Efficient Synthesis of N-Protected Trisubstituted Oxazolidines from Ketones, Vinyl Ethers, and Fluoroalkanesulfonyl Azides in Mild Conditions

Ping He,[a] Shizheng Zhu*[a,b]

[a] Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, P. R. China
Fax +86(21)64166128; E-mail: zhusz@mail.sioc.ac.cn

[b] College of Chemical Environment, South China Normal University, Guangzhou 510631, P. R. China

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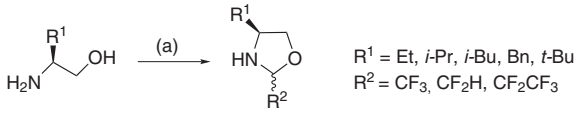
Abstract: A facile one-step method has been developed for the synthesis of 2,3,5-trisubstituted oxazolidines in moderate yields by the three-component reaction of ketones, vinyl ethers, and fluoroalkanesulfonyl azides at 0 °C within five minutes. This practical synthetic method provides a convenient and expeditious access to *N*-per(poly)fluoroalkanesulfonyl oxazolidines.

Key words: fluoroalkanesulfonyl azide, ketone, vinyl ether, oxazolidine, multi-component reactions

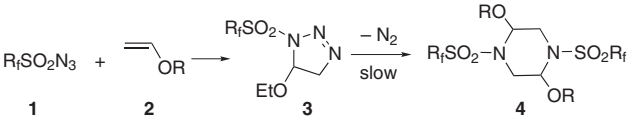
The increasing environmental consciousness of the chemical community has led to the search for more efficient and environmentally friendly methods for chemical syntheses.[1] Among them, multi-component reactions (MCRs), by virtue of their convergent, high productivity and facile execution, as well as the generally high yields of products obtained, have attracted much attention from the vantage point of combinatorial chemistry.[2] Oxazolidines, usually obtained from amino acids, have found widespread use as chiral non-racemic ligands in asymmetric catalysis.[3] Moreover, such oxazolidine derivatives were assumed to have potential as pro-drug forms,[4] as they undergo conversion to the parent compound. Semenov et al.[5] once reported their studies on the reactions of arylsulfonyl azides, vinyl ethers, and carbonyl compounds for the synthesis of oxazolidines but with a low yield. It is well known that the introduction of a fluorine atom can confer unusual chemical reactivity to organic molecules and often exert profound effects on the physical properties of biologically active compounds.[6] Thus, fluorine-containing oxazolidines should be expected to be of particular importance. However, there exist very few methods for the preparation of fluorine-containing oxazolidines.[7] Recently, Gosselin et al.[8] prepared these compounds by heating chiral amino alcohol with the corresponding perfluorinated aldehyde hemiacetal or aldehyde hydrate (Scheme 1).



Scheme 1 *Conditions*: (a) $CF_3CH(OMe)OH$ or $HCF_2CH(OH)Et$, PPTS, $PhCH_3$

During our studies on fluoroalkanesulfonyl azides **1**,[9] we found that it reacts smoothly with ketones and vinyl ethers to afford a series of N-protected oxazolidines in good yields. We were surprised to find that the reaction products were not the normal cycloaddition products 2,3,4-trisubstituted oxazolidines but the unexpected 2,3,5-trisubstituted isomers. This practical synthetic method provides a convenient and expeditious access to *N*-per(poly)fluoroalkanesulfonyl oxazolidines. Herein, we wish to report these results.

Recently, we reported the results of the 1,3-dipolar cycloaddition of **1** with acyclic vinyl ether.[10] Reactions of acyclic vinyl ethers with **1** at 0 °C or room temperature failed to give the corresponding *N*-fluoroalkanesulfonyl aziridines, but gave instead 1-fluoroalkanesulfonyl 1,2,3-triazolines **3** regiospecifically; these decomposed slowly at room temperature to give 1,4-fluoroalkanesulfonyl-2,5-alkoxy-piperazines **4** with elimination of nitrogen gas (Scheme 2).



Scheme 2

Initially we investigated the reaction of fluoroalkanesulfonyl azide **1a** with an equimolar amount of acetone **5a** in an excess of vinyl ether **2a** at 0 °C. Nitrogen gas was released immediately. TLC analysis showed that the azide **1a** disappeared within five minutes and two products were formed, they were separated and purified by column chromatography using petroleum ether–diethyl ether (100:1) as eluent. According to their NMR spectra and TLC analysis, one product obtained in 35% yield was identified as the 1-fluoroalkanesulfonyl 1,2,3-triazolines **3a**. Another major product, obtained in 54% yield, was a five-membered trisubstituted oxazolidine, isolated as a stable colorless oil. According to our previous results,[9] we deduced that the oxazolidine formed should be 2,3,4-trisubstituted, however, we finally found that this was incorrect. It is well documented in the literature that when a substituent was placed on the 5-position of the oxazolidine ring, the

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signal observed in ^{13}C NMR spectrum generally appears at lower field than that in the 4-substituted couterpart.[11] To determine the concrete position of the ethoxy group, the ^{13}C NMR spectrum of the oxazolidine **6** was further investigated. The chemical shift observed at 99.7 ppm in ^{13}C NMR spectrum of **6** indicated that the ethoxy group should be attached to the 5-C of the oxazolidine ring (Figure 1).

