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Design, Synthesis, Acaricidal Activities, and Structure–Activity Relationship Studies of Novel Oxazolines Containing Sulfonate Moieties

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Design, Synthesis, Acaricidal Activities, and Structure–Activity Relationship Studies of Novel Oxazolines Containing Sulfonate Moieties

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ABSTRACT

With the ultimate goal of addressing pest-related constraints on global agricultural production, we used combination principles to design and synthesize 2,4-diphenyl-1,3-oxazolines containing a sulfonate moiety at the *para*-position of the 4-phenyl group. The target compounds, which have strong affinity for lipids and can be expected to traverse cell membranes, were characterized by ^{1}H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry. Their activities against the larvae and eggs of carmine spider mites (*Tetranychus cinnabarinus*) were determined by a leaf-dipping method and compared with the activity of the commercial acaricide etoxazole. Most of the test compounds displayed good ovicidal and larvicidal activities. In particular, a *tert*-butylphenyl-substituent compound possessed better larvicidal activity (LC_{50} = 0.022 ± 0.009 mg/L) and ovicidal activity (0.044 ± 0.020 mg/L) than etoxazole (0.091 ± 0.051 and 0.095 ± 0.059 mg/L, respectively). Given its outstanding bioactivities, this compound deserves further attention as a pesticide candidate.

KEYWORDS: 2,4-diphenyl-1,3-oxazolines; etoxazole; acaricidal activity; sulfonate; structure–activity relationship

INTRODUCTION

Mites transmit human diseases and reduce the yields of agricultural crops.[1] For example, *Tetranychus cinnabarinus* (carmine spider mite), which is one of the most widely distributed polyphagous pests in agricultural areas around the world, feeds on more than 800 species of host plants, including fruit trees, potatoes, wheat, vegetables, corn, and cotton.[2] Mites generally feed directly on the cytosol, which results in the formation of punctate necrotic tissue, reduced photosynthetic activity, and leaf abscission in severe infestations.[3,4] Because mites have high reproductive potential and a short life cycle, mite infestations are a serious threat to agriculture; however, owing to the long-term use and abuse of existing traditional acaricides, mite infestations are hard to control.[5–7] Nevertheless, because chemical control by means of pesticides remains the most effective pest management method, new, highly effective acaricides with low toxicity are in great demand.

Etoxazole, a 2,4-diphenyl-1,3-oxazoline analogue, is widely used for control of pests, including mite species, because of its unique mode of action and low toxicities to mammals, birds, and aquatic organisms.[8–11] Research on the mechanism of action of etoxazole has been underway since the compound was discovered in 1994. Although there is some dispute about whether the target site of etoxazole is the sulfonylurea receptor[12–14] or chitin synthase,[15–22] it is generally accepted that etoxazole

inhibits chitin synthesis.[15] In 2006, Nauen and Smagghe used an isotopic tracer method to study etoxazole and the benzoylurea insecticide diflubenzuron and found that both compounds inhibit the synthesis of chitin from *N*-acetylglucosamine.[11] Nearly 20 benzoylurea insecticides are commercially available, but only one acaricide with a 2,4-diphenyl-1,3-oxazoline skeleton has entered the market to date; therefore, work on the development of new etoxazole analogues still generates considerable interest.

In 2016, our group designed and synthesized dozens of oxazoline derivatives containing sulfone or sulfoxide groups (I and II in Figure 1)[23] to target a sulfonylurea receptor protein, which has been reported[13,14] to be a binding site for chitin synthesis inhibitors. Most of the synthesized compounds showed excellent acaricidal activities against larvae and eggs. In addition, Takeda Chemical Industries synthesized a series of sulfonyl-group-containing compounds based on the commercially available insecticidal diflubenzuron (III in Figure 1) and found that they showed high activity against lepidopteran pests.[24]

