

Design, synthesis, and insecticidal activities of the novel sulfur-containing meta-amide compounds as potential pesticides

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Abstract

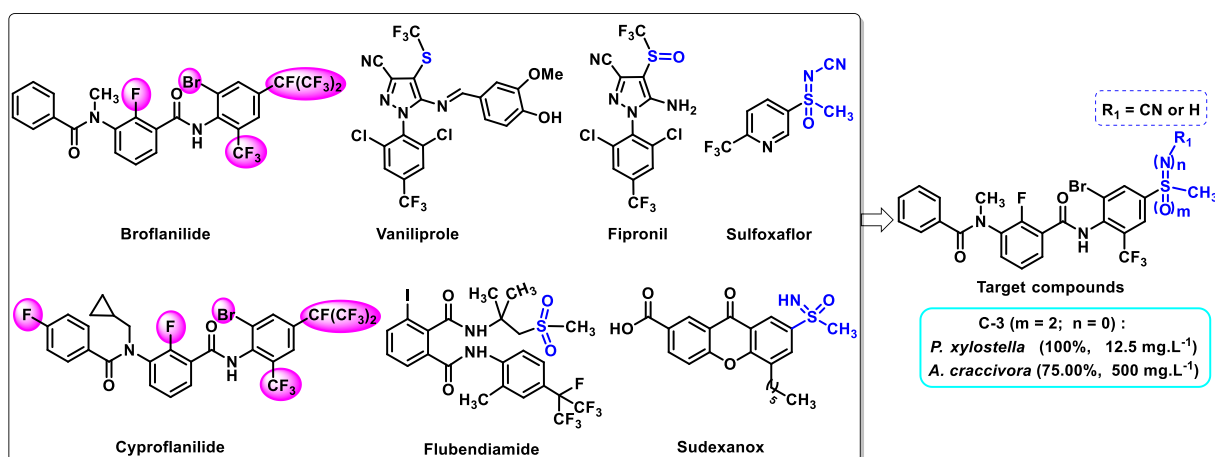
The potential risks associated with the high halogen content of typical meta-amide (*m*-diamide) insecticides aroused concerns among researchers. Hoping to make discoveries by introducing sulfur elements with good environmental compatibility, a series of novel sulfur-containing *m*-amide derivatives **C** were synthesized through exploration under mild conditions according to the literature. And the structures were confirmed by melting points, ¹H NMR, ¹³C NMR, ¹⁹F NMR, and HRMS. It was found that some target compounds **C** exhibited moderate to high insecticidal activities against *Aphis craccivora* (38.89%–75.00%) and *Plutella xylostella* (93.33%–100.00%) at 500 mg.L⁻¹. Especially, the sulfone-containing compound **C-3** revealed superior lethality rates against *P. xylostella* (100%, 12.5 mg.L⁻¹) and *A. craccivora* (75.00%, 500 mg.L⁻¹), suggesting its potential as a leading compound for further investigation.

Keywords

insecticidal activities, *m*-diamine, structure–activity relationship, sulfide, synthesis

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The novel sulfur-containing meta-amide (*m*-diamide) derivatives were synthesized through exploration, which had certain lethal rates against *A. craccivora* (38.89%–75.00%) and *P. xylostella* (93.33%–100.00%) at 500 mg.L⁻¹. Notably, the sulfone-containing compound **C-3** revealed lethal rates (100%, 12.5 mg.L⁻¹) against *P. xylostella* better than others, which could be further explored as a new leading compound. The results might provide valuable insights for future research on *m*-amide pesticides.



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Introduction

Broflanilide (BASF and Mitsui Chemicals, Inc.) and Cyproflanilide (Tahoe Group) (Figure 1) as the typical representatives of *m*-diamide insecticide that acts on γ -aminobutyric acid (GABA) receptors, which regulates the transmission of chloride ions into cells causing pests to vomit and excite until killing them.¹⁻³ The excellent insecticidal activities and unique meta-amide structure of these compounds have swiftly captured the attention of pesticide researchers.^{4,5} Structural analysis revealed that the halogen content in Broflanilide and Cycloflanilide accounts for more than 50% of the total molecular weight, primarily attributed to the presence of fluorine atom, bromine atom, trifluoromethyl, and heptafluoroisopropyl groups. The high halogen content in *m*-diamide insecticides raised concerns regarding their hydrophilicity and environmental compatibility.⁶ In particular, the fluorinated groups were often introduced into drug molecules since their excellent biological activities.⁷ However, the environmental impact of fluorinated organic compounds remains a significant concern. Consequently, the novel target compounds were designed to reduce fluorine content while preserving insecticidal efficacy, thereby enhancing environmental suitability.

