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Synthesis and insecticidal activity of novel heptafluoroisopropyl substituted 2,2-difluoro-1,3-benzodioxol-5-acetamide derivatives

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Abstract: In order to discover novel and environmentally benign pesticides, a series of novel heptafluoroisopropyl substituted 2,2-difluoro-1,3-benzodioxol-5-acetamide derivatives were synthesized via amide condensation reaction in aqueous solution. All the title compouds were characterized by ^{1}H NMR, ^{19}F NMR and HRMS. The bioassays showed that some of the compounds exhibited good insecticidal activities against bean aphids (*Aphis craccivora*) and armyworms (*Mythimna separata*). Preliminary structure-activity relationship studies suggested that the substituent groups played a key role in the insecticidal activities of the compounds.

Keywords: poly-fluorinated compounds; acetamide; TPGS-750-M/H_2O; insecticidal activity

新型七氟异丙基取代 2,2-二氟-1,3-苯并二氧-5-乙酰胺衍生物的合成与杀虫活性

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摘 要：为探索环境友好新型农药先导化合物，通过水相中酰胺缩合反应合成了 16 个未见文献报道的七氟异丙基苯基取代的 2,2-二氟-1,3-苯并二氧-5-乙酰胺类目标化合物。其结构通过核磁共振氢谱、氟谱以及高分辨质谱确认。初步生物活性测定表明，部分目标化合物对蚕豆蚜虫和粘虫表现出良好的杀虫活性，初步构效关系显示苯环上取代基的种类和位置在化合物的杀虫活性中起关键作用。

关键词: 多氟化合物； 乙酰胺； TPGS-750-M/H_2O； 杀虫活性

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The highly fluorinated groups have become an important bio-functional moiety in many bioactive compounds, mainly because of its high lipophilicity for crust penetration[1]. The introduction of fluorine atoms into organic molecules has been demonstrated in several widely used pesticides[2-3]. Flubendiamide, the first artificially synthesized insecticide targeting ryanodine receptors (RyRs), has shown extremely

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high activity against a broad spectrum of lepidopterous insects[4-5]. Since its discovery by Nihon Nohyaku and development with Bayer company in 1998, a series of pesticides containing polyfluorinated groups with high activities was reported, such as pyrifluquinazon[6-7] and pyflubumide[8](**Fig. 1**).

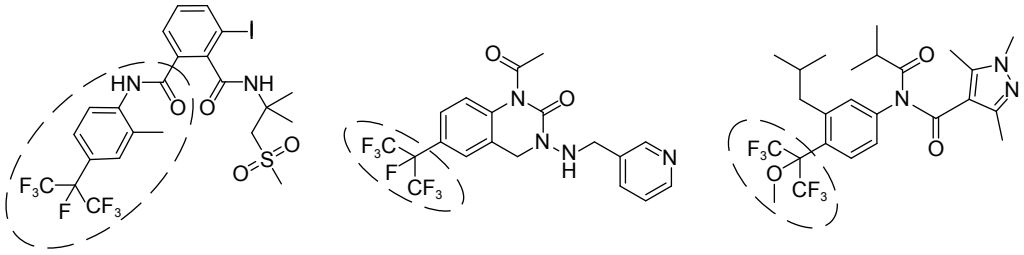


Fig. 1 Commercial pesticides with polyfluoroalkyl groups

Fludioxonil[9-11], a non-systemic fungicide, is the world's biggest seed treatment agent in terms of current unit sales. As a cereal seed treatment, it controls seed- and soil-borne diseases and gives particularly good control of *Fusarium roseum* and *Gerlachia nivalis* in small-grain cereals. The key moiety of the fungicide is 2,2-difluoro-1,3-benzodioxole.

In order to find some compounds with high biological activities and new action mode, herein we designed and synthesized a series of novel 2,2-difluoro-1,3-benzodioxol-5-acetamide compounds containing multi-fluorine atoms. As showed in **Fig. 2**, 2,2-difluoro-1,3-benzodioxole moiety from fludioxonil and heptafluoroisopropyl aniline moiety from flubendiamide were linked with amide group. These new 2,2-difluoro-1,3-benzodioxol-5-acetamide compounds are expected to exhibit desirable biological activities.

