# Synthesis, insecticidal evaluation of novel 1,3,4-thiadiazole chrysanthemamide derivatives formed by an EDCI/HOBt condensation

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A series of novel pesticides with two components derived from a 1,3,4-thiadiazole and chrysanthemic acid were synthesised via an EDCI/HOBt condensation. These 1,3,4-thiadiazole chrysanthemamides were identified by IR, $^1$H NMR and elemental analyses. Their insecticidal activity was also evaluated.

**Keywords**: 1,3,4-thiadiazole, chrysanthemamide, insecticidal activity

1,3,4-Thiadiazole derivatives have attracted considerable attention because of their diverse biological activity. It has been reported that many of these of these derivatives possess a wide spectrum of insecticidal,[1,2] herbicidal[3] and antimicrobial[4–8] activity. Because of their wide spectrum of biological activity, they have been widely used in agricultural and health pest control. L 1215[9] (Fig. 1), for example, was highly effective against mosquito larvae,[10] *Spodoptera eridania* larvae,[11] and Western Sprucebudworm.[12] Cyhalothrin (Fig. 1) has been reported to effectively control the major resistant strains of the cattle tick (*Boophilus microplus*) and the buffalo fly (*Haematobia irritans exigua*).[13]

1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDCI) is a reactive reagent for activating carboxylic acids in amide bond formation.[14–16] Under these reaction conditions, a number of side reactions can occur, including, racemisation of the amino acid and rearrangement of the active O-acylisourea adduct to the N-acyl urea and guanidine formation. Additives such as 1-hydoxybenzotriazole (HOBt) have often been added in catalytic amounts to help reduce racemisation and also to increase the rate of reaction. After the reaction the EDCI is converted into EDU (Scheme 3) which is easily washed out by water.

In order to develop new insecticidal agents of high potency, we have previously synthesised a series of 1,3,4-thiadiazole chrysanthemamide derivatives using catalysis by PDCP.[17] However, PDCP is caustic and requires harsh reaction conditions that are hazardous while EDC/HOBT is milder and more safer.

To solve the resistance problem, and to find new bioactive compounds with low toxicity, the effective parts of L1215 and cyhalothrin were combined by an amide linkage, and a series of novel chrysanthemamide derivatives were synthesised via EDCI/HOBt condensation. This gave a better synthetic route- and enabled us to investigate new structures which might have enhanced insecticidal activity.

## Results and discussion

The compounds **8a–l** were synthesised by the general route as shown in Scheme 1. The 5-aryl-1,3,4-thiadiazol-2-yl-chrysanthemamides (**8a–l**) were synthesised by treatment of the reaction of 2-amino-5-aryl-1,3,4-thiadiazoles (**7a–l**) with trifluorochrysanthemic acid via an EDCI/HOBt condensation in DMF. Compounds 7**a–l** were synthesised by substituted benzoic acids (**6a–l**) with thiosemicarbazide in the presence of phosphorus oxychloride.

Compounds **6g–i** were synthesised in four steps. The carboxylic acids (**1g–i**) were reacted with $SOCl_2$ to afford the acyl chlorides (**2g–i**), and then **2g–i** combined with benzene via a Friedel–Crafts acylation to afford **3g–i**. Reduction gave **4g–i**. Substituted hypnones (**5g–i**) were produced by the reaction of **4g–i** and acetic anhydride. Compounds **5g–i** reacted with sodium hypobromite to give the substituted benzoic acids (**6g–i**).

### *Insecticidal activities*

The preliminary insecticidal activity of compounds **8a–l** against *Plutella xylostella*, *Aphis craccivora* (Pea aphids) and *Tetranychus cinnabarinus* were measured. All bioassays were performed on representative test organisms reared in the laboratory. The bioassay was repeated at 25 ± 1 °C according