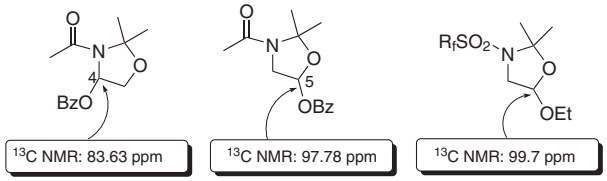


Figure 1 Determination of the ethoxy position in the ring of fluorinated oxazolidine **6**

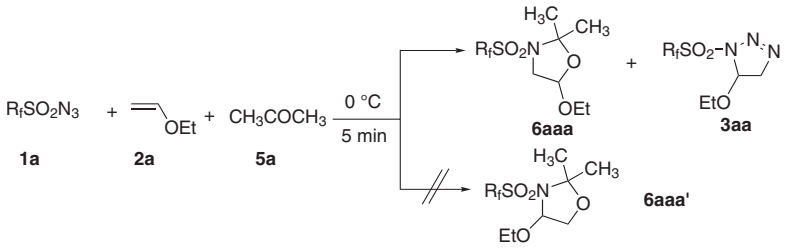
By comparison with results for arylsulfonyl azides, [5] all these data indicated that the product should be characterized as 5-ethoxy-2,2-dimethyl-3-fluoroalkanesulfonyloxazolidine **6aaa**, instead of the 4-ethoxy-2,2-dimethyl-3-fluoroalkanesulfonyloxazolidine **6aaa′**. This conclusion was supported by a further study with *trans*-cinnamaldehyde,[12] in which the major product oxazolidine was elucidated by single crystal X-ray diffraction analysis.[13] When this reaction was carried out in anhydrous diethyl ether or dichloromethane the yield of **6aaa** was improved to 66% and the amount of **3aa** decreased. Furthermore, it was found that the addition of activated MS 4Å could not catalyze this reaction, which indicated that the dehydration process was not involved in the formation of product **6aaa**.

Other azides **1b–d** reacted with vinyl ether **2** and ketone **5** in dichloromethane at 0 °C giving similar results. All these results were summarized in Table 1. The MCRs were found to be general and efficient. All the above reactions proceeded smoothly and were complete within five minutes. During the reaction process, the corresponding 1,2,3-triazolines **3** were obtained, however the yields of **6** varied from 61% to 75%. Varying the substituents on **2** and **5** did not have a great effect on the yields; even the cyclopentanone **5b** (R as a cyclic group) could generate the corresponding oxazolidine **6dbb** in 72% yield (Table 1, entry 16).

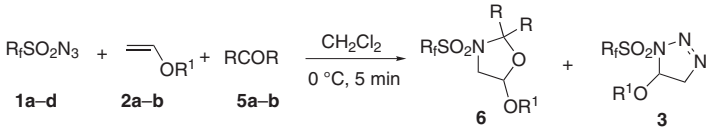
Table 1 Reaction Results of Fluoroalkanesulfonyl Azides, Vinyl Ethers, and Ketones[a]

Entry	Azides	Vinyl ethers	Ketones	Products	Yield (%)[b]	Product	Yield (%)[b]
1	**1a**	**2a**	**5a**	**6aaa**	66	**3aa**	24
2	**1a**	**2b**	**5a**	**6aba**	67	**3ab**	22
3	**1a**	**2a**	**5b**	**6aab**	62	**3aa**	20
4	**1a**	**2b**	**5b**	**6abb**	61	**3ab**	25
5	**1b**	**2a**	**5a**	**6baa**	68	**3ba**	18
6	**1b**	**2b**	**5a**	**6bba**	63	**3bb**	20
7	**1b**	**2a**	**5b**	**6bab**	64	**3bb**	18
8	**1b**	**2b**	**5b**	**6bbb**	64	**3bb**	20
9	**1c**	**2a**	**5a**	**6caa**	63	**3cb**	15
10	**1c**	**2b**	**5a**	**6cba**	75	**3cb**	15
11	**1c**	**2a**	**5b**	**6cab**	67	**3ca**	20
12	**1c**	**2b**	**5b**	**6cbb**	71	**3cb**	18
13	**1d**	**2a**	**5a**	**6daa**	72	**3da**	16
14	**1d**	**2b**	**5a**	**6dba**	66	**3db**	15
15	**1d**	**2a**	**5b**	**6dab**	64	**3da**	20
16	**1d**	**2b**	**5b**	**6dbb**	72	**3db**	17

[a] Reactant ratio: **1/2/5** = 1:1:1.
[b] Isolated yields based on **1**.

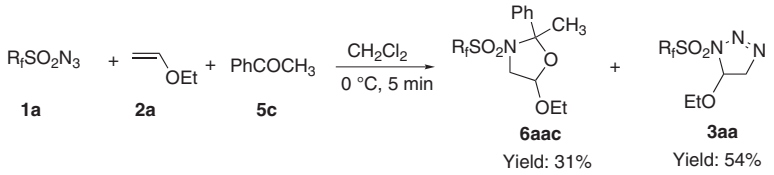


Scheme 3



R_f = $IC_2F_4OC_2F_4$ (**a**), $ClC_2F_4OC_2F_4$ (**b**), $HC_2F_4OC_2F_4$ (**c**), C_4F_9 (**d**)
R^1 = C_2H_5 (**a**), *i*-Bu (**b**)
R = CH_3 (**a**), -$(CH_2)_4$- (**b**)

