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Synthesis and herbicidal activity of 2-(substituted phenoxyacetoxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one containing fluorine

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ABSTRACT

A series of novel 2-(substituted phenoxyacetoxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one bearing fluorine **5a-n** and fluorine free **5o-q** were designed and synthesized. The results of bioassay showed that some of the target compounds exhibited excellent herbicidal activities to *Abutilon theophrasti*, *Brassica juncea*, *Amaranthus retroflexus* and *Eclipta prostrata* in post-emergence treatment at a dosage of 150 g ai/ha. It could be found that the type and position of fluorine-containing group as X or Y on benzene ring had a very important effect on herbicidal activity. Compound **5l** 2-[(2-chloro-4-fluorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one showed notable herbicidal activity, with 100% inhibition against *A. theophrasti* and *A. retroflexus*; and compound **5m** 2-(3-trifluoromethylphenoxyacetoxy)(methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one with 100% inhibition against *A. theophrasti* even at a dosage of 75 g ai/ha. Additional crop selectivity testing showed that compounds **5g** 2-(3-trifluoromethylphenoxyacetoxy)(phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one and **5l** are safe to rice, corn, cotton, rape and wheat.

1. Introduction

Due to unique properties of fluorine, such as the highest electronegativity, smallest size next to hydrogen, high thermal stability and lipophilicity, the substitution of hydrogen by fluorine has become a common strategy in drug development [1,2]. A variety of the reports regarding synthetic studies of organofluorine compounds have been presented because they can increase the herbicidal activity [3], fungicidal activity [4] and insecticidal activity [5] of certain compounds. And a number of fluorinated products (such as the herbicides flumioxazin, haloxyfop, flufenatet, tritosulfuron, carfentrazone-ethyl and flumetsulam etc.) have been launched into the market during the past decade (Scheme 1).

In our previous work, a series of 1-(substituted phenoxyacetoxy)alkylphosphonates **I** (Scheme 2) have been synthesized, which was confirmed as competitive inhibitors of pyruvate dehydrogenase complex with notable herbicidal activities [2,6–8]. The bioassay results showed that inhibitory potency of these compounds could be greatly affected by the chemical modification of R^1, R^2, R^3, X and Y in structure **I** (Scheme 2). On the other hand, it is well known that the introduction of cyclophosphonate may improve the properties and biological activities of the compounds by the replacement of simple phosphonate moiety in parent compound [9]. However, our previous work was not devoted to the synthesis of fluorine substituted cyclophosphonate analogs, which encourage us to design a series of 2-phenoxyacetoxymethyl-1,3,2-dioxaphosphinan-2-one derivatives. Based on the results of our previous work [6–8], the 2-Cl-4-F, 2-F-4-Cl, 2-F, 4-F and 3-CF_3 groups were introduced as X or Y. In this paper, fourteen novel 2-(substituted phenoxyacetoxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one containing fluorine **5a-n** and three fluorine free derivatives **5o-q** were conveniently synthesized. The results of bioassay showed that some of the target compounds display promising herbicidal activity and are safe to some tested crops.

2. Results and discussions

2.1. Synthesis

According to the reported method [10], substituted phenoxyacetic acids **1** were prepared starting from the substituted phenols and ethyl bromoacetate in good yields. Treatment of the 1,3,2-dioxaphosphinane **3** [11] with aldehydes in the presence of triethylamine readily led to the corresponding 1-hydroxycyclophosphonates **4**. The title compounds **5** were prepared by condensation of the intermediates **4** with substituted phenoxyacetyl chorides in chloroform at room temperature. The synthetic pathway is outlined in Scheme 3 and the structures of title compounds **5a–q** are given in Table 1.

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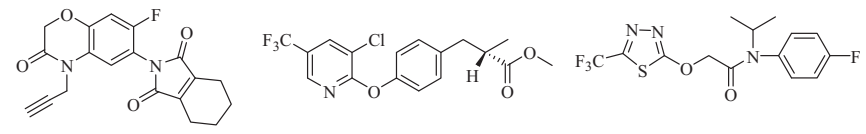
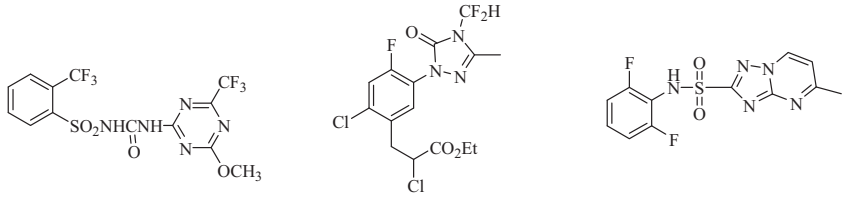
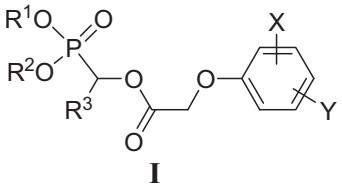


flumioxazin haloxyfop flufenatet



tritosulfuron carfentrazone-ethyl flumetsulam

Scheme 1.



