Synthesis and Herbicidal Activity of *O,O*-Dialkyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-substitutedbenzyl Phosphonates

Wu Tang and De-Qing Shi*

Key Laboratory of Pesticide and Chemical Biology of Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, Hubei, People's Republic of China
*E-mail: chshidq@mail.ccnu.edu.cn

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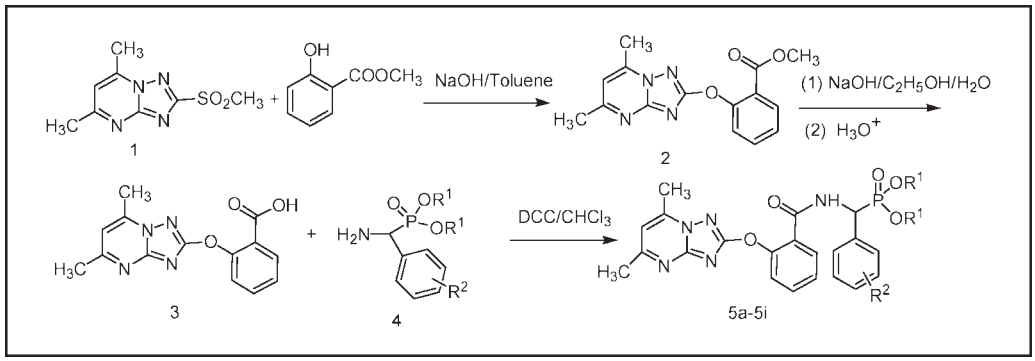

A series of novel 1,2,4-triazolo[1,5-a]pyrimidine derivatives containing an α-amino phosphonate moiety **5** were designed and synthesized by the multi-step reactions. Their structures were clearly confirmed by spectroscopic data (IR, ^{1}H NMR, ^{31}P NMR, MS) and elemental analysis, compound **5b** was further determined by X-ray diffraction crystallography. The results of preliminary bioassay indicated that some of the title compounds **5** possessed moderate herbicidal activities against dicotyledonous plants (*Brassica campestris L*) at the concentration of 100 mg/L. For example, compound **5i** possessed 92.0% inhibitory activity against *B. campestris L* and showed better activity than that of the commercialized herbicide Bispyribac-sodium; however, compounds **5** displayed weak herbicidal activity at the concentration of 10 mg/L.

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INTRODUCTION

α-Amino phosphonic acid and their ester derivatives, as bioisosteres of natural amino acids, are receiving an increasing 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 [1–7]. Recently, 1,2,4-Triazolopyrimidine derivatives exhibited wide biological activities and were used as herbicides in plant protection [8–12]. A lot of triazolopyrimidine sulfonamide herbicides, such as Cloransulam-methyl, Flumetsulam, Diclosulam, Penoxsulam and Metosulam (Fig. 1), were commercialized, these herbicides acted as acetolactate synthase (ALS) inhibitors, which have been identified as a very fruitful acting target for herbicides in the last decades [13]. To find novel potent and selective herbicide lead compounds, we have designed a series of novel 1,2,4-triazolo[1, 5-a]pyrimidine derivatives containing an α-amino phosphonate moiety **5**. The target compounds **5** were evaluated for herbicidal activities in this paper. The synthetic route is listed in Scheme 1, the molecular structure of compound **5b** is shown in Figure 2. Crystallographic data (excluding structure factors) for the structure have been deposited with the Cambridge Crystallographic Data Center as supplementary publication CCDC No. 734888 (available free of charge at http://www.ccdc.cam.ac.uk/conts/retrieving/html or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK).

