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Fluorinated phosphorus compounds Part 3. The synthesis of symmetrical and unsymmetrical fluoroalkyl phosphates

Christopher M. Timperley*, Ian Holden, Ian J. Morton, Matthew J. Waters

Chemical and Biological Defence Sector, Defence Evaluation and Research Agency, Porton Down, Salisbury, Wiltshire SP4 0JQ, UK

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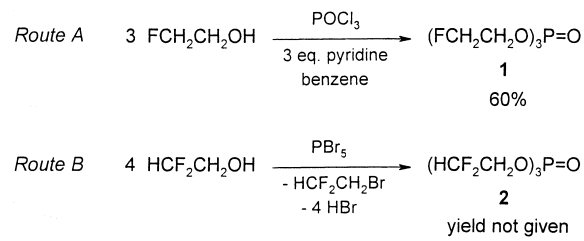
Abstract

Treatment of phosphorus pentachloride with four molar equivalents of fluoroalcohol gave symmetrical phosphates $(R_FO)_3P{=}O$ in isolated yields between 10–92% [$R_F{=}CF_3CH_2$, $C_2F_5CH_2$, $HCF_2CF_2CH_2$, $C_3F_7CH_2$, $(FCH_2)_2CH$, $(CF_3)_2CH$, $C_2F_5(CH_3)CH$]. The reaction proceeded best for fluoroalcohols having many fluorine atoms. 2,2-Difluoroethanol HCF_2CH_2OH and 1,3-difluoroisopropanol $(FCH_2)_2CHOH$ did not react cleanly and gave product mixtures. Hexafluoroisopropanol produced a 3:7 mixture of symmetrical phosphate $[(CF_3)_2CHO]_3P{=}O$ and chlorophosphorane $[(CF_3)_2CHO]_4PCl$. The latter reacted readily with water and alcohols. Heating the chloridates $CF_3CH_2OP(O)Cl_2$, $(CF_3CH_2O)_2P(O)Cl$ and $(C_2F_5CH_2O)_2P(O)Cl$ with various fluoroalcohols in the presence of calcium chloride catalyst gave unsymmetrical phosphates in isolated yields between 46–83%. The mixed phosphate $(CF_3CH_2O)_2P(O)OCH_2C_2F_5$ did not react with butanol or propylamine in dichloromethane at room temperature.

Keywords: Bis(fluoroalkyl)phosphorochloridate; Bis(fluoroalkyl)fluoroalkyl phosphate; Fluorinated phosphate; Tetra(hexafluoroisopropoxy)chlorophosphorane; Tris(fluoroalkyl)phosphate

1. Introduction

The lowest members of the symmetrical fluoroalkyl phosphate family were first made in the first half of the last century by two master fluorine chemists: tris(2-fluoroethyl) phosphate **1** by Knunyants *et al.* [1] and tris(2,2-difluoroethyl) phosphate **2** by Swarts [2].[1] The phosphates were prepared by the fluoroalcoholysis of phosphorus oxychloride (route A) or phosphorus pentabromide (route B). The first reaction requires a base and an inert solvent, whereas the second is conducted without solvent. Phosphate **2** has also been made by oxidation of tris(2,2-difluoroethyl)-phosphite $(HCF_2CH_2O)_3P$ with oxygen in the presence of chloral [3].



Modification of routes A and B has provided other symmetrical fluoroalkyl phosphates, including the third ethyl analogue, tris(2,2,2-trifluoroethyl) phosphate $(CF_3CH_2O)_3P{=}O$ [4–7]. Other homologues include $(C_2F_5CH_2O)_3P{=}O$ [6,7], $(C_3F_7CH_2O)_3P{=}O$ [5–10] and $[(CF_3)_2CHO]_3P{=}O$ [11]. Fluoroalkyl phosphates with more remote fluorine atoms have received little attention, although $(CF_3CH_2CH_2O)_3P{=}O$ has been made [6,7]. Some related phosphates have the general formula $[H(CF_2)_nCH_2O]_3P{=}O$. Members with an even number of difluoromethylene groups ($n = 2$, 4, 6 or 8) have been prepared by route A [12,13] or route B [5], by fluoroalcoholysis of phosphorus pentoxide [14], by dinitrogen tetraoxide oxidation of tris(fluoroalkyl) phosphites [15], or by pyrolysis of bis(fluoroalkyl) phosphoric acids [15].

* Corresponding author. Tel.: +44-1980-613566; fax: +44-1980-613371.

[1] Organic phosphorus compounds are named after the corresponding parent acids. Most of the substances described in this paper are derivatives of phosphoric acid $(HO)_3P{=}O$. Compounds of structure $(R_FO)_3P{=}O$ are symmetrical phosphates or tris(fluoroalkyl) phosphates, while those of structure $(R_FO)_2P(O)OR_F'$ are unsymmetrical phosphates or bis(fluoroalkyl) fluoroalkyl phosphates.

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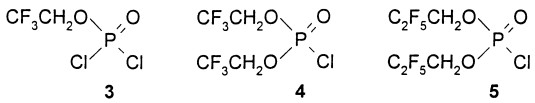
Surprisingly few unsymmetrical tris(fluoroalkyl) phosphates have been reported; the molecule $(CF_3CH_2O)_2P(O)OC(Me)_2(CF_2)_4H$ is a rare example [16].

Previous work from this laboratory described the preparation of dialkyl fluoroalkyl phosphates $(RO)_2P(O)OR_F$ [17] and bis(fluoroalkyl) alkyl phosphates $(R_FO)_2P(O)OR$ [18]. This paper addresses the synthesis of some symmetrical and unsymmetrical tris(fluoroalkyl) phosphates. Symmetrical phosphates were made by the direct interaction of phosphorus pentachloride with four molar equivalents of fluoroalcohol. The use of linear and branched fluoroalcohols permitted the mechanism of reaction to be deduced.



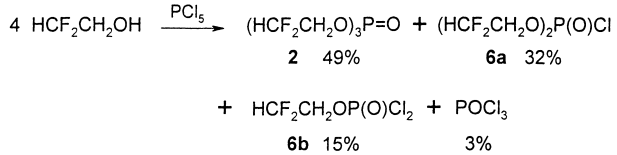
Unsymmetrical phosphates were prepared by heating phosphorochloridates **3–5** with fluoroalcohols in the presence of calcium chloride.

