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Synthesis and Herbicidal Activity of 2-(Substituted phenoxyacetoxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one

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ABSTRACT: A series of 2-(substituted phenoxyacetoxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-ones **IIa−s** were designed and synthesized on the basis of the previous work for the modification of alkylphosphonates **I**, and their structures were confirmed by ^{1}H NMR, ^{31}P NMR, ^{13}C NMR, IR, MS, and elemental analysis. Their herbicidal activities against seven species of weeds were evaluated in a greenhouse. A part of the title compounds such as **IIa−g**, **IIk**, **IIo**, and **IIr** exhibited significant postemergence herbicidal activity against *Abutilon theophrasti*, *Brassica juncea*, *Amaranthus retroflexus*, and *Eclipta prostrate* at a dosage of 150 g ai/ha. Structure−activity relationship analyses indicated that the introduction of a phosphorus-containing heterocyclic ring had a favorable effect on herbicidal activity, and their herbicidal activity could be further increased by a reasonable combination of X, Y, and R in parent structure **II**. It could be found that the title compounds **IIa** 2-[(2,4-dichlorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one and **IIr** 2-[(4-chloro-2-methyl-phenoxy)-acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one possess high activity and a broad spectrum against all of the test broadleaf weeds with 70−100% inhibition effect at a dosage of 75 g ai/ha, and the title compounds **IIa** and **IIr** are safe for corn and wheat at a dosage of 150 g ai/ha. Furthermore, the title compound **IIa** possesses low rat toxicity. These results suggest that the title compounds **IIa** and **IIr** could be potential and selective postemergence herbicides for further development.

KEYWORDS: *synthesis, herbicidal activity, cyclophosphonate, phosphonate*

INTRODUCTION

Reduced crop yield can be a major consequence of weeds in agriculture due mainly to the strong competition they pose for crops in obtaining light, water, nutrients, and physical space.[1−3] As the main weed control tool, herbicides play a very important role in modern agriculture. Unfortunately, an inevitable problem associated with the use of herbicides is the occurrence of herbicide-resistant weeds. Therefore, it is necessary to develop efficient herbicides with novel structures and modes of action to overcome the resistance of weeds.

As an important class of pesticides, organic phosphorus compounds display a wide range of biological activities and have attracted considerable attention as the main source of lead compounds in agrochemicals.[4−7] A detailed study of acylphosphinates and acylphosphonates revealed that these analogues of pyruvate could be designed as mechanism-based inhibitors of pyruvate dehydrogenase complex (PDHc).[8] However, they are not active enough for full development as herbicides.[8−10] These findings prompted us to perform our own study for novel PDHc inhibitors as potential herbicides.

In our previous work,[11−17] a series of alkylphosphonate derivatives with general structure **I** (Scheme 1) were designed and synthesized, and the ensuing bioassay results exhibited higher herbicidal activities in some cases. SAR analyses indicated that chlorine or fluorine atoms as X and Y at the 2- and 4-positions on a phenoxy ring and a smaller group (MeO) attached to the phosphorus as R^1 and R^2 in general structure **I** were beneficial to herbicidal activity. Among these alkylphosphonates **I**, the compound **I-1** (HW02) as a competitive inhibitor of PDHc was found to be the most effective compound against broadleaf weeds. The compound **I-1** as a novel postemergence herbicide was further developed and has got temporary registration from ICAMA in China.[18,19]

On the other hand, a variety of the reports regarding synthetic studies of cyclophosphonate analogues have been presented because phosphorus-containing heterocyclic moiety can increase bioactivity[20] and stability[21] through replacement of simple phosphonate. This encouraged us to design a series of cyclophosphonates (Scheme 1) on the basis of the alkylphosphonates **I** and further study the relationship of structure−herbicidal activity. It is very interesting to examine the effect on herbicidal activity by introduction of a phosphorus-containing heterocyclic ring. Here, we report the synthesis of a series of 2-(substituted phenoxyacetoxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-ones **IIa−s** and evaluation for their herbicidal activity.

MATERIALS AND METHODS

Synthesis Procedures. Chemicals and reagents were obtained from commercial sources, and all of the solvents were dried and purified by standard tecniques prior to use. Column chromatography was carried out with Merck silica gel (200−300 mesh). Melting points (mp) were measured on a Buchi B-545 melting point apparatus and were uncorrected. IR spectra were recorded as KBr pellets on a Perkin-Elmer Fourier transform infrared spectrophotometer. ^{1}H NMR were recorded on Varian XL-400 spectrometer at 400 MHz or Varian XL-600 spectrometer at 600 MHz using tetramethylsilane as internal standard (solvent $CDCl_3$). ^{13}C and ^{31}P NMR were recorded on a

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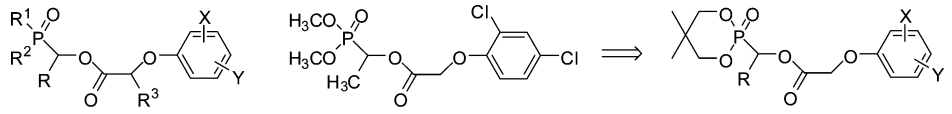
Scheme 1. Chemical Modification of Lead Structure I



I I-1 (HW02) IIa-s

Varian XL-400 spectrometer at 400 MHz (solvent $CDCl_3$). Chemical shifts (δ) are given in ppm, coupling constants (J) are in Hz, and multiplicities are implicated by s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). MS spectra were analyzed on a Finnigen TRACE spectrometer and API2000LC/MS. Elemental analyses were performed by a Vario EL III elemental analyzer.

Phosphorus trichloride, triethyl amine, and thionyl chloride were distilled before the reaction.

General Procedure for the Synthesis of Compounds ***2a−g***. Compounds **2a−g** could be prepared by the reaction of the intermediate **1** (10 mmol) and several kinds of aldehydes (10 mmol) in chloroform (10 mL) using triethylamine (5 mmol) as a catalyst in yield of 60−90%. Also, the intermediate **1** was synthesized from neopentyl glycol, which was used directly as obtained commercially.

All of the intermediates **2a−g** were synthesized according to the methods described in the literature,[22−24] in which the compounds **2b**,[23,24] **2c**,[22] **2d**,[22] **2e**,[22] and **2g**[22] have been reported.

Data for ***2a*** *(R = Me).* Yield, 65%; mp, 94−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.00 (s, 3H), 1.16 (s, 3H), 1.59−1.61 (m, 3H), 3.92−4.15 (m, 4H), 5.50−5.52 (m, 1H). ^{31}P NMR (160 MHz, $CDCl_3$): δ 19.39. Anal. Calcd for $C_7H_{15}O_4P$: C, 43.30; H, 7.79. Found: C, 43.41; H, 7.99.

