

## Electronic Supporting Information

### Formal $\alpha$ -trifluoromethylthiolation of carboxylic acid derivatives via *N*-acyl pyrazoles

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## General Methods

All reactions requiring dry or inert conditions were conducted in flame-dried glassware under a positive pressure of nitrogen. Anhydrous THF, toluene, methanol, 1,2-dichloroethane and acetonitrile were purchased from Aldrich and used as received, all other solvents were dried over molecular sieves. Molecular sieves (Aldrich Molecular Sieves, 3 Å, 1.6 mm pellets) were activated under vacuum at 200 °C overnight. Reactions were monitored by thin layer chromatography (TLC) on Macherey-Nagel pre-coated silica gel plates (0.25 mm) and visualized by UV light. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). <sup>1</sup>H NMR, <sup>13</sup>C NMR and <sup>19</sup>F NMR spectra were recorded on Bruker Avance III HD 600, Bruker Avance-400 or Bruker Avance-300 spectrometer in CDCl<sub>3</sub> as solvents at room temperature. Chemical shifts for protons are reported using residual solvent protons (<sup>1</sup>H NMR: δ = 7.26 ppm for CDCl<sub>3</sub>) as internal standard. Carbon spectra were referenced to the shift of the <sup>13</sup>C signal of CDCl<sub>3</sub> (δ = 77.0 ppm). The following abbreviations are used to indicate the multiplicity in NMR spectra: s - singlet; d - doublet; t - triplet; q - quartet; dd – double doublet; ddd – doublet of doublet of doublets; dq – doublet of quartets; m - multiplet; sept – septet; bs - broad signal.

IR measures were conducted on KBr pills using a Bruker Tensor 27 and maximum absorptions are reported in wavelength (cm<sup>-1</sup>). High resolution mass spectra (HRMS) were acquired using a Bruker solariX XR Fourier transform ion cyclotron resonance mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a 7 T refrigerated actively-shielded superconducting magnet. The samples were ionized in positive ion mode using a MALDI or ESI ionization sources. Melting points were measured with a Stuart Model SMP 30 melting point apparatus and are uncorrected.

Petrol ether (PE) refers to light petroleum ether (boiling point 40-60 °C). All starting materials (unless otherwise noted) were purchased from Aldrich and used as received.

N-bromophthalimide, N-chlorosuccinimide, dibenzensulfonamide and silver(I)trifluoromethanethiolate were purchased from TCI and used as received. Proton sponge was purchased from Sigma Aldrich and used as received. Reagents **2a-c** are known compounds, they were prepared according to the literature.<sup>1</sup> The pyrazolamides **1** were prepared by using general procedures reported in the literature.<sup>2</sup>

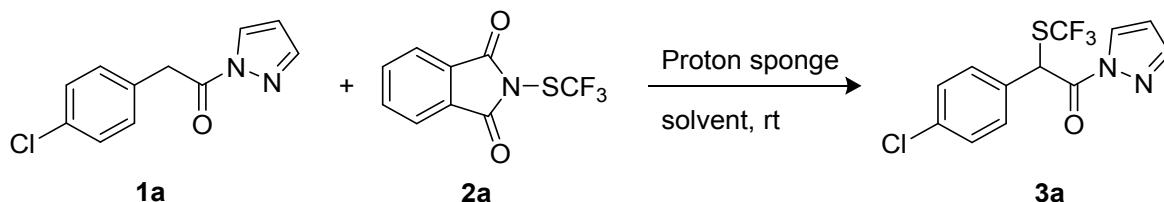
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<sup>1</sup> (a) Kang, K.; Xu, C.; Shen, Q. *Org. Chem. Front.* **2014**, *1*, 294; (b) Lefebvre, Q.; Fava, E.; Nikolaienko, P.; Rueping, M. *Chem. Commun.*, **2014**, *50*, 6617; (c) Zhang, P.; Li, M.; Xue, X.; Xu, C.; Zhao, Q.; Liu, Y.; Wang, H.; Guo, Y.; Lu, L.; Shen, Q. *J. Org. Chem.*, **2016**, *81*, 7486.

<sup>2</sup> Zhang, J.; Liu, X.; Wang, R. *Chem. Eur. J.* **2014**, *20*, 4911.

## Experimental Procedures and Compounds Characterization

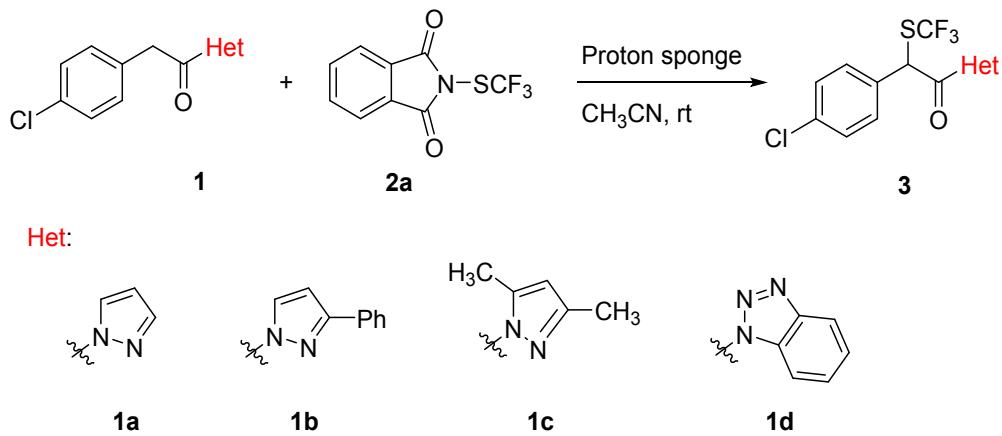
**Table S1. Solvent screening<sup>[a]</sup>**



Entry	solvent	t [h]	Conv. <b>3a</b> [%] <sup>[b]</sup>
1	CH <sub>3</sub> CN	6	75
2	CH <sub>2</sub> Cl <sub>2</sub>	6	10
3	toluene	6	16
4	MeO <i>t</i> Bu	6	31
5	AcOEt	6	21
6 <sup>[c]</sup>	DMF	6	41
7 <sup>[c]</sup>	DMSO	6	76

<sup>[a]</sup> Unless otherwise noted reactions were conducted with **1a** (0.1 mmol), **2a** (0.12 mmol), PS (20 mol%) in anhydrous solvent (0.5 mL) under nitrogen atmosphere. <sup>[b]</sup> Determined by <sup>1</sup>H NMR and <sup>19</sup>F NMR spectroscopy of crude reaction mixture using 1,3,5-trimethoxybenzene and  $\alpha,\alpha,\alpha$ -trifluorotoluene as internal standard. <sup>[c]</sup> After reaction, the solvent was removed with aqueous extraction and the product was hydrolyzed.

