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Fabien Petit-Cancelier, Samuel Couve-Bonnaire, Tatiana Besset. Synthesis of a library of SCF<sub>2</sub>CO<sub>2</sub>Et reagents: An access to original (ethoxycarbonyl)difluoromethylthioesters. *Tetrahedron*, 2021, 98, pp.132446. 10.1016/j.tet.2021.132446 . hal-03744618

**HAL Id: hal-03744618**

**<https://hal.science/hal-03744618>**

Submitted on 16 Nov 2022

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# Synthesis of a Library of SCF<sub>2</sub>CO<sub>2</sub>Et Reagents: An Access To Original (Ethoxycarbonyl)difluoromethylthioesters

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**Abstract:** A library of original and shelf-stable reagents, source of the (ethoxycarbonyl)difluoromethylthio group, is reported. These reagents are applied to the functionalization of a large panel of aldehydes via a transition metal-free protocol under mild reaction conditions. This approach offers an efficient access to valuable difluoromethylthioester derivatives.

**Keywords:** Difluoromethylthioester derivatives; Fluorine chemistry; Radical process; Mild reaction conditions; Aldehydes;

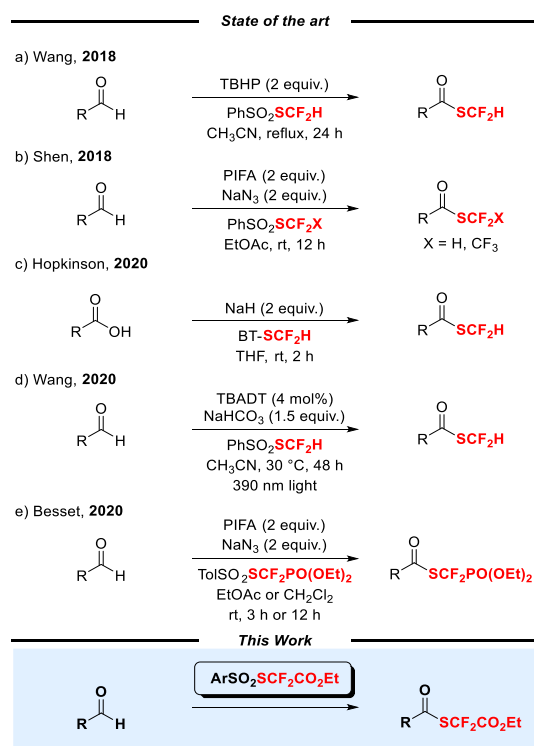
## Introduction

Over the years, the organofluorine chemistry field became a compulsory research area as fluorinated compounds are of paramount importance in material science, pharmaceutical and agrochemical industries.<sup>1</sup> Indeed, thanks to the specific properties of the fluorine atom and the fluorinated groups, their presence on a molecule generally modulate its physico-chemical and biological properties, offering an efficient tool for the discovery of compounds of interest.<sup>2</sup> Therefore, the development of original strategies to expand the portfolio of original fluorinated molecules is of major concern.<sup>3</sup>

Over the year, a special attention was paid to fluorinated groups such as SCF<sub>3</sub> and SCF<sub>2</sub>H groups,<sup>4</sup> thanks to their unique properties such as a strong withdrawing character and interesting lipophilicity (Hansch parameter  $\pi_R = 1.44$  and  $0.68$ , respectively).<sup>5</sup> More recently, the design of original SCF<sub>2</sub>FG groups (FG = CO<sub>2</sub>R, (R = Me, Et), PO(OEt)<sub>2</sub>, SO<sub>2</sub>Ph) has aroused the interest of the scientific community, as the physico-chemical properties of the molecules bearing such fluorinated groups might be fine-tuned.<sup>6</sup> Among them, the SCF<sub>2</sub>CO<sub>2</sub>R residue was recently studied and, thanks to the remarkable contributions of Shen<sup>7</sup> and Billard<sup>8</sup> who independently designed electrophilic reagents, its incorporation onto various molecules became possible.

Besides, considerable attention was paid to fluorinated thioesters,<sup>4f,4g,6b-d</sup> especially trifluoromethylthioesters. These later were synthesized by the direct introduction of the SCF<sub>3</sub> group onto acid chlorides,<sup>9</sup> aldehydes<sup>10</sup> or carboxylic acids.<sup>11</sup> In contrast, methods for the synthesis of difluoromethylthioesters remain limited. In 2018, Wang developed a new methodology for the difluoromethylthiolation of aldehydes using the PhSO<sub>2</sub>SCF<sub>2</sub>H reagent<sup>6b</sup> in the presence of di-*tert*-butyl peroxide (TBHP, (Scheme 1, eq. a).<sup>12</sup> The same year, taking benefit from the versatility of the PhSO<sub>2</sub>SR<sub>f</sub> (R<sub>f</sub> = CF<sub>3</sub>, CH<sub>2</sub>F, CF<sub>2</sub>H and CF<sub>2</sub>CF<sub>3</sub>) reagent, Shen reported the synthesis of various fluorinated thioesters (Scheme 1, eq. b).<sup>10b</sup> More recently, the group of Hopkinson developed an access to difluoromethylthioesters starting from carboxylic acids and the BT-SCF<sub>2</sub>H reagent (BT = benzothiazolium) (Scheme 1, eq.c).<sup>11b</sup> Then, a visible light-mediated synthesis of difluoromethylthioesters was depicted by the group of Wang using the tetrabutylammonium decatungstate (TBADT) photocatalyst with the PhSO<sub>2</sub>SCF<sub>2</sub>H reagent under oxidant-free reaction conditions (Scheme 1, eq. d).<sup>13</sup> Finally, our group developed a methodology for the direct introduction of the SCF<sub>2</sub>PO(OEt)<sub>2</sub> moiety onto aldehydes with the TolSO<sub>2</sub>SCF<sub>2</sub>PO(OEt)<sub>2</sub> reagent (Scheme 1, eq. e).<sup>14</sup> Despite these recent advances, the preparation of difluoromethylthioesters was restricted to few examples related to the incorporation of the SCF<sub>2</sub>H, SCF<sub>2</sub>CF<sub>3</sub> and SCF<sub>2</sub>PO(OEt)<sub>2</sub> motifs onto molecules and the quest for original tools to access novel fluorinated thioesters is really appealing. Herein, we report a straightforward methodology for the synthesis of original (ethoxycarbonyl)difluoromethyl-

