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The Synthesis and Herbicidal Evaluation of Fluorine-Containing Phenoxyacetoxyalkylphosphonate Derivatives

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*To investigate the influence of a fluorine moiety on the biological activity of phenoxyacetoxyalkylphosphonates, a series of fluorine-containing phenoxyacetoxyalkylphosphonates were synthesized and screened for herbicidal activity in a greenhouse. The majority of the title compounds showed better preemergence activity than postemergence activity against the test plants, especially on monocotyledon. Compound **5l** exhibited notable activity. Results showed that by introducing a fluorine moiety to the parent structure of phenoxyacetoxyalkylphosphonates, a series of new compounds with satisfactory herbicidal activity could be synthesized. A reasonable combination of a fluorine moiety and other substituents on the benzene ring had a great influence on the herbicidal activity.*

Keywords 1-hydroxyl alkylphosphonate; fluorophenoxyacetic acid; herbicidal activity; synthesis

INTRODUCTION

Fluorine is a very unique element with special biomimetic, high thermal stability and lipophilicity, which endows various prominent functionality in the organofluorine compounds. By introducing a fluorine atom into organic molecules, we can get compounds with improved physical,

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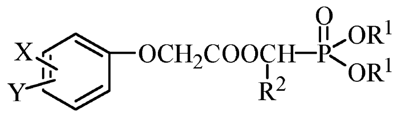


(1)

FIGURE 1 The general structure of 1-substituted phenoxyacetoxyalkylphosphonates.

chemical, and biological properties.[1–3] So the application of fluorides in pharmaceuticals and pesticides attracted more and more attention.

In our group, a recent study on 1-oxophosphonic acid derivatives revealed that 1-oxophosphonic acid derivatives, which possessed good herbicidal activities, could act as a leading structure for herbicide designing. The general structure (1) is shown in Figure 1. Structure modification has been attempted by introducing different substituents X and Y to the benzene ring.[4,5] But none of our previous work was devoted to the synthesis of fluorosubstituted phenoxyacetoxyalkylphosphonates, neither systematic structure-activity study of the this kind of compounds. So the fluorine moiety was introduced to the core structure (1) as a continued research of our previous work, and a novel series of *O*,*O*-dialkyl 1-(fluorophenoxyacetoxy)alkylphosphonates **5a–m** were synthesized and screened for herbicidal activity.

RESULTS AND DISCUSSION

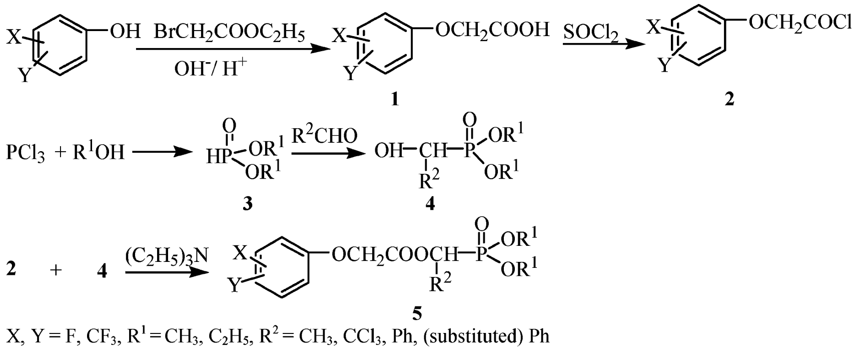
Chemistry

Compound **1** could be easily synthesized starting from fluorophenol and bromoacetic ester.[6] Dimethyl phosphite and diethyl phosphite were obtained by the reported method,[7] and compound **4** could be prepared by the reaction of compound **3** and several kinds of aldehydes using potassium fluoride and alumina (mass ratio was 1:1) as a catalyst in a yield of 65–94% according to the literature.[8,9]

The preparation of title compounds involved the condensation of fluorophenoxyacetyl chloride **2** and *O*,*O*-dimethyl 1-hydroxylalkylphosphonates or *O*,*O*-diethyl 1-hydroxylalkylphosphonates **4**. The synthetic pathway is outlined in Scheme 1, and the structures of **5a–m** are given in Table I.

