Pergamon

Tetrahedron 57 (2001) 669–674

TETRAHEDRON

A new route to fluorine-containing aziridines and α-amino esters

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Received 22 August 2000; revised 13 October 2000; accepted 2 November 2000

Abstract—The reaction of fluoroalkanesulfonyl azides with several silyl ketene acetals has been investigated. 1-Ethoxyl-1-trimethylsilyloxy-ethylene reacted readily with azides to afford *N*-fluoroalkanesulfonyl substituted glycinates in good yields. However, reaction of mono- or dialkyl-substituted silyl ketene acetals with azides gave rise to *N*-substituted α-amino esters and substituted *N*-perfluoroalkanesulfonyl aziridines. Acidic hydrolysis of the aziridines was also investigated. Mechanisms for the formation of the aziridines and α-amino esters are discussed.

1. Introduction

Using enolsilanes such as silyl enol ethers and silyl ketene acetals as enolates towards electrophilies has often been exploited in organic synthesis.[1] For instance, the Mukaiyama aldol reaction is one of the most powerful tools for the construction of new C–C bonds.[2] The development of efficient approaches to the synthesis of non-proteinogenic amino acids remains a topic of considerable interest.[3] In this field, some methods to effect the direct electrophilic amination of silyl ketene acetals were introduced by several research groups.[4] Recently, Tordella et al. studied the amination of silyl ketene acetals by thermolysis (110°C) or photolysis with ethyl azidoformate, which provided a variety of *N*-ethoxylcarbonyl α-amino esters.[5]

In recent years we reported the direct amination by per(poly)fluoroalkanesulfonyl azides of enol silyl ethers and enamines to produce *N*-substituted α-amino ketones and *N*-substituted amidines respectively.[6,7] The interest in these fluorine-containing compounds, precursors of biologically and pharmacologically active molecules, encouraged us to develop an introduction of the amino group to silyl ketene acetals. Furthermore, the lack of studies in the reaction of silyl ketene acetals with azides urged us to investigate the reaction of per(poly)fluoroalkanesulfonyl azides with silyl ketene acetals.

2. Results and discussion

In our previous work on the reaction of fluoroalkanesulfonyl azides with cyclohexene, it was found that the reaction occurred to give aziridines after 4 h at 90°C.[8] The silyl ketene acetal **1a** (1-ethoxyl-1-trimethylsilyloxy-ethylene) reacted with fluoroalkanesulfonyl azides **2** smoothly in acetonitrile at 0°C, the nitrogen evolved immediately and nearly quantitatively after stirring for 1 h. This reaction solely provided products **4**, which could be readily isolated by column chromatography or recrystallization, and were easily identified by analytical and spectral data as the *N*-substituted α-amino esters (ethyl glycinates).

However, the reactions of dialkyl substituted silyl ketene acetal **1c** and **1d** with azides **2** gave rise to two products. They could be separated by column chromatography. The first was identified as the *N*-perfluoroalkanesulfonyl aziridines **3**, and the second as the *N*-substituted α-amino esters **4**.

It was noticed that the reaction of monosubstituted silyl ketene acetal **1b** with azide **2** afforded both *N*-substituted aziridines and *N*-substituted α-amino esters in poor yields. For example, when **1b** was treated with **2b**, **3bb** was obtained in 25% yield and **4bb** in 5% yield. The low yield was attributed to the instability of the monoalkyl substituted *N*-fluoroalkanesulfonyl aziridines **3bb** and **3bc**, which decomposed to fluoroalkanesulfonyl amides quickly during chromatography on silica gel. In the reaction of **1b** with **2b** or **2c**, the fluoroalkanesulfonyl amides $R_fSO_2NH_2$ were obtained as by-products in 36 and 41% yield, respectively. Moreover, chromatography using neutral alumina gave complete decomposition of product **3**. Considering the instability of this kind of aziridines during chromatography, vacuum distillation was tried to purify the crude product. For example, the yield of **3bc** was increased to 35%. All the results are summarized in (Table 1, Scheme 1).

The reactions of silyl ketene acetals with perfluoroalkanesulfonyl azides occurred readily in many solvents. For example, the reaction of **1c** with **2c**, in solvents such as

Keywords: α-amino esters; aziridines; fluoroalkanesulfonyl azides; silyl ketene acetals.