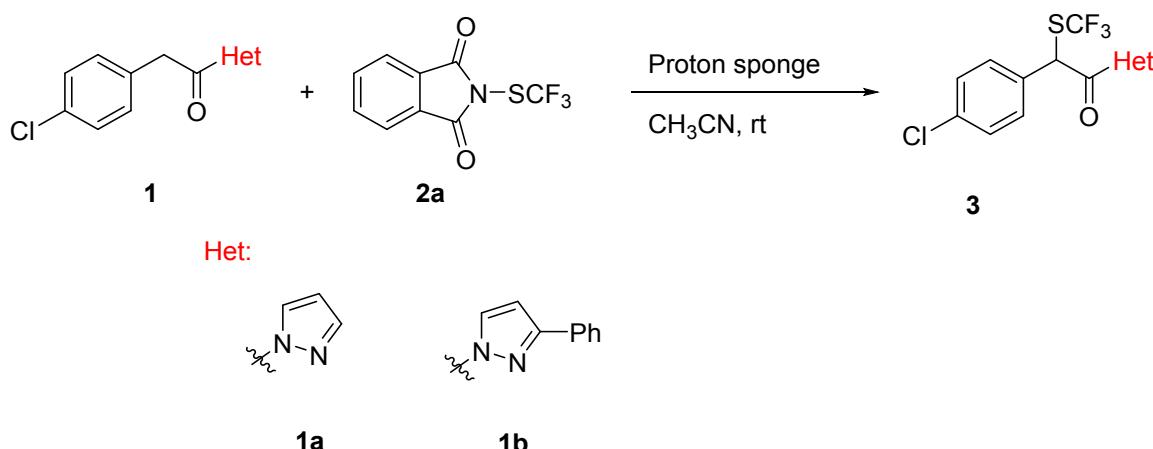
**Table S2. Substrate screening<sup>[a]</sup>**



Entry	<b>1</b>	t [h]	Conv. <b>3</b> [%] <sup>[b]</sup>	Yield [%] <sup>[c]</sup>
1	<b>1a</b>	6	75	63
2	<b>1b</b>	6	91	39
3	<b>1c</b>	6	7	-
4	<b>1d</b>	6	69	0

<sup>[a]</sup> Unless otherwise noted reactions were conducted with **1** (0.1 mmol), **2a** (0.12 mmol), **PS** (0.02 mmol), in anhydrous acetonitrile (0.5 mL) under nitrogen atmosphere. <sup>[b]</sup> Determined by <sup>1</sup>H NMR and <sup>19</sup>F NMR spectroscopy of crude reaction mixture using 1,3,5-trimethoxybenzene and  $\alpha,\alpha,\alpha$ -trifluorotoluene as internal standard. <sup>[c]</sup> Yield of isolated product.

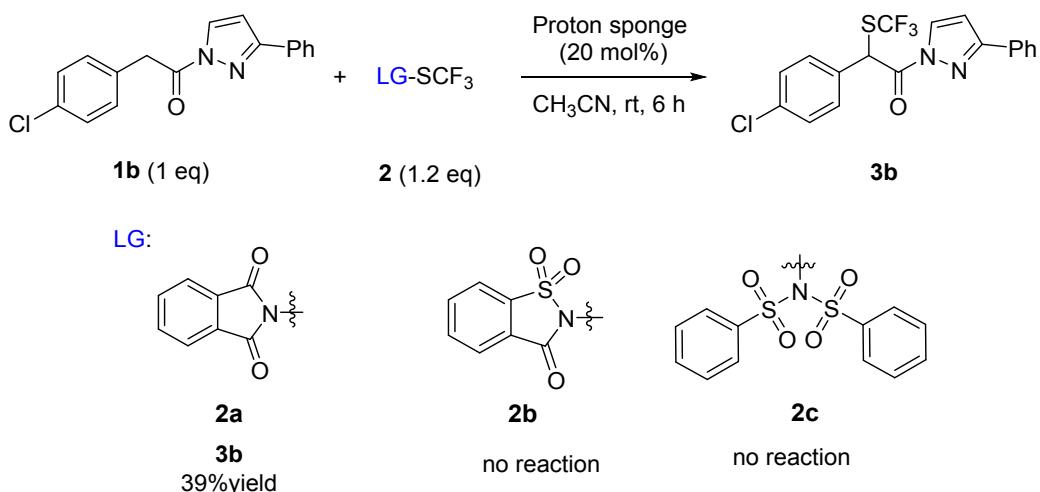
**Table S3. Optimization of reaction parameters<sup>[a]</sup>**



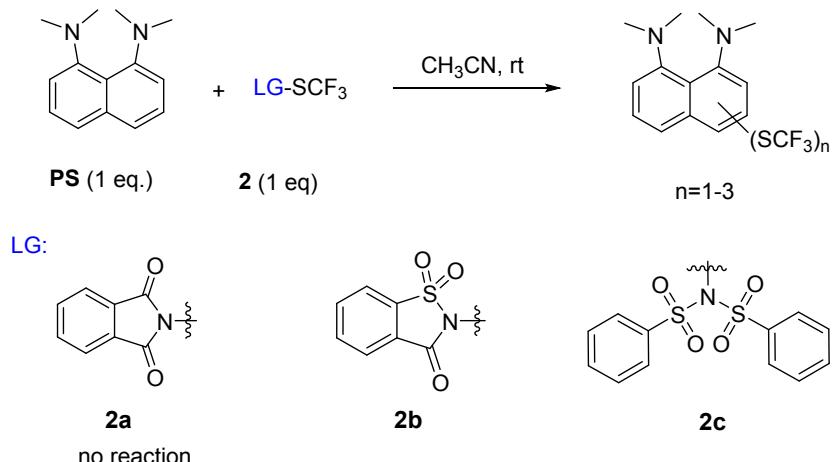
Entry	<b>1</b>	<b>1</b> [M]	<b>2a</b> (eq)	<b>PS</b> (eq)	t [h]	Conv. [%] <sup>[b]</sup>	Yield [%] <sup>[c]</sup>
1	<b>1a</b>	0.2	1.2	1	1	84	63%
2	<b>1b</b>	0.2	1.2	0.2	6	91	39%
3	<b>1b</b>	0.2	1.2	0.1	6	45	-
4	<b>1b</b>	0.5	1.2	0.2	6	60	-
5	<b>1b</b>	0.15	1.2	0.2	6	78	-
6 <sup>[d]</sup>	<b>1b</b>	0.2	1.2	0.2	4.5	68	-

<sup>[a]</sup> Unless otherwise noted reactions were conducted with **1a** (0.1 mmol), **2a** (0.12 mmol), **PS** (20 mol%) in anhydrous acetonitrile (0.5 mL) under nitrogen atmosphere. <sup>[b]</sup> Determined by <sup>1</sup>H NMR and <sup>19</sup>F NMR spectroscopy of crude reaction mixture using 1,3,5-trimethoxybenzene and  $\alpha,\alpha,\alpha$ -trifluorotoluene as internal standard. <sup>[c]</sup> Yield of isolated product. <sup>[d]</sup> T = 45°C.