The title compounds contained carboxylic ester bond which was sensitive to acid, base, and water, so the reaction required a temperature near r.t. and the reagent in anhydrous chloroform or dichoromethane.

All new compounds were identified by ^{1}H NMR, IR, MS, and elemental analysis. All the main functional groups were characterized in IR



SCHEME 1

spectra. A strong absorption near 1760 cm^{-1} was identified for the absorption C=O. A sharp and weak band at 3050–3100 cm^{-1} accounted for the C—H stretching of the benzene ring and a strong peak at 1260 cm^{-1} for P=O stretching. Another strong peak at 1330 cm^{-1} was the evidence for the Ar-CF_3 symmetry stretching. Doublets near 6.40 ppm confirmed the existence of O-CHP. The coupling constant of J_{PH} was 13.2 Hz.

Biological Assays

Herbicidal Activity Tests in Greenhouse

The herbicidal activities of title compounds **5a–m** were evaluated at a rate of 1.5 a.i. kg/ha in a set of an experiment in a greenhouse.

TABLE I The Preparation of *O,O*-Dialkyl 1-(Fluorophenoxyacetoxy) alkylphosphonates 5a–m

Compound	X	Y	R^1	R^2	Condition	Yield (%)
5a	H	3-CF_3	CH_3	2,4-2ClPh	2 h/20°C	65.3
5b	H	3-CF_3	C_2H_5	2,4-2ClPh	3 h/20°C	52.8
5c	H	3-CF_3	CH_3	3,4-2ClPh	2 h/20°C	73.2
5d	H	3-CF_3	C_2H_5	3,4-2ClPh	3 h/20°C	79.2
5e	H	3-CF_3	C_2H_5	2-ClPh	3 h/20°C	65.4
5f	H	3-CF_3	C_2H_5	3-NO_2Ph	3 h/20°C	78.5
5g	H	3-CF_3	C_2H_5	Ph	3 h/20°C	76.1
5h	H	4-F	CH_3	3-NO_2Ph	2 h/20°C	63.5
5i	H	4-F	CH_3	Ph	2 h/20°C	73.1
5j	H	4-CF_3	CH_3	CH_3	2 h/20°C	69.0
5k	H	4-CF_3	CH_3	CCl_3	2 h/20°C	66.5
5l	2-Cl	4-F	CH_3	CH_3	2 h/20°C	86.5
5m	2-Cl	4-F	CH_3	CCl_3	2 h/20°C	72.5

They were tested for a preemergence and postemergence inhibitory effect against *Echinochloa Crusgalli Beava* (barngard grass), *Digitaria Sanguinalis scop* (ascendant crabgrass), *Brassica napus L.* (rape), *Amaranthus retroflerus L.* (amaranth), and *Medicago sativa L.* (clover). Plastic pots were packed with sandy clay loam soil, and water was added up to 3 cm in depth. Fifteen to twenty seeds were sown in the soil at a depth of 5 mm and grown at 20–25°C for a few days. At the preemergence and postemergence, the diluted formulation of each compound containing acetone and Tween 80 were applied into the pots at 1.5 a.i. kg/ha. Twenty days later, the preemergence herbicidal activity against each weed was visually evaluated. At the postemergence, the solution of the chemicals tested was applied to the foliage of plants grown at 2 to 3 leaves stage with a sprayer at the rate of 1.5 a.i. kg/ha and with a spelling volume of 1000 L/ha. All treatments were replicated three times in a completely randomized design. Test plants were harvested 20 days after sowing, were determined for fresh weight, and were evaluated for postemergence herbicidal activity. The percentage growth inhibition of roots and aerial parts were calculated in relation to the mass of the roots and aerial parts of the control, respectively. The results are listed in Table II.

