Journal of Fluorine Chemistry 193 (2017) 8–16

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Synthesis and herbicidal activity of α-[(substituted phenoxybutyryloxy or valeryoxy)]alkylphosphonates and 2-(substituted phenoxybutyryloxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one containing fluorine

Wei Wang[a,b,1], Yuan Zhou[a,1], Hao Peng[a,*], Hong-Wu He[a,*], Xing-Tao Lu[c]

[a] Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, Institute of Pesticide Chemistry, College of Chemistry, Central China Normal University, Wuhan, 430079, PR China
[b] State Key Laboratory of Fluorine & Nitrogen Chemicals, Xi'an Modern Chemistry Research Institute, Xi'an, 710065, PR China
[c] Tai'an Academy of Agricultural Sciences, Tai'an, 271000, PR China

ARTICLE INFO

Article history:
Received 13 May 2016
Received in revised form 10 November 2016
Accepted 12 November 2016
Available online 14 November 2016

Keywords:
Synthesis
Herbiciadal activity
Fluorine
Phosphonate

ABSTRACT

Based on our previous work on the structural modification of the lead compound **I**, three series of novel fluorine-containing phosphonates derivatives (**II, III** and **IV**) were designed and synthesized. Their post-emergence herbicidal activities against some species of weeds were evaluated in a green house. The compounds **II** were synthesized by introducing of two methylene into the structure **I**. Compared with the commercial herbicidal clacyfos, compounds **II** showed moderate herbicidal activity with 60–85% inhibition effect against chingma abutilon (*Abutilon theophrasti*), common amaranth (*Amaranthus retroflexus*) and white eclipta (*Eclipta prostrate*) at a rate of 150 g ai/ha. The compounds **III** were designed by introducing open-chain phosphonates, which displayed notable herbicidal activity. Especially, the compounds **III-1**–**III-4**, **III-6**, **III-8**, **III-11** and **III-12** exhibited significant herbicidal activity (80–100%) comparing to the clacyfos against all tested broadleaf weeds, while compounds **IV** with five carbon atoms in the carboxylic acid chain were inactive against all of the tested weeds. Structure-activity relationship analyses indicated that the length of the carbon chain had a great effect on the herbicidal activity. Furthermore, a broad spectrum test confirmed that compounds **III-4** and **III-8** were comparable with glyphosate against all of the tested weeds at a rate of 75 g ai/ha.

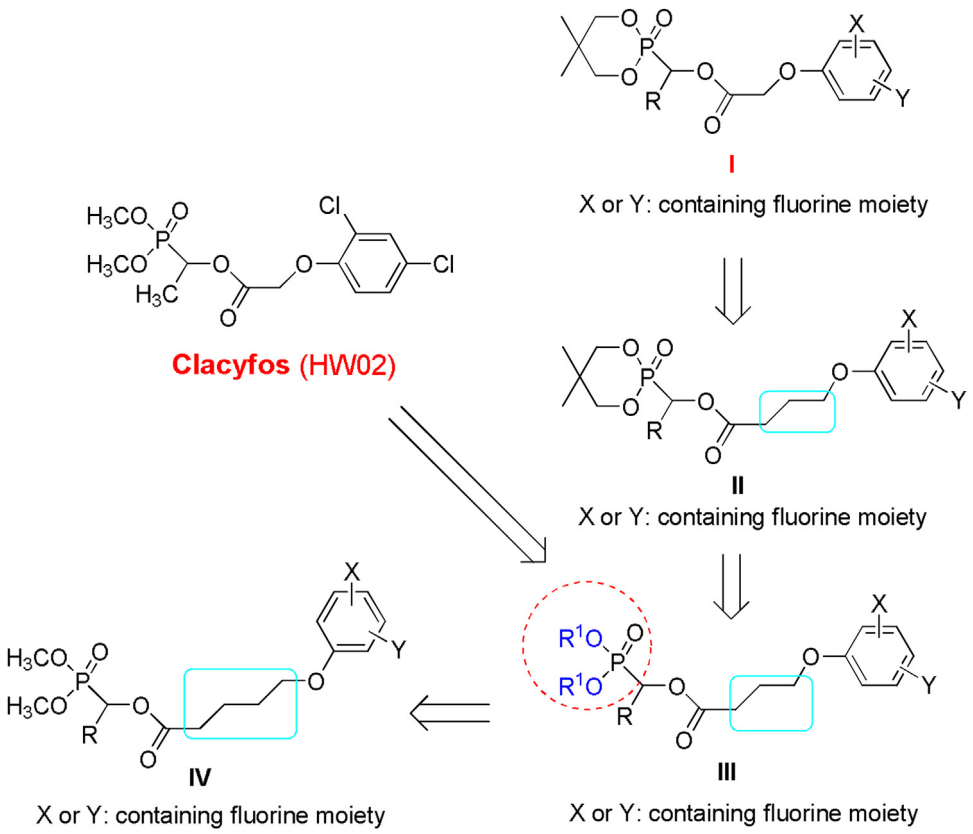
1. Introduction

Compounds containing fluorine have a wide range of bio-activities in agrochemical industries [1–3]. And a number of fluorinated products have been launched into the market during the past decade [4]. At the same time, organophosphorus compounds have attracted intense interest owing to their potential biological activities in pesticides, such as antiviral, antifungal, insecticidal and herbicidal activities [5–7]. In our previous work, the compound clacyfos as a competitive inhibitor of PDHc was found to be the most effective compound against broadleaf weeds and has got temporary registration from ICAMA in China [8–10]. Therefore, it is an interesting task to discover novel organophosphorus compounds with fluorine moieties with suitable post-emergence herbicidal activity. At first, the structure of compound **I** was designed and synthesized by introduction of a phosphorus-containing heterocyclic ring [11] and some fluorine-containing moieties such as 2-Cl-4-F, 2-F-4-Cl, 2-F, 4-F and 3-CF_3 as X or Y in our laboratory [4]. The results of herbicidal activity showed that some compounds **I** exhibited excellent herbicidal activities to some weeds in post-emergence treatment at a rate of 75 g ai/ha. A crop selectivity test indicated that they were safe for rice, corn, cotton, rape, and wheat.

Encouraged by these findings, we developed an idea that modification of the linkage part in the parent structure **I**. Moreover, it would be expected that alkyl homologation is an effective way to design bioactive compounds [12]. Therefore, the compounds **II** have been designed by introduction of two methylene into the structure **I** as shown in Scheme 1. Furthermore, compounds **III** have been designed and synthesized by the introduction of an

* Corresponding authors.
E-mail addresses: penghao@mail.ccnu.edu.cn (H. Peng), he1208@mail.ccnu.edu.cn (H.-W. He).
[1] These authors equally contributed to this work.

http://dx.doi.org/10.1016/j.jfluchem.2016.11.008
0022-1139/



Scheme 1. Chemical modification of lead structure **I**.

open-chain phosphonate into the structure **I**. As a comparison, the compounds **IV** have been designed by introducing of one methylene into the structure of compounds **III**. Herein, we report the preparation of the novel fluorine-containing alkylphosphonates **II**, **III**, and **IV**, and the evaluation of their herbicidal activities in detail.

2. Results and discussions

2.1. Chemistry

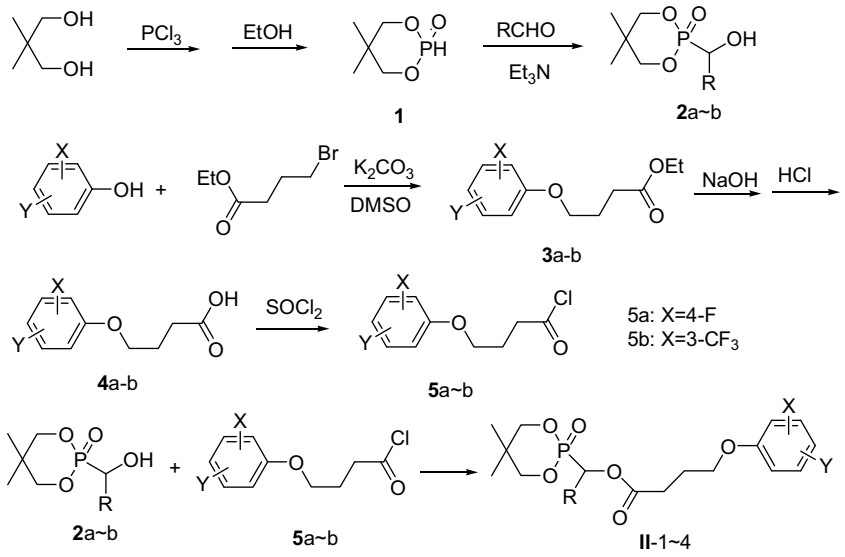
All of the intermediates 1-hydroxycyclophosphonates **2a**-**b** and *O*,*O*-dialkyl α-hydroxyalkylphosphonates **7a**-**f** were synthesized according to the methods described in the literature [13,14]. The substituted phenoxybutanoic acids **4a**-**d** and the substituted phenoxypentanoic acid **12** were synthesized by a standard method [11,15], respectively. The title compounds **II** and **III** were synthesized, as shown in Schemes 2 and 3, respectively. Thus, the substituted phenoxybutanoic acid **4a-d** was treated with thionyl chloride and then reacted with **2a**-**b** and **7a**-**f** to afford the title compounds **II** and **III**. The title compounds **IV** were prepared by condensation of the corresponding intermediates **7** with the intermediates **13** in dichloromethane at room temperature, as shown in Scheme 4. The structures of title compounds **II**, **III** and **IV** are given in Tables 1–3 , respectively.

