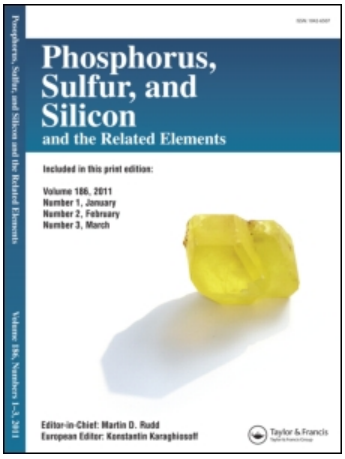


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# Synthesis and Herbicidal Activity of α-Amino Phosphonate Derivatives Containing Thiazole and Pyrazole Moieties

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# SYNTHESIS AND HERBICIDAL ACTIVITY OF α-AMINO PHOSPHONATE DERIVATIVES CONTAINING THIAZOLE AND PYRAZOLE MOIETIES

**Zhi-Hua Yu and De-Qing Shi**

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***A series of novel α-amino phosphonate derivatives containing the thiazole and pyrazole moieties 3 were synthesized by the Mannich-type reaction of substituted pyrazole-aldehyde 1, 2-amino-5-ethoxycarbonyl-4-methyl-thiazole 2, and dialkyl phosphites or triphenyl phosphite in the presence of a Lewis acid such as magnesium perchlorate as the catalyst under solvent-free conditions. Their structures were clearly confirmed by spectroscopy data (IR, $^{1}H$ NMR, $^{31}P$ NMR, MS) and elemental analysis. The results of a preliminary bioassay (in vitro) indicated that some of the title compounds 3 possessed moderate herbicidal activities against dicotyledonous plants (*Brassica campestris L*) or monocotyledonous plants (*Echinochloa crus-galli*) at the concerntration of 100 mg/L.***

***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; herbicidal activity; pyrazole; thiazole



## INTRODUCTION

Heterocyclic compounds containing nitrogen have played a major role in modern pesticide industry; it is reported that more than 85% of pesticides with high activity and low toxicity belong to nitrogen heterocyclic compounds. Pyrazole and thiazole are important two kinds of heterocyclic compounds with a wide spectrum of remarkable biological activities,[1–7] and many derivatives containing pyrazole and thiazole nucleus have been commercialized as herbicides, insecticides, and fungicides in plant protection[8–11] (see Figure 1). For example, pyraclofos and clothianidin were developed as insecticides, whereas pyrazolate and flurazole have been used as herbicides or their safeners, and furametpyr and ethaboxam as fungicides. Recently, α-amino phosphonic acids and their ester derivatives,

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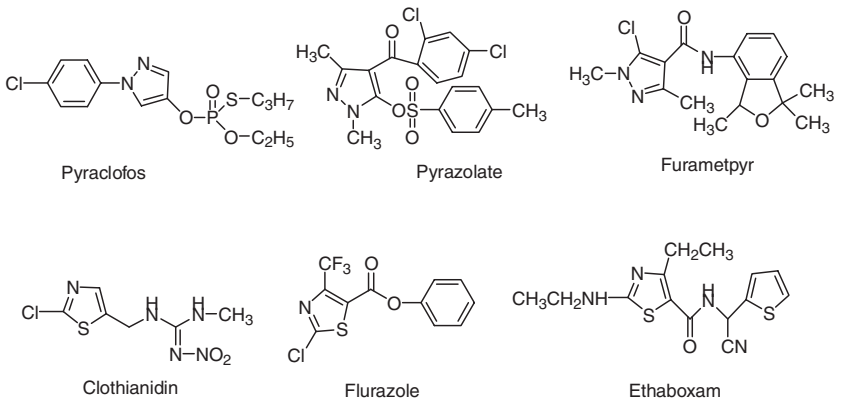
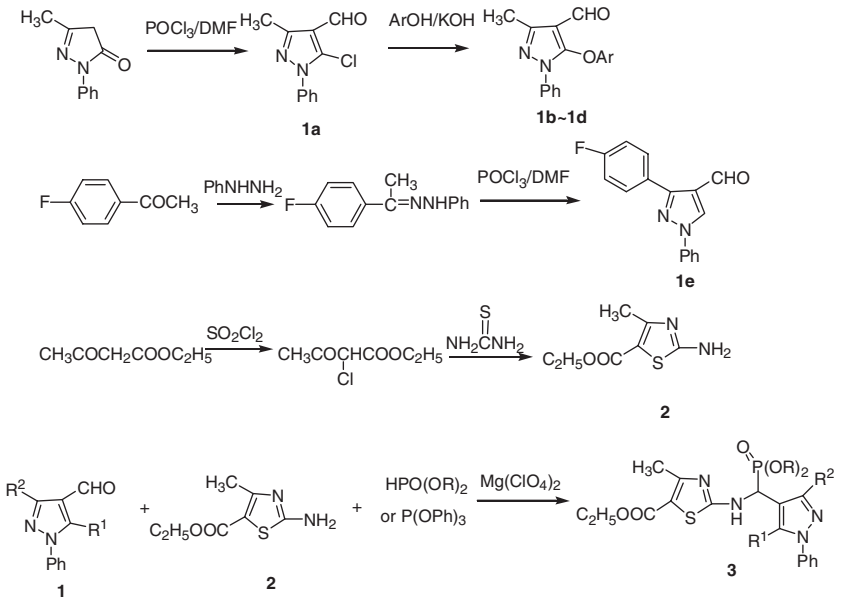