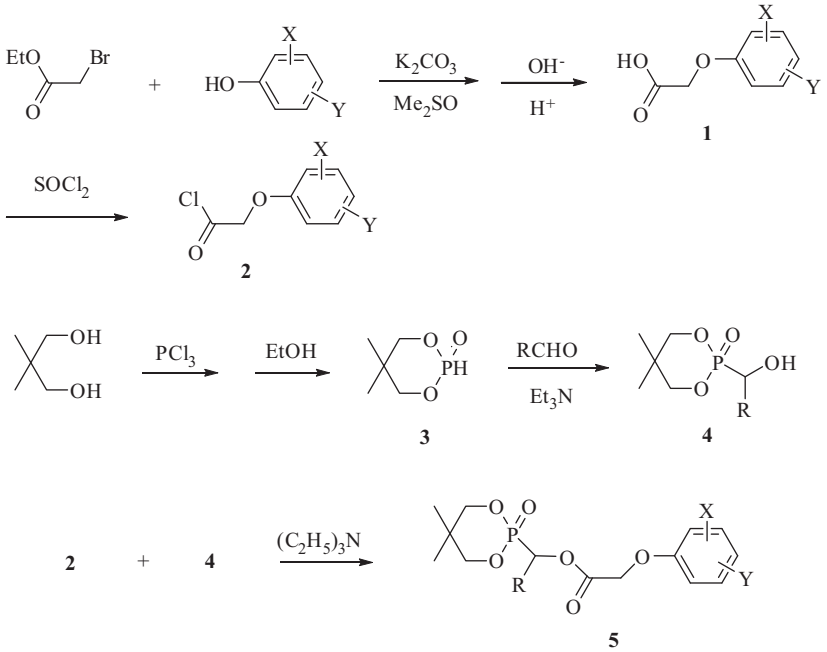
Scheme 2.

2.2. Greenhouse herbicidal activity and crop selectivity

The herbicidal activities of compounds **5a–q** were evaluated at a dosage of 150 g ai/ha in greenhouse using the previously reported procedure [6–8]. They were tested for post-emergence inhibitory effect against seven weeds. Monocotyledonous weeds such as *Digitaria sanguinalis, Echinochloa crusgalli, Setaira viridis* and dicotyledonous weeds such as *Abutilon theophrasti*, *Brassica juncea*, *Amaranthus retroflexus* and *Eclipta prostrate*.

Their herbicidal activities are summarized in Tables 1 and 2. And the results of the crop selectivity are shown in Table 3. Structure-activity relationship analysis indicated that the structure and position of substituents X, Y in benzene ring had great influence on the herbicidal activity. The compounds **5b**, **5g** and **5m** with 3-CF_3 on the phenoxy-benzene ring showed better herbicidal activities compared to the unsubstituted compounds **5o**–**5q** that are almost inactive. And the compounds **5e**, **5j**, **5l** with 2-Cl-4-F substitution as X and Y showed higher herbicidal activities even than those of compounds **5b**, **5g** and **5m**. However, the introduction of 2-F-4-Cl as X and Y, resulted in the compound **5d**, **5i** and **5k**, with some decrease in herbicidal activity. These results indicated that fluorine moiety introduced to the core cyclophosphonate structure was useful for the improvement of herbicidal activity. Especially, the introducing of 2-Cl-4-F groups made prominent enhancement on inhibitory activity.

As seen from Table 1, compounds **5a–q** displayed much higher herbicidal activity against dicotyledonous plants than monocotyledons ones. Especially compounds with 2-Cl, 4-F as X and Y, such as **5e**, **5j** and **5l** exhibited high and broad spectrum herbicidal activity (≥90% inhibition) at a dosage of 150 g ai/ha against dicotyledonous weeds such as *A. theophrasti*, *B. juncea*, *A. retroflexus* and *E. prostrate*. And the compounds with 3-CF_3 on the phenoxy-benzene ring, such



Scheme 3.

Table 1
Structures and herbicidal activity of compounds **5a–q** (150 g ai/ha).

