A Novel and Practical Preparation of α,α-Difluoro Functionalized Phosphonates from Iododifluoromethylphosphonate

Zhen-Yu Yang and Donald J. Burton*

Department of Chemistry, The University of Iowa, Iowa City, Iowa 52242

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The addition reaction of iododifluoromethylphosphonate 1 with alkenes is catalyzed by tetrakis(triphenylphosphine)palladium or copper metal under mild conditions. A variety of functional groups, including alkyl, trimethylsilyl, hydroxy, epoxy, acetoxy, ketone, and ester, in the alkenes could be tolerated under the reaction conditions. Reaction of 2 equiv of 1 with dienes gives the corresponding bisphosphonates. Although the palladium complex fails to induce addition of 1 to cyclohexene, the addition reaction proceeds readily with copper at 85 °C. With diallyl ether, a tetrahydrofuran derivative is obtained. Electron scavenger and radical inhibitors suppressed the addition reaction completely. A single electron transfer initiated radical mechanism is proposed. Treatment of the adducts with zinc in the presence of nickel chloride in moist THF at room temperature provides the corresponding α,α-difluoro-functionalized phosphonates in good yields.

Introduction

Phosphonic acids often exhibit important biological properties by virtue of their similarity to phosphates,[1] while substitution of a fluorine atom in a biological molecule often leads to pronounced activity enhancement.[2] Recently, the difluoromethylenephosphonate moiety has attracted much attention mainly due to the superior biological properties exhibited by this analogue as compared to those of analogous nonfluorinated phosphonates.[3] In addition, the analogues of pyro- and triphosphates where the bridging oxygen atoms were replaced by the difluoromethylene group have been successfully employed as substrates in enzymatic processes[4] and as probes of proteins.[5] More recently, 9-(5,5-difluoro-5-phosphonopentyl)guanine has been utilized as a multisubstrate analogue inhibitor of purine nucleoside phosphorylase.[6] It has been argued that the difluoromethylene group could be regarded as an isopolar–isosteric replacement for oxygen.[7]

Previous approaches to prepare α,α-difluorophosphonates have included Arbuzov reactions,[8-10] radical-based oligomerization,[11] oxidation–hydrolysis of diiodofluoroalkylphosphines,[12] oxidation of fluoroalkylphosphonites,[13] fluorination of phosphonate-stabilized anions,[14] and alkylation and allylation of difluoromethylphosphonate lithium,[15,16] cadmium,[17] and zinc[18,19] reagents. These methods exhibit little generality and utilize expensive, toxic, or unstable reagents. In our continued development of new methodologies for the preparation of precursors for the synthesis of potent biologically active molecules containing the difluoromethylene functionality,[20] we now describe a general approach for the preparation of α,α-difluoro functionalized phosphonates.

Results and Discussion

Recently, we reported a new approach to α,α-difluoro esters via addition–reduction processes.[20d] The success achieved in the addition–reduction sequence of iododifluoroacetates prompted us to examine the addition–reduction reaction of iododifluoromethylphosphonate with alkenes as a general route to α,α-difluoro phosphonates.

Addition of Iododifluoromethylphosphonate to Alkenes. Initially, we evaluated copper as a catalyst in the reaction of diethyl iododifluoromethylphosphonate (1) with alkenes. Although the adducts were obtained in the

$$RCH{=}CH_2 + \underset{\mathbf{1}}{ICF_2PO(OEt)_2} \xrightarrow[70-90\ ^\circ C]{Cu} RCHICH_2CF_2PO(OEt)_2$$

4: R = C_5H_{11}; 75%
6: R = Me_3Si; 75%
12: $MeCOCH_2CH_2$; 80%

case of the reaction of 1 with alkenes catalyzed by copper metal (15 mol %) in the absence of solvent, the reaction

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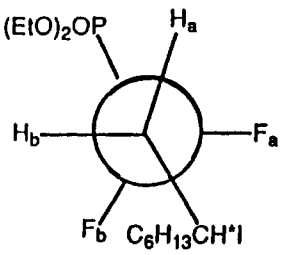
0022-3263/92/1957-4676$03.00/0

$C_6H_{13}\dot{C}HICH_2CF_2PO(OEt)_2$

$^2J_{Fa,Fb}$ = 298.3 Hz, $^2J_{F,P}$ = 105.9 Hz

$^3J_{Fb,Ha}$ = 26.4 Hz, $^3J_{Fb,Hb}$ = 12.2 Hz

$^3J_{Fa,Hb}$ = 29.2 Hz, $^3J_{Fa,Ha}$ = 10.2 Hz



-111.1 ppm (dddd);

-113.3 ppm (dddd).

Figure 1. Observed ^{19}F NMR spectrum.

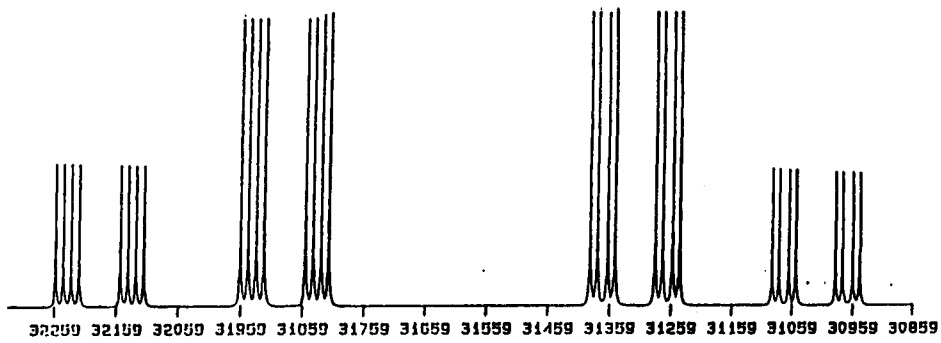


Figure 2. Computer-simulated ^{19}F NMR spectrum.

required a prolonged period (20 h) and elevated temperature (70–90 °C). Furthermore, a significant amount (15–20%) of diethyl difluoromethylphosphonate was observed. When the copper-catalyzed addition was conducted in a solvent, similar reaction conditions were necessary. For example, upon reaction of 1 with vinyltrimethylsilane and copper in acetonitrile or in benzene at 80 °C for 24 h, 6 was obtained in 63% and 75% yields, respectively. Likewise, reaction of 1 with 5-hexen-2-one in hexane at 80 °C for 2 days gave an 80% yield of 12.

We found that tetrakis(triphenylphosphine)palladium was a more effective catalyst in the addition reaction. The palladium-catalyzed reaction proceeded readily at room temperature in the absence of solvent and required only 10 min to be completed in most cases. The yields of

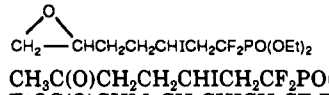
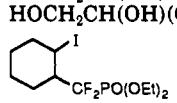
$$\underset{1}{ICF_2PO(OEt)_2} + CH_2{=}CHR \xrightarrow[rt]{Pd(PPh_3)_4} RCHICH_2CF_2PO(OEt)_2$$

63–91%

adducts were good to excellent, the products being easily isolated by either flash chromatography or simple distillation. No difluoromethylphosphonate was observed in

Table I. Palladium-Initiated Addition of 1 to Alkenes

$$ICF_2PO(OEt)_2 + CH_2{=}CHR \xrightarrow{Pd(PPh_3)_4} RCHICH_2CF_2PO(OEt)_2$$

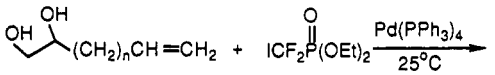
no.	product	yield (%)
2	n-$C_3H_7CHICH_2CF_2PO(OEt)_2$	85
3	n-$C_4H_9CHICH_2CF_2PO(OEt)_2$	91
4	n-$C_5H_{11}CHICH_2CF_2PO(OEt)_2$	81 (75)[a]
5	n-$C_6H_{13}CHICH_2CF_2PO(OEt)_2$	80
6	$Me_3SiCHICH_2CF_2PO(OEt)_2$	88 (75)[a]
7	$HOCH_2CHICH_2CF_2PO(OEt)_2$	81
8	$HO(CH_2)_3CHICH_2CF_2PO(OEt)_2$	79
9	$HO(CH_2)_8CHICH_2CF_2PO(OEt)_2$	76
10	$AcO(CH_2)_3CHICH_2CF_2PO(OEt)_2$	68
11		63
12	$CH_3C(O)CH_2CH_2CHICH_2CF_2PO(OEt)_2$	81 (80)[a]
13	$EtOC(O)CHMeCH_2CHICH_2CF_2PO(OEt)_2$	65
14	$HOCO(CH_2)_2CHICH_2CF_2PO(OEt)_2$	79
15	$HOCH_2CH(OH)CH_2CH_2CHICH_2CF_2PO(OEt)_2$	79
16	$HOCH_2CH(OH)(CH_2)_4CHICH_2CF_2PO(OEt)_2$	76
17		0 (69)[a]

[a] Copper-catalyzed addition reaction at 75–90 °C.

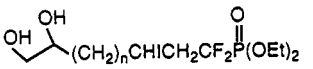
most cases. For example, upon reaction of 1 with 1-hexene in the presence of 2 mol % of palladium catalyst at room temperature for 10 min, 3 was isolated in 91% yield by flash chromatography. Similarly, alkenes containing functional groups, such as trimethylsilyl, epoxy, ester, ketone, and hydroxy, also gave the corresponding adducts in good yields. When a terminal alkenoic acid was used as a substrate, a solvent was necessary to avoid side reactions caused by the vigorous exothermic reaction (entry 14 in Table I). All results are summarized in Table I.

Since the two fluorines are nonequivalent, a typical AB pattern is always observed in the ^{19}F NMR spectrum. For example, Figure 1 illustrates an AB splitting pattern for diethyl 1,1-difluoro-3-iodononylphosphonate **5**. The coupling constant between the two fluorine atoms was 298.3 Hz, with a fluorine phosphorus coupling constant of 105.9 Hz. The coupling constants of the two vicinal hydrogens with fluorine were observed as 26.4 Hz and 12.2 Hz. The computer simulated spectrum[21] of the adduct is illustrated in Figure 2. Agreement between the observed and calculated spectrum is excellent.

