Synthesis and Insecticidal Evaluation of Novel *N*-pyridylpyrazole Derivatives Containing Diacylhydrazine/1,3,4-Oxadiazole Moieties

Wei Wang,* Xiao-Rui Zheng, Xiao-Ying Huang, Ming-Zhen Mao, Kang-Yun Liu, Chao Xue, Lie-Ping Wang,* and Bin-Ke Ning*

State Key Laboratory of Fluorine & Nitrogen Chemicals, Xi'an Modern Chemistry Research Institute, Xi'an, Shaanxi, People's Republic of China
*E-mail: wangwei204@aliyun.com; wlpcxm@qq.com; bkning@126.com

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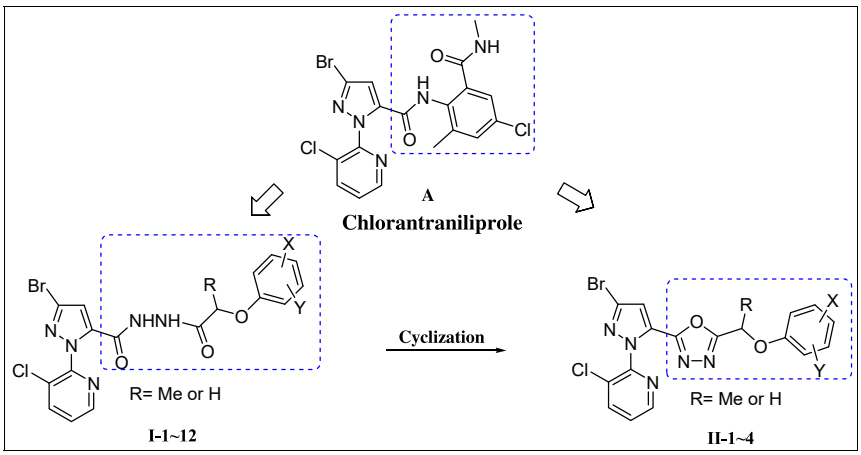

Two series of novel *N*-pyridylpyrazole derivatives containing diacylhydrazine/1,3,4-oxadiazole moieties were designed and synthesized based on the structure of chlorantraniliprole and characterized *via* ^{1}H-NMR, ^{13}C-NMR, IR, MS, and elemental analysis. The preliminary bioassay indicated that some of the title compounds **I** and **II** exhibited larvicidal activities against *Mythimna separata* with 90–100% death rates at 500 mg/L. The further test showed that these compounds had weak insecticidal activity against *Mythimna separata* and *Plutella xylostella* at 200 mg/L and might be not suitable as insecticide lead compound for further optimization.

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INTRODUCTION

As the main pests control tool, insecticides play a very important role in modern agriculture [1,2]. Because agricultural pests can develop resistance rapidly all over the world, it is necessary to develop efficient insecticides with novel structures and modes of action [2–6]. As a selective activator of the insect ryanodine receptor, chlorantraniliprole (**A**, Scheme 1) which has attracted considerable attention for decades because of its exceptional insecticidal activity on a broad spectrum and low mammalian toxicity [2–7]. Recently, Li and Song *et al*. have designed and synthesized series of novel *N*-pyridylpyrazole derivatives on the basis of the structure of chlorantraniliprole [2–11]. Their results demonstrated that the modifications in the structure of chlorantraniliprole are still attractive.

In our previous work, some series of novel *N*-pyridylpyrazole derivatives were designed and synthesized, and the ensuing bioassay results exhibited excellent larvicidal activity against *Mythimna separata* and *Plutella xylostella* in some cases [5–7,12]. On the other hand, among various biologically scaffolds, diacylhydrazine [13–19] and 1,3,4-oxadiazole [20–22] moieties have occupied important positions in pesticide chemistry and are often introduced in the design of bioactive compounds. On the basis of the aforementioned observations, a series of novel *N*-pyridylpyrazole derivatives containing diacylhydrazine moiety (**I-1–12**) and their corresponding 1,3,4-oxadiazole derivatives (**II-1–4**) (Figure 1) were designed and synthesized as part of our ongoing work amied at searching for new insecticidal compounds. Herein, we report the synthesis and insecticidal activity of the *N*-pyridylpyrazole derivatives **I** and **II**.

RESULTS AND DISCUSSION

The title compounds **I-1–12** were prepared by condensation of intermediate **7** with the pyrazole-5-carbonyl chloride **5** in the presence of K_2CO_3 as a base in tetrahydrofuran (THF) (Scheme 1). The 2-(substituted phenoxy)acetate carbonyl hydrazines **7** were prepared

Scheme 1. Synthetic route of compounds **I**-1–**I**-12. Reagents and conditions: (a) diethyl maleate, NaOEt, EtOH, reflux; (b) $POBr_3$, MeCN, 80°C; (c) $K_2S_2O_8$, H_2SO_4, MeCN, reflux; (d) (i) aqueous NaOH, MeOH and (ii) aqueous HCl; (e) $SOCl_2$, reflux; (f) Hydrazine hydrate, reflux; (g) K_2CO_3, THF, H_2O.

