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ORIGINAL PAPER

Design, synthesis, and bioactivity of cyanonitrovinyl neonicotinoids as potential insecticides

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Abstract A series of cyanonitrovinyl neonicotinoids were designed and synthesized via five steps in about 35% overall yields. All compounds were structurally characterized by ^{1}H nuclear magnetic resonance (NMR), ^{13}C NMR, infrared (IR), and high-resolution mass spectrometry (HRMS), and single-crystal X-ray diffraction analysis of 2-[1-[(6-chloropyridin-3-yl)methyl]-2-imidazolidinylidene]-2-nitroacetonitrile revealed that the double bond is (*E*)-configured. The preliminary agriculture bioassay indicated that one compound exhibited moderate insecticidal activity against pea aphid.

Keywords Neonicotinoids · Insecticides · (*E*)-configuration · Nitrovinyl compound · X-ray analysis

Introduction

Neonicotinoids, acting on insect nicotinic acetylcholine receptor (nAChR) [1, 2], are the major class of insecticides used throughout the world for crop protection. The first neonicotinoid, imidacloprid, was introduced to the market in 1991 (Fig. 1) [3], and in recent years monitoring results have revealed signs of resistance to it in some regions [4, 5]. One effective solution to this problem is to find novel neonicotinoids with higher insecticidal activity and higher nAChR binding affinity. Compared with imidacloprid, the nitrovinyl neonicotinoid 6-Cl-1-(pyridin-3-yl-methyl)-2-nitromethyleneimidazolidine (PMNI) has similar insecticidal activity and higher binding affinity [6], but 6-Cl-PMNI has never been commercialized because of its photolability [7].

Strong electron-withdrawing groups, such as nitro or cyano groups, play a crucial role in binding of neonicotinoids to nAChR [8–10], and high affinity confers them with high activity [11]. Kagabu et al. [12] reported that compound **2** with two cyano groups had higher activity than compound **1** with one cyano group. Therefore, it could be presumed that compound **3a** with nitro and cyano groups would have higher binding affinity and activity than 6-Cl-PMNI, in which there is only one electron-withdrawing group. Qian et al. [13, 14] reported that photostability was improved if the hydrogen atom of $=CHNO_2$ in 6-Cl-PMNI was replaced by another group. It is presumed that **3a** would have higher photostability than 6-Cl-PMNI. In addition, replacement of the chloropyridine ring by different heterocycles (Het) could adjust its lipophilicity (Scheme 1). Herein, we report the synthesis and bioactivity of the cyanonitrovinyl neonicotinoids **3**.

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Results and discussion

Synthesis of arylmethyl cyanonitrovinyl imidazolines ***3***

Starting from ethylenediamine, compounds **6** were synthesized in 56% yield according to the procedure reported previously [15]. Reaction of **6** with benzoyl isothiocyanate proceeded readily at room temperature to give **7** in 85% yield, and further oxidation of **7** with bromine gave **8** in

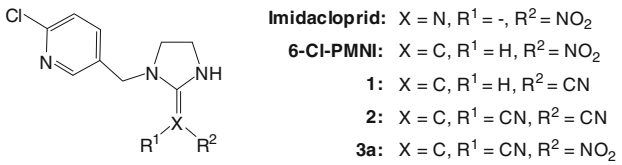


Fig. 1 Structure of neonicotinoids

94% yield. Compound **8** was subjected to fragmentation reaction, initiated by base and culminating in extrusion of sulfur with concomitant formation of **3** in 80% yield [16] (Scheme 1). The overall yield of the five steps of 36% based on ethylenediamine was similar to in previous reports [15, 16].

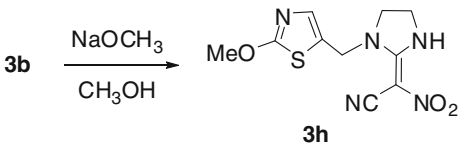
The synthesis of **3h** was different from **3a**–**3g** (Scheme 2). When the amount of sodium methoxide was two equivalents of **8b**, the final product was **3h**. When the amount of sodium methoxide was equivalent to **8b**, the final product was **3b**. This indicated that the formation of **3h** by substitution of chloride with methoxy group proceeded after the formation of **3b**.

