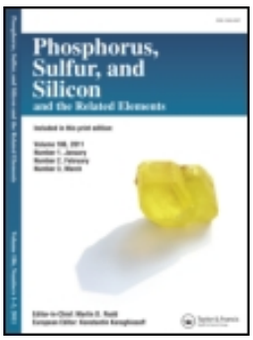

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Synthesis and insecticidal activities of *O,O*-dialkyl-2-[3-bromo-1-(3-chloropyridin-2-yl) -1*H*-pyrazole-5-carbonyloxy] (aryl) methylphosphonates

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ABSTRACT

A series of novel *O,O*-Dialkyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carbonyloxy](aryl) methylphosphonates **I-1**–**14** were designed and synthesized. The structures of all the title compounds were confirmed by ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR, IR and elemental analysis. Their insecticidal activities against *Mythimna separata* and *Plutella xylostella* were evaluated. The results of bioassays indicated that the title compounds exhibited 20–80% larvicidal activity against *Mythimna separata* at 1000 mg/L.

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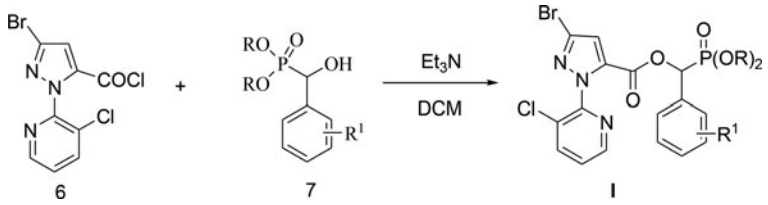
Synthesis; insecticidal activity; pyridylpyrazole; phosphonate

GRAPHICAL ABSTRACT



Introduction

Heterocyclic compounds display a wide range of biological activities and have attracted considerable attention as the main source of lead compounds in agrochemicals. Among various biologically nitrogen-containing heterocycles, pyrazole, pyridine, and their derivatives have occupied important positions in pesticide chemistry and are often introduced in the design of bioactive compounds.[1-3] Some of these compounds have been developed as commercial pesticides, such as Chlorantraniliprole (A),[4] Cyantraniliprole (B),[5] and Pyriprole (C)[6] (Figure 1).

On the other hand, organic phosphorus compounds represent another important type of bioactive compounds and have received special attention in agrochemicals.[7-13] Some novel phosphonate derivatives are widely employed as fungicides and herbicides, such as Dufulin (D)[8] and Clacyfos (E)[9](Figure 2). In our previous work, it was shown that some alkylphosphonate derivatives possessed good herbicide activities[3,10-12] and some α-aminophosphonate derivatives exhibited high cytotocity.[13] In order to find new phosphonates with improved pesticide activity, a series of novel phosphonate derivatives were designed by introducing the *N*-pyridylpyrazole structural unit into the phosphonate molecule. Here, we describe the synthesis of *O,O*-Dialkyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carbonyloxy](aryl)-methylphosphonates **I-1**–**14**. Their insecticidal activities against *Mythimna separata* and *Plutella xylostella* were evaluated accordingly.

Results and discussion

Synthesis

The synthetic procedures for the title compounds **I** are shown in Schemes 1-3. According to the literature,[1g] the key intermediate pyrazole carboxylic acid **5** was synthesized from 3-chloro-2-hydrazinylpyridine **1** which was used directly as obtained commercially. Pyrazole-5-carbonyl chloride **6** could be prepared by the reaction of pyrazole carboxylic acid **5** with thionyl chloride under reflux for 5–6 h[11]. The intermediate compounds **7** were synthesized via reaction of several aldehydes with dimethyl phosphite or diethyl phosphite in dichloromethane using triethylamine as a catalyst in yields of 80–90%.[10,11] Then, compound **6** was reacted with compounds **7** to afford the title compounds **I**. The structures of these newly synthesized compounds were confirmed by ^{1}H-NMR, ^{13}C-NMR, ^{31}P–NMR, IR, and elemental analysis. The ^{1}H-NMR, ^{13}C-NMR, ^{31}P–NMR of the title

