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Note

1-Diazinylmethyl-2-nitromethylene- and 2-Nitroimino-imidazolidines as New Potential Insecticides*

Koichi MORIYA, Katsuhiko SHIBUYA, Yumi HATTORI, Shin-ichi TSUBOI, Kozo SHIOKAWA and Shinzo KAGABU**

Yuki Research Center, Nihon Bayer Agrochem Co., Ltd., Nishi Hanjotsuka, Yuki 307, Japan

***Department of Chemistry, Faculty of Education, Gifu University, Yanagido, Gifu 501–11, Japan*

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INTRODUCTION

Nitromethylene insecticides have been drawing attention owing to their unique structure and hitherto unrecognized insecticidal mechanism.[2] We have studied their heterocyclic system chemically and biologically, and developed an epoch-making class of pesticides for practical application.[3,4] The structure of our novel insecticides features the attachment of 6-chloronicotinyl group to the original imidazolidine skeleton. This structural modification has increased the insecticidal potential of 2-nitromethylene-imidazolidine against *ex.*, green rice leafhopper (*Nephotettix cincticeps*) by over thirty centuplications and, in addition, broadened the spectrum markedly.** The study on the structure-activity relationship showed that the position of the ring nitrogen atom and the substituent was crucial to the exhibit the activity in the pyridylmethylimidazolidine system.[3] This paper deals with the insecticidal properties of diazinylmethylimidazolidines and compared them with the corresponding phenyl and pyridyl homologs (Table 1). Methyl group and chlorine atom were selected as ring substituents to simplify the comparison. The bioassay was carried out according to the previous procedure using green rice leafhoppers as test species.[3,4]

* Imidacloprid and Analogous Insecticides (Part IV). For Part III, see Ref. 1).

** 1-(6-chloronicotinyl)-2-nitromethylene-imidazolidine **8** and the 2-nitroimino analog **9** (common name: imidacloprid) have been extensively tested for commercial use.

MATERIALS AND METHODS

1. Preparation of Diazinylmethylimidazolidines

The synthetic scheme is depicted in Fig. 1. Diazinyl imidazolidine was prepared by either replacement of the two methyl-thio groups of 1,1-bis(methylthio)-2-nitroethylene **IV**[5] with diazinylmethylethylenediamine **III** or by diazinylmethylation of the nitrogen in the 1-position of 2-nitromethyleneimidazolidine or 2-nitroiminoimidazolidine.* Diazinylmethyl-ethylenediamine was prepared by mono *N*-alkylation of ethylenediamine with **I** or by reduction of the Schiff base from the diazinyl aldehyde **II**[6-8] and ethylenediamine, and chloromethyl-diazines were available by NCS chlorination[9] of the corresponding methyl-diazines.[10,11] The typical procedures for **IV** and **VI** are as below:

1-(5-Methyl-2-pyrazinyl)methyl-2-nitromethyleneimidazolidine **13**: A solution of 5-methyl-2-pyrazinylmethyl chloride (1.43 g) in acetonitrile (10 ml) was added dropwise to a solution of ethylenediamine (3 g) in acetonitrile (30 ml). The mixture was heated under reflux for 1 hr, cooled to room temperature, and stirred with 30% aqueous sodium hydroxide (1.33 g) for 30 min. The solvents and the excess ethylenediamine were removed *in vacuo*, and *N*-(5-methyl-2-pyrazinyl)-methylethylenediamine was extracted with ethanol (30 ml×2) from the residue. 1,1-Bis-(methylthio)-2-nitroethylene (1.65 g) was added to the combined extracts, and the mixture was heated under reflux for 6 hr. The solvent was distilled off, and the residue was chromatographed on silica gel, eluting with chloroform–ethanol (9: 1, v/v). Crude **13** was recrystallized from ethanol. Yield: 1.1 g (47%). ^{1}H NMR δ (DMSO-d$_6$) ppm: 2.47 (3H, s), 3.62 (4H, bs), 4.54 (2H, s), 6.60 (1H, s), 8.45 (2H, s), 8.80 (1H, bs).

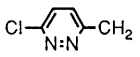
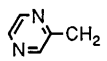
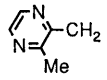
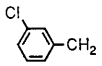
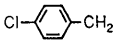
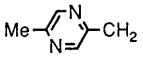
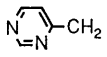
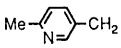
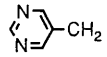
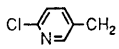
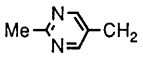
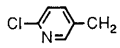
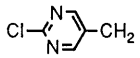
11 was prepared similarly.

