A Novel Intramolecular Horner–Wadsworth–Emmons Reaction: A Simple and General Route to α-Fluoro-α,β-unsaturated Diesters[1]

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Diethyl (fluorocarbethoxymethyl)phosphonate (**1**), prepared from triethyl phosphite and ethyl bromofluoroacetate, reacts with *n*-butyllithium in THF to give the phosphonate carbanion **2**. Addition of the pregenerated carbanion **2** to a THF solution of methyl or ethyl oxalyl chloride at −78 °C forms the acylated phosphonate $(EtO)_2P(O)CF(COCO_2R)CO_2Et$ (**3**). *In situ* reaction of **3** with Grignard reagents affords α-fluoro-α,β-unsaturated diesters $R'(CO_2R)C{=}CFCO_2Et$ in moderate to good yields with high *E*-stereoselectivity. The reaction is applicable to primary, secondary, and tertiary alkyl, alkenyl, alkynyl, aryl, cyclohexyl, and perfluorinated Grignard reagents. The assignment of *E* and *Z* configuration is based on NOE experiment. The *E*/*Z* ratio of unsaturated diesters formed in the reaction varies with the metal ion and cosolvent. However, solvents and bases have little influence on the stereoselectivity.

Introduction

α-Fluoro-α,β-unsaturated esters of defined stereochemistry have been used as precursors in the synthesis of biologically active 12-fluororetinal and 12-fluororhodopsin,[2] fluorinated analogues of insect sex pheromones,[3] and in the field of pyrethroids.[4] Replacement of the hydrogen atom by a fluorine atom has not only enhanced the biological activity of parent compounds but also increased their thermal and oxidative stabilities.[3] Biologically active molecules containing a vinylic fluorine atom are of special interest,[5] because of the presence of this group in a number of enzyme inhibitors.[6] Consequently, the synthesis of selectively fluorinated building blocks, such as α-fluoro-α,β-unsaturated diesters, has become an area of interest in recent years. Literature methods for the preparation of the α-fluoro-α,β-unsaturated diesters generally lack stereospecificity and generality and are often arduous to carry out on a practical scale. Thus, the reaction of diethyl oxalate with phosphonate carbanion **2** to give diethyl 2-fluoro-3-ethoxyfumarate only allows the introduction of the ethoxy group in the β-position of α-fluoro-α,β-unsaturated diesters.[7] The condensation of (carbethoxymethylene)triphenylphosphorane with diethyl oxalofluoroacetate in dimethylformamide (DMF) gives a 1:1 mixture of ethylenic triethyl esters $(EtO_2CCFH)(CO_2Et)C{=}CHCO_2Et$ and the isomerization product $(EtO_2CCH_2)(CO_2Et)C{=}CFCO_2Et$.[8] Alkylation of (ethylphenyl)sulfinyl fluoroacetate followed by subsequent thermal elimination leads to the preparation of α-fluoro-α,β-unsaturated diesters $(Et)(CO_2Et)C{=}CFCO_2Et$.[9] Herein, we describe a general one-pot synthesis of α-fluoro-α,β-unsaturated diesters, which permit variation of the group at the β-position *via* an intramolecular Horner–Wadsworth–Emmons reaction.

Results and Discussion

The Michaelis–Arbuzov reaction[7] of triethyl phosphites $(EtO)_3P$ with ethyl bromofluoroacetate ($CFHBrCO_2Et$) gives diethyl (fluorocarbethoxymethyl)phosphonate (**1**) (eq 1) in 71% yield.

$$(EtO)_3P + CFHBrCO_2Et \xrightarrow{140-150\ ^\circ C} \underset{\mathbf{1}}{(EtO)_2P(O)CFHCO_2Et} + EtBr \quad (1)$$

Addition of a tetrahydrofuran (THF) solution of anion $[(EtO)_2P(O)CFCO_2Et]^-Li^+$ (**2**) to a THF solution of an acid chloride such as methyl oxalyl chloride or ethyl oxalyl chloride forms the corresponding C-acylated phosphonates $(EtO)_2P(O)CF(COCO_2R)CO_2Et$ **3** in 90 to 92% ^{19}F NMR yields (eq 2). The acylated phosphonate $(EtO)_2P(O)CF(COCO_2Et)CO_2Et$ (**3a**) exhibited a resonance at −177.9 ppm in the ^{19}F NMR spectrum (d, J_{PCF} = 74 Hz) and the proton decoupled ^{31}P NMR signals occurred as a doublet at 5.14 ppm (d, J = 74 Hz).

$$\underset{\mathbf{2}}{\left[(EtO)_2P(O)CFCO_2Et\right]^-Li^+} + ClC(O)CO_2R \xrightarrow{THF/-78^\circ C} \underset{\mathbf{3}}{(EtO)_2P(O)CF(COCO_2R)CO_2Et} \quad (2)$$

3a: R = Et
b: R = Me

Treatment of the acylated phosphonate **3a** with 1 equiv of a Grignard reagent (RMgX) gives an *E*/*Z* mixture of

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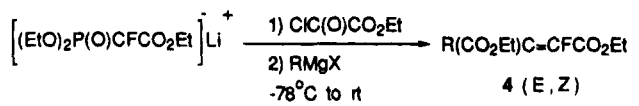
Table 1. Preparation of $R(CO_2Et)C{=}CFCO_2Et$

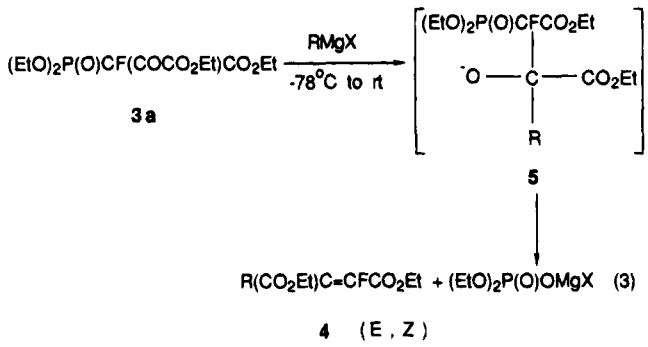


no.	R	X	E/Z[b]	NOE (%)	isolated yields (%)[a]
4a	Me	I	100/0	+6.2	52
4b	Et	Br	96/4		56
4c	n-C_3H_7	Cl	96/4		54
4d	i-C_3H_7	Cl	100/0		54
4e	t-Bu	Cl	100/0		49
4f	$H_2C{=}CH$	Br	85/15[c]	+17.2[d]	50
4g	C_6H_{11}	Cl	100/0		50
4h	Ph	Br	60/40		55
4i	n-C_3F_7	Br	0/100		63
4j	C_6F_5	Br	90/10		68
4k	$PhC{\equiv}C$	Br	0/100		65

[a] Isolated yields are based on $(EtO)_2P(O)CFHCO_2Et$. [b] *E/Z* ratio was obtained by ^{19}F NMR integration of the vinyl fluorine signals. [c] *E*- and *Z*-isomers were separated by flash chromatography. [d] No NOE was observed for the *Z*-isomer.

α-fluoro-α,β-unsaturated diesters $R(CO_2Et)C{=}CFCO_2Et$ **4** in 49–68% isolated yields. The R group can be alkyl, alkenyl, alkynyl, aryl, cyclohexyl, C_3F_7, and C_6F_5.

The initial step in the synthesis of **4** is the nucleophilic attack of the Grignard reagent at the ketone group of **3a** to form **5**, followed by intramolecular elimination of diethyl phosphate to afford **4** (eq 3).



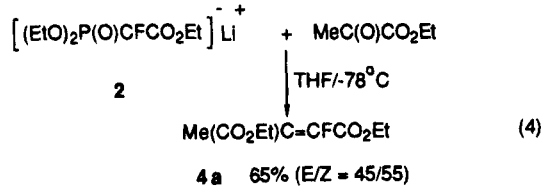
The results for the preparation of several α-fluoro-α,β-unsaturated diesters $R(CO_2Et)C{=}CFCO_2Et$ **4 (a–k)** are summarized in Table 1. The separation of the two isomers of $(CH_2{=}CH)(CO_2Et)C{=}CFCO_2Et$ (**4f**) (*E/Z* = 85/15) was accomplished *via* flash chromatography on a silica gel column *via* elution with *n*-hexane and ethyl acetate (24/1) to give the isomerically pure (*E*)-$(CH_2{=}CH)(CO_2Et)C{=}CFCO_2Et$ and (*Z*)-$(CH_2{=}CH)(CO_2Et)C{=}CFCO_2Et$. The *E/Z* ratio of **4** was determined by integration of the vinyl fluorine signals in the ^{19}F NMR spectrum, which appear as singlets between −99.2 and −130.6 ppm upfield from $CFCl_3$. The downfield chemical shift (−99.2 to −119.3 ppm) was assigned to the vinyl fluorine of the *Z*-isomer, whereas the upfield singlet (−101.9 to −130.6 ppm) was assigned to the vinyl fluorine of the *E*-isomer. For compounds with the general formula $R'(CO_2Et)C{=}CFCO_2Et$, the vinyl fluorine of the *Z*-isomer exhibits a downfield signal compared to the vinyl fluorine resonance of the *E*-isomer.

