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Preparation of α-fluorophosphonates

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Abstract

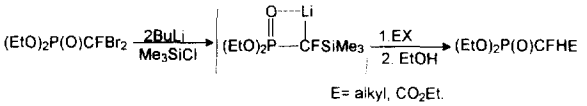
Two approaches to the preparation of α-fluorophosphonates are described. The first approach involved the free radical addition of $(EtO)_2P(O)CFBr_2$ to alkenes followed by reduction of the addition adducts with Bu_3SnH. The second approach utilized the $Pd(PPh_3)_4$ or Cu(O) catalyzed addition of $(RO)_2P(O)CFHI$ to alkenes followed by $Zn/NiCl_2 \cdot 6H_2O$ reduction of the addition adduct.

Keywords: α-Fluorophosphonates; Free radical addition; Reduction; Alkenes

1. Introduction

Phosphonates have long been known as important components in living species and have been called the backbone of biologically active compounds in the majority of life forms [1]. Recently, the introduction of the difluoromethylenephosphonate unit into organic molecules has attracted much attention due to the biological properties exhibited by these analogs as compared to the non-fluorinated analogs [2,3]. The preparation of α,α-difluoroalkylphosphonates has been well documented [4–17] and the biological properties of several α,α-difluoroalkylphosphonates have been described [3,18–24]. Recently, a general route to α,α-difluoroarylphosphonates has been reported [25].

A recent report of O'Hagan has suggested that α-fluorophosphonates may exhibit higher biological activity than the α,α-difluoroanalogs [26]. Classical approaches to the synthesis of α-fluorophosphonates generally involved fluorination with DAST, $FClO_3$ or a variety of N-F compounds [27–29]. An alternative method, developed by Blackburn [30], employed alkylation with $[(EtO)_2P(O)CFH^-]$. Patio and Savigac recently published a variation of this approach that utilized the $[(EtO)_2P(O)CFSiMe_3^-]$ anion [31,32]. This anion was generated in situ from $(EtO)_2P(O)CFBr_2$/RLi/Me_3SiCl; reaction of the anion with alkyl halides followed by treatment of the alkylation product with EtOH provided the desired alkylated phosphonates in good yields.



Previous work from our laboratory has demonstrated that the addition reaction of $(EtO)_2P(O)CF_2I$ to alkenes is readily catalyzed by either $Pd(PPh_3)_4$ or Cu(O) [5]. The corresponding addition adducts were readily reduced with $Zn/NiCl_2 \cdot 6H_2O$ in moist THF to give α,α-difluorophosphonates in good yields.

$$(EtO)_2P(O)CF_2I + CH_2=CHR \xrightarrow[\text{or Cu(O)}]{Pd(PPh_3)_4} \xrightarrow[\text{moist THF}]{Zn/NiCl_2} (EtO)_2P(O)CF_2CH_2CH_2R$$

We have attempted to utilize similar methodology for the synthesis of α-fluorophosphonates, and our approaches to this interesting class of compounds are outlined in subsequent sections of this manuscript.

2. Results and discussion

2.1. Approach [A]: Addition of $(EtO)_2P(O)CFBr_2$ (1) to alkenes

Since $(RO)_2P(O)CFBr_2$ is readily prepared from $CFBr_3$ and $(RO)_3P$ [26], we initially attempted the most simplistic route to α-fluorophosphonates; namely addition of (1) to

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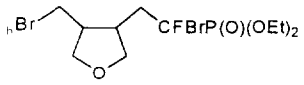
Table 1
The addition reaction of $(EtO)_2P(O)CFBr_2$ with various alkenes

$$(EtO)_2P(O)CFBr_2 + CH_2{=}CHR \xrightarrow[\text{Acetonitrile, reflux}]{\text{Benzoyl peroxide}} (EtO)_2P(O)CFBrCH_2CHBrR$$

Entry	R	The adducts	Yield [a]
5	C_4H_9	$(EtO)_2P(O)CFBrCH_2CHBrC_4H_9$	76
6	C_5H_{11}	$(EtO)_2P(O)CFBrCH_2CHBrC_5H_{11}$	75
7	C_6H_{13}	$(EtO)_2P(O)CFBrCH_2CHBrC_6H_{13}$	82
8	C_9H_{19}	$(EtO)_2P(O)CFBrCH_2CHBrC_9H_{19}$	79
9	$Si(CH_3)_3$	$(EtO)_2P(O)CFBrCH_2CHBrSi(CH_3)_3$	58
10	$CH_2OCH_2CH{=}CH_2$	Tetrahydrofuran derivative [b]	40

[a] Isolated yield.

[b] 

alkenes. This route would avoid the use of low temperatures and unstable phosphonate anions and the toxic and reactive reagents employed in the classical approaches. Preliminary experiments demonstrated that AIBN, Cu(O) and benzoyl peroxide catalyzed the addition reaction. Benzoyl peroxide gave the best results and was used in most later work. Best results were obtained in refluxing acetonitrile and most additions were completed in 24 h.

$$(EtO)_2P(O)CFBr_2 + CH_2{=}CHR \xrightarrow[\text{Reflux, } CH_3CN]{\text{Benzoyl peroxide}} (EtO)_2P(O)CFBrCH_2CHBrR$$

R = butyl, pentyl, hexyl, nonyl, $SiMe_3$

Typical by-products in this reaction are biphenyl, $(EtO)_2P(O)CFHBr$ and $(EtO)_2P(O)CFH_2$. Biphenyl can be removed by column chromatography, and the reduced phosphonates can be separated from the addition adducts by flash distillation.

Removal (reduction) of both bromine atoms was initially accomplished with $Zn/NiCl_2 \cdot 6H_2O$ in moist THF. ^{19}F NMR analysis of the reaction mixture indicated the desired α-fluorophosphonates as the major product as well as small amounts of elimination (dehydrohalogenation) products. Removal of these elimination products proved to be difficult either by column chromatography or distillation. However, tributyltin hydride easily reduced both bromines and the α-fluorophosphonates can be isolated in 60–80% yields, no elimination products were observed.

$$(EtO)_2P(O)CFBrCH_2CHBrR + Bu_3SnH \xrightarrow[\text{R.T.}]{Et_2O} (EtO)_2P(O)CFHCH_2CH_2R$$

Table 1 summarizes the addition reaction with 1-alkenes. When diallyl ether was substituted, tetrahydrofuran adduct was formed.

$$(EtO)_2P(O)CFBr_2 + (H_2C{=}CHCH_2)_2O \xrightarrow[\text{Reflux, } CH_3CN]{\text{Benzoyl peroxide}} \text{Br, CFBrP(O)(OEt)}_2 \quad 40\ \%$$

Although the addition reaction worked very well with 1-alkenes, functionalized alkenes, such as 1,2-epoxy-5-hexene, 1,2-epoxy-7-octene, allyl acetate, allyl benzene and 5-hexene-1-one proved troublesome. Generally, conversions with these functionalized derivatives were about 50%. Prolonged refluxing and the use of greater amounts of catalyst did not improve the conversion. In addition, removal of (**1**) from these lower conversion reactions proved difficult. Cyclohexene and 1-octyne did not react under the typical reaction conditions.

2.2. Approach [B]: Addition of $(RO)_2P(O)CFHI$ to alkenes

The reluctance of (**1**) to add to functionalized alkenes prompted us to investigate the addition of a more reactive α-fluoroiodophosphonate (cf. Ref. [5]). The requisite precursor was initially prepared in a one-flask procedure as outlined below.

$$(^iPrO)_2P(O)CFBr_2 \xrightarrow[\text{Moist THF}]{Zn} \left[(^iPrO)_2P(O)CFHZnBr\right] \xrightarrow[0^\circ C]{I_2} (^iPrO)_2P(O)CFHI \quad (\sim 50\%)\ (\mathbf{2})$$

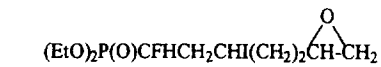
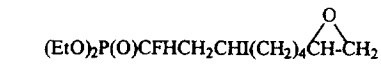
Presumably, the initially formed zinc reagent is quenched with water to give α-fluorobromophosphonate that reacts with additional zinc to give a zinc intermediate which gives **2** after the iodine quench. Although this route gave a reasonable yield (50%) of **2** in

$$(^iPrO)_2P(O)CFBr_2 \xrightarrow{Zn} [(^iPrO)_2P(O)CFBrZnBr] \xrightarrow{H_2O} (^iPrO)_2P(O)CFHBr$$
$$(^iPrO)_2P(O)CFHBr \xrightarrow{Zn} [(^iPrO)_2P(O)CFHZnBr] \xrightarrow{I_2} (^iPrO)_2P(O)CFHI$$

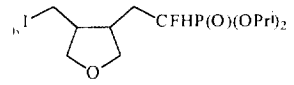
a one-flask procedure, the exotherm in the first step was