**Figure 1** Structures of some pesticides of pyrazole and thiazole derivatives.



as bioisosteres of natural amino acids, are receiving an increasing amount of attention in medicinal chemistry and pesticide science because some of their derivatives have been found to exhibit a wide range of biological activities such as enzyme inhibition, antibiotics, and haptens of catalytic antibodies, fungicides, herbicides, plant regulators, and plant virucides [for example, antiviral agent against tobacco mosaic virus (TMV)].[12–18] In order to find novel potent and selective herbicide lead compounds, we have synthesized a series of novel α-amino phosphonate derivatives containing pyrazole and thiazole hetercycles **3** via the Mannich-type reaction under solvent-free conditions. The target compounds **3** were evaluated for herbicidal activities. The synthetic route is listed in Scheme 1.




**Scheme 1** Synthetic route of the title compounds **3**.

## RESULTS AND DISCUSSION

### Synthesis and Structure Determination of Title Compounds 3

A series of novel $\alpha$-amino phosphonate derivatives containing thiazole and pyrazole moieties **3** were synthesized by the Mannich-type reactions of substituted pyrazole-aldehyde **1**, 2-amino-5-ethoxycarbonyl-4-methyl-thiazole **2**, and dialkyl phosphites or triphenyl phosphite in the presence of a Lewis acid such as magnesium perchlorate as the catalyst under solvent-free conditions. We found that the Lewis acid (magnesium perchlorate) can promote the reaction greatly, and without the use of magnesium perchlorate as the catalyst, the reaction was greatly slowed and the yields were very low (about 25%). The Mannich reaction might include two-step reactions: First, aldehydes are reacted with amines to form imines in the catalyst of magnesium perchlorate; second, phosphites are added to imines to generate $\alpha$-amino phosphonates. The structures of target compounds **3** were deduced from their spectral data (IR, $^1$H NMR, $^{31}$P NMR, EI-MS) and elemental analysis. In the $^1$H NMR spectra of **3**, the CH proton linking with the phosphonyl group displayed as a doublet due to coupling with P atom with the coupling constant of 23 Hz, while the NH proton appeared as a singlet with chemical shift $\delta$ 5.5–6.5. In some cases, the NH signal peaks disappeared in the $^1$H NMR spectrum. For $^{31}$P NMR spectra, the phosphorus atom of all compounds displayed as a singlet, giving chemical shifts $\delta$ 11.6–22.0. The IR spectra of compounds **3** showed normal stretching absorption bands, indicating the existence of the NH (3200–3300 cm$^{-1}$), C═O (∼1700 cm$^{-1}$), P═O (∼1225 cm$^{-1}$), P—O—C (∼1025 cm$^{-1}$) moieties. The EI-MS of compounds **3** revealed the existence of their molecular ion peaks, which were in accordance with the given structures of products **3**.