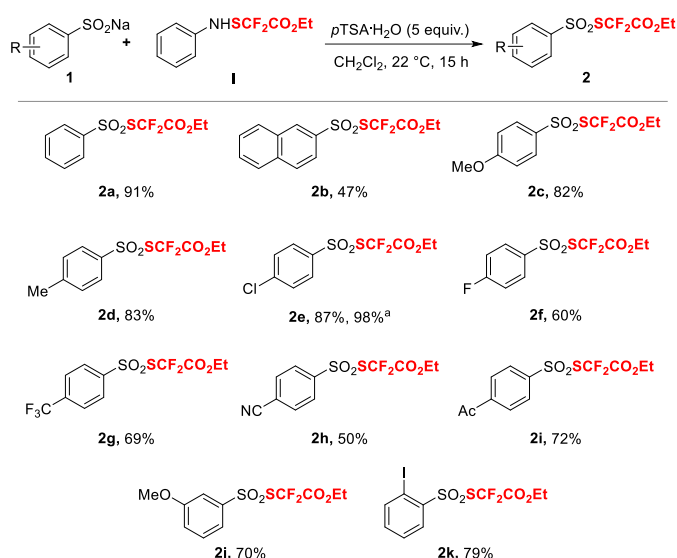
thioesters *via* a radical process. In that purpose, a library of reagents was synthesized and the direct introduction of the SCF<sub>2</sub>CO<sub>2</sub>Et moiety onto readily available aldehydes was then investigated.



**Scheme 1.** State of the Art: Approaches for the synthesis of difluoromethylthioesters. TBHP = di-*tert*-butyl peroxide; PIFA = (bistrifluoroacetoxy)iodobenzene; BT = benzothiazolium; TBADT = tetrabutylammonium decatungstate.

## Results and Discussion

At the outset of this study, we explored the synthesis of the ((ethoxycarbonyl)difluoromethyl)benzenesulfonylthioate **2a**. We imagined that this latter might be prepared starting from sodium benzenesulfinate and a suitable electrophilic SCF<sub>2</sub>CO<sub>2</sub>Et-containing source. Indeed, when the sodium benzenesulfinate **1a** was reacted with the (ethoxycarbonyl)difluoromethylsulfenamide **I** in presence of *para*-toluene sulfonic acid monohydrate, **2a** was isolated in 91% yield.<sup>15</sup> Note that the synthesis of the new reagent **I** employed in this transformation was successfully achieved following the procedure previously described by the group of Billard.<sup>8</sup> With these preliminary results in hand, we examined the scope of the reaction. It turned out that the transformation was versatile as a library of original SCF<sub>2</sub>CO<sub>2</sub>Et reagents was obtained starting from various sodium arylsulfonates **1** (Scheme 2).

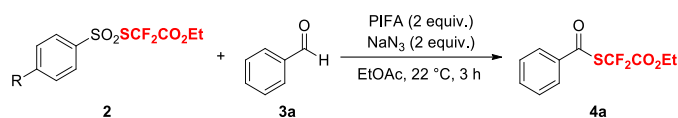


**Scheme 2.** (Ethoxycarbonyl)difluoromethylthiolation of sodium sulfonates **1**. Reaction conditions: Sodium sulfinate **1** (0.2 mmol, 1 equiv.), **I** (0.24 mmol, 1.2 equiv.), *p*TSA·H<sub>2</sub>O (1 mmol, 5.0 equiv.), CH<sub>2</sub>Cl<sub>2</sub> (0.08 M), 22 °C, 15 h, argon.  
<sup>a</sup> The reaction was carried out using 4.1 mmol of **1e**.

Pleasingly, several sodium arylsulfonates reacted well with the reagent **I** to give the desired difluoromethylated arylsulfonothioates **2**. Sodium benzenesulfinate (**1a**) and sodium naphthalenesulfinate (**1b**) turned out to be suitable substrates in this transformation. When arylsulfonates substituted at the *para* position with electron-donating groups (**1c-1d**) were reacted with **I**, the expected products (**2c-2d**) were obtained in high yields. The functionalization of arylsulfonates bearing halogens (**1e-1f**) and electron-withdrawing groups (**1g-1i**) went smoothly. Worth to mention that the transformation was tolerant to the presence of several functional groups such as cyano (**1h**), ketone (**1i**) and halogens (**1e** and **1f**), an asset for post-functionalization reactions. The reaction with the sodium 4-chlorobenzene sulfinate (**1e**) was successfully scaled up from 0.2 mmol to 4.1 mmol, giving the expected product **2e** in an excellent 98% yield. Finally, the functionalization of **1j** and **1k** went smoothly, suggesting that the substitution pattern of the arene did not have a significant impact on the outcome of the reaction.