Scheme 4



Scheme 5

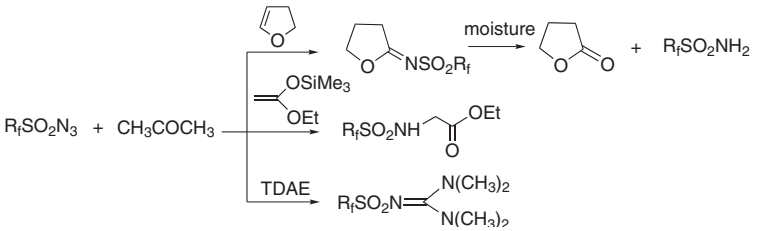
However, in the case of 1-phenylethanone **5c** ($PhCOCH_3$), it was found the yield of **6aac** decreased dramatically to 31% (Scheme 5). An interesting phenomenon was observed that although within five minutes **1a** was not detected in the reaction mixture, $PhCOCH_3$ was not consumed completely and the corresponding yield of triazolidine **3** increased to 54%.

Moreover, in the case of cyclic vinyl ethers such as 2,3-dihydrofuran, the expected 2,3,5-trisubstituted oxazolidine was not isolated, fluoroalkanesulfonylamide $R_fSO_2NH_2$ was obtained in high yield (Scheme 6). We assumed that the 2,3-dihydrofuran reacted easily with azides affording the corresponding sulfonylimines, which were moisture sensitive and were readily hydrolyzed to the corresponding γ-butyrolactone and polyfluoroalkanesulfonyl amine. Futhermore, when electron-rich alkenes such as silyl ketene acetals and tetrakis(dimethylamino)ethylene (TDAE) were employed, the expected fluoroalkanesulfonyl substituted oxazolidines were not obtained, but the corresponding results of the reaction of fluoroalkanesulfonyl azides with electron-rich alkenes, i.e. the third component ketone did not participate in the process.

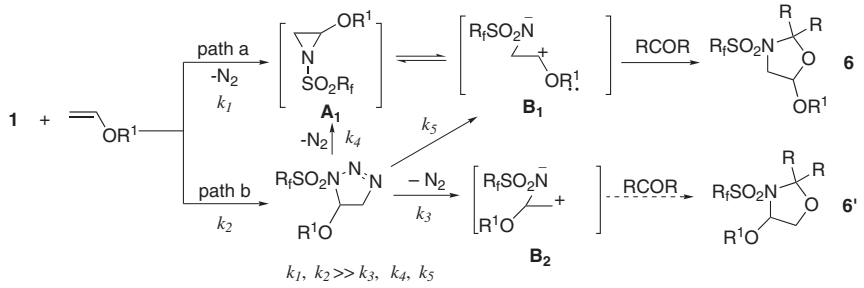
Based on the above results and a similar mechanism reported by Semenov et al.,[5] a possible reaction pathway for the formation of the fluorinated oxazolidines **6** was proposed (Scheme 7). A competing reaction between fluoroalkanesulfonyl azides **1** and vinyl ethers **2** occurred during the initial process. We propose that products **6** should be form through the intermediate $\mathbf{A_1}$ or zwitter ionic $\mathbf{B_1}$ (path a), though a reversible equilibrium process might exist. Due to the relative stability of the competing products triazolines, which could not release N_2 gas immediately under the same conditions, so the correlation of the reaction equilibrium constants during the process is $k_1,k_2 >> k_3,k_4,k_5$. In addition, due to the p-π conjugated action in the structure of $\mathbf{B_1}$, $\mathbf{B_1}$ is one a secondary carbonium, so $\mathbf{B_1}$ is more stable than $\mathbf{B_2}$ (primary carbonium), i.e., the formation of $\mathbf{B_1}$ is easier than the other zwitter ionic $\mathbf{B_2}$.[14] Thus, the isomers in **6′** could not be obtained (path b). To rationalize this proposal, further chemical transformation of triazolines was studied. No reaction was observed when mixing equimolar amounts of triazoline and ketone under the same reaction conditions, which indicated the formation of **6** was not through the competing products triazolines.

In conclusion, we have demonstrated a concise and efficient synthetic protocol for the synthesis of 2,3,5-trisubstituted fluorinated oxazolidines via the one-pot three-component reaction of ketones, vinyl ethers, and fluoroalkanesulfonyl azides under mild conditions. Further ring-opening chemical transformations are under investigation in our group.

Melting points were measured in a Temp-Melt apparatus and were uncorrected. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker AM-300 instruments with Me_4Si and $CFCl_3$ as the internal and external standards, respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Lower resolution mass spectra were obtained on a Finnigen MAT-8430 in-



Scheme 6



Scheme 7

strument using the electron impact ionization technique (70ev). Elemental analyses were performed by this Institute. All reactions as well as column chromatography were monitored routinely with the aid of TLC or ^{19}F NMR spectroscopy. All liquid ketones were distilled prior to use. All solvents were purified before use. The petroleum ether fraction used had a boiling range of 60–90 °C. Fluoroalkanesulfonyl azides **1** were prepared according to the literature.[15]

N-Protected 2,3,5-Trisubstituted Oxazolidines; Typical Procedure

To a 10 mL round-bottom flask containing vinyl ether **2a** (144 mg, 0.19 mL, 2.0 mmol) and ketone **5a** (116 mg, 0.15 mL, 2.0 mmol), in CH_2Cl_2 (2 mL) was added slowly fluoroalkanesulfonyl azides **1a** (898 mg, 2.0 mmol) at 0 °C over 2 min. TLC analysis showed the reaction finished within 5 min. Then the solvent was evaporated under reduced pressure and the residue was chromatographed on a silica column (petroleum ether–Et_2O, 100:1) to give **6aaa** (732 mg, 66%) as colorless oil. The second product fluoroalkanesulfonyl amide **3aa** (250 mg, 24%) was also obtained as colorless oil.

