J. Pesticide Sci. **18**, 41–48 (1993)

Original Article

Synthesis and Insecticidal Activity of Acyclic Nitroethene Compounds Containing a Heteroarylmethylamino Group*

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(Received April 23, 1992; Accepted July 23, 1992)

Several 1-[*N*-(heteroaromatic-methyl)-*N*-methyl]amino-1-methylamino-2-nitroethenes (**5a**) were prepared, and their insecticidal activities against *Nilaparvata lugens* were examined. Among them 6-chloro-3-pyridyl (**5a-8**), 6-bromo-3-pyridyl (**5a-9**), 6-fluoro-3-pyridyl (**5a-10**) and 2-chloro-5-thiazolyl (**5a-11**) congeners showed 100% mortality against the insect at 0.5 or 0.8 ppm. Modifications of these compounds and the 2-bromo-5-thiazolyl congener by changing the methylamino group to (substituted)amino groups and/or the methyl group attaching to the heteroaromatic-methylamino group to other groups revealed that a lot of compounds were effective against the insect at 0.5 or 0.8 ppm. Compounds that showed 100% mortality at 0.5 or 0.8 ppm, and **5b-1** whose activity at lower concentrations was not determined were chosen for further evaluations. As a result, 1-[*N*-(6-chloro-3-pyridylmethyl)-*N*-ethyl]amino-1-methylamino-2-nitroethene (**5b-8**, TI-304, nitenpyram) was selected as a candidate.

INTRODUCTION

In the preceding paper,[1] nitroethenes doubly substituted with a pyridylmethylamino and an alkylamino or its isosteric substituent at the β-position were synthesized and investigated for insecticidal activity. Among them, 1-methylamino-1-[*N*-methyl-*N*-(3-pyridylmethyl)]amino-2-nitroethene (**1**) and 1-methylamino-1-[*N*-ethyl-*N*-(3-pyridylmethyl)]amino-2-nitroethene (**2**) were chosen for the most potent activity against *Nilaparvata lugens*, *Nephotettix cincticeps* and *Laodelphax striatellus* (Fig. 1).

This paper describes trials and results of optimization of the activity by introduction of a substituent onto the pyridyl of **1** and **2**, and by substitution of the pyridyl group with other heterocyclic residues.

MATERIALS AND METHODS

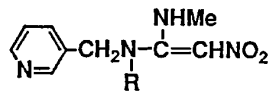
1. *Synthesis of Compounds*

General: See the preceding paper.[1]

All of the compounds in Tables 1, 2 and 3, if not otherwise stated, were prepared through five synthetic routes (Fig. 2). Method A, B and C were the same as reported.[1]

By Method D, 1,1-dichloro-2-nitroethene (**9**)[2,3] was treated with *N*-(heteroaromatic-methyl)-*N*-(substituted)amine to give 1-chloro-1-[*N*-(heteroaromatic-methyl)-*N*-(substituted)]-amino-2-nitroethene (**10**) *in situ*, which was then reacted with an amine successively to give **5**. By Method E, compounds **5** with a primary or

* Studies on Acyclic Nitroethene Compounds (Part 2). For Part 1, see Ref. 1).



1 R=Me
2 R=Et

Fig. 1 1-Methylamino-1-[*N*-methyl(ethyl)-*N*-(3-pyridylmethyl)]amino-2-nitroethene.

secondary amino group, which had been prepared by other methods, were formylated by sodium hydride and formic acetic anhydride.

Compound **5a-7** was prepared by direct substitution of compound **5a-8**.

Compounds **5b-30** and **5c-9** were obtained by reaction of 1-(*N*-methoxy-*N*-methyl)amino-1-methylthio-2-nitroethene with 6-chloro-3-pyridylmethylamine and reaction of 1-(*N*,*N*-dimethyl)amino-1-methylthio-2-nitroethene with 2-chloro-5-thiazolylmethylamine, respectively.

As to the configuration of the double bond of the compounds prepared, Rajappa's report[4] seems to be instructive. He has described: Nitrovinylamines, possessing an NH, seem to prefer the *Z* configuration in non-polar solvents, the stabilizing force being the formation of an intramolecular H-bond with the NO_2. .... Regarding the nitroenamines with no H-atom on the nitrogen, *i.e.* those nitroenamines which do not derive any stabilization by H-bonding, consensus appears to be that they exist in the *E*-configuration. .... This preference for the *E*-configuration is believed to be a consequence of the tendency to minimize steric crowding.