The sulfur-containing structure has consistently been a focal point in scientific research due to its diverse biological activities and easily derivatized structural characteristics.^{8,9} Thioethers, sulfoxides, sulfones, and sulfoximine are common derivative structures of sulfur, which make the corresponding compounds show excellent biological activities in the fields of pesticides and pharmaceuticals. For example, Vaniliprole,¹⁰ Fipronil,¹¹ Sulfoxaflor,¹² and Flubendiamide¹³ (Figure 1) revealed effective insecticidal and acaricidal properties. Moreover, sudexanox with sulfoximine structure was utilized as an antibacterial agent. Recently, the Long et al.¹⁴ group reported a series of compounds revealed good insecticidal activity against *Nilaparvata lugens* (98.92%, 100 mg·L⁻¹) by substituting sulfur for the trifluoromethyl group in the leading compound—Cyproflanilide. Therefore, developing new *m*-diamide compounds containing sulfur derivatives as potential insecticidal could be a significant avenue in future pesticide research.

Based on the above reasons, this report detailed the introduction of sulfur derivative structures into the leading *m*-diamide insecticide—Broflanilide. The modification replaced the high-fluorine group—heptafluoroisopropyl with sulfur derivatives, aiming to reduce the halogen content. Exploring the synthesis route and insecticide activities of target sulfur-containing compounds (Figure 1), and summarizing the structure–activity relationship (SAR), which might provide valuable insights for the future research on sulfur-containing *m*-diamide compounds.

Results and discussion

Chemistry

In Scheme 1, the key intermediate thioether-containing *m*-amide compound (**6**) could be smoothly prepared from 4-fluoro-2-(trifluoromethyl)nitrobenzene as the starting material *via* a linear reaction route through conventional reactions such as reduction reaction, nucleophilic addition reaction, and electrophilic substitution reaction. Regrettably, we endeavored to synthesize the target compound **C-1** as depicted in Scheme 1 during the exploration process, utilizing an electrophilic substitution reaction with *N*-bromosuccinimide (NBS). While the actual product obtained was verified by ¹H NMR and HRMS. It found that two amide hydrogens appeared in δ 10.25 and 10.11 indicating the loss of N-CH₃. However, the inferred structure could not be conclusively determined in conjunction with the HRMS data ($[M + H]^+$: 583.1355). Addressing this ambiguity remains an objective for our future research endeavors.

So, a bilinear synthesis route was proposed (Scheme 2) based on Aoki et al.¹⁵ In the course of exploration (Table 1), the reaction cannot proceed as effectively as reported in the literature when NaBr was used as the initiator.¹⁶ Therefore, a switch to KI was deemed necessary to facilitate the reaction,¹⁴ considering the nucleophilic substitution mechanism. The choice of KI was influenced by the superior nucleophilic and leaving group properties of iodide ions. Ultimately, the target compound **C-1** was successfully prepared with 2-bromo-4-(methylthio)-6-(trifluoromethyl)