### Herbicidal Activities

The herbicidal activity values of the title compounds **3** against *Brassica campestris L* (rape) and *Echinochloa crus-galli* (barnyard grass) have been investigated at the dosages of 100 mg/L and 10 mg/L compared with the commercially available herbicide, bispyribac-sodium, according to the method described in the Experimental section. The results of a preliminary bioassay (*in vitro*) indicated that some of the title compounds **3** possessed moderate herbicidal activities against dicotyledonous plants (*Brassica campestris L*) or monocotyledonous plants (*Echinochloa crus-galli*) at the concerntration of 100 mg/L. For example, compound **3b** possessed 47.2% inhibitory activity against *Brassica campestris L*, and compound **3f** showed 42.1% inhibitory activity against *Echinochloa crus-galli*; however, compounds **3** displayed weak herbicidal activity at the concentration of 10 mg/L. Further biological activity evaluation such as antiviral activity against TMV, herbicidal activity (*in vivo*), the structure–activity relationships, and lead compound optimization are underway.

## CONCLUSION

In summary, we have synthesized a series of novel $\alpha$-amino phosphonate derivatives containing thiazole and pyrazole moieties **3** via the Mannich-type reaction of substituted pyrazole-aldehydes **1**, 2-amino-5-ethoxycarbonyl-4-methyl-thiazole **2**, and dialkyl phosphites or triphenyl phosphite in the presence of a Lewis acid such as magnesium perchlorate as the catalyst under solvent -free conditions. Their structures were clearly confirmed by spectroscopy data (IR, $^1$H NMR, $^{31}$P NMR, MS) and elemental analysis. The results of a preliminary bioassay (in vitro) indicated that some of the title compounds **3** possessed

moderate herbicidal activities against dicotyledonous plants (*Brassica campestris L*) or monocotyledonous plants (*Echinochloa crus-galli*) at the concerntration of 100 mg/L.

## EXPERIMENTAL

### Instruments

The melting points of the products were determined on an XT-4 binocular microscope (Beijing Tech Instrument Co., Beijing, China) and were uncorrected. The IR spectra were recorded on a Nicolet NEXUS470 spectrometer as KBr pellets with absorption given in $cm^{-1}$. $^1H$ 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. Mass spectra were measured on a Finnigan TraceMS 2000 spectrometer at 70 eV using EI method. Elemental analysis was taken on a Vario EL III elemental analysis instrument. Analytical TLC was performed on silica gel GF254. Column chromatographic purification was carried out using silica gel. Unless otherwise noted, all materials were commercially available and were used directly without further purification. All solvents were dried and redistilled before use. 2-Amino-5-ethoxycarbonyl-4-methyl-thiazole **2** was prepared by chloridization of ethyl acetylacetate with $SO_2Cl_2$, followed by the cyclization with thiourea according to the reported procedure.[19] Yield 79%, mp 172.6–173.2°C; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 1.33 (t, $J = 7.2$ Hz, 3H, $OCH_2\mathbf{CH_3}$), 2.52 (s, 3H, $CH_3$), 4.26 (q, $J = 7.2$ Hz, 2H, $OCH_2$), 5.79 (s, 2H, $NH_2$). Compound **1a** was prepared by the Vilsmeier–Haack reaction of pyrazolone,[20] and compounds **1b**∼**1d** were obtained from the reaction of compound **1a** and substituted phenols under basic conditions according to the reported synthetic protocols.[21,22] Compound **1e** was obtained as a white solid by the condensation of 4-fluoroacetophenone with phenyl hydrazine and subsequent reaction with Vilsmeier–Haak reagent according to the reported method.[23] Yield, 63%; mp 152.2–153.6°C.



### General Synthetic Procedures for *O,O′*-Dialkyl (Diphenyl)-*N*-(5-ethoxycarbonyl-4-methyl-thiazol-2-yl)-α-amino-(substitutedpyrazol-4-yl)methylphosphonates 3

Substituted pyrazole-aldehyde **1a**∼**1e** (3 mmol), 2-amino-5-ethoxycarbonyl-4-methyl-thiazole **2** (0.56 g, 3 mmol), and dialkyl phosphite or triphenyl phosphite (3 mmol) and $Mg(ClO_4)_2$ (0.033 g, 0.15 mmol) were added to a 50 mL flask. The mixture was stirred at 80–120°C for 2–6 h (monitored by TLC). Acetone (10 mL) was added, the solid was filtered off, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a mixture of petroleum ether and acetone (2:1) as an eluent to give **3** as white solids in 53–80% yields.