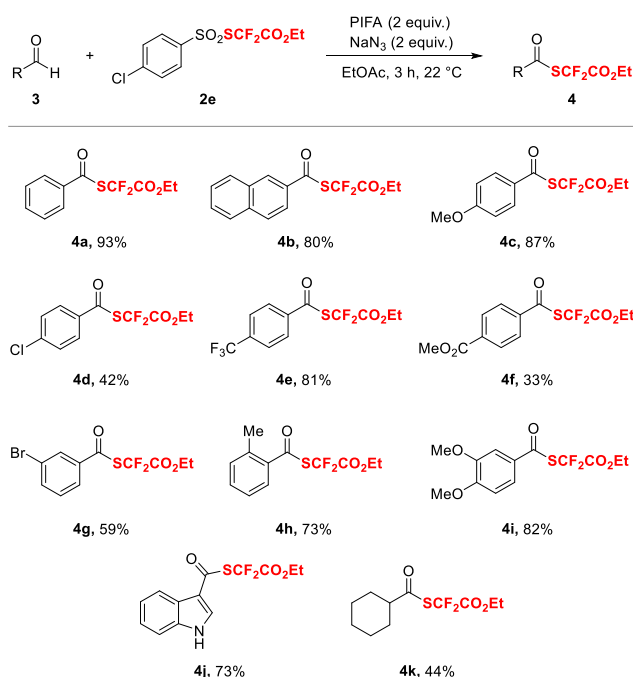
Then, we focused on the synthesis of (ethoxycarbonyl)difluoromethylthioesters **4**. Pleasingly, when the benzaldehyde **3a** was reacted with the reagent **2a** in the presence of PIFA and sodium azide, the expected product **4a** was obtained in a promising 56% yield (table 1, entry 1). To further optimize the reaction conditions, we wondered whether the electronic properties of the reagent **2** might have an influence on the outcome of the reaction (Table 1), the PhSO<sub>2</sub>SR<sub>f</sub> or TolSO<sub>2</sub>SR<sub>f</sub> being the most common reagents used in these transformations.<sup>6b</sup> When the reagent **2c** or the TolSO<sub>2</sub>SCF<sub>2</sub>CO<sub>2</sub>Et **2d** were used, **4a** was obtained in encouraging 76% and 64% yields, respectively (Table 1, entries 2 and 3). In contrast, the reagent **2g** turned out to be much less efficient providing **4a** in only 16% yield (Table 1, entry 4). Pleasingly, when the reaction was carried out with the reagent **2e** (Table 1, entry 5), **4a** was isolated in 93% yield, and we pursued our investigations using **2e** as the coupling partner.

**Table 1.** Study of the influence of the nature of the reagents **2** on the (ethoxycarbonyl)difluoromethylthiolation of the aldehyde **3a**



| Entry | R                             | Yield (%) |
|-------|-------------------------------|-----------|
| 1     | H ( <b>2a</b> )               | 56        |
| 2     | OMe ( <b>2c</b> )             | 76        |
| 3     | Me ( <b>2d</b> )              | 64        |
| 4     | CF <sub>3</sub> ( <b>2g</b> ) | 16        |
| 5     | Cl ( <b>2e</b> )              | 93        |

Reaction conditions: **3a** (0.2 mmol, 1 equiv.), **2** (0.3 mmol, 1.5 equiv.), PIFA (0.4 mmol, 2 equiv.), NaN<sub>3</sub> (0.4 mmol, 2 equiv.), EtOAc (0.4 M), 3 h, argon.



**Scheme 3.** Functionalization of aldehydes using the reagent **2e**. Reaction conditions: **3** (0.2 mmol, 1 equiv.), **2e** (0.3 mmol, 1.5 equiv.), PIFA (0.4 mmol, 2 equiv.), NaN<sub>3</sub> (0.4 mmol, 2 equiv.), EtOAc (0.4 M), 22 °C, 3 h, argon.

With the best reaction conditions in hand, we next investigated the scope of the reaction with various aldehydes (Scheme 3). Pleasingly, the (ethoxycarbonyl)difluoromethylthiolation of a myriad of aldehydes including (hetero)aromatic and aliphatic aldehydes was achieved. Indeed, benzaldehyde (**3a**) and naphthaldehyde (**3b**) were smoothly functionalized, leading to the corresponding products (**4a**) and (**4b**) in 93% yield and 80% yield, respectively. Aromatic aldehydes bearing an electron-donating group (**3c**), halogen (**3d**) and electron-withdrawing groups, such as CF<sub>3</sub> (**3e**) and ester (**3f**) at the *para* position were suitable substrates, the reaction being more efficient with electron-enriched compounds. When the 3-bromobenzaldehyde (**3g**) and the 2-methylbenzaldehyde (**3h**) reacted with **2e**, the expected products were obtained in 59% and 73% yields, respectively. The reaction using the 3,4-dimethoxybenzaldehyde (**3i**) proceeded also smoothly with a high yield. Gratifyingly, heteroaromatic and aliphatic substrates

such as the indole-3-carboxaldehyde (**3j**) and the cyclohexanecarboxaldehyde (**3k**) were also well converted to the corresponding products (**4j** and **4k**) with moderate to good yields.

In order to get a better understanding of the reaction mechanism, radical-trapping experiments were carried out. When the reaction was carried out under standard reaction conditions in the presence of 2 or 4 equivalents of TEMPO (2,2,6,6-tetramethyl-piperidinyloxy), no expected product **4a** was detected and the TEMPO-adduct was observed in GC-HRMS.<sup>16</sup> These results suggested that a radical process might be involved and based on the literature data,<sup>12,13,14,17</sup> a possible acyl radical might be generated from **3** in the presence of PIFA and NaN<sub>3</sub>, which would then react with the reagent **2e** to afford the expected compound **4**.

## Conclusion

In summary, we successfully synthesized a library of [(ethoxycarbonyl)difluoromethyl]arylsulfonothioate reagents (11 examples, up to 98% yield). These latter were applied to the (ethoxycarbonyl)difluoromethylthiolation of aldehyde derivatives. We demonstrated that the nature of the substituents on these reagents has a strong impact on the efficiency of the transformation. Hence, a straightforward synthetic route to (ethoxycarbonyl)difluoromethylthioesters was developed, affording the expected products in moderate to excellent yields (11 examples, up to 93% yield). Worth mentioning that this transition metal-free transformation was tolerant to halogens and functional groups such as ester. This approach offers an efficient and operationally simple tool for the construction of SCF<sub>2</sub>CO<sub>2</sub>Et-containing molecules. We do believe that this library of reagents will expand the portfolio of SCF<sub>2</sub>CO<sub>2</sub>Et-containing reagents and will, beyond doubt, open new avenues towards the synthesis of high-value added SCF<sub>2</sub>CO<sub>2</sub>Et-containing molecules.

