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Synthesis of 1-(N-Perfluoroalkanesulfonylamino)-2,2,2-(trichloroethyl)dialkylphosphonates and Phosphonic Acids

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ABSTRACT

A series of 1-(perfluoroalkanesulfonylamino)-2,2,2-(trichloroethyl)dialkylphosphonates $R_fSO_2NHCH(CCl_3)P(O)(OR)_2$ has been synthesized in good yields by addition of dialkyl phosphite to N-perfluoroalkanesulfonyltrichloroaldimines $R_fSO_2N=CHCCl_3$ that were prepared by treatment of N,N-dichloroperfluoroalkanesulfonylamines with trichloroethylene. Acidic hydrolysis of the phosphonates gave the corresponding phosphonic acids. © 1997 John Wiley & Sons, Inc.

INTRODUCTION

α-Aminophosphonates and their derivatives are of increasing interest in medicine and agriculture on account of their wide applications as active insecticides, fungicides, antibiotics, enzyme inhibitors, and virostatica [1–6]. Such an impressive array of applications has led to considerable effort toward their synthesis, and recently, many efforts have been devoted to the preparation of fluorine-containing analogs because the presence of a fluorine atom leads to a strong polarization and changes various physical and biological properties of the molecules (p*Ka*, lipoidal solubility, etc.). The standard syntheses of the α-aminophosphonates involve thermal addition of a dialkyl phosphite to an imine [7], using the Arbuzov-Michaelis-Becker reaction [8]; heating imines with phosphorous acid [9], and treatment of trimethylsilyloxy phosphorus(III) derivatives with an imine [10].

During a study on the N-pentafluorophenyl-aromatic aldimines $C_6F_5N=CHAr$, we have reported its addition reaction with dialkyl phosphites giving α-(N-pentafluorophenylamino)benzylphosphonates [11].

In this article, we report the syntheses of dialkyl 1-(N-perfluoroalkanesulfonylamino)-2,2,2-(trichloroethyl)phosphonates $R_fSO_2NHCH(CCl_3)P(O)(OR)_2$ and their derivatives.

RESULTS AND DISCUSSION

Considerable attention has been given to the preparation and reactions of N,N-dichloroperfluoroalkanesulfonylamines $R_fSO_2NCl_2$ **2** in our laboratory. Compounds **2** were conveniently prepared by one-pot reactions of perfluoroalkanesulfonylamines with KOH (aq.) and chlorine gas [12]:

$$\underset{\mathbf{1}}{R_fSO_2NH_2} \xrightarrow[0°C–20°C,\ 24\ h]{KOH(aq),\ CL_2} \underset{\mathbf{2}}{R_fSO_2NCl_2}$$

R_f: $I(CF_2)_2O(CF_2)_2$ (**a**); $H(CF_2)_2O(CF_2)_2$ (**b**); C_4F_9 (**c**); C_6F_{13} (**d**); C_8F_{17} (**e**).

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The products **2(a–c)** are yellowish liquids, and the compounds **2(d–e)** are solids, all being unstable on standing and easily decomposing to the corresponding perfluoroalkanesulfonylamines $R_fSO_2NH_2$. In the presence of zinc powder, they readily lose chlorine gas to form perfluoroalkanesulfonylnitrene intermediates. For example, each **2** reacted with tetramethylethylene to give the corresponding N-perfluoroalkanesulfonylaziridine. It was found that the reaction of each **2** with styrene occurred smoothly even in the absence of zinc powder and gave the corresponding 1:1 adduct [12–14].

We have now found that a similar treatment of each **2** with trichloroethylene without a catalyst at room temperature gave, not a 1:1 addition product, but rather the corresponding N-perfluoroalkanesulfonyltrichloroaldimine **4** and pentachloroethane **5**:

$$\underset{\mathbf{2}}{R_fSO_2NCl_2} + \underset{\mathbf{3}\ (\text{excess})}{CHCl=CCl_2} \xrightarrow[81\text{–}87\%]{\text{r.t., 10 h}} \underset{\mathbf{4}}{R_fSO_2N=CHCCl_3} + \underset{\mathbf{5}}{CHCl_2CCl_3}$$

R_f: $I(CF_2)_2O(CF_2)_2$ (**a**); $H(CF_2)_2O(CF_2)_2$ (**b**); $Cl(CF_2)_2O(CF_2)_2$ (**c**); C_4F_9 (**d**); C_6F_{13} (**e**); C_8F_{17} (**f**).

The results of the preparation of compounds **4** are listed in Table 1.

Compounds **4** are hygroscopic, and a small amount of each of them decomposed to **1** and trichloroacetaldhyde even during IR analysis. The products **4** are fully characterized by NMR, IR, MS, and HRMS spectroscopy. For instance, the chemical shifts (N=CH) of ^{13}C NMR and ^{1}H NMR for compound **4b** are δ 172.6 and 8.40, respectively. The characteristic IR absorptions are located at 1640–1670 cm^{-1} (C=N) and 1340–1360 cm^{-1} (SO_2). All the MS spectra of compounds **4** showed the characteristic isotopic peaks ($M^+ + 5$, $M^+ + 3$, $M^+ + 1$) for the CCl_3 group.

