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A convenient synthesis of perfluoroalkylated allylic sulfides

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Abstract

Perfluoroalkylated allylic sulfides can be synthesized by the reaction of thiophenoxymethyl lithium with fluorinated β-oxoalkylphosphonium salts in 51%–72% yields.

Keywords: Synthesis; Perfluoroalkylated allylic sulfides; NMR spectroscopy; IR spectroscopy; Mass spectrometry

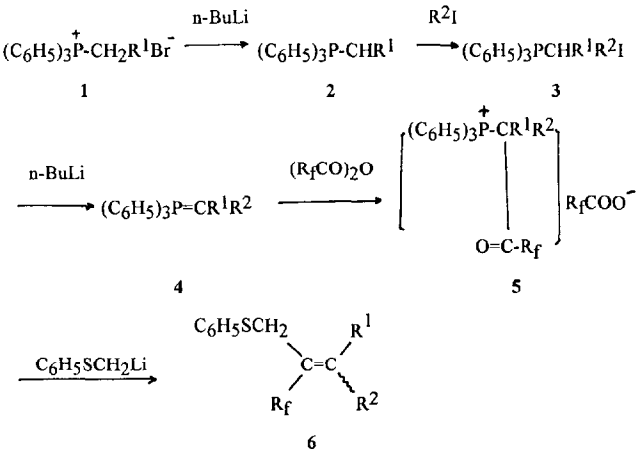
1. Introduction

Allylic sulfides are potentially useful intermediates in organic syntheses and may undergo many useful organic transformations [1]. The most important of the many uses of allylic sulfides in organic synthesis are the reactions of their carbanions with electrophiles [2]. They are useful as nucleophiles because of the presence of the sulfenyl group to stabilize adjacent carbanions which can subsequently react with electrophiles to give coupling products [3]. However, to the best of our knowledge perfluoroalkylated allylic sulfides have not been reported previously, although they would be expected to be useful intermediates for the synthesis of biologically active fluorinated compounds.

2. Results and discussion

In our previous papers we have reported that carbon nucleophiles can attack fluorinated β-oxoalkylphosphonium salts leading to formation of tetrasubstituted fluoroalkenes [4] and fluoroenynes [5], and phosphorus nucleophiles can attack these salts affording α-fluoroalkylvinyl or α-fluoroepoxyalkyl phosphonates [6]. In our continuing investigation to exploit the synthetic utility of fluorinated β-oxoalkylphosphonium salts in organic synthesis, we now wish to report the reaction of sulfur nucleophiles with β-oxoalkylphosphonium salts giving perfluoroalkylated allylic sulfides in 51%–72% yields (**6a–e** in three steps; **6f, g** in five steps).

The reaction sequence is as follows:



1 2 3 4 5 6

6a: $R^1 = CH_3$, $R^2 = CH_3$, $R_f = CF_3$

6b: $R^1 = CH_3$, $R^2 = CH_3$, $R_f = CF_3CF_2$

6c: $R^1, R^2 = -(CH_2)_4-$, $R_f = CF_3$

6d: $R^1, R^2 = -(CH_2)_4-$, $R_f = CF_3CF_2$

6e: $R^1 = C_6H_5$, $R^2 = CH_3$, $R_f = CF_3$

6f: $R^1 = n\text{-}C_3H_7$, $R^2 = CH_3$, $R_f = CF_3$

6g: $R^1 = n\text{-}C_4H_9$, $R^2 = CH_3$, $R_f = CF_3$

Phosphoranes **4** were acylated by the addition of perfluoroalkanoic anhydrides to give the fluorinated β-oxoalkylphosphonium salts **5** which were attacked by thiomethoxymethyl lithium ($C_6H_5SCH_2Li$) in the reaction medium, followed by elimination of triphenylphosphine oxide to give perfluoroalkylated allylic sulfides in good yield. The results are summarized in Table 1.

All products are new and were characterized by IR, NMR and MS methods, and by elemental analyses.