Each compound in Tables 1–3, except some (see footnotes), appears as a single isomer in TLC and ^{1}H NMR. And the configuration of **5b-8** is confirmed as *E* by X-ray analysis (unpublished data). It seems that the *E*-configuration of **5b-8** is attributed to the two factors (H-bonding and steric crowding) mentioned above. We believe compounds, as long as they possess an NH group and a tertiary amino group, exist in the *E*-configuration.

Typical examples of synthetic procedures are as follows.

1.1 Method D

1-[N-(6-Chloro-3-pyridylmethyl)-N-ethyl]-amino-1-pyrrolidino-2-nitroethene (***5b-35***)

In 20 ml of acetonitrile was dissolved 2.0 g of 1,1-dichloro-2-nitroethene,[2,3] followed by addition of 1.8 g of *N*-(6-chloro-3-pyridylmethyl)-*N*-ethylamine.[5] To the mixture was added dropwise 1.4 g of Et_3N under ice-cooling with stirring, followed by addition 0.8 g of pyrrolidine and 1.4 g of Et_3N. The mixture was stirred under ice-cooling for 0.5 hr and at

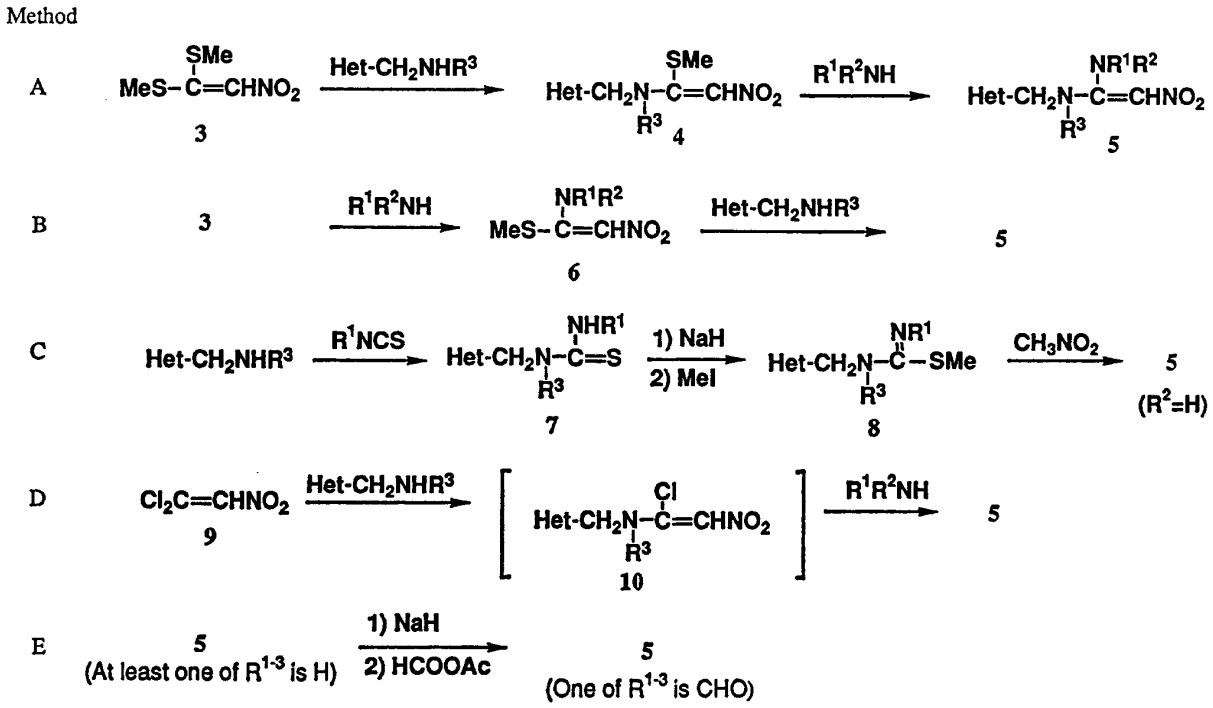


Fig. 2 Syntheses of acyclic nitroethene compounds containing a heteroaromatic-methylamino group.

room temperature for 0.5 hr, and concentrated *in vacuo*. The residue was diluted with 30 ml of cooled water and extracted with AcOEt (50, 30×2 ml). The combined extract was washed with brine, dried over $MgSO_4$ and concentrated. The residue was treated with a small amount of acetone to give 1.2 g of the title, compound as yellow crystals. mp 110–111°C. Anal. Found: C, 54.09; H, 6.17; N, 18.05, Calcd. for $C_{14}H_{19}N_4O_2Cl$: C, 54.11; H, 6.16; N, 18.03%. IR ν_{max}^{Nujol} cm^{-1}: 3100, 1585, 1560, 1535, 1510, 1460, 1365, 1330, 1260. ^1H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 1.19 (3H, t, J=7.2 Hz), 1.8–2.3 (4H, m), 3.18 (2H, q, J=7.1 Hz), 3.1–3.7 (4H, m), 4.42 (2H, s), 6.48 (1H, s), 7.35 (1H, d, J=8.4 Hz), 7.74 (1H, dd, J=8.1 & 2.6 Hz), 8.33 (1H, d, J=2.7 Hz).