Yield: 44%. ^{1}H NMR δ (DMSO-d$_6$) ppm: 3.62 (4H, bs), 4.62 (2H, s), 6.64 (1H, s), 8.59 (3H, m), 8.82 (1H, bs).

1-(2-Methyl-5-pyrimidinyl)methy-2-nitromethyleneimidazolidine **16**: A solution of 2-methyl-5-formylpyrimidine (1.22 g) in dichloromethane (10 ml) was added dropwise to a solution of ethyl-

* **VII** (mp 220–221°C) was prepared in a 45% yield by heating an aqueous solution of an equimolar mixture of nitroguanidine and ethylenediamine at 50°C for 1 hr.

Table 1 Biological activity against green rice leafhoppers.

No.	R	Y	LC_{90}[a)]	No.	R	Y	LC_{90}[a)]
1	H	CH	1000	**10**		CH	40
2		CH	200	**11**		CH	8
3		CH	—	**12**		CH	200
4		CH	200				
5		CH	40	**13**		CH	1.6
6		CH	8	**14**		CH	40
7		CH	1.6	**15**		CH	8
8		CH	0.32	**16**		CH	1.6
9	 (imidacloprid)	N	0.32	**17**		N	0.32

[a)] LC_{90} is the lowest concentration to kill over 90% of the insects in six stages from 1000–0.32 ppm.

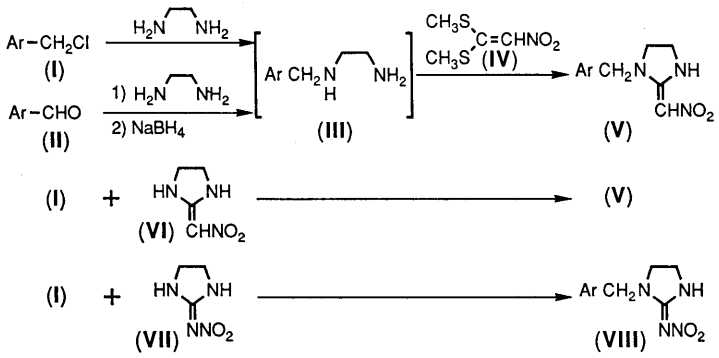


Fig. 1 Preparation scheme of 1-diazinylmethylimidazolidines.

enediamine (0.6 g) in dichloromethane (30 ml) at room temperature with stirring. After 4 hr of stirring, the solvent was removed *in vacuo*, and the residue was diluted with methanol (50 ml). To this solution was added sodium borohydride (0.38 g) by portions at 5°C and the mixture was stirred at room temperature for 5 hr. The solvents were removed *in vacuo* and the excess reducing reagent was decomposed with 2% hydrochloric acid (18 ml). Thirty-percent aqueous sodium hydroxide (1.33 g) was added to the mixture, and the water was distilled off *in vacuo*. *N*-(5-Methyl-2-pyrazinyl)methylethylenediamine was extracted with ethanol (30 ml×2) from the

residue. The combined extracts were heated under reflux for 6 hr together with 1,1-bis(methylthio)-2-nitroethylene (1.65 g). The solvent was removed, and the residue was chromatographed on silica gel, eluting with chloroform–ethanol (9: 1, v/v). Crude **16** was recrystallized from ethanol. Yield: 0.4 g (17%). ^{1}H NMR δ ($CDCl_3$) ppm: 2.74 (3H, s), 3.69 (4H, m), 4.30 (2H, s), 6.62 (1H, s), 8.51 (2H, s), 8.62 (1H, bs).

14 and **15** were prepared in a similar manner.

14; Yield: 10%. ^{1}H NMR δ (DMSO-d_6) ppm: 3.72 (4H, bs), 4.58 (2H, s), 6.54 (1H, s), 7.43 (1H, dd, J=5.2 and 1.0 Hz), 8.73 (1H, d, J=5.2 Hz), 8.96 (1H, bs), 9.10 (1H, d, J=1.0 Hz).

15; Yield: 7%. ^{1}H NMR δ ($CDCl_3$) ppm: 3.79 (4H, m), 4.59 (2H, s), 6.64 (1H, s), 8.70 (1H, bs), 8.81 (2H, s), 9.12 (1H, s).