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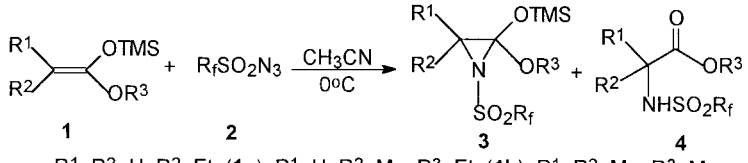
0040–4020/01/$ - see front matter
PII: S0040-4020(00)01050-4

Table 1. The reaction results of silyl ketene acetal **1** with **2**

Entry	Silyl ketene acetal **1**	Azides **2**	Reaction time (min)	Product **3** yield (%)	Product **4** yield (%)
1	**1a**	**2a**	30	–	**4aa** 51
2	**1a**	**2b**	30	–	**4ab** 80
3	**1a**	**2c**	30	–	**4ac** 94
4[a]	**1b**	**2b**	30	**3bb** 25	**4bb** 5
5[b]	**1b**	**2c**	30	**3bc** 20	**4bc** 4
6	**1c**	**2a**	60	**3ca** 45	**4ca** 16
7	**1c**	**2b**	60	**3cb** 48	**4cb** 17
8	**1c**	**2c**	60	**3cc** 47	**4cc** 29
9	**1d**	**2a**	30	**3da** 17	**4da** 45
10	**1d**	**2b**	30	**3db** 31	**4db** 44
11	**1d**	**2c**	30	**3dc** 44	**4dc** 52

[a] $C_4F_9SO_2NH_2$ was isolated in 36% yield.
[b] $IC_2F_4OC_2F_4SO_2NH_2$ was isolated in 41% yield.

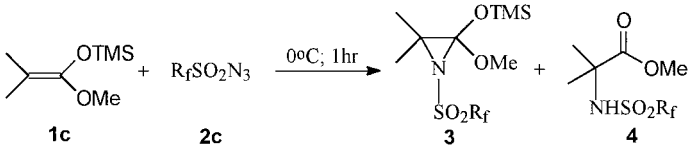


Scheme 1.

hexane, diethyl ether, anhydrous and moist acetonitrile was investigated. However, similar results were obtained and no significant solvent effect was observed. It is noteworthy that the use of moist acetonitrile did not change the distribution of products (Scheme 2, Table 2).

In the reactions of silyl ketene acetals with azides **2**, the triazoline **6** should be formed first by the 1,3-dipolar cycloaddation reaction.[9] The reaction should not involve a fluoroalkanesulfonyl nitrene intermediate, because the conversion of fluoroalkanesulfonyl azides into nitrenes requires thermolysis (≥100°C) or photolysis.[10] As the triazoline intermediate is the product of electronic control, the nitrogen atom bearing the sulfonyl group should be directed to the carbon of the olefinic bond bearing the oxygens.[11] Loss of nitrogen from the triazoline intermediate **6** may occur by two possible mechanisms, as illustrated in Scheme 3. Elmination of nitrogen from the triazoline adduct could give rise to aziridines, which possibly could undergo ring-opening to afford *N*-substituted α-amino esters (path A).[12] Alternatively, the triazoline adduct may fragment by loss of nitrogen with concomitant rearrangement of the sulfonyl amide to yield intermediate **9**, which produces α-amino esters **4** (path B). At the present time, we presume that the two possible pathways proceed simultaneously. At first, the isolation of aziridines **3** assures the existence of Path A. However, as mentioned above, when the reaction is carried out in moist acetonitrile, it did not alter the ratio of the α-amino esters and aziridines (see Table 2). From this observation, it could be concluded that the formation of α-amino esters does not exclusively proceed through the decomposition of aziridine **3**.

It is well known that activated aziridines undergo a ring-



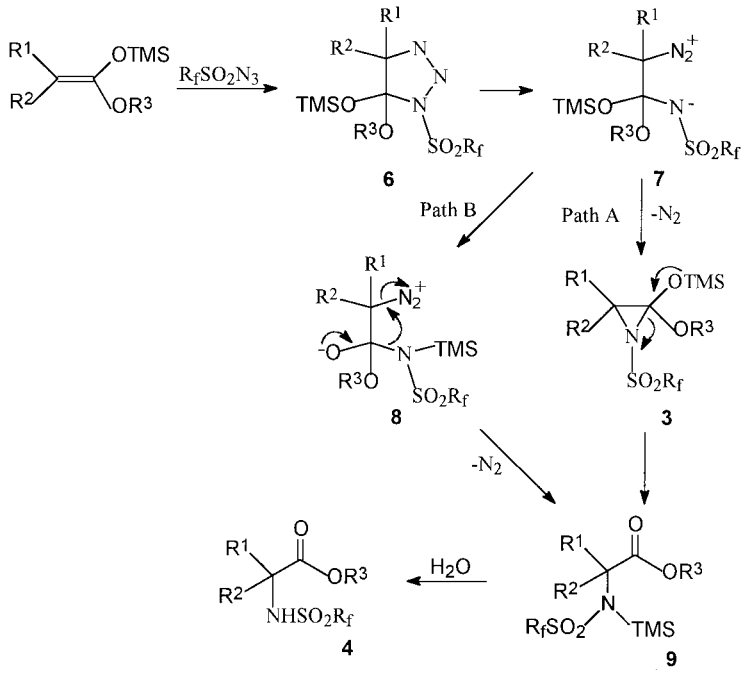
Scheme 2.

