## A Convenient Access to Perfluoroalkyl Selenoethers and Selenyl Chlorides

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**Abstract:** The treatment of diselenides with different perfluoroalkyl iodides in the presence of sodium hydroxymethanesulfinate led to perfluoroalkyl selenides in fair to good yields. The reaction between benzyl perfluorooctyl selenide and chlorine, or sulfuryl chloride, gave rise to the corresponding selenyl chloride and represents an easy route to perfluoroalkylselenyl chlorides.

**Key words:** fluorinated alkyl halides, selenium derivatives, electron transfer, selenyl chloride, cleavage by chlorine

The introduction of the trifluoromethylthio group has become an important field in organic chemistry.<sup>1</sup> Both the high lipophilicity and the electron-withdrawing abilities of this substituent modify the properties of molecules and its introduction is of great interest to the pharmaceutical and fine chemical industries.<sup>2</sup> The trifluoromethylseleno group is considered to show similar effects and it is thus very important to develop new approaches to perfluoromethyl selenides and their homologues.

Existing routes to perfluoroalkyl selenides are not numerous and usually employ toxic or expensive reagents. Moreover, these methods are often specific to trifluoromethyl alkyl- and aryl selenides and are not suited to long perfluoroalkyl chains. Some of them appear to be limited to aromatic substituents. Their synthesis was first described by Emeléus.<sup>3</sup> Methyl- and ethyl trifluoromethyl selenide were obtained by treatment of the corresponding alkyl iodide with bis(trifluoromethylselenyl) mercury, the latter prepared from selenium and mercury. Yagupolskii has described two methods to obtain various aryl perfluoroalkyl selenides. The first involves treating arylselenols or arylselenolates with perfluoroalkyl iodides (CF<sub>3</sub>I or  $C_3F_7I$ ) under irradiation.<sup>4</sup> The second is the substitution of different aryl iodides by toxic trifluoromethylseleno- and pentafluorophenylselenocopper compounds prepared by reaction between copper and the corresponding perfluoro diselenides.<sup>5</sup> More recently, Langlois has described two efficient syntheses of aryl- and alkyl trifluoromethyl selenides. The former were prepared by reaction of the selenocyanates with Ruppert's reagent (CF<sub>3</sub>SiMe<sub>3</sub>).<sup>6</sup> The second approach involved the addition of either Ruppert's reagent or the hemiaminal of trifluoroacetaldehyde to diselenides.<sup>7</sup> Finally, trifluoromethyl selenides are accessible to the nucleophilic displacement of chlorine in trifluoromethylselenyl chloride by various carbanions. This method is efficient but is limited by the difficult preparation of the latter compound.8a,b

Work within our group has demonstrated that disulfides can be employed as precursors for perfluoroalkyl sulfides in the presence of sulfoxylate anion radicals.<sup>2,9</sup> Aliphatic, aromatic and heteroaromatic disulfides are susceptible to perfluoroalkylation by perfluoroalkyl halides in the presence of sulfur dioxide radical anion. Among a variety of precursors for sulfur dioxide radical anion, sodium hydroxymethanesulfinate, NaO<sub>2</sub>SCH<sub>2</sub>OH (Rongalite<sup>®</sup>), proved to be one of the simplest and most efficient. It was thus thought that a similar process should work with the analogous diselenides (Scheme 1).



Scheme 1

Thus, treatment of diphenyl diselenide **1a** with a range of readily available perfluoroalkyl iodides gives rise to perfluoroalkyl selenides **2a-e** (Table; entries 1, 2, 3, 4 and 5).<sup>10,11</sup> This method is also efficient in the alkyl series as benzyl- and methyl perfluoroalkyl selenides **2f-g** are isolated in excellent yields (entries 6 and 7).