Data for ***2f*** *(R = n-Bu).* Yield, 68%; mp, 120−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91−0.86 (m, 3H), 1.02 (s, 3H), 1.15 (s, 3H), 1.35−1.31 (m, 4H), 1.94−1.93 (m, 2H), 4.16−3.91 (m, 4H), 5.58−5.59 (m, 1H). ^{31}P NMR (160 MHz, $CDCl_3$) δ 21.09. Anal. Calcd for $C_{10}H_{21}O_4P$: C, 50.84; H, 8.96. Found: C, 51.20; H, 9.23.

General Procedure for the Synthesis of Compounds ***3*** *and* ***4***. Compound **3** could be prepared from substituted phenol and chloroacetic acid according to the methods given in ref 25. A mixture containing substituted phenoxyacetyl acid **3** (4.0 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 **4** was obtained with a yield of 85−90%.

General Procedure for the Synthesis of the Title Compounds ***IIa−s***. A solution of substituted phenoxyacetyl chlorides **4** (3.3 mmol) in trichloromethane (15 mL) was added to a stirred mixture of α-hydroxyalkylphosphonates **2** (3 mmol) and triethylamine (3.3 mmol) in chloroform (20 mL) at 0−5 °C. The resultant mixture was stirred for 3−5 h at room temperature and then for 1−2 h at 40 °C. The chloroform 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 (2:1, v/v) to give the corresponding pure title compounds **IIa−s**. Their structures were confirmed by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR, MS, and elemental analysis. The physicochemical properties and spectroscopic data for all of the title compounds **IIa−s** are as follows.

2-[(2,4-Dichlorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one ***(IIa)***. White solid; yield, 64%; mp, 62−64 °C. IR (KBr, cm^{-1}): ν 3091, 2967, 1764, 1483, 1237, 1197, 1053, 1000, 844, 805. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−6.78 (m, 3H, $-C_6H_3$), 5.50 (m, 1H, PCHO), 4.76 (d, J = 4.0 Hz, 2H, $-OCH_2CO-$), 4.15−3.92 (m, 4H, 2 × (OCH_2)), 1.61−1.59 (m, 3H), 1.16 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.07, 153.97, 129.95, 127.82, 126.03, 123.75, 114.03, 65.50, 65.35 (d, $^1J_{C-P}$ = 165.30 Hz), 32.09, 21.07, 20.18, 14.37. ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.35. EI-MS m/z (%): 397 (M^+, 6), 178 (30), 133 (32), 111 (39), 95 (14), 69 (100). Anal. Calcd for $C_{15}H_{19}Cl_2O_6P$: C, 45.36; H, 4.82. Found: C, 45.11; H, 4.89.

2-[(2,4-Dichlorophenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one ***(IIb)***. White solid; yield 72%; mp, 110−113 °C. IR (KBr, cm^{-1}): ν 3114, 2966, 1769, 1483, 1282, 1194, 1072, 1009, 857, 805. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H, 5-furanyl-H), 7.37 (d, J = 2.4 Hz, 1H, 3-phenyl-H), 7.13−6.43 (m, 4H), 6.42 (d, J = 12.8 Hz, 1H, PCHO), 4.79 (s, 2H, OCH_2CO), 4.14−4.05 (m, 4H, 2 × (OCH_2)), 1.23 (s, 3H), 0.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.01, 156.11, 145.34, 145.01, 129.75, 127.61, 125.83, 123.79, 113.70, 113.10, 111.36, 65.29, 63.27 (d, $^1J_{C-P}$ = 168.99 Hz), 32.43, 21.55, 20.60. ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.16. EI-MS m/z (%): 449 (M^+, 1), 245 (25), 229 (40), 175 (29), 147 (21), 133 (70), 111 (22), 95 (34), 81 (41), 69 (100). Anal. Calcd for $C_{18}H_{19}Cl_2O_7P$: C, 48.13; H, 4.26. Found: C, 48.67; H, 3.87.

2-[(2,4-Dichlorophenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one ***(IIc)***. White solid; yield 67%; mp, 150−151 °C. IR (KBr, cm^{-1}): ν 3092, 2963, 1770, 1485, 1274, 1193, 1072, 1070, 864, 800. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−6.73 (m, 8H, $-C_6H_5$, $-C_6H_3$), 6.36 (d, J = 12.4 Hz, 1H, PCHO), 4.82 (s, 2H, OCH_2CO), 4.07−4.04 (m, 4H, 2 × (OCH_2)), 1.16 (s, 3H), 0.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.21, 152.09, 132.96, 130.35, 129.31, 128.73, 127.95, 127.67, 127.29, 123.86, 114.53, 71.12 (d, $^1J_{C-P}$ = 165.40 Hz), 66.17, 32.43, 21.60, 20.78. ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.38. EI-MS m/z (%): 458 (M^+ + 1, 13), 311 (9), 245 (11), 229 (28), 177 (43), 175 (77), 162 (11), 147 (16), 137 (15), 136 (26), 135 (90), 121 (100), 90 (90). Anal. Calcd for $C_{20}H_{21}Cl_2O_6P$: C, 52.30; H, 4.61. Found: C, 52.79; H, 4.47.

2-[(2,4-Dichlorophenoxy)acetoxy](2,4-dichlorophenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one ***(IId)***. White solid; yield 65%; mp, 169−170 °C. IR (KBr, cm^{-1}): ν 3102, 2974, 1772, 1480, 1288, 1179, 1057, 1006, 840, 813. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63−6.82 (m, 6H, $-C_6H_3$, $-C_6H_3$), 6.73 (d, J = 8.8 Hz, 1H, PCHO), 4.81 (d, J = 4.0 Hz, 2H, OCH_2CO), 4.17−4.01 (m, 4H), 1.21 (s, 3H), 0.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.31, 152.01, 138.62, 133.53, 132.89, 132.41, 131.64, 130.73, 130.29, 127.81, 126.64, 123.65, 114.38, 71.36 (d, $^1J_{C-P}$ = 165.90 Hz), 65.59, 32.24, 21.60, 20.78. ^{31}P NMR (160 MHz, $CDCl_3$): δ 5.84. EI-MS m/z (%): 528 (M^+, 5), 491 (5), 308 (28), 175 (57), 145 (23), 133 (100), 69 (71). Anal. Calcd for $C_{20}H_{19}Cl_4O_6P$: C, 45.48; H, 3.63. Found: C, 45.94; H, 3.44.

