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# Fluorinated phosphorus compounds
# Part 5. The boiling points of fluoroalkyl phosphoryl compounds

Christopher M. Timperley*, Matthew J. Waters

*Defence Science and Technology Laboratory, Chemical and Biological Defence Sector, Porton Down, Salisbury, Wiltshire SP4 0JQ, UK*

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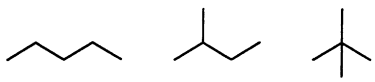
**Abstract**

The relationship between structure and boiling point for several classes of phosphoryl compounds having fluorinated or hydrocarbon ester groups is discussed, i.e. phosphoramidates $(R_2N)_2P(O)OCH_2R_F$ and $(R_FCH_2O)_2P(O)NR_2$, phosphates $(RO)_2P(O)OR_F$, $(R_FCH_2O)_2P(O)OR$, $(R_FO)_3P{=}O$ and $(R_FCH_2O)_2P(O)OCH_2R'_F$, and phosphonates $(R_FO)_2P(O)R$, where R= alkyl and $R_F$= fluoroalkyl. Fluorination generally produces compounds of similar or lower boiling point than the unfluorinated parent compounds. A key factor governing the boiling point of a fluorinated phosphoryl compound relative to its hydrocarbon analogue is not its molecular weight, but the position and number of fluorine atoms in the ester linkage(s). Molecules with an umbrella of fluorine atoms repel each other, leading to low intermolecular forces: the boiling points of $(C_3F_7CH_2O)_3P{=}O$ and $(C_3H_7CH_2O)_3P{=}O$ are close despite a molecular weight difference of 378. Molecules with protons capable of intermolecular hydrogen-fluorine bonding (i.e. those containing –NHR or $–CF_2H$ groups) have higher boiling points than those without, due to attractive forces in the liquid state. Synthetic procedures for four unfluorinated phosphates — $(MeO)_2P(O)O$-*i*-Pr, $(MeO)_2P(O)O$-*n*-Bu, $(EtO)_2P(O)O$-*i*-Pr and (*s*-$BuO)_3P{=}O$ are outlined. © 2001 Elsevier Science B.V. All rights reserved.

*Keywords:* Bis(fluoroalkyl) alkyl phosphates; Bis(fluoroalkyl) alkylphosphonates; Bis(fluoroalkyl) *N*,*N*-dialkylphosphoramidates; Fluoroalkyl phosphates; Fluoroalkyl *N*,*N*,*N*′,*N*′-tetraalkylphosphorodiamidates

## 1. Introduction

The unusual physical properties of organic molecules containing fluorine have fascinated chemists for years. An early surprise was the discovery that the boiling points of linear alkanes and perfluoroalkanes tracked each other closely despite large differences in molecular weight [1]. Branching, which tends to lower the boiling points of hydrocarbons, often has little effect on the boiling points of perfluorocarbons. Comparison of the boiling points of some isomers of pentane and perfluoropentane illustrates these generalisations [2].



| | | | |
|---|---|---|---|
| *bp* $C_5F_{12}$ | 29°C | 30°C | 30°C |
| *bp* $C_5H_{12}$ | 36°C | 28°C | 10°C |

Perfluorinated ethers and amines also boil at much lower temperatures than hydrocarbon analogues despite their much greater molecular weights [2]. Such trends reflect the extremely low intermolecular interactions in perfluoro-compounds. In most series of fluorinated compounds, the relationship between structure and boiling point is poorly established. Many fluoroalkyl phosphoryl compounds have been made in our laboratories to date [3–6] and, as most of their hydrocarbon counterparts were known, it was of interest to see how their boiling points compared. Classes of compounds considered were phosphoramidates A and B, phosphates C–F and phosphonates G (Fig. 1).[1] In the case of phosphates of structure F, a few unfluorinated analogues required preparation (their synthesis is described later — see Section 3).

The aim of this study is to examine how replacement of protons with fluorine atoms influences boiling point.

* Corresponding author. Tel.: +44-1980-613566; fax: +44-1980-613371.
*E-mail address*: cmtimperley@dera.gov.uk (C.M. Timperley).

[1] Organic phosphorus compounds are named after the corresponding parent acids. Most compounds described in this paper are derivatives of phosphoric acid $(HO)_3P{=}O$, except for compounds of type G which are derivatives of alkylphosphonic acids $(HO)_2P(O)R$. They are named as follows: A, fluoroalkyl *N*,*N*,*N*′,*N*′-tetraalkylphosphorodiamidates; B, bis(-fluoroalkyl) *N*,*N*-dialkylphosphoramidates; C, dialkyl fluoroalkyl phosphates; D, bis(fluoroalkyl) alkyl phosphates; E, tris(fluoroalkyl) phosphates; F, bis(fluoroalkyl) fluoroalkyl phosphates; and G bis(fluoroalkyl) alkylphosphonates.

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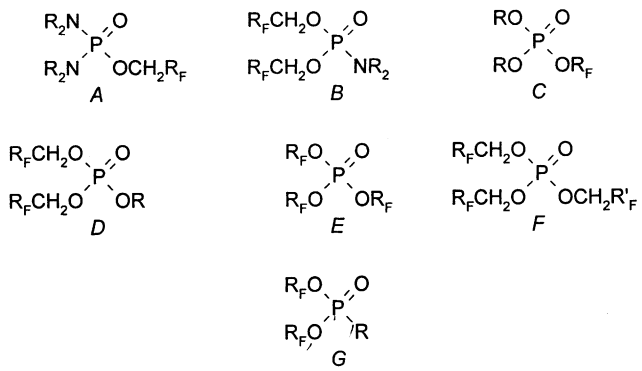


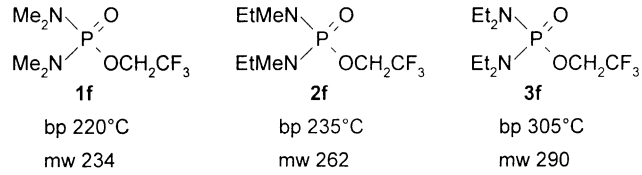

Fig. 1. Compounds investigated (R= alkyl and $R_F$= fluoroalkyl).

