新規1－アルキル－3－置換スルホニルオキシピラゾール－4－カルボキサミド誘導体の合成と殺虫活性

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Original Article

Synthesis and insecticidal activity of novel 1-alkyl-3-sulfonyloxypyrazole-4-carboxamide derivatives

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In the course of an agrochemical random screening test of 1-alkylpyrazole-4-carboxamide analogs showing herbicidal activity, it was discovered that some 1-alkyl-3-sulfonyloxypyrazole-4-carboxamides exhibited high insecticidal activity. These derivatives were readily synthesized through the reaction of various amines with mixed anhydrides of pyrazole-4-carboxylic acids. All pyrazole-4-carboxamides synthesized were evaluated for insecticidal activity and their structure–activity relationships are discussed. It was found that introduction of a methyl or an ethyl group at the 1-position of the pyrazole ring increased insecticidal activity, in particular, introduction of a methylsulfonyloxy group on the pyrazole ring at the 3-position induced potent activity. The level of activity varied with *N*-substituents of the carbamoyl group at the 4-position of the pyrazole ring. An α-branched alkyl group, such as an isopropyl or a *sec*-butyl group on the amide nitrogen atom, demonstrated the highest level of activity. Among the compounds evaluated, *N-sec*-butyl-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide showed the highest activity against *Nephotettix cincticeps,* and exhibited moderate activity against both adults and eggs of *Tetranychus urticae.* Interestingly, substitution of a cyano group induced a higher level of acaricidal activity, while *N*-(3-cyanopentan-3-yl)-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide gave excellent activity against *T. urticae* as well as *N. cincticeps*. © Pesticide Science Society of Japan

Keywords: pyrazole-4-carboxamide, synthesis, insecticidal activity, acaricidal activity, structure–activity relationships.

Introduction

Many substituted pyrazole derivatives with carboxamide moieties have the potential of being agrochemicals, and they are classified as an important class of compounds in the agrochemical industry. Some are used as practical agrochemicals, such as pyrazosulfuron-ethyl,[1] tebufenpyrad[2] and tolfenpyrad,[3] so active investigation of pyrazole carboxamide derivatives continues to be carried out in order to select useful compounds. DuPont's group found that *N-sec*-butyl-3-methylsulfonyloxypyrazole-1-carboxamide controlled *Diabrotica undecimpunctata howardi*, *Nilaparvata lugens* and *N. cincticeps* at a low rate of application and that pyrazole-1-carboxamide exhibited low acute mammalian toxicity.[4]

On the other hand, we previously reported that 3-(substituted oxy)pyrazole-4-carboxamides exhibited potent bleaching activity as carotenoid biosynthesis inhibitors, of which *N*-ethoxy-1-methyl-3-(3-trifluoromethylbenzyloxy)pyrazole-4-carboxamide (KPP-297) and *N*-(2,4-difluorophenyl)-1-ethyl-3-(3-trifluoromethylphenoxy)pyrazole-4-carboxamide (KPP-856) were the most promising rice herbicides[5,6]; however, in the course of agrochemical evaluation, there was no observable effect against targeted pests, such as *N. cincticeps* or *T. urticae*, even at a high rate of application. Through further structural studies on pyrazole, we assumed that the introduction of a methylsulfonyloxy group at the 3-position of the pyrazole ring would increase insecticidal activity. Accordingly, a number of new 1-alkyl-3-sulfonyloxypyrazole-4-carboxamides were synthesized and their insecticidal activities were evaluated to identify practical insecticides. As a result of structural modifications, a series of 1-alkyl-3-methylsulfony-

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loxypyrazole-4-carboxamides having an α-blanched alkyl group on the nitrogen atom of the carbamoyl group were found to be highly active against *N. cincticeps* and *T. urticae*.

This paper will report the synthesis of 1-alkyl-3-sulfonyloxypyrazole-4-carboxamides and their structure–activity relationships for insecticidal and acaricidal activity.

Materials and Methods

1. *Synthesis of Compounds*

1.1. *General procedure*

The preliminary synthetic route for 1-alkyl-3-substituted sulfonyloxypyrazole-4-carboxamides (**vi**) is shown in Fig. 1. The hydroxy group of ethyl 1-alkyl-3-hydroxypyrazole-4-carboxylates (**i**) [5,6] was protected by a reaction with benzyl chloride, and then the ester moiety of **ii** was converted to various amides by means of the usual amidation methods to afford 1-alkyl-3-benzyloxypyrazole-4-carboxamides (**iv**). After hydrogenolysis of the benzyloxy group, 1-alkyl-3-hydroxypyrazole-4-carboxamides (**v**) were treated with sulfonyl chlorides in the presence of potassium carbonate to yield the desired products (**vi**). As protection and deprotection with the benzyl group were ineffective, the synthetic route was improved (Fig. 2). Ethyl 1-alkyl-3-hydroxypyrazole-4-carboxylates (**i**) were hydrolyzed to give the acid (**vii**), which were treated with more than two equivalents of ethyl chloroformate in the presence of potassium carbonate to afford mixed anhydride-like intermediates (**viii**). Anhydrides (**viii**) were found to be useful intermediates and reacted with more than two equivalents of the desired amines to give 1-alkyl-3-hydroxypyrazole-4-carboxamides (**v**). Subsequent *O*-sulfonylation of 3-hydroxy group was easily performed to yield the targeting pyrazoles (**vi**); furthermore, it was not necessary to isolate the 1-alkyl-3-hydroxypyrazole-4-carboxamides (**v**). Namely, sulfonyl chlorides were added to the reaction mixture of the mixed anhydrides (**viii**) and amines to give the final products, 1-alkyl-3-sulfonyloxypyrazole-4-carboxamides (**vi**).

