Original Article

Synthesis and Insecticidal Activity of Acyclic Nitroethene Compounds Containing a 3-Pyridylmethylamino Group*

Isao MINAMIDA, Koichi IWANAGA,** Takanori TABUCHI,
Hideki UNEME, Hirokazu DANTSUJI and Tetsuo OKAUCHI

*Agricultural Research Laboratories, Agro Division, Takeda Chemical Industries, Ltd.,
Wadaï, Tsukuba 300-42, Japan*

***Animal Health Research Laboratories, Agro Division, Takeda Chemical Industries, Ltd.,
Yodogawa-ku, Osaka 532, Japan*

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A series of acyclic nitroethene compounds containing a 3-pyridylmethylamino group in the β -carbon atom were synthesized, and their insecticidal activities were examined. The compounds into whose 1-carbon atom of 1-(3-pyridylmethyl)amino-2-nitroethene a methylamino (**9a-5**) or a dimethylamino group (**9a-22**) was introduced were more effective against *Nilaparvata lugens* and *Laodelphax striatellus* than against *Nephotettix cincticeps*. An introduction of larger alkylamino groups decreased the activity. Successive modifications of the 1-methylamino-1-(3-pyridylmethyl)amino-2-nitroethene revealed that an introduction of a methyl or ethyl group into the nitrogen atom attached to the 3-pyridylmethyl group enhanced the activity. Compounds, such as 1-methylamino-1-[N-methyl(ethyl)-N-(3-pyridylmethyl)]amino-2-nitroethene (**9b-1,2**), exhibited potent activity against not only *N. lugens* and *L. striatellus* but also *N. cincticeps*.

INTRODUCTION

A recent report says that a series of nitrogen containing heterocycles bearing a nitromethylene substituent had potent insecticidal properties (Fig. 1) and that among them tetrahydro-2-nitromethylene-2*H*-1,3-thiazine (**1**) was particularly notable for a broad insecticidal spectrum with high activity against lepidopterous larvae.¹⁾ This compound was found unstable under sunlight, however, and efforts to avoid the drawback were undertaken. Thus, the *N*-formyl derivative WL 108477 (**2**) was chosen as a compound that has both greater photostability and comparable insecticidal activity.²⁾ Later, compounds **3**³⁻⁵⁾ and **4**,⁶⁾ which consist of the same heterocyclic skeleton as was reported in the precedent

paper¹⁾ and a 3-pyridylmethyl side chain in addition, were shown to exhibit exceedingly potent activity.

Incidentally, a random screening in our laboratories picked up acyclic nitromethylenes (**5** and **6**) as potential insecticides active against *Nilaparvata lugens* (unpublished data). Stimulated by the finding that seemed to contrary to Soloway's conclusion on SAR studies that the heterocyclic skeleton of **1** and **2** is essential to the activity,¹⁾ we were interested in replacing the heterocyclic skeleton of **1** to **4** with corresponding acyclic compartments.

This paper describes the synthesis and SAR studies of 1-methylamino-1-[N-methyl-N-(3-pyridylmethyl)]amino-2-nitroethene (**9b-1**) in which the pyridylmethylimidazoline portion of **3** was formally replaced by two separated acyclic fragments of this portion, *i.e.*, methylamino and *N*-methyl-N-(3-pyridylmethyl)-

* Studies on Acyclic Nitroethene Compounds (Part 1).

Fig. 1 Nitromethylene compounds.

amino, and its modified derivatives (**9a**, **b**, **c**) listed in Tables 1 to 3.

MATERIALS AND METHODS

1. Synthesis of Compounds

General: In the procedures of column chromatography, elution was carried out under monitoring by TLC, in which Merck Kieselgel 60 F₂₅₄ (Art. 5715), a column chromatographic eluent and an UV detector were used.

All solvents were evaporated by roto-evaporation *in vacuo*. All melting points are uncorrected.

All of the new compounds prepared showed corrective elemental analyses (except oily compounds), NMR charts and IR spectra. NMR spectra were recorded by proton NMR and

measured with tetramethylsilane as an internal reference standard with a Varian EM390 (90 MHz) spectrometer. All δ values are expressed in ppm. IR spectra were taken on a Shimadzu IR-435 spectrometer.

All of the compounds except **9a-1**, **9a-2**, **9a-3**, **9a-12**, **9c-9** and **9c-10** in Tables 1, 2 and 3 were prepared through three synthetic routes (Fig. 2). By Method A, 1,1-bis(methylthio)-2-nitroethene (**7**)⁷ was reacted with *N*-(3-pyridylmethyl)-*N*-(substituted)amine⁸ to give a compound of general formula **8**, which was then reacted with an amine to thereby give a compound of general formula **9**, 1-[*N*-(3-pyridylmethyl)-*N*-(substituted)]amino-1-(substituted)amino-2-nitroethene. Method B reversed the addition order of the reagents by Method A: an amine was added first and then *N*-(3-pyridylmethyl)-*N*-(substituted)amine. By Method C, *N*-(3-pyridylmethyl)-*N*-(substituted)amine was reacted with isothiocyanate to give a thiourea of general formula **11**, which was treated with sodium hydride and methyl iodide in tetrahydrofuran (THF) successively. The *S*-methylisothiurea obtained was refluxed in nitromethane to give **9** ($R^2=H$).⁹

We have got some information on the con

Fig. 2 Syntheses of acyclic nitroethene compounds.

figuration of the double bond of the compounds described in this and the following articles, which will be referred in the following paper.