## Experimental section

### 1. Material and instrumentation

All reactions were carried out using oven-dried glassware and magnetic stirring under argon unless otherwise stated. Reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. Analytical thin layer chromatography was performed on silica gel aluminum plates with F-254 indicator and visualized by UV light (254 nm) and/or chemical staining with a KMnO<sub>4</sub> solution. Flash column chromatography was performed using 0.040 – 0.063 mm silica gel. Reverse-phase chromatography was performed on InterchimS215 with Nacheray Magel PFP 21 × 250 mm as a column system. <sup>1</sup>H NMR spectra were recorded on a Bruker DXP 300 MHz spectrometer at 300.1 MHz, <sup>13</sup>C NMR spectra at 75.5 MHz, <sup>19</sup>F NMR spectra at 282.4 MHz. Chemical shifts ( $\delta$ ) are quoted in ppm relative to TMS (<sup>1</sup>H) and CFCl<sub>3</sub> (<sup>19</sup>F). Coupling constants ( $J$ ) are quoted in Hz. The following abbreviations were used to show the multiplicities: bs: broad singlet, s: singlet, d: doublet, t: triplet, q: quadruplet, dd: doublet of doublet, td, triplet of doublet and m: multiplet. The residual solvent signals were used as references (CDCl<sub>3</sub>:  $\delta_H$  = 7.26 ppm,  $\delta_C$  = 77.00 ppm or relative to external CFCl<sub>3</sub>,  $\delta_F$  = 0 ppm). High-resolution mass spectrometry (HRMS) were recorded on a Waters LCT Premier spectrometer with a micro-TOF analyzer. IR spectra were recorded on a PerkinElmer Spectrum 100, the wave numbers ( $\nu$ ) of recorded IR-signals (ATR) are quoted in cm<sup>-1</sup>.

Aniline was distilled over CaH<sub>2</sub>. Ethyl acetate (EtOAc) and dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>) were purified by distillation over CaH<sub>2</sub> and stored over Molecular Sieves (3Å). The sodium sulfonates **1b**, **1h** and **1j** were synthesized according to the literature.<sup>15</sup> The reagent **I** was prepared according to the literature procedure.<sup>8</sup>

### 2. General Experimental Procedures:

#### 2.1. General procedure for the synthesis of ethyl 2,2-difluoro-2-[(phenylamino)sulfonyl]acetate **I**:

The procedure was adapted from a previously reported procedure.<sup>8</sup> To a solution of DIPEA (3.4 mL, 19.8 mmol, 1.1 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> (36 mL), DAST (2.6 mL, 19.8 mmol, 1.1 equiv.) was slowly added under argon at -25 °C during 20 min. Then, TMSCF<sub>2</sub>CO<sub>2</sub>Et (3.4 mL, 18 mmol, 1 equiv.) was slowly added and the reaction mixture was stirred for 1.5 h at 25 °C. Once the aniline (1.6 mL, 18 mmol, 1 equiv.) was added, the reaction mixture was stirred at 25 °C for 16 h. The mixture was diluted in 100 mL of water and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 100 mL). The combined organic phases were washed with an aqueous saturated NaCl solution (100 mL), dried under Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated under reduced pressure. Purification of the crude reaction mixture by flash column chromatography on silica gel (height 15 cm, width 8 cm, pentane/diethyl ether = 95:5) afforded the desired product **I** (2.3 g, **52** %).

## 2.2. General procedure for the synthesis of the derivatives 2:

The procedure was adapted from a previously reported procedure.<sup>15a</sup> The reagent **1** (60 mg, 0.24 mmol, 1.2 equiv.), sodium sulfinate **1** (0.2 mmol, 1 equiv.) and *p*TSA.H<sub>2</sub>O (190 mg, 1 mmol, 5 equiv.) were charged in an oven-dried 10 mL tube equipped with a stirring bar and filled under argon. Then, 2.5 mL of distilled dichloromethane was added, and the resulting mixture was stirred at 25 °C for 16 h. The reaction completion was checked by <sup>19</sup>F NMR and then the reaction mixture was concentrated under reduced pressure and purified by flash column chromatography to afford the product **2**.

## 2.3. General procedure for the synthesis of the derivatives 4:

The aldehyde **3** (0.2 mmol, 1 equiv.) was charged in an oven-dried 10 mL tube equipped with a stirring bar and filled under argon followed by the reagent **2** (99.3 mg, 0.3 mmol, 1.5 equiv.), PIFA (172.0 mg, 0.4 mmol, 2 equiv.) and freshly distilled ethyl acetate (0.8 mL). Then, NaN<sub>3</sub> (26.8 mg, 0.4 mmol, 2 equiv.) was finally introduced. The reaction mixture was stirred at 22 °C for 3 h before removing the solvent under reduced pressure. The crude mixture was directly purified by flash column chromatography on silica gel to afford the desired product **4**.

