Fluorination of Trimethylsilyl Phosphites and Their Structural Analogues by Sulphuryl Chloride Fluoride. A Facile Preparation of Phosphorofluoridates† and Related Compounds

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Trimethylsilyl esters of general formula $RR'POSiMe_3$ react in a quantitative and fully chemoselective way with sulphuryl chloride fluoride to give phosphorofluoridates RR'P(O)F of high purity under extremely mild conditions.

Fluoro derivatives of phosphorus are of great importance in the chemistry of both elements. Sulphuryl chloride fluoride which is easy to handle and commercially available, has been used by us as a fluorinating reagent in organophosphorus–fluorine chemistry.[1]

The dialkyl phosphites and compounds of general formula RR'POH react with sulphuryl chloride fluoride only in the presence of bases or as their alkali metal salts (**1**). In this case, however, the reaction is not chemoselective and leads to a mixture of the fluoro- and chloro-compounds,[1b] equation (1).

$$\underset{(1)}{RR'P\text{-}O^-M^+} + SO_2ClF \longrightarrow \underset{-SO_2}{} RR'P(O)F + \underset{(2)}{RR'P(O)Cl} \quad (1)$$

Even under conditions where the fluoroproducts (**2**) are predominant, they are not readily separable from the corresponding chlorides.[2]

The compounds (**1**) can be readily transformed into their trimethylsilyl derivatives $RR'POSiMe_3$ (**3**).[3] We have found that these are very reactive towards sulphuryl chloride fluoride in a fully chemoselective manner, equation (2).

$$\underset{(3)}{RR'POSiMe_3} + SO_2ClF \longrightarrow \underset{(2)}{RR'P(O)F} + Me_3SiCl + SO_2 \quad (2)$$

† We would like to emphasize high toxicity of the phosphorofluoridates, which call for special precautions.

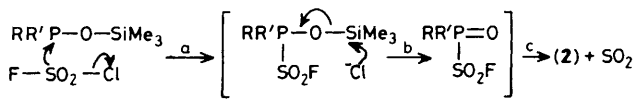
Phosphorofluoridates (**2**) of very high purity are formed in almost quantitative yield. The side products are volatile and readily separable. In our view, there are several contributing factors to this surprising chemoselectivity. Bond energies, although higher for Si–F than for P–F, are not very different and both heteroatoms are known to have a high affinity towards fluorine.[4] It is more likely that in the sulphuryl chloride fluoride molecule the S–Cl bond should be broken more readily than the S–F bond. The mechanistic pathway in Scheme 1 explains the 'high mobility' of chlorine and 'low mobility' of fluorine towards the silicon centre. Steps a and b proceed according to an Arbuzov reaction and step c *via* a radical pair in a solvent cage.

This discovery provides an easy access to all types of the fluoridates (**2**) from non-toxic starting materials. The method

Table 1. ^{31}P N.m.r. parameters for phosphorofluoridates (**2**).

R	R'	$\delta^{31}P$/p.p.m.[a]	J_{P-F}/Hz
EtO	EtO	−8.60	970.10
CF_3CH_2O	CF_3CH_2O	−10.22	995.10
Pr^iO	Pr^iO	−10.26	968.31
Bu^t	Ph	+58.63	1048
PhO	PhO	−19.73	995.99

[a] Positive chemical shifts are to high frequency of 85% H_3PO_4.



Scheme 1

can be used for preparation of the highly toxic fluoridates required in enzymatic studies, *e.g.* (**2**; R = R′ = Pr^{i}O).[5] The phosphorofluoridates derived from nucleosides can be synthesized efficiently from the corresponding trimethylsilyl phosphites.[6]

Table 1 shows ^{31}P n.m.r. data for some typical phosphorofluoridates we have synthesised. In a typical experiment 20 ml of a solution of (**3**) (0.01 mol) in dry dichloromethane was cooled to −50 °C and 2 g of SO_2ClF (excess) added with stirring and cooling. The reaction mixture was kept for 1 h at −50 °C and then for an additional 1 h at 20 °C. The solvent, sulphur dioxide, and the excess of SO_2ClF were removed *in vacuo*. Further purification by distillation is necessary only when the starting silyl ester (**3**) is not of high purity. The structures and purity of the phosphorofluoridates (**2**) were confirmed by ^{31}P n.m.r. spectroscopy, mass spectroscopy, and gas chromatography.

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