TABLE II The Herbicidal Activity of Title Compounds (1.5 a.i. kg/ha, Relative Inhibition of Growth %)

	Ech.[a]		*Dig.*		*Bra.*		*Ama.*		*Med.*	
Compound	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
5a	34.7	9.9	56.7	4.4	55.1	75.0	25.3	100	24.1	16.2
5b	21.6	30.6	63.8	0	0	44.0	86.4	88.5	89.9	100
5c	54.9	25.0	6.4	16.0	80.3	36.2	100	92.3	100	76.6
5d	48.0	30.6	97.9	20.0	37.4	49.6	72.3	96.2	93.2	100
5e	75.5	8.3	97.9	36.0	16.1	43.3	68.2	100	100	100
5f	88.3	0	97.9	32.0	33.9	61.7	100	84.6	100	83.3
5g	90.2	51.4	100	16.0	43.3	83.7	91.0	84.6	100	100
5h	64	31.0	76.7	55.2	16.6	44.8	38.9	79.1	52.1	38.9
5i	55.9	50.7	84.5	45.1	48.3	56.7	63.9	77.5	60.4	49.4
5j	0	34.3	10.1	12.6	17.9	28.8	0	63.1	8.3	26.0
5k	0	10.3	14.7	0	15.9	21.0	0	71.1	0	14.3
5l	94.8	76.1	100	67.5	96.9	82.4	97.2	100	97.9	92.2
5m	87.5	68.5	95.4	60.8	95.9	79.4	86.1	100	95.8	88.3

[a]*Ech: Echinochloa Crusgalli Beava*; *Dig: Digitaria Sanguinalis scop*; *Bra: Brassica napus L. Ama: Amaranthus retroflerus L.*; *Med: Medicago sativa*

Post: postemergence; Pre: preemergence.

IC_{50} Values Test

Based on the preliminary bioassays, title compounds were tested for IC_{50} values against the preemergence growth of *Cucumis sativa L*. at different concentrations by the following method. A compound with a certain concentration was dissolved in acetone and placed on a filter paper (5.5 cm diameter) in Petri dishes (9 cm), and 10 cucumber (*Cucumis sativa L.*) seeds (Jinyan 4) were placed on the filter paper after soaking in water for 6 h. The Petri dishes with cucumber seeds were placed in a LRH-250-G lighting culture tank at 28°C for 3 days with 10 h of lighting and 14 h in the dark. After 3 days of cultivation, the inhibition percentage was calculated by the corresponding control using the length of the taproot as an indicator. The concentrations were 24.0, 12.0, 6.0, 3.0, and 1.5 $\mu g\ g^{-1}$ for compounds **5b**, **5c**, **5d**, and **5e**; 18.0, 7.2, 2.88, and 1.152 $\mu g\ g^{-1}$ for compounds **5f** and **5g**; 4.0, 2.0, 1.0, 0.5, and 0.25 $\mu g\ g^{-1}$ for compound **5h**; 2.0, 1.0, 0.5, 0.25, and 0.125 $\mu g\ g^{-1}$ for compound **5i**; 240.0, 160.0, 106.67, 71.11, and 47.41 $\mu g\ g^{-1}$ for compound **5j**; 800.0, 400.0, 200.0, 100.0, and 50.0 $\mu g\ g^{-1}$ for compound **5k**; 0.5, 0.25, 0.125, 0.0625, and 0.01325 $\mu g\ g^{-1}$ for compound **5l**; and 1.0, 0.5, 0.25, 0.125, and 0.0625 $\mu g\ g^{-1}$ for compound **5m**. Three replications per concentration were performed. According to the average inhibition of cucumber root at five concentration for each test compound, IC_{50} was estimated by regression analysis using a logarithm of concentration and a probit of corresponding inhibition percentage. The results of bioassay are listed in Table III. As there was not enough sample for compound **5a**, only 12 results were listed.