**Table S4. Electrophile screening**

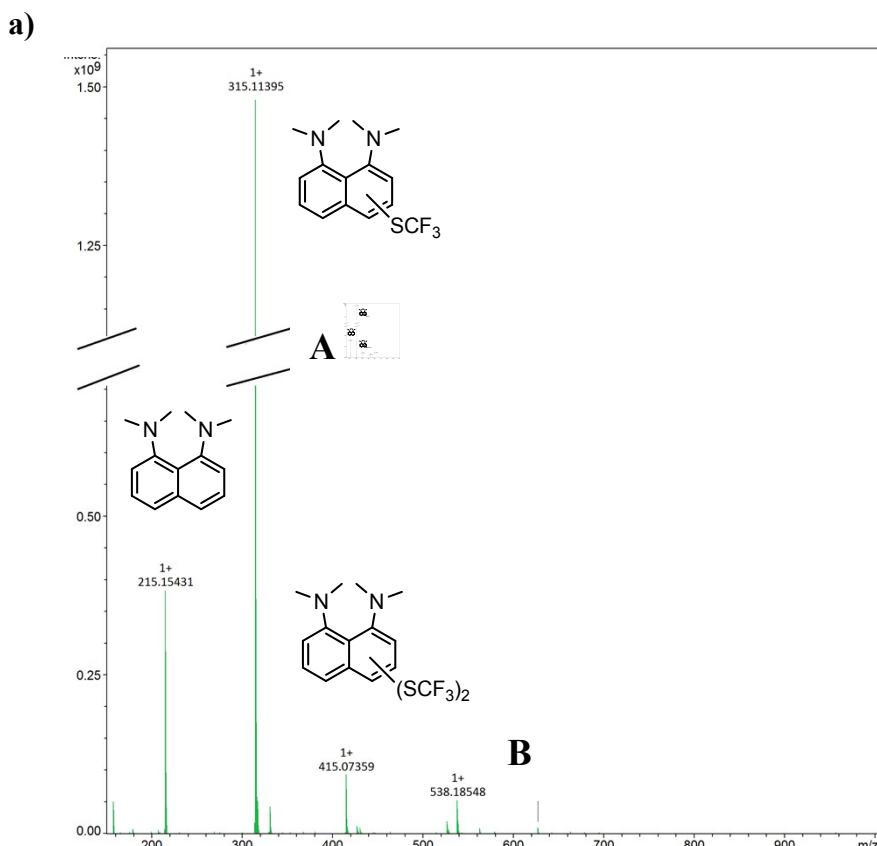


## Reaction between PS and trifluoromethylthiolating agents

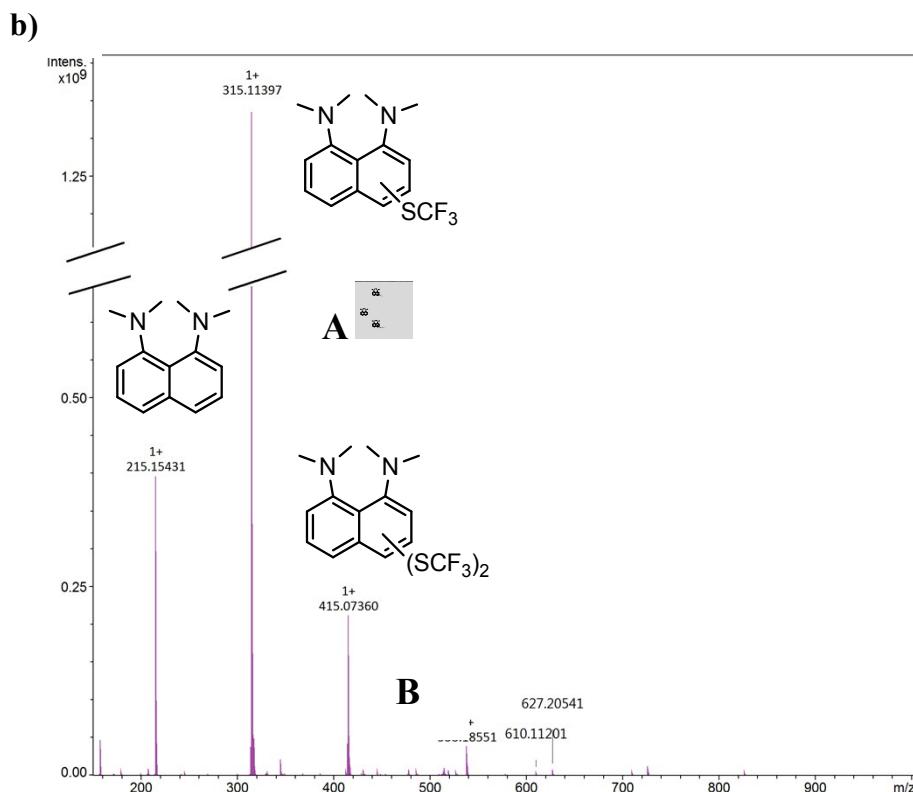


In an oven-dried vial, proton-sponge **PS** (0.2 mmol), trifluoromethylthiolating agent **2** (0.2 mmol) and anhydrous acetonitrile (1 mL) were introduced. The reaction mixture was stirred at room temperature and monitored by TLC for 6 h. When electrophilic reagents **2b** and **2c** were used, the formation of several products of trifluoromethylthiolation of **PS** at different positions of the aromatic moiety were observed after 30 minutes.<sup>3</sup> After completion, the crude mixture was filtrated and analyzed by high resolution mass spectrometry.

### HRMS (ESI-FT ICR) analysis of the crude reaction mixture a) using **2b**; b) using **2c**



<sup>3</sup> Sorokin, V.I.; Pozharskii, A. F.; Ozeryanskii, V. A. *J. Fluorine Chem.*, **2013**, 154, 67.



The high-resolution mass spectrometry analysis (HRMS) of the crude reaction mixture shows the formation of two main products reported in order of intensity of the corresponding molecular peaks:

a) The mono trifluoromethylthiolated proton sponge **A**

$[\mathbf{A}+\mathbf{H}]^+$  Found: m/z 315.1140, Calcd: m/z 315.1143

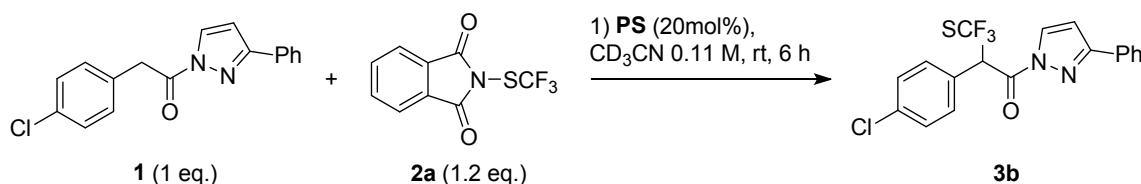
b) The bis trifluoromethylthiolated proton sponge **B**