Table 2
The addition reaction of $(EtO)_2P(O)CFHI$ with various alkenes

$$(EtO)_2P(O)CFHI + CH_2{=}CHR' \xrightarrow[\text{or Cu(O)}]{Pd(PPh_3)_4} (EtO)_2P(O)CFHCH_2CHIR'$$

Entry	Reaction temp. (°C) Pd(O)	Reaction temp. (°C) Cu(O)	The adducts	Yield[a] (%)
11	60	reflux	$(EtO)_2P(O)CFHCH_2CHI(CH_2)_3CH_3$	65 [b]
12	80	reflux	$(EtO)_2P(O)CFHCH_2CHI(CH_2)_4CH_3$	78
13	50	75	$(EtO)_2P(O)CFHCH_2CHI(CH_2)_5CH_3$	60 [b]
14	60	85	$(EtO)_2P(O)CFHCH_2CHI(CH_2)_5CH_3$	66
15	45	reflux	$(EtO)_2P(O)CFHCH_2CHISi(CH_3)_3$	60
16	75	–		69
17	75	–		65
18	50	–	$(EtO)_2P(O)CFHCH_2CHICH_2OCH_2CH_3$	63
19	70	–	$(EtO)_2P(O)CFHCH_2CHICH_2OH$	67
20	70	95	$(EtO)_2P(O)CFHCH_2CHICH_2Ph$	70
21	60	–	Tetrahydrofuran derivative [b]	77

[a] Isolated yield.
[b] NMR yield determined with trifluoromethyltoluene as an internal reference.

[b] 

difficult to control on scale-up (>50 mmol); thus the reaction sequence was modified to an amenable two-step scale-up process, as outlined below:

$$(EtO)_2P(O)CFBr_2 + Bu_3P + EtOH \xrightarrow[\text{R.T.}]{\text{THF}} (EtO)_2P(O)CFHBr\ (\mathbf{3})\quad (70\text{–}80\%)$$

$$(EtO)_2P(O)CFHBr + Zn \quad (\mathbf{3})$$

$$\xrightarrow[\text{Dry THF}]{} \left[(EtO)_2P(O)CFHZnBr\right] \xrightarrow[0\,^\circ C]{I_2} (EtO)_2P(O)CFHI\quad (70\text{–}80\%)\quad (\mathbf{4})$$

When **1** is treated with tributylphosphine and THF containing ethanol, a smooth, controllable conversion to **3** occurs. Subsequent treatment of **3** with zinc followed by an iodine quench gives **4** an overall 50–60% yield.

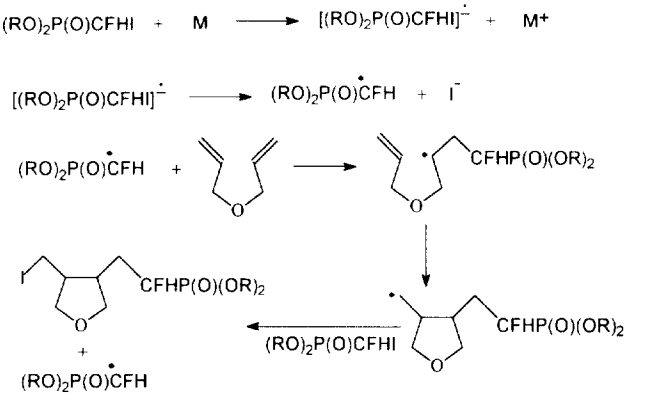
Similar to $(EtO)_2P(O)CF_2I$ [5], the addition of **4** to neat 1-alkenes is readily accomplished with $Pd(PPh_3)_4$ or Cu(O) catalysis. Approximately 20–25°C higher temperatures were required for the Cu(O) catalyzed reactions. With 1-alkenes, vinyl silane and epoxides, the

$$(RO)_2P(O)CFHI + CH_2{=}CHR' \xrightarrow[60\,^\circ C]{Pd(PPh_3)_4} (RO)_2P(O)CFHCH_2CHIR'$$

R = Et, ^{i}Pr

yields were good (Table 2). With unsaturated diols, allyl acetate and allyl phosphonates the yields were moderate to good, but purification was more difficult. The main impurity was $(EtO)_2P(O)CFH_2$. Cyclohexene and 1-hexyne did not react under these conditions.

The formation of the tetrahydrofuran addition product with diallyl ether is consistent with the expected initiation by an electron transfer mechanism.



Reaction with 4-pentene-1-ol gave two products. In addition to the expected addition adduct, a cyclized product was isolated in 21% yield.

Table 3
Preparation of 1-fluoro-functionalized phosphonates
$(EtO)_2P(O)CFHI + CH_2=CHR$

$$(EtO)_2P(O)CFHI + CH_2=CHR \xrightarrow[(2)\ Zn/NiCl_2\cdot 6H_2O,\ \text{moist THF}]{(1)\ Pd(PPh_3)_4} (EtO)_2P(O)CFHCH_2CH_2R$$

Entry	Products	Yield (%)[a]
24	$(EtO)_2P(O)CFHCH_2(CH_2)_4CH_3$	80
25	$(EtO)_2P(O)CFHCH_2(CH_2)_5CH_3$	60
26	$(EtO)_2P(O)CFHCH_2(CH_2)_6CH_3$	75
27	$(EtO)_2P(O)CFHCH_2(CH_2)_9CH_3$	65
28	$(EtO)_2P(O)CFHCH_2CH_2Si(CH_3)_3$	68
29	$(EtO)_2P(O)CFHCH_2CH_2CH_2OCH_2CH_3$	63
30	$(EtO)_2P(O)CFHCH_2(CH_2)_8CH_2OH$	60
31	$(EtO)_2P(O)CFHCH_2CH_2CH_2Ph$	71

[a]Isolated yield.

$$(^iPrO)_2P(O)CFHI + CH_2=CH(CH_2)_3OH \xrightarrow[65\ ^oC]{Pd(PPh_3)_4}$$

$$(^iPrO)_2P(O)CFHCH_2CHI(CH_2)_3OH \quad (\mathbf{22},\ 35\%) \qquad + \qquad \text{(tetrahydrofuran)}-CH_2CFHP(O)(OPr^i)_2 \quad (\mathbf{23},\ 21\%)$$

The NMR spectra of most of the adducts showed the presence of diastereomers (two ^{19}F, ^{13}C signals), and the diastereomers exhibited two distinct peaks in the GC–MS spectra.

Metal catalyzed addition of **3** to 1-alkenes was also attempted, but **3** exhibited insufficient activity to be useful.

The addition adducts of **4** were readily reduced with $Zn/NiCl_2\cdot 6H_2O$ in moist THF to give the α-fluorophosphonate derivatives. The overall addition–reduction sequence is amenable to a one-flask procedure (cf. Section 3). After the addition reaction was completed, the reaction mixture was diluted with hexane/ether and any solids removed by filtration. After solvent removal, the residue was treated with $Zn/NiCl_2\cdot 6H_2O$ in moist THF.

$$(EtO)_2P(O)CFHI + CH_2=CHR \xrightarrow[\text{or } Cu(O)]{Pd(PPh_3)_4} \xrightarrow[\text{moist THF}]{Zn/NiCl_2\cdot 6H_2O} (EtO)_2P(O)CFH(CH_2)_2R$$

Table 3 summarizes the results of the one-flask procedure. Occasionally, small amounts of an elimination product (loss of HI) were detected. In these cases, Bu_3SnH can be utilized in place of $Zn/NiCl_2\cdot 6H_2O$.

In conclusion, we have demonstrated the utility of the metal-catalyzed addition of $(RO)_2P(O)CFHI$ to 1-alkenes and 1-alkene derivatives. Reduction of the addition adducts gives the α-fluorophosphonates. The overall reaction is amenable to a one-flask procedure. The simplicity of the procedure, good yields and the ready availability of the phosphonate precursor make this an attractive route for the preparation of α-fluorophosphonates.

3. Experimental section

3.1. General

All reactions were performed in oven-dried apparatus that consisted of a two-necked flask equipped with a Teflon-coated magnetic stir bar and a reflux condenser (if necessary) connected to a nitrogen source and mineral oil bubbler. ^{19}F NMR, ^1H NMR, ^{13}C NMR, and ^{31}P NMR spectra were recorded on a Bruker AC 300-MHz spectrometer. All chemical shifts are reported in parts per million downfield of the standards. ^{19}F NMR spectra are referenced against internal $CFCl_3$, ^1H NMR and ^{13}C NMR spectra against internal TMS, and ^{31}P NMR against external H_3PO_4. FT-IR spectra were recorded as CCl_4 solutions using a solution cell with 0.1 cm path length. GC–MS spectra were performed with a Trio-1 spectrometer in the electron impact mode. High-resolution mass spectra determinations were made at the University of Iowa High Resolution Mass Spectrometry Facility. Most products are greater than 95% purity based on ^{19}F NMR and ^{13}C NMR spectroscopy and GC–MS. Column chromatography was carried out on 200–245 mesh silica gel.