These assignments were confirmed by nuclear Overhauser effect (NOE) experiments. For example, the fluorine signal in $Me(CO_2Et)C{=}CFCO_2Et$ (**4a**) appears at −125.5 ppm (q, J = 3.84 Hz). Irradiation of the Me group gives a positive (6.2% increase) NOE, in agreement with the syn relationship of the Me group and the vinyl fluorine (*E*-isomer).

Similar NOE experiments were carried out with pure (*E*)-$(CH_2{=}CH_a)(CO_2Et)C{=}CFCO_2Et$ and (*Z*)-$(CH_2{=}CH_b)(CO_2Et)C{=}CFCO_2Et$. The isomer which exhibits a fluorine signal at −128.1 ppm gives a positive (17.2% increase) NOE when H_a (6.73 ppm) is irradiated in agreement with the *E*-assignment. Similarly, the isomer which exhibits a fluorine signal −119.3 ppm gives a negative NOE when H_b (7.34 ppm) is irradiated in agreement with the *Z*-assignment. In general, the vinyl fluorine of the *Z*-isomer exhibits a downfield signal compared to the vinyl resonance of the *E*-isomer. Reduction of the *E* and *Z* mixture of $(CH_2{=}CH)(CO_2Et)C{=}CFCO_2Et$ (**4f**), which exhibited two fluorine signals at −128.1 and −119.3 ppm in the ^{19}F NMR spectrum (ratio = 85/15), with 5% Pd/C and hydrogen, gives (*E,Z*)-$Et(CO_2Et)C{=}CFCO_2Et$ (**4b**) (83/17 ratio of isomers). Compound **4b**, which showed signals at −127.5 and −116.1 ppm in the ^{19}F NMR spectrum, matched the authentic compound (*E,Z*)-$Et(CO_2Et)C{=}CFCO_2Et$ (−128.4 and −116.7 ppm for *E*- and *Z*-isomer in ^{19}F NMR spectrum, respectively), which was in turn prepared directly from the reaction between $(EtO)_2P(O)CF(COCO_2Et)CO_2Et$ (**3a**) and EtMgBr.

This assignment compares favorably to the case of (*E*)-$Me(CO_2Et)C{=}CFCO_2Et$ (**4a**) (−125.5 ppm in ^{19}F NMR spectrum), whose configuration was also confirmed *via* an NOE experiment.

An alternative approach to the compound **4a** is *via* the condensation of **2** with α-keto esters to give two isomers (*E/Z* = 45/55) which exhibit signals at −126.5 and −115.0 ppm in the ^{19}F NMR spectrum. These chemical shifts are consistent with the previously observed trend. The stereochemical preference, however, for our current approach (*E/Z* = 100/0) is superior to the α-keto ester condensation as indicated in eq 4. In addition, the current approach avoids the preparation of the requisite α-keto ester.



The steroselectivity of **4f** obtained in the current approach is dependent on the metal ions and solvent. The isomer ratios obtained with different bases and solvent are illustrated in Table 2. For example, the *E/Z* ratio changes from 88/12 to 71/29 when the base is changed from lithium diisopropylamide (LDA) or lithium bis(trimethylsilyl)amide ($LiN(TMS)_2$) to sodium hydride (NaH). Similarly, there is less preferential formation of *E*-isomer over *Z*-isomer in the presence of 18-crown-6 in potassium bis(trimethylsilyl)amide ($KN(TMS)_2$).[10]

The steroselectivity of **4f** in the current approach was unaffected when the solvent was changed from THF to diethyl ether. A higher ^{19}F NMR yield (62%) was observed using $LiN(TMS)_2$ as a base in THF. However, only 40% ^{19}F NMR yield was observed with potassium *tert*-butoxide (*t*-BuOK) as a base.

The stereoselectivity of **4f** changes significantly in the presence of hexamethylphosphoric triamide (HMPT) or *N,N'*-dimethylpropyleneurea (DMPU) as cosolvents[11] as

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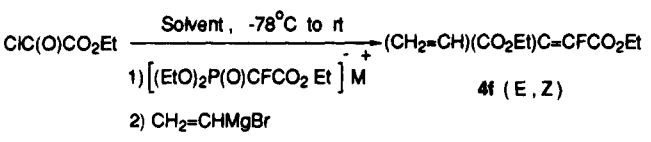
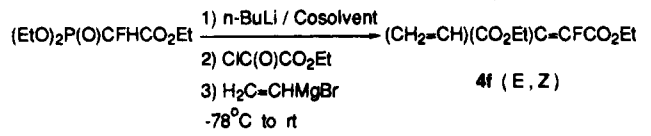
Table 2. Dependence of Solvent and Base on the Stereochemistry of 4f



no.	solvent	base	*E/Z*	yields (%)[a]
1	THF	*n*-BuLi	85/15	60
2	Et_2O	*n*-BuLi	80/20	58
3	THF	LDA	88/12	55
4	THF	$LiN(TMS)_2$	88/12	62
5	THF	*t*-BuOK	79/21	40
6	THF	$KN(TMS)_2$	76/24	54
7	THF	$KN(TMS)_2$/18-crown-6	72/28	52
8	THF	NaH	71/29	56
9	Et_2O	NaH	70/30	54

[a] ^{19}F NMR yields. $C_6H_5CF_3$ as internal standard.

Table 3. Dependence of Metal Ion and/or Cosolvent on the Stereochemistry of 4f



no.	metal ion or cosolvent	*E/Z*	yields (%)[a]
1	THF	85/15	60
2	THF/HMPT	99/1	60
3	THF/DMPU	98/2	59
4	THF/2LiCl	84/16	61

[a] ^{19}F NMR yields. $C_6H_5CF_3$ as internal standard.

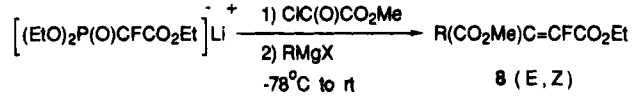
illustrated in Table 3. The use of a lithium base in a mixture of THF and HMPT or DMPU in the preparation of **4f** gave 98–99% *E*-stereoselectivity. However, the presence of lithium chloride (LiCl) in THF did not alter the *E/Z* ratio.[1,4,12,13]

A high degree of *E*-stereoselectivity was observed in most of the reactions reported in Table 1. For example, the *E*-isomer is the exclusive product when R = Me, *i*-C_3H_7, *t*-Bu, and C_6H_{11}. The *E*-isomer also predominates (96%) when R = Et and *n*-C_3H_7. However, *Z*-stereoselectivity increases when R = C_6H_5 and H_2C=CH. If R_F = C_3F_7 or C_6F_5, the *Z*-isomers were defined when R_F and fluorine were at the same side of the double bond in the products **4i** and **4j**. Thus, the *Z*-isomer is the exclusive product when R_F = C_3F_7 in compound **4i**.

In the preparation of (PhC≡C)(CO_2Et)C=$CFCO_2$Et (**4k**), attack of the salt PhC≡C^-M^+ (M = MgBr or Li) on the α-fluoro-β-keto phosphonate $(EtO)_2P(O)CF(COCO_2Et)CO_2Et$ (**3a**) gives exclusively the *Z*-isomer which exhibited a singlet at −112 ppm in the ^{19}F NMR spectrum. The repulsive interactions between phenylacetylide and fluorine led to the exclusive formation of *Z*-isomer in **4k**. Also, the repulsive interactions between C_6F_5 and fluorine resulted in the formation of *E*-isomer over *Z*-isomer in compound **4j**.

