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The addition of perfluoroalkanesulfinyl chlorides to alkoxyallenes

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ABSTRACT

The addition reaction of perfluoroalkanesulfinyl chlorides to alkoxyallenes was achieved under mild conditions. Two kinds of perfluoroalkyl alkenyl sulfoxides, β-alkoxyvinyl perfluoroalkyl sulfoxides and α-perfluoroalkanesulfinyl enones or enals, were obtained selectively depending on the structure of alkoxyallenes.

1. Introduction

Alkenyl sulfoxides are valuable intermediates for the construction of many biologically active molecules, particularly by virtue of their reactivity as dienophiles for Diels–Alder reactions, acceptors for Michael additions, and excellent partners in Pauson–Khand reactions [1–6]. Although the synthesis and reaction of alkenyl sulfoxides have been well studied, their fluorine-containing analogues are seldom reported [7]. Due to the strong electron-withdrawing effect of perfluoroalkyl group, it is reasonable to believe that the reactivity of perfluoroalkyl alkenyl sulfoxides can be enhanced by the introduction of perfluoroalkyl moiety [8]. Recently, Wakselman and coworkers reported the synthesis of some fluoroalkyl vinyl sulfoxides by the elimination of HCl from β-substituted perfluoroalkyl sulfoxides, and compared their activities with phenyl vinyl sulfoxides in Diels–Alder reaction [7,9].

During our continuous study on the reaction of perfluoroalkanesulfinyl chlorides (**1**) [10], it was found that perfluoroalkyl alkenyl sulfoxides could be easily prepared by the addition reaction of **1** and alkoxyallenes (**2**), and two kinds of perfluoroalkyl alkenyl sulfoxides, β-alkoxyvinyl perfluoroalkyl sulfoxides (**3**) and α-perfluoroalkanesulfinyl enones or enals (**4**), were obtained with different alkoxyallenes (Fig. 1). The results are reported in this paper.

2. Results and discussion

The investigation started with the addition reaction of the simplest alkoxyallene, methoxyallene (**2a**), with perfluoroalkanesulfinyl chlorides. Treatment of **2a** with 2-chlorotetrafluoroethanesulfinyl chloride (**1a**) in dichloromethane gave the desired product β-alkoxyvinyl sulfoxide (**3a**) in only 10% yield. To improve the yield of **3a**, various conditions were screened and the best result was obtained when the reaction was performed at 0 °C to room temperature without any solvents. Using the same conditions other alkoxyallenes and perfluoroalkanesulfinyl chlorides were examined. As shown in Table 1, changing the perfluoroalkyl group or alkyl group had little influence on the yield of the corresponding products.

It is noteworthy that only one isomer of **3** was formed in each addition reaction on the basis of carefully studying the ^{1}H NMR spectra of crude products. The configuration of **3** was further assigned as trans for R_FSO and alkoxy group by the NOE experiment of **3a**. The NOE effect was observed between proton H_a of CH_2Cl group and H_b of methoxy group (Fig. 2).

Under similar conditions, we next studied the reaction of **1a** and alkoxyallenes with alkyl substituent at α-position. To our surprise, no expected β-alkoxyvinyl sulfoxides (**3**) but α-(2-chlorotetrafluoroethanesulfinyl) enones (**4**) were obtained. The results are summarized in Table 2. With γ-substituted alkoxyallene **2h**, the reaction gave the corresponding α-(2-chlorotetrafluoroethanesulfinyl) enal **4d** in good yield.

When phenoxyallene (**2i**) was used, no addition reaction occurred (Table 1, entry 6). Similarly, alkyl substituted allenes, such as undeca-1,2-diene and nona-1,2-diene, did not react with **1**

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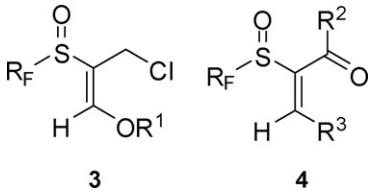
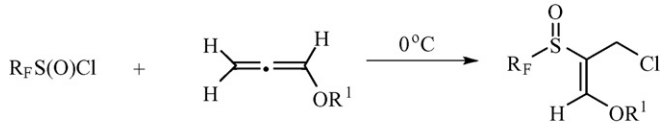


3 **4**

Fig. 1. β-Alkoxyvinyl perfluoroalkyl sulfoxides (**3**) and α-perfluoroalkanesulfinyl enones or enals (**4**).

Table 1
The reaction of perfluoroalkanesulfinyl chlorides with alkoxyallenes.



