

## Short and Efficient Preparation of Trifluoromethyl Vinyl Sulphides

Jean-Pierre Bégué,\* Danièle Bonnet-Delpon, Abderrahim M'Bida

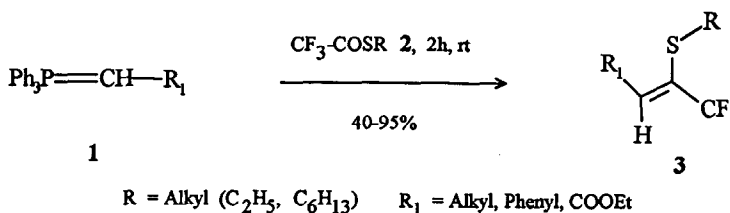
BioCIS-CNRS, Centre d'Etudes Pharmaceutiques, Rue J.B. Clément,  
F-92296 Châtenay-Malabry, France.

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**Abstract:** *S*-Alkyl trifluorothioacetate **2** reacts with stabilized and non-stabilized phosphoranes **1** to afford a new and general route to a wide range of trifluoromethyl vinyl sulphides **3**. Until now, no general methods allowed the preparation of these interesting compounds.

Vinyl sulphides have only recently emerged as valuable synthetic intermediates and their potential has been evaluated.<sup>1</sup> However trifluoromethylated vinyl sulphides were not available. The first reported example of this class of compounds was only obtained as a mixture with other products.<sup>2</sup> Since then, only few specific examples have been described.<sup>3-5</sup> Their preparations do not possess a broad generality and need too many steps to be efficient in a building block strategy.

We report in this note a novel synthetic approach to trifluoromethyl vinyl sulphides based on the reactivity of perfluorinated acid derivatives with phosphoranes.<sup>6</sup> We found that, upon treatment of a variety of phosphoranes **1** with *S*-alkyl trifluorothioacetate **2**, a clean reaction occurred, leading to the corresponding 1-trifluoromethyl vinyl sulphides **3** in good to excellent yields (Scheme 1 and Table 1). Such a Wittig olefination fails with non-fluorinated *S*-alkyl thioesters, with the condensation affording acylphosphoranes by loss of a thiolate anion.<sup>7</sup> The reaction succeeds only intramolecularly and only with stabilized phosphoranes.<sup>8</sup> Thus, as an example, when the phosphorane **1**, generated with one equiv. of NaH and HMDZ as catalyst in THF, was treated with one equiv. of *S*-



Scheme 1

alkyl trifluoro-thioacetate **2**, it afforded the 1-trifluoromethyl vinyl sulphide **3** in 40-95% yield after 2 hrs.<sup>9</sup> The reaction is stereoselective, the *Z* isomer being largely predominant. Remarkably, when the phosphorane is generated with BuLi, lithium salts do not favor the loss of the thiolate anion leading to a  $\beta$ -acylphosphorane.<sup>6,7</sup> Vinylsulphides **3** were obtained with comparable yields as with NaH, but with slightly poorer stereoselectivity. Relevant results are summarised in Table 1.

**Table 1: Wittig Olefination of S-alkyl trifluorothioacetates 2**

Entry	R	R <sup>1</sup>	Base	Yield (%) <sup>a,b</sup>	Z/E
1	C <sub>2</sub> H <sub>5</sub>	-CH <sub>2</sub> -CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	NaH	61.5	94:6
			BuLi <sup>f</sup>	50	85:15
2	C <sub>2</sub> H <sub>5</sub>	-cycloHexyl	NaH	60	80:20
			NaH <sup>d</sup>	77	90:10
3	C <sub>2</sub> H <sub>5</sub>	-CH <sub>2</sub> -cycloHexyl	NaH	48	98:2
			BuLi <sup>f</sup>	80	92:8
4	C <sub>2</sub> H <sub>5</sub>	-Phenyl	NaH	75	96:4
5	C <sub>2</sub> H <sub>5</sub>	-COOEt	NaH	80	93:7
6	C <sub>2</sub> H <sub>5</sub>	-CH=CH-C <sub>6</sub> H <sub>5</sub>	BuLi <sup>f</sup>	94	86:14
7	C <sub>6</sub> H <sub>13</sub>	-CH <sub>2</sub> -CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	NaH	45	100:0
8	C <sub>6</sub> H <sub>13</sub>	-COOEt	NaH	68	92:8
9	C <sub>6</sub> H <sub>5</sub>	-CH <sub>2</sub> -CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub>	NaH	0 <sup>c</sup>	

<sup>a</sup>All compounds showed spectroscopic and analytical data consistent with assigned structures.

<sup>b</sup>Yields refer to chromatographically pure materials. <sup>c</sup>Reactions with BuLi were performed at -78°C.

<sup>d</sup>Reaction was performed at -78°C. <sup>e</sup>1,1,1-Trifluoro-4-phenylbutan-2-one was isolated after hydrolysis.<sup>10</sup>

The reaction has a wide application, occurring smoothly with different substrates and affording a wide variety of trifluoromethylated vinyl sulphides. Synthetic applications of these versatile synthons are now in progress.

#### References and Notes

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- 9) Typical procedure: To a solution of the phosphorane prepared from phosphonium salt 1a (R<sub>1</sub> = (CH<sub>2</sub>)<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>) (.61 g, 10 mmol) and sodium hydride (0.4 g, 10 mmol) in THF (50 mL) with a catalytical amount of hexamethyldisilazane,<sup>6</sup> S-Ethyl trifluorothioacetate (1.89 g, 10 mmol, 1 mol. equiv.) was added dropwise at room temperature. The discoloration of the reaction mixture is fast; after 2 hrs petrol ether was added (200 mL) and the solution was filtered through a SiO<sub>2</sub> column in order to eliminate triphenylphosphine oxide. After evaporation of solvents, the crude product was purified by flash chromatography (pentane-Et<sub>2</sub>O 95:5) giving the pure vinyl sulphide 3a as a mixture Z/E 94:6 (1.6 g, 61.5%). <sup>19</sup>F NMR (CDCl<sub>3</sub>) δ -67 (minor E isomer -59.3); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.2 (t, J= 7.5 Hz, 3H), 2.6 (q, J= 7.5 Hz, 2H), 2.78 (m, 4H), 6.76 (t, J= 5.5 Hz), 7.2 (m, 5H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 14.6, 28.7, 31.3, 34.5, 123.3 (J= 273.2 Hz), 124.6 (q, 32 Hz), 125.1, 128.3, 128.5, 140.5, 144.9. Anal. Calc. for C<sub>13</sub>H<sub>15</sub>F<sub>3</sub>S: C 59.97, H 5.81; Found C 59.75, H 5.77.10.
- 10) The reaction failed in the case of S-phenyl trifluoroacetate, yielding 5-phenyl-1,1,1-trifluoropentan-2-one instead of the expected sulfides. This is probably due to the departure of the phenylthiolate anion, which is a very good leaving group, from the intermediate thiophenoxylbetaine.

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