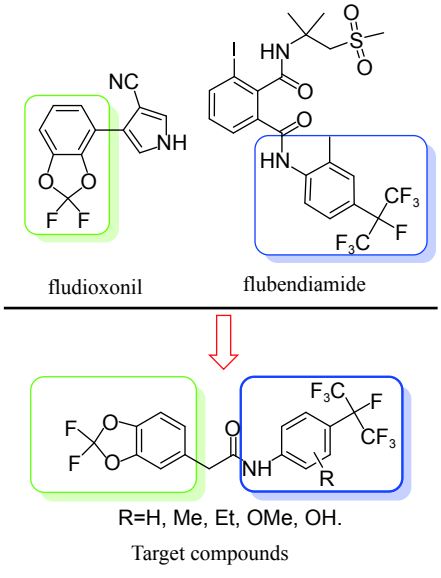


Fig. 2 Design of the title compounds

In addition, organic solvents represent the vast majority of mass consumption and waste generated by the chemical industry. Since most of chemical reactions are conducted in traditional organic solvents, a green protocol with reduced organic waste would be desirable[12-13]. The nanomicelle-forming amphiphile TPGS-750-M (**Fig. 3**) was reported recently, which can facilitate many reactions under mild conditions in water[14]. Encouraged by this, we have successfully improved the last key step of amidation using HATU as the coupling agent in 2 wt.% TPGS-750-M/H_2O under mild conditions[15-22]. Furthmore, a series of novel poly fluorinated 1,3-benzodioxol-5-acetamides (**h1-h16**) was designed and synthesized (**Scheme 1**). And the insecticidal activities were evaluated.

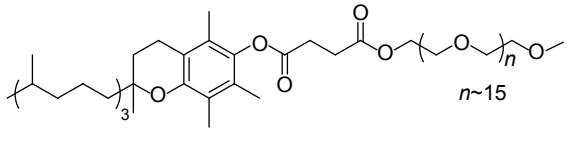
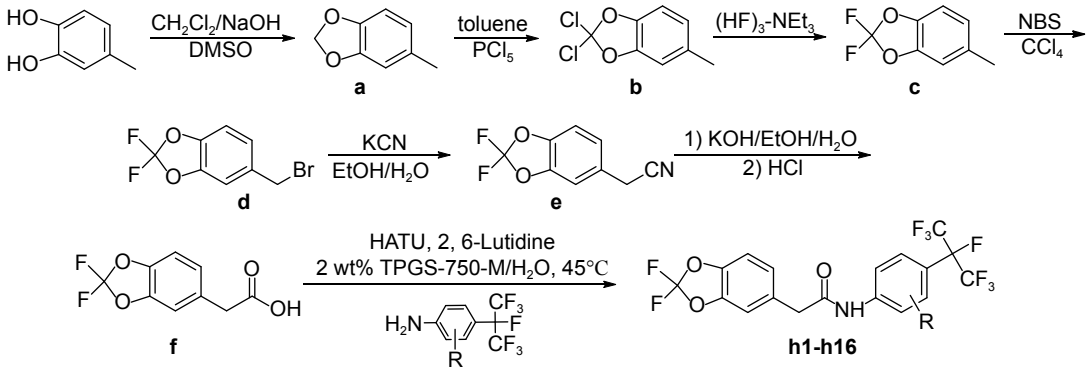


Fig. 3 Structural formula of TPGS-750-M

1 Materials and Methods

1.1 Instruments and reagents

All starting materials and reagents used were commercially available and were utilized without further purification (except as indicated). TPGS-750-M was synthesized according to the published procedure[14]. All the melting points were determined with an X-4 melting point apparatus while the thermometer was uncorrected. NMR spectra were recorded on a Varian INOVA spectrometer (400 MHz for ^{1}H NMR), or a Bruker Avance spectrometer (600



Scheme 1 General synthetic route of the title compound h1-h16

MHz for ^{1}H NMR, and 564 MHz for ^{19}F NMR spectroscopy). HRMS (ESI) were performed on an Agilent 6 210 TOF LC/MS instrument. Mass spectra were recorded on a Bruker Esquire 6 000 mass spectrometer (ESI).