Compd	R	X	Y	Post-emergence activity (%)						
				[a]DS	EC	SV	AT	BJ	AR	EP
5a	2-furyl	2-F	H	0	0	0	45	45	40	30
5b	2-furyl	3-CF_3	H	0	0	0	85	90	70	50
5c	2-furyl	4-F	H	70	50	30	80	70	30	40
5d	2-furyl	2-F	4-Cl	40	30	0	70	70	70	70
5e	2-furyl	2-Cl	4-F	70	75	50	100	95	100	90
5f	Ph	2-F	H	0	0	0	40	40	30	30
5g	Ph	3-CF_3	H	0	0	0	100	95	70	60
5h	Ph	4-F	H	0	0	0	40	55	70	70
5i	Ph	2-F	4-Cl	40	40	40	75	70	80	75
5j	Ph	2-Cl	4-F	30	70	60	100	95	100	90
5k	CH_3	2-F	4-Cl	0	0	0	75	75	60	60
5l	CH_3	2-Cl	4-F	70	85	70	100	95	100	95
5m	CH_3	3-CF_3	H	0	60	0	100	85	50	50
5n	CH_3	4-F	H	50	40	30	75	75	70	70
5o	2-furyl	H	H	0	0	0	10	40	30	10
5p	Ph	H	H	0	0	0	10	30	30	10
5q	CH_3	H	H	0	0	0	10	10	10	10

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

Table 2
Further herbicidal testing of compounds **5g**, **5l** and **5m**.

Compd	Dosage (g ai/ha)	Post-emergence activity (%)						
		[a]EC	SV	DS	AT	BJ	AR	EP
5g	37.5	0	0	0	/[b]	30	30	0
	75	0	0	0	/	60	40	0
5l	37.5	40	70	30	60	/	60	60
	75	75	60	60	100	/	100	85
5m	37.5	/	/	/	/	/	/	/
	75	40	0	0	100	/	0	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*.
[b] Not test.

Table 3
Crop Selectivity of Compound **5g** and **5l** post-emergence activity (%) 150 g ai/ha.

Compd	Crops					
	Rice	Corn	Cotton	Soybean	Rape	Wheat
5g	0	0	10	20	10	0
5l	10	10	10	20	10	0

>10% not safe to crops; 0–10% be safe to crops.

as **5b**, **5g** and **5m**, showed high herbicidal activities (>85% inhibition) at a dosage of 150 g ai/ha against *A. theophrasti* and *B. juncea*.

In addition, compounds **5g**, **5l** and **5m** were selected for further herbicidal evaluation and the results are listed in Table 2, which indicate that compound **5l** exhibited high herbicidal activity (100% inhibition) against *A. theophrasti* and *B. juncea*, and compound **5m** showed high herbicidal activity (100% inhibition) against *A. theophrasti* at a dosage of 75 g ai/ha. Even at a dosage as low as 37.5 g ai/ha, compound **5l** still exhibited broad herbicidal activity. Furthermore, compounds **5g** and **5l** were selected to evaluate their crop selectivity at a dosage of 150 g ai/ha. As shown in Table 3, compounds **5g** and **5l** are safe to rice, corn, cotton, rape and wheat, and compound **5g** has no injury to rice, corn and wheat.

3. Conclusion

A series of 2-(substituted phenoxyacetoxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one derivatives were synthesized, and their structure-activity relationships were studied. All of these compounds exhibited moderate to good herbicidal activities. Especially, compound **5l** showed good herbicidal activities even at a dose of 75 g ai/ha. It was found that a suitable group at the 2,4-positions of phenoxy-benzene ring was essential for high herbicidal activity. Furthermore, compound **5l** also showed good selectivity between weeds and crops, which could be a lead compound for further development. Our result showed fluorine or trifluoromethyl group as X or Y on benzene ring had a very important effect on herbicidal activity, however a satisfactory herbicidal activity of title compound **5** required a reasonable combination both type and position of fluorine – containing group as X or Y on benzene ring.

4. Experimental

Mass spectra were measured on a Finnigan TraceMS 2000 spectrometer. Infrared spectra were recorded in potassium bromide disks on a Nicolet Avatar360 FTIR spectrometer. ^{1}H, ^{13}C, ^{31}P and ^{19}F NMR spectra were recorded on a Varian Mercury-Plus400 or 600 spectrometer with $CDCl_3$ as the solvent and TMS as the internal standard. Elemental analysis was performed by Elementar Vario EL III elementary analyzer. Melting points (mp) were measured on an electrothermal melting point apparatus and temperature uncorrected. All of the solvents were anhydrous. Phosphorous trichloride, triethyl amine and thionyl chloride were distilled before the reaction. Samples were purified by flash chromatography with silica gel.

4.1. Synthesis of compounds *1* and *2*

The substituted phenoxyacetic acid **1** was synthesized by a standard method [2]. The corresponding substituted phenoxyacetyl chloride **2** could be easily obtained as a yellow liquid in 90% yield by treated compound **1** with thionyl chloride.