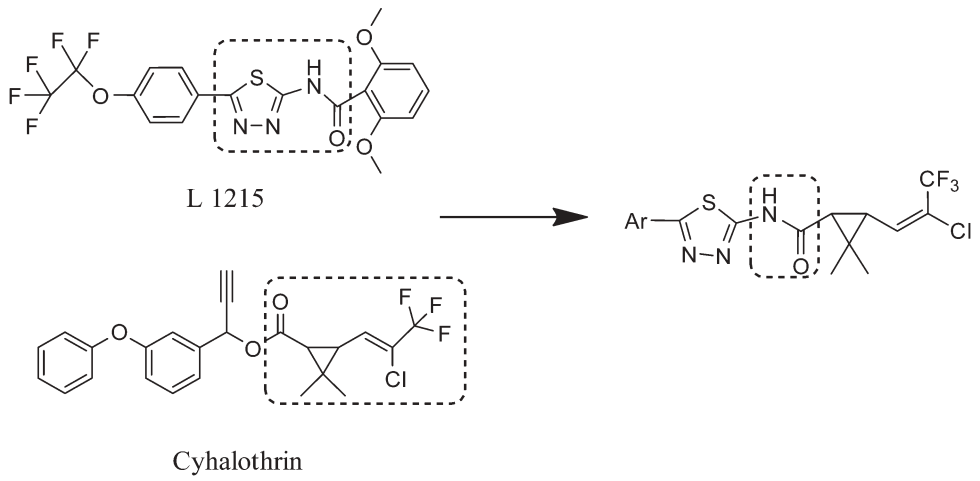


**Fig.1** Design strategy of the target compounds.

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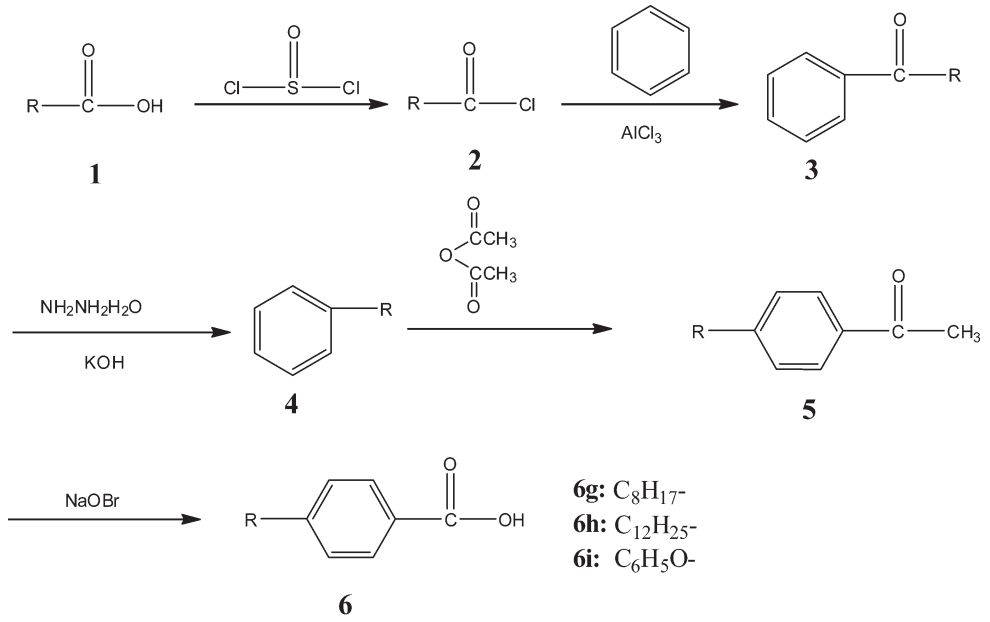
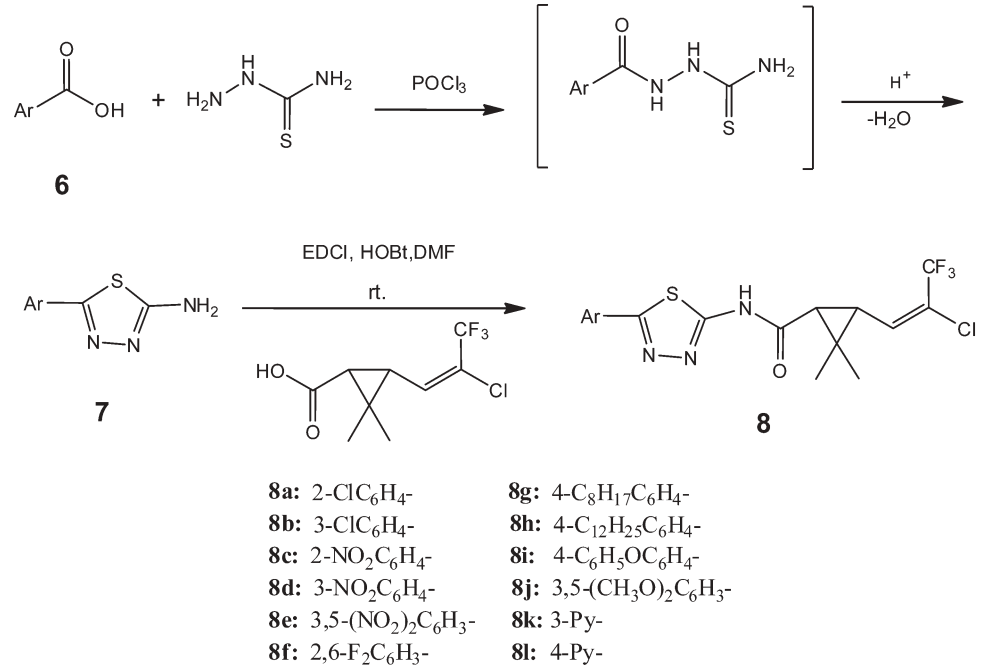



