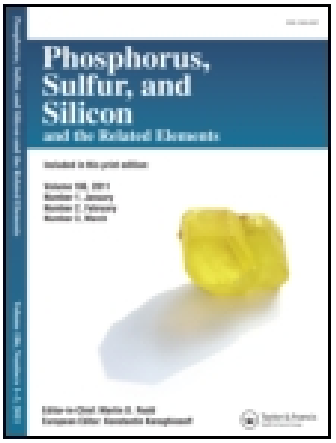


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# Synthesis and Herbicidal Activity of Novel Pyrimidinyl Derivatives Containing an α-Amino Phosphonate Moiety

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# SYNTHESIS AND HERBICIDAL ACTIVITY OF NOVEL PYRIMIDINYL DERIVATIVES CONTAINING AN α-AMINO PHOSPHONATE MOIETY

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***In order to find novel pyrimidinyl carboxylic acid analogs with high activity and low toxicity, a series of novel pyrimidinyl derivatives containing an α-amino phosphonate moiety 5 was synthesized by the condensation of 4-(4,6-dimethoxypyrimidin-2-yloxy)phenoxyacetic 3a or propionic acids 3b with dialkyl α-amino substitutedbenzyl phosphonates 4. Their structures were characterized by spectroscopic data (IR, $^{1}H$ NMR, $^{31}P$ NMR, MS) and elemental analyses. The results of preliminary herbicidal activities (in vitro) showed that most of these compounds exhibited higher herbicidal activities against dicotyledonous weeds (*Brassica campestris L*) than monocotyledonous weeds (*Echinochloa crus-galli*). Further bioassays (in vivo) indicated that some of compounds 5 possessed selective herbicidal activity against amaranth pigweed (*A. retroflexus*) in post-emergence treatment.***

***Supplemental materials are available for this article. Go to the publisher's online edition of* Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.***

**Keywords** α-Amino phosphonate; aryloxyphenoxy carboxylic acid; herbicidal activity; pyrimidinylcarboxylic acid



## INTRODUCTION

Since the late 1990s, pyrimidinyl carboxylic acid derivatives have been found to be effective herbicides against barnyard grass in different growth stages including pre-emergence treatment and excellent safety on transplanted rice crops, animals, fish, etc. These herbicides, known as inhibitors of branched chain amino acids (ALS or AHAS) synthase, have attracted considerable attention from pesticide scientists.[1–5] To date, several pyrimidyl carboxylic acid derivatives, such as bispyribac-sodium and pyriminobac-methyl, have been used as commercial herbicides (Figure 1). Aryloxyphenoxypropionate (APP) derivatives have been found to be the inhibitor of acetyl-coacarboxylase (ACCase) and they have acted as an important class of herbicides in plant protection.[6,7]

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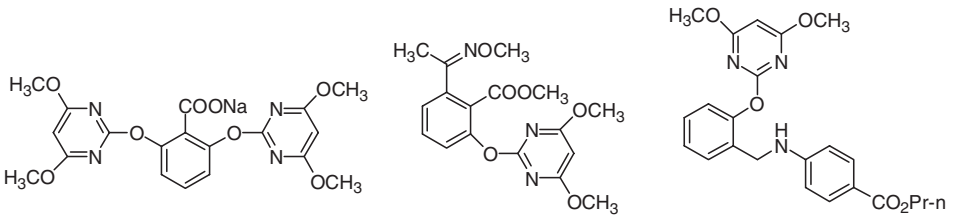
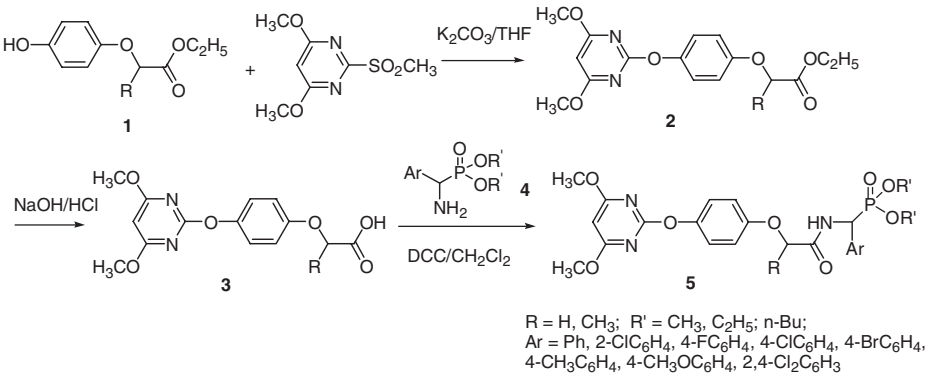