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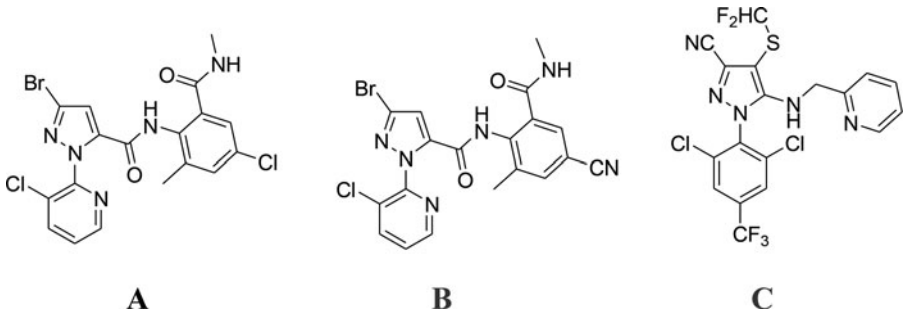


Figure 1. Chemical structures of chlorantraniliprole (**A**), cyantraniliprole (**B**), and pyriprole (**C**).

compounds **I-1–14** (Figures S1–S42) are presented in the Supplemental Materials.

In the ^{1}H-NMR spectra of the title compounds **I-1–14**, the chemical shifts of aromatic protons appeared at 6.86–8.50 ppm and the proton signal corresponding to OCHP displayed doublets at 6.10–6.71 ppm. The proton signal corresponding to the two methoxy groups (-OCH_3) attached with phosphorus appears as two doublets at 3.60 ± 0.06 and 3.72 ± 0.06 ppm, respectively. IR spectra of the title compounds **I-1–14** showed normal stretching absorption bands, indicating the existence of P═O (~1246 cm^{-1}), P–C (750–840 cm^{-1}), P–O–C (1010–1084 cm^{-1}), C═O (~1760 cm^{-1}), C–O (~1180 cm^{-1}), Ar-H (~3130 cm^{-1}), and C–H (2954–3002 cm^{-1}). The typical phosphorus resonance at 15.5–19.2 ppm in the ^{31}P–NMR spectra of **I-1–14** reveals the presence of a phosphorus center coupled to an adjacent CH. The EI mass spectra of the title compounds **I-1–4** 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 are in good agreement with the theoretical data.

Insecticidal activity

The preliminary results of insecticidal activity assessment indicate that the title compounds **I** exhibited 20–80% larvicidal activities against *Mythimna separata* at 1000 mg/L and the data are shown in Table S 1 (Supplemental Materials). Some of the title compounds were then selected for further test against *Mythimna separata* and *Plutella xylostella* at 500 mg/L using Chlorantraniliprol as a positive control. The subsequent results show that the title compounds **I-1**, **I-3**, **I-4**, **I-5**, **I-7**, **I-8** and **I-11** have certain insecticidal activity against *Mythimna separata* with 10–50% death rates and *Plutella xylostella* with 0–17.5% death rates at 500 mg/L. As shown in Table S1, compounds (such as **I**-1–3, **I**-6–8, **I**-12, **I**-14) with 2-Cl, 2-F, 4-Cl, 4-F, 2,4-Cl_2, 4-CF_3, 4-Br as R^1 show 30–80% larvicidal activity against *Mythimna separata* at 1000 mg/L. Compounds (such as **I**-4, **I**-9–11) with 2-CH_3, 4-CH_3, 2-OCH_3, 4-OCH_3 as R^1 show 40–70% larvicidal activity against *Mythimna separata* at 1000 mg/L. It can be found that the electronic factor does not seem to play a significant role as compounds with electron-rich and electron-poor substituents, respectively. Interestingly, when CH_3 as R, compounds with Cl or F or CH_3 as R^1 at *ortho* in phenyl ring show better larvicidal activities against *Mythimna separata* and *Plutella xylostella* at 500 mg/L compared to that substituted at *para* position.