Confirmation of configuration

The C=C double bond in compound **3** will lead to geometrical isomerism. To confirm its configuration, single-crystal X-ray diffraction analysis of **3a** was performed, which showed that **3a** is the (*E*)-diastereomer (Fig. 2).

Biological activity

Insecticidal activity of compounds **3** against pea aphid was tested. Only **3a** exhibited moderate activity, with 100% mortality at 500 ppm (Table 1), indicating that the chloropyridine is indispensable. Compared with 6-Cl-PMNI, compound **3a** had lower insecticidal activity. One possible



Scheme 2

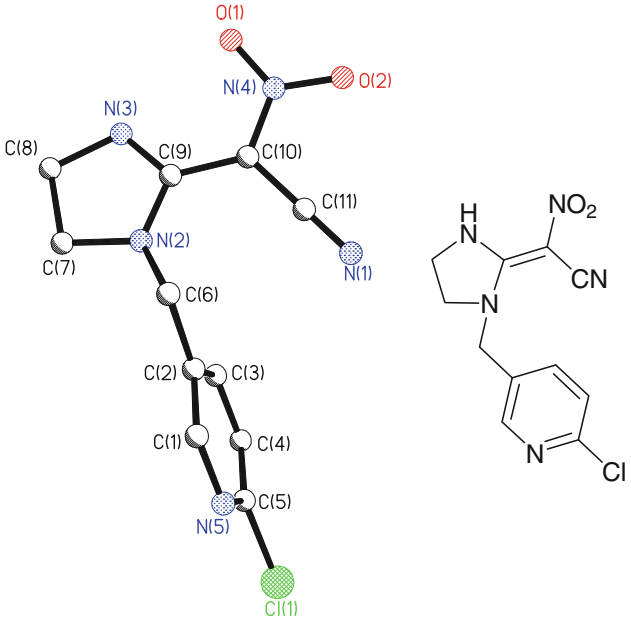
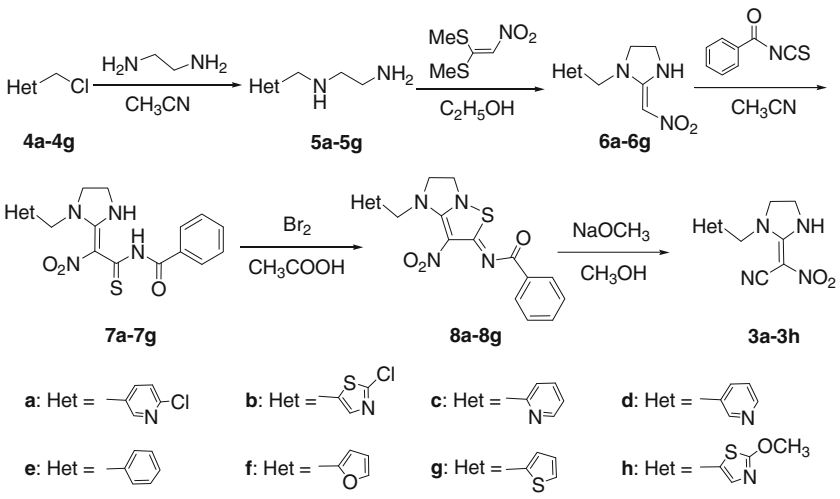


Fig. 2 X-ray single-crystal structure of **3a**

Table 1 Insecticidal activity of **3a** at different concentrations against pea aphid

Compound	Mortality (%)			
	500 ppm	150 ppm	30 ppm	5 ppm
3a	100	89.4	63.4	0
6-Cl-PMNI	100	100	100	81.0

Scheme 1



reason was that, in comparison with 6-Cl-PMNI, **3a** had lower lipophilicity because of the introduction of a cyano group instead of hydrogen. The low lipophilicity of **3a** made it difficult for it to diffuse through the insect's lipophilic cuticle to the site of action [17]. Additionally, in the single-crystal structure of **3a**, torsion angles of 6.5° between amidine and nitro group and 14.8° between amidine and cyano group were found. In 6-Cl-PMNI, the torsion angle between amidine and nitro group is about 0.6°. Coplanarity between amidine and nitro group was considered to be an essential feature for high affinity. The lack of coplanarity in compound **3a** could also be associated with the lower activity of **3a** [8, 11].