Typical examples of synthetic procedures are as follows.

1.1 Method A

1-Methylthio-1-(3-pyridylmethyl)amino-2-nitroethene (9a-4)

In 100 ml of EtOH was dissolved 5.0 g (0.03 mol) of 1,1-bis(methylthio)-2-nitroethene⁷⁾ with heating, and a 3.2 g (0.03 mol) solution of 3-pyridylmethylamine in 30 ml of EtOH was added dropwise in three installments at intervals of 20–30 min while refluxing. The mixture was further refluxed for 2 hr and the EtOH was distilled off *in vacuo*. The residue was subjected to silica gel column chromatography using MeOH–CHCl₃ (1:5) as an eluent. The procedure gave 4.0 g (59.2%) of the title compound and 0.5 g (5.8%) of 1,1-bis(3-pyridylmethylamino)-2-nitroethene (9a-12), respectively, each as a white powder. **9a-4**: mp 129–130°C. Anal. Found: C, 47.97; H, 4.93; N, 18.63, Calcd. for C₉H₁₁N₃O₂S: C, 47.99; H, 4.92; N, 18.65%. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 1560, 1425, 1360, 1350, 1330. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 2.48 (3H, s), 4.70 (2H, d, *J*=6 Hz), 6.62 (1H, s), 7.25–7.45 (1H, m), 7.6–7.8 (1H, m), 8.55–8.7 (2H, m), 10.76 (1H, br). **9a-12**: mp 141–143°C. Anal. Found: C, 58.68; H, 5.26; N, 24.47, Calcd. for C₁₄H₁₅N₅O₂: C, 58.94; H, 5.30; N, 24.55%. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3150, 1575, 1390. ¹H NMR $\delta_{\text{TMS}}^{\text{DMSO-d}_6}$ ppm: 4.55 (4H, d), 6.52 (2H, s), 7.25–7.5 (1H, m), 7.5–7.8 (1H, m), 8.4–8.6 (2H, m), 10.26 (2H, br s).

1-Methylamino-1-(3-pyridylmethyl)amino-2-nitroethene (9a-5)

In 50 ml of EtOH was dissolved 2.3 g (0.01 mol) of **9a-4** with heating, and a 1.2 g (0.015 mol) solution of 40% aqueous methylamine in 10 ml of EtOH was added dropwise over a period of 30 min while refluxing. The mixture was further refluxed for 2 hr and concentrated. The crystals were collected by filtration and recrystallized from acetonitrile to give 1.6 g of the title compound as white prisms. mp 159–160°C. Anal. Found: C, 51.67; H, 5.86; N, 26.96, Calcd. for C₉H₁₂N₄O₂: C, 51.92; H, 5.81; N, 26.91%. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 1620, 1580, 1390, 1215, 980. ¹H NMR $\delta_{\text{TMS}}^{\text{DMSO-d}_6}$ ppm: 2.86 (3H, s), 4.49 (2H, d, *J*=6 Hz), 6.46

(1H, s), 7.25–7.5 (1H, m), 7.6 (1H, br s), 7.6–7.85 (1H, m), 8.4–8.7 (2H, m), 10 (1H, br).

Compound **9a-4** was reacted with various amines in the same manner as in the preparation of **9a-5**, and the reaction product was purified by recrystallization or silica gel chromatography to give compounds listed in Table 1.

1.2 Method B

1-Piperidino-1-(3-pyridylmethyl)amino-2-nitroethene (9a-24)

In 20 ml of EtOH was dissolved 1.7 g (0.01 mol) of compound **7** under heating, and 0.9 g (0.01 mol) of piperidine dissolved in 10 ml of EtOH was added dropwise in three portions at 30 min intervals under reflux. After 2 hr of reflux, the solvent was distilled off, and the residue was chromatographed on a silica gel column and eluted with AcOEt–toluene (2:3). The above procedure yielded 0.8 g of 1-methylthio-1-piperidino-2-nitroethene as yellow prisms. mp 65–67°C. Anal. Found: C, 47.61; H, 6.87; N, 13.71, Calcd. for C₈H₁₄N₂O₂S: C, 47.50; H, 6.98; N, 13.85%. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 1650, 1530, 1380, 1300, 1255. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.6–1.9 (6H, m), 2.45 (3H, s), 3.4–3.7 (4H, m), 6.68 (1H, s).