1.2 Method E

1-[N-(6-Bromo-3-pyridylmethyl)-N-ethyl]-amino-1-(N-formyl-N-methyl)amino-2-nitroethene (***5b-44***)

In 10 ml of dry THF was suspended 0.1 g of petroleum ether-washed 60% sodium hydride, followed by addition of 0.7 g of 1-[*N*-(6-bromo-3-pyridylmethyl)-*N*-ethyl]amino-1-methylamino-2-nitroethene (**5b-39**). The mixture was stirred at room temperature for 1 hr. Then, 0.6 g of formic acetic anhydride was added under ice-cooling, and the mixture was stirred at the same temperature for 2.5 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×2). 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 MeOH–$CHCl_3$ (1 : 5). The procedure gave 0.5 g of the title compound as yellow crystals. mp 105–108 °C. Anal. Found: C, 41.97; H, 4.37; N, 15.99, Calcd. for $C_{12}H_{15}N_4O_3Br$: C, 42.00; H, 4.41; N, 16.33%. IR ν_{max}^{Nujol} cm^{-1}: 1705. ^1H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 1.13 (3H, t, J=7.2 Hz), 3.00 (3H, s), 3.1–3.7 (2H, m), 4.3–4.9 (2H, m), 6.97 (1H, s), 7.5–7.9 (2H, m), 8.21 (1H, s), 8.38 (1H, br s).

1.3 1-[N-(6-Methoxy-3-pyridylmethyl)-N-methyl]amino-1-methylamino-2-nitroethene (***5a-7***)

In 20 ml of DMF was dissolved 0.67 g of 1-[*N*-(6-chloro-3-pyridylmethyl)-*N*-methyl]-amino-1-methylamino-2-nitroethene (**5a-8**), followed by addition of 1.00 g of a 28% solution of sodium methoxide in MeOH. The mixture was stirred at 100°C for 5.5 hr. The MeOH and DMF were distilled off, and the residue was diluted with aqueous NaCl and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$, and the CH_2Cl_2 was distilled off. The residue was subjected to silica gel (230 g) column chromatography using MeOH–$CHCl_3$ (1 : 5) as an eluent to give 0.22 g of brown oil. A small amount of Et_2O was added to the oil, and the mixture was cooled and triturated. The resulting crystals were diluted with Et_2O, filtered and dried to give 0.128 g of the title compound as white-pale brown crystals. mp 77–78°C. Anal. Found: C, 52.02; H, 6.36; N, 22.07, Calcd. for $C_{11}H_{16}N_4O_3$: C, 52.37; H, 6.39; N, 22.21%. IR ν_{max}^{Nujol} cm^{-1}: 1605, 1455, 1310, 1250, 1025. ^1H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.75 (3H, s), 3.07 (3H, d, J=5 Hz), 3.93 (3H, s), 4.30 (2H, s), 6.53 (1H, s), 6.78 (1H, d, J=8 Hz), 7.45 (1H, dd, J=8 & 2 Hz), 8.05 (1H, d, J=2 Hz), 9.80 (1H, br).

1.4 1,1-Bis[(6-chloro-3-pyridylmethyl)amino]-2-nitroethene (***5b-30***)

A mixture of 7.0 g of 1,1-bis(methylthio)-2-nitroethene,[6] 4.5 g of *N*, *O*-dimethylhydroxylamine hydrochloride and 80 ml of EtOH was refluxed, and 6.4 ml of Et_3N was added dropwise over 1 hr. After completion of the dropwise addition, the mixture was further refluxed for 2 hr. The reaction mixture was then concentrated, and the resulting crystals were filtered off. The filtrate was concentrated, and the residue was subjected to silica gel column chromatography using EtOH–$CHCl_3$ (1 : 30) as the eluent. The procedure gave 1.0 g of 1-(*N*-methoxy-*N*-methyl)amino-1-methylthio-2-nitroethene as a yellow oil. ^1H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 2.43 (3H, s), 3.26 (3H, s), 3.68 (3H, s), 7.16 (1H, s).