RESULTS AND DISCUSSION

Synthesis and structure determination of title compounds 5. 5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-methylsulfone **1** were prepared using 3-amino-1,2,4-triazole-5-thiol and acetyl acetone as the starting materials, followed by S-alkylation and oxidation by H_2O_2 and $NaWO_4$ in good yield. 2-(5,7-Dimethyl-[1,2,4] triazolo[1,5-a]pyrimidin-2-yloxy)benzoic acid **3** was prepared by the reaction of **1** and methyl 2-hydroxybenzoate in the presence of sodium hydroxide in refluxing toluene, followed by the saponification in the presence

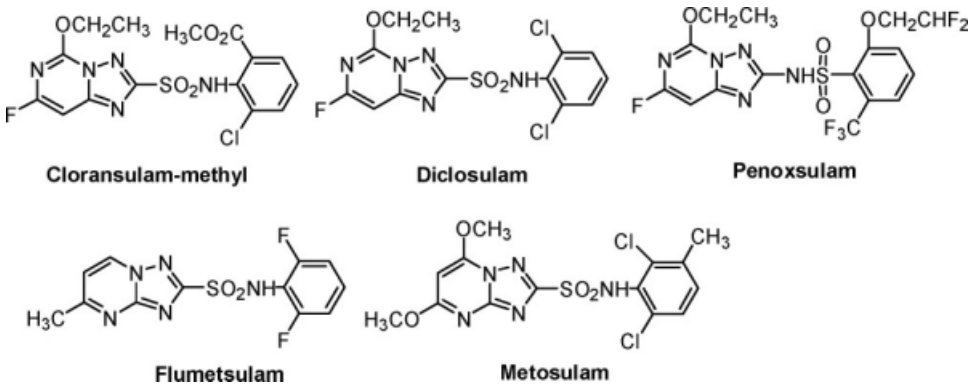


Figure 1. Structures of some commercial triazolopyrimidine-2-sulfonamide herbicides.

of aqueous sodium hydroxide. **3** reacted with α-amino-phosphonates **4** to generate the target compounds **5** in good yields in mild condition using dicyclohexylcarbodiimide (DCC) as the dehydration agent. The structures of target compounds **5** were characterized from their spectral data (IR, ^{1}H NMR, ^{31}P NMR, EI-MS) and elemental analysis, compound **5b** was further determined by single crystal X-ray diffraction analysis (see Fig. 2). In the ^{1}H NMR spectra of **5**, the CH proton linking with the phosphonyl group displayed doublet of doublet due to coupling with P atom and NH proton with the coupling constant of 21 and 9.0 Hz, respectively. While the NH and pyrimidine protons appeared as a singlet with chemical shift atδ 6.8 and 8.0, respectively. The IR spectra of compounds **5** showed normal stretching absorption bands indicating the existence of the NH (∼3240 cm^{-1}), C═O (∼1660 cm^{-1}), P═O (∼1225 cm^{-1}), P─O─C (∼1025 cm^{-1}) moieties. The ESI-MS of compounds **5** revealed the existence of their molecular ion peaks, which were in accordance with the given structures of products **5**.

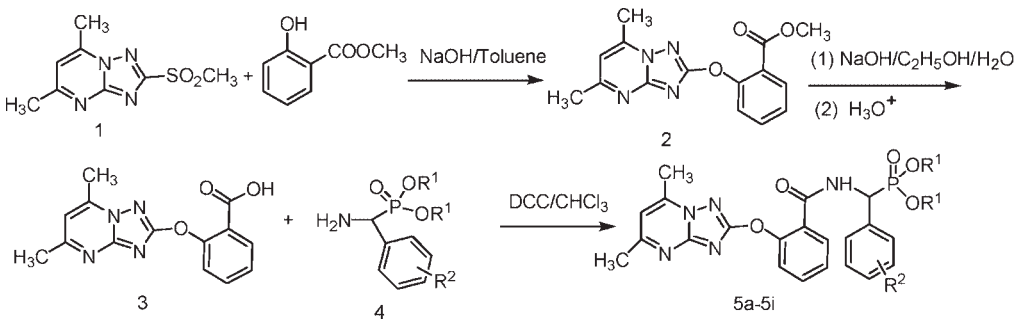
Herbicidal activities. The herbicidal activity values of the title compounds **5** against *Brassica campestris L* (rape) and *Echinochloa crus-galli* (barnyard grass) has been investigated at the dosages of 100 and 10 mg/L compared with the commercially available herbicide, Bispyribac-sodium according to the method described in the experimental section. The results of preliminary bioassy indicated that some of the title compounds **5** possessed moderate herbicidal activities against dicotyledonous plants (*B. campestris L*) at the concentration of 100 mg/L. For example, compound **5i** possessed 92.0% inhibitory activity against *B. campestris L* and showed better herbicidal activity than that of the commercialized herbicide Bispyribac-sodium. Futhermore, most of compounds **5** showed stronger inhibitory activity against dicotyledonous plants (*B. campestris L*) than that of monocotyledonous plants (*Radix E. crus-galli*). However, compounds **5** displayed weak herbicidal activity at the concentration of 10 mg/L. Further herbicidal evaluation (*in vivo*) and the structure–activity relationships are under investigation.

