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Short communication

1,4-Addition of tetraethyl fluoromethylenebisphosphonate to α,β-unsaturated compounds

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ABSTRACT

Tetraethyl fluoromethylenebisphosphonate in the presence of cesium carbonate in DMF undergoes efficient 1,4-addition to Michael acceptors having terminal double bond such as α,β-unsaturated ketones, esters, sulfones, sulfoxides, and phosphonates to yield the corresponding adducts (α-alkyl-α-fluoromethylenebisphosphonates) in good to excellent yields.

1. Introduction

Bisphosphonates are compounds of interesting biological properties. Currently, there is a number of drugs based on bisphosphonates that are used for the treatment of various bone diseases (such as osteoporosis, Paget's disease, tumor-induced osteolysis, and hypercalcemia) [1]. Bisphosphonates have also been found to have anticancer [2], antiparasitic [3], and herbicidal [4] properties. They are non-hydrolyzable analogues of the endogenous pyrophosphate in which the oxygen bridge is replaced by a carbon atom. The most potent bisphosphonates currently in use as anti-resorptive agents such as ibandronate, alendronate, risedronate and zoledronate consist of hydroxyl group and nitrogen-containing side chain attached to the bridging carbon atom. It was found recently by McKenna and co-workers that the replacement of hydroxyl group in risedronate for fluorine atom retains the biological activity but leads to reduced bone affinity, which can be useful therapeutically in certain situations [5]. These findings make α-alkyl-α-fluoromethylenebisphosphonates particularly interesting targets in the search for new biologically active bisphosphonates.

Previously, α-alkyl-α-fluoromethylenebisphosphonates have been prepared by one of these methods: (a) addition of carbon or nitrogen nucleophiles to bis(diethylphosphono)ethylene, followed by electrophilic fluorination [6], (b) alkylation of methylenebisphosphonate followed by electrophilic fluorination [5], (c) reaction of lithium salt of diethyl fluoromethylenebisphosphonate (**1**) with methylating agents such as iodomethane or dimethylsulfate (other alkylating reagents such as iodoethane fail in this reaction) [7]. Very recently, we have reported a general methodology towards α-alkyl-α-fluoromethylenebisphosphonates starting from **1** and employing alkylation with various alkyl halides using either cesium carbonate in DMF or sodium dimsyl [8]. Also it was shown by us that **1** undergoes Horner–Wadsworth–Emmons reactions with aromatic aldehydes in the presence of excess of cesium carbonate to provide α-fluorovinylphosphonates in excellent yields, however, with only moderate *E*:*Z* selectivity [9]. These results demonstrated that sodium or cesium salt of **1** is stable in polar aprotic solvents at room temperature and nucleophilic enough to affect the desired alkylation reaction, and prompted us to investigate 1,4-addition of carbanion of **1** to α,β-unsaturated compounds as a new method towards α-alkyl-α-fluoromethylenebisphosphonates.

Fluorinated carbanions often react as "hard" nucleophiles giving the products of 1,2-addition instead of 1,4-addition with Michael type acceptors. This is the general reactivity observed for the trifluoromethyl group transfer using the Ruppert–Prakash reagent ($TMSCF_3$) [10] unless a special reaction design is used such as protection of carbonyl function with a bulky Lewis acid [11]. However, electron deficient arylidenemalonitriles undergo efficient Michael additions [12] and 1,4-addition is also observed with 2-perfluoroalkylchromones [13], 3-arylchromones [14], quinolones [13] and coumarins [11]. Investigations of 1,2- and 1,4-additions to α,β-unsaturated ketones, esters and nitroolefins carried out by Hu and co-workers have shown that the order of soft to hard character of fluorinated sulfone-containing carbanions is as