The mechanism of this reaction is thought to involve generation of the perfluoroalkyl radical by reaction of the perfluoroalkyl halide with SO<sub>2</sub> radical anion.<sup>9</sup> A direct attack of the perfluoroalkyl radical at the selenium-selenium bond can give rise to the perfluoroalkyl selenide and to a selenyl radical, which probably dimerizes (Scheme 2). In all experiments, Rongalite<sup>®</sup> was added in portions over several hours to the reaction. In theory, this allows for the continuous production of sulfur dioxide radical anion and should thus facilitate radical formation over a longer time period. However, a selenide anion can be produced under these conditions by in situ reduction of the diselenide.<sup>12</sup> Thus, it is unclear as to whether the perfluoroalkyl radical is formed from the halide by direct reaction with the sulfoxylate radical anion or with the selenide anion.<sup>13</sup> Nevertheless. diselenides can be formed again from





Entry	R	R <sub>F</sub>	Product	Yield [%]	<sup>1</sup> Η NMR <sup>a</sup> [δ in ppm]	19 [δ	F NMR in ppm]
1	Ph	CF <sub>3</sub>	PhSeCF <sub>3</sub> 2a	28	7.79- 7.74 (m, 2H, H <sub>Ar</sub> ) 7.52- 7.46 (m, 1H, H <sub>Ar</sub> ) 7.44- 7.37 (m, 2H, H <sub>Ar</sub> )	- 36.6	
2	Ph	C <sub>2</sub> F <sub>5</sub>	PhSeC <sub>2</sub> F <sub>5</sub> 2b	62	7.79- 7.73 (m, 2H, H <sub>Ar</sub> ) 7.54- 7.47 (m, 1H, H <sub>Ar</sub> ) 7.45- 7.37 (m, 2H, H <sub>Ar</sub> )	- 83.3 - 92.1	
3	Ph	C <sub>4</sub> F <sub>9</sub>	PhSeC <sub>4</sub> F <sub>9</sub> 2c	57	7.80- 7.74 (m, 2H, H <sub>Ar</sub> ) 7.54- 7.47 (m, 1H, H <sub>Ar</sub> ) 7.45- 7.37 (m, 2H, H <sub>Ar</sub> )	- 81.6 - 87.3 - 119.3 - 126.2	
4	Ph	C <sub>6</sub> F <sub>13</sub>	PhSeC <sub>6</sub> F <sub>13</sub> 2d	67	7.79- 7.73 (m, 2H, H <sub>Ar</sub> ) 7.54- 7.47 (m, 1H, H <sub>Ar</sub> ) 7.45- 7.37 (m, 2H, H <sub>Ar</sub> )	- 81.4 - 87.0 - 118.4 - 122.1	- 123.3 - 126.6
5	Ph	C <sub>8</sub> F <sub>17</sub>	PhSeC <sub>8</sub> F <sub>17</sub> 2e	71	7.81- 7.73 (m, 2H, H <sub>Ar</sub> ) 7.54- 7.47 (m, 1H, H <sub>Ar</sub> ) 7.45- 7.37 (m, 2H, H <sub>Ar</sub> )	- 81.3 - 87.0 - 118.3 - 121.9	- 122.4 (4F) - 123.3 - 126.7
6	Ме	C <sub>8</sub> F <sub>17</sub>	MeSeC <sub>8</sub> F <sub>17</sub> <b>2f</b>	79	2.38 (s, 3H, Me)	- 83.4 - 89.7 - 119.0 - 121.9	- 122.5 (4F) - 123.3 - 126.7
7	Bn	C <sub>8</sub> F <sub>17</sub>	BnSeC <sub>8</sub> F <sub>17</sub> <b>2g</b>	80	7.36-7.23 (m, 5H, H <sub>Ar</sub> ) 4.30 (s, 2H, CH <sub>2</sub> )	- 81.2 - 87.2 - 118.7 - 121.8	- 122.3 (4F) - 123.2 - 126.6

Table	Preparation	and NMR	characteristics	of perfluoroalk	vl selenides 2a-g
					/

a) Bruker AC300; solvent CDCl<sub>3</sub>; references: TMS and CFCl<sub>3</sub>.

alkylselenide anions and perfluoroalkyl halides, by analogy with the behavior of alkylthiolates.<sup>14</sup> Consequently, the proposed mechanism (Scheme 2) seems reasonable, at least for aliphatic diselenides.