$[\mathbf{B}+\mathbf{H}]^+$  Found: m/z 415.0736, Calcd: m/z 415.0737

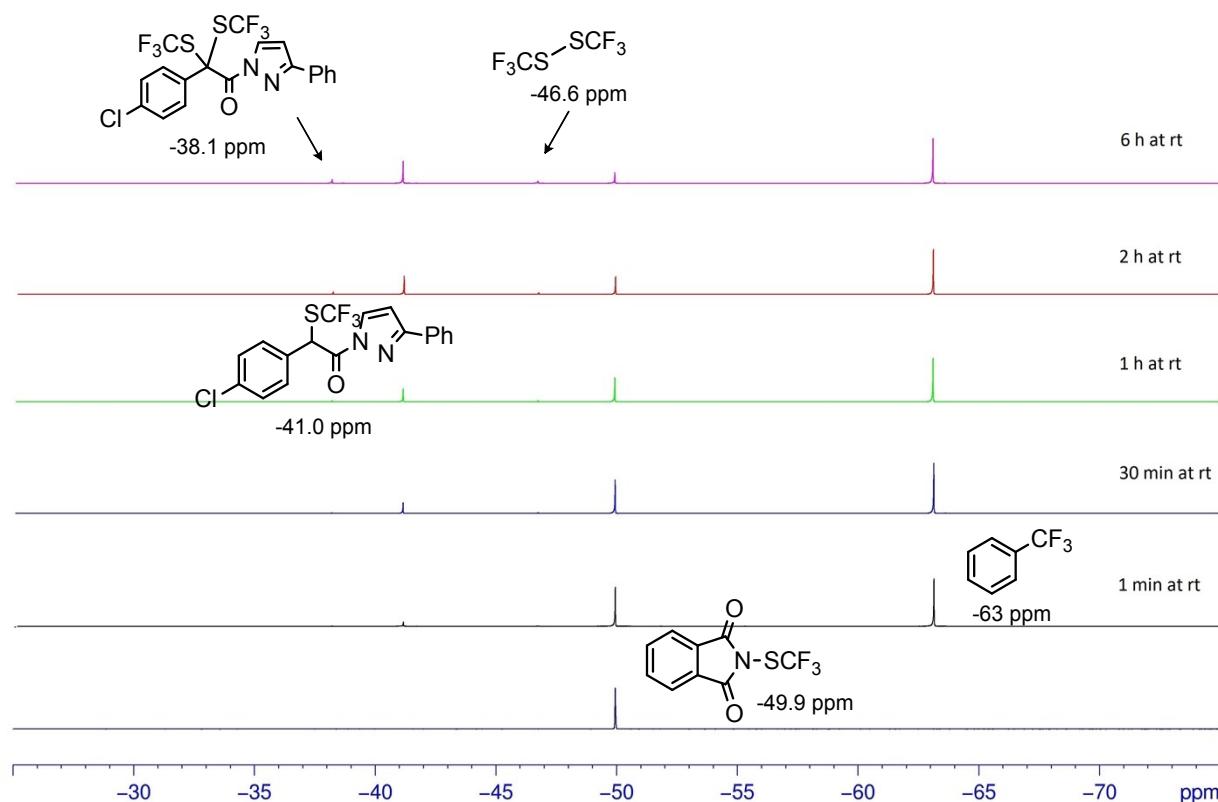
High resolution mass spectrometry analysis demonstrates, as expected from literature data,<sup>4</sup> that more electrophilic trifluoromethylthiolating reagents, such as **2b** or **2c**, are unsuitable reagents because of the occurrence of the side reaction with the base **PS**. It is important to mention that the formation of trifluoromethylthiolated-proton sponge products of type **A** and **B** was not observed when reagent **2a** was used, even at higher temperature.

<sup>4</sup> Zhang, J.; Yang, J.; Zheng, H.; Xue, X.; Mayr, H.; Cheng, J. *Angew. Chem. Int. Ed.* **2018**, *57*, 12690.

**Monitoring the reaction of **1b** and **2a** promoted by **PS** in deuterated acetonitrile by <sup>19</sup>F NMR spectroscopy**



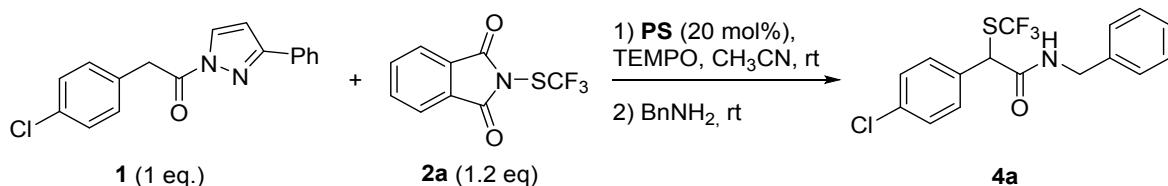
*N*-acylpyrazole **1b** (13.5 mg, 0.045 mmol, 1 equiv.), *N*-(trifluoromethylthio)phthalimide **2a** (13.5 mg, 0.054 mmol, 1.2 equiv.) and **PS** (1.95 mg, 0.009 mmol, 0.2 equiv.), were loaded into a NMR tube under nitrogen atmosphere and dissolved in anhydrous  $\text{CD}_3\text{CN}$  (0.4 mL). Trifluorotoluene (5.5  $\mu\text{L}$ , 0.045 mmol) was added as internal standard. The tube was shaken and the reaction was monitored by <sup>19</sup>F-NMR spectroscopy at 376 MHz at room temperature.



Product **3b** is rapidly formed, as demonstrated by the immediate formation of the corresponding peak at -41.0 ppm, after 1 minute. The gradual decrease of the intensity of the peak at -49.9 ppm, corresponding to the trifluoromethylthiolating agent **2a**, indicates its gradual consumption as the reaction proceeds. After 2 hours, the formation of two new peaks at -46.6 ppm and -38.1 ppm, corresponding to  $\text{CF}_3\text{SSCF}_3$  and the bis-trifluoromethylated product respectively, was observed.

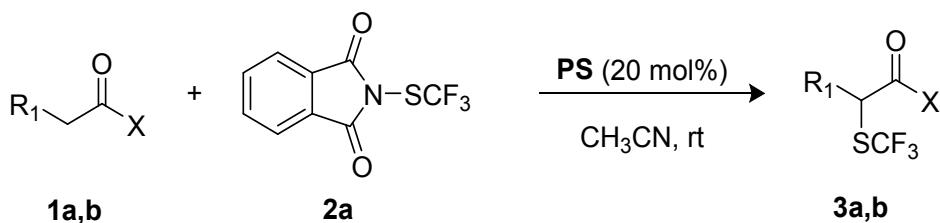
However, NMR spectra show that these products are present in traces, less than 5%, attesting that their formation is a negligible process.

### Synthesis of amide **4a** carried out in the presence of radical scavenger TEMPO



In an oven-dried vial, *N*-acylpyrazole **1b** (0.2 mmol), *N*-(trifluoromethylthio)phthalimide **2a** (0.24 mmol), 2,2,6,6-tetramethyl-1-piperidinyloxy TEMPO (0.2 mmol) and anhydrous acetonitrile (1 mL) were introduced, followed by the addition of **PS** (0.04 mmol) under nitrogen atmosphere. The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the first step, benzylamine (0.26 mmol) was added and the mixture was stirred at room temperature for the time reported in Table 2 in the paper. After completion, the solvent was evaporated, and the crude reaction mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 100/0 to 90/10) to afford product **4a** in 85% yield. This result demonstrated that in the presence of the radical scavenger, the amide **4a** was isolated with a comparable yield with respect to reaction performed in Table 2, thus ruling out the possibility that a radical mechanism is involved.

### General procedure for the synthesis of products **3a** and **3b**



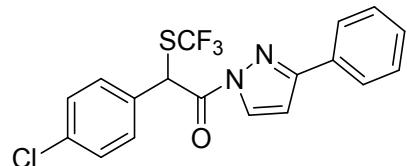
In an oven-dried vial *N*-acylpyrazole **1a** or **1b** (0.2 mmol), *N*-(trifluoromethylthio)phthalimide **2a** (0.24 mmol) and anhydrous acetonitrile (1 mL) were introduced. To this solution **PS** (0.04 mmol) was added under nitrogen atmosphere. The reaction mixture was stirred at rt and monitored by TLC. After completion, the crude mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 100/0 to 90/10) to afford products **3a** and **3b** in 39-63% yield. A significant decomposition of intermediates **3a** and **3b** was observed on silica gel, with respect to the conversion estimated by <sup>1</sup>H NMR analysis of the crude mixtures with the internal standard.