Discussion will focus on the relationship of structure to boiling point for each of the classes of compounds in Fig. 1. Data is presented in seven tables (the suffixes **f** and **h** after the compound numbers indicate fluorocarbon or hydrocarbon ester groups). As boiling points were recorded at different pressures, values at atmospheric pressure were estimated using a pressure–temperature nomograph. When close boiling points for unfluorinated phosphorus compounds appeared in the literature, the average was taken.

## 2. Boiling point comparisons

### 2.1. Phosphoramidates A and B

Hydrocarbon compounds of structure A contain two amino groups and boil at similar or lower temperatures than their fluoro analogues (Table 1). Increasing the size of the dialkylamino group raises the boiling point. In hydrocarbon and fluorocarbon pairs, the boiling point does not change much when $Me_2N$ is replaced by EtMeN, but increases appreciably when it is replaced by $Et_2N$. For example, compare **1f** with **2f** and **3f**.




Hydrocarbon compounds of structure B contain one amino group and have boiling points close to those of the fluorinated analogues (Table 2). Replacement of a $CH_3CH_2O$– group with a $CF_3CH_2O$– group does not affect the boiling point much, despite the weight difference of 54 mass units. Compounds with alkylamino groups boil 50–90°C higher than those with dialkylamino groups (compare **4f** with **5f** and **6f** with **7f**). The higher boiling points of the former can be ascribed to intermolecular hydrogen bonding between the amino proton and the fluoro-ester groups of associated molecules.

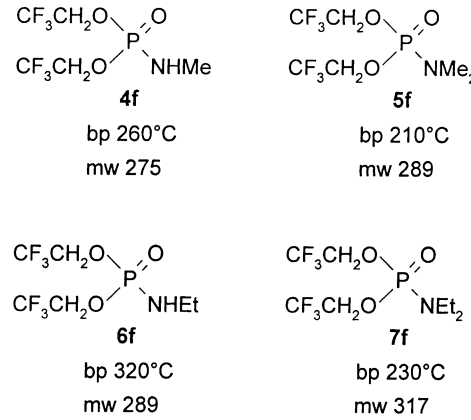



Table 1
Data for phosphorus amides of structure $(RR'N)_2P(O)OCH_2R_F$ (class A)

| Compound | R | R′ | $R_F$ | bp (°C/mmHg) | bp (°C/760 mmHg) | Reference |
|---|---|---|---|---|---|---|
| **1f** | Me | Me | $CF_3$ | 44/0.4 | 220 | [4] |
| **1h** | Me | Me | $CH_3$ | 103–104/18 | 220 | [7] |
| **2f** | Me | Et | $CF_3$ | 68/1 | 235 | [4] |
| **2h** | Me | Et | $CH_3$ | 56–58/1 | 225 | [8] |
| **3f** | Et | Et | $CF_3$ | 82/0.06 | 305 | [4] |
| **3h** | Et | Et | $CH_3$ | 79–80/0.8 | 255 | [9] |

Table 2
Data for phosphorus amides of structure $RR'NP(O)(OCH_2R_F)_2$ (class B)

| Compound | R | R′ | $R_F$ | bp (°C/mmHg) | bp (°C/760 mmHg) | Reference |
|---|---|---|---|---|---|---|
| **4f** | Me | H | $CF_3$ | 84–86/1 | 260 | [4] |
| **4h** | Me | H | $CH_3$ | 135/17, 130/15 | 260 | [10,11] |
| **5f** | Me | Me | $CF_3$ | 37/0.5 | 210 | [4] |
| **5h** | Me | Me | $CH_3$ | 84/12 | 210 | [12] |
| **6f** | Et | H | $CF_3$ | 96/0.1 | 320 | [4] |
| **6h** | Et | H | $CH_3$ | 80/0.03 | 315 | [13] |
| **7f** | Et | Et | $CF_3$ | 62/1 | 230 | [4] |
| **7h** | Et | Et | $CH_3$ | 91/6, 101/13 | 230 | [7,12] |

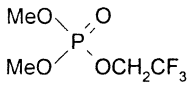
Table 3
Data for phosphorus esters of structure $(RO)_2P(O)OR_F$ (class C)

| Compound | R | $R_F$ | bp (°C/mmHg) | bp (°C/760 mmHg) | Reference |
|---|---|---|---|---|---|
| **8f** | Me | $CH_2CF_3$ | 54/1.8 | 205 | [3] |
| **8h** | Me | $CH_2CH_3$ | 112/41 | 205[a] | [14] |
| **9f** | Me | $CH_2C_2F_5$ | 61/1 | 230 | [3] |
| **9h** | Me | $CH_2C_2H_5$ | 116/15 | 240 | [15] |
| **10f** | Me | $CH(CF_3)_2$ | 50/6 | 180 | [3] |
| **10h** | Me | $CH(CH_3)_2$ | 61/0.03 | 290 | [16] |
| **11f** | Me | $CH_2C_3F_7$ | 42/0.06 | 250 | [3] |
| **11h** | Me | $CH_2C_3H_7$ | 70/0.02 | 305 | [16] |
| **12f** | Et | $CH_2CF_3$ | 90/13[b] | 215 | [3] |
| **12h** | Et | $CH_2CH_3$ | – | 215[a] | [16] |
| **13f** | Et | $CH_2C_2F_5$ | 90/12 | 210 | [3] |
| **13h** | Et | $CH_2C_2H_5$ | 130/20, 96–97/6 | 240 | [15,17] |
| **14f** | Et | $CH(CF_3)_2$ | 56/0.5 | 235 | [3] |
| **14h** | Et | $CH(CH_3)_2$ | 91/11 | 215 | [18] |
| **15f** | Et | $CH_2C_3F_7$ | 88/8 | 220 | [3] |
| **15h** | Et | $CH_2C_3H_7$ | 81/1, 123/15 | 245 | [17,19] |

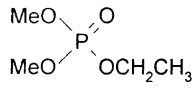
[a] This value is not extrapolated.
[b] Original figure 60–66°C/0.05 mmHg [3] is too high — a resynthesised sample of 98%+ purity (by multinuclear NMR) had the boiling point shown in the table.