## 3. Physical and spectral data

*Ethyl 2,2-difluoro-2-[(phenylamino)sulfanyl]-acetate 1*: **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.41. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 7.31 – 7.29 (m, 2H), 7.09 – 7.03 (m, 2H), 6.97 – 6.90 (m, 1H), 5.04 (bs, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ -92.9 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 161.8 (t, *J* = 31.9 Hz), 145.5, 129.0, 121.2, 120.0 (t, *J* = 289.8 Hz), 114.9, 63.6, 13.4. **IR** (neat, cm<sup>-1</sup>) *ν*: 3366, 2987, 1752, 1600, 1495, 1373, 1283, 1227, 1102, 1012, 917, 855, 749, 691, 596. **HRMS** (API<sup>+</sup>) for C<sub>10</sub>H<sub>12</sub>NO<sub>2</sub>F<sub>2</sub>S *m/z* 248.0557 [M+H]<sup>+</sup>, Found 248.0547 (Δ = -4.0 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-benzenesulfonothioate **2a**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2a** as a colorless oil (54.1 mg, **91%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.51. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 7.99 (d, *J* = 7.9 Hz, 2H), 7.74 – 7.67 (m, 1H), 7.64 – 7.54 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ -80.9 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 160.0 (t, *J* = 31.0 Hz), 145.1, 134.8, 129.4, 127.5, 119.2 (t, *J* = 294.5 Hz), 64.7, 13.7. **IR** (neat, cm<sup>-1</sup>) *ν*: 2988, 1772, 1582, 1449, 1352, 1294, 1152, 1078, 1013, 969, 714, 577. **HRMS** (ESI<sup>+</sup>) calcd for C<sub>10</sub>H<sub>10</sub>F<sub>2</sub>O<sub>4</sub>S<sub>2</sub>K *m/z* 334.9626 [M+K]<sup>+</sup>, Found 334.9634 (Δ = 2.4 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-2-naphthalene-sulfonothioate **2b**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2b** as a colorless oil (33.1 mg, **47%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.54. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 8.56 (s, 1H), 8.07 – 7.90 (m, 4H), 7.77 – 7.62 (m, 2H), 7.25 – 7.18 (m, 1H), 4.35 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ -81.0 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 160.1 (t, *J* = 31.2 Hz), 141.9, 135.6, 131.8, 130.1, 129.9, 129.9, 129.8, 128.1, 128.1, 121.9, 119.2 (t, *J* = 294.5 Hz), 64.7, 13.7. **IR** (neat, cm<sup>-1</sup>) *ν*: 2926, 1772, 1338, 1291, 1151, 1067, 811, 746, 650, 564. **HRMS** (ESI<sup>+</sup>) calcd for C<sub>14</sub>H<sub>16</sub>NF<sub>2</sub>O<sub>4</sub>S<sub>2</sub> *m/z* 364.0489 [M+NH<sub>4</sub>]<sup>+</sup>, Found 364.0501 (Δ = 3.3 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-methoxybenzene-sulfonothioate **2c**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2c** as a colorless oil (53.5 mg, **82%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.48. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 7.91 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 9.1 Hz, 2H), 4.38 (q, *J* = 7.2 Hz, 2H), 3.90 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ -81.4 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 164.6, 160.2 (t, *J* = 31.2 Hz), 136.8, 130.2, 119.2 (t, *J* = 293.7 Hz), 114.5, 64.6, 55.9, 13.8. **IR** (neat, cm<sup>-1</sup>) *ν*: 2986, 1771, 1591, 1496, 1347, 1264, 1142, 1016, 833, 658, 570. **HRMS** (API<sup>+</sup>) calcd for C<sub>11</sub>H<sub>13</sub>O<sub>5</sub>F<sub>2</sub>S<sub>2</sub> *m/z* 327.0172 [M+H]<sup>+</sup>, Found 327.0173 (Δ = 0.3 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-methylbenzene-sulfonothioate **2d**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2d** as a colorless oil (53.9 mg, **83%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.45. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.47 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ -81.1 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 160.1 (t, *J* = 31.1 Hz), 146.2, 142.3, 130.0, 127.6, 119.2 (t, *J* = 294.1 Hz), 64.6, 21.7, 13.7. **IR** (neat, cm<sup>-1</sup>) *ν*: 2980, 1773, 1593, 1448, 1294, 1149, 1015, 971, 812, 700, 650, 572. **HRMS** (ESI<sup>+</sup>) calcd for C<sub>11</sub>H<sub>12</sub>O<sub>4</sub>F<sub>2</sub>S<sub>2</sub>K *m/z* 348.8782 [M+K]<sup>+</sup>, Found 348.9793 (Δ = 3.2 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-chlorobenzene-sulfonothioate **2e**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2e** as a colorless oil (58.2 mg, **87%**). The reaction was also performed on 4.1 mmol scale starting from 794.4 mg of **1e** leading to the corresponding product **2e** (1.3 g, **98%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.37. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 7.92 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 8.8 Hz, 2H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ -80.8 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 159.9 (t, *J* = 30.8 Hz), 143.5, 141.6, 129.8, 129.1, 119.2 (t, *J* = 294.8 Hz), 64.8, 13.7. **IR** (neat, cm<sup>-1</sup>) *ν*: 2927, 1757, 1571, 1475, 1348, 1302, 1157, 1089, 1010, 826, 752, 561. **HRMS** (ESI<sup>+</sup>) calcd for C<sub>10</sub>H<sub>13</sub>F<sub>2</sub>NO<sub>4</sub>S<sub>2</sub>Cl *m/z* 347.9943 [M+NH<sub>4</sub>]<sup>+</sup>, Found 347.9946 (Δ = 0.9 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-fluorobenzene-sulfonylthioate **2f**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2f** as a colorless oil (37.7 mg, **60%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.41. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 8.08 – 7.95 (m, 2H), 7.31 – 7.21 (m, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –81.0 (s), –101.1 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 167.7 (d, *J* = 259.1 Hz), 160.0 (t, *J* = 30.9 Hz), 141.1, 130.8 (d, *J* = 9.9 Hz), 119.2 (t, *J* = 294.6 Hz), 116.8 (d, *J* = 23.1 Hz), 64.8, 13.7. IR (neat, cm<sup>–1</sup>) *v*: 2989, 1772, 1588, 1492, 1354, 1294, 1241, 1146, 970, 838, 656, 571. HRMS (ESI<sup>+</sup>) calcd for C<sub>10</sub>H<sub>13</sub>NF<sub>3</sub>O<sub>4</sub>S<sub>2</sub> *m/z* 332.0238 [M+NH<sub>4</sub>]<sup>+</sup>, Found 332.0234 (Δ = -1.2 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-trifluoromethyl-benzenesulfonylthioate **2g**: Purification by flash chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2g** as a colorless oil (50.3 mg, **69%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.32. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 8.13 (d, *J* = 8.3 Hz, 2H), 7.86 (d, *J* = 8.4 Hz, 2H), 4.39 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –63.8 (s), –80.4 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 159.8 (t, *J* = 30.7 Hz), 148.2, 136.2 (q, *J* = 33.4 Hz), 128.2, 126.7 (q, *J* = 3.7 Hz), 122.9 (q, *J* = 273.4 Hz), 119.2 (t, *J* = 295.4 Hz), 65.0, 13.7. IR (neat, cm<sup>–1</sup>) *v*: 3107, 2996, 1761, 1407, 1350, 1303, 1210, 1123, 1059, 1012, 847, 709, 549. HRMS (API) calcd for C<sub>11</sub>H<sub>9</sub>O<sub>4</sub>F<sub>5</sub>S<sub>2</sub>Cl *m/z* 398.9551 [M+Cl]<sup>+</sup>, Found 398.9550 (Δ = -0.3 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-cyanobenzene-sulfonylthioate **2h**: Purification by reverse flash chromatography (35 g column, 50 mL/min, H<sub>2</sub>O/MeCN=50/50 until H<sub>2</sub>O/MeCN=0/100) afforded **2h** as a colorless oil (32.0 mg, **50%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.35. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 8.11 (d, *J* = 8.6 Hz, 2H), 7.89 (d, *J* = 8.6 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –80.2 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 159.7 (t, *J* = 30.5 Hz), 148.5, 133.3, 128.2, 119.2 (t, *J* = 295.8 Hz), 118.4, 116.7, 65.0, 13.8. IR (neat, cm<sup>–1</sup>) *v*: 2987, 2237, 1772, 1355, 1288, 1154, 1015, 967, 837, 570. HRMS (API) calcd for C<sub>11</sub>H<sub>9</sub>F<sub>2</sub>NO<sub>4</sub>S<sub>2</sub> *m/z* 320.9941 [M]<sup>+</sup>, Found 320.9946 (Δ = 1.6 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-acetyl-benzene-sulfonylthioate **2i**: Purification by reverse flash column chromatography (35 g column, 50 mL/min, H<sub>2</sub>O/MeCN=50/50 until H<sub>2</sub>O/MeCN=0/100) afforded **2i** as a colorless oil (48.7 mg, **72%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.45. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 8.17 – 8.04 (m, 4H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.67 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –80.5 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 196.3, 159.9 (t, *J* = 30.9 Hz), 148.4, 141.3, 129.2, 128.0, 119.2 (t, *J* = 295.4 Hz), 64.9, 27.0, 13.8. IR (neat, cm<sup>–1</sup>) *v*: 2925, 1775, 1692, 1652, 1399, 1352, 1260, 1155, 965, 833, 594. HRMS (API) calcd for C<sub>12</sub>H<sub>12</sub>F<sub>2</sub>O<sub>5</sub>S<sub>2</sub>Cl *m/z* 372.9783 [M+Cl]<sup>+</sup>, Found 372.9781 (Δ = -0.5 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-3-methoxybenzene-sulfonylthioate **2j**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=90/10) afforded **2j** as a colorless oil (45.7 mg, **70%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.53. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 7.61 – 7.55 (m, 1H), 7.53 – 7.44 (m, 2H), 7.25 – 7.18 (m, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 3.89 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –80.8 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 160.1 (t, *J* = 31.0 Hz), 160.0, 146.1, 130.4, 121.6, 119.7, 119.2 (t, *J* = 294.4 Hz), 111.7, 64.7, 55.8, 13.8. IR (neat, cm<sup>–1</sup>) *v*: 2943, 1772, 1596, 1480, 1289, 1244, 1139, 969, 851, 783, 677, 608. HRMS (ESI<sup>+</sup>) calcd for C<sub>11</sub>H<sub>16</sub>NO<sub>5</sub>F<sub>2</sub>S<sub>2</sub> *m/z* 344.0438 [M+NH<sub>4</sub>]<sup>+</sup>, Found 344.0448 (Δ = 2.9 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-2-iodobenzene-sulfonylthioate **2k**: Purification by reverse flash column chromatography (35 g column, 50 mL/min, H<sub>2</sub>O/MeCN=50/50 until H<sub>2</sub>O/MeCN=0/100) afforded **2k** as a colorless oil (66.7 mg, **79%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.38. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 8.23 – 8.12 (m, 2H), 7.61 – 7.52 (m, 1H), 7.31 (td, *J* = 7.7 Hz and *J* = 1.5 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –80.9 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 160.1 (t, *J* = 31.0 Hz), 146.3, 143.1, 135.0, 130.9, 128.8, 119.2 (t, *J* = 294.9 Hz), 92.7, 64.7, 13.8. IR (neat, cm<sup>–1</sup>) *v*: 2988, 1770, 1566, 1446, 1350, 1298, 1156, 1011, 968, 759, 579. HRMS (ESI<sup>+</sup>) calcd for C<sub>10</sub>H<sub>10</sub>O<sub>4</sub>F<sub>2</sub>S<sub>2</sub>I *m/z* 422.9033 [M+H]<sup>+</sup>, Found 422.9024 (Δ = -2.1 ppm).