**Figure 1** Structures of some commercial pyrimidinyl carboxylic acid and pyrimidinyl benzylamine herbicides.



When heterocyclic units were introduced to the APP skeleton, some efficient herbicides were developed. Recently, $\alpha$-amino phosphonic acid and their ester derivatives, as bioisosteres of natural amino acids, have been receiving an increasing amount of attention in medicinal chemistry and pesticide science due to their wide biological activities such as enzyme inhibition, antibiotics, and haptens of catalytic antibodies, fungicides, herbicides, plant regulators, and plant virucides.[8–14] In order to find potent and selective herbicide lead structures, we have synthesized a series of novel pyrimidinyl derivatives bearing an $\alpha$-amino phosphonate moiety **5** (Scheme 1), which are similar to APP inhibitor in some extents, and compounds **5** were evaluated for herbicidal activities in this study.




**Scheme 1** Synthetic route to title compounds **5**.

## RESULTS AND DISCUSSION

### Synthesis

4-(4,6-Dimethoxypyrimidin-2-yloxy)phenoxyacetic or propionic acids (**3a**, **3b**) were prepared by the reaction of 2-(4-hydroxyphenoxy)-carboxylates with (4,6-dimethoxypyrimidin-2-yl)methylsulfone in potassium carbonate and refluxing THF, followed by saponification. Finally, 2-[4-(4,6-dimethoxypyrimidin-2-yloxy)phenoxy]acetic or propionic acid **3** reacted with $\alpha$-amino phosphonates **4** using DCC as the dehydration reagent to obtain the target compounds **5** in good yields. The structures of target compounds **5** were confirmed from their spectroscopic data (IR, $^1$H NMR, $^{31}$P NMR, EI-MS, or ESI-MS) and elemental analyses.

### Herbicidal Activities

The preliminary herbicidal activity (in vitro) of the title compounds **5** against *Brassica campestris L.* (rape) and *Echinochloa crus-galli* (barnyard grass) has been investigated at the dosages of 100 mg/L and 10 mg/L, compared with the commercially available herbicide, bispyribac-sodium, and is listed in Table S1 (Supplemental Materials, available online).

## CONCLUSIONS

In summary, we have synthesized a series of novel pyrimidinyl derivatives containing an $\alpha$-amino phosphonate moiety **5**. Their structures were clearly confirmed by spectroscopic data (IR, $^1$H NMR, $^{31}$P NMR, MS) and elemental analyses. The results of preliminary herbicidal activity of compounds **5** showed that some of the target compounds displayed good herbicidal activity against the root of *Brassica campestris L* at the concentration of 100 mg/L. Further bioassays (in vivo) indicated some of compounds **5** showed selective herbicidal activity against amaranth pigweed (*A. retroflexus*) in post-emergence treatments.



