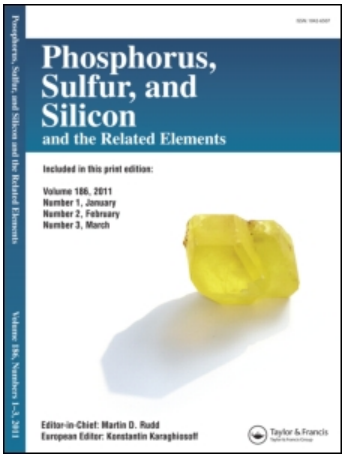

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Novel Heterocyclic Compounds Containing Sulfur: Synthesis and Insecticidal Activity of (2-Chlorothiazol-5-yl)methyl 2-Phenyliminothiazolidines

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A series of new (2-chlorothiazol-5-yl)methyl 2-phenyliminothiazolidines were designed and synthesized. All new compounds were characterized by ^{1}H *NMR and, in some cases, by* ^{13}C *NMR, IR, and HRMS. They are soluble in most organic solvents, which makes them easier to use. A preliminary bioassay showed that some of the new compounds display insecticidal activity against third-instar larvae of* Cx. pipiens pallens *at 50 mg/L and moderate insecticidal activity against* A. craccivora *at 1000 mg/L.*

Keywords Insecticidal activity; 2-phenyliminothiazolidine; synthesis; thiazolemethyl

INTRODUCTION

Crop protection continuously needs the discovery of novel pesticides. The agrochemical industry has successfully developed a wide array of pesticides with various chemical structures and modes of action.[1] Due to the emergence of resistant pests and toxicological issues associated with certain insecticides, there is a continuing need to discover novel chemical structures with potent activity.[2]

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Heterocyclic compounds play a very important role in drug design and synthesis, owing to their unique bioactivities. Sulfur-containing heterocyclic compounds such as 2-iminothiazolidine derivatives have gained much interest as potent inhibitors of indolethylamine *N*-methyltransferase,[3,4] octopaminergicagonists,[5,6] anthelmintics,[7,8] diuretic agents,[9] trehalase inhibitors,[10–12] and insecticidal agents.[13] It was presumed that this class of compounds may possess good potential with respect to agricultural bioactivities.

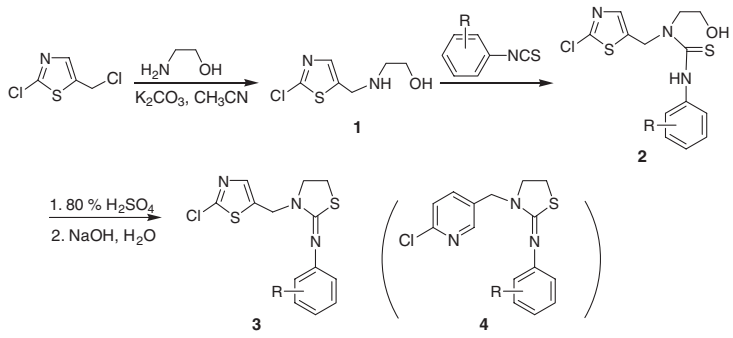
In the study of pharmaceuticals and agrochemicals, the introduction of pyridine into a parent compound may improve its properties and biological activities. In fact, many pyridyl-containing compounds possess a wide range of biological and pharmacological activities,[14–17] as well as low toxicity toward mammals. Bioisosterism is an important concept in bioactive compound design. Substitution of a 2-chloro-5-pyridyl group by a 2-chloro-5-thiazolyl group represents a successful example of bioisosterism, such as imidacloprid.[18–24] Encouraged by these reports, we developed the idea that the replacement of the 2-chloro-5-pyridyl with the 2-chloro-5-thiazolyl moiety in 2-phenyliminothiazolines could improve their insecticidal activities.

