Synthesis and Biological Activity of 4-[(Substituted Phenoxyacetoxy) methyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one

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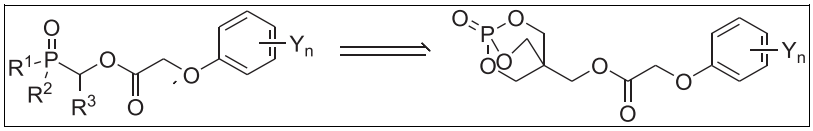

A series of novel 4-[(substituted phenoxyacetoxy)methyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one **4a–o** were synthesized. Their structures were confirmed by IR, ^{1}H NMR, mass spectroscopy, and elemental analyses. The results of preliminary bioassays show that some of the title compounds exhibit moderate to good herbicidal and fungicidal activities. For example, the title compounds **4b**, **4c**, **4f**, **4h**, **4i**, and **4j** possess 90–100% inhibition against the growth of roots of both rape and barnyard grass at 10 mg/L. Moreover, the title compounds **4f**, **4g**, and **4h** possess 75–89% inhibition against *Botrytis cinerea* at the concentration of 50 mg/L.

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INTRODUCTION

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. In our previous work, a series of 1-(substituted phenoxyacetoxy)alkylphosphonates, as potent pyruvate dehydrogenase complex (PDHc) inhibitors, were synthesized and showed notable bioactivities [1–3] (Scheme 1). To determine the effect of heterocyclic groups on the bioactivity, a series of heterocycle-containing 1-(substituted phenoxyacetoxy)alkylphosphonates [3] and phosphinates [4] were designed and synthesized, and some of them exhibited excellent herbicidal and fungicidal activities [3,4].

On the other hand, heterocyclic compounds containing a symmetric caged bicyclic phosphate have received much attention. Several of these compounds exhibited useful biological activity and could be particularly used as insecticides, herbicides, fungicides, and plant growth regulators [5–7]. Moreover, a variety of the reports regarding synthetic studies of cyclophosphonate analogs have been presented because phosphorus-containing heterocyclic moiety can increase bioactivity [8] and stability [9] by replacing the simple phosphonate. This encouraged us to replace the phosphonate group with symmetric caged bicyclic phosphate structure. Therefore, a series of novel 4-[(substituted phenoxyacetoxy)methyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one **4** (Scheme 2) was synthesized and their herbicidal and fungicidal activity were evaluated.

RESULTS AND DISCUSSION

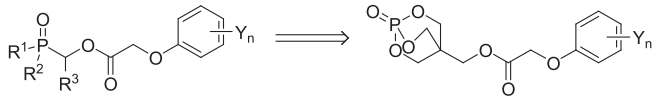
Caged bicyclic phosphate **4a–o** were synthesized by the condensation of 4-(hydroxymethyl)-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one **1** and substituted phenoxyacetyl chloride **3** in the presence of triethylamine (Scheme 2). Triethylamine is an important catalyst, which is essential to the condensation reaction, because the caged bicyclic phosphates **4** were easily regenerated to the starting material in strong alkaline medium. The 4-(hydroxy methyl)-2,6,7-trioxa-1-phosphabicyclo[2.2.2] octane-1-one **1** could be prepared by the treatment of the pentaerythritol with phosphorus oxychloride in dioxane. Substituted phenoxyacetic acids **2** and substituted phenoxyacetyl chlorides **3** were prepared according to the reported methods [3,4].

The structures of **4a–o** were characterized by ^{1}H NMR, IR, MS, and elemental analysis. Compound **4j** was analysed by X-ray single-crystal diffraction [10].