Experimental details and the insecticidal activities (Table S 1) are presented in the Supplemental Materials, together with sample ^{1}H, ^{13}C, and ^{31}P NMR spectra for the products (Figures S1–S42)

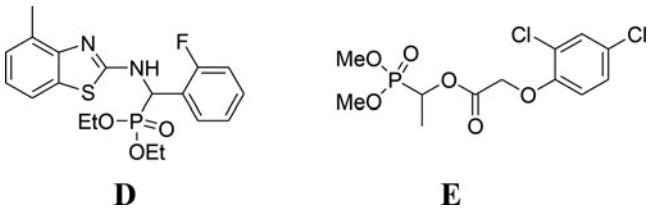


Figure 2. Chemical structures of dufulin (**D**) and clacyfos (**E**).

Conclusions

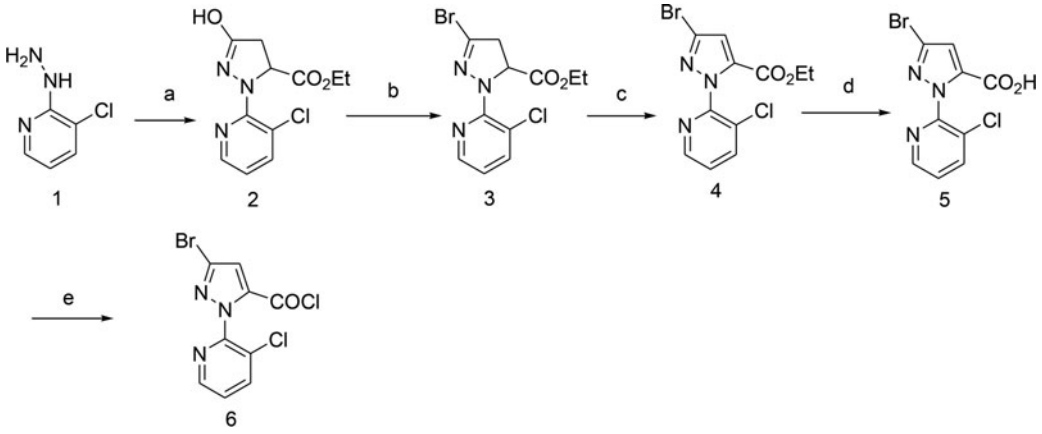
In summary, a series of phosphonates derivatives containing *N*-pyridylpyrazole structural unit were synthesized with moderate to good yields and screened for their insecticidal activity. Chlorantraniliprol was slected as a positive control. A preliminary bioassay shows that some of the title compounds exhibited certain insecticidal activities against *Mythimna separata* and *Plutella xylostella*.

Experimental

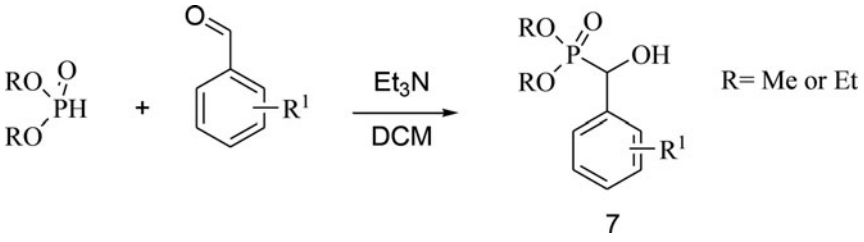
All the reagents were of analytical grade. Melting points were determined using an X-4 apparatus and uncorrected. ^{1}H NMR, ^{31}P NMR, ^{13}C NMR spectra were measured on a Bruker AC-P500 (500 Hz) instrument using TMS as an internal standard and $CDCl_3$ as solvent. MS spectra were analyzed on a Finnigen TRACE spectrometer and API2000LC/MS. Elemental analyses were performed by a Vario EL III elemental analyzer.

Synthesis of the intermediate 3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyl chloride 6

The intermediate compound **5** was synthesized according to the literature.[1g] A mixture containing the intermediate compound **5** (3.5 mmol) and thionyl chloride (3 mL) was added into a 25 mL flask and refluxed for 5–6 h. Excess thionyl chloride was evaporated off under reduced pressure, and a light yellow oil **6** was obtained in a yield of 94%.



Scheme 1. Synthesis of Compounds **6**. 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.



