Synthesis and Insecticidal, Anticancer Activity of Novel Pyrazole Acyl Urea Derivatives

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Summary: A series of novel acyl urea derivatives had been synthesized. Their structures were confirmed by NMR, FTIR and elemental analysis. Their antitumor activity was tested in A-549 lung cancer cell line, Bel7402 liver cancer cell line and HCT-8 intestine cancer cell line and insecticidal activity against *Mythimna separata* were evaluated. Among the tested compounds, compound **3h** held highest activity (45%) against Bel7402, but no activity against A-549 and HCT-8. Also compound **3c** (100%)**, 3e** (80%)**, 3f** (60%) and **3j** (60%) exhibited good insecticidal activity.

Keywords: Pyrazole, Acyl urea, Antitumor, Insecticidal.

Introduction

Pyrazole derivatives play an important role in industry, pharmaceutical, pesticidal fields. It is a classic five member heterocycle and often exhibit broad range of biological activities such as nematocidal [1-3], antifungal [4, 5], anti-inflammatory [6], anticancer [7], antioxidant [8], herbicidal [9], insecticidal [10], antimicrobial activity [11]. In past decades, many pyrazole derivatives, especially pyrazole linked pyridine compounds had been developed as commercial drugs or pesticides. For example, the high effective and broad spectra insecticides (phthalic diamides and anthranilic diamides) were discovered by Nihon Nohyaku, Bayer CropScience and DuPont respectively [12, 13]. On the other hand, urea structures are reported as a class of pharmacophore always used to discover novel drugs in pharmaceutical drug design and agrochemical industry [14-16] due to their diversity function. Many literatures reported that the compounds contain acyl urea group displayed broad activities, such as anticonvulsant [17], FAAH inhibitors [18], antinociceptive [19], anticancer [20], antischistosomal [21], S1P(2) antagonist activity [22].

In view of above and as continuation of our research on bioactive compounds [23-43], the insecticide chlorantraniliprole was selected as a lead compound. The urea bridge was introduced into chlorantraniliprole in order to discover new insecticides, the promising bioactive diversity of acyl urea compounds containing pyridine linked pyrazole moiety were designed and synthesized. Their insecticidal and antitumor activity was tested.

Experimental

Instruments

Chemicals and solvents were procured from commercial sourced in analytical grade purity. Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. Thin-layer chromatography (TLC) was carried out on aluminium-supported silica gel plates (Merck 60F 254) with visualization of components by UV light (254 nm). Column chromatography was carried out on silica gel (Merck 230-400 mesh). The IR spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wave numbers were given in cm^{-1}. The ^{1}H-NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Bruker-400 spectrometer (400 MHz). All chemical shifts are reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer.

Synthesis

The intermediate **1** and **2** was synthesized according to our previous references [44, 45], and the synthetic route was outlined in Scheme-1.

The mixture of 3-bromo-1-(3-chloropyridin -2-yl)-1*H*-pyrazole-5-carboxamide (5 mmole) and oxalyl chloride (10 mmole) in $ClCH_2CH_2Cl$ (30 mL) was stirred at refluxing for 12 h. After the reaction

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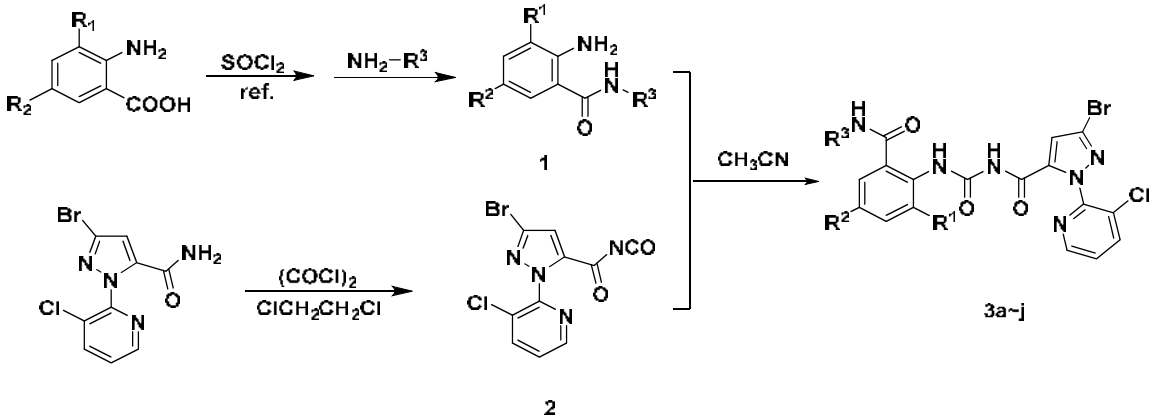
was complete according to TLC, the solution was evaporated in vacuum to get the crude residue. The crude residue was dissolved in CH_3CN (10 mL), then was slowly added into a solution of intermediate 1 (5 mmole) in CH_3CN (20 mL). After stirring at room temperature for 12 h, white solid was precipitated and filtered to get the white solid, which was washed and recrystallized with EtOH to obtain **3** (Scheme-1).