The formation of α-fluoro-α,β-unsaturated diesters is analogous to that of the Wittig reaction[14] and is illustrated in Scheme 1. For certain additions to the carbon–oxygen double bond of ketones containing an asymmetric α-carbon, the Felkin–Anh model of asymmetric induction[15] predicts the predominant diastereomer. The incoming nucleophile preferentially attacks the less hindered side of the plane containing the C=O bond. The intermediate alkoxide ion **6**, formed by the addition of R'MgX to α-fluoro-β-keto phosphonates $(EtO)_2P(O)CF(COCO_2Et)CO_2Et$ (**3a**), can exist in two diastereoisomeric forms **6a** and **6b**. The R' group attacks the carbonyl group on the side of the plane containing the fluorine atom. Thus, formation of **6a** will be favored over **6b**. Each of those intermediates decomposes *via* a syn elimination to give a specific diester ((*E*)-**4** and (*Z*)-**4**). Thus, the erythro form **6a** should lead to the *E*-isomer, while the threo form should lead to the *Z*-isomer. Different isomer ratios are possible for (*E*,*Z*)-(CH_2=CH)(CO_2Et)C=$CFCO_2$Et (**4f**) when the alkoxide ion **6a** or **6b** is associated with the lithium cation or if the cation is coordinated by HMPT or DMPU and removed from the reaction site.

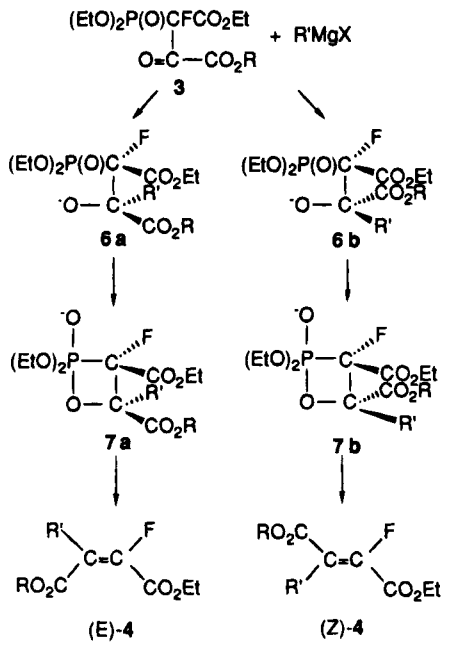
Table 4. Preparation of R(CO_2Me)C=$CFCO_2$Et



no.	R	X	*E/Z*[b]	NOE (%)	isolated yields (%)[a]
8a	Me	I	100/0	+8.0	51
8b	Et	Br	96/4		55
8c	*n*-C_3H_7	Cl	98/2		52
8d	*i*-C_3H_7	Cl	100/0		51
8e	*t*-Bu	Cl	100/0		49
8f	H_2C=CH	Br	87/13[c]	+9.2[d]	50
8g	C_6H_{11}	Cl	100/0		48
8h	Ph	Br	54/46		53

[a] Isolated yields are based on $(EtO)_2P(O)CFHCO_2Et$. [b] *E/Z* ratio was obtained by ^{19}F NMR integration of vinyl fluorine signals. [c] *E*- and *Z*-isomers were separated by flash chromatography. [d] No NOE was observed for the *Z*-isomer.

Scheme 1



Compounds R(CO_2Me)C=$CFCO_2$Et **8** were similarly prepared in 48–55% isolated yields, as summarized in

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(14) Wadsworth, W. S., Jr. *Org. React.* **1978**, *25*, 73.
(15) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353.

Table 4. Again, the assignments of the *E* and *Z* configurations were based on the chemical shift of the vinyl fluorine or confirmed by NOE. For example, Me(CO_2Me)C=$CFCO_2Et$ (**8a**) gives a positive (8.0% increase) NOE, in agreement with the *E*-assignment.

In summary, we have demonstrated that acylation of phosphonate carbanion $[(EtO)_2P(O)CFCO_2Et]^-Li^+$ (**2**) with methyl or ethyl oxalyl chloride followed by *in situ* reaction with Grignard reagents provides a direct entry to potentially useful α-fluoro-α,β-unsaturated diesters. By proper choice of Grignard reagents, the desired unsaturated diesters R′(CO_2R)C=$CFCO_2Et$ or R_F′(CO_2R)C=$CFCO_2Et$ were obtained in moderate to good yields with high *E*-stereoselectivity. When R′ is alkyl or cyclohexyl group, the *E*-isomer is the exclusive or predominant (96%) product. When R is alkenyl, alkynyl, or an aryl group, *Z*-stereoselectivity increases. However, the *E*-isomer is formed exclusively when HMPT or DMPU was used as a cosolvent in the preparation of (CH_2=CH)(CO_2Et)C=$CFCO_2Et$ (**4f**). Since the mild reaction conditions employed in this synthesis permit the presence of sensitive functionalities, this method provides a viable synthesis of biologically important α-fluoro-α,β-unsaturated diesters and permits variation of groups at the β-position.

Experimental Section

General. ^{19}F and $\{^1H\}^{31}P$ NMR spectra were recorded on a 90-MHz multinuclear spectrometer. 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 and ^{13}C NMR spectra against internal $(CH_3)_4Si$, and ^{31}P NMR spectra against an external 85% H_3PO_4 capillary. FTIR spectra were recorded as CCl_4 solutions using a solution cell with a 0.1 cm path length. All the mass spectral analyses were performed at 70 eV in the electron-impact mode on a single quadrapole instrument interfaced to a gas chromatograph fitted with an OV-101 column. High resolution mass spectral analyses were performed by the High Resolution Mass Spectroscopy Facility at 70 eV in the electron impact mode. GLPC analyses were performed on a 5% OV-101 column with a thermal conductivity detector.

Materials. $CFHBrCO_2Et$ was prepared similar to the reported preparation of ethyl chlorofluoroacetate ($CFHClCO_2$Et).[16] THF was purified by distillation from sodium benzophenone ketyl. $(EtO)_3P$ was distilled from Na metal at reduced pressure. The concentration of *n*-BuLi was determined *via* Duhamel's procedure.[17] $ClC(O)CO_2Me$, $ClC(O)CO_2Et$, Me$C(O)CO_2Et$, and HMPT were distilled prior to use. LDA, Li$N(TMS)_2$, K$N(TMS)_2$, *t*-BuOK, PhC≡CH, 18-crown-6, and DMPU were used without further purification. NaH (80% dispersion in mineral oil) was washed with *n*-hexane prior to use. Grignard reagents were prepared from RX and magnesium or by the hydrogen–metal exchange reaction for phenylacetylene–magnesium bromide. Normality of Grignard reagents was determined by the method of Bergbreiter and Pendergrass.[18] Perfluoro Grignard reagents (n-C_3F_7MgX and C_6F_5MgX) were prepared by the halogen–metal exchange reaction at low temperature.[19]

General Procedure for Preparation of R(CO_2Et)C=$CFCO_2Et$ 4 As Described for Preparation of (*E*)-Me(CO_2Et)C=$CFCO_2Et$ (4a). A 100 mL three-necked flask equipped with a septum port, a glass stopper, a magnetic stirring bar, and a reflux water condenser topped with a nitrogen T-tube leading to a source of nitrogen and mineral oil bubbler was charged sequentially with 30 mL of dry THF and 16.0 mmol (3.90 g) of $(EtO)_2P(O)CFHCO_2Et$. The contents of the flask were cooled to −78 °C in a dry ice/*i*-PrOH slush bath. To the cooled solution was added 16.0 mmol (6.4 mL) of a 2.5 M *n*-hexane solution of *n*-butyllithium dropwise *via* syringe. The resultant bright yellow solution was stirred at −78 °C and maintained at that temperature. Into another 250 mL three-necked flask equipped as above were placed 20 mL of dry THF and 16.0 mmol (2.18 g) of ethyl oxalyl chloride. The contents of the flask were stirred and cooled to −78 °C, and then the cold ylide solution generated in the first flask was added dropwise *via* syringe. The resulting mixture was stirred at −78 °C for 1 h and then allowed to warm to −10 °C over 5 h. ^{19}F NMR analysis of the reaction mixture revealed the complete consumption of the ylide and the presence of the product $(EtO)_2P(O)CF(COCO_2Et)CO_2Et$ (δ = −177.9 ppm, d, J = 73.3 Hz). The reaction mixture was cooled again to −78 °C; then 16 mmol (5.4 mL) of a 3.0 M diethyl ether solution of methylmagnesium iodide was added dropwise *via* syringe. The resultant mixture was allowed to warm to rt over 6 h and stirred at that temperature overnight. ^{19}F NMR analysis of the reaction mixture indicated the absence of **3a** and the formation of the title compound. The reaction mixture was poured into water (60 mL), and the water layer was extracted with ether (3 × 50 mL). The combined organic materials were washed with dilute HCl until the washings were neutral to litmus paper. The resulting solution was washed successively with brine (30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography (120 g of silica gel, 200–425 mesh) eluting with *n*-hexane/ethyl acetate (24/1) to give 1.69 g (52%) of the title compound (98% pure by GLPC analysis): ^{19}F NMR (δ) −125.5 (q, $^4J_{F,H}$ = 3.84); ^1H NMR (δ) 4.29 (q, 2H, $^3J_{H,H}$ = 7.18), 4.27 (q, 2H, $^3J_{H,H}$ = 7.17), 2.05 (d, 3H, $^4J_{H,F(cis)}$ = 3.87), 1.33 (t, 3H), 1.32 (t, 3H); ^{13}C NMR (δ) 169.9 (d, $^3J_{C,F}$ = 13 Hz), 159.7 (d, $^2J_{C,F}$ = 35 Hz), 147.9 (d, $^1J_{C,F}$ = 266 Hz), 121.7 (d, $^2J_{C,F}$ = 18 Hz), 62.1 (s), 61.8 (s), 13.9 (d, $^3J_{C,F}$ = 5 Hz), 13.8 (s); mass spectrum, *m/z* 204 (M^+, 0.4), 189 (4.9), 159 (11.0), 159 (11.0), 131 (100), 130 (12.8), 103 (7.5), 74 (28.2); FTIR 2984 (m), 1767 (m), 1739 (vs), 1675 (m), 1652 (m), 1456 (m), 1311 (s), 1287 (s), 1118 (m), 1111 (m); HRMS calcd 204.0798, found 204.0813.