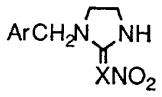
1-(6-Chloro-3-pyridazinyl)methyl-2-nitromethyleneimidazolidine **10**: To a solution of 2-nitromethylene-imidazolidine **VI**[5] (1.29 g) in DMF (30 ml) was added 0.4 g of sodium hydride (60% oil dispersion). After 1 hr of stirring, 6-chloro-3-pyridazinyl-methyl chloride (16.3 g) in DMF (10 ml) was added dropwise to the mixture, which was then stirred overnight. The solvent was removed *in vacuo*, and the residue was chromatographed on silica gel, eluting with chloroform–ethanol (9: 1, v/v). Crude **10** was recrystallized from ethanol. Yield: 0.3 g (12%). ^{1}H NMR δ (DMSO-d_6) ppm: 3.64 (4H, bs), 4.75 (2H, s), 6.65 (1H, s), 7.72 (1H, d, J=9.0 Hz), 7.92 (1H, d, J=9.0 Hz), 8.85 (1H, bs).

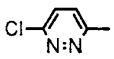
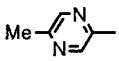
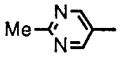
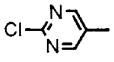
12 was prepared in a similar manner.

Yield: 7%. ^{1}H NMR δ (DMSO-d_6)ppm: 2.50 (3H, s), 3.63 (4H, bs), 4.67 (2H, s), 6.57 (1H, s), 8.38 (2H, bs), 8.84 (1H, bs).

1-(2-Chloro-5-pyrimidinyl)methyl-2-nitroiminoimidazolidine **17**: To a solution of 2-nitroimino-

Table 2 Characterization of imidazolidines.



No.	Ar	X	mp (°C)	HR-MS (M^+, m/z) or Anal	
				Calcd.	Found
10		CH	172–175	255.0523 ($C_9H_{10}ClN_5O_2$)	255.0506
11		CH	259–260	221.0912 ($C_9H_{11}N_5O_2$)	221.0920
12		CH	253 dec.	235.1069 ($C_{10}H_{13}N_5O_2$)	235.1092
13		CH	163–166	235.1069 ($C_{10}H_{13}N_5O_2$)	235.1068
14		CH	185–187	221.0912 ($C_9H_{11}N_5O_2$)	221.0917
15		CH	236 dec.	221.0912 ($C_9H_{11}N_5O_2$)	221.0895
16		CH	188–189	235.1069 ($C_{10}H_{13}N_5O_2$)	235.1069
17		N	181–183	C, 37.44% H, 3.53% N, 32.74% ($C_8H_9ClN_6O_2$)	C, 37.35% H, 3.49% N, 32.74%

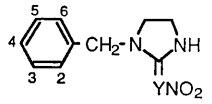


Fig. 2 Site notation for aromatic ring.

imidazolidine **VII**[6-8] (1.3 g) in DMF (30 ml) was added 0.4 g of sodium hydride (60% oil dispersion) with stirring. After 1 hr, a solution of 2-chloro-5-pyrimidinylmethyl chloride (1.63 g) in DMF (10 ml) was added dropwise to the mixture, which was then stirred continued overnight at room temperature. The solvent was removed *in vacuo*, and the residue was chromatographed on silica gel, eluting with chloroform–ethanol (15: 1, v/v). Crude **17** was recrystallized from ethanol. Yield: 0.02 g (1%). ^{1}H NMR δ ($CDCl_3$) ppm: 3.56 (4H, s), 4.49 (2H, s), 8.72 (2H, s), 8.95 (1H, bs).

The melting points and millimass or elemental analysis data on the diazinyl imidazolidines are listed in Table 2.

2. Biological Test

Paper towels were placed on the dent of the bottom part of a cage and watered. On them wet rice seeds were sown and stored for germination in the dark at 30°C for 4 days. After storage, the etiolated small rice plants about 2 cm tall were sprayed with a water solution of a test compound from the top. The concentration of the compound in a water-soluble concentrate was adjusted to six stages from 1000 to 0.32 ppm by diluting five times. After spraying, ten leafhopper nymphs were released on the plants, and the mortality was determined after 5 days.

