Bis(fluoroalkoxy)triphenylphosphorane: A New Reagent for the Preparation of Fluorinated Ketals†

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Ketals are widely used as synthetic intermediates in organic synthesis, but few fluorinated ketals $(R_F)_2C(OR)_2$ have been reported since there are no general methods for their preparation. Unlike hydrocarbon ketones, reaction of fluorinated ketones with alcohols ROH gives hemiketals instead of ketals.[1] The preparation of fluoroketals $(R_F)_2C(OR)_2$ is usually accomplished by reaction of the hemiketals with strong alkylating reagents such as dimethyl sulfate and alkyl halides in the presence of base.[2] However, this method is not applicable to the preparation of 1,1,1′,1′-tetrahydroperfluoroketals $(R_F)_2C(OCH_2R_F')_2$ since $R_F'CH_2X$ reacts poorly with nucleophiles.[3,4] Only one hydrofluoroketal, $(CF_3)_2C(OCH_2CF_2CF_2H)_2$, has been reported which was prepared from the reaction of hexafluoroacetone (HFA) with $P(OCH_2CF_2CF_2H)_5$.[5] However, this method is not general since reaction of HFA with $P(OCH_2CF_3)_5$ does not give the desired ketal product.[6] Given the affinity of triphenylphosphine for oxygen, we anticipated that fluorinated phosphoranes $Ph_3P(OCH_2R_F)_2$ might react with fluorinated ketones to form the desired ketals and triphenylphosphine oxide. We report herein the synthesis, structure and application of new bis(fluoroalkoxyl)triphenylphosphoranes $Ph_3P(OCH_2R_F)_2$ in making fluorinated ketals.

Although a number of methods for the preparation of bis(fluoroalkoxy)triphenylphosphorane are reported, only one compound, $Ph_3P(OCH_2CF_3)_2$, is known. The previous preparation of this compound was achieved by the reaction of Ph_3P with either CF_3CH_2OH in the presence of diethyl azodicarboxylate[7] or trifluoroethyl benzenesulfonate.[8] It could also be prepared by the reaction of Ph_3PBr_2 and $NaOCH_2CF_3$.[9] Our phosphoranes were readily prepared by the reaction of Ph_3PBr_2 with fluorinated alcohols in the presence of triethylamine at −30 °C to room temperature. For example, to a solution of Ph_3PBr_2 prepared in situ from bromine and triphenylphosphine in CH_2Cl_2 was added a mixture of fluorinated alcohol and triethylamine in ether at −40 to −30 °C. Pure phosphorane was readily obtained by filtration of the reaction mixture under N_2, followed by evaporation of the solvent and crystallization from methylene chloride and pentane. The yields are good to excellent for most cases and even a trifluorovinyl functionality can be tolerated in the reaction conditions. Typical results are summarized in Table 1.

$$Ph_3P \xrightarrow[2.\ R_FCH_2OH,\ Et_3N]{1.\ Br_2} Ph_3P(OCH_2R_F)_2 \quad 75\text{-}97\%$$

R_F=CH_3, $ClCF_2$, CF_3CF_2, $H(CF_2)_2$, $H(CF_2)_4$,

CF_2=$CFOCF_2CF(CF_3)OCF_2CF_2$

These fluorinated phosphoranes were characterized by NMR analysis. ^{31}P NMR spectra exhibited a singlet at −55.5 to −57.7 ppm (CH_2Cl_2, external 85% H_3PO_4), characteristic for phosphoranes (see Table 1).[10]

The $^{31}P-^{1}H$ coupling ($^3J_{H-P}$ = 2.1–4.3 Hz) was observed in ^1H NMR spectra. Single crystal X-ray analysis of compound $Ph_3P(OCH_2CF_2CF_3)_2$ indicated that the phosphorous atom was coordinated as a trigonal bipyramid to the two axial alkoxy groups and the three phenyl rings in the equatorial plane.[12] The two axial P–O distances are normal and almost equivalent (1.735 and 1.744 Å, respectively) with a linear O–P–O angle (178.4°) (Figure 1).

The fluorinated phosphoranes are thermally stable white solids. Thermal gravimetric analysis of $Ph_3P(OCH_2CF_2CF_3)_2$ shows no mass loss until 200 °C under nitrogen. Differential scanning calorimetry (DSC) indicated a sharp melting point at 134 °C. These phosphoranes readily hydrolyze to produce Ph_3PO and fluorinated alcohol R_FCH_2OH.