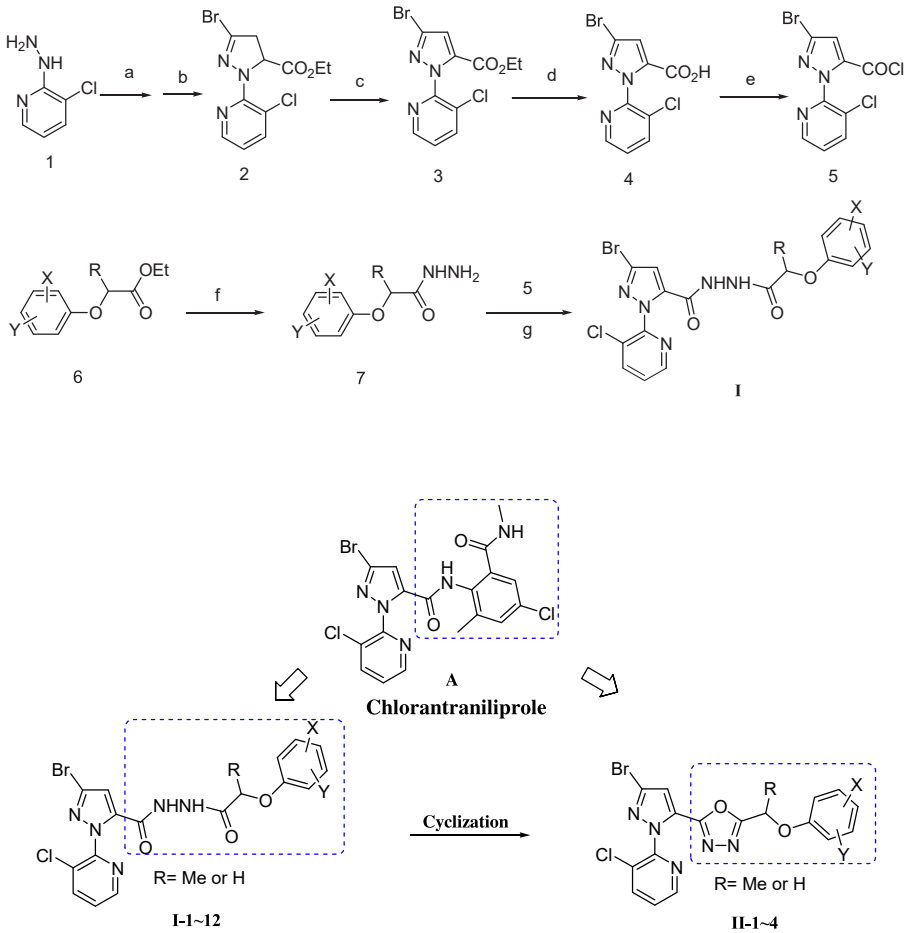

Figure 1. Chemical modification of lead structure **A** (chlorantraniliprole). [Color figure can be viewed at wileyonlinelibrary.com]

according to the reported methods [23]. The ethyl 2-(substituted phenoxy)acetate **6** could be synthesized from the corresponding substituted phenols and ethyl 2-bromoacetate in good yields [24]. According to the literature [2,4], the pyrazole carboxylic acid **4** was synthesized from 3-chloro-2-hydrazinylpyridine **1** which was used directly as obtained commercially. In addition, the pyrazole-5-carbonyl chloride **5** could be prepared by the reaction of pyrazole carboxylic acid **4** with thionyl chloride in reflux for 5–6 h. The synthetic route of the title compound **II** is shown in Scheme 2. The title compounds **II-1–4** could be obtained by the reaction of diacylhydrazines **I** with $POCl_3$ under the condition of refluxing [2,23].

The structures of the title compounds **I** and **II** were characterized by ^{1}H-NMR, ^{13}C-NMR, IR, MS, and

Scheme 2. Synthetic route of compounds **II**-1–**II**-4.

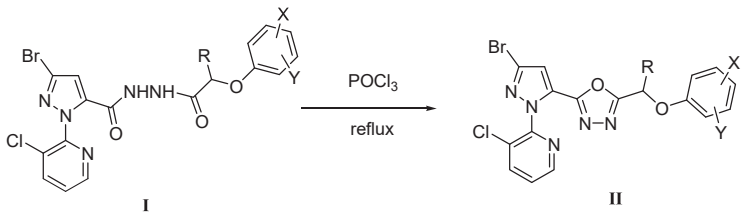

Table 1

Structure and insecticidal activity of compound **I**.