Therefore, we adopted the 2-iminothiazolidine ring as pharmacophore and simultaneously introduced a (2-chloro-5-pyridyl)methyl moiety and its bioisosteric 2-chloro-5-thiazole moiety into the 2-phenyliminothiazolidine system. In our previous work, we reported the synthesis of 2-phenyliminothiazolidines containing a pyridylmethyl group, which showed excellent herbicidal activity.[25,26] Herein we present the synthesis of a series of (2-chlorothiazol-5-yl)methyl 2-phenyliminothiazolidines by the replacement of the 2-chloro-5-pyridyl with the 2-chloro-5-thiazolyl moiety in 2-phenyliminothiazolines and a first evaluation of their insecticidal activities.

RESULTS AND DISCUSSION

Synthesis

The sulfur-containing compounds **3** were readily prepared in good yields as shown in Scheme 1. The thioureas **2** were obtained by reaction of the amino ethanol derivative **1** with the corresponding aryl isothiocyanates. Cyclization of **2** with 80% sulfuric acid provided the 2-phenyliminothiazolidine derivatives **3**. The overall yield of these two steps ranged from 40% to 86%. Compounds **3** were characterized by ^{1}H NMR and, in some cases, by ^{13}C NMR, IR, and HRMS. The IR spectra of compounds **3** showed C=N and C–S stretching bands at 1607–1629 cm^{-1} and 1221–1242 cm^{-1}, respectively. The ^{1}H NMR



2 - 4	R	2 - 4	R
a	H	**k**	4-F
b	2-NO_2	**l**	2,4-F_2
c	3-NO_2	**m**	2,6-F_2
d	4-NO_2	**n**	2-Cl
e	4-$N(CH_3)_2$	**o**	4-Cl
f	2-CH_3	**p**	4-CH_3
g	2,6-$(CH_3)_2$	**q**	4-CH_3-2-NO_2
h	2-CF_3	**r**	4-OCH_3-2-NO_2
i	3-CF_3	**s**	2-OCH_3
j	2-F	**t**	4-OCH_3

SCHEME 1 Synthesis of compounds **3**.

spectra of compounds **3** showed a singlet ($\delta = 4.67$–4.85 ppm), attributed to the CH_2 group linking to the thiazolidine ring. The two triplets at $\delta = 3.11$–3.24 ppm and $\delta = 3.47$–3.63 ppm were assigned to the two adjacent CH_2 groups of the thiazolidine ring.

Insecticidal Activity

Table I displays the insecticidal activities of selected compounds **3** and **4** against third-instar larvae of *Culex pipiens pallens* and *Aphis craccivora*. Some of the compounds exhibited high insecticidal activity against wiggler at 50 mg/L. 2-Chloro-5-thiazole is a bioisosteric analogue of 2-chloro-5-pyridine and corresponding compounds show similar insecticidal activity. We focused on the relationships between the type of substituents R at the phenyl ring and the biological activities. The compounds with a weakly electron donating or electron

TABLE I Insecticidal Activity Against Third-Instar Larvae of *Cx. pipiens pallens* of Some Compounds 3 and 4 at 50 mg/L

	R	Mortality rate (%)
3a	H	100
3f	2-CH_3	76.36
3g	2,6-$(CH_3)_2$	100
3i	3-CF_3	37.29
3k	4-F	52.0
3l	2,4-F,F	56.76
3n	2-Cl	100
3p	4-CH_3	42.55
3s	2-OCH_3	48.72
3t	4-OCH_3	90.91
4a	H	100
4f	2-CH_3	53.8
4g	2,6-$(CH_3)_2$	89.04
4j	2-F	100
4k	4-F	97.67
4l	2,4-F_2	81.69
4m	2,6-F_2	61.76
4n	2-Cl	59.38
4o	4-Cl	79.66
4s	2-OCH_3	55.84
4t	4-OCH_3	77.5

withdrawing group (CH_3, H, Cl, F) at the phenyl ring show good biological activities. The introduction of a strongly electron withdrawing group such as the *nitro* group at the phenyl ring results in a complete loss of activity (**3b–d**, **q**, **r/4b–d**, **q**, **r**), while the introduction of a strong electron donating group such as the *N*, *N*-dimethylamino group at the phenyl ring also results in a complete loss of activity (**3e/4e**). Among all compounds, **3a**, **g**, **n**, and **4a**, **n** possess significant biological activities, and the mortality rate against third-instar larvae of *Cx. pipiens pallens* reaches 100% at 50 mg/L. Further study of this aspect is underway.