2-[(2,4-Dichlorophenoxy)acetoxy](4-chlorophenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one ***(IIe)***. White solid; yield, 70%; mp, 120−121 °C. IR (KBr, cm^{-1}): ν 3090, 2978, 1768, 1484, 1273, 1189, 1073, 1020, 830, 815. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−6.72 (m, 7H, $-C_6H_4$, $-C_6H_3$), 6.30 (d, J = 12.4 Hz, 1H, PCHO), 4.80 (s, 2H, OCH_2CO), 4.10−3.91 (m, 4H, 2 × (OCH_2)), 1.16 (s, 3H), 0.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.28, 152.55, 141.90, 133.66, 131.82, 130.99, 128.07, 127.63, 127.15, 113.99, 69.98 (d, $^1J_{C-P}$ = 165.80 Hz), 66.01, 32.09, 21.56, 20.33. ^{31}P NMR (160 MHz, $CDCl_3$): δ 7.48. EI-MS m/z (%): 494 (M^+ + 1, 5), 274 (24), 175 (29), 133 (100), 69 (63). Anal. Calcd for $C_{20}H_{20}Cl_3O_6P$: C, 48.66; H, 4.08. Found: C, 48.89; H, 3.83.

2-[(2,4-Dichlorophenoxy)acetoxy](i-propyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one ***(IIf)***. White solid; yield, 86%; mp, 120−121 °C. IR (KBr, cm^{-1}): ν 3076, 2971, 1759, 1480, 1282, 1205, 1057, 1012, 834, 808. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, 1H, J = 2.4 Hz, 3-phenyl-H), 7.19−7.16 (dd, 1H, J = 2.4 Hz, J = 2.4 Hz, 5-phenyl-H), 6.78 (d, 1H, J = 8.8 Hz, 6-phenyl-H), 5.31−5.27 (t, 1H, J = 7.2 Hz, PCHO), 4.80 (d, J = 4.8 Hz, 2H, OCH_2CO), 4.15−3.92 (m, 4H, 2 × (OCH_2)), 2.37−2.33 (m, 1H), 1.15 (s, 3H), 1.13−1.01 (m, 6H), 0.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.65, 152.01, 133.73, 130.34, 127.51, 123.99, 114.38, 72.70 (d, $^1J_{C-P}$ = 159.60 Hz), 65.87, 32.36, 28.95, 21.51, 20.95, 18.13. ^{31}P NMR (160 MHz, $CDCl_3$):

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δ 20.13. EI-MS m/z (%): 426 (M^+ + 1, 4), 263 (14), 206 (36), 191 (100), 175 (34), 133 (71), 69 (72). Anal. Calcd for $C_{17}H_{23}Cl_2O_6P$: C, 48.02; H, 5.45. Found: C, 48.26; H, 5.04.

*2-[(2,4-Dichlorophenoxy)acetoxy](n-butyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIg**).* White solid; yield, 72%; mp, 75−76 °C. IR (KBr, cm^{-1}): ν 3070, 2953, 1755, 1478, 1281, 1198, 1068, 1009, 838, 799. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, 1H, J = 2.4 Hz, 3-phenyl-H), 7.19−7.16 (dd, 1H, J = 2.4 Hz, J = 2.4 Hz, 5-phenyl-H), 6.78 (d, 1H, J = 8.8 Hz, 6-phenyl-H), 5.50−5.47 (m, 1H, PCHO), 4.78−4.69 (s, 2H, OCH_2CO), 4.16−3.91 (m, 4H, 2 × (OCH_2)), 1.94−1.93 (m, 2H), 1.35−1.31 (m, 4H), 1.15 (s, 3H), 1.02 (s, 3H), 0.91−0.86 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.81, 152.26, 132.99, 130.47, 127.29, 124.13, 113.75, 71.65 (d, $^1J_{C-P}$ = 162.40 Hz), 66.11, 32.39, 24.31, 21.70, 21.31, 20.95, 18.76, 15.11. ^{31}P NMR (160 MHz, $CDCl_3$): δ 14.55. Anal. Calcd for $C_{18}H_{25}Cl_2O_6P$: C, 49.22; H, 5.74. Found: C, 49.55; H, 5.39.

*2-[(2-Chlorophenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIh**).* Yellow oil; yield, 82%; $n^{20}{}_D$ 1.5211. IR (KBr, cm^{-1}): ν 3124, 2971, 1765, 1596, 1492, 1291, 1170, 1061, 1011, 826. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−6.53 (m, 6H, C_6H_4, 5 and 4-furanyl-H), 6.49 (d, 1H, J = 14.4 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.71 (s, 2H, OCH_2CO), 4.12−4.05 (m, 4H, 2 × (OCH_2)), 1.23 (s, 3H), 0.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.19, 155.08, 144.89, 143.91, 129.17, 128.82, 126.34, 115.72, 115.47, 113.11, 111.33, 65.32, 63.41 (d, $^1J_{C-P}$ = 170.80 Hz), 32.37, 21.59, 20.21. ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.08. EI-MS m/z (%): 414 (M^+, 3), 245 (30), 229 (17), 141 (37), 133 (75), 113 (35), 95 (32), 81 (45), 69 (100). Anal. Calcd for $C_{18}H_{20}ClO_7P$: C, 52.12; H, 4.86. Found: C, 52.33; H, 4.52.

*2-[(4-Chlorophenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIi**).* Yellow oil; yield, 80%; $n^{20}{}_D$ 1.5213. IR (KBr, cm^{-1}): ν 3125, 2970, 1766, 1595, 1492, 1291, 1170, 1062, 1011, 826. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H, 5-furanyl-H), 7.23 (d, 2H, J = 8.4 Hz, 3 and 5-phenyl-H), 6.81 (d, 2H, J = 8.4 Hz, 2 and 6-phenyl-H), 6.72 (s, 1H, 4-furanyl-H), 6.50 (d, 1H, J = 13.2 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.76 (s, 2H, OCH_2CO), 4.14−4.02 (m, 4H, 2 × (OCH_2)), 1.22 (s, 3H), 0.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.27, 155.90, 145.01, 144.11, 129.40, 115.79, 113.10, 113.05, 111.05, 65.20, 63.35 (d, $^1J_{C-P}$ = 170.80 Hz), 32.41, 21.57, 20.58. ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.02. EI-MS m/z (%): 414 (M^+, 2), 245 (12), 229 (39), 175 (5), 141 (21), 133 (63), 111 (14), 95 (35), 81 (50), 69 (100). Anal. Calcd for $C_{18}H_{20}ClO_7P$: C, 52.12; H, 4.86. Found: C, 52.46; H, 5.38.