3-Bromo-1-(3-chloropyridin-2-yl)-N-((2-(isopropylcarbamoyl)-6-methylphenyl)carbamoyl)-1H-pyrazole-5-carboxamide (**3a**) White solid (77.8%); m.p. 184-186 ℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.01 (d, 6H, *J* = 6.8 Hz, CH(C$\underline{H_3}$)$_2$), 2.16 (s, 3H, CH_3), 3.84-3.92 (m, 1H, NHC$\underline{H}$), 7.21-7.32 (m, 3H, Ar—H), 7.65 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.4 Hz, pyridyl—H), 8.03 (d, 1H, *J* = 7.6 Hz, C$\underline{H}$NHCH), 8.26 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.55 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 9.80 (br, 1H, CONHCO), 11.35 (br, 1H, C$\underline{H}$NHCO). Anal. Calculated for $C_{21}H_{20}BrClN_6O_3$: C 48.53, H 3.88, N 16.17; found: C 48.39, H 4.11, N 15.86.

3-bromo-N-((4-chloro-2-(isopropylcarbamoyl)phenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3b**) White solid (83.6%); m.p.204-206℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.03 (d, 6H, *J* = 6.4 Hz, CH(C$\underline{H_3}$)$_2$), 3.80-3.88 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 7.51-7.52 (m, 2H, Ar—H), 7.60 (s, 1H, pyrazolyl—H), 7.68 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.13 (d, 1H, *J* = 9.6 Hz, Ar—H), 8.25 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.46 (d, 1H, *J* = 8.0 Hz, N$\underline{H}$CH), 8.54 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 11.06 (br, 1H, CONHCO), 11.41 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{20}H_{17}BrCl_2N_6O_3$: C 44.47, H 3.17, N 15.56; found: C 44.43, H 3.28, N 15.21.

3-bromo-N-((4-chloro-2-methyl-6-(methylcarbamoyl)phenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3c**) White solid (68.3%); m.p. 201-206℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 2.16 (s, 3H, CH_3), 2.63 (d, 3H, *J* = 4.4 Hz, NHC$\underline{H_3}$), 7.32 (d, 1H, *J* = 2.4 Hz, Ar—H), 7.45 (d, 1H, *J* = 2.4 Hz, Ar—H), 7.64 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.27 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.36 (q, 1H, *J* = 4.4 Hz, N$\underline{H}$CH$_3$), 8.56 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 9.93 (br, 1H, CONHCO), 11.39 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{19}H_{15}BrCl_2N_6O_3$: C 43.37, H 2.87, N 15.97; found: C 43.07, H 3.11, N 15.55.

3-bromo-N-((4-chloro-2-methyl-6-(propylcarbamoyl)phenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3d**) White solid (86.4%); m.p.186-189℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 0.81 (t, 3H, *J* = 7.6 Hz, CH$_2$C$\underline{H_3}$), 1.39 (q, 2H, *J* = 7.2 Hz, C$\underline{H_2}$CH$_3$), 2.16 (s, 3H, CH_3), 3.02-3.07 (m, 2H, NHC$\underline{H_2}$), 7.28 (d, 1H, *J* = 2.4 Hz, Ar—H), 7.45 (d, 1H, *J* = 2.0 Hz, Ar—H), 7.64 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.27 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.34 (t, 1H, *J* = 4.8 Hz, N$\underline{H}$CH$_2$), 8.56 (d, 1H, *J* = 4.4 Hz, pyridyl—H), 9.82 (br, 1H, CONHCO), 11.39 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{21}H_{19}BrCl_2N_6O_3$: C 45.51, H 3.46, N 15.16; found: C 45.73, H 3.24, N 15.37.