### 2.2. Phosphates C

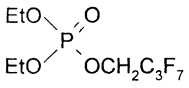
Dialkyl fluoroalkyl phosphates of structure C contain one fluoro-ester group and have similar or lower boiling points than their unfluorinated analogues (Table 3). For example, compare **8f** with **8h** and **15f** with **15h**.



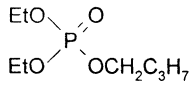

**8f**
bp 205°C
mw 208




**8h**
bp 205°C
mw 154



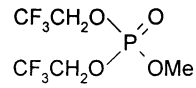

**15f**
bp 220°C
mw 336



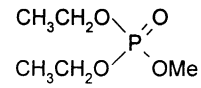

**15h**
bp 245°C
mw 210

### 2.3. Phosphates D

Bis(fluoroalkyl) alkyl phosphates of structure D contain two fluoro-ester groups and have boiling points 10–40°C higher than their hydrocarbon analogues (Table 4). For example, compare **16f** with **16h**.




**16f**
bp 245°C
mw 276




**16h**
bp 208°C
mw 168

The higher boiling points of the fluoro compounds might arise from increased attractions between the fluoro-ester groups of one molecule and the electron-deficient alkoxy groups of another. The alkoxy groups in molecules of structure *D* are unusually polarised: the methoxy group in compounds $(R_FCH_2O)_2P(O)OMe$, where $R_F$ is $CF_3$ or $C_2F_5$, can be displaced under mild conditions [4].

Table 4
Data for phosphorus esters of structure $ROP(O)(OCH_2R_F)_2$ (class D)

| Compound | R | $R_F$ | bp (°C/mmHg) | bp (°C/760 mmHg) | Reference |
|---|---|---|---|---|---|
| **16f** | Me | $CF_3$ | 42/0.1 | 245 | [4] |
| **16h** | Me | $CH_3$ | 101/24, 208 | 208[a] | [18,20] |
| **17f** | Et | $CF_3$ | 37/0.01 | 250 | [4] |
| **12h** | Et | $CH_3$ | – | 215[a] | [21] |
| **18f** | *n*-Pr | $CF_3$ | 45/0.015 | 270 | [4] |
| **13h** | *n*-Pr | $CH_3$ | 130/20, 96–97/6 | 240 | [15,17] |
| **19f** | *i*-Pr | $CF_3$ | 37/0.015 | 260 | [4] |
| **19h** | *i*-Pr | $CH_3$ | 46/0.03 | 270 | [16] |

[a] This value is not extrapolated.

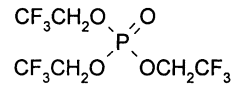
Table 5
Data for phosphorus esters of structure $(R_FO)_3P{=}O$ (class E)

| Compound | $R_F$ | bp (°C/mmHg) | bp (°C/760 mmHg) | Reference |
|---|---|---|---|---|
| **20f** | $CH_2CF_3$ | 40/0.6 | 210 | [6] |
| **12h** | $CH_2CH_3$ | – | 215[a] | [22] |
| **21f** | $CH_2C_2F_5$ | 64/0.9 | 235 | [6] |
| **21h** | $CH_2C_2H_5$ | – | 252[a] | [22] |
| **22f** | $CH_2(CF_2)_2H$ | 102/0.015 | 360 | [6] |
| **23f** | $CH(CF_3)_2$ | 24°C (mp) | – | [6] |
| **24f** | $CH(CH_2F)_2$ | 49/0.02 | 275 | [6] |
| **24h** | $CH(CH_3)_2$ | 84/5 | 225 | [23] |
| **25f** | $CH_2C_3F_7$ | 63/0.08 | 275 | [6] |
| **25h** | $CH_2C_3H_7$ | – | 289[a] | [22,24] |
| **26f** | $CH(CH_3)C_2F_5$ | 62/0.8 | 230 | [6] |
| **26h** | $CH(CH_3)C_2H_5$ | 80/0.015 | 325 | [16] |

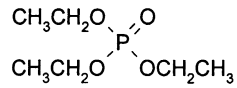
[a] This value is not extrapolated.

### 2.4. Phosphates E

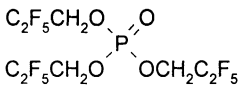
Symmetrical tris(fluoroalkyl) phosphates of structure E contain three identical fluoro-ester groups and have boiling points determined by the number and position of the fluorine atoms. Compounds with terminal perfluoroalkyl groups boil slightly lower than their unfluorinated counterparts despite large differences in molecular weight (Table 5). For example, compare **20f** with **12h** and **21f** with **21h**.



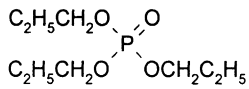
**20f**
bp 210°C
mw 344



**12h**
bp 215°C
mw 182

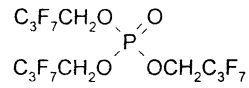


**21f**
bp 235°C
mw 494

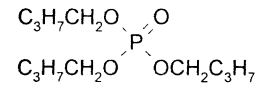


**21h**
bp 252°C
mw 224

Tris(heptafluorobutyl) phosphate **25f** has an extrapolated boiling point lower than that of tributyl phosphate **25h** despite a molecular weight difference of 378 mass units!