4.2. Synthesis of 1-hydroxylcyclophosphonate *4*

1-Hydroxycyclophosphonate **4** could be prepared by the reaction of 1,3,2-dioxaphosphinane **3** and several kinds of aldehydes using triethylamine as catalyst in yield of 65–94% according to literatures [12,13].

4.3. General synthesis of title compounds *5a–q*

A solution of substituted phenoxyacetyl chloride **2** (0.011 mol) in chloroform (15 mL) was added to stirred mixture of 1-hydroxycyclophosphonate **4** (0.01 mol) and triethylamine (0.011 mol) in chloroform (15 mL) at 2–4 °C. The resulting mixture was stirred at ambient temperature for 2–3 h, then washed with 0.1 mol/L HCl, saturated $NaHCO_3$ and brine separately, dried and evaporated. The residue was chromatographed on silica gel using acetone-petroleum ether (1:4) as the eluent to afford the compounds **5a–q** as a yellow oil or white solid.

4.3.1. 2-[(2-Fluorophenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (*5a*)

Yellow oil; yield 75%; n_D^{20} 1.5051; IR (KBr): ν 3124, 2973, 1765, 1506, 1288, 1173, 1062, 1012, 831 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–6.70 (m, 6H, $-C_6H_4$, 5 and 4-furanyl-H), 6.53–6.49 (d, J = 14.4 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.79 (s, 2H, OCH_2CO), 4.25–4.05 (m, 4H, 2 × (OCH_2)), 1.28 (s, 3H), 0.93 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-134.56; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.07, 152.47 (d, $^1J_{C-F}$ = 243.5 Hz), 149.67, 145.16, 144.11, 124.42, 122.82, 116.60 (d, J = 17.9 Hz), 115.74 (d, J = 19.5 Hz), 113.05, 111.04, 66.38, 64.07 (d, $^1J_{C-P}$ = 170.7 Hz), 32.39, 21.69, 20.43; ^{31}P

NMR (160 MHz, $CDCl_3$): δ 5.85; EI-MS (70 eV): m/z 398 (M^+); Anal. Calcd for $C_{18}H_{20}FO_7P$: C, 54.28; H, 5.06; Found: C, 53.89; H, 4.73.

*4.3.2. 2-[(3-Trifluoromethylphenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphian-2-one (**5b**)*

Yellow oil; yield 75%; n_D^{20} 1.5612; IR (KBr): ν 2972, 1742, 1596, 1492, 1261, 1170, 1062, 1008, 827 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (s, 1H, 5-furanyl-H), 7.32–6.70 (m, 5H, $-C_6H_4$, 4-furanyl-H), 6.53–6.49 (d, 1H, J = 13.2 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.78 (s, 2H, OCH_2CO), 4.20–4.01 (m, 4H, 2 × (OCH_2)), 1.22 (s, 3H), 0.92 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-63.69; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.92, 157.33, 144.93, 144.02, 131.70 (q, $^2J_{C\text{-}F}$ = 30.76 Hz), 130.12, 123.49 (q, $^1J_{C\text{-}F}$ = 270.80 Hz), 118.50, 117.71, 111.45, 111.39, 110.94, 64.93, 63.42 (d, $^1J_{C\text{-}P}$ = 170.70 Hz), 32.23, 21.39, 20.33; ^{31}P NMR (160 MHz, $CDCl_3$): δ 5.94; EI-MS (70 eV): m/z 448 (M^+); Anal. Calcd for $C_{19}H_{20}F_3O_7P$: C, 50.90; H, 4.50; Found: C, 50.68; H, 4.16.

*4.3.3. 2-[(4-Fluorophenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5c**)*

White solid; yield 76%; mp 67–70 °C; IR (KBr): ν 3077, 2972, 1770, 1506, 1290, 1173, 1061, 1012, 947,830, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H, 5-furanyl-H), 6.99–6.95 (m, 2H, 3 and 5-phenyl-H), 6.84–6.80 (m, 2H, 2 and 6-phenyl-H), 6.73–6.71 (m, 1H, 4-furanyl-H), 6.53–6.49 (d, 1H, J = 12.0 Hz, PCHO), 6.42–6.41 (m, 1H, 3-furanyl-H), 4.69 (s, 1H, OCH_2CO), 4.16–4.01 (m, 4H, 2 × (OCH_2)), 1.22 (s, 3H), 0.94 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-123.12; ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.18, 157.15 (d, $^1J_{C\text{-}F}$ = 236.30 Hz), 154.74, 146.16, 143.82, 115.70 (d, J = 22.90 Hz), 115.29 (d, J = 8.10 Hz), 112.04, 110.87, 65.78, 63.38 (d, $^1J_{C\text{-}P}$ = 172.30 Hz), 32.42, 21.65, 20.71; ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.45; EI-MS (70 eV): m/z 398 (M^+); Anal. Calcd for $C_{18}H_{20}FO_7P$: C, 54.28; H, 5.06; found: C, 54.48; H, 5.39.