2.2. Greenhouse herbicidal activity and crop selectivity

The herbicidal activities of compounds **II**, **III** and **IV** were evaluated at a rate of 150 g ai/ha in greenhouse according to a previously reported procedure [11]. That is, with these compounds post-emergence inhibitory effect against monocotyledonous weeds such as barnyard grass (*Echinochloa crusgalli*), crab grass (*Setaira viridis*) and green bristlegrass (*Digitaria sanguinalis*) and dicotyledonous weeds such as chingma abutilon (*Abutilon theophrasti*), common amaranth (*Amaranthus retroflexus*) and white eclipta (*Eclipta prostrate*) were measured at 150 g ai/ha. The commercial herbicide clacyfos was used as positive control [9,10]. Furthermore, a broad spectrum test was made using more weed species such as chingma abutilon (*Abutilon theophrasti*), white eclipta (*Eclipta prostrata*), bok choy (*Brassica chinensis* L.), tomato (*Solanum lycopersicum*), leaf mustard (*Brassica juncea*), glory (*Pharbitisnil (Linn.) Choisy*), common vetch (*Vicia sativa* L.), goosefoot (*Chenopodium album*), cabbage (*Brassica oleracea L*), turnip (*Raphanus sativus* L.) for the compounds **III-1**, **III-4** and **III-8** at 150 and 75 g ai/ha, which displayed much higher herbicidal activity than the other compounds in preliminary bioassays. Here the commercial glyphosate was selected as a positive control.

Their herbicidal activities are summarized in Tables 1–4. Structure-activity relationship analysis indicated that the linkage part in the parent structure containing fluorine had great influence on the herbicidal activity. Comparing herbicidal activity among the title compounds **II**, **III** and **IV** in Tables 1–3, the title compounds containing fluorine with three methylene of the linkage part have a favorable herbicidal activity, regardless of the position of substituents X, Y in benzene ring. And the herbicidal activity of the title compounds **III** was greatly improved when a phosphorus-containing heterocyclic ring of the title compound **II** was replaced by EtO or MeO group.

Compounds **III** exhibited the best herbicidal activities than those of compounds **II**, followed by compounds **IV** as shown in Tables 1–3. The compounds **II** displayed much higher herbicidal activity against dicotyledonous weeds than against monocotyledons weeds (shown in Table 1). For instance, the herbicidal activities of compounds **II** were 60–85% against dicotyledonous weeds at a rate of 150 g ai/ha, while 20–30% against



Scheme 2. Synthetic route of 2-(substituted phenoxybutyryloxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one containing fluorine **II-14**.

monocotyledons at the same rate. Compounds **III** also displayed much higher herbicidal activity against dicotyledonous plants than monocotyledonous plants (shown in Table 2). It is worthwhile to note that the compounds such as **III-1–3**, **III-4**, **III-6**, **III-8** and **III-11–12** exhibited significant herbicidal activity comparaing to that of clacyfos against all tested broadleaf weeds with 85–100% inhibition effect at a rate of 150 g ai/ha. And compounds **III-20–21** and **III-24** displayed 85–100% inhibition effect against chingma abutilon and common amaranth at the same dose. Structure-activity relationship analysis of compounds **III** indicated that modification of the linkage part in the parent structure **I** by introduction of two methylene seems to have a favorable effect on herbicidal activity. As shown in Table 3, compounds **IV** were inactive against all tested weeds at a rate of 150 g ai/ha for post-emergence, no matter what the different of substituents R and X, Y.

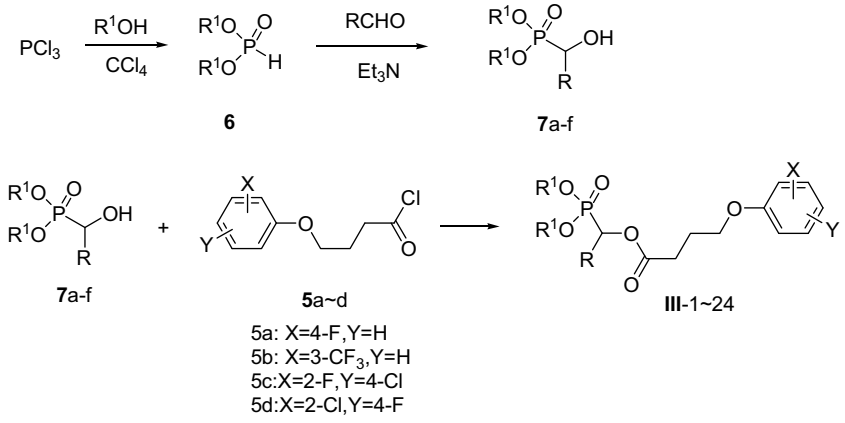
Based on the preliminary bioassay results, compounds **III-3**, **III-4** and **III-8** were selected for a broad spectrum test (shown in Table 4). Compounds **III-4** and **III-8** were comparable with glyphosate against chingma abutilon, leaf mustard, glory, goose-foot, cabbage and turnip at the rate of 75 g ai/ha.

3. Conclusion

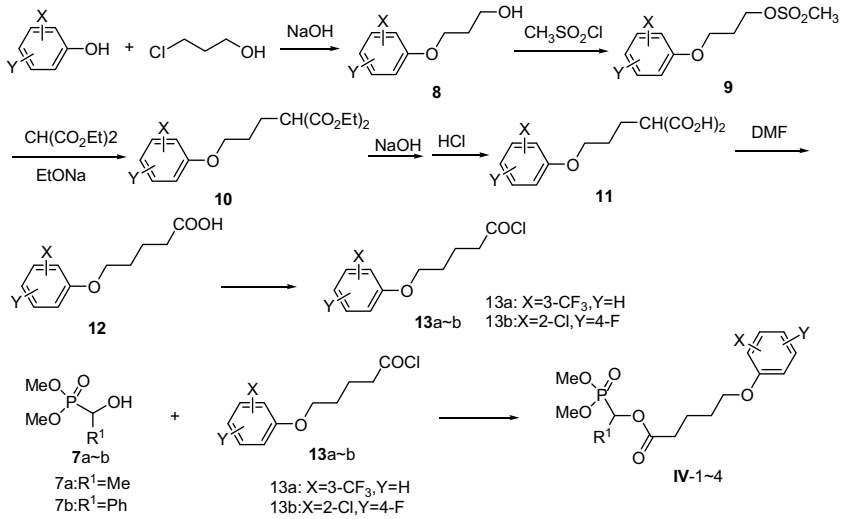
In summary, three series of novel fluorine-containing phosphorus derivatives **II**, **III** and **IV** were designed and synthesized based on the structural modification of **I** and their post-emergence herbicidal activity against six species of weeds were evaluated. The compounds **II** showed moderate herbicidal activities against dicotyledonous plants. And some compounds **III** showed good herbicidal activities against dicotyledonous plants. But compounds **IV** showed inactives against tested plants. It was found that the linkage part in the parent structure **I** by introduction of two methylene seems to have a favorable effect on herbicidal activity. Furthermore, the compounds **III-4** and **III-8** showed good herbicidal activities and a broad spectrum, which could be a lead compound for further development. Our result showed a reasonable linkage part of the containing fluorine analogs in the parent structure **I** had a very important effect on herbicidal activity.

4. Experimental

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 and ^{13}C NMR were recorded on Varian XL-400 spectrometer at 400 MHz for ^{1}H and 100 MHz for ^{13}C or Varian XL-600



Scheme 3. Synthetic route of α-[(substituted phenoxybutyryloxy)alkyl]-α-alkylmethylphosphonates containing fluorine **III-1~24**.



Scheme 4. Synthetic route of α-[(substituted phenoxyvaleryoxy)alkyl]-alkylmethylphosphonates containing fluorine **IV-1 4**.

Table 1
Herbicidal activity of compounds **II-1–4**.

Compd.	R	X	Y	Dosage	Post-emergence activity(%)					
				g ai/ha	[a]EC	DS	SV	AT	AR	EP
II-1	Me	4-F	H	150	30	30	30	80	70	70
II-2	Me	3-CF_3	H	150	20	20	20	70	80	80
II-3	Ph	4-F	H	150	30	30	30	60	70	70
II-4	Ph	3-CF_3	H	150	30	30	30	75	80	85
Clacyfos				150	0	0	0	100	85	90

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

Table 2
Herbicidal activity of compounds **III-1–24**.

Compd	R	R^1	X	Y	Dosage	post-emergence activity (%)					
					g ai/ha	EC[a]	DS[a]	SV[a]	AT[a]	AR[a]	EP[a]
III-1	Me	Me	4-F	H	150	0	60	60	100	85	100
III-2	Me	Me	3-CF_3	H	150	20	40	60	90	80	100
III-3	Me	Me	2-F	4-Cl	150	40	50	40	95	100	100
III-4	Me	Me	2-Cl	4-F	150	0	50	40	98	100	98
III-5	Me	Ph	4-F	H	150	60	70	40	85	70	75
III-6	Me	Ph	3-CF_3	H	150	0	0	0	100	100	85
III-7	Me	Ph	2-F	4-Cl	150	0	0	40	60	70	70
III-8	Me	Ph	2-Cl	4-F	150	50	50	50	90	85	100
III-9	Me	Et	4-F	H	150	30	40	0	70	60	60
III-10	Me	Et	3-CF_3	H	150	0	0	0	50	0	0
III-11	Me	Et	2-F	4-Cl	150	40	20	30	100	100	90
III-12	Me	Et	2-Cl	4-F	150	60	40	40	100	100	85
III-13	Me	Pr	4-F	H	150	40	70	40	80	70	70
III-14	Me	Pr	3-CF_3	H	150	0	0	0	100	40	0
III-15	Me	Pr	2-F	4-Cl	150	50	30	50	70	70	70
III-16	Me	Pr	2-Cl	4-F	150	30	50	50	90	90	70
III-17	Et	Ph	4-F	H	150	30	60	40	85	70	60
III-18	Et	Ph	3-CF_3	H	150	50	30	30	90	40	30
III-19	Et	Ph	2-F	4-Cl	150	0	40	30	60	70	70
III-20	Et	Ph	2-Cl	4-F	150	70	50	50	100	100	70
III-21	Et	Me	4-F	H	150	40	60	60	100	85	75
III-22	Et	Me	3-CF_3	H	150	0	0	0	100	70	70
III-23	Et	Me	2-F	4-Cl	150	0	0	0	80	80	40
III-24	Et	Me	2-Cl	4-F	150	50	40	40	100	90	70
Clacyfos					150	0	0	0	100	85	90

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

spectrometer at 600 MHz for ^{1}H and 150 MHz for ^{13}C, respectively. ^{19}F NMR and ^{31}P NMR were recorded on Varian XL-400 spectrometer at 376 MHz for ^{19}F and 162 MHz for ^{31}P, respectively (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). Mass spectra were analyzed on a Finnigen TRACE spectrometer and API2000LC/MS. Elemental analyses were performed by a Vario EL III elemental analyzer.