There are some literature reports on reactions of $RNCl_2$ with $CHCl=CCl_2$ [16–19], and a radical mechanism for these reactions has been proposed. The mechanism of this reaction was supported by ESR results. Generally, the radical intermediate could be captured by a spin trapping reagent, 2-methyl-2-nitrosopropane, *t*-BuNO. However, recently [20], we found that compound **2** readily reacted with *t*-BuNO to give either the unsymmetrical nitroxide $R_fN(O)$-Bu-*t* or the symmetrical nitroxide $R_fN(O)$-R_f, depending on the nature of the solvent and the amount of **2** used. Because of this, the use of *t*-BuNO is unsuitable for investigating the mechanism of this reaction. When $C_6H_5CH=N(O)Bu$-*t* was used, the ESR spectrum showed a triplet peak (a_N = 29.99 G; g = 2.0098), but the hyperfine structure was not observed [21]. Accordingly, the reaction involves a radical procedure and may be suggested to occur as in Scheme 1.

In our previous work, it was found that the N-sulfinylperfluoroalkanesulfonylamines R_fSO_2NSO **6** readily react with many carbonyl compounds such as aldehydes, DMF, and formates, forming N-perfluoroalkanesulfonylimines $R_fSO_2N=CHR$ (R: Ar, NR'_2, OR′). However, very reactive carbonyl reagents, such as CF_3COCF_3 and CCl_3CHO do not react with **6**, except in the presence of CsF, giving the corresponding $R_fSO_2N=C(CF_3)_2$ or $R_fSO_2N=CHCCl_3$ **4** in very low yield [15,22].

Compared with ArN=CHAr or RN=CHAr, compounds **4** are more reactive toward the addition of a dialkyl phosphite. In the literature, it is reported that the temperature of addition of ArN=CHAr or RN=CHAr to $HP(O)(OR)_2$ is generally around 140°C, and, in some cases, Lewis acids such as $AlCl_3$ or BF_3–OEt_2 must be used as catalysts [23–25].

Quang et al. [26] have synthesized the 1-acylamino-2,2-2-trichloroethanephosphonates by the Arbusov–Michaelis reaction of 1,2,2,2-tetrachloro-N-acylethylamines with trialkyl phosphites. Ulrich and co-workers [27] have also added hydrogen phosphite to anhydrochloralurethans, $Cl_3CCH=NCOOR$, to prepare the corresponding 1:1 adducts, but the reaction was quite sluggish and required a basic catalyst.

An exothermic reaction occurred for an equimolar mixture of **4** and **7** at room temperature. Raising the temperature to 70°C improved the reaction and readily gave high yields of **8**; thus,

$$\underset{\mathbf{4}}{R_fSO_2N=CHCCl_3} + \underset{\mathbf{7}}{HP(O)(OR)_2} \xrightarrow[70^\circ C]{8\text{ h}} \underset{\mathbf{8}}{R_fSO_2NHCH(CCl_3)P(O)(OR)_2}$$

R_f: $I(CF_2)_2O(CF_2)_2$ (**a**); $H(CF_2)_2O(CF_2)_2$ (**b**); C_4F_9 (**c**); C_6F_{13} (**d**). R:CH_3, C_2H_5.

TABLE 1 N-Perfluoroalkanesulfonyltrichloroaldimines **4**

Compounds		*Boiling Point*	*Yield*[b]
R_f	**4**	(°C/Torr)	(%)
$I(CF_2)_2O(CF_2)_2$	**4a**	93/2	87
$H(CF_2)_2O(CF_2)_2$	**4b**	54–55/2	86
$Cl(CF_2)_2O(CF_2)_2$	**4c**	76/2	83
C_4F_9	**4d**	60/2[a]	82
C_6F_{13}	**4e**	74–75/2	83
C_8F_{17}	**4f**	98/2	81

[a]Known compound [15].
[b]Isolated yields based on compounds **2**.

$$R_fSO_2NCl_2 \rightarrow R_fSO_2NCl\cdot + Cl\cdot$$

$$R_fSO_2\dot{N}Cl + CHCl{=}CCl_2 \rightarrow R_fSO_2NCl{-}CHCl{-}\dot{C}Cl_2$$

$$R_fSO_2NCl{-}CHCl{-}\dot{C}Cl_2 + R_fSO_2NCl_2 \rightarrow [R_fSO_2NClCHClCCl_3] + R_fSO_2\dot{N}Cl$$

$$[R_fSO_2NClCHClCCl_3] \rightarrow R_fSO_2N{=}CHCCl_3 + Cl_2\,Cl_2 + CHCl{=}CCl_2 \rightarrow CHCl_2CCl_3$$

SCHEME 1

The addition products **8** are really separated by column chromatography (ethyl acetate:petroleum ether = 1:3.5 as eluant) from the reaction mixture. Recrystallization from chloroform gave pure samples as white solids.

The ^{1}H NMR, ^{19}F NMR, IR, MS, elemental analyses, or HRMS were consistent with the structures given above. Furthermore, the structures were confirmed by the determination of the X-ray molecular structure of **8b** (see Figure 1). Selective bond lengths and bond angles are collected in Table 3 and Table 4.

In the 90 MHz NMR spectra, the alkyloxy groups gave rise to signals that are typical of those for dialkyl phosphoryl compounds in general. For example, the methyloxy group in compounds **8a** and **8c** appeared as a d-d peak at δ 3.83–3.96 ($^3J_{H-P}$ = 7.2 Hz). The NH–CH-proton felt within fairly narrow ranges δ 4.60–4.65 and were also split by the P-atom to give a double peak ($^2J_{H-P}$ = 19.8 Hz). The chemical shift of the NH proton, shown as a broad signal varied somewhat from δ 6.53–7.50 and disappeared when the compound was treated with D_2O.