In 2013, our group found that a diflubenzuron derivative in which the Cl atom has been replaced with a sulfonate moiety (IV in Figure 1) exhibits bioactivity similar to that of a commercial insecticide.[25] Many of the early commercial pesticides contained a sulfonate moiety (Fenson, Genite, and chlorfenson)[26,27] or a thiosulfonate moiety (Bensultap).[28]

Owing to their physicochemical properties, sulfonate-bearing compounds have strong affinity for lipid phases and can cross the cuticle membrane easily to bind to target sites. Therefore, in this study, with the goal of developing new chitin synthesis inhibitors, we used combination principles to design a series of 2,4-diphenyl-1,3-oxazolines containing a sulfonate moiety at the *para*-position of the 4-phenyl substituent on the oxazoline ring, and we synthesized the compounds and evaluated their acaricidal activities.

MATERIALS AND METHODS

Chemicals: All regular reagents and solvents were purchased from Tianjin Chemical Reagents Supply and Marketing Company without any extra treatment unless otherwise noted. All required anhydrous solvents were treated according to standard techniques just before use. Compounds 2,6-difluorobenzamide (Beijing Ouhe Technology Co., Ltd), dimethylchloroacetal (Shanghai Macklin Biochemical Technology Co., Ltd), anisole (Tianjin Chemical Reagents Supply and Marketing Company), $AlCl_3$ (Tianjin Chemical Reagents Supply and Marketing Company), BBr_3 (Beijing Innochem Technology Co., Ltd), different substituted sulfonyl chloride (Tiajin Heowns Biochemical Technology Co., Ltd; Beijing Innochem Technology Co., Ltd; Beijing J&K Technology Co., Ltd; Shanghai Bidepharm Technology Co., Ltd; Shanghai Boka-chemical Technology Co., Ltd; or SAEN Chemical

Technology (Shanghai) Co., Ltd) and trifluoromethanesulfonic anhydride (Beijing Innochem Technology Co., Ltd) were purchased separately from different commercial sources listed above.

Instruments: Reaction progress was monitored by thin-layer chromatography on silica gel GF254 with ultraviolet (UV) detection. Melting points were obtained using an X-4 binocular microscope melting point (mp) apparatus and are uncorrected. Yields were not optimized. ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded utilizing a Bruker AV400 spectrometer with $CDCl_3$ or DMSO-d_6 as solvent and tetramethylsilane as internal standard. High-resolution mass spectra (HRMS) data were obtained with a Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (FTICR-MS) spectrometer (ionspec, 7.0T).

Procedures for the Synthesis of Compounds in Scheme 1.

Synthesis of N-(2-chloro-1-methoxyethyl)-2,6-difluorobenzamide (2).

Compound **2** (21.7 g, yield 87%) was synthesized by the reaction of 2,6-difluorobenzamide (15.7 g，100 mmol) and dimethylchloroacetal (44 mL，300 mmol) catalyzed with concentrated sulfuric acid (6.5 mL，120 mmol) according to the method reported in our previous study.[29] The physical data are included in Supporting Information.

Synthesis of N-(2-chloro-1-(4-methoxyphenyl)ethyl)-2,6-difluorobenzamide (3).

A mixture of **2** (5.0 g, 20 mmol) and anisole (2.6 mL, 24 mmol) in 30 mL of dry CH_2Cl_2 was cooled to below 0 °C. The anhydrous $AlCl_3$ (5.34 g, 40 mmol) was slowly added to the mixture under stirring, and the reaction was carried out at room temperature subsequently until the reaction was complete as indicated by TLC. The mixture was poured into ice water to quench $AlCl_3$. After separation of the organic phase, the aqueous phase was extracted with dichloromethane three times. The combined organic phase was washed with saturated brine, dried with anhydrous sodium sulfate, filtered, and evaporated to give **3** (with a small amount of 2-methoxyphenyl isomer) (5.86 g, yield 90%).

Synthesis of N-(2-chloro-1-(4-hydroxyphenyl)ethyl)-2,6-difluorobenzamide (4).