Conclusion. In summary, we have designed and synthesized one series of novel 1,2,4-triazolo[1,5-a]pyrimidine derivatives containing an α-amino phosphonate moiety **5**. The results of preliminary bioassy indicated that some of the title compounds **5** possessed moderate herbicidal activities against dicotyledonous plants (*B. campestris L*) at the concerntration of 100 mg/L.

EXPERIMENTAL

The melting points of the products were determined on an XT-4 binocular microscope (Beijing Tech Instrument, Beijing,

Scheme 1. Synthesis of the title compounds **5**.



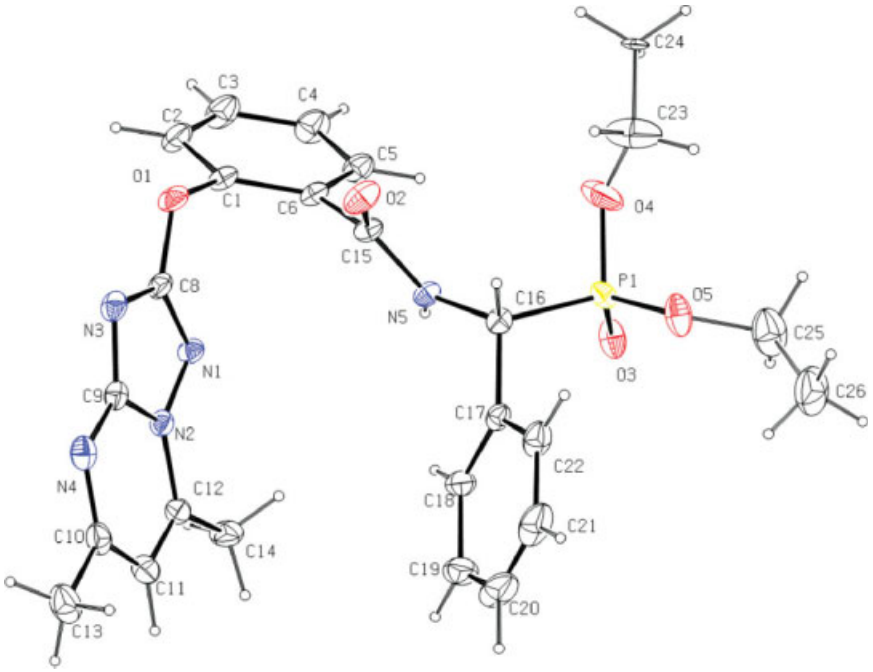


Figure 2. Molecular structure of compound **5b**. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

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-PLUS400 (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 was measured on an Applied Biosystems API 2000 LC/MS/MS (ESI-MS) spectrometer. Elemental analysis was taken on a Elementar Vario EL III elemental analysis instrument. X-ray diffraction was carried out on a Bruker Smart 1000 CCD diffractometer (Germany). Analytical thin layer chromatography (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. 5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-methylsulfone **1** were prepared by the annulation reaction of 3-amino-1,2,4-triazole-5-thiol with acetyl acetone, followed by S-alkylation and oxidation by H_2O_2 and $NaWO_4$ according to the reported procedure [14], yield 82%, m.p. 187–188°C. Dialkyl α-amino phosphonates **4** were prepared from aromatic aldehyde, ammonium hydroxide and dialkyl phosphites in moderate yields according to the reported synthetic protocols [15,16].