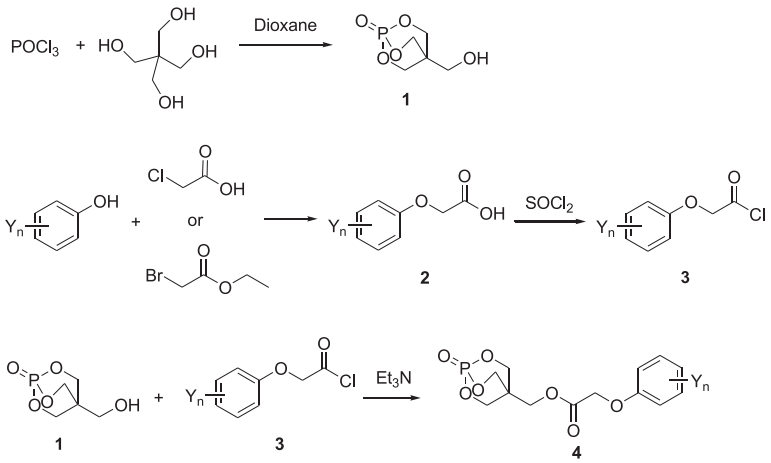
The ^{1}H NMR spectrum showed that the chemical shifts of aromatic protons appeared at 6.8–7.6 ppm. The proton signal corresponding to three methylene groups on the bicyclic ring appeared as a doublet due to the coupling with phosphorus. The protons of the methylene group between the bicyclic ring and oxygen appeared as a singlet at about 4.0 ppm. The protons of the methylene group between phenoxy group and carbonyl group also appeared as a singlet at 4.8–4.9 ppm.

The corresponding IR spectrum revealed normal absorption bands at 1750–1760 cm^{-1} (C=O). The two or three bands in the 1490–1640 cm^{-1} region were attributed to

Scheme 1. Design of caged bicyclic phosphates.



Scheme 2. Synthesis of caged bicyclic phosphates **4**.



aromatic rings systems. A stretching vibration for P-O-C appeared at 1020–1040 cm^{-1}. An asymmetric stretching vibration for C-O-C appeared near 1210 cm^{-1} and a symmetric stretching vibration for C-O-C was found near 1090 cm^{-1}. The mass spectra of the title compounds **4** revealed the existence of the molecular ion peaks, which were in good accordance with the given structures of products.

Biological activity. ***Herbicidal activity.*** The preliminary herbicidal activity of **4a–o** were evaluated against *Brassica napus* (rape) and *Echinochloa crusgalli* (barnyard grass) at the concentration of 100 and 10 mg/L using the known procedure [11]. 2,4-Dichlorophenoxy acetic acid (2,4-D), a commercially available herbicide, was selected as a positive control. As shown in Table 1, most of title compounds displayed good inhibitory effect on the growth

Table 1

Structure and herbicidal activity of compounds **4a–o**.

		Relative inhibition (stem%/root%)			
		Barnyard grass		Rape	
Compound	Y_n	100 mg/L	10 mg/L	100 mg/L	10 mg/L
4a	H	82/94	0/89	83/99	23/82
4b	2,4-Cl_2	52/97	52/94	99/99	92/95
4c	2-Cl	55/97	48/91	97/99	90/95
4d	4-Cl	42/97	37/83	90/97	63/92
4e	2-F	55/80	31/69	49/92	24/53
4f	3-CF_3	78/97	50/91	97/99	87/92
4g	4-CH_3	22/94	4/51	88/97	34/79
4h	2-CH_3, 4-Cl	65/97	50/97	99/100	92/98
4i	3-CH_3, 4-Cl	63/97	55/91	97/100	90/98
4j	2-Cl, 4-F	54/95	43/95	99/100	93/100
4k	2-Cl, 5-CH_3	37/92	3/54	88/99	75/93
4l	2,3-$(CH_3)_2$	50/89	18/44	97/99	64/86
4m	4-F	78/94	18/89	97/99	64/86
4n	3-Me	39/94	0/83	77/99	36/91
4o	4-*t*-Bu	43/72	25/67	49/79	5/9
2,4-D		34/98	33/98	94/100	94/99

Table 2

Structure and post-emergence herbicidal activity of compounds **4a–o**.