Palladium-initiated reaction of 1 with terminal alkene-1,2-diols provides a general approach to a variety of dihydroxy-substituted 1,1-difluoroalkylphosphonates, which have been demonstrated to be enzyme inhibitors.[4c,17b] For example, when neat 5-hexene-1,2-diol was treated with 1 in the presence of 2 mol % of palladium at room temperature for 40 min, **15** was isolated in 79% yield. Similarly, 7-octene-1,2-diol gave **16** in 76% isolated yield



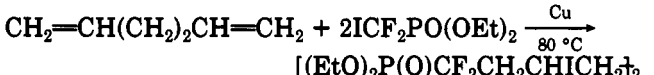
1



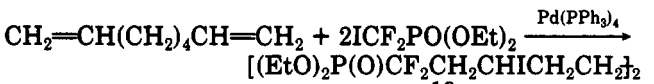
15: n = 2: 79%

16: n = 4: 76%

Addition of 2 equiv of 1 to dienes affords the corresponding bisphosphonates in good yields. Upon reaction of 1,5-hexadiene with 2.1 equiv of 1 and 30 mol % of copper metal at 85 °C for 48 h, the bisphosphonate **18** was isolated in 92% yield. Similarly, when 1,7-octadiene was treated with 2 equiv of 1 and 5 mol % of tetrakis(triphenylphosphine)palladium in hexane at 40 °C overnight, bisphosphonate **19** was isolated in 73% yield.

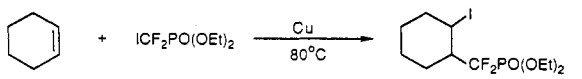


18
92%



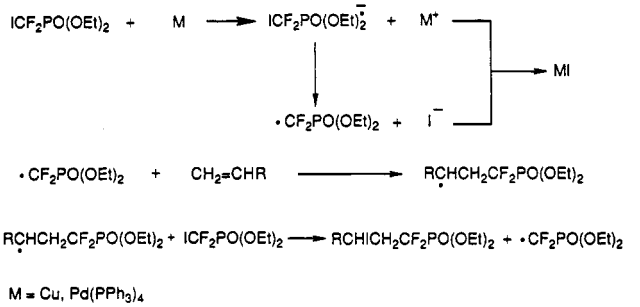
19
73%

Palladium-catalyzed addition of 1 to cyclohexene either at room temperature or at 60 °C failed to produce the addition product. However, when 15 mol % of copper metal was used as a catalyst at 80 °C, **17** was obtained in 69% yield, as a mixture of cis and trans isomers.



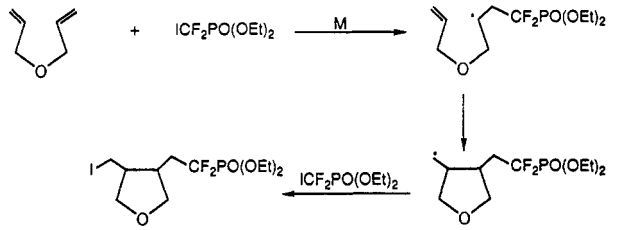
17
69%

Previous reports by Chen and co-workers documented that the addition of perfluoroalkyl iodides to alkenes and alkynes could be catalyzed by copper[22] or tetrakis(triphenylphosphine)palladium,[23] and they proposed a single electron transfer initiated radical chain process. We also suggested a single electron transfer mechanism for the copper-initiated reaction of iododifluoroacetates with alkenes.[20g] Accordingly, we propose that the palladium or copper-initiated reaction of 1 with alkenes similarly involves a single electron transfer mechanism.



Evidence consistent with the proposed mechanism is that the reaction can be inhibited by both electron transfer and radical inhibitors. For example, after reaction of 1 with 1-heptene and 3 mol % palladium catalyst in the presence of 3 mol % of *p*-dinitrobenzene at room temperature for 4 h, no reaction was observed by ^{19}F NMR analysis of the reaction mixture. Similarly, both di-*tert*-butyl nitroxide and galvinoxyl completely suppressed the reaction under the same conditions.

Consistent with a radical intermediate in the reaction, we reacted 1 with diallyl ether in the presence of copper or palladium catalyst and obtained the cyclization product. This result is similar to the palladium- or copper-initiated reaction of perfluoroalkyl iodides or iododifluoroacetates with diallyl ether.[20g,22a,c,23a,b]



20

M = Cu: 73%

M = $Pd(PPh_3)_4$: 82%

Reduction of the Adducts. Hydrogenolysis of the carbon–halogen bond has been widely used to reduce a variety of organohalides.[24] A mixture of metal hydrides with transition-metal salts such as $CoCl_2$,[25] $NiCl_2$,[26] CuCl,[27]

(21) Spectral simulation program written by Dr. W. E. Bennett at the University of Iowa.

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Table II. Preparation of 1,1-Difluoro-Functionalized Phosphonates

$$ICF_2PO(OEt)_2 + CH_2{=}CHR \xrightarrow[(2)\ NiCl_2{\cdot}6H_2O/Zn]{(1)\ Pd(PPh_3)_4} RCH_2CH_2CF_2PO(OEt)_2$$

no.	product	yield[a] (%)
2a	n-$C_3H_7CH_2CH_2CF_2PO(OEt)_2$	64[b]
4a	n-$C_5H_{11}CH_2CH_2CF_2PO(OEt)_2$	52[b]
5a	n-$C_6H_{13}CH_2CH_2CF_2PO(OEt)_2$	80
6a	$Me_3SiCH_2CH_2CF_2PO(OEt)_2$	84
9a	$HO(CH_2)_8CH_2CH_2CF_2PO(OEt)_2$	75
10a	$AcO(CH_2)_3CH_2CH_2CF_2PO(OEt)_2$	61[b]
12a	$CH_3COCH_2CH_2CH_2CH_2CF_2PO(OEt)_2$	55[b]
13a	$EtOCOCHMeCH_2CH_2CH_2CF_2PO(OEt)_2$	61[b]
16a	$HOCH_2CH(OH)(CH_2)_6CF_2PO(OEt)_2$	71

[a] The purified adducts were reduced, and the isolated yields are based on the corresponding adducts. [b] The crude adducts were directly reduced and the isolated yields are based on diethyl iodofluoromethylphosphonate **1**.

$RhCl_3$,[28] $TiCl_3$,[29] and Zn/acid[30] are effective for the removal of halogen from organic halides. Radical reduction with organotin hydrides provides an alternative reducing agent with excellent selectivity.[31]

Preliminary work with tributyltin hydride demonstrated that the adduct can be readily converted to the corresponding α,α-difluoro phosphonates. However, it is difficult to separate the product from the reaction mixture by simple distillation in some cases. Thus, a small but significant amount of tributyltin iodide was always present as a contaminant in the final product. Recently we have reported that $NiCl_2{\cdot}6H_2O$/Zn could readily reduce 1,1-difluoro-3-iodo esters to the corresponding 1,1-difluoro esters.[20g] Accordingly, we found that 1,1-difluoro-3-iodoalkylphosphonates could also be converted into the 1,1-difluorophosphonates in good yields upon treatment with $NiCl_2{\cdot}6H_2O$/Zn in moist THF. For example, when **5** was added to a mixture of zinc in the presence of nickel chloride hexahydrate in moist THF and the resultant mixture was stirred at room temperature for several hours, ^{19}F NMR analysis indicated that only α,α-difluorononylphosphonate **5a** (−112.2 ppm, dt, $^2J_{F,P}$ = 110.0 Hz, $^3J_{F,H}$ = 19.5 Hz) was formed, which was readily isolated in 80% yield by simple distillation. As illustrated in Table II, **5**, **6**, **9**, and **16** could be readily converted to the corresponding iodine-free α,α-difluoro phosphonates **5a**, **6a**, **9a**, and **16a** in good yields, respectively.

$$RCHICH_2CF_2PO(OEt)_2 + Zn \xrightarrow[THF,\ rt]{NiCl_2{\cdot}6H_2O} RCH_2CH_2CF_2PO(OEt)_2$$

5: R = n-C_6H_{13}
6: R = Me_3Si

5a: R = n-C_6H_{13}; 80%
6a: R = Me_3Si; 84%

However, when ω-hydroxy-γ-iodo-α,α-difluoroalkylphosphonates were used as substrates, reduction with $NiCl_2{\cdot}6H_2O$/Zn in moist THF gave the desired ω-hydroxy-α,α-difluoro phosphonates along with significant amounts (10–15%) of dehydroiodination products, which were observed by ^{19}F and ^{31}P NMR analysis. For example, upon treatment of **9** with zinc in the presence of 5 mol % of $NiCl_2{\cdot}6H_2O$ in THF at 25 °C, the ^{19}F NMR spectrum of the reaction mixture exhibited two sets of doublets of triplets at −111.7 ppm (dt, $^2J_{F,P}$ = 108.8 Hz, $^3J_{H,F}$ = 17.3 Hz) and −112.3 ppm (dt, $^2J_{F,P}$ = 109.9 Hz, $^3J_{H,F}$ = 19.6 Hz), respectively. Similarly, the ^{31}P NMR spectrum of the crude product exhibited signals at 7.51 (t, $^2J_{F,P}$ = 109.9 Hz) and 7.23 ppm (t, $^2J_{F,P}$ = 108.4 Hz), respectively. The presence of two sets of signals in the ^{19}F NMR and ^{31}P NMR spectra indicated that the desired reduction product **9a** and the dehydroiodination product were formed upon reduction of **9**. Although we did not separate the elimination product from the desired reduction product **9a**, this phenomenon in a similar system had been observed in our laboratory and the elimination product was isolated and identified, indicating regiospecific dehydroiodination.[31] Further evidence for the formation of the elimination product is that when the crude products (reduction product and elimination product) were hydrogenated with 5% of palladium on carbon as the catalyst, only **9a** was detected.

$$HO(CH_2)_8CHICH_2CF_2PO(OEt)_2\ (\mathbf{9}) \xrightarrow{NiCl_2{\cdot}6H_2O} \underset{85\%}{HO(CH_2)_8CH_2CH_2CF_2PO(OEt)_2} + \underset{15\%}{HO(CH_2)_7CH{=}CHCH_2CF_2PO(OEt)_2} \xrightarrow[Pd/C]{H_2} HO(CH_2)_8CH_2CH_2CF_2PO(OEt)_2\ (\mathbf{9a})$$

75% isolated yield

The addition–reduction two-step sequence for the preparation of α,α-difluoro-functionalized phosphonates could be simplfied without purification of the adducts. After the Pd-catalyzed addition reaction was completed, addition of a mixture of ether and hexane to the reaction mixture resulted in the precipitation of brown solids, which were readily removed by filtration. Concentration by rotary evaporation of the filtrate gave a residue, which was then transferred to a flask with zinc and a catalytic amount of nickel chloride hexahydrate in moist THF. The corresponding α,α-difluoro phosphonate was obtained upon stirring the resultant mixture at room temperature for a few hours (cf. Table II).

