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SYNTHESIS AND CHARACTERIZATION OF (E) AND (Z)-1,2-DIFLUOROETHENEDIYL*BIS*PHOSPHONATES*

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SUMMARY

Cuprous halide mediated decomposition of (diethoxyphosphinyl)difluoromethylzinc bromide, $(EtO)_2P(O)CF_2ZnBr$, forms the title *bis*phosphonates in 50% isolated yield. The ^{19}F and ^{31}P NMR spectra of these isomeric *bis*phosphonates exhibit non-first order AA'XX' patterns. Computer simulation permitted the determination of the $J_{P\text{-}F}$, $J_{F\text{-}F}$, and $J_{P\text{-}P}$ coupling constants for these compounds. Silylation and hydrolysis of the *bis*phosphonate mixture gave the silylated *bis*phosphonates and *bis*phosphonic acids respectively, as expected Metathesis of the zinc reagent also yielded phenyl (diethoxyphosphinyl)difluoromethylmercury, $(EtO)_2P(O)CF_2HgPh$, in good yield. However, attempts to generate fluoro(diethoxyphosphinyl)carbene from this mercurial were unsuccessful.

INTRODUCTION

Perfluorinated vinyl phosphonates are generally prepared *via* the nucleophilic addition-elimination reaction between a trialkylphosphite and a perfluoroolefin[1] An interesting example of this type of reaction was reported by Dittrich and Hägele[2], who described the reaction of triisopropyl phosphite with iodotrifluoroethene to yield (E) and (Z)-1,2-difluoro-2-iodoethenylphosphonate. When excess triisopropyl phosphite was used, they also obtained a low yield of (E)-1,2-difluoroethenediyl*bis*phosphonate. The (Z) isomer was not observed.

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* Abstracted in part from the Ph.D. thesis of L.G. Sprague, University of Iowa, 1986.

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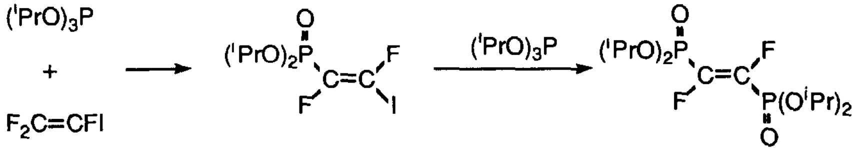

Recently, we reported that both geometrical isomers of the corresponding ethyl analog were formed as by-products in the cuprous bromide catalyzed acylation[3] and alkylation[4] of [(diethoxyphosphinyl)difluoromethyl]zinc bromide. Subsequently, we have found that, in the absence of an organic electrophile, cuprous halide decomposition[1] of the zinc reagent gives a modest isolated yield of the 1,2-difluoroethenediyl*bis*phosphonate isomers as the sole product.

RESULTS

The zinc reagent (**2**) prepared from bromodifluoromethylphosphonate (**1**) [5] is thermally stable [4, 6], and does not decompose to yield the ethene *bis*-phosphonate (**3**).

$$\begin{tikzcd} (EtO)_3P + CF_2Br_2 \arrow[r, "ether", "reflux"'] & \underset{(\mathbf{1}),\ 95\%}{(EtO)_2P(O)CF_2Br} \arrow[d, "Zn\ glyme"] \\ \underset{(\mathbf{3})}{(EtO)_2P(O)CF{=}CFP(O)(OEt)_2} & \underset{(\mathbf{2})}{(EtO)_2P(O)CF_2ZnBr} \arrow[l, "/" marking] \end{tikzcd}$$

However, in the presence of a catalytic amount of cuprous halide, the zinc reagent slowly, but spontaneously, decomposes to yield both geometrical isomers of the 1,2-difluoroethenediyl*bis*phosphonate (**3**). This mixture of isomers is

$$(EtO)_2P(O)CF_2ZnBr \xrightarrow[glyme]{CuBr} \underset{(\mathbf{3}),\ 50\%,\ E{:}Z = 7{:}3}{(EtO)_2P(O)CF{=}CFP(O)(OEt)_2}$$

liquid at room temperature, with a boiling point range of 112-155°C (0.02 mm Hg). The Z-isomer boils at the lower end of this range, while the E-isomer boils at the higher end. Simple distillation through a Vigreux column partially separates the two isomers; the final fraction consisted solely of the E-isomer.

