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An efficient synthesis of (*Z*)-γ-fluoroallylphosphonates using a base-promoted deconjugation of (*E*)-γ-fluorovinylphosphonates, and its utility as fluoroolefin-containing building block

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Dedicated to Professor Paul Tarrant on the occasion of his 85th birthday

Abstract

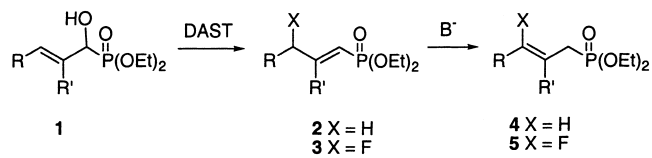
A three-step synthesis of γ-fluoroallylphosphonates starting with α,β-unsaturated aldehydes is described. Treatment with diethyl phosphite in the presence of KF gives α-hydroxyallyl phosphonate in excellent yield; DAST deoxofluorination produces the corresponding γ-fluorovinylphosphonate through a S_N2' mechanism, and finally, a base-promoted double bond migration leads to the desired γ-fluoroallylphosphonate. γ-Fluoroallylphosphonate is a useful building block in the synthesis of fluoroolefins. An exploratory study yielded excellent yields of (*Z*)-diethyl 1-benzyl-3-fluoro-2-butenylphosphonate and (*Z*)-diethyl 1,3-difluoro-2-hexenylphosphonate. Treatment of (*E*)-diethyl 3-fluoro-2-hexenylphosphonate with $LiN(TMS)_2$ and benzaldehyde in THF led to the preferential formation of *syn*-(*Z*)-diethyl 3-fluoro-1-(hydroxybenzyl)-2-butenylphosphonate.

Keywords: Fluoroallylphosphonate; Fluorovinylphosphonate; Hydroxyallylphosphonate; HWE olefination

1. Introduction

The selective replacement of a vinyl hydrogen by fluorine enhances the biological activity of olefin-containing molecules such as pheromones [1–4], and retinoids [5–8]. Of paramount importance in the synthesis of the latter is the regio- and stereocontrol of the olefinic bond. In this context, allylic phosphonate (**4**) provides a powerful building block for the formation of conjugated dienes — via a modified Wadsworth–Horner olefination of the phosphoryl-stabilized α-carbanion [9–11]; and olefins — after alkylation with alkyl halides followed by $LiAlH_4$ reduction and simultaneous elimination of the phosphonate group [12–14]. Literature preparations of **4** are numerous and include the rearrangement of the corresponding phosphites [15–17], metal-coordinated allyl addition to $P(OEt)_3$ [18], phosphonium salts [19], and base-catalyzed isomerization of vinylphosphonates [20] (**2** → **4**, Eq. (1)).

During our studies on fluorinated phosphonate synthons [21–23], it occurred to us that γ-fluoroallylphosphonate (**5**) might be capable of playing a similar role to that of its nonfluorinated counterpart (**4**). Despite its importance as a synthetic intermediate, **5** has received scarce attention in the literature [5–7]. For the synthesis of **5** we adapted Kiddle and Babbler's methodology [20] because the required γ-fluorovinylphosphonate (**3**) can be easily prepared by a two-step sequence involving Pudovik reaction [24] of α,β-unsaturated aldehydes with diethyl phosphite [$HP(O)(OEt)_2$] followed by DAST deoxofluorination of allylic α-hydroxyphosphonate (**1**) (Eq. (1)).



1 **2** X = H, **3** X = F; **4** X = H, **5** X = F (1)

2. Results and discussion

In our laboratory, α-hydroxyallylphosphonate (**1**) was obtained in higher yields than previously reported [25] (Table 1) when the reaction was carried out neat in the presence of $KF{\cdot}2H_2O$ and a slight excess of $HP(O)(OEt)_2$ [26]. α-Hydroxyallyl phosphonates were very stable except

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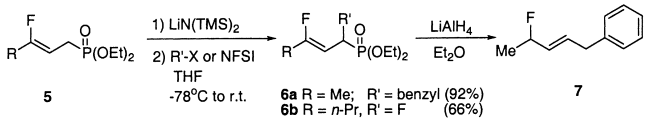
for **1f** (entry 6) who underwent gradual decomposition at room temperature. The deoxofluorination of α-hydroxyallylphosphonate (**1**) with DAST was first studied by Blackburn using only acyclic substrates [25]. We extended this fluorination method to substituted, conjugated and cyclic α-hydroxyallyl phosphonates, and in all cases but one (entry 6)[1], good to excellent yields of (*E*)-γ-fluorovinylphosphonates **3** were obtained (Table 1). The stereochemical assignment was based on vicinal ^{13}C–^{31}P coupling constants [28] and Blackburn's NMR data [25]. DAST fluorination of 2,4-hexadienyl hydroxyphosphonate (**1d**) occurred exclusively on the ϵ-carbon, ruling out a S_Ni' mechanism in this conjugated system (entry 4). The stereochemistry of the vinylphosphonate moiety in the five- and six-membered rings exocyclic olefins (**3g,h**) showed a remarkable preference for the *E*-isomer, as determined by NOE studies (entries 7 and 8). A competing dehydrofluorination produced five- and six-membered ring conjugated dienylphosphonate byproducts (5% and 24%).

With an effective synthesis of **3** in hand we proceeded to investigate the base-catalyzed double bond migration (i.e., **3** → **5**). Presumably, the first step in this process is the deprotonation of the γ-carbon, leading to a resonance stabilized system in which the α-anion of **5** should be the major contributor and therefore the predominant isomer after workup. Semiempirical calculations (AM1) predicted acyclic compounds **5a,b,c** to be more stable than **3a,c,e**. Similar calculations also predicted that the difference in stabilization energy between cyclic fluorophosphonates **3g** and **5d**, and between **3h** and **5e**, was negligible. Experimental evidence on the prototropic equilibria of diethyl alkenylphosphonates had shown that the PO_3Et_2 group provided only a very weak stabilizing effect of on the adjacent carbon–carbon double bond [29]. Preliminary trials to synthesize **5** from **3** using Kiddle and Babbler's conditions (KO*t*-Bu in DMSO at room temperature) [20], met with partial success, yields ranging between 30% and 50%. We speculated that the presence of DMSO in the workup might have contributed to the low yields because of the partial solubility of the phosphonate product in the DMSO-containing aqueous layer. We succeeded in promoting the double bond migration from **3** to (*Z*)**-5**, in excellent yield and with great stereospecificity, using strongly basic but experimentally more friendly conditions ($KNTMS_2$, 18-crown-6 and THF rather than DMSO) (entries 1, 3, and 5). Analysis of the vinylic $^3J_{FH}$ coupling constants permitted an unequivocal assignment of the sterochemistry of the double bond. In the case of five- and six-membered rings (entries 7 and 8), the regiochemical outcome of the migration protocol was less specific. Whereas **3h** produced predominantly the vinylfluoro isomer (**5e**) (vinyl:allyl 90:10), **3g** produced exclusively the allylfluoro isomer (**5d**) regardless of whether kinetic or thermodynamic conditions were applied.