Hydrolysis of **8** with concentrated hydrochloric acid (36%) gave the corresponding phosphonic acid **9**.

$$\underset{\mathbf{8}}{R_fSO_2NHCH(CCl_3)P(O)(OR)_2} \xrightarrow[15\ h,\ 100°C]{HCl(36\%)} \underset{\mathbf{9}}{R_fSO_2NHCH(CCl_3)P(O)(OH)_2}$$

R_f: $I(CF_2)_2O(CF_2)_2$ (**a**); $H(CF_2)_2O(CF_2)_2$ (**b**). R: CH_3; C_2H_5.

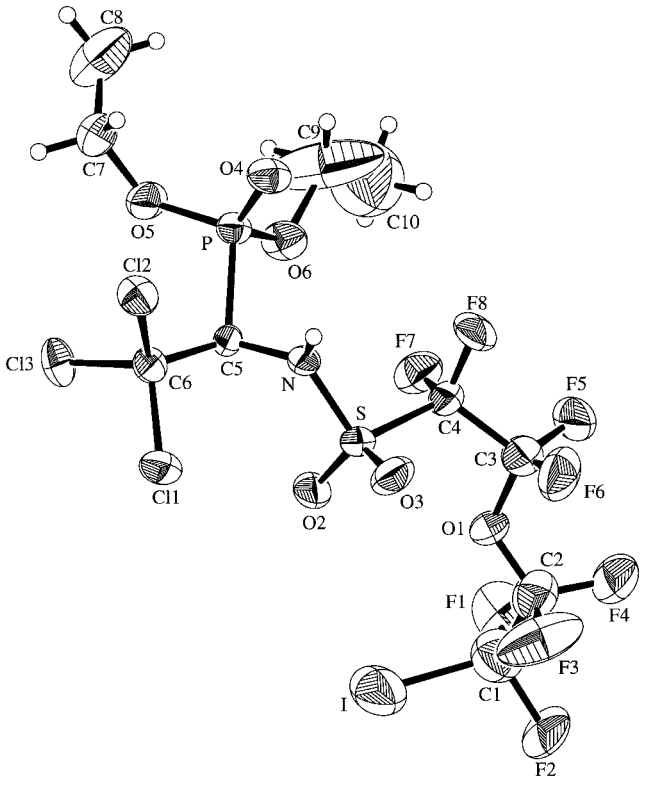


FIGURE 1 The molecular structure of compound **8b**. (A copy of the ESR Spectrum may be obtained by a written request to Professor Shizneng Zhu.)

TABLE 2 Compounds **8** and **9** Prepared

Compounds **8** *and* **9**			*Melting Points*[a]	*Yields*[b]
R_f	*R*		(°C)	(%)
$I(CF_2)_2O(CF_2)_2$	Me	**8a**	122–123	86
$I(CF_2)_2O(CF_2)_2$	Et	**8b**	105–106	90
$H(CF_2)_2O(CF_2)_2$	Me	**8c**	119–120	88
C_4F_9	Et	**8d**	108–109	85
C_6F_{13}	Et	**8e**	90–92	78
$I(CF_2)_2O(CF_2)_2$	H	**9a**	—	65
$H(CF_2)_2O(CF_2)_2$	H	**9b**	—	60

[a]Recrystallized from $CHCl_3$.
[b]Isolated yield based on **4**.

TABLE 3 Select Bond Lengths (Å) of Compound **8b**

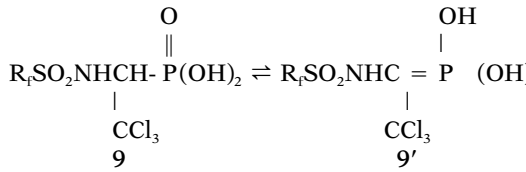
Atom	*Atom*	*Distance*	*Atom*	*Atom*	*Distance*
I	C(1)	2.03(2)	Cl(1)	C(6)	1.76(1)
Cl(2)	C(6)	1.76(1)	Cl(3)	C(6)	1.77(1)
S	O(2)	1.433(8)	S	O(3)	1.404(10)
S	N	1.603(8)	S	C(4)	1.84(1)
P	O(4)	1.460(7)	P	O(5)	1.552(9)
P	O(6)	1.526(9)	P	C(5)	1.854(10)
F(1)	C(1)	1.29(2)	F(8)	C(4)	1.34(1)
O(1)	C(2)	1.31(2)	O(1)	C(3)	1.40(2)
O(5)	C(7)	1.44(2)	O(6)	C(9)	1.57(4)
N	C(5)	1.42(1)	C(1)	C(2)	1.64(3)
C(5)	C(6)	1.57(2)	C(9)	C(10)	1.22(5)

Compounds **9** were obtained as dark liquids. In the ^{1}H NMR spectra, with CD_3COCD_3 and D_2O added, no expected double peak appeared (C<u>H</u>). In order to solve this problem, we propose a possible explanation. Because of the presence of the electron-withdrawing groups CCl_3- and R_fSO_2N- [28,29], the hydrogen of the C<u>H</u> has acidic power, and the compounds **9** can exist in an equilibrium with its enolate-like form **9′** [30]. When D_2O was added, the resonances of all reactive hydrogen atoms disappeared (see Scheme 2).

All of the yields and properties of compounds **8** and **9** are collected in Tables 2–4. The biological activities of **8** and **9** are now under investigation.