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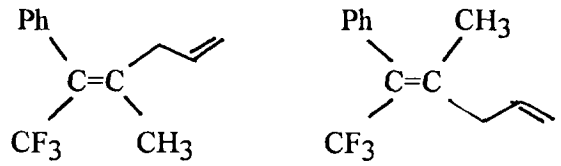
Table 1
Perfluoroalkylated allylic sulfides prepared

Compound	Method [a]	Yield [b] (%)	Ratio [c] E/Z
6a	B	65	
6b	B	53	
6c	B	57	
6d	B	51	
6e	B	72	0:100
6f	A	63	45:55
6g	A	68	44:56

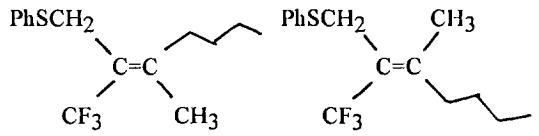
[a] Method A: from **1** as starting material. Method B: from **3** as starting material.
[b] Isolated yields.
[c] Estimated on the basis of NMR spectra.

The configurations of **6f** and **6g** were ascertained on the basis of their ^{19}F NMR data. It has been reported that if the trifluoromethyl group is *trans* with respect to the methyl group, the chemical shifts of the trifluoromethyl group appear downfield, while those *cis* with respect to the methyl group are shifted slightly upfield [7]. For example:



Therefore we can predicate as follows:

4f:



3. Experimental details

All melting points and boiling points are reported uncorrected. IR spectra of solid products were obtained as KCl disks and of liquid products as films on a Shimadzu IR-440 spectrometer. NMR spectra (chemical shifts in ppm from TMS for ^1H NMR and from external TFA for ^{19}F NMR, positive for upfield shifts) were obtained on a Varian EM-360 (60 MHz) or XL-200 (200 MHz) spectrometer. Coupling constants are given in Hz. Mass spectra were recorded on a Finnigan GC-MS 4021 spectrometer.

3.1. General procedure for the preparation of compound 6

Method A

A solution of phosphorane **2**, generated from the phosphonium bromide **1** (3.0 mmol) and n-butyllithium (3.0 mmol) at −20 °C in absolute THF (30 ml), was stirred at 0 °C under nitrogen while methyl iodide (0.43 g, 3 mmol) was added slowly. After stirring at 20 °C for 1 h and cooling to −20 °C, a second portion of n-butyllithium (3 mmol) was added. The mixture was again stirred for an additional 1 h, cooled to −78 °C and perfluoroalkanoic anhydride (3 mmol) slowly added. After addition and stirring at −78 °C for 1 h, thiophenoxymethyllithium (3 mmol) was added slowly. The mixture was allowed to warm to room temperature and stirred for an additional 1 h. After standing overnight, the filtrate was collected and diluted with petroleum ether (100 ml, 60–90 °C). Filtration and evaporation of the filtrate gave a residue which was purified by column chromatography on silica gel with light petroleum (60–90 °C) ethyl ether (10:1) as eluent to give the products **6**.

Method B

A similar procedure was used as in method A, but the first two operations were omitted as the intermediates **3** were readily available [7].

2-Trifluoromethyl-3-methyl-2-butenyl phenyl sulfide (**6a**): yield 65%, b.p. 82 °C/0.7 Torr. Analysis: calc. for $C_{12}H_{13}F_3S$ (246.29): C, 58.52; H, 5.32%. Found: C, 58.54; H, 5.32%. MS *m/z*: 246 (M^+); 137; 110; 77. IR (film) (cm^{-1}): 1660; 1590; 1490; 1440; 1330; 1110. ^1H NMR ($CDCl_3$/TMS) δ: 1.76 (s, 3H); 2.10 (s, 3H); 3.80 (s, 2H); 7.40–7.60 (m, 5H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: −19.6 (s) ppm.

2-Pentafluoroethyl-3-methyl-2-butenyl phenyl sulfide (**6b**): yield 53%, m.p. 37 °C. Analysis: calc. for $C_{13}H_{13}F_5S$ (296.30): C, 52.70; H, 4.42%. Found: C, 52.49; H, 4.27%. MS *m/z*: 296 (M^+); 77. IR (KCl) (cm^{-1}): 1580; 1490; 1440; 1320; 1070. ^1H NMR ($CDCl_3$/TMS) δ: 1.93 (s, 3H); 1.88 (s, 3H); 3.66 (s, 2H); 7.25–7.45 (m, 5H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 6.7 (s, 3F); 32.0 (s, 2F) ppm.