To the solution of crude **3** (10 mmol, 3.26 g) in 20 mL of dry CH_2Cl_2 was added dropwise BBr_3 (2.4 mL, 24 mmol) at -10 °C under the argon protection, followed by stirring at room temperature for 4 h. After the reaction was complete, the reaction solution was poured into ice-water slowly to quench BBr_3, and then the mixture was stirred until the precipitates disappeared. The organic phase was collected and the aqueous phase was extracted with dichloromethane three times. After the combined organic phase was washed with saturated brine, dried with anhydrous sodium sulfate, filtered and evaporated, compound **4** (with a small amount of 2-hydroxyphenyl isomer) (2.84 g, yield 91%) was

obtained.

Synthesis of 4-(2-(2,6-difluorophenyl)-4,5-dihydrooxazol-4-yl)phenol (5).

Crude **4** (1.87 g, 6 mmol) was dissolved in 10 mL of methanol. The solution was stirred for 1 h after the addition of NaOH (0.48 g, 12 mmol). After most of the methanol was removed under reduced pressure, the aqueous phase was extracted with ethyl acetate three times. The combined organic phase was washed, dried, filtrated, concentrated in vacuo, and further purified by flash chromatography on silica gel using petroleum ether and ethyl acetate (v/v = 5:1) to give the target compound **5** (0.84 g, yield 51%).

Synthesis of 4-(2-(2,6-difluorophenyl)-4,5-dihydrooxazol-4-yl)phenyl methanesulfonate (6a)

To a solution of **5** (0.55 g, 2 mmol) and triethylamine (0.57 mL, 4 mmol) in 10 mL of dry THF was added slowly the solution of methanesulfonyl chloride (0.19 mL, 2.4 mmol) in 10 mL of dry THF at room temperature under stirring, the mixture was then continuously stirred until the reaction was complete as indicated by TLC. After THF was removed under reduced pressure, ethyl acetate and water were added to separate the organic phase, and the aqueous phase was extracted with ethyl acetate three times. The combined organic phase was washed, dried, concentrated in vacuo, and further purified by flash chromatography on

164 silica gel using petroleum ether and ethyl acetate (v/v = 6:1) to give the
165 target compound **6a** (1.16 g, yield 71%).

166 Compounds **6b-w** were synthesized according to the similar procedure
167 used for compound **6a**. The physical data are in datail in the Supporting
168 Information.

169 **Synthesis of 4-(2-(2,6-difluorophenyl)-4,5-dihydrooxazol-4-yl)phenyl**
170 **trifluoromethanesulfonate (6x)**

171 To a solution of **5** (0.55 g, 2 mmol) and NaOH (0.10 g, 2.4 mmol) in
172 10 mL of solvent (H_2O/CCl_4 = 1/1) was slowly added a solution of
173 trifluoromethanesulfonic anhydride (0.19 mL, 2.4 mmol) in 5 mL of CCl_4
174 at 0 °C under stirring, and the mixture was continuously stirred for 3 h
175 until the reaction was complete as indicated by TLC. Dichloromethane
176 and water were added to separate the organic phase, and the aqueous
177 phase was extract with dichloromethane three times. The combined
178 organic phase was washed, dried, concentrated in vacuo, and further
179 purified by flash chromatography on silica gel using petroleum ether and
180 ethyl acetate (v/v = 5:1) to give the target compound **6x** (0.58 g, yield
181 71%).

182

183 **Biological Assays**

184 Biological assays of the activities of the test compounds against mites and
185 various insects were conducted according to literature procedures[29–32] at

186 25 ± 1 °C in a greenhouse. The assay details are provided in Supporting
187 Information.