**Scheme 1** General synthetic route for substituted benzoic acid **6g–i**.




**Scheme 2** General synthetic route for the target compounds **8a–l**.

to statistical requirements. All compounds were dissolved in acetone and diluted with water containing Tween 80 (500 mg $L^{-1}$) to obtain a serial concentrations of 400.0 mg $L^{-1}$ for bioassays. The numbers of live and dead insects were counted after 72 h. Each treatment was performed three times. For comparative purposes, the commercial insecticide avermectin was tested under the same conditions. The results are listed in Table 2.

## Experimental

Unless otherwise noted, all reagents and solvents were used as received. Reactions were monitored by TLC with visualisation by UV light. Melting points were recorded on an X-4 binocular microscope melting point apparatus (Beijing Tech Instruments Co., Beijing, China) and were corrected. Elemental analyses were performed on an Elementer Vario EL III elementary analysis instrument. $^1$H NMR spectra were obtained in $CDCl_3$ or DMSO-$d_6$, and were recorded on a Bruker DRX500 spectrometer and resonance were given in ppm (δ) relative to TMS, and peak multiplicity is reported as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or b (broad). IR spectra in KBr were recorded on a Perkin-Elmer PE-683 IR spectrometer.

*Preparation of* **2***; general procedure*

$SOCl_2$ (0.45mol) was added dropwise to carboxylic acids (**1g–i**) (0.25 mol) were added in an ice bath. The reaction mixture was heated to reflux and stirred for 2 h. After cooling, the remaining $SOCl_2$ was evaporated under reduced pressure to afford compound **2**.

*Preparation of* **3***; general procedure*

To a mixture of benzene (0.28 mol) and aluminium trichloride (0.11 mol) was added **2** (0.1 mol) dropwise in the ice bath. The reaction mixture was heated to reflux and stirred for 3 h. After completion

**Table 1** Physical constants of products **7a–l**

| Compd | Ar | Recrystallisation solvent | Yield /% | M.p. /°C | M.p.(lit.) /°C |
|---|---|---|---|---|---|
| **7a** | 2-Chlorophenyl | Ethanol | 73.2 | 180–181 | 182–184 [18] |
| **7b** | 3-Chlorophenyl | Ethanol | 78.4 | 223–224 | 226 [19] |
| **7c** | 2-Nitrophenyl | Ethanol | 76.2 | 239–240 | 232–234 [20] |
| **7d** | 3-Nitrophenyl | Ethanol | 75.9 | 248–250 | – |
| **7e** | 3,5-Dinitrophenyl | Ethanol | 70.5 | 216–218 | 212–214 [21] |
| **7f** | 2,6-Difluorophenyl | Acetone | 82.1 | 185–186 | – |
| **7g** | 4-Octylphenyl | Ethanol | 68.9 | 141–142 | – |
| **7h** | 4-Dodecylphenyl | Methanol | 65.2 | 191–194 | – |
| **7i** | 4-Phenoxyphenyl | Ethanol | 72.3 | 187–191 | – |
| **7j** | 3,5-Dimethylphenyl | Ethanol | 82.5 | 171–173 | 170–173 [18] |
| **7k** | Pyridine-3-yl | Ethanol | 74.6 | 222–224 | 230–232 [18] |
| **7l** | Pyridine-4-yl | Acetone | 79.3 | 228–230 | 225 [22] |