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

4.1. General procedure for synthesis compounds *2a-b* and *7a-f*

All of intermediates **2a-b** and **7a-f** were synthesized according to the methods described in the literature [13,14], in which all of them have been reported.

4.2. General procedure for synthesis compounds *4* and *5*

The substituted phenoxybutanoic acid **4** was synthesized by a standard method [11]. A mixture containing substituted phenoxybutanoic acid **4** (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 **5a-d** was obtained with a yield of 85–90%.

4.3. General procedure for synthesis compounds *12*

The substituted phenoxypentanoic acid **12** was synthesized by a standard method [15]. The substituted 3-phenoxypropanol **8** could be prepared from substituted phenol and 1-chloro-3-hydroxypropane according to the methods given in the literature [15]. A solution of methanesulfonyl chloride (6 mmol) in dichloromethane (5 mL) was added to a stirred mixture of substituted 3-phenoxypropanol **8** (5 mmol) and triethylamine (6 mmol) in dichloromethane (10 mL) at 0–5 °C. The resultant mixture was stirred for 3–5 h at room temperature. The solvent was filtered, and the filtrate was evaporated under reduced pressure to afford crude product **9**, and then, a mixture of ethanol (10 mL) and sodium (5 mmol) was heated under refluxed for 2 h, and diethyl malonate (5 mmol) was added dropwise over about 1 h. The resultant mixture was refluxed for 5–8 h at 70–80 °C, and filtered, the filtrate was evaporated under reduced pressure to afford crude product **10**

Table 3
Herbicidal activity of compounds **IV-1–4.**

Compd.	R	X	Y	post-emergence, 150 g ai/ha					
				[a]EC	SV	DS	AT	AR	EP
IV-1	Me	3-CF_3	H	0	0	0	0	0	0
IV-2	Me	2-Cl	4-F	0	0	0	0	0	0
IV-3	Ph	3-CF_3	H	0	0	0	0	0	0
IV-4	Ph	2-Cl	4-F	0	0	0	0	0	0
Clacyfos (HW02)				0	0	0	100	85	90

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

Table 4
Broad Spectrum Testing of the Title Compounds **III-1**, **4**, **8.**

Compd	Dosage	post-emergence activity (%)							
	g ai/ha	[a]AT	EP	BC	BJ	PC	CA	*BO*	RS
III-1	150	100	100	80	80	100	70	75	85
	75	40	80	70	80	90	60	70	80
III-4	150	98	98	80	90	100	80	80	80
	75	100	80	70	85	100	75	60	80
III-8	150	90	100	80	80	80	75	75	50
	75	100	70	70	80	80	70	60	50
Glyphosate	150	100	100	80	80	60	90	80	65
	75	80	90	70	30	60	70	70	60

[a] AT for *Abutilon theophrasti*; EP for *Eclipta prostrata;* BC *for Brassica chinensis* L.; BJ for *Brassica juncea*; PC for *Pharbitis nil* (Linn.) Choisy; CA for *Chenopodium album*;BO for *Brassica oleracea*; RS for *Raphanus sativus* L.

which was used without further purification (Scheme 4). To a solution of sodium hydroxide (2 M, 80 mL), an intermediate **10** was added. The resulting mixture was then stirred for 18 h at room temperature, and acidified with dilute hydrochloric acid. The acid **11** was precipitated, filtered off, and subsequently washed with water, and then dissolved into dimethylformamide (10 mL), refluxed for 8 h at 110–120 °C, and cooled to room temperature. Then ice water (30 mL) was added to the mixture, and the precipitate was filtered off. A colorless crystal (**12**) was obtained with a yield of 90–96% (Scheme 4).

*4.4. General procedure for synthesis compounds **13a-b***

A mixture containing substituted phenoxypentanoic acid **12** (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 the substituted phenoxypentanoyl chlorides, which is a light yellow oil **13a-b** was obtained with a yield of 71–84%.

4.5. General procedure for synthesis compounds II-1–4

A solution of substituted phenoxyacetyl chloride **5a–b** (3.3 mmol) in dichloromethane (15 mL) was added to a stirred mixture of α-hydroxyalkylphosphonates **2a–b** (3 mmol) and triethylamine (3.3 mmol) in dichloromethane (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 dichloromethane 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 eluted with petroleum ether/acetone (2:1, v/v) to give the corresponding title compounds **II-1–4** in pure form. Their structures were confirmed by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, ^{19}F NMR, IR, MS and elemental analysis. And the physicochemical properties and spectroscopic data for all of the title compounds **II-1–4** are as follows.

*4.5.1. 2-{[(4-fluorophenoxybutyryloxy)(methyl)methyl]}-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**II-1**)*

White solid; yield 81%; m.p. 63–65 °C; **IR** (KBr, cm^{-1}): 3148, 2982, 1729(C=O), 1647, 1568, 1493, 1462, 1445, 1346, 1296, 1247, 1190, 1133, 1027, 965, 873, 795 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.03 (s, 3H), 1.11 (s, 3H), 1.54 (dd, 3H, *J* = 6.8 Hz, *J* = 15.6 Hz, P—$CHCH_3$), 2.09–2.17 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.60 (t, 2H, *J* = 7.2 Hz, $CO_2CH_2CH_2CH_2O$), 3.90–4.15 (m, 4H + 2H, 2 × (OCH_2), $CO_2CH_2CH_2CH_2O$), 5.40–5.46 (m, 1H, P—$CHCH_3$), 6.79–6.99 (m, 4H, ^{2,3,5and6}H-Ph); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 14.76, 20.95, 21.40, 24.36, 30.47, 32.42, 63.84 (d, $^1J_{C\text{-}P}$ = 165.8 Hz), 66.75, 115.38 (d, *J* = 8.1 Hz), 115.59 (d, *J* = 23.2 Hz), 153.23, 157.29 (d, $^1J_{C\text{-}F}$ = 238.2 Hz), 171.55; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.83; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 15·22; **EI-MS** (70 eV): *m*/*z* 374 (M^+); **Anal. Calcd for** $C_{17}H_{24}FO_6P$: C, 54.54; H, 6.46; Found: C, 54.70; H, 6.60.

*4.5.2. 2-{[(3-trifluoromethylphenoxybutyryloxy)(methyl)methyl]}-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**II-2**)*

Oil; yield 77%; n_D^{20}1.5051; **IR** (KBr, cm^{-1}): 3178, 2932, 1729 (C=O), 1647, 1568, 1493, 1462, 1415, 1346, 1284, 1247, 1169, 1133, 1027, 932, 863, 801 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.03 (s, 3H), 1.10 (s, 3H), 1.54 (dd, 3H, *J* = 7.2 Hz, *J* = 16.4 Hz, $PCHCH_3$), 2.14–2.20 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.61 (t, 2H, *J* = 7.2 Hz, $CO_2CH_2CH_2CH_2O$), 3.89–4.15 (m, 4H + 2H, 2 × (OCH_2), $CO_2CH_2CH_2CH_2O$), 5.41–5.46 (m, 1H, $PCHCH_3$), 7.04–7.41 (m, 4H, ^{2,4,5and6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 15.10, 21.31, 21.72, 24.56, 30.72, 32.78, 64.15 (d, $^1J_{C\text{-}P}$ = 165.4 Hz), 66.80, 111.41, 117.57, 118.16, 124.13 (q, $^1J_{C\text{-}F}$ = 270.5 Hz), 130.30, 131.93 (q, $^2J_{C\text{-}F}$ = 32.1 Hz), 159.00, 172.04; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −63.60; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 15·30; **EI-MS** (70 eV): *m*/*z* 424 (M^+); **Anal. Calcd for** $C_{18}H_{24}F_3O_6P$: C, 50.95; H, 5.70; Found: C, 51.10; H, 6.03.

*4.5.3. 2-{[(4-fluorophenoxybutyryloxy)(phenyl)methyl]}-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**II-3**)*

White solid; yield 83%; mp 83–85 °C; **IR** (KBr, cm^{-1}): 3310, 3019, 1729(C=O), 1647, 1568, 1493, 1457, 1421, 1346, 1292, 1247, 1169, 1099, 1027, 932, 863, 824 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.92 (s, 3H), 1.11 (s, 3H), 2.11–2.15 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.68 (t, 2H, *J* = 6.8 Hz, $CO_2CH_2CH_2CH_2O$), 3.89–4.11 (m, 4H + 2H, 2 × (OCH_2), $CO_2CH_2CH_2CH_2O$), 6.30 (d, 1H, *J* = 12.8 Hz, PCH), 6.75–7.49 (m, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 20.92, 21.56, 24.45, 30.58, 32.42, 66.77, 69.86 (d, $^1J_{C\text{-}P}$ = 165.4 Hz), 115.23 (d, *J* = 7.6 Hz), 115.73 (d, *J* = 22.8 Hz), 127.74 (d, *J* = 5.2 Hz), 128.68, 128.99, 133.03, 154.70, 157.15 (d, $^1J_{C\text{-}F}$ = 236.6 Hz), 171.62; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.95; 160 MHz, $CDCl_3$): δ 10·26; **EI-MS** (70 eV): *m*/*z* 436 (M^+); **Anal. Calcd for** $C_{22}H_{26}FO_6P$: C, 60.55; H, 6.00; Found: C, 60.72; H, 6.35.