	Chemical structure		MS		PX	
Compd	R	X,Y	500 mg/L	200 mg/L	500 mg/L	200 mg/L
I-1	H	4-Cl	73	NT	58	NT
I-2	CH_3	4-Cl	100	10	85	5
I-3	H	2,4-diCl	75	NT	68	NT
I-4	CH_3	2,4-diCl	80	NT	70	NT
I-5	H	3-Cl	65	NT	53	NT
I-6	CH_3	3-Cl	98	10	70	0
I-7	H	2-Cl	20	NT	13	NT
I-8	CH_3	2-Cl	25	NT	15	NT
I-9	H	4-CH_3	50	NT	35	NT
I-10	CH_3	4-CH_3	55	NT	35	NT
I-11	H	2-CH_3	55	NT	35	NT
I-12	CH_3	2-CH_3	95	0	68	0
Chlorantraniliprol			100	100	100	100

NT, not test; MS, *Mythimna separata*; PX, *Plutella xylostella*.

Table 2

Structure and insecticidal activity of compound **II**.

	Chemical structure		MS		PX	
Compd	R	X,Y	500 mg/L	200 mg/L	500 mg/L	200 mg/L
II-1	H	2-Cl	90	0	65	0
II-2	CH_3	2-Cl	10	NT	5	NT
II-3	H	4-Cl	33	NT	28	NT
II-4	H	2,4-diCl	30	NT	20	NT
Chlorantraniliprol			100	100	100	100

NT, not test; MS, *Mythimna separata*; PX, *Plutella xylostella*.

elemental analysis. In the ^{1}H-NMR spectra of the title compounds **I-1**–**12**, the proton signal corresponding to –CONHNHCO– appears as two singlets at δ 10.20–10.85. IR spectra of the title compounds **I-1**–**12** showed normal stretching absorption bands, indicating the existence of C=O (~1718 cm^{-1}). The typical carbon resonance at δ_c 155–171 in the ^{13}C-NMR spectra of **I-2**–**12** also confirms the presence of two carbon–oxygen double bonds. The ESI mass spectra of the title compounds **I** and **II** revealed the existence of the molecular ion peaks, which were in good accordance with the given structures of title compounds. The elemental analysis of all target compounds is in good agreement with the theoretical data.

Insecticidal activity. The preliminary insecticidal activity of **I** and **II** was evaluated against *M. separata* and *P. xylostella* at 500 mg/L using the known procedure [12] and chlorantraniliprol as a positive control. As shown in Tables 1, 2, compounds **I** and **II** exhibited 10–100% and 5–85% larvicidal activities against *M. separata* and *P. xylostella* at 500 mg/L, respectively. Bioassay results indicated that some compounds had excellent larvicidal activities against *M. separata* at the tested concentration. For example, the larvicidal activities of compounds **I-1**, **I-6**, **I-12**, and **II-1** against *M. separata* at 500 mg/L were 90–100%. Especially, compounds **I-1** exhibited 100% larvicidal activities against *M. separata*. Then, some of compounds were selected for further test against *M. separata* and *P. xylostella* at 200 mg/L. The subsequent results showed that compounds **I**-2, **I-6**, **I-12**, and **II-1** had weak insecticidal activity against *M. separata* and *P. xylostella* with 0–10% death rates. Comparing insecticidal activities among the title compounds in Table 1, it was found that the R group and the substituents X,Y have an impact on the insecticidal activity. For example, when the kind and positions of substituents X,Y were kept constant, compound **I** with R as CH_3 showed better activity than that of compounds with R as H. Comparing insecticidal activities among the title compound **II** in Table 2, it is noteworthy that compound with X, Y as 2-Cl and R as H showed higher insecticidal activities against *M. separata* and *P. xylostella* at 500 mg/L compared to those compounds containing X,Y as 2-Cl and R as CH_3 or X,Y as 4-Cl, 2,4-Cl_2, and R as H. However, further exploring of

structure–activity relationship about compound **II** could not be successfully ascertained due to lack of structural diversity.

CONCLUSION

In conclusion, two series of novel *N*-pyridylpyrazole derivatives **I** and **II** were designed and synthesized based on the structure of chlorantraniliprole. The insecticidal activities of the new compounds against *M. separata* and *P. xylostella* were evaluated. Some of the *N*-pyridylpyrazole derivatives (compounds **I-2**, **6**, **12**, and **II**-1) exhibited larvicidal activities against *M. separata* with 90–100% death rates at 500 mg/L. The results of further test showed that these compounds had weak insecticidal activity against *M. separata* and *P. xylostella* with 0–10% death rates at 200 mg/L. Generally speaking, these types of compounds might be not suitable as insecticide lead compound for further optimization.