Reaction of $Ph_3P(OCH_2R_F)_2$ with hexafluoroacetone in CH_2Cl_2 in a shaker tube at 150–200 °C gave the corresponding ketals in good yields in most cases. When a longer chain ketone such as perfluoropentanone-3 was used as a substrate, the fluorinated ketal was also obtained under similar conditions.

$$Ph_3P(OCH_2R_F)_2 + \begin{matrix} CF_3 \\ \diagdown \\ \quad =O \\ \diagup \\ CF_3 \end{matrix} \longrightarrow \begin{matrix} CF_3 & OCH_2R_F \\ \diagdown & \diagup \\ C & \\ \diagup & \diagdown \\ CF_3 & OCH_2R_F \end{matrix} + Ph_3P{=}O$$

R_F=CF_3 (66%); CF_3CF_2 (73%); $(CF_2)_2H$ (56%); $(CF_2)_4H$ (46%)

This method has been used to prepare functionalized fluoroketals. $Ph_3P(OCH_2CF_2CF_2OCF(CF_3)CF_2OCF{=}CF_2)_2$ reacted with HFA to afford $(CF_3)_2C(OCH_2CF_2CF_2OCF(CF_3)CF_2OCF{=}CF_2)_2$. The yield was relatively low, and viscous byproducts were observed. Presumably, the trifluorovinyl ether functionality participated in side reactions.

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(12) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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Table 1. Preparation of Bis(fluoroalkoxy)triphenylphosphorane, $Ph_3P(OCH_2R_F)_2$

R_F	yield (%)	^{31}P NMR, δ	^1H NMR of CH_2, δ (J, Hz)
CF_3	96	−57.7	2.88 (qd, 8.9, 4.3)
$ClCF_2$	97	−57.7	3.00 (td, 11, 3.8)
CF_3CF_2	94	−57.2	2.95 (td, 13.1, 2.8)
HCF_2CF_2	92	−56.0	2.88 (td, 11.1, 2.1)
$H(CF_2)_4$	90	−55.5	3.02 (td, 14.0, 3.9)
$CF_2ClCFCl$	83	−56.4	3.11 (dd, 24.6, 3.5)
EVE[a]	75	−56.2	2.95 (td, 13.7, 4.0)

[a] EVE = CF_2=$CFOCF_2CF(CF_3)OCF_2CF_2$

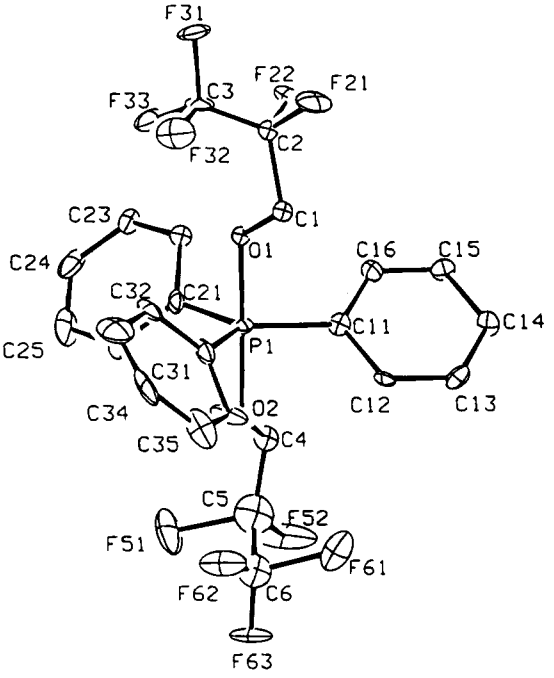

Figure 1. Crystal structure of $Ph_3P(OCH_2CF_2CF_3)_2$.

In conclusion, we have synthesized new fluorinated bis(fluoroalkoxy)triphenylphosphoranes which readily react with perfluoroketones to form a new class of fluorinated ketals.