## EXPERIMENTAL

### Instruments

$^1$H and $^{31}$P NMR spectra were performed on a Varian Mercury Plus-400 (400 MHz) or Varian Mercury Plus-600 (600 MHz) spectrometer at room temperature in $CDCl_3$ with TMS and 85% $H_3PO_4$ as the internal and external standards, respectively; chemical shift values ($\delta$) were given in ppm. Elemental analyses were taken on a Germany Elementar Vario EL III elemental analyses instrument. Mass spectra were measured on a Finnigan TraceMS 2000 spectrometer at 70 eV using EI method or Applied Biosystems API 2000 LC/MS/MS (ESI-MS) spectrometer. The IR spectra were recorded on a Nicolet NEXUS470 spectrometer as KBr pellets with absorption given in $cm^{-1}$. The melting points were determined on an X-4 binocular microscope melting point apparatus (Beijing Tech. Instruments Co., Beijing, China) and were uncorrected. Analytical TLC was performed on silica gel GF254. Column chromatographic purification was carried out using silica gel. Yields were not optimized. Unless otherwise noted, all materials were commercially available and were used directly without further purification. All solvents were dried and redistilled before use. Ethyl 2-(4-hydroxyphenoxy)-acetate or -propionate were prepared from hydroquinone and ethyl 2-chloroacetate or 2-bromopropionate in sodium ethoxide ethanol solution according to the reported methods.[15] For acetate, yield 66%, mp 124.3–125.8°C; and for propionate, yield 58%, mp 120.5–121.9°C. Dialkyl $\alpha$-amino phosphonates **4** were synthesized from aromatic aldehyde, ammonium hydroxide, and dialkyl phosphites in moderate yields according to the reported synthetic protocols.[16,17]

### Synthesis of 4-(4,6-Dimethoxypyrimidin-2-yloxy)phenoxyacetic or -propionic Acids (3a, 3b)

Ethyl 2-(4-hydroxyphenoxy)-propionate (2.10 g, 10 mmol), 4,6-dimethoxypyrimidin-2-yl-methylsulfone (2.18 g, 10 mmol), and anhydrous potassium carbonate (2.07 g, 15 mmol) in dry THF (30 mL) were stirred under reflux for 5 h (monitored by TLC). The solid was filtered off, and the liquid was poured into ice water (50 mL). The crude product was collected by filtration. After recrystallization from ethyl acetate, ethyl 4-(4,6-dimethoxypyrimidin-2-yloxy)propionate was obtained as a light yellow crystals

(2.68 g), yield: 77%, mp: 83.2–84.4°C, which can be used for the next step without further purification.

Ethyl 4-(4,6-dimethoxypyrimidin-2-yloxy)propionate (3.48 g, 10 mmol), sodium hydroxide (0.64 g, 16 mmol), water (10 mL), and ethanol (10 mL) were stirred at 80–90°C for 1–2 h (monitored by TLC). The solution was acidified by dilute hydrochloride. The crude product was collected by filtration, washed by ethyl ether, and **3b** was obtained as a yellow solid, yield: 92%, mp: 153.2–154.6°C. $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.67 (d, $J = 7.2$ Hz, 3H, $CH_3$), 3.82 (s, 6H, $2OCH_3$), 4.77 (q, $J = 7.2$ Hz, 1H, CH), 5.76 (s, 1H, pyrimidine-H), 6.90 (d, $J = 8.4$ Hz, 2H, ArH), 7.10 (d, $J = 9.0$ Hz, 2H, ArH), 13.06 (s, 1H, OH). Anal. Calcd for $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.04; N, 8.75. Found: C, 56.06; H, 4.84; N, 8.93.

**3a** was prepared in a similar procedure, yield, 86%; yellow solid, mp 136.5–137.4°C. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 3.84 (s, 6H, $2OCH_3$), 4.51 (s, 2H, $CH_2$), 5.79 (s, 1H, pyrimidine-H), 6.94 (d, $J = 8.2$ Hz, 2H, ArH), 7.06 (d, $J = 8.8$ Hz, 2H, ArH), 12.95 (s, 1H, OH). Anal. Calcd for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15. Found: C, 55.13; H, 4.79; N, 9.44.



### General Synthetic Procedures for O,O′-Dialkyl {2-[4-(4,6-Dimethoxypyrimidin-2-yloxy)phenoxy]acetamido or -propionamido}substitutedphenyl Methylphosphonates 5

To a solution of $\alpha$-aminophosphonate **4** (2.0 mmol) and 2-[4-(4,6-dimethoxypyrimidin-2-yloxy)phenoxy]acetic or propionic acid **3** (2.0 mmol) in anhydrous methylene chloride (10 mL), dicyclohexylcarbodiimide (DCC, 0.45 g, 2.2 mmol) in anhydrous methylene chloride (3 mL) was added dropwise at 0–5°C under stirring for 0.5 h. The mixture was allowed to be stirred at room temperature for 10–24 h (monitored by TLC). The solid was filtered off, the solvent was removed, acetone (5 mL) was added to the crude product, and the solid formed was filtered off again. After the removal of the solvent followed by column chromatography of the crude product on silica gel using a mixture of petroleum ether and acetone (*v/v*, 2:1) as the eluent, compounds **5** were obtained as white solids or yellow liquids in 61–86% yields.