3.2. Materials

Cu(O) and $Pd(PPh_3)_4$ were prepared by the literature procedures [33,34]. $(EtO)_2P(O)CFBr_2$ (**1**) was prepared by the method of Burton and Flynn [35]. Nickel chloride hexahydrate, iodine, all alkenes and benzoyl peroxide were obtained from Aldrich Chemical and used without purification. Zinc metal powder was washed with acid, water and acetone and dried under full vacuum overnight. Hexanes, diethyl ether, and acetonitrile were purchased from Fisher Scientific and used without further purification.

3.3. Preparation of diethyl 1,3-dibromo-1-fluoroalkylphosphonates

3.3.1. General procedure

A mixture of 3.28 g (10 mmol) of **1**, (11 mmol) of the respective alkenes, 0.15 g (0.6 mmol) benzoyl peroxide and 20 ml acetonitrile was refluxed under N_2 overnight. The reaction mixture was concentrated to give a residue which was purified by column chromatography (hexane:ethyl acetate = 7:3) to give corresponding adducts.

3.3.2. Diethyl 1,3-dibromo-1-fluoroheptylphosphonate (5)

Via the general procedure, 3.15 g (76%) of **5** was obtained. ^{19}F NMR ($CDCl_3$): −126.1 (m), −128.0 (m) ppm. ^1H NMR ($CDCl_3$): 4.34–4.62 (m, 5H), 2.76–3.14 (m, 2H), 1.75–2.12 (m, 2H), 1.28–1.61 (m, 10H), 0.91 (t, J = 7.2 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 8.91 (d, J = 83.2 Hz), 8.58 (d, J = 83.1 Hz) ppm. ^{13}C NMR ($CDCl_3$): 102.72 (dd, J = 269.8 Hz, J = 191 Hz), 102.67 (dd, J = 272.5 Hz, J = 190.9 Hz), 65.79 (dd, J = 9.5 Hz, J = 7.4 Hz), 65.08 (dd, J = 8.2 Hz, J = 7.6 Hz), 50.58 (d, J = 11.3 Hz), 48.54 (d,

J=8.2 Hz), 48.22 (dd, J=17.9 Hz, J=7.1 Hz), 47.47 (dd, J=17.7 Hz, J=6.7 Hz), 39.46, 38.17 (d, J=3.1 Hz), 29.36, 29.35, 21.94, 21.86, 16.45 (m), 16.38 (m), 13.90 (overlap) ppm. GC–MS: 413 (M^++1, 0.3), 367 (0.5), 369 (0.72), 371 (0.3), 333 (291), 248 (100), 250 (98.9), 233 (2.0), 195 (16.9), 183 (15.5), 111 (24.1), 109 (47.7), 93 (42.4). FT-IR (cm^{-1}): 2982 (s), 2958 (s), 1392 (m), 1231 (s), 1118 (m), 925 (vs). R_f: 0.33 (hexanes:ethyl acetate = 1:1).

3.3.3. Diethyl 1,3-dibromo-1-fluorooctylphosphonate (6)

Via the general procedure, 3.21 g (75%) of **6** was obtained. ^{19}F NMR ($CDCl_3$): −126.1 (m), −128.1 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.15–4.66 (m, 5H), 2.75–3.15 (m, 2H), 1.75–2.14 (m, 2H), 1.24–1.53 (m, 12H), 0.83–0.96 (m, 3H) ppm. ^{31}P NMR ($CDCl_3$): 9.07 (d, J=82.3 Hz), 8.78 (d, J=82.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): 102.76 (dd, J=270.1 Hz, J=191.2 Hz), 102.7 (dd, J=272.5 Hz, J=190.3 Hz), 65.79 (dd, J=10.7 Hz, J=7.3 Hz), 65.09 (dd, J=7.9 Hz, J=7.9 Hz), 50.73 (d, J=11.5 Hz), 48.63 (d, J=8.2 Hz), 48.21 (dd, J=17.6 Hz, J=7.1 Hz), 47.45 (dd, J=17.7 Hz, J=6.7 Hz), 39.74, 38.43 (d, J=3.0 Hz), 30.99, 30.92, 26.9 (overlap), 22.46 (overlap), 16.44 (d, J=5.2 Hz) (overlap), 13.90 (overlap) ppm. GC–MS: 345 (M^+ − Br, 49), 347 (M^+ − Br, 47), 317 (8.2), 289 (5.3), 265 (14.7), 248 (92), 189 (40.7), 109 (76.7), 81 (85.0), 55 (100). FT-IR (cm^{-1}): 2981 (m), 2931 (m), 1379 (s), 1229 (vs) 1117 (m), 1023 (m). R_f: 0.33 (hexanes:ethyl acetate = 1:1).

3.3.4. Diethyl 1,3-dibromo-1-fluorononylphosphonate (7)

Via the general procedure, 3.63 g (82%) of (**7**) was obtained. ^{19}F NMR ($CDCl_3$): −126.0 (m), −128.0 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.15–4.56 (m, 5H), 2.71–3.13 (m, 2H), 1.70–2.10 (m, 2H), 1.18–1.63 (m, 14H), 0.91 (m, 3H) ppm. ^{31}P NMR ($CDCl_3$): 9.10 (d, J=82.4 Hz), 8.74 (d, J=82.9 Hz) ppm. ^{13}C NMR ($CDCl_3$): 102.76 (dd, J=269.8 Hz, J=190.8 Hz), 102.7 (dd, J=272.5 Hz, J=190.8 Hz), 65.71 (dd, J=8.1 Hz, J=6.7 Hz), 65.02 (dd, J=7.9 Hz, J=7.7 Hz), 50.59 (d, J=11.2 Hz), 48.57 (d, J=8.2 Hz), 48.30 (dd, J=18.0 Hz, J=7.0 Hz), 47.53 (dd, J=17.7 Hz, J=6.3 Hz), 39.76, 38.49 (d, J=2.8 Hz), 31.60, 31.59, 28.47, 28.39, 27.2 (overlap), 22.53 (overlap), 16.46 (d, J=4.9 Hz), 16.39 (d, J=4.2 Hz), 14.03 (overlap) ppm. GC–MS: 359 (M^+ − Br, 55), 361 (M^+ − Br, 53), 279 (17.4), 248 (70), 250 (64), 223 (16.3), 183 (23), 139 (40), 109 (73.8), 81 (84.4), 55 (100). R_f: 0.33 (hexanes:ethyl acetate = 1:1). HRMS: Found 439.0038 (calc. 439.0048 for $C_{13}H_{26}{}^{79}Br_2FO_3P$).

3.3.5. Diethyl 1,3-dibromo-1-fluorododecylphosphonate (8)

Via the general procedure, 3.93 g (79%) of (**8**) was obtained. ^{19}F NMR ($CDCl_3$): −126.1 (m), −128.0 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.24–4.60 (m, 5H), 2.73–3.13 (m, 2H), 1.73–2.09 (m, 2H), 1.20–1.65 (m, 20H), 0.88 (m, 3H) ppm. ^{31}P NMR ($CDCl_3$): 9.06 (d, J=82.4 Hz), 8.72 (d, J=83.9 Hz) ppm. ^{13}C NMR ($CDCl_3$): 102.63 (dd, J=270.0 Hz, J=191.2 Hz), 102.6 (dd, J=272.3 Hz, J=191.0 Hz), 65.65 (dd, J=11.3 Hz, J=7.3 Hz), 64.94 (dd, J=7.7 Hz, J=7.7 Hz), 50.60 (d, J=11.3 Hz), 48.48 (d, J=8.3 Hz), 48.04 (dd, J=17.8 Hz, J=7.2 Hz), 47.33 (dd, J=17.4 Hz, J=6.7 Hz), 39.60, 38.34 (d, J=2.8 Hz), 31.74 (overlap), 29.36 (overlap), 29.29 (overlap), 29.22 (overlap), 28.70, 28.60, 27.12 (overlap), 22.53 (overlap), 16.30 (d, J=4.9 Hz) (overlap), 13.97 (overlap) ppm. DIP–MS: 401 (M^+ − Br, 29.7), 403 (M^+ − Br, 28.5), 321 (10.9), 248 (88.6), 250 (84.2), 183 (35.8), 127 (42.9), 109 (76.1), 81 (69.2), 55 (63.0), 43 (100). FT-IR (cm^{-1}): 2981 (s), 2955 (m), 1392 (s), 1223 (vs), 1185 (s), 1163 (s). R_f: 0.33 (hexanes:ethyl acetate = 1:1).