Compound	Y_n	Ech	Dig	Bra	Brj	Amr	Chs
4a	H	28	25	4	0	26	0
4b	2,4-Cl_2	0	0	0	0	0	0
4c	2-Cl	0	0	0	90	70	80
4d	4-Cl	0	0	0	0	0	70
4e	2-F	0	0	0	100	100	100
4f	3-CF_3	0	0	0	0	0	60
4g	4-Me	0	0	0	100	80	80
4h	2-Me, 4-Cl	0	0	0	0	0	70
4i	3-Me, 4-Cl	0	0	0	0	0	70
4j	2-Cl, 4-F	0	0	0	60	40	70
4k	2-Cl, 5-Me	0	0	0	0	40	0
4l	2,3-Me_2	22	0	12	40	33	0
4m	4-F	20	0	41	0	39	0
4n	3-Me	30	13	0	0	21	0
4o	4-*t*-Bu	25	30	79	0	85	0
Clacyfos		0	15	92	93	96	93

Inhibitory potency (%) on the growth of plants at a rate of 150 g ai/ha in the greenhouse.
Ech, barnyard grass; Dig, crab grass; Bra, rape; Brj, leaf mustard; Amr, common amaranth; Chs, small goosefoot.

of roots of dicotyledons and monocotyledons, especially compounds **4b**, **4c**, **4f**, and **4h–j** with >90% inhibitory effect against the growth of roots of rape and barnyard grass at 100 and 10 mg/L. The title compounds showed much higher herbicidal activities against dicotyledons than monocotyledons. For example, compounds **4b**, **4c**, and **4h–j** with >90% inhibitory effect against the growth of stems of dicotyledonous rape at 10 mg/L, but none of compounds **4** showed more than 55% inhibitory effect against the growth of stems of monocotyledonous barnyard grass at the same concentration.

On the basis of the preliminary bioassay, further bioassays were carried out in the greenhouse to confirm their post-emergence herbicidal activity on barnyard grass (*Echinochloa crusgalli*), crab grass (*Digitaria sanguinalis*), rape (*Brassica napus*), leaf mustard (*Brassica juncea*), common amaranth (*Amaranthus retroflexus*), and small goosefoot (*Chenopodium serotinum*). A commercially available herbicide, 1-(2,4-dichlorophenoxyacetoxy)ethylphosphonate (clacyfos), was selected as a positive control.

As shown in Table 2, compounds **4c**, **4e**, and **4g** exhibited good post-emergence herbicidal activity against tested dicotyledonous plants, especially **4e** displayed a 100% inhibition effect against all tested broad-leaved weeds at a rate of 150 g ai/ha. However, there was no activity against monocot weeds. It was observed that compounds with one substitution as Y_n showed better herbicidal activity than the compounds with two substitutions. The compounds with 2,4-Cl_2; 2-Me,4-Cl; 3-Me,4-Cl; 2-Cl,4-F; 2-Cl,5-Me; and 2,3-Me_2 as Y_n showed much weaker or no herbicidal activity. The 2-F substitution on the phenoxybenzene ring was most promotive for herbicidal activity followed by 4-Me or 2-Cl.

Fungicidal activity. The fungicidal activities of compounds **4a–o** were evaluated by the classic plate method at the concentration of 50 mg/L, which was described in the experimental part. The six fungi *Fusarium oxysporum* (fusarium wilt of cotton), *Rhizoctonia solani* (rice sheath blight), *Botrytis cinerea* (cucumber gray mold), *Gibberella zeae* (wheat head scab), *Dothiorella gregaria* (apple ring dot), and *Colletotrichum gossypii* (cotton anthracnose) belong to the group of field fungi and were isolated from corresponding crops. As listed in Table 3, most of the compounds display moderate fungicidal activity against the aforementioned six fungi. For example, compounds **4f–h** possessed 75–89% inhibitory activity against cucumber gray mold.

In conclusion, a series of novel 4-(substituted phenoxyacetoxy)methyl-2,6,7-trioxa-1-phosphabicyclo [2.2.2]octane-1-one **4a–o** were synthesized. The results of preliminary bioassays showed compounds **4b**, **4c**, **4f**, and **4h–j** displayed notable herbicidal activity against the tested plants, with more than 90% inhibitory rate to the root growth at the concentration of 10 mg/L. In addition, compounds **4f–h** possessed 75–89% inhibitory activity against cucumber gray mold. These results indicated that the title compounds **4** could be modified and used as lead compounds for further study.

EXPERIMENTAL

Chemicals and reagents were obtained from commercial sources, and all of the solvents were dried and purified by standard techniques prior to use. Column chromatography was carried out with Merck silica gel (200–300 mesh).

Table 3

Fungicidal activity of compounds **4a–o**.