**25f**
bp 275°C
mw 644



**25h**
bp 289°C
mw 266

### 2.5. Phosphates F

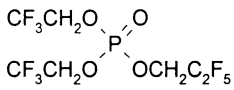
Unsymmetrical tris(fluoroalkyl) phosphates of structure F contain two different fluoro-ester groups. Like the symmetrical phosphates, they boil at similar or lower temperatures than their hydrocarbon counterparts (Table 6). Three fluoroalkyl groups around the phosphoryl core P=O gives molecules shielded by an umbrella of fluorine atoms. Electronic repulsion between the molecules gives rise to low intermolecular forces and accounts for their low boiling points; compare, for example, **28f** with **13h**. This principle also

Table 6
Data for phosphorus esters of structure $(R_FCH_2O)_2P(O)OCH_2R'_F$ (class F)

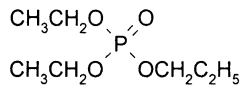
| Compound | $R_F$ | $R'_F$ | bp (°C/mmHg) | bp (°C/760 mmHg) | Reference |
|---|---|---|---|---|---|
| **27f** | $CF_3$ | $(CF_2)_2H$ | 100/10 | 225 | [6] |
| **28f** | $CF_3$ | $C_2F_5$ | 82/10 | 205 | [6] |
| **13h** | $CH_3$ | $C_2H_5$ | 130/20, [15] | 240 | [15,18] |
| **29f** | $CF_3$ | $C_3F_7$ | 85/10 | 210 | [6] |
| **29h** | $CH_3$ | $C_3H_7$ | 85/4, 123/15 | 240 | [18,19] |
| **30f** | $C_2F_5$ | $CF_3$ | 100/10 | 225 | [6] |
| **31f** | $(CF_2)_2H$ | $CF_3$ | 124/5 | 275 | [6] |
| **31h** | $C_2H_5$ | $CH_3$ | 145/20 | 265 | [15] |
| **32f** | $C_2F_5$ | $(CF_2)_2H$ | 94/5 | 235 | [6] |
| **21h** | $C_2H_5$ | $C_2H_5$ | – | 252[a] | [22] |
| **33f** | $C_2F_5$ | $C_3F_7$ | 104/10 | 230 | [6] |
| **33h** | $C_2H_5$ | $C_3H_7$ | 60/0.02 | 295 | [16] |
| **34f** | $C_3F_7$ | $CF_3$ | 100/1 | 280 | [6] |
| **34h** | $C_3H_7$ | $CH_3$ | 95–96/3–4 | 245 | [25] |

[a] This value is not extraploated.

operates when fluoroalkyl groups are bound directly to the phosphoryl core; tris(trifluoromethyl)phosphine oxide $(CF_3)_3P{=}O$ is a liquid that boils at 24°C at atmospheric pressure [26], yet its unfluorinated analogue, trimethylphosphine oxide $(CH_3)_3P{=}O$ is a solid that melts at 140°C.



**28f**
bp 205°C
mw 394



**13h**
bp 240°C
mw 196

Symmetric and unsymmetric tris(fluoroalkyl) phosphates containing the tetrafluoropropyl group $-CH_2(CF_2)_2H$ boil at much higher temperatures than those with pentafluoropropyl groups $-OCH_2C_2F_5$, presumably because the ω-proton of the former can participate in intermolecular hydrogen-fluorine bonding.

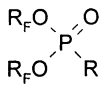
### 2.6. Phosphonates G

Bis(fluoroalkyl) alkylphosphonates of structure G follow similar boiling point trends as the tris(fluoroalkyl) phosphates of structures E and F (Table 7); they generally boil at lower temperatures than their hydrocarbon counterparts. Again an umbrella of fluorine atoms depresses the boiling point. Branched fluoro-ester groups in bis(hexafluoroisopropyl) alkylphosphonates give rise to much lower forces of attraction than present in di-isopropyl analogues (the

Table 7
Data for phosphorus esters of structure $RP(O)(OR_F)_2$ (class G)