5-Ethoxy-3-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)ethanesulfonyl]-2,2-dimethyloxazolidine (6aaa)
Colorless oil.

IR (KBr): 2984, 1384, 1293, 1200, 1156, 1045, 915 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.21 (dd, *J* = 4.2 Hz, 1.5 Hz, 1 H), 3.83–3.71 (m, 3 H), 3.53–3.45 (m, 1 H), 1.72 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.19 (t, *J* = 6.9 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –65.5 (s, 2 F, ICF_2), –82.4 (d, *J* = 7.3 Hz, 2 F, CF_2O), –86.2 (t, *J* = 6.5 Hz, 2 F, OCF_2), –114.9 (br, 2 F, CF_2S).

MS (EI, 70 eV): *m/z* (%) = 536 (M^+ – Me, 9), 506 (M^+ – EtO, 2), 227 ($IC_2F_4^+$, 9), 177 (ICF_2^+, 7), 129 ($M^+ – R_fSO_2NH$, 100), 70($M^+ – R_fSO_2NHC_3H_6O$, 89), 43 ($C_3H_7^+$, 76). Anal. Calcd for $C_{11}H_{14}F_8INO_5S$: C, 23.96; H, 2.54; N, 2.54. Found: C, 24.14; H, 2.45; N, 2.69.

5-Isobutoxy-3-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)ethanesulfonyl]-2,2-dimethyloxazolidine (6aba)
Colorless oil.

IR (KBr): 2962, 1384, 1293, 1200, 1156, 1032, 915 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.22 (dd, *J* = 3.9 Hz, 1.8 Hz, 1 H), 3.87–3.78 (m, 2 H), 3.53 (dd, *J* = 9.0 Hz, 6.6 Hz, 1 H), 3.20 (dd, *J* = 9.0 Hz, 6.0 Hz, 1 H), 1.92–1.81 (m, 1 H), 1.75 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 0.924 (d, *J* = 6.6 Hz, 3 H, CH_3), 0.917 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –65.2 (d, *J* = 2.2 Hz, 2 F, ICF_2), –82.2 (s, 2 F, CF_2O), –85.9 (d, *J* = 11.6 Hz, 2 F, OCF_2), –114.5 (br, 2 F, CF_2S).

MS (EI, 70 eV): *m/z* (%) = 564 (M^+ – Me, 26), 506 (M^+ – *i*-BuO, 22), 227 ($IC_2F_4^+$, 3), 177 (ICF_2^+, 3), 70 ($M^+ – R_fSO_2NHC_3H_6O$, 73), 57 (*i*-Bu^+, 100), 43 ($C_3H_7^+$, 71).

Anal. Calcd for $C_{13}H_{18}F_8INO_5S$: C, 26.94; H, 3.11; N, 2.42. Found: C, 27.11; H, 3.12; N, 2.62.

2-Ethoxy-4-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)ethanesulfonyl]-1-oxa-4-azaspiro[4.4]nonane (6aab)
Colorless oil.

IR (KBr): 2978, 1395, 1293, 1153, 1095, 915 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.24 (dd, *J* = 4.8 Hz, 2.1 Hz, 1 H), 3.88–3.72 (m, 3 H), 3.51 (dq, *J* = 7.2 Hz, 9.3 Hz, 1 H), 2.39–2.34 (m, 1 H), 2.16 (br, 2 H), 1.85–1.64 (m, 5 H), 1.22 (t, *J* = 7.1 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –65.3 (d, *J* = 5.4 Hz, 2 F, ICF_2), –82.3 (t, *J* = 12.4 Hz, 2 F, CF_2O), –86.0 (m, 2 F, OCF_2), –114.0 (s, 2 F, CF_2S).

MS (EI, 70 eV): *m/z* (%) = 577 (M^+, 11), 548 (M^+ – Et, 53), 532 (M^+ – EtO, 9), 227 ($IC_2F_4^+$, 14), 177 (ICF_2^+, 11), 170 ($M^+ – R_fSO_2$, 48), 141 ($M^+ – R_fSO_2Et$, 63), 96 ($C_6H_8O^+$, 53), 67 ($C_5H_7^+$, 48), 55 ($C_4H_7^+$, 100), 41 ($C_3H_5^+$, 66).

Anal. Calcd for $C_{13}H_{16}F_8INO_5S$: C, 27.04; H, 2.77; N, 2.43. Found: C, 27.22; H, 2.72; N, 2.64.

2-Isobutoxy-4-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)ethanesulfonyl]-1-oxa-4-azaspiro[4.4]nonane (6abb)
Colorless oil.