Experimental Section

Synthesis of $Ph_3P(OCH_2CF_3)_2$. To a stirred solution of 136.2 g (0.52 mol) of Ph_3P in 300 mL of CH_2Cl_2 was added a solution of 41.6 g (0.52 mol) of Br_2 in 100 mL of CH_2Cl_2 at −40 °C over 1 h. After the addition was complete, the mixture was stirred at −40 °C to room temperature for 1 h and then cooled to −40 °C. A mixture of 100.0 g (1.0 mol) of CF_3CH_2OH and 101.0 g (1 mol) of Et_3N in 400 mL of ether was added at this temperature over 1 h, and then the resulting reaction mixture was warmed to room temperature and stirred for an additional 3.5 h. After the solids were removed by filtration under nitrogen, the filtrate was evaporated under vacuum at room temperature to give 209.3 g solids (91%). Analytic sample was obtained by slow evaporation of CH_2Cl_2 and pentane solution, mp 138.4 °C. ^1H NMR ($CDCl_3$): 8.11−8.04 (m, 6H), 7.57−7.33 (m, 9H), 2.88 (qd, J = 8.9 Hz, J = 4.2 Hz, 4H). ^{19}F NMR ($CDCl_3$): 74.7 (t, J =8.9 Hz). ^{31}P NMR (CH_2Cl_2): −58.0 (s). Anal. Calcd for $C_{22}H_{19}F_6PO_2$: C, 57.39; H, 4.13; F, 24.78; P, 6.74. Found: C, 57.27; H, 4.32; F, 24.91; P, 7.06.

Synthesis of $Ph_3P(OCH_2CF_2Cl)_2$. A similar experiment using 30.0 g (0.115 mol) of Ph_3P, 18.3 g (0.115 mol) of Br_2, 25.0 g (0.21 mol) of $ClCF_2CH_2OH$, and 21.2 g (0.21 mol) of Et_3N in 100 mL of ether and 100 mL of CH_2Cl_2 gave 50.1 g (96.7%) of $Ph_3P(OCH_2CF_2Cl)_2$. ^1H NMR ($CDCl_3$): 8.14−8.06 (m, 6H), 7.71−7.49 (m, 9H), 3.00 (td, J = 11.1 Hz, J = 3.8 Hz, 4H). ^{19}F NMR: −61.2 (t, J = 11.0 Hz). ^{31}P NMR(CH_2Cl_2): −57.7 (s). An analytic sample was obtained by slow evaporation of solution in CH_2Cl_2 and pentane. Anal. Calcd for $C_{22}H_{19}F_4Cl_2PO_2$: C, 53.57; H, 3.88; F, 15.41; Cl, 14.37; P, 6.28. Found: C, 53.55; H, 4.19; F, 17.39; Cl, 13.33, P, 6.84.

Synthesis of $Ph_3P(OCH_2CF_2CF_3)_2$. A similar experiment using 52.4 g (0.2 mol) of Ph_3P, 32.0 g (0.2 mol) of Br_2, 60.0 g (0.4 mol) of $CF_3CF_2CH_2OH$, and 41.8 g of Et_3N in 150 mL of CH_2Cl_2 and 200 mL of ether gave 105.1 g (94%) of $Ph_3P(OCH_2CF_2CF_3)_2$. ^1H NMR ($CDCl_3$): 8.07−8.01 (m, 6H), 7.54−7.33 (m, 9H), 2.95 (td, J = 13.1 Hz, J = 2.8 Hz, 4H). ^{19}F NMR ($CDCl_3$): −83.7 (s, 6F), −123.7 (t, J = 13.2 Hz, 4F). ^{31}P NMR (CH_2Cl_2): −57.2 (s). Single crystals for X-ray analysis were obtained by slow evaporation of a CH_2Cl_2/pentane solution at 25 °C in an N_2 box.

Synthesis of $Ph_3P(OCH_2CF_2CF_2H)_2$. A similar experiment using 52.4 g (0.2 mol) of Ph_3P, 32.0 g (0.2 mol) of Br_2, 54.1 g (0.41 mol) of $HCF_2CF_2CH_2OH$, and 41.4 g (0.41 mol) of Et_3N in 250 mL of CH_2Cl_2 and 250 mL of ether gave 96.6 g (92%) of $Ph_3P(OCH_2CF_2CF_2H)_2$. ^1H NMR ($CDCl_3$): 8.04−9.76 (m, 4H), 7.52−7.48 (m, 9H), 5.74 (tt, J = 53.4 Hz, J = 5.5 Hz, 2H), 2.88 (td, J = 11.1 Hz, J = 2.1 Hz, 4H). ^{19}F NMR ($CDCl_3$): −126.5 (m, 4F), −141.2 (t, J = 54 Hz, 4F); ^{31}P NMR (CH_2Cl_2): −56.0 (s).

Synthesis of $Ph_3P(OCH_2CFClCF_2Cl)_2$. A similar experiment using 21.0 g (0.08 mol) of Ph_3P, 12.8 g (0.08 mol) of Br_2, 27.0 g (0.147 mol) of $ClCF_2CFClCH_2OH$, and 15.0 g (0.148 mol) of Et_3N in 100 mL of CH_2Cl_2 and 100 mL of ether gave 38.1 g (83%) of $Ph_3P(OCH_2CFClCF_2Cl)_2$. ^1H NMR ($CDCl_3$): 8.11−8.03 (m, 6H), 7.50−7.32 (m, 9H), 3.11 (dd, J = 24.6 Hz, J = 3.5 Hz, 4H). ^{31}P NMR(CH_2Cl_2): −56.4 (s).