**2-(4-chlorophenyl)-1-(1H-pyrazol-1-yl)-2-((trifluoromethyl)thio)ethanone (3a)**



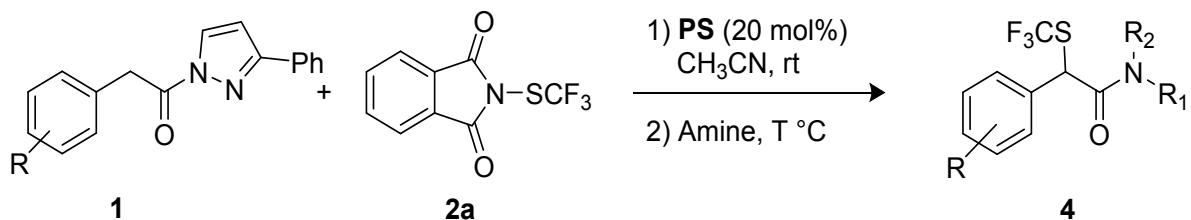
Colorless oil, 40.4 mg, 63% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3464, 1641, 1386, 1113, 757.  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  8.21 (d, 1H,  $J = 2.9$  Hz), 7.73 (d, 1H,  $J = 1.3$  Hz), 7.52 (d, 2H,  $J = 8.6$  Hz), 7.33 (d, 2H,  $J = 8.6$ ), 6.56 (s, 1H), 6.48 (dd, 1H,  $J = 2.9$  Hz,  $J = 1.3$  Hz).  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  166.9, 145.0, 135.2, 132.3, 130.1, 129.8 (q  $^1J_{\text{CF}} = 307.5$  Hz), 129.4, 129.1, 111.2, 49.1.  **$^{19}\text{F NMR}$**  ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.8. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_8\text{ClF}_3\text{N}_2\text{OS}$ : 320.9998, found: 320.9915.

**2-(4-chlorophenyl)-1-(3-phenyl-1H-pyrazol-1-yl)-2-((trifluoromethyl)thio)ethanone (3b)**



Colorless oil, 30.9 mg, 39% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3460, 1699, 1661, 1652, 1558, 1505, 1114, 758.  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  8.24 (d, 1H,  $J = 2.8$  Hz), 7.86 (d, 2H,  $J = 6.5$  Hz), 7.58 (d, 2H,  $J = 8.5$  Hz), 7.51-7.45 (m, 3H), 7.35 (d, 2H,  $J = 8.5$  Hz), 6.81 (d, 1H,  $J = 2.8$  Hz), 6.63 (s, 1H).  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  166.6, 156.4, 135.2, 132.6, 131.0, 130.3, 130.1, 129.9 (q  $^1J_{\text{CF}} = 307.6$  Hz), 129.7, 129.3, 128.9, 126.4, 109.1, 49.5.  **$^{19}\text{F NMR}$**  ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.7. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{18}\text{H}_{12}\text{ClF}_3\text{N}_2\text{OS}$ : 397.0311 found: 397.0348.

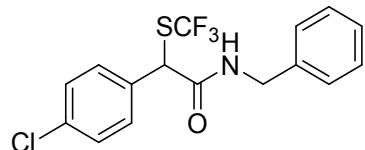
**General procedure for one-pot synthesis of  $\alpha$ -trifluoromethylthio amides**



In an oven-dried vial, under nitrogen atmosphere, **PS** (0.02 mmol) was added to a mixture of *N*-acylpyrazole **1** (0.2 mmol) and *N*-(trifluoromethylthio)phthalimide **2a** (0.24 mmol) in anhydrous acetonitrile (1 mL). The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the first step, the opportune amine (0.26 mmol) was added and the mixture was stirred for the time and at the temperature reported in Table 2 of the paper. After completion, the

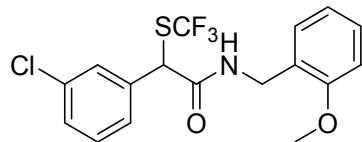
solvent was evaporated, and the crude mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 100/0 to 70/30) to afford products **4a-q** in 64-98% yield.

**N-benzyl-2-(4-chlorophenyl)-2-((trifluoromethyl)thio)acetamide (4a)**



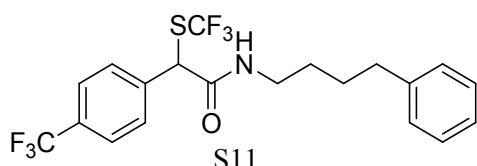
White solid, 64.7 mg, 90% yield. **mp** 127.8-129.1 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3460, 1649, 1560, 1491, 1154, 1115, 697. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.33-7.29 (m, 5H), 7.31 (d, 2H,  $J$  = 7.2 Hz), 7.17 (d, 2H,  $J$  = 7.2 Hz), 6.51 (bs, 1H), 5.01 (s, 1H), 4.45 (dd, 1H,  $J$  = 14.8 Hz,  $J$  = 5.8 Hz), 4.37 (dd, 1H,  $J$  = 14.8 Hz,  $J$  = 5.8 Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  167.1, 137.0, 135.1, 133.8, 129.7 (q,  $^1J_{\text{CF}} = 308.3$  Hz), 129.4 (2H), 128.8, 127.9, 127.7, 52.9, 44.3. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.6. **HRMS (MALDI-FT ICR)** exact mass [M+H]<sup>+</sup> calculated for  $\text{C}_{16}\text{H}_{13}\text{ClF}_3\text{NOS}$ : 360.0358, found: 360.0427.

**2-(3-chlorophenyl)-N-(2-methoxybenzyl)-2-((trifluoromethyl)thio)acetamide (4b)**



White solid, 56.1 mg, 72% yield. **mp** 97.0-98.8 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3450, 3304, 1652, 1558, 1495, 1464, 1246, 1155, 1115, 1030, 755. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.38 (s, 1H), 7.31-7.26 (m, 4H), 7.19 (d, 1H,  $J$  = 7.5 Hz), 6.90 (t, 1H,  $J$  = 7.5 Hz), 6.86 (d, 1H,  $J$  = 8.3 Hz), 6.70 (bs, 1H), 4.96 (s, 1H), 4.46 (dd, 1H,  $J$  = 14.3 Hz,  $J$  = 5.8 Hz), 4.41 (dd, 1H,  $J$  = 14.3 Hz,  $J$  = 5.8 Hz), 3.78 (s, 3H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  166.5, 157.4, 137.5, 134.9, 134.3, 130.3, 129.9, 129.7 (q,  $^1J_{\text{CF}} = 309.7$  Hz), 129.3, 129.1, 128.2, 126.4, 124.9, 120.7, 110.3, 55.1, 53.1, 40.7. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.7. **HRMS (MALDI-FT ICR)** exact mass [M+H]<sup>+</sup> calculated for  $\text{C}_{17}\text{H}_{15}\text{ClF}_3\text{NO}_2\text{S}$ : 390.0464, found: 390.0424.