IR (KBr): 2963,1395, 1293, 1153, 1033, 914 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.22 (dd, *J* = 4.8 Hz, 1.8 Hz, 1 H), 3.90–3.76 (m, 2 H), 3.51 (dd, *J* = 9.0 Hz, 6.6 Hz, 1 H), 3.20 (dd, *J* = 9.0 Hz, 6.0 Hz, 1 H), 2.39–2.35 (m, 1 H), 2.16 (br, 2 H), 1.92–1.70 (m, 6 H), 0.93 (d, *J* = 7.2 Hz, 3 H, CH_3), 0.92 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –65.2 (CF_2, d, *J* = 6.2 Hz), –82.2 (CF_2, d, *J* = 7.3 Hz), –85.9 (CF_2, s), –114.0 (CF_2, s).

MS (EI, 70 eV): *m/z* (%) = 605 (M^+, 10), 576 (M^+ – Et, 16), 532 (M^+ – *i*-BuO, 9), 198 ($M^+ – R_fSO_2$, 15), 142 ($M^+ – R_fSO_2$-*i*-Bu, 24), 96 ($C_6H_8O^+$, 32), 57 (*i*-Bu^+, 100), 41 ($C_3H_5^+$, 48).

Anal. Calcd for $C_{15}H_{20}F_8INO_5S$: C, 29.75; H, 3.31; N, 2.31. Found: C, 29.89; H, 3.25; N, 2.60.

5-Ethoxy-3-[2-(2-chloro-1,1,2,2-tetrafluoroethoxy)-1,1,2,2-tetrafluoroethanesulfonyl]-2,2-dimethyloxazolidine (6baa)
Colorless oil.

IR (KBr): 2984, 1385, 1306, 1174, 1046, 969 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.24 (dd, *J* = 4.2 Hz, 1.5 Hz, 1 H), 3.86–3.75 (m, 3 H), 3.51 (dq, *J* = 7.2 Hz, 9.6 Hz, 1 H), 1.75 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 1.22 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 99.7, 63.1, 54.0, 29.1, 27.9, 14.5.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.2 (s, 2 F, $ClCF_2$,), –82.2 (s, 2 F, CF_2O), –87.2 (t, *J* = 13.4 Hz, 2 F, OCF_2,), –114.7 (br, 2 F, CF_2S).

MS (EI, 70 eV): *m/z* (%) = 446/444 (M^+ – Me, 21/57), 416/414 (M^+ – EtO, 10/27), 129 ($M^+ – R_fSO_2NH$, 84), 70 ($M^+ – R_fSO_2NH$-C_3H_6O, 100), 43 ($C_3H_7^+$, 64).

Anal. Calcd for $C_{11}H_{14}ClF_8NO_5S$: C, 28.73; H, 3.05; N, 3.05. Found: C, 29.03; H, 3.11; N, 3.36.

5-Isobutoxy-3-[2-(2-chloro-1,1,2,2-tetrafluoroethoxy)-1,1,2,2-tetrafluoroethanesulfonyl]-2,2-dimethyloxazolidine (6bba)
Colorless oil.

IR (KBr): 2962, 1385, 1203, 1200, 1174, 1033, 969 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.22 (dd, *J* = 3.9 Hz, 1.8 Hz, 1 H), 3.87–3.79 (m, 2 H), 3.53 (dd, *J* = 9.3 Hz, 6.9 Hz, 1 H), 3.20 (dd, *J* = 9.3 Hz, 6.9 Hz, 1 H), 1.92–1.81 (m, 1 H), 1.75 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 0.924 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.918 (d, *J* = 6.9 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.1 (s, 2 F, $ClCF_2$,), –82.2 (d, *J* = 9.9Hz, 2 F, CF_2O), –87.2 (t, *J* = 13.3Hz, 2 F, OCF_2), –114.5 (br, 2 F, CF_2S).

MS (EI, 70 eV): *m/z* (%) = 474/472 (M^+ – Me, 18/47), 416/414 (M^+ – *i*-BuO, 51/100), 70 ($M^+ – R_fSO_2NHC_3H_6O$, 93), 57 (*i* -Bu^+, 77), 43 ($C_3H_7^+$, 38).

Anal. Calcd for $C_{13}H_{18}ClF_8NO_5S$: C, 32.00; H, 3.69; N, 2.87. Found: C, 32.20; H, 3.95; N, 3.26.

2-Ethoxy-4-[2-(2-chloro-1,1,2,2-tetrafluoroethoxy)-1,1,2,2-tetrafluoroethanesulfonyl]-1-oxa-4-azaspiro[4.4]nonane (6bab)
Colorless oil.

IR (KBr): 2979, 1396, 1305, 1204, 1174, 1047, 970 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.25 (dd, *J* = 5.1 Hz, 1.8 Hz, 1 H), 3.90–3.73 (m, 3 H), 3.52 (dq, *J* = 7.2 Hz, 9.6 Hz, 1 H), 2.39–2.32 (m, 1 H), 2.16 (br, 2 H), 1.86–1.67 (m, 5 H), 1.23 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.1 (s, 2 F, $ClCF_2$), –82.2 (t, *J* = 13 Hz, 2 F, CF_2O), –87.2 (t, *J* = 12.3 Hz, 2 F, OCF_2), –114.1 (s, 2 F, CF_2S).

MS (EI, 70 eV): *m/z* (%) = 487/485 (M^+, 11/27), 458/456 (M^+ – Et, 37/96), 442/440 (M^+ – EtO, 13/35), 170 (M^+ – R_fSO_2, 63), 141 (M^+ – R_fSO_2Et, 99), 96 ($C_6H_8O^+$, 80), 67 ($C_5H_7^+$, 54), 55 ($C_4H_7^+$, 100), 41($C_3H_5^+$, 58).

