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Synthesis, Insecticidal Activity and Structure-Activity Relationship of 2-(3,3-Dichloro-2-propenyloxy)phenyl-containing Phthalic Acid Diamide Derivatives

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A series of novel 2-(3,3-dichloro-2-propenyloxy)phenyl-containing phthalic acid diamide derivatives (**3I-3IV**) were designed and synthesized. Their chemical structures were characterized by ^{1}H NMR, mass spectrometry and elemental analyses. The insecticidal activities of these compounds against *Plutella xylostella* were evaluated at the concentration of 100 mg/L. Their insecticidal activity is effected by the substituent on the aliphatic amide moiety, which follows the trend of H (**3I**) > -SCH_3 (**3II**) and -$S(O)_2CH_3$ (**3IV**) > -OCH_3 (**3III**). Meanwhile, when the substituent (-CH_3, -CF_3, -Cl) on the aniline ring was introduced to the 3,3-dichloro-2-propenyloxy group in different positons, the *meta*-derivatives exhibit better insecticidal activity than the *para*-derivatives. Compared with the compounds bearing 3,3-dichloro-2-propenyloxy group on the 2-positon of the aniline ring, the compounds with that substituent on the 4-positon exhibit almost the same insecticidal activity trend but much better bioactivity.

Keywords: Phthalic acid diamides, 3,3-Dichloro-2-propenyloxy, Insecticidal activity, Synthesis.

INTRODUCTION

Flubendiamide[1] (Fig. 1) is an efficient insecticide having an unique chemical structure that being codeveloped by Nihon Nohyaku and Bayer Crop Science[2] and acts on ryanodine-sensitive intracellular calcium release channels (ryanodine receptors: RyRs) in insects[3]. It is widely used for vegetables, fruits, crops and cotton to control lepidopterous insects, also low acute toxicity to mammals[1]. As a typical representative belongs to the phthalic acid diamides, the general structure of potent phthalic acid diamides can be characterized by three parts, as shown in Fig. 2: (A) the phthaloyl moiety, (B) the aliphatic amide moiety and (C) the aromatic amide moiety[4]. Previous researchers have paid primarily attention concentrated on the substitutions of the aniline ring and the aliphatic side chain[5-12].

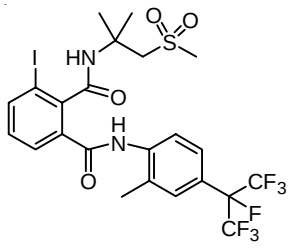
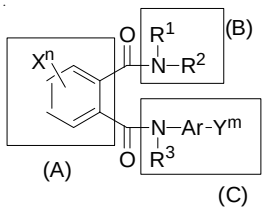


Fig. 1. Chemical structure of flubendiamidetec



General structure 1

Fig. 2. General formula of phthalic acid diamides

Pyridalyl (Fig. 3) is another commercially successful insecticide that shows high insecticidal activity against lepidopterous insects[13,14]. It has already been proved that 3,3-dichloro-2-propenyloxy group plays an essential role in the bioactivity of pyridyl derivatives[13-15]. Be intrigued by these results, our group has introduced the 3,3-dichloro-2-propenyloxy group on the phthalic acid diamide structure at the 4-position of aniline ring, which exhibited excellent insecticidal activities against *Plutella xylostella*[3]. In view of this, in order to investigate the structure-activity relationship between different substitution positions of 3,3-dichloro-2-propenyloxy group on the aniline ring, we designed and synthesized a series of new 3,3-dichloro-2-propenyloxy-containing phthalic acid diamides by introducing 3,3-dichloro-2-propenyloxy group to the 2-position of the aniline ring as shown in Fig. 4. Their insecticidal

activities against *Plutella xylostella* were evaluated systematically, although they do not exhibit satisfied insecticidal activities as anticipated. However, the preparation, insecticidal activity test results and the structure-activity relationship discussions would be useful for understanding the structure-property correlations and rational design of new insecticide with high insecticidal activity. The synthetic routes for title compounds (**3I-3IV**) are shown in **Scheme-I**.

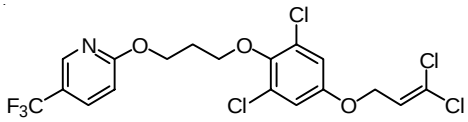
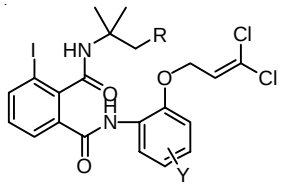