Table 2. The solvent effect on the reaction of silyl ketene acetal **1c** with azide **2c**

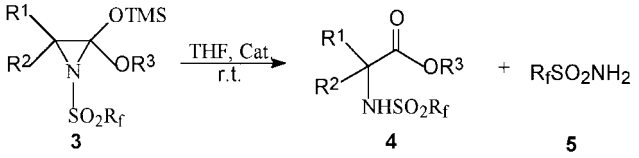
Entry	Solvent	Product **3** yield (%)	Product **4** yield (%)
1	Hexane	45	30
2	Diethyl ether	39	26
3	Acetonitrile	47	29
4[a]	Acetonitrile(moist)	46	29

[a] 1.5 equiv. of silyl ketene acetal was used.

opening reaction in the presence of an acid catalyst, especially *N*-sulfonyl substituted aziridines.[13] The hydrolysis of substituted aziridines **3** under acidic conditions was studied and some different results were observed. In the case of mono- or dimethyl substituted aziridines, the only isolated products were fluoroalkanesulfonyl amides **5**. However, the acidic hydrolysis of cyclohexane substituted aziridines produced two products, α-amino esters **4** and amides **5**. Unfortunately, the Bu_4NF induced ring-opening reaction offered complications (Scheme 4, Table 3).



Scheme 3.



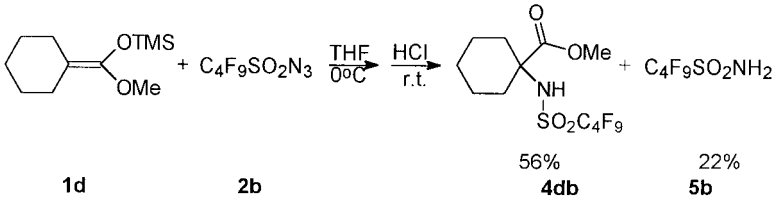
Scheme 4.

Table 3. Hydrolysis of aziridines **3**

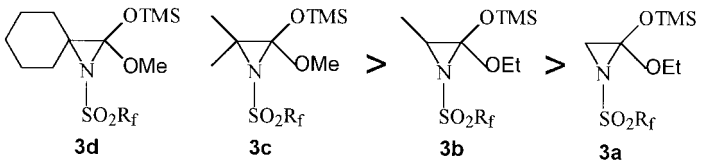
Entry	Aziridine	Catalyst	Time (h)	Product **4** (%)	Product **5** (%)
1	**3cc**	HCl (6N)	3	–	95
2	**3cc**	HCl (1N)	20	–	91
3	**3cc**	CH_3CO_2H	72	–	90
4	**3cc**	SiO_2	8	–	94
5	**3bb**	HCl (6N)	1	–	87
6	**3db**	HCl (6N)	2	67	27

As aziridine **3db** can be hydrolyzed to α-amino ester **4db** in moderate yield (67%), the one-pot hydrolysis directly from the reaction of silyl ketene acetal with azide was tried. After stirring of the mixture of silyl ketene acetal **1d** and azide **2b** in tetrahydrofuran at 0°C for 30 min, the temperature was raised to rt and catalytic hydrochloric acid was added. The expected α-amino ester **4db** was obtained in 56% yield, which was better than in the case of non-hydrolysis (44%) (see Scheme 5).

Open-chain and cyclic α,α-disubstituted glycines are an important class of non-proteinogenic amino acids and the focus of many investigations, such as those on α-amino isobutyric acid (Aib) and 1-aminocycloalkane-1-carboxylic acid (Ac_nc), etc.[14] They play an important role in the design of conformationally restricted peptides.[15] Although many synthetic methods are available for the preparation of these α,α-disubstituted α-amino acids, they have some



Scheme 5.



Scheme 6.

limitations.[16] It is obvious that the reaction of silyl ketene acetal with azides provides an alternative method for the preparation of α,α-disubstituted α-amino acid derivatives.

Comparing the stability of aziridines **3bb**, **3cb** and **3db**, it was quite evident that the more substituted aziridines had a greater stability. In fact, aziridine **3a** which had no alkyl substituent was too unstable to exist, and **3b** was unstable during the process of chromatography using silica gel. Aziridines **3c** and **3d**, which have dialkyl substituents, were more stable and could be purified by chromatography using silica gel (Scheme 6).

3. Conclusions

In conclusion, we have developed a novel and facile method for the synthesis of *N*-fluoroalkanesulfonyl substituted α-amino esters and highly functionalized *N*-fluoroalkanesulfonyl substituted aziridines from the reaction of silyl ketene acetals with fluoroalkanesulfonyl azides, which could be utilized in a variety of ways such as nucleophile induced ring-opening etc. Further investigation of these highly functionalized aziridines is being pursued. Moreover, cyclic α-amino esters were synthesized directly from the silyl ketene acetal, which provided an extremely attractive method for the preparation of conformationally constrained cyclic α-amino acid derivatives.