Data for **5a** (Ar = 4-$CH_3C_6H_4$, R = $CH_3$, R′ = $C_2H_5$): yield, 79%; white solid; mp 130.4–131.9°C; IR (KBr): $\nu$ 3423 (N—H), 3226 (C-H), 1693 (C=O), 1403, 1210 (P=O), 1029 (P—O—C), 982 (P—C) cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.14 (t, $J = 7.2$ Hz, 3H, $CH_3$), 1.31 (t, $J = 7.2$ Hz, 3H, $CH_3$), 1.62 (d, $J = 6.8$ Hz, 3H, $CH_3$), 2.28 (s, 3H, $CH_3$), 3.84 (s, 6H, 2 $CH_3O$), 3.86–4.14 (m, 4H, $2CH_2$), 4.68 (q, $J = 6.8$ Hz, 1H, CH), 5.45 (dd, $J = 10.0$ Hz, $J = 20.8$ Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.86–7.12 (m, 8H, ArH), 7.30 (d, $J = 8.8$ Hz, 1H, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 18.65; EI-MS (70ev): *m/z* 559.5 ($M^+$, 15.8), 422 (37.5), 396.5 (80.3), 259 (96.4), 256 (31.1), 141 (77.7), 139 (100), 120 (28.7), 112 (81.8), 91(29.3), 80.5 (15.8), 77.5 (4.8), 70 (28.4). Anal. Calcd for $C_{27}H_{34}N_3O_8P$: C, 57.96; H, 6.12; N, 7.51. Found: C, 58.04; H, 6.03; N, 7.76.

Data for **5b** (Ar = Ph, R = $CH_3$, R′ = $C_2H_5$): yield, 84%; white solid; mp 147.7–148.5°C; $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.13 (t, $J = 7.2$ Hz, 3H, $CH_3$), 1.31 (t, $J = 7.2$ Hz, 3H, $CH_3$), 1.63 (d, $J = 7.2$ Hz, 3H, $CH_3$), 3.83 (s, 6H, $2CH_3O$), 3.74–4.14 (m, 4H, $2CH_2$), 4.68 (q, $J = 6.6$ Hz, 1H, CH), 5.48 (dd, $J = 10.2$ Hz, $J = 20.7$ Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.86–7.32 (m, 9H, ArH), 7.32 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 243 MHz): $\delta$ 19.53; ESI-MS: *m/z* 583 ($M^+$+K-1, 8), 559 (18), 545.0 ($M^+$, 100). Anal. Calcd for $C_{26}H_{32}N_3O_8P$: C, 57.24; H, 5.91; N, 7.70. Found: C, 57.01; H, 5.77; N, 7.95.

Data for **5c** (Ar = 4-$CH_3O$ $C_6H_4$, R = $CH_3$, R′ = $C_2H_5$): yield, 82%; white solid; mp 147.0–147.9°C; $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.14 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.31 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.62 (d, $J$ = 7.2 Hz, 3H, $CH_3$), 3.75 (s, 3H, $OCH_3$), 3.81 (s, 6H, $2CH_3O$), 3.84–4.12 (m, 4H, $2CH_2$), 4.67 (q, $J$ = 7.2 Hz, 1H, CH), 5.40 (dd, $J$ = 10.2 Hz, $J$ = 20.7 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.76 (d, $J$ = 8.4 Hz, 2H, ArH), 6.86 (d, $J$ = 8.4 Hz, 2H, ArH), 7.09–7.14 (m, 4H, ArH), 7.29 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 243 MHz): $\delta$ 19.26; ESI-MS: *m/z* 612.5 ($M^+$+K-1, 12), 597.5 ($M^+$+Na-1, 38), 575.5 ($M^+$, 100). Anal. Calcd for $C_{27}H_{34}N_3O_9P$: C, 56.34; H, 5.95; N, 7.30. Found: C, 56.48; H, 6.13; N, 7.17.