2-Trifluoromethyl-3,3-(1,4-butylene)-2-allyl phenyl sulfide (**6c**): yield 57%, b.p. 95–97 °C/0.2 Torr. Analysis: calc. for $C_{14}H_{15}F_3S$ (272.08): C, 61.75; H, 5.55%. Found: C, 61.47; H, 5.41%. MS *m/z*: 272 (M^+); 253. IR (film) (cm^{-1}): 1665; 1690; 1480; 1440; 1340; 1110. ^1H NMR ($CDCl_3$/TMS) δ: 1.45–1.75 (m, 4H); 1.95–2.25 (m, 2H); 2.35–2.60 (m, 2H); 3.53 (s, 2H); 7.10–7.30 (m, 5H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: −16.5 (s) ppm.

2-Pentafluoroethyl-3,3-(butylene)-2-allyl phenyl sulfide (**6d**): yield 51%, m.p. 42–43 °C. Analysis: calc. for $C_{15}H_{15}F_5S$ (322.08): C, 55.89; H, 4.69%. Found: C, 56.14; H, 4.62%. MS *m/z*: 322 (M^+); 213; 110. IR (KCl) (cm^{-1}): 1650; 1480; 1390; 1200; 1100. ^1H NMR ($CDCl_3$/TMS) δ: 1.55–1.72 (m, 4H); 2.44–2.60 (m, 4H); 3.65 (s, 2H); 7.20–7.41 (m, 5H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: 6.5 (s, 3F); 35.2 (s, 2F) ppm.

2-Trifluoromethyl-3-phenyl-1-thiophenoxy-2-butene (**6e**): yield 72%, m.p. 73.0–73.5 °C. Analysis: calc. for $C_{17}H_{15}F_3S$ (308.08): C, 66.22; H, 4.91%. Found: C, 66.43; H. 4.44%. MS *m/z*: 308 (M^+); 199; 179. IR (KCl) (cm^{-1}): 1650; 1580; 1480; 1440; 1340; 1110. ^1H NMR ($CDCl_3$/TMS) δ: 1.82 (s, 3H); 3.84 (s, 2H); 7.04–7.64 (m, 10H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: −21.3 (s) ppm.

2-Trifluoromethyl-3-methyl-1-thiophenoxy-2-hexene (**6f**): yield 63%, b.p. 90–92 °C/0.3 Torr. Analysis: calc. for $C_{14}H_{17}F_3S$ (274.10): C, 61.29; H, 6.25%. Found: C, 60.94; H, 6.12%. MS *m/z*: 274 (M^+). IR (KCl) (cm^{-1}): 1650; 1580; 1480; 1440; 1330; 1110. ^1H NMR ($CDCl_3$/TMS) δ: 0.82 (t, J=7.3 Hz, 0.55×3H, CH_3-*Z*); 0.99 (t, J=7.3 Hz, 0.45×3H, CH_3-*E*); 1.25–1.53 (m, 2H); 1.64 (q, J=2.2 Hz, 0.45×3H, CH_3-*E*); 1.85–1.94 (m, 0.55×2H, CH_2-*Z*); 1.94 (q, J=2.2 Hz, 0.55×3H, CH_3-*Z*); 2.24–2.35 (m, 0.45×2H, CH_2-*E*); 3.60 (s, 2H); 7.10–7.35 (m, 5H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: −21.2 (s, 0.45×3F-*E*); −20.2 (s, 0.55×3F-*Z*) ppm.

2-Trifluoromethyl-3-methyl-1-thiophenoxy-2-heptene (**6g**); yield 68%, b.p. 95–96 °C/0.3 Torr. Analysis: calc. for $C_{15}H_{19}F_3S$ (288.12); C, 62.47; H, 6.65%. Found: C, 62.15; H, 6.64%. MS *m/z*: 288 (M^+); 269. IR (KCl) (cm^{-1}): 1650; 1580; 1480; 1440; 1330; 1110. ^1H NMR ($CDCl_3$/TMS) δ: 0.81 (t, J=7.3 Hz, 0.56×3H, CH_3-*Z*); 0.98 (t, J=7.3 Hz, 0.44×3H, CH_3-*E*); 1.13–1.58 (m, 4H); 1.63 (q, J=2.2 Hz, 0.44×3H, CH_3-*E*); 1.84–1.95 (m, 0.56×2H, CH_2-*Z*); 1.95 (q, J=2.2 Hz, 0.56×3H, CH_3-*Z*); 2.25–2.36 (m, 0.44×2H, CH_2-*E*); 3.62 (s, 2H); 7.12–7.34 (m, 5H) ppm. ^{19}F NMR ($CDCl_3$/TFA) δ: −20.6 (s, 0.44×3F-*E*); −19.8 (s, 0.56×3F-*Z*) ppm.

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