3.3.6. Diethyl 1,3-dibromo-1-fluoro-3-trimethylsilyl-phosphonate (9)

A mixture of 3.28 g (10 mmol) of (**1**), 1.5 g (15 mmol) of vinyltrimethyl silane, 0.15 g (0.6 mmol) benzoyl peroxide and 20 ml acetonitrile was refluxed under N_2 overnight. The reaction mixture was concentrated to give a residue which was purified by column chromatography (hexane:ethyl acetate = 7:3) to give 2.5 g (58%) of (**9**). ^{19}F NMR ($CDCl_3$): −128.1 (m), −129.8 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.31 (m, 4H), 3.61 (m, 1H), 2.63–3.05 (m, 2H), 1.37 (m, 6H), 0.14 (d, 9H) ppm. ^{31}P NMR ($CDCl_3$): 9.09 (d, J=80.1 Hz), 9.07 (d, J=86.2 Hz) ppm. ^{13}C NMR ($CDCl_3$): 106.1 (dd, J=211.3 Hz, J=188.7 Hz), 102.5 (dd, J=207.0 Hz, J=188.7 Hz), 65.62 (dd, J=7.0 Hz, J=5.5 Hz), 64.91 (dd, J=7.2 Hz, J=5.4 Hz), 44.57 (dd, J=19.1 Hz, J=6.9 Hz), 42.40 (dd, J=18.0 Hz, J=7.3 Hz), 33.53 (d, J=5.8 Hz), 32.79 (d, J=7.0 Hz), 16.44 (d, J=5.5 Hz), 16.37 (d, J=7.2 Hz), −3.06, −3.26 ppm. GC–MS: 347 (M^+ − Br, 1.4), 349 (M^+ − Br, 1.3), 320 (7.7), 322 (7.4), 293 (4.8), 255 (4.6), 199 (6.2), 165 (22.3), 137 (34.8), 109 (30.7), 73 (100). R_f: 0.36 (hexanes:ethyl acetate = 1:1).

3.3.7. Dibromo tetrahydrofuran derivative (10)

Via the general procedure, 1.71 g (40%) of (**10**) was obtained. ^{19}F NMR ($CDCl_3$): −127.8 (m), −126.6 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.25–4.45 (m, 4H), 3.26–4.21 (m, 6H), 2.19–3.03 (m, 4H), 1.37–1.45 (m, 6H) ppm. ^{31}P NMR ($CDCl_3$): 9.16 (d, J=83.4 Hz), 9.24 (d, J=83.1 Hz) ppm. ^{13}C NMR ($CDCl_3$): 16.44 (m), 31.75 (d, J=2.1 Hz), 34.19, 34.46 (d, J=1.2 Hz), 38.64 (d, J=8.2 Hz), 38.91 (d, J=8.6 Hz), 40.83 (d, J=7.0 Hz), 44.27 (d, J=8.8 Hz), 36.84 (dd, J=19.2 Hz, J=6.9 Hz), 37.26 (dd, J=19.2 Hz, J=7.0 Hz), 42.14 (dd, J=19.2 Hz, J=6.7 Hz), 43.36 (dd, J=19.0 Hz, J=6.7 Hz), 43.36 (dd, J=18.7 Hz, J=6.4 Hz), 44.29, 44.68, 47.63, 47.91, 64.96 (m), 65.66 (m), 71.68, 71.76, 71.83, 72.07, 72.15, 73.85, 73.92, 74.28, 103.4 (dd, J=267.4 Hz, J=190.2 Hz), 103.4 (dd, J=267.6 Hz, J=190.7 Hz), 103.9 (dd, J=267.0 Hz, J=190.8 Hz), 104.3 (dd, J=268.0 Hz, J=191.4 Hz) ppm. DIP–MS: 425 (M^+ − 1, 0.06), 427 (M^+ − 1, 0.10), 399 (0.12), 401 (0.10), 347 (2), 317 (3.5), 289 (2.5), 248 (2.1), 207 (1.8), 183 (100), 155 (14.0), 127 (15.3), 109 (13.6). FT-IR (cm^{-1}): 2981 (m), 2912

(s), 1717 (m), 1392 (vs), 1163 (m), 1096 (s), 916 (m). R_f: 0.17 (hexanes:ethyl acetate = 1:1).

3.4. General procedure for the treatment of the adducts with tributyltin hydride

A total of 4.4 mmol tributyltin hydride was slowly added to a mixture of 2 mmol of the addition adducts and 10 ml diethyl ether. The resulting reaction mixture was stirred at room temperature overnight. The reaction mixture was poured into 20 ml of acetonitrile and the solution was washed with hexanes (4×10 ml) [36]. The acetonitrile layer was concentrated by distillation and the remaining residue was purified by column chromatography (hexanes:ethyl acetate = 7:3) to afford the desired reduction products.

3.5. Preparation of diethyl bromofluoromethylphosphonate (3)

A total of 20.2 g (100 mmol) of tributylphosphine was rapidly added to a mixture of 32.8 g (100 mmol) of $(EtO)_2P(O)CFBr_2$, 4.7 g (100 mmol) EtOH and 200 ml THF. In the initial stage of the reaction, the reaction temperature should be maintained under 50°C. The mixture was stirred at room temperature overnight and then was poured into 300 ml diethyl ether. The resulting ether solution was washed with water (3×40 ml) and brine solution (2×50 ml). The organic solution was then dried over anhydrous $MgSO_4$. After ether was removed by rotary evaporation, the residue was distilled under reduced pressure to give 18.5 g (74%) of (**3**); bp: 50–52°C/0.05 mm Hg. ^{19}F NMR ($CDCl_3$): −166.3 (dd, J=73.7 Hz, J=47.2 Hz) ppm. ^1H NMR ($CDCl_3$):1.40 (dt, J=7.1 Hz, J=4.5 Hz, 6H), 4.32 (m, 4H), 6.51 (dd, J=47.0 Hz, J=10 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$): 15.8, 64.4 (dd, J=40.9 Hz, J=6.7 Hz), 83.6 (J=264.5 Hz, J=189.0 Hz) ppm. ^{31}P NMR (H_3PO_4 external ref.): 7.9 (d, J=74.1 Hz) ppm. GC–MS: 250 (M^++1, 1.3), 221 (5.4), 193 (3.8), 157 (3.6), 137 (82), 109 (100), 81 (78).

3.6. Preparation of diethyl fluoroiodomethylphosphonate (4)

A mixture of $(EtO)_2P(O)CFHBr$ (100 mmol, 24.9 g), Zn powder (110 mmol, 7.3 g), 150 ml THF was stirred at room temperature for 8 h. The THF solution was syringed into another dry flask which contained I_2 (100 mmol, 25.4 g) at 0°C and the mixture was stirred at room temperature overnight. This mixture was then poured into 300 ml diethyl ether. This ether solution was washed with $NaHSO_3$ solution, water and brine solution. The organic solution was dried over anhydrous $MgSO_4$. After ether was removed by rotary evaporation, the resulting residue was distilled at reduced pressure to give 20.7 g (~70%) of (**4**); bp: 82–83/0.05 mm Hg. ^{19}F NMR ($CDCl_3$): −178.7 (dd, J=70.5 Hz, J=48.0 Hz) ppm. ^1H NMR ($CDCl_3$): 1.40 (qd, J=6.5 Hz, J=0.6 Hz, 6H), 4.31 (m, 4H), 6.97 (dd, J=48.0 Hz, J=7.6 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$): 16.4 (t, J=5.2 Hz), 60.6 (dd, J=263.9 Hz, J=182.1 Hz), 65.1 (J=55.4 Hz, J=7.0 Hz) ppm. ^{31}P NMR (H_3PO_4 external ref.): 9.32 (d, J=71.0 Hz) ppm. GC–MS: 296 (M^+, 2.7), 225 (2.0), 191 (2.7), 175 (10.9), 169 (M^+−I, 51.5), 109 (58.2), 93 (68.2), 77 (65.8), 65 (100).

3.6.1. Diisopropyl fluoroiodomethylphosphonate (2)

2 was prepared in the same manner as **4**; bp: 92°C–93°C/0.1 mm Hg. ^{19}F NMR ($CDCl_3$): −178.4 (dd, J=71.0 Hz, J=48.0 Hz) ppm. ^1H NMR ($CDCl_3$): 1.40 (m, 12H), 4.89 (m, 2H), 6.92 (dd, J=48.0 Hz, J=8.0 Hz, 1H) ppm. ^{13}C NMR ($CDCl_3$): 24.0 (dd, J=31.0 Hz, J=5.0 Hz), 61.6 (dd, J=264 Hz, J=183.0 Hz), 74.0 (dd, J=42.0 Hz, J=7.0 Hz) ppm. ^{31}P NMR (H_3PO_4 external ref.): 7.0 (d, J=70.0 Hz) ppm. GC–MS: 324 (M^+), 197 (M^+−I), 155 (M^+−I−CH_2=$CHCH_3$), 113 (M^+−I−2CH_2=$CHCH_3$).