Fig. 3. Chemical structure of pyridalyl



General structure 2

Fig. 4. General structure of the title compounds

EXPERIMENTAL

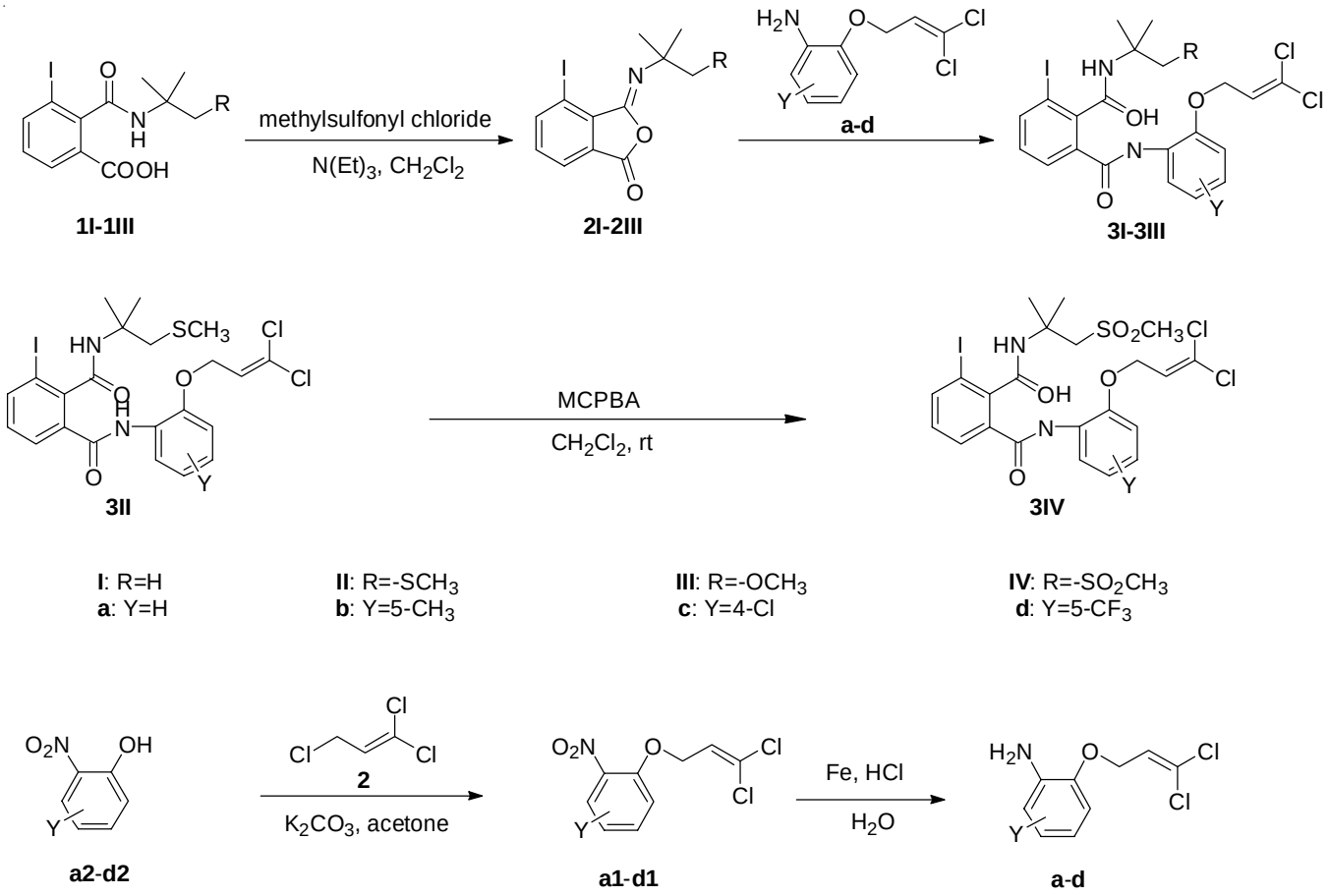
Melting points (m.p.) were measured by an X-4 microscope electrothermal apparatus (Taike, China) without correcting the thermometer. ^{1}H nuclear magnetic resonance (^{1}H NMR) spectra were measured on a Bruker AV-400 spectrometer using tetramethylsilane (TMS) as an internal standard and $CDCl_3$ as solvent. Elemental analyses were performed on a Yanaco Corder MT-3 (Yanaco Co., Ltd.) elemental analyzer. Mass spectra were recorded on a mass spectrometry (MS) spectrometer VG12-250 MS (Agilent Co.).

Compounds **a-d**[15,16], phthalamic acids (**1I** to **1III**) were prepared following the references and did some modification[17,18]. All of the starting materials and reagents were purchased directly and used without further purification unless otherwise indicated.

Synthesis

General procedure for synthesizing compounds 2I-2III[3]: 1I-1III (1.27 mmol) in dichloromethane (30 mL) was cooled in ice while triethylamine (0.13 g, 1.27 mmol) was added with stirring. The solution was cooled below 0 °C, followed by adding methylsulfonyl chloride (0.15 g, 1.27 mmol) that kept the reaction temperature at below 5 °C. Then the reaction was kept in an ice bath. The reaction was monitored by TLC and the reaction was ended when the point of **1I**-**1III** was disappeared. The solution was used directly in the next step without work-up.

General procedure for synthesizing compounds 3I-3III[3]: Aromatic amine (**a-d**) (1.27 mmol) was added into the above reaction solution of **2I-2III** (1.27 mmol) in dichloromethane under an ice bath and then warmed to room temperature.



Scheme-I: General synthetic route for the compounds **3I-3IV, a-d**

The reaction was monitored by TLC. The solution was successively washed by dilute hydrochloric acid, water, aqueous sodium carbonate solution and water last and was dried by anhydrous sodium sulfate. The organic layer was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel eluted with petroleum ether: ethyl acetate (10:1-8:1, by volume) to obtain compounds **3I-3III** as white or yellow powders.

N-*tert*-Butyl-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-phenyl]-1,2-benzenedicarboxamine (3Ia): Yield: 67 %; yellow solid. m.p.: 159-164 °C. ^{1}H NMR δ_H($CDCl_3$): 1.33 (s, 9H, $C(CH_3)_3$), 4.77 (d, J = 6.0 Hz, 2H, $OC\underline{H}_2CH$), 5.67 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.37 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.87 (d, J = 8.0 Hz, 1H, N^1-3-ArH), 7.00-7.08 (m, 2H, N^1-4-ArH, N^1-5-ArH), 7.18 (t, J = 7.8 Hz, 1H, 5-ArH), 7.75 (d, J = 7.4 Hz, 1H, 4-ArH), 7.95 (d, J = 7.9 Hz, 1H, 6-ArH), 8.50 (d, J = 7.9 Hz, 1H, N^1-6-ArH), 8.82 (s, 1H, O=C-NH-Ar). MS *m/z*: 547.0 (M). Elemental analysis: Found: C, 46.01; H, 3.80; N, 4.99 %. Calcd. for $C_{21}H_{21}N_2O_3Cl_2I$: C, 46.09; H, 3.87; N, 5.12 %.