4. Experimental

Mps were measured in Temp-Melt apparatus. ^{1}H NMR and ^{19}F NMR spectra were recorded on Varian-360 L or Bruker AM-300 instruments with Me_4Si and $CFCl_3$ (with upfield negative) as internal and external standards, respectively. NMR spectra were recorded in chloroform-d unless otherwise stated. IR spectra were obtained with an Perkin Elmer 983 G spectrophotometer using KBr disks of the compounds. Low mass spectra was obtained with HP 5989a instrument. Elemental analyzes 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. Ether, THF and hexane were dried over sodium wire, and acetonitrile was distilled from CaH_2. Reagents were purified before use. Silyl ketene acetals were prepared by the method of Ainsworth.[17] Per(poly)fluoroalkanesulfonyl azides were prepared as previous described.[18]

4.1. General method for the reaction of silyl ketene acetal 1 with azides 2

To a solution of perfluorobutanesulfonyl azides **2b** (0.573 g, 1.763 mmol) and acetonitrile 5 mL, was added **1c** (0.282 g, 1.763 mmol) dropwise with stirring under a nitrogen atmosphere at 0°C. The resulting mixture was stirred at 0°C until the starting reagents had disappeared (about 60 min, monitored by TLC). After removal of the excess solvent, the residue was chromatographed on a silica gel column. Elution with light petroleum ether (bp 60–90°C)–ethyl acetate (10:1) gave aziridine **3cb** (0.395 g, 0.846 mmol, 48%), and elution with light petroleum ether (bp 60–90°C)–ethyl acetate (5:1) gave α-amino ester **4cb** (0.116 g, 0.291 mmol, 17%).

4.2. General procedure for the hydrolysis of aziridine 3

Concentrated hydrochloric acid (0.05 mL) was added to a solution of **3db** (45 mg, 0.088 mmol) in moist THF (3 mL) at room temperature. After the reaction was complete, water (5 mL) was added. The reaction mixture was extracted with ether (10 mL×3). The organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent, the residue was chromatographed with light petroleum ether (bp 60–90°C)–ethyl acetate (5:1) on silica gel to give **4db** in 67% yield.

4.2.1. Ethyl *N*-trifluoromethanesulfonyl glycinate (4aa). Colorless crystals, mp 93–4°C (lit.[19] 93–4°C). ν_{max} (KBr)/cm^{-1} 3242 s, 2993 w, 1730 vs, 1459 m, 1376 s, 1232–1117 vs. $\delta_H(CDCl_3)$: 5.98 (1H, s, NH), 4.18 (2H, q, J=7.2 Hz, CH_2CH_3), 3.95 (2H, d, J=4.4 Hz, CH_2), 1.32 (3H, t, J=7.2 Hz, CH_2CH_3). $\delta_F(CDCl_3)$: −76.5 (CF_3, s); m/z 236 (M^++1, 28.28), 162 (M^+-CO_2Et, 100.00), 133 ($CF_3SO_2^+$, 10.67), 69 (CF_3^+, 58.37). (Found: C, 25.61; H, 3.52; N, 6.16%. Calcd for $C_5H_8F_3NO_4S$ C, 25.53; H, 3.40; N, 5.96%).

4.2.2. Ethyl *N*-perfluorobutanesulfonyl glycinate (4ab). Colorless crystals, mp 56–7°C. ν_{max} (KBr)/cm^{-1} 3222 s, 2985 w, 1738 vs, 1465 m, 1387 s, 1254 vs, 1180 m, 1135 m. $\delta_H(CDCl_3)$: 6.10 (1H, s, NH), 4.29 (2H, q, J=7.2 Hz, CH_2CH_3), 4.09 (2H, d, J=4.4 Hz, CH_2), 1.32 (3H, t, J=7.2 Hz, CH_2CH_3). $\delta_F(CDCl_3)$: −79.9 (CF_3, s), −111.9 (CF_3CF_2, m), −120.6 ($C_2F_5CF_2$, m), −125.3 (SO_2CF_2, m); m/z 386 (M^++1, 14.29), 312 (M^+-CO_2Et, 100.00), 219 ($C_4F_9^+$, 32.80), 69 (CF_3^+, 45.16). (Found: C, 24.94; H, 2.18; N, 3.73%. Calcd for $C_8H_8F_9NO_4S$ C, 24.94; H, 2.08; N, 3.64%).

