Alcohols 2 and 3[18] **(X = OH)** were prepared from the acetates (see above) or directly from acetoxymercuration following the standard procedure[19] in 55% yeld; the alcohols (**3:2** = 50:50) were separated on a alumina (neutral) column (200 cm/3 cm, with dichloromethane): ^{1}H NMR [**2**, X = OH] 0.97 (2 Me), 4.13 ppm, [**3**, X = OH] 0.90, 0.97 (Me), 3.63 ppm.

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The Use of Organosilicon Esters for the Synthesis of Alkyl Phosphonofluoridates

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Introduction

The alkyl methylphosphonofluoridates are an important class of highly toxic compounds. In order to minimize the safety hazards associated with preparing these esters, simple high yield syntheses are highly desirable. The method that is usually employed to prepare these compounds involves the reaction of an alcohol with methylphosphonic difluoride (**1**) in the presence of an HF acceptor such as an alkyl amine.[1] Another reaction that is sometimes used to prepare the alkyl methylphosphonofluoridates involves the controlled addition of an alcohol to an equimolar mixture of **1** and methylphosphonic dichloride dissolved in refluxing methylene chloride.[2] Both of these methods suffer from the necessity of controlling the addition of the alcohol in order to moderate the heat from the reaction and from the workup procedures that are necessary to obtain pure products that are free from a solvent or an ammonium fluoride salt.

In the chemistry of organosilicon compounds, the reactions in which Si–F bonds are formed are usually highly exothermic. In reactions in which silicon tetrafluoride is formed, the Si–F bond energy[3] of 160 kcal/mol provides the driving force for these reactions. In view of the affinity of silicon for fluorine, and the lability of the fluorine atoms of **1**, it seemed logical to investigate the potential reactivity of alkoxy-substituted silanes with **1**. It seemed reasonable to suppose that a ligand exchange reaction with P–F systems might occur by a simple redistribution mechanism.

Results and Discussion

We found that **1** reacts with the tetraalkoxysilanes **2a–c** to give the alkyl methyphosphonofluoridates **3a–c** together with the dialkyl methylphosphonates **4a–c** and silicon tetrafluoride (eq 1). The difluoride **1** also undergoes an

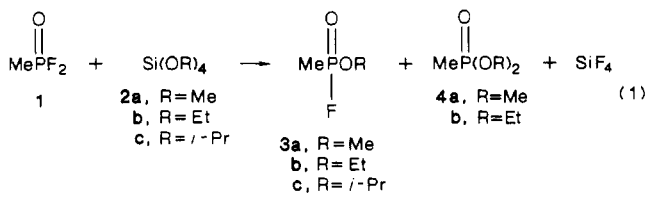


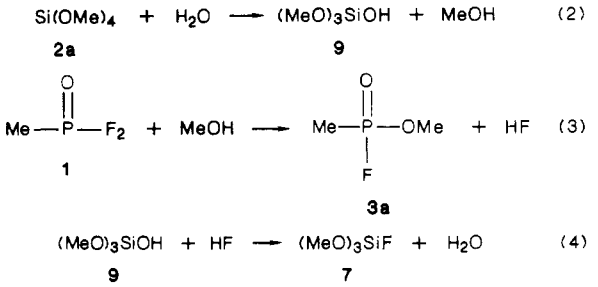
Table I. Reactions of 1 with the Alkoxysilanes

alkoxysilane	ratio[a]	reactn time	products (% yield)[b]
2a	1:3	15 min	**3a** (79), **4a** (19)[c]
2a	1:1	20 h	**4a** (>95)
2a + 7 + 8	1:1[d]	4 min	**3a** (80), 1 (20)
2a + H_2O[e]	1:4	15 s	**3a** (92), **4a** (6)
2b	1:4	1.5 h	**3b** (81)[f]
2c	1:4	48	**3c** (85)
2c + H_2O[g]	1:4	15 s	**10** (90)
2c + H_2O[h]	1:4	4 min	**3c** (60), **10** (19), 1 (20)
5	1:3	10 min	**3a** (80), **4a** (10), 1 (10)
6	1:1	5 days	**3a** (86), **4a** (5)

[a] Molar ratio of alkoxysilane to **1**. [b] Product yields by ^{1}H NMR. [c] Product yield by ^{31}P NMR. [d] Equimolar ratio of total methoxy groups to **1**. [e] Equimolar ratio of H_2O and **2a**. [f] Isolated yield after distillation. [g] Equimolar ratio of H_2O and **1**. [h] Equimolar ratio of H_2O and **2c**.