The ^{19}F and ^{31}P NMR spectra of both isomers were observed as non-first order AA'XX' patterns[7]; the ^{19}F spectra are illustrated in Figures 1 and 3. Computer simulated spectra of these isomeric *bis*phosphonates are illustrated in Figures 2 and 4[*]. Table 1 summarizes the ^{19}F and ^{31}P NMR data for these isomers. Agreement between the observed and calculated spectra is excellent. Recently, Russian workers [8] have also reported the preparation of these isomeric *bis*phosphonates *via* the reaction of tetrafluoroethylene, diethyl trifluorovinylphosphonate, or iodotrifluoroethene with either triethylphosphite or diethyl(trimethylsilyl)phosphite. These workers also computer simulated the spectra of these isomers; however, no spectral representations of observed and simulated spectra were given for comparison. We have utilized the data reported in this paper [8] in our computer program to simulate the spectra The spectra obtained did not match our simulated or observed spectra. In addition, the theoretical calculated coupling constants reported by these workers [8] did not agree with our values. We have no obvious explanation for this disagreement.

The isomeric *bis*phosphonates are readily silylated[**], as expected, and the silylated ester is readily hydrolyzed to the *bis*phosphonic acid. Similar reactions had been previously observed with the difluoromethylene*bis*-phosphonate [9] and the difluorophosphonoacetate [3].

$$\begin{tikzcd}
(\mathbf{3}) + \text{xs } Me_3SiCl \arrow[r, "NaBr", "CH_3CN,\ \text{reflux}"'] & \begin{array}{c}(Me_3SiO)_2P(O)CF{=}CFP(O)(OSiMe_3)_2 \\ (\mathbf{4}),\ 78\%,\ \underline{E}{:}\underline{Z} = 7{:}3\end{array} \arrow[d, "H_2O"] \\
& \begin{array}{c}(HO)_2P(O)CF{=}CFP(O)(OH)_2 \\ \underline{E}{:}\underline{Z} = 7{:}3\end{array}
\end{tikzcd}$$

Attempted bromination of (**3**) did not yield the addition product; instead, halogenation of the ethoxy groups occurred. Also, attempted isomerization of E-(**3**) on a 3:1 mixture of E/Z (**3**) with KF/DMF was unsuccessful. Only slow decomposition of (**3**) occurred.

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[*] The ^{19}F NMR spectra were calculated and plotted utilizing NMR.COM and PLOT.COM, spectral simulation programs designed and written by Dr. W.E. Bennett at the University of Iowa.

[**] Although bromotrimethylsilane is the usual silylating reagent in these systems, the less expensive chlorotrimethylsilane can also be used in the presence of NaBr and acetonitrile as solvent.

The most likely mechanism for the formation of (**3**) is *via* the formation of the intermediate [(diethoxyphosphinyl)difluoromethyl]copper complex (**5**). Conversion

$$(EtO)_2P(O)CF_2ZnBr + CuBr \longrightarrow (EtO)_2P(O)CF_2Cu \cdot ZnBr_2$$

(**5**)

of (**5**) to (**3**) could occur *via* formation of fluoro(diethoxyphosphinyl)carbene or its copper carbenoid intermediate. Attempts to trap $(EtO)_2P(O)FC.$ with conventional alkene traps were unsuccessful.

We then attempted to generate this phosphinyl carbene *via* a route analogous to the Seyferth reagents[10]. Metathesis of (**2**) with phenyl mercuric chloride gave the phenyl [(diethoxyphosphinyl)difluoromethyl]mercury (**6**) in good yield.

$$(\mathbf{2}) + PhHgCl \longrightarrow (EtO)_2P(O)CF_2HgPh$$

(**6**), 61%

However, subsequent reaction of (**6**) with sodium iodide did not extrude the phosphinyl carbene. Only dealkylation of (**6**) or the dealkylated product of the protonated phosphonate carbanion were detected in a 82/18 ratio*. No fluorinated norcaranes were detected.

$$(\mathbf{6}) + NaI \xrightarrow[\text{, 146°C}]{\text{xylenes}} Na^+[(EtO)OP(O)CF_2HgPh]^- + Na^+[(EtO)OP(O)CF_2H]^-$$

In summary, the *E* and *Z* isomers of the 1,2-difluoroethenediyl*bis*–phosphonates have been prepared by a novel cuprous salt catalyzed decomposition of $(EtO)_2P(O)CF_2ZnBr$. Both the *E* and *Z* isomers have been completely characterized and the AA'XX' spin system computer simulated to obtain the coupling constants for both isomers. The ready availability of $(EtO)_2P(O)CF_2Br$ and the ease of formation of the corresponding zinc reagent provide a convenient, easily scaled-up entry to these novel, unsaturated *bis*phosphonates and *bis*phosphonic acids.