*2-[(4-Chloro-3-methylphenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIj**).* Yellow oil; yield, 82%; $n^{20}{}_D$ 1.5230. IR (KBr, cm^{-1}): ν 3124, 2968, 1770, 1600, 1482, 1291, 1166, 1062, 1012, 828. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H, 5-furanyl-H), 7.24−6.69 (m, 4H, 2, 5, and 6-phenyl-H, 4-furanyl-H), 6.50 (d, H, J = 14.4 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.70 (s, 2H), 4.16−4.03 (m, 4H), 2.32 (s, 3H), 1.23 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.31, 156.11, 145.30, 143.87, 137.23, 129.80, 127.03, 117.01, 112.92, 112.74, 111.03, 65.07, 63.78 (d, $^1J_{C-P}$ = 170.10 Hz), 32.19, 21.47, 20.61, 20.25. ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.11. EI-MS m/z (%): 428 (M^+, 8), 278 (20), 234 (37), 230 (10), 155 (57), 125 (55), 81 (58), 69 (100). Anal. Calcd for $C_{19}H_{22}ClO_7P$: C, 53.22; H, 5.17. Found: C, 53.95; H, 6.15.

*2-[(4-Chloro-2-methylphenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIk**).* White solid; yield, 80%; mp, 63−65 °C. IR (KBr, cm^{-1}): ν 3122, 2971, 1771, 1492, 1291, 1171, 1063, 1012, 947, 918, 808. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H, 5-furanyl-H), 7.13−7.03 (m, 2H, 3 and 5-phenyl-H), 6.72 (s, 1H, 6-phenyl-H), 6.57 (d, 1H, J = 8.4 Hz, 4-furanyl-H), 6.50 (d, 1H, J = 14.4 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.72 (s, 1H, OCH_2CO), 4.11−3.98 (m, 4H, 2 × (OCH_2)), 2.25 (s, 3H, $PhCH_3$), 1.21 (s, 3H), 0.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.37, 156.99, 145.01, 143.73, 130.89, 129.24, 127.93, 126.55, 126.07, 113.11, 110.97, 65.13, 63.87 (d, $^1J_{C-P}$ = 170.60 Hz), 32.57, 21.39, 20.78, 16.09. ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.23. EI-MS m/z (%): 428 (M^+, 6), 384 (1), 278 (11), 234 (37), 230 (10), 155 (57), 125 (55), 81 (58), 69 (79). Anal. Calcd for $C_{19}H_{22}ClO_7P$: C, 53.22; H, 5.17. Found: C, 53.32; H, 5.34.

*2-[(2-Chlorophenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIl**).* Yellow solid; yield, 82%; mp, 87−88 °C. IR (KBr, cm^{-1}): ν 3014, 2968, 1752, 1590, 1493, 1293, 1190, 1056, 837. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−6.79 (m, 9H, $-C_6H_5$, $-C_6H_4$), 6.37 (d, 1H, J = 12.4 Hz, PCHO), 4.84 (s, 2H, OCH_2CO), 4.16−3.96 (m, 4H, 2 × (OCH_2)), 1.17 (s, 3H), 0.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 166.96, 156.02, 132.05, 129.15, 128.88, 128.73, 128.67, 127.90, 127.83, 122.87, 113.68, 71.45 (d, $^1J_{C-P}$ = 164.60 Hz), 66.06, 32.30, 21.67, 20.71. ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.24. EI-MS m/z (%): 424 (M^+, 3), 240 (22), 141 (34), 133 (86), 105 (45), 91 (14), 77 (51), 69 (100). Anal. Calcd for $C_{20}H_{22}ClO_6P$: C, 56.55; H, 5.22. Found: C, 56.74; H, 5.46.

*2-[(4-Chlorophenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIm**).* White solid; yield, 78%; mp, 59−60 °C. IR (KBr, cm^{-1}): ν 3064, 2967, 1755, 1594, 1492, 1291, 1190, 1057, 1008, 835. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44−6.80 (m, 9H, $-C_6H_5$, $-C_6H_4$), 6.36 (d, 1H, J = 12.0 Hz, PCHO), 4.80−4.69 (m, 2H, OCH_2CO), 4.11−3.92 (m, 4H, 2 × (OCH_2)), 1.16 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.30, 156.02, 129.73, 129.28, 128.85, 127.99, 127.93, 125.51, 115.85, 70.86 (d, $^1J_{C-P}$ = 165.30 Hz), 65.40, 32.13, 21.59, 20.80. ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.72. EI-MS m/z (%): 424 (M^+, 1), 240 (43), 172 (4), 141 (30), 133 (85), 105 (39), 91 (7), 77 (50), 69 (100). Anal. Calcd for $C_{20}H_{22}ClO_6P$: C, 56.55; H, 5.22. Found: C, 56.93; H, 5.51.

*2-[(4-Chloro-3-methylphenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIn**).* Yellow solid; yield, 80%; mp, 70−71 °C. IR (KBr, cm^{-1}): ν 3065, 2966, 1766, 1607, 1479, 1277, 1165, 1059, 1008, 837. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43−6.64 (m, 8H), 6.35 (d, 1H, J = 16.0 Hz, PCHO), 4.73 (d, 2H, J = 2.4 Hz, OCH_2CO), 4.08−3.97 (m, 4H, 2 × (OCH_2)), 2.31 (s, 3H, $PhCH_3$), 1.16 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.31, 155.63, 137.55, 132.33, 129.67, 128.83, 128.51, 127.39, 126.77, 117.03, 113.44, 71.71 (d, $^1J_{C-P}$ = 165.90 Hz), 65.29, 32.11, 21.49, 20.61, 20.38. ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.89. EI-MS m/z (%): 438 (M^+, 3), 295 (6), 241 (2), 240 (12), 175 (39), 145 (46), 133 (91), 105 (38), 91 (13), 77 (26), 69 (100). Anal. Calcd for $C_{21}H_{24}ClO_6P$: C, 57.48; H, 5.51. Found: C, 57.39; H, 5.73.

*2-[(4-Chloro-2-methylphenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIo**).* Yellow solid; yield, 80%; mp, 98−100 °C. IR (KBr, cm^{-1}): ν 3124, 2975, 1770, 1601, 1494, 1276, 1177, 1071, 1012, 952, 837. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45−6.56 (m, 8H, $-C_6H_5$, $-C_6H_3$), 6.36 (d, 1H, J = 12.0 Hz, PCHO), 4.76 (s, 2H, OCH_2CO), 4.11−3.86 (m, 4H, 2 × (OCH_2)), 2.26 (s, 3H, $PhCH_3$), 1.13 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.36, 154.27, 132.16, 130.71, 129.17, 128.94, 128.66, 127.89, 126.31, 126.17, 117.16, 70.53 (d, $^1J_{C-P}$ = 164.60 Hz), 65.47, 32.33, 21.46, 20.61, 16.07. ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.55. EI-MS m/z (%): 438 (M^+, 10), 288 (16), 244 (51), 241 (13), 240 (100), 173 (21), 155 (36), 133 (59), 125 (46), 105 (33), 91 (26), 77 (39), 69 (72). Anal. Calcd for $C_{21}H_{24}ClO_6P$: C, 57.48; H, 5.51. Found: C, 57.59; H, 5.63.