EXPERIMENTAL

Chemicals and reagents were obtained from commercial sources, and all of the solvents were dried and purified by standard techniques prior to use. Column chromatography was carried out with Merck silica gel (200–300 mesh). Melting points (mp) were measured on a Buchi B-545 melting point apparatus and were uncorrected. IR spectra were recorded as KBr pellets on a Perkin-Elmer Fourier transform infrared spectrophotometer. ^{1}H-NMR were recorded on Varian XL-500 spectrometer at 500 MHz using tetramethylsilane as internal standard (solvent $CDCl_3$). Chemical shifts (δ) are given in ppm, coupling constants (J) are in Hz, and multiplicities are implicated by s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). MS spectra were analyzed on a Finnigen TRACE spectrometer and API2000LC/MS. Elemental analyses were performed by a Vario EL III elemental analyzer.

General procedure for the synthesis of 5. The intermediate compound **4** was synthesized according to the literature [2,4]. A mixture containing the intermediate compound **4** (3.5 mmol) and thionyl chloride (3 mL) was added into a 25 mL of flask and refluxed for 5–6 h. Excess thionyl chloride was evaporated off under reduced pressure, and a light yellow oil **5** was obtained with a yield of 94%.

General procedure for the synthesis of 7. The intermediate compound **6** was synthesized according to the literature [24]. A mixture of **6** (4 mmol) and hydrazine hydrate (4.4 mmol) was refluxed for 5–8 h. The mixture was then stirred over night at room temperature. After evaporation under reduced pressure, the residue was washed with 30 mL of petroleum ether and then filtered to give compound **7** with yield of 80–95%.

General procedure for the synthesis of I-1–I-12. A mixture of intermediate **7** (2 mmol) and K_2CO_3 (1 mmol) in THF/H_2O 10 mL (1:1, *v*/v) was stirred, and intermediate **5** (2 mmol) in THF (5 mL) was added. After stirring for 3–4 h at room temperature, the reaction mixture was evaporated off under reduced pressure, poured into water, and then filtered and recrystallized from ethanol to afford compounds **I-1**–**I-12**.

N′-(2-(4-Chlorophenoxy)acetyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-1). White solid; yield, 89%; mp, 158–160°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 4.61 (s, 2H, -C$\underline{H_2}$-), 6.97–7.01 (m, 2H, ^{2,6}H-Ar), 7.30 (s, 1H, ^{4}H-pyrazole), 7.31–7.34 (m, 2H, ^{3,5}H-Ar), 7.64–7.67 (dd, J = 5 Hz, J = 8 Hz, 1H, ^{5}H-pyridine), 8.20–8.22 (m, 1H, ^{4}H-pyridine), 8.50–8.52 (m, 1H, ^{6}H-pyridine), 10.31 (s, 1H, CON$\underline{H}$), 10.77 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3389, 3296, 3120, 3072, 3001, 1717, 1692, 1599, 1582, 1519, 1504, 1466, 1418, 1360, 1245, 1206, 1120, 1094, 1052, 965, 884, 919, 830, 799, 753; ESI-MS *m/z*: 482.95 (M^+); *Anal*. Calcd for $C_{17}H_{12}BrCl_2N_5O_3$: C, 42.09; H, 2.49; N, 14.44; Found: C, 42.12; H, 2.44; N, 14.39.

N′-(2-(4-Chlorophenoxy)propanoyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-2). White solid; yield, 90%; mp, 165–167°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.43 (d, 3H, J = 6.5 Hz, CH-C$\underline{H_3}$),4.82 (q, 1H, J = 6.0 Hz, C$\underline{H}$-CH_3), 6.94 (s, 1H), 6.96 (s, 1H), 7.26 (s, 1H, ^{4}H-pyrazole), 7.29–8.51 (m, 4H), 10.34 (s, 1H, CON$\underline{H}$), 10.78 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3391, 3270, 3078, 2854, 1706, 1673, 1579, 1539, 1506, 1465, 1415, 1355, 1235, 1213, 1200, 1100, 1080, 1046, 979, 961, 809, 778, 762; ^{13}C-NMR (125 MHz, DMSO-d_6): 19.0, 73.3, 110.7, 117.6, 125.5, 127.3, 129.1, 129.7, 130.1, 133.2, 139.8, 147.6, 148.9, 156.3, 156.4, 170.4; ESI-MS *m/z*: 496.97 (M^+); *Anal*. Calcd for $C_{18}H_{14}BrCl_2N_5O_3$: C, 43.31; H, 2.83; N, 14.03; Found: C, 43.26; H, 2.87; N, 14.08.