Previous work in our laboratory described an efficient synthesis of trifluoromethanesulfonyl chloride by oxidative chlorination of benzyl trifluoromethyl sulfide in aqueous medium.<sup>15</sup> Thus, treatment of benzyl perfluorooctyl selenide **2g** with chlorine under non oxidative conditions (CCl<sub>4</sub> as solvent) gives rise to a mixture of benzyl chloride **4** and perfluorooctylselenyl chloride **3** in quantitative yield.<sup>16a</sup> Interestingly, the same result is obtained when compound **2g** is treated with sulfuryl chloride in dichloromethane. Cleavage of the carbon-selenium bond is easy in the case of a benzyl substituent (Scheme 3).

No trace of perfluorooctylselenyl trichloride was detected by <sup>77</sup>Se NMR.<sup>17</sup> The crude mixture was purified by pre-





parative GC and the selenyl chloride **3** was characterized by NMR analysis (<sup>19</sup>F, <sup>77</sup>Se) and HRMS.<sup>16</sup> The crude mixture can be used in further experiments without any purification (Scheme 3). Direct addition of sodium diethylmalonate in ether in the previous mixture gives rise to the corresponding selenoether **5**.<sup>18</sup> In summary, we have shown that aryl- and alkyl perfluoroalkyl selenides can be obtained in one step from diselenides in a simple way and in good yields. We have also developed a new access to perfluoroalkylselenyl chlorides.

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- (10) **Preparation of 2g** : Dibenzyl diselenide (3.00 g, 8.82 mmol) was dissolved in DMF (30 mL) under argon. Perfluorooctyl iodide  $C_8F_{17}I$  (4.72 mL, 17.60 mmol), prewashed with a 10% aqueous solution of  $Na_2S_2O_5$ , was added followed by water (1 mL). Lastly sodium hydroxymethanesulfinate (4.07 g, 26.40 mmol) was added in portions over 3 h. The solution was stirred at room temperature for 20 h. The mixture was extracted with  $Et_2O$  and the organic layer washed with NaHCO<sub>3</sub> (5% in H<sub>2</sub>O) and water, then dried over MgSO<sub>4</sub>, and concentrated under reduced pressure. The product was purified by flash chromatography on silica gel using pentane as eluent ( $R_f$ : 0,70) to afford 8.25 g (80% calculated from  $C_8F_{17}I$ ) of **2g**. See Table for <sup>1</sup>H and <sup>19</sup>F NMR. All compounds were also characterized by mass spectra and <sup>13</sup>C NMR.
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- (16) a) Preparation of 3 with chlorine : Benzyl perfluorooctyl selenide 2g (3.00 g, 5.10 mmol) was dissolved in CCl<sub>4</sub> (25 mL, 0.2 M). Chlorine was bubbled to this solution cooled at 0 °C during 10 min. After 30 min, distillation of the solvent through a Vigreux column left a mixture of benzyl chloride 4 and of selenyl chloride 3. These compounds were separated by preparative GC (Shimadzu GC-8A, with SE30 column on chromosorb WAW 45/60, length 2,5 m) to afford 2.6 g (95%) of **3**. Retention times : 40 min for **3** and 17.5 min for **4**. <sup>19</sup>F NMR (288 MHz, CFCl<sub>3</sub>):  $\delta = -81.5$  (3F, m), -90.4 (2F, m), -118.9 (2F, m), -122.1 (2F, m), -122.4 (4F, m), -123.3 (2F, m), -126.8 (2F, m); <sup>77</sup>Se NMR (57 MHz, SeMe<sub>2</sub>):  $\delta = 1059$ ; HRMS m/z calcd for  $C_8F_{17}$ ClSe 533.8583, found 533.8579. b) Preparation of 3 with sulfuryl chloride : Benzyl perfluorooctyl selenide 2g (0.80 g, 1.35 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (7 mL, 0.2 M). Sulfuryl chloride (0.16 mL, 2.03 mmol) was added slowly at 0 °C and the temperature was raised to room temperature for 1 h. Work-up and yield were identical to those described above.
- (17) a) Gombler, W. Z. Naturforsch. **1981**, *36b*, 535. b) The <sup>77</sup>Se NMR chemical shift for compound **3** is 1059 ppm which is consistent with the litterature ( $\delta = 953$  for CF<sub>3</sub>SeCl<sub>3</sub> versus 1077 for CF<sub>3</sub>SeCl).
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