In conclusion, we have designed and synthesized a series of novel cyanonitrovinyl neonicotinoids with nitro in (*E*)-configuration. Bioactivity results showed that **3a** exhibited moderate insecticidal activity against pea aphid. A possible explanation for the decrease in its insecticidal activity compared with 6-Cl-PMNI is the effect of its lower lipophilicity. Further work is in progress to improve its lipophilicity to design more active neonicotinoid insecticides.

Experimental

Melting points were obtained with an X-6 micro-melting point apparatus and are reported corrected. Infrared (IR) spectra were recorded on a Nicolet 20DXB Fourier-transform (FT)-IR spectrometer using potassium bromide pellets or films. ^{1}H NMR spectra were obtained on a Varian INOVA 400-MHz NMR spectrometer with dimethyl sulfoxide (DMSO)-d_6 as solvent and tetramethylsilane (TMS) as internal standard. High-resolution mass spectra (HRMS) were obtained on HPLC-Q-Tof MS (Micro) spectrometer. X-ray single-crystal diffraction experiments were carried out on a Bruker Smart APEXII diffractometer at 25 °C. All solvents were of analytic grade. All chemicals and reagents were purchased from commercial suppliers. Nitrovinyl imidazolidines **6** were synthesized according to the procedure reported previously [15].

General synthesis procedure for 7

Benzoyl chloride (0.43 g, 3 mmol) in 5 cm^3 acetonitrile was added dropwise to freshly prepared solution of 0.24 g ammonium thiocyanate (3.1 mmol) in 10 cm^3 acetonitrile, which was refluxed for 30 min and cooled to room temperature, and the solid was filtered off. The filtrate was added dropwise to solution of 0.76 g **6a** (3 mmol) in 20 cm^3 acetonitrile and stirred at room temperature for 4 h. The suspension was filtered to give 1.09 g **7a** (85% yield). Compounds **7b**–**7g** were prepared similarly.

(Z)-N-[2-[1-[(6-Chloropyridin-3-yl)methyl]-2-imidazolidinylidene]-2-nitrothioacetyl]benzamide (**7a**, $C_{18}H_{16}N_5O_3SCl$)
Yield 85%; red powder; m.p.: 140.1–142.0 °C; IR (KBr): $\bar{\nu}$ = 3,432, 1,591, 1,579, 1,141 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.02 (s, 1H), 10.35 (s, 1H), 8.42 (s, 1H), 7.91 (d, 5H, J = 7.6 Hz), 7.84 (dd, 1H, J = 8.4 Hz, J = 2.4 Hz), 7.69–7.56 (m, 4H), 4.58 (s, 2H), 3.91–3.81 (m, 4H) ppm; HRMS (ESI): calculated for $C_{18}H_{16}N_5O_3NaSCl$ [M + Na$^+$] 440.0560, found 440.0580.

(Z)-N-[2-[1-[(2-Chlorothiazol-5-yl)methyl]-2-imidazolidinylidene]-2-nitrothioacetyl]benzamide (**7b**, $C_{16}H_{14}N_5O_3S_2Cl$)
Yield 88%; red powder; m.p.: 125.4–126.9 °C; IR (KBr): $\bar{\nu}$ = 3,438, 1,586, 1,572, 1,139 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.00 (s, 1H), 10.38 (s, 1H), 7.92 (d, 2H, J = 7.6 Hz), 7.69–7.59 (m, 4H), 4.79 (s, 2H), 3.95–3.83 (m, 4H) ppm; HRMS (ESI): calculated for $C_{16}H_{14}N_5O_3NaS_2Cl$ [M + Na$^+$] 446.0124, found 446.0123.