*4.5.4. 2-{[(3-trifluoromethylphenoxybutyryloxy)(phenyl)methyl]}-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one (**II-4**)*

White solid; yield 76%; mp 97–99 °C; **IR** (KBr, cm^{-1}): 3293, 2896, 1729(C=O), 1652, 1573, 1489, 1462, 1425, 1346, 1298, 1239, 1156, 1088, 1027, 932, 859, 799 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.92 (s, 3H), 1.11 (s, 3H), 2.15–2.19 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.69 (t, 2H, *J* = 7.2 Hz, $CO_2CH_2CH_2CH_2O$), 3.85–4.11 (m, 4H + 2H, 2 × (OCH_2), $CO_2CH_2CH_2CH_2O$), 6.31 (d, 1H, *J* = 13.2 Hz, PCH), 6.99–7.50 (m, 9H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 20.87, 21.49, 24.29, 30.48, 32.39, 66.46, 69.85 (d, $^1J_{C\text{-}P}$ = 165.3 Hz), 111.02, 117.42, 117.83, 126.52 (q, $^1J_{C\text{-}F}$ = 264.6 Hz), 127.77, 128.63, 128.98, 129.94 (q, $^2J_{C\text{-}F}$ = 30.3 Hz), 129.94, 132.71, 158.68, 171.38; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −63.59; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 10·23; **EI-MS** (70 eV): *m*/*z* 486 (M^+); **Anal. Calcd for** $C_{23}H_{26}F_3O_6P$: C, 56.79; H, 5.39; Found: C, 60.10; H, 5.75.

4.6. General procedure for synthesis compounds III-1–24

Following the procedure described for **II-1**–**II-4**, compounds **III-1**–**III-24** were obtained. Their structures were confirmed by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR, ^{19}F NMR, IR, MS and elemental analysis. And the physicochemical properties and spectroscopic data for all of the title compounds **III-1**–**24** are as follows.

4.6.1. O,O-*Dimethyl(4-fluorophenoxybutyryloxy)(methyl) methylphosphonate (**III-1**)*

Oil; yield 81%; n_D^{20} 1.5110; **IR** (KBr): 3396, 2962, 1744(C=O), 1656, 1567, 1442, 1378, 1326, 1291, 1242, 1174, 1126, 1037, 939, 762 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.47 (dd, 3H, J = 8.6 Hz, J = 20.6 Hz, P—CH—CH_3), 2.08–2.14 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.59 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2$), 3.77 (d, 3H, J = 6.4 Hz, P—O—CH_3), 3.80 (d, 3H, J = 6.0 Hz, P—O—CH_3), 3.97 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2$), 5.30–5.35 (m, 1H, P—CH), 6.80-6.83 (m, 2H, ^{2,6}H-Ph), 6.94–6.98 (m, 2H, ^{3,5}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 14.94, 24.39, 30.45, 53.15, 63.90 (d, $^{1}J_{C\text{-}P}$ = 169.8 Hz), 66.82, 115.18 (d, J = 7.6 Hz), 115.61 (d, J = 22.8 Hz), 154.68, 156.44 (d, $^{1}J_{C\text{-}F}$ = 236.6 Hz), 171.76; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.94; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 22.54; **MS** (EI) (m/z): 334 (M^+); **Anal. Calcd for** $C_{14}H_{20}FO_6P$: C, 50.30; H, 6.03; Found: C, 50.20; H, 6.10.

4.6.2. O,O-*Dimethyl(3-trifluoromethylphenoxybutyryloxy)(methyl) methylphosphonate 5 (**III-2**)*

Oil; yield 74%; n_D^{20} 1.5231; **IR** (KBr): 3406, 2958, 1744(C=O), 1656, 1592, 1452, 1378, 1330, 1291, 1242, 1168, 1126, 1037, 962, 786 cm^{-1};**^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.47 (dd, 3H, J = 7.2 Hz, J = 17.2 Hz, P—CH—CH_3), 2.12–2.19 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.60 (t, 2H, J = 7.6 Hz, $CO_2CH_2CH_2CH_2$), 3.77 (d, 3H, J = 6.4 Hz, P—O—CH_3), 3.80 (d, 3H, J = 4.8 Hz, P—O—CH_3—CH_3), 4.05 (t, 2H, J = 6.4 Hz, $CO_2CH_2CH_2CH_2$), 5.31-5.35 (m, 1H, P—CH), 7.04–7.41 (m, 4H, ^{2,4,5,6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 14.80, 24.16, 30.24, 53.00, 63.86 (d, $^{1}J_{C\text{-}P}$ = 169.5 Hz), 66.43, 110.91, 117.14, 117.66, 123.73 (q, $^{1}J_{C\text{-}F}$ = 270.5 Hz), 129.79, 131.43(q, $^{2}J_{C\text{-}F}$ = 32.0 Hz), 158.64, 171.48; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −63.63; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 22.49; **MS** (EI) (m/z): 384 (M^+); **Anal. Calcd for** $C_{15}H_{20}F_3O_6P$: C, 46.88; H, 5.25; Found: C, 47.05; H, 5.17.

4.6.3. O,O-*Dimethyl(4-chloro-2-fluorophenoxybutyryloxy)(methyl) methylphosphonate (**III-3**)*

Oil; yield 78%; n_D^{20} 1.5155; **IR** (KBr): 3030, 2980, 2860, 1745 (C=O), 1580, 1260, 1170, 1060, 810 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.47 (dd, 3H, J = 7.2 Hz, J = 10.8 Hz, P—$CHCH_3$), 2.13–2.20 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.65 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2$), 3.77 (d, 3H, J = 8.8 Hz, P—O—CH_3), 3.80 (d, 3H, J = 8.8 Hz, P—O—CH_3), 4.05 (t, 2H, J = 7.8 Hz, $CO_2CH_2CH_2CH_2$), 5.31–5.33 (m, 1H, P—CH), 6.85–7.14 (m, 3H, ^{3,5,6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 14.92, 24.26, 30.21, 53.14, 63.95 (d, $^{1}J_{C\text{-}P}$ = 170.3 Hz), 68.08, 113.72, 114.02 (d, J = 8.9 Hz), 117.15 (d, J = 21.7 Hz), 123.40, 150.64, 156.31 (d, $^{1}J_{C\text{-}F}$ = 244.1 Hz), 171.67; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −122.51; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 22.49; **MS** (EI) (m/z): 368 (M^+); **Anal. Calcd for** $C_{14}H_{19}ClFO_6P$: C, 45.60; H, 5.19; Found: C, 45.76; H, 5.53.

4.6.4. O,O-*Dimethyl(2-chloro-4-fluorophenoxybutyryloxy)(methyl) methylphosphonate (**III-4**)*

Oil; yield 76%; n_D^{20} 1.5161; **IR** (KBr): 3030, 2980, 2860, 1745 (C=O), 1580, 1260, 1170, 1060, 810 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.47 (dd, 3H, J = 7.2 Hz, J = 17.2 Hz, P—$CHCH_3$), 2.13–2.20 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.65 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2$), 3.77 (d, 3H, J = 8.8 Hz, P—O—CH_3), 3.80 (d, 3H, J = 8.8 Hz, P—O—CH_3), 4.04 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2$), 5.32–5.33 (m, 1H, P—CH), 6.85–7.14 (m, 3H, ^{3,5,6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 14.92, 24.26, 30.21, 53.14, 63.95 (d, $^{1}J_{C\text{-}P}$ = 169.7 Hz), 68.08, 113.72, 114.03 (d, J = 8.9 Hz), 117.29 (d, J = 25.9 Hz), 123.35, 150.64, 156.31(d, $^{1}J_{C\text{-}F}$ = 240.5 Hz), 171.67; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −122.44; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 22.48; **MS** (EI) (m/z): 368 (M^+); **Anal. Calcd for** $C_{14}H_{19}ClFO_6P$: C, 45.60; H, 5.19; Found: C, 45.87; H, 5.30.

4.6.5. O,O-*Dimethyl(4-fluorophenoxybutyryloxy)(phenyl) methylphosphonate (**III-5**)*

Oil; n_D^{20} 1.5228; yield 74%; **IR** (KBr): 3365, 2955, 1743(C=O), 1656, 1603, 1571, 1506, 1452, 1248, 1208, 1046, 948, 830 cm^{-1};**^{1}H NMR** (600 MHz, $CDCl_3$): δ 2.11–2.14 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.63–2.70 (m, 2H, $CO_2CH_2CH_2CH_2$), 3.63 (d, 3H, J = 10.8 Hz, P—O—CH_3), 3.70 (d, 3H, J = 10.8 Hz, P—O—CH_3), 3.94 (m, 2H, $CO_2CH_2CH_2CH_2$), 6.19 (d, 1H, J = 13.2 Hz, P—CH), 6.76–7.48 (m, 9H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 24.50, 30.59, 53.74, 66.86, 69.99 (d, $^{1}J_{C\text{-}P}$ = 168.8 Hz), 115.27 (d, J = 7.7 Hz), 115.69 (d, J = 22.9 Hz), 127.72 (d, J = 5.2 Hz), 128.59, 128.84, 133.02, 154.74, 157.15 (d, $^{1}J_{C\text{-}F}$ = 236.6 Hz), 171.51; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.94; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 18δ 18.68; **MS** (EI) (m/z): 396 (M^+); **Anal. Calcd for** $C_{19}H_{22}FO_6P$: C, 57.58; H, 5.59; Found: C, 57.14; H, 5.42.