Synthesis of methyl 2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoate 2. Methyl 2-hydroxy-benzoate (0.91 g, 6 mmol), sodium hydroxide (0.24 g, 6 mmol) and anhydrous toluene (60 mL) were stirred under reflux for 3h, while the water was removed away during the reaction time. 5,7-Dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-methylsulfone **1** (2.26 g, 10 mmol) was added and stirred under reflux for 10 h till the reaction completed (monitored by TLC). The solid was filtered off, and the solvent was removed under a reduced pressure, the residue was purified by column chromatography on silica gel using petroleum ether/acetone (1:1 *v*/*v*) as the eluent, giving a white solid, yield: 68%, mp: 141–142°C. Anal. Cacld for $C_{15}H_{14}N_3O_3$: C, 60.40; H, 4.73; N, 18.78. Found: C, 60.17; H, 4.91; N, 18.55.

Synthesis of 2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoic acid 3. Methyl 2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-loxy)benzoate **2** (1.19 g, 4 mmol), sodium hydroxide (0.32 g, 8 mmol), water (10 mL) and ethanol (10 mL) were stirred at 80–90°C for 1–2 h. The solution was acidified by dilute hydrochloride, The crude product was collected by filtration, washed by ethyl ether, the product was obtained as a yellow solid, yield: 80%, mp: 103–104°C. Anal. Cacld for $C_{14}H_{12}N_4O_3$: C, 59.15; H, 4.25; N, 19.71. Found: C, 59.30; H, 4.19; N, 19.47.

General synthetic procedure for *O,O*-dialkyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-substitutedbenzyl phosphonate 5. 2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoic acid **3** (0.284 g, 1.0 mmol), *O,O′*-diethyl α-amino (substituted phenyl) methylphosphonate **4** (1.0 mmol) and anhydrous chloroform (5 mL) were added to a 50 mL three-necked flask at 273 K, DCC (0.225 g, 1.1 mmol) in anhydrous chloroform (5 mL) was added dropwise slowly. The mixture was allowed to be stirred at room temperature overnight. After the solvent was removed under a reduced pressure, the residue was purified by column chromatography on silica gel using petroleum ether/acetone (1:2 *v*/*v*) as the eluent, giving the target compounds as a light yellow solid or liquid.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(*p*-tolyl) methyl phosphonate (5a).** Yellow oil, yield 68%; IR (KBr): υ 3230 (N—H), 2985 (Ph-H), 1652 (C=O), 1562, 1465, 1426 (Ph), 1248 (P=O), 1025 (P—O—C) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 1.12 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.21 (t, J = 7.2

