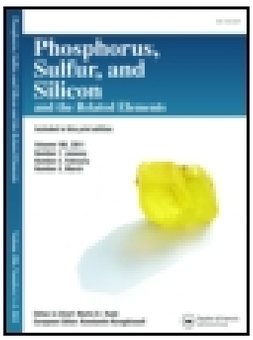

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Design, synthesis and herbicidal activity of novel cyclic phosphonates with diaryl ethers containing pyrimidine

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ABSTRACT

Thirteen novel cyclic phosphates were rationally designed and synthesized by introducing diary ethers containing pyrimidine. All the target compounds were characterized by ^{1}H, ^{13}C, ^{31}P NMR and HRMS. The test of herbicidal activity indicated that most of the compounds showed good herbicidal activities against *Amaranthus retroflexus*. The compounds **IA-2** (1-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)propyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate) and **IA-3** ((5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(phenyl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)-benzoate) exhibited remarkable post-emergency herbicidal activity against the tested monocotyledonous weed at the dosage of 112.5 g ai/ha.

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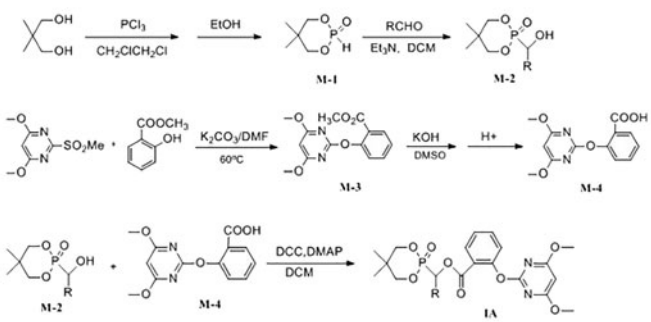
Synthesis; herbicidal activity; diary ether; heterocyclic phosphonate

GRAPHICAL ABSTRACT



Introduction

Pyruvate dehydrogenase complex (PDHc) is known to be one target enzyme attacked by some herbicidally active compounds.[1–3] α-Substituted alkylphosphonate derivatives have received considerable attention over the past two decades in medicine and pesticide chemistry due to their biological, activities.[4–6]

Studies indicated that α-(substituted phenoxyacetoxy)alkylphosphonates possess excellent herbicidal activities as potent pyruvate dehydrogenase complex (PDHc) inhibitors.[7–10] Clacyfos (**HW02**), the only herbicide developed by China included in The Pesticide Manual (17th version), as a selective post-emergency herbicide, displayed outstanding herbicidal activity on broad-leaved weeds. In our previous work, the introduction of a cyclophosphonate moiety into the phosphonate part of structure could promote the herbicidal activity of the phosphonates.[11–12] Introducing diaryl ethers to some pesticides could improve physical and chemical properties and biological activity, such as photostability, improving efficiency and biological activity spectra.[13]

In order to design and synthesize new phosphonate derivatives with better herbicidal activity, the pyrimidinyl benzoate structural unit and heterocyclic were introduced into phosphonate molecules to design and synthesis a novel series of 1′-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphoryl)alkyl-2-(4,6-dimethoxy-pyrimidin-2-yloxy)benzoates. Here the preparation of the target compounds and their herbicidal activity were reported.

Results and discussion

Synthesis

According to the reported literatures,[14–16] α-substituted-1,3,2-dioxaphosphorinane **M-2** was the key intermediate for the synthesis of title compound **IA**. Condensation of