1 **2** **3**

Entry	1	R_F	2	R^1	Product	Isolated yield (%)
1	**1a**	ClC_2F_4	**2a**	Me	**3a**	47
2	**1a**	ClC_2F_4	**2b**	Et	**3b**	61
3	**1a**	ClC_2F_4	**2c**	Bn	**3c**	77
4	**1b**	n-C_4F_9	**2b**	Et	**3d**	78
5	**1c**	n-C_6F_{13}	**2b**	Et	**3e**	68
6	**1a**	ClC_2F_4	**2i**	Ph	–	NR

either. As a comparison, the reaction of *tert*-butanesulfinyl chloride with methoxyallene under similar conditions was tried, but it was very complicated and no desired product was obtained.

In all reactions, the addition took place at β-carbon of allenes selectively. On the basis of the above results, a possible mechanism was proposed for this addition reaction as shown in Scheme 1. The reaction of **2** and perfluoroalkanesulfinyl chlorides gives intermediate **B**, which undergoes further transformations to give the final product through path 1 or path 2 depending on the structure of **2**. In the case of unsubstituted alkoxyallenes (R^2=R^3=H), the reaction gives the usual addition products **3** through path 1, while α-sulfinyl enones or enals **4** are formed through path 2 when substituted alkoxyallenes are used, probably due to both steric and conjugation effects. Alkoxy group is essential to this reaction and it might act as an electron-donor to make **2** form intermediate A. This can be further proved by the fact that alkyl allenes and phenoxyallene do not react with **1**. In the latter case the conjugation between the lone electron pair of oxygen and aromatic ring weakens the electron-donor ability of oxygen.

In summary, the reaction of perfluoroalkanesulfinyl chlorides with alkoxyallenes was achieved under mild conditions with good regio- and stereoselectivity, providing a novel method for the preparation of multi-functional perfluoroalkyl alkenyl sulfoxides.

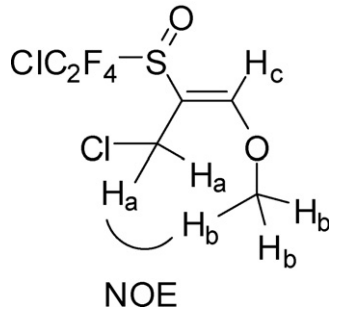
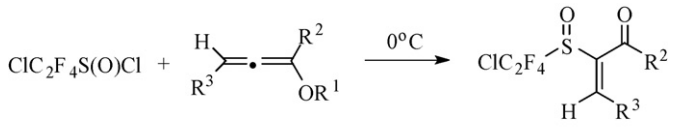


Fig. 2. ^{1}H-^{1}H NOESY of **3a**.

Table 2
The reaction of perfluoroalkanesulfinyl chlorides with substituted alkoxyallenes.



1a **2** **4**

Entry	2	R^1	R^2	R^3	Product	Isolated yield (%)
1	**2e**	Me	n-Pr	H	**4a**	67
2	**2f**	Me	n-Bu	H	**4b**	76
3	**2g**	Et	$Ph(CH_2)_3$	H	**4c**	65
4	**2h**	Et	H	$Me_2C(OEt)$	**4d**	82

3. Experimental

3.1. General

Melting points were uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker AM-300 spectrometer (300 MHz) with TMS as internal standard. ^{19}F NMR spectra were taken on a Bruker AM-300 (282 MHz) spectrometer using $CFCl_3$ as external standard. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Mass spectra and high-resolution mass spectra (HRMS) were obtained on a Finnigan GC-MS 4021 and a Finnigan MAT-8430 spectrometer, respectively. Alkoxyallenes **2a**–**2i** were prepared *via* base induced isomerization of alkynyl ether using the Brandsma's procedure [11–13].