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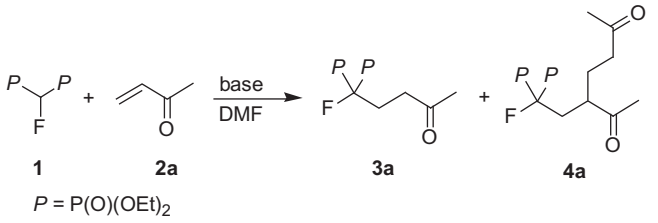
follows: $(PhSO_2)_2CF^- > PhSO_2CHF^- > PhSO_2CF_2^-$ [15]. 1,4-Additions of monofluoromethylene moieties are known. For example, Prakash and co-workers have described efficient conjugate additions of $PhSO_2CHFR$ (R = NO_2, CN, CO_2Et, SO_2Ph) to α,β-unsaturated compounds using either trimethylphosphine or potassium carbonate at room temperature [16]. Michael addition reactions between α-fluoro-β-keto esters and α,β-unsaturated ketones or esters proceed at room temperature in the presence of spray-dried potassium fluoride [17]. Using the same base α-fluoronitroalkanes undergo 1,4-addition to methyl vinyl ketone or acrylonitrile [18]. Some enantioselective Michael additions of monofluoromethylene moieties have been published recently. Enantioselective Michael addition of 1-fluoro-bis(phenylsulfonyl)-methane to α,β-unsaturated ketones catalyzed by ammonium salts of cinchona alkaloids in the presence of excess of cesium carbonate have been reported by Shibata and co-workers [19] and highly efficient stereoselective Michael addition of α-fluoro-α-nitro(phenylsulfonyl)methane to chalcones catalyzed by cinchona alkaloid-derived chiral bifunctional triourea organocatalysts have been reported by Prakash and co-workers [20].

2. Results and discussion

First, 1,4-addition of tetraethyl fluoromethylenebisphosphonate (**1**) to model Michael acceptor – methyl vinyl ketone (**2a**) was tested in the presence of equimolar amounts of triphenylphosphine as nucleophilic initiator in THF. However, even after 24 h at ambient temperature, no addition product **3a** was observed. The use of two-fold excess of potassium carbonate in DMF was more successful and low conversions of the desired adduct **3a** were observed accompanied by small amounts of double addition product **4a** after prolonged reaction time (Table 1, entries 1 and 2). Employment of cesium carbonate led to considerable improvements in the reaction outcome. Further optimization experiments revealed that conducting the reaction at room temperature with two equivalents of cesium carbonate provided good yield of the desired product **3a** while the formation of the double addition side product **4a** was negligible (Table 1, entry 4).

Optimized reaction conditions were used in the scope and limitation study of the 1,4-addition of **1** to various α,β-unsaturated compounds (Table 2). Addition to methyl vinyl ketone proceeded smoothly to give the addition adduct **3a** in 67% isolated yield (Table 2, entry 1). The use of methyl acrylate gave **3b** in 81% yield in 22 h (Table 2, entry 2). Diethyl vinylphosphonate **2c** provided the corresponding adduct **3c** in a good yield (Table 2, entry 3) and it was found that the long reaction time could be shortened to 48 h by conducting the reaction at 50 °C with similar product conversion. Very good 80% yield was obtained by using phenyl vinyl sulfoxide (**2d**). Phenyl vinyl sulfone represented the most reactive Michael acceptor tested; the corresponding adduct **3e** was obtained in 90% isolated yield. Addition to the triple bond of ethyl propiolate (**2f**) gave the adducts in combined 48% yield. Each stereoisomer was isolated by column chromatography and the major *Z*-isomer was obtained in 35% yield (Table 2, entry 6). α-Alkyl substitution on the Michael acceptor dramatically slows down the reaction as observed for methyl methacrylate (**2g**). Unfortunately, β-substituted Michael acceptors were not reactive as judged by ^{19}F and ^{31}P NMR of reaction mixtures, which showed only signals corresponding to starting bisphosphonate **1**. This was the case for 2-cyclohexenone, chalcone and even strongly activated acceptors such as nitrostyrene or benzylidenemalononitrile (Table 2, entries 8–11). As shown by Dilman and co-workers [12] the trifluoromethyl, pentafluoroethyl and pentafluorophenyl group could be efficiently transferred to **2k** using corresponding silanes in the presence of sodium acetate as a nucleophilic initiator. Highly sterically demanding character of the carbanion of fluoromethy-