N-*tert*-Butyl-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-methylphenyl]-1,2-benzenedicarboxamine (3Ib): Yield: 62 %; yellow solid. m.p.: 176-180 °C. ^{1}H NMR δ_H($CDCl_3$): 1.34 (s, 9H, $C(CH_3)_3$), 2.33 (s, 3H, Ar-CH_3), 4.73 (d, J = 6.0 Hz, 2H, $OC\underline{H}_2CH$), 5.67 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.36 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.75 (d, J = 8.3 Hz, 1H, N^1-4-ArH), 6.86 (d, J = 8.3 Hz, 1H, N^1-3-ArH), 7.18 (t, J = 7.8 Hz, 1H, 5-ArH), 7.74 (d, J = 7.7 Hz, 1H, 4-ArH), 7.94 (d, J = 7.9 Hz, 1H, 6-ArH), 8.34 (s, 1H, N^1-6-ArH), 8.79 (s, 1H, O=C-NH-Ar). MS *m/z*: 560.9 (M). Elemental analysis: Found: C, 47.23; H, 4.22; N, 4.83 %. Calcd. for $C_{22}H_{23}N_2O_3Cl_2I$: C, 47.08; H, 4.13; N, 4.99 %.

N-*tert*-Butyl-3-iodo-N'-[4-chloro-2-(3,3-dichloro-2-propenyloxy)phenyl]-1,2-benzenedicarboxamine (3Ic): Yield: 58 %; yellow solid. m.p.: 152-156 °C. ^{1}H NMR δ_H($CDCl_3$): 1.33 (s, 9H, $C(CH_3)_3$), 4.75 (d, J = 6.0 Hz, 2H, $OC\underline{H}_2CH$), 5.65 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.39 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.86 (d, J = 2.2 Hz, 1H, N^1-3-ArH), 6.99 (d, J = 8.7 Hz, 1H, N^1-6-ArH), 7.19 (t, J = 7.8 Hz, 1H, 5-ArH), 7.75 (d, J = 7.8 Hz, 1H, 4-ArH), 7.95 (d, J = 7.9 Hz, 1H, 6-ArH), 8.47 (d, J = 8.7 Hz, 1H, N^1-5-ArH), 8.83 (s, 1H, O=C-NH-Ar). MS *m/z*: 581.0 (M). Elemental analysis: Found: C, 43.48; H, 3.62; N, 4.66 %. Calcd. for $C_{21}H_{20}N_2O_3Cl_3I$: C, 43.36; H, 3.47; N, 4.82 %.

N-*tert*-Butyl-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-(trifluoromethyl)phenyl]-1,2-benzenedicarboxamine (3Id): Yield: 54 %; white solid. m.p.: 124-127 °C. ^{1}H NMR δ_H($CDCl_3$): 1.33 (s, 9H, $C(CH_3)_3$), 4.83 (d, J = 5.4 Hz, 2H, $OC\underline{H}_2CH$), 5.74 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.40 (t, J = 5.3 Hz, 1H, $OCH_2C\underline{H}$), 6.93 (d, J = 8.2 Hz, 1H, N^1-4-ArH), 7.19 (t, J = 7.5 Hz, 1H, 5-ArH), 7.35 (d, J = 8.0 Hz, 1H, N^1-3-ArH), 7.76 (d, J = 7.4 Hz, 1H, 4-ArH), 7.96 (d, J = 7.6 Hz, 1H, 6-ArH), 8.87 (s, 1H, N^1-6-ArH), 9.02 (s, 1H, O=C-NH-Ar). MS *m/z*: 615.0 (M). Elemental analysis: Found: C, 42.81; H, 3.39; N, 4.48 %. Calcd. for $C_{22}H_{20}N_2O_3Cl_2F_3I$: C, 42.95; H, 3.28; N, 4.55 %.

N-[1,1-Dimethyl-2-(methylthio)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)phenyl]-1,2-benzenedicarboxamine (3IIa): Yield: 46 %; yellow solid. m.p.: 107-110 °C. ^{1}H NMR δ_H($CDCl_3$): 1.41 (s, 6H, CH_3-C-CH_3), 2.01 (s, 3H, $C\underline{H}_3$-S-CH_2), 2.84 (s, 2H, CH_3-S-$C\underline{H}_2$), 4.77 (d, J = 6.0 Hz, 2H, $OC\underline{H}_2CH$), 5.97 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.34 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.87 (d, J = 8.0 Hz, 1H, N^1-6-ArH), 7.03 (m, 2H, N^1-4-ArH, N^1-5-ArH), 7.19 (t, J = 7.8 Hz, 1H, 5-ArH), 7.74 (d, J = 7.7 Hz, 1H, 4-ArH), 7.96 (d, J = 8.3 Hz, 1H, 6-ArH), 8.51 (d, J = 7.3 Hz, 1H, N^1-3-ArH), 8.74 (s, 1H, O=C-NH-Ar). MS *m/z*: 592.9 (M). Elemental analysis: Found: C, 44.49; H, 3.78; N, 4.57 %. Calcd. for $C_{22}H_{23}N_2O_3SCl_2I$: C, 44.54; H, 3.91; N, 4.72 %.

