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A convenient one-pot synthesis of per-(or poly-)fluoroalkanesulfonyl substituted cyclopropanes

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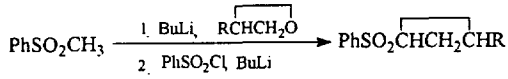
Abstract

Per-(or poly-)fluoroalkanesulfonyl substituted cyclopropanes are prepared by a facile one-pot reaction of methyl per-(or poly-)fluoroalkanesulfones with 1,2-dibromoethane under basic reaction conditions. Similarly treatment of benzyl per-(or poly-)fluoroalkanesulfones gave 1-phenyl-1-per-(or poly-)fluoroalkanesulfonyl cyclopropanes and *trans*-1,2-diphenylethene as the by-product which was formed by coupling of phenylcarbene.

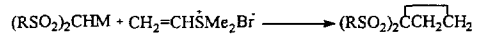
Keywords: Per-(or poly-)fluoroalkanesulfonyl; Cyclopropanes; Synthesis; α-elimination; Carbenes

1. Introduction

Functionalized cyclopropanes have received substantial attention due to their unusual structural, spectroscopic, chemical and biological properties [1]. They serve as important intermediates for the preparation of four, five and seven-membered rings, and can also be considered as precursors to specifically ring opened derivatives [2–4]. Thus, many studies on the synthesis and chemical properties of such cyclopropane derivatives have been reported [5,6]. For example, Tanaka reported a one-pot synthesis of phenylsulfonyl substituted cyclopropanes via successive alkylation and cyclization of sulfone stabilized carbanions [7].



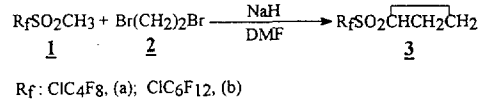
1,1-disulfonyl substituted cyclopropanes were also obtained by the following reaction [8]:



Cyclopropane derivatives bearing a fluorine containing group have drawn attention and some perfluoroalkyl substituted cyclopropanes have been synthesized [9,10]. However, the perfluoroalkanesulfonyl substituted derivatives have been rarely studied. In one paper, cyclopropyl triflone was mentioned but no details were given [11]. Here we report a facile, one-pot, method for the preparation of per-(or poly-)fluoroalkanesulfonyl substituted cyclopropanes.

2. Results and discussion

Methyl polyfluoroalkylsulfones $R_fSO_2CH_3$ obtained from the reaction of R_fSO_2Na with CH_3I, reacted in DMF with 1,2-dibromoethane in the presence of two molar ratio of NaH to afford 1-perfluoroalkanesulfonyl cyclopropane in moderate yields (60–68%).



R_f: ClC_4F_8, (a); ClC_6F_{12}, (b)

This reaction was readily carried out in DMF, and the ^{19}F NMR spectrum was used to follow the reaction process; after stirring for 24 h at 110°C, the reaction was nearly completed. Since the products **3** did not dissolve in water, they were separated from the reaction mixture by an aqueous work-up. Vacuum fractional distillation of the crude product gave a pure sample. When this reaction was carried out in diethylene glycol dimethyl ether (110°C, 24 h), the yield of **3** was only 25%. It was note worthy that, reflux of the reaction

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mixture in tetrahydrofuran did not give the expected product **3**.

The ^{1}H NMR spectrum of **3** have three resonances for the three membered ring protons, for example, the chemical shifts of compound **3b** are at 2.50 ppm (1H), 1.45 ppm (2H), and 1.30 ppm (2H). Because the two ring CH_2 groups are chemically equal, the observed chemical differences should be attributed to a stereo effect. The down-field chemical shift at 1.45 ppm is tentatively assigned to the two protons located on the same side as the R_fSO_2 group.

This synthetic method was also applicable to benzyl perfluoroalkylsulfones $R_fSO_2CH_2Ph$, which were similarly synthesized as compounds **1**. Hendrickson et al. have reported the preparation of compound **4a**, with iodide ion catalysis, potassium triflinate reacted with benzyl bromide in boiling CH_3CN for 7 days gave benzyl triflone in 70% yield [12]. In our case, treatment of R_fSO_2Na with $PhCH_2Br$ in CH_3CN at 80°C for 24 h without catalysis gave 72–78% yields of products **4**. A similar treatment of **4** with **2** and potassium carbonate in DMF gave 1-phenyl-1-perfluoroalkanesulfonyl cyclopropanes **5** in good yields. (see Table 1). As found with compounds **3**, the ^{1}H NMR of the CH_2 groups in compounds **5** also have different chemical shifts. For example, in the compound **5a** they are at 1.51 ppm and 2.05 ppm, respectively. Compared with compound **3b**, the larger differences of the chemical shift (0.54 ppm) in compound **5a** would be caused by the 1-phenyl substitution.