Table II shows that some compounds **3** and **4** exhibit moderate insecticidal activity against *A. craccivora* at 1000 mg/L. Selected compounds containing the 2-chlorothiazol-5-yl unit showed insecticidal activity. Among the compounds containing a 2-chloro-5-pyridyl moiety, only **4g** exhibited 55.7% of mortality rate against *A. craccivora* at 1000 mg/L.

In conclusion, we have presented the design and synthesis of novel 2-phenyliminothiazolidine derivatives containing thiazolemethyl and pyridinemethyl moiety. A first biological assay indicated that they possess good insecticidal activities against third-instar larvae of *Cx.*

TABLE II Insecticidal Activity Against *A. craccivora* of Some Compounds 3 and 4 at 1000 mg/L

	R	Mortality rate
3d	4-NO_2	37.13
3f	2-CH_3	36.23
3h	2-CF_3	69.64
3k	4-F	49.18
3l	2,4-F_2	38.37
3m	2,6-F_2	42.11
4g	2,6-$(CH_3)_2$	55.70

pipiens pallens. It is shown that a systematic study on the structure–activity relationships will benefit the prediction of new compounds with better insecticidal activity. The 2-phenyliminothiazolidine framework might be identified as a novel insecticidal lead structure.

EXPERIMENTAL

Melting points were obtained with an X-6 micro melting point apparatus and are uncorrected. The IR spectra were recorded with a Nicolet 20DXB FR-IR spectrometer using KBr pellets or films. The ^{1}H NMR spectra were measured with a Varian INOVA-400 spectrometer (400 MHz) in $CDCl_3$ with TMS as internal standard; chemical shifts are reported in ppm. The ^{13}C NMR spectra were measured with a Bruker AVANCE-500 spectrometer (125 MHz) in $CDCl_3$ using TMS as internal standard. High-resolution mass spectra (HRMS) were obtained with a HPLC-Q-Tof MS (Mcrio) spectrometer. Flash chromatography was performed on silica gel. All the solvents were of analytical grade. All chemicals or reagents were purchased from standard commercial suppliers.

Synthesis of 2-[(2-Chlorothiazol-5-yl)methylamino]ethanol (1)

2-Chloro-5-(chloromethyl)thiazole (10 mmol, 1.68 g) dissolved in 100 mL of acetonitrile was added dropwise to a K_2CO_3 (10 mmol, 1.38 g)-containing solution of ethanolamine (10 mmol, 0.61 g) in 25 mL of acetonitrile over a period of 2 h at room temperature. The resulting mixture was refluxed for 4.5 h. The solvent was evaporated in vacuo, and the residue was purified by column chromatography on silica gel using 10% methanol/chloroform as eluent (v/v, $R_f = 0.20$) to give **1** as a yellowish oil in 79% yield (1.52 g). API-ES-MS (positive) *m/z*193.0

([M + H]$^+$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.81$ (t, $J = 5.0$ Hz, 2H), 3.69 (t, $J = 5.0$ Hz, 2H), 3.98 (s, 2H), 7.37 (s, 1H).

Synthesis of 2-Phenyliminothiazolidines 3: General Procedure

To a solution of **1** (1.0 mmol, 192.7 mg) in 50 mL of ethanol, the corresponding phenyl isothiocyanate (1.0 mmol) was added over a period of 10 min, and the mixture was stirred at room temperature for 30–60 min. The solvent was evaporated in vacuo, and the residue was washed with Et_2O (3 × 10 mL) and H_2O (3 × 10 mL) to afford **2**, which was used directly without further purification.