**Table 2** The insecticidal activities of the title compounds **8a–l**

| Comp. | Concentration (ppm) | Insecticidal target[a] | | |
|---|---|---|---|---|
| | | *Plutella xylostella* | *Aphis craccivora* (Pea aphids) | *Tetranychus cinnabarinus* |
| **8a** | 400 | – | + | – |
| **8b** | 400 | – | + | – |
| **8c** | 400 | – | + | – |
| **8d** | 400 | + | + | – |
| **8e** | 400 | – | + | + |
| **8f** | 400 | – | + | + |
| **8g** | 400 | – | – | – |
| **8h** | 400 | – | + | + |
| **8i** | 400 | – | – | + |
| **8j** | 400 | – | + | – |
| **8k** | 400 | – | – | – |
| **8l** | 400 | – | + | ++ |
| **Avermectins** | 400 | +++ | +++ | +++ |

[a] Activity is expressed in four categories: (–) < 50%, (+) 51 –70%, (++) 71 –90%, (+++) > 90%.

of the reaction, the mixture was poured into ice water. The pH was adjusted to 5–6 with concentrated hydrochloric acid. It was then extracted with benzene (3×30 mL) and washed by 10% sodium bicarbonate and pure water until the pH reached 7. The benzene layer was dried over anhydrous $MgSO_4$ and distilled under reduced pressure to afford yellow liquid **3**.

*Preparation of* **4***; general procedure*

Hydrazine hydrate (0.38 mol) was added to a mixture of **3** (0.11 mol) and diglycol at room temperature. The mixture was heated to reflux and stirred for 2.5 h. Refluxing was continued for a further 4 h after adding potassium hydroxide (25.5 g). At the end of the reaction, the mixture was extracted, washed to neutral, dried and distilled under reduced pressure to afford **4**.

*Preparation of* **5***; general procedure*

Acetic anhydride (0.04 mol) was added dropwise to a mixture of **4** (0.04 mol) and anhydrous $CS_2$ (20 mL) was added at room temperature and the mixture was subsequently stirred at 50 °C. After completion of the reaction, the mixture was poured into ice water (100 mL) and concentrated hydrochloric acid (20 mL) was added. It was then extracted with benzene (3×30 mL) and washed by 10% sodium bicarbonate and pure water until the pH reached 7. The organic phase was dried over anhydrous $MgSO_4$ and distilled under reduced pressure to afford yellow oily liquid **5**.

*Preparation of* **6***; general procedure*

**5** (0.04 mol) was added dropwise to a mixture of sodium hypobromite (75 mL) and tetrahydrofuran (70 mL) was added at 0–5 °C. After 1 h ice-bath reaction, the mixture was heated until reflux and stirred for 2 h. The mixture was separated and the aqueous phase was acidified and filtered to obtain the crude product. The crude product was recrystallised from toluene to give compound **6** (**6g**, m.p. 95–96 ºC, **6h**, m. p. 90–91 ºC (lit.[23] 93–95 ºC) and **6i**, m.p. 167–169 ºC). Registry CAS No.: **6g** 3575-31-3, **6h** 21021-55-6, **6i** 2215-77-2.

*Preparation of 5-aryl-1,3,4-thiadiazol-2-amines* **7a–l**: *general procedure*

A mixture of substituted benzoic acid **I** (0.1 mol) and thiosemicarbazide (0.1 mol) was treated with $POCl_3$ (0.3 mol) dropwise at 0–5 °C and maintained at this temperature for 30 minutes. The reaction mixture was heated until reflux and stirred for 4 h. After cooling, 50 mL water was added to the reaction mixture. The pH of the reaction solution was adjusted to the range of 8–9 with the solution of 50% NaOH. The crude product precipitated, filtered, washed with water, dried, and recrystallised from ethanol to afford compounds **7a–l** as listed in Table 1.

*5-(3-Nitrophenyl)-1,3,4-thiadiazol-2-amine* (**7d**): IR (KBr) ν: 3420, 3108, 1623, 1506, 1342, 1270, 1131 $cm^{-1}$. Anal. Calcd for $C_8H_6N_4O_2S$: C, 43.24; H, 2.72; N, 25.21. Found: C, 43.19; H, 2.73; N, 25.13%.