4.6.6. O,O-*Dimethyl(3-trifluoromethylphenoxybutyryloxy)(phenyl) methylphosphonate (**III-6**)*

Oil; n_D^{20} 1.5025; yield 75%; **IR** (KBr): 3416, 2954, 1743(C=O), 1652, 1570, 1452, 1397, 1330, 1166, 1049, 959, 884 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 2.15–2.19 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.66–2.71 (m, 2H, $CO_2CH_2CH_2CH_2$), 3.63 (d, 3H, J = 10.8 Hz, P—O—CH_3), 3.70 (d, 3H, J = 10.8 Hz, P—O—CH_3), 4.02 (m, 2H, $CO_2CH_2CH_2CH_2$), 6.20 (d, 1H, J = 13.8 Hz, P—CH), 6.99–7.49 (m, 9H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 24.50, 30.59, 53.80, 66.56, 70.07 (d, $^{1}J_{C\text{-}P}$ = 169.2 Hz), 111.08, 117.43, 117.88, 125.56 (q, $^{1}J_{C\text{-}F}$ = 270.5 Hz), 127.77, 128.62, 128.89, 129.93 (q, $^{2}J_{C\text{-}F}$ = 32.3 Hz), 132.99, 155.61, 158.75, 171.49; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −63.70; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 18.68; **MS** (EI) (m/z): 446 (M^+); **Anal. Calcd for** $C_{20}H_{22}F_3O_6P$: C, 53.82; H, 4.97; Found: C, 53.84; H, 5.02.

4.6.7. O,O-*Dimethyl(4-chloro-2-fluorophenoxybutyryloxy)(phenyl) methylphosphonate (**III-7**)*

Oil; n_D^{20} 1.5319; yield 78%; **IR** (KBr): 3412, 2953, 1741(C=O), 1656, 1572, 1472, 1450, 1399, 1305, 1265, 1193, 1132, 1050, 949, 894, 860, 803, 700 cm^{-1};**^{1}H NMR** (600 MHz, $CDCl_3$): δ 2.13–2.18 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.65–2.73 (m, 2H, $CO_2CH_2CH_2CH_2$), 3.64 (d, 3H, J = 10.8 Hz, P—O—CH_3), 3.70 (d, 3H, J = 10.8 Hz, P—O—CH_3), 4.03 (m, 2H, $CO_2CH_2CH_2CH_2$), 6.19 (d, 1H, J = 13.2 Hz, P—CH), 6.82–7.48 (m, 8H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 24.36, 30.32, 53.76, 68.04, 70.07 (d, $^{1}J_{C\text{-}P}$ = 164.6 Hz), 115.54, 116.90 (d, J = 21.7 Hz), 124.16, 126.60 (d, J = 8.8 Hz), 127.72 (d, J = 5.5 Hz), 128.58, 128.84, 132.98, 143.95 (d, J = 9.8 Hz), 152.67 (d, $^{1}J_{C\text{-}F}$ = 249.2 Hz), 171.39; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −123.04; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 18.68; **MS** (EI) (m/z): 430 (M^+); **Anal. Calcd for** $C_{19}H_{21}ClFO_6P$: C, 52.97; H, 4.91; Found: C, 52.71; H, 4.88.

4.6.8. O,O-*Dimethyl(2-chloro-4-fluorophenoxybutyryloxy)(phenyl) methylphosphonate (**III-8**)*

Oil; n_D^{20} 1.5261;yield 80%; **IR** (KBr): 3396, 2956, 1744(C=O), 1657, 1600, 1572, 1495, 1452, 1398, 1261, 1193, 1052, 950, 905, 860, 803, 769 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 2.14–2.19 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.69–2.77 (m, 2H, $CO_2CH_2CH_2CH_2$), 3.64 (d, 3H, J = 10.8 Hz, P—O—CH_3), 3.70 (d, 3H, J = 10.8 Hz, P—O—CH_3), 3.99–4.04 (m, 2H, $CO_2CH_2CH_2CH_2$), 6.19 (d, 1H, J = 13.2 Hz, P—CH), 6.81-7.48 (m, 8H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 24.38, 30.32, 53.80, 68.12, 70.05 (d, $^{1}J_{C\text{-}P}$ = 168.9 Hz), 113.81, 114.17 (d, J = 8.5 Hz), 117.31, 117.56, 127.71, 128.57, 128.82, 133.02, 150.74, 156.44 (d, $^{1}J_{C\text{-}F}$ = 240.9 Hz), 171.47; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.94; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 18.63; **MS** (EI) (m/z): 430 (M^+); **Anal. Calcd for** $C_{19}H_{21}ClFO_6P$: C, 52.97; H, 4.91; Found: C, 52.65; H, 5.08.

4.6.9. O,O-*Dimethyl(4-fluorophenoxybutyryloxy)(ethyl) methylphosphonate (**III-9**)*

Oil; n_D^{20} 1.5118; yield 79%; **IR** (KBr): 3416, 2939, 1742(C=O), 1648, 1587, 1563, 1457, 1392, 1329, 1286, 1240, 1168, 1126, 1095, 1049, 937, 826, 790, 752 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.97 (t, 3H, J = 7.2 Hz, P—$CHCH_2CH_3$), 1.86–1.98 (m, 2H, P—$CHCH_2CH_3$), 2.10–2.16 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.63 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2$), 3.75 (d, 3H, J = 6.4 Hz, P—O—CH_3), 3.78 (d, 3H, J = 6.4 Hz, P—O—CH_3), 3.97 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2$), 5.23–5.28 (m, 1H, P—$CHCH_2CH_3$), 6.80–6.84 (m, 2H, ^{2,6}H-Ph), 6.94–6.99 (m, 2H, ^{3,5}H-Ph); **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.94; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 23.04; **MS** (EI) (*m/z*): 348 (M^+); **Anal. Calcd for** $C_{15}H_{22}FO_6P$: C, 51.73; H, 6.37; Found: C, 52.05; H, 6.08.

4.6.10. O,O-*Dimethyl(3-trifluoromethylphenoxybutyryloxy)(ethyl) methylphosphonate (**III-10**)*

Oil; n_D^{20} 1.4948; yield 79%; **IR** (KBr): 3420, 2958, 1742(C=O), 1657, 1592, 1572, 1453, 1399, 1331, 1286, 1240, 1168, 1126, 1095, 1049, 957, 826, 794, 747 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.97 (t, 3H, J = 7.6 Hz, P—$CHCH_2CH_3$), 1.80–1.97 (m, 2H, P—$CHCH_2CH_3$), 2.13–2.21 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.64 (t, 2H, J = 7.6 Hz, $CO_2CH_2CH_2CH_2$), 3.75 (d, 3H, J = 6.0 Hz, P—O—CH_3), 3.78 (d, 3H, J = 6.0 Hz, P—O—CH_3), 4.06 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2$), 5.22–5.28 (m, 1H, P—$CHCH_2CH_3$), 7.04–7.41 (m, 4H, ^{2,4,5,6}H-Ph); **^{19}FNMR** (376 MHz, $CDCl_3$): δ −63.63; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 23.02; **MS** (EI) (*m/z*): 398 (M^+); **Anal. Calcd for** $C_{16}H_{22}F_3O_6P$: C, 48.25; H, 5.57; Found: C, 48.65; H, 5.22.

4.6.11. O,O-*Dimethyl(4-chloro-2-fluorophenoxybutyryloxy)(ethyl) methylphosphonate (**III-11**)*

Oil; n_D^{20} 1.5111; yield 77%; **IR** (KBr): 3398, 2949, 1742(C=O), 1639, 1588, 1569, 1453, 1389, 1331, 1286, 1248, 1173, 1126, 1095, 1046, 957, 826, 794, 736 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 0.97 (t, 3H, J = 7.80 Hz, P—$CHCH_2CH_3$), 1.80–1.96 (m, 2H, P—$CHCH_2CH_3$), 2.14–2.19 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.64 (t, 2H, J = 7.8 Hz, $CO_2CH_2CH_2CH_2$), 3.76 (d, 3H, J = 10.2 Hz, P—O—CH_3), 3.78 (d, 3H, J = 10.8 Hz, P—O—CH_3), 4.07 (t, 2H, J = 6.6 Hz, $CO_2CH_2CH_2CH_2$), 5.22–5.26 (m, 1H, P—$CHCH_2CH_3$), 6.89 (t, 1H, J = 9.0 Hz, ^{6}H-Ph), 7.02-7.11 (m, 2H, ^{3,5}H-Ph); **^{19}FNMR** (376 MHz, $CDCl_3$): δ-122.40; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 22.95; **MS** (EI) (*m/z*): 382 (M^+); **Anal. Calcd for** $C_{15}H_{21}ClFO_6P$: C, 47.07; H, 5.53; Found: C, 47.35; H, 5.48.

4.6.12. O,O-*Dimethyl(2-chloro-4-fluorophenoxybutyryloxy)(ethyl) methylphosphonate (**III-12**)*

Oil; n_D^{20} 1.5201; yield 71%; **IR** (KBr): 3438, 2948, 1742(C=O), 1658, 1582, 1506, 1395, 1294, 1251, 1208, 1165, 1094, 1038, 937, 841 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 0.97 (t, 3H, J = 7.2 Hz, P—$CHCH_2CH_3$), 1.83–1.98 (m, 2H, P—$CHCH_2CH_3$), 2.14–2.20 (m, 2H, $CO_2CH_2CH_2CH_2$), 2.68 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2$), 3.75 (d, 3H, J = 10.2 Hz, P—O—CH_3), 3.78 (d, 3H, J = 10.8 Hz, P—O—CH_3), 4.06 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2$), 5.22–5.27 (m, 1H, P—$CHCH_2CH_3$), 6.84–7.13 (m, 3H, ^{6}H-Ph, ^{5}H-Ph, ^{3}H-Ph); **^{19}FNMR** (376 MHz, $CDCl_3$): δ −122.44; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 22.95; **MS** (EI) (*m/z*): 382 (M^+); **Anal. Calcd for** $C_{15}H_{21}ClFO_6P$: C, 47.07; H, 5.53; Found: C, 47.05; H, 5.08.