4.2.3. Ethyl *N*-1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)-ethanesulfonyl glycinate (4ac). Colorless liquid. ν_{max} (KBr)/cm^{-1} 3258 s, 2989 m, 1737 s, 1440 m, 1337 m, 1220–1090 vs. $\delta_H(CDCl_3)$: 6.10 (1H, s, NH), 4.29 (2H, q, J=7.2 Hz, CH_2CH_3), 4.09 (2H, d, J=4.4 Hz, CH_2), 1.32 (3H, t, J=7.2 Hz, CH_2CH_3). $\delta_F(CDCl_3)$: −63.8 (ICF_2, s), −81.1 (ICF_2CF_2, t, J=17 Hz), −84.8 (OCF_2, t, J=17 Hz), −115.8 (SO_2CF_2, s); m/z 510 (M^++1, 43.09), 436 (M^+-CO_2Et, 100.00), 227 ($C_2F_4I^+$, 29.55), 177 (CF_2I^+, 13.27). (Found: C, 19.12; H, 1.80; N, 2.92%. Calcd for $C_8H_8F_8INO_5S$ C, 18.86; H, 1.57; N, 2.75%).

4.2.4. 1-Perfluorobutanesulfonyl-2-ethoxyl-2-trimethylsilyloxy-3-methyl-aziridine (3bb). Colorless liquid. ν_{max} (KBr)/cm^{-1} 2958 m, 1617 m, 1448 m, 1376 m, 1231 vs. $\delta_H(CDCl_3)$: 4.87 (1H, q, J=6.6 Hz, CH), 4.33 (2H, q, J=7.1 Hz, CH_2CH_3), 1.51 (3H, d, J=6.6 Hz, CH_3), 1.39 (2H, t, J=7.1 Hz, CH_2CH_3), 0.16 (9H, s, $3CH_3$). $\delta_F(CDCl_3)$: −79.4 (CF_3, s), −112.4 (CF_3CF_2, m), −119.6 ($C_2F_5CF_2$, m), −124.8 (SO_2CF_2, m); m/z 456 (M^+-CH_3, 1.87), 428 (M^++2−OEt, 23.98), 400 (M^++2−TMS, 36.38), 219 ($C_4F_9^+$, 26.95), 149 (M^+-R_f–TMS–C_2H_6, 100.00), 73 (TMS^+, 62.02). (Found: C, 30.94; H, 3.93; N, 3.20%. Calcd for $C_{12}H_{18}F_9NO_4SSi$ C, 30.57; H, 3.82; N, 2.97%).

4.2.5. Ethyl *N*-perfluorobutaneanesulfonyl alaninate (4bb). White solid, mp 55–6°C. ν_{max} (KBr)/cm^{-1} 3246 s, 2989 m, 1726 s, 1448 m, 1385 m, 1240–1145 vs. δ_H($CDCl_3$): 6.02 (1H, d, J=8.36 Hz, NH), 4.30 (3H, m, CH, CH_2CH_3), 1.55 (3H, d, J=7.1 Hz, CH_3CH), 1.27 (3H, t, J=7.1 Hz, CH_2CH_3). δ_F($CDCl_3$): −79.3 (CF_3, s), −111.3 (CF_3CF_2, m), −120.8 ($C_2F_5CF_2$, m), −124.7 (SO_2CF_2, m); *m/z* 400 (M^++1, 28.68), 326 (M^+-CO_2Et, 100.00), 219 ($C_4F_9^+$, 7.37), 69 (CF_3^+, 13.55). (Found: C, 27.44; H, 2.56; N, 3.61%. Calcd for $C_9H_{10}F_9NO_4S$ C, 27.07; H, 2.51; N, 3.51%).

4.2.6. 1-(1,1,2,2-Tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)-ethanesulfonyl)-2-ethoxyl-2-trimethylsilyloxy-3-methyl-aziridine (3bc). Colorless liquid. ν_{max} (KBr)/cm^{-1} 2958 w, 1617 m, 1449 m, 1364 m, 1229 vs, 1190–1096 vs. δ_H($CDCl_3$): 4.92 (1H, q, J=6.6 Hz, CH), 4.35 (2H, q, J=7.1 Hz, CH_2CH_3), 1.51 (3H, d, J=6.6 Hz, CH_3CH), 1.39 (3H, t, J=7.1 Hz, CH_2CH_3), 0.16 (9H, s, $3CH_3$). δ_F($CDCl_3$): −63.6 (ICF_2, s), −79.8 (ICF_2CF_2, t, J=17 Hz), −84.2 (OCF_2, t, J=17 Hz), −116.1 (SO_2CF_2, s); *m/z* 580 (M^+-CH_3, 21.86), 552 (M^++2−OEt, 90.97), 524 (M^++2−OTMS, 100.00), 227 ($C_2F_4I^+$, 34.63), 117 (M^++2−TMS, 84.38), 73 (TMS^+, 53.25). (Found: C, 24.56; H, 3.02; N, 2.50%. Calcd for $C_{12}H_{18}F_8NIO_5SSi$ C, 24.20; H, 3.03; N, 2.35%).