3.2. Typical experiment procedure for the preparation of perfluoroalkyl alkenyl sulfoxides

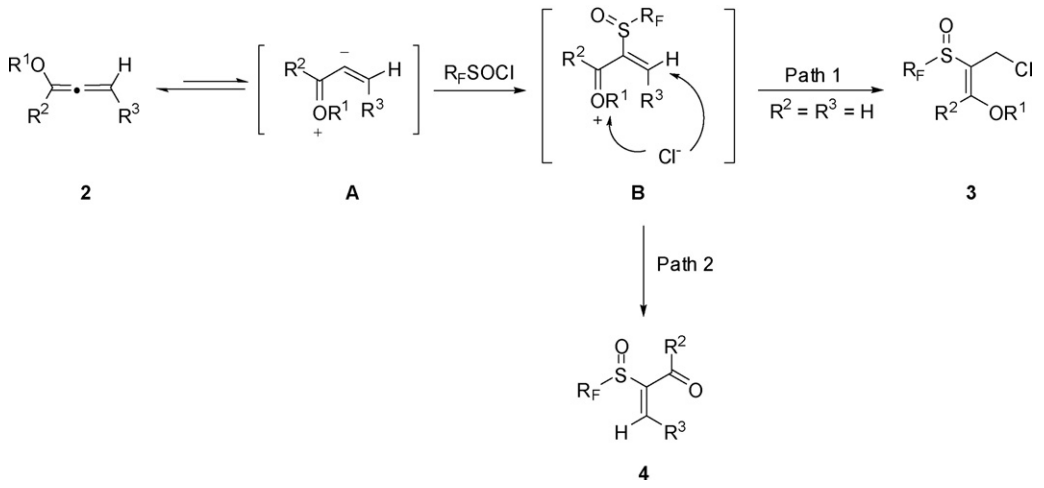
Under stirring, **1a** (0.5 mmol) was added dropwise to **2a** (1 mmol) at 0 °C. After addition, the mixture was warmed to room temperature over 2 h, and then stirred at room temperature for 1 h (monitored by TLC). After completion of the reaction, the mixture was concentrated to remove volatile compounds. The residue was purified by column chromatography on silica gel (ethyl acetate: hexane = 1:10) to give **3a**.

3.2.1. (E)-3-Chloro-2-(2-chlorotetrafluoroethanesulfinyl)-1-methoxyprop-1-ene (3a)

White solid, m.p.: 34–35 °C. IR (KBr): ν 2953, 1635, 1160, 1121, 1018 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.05 (s, 1H), 4.42, 4.30 (AB, J_{AB} = 12.9 Hz, 2H), 4.05 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −67.52 (m, 2F); −108.53, −122.06 (AB, J_{AB} = 230.1 Hz, 2F). ESI-MS *m*/*z*: 289 $[M+1]^+$. Anal. Calcd for $C_6H_6Cl_2F_4O_2S$: C, 24.93; H, 2.09. Found: C, 25.28; H, 2.07.

3.2.2. (E)-3-Chloro-2-(2-chlorotetrafluoroethanesulfinyl)-1-ethoxyprop-1-ene (3b)

Oil. IR (neat): ν 2985, 1631, 1167, 1122, 1017 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.13 (s, 1H), 4.43, 4.32 (AB, J_{AB} = 12.3 Hz, 2H), 4.27 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −67.10 (m, 2F), −108.21, −121.48 (AB, J_{AB} = 229.7 Hz, 2F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.28, 112.38, 72.68, 32.33, 15.29. EI-MS *m*/*z*: 303 $[M+1]^+$, 167 $[M-ClC_2F_4]^+$. HRMS Calcd for $C_7H_8Cl_2F_4O_2S$ $[M]^+$: 301.9612. Found: 301.9558.



Scheme 1. Proposed mechanism for the addition reaction.

*3.2.3. (E)-3-Chloro-2-(2-chlorotetrafluoroethanesulfinyl)-1-benzyloxy-1-ene (**3c**)*

Oil. IR (neat): ν 3036, 1633, 1184, 1119, 800, 737, 698 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.43–7.34 (m, 5H), 7.18 (s, 1H), 5.22, 5.19 (AB, J_{AB} = 12.6 Hz, 2H), 4.44, 4.34 (AB, J_{AB} = 12.6 Hz, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −69.98 (m, 2F), −108.15, −121.02 (AB, J_{AB} = 231.3 Hz, 2F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.84, 134.53, 129.28, 129.08, 127.76, 113.27, 77.64, 32.23. ESI-MS *m/z*: 365 $[M+1]^+$. HRMS Calcd for $C_{12}H_{10}Cl_2F_4O_2S$ $[M+1]^+$: 364.9799. Found: 364.9787.

*3.2.4. (E)-3-Chloro-2-perfluorobutanesulfinyl-1-ethoxyprop-1-ene (**3d**)*

Oil. IR (neat): ν 2987, 1632, 1240, 1207, 1149 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.14 (s, 1H), 4.43, 4.30 (AB, J_{AB} = 12.6 Hz, 2H), 4.28 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −81.26 (m, 3F), −109.95, −123.15 (AB, J_{AB} = 245.2 Hz, 2F), −121.31, −122.67 (AB, J_{AB} = 301.3 Hz, 2F), −126.43 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.72, 112.10, 72.75, 32.13, 15.17. ESI-MS *m/z*: 387.0 $[M+1]^+$. HRMS Calcd for $C_9H_8ClF_9O_2S$ $[M+1]^+$: 386.9877. Found: 386.9863.