N-[1,1-Dimethyl-2-(methylthio)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-methylphenyl]-1,2-benzenedicarboxamine (3IIb): Yield: 58 %; yellow solid. m.p.: 121-124 °C. ^{1}H NMR δ_H($CDCl_3$): 1.42 (s, 6H, CH_3-C-CH_3), 2.02 (s, 3H, $C\underline{H}_3$-S-CH_2), 2.33 (s, 3H, Ar-CH_3), 2.85 (s, 2H, CH_3-S-$C\underline{H}_2$), 4.73 (d, J = 6.0 Hz, 2H, $OCH_2C\underline{H}$), 5.96 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.33 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.75 (d, J = 8.3 Hz, 1H, N^1-4-ArH), 6.87 (d, J = 9.0 Hz, 1H, N^1-3-ArH), 7.19 (t, J = 7.8 Hz, 1H, 5-ArH), 7.74 (d, J = 7.3 Hz, 1H, 4-ArH), 7.95 (d, J = 7.9 Hz, 1H, 6-ArH), 8.35 (s, 1H, N^1-6-ArH), 8.71 (s, 1H, O=C-NH-Ar). MS *m/z*: 606.9 (M). Elemental analysis: Found: C, 45.32; H, 4.01; N, 4.49 %. Calcd. for $C_{23}H_{25}N_2O_3SCl_2I$: C, 45.49; H, 4.15; N, 4.61 %.

N-[1,1-Dimethyl-2-(methylthio)ethyl]-3-iodo-N'-[4-chloro-2-(3,3-dichloro-2-propenyloxy)phenyl]-1,2-benzenedicarboxamine (3IIc): Yield: 52 %; yellow solid. m.p.: 105-108 °C. ^{1}H NMR δ_H($CDCl_3$): 1.41 (s, 6H, CH_3-C-CH_3), 2.03 (s, 3H, $C\underline{H}_3$-S-CH_2), 2.84 (s, 2H, CH_3-S-$C\underline{H}_2$), 4.75 (d, J = 6.0 Hz, 2H, $OC\underline{H}_2CH$), 5.97 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.36 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.86 (d, J = 2.1 Hz, 1H, N^1-3-ArH), 7.01 (d, J = 8.7 Hz, 1H, N^1-5-ArH), 7.20 (t, J = 7.8 Hz, 1H, 5-ArH), 7.75 (d, J = 7.6 Hz, 1H, 4-ArH), 7.97 (d, J = 8.0 Hz, 1H, 6-ArH), 8.49 (d, J = 8.7 Hz, 1H, N^1-6-ArH), 8.76 (s, 1H, O=C-NH-Ar). MS *m/z*: 626.9 (M). Elemental analysis: Found: C, 42.33; H, 3.41; N, 4.28 %. Calcd. for $C_{22}H_{22}N_2O_3SCl_3I$: C, 42.09; H, 3.53; N, 4.46 %.

N-[1,1-Dimethyl-2-(methylthio)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-(trifluoromethyl)phenyl]-1,2-benzenedicarboxamine (3IId): Yield: 61 %; yellow solid. m.p.: 126-130 °C. ^{1}H NMR δ_H($CDCl_3$): 1.42 (s, 6H, CH_3-C-CH_3), 2.01 (s, 3H, $C\underline{H}_3$-S-CH_2), 2.83 (s, 2H, CH_3-S-$C\underline{H}_2$), 4.83 (d, J = 6.0 Hz, 2H, $OC\underline{H}_2CH$), 5.98 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.36 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.93 (d, J = 6.2 Hz, 1H, N^1-4-ArH), 7.22 (t, J = 7.9 Hz, 1H, 5-ArH), 7.36 (d, J = 8.5 Hz, 1H, N^1-3-ArH), 7.77 (d, J = 7.8 Hz, 1H, 4-ArH), 7.98 (d, J = 7.9 Hz, 1H, 6-ArH), 8.89 (d, J = 1.8 Hz, 1H, N^1-6-ArH), 8.92 (s, 1H, O=C-NH-Ar). MS *m/z*: 661.1 (M). Elemental analysis: Found: C, 41.91; H, 3.52; N, 4.27 %. Calcd. for $C_{23}H_{22}N_2O_3SCl_2F_3I$: C, 41.77; H, 3.35; N, 4.24 %.

N-[1,1-Dimethyl-2-(methoxy)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)phenyl]-1,2-benzenedicarboxamine (3IIIa): Yield: 57 %; yellow solid. m.p.: 113-116 °C. ^{1}H NMR δ_H($CDCl_3$): 1.34 (s, 6H, CH_3-C-CH_3), 3.23 (s, 3H, $C\underline{H}_3$-O-CH_2), 3.25 (s, 2H, CH_3-O-$C\underline{H}_2$), 4.77 (d, J = 6.0 Hz, 2H, $OC\underline{H}_2CH$), 6.03 (s, 1H, O=C-N$\underline{H}$-C-CH_3), 6.36 (t, J = 6.0 Hz, 1H, $OCH_2C\underline{H}$), 6.87 (d, J = 8.0 Hz, 1H, N^1-3-ArH), 7.03 (m, 2H, N^1-4-ArH, N^1-5-ArH), 7.17 (t, J = 7.8 Hz, 1H, 5-ArH), 7.76 (d, J = 7.9 Hz, 1H, 4-ArH), 7.95 (d, J = 7.9 Hz, 1H, 6-ArH), 8.50 (d, J = 7.9 Hz, 1H, N^1-6-ArH), 8.82 (s, 1H, O=C-NH-Ar). MS *m/z*: 576.8

(M). Elemental analysis: Found: C, 45.72; H, 4.05; N, 4.98 %. Calcd. for $C_{22}H_{23}N_2O_4Cl_2I$: C, 45.78; H, 4.02; N, 4.85 %.