Preparation of (*E*)- and (*Z*)-Et(CO_2Et)C=$CFCO_2Et$ (4b). Yield: 1.95 g (56%). GLPC purity: 98%. **(*E*)-4b:** ^{19}F NMR (δ) −128.4 (t, $^4J_{F,H}$ = 2.87); ^1H NMR (δ) 4.29 (q, 2H, $^3J_{H,H}$ = 7.14), 4.28 (q, 2H, $^3J_{H,H}$ = 7.15), 2.46 (d, q, 2H, $^4J_{H,F(cis)}$ = 2.97), 1.33 (t, 3H), 1.32 (t, 3H), 1.12 (t, 3H, $^3J_{H,H}$ = 7.58); ^{13}C NMR (δ) 166.5 (d, $^3J_{C,F}$ = 13 Hz), 159.8 (d, $^2J_{C,F}$ = 35 Hz), 146.7 (d, $^1J_{C,F}$ = 265 Hz), 127.9 (d, $^2J_{C,F}$ = 17 Hz), 62.7 (s), 62.1 (s), 20.9 (d, $^3J_{C,F}$ = 4 Hz), 14.0 (s), 13.9 (s), 11.7 (s); mass spectrum, *m/z* 218 (M^+, 0.7), 189 (11.8), 173 (16.7), 172 (11.3), 145 (100), 144 (52.0), 117 (18.9), 116 (11.2), 99 (10.5); FTIR 2982 (m), 2940 (m), 1744 (s), 1741 (s), 1737 (s), 1735 (s), 1669 (m), 1370 (m), 1313 (s), 1288 (m), 1252 (m), 1184 (m), 1124 (m). **(*Z*)-4b:** ^{19}F NMR (δ) −116.7 (s); mass spectrum, *m/z* 173 (36.8), 172 (32.0), 145 (21.5), 144 (100), 117 (11.0), 116 (21.1), 115 (11.0).

Preparation of (*E*)-and (*Z*)-(n-C_3H_7)(CO_2Et)C=$CFCO_2Et$ (4c). Yield: 1.92 g (54%). GLPC purity: 99%. **(*E*)-4c:** ^{19}F NMR (δ) −127.8 (t, $^4J_{F,H}$ = 2.82); ^1H NMR (δ) 4.29 (q, 2H, $^3J_{H,H}$ = 7.08), 4.27 (q, 2H, $^3J_{H,H}$ = 7.05), 2.41 (t, d, 2H, $^4J_{H,F(cis)}$ = 2.95), 1.54 (sextet, 2H, $^3J_{H,H}$ = 7.05), 1.32 (t, 3H), 1.32 (t, 3H), 0.97 (t, 3H, $^3J_{H,H}$ = 7.35); ^{13}C NMR (δ) 166.6 (d, $^3J_{C,F}$ = 13 Hz), 159.8 (d, $^2J_{C,F}$ = 35 Hz), 147.3 (d, $^1J_{C,F}$ = 265 Hz), 126.6 (d, $^2J_{C,F}$ = 16 Hz), 62.1 (s), 61.7 (s), 26.4 (d, $^3J_{C,F}$ = 3 Hz), 20.6 (s), 14.0 (s), 13.9 (s), 13.6 (s); mass spectrum, *m/z* 232 (M^+, 3.4), 204 (6.6), 203 (28.0), 187 (27.5), 186 (18.8), 175 (10.2), 159 (100), 158 (69.2), 131 (14.5); FTIR 2967 (m), 2936 (m), 1740 (s), 1738 (s), 1734 (s), 1684 (m), 1669 (m), 1653 (m), 1370 (s), 1312 (s), 1288 (s), 1184 (s). **(*Z*)-4c:** ^{19}F NMR (δ) −115.8 (s); mass spectrum, *m/z* 232 (M^+, 100), 204 (10.8), 203 (12.1), 168 (10.4), 165 (14.6), 157 (10.1), 152 (37.8), 134 (27.9), 128 (20.6), 127 (17.8), 109 (18.4).

Preparation of (*E*)-(i-C_3H_7)(CO_2Et)C=$CFCO_2Et$ (4d). Yield: 2.00 g (54%). GLPC purity: 98%. **4d:** ^{19}F NMR (δ) −130.3 (s); ^1H NMR (δ) 4.30 (q, 2H, $^3J_{H,H}$ = 7.07), 4.29 (q, 2H, $^3J_{H,H}$ = 7.06), 3.11 (hep, d, 1H, $^4J_{H,F}$ = 0.99), 1.34 (t, 3H), 1.32 (t, 3H), 1.15 (d, 6H, $^3J_{H,H}$ = 6.89); ^{13}C NMR (δ) 165.5 (d, $^3J_{C,F}$ = 13 Hz), 159.7 (d, $^2J_{C,F}$ = 35 Hz), 144.9 (d, $^1J_{C,F}$ = 265 Hz),

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(18) Bergbreiter, D. E.; Pendergrass, E. *J. Org. Chem.* **1981**, *46*, 219.
(19) Denson, D. D.; Smith, C. F.; Tamborski, C. *J. Fluorine Chem.* **1973/74**, *3*, 47.

132.7 (d, $^2J_{C,F}$ = 16 Hz), 62.0 (s), 61.5 (s), 27.2 (d, $^3J_{C,F}$ = 4 Hz), 20.3 (s), 14.0 (s), 13.9 (s); mass spectrum, *m/z* 203 (1.2), 187 (18.8), 160 (10.8), 159 (100), 158 (30.1), 131 (38.0), 130 (10.4); FTIR 2973 (m), 2874 (m), 2861 (m), 1745 (s), 1740 (s), 1737 (s), 1663 (m), 1558 (m), 1313 (s), 1308 (s), 1305 (s), 1273 (s).

Preparation of (*E*)-(*t*-Bu)(CO$_2$Et)C=CFCO$_2$Et (4e). Yield: 2.00 g (49%). GLPC purity: 98%. **4e:** ^{19}F NMR (δ) −124.7 (s); ^{1}H NMR (δ) 4.32 (q, 2H, $^3J_{H,H}$ = 7.12), 4.24 (q, 2H, $^3J_{H,H}$ = 7.14), 1.38 (t, 3H), 1.27 (d, 9H, $^4J_{H,F}$ = 1.11), 1.31 (t, 3H); ^{13}C NMR (δ) 166.2 (d, $^3J_{C,F}$ = 15 Hz), 160.1 (d, $^2J_{C,F}$ = 35 Hz), 146.1 (d, $^1J_{C,F}$ = 270 Hz), 135.4 (d, $^2J_{C,F}$ = 12 Hz), 62.0 (s), 61.4 (s), 28.8 (d, $^3J_{C,F}$ = 4 Hz), 27.8 (s), 14.0 (s), 13.9 (s); mass spectrum, *m/z* 231 (2.1), 201 (18.2), 173 (100), 157 (48.9), 145 (80.4), 131 (11.9), 129 (14.4), 127 (61.3), 125 (19.6); FTIR 2981 (m), 1739 (s), 1734 (s), 1652 (m), 1575 (m), 1558 (m), 1369 (s), 1306 (s), 1261 (m), 1242 (s).