The appropriate thiourea **2** (10 mmol) was dissolved in 10 mL of 80% sulfuric acid and heated at 90°C for 45 min. The cooled mixture was basified with 10 *M* NaOH in an ice bath. The precipitated gummy residue was extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was washed with brine, dried ($MgSO_4$), and the solvent was evaporated to give crude **3**, which was purified by column chromatography on silica gel using petroleum ether and acetone as eluents. The overall yields of these two steps ranged from 45% to 84%.

2-(Phenylimino)-3-(2-chlorothiazol-5-yl)methylthiazolidine (3a)

Yield: 65% (201.4 mg); mp 75.3–76.2°C; IR (KBr): $\upsilon_{max} = 1615, 1587, 1233, 768, 699\ cm^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.16$ (t, $J = 6.8$ Hz, 2H), 3.53 (t, $J = 6.8$ Hz, 2H), 4.76 (s, 2H), 6.98–7.20 (m, 2H), 7.05–7.10 (m, 1H), 7.29–7.34 (m, 2H), 7.45 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 26.9, 42.8, 49.8, 121.7, 123.5, 129.0, 135.0, 140.3, 151.4, 153.2, 158.5$; HRMS (ESI) calcd for $C_{13}H_{13}ClN_3S_2$ [M + H]$^+$ 310.0239, found 310.0237.

2-(2-Nitrophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3b)

Yield: 82% (291.0 mg); mp 102.8–103.8°C; IR (KBr): $\upsilon_{max} = 1628, 1601, 1517, 1228, 761\ cm^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.23$ (t, $J = 6.8$ Hz, 2H), 3.63 (t, $J = 6.8$ Hz, 2H), 4.79 (s, 2H), 7.07 (dd, $J = 1.2$ Hz, 8.2 Hz, 1H), 7.11–7.17 (m, 1H), 7.44–7.52 (m, 2H), 7.89 (dd, $J = 1.2$ Hz, 8.2 Hz, 1H); HRMS (ESI) calcd for $C_{13}H_{12}ClN_4O_2S_2$ [M + H]$^+$ 355.0090, found 355.0077.

2-(3-Nitrophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3c)

Yield: 70% (248.4 mg); mp 102.1–103.9°C; IR (KBr): $\upsilon_{max} = 1625, 1607, 1514, 1233, 745, 690\ cm^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$

3.24 (t, $J = 6.8$ Hz, 2H), 3.61 (t, $J = 6.8$ Hz, 2H), 4.79 (s, 2H), 7.33 (d, $J = 8.4$ Hz, 1H), 7.45 (d, $J = 8.0$ Hz, 1H), 7.48 (s, 1H), 7.82–7.85 (m, 1H), 7.90–7.96 (m, 1H); HRMS calcd for $C_{13}H_{12}ClN_4O_2S_2$ $[M + H]^+$ 355.0090, found 355.0081.

2-(4-Nitrophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3d)

Yield: 76% (269.7 mg); mp 140.3–141.6°C; IR (KBr): $\upsilon_{max} = 1620$, 1581, 1499, 1240, 855 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.25$ (t, $J = 7.0$ Hz, 2H), 3.62 (t, $J = 7.0$ Hz, 2H), 4.78 (s, 2H), 6.90–7.40 (m, 2H), 7.48 (s, 1H), 8.17–8.21 (m, 2H); HRMS (ESI) calcd for $C_{13}H_{12}ClN_4O_2S_2$ $[M + H]^+$ 355.0090, found 355.0084.

2-(4-N,N-Dimethylaminophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3e)

Yield: 70% (247.0 mg); oil; IR (film): $\upsilon_{max} = 1615$, 1513, 1236, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.92$ (s, 6H), 3.13 (t, $J = 6.8$ Hz, 2H), 3.47 (t, $J = 6.8$ Hz, 2H), 4.73 (s, 2H), 6.74 (d, $J = 8.8$ Hz, 2H), 6.93 (d, $J = 8.8$ Hz, 2H), 7.43 (s, 1H); HRMS calcd for $C_{15}H_{18}ClN_4S_2$ $[M + H]^+$ 353.0661, found 353.0665.

