Synthesis of novel partially fluorinated phosphonic/sulfonic acids

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Abstract

A new synthesis of $(EtO)_2P(O)CH_2OCH_2CH=CH_2$ (**1**) has been developed. Addition of $I(CF_2)_4SO_2F$ or $I(CF_2)_2O(CF_2)_2SO_2F$ to **1** followed by hydrolysis, reduction and ion exchange of the addition adducts gave $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H\cdot 2H_2O$ and $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H\cdot 3H_2O$, respectively.

Introduction

Significant changes in the acidity of organic acids are observed when hydrogen atoms are replaced by fluorine. For example, fluorinated sulfonic or phosphonic acids are much stronger acids than their hydrocarbon analogs [1]. Perfluorinated sulfonic acids are the strongest organic acids known. On the other hand, some fluorinated sulfonic acids, such as trifluoromethanesulfonic acid and its derivatives, play an important role in organic synthesis [2]. The perfluoroalkylphosphonic acids have recently attracted attention as biological chelating agents [3] and electrolytes [4]. The mixed fluorinated phosphonic/sulfonic acids $(HO)_2P(O)CF_2SO_3H$ [5], $(HO)_2P(O)CFHSO_3H$ and $(HO)_2P(O)(CF_2)_4O(CF_2)_2SO_3H$ [6] have recently been reported. Incorporation of oxygen atoms into the skeleton of polymers is known to enhance their flexibility [7]. Mixed acids of the type $(HO)_2P(O)(CH_2)_xO(CH_2)_y(CF_2)_zSO_3H$ could be suitable precursors for the preparation of polymer-supported superacid catalysts by attachment to a polymer support via the phosphonic acid group. The mixed phosphonic/sulfonic acids $(HO)_2P(O)(CH_2)_xO(CH_2)_y(CF_2)_zSO_3H$ have not been reported, although Gard *et al.* [8] have recently reported the preparation of $(EtO)_2P(O)CH_2CH_2O(CF_2)_2SO_2F$ by the reaction of tetrafluoroethane sultone with CsF or KF in the presence of diethyl 2-bromoethylphosphonate. In this work, we report the synthesis of novel partially fluorinated phosphonic/sulfonic acids $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H\cdot 3H_2O$ and $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H\cdot 2H_2O$ isolated as their hydrates, **8** and **12**, respectively.

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Results and discussion

Synthesis of $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H \cdot 3H_2O$ *(8)*

The key step in the synthesis of the mixed sulfonic/phosphonic acid **8** is the radical addition of 2-(2-iodotetrafluoroethoxy)tetrafluoroethanesulfonyl fluoride (**2**)* to phosphonate **1**. The precursor **1** can be readily prepared under mild conditions from diethyl phosphite by a three-step one-pot reaction in 66% overall yield†. The transformation of sulfonyl fluoride **3** into acid **8** has been accomplished in 64% overall yield via hydrolysis, reduction and an ion-exchange reaction. The synthetic route to acid **8** is outlined in Scheme 1.

$$(EtO)_2P(O)H \xrightarrow[\substack{(2)\ (HCHO)_n/0\ ^\circ C\text{–}RT \\ (3)\ H_2C{=}CHCH_2Br/0\ ^\circ C\text{–}RT}]{(1)\ Na/RT/Et_2O} (EtO)_2P(O)CH_2OCH_2CH{=}CH_2$$
(1) (66%)

$$\mathbf{1} \xrightarrow[(PhCO_2)_2/110\ ^\circ C]{I(CF_2)_2O(CF_2)_2SO_2F\ (2)} (EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_2O(CF_2)_2SO_2F$$
(3) (70%)

$$\mathbf{3} \xrightarrow{Et_3N/MeOH/RT} [(EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_2O(CF_2)_2SO_3^-\ \overset{+}{N}HEt_3]$$
(4)

$$\mathbf{4} \xrightarrow[MeOH/Et_3N]{H_2/Pd\text{–}C(5\%)} [(EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3^-\ \overset{+}{N}HEt_3]$$
(5)

$$\mathbf{5} \xrightarrow{NaOH/RT} [(EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3Na]$$
(6)

$$\mathbf{6} \xrightarrow{\text{ion exchange}} (EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H$$
(7) (82%)

$$\mathbf{7} \xrightarrow{\text{conc. HCl/110 °C}} (HO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H \cdot 3H_2O$$
(8) (80%)

Scheme 1.