a: R^1 = CH_3, R^2 = H, R^3 = *i*-Pr; b: R^1 = H, R^2 = Cl, R^3 = *i*-Pr; c: R^1 = CH_3, R^2 = Cl, R^3 = CH_3; d: R^1 = CH_3, R^2 = Cl, R^3 = *n*-Pr; e: R^1 = CH_3, R^2 = Cl, R^3 = *i*-Pr; f: R^1 = CH_3, R^2 = Cl, R^3 = cyclopropyl; g: R^1 = CH_3, R^2 = Cl, R^3 = *n*-butyl; h: R^1 = CH_3, R^2 = Cl, R^3 = *t*-butyl; i: R^1 = CH_3, R^2 = Cl, R^3 = cyclohexyl; j: R^1 = CH_3, R^2 = Br, R^3 = *i*-Pr; k: R^1 = Cl, R^2 = Cl, R^3 = *i*-Pr

Scheme-1: Synthetic route of title compounds.

3-bromo-N-((4-chloro-2-(isopropylcarbamoyl)-6-methylphenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3e**) White solid (82.3%); m.p. 202-203℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.01 (d, 6H, *J* = 6.4 Hz, CH(C$\underline{H_3}$)$_2$), 2.16 (s, 3H, CH_3), 3.82-3.91 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 7.25 (s, 1H, Ar－H), 7.43 (s, 1H, Ar－H), 7.65 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.15 (d, 1H, *J* = 7.6 Hz, N$\underline{H}$CH), 8.26 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.55 (d, 1H, *J* = 4.4 Hz, pyridyl—H), 9.77 (br, 1H, CON$\underline{H}$CO), 11.41 (br, 1H, N$\underline{H}$CO). FTIR, ν, cm^{-1}: 3422, 3317, 3208, 2972, 1696, 1652, 1577, 1484, 1459, 1356, 1255, 1239, 1209, 810, 786; Anal. Calculated for $C_{21}H_{19}BrCl_2N_6O_3$: C 45.51, H 3.46, N 15.16; found: C 45.63, H 3.12, N 14.86.

3-bromo-N-((4-chloro-2-(cyclopropylcarbamoyl)-6-methylphenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3f**) White solid (80.6%); m.p.195-198℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 0.36-0.40 (m, 2H, CH_2CH_2), 0.58-0.63 (m, 2H, CH_2CH_2), 2.15 (s, 3H, CH_3), 2.62-2.68 (m, 1H, CH), 7.27 (s, 1H, Ar－H), 7.44 (s, 1H, Ar－H), 7.66 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.27 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.37 (d, 1H, *J* = 4.0 Hz, N$\underline{H}$CH), 8.56 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 9.78 (br, 1H, CON$\underline{H}$CO), 11.42 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{21}H_{17}BrCl_2N_6O_3$: C 45.68, H 3.10, N 15.22; found: C 45.39, H 3.15, N 15.08.

3-bromo-N-((2-(butylcarbamoyl)-4-chloro-6-methylphenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3g**) White solid (73.6%); m.p. 191-193℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 0.82 (t, 3H, *J* = 7.2 Hz, $CH_2\underline{CH_3}$), 1.20-1.29 (m, 2H, $\underline{CH_2}CH_3$), 1.33-1.39 (m, 2H, $\underline{CH_2}CH_2CH_3$), 2.16 (s, 3H, CH_3), 3.09 (q, 2H, *J* = 6.8 Hz, NH$\underline{CH_2}$), 7.27 (d, 1H, *J* = 2.4 Hz, Ar－H), 7.44 (d, 1H, *J* = 2.0 Hz, Ar－H), 7.65 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.26 (d, 1H, *J* = 7.6 Hz, pyridyl—H), 8.32 (t, 1H, *J* = 5.6 Hz, N$\underline{H}$CH$_2$), 8.56 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 9.81 (br, 1H, CON$\underline{H}$CO), 11.39 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{22}H_{21}BrCl_2N_6O_3$: C 46.50, H 3.72, N 14.79; found: C 46.79, H 3.51, N 15.02.