2-(2-Methylphenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3f)

Yield: 79% (255.8 mg); mp 76.1–77.2°C; IR (KBr): $\upsilon_{max} = 1622$, 1595, 1228, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.21$ (s, 3H), 3.15 (t, $J = 6.8$ Hz, 2H), 3.54 (t, $J = 6.8$ Hz, 2H), 4.80 (s, 2H), 6.87 (d, $J = 8.0$ Hz, 1H), 6.99 (d, $J = 7.6$ Hz, 1H), 7.11–7.20 (m, 2H), 7.46 (s, 1H); HRMS (ESI) calcd for $C_{14}H_{15}ClN_3S_2$ $[M + H]^+$ 324.0396, found 324.0409.

2-(2,6-Dimethylphenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3g)

Yield: 80% (270.3 mg); mp 78.9–80.3°C; IR (KBr): $\upsilon_{max} = 1628$, 1587, 1232, 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.15$ (s, 6H), 3.12 (t, $J = 7.0$ Hz, 2H), 3.57 (t, $J = 7.0$ Hz, 2H), 4.85 (s, 2H), 6.89 (t, $J = 7.6$ Hz, 1H), 7.02 (d, $J = 7.6$ Hz, 2H), 7.49 (s, 1H); HRMS (ESI) calcd for $C_{15}H_{17}ClN_3S_2$ $[M + H]^+$ 338.0552, found 338.0557.

2-(2-Trifluoromethylphenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3h)

Yield: 80% (302.3 mg); mp 102.7–103.4°C; IR (KBr): $\upsilon_{max} = 1626$, 1599, 1230, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.19$ (t, $J = 7.0$ Hz, 2H), 3.59 (t, $J = 7.0$ Hz, 2H), 4.80 (s, 2H), 7.02 (d, $J = 8.0$ Hz,

1H), 7.12 (t, $J = 7.6$ Hz, 1H), 7.42–7.49 (m, 2H), 7.61 (d, $J = 8.0$ Hz, 1H); HRMS (ESI) calcd for $C_{14}H_{12}ClF_3N_3S_2$ $[M + H]^+$ 378.0113, found 378.0123.

2-(3-Trifluoromethylphenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3i)

Yield: 60% (226.7 mg); oil; IR (film): $\upsilon_{max} = 1622$, 1601, 1585, 1230, 799, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.16$ (t, $J = 6.8$ Hz, 2H), 3.53 (t, $J = 6.8$ Hz, 2H), 4.74 (s, 2H), 7.17 (d, $J = 8.0$ Hz, 1H), 7.25 (s, 1H), 7.31 (t, $J = 8.0$ Hz, 1H), 7.40 (d, $J = 8.0$ Hz, 1H), 7.45 (s, 1H); HRMS (ESI) calcd for $C_{14}H_{12}ClF_3N_3S_2$ $[M + H]^+$ 378.0113, found 378.0109.

2-(2-Fluorophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3j)

Yield: 76% (249.2 mg); mp 96.2–97.0°C; IR (KBr): $\upsilon_{max} = 1621$, 1603, 1235, 766 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.19$ (t, $J = 7.0$ Hz, 2H), 3.58 (t, $J = 7.0$ Hz, 2H), 4.80 (s, 2H), 6.98–7.12 (m, 4H), 7.47 (s, 1H); HRMS (ESI) calcd for $C_{13}H_{12}ClFN_3S_2$ $[M + H]^+$ 328.0144, found 328.0145.

2-(4-Fluorophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3k)

Yield: 84% (275.4 mg); mp 91.7–92.6°C; IR (KBr): $\upsilon_{max} = 1613$, 1502, 1223, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.17$ (t, $J = 6.8$ Hz, 2H), 3.53 (t, $J = 6.8$ Hz, 2H), 4.74 (s, 2H), 6.91–7.03 (m, 4H), 7.45 (s, 1H); HRMS (ESI) calcd for $C_{13}H_{12}ClFN_3S_2$ $[M + H]^+$ 328.0144, found 328.0145.