Table 1
Optimization of the 1,4-addition of tetraethyl fluoromethylenebisphosphonate (**1**) to methyl vinyl ketone (**2a**)[a]



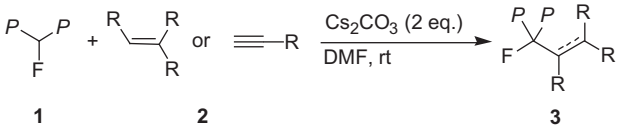
1 **2a** **3a** **4a**

P = P(O)(OEt)$_2$

Entry	Base (eq.)	Temp. (°C)	Time (h)	**3a**, Yield (%)	**4a**, Conv. (%)[b]
1	K_2CO_3 (2)	rt	21	17[b]	0
2	K_2CO_3 (2)	rt	49	45[b]	4
3	Cs_2CO_3 (1)	rt	19	44[c]	0
4	Cs_2CO_3 (2)	rt	6	88[c], 67[d]	2
5	Cs_2CO_3 (3)	rt	6	61[c], 48[d]	2
6	Cs_2CO_3 (2)	50	0.75	74[b]	9

[a] Reactions were carried out using **1** (0.3 mmol, 1 eq.), **2a** (0.75 mmol, 2.5 eq.), base (0.3–0.9 mmol, 1–3 eq.) in DMF (2 mL).
[b] Conversion estimated by GC–MS analysis.
[c] ^{19}F NMR yield using 4-fluoroanisole as internal standard (20 s relaxation time).
[d] Isolated yield.

Table 2
1,4-Addition of tetraethyl fluoromethylenebisphosphonate (**1**) to α,β-unsaturated compounds (**2**)[a]



1 **2** **3**

P = P(O)(OEt)$_2$

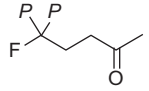
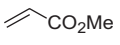
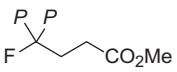
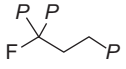
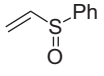
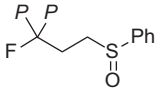
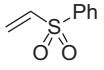
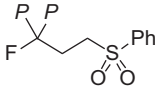
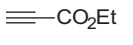
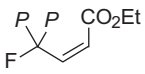
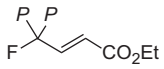
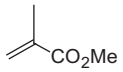
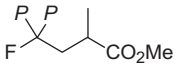
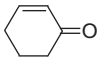
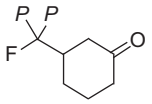
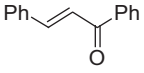
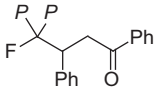
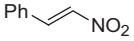
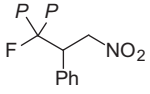
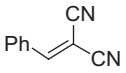
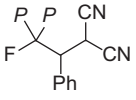
Entry	**2**	Michael acceptor (eq.)	Time (h)	**3**	Product	Yield (%)[b]
1	**2a**		2.5 6	**3a**		67
2	**2b**		1.5 22	**3b**		81
3	**2c**		2.0 144	**3c**		77
4	**2d**		2.5 18	**3d**		80
5	**2e**		1.2 3	**3e**		90

Table 2 (*Continued*)

Entry	2	Michael acceptor (eq.)	Time (h)	3	Product	Yield (%)[b]
6	**2f**		2.5 18	(*Z*)-**3f**		35
				(*E*)-**3f**		13
7	**2g**		2.5 168	**3g**		25[c]
8	**2h**		2.5 72	**3h**		0
9	**2i**		1.3 168	**3i**		0
10	**2j**		2.5 72	**3j**		0
11	**2k**		2.5 72	**3k**		0

[a] Reactions were carried out using **1** (0.3 mmol, 1 eq.), **2** (0.36–0.75 mmol, 1.2–2.5 eq.), Cs_2CO_3 (0.6 mmol, 2 eq.) in DMF (1 mL) at rt.
[b] Isolated yield.
[c] ^{19}F NMR yield using 4-fluoroanisole as internal standard (20 s relaxation time).

lenebisphoshonate **1** explains the observed lack of reactivity with **2k**.