Conclusion

We have demonstrated that copper- or palladium-initiated addition of **1** to alkenes produces the corresponding adducts in good yields. The α,α,ω,ω-tetrafluoroalkylene bisphosphonate precursors can also be prepared from the reaction of **1** with dienes. A single electron transfer mechanism is proposed. The adducts can be reduced with zinc in the presence of nickel chloride in moist THF to give the corresponding α,α-difluoro-functionalized phosphonates. The mild reaction conditions, readily available starting materials and catalysts, and simple procedure provide a convenient and practical method for the preparation of compounds of biological importance.

Experimental Section

General. All reactions were performed in an oven-dried apparatus that consisted of a two- or three-necked flask equipped with a Teflon-coated magnetic stirring bar and a reflux condenser connected to a nitrogen source and mineral oil bubbler. All boiling points were determined during fractional distillation using a partial immersion thermometer and are uncorrected. ^{19}F NMR, ^1H NMR,

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^{13}C NMR, and ^{31}P NMR spectra were recorded on JEOL FX 90Q 90-MHz multinuclear and Bruker AC-300-MHz spectrometers. All chemical shifts are reported in parts per million downfield (positive) of the standard. ^{19}F NMR spectra are referenced against internal $CFCl_3$, ^1H NMR and ^{13}C NMR spectra against internal tetramethylsilane, and ^{31}P NMR against external H_3PO_4. FT-IR spectra were recorded as CCl_4 solutions using a solution cell with a 0.1-cm path length. GC–MS spectra were performed at 70 eV, in the electron impact mode. GLPC analyses were performed on a 5% OV-101 column with a thermal conductivity detector. Most products are greater than 95% purity based on ^{19}F and ^{13}C NMR and GC–MS analysis.

Materials. Diethyl iododifluoromethylphosphonate (1) was prepared by iodination of the corresponding zinc or cadmium reagents.[17a,19] Cu[32] and $Pd(PPh_3)_4$[33] were prepared by literature procedures. Nickel chloride hexahydrate, iodine, Zn, all alkenes, and THF were obtained from Aldrich Chemical Co. and used without purification except Zn, which was washed with acid, water, and acetone.

Representative General Procedure for the Preparation of α,α-Difluoro-Functionalized Phosphonates. Preparation of Diethyl 1,1-Difluoro-3-iodohexylphosphonate (2). To a stirred solution of 0.3 g (0.26 mmol) of $Pd(PPh_3)_4$ and 0.7 g (10 mmol) of 1-pentene at 25 °C was added 1.6 g (5 mmol) of 1, and the resultant mixture was stirred for 10 min. Distillation of the reaction mixture gave 1.7 g (85%) of 2, bp 112–114 °C (0.1 mmHg). ^{19}F NMR ($CDCl_3$): −110.2 (dddd, $^2J_{F,F}$ = 298 Hz, $^2J_{F,P}$ = 106.4 Hz, $^3J_{F,H}$ = 29.0 Hz, $^3J_{F,H}$ = 11.0 Hz, 1 F), −113.4 (dddd, $^2J_{F,F}$ = 297.9 Hz, $^2J_{F,P}$ = 106.4 Hz, $^3J_{F,H}$ = 26.5 Hz, $^3J_{F,H}$ = 11.1 Hz, 1 F). ^1H NMR ($CDCl_3$): 4.43 (m, 1 H), 4.28 (m, 4 H), 3.00–2.67 (m, 2 H), 1.83–1.70 (m, 2 H), 1.64–1.45 (m, 2 H), 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 1.24 (t, $^3J_{H,H}$ = 6.9 Hz, 3 H). ^{31}P NMR ($CDCl_3$): 6.05 (t, $^2J_{P,F}$ = 117 Hz). ^{13}C NMR ($CDCl_3$): 120.20 (td, $^1J_{F,C}$ = 262.7 Hz, $^1J_{P,C}$ = 215.2 Hz), 64.85 (d, $^3J_{C,P}$ = 6.8 Hz), 44.80 (td, $^2J_{F,C}$ = 19.6 Hz, $^2J_{P,C}$ = 14.6 Hz), 42.65, 22.99, 16.44, 12.99. FT-IR (CCl_4): 2983 (m), 2964 (m), 1274 (s), 1166 (s), 1120 (m), 1080 (m), 1038 (s), 1024 (s). GC–MS: 339 (M^+ − EtO, 1.4), 257 (91.5), 201 (36.3), 181 (25.0), 119 (100.0), 117 (50.5), 97 (39.2), 81 (36.1), 55 (54.3).

Preparation of Diethyl 1,1-Difluoro-3-iodoheptylphosphonate (3). Similarly, 3 was prepared from 0.84 g (10 mmol) of 1-hexene, 1.6 g (5 mmol) of 1, and 0.3 g (0.26 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (hexane:ethyl acetate = 70:30) gave 1.85 g (91%) of 3. ^{19}F NMR ($CDCl_3$): −109.9 (dddd, $^2J_{F,F}$ = 297.1 Hz, $^2J_{F,P}$ = 104.4 Hz, $^3J_{F,H}$ = 26.1 Hz, $^3J_{F,H}$ = 11.6 Hz, 1 F), −112.6 (dddd, $^2J_{F,F}$ = 297.1 Hz, $^2J_{F,P}$ = 104.4 Hz, $^3J_{F,H}$ = 25.1 Hz, $^3J_{F,H}$ = 13.0 Hz, 1 F). ^1H NMR ($CDCl_3$): 4.46 (m, 5 H), 3.11–2.66 (m, 2 H), 1.77–1.26 (m, 6 H), 1.39 (t, $^3J_{H,H}$ = 6.8 Hz, 6 H), 0.93 (m, 3 H). ^{31}P NMR ($CDCl_3$): 5.80 (t, $^2J_{F,P}$ = 106.0 Hz). FT-IR (CCl_4): 2962 (s), 1272 (s), 1167 (s), 1077 (s), 979 (s). GC–MS: 271 (M^+ − I, 100), 215 (6.25), 195 (4.10), 127 (2.27), 40 (23.99).

Preparation of Diethyl 1,1-Difluoro-3-iodooctylphosphonate (4). Similarly, 4 was prepared from 1.0 g (10 mmol) of 1-heptene, 1.6 g (5 mmol) of 1, and 0.3 g (0.26 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (hexane:ethyl acetate = 70:30) gave 2.1 g (81%) of 4. ^{19}F NMR ($CDCl_3$): −110.1 (dddd, $^2J_{F,F}$ = 297.6 Hz, $^2J_{F,P}$ = 105.9 Hz, $^3J_{F,H}$ = 29.2 Hz, $^3J_{F,H}$ = 10.7 Hz, 1 F), −112.9 (dddd, $^2J_{F,F}$ = 297.6 Hz, $^2J_{F,P}$ = 105.9 Hz, $^3J_{F,H}$ = 29.2 Hz, $^3J_{F,H}$ = 10.7 Hz, 1 F). ^1H NMR ($CDCl_3$): 4.43 (m, 1 H), 4.28 (m, 4 H), 3.02–2.69 (m, 2 H), 1.79 (m, 2 H), 1.39 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 1.54–1.20 (m, 6 H), 0.92 (t, $^3J_{H,H}$ = 7.1 Hz, 3 H). ^{31}P NMR ($CDCl_3$): 6.1 (t, $^2J_{F,P}$ = 106 Hz). ^{13}C NMR ($CDCl_3$): 120.75 (td, $^1J_{F,C}$ = 262.0 Hz, $^1J_{P,C}$ = 215.0 Hz), 64.70 (d, $^2J_{C,P}$ = 6.8 Hz), 44.72 (td, $^2J_{F,C}$ = 20.0 Hz, $^2J_{P,C}$ = 14.7 Hz), 40.25, 31.78, 23.42 (t, $^3J_{F,C}$ = 4.0 Hz), 21.73, 16.42 (d, $^3J_{P,C}$ = 5.0 Hz), 13.90. FT-IR (CCl_4): 2961 (s), 1275 (s), 1165 (s), 1083 (s), 980 (s). GC–MS: 413 (M^+ + 1, 0.3), 285 (76.6), 257 (13.3), 229 (16.4), 187 (20.1), 147 (60.9), 145 (37.5), 127 (41.6), 109 (48.4), 81 (47.7), 65 (51.6), 55 (100), 43 (50).

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Preparation of Diethyl 1,1-Difluoro-3-iodononylphosphonate (5). Similarly, 5 was prepared frm 2.5 g (22 mmol) of 1-octene, 6.3 g (20 mmol) of 1, and 0.5 g (0.43 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (hexane:ethyl acetate = 90:10–40:60) gave 6.8 g (80%) of 5. ^{19}F NMR ($CDCl_3$): −110.1 (dddd, $^2J_{F,F}$ = 298.3 Hz, $^2J_{F,P}$ = 105.9 Hz, $^3J_{H,F}$ = 29.2 Hz, $^3J_{F,H}$ = 10.2 Hz, 1 F), −113.3 (dddd, $^2J_{F,F}$ = 298.3 Hz, $^2J_{F,P}$ = 105.9 Hz, $^3J_{F,H}$ = 26.4 Hz, $^3J_{F,H}$ = 12.2 Hz, 1 F). ^1H NMR ($CDCl_3$): 4.42 (m, 1 H), 4.28 (m, 4 H), 3.01–2.71 (m, 2 H), 1.78 (m, 2 H), 1.39 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 1.30 (m, 8 H), 0.89 (t, $^3J_{H,H}$ = 6.8 Hz, 3 H). ^{31}P NMR ($CDCl_3$): 7.51 (t, $^2J_{F,P}$ = 107.0 Hz). ^{13}C NMR ($CDCl_3$): 119.8 (td, $^1J_{F,C}$ = 262.6 Hz, $^1J_{P,C}$ = 215.8 Hz), 64.64 (d, $^2J_{F,C}$ = 7.2 Hz), 44.37 (td, $^2J_{F,C}$ = 19.6 Hz, $^2J_{P,C}$ = 14.7 Hz), 40.53, 31.60, 29.58, 28.24, 23.42 (t, $^3J_{F,C}$ = 3.7 Hz), 22.56, 16.40 (d, $^3J_{P,C}$ = 5.2 Hz), 14.02. FT-IR (CCl_4): 2959 (s), 1275 (s), 1166 (s), 1041 (s), 979 (s). DIP-MS: 299 (M^+ − I, 99.5), 187 (56.9), 109 (43.6), 81 (54.4), 69 (42.1), 55 (82.0), 43 (100), 41 (90.3).