(Z)-N-[2-Nitro-2-[1-(2-pyridinylmethyl)-2-imidazolidinylidene]thioacetyl]benzamide (**7c**, $C_{18}H_{17}N_5O_3S$)
Yield 83%; red powder; m.p.: 131.8–133.1 °C; IR (KBr): $\bar{\nu}$ = 3,431, 1,587, 1,567, 1,139 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.00 (s, 1H), 10.45 (s, 1H), 8.71 (d, 1H, J = 4.4 Hz), 8.28–8.0 (m, 3H), 7.95–7.62 (m, 5H), 4.70 (s, 2H), 3.94–3.88 (m, 4H) ppm; HRMS (ESI): calculated for $C_{18}H_{17}N_5O_3NaS$ [M + Na$^+$] 406.0950, found 406.0946.

(Z)-N-[2-Nitro-2-[1-(3-pyridinylmethyl)-2-imidazolidinylidene]thioacetyl]benzamide (**7d**, $C_{18}H_{17}N_5O_3S$)
Yield 87%; red powder; m.p.: 136.1–137.4 °C; IR (KBr): $\bar{\nu}$ = 3,441, 1,584, 1,574, 1,134 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.01 (s, 1H), 10.40 (s, 1H), 8.77 (s, 2H), 8.24 (d, 1H, J = 4.0 Hz), 7.90 (d, 2H, J = 7.6 Hz), 7.83 (t, 1H, J = 7.6 Hz), 7.68 (t, 1H, J = 7.2 Hz), 7.60 (d, 2H, J = 7.2 Hz), 4.70 (s, 2H), 3.90–3.85 (m, 4H) ppm; HRMS (ESI): calculated for $C_{18}H_{17}N_5O_3NaS$ [M + Na$^+$] 406.0950, found 406.0955.

(Z)-N-[2-Nitro-2-[1-(phenylmethyl)-2-imidazolidinylidene]thioacetyl]benzamide (**7e**, $C_{19}H_{18}N_4O_3S$)
Yield 85%; red powder; m.p.: 157.1–158.8 °C; IR (KBr): $\bar{\nu}$ = 3,437, 1,589, 1,570, 1,128 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.06 (s, 1H), 10.22 (s, 1H), 7.91 (d, 2H, J = 7.2 Hz), 7.67 (t, 1H, J = 7.6 Hz), 7.59 (t, 2H, J = 7.6 Hz), 7.39–7.32 (m, 5H), 4.49 (s, 2H), 3.92–3.74 (m, 4H) ppm; HRMS (ESI): calculated for $C_{19}H_{18}N_4O_3NaS$ [M + Na$^+$] 405.0997, found 405.0997.

(Z)-N-[2-[1-(2-Furanylmethyl)-2-imidazolidinylidene]-2-nitrothioacetyl]benzamide (**7f**, $C_{17}H_{16}N_4O_4S$)
Yield 86%; red powder; m.p.: 128.3–129.9 °C; IR (KBr): $\bar{\nu}$ = 3,434, 1,589, 1,577, 1,137 cm^{-1}; ^{1}H NMR (400 MHz,

DMSO-d_6): δ = 14.05 (s, 1H), 10.26 (s, 1H), 7.92 (d, 2H, J = 7.6 Hz), 7.66 (d, 2H, J = 7.2 Hz), 7.60 (t, 2H, J = 7.2 Hz), 6.44 (s, 2H), 4.52 (s, 2H), 3.89–3.78 (m, 4H) ppm; HRMS (ESI): calculated for $C_{17}H_{16}N_4O_4NaS$ [M + Na^+] 395.0790, found 395.0788.