3. Conclusion

In conclusion, tetraethyl fluoromethylenebisphosphonate (**1**) in the presence of two-fold excess of cesium carbonate in DMF reacts with Michael acceptors having terminal double or triple bond in 1,4-addition fashion to provide α-alkyl or α-alkenyl-α-fluoromethylenebisphosphonates **3** in moderate to excellent yields. Michael acceptors with substituted double bond in β position were found to be unreactive.

4. Experimental

^1H, ^{13}C {^1H}, ^{19}F and ^{31}P {^1H} NMR spectra were recorded in $CDCl_3$ on a Bruker 400 MHz instrument at 400, 100.6, 376, and 162 MHz, respectively. Chemical shifts (δ) are reported in ppm relative to Me_4Si (0 ppm, for ^1H NMR), residual $CHCl_3$ (7.26 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR), internal $CFCl_3$ (0 ppm for ^{19}F NMR), and external H_3PO_4 in water (0 ppm for ^{31}P NMR). GC–MS spectra were recorded on an Agilent 7890A gas chromatograph coupled with 5975C quadrupole mass selective electron impact (EI) detector (70 eV). High resolution mass spectra (HRMS) were recorded on a LTQ Orbitrap XL instrument using electrospray (ESI) ionization. Reactions were conducted under Ar. DMF was dried by refluxing with calcium hydride followed by distillation and kept over molecular sieves (3 Å). All other chemicals were used as received.

4.1. General preparation of tetraethyl α-alkyl-α-fluoromethylenebisphosphonates 3

Tetraethyl fluoromethylenebisphosphonate (**1**) (92 mg, 0.3 mmol, 1 eq.) and Michael acceptor **2** (0.36–0.75 mmol, 1.2–2.5 eq.) were added to a mixture of cesium carbonate (195 mg, 0.6 mmol, 2 eq.) in dry DMF (2.0 mL) in a Shlenk flask. The reaction mixture was stirred at rt for appropriate time and then poured into saturated aqueous solution of ammonium chloride (25 mL). The product was extracted into diethyl ether (3 × 25 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography using silica gel gave pure products **3** (new compounds).

4.1.1. Diethyl [1-(diethoxy-phosphoryl)-1-fluoro-4-oxo-pentyl]-phosphonate, 3a

Prepared according to the general procedure using **2a** (53 mg, 0.75 mmol, 2.5 eq.) in 6 h at rt giving **3a** (76 mg, 67%) as a colorless liquid: R_f = 0.17 (EtOAc); ^1H NMR: δ 1.38 (t, 12H, $^3J_{HH}$ = 7.1 Hz, 4 × OCH_2CH_3), 2.18 (s, 3H, $COCH_3$), 2.39–2.57 (m, 2H, CH_2), 2.86–2.92 (m, 2H, CH_2), 4.23–4.34 (m, 8H, 4 × OCH_2); ^{13}C NMR: δ 16.3–16.5 (m), 26.6 (d, $^2J_{CF}$ = 20.3 Hz, $CFCH_2$), 29.9, 37.1–37.3 (m), 64.0–64.2 (m), 94.8 (dt, $^1J_{CF}$ = 187.6 Hz, $^1J_{CP}$ = 157.2 Hz, CF), 206.7 (C=O); ^{19}F NMR: δ −193.4 (tt, $^2J_{FP}$ = 75.0 Hz, $^3J_{FH}$ = 22.5 Hz); ^{31}P NMR: δ 14.1 (d, $^2J_{PF}$ = 75.0 Hz); GC–MS (EI) *m/z* 334 (16%), 306 (100), 291 (15), 279 (35), 251 (17), 239 (38), 219 (17), 207 (44), 197 (49), 183 (38), 170 (42), 127 (35), 43 (32); HRMS (ESI^+) *m/z* calcd. for $C_{13}H_{28}FO_7P_2$ $(M+H)^+$: 377.1289, found: 377.1286.