**N-(4-phenylbutyl)-2-(4-(trifluoromethyl)phenyl)-2-((trifluoromethyl)thio)acetamide (4c)**



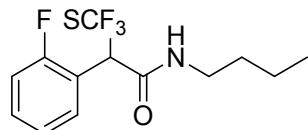
White solid, 85.3 mg, 98% yield. **mp** 86.6-88.4 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3460, 1654, 1326, 1169, 1112, 1064. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz): 7.63 (d, 2H,  $J = 8.2$  Hz), 7.53 (d, 2H,  $J = 8.2$  Hz), 7.30-7.25 (m, 2H), 7.20 (dt, 1H,  $J = 7.2$  Hz,  $J = 1.5$  Hz), 7.12 (dd, 2H,  $J = 7.2$  Hz,  $J = 1.5$  Hz), 6.04 (bs, 1H), 4.99, (s, 1H), 3.30 (q, 2H,  $J = 6.5$  Hz), 2.60 (t, 2H,  $J = 7.3$  Hz), 1.62-1.53 (m, 4H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  166.7, 141.8, 139.5, 131.2 (q,  ${}^2J_{\text{CF}} = 32.7$  Hz), 129.7 (q,  $J_{\text{CF}} = 307.9$  Hz), 128.5, 128.4, 128.3, 126.2 (q,  ${}^2J_{\text{CF}} = 3.3$  Hz), 125.9, 122.7 (q,  ${}^1J_{\text{CF}} = 272.6$  Hz), 53.0, 40.2, 35.3, 28.8, 28.4. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.6, -62.8. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{20}\text{H}_{19}\text{F}_6\text{NOS}$ : 436.1092, found: 436.1054.

### 2-(4-fluorophenyl)-N-(prop-2-yn-1-yl)-2-((trifluoromethyl)thio)acetamide (4d)



White solid, 42.0 mg, 74% yield. **mp** 117.8-118.7 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3460, 2032, 1646, 1508, 1231, 1112. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.39 (dd, 2H,  $J = 8.6$  Hz,  $J = 5.0$  Hz), 7.07 (dd, 2H,  $J = 8.6$  Hz), 6.31 (bs, 1H), 5.01 (s, 1H), 4.13 (ddd, 1H,  $J = 17.6$  Hz,  $J = 5.4$  Hz,  $J = 2.6$  Hz), 4.08 (ddd, 1H,  $J = 17.6$  Hz,  $J = 5.4$  Hz,  $J = 2.6$  Hz), 2.25 (dd, 1H,  ${}^1J = {}^2J = 2.6$  Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  167.2, 162.9 (d,  ${}^1J_{\text{CF}} = 248.0$  Hz), 130.6, 130.0 (d,  ${}^3J_{\text{CF}} = 8.4$  Hz), 129.6 (q,  ${}^1J_{\text{CF}} = 308.7$  Hz), 116.4 (d,  ${}^2J_{\text{CF}} = 21.8$  Hz), 78.2, 72.4, 52.4, 30.0. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.7, -111.7. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{Na}]^+$  calculated for  $\text{C}_{12}\text{H}_9\text{F}_4\text{NOS}$ : 314.0233 found: 314.0237.

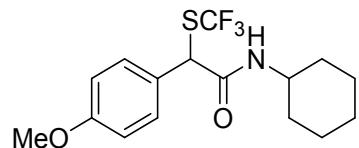
### N-butyl-2-(2-fluorophenyl)-2-((trifluoromethyl)thio)acetamide (4e)



White solid, 40.8 mg, 66% yield. **mp** 58.8-59.5 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3299, 3086, 2962, 2936, 2876, 1652, 1558, 1491, 1456, 1244, 1152, 1116. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.52 (t, 1H,  $J = 7.4$  Hz), 7.37-7.30 (m, 1H), 7.19-7.09 (m, 2H), 6.19 (bs, 1H), 5.28 (s, 1H), 3.27 (ddd, 2H,  $J = J = J = 7.2$  Hz), 1.48 (quint, 2H,  $J = 7.2$  Hz), 1.29 (sextet, 2H,  $J = 7.2$  Hz), 0.89 (t, 3H,  $J = 7.2$  Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  166.7, 159.7 (d,  ${}^1J_{\text{CF}} = 248.3$  Hz), 130.7 (d,  ${}^3J_{\text{CF}} = 8.5$  Hz), 129.9 (q,  ${}^1J_{\text{CF}}$

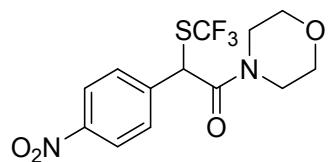
$= 309.0$  Hz), 129.7 (d,  $^4J_{CF} = 1.9$  Hz), 125.0 (d,  $^3J_{CF} = 3.5$  Hz), 123.2 (d,  $^2J_{CF} = 13.7$  Hz), 115.7 (d,  $^2J_{CF} = 25.4$  Hz), 46.3, 40.1, 31.2, 19.8, 13.6.  **$^{19}F$  NMR** ( $CDCl_3$ , 376 MHz):  $\delta$  -41.1, -117.3. **HRMS (MALDI-FT ICR)** exact mass  $[M+H]^+$  calculated for  $C_{13}H_{15}F_4NOS$ : 310.0810, found: 310.0856.

#### *N*-cyclohexyl-2-(4-methoxyphenyl)-2-((trifluoromethyl)thio)acetamide (4f)



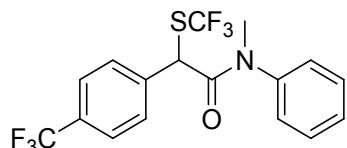
Pale yellow solid, 52.1 mg, 75% yield. **mp** 141.0-143.3 °C. **FTIR**  $\nu_{max}(KBr)/cm^{-1}$ : 3469, 2934, 2856, 1648, 1449, 1255, 1114, 526.  **$^1H$  NMR** ( $CDCl_3$ , 300 MHz):  $\delta$  7.31 (d, 2H,  $J = 8.7$  Hz), 6.88 (d, 2H,  $J = 8.7$  Hz), 6.02 (bs, 1H), 4.97 (s, 1H), 3.80 (s, 3H), 1.89-1.09 (m, 11 H).  **$^{13}C$  NMR** ( $CDCl_3$ , 75 MHz):  $\delta$  166.8, 159.9, 129.8 (q,  $^1J_{CF} = 308.6$  Hz), 129.3, 127.0, 114.5, 55.3, 53.2, 49.0, 32.8, 32.5, 25.3, 24.7, 24.6.  **$^{19}F$  NMR** ( $CDCl_3$ , 376 MHz):  $\delta$  -40.7. **HRMS (MALDI-FT ICR)** exact mass  $[M+H]^+$  calculated for  $C_{16}H_{20}F_3NO_2S$ : 348.1235, found: 348.1239.

#### 1-morpholino-2-(4-nitrophenyl)-2-((trifluoromethyl)thio)ethenone (4g)



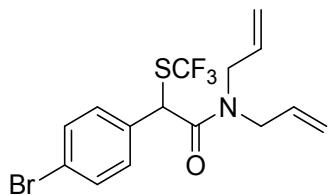
Brown solid, 65.2 mg, 93% yield. **mp** 147.8-153.9 °C. **FTIR**  $\nu_{max}(KBr)/cm^{-1}$ : 3453, 2365, 1645, 1524, 1445, 1349, 1113.  **$^1H$  NMR** ( $CDCl_3$ , 400 MHz):  $\delta$  8.25 (d, 2H,  $J = 8.4$  Hz), 7.63 (d, 2H,  $J = 8.4$  Hz), 5.43 (s, 1H), 3.70-3.52 (m, 6H), 3.35-3.26 (m, 2H).  **$^{13}C$  NMR** ( $CDCl_3$ , 100 MHz):  $\delta$  165.2, 148.0, 143.3, 130.2 (q,  $^1J_{CF} = 309.6$  Hz), 129.1, 124.4, 66.4, 65.9, 51.1, 46.6, 43.0.  **$^{19}F$  NMR** ( $CDCl_3$ , 376 MHz):  $\delta$  -40.1. **HRMS (MALDI-FT ICR)** exact mass  $[M+H]^+$  calculated for  $C_{13}H_{13}F_3N_2O_4S$ : 351.0548, found: 351.0593.