2. Results and discussion

2.1. Synthesis of tris(fluoroalkyl) phosphates

The reaction of phosphorus pentabromide [2] or pentachloride [5] with four moles of fluoroalcohol generates one mole of tris(trifluoroalkyl) phosphate, one mole of fluoroalkyl halide, and four moles of hydrogen halide (refer to route B in the Section 1). Chuganov and Sapgir [5] reported the reactions of phosphorus pentachloride with primary fluoroalcohols, but experimental details and spectroscopic data for the products were not recorded. Their postulated mechanism involved instant generation of $POCl_3$ (via elimination of fluoroalkyl halide from the phosphorane $R_FCH_2OPCl_4$) and its subsequent reaction with three molecules of fluoroalcohol. However, phosphorus oxychloride is normally unreactive towards fluoroalcohols under neutral or acidic conditions [8,18]. Our studies were directed at solving this apparent contradiction.

The reaction of 2-fluoroethanol with phosphorus pentachloride was not pursued owing to the high toxicity of the alcohol [19]. The next homologue, 2,2-difluoroethanol, yielded a mixture of tris(difluoroethyl) phosphate **2**, phosphorochloridates **6a** and **6b**, and phosphorus oxychloride.



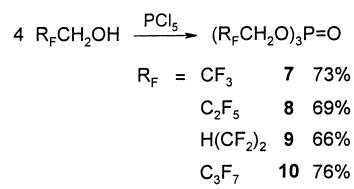
The individual yields parallel the stabilities of the phosphorane intermediates and their ease of elimination of 2-chloro-1,1-difluoroethane. The stabilities decrease in the order $(HCF_2CH_2O)_4PCl > (HCF_2CH_2O)_3PCl_2 > (HCF_2CH_2O)_2PCl_3 > HCF_2CH_2OPCl_4$. It is recognised that electron-acceptor groups on phosphorus stabilise the five coordinate state [20]; e.g. penta(trifluoroethoxy)phosphorane $(CF_3CH_2O)_5P$ can be distilled without decomposition [21].

Table 1
Experimental data for symmetrical phosphates $(R_FO)_3P=O$

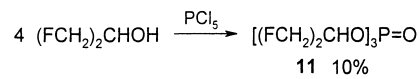
Compound	R_F	Yield (%)	Bp (°C/mmHg)
7	CF_3CH_2	73	40/0.6[a]
8	$C_2F_5CH_2$	69	64/0.9[b]
9	$H(CF_2)_2CH_2$	66	102/0.015[c]
10	$C_3F_7CH_2$	76	63/0.08[d]
11	$(FCH_2)_2CH$	10	49/0.02
12a	$(CF_3)_2CH$	92	mp 24°C[e]
18	$C_2F_5(CH_3)CH$	21	62/0.8

[a] 74–75°C/9 mmHg [4], 186–189°C [5] and 73°C/8 mmHg [6,7].
[b] 67°C/1.5 mmHg [6,7].
[c] 250–255°C [5], 121°C/2 mmHg [13] and 115°C/1 mmHg [14].
[d] 220–223°C [5], 96°C/2.5 mmHg [6,7] and 78–80°C/0.5 mmHg [10].
[e] This compound has also been prepared by treatment of phosphorus oxychloride with three molar equivalents of $(CF_3)_2CHOLi$ in ether (90% yield and mp 23°C) [11].

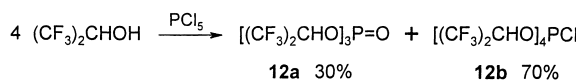
Primary fluoroalcohols containing three or more fluorine atoms reacted rapidly with phosphorus pentachloride to afford phosphates **7–10** in good yield (Table 1).



The secondary fluoroalcohol, 1,3-difluoroisopropanol, gave a mixture of products identifiable by GC–MS, which included mono- and bis-fluoroalkyl phosphorochloridates $(FCH_2)_2CHOP(O)Cl_2$ and $[(FCH_2)_2CHO]_2P(O)Cl$. Symmetrical phosphate **11** was separated by fractionation. The low yield, like that found with 2,2-difluoroethanol, shows that sparsely fluorinated alcohols cannot form phosphates as easily as highly fluorinated ones (perhaps as a consequence of the lower stabilities of the phosphorane intermediates).



The reaction of hexafluoroisopropanol with phosphorus pentachloride followed an unexpected course and furnished two products: desired phosphate **12a** and stable intermediate **12b** in a 3:7 ratio. The composition of the mixture remained constant for repeat experiments and could not be altered by fractionation as both products co-distilled. The origin of the phosphate is not obvious; it did not originate from phosphorane hydrolysis as anhydrous conditions were used.



Tetra(hexafluoroisopropoxy)chlorophosphorane **12b** is a missing link in the hexafluoroisopropoxy-phosphorane family: the related entities $[(CF_3)_2CHO]_3PCl_2$ and $[(CF_3)_2CHO]_5P$ have already been isolated [11]. Like these, the former is covalent, and is expected to have a trigonal bipyramidal structure. The phosphorus chemical shift of chlorophosphorane **12b** is δ 67 ppm, i.e. in the region typical of covalent phosphoranes. It did not give a molecular ion in the high-resolution mass spectrum, but ions of *m/z* 715 and *m/z* 699 were prominent, corresponding respectively to loss of F and Cl from the molecule. The high stability of **12b** compared to analogues derived from primary fluoroalcohols, e.g. $(C_2F_5CH_2O)_4PCl$, is due to the greater electron-withdrawing ability of the hexafluoroisopropoxy group and its greater bulk which disfavours the Arbusov rearrangement:

$$[(CF_3)_2CHO]_4PCl \not\longrightarrow [(CF_3)_2CHO]_3P{=}O + (CF_3)_2CHCl$$

Tetra(hexafluoroisopropoxy)chlorophosphorane **12b** is sensitive to moisture. Addition of water to the 3:7 phosphate–phosphorane mixture resulted in rapid hydrolysis of the phosphorane, allowing the isolation of pure tris(hexafluoroisopropyl) phosphate **12a**. Alternative routes to this compound involve hydrolysis of the phosphoranes $[(CF_3)_2CHO]_3PCl_2$ and $[(CF_3)_2CHO]_5P$ [11].

$$\underset{\substack{\textbf{12b}\\ \delta_P\ -67}}{[(CF_3)_2CHO]_4PCl} \xrightarrow[\text{quantitative}]{H_2O} \underset{\substack{\textbf{12a}\\ \delta_P\ -3.6}}{[(CF_3)_2CHO]_3P{=}O} + (CF_3)_2CHOH$$

Methanolysis of **12b** resulted in substitution of the chlorine atom, probably via an octahedral intermediate [21], to give 50% methoxyphosphorane **13** (Fig. 1). Further reaction gave the unstable dimethoxyphosphorane **14** which collapsed by two pathways to give 12% bis(hexafluoroisopropyl) methyl phosphate **15** (via loss of hexafluoroisopropyl methyl ether) and 6% dimethyl hexafluoroisopropyl phosphate **16** (via loss of bis(hexafluoroisopropyl)ether). Unstable dimethoxyphosphorane **14** also underwent methanolysis to trimethoxyphosphorane **17** which collapsed, presumably by loss of bis(hexafluoroisopropyl)ether, to give a trace of trimethyl phosphate.