3.7. Preparation procedures for the adducts of 4 with various alkenes

3.7.1. Diethyl 1-fluoro-3-iodooctylphosphonate (12)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 2.0 g (20 mmol) of 1-heptene was stirred at 80°C for 4 h. The reaction mixture was dissolved in 50 ml of hexanes/ether (1:1) mixture. The resulting solid was removed by filtration and the solid was washed with 20 ml of the hexanes/ether mixture. The combined solutions were then concentrated to give a residue which was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 1.57 g (78%) of (**12**). ^{19}F NMR ($CDCl_3$): −207.9 (m), −212.9 (m) ppm. ^1H NMR ($CDCl_3$): 4.86–5.15 (m, 1H), 4.16–4.31 (m, 4H), 2.14–2.68 (m, 2H), 1.28–2.00 (m, 15H), 0.88–0.93 (m, 3H) ppm. ^{31}P NMR ($CDCl_3$): 17.89 (d, J=74.0 Hz), 17.25 (d, J=74.7 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.64 (dd, J=170.5 Hz, J=180.2 Hz), 88.12 (dd, J=169.9 Hz, J=180.6 Hz), 63.39 (d, J=2.8 Hz), 62.98 (d, J=3.4 Hz), 41.15, 40.86, 40.77, 39.27, 33.45 (d, J=16.5 Hz), 33.17 (d, J=12.2 Hz), 30.85, 30.81, 28.97, 29.15, 22.42 (overlap), 16.48 (d, J=3.0 Hz), 16.45 (d, J=2.2 Hz), 13.97 (overlap) ppm. GC–MS: 267 (M^+−I, 31.9), 247 (4.9), 219 (3.75), 191 (4.0), 155 (10.7), 137 (5.7), 127 (18.13), 109 (100), 91 (10.2), 85 (20.4), 81 (30.2), 67 (31.46). FT-IR (cm^{-1}): 2980 (s), 2870 (s), 1369 (vs), 1097 (s), 972 (m). R_f: 0.35 (hexanes:ethyl acetate = 1:1).

3.7.2. Diethyl 1-fluoro-3-iodododecylphosphonate (14)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 3.08 g (20 mmol) of 1-undecene was stirred at 60°C for 4 h. The reaction mixture was dissolved in 50 ml of a hexanes/ether (1:1) mixture. The resulting solid was removed by filtration and the solid was washed with 20 ml of the hexanes/ether mixture. The combined solutions were then concentrated to give a residue which was purified by column chromatography on silica gel

(hexanes:ethyl acetate = 7:3) to give 1.49 g (66%) of **14**. ^{19}F NMR ($CDCl_3$): −207.9 (m), −212.9 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.86–5.15 (m, 1H), 4.16–4.34 (m, 4H), 2.14–2.66 (m, 2H), 1.65–2.01 (m, 2H), 1.26–1.60 (m, 21H), 0.88 (t, J = 6.7 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 18.12 (d, J = 74.0 Hz), 17.48 (d, J = 75.5 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.68 (dd, J = 171.3 Hz, J = 180.8 Hz), 88.17 (dd, J = 170.4 Hz, J = 180.7 Hz), 63.29 (dd, J = 33.5 Hz, J = 6.5 Hz), 63.20 (dd, J = 33.1 Hz, J = 6.5 Hz), 40.67 (d, J = 31 Hz), 41.16 (d, J = 2.1 Hz), 40.93, 39.32, 33.51 (dd, J = 16.5 Hz, J = 2.8 Hz), 33.22 (dd, J = 12.6 Hz, J = 3.8 Hz), 31.86, 29.54, 29.49 (overlap), 29.42 (overlap), 29.33 (overlap), 29.26 (overlap), 28.72, 28.67, 22.66, 16.52 (d, J = 2.5 Hz), 16.44 (d, J = 2.5 Hz), 14.11 (overlap) ppm. GC–MS: 323 (M^+ − I, 100), 303 (8.4), 275 (2.9), 211 (6.8), 197 (2.6), 181 (6.3), 165 (6.4), 127 (4.15), 109 (12.76), 81 (17.9), 71 (7.63), 55 (10.11). FT-IR (cm^{-1}): 2980 (s), 2855 (m), 1392 (s), 1163 (s), 1127 (vs), 1099 (s), 1025 (m), 974 (m). R_f: 0.33 (hexanes:ethyl acetate = 1:1).

3.7.3. Diethyl 1-fluoro-3-iodo-3-trimethylsilylpropyl-phosphonate (15)

A mixture of 1.48 g (5.0 mmol) of (EtO)2P(O)CFHI, 0.20 g (0.18 mmol) of Pd(PPh3)4 and 1.92 g (20 mmol) of vinyltrimethyl silane was stirred at 45°C for 4 h. The reaction mixture was dissolved in 50 ml of a hexanes/ether (1:1) mixture. The resulting solid was removed by filtration and the solid was washed with 20 ml of a hexanes/ether solution. The combined solutions were concentrated to give a residue which was then purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 1.18 g (60%) of **15**. 19F NMR ($CDCl_3$): −203.3 (m), −214.13 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.88–5.15 (dm, J = 47.0 Hz, 1H), 4.16–4.28 (m, 4H), 3.30–3.38 (m, 1H), 1.82–2.52 (m, 2H), 1.37 (td, J = 7.1 Hz, J = 1.2 Hz, 6H), 0.19 (s, 9H) ppm. ^{31}P NMR ($CDCl_3$): 17.95 (d, J = 75.7 Hz), 18.73 (d, J = 74.8 Hz) ppm. ^{13}C NMR ($CDCl_3$): 89.04 (dd, J = 181.6 Hz, J = 169.1 Hz), 88.01 (dd, J = 180.6 Hz, J = 169.8 Hz), 62.84 (d, J = 6.7 Hz), 62.39 (d, J = 6.7 Hz), 34.91 (dd, J = 21.2 Hz, J = 2.3 Hz), 33.69 (dd, J = 20.7 Hz, J = 3.6 Hz), 16.43 (dd, J = 5.7 Hz, J = 2.3 Hz), 15.78 (dd, J = 11.8 Hz, J = 1.2 Hz), 14.28 (d, J = 14.2 Hz), 14.18 (d, J = 14.2 Hz), −2.81, −2.61 ppm. GC–MS: 325 (6.9), 269 (M^+ − I, 22.9), 242 (18), 215 (16.9), 177 (90), 165 (14.5), 121 (58.5), 73 (100). R_f: 0.33 (hexanes:ethyl acetate = 1:1).

3.7.4. Diethyl 1-fluoro-3-iodo-6,7-epoxy-heptylphosphonate (16)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 2.0 g (20 mmol) of 1,2-epoxy-5-hexene was stirred at 75°C for 4 h. The reaction mixture was dissolved in 50 ml of a hexanes/ether (1:1) mixture. The resulting solid was removed by filtration and the solid was washed with 20 ml of a hexane/ether mixture. The combined solution was then concentrated to give a residue which was purified by column chromatography on silica gel (hexane:ethyl acetate = 7:3 to 1:10) to give 1.37 g (69%) of **16**. ^{1}H NMR ($CDCl_3$): 4.86–5.15 (dm, J = 45.6 Hz, 1H), 4.15–4.40 (m, 5H), 2.93–2.98 (m, 1H), 2.76–2.80 (m, 1H), 1.5–2.6 (m, 7H), 1.38 (td, J = 7.1 Hz, J = 0.5 Hz, 6H) ppm. ^{19}F NMR ($CDCl_3$): −207.7 (m), −212.6 (m) ppm. ^{31}P NMR ($CDCl_3$): 17.71 (d, J = 73.2 Hz), 17.16 (d, J = 74.8 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.47 (dd, J = 171.5 Hz, J = 181.2 Hz), 88.01 (dd, J = 170.4 Hz, J = 180.7 Hz), 63.40 (d, J = 6.1 Hz), 63.03 (d, J = 6.7 Hz), 51.27, 50.9, 46.85 (d, J = 8.9 Hz), 46.82 (d, J = 8.8 Hz), 40.88, 40.63, 37.11 (d, J = 39 Hz), 35.72 (d, J = 40.6 Hz), 32.28 (d, J = 33.6 Hz), 32.49 (d, J = 42.8 Hz), 32.08 (ddd, J = 3.3 Hz, J = 10.4 Hz, J = 14.9 Hz), 29.96 (ddd, J = 3.6 Hz, J = 12.8 Hz, J = 17.1 Hz), 16.50 (d, J = 2.1 Hz), 16.42 (d, J = 2.1 Hz) ppm. GC–MS: 267 (M^+ − I, 31.1), 239 (8.0), 219 (4.0), 211 (8.7), 191 (8.8), 173 (38.7), 155 (12.8), 137 (13.4), 112 (1.9), 109 (57.7), 91 (54.9), 81 (100), 65 (20.2). R_f: 0.27 (hexanes:ethyl acetate = 1:1).