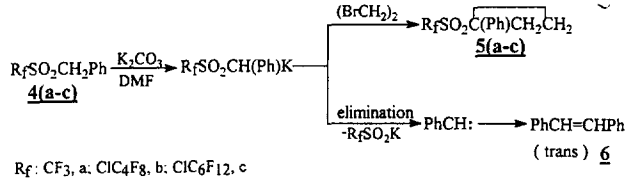
It was interesting to find that in all these reactions, another product was also separated: *trans*-1,2-diphenyl ethene PhCH=CHPh **6**. This product may be formed by a coupling reaction of phenyl carbene PhCH: which was formed from the α-elimination of $R_fSO_2CH(Ph)K$ (see Scheme 1). When $R_fSO_2CH(Ph)K$ was heated in DMF at 110°C for 24 h, compound **6** was isolated in 35% yield.

It is well-known that the $CF_3SO_2^-$ can be removed either by basic β-elimination or by thermolysis [11]. For example, heating of $CF_3SO_2C(CH_3)(Ph)CH_2Ph$ with K_2CO_3 in CH_3CN gave the 1,2-eliminated product $PhCH{=}C(CH_3)Ph$. However, α-elimination of per-(or poly-)fluoroalkanesulfinate has not been reported. Further exploration of the formation and trapping reactions of phenyl carbene are now in progress and these results will be published elsewhere.

The prepared per-(or poly-)fluoroalkanesulfonyl substituted cyclopropanes are listed in Table 1.

Table 1
Per-(or poly-)fluoroalkanesulfonyl substituted cyclopropanes $R_fSO_2C(R)$-CH_2CH_2 **3** and **5** prepared

Products (**3** and **5**)		Melting point (°C)	Yield (%)	Elemental analysis
R_f	*R*			(Calcd/Found)
ClC_4F_8	H **3a**	22–24	72	C, 24.71/24.43; H, 1.47/1.25
ClC_6F_{12}	H **3b**	32–33	64	C, 24.52/24.66; H, 1.14/1.13
CF_3	Ph **5a**	72–73	72	C, 48.00/47.60; H, 3.60/3.60
ClC_4F_8	Ph **5b**	37–39	68	C, 39.45/39.88; H, 2.16/2.43
ClC_6F_{12}	Ph **5c**	38–39	65	C, 34.85/35.19; H, 1.74/1.74



Scheme 1.

3. Experimental details

The reported melting points are measured on a Mel-temp apparatus and are uncorrected. Solvents were purified and dried before use. ^{1}H NMR (90 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 ($\delta_{CFCl3} = \delta_{TFA} + 77.6$ ppm, and with upfield positive) as internal and external standard, respectively. IR spectra were obtained on an IR-440 Shimadzu spectrophotometer. Low resolution mass spectra were measured on a Finnigan GC-MS 4021 instrument. Elemental analysis were performed by this Institute.

Methyl perfluoroalkylsulfones $R_fSO_2CH_3$ **1** were prepared according to the literature [12].

$ClC_4F_8SO_2Na$ (6.4 g, 20 mmol), CH_3I (2.8 g, 20 mmol) and 20 ml DMSO were added into a 50 ml flask equipped with a reflux condenser and a magnetic stirring bar. After stirring at 60°C for 24 h, the mixture was poured into 100 ml ice-water. The solid was filtered and the aqueous layer was extracted by ether (30 ml×2). The ether was removed by a rotary evaporator, the residue was combined with the filtered solid and the crude product was distilled to give the pure product **1a** (4.3 g, 70%).

Similarly compound **1b** (75%) was prepared.

$ClC_4F_8SO_2CH_3$ **1a** m.p. 25–26°C

^{1}H NMR ($CDCl_3$) δ (ppm): 3.10 (s, 3H).

^{19}F NMR ($CDCl_3$) δ (ppm): −68.6 (s, $ClCF_2$), −115.0 (s, SCF_2), −120.9 (m, CF_2CF_2)

IR (ν_{max}, cm^{-1}): 3020 (w), 2990 (w), 1370 (s), 1200–1120 (vs).

$ClC_6F_{12}SO_2CH_3$ **1b** m.p. 58–59°C

^{1}H NMR ($CDCl_3$) δ (ppm): 3.12 (s, 3H).