1.2 Synthetic procedures

1.2.1 Synthesis of 5-methyl-1,3-benzodioxole (a)

Methylene chloride (300.0 g, 3.56 mol) and dimethylsulphoxide (1 000.0 g, 12.80 mol) were added to a flask and stirred under reflux at 90 °C to 100 °C for 1 h. A solution of sodium hydroxide (144.0 g, 3.60 mol) and 4-methylbenzene-1, 2-diol (195.2 g, 1.57 mol) in water (300 mL) were added dropwise in 1 h. At the end of the addition, the mixture was subsequently stirred for a further 2 h under reflux. Then 500 mL of water was added to the reaction solution and steam distillation was conducted. The distillation fractions at 110 °C was collected and separated. Aqueous phase was extracted with dichloromethane (200 mL). The combined organic phases were dried, concentrated and 5-methyl-1,3-benzodioxole (**a**) was obtained as a colorlesstaine oil, yield: 149.7 g (70%). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.30 (s, 3H, -CH_3), 6.05 (s, 2H, -CH_2-), 6.90-7.05 (m, 3H, Ar-H).

1.2.2 Synthesis of 2,2-dichloro-5-methyl-1,3-benzodioxole (b)

5-Methyl-1,3-benzodioxole (13.6 g, 0.10 mol) was added dropwise to phosphorus pentachloride (25.0 g, 0.12 mol) in toluene (50 mL) with stirring. Vigorous evolution of hydrogen chloride started immediately. The mixture was then heated under reflux for 3 h. After distillation, phosphorus trichloride, phosphorus pentachloride and toluene were recovered and 2,2-dichloro-5-methyl-1,3-benzodioxole (**b**) was obtained as a pale-yellow oil at boiling point: 98-99 °C (2 200 Pa), yield: 17.0 g (82%). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.28 (s, 3H, -CH_3), 6.70-6.80 (m, 3H, Ar-H).

1.2.3 Synthesis of 2,2-difluoro-5-methyl-1,3-benzodioxole (c)

A mixture of 2,2-dichloro-5-methyl-1,3-benzodioxole (16.4 g, 0.08 mol) and triethylamine tris (hydrogen fluoride) (9.6 g, 0.06 mol) was stirred under nitrogen at room temperature. The progress was monitored by TLC (V(ethyl acetate) : V(hexane) = 1 : 20). At the end of the reaction, the mixture was filtered. The filtrate was distilled under reduced pressure to yield 2,2-difluoro-5-methyl-1,3-benzodioxole (**c**) as a colorless oil at boiling point：60-62 °C(1 600 Pa), yield: 11.7 g (85%). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.28 (s, 3H, -CH_3), 6.70-6.80 (m, 3H, Ar-H).

1.2.4 Synthesis of 2,2-difluoro-5-bromomethyl-1,3-benzodioxole (d)

To a solution of 2,2-difluoro-5-methyl-1,3-benzodioxole (11.5 g, 0.07 mol) in carbon tetrachloride (50 mL) was added *N*-bromosuccinimide (NBS) (12.3 g, 0.07 mol) and a catalytic amount of benzoyl peroxide (0.2 g, 0.001 mol). After stirred at refluxed for 3 h, the reaction mixture was cooled to room temperature and filtered. The filtrate was concentrated to give 2,2-difluoro-5-bromomethyl-1,3-benzodioxole (**d**) as a brown oil, yield: 16.0 g (95%). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 4.38 (s, 2H, -CH_2-), 6.80-7.40 (m, 3H, Ar-H). The product was used without purification in the next step.

1.2.5 Synthesis of 2-(2,2-difluoro-1,3-benzodioxole-5-yl) acetonitrile (e)

A solution of

2,2-difluoro-5-bromomethyl-1,3-benzodioxole (12.6 g, 0.05 mol) and potassium cyanide (3.9 g, 0.06 mol) in 80% aqueous ethanol (60 mL) was heated under reflux for 6 h and then cooled to room temperature. After the addition of water (20 mL), the organic product was extracted with ethyl acetate (3 × 25 mL). The combined organic layer was washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated to afford 2-(2,2-difluoro-1,3-benzodioxole-5-yl) acetonitrile (**e**) as a pale-yellow liquid that was used directly in the next step, yield: 4.0 g (40%). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.78 (s, 2H, -CH_2-), 7.01-7.03 (m, 3H, Ar-H).