*3.2.5. (E)-3-Chloro-2-perfluorohexylsulfinyl-1-ethoxyprop-1-ene (**3e**)*

Oil. IR (neat): ν 2985, 1632, 1236, 1140, 1089 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.13 (s, 1H), 4.37, 4.30 (AB, J_{AB} = 12.6 Hz, 2H), 4.28 (q, J = 6.9 Hz, 2H), 1.43 (t, J = 6.9 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −81.22 (m, 3F), −109.75, −122.80 (AB, J_{AB} = 249.7 Hz, 2F), −120.25, −121.80 (AB, J_{AB} = 305.4 Hz, 2F), −122.84 (m, 2F), −123.33 (m, 2F), −126.59 (m, 2F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.58, 112.16, 72.73, 32.22, 15.21. ESI-MS *m/z*: 486.9 $[M+1]^+$, 509.0 $[M+Na]^+$. HRMS Calcd for $C_{11}H_8ClF_{13}O_2S$ $[M+1]^+$: 486.9809. Found: 486.9769.

*3.2.6. 2-(2-Chlorotetrafluoroethanesulfinyl)-hex-1-en-3-one (**4a**)*

Oil. IR (neat): ν 2966, 1712, 1625, 1179, 1122 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.03 (d, J = 2.1 Hz, 1H), 6.93 (d, J = 2.1 Hz, 1H), 2.80 (td, J_1 = 7.2 Hz, J_2 = 3.0 Hz, 2H), 1.75–1.68 (m, 2H), 0.98 (t, J = 7.2 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −68.30 (m, 2F), −107.69, −121.325 (AB, J_{AB} = 219.3 Hz, 2F). EI-MS *m/z*: 281 $[M+1]^+$, 145 $[M-C_2F_4Cl]^+$. Anal. Calcd for $C_8H_9ClF_4O_2S$: C, 34.23; H, 3.23. Found: C, 34.03; H, 3.72.

*3.2.7. 2-(2-Chlorotetrafluoroethanesulfinyl)-hept-1-en-3-one (**4b**)*

Oil. IR (neat): ν 2964, 1712, 1625, 1164, 1121 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.26 (d, J = 2.1 Hz, 1H), 6.93 (d, J = 2.1 Hz, 1H), 2.82 (td, J_1 = 7.5 Hz, J_2 = 3.0 Hz, 2H), 1.69–1.64 (m, 2H), 1.41–1.34 (m, 2H), 0.98 (t, J = 7.5 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −68.37 (m, 2F), −107.73, −121.40 (AB, J_{AB} = 225.7 Hz, 2F). ESI-MS *m/z*: 316.7 $[M+Na]^+$, 348.8 $[M+MeOH+Na]^+$. Anal. Calcd for $C_9H_{11}ClF_4O_2S$: C, 36.68; H, 3.76. Found: C, 37.08; H, 3.98.

*3.2.8. 2-(2-Chlorotetrafluoroethanesulfinyl)-6-phenylhex-1-en-3-one (**4c**)*

Oil. IR (neat): ν 2936, 1719, 1686, 1180, 1122 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.16 (m, 5H), 6.91, 6.89 (AB, J = 2.4 Hz, 2H), 2.82–2.78 (m, 2H), 2.68 (t, J = 7.5 Hz, 2H), 1.69–1.64 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −68.26 to −68.28 (m, 2F), −107.58, −121.32 (AB, J = 221.4 Hz, 2F). ESI-MS *m/z*: 378.9 $[M+Na]^+$, 410.8 $[M+MeOH+Na]^+$. Anal. Calcd for $C_{14}H_{13}ClF_4O_2S$: C, 47.13; H, 3.67; Found: C, 47.18; H, 3.96.

*3.2.9. 2-(2-Chlorotetrafluoroethanesulfinyl)-4-ethoxy-4-methylpent-2-enal (**4d**)*

Oil. IR (neat): ν 2982, 1676, 1623, 1181, 1122, 1070 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 10.68 (s, 1H), 7.17 (s, 1H), 3.54 (qd, J_1 = 6.9 Hz, J_2 = 2.1 Hz, 2H), 1.55 (s, 6H), 1.21 (t, J = 6.9 Hz, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −67.98 (m, 2F), −107.98, −122.61 (AB, J_{AB} = 223.4 Hz, 2F). ESI-MS *m/z*: 325.0 $[M+1]^+$, 357.0 $[M+1+MeOH]^+$. Anal. Calcd for $C_{10}H_{13}ClF_4O_3S$: C, 36.99; H, 4.04; Found: C, 37.28; H, 4.22.

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