188 *Acaricidal Activity against Eggs and Larvae of T. cinnabarinus.* Each test
189 compound was dissolved in acetone, and the acetone solution was diluted
190 with distilled water to the desired concentration (200–0.05 mg/L). Fresh
191 sieva bean leaves infested with mite eggs or larvae (60–100 eggs or
192 larvae per leaf) were dipped into the test solution and swirled around for 3
193 s and then placed in a tube (10 cm inner diameter) lined with a piece of
194 filter paper. The bioactivities were evaluated 4 days after treatment and
195 are reported as mortality percentages, where 0% indicates no activity and
196 100% indicates total kill.

197 *Larvicidal Activities against Cotton Bollworm (Helicoverpa armigera),*
198 *Corn Borer (Ostrinia nubilalis), and Oriental Armyworm (Mythimna*
199 *separata)*. Disks (diameter approximately 5 cm) were cut from fresh corn
200 leaves and then dipped into the prepared test solution and swirled around
201 for 3–5 s. After air-drying, each treated leaf disk was placed in a glass
202 vessel (7 cm diameter), and 10 third-instar larvae were added to the vessel
203 and lined with a piece of filter paper. Percentage mortality was evaluated
204 4 days after treatment. Leaves treated with acetone were used as controls.

205 *Larvicidal Activity against Mosquito (Culex pipiens pallens).* Twenty
206 fourth-instar mosquito larvae were placed in 10 mL of the test solution,
207 and after 8 days, the number of dead larvae were counted. Results are

expressed as mortality percentages.

Statistical Analysis

Each treatment was carried out three times. The mortality data given in Tables 1–4 are means ± SDs for the three replicates. Linear regression equations and correlation coefficients were obtained with four or five sets of data in Tables 2 and 3 by means of the DPS Data Processing System software. LC_{50} values were auto-calculated and are reported with 95% confidence intervals.

RESULT AND DISCUSSION

Chemistry

The route used to synthesize the test compounds is outlined in Scheme 1. Briefly, key intermediate **5** was prepared from 2,6-difluorobenzamide (**1**) via a sequence involving condensation with dimethylchloroacetal, a Friedel–Crafts reaction with anisole, demethylation with BBr_3, and oxazoline ring formation. Because a mixture of *para*- and *ortho*-methoxy-substituted isomers was obtained from the Friedel–Crafts reaction and the isomers had similar polarities, they were not separated prior to the demethylation reaction. After the methyl group had been removed, the reaction mixture was allowed to stir long enough to ensure that phenol **4** was completely dissolved in the solvent, so that it could be separated by filtration from the precipitate (H_3BO_3) that formed when the

BBr_3 was quenched.[33] Under alkaline conditions, **4** cyclized to give oxazoline **5**. Analysis of structure–activity relationships has indicated that *para*-substitution on the 4-phenyl group is beneficial for bioactivity,[9,10] so *para*-hydroxyphenyl compound **5** was purified from other isomers by means of column chromatography. Note that in an attempt to avoid the formation of *ortho*-isomers in the Friedel–Crafts reaction, we explored the use of various phenyl ethers, but only *t*-butoxybenzene worked. However, owing to the difficulty of synthesizing *t*-butoxybenzene and the high cost of obtaining it from commercial suppliers, we chose anisole. Isoxazole **5** reacted with various sulfonyl chlorides and sulfonyl anhydride to afford target compounds **6a–x** (60–96%) in moderate to high yields, except in the cases of **6r** and **6s** (22 and 44%, respectively).

Biological Activities and Structure–Activity Relationships

Activities against T. cinnabarinus Larvae and Eggs. The acaricidal activities of compounds **6a–x** and etoxazole (as a control) against larvae and eggs of mites were tested (Table 1). Most of the sulfonate--containing compounds displayed good to excellent larvicidal and ovicidal activities. Among the alkanesulfonates (**6a–e**), **6c** (which has a medium-length *n*-propyl group) had much higher activities than **6a** (methyl), **6b** (ethyl), and **6d** (*n*-butyl). Benzenesulfonates with a straight-chain alkane substituent (**6a**–**d)** showed similar or better larvicidal activities than cyclohexane-substituted compound **6e**. For