Several catalysts were tried for the addition of **2** to **1**. The $Zn/NiCl_2 \cdot 6H_2O$ catalyst system [11] gave only the reduced product, $H(CF_2)_2O(CF_2)_2SO_2F$. Tetrakis(triphenylphosphine)palladium [12] did not catalyze the addition reaction at room temperature. In the presence of triethylborane [13], addition of **2** to 1-hexene produced the corresponding addition product in 79% yield. However, triethylborane catalyzed addition of **2** to **1** gave **3** in only 18% yield.

$$Bu^nCH{=}CH_2 + \mathbf{2} \xrightarrow{Et_3B/40\text{–}60\ ^\circ C/6\ h} Bu^nCHICH_2(CF_2)_2O(CF_2)_2SO_2F$$
(79%)

$$\mathbf{1} + \mathbf{2} \xrightarrow{Et_3B/110\ ^\circ C/24\ h} (EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_2O(CF_2)_2SO_2F$$
(3) (18%)

*Obtained from Shanghai Institute of Chemistry, Shanghai, China. See also ref. 9.

†The analog, $(BuO)_2P(O)CH_2OCH_2CH{=}CH_2$, has been prepared by treatment of $(BuO)_2PCl$ with $ClCH_2OCH_2CH{=}CH_2$ in the presence of a Lewis acid at high temperature [10].

Finally, it was found that benzoyl peroxide [14] catalyzed the addition of **2** to **1** at 110 °C affording $(EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_2O(CF_2)_2SO_2F$ (**3**) in 70% isolated yield. Sulfonyl fluoride **3** was hydrolyzed by triethylamine in methanol at room temperature to form sulfonate **4**. In the presence of triethylamine, removal of iodine from sulfonate **4** was accomplished by hydrogenation utilizing 5% palladium on activated carbon [15] as a catalyst in methanol to yield the corresponding sulfonate **5**. Sulfonate **5** was treated with sodium hydroxide in methanol to give the sulfonate $(EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3Na$ (**6**) which was passed through a Dowex 50X8-200 ion-exchange resin column to form crude **7** in 82% overall yield from sulfonyl fluoride **3**. Sulfonates **4**, **5** and **6** were not isolated as pure products because it was difficult to remove Et_3NHF, Et_3NHI, NaF and NaI from the sulfonates. Sulfonic acid **7** was hydrolyzed in concentrated HCl at 110–120 °C to yield the mixed acid $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O$-$(CF_2)_2SO_3H \cdot 3H_2O$ (**8**) in 80% yield (based on **7**). Titration of acid **8** with NaOH (0.0312 N) gave rise to two inflection points, one for 2 equiv. (the sulfonic acid proton and one phosphonic acid proton) and another for 1 equiv. (the second phosphonic acid proton) of the acid. Based on the molecular weight of 504 g mol^{-1}, which is that of the acid trihydrate $(HO)_2P(O)$-$CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H \cdot 3H_2O$, the total titer gave 99.9% purity.

*Synthesis of $(HO)_2P(O)CH_2O(CH_2)_3(CF_2CF_2)_2SO_3H \cdot 2H_2O$ (**12**)*

Initially, we designed the following route (Scheme 2) to prepare the mixed acid **12**:

$$\mathbf{1} \xrightarrow{I(CF_2)_4I} (EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_4I \quad (\mathbf{9})$$

$$\mathbf{9} \xrightarrow[(2)\ H_2O_2]{(1)\ Na_2S_2O_4/NaHCO_3} (EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_4SO_3Na \quad (\mathbf{11})$$

$$\mathbf{11} \xrightarrow[(2)\ \text{ion exchange}]{(1)\ \text{hydrolysis}} (HO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H \quad (\mathbf{12})$$

Scheme 2.

In the presence of 1 mol% $Pd(PPh_3)_4$, the reaction of **1** (12.5 mmol) with $I(CF_2)_4I$ (16.5 mmol) gave the mono adduct **9** (68%) and the bis adduct $\{(EtO)_2P(O)CH_2OCH_2CHICH_2CF_2CF_2\}_2$ (**9a**) (29%), which were easily separated by column chromatography. The addition reaction did not work well when Cu [16] was utilized as a catalyst. Treatment of monoadduct **9** with sodium dithionite and sodium bicarbonate followed by oxidation with hydrogen peroxide gave less than 5% of the expected sulfonate **11** as well as significant amounts of decomposition products.