In 20 ml of EtOH was dissolved 0.8 g (0.004 mol) of 1-methylthio-1-piperidino-2-nitroethene, followed by addition of 0.4 g (0.004 mol) of 3-pyridylmethylamine. The mixture was refluxed for 2 hr. The EtOH was distilled off, and the residue was purified by silica gel chromatography to give 0.3 g (28.6%) of the title compound as a pale yellow powder. mp 106–108°C. Anal. Found: C, 59.36; H, 6.93; N, 21.12, Calcd. for C₁₃H₁₈N₄O₂: C, 59.53; H, 6.92; N, 21.36%. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 1595, 1380, 1280, 1200, 975. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.66 (6H, br s), 3.1–3.35 (4H, m), 4.50 (2H, d, *J*=6 Hz), 6.50 (1H, s), 7.31 (1H, dd, *J*=8 & 5 Hz), 7.73 (1H, dt, *J*=8 & 1 Hz), 8.59 (2H, m), 9.80 (1H, br t, *J*=6 Hz).

The two procedures above were repeated with 1,1-dimethylhydrazine or dimethyl amine instead of piperidine to give compound **9a-21** or **9c-8**.

1.3 Method C

1-[N-Ethyl-N-(3-pyridylmethyl)]amino-1-methylamino-2-nitroethene (9b-2)

In 50 ml of Et₂O was dissolved 2.4 g of *N*-

ethyl-*N*-(3-pyridylmethyl)amine,⁹⁾ followed by addition of 1.3 g of methyl isothiocyanate. The mixture was stirred at room temperature for 1 hr. The resulting precipitate was collected by filtration, washed with a small amount of Et₂O and dried to give 3.7 g of *N*-ethyl-*N'*-methyl-*N*-(3-pyridylmethyl)thiourea as white prisms. mp 122–123°C. Anal. Found: C, 57.35; H, 7.31; N, 19.89. Calcd. for C₁₀H₁₅N₃S: C, 57.38; H, 7.22; N, 20.08%. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1540, 1475, 1425, 1340, 1240, 1040. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.16 (3H, t, *J*=7 Hz), 3.16 (3H, d, *J*=5 Hz), 3.55 (2H, q, *J*=8 Hz), 5.12 (2H, s), 5.95 (1H, br s), 7.27 (1H, dd, *J*=8 & 5 Hz), 7.74 (1H, dt, *J*=8 & 1 Hz), 8.53 (2H, m).

In 30 ml of dry THF was dissolved 3.1 g of *N*-ethyl-*N'*-methyl-*N*-(3-pyridylmethyl)thiourea, followed by addition of 0.6 g of 60% sodium hydride. The mixture was stirred at room temperature for 1 hr. Then, 2.1 g of methyl iodide was added dropwise, and the mixture was further stirred for 3 hr. The reaction mixture was concentrated, and the residue was diluted with 50 ml of a saturated solution of NaCl and extracted three times with 50 ml portions of AcOEt. The extracts were pooled and dried over MgSO₄. The solvent was then distilled off to give 3.1 g of *S*, *N'*-dimethyl-*N*-ethyl-*N*-(3-pyridylmethyl)isothiourea as a yellow oil. IR $\nu_{\text{max}}^{\text{Neat}}$ cm⁻¹: 1600, 1420, 1225, 1020, 710. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.06 (3H, t, *J*=7 Hz), 2.30 (3H, s), 3.23 (3H, s), 3.35 (2H, q, *J*=7 Hz), 4.53 (2H, s), 7.22 (1H, dd, *J*=8 & 5 Hz), 7.59 (1H, dt, *J*=8 & 1 Hz), 8.50 (2H, m).

To 2.2 g of *S*, *N'*-dimethyl-*N*-ethyl-*N*-(3-pyridylmethyl)isothiourea was added 10 ml of nitromethane, and the mixture was refluxed for 16 hr.⁹⁾ The reaction mixture was concentrated, and the residue was subjected to silica gel column chromatography using MeOH–CHCl₃ (1:5) as an eluent to give 1.4 g of the title compound as a yellow viscous oil. IR $\nu_{\text{max}}^{\text{Neat}}$ cm⁻¹: 1600, 1420, 1360, 1210, 1010. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.20 (3H, t, *J*=7 Hz), 3.08 (3H, d, *J*=5 Hz), 3.18 (2H, q, *J*=7 Hz), 4.46 (2H, s), 6.53 (1H, s), 7.33 (1H, dd, *J*=8 & 5 Hz), 7.60 (1H, dt, *J*=8 & 1 Hz), 8.57 (2H, m), 9.86 (1H, br).

1.4 1-[*N*-Methyl-*N*-(3-pyridylmethyl)]amino-2-nitroethene (9a-1)

This compound was prepared according to the Royer's method.¹⁰⁾ The mixture of 3.5 g (0.05 mol) of ethyl orthoformate, 3.0 g (0.02 mol) of nitromethane, 1.2 g of *N*-methyl-*N*-(3-pyridylmethyl)amine and 0.1 g of *p*-TsOH was heated at 120°C in an oil bath for 1 hr. Volatile materials were evaporated under reduced pressure, and the residue was purified on silica gel column chromatography to give 1.5 g (80%) of the title compound as pale yellow crystals. mp 94–95°C. Anal. Found: C, 55.83; H, 5.62; N, 21.63. Calcd. for C₉H₁₁N₃O₂: C, 55.95; H, 5.74; N, 21.75%. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 1620, 1320, 1250. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 2.90 (3H, br s), 4.55 (2H, br s), 6.75 (1H, d, *J*=14 Hz), 7.36 (1H, dd, *J*=8 & 5 Hz), 7.66 (1H, br d, *J*=8 Hz), 8.36 (1H, d, *J*=14 Hz), 8.60 (1H, dd, *J*=5 & 2 Hz), 8.68 (1H, d, *J*=1 Hz).