Preparation of (*E*)- and (*Z*)-(H$_2$C=CH)(CO$_2$Et)C=CFCO$_2$Et (4f). Yield: 50%. **(*E*)-4f:** 1.46 g; GLPC purity: 98%. **(*Z*)-4f:** 0.26 g; GLPC purity: 98%. **(*E*)-4f:** ^{19}F NMR (δ) −128.1 (m, $^4J_{H,F}$ = 0.99); ^{1}H NMR (δ) 6.73 (d,d,d, 1H, $^4J_{H,F}$ = 0.99), 5.56 (d,d, 1H, $^3J_{H,H(cis)}$ = 10.57, $^2J_{H,H}$ = 1.93), 5.51 (d, 1H, $^3J_{H,H(trans)}$ = 17.1), 4.40 (q, 2H, $^3J_{H,H}$ = 7.16), 4.28 (q, 2H, $^3J_{H,H}$ = 7.10), 1.38 (t, 3H), 1.31 (t, 3H); ^{13}C NMR (δ) 164.5 (d, $^3J_{C,F}$ = 11 Hz), 159.7 (d, $^2J_{C,F}$ = 53 Hz), 144.9 (d, $^1J_{C,F}$ = 276 Hz), 125.8 (d, $^2J_{C,F}$ = 5 Hz), 125.6 (s), 123.0 (d, $^3J_{C,F}$ = 5 Hz), 62.3 (s), 62.1 (s), 14.0 (s), 13.9 (s); mass spectrum, *m/z* 217 (4.56), 216 (M$^+$, 43.2), 189 (3.3), 188 (34.3), 171 (23.9), 160 (58.2), 143 (49.3), 142 (100), 115 (6.23); FTIR 2984 (w), 1742 (s), 1734 (m), 1652 (m), 1635 (m), 1371 (s), 1324 (s), 1286 (s), 1194 (m). **(*Z*)-4f:** ^{19}F NMR (δ) −119.3 (s); ^{1}H NMR (δ) 7.34 (d,d,d, 1H, $^4J_{H,F}$ = 1.26), 5.52 (d,d, 1H, $^3J_{H,H(cis)}$ = 10.91, $^2J_{H,H}$ = 1.74), 5.50 (d, 1H, $^3J_{H,H(trans)}$ = 17.7), 4.37 (q, $^3J_{H,H}$ = 7.15), 4.34 (q, $^3J_{H,H}$ = 7.13), 1.36 (t), 1.35 (t); ^{13}C NMR (δ) 163.9 (d, $^3J_{C,F}$ = 4 Hz), 160.0 (d, $^2J_{C,F}$ = 34 Hz), 144.8 (d, $^1J_{C,F}$ = 268 Hz), 127.2 (d, $^2J_{C,F}$ = 19 Hz), 126.9 (s), 123.3 (d, $^3J_{C,F}$ = 11 Hz), 62.2 (s), 62.0 (s), 14.2 (s), 14.1 (s); mass spectrum, *m/z* 217 (1.37), 216 (M$^+$, 13.6), 189 (1.5), 171 (24.7), 160 (47.1), 143 (13.7), 142 (100), 51 (18.9); FTIR 2962 (m), 2935 (m), 1761 (m), 1740 (s), 1371 (m), 1334 (s), 1302 (s), 1261 (s), 1189 (m); HRMS calcd 216.0798, found 216.0803.

Preparation of (*E*)-(C$_6$H$_{11}$)(CO$_2$Et)C=CFCO$_2$Et (4g). Yield: 2.17 g (50%). GLPC purity: 97%. **4g:** ^{19}F NMR (δ) −130.6 (s); ^{1}H NMR (δ) 4.26 (q, 2H, $^3J_{H,H}$ = 1.72), 4.31 (q, 2H, $^3J_{H,H}$ = 7.12), 2.74 (m, 1H), 1.79–1.67 (m, 4H), 1.35–1.29 (m, 12H); ^{13}C NMR (δ) 165.7 (d, $^3J_{C,F}$ = 12 Hz), 159.8 (d, $^2J_{C,F}$ = 35 Hz), 145.1 (d, $^1J_{C,F}$ = 267 Hz), 132.2 (d, $^2J_{C,F}$ = 16 Hz), 62.2 (s), 61.5 (s), 37.2 (d, $^3J_{C,F}$ = 3 Hz), 30.4, 26.1, 25.6, 14.1 (s), 14.0 (s); mass spectrum, *m/z* 243 (2.2), 227 (4.1), 199 (34.8), 198 (18.6), 197 (11.0), 153 (23.7), 142 (11.2), 105 (29.6), 97 (17.8), 83 (34.6), 79 (29.0), 67 (56.4), 65 (15.4), 55 (100), 41 (68.1); FTIR 2982 (m), 1739 (s), 1662 (m), 1450 (m), 1330 (s), 1274 (s), 1268 (s).

Preparation of (*E*)-and (*Z*)-(C$_6$H$_5$)(CO$_2$Et)C=CFCO$_2$Et (4h). Yield: 2.34 g (55%). GLPC purity: 98%. **(*E*)-4h:** ^{19}F NMR (δ) −128.6 (s); ^{1}H NMR (δ) 7.55–7.26 (m, 5H), 4.35 (q, 2H, $^3J_{H,H}$ = 7.12), 4.28 (q, 2H, $^3J_{H,H}$ = 7.14), 1.37 (t, 3H), 1.27 (t, 3H); ^{13}C NMR (δ) 165.0 (d, $^3J_{C,F}$ = 12 Hz), 164.0 (s), 160.0 (d, $^2J_{C,F}$ = 36 Hz), 159.0 (d, $^2J_{C,F}$ = 34 Hz), 148.0 (d, $^1J_{C,F}$ = 273 Hz), 147.0 (d, $^1J_{C,F}$ = 275 Hz), 134 (s), 131 (s), 130 (s), 129 (s), 128.8 (d, $^2J_{C,F}$ = 15 Hz), 128.0 (d), 62.1 (s), 62.0 (s), 13.1 (s), 13.0 (s); mass spectrum, *m/z* 266 (M$^+$, 56.8), 221 (21.0), 193 (85.0), 190 (100), 165 (96.8), 164 (37.1); FTIR 3026 (m), 2939 (m), 1748 (s), 1738 (s), 1735 (s), 1652 (m), 1370 (s), 1304 (s), 1296 (s), 1291 (m), 1256 (s), 1241 (s), 1233 (s). **(*Z*)-4h:** ^{19}F NMR (δ) −113.3 (s); mass spectrum, *m/z* 266 (M$^+$, 43.2), 221 (26.4), 193 (54.6), 190 (95.6), 165 (100), 164 (38.2).

Preparation of (*Z*)-(*n*-C$_3$F$_7$)(CO$_2$Et)C=CFCO$_2$Et (4i). Yield: 3.6 g (63%). GLPC purity: 98%. **4i:** ^{19}F NMR (δ) −126.3 (d), −109.6 (d, q, $^4J_{F,F}$ = 10), −107.1 (t, t, $^4J_{F,F}$ = 39, $^5J_{F,F}$ = 18), −80.9 (t); ^{1}H NMR (δ) 4.37 (q, 2H, $^3J_{H,H}$ = 7.09), 4.34 (q, 2H, $^3J_{H,H}$ = 7.15), 1.37 (t, 3H), 1.33 (t, 3H); ^{13}C NMR (δ) 159.5 (d, $^3J_{C,F}$ = 11 Hz), 159.5 (t, $^3J_{C,F}$ = 3 Hz), 158.4 (d, $^2J_{C,F}$ = 33 Hz), 153.0 (d, $^1J_{C,F}$ = 296 Hz), 153.0 (t, $^3J_{C,F}$ = 6 Hz), 114.0 (q, t, $^1J_{C,F}$ = 285, $^3J_{C,F}$ = 34 Hz), 112.9 (t, q, $^1J_{C,F}$ = 295 Hz, $^3J_{C,F}$ = 33 Hz), 105.2 (d, $^2J_{C,F}$ = 37 Hz), 105.2 (t, $^2J_{C,F}$ = 36 Hz), 63.7 (s), 63.3 (s), 13.9 (s), 13.8 (s); mass spectrum, *m/z* 313 (8.2), 285 (92.0), 193 (20.1), 189 (26.6), 32 (100); FTIR 2940 (m), 1755 (s), 1752 (s), 1749 (s), 1675 (m), 1325 (s), 1263 (s), 1257 (s), 1243 (s), 1240 (s), 1237 (s), 1233 (s).