#### *N*-methyl-*N*-phenyl-2-(4-(trifluoromethyl)phenyl)-2-((trifluoromethyl)thio)acetamide (4h)



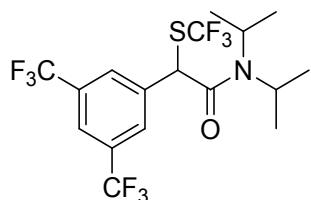
Yellow oil, 53.5 mg, 68% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3455, 1558, 1496, 1386, 1325, 1173, 1110, 1068, 1020. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.51 (d, 2H,  $J = 8.1$  Hz), 7.44 (bs, 3H), 7.23 (d, 2H,  $J = 8.1$  Hz), 7.03 (bs, 2H), 5.08 (s, 1H), 3.28 (s, 3H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  167.3, 142.2, 139.9, 130.7 (q,  $^2J_{\text{CF}} = 32.8$  Hz), 130.1 (q,  $^1J_{\text{CF}} = 308.3$  Hz), 130.0, 129.0, 128.7, 127.4, 125.6 (q,  $^3J_{\text{CF}} = 3.3$  Hz), 123.8 (q,  $^1J_{\text{CF}} = 272.5$  Hz), 50.3, 38.1. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.9, -62.7. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{17}\text{H}_{13}\text{F}_6\text{NOS}$ : 394.0622, found: 394.0694.

#### ***N,N-diallyl-2-(4-bromophenyl)-2-((trifluoromethyl)thio)acetamide (4i)***



Colorless oil, 56.2 mg, 72% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3464, 1645, 1555, 1398, 1210, 1115, 544. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.81 (d, 2H,  $J = 8.3$  Hz), 7.65 (d, 2H,  $J = 8.3$  Hz), 5.87-5.81 (m, 1H), 5.73-7.66 (m, 1H), 5.31-5.13 (m, 5H), 4.13 (d, 2H,  $J = 6.0$  Hz), 3.80 (d, 2H,  $J = 6.0$  Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  189.9, 166.4, 132.4, 132.0, 131.6, 131.1, 130.2 (q,  $^1J_{\text{CF}} = 310.8$  Hz), 130.2, 119.4, 118.8, 49.4, 46.1, 29.7. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.4. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{15}\text{H}_{15}\text{BrF}_3\text{NOS}$ : 394.0010, found: 394.0025.

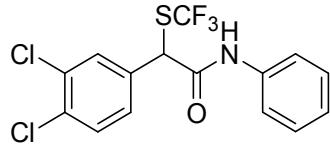
#### ***2-(3,5-bis(trifluoromethyl)phenyl)-N,N-diisopropyl-2-((trifluoromethyl)thio)acetamide (4j)***



White solid, 66.5 mg, 73% yield. **mp** 82.3-84.4 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3406, 3049, 2370, 1653, 1558, 1505, 1117. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.89 (s, 2H), 7.86 (s, 1H), 5.52 (s, 1H), 3.86 (sept, 1H,  $J = 6.6$  Hz), 3.36 (sept, 1H,  $J = 6.7$  Hz), 1.44 (d, 3H,  $J = 6.7$  Hz), 1.28 (d, 3H,  $J = 6.7$  Hz), 1.26 (d, 3H,  $J = 6.6$  Hz), 0.61 (d, 3H,  $J = 6.6$  Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  164.9, 140.4, 132.5 (q,  $^2J_{\text{CF}} = 33.5$  Hz), 130.4 (q,  $^1J_{\text{CF}} = 308.9$  Hz), 128.3, 122.8 (q,  $^1J_{\text{CF}} = 273.1$  Hz), 122.4 (q,  $^3J_{\text{CF}} = 3.6$  Hz), 53.7, 50.2, 47.0, 20.8, 20.3, 19.6, 19.2. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.1, -

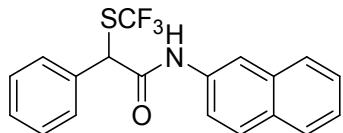
63.0. **HRMS (MALDI-FT ICR)** exact mass  $[M+H]^+$  calculated for  $C_{17}H_{18}F_9NOS$ : 456.0965, found: 456.0986.

**2-(3,4-dichlorophenyl)-*N*-phenyl-2-((trifluoromethyl)thio)acetamide (4k)**



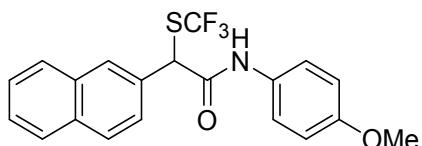
Yellow solid, 63.1 mg, 83% yield. **mp** 109.8-111.5 °C. **FTIR**  $\nu_{max}(KBr)/cm^{-1}$ : 3450, 1654, 1560, 1500, 1446, 1111, 756.  **$^1H$  NMR** ( $CDCl_3$ , 400 MHz):  $\delta$  7.81 (bs, 1H), 7.58 (d, 1H,  $J$  = 1.4 Hz), 7.47 (m, 3H), 7.34 (t, 3H,  $J$  = 7.6 Hz), 7.17 (t, 1H,  $J$  = 7.4 Hz), 5.07 (s, 1H).  **$^{13}C$  NMR** ( $CDCl_3$ , 75 MHz):  $\delta$  164.8, 136.4, 135.0, 133.7, 133.5, 131.2, 130.1, 129.6 (q,  $^{1}J_{CF}$  = 308.6 Hz), 129.2, 127.4, 125.6, 120.3, 53.0.  **$^{19}F$  NMR** ( $CDCl_3$ , 376 MHz):  $\delta$  -40.4. **HRMS (MALDI-FT ICR)** exact mass  $[M+H]^+$  calculated for  $C_{15}H_{10}Cl_2F_3NO$ : 379.9812, found: 379.9853.

***N*-(naphthalen-2-yl)-2-phenyl-2-((trifluoromethyl)thio)acetamide (4l)**



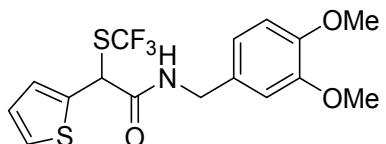
Brown solid, 57.1 mg, 79% yield. **mp** 151.2-153.3 °C. **FTIR**  $\nu_{max}(KBr)/cm^{-1}$ : 3460, 1652, 1508, 1152, 1113, 767, 696.  **$^1H$  NMR** ( $CDCl_3$ , 400 MHz):  $\delta$  8.19 (bs, 1H), 7.91 (m, 2H), 7.75 (d, 1H,  $J$  = 8.3 Hz), 7.60 (d, 2H,  $J$  = 7.0 Hz), 7.53-7.48 (m, 7H), 5.39 (s, 1H).  **$^{13}C$  NMR** ( $CDCl_3$ , 100 MHz):  $\delta$  166.0, 134.7, 134.2, 133.6, 131.0, 129.8 (q,  $^{1}J_{CF}$  = 307.3 Hz), 129.4, 129.3, 128.9, 128.2, 127.7, 127.5, 126.7, 125.5, 119.7, 117.4, 54.4.  **$^{19}F$  NMR** ( $CDCl_3$ , 376 MHz):  $\delta$  -40.6. **HRMS (MALDI-FT ICR)** exact mass  $[M+H]^+$  calculated for  $C_{19}H_{14}F_3NOS$ : 362.0748, found: 362.0712.