*4.3.4. 2-[(4-Chloro-2-fluorophenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5d**)*

White solid; yield 80%; mp 78–80 °C; IR (KBr): ν 3070, 2979, 1502, 1289, 1174, 1061, 1013, 947, 861, 799 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (s, 1H, 5-furanyl-H), 7.15–6.78 (m, 3H, 3,5,6-phenyl-H), 6.71 (s, 1H, 4-furanyl-H), 6.50–6.45 (d, 1H, J = 14.0 Hz, PCHO), 6.41 (s, 1H, 3-furanyl-H), 4.78 (s, 1H, OCH_2CO), 4.19–4.00 (m, 4H, 2 × (OCH_2)), 1.21 (s, 3H), 0.93 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-131.19; ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.07, 152.30 (d, $^1J_{C\text{-}F}$ = 248 Hz), 146.13, 145.54 (d, J = 10.30 Hz), 143.82, 125.40, 124.14, 116.87 (d, J = 21.70 Hz), 115.55, 112.02 (d, J = 6.10 Hz), 110.87, 65.63, 63.30 (d, $^1J_{C\text{-}P}$ = 172.30 Hz), 32.12, 21.23, 20.41; ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.11; EI-MS (70 eV): m/z 432 (M^+); Anal. Calcd for $C_{18}H_{19}ClFO_7P$: C, 49.96; H, 4.43; Found: C, 50.11; H, 4.49.

*4.3.5. 2-[(2-Chloro-4-fluorophenoxy)acetoxy](furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5e**)*

White solid; yield 78%; mp 58–61 °C; IR (KBr): ν 3076, 2972, 1771, 1499, 1292, 1174, 1059, 947, 861, 801 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (s, 1H, 5-furanyl-H), 7.16–7.13 (dd, 1H, J = 3.2 Hz, J = 3.2 Hz, 3-phenyl-H), 6.92–6.87 (m, 1H, 5-phenyl-H), 6.83–6.79 (dd, 1H, J = 4.8 Hz, J = 4.8 Hz, 6-phenyl-H), 6.71 (s, 1H, 4-furanyl-H), 6.52-6.48 (d, 1H, J = 14.0 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.76 (s, 1H, OCH_2CO), 4.18–4.02 (m, 4H, 2 × (OCH_2)), 1.22 (s, 3H), 0.93 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-120.30; ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.13, 156.38 (d, $^1J_{C\text{-}F}$ = 240.10 Hz), 150.70, 146.09, 143.80, 117.53, 117.27, 114.17 (d, J = 8.80 Hz), 113.88 (d, J = 22.10 Hz), 111.99 (d, J = 6.10 Hz), 110.83, 65.61, 63.29 (d, $^1J_{C\text{-}P}$ = 172.30 Hz), 32.11, 21.22, 20.40; ^{31}P NMR (160 MHz, $CDCl_3$): δ 6.24; EI-MS (70 eV): m/z 432 (M^+); Anal. Calcd for $C_{18}H_{19}ClFO_7P$: C, 49.96; H, 4.43; Found: C, 50.05; H, 4.59.

*4.3.6. 2-[(2-Fluorophenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5f**)*

Yellow solid; yield 77%; mp 70–71 °C; IR (KBr): ν 3068, 2972, 1751, 1613, 1505, 1291, 1190, 1055, 1005, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44–6.89 (m, 9H), 6.36 (d, 1H, J = 12.4 Hz, PCHO), 4.83 (d, 2H, J = 3.6 Hz, OCH_2CO), 4.16–4.04 (m, 4H, 2 × (OCH_2)), 1.18 (s, 3H), 0.91 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-134.72; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.75, 152.06 (d, $^1J_{C\text{-}F}$ = 244.20 Hz), 145.09 (d, J = 10.30 Hz), 131.99, 128.81, 128.37, 127.44 (d, J = 5.30 Hz), 126.66, 122.41 (d, J = 6.50 Hz), 116.29 (d, J = 17.90 Hz), 115.12, 71.33 (d, $^1J_{C\text{-}P}$ = 164.60 Hz), 65.99, 32.08, 21.29, 20.07; ^{31}P NMR (160 MHz, $CDCl_3$): δ 7.94; EI-MS (70 eV): m/z 408 (M^+); Anal. Calcd for $C_{20}H_{22}FO_6P$: C, 58.82; H, 5.43. Found: C, 58.81; H, 5.15.