As Table II indicates, there were remarkable differences among the herbicidal activity of the title compounds, and they showed acceptable herbicidal activity except for compounds **5h**, **5i**, **5j**, and **5k**. The majority of title compounds showed better preemergence activity

TABLE III The IC_{50} of Title Compounds Against *Cucumis sativa L.*

No.	Regression Equation	IC_{50} ($\mu g\ g^{-1}$)	No.	Regression Equation	IC_{50} ($\mu g\ g^{-1}$)
5b	$Y = 4.44 + 0.91x$	4.14 (4.01–4.27)	**5h**	$Y = 5.15 + 0.10x$	0.73 (0.60–0.86)
5c	$Y = 4.46 + 0.89x$	4.04 (3.93–4.15)	**5i**	$Y = 5.15 + 1.22x$	0.75 (0.68–0.82)
5d	$Y = 4.28 + 0.82x$	7.58 (7.40–7.70)	**5j**	$Y = 0.85 + 2.14x$	87.94 (87.81–88.07)
5e	$Y = 4.47 + 0.94x$	3.68 (3.56–3.76)	**5k**	$Y = 1.18 + 1.83x$	119.92 (119.02–119.28)
5f	$Y = 4.53 + 0.72x$	4.56 (4.35–4.64)	**5l**	$Y = 6.45 + 1.43x$	0.10 (0.02–0.21)
5g	$Y = 4.59 + 0.81x$	3.19 (3.00–3.25)	**5m**	$Y = 5.99 + 1.10x$	0.13 (0.055–0.20)

[a] IC_{50} value is defined as the micromolar concentration required for 50% inhibition in the growth of a root length of Cucumber (*Cucumis sativa L.*)
[b] The fiducial limit was 95%.

than postemergence activity against the test plants especially on monocotyledon, such as compounds **5l**, and **5m**, **5f**, and **5g** exhibited notable preemergence inhibitory effects against 5 plants species and 4 plants species, except *Brassica napus L.*, respectively, and compounds **5d** and **5e** also exhibited good preemergence inhibitory effects against *Digitaria Sanguinalis scop*. On the other hand, the title compounds showed better postemergence activity on dicotyledon than monocotyledon. Compounds **5a**, **5b**, **5c**, **5g**, and **5m** exhibited obvious postemergence inhibitory effects (>90%) against *Amaranthus retroflerus L. or Medicago sativa,* especially compounds **5d**, **5e**, and **5l**, which exhibited 92–100% inhibitory effects against both *Amaranthus retroflerus L.* and *Medicago sativa.* According to the IC_{50} value shown in Table III, compounds **5l** and **5m**, for which the IC_{50} were 0.10 and 0.13 $\mu g\ g^{-1}$, respectively, displayed higher inhibitory activity, whereas **5j** and **5k**, for which the IC_{50} were 87.94 $\mu g\ g^{-1}$ and 119.92 $\mu g\ g^{-1}$, respectively, displayed lower inhibitory activity against the growth of the root of *Cucumis sativa L.* The IC_{50} results well corresponded to the results in Table II except for compounds **5h** and **5i**, which showed much better inhibitory activity against the growth of *Cucumis sativa L.* than other test dicotyledon. As seen from Table II, compounds **5l** and **5m** exhibited higher inhibitory activity, whereas **5j** and **5k** exhibited lower inhibitory activity, of only 0–28% against the test plants except for the postemergence inhibition against *Amaranthus retroflerus* in 63.1% and 71.3%, respectively, in the greenhouse.

Among all the compounds, compound **5l** showed the highest activity, which exhibited 94.8–100% preemergence inhibitory activity against all the test plants, 92.2–100% post-emergence inhibition against both *Amaranthus retroflerus L.* and *Medicago sativa*, and 67–82% post-emergence inhibition against other test plants. Its IC_{50} value also showed the highest activity against the growth of the root of *Cucumis sativa L.*

We found the structure of substituents X and Y in the benzene ring had great influence on the herbicidal activity: such herbicidal activity could be enhanced by introducing 2-Cl-4-F to the benzene ring, whereas the introduction of X and Y as 1-H-4-CF_3 resulted in a sharp decrease in their herbicidal activity toward test plants. As a typical example, the herbicidal activity of compounds **5l** and **5m (**X and Y as 2-Cl-4-F, R^1 as CH_3, R^2 as CH_3 or CCl_3**)** was much higher than that of compounds **5j** and **5k (**X and Y as 1-H-4-CF_3, R^1 as CH_3, R^2 as CH_3 or CCl_3**)** and also higher than others. So we can conclude that the herbicidal activity of title compounds highly depends upon the structure of the substituents on the benzene ring.