1.5 1-Nitro-2-(3-pyridylmethyl)amino-1-butene (9a-2)

To 6.51 g (0.05 mol) of propionic anhydride was added 5.41 g of 3-pyridylmethylamine under ice-cooling for 20 min, and the mixture was stirred at room temperature for 1 hr. Propionic acid produced was removed *in vacuo* to give 7.81 g (95.4%) of *N*-(3-pyridylmethyl)propionamide as an oil. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.13 (3H, t, *J*=7.6 Hz), 2.24 (2H, q, *J*=7.6 Hz), 4.40 (2H, d, *J*=6.0 Hz), 7.10 (1H, br s), 7.26 (1H, dd, *J*=8.0 & 5.0 Hz), 7.55–7.75 (1H, m), 8.4–8.6 (2H, m).

A mixture of 1.64 g (0.01 mol) of *N*-(3-pyridylmethyl)propionamide, 6.67 g (0.03 mol) of P₂S₅ and 100 ml of toluene was stirred at 70°C for 6.5 hr. To this mixture were added 80 ml of water and 15.1 g (0.18 mol) of NaHCO₃ under ice-cooling, followed by stirring at room temperature for 1 hr. The organic phase was separated, and the aqueous phase was extracted with CHCl₃ after saturation with NaCl. The organic phase combined was dried over MgSO₄ and evaporated. The residue was purified on silica gel column chromatography using MeOH–CH₂Cl₂ (1:10) as an eluent to give 1.45 g (80.4%) of *N*-(3-pyridylmethyl)propionthioamide as an oil. ¹H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.30 (3H, t, *J*=7.6 Hz), 2.73 (2H, q, *J*=7.6 Hz), 4.90 (2H, d, *J*=5.6 Hz), 7.30 (1H, dd, *J*=8.1 & 5.1 Hz), 7.65–7.85 (1H, m), 8.4–

8.55 (2H, m), 8.87 (1H, br s).

To a solution of 1.45 g (0.008 mol) of *N*-(3-pyridylmethyl)propionthioamide in 10 ml of dry THF was added 0.21 g (0.009 mol) of 60% sodium hydride in small portions for 1 min. After stirring for 30 min, a solution 1.26 g (0.009 mol) of methyl iodide in 1 ml of dry THF was added dropwise for 10 min, and the mixture was further stirred at room temperature. The mixture was concentrated, and the residue was diluted with 10 ml of water and extracted twice with CH_2Cl_2 . The solvent was then distilled off to give 1.62 g (103.7%) of *S*-methyl-*N*-(3-pyridylmethyl)propionthioimide (*E,Z*-mixture) as a crude oil. ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.1–1.35 (3H, m), 2.3–2.75 (5H, m), 4.53 (0.5H, s), 4.60 (0.5H, s), 7.15–7.35 (1H, m), 7.6–7.85 (1H, m), 8.4–8.7 (2H, m).

To 1.62 g of *S*-methyl-*N*-(3-pyridylmethyl)propionthioimide was added 15 ml of nitromethane, and the mixture was refluxed for 27.5 hr. The reaction mixture was concentrated, and the residue was subjected to silica gel column chromatography using $\text{MeOH}-\text{CH}_2\text{Cl}_2$ (1:10) as an eluent to give 1.00 g (60%) of the title compound as a syrup. Anal. Found: C, 57.54; H, 6.22; N, 19.86, Calcd. for $\text{C}_{10}\text{H}_{13}\text{N}_3\text{O}_2$: C, 57.96; H, 6.32; N, 20.28%. IR $\nu_{\text{max}}^{\text{Neat}}$ cm^{-1} : 3200, 1590. ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 1.17 (3H, t, $J=7.5$ Hz), 2.38 (2H, q, $J=7.5$ Hz), 4.68 (2H, d, $J=6.6$ Hz), 6.63 (1H, s), 7.38 (1H, dd, $J=8.1$ & 4.8 Hz), 7.6–7.8 (1H, m), 8.5–8.7 (2H, m), 10.47 (1H, br s).

1.6 1-Methoxy-1-(3-pyridylmethyl)amino-2-nitroethene (9a-3)

In 1 l of MeOH was dissolved 16.5 g (0.1 mol) of **7** with heating on reflux. A solution of 11.0 g (0.1 mol) of 3-pyridylmethylamine in 200 ml of MeOH was added dropwise in four installments at 1 hr intervals. The mixture was further refluxed for 3 hr, and the MeOH was distilled off. The residue was purified by silica gel column chromatography to give 5.9 g (28.2%) of the title compound as white prisms. (In this procedure, compound **9a-4** was also produced as a major product.) mp 129–130°C. Anal. Found: C, 51.38; H, 5.28; N, 19.93, Calcd. for $\text{C}_9\text{H}_{11}\text{N}_3\text{O}_3$: C, 51.67; H, 5.30; N, 20.09%. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1610, 1425, 1370, 1210, 1090. ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 3.86 (3H, s), 4.60 (2H, d, $J=6$ Hz), 6.68 (1H, s), 7.30

(1H, dd, $J=8$ & 5 Hz), 7.66 (1H, dt, $J=8$ & 1 Hz), 8.59 (2H, m), 10.15 (1H, br).