4.1.2. Methyl 4,4-bis-(diethoxy-phosphoryl)-4-fluoro-butyrate, 3b

Prepared according to the general procedure using **2b** (39 mg, 0.45 mmol, 1.5 eq.) in 22 h at rt giving **3b** (95 mg, 81%) as a colorless liquid: R_f = 0.22 (EtOAc); ^1H NMR: δ 1.38 (t, 12H, $^3J_{HH}$ = 7.1 Hz, 4 × OCH_2CH_3), 2.45–2.62 (m, 2H, CH_2), 2.70 c −2.78 (m, 2H, CH_2), 3.69 (s, 3H, CO_2CH_3), 4.22–4.35 (m, 8H, 4 × OCH_2); ^{13}C NMR: δ 16.2–16.4 (m), 27.8–28.1 (m), 28.0 (d, $^2J_{CF}$ = 20.1 Hz, $CFCH_2$), 51.6, 63.8–64.3 (m), 94.5 (dt, $^1J_{CF}$ = 188.9 Hz, $^1J_{CP}$ = 156.7 Hz, CF), 172.9 (C=O); ^{19}F NMR: δ −194.5 (tt, $^2J_{FP}$ = 74.0 Hz, $^3J_{FH}$ = 22.3 Hz); ^{31}P NMR: δ 14.0 (d, $^2J_{PF}$ = 74.0 Hz); GC–MS (EI) *m/z* 361 (16%), 319 (59), 306 (31), 291 (93), 263 (58), 255 (41), 235 (52), 207 (100), 183 (39), 127 (34); HRMS (ESI^+) *m/z* calcd. for $C_{13}H_{28}FO_8P_2$ $(M+H)^+$: 393.12380, found: 393.12367.

4.1.3. Diethyl [1,3-dis-(diethoxy-phosphoryl)-1-fluoro-propyl]-phosphonate, 3c

Prepared according to the general procedure using **2c** (98 mg, 0.6 mmol, 2.0 eq.) in 144 h at rt giving **3c** (109 mg, 77%) as a colorless liquid: R_f = 0.27 (EtOAc–MeOH, 9:1); ^1H NMR: δ = 1.32–1.40 (m, 18H, 6 × OCH_2CH_3), 2.03–2.22 (m, 2H, CH_2), 2.35–2.57 (m, 2H, CH_2), 4.05–4.16 (m, 4H, 2 × OCH_2), 4.18–4.35 (m, 8H, 4 × OCH_2); ^{13}C NMR: δ 16.1–16.2 (m), 16.2–16.3 (m), 19.5 (dq, $^1J_{CP}$ = 142.4 Hz, $^3J_{CF}$ = $^3J_{CP}$ = 5.8 Hz, CH_2PO), 26.3 (dd, $^2J_{CF}$ = 21.0 Hz, $^2J_{CP}$ = 2.7 Hz $CFCH_2$), 61.6 (d, $^2J_{CP}$ = 6.4 Hz, 2 × OCH_2), 63.8–64.2 (m), 94.2 (ddt, $^1J_{CF}$ = 190.0 Hz, $^1J_{CP}$ = 156.7 Hz, $^3J_{CP}$ = 18.6 Hz, CF); ^{19}F NMR: δ −194.0 (tt, $^2J_{FP}$ = 74.1 Hz, $^3J_{FH}$ = 21.7 Hz); ^{31}P NMR: δ = 13.7 (d, 2P, $^2J_{PF}$ = 74.1 Hz, CFP_2), 30.6 (s, 1P, CH_2P); GC–MS (EI) *m/z* 425 (16%), 333 (97), 319 (26), 306 (100), 285 (28), 261 (26), 221 (25), 207 (23), 170 (20), 165 (22), 109 (21); HRMS (ESI^+) *m/z* calcd. for $C_{15}H_{35}FO_9P_3$ $(M+H)^+$: 471.14725, found: 471.14699.