Compound	Y_n	Fus	Rhi	Bot	Gib	Dot	Col
4a	H	20.83	15.46	22.73	22.22	4.17	16.67
4b	2,4-Cl_2	45.45	35.92	72.97	25.93	34.78	18.45
4c	2-Cl	22.73	60.19	70.27	29.63	30.43	15.30
4d	4-Cl	22.73	38.83	64.86	29.63	34.78	38.76
4e	2-F	36.36	63.11	59.46	33.33	39.13	33.90
4f	3-CF_3	45.45	34.95	89.19	37.04	26.09	45.45
4g	4-Me	31.82	55.34	75.68	18.52	26.09	13.64
4h	2-Me, 4-Cl	27.27	44.66	78.38	25.93	39.13	27.82
4i	3-Me, 4-Cl	40.91	57.28	70.27	29.63	39.13	29.63
4j	2-Cl, 4-F	38.56	35.99	62.95	24.93	36.76	18.55
4k	2-Cl, 5-Me	36.92	47.25	60.12	25.43	28.29	16.45
4l	2,3-Me_2	4.17	36.08	27.27	25.93	37.50	4.17
4m	4-F	4.17	27.84	36.36	33.33	16.67	8.33
4n	3-Me	8.33	15.46	31.82	18.52	8.33	0.00
4o	4-*t*-Bu	16.67	5.15	36.36	0.00	-12.50	12.50

Fus, *Fusarium oxysporum*; Rhi, *Rhizoctonia solani*; Bot, *Botrytis cinerea*; Gib, *Gibberella zeae*; Dot, *Dothiorella gregaria*; Col, *Colletotrichum gossypii*.

Melting points (mp) were measured on an X-4 melting point apparatus (Beijing, China) and were uncorrected. IR spectra were recorded as KBr pellets on a Perkin-Elmer Fourier transform infrared spectrophotometer (USA). ^{1}H NMR was recorded on Varian XL-400 spectrometer (Salt Lake City, USA) at 400 MHz using tetramethylsilane as internal standard (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), and m (multiplet). MS spectra were analysed on a Finnigan Trace MS spectrometer (Ramsey, USA). Elemental analyses were performed by a Vario EL III elemental analyser (Hanau, Germany).

Procedure for the synthesis of intermediate 1. To a solution of pentaerythritol (50 mmol) in 1,4-dioxane (30 mL), phosphorus oxychloride (50 mmol) was added dropwise under 90°C. After stirring for 2 h, the reaction solution was heated under reflux for 6 h. A white solid was precipitated, filtered off, and subsequently washed with 1,4-dioxane. The crude product was recrystallized from absolute ethanol, giving 4-(hydroxymethyl)-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one **1** in 94% yield as a white solid.

General procedure for the synthesis of intermediates 3. A mixture containing substituted phenoxyacetyl acid **2** (4.0 mmol) and thionyl chloride (6 mL) was added into a 15 mL flask and refluxed for 5–6 h. Excess thionyl chloride was evaporated off under reduced pressure, and a light yellow oil **3** was obtained, which was used directly without further purification.

General procedure for the synthesis of title compounds 4a–o. A solution of substituted phenoxyacetyl chlorides **3** (5.5 mmol) in acetonitrile (15 mL) was added to a stirred mixture of 4-(hydroxymethyl)-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one **1** (5 mmol) and triethylamine (5.5 mmol) in acetonitrile (20 mL) at 0–5°C. The resultant mixture was stirred for 1 h at room temperature. Acetonitrile was evaporated under reduced pressure, and the crude product was washed with brine. Then the residue was purified by recrystallized with acetonitrile to give the corresponding pure title compounds **4a–o**. Their structures were confirmed by ^{1}H NMR, IR, MS, and elemental analysis. And the physicochemical properties and spectroscopic data for compounds **4a–o** are as follows.

4-[(Phenoxyl)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo [2.2.2]octane-1-one (4a). White solid; yield, 69%; mp, 154–155°C; IR (KBr, cm^{-1}): ν 1768, 1326, 1215, 1160, 1042, 962, 850. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.07 (s, 2H, CH_2O), 4.60 (d, J = 6.4 Hz, 6H, $(CH_2O)_3$), 4.87 (s, 2H, CH_2CO), 6.94-7.31 (m, 4H, Ar-H); MS (70 eV): *m/z*: 314 (M^+); *Anal.* Calcd for $C_{13}H_{15}O_7P$: C, 49.69; H, 4.81. Found: C, 49.20; H, 4.40.