(Z)-N-[2-Nitro-2-[1-(2-thienylmethyl)-2-imidazolidinylidene]thioacetyl]benzamide (**7g**, $C_{17}H_{16}N_4O_3S_2$)
Yield 88%; red powder; m.p.: 168.5–169.4 °C; IR (KBr): $\bar{\nu}$ = 3,442, 1,588, 1,567, 1,138 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 14.26 (s, 1H), 9.94 (s, 1H), 7.92 (d, 2H, J = 7.6 Hz), 7.67 (t, 1H, J = 7.2 Hz), 7.59 (t, 2H, J = 7.6 Hz), 7.54 (t, 1H, J = 7.6 Hz), 7.16–7.15 (m, 2H), 4.70 (s, 2H), 3.83–3.73 (m, 4H) ppm; HRMS (ESI): calculated for $C_{17}H_{16}N_4O_3NaS_2$ [M + Na^+] 411.0718, found 411.0722.

General synthesis procedure for ***8***

To a stirred solution of 1.00 g **7a** (2.4 mmol) in 10 cm^3 warm acetic acid was added dropwise 0.43 g bromine (2.6 mmol) in 2 cm^3 acetic acid, with stirring for 10 min. The solvent was removed by evaporation under reduced pressure, and the residue was washed with water to afford 0.94 g **8a** (94% yield). Compounds **8b**–**8g** were prepared similarly.

(Z)-N-[1-[(6-Chloropyridin-3-yl)methyl]-2,3-dihydro-7-nitro-1H-imidazo[1,2-b]isothiazol-6-ylidene]benzamide
(**8a**, $C_{18}H_{14}N_5O_3SCl$)
Yield 94%; light-red powder; m.p.: 229.1–231.0 °C; IR (KBr): $\bar{\nu}$ = 1,605, 1,577 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.40 (d, 1H, J = 1.6 Hz), 8.23 (d, 2H, J = 7.2 Hz), 7.91–7.53 (m, 5H) 4.84 (s, 2H), 4.09 (s, 4H) ppm; HRMS (ESI): calculated for $C_{18}H_{14}N_5O_3NaSCl$ [M + Na^+] 438.0404, found 438.0405.

(Z)-N-[1-[(2-Chlorothiazol-5-yl)methyl]-2,3-dihydro-7-nitro-1H-imidazo[1,2-b]isothiazol-6-ylidene]benzamide
(**8b**, $C_{16}H_{12}N_5O_3S_2Cl$)
Yield 96%; light-red powder; m.p.: 215.4–216.8 °C; IR (KBr): $\bar{\nu}$ = 1,602, 1,571 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.24 (d, 2H, J = 7.6 Hz), 7.74 (s, 1H), 7.65–7.54 (m, 3H) 4.99 (s, 2H), 4.09 (s, 4H) ppm; HRMS (ESI): calculated for $C_{16}H_{12}N_5O_3NaS_2Cl$ [M + Na^+] 443.9968, found 443.9965.

(Z)-N-[2,3-Dihydro-7-nitro-1-(2-pyridinylmethyl)-1H-imidazo[1,2-b]isothiazol-6-ylidene]benzamide
(**8c**, $C_{18}H_{16}N_5O_3S$)
Yield 95%; light-red powder; m.p.: 243.7–245.5 °C; IR (KBr): $\bar{\nu}$ = 1,597, 1,572 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.73 (d, 1H, J = 4.2 Hz), 8.31–8.22 (m, 3H), 7.87–7.53 (m, 5H), 5.10 (s, 2H), 4.15 (s, 4H) ppm; HRMS (ESI): calculated for $C_{18}H_{16}N_5O_3S$ [M + H^+] 382.0974, found 382.0978.

(Z)-N-[2,3-Dihydro-7-nitro-1-(3-pyridinylmethyl)-1H-imidazo[1,2-b]isothiazol-6-ylidene]benzamide
(**8d**, $C_{18}H_{16}N_5O_3S$)
Yield 92%; light-red powder; m.p.: 235.0–236.9 °C; IR (KBr): $\bar{\nu}$ = 1,591, 1,573 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.95 (s, 1H), 8.84 (d, 1H, J = 4.2 Hz), 8.50 (d, 1H, J = 8.0 Hz), 8.23 (d, 2H, J = 7.2 Hz), 8.00 (d, 1H, J = 7.2 Hz), 7.65–7.54 (m, 3H), 4.99 (s, 2H), 4.14 (s, 4H) ppm; HRMS (ESI): calculated for $C_{18}H_{16}N_5O_3S$ [M + H^+] 382.0974, found 382.0980.