The products were identified by analysis by NMR and GC–MS, a standard of compound **15** existing from current work[2] and one of compound **16** existing from previous work [17]; trimethyl phosphate is available commercially. Methoxyphosphorane **13**, like other fluoroalkoxy-substituted phosphoranes [11], did not give a molecular ion in its mass spectrum, but gave a minor peak at *m/z* 699 (loss of a methoxy group) and a major peak at *m/z* 563 (loss of a hexafluoroisopropoxy group). Its phosphorus chemical shift is δ-83 ppm. The formation of fluoroethers as by-products is assumed. It is however known that $Ph_3P(OCH_2CF_3)_2$ reacts

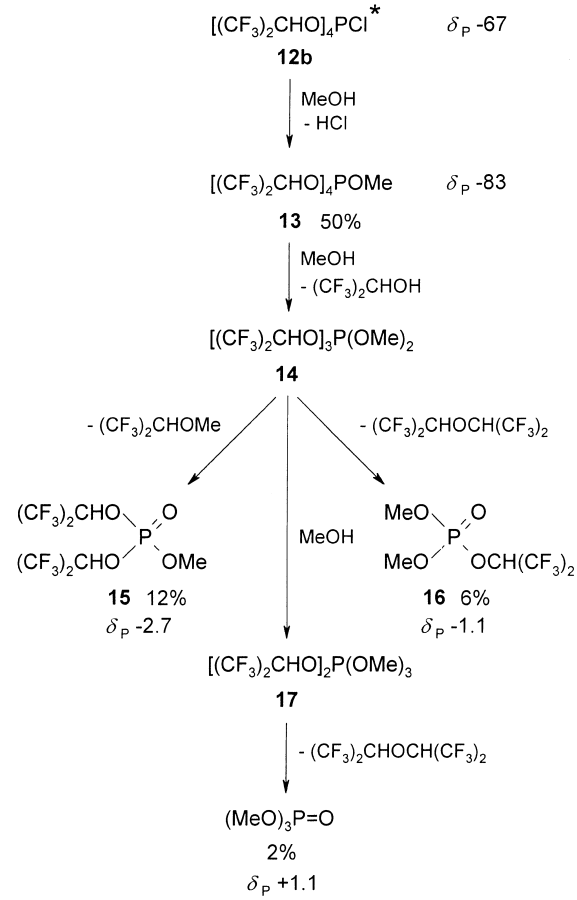


Fig. 1. The methanolysis of tetra(hexafluoroisopropoxy)chlorophosphorane.

rapidly with alcohols to afford trifluoroethyl ethers [22]. The possibility that phosphates **15** and **16** might arise from transesterification of the tris(hexafluoroisopropyl) phosphate in the starting mixture was excluded as its proportion remained constant before and after the reaction. Tris(fluoroalkyl) phosphates are also unreactive towards alcohols such as butanol (see Section 2.3).

The multiple reaction pathways clearly show the destabilising effect of increased alkoxy substitution on pentacoordinate phosphorus. Interestingly, phosphorane **14** bearing hexafluoroisopropyl and methoxy groups eliminated a larger proportion of the unsymmetrical methoxy ether $(CF_3)_2CHOMe$ compared to the symmetrical fluoroether $(CF_3)_2CHOCH(CF_3)_2$; ejection of dimethyl ether was not apparent (see Fig. 1).

The reaction of racemic 3,3,4,4,4-pentafluoro-2-butanol with phosphorus pentachloride did not provide a stable phosphorane, but instead gave the symmetrical phosphate **18** in poor yield. This phosphate contains three chiral ester groups. A pair of diastereoisomers form, one when the three

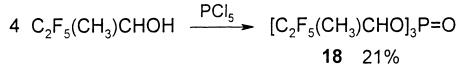
[2] The synthesis of pure bis(hexafluoroisopropyl) phosphorochloridate $[(CF_3)_2CHO]_2P(O)Cl$, a potent electrophile, and its reaction with methanol and triethylamine in ether to furnish phosphate **15** will be discussed in a later paper.

Table 2
Spectroscopic data for symmetrical tris(fluoroalkyl) phosphates $(R_FO)_3P{=}O$ (NMR data measured in $CDCl_3$)