N-[1,1-Dimethyl-2-(methoxy)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-methylphenyl]-1,2-benzenedicarboxamine (3IIIb): Yield: 58 %; yellow solid. m.p.: 135-137 °C. ^{1}H NMR δ_H($CDCl_3$): 1.35 (s, 6H, CH_3-C-CH_3), 2.33 (s, 3H, Ar-CH_3), 3.24 (d, 5H, C<u>H</u>$_3$-O-CH_2, CH_3-O-C<u>H</u>$_2$), 4.73 (d, *J* = 5.5 Hz, 2H, OC<u>H</u>$_2$CH), 6.01 (s, 1H, O=C-N<u>H</u>-C-CH_3), 6.35 (t, *J* = 5.4 Hz, 1H, OCH_2C<u>H</u>), 6.75 (d, *J* = 8.0 Hz, 1H, N^1-4-ArH), 6.86 (d, *J* = 7.4 Hz, 1H, N^1-3-ArH), 7.18 (t, *J* = 7.7 Hz, 1H, 5-ArH), 7.75 (d, *J* = 7.3Hz, 1H, 4-ArH), 7.95 (d, *J* = 7.3 Hz, 1H, 6-ArH), 8.34 (s, 1H, N^1-6-ArH), 8.78 (s, 1H, O=C-NH-Ar). MS *m/z*: 591.0 (M). Elemental analysis: Found: C, 46.68; H, 4.27; N, 4.66 %. Calcd. for $C_{23}H_{25}N_2O_4Cl_2I$: C, 46.72; H, 4.26; N, 4.74 %.

N-[1,1-Dimethyl-2-(methoxy)ethyl]-3-iodo-N'-[4-chloro-2-(3,3-dichloro-2-propenyloxy)phenyl]-1,2-benzenedicarboxamine (3IIIc): Yield: 63 %; yellow solid. m.p.: 106-109 °C. ^{1}H NMR δ_H($CDCl_3$): 1.34 (s, 6H, CH_3-C-CH_3), 3.24 (s, 5H, C<u>H</u>$_3$-O-CH_2, CH_3-O-C<u>H</u>$_2$), 4.75 (d, *J* = 6.0 Hz, 2H, OC<u>H</u>$_2$CH), 6.04 (s, 1H, O=C-N<u>H</u>-C-CH_3), 6.38 (t, *J* = 6.0 Hz, 1H, OCH_2C<u>H</u>), 6.86 (d, *J* = 2.2 Hz, 1H, N^1-3-ArH), 7.00 (d, *J* = 8.7 Hz, 1H, N^1-5-ArH), 7.19 (t, *J* = 7.8 Hz, 1H, 5-ArH), 7.77 (d, *J* = 7.8 Hz, 1H, 4-ArH), 7.96 (d, *J* = 7.9 Hz, 1H, 6-ArH), 8.48 (d, *J* = 8.7 Hz, 1H, N^1-6-ArH), 8.84 (s, 1H, O=C-NH-Ar). MS *m/z*: 610.8 (M). Elemental analysis: Found: C, 43.05; H, 3.85; N, 4.45 %. Calcd. for $C_{22}H_{22}N_2O_4Cl_3I$: C, 43.20; H, 3.63; N, 4.58 %.

N-[1,1-Dimethyl-2-(methoxy)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-(trifluoromethyl)phenyl]-1,2-benzenedicarboxamine (3IIId): Yield: 65 %; yellow solid. m.p.: 121-124 °C. ^{1}H NMR δ_H($CDCl_3$): 1.34 (s, 6H, CH_3-C-CH_3), 3.24 (s, 5H, C<u>H</u>$_3$-O-CH_2, CH_3-O-C<u>H</u>$_2$), 4.83 (d, *J* = 5.1 Hz, 2H, OC<u>H</u>$_2$CH), 6.06 (s, 1H, O=C-N<u>H</u>-C-CH_3), 6.38 (t, *J* = 5.2 Hz, 1H, OCH_2C<u>H</u>), 6.93 (d, *J* = 8.1 Hz, 1H, N^1-4-ArH), 7.19 (t, *J* = 7.2 Hz, 1H, 5-ArH), 7.35 (d, *J* = 7.7 Hz, 1H, N^1-3-ArH), 7.78 (d, *J* = 7.2 Hz, 1H, 4-ArH), 7.97 (d, *J* = 7.4 Hz, 1H, 6-ArH), 8.89 (s, 1H, N^1-6-ArH), 9.00 (s, 1H, O=C-NH-Ar). MS *m/z*: 645.3 (M). Elemental analysis: Found: C, 42.69; H, 3.45; N, 4.48 %. Calcd. for $C_{23}H_{22}N_2O_4Cl_2F_3I$: C, 42.81; H, 3.44; N, 4.34 %.

General procedure for synthesizing compounds 3IV[3]: Added MCPBA (0.21 g, 1.02 mmol) into a solution of **3II** (0.51 mmol) in dichloromethane (20 mL). The reaction was kept at room temperature. The reaction was monitored by TLC. After **3II** disappeared, the solution was successively washed by aqueous sodium dithionite solution, water, aqueous sodium carbonate solution and finally water and was dried by anhydrous sodium sulfate. The organic layer was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel eluted with petroleum ether: ethyl acetate (2:1, by volume) to obtain compounds **3IV** as yellow powders.