Anal. Calcd for $C_{13}H_{16}ClF_8NO_5S$: C, 32.13; H, 3.30; N, 2.88. Found: C, 32.45; H, 3.13; N, 3.23.

2-Isobutoxy-4-[2-(2-chloro-1,1,2,2-tetrafluoroethoxy)-1,1,2,2-tetrafluoroethanesulfonyl]-1-oxa-4-azaspiro[4.4]nonane (6bbb)
Colorless oil.

IR (KBr): 2963, 1397, 1205, 1174, 1041, 970 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.22 (dd, *J* = 5.1 Hz, 1.5 Hz, 1 H,), 3.88 (dd, *J* = 10.2 Hz, 5.1 Hz, 1 H), 3.78 (dd, *J* = 10.2 Hz, 6.0 Hz, 1 H), 3.51 (dd, *J* = 9.0 Hz, 6.6 Hz, 1 H), 3.20 (dd, *J* = 9.0 Hz, 6.0 Hz, 1 H), 2.39–2.34 (m, 1 H), 2.16 (br, 2 H), 1.92–1.67 (m, 6 H), 0.93 (d, *J* = 6.9 Hz, 3 H, CH_3), 0.92 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –74.1 (s, 2 F, $ClCF_2$), –82.2 (t, *J* = 12.8 Hz, 2 F, CF_2O), –87.1 (t, *J* = 12.7 Hz, 2 F, OCF_2), –114.2 (s, 2 F, CF_2S).

MS (EI, 70 eV): *m/z* (%) = 515/513 (M^+, 3/8), 486/484 (M^+ – Et, 5/13), 442/440 (M^+ – *i*-BuO, 5/14), 198 (M^+ –R_fSO_2, 11), 142 (M^+ – R_fSO_2-*i*-Bu, 29), 96 ($C_6H_8O^+$, 30), 57 (*i*-Bu^+, 100), 41 ($C_3H_5^+$, 40).

Anal. Calcd for $C_{15}H_{20}ClF_8NO_5S$: C, 35.05; H, 3.89; N, 2.73. Found: C, 35.27; H, 4.07; N, 2.80.

5-Ethoxy-3-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)ethanesulfonyl]-2,2-dimethyloxazolidine (6caa)
Colorless oil.

IR (KBr): 2985, 1384, 1284, 1163, 1046, 1000 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.86 (tt, *J* = 52.5 Hz, 3.0 Hz, 1 H, HCF_2), 5.24 (dd, *J* = 4.5 Hz, 1.8 Hz, 1 H), 3.86–3.75 (m, 3 H), 3.52 (dq, *J* = 7.2 Hz, 9.3 Hz, 1 H), 1.75 (s, 3 H, CH_3), 1.64 (s, 3 H, CH_3), 1.23 (t, *J* = 7.0 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.8 (t, *J* = 11.0 Hz, 2 F, CF_2O), –88.9 (m, 2 F, OCF_2), –114.6 (br, 2 F, CF_2S), –137.8 (dt, *J* = 54 Hz, 5.5 Hz, 2 F, HCF_2).

MS (EI, 70 eV): *m/z* (%) = 410 (M^+ – Me, 100), 380 (M^+ – EtO, 30), 129 (M^+ – R_fSO_2NH, 62), 70 (M^+ – R_fSO_2NH-C_3H_6O, 39).

Anal. Calcd for $C_{11}H_{15}F_8NO_5S$: C, 31.06; H, 3.53; N, 3.29. Found: C, 31.01; H, 3.82; N, 3.35.

5-Isobutoxy-3-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)ethanesulfony]-2,2-dimethyloxazolidine (6cba)
Colorless oil.

IR (KBr): 2963, 1384, 1196, 1162, 1032 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.87 (tt, *J* = 52.2 Hz, 3.0 Hz, 1 H, HCF_2), 5.22 (dd, *J* = 4.5 Hz, 1.8 Hz, 1 H), 3.87–3.78 (m, 2 H), 3.53 (dd, *J* = 9.0 Hz, 6.3 Hz, 1 H), 3.19 (dd, *J* = 9.0 Hz, 6.3 Hz, 1 H), 1.92–1.81 (m, 1 H), 1.75 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 0.923 (d, *J* = 6.6 Hz, 3 H, CH_3), 0.916 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.8 (s, 2 F, CF_2O), –88.9 (s, 2 F, OCF_2), –114.8 (br, 2 F, CF_2S), –137.8 (dt, *J* = 53.6 Hz, 5.0 Hz, HCF_2).

MS (EI, 70 eV): *m/z* (%) = 438 (M^+ – Me, 29), 380 (M^+ – *i*-BuO, 81), 70 (M^+ – $R_fSO_2NHC_3H_6O$, 88), 57 (*i*-Bu^+, 100), 43 ($C_3H_7^+$, 61).

Anal. Calcd for $C_{13}H_{19}F_8NO_5S$: C, 34.44; H, 4.19; N, 3.09. Found: C, 34.77; H, 4.30; N, 3.38.

2-Ethoxy-4-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)ethanesulfonyl]-1-oxa-4-azaspiro[4.4]nonane (6cab)
Colorless oil.