| Compound | R | $R_F$ | bp (°C/mmHg) | bp (°C/760 mmHg) | Reference |
|---|---|---|---|---|---|
| Dialkyl methylphosphonates | | | | | |
| **35f** | Me | $CH_2CF_3$ | 55/4 (mp 22°C) | 195 | [5] |
| **35h** | Me | $CH_2CH_3$ | 64/2 | 215 | [27] |
| **36f** | Me | $CH_2C_2F_5$ | 45/1 (mp 15°C) | 205 | [5] |
| **37f** | Me | $CH_2(CF_2)_2H$ | 97/0.015 | 350 | [5] |
| **37h** | Me | $CH_2C_2H_5$ | 94/9 | 225 | [28] |
| **38f** | Me | $CH(CF_3)_2$ | 38/2.5 | 180 | [5] |
| **38h** | Me | $CH(CH_3)_2$ | 66/3 | 210 | [27] |
| **39f** | Me | $CH_2C_3F_7$ | 73/0.02 (mp 20°C) | 315 | [5] |
| **39h** | Me | $CH_2C_3H_7$ | 86–91/1.5 | 260 | [29] |
| Dialkyl ethylphosphonates | | | | | |
| **40f** | Et | $CH_2CF_3$ | 59/4 | 200 | [5] |
| **40h** | Et | $CH_2CH_3$ | 62/2 | 210 | [27] |
| **41f** | Et | $CH_2C_2F_5$ | 35/0.1 (mp 19°C) | 230 | [5] |
| **42f** | Et | $CH_2(CF_2)_2H$ | 98/0.015 | 355 | [5] |
| **42h** | Et | $CH_2C_2H_5$ | 48/0.2 | 240 | [30] |
| **43f** | Et | $CH(CF_3)_2$ | 41/0.15 | 235 | [5] |
| **43h** | Et | $CH(CH_3)_2$ | 54/0.2 | 240 | [16] |
| **44f** | Et | $CH_2C_3F_7$ | 73/0.015 | 315 | [5] |
| **44h** | Et | $CH_2C_3H_7$ | 138/17 | 265 | [31] |
| Dialkyl propylphosphonates | | | | | |
| **45f** | *n*-Pr | $CH_2CF_3$ | 47/1 | 210 | [5] |
| **45h** | *n*-Pr | $CH_2CH_3$ | 53/0.8 | 220 | [16] |
| **46f** | *n*-Pr | $CH_2C_2F_5$ | 49/0.5 | 225 | [5] |
| **47f** | *n*-Pr | $CH_2(CF_2)_2H$ | 95/0.015 | 350 | [5] |
| **47h** | *n*-Pr | $CH_2C_2H_5$ | 76/0.04 | 305 | [16] |
| **48f** | *n*-Pr | $CH(CF_3)_2$ | 34/0.3 | 215 | [5] |
| **48h** | *n*-Pr | $CH(CH_3)_2$ | 53/0.01 | 290 | [16] |
| **49f** | *n*-Pr | $CH_2C_3F_7$ | 80/0.015 | 325 | [5] |
| **49h** | *n*-Pr | $CH_2C_3H_7$ | 96/0.025 | 345 | [16] |
| Dialkyl isopropylphosphonates | | | | | |
| **50f** | *i*-Pr | $CH_2CF_3$ | 57/0.04 | 200 | [5] |
| **50h** | *i*-Pr | $CH_2CH_3$ | 68/4 | 210 | [16] |
| **51f** | *i*-Pr | $CH_2C_2F_5$ | 64/3 | 210 | [5] |
| **52f** | *i*-Pr | $CH_2(CF_2)_2H$ | 91/0.015 | 340 | [5] |
| **52h** | *i*-Pr | $CH_2C_2H_5$ | 69/0.03 | 300 | [16] |
| **53f** | *i*-Pr | $CH(CF_3)_2$ | 46/0.8 | 215 | [5] |
| **53h** | *i*-Pr | $CH(CH_3)_2$ | 65/0.1 | 270 | [16] |
| **54f** | *i*-Pr | $CH_2C_3F_7$ | 71/0.02 | 310 | [5] |
| **54h** | *i*-Pr | $CH_2C_3H_7$ | 74/0.01 | 320 | [16] |

molecular weight difference between the fluorinated and unfluorinated compounds is 216 mass units).

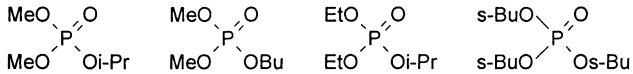


| R | $R_F = CH(CF_3)_2$ | $R_F = CH(CH_3)_2$ |
|---|---|---|
| Me | 180 °C | 210 °C |
| Et | 235 °C | 240 °C |
| *n*-Pr | 215 °C | 290 °C |
| *i*-Pr | 215 °C | 270 °C |

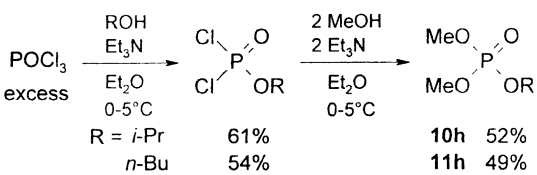
Bis(fluoroalkyl) alkylphosphonates containing the tetrafluoropropyl group $–CH_2(CF_2)_2H$ are exceptional as they boil at much higher temperatures than those with pentafluoropropyl or propyl groups; cf. tris(fluoroalkyl) phosphates of structures E and F (see Section 2.5).

## 3. Synthetic work

Compounds required to complete the boiling point tables were dimethyl isopropyl phosphate **10h**, dimethyl butyl phosphate **11h**, diethyl isopropyl phosphate **14h** and tri(*s*-butyl) phosphate **26h**.

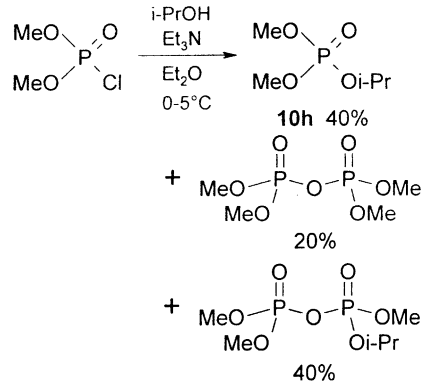



A simple method for the preparation of alkyl phosphorochloridates consists of the alcoholysis of phosphorus oxychloride; the hydrogen atom of the hydroxyl and the chlorine of the phosphorus compound are removed as hydrogen chloride. The formation of either the primary or the secondary derivatives depends upon the relative proportions of the reagents and the reactivity of the alcohol. Slow dropwise addition of isopropanol or butanol and triethylamine to an excess of phosphorus oxychloride with cooling allowed the phosphorodichloridates to be isolated in good yield.[2] Methanolysis of these in the presence of triethylamine furnished phosphates **10h** and **11h**.

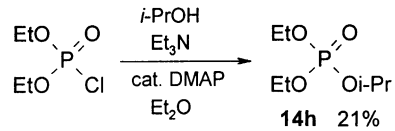



[2] Dichloridates $Cl_2P(O)OR$ where R = *i*-Pr or *n*-Bu have been made in yields of 40 or 75%, respectively by the alcoholysis of pyrophosphate $Cl_2P(O)OP(O)Cl_2$ between −30 and 0°C [32]. Isopropyl phosphorodichloridate $Cl_2P(O)O$-*i*-Pr has been prepared in 60% yield by mixing phosphorus oxychloride with isopropanol, with removal of HCl after 2 h by bubbling a stream of dry nitrogen through the solution [33].