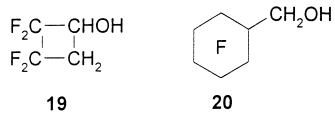
Compound	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)	^{19}F NMR δ, J (Hz)	^{31}P NMR δ	IR ν (cm^{-1})	HRMS analysis
7	4.43 (6H, dq, $J = 8$, 12, OCH_2)	122 (dq, $J = 9$, 276, CF_3), 64.3 (dq, $J = 4$, 40, OCH_2)	−74.5 (9F, t, $J = 7$, CF_3)	−3.7	1460, 1425, 1288 (P=O), 1178, 1084, 964, 899, 845	Calculated $C_6H_6F_9O_4P$ 343.986, found 343.985 (error 3.4 ppm)
8	4.5 (6H, dt, $J = 8$, 12, OCH_2)	118.2 (tq, $J = 35$, 285, CF_3), 111.2 (dtq, $J = 10$, 257, 36, CF_2), 63.5 (dt, $J = 4$, 28, OCH_2)	−124.5 (6F, t, $J = 12$, CF_2), −83.2 (9F, m, $J = 12$, CF_3)	−4.0	1356, 1308 (P=O), 1205, 1163, 1113, 1068, 1032, 937, 897	Calculated $C_9H_6F_{15}O_4P$ 493.976, found 493.975 (error 2.4 ppm)
9	5.92 (3H, tt, $J = 3$, 43, CF_2H), 4.46 (6H, dt, $J = 5$, 13, OCH_2)	113.3 (dtt, $J = 9$, 30, 250, CF_2), 107 (tt, $J = 37$, 287, CF_2H), 63.6 (dt, $J = 6$, 31, OCH_2)	−136.5 (6F, d, $J = 43$, CF_2H), −123.7 (6F, dt, $J = 3$, 13, CF_2)	−3.5	1460, 1404, 1294 (P=O), 1240, 1215, 1109, 1070, 951, 899, 835	Calculated $C_9H_9F_{12}O_4P$ 440.005, found 439.999 (error 12.7 ppm)
10	4.55 (6H, dt, $J = 8$, 12, OCH_2)	117.2 (tq, $J = 34$, 287, CF_3), 113.1 (ttd, $J = 258$, 31, 9, OCH_2CF_2), 108.4[a] (t, $J = 265$, CF_2CF_3), 63.7 (td, $J = 25$, 3, OCH_2)	−127.3 (6F, m, CH_2CF_2), −121.5 (6F, m, CF_2CF_3), −80.7 (9F, m, CF_3)	−3.4	1460, 1410, 1356, 1301 (P=O), 1232, 1186, 1126, 1086, 1016, 931	Calculated $C_{12}H_6F_{21}O_4P$ 643.967, found 643.966 (error 0.7 ppm)
11	5.1 (3H, complex m, OCH), 4.6 and 4.8 (12H, complex m, CH_2F)[b]	80 (ddd, $J = 174$, 7, 7, CH_2F), 78.6 (dt, $J = 9$, 21, OCH)	−46.3 (6F, dt, $J = 18$, 47, CH_2F)	8.6	1460, 1412, 1290 (P=O), 1088, 1051, 999, 908	Calculated $C_9H_{15}F_6O_4P$ 332.061 ($[M–CH_2F]^+ = 299.047$), found 299.046 (error 4.7)
12a	5.1 (3H, br m, OCH)	119.7 (dq, $J = 10$, 282, CF_3), 74.4 (dsep, $J = 14$, 35, OCH)	−73.3 (18F, d, $J = 5$, CF_3)	−3.6	1379, 1355, 1290 (P=O), 1237, 1115, 909, 881, 819	Calculated $C_9H_3F_{18}O_4P$ 547.948, found 547.948 (error −0.5 ppm)
18	4.87 (3H, m, OCH), 1.55 (9H, br m, CH_3)	118 (tq, $J = 38$, 285, CF_3), 112 (m, CF_2), 72 (br t, OCH), 14.3 (s, CH_3)	Very complex due to the existence of two diastereoisomers	−6.2 and −4.7	1458, 1394, 1327, 1288 (P=O), 1253, 1203, 1159, 1130, 1080, 1045, 991, 968, 843	Calculated $C_{12}H_{12}F_{15}O_4P$ 536.023, found 536.017 (error 11 ppm)

[a] Complicated by two sets of $^2J_{C-F}$.
[b] The proton spectrum is second order and is very complex (perhaps an AA′BB′CMX system; this would need a computer simulation to resolve and is not amenable to first order analysis).

ester groups are of equal configuration (i.e. RRR or SSS — two possibilities), and the other when they are of mixed configuration (i.e. RSS, SSR, RSR, SRS, SRR, RRS — six possibilities). The expected 1:3 mixture was observed by phosphorus NMR spectroscopy (see Table 2).



Tertiary fluoroalcohols did not combine with phosphorus pentachloride; $CF_3(CH_3)_2COH$, $CH_3(CF_3)_2COH$ and $(CF_3)_3COH$ remained unchanged. The cyclic fluoroalcohols, 2,2,3,3-tetrafluorocyclobutanol **19** and (perfluorocyclohexyl)methanol **20**, gave complex mixtures; no attempt was made to purify and characterise the individual components.

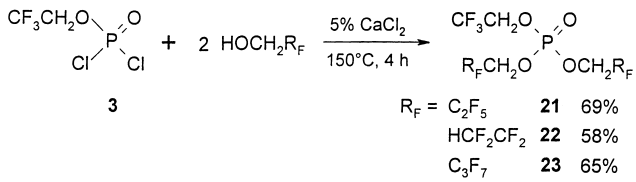


The symmetrical fluoroalkyl phosphates that were isolated were colourless stable liquids. Their yields and boiling points are given in Table 1 and spectroscopic data in Table 2.

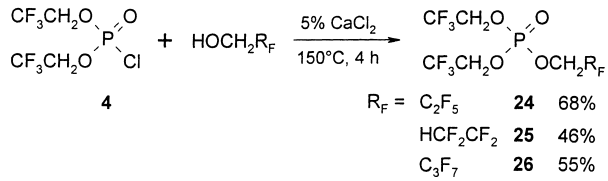
2.2. Synthesis of bis(fluoroalkyl) fluoroalkyl phosphates

The reaction of fluorinated alcohols with phosphoryl chlorides generally takes place in the presence of base [8,18] but not under neutral or acidic conditions. One way of facilitating nucleophilic attack is to use a Lewis acid which increases the positive charge on phosphorus by coordination to the oxygen atom of the P=O group [16]. Unfluorinated phosphorus ester groups often undergo cleavage of the carbon–oxygen bond under these conditions due to release of hydrogen chloride. However, as shown in the fluoroalcoholysis of phosphorus pentachloride, fluorinated phosphorus ester groups are not cleaved by hydrogen chloride even on prolonged heating. This has enabled the synthesis of many symmetrical phosphates having fluoro aliphatic [7,10,16,23,24] and aromatic [16,25–32] substituents, with Group I–III metal salts being used as catalysts. In the present study, some fluoroalkyl-substituted phosphoryl chlorides were found to react with several aliphatic fluoroalcohols in the presence of 5% calcium chloride catalyst to afford unsymmetrical fluoroalkyl phosphates.