Preparation of Diethyl 1,1-Difluoro-3-iodo-3-(trimethylsilyl)propylphosphonate (6). A mixture of 1.4 g (14 mmol) of vinyltrimethylsilane, 3.2 g (10 mmol) of 1, and 0.1 g (1.6 mmol) of Cu in 10 mL of benzene was stirred at 80 °C for 2 days. After removal of the solids by filtration, evaporation gave a residue, which was purified by chromatography on silica gel (hexane:ethyl acetate = 8:2) to give 3.1 g (75%) of 6. ^{19}F NMR ($CDCl_3$): −111.4 (dddd, $^2J_{F,F}$ = 294.8 Hz, $^2J_{F,P}$ = 105.4 Hz, $^3J_{F,H}$ = 26.0 Hz, $^3J_{F,H}$ = 8.7 Hz, 1 F), −114.5 (dddd, $^2J_{F,F}$ = 294.8 Hz, $^2J_{F,P}$ = 108.5 Hz, $^3J_{F,H}$ = 27.2 Hz, $^3J_{F,H}$ = 13.1 Hz, 1 F). ^1H NMR ($CDCl_3$): 4.29 (m, 4 H), 3.31 (dd, $^3J_{H,H}$ = 9.7 Hz, $^3J_{H,H}$ = 3.2 Hz, 1 H), 2.85–2.47 (m, 2 H), 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 0.19 (s, 9 H). ^{31}P NMR ($CDCl_3$): 6.96 (t, $^2J_{F,P}$ = 105.7 Hz). FT-IR (CCl_4): 2984 (s), 1276 (s), 1166 (s), 1099 (s), 1042 (s), 978 (s). GC–MS: 414 (M^+, 0.3), 399 (M^+ − Me, 12.6), 287 (61.5), 259 (44.3), 233 (62.0), 185 (50.5), 165 (100), 141 (66.4), 139 (78.1), 109 (54.2), 81 (58.9), 77 (66.4), 73 (99.0), 45 (42.2).

Preparation of Diethyl 1,1-Difluoro-3-iodo-4-hydroxybutylphosphonate (7). Similarly, 7 was prepared from 0.58 g (10 mmol) of allyl alcohol, 1.6 g (5 mmol) of 1, and 0.16 g (0.13 mmol) of $Pd(PPh_3)_4$ in 4 mL of hexane at room temperature. Purification of the reaction mixture by flash chromatography on silica gel (hexane:CH_2Cl_2 = 1:1 to CH_3OH) gave 1.5 g (81%) of 7. ^{19}F NMR ($CDCl_3$): −111.7 (dt, $^2J_{F,P}$ = 107.4 Hz, $^3J_{F,H}$ = 19.5 Hz). ^1H NMR ($CDCl_3$): 4.44 (pent, $^3J_{H,H}$ = 6.0 Hz, 1 H), 4.28 (m, 4 H), 4.11 (br, 1 H), 3.80 (dd, $^3J_{H,H}$ = 12 Hz, $^3J_{H,H}$ = 5.6 Hz, 1 H), 3.74 (dd, $^3J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 5.6 Hz, 1 H), 3.11–2.94 (m, 1 H), 2.83–2.64 (m, 1 H), 1.39 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H). FT-IR (CCl_4): 3450 (m), 2986 (m), 1272 (s), 1165 (s), 1022 (s), 981 (m). DIP-MS: 342 (M^+ − CH_2O, 0.9), 245 (10.2), 199 (14.5), 171 (100), 109 (37.20), 101 (31.6), 81 (43.2), 65 (30.0), 43 (82.8).

Preparation of Diethyl 1,1-Difluoro-3-iodo-6-hydroxyhexylphosphonate (8). Similarly, 8 was prepared from 1.7 g (20 mmol) of 4-penten-1-ol, 6.3 g (20 mmol) of 1, and 0.25 g (0.22 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (CH_2Cl_2:hexane = 1:1 to CH_2Cl_2:CH_3CO_2Et = 1:3) gave 6.3 g (79%) of 8. ^{19}F NMR ($CDCl_3$): −109.6 (dddd, $^2J_{F,F}$ = 297.2 Hz, $^2J_{F,P}$ = 105.2 Hz, $^3J_{F,H}$ = 24.7 Hz, $^3J_{F,H}$ = 10.4 Hz, 1 F), −112.5 (dddd, $^2J_{F,F}$ = 297.2 Hz, $^2J_{F,P}$ = 105.2 Hz, $^3J_{F,H}$ = 25.3 Hz, $^3J_{F,H}$ = 13.0 Hz, 1 F). ^1H NMR ($CDCl_3$): 4.45 (m, 1 H), 4.26 (m, 4 H), 3.64 (s, 1 H), 3.63 (t, $^3J_{H,H}$ = 6.0 Hz, 2 H), 2.98–2.74 (m, 2 H), 1.95–1.57 (m, 4 H), 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H). ^{13}C NMR ($CDCl_3$): 120.02 (td, $^1J_{C,F}$ = 261.5 Hz, $^1J_{C,P}$ = 215.21 Hz), 64.95 (d, $^2J_{C,P}$ = 7.0 Hz), 60.94, 44.90 (td, $^2J_{C,F}$ = 19.6 Hz, $^2J_{C,P}$ = 14.8 Hz), 36.98, 32.74, 22.94, 16.42 (d, $^3J_{C,F}$ = 7.3 Hz). ^{31}P ($CDCl_3$): 6.05 (t, $^2J_{F,P}$ = 105.5 Hz). FT-IR (CCl_4): 3494 (br), 2985 (m), 1271 (s), 1165 (m), 1063 (s), 1034 (s). GC–MS: 273 (M^+ − I, 2.3), 244 (25.6), 202 (13.1), 138 (100.0), 111 (29.5), 85 (17.2), 81 (16.6), 71 (93.0), 65 (17.8), 43 (36.8).

Preparation of Diethyl 1,1-Difluoro-3-iodo-11-hydroxyundecylphosphonate (9). Similarly, 9 was prepared from 3.3 g (20 mmol) of 9-decen-1-ol, 6.3 g (20 mmol) of 1, and 0.4 g (0.35 mmol) of $Pd(PPh_3)_4$ at room temperature. After a mixture of ether and hexane (1:1) was added to the reaction mixture, solids were precipitated and removed by filtration. The filtrates were evaporated and purified by chromatography on silica gel (CH_2Cl_2:hexane = 1:2–2:1 then ethyl acetate) to give 7.1 g (76%) of 9. ^1H NMR ($CDCl_3$): 4.65 (m, 1 H), 4.41 (m, 4 H), 3.71 (s, 1 H), 3.57 (t, $^3J_{H,H}$ = 6.5 Hz, 2 H), 3.01–2.66 (m, 2 H), 1.77 (m, 2

H), 1.52 (m, 2 H), 1.39 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H), 1.32–1.16 (m, 10 H). ^{19}F NMR ($CDCl_3$): −110.1 (dddd, $^2J_{F,F}$ = 298.3 Hz, $^2J_{F,P}$ = 105.9 Hz, $^3J_{F,H}$ = 28.7 Hz, $^3J_{F,H}$ = 12.8 Hz, 1 F), −113.2 (dddd, $^2J_{F,F}$ = 298.3 Hz, $^2J_{F,P}$ = 106.0 Hz, $^3J_{F,H}$ = 25.9 Hz, $^3J_{F,H}$ = 12.0 Hz, 1 F). ^{13}C NMR ($CDCl_3$): 120.05 (td, $^1J_{C,F}$ = 262.4 Hz, $^1J_{C,P}$ = 215.7 Hz), 64.76 (d, $^2J_{C,P}$ = 5.6 Hz), 62.32, 44.64 (dt, $^2J_{C,P}$ = 14.8 Hz, $^2J_{C,F}$ = 19.5 Hz), 40.44, 32.64, 29.54, 29.31, 28.44, 25.73, 23.13 (d, $^3J_{C,F}$ = 7.2 Hz), 16.37 (d, $^3J_{C,P}$ = 5.1 Hz). ^{31}P NMR ($CDCl_3$): 6.01 (t, $^2J_{F,P}$ = 107.7 Hz). FT-IR (CCl_4): 3480 (w), 2984 (w), 1272 (s), 1166 (s), 1031 (s), 981 (s). DIP-MS: 329 (2.4), 287 (24.7), 131 (54.7), 111 (49.3), 91 (43.6), 81 (49.7), 55 (30.1), 43 (100).

Preparation of Diethyl 1,1-Difluoro-3-iodo-6-acetoxyhexylphosphonate (10). Similarly, **10** was prepared from 0.77 g (6 mmol) of 4-penten-1-yl acetate, 1.6 g (5 mmol) of **1**, and 0.2 g (0.17 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (hexane:CH_2Cl_2 = 1:1–5:95) gave 1.5 g (68%) of **10**. ^{19}F NMR ($CDCl_3$): −109.9 (dddd, $^2J_{F,F}$ = 299.8 Hz, $^2J_{F,P}$ = 103.0 Hz, $^3J_{F,H}$ = 29.8 Hz, $^3J_{F,H}$ = 9.0 Hz, 1 F), −113.4 (dddd, $^2J_{F,F}$ = 299.8 Hz, $^2J_{F,P}$ = 103.0 Hz, $^3J_{F,H}$ = 25.9 Hz, $^3J_{F,H}$ = 9.5 Hz, 1 F). ^{1}H NMR ($CDCl_3$): 4.47 (m, 1 H), 4.28 (m, 4 H), 4.10 (t, $^3J_{H,H}$ = 6.1 Hz, 2 H), 3.06–2.67 (m, 2 H), 2.04 (s, 3 H), 1.93–1.72 (m, 4 H), 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H). ^{13}C NMR ($CDCl_3$): 170.79, 120.10 (td, $^1J_{F,C}$ = 262.5 Hz, $^1J_{P,C}$ = 214.9 Hz), 64.74 (d, $^2J_{C,P}$ = 6.8 Hz), 63.16, 44.70 (td, $^2J_{F,C}$ = 20.0 Hz, $^2J_{P,C}$ = 14.9 Hz), 37.00, 28.91, 22.06, 20.83, 16.40 (d, $^3J_{P,C}$ = 5.5 Hz). FT-IR (CCl_4): 2984 (m), 1744 (s), 1274 (s), 1047 (s), 980 (s). DIP-MS: 442 (M^+, 0.05), 315 (9.0), 273 (34.6), 117 (55.8), 81 (16.2), 43 (100).

