Journal of Fluorine Chemistry, 10 (1977) 329–332

Received: July 28, 1977

PRELIMINARY NOTE

Michaelis-Arbuzov Preparation of Halo-F-Methylphosphonates

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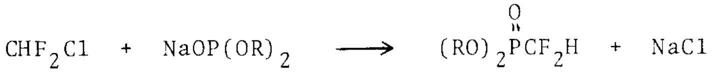
The preparation and chemistry of polyfluoroalkyl phosphines and phosphoranes has received considerable attention in the chemical literature [1]. More recently, polyfluorinated phosphonium salts have been prepared and employed as ylide precursors in the preparation of a wide variety of fluoromethylene olefins [2]. In contrast to the extensively investigated chemistry of these aforementioned fluoroalkyl phosphorus derivatives, there is almost a total void in our knowledge of fluoroalkyl phosphonates, especially the halo-F-methyl derivatives, even though phosphonic acids and their derivatives outnumber all other compounds which contain the carbon-phosphorus bond [3].

Emeleus and co-workers [4] have reported the preparation of trifluoromethyl phosphonic, phosphorous, and phosphinous acids *via* oxidative hydrolysis of trifluoromethylphosphine derivatives. However, the preparation and chemistry of the ester derivatives of these compounds was not reported. Similarly, Mc Ivor [5] has reported some details of the infrared spectrum of diethyltrifluoromethylphosphonate, but no details of its preparation are given. The only unequivocal preparation of a fluoromethylphosphonate in the literature is that of Soborovskii and Baina, who prepared esters of difluoromethylphosphonic acid *via* the reaction of chlorodifluoromethane and sodium dialkylphosphites [6]. Although the mechanism of this reaction

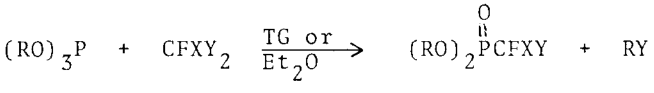


$$CHF_2Cl + NaOP(OR)_2 \longrightarrow (RO)_2\overset{O}{\overset{\|}{P}}CF_2H + NaCl$$

was inferred as SN_2, most likely the phosphonate is formed *via* trapping of difluorocarbene by the phosphite anion similarly to carbene trapping by other strong bases in their reaction with chlorodifluoromethane [7]. Consequently, this mode of phosphonate preparation is specific for the difluoromethyl analog and is not of general applicability.

The Michaelis-Arbuzov reaction is the most widely employed method for the synthesis of phosphonate esters [8]. Unfortunately, halo-*F*-methanes, such as CF_3Cl, CF_3I, and $CFCl_3$, have been reported to be inert under the normal reaction conditions used in this approach [9, 10]. These early failures have no doubt discouraged additional work *via* this type of reaction and have contributed to the lack of fluoroalkylphosphonates reported in the literature.

We now wish to report that dibromo-*F*-methane (I) and tribromo-*F*-methane (II) undergo a facile Michaelis-Arbuzov reaction [11] with alkyl phosphites to give the appropriate bromo-*F*-methylphosphonate esters. The reactions are conveniently carried out in triglyme (TG) or diethyl ether (Et_2O) at 25 to 50°C and give reasonably good yields of the phosphonate esters.



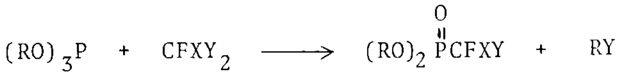
$$(RO)_3P + CFXY_2 \xrightarrow[Et_2O]{TG\ or} (RO)_2\overset{O}{\overset{\|}{P}}CFXY + RY$$

X = F, Br

Y = Br

Data for the results obtained with some typical phosphites *via* this procedure are summarized in Table I. A typical experimental procedure is exemplified by the following description of the preparation of bromo-*F*-methyldiethylphosphonate from (I) and triethylphosphite.

TABLE I



$$(RO)_3P + CFXY_2 \longrightarrow (RO)_2\overset{O}{\overset{\|}{P}}CFXY + RY$$

R	$CFXY_2$	Solvent	$\%, (RO)_2\overset{O}{\overset{\|}{P}}CFXY$[12,13]
Me	I	TG	55
Et	I	Et_2O	95
Et	I	TG	55
n-Bu	I	Et_2O	65
iso-Pr	I	TG	42
Et	II	Et_2O	78
Et	II	TG	60
iso-Pr	II	Et_2O	22

Dibromo-*F*-methane (134 g, 0.64 mol) was added to a stirred (magnetically) cold (ice bath) solution of triethylphosphite (100 g, 0.60 mol) in 300 ml of dry diethyl ether. Under a nitrogen atmosphere the colorless solution was warmed to room temperature and then refluxed for 24 hours. After concentration of the reaction mixture, vacuum distillation yielded 152 g (0.57 mol, 95%) of bromo-*F*-methyldiethylphosphonate, b.p. 99-102°C/16 mm. The ^{19}F nmr spectrum (in $CDCl_3$ with internal $CFCl_3$) consisted of a doublet at 61.9 ppm, and the ^{31}P nmr spectrum (in $CDCl_3$ with H_3PO_4 capillary) consisted of a triplet at -1.16 ppm, $J_{P,F}$ 93 Hz. The ^{13}C nmr spectrum (in $CDCl_3$ with internal TMS) consisted of a triplet of doublets at 116.8 ppm, J_{PC} 238 Hz, J_{CF} 330 Hz, for the bromo-*F*-methyl carbon. The mass spectrum showed a molecular ion at m/e 268 and 266 (1:1 ratio) consistent with the assigned structure.

The ease of preparation of these phosphonates on a large scale now permits a detailed investigation of the chemistry of this important class of phosphorus fluorine compounds. These interesting molecules offer several sites of attack, which can potentially be controlled by the proper selection of the attacking agent. Attack at the alkyl group, attack at phosphorus, attack at the halo-*F*-methyl carbon, and attack on halogen itself offer several interesting selective reactions. Additional work is in progress with these and other halo-*F*-methylphosphonates and future reports will elucidate the overall preparation and synthetic utility of these intermediates.

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2 For recent references to fluoromethylene ylides, cf: D. J. Burton and co-workers; (a) J. Org. Chem., 40 (1975), 2796; (b) Syn. Comm., 3 (1973), 197; (c) J. Fluorine Chem., 1 (1972), 381; and (d) J. Fluorine Chem., 1 (1971), 123.

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7 W. A. Sheppard and C. M. Sharts, Organic Fluorine Chemistry, W. A. Benjamin, New York, (1969), 252.

8 R. G. Harvey and E. R. De Sombre, Topics In Phosphorus Chemistry, Interscience, New York, 1 (1964), 57.

9 G. Kamai, C. A., 46 (1952), 6081.

10 A. F. Isbell, C. A., 58 (1963), 11394.

11 Although the products of these reactions are the expected Michaelis-Arbuzov type of products, the mechanism of this process is probably not the expected SN2 reaction. Additional work is in progress to delineate some of the mechanistic features of this reaction sequence.

12 The yield of phosphonate is an isolated yield based on phosphite.

13 The spectroscopic data (^{1}H, ^{19}F, ^{31}P, and ^{13}C nmr) of the phosphonates were consistent with the assigned structures.