benzenesulfonates **6g** to **6j**, the phenyl group of which has a *para*-halogen atom, the activities against both larvae and eggs increased as the electronegativity of the halogen atom decreased, except in the case of I-substituted compound **6j**. There were no obvious differences between the activities of *para*-F-, *ortho*-F-, and *meta*-F-substituted compounds **6g**, **6k**, and **6l**. The activities of **6n** and **6o** (which have two and three F atoms, respectively) were higher than the activities of the mono-F-substituted compounds (**6g**, **6k**, and **6l**). Compared with compounds bearing a strongly electron-withdrawing group, such as **6m** and **6w**, compound **6q**, which has an electron-donating *t*-butyl group, possessed higher larvicidal and ovicidal activities. Finally, vinyl-substituted compound **6f** and trifluoromethyl-substituted compound **6x** showed only moderate acaricidal activities.

Because **6c**, **6i**, and **6q** showed the best bioactivities against both larvae and eggs, their activities were assayed at lower concentrations, and LC_{50} values were calculated for both larvae and eggs (Tables 2 and 3). Compounds **6c** and **6i** (LC_{50} = 0.066 ± 0.021 and 0.073 ± 0.021 mg/L, respectively) showed larvicidal activities comparable to that of etoxazole (0.091 ± 0.051 mg/L). Remarkably, however, *t*-butylphenyl-substituted compound **6q** exhibited a lower LC_{50} (0.022 ± 0.009 mg/L) against larvae than that of etoxazole. In addition, the ovicidal activities of **6c** and **6q** (0.043 ± 0.031 and 0.044 ± 0.020 mg/L) were lower than that of

etoxazole (0.095 ± 0.059 mg/L). Taken together, these results suggest that benzenesulfonate **6q** deserves to be further studied.

Activity against Mosquito Larvae and Lepidopteran Pests. We also evaluated the activities of **6a–x** and etoxazole against mosquito larvae (Table 4). Most of the compounds showed 100% mortality at 10 mg/L, whereas treatment with etoxazole resulted in only 70% mortality. Notably, the mortalities of **6d**, **6g**, **6h**, and **6k** were 60% or more at 2 mg/L. Compound **6h** showed 100% mortality at 2 mg/L, exhibiting the best insecticidal activity against mosquito larvae of all the tested compounds. In contrast, the activities of **6a**–**x** against lepidopteran pests (cotton bollworm, corn borer, and oriental armyworm) (see Supporting information) were not as high as those against mosquito: most of the test compounds showed mortalities lower than 60% even at a concentration of 600 mg/L.

In summary, we designed and synthesized a series of novel sulfonate-containing 2,4-diphenyl-1,3-oxazoline derivatives and assayed their acaricidal activity. All of the test compounds exhibited good larvicidal and ovicidal activity against spider mites, and one compound in particular—4-*t*-butylphenyl-substituted compound **6q**—showed higher activities than etoxazole. Our results indicate that oxazoline derivatives containing a sulfonate group are worthy of further study.

ASSOCIATED CONTENT

Supporting Information. The physical data and spectra of all target compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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410
411

413 **Figure Captions**

414 Figure 1. Inspirations for the Design of Sulfonate-Containing Oxazolines **6a**–**x**.

415 Scheme 1. Synthesis and Chemical Structures of Sulfonate-Containing Oxazolines

416 **6a**–**x**.