Scheme 2. Synthesis of compounds **7**.

Synthesis of the intermediate O,O-dialkyl-1-hydroxyalkylphosphonates 7

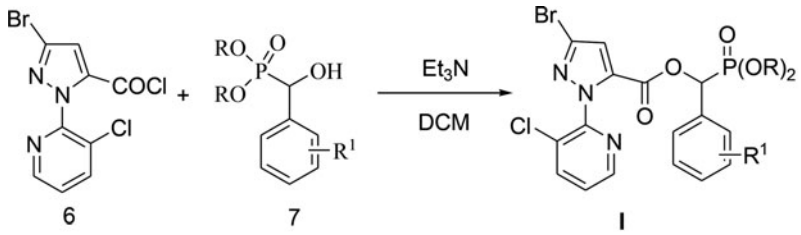
The intermediate compounds **7** could be prepared by the reaction of several aldehydes (4 mmol) and dimethyl phosphite or diethyl phosphite (4 mmol) in dichloromethane (15 mL) using triethylamine (2 mmol) as a catalyst in yields of 80–90%[10,11].

General procedure for the synthesis of the title compounds I-1–14

A solution of pyrazole carbonyl chloride **6** (3.3 mmol) in dichloromethane (15 mL) was added to a stirred mixture of **7** (3 mmol) and triethylamine (3.3 mmol) in dichloromethane (20 mL) at 0–5 °C. The resulting mixture was stirred for 3–5 h at room temperature and then for 1–2 h at 40 °C. The dichloromethane layer was washed with 0.1 M hydrochloric acid, saturated sodium hydrogen carbonate solution, and brine, dried, and concentrated. The residue was purified by column chromatography on silica gel and elution with petroleum ether/acetone (4:1, v/v) to give the corresponding pure title compounds **I-1–14** in 66–90% yields.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](2-chlorophenyl)methylphosphonate I-1:

White solid; yield, 82%; mp, 95–96 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.61 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 3.78 (d, 3H,



I-1: R= Me, R^1=2-Cl; **I-2**:R=Et,R^1=2-Cl; **I-3**:R= Me,R^1=4-Cl;
I-4:R= Me,R^1=4-CH_3;**I-5**:R= Me, R^1-Phenyl=2,2-difluorobenzo[d][1,3]dioxole-4-yl
I-6:R= Me,R^1=2,4-Cl_2;**I-7**:R=Me,R^1=2-F; **I-8**:R=Me,R^1=4-F;
I-9:R=Me,R^1=2-OCH_3;**I-10**:R=Me,R^1=4-OCH_3;**I-11**:R=Me,R^1=2-CH_3;
I-12:R=Me,R^1=4-CF_3;**I-13**:R=Me,R^1=H; **I-14**:R=Me,R^1=4-Br;

Scheme 3. Synthesis of the target compounds **I**.

J = 10.5 Hz, P-O-C$\underline{H}_3$), 6.70 (d, 1H, J = 13.5 Hz, P-C$\underline{H}$), 7.19 (s, 1H, ^{4}H-Pyrazole), 7.26–8.50 (m, 7H, ^{3,4,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.9, 67.4 (d, $^1J_{C\text{-}P}$ = 168.99 Hz), 115.0, 126.4, 127.3, 128.3, 129.1, 129.6, 130.4, 133.4, 134.9, 139.3, 147.1, 148.3, 155.6, 155.7; ^{31}P NMR (202 MHz, $CDCl_3$): δ 17.9; IR (KBr)/cm^{-1}: 3456, 3119, 3071, 2963, 2938, 2906, 1741, 1580, 1511, 1469, 1358, 1291, 1255, 1226, 1134, 1073, 1040, 1025, 960, 759; EI-MS m/z (%): 532 (M^+, 8); *Anal.* Calcd for $C_{18}H_{15}BrCl_2N_3O_5P$: C, 40.40; H, 2.83; N, 7.85. Found: C, 40.48; H, 2.92; N, 7.59.