**Data for 3a.** (R = Et, $R^1$ = PhO, $R^2$ = $CH_3$): yield 61%, white solid, mp 157.6–158.3°C; IR (KBr): $\upsilon$ 3218 (N—H), 2984 (Ph—H), 1708 (C=O), 1560, 1495, 1427 (Ph), 1270, 1245 (P=O), 1036 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): $\delta$ 1.24 (t, $J = 7.2$ Hz, 3H, $CH_2\mathbf{CH_3}$), 1.28 (t, $J = 7.2$ Hz, 3H, $CH_2\mathbf{CH_3}$), 1.32 (t, $J = 7.2$ Hz, 3H, $CH_2\mathbf{CH_3}$), 2.45 (s, 3H, $CH_3$), 2.48 (s, 3H, $CH_3$), 3.96–4.02 (m, 1H, $OCH_2$), 4.09–4.14 (m, 3H, $OCH_2$), 4.25 (q, $J = 7.2$ Hz, 2H, $OCH_2$), 4.96 (d, $J = 22.8$ Hz, 1H, PCH), 5.90 (s, 1H, NH), 6.85 (d, $J = 7.8$ Hz, 2H, ArH), 6.98 (t, $J = 7.2$ Hz, 1H, ArH), 7.16–7.20 (m, 3H, ArH), 7.30 (d, $J = 7.8$ Hz, 2H, ArH), 7.56 (d, $J = 7.2$ Hz, 2H, ArH);$^{31}P$ $\{^1H\}$ NMR ($CDCl_3$, 243 MHz): $\delta$ 19.55. Anal. Calcd for $C_{28}H_{33}N_4O_6PS$: C 57.52, H 5.69, N 9.58; found C 57.60, H 5.35, N 9.81.

**Data for 3b.** (R = *n*-Bu, $R^1$ = Cl, $R^2$ = $CH_3$): yield 59%, white solid, mp 159.7–160.5°C; IR (KBr): $\upsilon$ 3257 (N—H), 1701 (C=O), 1552, 1491, 1418 (Ph), 1268, 1196 (P=O), 1020 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): $\delta$ 0.87 (t, $J$ = 7.8 Hz, 3H, $CH_2\mathbf{CH_3}$), 0.91 (t, $J$ = 7.8 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.28–1.33(m, 5H, $OCH_2\mathbf{CH_3}$, $CH_2$), 1.36–1.40 (m, 2H, $CH_2$), 1.52–1.55 (m, 2H, $CH_2$), 1.63–1.67 (m, 2H, $CH_2$), 2.45 (s, 3H, $CH_3$), 2.54 (s, 3H, $CH_3$), 3.91 (q, $J$ = 7.8 Hz, 1H, $OCH_2$), 4.05 (q, $J$ = 7.8 Hz, 1H, $OCH_2$), 4.12 (q, $J$ = 7.2 Hz, 2H, $OCH_2$), 4.23–4.27 (m, 2H, $OCH_2$), 5.10 (d, $J$ = 23.4 Hz, 1H, PCH), 6.51 (s, 1H, NH), 7.41 (t, $J$ = 7.2 Hz, 1H, ArH), 7.47 (t, $J$ = 7.8 Hz, 2H, ArH), 7.52 (d, $J$ = 7.8 Hz, 2H, ArH); $^{31}P$ $\{^1H\}$NMR ($CDCl_3$, 243 MHz): $\delta$ 20.03. Anal. Calcd for $C_{26}H_{36}ClN_4O_5PS$: C 53.56, H 6.22, N 9.61; found C 53.78, H 6.01, N 9.54.