417

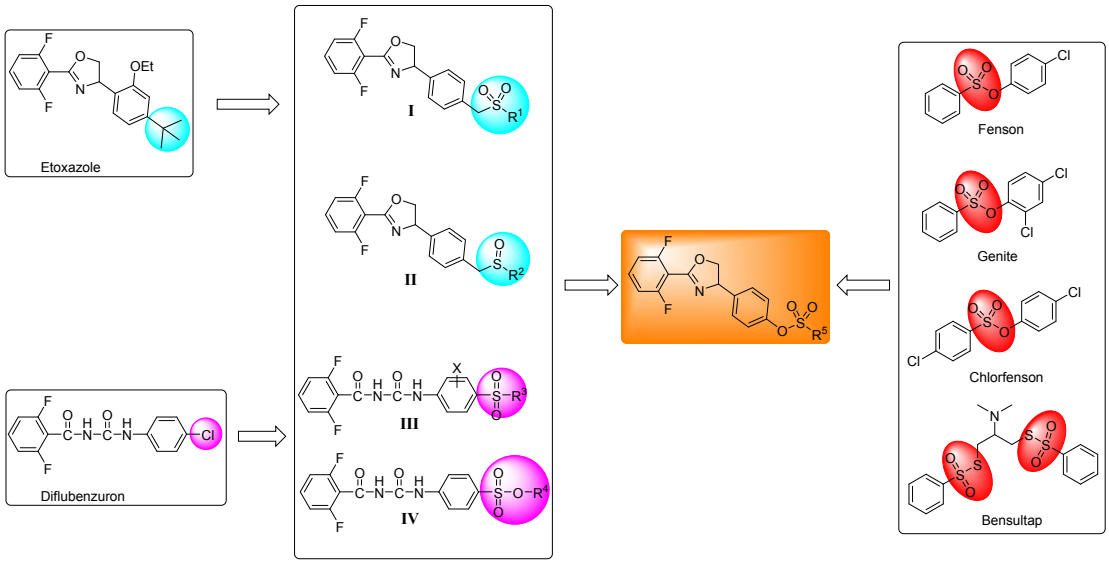
418

419

420

422 Figure 1

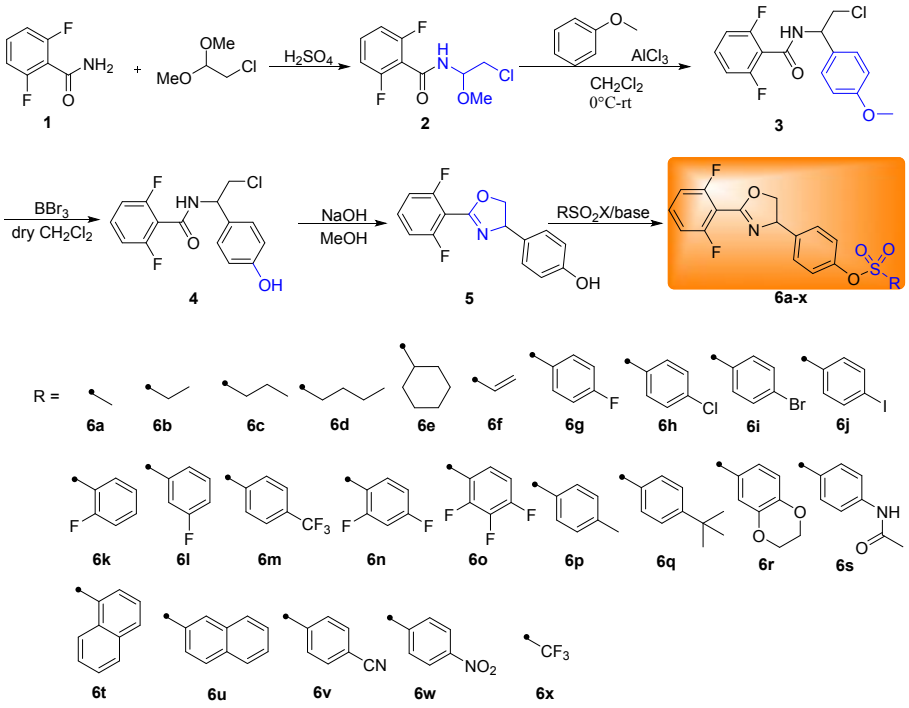
423



424

425

427 Scheme 1



428

430 Table 1. Mortalities of Oxazolines **6a**–**x** and Etoxazole against Carmine Spider Mite

431 Larvae and Eggs[a]

Compound	Mortality (%) against larvae					Mortality (%) against eggs				
	200 mg/L	100 mg/L	10 mg/L	1 mg/L	0.1 mg/L	200 mg/L	100 mg/L	10 mg/L	1 mg/L	0.1 mg/L
6a	100	100	100	80 ± 5	50 ± 0	100	93.3 ± 2.9	80 ± 0	70 ± 0	—
6b	100	100	90 ± 0	60 ± 0	—	100	93.3 ± 2.9	80 ± 0	50 ± 0	—
6c	**100**	**100**	**100**	**100**	**80 ± 0**	**100**	**100**	**100**	**90 ± 0**	**50 ± 0**
6d	100	100	100	90 ± 0	60 ± 0	100	93.3 ± 2.9	85 ± 5	60 ± 0	—
6e	100	100	90 ± 0	60 ± 0	—	100	100	90 ± 0	70 ± 0	—
6f	100	80 ± 0	80 ± 0	60 ± 0	—	100	80 ± 0	60 ± 0	—	—
6g	100	100	90 ± 0	50 ± 0	—	100	100	90 ± 0	58.3 ± 5.8	—
6h	100	100	95 ± 0	86.6 ± 5.8	60 ± 0	100	95 ± 0	90 ± 0	70±0	—
6i	**100**	**100**	**100**	**100**	**70** ± 0	**100**	**100**	**90 ± 0**	**73.3 ± 5.8**	**30 ± 0**