Synthesis of $Ph_3P[OCH_2(CF_2)_4H]_2$. A similar experiment using 78.6 g (0.3 mol) of Ph_3P, 48.0 g (0.3 mol) of Br_2, 140.0 g (0.6 mol) of $H(CF_2)_4CH_2OH$, and 61.0 g (0.6 mol) of Et_3N in 300 mL of CH_2Cl_2 and 300 mL of ether gave 196.7 g (90%) of $Ph_3P[OCH_2(CF_2)_4H]_2$. ^1H NMR ($CDCl_3$): 8.09−8.01 (m, 6H), 7.66−7.47 (m, 9H), 5.88 (tt, J = 52.0 Hz, J = 5.6 Hz, 2H), 3.02 (td, J =14.0 Hz, J = 3.9 Hz). ^{19}F NMR: −119.7 (t, J = 11.6 Hz, 4F), −125.8 (s, 4F), −131.2 (m, 4F), −138.0 (d, J = 52.0 Hz, 4F). ^{31}P NMR (CH_2Cl_2): −55.5 (s).

Synthesis of $Ph_3P(OCH_2CF_2CF_2OCF_2CFCF_3OCF{=}CF_2)_2$. A similar experiment using 22.0 g (0.084 mol) of Ph_3P, 13.4 g (0.084 mol) of Br_2, 59.5 g (0.15 mol) of CF_2=$CFOCF_2CF(CF_3)OCF_2CF_2CH_2OH$ (EVEOH),[11] and 15.2 g (0.15 mol) of Et_3N in 100 mL of CH_2Cl_2 and 100 mL of ether gave 59.6 g (75.3%) of $Ph_3P(OEVE)_2$. ^1H NMR ($CDCl_3$): 8.08−8.01 (m, 6H), 7.48-7.32 (m, 9H), 2.95 (td, J = 13.7 Hz, J = 4.0 Hz, 4H). ^{19}F NMR ($CDCl_3$): −80.3 (s, 6F), −83.9 (m, 4F), −85.1 (m, 4H), −113.9 (dd, J = 83.8 Hz, J = 65.6 Hz, 2F), −122.1 (dd, J = 112.3 Hz, J = 83.8 Hz, 2F), −123.2 (t, J = 13.8 Hz, 4F), −135.6 (dd, J = 112.3 Hz, J = 65.5 Hz, 2F), −145.4 (t, J = 21.9 Hz, 2F). ^{31}P NMR (CH_2Cl_2): −56.2 (s).

Synthesis of $(CF_3)_2C(OCH_2CF_3)_2$. A solution of 420.0 g of $Ph_3P(OCH_2CF_3)_2$ in 300 mL of CH_2Cl_2 was transfered into a 1-L autoclave under N_2 and then pressured with 180 g of hexafluoroacetone. After being heated at 150 °C for 3 h and 200 °C for 4 h, the reaction mixture was poured into a flask and distilled to give the desired product (208.9 g, bp 95.5−96 °C, 99.8% purity). ^{19}F NMR ($CDCl_3$): −75.1 (t, J = 7.5 Hz, 6F), −76.1 (s, 6F). ^1H NMR ($CDCl_3$): 4,18 (q, J = 7.7 Hz). ^{13}C NMR: 122.6 (q, J = 276.7 Hz), 119.8 (q, J = 291.7 Hz); 62.5 (q, J = 37.7 Hz). Anal. Calcd for $C_7H_4F_{12}O_2$: C, 24.15; H, 1.16; F, 65.49. Found: C, 24.21; H, 1.49; F, 65.53.

Synthesis of $(CF_3)_2C(OCH_2CF_2CF_3)_2$. A mixture of 95.0 g of $Ph_3P(OCH_2CF_2CF_3)_2$ and 34.0 g of hexafluoroacetone in 120 mL of CH_2Cl_2 was heated in a shaker tube at 150 °C for 3 h and at 210 °C for 2 h. Two layers were observed, and the lower layer was separated and distilled to give 55.3 g of desired product (99% purity), bp 120−121 °C. ^{19}F NMR ($CDCl_3$): −76.0 (s, 6F), −84.4 (s, 6F), −124.7 (t, J = 11.8 Hz, 4F). ^1H NMR ($CDCl_3$): 4.22 (t, J = 8.0 Hz). Anal. Calcd for $C_9H_4F_{16}O_2$: C, 24.12; H, 0.90. Found: C, 24.48; H, 1.04.