exchange reaction with trimethoxysilane (**5**) as well as with trimethylmethoxysilane (**6**) when a catalytic amount of a KF-saturated acetonitrile solution containing 1% (w/v) 18-crown-6 is employed. In order to further explore the reaction between **1** and **2a**, the synthesis of the fluorinated methoxysilane intermediates was attempted. A mixture consisting of 20% **2a**, 56% trimethoxyfluorosilane (**7**), and 23% dimethoxydifluorosilane (**8**) was obtained upon treating **2a** with antimony trifluoride. Trifluoromethoxysilane should also have been formed, but it reportedly[4] disproportionates to give **2a** and silicon tetrafluoride. From these experiments (Table I) it is evident that the fluorinated methoxysilanes are more reactive toward the exchange reaction with **1** than is **2a**.

As part of our attempts to determine the mechanism of this reaction, a number of potential catalysts were screened. Among the reagents tested for catalytic activity were potassium fluoride/18-crown-6, pyridine–HF, boron trifluoride etherate, triethylamine, and methanol. In these trials a 4:1 molar ratio of **1** to **2a** was employed, because the end of the reaction could be visualized by the emission of SiF_4. In all cases, instead of increasing the rate of reaction, the presence of the potential catalysts delayed the emission of SiF_4 (end of reaction) from 15–20 min (absence of added catalyst) to 25–40 min. In these experiments it was noted that a rise in the reaction temperature to 55–65 °C occurs simultaneously with the emission of SiF_4. The presence of water, however, causes a marked acceleration in the rate of the reaction. A possible mechanism that would account for these results is suggested in eq 2–4.



In this mechanism, methanol is produced by the hydrolysis of **2a** (eq 2) and reacts with **1** to give **3a** and HF (eq 3). The HF dehydrates trimethoxysilanol (**9**) that is formed in eq 2, resulting in the regeneration of H_2O and the formation of **7** (eq 4). The fluorosilane **7** then reacts with water and continues this cycle until SiF_4 is formed.

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The diester **4b** has been reported[5] to result from the reaction of **1** with 1-ethoxysilatrane. It is likely that the pentacoordinate silicon atom enhances the reactivity of the ethoxy group toward the exchange reaction with **1** and with **3b** because the formation of **3b** was not reported.[5] In our systems, the uncatalyzed reactions of the three tetraalkoxysilanes **2a-c** with **1** proceed at different rates. Tetramethoxysilane (**2a**) is the most reactive toward **1**, whereas tetraisopropoxysilane (**2c**) is the least reactive. Steric interactions, which develop in the transition state leading to the alkyl phosphonofluoridate products, can be invoked to explain the observed order of relative reactivity.

Experimental Section

General Procedures. ^1H NMR spectra were obtained on a Varian EM-360A spectrometer, generally with carbon tetrachloride as the solvent, with tetramethylsilane as an external standard. ^{31}P and ^{19}F spectra were recorded on a Varian FT-80A or Varian XL-200 spectrometer using neat liquid samples. A positive chemical shift value (δ, ppm) is taken downfield from 85% phosphoric acid as an external reference for the ^{31}P NMR spectra and downfield from $CFCl_3$ for the ^{19}F spectra. Tetramethoxysilane (**2a**), trimethoxysilane (**5**), trimethylmethoxysilane (**6**), and tetraethoxysilane (**2b**) were used as received from Petrarch. Methylphosphonic difluoride (**1**)[6] was distilled from dicyclohexylcarbodiimide prior to use. Tetraisopropoxysilane (**2c**) was prepared by Regis Chemical Company[7] according to the method of Sumrell and Ham.[8]

Fluorinated Methoxy Silanes (7 and 8). The mixture of **7** and **8** was prepared as described by Noskov.[4] Analysis of the crude distillate by ^1H and ^{19}F NMR revealed that the composition of the product mixture was 20% **2a**, 56% **7**, and 23% **8**. ^{19}F NMR: δ -157.05 (d, J_{Si-F} = 196 Hz, **6**), -158.15 (d, J_{Si-F} = 196 Hz, **7**). ^1H NMR: δ 3.38 (s, **2a**), 3.46 (s, **7**), 3.56 (s, **8**).