4.6.13. O,O-*Dimethyl(4-fluorophenoxybutyryloxy)(propyl) methylphosphonate (**III-13**)*

Oil; n_D^{20} 1.5118; yield 80%; **IR** (KBr): 3441, 2959, 1742(C=O), 1658, 1571, 1506, 1395, 1294, 1247, 1208, 1165, 1097, 1038, 948, 829 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, J = 7.6 Hz, P—$CHCH_2CH_2CH_3$), 1.42 (m, 2H, P—$CHCH_2CH_2CH_3$), 1.82–1.96 (m, 2H, P—$CHCH_2CH_2CH_3$), 2.12–2.18 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.61 (m, 2H, $CO_2CH_2CH_2CH_2O$), 3.76 (d, 3H, J = 10.2 Hz, P—O—CH_3), 3.78 (d, 3H, J = 10.2 Hz, P—O—CH_3), 3.97 (m, 2H, $CO_2CH_2CH_2CH_2O$), 5.34 (m, 1H, P—$CHCH_2CH_2CH_3$), 6.82–6.96 (m, 4H, ^{2,6}H-Ph, ^{3,5}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 13.44, 18.76, 24.53, 30.40, 31.10, 53.21, 66.87, 66.96 (d, $^1J_{C-P}$ = 165.7 Hz), 115.26 (d, J = 8.0 Hz), 115.73 (d, J = 23.0 Hz), 154.76, 156.04 (d, $^1J_{C-F}$ = 238.1 Hz), 172.15; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.94; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 23.28; **MS** (EI) (*m/z*): 362 (M^+); **Anal. Calcd for** $C_{16}H_{24}FO_6P$: C, 53.04; H, 6.68; Found: C, 53.05; H, 7.08.

4.6.14. O,O-*Dimethyl(3-trifluoromethylphenoxybutyryloxy)(propyl) methylphosphonate (**III-14**)*

Oil; n_D^{20} 1.5085; yield 80%; **IR** (KBr): 3429, 2967, 1742(C=O), 1653, 1582, 1515, 1468(ArC-C), 1391, 1294, 1247, 1208, 1156, 1097, 1038, 954, 831 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, J = 7.2 Hz, P—$CHCH_2CH_2CH_3$), 1.25–1.45 (m, 2H, P—$CHCH_2CH_2CH_3$), 1.78–1.88 (m, 2H, P—$CHCH_2CH_2CH_3$), 2.13–2.18 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.63 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2O$), 3.75 (d, 3H, J = 6.8 Hz, P—O—CH_3), 3.78 (d, 3H, J = 6.8 Hz, P—O—CH_3), 4.05 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2O$), 5.31–5.36 (m, 1H, P—$CHCH_2CH_2CH_3$), 7.05–7.41 (m, 4H, ^{2,4,5,6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 13.41, 18.91, 24.38, 30.31, 31.11, 53.15, 66.55, 67.06 (d, $^1J_{C-P}$ = 166.0 Hz), 111.09, 117.41, 117.82, 121.78 (q, $^1J_{C-F}$ = 270.1 Hz), 129.91, 131.86 (q, J = 32.5 Hz), 158.76, 171.92; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −63.66; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 23.25; **MS** (EI) (*m/z*): 412 (M^+); **Anal. Calcd for** $C_{17}H_{24}FO_6P$: C, 49.52; H, 5.87; Found: C, 49.71; H, 6.13.

4.6.15. O,O-*Dimethyl(4-chloro-2-fluorophenoxybutyryloxy)(propyl) methylphosphonate (**III-15**)*

Oil; n_D^{20} 1.5353; yield 82%; **IR** (KBr): 3421, 2960, 2875, 1740 (C=O), 1657, 1573, 1497, 1472, 1400, 1293, 1261, 1193, 1053, 949, 913, 905, 860, 825, 762 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, J = 7.2 Hz, P—$CHCH_2CH_2CH_3$), 1.25–1.47 (m, 2H, P—$CHCH_2CH_2CH_3$), 1.78–1.87 (m, 2H, P—$CHCH_2CH_2CH_3$), 2.14–2.21 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.68 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2O$), 3.75 (d, 3H, J = 10.8 Hz, P—O—CH_3), 3.78 (d, 3H, J = 10.8 Hz, P—O—CH_3), 4.05 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2O$), 5.30–5.37 (m, 1H, P—$CHCH_2CH_2CH_3$), 6.85–7.14 (m, 3H, ^{3,5,6}H-Ph); **^{19}FNMR** (376 MHz, $CDCl_3$): δ −122.47; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 23.20; **MS** (EI) (*m/z*): 396 (M^+); **Anal. Calcd for** $C_{16}H_{23}ClFO_6P$: C, 48.43; H, 5.84; Found: C, 48.51; H, 5.93.

4.6.16. O,O-*Dimethyl(2-chloro-4-fluorophenoxybutyryloxy)(propyl) methylphosphonate (**III-16**)*

Oil; n_D^{20} 1.5129; yield 83%; **IR** (KBr): 3426, 2959, 1741(C=O), 1656, 1572, 1502, 1471, 1399, 1306, 1268, 1209, 1131, 1038, 948, 894, 858, 825, 759 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.91 (t, 3H, J = 7.6 Hz, P—$CHCH_2CH_2CH_3$), 1.25–1.48 (m, 2H, P—$CHCH_2CH_2CH_3$), 1.78–1.87 (m, 2H, P—$CHCH_2CH_2CH_3$), 2.12–2.20 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.64 (t, 2H, J = 7.2 Hz, $CO_2CH_2CH_2CH_2O$), 3.76 (d, 3H, J = 10.4 Hz, P—O—CH_3), 3.79 (d, 3H, J = 10.4 Hz, P—O—CH_3), 4.07 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2O$), 5.30–5.37 (m, 1H, P—$CHCH_2CH_2CH_3$), 6.86–7.12 (m, 3H, ^{3,5and6}H-Ph); **^{19}FNMR** (376 MHz, $CDCl_3$): δ −132.36; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 23.22; **MS** (EI) (*m/z*): 396 (M^+); **Anal. Calcd for** $C_{16}H_{23}ClFO_6P$: C, 48.43; H, 5.84; Found: C, 48.79; H, 6.03.

4.6.17. O,O-*Diethyl(4-fluorophenoxybutyryloxy)(phenyl) methylphosphonate (**III-17**)*

Oil; n_D^{20} 1.5129; yield 80%; **IR** (KBr): 3065, 2982, 1746(C=O), 1652, 1568, 1507, 1475, 1452, 1392, 1290, 1209, 1050, 972, 830 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.18 (t, 3H, J = 6.6 Hz, P—O—CH_2CH_3), 1.24 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 2.09–2.14 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.62–2.70 (m, 2H, $CO_2CH_2CH_2CH_2O$), 3.90–4.09 (m, 6H, $CO_2CH_2CH_2CH_2O$, 2 × P—O—CH_2CH_3), 6.16 (d, 1H, J = 13.8 Hz, P—CH), 6.75–7.48 (m, 9H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ

16.19, 24.45, 30.50, 63.17, 66.78, 70.32 (d, $^1J_{C-P}$ = 169.0 Hz), 115.23 (d, J = 8.0 Hz), 115.61 (d, J = 23.0 Hz), 127.69, 127.74, 128.51 (d, J = 19.0 Hz), 133.29, 154.72, 157.05 (d, $^1J_{C-F}$ = 236.6 Hz), 171.47; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −132.36; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 16.26; **MS** (EI) (*m/z*): 424 (M^+); **Anal. Calcd for** $C_{21}H_{26}FO_6P$: C, 59.43; H, 6.17; Found: C, 59.45; H, 6.31.

4.6.18. O,O-*Diethyl(3-trifluoromethylphenoxybutyryloxy)(phenyl) methylphosphonate (**III-18**)*

Oil; n_D^{20} 1.4941; yield 81%; **IR** (KBr): 3065, 2982, 1744(C=O), 1651, 1568, 1494, 1452, 1393, 1330, 1238, 1167, 1125, 1049, 961, 883, 793 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.18 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 1.24 (t, 3H, J = 6.6 Hz, P—O—CH_2CH_3), 2.14–2.18 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.66–2.70 (m, 2H, $CO_2CH_2CH_2CH_2O$), 3.92–4.09 (m, 6H, $CO_2CH_2CH_2CH_2O$, 2 × P—O—CH_2CH_3), 6.17 (d, 1H, J = 13.2 Hz, P—CH), 6.99–7.48 (m, 9H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 16.18, 24.31, 30.45, 63.17, 66.47, 70.38 (d, $^1J_{C-P}$ = 169.0 Hz), 110.99, 117.31, 117.80, 127.69 (q, $^1J_{C-F}$ = 266.9 Hz), 127.74, 128.39, 128.66, 129.85, 131.44 (q, $^2J_{C-F}$ = 32.0 Hz), 133.22, 158.69, 171.37; **^{19}FNMR** (376 MHz, $CDCl_3$): δ-65.36; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 16.22; **MS** (EI) (*m/z*): 474 (M^+); **Anal. Calcd for** $C_{22}H_{26}F_3O_6P$: C, 55.70; H, 5.52; Found: C, 55.85; H, 5.66.