EXPERIMENTAL

The melting points and boiling points reported are uncorrected. Solvents were purified and dried before use. ^{1}H NMR (60 MHz), ^{13}C NMR (300 MHz), and ^{19}F NMR (54.6 MHz) spectra were recorded on a Varian-360L instrument or a Bruker AM-300 spectrometer with TMS and TFA ($\delta_{CFCl3} = \delta_{TFA} + 76.6$ ppm, and with upfield positive) being used as an internal and external standard, respectively. X-ray structure analyses were performed with a Rigaku AFC 7R diffractometer. IR spectra were obtained with an IR-440 Shimadzu or Perkin-Elmer 983G spectrophotometer. Lower resolution mass spectra and high resolution mass spectra (HRMS) were obtained on a Finnigan GC-MS 4021 and Finnigan MAT-8430 instrument, respectively.



SCHEME 2

TABLE 4 Select Bond Angles of Compound **8b**

Atom	*Atom*	*Atom*	*Angle*	*Atom*	*Atom*	*Atom*	*Angle*
I	C(1)	F(2)	106(1)	Cl(1)	C(6)	Cl(2)	108.8(6)
Cl(1)	C(6)	Cl(3)	107.5(5)	Cl(1)	C(6)	Cl(5)	110.2(7)
Cl(2)	C(6)	Cl(3)	109.1(6)	Cl(2)	C(6)	C(5)	111.3(7)
Cl(3)	C(6)	C(5)	109.7(7)	P	C(5)	C(6)	115.1(7)
N	C(5)	C(6)	112.5(5)	P	O(5)	C(7)	125.6(8)
P	O(6)	C(9)	121.1	S	N	C(5)	123.1(6)
P	C(5)	N	106.7(6)	O(2)	S	O(3)	122.7(5)
F(1)	C(1)	C(2)	106(1)	F(6)	C(3)	C(4)	110(1)
N	S	C(4)	103.4(5)	S	C(4)	C(3)	118(10)

General Preparation of Compounds **4**

Compound **2a** (1.33 g, 2.7 mmol), generated according to the literature Ref. [8], was mixed with excess trichloroethylene in a 10 mL flask. After the mixture had been stirred for 10 hours at room temperature, excess trichloroethylene was removed. Vacuum distillation gave a colorless liquid **4a** (1.3 g), yield 87%. Similar treatments gave compounds **4b–f**.

$ICF_2CF_2OCF_2CF_2SO_2N=CHCCl_3$ **4a.** ^{1}H NMR ($CDCl_3$: δ 8.30 (s, N=CH). ^{19}F NMR: δ −12.3 (s, ICF_1), 4.0 (s, OCF_2), 8.2 (s, CF_2O), 38.0 (s, SCF_2). IR (film) (ν_{max}, cm^{-1}): 1640 (m), 1445 (m), 1390 (s), 1340 (m), 1300 (m), 1230–1090 (vs), 990 (m), 910 (m), 870 (m), 800 (m). MS (m/e, %): 521/519/517 ($M^+ + 5 - Cl/M^+ + 3 - Cl/M^+ + 1 - Cl$, 6.61/33.39/46.84), 485/483 ($M^+ + 4 - 2 \times Cl/M^+ + 2 - 2 \times Cl$, 1.17/3.20), 227 ($IC_2F_4^+$, 85.25), 210/208/206 ($M^+ + 2 - IR_f/M^+ - IR_f/M^+ - 2 - IR_f$, 0.68/0.97/1.91), 177 ($ICF_2^+$, 42.25), 144/142/140 ($M^+ + 6 - IR_f - 2 \times Cl/M^+ + 4 - IR_f - 2 \times Cl/M^+ + 2 - IR_f - 2 \times Cl$, 1.05/1.06/2.07), 144 ($^+N=CHCCl_3$, 1.05), 130 ($^+CHCCl_3$, 2.18), 117 ($^+CCl_3$, 3.11), 114/112/110 ($M^+ + 5 - IR_fSO_2 - Cl/M^+ + 3 - IR_fSO_2 - Cl/M^+ + 1 - IR_fSO_2 - Cl$, 11.82/68.52/100.00), 83 ($^+SO_2F$ or $HCCl_2^+$, 42.25), 64 (SO_2^+, 11.27). Elemental Anal. for $C_8H_8Cl_3F_8INO_6PS$. Required: C, 13.03; H, 0.18; N, 2.53; F, 27.51%. Found: C, 13.23; H, 0.47; N, 2.25; F, 27.32%.