4.2.7. Ethyl *N*-1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)-ethanesulfonyl alainate (4bc). Colorless liquid. ν_{max} (KBr)/cm^{-1} 3254 m, 2988 m, 1730 s, 1448 m, 1385 m, 1230 vs, 1148 s. δ_H($CDCl_3$): 5.89 (1H, d, J=8.40 Hz, NH), 4.35 (3H, m, CH, CH_2CH_3), 1.55 (3H, d, J=7.1 Hz, CH_3CH), 1.30 (3H, t, J=7.1 Hz, CH_2CH_3). δ_F($CDCl_3$): −63.8 (ICF_2, s), −80.3 (ICF_2CF_2, t, J=17 Hz), −84.3 (OCF_2, t, J=17 Hz), −116.4 (SO_2CF_2, s); *m/z* 524 (M^++1, 18.97), 450 (M^+−TMS, 100.00), 227 ($IC_2F_4^+$, 11.91), 177 (ICF_2^+, 6.09). (Found: C, 20.82; H, 2.05; N, 2.65%. Calcd for $C_9H_{10}F_8INO_5S$ C, 20.65; H, 1.91; N, 2.68%).

4.2.8. 1-Trifluoromethanesulfonyl-2-methoxyl-2-trimethylsilyloxy-3,3-dimethyl-aziridine (3ca). Colorless solid. mp 60–1°C. ν_{max} (KBr)/cm^{-1} 2962 m, 1616 s, 1471 m, 1448 m, 1363 s, 1257–1179 vs. δ_H($CDCl_3$): 3.82 (3H, s, OCH_3), 1.61 (6H, s, $2CH_3$), 0.30 (9H, s, $3CH_3$). δ_F($CDCl_3$): −79.6 (CF_3, s); *m/z* 307 (M^++1−CH_3, 12.58), 306 (M^+− CH_3, 67.78), 89 ($OTMS^+$, 72.85), 73 (TMS^+, 100.00). (Found: C, 33.91; H, 5.78; N, 4.31%. Calcd for $C_9H_{18}F_3NO_4SSi$ C, 33.64; H, 5.61; N, 4.36%).

4.2.9. Methyl 2-methyl-*N*-trifluoromethaneanesulfonyl alaninate (4ca). Colorless solid, mp 38–9°C. ν_{max} (KBr)/cm^{-1} 3208 s, 2939 s, 1722 vs, 1455 m, 1433 m, 1369 s, 1294 s, 1220–1094 vs. δ_H($CDCl_3$): 5.87 (1H, s, NH), 3.83 (3H, s, OCH_3), 1.69 (6H, s, $2CH_3$). δ_F($CDCl_3$): −77.3 (CF_3, s); *m/z* 234 (M^+−Me, 1.86), 190 (M^+-CO_2Me, 100.00), 133 ($CF_3SO_2^+$, 1.84), 69 (CF_3^+, 19.18). (Found: C, 29.03; H, 3.98; N, 5.43%. Calcd for $C_6H_{10}F_3NO_4S$ C, 28.92; H, 4.02; N, 5.62%).

4.2.10. 1-Perfluorobutanesulfonyl-2-methoxyl-2-trimethylsilyloxy-3,3-dimethyl-aziridine (3cb). Colorless liquid. ν_{max} (KBr)/cm^{-1} 2959 m, 1623 s, 1467 s, 1374 s, 1216–1160 vs. δ_H($CDCl_3$): 3.87 (3H, s, OCH_3), 1.58 (6H, s, $2CH_3$), 0.27 (9H, s, $3CH_3$). δ_F($CDCl_3$): −79.5 (CF_3, s), −112.4 (CF_3CF_2, m), −119.5 ($C_2F_5CF_2$, m), −124.9 (SO_2CF_2, m); *m/z* 472 (M^++1, 5.72), 456 (M^+-CH_3, 100.00), 131 ($C_5H_{13}O_2Si$, 57.17), 89 ($OTMS^+$, 39.34), 73 (TMS^+, 68.42). (Found: C, 30.75; H, 3.84; N, 3.08%. Calcd for $C_{12}H_{18}F_9NO_4SSi$ C, 30.57; H, 3.82; N, 2.97%).

4.2.11. Methyl 2-methyl-*N*-perfluorobutaneanesulfonyl alaninate (4cb). Colorless solid, mp 56–7°C. ν_{max} (KBr)/cm^{-1} 3230 s, 2962 m, 1722 vs., 1449 m, 1369 s, 1265–1195 vs. δ_H($CDCl_3$): 5.98 (1H, s, NH), 3.83 (3H, s, OCH_3), 1.67 (6H, s, $2CH_3$). δ_F($CDCl_3$): −79.7 (CF_3, s), −111.1 (CF_3CF_2, m), −120.1 ($C_2F_5CF_2$, m), −125.0 (SO_2CF_2, m); *m/z* 400 (M^++1, 0.59), 384 (M^+-CH_3, 1.36), 340 (M^+-CO_2Me, 100.00), 219 ($C_4F_9^+$, 5.16), 101 ($M^+-R_fSO_2NH$, 3.06), 69 (CF_3^+, 20.81). (Found: C, 27.19; H, 2.43; N, 3.38%. Calcd For $C_9H_{10}F_9NO_4S$ C, 27.07; H, 2.51; N,3.51%).