Treatment of dimethyl phosphorochloridate with isopropanol under analogous conditions gave, in addition to dimethyl isopropyl phosphate **10h**, a mixture of pyrophosphates (from attack of the phosphate on the starting phosphorochloridate and loss of isopropyl or methyl chloride). The pyrophosphate ratios, determined by GC–MS, reflect the ease of dealkylation of the methoxy group of the phosphonium intermediate by chloride ion (the isopropoxy group is less vulnerable to dealkylation). No attempt was made to separate the desired phosphate from the mixture.



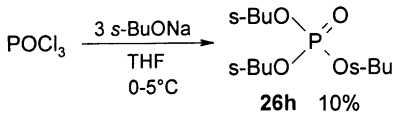

A cleaner reaction ensued between diethyl phosphorochloridate and isopropanol. A catalytic amount of 4-dimethylaminopyridine (DMAP) was used to accelerate the otherwise sluggish addition and, after distillation, phosphate **14h** could be isolated in low yield.



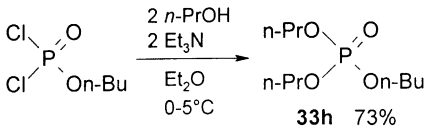

It can be concluded that the easiest way to make dialkyl alkyl phosphates is to put the largest alkoxy group on phosphorus first (to give an alkyl phosphorodichloridate) and then introduce the smaller alkoxy groups. The inverse sequence, i.e. alcoholysis of the dialkyl phosphorochloridate, requires harsher conditions.

The action of three molar equivalents of *s*-butanol and triethylamine on phosphorus oxychloride in the presence of DMAP gave only di-*s*-butyl phosphorochloridate $(s\text{-BuO})_2P(O)Cl$ even on prolonged reflux in ether. Work-up was carried out in the usual way but the crude product underwent decomposition on attempted distillation. The poor reactivity of di-*s*-butyl phosphorochloridate necessitates harsher conditions for forcing the third group onto phosphorus. Slightly more than three molar equivalents of sodium *s*-butoxide in tetrahydrofuran resulted in complete displacement of chloride from phosphorus oxychloride (shown by GC–MS analysis). Although, the required phosphate **26h** decomposed on vacuum distillation, a small amount could be isolated and characterised. It contains

three chiral groups and exists as a statistically correct 3:1 mixture of RRR/SSS and RSS/SRR diastereoisomers as determined by phosphorus NMR spectroscopy (see experimental Section 4.4).




Dipropyl butyl phosphate **33h**, the last of the missing compounds, was isolated in good yield from the reaction of butyl phosphorodichloridate with propanol and triethylamine.




The analogue, diethyl butyl phosphate $(EtO)_2P(O)On$-Bu was produced similarly by Gerrard by the addition of the same dichloridate to an ethereal solution of ethanol and pyridine [19].

## 4. Experimental details

All reagents were of commercial quality. DMAP refers to 4-dimethylaminopyridine. Anhydrous solvents were used for reactions; tetrahydrofuran was distilled from sodium wire/benzophenone. Triethylamine was distilled from $CaH_2$ and stored over $CaH_2$. NMR spectra were obtained on a JEOL Lambda 500 instrument (operating at 500 MHz for $^1H$, 125 MHz for $^{13}C$, 470 MHz for $^{19}F$, and 202 MHz for $^{31}P$ spectra) or a JEOL Lambda 300 instrument (operating at 300 MHz for $^1H$, 75 MHz for $^{13}C$, 282 MHz for $^{19}F$, and 121.5 MHz for $^{31}P$ spectra) as solutions in $CDCl_3$, with internal reference $SiMe_4$ for $^1H$ and $^{13}C$, external $CFCl_3$ for $^{19}F$ and external $(MeO)_3P$ ($\delta = 140$ ppm) for $^{31}P$ spectra. Data are recorded as follows: chemical shifts in ppm from reference on the $\delta$ scale, integration, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet and sep: septet; br: broad), coupling constant ($J$, Hz) and assignment. IR spectra were recorded as liquid films on a Nicolet SP210 instrument using Omnic software. Reaction mixtures were monitored by gas chromatography-mass spectrometry (GC–MS) using a Finnigan MAT GCQ instrument with chemical ionisation (CI) using methane as reagent gas. Molecular weights of pure products were confirmed with methane positive CI data. Elemental analysis was carried out on the largest stable fragment ion, using high resolution mass spectrometry (HRMS) on a Micromass Autospec SQ Double Focusing Magnetic Sector instrument. Mode: positive ion electron impact, magnet scan $m/z$ 400–100 (seconds per decade), resolution 2900. Inlet: septum (160°C), 0.2 ml introduced. Source conditions: temperature 200°C, electron energy 70 eV, and accelerating voltage 8000 V.

### 4.1. General procedure for alkyl phosphorodichloridates

A solution of the appropriate alcohol (0.04 mol) and triethylamine (0.04 mol) in ether (50 ml) was added dropwise to a stirred solution of phosphorus oxychloride (0.06 mol) in ether (75 ml) cooled to 0–5°C. After addition the mixture was allowed to warm to room temperature and left for 14 h. The precipitate was removed by filtration and the filtrate concentrated to give a liquid. This was distilled under reduced pressure to give the dichloridate as colourless liquid.

#### 4.1.1. Isopropyl phosphorodichloridate

Yield 61% and purity 99% by phosphorus NMR analysis (bp 40°C/4 mmHg, lit. bp 60°C/12 mmHg [32] and 64–66°C/14 mmHg [33]). This material discoloured on standing for several days in a refrigerator and was best used immediately for phosphate synthesis. $^1H$ NMR $\delta = 5.04$ (1H, dsep, $J = 11.2$ and 6.2 Hz, OCH), 1.49 (6H, dd, $J = 1$ and 6.2 Hz, $CH_3$). $^{13}C$ NMR $\delta = 79.6$ (OCH), 23.2 ($CH_3$). $^{31}P$ NMR $\delta = 4.7$. IR (film) $\nu = 1466, 1390, 1381, 1304$ (P=O), 1182, 1146, 1097, 1012, 991, 918, 893, 737, 598, 577, 519 $cm^{-1}$. HRMS calculated $C_3H_7Cl_2O_2P$ 175.956. The compound did not give a useful mass spectrum.