Our efficient synthesis of acyclic γ-fluoroallyl phosphonate (**5**) unmasked a new active methylene site on the α-carbon capable of producing a phosphoryl-stabilized carbanion and the possibility of further functionalization at the α-position. With this purpose in mind, we explored the alkylation and electrophilic fluorination of **5**. It is well documented in the literature that lithio derivatives of γ-substituted allylphosphonate (**4**) undergo alkylation at the α-carbon when alkyl halides are utilized [12–14,30][2]. Thus, it came as no surprise that the alkylation of **5a** and **5b** ($LiNTMS_2$ in THF at −78°C) with benzyl bromide produced α-substituted-γ-fluoroallylphosphonate (**6a**) in excellent yield (Eq. (2)). Analogously, treatment of the α-carbanion of **5b** with N-fluorobenzenesulfonimide (NFSI), an electrophilic fluorinating agent, yielded 1,3-difluorobutenylphosphonate (**6b**) in 66% yield after chromatography. Kondo and coworkers [12–14] have used α-substituted allylphosphonates as a template for the synthesis of *trans*-olefins by means of a $LiAlH_4$-induced reductive cleavage of the phosphonate group. To probe whether our α-substituted-γ-fluoroallylphosphonate (**6**) would behave in a similar fashion, **6a** was treated with $LiAlH_4$ (THF, −78°C to room temperature) and the reaction was monitored using ^{31}P and ^{19}F NMR spectroscopy. After 2 h, disappearance of the phosphonate signal was accompanied by the appearance of two new allylic fluorine signals at δ 165 (85%) and δ 168 ppm (15%) corresponding to *Z*/*E* isomers of **7** generated by S_N2' hydride displacement of phosphorus and concomitant double bond transposition. Unfortunately, attempted purification of **7** by chromatography or vacuum distillation led to loss of HF.

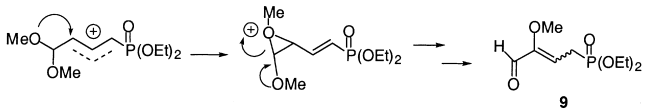


5 7

(2)

It can be argued that if the α-carbanion of **5** was trapped with an electrophilic reagent (e.g., benzaldehyde), and if the resulting pair of diastereomeric β-hydroxyphosphonates (e.g., **8c** and **8d**) could be separated and the phosphate group eliminated, then it would be possible to synthesize (*E*) and (*Z*)-fluoroalkenes almost at will (Scheme 1). Toward this goal, we turned our attention to Warren's pioneering

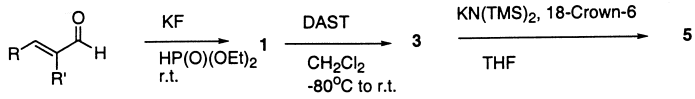
[1] Reaction mixture gave **3f** [^{31}P NMR: δ 17.8 (46%)] and a major byproduct tentatively identified as **9** [^{31}P NMR: δ 25.3 (54%)]. The structure of **9** was assigned based on ^1H NMR and decoupling experiments. Compound **9** could have been produced by migration of the methoxy group in **1f**, triggered by the γ-allylic cationic intermediate shown below:

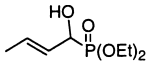
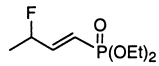
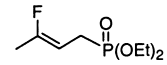
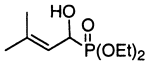
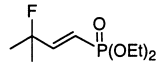
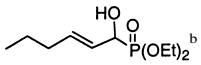
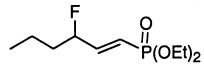
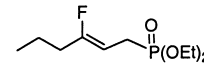
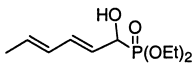
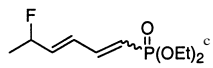
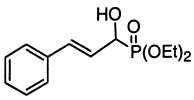
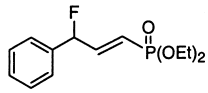
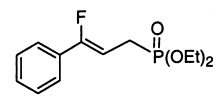
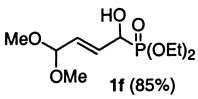
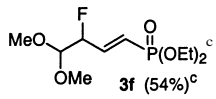
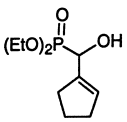
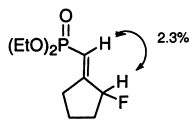
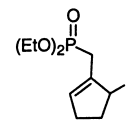
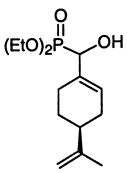
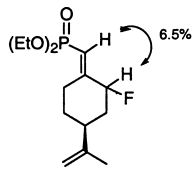
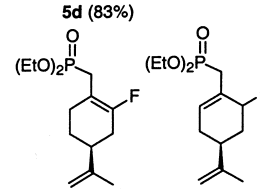


9

[2] Modro has reported that diethyl prop-2-enylphosphonate (allylic phosphonate), when treated with *n*-BuLi gives a lithiated derivative that adds to aromatic aldehydes via the α- or γ-carbon atom of the allylic system. See [30].

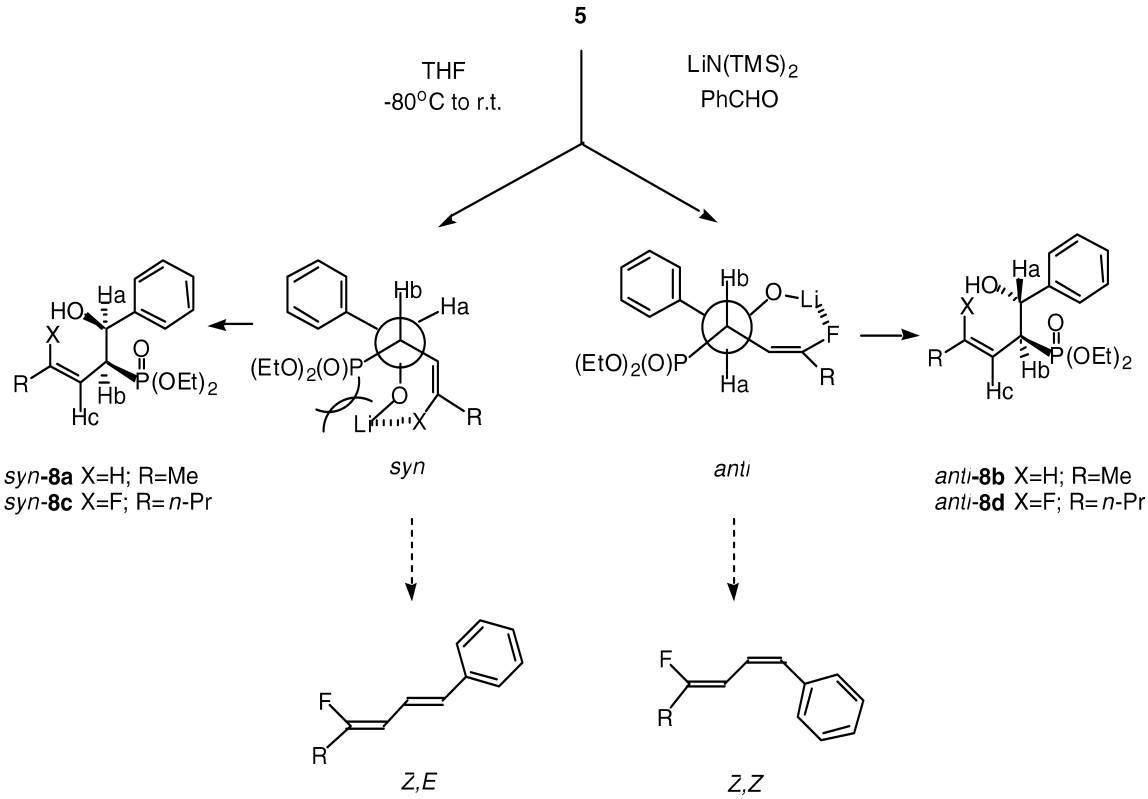
Table 1
Synthesis of γ-fluoroallylphosphonate **5**