4.1.4. Diethyl [3-benzenesulfinyl-1-(diethoxy-phosphoryl)-1-fluoro-propyl]-phosphonate, 3d

Prepared according to the general procedure using **2d** (114 mg, 0.75 mmol, 2.5 eq.) in 18 h at rt giving **3d** (110 mg, 80%) as a colorless liquid: R_f = 0.43 (EtOAc–MeOH, 9:1); ^{1}H NMR: δ = 1.38–1.49 (m, 12H, 4 × CH_3), 2.31–2.53 (m, 1H, CH^aH^b), 2.63–2.87 (m, 1H, CH^aH^b), 3.15–3.23 (m, 1H, CH^aH^b), 3.42–3.53 (m, 1H, CH^aH^b), 4.26–4.42 (m, 8H, 4 × OCH_2), 7.59–7.67 (m, 3H, C_{Ar}H), 7.72–7.76 (m, 2H, C_{Ar}H); ^{13}C NMR: δ 16.3–16.5 (m), 25.2 (d, $^2J_{CF}$ = 20.8 Hz, CFC*H*), 49.7–49.9 (m), 64.0–64.5 (m), 94.3 (dt, $^1J_{CF}$ = 189.7 Hz, $^1J_{CP}$ = 156.9 Hz, CF), 124.2, 129.2, 131.0, 143.2; ^{19}F NMR: δ = −193.0 (tt, $^2J_{FP}$ = 73.9 Hz, $^3J_{FH}$ = 22.0 Hz); ^{31}P NMR: δ 13.3 (d, $^2J_{PF}$ = 73.9 Hz); HRMS (ESI$^+$) *m/z* calcd. for $C_{17}H_{30}FO_7P_2S$ (M + H)$^+$: 459.1166, found: 459.1166.

4.1.5. Diethyl [3-benzenesulfonyl-1-(diethoxy-phosphoryl)-1-fluoro-propyl]-phosphonate, 3e

Prepared according to the general procedure using **2e** (61 mg, 0.36 mmol, 1.2 eq.) in 3 h at rt giving **3e** (128 mg, 90%) as a colorless liquid: R_f = 0.29 (EtOAc); ^{1}H NMR: δ 1.32 (t, 6H, $^3J_{HH}$ = 7.1 Hz, 2 × CH_3), 1.33 (t, 6H, $^3J_{HH}$ = 7.1 Hz, 2 × CH_3), 2.47–2.64 (m, 2H, CH_2), 3.51–3.55 (m, 2H, CH_2), 4.16–4.29 (m, 8H, 4 × OCH_2), 7.55–7.61 (m, 2H, C_{Ar}H), 7.66–7.71 (m, 1H, C_{Ar}H), 7.92–7.94 (m, 2H, C_{Ar}H); ^{13}C NMR: δ 16.2–16.3 (m), 26.4 (d, $^2J_{CF}$ = 21.0 Hz, $CFCH_2$), 50.3–50.5 (m), 64.1–64.4 (m), 93.2 (dt, $^1J_{CF}$ = 190.8 Hz, $^1J_{CP}$ = 157.0 Hz, CF), 128.0, 129.2, 133.7, 138.6; ^{19}F NMR: δ −193.4 (tt, $^2J_{FP}$ = 73.2 Hz, $^3J_{FH}$ = 21.2 Hz); ^{31}P NMR: δ 12.9 (d, $^2J_{PF}$ = 73.2 Hz); GC–MS (EI) *m/z* 382 (20%), 333 (82), 317 (74), 306 (91), 291 (81), 277 (40), 263 (46), 249 (43), 235 (43), 221 (100), 207 (73), 183 (41), 125 (73), 99 (50), 77 (73), 65 (47); HRMS (ESI$^+$) *m/z* calcd. for $C_{17}H_{30}FO_8P_2S$ (M + H)$^+$: 475.1115, found: 475.1115.