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* $Na^+[(EtO)OP(O)CF_2HgPh]^-$: ^{19}F NMR (MeOH): ϕ = -105.9 ppm (d with Hg satellites, $J_{F\text{-}P}$ = 71 Hz, $J_{F\text{-}Hg}$ = 725 Hz); ^{31}P NMR (MeOH): δ = 0.45 ppm (t). $Na^+[(EtO)OP(O)CF_2H]^-$: ^{19}F NMR (MeOH): ϕ = -133.8 ppm (dd, $J_{F\text{-}P}$ = 78 Hz, $J_{F\text{-}H}$ = 49 Hz); ^{31}P NMR (MeOH): δ = 2.2 ppm (t).

TABLE 1

^{19}F and ^{31}P NMR Spectroscopic Data

Phosphonate	^{19}F-NMR[a]	^{31}P-NMR[b]	Coupling Constants
E-$(EtO)_2P(O)CF{=}CFP(O)(OEt)_2$ (**3**)[c]	-150.6 ppm	-1.23 ppm	^3J (F-F) = 147 Hz ^2J (F-P) = 89 Hz ^3J (F-P) = -6 Hz ^3J (P-P) = 35±2 Hz
Z-$(EtO)_2P(O)CF{=}CFP(O)(OEt)_2$ (**3**)[c]	-128.3 ppm	-0.34 ppm	^3J (F-F) = 15 Hz ^2J (F-P) = 82 Hz ^3J (F-P) = 18 Hz (^3J (P-P) ≈ 0 Hz)
$(EtO)_2P(O)CF_2ZnBr$ (**2**)[d]	-126.1 ppm (d)	14.1 ppm (t)	^2J (F-P) = 89 Hz
$(EtO)_2P(O)CF_2Cu \cdot ZnBr_2$ (**5**)[d]	-116.0 ppm (d)	13.0 ppm (t)	^2J (F-P) = 99 Hz
$(EtO)_2P(O)CF_2HgPh$ (**6**)[c]	-111.0 ppm (d, Hg sat)	13.6 ppm (t, Hg sat)	^2J (F-P) = 80 Hz ^2J (F-Hg) = 617 Hz ^2J(P-Hg) = 393 Hz
E-$(Me_3SiO)_2P(O)CF{=}CFP(O)(OSiMe_3)_2$ (**4**)[c]	-152.6 ppm (m, AA'XX')	-19.8 ppm (m, AA'XX')	(not calculated)
Z-$(Me_3SiO)_2P(O)CF{=}CFP(O)(OSiMe_3)_2$ (**4**)[c]	-132.7 ppm (m, AA'XX')	-19.5 ppm (m, AA'XX')	(not calculated)
E-$(HO)_2P(O)CF{=}CFP(O)(OH)_2$ [e]	-155.4 ppm (m, AA'XX')	-2.5 ppm (m, AA'XX')	(not calculated)
Z-$(HO)_2P(O)CF{=}CFP(O)(OH)_2$ [e]	-137.7 ppm (m, AA'XX')	-2.5 ppm (m, AA'XX')	(not calculated)

[a] Relative to internal $CFCl_3$.

[b] Relative to external 85% H_3PO_4.

[c] $CDCl_3$ as solvent.

[d] 50% DMF/50% monoglyme as solvent.

[e] Water as solvent.