Entry 1(%)[a]	3(%)[a]	5(%)[a]
 **1a** (95%)	 **3a** (76%)	 **5a** (67%)
 **1b**[b]	 **3b** (51%)	–[d]
 **1c** (76%)	 **3c** (78%)	 **5b** (78%)
 **1d** (92%)	 **3d** (92%)[c]	–[d]
 **1e** (75%)	 **3e** (73%)	 **5c** (83%)
 **1f** (85%)	 **3f** (54%)[c]	–[d]
 **1g** (70%)	 **3g** (60%) *E*:*Z* 94:6	 **5d** (83%)
 **1h** (77%)	 **3h** (59%) *E*:*Z* 78:22	 91 : 9 **5e** (77%)

[a] Isolated yields.
[b] See [35] for preparation.
[c] NMR yields.
[d] This reaction was not attempted.

work on olefin stereocontrol using the Horner–Wittig reaction [31]. By performing first the addition of a lithiated alkyldiphenylphosphine oxide to an aldehyde, separating the two diastereomeric β-hydroxyphosphine oxide intermediates and then proceeding with the extrusion of diphenylphosphinic acid, Warren was able to synthesize exclusively (*E*) or (*Z*)-alkenes [32]. Hitherto, this level of stereocontrol has rarely been achieved using dialkylphosphonates (i.e., HWE olefination) [27] mainly because the oxyanion intermediate decomposes via a transient oxaphosphetane to yield usually *E*-enriched olefins [33]. To our knowledge, the only literature isolation of β-hydroxyallylphosphonates was reported by Collignon and coworkers [9], who obtained a slight predominance of the *syn* adduct [e.g., *syn*-**8a** (58%), *anti*-**8b** (42%)] after acidic hydrolysis at −70°C. When we generated the carbanion of **5b** using $LiNTMS_2$ (two equivalents) in THF, added benzaldehyde (1.5 equivalents) at −80°C, and warmed up the mixture to room temperature, the reaction not only stopped short of oxaphosphetane elimination but, more importantly, it



Scheme 1. HWE addition of benzaldehyde to **5**.

favored the preferential formation of the *anti* adduct [*anti*-**8d** (62%), *syn*-**8c** (13%)]. The only major contaminant was unreacted starting material (25%). The high degree of selectivity observed in this reaction is comparable to Warren's Horner–Wittig reaction using the diphenylphosphoryl group [31]. Diastereomers *anti*-**8d** and *syn*-**8c** were identified according to $^{3}J_{HaHb}$, $^{2}J_{HbP}$, $^{3}J_{HaHb}$ and $^{3}J_{HbHc}$ coupling constant measurements in the ^{1}H NMR spectrum which were compared with existing data (Table 2) [9,34]. The diastereomeric ratios were determined by ^{31}P and/or ^{19}F NMR spectroscopy in the crude mixture (Table 3).

To account for the diastereoselective formation of **8d** we hypothesized that fluorine exerts an influence on the direction of approach of the carbonyl group through a C–F---Li–O–C coordination that favors the *anti* isomer on steric grounds (Scheme 1, X = F). The alternative pathway, leading to *syn* isomer (**8c**), would have entailed an unfavorable *gauche* interaction between the Li–O–C moiety and the phosphoryl group. To determine whether fluorine indeed plays a determining role in the stereoselective outcome of this reaction we conducted a similar reaction using a non-fluorinated substrate (e.g., **4** R^{1} = H, R = *n*-Pr) and found approximately equal amounts of *syn* and *anti* diastereomers in the crude mixture, very much in agreement with Collignon's results. An investigation of the chiral impact of using γ-fluoroallyl phosphonate (**5**) in asymmetric HWE reactions is in progress.

In summary, we have reported a new general synthesis of γ-fluoroallylic phosphonates (**5**) from commercially available aldehydes, using a base-promoted deconjugation of γ-fluorovinyl phosphonates. We have also demonstrated the preference of DAST for S_N2' deoxofluorination using cyclic

Table 2
^{1}H NMR data for *anti*-**8** ($CDCl_3$)[a]

	Ha (δ)	Hb (δ)	Hc (δ)	$^{3}J_{aP}$ (Hz)	$^{2}J_{bP}$ (Hz)	$^{3}J_{ab}$ (Hz)	$^{3}J_{bc}$ (Hz)	J_{cF} (Hz)
anti-**8b**	5.3, dd	3.0, ddd	5.4, m	–[b]	21.8[c]	3.1[d]	9.8	–
anti-**8d**	5.28, dd	3.31, ddd	4.76, ddd	8.9	22.0	2.2	10.8	35.9

[a] Values for **8a,b** were obtained from [9].
[b] Not reported.
[c] In the case of *syn*-**8a**, $^{2}J_{bP}$ = 17.5 Hz.
[d] For *syn*-8a, $^{3}J_{ab}$ 8.8 Hz.

Table 3
^{31}P and ^{19}F NMR data for **8** ($CDCl_3$)[a]

	^{31}P (δ)	^{19}F (δ)	$^{4}J_{PF}$ (Hz)
syn-**8a**	27.0	–	–
syn-**8c**	28.8	−103.9	8.5
anti **8b**	26.8	–	–
anti **8d**	28.5	−103.1	13.0

[a] Values for **8a,b** were obtained from [9].

and acyclic hydroxyphosphonates and have provided a glimpse of the building block potential of **5** in the regiospecific synthesis of acyclic α-substituted-γ-fluoroallylphosphonates.

3. Experimental

All moisture sensitive reactions were done using flame-dried glassware flushed with argon, magnetic stirring, and dry, freshly distilled solvents. THF was distilled from Na/benzophenone. Toluene and methylene chloride (CH_2Cl_2) were distilled from calcium hydride. Other solvents were HPLC grade and were used without purification. Diethyl phosphite [$HP(O)(OEt)_2$], benzyl bromide, benzaldehyde, and decyl iodide were distilled prior to use. All other reagents were used as received. All reactions were monitored using one of the following techniques: TLC, GC–MS, ^{31}P and/or ^{19}F NMR. Preparative TLC was performed using E.Merck Silica Gel 60 F_{254}. Analytical TLC was performed using Macherey–Nagel Polygram Sil G/UV_{254} precoated plates. Flash chromatography was performed using silica gel 230–400 mesh, 40–63 μ (Lagand). Dry-column chromatography was performed using Florisil®, 60–100 mesh. Solid phase extraction was performed using Extract–Clean™ columns (silica gel, 60 Å). Melting points are uncorrected. IR spectra were recorded on neat liquids. ^{1}H, ^{19}F and ^{31}P NMR spectra were recorded in $CDCl_3$ at 300, 282, and 121 MHz respectively. ^{19}F NMR spectra are referenced against external $CFCl_3$, ^{1}H NMR spectra against internal $(CH_3)_4Si$, and ^{31}P NMR spectra against 85% H_3PO_4. ^{31}P and ^{19}F NMR spectra were broadband decoupled from hydrogen nuclei. *J* values are given in Hertz (Hz). Low resolution EI mass spectra were recorded with an ionization voltage of 70 eV; peaks are reported as *m/e* (% intensity relative to base peak). Elemental analyses were performed by Atlantic Microlab, Norcross, GA. High resolution MS was performed at the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln.