3.7.5. Diethyl 1-fluoro-3-iodo-8,9-epoxy-nonylphosphonate (17)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 2.2 g (20 mmol) of 1,2-epoxy-7-octene was stirred at 75°C for 4 h. The reaction mixture was dissolved in 50 ml of mixture of hexanes/ether (1:1). The resulting solid was removed by filtration and the solid was washed with solvent (hexanes/ether mixture). The combined solutions were then concentrated to give a residue which was purified by column chromatography on silica gel (hexane:ethyl acetate = 7:3 to 1:10) to give 1.37 g (65%) of **17**. ^{1}H NMR ($CDCl_3$): 4.86–5.15 (dm, J = 45.6 Hz, 1H), 4.15–4.40 (m, 5H), 1.33–2.89 (m, 19H) ppm. ^{19}F NMR ($CDCl_3$): −207.7 (m), −212.6 (m) ppm. ^{31}P NMR ($CDCl_3$): 17.79 (d, J = 74.8 Hz), 17.17 (d, J = 76.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.52 (dd, J = 171.5 Hz, J = 180.9 Hz), 88.04 (dd, J = 170.4 Hz, J = 180.6 Hz), 63.20 (dd, J = 38.5 Hz, J = 6.1 Hz), 63.14 (dd, J = 39.9 Hz, J = 6.1 Hz), 51.99 (overlap), 46.95, 46.91, 40.63 (overlap), 39.07, 39.02, 32.90, 30.67, 32 (overlap), 29.25 (d, J = 6.5 Hz), 29.04 (d, J = 2.2 Hz), 25.04, 24.97, 16.42 (d, J = 2.1 Hz), 16.34 (d, J = 2.1 Hz) ppm. GC–MS: 295 (M^+ − I, 7), 257 (5.4), 229 (5.4), 201 (9.3), 183 (4.9), 137 (16.7), 119 (100), 103 (31.3), 91 (38). FT-IR (cm^{-1}): 2983 (s), 2860 (s), 1480 (s), 1369 (s), 1163 (m), 1097 (m), 1051 (m). R_f: 0.27 (hexanes:ethyl acetate = 1:1).

3.7.6. Diethyl 1-fluoro-3-iodo-4-ethoxy-butylphosphonate (18)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.72 g (20 mmol) of allyl ethyl ether was stirred at 50°C for 4 h. The reaction mixture was dissolved in 50 ml of a hexanes/ether (1:1) mixture. The resulting solid was removed by filtration and the solid was washed with the hexanes/ether mixture. The combined solutions were then concentrated to give a residue

which was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3–6:4) to give 1.2 g (63%) of **18**. ^{19}F NMR ($CDCl_3$): −208.1 (m), −212.6 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.89–6.12 (dm, J = 47.1 Hz, 1H), 4.16–4.44 (m, 5H), 3.50–3.81 (m, 4H), 2.05–2.65 (m, 2H), 1.37 (t, J = 7.0 Hz, 6H), 1.18–1.24 (md, J = 7.0 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 17.93 (d, J = 73.3 Hz), 17.28 (d, J = 74.8 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.35 (dd, J = 172.4 Hz, J = 181.0 Hz), 88.49 (dd, J = 169.4 Hz, J = 180.7 Hz), 75.94, 75.60, 66.46, 66.45, 63.40 (d, J = 6.7 Hz), 63.00 (d, J = 6.7 Hz), 37.13 (dd, J = 3.6 Hz, J = 19.5 Hz), 37.84 (dd, J = 2.1 Hz, J = 20.5 Hz), 27.97 (dd, J = 16.5 Hz, J = 3.0 Hz), 25.10 (dd, J = 13.0 Hz, J = 3.5 Hz), 16.48 (d, J = 5.5 Hz), 16.45 (d, J = 5.5 Hz), 15.05 ppm. GC–MS: 255 (M^+ − I, 28.5), 227 (5.6), 209 (21.1), 181 (15.7), 171 (43), 153 (100), 133 (14), 109 (26.4), 81 (28.0). R_f: 0.40 (hexanes:ethyl acetate = 1:1).

3.7.7. Diethyl 1-fluoro-3-iodo-4-hydroxy-butylphosphonate (19)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.16 g (20 mmol) of allyl alcohol was stirred at 70°C for 4 h. The reaction mixture was dissolved in 50 ml of a hexanes/ether (1:1) mixture. The resulting solid was removed by filtration, the solid was washed with the hexanes/ether mixture. The combined solutions were then concentrated to give a residue which was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7.3–1:10) to give 1.20 g (67%) of **19**. ^{19}F NMR ($CDCl_3$): −207.8 (m), −212.4 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.14 (dm, $J_{H,F}$ = 47 Hz, 1H), 3.59–3.73 (m, J = 6.0 Hz, 1H), 3.27–3.51 (m, 5H), 2.84–3.07 (m, 2H), 1.16–1.77 (m, 2H), 0.49 (t, J = 7.1 Hz, 6H) ppm. ^{31}P NMR ($CDCl_3$): 17.80 (d, J = 74.8 Hz), 17.17 (d, J = 76.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): 87.93 (dd, J = 172.3 Hz, J = 181.1 Hz), 87.97 (dd, J = 170.3 Hz, J = 180.4 Hz), 67.78, 67.17, 62.95, 36.26 (dd, J = 3.3 Hz, J = 19.8 Hz), 36.79 (dd, J = 2.2 Hz, J = 20.5 Hz), 32.76 (dd, J = 2.4 Hz, J = 15.8 Hz), 29.92 (dd, J = 3.2 Hz, J = 12.6 Hz), 16.02 (d, J = 2.2 Hz), 16.1 (d, J = 1.9 Hz) ppm. DIP–MS: 253 (1.12), 227 (M^+ − I, 12.4), 209 (28.0), 197 (9.8), 181 (22.3), 153 (100), 127 (22.7), 109 (58.9), 81 (69.7), 69 (53.5), 65 (42.2). FT-IR (cm^{-1}): 3382 (br), 2984 (s), 2934 (s), 2871 (vs), 1477 (s), 1163 (m), 1096 (m), 975 (m). R_f: 0.17 (hexanes:ethyl acetate = 1:1).

3.7.8. Diethyl 1-fluoro-3-iodo-4-phenylbutylphosphonate (20)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 2.36 g (20 mmol) of allyl benzene was stirred at 70°C for 8 h. The reaction mixture was dissolved in 50 ml of a hexane/ether (1:1) mixture. The resulting solid was removed by filtration and the solid was washed with the hexane/ether mixture. The combined solutions were concentrated to give a residue which was then purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 1.45 g (70%) of **20**. ^{19}F NMR ($CDCl_3$): −206.7 (m), −212.9 (m) ppm. ^{1}H NMR ($CDCl_3$): 7.07–7.36 (m, 5H), 4.95–5.12 (dm, J = 48.8 Hz, 1H), 4.47 (m, 1H), 4.15 (m, 4H), 3.15 (m, 2H), 2.26–2.49 (m, 2H), 1.32 (m, 6H) ppm. ^{31}P NMR ($CDCl_3$): 17.22 (d, J = 74.0 Hz), 17.71 (d, J = 73.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): 138.56, 138.22, 128.47, 128.42, 127.97, 127.94, 126.48, 126.41, 88.05 (dd, J = 180.4 Hz, J = 169.6 Hz), 85.68 (dd, J = 181.3 Hz, J = 171.2 Hz), 62.82 (d, J = 7.0 Hz), 62.42 (d, J = 6.7 Hz), 46.78, 45.88, 39.35 (d, J = 2.2 Hz), 39.10 (d, J = 2.1 Hz), 31.58 (dd, J = 11.6 Hz, J = 2.9 Hz), 29.73 (dd, J = 11.3 Hz, J = 3.7 Hz), 15.95, 15.87 ppm. DIP–MS: 287 (M^+ − I, 53), 259 (16.8), 211 (13), 193 (2), 147 (8.0), 129 (100), 104 (16.8), 91 (53). FT-IR (cm^{-1}): 3086 (vs), 3064 (s), 1029 (s), 2984 (m), 2870 (vs), 1369 (s), 1163 (s), 1095 (s). R_f: 0.27 (hexanes:ethyl acetate = 1:1).

3.7.9. Iodotetrahydrofuran derivative (21)

A mixture of 1.1 g (3.4 mmol) of $(^iPrO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.5 g (15 mmol) of allyl ether was stirred at 60°C for 2 h. After the usual workup, the residue was purified by column chromatography on silica gel (methylene chloride:hexanes = 6:1–4:1) to give 1.1 g (77%) of **21**. ^{19}F NMR ($CDCl_3$): −207.9 (m), −208.5 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.79 (m, 2H), 4.67 (m, 1H), 3.95–4.17 (m, 2H), 3.49–3.74 (m, 2H), 3.00–3.30 (m, 6H), 2.51 and 2.79 (2m, 2H), 1.80–2.30 (m, 2H), 1.37 (m, 12H) ppm. ^{31}P NMR ($CDCl_3$): 15.0 (d, J = 76 Hz), 15.5 (d, J = 76 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.8 (dd, J = 179.8 Hz, J = 170.0 Hz), 88.2 (dd, J = 179.8 Hz, J = 170.0 Hz), 74.2, 73.8, 73.5, 72.1, 72 (m), 47.7, 45.3, 43.9 (d, J = 14.0 Hz), 41.0 (d, J = 14 Hz), 33.3 (d, J = 20.1 Hz), 26.9 (d, J = 20.1 Hz), 24.1 (m), 4.0, 8.1 ppm. GC–MS: 337 (M^+ − $2CH_2$=$CHCH_3$ − 1), 321 (M + − $2CH_2$=$CHCH_3$–OH), 253, 211.