4-[(2,4-Dichlorophenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4b). White solid; yield, 78%; mp, 164–165°C; IR (KBr, cm^{-1}): ν 1765, 1324, 1216, 1091, 1042, 963, 852, 820. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.08 (s, 2H, CH_2O), 4.63 (d, J = 6.4 Hz, 6H, $(CH_2O)_3$), 5.02 (s, 2H, CH_2CO), 7.18–7.64 (m, 3H, Ar-H); MS (70 eV): *m/z*: 382 (M^+); *Anal.* Calcd for $C_{13}H_{13}Cl_2O_7P$: C, 40.75; H, 3.42. Found: C, 40.43; H, 3.59.

4-[(2-Chlorophenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4c). White solid; yield, 68%; mp, 140–142°C; IR (KBr, cm^{-1}): ν 1766, 1325, 1213, 1082, 1043, 962, 851, 827. ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.07 (s, 2H, CH_2O), 4.62 (d, J = 6.4 Hz, 6H, $(CH_2O)_3$), 4.88 (s, 2H, CH_2CO), 6.99–7.36 (m, 4H, Ar-H); MS (70 eV): *m/z*: 348 (M^+); *Anal.* Calcd for $C_{13}H_{14}ClO_7P$: C, 44.78; H, 4.05. Found: C, 44.36; H, 4.15.

4-[(4-Chlorophenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4d). White solid; yield, 67%; mp, 182–183°C; IR (KBr, cm^{-1}): *v* 1779, 1325, 1209, 1164, 1044, 965, 851, 803. ^1H NMR (400 MHz, DMSO-d_6) δ 4.07 (s, 2H, CH_2O), 4.63 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.88 (s, 2H, CH_2CO), 7.00–7.35 (m, 4H, Ar-H); MS (70 eV): *m/z*: 348 (M^+); *Anal.* Calcd for $C_{13}H_{14}ClO_7P$: C, 44.78; H, 4.05. Found: C, 44.60; H, 3.90.

4-[(2-Fluorophenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4e). White solid; yield, 73%; mp, 147–148°C; IR (KBr, cm^{-1}): *v* 1767, 1324, 1234, 1199, 1043, 961, 850. ^1H NMR (400 MHz, DMSO-d_6) δ 4.08 (s, 2 H, CH_2O), 4.62 (d, $J = 6.8$ Hz, 6H, $(CH_2O)_3$), 4.96 (s, 2H, CH_2CO), 6.99–7.28 (m, 4H, Ar-H); MS (70 eV): *m/z*: 332 (M^+); *Anal.* Calcd for $C_{13}H_{14}FO_7P$: C, 47.00; H, 4.25. Found: C, 46.69; H, 4.41.

4-[(3-Trifluoromethylphenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4f). White solid; yield, 69%; mp, 137–139°C; IR (KBr, cm^{-1}): *v* 1766, 1325, 1212, 1082, 1043, 962, 851, 827. ^1H NMR (400 MHz, DMSO-d_6) δ 4.09 (s, 2H, CH_2O), 4.62 (d, $J = 6.0$ Hz, 6H, $(CH_2O)_3$), 5.01 (s, 2H, CH_2CO), 7.29–7.55 (m, 4H, Ar-H); MS (70 eV): *m/z*: 382 (M^+); *Anal.* Calcd for $C_{14}H_{14}F_3O_7P$: C, 43.99; H, 3.69. Found: C, 43.78; H, 4.28.

4-[(4-Methylphenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4g). White solid; yield, 71%; mp, 158–159°C; IR (KBr, cm^{-1}): *v* 1766, 1326, 1214, 1087, 1043, 961, 850, 818. ^1H NMR (400 MHz, DMSO-d_6) δ 2.23 (s, 3H, CH_3), 4.06 (s, 2H, CH_2O), 4.60 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.82 (s, 2H, CH_2CO), 6.84–7.10 (m, 4H, Ar-H); MS (70 eV): *m/z*: 328 (M^+); *Anal.* Calcd for $C_{14}H_{17}O_7P$: C, 51.23; H, 5.22. Found: C, 50.94; H, 51.23.