Preparation of Diethyl 1,1-Difluoro-3-iodo-6,7-epoxyheptylphosphonate (11). Similarly, **11** was prepared from 1.1 g (11 mmol) of 1,2-epoxy-5-hexene, 3.1 g (10 mmol) of **1**, and 0.3 g (0.26 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (hexane:ethyl acetate = 1:1–3:7) gave 2.6 g (63%) of **11**. ^{19}F NMR ($CDCl_3$): −110.2 (dddd, $^2J_{F,F}$ = 297.7 Hz, $^2J_{F,P}$ = 105.4 Hz, $^3J_{F,H}$ = 30.2 Hz, $^3J_{F,H}$ = 10.2 Hz, 1 F), −113.3 (dddd, $^2J_{F,F}$ = 297.7 Hz, $^2J_{F,P}$ = 105.4 Hz, $^3J_{F,H}$ = 11.1 Hz, $^3J_{F,H}$ = 2.7 Hz, 1 F). ^{1}H NMR ($CDCl_3$): 4.46 (m, 1 H), 4.28 (m, 4 H), 2.95 (m, 2 H), 2.76 (m, 2 H), 2.51 (m, 1 H), 2.16–1.71 (m, 4 H), 1.40 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H). ^{13}C NMR ($CDCl_3$): 120.13 (td, $^1J_{F,C}$ = 262.2 Hz, $^1J_{P,C}$ = 215.1 Hz), 64.51 (d, $^2J_{P,C}$ = 6.9 Hz), 51.23, 50.88, 46.86, 46.67, 44.84 (td, $^2J_{F,C}$ = 19.6 Hz, $^2J_{P,C}$ = 16.0 Hz), 37.10, 36.65, 32.81, 32.48, 22.07 (m), 16.40 (d, $^3J_{P,C}$ = 5.5 Hz). ^{31}P NMR ($CDCl_3$): 5.77 (t, $^2J_{F,P}$ = 105.5 Hz). FT-IR (CCl_4): 2985 (s), 1272 (s), 1165 (s), 1028 (s), 981 (s). GC–MS: 285 (M^+ − I, 4.6), 171 (64.20), 97 (60.5), 83 (98.00), 81 (69.00), 69 (98.00), 43 (100).

Preparation of Diethyl 1,1-Difluoro-3-iodo-6-oxoheptylphosphonate (12). Similarly, **12** was prepared from 0.6 g (6 mmol) of 5-hexen-2-one, 1.6 g (5 mmol) of **1**, and 0.15 g (0.13 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (hexane:ethyl acetate = 7:3–3:7) gave 1.7 g (81%) of **12**. ^{19}F NMR ($CDCl_3$): −110.2 (dddd, $^2J_{F,F}$ = 299.4 Hz, $^2J_{F,P}$ = 106.0 Hz, $^3J_{F,H}$ = 30.5 Hz, $^3J_{F,H}$ = 10.0 Hz, 1 F), −133.2 (dddd, $^2J_{F,F}$ = 299.4 Hz, $^2J_{F,P}$ = 106.0 Hz, $^3J_{F,H}$ = 26.4 Hz, $^3J_{F,H}$ = 11.5 Hz, 1 F). ^{1}H NMR ($CDCl_3$): 4.46 (m, 1 H), 4.10 (m, 4 H), 3.05–2.57 (m, 4 H), 2.17 (s, 3 H), 2.14 (m, 2 H), 1.39 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H). ^{31}P NMR ($CDCl_3$): 5.81 (t, $^2J_{F,P}$ = 106.0 Hz). ^{13}C NMR ($CDCl_3$): 206.34, 119.98 (td, $^1J_{F,C}$ = 263.0 Hz, $^1J_{P,C}$ = 215.0 Hz), 64.74 (d, $^2J_{P,C}$ = 7.1 Hz), 44.78 (td, $^2J_{F,c}$ = 20.2 20.2 Hz, $^2J_{C,P}$ = 15.0 Hz), 43.63, 34.36, 29.97, 22.17 (td, $^3J_{F,C}$ = 7.0 Hz, $^3J_{P,C}$ = 3.6 Hz), 16.42. FT-IR (CCl_4): 2984 (m), 1722 (s), 1275 (s), 1169 (s), 1071 (s), 1031 (s). DIP-MS: 367 (M^+ − OEt, 0.3), 285 (20.4), 187 (30.8), 109 (10.1), 81 (17.5), 43 (100).

Reaction of 1 with 5-Hexen-2-one in the Presence of Copper. A mixture of 4.7 g (15 mmol) of **1**, 1.7 g (17 mmol) of 5-hexen-2-one, and 0.2 g (3.1 mmol) of Cu in 20 mL of hexane was stirred at 70–80 °C for 18 h. Solids were removed by filtration and washed with ether (3 × 20 mL). The combined organic layers were evaporated to give a residue, which was purified by chromatography on silica gel (hexane:ethyl acetate = 7:3) to give 5.0 g (80%) of **12**.

Preparation of Diethyl 1,1-Difluoro-3-iodo-5-carbethoxyhexylphosphonate (13). Similarly, **13** was prepared from 0.85 g (6 mmol) of ethyl 2-methyl-4-pentenoate, 1.6 g (5 mmol) of **1**, and 0.15 g (0.13 mmol) of $Pd(PPh_3)_4$ at room temperature. Purification of the reaction mixture by chromatography on silica gel (CH_2Cl_2) gave 1.5 g (65%) of **13**, as a mixture of diastereoisomers in a 1:1 ratio. ^{19}F NMR ($CDCl_3$): (a) −109.7 (dddd, $^2J_{F,F}$ = 298.1 Hz, $^2J_{F,P}$ = 104.8 Hz, $^3J_{F,H}$ = 28.2 Hz, $^3J_{F,H}$ = 10.7 Hz, 1 F), −113.2 (dddd, $^2J_{F,F}$ = 298.1 Hz, $^2J_{P,F}$ = 105.1 Hz, $^3J_{F,H}$ = 25.8 Hz, $^3J_{F,H}$ = 11.6 Hz, 1 F); (b) −110.3 (dddd, $^2J_{F,F}$ = 298.1 Hz, $^2J_{F,P}$ = 105.1 Hz, $^3J_{F,H}$ = 31.7 Hz, $^3J_{F,H}$ = 10.7 Hz, 1 F), −113.6 (dddd, $^2J_{F,F}$ = 298.1 Hz, $^2J_{F,P}$ = 105.1 Hz, $^3J_{F,H}$ = 27.5 Hz, $^3J_{F,H}$ = 9.0 Hz, 1 F). ^{1}H NMR ($CDCl_3$): 4.40 (m, 1 H), 4.31 (m, 4 H), 4.17–4.11 (m, 2 H), 3.10–2.72 (m, 2 H), 2.32–2.11 (m, 2 H), 1.85–1.75 (m, 1 H), 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 1.30–1.22 (m, 3 H), 1.15 (d, $^3J_{H,H}$ = 7.0 Hz, 3 H). FT-IR (CCl_4): 2983 (s), 1734 (s), 1274 (s), 1181 (s), 1070 (s), 1029 (s). GC–MS: 411 (M^+ − OEt, 8.7), 329 (43.2), 255 (46.2), 179 (28.5), 117 (100), 95 (43.2), 81 (40.2), 65 (27.5), 55 (32.2), 43 (32.2).

Preparation of 6,6-Difluoro-6-(diethoxyphosphinyl)-4-iodohexanoic Acid (14). A mixture of 0.5 g (5 mmol) of 4-pentenoic acid, 1.6 g (5 mmol) of **1**, and 0.25 g (0.22 mmol) of $Pd(PPh_3)_4$ in 3 mL of hexane was stirred at room temperature for 20 min. Solids were removed by filtration and washed with ether. The filtrate was concentrated, and the residue was purified by chromatography on silica gel (CH_2Cl_2 to CH_3OH) to give 1.7 (79%) of **14**. ^{19}F NMR ($CDCl_3$): −110.2 (dddd, $^2J_{F,F}$ = 298.1 Hz, $^2J_{F,P}$ = 106.6 Hz, $^3J_{F,H}$ = 28.5 Hz, $^3J_{F,H}$ = 10.2 Hz, 1 F), −113.4 (dddd, $^2J_{F,F}$ = 299.5 Hz, $^2J_{F,P}$ = 106.4 Hz, $^3J_{F,H}$ = 25.6 Hz, $^3J_{F,H}$ = 11.2 Hz, 1 F). ^{1}H NMR ($CDCl_3$): 9.22 (br, 1 H), 4.47 (m, 1 H), 4.30 (m, 4 H), 2.91–2.49 (m, 4 H), 2.20–2.04 (m, 2 H), 1.40 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H). ^{31}P NMR ($CDCl_3$): 5.52 (t, $^2J_{F,P}$ = 107.0 Hz). FT-IR (CCl_4): 3233–2854 (br), 2985 (m), 1714 (s), 1274 (s), 1168 (s), 1065 (s). DIP-MS: 414 (M^+, 0.2), 149 (33.0), 97 (25.5), 81 (55.7), 69 (100), 55 (63.9), 43 (84.5).