1.2.6 Synthesis of 2- (2,2-difluoro-1,3-benzodioxole-5-yl) acetic acid (f) A mixture of 2-(2,2-difluoro-1,3-benzodioxole-5-yl) acetonitrile (4.0 g, 0.02 mol), potassium hydroxide pellets (3.4 g, 0.06 mol) in ethanol (20 mL) and water (10 mL) was heated under reflux for 3 h. After cooling, the reaction mixture was poured into ice-water, acidified with dilute hydrochloric acid and extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed with water (2 × 20 mL), dried over sodium sulfate and evaporated under vacuum. Recrystallization of the solid residue from heptane affords 2-(2,2-difluoro-1,3-benzodioxole-5-yl)acetic acid (**f**) as a pale yellow solid, yield: 8.8 g (82%), m.p. 94-96 °C. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.65 (s, 2H, -CH_2-), 6.97-7.04 (m, 3H, Ar-H).

1.2.7 General synthetic procedure for 2-(2,2-difluoro-1,3-benzodioxole-5-yl)-*N*-(2-methyl-4-(perfluoropropan-2-yl) phenyl) acetamide (h1) To a dried 5 mL reaction vial was added a mixture of 2,2-difluoro-1,3-benzodioxole-5-acetic acid (**f**) (0.2 g, 0.001 mol), 2, 6-lutidine (0.3 g, 0.003 mol) in 2 wt.% TPGS-750-M/H_2O (2 mL), HATU (0.418 g, 0.001 mol) and 2-methyl-4-(perfluoropropan-2-yl) aniline (0.5 g, 0.001 mol). The reaction was allowed to stir for 24 hours at 45 °C. The reaction progress was monitored by HPLC. The aqueous reaction mixture was extracted with EtOAc (3 × 2 mL). The organic extracts were then washed with 1 mol/L HCl (3 × 2 mL) and Na_2CO_3 (3 × 6 mL) saturated solution in water[25]. The organic phase was concentrated under reduced pressure to give a crude product. The product was purified by column chromatography on silica gel (V (ethyl acetate) : V(hexane) = 1 : 1) to give compound **h1**. The synthetic procedure for compounds **h2-h16** is the same as the synthesis of compound **h1**.

1.3 Insecticidal activity

The preliminary bioactivity tests were performed on representative test organisms reared in the laboratory. All compounds were dissolved in *N*, *N*-dimethylformamide (DMF) and diluted with distilled water containing 0.1% tween-80 to achieve the testing solution with the desired concentration. For insecticidal activity test, flubendiamide and abamectin were tested under the same conditions as the control.

1.3.1 Insecticidal activity against Homoptera pest—*Aphis craccivora* The foliar contact activity against bean aphid (*A. craccivora*) was tested. Tender shoots of soybean with 60 insects of each species were dipped in the diluted solutions of the chemicals for 5 s. Then the superfluous liquor was removed, and they were kept in the conditioned room for normal cultivation. The mortality was evaluated by the number of live larvae in the treated bottles relative to that in the untreated controls after 48 h. Controls were performed under the same conditions.

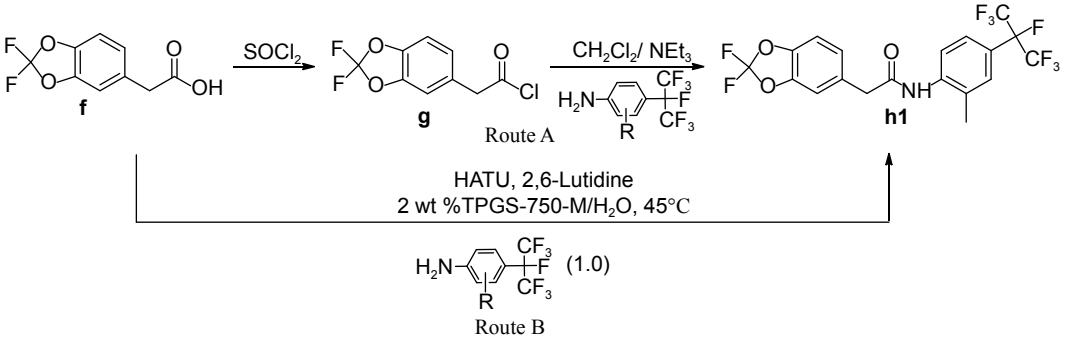
1.3.2 Insecticidal activity against Lepidopteran pest—*Mythimna separata* The insecticidal activity against armyworms (*M. separata*) was also tested by foliar application. Individual corn leaves were placed on moistened pieces of filter paper in petri-dishes. The leaves were then sprayed with the testing solution and exposed to dry. The dishes were infested with 10 third-instar larvae and maintained in the conditioned room. The mortality rates were evaluated 48 h after treatment.