3-bromo-N-((2-(tert-butylcarbamoyl)-4-chloro-6-methylphenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3h**) White solid (79.5%); m.p. 187-189℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.19 (s, 9H, C(C$\underline{H_3}$)$_3$), 2.15 (s, 3H, CH_3), 7.18 (d, 1H, *J* = 2.0 Hz, Ar－H), 7.39 (d, 1H, *J* = 2.0 Hz, Ar－H), 7.67 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 7.82 (s, 1H, N$\underline{H}$C(CH$_3$)$_3$), 8.25 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.54 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 9.73 (br, 1H, CON$\underline{H}$CO), 11.43 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{22}H_{21}BrCl_2N_6O_3$: C 46.50, H 3.72, N 14.79; found: C 46.39, H 3.47, N 14.98.

3-bromo-N-((4-chloro-2-(cyclohexylcarbamoyl)-6-methylphenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3i**) White solid (80.5%); m.p. 205-210℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.04-1.72 (m, 10H, cyclohexyl－H), 2.15 (s, 3H, CH_3), 3.54-3.61 (m, 1H, cyclohexyl－H), 7.25 (d, 1H, *J* = 2.0 Hz, Ar－H), 7.43 (d, 1H, *J* = 2.0 Hz, Ar－H), 7.66 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.14 (d, 1H, *J* = 7.6 Hz, N$\underline{H}$CH), 8.26 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.55 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 9.76 (br, 1H, CON$\underline{H}$CO), 11.40 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{24}H_{23}BrCl_2N_6O_3$: C 48.50, H 3.90, N 14.14; found: C 47.99, H 4.20, N 13.95.

3-bromo-N-((4-bromo-2-(isopropylcarbamoyl)-6-methylphenyl)carbamoyl)-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carboxamide (**3j**) White solid (81.9%); m.p. 186-188℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.01 (d, 6H, *J* = 6.4 Hz, CH(C$\underline{H_3}$)$_2$), 2.15 (s, 3H, CH_3), 3.82-3.91 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 7.37 (s, 1H, Ar－H), 7.56 (s, 1H, Ar－H), 7.65 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 8.15 (d, 1H, *J* = 7.6 Hz, N$\underline{H}$CH), 8.26 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.55 (d, 1H, *J* = 4.8 Hz, pyridyl—H), 9.77 (br, 1H, CON$\underline{H}$CO), 11.41 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{21}H_{19}Br_2ClN_6O_3$: C 42.13, H 3.20, N 14.04; found: C 42.04, H 3.30, N 13.89.

3-bromo-1-(3-chloropyridin-2-yl)-N-((2,4-dichloro-6-(isopropylcarbamoyl)phenyl)carbamoyl)-1H-pyrazole-5-carboxamide (**3k**) White solid (75.8%); m.p. 192-194℃; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 1.01 (d, 6H, *J* = 6.8 Hz, CH(C$\underline{H_3}$)$_2$), 3.83-3.92 (m, 1H, C$\underline{H}$(CH$_3$)$_2$), 7.44 (s, 1H, Ar－H), 7.65 (s, 1H, pyrazolyl—H), 7.69 (dd, 1H, *J* = 4.8, 8.0 Hz, pyridyl—H), 7.80 (s, 1H, Ar－H), 8.17 (d, 1H, *J* = 7.6 Hz, N$\underline{H}$CH), 8.27 (d, 1H, *J* = 8.0 Hz, pyridyl—H), 8.56 (d, 1H, *J* = 4.4 Hz, pyridyl—H), 9.83 (br, 1H, CON$\underline{H}$CO), 11.58 (br, 1H, N$\underline{H}$CO). Anal. Calculated for $C_{20}H_{16}BrCl_3N_6O_3$: C 41.80, H 2.81, N 14.62; found: C 41.73, H 2.72, N 14.31.

Anticancer and Insecticidal Activity

The anticancer and insecticidal activity of compounds was evaluated according to references [46, 47].

Anticancer activity

Three different human cancer cell lines, A-549, Bel7402 and HCT-8, were obtained from National Center for Pharmaceutical Screening, Institute of Materia Medica, and cultured on RPMI1640 medium at 37 °C in a humidified atmosphere with 5% CO_2 for 24 h. All cells to be tested in the following assays had a passage number of 3–6.

For the drug treatment experiments, the cancer cells were treated with the compounds (predissolved in DMSO) at 5 μg/mL for a period of 3 days. At the end of the drug treatment period, MTT solution (150 μL, 0.5 mg/mL) in PBS (PBS without MTT as the blank) was fed to each well of the culture plate. After 4 h incubation, the formazan crystal formed in the well was dissolved with 150 μL of DMSO for optical density reading at 544 nm.