3.1. Diethyl 1-hydroxy-2-butenylphosphonate (*1a*). General method

A mixture of $KF{\cdot}2H_2O$ (4.92 g, 52.26 mmol) and diethyl phosphite (3.32 g, 24.04 mmol) was magnetically stirred for 30 min at room temperature. To the slurry was added dropwise *trans*-crotonaldehyde (0.998 g, 10.4 mmol). The resulting mixture was allowed to stir overnight before adding ether (75 ml) and water (25 ml). The aqueous phase was extracted with ether (2 × 25 ml), dried ($MgSO_4$) and concentrated to provide **1a** as a viscous oil (1.74 g, 24.9 mmol) which was purified using column chromatography (silica, EtOAc:hexane 1:1) yielding **1a** (4.76 g, 95.3%). Although this compound has been reported previously [35], only physical constants were supplied. ^{1}H NMR: δ 5.96–5.82 (m, 1H), 5.68–5.57 (m, 1H), 4.40 (ddt, $^{2}J_{PH} = 10.6$ Hz, $^{3}J_{HH} = 6.9$ Hz, $^{4}J_{HH} = 1.2$ Hz, 1H), 4.17 (quintet, $J = 7.2$ Hz, 4H), 3.55 (br. s, 1H), 1.76 (dt, $^{3}J_{HH} = 5.1$ Hz, $^{4,5}J_{HH} = 1.3$ Hz, 3H), 1.32 (td, $^{3}J_{HH} = 7.1$ Hz, $^{4}J_{HP} = 1.2$ Hz, 6H); ^{31}P NMR: δ 23.2 (s); ^{13}C NMR: δ 129.9 (d, $^{2}J_{CP} = 14.0$ Hz), 125.5 (d, $^{3}J_{CP} = 3.47$ Hz), 69.25 (d, $^{1}J_{CP} = 161$ Hz), 62.9 (t, $^{2}J_{CP} = 7$ Hz), 17.9, 16.4 (d, $^{3}J_{CP} = 6$ Hz); *m/e* 179, 151, 138, 111, 99, 82, 53, 29.

3.2. Diethyl 1-hydroxy-2-hexenylphosphonate (*1c*)

trans-2-Hexenal (2.09 g, 21.3 mmol), diethyl phosphite (2.94 g, 21.3 mmol) and $KF{\cdot}2H_2O$ (5.08 g, 53 mmol) were stirred overnight to yield **1c** (3.8 g, 76%) after column chromatography (silica, hexane:EtOAc 1:1). ^{1}H NMR: δ 5.92–5.81 (m, 1H), 5.64–5.54 (m, 1H), 4.41 (m, 1H), 4.17 (quintet, $J = 7.2$ Hz, 4H), 3.84 (t, $J = 6.3$ Hz, 1H), 2.11–2.02 (m, 2H), 1.42 (sextet, $J = 7.4$ Hz, 2H), 1.33 (td, $^{3}J_{HH} = 7.0$ Hz, $^{4}J_{HP} = 1.1$ Hz, 6H), 0.91 (t, $^{3}J_{HH} = 7.4$, 3H); ^{31}P NMR: δ 23.1(s); ^{13}C NMR: δ 134.9 (d, $^{2}J_{CP} = 13.0$ Hz), 124.4 (d, $^{3}J_{CP} = 3.7$ Hz), 69.30 (d, $^{1}J_{CP} = 161$ Hz), 62.9 (t, $^{2}J_{CP} = 8$ Hz), 34.4, 22.05 (d, $^{4}J_{CP} = 3$ Hz), 3 Hz), 16.4 (d, $^{3}J_{CP} = 5$ Hz), 13.5; *m/e* 207 ($M^+ - 29$, 9), 151 (7), 138 (40), 111 (100), 83 (50), 82 (80). Anal.: Calcd. for $C_{10}H_{21}O_4P$: C, 50.84; H, 8.96. Found: C, 50.82; H, 9.08.

3.3. (E, E)-Diethyl 1-hydroxy-2,4-hexadienylphosphonate (*1d*)

A mixture of $KF{\cdot}2H_2O$ (3.29 g, 34.9 mmol) and diethyl phosphite (1.44 g, 10.4 mmol) was stirred for 30 min. To the slurry was added dropwise *trans,trans*-2,4-hexadienal (0.99 g, 10.4 mmol). The resulting mixture was allowed to stir overnight and worked up as above to yield **1d** (2.37 g, 97%) ^{31}P NMR: δ 22.7 (s); *m/e* 234 (M^+, 2), 205 (10), 177 (5), 138 (12), 111 (75), 82 (90), 41 (100); IR (film): 3280, 3000–2860, 1639 cm^{-1}.

3.4. Diethyl 1-hydroxy-3-phenyl-2-propenylphosphonate (*1e*)

trans-Cinnamaldehyde (3.96 g, 30.0 mmol), $KF{\cdot}2H_2O$ (14.14 g, 150.2 mmol) and diethyl phosphite (4.17 g, 30.2 mmol) were stirred overnight under standard reaction and workup conditions to produce a solid which was

recrystallized from cyclohexane to yield **1e** (6.09 g, 75%). Although this compound has been reported previously 25 no comprehensive NMR data was supplied. ^{1}H NMR:δ 7.41–7.25 (m, 5H), 6.78 (ddd, $^3J_{HH} = 16.0$ Hz, $^4J_{HP} = 4.80$ Hz, $^4J_{HH} = 1.48$ Hz, 1H, H–C–Ph), 6.32 (ddd, $^3J_{HH} = 16.0$ Hz, $^3J_{HH} = 6.1$ Hz, $^3J_{HP} = 0.6$ Hz, 1H, H–C = C), 4.67 (ddd, $^2J_{HP} = 12.9$ Hz, $^3J_{HH} = 6.1$ Hz, $^4J_{HH} = 1.6$ Hz, 1H), 4.19 (quintet, $J = 7.2$ Hz, 4H), 1.33 (td, $^3J_{HH} = 7.1$ Hz, $^4J_{HP} = 2.0$ Hz, 6H); ^{31}P NMR: δ 22.2 (s); ^{13}C NMR: δ 136.4 (d, $^4J_{CP} = 4$ Hz), 132.2 (d, $^2J_{CP} = 14$ Hz), 128.5, 127.8, 126.6 (d, $^5J_{CP} = 2$ Hz), 123.9 (d, $^3J_{CP} = 5$ Hz), 69.40 (d, $^1J_{CP} = 162$ Hz), 63.2 (d, $^2J_{CP} = 7$ Hz), 63.1 (d, $^2J_{CP} = 7$ Hz), 16.4 (d, $^3J_{CP} = 5$ Hz), 13.5.

3.5. Diethyl 1-hydroxy-4,4-dimethoxy-2-butenylphosphonate (*1f*)

Under standard reaction and workup conditions, fumaraldehyde monodimethylacetal [36] (0.501 g, 3.84 mmol). KF·2H$_2$O (0.964 g, 8.5 mmol), and diethyl phosphite (0.447 g, 3.21 mmol) produced **1f** (0.793 g, 85%) after chromatographic purification (silica, gradient hexane/EtOAc). ^{1}H NMR: 6.07–5.83 (m, 2H), 4.83 (br. s, 1H), 4.55 (dd, $^2J_{HP} = 16$ Hz, $^3J_{HH} = 5$ Hz, 1H), 4.12 (quintet, $J = 7.2$ Hz, 4H), 3.3 (s, 6H), 1.32 (td, $^3J_{HH} = 7.0$ Hz, $^4J_{HP} = 1.7$ Hz, 6H); ^{31}P NMR: δ 22.1 (s). This compound decomposed gradually upon standing and could not be sent out for elemental analysis.