^{19}F NMR ($CDCl_3$) δ (ppm): −68.2 (s, $ClCF_2$), −115.0 (s, SCF_2), −121 (m, CF_2CF_2), −122 (m, CF_2)

IR (ν_{max}, cm^{-1}): 3018 (w), 2994 (w), 1360 (s), 1215–1120 (vs)

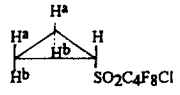
MS (m/e, %): 280(M^+H–ClC_2F_4, 1.06), 100(C_2F_4, 100.00), 85/87($ClCF_2^+$, 18.45/5.71).

Elemental analysis for the compound $C_7H_3ClF_{12}O_2S$:

Calcd: C, 20.27; H, 0.72%
Found: C, 19.80; H, 0.41%.

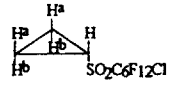
3.1. Preparation of 1-perfluoroalkanesulfonyl propane 3

General procedure: A mixture of $ClC_4F_8SO_2CH_3$ (3.2 g, 10 mmol), NaH (85%, 0.6 g, 21 mmol), 1,2-dibromoethane (1.9 g, 10 mmol) and 20 ml DMF in a 50 ml flask equipped with a reflux condenser and a stirring bar were heated to 100°C for 24 h. The reaction mixture was poured into a 100 ml beaker containing 50 ml ice-water and the solid was filtered out. The aqueous layer was extracted by ether (30 ml×2) and the ether layer was separated and dried over Na_2SO_4. The ether was removed by a rotary evaporator, the residue and the filtered solid were combined and sublimed to gave the product **3a** (2.4 g, 72%). Similarly, compound **3b** (64%) was prepared.



3a

^{1}H NMR ($CDCl_3$) δ (ppm): 2.50 (m, 1H), 1.42 (m, 2H^b), 1.29 (m, 2H^a).
^{19}F NMR ($CDCl_3$) δ (ppm): −68.8 (s, $ClCF_2$), −113.5 (s, SCF_2), −120.1 (m, CF_2), −120.5 (m, CF_2)
IR (ν_{max}, cm^{-1}): 3020 (w), 1432 (w), 1370 (s), 1215–1120 (vs)



3b

^{1}H NMR ($CDCl_3$) δ (ppm): 2.50 (m, 1H), 1.45 (m, 2H^b), 1.30 (m, 2H^a).
^{19}F NMR ($CDCl_3$) δ (ppm): −68.3 (s, $ClCF_2$), −113.5 (s, SCF_2), −120.8 (m, CF_2CF_2), −121 (m, CF_2)
IR (ν_{max}, cm^{-1}): 3020 (w), 1432 (w), 1360 (s), 1210–1120 (vs)
MS (m/e, %): 441/443(M^+H, 2.14/0.79), 169($CF_3CF_2CF_2^+$, 6.47), 105(M^+–ClC_6F_{12}, 100.00), 85/87($ClCF_2^+$, 14.60/5.17).

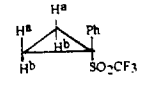
3.2. Preparation of benzyl perfluoroalkanesulfones $R_fSO_2CH_2Ph$

CF_3SO_2Na (3.2 g, 20 mmol), $PhCH_2Br$ (3.6 g, 20 mmol) and 20 ml CH_3CN were added into a 50 ml flask equipped with a reflux condenser and a magnetic stirring bar. After refluxing for 12 h, the reaction mixture was poured into 50 ml ice-water. The solid was filtered out and the aqueous layer was extracted by ether (30 ml×2). The ether was removed by a rotary evaporator, the residue was combined with the filtered solid, the crude product was sublimed to give the pure product **4a** (3.4 g, 76%). M.p. 102–103°C identical with the literature data [12].