We were unable to prepare sulfonate **11**, a precursor to mixed **12**, by sulfination and oxidation of **9** as shown in Scheme 2. However, the mixed acid **12** was prepared in good yield by the six-step procedure shown in Scheme 3 from **1** and 4-iodoperfluorobutanesulfonyl fluoride (**13**) [17]. In

the presence of benzoyl peroxide, the addition of **13** to **1** gave **14** in 80% yield. The transformation of **14** into **18** has been accomplished in 79% crude yield via hydrolysis, reduction and ion exchange. The sulfonic acid **18** was hydrolyzed in concentrated HCl at 110–120 °C to yield the mixed acid **12** in 84% yield (based on **18**). Titration of acid **12** with NaOH (0.0312 N) gave rise to two inflection points, one for 2 equiv. (the sulfonic acid proton and one phosphonic acid proton) and another for 1 equiv. (the second phosphonic acid proton) of the acid. Based on the molecular weight of 470 g mol^{-1}, which is that of the acid dihydrate $(HO)_2P(O)CH_2O(CH_2)_3(CF_2CF_2)_2SO_3H \cdot 2H_2O$, the total titer gave 99.5% purity.

$$\mathbf{1} \xrightarrow[(PhCO_2)_2/110\,^\circ C]{I(CF_2)_4SO_2F\ (\mathbf{13})} (EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_4SO_2F \quad (\mathbf{14})\ (80\%)$$

$$\mathbf{14} \xrightarrow{Et_3N/MeOH/RT} [(EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_4SO_3^-\ \overset{+}{N}HEt_3] \quad (\mathbf{15})$$

$$\mathbf{15} \xrightarrow[MeOH/Et_3N/RT]{H_2/Pd\text{–}C(5\%)} [(EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3^-\ \overset{+}{N}HEt_3] \quad (\mathbf{16})$$

$$\mathbf{16} \xrightarrow{NaOH/RT} [(EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3Na] \quad (\mathbf{17})$$

$$\mathbf{17} \xrightarrow{\text{ion exchange}} (EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H \quad (\mathbf{18})\ (79\%)$$

$$\mathbf{18} \xrightarrow{\text{conc. HCl/110 °C}} (HO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H \cdot 2H_2O \quad (\mathbf{12})\ (84\%)$$

Scheme 3.

Experimental

All boiling points were determined during distillation and are uncorrected. ^{19}F NMR (83.9 MHz) and ^{31}P NMR (36 MHz) spectra were recorded on a JEOL FX 90Q spectrometer; ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AC 300 spectrometer. All chemical shifts are reported in parts per million (ppm) downfield (positive) from the standard. ^1H NMR and ^{13}C NMR chemical shifts are reported relative to internal TMS. ^{19}F NMR chemical shifts are reported relative to internal $CFCl_3$ and ^{31}P NMR chemical shifts against external H_3PO_4 (85%). ^{13}C NMR spectra were broad band decoupled from hydrogen nuclei. $CDCl_3$ served as the solvent for all NMR spectra except where indicated. IR spectra were recorded on a Mattson Cygnus 100 FT-IR spectrometer. GC MS and DIP MS spectra were recorded on a VG TRIO-1 spectrometer operating at 70 eV.

Preparation of $(EtO)_2P(O)CH_2OCH_2CH{=}CH_2$ (1) [18] (nc)