Preparation of Diethyl 1,1-Difluoro-3-iodo-6,7-dihydroxyheptylphosphonate (15). A mixture of 2.3 g (20 mmol, 90% purity) of 5-hexene-1,2-diol, 4.9 g (15 mmol) of **1**, and 0.4 g (0.35 mmol) of $Pd(PPh_3)_4$ was stirred at room temperature for 1 h. Ether (50 mL) was added to the reaction mixture, and the solids were removed by filtration. After evaporation of the ether, the residue was purified by chromatography on silica gel (CH_2Cl_2 to CH_3CO_2Et:MeOH = 90:10) to give 5.1 g (79%) of **15**. ^{19}F NMR ($CDCl_3$): −108.7, −111.8 (m, 2 F). ^{1}H NMR ($CDCl_3$): 5.35 (br, 2 H), 4.33 (m, 4 H), 3.86 (br, 1 H), 3.73 (m, 1 H), 3.57 (m, 1 H), 2.17–1.97 (m, 2 H), 1.56 (m, 5 H), 1.38 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H). ^{31}P NMR ($CDCl_3$): 5.9 (t, $^2J_{P,F}$ = 106.5 Hz). ^{13}C NMR ($CDCl_3$): 119.49 (td, $^1J_{C,F}$ = 262.4 Hz, $^1J_{C,P}$ = 212.7 Hz), 71.03, 70.22, 66.03 (d, $^2J_{C,P}$ = 7.5 Hz), 64.49 (d, $^2J_{C,P}$ = 7.0 Hz), 44.26 (m), 36.60, 35.97, 32.87, 32.56, 22.52 (t, $^3J_{C,F}$ = 4.0 Hz), 22.26 (t, $^3J_{C,F}$ = 5.6 Hz), 15.88 (d, $^3J_{C,P}$ = 5.2 Hz). FT-IR (CCl4): 3551–3425 (br), 2985 (m), 1270 (s), 1259 (s), 1164 (m), 1034 (s), 1027 (s), 982 (m). GC–MS: 399 (M^+ − CH_2OH, 3.59), 303 (M^+ − I, 5.27), 156 (35.87), 127 (38.57), 109 (14.13), 69 (16.93), 55 (23.65), 44 (100).

Preparation of Diethyl 1,1-Difluoro-3-iodo-8,9-dihydroxynonylphosphonate (16). A mixture of 2.1 g (14.6 mmol) of 7-octene-1,2-diol, 4.7 g (15 mmol) of **1**, and 0.35 g (0.3 mmol) of $Pd(PPh_3)_4$ was stirred at room temperature 2 h. The reaction mixture was passed through a short column with silica gel (CH_2Cl_2 to CH_3CO_2Et:MeOH = 95:5) to give 5.2 g (76%) of **16**. ^{19}F NMR ($CDCl_3$): −109.9 (ddm, $^2J_{F,F}$ = 298.9 Hz, $^2J_{F,P}$ = 106.5 Hz), −113.0 (ddm, $^2J_{F,F}$ = 298.9 Hz, $^2J_{F,P}$ = 106.5 Hz). ^{1}H NMR ($CDCl_3$): 4.41 (m, 1 H), 4.28 (m, 4 H), 4.12 (br, 1 H), 3.64 (br, 1 H), 3.56 (m, 1 H), 3.39 (m, 1 H), 2.97–2.72 (m, 2 H), 1.80 (m, 2 H), 1.60–1.23 (m, 13 H). ^{13}C NMR ($CDCl_3$): 119.54 (td, $^1J_{C,F}$ = 262.4 Hz, $^1J_{C,P}$ = 215.6 Hz), 71.46, 66.10 (d, $^2J_{C,P}$ = 5.0 Hz), 64.39 (d, $^2J_{C,P}$ = 6.9 Hz), 44.04 (m), 39.85, 32.32 (m), 29.18, 24.06, 22.56, 20.46, 15.88 (d, $^3J_{C,P}$ = 5.2 Hz), 13.67. FT-IR (CCl_4): 3472–3402 (br), 2985 (m), 2936 (s), 1271 (s), 1166 (s), 1044 (s), 1026 (s), 981 (m). GC–MS: 427 (M^+ − CH_2OH, 9.2), 331 (5.0), 157 (77.0), 128 (90.5), 127 (78.6), 109 (58.0), 83 (51.6), 67 (52.4), 55 (88.1), 45 (54.0), 41 (100).

Preparation of Diethyl 1,1-Difluoro-1-(2-iodocyclohexyl)methylphosphonate (17). A mixture of 4.7 g (15 mmol) of **1**, 2.4 g (30 mmol) of cyclohexene, and 0.19 g (3 mmol) of Cu was stirred at 70 °C for 24 h. The reaction mixture was diluted with 40 mL of ether, and solids were removed by filtration. After evaporation of the ether, the residue was evacuated at 70 °C under reduced pressure (0.1 mmHg) for 4 h to give 4.1 g (69%) of **17**, which was a mixture of *cis*- and *trans*-**17** in a 2:1 ratio. ^{19}F NMR ($CDCl_3$): (a) −106.9 (ddd, $^2J_{F,F}$ = 302.2 Hz, $^2J_{F,P}$ = 110.7 Hz, $^3J_{F,H}$

= 26.4 Hz), -109.6 (ddd, $^2J_{F,F}$ = 302.0 Hz, $^2J_{F,P}$ = 110.7 Hz, $^3J_{F,H}$ = 21.6 Hz); (b) -116.0 (ddd, $^2J_{F,F}$ = 300.0 Hz, $^2J_{F,P}$ = 110.0 Hz, $^3J_{F,H}$ = 19.8 Hz), -118.8 (ddd, $^2J_{F,F}$ = 304.1 Hz, $^2J_{F,P}$ = 110.1 Hz, $^3J_{F,H}$ = 21.6 Hz). ^{1}H NMR ($CDCl_3$): 5.03 (m, 0.5 H), 4.82 (m, 0.5 H), 4.26 (m, 4 H), 2.57 (m, 1 H), 2.17 (m, 8 H), 1.39 (m, 6 H). FT-IR (CCl_4): 2984 (m), 2941 (s), 1271 (s), 1171 (s), 1099 (s), 1043 (s), 1027 (s). GC-MS: (a) 269 (M^+ - I, 2.3), 161 (34.1), 138 (47.6), 132 (80.7), 130 (84.2), 111 (83.1), 109 (58.8), 81 (100.0), 77 (40.5), 65 (41.6); (b) 269 (M^+ - I, 3.4), 268 (35.8), 192 (18.3), 138 (42.9), 131 (60.4), 130 (100.0), 111 (99.2), 109 (99.6), 91 (54.6), 81 (64.2), 79 (63.3), 65 (52.9).

Preparation of Tetraethyl 1,1,8,8-Tetrafluoro-3,6-diiodo-1,8-octanediylbis(phosphonate) (18). A tube, charged with 1.85 g (15 mmol) of 1,5-hexadiene, 9.7 g (31 mmol) of 1, and 0.3 g (4.7 mmol) of copper, was cooled with liquid N_2, degassed, and sealed. The reaction mixture was stirred at 75-80 °C for 48 h, and then 30 mL of ether was added and the solids were removed by filtration. After evaporation of the ether, the residue was purified by chromatography on silica gel (hexane:CH_2Cl_2 = 1:1 to ethyl acetate:CH_2Cl_2 = 5:1) to give 9.7 g (92%) of 18. ^{19}F NMR ($CDCl_3$): -110.2 (dm, $^2J_{F,F}$ = 297.8 Hz, 1 F), -113.5 (ddm, $^2J_{F,F}$ = 298.0 Hz, $^2J_{F,P}$ = 105.5 Hz, 1 F). ^{1}H NMR ($CDCl_3$): 4.43 (m, 2 H), 4.29 (m, 8 H), 3.04-2.71 (m, 4 H), 2.18-1.88 (m, 4 H), 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 12 H). ^{13}C NMR ($CDCl_3$): 120.04 (td, $^1J_{C,F}$ = 262.6 Hz, $^1J_{C,P}$ = 215.2 Hz), 64.80 (d, $^2J_{C,P}$ = 6.5 Hz), 44.76 (td, $^2J_{C,F}$ = 19.2 Hz, $^2J_{C,P}$ = 15.3 Hz), 40.40, 20.50 (t, $^3J_{C,F}$ = 14.0 Hz), 16.40 (d, $^3J_{C,P}$ = 3.8 Hz. ^{31}P NMR ($CDCl_3$): 5.8 (t, $^2J_{P,F}$ = 105.5 Hz). FT-IR (CCl_4): 2985 (m), 1394 (m), 1275 (s), 1165 (s), 1097 (s), 1026 (s), 980 (s). GC-MS: 583 (M^+ - I, 31.9), 223 (21.1), 156 (32.4), 141 (39.2), 128 (100.0), 127 (80.4), 109 (82.4), 81 (65.7), 77 (50.3), 65 (54.9).

Preparation of Tetraethyl 1,1,10,10-Tetrafluoro-3,8-diiodo-1,10-decanediylbis(phosphonate) (19). Similarly, 19 was prepared from 0.55 g (5 mmol) of 1,7-octadiene, 3.2 g (10 mmol) of 1, and 0.4 g (0.35 mmol) of $Pd(PPh_3)_4$ in 5 mL of hexane at 40 °C overnight. Usual workup gave a residue, which was purified by flash chromatography on silica gel (hexane:CH_2Cl_2 = 1:1 and ethyl acetate:CH_2Cl_2 = 10:2) to give 2.7 g (73%) of 19. ^{19}F NMR ($CDCl_3$): -110.0 (ddm, $^2J_{F,F}$ = 297.6 Hz, $^2J_{F,P}$ = 105.0 Hz, 1 F), -113.3 (dddd, $^2J_{F,F}$ = 297.6 Hz, $^2J_{F,P}$ = 105.0 Hz, $^3J_{H,H}$ = 26.6 Hz, $^3J_{H,H}$ = 11.4 Hz, 1 F), 4.42 (m, 2 H), 4.26 (m, 8 H), 3.02-2.67 (m, 4 H), 1.82 (m, 4 H), 1.61-1.48 (m, 4 H), 1.40 (t, $^3J_{H,H}$ = 7.1 Hz, 10 H). ^{13}C NMR ($CDCl_3$): 120.09 (td, $^1J_{C,F}$ = 262.5 Hz, $^1J_{C,P}$ = 214.8 Hz), 64.70 (d, $^2J_{C,P}$ = 6.7 Hz), 44.78 (m), 40.09 (d, $^3J_{C,P}$ = 5.0 Hz), 28.65, 22.94 (t, $^3J_{C,F}$ = 3.2 Hz), 16.41 (d, $^3J_{C,P}$ = 5.5 Hz). FT-IR (CCl_4): 2986 (s), 2934 (s), 1281 (s), 1273 (s), 1167 (s), 1062 (s), 1029 (s), 980 (s). GC-MS: (M^+ - I, 56.6), 583 (11.1), 379 (9.2), 229 (17.7), 186 (27.9), 169 (28.3), 127 (63.6), 117 (53.3), 103 (88.3), 91 (57.4), 81 (100), 77 (71.3), 65 (73.2).