3.8. The reaction of diisopropyl fluoroiodomethylphosphonate with 4-pentene-1-ol

A mixture of 1.1 g (3.4 mmol) of $(^iPrO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.5 g (17 mmol) of 4-pentene-1-ol was stirred at 65°C for 2 h. The reaction mixture was dissolved 50 ml of a hexanes/ether (1:1) mixture. The resulting solid was removed by filtration and the solid was washed with the hexanes/ether mixture. The combined solutions were concentrated to give a residue which was then purified by column chromatography on silica gel (CH_2Cl_2:EtOAc = 7:1) to give 0.2 g tetrahydrofuran derivative (**23**) in 21% yield, with (CH_2Cl_2:EtOAc = 3:1 to 0:10) to afford 0.48 g of **22** in 35% yield.

3.8.1. Compound (22)

^{19}F NMR ($CDCl_3$): −207.7 (m), −212.5 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.71–4.91 (m, 3H), 4.07 (p, J = 6.0 Hz, 2H), 3.70–3.90 (m, 2H), 1.54–2.23 (m, 6H), 1.35 (m, 12H) ppm.

^{31}P NMR ($CDCl_3$): 15.0 (d, J=76 Hz), 15.5 (d, J=76 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.7 (dd, J=181 Hz, J=173 Hz), 88.2 (dd, J=181 Hz, J=173 Hz), 72.3 (m), 61.1, 61.0, 41.0 (m), 37.4, 35.8, 33.4 (m), 31.3 (m), 32.5, 32.4, 24.1 (m) ppm. FT−IR (cm^{-1}): 3435 (br), 2983 (s), 2938 (m), 1387 (m), 1377 (m), 1258 (s), 1006 (vs), 994 (vs).

*3.8.2. Compound (**23**)*

^{19}F NMR ($CDCl_3$): −207.5 (m), −212.3 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.85–5.07 (m, 1H), 4.79 (m, 2H), 4.29 (m, 1H), 4.15 (s, 1H), 3.65 (t, J=6 Hz, 2H), 1.65–2.36 (m, 6H), 1.37 (m, 12H) ppm. ^{13}C NMR ($CDCl_3$): 88.6 (dd, J=180 Hz, J=173 Hz), 87.2 (dd, J=180 Hz, J=173 Hz), 75.9 (m), 74.3 (m), 71.9 (m), 68.0, 67.6, 36.3 (d, J=19.0 Hz), 35.8 (d, J=19.0 Hz), 31.7, 31.0, 25.8, 25.7, 24.1 (m) ppm. GC–MS: 283 (M^++1), 254 (M^+−CH_2=CH_2), 239 (M^+−CH_2=CH_2–CH_3), 212 (M^+−THF+1), 197 ((^{i}PrO)$_2$P (O)CFH$^+$), 71 (THF$^+$−1). FT-IR (cm^{-1}): 2981 (s), 2939 (m), 1387 (m), 1262 (s), 1107 (s), 992 (vs).

3.9. General procedure for the reduction reaction of the adducts with tributyltin hydride

A total of 3.3 mmol tributyltin hydride was slowly added to a mixture of 3 mmol (1.18 g) of **12** and 10 ml diethyl ether. The reaction mixture was stirred at room temperature overnight. The reaction mixture was poured into 20 ml of acetonitrile and the resulting solutions was washed with hexanes (4×10 ml) [36]. The acetonitrile layer was concentrated by distillation and the remaining residue was purified by column chromatography (hexanes:ethyl acetate = 3:1) to give 0.60 g (74%) of **25**.

3.10. General procedure for the one-flask preparation of α-fluorophosphonates

A mixture of olefin (20 mmol), 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.48 g (5.0 mmol) of (EtO)$_2$P(O)CFHI (**4**) was stirred at the indicated temperature. After the reaction was completed, 50 ml of a hexanes/ether (1:1) solution was added to the reaction mixture. The resulting solid was removed by filtration and the solid washed with 20 ml of the hexanes/ether mixture. The combined solutions were concentrated to give a residue which was then treated with Zn/$NiCl_2 \cdot 6H_2O$ in moist THF solution at room temperature for several hours. The reaction mixture was diluted with 100 ml diethyl ether, washed with 30 ml of saturated NH_4Cl(aq) and water. The organic layer was dried over anhydrous $MgSO_4$ and concentrated to give a residue which was purified by column chromatography to give the desired product.

*3.10.1. Diethyl 1-fluoro-heptylphosphonate (**24**)*

A mixture of 1.48 g (5.0 mmol) of (EtO)$_2$P(O)CFHI, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.68 g (20 mmol) of 1-hexene was stirred at 65°C for 2 h, followed by treatment with Zn (0.38 g) and $NiCl_2$•$6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 1.02 g (80%) of **24**. ^{19}F NMR ($CDCl_3$): −209.8 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.62 (dm, J=46.7 Hz, 1H), 4.13 (dm, J=6.9 Hz, 4H), 1.2–1.9 (m, 16H), 0.82 (t, J=6.8 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 19.03 (d, J=75.5 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.66 (dd, J=179.7 Hz, J=169.9 Hz), 62.92 (dd, J=29.7 Hz, J=6.3 Hz), 31.64, 30.16 (d, J=20.2 Hz), 28.84, 25.30 (dd, J=12.5 Hz, J=3.4 Hz), 22.60, 16.52 (dd, J=5.5 Hz, J=2.7 Hz), 14.05 ppm. GC–MS: 225 (M^+−CH_2CH_3, 1.8), 211 (16), 197 (5.0), 183 (18), 170 (68), 155 (10), 143 (45), 138 (100), 109 (51). FT-IR (cm^{-1}): 2982 (s), 2955 (s), 2871 (s), 1467 (s), 1393 (vs), 1164 (s), 1054 (m), 969 (m). R_f: 0.33 (hexanes:ethyl acetate = 1:1). HRMS (FAB, M+Na)$^+$: obs. 277.1341, calc. 277.1344.

*3.10.2. Diethyl 1-fluoro-octylphosphonate (**25**)*

A mixture of 1.48 g (5.0 mmol) of (EtO)$_2$P(O)CFHI, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.96 g (20 mmol) of 1-heptene was stirred at 80°C for 4 h, followed by treatment with Zn (0.38 g) and $NiCl_2 \cdot 6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 0.81 g (60%) of **25**. ^{19}F NMR ($CDCl_3$): −209.4 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.62 (dm, J=47.0 Hz, 1H), 4.13 (dm, J=7.0 Hz, 4H), 1.17–1.93 (m, 18H), 0.81 (t, J=6.5 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 18.91 (d, J=76.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.78 (dd, J=179.8 Hz, J=169.7 Hz), 62.73 (dd, J=29.7 Hz, J=6.8 Hz), 31.56, 29.93 (d, J=20.1 Hz), 28.87, 28.85, 25.16 (dd, J=12.5 Hz, J=3.4 Hz), 22.44, 16.30 (dd, J=5.5 Hz, J=2.5 Hz), 13.88 ppm. GC–MS: 269 (M^++1, 3), 239 (2), 225 (2), 211 (13), 183 (20), 170 (46), 143 (48), 138 (100), 129 (12), 111 (28), 101 (23), 81 (25). R_f: 0.33 (hexanes:ethyl acetate = 1:1).

*3.10.3. Diethyl 1-fluorononylphosphonate (**26**)*

A mixture of 1.48 g (5.0 mmol) of (EtO)$_2$P(O)CFHI, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 2.24 g (20 mmol) of 1-octene was stirred at 50°C for 2 h, followed by treatment with Zn (0.38 g) and $NiCl_2 \cdot 6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 1.06 g (75%) of **26**. ^{19}F NMR ($CDCl_3$): −209.4 (m) ppm. ^{1}H NMR ($CDCl_3$): 4.69 (dm, J=47.3 Hz, 1H), 4.19 (dm, J=21.2 Hz, 4H), 1.19–2.15 (m, 20H), 0.88 (t, J=6.5 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 18.95 (d, J=76.2 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.48 (dd, J=179.8 Hz, J=169.8 Hz), 62.48 (dd, J=29.8 Hz, J=6.2 Hz), 31.43, 29.71 (d, J=20.1 Hz), 28.87, 28.85, 28.70, 24.92 (dd, J=12.5 Hz, J=3.4 Hz), 22.24, 16.03 (dd, J=5.5 Hz, J=2.5 Hz), 13.62 ppm. DIP–MS: 281 (M^+−1, 100), 261 (11), 233 (7), 205 (5), 183 (5), 169 (21), 141 (20), 123 (64), 109 (34), 81 (79). R_f: 0.33 (hexanes:ethyl acetate = 1:1).).