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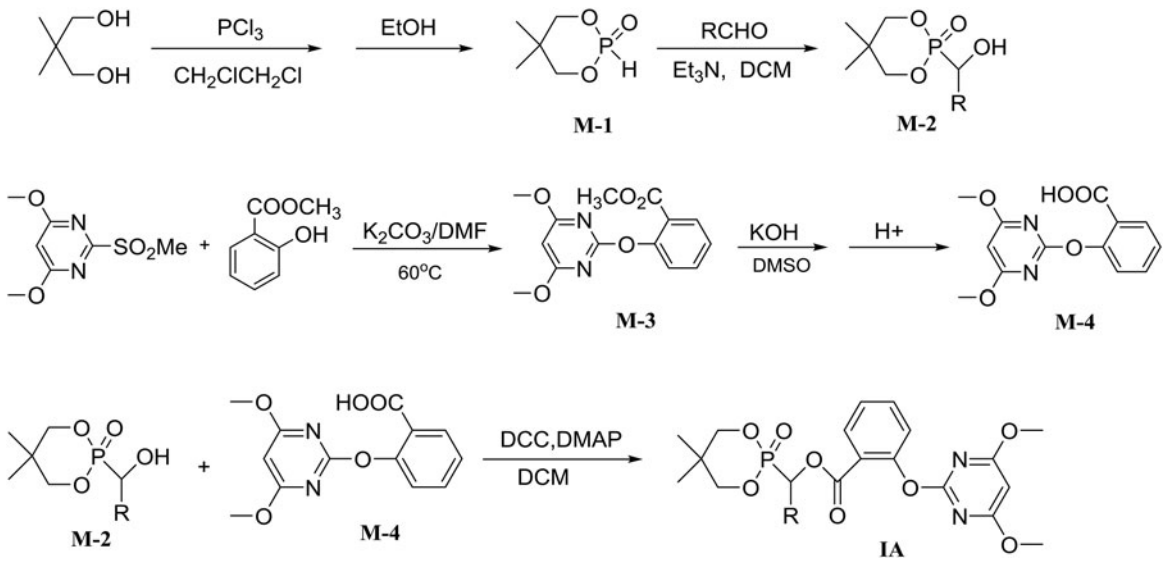

Scheme 1. Synthetic route for the title compounds **IA**.

neopentyl glycol, phosphorus trichloride and ethanol yielded **M-1**, which was then reacted with substituted aldehyde in DCM using triethylamine as catalyst to give **M-2**. The title compound **IA** could be synthesized by condensation of **M-2** and **M-4**, which was prepared by the hydrolysis of compound **M-3**. **M-3** was obtained starting from methyl 2-hydroxybenzoate by reacting with 4,6-dimethoxy-2-(methylsulfonyl)pyrimidine in DMF with K_2CO_3 as base (Scheme 1).

All the title compounds were characterized with ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and HRMS, all the title compounds excepted **IA-2** and **IA-4** were further identified via elemental analysis. Physical properties are summarized in Table S1 (Supplemental Materials).

In the ^{1}H NMR spectra, the signal of pyrimidin-2-y proton appeared as singlet. The proton signals corresponding to methyl, methoxy and methylidyne attached with phosphorus appear as singlet, singlet and two doublets, respectively. In the ^{1}H NMR spectra of the title compounds, the chemical shifts of aromatic protons appeared at 6.85–8.18 ppm. As for the compounds with aromatic groups as R, the proton signal corresponding to the methylidyne group attached with phosphorus appears at 5.37–6.92 as symmetric doublets, due to the coupling with phosphorus. ^{31}P NMR chemical shifts of the title compounds appeared as a singlet at δ 6.04-13.18 ppm.

Herbicidal activity tests

The herbicidal activities of the phosphonates **IA-1**-**IA-13** were evaluated at a rate of 200 g ai/ha in a set of experiments in a greenhouse. They were tested for a pre-emergency and post-emergency inhibitory effect against *Triticum aestivum*, *Echinochloa crusgalli*, *Sorghum bicolor*, *Brassica campestris*, *Raphanus sativus* L, and *Cucumis sativus*.

The bioassay of the herbicidal activities of the title compounds **IA** were carried out at a dose of 200 mg/L in a set of experiments in a greenhouse. All the title compounds **IA** were tested for the growth inhibitory effect of the weed root and stem against wheat, barnyard grass, broomcorn, rape, radish, and cucumber.

From the data of Tables S2 and S3, most of the title compounds exhibited poor inhibitory effect on the growth of the root and stem against the tested barnyard grass, and broomcorn. A part of title compounds showed good to excellent inhibitory activity on the growth of the root and stem against rape, radish, and cucumber. Especially, compounds **IA-2** and **IA-3** shown excellent inhibitory activity against almost all the tested weeds. Compounds **IA-2** and **IA-3** were further tested at the rates of 450, 225, and 112.5 g ai/ha for pre-emergency and post-emergency herbicidal activity and against barnyard grass, crab grass, green bristlegrass, small goosefoot, leaf mustard and common amaranth. As shown in Tables S4 and S5, compounds **IA-2** and **IA-3** exhibited good to excellent inhibitory activity for pre-emergency and post-emergency herbicidal activity against small goosefoot, leaf mustard and common amaranth at the rates of 450, 225, and 112.5 g ai/ha, which shown that compounds **IA-2** and **IA-3** exhibited better herbicidal activity against the tested monocotyledonous weeds than that against dicotyledonous weeds.