2 Results and Discussion

2.1 Synthesis of the title compounds

As shown in **Scheme 1**, 2,2-difluoro-5-methyl-1,3-benzodioxole (**c**) is the key intermediate for the synthesis of title compounds and was prepared

starting from 4-methylbenzene-1, 2-diol by cyclization, chlorination and fluorination reaction [23-26]. During the fluorination reaction, triethylamine trihydrogen-fluoride was employed as the fluorinating agent and high yields were obtained under ambient reaction conditions. Then the intermediate **c** was converted to another key intermediate 2,2-difluoro-1,3-benzodi-oxole-5-acetic acid (**f**) by bromination, cyanation and hydrolysis. In traditional synthetic procedure, the intermediate **f** was converted to compound **h1** by acylchlorination and acylation reaction in 45% total yield[27](**Scheme 2**, Route A). In the improved route, compound **h1** was prepared in 60% yield by coupling intermediate **f** and 2-methyl-4-heptafluoroisopropyl aniline using TPGS-750-M in water (**Scheme 2**, Route B). With the above mentioned environment-friendly and easy operative method, title compounds **h2-h16** were synthesized with moderate yields. Physical and chemical data of the title compounds **h1-h16** were listed in **Table 1**. ^{1}H NMR, ^{19}F NMR and



Scheme 2 Route improvement for the synthesis of the title compounds h1

Table 1 Physical and chemical data of title compounds h1-h16

Entry	Compd.	R	Appearance	m.p./°C	Yield/%
1	**h1**	2-CH_3	White solid	125-127	60
2	**h2**	H	White solid	103-105	63
3	**h3**	2, 3-$(CH_3)_2$	White solid	135-137	60
4	**h4**	3-CH_3	White solid	112-114	59
5	**h5**	2, 5-$(CH_3)_2$	White solid	127-129	61
6	**h6**	3-OCH_3	White solid	134-136	55
7	**h7**	2, 6-$(CH_2CH_3)_2$	White solid	111-113	53
8	**h8**	2-CH_3-6-CH_2CH_3	White solid	118-120	56
9	**h9**	2-OH	White solid	130-132	43
10	**h10**	2, 6-$(CH_3)_2$	White solid	132-134	58
11	**h11**	2-OCH_3	White solid	114-116	56
12	**h12**	2-CH_2CH_3	White solid	120-122	57
13	**h13**	2-OCH_2CH_3	White solid	105-107	60
14	**h14**	3-CH_2CH_3	White solid	128-130	55
15	**h15**	2, 5-$(OCH_3)_2$	White solid	122-124	52
16	**h16**	2, 6-$(OCH_3)_2$	White solid	123-125	58

HRMS spectra were listed in **Table 2**.

2.2 Insecticidal activity

The insecticidal activity of the above compounds against bean aphids (*A. craccivora*) and armyworms (*M. separata*) *in vivo* was evaluated. The results were listed in **Table 3**. **h5**, **h8**, **h10** and **h16** exhibited 100% mortality against *A. craccivora* at the concentration of 500 mg/L. **h1**, **h7**, **h12** and **h15** also showed high activities, and displayed mortalities higher than 80%. As for the insecticidal activities against *M. separata*, compounds **h2**, **h4** and **h14** exhibited mortalities higher than 80% at the