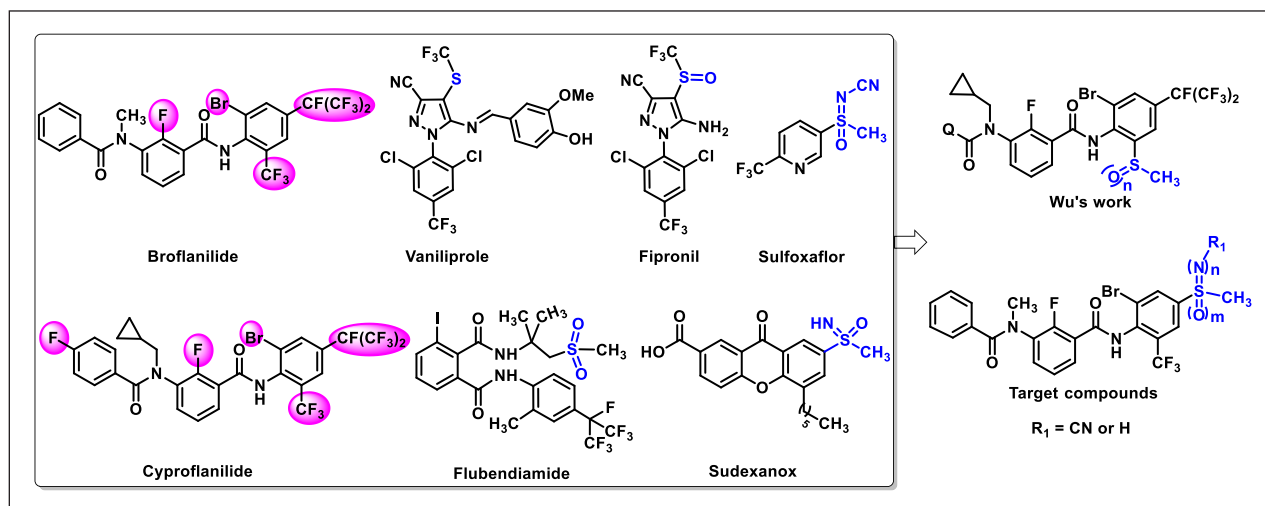
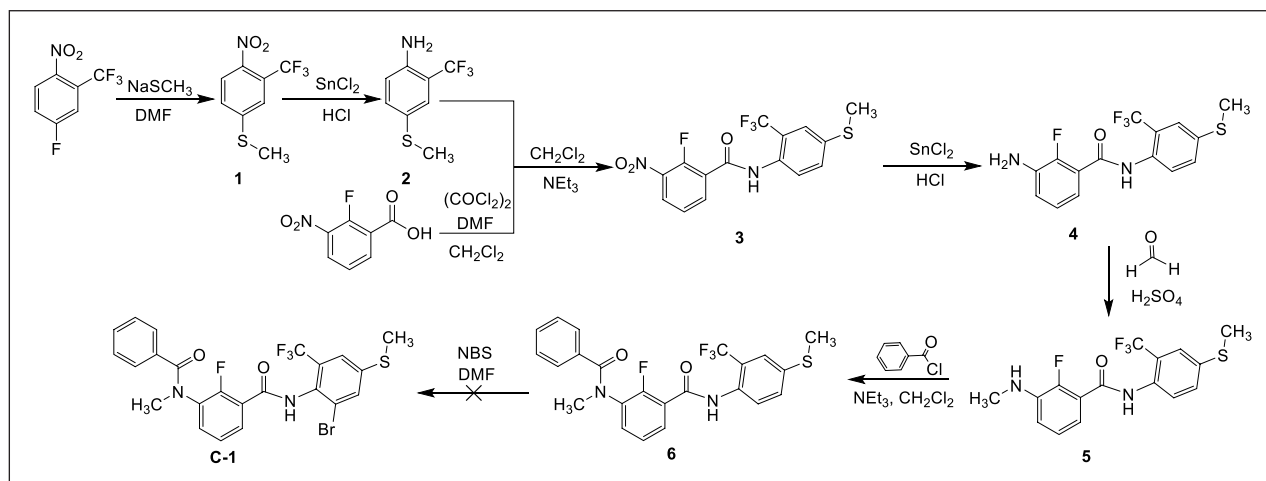
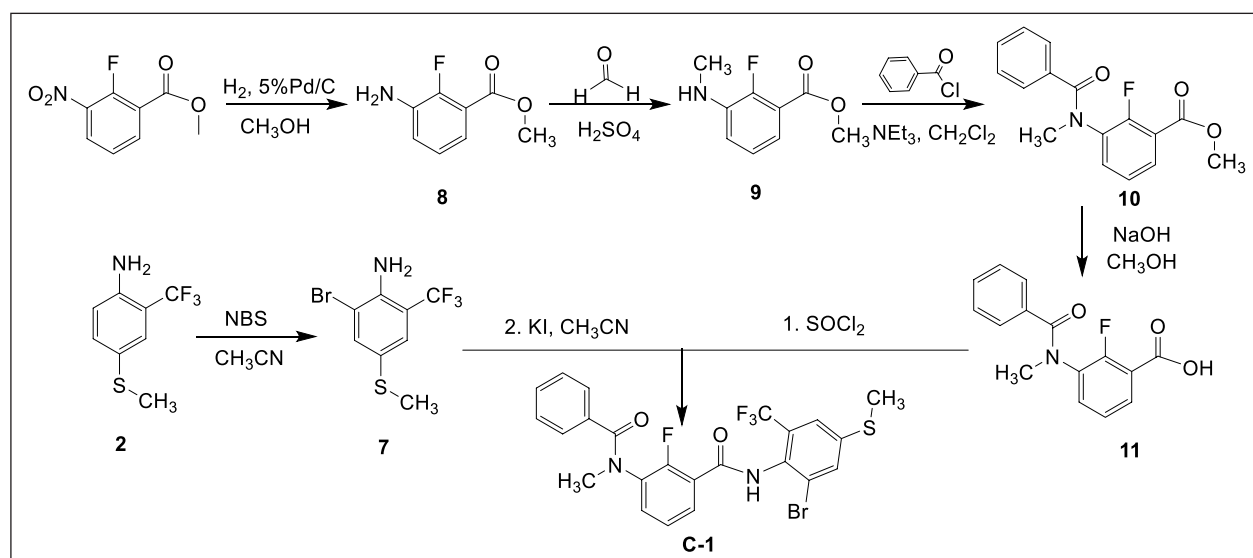


Figure 1. The structures of two *m*-diamide and sulfur-containing drugs, and the designed target compounds in this paper.



Scheme 1. Linear synthesis route for a novel *m*-diamide compound containing thioether (**C-I**).



Scheme 2. Bilinear synthesis route for a novel *m*-diamide compound containing thioether (**C-I**).

Table 1. Optimization of reaction conditions for the synthesis compound **C-I** starting with compounds **6** and **11**.