Data for **5d** (Ar = 2-$ClC_6H_4$, R = $CH_3$, R′ = $C_2H_5$): yield, 70%; white solid; mp 53.2–54.7°C; $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.17 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.36 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.63 (d, $J$ = 7.2 Hz, 3H, $CH_3$), 3.68–4.20 (m, 4H, $2CH_2$), 3.83 (s, 6H, $2CH_3O$), 4.66 (q, $J$ = 7.2 Hz, 1H, CH), 5.78 (s, 1H, pyrimidine-H), 5.99 (dd, $J$ = 9.6 Hz, $J$ = 21.0 Hz, 1H, PCH), 6.85–7.43 (m, 8H, ArH), 7.48 (s, 1, NH); $^{31}$P NMR ($CDCl_3$, 243 MHz): $\delta$ 18.91; ESI-MS: *m/z* 579.5 ($M^+$, 100). Anal. Calcd for $C_{26}H_{31}ClN_3O_8P$: C, 53.84; H, 5.39; N, 7.25. Found: C, 54.03; H, 5.50; N, 7.49.

Data for **5e** (Ar = 4-$CH_3C_6H_4$, R = $CH_3$, R′ = $CH_3$): yield, 74%; white solid; mp 81.3–82.5°C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.63 (d, $J$ = 7.2 Hz, 3H, $CH_3$), 2.35 (s, 3H, $CH_3$), 3.48 (d, $J$ = 10.0 Hz, 3H, $OCH_3$), 3.78 (d, $J$ = 10.8 Hz, 3H, $OCH_3$), 3.83 (s, 6H, $2CH_3O$), 4.68 (q, $J$ = 7.2 Hz, 1H, CH), 5.50 (dd, $J$ = 10.0 Hz, $J$ = 20.8 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.86–7.32 (m, 8H, ArH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 22.19; ESI-MS: *m/z* 569 ($M^+$+K-1, 27), 553 ($M^+$+Na-1, 64), 531 ($M^+$, 100). Anal. Calcd for $C_{25}H_{30}N_3O_8P$: C, 56.49; H, 5.69; N, 7.91. Found: C, 56.71; H, 5.55; N, 7.62.

Data for **5f** (Ar = 2,4-$Cl_2C_6H_3$, R = $CH_3$, R′ = $C_2H_5$): yield, 69%; white solid; mp 82.7–84.3°C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.26 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.51 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.63 (d, $J$ = 7.2 Hz, 3H, $CH_3$), 3.66–4.19 (m, 4H, $2CH_2$), 3.84 (s, 6H, $2CH_3O$), 4.67 (q, $J$ = 7.2 Hz, 1H, CH), 5.79 (s, 1H, pyrimidine-H), 5.87 (dd, $J$ = 10.6 Hz, $J$ = 20.8 Hz, 1H, PCH), 6.85–7.40 (m, 7H, ArH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 19.07; ESI-MS: *m/z* 635 ($M^+$+Na-1, 58), 615 (25), 613 ($M^+$, 100). Anal. Calcd for $C_{26}H_{30}Cl_2N_3O_8P$: C, 50.83; H, 4.92; N, 6.84. Found: C, 50.57; H, 5.11; N, 6.53.

Data for **5g** (Ar = 4-$FC_6H_4$, R = $CH_3$, R′ = $C_2H_5$): yield, 85%; white solid; mp 139.9–141.1°C; IR (KBr): $\nu$ 3428 (N—H), 1693 (C=O), 1401, 1211 (P=O), 1034 (P—O—C), 984 (P—C) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.15 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 1.31 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.63 (d, $J$ = 6.8 Hz, 3H, $CH_3$), 3.80–4.14 (m, 4H, $2CH_2$), 3.83 (s, 6H, $2CH_3O$), 4.69 (q, $J$ = 6.8 Hz, 1H, CH), 5.41 (dd, $J$ = 10.6 Hz, $J$ = 20.8 Hz, 1H, PCH), 5.79 (s, 1H, pyrimidine-H), 6.86–7.17 (m, 8H, ArH), 7.31 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 18.55; ESI-MS: *m/z* 602 ($M^+$+K-1, 36), 585 ($M^+$+Na-1, 85), 563.7 ($M^+$, 100). Anal. Cacld for $C_{26}H_{31}FN_3O_8P$: C, 55.42; H, 5.54; N, 7.46. Found: C, 55.25; H, 5.39; N, 7.20.