*S*-(Ethoxycarbonyl)difluoromethylbenzothioate **4a**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4a** as a colorless oil (48.4 mg, **93%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.35. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 7.89 – 7.82 (m, 2H), 7.69 – 7.61 (m, 1H), 7.53 – 7.43 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –85.8 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 187.3 (t, *J* = 3.5 Hz), 161.2 (t, *J* = 30.9 Hz), 135.2 (t, *J* = 2.9 Hz), 134.9, 129.1, 127.6, 120.4 (t, *J* = 284.9 Hz), 64.1, 13.8. IR (neat, cm<sup>–1</sup>) *v*: 2987, 2130, 1767, 1683, 1583, 1450, 1372, 1301, 1210, 1131, 1026, 894, 772, 683. HRMS (CI<sup>+</sup>) calcd for C<sub>11</sub>H<sub>11</sub>F<sub>2</sub>O<sub>3</sub>S *m/z* 261.0397 [M+H]<sup>+</sup>, Found 261.0405 (Δ = 3.2 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-2-naphthothioate **4b**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4b** as a colorless oil (49.6 mg, **80%**). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.38. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>) δ 8.42 (s, 1H), 8.01 – 7.80 (m, 4H), 7.70 – 7.51 (m, 2H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>) δ –85.6 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 187.1 (t, *J* = 3.2 Hz), 161.3 (t, *J* = 30.9 Hz), 136.3, 132.4 (t, *J* = 2.8 Hz), 132.2, 129.8, 129.7, 129.4, 129.1, 127.9, 127.4, 122.5, 120.5 (t, *J* = 284.9 Hz), 64.1, 13.8. IR (neat, cm<sup>–1</sup>) *v*: 2986, 1766, 1681, 1626, 1466, 1370, 1300,