Preparation of (*E*)- and (*Z*)-(C$_6$F$_5$)(CO$_2$Et)C=CFCO$_2$Et (4j). Yield: 3.87 g (68%). GLPC purity: 98%. **4j:** ^{19}F NMR (δ) **(*E*)-4j** −163.8 (m), −153.4 (t, $^3J_{F(m),F(p)}$ = 21), −139.5 (d, d, $^3J_{F(o),F(m)}$ = 23, $^4J_{F(o),F}$ = 13), −101.9 (t, $^4J_{F,F(o)}$ = 10); **(*Z*)-4j** −163.0 (m), −153.0 (t, $^3J_{F(m),F(p)}$ = 19), −141.0 (d, $^3J_{F(o),F(m)}$ = 22), −99.2 (s); ^{1}H NMR (δ) 4.42 (q, 2H, $J_{H,H}$ = 7.13), 4.30 (q, 2H, $J_{H,H}$ = 7.13), 1.41 (t, 3H), 1.31 (t, 3H); ^{13}C NMR (δ) 162.7 (d, $^3J_{C,F}$ = 12 Hz), 159.0 (d, $^2J_{C,F}$ = 34 Hz), 155.0 (d, $^1J_{C,F}$ = 286 Hz), 146.3 (s), 142.9 (s), 139.6 (s), 136.2 (s), 108.0 (d, $^2J_{C,F}$ = 15 Hz), 63.3 (s), 62.8 (s), 13.8 (s), 13.7 (s); mass spectrum, *m/z* 356 (M$^+$, 7.3), 311 (6.4), 284 (9.9), 283 (76.8), 280 (22.56), 255 (100), 236 (17.5), 45 (35.3); FTIR 2940 (m), 1741 (s), 1737 (s), 1669 (m), 1504 (s), 1501 (s), 1499 (s), 1444 (s), 1305 (s), 1279 (s), 1276 (s), 1272 (s), 1063 (s), 995 (s); HRMS calcd 356.0483, found 356.0461.

Preparation of (*Z*)-(PhC≡C)(CO$_2$Et)C=CFCO$_2$Et (4k). Yield: 3.02 g (65%). GLPC purity: 99%. **4k:** ^{19}F NMR (δ) −112.0 (s); ^{1}H NMR (δ) 7.55 (m, 2H), 7.35 (m, 3H), 4.36 (q, 2H, $^3J_{H,H}$ = 7.13), 4.34 (q, 2H, $^3J_{H,H}$ = 7.13), 1.37 (t), 1.35 (t); ^{13}C NMR (δ) 162 (s), 159 (s), 151 (s), 131 (s), 130 (d, $^1J_{C,F}$ = 270 Hz), 129 (s), 77.1 (d, $^3J_{C,F}$ = 4.5 Hz), 76.8 (s), 62.8 (s), 62.7 (s), 13.9 (s), 13.8 (s); mass spectrum, *m/z* 290 (22.8), 261 (25.2), 233 (92.7), 218 (15.4), 217 (41.0), 214 (24.8), 190 (22.4), 189 (46.5), 170 (19.7), 161 (22.1), 144 (100), 133 (78.7); FTIR 2985 (s), 1745 (vs), 1739 (vs), 1629 (s), 1371 (s), 1312 (vs), 1244 (s), 1184 (s), 1088 (s); HRMS calcd 290.0955, found 290.0961.

General Procedure for Dependence of Solvent and Base on the Stereochemistry of (*E*,*Z*)-(CH$_2$=CH)(CO$_2$Et)-C=CFCO$_2$Et (4f) As Described by Reaction of the Anion Derived from (EtO)$_2$P(O)CFHCO$_2$Et Using KN(TMS)$_2$/18-Crown-6 in THF with ClC(O)CO$_2$Et and CH$_2$=CHMgBr. A solution of 4.1 mmol (1.0 g) of (EtO)$_2$P(O)CFHCO$_2$Et and 8 mL of dry THF was cooled to −78 °C in a dry ice/*i*-PrOH slush bath under N$_2$. To the cooled solution was added 4.1 mmol (8.2 mL) of a 0.5 M toluene solution of potassium bis-(trimethylsilyl)amide dropwise *via* syringe. The resultant bright yellow solution was allowed to warm to 5 °C and maintained at that temperature. Into another 100 mL three-necked flask equipped as above were placed 8 mL of dry THF, 4.1 mmol (0.55 g) of ethyl oxalyl chloride, and 4.1 mmol (1.1 g) of 18-crown-6. The contents of the flask were stirred and cooled to −78 °C, and then the cold ylide solution generated in the first flask was added dropwise *via* syringe. The resulting mixture was stirred at −78 °C for 1 h and then allowed to warm to −10 °C over 5 h. ^{19}F NMR analysis of the reaction mixture revealed the complete consumption of the ylide and the presence of the product (EtO)$_2$P(O)CF(COCO$_2$-Et)CO$_2$Et (δ = −177.9 ppm, d, J = 73.3 Hz). The reaction mixture was cooled again to −78 °C; then 4.0 mmol (4.0 mL) of a 1.0 M THF solution of vinylmagnesium bromide was added dropwise *via* syringe. The resultant mixture was allowed to warm to rt over 6 h and stirred at that temperature overnight. ^{19}F NMR analysis of the reaction mixture indicated the absence of **3a** and the formation of the diester compound **4f**. The reaction mixture was poured into water (45 mL), and the water layer was extracted with ether (3 × 30 mL). The combined organic extracts were washed with dilute HCl until the washings were neutral to litmus paper. The resulting solution was washed successively with brine (20 mL) and water (20 mL), dried over MgSO$_4$, and concentrated in vacuo to give 52% ^{19}F NMR yield of the title compound **4f**. The *E*/*Z* ratio of the unsaturated diester, determined by the integration of vinyl fluorine signals in the ^{19}F NMR spectrum, was 72 to 28.

General Procedure for Dependence of Metal ion and/or Cosolvent on the Stereochemistry of (*E*,*Z*)-(CH$_2$=CH)-(CO$_2$Et)C=CFCO$_2$Et (4f) As Described by Reaction of the Anion Derived from (EtO)$_2$P(O)CFHCO$_2$Et Using *n*-BuLi in THF/HMPT with ClC(O)CO$_2$Et and CH$_2$=CHMgBr. A solution of 4.1 mmol (1.0 g) of (EtO)$_2$P(O)CFHCO$_2$Et and 8 mL of dry THF was cooled to −78 °C in a dry ice/*i*-PrOH slush bath under N$_2$. To the cooled solution was added 4.1 mmol (1.7 mL) of a 2.5 M *n*-hexane solution of *n*-butyllithium

dropwise *via* syringe. The resultant bright yellow solution was allowed to warm to 5 °C and maintained at that temperature. Into another 100 mL three-necked flask equipped as above was placed 8 mL of dry THF, 4 mmol (0.6 mL) of HMPT, and 4.1 mmol (0.55 g) of ethyl oxalyl chloride. The contents of the flask were stirred and cooled to −78 °C, and then the cold ylide solution generated in the first flask was added dropwise *via* syringe. The resulting mixture was stirred at −78 °C for 1 h and then allowed to warm to −10 °C over 5 h. ^{19}F NMR analysis of the reaction mixture revealed the complete consumption of the ylide and the presence of the product $(EtO)_2P(O)CF(COCO_2Et)CO_2Et$ (δ = −177.9 ppm, d, J = 73.3 Hz). The reaction mixture was cooled again to −78 °C; then 4.0 mmol (4.0 mL) of a 1.0 M THF solution of vinylmagnesium bromide was added dropwise *via* syringe. The resultant mixture was allowed to warm to rt over 6 h and stirred at that temperature overnight. ^{19}F NMR analysis of the reaction mixture indicated the absence of **3a** and the formation of the diester compound **4f**. The reaction mixture was poured into water (45 mL), and the water layer was extracted with ether (3 × 30 mL). The combined organic extracts were washed with dilute HCl until the washings were neutral to litmus paper. The resulting solution was washed successively with brine (20 mL) and water (20 mL), dried over $MgSO_4$, and concentrated in vacuo to give 60% ^{19}F NMR yield of **4f**. The *E*/*Z* ratio of the unsaturated diester, determined by the integration of vinyl fluorine signals in the ^{19}F NMR spectrum, was 99 to 1.