6j	100	100	86.7 ± 5.8	63.3 ± 5.8	—	100	100	86.7 ± 5.8	58.3 ± 5.8	—
6k	100	100	90±0	80 ± 0	50 ± 0	100	93.3 ± 2.9	80 ± 0	50 ± 0	—
6l	100	100	90±0	50 ± 0	—	100	100	90 ± 0	56.7 ± 5.8	—
6m	100	100	95±0	80 ± 0	58.3 ± 5.8	100	100	90 ± 0	70 ± 0	—
6n	100	100	95±0	80 ± 0	58.3 ± 5.8	100	90 ± 0	86.7 ± 5.8	50 ± 0	—
6o	100	100	100	90 ± 0	58.3 ± 5.8	100	100	93.3 ± 5.8	66.7 ± 5.8	—
6p	100	100	86.7 ± 5.8	70 ± 0	—	100	91.7 ± 2.9	70 ± 0	50 ± 0	—
6q	**100**	**100**	**100**	**96.7 ± 2.8**	**85**	**100**	**100**	**96.7 ± 2.9**	**90 ± 0**	**46.7 ± 5.8**
6r	100	90 ± 0	70 ± 0	50 ± 0	—	100	70 ± 0	50 ± 0	—	—

6s	100	100	93.3 ± 2.8	70 ± 0	—	100	95 ± 0	90 ± 0	60 ± 0	—
6t	100	90 ± 0	80 ± 0	53.3 ± 5.8	—	100	80 ± 0	70 ± 0	30 ± 10	—
6u	100	100	100	95 ± 0	63.3 ± 5.8	100	95 ± 0	90 ± 0	63.3 ± 5.8	—
6v	100	95 ± 0	70 ± 0	40 ± 0	—	100	93.3 ± 2.9	70 ± 0	46.7 ± 5.8	—
6w	100	70 ± 0	30 ± 10	—	—	90	80 ± 0	40 ± 0	—	—
6x	100	90 ± 5	73.3 ± 5.8	60 ± 0	—	100	90 ± 0	70 ± 0	56.7 ± 5.8	—
Etoxazole	100	100	100	90 ± 0	63.3 ± 5.8	100	100	95 ± 0	80 ± 0	30 ± 0

[a]Values are means ± SDs (n = 3).