4.6.19. O,O-*Diethyl(4-chloro-2-fluorophenoxybutyryloxy)(phenyl) methylphosphonate (**III-19**)*

Oil; n_D^{20} 1.5205; yield 79%; **IR** (KBr): 3067, 2981, 1743(C=O), 1651, 1568, 1505, 1474, 1306, 1268, 1208, 1164, 1049, 948, 894 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.18 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 1.22 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 2.12–2.15 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.64–2.71 (m, 2H, $CO_2CH_2CH_2CH_2O$), 3.91–4.05 (m, 6H, $CO_2CH_2CH_2CH_2O$, 2 × P—O—CH_2CH_3), 6.16 (d, 1H, J = 13.6 Hz, P—CH), 6.82–7.47 (m, 8H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 16.30, 24.35, 30.27, 63.28, 67.98, 70.43 (d, $^1J_{C-P}$ = 168.8 Hz), 115.49, 116.84 (d, J = 21.5 Hz), 124.14, 125.40 (d, J = 8.5 Hz), 127.71 (d, J = 5.2 Hz), 128.42, 128.66, 133.25, 145.56 (d, J = 10.3 Hz), 152.27 (d, $^1J_{C-F}$ = 248.4 Hz), 171.38; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −126.36; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 16.18; **MS** (EI) (*m/z*): 458 (M^+); **Anal. Calcd for** $C_{21}H_{25}ClFO_6P$: C, 54.97; H, 5.49; Found: C, 55.15; H, 5.61.

4.6.20. O,O-*Diethyl(2-chloro-4-fluorophenoxybutyryloxy)(phenyl) methylphosphonate (**III-20**)*

Oil; n_D^{20} 1.5169; yield 78%; **IR** (KBr): 3066, 2973, 1744(C=O), 1653, 1569, 1495, 1473, 1452, 1330, 1243, 1165, 1051, 958, 859 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.19 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 1.24 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 2.15–2.18 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.70–2.75 (m, 2H, $CO_2CH_2CH_2CH_2O$), 3.93–4.08 (m, 6H, $CO_2CH_2CH_2CH_2O$, 2 × P—O—CH_2CH_3), 6.16 (d, 1H, J = 13.8 Hz, P—CH), 6.81–7.48 (m, 8H); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 16.23, 24.39, 30.31, 63.24, 68.08, 70.43 (d, $^1J_{C-P}$ = 168.8 Hz), 113.79, 114.11 (d, J = 9.0 Hz), 117.42 (d, J = 26.4 Hz), 127.75, 128.43, 128.66, 128.89, 133.29, 150.31, 156.44 (d, $^1J_{C-F}$ = 242.1 Hz), 171.54; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −128.33; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 16.17; **MS** (EI) (*m/z*): 458 (M^+); **Anal. Calcd for** $C_{21}H_{25}ClFO_6P$: C, 54.97; H, 5.49; Found: C, 55.30; H, 5.53.

4.6.21. O,O-*Diethyl(4-fluorophenoxybutyryloxy)(methyl) methylphosphonate (**III-21**)*

Oil; n_D^{20} 1.4762; yield 87%; **IR** (KBr): 3055, 2984, 1744(C=O), 1651, 1508, 1476, 1448, 1392, 1329, 1291, 1246, 1165, 1098, 1048, 967, 831, 794 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.31 (t, 3H, J = 6.6 Hz, P—O—CH_2CH_3), 1.33 (t, 3H, J = 6.6 Hz, P—O—CH_2CH_3), 1.44–1.48 (m, 3H, P—CH-CH_3), 2.10–2.14 (m, 2H, $CO_2CH_2CH_2$-CH_2O), 2.58 (m, 2H, $CO_2CH_2CH_2CH_2O$), 3.97 (t, 2H, J = 5.4 Hz, $CO_2CH_2CH_2CH_2O$), 4.13–4.17 (m, 2 × 2H, 2 × P—O—CH_2CH_3), 5.27–5.31 (m, 1H, P—CH-CH_3), 6.81–6.97 (m, 4H, ^{2,3,5,6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 15.02, 16.34, 24.46, 30.52, 62.65, 64.36 (d, $^1J_{C-P}$ = 170.2 Hz), 66.88, 115.23 (d, J = 7.7 Hz), 115.65 (d, J = 22.9 Hz), 154.74, 157.09 (d, $^1J_{C-F}$ = 236.6 Hz), 171.82; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −123.36; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 19.83; **MS** (EI) (*m/z*): 362 (M^+); **Anal. Calcd for** $C_{16}H_{24}FO_6P$: C, 53.04; H, 6.68; Found: C, 53.33; H, 6.81.

4.6.22. O,O-*Diethyl(3-trifluoromethylphenoxybutyryloxy)(methyl) methylphosphonate (**III-22**)*

Oil; n_D^{20} 1.4582; yield 78%; **IR** (KBr): 3458, 2984, 2938, 1744 (C=O), 1650, 1609, 1591, 1493, 1452, 1331, 1290, 1241, 1167, 1126, 1097, 1047, 966, 793 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.29 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 1.32 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 1.47 (dd, 3H, J = 7.2 Hz, J = 6.6 Hz, P—$CHCH_3$), 2.14–2.17 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.59–2.62 (m, 2H, $CO_2CH_2CH_2CH_2O$), 4.07 (t, 2H, J = 6.0 Hz, $CO_2CH_2CH_2CH_2O$), 4.13–4.18 (m, 2 × 2H, 2 × P—O—CH_2CH_3), 5.29–5.33 (m, 1H, P—CH-CH_3), 7.04-7.40 (m, 4H, ^{2,4,5,6}H-Ph); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 14.88, 16.19, 24.21, 30.29, 62.53, 64.29 (d, $^1J_{C-P}$ = 170.1 Hz), 66.45, 110.91, 117.15, 117.67, 123.73 (q, $^1J_{C-F}$ = 270.5 Hz), 129.78, 131.50 (q, $^2J_{C-F}$ = 31.5 Hz), 158.63, 171.57; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −64.41; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 20.01; **MS** (EI) (*m/z*): 412 (M^+); **Anal. Calcd for** $C_{17}H_{24}F_3O_6P$: C, 49.52; H, 5.87; Found: C, 50.01; H, 5.99.

4.6.23. O,O-*Diethyl(4-chloro-2-fluorophenoxybutyryloxy)(methyl) methylphosphonate (**III-23**)*

Oil; n_D^{20} 1.4859; yield 79%; **IR** (KBr): 3471, 2984, 2937, 1744 (C=O), 1654, 1607, 1587, 1504, 1446, 1416, 1392, 1306, 1244, 1208, 1166, 1131, 1026, 968, 859, 858, 799 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.31 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 1.33 (t, 3H, J = 7.2 Hz, P—O—CH_2CH_3), 1.47 (dd, 3H, J = 7.2 Hz, J = 16.8 Hz, P—$CHCH_3$), 2.13–2.16 (m, 2H, $CO_2CH_2CH_2CH_2O$), 2.59–2.62 (m, 2H, $CO_2CH_2CH_2$-CH_2O), 4.06–4.16 (m, 2H + 2 × 2H, $CO_2CH_2CH_2CH_2O$, 2 × P—O—CH_2CH_3), 5.26–5.32 (m, 1H, P—CH-CH_3), 6.87–7.10 (m, 3H, ^{3,5,6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 14.97, 16.31, 24.30, 30.26, 62.63, 64.41(d, $^1J_{C-P}$ = 170.1 Hz), 68.02, 115.43, 116.79 (d, J = 21.4 Hz), 124.08 (d, J = 3.5 Hz), 125.34 (d, J = 8.4 Hz), 145.44 (d, J = 10.4 Hz), 152.21 (d, $^1J_{C-F}$ = 248.2 Hz), 171.70; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −123.31; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 19.96; **MS** (EI) (*m/z*): 396 (M^+); **Anal. Calcd for** $C_{16}H_{23}ClFO_6P$: C, 48.43; H, 5.84; Found: C, 48.69; H, 5.96.

4.6.24. O,O-*Diethyl(2-chloro-4-fluorophenoxybutyryloxy)(methyl) methylphosphonate (**III-24**)*

Oil; n_D^{20} 1.4826; yield 78%; **IR** (KBr): 3396, 2985, 1744(C=O), 1647, 1498, 1474, 1445, 1404, 1292, 1261, 1194, 1165, 1026, 969, 905, 860, 801 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$): δ 1.29 (m, 3H, P—O—CH_2CH_3), 1.33 (m, 3H, P—O—CH_2CH_3), 1.47 (dd, 3H, J = 7.2 Hz, J = 16.8 Hz, P—$CHCH_3$), 2.15–2.18 (m, 2H, $CO_2CH_2CH_2$-CH_2O), 2.63–2.67 (m, 2H, $CO_2CH_2CH_2CH_2O$), 4.04–4.19 (m, 2H + 2 × 2H, $CO_2CH_2CH_2CH_2O$, 2 × P—O—CH_2CH_3), 5.27–5.33 (m, 1H, P—CH-CH_3), 6.85–7.13 (m, 3H, ^{3,5,6}H-Ph); **^{13}CNMR** (100 MHz, $CDCl_3$): δ 15.02, 16.34, 24.37, 30.31, 62.70, 64.41 (d, $^1J_{C-P}$ = 170.3 Hz), 68.15, 113.78, 114.05 (d, J = 9.1 Hz), 117.38 (d, J = 25.7 Hz), 123.49, 150.71, 156.38 (d, $^1J_{C-F}$ = 240.7 Hz), 171.80; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.46; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 20.04; **MS** (EI) (*m/z*): 396 (M^+); **Anal. Calcd for** $C_{16}H_{23}ClFO_6P$: C, 48.43; H, 5.84; Found: C, 48.51; H, 6.03.

4.7. General procedure for Synthesis Compounds IV–1–4

Following the procedure described for **II-1–4**, compounds **IV-1–4** were obtained. Their structures were confirmed by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, ^{31}P NMR, IR, MS and elemental analysis. And the physicochemical properties and spectroscopic data for all of the title compounds **IV-1–4** are as follows.

