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PRELIMINARY NOTE

A New, Effective Method for the Synthesis of 1H-F-1-Alkene-1-phosphonates from F-Alkanoic Acid Chlorides

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SUMMARY

Diethyl (Z)-1H-F-1-alkene-1-phosphonates were synthesized in good yields by the treatment of diethyl (Z)-1-[(diethoxyphosphinyl)oxy]-F-1-alkene-1-phosphonates, prepared from F-alkanoic acid chlorides and triethyl phosphite, with butylcopper(I) reagent in tetrahydrofuran-tetramethylethylenediamine at -78 °C.

Electron-deficient olefinic compounds, e.g., vinyl ketones [1], vinyl sulfoxides [2], nitroolefins [3], and vinyl phosphorus compounds [4] have been revealed to be useful building blocks as acceptors in the Michael addition reaction of various nucleophiles and as dienophiles in the Diels-Alder reaction. In contrast, the synthetic application of fluorine-containing analogs, whose olefinic linkages are more electron-deficient, is relatively limited because of the difficulties and tediousness in preparing such compounds [5].

In our continuing studies on the synthesis and application of fluorinated vinylic compounds bearing hetero-functional group(s) [6], we have now developed a new, efficient method for the two-step synthesis of 1H-F-1-alkene-1-phosphonates from F-alkanoic acid chlorides.

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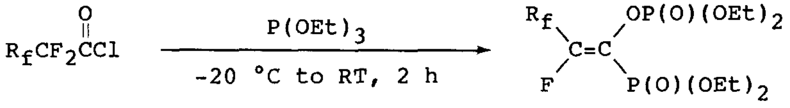
F-Alkanoic acid chlorides (1) were allowed to react with 2 equivalents of triethyl phosphite at -20 °C to room temperature to afford diethyl (Z)-1-[(diethoxyphosphinyl)oxy]-F-1-alkene-1-phosphonates (2) [7].



1 **2**

R_f = CF_3 77%

R_f = CF_3CF_2 79%

R_f = $CF_3(CF_2)_4CF_2$ 67%

R_f = $CF_3(CF_2)_6CF_2$ 66%

R_f = $CHF_2(CF_2)_7CF_2$ 69%

When above-obtained phosphonate **2** was treated with an organocopper(I) reagent at -78 °C, the corresponding (Z)-1H-F-1-alkene-1-phosphonate (**3**) was obtained in good yields*. Out of the organocopper(I) reagents examined, dibutylcopper(I) lithium was the most effective for the reaction. Neither dimethyl- nor diphenylcopper(I) lithium caused the expected reaction at all, the starting phosphonate **2** being recovered unchanged. Tetrahydrofuran (THF) or diethyl ether could be used as solvent. The addition of tetramethylethylenediamine (TMEDA) to the solvent improved the reproducibility of the reaction. The results are summarized in Table 1.

TABLE 1

Synthesis of (Z)-1H-F-1-Alkene-1-phosphonates **3**

Product **3** R_f	Yield of **3** %	J_{H-F} [a] Hz
CF_3	65	40.0
CF_3CF_2	81	38.9
$CF_3(CF_2)_4CF_2$	62	37.9
$CF_3(CF_2)_6CF_2$	80	39.3
$CHF_2(CF_2)_7CF_2$	70	40.5

[a] Determined by ^1H and ^{19}F NMR.

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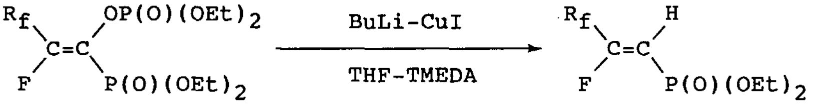
*The spectroscopic (IR, Mass, ^1H, ^{19}F, and ^{31}P NMR) and analytical data of all new compounds were in good accord with the assigned structures.



2 → 3

It is noteworthy that no butylated product was formed in any case [8], and that the reaction occurred selectively on the enol phosphate moiety in **2** and with complete retention of configuration. To our knowledge, this is the first example showing that the effective reduction of an enol oxygen moiety is by using organocopper(I) reagent [9].

Procedure: In a four-necked flask fitted with a thermometer, a mechanical stirrer, an inlet tube for nitrogen, and a rubber septum were placed cuprous iodide (125.0 mmol), anhydrous TMEDA (125.0 mmol), and 250 mL of dry THF. This suspension was cooled to -78 °C by immersing in a dry ice-methanol bath and butyllithium (220.0 mmol) in hexane (1.5 M) was gradually added to it by use of a syringe. After stirring for 30 min at -78 °C, a solution of **2** (50.0 mmol) in 25 mL of dry THF was added to the resulting dark-brown solution at such a rate that the reaction temperature should not rise above -60 °C. The whole mixture was stirred for 15 min at -78 °C. To this reaction mixture, which had been brought to -50 to -40 °C, was added 10 mL of water and successively 200 mL of a saturated aqueous solution of ammonium chloride. After being stirred for a while at room temperature, the mixture was subjected to extraction with ether (4 x 100 mL). The ethereal extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residual oil was distilled *in vacuo* or chromatographed on silica gel (Wako gel C-200) by using ether as an eluent to give analytically pure phosphonate 3.*

Further studies on the synthetic application of these new phosphonates as well as the mechanism of the present reaction are now in progress.

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*See footnote p. 272.

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7 T. Ishihara, T. Maekawa, Y. Yamasaki, and T. Ando, J. Fluorine Chem., 34 (1986) 323.

8 It was reported that the reaction of a fluorine-free enol phosphate with dibutylcopper(I) lithium gave the corresponding butylated alkene. See, L. Blaszczak, J. Winkler and S. O'Kuhn, Tetrahedron Lett., (1976) 4405.

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