#### 4.1.2. Butyl phosphorodichloridate

Yield 54% and purity 99% by phosphorus NMR analysis (bp 50°C/1.5 mmHg, lit. bp 85°C/13 mmHg [19]). $^1H$ NMR $\delta = 4.35$ (2H, dt, $J = 10$ and 6.4 Hz, $OCH_2$), 1.80 (2H, m, $J = 7$ Hz, $CH_2$), 1.47 (2H, m, $J = 7$, $CH_2CH_3$), 0.98 (3H, t, $J = 7.2$, $CH_3$). $^{13}C$ NMR $\delta = 72.1$ ($OCH_2$), 31.5 ($CH_2$), 18.5 ($CH_2CH_3$), 13.4 ($CH_3$). $^{31}P$ NMR $\delta = 6.0$. IR (film) $\nu = 1466, 1431, 1387, 1300$ (P=O), 1147, 1120, 1055, 1032, 1016, 897, 833, 789, 727, 579, 528, 496, 405 $cm^{-1}$. HRMS calculated $C_4H_9Cl_2O_2P$ 189.972. Found 134.918 [$M$-$C_4H_9$ ($2 \times {}^{35}Cl$)] (error −7.9), 136.915 [$M$-$C_4H_9$ ($1 \times {}^{35}Cl$, $1 \times {}^{37}Cl$)] (error −4.7) and 138.912 [$M$-$C_4H_9$ ($2 \times {}^{37}Cl$)] (error −5.4).

### 4.2. General procedure for dialkyl alkyl phosphates

A solution of the appropriate alcohol (0.025 mol) and triethylamine (0.025 mol) in ether (15 ml) was added dropwise by cannula to a stirred solution of the appropriate alkyl phosphorodichloridate (0.011 mol) in ether (35 ml) cooled to 0–5°C under argon. The mixture was allowed to warm to room temperature and left for 14 h; GC–MS analysis showed varying extents of reaction. To ensure full conversion to the phosphate, a catalytic amount of DMAP was added before refluxing the mixtures (5–15 h). The precipitate was removed and the filtrate concentrated to give a mobile liquid that was distilled under reduced pressure (vacuum between 0.02–0.03 mmHg).

*4.2.1. Dimethyl isopropyl phosphate (**10h**)*

Synthesised by methanolysis of isopropyl phosphorodichloridate; 15 h of reflux were required to drive the reaction to completion. The crude product was distilled using a Kugelrohr apparatus to give the title compound as a colourless liquid (bp 61°C/0.03 mmHg). Yield 52% and purity >97% by phosphorus NMR analysis. $^{1}$H NMR $\delta = 4.66$ (1H, dsep, $J = 6.1$ Hz, OCH), 3.75 (6H, d, $J = 10.4$ Hz, $OCH_3$), 1.35 (6H, d, $J = 6.4$ Hz, $CH_3$). $^{13}$C NMR $\delta = 72.6$ (OCH), 53.9 ($OCH_3$), 23.4 ($CH_3$). $^{31}$P NMR $\delta = -0.6$. IR (film) $\nu = 1466, 1389, 1269$ (P=O), 1182, 1144, 1009, 899, 847, 802, 746, 513 cm$^{-1}$. HRMS calculated $C_5H_{13}O_4P$ 168.055 ($[M\text{-}CH_3]^+ = 153.020$). Found 153.032 [$M$-$CH_3$] (error 0).

*4.2.2. Dimethyl butyl phosphate (**11h**)*

Synthesised by methanolysis of butyl phosphorodichloridate; 5 h of reflux were required to drive the reaction to completion. The crude product was distilled using a Kugelrohr apparatus to give the title compound as a colourless liquid (bp 70°C/0.02 mmHg). Yield 49% and purity >95% by phosphorus NMR analysis. $^{1}$H NMR $\delta = 4.06$ (2H, dt, $J = 6.7$ and 6.7 Hz, $OCH_2$), 3.77 (6H, d, $J = 9$ Hz, $OCH_3$), 1.67 (2H, m, $J = 7$ Hz, $CH_2$), 1.43 (2H, m, $J = 7$ Hz, $CH_2CH_3$), 0.95 (3H, t, $J = 7$ Hz, $CH_3$). $^{13}$C NMR $\delta = 67.6$ ($OCH_2$), 54.1 ($OCH_3$), 32.1 ($CH_2$), 18.5 ($CH_2CH_3$), 13.4 ($CH_3$). $^{31}$P NMR $\delta = -0.5$. IR (film) $\nu = 1646, 1466, 1398, 1282$ (P=O), 1188, 1036, 906, 850, 760, 511 cm$^{-1}$. HRMS calculated $C_6H_{15}O_4P$ 182.071 ($[M\text{-}C_2H_5]^+ = 153.009$). Found 153.031 [$M$-$C_2H_5$] (error 1.2).