1.2. *Typical Procedure*

Chemical structures of all compounds were confirmed by ^{1}H NMR spectra, which were recorded on a Bruker DPX-250 NMR spectrometer with tetramethylsilane (TMS) as an internal standard. All melting points were measured by a BÜCHI-530 micro melting point apparatus and are uncorrected.

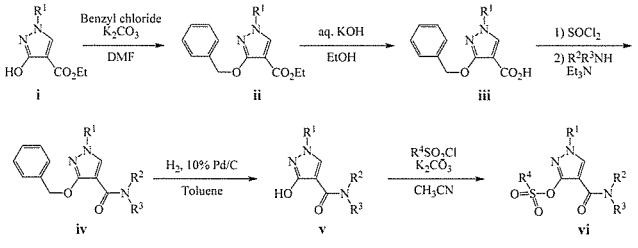


Fig. 1. Synthetic route of 1-alkyl-3-substituted sulfonyloxypyrazole-4-carboxamides.

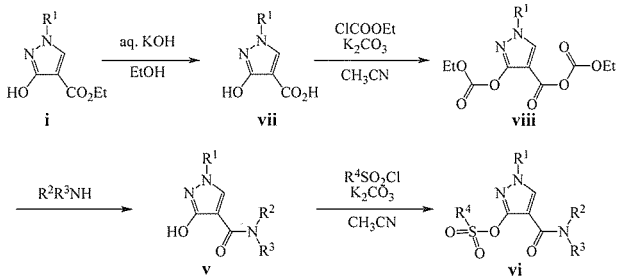


Fig. 2. Alternative synthetic route of 1-alkyl-3-substituted sulfonyloxypyrazole-4-carboxamides.

1.2.1. *Ethyl 3-benzyloxy-1-methylpyrazole-4-carboxylate* (**ii**; R^1 : Me)

Benzylchloride (29.9 ml, 259 mmol) was added to an *N,N*-dimethylformamide (DMF; 300 ml) solution of ethyl 3-hydroxy-1-methylpyrazole-4-carboxylate (40.0 g, 235 mmol) and potassium carbonate (39.0 g, 282 mmol) and the mixture was heated at 70°C for 9 hr with stirring. The resulting mixture was poured into 2 M-hydrochloric acid solution (1 L). A solid deposit was isolated by filtration, washed with water and hexane, and then well dried to give ethyl 3-benzyloxy-1-methylpyrazole-4-carboxylate (52.7 g, 202 mmol) in 86% yield as a pale yellow solid. mp: 48–50°C; ^{1}H NMR δ_H ($CDCl_3$, TMS): 1.33 (3H, t, *J*=7.1 Hz, CH_3CH_2O), 3.76 (3H, s, CH_3N), 4.27 (2H, q, *J*=7.1 Hz, CH_3CH_2O), 5.33 (2H, s, CH_2O), 7.34–7.36 (3H, m, benzene), 7.49–7.51 (2H, m, benzene), 7.68 (1H, s, pyrazole).

1.2.2. *3-Benzyloxy-1-methylpyrazole-4-carboxylic acid* (**iii**; R^1 : Me)

A 20% aqueous solution (30 ml) of potassium hydroxide was added to an ethanol solution (100 ml) of ethyl 3-benzyloxy-1-methylpyrazole-4-carboxylate (30.0 g, 115 mmol) and the mixture was stirred under reflux for 3 hr. The resulting mixture was poured into 4 M-hydrochloric acid solution (300 ml). A solid deposit was isolated by filtration, washed with water and well dried to give 3-benzyloxy-1-methylpyrazole-4-carboxylic acid (20.9 g, 90.0 mmol) in 78% yield as a colorless solid. mp: 169–171°C; ^{1}H NMR δ_H (DMSO-d_6): 3.78 (3H, s, CH_3N), 5.36 (2H, s, CH_2O), 7.29–7.44 (3H, m, benzene), 7.44–7.52 (2H, m, benzene), 7.68 (1H, s, pyrazole), 11.7–12.4 (1H, bs, OH).