A mixture of 0.8 g of 1-(*N*-methoxy-*N*-methyl)amino-1-methylthio-2-nitroethene, 0.7 g of 6-chloro-3-pyridylmethylamine and 30 ml of EtOH was refluxed for 4 hr. The resulting crystals were collected by filtration and dried to give 150 mg of the title compound as crystals. mp 238–240°C (dec.). Anal. Found: C, 47.32; H, 3.92; N, 19.65, Calcd. for $C_{14}H_{13}N_5O_2Cl_2$: C, 47.46; H, 3.70; N, 19.77%. IR ν_{max}^{Nujol}

cm^{-1}: 3240, 1620, 1575, 1460, 1395, 1220. ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 4.53 (4H, d, J=5.7 Hz), 6.51 (1H, s), 7.50 (2H, d, J=8.7 Hz), 7.76 (2H, dd, J=8.7 & 2.4 Hz), 8.37 (2H, d, J=2.4 Hz), 9.8–10.8 (2H, br).

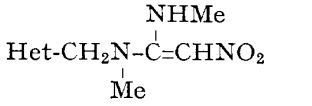
1.5 1,1-Bis[(2-chloro-5-thiazolylmethyl)amino]-2-nitroethene (**5c-9**)

A mixture of 0.60 g of 1-dimethylamino-1-methylthio-2-nitroethene, 0.55 g of 2-chloro-5-thiazolylmethylamine and 30 ml of EtOH was refluxed for 1.5 hr. After cooling, the resulting crystals of 1-*N*-(2-chloro-5-thiazolylmethyl)-amino-1-methylthio-2-nitroethene (0.20 g) were filtered off, and the filtrate was concentrated and subjected to silica gel column chromatography using EtOH–$CHCl_3$ (1 : 10) as the eluent. The procedure gave 0.034 g of the title compound along with 0.07 g of 1-dimethylamino-1-[*N*-(2-chloro-5-thiazolylmethyl)]-amino-2-nitroethene (**5c-4**). mp 211°C (dec.). Anal. Found: C, 32.58; H, 2.56; N, 19.27, Calcd. for $C_{10}H_9N_5O_2S_2Cl_2$: C, 32.79; H, 2.49; N, 19.12%. IR ν_{max}^{Nujol} cm^{-1}: 3120, 1610, 1210, 1040. ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 4.5–4.8 (4H, m), 6.63 (1H, s), 7.63 (2H, s).

2. Biological Tests

Each test compound was sprayed at the indicated concentrations 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* were released in each tube, which was then capped with an aluminum cap. The test tubes were main

Table 1 Insecticidal activity against *Nilaparvata lugens* of 1-[*N*-(heteroaromatic-methyl)-*N*-methyl]amino-1-methylamino-2-nitroethenes.

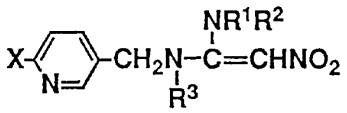


5a

Compd. No.	Het	Method[a]	mp (°C)	Yield[b] (%)	Mortality (%)				
					500	100	4	0.8	0.16
					200 (ppm)	40 (ppm)	2.5 (ppm)	0.5 (ppm)	0.1 (ppm)
5a-1	3-pyridyl	C	86–87	28	100 100	100	100	80	0
-2	4-pyridyl	C	145–146	66	100 100	100	60	30	10
-3	pyradinyl	C	132–133	65	100 100	85	10	0	0
-4	4-thiazolyl	C	155–156	54	100	5	0	10	
-5	5-bromo-3-pyridyl	C	116–117	59	100 60	15	0	0	
-6	6-methyl-3-pyridyl	C	102–103	66	100 100	100	100	80	0
-7	6-methoxy-3-pyridyl	[c]	77–78	[c]	100 100	75			
-8	6-chloro-3-pyridyl	C	103–104	20	100 100	100	100	100	65
-9	6-bromo-3-pyridyl	C	130–131	51	100		100	100	90
-10	6-fluoro-3-pyridyl	C	100–100.5	27	100		100	100	0
-11	2-chloro-5-thiazolyl	C	131–133	47	100		100	100	10
-12	4-chlorophenyl	C	98–99	70	100 60	10			

[a] Synthetic method described in the text. [b] Based on **8**. [c] See the text.

Table 2 Insecticidal activity against *Nilaparvata lugens* of 1-[*N*-(6-halogeno-3-pyridylmethyl)-*N*-(substituted)]amino-1-(substituted)amino-2-nitroethenes.