N′-(2-(2,4-Dichlorophenoxy)acetyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-3). White solid; yield, 92%; mp, 199–201°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 4.74 (s, 2H, C$\underline{H_2}$), 7.02 (d, 1H, J = 9.0 Hz, ^{6}H-Ar), 7.29 (s, 1H, ^{4}H-pyrazole), 7.32–8.51 (m, 5H, ^{4,5,6}H-Py, ^{3,5}H-Ar), 10.34 (s, 1H, CON$\underline{H}$), 10.85 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3460, 3371, 3188, 2953, 1701, 1630, 1574, 1519, 1479, 1456, 1292, 1267, 1071, 1033, 999, 960, 819, 763; ^{13}C-NMR (125 MHz, DMSO-d_6): 67.2, 110.8, 115.9, 123.1, 125.7, 127.3, 127.4, 128.4, 129.9, 130.1, 133.2, 139.8, 147.6, 148.9, 152.9, 156.3, 166.7; ESI-MS *m/z*: 516.91 (M^+); *Anal*. Calcd for $C_{17}H_{11}BrCl_3N_5O_3$: C, 39.30; H, 2.13; N, 13.48; Found: C, 39.34; H, 2.14; N, 13.46.

N′-(2-(2,4-Dichlorophenoxy)propanoyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-4). White solid; yield, 88%; mp, 102–104°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.48 (d, 3H, J = 6.5 Hz, CH-C$\underline{H}_3$), 4.87 (q, 1H, J = 6.5 Hz, C$\underline{H}$-CH$_3$), 7.03 (d, 1H, J = 8.5 Hz, ^{6}H-Ar), 7.26–8.52 (m, 6H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{3,5}H-Ar), 10.39 (s, 1H, CON$\underline{H}$), 10.84 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3389, 3209, 2988, 2872, 1714, 1682, 1645, 1576, 1524, 1476, 1416, 1358, 1285, 1244, 1105, 1060, 1046, 1027, 961, 872, 803, 763; ^{13}C-NMR (125 MHz, DMSO-d_6): 19.1, 74.3, 110.8, 116.8, 123.8, 125.9, 127.3, 127.3, 128.4, 129.1, 129.9, 130.1, 133.2, 139.8, 147.6, 152.3, 156.3, 169.8; ESI-MS *m/z*: 530.93 (M$^+$); *Anal*. Calcd for $C_{18}H_{13}BrCl_3N_5O_3$: C, 40.52; H, 2.46; N, 13.12; Found: C, 40.48; H, 2.50; N, 13.09.

N′-(2-(3-Chlorophenoxy)acetyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-5). White solid; yield, 91%; mp, 191–193°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 4.65 (s, 2H, -C$\underline{H}_2$-), 6.95 (d, 1H, J = 8.0 Hz, ^{6}H-Ar), 7.02–8.52 (m, 7H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{2,4,5}H-Ar), 10.33 (s, 1H, CON$\underline{H}$), 10.79 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3607, 3298, 3179, 3136, 3072, 3026, 2979, 1708, 1677, 1596, 1581, 1544, 1512, 1467, 1439, 1359, 1282, 1225, 1076, 1060, 962, 898, 814, 774, 760; ^{13}C-NMR (125 MHz, DMSO-d_6): 66.7, 110.7, 114.3, 115.4, 121.8, 127.3, 127.3, 129.1, 130.1, 131.3, 134.1, 139.8, 147.6, 148.9, 156.4, 158.9, 167.1; ESI-MS *m/z*: 482.95 (M$^+$); *Anal*. Calcd for $C_{17}H_{12}BrCl_2N_5O_3$: C, 42.09; H, 2.49; N, 14.44; Found: C, 42.13; H, 2.46; N, 14.41.

N′-(2-(3-Chlorophenoxy)propanoyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-6). White solid; yield, 89%; mp, 148–150°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.45 (d, 3H, J = 6.5 Hz, CH-C$\underline{H}_3$), 4.87 (q, 1H, J = 6.5 Hz, C$\underline{H}$-CH$_3$), 6.92 (d, 1H, J = 7.5 Hz, ^{6}H-Ar), 6.99–8.52 (m, 7H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{2,4,5}H-Ar), 10.35 (s, 1H, CON$\underline{H}$), 10.78 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3607, 3288, 3270, 3179, 3078, 3026, 2979, 1706, 1673, 1579, 1539, 1506, 1465, 1439, 1415, 1355, 1288, 1213, 1080, 1046, 961, 869, 809, 778, 762; ^{13}C-NMR (125 MHz, DMSO-d_6): 18.6, 72.8, 110.3, 114.3, 115.5, 121.3, 126.9, 126.9, 128.6, 129.7, 130.9, 133.7, 139.4, 147.2, 148.5, 155.9, 158.0, 170.0; ESI-MS *m/z*: 496.97 (M$^+$); *Anal*. Calcd for $C_{18}H_{14}BrCl_2N_5O_3$: C, 43.31; H, 2.83; N, 14.03; Found: C, 43.29; H, 2.85; N, 14.07.