*2-[(4-Chloro-3-methylphenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIp**).* White solid; yield, 64%; mp, 104−106 °C. IR (KBr, cm^{-1}): ν 3077, 2970, 1764, 1485, 1285, 1206, 1060, 1009, 953, 839, 801. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.24 (d, 1H, J = 9.0 Hz, 5-phenyl-H), 6.78−6.64 (m, 2H, 2 and 6-phenyl-H), 5.52−5.47 (m, 1H, PCHO), 4.67 (s, 2H, OCH_2CO), 4.13−3.98 (m, 4H, 2 × (OCH_2)), 2.33 (s, 3H, $PhCH_3$), 1.60−1.56 (dd, 3H, J = 7.2 Hz, J = 7.2 Hz, $PCH(CH_3)O$), 1.17 (s, 3H), 0.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.54, 155.83, 137.21, 129.62, 126.91, 117.02, 112.92, 65.23, 65.06 (d, $^1J_{C-P}$ = 165.30 Hz), 32.38, 21.44, 20.67, 20.21, 14.69. ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.65. EI-MS m/z (%): 376 (M^+, 3), 178 (54), 158 (17), 155 (16), 150 (19), 133 (26), 124 (33), 111 (92), 88 (23), 69 (100). Anal. Calcd for $C_{16}H_{22}ClO_6P$: C, 51.01; H, 5.89. Found: C, 51.28; H, 6.03.

*2-[(2-Chlorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIq**).* White solid; yield, 68%; mp, 99−101 °C. IR (KBr, cm^{-1}): ν 3098, 2974, 1775, 1493, 1286, 1194, 1066,

1003, 953, 799. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.27−6.81 (m, 4H, C_6H_4), 5.50−5.48 (m, 1H, PCHO), 4.68 (s, 2H, OCH_2CO), 4.14−3.97 (m, 4H, 2 × (OCH_2)), 1.60−1.56 (q, 3H, J = 7.8 Hz, PCH($\underline{CH_3}$)O), 1.16 (s, 3H), 1.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.17, 155.71, 129.15, 128.92, 126.42, 115.60, 115.53, 65.04, 64.81 (d, $^1J_{C-P}$ = 165.30 Hz), 32.11, 21.13, 20.46, 14.41. ^{31}P NMR (160 MHz, $CDCl_3$): δ 13.53. EI-MS m/z (%): 362 (M^+, 3), 178 (33), 150 (11), 141 (17), 133 (23), 111 (100), 96 (9), 75 (24), 69 (80). Anal. Calcd for $C_{15}H_{20}ClO_6P$: C, 49.67; H, 5.56. Found: C, 50.03; H, 5.83.

*2-[(4-Chloro-2-methylphenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIr**).* White solid; yield, 68%; mp, 82−84 °C. IR (KBr, cm^{-1}): ν 3079, 2972, 1768, 1491, 1231, 1184, 1056, 1010, 947, 877, 805. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.14 (s, 1H, 3-phenyl-H), 7.10−7.07 (m, 1H, 5-phenyl-H), 6.61 (d, 1H, J = 8.4 Hz, 6-phenyl-H), 5.50−5.46 (m, 1H, PCHO), 4.69 (d, 2H, J = 4.2 Hz, OCH_2CO), 4.14−3.91 (m, 4H, 2 × (OCH_2)), 2.25 (s, 3H, Ph$\underline{CH_3}$), 1.60−1.55 (q, 3H, J = 8.4 Hz, PCH($\underline{CH_3}$)O), 1.14 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.44, 153.99, 136.56, 130.11, 127.05, 117.23, 113.04, 65.49, 65.30 (d, $^1J_{C-P}$ = 164.90 Hz), 32.31, 21.43, 20.66, 20.37, 14.88. ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.33. EI-MS m/z (%): 376 (M^+, 5), 236 (4), 193 (16), 178 (38), 155 (28), 133 (49), 111 (43), 77 (37), 69 (100). Anal. Calcd for $C_{16}H_{22}ClO_6P$: C, 51.01; H, 5.89. Found: C, 51.08; H, 6.23.

*2-[(4-Chlorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**IIs**).* White solid; yield, 74%; mp, 62−64 °C. IR (KBr, cm^{-1}): ν 3093, 2976, 1776, 1495, 1286, 1191, 1070, 1004, 952, 838, 798. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 (d, 2H, J = 8.4 Hz, 3 and 5-phenyl-H), 6.83 (d, 2H, J = 8.4 Hz, 2 and 6-phenyl-H), 5.52−5.47 (m, 1H, PCHO), 4.68 (s, 2H, OCH_2CO), 4.14−3.97 (m, 4H, 2 × (OCH_2)), 1.60−1.56 (dd, 3H, J = 7.2 Hz, J = 7.2 Hz, PCH($\underline{CH_3}$)O), 1.16 (s, 3H), 1.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 167.19, 153.91, 129.55, 125.38, 114.01, 66.70, 65.55 (d, $^1J_{C-P}$ = 165.60 Hz), 32.12, 21.18, 20.33, 14.75. ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.14. EI-MS m/z (%): 362 (M^+, 5), 178 (40), 150 (11), 141 (25), 133 (33), 111 (91), 99 (6), 77 (13), 74 (18), 69 (100). Anal. Calcd for $C_{15}H_{20}ClO_6P$: C, 49.67; H, 5.56. Found: C, 49.81; H, 5.76.

Greenhouse Herbicidal Activity. The herbicidal activities of the title compounds **IIa−s** against monocotyledonous weeds such as *Echinochloa crusgalli*, *Setaira viridis*, and *Digitaria sanguinalis* and dicotyledonous weeds such as *Abutilon theophrasti*, *Brassica juncea*, *Amaranthus retroflexus*, and *Eclipta prostrate* were evaluated at 150 g ai/ha using the compounds **I-1** (HW02) and **I-2** as references according to a previous reported procedure.[18,19] Some of the title compounds **IIa-g** and **IIr** were then selected for further test at 75 and 37.5 g ai/ha using the compound **I-1** (HW02) as a positive control, and the weed species were the same as the first test except for *Abutilon theophrasti*. Finally, a broad spectrum test was made using more weed species such as *Amaranthus retroflexus*, *Brassica chinensis*, *Pharbitis nil*, *Raphanus sativus*, *Ammannia baccifera*, *Monochoia vaginalis*, *Brassica oleracea*, *Brassica campestris*, *Chenopodium album*, and *Brassica juncea* for the title compounds **IIa** and **IIb** at 150 and 75 g ai/ha. Glyphosate was selected as a positive control.