5b

Compd. No.	X	R^1	R^2	R^3	Method[a]	mp (°C)	Yield[b] (%)	Mortality (%) 500 ppm	200 ppm	100 ppm	40 ppm	4 ppm	2.5 ppm	0.8 ppm	0.5 ppm	0.16 ppm	0.1 ppm
5a-8	Cl	Me	H	Me	C	103–104	20	100	100		100		100	100		65	
-9	Br	Me	H	Me	C	130–131	51	100			100		100	100		90	
5b-1	Cl	H	H	Me	A	206–207	88	100	100		100						
-2	Cl	H	H	Et	A	159–161	30	100	100		100		100	80		20	
-3	Cl	H	H	*n*-Pr	A	185–186 (dec.)	55	100	90		15		40	0		0	
-4	Cl	H	H	*i*-Pr	A	Powder[c]	36	100	10		0		10	0		0	
-5	Cl	H	H	*c*-Pr	D	128–129	68			100		100		100			
-6	Cl	H	H	FCH_2CH_2	D	152–153	38			100		100		90			
-7	Cl	Me	H	H	A	181–183	54	100	100		100			100		80	
-8	Cl	Me	H	Et	C	83–84	69	100	100		100			100			
-9	Cl	Me	H	FCH_2CH_2	D	78–79	12			100		100		0			
-10	Cl	Me	H	CF_3CH_2	C	110–111	11	100			100		100	50			
-11	Cl	Me	H	*n*-Pr	C	102–103	62	100	100		100		100	90		20	
-12	Cl	Me	H	*i*-Pr	C	119–120	34	100	100		80		40	10		10	
-13	Cl	Me	H	*c*-Pr	D	115–116	54			100		100		100			
-14	Cl	Me	Me	H	B	124–125	52	100	100		100		100	100		90	
-15	Cl	Me	Me	Me	B	110–112	14	100	100		100		100	100		90	
-16	Cl	Me	Me	CHO	E	105–106	32	100			100		100	80			
-17	Cl	Me	Me	Et	D	Oil[d]	53			100	100		100	100			
-18	Cl	Me	Me	FCH_2CH_2	D	90–91	34			100		100		70			
-19	Cl	Me	Me	*c*-Pr	D	73–75	62			100		100		100			
-20	Cl	Et	H	Me	C	132–133	80	100	100		100		100	100		0	
-21	Cl	Et	H	Et	D	123–125	55			100		100		70			
-22[e]	Cl	Me	CHO	H	E	80–85	22	100			100		100	70			
-23	Cl	Me	CHO	Me	E	Syrup[f]	45	100			100		100	60			
-24	Cl	Me	CHO	Et	E	Syrup[g]	44	100			100		100	90			
-25	Cl	Me	Et	H	B	87–88	45	100	100		100		90				
-26	Cl	Me	Et	Et	D	Oil[h]	79			100		100					
-27	Cl	*c*-Pr	H	Et	D	74–75	50			100		100		20			
-28	Cl	H_2N	H	H	A	188–190 (dec.)	93	100	25		0						
-29	Cl	Me_2N	H	H	B	170–172	26	100	85		15						

Table 2 (Continued)

Compd. No.	X	R^1	R^2	R^3	Method[a]	mp (°C)	Yield[b] (%)	Mortality (%) 500 / 200 (ppm)	100 / 40 (ppm)	4 / 2.5 (ppm)	0.8 / 0.5 (ppm)	0.16 / 0.1 (ppm)
-30	Cl	[i]	H	H	[j]	238–240	[j]	100				
								15	0			
-31[k]	Cl	MeO	H	Et	D	Oil[l]	76		100	0	0	
-32	Cl	MeO	Me	Et	D	Oil[m]	44		100	90	40	
-33	Cl	*i*-Pr	H	Et	D	126–127.5	41		100	100	0	
-34	Cl	Et	Et	Et	D	105–106	55		100	90	10	
-35	Cl	$-(CH_2)_4-$		Et	D	110–111	37		100	40	10	
-36	Br	H	H	Me	A	206–207	65	100				
										100	100	50
-37	Br	Me	H	H	C	184–186 (dec.)	33	100				
										100	90	30
-38[n]	Br	Me	H	CHO	E	Syrup[o]	14	100				
										100	100	60
-39	Br	Me	H	Et	C	79–80	55	100				
										100	90	10
-40	Br	Me	Me	H	C	158–159	34	100				
										100	100	20
-41	Br	Me	Me	CHO	E	96–97	40	100				
										100	100	90
-42[p]	Br	Me	CHO	H	E	115–127[q]	11	100				
										100	100	80
-43	Br	Me	CHO	Me	E	Syrup[r]	76	100				
										100	100	80
-44	Br	Me	CHO	Et	E	105–108	66	100				
										100	100	100
-45	F	Me	H	Me	C	100–100.5	27	100				
										100	100	0
-46	F	Me	H	Et	C	Oil[s]	34	100				
										100	100	20