(Z)-N-[2,3-Dihydro-7-nitro-1-(phenylmethyl)-1H-imidazo-[1,2-b]isothiazol-6-ylidene]benzamide
(**8e**, $C_{19}H_{16}N_4O_3S$)
Yield 95%; light-red powder; m.p.: 204.3–205.9 °C; IR (KBr): $\bar{\nu}$ = 1,599, 1,572 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.22 (d, 2H, J = 7.2 Hz), 7.64–7.53 (m, 3H), 7.41–7.30 (m, 5H), 4.81 (s, 2H), 4.07 (s, 4H) ppm; HRMS (ESI): calculated for $C_{19}H_{16}N_4O_3NaS$ [M + Na^+] 403.0841, found 403.0845.

(Z)-N-[1-(2-Furanylmethyl)-2,3-dihydro-7-nitro-1H-imidazo[1,2-b]isothiazol-6-ylidene]benzamide
(**8f**, $C_{17}H_{14}N_4O_4S$)
Yield 97%; light-red powder; m.p.: 200.6–202.4 °C; IR (KBr): $\bar{\nu}$ = 1,603, 1,575 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.92 (d, 1H, J = 7.6 Hz), 7.67–7.58 (m, 4H), 6.45 (s, 2H), 4.52 (s, 2H), 3.89 (s, 4H) ppm; HRMS (ESI): calculated for $C_{17}H_{14}N_4O_4NaS$ [M + Na^+] 393.07558, found 393.0768.

(Z)-N-[2,3-Dihydro-7-nitro-1-(2-thienylmethyl)-1H-imidazo[1,2-b]isothiazol-6-ylidene]benzamide
(**8g**, $C_{17}H_{14}N_4O_3S_2$)
Yield 96%; light-red powder; m.p.: 198.7–200.3 °C; IR (KBr): $\bar{\nu}$ = 1,608, 1,565 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.25 (d, 2H, J = 6.0 Hz), 7.64–7.52 (m, 4H), 7.11–7.02 (m, 2H), 5.00 (s, 2H), 4.10 (s, 4H) ppm; HRMS (ESI): calculated for $C_{17}H_{14}N_4O_3NaS_2$ [M + Na^+] 409.0405, found 409.0400.

General synthesis procedure for ***3***

To compound **8a** (0.83 g, 2 mmol) in 20 cm^3 methanol was added 0.11 g sodium methoxide (2.1 mmol), with reflux for 10 min. The solvent was evaporated in vacuo, and the residue was washed with water and diethyl ether to afford 0.44 g **3a** (80% yield). Compounds **3b**–**3g** were prepared similarly.

(E)-2-[1-[(6-Chloropyridin-3-yl)methyl]-2-imidazolidinylidene]-2-nitroacetonitrile
(**3a**, $C_{11}H_{10}ClN_5O_2$)
Yield 78%; light-yellow powder; m.p.: 174.8–175.9 °C; IR (KBr): $\bar{\nu}$ = 2,213, 1,544, 1,325 cm^{-1}; ^{1}H NMR (400 MHz,

DMSO-d_6): $\delta = 9.49$ (br, 1H), 8.40 (d, 1H, $J = 2.4$ Hz), 7.83 (dd, 1H, $J = 2.4$ Hz, $J = 8.0$ Hz), 7.56 (d, 1H, $J = 8.0$ Hz), 4.80 (s, 2H), 3.71 (s, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 158.9$, 149.8, 149.0, 139.0, 131.3, 124.5, 115.2, 90.5, 50.0, 48.3, 42.6 ppm; HRMS (ESI): calculated for $C_{11}H_{10}ClN_5NaO_2$ [M + Na^+] 302.0421, found 302.0410.