IR (KBr): 2979, 1394, 1284, 1142, 1046 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.87 (tt, *J* = 52.8 Hz, 3.0 Hz, 1 H, HCF_2), 5.25 (dd, *J* = 4.8 Hz, 1.8 Hz, 1 H), 3.90–3.73 (m, 3 H), 3.52 (dq, *J* = 6.6 Hz, 9.6 Hz, 1 H), 2.39–2.32 (m, 1 H), 2.16 (br, 2 H), 1.86–1.64 (m, 5 H), 1.23 (t, *J* = 7.1 Hz, 3 H, CH_3). ^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.8 (t, *J* = 12.1 Hz, 2 F, CF_2O), –88.8 (d, *J* = 8.2 Hz, 2 F, OCF_2), –114.2 (br, 2 F, CF_2S), –137.7 (dt, *J* = 56 Hz, 5.1 Hz, 2 F, HCF_2).

MS (EI, 70 eV): *m/z* (%) = 451 (M^+, 32), 422 (M^+ – Et, 100), 406 (M^+ – EtO, 43), 170 (M^+ – R_fSO_2, 53), 141 (M^+ – R_fSO_2Et, 81), 96 ($C_6H_8O^+$, 70), 67 ($C_5H_7^+$, 46), 55 ($C_4H_7^+$, 85), 41 ($C_3H_5^+$, 50).

Anal. Calcd for $C_{13}H_{17}F_8NO_5S$: C, 34.59; H, 3.77; N, 3.10. Found: C, 34.99; H, 3.80; N, 3.50.

2-Isobutoxy-4-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)ethanesulfonyl]-1-oxa-4-azaspiro[4.4]nonane (6cbb)
Colorless oil.

IR (KBr): 2963, 1395, 1284, 1143, 1034 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.86 (tt, *J* = 52.5 Hz, 3.0 Hz, 1 H, HCF_2), 5.22 (dd, *J* = 4.8 Hz, 1.5 Hz, 1 H), 3.87 (dd, *J* = 10.2 Hz, 5.1 Hz, 1 H), 3.77 (dd, *J* = 10.5 Hz, 1.8 Hz, 1 H), 3.51 (dd, *J* = 9.3 Hz, 6.9 Hz, 1 H), 3.20 (dd, *J* = 9.3 Hz, 6.3 Hz, 1 H), 2.38–2.32 (m, 1 H), 2.15 (br, 2 H), 1.92–1.69 (m, 6 H), 0.926 (d, *J* = 6.6 Hz, 3 H, CH_3), 0.919 (d, *J* = 6.9Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 99.7, 74.6, 54.3, 28.3, 22.6, 22.1, 27.9, 19.1, 18.8.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.8 (t, *J* = 13.1 Hz, 2 F, CF_2O), –88.8 (d, *J* = 9.0 Hz, 2 F, OCF_2), –114.3 (br, 2 F, CF_2S), –137.8 (dt, *J* = 53.9 Hz, 5.1 Hz, HCF_2).

MS (EI, 70 eV): *m/z* (%) = 479 (M^+, 11), 450 (M^+ – Et, 20), 406 (M^+ – *i*-BuO, 18), 198 (M^+ – R_fSO_2, 12), 142 (M^+ –R_fSO_2-*i*-Bu, 31), 96 ($C_6H_8O^+$, 31), 57 (*i*-Bu^+, 100), 41 ($C_3H_5^+$, 43).

Anal. Calcd for $C_{15}H_{21}F_8NO_5S$: C, 37.58; H, 4.38; N, 2.92. Found: C, 37.74; H, 4.64; N, 2.96.

5-Ethoxy-3-(nonafluorobutane-1-sulfonyl)-2,2-dimethyloxazolidine (6daa)
Colorless oil.

IR (KBr): 2985, 1385, 1238, 1140, 1046, 1005 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.25 (dd, *J* = 4.2 Hz, 1.8 Hz, 1 H), 3.87–3.75 (m, 3 H), 3.51 (dq, *J* = 7.2 Hz, 9.6 Hz, 1 H), 1.76 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 1.24 (t, *J* = 6.3 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.3 (m, 3 F, CF_3), –111.3 (br, 2 F, CF_2S), –121.5 (s, 2 F, CF_2), –126.4 (m, 2 F, CF_2).

MS (EI, 70 eV): *m/z* (%) = 412 (M^+ – Me, 91), 382 (M^+ – EtO, 31), 129 (M^+ – R_fSO_2NH, 84), 70 (M^+ – $R_fSO_2NHC_3H_6O$, 100), 43 ($C_3H_7^+$, 60).

Anal. Calcd for $C_{11}H_{14}F_9NO_4S$: C, 30.91; H, 3.28; N, 3.28. Found: C, 30.75; H, 3.59; N, 3.35.

5-Isobutoxy-3-(nonafluorobutane-1-sulfonyl)-2,2-dimethyloxazolidine (6dba)
Colorless oil.

IR (KBr): 2962, 1385, 1238, 1154, 1034 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.22 (dd, *J* = 3.6 Hz, 2.0 Hz, 1 H), 3.86–3.82 (m, 2 H), 3.53 (dd, *J* = 9.0 Hz, 6.9 Hz, 1 H), 3.20 (dd, *J* = 9.0 Hz, 6.3 Hz, 1 H), 1.92–1.81 (m, 1 H), 1.76 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 0.921 (d, *J* = 7.2 Hz, 3 H, CH_3), 0.914 (d, *J* = 6.0 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 99.9, 74.6, 54.1, 28.5, 28.2, 18.9, 18.8.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.2 (t, *J* = 9.6 Hz, 3 F, CF_3), –111.3 (br, 2 F, CF_2S), –121.5 (s, 2 F, CF_2), –126.3 (m, 2 F, CF_2).