*5-(2,6-Difluorophenyl)-1,3,4-thiadiazol-2-amine* (**7f**): IR (KBr) ν: 3279, 3109, 1633, 1513, 1312, 1275, 1181, Anal. Calcd for $C_8H_5F_2N_3S$: C, 45.07; H, 2.36; N, 19.71. Found: C, 45.01; H, 2.42; N, 19.59%.

*5-(4-Octylphenyl)-1,3,4-thiadiazol-2-amine* (**7g**): IR (KBr) ν: 3269, 3101, 2921, 2850, 1620, 1510, 1265, 1135 $cm^{-1}$. Anal. Calcd for $C_{16}H_{23}N_3S$: C, 66.39; H, 8.01; N, 14.52. Found: C, 66.49; H, 8.03; N, 14.72%.

*5-(4-Dodecylphenyl)-1,3,4-thiadiazol-2-amine* (**7h**): IR (KBr) ν: 3272, 3161, 2921, 2850, 1683, 1558, 1303, 1145. Anal. Calcd for $C_{20}H_{31}N_3S$: C, 69.52; H, 9.04; N, 12.16. Found: C, 69.63; H, 9.08; N, 12.26%.

*5-(4-Phenoxyphenyl)-1,3,4-thiadiazol-2-amine* (**7i**): IR (KBr) ν: 3265, 3101, 1620, 1558, 1265, 1134, 981 $cm^{-1}$. Anal. Calcd for $C_{14}H_{11}N_3OS$: C, 62.43; H, 4.12; N, 15.60. Found: C, 63.21; H, 3.93; N, 15.82%.

*Preparation of 1,3,4-thiadiazole chrysanthemamides* **8a–l***; general procedure*

A solution of **7a–l** (2.5 mmol) and trifluorochrysanthemic acid (2.3 mmol) in DMF (40 mL) was treated with EDCI (2.5 mmol) and HOBt (2.5 mmol). The mixture was stirred overnight at room temperature, monitored by TLC. After the reaction was complete, the mixture was poured into water. The crude precipitate was filtered and washed with water to obtain the crude product. The crude products were recrystallised from ethanol to give compounds **8a–l**.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-N-(5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl)-2,2-dimethylcyclopropanecarboxamide* (**8a**): Yield 85.2%; m.p. 201–203 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ (ppm): 1.37 (s, 6H, $CH_3$), 2.29 (t, 1H, CH), 2.40 (d, 1H, CH), 7.11 (d, 1H, C=CH), 7.38–8.16 (m, 4H, Ph), 12.68 (s, 1H, NH). IR (KBr) ν: 3244, 3157, 3080, 2958, 2898, 1681, 1652, 1560, 1299, 1276, 1134, 1118, 781$cm^{-1}$. Anal. Calcd for $C_{17}H_{14}Cl_2F_3N_3OS$: C, 46.80; H, 3.23; N, 9.63. Found: C, 46.78; H, 3.33; N, 9.62%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-N-(5-(3-chlorophenyl)-1,3,4-thiadiazol-2-yl)-2,2-dimethylcyclopropanecarboxamide* (**8b**): Yield 83.1%; m.p. 209–211 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ (ppm): 1.35 (s, 6H, $CH_3$), 2.28 (t, 1H, CH), 2.42 (d, 1H, CH), 7.10 (d, 1H, C=CH), 7.42–7.97 (m, 4H, Ph), 12.79 (s, 1H, NH). IR (KBr) ν: 3251, 3161, 3080, 2960, 2866, 1683, 1652, 1568, 1303, 1272, 1145, 1116, 784 $cm^{-1}$. Anal. Calcd for $C_{17}H_{14}Cl_2F_3N_3OS$: C, 46.80; H, 3.23; N, 9.63. Found: C, 45.97; H, 3.27; N, 9.66%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethyl-N-(5-(2-nitrophenyl)-1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide* (**8c**): Yield 79.1%; m.p. 235–237 °C. $^1$H NMR (500 MHz, $CDCl_3$) δ (ppm):