*4.3.7. 2-[(3-Trifluoromethylphenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5g**)*

White solid; yield 75%; mp 101–102 °C; IR (KBr): ν 3066, 2972, 1594, 1494, 1771, 1288, 1171, 1063, 1012, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45–7.05 (m, 9H), 6.37 (d, 1H, J = 12.8 Hz, PCHO), 4.81 (d, 2H, J = 4.8 Hz, OCH_2CO), 4.09–3.94 (m, 4H, 2 × (OCH_2)), 1.26 (s, 3H), 0.92 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-63.69; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.90, 157.41, 131.97, 131.60 (q, $^2J_{C\text{-}F}$ = 32.33 Hz), 130.18, 129.13, 128.61, 127.75, 123.47 (q, $^1J_{C\text{-}F}$ = 268.30 Hz), 118.53, 117.70, 111.57, 70.83 (d, $^1J_{C\text{-}P}$ = 165.00 Hz), 65.09, 32.27, 21.37, 20.53; ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.57; EI-MS (70 eV): m/z 458 (M^+); Anal. Calcd for $C_{21}H_{22}F_3O_6P$: C, 55.03; H, 4.84. Found: C, 55.35; H, 4.55.

*4.3.8. 2-[(4-Fluorophenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5h**)*

Yellow solid; yield 77%; mp 110–113 °C; IR (KBr): ν 3073, 2969, 1769, 1603, 1507, 1387, 1287, 1191, 1058, 997, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45–6.81 (m, 9H, $-C_6H_5$, $-C_6H_3$), 6.38–6.34 (d, 1H, J = 12.0 Hz, PCHO), 4.78–4.68 (dd, 2H, J = 16.8 Hz, J = 16.4 Hz, OCH_2CO), 4.11–3.93 (m, 4H, 2 × (OCH_2)), 1.15 (s, 3H), 0.91 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-123.15; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.31, 157.66 (d, $^1J_{C\text{-}F}$ = 238.20 Hz), 153.45, 132.01, 129.07, 128.46 (d, J = 19.00 Hz), 127.76 (d, J = 6.10 Hz), 115.91 (d, J = 23.30 Hz), 115.64 (d, J = 8.00 Hz), 70.80 (d, $^1J_{C\text{-}P}$ = 165.00 Hz), 65.51, 32.27, 21.41, 20.55; ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.55; EI-MS (70 eV): m/z 408 (M^+); Anal. Calcd for $C_{20}H_{22}FO_6P$: C, 58.82; H, 5.43. Found: C, 59.01; H, 5.65.

*4.3.9. 2-[(2-Fluoro-4-chlorophenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5i**)*

Yellow solid; yield 75%; mp 117–119 °C; IR (KBr): ν 3067, 2974, 2895, 1753, 1604, 1494, 1275, 1188, 1057, 943, 745 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 7.43–6.82 (m, 8H, $-C_6H_5$, $-C_6H_3$), 6.36–6.33 (d, 1H, J = 12.0 Hz, PCHO), 4.80 (s, 2H, OCH_2CO), 4.10–3.96 (m, 4H, 2 × (OCH_2)), 1.16 (s, 3H), 0.90 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-131.03; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.33, 151.75 (d, $^1J_{C\text{-}F}$ = 249.20 Hz), 143.90 (d, J = 9.90 Hz), 131.69, 128.80, 128.27, 127.42 (d, J = 5.30 Hz), 126.63 (d, J = 8.80 Hz), 124.01, 116.89 (d, J = 21.70 Hz), 116.01, 70.85 (d, $^1J_{C\text{-}P}$ = 164.60 Hz), 66.05, 31.97, 21.14, 20.13; ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.25; EI-MS (70 eV): m/z 442 (M^+); Anal. Calcd for $C_{20}H_{21}ClFO_6P$: C, 54.25; H, 4.78; Found: C, 54.55; H, 4.98.

*4.3.10. 2-[(2-Chloro-4-fluorophenoxy)acetoxy](phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5j**)*

Yellow solid; yield 77%; mp 110–112 °C; IR (KBr): ν 3078, 2971, 1753, 1623, 1500, 1281, 1189, 1048, 995, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45–6.81 (m, 8H, Phenyl-H), 6.38–6.34 (d, 1H, J = 12.4 Hz, PCHO), 4.80 (s, 2H, OCH_2CO), 4.11–3.92 (m, 4H, 2 × (OCH_2)), 1.16 (s, 3H), 0.90 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$):

δ-120.36; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.46, 156.79 (d, $^1J_{C-F}$ = 242.30 Hz), 149.30, 131.74, 128.66, 128.43, 127.75, 123.42, 117.38, 114.72 (d, J = 8.30 Hz), 113.79, 70.75 (d, $^1J_{C-P}$ = 164.60 Hz), 66.31, 31.98, 21.13, 20.22; ^{31}P NMR (160 MHz, $CDCl_3$): δ 8.48; EI-MS (70 eV): m/z 442 (M^+); Anal. Calcd for $C_{20}H_{21}ClFO_6P$: C, 54.25; H, 4.78; Found: C, 54.55; H, 4.98.