Weed seeds were planted in 9 cm-diameter plastic boxes containing artificial mixed soil. Before plant emergence, the boxes were covered with plastic film to keep moist. Plants were grown in the greenhouse. Fresh weight of the above ground tissues was measured 10 days after treatment. The inhibition percent is used to describe the control efficiency of compounds. All test compounds were dissolved in *N*,*N*-dimethylformamide with the addition of a little Tween 20 and then were sprayed using a laboratory belt sprayer delivering at 750 L/ha-spray-volume. The mixture of the same amount of water, *N*,*N*-dimethylformamide, and Tween 20 was sprayed as control. Activity numbers represent percent displaying herbicidal damage as compared to control. The diluted formulation solutions were applied for postemergence treatment,; dicotyledon weeds were treated at the two-leaf stage, and monocotyledon weeds were treated at the one-leaf stage, respectively.

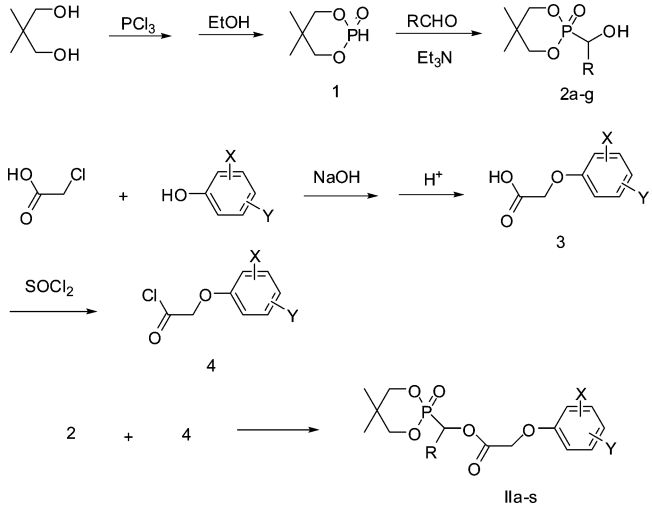
Crop Selectivity. Conventional rice, corn, cotton, soybean, rape, and wheat were respectively planted in plots (diameter = 12 cm) containing test soil and grown in a greenhouse at 20−25 °C. After the plants had reached the four-leaf stage, the spraying treatment was conducted at different dosages by diluting the formulation of the selected compounds. The visual injury and growth state of the individual plant were observed at regular intervals. The final evaluation for crops safety of the selected compounds was conducted by visual observation in 30 days after treatment on the 0−100 scale (0 = no injury, 10 = chlorosis, 100 = death).

Toxicity. Mammalian toxicity was performed according to the Chinese standard procedure. The title compound **IIa** was selected for mammalian toxicity testing.

RESULTS AND DISCUSSION

Synthesis of the Title Compounds IIa−s. The title compounds **IIa−s** were prepared by condensation of intermediates **2a−g** with substituted phenoxyacetyl chlorides **4** in the presence of triethylamine or pyridine as a base and chloroform as a solvent (Scheme 2). The intermediates **2a−g**

Scheme 2. Synthetic Route of 2-[(Substituted phenoxyacetoxy)alkyl]-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one IIa−s



were prepared according to existing methods.[22−24] The substituted phenoxyacetic acids **3** were prepared by condensation of corresponding substituted phenols with chloroacetic acid in the presence of alkali such as sodium hydroxide. The structures of the title compounds **IIa−s** were characterized by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, IR, MS, and elemental analysis. The title compounds **IIa−s** exhibit some characteristic peakes at δ = 0.89−1.23 (2s, 6H, $2CH_3$) and δ = 5.45−6.74 (d or t or m, 1H, P$\underline{CH}$O), respectively, in the ^{1}H NMR. The typical carbon resonance at δ_C 166−168 in the ^{13}C NMR spectra of **IIa−s** also confirms the presence of a carbon−oxygen double bond. The typical phosphorus resonance at δ_P 5.85−13.09 in the ^{31}P NMR spectra of **IIa−s** reveals the presence of a phosphorus center coupled to an adjacent CH.

Greenhouse Herbicidal Activity and Crop Selectivity. The herbicidal activities of title compounds **IIa−s** were evaluated at different doses in a set of experiments in a greenhouse. As an initial evaluation, all of the title compounds were tested at a dosage of 150 g ai/ha for postemergence herbicidal activity on *E. crusgalli*, *S. viridis*, *D. sanguinalis*, *A. theophrasti*, *B. juncea*, *A. retroflexus*, and *E. prostrate*. Compounds **I-1** (HW02) and **I-2** (R^1 and R^2 = MeO, R = Me, R^3 = H in structure **I**) were selected as control. The results

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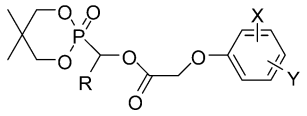
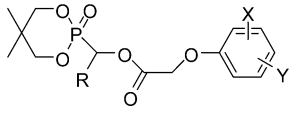
Table 1. Structures and Herbicidal Activity of the Title Compounds IIa−s (Percent Inhibition)