Reaction of 1 with Diallyl Ether. A mixture of 1.5 g (15 mmol) of diallyl ether, 3.2 g (10 mmol) of 1, and 0.1 g (1.6 mmol) of Cu was stirred at 80 °C for 26 h. The reaction mixture was poured into water and extracted with ether (2 × 30 mL), and the combined organic layers were dried over $MgSO_4$. After evaporation of the ether, the residue was purified by chromatography on silica gel (hexane:ethyl acetate = 1:1) to give 3.1 g (73%) of 20 as a mixture of cis and trans isomers. ^{19}F NMR ($CDCl_3$): (a) -110.7 (dddd, $^2J_{F,F}$ = 296.4 Hz, $^2J_{F,P}$ = 106.0 Hz, $^3J_{F,H}$ = 30.1 Hz, $^3J_{F,H}$ = 10.6 Hz, 0.7 F), -113.4 (dddd, $^2J_{F,F}$ = 296.4 Hz, $^2J_{F,P}$ = 106.0 Hz, $^3J_{F,H}$ = 28.4 Hz, $^3J_{F,H}$ = 12.4 Hz, 0.7 F); (b) -110.6 (dddd, $^2J_{F,F}$ = 296.4 Hz, $^2J_{F,P}$ = 106.0 Hz, $^3J_{F,H}$ = 30.0 Hz, $^3J_{F,H}$ = 10.6 Hz, 0.3 F), -112.8 (dddd, $^2J_{F,F}$ = 296.4 Hz, $^2J_{F,P}$ = 106.0 Hz, $^3J_{F,H}$ = 28.4 Hz, $^3J_{F,H}$ = 13.3 Hz, 0.3 F). ^{1}H NMR ($CDCl_3$): 4.24 (m, 4 H), 3.99-3.90 (m, 2 H), 3.72-3.50 (m, 2 H), 3.33-2.99 (m, 2 H), 2.75-2.67 (m, 2 H), 2.34-1.98 (m, 2 H), 1.35 (t, $^3J_{H,H}$ = 7.2 Hz, 6 H). ^{31}P NMR ($CDCl_3$): 6.6 (t, $^2J_{P,F}$ = 106.0 Hz). FT-IR (CCl_4): 2984 (m), 2866 (m), 1273 (s), 1269 (s), 1177 (s), 1164 (s), 1097 (s), 1086 (s). GC-MS: (a) 383 (M^+ - Et, 0.2), 285 (M^+ - I, 56.0), 229 (24.8), 138 (97.3), 129 (43.3), 117 (100), 109 (50), 77 (46.7), 65 (46); (b) 339 (4.7), 285 (M^+ - I, 100), 257 (14.5), 138 (31.8), 117 (27.7), 97 (13.6), 77 (10.2), 55 (10.3).

Reduction of Adducts with Zinc in the Presence of Nickel Dichloride Hexahydrate: Diethyl 1,1-Difluorononylphosphonate (5a). A mixture of 0.65 g (10 mmol) of Zn, 0.1 g (0.4 mmol) of $NiCl_2$·$6H_2O$, a drop of water, and 10 mL of THF was stirred for 15 min; 2.1 g (5 mmol) of 5 was added, and the resultant mixture was stirred overnight and then poured into a beaker with NH_4Cl solution and ether. Solids were removed by filtration, and the organic layer was separated. The aqueous layer was extracted with ether (2 × 40 mL), and the combined extracts were combined with the organic layer, subsequently washed with water, and dried over $MgSO_4$. After evaporation of the ether, the residue was distilled to give 1.2 g (80%) of **5a**, bp 95-96 °C (0.05 mmHg). ^{19}F NMR ($CDCl_3$): -112.2 (dt, $^2J_{F,P}$ = 110.0 Hz, $^3J_{F,H}$ = 19.5 Hz). ^{1}H NMR: 4.27 (m, 4 H), 2.17-1.94 (m, 2 H), 1.63-1.53 (m, 2 H), 1.38 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 1.36-1.28 (m, 10 H), 0.88 (t, $^3J_{H,H}$ = 6.5 Hz, 3 H). ^{31}P NMR ($CDCl_3$): 7.51 (t, $^2J_{F,P}$ = 110 Hz). ^{13}C NMR ($CDCl_3$): 121.06 (td, $^1J_{F,C}$ = 259 Hz, $^1J_{P,C}$ = 215.0 Hz), 64.30 (d, $^2J_{C,P}$ = 7.2 Hz), 34.10 (td, $^2J_{F,C}$ = 20.7 Hz, $^2J_{P,C}$ = 14.5 Hz), 31.58, 29.41, 29.33, 29.17, 22.69, 20.67 (dt, $^3J_{P,C}$ = 4.7 Hz, $^3J_{F,C}$ = 4.8 Hz), 16.47, 16.40, 14.08. IR (CCl_4): 2960 (s), 1271 (s), 1165 (s), 1027 (s), 977 (s), 955 (m). GC-MS: 257 (1.9), 243 (2.6), 215 (9.3), 160 (13.9), 138 (100), 129 (17.0), 111 (17.0), 109 (35.0), 81 (18.5), 65 (13.1), 41 (18.0).

Preparation of Diethyl 1,1-Difluoro-3-(trimethylsilyl)-propylphosphonate (6a). Similarly, **6a** was prepared from 2.1 g (5 mmol) of 6, 0.65 g (10 mmol) of Zn, and 0.1 g (0.4 mmol) of $NiCl_2$·$6H_2O$ in 10 mL of THF at room temperature. Usual workup gave a residue, which was distilled to give 1.2 g (84%) of **6a**, bp 76-78 °C (0.1 mmHg). ^{19}F NMR ($CDCl_3$): -113.9 (dt, $^2J_{F,P}$ = 109.2 Hz, $^3J_{F,H}$ = 19.0 Hz). ^{1}H NMR ($CDCl_3$): 4.27 (m, 4 H), 2.11-1.89 (m, 2 H), 1.38 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 0.74 (m, 2 H), 0.03 (s, 9 H). ^{31}P NMR ($CDCl_3$): 7.80 (t, $^2J_{F,P}$ = 109.2 Hz). ^{13}C NMR ($CDCl_3$): 123.07 (td, $^1J_{F,C}$ = 259.7 Hz, $^1J_{P,C}$ = 213.6 Hz), 66.24 (d, $^2J_{C,P}$ = 7.2 Hz), 30.85 (td, $^2J_{F,C}$ = 22.0 Hz, $^2J_{P,C}$ = 15.0 Hz), 18.45, 18.37, 8.49, 2.00. IR (CCl_4): 2984 (m), 1270 (s), 1178 (s), 1093 (s), 976 (s). GC-MS: 287 (M^+ - 1, 0.1), 210 (40.0), 165 (55.0), 141 (57.1), 81 (39.6), 77 (61.8), 73 (100), 65 (22.7), 54 (26.1).

Preparation of Diethyl 1,1-Difluoro-8,9-dihydroxynonylphosphonate (16a). A mixture of 0.09 g (0.33 mmol) of $NiCl_2$·$6H_2O$, 0.85 g (13 mmol) of Zn, and 10 mL of THF was stirred for 15 min, 3.0 g (6.55 mmol) of **16** in 5 mL of THF was added, and the resultant mixture was stirred for 2 h. THF was removed under reduced pressure, and 50 mL of CH_3CO_2Et was added. The solids were removed by filtration and washed with CH_3CO_2Et. After evaporation of the CH_3CO_2Et, the residue was purified by chromatography on silica gel (CH_2Cl_2:CH_3CO_2Et = 50:50 to CH_3CO_2Et:MeOH = 95:5) to give 1.5 g (71%) of **16a**. ^{19}F NMR ($CDCl_3$): -112.1 (dt, $^2J_{F,P}$ = 112.3 Hz, $^3J_{F,H}$ = 19.5 Hz). ^{1}H NMR ($CDCl_3$): 4.27 (m, 4 H), 3.67 (m, 2 H), 3.43 (m, 1 H), 2.44 (br, 2 H), 2.14-1.94 (m, 2 H), 1.57 (m, 2 H), 1.38 (m, 14 H). ^{31}P NMR ($CDCl_3$): 7.4 (t, $^2J_{F,P}$ = 112.0 Hz). ^{13}C NMR ($CDCl_3$): 120.94 (td, $^1J_{F,C}$ = 259.1 Hz, $^1J_{C,P}$ = 215.9 Hz), 72.21, 66.68, 64.65 (d, $^2J_{C,P}$ = 6.9 Hz), 33.97 (td, $^2J_{C,F}$ = 20.8 Hz, $^3J_{C,P}$ = 14.5 Hz), 33.12, 29.41, 29.25, 25.48, 16.41 (d, $^3J_{C,P}$ = 5.2 Hz). GC-MS: 301 (M^+ - OMe, 2.5), 215 (2.1), 149 (18.3), 138 (17.6), 109 (21.8), 81 (12.7), 69 (22.2), 43 (100).

Preparation of 1,1-Difluoro-11-hydroxyundecylphosphonate (9a). A mixture of 0.9 g (13.8 mmol) of Zn, 0.12 g (0.5 mmol) of $NiCl_2$·$6H_2O$, and a drop of water in 20 mL of THF was stirred at room temperature for 20 min; 3.3 g (7 mmol) of 9 was added, and the resultant mixture was stirred overnight. The ^{19}F NMR spectrum of the reaction mixture exhibited two sets of doublets of triplets in a 1:5 ratio at -111.7 (dt, $^2J_{F,P}$ = 110.0 Hz, $^3J_{F,H}$ = 19.5 Hz) and -112.3 (dt, $^2J_{F,P}$ = 110.0 Hz, $^3J_{F,H}$ = 19.5 Hz), respectively. The mixture was poured into a beaker with NH_4Cl solution and ether, and solids were removed by filtration. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were washed with water and dried over $MgSO_4$. After evaporation of the ether, the residue was added to a flask with 0.18 g of 5% Pd/C in 30 mL of methanol, and then H_2 was bubbled into the solution for 5 days. The Pd/C was removed by filtration, and methanol was evaporated. The residue was diluted with 50 mL of ether and dried over $MgSO_4$. After evaporation of the ether, 1.8 g (75%) of **9a** was obtained. ^{19}F NMR ($CDCl_3$): -112.26 (dt, $^2J_{F,P}$ = 110.4 Hz, $^3J_{F,H}$ = 20.1 Hz). ^{1}H NMR ($CDCl_3$): 4.26 (m, 4 H), 3.57 (m, 3 H), 2.11-1.95 (m, 2 H), 1.54 (m, 4 H), 1.40-1.30 (m, 18 H). ^{13}C NMR ($CDCl_3$): 120.98 (td, $^1J_{F,C}$ = 258.9 Hz, $^1J_{C,P}$ = 215.1 Hz), 64.47 (d, $^2J_{C,P}$ = 7.1 Hz), 62.45, 34.05 (td, $^2J_{C,F}$ = 20.7 Hz, $^2J_{C,P}$ = 14.5 Hz), 32.86, 29.65, 29.57, 29.47, 29.37, 25.96, 20.75, 20.67 (d, $^3J_{C,P}$ = 4.5 Hz), 16.43 (d, $^3J_{C,P}$ = 5.9 Hz). ^{31}P NMR ($CDCl_3$):

7.60 (t, $^2J_{P,F}$ = 110.4 Hz). GC–MS: 344 (M^+, 1.3), 215 (8.7), 138 (100.0), 111 (19.3), 109 (22.9), 91 (10.1), 81 (19.6), 69 (13.7), 55 (27.5).