Table 2 The ^{1}H NMR, ^{19}F NMR and HRMS of the title compounds h1-h16

Compd.	^{1}H NMR($CDCl_3$, 400 MHz), δ	^{19}F NMR ($CDCl_3$, 564 MHz), δ	HRMS $[M+H]^+$, *m/z*	
			Calcd.	Found
h1	2.26 (s, 3H, -CH_3), 3.68 (s, 2H, -CH_2-), 7.02-7.07 (m, 4H, Ar-H × 3, N-H), 7.19-7.33 (m, 3H, Ar-H).	–181.70 (m, 1F, CF), –75.82 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –49.94 (s, 2F, CF_2).	474.074 6	474.075 0
h2	3.69 (s, 2H, -CH_2-), 7.00-7.04 (m, 3H, Ar-H), 7.51 (d, 2H, *J* = 9.0 Hz, Ar-H), 7.60 (d, 2 H, *J* = 9.0 Hz, Ar-H), 7.74 (br, 1H, N-H).	–182.32 (m, 1F, CF), –75.87 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –49.96 (s, 2F, C F_2).	460.059 0	460.058 7
h3	2.01 (s, 3H, -CH_3), 2.38 (d, 3 H, *J* = 5.4 Hz, -CH_3), 3.74 (s, 2H, -CH_2-), 7.07-7.09 (m, 3H, Ar-H), 7.17 (br, 1H, N-H), 7.34 (d, 1H, *J* = 7.8 Hz, Ar-H), 7.64 (d, 1H, *J* = 7.8 Hz, Ar-H).	–174.74 (m, 1F, CF), –74.06 (d, 6 F, *J* = 6.2 Hz, CF_3 × 2), –50.04 (s, 2 F, CF_2).	488.090 3	488.089 9
h4	2.46 (d, 3H, *J* = 8.8 Hz, -CH_3), 3.71 (s, 2H, -CH_2-), 7.04-7.08 (m, 2H, Ar-H), 7.38-7.44 (m, 2H, Ar-H × 1, N-H), 7.68-7.79 (m, 3H, Ar-H)	–175.08 (m, 1F, CF), –74.11 (d, 6F, *J* = 6.2 Hz, CF_3 × 2), –50.02 (s, 2F, CF_2)	474.074 6	474.074 3
h5	2.05 (s, 3H, -CH_3-), 2.46 (d, 3H, *J* = 9.2 Hz, -CH_3), 3.76 (s, 2H, -CH_2-), 7.00 (br, 1H, N-H), 7.05-7.10 (m, 3H, Ar-H × 3), 7.20 (s, 1H, Ar-H), 7.68-7.69 (m, 1H, Ar-H).	–174.33 (m, 1F, CF), –74.04 (d, 6F, *J* = 6.2 Hz, CF_3 × 2), –50.03 (s, 2F, C F_2)	488.090 3	488.091 0
h6	3.72 (s, 2H, -CH_2-), 3.81 (s, 3H, -OCH_3), 7.04-7.08 (m, 3H, Ar-H × 2, N-H × 1), 7.67-7.79 (m, 4H, Ar-H).	–173.14 (m, 1F, CF), –73.62 (d, 6F, *J* = 6.2 Hz, CF_3 × 2), –50.01 (s, 2F, CF_2).	490.069 5	490.069 0
h7	1.17 (t, 6H, *J* = 7.2 Hz, -$CH_2\underline{CH_3}$ × 2), 2.72 (q, 4H, *J* = 7.2 Hz, -$\underline{CH_2}$ CH_3 × 2), 3.74 (s, 2H, -CH_2-), 7.03-7.07 (m, 3H, Ar-H), 7.36 (s, 2H, Ar-H). 7.42 (br, 1H, N-H).	–180.52 (m, 1F, CF), –75.51 (d, 6F, *J* = 5.6 Hz, CF_3×2), –49.95 (s, 2F, CF_2).	516.121 6	516.122 1
h8	1.15 (t, 3H, *J* = 7.2 Hz, -$CH_2\underline{CH_3}$), 2.26 (s, 3H, -CH_3), 2.72 (q, 2H, *J* = 7.2 Hz, -$\underline{CH_2}CH_3$), 3.73 (s, 2H, -CH_2-), 7.00-7.05 (m, 3H, Ar-H), 7.34 (s, 1H, Ar-H), 7.38 (s, 1H, Ar-H), 7.44 (br, 1H, N-H).	–181.03 (m, 1F, CF), –75.55 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –50.00 (s, 2F, CF_2).	502.105 9	502.105 3
h9	3.72 (s, 2H, -CH_2-), 7.02-7.07 (m, 3H, Ar-H), 7.09 (d, 1H, *J* = 8.4 Hz, Ar-H), 7.14 (s, 1H, Ar-H), 7.34 (br, 1H, N-H), 8.10 (d, 1H, *J* = 8.4 Hz, Ar-H).	–182.45 (m, 1F, CF), –75.89 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –49.92 (s, 2F, CF_2).	476.053 9	476.054 3
h10	2.25 (s, 6H, -CH_3 × 2), 3.70 (s, 2H, -CH_2-), 7.01-7.06 (m, 3H, Ar-H), 7.35 (s, 2H, Ar-H), 7.46 (s, br H, N-H).	–182.30 (m, 1F, CF), –75.80 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –49.95 (s, 2F, CF_2).	488.090 3	488.090 7
h11	3.75 (s, 2H, -CH_2-), 3.85 (s, 3H, -OCH_3), 7.02-7.09 (m, 4H, Ar-H), 7.19 (d, *J* =8.4 Hz, 1H, Ar-H), 7.87 (br, 1H, N-H), 8.47 (d, *J* =8.4 Hz, 1H, Ar-H).	–182.50 (m, 1F, CF), –75.90 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –49.98 (s, 2F, CF_2).	490.069 5	490.070 1
h12	1.16 (t, 3H, *J* = 7.2 Hz, -$CH_2\underline{CH_3}$), 2.72 (q, 2H, *J* = 7.2 Hz, -$\underline{CH_2}CH_3$), 3.71 (s, 2H, -CH_2-), 7.01-7.05 (m, 3H, Ar-H), 7.32-7.47 (m, 4H, Ar-H × 3, NH).	–181.81 (m, 1F, CF), –75.67 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –49.93 (s, 2F, CF_2).	488.090 3	488.091 2
h13	1.39 (t, 3H, *J* = 6.8 Hz, -$OCH_2\underline{CH_3}$), 3.74 (s, 2H, -CH_2-), 3.83 (q, 2H, *J* = 6.8 Hz, -$O\underline{CH_2}CH_3$), 7.03-7.10 (m, 4H, Ar-H), 7.20 (d, *J* = 8.4 Hz, 1H, Ar-H), 7.88 (br, 1H, N-H), 8.49 (d, *J* = 8.4 Hz, 1H, Ar-H).	–182.48 (m, 1F, CF), –75.89 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –49.97 (s, 2F, CF_2).	504.085 2	504.084 5
h14	1.11 (t, 3H, *J* = 7.2 Hz, -$CH_2\underline{CH_3}$), 2.60 (q, 2H, *J* = 7.2 Hz, -$\underline{CH_2}$ CH_3), 3.72 (s, 2H, -CH_2-), 7.07-7.10 (m, 2H, Ar-H), 7.41-7.48 (m, 2H, Ar-H × 1, N-H), 7.71-7.82 (m, 3H, Ar-H).	–175.15 (m, 1F, CF), –74.17 (d, 6F, *J* = 6.2 Hz, CF_3 × 2), –50.00 (s, 2F, CF_2).	488.090 3	488.091 0
h15	3.74 (s, 2H, -CH_2-), 3.76 (s, 3H, -OCH_3), 3.80 (s, 3H, -OCH_3), 7.62-7.24 (m, 6H, Ar-H × 5, N-H).	–178.54 (m, 1F, CF), –75.12 (d, 6F, *J* = 6.0 Hz, CF_3 × 2), –50.06 (s, 2F, CF_2).	520.080 1	520.080 9
h16	3.75 (s, 2H, -CH_2-), 3.79 (s, 6H, -OCH_3 × 2), 7.68-7.33 (m, 5H, Ar-H × 5). 7.44 (br, 1H, N-H).	–180.10 (m, 1F, CF), –75.52 (d, 6F, *J* = 5.6 Hz, CF_3 × 2), –50.03 (s, 2F, CF_2).	520.080 1	520.080 6