4.2.12. 1-(1,1,2,2-Tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)-ethanesulfonyl)-2-methoxyl-2-trimethylsilyloxy-3,3-dimethyl-aziridine (3cc). Colorless liquid. ν_{max} (KBr)/cm^{-1} 2958 s, 1623 s, 1467 s, 1444 m, 1362 s, 1295 s, 1240–1080 vs. δ_H($CDCl_3$): 3.80 (3H, s, OCH_3), 1.60 (6H, s, $2CH_3$), 0.28 (9H, s, $3CH_3$). δ_F($CDCl_3$): −63.8 (ICF_2, s), −80.0 (ICF_2CF_2, t, J=17 Hz), −84.8 (OCF_2, t, J=17 Hz), −116.4 (SO_2CF_2, s); *m/z* 596 (M^++1, 9.85), 580 (M^+-CH_3, 100.00), 252 (M^+-R_f, 4.74), 236 (M^+-OR_f, 6.96), 131 ($C_5H_{13}O_2Si$, 47.67), 73 (TMS^+, 33.58). (Found: C, 24.30; H, 3.12; N, 2.33%. Calcd for $C_{12}H_{18}F_8INO_5SSi$ C, 24.20; H, 3.03; N, 2.35%).

4.2.13. Methyl 2-methyl-*N*-1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)-ethanesulfonyl alaninate (4cc). Colorless liquid. ν_{max} (KBr)/cm^{-1} 3263 s, 2958 w, 1730 s, 1440 m, 1230–1100 vs. δ_H($CDCl_3$): 6.13 (1H, s, NH), 4.04 (3H, s, OCH_3), 1.86 (6H, s, $2CH_3$). δ_F($CDCl_3$): −63.4 (ICF_2, s), −80.8 (ICF_2CF_2, t, J=17 Hz), −84.9 (OCF_2, t, J=17 Hz), −117.2 (SO_2CF_2, s); *m/z* 524 (M^++1, 4.54), 464 (M^+-CO_2Me, 100.00), 101 ($M^+-R_fSO_2NH$, 5.19). (Found: C, 20.70; H, 2.00; N, 2.55%. Calcd for $C_9H_{10}F_8INO_5S$ C, 20.65; H, 1.91; N, 2.68%).

4.2.14. 1-Trifluoromethanesulfonyl-2-methoxyl-2-trimethylsilyloxy-1-azaspiro[2,5]octane (3da). Colorless liquid. ν_{max} (KBr)/cm^{-1} 2938 m, 1616 s, 1449 m, 1322 s, 1227 vs, 1199 vs. δ_H($CDCl_3$): 3.96 (3H, s, OCH_3), 2.03–1.86 (4H, m, CH_2, CH_2), 1.70–1.50 (6H, m, C_3H_6), 0.24 (9H, s, $3CH_3$). δ_F($CDCl_3$): −79.3 (CF_3, s); *m/z* 362 (M^++1, 0.79), 346 (M^+-CH_3, 39.45), 171 (M^+-OR_f–OTMS–CH_4, 100.00), 89 ($OTMS^+$, 28.15), 73 (TMS^+, 55.32), 69 (CF_3^+, 12.10). (Found: C, 40.10; H, 6.17; N, 3.83%. Calcd for $C_{12}H_{22}F_3NO_4SSi$ C, 39.89; H, 6.09; N, 3.88%).

4.2.15. Methyl 1-*N*-(trifluoromethanesulfonyl)-amino cyclohexanecarboxylate (4da). Colorless solid, mp 117–8°C. ν_{max} (KBr)/cm^{-1} 3194 s, 2957 m, 1716 s, 1458 m, 1440 m, 1371 s, 1288 vs, 1196 vs. δ_H($CDCl_3$): 5.17 (1H, s, NH), 3.81 (3H, s, OCH_3), 2.03–1.93 (4H, m, CH_2, CH_2), 1.66–1.59 (6H, m, C_3H_6). δ_F($CDCl_3$): −77.1 (CF_3, s); *m/z* 290 (M^++1, 4.39), 230 (M^+-CO_2Me, 100.00), 141 ($M^+-CF_3SO_2NH$, 16.50), 81 ($C_6H_9^+$, 81.59), 69 (CF_3^+,

18.76). (Found: C, 37.38; H, 4.83; N, 4.83%. Calcd for $C_9H_{14}F_3NO_4S$ C, 37.37; H, 4.84; N, 4.84%).