1.2.3. N-*Isopropyl-3-benzyloxy-1-methylpyrazole-4-carboxamide* (**iv**; R^1 : Me, R^2 : Isopropyl, R^3 : H)

A toluene (20 ml) solution of 3-benzyloxy-1-methylpyrazole-4-carboxylic acid (2.00 g, 8.61 mmol) and thionyl chloride (6 ml) was stirred under reflux for 3 hr. After the distillation of toluene and excess thionyl chloride, dichloromethane (20 ml), triethylamine (1.13 g, 11.2 mmol), and isopropylamine (0.56 g, 9.47 mmol) were added in turn with cooling in an ice-cold water bath. The mixture was stirred at 0°C for 1 hr and at room temperature for 12 hr. The resulting mixture was quenched by 1 M-hydrochloric acid solution (40 ml) and ex-

tracted twice with ethyl acetate (50 ml×2). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate and evaporated. The residue was purified by silica gel column chromatography (ethyl acetate/hexane=2/1) to give *N*-isopropyl-3-benzyloxy-1-methylpyrazole-4-carboxamide (1.90 g, 7.02 mmol) in 82% yield as a colorless solid. ^{1}H NMR δ_H ($CDCl_3$, TMS): 1.14 (6H, d, J=6.5 Hz, isopropyl), 3.76 (3H, s, CH_3N), 4.16 (1H, dsep, J=6.5 and 7.5 Hz, isopropyl), 5.32 (2H, s, CH_2O), 6.61 (1H, bd, J=7.5 Hz, NH), 7.30–7.54 (5H, m, benzene), 7.71 (1H, s, pyrazole).

1.2.4. N-*Isopropyl-3-hydroxy-1-methylpyrazole-4-carboxamide* (**v**; R^1 : CH_3, R^2 : Isopropyl, R^3 : H)

N-Isopropyl-3-benzyloxy-1-methylpyrazole-4-carboxamide (1.90 g, 6.96 mmol), ethanol (100 ml) and 10% palladium on charcoal (0.3 g) were put in a stainless steel autoclave, and the mixture was stirred under 0.39 MPa hydrogen gas at room temperature until the gas was no longer absorbed. After the reaction, the catalyst was filtered off and the filtrate was evaporated. A solid deposit was washed with hexane and well dried to give *N*-isopropyl-3-hydroxy-1-methylpyrazole-4-carboxamide (1.23 g, 6.72 mmol) in 97% yield as a colorless solid. mp: 143–145°C; ^{1}H NMR δ_H ($CDCl_3$, TMS): 1.24 (6H, d, J=6.6 Hz, isopropyl), 3.76 (3H, s, CH_3N), 4.24 (1H, dsep, J=6.6 and 7.1 Hz, isopropyl), 6.51 (1H, bd, J=7.1 Hz, NH), 7.65 (1H, s, pyrazole). (OH: not detected).

1.2.5. N-*Isopropyl-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide* (**1**)

Methylsulfonyl chloride (0.10 ml, 1.20 mmol) was added to a DMF (15 ml) solution of *N*-isopropyl-3-hydroxy-1-methylpyrazole-4-carboxamide (0.2 g, 1.09 mmol) and triethylamine (0.14 g, 1.42 mmol), and the mixture was stirred for 2 days. The resulting mixture was quenched by 1 M-hydrochloric acid solution (40 ml) and extracted twice with ethyl acetate (50 ml×2). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was purified by silica gel column chromatography (ethyl acetate/hexane=1/2) to give *N*-isopropyl-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide (0.23 g, 0.86 mmol) in 79% yield as a colorless solid. mp: 88–89°C; ^{1}H NMR δ_H ($CDCl_3$, TMS): 1.23 (6H, d, J=6.5 Hz, isopropyl), 3.47 (3H, s, CH_3SO_3), 3.84 (3H, s, CH_3N), 4.19 (1H, dsep, J=5.9 and 6.5Hz, isopropyl), 6.22 (1H, bd, J=5.9 Hz, NH), 7.81 (1H, s, pyrazole).

1.2.6. *1-Methyl-3-hydroxypyrazole-4-carboxylic acid* (**vii**; R^1 : CH_3)

A 20% aqueous solution (100 ml) of sodium hydroxide was added to an ethanol solution (200 ml) of ethyl 3-hydroxy-1-methylpyrazole-4-carboxylate (50.0 g, 192 mmol) and the mixture was stirred under reflux for 4 hr. The resulting mixture was poured into a 4 M-hydrochloric acid solution (500 ml). A solid deposit was isolated by filtration, washed with water and well dried to give 3-hydroxy-1-methylpyrazole-4-carboxylic acid (43.2 g, 188 mmol) in 98% yield as a colorless solid. mp: 218–219°C; ^{1}H NMR δ_H (DMSO-d_6): 3.64 (3H, s, CH_3N), 7.89 (1H, s, pyrazole). (OH and COOH: not detected).