The herbicidal activities (Tables S2–S5) are presented in the Supplemental Materials.

Experimental

All melting points (m.p.) were obtained with a digital model X-5 apparatus and are uncorrected. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded at Varian Mercury-Plus 600 or plus-400 using $CDCl_3$ or DMSO-d_6 as the solvent and tetramethysilane as internal standards. Infrared spectra were recorded in potassium bromide pellets with a Nicolet Avatar 360 Fourier transform infrared (FTIR) spectrophotometer. Elemental analysis was measured with an Elementar Vario EL III elementary analyzer. Mass spectra were performed on a Finnigan Trace MS 2000 spectrometer. All chemicals or reagents used for syntheses were commercially available,

were of AR grade, and were used as received. Furfural, 2-thiophene formaldehyde, triethylamine are distilled before use. Dichloromethane need to be treated to be anhydrous before use. All other solvents and reagents were analytical reagent and used directly without purification.

All of the compounds **IA** were synthesized according to the reported methods (Scheme 1).[14–16] The details of the synthetic procedure were supplied in the Supplemental Materials together with sample 1H and ^{13}C NMR spectra and HRMS of the products (Figures S1–S52).

1-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)ethyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-1)

White solid; yield: 85%, m.p. 95-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, J = 7.8 Hz, 1H, phenyl-H), 7.66 (t, J = 7.7 Hz, 1H, phenyl-H), 7.39 (t, J = 7.6 Hz, 1H, phenyl-H), 7.31 (s, 1H, phenyl-H), 5.80 (s, 1H, pyrimidinyl-H), 5.55 (p, J = 7.2 Hz, 1H, PCHO), 4.12-3.93 (m, 4H, 2×(OCH_2)), 3.82 (s, 6 H, 2×(OCH_3)), 1.63 (s, 3H, CH_3), 1.24 (s, 3H, CH_3) , 0.92 (s, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 173.06, 163.96, 151.60, 135.30, 131.63, 126.50, 124.13, 123.87, 84.42, 77.85, 77.78, 77.15, 77.08, 65.28, 63.67, 54.63, 32.39, 32.31, 21.55, 20.16, 14.77; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 13.16; HRMS (ESI): calcd. for $C_{20}H_{25}N_2O_8P$; $[M+H]^+$ 453.1421, found: 453.1429. Elemental Anal. Calcd for $C_{20}H_{25}N_2O_8P$: C, 53.10; H, 5.57. N, 6.19; Found: C, 53.21; H, 5.77; N, 6.01.

1-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)propyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-2)

White solid; yield: 63%, m.p. 80-81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (dd, J = 7.8, 1.5 Hz, 1H, phenyl-H), 7.56 (td, J = 8.1, 1.6 Hz, 1H, phenyl-H), 7.31-7.25 (m, 1H, phenyl-H), 7.19 (s, 1H, phenyl-H), 5.68 (s, 1H, pyrimidinyl-H), 5.44-5.37 (m, 1H, PCHO), 4.34-3.84 (m, 4H, 2×(OCH_2)), 3.71 (s, 6H, 2×(OCH_3)), 1.12 (s, 2H, CH_2CH_3), 0.84-0.77 (m, 3H, CH_3), 0.78 (s, 6H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 173.10, 164.16, 164.00, 163.95, 151.98, 135.48, 131.89, 126.59, 124.60, 123.26, 84.17, 77.75, 77.68, 77.01, 76.95, 69.88, 68.31, 54.59, 32.35, 32.28, 31.42, 22.81, 22.52, 21.54, 20.09, 14.42, 10.24, 10.12; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 12.66; HRMS (ESI): calcd. for $C_{21}H_{27}N_2O_8P$; $[M+H]^+$ 467.1578, found: 467.1580.