N′-(2-(2-Chlorophenoxy)acetyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-7). White solid; yield, 91%; mp, 127–129°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 4.72 (s, 2H, -C$\underline{H}_2$-), 6.96–8.52 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{3,4,5,6}H-Ar), 10.32 (s, 1H, CON$\underline{H}$), 10.84 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3428, 3296, 3072, 3030, 3001, 2996, 1717, 1692, 1599, 1582, 1519, 1504, 1479, 1466, 1389, 1360, 1278, 1245, 1206, 1147, 1094, 1052, 965, 919, 884, 799, 753; ^{13}C-NMR (125 MHz, DMSO-d_6): 66.6, 110.5, 114.3, 121.7, 122.5, 126.9, 128.3, 128.7, 129.7, 130.2, 137.4, 139.5, 147.3, 148.5, 153.4, 155.9, 166.6; ESI-MS *m/z*: 482.95 (M$^+$); *Anal*. Calcd for $C_{17}H_{12}BrCl_2N_5O_3$: C, 42.09; H, 2.49; N, 14.44; Found: C, 42.11; H, 2.46; N, 14.49.

N′-(2-(2-Chlorophenoxy)propanoyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-8). White solid; yield, 90%; mp, 144–146°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.49 (d, 3H, J = 6.5 Hz, CH-C$\underline{H}_3$), 4.85 (q, 1H, J = 6.5 Hz, C$\underline{H}$-CH$_3$), 6.95–8.52 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{3,4,5,6}H-Ar), 10.38 (s, 1H, CON$\underline{H}$), 10.83 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3428, 3273, 3124, 3030, 2996, 2938, 1714, 1688, 1658, 1583, 1521, 1479, 1470, 1389, 1278, 1243, 1147, 1093, 1059, 965, 916, 883, 797, 759; ^{13}C-NMR (125 MHz, DMSO-d_6): 18.8, 73.6, 110.4, 115.3, 122.3, 122.5, 126.9, 126.9, 128.2, 128.7, 129.7, 130.2, 139.5, 147.3, 148.5, 152.8, 155.9, 169.9; ESI-MS *m/z*: 496.97 (M$^+$); *Anal*. Calcd for $C_{18}H_{14}BrCl_2N_5O_3$: C, 43.31; H, 2.83; N, 14.03; Found: C, 43.35; H, 2.84; N, 13.99.

N′-(2-(4-Methylphenoxy)acetyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-9). White solid; yield, 79%; mp, 128–130°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 2.2 (s, 3H, Ar-C$\underline{H}_3$), 4.54 (s, 2H, -C$\underline{H}_2$-), 6.84–8.52 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{3,4,5,6}H-Ar), 10.27 (s, 1H, CON$\underline{H}$), 10.77 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3438, 3241, 3131, 3055, 2990, 1699, 1676, 1616, 1579, 1545, 1511, 1462, 1417, 1359, 1275, 1230, 1171, 1098, 1055, 1030, 968, 889, 812, 760; ^{13}C-NMR (125 MHz, DMSO-d_6): 20.1, 66.2, 110.3, 114.6, 125.4, 126.9, 126.9, 128.2, 128.3, 129.8, 132.8, 139.4, 147.2, 155.6, 155.9, 167.1; ESI-MS *m/z*: 463.00 (M$^+$); *Anal*. Calcd for $C_{18}H_{15}BrClN_5O_3$: C, 46.52; H, 3.25; N, 15.07; Found: C, 46.50; H, 3.28; N, 15.11.

N′-(2-(4-Methylphenoxy)propanoyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-10). White solid; yield, 79%; mp, 185–187°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.42 (d, 3H, J = 6.5 Hz, CH-C$\underline{H}_3$), 2.21 (s, 3H, Ar-C$\underline{H}_3$), 4.75 (q, 1H, J = 6.5 Hz, C$\underline{H}$-CH$_3$), 6.81–8.52 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{2,3,5,6}H-Ar), 10.29 (s, 1H, CON$\underline{H}$), 10.73 (s, 1H, CON$\underline{H}$); IR (KBr)/cm^{-1}: 3418, 3249, 3137, 3060, 2986, 1697, 1660, 1613, 1582, 1537, 1509, 1467, 1417, 1359, 1285, 1227, 1177, 1124, 1097, 1050, 1030, 962, 886, 812, 764; ^{13}C-NMR (125 MHz, DMSO-d_6):18.7, 20.1, 72.6, 110.4, 115.3, 126.9, 126.9, 128.2, 128.6, 129.8, 137.4, 139.4, 147.2, 148.5, 155.0, 155.9, 170.6; ESI-MS *m/z*: 477.02 (M$^+$); *Anal*. Calcd for $C_{19}H_{17}BrClN_5O_3$: C, 47.67; H, 3.58; N, 14.63; Found: C, 47.64; H, 3.58; N, 14.66.