1.2.7. *(3-Ethoxycarbonyloxy-1-methylpyrazol-4-yl) ethyl carbonate* (**viii**; R^1 : CH_3)

Ethyl chlorofomate (2.11 ml, 22.1 mmol) was added to an acetone solution (20 ml) of 3-hydroxy-1-methylpyrazole-4-carboxylic acid (1.50 g, 10.6 mmol) and potassium carbonate (1.60 g, 11.6 mmol) with cooling in an ice-cold water bath. The mixture was stirred at 0°C for 1 hr and at room temperature for 1 hr. After the reaction, the solid deposit was filtered off and the filtrate was evaporated to give (3-ethoxycarbonyloxy-1-methylpyrazol-4-yl) ethyl carbonate (3.03 g, 10.6 mmol) quantitatively as a colorless oil. ^{1}H NMR δ_H ($CDCl_3$, TMS): 1.37(3H, t, J=7.1 Hz, CH_3CH_2O), 1.39(3H, t, J=7.1 Hz, CH_3CH_2O), 3.88 (3H, s, CH_3N), 4.34 (2H, q, J=7.1 Hz, CH_3CH_2O), 4.35 (2H, q, J=7.1 Hz, CH_3CH_2O), 7.88 (1H, s, pyrazole).

1.2.8. *N-Isopropyl-1-methyl-3-methylsulfonyloxypyrazoele-4-carboxamide (**1**; One-pot synthesis)*

Isopropylamine (2.60 g, 44.0 mmol) was added to an acetonitrile solution (50 ml) of (3-ethoxycarbonyloxy-1-methylpyrazol-4-yl)carbonyl ethyl carbonate (4.42 g, 14.7 mmol) with cooling in an ice-cold water bath. The mixture was stirred at 0°C for 1 hr and at room temperature overnight. Potassium carbonate (6.10 g, 44.1 mmol) and methylsulfonyl chloride (5.04 g, 44.1 mmol) was added and the mixture was stirred under reflux for 8 hr. The resulting mixture was quenched by 1 M-hydrochloric acid solution (200 ml) and extracted twice with ethyl acetate (200 ml×2). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate and evaporated. The residue was purified by silica gel column chromatography (ethyl acetate/hexane=1/1) to give *N*-isopropyl-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide (2.54 g, 9.70 mmol) in 66% yield as a colorless solid.

1.2.9. *N-(3-Cyanopentan-3-yl)-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide* (**28**)

3-Amino-3-pentylcyanide (5.88 g, 52.4 mmol) was added to an acetonitrile solution (15 ml) of (3-ethoxycarbonyloxy-1-methylpyrazol-4-yl) ethyl carbonate (1.50 g, 5.24 mmol) with cooling in an ice-cold water bath and the mixture was stirred at 0°C for 1 hr. Acetonitrile (15 ml), potassium carbonate (3.62g, 26.2 mmol) and methylsulfonyl chloride (2.0 ml, 26.2 mmol) was added to the mixture and the mixture was stirred at 60°C for 12 hr. The resulting mixture was quenched with 1 M-hydrochloric acid solution (80 ml) and extracted twice with ethyl acetate (60 ml×2). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate and evaporated. The residue was purified by silica gel column chromatography (ethyl acetate/hexane=1/1) to give *N*-(3-cyanopentan-3-yl)-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide (0.62 g, 1.99 mmol) in 38% yield as a colorless solid. mp: 96–97°C; ^{1}H NMR δ_H ($CDCl_3$, TMS): 1.09 (6H, t,

J=7.5 Hz, CH_3CH_2), 1.91–2.20 (4H, m, CH_3CH_2), 3.48 (3H, s, CH_3), 3.87 (3H, s, CH_3), 6.41 (1H, bs, NH), 7.87 (1H, s, pyrazole).

Similar to the methods described above, all 1-alkyl-3-sulfonyloxypyrazole-4-carboxamides were prepared through the synthetic route shown in Fig. 2.

2. *Evaluation of Insecticidal Activity*

Each test compound was dissolved in 0.2 ml dimethyl sulfoxide, and the solution was diluted with water containing an emulsifier (Sorpol 2564) and spreader (Neoesterin).

2.1. *Green rice leafhopper* (N. cincticeps)

Rice seedlings (5-cm tall: two-leaf stage) were sprayed with a water solution (10 ml) of the test compound. After spraying, 20 leafhopper nymphs (3rd instar nymph) were released onto the rice seedling. Leafhopper nymphs were reared under 16 h light–8 h dark cycles at 25°C. Mortality was determined 7 days after treatment.

2.2. *Two-spotted spider mite* (T. urticae)

Acaricidal and ovicidal activity was evaluated by the leaf disk assay as follows. Twenty female adults were applied to a leaf disk of kidney bean (*Phaseolus vulgaris)* (5-cm diameter : two-leaf stage) for 24 hr. Animals were removed only for the treatment for ovicidal activity, after which a leaf disk was sprayed with a water solution (10 ml) of the test compound. Animals and eggs were reared under 16 hr light–8 hr dark cycles at 25°C. Mortality was determined 2 days and ovicidal activity was determined 7 days after treatment.