[a] Synthetic method described in the text. [b] Based on **4**, **6**, **8**, Het-CH_2NHR^3 or **5** in Method A–E. [c] ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 1.13 (6H, d, J=7 Hz), 4.30 (1H, sept, J=7 Hz), 4.62 (2H, s), 6.50 (1H, s), 7.49 (1H, d, J=8 Hz), 7.69 (1H, dd, J=8 & 2 Hz), 8.30 (1H, d, J=2 Hz), 9.04 (2H, br). [d] ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 1.18 (3H, t, J=7 Hz), 2.96 (6H, s), 3.16 (2H, q, J=7.3 Hz), 4.40 (2H, s), 6.39 (1H, s), 7.36 (1H, d, J=8.7 Hz), 7.66 (1H, dd, J=8.1 & 2.3 Hz), 8.31 (1H, d, J=2.4 Hz). [e] Contained 30% of *N'*-CHO isomer by NMR integration. (Main isomer) ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 3.50 (3H, s), 4.53 (2H, d, J=6 Hz), 6.76 (1H, s), 7.49 (1H, d, J=8 Hz), 7.86 (1H, dd, J=8 & 2 Hz), 8.30 (1H, s), 8.42 (1H, d, J=2 Hz), 9.45 (1H, br). (Minor isomer) ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 2.95 (3H, d, J=5 Hz), 4.83 (2H, s), 6.66 (1H, s), 7.46 (1H, d, J=8 Hz), 7.86 (1H, dd, J=8 & 2 Hz), 8.30 (1H, s), 8.42 (1H, d, J=2 Hz), 9.45 (1H, br). [f] ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 1.13 (3H, t, J=7 Hz), 3.00 (3H, s), 3.10–3.53 (2H, m), 4.60 (2H, br), 6.96 (1H, s), 7.48 (1H, d, J=8 Hz), 7.82 (1H, dd, J=8 & 2 Hz), 8.20 (1H, s), 8.39 (1H, d, J=2 Hz). [g] ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 1.13 (3H, t, J=7 Hz), 3.00 (3H, s), 3.10–3.53 (2H, m), 4.60 (2H, br), 6.96 (1H, s), 7.48 (1H, d, J=8 Hz), 7.82 (1H, dd, J=8 & 2 Hz), 8.20 (1H, s), 8.39 (1H, d, J=2 Hz). [h] ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 1.18 (6H, t, J=7.2 Hz), 2.90 (3H, s), 3.14 (2H, q, J=6.7 Hz), 3.30 (2H, q, J=6.9 Hz), 4.39 (2H, s), 6.41 (1H, s), 7.35 (1H, d, J=7.8 Hz), 7.67 (1H, dd, J=8.1 & 2.4 Hz), 8.30 (1H, d, J=2.4 Hz). [i] 6-chloro-3-pyridylmethyl. [j] See the text. [k] Existed in N^1-(6-chloro-3-pyridylmethyl)-N^1-ethyl-N^2-methoxy-2-nitroacetamidine form. [l] ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 1.12 (3H, t, J=7.4 Hz), 3.23 (2H, q, J=7 Hz), 3.70 (3H, s), 4.39 (2H, s), 5.34 (2H, s), 7.30 (1H, d, J=8.1 Hz), 7.66 (1H, dd, J=8.4 & 2.1 Hz), 8.32 (1H, d, J=2.4 Hz). [m] ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 1.21 (3H, t, J=7.4 Hz), 3.14 (3H, s), 3.29 (2H, q, J=7.1 Hz), 3.63 (3H, s), 4.49 (2H, s), 6.50 (1H, s), 7.35 (1H, d, J=8.1 Hz), 7.68 (1H, dd, J=8.1 & 2.6 Hz), 8.31 (1H, d, J=2.4 Hz). [n] Contained 40% of *N'*-CHO isomer by NMR integration. [o] (Main isomer) ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 3.01 (3H, d, J=5 Hz), 4.73 (2H, s), 6.36 (1H, s), 7.53 (2H, br s), 8.34 (2H, br s), 9.35 (1H, br). [p] Contained 10% of *N'*-CHO isomer by NMR integration. [q] (Main isomer) ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 3.13 (3H, s), 4.48 (2H, d, J=6 Hz), 6.57 (1H, s), 7.53 (2H, m), 8.33 (2H, m), 9.46 (1H, br). [r] ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 2.93 (3H, s), 3.02 (3H, s), 4.3–4.9 (2H, m), 6.87 (1H, s), 7.68 (2H, br s), 8.23 (1H, s), 8.3–8.5 (1H, m). [s] ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 1.19 (3H, t), 3.08 (3H, d), 3.16 (2H, q), 4.37 (2H, s), 6.54 (1H, s), 6.98 (1H, dd, J=8.4 & 2.7 Hz), 7.80 (1H, ddd, J=8.4, 2.4 & 8.4 Hz), 8.15 (1H, d, J=2.4 Hz).