FT-IR (cm^{-1}): 2981 (s), 2855 (m), 2361 (vs), 1466 (s), 1393 (vs), 1164 (s), 1054 (m), 969 (m).

3.10.4. Preparation of diethyl 1-fluorododenylphosphonate (27)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 3.08 g (20 mmol) of 1-undecene was stirred at 60°C for 4 h, followed by treatment with Zn (0.38 g) and $NiCl_2 \cdot 6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 8:2) to give 1.06 g (65%) of **27**. ^{19}F NMR ($CDCl_3$): −209.5 (m) ppm. ^1H NMR ($CDCl_3$): 4.69 (dm, J = 47.0 Hz, 1H), 4.20 (dm, J = 7.2 Hz, 4H), 1.26–2.00 (m, 26H), 0.88 (t, J = 6.7 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 18.88 (d, J = 76.6 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.78 (dd, J = 179.8 Hz, J = 170.0 Hz), 62.75 (dd, J = 29.3 Hz, J = 6.1 Hz), 31.77, 29.93 (d, J = 20.1 Hz), 29.47, 29.47, 29.37, 29.20, 29.20, 28.94, 25.18 (dd, J = 12.5 Hz, J = 3.4 Hz), 22.54, 16.31 (dd, J = 5.5 Hz, J = 2.5 Hz), 13.95 ppm. GC–MS: 323 ($M^+ - 1$, 1), 295 (1), 267 (2), 225 (3), 211 (10), 183 (24), 170 (38), 143 (24), 138 (100), 109 (20). R_f: 0.35 (hexanes:ethyl acetate = 1:1).). FT-IR (cm^{-1}): 2981 (s), 1466 (vs), 1392 (vs), 1369 (vs), 1164 (s), 1096 (m), 970 (m). HRMS (FAB, M + H)$^+$: obs. 325.2308, calc. 325.2307.

3.10.5. Diethyl 1-fluoro-3-trimethylsilylpropylphosphonate (28)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 2.28 g (20 mmol) of vinyl trimethylsilane was stirred at 45°C for 4 h, followed by treatment with Zn (0.38 g) and $NiCl_2 \cdot 6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7.3) to give 0.92 g (68%) of **28**. ^{19}F NMR ($CDCl_3$): −208.7 (m) ppm. ^1H NMR ($CDCl_3$): 4.48 (dm, J = 47.2 Hz, 1H), 4.09 (dq, J = 14.2 Hz, J = 7.1 Hz, 4H), 1.78 (m, 2H), 1.26 (t, J = 7.2 Hz, 6H), 0.75 (m, 1H), 0.48 (m, 1H), −0.08 (s, 9H) ppm. ^{31}P NMR ($CDCl_3$): 16.8 (d, J = 74.6 Hz) ppm. ^{13}C NMR ($CDCl_3$): 90.75 (dd, J = 180.7 Hz, J = 167.0 Hz), 63.90 (dd, J = 33 Hz, J = 6.3 Hz), 24.77 (dd, J = 21.0 Hz, J = 0.9 Hz), 16.27 (dd, J = 5.8 Hz, J = 2.4 Hz), 11.9 (dd, J = 10.4 Hz, J = 2.4 Hz), −2.1 ppm. GC–MS: 255 ($M^+ - CH_3$, 11), 242 (9), 227 (8), 215 (24), 210 (35), 199 (45), 165 (63), 157 (22), 137 (31), 109 (34), 73 (100). FT-IR (cm^{-1}): 2983 (s), 2955 (s), 2910 (s), 1393 (vs), 1250 (s), 1031 (s), 969.6 (m). R_f: 0.33 (hexanes:ethyl acetate = 1:1).

3.10.6. Diethyl 1-fluoro-4-ethoxylbutylphosphonate (29)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 1.72 g (20 mmol) of allyl ethyl ether was stirred at 50°C for 6 h, followed by treatment with Zn (0.38 g) and $NiCl_2 \cdot 6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 0.81 g (63%) (**29**). ^{19}F NMR ($CDCl_3$): −209.7 (m) ppm. ^1H NMR ($CDCl_3$): 4.67 (dm,J = 47.1 Hz, 1H), 4.13 (m, 4H), 3.39 (m. 4H), 1.6–2.1 (m, 4H), 1.29 (t, J = 7.1 Hz, 6H), 1.12 (t, J = 7.0 Hz, 3H) ppm. ^{31}P NMR ($CDCl_3$): 18.50 (d, J = 76.5 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.66 (dd, J = 179.7 Hz, J = 170.3 Hz), 69.43, 65.99, 62.78 (dd, J = 27.8 Hz, J = 6.7 Hz), 27.02 (dd, J = 20.1 Hz, J = 0.9 Hz), 25.43 (dd, J = 12.8 Hz, J = 3.6 Hz), 16.29 (dd, J = 5.5 Hz, J = 2.5 Hz), 15.00 ppm. GC–MS: 257 ($M^+ + 1$, 5.0), 227 (63), 211 (34), 183 (100), 153 (42), 138 (37), 111 (15), 81 (51), 71 (62), 59 (100). R_f: 0.30 (hexanes:ethyl acetate = 1:1).). FT-IR (cm^{-1}): 2978 (s), 2867 (m), 1479 (vs), 1445 (vs), 1392 (vs), 1379 (vs), 1164 (m). HRMS (FAB, M + Na)$^+$: obs. 279.1135, calc. 279.1137.

3.10.7. Diethyl 1-fluoro-11-hydroxyundecylphosphonate (30)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 3.12 g (20 mmol) of 1-decenol was stirred at 60°C for 4 h, followed by treatment with Zn (0.38 g) and $NiCl_2 \cdot 6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 2:8) to give 0.98 g (60%) of **30**. ^{19}F NMR ($CDCl_3$): −209.4 (m) ppm. ^1H NMR ($CDCl_3$): 4.70 (dm, J = 46.9 Hz, 1H), 4.20 (m, J = 7.1 Hz, 4H), 3.61 (t, J = 6.6 Hz, 2H), 2.4 (s, 1H), 1.30 ~ 1.96 (m, 24H) ppm. ^{31}P NMR ($CDCl_3$): 18.85 (d, J = 76.3 Hz) ppm. ^{13}C NMR ($CDCl_3$): 88.71 (dd, J = 179.8 Hz, J = 170.1 Hz), 62.93 (dd, J = 28.7 Hz, J = 6.1 Hz), 62.62, 32.60, 29.88 (d, J = 19.9 Hz), 29.35, 29.23, 29.22, 29.11, 28.86, 25.6, 25.10 (dd, J = 3.8 Hz, J = 3.0 Hz), 16.28 (dd, J = 5.5 Hz, J = 2.5 Hz) ppm. DIP–MS: 325 ($M^+ - 1$, 0.67), 296 (3.35), 267 (3.02), 211 (10.6), 183 (29.7), 138 (100), 109 (27.8), 81 (25.6). R_f: 0.17 (hexanes:ethyl acetate = 1:1).

3.10.8. Diethyl 1-fluoro-4-phenylbutylphosphonate (31)

A mixture of 1.48 g (5.0 mmol) of $(EtO)_2P(O)CFHI$, 0.20 g (0.18 mmol) of $Pd(PPh_3)_4$ and 2.36 g (20 mmol) of allyl benzene was stirred at 70°C for 8 h, followed by treatment of Zn (0.38 g) and $NiCl_2 \cdot 6H_2O$ (50 mg) in moist THF. After the usual workup, the residue was purified by column chromatography on silica gel (hexanes:ethyl acetate = 7:3) to give 1.02 g (71%) of **31**. ^{19}F NMR ($CDCl_3$): −210.4 (m) ppm. ^1H NMR ($CDCl_3$): 7.20 (m, 5H), 4.91 (dm, J = 48.6 Hz, 1H), 4.30 (m, 4H), 2.68 (m, 2H), 1.92 (m, 4H), 1.38 (m, 6H) ppm. ^{31}P NMR ($CDCl_3$): 17.76 (d, J = 75.4 Hz) ppm. ^{13}C NMR ($CDCl_3$): 140.9, 128.1, 127.9, 125.5, 87.94 (dd, J = 180.5 Hz, J = 171.6 Hz), 63.68 (dd, J = 22.1 Hz, J = 6.9 Hz), 34.67 (m), 29.01 (d, J = 20.1 Hz), 26.43 (dd, J = 13.1 Hz, J = 3.3 Hz), 15.91 (dd, J = 5.5 Hz, J = 1.9 Hz) ppm. GC–MS: 288 (M^+, 21), 268 (3), 211 (3), 183 (18), 170 (13), 138 (97), 111 (35), 91 (100). R_f: 0.25 (hexanes:ethyl acetate = 1:1). FT-IR (cm^{-1}): 3084 (s), 2984 (s), 2866 (s), 1499 (vs), 1393 (s), 1370 (vs), 1291

(vs), 974 (m). HRMS (FAB, M+Na)$^+$: obs. 311.90, calc. 311.1188.

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