1.7 1-(*N*-Formyl-*N*-methyl)amino-1-[*N*-methyl-*N*-(3-pyridylmethyl)]amino-2-nitroethene (9c-9)

In 10 ml of dry THF was suspended 0.1 g of petroleum ether-washed 60% sodium hydride, followed by addition of 0.51 g (0.0023 mol) of the compound (**9b-1**). The mixture was stirred at room temperature overnight, and to it 0.6 g of formic acetic anhydride was added under ice-cooling. The mixture was stirred at the same temperature for 1 hr. The solvent was distilled off, and the residue was diluted with 30 ml of water, neutralized with NaHCO_3 and extracted with CH_2Cl_2 (30 ml $\times$ 3). The extract was dried over MgSO_4 , the CH_2Cl_2 was removed by distillation, and the residue was subjected to silica gel column chromatography, elution being carried out with $\text{MeOH}-\text{CHCl}_3$ (1:5). The procedure gave 0.25 g of the title compound as pale yellow prisms. mp 97–98°C. Anal. Found: C, 52.81; H, 5.58; N, 22.11, Calcd. for $\text{C}_{11}\text{H}_{14}\text{N}_4\text{O}_3$: C, 52.79; H, 5.64; N, 22.39%. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1700, 1560, 1350, 1285, 1260, 890. ^1H NMR $\delta_{\text{TMS}}^{\text{DMSO}-d_6}$ ppm: 2.93 (3H, s), 3.03 (3H, s), 4.62 (2H, br), 6.86 (1H, s), 7.42 (1H, dd, $J=8$ & 5 Hz), 7.73 (1H, br d, $J=8$ Hz), 8.25 (1H, s), 8.55 (2H, br).

1.8 1,1-Bis[*N*-methyl-*N*-(3-pyridylmethyl)]amino-2-nitroethene (9c-10)

A mixture of 2.0 g (0.012 mol) 1-dimethylamino-1-methylthio-2-nitroethene and 1.5 g (0.012 mol) *N*-methyl-*N*-(3-pyridylmethyl)amine was stirred at 120°C for 40 min. The reaction mixture was subjected to column chromatography, elution being carried out with $\text{MeOH}-\text{CHCl}_3$ (1:10) to give two fractions containing compounds **9c-8** and **9c-10**, respectively. One of the fractions was further purified by silica gel column chromatography using $\text{MeOH}-\text{CHCl}_3$ (1:10) and acetone- CHCl_3 (2:1) in succession, whereby 0.4 g of compound **9c-8** was obtained as pale yellow crystals. The other fraction was also chromatographed on a silica gel column and eluted with $\text{MeOH}-\text{CHCl}_3$ (1:10) and acetone- CHCl_3 (2:1) in that order to give 0.35 g of compound **9c-10** as a yellow oil. ^1H NMR $\delta_{\text{TMS}}^{\text{CDCl}_3}$ ppm: 2.83 (6H, s), 4.48 (4H, s), 6.52

(1H, s), 7.34 (2H, dd, $J=8.4$ & 5.1 Hz), 7.62 (2H, dt, $J=8.4$ & 1.5 Hz), 8.4–8.8 (4H, m).

2. Biological Tests

Each test compound at 500 (200 or 40) ppm was sprayed over stems and leaves of rice seedlings in the 2-leaf stage at a rate of 10 ml per paper pot. Water was put in test tubes, and the treated rice seedlings were placed therein. Then 10 (or 20) 3rd-instar larvae of *Nilaparvata lugens* (*Nephotettix cincticeps* or *Laodelphax striatellus*) were released in each tube, which was then capped with an aluminum cap. The test tubes were maintained in an incubator at 25°C , and dead insects were counted 7 days after release. The % mortality was calculated using the following formula.

$$\text{Mortality (\%)} = \left(\frac{\text{Number of dead insects}}{\text{Number of insects released}} \right) \times 100$$