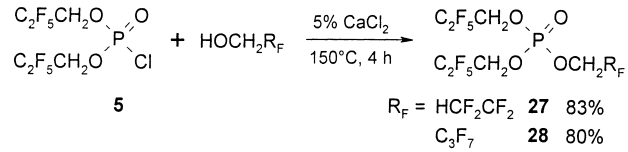
Trifluoroethyl phosphorodichloridate **3** combined with primary fluoroalcohols to give phosphates **21–23** in moderate yield (Table 3). The secondary fluoroalcohol $(CF_3)_2CHOH$, or the tertiary fluoroalcohols $CF_3(CH_3)_2COH$ and $CH_3(CF_3)_2COH$, did not react.



Bis(fluoroethyl)phosphorodichloridate **4** also combined with primary fluoroalcohols to give unsymmetrical phosphates **24–26** in reasonable yield (Table 3). The reaction with pentafluoropropanol was scaled up to provide over 50 g of pure bis(trifluoroethyl) pentafluoropropyl phosphate **24** (see Section 4.8)



Similarly, bis(pentafluoropropyl)phosphorochloridate **5** combined with tetrafluoropropanol and heptafluorobutanol to afford phosphates **27** and **28** in good yields.



Like the symmetrical phosphates, the unsymmetrical fluoroalkyl phosphates were isolated as colourless stable liquids. Their yields and boiling points are given in Table 3 and spectroscopic data in Table 4.

2.3. The reactivity of bis(trifluoroethyl) pentafluoropropyl phosphate to nucleophiles

To end speculation concerning the potential reactivity of the mixed phosphates to nucleophiles, compound **24** was treated in separate experiments with molar equivalents of butanol and propylamine. In both cases, no products were detected by GC–MS analyses and the starting phosphate was recovered unchanged (see Section 4.9).

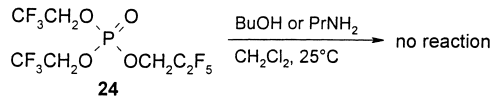


Table 3
Experimental data for unsymmetrical phosphates

Compound	R_F	R_F'	Yield (%)	Bp (°C/mmHg)
Products of general formula $R_FCH_2OP(O)(OCH_2R_F')_2$				
21	CF_3	C_2F_5	69	100/10
22	CF_3	$(CF_2)_2H$	58	124/5
23	CF_3	C_3F_7	65	100/1
Products of general formula $(R_FCH_2O)_2P(O)OCH_2R_F'$				
24	CF_3	C_2F_5	68[a]	82/10
25	CF_3	$(CF_2)_2H$	46	100/10
26	CF_3	C_3F_7	55	85/10
27	C_2F_5	$(CF_2)_2H$	83	94/5
28	C_2F_5	C_3F_7	80	104/10

[a] In the scale-up reaction, an improved yield of 77% was achieved, the boiling point being 73°C/5 mmHg (see Section 4.8).

Table 4
Spectroscopic data for unsymmetrical phosphates $R_FCH_2OP(O)(OCH_2R_F')_2$ and $(R_FCH_2O)_2P(O)OCH_2R_F'$ (NMR data measured in $CDCl_3$)