2-(2,4-Difluorophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3l)

Yield: 80% (276.7 mg); mp 116.8–117.3°C; IR (KBr): $\upsilon_{max} = 1619$, 1527, 1236, 848, 806 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.20$ (t, $J = 7.0$ Hz, 2H), 3.58 (t, $J = 7.0$ Hz, 2H), 4.78 (s, 2H), 6.77–6.89 (m, 2H), 6.92–7.00 (m, 1H), 7.47 (s, 1H); HRMS (ESI) calcd for $C_{13}H_{11}ClF_2N_3S_2$ $[M + H]^+$ 346.0051, found 346.0036.

2-(2,6-Difluorophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3m)

Yield: 81% (280.1 mg); mp 155.1–156.0°C; IR (KBr): $\upsilon_{max} = 1622$, 1528, 1236, 789, 743 cm^{-1};^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.22$ (t, $J = 7.0$ Hz, 2H), 3.63 (t, $J = 7.0$ Hz, 2H), 4.83 (s, 2H), 6.85–7.02 (m, 3H),

7.48 (s, 1H); HRMS (ESI) calcd for $C_{13}H_{11}ClF_2N_3S_2$ $[M + H]^+$ 346.0051, found 346.0036.

2-(2-Chlorophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3n)

Yield: 67% (230.7 mg); mp 100.4–101.4°C; IR (KBr): $\upsilon_{max} = 1619$, 1584, 1230, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.19$ (t, $J =$ 6.8 Hz, 2H), 3.59 (t, $J = 6.8$ Hz, 2H), 4.83 (s, 2H), 6.96–7.02 (m, 2H), 7.17–7.23 (m, 1H), 7.39 (d, $J = 8.0$ Hz, 1H), 7.49 (s, 1H), ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 26.8, 42.5, 50.1, 122.9, 124.3, 127.2, 127.3, 129.8, 135.2, 140.4, 148.4, 153.0, 159.6; HRMS (ESI) calcd for $C_{13}H_{12}Cl_2N_3S_2$ $[M + H]^+$ 343.9850, found 343.9862.

2-(4-Chlorophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3o)

Yield: 70% (241.0 mg); mp 108.3–109.1°C; IR (KBr): $\upsilon_{max} = 1608$, 1579, 1235, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.17$ (t, $J =$ 7.0 Hz, 2H), 3.53 (t, $J = 7.0$ Hz, 2H), 4.74 (s, 2H), 6.93 (d, $J = 8.8$ Hz, 2H), 7.26 (d, $J = 8.8$ Hz, 2H), 7.45 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 26.9, 42.7, 49.9, 123.1, 128.6, 129.0, 134.8, 140.4, 149.9, 153.2, 159.0; HRMS (ESI) calcd for $C_{13}H_{12}Cl_2FN_3S_2$ $[M + H]^+$ 343.9850, found 343.9863.

2-(4-Methylphenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3p)

Yield: 84% (272.0 mg); mp 65.0–65.7°C; IR (KBr): $\upsilon_{max} = 1621$, 1602, 1505, 1231, 825 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.33$ (s, 3H), 3.15 (t, $J = 6.8$ Hz, 2H), 3.51 (t, $J = 6.8$ Hz, 2H), 4.75 (s, 2H), 6.90 (d, $J =$ 8.2 Hz, 2H), 7.12 (d, $J = 8.2$ Hz, 2H), 7.44 (s, 1H); HRMS (ESI) calcd for $C_{14}H_{15}ClN_3S_2$ $[M + H]^+$ 324.0396, found 324.0391.

2-(4-Methyl-2-nitrophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3q)

Yield: 80% (295.1 mg); mp 86.8–87.7°C; IR (KBr): $\upsilon_{max} = 1613$, 1557, 1237, 828, 794 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.38$ (s, 3H), 3.21 (t, $J = 7.0$ Hz, 2H), 3.61 (t, $J = 7.0$ Hz, 2H), 4.79 (s, 2H), 6.96 (d, $J =$ 8.4 Hz, 1H), 7.30 (dd, $J = 1.2$ Hz, 8.4 Hz, 1H), 7.46 (s, 1H), 7.71 (d, $J =$ 1.2 Hz, 1H); HRMS (ESI) calcd for $C_{14}H_{14}ClN_4O_2S_2$ $[M + H]^+$ 369.0247, found 369.0257.

