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Note

Insecticidal Activity of *N*-Acyl-*N*-(4-aryloxybenzyl)pyrazole-5-carboxamides

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INTRODUCTION

Previously, we reported the structure-activity relationships of insecticidal *N*-(4-aryloxybenzyl)pyrazole-5-carboxamides.[1] Meanwhile, Obata *et al.* reported that *N*-acyl-*N*-phenoxyethylpyrazole-5-carboxamides were highly effective against two-spotted spider mite (*Tetranychus urticae*) and less toxic against fish.[2]

With these results in mind, we synthesized *N*-acyl-*N*-(4-aryloxybenzyl)pyrazole-5-carboxamides (**I**) and found them to be highly active insecticides.[3] This paper describes their structure-activity relationships.

MATERIALS AND METHODS

1. Synthesis of Compounds

I were prepared by the *N*-acylation of corresponding carboxamides.[3] A typical example is described below.

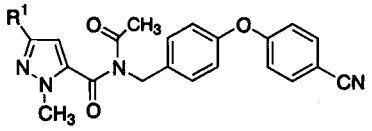
*1.1. N-[4-(4-Cyanophenoxy)benzyl]-3-ethyl-1-methylpyrazole-5-carboxamide (**23**)*

A mixture of 3-ethyl-1-methylpyrazole-5-carboxylic acid (15.4 g, 100 mmol) and thionyl chloride (20 ml) was refluxed for 1 hr. The reaction mixture was cooled and excess thionyl chloride was removed under reduced pressure. The residue was dissolved in toluene (200 ml) and added dropwise to a mixture of 4-(4-cyanophenoxy)benzylamine (26.9 g, 120 mmol), triethylamine (12.1 g, 120 mml) and toluene (100 ml) on ice. The mixture was stirred at room temperature for 2 hr, poured into ice water and extracted with toluene (100 ml). The organic layer was separated, washed with water and saturated aqueous sodium chloride, and dried over anhydrous sodium sulfate. After the solvent had been removed under reduced pressure, the residue was purified by column chromatography on silica gel with hexane/ethyl acetate (3/1) to give 30. 6 g (85%) of **23** as colorless crystals. mp : 134–135°C ; ^{1}H NMR ($CDCl_3$) δ (ppm) : 1.23 (3H, t, J=7.8 Hz), 2.63 (2H, q, J=7.8 Hz), 4.15 (3H, s), 4.59 (2H, d, J=6.0 Hz), 6.30 (1H, br), 6.32 (1H, s), 6.99–7.07 (4H, m), 7.38 (2H, d, J=8.4 Hz), 7.60 (2H, d, J=9.0 H).

*1.2. N-Acetyl-N-[4-(4-cyanophenoxy)benzyl]-3-ethyl-1-methylpyrazole-5-carboxamide (**2**)*

A solution of **23** (6.00 g, 16.6 mmol) in *N*-methylpyrrolidone (20 ml) was added dropwise to a mixture of sodium hydride (60% dispersion in mineral oil, 1.00 g, 25 mmol) in *N*-methylpyrrolidone (20 ml) on ice. After 30 min at room temperature, acetyl chloride (3.0 ml, 42 mmol) was added dropwise on ice. After stirring for 1 hr at room temperature, the reaction mixture was poured into a mixture of ice (100 g) and saturated aqueous ammonium chloride (100 ml), and extracted with ethyl acetate (100 ml). The organic layer was washed with water and saturated aqueous sodium chloride, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by chromatography on silica gel with hexane/ethyl acetate (2/1) to give 2.20 g (33%) of **2** as a colorless oil. n_D^{25} 1.5898 ; ^{1}H NMR ($CDCl_3$) δ (ppm) : 1.22 (3H, t, J=7.8 Hz), 2.28 (3H, s), 2.64 (2H, q, J=7.8 Hz), 3.89 (3H, s), 5.02 (2H, s), 6.29 (1H, s), 6.94–7.03 (4H, m), 7.11 (2H, d, J

Table 1. 3-Substituted-*N*-acetyl-*N*-[4-(4-cyanophenoxy)benzyl]-1-methylpyrazole-5-carboxamides and their insecticidal activity against *Spodoptera litura*



No.	R^1	mp or n_D (°C)	Activity rating[a)]
1	methyl	1.5950 (25)	C
2	ethyl	1.5898 (25)	A
3	propyl	1.5837 (24)	B
4	isopropyl	1.5830 (23)	C
5	cyclopropyl	1.5981 (24)	B
6	butyl	1.5698 (25)	E
7	isobutyl	1.5770 (25)	D
8	*sec*-butyl	1.5730 (23)	B
9	*tert*-butyl	1.5588 (23)	E
10	pentyl	1.5710 (23)	E
11	methoxy	57-59	C
12	ethoxy	1.5840 (25)	C
13	isopropoxy	1.5790 (25)	C
14	butoxy	1.5770 (25)	D

[a)] Expressed as indices of A, B, C, D and E corresponding to more than 80% mortality at 3.1, 13, 50 and 200 ppm and less than 80% mortality at 200 ppm, respectively.