3.6. 1-(Diethoxyphosphono-α-hydroxymethyl)cyclopentene (*1g*)

Cyclopentene-1-carboxaldehyde [37] (0.77 g, 8.0 mmol) was stirred with diethyl phosphite (1.27 g, 9.2 mmol) and KF·2H$_2$O (1.80 g, 19 mmol) for 2 h under standard reaction and workup conditions. Flash chromatography (silica, CH_2Cl_2:EtOAc 1:1) of the residual oil and collection of the fractions with Rf 0.32 yielded a clear oil (1.30 g, 70%). ^{1}H NMR: 5.9 (br. s, 1H), 4.59 (d, $^2J_{HP} = 12.1$ Hz, 1H), 4.21–4.16 (quintet, $J = 7.2$ Hz, 4H), 3.0 (br. s, 1H), 2.56–2.47 (m, 2H, CH_2–CH=), 2.42–2.34 (m, 2H, CH_2–C=), 1.91 (quintet, $^3J_{HH} = 7.4$ Hz, 2H), 1.32 (td, $^3J_{HH} = 7.0$ Hz, $^4J_{HP} = 1.7$ Hz, 6H); ^{31}P NMR: δ 22.4 (s); ^{13}C NMR: 139.6, 128.7 (d, $^2J_{CP} = 12$ Hz), 68.2 (d, $^1J_{CP} = 160$ Hz), 62.8 (m), 32.6 (d, $^3J_{CP} = 3$ Hz), 32.3 (d, $^4J_{CP} = 3$ Hz), 23.3, 16.3 (d, $^3J_{CP} = 6$ Hz). Anal.: Calcd. for $C_{10}H_{19}O_4P$: C, 51.28; H, 8.18. Found: C, 51.10; H, 8.28.

3.7. 1-(Diethoxyphosphono-α-hydroxymethyl)-4-isopropylidenecyclohexene (*1h*)

(S)-(−) Perillaldehyde (2.42 g, 16.1 mmol) was stirred with diethyl phosphite (2.67 g, 19.3 mmol) and KF·2H$_2$O (3.6 g, 38.3 mmol) overnight under standard reaction and workup conditions to give **1h** (3.6 g, 77%) after column chromatography (silica, gradient hexane:EtOAc 1:1); Rf 0.29 (hexane:EtOAc 1:3) ^{1}H NMR: δ 5.87 (bs, 1H), 4.72 (d, $^2J_{HH} = 4.1$ Hz, 2H), 4.32 (dd, $^2J_{HP} = 11.2$ Hz, $^3J_{HP} = 4.5$ Hz, 1H), 4.22–4.11 (m, 4H), 3.07 (pseudo quartet, $^3J_{HH} = 6.5$ Hz, 1H), 2.4–1.8 (m, 5H), 1.74 (s, 3H), 1.55–1.40 (m, 1H), 1.33 (td, $^3J_{HH} = 7.0$ Hz, $^4J_{HP} = 1.5$ Hz, 6H); ^{31}P NMR: δ 23.1 (s); ^{13}C NMR: two diastereomers: 149.74 [139,7], 133.62 (d, $^3J_{CP} = 4$ Hz) [133.24 (d, $^3J_{CP} = 4$ Hz)], 125.94 (d, $^2J_{CP} = 12$ Hz) [125.35 (d, $^2J_{CP} = 12$ Hz)], 108.9, 72.6 (d, $^1J_{CP} = 158$ Hz) [72.1 (d, $^1J_{CP} = 158$ Hz)], 63.0 (m), 41.06 [40.96], 30.85 (d, $^3J_{CP} = 2$ Hz) [30.76 (d, $^3J_{CP} = 2$ Hz)], 27.7 [27.6], 26.31 (d, $^3J_{CP} = 2$ Hz) [26.0 (d, $J_{CP} = 2$ Hz)], 20.94, 16.7 (d, $^3J_{CP} = 5$ Hz); IR (film) ν 3280, 3060, 1639 cm^{-1}. Anal.: Calcd. for $C_{14}H_{25}O_4P$: C, 58.32; H, 8.74. Found: C, 58.04; H, 8.67.

3.8. (E)-Diethyl 3-fluoro-1-butenylphosphonate (*3a*). General method

To a solution of **1a** (2.99 g, 14.4 mmol) in CH_2Cl_2 (75 ml) at −80°C was added DAST (2.4 ml, 17.3 mmol, 1.2 eq) dropwise via syringe. The resulting solution was allowed to warm slowly overnight before quenching with saturated $NaHCO_3$ (100 ml). The layers were separated and the aqueous was extracted with CH_2Cl_2 (3 × 25 ml). The organic layer was washed with H_2O (40 ml). The combined organic layers were washed with brine (25 ml), dried ($MgSO_4$) and concentrated to give a viscous amber oil (2.71 g) containing **3a** (δ 178.2 ppm, 98%) and its α-fluorophosphonate isomer (δ 196.9 ppm, 2%). Kugelrohr distillation (108°C/0.07 mmHg) afforded pure **3a** (2.30 g, 76%). [Note: Although this compound has been reported previously by Blackburn and coworkers [25] our ^{1}H NMR analysis differs from theirs on the chemical shift of the vinylic hydrogen on carbon No. 1] ^{1}H NMR: δ 6.75 (m, $^3J_{HH} = 17.2$ Hz, 1H, C–CH=), 5.95 (ddt, $^2J_{HP} = 19.2$ Hz, $^3J_{HH} = 17.2$ Hz, $^5J_{HF} = 1.6$ Hz, 1H, CHP), 5.21 (dm, $^2J_{HF} = 46.8$ Hz, 1H), 4.09 (quintet, $^3J_{HP} = 7.1$ Hz, 4H), 1.46 (dd, $^3J_{HF} = 23.4$ Hz, $^3J_{HH} = 6.6$ Hz, 1H), 1.34 (td, $^3J_{HH} = 7.0$ Hz, $^4J_{HP} = 0.7$ Hz, 6H); ^{31}P NMR: δ 18.3 (s); ^{19}F NMR: δ 178.2 (s); ^{13}C NMR: δ 149.8 (dd, $^2J_{CF} = 19.4$ Hz, $^2J_{CP} = 5$ Hz, C2), 115.5 (dd, $^1J_{CF} = 188.7$ Hz, $^3J_{CP} = 9$ Hz, C1), 87.7 (dd, $^1J_{CP} = 173$ Hz, $^3J_{CF} = 22$ Hz, C3), 61.3 (d, $^2J_{CP} = 6$ Hz), 19.5 (dd, $^2J_{CF} = 23$ Hz, $^4J_{CP} = 2$ Hz, C4); *m/z* 163 (37), 155 (43), 135 (98), 119 (19), 109 (18), 82 (47), 81 (100), 73 (46), 65 (61).