Data for **5h** (Ar = 4-$ClC_6H_4$, R = $CH_3$, R′ = $C_2H_5$): yield, 81%; white solid; mp 109.7–111.2°C; $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.17 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.31 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.62 (d, $J$ = 6.6 Hz, 3H, $CH_3$), 3.81 (s, 6H, $2CH_3O$), 3.83–4.14 (m, 4H, $2CH_2$), 4.69 (q, $J$ = 6.8 Hz, 1H, CH), 5.42 (dd, $J$ = 10.8 Hz, $J$ = 21.0 Hz, 1H, PCH), 5.79 (s, 1H, pyrimidine-H), 6.88 (d, $J$ = 9.0 Hz, 2H, ArH), 7.11–7.27 (m, 6H, ArH), 7.32 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 243 MHz): $\delta$ 18.95; EI-MS (70ev): *m/z* 581(6), 579 ($M^+$, 16), 139 (100). Anal. Calcd for $C_{26}H_{31}ClN_3O_8P$: C, 53.84; H, 5.39; N, 7.25. Found: C, 53.97; H, 5.13; N, 7.40.

Data for **5i** (Ar = Ph, R = $CH_3$, R′ = $n$-$C_4H_9$): yield, 77%; white solid; mp 86.7–87.5°C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 0.83 (t, $J$ = 7.6 Hz, 3H, $CH_3$), 0.93 (t, $J$ = 7.6 Hz, 3H, $CH_3$), 1.22–1.45 (m, 8H, $2CH_2CH_2$), 1.62 (d, $J$ = 6.8 Hz, 3H, $CH_3$), 3.62–4.12 (m, 4H, $2CH_2$), 3.85 (s, 6H, 2 $CH_3O$), 4.68 (q, $J$ = 6.8 Hz, 1H, CH), 5.45 (dd, $J$ = 10.8 Hz, $J$ = 21.0 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.86 (d, $J$ = 9.2 Hz, 2H, ArH), 7.10 (d, $J$ = 9.2 Hz, 2H, ArH), 7.17–7.27 (m, 5H, ArH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 18.14; ESI-MS: *m/z* 639 ($M^+$+K-1, 22), 623.4 ($M^+$+Na-1, 64), 601.2 ($M^+$, 100). Anal. Calcd for $C_{30}H_{40}N_3O_8P$: C, 59.89; H, 6.70; N, 6.98. Found: C, 60.14; H, 6.69; N, 7.17.

Data for **5j** (Ar = Ph, R = H, R′ = $C_2H_5$): yield, 71%; yellow oil; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.12 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.27 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 3.75–4.12 (m, 4H, $2CH_2$), 3.83 (s, 6H, $2CH_3O$), 4.54 (2d, $J$ = 15.6 Hz, 2H, $CH_2$), 5.55 (dd, $J$ = 9.6 Hz, $J$ = 20.8 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.94 (d, $J$ = 8.8 Hz, 2H, ArH), 7.17 (d, $J$ = 8.8 Hz, 2H, ArH), 7.31–7.51 (m, 6H, ArH, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 19.79; ESI-MS: *m/z* 553 ($M^+$+Na-1, 64), 531 ($M^+$, 100). Anal. Calcd for $C_{25}H_{30}N_3O_8P$: C, 56.49; H, 5.69; N, 7.91. Found: C, 56.74; H, 5.48; N, 8.13.