A 500 ml flask was charged with sodium (11.5 g, 0.5 mol) and 250 ml dry diethyl ether. Diethyl phosphite (69 g, 0.5 mol) was slowly syringed into

the mixture at 0 °C with stirring. The mixture was allowed to warm to room temperature with stirring until the sodium disappeared (*c.* 3 h). Under nitrogen, paraformaldehyde (18 g, 0.6 mol) was slowly added to the flask and the resultant mixture was stirred at room temperature for 2 h. Allyl bromide (61.5 g, 0.51 mol) was added dropwise at 0 °C and the mixture was allowed to stir overnight at room temperature. After removal of the solid salts by filtration, the filtrate was washed with 100 ml water and dried over anhydrous sodium sulfate. The solvent was removed and the residue was distilled to afford 68.3 g (66% yield based on phosphite) of **1**, b.p. 75–78 °C/0.7 mmHg. ^{1}H NMR δ: 1.35 (t, $J=7$ Hz, 6H, CH_3); 3.77 (d, $J=9$ Hz, 2H, PCH_2); 4.11 (d, $J=6$ Hz, 2H, CH_2C=); 4.18 (m, 4H, CH_2CH_3); 5.28 (m, 2H, =CH_2); 5.88 (ddt, $J=17$, 10, 6 Hz, 1H, –CH=) ppm. ^{13}C NMR δ: 16.5 (CH_3); 62.4 (d, $J=7$ Hz, CH_2CH_3); 63.7 (d, $J=167$ Hz, PCH_2); 74.0 (d, $J=13$ Hz, CH_2CH=); 118.4 and 133.6 (CH=CH) ppm. ^{31}P NMR δ: 21.0 (s) ppm. GC MS (*m/z*); 208 (M^+, 0.08); 193 (0.29); 181 (0.22); 167 (0.76); 152 (36.65); 125 (100); 109 (35.06). FT-IR (CCl_4) (cm^{-1}); 2986 (m); 2983 (m); 2933 (w); 2907 (w); 1261 (s); 1056 (s); 1031 (s); 968 (s).

*Preparation of $(EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_2O(CF_2)_2SO_2F$ (**3**) (nc) using $(PhCO_2)_2$ as the catalyst*

A 50 ml glass Ace reactor with a Teflon screw-cap was charged with 2.1 g (10 mmol) of **1**, 4.9 g (11.5 mmol) of **2** and 0.25 g (1 mmol) of benzoyl peroxide. The mixture was stirred at 110–120 °C for 22 h. Column chromatography (silica gel 400×30 mm) with methylene chloride and ethyl acetate (2:1) eluent gave 4.5 g (70% yield) of **3** as an oil. ^{19}F NMR δ: +45.0 (s, 1F, SO_2F); −82.7 (s, 2F, $CF_2CF_2SO_2F$); −88.2 (s, 2F, $CH_2CF_2CF_2O$); −112.8 (s, 2F, CF_2SO_2F); −118.1 (t, $J=17$ Hz, 2F, CH_2CF_2) ppm. ^{1}H NMR δ: 1.35 (td, $J=7$, 1.2 Hz, 6H, CH_3); 2.54–3.11 (m, 2H, CH_2CF_2); 3.79–3.91 (m, 4H, PCH_2OCH_2); 4.22 (m, 4H, CH_2CH_3); 4.33 (m, 1H, CHI) ppm. ^{13}C NMR δ: 12.9 (s, CHI); 16.5 (s, CH_3); 37.2 (t, $J=21$ Hz, CH_2CF_2); 62.7 (CH_2CH_3); 65.3 (d, $J=166$ Hz, PCH_2); 77.7 (s, OCH_2CHI); 112.0–121.3 (m, 4 CF_2) ppm. ^{31}P NMR δ: 20.3 (s) ppm. FT-IR (CCl_4) (cm^{-1}): 2987 (w); 2984 (w); 1462 (vs); 1267 (s); 1243 (s); 1208 (s); 1193 (s); 1152 (vs); 1115 (s); 1055 (s); 1030 (s). DIP/MS (*m/z*): 507 (M^+-I, 0.23); 451 ($M^+-CF_2CF_2SO_2F$, 0.18); 137 (6.11).

*Preparation of **3** with triethylborane initiation*

A mixture consisting of 6.7 g (32 mmol) of phosphonate **1**, 15 g (35 mmol) of **2** and 15 mmol of Et_3B (1.0 M in hexane) was stirred overnight at 65 °C. ^{19}F NMR analysis indicated that only a trace of the addition product was formed. An additional 15 mmol of Et_3B were added and the mixture was stirred at 110 °C for another day. ^{19}F NMR analysis revealed that **2** was the major component, while a small amount of addition product was formed. Chromatography on silica gel gave 3.7 g (18% yield) of **3**.