(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(phenyl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-3)

Yellow solid; yield: 81%, m.p.107-109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13 (dd, J = 7.8, 1.5 Hz, 1H, phenyl-H), 7.61 (td, J = 8.1, 1.7 Hz, 1H, phenyl-H), 7.46-7.41 (m, 2H, phenyl-H), 7.35 (dd, J = 11.4, 3.9 Hz, 1H, phenyl-H), 7.31-7.28 (m, 3H, phenyl-H), 7.24 (s, 1H, phenyl-H), 6.45 (d, J = 12.5 Hz, 1H, PCHO), 5.67 (s, 1H, pyrimidinyl-H), 4.32-3.95 (m, 4H, 2×(OCH_2)), 3.72 (s, 6H, 2×(OCH_3)), 1.18 (s, 3H, CH_3), 0.85 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 172.95, 163.87, 163.41, 163.32, 151.95, 135.41, 133.67, 131.68, 129.10, 128.76, 128.37, 128.32, 126.55, 124.45, 123.53, 84.37, 77.76, 77.70, 77.27, 77.20, 70.25, 68.68, 55.37, 54.52, 32.43, 21.60, 19.93, 14.43; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 9.15; HRMS (ESI): calcd. for $C_{25}H_{27}N_2O_8P$; $[M+H]^+$ 515.1578, found: 515.1574; Elemental Anal. Calcd for $C_{25}H_{27}N_2O_8P$: C, 58.37; H, 5.29. N, 5.45; Found: C, 58.54; H, 5.46; N, 5.43.

(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(furan-2-yl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-4)

Yellow solid; yield: 67%, 139-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (dd, J = 7.8, 1.5 Hz, 1H, phenyl-H), 7.55 (td, J = 8.1, 1.6 Hz, 1H, furyl-H), 7.28 (d, J = 7.6 Hz, 1H, phenyl-H), 7.24 (s, 1H, phenyl-H), 7.17 (d, J = 8.1 Hz, 1H, furan-2-yl), 6.54-6.48 (m, 2H, furyl-H), 6.23 (s, 1H, PCHO), 5.55 (s, 1H, pyrimidinyl-H), 4.57-3.82 (m, 4H, 2×(OCH_2)), 3.65 (s, 6H, 2×(OCH_3)), 1.20 (s, 3H, CH_3), 0.80 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 172.81, 163.73, 163.42, 163.35, 151.77, 146.20, 144.96, 135.54, 131.65, 126.52, 124.17, 123.51, 112.64, 112.58, 111.28, 84.43, 78.22, 78.16, 77.59, 77.53, 63.91, 62.27, 54.42, 32.41, 32.33, 21.57, 19.90; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 6.04; HRMS (ESI): calcd. for $C_{23}H_{25}N_2O_9P$; $[M+H]^+$ 505.1370, found: 505.1371.

(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(4-fluorophenyl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-5)

White solid; yield: 85%, m.p. 110-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (dd, J = 7.8, 1.5 Hz, 1H, phenyl-H), 7.55 (td, J = 8.1, 1.6 Hz, 1H, phenyl-H), 7.36 (td, J = 6.9, 1.5 Hz, 2H, phenyl-H), 7.29 (dd, J = 11.4, 3.8 Hz, 1H, phenyl-H), 7.18(s, 1H, phenyl-H),6.90 (t, J = 8.6 Hz, 2H, phenyl-H) , 6.35 (d, J = 12.6 Hz, 1H, PCHO), 5.61 (s, 1H, pyrimidinyl-H), 4.30-3.89 (m, 4H, 2×(OCH_2)), 3.65 (s, 6H, 2×(OCH_3)), 1.11 (s, 3H, CH_3), 0.80 (s, 3H, CH_3); ^{13}C NMR (101 Hz, DMSO-d_6) δ: 172.89, 163.87, 163.76, 163.41, 163.33, 161.42, 151.84, 135.39, 131.59, 130.83, 130.75, 130.69, 129.86, 126.51, 124.33, 123.54, 84.29, 77.68, 77.60, 77.23, 77.17, 69.17, 67.60, 54.49, 32.41, 32.33, 21.55, 19.87; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 9.04. HRMS (ESI): calcd. for $C_{25}H_{26}FN_2O_8P$; $[M+H]^+$ 533.1482, found:533.1486; Elemental Anal. Calcd for $C_{25}H_{26}FN_2O_8P$: C, 56.39; H, 4.92; N, 5.26; Found:56.67; H, 4.68; N,; 5.05.