Hz, 3H, $CH_2\mathbf{CH_3}$), 2.26 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.83–3.85 (m, 1H, CH_2), 3.95–3.97 (m, 1H, CH_2), 4.00–4.04 (m, 2H, CH_2), 5.67 (dd, J = 9.6 Hz, J = 20.1 Hz, 1H, PCH), 6.80 (s, 1H, pyrimidine-H), 7.01 (d, J = 7.8 Hz, 2H, ArH), 7.28–7.37 (m, 4H, ArH), 7.49 (t, J = 7.8 Hz, 1H, ArH), 7.99 (d, J = 7.8 Hz, 1H, ArH), 8.09 (s, 1H, NH); ESI-MS: *m/z* 562 (M^+ + K-1, 5%), 546 (M^+ + Na-1, 23%), 523.7 (M^+, 100%), 267 (10%). Anal. Cacld for $C_{26}H_{30}N_5O_5P$: C, 59.65; H, 5.78; N, 13.38. Found: C, 59.47; H, 5.51; N, 13.24.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-phenylmethyl phosphonate (5b).** Yellow solid, m.p. 136–137°C, yield 69%; IR (KBr): υ 3238 (N—H), 2982 (Ph-H), 1658 (C=O), 1558, 1463, 1420 (Ph), 1252 (P=O), 1026 (P—O—C) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.12 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.21 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 2.65 (s, 3H, CH_3), 2.69 (s, 3H, CH_3), 3.81–3.87 (m, 1H, CH_2), 3.93–4.05 (m, 3H, $2CH_2$), 5.71 (dd, J = 9.6 Hz, J = 20.6 Hz, 1H, PCH), 6.81 (s, 1H, pyrimidine-H), 7.18–7.25 (m, 3H, ArH), 7.27–7.43 (m, 4H, ArH), 7.50 (t, J = 8.0 Hz, 1H, ArH), 8.01 (d, J = 7.6 Hz, 1H, ArH), 8.15 (dd, J = 4.0 Hz, J = 9.0 Hz, 1H, NH); ^{31}P NMR ($CDCl_3$, 162 MHz): δ 19.58; ESI-MS: *m/z* 547 (M^+ + K-1, 5%), 531.5 (M^+ + Na-1, 14%), 509.1 (M^+, 100%), 266.6 (5%). Anal. Cacld for $C_{25}H_{28}N_5O_5P$: C, 58.93; H, 5.54; N, 13.75. Found: C, 59.12; H, 5.68; N, 13.51.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(4-chlorophenyl) methyl phosphonate (5c).** yellow solid, m.p. 121–123°C, yield 75%; IR (KBr): υ 3228 (N—H), 2987 (Ph-H), 1663 (C=O), 1561, 1468, 1418 (Ph), 1246 (P=O), 1019 (P—O=C) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.15 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.23 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 2.66 (s, 6H, CH_3), 3.88–4.07 (m, 4H, $2CH_2$), 5.68 (dd, J = 8.0 Hz, J = 20.8 Hz, 1H, PCH), 6.83 (s, 1H, pyrimidine-H), 7.15 (d, J = 8.0 Hz, 2H, ArH), 7.34–7.38 (m, 4H, ArH), 7.52 (t, J = 6.8 Hz, 1H, ArH), 8.00 (d, J = 8.0 Hz, 1H, ArH), 8.07 (s, 1H, NH); ESI-MS: *m/z* 565.8 (M^+ + Na-1, 17%), 543.8 (M^+, 100%), 266.9 (12%). Anal. Cacld for $C_{25}H_{27}ClN_5O_5P$: C, 55.20; H, 5.00; N, 12.88. Found: C, 55.03; H, 4.87; N, 12.95.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(4-methoxyphenyl) methyl phosphonate (5d).** Yellow solid, m.p. 89–90°C, yield 67%; IR (KBr): υ 3236 (N—H), 2992 (Ph-H), 1661 (C=O), 1564, 1466, 1425 (Ph), 1242 (P=O), 1025 (P—O—C) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.24 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 2.67 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 3.86–4.05 (m, 4H, $2CH_2$), 5.68 (dd, J = 9.4 Hz, J = 20.8 Hz, 1H, PCH), 6.83 (s, 1H, pyrimidine-H), 7.01 (d, J = 8.8 Hz, 2H, ArH), 7.27–7.37 (m, 4H, ArH), 7.51 (d, J = 7.6 Hz, 1H, ArH), 7.98 (d, J = 9.6 Hz, 1H, ArH), 8.10 (s, 1H, NH). Anal. Cacld for $C_{26}H_{30}N_5O_6P$: C, 57.88; H, 5.60; N, 12.98. Found: C, 58.05; H, 5.85; N, 12.81.