Preparation of $CH_3(CH_2)_3CHICH_2(CF_2)_2O(CF_2)_2SO_2F$ with triethylborane initiation

A mixture consisting of 0.9 g (2.1 mmol) of **2**, 0.35 g (4.2 mmol) of 1-hexene and 2 mmol of Et_3B was stirred at 40 °C for 3 h, then at 60 °C for 3 h. ^{19}F NMR analysis indicated that **2** was converted into the corresponding addition product. The mixture was concentrated and dried under vacuum to give 0.85 g (79% yield) of the product as an oil. ^{19}F NMR δ: +44.9 (1F, SO_2F); −82.2 (s, 2F, $OCF_2CF_2SO_2F$); −88.4 (m, 2F, $CH_2CF_2CF_2O$); −112.7 (s, 2F, CF_2SO_2F); −115.5 (m, 2F, CH_2CF_2) ppm.

Preparation of $(EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H$ (7)

A 50 ml flask was charged with 3.5 g (5.5 mmol) of **3** and 5 ml of methanol. Triethylamine (3.5 g, 35 mmol) was added dropwise and an exothermic reaction was observed immediately. ^{19}F NMR analysis indicated that the sulfonyl fluoride had been converted to the sulfonate **4**. Pd (5% on activated carbon, 0.5 g) was added and the mixture was stirred overnight at room temperature under H_2 (1 atm). After removal of the Pd–C by filtration, the filtrate was concentrated and dried under vacuum to give 5.2 g of residue. The residue was dissolved in 5 ml of methanol and added to 0.65 g NaOH in 20 ml of methanol. The mixture was concentrated to afford a residue which was dissolved in 20 ml of water and passed through an ion-exchange column packed with Dowex 50X8-200 ion-exchange resin to give 2.3 g (82% crude yield) of acid **7**.

Compound **4**: ^{19}F NMR (MeOH) δ: −82.9 (2F, OCF_2CF_2SO); −88.8 (2F, $CH_2CF_2CF_2$); −117.2 (2F, CH_2CF_2); −118.4 (2F, CF_2S) ppm.

Compound **5**: ^{19}F NMR (MeOH external $CFCl_3$) δ: −84.3 (2F, OCF_2CF_2SO); −89.9 (2F, $CH_2CF_2CF_2$); −119.4 (t, J = 16 Hz, 2F, CH_2CF_2); −119.8 (2F, CF_2SO) ppm.

Compound **7**: ^{19}F NMR (DMSO-d_6) δ: −82.2 (2F, OCF_2CF_2S); −87.6 (2F, $OCF_2CF_2CH_2$); −116.9 (t, J = 20 Hz, 2F, CF_2CH_2); −117.9 (2F, CF_2S) ppm.

Preparation of $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H \cdot 3H_2O$ (8) (nc)

The crude sulfonic acid **7** (2.3 g) was dissolved in 3 ml of concentrated HCl and stirred at 110–120 °C for 6 h. After removal of HCl by vacuum, 20 ml of water and 0.3 g charcoal were added and the mixture was stirred at room temperature for 6 h. After removal of the charcoal by filtration, the filtrate was concentrated to form a residue which was pumped under vacuum for 5 d to give 1.83 g (80% yield) of **8** as a viscous oil. ^{19}F NMR (DMSO-d_6) δ: −82.3 (2F, OCF_2CF_2S); −87.4 (2F, $OCF_2CF_2CH_2$); −116.8 (t, J = 17 Hz, 2F, CH_2CF_2); −117.8 (2F, CF_2SO_3H) ppm. ^1H NMR (DMSO-d_6) δ: 1.75 (m, 2H, $CH_2CH_2CF_2$); 2.20 (m, 2H, CH_2CF_2); 3.57 (t, J = 7 Hz, 2H, OCH_2CH_2); 3.60 (d, J = 9 Hz, 2H, PCH_2); 7.21 (s, 7H, $OH + H_2O$) ppm. ^{13}C NMR (DMSO-d_6) δ: 20.4 (s, OCH_2CH_2); 26.6 (t, J = 22 Hz, CH_2CF_2); 65.4 (d, J = 161 Hz,

PCH_2); 70.8 (s, OCH_2CH_2); 108.0–120.8 (m, 4 CF_2) ppm. ^{31}P NMR (DMSO-d_6) δ: 17.6 (s) ppm.