$HCF_2CF_2OCF_2CF_2SO_2N=CHCCl_3$ **4b.** ^{1}H NMR ($CDCl_3$) δ 8.40 (s, N=CH), 5.60 (*t-t*, $^2J_{H-F}$ = 54.0 Hz). ^{19}F NMR: δ 4.0 (*t*, OCF_2), 11.5 (s, CF_2O), 38.3 (s, SCF_2), 61.0 (d, HCF_2, $^2J_{H-F}$ = 54.0 Hz). ^{13}C NMR ($CDCl_3$) δ 172.642 (N=<u>C</u>H), 116.803 (*t-t*, SCF_2, $^1J_{C-F}$ = 284.93 Hz, $^2J_{C-F}$ = 30.12 Hz), 115.830 (*t-t*, CF_2, $^1J_{C-F}$ = 288.64 Hz, $^2J_{C-F}$ = 30.27 Hz), 113.028 (*t-t*, CF_2, $^1J_{C-F}$ = 301.54 Hz, $^2J_{C-F}$ = 37.97 Hz), 107.015 (*t-t*, HCF_2, $^1J_{C-F}$ = 253.43 Hz, $^2J_{C-F}$ = 38.50 Hz), 90.657 (<u>C</u>Cl_3). IR (film)(ν_{max}, cm^{-1}): 1644 (s), 1440 (s), 1394 (s), 1334 (m), 1292 (s), 1240–1137 (vs), 1064 (m), 1010 (m), 870 (m), 836 (m), 702 (m). MS (m/e, %): 430/428/426 ($M^+ + 5/M^+ + 3/M^+ + 1$, 4.78/13.65/13.65), 393/391 ($M^+ + 3 - Cl/M^+ + 1 - Cl$, 1.04/1.51), 217 ($HR_f^+$, 3.98), 194/192 ($M^+ + 3 - HC_2F_4O$-$CCl_3/M^+ + 1 - HC_2F_4O - CCl_3$, 18.31/14.87), 146/144 ($M^+ + 2 - HR_fSO_2/M^+ - HR_fSO_2$, 16.31/1.19), 130 ($^+CHCCl_3$, 2.39), 119 ($C_2F_5^+$, 100.00), 117 ($^+CCl_3$, 19.16), 101 ($HC_2F_4^+$, 72.90), 84 ($^+N=CHCCl$, 16.01), 83 ($HCCl_2^+$, 16.96), 82 ($CCl_2^+$, 30.68), 64 ($SO_2^+$, 28.48). HRMS for $C_6H_2NO_3Cl_2F_8S$: found: 389.8963; diff.: −4.2.

$C_4F_9SO_2N=CHCCl_3$ **4d.** ^{1}H NMR ($CDCl_3$) δ 8.65 (s, N=CH). ^{19}F NMR: δ 4.0 (*t*, CF_3), 33.2 (*t*, SCF_2),

43.0 (s, CF_2), 48.2 (s, CF_2). IR (film)(ν_{max}, cm^{-1}): 1640 (s), 1460 (s), 1420 (s), 1360 (m), 1250–1180 (vs), 1140 (s), 1120 (m), 1030 (m), 1000 (m), 980 (w), 870 (m), 690 (m). MS (m/e, %): 432/430/428 (M^+ + 5/M^+ + 3/M^+ + 1, 4.77/13.45/13.32), 395/393 (M^+ + 3 − Cl/M^+ + 1 − Cl, 1.39/2.05), 246 (M^+ − 1 − CF_2 − $CHCCl_3$, 21.97), 219 ($C_4F_9^+$, 100.00), 169 ($C_3F_7^+$, 4.27), 131 (M^+ + 1 − $C_4F_9SO_2N$, 51.93), 119 ($C_2F_5^+$, 32.17), 117 ($^+CCl_3$, 17.52), 83 ($^+SO_2F$ or $HCCl_2^+$, 14.55), 64 (SO_2^+, 21.91).

$C_6F_{13}SO_2N{=}CHCCl_3$ **4e.** ^{1}H NMR ($CDCl_3$) δ 8.20 (s, N=CH). ^{19}F NMR: δ 4.0 (*t*, CF_3), 33.8 (*t*, SCF_2), 42.6 (s, CF_2), 44.6 (s, CF_2), 45.8 (s, CF_2), 49.3 (s, CF_2). IR (film) (ν_{max}, cm^{-1}): 1650 (s), 1460 (s), 1390 (s), 1370 (m), 1250–1170 (vs), 1150 (s), 1060 (m), 790 (m), 690 (m). MS (m/e, %): 532/530/528 (M^+ + 5/M^+ + 3/M^+ + 1, 2.95/8.51/8.40), 495/493 (M^+ + 3 − Cl/M^+ + 1 − Cl, 0.53/0.75), 402/400 (M^+ + 5-$CHCCl_3$/M^+ + 3 − $CHCCl_3$, 4.58/88.68), 319 ($C_6F_{13}^+$, 6.58), 169 ($C_3F_7^+$, 4.27), 131 (M^+ + 1 − $C_6F_{13}SO_2N$, 41.58), 119 ($C_2F_5^+$, 39.59), 117 ($^+CCl_3$, 7.02), 83 ($HCCl_2^+$, 14.55), 111 (M^+ + 2 − $C_6F_{13}SO_2$ − Cl, 24.46), 82 (CCl_2^+, 24.59), 80 (SO_3^+, 100.00), 69 (CF_3^+, 48.85), 64 (SO_2^+, 21.91). HRMS for $C_8H_2NO_2Cl_2Cl{*}F_{13}S$; found: 529.8646; diff.: 1.2.

$C_8F_{17}SO_2N{=}CHCCl_3$ **4f.** ^{1}H NMR ($CDCl_3$) δ 8.78 (s, N=CH). ^{19}F NMR: δ 3.4 (*t*, CF_3), 33.3 (s, SCF_2), 42.3 (s, CF_2), 44.3 (m, 4 × CF_2), 48.8 (s, CF_2), 49.3 (s, CF_2). IR (film)(ν_{max}, cm^{-1}): 1670 (m), 1450 (s), 1380 (s), 1240–1180 (vs), 1150 (s), 1060 (m), 790 (m). MS (m/e, %): 632/630/628 (M^+ + 5/M^+ + 3/M^+ + 1, 0.41/1.15/1.09), 593 (M^+ + 1 − Cl, 0.42), 500 (M^+ + 3 − $CHCCl_3$, 23.30), 169 ($C_3F_7^+$, 24.40), 131 (M^+ + 1 − $C_8F_{17}SO_2N$, 40.97), 119 ($C_2F_5^+$, 26.10), 117 ($^+CCl_3$, 7.02), 111 (M^+ + 2 − $C_8F_{17}SO_2$ − Cl, 11.52), 83 ($HCCl_2^+$, 14.55), 82 (CCl_2^+, 18.90), 80 (SO_3^+, 100.00), 64 (SO_2^+, 46.50).