**Data for 3c.** (R = Ph, $R^1$ = Cl, $R^2$ = $CH_3$): yield 78%, white solid, mp 136–137°C; IR (KBr): $\upsilon$ 3270 (N—H), 1697 (C=O), 1549, 1489, 1416 (Ph), 1270, 1187 (P=O), 1094, 1024 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): $\delta$ 1.33 (t, $J$ = 7.2Hz, 3H, $CH_2\mathbf{CH_3}$), 2.46 (s, 3H, $CH_3$), 2.55 (s, 3H, $CH_3$), 4.27 (q, $J$ = 7.2 Hz, 2H, $OCH_2$), 5.61 (d, $J$ = 21.6 Hz, 1H, PCH), 7.04 (d, $J$ = 7.8 Hz, 2H, ArH), 7.14–7.24 (m, 3H, ArH), 7.27–7.30 (m, 3H, ArH), 7.32 (t, $J$ = 7.8 Hz, 2H, ArH), 7.40–7.47 (m, 5H, ArH); $^{31}P$ $\{^1H\}$NMR ($CDCl_3$, 243 MHz): $\delta$ 21.45; EI-MS (70 eV): *m/z* 622 ($M^+$, 5), 389 (30), 353 (14), 245 (14.7), 205 (15.6), 171 (22), 140 (29), 94 (100), 77 (22), 45 (53.8). Anal. Calcd for $C_{30}H_{28}ClN_4O_5PS$: C 57.83, H 4.53, N 8.99; found C 58.11, H 4.27, N 9.13.

**Data for 3d.** (R = Ph, $R^1$ = H, $R^2$ = 4-$FC_6H_4$): yield 53%, white solid, mp 189.7–191.2°C; IR (KBr): $\upsilon$ 3265 (N—H), 1692 (C=O), 1560, 1482, 1450 (Ph), 1248 (P=O), 1028 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): $\delta$ 1.36 (t, $J$ = 7.2 Hz, 3 H, $OCH_2\mathbf{CH_3}$), 2.63 (s, 3H, $CH_3$), 4.31 (q, $J$ = 7.6 Hz, 2 H, $OCH_2$), 5.38 (d, $J$ = 23.4 Hz, 1H, PCH), 6.78 (d, $J$ = 7.6 Hz, 2H, ArH), 6.96–7.25 (m, 6H, ArH), 7.27–7.55 (m, 9H, ArH), 7.72 (d, $J$ = 7.6 Hz, 2H, ArH), 8.26 (s, 1H, pyrazol-H); $^{31}P$ $\{^1H\}$NMR ($CDCl_3$, 162 MHz): $\delta$ 22.38. Anal. Calcd for $C_{35}H_{30}FN_4O_5PS$: C 62.87, H 4.52, N 8.38; found C 62.57, H 4.42, N 8.24.

**Data for 3e.** (R = Et, $R^1$ = Cl, $R^2$ = $CH_3$): yield 68%, white solid, mp 145.4–146.7°C; IR (KBr): $\upsilon$ 3268 (N—H), 1691 (C=O), 1552, 1484, 1453 (Ph), 1235 (P=O), 1026 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): $\delta$ 1.23 (t, $J$ = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.33 (t, $J$ = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.35 (t, $J$ = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 2.44 (s, 3H, $CH_3$), 2.55 (s, 3H, $CH_3$), 4.00–4.02 (m, 1H, $O\mathbf{CH_2}CH_3$), 4.10–4.14 (m, 1H, $O\mathbf{CH_2}CH_3$), 4.20–4.27 (m, 4H, $2O\mathbf{CH_2}CH_3$), 5.06 (d, $J$ = 23.4 Hz, 1H, PCH), 5.71 (s, 1H, NH), 7.41(t, $J$ = 7.2 Hz, 1H, ArH), 7.48 (t, $J$ = 7.2 Hz, 2H, ArH), 7.52 (d, $J$ = 7.2 Hz, 2H, ArH); $^{31}P$ $\{^1H\}$ NMR ($CDCl_3$, 243 MHz): $\delta$ 21.75; EI-MS (70 eV): *m/z* 526 ($M^+$, 5), 389 (8), 221 (31), 186 (100), 185 (48), 158 (83), 141 (39), 113 (43), 87 (7.0), 71 (9.5). Anal. Calcd for $C_{22}H_{28}ClN_4O_5PS$: C 50.14, H 5.36, N 10.63; found C 50.35, H 5.24, N 10.40.