Synthesis of $(CF_3)_2C(OCH_2CF_2CF_2H)_2$. A mixture of 84.0 g of $Ph_3P(OCH_2CF_2CF_2H)_2$ and 27.0 g of hexafluoroacetone in 100 mL of CH_2Cl_2 was heated in a shaker tube at 150 °C for 6 h. After evaporation of the CH_2Cl_2, the residue was distilled under partial vacuum (30 mmHg) to give 56.8 g of crude product (88% purity). Redistillation gave 36.8 g of pure product (99.8% purity), bp 72 °C/30 mmHg). ^{19}F NMR ($CDCl_3$): −75.9 (s, 6F), −124.7 (t, J =12.2 Hz, 4F), −138.4 (d, J = 53. 0 Hz, 4F). ^1H NMR ($CDCl_3$): 5.92 (tt, J = 53.0 Hz, J = 3.8 Hz, 2H), 4.20 (t, J = 12.0 Hz, 4H).

Synthesis of $(CF_3CF_2)_2C(OCH_2CF_3)_2$. A mixture of 23.0 g of $Ph_3P(OCH_2CF_3)_2$ and 13.3 g of perfluoropentanone-3 in 30 mL of CH_2Cl_2 was heated in a shaker tube at 150 °C for 3 h and 210 °C for 3 h. After evaporation of the CH_2Cl_2, the residue was distilled under partial vacuum (-30 mmHg) to give 7.2 g of crude product. Redistillation gave 6.8 g of pure product, bp 125–128 °C. ^{19}F NMR ($CDCl_3$): −74.4 (t, J = 7.5 Hz, 6F), −79.0 (s, 6F), −117.2 (s, 4F). ^1H NMR ($CDCl_3$): 4.27 (q, J = 7.6 Hz). Anal. Calcd for $C_9H_4F_{16}O_2$: C, 24.12; H, 0.90; F, 67.84. Found: C, 24.45; H, 0.95; F, 67.04.

Synthesis of $(CF_3)_2C(OCH_2CF_2CF_2CF_2CF_2H)_2$. A mixture of 74.0 g of $Ph_3P(OCH_2CF_2CF_2CF_2CF_2H)_2$ containing 16% $H(CF_2)_4CH_2OH$ and 33.2 g of HFA in 70 mL of CH_2Cl_2 was heated in a shaker tube at 150 °C for 3 h and 210 °C for 3 h. After evaporation of the CH_2Cl_2, the residue was distilled to give 28.8 g of product with 89% purity. Redistillation gave 21.0 g of pure product, bp 85 °C/5 mmHg. ^{19}F NMR ($CDCl_3$): −76.0 (s, 6F), −121.1 (t, J = 11.6 Hz, 4F), −125.7 (s, 4F), −130.4 (s, 4F), −137.8 (d, J = 50.1 Hz, 4F). Anal. Calcd for $C_{13}H_6F_{22}O_2$: C, 25.51; H, 0.99; F, 68.28. Found: C, 25.68; H, 1.05; F, 68.01.

Synthesis of $(CF_3)_2C(OEVE)_2$. A mixture of 59.6 g of $Ph_3P(OEVE)_2$ and 13.0 g of HFA in 30 mL of CH_2Cl_2 was heated in a shaker tube for 6 h. The reaction mixture was poured into a jar and the lower layer was separated and distilled under reduced pressure to give 8.5 g of $(CF_3)_2C(OEVE)_2$ (bp 65–66 °C/0.3 mmHg). ^1H NMR: 4.54 (t, J = 12.4 Hz). ^{19}F NMR: −75.7 (s, 6F), −80.0 (t, J = 7.4 Hz, 6F), −83.3 (m, 4F), −84.7 (m, 4F), −113.3 (dd, J = 85.0 Hz, J = 65.6 Hz, 2F), −121.8 (dd, J = 111.8 Hz, J = 85.0 Hz, 2H), −123.5 (t, J = 12.3 Hz, 4F), −136.1 (ddt, J = 111.8 Hz, J = 65.5 Hz, J = 5.6 Hz, 2F), −145.2 (t, J = 21.9 Hz, 2F). IR (neat): 2976 (w), 1839 (m), 1342 (s), 1315 (s), 1234 (s), 1162 (s). HRMS: calcd for $C_{18}H_4F_{29}O_6$ (M − CF_3): 867.1826. Found: 866.9549.

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