N′-(2-(2-Methylphenoxy)acetyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-11). White solid; yield, 85%; mp, 171–173°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 2.20 (s, 3H, Ar-C$\underline{H}_3$), 4.60 (s, 2H,-C$\underline{H}_2$-), 6.83–8.52 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{3,4,5,6}H-Ar), 10.20 (s, 1H, CON$\underline{H}$), 10.78 (s, 1H, CON$\underline{H}$); IR (KBr)/

cm^{-1}: 3401, 3223, 3099, 2998, 2917, 1709, 1679, 1669, 1583, 1499, 1470, 1351, 1313, 1227, 1193, 1139, 1139, 1058, 964, 919, 883, 809, 759; ^{13}C-NMR (125 MHz, DMSO-d_6):16.1, 66.3, 110.3, 111.6, 121.1, 126.3, 126.9, 128.2, 128.6, 129.6, 130.6, 132.7, 137.4, 139.4, 147.2, 148.5, 155.9, 167.1; ESI-MS *m/z*: 463.00 (M^+); *Anal*. Calcd for $C_{18}H_{15}BrClN_5O_3$: C, 46.52; H, 3.25; N, 15.07; Found: C, 46.51; H, 3.27; N, 15.06.

N′-(2-(2-Methylphenoxy)propanoyl)-3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbohydrazide (I-12). White solid; yield, 77%; mp, 175–177°C; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 1.45 (d, 3H, J = 6.5 Hz, CH-C<u>H</u>$_3$), 2.18 (s, 3H, Ar-C<u>H</u>$_3$), 4.76 (q, 1H, J = 6.5 Hz, C<u>H</u>-CH$_3$), 6.81–8.52 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{2,3,5,6}H-Ar), 10.25 (s, 1H, CON<u>H</u>), 10.74 (s, 1H, CON<u>H</u>); IR (KBr)/cm^{-1}: 3427, 3278, 3124, 3025, 2990, 2937, 1715, 1689, 1675, 1583, 1521, 1493, 1464, 1358, 1303, 1238, 1193, 1147, 1131, 1052, 964, 917, 883, 800, 756; ^{13}C-NMR (125 MHz, DMSO-d_6):16.2, 18.9, 72.8, 110.4, 112.5, 121.0, 126.8, 126.9, 128.6, 129.6, 130.6, 132.7, 137.4, 139.4, 147.2, 148.5, 155.4, 155.9, 170.6; ESI-MS *m/z*: 477.02 (M^+); *Anal*. Calcd for $C_{19}H_{17}BrClN_5O_3$: C, 47.67; H, 3.58; N, 14.63; Found: C, 47.71; H, 3.57; N, 14.66.

General procedure for the synthesis of II-1–II-4. A mixture of compound **I** (3 mmol) and $POCl_3$ (4 mL) was heated at 120°C for 6 h. Ice water (40 mL) was added, and then, the mixture was neutralized with concentrated ammonia and extracted with dichloromethane (3 × 15 mL). After drying with anhydrous Na_2SO_4, the solvent was evaporated off under reduced pressure to give crude products. These compounds were purified by column chrimatography with silica gel using ethyl accetate/petroleum ether (3:1, *v*/v) as an eluent.

2-(5-(5-((2-Chlorophenoxy)methyl)-1,3,4-oxadiazol-2-yl)-3-bromo-1H-pyrazol-1-yl)-3-chloropyridine (II-1). White solid; yield, 65%; mp, 126–128°C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.29 (s, 2H, -C<u>H</u>$_2$-), 6.86–8.44 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{3,4,5,6}H-Ar); IR (KBr)/cm^{-1}: 3138, 2925, 2854, 1699, 1621, 1575, 1483, 1461, 1426, 1352, 1277, 1229, 1128, 1063, 1042, 1019, 959, 879, 801, 748; ESI-MS *m/z*: 464.94 (M^+); *Anal*. Calcd for $C_{17}H_{10}BrCl_2N_5O_2$: C, 43.71; H, 2.16; N, 14.99; Found: C, 43.68; H, 2.15; N, 14.98.