(4-bromophenyl)(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)methyl 2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-6)

White solid; yield: 63%, m.p. 135-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (d, J = 1.5 Hz, 1H, phenyl-H), 7.58 (td, J = 8.1, 1.6 Hz, 1H, phenyl-H), 7.40 (d, J = 1.5 Hz, 2H, phenyl-H), 7.31 (d, J = 11.4, 3.8 Hz, 1H, phenyl-H), 7.20(s, 1H, phenyl-H), 6.90 (t, J = 8.6 Hz, 2H, phenyl-H) , 6.40 (d, J = 12.6 Hz, 1H, PCHO), 5.57 (s, 1H, pyrimidinyl-H), 4.31-3.90 (m, 4H, 2×(OCH_2)), 3.66 (s, 6H, 2×(OCH_3)), 1.14 (s, 3H, CH_3), 0.83 (s, 3H, CH_3); ^{13}C NMR (101 MHz,

DMSO-d_6) δ: 166.40, 166.31, 159.91, 136.38, 133.61, 133.59, 131.94, 131.29, 130.21, 130.16, 122.48, 122.45, 120.02, 118.13, 113.88, 78.21, 78.14, 77.57, 77.50, 70.33, 68.75, 32.55, 32.47, 21.60, 20.01; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 9.51; HRMS (ESI): calcd. for $C_{25}H_{26}BrN_2O_8P$; $[M+H]^+$ 593.0683, found:593.0683; Elemental Anal. Calcd for $C_{25}H_{26}BrN_2O_8P$: C, 50.60; H, 4.42; N, 4.72; Found: C, 50.63; H, 4.60; N, 4.60.

(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(3-nitrophenyl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy) benzoate (IA-7)

White solid; yield: 66%, m.p.150-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (d, J = 1.6 Hz, 1H, phenyl-H), 8.18 (d, J = 8.1 Hz, 1H, phenyl-H), 8.13 (dd, J = 7.9, 1.5 Hz, 1H, phenyl-H), 7.83 (d, J = 7.9 Hz, 1H, phenyl-H), 7.68-7.61 (m, 1H, phenyl-H), 7.49 (t, J = 8.0 Hz, 1H, phenyl-H), 7.38 (td, J = 7.8, 0.9 Hz, 1H, phenyl-H), 7.29 (d, J = 0.6 Hz, 1H, phenyl-H), 7.23 (s, 1H, phenyl-H), 6.51 (d, J = 13.5 Hz, 1H, PCHO), 5.65 (s, 1H, pyrimidinyl-H), 4.47-4.01 (m, 4H, 2×(OCH_2)), 3.72 (s, 6H, 2×(OCH_3)), 1.20 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 172.88, 163.71, 163.45, 163.36, 151.87, 148.06, 135.88, 135.53, 135.08, 135.02, 131.56, 130.57, 126.57, 124.33, 124.20, 123.36, 123.27, 84.23, 77.90, 77.83, 77.45, 77.39, 68.81, 67.26, 54.50, 32.46, 32.39, 21.55, 19.83; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 7.94; HRMS (ESI): calcd. for $C_{25}H_{26}N_3O_{10}P$; $[M+H]^+$ 560.1429, found:560.1438.

(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(p-tolyl) methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-8)

White solid; yield 56%, m.p. 132-135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (dd, J = 7.7, 1.5 Hz, 1H, phenyl-H), 7.59 (t, J = 7.8 Hz, 1H, phenyl-H), 7.36-7.28 (m, 3H, phenyl-H), 7.22 (s, 1H, phenyl-H), 7.07 (d, J = 8.0 Hz, 2H, phenyl-H), 6.40 (d, J = 12.4 Hz, 1H, PCHO), 5.64 (s, 1H, pyrimidinyl-H), 4.31-3.93 (m, 4H, 2×(OCH_2)), 3.70 (s, 6H, 2×(OCH_3)), 2.30 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 0.84 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 172.94, 163.84, 163.50, 163.41, 151.88, 138.65, 138.63, 135.35, 131.64, 130.58, 130.56, 129.33, 128.45, 128.39, 126.54, 124.42, 123.67, 84.34, 77.72, 77.65, 77.24, 77.17, 70.06, 68.47, 54.52, 32.44, 32.36, 21.62, 21.23, 19.94; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 9.46. HRMS (ESI): calcd. for $C_{26}H_{29}N_2O_8P$; $[M+H]^+$ 529.1734, found: 529.1736. Elemental Anal. Calcd for $C_{26}H_{29}N_2O_8P$: C, 59.09; H, 5.53; N, 5.30; Found: C, 59.53; H, 5.85; N, 5.12.