1214, 1121, 1018, 977, 904, 862, 790, 748, 597. **HRMS** (API<sup>+</sup>) calcd for C<sub>15</sub>H<sub>13</sub>F<sub>2</sub>O<sub>3</sub>S *m/z* 311.0553 [M+H]<sup>+</sup>, Found 311.0563 (Δ = 3.9 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-methoxy-benzothioate **4c**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4c** as a colorless oil (50.5 mg, **87%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.42. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 7.82 (d, *J* = 8.9 Hz, 2H), 6.94 (d, *J* = 8.9 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz, CDCl<sub>3</sub>) δ -85.7 (s). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 185.4 (t, *J* = 3.4 Hz), 165.0, 161.4 (t, *J* = 31.0 Hz), 130.0, 127.8 (t, *J* = 2.9 Hz), 120.5 (t, *J* = 284.1 Hz), 114.2, 64.0, 55.6, 13.8. **IR** (neat, cm<sup>-1</sup>) *v*: 2985, 1770, 1671, 1598, 1509, 1464, 1265, 1221, 1168, 1129, 1023, 896, 836, 617. **HRMS** (API<sup>+</sup>) calcd for C<sub>12</sub>H<sub>13</sub>F<sub>2</sub>O<sub>4</sub>S *m/z* 291.0503 [M+H]<sup>+</sup>, Found 291.0504 (Δ = 2.9 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-chloro-benzothioate **4d**: Purification by reverse flash column chromatography (35 g column, 50 mL/min, H<sub>2</sub>O/MeCN=50/50 until H<sub>2</sub>O/MeCN=0/100) afforded **4d** as a colorless oil (24.7 mg, **42%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.35. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 8.8 Hz, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz, CDCl<sub>3</sub>) δ -85.6 (s). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 186.1 (t, *J* = 3.5 Hz), 161.1 (t, *J* = 30.7 Hz), 141.6, 133.4 (t, *J* = 2.9 Hz), 129.5, 128.9, 120.3 (t, *J* = 285.7 Hz), 64.2, 13.8. **IR** (neat, cm<sup>-1</sup>) *v*: 2987, 1767, 1683, 1587, 1488, 1401, 1301, 1207, 1088, 1012, 895, 835, 732, 584. **HRMS** (API<sup>+</sup>) calcd for C<sub>11</sub>H<sub>10</sub>ClF<sub>2</sub>O<sub>3</sub>S *m/z* 295.0007 [M+H]<sup>+</sup>, Found 295.0007 (Δ = 0.0 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-trifluoromethyl-benzothioate **4e**: Purification by reverse flash column chromatography (35 g column, 50 mL/min, H<sub>2</sub>O/MeCN=50/50 until H<sub>2</sub>O/MeCN=0/100) afforded **4e** as a colorless oil (53.2 mg, **81%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.31. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz, CDCl<sub>3</sub>) δ -63.9 (s), -85.5 (s). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 186.6 (t, *J* = 3.6 Hz), 160.9 (t, *J* = 30.7 Hz), 136.1 (q, *J* = 33.1 Hz), 127.9, 126.2 (q, *J* = 3.7 Hz), 122.7 (q, *J* = 273.2 Hz), 120.2 (t, *J* = 286.4 Hz), 64.3, 13.8. **IR** (neat, cm<sup>-1</sup>) *v*: 2987, 1774, 1695, 1448, 1410, 1323, 1210, 1173, 1132, 1066, 1015, 905, 650. **HRMS** (API<sup>+</sup>) calcd for C<sub>12</sub>H<sub>10</sub>F<sub>5</sub>O<sub>3</sub>S *m/z* 329.0271 [M+H]<sup>+</sup>, Found 329.0269 (Δ = -0.6 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-4-methyl-carboxylatebenzothioate **4f**: Purification by reverse flash column chromatography (35 g column, 50 mL/min, H<sub>2</sub>O/MeCN=50/50 until H<sub>2</sub>O/MeCN=0/100) afforded **4f** as a colorless oil (21.2 mg, **33%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.37. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 8.15 (d, *J* = 8.7 Hz, 2H), 7.92 (d, *J* = 8.7 Hz, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz, CDCl<sub>3</sub>) δ -85.6 (s). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 186.9 (t, *J* = 3.5 Hz), 165.6, 161.0 (t, *J* = 30.6 Hz), 138.2 (t, *J* = 2.8 Hz), 135.5, 130.2, 127.5, 120.3 (t, *J* = 286.1 Hz), 64.2, 52.7, 13.8. **IR** (neat, cm<sup>-1</sup>) *v*: 2956, 1769, 1721, 1682, 1500, 1438, 1406, 1372, 1281, 1207, 1089, 1000, 897, 823, 774, 697. **HRMS** (ESI<sup>+</sup>) calcd for C<sub>13</sub>H<sub>12</sub>F<sub>2</sub>O<sub>5</sub>SNa *m/z* 341.0271 [M+Na]<sup>+</sup>, Found 341.0268 (Δ = -0.9 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-3-bromobenzothioate **4g**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4g** as a colorless oil (40.0 mg, **59%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.33. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 8.01 – 7.95 (m, 1H), 7.82 – 7.73 (m, 2H), 7.42 – 7.34 (m, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz, CDCl<sub>3</sub>) δ -85.5 (s). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 186.1 (t, *J* = 3.6 Hz), 161.0 (t, *J* = 30.7 Hz), 137.7, 136.7 (t, *J* = 2.8 Hz), 130.6, 130.4, 126.1, 123.3, 120.2 (t, *J* = 286.1 Hz), 64.2, 16.8. **IR** (neat, cm<sup>-1</sup>) *v*: 2987, 1766, 1688, 1567, 1471, 1418, 1372, 1300, 1197, 1133, 997, 914, 710. **HRMS** (CI<sup>+</sup>) calcd for C<sub>11</sub>H<sub>10</sub>BrF<sub>2</sub>O<sub>3</sub>S *m/z* 338.9502 [M+H]<sup>+</sup>, Found 338.9503 (Δ = 0.3 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-2-methyl-benzothioate **4h**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4h** as a colorless oil (40.0 mg, **73%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.39. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 7.75 (d, *J* = 7.9 Hz, 1H), 7.51 – 7.44 (td, *J* = 7.6 Hz and *J* = 1.3 Hz, 1H), 7.35 – 7.25 (m, 2H), 4.44 (q, *J* = 7.1 Hz, 2H), 2.49 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz, CDCl<sub>3</sub>) δ -86.4 (s). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 188.7 (t, *J* = 3.2 Hz), 161.3 (t, *J* = 31.0 Hz), 138.4, 134.7 (t, *J* = 2.8 Hz), 133.3, 132.2, 129.0, 126.2, 120.3 (t, *J* = 284.4 Hz), 64.0, 20.8, 13.8. **IR** (neat, cm<sup>-1</sup>) *v*: 2986, 2131, 1774, 1696, 1571, 1457, 1372, 1285, 1195, 1132, 1015, 890, 766, 648. **HRMS** (CI<sup>+</sup>) calcd for C<sub>12</sub>H<sub>13</sub>F<sub>2</sub>O<sub>3</sub>S *m/z* 275.0542 [M]<sup>+</sup>, Found 275.0546 (Δ = 1.6 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-3,4-dimethoxy-benzothioate **4i**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4i** as a colorless oil (52.5 mg, **82%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.43. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 7.51 (dd, *J* = 8.5 Hz and *J* = 2.1 Hz, 1H), 7.32 (d, *J* = 2.1 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.95 (s), 3.90 (s), 1.38 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz, CDCl<sub>3</sub>) δ -85.7 (s). **<sup>13</sup>C NMR** (75.5 MHz, CDCl<sub>3</sub>) δ 185.6 (t, *J* = 3.5 Hz), 161.4 (t, *J* = 30.9 Hz), 154.8, 149.3, 128.0 (t, *J* = 2.9 Hz), 122.7, 120.5 (t, *J* = 284.4 Hz), 110.4, 109.3, 64.0, 56.2, 56.1, 13.8. **IR** (neat, cm<sup>-1</sup>) *v*: 2942, 1771, 1666, 1583, 1512, 1468, 1418, 1268, 1141, 1016, 977, 861, 803, 763, 658. **HRMS** (API<sup>+</sup>) calcd for C<sub>13</sub>H<sub>15</sub>F<sub>2</sub>O<sub>5</sub>S *m/z* 321.0608 [M+H]<sup>+</sup>, Found 321.0609 (Δ = 0.3 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-1*H*-indole-3-carbo-thioate **4j**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4j** as a colorless oil (43.7 mg, **73%**). **R<sub>f</sub>** (Petroleum ether/EtOAc=90/10): 0.27. **<sup>1</sup>H NMR** (300.1 MHz, CDCl<sub>3</sub>) δ 9.20 (bs, 1H), 8.16 – 8.08 (m, 1H), 7.91 (d, *J* = 3.0 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.35 – 7.26 (m, 2H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). **<sup>19</sup>F{<sup>1</sup>H} NMR** (282.4 MHz,