4-[(4-Chloro-2-mehtyphenoxyl)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4h). White solid; yield, 71%; mp, 143–145°C; IR (KBr, cm^{-1}): *v* 1765, 1325, 1219, 1185, 1043, 962, 850, 822. ^1H NMR (400 MHz, DMSO-d_6) δ 2.19 (s, 3H, CH_3), 4.07 (s, 2H, CH_2O), 4.62 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.90 (s, 2H, CH_2CO), 6.91–7.26 (m, 3H, Ar-H); MS (70 eV): *m/z*: 362 (M^+); *Anal.* Calcd for $C_{14}H_{16}ClO_7P$: C, 46.36; H, 4.45. Found: C, 46.37; H, 4.57.

4-[(4-Chloro-3-methylphenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4i). Yellowish solid; yield, 65%; mp, 122–123°C; IR (KBr, cm^{-1}): *v* 1766, 1324, 1244, 1168, 1044, 962, 849, 811. ^1H NMR (400 MHz, DMSO-d_6) δ 2.28 (s, 3H, CH_3), 4.07 (s, 2H, CH_2O), 4.63 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.86 (s, 2H, CH_2CO), 6.75–7.33 (m, 3H, Ar-H); MS (70 eV): *m/z*: 362 (M^+); *Anal.* Calcd for $C_{14}H_{16}ClO_7P$: C, 46.36; H, 4.45. Found: C, 45.99; H, 4.54.

4-[(2-Chloro-4-fluorophenoxy)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4j). Yellowish solid; yield, 78%; mp, 148–151°C; IR (KBr, cm^{-1}): *v* 1766, 1325, 1229, 1190, 1040, 963, 851. ^1H NMR (400 MHz, DMSO-d_6) δ 4.08 (s, 2H, CH_2O), 4.63 (d, $J = 6.8$ Hz, 6H, $(CH_2O)_3$), 4.99 (s, 2H, CH_2CO), 7.17–7.50 (m, 3H, Ar-H); MS (70 eV): *m/z*: 366 (M^+); *Anal.* Calcd for $C_{13}H_{13}ClFO_7P$: C, 42.58; H, 3.57. Found: C, 42.51; H, 3.57.

4-[(2-Chloro-5-methylphenoxyl)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4k). White solid; yield, 38%; mp, 170–173°C; IR (KBr, cm^{-1}): *v* 1766, 1321, 1202, 1176, 1039, 966, 852, 804. ^1H NMR (400 MHz, DMSO-d_6) δ 2.33 (s, 3H, CH_3), 4.01 (s, 2H, CH_2O), 4.48 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.76 (s, 2H, CH_2CO), 6.64–7.31 (m, 3H, Ar-H); MS (70 eV): *m/z*: 362 (M^+); *Anal.* Calcd for $C_{14}H_{16}ClO_7P$: C, 46.36; H 4.45. Found: C, 46.35; H, 4.47.

4-[(2,3-Dimethylphenoxyl)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4l). White solid; yield, 24%; mp, 183–184°C; IR (KBr, cm^{-1}): *v* 1769, 1309, 1193, 1131, 1038, 970, 855. ^1H NMR (400 MHz, DMSO-d_6) δ 2.21 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 3.98 (s, 2H, CH_2O), 4.43 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.71 (s, 2H, CH_2CO), 6.52–7.06 (m, 3H, Ar-H); MS (70 eV): *m/z*: 342 (M^+);*Anal.* Calcd for $C_{15}H_{19}O_7P$: C, 52.64; H, 5.60. Found: C, 52.86; H, 5.38.

4-[(4-Fluorophenoxyl)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4m). White solid; yield, 84%; mp, 139–140°C; IR (KBr, cm^{-1}): *v* 1768, 1326, 1204, 1159, 1043, 962, 850, 833. ^1H NMR (400 MHz, DMSO-d_6) δ 4.02 (s, 2H, CH_2O), 4.52 (d, $J = 6.8$ Hz, 6H, $(CH_2O)_3$), 4.66 (s, 2H, CH_2CO), 6.85–7.02 (m, 4H, Ar-H); MS (70 eV): *m/z*: 332 (M^+); *Anal.* Calcd for $C_{13}H_{14}FO_7P$: C, 47.00; H, 4.25. Found: C, 47.42; H, 4.03.