Compound	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)[a]	^{19}F NMR δ, J (Hz)	^{31}P NMR δ	IR ν (cm^{-1})	HRMS analysis
21	4.51 (4H, dt, $J = 4$, 12, $OCH_2C_2F_5$), 4.51 (2H, dq, $J = 9$, 7, OCH_2CF_3)	122 (tq, $J = 34$, 286, CF_2CF_3), 121.9 (dq, $J = 13$, 286, CF_3), 113.3 (dtq, $J = 9$, 255, 37, CF_2), 64.3 (q, $J = 39$, OCH_2CF_3), 63.4 (t, $J = 30$, OCH_2CF_2)	−124.5 (4F, t, $J = 13$, CF_2), −83.2 (6F, br m, CF_3), −75.2 (3F, t, $J = 8$, CH_2CF_3)	−3.9	1460, 1356, 1308, 1282 (P=O), 1207, 1074, 1034, 966, 897	Calculated $C_8H_6F_{13}O_4P$ 443.980, found 443.978 (error 4.5 ppm)
22	5.92 (2H, tt, $J = 4$, 36, CF_2H), 4.46 (4H, dtt, $J = 8$, 1, 12, $OCH_2CF_2CF_2$), 4.42 (2H, dq, $J = 8$, 9, OCH_2CF_3)	122 (dq, $J = 11$, 278, CF_3), 113.3 (dtt, $J = 9$, 29, 250, CH_2CF_2), 109 (tt, $J = 39$, 251, CF_2H), 64.3 (dq, $J = 5$, 39, CH_2CF_3), 63.6 (dt, $J = 6$, 30, CH_2CF_2)	−137.3 (4F, d, $J = 52$, CF_2H), −124.5 (4F, t, $J = 13$, CH_2CF_2), −75.3 (3F, t, $J = 6$, CF_3)	−3.6	1458, 1423, 1282 (P=O), 1240, 1184, 1076, 964, 899, 835	Calculated $C_8H_8F_{11}O_4P$ 407.998 ($[M–F]^+$=389.000), found 388.998 (error 4.2 ppm)
23	4.55 (4H, dt, $J = 9$, 13, OCH_2CF_2), 4.43 (2H, dq, $J = 9$, 8, OCH_2CF_3)	121.9 (dq, $J = 10$, 278, CH_2CF_3), 115-110 (m, J obs, CF_2CF_2), 107 (m, J obs, CF_3), 64.4 (dq, $J = 4$, 38, CH_2CF_3), 63.6 (br t, $J = 26$, CH_2CF_2)	−126.7 (4F, br m, CH_2CF_2), −120.9 (4F, br m, CF_2), −80.1 (6F, t, $J = 10$, CF_3), −74.7 (3F, t, $J = 9$, CH_2CF_3)	−3.8	1458, 1356, 1282 (P=O), 1230, 1182, 1082, 1016, 966, 930	Calculated $C_{10}H_6F_{17}O_4P$ 543.973, found 543.972 (error 2.8 ppm)
24	4.51 (2H, dtq, $J = 8$, 12, 1, OCH_2CF_2), 4.43 (4H, dq, $J = 9$, 8, OCH_2CF_3)	122 (dq, $J = 10$, 278, CH_2CF_3), 118 (tq, $J = 34$, 286, CF_3), 113 (dtq, $J = 8$, 38, 278, CF_2), 64.3 (dq, $J = 5$, 38, CH_2CF_3), 63.3 (dt, $J = 4$, 29, CH_2CF_2)	−124.5 (2F, m, CH_2CF_2), −83.3 (3F, m, CF_3), −75.2 (6F, m, CH_2CF_3)	−3.8	1459, 1424, 1305, 1279 (P=O), 1179, 1081, 1033, 965, 898, 845, 810	Calculated $C_7H_6F_{11}O_4P$ 393.983, found 393.982 (error 0.9 ppm)
25	5.92 (1H, tt, $J = 4$, 56, CF_2H), 4.48 (2H, br dt, $J = 8$, OCH_2CF_2), 4.43 (4H, dq, $J = 9$, 8, OCH_2CF_3)	122.1 (dq, $J = 9$, 278, CF_3), 113.5 (dtt, $J = 9$, 28, 250, CF_2), 109.1 (tt, $J = 36$, 251, CF_2H), 64.4 (dq, $J = 5$, 38, OCH_2CF_3), 63.8 (dt, $J = 4$, 29, OCH_2CF_2)	−137.2 (2F, m, $J = 61$, CF_2H), −124.5 (2F, br m, CF_2), −75.2 (6F, br m, CF_3)	−3.7	1458, 1424, 1274 (P=O), 1239, 1109, 964, 938, 898, 840	Calculated $C_7H_7F_{10}O_4P$ 375.992, found 375.990 (error 6.8 ppm)
26	4.6 (2H, dt, $J = 7$, 13, $OCH_2C_3F_7$), 4.43 (4H, dq, $J = 8$, 8, OCH_2CF_3)	121.9 (dq, $J = 13$, 280, OCH_2CF_3), 117.4 (tq, $J = 39$, 287, $CF_2CF_2CF_3$), 113 (dtt, $J = 10$, 33, 258, OCH_2CF_2), 109 (tq, $J = 271$, 37, $CF_2CF_2CF_3$)	−126.5 (2F, m, OCH_2CF_2), −121 (2F, m, CF_2CF_3), −80 (3F, CF_2CF_3), −72.5 (6F, m, CH_2CF_3)	−3.7	1458, 1306, 1279 (P=O), 1234, 1182, 1086, 1016, 966, 903, 845	Calculated $C_8H_6F_{13}O_4P$ 443.980, found 443.789 (error 2.1 ppm)
27	5.91 (1H, tt, $J = 3$, 52, CF_2H), 4.5 (4H, m, $J = 8$, 14, OCH_2CF_3), 4.48 (2H, m, $J = 8$, 6, $OCH_2CF_2CF_2H$)	118.1 (tq, $J = 33$, 288, CF_3), 111 (m, J obs, ~64, both types of CF_2), 109 (tt, $J = 36$, 251, CF_2H), 63.7 (dt, $J = 6$, 31, $CH_2CF_2CF_2$), 63.4 (dt, $J = 5$, 29, $CH_2C_2F_5$)	−136.4 (2F, d, $J = 52$, CF_2H), −123.6 (2F, t, $J = 14$, CF_2CF_2H), −123.6 (4F, t, $J = 13$, CF_2CF_3), −82.6 (6F, s, CF_3)	−3.8	1460, 1356, 1306 (P=O), 1209, 1113, 1070, 1032, 937, 897, 835	Calculated $C_9H_7F_{14}O_4P$ 475.986, found 475.983 (error 5 ppm)
28	4.55 and 4.51 (4H, each pair ddd, $J = 7$, 13, one of coupling constants obscured because of overlap, pair of enantiotopic protons in $OCH_2C_2F_5$ groups), 4.51 (2H, dt, $J = 8$, 12, $OCH_2C_3F_7$)	118.3 (tq, $J = 36$, 284, $CH_2CF_2CF_3$), 117.7 (tq, $J = 29$, 287), 111.5 (dtq, $J = 9$, 257, 36, $CH_2CF_2CF_3$), 111 and 107 (m, J obs, $CH_2CF_2CF_2$), 63.8 (dt, $J = 4$, 27, $OCH_2C_3F_7$), 63.6 (dt, $J = 4$, 29, $OCH_2C_2F_5$)	−126.6 (2F, m, CF_2CF_2), −123.8 (4F, m, CF_2CF_3), −120.9 (2F, m, $CF_2C_2F_5$), −82.7 (6F, m, CF_2CF_3), −80 (3F, m, $CF_2CF_2CF_3$)	−3.9	1460, 1377, 1356, 1307 (P=O), 1209, 1126, 1074, 1034, 937, 897, 820	Calculated $C_{10}H_6F_{17}O_4P$ 543.973, found 543.971 (error 3.3 ppm)

[a] In the carbon spectra, obs indicates that the signals are obscured due to complex splitting patterns and signal-to-noise problems.

3. Conclusion

Symmetrical fluoroalkyl phosphates can be prepared from the interaction of primary or secondary fluoroalcohols with phosphorus pentachloride; tertiary fluoroalcohols do not react under these conditions. A requirement for a high yield of phosphate is the presence of many fluorine atoms in the fluoroalcohol. With hexafluoroisopropanol the reaction followed a surprising course, giving the expected symmetrical phosphate and the unexpected tetra-(hexafluoroisopropoxy) chlorophosphorane. This outcome indicates that fluoroalcoholysis of PCl_5 is mediated through chlorophosphorane intermediates, rather than by formation of $POCl_3$ and its subsequent transformation (as proposed by Chuganov and Sapgir [5]). Unsymmetrical fluoroalkyl phosphates can be prepared from the interaction of primary fluoroalcohols with phosphoryl chlorides in the presence of calcium chloride; secondary or tertiary fluoroalcohols are unreactive under these conditions.