				post-emergence, 150 g ai/ha						
compound	R	X	Y	EC[a]	SV[a]	DS[a]	AT[a]	BJ[a]	AR[a]	EP[a]
IIa	CH_3	2-Cl	4-Cl	30 ± 3.5	30 ± 0	30 ± 1.0	95 ± 2.0	95 ± 5.0	95 ± 1.0	85 ± 2.0
IIb	2-furyl	2-Cl	4-Cl	30 ± 0	30 ± 2.5	40 ± 1.5	90 ± 3.0	95 ± 5.0	80 ± 1.0	80 ± 3.5
IIc	Ph	2-Cl	4-Cl	0	0	0	98 ± 0	100	90 ± 2.5	80 ± 2.0
IId	2,4-Cl_2−Ph	2-Cl	4-Cl	0	0	0	95 ± 1.0	100	80 ± 0	70 ± 1.0
IIe	4-Cl−Ph	2-Cl	4-Cl	0	0	0	90 ± 1.0	98 ± 0	80 ± 1.5	70 ± 0
IIf	*i*-Pr	2-Cl	4-Cl	0	0	0	95 ± 1.0	100	85 ± 2.5	75 ± 2.0
IIg	*n*-Bu	2-Cl	4-Cl	0	0	0	90 ± 0	100	85 ± 1.0	75 ± 1.5
IIh	2-furyl	2-Cl	H	0	0	0	70 ± 2.0	90 ± 1.5	85 ± 0	70 ± 3.5
IIi	2-furyl	4-Cl	H	0	0	0	70 ± 0	70 ± 2.5	55 ± 5.0	50 ± 1.0
IIj	2-furyl	3-CH_3	4-Cl	0	0	0	70 ± 4.0	65 ± 0	60 ± 1.0	55 ± 2.0
IIk	2-furyl	2-CH_3	4-Cl	60 ± 4.0	0	0	100	90 ± 1.0	100	70 ± 3.0
IIl	Ph	2-Cl	H	0	0	0	70 ± 1.5	75 ± 0	75 ± 1.0	65 ± 3.0
IIm	Ph	4-Cl	H	0	0	0	65 ± 1.0	70 ± 2.5	60 ± 0	50 ± 2.0
IIn	Ph	3-CH_3	4-Cl	0	0	0	65 ± 0	65 ± 1.0	65 ± 1.5	60 ± 3.5
IIo	Ph	2-CH_3	4-Cl	40 ± 0	0	0	100	90 ± 1.0	100	75 ± 2.5
IIp	CH_3	4-Cl	3-CH_3	0	0	0	70 ± 2.5	70 ± 1.0	60 ± 2.0	60 ± 0
IIq	CH_3	2-Cl	H	20 ± 5.0	0	0	70 ± 3.0	90 ± 0	90 ± 1.5	75 ± 0
IIr	CH_3	2-CH_3	4-Cl	30 ± 1.5	0	0	100	100	100	90 ± 2.5
IIs	CH_3	4-Cl	H	10 ± 2.5	0	0	70 ± 0	75 ± 1.5	70 ± 1.0	60 ± 2.0
I-1	CH_3	2-Cl	4-Cl	0	0	0	100	85 ± 2.0	96 ± 2.0	90 ± 2.0
I-2	CH_3	2-CH_3	4-Cl	0	0	0	82 ± 2.0	20 ± 5.0	10 ± 2.0	30 ± 5.0

[a]EC for *Echinochloa crusgalli*; SV for *Setaira viridis*; DS for *Digitaria sanguinalis*; AT for *Abutilon theophrasti*; BJ for *Brassica juncea*; AR for *Amaranthus retroflexus*; EP for *Eclipta prostrate*.

Table 2. Further Herbicidal Testing of the Title Compounds IIa−g and IIr (Percent Inhibition)



compound	dosage (g ai/ha)	EC[a]	SV[a]	DS[a]	BJ[a]	AR[a]	EP[a]
IIa	37.5	0	0	0	90 ± 2.0	70 ± 1.5	50 ± 1.5
	75	0	0	0	95 ± 5.0	75 ± 3.0	70 ± 0
IIb	37.5	0	0	0	85 ± 5.0	50 ± 2.5	60 ± 2.0
	75	0	0	0	90 ± 3.0	70 ± 2.0	62 ± 3.0
IIc	37.5	0	0	0	90 ± 2.0	50 ± 0	50 ± 1.0
	75	0	0	0	95 ± 0	80 ± 2.0	55 ± 2.0
IId	37.5	0	0	0	50 ± 2.5	20 ± 0	30 ± 1.0
	75	0	0	0	55 ± 2.0	20 ± 0	34 ± 2.0
IIe	37.5	0	0	0	80 ± 2.0	30 ± 1.5	0
	75	0	0	0	90 ± 0	50 ± 2.0	0
IIf	37.5	0	0	0	90 ± 1.0	30 ± 5.0	30 ± 0
	75	0	0	0	100	80 ± 1.0	35 ± 2.0
IIg	37.5	0	0	0	90 ± 0	50 ± 3.5	30 ± 2.0
	75	0	0	0	100	70 ± 1.5	40 ± 2.5
IIr	37.5	0	0	0	80 ± 2.0	80 ± 0	80 ± 1.5
	75	0	0	0	100	100	85 ± 1.0
I-1 HW02	37.5	0	0	0	90 ± 2.0	70 ± 1.5	60 ± 1.0
	75	0	0	0	95 ± 0	95 ± 1.0	80 ± 2.0

[a]EC for *Echinochloa crusgalli*; SV for *Setaira viridis*; DS for *Digitaria sanguinalis*; BJ for *Brassica juncea*; AR for *Amaranthus retroflexus*; EP for *Eclipta prostrate*.

are listed in Table 1. All of the title compounds displayed much higher herbicidal activity against dicotyledonous plants than against monocotyledons plants. A part of the title compounds such as **IIa−g**, **IIk**, **IIo**, and **IIr** exhibited significant herbicidal activity against *A. theophrasti*, *B. juncea*, *A. retroflexus*, and *E. prostrate*. Especially, the title compounds **IIa** and **IIr** displayed

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Table 3. Broad Spectrum Testing of the Title Compounds IIa,b and IIr

		postemergence									
compound	dosage (g ai/ha)	AR[a]	BR[a]	PN[a]	RS[a]	AB[a]	MV[a]	BO[a]	BC[a]	CA[a]	BJ[a]
IIa	75	75 ± 3.0	80 ± 1.0	100	90 ± 2.0	100	100	80 ± 2.0	90 ± 1.0	80 ± 1.0	95 ± 2.0
	150	95 ± 1.0	85 ± 2.0	100	95 ± 1.0	100	100	90 ± 1.0	100	85 ± 1.0	95 ± 2.0
IIb	75	70 ± 2.0	70 ± 2.0	100	80 ± 1.0	100	100	80 ± 1.0	80 ± 2.5	70 ± 3.0	90 ± 3.0
	150	80 ± 1.0	80 ± 3.0	100	85 ± 3.0	100	100	85 ± 1.5	95 ± 1.0	80 ± 2.0	95 ± 5.0
IIr	75	100	70 ± 1.0	100	80 ± 1.0	100	100	/	/	70 ± 1.5	100
	150	100	80 ± 1.0	100	80 ± 1.0	100	100	/	/	75 ± 1.0	100
glyphosate	75	90 ± 3.0	70 ± 2.0	60 ± 0	60 ± 2.0	100	100	70 ± 2.0	100	70 ± 2.0	30 ± 1.0
	150	90 ± 2.0	80 ± 1.0	60 ± 0	65 ± 3.0	100	100	80 ± 2.5	100	90 ± 1.0	80 ± 2.0

[a]AR for *Amaranthus retroflexus*; BR for *Brassica chinensis*; PN for *Pharbitis nil*; RS for *Raphanus sativus*; AB for *Ammannia baccifera*; MV for *Monochoia vaginalis*; BO for *Brassica oleracea*; BC for *Brassica campestris*; CA for *Chenopodium album*; BJ for *Brassica juncea*; /, not tested.