concentration of 500 mg/L.

Preliminary structure-activity relationship studies suggested that the insecticidal activities were significantly influenced by the substituent on the benzene ring of *p*-heptafluoroisopropyl aniline. For example, alkyl and alkoxy substituted compounds (**h1-h8**, **h10-h16**) showed good insecticidal activities, whereas hydroxyl substituted compound **h9** exhibited no insecticidal activity. The target compounds displayed high selectivity between *A. craccivora* and *M. separate*, and compounds with substituent on 2-position of heptafluoroisopropyl aniline exhibited obvious insecticidal effect against *A. craccivora*. Whereas 3-position substituted compounds (**h4** and

Table 3 Insecticidal activity of title compounds h1 to h16

Compd.	Concentration/(mg/L)	Mortality/%	
		A. craccivora	*M. separata*
h1	500	80	0
h2	500	0	100
h3	500	70	0
h4	500	20	100
h5	500	100	0
h6	500	0	80
h7	500	90	0
h8	500	100	0
h9	500	0	0
h10	500	100	0
h11	500	60	0
h12	500	90	0
h13	500	70	0
h14	500	0	90
h15	500	80	0
h16	500	100	0
flubendiamide	500	0	100
abamectin	50	100	100

h6) and unsubstituted compound **h2** showed insecticidal activities against *M. separata*. Further studies on structure optimization are currently in progress.

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