In conclusion, a series of new compounds with satisfactory herbicidal activity could be attained by the introduction of a fluorine moiety. A reasonable combination of a fluorine moiety and other substituents had great influence on their herbicidal activity. These results provided some interesting hints for further study of the structure modification and structure-activity relationship of this kind of phenoxyacetoxyalkylphosphate derivatives.

EXPERIMENTAL

Mass spectra were measured on a Finnigan Trace MS 2000 spectrometer. Infrared spectra were recorded in potassium bromide disks on a Nicolet Avatar360 FTIR spectrometer. ^{1}H NMR was recorded in deuterocholroform solution at 400 MHz using tetramethysilane as internal standard on Varian Mercury-Plus 400 spectrometer. Elemental analysis was performed by an Elementar Vario EL III elementary analyzer. Melting points (m.p.) were measured on an electrothermal melting-point apparatus, and the temperature was uncorrected.

The General Synthetic Procedure for 1 and 2

To a three-neck boiling flask, fluorophenol (40 mmol), bromoacetic ester (7.01 g, 42 mmol), and potassium carbonate (6.0 g, 43.5 mmol) were added by order; then anhydrous DMSO (150 mL) was added. The mixture was stirred and kept at 70–80°C for 5 h and then was treated with ice water immediately. After the yellow solid was filtered off and dissolved in acetone (20 mL), sodium hydrate (2 mol/L, 30 mL) was added and then stirred for another 2 h at r.t. Then hydrochloric acid (2 mol/L, 30 mL) was added, and the fluorophenoxyacetic acid **1** formed. The solid can be recrystalized as a white crystal in a yield of 70%. The corresponding fluorophenoxyacetyl chloride **2** can be easily obtained as a yellow liquid in a 90% yield by treating compound **1** with thionyl chloride.

The General Synthetic Procedure for 4

Dimethyl phosphite (1.38 g, 10 mmol) or diethyl phosphite **3** (1.10 g, 10 mmol) and several kinds of aldehydes (10 mmol) were stirred at r.t. for 10 min; then potassium fluoride and alumina (mass ratio was 1:1, 3 g) were added. The mixture was stirred for another 30 min, dissolved in dichoromethane (15 mL), and filtered. Dichoromethane was evaporated under reduced pressure, and the products were formed as white solids or a colorless liquid in a yield of 65–94%.

The General Synthetic Procedure for 5a–m

A solution of fluorophenoxyacetyl chloride **2** (5.2 mmol) in trichloromethane (10 mL) was added dropwise to stirred mixture of 1-hydroxyalkylphosphonate **4** (5 mmol) and triethylamine (0.53 g, 5 mmol) in trichloromethane (15 mL) at 2∼4°C. The resultant mixture was stirred at an ambient temperature for 2∼3 h, washed with hydrochloric acid (0.1 mol/L, 25 mL), saturated sodium hydrate solution (25 mL) and brine (25 mL) separately; dried; and evaporated. The residue was chromatographed on silica with 20% acetone in petroleum ether as an eluent to give **5a–m** as a yellow liquid or white solid.

O,O-Dimethyl1-(3-trifluoromethylphenoxyacetoxy)2,4-dichlorobenzylphosphonate (5a)

Yellow liquid, n_D^{20} 1.5221; ^1H NMR (400 MHz, $CDCl_3$): δ 3.58–3.71 (d, 6H, J_{HP} = 9.7 Hz, $2OCH_3$), 4.74 (s, 2H, OCH_2CO), 6.40–6.42 (d, 1H, J_{HP} = 13.3 Hz, OCHP), 7.01–7.40 (m, 7H, C_6H_4, C_6H_3); IR (ν_{max}, cm^{-1}): 3076 (Ar-H), 1754 (C=O), 1330 (Ar-CF_3), 1265 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 93 (76), 125 (42), 127 (43), 175 (94), 255 (100), 487 (33); anal. calcd. for $C_{18}H_{16}O_6PF_3Cl_2$: C, 44.35; H, 3.29. Found: C, 44.60; H, 3.31%.