General Procedure for Preparation of R(CO_2Me)C=CFCO_2Et (8) As Described by Preparation of (*E*)-Me(CO_2Et)C=CFCO_2Et (8a). A solution of 16.0 mmol (3.90 g) of $(EtO)_2P(O)CFHCO_2Et$ and 30 mL of dry THF was cooled to −78 °C in a dry ice/*i*-PrOH slush bath under N_2. To the cooled solution was added 16.0 mmol (6.4 mL) of a 2.5 M *n*-hexane solution of *n*-butyllithium dropwise *via* syringe. The resultant bright yellow solution was stirred at −78 °C and maintained at that temperature. Into another 250 mL three-necked flask equipped as above were placed 20 mL of dry THF and 16.0 mmol (1.96 g) of methyl oxalyl chloride. The contents of the flask were stirred and cooled to −78 °C, and then the cold ylide solution generated in the first flask was added dropwise *via* syringe. The resulting mixture was stirred at −78 °C for 1 h and then allowed to warm to −10 °C over 5 h. ^{19}F NMR analysis of the reaction mixture revealed the complete consumption of the ylide and the presence of the product $(EtO)_2P(O)CF(COCO_2Me)CO_2Et$ (δ = −178.3 ppm, d, J = 73.3 Hz). The reaction mixture was cooled again; then 16 mmol (5.4 mL) of a 3.0 M diethyl ether solution of methylmagnesium iodide was added dropwise *via* syringe. The resultant mixture was allowed to warm to rt over 6 h and stirred at that temperature overnight. ^{19}F NMR analysis of the reaction mixture indicated the absence of **3b** and the formation of the title compound. The reaction mixture was poured into water (60 mL), and the water layer was extracted with ether (3 × 50 mL). The combined organic extracts were washed with dilute HCl until the washings were neutral to litmus paper. The resulting solution was washed successively with brine (30 mL) and water (30 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography (120 g of silica gel, 200−425 mesh) eluting with *n*-hexane/ethyl acetate (24/1) to give 1.55 g (51%) of the title compound (98% pure by GLPC analysis): ^{19}F NMR (δ) −125.1 (q, $^4J_{F,H}$ = 3.87); ^{1}H NMR (δ) 4.30 (q, 2H, $^3J_{H,H}$ = 7.33), 3.83 (s, 3H), 2.03 (d, 3H, $^4J_{H,F(cis)}$ = 3.91), 1.35 (t, 3H); ^{13}C NMR (δ) 167.5 (d, $^3J_{C,F}$ = 13 Hz), 159.7 (d, $^2J_{C,F}$ = 35 Hz), 148.0 (d, $^1J_{C,F}$ = 266 Hz), 121.5 (d, $^2J_{C,F}$ = 18 Hz), 62.2 (s), 52.6 (s), 14.0 (s), 12.9 (d, $^4J_{C,F}$ = 5 Hz); mass spectrum, *m*/*z* 190 (M^+, 1.2), 159 (13.9), 158 (15.5), 145 (48.9), 131 (100), 130 (28.9), 117 (20.9); FTIR 2985 (m), 1746 (s), 1743 (s), 1740 (s), 1736 (s), 1676 (m), 1378 (m), 1307 (s), 1305 (s), 1303 (s), 1298 (s), 1295 (s).

Preparation of (*E*)- and (*Z*)-Et(CO_2Me)C=CFCO_2Et (8b). Yield: 1.79 g (55%). GLPC purity: 98%. **(*E*)-8b:** ^{19}F NMR (δ) −128.0 (t, $^4J_{F,H}$ = 2.96); ^{1}H NMR (δ) 4.25 (q, 2H, $^3J_{H,H}$ = 7.12), 3.78 (s, 3H), 2.42 (q, d, 2H, $^4J_{H,F(cis)}$ = 2.39), 1.29 (t, 3H), 1.07 (t, 3H, $^3J_{H,H}$ = 7.59); ^{13}C NMR (δ) 167.0 (d, $^3J_{C,F}$ = 13 Hz), 159.7 (d, $^2J_{C,F}$ = 34 Hz), 146.8 (d, $^1J_{C,F}$ = 266 Hz), 127.7 (d, $^2J_{C,F}$ = 17 Hz), 62.1 (s), 52.5 (s), 20.9 (d, $^4J_{C,F}$ = 4 Hz), 14.0 (s), 11.7 (s); mass spectrum, *m*/*z* 204 (M^+, 2.13), 172 (26.9), 159 (40.2), 158 (11.2), 145 (100), 144 (89.4), 131 (25.8), 117 (22.1), 116 (20.2), 115 (26.6), 99 (23.7), 71 (42.0), 69 (22.3); FTIR 2952 (m), 2880 (m), 1742 (s), 1739 (s), 1734 (s), 1684 (w), 1670 (m), 1653 (m), 1371 (s), 1314 (s), 1292 (s). **(*Z*)-8b:** ^{19}F NMR (δ) −116.8 (s); mass spectrum, *m*/*z* 172 (17.5), 159 (24.7), 145 (61.3), 144 (50.4), 117 (23.7), 116 (17.9), 115 (21.6), 99 (30.0), 72 (32.5), 71 (80.4), 69 (44.6), 59 (100), 57 (47.9).

Preparation of (*E*)- and (*Z*)-(*n*-C_3H_7)(CO_2Me)C=CFCO_2Et (8c). Yield: 1.78 g (52%). GLPC purity: 99%. **(*E*)-8c:** ^{19}F NMR (δ) −127.5 (t, $^4J_{F,H}$ = 2.86); ^{1}H NMR (δ) 4.29 (q, 2H, $^3J_{H,H}$ = 7.13), 3.81 (s, 3H), 2.41 (t, d, 2H, $^4J_{C,F(cis)}$ = 3.03), 1.52 (sextet, 2H, $^3J_{H,H}$ = 7.48), 1.33 (t, 3H), 0.96 (t, 3H, $^3J_{H,H}$ = 7.36); ^{13}C NMR (δ) 167.2 (d, $^3J_{C,F}$ = 13 Hz), 159.8 (d, $^2J_{C,F}$ = 35 Hz), 147.3 (d, $^1J_{C,F}$ = 265 Hz), 126.4 (d, $^3J_{C,F}$ =17 Hz), 62.2 (s), 52.5 (s), 29.4 (d, $^3J_{C,F}$ = 3.4 Hz), 20.5 (s), 14.0 (s), 13.6 (s); mass spectrum, *m*/*z* 218 (M^+, 4.9), 189 (27.6), 187 (17.7), 186 (26.1), 173 (44.8), 159 (80.4), 158 (100), 157 (21.7), 145 (25.4), 130 (57.3), 113 (48.3), 59 (70.6); FTIR 2953 (m), 1740 (s), 1718 (s), 1700 (s), 1669 (m), 1313 (s), 1291 (s), 1226 (s), 1180 (m). **(*Z*)-8c:** ^{19}F NMR (δ) −116.9 (s); mass spectrum, *m*/*z* 203 (9.4), 187 (11.3), 159 (100), 158 (71.0), 131 (29.6), 130 (67.3), 113 (37.0), 102 (25.6), 101 (10.5).

Preparation of (*E*)-(*i*-C_3H_7)(CO_2Me)C=CFCO_2Et (8d). Yield: 1.74 g (51%). GLPC purity: 98%. **8d:** ^{19}F NMR (δ) −129.9 (s); ^{1}H NMR (δ) 4.28 (q, $^3J_{H,H}$ = 7.15), 3.82 (s), 3.10 (hep, d, $^4J_{H,F}$ = 1.02), 1.32 (t, 3H), 1.15 (d, 6H, $^3J_{H,H}$ = 6.96); ^{13}C NMR (δ) 166.1 (d, $^3J_{C,F}$ = 13 Hz), 159.8 (d, $^2J_{C,F}$ = 34 Hz), 145.2 (d, $^1J_{C,F}$ = 264 Hz), 132.6 (d, $^2J_{C,F}$ = 16 Hz), 62.1 (s), 52.3 (s), 27.3 (d), 20.3 (s), 14.0 (s); mass spectrum, *m*/*z* 219 (0.1), 218 (M^+, 1.0), 187 (13.5), 173 (23.0), 159 (100), 158 (44.1), 145 (48.0), 131 (54.9), 113 (51.0); FTIR 2952 (m), 1767 (s), 1741 (s), 1664 (m), 1311 (s), 1276 (s), 1198 (s), 1182 (m).