Entry	Initiator	Temp. (°C)	Time(h)	Yield of C-I (%) ^a
1	NaBr	rt	6	0
2	NaBr	reflux	6	0
3	NaBr	reflux	10	0
4	KI	rt	6	0
5	KI	reflux	6	32

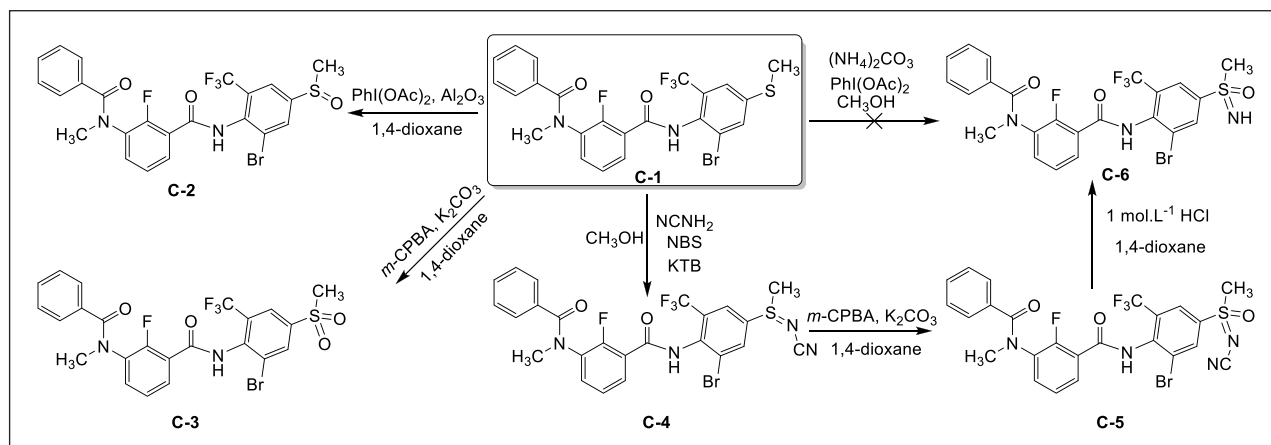
^aIsolated yields.

aniline (**7**) and the corresponding acyl chloride, achieving a yield of 32% with KI as a nucleophilic catalyst.

The intermediate compounds **1–11** were smoothly synthesized through exploration according to Aoki et al.¹⁵ and Zhang et al.,¹⁶ which were applicable exclusively for exploring the synthetic pathways of the intermediate compounds. Compounds **1–7** are novel, whereas compounds **8–11** have been previously reported;¹⁵ however, their

relevant data have not been provided. So comprehensive characterization data and specific synthesis routes for intermediates **1–11** were presented in the Supplemental materials. A significant number of synthetic routes were reported for *m*-diamide pesticides in recent years due to the wonderful insecticidal activities.^{17–19} Consequently, two synthetic routes for novel *m*-diamide target compounds containing thioether were conceptualized depending on literature reports and previous synthesis work experience.

The sulfoxide-containing compound **C-2** (PhI(OAc)₂-Al₂O₃) and sulfone-containing compound **C-3** (*m*-CPBA-K₂CO₃) can be obtained by treating thioether-containing product (**C-1**) with 1,4-dioxane under different oxidant reflux conditions (Scheme 3). For *N*-cyanosulfilimine, **C-4** (Table 2)²⁰ was prepared by NCNH₂ as the nitrogen source with different conditions. Notably, the use of PhI(OAc)₂ as an oxidant at various temperatures yielded suboptimal results for compound **C-4**. When employing NBS and KTB in CH₃OH, and maintaining the reaction at room temperature for 2 h, enhanced the yield to 42%. However, it was



Scheme 3. Synthesis route for novel *m*-diamide compounds containing sulfoxide (**C-2**), sulfone (**C-3**), *N*-cyanosulfilimine (**C-4**), *N*-cyanosulfoximine (**C-5**), and *NH*-sulfoximine (**C-6**).

Table 2. Optimization of reaction conditions for the synthesis compound **C-4** starting with compound **C-1**.

Entry	Reaction condition	Temperature	Yield of C-4 (%) ^a
1 ²⁰	NCNH ₂ , PhI(OAc) ₂ , CH ₃ OH	Room temperature	38
2	NCNH ₂ , PhI(OAc) ₂ , CH ₃ OH	Reflux	35
3	NCNH ₂ , NBS, <i>t</i> -BuOK, CH ₃ OH	Room temperature	42
4	NCNH ₂ , NBS, <i>t</i> -BuOK, CH ₃ OH	Reflux	-

^aIsolated yields.

observed that reflux conditions introduced complexity to the system and hindered the formation of the target product. Treating the *N*-cyanosulfilimine, **C-4** with *m*-CPBA facilitated the smooth conversion to the *N*-cyanosulfoximine compound **C-5**. It was unsuccessful when attempted to synthesize target compound **C-6** from thioether-containing compound **C-1** in a single step according to literature reports.²¹ Instead, it was found necessary to implement an acid dissociation reaction using 1 mol.L⁻¹ HCl, with *N*-cyanosulfoximine **C-5** as the starting material, to synthesize *NH*-sulfoximine **C-6**. However, there was a significant loss during their separation and purification due to the low solubility of the novel compounds (**C-1-C-6**) resulting in low yields (32%–48%).