tained in an incubator at 25°C, and dead insects were counted 7 days after release. The % mortality was calculated using the following formula.

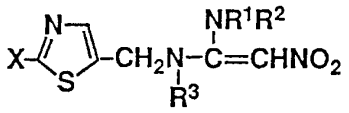
$$\text{Mortality}(\%) = (\text{Number of dead insects} / \text{Number of insects released}) \times 100$$

RESULTS AND DISCUSSION

Table 1 shows insecticidal activity of some 1-[*N*-(heteroaromatic-methyl)-*N*-methyl]-amino-1-methylamino-2-nitroethenes (**5a**) against *Nilaparvata lugens*. Compounds bearing 3-pyridyl (**5a-1**), 4-pyridyl (**5a-2**), pyradinyl (**5a-3**), 4-thiazolyl (**5a-4**), 5-bromo-3-pyridyl (**5a-5**), 6-methyl-3-pyridyl (**5a-6**), 6-methoxy-3-pyridyl (**5a-7**) and 4-chlorophenyl (**5a-12**) showed the activity, while **5a-2–5**, **7**, **12** were not effective at 0.5 ppm. Compounds **5a-1** and **5a-6** were moderately effective at 0.5 ppm. On the other hand, compounds possessing 6-halogeno-3-pyridyl (**5a-8–10**) and 2-chloro-5-thiazolyl (**5a-11**) showed potent activity, being effective at 0.5 or 0.8 ppm.

Encouraged by the above results, we tried to optimize the activity focusing on heteroaromatic 6-halogeno-3-pyridyl or 2-chloro (or bromo)-5-thiazolyl (Tables 2 and 3).

Table 3 Insecticidal activity against *Nilaparvata lugens* of 1-[*N*-(2-halogeno-5-thiazolylmethyl)-*N*-(substituted)]amino-1-(substituted)amino-2-nitroethenes.



5c

Compd. No.	X	R^1	R^2	R^3	Method[a]	mp (°C)	Yield[b] (%)	Mortality (%) 500 ppm	200 ppm	100 ppm	40 ppm	4 ppm	2.5 ppm	0.8 ppm	0.5 ppm	0.16 ppm	0.1 ppm
5a-11	Cl	Me	H	Me	C	131–133	47	100		100		100		100		10	
5c-1	Cl	Me	H	H	A	181 (dec.)	68	100		100		100		100		60	
-2	Cl	Me	H	CHO	E	125–126 (dec.)	1.8			100		100		100		100	
-3	Cl	Me	H	Et	C	110–112	16	100		100		100		100		80	
-4	Cl	Me	Me	H	B	101–102	7.2	100		100		100		100		100	
-5	Cl	Me	Me	CHO	E	139–142	53	100		100		100		100		100	
-6[c]	Cl	Me	CHO	H	E	Syrup[d]	14	100		100		100		100		70	
-7	Cl	Me	CHO	Me	E	Syrup[e]	42	100		100		100		100		40	
-8	Cl	Me	CHO	Et	E	99–100	31	100		100		100		100		70	
-9	Cl	[f]	H	H	[g]	211 (dec.)	[g]	100		100		80		10			
-10	Br	Me	H	H	A	167–169 (dec.)	83	100		100		100		100		100	
-11	Br	Me	Me	H	B	125 (dec.)	9	100		100		100		100		100	

[a] Synthetic method described in the text. [b] Based on **4**, **6**, **8** or **5** in Method A, B, C or E. [c] Contained 30% of *N'*-CHO isomer by NMR integration. [d] (Main isomer) ^{1}H NMR $\delta_{TMS}^{CDCl_3}$ ppm: 3.16 (3H, s), 4.63 (2H, d, J=5.7 Hz), 6.57 (1H, s), 7.49 (1H, s), 8.35 (1H, s), 9.1–9.6 (1H, br). [e] ^{1}H NMR $\delta_{TMS}^{DMSO\text{-}d_6}$ ppm: 2.92 (3H, s), 2.99 (3H, s), 4.74 (2H, br s), 6.90 (1H, s), 7.71 (1H, s), 8.19 (1H, s). [f] 2-Chloro-5-thiazolylmethyl. [g] See the text.