Preparation of (*E*)-(*t*-Bu)(CO_2Me)C=CFCO_2Et (8e). Yield: 1.82 g (49%). GLPC purity: 98%. **8e:** ^{19}F NMR (δ) −124.3 (s); ^{1}H NMR (δ) 4.27 (q, 2H, $^3J_{H,H}$ = 7.17), 3.81 (s, 3H), 1.30 (t, 3H), 1.27 (d, 9H, $^3J_{H,F}$ = 1.00); ^{13}C NMR (δ) 166.7 (d, $^3J_{C,F}$ = 16 Hz), 158.9 (d, $^2J_{C,F}$ = 34 Hz), 146.1 (d, $^1J_{C,F}$ = 270 Hz), 135.4 (d, $^2J_{C,F}$ = 12 Hz), 62.2 (s), 52.2 (s), 34.8 (d, $^3J_{C,F}$ = 2.4 Hz), 28.8 (s), 14.0 (s); mass spectrum, *m*/*z* 217 (4.9), 201 (12.2), 187 (12.7), 173 (100), 159 (34.2), 157 (66.8), 145 (71.1), 127 (58.8), 73 (53.0), 57 (62.6), 41 (30.6); FTIR 2973 (m), 2875 (m), 1749 (s), 1738 (s), 1734 (s), 1732 (s), 1652 (m), 1585 (s), 1554 (s), 1370 (s), 1311 (s), 1301 (s), 1269 (s), 1180 (m), 1164 (s), 1160 (s).

Preparation of (*E*)- and (*Z*)-(H_2C=CH)(CO_2Me)C=CFCO_2Et (8f). Yield: 50%. **(*E*)-8f:** 1.41 g; GLPC purity: 98%. **(*Z*)-8f:** 0.21 g; GLPC purity: 98%. **(*E*)-8f:** ^{19}F NMR (δ) −127.0 (m); ^{1}H NMR (δ) 6.72 (d, d, d, $^4J_{H,F}$ = 0.94), 5.55 (d, d, $^3J_{H,H(cis)}$ = 10.85, $^2J_{H,H}$ = 1.94), 5.49 (d, $^3J_{H,H(trans)}$ = 17.7), 4.31 (q, 2H, $^3J_{H,H}$ = 7.11), 3.86 (s, 3H), 1.34 (t, 3H); ^{13}C NMR (δ) 165.0 (d, $^3J_{C,F}$ = 11 Hz), 159.8 (d, $^2J_{C,F}$ = 33 Hz), 145.1 (d, $^1J_{C,F}$ = 276 Hz), 125.7 (d, $^2J_{C,F}$ = 5 Hz), 123.1 (d, $^3J_{C,F}$ = 5 Hz), 115.5 (s), 62.4 (s), 52.8 (s), 14.0 (s); mass spectrum, *m*/*z* 202 (M^+, 39.7), 174 (100), 159 (25.0), 157 (32.2), 143 (58.2), 129 (63.4), 114 (30.0), 87 (68.2), 86 (41.8), 70 (58.2), 59 (57.5), 51 (43.5); FTIR 2951 (m), 1739 (s), 1735 (s), 1721 (s), 1718 (s), 1321 (s), 1300 (s), 1297 (s), 1186 (m). **(*Z*)-8f:** ^{19}F NMR (δ) −117.6 (s); ^{1}H NMR (δ) 7.34 (d, d, d, 1H, $^4J_{H,F}$ = 1.28), 5.52 (d, d, d, 1H, $^3J_{H,H(cis)}$ = 10.99, $^2J_{H,H}$ = 0.88, $^3J_{H,F}$ = 0.44), 5.47 (d, 1H, $^3J_{H,H(trans)}$ = 17.6), 4.34 (q, 2H, $^3J_{H,H}$ = 7.12), 3.89 (s, 3H), 1.36 (t, 3H); ^{13}C NMR (δ) 164.4 (d, $^3J_{C,F}$ = 4 Hz), 159.9 (d, $^2J_{C,F}$ = 34 Hz), 144.9 (d, $^1J_{C,F}$ = 268 Hz), 126.8 (s), 125.5 (d, $^3J_{C,F}$ = 11 Hz), 123.5 (d, $^2J_{C,F}$ =14 Hz), 62.2 (s), 52.7 (s), 14.1 (s); mass spectrum, *m*/*z* 202 (M^+, 2.5), 129 (4.5), 40 (14.7), 32 (100); FTIR 2955 (m), 2924 (m), 1743 (s), 1740 (s), 1730 (s), 1650 (w), 1371 (s), 1339 (s), 1269 (s).

Preparation of (*E*)-(C_6H_{11})(CO_2Me)C=CFCO_2Et (8g). Yield: 1.98 g (48%). GLPC purity: 96%. **8g:** ^{19}F NMR (δ) −130.3 (s); ^{1}H NMR (δ) 4.27 (q, 2H, $^3J_{H,H}$ = 7.15), 3.82 (s, 3H), 2.74 (m, 1H), 1.78−1.67 (m, 4H), 1.34−1.28 (m, 9H); ^{13}C NMR (δ) 166.0 (d, $^3J_{C,F}$ = 13 Hz), 159.8 (d, $^2J_{C,F}$ = 34 Hz), 145.2 (d, $^1J_{C,F}$ = 264 Hz), 132.1 (d, $^2J_{C,F}$ = 16 Hz), 62.1 (s), 52.3 (s), 37.0 (d, $^3J_{C,F}$ = 2 Hz), 30.4 (s), 26.1 (s), 25.5 (s), 14.0 (s); mass spectrum, *m*/*z* 258 (M^+, 1.2), 227 (15.4), 226 (45.7), 213 (21.3), 199 (40.6), 198 (53.2), 197 (26.0), 185 (61.4), 177 (26.0), 169

(26.8), 153 (53.9); FTIR 2857 (m), 1744 (s), 1741 (s), 1736 (s), 1662 (m), 1450 (m), 1437 (s), 1308 (s), 1276 (s), 1237 (s), 1179 (m).

Preparation of (*E*)- and (*Z*)-(C_6H_5)(CO_2Me)C=CFCO_2Et (8h). Yield: 2.13 g (53%). GLPC purity: 98%. **(*E*)-8h:** ^{19}F NMR (δ) −128.1 (s); ^{1}H NMR (δ) 7.55–7.31 (m, 5H), 4.35 (q, 2H, $^3J_{H,H}$ = 7.15), 3.87 (s, 3H), 1.36 (t, 3H); ^{13}C NMR (δ) 166.0 (d, $^3J_{C,F}$ = 11 Hz), 165.0 (s), 160.0 (d, $^2J_{C,F}$ = 33 Hz), 159.0 (d, $^2J_{C,F}$ = 35 Hz), 148.2 (d, $^1J_{C,F}$ = 274 Hz), 145.5 (d, $^1J_{C,F}$ = 273 Hz), 130–128 (m), 125.0 (d, $^2J_{C,F}$ = 14 Hz), 124.0 (d, $^2J_{C,F}$ = 15 Hz), 62.5 (s), 62.0 (s), 53.0 (s), 52.8 (s), 14.0 (s), 13.5 (s); mass spectrum, *m/z* 252 (9.2), 193 (15.6), 179 (100), 176 (28.7), 165 (18.8), 164 (14.1), 120 (56.3), 109 (51.9), 108 (23.6), 103 (28.0), 101 (31.7), 94 (20.2), 87 (50.4); FTIR 2953 (m), 1746 (s), 1744 (s), 1652 (m), 1558 (s), 1545 (s), 1542 (s), 1371 (s), 1322 (s), 1303 (s), 1255 (s), 1229 (s), 1227 (s). **(*Z*)-8h:** ^{19}F NMR (δ) −111.9 (s); ^{1}H NMR (δ) 7.55–7.31 (m, 5H), 4.07 (q, 2H, $^3J_{H,H}$ = 7.15), 3.81 (s, 3H), 1.02 (t, 3H); mass spectrum, *m/z* 252 (35.3), 221 (10.7), 180 (11.5), 179 (100), 176 (27.9), 165 (14.8), 164 (10.5), 120 (13.6).

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