*4.3.11. 2-[(4-Chloro-2-fluorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5k**)*

White solid; yield 80%; mp 107–109 °C; IR (KBr): ν 3079, 2974, 1775, 1494, 1287,1246, 1194, 1085, 1047, 1004, 975, 841, 798 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.15–6.82 (m, 3H, 3, 5 and 6-phenyl-H), 5.50–5.46 (q, 1H, J = 7.0 Hz, PCHO), 4.78–4.68 (s, 2H, OCH_2CO), 4.14–3.99 (m, 4H, 2 × (OCH_2)), 1.60–1.55 (dd, 3H, J = 7.2 Hz, J = 7.2 Hz, PCH(CH_3)O), 1.17 (s, 3H), 0.99 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-131.29; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.22, 152.87 (d, $^1J_{C-F}$ = 248.40 Hz), 144.47 (d, J = 10.10 Hz), 125.61, 124.37 (d, J = 3.40 Hz), 117.73 (d, J = 21.7 Hz), 115.74, 66.59, 65.15 (d, $^1J_{C-P}$ = 165.80 Hz), 32.33, 21.30, 20.61 14.57; ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.36; EI-MS (70 eV): m/z 380 (M^+); Anal. Calcd for $C_{15}H_{19}ClFO_6P$: C, 47.32; H, 5.03; Found: C, 47.65; H, 5.23.

*4.3.12. 2-[(2-Chloro-4-fluorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5l**)*

White solid; yield 78%; mp 82–84 °C; IR (KBr): ν 3062, 2967, 1738, 1496, 1247, 1195, 1070, 1001, 965, 829, 800 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.17–7.15 (dd, 1H, J = 2.4 Hz, J = 2.4 Hz, 3-phenyl-H), 6.96-6.84 (m, 2H, 5 and 6-phenyl-H), 5.53–5.47 (m, 1H, PCHO), 4.77–4.70 (dd, 2H, J = 16.8 Hz, J = 16.2 Hz, OCH_2CO), 4.13–3.97 (m, 4H, 2 × (OCH_2)), 1.60–1.56 (dd, 3H, J = 7.2 Hz, J = 6.6 Hz, PCH(CH_3)O), 1.16 (s, 3H), 0.99 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-120.23; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.02, 157.04 (d, $^1J_{C-F}$ = 240.80 Hz), 149.57, 123.70, 117.67 (d, J = 25.9 Hz), 114.98 (d, J = 9.10 Hz), 114.08 (d, J = 22.9 Hz), 66.60, 65.15 (d, $^1J_{C-P}$ = 166.10 Hz), 32.34, 21.31, 20.64 14.59; ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.22; EI-MS (70 eV): m/z 380 (M^+); Anal. Calcd for $C_{15}H_{19}ClFO_6P$: C, 47.32; H, 5.03; Found: C, 47.41; H, 5.30.

*4.3.13. 2-[(3-Trifluoromethylphenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5m**)*

White solid; yield 76%; mp 69–71 °C; IR (KBr): ν 3094, 2974, 1767,1594, 1494, 1331, 1171, 1065, 1012, 947, 877, 800 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.06 (m, 4H, –C_6H_4), 5.55–5.47 (m, 1H, PCHO), 4.75 (s, 2H, OCH_2CO), 4.16–3.95 (m, 4H, 2 × (OCH_2)), 1.61–1.55 (dd, 3H, J = 7.2 Hz, J = 7.2 Hz, PCH(CH_3)O), 1.15 (s, 3H), 1.02 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-63.72; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.51, 158.63, 131.43 (q, $^2J_{C-F}$ = 32.00 Hz), 129.79, 123.73 (q, $^1J_{C-F}$ = 270.50 Hz), 117.66, 117.14, 110.91, 65.32, 64.35 (d, $^1J_{C-P}$ = 145.98 Hz), 31.51, 20.53, 19.78, 14.09; ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.50; EI-MS (70 eV): m/z 396 (M^+); Anal. Calcd for $C_{16}H_{20}F_3O_6P$: C, 48.49; H, 5.09; Found: C, 48.71; H, 5.38.