(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(4-methoxyphenyl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy) benzoate (IA-9)

White solid; yield: 79%, m.p. 112-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (dd, J = 7.2, 1.5 Hz, 1H, phenyl-H), 7.62 (td, J = 8.2, 1.6 Hz, 1H, phenyl-H), 7.43 (td, J = 6.8, 1.5 Hz, 1H, phenyl-H), 7.36 (dd, J = 11.5, 3.8 Hz, 2H, phenyl-H), 6.97 (t, J = 8.6 Hz, 2H, phenyl-H), 6.42 (d, J = 12.6 Hz, 1H, PCHO), 5.68 (s, 1H, pyrimidinyl-H), 4.37-3.96 (m, 1H, 2×(OCH_2)), 3.72, (s, 3H, CH_3), 3.72 (s, 6H, 2×(OCH_3)), 1.18 (s, 3H, CH_3), 0.87 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 166.70, 166.60, 160.05, 136.38, 131.10, 129.86, 129.81, 125.68, 120.02, 118.08, 114.41, 113.73, 77.92, 77.85, 77.36, 77.29, 70.36, 68.76, 55.65, 32.52, 32.44, 21.61, 20.03; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 10.38; HRMS (ESI): calcd. for $C_{26}H_{29}N_2O_9P$; $[M+Na]^+$ 583.1242, found: 583.1256; Elemental Anal. Calcd for $C_{26}H_{29}N_2O_9P$: C, 57.35; H, 5.37; N, 5.14; Found: C, 57.46; H, 5.76; N, 5.01.

(3-chlorophenyl)(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-10)

White solid; yield: 62%, m.p. 127-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (dd, J = 7.8, 1.4 Hz, 1H, phenyl-H), 7.63 (td, J = 8.1, 1.6 Hz, 1H, phenyl-H), 7.45 (d, J = 1.3 Hz, 1H, phenyl-H), 7.39-7.32 (m, 2 H, phenyl-H), 7.28-7.26 (m, 1H, phenyl-H), 7.25-7.20 (m, 1H, phenyl-H), 6.41 (d, J = 13.1 Hz, 1H, PCHO), 5.69 (s, 1H, pyrimidinyl-H), 4.40-3.98 (m, 3H, 2×(OCH_2)), 3.73 (s, 6H, 2×(OCH_3)), 1.18 (s, 3H, CH_3), 0.87 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 172.94, 163.80, 163.42, 163.34, 151.94, 136.08, 135.50, 133.46, 131.69, 130.73, 129.19, 128.20, 128.15, 127.08, 127.03, 126.47, 124.44, 123.34, 84.40, 77.84, 77.78, 69.35, 67.78, 54.53, 32.44, 32.37, 21.56, 19.87; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 8.49; HRMS (ESI): calcd. for $C_{25}H_{26}ClN_2O_8P$; $[M+H]^+$ 549.1188, found: 549.1185; Elemental Anal. Calcd for $C_{25}H_{26}ClN_2O_8P$: C, 54.70; H, 4.77; N, 5.10; Found: C, 54.87; H, 5.15; N, 5.96.

(2,4-dichlorophenyl)(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy) benzoate (IA-11)

White solid; yield: 67%, m.p. 141-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, J = 7.8 Hz, 1H, phenyl-H), 7.71 (d, J = 8.4 Hz, 1H, phenyl-H), 7.62 (t, J = 7.7 Hz, 1H, phenyl-H), 7.38 (s, 1H, phenyl-H), 7.34 (d, J = 7.5 Hz, 1H, phenyl-H), 7.27 (s, 1H, phenyl-H),7.24 (d, J = 8.9 Hz, 1H, phenyl-H), 6.92 (d, J = 10.8 Hz, 1H, PCHO), 5.70 (s, 1H, pyrimidinyl-H),4.30-3.92 (m, 4H, 2×(OCH_2)), 3.75 (s, 6H, 2×(OCH_3)), 1.21 (s, 3H, CH_3), 0.90 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 172.94, 163.66, 151.69, 135.53, 134.96, 134.93, 134.02, 133.90, 131.75, 130.47, 129.32, 128.07, 126.59, 124.44, 123.30, 84.31, 78.31, 66.83, 65.22, 54.57, 32.46, 32.39, 21.34, 20.04; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 7.96; HRMS (ESI): calcd. for $C_{25}H_{25}Cl_2N_2O_8P$; $[M+H]^+$ 583.0798, found: 583.0798; Elemental Anal. Calcd for $C_{25}H_{25}Cl_2N_2O_8P$: C, 51.47; H, 4.32; N, 4.80; Found: C, 51. 08; H, 5.56; N, 4. 59.