4.7.1. O,O-*Dimethyl(3-trifluoromethylphenoxyvaleryloxy)(methyl) methylphosphonate (**IV-1**)*

Oil; yield 86%; n_D^{20} 1.4971; **IR** (KBr): 3180, 2982, 2857, 1784 (C=O), 1563, 1492, 1260, 1170, 1065, 815 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.48 (dd, 3H, *J* = 6.8 Hz, *J* = 20.4 Hz, P—$CHCH_3$), 1.84–1.87 (m, 2 × 2H, $CO_2CH_2CH_2CH_2CH_2$), 2.45–2.48 (m, 2H, $CO_2CH_2CH_2CH_2CH_2$), 3.79 (d, 3H, *J* = 6.4 Hz, P—O—CH_3), 3.82 (d, 3H, *J* = 6.4 Hz, P—O—CH_3), 3.99–4.01 (m, 2H, $CO_2CH_2CH_2CH_2CH_2$), 5.31–5.36 (m, 1H, P—CH-CH_3), 7.04–7.41 (m, 4H, ^{2,4,5,6}H-Ph); **^{13}CNMR** (150 MHz, $CDCl_3$): δ 15.01, 21.47, 28.29, 33.59, 53.21, 63.88 (d, $^1J_{C\text{-}P}$ = 169.8 Hz), 67.48, 111.18, 117.13, 117.78, 123.88 (q, $^1J_{C\text{-}F}$ = 270.5 Hz), 129.94, 131.69 (q, $^2J_{C\text{-}F}$ = 32.1 Hz), 158.93, 171.95; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −63.36; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 24.04; **MS** (EI) (*m/z*): 398 (M^+); **Anal. Calcd for** $C_{16}H_{22}F_3O_6P$: C, 48.25; H, 5.57; Found: C, 48.48; H, 5.83.

4.7.2. O,O-*Dimethyl(2-chloro-4-fluorophenoxyvaleryloxy)(methyl) methylphosphonate (**IV-2**)*

Oil; yield 77%; n_D^{20} 1.4198; **IR** (KBr): 3218, 2967, 2831, 1784 (C=O), 1601, 1488, 1260, 1165, 1073, 809 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.47 (dd, 3H, *J* = 6.8 Hz, *J* = 17.2 Hz, P—$CHCH_3$), 1.88–1.89 (m, 2 × 2H, $CO_2CH_2CH_2CH_2CH_2$), 2.47–2.50 (m, 2H, $CO_2CH_2CH_2CH_2CH_2$), 3.79 (d, 3H, *J* = 6.8 Hz, P—O—CH_3), 3.82 (d, 3H, *J* = 6.8 Hz, P—O—CH_3), 3.99-4.01 (m, 2H, $CO_2CH_2CH_2CH_2CH_2$), 5.31–5.35 (m, 1H, P—CH-CH_3), 6.83–7.14 (m, 3H, ^{3,5,6}H-Ph); **^{13}CNMR** (150 MHz, $CDCl_3$): δ 15.17, 21.69, 28.53, 33.83, 53.45, 64.21 (d, $^1J_{C\text{-}P}$ = 169.8 Hz), 69.38, 113.97 (d, *J* = 26.6 Hz), 114.17 (d, *J* = 10.2 Hz), 117.61 (d, *J* = 24.3 Hz), 123.69, 151.13, 156.57(d, $^1J_{C\text{-}F}$ = 240.8 Hz), 172.16; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −124.46; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 23.96; **MS** (EI) (*m/z*): 382 (M^+); **Anal. Calcd for** $C_{15}H_{21}ClFO_6P$: C, 47.07; H, 5.53; Found: C, 47.36; H, 5.78.

4.7.3. O,O-*Dimethyl(3-trifluoromethylphenoxyvaleryloxy)(phenyl) methylphosphonate (**IV-3**)*

Oil; yield 80%; n_D^{20} 1.5110; **IR** (KBr): 3286, 2953, 1744(C=O), 1702, 1600, 1564, 1495, 1472, 1452, 1398, 1261, 1193, 1052, 950, 905, 860, 803, 769 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.79–186 (m, 2 × 2H, $CO_2CH_2CH_2CH_2CH_2$), 2.53–2.58 (m, 2H, $CO_2CH_2CH_2CH_2CH_2$), 3.65 (d, 3H, *J* = 10.8 Hz, P—O—CH_3), 3.72 (d, 3H, *J* = 10.8 Hz, P—O—CH_3), 3.98 (t, 2H, *J* = 5.6 Hz, $CO_2CH_2CH_2CH_2CH_2$), 6.20 (d, 1H, *J* = 13.6 Hz, P—CH), 7.02–7.51 (m, 9H); **^{13}CNMR** (150 MHz, $CDCl_3$): δ 21.43, 28.26, 33.59, 53.67, 67.44, 69.93 (d, $^1J_{C\text{-}P}$ = 169.9 Hz), 110.07, 117.25, 117.81, 123.88 (q, $^1J_{C\text{-}F}$ = 270.5 Hz), 127.67, 128.56, 129.13, 130.19, 131.67 (q, $^2J_{C\text{-}F}$ = 32.5 Hz), 133.08, 158.92, 171.48; **^{19}FNMR** (376 MHz, $CDCl_3$): δ −65.56; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 20.13; **MS** (EI) (*m/z*): 460 (M^+); **Anal. Calcd for** $C_{21}H_{24}F_3O_6P$: C, 54.79; H, 5.25; Found: C, 60.01; H, 7.56.

4.7.4. O,O-*Dimethyl(2-chloro-4-fluorophenoxyvaleryloxy)(phenyl) methylphosphonate (**IV-4**)*

Oil; yield 79%; n_D^{20} 1.4692; **IR** (KBr): 3306, 2973, 1744(C=O), 1657, 1592, 1561, 1495, 1483, 1452, 1398, 1261, 1193, 1052, 964, 916, 843, 799, 754 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.84–188 (m, 2 × 2H, $CO_2CH_2CH_2CH_2CH_2$), 2.53–2.59 (m, 2H, $CO_2CH_2CH_2CH_2CH_2$), 3.65 (d, 3H, *J* = 10.4 Hz, P—O—CH_3), 3.72 (d, 3H, *J* = 10.4 Hz, P—O—CH_3), 3.98 (t, 2H, *J* = 6.0 Hz, $CO_2CH_2CH_2CH_2CH_2$), 6.20 (d, 1H, *J* = 13.2 Hz, P—CH), 6.81–7.50 (m, 8H); **^{13}CNMR** (150 MHz, $CDCl_3$): δ 21.48, 28.31, 33.65, 53.68, 69.16, 69.95 (d, $^1J_{C\text{-}P}$ = 169.9 Hz), 113.70, 113.92 (d, *J* = 8.3 Hz), 117.41 (d, *J* = 22.5 Hz), 123.46, 127.68, 128.50, 128.62, 133.09, 150.92, 156.37 (d, $^1J_{C\text{-}F}$ = 240.8 Hz), 171.55; **^{19}F NMR** (376 MHz, $CDCl_3$): δ −128.26; **^{31}P NMR** (160 MHz, $CDCl_3$): δ 20.03; **MS** (EI) (*m/z*): 444 (M^+); **Anal. Calcd for** $C_{20}H_{23}ClFO_6P$: C, 54.0; H, 5.21; Found: C, 54.36; H, 5.42.

Acknowledgements

This research was supported in part by the Natural Science Foundation of Hubei Province of China (No. 2014CFA111) and the National Natural Science Foundation of China (No. 21172090 and 21472062).

References

[1] Y.X. Liu, Q.Q. Zhao, Q.M. Wang, H. Li, R.Q. Huang, Y.H. Li, J. Fluor. Chem. 126 (2005) 345–348.
[2] X.Y. Xua, X.H. Qian, Z. Li, G.H. Song, W.D. Chen, J. Fluor. Chem. 126 (2005) 297–300.
[3] X.M. Zheng, Z. Li, Y.L. Wang, W.D. Chen, Q.C. Huang, C.X. Liu, G.H. Song, J. Fluor. Chem. 123 (2003) 163–169.
[4] W. Wang, H.W. He, N. Zuo, X. Zhang, J.S. Lin, W. Chen, H. Peng, J. Fluor. Chem. 142 (2012) 24–28.
[5] L.H. Ning, W. Wang, Y.J. Liang, H. Peng, L.W. Fu, H.W. He, Eur. J. Med. 48 (2012) 379–384.
[6] M.H. Chen, Z. Chen, B.A. Song, P.S. Bhadury, S. Yang, X.J. Hu, W. Xue, S. Zheng, J. Agric. Food. Chem. 57 (2009) 1383–1388.
[7] T. Wang, W. Wang, H. Peng, H.W. He, J. Heterocycl. Chem. 52 (2015) 173–179.
[8] H. Peng, T. Wang, P. Xie, T. Chen, H.W. He, J. Wan, J. Agric. Food Chem. 55 (2007) 1871–1880.
[9] H.W. He, J.L. Yuan, H. Peng, T. Chen, P. Shen, S.Q. Wan, Y.J. Li, H.L. Tan, Y.H. He, J. B. He, Y. Li, J. Agric. Food Chem. 59 (2011) 4801–4813.
[10] H.W. He, H. Peng, T. Wang, C.B. Wang, J.L. Yuan, T. Chen, J.B. He, X.S. Tan, J. Agric. Food Chem. 61 (2013) 2479–2488.
[11] W. Wang, H.W. He, N. Zuo, H.F. He, H. Peng, X.S. Tan, J. Agric. Food Chem. 60 (2012) 7581–7587.
[12] Q.D. You, Medicinal Chemistry, Chemical Industry Press, Beijing, 2003.
[13] C.B. Wang, C. Xu, X.S. Tan, H. Peng, H.W. He, Org. Biomol. Chem. 10 (2012) 1680–1685.
[14] H.W. He, T. Wang, J.L. Yuan, J. Organomet. Chem. 690 (2005) 2608–2613.
[15] R. Wen, Organic Reactions for Drug Synthesis, Chemical Industry Press, Beijing, 2002.