1.36 (s, 6H, $CH_3$), 2.48 (t, 1H, CH), 2.62 (d, 1H, CH), 7.09 (d, 1H, C=CH), 7.64–7.91 (m, 4H, Ph), 13.89 (s, 1H, NH). IR (KBr) ν: 3244, 3155, 3078, 2908, 2740, 1699, 1652, 1558, 1544, 1299, 1141, 1120, 771 $cm^{-1}$. Anal. Calcd for $C_{17}H_{14}ClF_3N_4O_3S$: C, 45.70; H, 3.16; N, 12.54. Found: C, 45.73; H, 3.12; N, 12.58%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethyl-N-(5-(3-nitrophenyl)-1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide* (**8d**): Yield 78.3%; m.p. 216–218 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 1.37 (s, 6H, $CH_3$), 2.49 (t, 1H, CH), 2.63 (d, 1H, CH), 7.08 (d, 1H, C=CH), 7.64–7.71 (m, 4H, Ph), 13.89 (s, 1H, NH). IR (KBr) ν: 3452, 3149, 3031, 2958, 2866, 1695, 1652, 1556, 1529, 1299, 1147, 1116, 727 $cm^{-1}$. Anal. Calcd for $C_{17}H_{14}ClF_3N_4O_3S$: C, 45.70; H, 3.16; N, 12.54. Found: C, 45.89; H, 3.22; N, 12.64%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-N-(5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-yl)-2,2-dimethylcyclopropanecarboxamide* (**8e**): Yield 77.6%; m.p. 232–234 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 1.39 (s, 6H, $CH_3$), 2.33 (t, 1H, CH), 2.44 (d, 1H, CH), 7.10 (d, 1H, C=CH), 9.03–9.11 (m, 3H, Ph), 13.07 (s, 1H, NH). IR (KBr) ν: 3458, 3097, 3008, 2962, 2885, 1683, 1654, 1548, 1508, 1296, 1139, 1116, 730 $cm^{-1}$. Anal. Calcd for $C_{17}H_{13}ClF_3N_5O_5S$: C, 41.51; H, 2.66; N, 14.24. Found: C, 41.58; H, 2.64; N, 14.29%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-N-(5-(2,6-difluorophenyl)-1,3,4-thiadiazol-2-yl)-2,2-dimethylcyclopropanecarboxamide* (**8f**): Yield 87.3%; m.p. 226–228 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 1.37 (s, 6H, $CH_3$), 2.33 (t, 1H, CH), 2.48 (d, 1H, CH), 7.07–7.12 (m, 3H, Ph), 7.42 (d, 1H, C=CH), 12.96 (s, 1H, NH). IR (KBr) ν: 3149, 3083, 2968, 2896, 1683, 1654, 1558, 1298, 1276, 1143, 1118, 781 $cm^{-1}$. Anal. Calcd for $C_{17}H_{13}ClF_5N_3OS$: C, 46.64; H, 2.99; N, 9.60. Found: C, 46.36; H, 2.92; N, 9.52%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethyl-N-(5-(4-octylphenyl)-1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide* (**8g**): Yield 68.6%; m.p. 203–209 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 0.88 (t, 3H, $CH_3$), 1.31 (s, 3H, $CH_3$), 1.50 (m, 10H, $CH_3$), 1.62 (s, 3H, $CH_3$), 1.64 (m, 2H, $CH_2$) 2.45 (d, 1H, CH), 2.63 (t, 2H, $CH_2$), 2.91 (d, 1H, CH), 7.17 (d, 1H, C=CH), 7.29–7.79 (m, 4H, Ph), 14.13 (s, 1H, NH). IR (KBr) ν: 3244, 3151, 3064, 2958, 2854, 1683, 1652, 1564, 1299, 1137, 950, 727 $cm^{-1}$. Anal. Calcd for $C_{25}H_{31}ClF_3N_3OS$: C, 58.41; H, 6.08; N, 8.17. Found: C, 58.49; H, 6.03; N, 8.19%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-N-(5-(4-dodecylphenyl)-1,3,4-thiadiazol-2-yl)-2,2-dimethylcyclopropanecarboxamide* (**8h**): Yield 66.4%; m.p. 216–217 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 0.87 (t, 3H, $CH_3$), 1.25 (m, 18H, $CH_2$), 1.31 (s, 3H, $CH_3$), 1.49 (s, 3H, $CH_3$), 1.64 (m, 2H, $CH_2$), 2.41 (t, 1H, CH), 2.63 (m, 2H, $CH_2$), 2.90 (t, 1H, CH), 7.16 (d, 1H, C=CH), 7.27–7.81 (m, 4H, Ph), 14.09 (s, 1H, NH). IR (KBr) ν: 3244, 3163, 3080, 2958, 2852, 1683, 1652, 1573, 1303, 1145, 952, 729 $cm^{-1}$. Anal. Calcd for $C_{29}H_{39}ClF_3N_3OS$: C, 61.09; H, 6.89; N, 7.37. Found: C, 61.03; H, 6.84; N, 7.39%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethyl-N-(5-(4-phenoxyphenyl)-1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide* (**8i**): Yield 76.2%; m.p. 204–206 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 1.25 (s, 3H, $CH_3$), 1.47 (s, 3H, $CH_3$), 2.43 (t, 1H, CH), 2.87 (d, 1H, CH), 7.15 (d, 1H, C=CH), 7.05–7.86 (m, 9H, Ph), 14.04 (s, 1H, NH). IR (KBr) ν: 3452, 3170, 3072, 2960, 2875, 1683, 1650, 1569, 1303, 1145, 1053, 954, 752 $cm^{-1}$. Anal. Calcd for $C_{23}H_{19}ClF_3N_3O_2S$: C, 55.93; H, 3.88; N, 8.51. Found: C, 55.98; H, 3.85; N, 8.53%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-N-(5-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-2-yl)-2,2-dimethylcyclopropanecarboxamide* (**8j**): Yield 83.1%; m.p. 229–230 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 1.42 (s, 6H, $CH_3$), 2.28 (t, 1H, CH), 2.58 (d, 1H, CH), 3.88 (s, 6H, $CH_3$), 6.69 (d, 1H, C=CH), 7.12–7.67 (m, 3H, Ph), 12.66 (s, 1H, NH). IR (KBr) ν: 3452, 3164, 3083, 2958, 2854, 1676, 1654, 1569, 1303, 1176, 1134, 1118, 779 $cm^{-1}$. Anal. Calcd for $C_{19}H_{19}ClF_3N_3O_3S$: C, 49.41; H, 4.15; N, 9.10. Found: C, 49.32; H, 4.12; N, 9.05%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethyl-N-(5-(pyridin-3-yl)-1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide* (**8k**): Yield 81.2%; m.p. 238–239 °C. $^1H$ NMR (500 MHz, DMSO-$d_6$) δ (ppm): 1.31 (s, 6H, $CH_3$), 2.23 (t, 1H, CH), 2.58 (d, 1H, CH), 7.10 (d, 1H, C=CH), 7.27–8.25 (m, 4H, Ph), 12.79 (s, 1H, NH). IR (KBr) ν: 3452, 3159, 3080, 2960, 2871, 1683, 1652, 1569, 1305, 1143, 1120, 705 $cm^{-1}$. Anal. Calcd for $C_{16}H_{14}ClF_3N_4OS$: C, 47.71; H, 3.50; N, 13.91. Found: C, 47.79; H, 3.49; N, 13.94%.