*Preparation of $(EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_4I$ (**9**) (nc)*

A 50 ml flask was charged with 0.1 g (0.09 mmol) of $Pd(PPh_3)_4$ and 2.6 g (12.5 mmol) of **1**. $I(CF_2)_4I$ (7.5 g, 16.5 mmol) was added to the reaction mixture under nitrogen at room temperature and an exothermic reaction occurred after a few minutes. After the mixture had been stirred at room temperature for 1 h, ^1H NMR analysis indicated that **1** had been completely consumed. Chromatography on silica gel (300×35 mm) with ethyl acetate eluent gave 5.6 g of the mono adduct **9** (68%). Further elution with methanol eluent gave 1.6 g of the bis adduct **9a** (29%). A similar reaction, but with a 1:1.1 ratio of **1** to $I(CF_2)_4I$, afforded 53% of the mono adduct **9** and 43% of the bis adduct **9a**.

Compound **9**: ^{19}F NMR δ: −59.4 (2F, CF_2I); −113.2 (2F, CF_2CF_2I); −114.3 (2F, CH_2CF_2); −123.2 (2F, $CF_2CF_2CH_2$) ppm. ^1H NMR δ: 1.35 (t, J=7 Hz, 6H, CH_3); 2.66–3.07 (m, 2H, CH_2CF_2); 3.79–3.91 (m, 4H, PCH_2OCH_2); 4.18 (m, 4H, OCH_2CH_3); 4.36 (p, J=6 Hz, 1H, *CHI*) ppm. ^{13}C NMR δ: 13.4 (s, *CHI*); 16.5 (s, CH_3); 37.5 (t, J=21 Hz, CH_2CF_2); 62.6 (s, OCH_2CH_3); 65.1 (d, J=166 Hz, PCH_2); 77.6 (d, J=10 Hz, OCH_2CHI); 94.1 (tt, J=322, 42 Hz, CF_2I); 108.3–117.6 (m, 3 CF_2) ppm. ^{31}P NMR δ: 20.1 (s) ppm. FT-IR (CCl_4) (cm^{-1}) 1187 (vs); 1263 (s); 2983 (w).

Compound **9a**: ^{31}P NMR δ: 20.4 (s). ^{19}F NMR δ: −114.3 (s, 4F); −124.0 (s, 4F) ppm. ^1H NMR δ: 1.35 (t, J=7 Hz, 12H, CH_3); 2.70–3.02 (m, 4H, CH_2CF_2); 3.86 (m, 8H, PCH_2OCH_2); 4.18 (m, 8H, OCH_2CH_3); 4.36 (p, J=6 Hz, 2H, *CHI*) ppm.

*Preparation of $(EtO)_2P(O)CH_2OCH_2CHICH_2(CF_2)_4SO_2F$ (**14**) (nc)*

A mixture consisting of **13** (2 g, 4.9 mmol), **1** (1.0 g, 4.8 mmol) and benzoyl peroxide (0.12 g, 0.5 mmol) was stirred at 110 °C for 1 h. ^{19}F NMR analysis indicated that the addition product had formed. Column chromatography on silica gel (300×35 mm) with methylene chloride and ethyl acetate (3:1) eluent gave 2.4 g (80% yield) of **14** as an oil. ^{19}F NMR δ: +45.9 (1F, SO_2F); −108.0 (2F, CF_2S); −114.1 (2F, CF_2CH_2); −120.3 (2F, CF_2CF_2S); −123.6 (2F, $CF_2CF_2CH_2$) ppm. ^1H NMR δ: 1.36 (td, J=7, 1.2 Hz, 6H, CH_3); 2.66–3.15 (m, 2H, CH_2CF_2); 3.80–3.94 (m, 4H, PCH_2OCH_2); 4.20 (m, 4H, CH_2CH_3); 4.35 (p, J=7 Hz, 1H, *CHI*) ppm. ^{13}C NMR δ: 12.7 (s, *CHI*); 16.6 (s, CH_3); 37.5 (t, J=21 Hz, CH_2CF_2); 62.8 (CH_2CH_3); 65.3 (d, J=166 Hz, PCH_2); 77.7 (s, OCH_2CHI); 110.5–121.2 (m, 4 CF_2) ppm. ^{31}P NMR δ: 20.4 (s) ppm. FT-IR (CCl_4) (cm^{-1}): 2986 (w); 2983 (w); 1461 (vs); 1262 (s); 1240 (s); 1212 (s); 1168 (m); 1142 (s); 1030 (s). DIP/MS (*m/z*): 491 (M^+ −I, 0.77); 435 ($M^+ - CF_2CF_2SO_2F$, 0.69); 137 (8.45); 109 (12.67).