RESULTS AND DISCUSSION

First we prepared a series of 1-(3-pyridylmethyl)amino-1-(substituted)-2-nitroethenes (**9a**) by introducing a substituent into the 1-position of 1-(3-pyridylmethyl)amino-2-nitroethene and tested against *N. lugens*, *N. cincticeps* and *L. striatellus*. 1-[N-Methyl-N-(3-pyridylmethyl)]amino-2-nitroethene (**9a-1**) showed weak activity against *N. lugens* probably owing to the methyl group attached to the nitrogen atom bearing a 3-pyridylmethyl group (*vide infra*). On the other hand, compounds substituted with ethyl (**9a-2**), methoxy (**9a-3**) or methylthio (**9a-4**) did not show activity. Surprisingly, compounds with methylamino (**9a-5**) and ethylamino (**9a-6**) showed potent activity. But sterically large alkylamino groups (**9a-7**, **9**, **10**) decreased the activity to less than that of **9a-5** and **9a-6**. Anilino (**9a-11**) and (3-pyridylmethyl)amino (**9a-12**) also showed a similar effect on the activity. Substituted ethylamino groups behaved differently according to their substituents. Hydroxy (**9a-14**), dimethoxy (**9a-16**), *n*-propylthio (**9a-18**) and trifluoro (**9a-19**) showed weak or moderate activity against *N. lugens* at 500 ppm, while a methoxy (**9a-15**) or dimethylamino (**9a-17**) group on ethyl caused 100% mortality. Compounds into which a hydrazino group (**9a-20**, **21**) was intro-

duced showed 100% mortality. It is interesting that dimethylamino (**9a-22**) or pyrrolidino (**9a-23**) increased the activity, while piperidino (**9a-24**) or morpholino (**9a-25**) did not so much. Among all the compounds listed in Table 1, methylamino (**9a-5**) or dimethylamino (**9a-22**) substrates seemed most active, when the activity against *L. striatellus* was taken into consideration.

According to the result described we tried to prepare 1-methylamino-1-[N-(3-pyridylmethyl)-N-substituted]amino-2-nitroethenes (**9b**) by fixing a 1-methylamino group as position 1's substituent, which was one of the most promising substituents, and by changing the substituent on the nitrogen atom attached to the 3-pyridylmethyl group.

Most compounds shown in Table 2 exhibited potent insecticidal activity against *N. lugens* even at 40 ppm. Against *L. striatellus* these compounds showed 100% mortality at 200 ppm, but the efficacy at 40 ppm was low except for three compounds (**9a-5**, **9b-1**, **2**). Only two compounds showed 100% mortality against *N. cincticeps* at 40 ppm. These results revealed the susceptibility against these insects decreased in the order of *N. lugens*, *L. striatellus* and *N. cincticeps*.

It is apparent that an introduction of a substituent on the nitrogen atom bearing a 3-pyridylmethyl group enhanced the activity against these insects. Not only alkyl groups (**9b-1-4**) and substituted alkyl groups (**9b-5-7**) but also methoxy and dimethylamino groups were effective. Among them relatively smaller alkyl groups (Me and Et) were most effective.

The activity of the reported compounds **3** and **4** are also listed in Table 2. Compounds **9b-1** and **9b-2** are superior to **3** and **4** in the activity against *L. striatellus* and *N. cincticeps*.

According to the results above, we were obliged to reinvestigate structure-activity relationships by fixing a substituent on the nitrogen atom bearing 3-pyridylmethyl as methyl (the smallest alkyl). 1-[N-(3-pyridylmethyl)-N-methyl]amino-1-(substituted)-amino-2-nitroethenes were prepared and tested against the same insects. Changing the methylamino group into larger alkylamino (**9c-2**, **3**, **5**), alkenylamino (**9c-4**), substituted alkylamino

Table 1 Insecticidal activity of 1-(3-pyridylmethyl)amino-1-(substituted)-2-nitroethenes.

Compd. No.	R	R ³	Method ^{a)}	mp (°C)	Yield ^{b)} (%)	Mortality (%)						
						N.l. ^{c)}		L.s. ^{d)}			N.c. ^{e)}	
						500	200	40	200	40	200	40 ppm
9a-1	H	Me	f)	94-95	f)	40	— ^{g)}	—	—	—	—	—
-2	Et	H	f)	oil ^{f)}	f)	0	—	—	—	—	—	—
-3	MeO	H	f)	129-130	f)	0	—	—	—	—	—	—
-4	MeS	H	A	129-130	59.2	0	—	—	—	—	—	—
-5	MeNH	H	A	159-160	76.8	100	100	100	100	100	5	0
-6	EtNH	H	A	161-162	72.0	100	60	10	15	10	15	5
-7	<i>i</i> -PrNH	H	A	148-150	33.9	60	—	—	—	—	—	—
-8	CH ₂ =CHCH ₂ NH	H	A	114-115	59.8	100	10	5	—	—	15	10
-9	<i>n</i> -BuNH	H	A	110-112	63.9	20	—	—	—	—	—	—
-10	<i>n</i> -C ₈ H ₁₇ NH	H	A	97-98	68.1	30	—	—	—	—	—	—
-11	C ₆ H ₅ NH	H	A	217-218	59.2	40	—	—	—	—	—	—
-12	3-pyridyl-CH ₂ NH	H	A ^{f)}	141-143	f)	30	—	—	—	—	—	—
-13	Me ₃ SiCH ₂ NH	H	A	156-157	35.7	100	20	20	5	0	35	20
-14	HOCH ₂ CH ₂ NH	H	A	161-163	58.8	60	—	—	—	—	—	—
-15	MeOCH ₂ CH ₂ NH	H	A	108-109	63.4	100	55	10	10	5	35	5
-16	(MeO) ₂ CHCH ₂ NH	H	A	96-98	49.6	50	—	—	—	—	—	—
-17	Me ₂ NCH ₂ CH ₂ NH	H	A	110-111	52.8	100	10	0	25	10	15	10
-18	<i>n</i> -PrSCH ₂ CH ₂ NH	H	A	93-94	54.1	10	—	—	—	—	—	—
-19	CF ₃ CH ₂ NH	H	A	164-165	2.9	60	—	—	—	—	—	—
-20	NH ₂ NH	H	A	176-177 (dec.)	95.6	100	30	5	10	0	30	5
-21	Me ₂ NNH	H	B	158-159	11.0	100	30	15	5	0	25	10
-22	Me ₃ N	H	A	68-70	36.0	100	100	100	100	100	25	5
-23	Pyrrolidino	H	A	103-105	56.4	100	10	10	5	5	45	10
-24	Piperidino	H	B	106-108	28.6	20	—	—	—	—	—	—
-25	Morpholino	H	A	102-103	18.9	10	—	—	—	—	—	—