$CHCl_2CCl_3$ **5.** ^{1}H NMR δ 6.15 (s, CH).

Preparation of Compound **8**

Dimethyl phosphonite (0.2 g, 2.5 mmol) was added dropwise into a 10 mL flask containing **4a** (1.4 g, 2.5 mmol) with magnetic stirring at room temperature. The reaction was exothermic, and the mixture became viscous. The temperature was then raised to 70°C for 7 hours. After cooling, the crude product was treated by column chromatography (ethyl acetate: petroleum ether = 1:3.5) to give **8a** (1.4 g), yield 86%.

$ICF_2CF_2OCF_2CF_2SO_2NHCH(CCl_3)P(O)(OCH_3)_2$
8a. ^{1}H NMR ($CDCl_3$) δ 7.33 (br, NH), 4.65 (d, CH, $^2J_{H-P}$ = 19.8 Hz), 3.84, 3.96 (s, OCH_3). *^{19}F NMR:* δ −13.3 (*t*, ICF_2), 3.80 (s, OCF_2), 7.5 (s, CF_2O), 37.0 (s, SCF_2). IR (KBr) (ν_{max}, cm^{-1}): 3030 (s), 2840 (m), 2834 (m), 2760 (m), 1476 (s), 1386 (s), 1266 (s), 1148 (vs), 1056 (vs), 1004 (vs), 926 (s), 874 (s), 826 (s), 796 (m), 726 (s). MS (m/e, %): 664/662 (M^+ + 3/M^+ + 1, 0.91/1.00), 626 (M^+ − Cl, 0.5), 544 (M^+ − CCl_3, 41.36), 519/517 (M^+ + 2 − Cl − $P(O)(OCH_3)_2$/M^+ − Cl − $P(O)(OCH_3)_2$, 2.91/4.30), 418 (M^+H − CCl_3 − I, 8.42), 227 ($IC_2F_4^+$, 20.34), 119 ($C_2F_5^+$, 26.15), 117 (CCl_3^+, 1.95), 112 ($C_3F_4^+$, 9.57), 110 (M^+ H − CCl_3 − IR_fSO_2NHCH, 100.00), 109 ($^+P(O)(OCH_3)_2$, 87.58), 79 ($^+HP(O)(OCH_3)_2$, 25.40), 64 (SO_2^+, 1.78). Elemental anal. for $C_8H_8Cl_3F_8INO_6PS$. Required: C, 14.51; H, 1.20; N, 2.11%. Found: C, 14.59; H, 0.85; N, 1.90%.

$ICF_2CF_2OCF_2CF_2SO_2NHCH(CCl_3)P(O)(OEt)_2$
8b. ^{1}H NMR ($CDCl_3$) δ 7.50 (br, NH), 4.60 (d, CH, $^2J_{H-P}$ = 19.8 Hz), 4.40–4.0 (m, 2 × OCH_2), 1.5–1.2 (m, 2 × CH_3). ^{19}F NMR: δ −10.3 (s, ICF_2), 4.0 (*t*, OCF_2), 8.0 (s, CF_2O), 37.0 (s, SCF_2). IR (KBr) (ν_{max}, cm^{-1}): 3436 (br), 3022 (m), 2892 (m), 2830 (m), 2755 (m), 1485 (m), 1386 (s), 1336 (s), 1295 (m), 1205, 1155, 1102 (vs), 1006 (m), 916 (s), 727 (m). MS (m/e, %): 692/690 (M^+ + 3/M^+ + 1, 3.16/3.10), 572 (M^+ − CCl_3, 26.52), 544 (M^+ + 1 − CCl_3 − Et, 12.05), 517 (M^+ − I − OEt, 15.36), 516 (M^+ − 1 − I − OEt, 30.10), 330 (M^+ − IR_f − O, 6.49), 282 ($^+NHCH(CCl_3)P(O)(OEt)_2$, 3.35), 227 ($IC_2F_4^+$, 38.51), 137 ($^+P(O)(OEt)_2$, 85.53), 130 ($^+CHCCl_3$, 2.66), 117 ($^+CCl_3$, 33.02), 109 ($^+P(O)(OEt)(OH)$, 100.00), 92 ($^+P(O)(OEt)$, 6.22). Elemental anal. for $C_{10}H_{12}Cl_3F_8INO_6PS$. Required: C, 17.43; H, 1.75; N, 2.03%. Found: C, 18.11; H, 1.69; N, 2.06%.