**Data for 3f.** (R = Et, $R^1$ = 4-$FC_6H_4O$, $R^2$ = $CH_3$): yield 70%, white solid, mp 163.8–164.7°C; IR (KBr): $\upsilon$ 3272 (N—H), 1698 (C=O), 1554, 1481, 1456 (Ph), 1228 (P=O), 1032 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): $\delta$ 1.25 (t, $J$ = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.29 (t, $J$ = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.33 (t, $J$ = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 2.45 (s, 3H, $CH_3$), 2.47 (s, 3H, $CH_3$), 4.00–4.03 (m, 1H, $O\mathbf{CH_2}CH_3$), 4.10–4.16 (m, 3H, $O\mathbf{CH_2}CH_3$), 4.25 (q, $J$ = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 4.97 (d, $J$ = 22.8 Hz, 1H, PCH), 6.78 (dd, $J$ = 4.2 Hz, $J$ = 9.0 Hz, 2H, ArH), 6.84 (t, $J$ = 7.8 Hz, 2H, ArH), 7.20 (t, $J$ = 7.2 Hz, 1H, ArH), 7.31 (t, $J$ = 7.8 Hz, 2H, ArH), 7.54 (d, $J$ = 7.8 Hz, 2H, ArH);$^{31}P$ $\{^1H\}$ NMR ($CDCl_3$, 243 MHz): $\delta$ 23.60; EI-MS (70 eV): *m/z* 602.5 ($M^+$, 2), 465 (47), 417 (6.0), 278.5 (16.0), 186 (40.1), 185 (100), 157 (6), 111 (11). Anal. Calcd for $C_{28}H_{32}FN_4O_6PS$: C 55.81, H 5.35, N 9.30; found C 55.53, H 5.48, N 9.15.

**Data for 3g.** (R = Ph, $R^1$ = 4-$FC_6H_4O$, $R^2$ = $CH_3$): yield 81%, white solid, mp 142.1–143.7°C; IR (KBr): υ 3288 (N—H), 1692 (C═O), 1550, 1485, 1464 (Ph), 1236 (P═O), 1025 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): δ 1.32 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 2.47 (s, 3H, $CH_3$), 2.49 (s, 3H, $CH_3$), 4.25 (q, *J* = 7.6 Hz, 2H, $O\mathbf{CH_2}CH_3$), 5.54 (d, *J* = 22.8 Hz, 1H, PCH), 6.74 (dd, *J* = 4.2 Hz, *J* = 9.0 Hz, 2H, ArH), 6.79 (t, *J* = 9.0 Hz, 2H, ArH), 7.02 (d, *J* = 8.4 Hz, 2H, ArH), 7.07 (d, *J* = 8.4 Hz, 2H, ArH), 7.13–7.21 (m, 3H, ArH), 7.25–7.31 (m, 6H, ArH), 7.46 (d, *J* = 7.8 Hz, 2H, ArH);$^{31}P$ $\{^1H\}$ NMR ($CDCl_3$, 243 MHz): δ 11.66; EI-MS (70 eV): *m/z* 698.4 ($M^+$, 2.5), 512 (18), 466 (40), 461 (13.1), 353 (12), 279 (31), 235 (17.2), 185 (100), 170 (11), 140 (7), 94 (3.6), 77 (3.1). Anal. Calcd for $C_{36}H_{32}FN_4O_6PS$: C 61.88, H 4.62, N 8.02; found C 62.11, H 4.58, N 7.89.

**Data for 3h.** (R = Et, $R^1$ = H, $R^2$ = 4-$FC_6H_4$): yield 67%, white solid, mp 128.2–129.8°C; IR (KBr): υ 3209 (N—H), 2986 (Ph), 1702 (C═O), 1557, 1554, 1494 (Ph), 1272, 1223 (P═O), 1088, 1053 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): δ 1.13 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.20 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.27 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 2.51 (s, 3H, $CH_3$), 3.91–3.95 (m, 1H, $O\mathbf{CH_2}CH_3$), 4.02–4.09 (m, 2H, $O\mathbf{CH_2}CH_3$), 4.15–4.22 (m, 3H, $O\mathbf{CH_2}CH_3$), 5.58 (d, *J* = 19.8 Hz, 1H, PCH), 7.18 (t, *J* = 7.8 Hz, 2H, ArH), 7.25 (d, *J* = 7.8 Hz, 1H, ArH), 7.37 (t, *J* = 7.8 Hz, 2H, ArH), 7.65 (t, *J* = 7.8 Hz, 2H, ArH), 7.81 (dd, *J* = 6.0 Hz, *J* = 8.1 Hz, 2H, ArH), 8.43 (s, 1H, pyrazol-H); $^{31}P$ $\{^1H\}$ NMR ($CDCl_3$, 243 MHz): δ 18.35; EI-MS (70 eV): *m/z* 572 ($M^+$, 3.6), 436 (11.7), 396.5 (57.1), 259 (100), 258 (61.8), 256 (47.3), 186.5 (15.2), 140 (26), 139 (37.7), 120 (15.7), 71 (7.9). Anal. Calcd for $C_{27}H_{30}FN_4O_5PS$: C 56.64, H 5.28, N 9.78; found C 56.70, H 5.47, N 10.03.