^{a)} Synthetic method described in the text. ^{b)} Based on **8** or **10**. ^{c)} *Nilaparvata lugens*. ^{d)} *Laodelphax striatellus*. ^{e)} *Nephotettix cincticeps*.

^{f)} See the text. ^{g)} Not tested.

Table 2 Insecticidal activity of 1-methylamino-1-[N-(3-pyridylmethyl)-N-substituted]amino-2-nitroethenes, compounds **3** and **4**.

Compd. No.	R ³	Method ^{a)}	mp (°C)	Yield ^{b)} (%)	Mortality (%)					
					N.I. ^{c)}		L.s. ^{d)}		N.Z. ^{e)}	
					500	200	40	200	40	200
9a-5	H	A	159-160	76.8	100	100	100	100	100	5
9b-1	Me	C	86-87	28.1	100	100	100	100	100	0
-2	Et	C	oil ^{f)}	59.3	100	100	100	100	100	100
-3	<i>n</i> -Pr	C	oil ^{g)}	60.0	100	100	100	100	100	0
-4	<i>n</i> -Bu	C	oil ^{h)}	64.3	100	100	100	100	85	15
-5	Benzyl	C	118-119	43.6	100	100	100	— ⁱ⁾	—	100
-6	MeOCH ₂ CH ₂	C	oil ^{j)}	45.1	100	100	100	100	40	80
-7	(MeO) ₂ CHCH ₂	C	oil ^{k)}	33.7	100	100	95	100	5	75
-8	MeO	C	100-101	47.7	100	100	65	—	—	65
-9	Me ₂ N	C	109-110	44.2	100	100	100	100	95	80
3			164-165 ^{l)}		100	100	100	100	85	65
4			124-125 ^{m)}		100	100	100	90	70	25

^{a)} Synthetic method described in the text. ^{b)} Based on **8** or **13**. ^{c)} *Nilaparvata lugens*. ^{d)} *Laodelphax striatellus*. ^{e)} *Nephotettix cincticeps*. ^{f)} ¹H NMR δ_{TMS}¹³ ppm: 1.20 (t), 3.08 (d), 3.18 (q), 4.46 (s), 6.53 (s), 9.86 (br s). ^{g)} ¹H NMR δ_{TMS}¹³ ppm: 0.86 (t), 1.40-1.90 (2H, m), 2.95-3.30 (2H, m), 3.05 (d), 4.53 (s), 6.55 (s), 7.34 (dd), 7.66 (dt), 8.43-8.66 (2H, m), 9.56 (br d). ^{h)} ¹H NMR δ_{TMS}¹³ ppm: 0.90 (t), 1.06-1.80 (4H, m), 2.96-3.23 (2H, m), 3.07 (d), 4.40 (s), 6.56 (s), 7.33 (dd), 7.60 (dt), 8.46-8.66 (2H, m), 9.82 (br d). ⁱ⁾ Not tested. ^{j)} ¹H NMR δ_{TMS}¹³ ppm: 3.06 (d), 3.35 (s), 3.43 (m), 4.53 (s), 6.55 (s), 9.10 (br s). ^{k)} ¹H NMR δ_{TMS}¹³ ppm: 1.20 (t), 3.08 (d), 3.18 (q), 4.46 (s), 6.53 (s), 9.86 (br s). ^{l)} Shiokawa *et al.* give the mp as 169-171°C. ^{m)} Shiokawa *et al.* give the mp as 96-100°C.

Table 3 Insecticidal activity of 1-[N-(3-pyridylmethyl)-N-methyl]amino-1-(substituted)amino-2-nitroethenes.