Reactions of Methylphosphonic Difluoride with the Alkoxy-Substituted Silanes. General Procedures. *WARNING! The alkyl phosphonofluoridates are highly toxic acetylcholineesterase inhibitors; trained medical personnel should be available and the proper safety procedures should be followed while synthesizing or performing other experiments with these compounds.*[9] It is recommended that the water catalysis of these reactions not be attempted and that the reaction flask never be filled above half-full in order to ensure the retention of the alkyl methylphosphonofluoridate product in the reaction flask during the emission of silicon tetrafluoride. These reactions were conducted by using 1 to 2 g (10-20 mmol) of **1**. The neat reaction mixtures were stirred for the times specified (Table I) in flasks fitted with calcium sulfate drying tubes. Reactions were monitored by ^1H NMR analysis of a small aliquot of the reaction mixture dissolved in carbon tetrachloride. In some cases, the reaction temperature was measured with a thermocouple inserted into a septum-fitted two-necked flask. At the end of the reactions, the product composition was determined by ^1H or ^{31}P NMR analysis. The results are summarized in Table I.

Methyl Methylphosphonofluoridate (3a). ^{31}P NMR: δ 33.4 (d, J = 1039 Hz). ^1H NMR: δ 1.55 (dd, J_{P-H} = 18.4 Hz, 3 H, CH_3-P, $^2J_{F-H}$ = 6.0 Hz), 3.80 (d, J_{P-H} = 11.8 Hz, CH_3OP).

Dimethyl Methylphosphonate (5). ^{31}P NMR: δ 37.8 ^1H NMR: δ 1.37 (d, J = 17.8 Hz, 3 H, CH_3-P), 3.67 (d, J = 10.9 Hz, 6 H, CH_3OP).

Isopropyl Methylphosphonofluoridate (11). ^1H NMR: δ 1.25 (d, J = 6.1 Hz, 6 H, $OCH(CH_3)_2$), 1.45 (dd, J_{P-H} = 18.3 Hz, 3 H, CH_3-P, $^2J_{F-H}$ = 5.5 Hz), 4.4-5.1 (m, 1 H, $OCH(CH_3)_2$).

Methylphosphonofluoridic Acid (13). ^1H NMR: δ 1.49 (dd, J_{P-H} = 18.8 Hz, 3 H, CH_3-P, $^2J_{F-H}$ = 6.0 Hz), 9.75 (s, 1 H, P-OH).

Ethyl Methylphosphonofluoridate (2b). A preparative scale synthesis of this compound was performed by employing 14.5 g (69 mmol) of silane **2b** and 27.2 g (272 mmol) of **1**. The temperature of the reaction mixture rose gradually from room temperature to 33 °C over a period of 50 min. During the next 5-6 min the reaction temperature rose to 70 °C as the solution darkened and SiF_4 was emitted. The resulting product was purified by vacuum distillation (bp 53-54 °C/12 mm) to afford 27.9 g (81%) of **3b**. The product was 97.4% pure by ^{31}P NMR and contained 2.1% of unreacted **1**. ^{31}P NMR: δ 31.2 (d, J = 1038 Hz). ^1H NMR: δ 1.39 (t, J = 6.9 Hz, 3 H, OCH_2CH_3), 1.54 (dd, J_{P-H} = 18.5 Hz, 3 H, CH_3-P, $^2J_{F-H}$ = 5.8 Hz), 3.8-4.5 (m, 2 H, OCH_2CH_3).

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Registry No. **1**, 676-99-3; **2a**, 681-84-5; **2b**, 78-10-4; **2c**, 1992-48-9; **3a**, 353-88-8; **3b**, 673-97-2; **3c**, 107-44-8; **4a**, 756-79-6; **5**, 2487-90-3; **6**, 1825-61-2; **7**, 39486-13-0; **8**, 25111-12-0; **13**, 1511-67-7; antimony trifluoride, 7783-56-4.

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Facile Conversion of Chloromethylated Polystyrene to the Lithium or Potassium Derivatives

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Functionalization of chloromethylated polystyrene (Merrifield resin) is an important process in the synthesis of polymer-supported reagents or catalysts.[1] As pointed out recently by Fréchet et al.,[2] organometallic substituents on the polymer are ideal reagents for C-C bond formation. They were able to prepare an insoluble Grignard reagent directly from Merrifield resin by reaction with magnesium-anthracene/THF. However, they remark in their paper that the lithiated derivative of chloromethylated polystyrene "has never been prepared successfully", in contrast to polystyrene lithiated on the phenyl ring, which is readily available from the aryl bromide.[2] We now report that both the lithium and potassium derivatives can be prepared quantitatively from chloromethylated polystyrene by a simple two-step procedure.

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