(E)-2-[1-[(2-Chlorothiazol-5-yl)methyl]-2-imidazolidinylidene]-2-nitroacetonitrile (**3b**, $C_9H_8ClN_5O_2S$)
Yield 75%; yellow powder; m.p.: 178.9–180.3 °C; IR (KBr): $\bar{\nu} = 2{,}206$, 1,542, 1,343 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 9.59$ (br, 1H), 7.73 (s, 1H), 4.88 (s, 2H), 3.67 (s, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 158.4$, 141.7, 135.6, 123.9, 115.6, 90.5, 59.1, 49.5, 42.6 ppm; HRMS (ESI): calculated for $C_9H_8ClN_5NaO_2S$ [M + Na^+] 307.9985, found 307.9996.

(E)-2-Nitro-2-[1-(2-pyridinylmethyl)-2-imidazolidinylidene]acetonitrile (**3c**, $C_{11}H_{11}N_5O_2$)
Yield 70%; light-yellow powder; m.p.: 174.1–175.9 °C; IR (KBr): $\bar{\nu} = 2{,}210$, 1,544, 1,359 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 9.46$ (br, 1H), 8.54 (d, 1H, $J = 4.4$ Hz), 7.82 (t, 1H, $J = 6.8$ Hz), 7.37 (d, 1H, $J = 8.0$ Hz), 7.33 (t, 1H, $J = 6.8$ Hz), 4.92 (s, 2H), 3.83–3.69 (m, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 159.3$, 155.4, 149.8, 137.6, 123.2, 122.1, 115.3, 91.1, 51.7, 50.9, 42.6 ppm; HRMS (ESI): calculated for $C_{11}H_{11}N_5NaO_2$ [M + Na^+] 268.0810, found 268.0818.

(E)-2-Nitro-2-[1-(3-pyridinylmethyl)-2-imidazolidinylidene]acetonitrile (**3d**, $C_{11}H_{11}N_5O_2$)
Yield 72%; light-yellow powder; m.p.: 172.4–173.8 °C; IR (KBr): $\bar{\nu} = 2{,}205$, 1,548, 1,340 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 9.47$ (br, 1H), 8.55 (s, 2H), 7.75 (d, 1H, $J = 7.2$ Hz), 7.43 (t, 1H, $J = 7.2$ Hz), 4.82 (s, 2H), 3.71 (s, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 158.9$, 149.4, 149.0, 135.5, 131.6, 124.1, 115.4, 90.7, 50.2, 48.9, 42.6 ppm; HRMS (ESI): calculated for $C_{11}H_{11}N_5NaO_2$ [M + Na^+] 268.0810, found 268.0817.

(E)-2-Nitro-2-[1-(phenylmethyl)-2-imidazolidinylidene]-acetonitrile (**3e**, $C_{12}H_{12}N_4O_2$)
Yield 75%; light-yellow powder; m.p.: 167.9–169.8 °C; IR (KBr): $\bar{\nu} = 2{,}207$, 1,542, 1,338 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 9.47$ (br, 1H), 7.39–7.31 (m, 5H), 4.76 (s, 2H), 3.66 (s, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 158.1$, 135.2, 128.7, 127.7, 127.2, 114.9, 90.3, 50.4, 49.5, 42.0 ppm; HRMS (ESI): calculated for $C_{12}H_{12}N_4NaO_2$ [M + Na^+] 267.0858, found 267.0868.

(E)-2-[1-(2-Furanylmethyl)-2-imidazolidinylidene]-2-nitroacetonitrile (**3f**, $C_{10}H_{10}N_4O_3$)
Yield 74%; light-yellow powder; m.p.: 164.9–166.8 °C; IR (KBr): $\bar{\nu} = 2{,}208$, 1,548, 1,355 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 9.44$ (br, 1H), 7.69 (d, 1H, $J = 0.8$ Hz), 6.49–6.46 (m, 2H), 4.79 (s, 2H), 3.76–3.63 (m, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 158.5$, 148.9, 144.1, 115.5, 111.1, 109.9, 91.0, 50.0, 43.9, 42.5 ppm; HRMS (ESI): calculated for $C_{10}H_{10}N_4NaO_3$ [M + Na^+] 257.0651, found 257.0644.