2-(4-Methoxy-2-nitrophenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3r)

Yield: 81% (311.7 mg); mp 112.8–113.6°C; IR (KBr): υ_{max} = 1607, 1561, 1225, 828, 794 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.21 (t, J = 7.0 Hz, 2H), 3.61 (t, J = 7.0 Hz, 2H), 3.85 (s, 3H), 4.79 (s, 2H), 6.99 (d, J = 8.8 Hz, 1H), 7.09 (dd, J = 2.8 Hz, 8.8 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.46 (s, 1H); HRMS (ESI) calcd for $C_{14}H_{14}ClN_4O_3S_2$ $[M + H]^+$ 385.0196, found 385.0193.

2-(2-Methoxyphenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3s)

Yield: 45% (152.9 mg); oil; IR (film): υ_{max} = 1622, 1586, 1247, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.11 (t, J = 6.8 Hz, 2H), 3.50 (t, J = 6.8 Hz, 2H), 3.83 (s, 3H), 4.79 (s, 2H), 6.87–6.93 (m, 3H), 7.02–7.08 (m, 1H), 7.48 (s, 1H); HRMS (ESI) calcd for $C_{14}H_{15}ClN_3OS_2$ $[M + H]^+$ 340.0345, found 340.0358.

2-(4-Methoxyphenyl)imino-3-(2-chlorothiazol-5-yl)methylthiazolidine (3t)

Yield: 40% (135.9 mg); mp 78.5–79.6°C; IR (KBr): υ_{max} = 1619, 1502, 1229, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.15 (t, J = 6.8 Hz, 2H), 3.50 (t, J = 6.8 Hz, 2H), 3.80 (s, 3H), 4.75 (s, 2H), 6.86 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.44 (s, 1H); HRMS (ESI) calcd for $C_{14}H_{15}ClN_3OS_2$ $[M + H]^+$ 340.0345, found 340.0337.

Biological Assay

All compounds were dissolved in a mixture of DMF, emulsifier 0201 (a mixture of anionic and nonionic surfactant), and water to give a solution of the required concentration according to the experimental needs. The concentration of the surfactant was not higher than 0.1%. The insecticidal bioassay tests were carried out by following the FAO (1971) and IRAC (2004) test method.[27,28]

Activity Against Third-Instar Larvae of Cx. pipiens pallens

A solution of 50 mg/L was added into each well of 96 well plates. Twenty third-instar larvae of *Cx. pipiens pallens* were used in each well and kept at 24 ± 1°C in the thermostatic chamber for 24 h. The mortality rates (%) of test worm were determined (Table I). The experiments were conducted in three replicates for each concentration.

Activity Against A. Craccivora

A leaf-dipping method was used to evaluate the activity of the test samples. Thirty apterous adults of *A. craccivora* placed on pea sprouts

were dipped into 1000 mg/L solutions for 5 s, and then excrescent solution on pea sprouts were removed. All treated samples were maintained at 24 ± 1°C in the thermostatic chamber for 24 h. The mortality rates (%) of test worm were determined (Table II). The experiments were conducted in three replicates for each concentration.