N-[1,1-Dimethyl-2-(methylsulfonyl)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)phenyl]-1,2-benzenedicarboxamine (3IVa): Yield: 71 %; yellow solid. m.p.: 130-134 °C. ^{1}H NMR δ_H($CDCl_3$): 1.60 (s, 6H, CH_3-C-CH_3), 2.64 (s, 3H, C<u>H</u>$_3$-S(O)$_2$-CH_2), 3.51 (s, 2H, CH_3-S(O)$_2$-C<u>H</u>$_2$), 4.70 (d, *J* = 6.1 Hz, 2H, OC<u>H</u>$_2$CH), 6.13 (s, 1H, O=C-N<u>H</u>-C-CH_3), 6.21 (t, *J* = 6.1 Hz, 1H, OCH_2C<u>H</u>), 6.82 (d, *J* = 8.0 Hz, 1H, N^1-6-ArH), 6.99 (m, 2H, N^1-4-ArH, N^1-5-ArH), 7.15 (t, *J* = 7.8 Hz, 1H, 5-ArH), 7.63 (d, *J* = 7.4 Hz, 1H, 4-ArH), 7.90 (d, *J* = 7.9 Hz, 1H, 6-ArH), 8.40 (d, *J* = 7.6 Hz, 1H, N^1-3-ArH), 8.48 (s, 1H, O=C-NH-Ar). MS *m/z*: 625.2 (M). Elemental analysis: Found: C, 42.31; H, 3.74; N, 4.47 %. Calcd. for $C_{22}H_{23}N_2O_5SCl_2I$: C, 42.26; H, 3.71; N, 4.48 %.

N-[1,1-Dimethyl-2-(methylsulfonyl)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-methylphenyl]-1,2-benzenedicarboxamine (3IVb): Yield: 90 %; yellow solid. m.p.: 133-136 °C. ^{1}H NMR δ_H($CDCl_3$): 1.67 (s, 6H, CH_3-C-CH_3), 2.33 (s, 3H, Ar-CH_3), 2.72 (s, 3H, C<u>H</u>$_3$-S(O)$_2$-CH_2), 3.59 (s, 2H, CH_3-S(O)$_2$-C<u>H</u>$_2$), 4.73 (d, *J* = 6.1 Hz, 2H, OC<u>H</u>$_2$CH), 6.21 (s, 1H, O=C-N<u>H</u>-C-CH_3), 6.27 (t, *J* = 6.1 Hz, 1H, OCH_2C<u>H</u>), 6.77 (d, *J* = 8.3 Hz, 1H, N^1-4-ArH), 6.88 (d, *J* = 7.6 Hz, 1H, N^1-3-ArH), 7.20 (t, *J* = 7.8 Hz, 1H, 5-ArH), 7.69 (d, *J* = 7.6 Hz, 1H, 4-ArH), 7.97 (d, *J* = 7.3 Hz, 1H, 6-ArH), 8.31 (s, 1H, N^1-6-ArH), 8.51 (s, 1H, O=C-NH-Ar). MS *m/z*: 638.7 (M). Elemental analysis: Found: C, 43.16; H, 3.89; N, 4.41 %. Calcd. for $C_{23}H_{25}N_2O_5SCl_2I$: C, 43.21; H, 3.94; N, 4.38 %.

N-[1,1-Dimethyl-2-(methylsulfonyl)ethyl]-3-iodo-N'-[4-chloro-2-(3,3-dichloro-2-propenyloxy)phenyl]-1,2-benzenedicarboxamine (3IVc): Yield: 80 %; yellow solid. m.p.: 134-136 °C. ^{1}H NMR δ_H($CDCl_3$): 1.65 (s, 6H, CH_3-C-CH_3), 2.78 (s, 3H, C<u>H</u>$_3$-S(O)$_2$-CH_2), 3.58 (s, 2H, CH_3-S(O)$_2$-C<u>H</u>$_2$), 4.74 (d, *J* = 6.2 Hz, 2H, OC<u>H</u>$_2$CH), 6.28 (t, *J* = 6.2 Hz, 2H, O=C-N<u>H</u>-C-CH_3, OCH_2C<u>H</u>), 6.88 (d, *J* = 2.2 Hz, 1H, N^1-3-ArH), 7.01 (d, *J* = 8.7 Hz, 1H, N^1-5-ArH), 7.21 (t, *J* = 7.8 Hz, 1H, 5-ArH), 7.69 (d, *J* = 7.6 Hz, 1H, 4-ArH), 7.97 (d, *J* = 7.9 Hz, 1H, 6-ArH), 8.43 (d, *J* = 8.7 Hz, 1H, N^1-6-ArH), 8.51 (s, 1H, O=C-NH-Ar). MS *m/z*: 659.2 (M). Elemental analysis: Found: C, 40.11; H, 3.34; N, 4.27 %. Calcd. for $C_{22}H_{22}N_2O_5SCl_3I$: C, 40.05; H, 3.36; N, 4.25 %.