*4.3.14. 2-[(4-Fluorophenoxy)acetoxy](methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5n**)*

White solid; yield 75%; mp 67–69 °C; IR (KBr): ν 3117, 2972, 1768, 1508, 1272, 1207, 1065, 1006, 952, 833, 799 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.01–6.83 (m, 4H, –C_6H_4), 5.53–5.49 (m, 1H, PCHO), 4.67 (s, 2H, OCH_2CO), 4.11–4.00 (m, 4H, 2 × (OCH_2)), 1.60–1.56 (q, 3H, J = 7.8 Hz, PCH(CH_3)O), 1.16 (s, 3H), 1.00 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ-120.09; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.31, 157.30 (d, $^1J_{C-F}$ = 238.20), 153.21, 115.59 (d, J = 23.20 Hz), 115.38 (d, J = 8.00 Hz), 65.61, 64.69 (d, $^1J_{C-P}$ = 146.30 Hz), 31.99, 21.01, 20.27, 14.29; ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.42; EI-MS (70 eV): m/z 346 (M^+); Anal. Calcd for $C_{15}H_{20}FO_6P$: C, 52.03; H, 5.82; Found: C, 52.43; H, 5.95.

*4.3.15. 2-phenoxyacetoxy(furan-2-yl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5o**)*

yellow oil; yield, 78%; n_D^{20} 1.5169; IR (KBr, cm^{-1}): ν 3060, 2970, 1744, 1600, 1494, 1264, 1174, 1060, 1009, 833. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–6.72 (m, 7H, –C_6H_5, 5 and 4-furanyl-H), 6.55–6.51 (d, J = 14.4 Hz, PCHO), 6.42 (s, 1H, 3-furanyl-H), 4.74 (s, 2 H, OCH_2CO), 4.19–4.04 (m, 4H, 2 × (OCH_2)), 1.24 (s, 3H), 0.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.42, 157.23, 145.22, 143.94, 129.47, 121.81, 114.35, 112.76, 110.93, 64.96, 63.72 (d, $^1J_{C-P}$ = 169.90 Hz), 32.28, 21.51, 20.34; ^{31}P NMR (160 MHz, $CDCl_3$): δ 5.72; EI-MS m/z (%): 380 (M^+, 7); Anal.Calcd for $C_{18}H_{21}O_7P$: C, 56.84; H, 5.57. Found: C, 56.70; H, 5.18.

*4.3.16. 2-phenoxyacetoxy(phenyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5p**)*

yellow solid; yield, 80%; mp, 80–81 °C; IR (KBr, cm^{-1}): ν 3064, 2971, 1765, 1598, 1492, 1290, 1194, 1054, 1004, 830. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–6.87 (m, 10H, –C_6H_5, –C_6H_5), 6.38–6.34 (d, 1H, J = 12.0 Hz, PCHO), 4.77–4.76 (d, 2H, J = 3.6 Hz, OCH_2CO), 4.13–3.98 (m, 4H, 2 × (OCH_2)), 1.17 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.58, 157.35, 132.32, 129.68, 129.10, 128.65, 127.83, 121.97, 114.42, 71.27 (d, $^1J_{C-P}$ = 163.80 Hz), 65.13, 32.34, 21.61, 20.56; ^{31}P NMR (160 MHz, $CDCl_3$): δ 7.97; EI-MS m/z (%): 390 (M^+, 1); Anal. Calcd for $C_{20}H_{23}O_6P$: C, 61.54; H, 5.94. Found: C, 61.25; H, 5.68.

*4.3.17. 2-phenoxyacetoxy(methyl)methyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**5q**)*

white oil; yield, 81%; n_D^{20} 1.3690; IR (KBr, cm^{-1}): ν 3091, 2967, 1764, 1483, 1237, 1197, 1053, 1000, 844, 805. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32–6.88 (m, 5H, –C_6H_5), 5.53–5.47 (m, 1H, PCHO), 4.71 (s, 2H, OCH_2CO), 4.12–3.98 (m, 4H, 2 × (OCH_2)), 1.60–1.55 (dd, 3H, J = 7.2 Hz, J = 7.2 Hz, PCH(CH_3)O), 1.17 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.30, 156.89, 129.09, 121.43, 113.91, 64.87 (d, $^1J_{C-P}$ = 146.00 Hz), 64.73, 31.90, 20.04, 20.21, 14.25; ^{31}P NMR (160 MHz, $CDCl_3$): δ 12.26; EI-MS m/z (%): 328 (M^+, 5); Anal. Calcd for $C_{15}H_{21}O_6P$: C, 54.88; H, 6.45. Found: C, 55.23; H, 6.81.

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