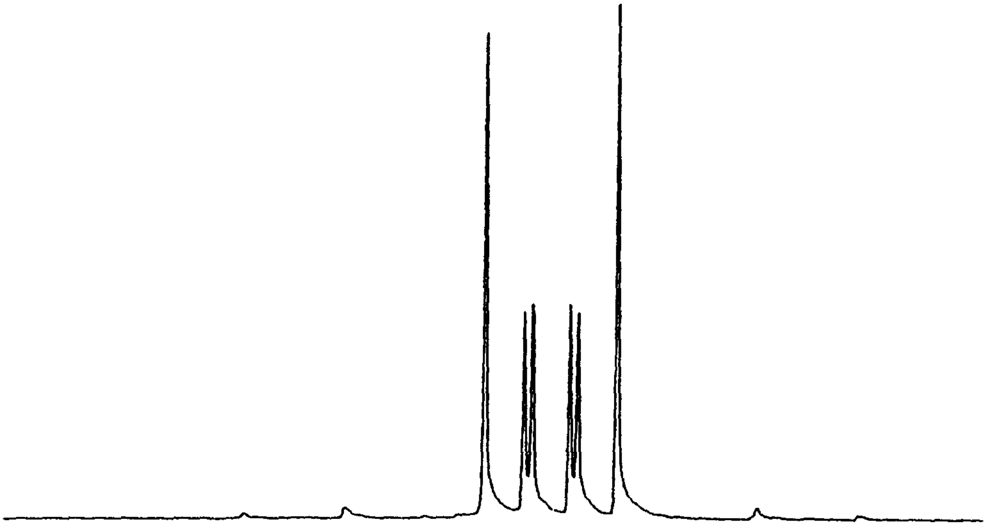

Fig. 1. The Observed ^{19}F NMR Spectrum of E-$(EtO)_2P(O)CF{=}CFP(O)(OEt)_2$, **3**.

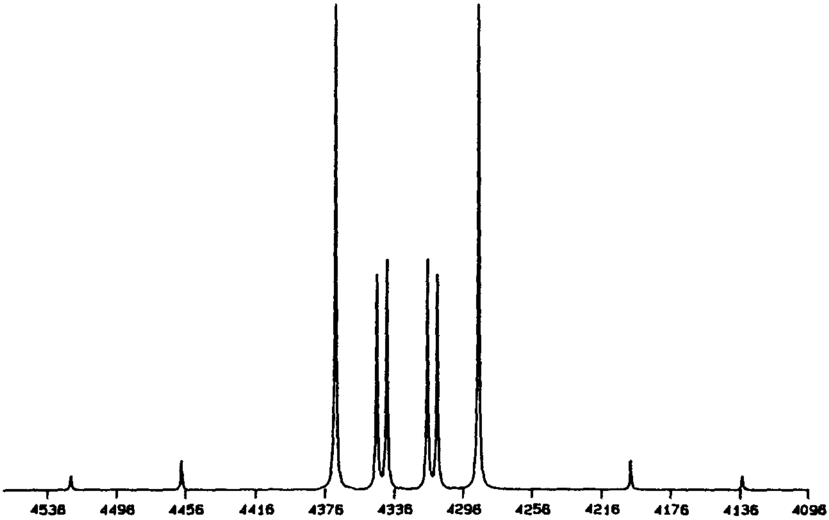

Fig. 2. The Computer Simulated ^{19}F NMR Spectrum of E-$(EtO)_2P(O)CF{=}CFP(O)(OEt)_2$, **3**.

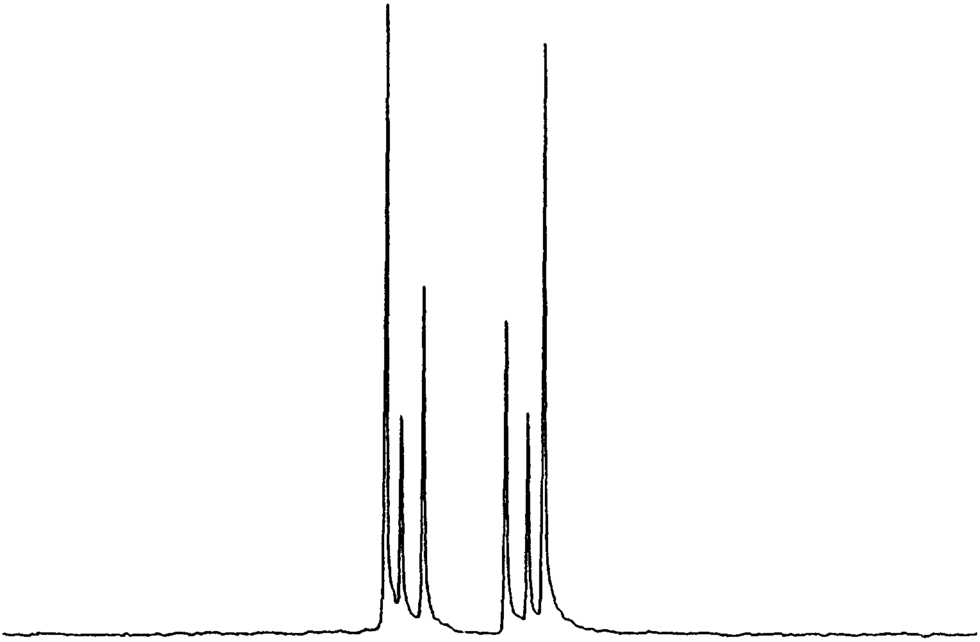

Fig. **3.** The Observed ^{19}F NMR Spectrum of Z-$(EtO)_2P(O)CF{=}CFP(O)(OEt)_2$, **3**.