4.2.16. 1-Perfluorobutanesulfonyl-2-methoxyl-2-trimethylsilyloxy-1-azaspiro[2,5]octane (3db). Colorless liquid. ν_{max} (KBr)/cm^{-1} 2938 m, 1608 s, 1449 m, 1372 m, 1239–1142 vs. $\delta_H(CDCl_3)$: 3.94 (3H, s, OCH_3), 2.15–1.85 (4H, m, CH_2, CH_2), 1.68–1.55 (6H, m, C_3H_6), 0.25 (9H, s, $3CH_3$). $\delta_F(CDCl_3)$: −79.8 (CF_3, s), −112.4 (CF_3CF_2, m), −119.8 ($C_2F_5CF_2$, m), −125.3 (SO_2CF_2, m); *m/z* 512 (M^++1, 0.76), 496 (M^+-CH_3, 51.54), 187 (M^+-OR_f–OTMS, 29.70), 171 (M^+-OR_f–OTMS–CH_4, 100.00), 89 ($OTMS^+$, 35.11), 73 (TMS^+, 60.79).(Found: C, 35.57; H, 4.32; N, 2.77%. Calcd for $C_{15}H_{22}F_9NO_4SSi$ C, 35.23; H, 4.31; N, 2.74%).

4.2.17. Methyl 1-*N*-(perfluorobutanesulfonyl)-amino cyclohexanecarboxylate (4db). Colorless solid, mp 75–6°C. ν_{max} (KBr)/cm^{-1} 3222 m, 2950 m, 1716 s, 1456 m, 1373 m, 1288 s, 1237–1146 vs. $\delta_H(CDCl_3)$: 5.30 (1H, s, NH), 3.80 (3H, s, OCH_3), 2.05–1.90 (4H, m, CH_2, CH_2), 1.65–1.55 (6H, m, C_3H_6). $\delta_F(CDCl_3)$: −79.0 (CF_3, s), −111.2 (CF_3CF_2, m), −119.6 ($C_2F_5CF_2$, m), −124.6 (SO_2CF_2, m); *m/z* 440 (M^++1, 0.45), 380 ($M^+-CO_2CH_3$, 100.00), 81 ($C_6H_9^+$, 20.69), 69 (CF_3^+, 20.81). (Found: C, 32.63; H, 3.19; N, 3.26%. Calcd for $C_{12}H_{14}F_9NO_4S$ C, 32.80; H, 3.19; N,3.19%).

4.2.18. 1-(1,1,2,2-Tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)-ethanesulfonyl)-2-methoxyl-2-trimethylsilyloxy-1-azaspiro[2,5]octane (3dc). Colorless liquid. ν_{max} (KBr)/cm^{-1} 2938 m, 1608 s, 1499 m, 1333 m, 1220–1094 vs. $\delta_H(CDCl_3)$: 3.93 (3H, s, OCH_3), 2.06–1.83 (4H, m, CH_2, CH_2), 1.73–1.43 (6H, m, C_3H_6), 0.23 (9H, s, $3CH_3$). $\delta_F(CDCl_3)$: −63.7 (ICF_2, s), −80.0 (ICF_2CF_2, t, J=17 Hz), −84.8 (OCF_2, t, J=17 Hz), −116.1 (SO_2CF_2, s); *m/z* 636 (M^++1, 4.28), 620 (M^+-CH_3, 73.95), 276 (M^+-OR_f, 7.76), 228 ($M^+-SO_2R_f$, 4.58), 187 (M^+-OR_f–OTMS, 25.19), 171 (M^+-OR_f–OTMS–CH_4, 100.00),. (Found: C, 28.34; H, 3.42; N, 2.25%. Calcd for $C_{15}H_{22}F_8INO_5SSi$ C, 28.35; H, 3.46; N, 2.20%).

4.2.19. Methyl 1-*N*-(1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoro-2-iodoethoxy)-ethanesulfonyl)-amino cyclohexanecarboxylate (4dc). Colorless solid, mp 70–1°C. ν_{max} (KBr)/cm^{-1} 3208 s, 2954 m, 1716 s, 1437 m, 1336 s, 1285–1080 vs. $\delta_H(CDCl_3)$: 5.44 (1H, s, NH), 3.79 (3H, s, OCH_3), 1.99 (4H, m, CH_2, CH_2), 1.62 (6H, m, C_3H_6). $\delta_F(CDCl_3)$: −63.4 (ICF_2, s), −80.1 (ICF_2CF_2, t, J=17 Hz), −84.2 (OCF_2, t, J=17 Hz), −115.1 (SO_2CF_2, s); *m/z* 564 (M^++1, 0.66), 504 (M^+-CO_2Me, 100.00), 436 (M^+-I, 2.75), 141 ($M^+-R_fSO_2NH$, 6.98), 81 ($C_6H_9^+$, 17.02), 227 ($C_2F_4I^+$, 2.94). (Found: C, 25.78; H, 2.41; N, 2.46%. Calcd for $C_{12}H_{14}F_8INO_5S$ C, 25.58; H, 2.49; N, 2.49%).

Acknowledgements

The authors thank the National Natural Science Foundation of China (NNSFC) (No. 2972051) and Innovation Found of Chinese Academy of Sciences for financial support.

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