3.9. (E)-Diethyl 3-fluoro-3-methyl-1-butenylphosphonate (*3b*)

Using the general fluorination procedure **1b** [35] (2.52 g, 11.362 mmol) was fluorinated with DAST (1.5 ml, 11.0 mmol). Kugelrohr distillation (b.p. 104°C/0.07 mmHg) afforded **3b** (1.29 g, 51%). ^{1}H NMR (400 MHz): δ 6.79 (m, $^3J_{HF} = 22.9$ Hz, $^3J_{HH} = 17.2$ Hz, 1H, C–CH=), 5.92 (ddd, $^2J_{HP} = 19.4$ Hz, $^3J_{HH} = 17.2$ Hz, $^4J_{HF} = 0.58$ Hz, 1H, CHP), 4.10 (quintet, $^3J_{HP} = 7.1$ Hz, 2H), 1.66 (d,

$^3J_{HF}$ = 20 Hz, 6H) 1.34 (t, $^3J_{HH}$ = 7.1 Hz, 6H); ^{31}P NMR: δ 18.9 (s), ^{19}F NMR: δ 143.6 (s); *m/e* 204 ($M^+ - 20$, 10), 163 (20), 149 (20), 148 (20), 135 (50), 133 (45), 95 (60), 81 (70), 67 (100). Anal.: Calcd. for $C_9H_{18}O_3PF$: C, 48.21; H, 8.09. Found: C, 47.73; H, 8.33.

3.10. (E)-Diethyl 3-fluoro-1-hexenylphosphonate (**3c**)

Using the standard fluorination conditions, **1c** (5.49 g, 23.0 mmol) in CH_2Cl_2 (80 ml) was treated with DAST (3.3 ml, 25.0 mmol) to yield an amber oil (6.24 g) which yielded **3c** (4.27 g, 78%) after vacuum distillation (90°C/0.35 mmHg). ^{1}H NMR ($CDCl_3$): δ 6.88–6.62 (m, 1H, C–CH=), 5.94 (dddd, $^2J_{HP}$ = 19.7 Hz, $^3J_{HH}$ = 17.2 Hz, $^5J_{HF}$ = 1.8 Hz, $^5J_{HH}$ = 0.4 Hz, 1H, CHP), 5.04 (dm, $^2J_{HF}$ = 49.1 Hz, 1H), 4.088 (quintet, $^3J_{HP}$ = 7.1 Hz, 2H), 4.085 (quintet, $^3J_{HP}$ = 7.1 Hz, 2H), 1.75–1.65 (m, 2H), 1.46 (sextet, $^3J_{HH}$ = 7.4, 2H), 1.32 (t, $^3J_{HH}$ = 7.1 Hz, 6H), 0.94 (t, $^3J_{HH}$ = 7.2 Hz, 3H); ^{31}P NMR: δ 18.4 (s); ^{19}F NMR: δ 185.9 (s); Anal.: Calcd for $C_{10}H_{20}O_3PF$: C, 50.42; H, 8.46. Found: C, 50.14; H, 8.47.

3.11. Diethyl 5-fluoro-1,3-hexadienyl-1-phosphonate (**3d**)

To **1d** (1.02 g, 4.36 mmol) in CH_2Cl_2 (10 ml) was added a solution of DAST (0.75 ml, 5.7 mmol) in CH_2Cl_2 (10 ml) dropwise. After workup a viscous amber oil resulted (1.03 g, 92%) which was judged homogeneous by TLC. ^{1}H NMR: δ 7.10 (m, 1H), 6.36 (td, $^3J_{HH}$ = 13.0 Hz, 1 Hz, 1H), 6.08 (td, $^3J_{HH}$ = 15.6 Hz, J = 5.2 Hz, 1H), 5.77 (t, $^3J_{HH}$ = 17.9 Hz, 1H), 5.18 (dm, $^3J_{HF}$ = 47.8 Hz, 1H), 4.09 (quintet, $^3J_{HH}$ = 7.3 Hz, 4H), 1.45 (dd, $^3J_{HF}$ = 23.6 Hz, $^3J_{HH}$ = 6.5 Hz, 3H), 1.34 (t, $^3J_{HH}$ = 7.1 Hz, 6H); ^{31}P NMR: δ 19.09 (s); ^{19}F NMR: δ 172.3 (s); *m/z* = 236 (M^+, 25), 216 (8), 189 (75), 160 (55), 135 (40), 111 (20), 84 (100), 79 (90), 65 (35), 51 (38). HRMS $C_{10}H_{18}O_3PF$ requires 236.09773; Found: 236.09772.

3.12. (E) Diethyl 3-fluoro-3-phenyl-1-propenylphosphonate (**3e**)

1e (3.66 g, 13.5 mmol) in CH_2Cl_2 (35 ml) was treated with DAST (2.4 ml, 18.16 mmol) to afford **3e** (2.69 g, 73%). ^{1}H NMR were consistent with that previously reported for this compound [25] and confirmed the absence of the (*Z*)-stereoisomer. ^{31}P NMR: δ 17.8 (s); ^{19}F NMR: δ 174.4 (s).

3.13. Diethyl 3-fluoro-4,4-dimethoxy-2-butenylphosphonate (**3f**)

Under the general fluorination protocol, **1f** (202 mg, 0.75 mmol), CH_2Cl_2 (15 ml) and DAST (0.14 ml, 0.95 mmol) produced an oily residue (173 mg, 85% recovery) which was chromatographed (silica, EtOAc) to give a mixture of two compounds (**3f**) (46%) and diethyl 4-oxo-3-methoxy-2-butenylphosphonate (**9**) (54%) accompanied by smaller amounts of an unidentified non-fluorinated vinylphosphonate [^{31}P NMR: δ 18.5 (s)]. **3f**: ^{1}H NMR: δ 6.9–6.6 (m, 1H), 6.14–6.00 (m, 1H), 5.0 (dm, $^3J_{HF}$ = 47.4 Hz, 1H), 4.35 (t, J = 6 Hz, 1H), 4.25–4.05 (m, 4H), 3.47 (s, 3H), 3.43 (s, 3H), 1.34 (m, 6H); ^{31}P NMR: δ 17.8 (s), ^{19}F NMR: δ 198.5 (s) ppm.

3.14. (E)-1-(Diethoxyphosphonomethylene)-2-fluorocyclopentane (**3g**)

Using the general fluorination protocol, **1g** (311 mg, 1.33 mmol) in CH_2Cl_2 (15 ml) was treated with DAST (0.25 ml, 1.65 mmol) to give an amber oil (294 mg, 95% mass recovery). ^{19}F and ^{31}P NMR indicated the presence of the *E*-isomer (^{31}P NMR: δ 17.1 ppm, ^{19}F NMR: δ 175.7 ppm) (87%), and *Z*-isomer (^{31}P NMR: δ 15.4 ppm, ^{19}F NMR: δ 167.5 ppm) (8%) and dehydrofluorinated product (^{31}P NMR: δ 20.5 ppm) (5%). Kugelrohr distillation (b.p. 100°C/0.07 mmHg) did not separate the desired product from mixture. Flash chromatography (silica, hexane:EtOAc 1:2) of an aliquot (1.024 g) led to the isolation of **3g** (181 mg, 60%) as *E*:*Z* 94:6 mixture. ^{1}H NMR: δ 5.85 (dm, $^2J_{HP}$ = 17.7 Hz, 1H), 5.18 (dm, $^2J_{HF}$ = 53.9 Hz, 1H), 4.083 (quintet, $^3J_{HP}$ = 7.1 Hz, 2H), 4.080 (quintet, $^3J_{HP}$ = 7.1 Hz, 2H), 2.89–2.80 (m, 1H), 2.66–2.48 (m, 1H), 2.08–1.83 (m, 3H), 1.80–1.65 (m, 1H), 1.33 (t, $^3J_{HH}$ = 7.1 Hz, 6H); ^{31}P NMR: δ 17.1 (s); ^{19}F NMR: δ 175.5 (s). *m/z* = 216, 188, 160, 141, 106, 78, 51, 29. Anal.: Calcd. for $C_{10}H_{18}O_3PF$: C, 50.85; H, 7.68. Found: C, 50.95; H, 7.71.