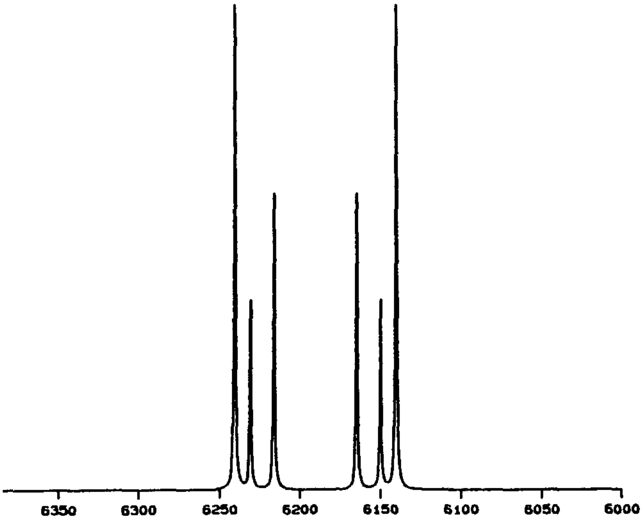

Fig. **4.** The Computer Simulated ^{19}F NMR Spectrum of Z-$(EtO)_2P(O)CF{=}CFP(O)(OEt)_2$, **3**.

EXPERIMENTAL

General

The reaction flasks and other glass equipment were dried in an oven at 130°C, and assembled under a stream of dry nitrogen. All boiling points were determined during fractional distillation by means of a partial immersion thermometer, and are uncorrected. ^{19}F and ^{31}P NMR spectra were recorded on a Jeol FX90-Q multinuclear spectrometer, while ^{1}H and ^{13}C NMR spectra were obtained either on the Jeol or on a Bruker WM360X spectrometer. ^{19}F NMR spectra are referenced against internal $CFCl_3$, and ^{31}P NMR against external 85% H_3PO_4. ^{31}P and, where indicated, ^{13}C NMR spectra were broadband decoupled from hydrogen nuclei ^{1}H and ^{13}C NMR spectra were referenced against internal tetramethylsilane.

Diethyl bromodifluoromethylphosphonate was prepared by the method of Burton and Flynn[5] Monoglyme was distilled from sodium benzophenone ketyl, and acetonitrile from phosphorus pentoxide Cuprous bromide was purified by a method similar to that of Osterlof[11] Zinc powder was washed with 1% HCl, water, and acetone, then dried under vacuum.

Tetraethyl (E) & (Z)-1,2-difluoroethenediyl*bis*phosphonate (3)

A 500 ml, round bottomed flask was equipped with a Teflon coated spinbar and a nitrogen inlet. Into the flask was filtered, through a medium frit Schlenk filter funnel, a solution of [(diethoxyphosphinyl)difluoromethyl]zinc bromide[3], prepared from diethyl bromodifluoromethylphosphonate (66.8 g, 0.25 mol), zinc powder (16.4 g, 0.25 mol), and monoglyme (125 ml). To this solution was added CuBr (1.06 g, 0.007 mol), and the mixture was allowed to stir for 2 days at room temperature. The volume of reaction mixture was reduced by half, by rotary evaporation, and the remainder poured into water (100 ml). The insoluble inorganic salts were removed by suction filtration, and the filtrate extracted with 3X35 ml of CH_2Cl_2. The combined organic phases were dried over anh. Na_2SO_4, filtered, concentrated on a rotary evaporator, and distilled under vacuum. Combination of the fractions in the boiling range 112-155°C (0.02 mm Hg) gave **E** and **Z-3**. The yield was 21.1 g (0.63 mol, 50%). GLPC purity 95%; $n_D^{24} = 1.4327$.