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(2,4-dichlorophenyl) methyl phosphonate (5e).** Yellow solid, m.p. 96–97°C, yield 85%; IR (KBr): υ 3232 (N—H), 2996 (Ph-H), 1668 (C=O), 1560, 1461, 1432 (Ph), 1246 (P=O), 1028 (P—O—C) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.13 (t, J = 8.0 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.29 (t, J = 8.0 Hz, 3H, $CH_2\mathbf{CH_3}$), 2.66 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 3.86–3.99 (m, 2H, CH_2), 4.11–4.15 (m, 2H, CH_2), 6.18 (dd, J = 8.8 Hz, J = 21.0 Hz, 1H, PCH), 6.83 (s, 1H, pyrimidine-H), 7.08 (d, J = 8.0 Hz, 1H, ArH), 7.29–7.39 (m, 3H, ArH), 7.46–7.53 (m, 2H, ArH), 8.02 (d, J = 8.0 Hz, 1H, ArH), 8.22 (s, 1H, NH). Anal. Cacld for $C_{25}H_{26}Cl_2N_5O_5P$: C, 51.91; H, 4.53; N, 12.11. Found: C, 52.13; H, 4.27; N, 12.04.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(4-bromophenyl) methyl phosphonate (5f).** Yellow solid, m.p. 119–120°C, yield 88%; IR (KBr): υ 3235 (N—H), 2992 (Ph-H), 1672 (C=O), 1556, 1459, 1430 (Ph), 1245 (P=O), 1026 (P—O—C) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.15 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.24 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 2.66 (s, 6H, $2CH_3$), 3.90–4.06 (m, 4H, $2CH_2$), 5.65 (dd, J = 9.2 Hz, J = 20.6 Hz, 1H, PCH), 6.83 (s, 1H, pyrimidine-H), 7.29–7.38 (m, 4H, ArH), 7.51 (t, J = 7.6 Hz, 1H, ArH), 7.98 (d, J = 8.0 Hz, 1H, ArH), 8.10 (s, 1H, NH). Anal. Cacld for $C_{25}H_{27}BrN_5O_5P$: C, 51.03; H, 4.63; N, 11.90. Found: C, 51.34; H, 4.90; N, 11.73.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(2-chlorophenyl) methyl phosphonate (5g).** white solid, m.p. 144–145°C, yield 68%; IR (KBr): υ 3417, 3236 (N—H), 2990 (Ph-H), 1665(C=O), 1626, 1557, 1479 (Ph), 1233 (P=O), 1025 (P—O—C) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.10 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.26 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 2.65 (s, 3H, CH_3), 270 (s, 3H, CH_3), 3.80–3.82 (m, 1H, CH_2), 3.92–3.95 (m, 1H, CH_2), 4.11–4.14 (m, 2H, CH_2), 6.26 (dd, J =9.0 Hz, J = 20.7 Hz, 1H, PCH), 6.81 (s, 1H, pyrimidine-H), 7.10–7.14 (m, 2H, ArH), 7.32 (d, J = 10.2 Hz, 2H, ArH), 7.37 (d, J = 7.8 Hz, 1H, ArH), 7.49 (d, J = 7.8 Hz, 1H, ArH), 7.53 (d, J = 7.2 Hz, 1H, ArH), 8.02 (d, J = 8.4 Hz, 1H, ArH), 8.27 (s, 1H, NH); ^{31}P NMR ($CDCl_3$, 243 MHz): δ 18.89; ESI-MS: *m/z* 581.6 (M^+ + K-1, 3%), 563.8 (M^+ + Na-1, 7%), 543.4 (M^+, 100%), 266.8 (2%). Anal. Cacld for $C_{25}H_{27}ClN_5O_5P$: C, 55.20; H, 5.00; N, 12.88. Found: C, 54.97; H, 4.73; N, 12.60.