*4.2.3. Dipropyl butyl phosphate (**33h**)*

Synthesised by propanolysis of butyl phosphorodichloridate; 5 h of reflux were required to drive the reaction to completion. The crude product was distilled using a Kugelrohr apparatus to give the title compound as a colourless liquid (bp 60°C/0.02 mmHg). Yield 73% and purity >99% by phosphorus NMR analysis. $^{1}$H NMR $\delta = 4.05$ (2H, dt, $J = 6.7$ and 6.7 Hz, butyl $OCH_2$), 3.99 (4H, dt, $J = 6.7$ and 6.7 Hz, propyl $OCH_2$), 1.71 (6H, complex m, $J = 7$ Hz, butyl and propyl $CH_2$), 1.42 (2H, m, $J = 7$ Hz, butyl $CH_2CH_3$), 0.97 (6H, t, $J = 7$ Hz, propyl $CH_3$), 0.94 (3H, t, $J = 7$ Hz, $CH_3$). $^{13}$C NMR $\delta = 69$ (propyl $OCH_2$), 67.3 (butyl $OCH_2$), 32.2 (butyl $CH_2$), 23.6 (propyl $CH_2$), 18.6 (butyl $CH_2CH_3$), 13.5 (butyl $CH_3$), 10 (propyl $CH_3$). $^{31}$P NMR $\delta = -1.6$. IR (film) $\nu = 1599, 1466, 1379, 1279$ (P=O), 1151, 1007, 864, 750, 546, 403 cm$^{-1}$. HRMS calculated $C_{10}H_{23}O_4P$ 238.133 ($[M\text{-}C_3H_5]^+ = 197.060$). Found 197.097 [$M$-$C_3H_5$] (error −14.1).

*4.3. Synthesis of diethyl isopropyl phosphate (**14h**)*

A solution of isopropanol (0.03 mol) and triethylamine (0.03 mol) in ether (20 ml) was added dropwise to a stirred solution of diethyl phosphorochloridate (0.03 mol) in ether (40 ml) cooled to 0–5°C. The mixture was allowed to warm to room temperature and left for 14 h; analysis by GC–MS showed incomplete conversion to the phosphate. To drive the reaction to completion, a catalytic amount of DMAP was added and the mixture refluxed for 5 h. The precipitate was removed by filtration and the filtrate concentrated. Fractionation of the residue under reduced pressure gave the title compound as a colourless liquid (bp 46°C/0.03 mmHg). Yield 21% and purity >90% by phosphorus NMR analysis. $^{1}$H NMR $\delta = 4.65$ (1H, dsep, $J = 7$ and 7 Hz, OCH), 4.1 (4H, dq, $J = 7$ and 7 Hz, $OCH_2$), 1.3 (6H, dt, $J = 1.2$ and 7 Hz, ethyl $CH_3$), 1.3 (6H, d, $J = 6$ Hz, isopropyl $CH_3$). $^{13}$C NMR $\delta = 72.4$ (OCH), 63.4 ($OCH_2$), 23.6 (isopropyl $CH_3$), 16.1 (ethyl $CH_3$). $^{31}$P NMR $\delta = -2.8$. IR (film) $\nu = 1466, 1389, 1377, 1263$ (P=O), 1167, 1144, 1101, 1034, 1009, 895, 800, 746, 552, 492, 434 cm$^{-1}$. HRMS calculated $C_7H_{17}O_4P$ 196.086 ($[M\text{-}C_3H_3]^+ = 157.029$). Found 155.047 [$M$-$C_3H_3$] (error −15.3).

*4.4. Synthesis of tri(s-butyl) phosphate (**26h**)*

A solution of *s*-butanol (0.115 mol) in THF (40 ml) was added dropwise to a stirred suspension of sodium hydride (0.115 mol) in THF (40 ml) cooled to 0–5°C. The mixture was warmed to room temperature and left for 2 h. A solution of phosphorus oxychloride (0.033 mol) in THF (50 ml) was added dropwise to the mixture at 0–5°C. After addition, the reaction mixture was allowed to warm to room temperature and left for 14 h; analysis by GC–MS revealed >95% product. The very fine precipitate was removed using special filter paper (Whatman® silicone-treated phase-separator) and the filtrate concentrated to give a liquid. Distillation under reduced pressure gave the title compound as a colourless liquid (bp 80°C/0.015 mmHg, lit. 119–129°C/8–12mm Hg [24] ). Yield 10% and purity >95% by phosphorus NMR analysis. $^{1}$H NMR $\delta = 4.42$ (3H, m, OCH), 1.67 (3H, m, $J = 14$, 7 and 7 Hz, proton of $CH_2$ group), 1.59 (3H, m, $J = 14$, 6 and 6 Hz, proton of $CH_2$ group), 1.31 (9H, d, $J = 6.4$ Hz, $OCHCH_3$), 0.95 (9H, t, $J = 7.3$ Hz, $CH_3$). $^{13}$C NMR $\delta = 76.5$ (OCH), 30.2 ($CH_2$), 20.8 ($OCHCH_3$), 9.3 ($CH_3$). $^{31}$P NMR $\delta = -3.44$ and −3.48. IR (film) $\nu = 1464, 1383, 1259$ (P=O), 1174, 1149, 1126, 1097, 1028, 997, 866, 818, 746, 592, 550 cm$^{-1}$. HRMS calculated $C_{12}H_{27}O_4P$ 266.165. The compound did not give a useful mass spectrum.

## 5. Conclusion

Fluorination of phosphoryl compounds generally produces compounds of similar or lower boiling point than the unfluorinated parent compounds. Those with terminal –$CF_3$ in the ester groups have the lowest boiling points due to low forces of attraction in the liquid state. Those with terminal –$CF_2H$ in the ester groups are an exception — they have high boiling points due presumably to strong

intermolecular hydrogen–fluorine bonds. Compounds shielded by an umbrella of fluorine atoms boil at the lowest temperatures. The boiling points (at atmospheric pressure) quoted in the tables were derived from extrapolation using a pressure–temperature nomograph. Any error in the extrapolation will be the same for all compounds. This has allowed comparative trends to be seen. However, accurate measurement of boiling point for a range of fluorinated and unfluorinated phosphoryl compounds at 760 mmHg are required before a detailed analysis of the physical effects of fluorination can be undertaken.

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