CDCl<sub>3</sub>)  $\delta$  -84.9 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta$  178.8 (t,  $J$  = 3.2 Hz), 162.0 (t,  $J$  = 31.5 Hz), 136.2, 132.1, 124.5, 124.4, 121.5, 120.6 (t,  $J$  = 284.8 Hz), 115.8 (t,  $J$  = 3.2 Hz), 112.0, 64.2, 13.8. IR (neat, cm<sup>-1</sup>)  $\nu$ : 3371, 2922, 1752, 1664, 1514, 1416, 1297, 1123, 1001, 884, 822, 746, 651. HRMS (API<sup>+</sup>) calcd for C<sub>13</sub>H<sub>12</sub>NF<sub>2</sub>O<sub>3</sub>S  $m/z$  300.0506 [M+H]<sup>+</sup>, Found 300.0503 ( $\Delta$  = -1.0 ppm).

*S*-(Ethoxycarbonyl)difluoromethyl-cyclohexanethioate **4k**: Purification by flash column chromatography (height: 15 cm, width: 3 cm, pentane/diethyl ether=95/05) afforded **4k** as a colorless oil (23.4 mg, 44%). *R<sub>f</sub>* (Petroleum ether/EtOAc=90/10): 0.40. <sup>1</sup>H NMR (300.1 MHz, CDCl<sub>3</sub>)  $\delta$  4.37 (q,  $J$  = 7.1 Hz, 2H), 2.55 – 2.41 (m, 2H), 1.86 – 1.71 (m, 2H), 1.71 – 1.58 (m, 1H), 1.54 – 1.38 (m, 2H), 1.36 (t,  $J$  = 7.1 Hz, 2H), 1.32 – 1.12 (m, 3H). <sup>19</sup>F{<sup>1</sup>H} NMR (282.4 MHz, CDCl<sub>3</sub>)  $\delta$  -86.1 (s). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta$  198.2 (t,  $J$  = 2.0 Hz), 161.2 (t,  $J$  = 31.0 Hz), 120.2 (t,  $J$  = 284.6 Hz), 63.9, 52.8 (t,  $J$  = 2.4 Hz), 28.8, 25.4, 25.1, 13.8. IR (neat, cm<sup>-1</sup>)  $\nu$ : 2935, 2959, 1776, 1709, 1451, 1371, 1288, 1131, 1078, 1024, 957, 742. HRMS (API<sup>+</sup>) calcd for C<sub>11</sub>H<sub>17</sub>F<sub>2</sub>O<sub>3</sub>S  $m/z$  267.0866 [M+H]<sup>+</sup>, Found 267.0866 ( $\Delta$  = 0.0 ppm).

## Acknowledgements

This work has been partially supported by University of Rouen Normandy, INSA Rouen Normandy, the Centre National de la Recherche Scientifique (CNRS), European Regional Development Fund (ERDF), Labex SynOrg (ANR-11-LABX-0029), Carnot Institute I2C, the graduate school for research XL-Chem (ANR-18-EURE-0020 XL CHEM), and by Region Normandie. F.P.-C. and T.B. thank the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement no. 758710). F.P.-C. thanks the Region Normandy for a doctoral fellowship.

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