435 Table 2. Mortalities and LC_{50} Values for Oxazolines **6c**, **6i**, and **6q** and Etoxazole

436 against Carmine Spider Mite Larvae

Compound	Mortality (%)[a] against larvae and LC_{50} values								
	10 mg/L	1 mg/L	0.5 mg/L	0.1 mg/L	0.05 mg/L	0.01 mg/L	Formula (y = ax + b)	LC_{50}[b]	Correlation coefficient
6c	100[a]	100	95 ± 5	80 ± 0	40 ± 0	—	$y = 3.39x + 9.01$	0.066 ± 0.021	0.90
6i	100	100	90 ± 0	70 ± 0	40 ± 0	—	$y = 3.38x + 8.83$	0.073 ± 0.021	0.87
6q	100	95 ± 5	90 ± 0	86.7 ± 5.8	50 ± 0	36.7 ± 5.8	$y = 1.67x + 7.45$	**0.022** ± 0.009	0.94
Etoxazole	100	90 ± 0	80 ± 0	63.3 ± 5.8	30 ± 0	—	$y = 1.24x + 6.29$	0.091 ± 0.051	0.96

437 [a]Mortality percentages are means ± SDs (n = 3). [b]Values are given with 95% confidence intervals.

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Table 3. Mortalities and LC_{50} Values for Oxazolines **6c**, **6i**, and **6q** and Etoxazole against Carmine Spider Mite Eggs

Compound	Mortality (%)[a] against eggs and LC_{50} values							
	1 mg/L	0.5 mg/L	0.1 mg/L	0.05 mg/L	0.01 mg/L	Formula (y = ax + b)	LC_{50}[b]	Correlation coefficient
6c	100	90 ± 5	76.7 ± 5.8	50 ± 0	20 ± 0	$y = 1.28x + 6.75$	**0.043** ± 0.031	0.99
6i	90 ± 0	75 ± 5	60 ± 0	30 ± 0		$y = 1.21x + 6.21$	0.101 ± 0.058	0.96
6q	96.7 ± 2.9	90 ± 5	78.3 ± 2.9	45 ± 5		$y = 1.33x + 6.81$	**0.044** ± 0.020	0.96
Etoxazole	95 ± 5	80 ± 0	60 ± 0	30 ± 0		$y = 1.48x + 6.52$	0.095 ± 0.059	0.97

[a]Mortality percentages are means ± SDs (n = 3). [b]Values are given with 95% confidence intervals.

446 Table 4. Mortalities of Oxazolines **6a**–**x** and Etoxazole against Mosquito Larvae

Compound	Mortality (%)[a] against mosquito larvae			
	10 mg/L	5 mg/L	2 mg/L	1 mg/L
6a	100	20 ± 10	—	—
6b	100	60 ± 5	—	—
6c	100	31.3 ± 2.9	—	—
6d	**100**	**100**	**68.3 ± 2.9**	—
6e	100	50 ± 5	—	—
6f	61.7 ± 2.9	—	—	—
6g	**100**	**100**	**60 ± 5**	—
6h	**100**	**100**	**100**	**20 ± 5**
6i	68.3 ± 5.8	—	—	—
6j	100	63.3 ± 5.8	—	—
6k	**100**	**100**	**78.3 ± 2.9**	—
6l	100	50 ± 0	—	—
6m	100	30 ± 5	—	—
6n	100	30 ± 10	—	—
6o	100	50 ± 5	—	—
6p	100	51.7 ± 2.9	—	—
6q	71.7 ± 2.9	—	—	—
6r	100	53.3 ± 5.8	—	—
6s	60 ± 5	—	—	—
6t	60 ± 0	—	—	—
6u	40 ± 10	—	—	—
6v	100	40 ± 0	—	—
6w	61.7 ± 2.9	—	—	—
6x	68.3 ± 2.9	—	—	—
Etoxazole	70 ± 5	—	—	—

447 [a]Mortality percentages are means ± SDs (n = 3).

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Graphical Abstract

Agricultural and Environmental Chemistry