3.15. (E)-1-(Diethoxyphosphonomethylene)-2-fluoro-4-isopropylidene cyclohexane (**3h**)

Using the general method, **1h** (1.40 g, 4.86 mmol), CH_2Cl_2 (80 ml) and DAST (0.80 ml, 6.05 mmol) produced an oily mixture (1.17 g). ^{19}F and ^{31}P NMR indicated the presence of the *E*-isomer (^{31}P NMR: δ 17.0 ppm, ^{19}F NMR: δ 174.8 ppm) (45%), *Z*-isomer (^{31}P NMR: δ 18.7 ppm, $^4J_{PF}$ = 4.8 Hz, ^{19}F NMR: δ 179.4, $^4J_{PF}$ = 5.1 Hz) (31%) and dehydrofluorinated product (^{31}P NMR: δ 19.4 ppm) (24%). Kugelrohr distillation (b.p. 114°C/0.05 mmHg) did not separate the desired product from mixture. Flash chromatography (silica, gradient hexane:EtOAc 7:3–4:6) of an aliquot (0.97 g) led to the isolation of **3h** (570 mg, 59%) as *E*:*Z* 78:22 mixture. ***E*-3g** ^{1}H NMR: δ 5.59 (dd, $^2J_{HP}$ = 17.2 Hz, $^4J_{HF}$ = 2.9 Hz, 1H), 4.93 (dm, $^2J_{HF}$ = 49.0 Hz, 1H), 4.75 (d, $^2J_{HH}$ = 11.8 Hz, 2H) 4.092 (quintet, $^3J_{HP}$ = 7.3 Hz, 2H), 4.085 (quintet, $^3J_{HP}$ = 7.3 Hz, 2H), 3.18 (dt, $^3J_{HF}$ = 14.0 Hz, J_{HF} = 3.7 Hz, 1H), 2.59–2.43 (m, 2H), 2.28–2.15 (m, 1H), 1.96–1.90 (m, 1H), 1.72 (s, 3H), 1.8–1.3 (m, 2H), 1.33 (t, $^3J_{HH}$ = 7.1 Hz, 6H); ^{31}P NMR: δ 17.0 (s); ^{19}F NMR: δ 174.8 (s); *m/e* 290 (M^+, 20), 270 (65), 244 (20), 202 (50), 174 (25), 146 (50), 132 (100), 117 (48), 105 (25), 91 (70), 65 (25), 53 (28). $C_{14}H_{24}O_3PF$ required 290.14467. Found 290.14468.

3.16. (Z)-Diethyl 3-fluoro-2-butenylphosphonate (**5a**). General method

Into a vacuum–dried mixture of $KN(TMS)_2$ (0.637 g, 3.15 mmol) and 18-crown-6 (1.614 g, 5.72 mmol) dissolved in THF (30 ml) and cooled to −80°C was added a cold (−80°C) solution of **3a** (0.602 g, 2.86 mmol) in THF (10 ml) via cannula, and the resulting mixture was stirred for 4 h at −80°C before addition of saturated aqueous NH_4Cl (30 ml). The layers were separated and the aqueous phase was extracted with diethyl ether (2 × 25 ml). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to give an oil (0.554 g). An aliquot (77 mg) was purified using flash chromatography (silica, hexane:EtOAc 3:7) yielding **5a** (56 mg, 67%). ^{1}H NMR: δ 4.62 (dq, $^3J_{HF} = 34.7$ Hz, $^3J = 7.2$ Hz, 1H, HC=), 4.11 (quintet, $^3J_{HP} = 7.2$ Hz, 4H), 2.60 (ddd, $^2J_{HP} = 21.3$ Hz, $^3J_{HH} = 7.8$ Hz, $^4J = 1.1$ Hz, 2H), 1.92 (ddd, $^3J_{HF} = 16.7$ Hz, $^4J_{HH} = 5.2$ Hz, $^5J = 1.1$ Hz, 3H), 1.32 (t, $^3J_{HH} = 7.1$ Hz, 6H); ^{31}P NMR: δ 28.1 (d, $^4J_{FP} = 10$ Hz); ^{19}F NMR: δ 99.2 (d, $^4J_{FP} = 10$ Hz); *m/z* = 210 (M^+, 32), 162 (14), 138 (52), 134 (42), 111 (75), 109 (57), 101 (30), 91 (38), 81 (100), 73 (88). Anal.: Calcd. for $C_8H_{16}O_3PF$: C, 45.72; H, 7.67. Found: C, 45.85; H, 7.75.

3.17. (Z)-Diethyl 3-fluoro-2-hexenylphosphonate (**5b**)

$KN(TMS)_2$ (479 mg, 2.40 mmol), 18-crown-6 (1.52 g, 5.75 mmol), THF (60 ml) and a solution of **3c** (440 mg, 1.85 mmol) in THF (20 ml)were mixed and stirred for 4.5 h to yield a pale yellow oil (422 mg). Purification using flash chromatography produced **5b** (343 mg, 78%). ^{1}H NMR δ 4.61 (dq, $^3J_{HF} = 35.2$ Hz, $^3J = 7.8$ Hz, 1H, HC=), 4.105 (quintet, $^3J_{HP} = 7.2$ Hz, 2H), 4.102 (quintet, $^3J_{HP}$= 7.2 Hz, 2H), 2.61 (ddd, $^2J_{HP} = 21.3$ Hz, $^3J_{HH} = 7.8$ Hz, $^4J = 0.9$ Hz, 2H), 2.23–2.11(m, 2H), 1.54 (sextet, $^3J_{HH} = 7.4$ Hz, 2H), 1.32 (t, $^3J_{HH} = 7.1$ Hz, 6H), 0.94 (t, $^3J_{HH} = 7.4$ Hz, 3H); ^{31}P NMR: δ 28.1 (d, $^4J_{FP} = 10.2$ Hz); ^{19}F NMR: δ 105.7 (d, $^4J_{FP} = 8.2$ Hz); *m/z* = 238 (M^+, 12), 162 (11), 152 (31), 138 (31), 111 (57), 81 (100), 59 (48). Anal.: Calcd. for $C_{10}H_{20}O_3PF$: C, 50.42; H, 8.46. Found: C, 49.90; H, 8.48.

3.18. (Z)-Diethyl 3-fluoro-3-phenyl-2-propenylphosphonate (**5c**)

Compound **5a**, $KN(TMS)_2$ (83 mg, 0.42 mmol), 18-crown-6 (297 mg, 1.12 mmol), THF (10 ml) and a solution of **3e** (99 mg, 0.36 mmol) in THF (5 ml) were allowed to warm up to room temperature with stirring during 20 h to yield **5c** (82 mg, 83%). An analytical sample was isolated following filtration using a silica plug (hexane:EtOAc 1:1).^{1}H NMR: δ 7.58–7.32 (m, 5H), 5.46 (dq, $^3J_{HF} = 34.0$ Hz, $^3J = 7.6$ Hz, 1H, HC=), 4.14 (quintet, $^3J_{HP} = 7.2$ Hz, 4H), 2.84 (dd, $^2J_{HP} = 22.7$ Hz, $^3J_{HH} = 7.6$ Hz, 2H), 1.32 (t, $^3J_{HH} = 7.2$ Hz, 6H); ^{31}P NMR: δ 27.5 (d, $J = 10.9$); ^{19}F NMR: δ 117.3 (d, $^4J_{FP} = 13.8$ Hz); *m/z* = 272 (M^+, 15), 216 (7), 199 (10), 135 (100), 133 (44), 115 (98), 109 (38), 81 (39), 29 (39). Anal.: Calcd. for $C_{13}H_{18}O_3PF$: C, 57.35; H, 6.66. Found: C, 57.20; H, 6.57.