Results and Discussion

1. *Synthesis*

The desired 3-sulfonyloxypyrazole-4-carboxamides (**vi**) were easily synthesized by sulfonylation of 3-hydroxypyrazole-4-carboxamides (**v**), although synthesis of **vi** by amidation of 3-sulfonyloxypyrazole-4-carboxylates, which were prepared by sulfonylation of 3-hydroxypyrazole-4-carboxylates (**i**), was unsuccessful because of easy hydrolysis of the 3-sulfonyloxy group; therefore, facile preparation of the key precursor (**v**) was very important to supply a wide variety of targeting compounds (**vi**). From the point of view of synthetic efficiency, the synthetic route shown in Fig. 1, which consists of five common reactions, provides a good yield for each step, but it is desirable for the protection and de-protection processes of the 3-hydroxyl group to be omitted.

On the other hand, the improved synthetic method *via* mixed anhydride-like intermediates (**viii**) has the advantage of giving the desired compounds through four steps, as shown in Fig. 2. Moreover, since the amidation of **viii** and the subsequent sulfonylation of 3-hydroxypyrazole-4-carboxamides (**v**) generated *in situ* can be carried out in one flask, it is essentially possible to obtain the final products (**vi**) through only three steps from the starting materials (**i**), provided that there is much scope for the improvement of chemical yield. Concretely, compound 1, *N*-isopropyl-1-methyl-3-methylsulfonyloxypyrazole-4-carboxamide, was prepared in 42% overall yield from the starting materials (**i**) through the synthetic route shown in Fig. 1; however, the adoption of the synthetic route illustrated in Fig. 2 gave compound 1 in 66% overall yield.

As described above, the mixed anhydrides (**viii**), which were readily prepared by the reaction of **vii** with two equivalents of ethyl chloroformate in the presence of potassium carbonate, were considered to be extremely useful intermediates for shortening the synthetic pathway. Although the compounds (**viii**) are very stable at room temperature under neutral and acidic conditions, **viii** reacted with amines under basic conditions to give amides (**v**) owing to moderate activation of the 4-carboxyl group by the ethoxycarbonyl group. Simultaneously, the 3-hydroxyl group was reformed by de-protection of the carbonate moiety with excess amine or ethanol formed *in situ*; that is, two ethoxycarbonyl groups of **viii** performed well in both activation of the 4-carboxyl group and protection of the 3-hydroxyl group. Therefore, the present synthetic method could be applied to other compounds having such a carboxyl group and a hydroxyl group in a molecule.

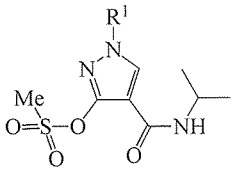
2. *Insecticidal and Acaricidal Activities*

Insecticidal and acaricidal activities against *N. cincticeps* and *T. urticae* were evaluated for 31 kinds of 1-alkyl-3-sulfonyloxypyrazole-4-carboxamides (**1–31**) and their results are summarized in Tables 1–4.

Table 1 shows the substituent effect of R^1 on insecticidal and acaricidal activities in the series of *N*-isopropyl-1-alkyl-3-methylsulfonyloxypyrazole-4-carboxamides (**1–7**), whose substituents on the pyrazole ring, 4-isopropylcarbamoyl and 3-methylsulfonyloxy groups are much more important for potent insecticidal and acaricidal activities, as described below. As shown in Table 1, methyl, ethyl, 2-chloroethyl, 2-fluoroethyl, and propyl and isopropyl derivatives (**1–6**) exhibited good insecticidal activity against *N. cincticeps*. Among them, compounds **1**, **2** and **3** were active at a low application rate of 3.1 ppm, while compounds **4**, **5** and **6** showed moderate to low levels of activity at the same rate; in particular, *tert*-butyl derivative (**7**) was inactive even at a rate of 500 ppm. These results obviously suggest that the hydrophobicity and bulkiness of R^1 influenced activity significantly and the methyl group was the most suitable substituent for controlling *N. cincticeps*. On the other hand, marked acaricidal activity against *T. urticae* was not observed in the series of compounds **1–7**, although compounds **1** and **3** showed more than 80% efficacy for adults of *T. urticae*.