***O,O*-Diethyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(4-fluorophenyl) methyl phosphonate (5h).** Yellow solid, m.p. 147–148°C, yield 73%; IR (KBr): υ 3241 (N—H), 2995 (Ph-H), 1662 (C=O), 1622, 1554, 1485 (Ph), 1230 (P=O), 1021 (P—O—C) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.14 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.22 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 2.65 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.87–3.90 (m, 1H, CH_2), 3.96–3.99 (m, 1H, CH_2), 4.00–4.06 (m, 2H, CH_2), 5.68 (dd, J = 9.0 Hz, J = 20.4 Hz, 1H, PCH), 6.81 (s, 1H, pyrimidine-H), 6.88 (t, J = 9.0 Hz, 2H, ArH), 7.33–7.42 (m, 4H, ArH), 7.51 (t, J = 7.2 Hz, 1H, ArH), 8.00 (d, J = 8.4 Hz, 1H, ArH), 8.08 (s, 1H, NH). Anal. Cacld for $C_{25}H_{27}FN_5O_5P$: C, 56.92; H, 5.16; N, 13.28. Found: C, 57.12; H, 5.27; N, 13.65.

***O,O*-Dibutyl *N*-[2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yloxy)benzoxyl]-1-amino-1-(phenyl) methyl phosphonate (5i).** Yellow oil, yield 52%; IR (KBr): υ 3236 (N—H), 2998 (Ph-H), 1654 (C=O), 1618, 1550, 1482 (Ph), 1225 (P=O), 1025 (P—O—C) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ: 0.79 (t, J = 7.8 Hz, 3H, $CH_2\mathbf{CH_3}$), 0.83 (t, J = 7.2 Hz, 3H, $CH_2\mathbf{CH_3}$), 1.20–1.53 (m, 8H, $2CH_2CH_2$), 2.68 (s, 3H, CH_3), 2.70 (s, 3H, CH_3), 3.72–3.75 (m, 1H, CH_2), 3.87–3.90 (m, 1H, CH_2), 3.93–3.99 (m, 2H, CH_2), 5.72 (dd, J = 9.0 Hz, J = 20.4 Hz, 1H, PCH), 6.80 (s, 1H, pyrimidine-H), 7.17–7.22 (m, 3H, ArH), 7.33 (t, J = 7.2 Hz, 1H, ArH), 7.35 (d, J = 8.0 Hz, 1H, ArH), 7.42 (d, J = 7.2 Hz, 2H, ArH), 7.49 (t, J = 7.2

Table 1

The herbicidal activities of compounds **5a–5i** (*in vitro*, relative inhibitory rate %, concentration, mg/L).

	Brassica campestris root test		*Echinochloa crusgalli* cup test	
Compounds	100	10	100	10
5a	42.9	15.4	25.9	13.1
5b	52.1	26.6	30.5	21.0
5c	39.7	0	29.5	0
5d	29.0	19.2	19.5	11.7
5e	45.3	14.0	15.1	9.0
5f	33.6	4.7	14.6	0
5g	34.1	0	11.6	6.2
5h	7.0	0	20.0	6.2
5i	92.0	31.3	23.4	7.6
Bispyribac-sodium	69.8	65.6	72.4	46.9

Hz, 1H, ArH), 8.00 (d, J = 7.2 Hz, 1H, ArH), 8.15 (s, 1H, NH); ^{31}P NMR ($CDCl_3$, 243 MHz): δ 19.61. Anal. Cacld for $C_{29}H_{36}N_5O_5P$: C, 61.58; H, 6.42; N, 12.38. Found: C, 61.84; H, 6.35; N, 12.07.

Herbicidal activity (*in vitro*). The herbicidal evaluation of compounds **5** were carried out in the laboratory of biological activities test, Nankai University, China. Compounds **5** were determined with *B. campestris L.* and *Radix E. crus-galli* as samples of annual dicotyledonous and monocotyledonous plants, respectively, using a previously reported procedure [17]. For all of the bioassay tests, each treatment was repeated two times.

Treatment. The emulsions of purified compounds were prepared by dissolving them in 100 μL of *N*,*N*-dimethylformamide with the addition of 2 μL of Tween 20. The mixture of the same amount of water, *N*,*N*-dimethylformamide, and Tween 20 was used as control. The commercially available herbicide, Bispyribac-sodium was used as a compared sample to evaluate the herbicidal activity of the target compounds **5**.

Inhibition of the root-growth of rape (*B. campestris* L.). Rape seeds were soaked in distilled water for 4 h before being placed on a filter paper in a 6 cm Petri plate, to which 2 mL of inhibitor solution had been added in advance. Usually, 10 seeds were used on each plate. The plate was placed in a dark room and allowed to germinate for 72 h at 28 ± 1°C. The lengths of 10 rape roots selected from each plate were measured, and the means were calculated. The percentage inhibition was used to describe the control efficiency of the compounds. The herbicidal activity was listed in Table 1.

Inhibition of the seedling growth of barnyard grass [*Radix Echinochloa crus-galli*]. Ten *Radix E. crus-galli* seeds were placed into a 50 mL cup covered with a layer of glass beads and a piece of filter paper at the bottom, to which 6 mL of inhibitor solution had been added in advance. The cup was placed in a bright room, and the seeds were allowed to germinate for 72 h at 28 ± 1°C. The heights of the above-ground parts of the seedlings in each cup were measured, and the mean values were calculated. The percentage inhibition was used to describe the control efficiency of the compounds. The herbicidal activity is also listed in Table 1.

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