3.19. 1-Diethoxyphosphonomethyl-5-fluorocyclopentene (**5d**)

Applying the general methodology described for **5a**, $KN(TMS)_2$ (181 mg, 0.91 mmol), 18-crown-6 (523 mg, 1.98 mmol), THF (20 ml) and a solution of **3g** (170 mg, 0.72 mmol) in THF (4 ml) were stirred at −85°C for 0.5 h and then slowly warmed to −15°C over 3 h. yielding **5d** (141 mg, 83%). An aliquot (120 mg) was chromatographed (silica, gradient hexane:EtOAc) yielding a very low recovery of **5d** (40 mg, 34%), probably as a result of HF loss and concomitant diene formation. ^{1}H NMR: δ 6.03 (br. s, 1H), 5.58 (dm, $^2J_{FH} = 57$ Hz, 1H), 4.11 (quintet, $^3J_{HP} = 7.2$ Hz, 4H), 2.74 (br. d, $^2J_{HP} = 20.5$ Hz, 2H), 2.9–1.75 (m, 4H), 1.30 (t, $^3J_{HH} = 7.2$ Hz, 6H); ^{31}P: δ 27.2 (d, $^4J_{FP} = 8.0$); ^{19}F NMR: δ 166.1 (d, $^4J_{FP} = 8.8$ Hz). Anal.: Calcd. for $C_{10}H_{18}O_3PF$: C, 50.85; H, 7.68. Found: C, 50.69; H, 7.71.

3.20. 1-Diethoxyphosphonomethyl-2-fluoro-4-isopropylidenecyclohexane (**5e**)

$KN(TMS)_2$ (96 mg, 0.48 mmol), 18-crown-6 (277 mg, 1.16 mmol), THF (10 ml) and a solution of **3h** (105 mg, 0.36 mmol) in THF (4 ml) were stirred at −85°C for 0.5 h and then slowly warmed to room temperature overnight yielding **5e** (81 mg, 77%) as a 91:9 mixture of vinylfluoro and allylfluoro isomers. An aliquot (77 mg) underwent extensive degradation when chromatographed (silica, gradient hexane:EtOAc) yielding a considerably low amount of **5e** (11 mg, 14%). ^{1}H NMR: δ 4.75 (d, $^2J_{HH} = 8$ Hz, 2H) 4.1 (quintet, $^3J_{HP} = 7.3$ Hz, 4H), 2.65 (d, $^3J_{HF} = 22$ Hz, 2H), 2.4–2.2 (m, 5H), 1.9–1.70 (m, 1H), 1.75 (s, 3H), 1.5–1.3 (m, 1H), 1.33 (t, $^3J_{HH} = 7.1$ Hz, 6H); ^{31}P NMR: δ 27.5 (d, $^4J_{FP} = 11$ Hz); ^{19}F NMR: δ 105.6 (d, $^4J_{FP} = 13$ Hz). Anal.: Calcd. for $C_{14}H_{24}O_3PF$: C, 57.92; H, 8.33. Found: C, 57.82; H, 8.36.

3.21. (Z)-Diethyl 1-benzyl-3-fluoro-2-butenylphosphonate (**6a**)

To a solution of **5a** (112 mg, 0.53 mmol) in THF (15 ml) cooled to −60°C was added $LiN(TMS)_2$ (1.1 ml, 1 M in THF, 2 eq), the resulting mixture was removed from the cold bath for 15 min and then cooled down to −60°C before addition of benzyl bromide (136 mg, 0.79 mmol). The resulting mixture was allowed to warm to room temperature overnight and quenched with saturated NH_4Cl (25 ml). The layers were separated and the aqueous phase was extracted with diethyl ether (2 × 25 ml). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, concentrated

and purified using flash chromatography (silica, gradient hexane:EtOAc) to give **6a** (147 mg, 92%). ^{1}H NMR: δ 7.3–7.1 (m, 5H), 4.46 (dm, $^3J_{HF} = 34.6$ Hz, 1H, HC=), 4.11 (quintet, $^3J_{HP} = 7.1$ Hz, 4H), 3.36–3.18 (m, 2H), 2.76–2.64 (m, 1H), 1.81 (ddd, $^3J_{HF} = 16.7$ Hz, $^4J_{HH} = 5.0$ Hz, $^5J = 0.6$ Hz, 3H), 1.32 (td, $^3J_{HH} = 7.2$ Hz, $^4J_{HP} = 1.9$ Hz, 6H); ^{31}P NMR: δ 29.2 (d, $^4J_{FP} = 8$ Hz); ^{19}F NMR: δ 98.0 (d, $^4J_{FP} = 8$ Hz); Anal.: Calcd. for $C_{15}H_{22}O_3PF$: C, 59.99; H, 7.58. Found: C, 59.42; H, 7.44.

*3.22. (Z)-Diethyl 1,3-dfluoro-2-hexenylphosphonate (**6b**)*

To a solution of **5b** (107 mg, 0.45 mmol) in THF (15 ml cooled to −78°C was added $LiN(TMS)_2$ (0.65 ml, 1 M in THF, 1.3 eq), the resulting mixture was removed from the cold bath for 15 min and then cooled down to −78°C before addition of NFSI (187 mg, 0.59 mmol). The resulting mixture was allowed to warm to room temperature overnight before addition of brine (20 ml), diethyl ether (50 ml) and NaOH 14% (7 ml). The layers were separated and the aqueous phase was extracted with diethyl ether (2×25 ml). The combined organic layers were washed with water, dried over anhydrous $MgSO_4$, filtered, concentrated and purified using flash chromatography (silica, gradient hexane:EtOAc) to give **6b** (77 mg, 66%). ^{1}H NMR: δ 5.57 (ddd, $^2J_{HF} = 41.0$ Hz, $^2J_{HP} = 10.3$ Hz, $^3J_{HH} = 6.0$ Hz, 1H), 5.08–4.88 (m, 1H, HC=), 4.27–4.07 (m, 4H), 2.28–2.04 (m, 2H), 1.5–1.4 (m, 2H), 1.39–1.25 (m, 6H), 0.94 (t, $^3J_{HH} = 7.4$ Hz, 3H); ^{31}P NMR: δ 16.7 (dd, $^2J_{FP} = 88.1$ Hz, $^4J_{PF} = 9.8$ Hz); ^{13}C NMR: δ 166.2 (ddd, $^1J_{CF} = 256.6$ Hz, $^3J_{CF} = 12.4$ Hz, $^3J_{CP} = 11.0$ Hz), 98.3 (dd, $^2J_{CF} = 21.4$ Hz, $^2J_{CP} = 11.5$ Hz), 81.4 (ddd, $^1J_{CF} = 179.5$ Hz, $^1J_{CP} = 174.8$ Hz, $^3J_{CF} = 7.2$ Hz), 63.4 (d, $^2J_{CP} = 6.7$ Hz), 63.2 (d, $^2J_{CP} = 6.7$ Hz), 33.9 (d, $^2J_{CF} = 24.8$ Hz), 18.9, 16.3 (d, $^3J_{CP} = 5.9$ Hz), 13.2; Anal.: Calcd. for $C_{10}H_{19}O_3PF_2$: C, 46.88; H, 7.47. Found: C, 46.58; H, 7.36.

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