Insecticidal activity

The insecticidal activity against Oriental armyworm was 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 test solution and allowed to dry. The dishes were infested 10 fourth-instar Oriental armyworm larvae. Percentage mortalities were evaluated 2 days after treatment. Each treatment was performed three times. For comparative purposes, Chlorantraniliprole was tested under the same conditions.

Results and Discussion

Synthesis

All the key intermediate **1** and **2** were synthesized according to our previous work [45]. The isocyanate 2 was obtained under room temperature without separation. The final amide derivatives **3** (Scheme 1) were produced by reaction of the amide of **1** with appropriate isocyanate at room temperature in CH_3CN. The final product was given by recrystallized in EtOH.

All the title pyrazole compounds were confirmed by ^{1}H-NMR, MS and elemental analysis. In the ^{1}H-NMR spectra of target compound **3e**, the singles of pyridine ring observed at 7.69, 8.26 and 8.55 ppm respectively, the -CH proton signal of pyrazole ring can be found around 7.65 ppm. The appearance of signals around at 8.15, 9.77 and 11.41 ppm is assigned to the NH respectively. The infrared spectrum of amide derivative **3e** showed absorption bands at 3422cm^{-1}, 3317cm^{-1}, 3208 cm^{-1} for the three N-H stretching. The characteristic stretching vibrations ν (C=O) and ν (C=N) appears at 1696 cm^{-1}, 1652 cm^{-1} and 1577 cm^{-1} respectively.

Anticancer, Insecticidal Activities and SAR

The anticancer results of title compounds are listed in Table-1, 5-Fluorouracil was used as control. As shown in Table-1, most of the title compounds showed weak inhibitory against A-549, Bel7402, and HCT-8 cell lines at a concentration of 5 μg/mL. Among them, only compound 3h (45%) exhibited moderate activity against Bel7402. meanwhile, compound **3k** (38%) and **3j** (34%) possessed moderate activity against A-549 and HCT-8 respectively. Surprisingly, most of title compound can increase the HCT-8 cell growth.

Table-1: The anticancer activity of title compounds at 5μg/mL(%, inhibitory).

No.	A-549	Bel7402	HCT-8
3a	11.07	13.26	-0.44
3b	4.39	13.16	-6.37
3c	2.37	3.37	-5.55
3d	21.97	6.29	6.66
3e	13.29	5.62	0.34
3f	5.78	2.88	0.96
3g	11.16	-2.06	2.50
3h	17.63	45.29	-0.42
3i	18.98	13.49	33.95
3j	21.25	3.00	8.43
3k	38.55	10.93	0.27
5-Fluorouracil	56.51	75.08	78.56

The insecticidal results of title compounds are listed in Table 2, Chlorantraniliprole was used as control. As shown in Table 2, some of the title compounds showed good inhibitory against *Mythimna separata* at a concentration of 200 μg/mL, such as compound **3c** (100%) and **3e** (80%), which is a little lower than that of control. Also the compound **3f** (60%) and **3j** (60%) exhibited moderate activity against *Mythimna separata* at a concentration of 200 μg/mL. Furthermore, compound **3c** (60%) showed moderate activity even at 100 ppm, but the activity of compound **3e** (80%) decreased quickly while the concentration was decreased (200ppm to 100 ppm). From the insecticidal data, we can found that R^2 was

substituted by halo, the activity is higher. For the halo, the activity is much higher when the halo is Cl. Meanwhile, the R^3 is not straight chain alkane substituted, the activity is high.

Table-2: The insecticidal activity of title compounds (%, death rate).

No.	Concentration	Death rate
3a	**200**	**0**
3b	**200**	**0**
3c	**200**	**100**
	100	**60**
3d	**200**	**0**
3e	**200**	**80**
	100	**10**
3f	**200**	**60**
3g	**200**	**0**
3h	**200**	**0**
3i	**200**	**0**
3j	**200**	**60**
3k	**200**	**0**
Chlorantraniliprole	**100**	**100**

Conclusion

Some interesting acyl urea derivatives containing pyrazole moiety were designed and synthesized. The primarily bioassay results indicated that showed some of them exhibited moderate anticancer activities and insecticidal activities. Among all these synthesized compounds, compound **3c**, **3e**, **3f** and **3j** are highly insecticidal activity with the range 60%~100% at 200 ppm. In particular, compound 3c still exhibited moderate inhibitory (60%) at 100 ppm. All these compounds displayed weak anticancer activity.

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