Taking into account the availability of the methylsulfonyloxy group in pyrazole-1-carboxamides presented by DuPont's group[4], the desired biological activity should also be affected by the substituent, R^4, on the sulfonyloxy group at the 3-position of the pyrazole ring. Table 2 summarizes insecticidal and acaricidal activities of compounds **1** and **8–11**, whose sulfonyl groups are substituted by representative groups, such as

Table 1. Insecticidal and acaricidal activities of *N*-isopropyl-1-alkyl-3-methylsulfonyloxypyrazole-4-carboxamides

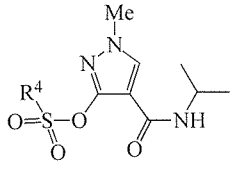


1–7

Compound No.	R^1	mp (°C)	Concentration (ppm)	Mortality (%)		
				Nc[a]	Tu[b] (Adults)	Tu (Eggs)
1	Methyl	88–89	62.5	100	100	37
			3.1	100	17	23
2	Ethyl	65–67	62.5	100	51	13
			3.1	100	—	—
3	$ClCH_2CH_2$	112–113	62.5	100	80	34
			3.1	96	15	30
4	FCH_2CH_2	86–87	62.5	100	50	69
			3.1	43	—	—
5	Propyl	70–71	62.5	100	36	26
			3.1	76	—	—
6	Isopropyl	86–87	62.5	100	50	47
			3.1	74	—	—
7	*tert*-Butyl	78–80	500	0	50	0

Activity was evaluated 7 days after treatment: 0 (no activity)−100 (complete kill). [a] Nc: *Nephotettix cincticeps*. [b] Tu: *Tetranychus urticae*.

Table 2. Insecticidal and acaricidal activities of *N*-isopropyl-1-alkyl-3-subustituted sulfonyloxypyrazole-4-carboxamides



1, 8–11

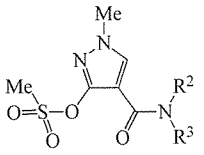
Compound No.	R^4	mp (°C)	Concentration (ppm)	Mortality (%)		
				Nc[a]	Tu[b] (Adults)	Tu (Eggs)
1	Methyl	88–89	62.5	100	100	37
			3.1	100	17	23
8	Ethyl	oil	62.5	100	14	2
			3.1	55	—	—
9	CF_3	139–140	62.5	24	15	10
10	$ClCH_2$	79–81	62.5	100	15	13
			3.1	10	—	—
11	Me_2N	67–69	62.5	0	0	0

Activity was evaluated 7 days after treatment: 0 (no activity)−100 (complete kill). [a] Nc: *Nephotettix cincticeps*. [b] Tu: *Tetranychus urticae*.

methyl, ethyl, trifluoromethyl, chloromethyl, and dimethylamino groups. Other substituents on the pyrazole ring were fixed to the *N*-isopropylcarbamoyl group at the 4-position and the 1-methyl group that exhibited the highest insecticidal activity, as shown in Table 1. The results in Table 2 clearly indicate that compounds **8** (R^4=ethyl) and **10** (R^4=chloromethyl) perfectly controlled *N. cincticeps* at a rate of 62.5 ppm; however, their activities at 3.1 ppm were far lower than that of a methyl derivative (**1**). Substitution of an electron-withdrawing group such as **9** (R^4=CF_3) markedly decreased the activity, and the dimethylamino derivative (**11**) showed no insecticidal activity. These results evidently suggested that the methylsulfonyloxy derivative (**1**) was also the most active compound for controlling *N. cincticeps*. Additionally, all compounds except for **1** exhibited no or lower acaricidal activity against *T. urticae*.

As discussed above and based on the results in Tables 1 and 2, after modification of both substituents on the 1-nitrogen atom and the 3-sulfonyloxy group of the pyrazole ring, we came to the conclusion that compound **1** is still the most active among the compounds (**1–11**). Then, we attempted to modify the substituents (R^2 and R^3) on the nitrogen atom of the 4-carbamoyl group in order to obtain more active derivatives. Table 3 summarizes the insecticidal and acaricidal activities of 1-methyl-3-methylsulfonyloxypyrazole-4-carboxamides (**1**, **12–22**). As shown in Table 3, compounds **16** (cyclopropyl), **17** (*sec*-butyl), **18** (*tert*-butyl), **19** (2-pentyl), **20** (3-pentyl) and **21** (2-heptyl) induced more than 90% mortality against *N. cincticeps* at 62.5 ppm. We thus assumed that the α-blanched alky group on the nitrogen atom of the carbamoyl group would be effective for higher insecticidal activity. The low activity of *N*-methyl (**12**), *N*-ethyl (**13**), and *N*-propyl (**14**)

Table 3. Insecticidal and acaricidal activities of 1-alkyl-3-methylsulufonyloxypyrazole-4-carboxamides



1, 12–22

Compound No.	R^2	R^3	mp (°C)	Concentration (ppm)	Mortality (%)		
					Nc[a]	Tu[b] (Adults)	Tu (Eggs)
1	Isopropyl	H	88–89	62.5	100	100	37
				3.1	100	17	23
				1.3	74	16	22
12	Methyl	H	88–89	62.5	20	19	4
13	Ethyl	H	57–59	62.5	0	0	0
14	Propyl	H	85–86	62.5	87	25	7
15	Isopropyl	Me	101–102	62.5	41	10	5
16	Cyclopropyl	H	96–97	62.5	97	21	9
				3.1	10	—	—
17	*sec*-Butyl	H	71–73	62.5	100	89	12
				3.1	100	—	—
				1.3	97	—	—
18	*tert*-Butyl	H	122–123	62.5	100	23	3
				3.1	80	—	—
19	2-Pentyl	H	oil	62.5	100	94	44
				3.1	95	7	6
20	3-Pentyl	H	78–80	62.5	100	100	19
				3.1	65	10	—
21	2-Heptyl	H	73–74	62.5	94	29	6
				3.1	8	—	—
22	1-Phenylethyl	H	125–126	62.5	81	0	0