All of the target *m*-diamide compounds (**C-1-C-6**) were characterized by melting points, ¹H NMR, ¹³C NMR, and ¹⁹F NMR, the consistency between the theoretical and measured values of HRMS further proved the correctness. In ¹H NMR spectra, the characteristic proton peak of amide bond N-H appeared at δ 10.06–10.80 ppm for all *m*-diamide products, among which the signal for compound **6** appeared at δ 10.06 ppm. Chemical structure analysis suggested that this shift toward a lower field and higher position may be attributed to the electron-withdrawing effect of the Br atom adjacent to the amino group. Notably, the *N*-CH₃ signal was consistently found at δ 3.32–3.39 ppm, while the chemical shift range of (X)_n = S-CH₃, influenced by the varying oxidation states of sulfur, was broader (δ 2.56–3.96) exhibiting a discernible pattern. The electron-withdrawing capacity of sulfur-containing groups was observed to increase with the sulfur oxidation state, leading to a sequential trend in chemical shift for (X)_n = S-CH₃:

sulfone (**C-3**, δ 3.46 ppm), *N*-cyanosulfilimine (**C-5**, δ 3.96 ppm), and *NH*-sulfoximine (**C-6**, δ 3.53 ppm) > sulfoxide (**C-2**, δ 2.90 ppm) and *N*-cyanosulfoximine (**C-4**, δ 3.28 ppm) > thioether (**C-1**, δ 2.85 ppm). When the sulfur oxidation state remained constant, it was evident that compounds with X = *N*-CN exhibited higher shifts than those with X = O, due to the stronger electron-withdrawing ability of *N*-CN group (**C-4** (δ 3.28 ppm) > **C-2** (δ 2.90 ppm); **C-5** (δ 3.96 ppm) > **C-3** (δ 3.46 ppm)). Moreover, the typical proton chemical shift for the O = S = NH group of **C-6** appeared at δ 4.04 ppm. The ¹⁹F NMR spectra distinctly and clearly resolved the signals for the CF₃ (δ -60.83 to -60.53 ppm) and F (δ -123.31 to 123.05 ppm) in the target compounds.

Biology

The insecticidal activities data of target compounds **C-1-C-6** against *Plutella xylostella*, *N. lugens*, and *Aphis craccivora* Koch are listed in Table 3. Most compounds exhibited 100.00% larvicidal activity against *P. xylostella* at 500 mg·L⁻¹, with compound **C-3** exhibiting remarkable inhibitory rates, which maintained 100.00% inhibition rate even at the concentration of 12.5 mg·L⁻¹ keeping pace with Broflanilide. While for *N. lugens* at the same concentration, all of the compounds showed poor lethal rates, leading to the inference that these sulfur-containing compounds had no significant inhibitory effect on *Delphacidae*. The target compounds had certain lethal rates (4.60%–75.00%) against *A. craccivora* at 500 mg·L⁻¹, it was noteworthy that compounds **C-2** (75.00%) and **C-3** (74.07%) showed better insecticidal activities than Broflanilide.

Table 3. Insecticidal activity of target compounds against *P. xylostella*, *N. lugens*, and *Aphis craccivora* Koch.

No.	Lethal rate (%) at a concentration of (mg·L ⁻¹)						
	<i>P. xylostella</i>					<i>N. lugens</i>	<i>A. craccivora</i>
	500	200	50	25	12.5	500	500
C-1	100.00	100.00	0.00	-*	-	0.00	47.25
C-2	100.00	60.00	-	-	-	3.13	75.00
C-3	93.33	100.00	100.00	100.00	100.00	0.00	74.07
C-4	93.33	0.00	-	-	-	0.00	38.89
C-5	0.00	-	-	-	-	4.76	45.65
C-6	100.00	0.00	-	-	-	0.00	4.60
Broflanilide	100.00	100.00	100.00	100.00	100.00	0.00	50.00
Dinotefuran	-	-	-	-	-	100	100
Blank control	0	0	0	0	0	0	0

* -: not test.

As shown in Table 3, the SARs can be deduced: For *P. xylostella*, the larvicidal activity sequence of the (X)_n = S-CH₃ was identified as sulfone (**C-3**, 12.5 mg·L⁻¹: 100.00%) > thioether (**C-1**, 200 mg·L⁻¹: 100%) > sulfoxide (**C-2**, 200 mg·L⁻¹: 60%) > NH-sulfoximine (**C-6**, 500 mg·L⁻¹: 100%) > N-cyanosulfoximine (**C-4**, 500 mg·L⁻¹: 93.33%) > N-cyanosulfilimine (**C-5**, 500 mg·L⁻¹: 0.00%). It indicated that the insecticidal activity of sulfur oxides (**C-3** and **C-2**) was significantly superior to that of sulfur nitrogen oxides (**C-6**, **C-4**, and **C-5**). Especially the sulfone compound (**C-3**) with stronger electron-withdrawing ability was favorable for the improvement of the bioactivity. Through SAR analysis, it was found that sulfur oxides compounds (**C-2** (75.00%) and **C-3** (74.07%)) were markedly more effective than the thioether compound (**C-1** (47.25%)) and sulfur nitrogen oxides compounds (**C-6** (45.65%), **C-4** (38.89%), and **C-5** (4.60%)) against *A. craccivora*, mirroring the pattern observed against *P. xylostella*. Based on these findings, we speculated that the sulfur-containing *m*-amide compounds as design in the paper possess significant insecticidal activities against *P. xylostella* and *A. craccivora*. In addition, the sulfone-containing target compound **C-3** exhibited substantially higher bioactivities compared with the others.