O,O-Diethyl 1-(3-trifluoromethylphenoxyacetoxy)2,4-dichlorobenzylphosphonate (5b)

Yellow liquid, n_D^{20} 1.5139; ^1H NMR (400 MHz, $CDCl_3$): δ 1.18–1.30 (m, 6H, J_{HH} = 7.0 Hz, $2OCH_2C\underline{H_3}$), 3.94–4.10 (m, 4H, J_{HH} = 7.2 Hz, 2O $\underline{CH_2}CH_3$), 4.78 (s, 2H, OCH_2CO), 6.60–6.63 (d, 1H, J_{HP} = 13.3 Hz, OCHP), 7.04–7.47 (m, 7H, C_6H_4, C_6H_3); IR (ν_{max}, cm^{-1}): 3079 (Ar-H), 1758 (C=O), 1331 (Ar-CF_3), 1266 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 93 (82), 121 (100), 145 (94), 173 (96), 231 (65), 516 (5.8); anal. calcd. for $C_{20}H_{20}O_6PF_3Cl_2$: C, 46.60; H, 3.88. Found: C, 46.50; H, 3.99%.

O,O-Dimethyl 1-(3-trifluoromethylphenoxyacetoxy) 3,4-dichlorobenzy phosphonate (5c)

Yellow liquid, n_D^{20} 1.5320; ^1H NMR (400 MHz, $CDCl_3$): δ 3.50–3.58 (d, 6H, J_{HP} = 10.2 Hz, $2OCH_3$), 4.49 (s, 2H, OCH_2CO), 6.50–6.64 (d, 1H, J_{HP} = 13.2 Hz, OCHP), 7.04–7.42 (m, 7H, C_6H_4, C_6H_3); IR (ν_{max}, cm^{-1}): 3079 (Ar-H), 1775 (C=O), 1333 (Ar-CF_3), 1267 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 93 (95), 109 (74), 127 (47), 145 (81), 175 (100), 486 (2.6); anal. calcd. for $C_{18}H_{16}O_6PF_3Cl_2$: C, 44.35; H, 3.29. Found: C, 44.85; H, 3.48%.

O,O-Diethyl 1-(3-trifluoromethylphenoxyacetoxy) 3,4-dichlorobenzylphosphonate (5d)

Yellow liquid, n_D^{20} 1.5159; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.10–1.30 (m, 6H, J_{HH} = 7.2 Hz, $2OCH_2C\underline{H}_3$), 3.99–4.22 (m, 4H, J_{HH} = 7.0 Hz, 2O $\underline{CH_2}CH_3$), 4.78 (2H, OCH_2CO), 6.09–6.10 (d, 1H, J_{HP} = 13.3 Hz, $\overline{OCHP)}$, 7.00–7.40 (m, 7H, C_6H_4, C_6H_3); IR (ν_{max}, cm^{-1}): 3075 (Ar-H), 1777 (C=O), 1330 (Ar-CF_3), 1264 (P=O), 740 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 121 (100), 145 (92), 175 (83), 516 (80); anal. calcd. for $C_{20}H_{20}O_6PF_3Cl_2$: C, 46.60; H, 3.88. Found: C, 46.58; H, 3.93%.

O,O-Diethyl 1-(3-trifluoromethylphenoxyacetoxy) 2-chlorobenzylphosphonate (5e)

Yellow liquid, n_D^{20} 1.4932; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28–1.30 (m, 6H, J_{HH} = 6.9 Hz, $2OCH_2\underline{CH_3}$), 3.91–4.20 (m, 4H, J_{HH} = 7.0 Hz, 2O $\underline{CH_2}CH_3$), 4.75 (2H, $OCH_2\overline{CO)}$, 6.71–6.73 (d, 1H, J_{HP} = 13.3 Hz, $\overline{OCHP)}$, 7.02–7.54 (m, 8H, $2C_6H_4$); IR (ν_{max}, cm^{-1}): 3070 (Ar-H), 1750 (C=O), 1333 (Ar-CF_3), 1263 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 108.9 (82), 121 (100), 138 (98), 175 (94), 197 (85), 480 (4.5); anal. calcd. for $C_{20}H_{21}O_6PF_3Cl$: C, 49.95; H, 4.37. Found: C, 49.392; H, 4.42%.