$HCF_2CF_2OCF_2CF_2SO_2NHCH(CCl_3)P(O)(OCH_3)_2$
8c. ^{1}H NMR ($CDCl_3$) δ 6.63 (br, NH), 5.85 (*t* − *t*, $^2J_{H-F}$ = 54 Hz, $^3J_{H-F}$ = 3.6 Hz), 4.63 (d, CH, $^2J_{H-P}$ = 19.8 Hz), 3.83, 3.95 (s, OCH_3). ^{19}F NMR δ 3.0 (s, OCF_2), 10.0 (s, CF_2O), 37.0 (s, SCF_2), 59.5 (d, HCF_2, $^2J_{H-F}$ = 54.0 Hz). IR (KBr) (ν_{max}, cm^{-1}): 3030 (s), 2920 (m), 2840 (m), 2790 (m), 1490 (s), 1390 (s), 1270 (s), 1230 (s), 1210 (s), 1150 (s), 1110 (s), 1070 (s), 1050 (s), 930 (s), 810 (s), 730 (m), 620 (m). MS (m/e, %): 540/538/536 (M^+ + 5/M^+ + 3/M^+ + 1, 6.07/17.59/466 (M + − 2 − Cl/M^+ − Cl, 2.72/2.83), 418 (M^+ − CCl_3, 41.36), 17.59), 502/500 (M^+ + CF_3, 1.21), 393/391 (M^+ + 2 − Cl − $P(O)(OCH_3)_2$/M^+ − Cl − $P(O)(OCH_3)_2$, 4.28/6.31), 117 (CCl_3^+, 2.94), 110 (M^+ H − CCl_3 − HR_fSO_2NHCH, 100.00), 109 ($^+P(O)(OCH_3)_2$, 92.28), 101 ($HC_2F_4^+$, 29.07), 95 ($^+P(O)(OCH_3)(OH)$, 7.85), 69 (CF_3^+, 3.33), 64 (SO_2^+,

2.04). Elemental anal. for $C_8H_9Cl_3F_8NO_6PS$. Required: C, 17.90; H, 1.67; N, 2.61%. Found: C, 17.85; H, 1.35; N, 2.32%.

$C_4F_9SO_2NHCH(CCl_3)P(O)(OEt)_2$ **8d.** ^{1}H NMR ($CDCl_3$) δ 7.43 (br, NH), 4.61 (d, CH, $^2J_{H-P}$ = 19.8 Hz), 4.45–4.01 (m, 2 × OCH_2), 1.5–1.2 (m, 2 × CH_3). ^{19}F NMR: δ 3.3 (s, CF_3), 33.3 (*t*, SCF_2), 43.5 (s, CF_2), 48.5 (s, CF_2). IR (KBr) (ν_{max}, cm^{-1}): 3402 (br), 3022 (m), 2961 (m), 2895 (m), 2755 (m), 1485 (m), 1447 (s), 1391 (s), 1354 (s), 1256 (m), 1207, 1147, 1102 (vs), 965 (m), 852 (m), 737 (m). MS (m/e, %): 570/568/566 (M^+ + 5/M^+ + 3/M^+ + 1, 5.37/15.18/15.63), 538 (M^+ + 2 − Et, 2.18), 448 (M^+ − CCl_3, 14.12), 420 (M^+ + 1 − CCl_3 − Et, 9.83), 392 (M^+ − 1 − Cl − $P(O)(OEt)_2$, 30.17), 282 ($^+NHCH(CCl_3)P(O)(OEt)_2$, 1.97), 219 ($C_4F_9^+$, 15.30), 169 ($C_3F_7^+$, 2.69), 137 ($^+P(O)(OEt)_2$, 66.20), 117 ($^+CCl_3$, 35.55), 109 ($^+P(O)(OEt)(OH)$, 100.00), 92 ($^+P(O)(OEt)$, 6.03), 69 (CF_3^+, 45.73). HRMS for $C_{10}H_{13}NO_5Cl_3F_9SP$. Found: 565.9155; diff.: −1.9.

$C_6F_{13}SO_2NHCH(CCl_3)P(O)(OEt)_2$ **8e.** ^{1}H NMR ($CDCl_3$) δ 6.53 (br, NH), 4.64 (d, CH, $^2J_{H-P}$ = 19.8 Hz), 4.48–4.03 (m, 2 × OCH_2), 1.48–1.18 (m, 2 × CH_3). ^{19}F NMR: δ 2.7 (s, CF_3), 32.8 (s, SCF_2), 42.0 (s, CF_2), 42.7 (s, CF_2), 45.7 (s, CF_2), 48.2 (s, CF_2). IR (KBr) (ν_{max}, cm^{-1}): 3398 (br), 3056 (m), 2953 (m), 2904 (m), 2840 (m), 1485 (s), 1447 (s), 1390 (s), 1367 (s), 1255–1107 (vs), 703 (m), 639 (m). MS (m/e, %): 670/668/666 (M^+ + 5/M^+ + 3/M^+ + 1, 9.77/26.90/25.23), 632/630 (M^+ + 2 − Cl/M^+ − Cl, 3.96/5.22), 596 (M^+ − CF_3, 3.46), 548 (M^+ − CCl_3, 6.07), 495/493 (M^+ + 2 − Cl − $P(O)(OEt)_2$/M^+ − Cl − $P(O)(OEt)_2$, 5.33/8.50), 231 (M^+ − 1 − $C_6F_{13}SO_2NH$ − Cl, 9.86), 137 ($^+P(O)(OEt)_2$, 54.72), 119 ($C_2F_5^+$, 47.54), 117 ($^+CCl_3$, 19.92), 109 ($^+(O)(OEt)(OH)$, 100.00), 83 ($HCCl_2^+$, 33.50), 69 (CF_3^+, 69.78). HRMS for $C_{12}H_{13}NO_5Cl_3F_{13}SP$. Found: 664.9069; diff.: 3.8.