Conclusion

Novel sulfur-containing *m*-amide target compounds **C-1**–**C-6** were synthesized through exploration by referencing and improving literature, which were characterized by melting points, ¹H NMR, ¹³C NMR, ¹⁹F NMR, and HRMS. The mild preparation of thioether-containing compound (**C-1**) was achieved by cleverly utilizing I⁻ with good nucleophilicity and departure properties, thereby circumventing the need for harsh conditions such as strong bases and low temperatures. The biological activity assays revealed that the target compounds **C** exhibited moderate to high insecticidal activities in preliminary screenings against *A. craccivora* and *P. xylostella*. Particularly noteworthy was the sulfone-containing compound **C-3**, which demonstrated superior lethal rates against *P. xylostella* (100% at 12.5 mg·L⁻¹) and *A. craccivora* (75.00% at 500 mg·L⁻¹) compared with the other compounds. And the SAR of these

compounds was investigated, offering valuable insights for the synthesis of novel sulfur-containing *m*-amide structures with potent insecticidal properties. However, it should be noted that the racemic compounds **C-2**, **C-4**, **C-5**, and **C-6** are chiral with respect to their sulfur atoms. The two enantiomers in each case of these compounds are likely to possess different biological activities, which should be given sufficient attention in future biological activities exploration work.

Experimental

Chemistry

Reagents and solvents were purchased from Titan Corporation and used without further purification. Melting points were measured by the SGWX-4B melting point analyzer and uncorrected. NMR spectra were recorded on a Bruker Avance NEO (400, 101, 376 MHz) spectrometer, using DMSO-*d*₆ (TMS as the 0 point internal standard) as the solvent. EI-MS data were analyzed by LCMS-8040 with ESI ionization. HRMS data were obtained on Thermo Q Exactive Focus with ESI ionization.

Synthesis

Synthesis of compound **C-1**; general procedure

Method 1. The thioether-containing target compound **C-1** was prepared by compound **6** (2 mmol), and NBS (2.4 mmol) was added to 5 mL of *N,N*-dimethylformamide (DMF), and the reaction system was heated to reflux state and monitored by Thin Layer Chromatography (TLC) until the reaction was complete (about 6 h) (Scheme 1).¹⁶ Upon completion of the reaction, 20 mL of water was added into the system, extraction and drying were performed, and then the target product was obtained by column chromatography purification. Despite these efforts, the anticipated product **C-1** was not obtained, as determined through structural analysis.

Method 2. The synthesis of the target compound **C-1** began with the preparation of benzoyl chloride, which was achieved by reacting the corresponding acid **11** (5

mmol) with thionyl chloride (SOCl₂) in a 100 mL round-bottom flask (Scheme 2). Then, 2-bromo-4-(methylthio)-6-(trifluoromethyl)aniline (**7**, 5 mmol), potassium iodide (6.5 mmol), and 10 mL of acetonitrile were added.¹⁵ After that, the reaction mixture was warmed to a reflux state and maintained for 6 h (monitored by TLC). The residue was dissolved in dichloromethane (30 mL) and was washed with salt water. The organic phase was dried using Na₂SO₄ and column chromatography gave the target compound **C-1**.

Compound C-1: Brown solid; 32%; m.p. 125-126 °C; ¹H NMR (400 MHz, DMSO) δ 10.24 (s, 1H, -NH), 8.08 (s, 1H, Ph-H), 8.04 (s, 1H, Ph-H), 7.84 (d, *J* = 8.2 Hz, 1H, Ph-H), 7.59-7.52 (m, 2H, Ph-H), 7.36-7.28 (m, 5H, Ph-H), 3.32 (s, 3H, N-CH₃), 2.85 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO) δ 170.6, 163.4, 146.1, 137.3, 135.9, 134.1, 133.2, 131.7, 130.4, 129.6, 129.5, 129.4, 129.0, 128.5, 128.0, 126.4, 125.4, 124.8, 122.6, 43.5, 39.5. ¹⁹F NMR (376 MHz, DMSO) δ -60.53 (-CF₃), -123.22 (-F). HRMS (ESI): *m/z* calcd for C₂₃H₁₈BrF₄N₂O₂S [M + H]⁺ 541.0208, found 541.0203.

Synthesis of compound C-2; general procedure. Thioether-containing compound (**C-1**, 1 mmol) was dissolved in 10 mL of 1,4-dioxane with 3 mmol of PhI(OAc)₂ and 1 mmol of Al₂O₃ and then warmed to reflux stirring for 6 h (monitored by TLC).²² After that concentrated, the residue was dissolved in 20 mL of CH₂Cl₂. The organic phase was washed with brine and dried by Na₂SO₄. The sulfoxide-containing compound **C-2** was afforded by further purification through column chromatography.