Table 4. Crop Selectivity of the Title Compounds IIa−g and IIr

		crops (percent inhibition, postemergence)[a]					
compound	dosage (g ai/ha)	rice	corn	cotton	soybean	rape	wheat
IIa	150	10 ± 1.5	0	30 ± 2.0	30 ± 1.0	40 ± 2.5	0
IIb	150	40 ± 0	0	30 ± 1.0	30 ± 2.5	40 ± 0	10 ± 1.0
IIc	150	10 ± 2.0	0	40 ± 1.0	30 ± 0	40 ± 2.5	10 ± 0
IId	150	10 ± 1.0	10 ± 2.0	20 ± 5.0	30 ± 3.0	40 ± 0	0
IIe	150	10 ± 0	0	20 ± 3.5	20 ± 2.5	40 ± 4.0	0
IIf	150	20 ± 1.0	0	20 ± 0	30 ± 1.5	50 ± 2.5	10 ± 0
IIg	150	30 ± 0	0	20 ± 1.5	30 ± 2.0	40 ± 0	10 ± 0
IIr	150	10 ± 2.0	0	20 ± 3.0	20 ± 5.0	40 ± 5.0	0

[a]>10%, not safe to crops; 0−10%, safe to crops.

notable herbicidal activity against all tested broadleaf weeds with 85−100% inhibition effect. However, they were almost inactive against monocot weeds.

Comparing herbicidal activity among the title compounds **IIa−s** in Table 1, the title compounds with 2,4-Cl_2 or 2-CH_3, 4-Cl as X and Y (such as **IIa−g**, **IIk**, **IIo**, and **IIr**), exhibit significant herbicidal activity against tested dicotyledons for postemergence at a dosage of 150 g ai/ha, irrespective of different substituents in the R moiety (such as CH_3, 2-furyl, Ph, 2,4-Cl_2−Ph, 4-Cl−Ph, *i*-Pr, and *n*-Bu).

On the basis of the preliminary bioassays, the title compounds with 2,4-Cl_2 and 2-CH_3, 4-Cl as X and Y were selected for further bioassay at lower dose for postemergence herbicidal activity. The subsequent results in Table 2 show that the title compounds **IIa-c**, **IIf**, **IIg**, and **IIr** have an herbicidal activity comparable to that of compound **I-1** (HW02) against *B. juncea* with >90% inhibition in a dosage of 75 g ai/ha, and it can be found that the title compound **IIr** with 2-CH_3, 4-Cl as X and Y has the most effective inhibition against all tested broadleaf weeds, even at a dosage as low as 37.5 g ai/ha. Comparing the title compound **IIr** with compound **I-2**, both with 2-CH_3, 4-Cl as X and Y, however, the title compound **IIr** containing phosphorus-heterocyclic ring exhibits much higher herbicidal activity than that of compound **I-2**. From the data in Table 1, the compound **I-2** displays very poor herbicidal activity against *B. juncea*, *A. retroflexus*, and *E. prostrate* at a dose of 150 g ai/ha, and it has almost no herbicidal activity at a lower dose. This finding illustrates that the herbicidal activity of the compound can be greatly enhanced by replacement of MeO group attached to phosphorus moiety in the structure **I** with a phosphorus-containing heterocyclic ring when keeping 2-CH_3, 4-Cl as X and Y. Also, it has come to our notice that the herbicidal activity of the title compound **IIr** against *A. retroflexus* and *E. prostrate* seems also better than the compound **I-1** (HW02). Besides, the introduction of 2,4-Cl_2−Ph or 4-Cl−Ph as R results in a decrease in herbicidal activity when 2,4-Cl_2 is kept constant as X and Y; for example, the title compounds **IId** and **IIe** are very weak or inactive against tested broadleaf weeds at a dosage of 37.5 or 75 g ai/ha.

Structure−activity relationship analysis indicates that the introduction of a phosphorus-containing heterocyclic ring seems to have a favorable effect on herbicidal activity, and substituents X and Y on the benzene ring still greatly affect activity. However, it is noteworthy that the title compounds **II** with 2-CH_3, 4-Cl as X and Y show higher or the same herbicidal activity as compared to those of compounds containing 2,4-Cl_2 as X and Y, such as compound **I-1** (HW02) and the title compound **IIa**. This finding is much different from SAR analyses for compounds **I**.[19]

Novel herbicides must possess broad spectrum and high activities against weeds. Hereby, some of the title compounds **IIa**, **IIb**, and **IIr** were chosen for a broad spectrum test to confirm their activity and potential application as novel herbicides using *A. retroflexus*, *B. chinensis*, *P. nil*, *R. sativus*, *A. baccifera*, *M. vaginalis*, *B. oleracea*, *B. campestris*, *C. album*, and *B. juncea*. The results in Table 3 show the herbicidal activity and spectrum of the title compounds **IIa**, **IIb**, and **IIr** are comparable with glyphosate. Especially, the title compounds **IIa**, **IIb**, and **IIr** show higher herbicidal activity than glyphosate against *P. nil*, *R. sativus*, *B. oleracea*, and *B. juncea* at a dosage of 75 g ai/ha.

In addition, we also tested the crop selectivity of the title compounds (**IIa−g** and **IIr**) as shown in Table 4. The title compounds **IIa**, **IIe**, and **IIr** have a higher level of selectivity for corn and wheat by postemergence application at the dosages of 150 g ai/ha among the eight tested compounds, thus indicating that further development could be carried out for purposes of weed control in corn or wheat fields.

Toxicity. The title compound **IIa** as a representative compound was selected for testing of toxicity to mammal (rat) according to the pesticide standard procedure. The title compound **IIa** exhibited low toxicity against rat (LD_{50}: percutaneous, 2330 mg/kg; oral, >2000 mg/kg).

In conclusion, a series of novel 1,3,2-dioxaphosphinan-2-one derivatives **II** were designed and synthesized on the basis of the structural modification of **I**, and their postemergence herbicidal activity against seven species of weeds was evaluated. SAR analyses indicate that the introduction of a phosphorus-containing heterocyclic ring has a favorable effect on herbicidal activity and their herbicidal activity is further increased by a reasonable combination of X, Y, and R in parent compound **II**. The title compounds **IIa** and **IIr** possess high activity and broad spectrum against all of the test broadleaf weeds with 70−100% inhibition effect at a dosage of 75 g ai/ha, and they are very safe for corn and wheat at a dosage of 150 g ai/ha. Furthermore, the title compound **IIa** exhibits low toxicity against rat. These findings demonstrate that the title compounds **IIa** and **IIr** can be potential and selective postemergence herbicides for further development.

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Notes

The authors declare no competing financial interest.

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