*O,O-Diethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-*1H*-pyrazole-5-carbonyloxy](2- chlorophenyl)methylphosphonate I-2:*

White solid; yield, 79%; mp, 85–87 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.16 (t, 3H, J = 7.0 Hz, P-O-$CH_2C\underline{H}_3$), 1.30 (t, 3H, J = 7.0 Hz, P-O-$CH_2C\underline{H}_3$), 3.85–4.18 (m, 2×2H, 2×P-O-$\underline{CH}_2CH_3$), 6.67 (d, 1H, J = 13.5Hz, P-C$\underline{H}$), 7.19(s, 1H, ^{4}H-Pyrazole), 7.26–8.47 (m, 7H, ^{3,4,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.5, 63.6, 67.8 (d, $^1J_{C\text{-}P}$ = 171.9 Hz), 114.9, 126.3, 127.2, 128.3, 129.2, 129.6, 129.8, 130.3, 133.6, 135.1, 139.3, 147.1, 148.4, 155.7, 155.8; ^{31}P NMR (202 MHz, $CDCl_3$): δ 15.5; IR (KBr)/cm^{-1}: 3457, 3119, 3073, 2988, 2963, 2939, 2906, 1738, 1575, 1510, 1469, 1358, 1291, 1255, 1226, 1134, 1076, 1043, 960, 759; EI-MS m/z (%):561 (M^+, 4); *Anal.* Calcd for $C_{20}H_{19}BrCl_2N_3O_5P$: C, 42.65; H, 3.40; N, 7.46; Found: C, 42.88, H, 3.82, N, 7.49.

*O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-*1H*-pyrazole-5-carbonyloxy](4-chlorophenyl)methylphosphonate I-3:*

White solid; yield, 84%; mp, 109–111 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.63 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.69 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 6.13 (d, 1H, J = 13.5 Hz, P-C$\underline{H}$), 7.19(s, 1H, ^{4}H-Pyrazole), 7.32–8.50 (m, 7H, ^{2,3,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.9, 70.4 (d, $^1J_{C\text{-}P}$ = 169.8 Hz), 115.0, 126.3, 128.4, 128.9, 129.2, 130.7, 134.9, 139.2, 147.1, 148.4, 155.8, 155.9; ^{31}P NMR (202 MHz, $CDCl_3$): δ 18.1; IR (KBr)/cm^{-1}: 3443, 3132, 3097, 2956, 2918, 2851, 1739, 1650, 1578, 1469, 1358, 1292, 1256, 1239, 1184, 1149, 1084, 1063, 1047, 960, 759; EI-MS m/z (%): 532 (M^+, 6); *Anal.* Calcd for $C_{18}H_{15}BrCl_2N_3O_5P$: C, 40.40; H, 2.83; N, 7.85; Found: C, 40.42; H, 2.86; N, 7.89.

*O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-*1H*-pyrazole-5-carbonyloxy](4-methyl-phenyl)methylphosphonate I-4:*

White solid; yield, 77%; mp, 68–70 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.33 (s, 3H, Ar-C$\underline{H}_3$), 3.60 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.68 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 6.14 (d, 1H, J = 13.0 Hz, P-C$\underline{H}$), 7.14–8.50 (m, 8H, ^{4}H-Pyrazole, ^{2,3,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.3, 54.1, 70.9 (d, $^1J_{C\text{-}P}$ = 170.5 Hz), 105.4, 113.9, 114.9, 126.3, 127.1, 127.8, 128.9, 129.4, 135.8, 139.3, 147.0, 156.4, 156.5; ^{31}P NMR (202 MHz, $CDCl_3$): δ 18.8; IR (KBr)/cm^{-1}: 3441, 3112, 3087, 2966, 2908, 2860, 1741, 1647, 1577, 1468, 1358, 1290, 1255, 1237, 1183, 1150, 1080, 1064, 1046, 961, 759; EI-MS m/z (%): 513 (M^+, 8); *Anal.* Calcd for $C_{19}H_{18}BrClN_3O_5P$: C, 44.34; H, 3.52; N, 8.16; Found: C, 44.38; H, 3.92; N, 8.29.