General Procedure for the Preparation of α,α-Difluoro Phosphonates without Purification of Adducts: Preparation of Diethyl 1,1-Difluorooctylphosphonate (4a). To a stirred mixture of 0.22 g (0.2 mmol) of $Pd(PPh_3)_4$ and 2.0 g (20 mmol) of 1-heptene was added 3.1 g (10 mmol) of 1, and the reaction mixture was stirred at room temperature for 20 min. Then, a mixture of 10 mL of hexane and 10 mL of ether was added to the flask, which resulted in the precipitation of solids. The solids were removed by filtration and washed with hexane. The combined filtrates were evaporated to give a residue, which was added to a flask charged with 0.1 g (0.37 mmol) of nickel chloride hexahydrate and 1.3 g (20 mmol) of zinc in 10 mL of moist THF. The resulting mixture was stirred at room temperature for 2 h and then poured into a beaker with 50 mL of NH_4Cl solution and 40 mL of ether. The solids were removed by filtration and washed with ether. The combined organic layers were washed with water and dried over $MgSO_4$. After evaporation of the ether, the residue was distilled at reduced pressure to give 1.5 g (52%) of **4a**, bp 95–98 °C (0.05 mmHg). ^{19}F NMR ($CDCl_3$): −111.8 (dt, $^2J_{P,F}$ = 110.0 Hz, $^1J_{H,F}$ = 19.5 Hz). ^{31}P NMR ($CDCl_3$): 7.72 (t, $^2J_{P,F}$ = 110.0 Hz). ^1H NMR ($CDCl_3$): 4.27 (m, 4 H), 2.15–1.93 (m, 2 H), 1.58 (m, 2 H), 1.38 (t, $^3J_{H,H}$ = 7.2 Hz, 6 H), 1.41–1.29 (m, 8 H), 0.89 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H). ^{13}C NMR ($CDCl_3$): 121.11 (td, $^1J_{F,C}$ = 259.5 Hz, $^1J_{P,C}$ = 215.0 Hz), 64.33 (d, Hz), = 6.7 Hz), 34.17 (td, $^2J_{C,F}$ = 20.8 Hz, $^2J_{C,P}$ = 14.3 Hz), 31.78, 29.42, 29.08, 22.69, 20.75 (dt, $^2J_{C,P}$ = 4.7 Hz, $^2J_{C,F}$ = 4.5 Hz), 16.46 (d, J = 5.6 Hz), 14.07. IR (CCl_4): 2960 (s), 2931 (s), 1394 (m), 1272 (vs), 1165 (m), 1098 (m), 979 (s), 952 (m). GC–MS: 286 (M^+, 0.06) 229 (11.2), 138 (100), 129 (24.4), 111 (21.3), 109 (48.6), 65 (14.5), 43 (16.9). HRMS calcd for $C_{12}H_{25}O_3PF_2$ 286.1497, found 286.1524.

Preparation of Diethyl 1,1-Difluorohexylphosphonate (2a). Similarly, a mixture of 0.7 g (10 mmol) of 1-pentene, 1.6 g (5 mmol) of 1, and 0.1 g (0.08 mmol) of $Pd(PPh_3)_4$ was stirred for 10 min, followed by treatment with 0.65 g (10 mmol) of Zn and $NiCl_2{\cdot}6H_2O$ in 8 mL of moist THF. Usual workup gave a residue, which was distilled to give 0.82 g (64%) of **2a**, bp 64–65 °C (0.1 mmHg). ^{19}F NMR ($CDCl_3$): −112.3 (dt, $^2J_{F,P}$ = 110.0 Hz, $^3J_{F,H}$ = 19.8 Hz). ^1H NMR ($CDCl_3$): 4.25 (m, 4 H), 2.12–1.94 (m, 2 H), 1.58 (m, 2 H), 1.24 (m, 10 H), 0.90 (t, $^3J_{H,H}$ = 6.8 Hz, 3 H). ^{31}P NMR ($CDCl_3$): 7.59 (t, $^2J_{F,P}$ = 110.0 Hz). FT-IR (CCl_4): 2962 (s), 1271 (s), 1165 (s), 1036 (s), 978 (s). GC–MS: 258 (M^+, 1.1), 229 (34.2), 138 (64.0), 109 (100), 101 (55.4), 81 (50.4), 65 (35.8), 65 (35.82), 41 (27.0).

Preparation of Diethyl 1,1-Difluoro-6-acetoxyhexylphosphonate (10a). Similarly, a mixture of 1.4 g (11 mmol) of 4-penten-1-yl acetate, 3.1 g (10 mmol) of 1, and 0.3 g (0.26 mmol) of $Pd(PPh_3)_4$ was stirred at room temperature for 10 min, with subsequent treatment with 1.3 g (20 mmol) of Zn and 0.2 g (0.84 mmol) of $NiCl_2{\cdot}6H_2O$ in 10 mL of moist THF. Usual workup gave a residue, which was distilled to give 1.9 g (62%) of **10a**, bp 109–112 °C (0.05 mmHg). ^{19}F NMR ($CDCl_3$): −112.5 (dt, $^2J_{F,P}$ = 109.6 Hz, $^3J_{F,H}$ = 20.2 Hz). ^1H NMR ($CDCl_3$): 4.27 (m, 4 H), 4.07 (t, $^3J_{H,H}$ = 7.1 Hz, 2 H), 2.10–1.96 (m, 5 H), 1.71–1.57 (m, 4 H), 1.48–1.39 (m, 2 H), 1.39 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H). IR (CCl_4): 2983 (s), 1742 (s), 1272 (s), 1165 (s), 1028 (s), 977 (s). GC–MS: 273 (M^+ − OEt, 4.1), 229 (30.8), 155 (55.8), 138 (100), 111 (28.0), 109 (50.8), 81 (29.5), 65 (19.5), 43 (77.0).

Preparation of Diethyl 1,1-Difluoro-5-carbethoxyhexylphosphonate (13a). Similarly, a mixture of 0.85 g (6 mmol) of ethyl 2-methyl-4-pentenoate, 1.6 g (5 mmol) of 1, and 0.2 g (0.17 mmol) of $Pd(PPh_3)_4$ was stirred for 20 min, with subsequent treatment with 0.65 g (10 mmol) of Zn and 0.1 g (0.42 mmol) of $NiCl_2{\cdot}6H_2O$ in 10 mL of moist THF. Usual workup gave a residue, which was distilled to give 1.0 g (61%) of **13a**, bp 108–110 °C (0.1 mmHg). ^{19}F NMR ($CDCl_3$): −112.5 (dt, $^2J_{F,P}$ = 110 Hz, $^3J_{F,H}$ = 19.8 Hz). ^1H NMR ($CDCl_3$): 4.26 (m, 4 H), 2.14–1.97 (m, 2 H), 1.77–1.41 (m, 4 H), 1.38 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H), 1.26 (t, $^3J_{H,H}$ = 7.1 Hz, 3 H), 1.16 (d, $^3J_{H,H}$ = 7.0 Hz, 3 H). ^{31}P NMR ($CDCl_3$): 7.4 (t, $^2J_{F,P}$ = 110.0 Hz). ^{13}C NMR ($CDCl_3$): 176.22, 120.70 (td, $^1J_{F,C}$ = 259.0 Hz, $^1J_{P,F}$ = 215.2 Hz), 64.36 (d, $^2J_{P,C}$ = 7.1 Hz), 60.26, 39.32, 33.88 (td, $^2J_{F,C}$ = 20.6 Hz, $^2J_{P,C}$ = 14.6 Hz), 17.07, 16.45, 16.40, 14.26. IR (CCl_4): 2983 (s), 1735 (s), 1271 (s), 1179 (s), 1034 (s), 987 (s). GC–MS: 285 (M^+ − OEt, 8.7), 229 (100), 173 (54.7), 109 (59.8), 69 (47.9), 55 (45.2).

Preparation of Diethyl 1,1-Difluoro-6-oxo-heptylphosphonate (12a). Similarly, a mixture of 1.1 g (11 mmol) of 5-hexen-2-one, 3.2 g (10 mmol) of 1, and 0.3 g (0.26 mmol) of $Pd(PPh_3)_4$ was stirred for 20 min, with subsequent treatment with 1.3 g (20 mmol) of Zn and 0.1 g (0.42 mmol) of $NiCl_2{\cdot}6H_2O$ in 10 mL of moist THF. Usual workup gave a residue, which was distilled to give 1.6 g (55%) of **12a**, bp 114–116 °C (0.1 mmHg). ^{19}F NMR ($CDCl_3$): −112.2 (dt, $^2J_{F,P}$ = 107.4 Hz, $^3J_{F,H}$ = 19.5 Hz). ^1H NMR ($CDCl_3$): 4.28 (m, 4 H), 2.48 (t, $^3J_{H,H}$ = 6.7 Hz, 2 H), 2.14 (s, 3 H), 2.15–1.96 (m, 2 H), 1.67–1.55 (m, 4 H), 1.38 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H). IR (CCl_4): 2985 (s), 1722 (s), 1275 (s), 1165 (s), 1040 (s), 980 (s). GC–MS: 286 (M^+, 3.11), 229 (61.7), 173 (40.0), 138 (92.1), 81 (39.0), 43 (100).

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Supplementary Material Available: ^1H or ^{13}C NMR spectra of all compounds found in Experimental Section (27 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.