4-[(3-Mehthylphenoxyl)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4n). Yellowish solid; yield, 12%; mp, 144–145°C; IR (KBr, cm^{-1}): *v* 1769, 1322, 1206, 1171, 1041, 966, 857. ^1H NMR (400 MHz, DMSO-d_6) δ 2.28 (s, 3H, CH_3), 4.06 (s, 2H, CH_2O), 4.59 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.84 (s, 2H, CH_2CO), 6.78–7.19 (m, 4H, Ar-H); MS (70 eV): *m/z*: 328 (M^+); *Anal.* Calcd for $C_{14}H_{17}O_7P$: C, 51.23; H, 5.22. Found: C, 51.09; H, 4.89.

4-[(4-Butylphenoxyl)acetyloxymethyl]-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-1-one (4o). Yellowish solid; yield, 21%; mp, 200–202°C; IR (KBr, cm^{-1}): *v* 1774, 1325, 1204, 1188, 1047, 965, 852. ^1H NMR (400 MHz, DMSO-d_6) δ 1.25 (s, 9H, $(CH_3)_3$), 4.05 (s, 2H, CH_2O), 4.55 (d, $J = 6.4$ Hz, 6H, $(CH_2O)_3$), 4.84 (s, 2H, CH_2CO), 6.87–7.31 (m, 4H, Ar-H); MS (70 eV): *m/z*: 370 (M^+); *Anal.* Calcd for $C_{17}H_{23}O_7P$: C, 55.13; H, 6.26. Found: C, 55.33; H, 5.93.

Biological activity testing. The preliminary herbicidal activity of title compounds **4a–o** was measured according

to the modified method described previously [11]. A set amount of each sample was dissolved in *N*,*N*-dimethylformamide (DMF) to which a drop of an emulsifier, Tween 80, was added. The solution was then diluted with water until it reached the concentrations required. The amounts of DMF and the emulsifier were set as low as possible but still sufficient to make a uniform emulsion even at high concentrations. A solution (5 mL) was placed on a filter paper (diameter = 5.5 cm) in Petri dishes (diameter = 9.0 cm), and 10 rape seeds were placed on the filter paper after soaking in water for 6 h. The Petri dishes were kept at 28°C for 3 days with 10 h of lighting and 14 h in the dark. The experiments were conducted in three replicates. The lengths of roots and shoots were measured after 72 h of treatment, and the growth inhibitory rate related to untreated control was determined.

The title compounds **4a–o** were further evaluated on dicotyledonous weeds such as rape (*Brassica napus*), leaf mustard (*Brassica juncea*), common amaranth (*Amaranthus retroflexus*) and small goosefoot (*Chenopodium serotinum*), and monocotyledonous weeds such as barnyard grass (*Echinochloa crusgalli*), and crab grass (*Digitaria sanguinalis*) at the rate of 150 g ai/ha. Plastic pots were packed with sandy clay loam soil and water was added up to 3 cm in depth. About 15–20 seeds of plants were sown in the soil at a depth of 5 mm and grown at 20–25°C for a few days. The solution was applied to the foliage of plants grown at two or three leaves with a sprayer at the rate of 150 g ai/ha. All the treatments were replicated three times in a completely randomized design. The test plants were harvested 20 days after sowing and determined for fresh weight.

The fungicidal activity was evaluated by the classic plate method. The samples were dissolved in DMF (0.5–1.0 mL) to the concentration of 1000 mg/L. The solutions (1 mL) were mixed rapidly with thawed potato glucose agar culture medium (9 mL) under 50°C. The mixtures were poured into Petri dishes. After the dishes were cooled, the solidified plates were incubated with 4-mm mycelium disk, inverted, and incubated at 28°C for 48 h. Distilled water was used as the blank control. Three replicates of each test were carried out. The mycelial elongationradius (mm) of fungi settlements was measured after 48 h of culture. The growth inhibitory rates were calculated with the following equation: $I = [(C-T)/C] \times 100\%$. Here, I is the growth inhibitory rate (%), T is the treatment group fungi settlement radius (mm), and C is the radius of the blank control.

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