MS (EI, 70 eV): *m*/*z* (%) = 440 (M^+ – Me, 28), 382 (M^+ – *i*-BuO, 29), 70 ($M^+ – R_fSO_2NHC_3H_6O$, 57), 57 (*i*-Bu^+, 100), 43 ($C_3H_7^+$, 47).

Anal. Calcd for $C_{13}H_{18}F_9NO_4S$: C, 34.29; H, 3.96; N, 3.08. Found: C, 34.51; H, 3.94; N, 3.21.

2-Ethoxy-4-(nonafluorobutane-1-sulfonyl)-1-oxa-4-aza-spiro[4.4]nonane (6dab)
Colorless oil.

IR (KBr): 2979, 1397, 1239, 1195, 1142, 1046 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.25 (dd, *J* = 5.1 Hz, 1.5 Hz, 1 H), 3.92–3.74 (m, 3 H), 3.53 (dq, *J* = 7.2 Hz, 9.6 Hz, 1 H), 2.40–2.32 (m, 1 H), 2.17 (br, 2 H), 1.87–1.65 (m, 5 H), 1.23 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.1 (m, 3 F, CF_3), –110.6 (br, 2 F, CF_2S), –121.5 (s, 2 F, CF_2), –126.2 (m, 2 F, CF_2).

MS (EI, 70 eV): *m*/*z* (%) = 453 (M^+, 35), 424 (M^+ – Et, 100), 408 (M^+ – EtO, 58), 170 ($M^+ – R_fSO_2$, 58), 141 ($M^+ – R_fSO_2Et$, 86), 96 ($C_6H_8O^+$, 77), 67 ($C_5H_7^+$, 51), 55 ($C_4H_7^+$, 85), 41 ($C_3H_5^+$, 55).

Anal. Calcd for $C_{13}H_{16}F_9NO_4S$: C, 34.44; H, 3.53; N, 3.09. Found: C, 34.51; H, 3.52; N, 3.21.

2-Isobutoxy-4-(nonafluorobutane-1-sulfonyl)-1-oxa-4-aza-spiro[4.4]nonane (6dbb)
Colorless oil.

IR (KBr): 2963, 1397, 1238, 1142, 1034 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.22 (dd, *J* = 4.5 Hz, 1.5 Hz, 1 H), 3.90–3.78 (m, 2 H), 3.51 (dd, *J* = 9.0 Hz, 6.9 Hz, 1 H), 3.21 (dd, *J* = 9.0 Hz, 6.0 Hz, 1 H), 2.39–2.32 (m, 1 H), 2.16 (br, 2 H), 1.94–1.68 (m, 6 H), 0.926 (d, *J* = 6.6 Hz, 3 H, CH_3), 0.919 (d, *J* = 6.6 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –81.1 (m, 3 F, CF_3), –110.9 (br, 2 F, CF_2S), –121.4 (s, 2 F, CF_2), –126.2 (m, 2 F, CF_2).

MS (EI, 70 eV): *m*/*z* (%) = 481 (M^+, 16), 452 (M^+ – Et, 21), 408 (M^+ – *i*-BuO, 43), 198 ($M^+ – R_fSO_2$, 15), 142 ($M^+ – R_fSO_2$-*i*-Bu, 29), 96 ($C_6H_8O^+$, 36), 57 (*i*-Bu^+, 100), 41 ($C_3H_5^+$, 45).

Anal. Calcd for $C_{15}H_{20}F_9NO_4S$: C, 37.42; H, 4.16; N, 2.91. Found: C, 37.30; H, 4.16; N, 3.17.

5-Ethoxy-3-[1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)ethanesulfonyl]-2-methyl-2-phenyloxazolidine (6aac)
Colorless oil.

IR (KBr): 2980, 1398, 1292, 1151, 915 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.59–7.33 (m, 5 H, ArH), 5.36 (t, *J* = 4.8 Hz, 1 H), 4.13 (dd, *J* = 5.7 Hz, 11.4 Hz, 1 H), 3.71 (t, *J* = 7.2 Hz, 1 H), 3.56–3.45 (m, 2 H), 1.99 (s, 3 H, CH_3), 1.01 (t, *J* = 7.2 Hz, 3 H, CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –65.2 (t, *J* = 5.6 Hz, 2 F, ICF_2), –82.1 (d, *J* = 13.0 Hz, 2 F, CF_2O), –85.8 (m, 2 F, OCF_2), –113.5 (m, 2 F, CF_2S).

MS (EI, 70 eV): *m*/*z* (%) = 598 (M^+ – CH_3, 22), 536 (M^+ – Ph, 32), 227 ($IC_2F_4^+$, 8), 177 (ICF_2^+, 6), 191 ($M^+ – R_fSO_2CH_3$, 30), 91 ($C_7H_7^+$, 100).

Anal. Calcd for $C_{16}H_{16}F_8INO_5S$: C, 31.32; H, 2.61; N, 2.28. Found: C, 31.65; H, 2.70; N, 2.32.

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