O,O-Diethyl 1-(3-trifluoromethylphenoxyacetoxy)3-nitrobenzylphosphonate (5f)

Yellow solid, m.p. 86.7–87.7°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.23–1.30 (m, 6H, J_{HH} = 7.0 Hz, $2OCH_2\underline{CH_3}$), 3.80–4.20 (m, 4H, J_{HH} = 7.2 Hz, $2O\underline{CH_2}CH_3$), 4.77 (s, 2H, $OCH_2\overline{CO)}$, 6.50–6.60 (d, 1H, J_{HP} = 13.3 Hz, $\overline{OCHP)}$, 7.05–7.36 (m, 8H, $2C_6H_4$); IR (ν_{max}, cm^{-1}): 3074 (Ar-H), 1761 (C=O), 1335 (Ar-CF_3), 1250 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 121 (100), 145 (91), 175 (98), 491 (49); anal. calcd. for $C_{20}H_{21}O_8PF_3N$: C, 48.88; H, 4.28; N, 2.85. Found: C, 48.55; H, 4.06; N, 2.63%.

O,O-Diethyl 1-(3-trifluoromethylphenoxyacetoxy) benzylphosphonate (5g).

White solid, m.p. 92.5–93.6°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18–1.24 (m, 6H, J_{HH} = 7.4 Hz, $2OCH_2\underline{CH_3}$), 3.90–4.07 (m, 4H, J_{HH} = 7.2 Hz, $2O\underline{CH_2}CH_3$), 4.74 (s, 2H, $OCH_2\overline{CO)}$, 6.70–6.74 (d, 1H, J_{HP} = 13.2 Hz, $\overline{OCHP)}$, 7.04–7.30 (m, 9H, C_6H_4, C_6H_5); IR (ν_{max}, cm^{-1}): 3076 (Ar-H), 1770 (C=O), 1330 (Ar-CF_3), 1267 (P=O), 743 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 121 (100), 145 (85), 175 (98), 446 (15); anal. calcd. for $C_{20}H_{22}O6PF_3$: C, 53.81; H, 4.93. Found: C, 53.59, H, 4.61%.

O,O-Dimethyl 1-(4-fluorophenoxyacetoxy) 3-nitrobenzylphosphonate (5h)

Yellow liquid (63.5% yield): n_D^{20} 1.5225; ^1H NMR (400 MHz, $CDCl_3$): δ 3.70–3.81 (d, 6H, $J_{HP} = 9.7$ Hz, $2OCH_3$), 4.78 (s, 2H, OCH_2CO), 6.32–6.34 (d, 1H, $J_{HP} = 13.1$ Hz, OCHP), 6.85–7.42 (m, 8H, C_6H_4); IR (ν_{max}, cm^{-1}): 3080 (Ar-H), 1767 (C=O), 1260 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 93 (100), 109 (98), 151 (63), 170 (97), 261 (66), 413 (6); anal. calcd. for $C_{17}H_{17}O_8PNF$: C, 49.40; H, 4.15; N, 3.39, Found: C, 50.08; H, 4.35; N, 3.18%.

O,O-Dimethyl 1-(4-fluorophenoxyacetoxy) benzylphosphonate (5i).

Yellow solid, m.p. 131.1–131.3°C; ^1H NMR (400 MHz, $CDCl_3$): δ 3.62–3.72 (d, 6H, $J_{HP} = 10.4$ Hz, $2OCH_3$), 4.72 (s, 2H, OCH_2CO), 6.26–6.34 (d, 1H, $J_{HP} = 13.2$ Hz, OCHP), 6.88–7.42 (m, 9H, C_6H_5, C_6H_4); IR (ν_{max}, cm^{-1}): 3077 (Ar-H), 1770 (C=O), 1263 (P=O), 735 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 93 (99), 109 (100), 151 (11), 170 (98), 199 (80), 216 (27), 368 (18); anal. calcd. for $C_{17}H_{18}O_6PF$: C, 55.44; H, 4.93. Found: C, 55.12; H, 4.70%.