4.1.6. Ethyl 4,4-bis-(diethoxy-phosphoryl)-4-fluoro-but-2-enoate, 3f

Prepared according to the general procedure using **2f** (74 mg, 0.75 mmol, 2.5 eq.) in 18 h at rt giving (*Z*)-**3f** (43 mg, 35%) as a colorless liquid: R_f = 0.24 (EtOAc); ^{1}H NMR: δ 1.26–1.39 (m, 15H, 5 × CH_3), 4.18–4.24 (m, 2H, CO_2CH_2), 4.27–4.36 (m, 8H, 4 × OCH_2), 6.03–6.07 (m, 1H, CH=), 6.07–6.16 (m, 1H, CH=); ^{13}C NMR: δ 14.0, 16.2–16.4 (m), 60.8, 64.8–65.1 (m), 97.1 (dt, $^1J_{CF}$ = 202.8 Hz, $^1J_{CP}$ = 154.1 Hz, CF), 122.8 (dt, $^3J_{CF}$ = 10.5 Hz, $^3J_{CP}$ = 5.4 Hz, CFCH = *C*H), 126.8 (dt, $^2J_{CF}$ = 13.6 Hz, $^2J_{CP}$ = 4.9 Hz, CFCH =), 166.3 (C = O); ^{19}F NMR: δ −193.7 (dt, $^2J_{FP}$ = 68.0 Hz, $^3J_{FH}$ = 27.6 Hz); ^{31}P NMR: δ 8.8 (d, $^2J_{PF}$ = 68.0 Hz); GC–MS (EI) *m/z* 359 (15%), 246 (21), 223 (28), 222 (96), 194 (78), 166 (100), 138 (51); HRMS (ESI$^+$) *m/z* calcd. for $C_{14}H_{28}FO_8P_2$ (M + H)$^+$: 405.12380, found: 405.12375; and (*E*)-**3f** (17 mg, 13%) as a colorless liquid: R_f = 0.38 (EtOAc); ^{1}H NMR: δ 1.29–1.39 (m, 15H, 5 × CH_3), 4.15–4.35 (m, 10H, 5 × OCH_2), 6.20 (dt, 1H, $^3J_{HH}$ = 15.6 Hz, $^4J_{HP}$ = 4.9 Hz, CH), 7.15 (ddt, 1H, $^3J_{HF}$ = 25.5 Hz, $^3J_{HH}$ = 15.6 Hz, $^3J_{HP}$ = 3.6 Hz, CH); ^{13}C NMR: δ 14.2, 16.3–16.4 (m), 60.9, 64.8–65.0 (m), 122.1 (dt, $^3J_{CF}$ = 12.1 Hz, $^3J_{CP}$ = 9.3 Hz, CFCH=*C*H), 137.9 (dt, $^2J_{CF}$ = 14.2 Hz, $^2J_{CP}$ = 4.9 Hz, *C*FCH=), 165.0 (C=O); ^{19}F NMR: δ −192.6 (dt, $^2J_{FP}$ = 69.2 Hz, $^3J_{FH}$ = 25.5 Hz); ^{31}P NMR: δ = 9.3 (d, $^2J_{PF}$ = 69.2 Hz); GC–MS (EI) *m/z* 359 (16%), 246 (21), 223 (28), 222 (96), 194 (79), 166 (100), 138 (50); HRMS (ESI$^+$) *m/z* calcd. for $C_{14}H_{28}FO_8P_2$ (M + H)$^+$: 405.12380, found: 405.12382.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jfluchem.2011.03.011.

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