Data for **5k** (Ar = 4-$CH_3C_6H_4$, R = H, R′ = $C_2H_5$): yield, 69%; white solid; mp 86.9–88.2°C; $^1$H NMR ($CDCl_3$, 600 MHz): $\delta$ 1.14 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.29 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 2.33 (s, 3H, $CH_3$), 3.75–3.77 (m, 1H, $CH_2$), 3.84 (s, 6H, $2CH_3O$), 3.96–4.11 (m, 3H, $2CH_2$), 4.52 (2d, $J$ = 15.6 Hz, 2H, $CH_2$), 5.52 (dd, $J$ = 9.6 Hz, $J$ = 24.0 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.95 (d, $J$ = 9.0 Hz, 2H, ArH), 7.15–7.17 (m, 4H, ArH), 7.31 (d, $J$ = 6.6 Hz, 2H, ArH), 7.44 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 243 MHz): $\delta$ 19.82; ESI-MS: *m/z* 584 ($M^+$+K-1, 16), 567 ($M^+$+Na-1, 18), 545.0 ($M^+$, 100). Anal. Calcd for $C_{26}H_{32}N_3O_8P$: C, 57.24; H, 5.91; N, 7.70. Found: C, 57.40; H, 6.09; N, 7.42.

Data for **5l** (Ar = 4-$CH_3OC_6H_4$, R = H, R′ = $C_2H_5$): yield, 76%; white solid; mp 82.4–84.1°C; IR (KBr): $\nu$ 3428 (N—H), 1696 (C=O), 1404, 1205 (P=O), 1024 (P—O—C), 981(P—C) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.39 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 1.29 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 3.76 (s, 3H, $OCH_3$), 3.80 (s, 6H, $2CH_3O$), 3.84–4.12 (m, 4H, $2CH_2$), 5.52 (2d, $J$ = 14.8 Hz, 2H, $CH_2$), 5.50 (dd, $J$ = 9.6 Hz, $J$ = 20.4 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.88 (d, $J$ = 8.4 Hz, 2H, ArH), 6.95 (d, $J$ = 8.8 Hz, 2H, ArH), 7.16 (d, $J$ = 8.8 Hz, 2H, ArH), 7.41 (d, $J$ = 8.5 Hz, 2H, ArH), 7.42 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 19.30; ESI-MS: *m/z* 561.5 ($M^+$, 100), 256.5 (14). Anal. Calcd for $C_{26}H_{32}N_3O_9P$: C, 55.61; H, 5.74; N, 7.48. Found: C, 55.83; H, 5.91; N, 7.27.

Data for **5m** (Ar = 4-$ClC_6H_4$, R = H, R′ = $C_2H_5$): yield, 68%; yellow oil; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.16 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 1.31 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 3.86 (s, 6H, $2CH_3O$), 3.98–4.12 (m, 4H, $2CH_2$), 4.56 (2d, $J$ = 14.8 Hz, 2H, $CH_2$), 5.51 (dd, $J$ = 9.6 Hz, $J$ = 23.0 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.96 (d, $J$ = 8.8 Hz, 2H, ArH), 7.17 (d, $J$ = 8.4 Hz, 2H, ArH), 7.31–7.41(m, 4H, ArH), 7.43 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 19.86; ESI-MS: *m/z* 587 ($M^+$+Na-1, 37), 565.5 ($M^+$, 100). Anal. Calcd for $C_{25}H_{29}ClN_3O_8P$: C, 53.06; H 5.16; N, 7.42. Found: C, 52.81; H, 5.45; N, 7.28.

Data for **5n** (Ar = 4-$CH_3C_6H_4$, R = H, R′ = $CH_3$): yield, 72%; yellow oil; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 2.34 (s, 3H, $CH_3$), 3.52 (d, $J$ = 10.4 Hz, 3H, $CH_3$), 3.72 (d, $J$ = 10.8 Hz, 3H, $CH_3$), 3.85(s, 6H, $2CH_3O$), 4.57 (2d, $J$ = 14.0 Hz, 2H, $CH_2$), 5.61 (dd, $J$ = 9.6 Hz, $J$ = 22.4 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.95 (d, $J$ = 9.2 Hz, 2H, ArH), 7.15–7.18 (m, 4H, ArH), 7.30 (d, $J$ = 8.8 Hz, 2H, ArH), 7.51 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 22.03; ESI-MS: *m/z* 555 ($M^+$+K-1, 23), 539 ($M^+$+Na-1, 41), 517 ($M^+$, 100). Anal. Calcd for $C_{24}H_{28}N_3O_8P$: C, 55.71; H, 5.45; N, 8.12. Found: C, 55.63; H, 5.20; N, 8.30.