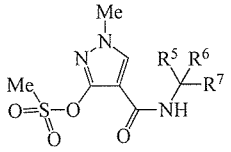
Activity was evaluated 7 days after treatment: 0 (no activity)−100 (complete kill). [a] Nc: *Nephotettix cincticeps*. [b] Tu: *Tetranychus urticae*.

analog supported this presumption. It is also noteworthy that additional substitution on the nitrogen atom of the carbamoyl group markedly reduced activity; in fact, *N*-isopropyl-*N*-methyl analog (**15**) was markedly inferior to *N*-isopropyl analog (**1**), even though **15** had the α-blanched alky group; that is, a hydrogen atom on the nitrogen atom of the carbamoyl group is essential to increase mortality. Among the active compounds (**16–21**), *sec*-butyl and 2-pentyl derivatives (**17** and **19**) were particularly active against *N. cincticeps*; furthermore, the insecticidal activity of **17** was superior to **1** at a rate of 1.3 ppm. In spite of being an *N*-monosubstituted analog with an α-blanched aralkyl group, the 1-phenylethyl derivative (**22**) showed no more than 80% mortality at 500 ppm application. On the other hand, almost all compounds shown in Table 3 exhibited unsatisfactory acaricidal activity against *T. urticae*, except for **17**, **19** and **20**.

As it was considered that further modifications were required in order to improve acaricidal activity, we tried to introduce an electron-withdrawing group, such as a cyano or a trifluoromethyl group, onto the alkyl group of the *N*-alkylcarbamoyl group. Table 4 shows the insecticidal and acaricidal activities of further modified compounds (**23–31**). When the acaricidal activity of **12** was compared with that of **23**, substitution of the cyano group remarkably increased acaricidal activity. A similar tendency was observed when **14** and **24**, **17** and **25** or **20** and **28** were compared; however, we could not evaluate the activity of the compound with a cyano group corresponding to **1**, which was the most potent against *T. urticae* in Table 3, because the targeted compound (R^5=R^6=CH_3, R^7=CN) was not obtained even through the synthetic routes depicted in Fig. 1 and 2. Comparison of **19** and **26** indicated that introduction of the cyano group was not always effective for eliciting higher activity. A spiro compound (**29**) reduced the activity compared with **28**. Substitution of a trifluoromethyl group (**31**) was not advantageous for eliciting high acaricidal activity. Among the compounds with a cyano group (**23–30**), **28** controlled *T. urticae* perfectly even at 3.1 ppm application, although the efficacy against *N. cincticeps* was slightly inferior. It was assumed that the cyano group was readily metabolized for *N. cincticeps* so that compounds with a cyano group could not exhibit excellent activity against *N. cincticeps*.

In conclusion, our findings indicated that *N-sec*-butyl-1-methyl-3-methylsulfonylpyrazole-4-carboxamide controlled *N. cincticeps* even at 1.3 ppm application and that *N*-(3-cyanopentan-3-yl)-1-methyl-3-methylsulfonyloxypyrazole-4-

Table 4. Insecticidal and acaricidal activities of 1-alkyl-3-methylsulfonyloxypyrazole-4-carboxamides



23–31

Compound No.	R^5	R^6	R^7	mp (°C)	Concentration (ppm)	Mortality (%)		
						Nc[a]	Tu[b] (Adults)	Tu (Eggs)
23	H	H	CN	111–113	62.5	47	100	100
					3.1	—	8	8
24	H	Ethyl	CN	oil	62.5	100	100	94
					3.1	10	7	3
25	Methyl	Ethyl	CN	109–112	62.5	100	100	100
					3.1	88	15	9
26	Methyl	Propyl	CN	109–112	62.5	100	64	67
					3.1	81	8	3
27	Methyl	Isopropyl	CN	80–82	62.5	100	100	100
					3.1	32	11	26
28	Ethyl	Ethyl	CN	96–97	62.5	100	100	100
					3.1	55	100	100
29	$-(CH_2)_5-$		CN	108–111	62.5	50	93	20
30	Ethyl	Propyl	CN	120–121	62.5	22	15	39
31	H	H	CF_3	67–68	62.5	22	86	61

Activity was evaluated 7 days after treatment: 0 (no activity)–100 (complete kill). [a] Nc: *Nephotettix cincticeps*. [b] Tu: *Tetranychus urticae*.

carboxamide exhibited the highest level of acaricidal activity in the pyrazole derivatives presented.