*3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethyl-N-(5-(pyridin-4-yl)-1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide* (**8l**): Yield 83.1%; m.p. 240–242 °C. $^1H$ NMR (500 MHz, $CDCl_3$) δ (ppm): 1.47 (s, 6H, $CH_3$), 2.41 (t, 1H, CH), 2.52 (d, 1H, CH), 7.22 (d, 1H, C=CH), 7.77–8.82 (m, 4H, Ph), 13.01 (s, 1H, NH). IR (KBr) ν: 3452, 3155, 3082, 2966, 2896, 1683, 1652, 1568, 1303, 1143, 1118, 823 $cm^{-1}$. Anal. Calcd for $C_{16}H_{14}ClF_3N_4OS$: C, 47.71; H, 3.50; N, 13.91. Found: C, 47.73; H, 3.59; N, 13.90%.

*Biological assay*

The results indicated that most of the title compounds showed low activity against *Plutella xylostella* while exhibiting moderate activity against *Aphis craccivora* (Pea aphids). Compounds **8e**, **8f**, **8h**, **8i** and **8l** also showed moderate activities against *Tetranychus cinnabarinus*. The results showed that compounds containing electron withdrawing groups especially, $–NO_2$, –F group, would enhance the insecticidal activity against *Aphis craccivora* (Pea aphids). It is worth mentioning that compound **8h** exhibited better activity than **8g** might be better absorbed because of its higher lipophilicity.

Analysis of the results reveals that a change in the HLB value of molecule by modifying the substitutent on the phenyl from an electron-donating group to electron-withdrawing group can enhance the biological activity. Other heterocyclic compounds might be introduced instead of the substituted phenyl groups.

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