4. Experimental details

All reagents were of commercial quality: fluoroalcohols were purchased from Apollo Scientific Ltd (Derbyshire, UK) or from Lancaster Synthesis (Morecambe, UK). Anhydrous solvents were used for reactions. NMR spectra were obtained on a JEOL Lambda 500 instrument (operating at 500 MHz for ^{1}H, 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 ^{1}H, 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 ^{1}H and ^{13}C, external $CFCl_3$ for ^{19}F and external $(MeO)_3P$ (δ 140 ppm) for ^{31}P spectra. Data in Tables 2 and 4 are recorded as follows: chemical shifts in ppm from reference on the δ scale, integration, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet and sep: septet, br: broad, obs: obscured signal from which coupling constants could not be extracted), coupling constant (Hz) and assignment. IR spectra were recorded as liquid films on a Nicolet SP210 instrument using Omnic sofware. 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 masses of pure products were confirmed with methane +ve 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: +ve ion electron impact, magnet scan *m/z* 400–100 (seconds/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. Reaction of fluoroalcohols with phosphorus pentachloride

The fluoroalcohol (0.2 mol) was added dropwise using a pressure-equalising dropping funnel (equipped with a calcium chloride guard tube) to finely-divided phosphorus pentachloride (0.05 mol) in a round-bottom flask cooled to 0–5°C. Contact of the fluoroalcohol with the solid phosphorus pentachloride resulted in dissolution, giving a colourless solution that effervesced due to liberation of HCl and the respective fluoroalkyl chloride. After addition, the mixture was warmed to room temperature and left for 12 h. An aliquot was then analysed by GC–MS. In cases where good conversion to the required product had occurred, residual phosphorus pentachloride was removed by filtration. Fractionation under reduced pressure (0.015–0.9 mmHg) gave tris(fluoroalkyl)phosphates **7–11** and **18** as colourless liquids. Yields ranged from 10 to 76% (see Table 1).

4.2. Reaction of hexafluoroisopropanol with phosphorus pentachloride

The previous procedure was followed. As some unreacted phosphorus pentachloride remained after addition of hexafluoroisopropanol, the mixture was refluxed for 2 h, then distilled under reduced pressure (bp 40°C/0.08 mmHg). Multinuclear NMR analysis showed the distillate to comprise 30% tris(hexafluoroisopropyl)phosphate **12a** and 70% tetra(hexafluoroisopropoxy)chlorophosphorane **12b**. A portion of the mixture (10 g) was treated with ice water (5 g) in chloroform (20 ml). The product, the lowest of three layers, was separated and concentrated under reduced pressure to give pure tris(hexafluoroisopropyl)phosphate **12a** as white crystals (11.2 g, 92%); mp 24°C (lit. mp 23°C [11]). HRMS for phosphorane **12b**: calculated for $C_{12}H_4ClF_{24}O_4P$ 733.915 ($[M–F]^+ = 714.917$ and $[M–Cl]^+ = 698.946$), found 714.916 (error 1.1 ppm) and 698.946 (error 1.1 ppm).

4.3. Attempted synthesis of tris(2,2,3,3-tetrafluorocyclobutyl) phosphate

The method was essentially the same as that outlined in Section 4.1. After addition of 2,2,3,3-tetrafluorocyclobutanol **19**, the reaction mixture set solid and was left for 14 h. On heating, it melted and the resulting liquid was refluxed for 3 h, then distilled to give a colourless oil (bp 118°C/0.5 mmHg) which on standing crystallised to give a white solid (mp 40–42°C). The solid contained two phosphorus compounds that were not separated or characterised.

4.4. Attempted synthesis of tris[(perfluorocyclohexyl) methyl] phosphate

The method was essentially the same as that outlined in Section 4.1. After addition of the (perfluorocyclohexyl)-

methanol **20**, the mixture was allowed to warm to room temperature and then refluxed for 6 h (until all the solid went into solution) to produce a very viscous oil. The oil was distilled (bp 134°C/0.01 mmHg) and shown by multinuclear NMR analysis to contain five different phosphorus compounds. No attempt was made to separate or characterise the individual compounds.

*4.5. Methanolysis of tetra(1,1,1,3,3,3-hexafluoroisopropoxy)chlorophosphorane (**12b**)*

The 3:7 mixture of tris(hexafluoroisopropyl)phosphate **12a** and tetra(hexafluoro-isopropoxy)chlorophosphorane **12b** (2 g), made according to the procedure in Section 4.2, was weighed into an oven-dried separating funnel and methanol added by syringe (0.1 ml). The methanol formed a top layer that dissolved slowly with evolution of HCl gas. Analysis by GC–MS and NMR spectroscopy showed the mixture to comprise phosphate **12a**, tetra(hexafluoroisopropoxy)methoxyphosphorane **13**, bis-(hexafluoroisopropyl) methyl phosphate **15**, dimethyl hexafluoroisopropyl phosphate **16** and trimethyl phosphate.

*4.6. The synthesis of bis(fluoroalkyl) 2,2,2-trifluoroethyl phosphates (**21**)–(**23**)*

2,2,2-Trifluoroethyl phosphorodichloridate **3** (10 mmol) was weighed into a 25 ml round-bottom flask equipped with a magnetic flea and a Liebig condenser with a calcium chloride guard tube. To the reaction mixture was added finely powdered anhydrous $CaCl_2$ (0.5 mmol) in one portion and the appropriate fluoroalcohol (20 mmol) by syringe. The mixture was maintained at 150°C for 2 h. Evolution of HCl was observed; beads of hydrochloric acid formed on the inner surface of the guard tube. The reaction mixture was analysed by GC–MS. The title compounds were isolated after fractionation in a micro-distillation apparatus.

*4.7. General procedure for the synthesis of unsymmetrical phosphates (**24**)–(**28**)*

The procedure was the same as that in the previous section, only bis(2,2,2-trifluoroethyl)phosphorochloridate **4** or bis(2,2,3,3,3-pentafluoropropyl)phosphorochloridate **5** (10 mmol) was treated with the appropriate fluoroalcohol (10 mmol).

*4.8. Scaled-up synthesis of bis(2,2,2-trifluoroethyl) 2,2,3,3,3-pentafluoropropyl phosphate (**24**)*

Finely-powdered anhydrous $CaCl_2$ (0.9 g, 8.5 mmol) was added in one portion to a magnetically stirred mixture of bis(2,2,2-trifluoroethyl)phosphorochloridate **4** (47.5 g, 0.17 mol) and 2,2,3,3,3-pentafluoropropanol (21.5 g, 0.17 mol). The mixture was heated under reflux for 4 h. Evolution of HCl took place. Fractionation under reduced pressure gave the title compound as a colourless mobile liquid (51.8 g, 77%); bp 73°C/5 mmHg.

*4.9. Attempted reaction of unsymmetrical phosphate (**24**) with butanol or propylamine*

Butanol or propylamine (6 mmol) were introduced by syringe into a solution of bis(2,2,2-trifluoroethyl) 2,2,3,3,3-pentafluoropropyl phosphate **24** (6 mmol) in dichloromethane (10 ml) at room temperature under argon. Analysis by GC–MS showed no reaction to have taken place after 12 h. The starting phosphate was recovered by distillation under reduced pressure (bp 52°C/1 mmHg).