Acidic Hydrolysis of **8**

8a (0.5 g, 0.75 mmol) was mixed with hydrochloric acid (10 mL, 36%) at room temperature and then refluxed for 15 hours. After cooling, the mixture was evaporated to dryness and then extracted with ether (3 × 20 mL). The organic layers were combined, and, after removal of the solvent, a dark oil **9a** (0.3 g) remained (yield 65%). A similar procedure was used to prepare compound **9b**.

$ICF_2CF_2OCF_2CF_2SO_2NHCH(CCl_3)P(O)(OH)_2$
9a. ^{19}F NMR (D_2O, CD_3COCD_3): δ − 12.0 (s, ICF_2), 4.0 (s, OCF_2), 8.0 (s, CF_2O), 39.0 (s, SCF_2). IR (film) (ν_{max}, cm^{-1}): 3450 (br), 3274 (br), 1377 (s), 1350 (m), 1310 (s), 1230–1100 (vs), 930 (m), 810 (m), 740 (m). MS (m/e, %): 521/519/517 (M^+ + 4 − $P(O)(OH)_2$ − Cl/M^+ + 2 − $P(O)(OH)_2$ − Cl/M^+ − $P(O)(OH)_2$ − Cl, 10.07/51.56/75.34), 390 (M^+ H − CCl_3 − I, 1.53), 227 ($IC_2F_4^+$, 96.35), 221 (M^+ − IR_fSO_2NH, 3.70), 144 ($^+NCHCCl_3$, 2.47), 117 (CCl_3^+, 1.56), 114/112/110 (M^+ + 4 − $P(O)(OH)_2$ − Cl − IR_fSO_2/M^+ + 2 − $P(O)(OH)_2$ − Cl − IR_fSO_2/M^+ − $P(O)(OH)_2$ − Cl − IR_fSO_2, 16.70/100.00/82.01), 83 ($HCCl_2^+$, 83.19), 81 ($^+P(O)(OH)_2$, 4.93), 80 (SO_3^+, 25.91), 69 (CF_3^+, 15.73), 64 (SO_2^+, 28.68).

$HCF_2CF_2OCF_2CF_2SO_2NHCH(CCl_3)P(O)(OH)_2$
9b. ^{1}H NMR (D_2O, CD_3COCD_3) δ 5.75 (*t* − *t*, $^2J_{H-F}$ = 54 Hz, $^3J_{H-F}$ = 3.6 Hz). ^{19}F NMR δ 4.0 (s, OCF_2), 11.0 (s, CF_2O), 39.0 (s, SCF_2), 60.0 (d, HCF_2, $^2J_{H-F}$ = 54.0 Hz). IR (film) (ν_{max}, cm^{-1}): 3420 (br), 3299 (br), 1400 (s), 1350 (m), 1300 (m), 1220–1120 (vs), 940 (m), 870 (m), 820 (m), 770 (m). MS (m/e, %): 395/393/391 (M^+ + 4 − $P(O)(OH)_2$ − Cl/M^+ + 2 − $P(O)(OH)_2$ − Cl/M^+ − $P(O)(OH)_2$ − Cl, 4.61/23.66/34.10), 357 (M^+H − CCl_3 − 2 × OH, 1.14), 291 (M^+H − HR_f, 1.14), 275 ($^+SO_2CH(CCl_3)P(O)(OH)_2$, 8.66), 211 ($^+CH(CCl_3)P(O)(OH)_2$, 3.04), 119 ($C_2F_5^+$, 83.39), 117 ($CCl_3^+$, 2.47), 114/112/110 ($^+NHCHCCl_2$ + 4/$^+NHCHCCl_2$ + 2/$^+NHCHCCl_2$, 11.3/63.21/95.11), 101 ($HC_2F_4^+$, 100.00), 94 ($^+CHP(O)(OH)_2$, 2.95), 87/85/83 ($^+HCCl_2$ + 4/$^+HCCl_2$ + 2/$^+HCCl_2$, 6.23/35.89/54.39), 81 ($^+P(O)(OH)_2$, 5.86), 64 (SO_2^+, 24.29).

Crystal Structure Analysis

$C_{10}H_{10}Cl_3F_8INO_6PS$: M = 688.48, monoclinic, space group $P2_1/c$, a = 11.679 (4), b = 10.100 (3), c = 19.766 (6) Å, β = 91.39 (3) Å, V = 2330 (1) Å^3, Z = 4, D_c = 1.962 g/cm^3. F (000) = 1328.00. Radiation, Mo − K_α (λ = 0.71069 Å). Crystal dimensions, 0.2 × 0.2 × 0.3 mm. Intensity data were collected at 20°C with a Rigaku AFC 7R diffractometer using graphite-monochromated Mo-K_α radiation (μ = 19.65 cm^{-1}). A total of 2812 independent reflections were measured in the range $18.2 < 2\theta < 21.5°$. The structure was solved via a direct method using a Siemens system. The positions for all H atoms were obtained by theoretical calculations. All positional parameters and anisotropic thermal parameters for non-H atoms were refined by means of a full-matrix least-squares technique. The final R and R_w values were 0.075 and 0.097, respectively, based on 1899 observed reflections [$I > 3.00\ \sigma$ (I)]. All calculations were performed on a MICRO VAXII computer with SHELX86 and ORTEP programs.

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