^{1}H NMR: $\delta = 1.39$ ppm (t, J = 7 Hz), 4.26 ppm (dq (5 lines), J = 6 Hz). ^{13}C NMR: $\delta =$ 13.4 ppm (q, J = 126 Hz), 64.4 ppm (t, J = 150 Hz), 153.2 ppm (m). IR (neat film):

1625 (m, C=C), 1460 (w), 1430 (w), 1375 (m), 1350 (w), 1270 (s, P=O), 1150 (s), and 1000 (vs) cm^{-1}.

Analytical. Calculated for $C_{10}H_{20}F_2O_6P_2$: C, 35.72%; H, 6.00%. Found: C, 36.05%, H, 5.95%.

Tetrakis(trimethylsilyl) (E) & (Z)-1,2-difluoroethenediyl*bis*phosphonate (4)

A 250 ml, 3-necked flask was equipped with a Teflon coated stirbar and a reflux condenser topped by a nitrogen inlet. Acetonitrile (50 ml), sodium bromide (25.7 g), **3** (E/Z mixture, 16.8 g, 50 mmol), and chlorotrimethylsilane (51 ml, 0.4 mol) were successively introduced, and the mixture was refluxed with vigorous stirring for 3 days. It was then filtered through a medium frit Schlenk filter funnel under N_2, into a 200 ml boiling flask. The solvent and volatile materials were distilled off at atmospheric pressure, and the residue fractionally distilled under vacuum to give E and Z-**4**, b.p. 125-143°C (0.08 mm Hg). The yield was 19.9 g (38.8 mmol, 78%).

(E) & (Z)-1,2-difluoroethenediyl*bis*phosphonic acid

The tetrakis(trimethylsilyl) phosphonate (**4**) (19.6 g, 38.2 mmol) was placed in a 100 ml, round bottomed flask with a Teflon coated stirbar, and deionized water (40 ml) was added. The mixture was stirred for 1 hr. A slight exotherm was observed initially, and 2 layers were formed. The layers were separated, and the aqueous (lower) layer concentrated under vacuum, to give the product acid as a colorless, syrupy, concentrated aqueous solution.

Phenyl [(diethoxyphosphinyl)difluoromethyl]mercury (6)

A 500 ml, round bottomed flask was equipped with a Teflon coated spinbar and a nitrogen inlet. Into the flask was filtered, through a medium frit Schlenk filter funnel, a solution of [(diethoxyphosphinyl)difluoromethyl]zinc bromide, prepared from diethyl bromodifluoromethylphosphonate (66.8 g, 0.25 mol), zinc powder (16.4 g, 0.25 mol), and monoglyme (250 ml). To this solution was added phenyl mercuric chloride (78.5 g, 0.25 mol). The resultant slurry was allowed to stir at room temperature for 12 days. The mixture was filtered through a medium frit glass Büchner funnel under aspirator vacuum, and concentrated by rotary evaporation. The resulting slush was dissolved in benzene (350 ml), and water (100 ml) was added with shaking. The mixture was again filtered under vacuum, and the filtrate washed with water (3X100 ml) Concentration by rotary evaporation left a residue, which, upon recrystallization from $CHCl_3$: hexane (1:3), gave a combined yield of 70.3 g (61%) of white, crystalline **6** from 2 crops. The crystals had a poorly defined melting point slightly above room temperature.

An analytically pure sample of **6** was prepared by heating 8.0 g of the crystals at 68°C *in vacuo* overnight, to obtain a clear glass, which was recrystallized from $CHCl_3$ to give 2.8 g; m.p. 59-61°C. ^1H NMR: δ = 1.39 ppm (6H, t, J = 7 Hz); 4.27 ppm (4H, dq (5 lines), J = 7 Hz); 7.28 ppm (5H, s). $^{13}C\{^1H\}$ NMR: δ = 16.5 ppm (d, $J_{C\text{-}P}$ = 4 Hz); 64.0 ppm (d, $J_{C\text{-}P}$ = 7 Hz); 137.3 ppm (s with Hg satellites, *meta* C, $J_{C\text{-}Hg}$ = 95 Hz); 128.7 ppm (s with Hg satellites, *ortho* C, $J_{C\text{-}Hg}$ = 120 Hz); 129.0 ppm (s, *para* C); 160.8 ppm (td, $J_{C\text{-}F}$ = 301 Hz, $J_{C\text{-}P}$ = 161 Hz); ~162 ppm (s, *ipso* C).

Analytical. Calculated for $C_{11}H_{15}F_2HgO_3P$· C, 28.43%; H, 3.25%. Found: C, 28.60%; H, 3.21%.

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