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References

[1] I.L. Knunyants, O.V. Kil'dasheva, E. Bykovskaya, Zh. Obshch. Khim. 19 (1949) 93 (English Translation).
[2] F. Swarts, Recl. Trav. Chim. Pays-Bas 28 (1909) 166.
[3] T.N. Sintashina, V.F. Mironov, E.N. Ofitserov, I.V. Konovalova, A.N. Pudovik, Izv. Akad. Nauk. SSSR (1988) 1451, Chem. Abs. 95 (1989) 186571.
[4] L.C. Krogh, T.S. Reid, H.A. Brown, J. Org. Chem. 19 (1954) 1124.
[5] V.S. Chuganov, E.V. Sapgir, Zh. Obshch. Khim. 38 (1968) 412 (English Translation).
[6] L.S. Zakharov, V.V. Pisarenko, N.N. Godovikov, M.I. Kabachnik, Izv. Akad. Nauk. SSSR, Ser. Khim. (1969) 1729 (English Translation).
[7] L.S. Zakharov, V.V. Pisarenko, N.N. Godovikov, M.I. Kabachnik, Bull. Acad. Sci. USSR, Div. Chem. Sci. 20 (1971) 2373 (English Translation).
[8] K. Sellars, J. Appl. Chem. (London) 6 (1956) 45.
[9] J.C. Conly, US Patents 2 754 316, 2 754 317 and 2 754 318 (1956); Chem. Abs. 51 (1957) 1244.
[10] I. Yu Kudryavtsev, L.S. Zakharov, M.I. Kabachnik, Russ. Chem. Bull. 47 (1998) 2015.
[11] D. Dakternieks, G.V. Roschenthaler, R. Schmutzler, J. Fluorine Chem. 1 (1978) 387.
[12] A.F. Benning, US Patent 2 597 702 (1952), Chem. Abs. 47 (1953) 2196c
[13] P.O. Gitel', L.F. Osipova, O.P. Solovova, A.Ya Yakubovich, Zh. Obshch. Khim. 39 (1969) 281 (English Translation).
[14] A.V. Fokin, V.A. Komarov, A.F. Kolomiets, A.I. Rapkin, K.I. Pasevina, T.M. Potarina, O.V. Verenikin, Izv. Akad. Nauk. SSSR, Ser. Khim. 7 (1978) 1375 (English Translation).
[15] A.V. Fokin, N. Studnev, A.I. Rapkin, K.I. Posevina, A.F. Kolomiets, Izv. Akad. SSSR Ser. Khim. 7 (1981) 1641.
[16] M.I. Kabachnik, L.S. Zakharov, E.I. Goryunov, I.Yu. Kudryavtsev, G.N. Molchanova, M.A. Kurykin, P.V. Petrovskii, T.M. Shcherbina, A.P. Laretina, Russ. J. Gen. Chem. 64 (1994) 812 (English Translation).
[17] C.M. Timperley, I.J. Morton, M.J. Waters, J.L. Yarwood, J. Fluorine Chem. 96 (1999) 95.
[18] C.M. Timperley, M. Bird, J.F. Broderick, I. Holden, I.J. Morton, M.J. Waters, J. Fluorine Chem. (2000), in press.

[19] C.M. Timperley, Highly Toxic Fluorine Compounds, in: R.E. Banks (Ed.), Fluorine Chemistry at the Millennium: Fascinated by Fluorine, Chapter 29, 2000, in press.
[20] L.N. Markovskii, A.V. Solov'ev, V.E. Pashinnik, Y.G. Shermolovich, Zh. Obshch. Khim. 50 (1980) 644 (English Translation).
[21] D.B. Denney, D.Z. Denney, P.J. Hammond, Y.-P. Wang, J. Am. Chem. Soc. 103 (1981) 1785.
[22] T. Kubota, S. Miyashita, T. Kitazume, N. Ishikawa, J. Org. Chem. 45 (1980) 5052.
[23] L.S. Zakharov, V.V. Pisarenko, N.N. Godovikov, M.I. Kabachnik, Bull. Acad. Sci. USSR, Div. Chem. Sci., 20 (1971) 2536 (English Translation).
[24] M.I. Kabachnik, L.S. Zakharov, E.I. Goryunov, V.S. Shaidurov, A.V. Kashkin, Y.L. Bakhmutov, V.F. Zabolotskikh, Izv. Akad. Nauk. SSSR, Ser. Khim. 4 (1985) 875 (English Translation).
[25] L.S. Zakharov, V.V. Pisarenko, N.N. Godovikov, M.I. Kabachnik, Izv. Akad. Nauk. SSSR Ser. Khim. 12 (1969) 2699 (English Translation).
[26] L.S. Zakharov, E.I. Goryunov, S.T. Ioffe, L.L. Morozov, T.M. Shcherbina, M.I. Kabachnik, Izv. Akad. Nauk. SSSR Ser. Khim. 8 (1976) 1727 (English Translation).
[27] L.S. Zakharov, E.I. Goryunov, L.L. Morozov, V.A. Svoren', E.P. Lur'e, T.M. Shcherbina, M.I. Kabachnik, Izv. Akad. Nauk. SSSR, Ser. Khim. 9 (1978) 1843 (English Translation).
[28] E.I. Goryunov, L.S. Zakharov, P.V. Petrovskii, M.I. Kabachnik, Izv. Akad. Nauk. SSSR, Ser. Khim. 7 (1984) 1463 (English Translation).
[29] E.I. Goryunov, L.S. Zakharov, P.V. Petrovskii, M.I. Kabachnik, Izv. Akad. Nauk. SSSR, Ser. Khim. 4 (1985) 799 (English Translation).
[30] E.I. Goryunov, P.V. Petrovskii, T.M. Shcherbina, L.S. Zakharov, M.I. Kabachnik, Izv. Akad. Nauk. SSSR, Ser. Khim. 8 (1989) 1700 (English Translation).
[31] E.I. Goryunov, P.V. Petrovskii, L.S. Zakharov, M.I. Kabachnik, Izv. Akad. Nauk. SSSR, Ser. Khim. 2 (1990) 371 (English Translation).
[32] E.I. Goryunov, G.N. Molchanova, P.V. Petrovskii, L.S. Zakharov, M.I. Kabachnik, Russ. Chem. Bull. 47 (1998) 1728.