(3,4-dichlorophenyl)(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy) benzoate (IA-12)

White solid; yield: 82%, m.p. 131-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (t, J = 7.8 Hz, 1H, phenyl-H), 7.56

(s, 1H, phenyl-H), 7.42-7.35 (m, 2H, phenyl-H), 7.33-7.31 (m, 2H, phenyl-H), 7.26 (s, 1H, phenyl-H), 6.40 (d, $J = 13.2$ Hz, 1H, PCHO), 5.71 (s, 1H, pyrimidinyl-H), 4.47-4.01 (m, 4H, 2×(OCH_2)), 3.75 (s, 6H, 2×(OCH_3)), 1.21 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ: 172.91, 163.73, 163.53, 163.45, 151.85, 135.49, 134.66, 132.16, 132.14, 131.66, 131.58, 131.12, 130.48, 130.42, 128.81, 128.76, 126.56, 124.36, 123.41, 84.32, 77.87, 77.81, 77.44, 77.37, 68.58, 67.02, 54.53, 32.45, 32.38, 21.55, 19.85; ^{31}P NMR (162 MHz, $CDCl_3$) δ: 8.14. HRMS (ESI): calcd. for $C_{25}H_{25}Cl_2N_2O_8P$; $[M+H]^+$ 583.0798, found: 583.0801; Elemental Anal. Calcd for $C_{25}H_{25}Cl_2N_2O_8P$: C, 51.47; H, 4.32; N, 4.80; Found: C, 51. 97; H, 4.80; N, 4. 89.

(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphinan-2-yl)(thiophen-2-yl)methyl-2-((4,6-dimethoxypyrimidin-2-yl)oxy)benzoate (IA-13)

White solid; yield:55%, m.p.115-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (d, $J = 7.7$ Hz, 1H, phenyl-H), 7.63 (t, $J = 7.7$ Hz, 1H, phenyl-H), 7.36 (t, $J = 7.6$ Hz, 1H, phenyl-H), 7.30 (d, $J = 5.1$ Hz, 1H, phenyl-H), 7.25 (d, $J = 7.4$ Hz, 2H, thienyl-H), 6.95 (t, $J = 4.3$ Hz, 1H, thienyl-H), 6.73 (d, $J = 13.4$ Hz, 1H, PCHO), 5.60 (s, 1H, pyrimidinyl-H), 4.61-4.03 (m, 4H, 2×(OCH_2)), 3.72 (s, 6H, 2×(OCH_3)), 1.28 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^{13}C NMR (151 MHz, DMSO-d_6) δ: 173.83, 164.74, 164.25, 164.20, 152.88, 136.50, 135.45, 132.53, 130.77, 130.72, 129.83, 128.24, 127.51, 125.22, 124.48, 85.40, 78.92, 78.88, 78.45, 78.41, 66.10, 65.01, 55.45, 33.42, 33.37, 22.63, 20.83. ^{31}P NMR (162 MHz, $CDCl_3$) δ: 7.19. HRMS (ESI): calcd. for $C_{23}H_{25}N_2O_8PS$; $[M+H]^+$ 521.1142, found: 521.1142; Elemental Anal. Calcd for $C_{23}H_{25}Cl_2N2O_8PS$: C, 53.07; H, 4.84; N, 5.38; S, 6.16; Found: C, 52.69; H, 5.18; N,5.09; S, 6.39.

Conclusions

In conclusion, novel substituted heterocyclic phosphorus compounds containing pyrimidine structure of diaryl ethers were rationally designed and synthesized. The herbicidal activity of the title compounds against the growth of the root and stem against rape, radish and cucumber was carried out. The bioassay of herbicidal activity revealed that most of the compounds showed good herbicidal inhibitory activities against *Amaranthus retroflexus*. The compounds **IA-2** and **IA-3** exhibited remarkable post-emergency herbicidal activity against the tested monocotyledonous weed at the dosage of 112.5 g ai/ha, which will provide more useful information for the further design and discovery of compounds with high herbicidal activity.

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