N-[1,1-Dimethyl-2-(methylsulfonyl)ethyl]-3-iodo-N'-[2-(3,3-dichloro-2-propenyloxy)-5-(trifluoromethyl)phenyl]-1,2-benzenedicarboxamine (3IVd): Yield: 86 %; yellow solid. m.p.: 95-97 °C. ^{1}H NMR δ_H($CDCl_3$): 1.68 (s, 6H, CH_3-C-CH_3), 2.81 (s, 3H, C<u>H</u>$_3$-S(O)$_2$-CH_2), 3.61 (s, 2H, CH_3-S(O)$_2$-C<u>H</u>$_2$), 4.82 (d, *J* = 6.2 Hz, 2H, OC<u>H</u>$_2$CH), 6.27 (t, *J* = 6.2 Hz, 2H, O=C-N<u>H</u>-C-CH_3, OCH_2C<u>H</u>), 6.95 (d, *J* = 8.6 Hz, 1H, N^1-4-ArH), 7.22 (t, *J* = 7.8 Hz, 1H, 5-ArH), 7.37 (d, *J* = 7.8 Hz, 1H, N^1-3-ArH), 7.70 (d, *J* = 7.4 Hz, 1H, 4-ArH), 7.99 (d, *J* = 7.9 Hz, 1H, 6-ArH), 8.62 (s, 1H, O=C-NH-Ar), 8.83 (d, *J* = 1.56 Hz, 1H, N^1-6-ArH). MS *m/z*: 692.7 (M). Elemental analysis: Found: C, 39.78; H, 3.15; N, 4.06 %. Calcd. for $C_{23}H_{22}N_2O_5SCl_2F_3I$: C, 39.84; H, 3.20; N, 4.04 %.

Evaluation of insecticidal activities: According to a previously reported method, the insecticidal activities of the title compounds (**3I-3IV**) *in vivo* were tested against *Plutella xylostella*[4]. Dipping method was used for testing the insecticidal activity against *Plutella xylostella*. Dipped the cabbage leaf discs (8 cm diameter) into a test solution for 10 s and then dried by air on filter paper. The leaf was released into a petri dish and then introduced seven third-instar *Plutella xylostella* into the dish. *Plutella xylostella* was showed abnormal symptoms such as body contraction, feeding cessation, paralysis or dead even. Percentage mortalities were evaluated for 3 days after the treatment. Evaluation was based on a percentage scale

of 0-100, where 0 was meant as no activity and 100 as total kill. The results are listed in Table-1. Flubendiamide and pyridalyl were used as controls.

RESULTS AND DISCUSSION

The reaction routes employed for the synthesis of **a-d** (2-(3,3-dichloro-2-propenyloxy)benzenamine, 2-(3,3-dichloro-2-propenyloxy)-5-methylbenzenamine, 4-chloro-2-(3,3-dichloro-2-propenyloxy)benzeneamine, 2-(3,3- dichloro-2-propenyloxy)-5-(trifluoromethyl)benzenamine) are shown in **Scheme-I**. According to the previously reported methods[15,16], iron powder was used in preparation of compounds **a-d** and the filtrate was extracted by ethyl acetate in work-up. However, by washing the filter cake with ethyl acetate, the yield could be increased up to 35-42 %. These results are shown in Table-1.

TABLE-1
SYNTHESIS OF **a-d** UNDER BOTH OPTIMAL AND CONVENTIONAL METHODS

No.	Yield (%)	
	Optimal	Conventional
a	73	43
b	88	46
c	67	29
d	70	35

The structures of all the synthesized compounds were confirmed by ^{1}H NMR, mass spectrometry and elemental analyses. The aromatic amide proton of title compounds show up at low field (δ 8.48-9.02) in the ^{1}H NMR, while the aliphatic amide moiety proton appears at δ 5.65-6.28 in $CDCl_3$ by solvent influence. The chemical shift of CH_2 and CH proton of the dichloro-propenyloxy group are around at δ 4.70-4.83 and 6.21-6.40, respectively. The chemical shift of CH_2 proton in the aliphatic side chain of title compounds **3II**, **3III** and **3IV** are at δ 2.83-2.85, 3.24-3.25 and 3.51-3.61, respectively. Meanwhile, the CH_3 group in the aliphatic side chain attaching to the hetero atom are at δ 2.01-2.03, 3.23-3.24 and 2.64-2.81, respectively, due to the difference in shielding effect induced by S, O and O=S=O group. The chemical shift of the 4-ArH, 5-ArH and 6-ArH of the 3-iodo-1,2-benzenedicar-boxamide derivatives were identified at δ 7.63-7.78, 7.15-7.22 and 7.90-7.99, respectively.

Bioactivity and the structure-activity relationship: The biological activities of the selected compounds **3I-3IV** against Diamondback moth at the concentration of 100 mg/L are shown in Table-2.

As summarized in Table-2, the insecticidal activities against *Diamondback moth* of the target compounds **3I-3IV** are lower than we reported previously[3]. Although it is difficult to found a specific structure-activity relationship from these data, it still shows the following general trend. To discuss the structure-activity relationship about the effect of the aliphatic amide moiety substituent R, compounds **3I-3IV** were designed to contain $-OCH_3$, $-SCH_3$ and $-S(O)_2CH_3$ substituents, respectively. As shown in Table-2, the general trend of insecticidal activity for the substituents R is H (**3I**) > $-SCH_3$ (**3II**) and $-S(O)_2CH_3$ (**3IV**) > $-OCH_3$ (**3III**), which is similar to our early study[3]. For example, compound **3Ia** (Y = H, 33.33 %) displays higher insecticidal activity than **3IIa** (Y = H, 9.52 %) at 100 mg/L. For compounds **3IIId** and **3IVd** (Y = 5-CF_3), compound **3IVd** exhibits 14.29 % mortality at 100 mg/L, while the former only had 9.52 % mortality at the same concentration.