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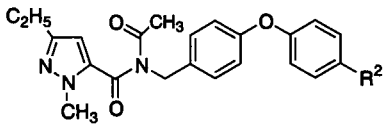
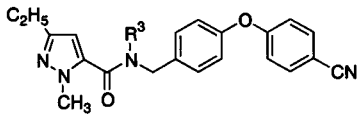
Table 2. *N*-[4-[(4-Substituted)phenoxy]benzyl]-*N*-acetyl-3-ethyl-1-methylpyrazole-5-carboxamides and their insecticidal activity against *Spodoptera litura*



No.	R^2	n_D (°C)	Activity rating[a)]
2	cyano	1.5898 (25)	A
15	methylthio	1.5979 (23)	A
16	trifluoromethyl	1.5448 (24)	B
17	nitro	1.6000 (23)	B
18	fluoro	1.5664 (23)	D
19	chloro	1.5790 (23)	D
20	methyl	1.5690 (24)	D
21	methoxy	1.5730 (23)	E
22	H	1.5669 (23)	E

[a)] Expressed as indices of A, B, C, D and E corresponding to more than 80% mortality at 3.1, 13, 50 and 200 ppm and less than 80% mortality at 200 ppm, respectively.

Table 3. *N*-Substituted-*N*-[4-(4-cyanophenoxy)benzyl]-3-ethyl-1-methylpyrazole-5-carboxamides and their insecticidal activity against *Spodoptera litura*



No.	R^3	mp or n_D (°C)	Activity rating[a)]
23	H	134-135	C
2	acetyl	1.5898 (25)	A
24	propionyl	1.5828 (24)	B
25	butyryl	1.5755 (23)	B
26	isobutyryl	94-96	A
27	cyclopropanecarbonyl	1.5901 (23)	B
28	valeryl	1.5681 (25)	B
29	isovaleryl	1.5612 (24)	B
30	2-methylbutyryl	1.5691 (25)	B
31	pivaloyl	1.5717 (24)	C

[a)] Expressed as indices of A, B, C, D and E corresponding to more than 80% mortality at 3.1, 13, 50 and 200 ppm and less than 80% mortality at 200 ppm, respectively.

=7.8 Hz), 7.60 (2H, d, J=8.7 Hz).

2. Biological Tests

2.1. Formulation

A mixture of 20 parts of the compound, 20 parts of white carbon, 52 parts of kaolin and 8 parts of surfactant was mixed to give a wettable powder containing 20% of the active ingredient.

2.2. Insecticidal evaluation

Tests described below were repeated twice for each concentration. The activity rating was expressed as indices of A, B, C, D and E corresponding to more than 80% mortality at 3.1, 13, 50 and 200 ppm and less than 80% mortality at 200 ppm, respectively.

A leaf disk of cabbage (6 cm in diameter) was dipped in a suspension prepared by diluting the wettable powder described above with water to predetermined concentrations. Five third-instar larvae of common cutworms (*Spodoptera litura*) were maintained with the treated leaf disk in a plastic cup (7 cm in diameter) and kept at 25°C during the test period. The mortality was observed 5 days after treatment.

RESULTS AND DISCUSSION

Table 1 shows some 3-substituted-*N*-acetyl-*N*-[4-(4-cyanophenoxy)benzyl]-1-methylpyrazole-5-carboxamides and their insecticidal activity against *Spodoptera litura*. Among alkyl analogs, the ethyl analog (**2**) showed the highest level of activity. The relative order of activity was : ethyl (**2**) > propyl (**3**), cyclopropyl (**5**), *sec*-butyl (**8**) > methyl (**1**), isopropyl (**4**) > isobutyl (**7**) > *tert*-butyl (**9**), pentyl (**10**). Some alkoxy groups were then introduced to examine the electronic effect. The methoxy (**11**), ethoxy (**12**) and isopropoxy (**13**) analogs were active at 50 ppm, but less active than the ethyl analog (**2**), so electron-donating substitution seems to have a negative effect.

Table 2 shows the effect of substituents (R^2) of the phenoxy moiety. The unsubstituted (**22**) and the methoxy (**21**) analog were inactive at 200 ppm. Cyano (**2**) and methylthio (**15**) anologs were the most active, followed by trifluoromethyl (**16**) and nitro (**17**) analogs. These results are very similar to those obtained for *N*-(aryloxybenzyl)pyrazolecarboxamides.[1)]

Table 3 shows the effect of the acyl group at the amide nitrogen. Almost all *N*-acylated analogs were more active than the unsubstituted analog (**23**). Among them, the acetyl (**2**) and isobutyryl (**26**) analogs were the most active. This positive effect of acyl substitution may be explained by the lipophilicity of the *N*-acylated compounds. These compounds may penetrate a target site more easily than unacylated compounds.

In this study, the insecticidal activity of thirty *N*-acyl-*N*-(4-aryloxybenzyl)pyrazole-5-carboxamides was examined. *N*-Acetyl-*N*-[4-(4-cyanophenoxy)benzyl]-3-ethyl-1-methylpyrazole-5-carboxamide (**2**), *N*-acetyl-3-ethyl-1-methyl-*N*-[4-[4-(methylthio)-phenoxy]benzyl]pyrazole-5-carboxamide (**15**) and *N*-[4-(4-cyanophenoxy)benzyl]-3-ethyl-*N*-isobutyryl-1-methylpyrazole-5-carboxamide (**26**) were found to be most active against *Spodoptera litura*.

REFERENCES

1) I. Okada, S. Okui, M. Wada and Y. Takahashi : *J. Pestic. Sci.* **21**, 305–310 (1996).
2) T. Obata, K. Fujii, E. Funaki, K. Tsutsumiuti, A. Ohoka, S. Suizu and Y. Kanetsuki : *J. Pestic. Sci.* **24**, 33–37 (1999).
3) I. Okada, Y. Ikeda, Y. Shiga and T. Fukuchi (Mitsubishi Chemical Corp.) : Jpn Kokai Tokkyo Koho JP 2001–172261 (2001).