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英文編掲載報文・短報等の要旨

報　文

アワヨトウに寄生する単寄生蜂ギンケハラボソコマユバチと多寄生蜂カリヤコマユバチの4種殺虫剤に対する異なった反応

神崎真悟，田中利治

本研究は，4種類の殺虫剤（フェニトロチオン，サイパーメスリン，ピリプロキシフェン，ピリダリル）を使って，内部多寄生蜂カリヤコマユバチ（カリヤ）と内部単寄生蜂ギンケハラボソコマユバチ（ギンケ）の寄生後の発育段階にそって，それぞれ寄生された被寄生寄主を通した薬剤の影響を調べた．被寄生寄主は，内部寄生蜂によって生理的に調整されていることから，被寄生寄主の解毒代謝能力が変化していることが予測された．それぞれの薬剤の2種の寄生バチの発生・発育に対する影響は，未寄生寄主のLD_{50}あるいはLD_{95}値を用いた．フェニトロチオンとサイパーメスリンは，カリヤでは寄生後のどのステージの処理でも影響が強かったが，単寄生蜂のギンケは，寄生後3日以降の処理では低い死亡率となった．ピリプロキシフェンは，カリヤの発育には影響がなかったが，ギンケでは幼虫期における処理で50 ppm（LD10）より低い値で影響を受けた．パラフィン切片で，ギンケの蛹期での腹部の発育停止によるものと分かった．ピリダリルはカリヤ（卵－幼虫期間は約10日）の寄生後7日までのステージで寄主からの脱出に大きな影響を与えたが，8日目以降は脱出し，正常に羽化した．理由はピリダリル処理によって被寄生寄主が動けなくなりえさの摂取が困難であるためと思われた．一方，ギンケではLD_{50}のピリダリル処理で，幼虫脱出・成虫羽化ともに影響が少なかった．多寄生と単寄生ではそれぞれ感受性の違いが見られた．

新規殺菌剤ピリベンカルブの灰色かび病に対する防除効果

高垣真喜一，片岡　智，貴田健一，三浦一郎，福本俊一郎，玉井龍二

ピリベンカルブは，クミアイ化学工業（株）とイハラケミカル工業（株）が開発したワイドスペクトラムな新規殺菌剤であり，特に各種灰色かび病に対して優れた防除効果を発揮する．本剤は予防効果だけでなく治療効果も有し，また，キュウリ灰色かび病のポット試験において，予防効果に明らかに優る病徴進展阻害効果を示した．本剤は浸達性を有し，耐雨性，残効性にも優れていることから，圃場でも高い防除効果を発揮すると考えられた．圃場試験にて，ナス灰色かび病およびインゲンマメ灰色かび病に対するピリベンカルブの防除効果を確認したところ，200～100 ppmで市販剤と同等～優る防除効果を示した．

新規1-アルキル-3-置換スルホニルオキシピラゾール-4-カルボキサミド誘導体の合成と殺虫活性

大野竜太，長岡真帆，平井憲次，内田　淳，河内真一郎，山田　修，徳村　潤

様々な置換基を有する1-アルキル-3-置換スルホニルオキシピラゾール-4-カルボキサミド誘導体を合成し，殺虫活性を調べた．その結果，3-メチルスルホニルオキシピラゾール-4-カルボキサミドが強力な殺虫活性を示すことを見いだした．さらにピラゾール環4位のカルバモイル基の窒素原子上に分枝アルキル基を導入すると活性が向上し，*N*-sec-ブチル-1-メチル-3-メチルスルホニルオキシピラゾール-4-カルボキサミドは1.3 ppmという低濃度でもツマグロヨコバイをほぼ完全に防除できることが分かった．また，カルバモイル基の窒素原子上にシアノ基を有するアルキル基を導入するとナミハダニに対する活性が飛躍的に向上することが分かり，*N*-(3-シアノペンタン-3-イル)-1-メチル-3-メチルスルホニルオキシピラゾール-4-カルボキサミドが3.1 ppmの処理濃度にてナミハダニの卵および成虫を完全に防除できることを見いだした．

短　報

ヨトウガの一種 *Spodoptera frugiperda* のフェロモンに対する電気生理学的応答の抑制

Celia Patricia Pérez Luis, Angel Guerrero, Edi A. Malo

ヨトウガ（fall armyworm, FAW）の一種である *Spodoptera frugiperda*（Lepidoptera: Noctuidae）を制御する新手法を探るため，我々は3-オクチルチオ-1,1,1-トリフルオロプロパン-2-オン(3-octylthio-1,1,1-trifluoropropan-2-one, OTFP）によるフェロモンに対する電気生理学的応答（EGA応答）の抑制を検討した．トリフルオロメチルケトン類の一種として，OTFPはセリンエステラーゼ，特に昆虫触角のセリンエステラーゼの強力なインヒビターである．触角レセプターをOTFPの蒸気に曝すことによって，フェロモンに対するEGA反応の強度および再分極に要する総時間の2/3の値（2/3 RT）はともに低下した．このOTFPによる低下効果は可逆