According to the relative position of the 3,3-dichloro-2-propenyloxy group and the substituents Y on the aniline ring, compounds **3Ic-3IVc** are defined as *meta*-derivatives, while compounds **3Ib-3IVb** and **3Id-3IVd** are representative the *para*-ones. As shown in Table-2, compared with compounds **3II**, **3III** and **3IV**, the trend of insecticidal activity is *meta*-derivatives > *para*-derivatives. For example, *meta*-derivatives **3Ic**, **3IIIc** and **3IVc** display higher insecticidal activity than the *para*-derivatives **3Ib** and **3Id**, **3IIIb** and **3IIId** and **3IVb**,

TABLE-2
STRUCTURES AND INSECTICIDAL ACTIVITIES AGAINST *Diamondback moth* OF COMPOUNDS **3I-3IV**, FLUBENDIAMIDE AND PYRIDYL

Compound	R	Y	Concentration	Mortality (%)	
			(μg/mL)	1 days	3 days
3Ia	H	H	100	0	33.33
3Ib	H	5-CH_3	100	0	4.76
3Ic	H	4-Cl	100	0	14.29
3Id	H	5-CF_3	100	0	9.52
3IIa	SCH_3	H	100	0	9.52
3IIb	SCH_3	5-CH_3	100	0	4.76
3IIc	SCH_3	4-Cl	100	0	4.76
3IId	SCH_3	5-CF_3	100	0	4.55
3IIIa	OCH_3	H	100	0	4.76
3IIIb	OCH_3	5-CH_3	100	0	4.55
3IIIc	OCH_3	4-Cl	100	4.76	14.29
3IIId	OCH_3	5-CF_3	100	0	9.52
3IVa	$S(O)_2CH_3$	H	100	0	4.55
3IVb	$S(O)_2CH_3$	5-CH_3	100	4.76	4.76
3IVc	$S(O)_2CH_3$	4-Cl	100	0	14.29
3IVd	$S(O)_2CH_3$	5-CF_3	100	0	14.29
Flubendiamide	-	-	100	100	-
Pyridyl	-	-	100	100	-

respectively, while the non-derivatives **3IIa**, **3IIIa** and **3IVa** do not exhibit obvious bioactivity. Compound **3Ic** (14.29 %) displays higher insecticidal activity than the corresponding *para*-derivatives **3Ib** (4.76 %) and **3Id** (9.52 %) at 100 mg/L, while compound **3IIIc** (14.29 %) also shows higher potency than the corresponding *para*-derivatives **3IIIb** (4.55 %) and **3IIId** (9.52 %) at 100 mg/L.

In order to discuss the electronic effect of substituent Y on the aniline ring, the electron-withdrawing substituents (-Cl and -CF_3) and the electron-donating substituent (-CH_3) were introduced, which is different with the rule we reported before[3]. The insecticidal activity of the compounds with the electron-withdrawing substituents (-Cl and -CF_3) is better than those with electron-donating substituent. For example, the introduction of electron-donating substituent -CH_3 on the 5-position of the aniline ring makes the insecticidal activity lower than the electron-withdrawing substituent -CF_3 in the same condition. Compound **3IVd** (Y = 5-CF_3, 14.29 %) displays a little bit higher insecticidal activity than **3IVb** (Y = 5-CH_3, 4.76 %). The introduction of Cl substituent is advantageous to improve the bioactivity.

In summary, the insecticidal activity of the title compounds bearing the 3,3-dichloro-2-propenyloxy group on the 2-position of the aniline ring substantially follows the same trend of H (**3I**) > -SCH_3 (**3II**) and -$S(O)_2CH_3$ (**3IV**) > -OCH_3 (**3III**), as those contained the same substituents on the 4-position of the aniline ring. Meanwhile, when the substituent (-CH_3, CF_3, -Cl) on the aniline ring was introduced to the different position of the 3,3-dichloro-2-propenyloxy group, the *meta*-derivatives exhibit better insecticidal activity than the *para*-derivatives. Although the insecticidal activity of the title compounds against *Plutella xylostella* is not as high as the 4-(3,3-dichloro-2-propenyloxy) phenyl-containing phthalic acid diamides, the 3,3-dichloro-2-propenyloxy group is worthy and significant for being incorporated into phthalic acid diamide derivatives. Maybe on the 3-position of the aniline ring where the 3,3-dichloro-2-propenyloxy group substituted can contribute to activity improving. Furthermore, the structure-activity relationship of the 3,3-dichloro-2-propenylxyphenyl-containing phthalic acid diamides will be more meaningful. The research of this sort is on the way.

Conclusion

A series of novel 2-(3,3-dichloro-2-propenyloxy)phenyl-containing phthalic acid diamide derivatives were designed and synthesized. Their chemical structures were characterized and confirmed. The insecticidal activities of these compounds against *P. xylostella* were evaluated at the concentration of 100 mg/L. Their insecticidal activity follows the trend of H (**3I**) > -SCH_3 (**3II**) and -$S(O)_2CH_3$ (**3IV**) > -OCH_3 (**3III**) which substitutes on the aliphatic amide moiety. Meanwhile, when the substituent (-CH_3, -CF_3, -Cl) on the aniline ring was introduced to the 3,3-dichloro-2-propenyloxy group in different positions, the *meta*-derivatives exhibit better insecticidal activity than the *para*-derivatives. Compared with the compounds bearing 3,3-dichloro-2-propenyloxy group on the 2-positon of the aniline ring, the compounds with that substituent on the 4-positon exhibit almost the same insecticidal activity trend but much better bioactivity.

Nevertheless, further studies on the structure-activity relationships of compounds of this sort, for example combined the 3,3-dichloro-2-propenyloxy group on the 3-positon of the aniline ring, could help for the detailed structure-activity relationship of these compounds, aid for the design of novel insecticidal structures with superior performance.

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