O,O-Dimethyl 1-(4-trifluoromethylphenoxyacetoxy) ethylphosphonate (5j)

'Yellow liquid, n_D^{20} 1.4609; ^1H NMR (400 MHz, $CDCl_3$): δ 1.50–1.51 (dd, 3H, $J_{HH} = 7.1$ Hz, $J_{HP} = 13.3$ Hz, CH_3), 3.76–3.84 (d, 6H, $J_{HP} = 10.0$ Hz, $2OCH_3$), 4.75 (s, 2H, OCH_2CO), 5.39–5.43 (m, 1H, $J_{HH} = 7.1$ Hz, $J_{HP} = 13.3$ Hz, OCHP), 6.97–7.58 (m, 4H, C_6H_4); IR (ν_{max}, cm^{-1}): 3087 (Ar-H), 1769 (C=O), 1330 (Ar-CF_3), 1271 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 79 (45), 93 (98), 109 (100), 138 (98), 195 (62), 356 (40); anal. calcd. for $C_{13}H_{16}O_6PF_3$: C, 43.83; H, 4.53. Found: C, 43.97; H, 4.28%.

O,O-Dimethyl 1-(4-trifluoromethylphenoxyacetoxy) trichloromethylmethylphosphonate (5k)

Yellow liquid, n_D^{20} 1.4850; ^1H NMR (400 MHz, $CDCl_3$): δ 3.76–3.91 (d, 6H, $J_{HP} = 10.0$ Hz, $2OCH_3$), 4.90 (s, 2H, OCH_2CO), 5.89–5.96 (d, 1H, $J_{HP} = 13.2$ Hz, OCHP), 6.94–7.56 (m, 4H, C_6H_4); IR (ν_{max}, cm^{-1}): 3081 (Ar-H), 1786 (C=O), 1330 (Ar-CF_3), 1271 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 79 (63), 93 (75), 109 (82), 139 (15), 175 (100), 458 (27); anal. calcd. for $C_{13}H_{13}Cl_3O_6PF_3$: C, 33.98; H, 2.85. Found: C, 33.89; H, 2.76%.

O,O-Dimethyl 1-(2-chloro-4-fluorophenoxyacetoxy) ethylphosphonate (5l)

White solid, m.p. 118.9–120.1°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48–1.54 (dd, 3H, J_{HH} = 7.1 Hz, J_{HP} = 13.1 Hz, CH_3), 3.78–3.86 (d, 6H, J_{HP} = 10.4 Hz, $2OCH_3$), 4.72 (s, 2H, OCH_2CO), 5.40–5.43 (m, 1H, J_{HH} = 7.1 Hz, J_{HP} =13.1 Hz, OCHP), 6.84–7.27 (m, 3H, C_6H_3); IR (ν_{max}, cm^{-1}): 3081(Ar-H), 1750 (C=O), 1263 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 79 (43), 93 (85), 109 (100), 138 (99), 195 (49), 340 (75); anal. calcd. for $C_{12}H_{15}ClO_6PF$: C, 42.31; H, 4.44. Found: C, 42.29; H, 4.44%.

O,O-Dimethyl 1-(2-chloro-4-fluorophenoxyacetoxy) trichloromethylmethylphosphonate (5m)

White solid, m.p. 104–105.2°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.86–3.90 (d, 6H, J_{HP} = 10.2 Hz, $2OCH_3$), 4.91 (s, 2H, OCH_2CO), 5.40–5.44 (d, 1H, J_{HP} = 13.3 Hz, OCHP), 6.91–7.27 (m, 3H, C_6H_3); IR (ν_{max}, cm^{-1}): 3089 (Ar-H), 1779 (C=O), 1266 (P=O), 742 (P—C); EIMS (probe) 70 eV, *m/z* (rel. int.): 79 (56), 93 (82), 109 (100), 159 (94), 205 (57), 442 (17); anal. calcd. for $C_{12}H_{12}Cl_4O_6PF$: C, 32.46; H, 2.72. Found: C, 32.65; H, 2.55%.

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