REFERENCES

[1] P. Böger, K. Wakabayashi, and K. Hirai, *Herbicide Classes in Development: Mode of Action, Targets, Genetic Engineering, Chemistry* (Springer, Berlin, 2002), p. 364.
[2] M. A. Dekeyser and R. G. H. Downer, *Pestic. Sci.*, **40,** 85 (1994).
[3] J. Rokach, P. Hamel, N. R. Hunter, G. Reader, C. S. Rooney, P. S. Anderson, E. J. Cragoe, and L. R. Mandel, *J. Med. Chem.*, **22,** 237 (1979).
[4] J. Rokach, Y. Girard, P. Hamel, G. Reader, C. S. Rooney, L. R. Mandel, E. J. Cragoe, and A. G. Zacchei, *J. Med. Chem.*, **23,** 773 (1980).
[5] A. Hirashima, A. Rafaeli, C. Gileadi, and E. Kuwano, *Bioorg. Med. Chem.*, **7,** 2621 (1999).
[6] A. Hirashima, M. Morimoto, E. Kuwano, E. Taniguchic, and M. Eto, *Bioorg. Med. Chem.*, **10,** 117 (2002).
[7] A. H. M. Raeymaekers, F. T. N. Allewijn, J. Vandenberk, P. J. A. Demoen, T. T. T. Offenwert, and P. A. J. Janssen, *J. Med. Chem.*, **9,** 545 (1966).
[8] R. Caujolle, H. Amarouch, M. Payard, P. R. Loiseau, C. Bories, P. M. Loiseau, and P. Garyral, *Eur. J. Med. Chem.*, **24,** 287 (1989).
[9] R. Jozsef, T. Lajos, B. Jozsef, S. Inge, K. Ildiko, and S. Jozsef, HU 13936 (1977) .
[10] X.-Y. Xu, X.-H Qian, Z. Li, G.-H. Song, and W.-D. Chen, *J. Fluorine Chem.*, **125,** 1159 (2004).
[11] X.-H. Qian, X.-Y. Xu, Z.-B. Li, Z. Li, and G.-H. Song, *J. Fluorine Chem.*, **125,** 1609 (2004).
[12] C.-X. Liu, X.-Y. Xu, Z. Li, W.-D. Chen, Q.-C. Huang, and X.-H. Qian, *J. Fluorine Chem.*, **126,** 53 (2005).
[13] D. Duerr, DE 2741378 (1978).
[14] M.-C. Liu, T.-S. Lin, J. G. Cory, A. H. Cory, and A. C. Sartorelli, *J. Med. Chem.*, **39,** 2586 (1996).
[15] B. L. Finkelstein, M. A. Martz, and C. J. Strock, *Pestic. Sci.*, **50,** 319 (1997).
[16] Q. M. Wang, H. K. Sun, H. Y. Cao, M. R. Cheng, and R. Q. Huang, *J. Agric. Food Chem.*, **51,** 5030 (2003).
[17] Y. W. Jo, W. B. Im, J. K. Rhee, M. J. Shim, W. B. Kim, and E. C. Choi, *Bioorg. Med. Chem.*, **12,** 5909 (2004).
[18] I. Yamamoto, *Agrochem. Jpn.*, **68,** 14 (1996).
[19] A. Elbert, H. Overbeck, K. Iwaya, and S. Tsuboi, *Pests and Diseases*, **1,** 21 (1990).
[20] I. Minamida, K. Iwanaga, and T. J. Tabuchi, *Pestic. Sci.*, **18,** 41 (1993).
[21] H. Takahashi, J. Mitsui, and N. Takakusa, *Pests and Diseases*, **1,** 89 (1992).
[22] P. Maienfisch, and L. Gsell, EP 580553 (1992).
[23] P. Maienfisch, L. Gsell, and A. Rindlisbacher, *Pestic. Sci.*, **55,** 351 (1999).
[24] H. Uneme, K. Iwanaga, N. Higuchi, Y. Kando, T. Okauchi, A. Akayama, and I. Minamida, *Pestic. Sci.*, **55,** 202 (1999).
[25] G.-Y. Li, X.-H. Qian, J.-N. Cui, Q.-C. Huang, D.-W. Cui, R. Zhang, and F.-Y Liu, *J. Fluorine Chem.*, **127,** 182 (2006).

[26] G.-Y. Li, X.-H. Qian, S.-G. Yan, J.-N. Cui, R. Zhang, and Y. Xiao, *Monatsh. Chem.*, **139,** 169 (2008).
[27] Food and Agriculture Organization of the United Nations. Recommended Methods of Measurement of Pest Resistance to Pesticides. FAO Plant Production and Protection Paper. (1980).
[28] Insecticide Resistance Action Committee. http://www.irac-online.org/resources/methods.asp (2004).