*O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-*1H*-pyrazole-5-carbonyloxy](2,2-difluorobenzo[d][1,3]dioxole-4-yl)methylphosphonate I-5:*

White solid; yield, 68%; mp, 121–123 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.64 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.76 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 6.31 (d, 1H, J = 13.5 Hz, P-C$\underline{H}$), 7.02–8.50 (m, 7H, ^{4}H-Pyrazole, ^{4,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.8, 64.9 (d, $^1J_{C\text{-}P}$ = 163.6 Hz), 109.0, 109.1, 115.1, 119.9, 122.4, 123.7, 123.8, 126.2, 128.4, 131.5, 134.6, 136.8, 137.7, 139.3, 140.9, 141.0, 143.3, 147.1, 148.3, 155.6, 155.8; ^{31}P NMR (202 MHz, $CDCl_3$): δ 16.9; IR (KBr)/cm^{-1}: 3454, 3131, 3090, 2976, 2911, 2868, 1749, 1643, 1575, 1466, 1358, 1291, 1256, 1239, 1185, 1149, 1082, 1063, 1046, 960, 758; *Anal.* Calcd for $C_{19}H_{14}BrClF_2N_3O_7P$: C, 39.30; H, 2.43; N, 7.24; Found: C, 39.38; H, 2.52; N, 7.28.

*O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-*1H*-pyrazole-5-carbonyloxy](2,4-dichlorophenyl) methylphosphonate I-6:*

White solid; yield, 88%; mp, 117–119 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.64 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.78 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 6.60 (d, 1H, J = 13.5 Hz, P-C$\underline{H}$), 7.18(s, 1H, ^{4}H-Pyrazole), 7.26–8.50 (m, 6H, ^{3,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 54.2, 67.0 (d, $^1J_{C\text{-}P}$ = 172.3 Hz), 115.1, 126.3, 127.7, 128.0, 128.4, 129.2, 129.3, 129.6, 130.6, 134.3, 134.8, 135.9, 139.3, 147.1, 148.3, 155.5, 155.6; ^{31}P NMR (202 MHz, $CDCl_3$): δ 17.6; IR (KBr)/cm^{-1}: 3449, 3113, 3088, 2976, 2911, 2869, 1747, 1640, 1576, 1468, 1357, 1290, 1258, 1236, 1185, 1150, 1083, 1065, 1046, 960, 759; *Anal.* Calcd for $C_{18}H_{14}BrCl_3N_3O_5P$: C, 37.96; H, 2.48; N, 7.38; Found: C, 38.08; H, 2.72; N, 7.69.

*O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-*1H*-pyrazole-5-carbonyloxy](2-fluorophenyl)methylphosphonate I-7:*

White solid; yield, 86%; mp, 101–103 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.64 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.76 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 6.52 (d, 1H, J = 13.0 Hz, P-C$\underline{H}$), 7.03–8.48 (m, 8H, ^{4}H-Pyrazole, ^{3,4,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 54.1, 64.2 (d, $^1J_{C\text{-}P}$ = 173.3 Hz), 105.1, 115.0, 115.6, 115.7, 119.9, 120.0, 124.6, 126.3, 128.3, 129.2, 129.3, 129.4, 131.0, 131.1, 134.9, 139.2, 147.1, 148.4, 155.7, 155.8; ^{31}P NMR (202 MHz, $CDCl_3$): δ 17.9; IR (KBr)/cm^{-1}: 3451, 3123, 3097, 2986, 2909, 2860, 1750, 1645, 1576, 1466, 1358, 1290, 1257, 1238, 1180, 1152, 1081, 1065, 1044, 960, 758; *Anal.* Calcd for $C_{18}H_{15}BrClFN_3O_5P$: C, 41.68; H, 2.92; N, 8.10; Found: C, 42.08; H, 3.02; N, 8.19.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](4-fluorophenyl)methylphosphonate I-8:

White solid; yield, 79%; mp, 131–133 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.61 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.70 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 6.14 (d, 1H, J = 13.5 Hz, P-C$\underline{H}$), 7.01–8.50 (m, 8H, ^{4}H-Pyrazole, ^{2,3,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.7, 69.9 (d, $^{1}J_{C\text{-}P}$ = 160.5 Hz), 105.2, 115.2, 115.3, 115.4, 126.3, 128.7, 128.8, 128.9, 129.0, 132.4, 136.9, 137.7, 139.3, 147.1, 159.4, 161.6, 163.6; ^{31}P NMR (202 MHz, $CDCl_3$): δ 18.4; IR (KBr)/cm^{-1}: 3455, 3119, 3094, 2970, 2906, 2863, 1742, 1649, 1578, 1465, 1358, 1291, 1256, 1236, 1180, 1150, 1081, 1065, 1045, 960, 759; *Anal.* Calcd for $C_{18}H_{15}BrClFN_3O_5P$: C, 41.68; H, 2.92; N, 8.10; Found: C, 41.81; H, 3.13; N, 8.11.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](2-methoxyphenyl)methylphosphonate I-9:

White solid; yield, 66%; mp, 126–128 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.55 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 3.68 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.77 (s, 3H, -OC$\underline{H}_3$), 6.73 (d, 1H, J = 12.5 Hz, P-C$\underline{H}$), 6.81–8.42 (m, 8H, ^{4}H-Pyrazole, ^{3,4,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.8, 55.8, 64.6 (d, $^{1}J_{C\text{-}P}$ = 172.0 Hz), 105.1, 110.9, 114.9, 120.8, 126.2, 128.2, 129.2, 135.4, 137.0, 137.7, 139.2, 147.0, 148.4, 155.9, 156.7; ^{31}P NMR (202 MHz, $CDCl_3$): δ 16.9; IR (KBr)/cm^{-1}: 3441, 3121, 3099, 2969, 2905, 2862, 1748, 1644, 1576, 1468, 1355, 1291, 1256, 1236, 1181, 1152, 1080, 1065, 1047, 957, 758; *Anal.* Calcd for $C_{19}H_{18}BrClN_3O_6P$: C, 43.00; H, 3.42; N, 7.92; Found: C, 43.08; H, 3.52; N, 8.09.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](4-methoxyphenyl)methylphosphonate I-10:

White solid; yield, 72%; mp, 117–119 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.59 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 3.69 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 3.79 (s, 3H, -OC$\underline{H}_3$), 6.11 (d, 1H, J = 13.0 Hz, P-C$\underline{H}$), 6.86–8.49 (m, 8H, ^{4}H-Pyrazole, ^{2,3,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.9, 55.3, 70.7 (d, $^{1}J_{C\text{-}P}$ = 171.9 Hz), 114.2, 114.9, 126.2, 128.3, 129.3, 129.6, 135.3, 139.2, 147.1, 148.5, 156.0, 156.1, 160.3; ^{31}P NMR (202 MHz, $CDCl_3$): δ 18.9; IR (KBr)/cm^{-1}: 3440, 3129, 3082, 2955, 2930, 2851, 1736, 1644, 1611, 1578, 1514, 1471, 1360, 1293, 1246, 1180, 1134, 1047, 959, 815, 762; *Anal.* Calcd for $C_{19}H_{18}BrClN_3O_6P$: C, 43.00; H, 3.42; N, 7.92; Found: C, 43.13; H, 3.47; N, 8.11.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](2-methylphenyl)methylphosphonate I-11:

White solid; yield, 83%; mp, 125–127 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.41 (s, 1H, Ar-C$\underline{H}_3$), 3.57 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 3.69 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 6.40 (d, 1H, J = 13.5Hz, P-C$\underline{H}$), 7.14–8.50 (m, 8H, ^{4}H-Pyrazole, ^{3,4,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.5, 53.9, 67.8 (d, $^{1}J_{C\text{-}P}$ = 170.9 Hz), 114.9, 126.2, 126.4, 128.0, 128.3, 129.1, 129.3, 130.6, 135.3, 136.6, 139.2, 147.1, 148.5, 155.9, 156.1; ^{31}P NMR (202 MHz, $CDCl_3$): δ 19.2; IR (KBr)/cm^{-1}: 3441, 3150, 3054, 2955, 2852, 1740, 1645, 1579, 1472, 1358, 1297, 1263, 1240, 1174, 1151, 1078, 1057, 1027, 961, 763; *Anal.* Calcd for $C_{19}H_{18}BrClN_3O_5P$: C, 44.34; H, 3.52; N, 8.16; Found: C, 44.38; H, 3.92; N, 8.29.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](4-trifluoromethylphenyl)methylphosphonate I-12:

White solid; yield, 70%; mp, 138–140 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.66 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 3.70 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 6.22 (d, 1H, J = 14.0 Hz, P-C$\underline{H}$), 7.21 (s, 1H, ^{4}H-Pyrazole), 7.44–8.50 (m, 7H, ^{2,3,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.9, 70.4 (d, $^{1}J_{C\text{-}P}$ = 168.0 Hz), 115.1, 125.6, 125.7, 125.8, 126.3, 127.9, 128.0, 129.2, 130.8, 131.0, 131.1, 131.3, 131.4, 131.6, 134.7, 136.2, 139.3, 147.1, 148.4, 155.8, 155.9; ^{31}P NMR (202 MHz, $CDCl_3$): δ 17.8; IR (KBr)/cm^{-1}: 3440, 3130, 3044, 2965, 2858, 1741, 1645, 1578, 1471, 1358, 1296, 1261, 1239, 1173, 1150, 1079, 1055, 1030, 960, 762; *Anal.* Calcd for $C_{19}H_{15}BrClF_3N_3O_5P$: C, 40.13; H, 2.66; N, 7.39; Found: C, 40.38; H, 2.72; N, 7.41.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](phenyl)methylphosphonate I-13:

White solid; yield, 90%; mp, 141–143 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ3.60 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 3.67 (d, 3H, J = 11.0 Hz, P-O-C$\underline{H}_3$), 6.18 (d, 1H, J = 13.0 Hz, P-C$\underline{H}$), 7.20 (s, 1H, ^{4}H-Pyrazole), 7.33–8.50 (m, 8H, Ar-H, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.9, 71.0 (d, $^{1}J_{C\text{-}P}$ = 169.3 Hz), 105.2, 114.9, 126.3, 127.8, 128.3, 128.7, 129.3, 135.1, 137.7, 139.2, 147.1, 155.9, 156.0; ^{31}P NMR (202 MHz, $CDCl_3$): δ 18.6; IR (KBr)/cm^{-1}: 3443, 3122, 3054, 2961, 2855, 1740, 1646, 1579, 1474, 1358, 1295, 1260, 1237, 1174, 1150, 1081, 1054, 1033, 961, 759; *Anal.* Calcd for $C_{18}H_{16}BrClN_3O_5P$: C, 43.18; H, 3.22; N, 8.39; Found: C, 43.31; H, 3.52; N, 8.44.

O,O-Dimethyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1H-pyrazole-5-carbonyloxy](4-bromophenyl)methylphosphonate I-14:

White solid; yield, 71%; mp, 148–150 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.63 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 3.69 (d, 3H, J = 10.5 Hz, P-O-C$\underline{H}_3$), 6.12 (d, 1H, J = 13.5 Hz, P-C$\underline{H}$), 7.19 (s, 1H, ^{4}H-Pyrazole), 7.24–8.50 (m, 7H, ^{2,3,5,6}H-Ar, ^{4,5,6}H-Py); ^{13}C NMR (125 MHz, $CDCl_3$): δ 53.9, 70.4 (d, $^{1}J_{C\text{-}P}$ = 169.5 Hz), 115.0, 123.5, 126.3, 128.4, 129.2, 129.4, 131.2, 131.9, 134.9, 139.2, 147.1, 148.4, 155.8, 155.9; ^{31}P NMR (202 MHz, $CDCl_3$): δ 18.0; IR (KBr)/cm^{-1}: 3437, 3131, 3096, 2954, 2920, 2851, 1740, 1651, 1578, 1512, 1469, 1358, 1238, 1184, 1135, 1062, 1047, 960, 815, 763; *Anal.* Calcd for $C_{18}H_{15}Br_2ClN_3O_5P$: C, 37.30; H, 2.61; N, 7.25; Found: C, 37.51; H, 3.02; N, 7.46.

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