*Preparation of $(EtO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H$ (**18**)*

The adduct **14** (7.7 g, 12.5 mmol) was dissolved in 20 ml of methanol. Et_3N (5 ml) was added slowly and an exothermic reaction was observed.

^{19}F NMR analysis of the reaction mixture indicated that **14** had been hydrolyzed to sulfonate **15**. Pd (5% on activated carbon, 0.25 g) was added to the reaction mixture and the resultant mixture was stirred at room temperature under H_2 (1 atm) for 20 h. After removal of the Pd–C by filtration, NaOH (1.5 g) was added. The mixture was concentrated to give 9.1 g of solid residue which was dissolved in 37 ml of water and passed through an ion-exchange column packed with Dowex 50X8-200 ion-exchange resin to give 4.85 g (79% yield) of crude **18** which contained some partially hydrolyzed acid $(EtO)(HO)P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H$.

Compound **15**: ^{19}F NMR (MeOH) δ: −115.5 (2F); −116.2 (2F); −121.8 (2F); −125.7 (2F) ppm.

Compound **16**: ^{19}F NMR (MeOH) δ: −116.4 (4F); −122.2 (2F); −125.7 (2F) ppm.

Compound **18**: ^{19}F NMR (DMSO-d_6) δ: −114.2 (2F); −114.3 (2F); −119.7 (2F); −123.2 (2F) ppm.

Preparation of $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H\cdot 2H_2O$ (12) (nc)

The crude acid **18** (6.2 g, 12.7 mmol) was dissolved in 30 ml of concentrated HCl and refluxed for 5 h. After removal of the HCl, 60 ml of water and charcoal (2 g) were added. The resultant mixture was stirred at room temperature overnight. After removal of charcoal by filtration, the aqueous solution was concentrated to form a residue which was pumped under vacuum for 4 d at room temperature to give 5 g (84% yield) of **12** as a hygroscopic solid. ^{19}F NMR (DMSO-d_6) δ: −113.1 (m, 2F, CF_2CH_2); −114.2 (t, $J=15$ Hz, 2F, CF_2S); −119.8 (m, 2F, CF_2CF_2S); −123.1 (t, $J=10$ Hz, 2F, $CF_2CF_2CH_2$) ppm. ^1H NMR (DMSO-d_6) δ: 1.78 (m, OCH_2CH_2); 2.22 (m, CH_2CF_2); 3.56 (m, PCH_2OCH_2); 5.72 (s, $OH+H_2O$) ppm. ^{31}P NMR (DMSO-d_6) δ: 17.3 (s) ppm. ^{13}C NMR (DMSO-d_6) δ: 20.3 (s, OCH_2CH_2); 27.4 (t, $J=22$ Hz, CH_2CF_2); 66.0 (d, $J=161$ Hz, PCH_2); 70.7 (d, $J=11$ Hz, OCH_2CH_2); 108.2–122.1 (m, 4 CF_2) ppm.

Titration of $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3H\cdot 3H_2O$ (8)

The acid **8** (76.9 mg) was dissolved in 10 ml of 0.1 N NaCl (aq.), then titrated with 0.0312 N NaOH which had been standardized with primary standard potassium acid phthalate. A pH meter was used to monitor the titration. Two breaks were observed. The first break was at $V=9.70$ ml and the second break at 14.65 ml. The total titration purity was 99.9% (based on the acid trihydrate, MW = 504).

Titration of $(HO)_2P(O)CH_2O(CH_2)_3(CF_2)_4SO_3H\cdot 2H_2O$ (12)

The acid **12** (30.2 mg) was dissolved in 10 ml of 0.1 N NaCl (aq.), then titrated by 0.0312 N NaOH. The first break was at $V=4.00$ ml and the second break at 6.15 ml. The total titration purity was 99.5% (based on the acid dihydrate with MW = 470).

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