When heteroaromatic was 6-chloro-3-pyridyl, and R^1 and R^2 were hydrogen atoms, only one compound (**5b-5**) showed 100% mortality at 0.8 ppm, although ineffective concentrations were not determined for **5b-1**, and the compounds other than **5b-5** were effective at higher concentrations. When heteroaromatic was 6-chloro-3-pyridyl, and R^1R^2N was methylamino, dimethylamino or *N*-formyl-*N*-methylamino, a lot of compounds showed 100% mortality at 0.5 or 0.8 ppm. One compound (**5b-20**), whose R^1R^2N was ethylamino, showed 100% mortality at 0.5 ppm, and one compound (**5b-26**), whose R^1R^2N was *N*-ethyl-*N*-methylamino, showed 100% mortality at 4 ppm, but these substituents seemed to be not as good as methylamino, dimethylamino or *N*-formyl-*N*-methylamino. When R^1R^2N was cyclopropylamino, hydrazino, dimethylhydrazino, (6-chloro-3-pyridylmethyl)amino, methoxyamino, *N*-methoxy-*N*-methylamino isopropylamino, diethylamino or pyrrolidino, compounds did not show 100% mortality at 0.8 ppm, although they were effective at higher concentrations.

It seemed that these substituents, *e.g.*, methylamino, dimethylamino and *N*-formyl-*N*-methylamino were superior to others even when heteroaromatic was 6-bromo-3-pyridyl, 6-fluoro-3-pyridyl, 2-chloro-5-thiazolyl or 2-bromo-5-thiazolyl.

As to the R^3, it seemed to the authors that hydrogen, methyl, ethyl, formyl and cyclopropyl are favorable.

All the compounds that showed 100% mortality at 0.5 or 0.8 ppm, and **5b-1** whose activity at lower concentrations were not determined were further evaluated for acute activity, residual activity, insecticidal spectrum against other insects, paddy-water application, seedling-box application, foliar application, soil application, field test, *etc.* As a result, 1-[*N*-(6-chloro-3-pyridylmethyl)-*N*-ethyl]amino-1-methylamino-2-nitroethene (**5b-8**, TI-304, nitenpyram*) was selected as a candidate.

Several compounds including **5a-8** and **5b-8** were superior to cyclic 1-(6-chloro-3-pyridylmethyl)-2-(nitromethylene)imidazolidine, especially in residual activity (unpublished data).

* ISO name under application.

ACKNOWLEDGMENTS

The authors wish to thank Dr. Atsuo Akayama for his assistance in the biological test, and helpful and stimulating discussions and suggestions.

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要　　約

芳香族複素環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*

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符阪隆文，石塚　仁，岡内哲夫

1-メチルアミノ-1-[*N*-メチル-*N*-(3-ピリジルメチル)]アミノ-2-ニトロエテンがトビイロウンカ，ツマグロヨコバイ，ヒメトビウンカに対して強い活性を示すことを前報で報告した．本報では3-ピリジル基を他の芳香族複素環に変換し，トビイロウンカに対する活性を検討した．その結果6-クロロ-3-ピリジル，6-ブロモ-3-ピリジル，6-フルオロ-3-ピリジル，2-クロロ-5-チアゾリル基を有する化合物は0.5または0.8 ppmで100%の死虫率を示したので，芳香族複素環を6-ハロゲノ-3-ピリジル，2-クロロ(またはブロモ)-5-チアゾリル基に固定して構造-活性相関を検討した．アミノ基としてはメチルアミノ，ジメチルアミノ，*N*-ホルミル-*N*-メチルアミノ基が，芳香族複素環メチル基が結合した窒素原子の置換基としては水素，メチル，エチル，ホルミル，シクロプロピル基が好ましいことが判明し，0.5または0.8 ppmで100%の死虫率を示す化合物および低濃度での試験を実施しなかった化合物**5b-1**はさらに評価を行なった．その結果1-[*N*-(6-クロロ-3-ピリジルメチル)-*N*-エチル]アミノ-1-メチルアミノ-2-ニトロエテン(**5b-8**, TI-304，ニテンピラム)が候補化合物として選ばれた．

* 非環状ニトロエテン化合物の研究（第2報）