Compound C-2: Yellow solid; 43%; m.p. 105-106 °C; ¹H NMR (400 MHz, DMSO) δ 10.60 (s, 1H, NH), 8.33 (s, 1H, Ph-H), 8.09 (s, 1H, Ph-H), 7.57-7.54 (m, 2H, Ph-H), 7.40-7.28 (m, 6H, Ph-H), 3.35 (s, 3H, N-CH₃), 2.90 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO) δ 170.6, 163.1, 156.0, 153.5, 136.0, 133.2, 133.0, 132.62, 132.6, 132.5, 130.4, 129.2, 128.4, 128.0, 125.1, 124.3, 121.9, 121.6, 120.6, 43.4, 40.3. ¹⁹F NMR (376 MHz, DMSO) δ -60.64 (-CF₃), -123.31 (-F). HRMS (ESI): *m/z* calcd for C₂₃H₁₈BrF₄N₂O₃S [M + H]⁺ 557.0158, found 557.0153.

Synthesis of compound C-3; general procedure. Thioether-containing compound (**C-1**, 1 mmol) was dissolved in 10 mL of 1,4-dioxane with 3 mmol of *m*-CPBA and 1 mmol of K₂CO₃, warmed to reflux, and maintained for about 4 h (monitored by TLC).²² After that concentrated, the residue was dissolved 20 mL of CH₂Cl₂. The organic phase was washed with brine and dried by Na₂SO₄. The sulfone-containing compound **C-3** was afforded by further purification through column chromatography.

Compound C-3: Yellow solid; 40%; m.p. 120-121 °C; ¹H NMR (400 MHz, DMSO) δ 10.73 (s, 1H, NH), 8.62 (s, 1H, Ph-H), 8.29 (s, 1H, Ph-H), 7.93-7.90 (m, 1H, Ph-H), 7.62-7.53 (m, 2H, Ph-H), 7.40-7.25 (m, 5H, Ph-H), 3.49 (s, 3H, CH₃), 3.36 (s, 3H, N-CH₃). ¹³C NMR (101 MHz, DMSO) δ 170.7, 166.6, 163.1, 142.2, 140.0, 136.1, 135.9, 133.8, 133.2, 131.1, 130.4, 129.3, 129.1, 128.5, 128.2, 127.8, 125.4, 124.0, 121.0, 43.4, 39.5. ¹⁹F NMR (376 MHz, DMSO) δ -60.78 (-CF₃), -123.07 (-F). HRMS (ESI): *m/z*

calcd for C₂₃H₁₈BrF₄N₂O₄S [M + H]⁺ 573.0107, found 573.0102.

Synthesis of compound C-4; general procedure. In the presence of *t*-BuOK as a base, thioether-containing *m*-amide compound (**C-1**, 10 mmol), NCNH₂ (13 mmol), and halogen source NBS (30 mmol) were added in methanol, and the reaction system was maintained for 2 h (monitored by TLC).²³ The reaction system was concentrated under reduced pressure, then the residue was dissolved in 20 mL of CH₂Cl₂, the mixture was washed with brine, and the organic phase was dried over anhydrous Na₂SO₄. After removal of the solvent, the residue was further purified by column chromatography with ethyl acetate, petroleum ether, and methanol (100:100:1) as solvents to afford *N*-cyanosulfilimine **C-4**.

Compound C-4: Brown solid; 42%; 121-122 °C; ¹H NMR (400 MHz, DMSO) δ 10.69 (s, 1H, -NH), 8.61 (s, 1H, Ph-H), 8.33 (s, 1H, Ph-H), 7.60-7.56 (m, 2H, Ph-H), 7.38-7.30 (m, 6H, Ph-H), 3.36 (s, 3H, N-CH₃), 3.28 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO) δ 170.7, 163.2, 155.9, 153.4, 139.2, 138.7, 135.9, 135.1, 133.2, 131.2 (d, *J* = 31.3 Hz), 130.4, 129.1, 128.5, 128.0, 125.4 (d, *J* = 4.0 Hz), 124.5(q, *J* = 273.7 Hz, CF₃), 123.9, 121.1, 39.3, 36.1. ¹⁹F NMR (376 MHz, DMSO) δ -60.67 (-CF₃), -123.11 (-F). HRMS (ESI): *m/z* calcd for C₂₄H₁₇BrF₄N₄O₂S [M + H]⁺ 581.0270, found 581.0262.

Synthesis of compound C-5; general procedure. *N*-cyanosulfilimine **C-4** (4 mmol), *m*-CPBA (12 mmol), and K₂CO₃ (4 mmol) were mixed in methanol (50 mL), and the reaction system was heated to reflux for 3 h (monitored by TLC) and then concentrated under reduced pressure.²³ To the residue, CH₂Cl₂ (30 mL) was added, the mixture was washed with brine, and the organic phase was dried over anhydrous Na₂SO₄. After removal of the solvent, the residue was further purified by column chromatography with ethyl acetate, petroleum ether, and methanol (100:100:2) as solvents to afford the *N*-cyanosulfoximine **C-5**.