(E)-2-Nitro-2-[1-(2-thienylmethyl)-2-imidazolidinylidene]acetonitrile (**3g**, $C_{10}H_{10}N_4O_2S$)
Yield 76%; light-yellow powder; m.p.: 165.5–167.1 °C; IR (KBr): $\bar{\nu} = 2{,}209$, 1,550, 1,332 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 9.38$ (br, 1H), 7.55 (dd, 1H, $J = 1.2$ Hz, $J = 5.2$ Hz), 7.15 (d, 1H, $J = 6.4$ Hz), 7.04 (t, 1H, $J = 3.2$ Hz), 4.95 (s, 2H), 3.75–3.63 (m, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 163.1$, 142.2, 133.4, 132.3, 132.1, 120.2, 95.6, 54.3, 50.6, 47.3 ppm; HRMS (ESI) calculated for $C_{10}H_{10}N_4NaO_2S$ [M + Na^+] 273.0422, found 273.0419.

(E)-2-[1-[(2-Methoxythiazol-5-yl)methyl]-2-imidazolidinylidene]-2-nitroacetonitrile (**3h**, $C_{10}H_{11}N_5O_3S$)
To compound **8b** (0.84 g, 2 mmol) in 20 cm^3 methanol was added 0.26 g sodium methoxide (4.8 mmol), with reflux for 10 min. The solvent was evaporated, and the residue was washed with water and diethyl ether to afford 0.45 g **3h** (79% yield). Light-yellow powder; m.p.: 169.4–170.8 °C; IR (KBr): $\bar{\nu} = 2{,}205$, 1,538, 1,341 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 9.47$ (br, 1H), 7.24 (s, 1H), 4.81 (s, 2H), 4.01 (s, 3H), 3.73–3.64 (m, 4H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): $\delta = 175.4$, 158.4, 137.7, 123.9, 115.7, 90.6, 59.0, 49.4, 44.4, 42.7 ppm; HRMS (ESI): calculated for $C_{10}H_{11}N_5NaO_3S$ [M + Na^+] 304.0480, found 304.0485.

*X-ray data for **3a***

$C_{11}H_{10}ClN_5O_2$, unit cell parameters: $a = 11.7507(4)$, $b = 9.0996(14)$, $c = 10.9721(17)$, $\alpha = 90.00$, $\beta = 90.00$, $\gamma = 90.00$, space group *Pbca*. The crystallographic data for the structure **3a** reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication No. CCDC 747419 for compound **3a**. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; email: deposit@ccdc.cam.ac.uk).

Bioassay

All bioassays were performed on representative test organisms reared in the laboratory. The bioassay was repeated at 25 ± 1 °C according to statistical requirements. All compounds were dissolved in *N*,*N*-dimethylformamide (AP, Shanghai Chemical Reagent Co., Ltd., Shanghai, China) and

diluted with distilled water containing Triton X-100 (0.1 mg dm^{-3}) to obtain series concentrations of 500.0, 250.0, and 125.0 mg dm^{-3} and others for bioassays. For comparative purposes, 6-Cl-PMNI was tested under the same conditions.

Insecticidal test for cowpea aphid (Aphis craccivora)

Activities of insecticidal compounds against cowpea aphid were tested by the leaf-dip method according to our previously reported procedure [14]. Horsebean plant leaves with 40–60 apterous adults were dipped into diluted solutions of the chemicals containing Triton X-100 (0.1 mg dm^{-3}) for 5 s, and the excess dilution was sucked out with filter paper; the burgeons were placed in the conditioned room [25 ± 1 °C, 50% relative humidity (RH)]. Water containing Triton X-100 (0.1 mg dm^{-3}) was used as control. Mortality rates were evaluated 24 h after treatment. Each treatment had three repetitions, and data were adjusted and subjected to probit analysis as before.

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