Data for **5o** (Ar = 4-$BrC_6H_4$, R = H, R′ = $C_2H_5$): yield, 64%; yellow oil; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.17 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 1.30 (t, $J$ = 6.8 Hz, 3H, $CH_3$), 3.82 (s, 6H, $2CH_3O$), 3.98–4.12 (m, 4H, $2CH_2$), 4.54 (2d, $J$ = 15.2 Hz, 2H, $CH_2$), 5.49 (dd, $J$ = 9.6 Hz, $J$ = 21.0 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.95 (d, $J$ = 9.2 Hz, 2H, ArH), 7.16 (d, $J$ = 7.2 Hz, 2H, ArH), 7.28–7.51 (m, 5H, ArH, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 18.79; EI-MS (70ev): *m/z* 611(12), 609 ($M^+$, 12.5), 275 (28), 139 ($M^+$, 100), 111 (73). Anal. Calcd for $C_{25}H_{29}BrN_3O_8P$: C, 49.19; H, 4.79; N, 6.88. Found: C, 49.40; H, 4.97; N, 7.05.

Data for **5p** (Ar = 4-$FC_6H_4$, R = H, R′ = $C_2H_5$): yield, 68%; yellow oil; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 1.15 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 1.29 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 3.84 (s, 6H, $2CH_3O$), 3.92–4.14 (m, 4H, $2CH_2$), 4.55 (2d, $J$ = 15.2 Hz, 2H, $CH_2$), 5.75 (dd, $J$ = 10.8 Hz, $J$ = 21.4 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.94 (d, $J$ = 8.8 Hz, 2H, ArH), 6.96–7.05 (m, 2H, ArH), 7.17 (d, $J$ = 8.8 Hz, 2H, ArH), 7.28–7.34 (m, 3H, ArH, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 19.27; ESI-MS: *m/z* 587 ($M^+$+K-1, 72), 549 ($M^+$, 100). Anal. Calcd for $C_{25}H_{29}FN_3O_8P$: C, 54.65; H, 5.32; N, 7.65. Found: C, 54.83; H, 5.11; N, 7.47.

Data for **5q** (Ar = Ph, R = H, R′ = *n*-$C_4H_9$): yield, 61%; white solid; mp 76.1–77.0°C; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ 0.83 (t, $J$ = 7.2 Hz, 3H, $CH_3$), 0.90 (t, $J$ = 7.6 Hz, 3H, $CH_3$), 1.20–1.46 (m, 6H, $CH_2$), 1.57–1.68 (m, 2H, $CH_2$), 3.65–4.06 (m, 4H, $2CH_2$), 3.88 (s, 6H, $2CH_3O$), 4.55 (2d, $J$ = 14.8 Hz, 2H, $CH_2$), 5.56 (dd, $J$ = 10.0 Hz, $J$ = 20.6 Hz, 1H, PCH), 5.78 (s, 1H, pyrimidine-H), 6.95 (d, $J$ = 8.8 Hz, 2H, ArH), 7.17 (d, $J$ = 8.8 Hz, 2H, ArH), 7.29–7.47 (m, 5H, ArH). 7.50 (s, 1H, NH); $^{31}$P NMR ($CDCl_3$, 162 MHz): $\delta$ 17.87; ESI-MS: *m/z* 624.7 ($M^+$+K-1, 12), 609.4 ($M^+$+Na-1, 27), 587.6 ($M^+$, 100), 582.9 (13). Anal. Calcd for $C_{29}H_{38}N_3O_8P$: C, 59.28; H, 6.52; N, 7.15. Found: C, 59.47; H, 6.73; N, 6.91.

### Herbicidal Activity (In Vitro)

The herbicidal evaluation of compounds **5** were carried out in the laboratory of biological activities test, State Key Laboratory of Elemento-organic Chemistry, Nankai University. The results are summarized in Table S2 (Supplemental Materials).

### Herbicidal Activity (In Vivo)

The herbicidal activities of some of compounds **5** were evaluated using a previously reported procedure.[19] See the Supplemental Materials for complete details.

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