**Data for 3i.** (R = Ph, $R^1$ = 4-*t*-Bu-$C_6H_4O$, $R^2$ = $CH_3$): yield 58%, white solid, mp 121.4–123.0°C; IR (KBr): υ 3238 (N—H), 2975 (Ph), 1700 (C═O), 1545, 1492, 1436 (Ph), 1262, 1235 (P═O), 1090, 1025 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): δ 1.23 (s, 9H, $3CH_3$), 1.31 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 2.47 (s, 3H, $CH_3$), 2.48 (s, 3H, $CH_3$), 4.23 (q, *J* = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 5.61(d, *J* = 23.4 Hz, 1H, PCH), 6.74 (d, *J* = 8.4 Hz, 2H, ArH), 7.02 (d, *J* = 8.4 Hz, 2H, ArH), 7.07 (d, *J* = 8.4 Hz, 2H, ArH), 7.13–7.32 (m, 11H, ArH), 7.52 (d, *J* = 7.8 Hz, 2H, ArH); $^{31}P$ $\{^1H\}$ NMR ($CDCl_3$, 243 MHz): δ 21.47. Anal. Calcd for $C_{40}H_{41}N_4O_6PS$: C 65.20, H 5.61, N 7.60; found C 64.92, H 5.54, N 7.89.

**Data for 3j.** (R = Et, $R^1$ = 4-*t*-Bu-$C_6H_4O$, $R^2$ = $CH_3$): yield 61%, white solid, mp 197.1–198.3°C; IR (KBr): υ 3243 (N—H), 2966 (Ph), 1704 (C═O), 1547, 1494, 1433 (Ph), 1268, 1238 (P═O), 1094, 1020 (P—O—C) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 600 MHz): δ 1.21 (s, 9H, $3CH_3$), 1.23 (t, *J* = 7.8 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.27 (t, *J* = 7.8 Hz, 3H, $OCH_2\mathbf{CH_3}$), 1.30 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 2.47 (s, 3H, $CH_3$), 2.48 (s, 3H, $CH_3$), 3.96–4.05 (m, 1H, $O\mathbf{CH_2}CH_3$), 4.08–4.13 (m, 3H, $O\mathbf{CH_2}CH_3$), 4.21–4.23 (m, 2H, $O\mathbf{CH_2}CH_3$), 5.16 (d, *J* = 22.4 Hz, 1H, PCH), 5.74 (s, 1H, NH), 6.77 (d, *J* = 7.8 Hz, 2H, ArH), 7.20 (t, *J* = 8.4 Hz, 3H, ArH), 7.32 (t, *J* = 7.8 Hz, 2H, ArH), 7.59 (d, *J* = 8.4 Hz, 2H, ArH); $^{31}P$ $\{^1H\}$ NMR ($CDCl_3$, 243 MHz): δ 19.81. EI-MS (70 eV): *m/z* 641.6 ($M^+$, 68.7), 487 (3.3), 355 (20.1), 353 (48.2), 344 (10.2), 287 (12.3), 275 (12.6), 208 (6.5), 135 (14.5), 109 (7.0), 91 (100), 77 (38.8). Anal. Calcd for $C_{32}H_{41}N_4O_6PS$: C 59.99, H 6.45, N 8.74; found C 60. 18, H 6.30, N 8.96.

## Herbicidal Activity (*In Vitro*)

The herbicidal evaluation of compounds **3** was carried out in the laboratory of biological activities test, Nankai University, Tianjin, China, and the results are summarized in the Supplemental Materials and Table S1 (available online).

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