2-(5-(5-(1-(2-Chlorophenoxy)ethyl)-1,3,4-oxadiazol-2-yl)-3-bromo-1H-pyrazol-1-yl)-3-chloropyridine (II-2). White solid; yield, 62%; mp, 115–117°C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.77 (d, 3H, J = 6.5 Hz, CH-C<u>H</u>$_3$), 5.53 (q, 1H, J = 6.5 Hz, C<u>H</u>-CH$_3$), 6.94–8.43 (m, 8H, ^{4}H-pyrazole, ^{4,5,6}H-Py, ^{3,4,5,6}H-Ar); IR (KBr)/cm^{-1}: 3140, 2928, 2854, 1700, 1626, 1580, 1483, 1464, 1379, 1287, 1232, 1130, 1061, 1042, 1021, 958, 851, 803, 748; ESI-MS *m/z*: 478.96 (M^+); *Anal*. Calcd for $C_{18}H_{12}BrCl_2N_5O_2$: C, 44.93; H, 2.51; N, 14.56; Found: C, 44.94; H, 2.54; N, 14.52.

2-(5-(5-((4-Chlorophenoxy)methyl)-1,3,4-oxadiazol-2-yl)-3-bromo-1H-pyrazol-1-yl)-3-chloropyridine (II-3). White solid; yield, 57%; mp, 130–132°C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.20 (s, 2H, -C<u>H</u>$_2$-), 6.88 (d, 2H, J = 9.0 Hz, ^{2,6}H-Ar), 7.12 (s, 1H, ^{4}H-pyrazole), 7.25 (d, 2H, J = 9.0 Hz, ^{3,5}H-Ar),7.42–8.45 (m, 3H, ^{4,5,6}H-Py); IR (KBr)/cm^{-1}: 3129, 2929, 2856, 1699, 1625, 1580, 1509, 1461, 1426, 1377, 1273, 1225, 1131, 1060, 1041, 1016, 959, 879, 851, 801, 748; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 59.9, 112.5, 116.2, 126.6, 127.5, 128.9, 129.4, 129.7, 129.9, 130.9, 139.6, 147.8, 155.9, 156.5, 162.1; ESI-MS *m/z*: 464.94 (M^+); *Anal*. Calcd for $C_{17}H_{10}BrCl_2N_5O_2$: C, 43.71; H, 2.16; N, 14.99; Found: C, 43.73; H, 2.14; N, 14.97.

2-(5-(5-((2,4-Dichlorophenoxy)methyl)-1,3,4-oxadiazol-2-yl)-3-bromo-1H-pyrazol-1-yl)-3-chloropyridine (II-4). White solid; yield, 71%; mp, 126–128°C; ^{1}H-NMR (500 MHz, $CDCl_3$): δ 5.28 (s, 2H, -C<u>H</u>$_2$-), 6.96 (d, 1H, J = 4.5 Hz, ^{6}H-Ar), 7.14 (s, 1H, ^{4}H-pyrazole), 7.16–7.46 (m, 5H, ^{3,5}H-Ar, ^{4,5,6}H-Py); IR (KBr)/cm^{-1}: 3131, 2930, 2925, 2854, 1701, 1621, 1577, 1489, 1463, 1421, 1379, 1352, 1277, 1129, 1128, 1063, 1042, 1019, 957, 879, 850, 800, 749; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 61.0, 112.6, 115.7, 124.7, 126.6, 127.9, 128.2, 128.9, 129.3, 129.8, 130.6, 139.6, 147.2, 147.8, 151.8, 156.7, 161.6; ESI-MS *m/z*: 498.90 (M^+); *Anal*. Calcd for $C_{17}H_9BrCl_3N_5O_2$: C, 40.71; H, 1.81; N, 13.96; Found: C, 40.72; H, 1.80; N, 13.99.

Insecticidal activity testing.

Larvicidal activity against Mythimna separata. The larvicidal activities of compounds **I**, **II**, and chlorantraniliprol were determined according the reference methods [12]. The insecticial activity against *M. separata* was tested by foliar application; individual corn (Tangyu10, *Zea mays L*.) leaves were placed on moistened pieces of filter paper in Petri dishes. The leaves were then sprayed with the test solution and allowed to dry. The dishes were infested with 10 third-instar oriental aymyworm larvae. Percentage mortalities were evaluated 2 days after treatment. Each treatment was replicated three times.

Larvicidal activity against Plutella xylostella. The larvicidal activity of compounds **I**, **II**, and chlorantraniliprol were tested by the leaf-dip method [12]. At first, a solution of each test sample in dimethylformamide at a concentration of 500 mg/L was prepared. Leafs disks (6 × 2 cm) were cut from fresh cabbage leaves and then sprayed with the test solution for 3 s and allowed to dry. The resulting leaf disks were placed individually into glass tubes. Each disk was infested with 30 s of instar diamondback moth larvae. Percentage mortalities were evaluated 2 days after treatment. Each treatment was performed three times.

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