RESULTS AND DISCUSSION

Bioassay of *N*-benzyl-imidazolidines revealed the efficacy depended on the position of a substituent on the phenyl ring. While 2-chloro derivative (**3**) showed no activity, 4-chloro derivative (**5**) multiplied the activity of **2** by five times. In nicotinyl derivatives that possessed iminyl nitrogen at 3-position on the aromatic ring, an introduction of methyl or chloro moiety at 4-position on the aromatic ring multiplied the activity of **6** by five times or twentyfive times, respectively (**6**–**8**).

In diazine derivatives that possessed iminyl nitrogen at 3-position on aryl ring, the magnitude of the activity depended on the position of the other nitrogen and substituents. Pyridazine derivative (**10**) that possessed the other nitrogen at 2-position was less active than the most active pyridine derivative (**8**). Pyrazine derivatives (**11**, **13**) that possessed the other nitrogen at 6-position were as active as the corresponding pyridine derivatives (**6**, **7**). An introduction of a methyl substituent at 4-position on the aryl ring increased the activity, while an introduction of a methyl substituent at 2-position reduced the activity (**11**–**13**). Pyrimidine derivative **14** having no nitrogen atom at 3-position on the aromatic ring was less active than the corresponding isomer **15**. The pyrimidine derivatives (**14**, **15**) that possessed the other nitrogen at 5-position were as active as the corresponding pyridine derivatives (**6**, **7**). We remarked on the favorable effect of some substituents at 4-position with iminyl nitrogen at 3-position on the aryl group in the nitromethylene series.[8] This effect of substituents was also observed in the diazine system. The methyl and chloro derivatives (**13**, **16**, **17**) showed high insecticidal activity, and 1-(2-chloro-5-pyrimidinyl)methyl-2-nitroimino-imidazolidine **17**, in particular, had a high insecticidal potential, controlling the test species at a 0.32 ppm dose, comparable to imidacloprid **9**.

REFERENCES

1) K. Shiokawa, K. Moriya, K. Shibuya, Y. Hattori, S. Tsuboi & S. Kagabu: *Biosci. Biotech. Biochem.* **56**, 1364 (1992)
2) S. B. Soloway, A. C. Henry, W. D. Kollmeyer, W. M. Padgent, J. E. Powell, S. A. Roman, C. H. Tieman, R. A. Corey & C. A. Horne: Abstracts of Papers "Advances in Pesticide Science," July 1978, Part 2, pp. 206–217
3) S. Kagabu, K. Moriya, K. Shibuya, Y. Hattori, S. Tsuboi & K. Shiokawa: *Biosci. Biotech. Biochem.* **56**, 362 (1992)
4) K. Moriya, K. Shibuya, Y. Hattori, S. Tsuboi, K. Shiokawa & S. Kagabu: *Biosci. Biotech. Biochem.* **56**, 364 (1992)
5) R. Gomper & H. Schaefer: *Chem. Ber.* **100**, 591 (1967)
6) H. Bredereck, R. Sell & F. Effenberger: *Chem. Ber.* **97**, 591 (1964)
7) H. Bredereck, G. Simchen, A. Santos & H. Wagner: *Angew. Chem. Int. Ed. Engl.* **5**, 671 (1966)
8) K. G. Watson (ICI Australia Ltd.): Jpn. Kokai Tokkyo Koho JP 59–59669 (1984)
9) G. R. Newkome, G. E. Kiefer, U. J. Xia & V. K. Gupta: *Synthesis* **1984**, 676
10) G. Karmas & P. E. Spoerri: *J. Am. Chem. Soc.* **74**, 1580 (1952)
11) D. J. Brown & T. Nagamatsu: *Aust. J. Chem.* **30**, 2515 (1977)

要　約

殺虫活性を有する 1-ジアジニルメチル-2-ニトロメチレンイミダゾリジンとそのニトロイミノ誘導体

盛家晃一，渋谷克彦，服部ゆみ
坪井真一，塩川紘三，利部伸三

先にわれわれは，1-(6-クロロ-3-ピリジル)メチル-2-ニトロメチレン-イミダゾリジンとそのニトロイミノ誘導体 (imidacloprid, Admire®) が，高い殺虫活性を有することを報告した．さらに高活性な化合物を目標に，上記化合物のピリジン環の代わりにジアジン環を導入したイミダゾリジン誘導体を8種合成し殺虫活性を試験したところ，1-(2-クロロ-5-ピリミジニル)メチル-2-ニトロイミノ-イミダゾリジン (**17**) が最も高い活性を示し，ツマグロヨコバイに対して imidacloprid と同等の活性を示すことがわかった．