Compound C-5: White solid; 35%; 155-157 °C; ¹H NMR (400 MHz, DMSO) δ 10.80 (s, 1H, -NH), 8.76 (s, 1H, Ph-H), 8.39 (s, 1H), 7.92-7.90 (m, 1H, Ph-H), 7.73-7.54 (m, 3H, Ph-H), 7.38-7.30 (m, 4H, Ph-H), 3.96 (s, 3H, CH₃), 3.39 (s, 3H, N-CH₃). ¹³C NMR (101 MHz, DMSO) δ 170.6, 166.6, 163.1, 141.6, 137.8, 136.7, 135.9, 133.8, 133.2, 131.1, 130.4, 129.3, 128.4, 128.0, 125.4 (d, *J* = 4.0 Hz), 124.3, 122.3(q, *J* = 273.7 Hz, CF₃), 112.0, 42.5, 39.3. ¹⁹F NMR (376 MHz, DMSO) δ -60.83 (-CF₃), -123.05 (-F). HRMS (ESI): *m/z* calcd for C₂₄H₁₇BrF₄N₄O₂S [M + H]⁺ 597.0219, found 597.0212.

Synthesis of compound C-6; general procedure. NH-sulfoximine (**C-6**) was obtained by the treatment of *N*-cyanosulfoximine (**C-5**) with 1 mol.L⁻¹ HCl in dioxane refluxing 4 h (monitored by TLC).²⁴ And the reaction system was concentrated under reduced pressure, then the residue was dissolved in 20 mL of CH₂Cl₂, and the mixture was sequentially washed with saturated Na₂HCO₃ and brine. The organic phase was dried over anhydrous Na₂SO₄. After removal of the solvent, the residue was further purified by column

chromatography with ethyl acetate and petroleum ether (2:1) as solvents to afford **C-6**.

Compound C-6: White solid; 60%; 164–166 °C; ¹H NMR (400 MHz, DMSO) δ 10.71 (s, 1H, -NH), 8.53 (s, 1H, Ph-H), 8.22 (s, 1H, Ph-H), 7.62–7.57 (m, 2H, Ph-H), 7.40–7.29 (m, 6H, Ph-H), 4.04 (s, 1H, S = NH), 3.53 (s, 3H, CH₃), 3.36 (s, 3H, CH₃). ¹³C NMR (101 MHz, DMSO) δ 165.8, 163.9, 154.5, 152.0, 134.0, 132.3, 132.2, 130.6, 123.0, 128.7, 128.0, 126.9, 126.8, 126.6, 126.1, 126.0, 125.3, 124.3 (d, *J* = 4.0 Hz), 121.9, 45.6, 39.1. ¹⁹F NMR (376 MHz, DMSO) δ -60.77 (-CF₃), -123.06 (-F). HRMS (ESI): *m/z* calcd for C₂₄H₁₇BrF₄N₄O₂S [M + H]⁺ 572.0267, found 572.0262.

Insecticidal activity assay^{25–27}

Feeding conditions

P. xylostella: Raised indoors with radish seedlings at a temperature of 22 ± 2 °C and a light intensity of 12L:12D.^{25–27}

N. lugens: Raised indoors with water rice seedlings at a temperature of 26 ± 2 °C and a light intensity of 12L:12D.

A. craccivora: Reared indoors with silkworm bean seedlings at a temperature of 22 ± 2 °C and a light intensity of 12L:12D.

Drug preparation. Dissolve the raw materials in DMF to prepare a 1% mother liquor, and dilute with distilled water containing 0.1% Tween 80 to achieve the desired concentration.

Insecticidal activity methods. The lethal rates of the target compounds against *P. xylostella*, *N. lugens*, and *A. craccivora* were investigated in a greenhouse, compared to Broflanilide and a blank control group without medication.

Determination of the activity of *P. xylostella*²⁶: Using the leaf soaking method, gently immerse radish leaves in the prepared test solution for 30 s. Then, transfer the leaves onto plastic culture dishes lined with filter paper and allow them to air-dry in the shade. Each dish was infested with 8 s-instar diamondback moths and placed in an observation room at a temperature of 25 °C. Test results were observed after 48 h. Insects were considered deceased if they exhibited no response or were unable to crawl normally when lightly touched with a brush. Repeat three times for each sample.

Determination of the activity of *N. lugens*²⁷: Using the spray method, select a rice seedling with two leaves and one core and place it in a 6-cm Petri dish. Then, quartz sand was spread on the Petri dish. Each dish was infested with 20 third-instar early brown planthopper nymphs and treated with 2.5-mL spray with Potter spray tower. The dishes were placed in an observation room at a temperature of 25 °C. Test results were observed after 48 h. Insect was deemed deceased if it exhibited no response or was unable to crawl normally when lightly touched with a brush. Repeat three times for each sample.

Determination of the activity of *A. craccivora*²⁷: Using the spray method. Infested with 30 alfalfa aphid nymphs

and treated with 2.5 mL spray with Potter spray tower, and then placed the treated aphids in a 25 °C observation room for cultivation. After 48 h of investigation, the insect bodies were gently touched with tweezers, and the absence of a response was considered an indicator of mortality. Repeat three times for each sample.

Data statistics and analysis. The number of deaths of each processed target was counted and the lethal rate was calculated as follows:

$$\text{Lethal rate (\%)} = \frac{\text{number of dead insects}}{\text{total number of insects}} \times 100\%$$

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Supplemental material

Supplemental material for this article is available online.

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