Similarly compounds **4b** (72%) and **4c** (78%) were prepared. $ClC_4F_8SO_2CH_2Ph$ **4b** m.p. 80–81°C
^{1}H NMR ($CDCl_3$) δ (ppm): 7.31 (s, 5H), 4.36 (s, 2H).
^{19}F NMR ($CDCl_3$) δ (ppm): −68.0 (s, $ClCF_2$), −112.4 (s, SCF_2), −120.3 (m, CF_2CF_2), −121.8 (m, CF_2)
IR (ν_{max}, cm^{-1}): 2950 (w), 1491 (m), 1445 (m), 1403 (w), 1357 (s), 1240–1170 (vs)
MS (m/e, %): 328/326(M^+–SO_2, 0.47/0.15), 249($C_4F_8SOH^+$, 0.12), 155(M^+–R_f, 1.90), 91(C_6H_5–CH_2^+, 100.00), 77 ($C_6H_5^+$ 0.65), 69(CF_3^+, 6.87)
Elemental analysis for the compound $C_{11}H_7ClF_8O_2S$:
Calcd: C, 33.80; H, 1.79%
Found: C, 33.48; H, 1.45%
$ClC_6F_{12}SO_2CH_2Ph$ **4c** m.p. 82–83°C
^{1}H NMR ($CDCl_3$) δ (ppm): 7.42 (s, 5H), 4.48 (s, 2H).
^{19}F NMR ($CDCl_3$) δ (ppm): −68.5 (s, $ClCF_2$), −112.7 (s, SCF_2), −121.4 (m, CF_2), −121.6 (m, CF_2)
IR (ν_{max}, cm^{-1}): 3000 (w), 1493 (m), 1455 (m), 1415 (w), 1359 (s), 1240–1170 (vs)
MS (m/e, %): 491/493(M^+H, 0.41/0.13), 91($C_6H_5CH_2^+$, 100.00), 77 ($C_6H_5^+$, 0.46), 69(CF_3^+, 4.16)
Elemental analysis for the compound $C_{13}H_7ClF_{12}O_2S$:
Calcd: C, 31.80; H, 1.43%
Found: C, 31.78; H, 1.26%.

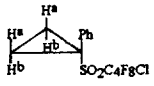
3.3. Preparation of 1-phenyl-1-perfluoroalkanesulfonyl cyclopropanes 5

$CF_3SO_2CH_2C_6H_5$ (2.3 g, 10 mmol), 1,2-dibromoethane (1.98 g, 10 mmol), K_2CO_3(98%, 1.5 g, 11 mmol) and 20 ml DMF were added into a 50 ml flask equipped with a reflux condenser and a stirring bar. This reaction mixture was stirred at 110°C for 24 h. In a similar fashion, as reported above for compound **3**, compound **5a** was formed (1.8 g, 72%). Vacuum sublimation of the crude product gave the pure compound. Similar treatment of **4b** and **4c** gave the compounds **5b** and **5c**.



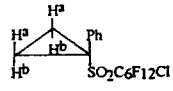
5a

^{1}H NMR ($CDCl_3$) δ (ppm): 7.40 (m, 5H), 2.05 (t, 2H^b), 1.51 (t, 2H^a).
^{19}F NMR ($CDCl_3$) δ (ppm): −73.0 (s, CF_3)
IR (ν_{max}, cm^{-1}): 3020 (w), 1680 (m), 1495 (m), 1455 (m), 1420 (w), 1350 (s), 1250–1170 (vs)
MS (m/e, %): 250 (M^+, 2.70), 133 (M^+–$C_6H_5C(CH_2)_2$, 1.22), 117(M^+–SO_2CF_3, 100.00), 91($C_6H_5CH_2^+$, 24.82), 77($C_6H_5^+$, 7.41), 69(CF_3^+, 6.01)



5b

^{1}H NMR (CCl_4) δ (ppm): 7.17 (m, 5H), 2.00 (t, $2H^b$), 1.38 (t, $2H^a$).
^{19}F NMR (CCl_4) δ (ppm): −68.5 (s, $ClCF_2$), −107.0 (s, SCF_2), −119.6 (m, CF_2), −119.8 (m, CF_2),
IR (ν_{max}, cm^{-1}): 3020 (w), 3015 (w), 1500 (m), 1458 (m), 1360 (s), 1210–1108 (s)
MS (m/e, %): 416/418 (M^+, 0.38/0.10), 299(M^+–$C_6H_5C(CH_2)$, 0.73), 117(M^+–SO_2R_f, 100.00), 91($C_6H_5CH_2^+$, 14.85), 77($C_6H_5^+$, 3.85)



5c

^{1}H NMR ($CDCl_3$) δ (ppm): 7.41 (m, 5H), 2.07 (t, $2H^b$), 1.51 (t, $2H^a$).
^{19}F NMR ($CDCl_3$) δ (ppm): −68.4 (s, $ClCF_2$), −107.6 (s, SCF_2), −120.9 (m, CF_2), −121.0 (m, CF_2), −122.00 (m, CF_2)
IR (ν_{max}, cm^{-1}): 3010 (w), 1490 (m), 1450 (m), 1420 (w), 1350 (s), 1260–1170 (vs)
MS (m/e, %): 516/518 (M^+, 1.21/0.43), 117(M^+–SO_2R_f, 100.00), 91($C_6H_5CH_2^+$, 16.13), 77($C_6H_5^+$, 2.93)

Acknowledgements

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