Compd. No.	R ¹	R ²	Method ^{a)}	mp (°C)	Yield ^{b)} (%)	Mortality (%)					
						N.I. ^{c)}		L.s. ^{d)}		N.c. ^{e)}	
						500	200	40	200	40	40 ppm
9b-1	Me	H	C	86-87	28.1	100	100	100	100	100	100
9c-1	H	H	A	158-159	24.0	100	100	100	100	30	95
-2	Et	H	C	oil ^{f)}	13.7	100	100	100	30	5	25
-3	i-Pr	H	C	119-121	43.2	100	100	100	30	5	20
-4	CH ₂ =CHCH ₂	H	C	oil ^{g,h)}	4.8	— ⁱ⁾	—	—	—	—	—
-5	n-Bu	H	C	oil ⁱ⁾	24.3	100	100	100	—	—	5
-6	Benzyl	H	C	oil ^{j)}	37.4	100	100	95	40	10	50
-7	MeOCH ₂ CH ₂	H	C	55-57	50.4	100	100	100	—	—	5
-8	Me	Me	B	103-105	13.8	100	100	100	—	—	30
-9	Me	CHO	k)	97-98	k)	100	100	100	—	—	100
-10	3-pyridylmethyl	Me	k)	oil ^{k)}	k)	100	100	55	—	—	15

^{a)} Synthetic method described in the text. ^{b)} Based on **8**, **10** or **13**. ^{c)} *Nilaparvata lugens*. ^{d)} *Laodelphax striatellus*. ^{e)} *Nephotettix cincticeps*.

^{f)} ¹H NMR $\delta_{\text{HMS}}^{\text{ppm}}$: 1.34 (3H, t, $J=7.5$ Hz), 2.82 (3H, s), 3.1-3.6 (2H, m), 4.43 (2H, s), 6.52 (1H, s), 7.32 (1H, dd, $J=8.4$ & 5.4 Hz), 7.58 (1H, dt, $J=8.4$ & 1.5 Hz), 8.4-8.7 (2H, m), 9.3-9.8 (1H, br). ^{g)} ¹H NMR $\delta_{\text{HMS}}^{\text{ppm}}$: 2.81 (3H, s), 3.9-4.2 (2H, m), 4.43 (2H, s), 5.1-5.6 (2H, m), 5.7-6.2 (1H, m), 6.55 (1H, s), 7.35 (1H, dd, $J=8.4$ & 5.1 Hz), 7.60 (1H, dt, $J=8.4$ & 1.5 Hz), 8.4-8.7 (2H, m), 9.4-9.9 (1H, br). ^{h)} Polymerized on standing. ⁱ⁾ ¹H NMR $\delta_{\text{HMS}}^{\text{ppm}}$: 0.94 (3H, t, $J=7.8$ Hz), 1.2-1.9 (4H, m), 2.80 (3H, s), 3.34 (2H, m), 4.42 (2H, s), 6.54 (1H, s), 7.34 (1H, dd, $J=8.4$ & 5.4 Hz), 7.58 (1H, dt, $J=8.4$ & 1.5 Hz), 8.4-8.7 (2H, m), 9.4-9.9 (br). ^{j)} ¹H NMR $\delta_{\text{HMS}}^{\text{ppm}}$: 2.78 (3H, s), 4.36 (2H, s), 4.53 (2H, d, $J=6.0$ Hz), 6.56 (1H, s), 7.1-7.5 (7H, m), 8.3-8.5 (1H, m), 8.57 (1H, dd, $J=5.2$ & 1.5 Hz), 9.7-10.2 (1H, br). ^{k)} See the text. ^{l)} Not tested.

(9c-6, 7) and secondary amino (9c-8, 10) groups resulted in the decrease of the activity. Only one exception was (*N*-formyl-*N*-methyl)-amino (9c-9), which exhibited similar activity against the pests.

The summary: we prepared a lot of acyclic nitroethene compounds bearing a 3-pyridyl-methylamino group and tested the activity against *N. lugens*, *N. cincticeps* and *L. striatellus*. Among them two (9b-1, 2) or three compounds (9c-9) showed 100% mortality against these insects at 40 ppm.

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要 約

3-ピリジルメチルアミノ基を有する非環状ニトロエテン化合物の合成と殺虫活性*

南田 勲, 岩永幸一, 田渕学典
采女英樹, 塩辻寛和, 岡内哲夫

β-炭素上に 3-ピリジルメチルアミノ基を有する非環状ニトロエテン化合物を合成し, その殺虫活性を検討した。1-(3-ピリジルメチル)アミノ-2-ニトロエテンの 1 位炭素にメチルアミノ基またはジメチルアミノ基を導入した化合物はトビイロウンカ, ヒメトビウンカに対する活性は強かったが, ツマグロヨコバイに対する活性は弱かった。またより大きいアルキルアミノ基を導入すると活性は減少した。1 位をメチルアミノ基に固定し, 1-メチルアミノ-1-(3-ピリジルメチル)アミノ-2-ニトロエテンの 3-ピリジルメチル基の結合した窒素原子を次に修飾した。この窒素原子にメチル基あるいはエチル基を導入すると殺虫活性は上昇し, 1-メチルアミノ-1-[*N*-メチル(エチル)-*N*-(3-ピリジルメチル)]アミノ-2-ニトロエテン(9b-1, 2) はトビイロウンカ, ヒメトビウンカだけでなく, ツマグロヨコバイに対しても強い活性を示した。

* 非環状ニトロエテン化合物の研究 (第1報)