***N*-(4-methoxyphenyl)-2-(naphthalen-2-yl)-2-((trifluoromethyl)thio)acetamide (4m)**



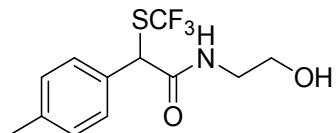
White solid, 57.1 mg, 73% yield. **mp** 164.2-165.7 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3489, 2057, 1637, 1512, 1249, 1155, 1108, 714, 478. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.91-7.83 (m, 4H), 7.68 (bs, 1H), 7.59-7.52 (m, 3H), 7.35 (d, 2H,  $J$  = 8.6 Hz), 6.83 (d, 2H,  $J$  = 8.6 Hz), 5.35 (s, 1H), 3.77 (s, 3H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  165.5, 157.1, 133.3, 133.2, 132.2, 129.8, 129.8 (q,  $^1J_{\text{CF}}$  = 307.1 Hz), 129.6, 128.1, 127.8, 127.7, 127.1, 126.9, 125.1, 122.1, 114.2, 55.5, 54.8. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.5. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{20}\text{H}_{16}\text{F}_3\text{NO}_2\text{S}$ : 392.0854, found: 392.0813.

#### ***N-(3,4-dimethoxybenzyl)-2-(thiophen-2-yl)-2-((trifluoromethyl)thio)acetamide (4n)***



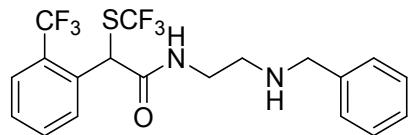
Brown solid, 56.4 mg, 72% yield. **mp** 113.1-115.3 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3043, 1735, 1701, 1685, 1654, 1648, 1560, 1541, 1518, 1459, 1267, 1114. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.33 (d, 1H, ,  $J$  = 4.5 Hz), 7.12 (d, 1H, ,  $J$  = 2.9 Hz), 6.97 (t, 1H, ,  $J$  = 4.5 Hz), 6.78 (m, 2H), 6.74 (s, 1H), 6.39 (bs, 1H), 5.34 (s, 1H), 4.43 (d, 2H,  $J$  = 5.7 Hz), 3.86 (s, 3H), 3.91 (s, 3H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  166.9, 149.2, 148.6, 136.6, 129.7, 129.6 (q,  $^1J_{\text{CF}}$  = 308.5 Hz), 127.9, 127.4, 127.2, 120.1, 111.1, 110.8, 55.9, 55.7, 48.9, 44.1. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.9. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{K}]^+$  calculated for  $\text{C}_{16}\text{H}_{16}\text{F}_3\text{NO}_3\text{S}_2$ : 430.0155, found: 430.0161.

#### ***N-(2-hydroxyethyl)-2-(p-tolyl)-2-((trifluoromethyl)thio)acetamide (4o)***



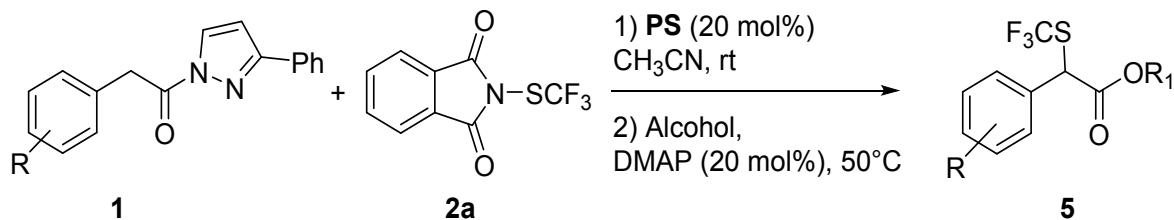
Pink solid, 41.1 mg, 70% yield. **mp** 89.0-91.6 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3440, 2927, 1652, 1558, 1512, 1456, 1464, 1246, 1155, 1115, 1030. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.29 (d, 2H,  $J$  = 8.0 Hz), 7.18 (d, 2H;  $J$  = 8.0 Hz), 6.58 (bs, 1H), 5.01 (s, 1H), 3.70 (m, 2H), 3.49-3.38 (m, 2H), 2.34 (s, 3H), 2.19 (bs, 1H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  168.7, 139.1, 132.0, 129.9, 129.8 (q,  $^1J_{\text{CF}}$  = 308.6 Hz), 127.9, 61.7, 53.4, 42.7, 21.2. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.8. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_{14}\text{F}_3\text{NO}_2\text{S}$ : 294.0697, found: 294.0658.

***N*-(2-(benzylamino)ethyl)-2-(2-(trifluoromethyl)phenyl)-2-((trifluoromethyl)thio)acetamide  
(4p)**



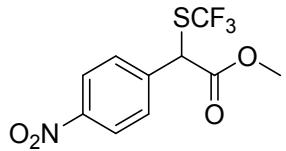
Dark red oil, 69.8 mg, 80% yield. **FTIR**  $\nu_{\text{max}}$ (KBr)/cm<sup>-1</sup>: 3445, 1670, 1519, 1454, 1315, 1154, 1123, 1061, 1038. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 300 MHz):  $\delta$  7.90 (d, 1H, *J* = 7.7 Hz), 7.68 (d, 1H, *J* = 7.7 Hz), 7.59 (t, 1H, *J* = 7.7 Hz), 7.45 (t, 1H, *J* = 7.7 Hz), 7.34-7.23 (m, 5H), 6.65 (bs, 1H), 5.38 (s, 1H), 3.72 (s, 2H), 3.39-3.32 (m, 1H), 3.29-3.21 (m, 1H), 2.80 (bs, 1H), 2.76-2.71 (m, 2H). **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz):  $\delta$  167.7, 140.9, 135.8, 133.7, 131.6, 130.7 (q, *J*<sub>CF</sub> = 307.4 Hz), 129.7, 129.4, 128.9, 128.5 (q, *J*<sub>CF</sub> = 29.9 Hz), 128.1, 127.0 (q, *J*<sub>CF</sub> = 5.5 Hz), 125.1 (q, *J*<sub>CF</sub> = 275.1 Hz), 54.3, 49.7, 48.1, 40.6. **<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz):  $\delta$  -41.1, -57.8. **HRMS (MALDI-FT ICR)** exact mass [M+H]<sup>+</sup> calculated for C<sub>19</sub>H<sub>18</sub>F<sub>6</sub>N<sub>2</sub>OS: 437.1044, found: 437.1027.

**General procedure for one-pot synthesis of  $\alpha$ -trifluoromethylthio esters**



In an oven-dried vial, under nitrogen atmosphere, **PS** (0.02 mmol) was added to a mixture of *N*-acylpyrazole **1** (0.2 mmol) and *N*-(trifluoromethylthio)phthalimide **2a** (0.24 mmol) in anhydrous acetonitrile (1 mL). The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the first step, acetonitrile was evaporated, then DMAP (0.04 mmol) and anhydrous alcohol (2 mL) were added and the mixture was stirred at 50°C for the time reported in Table 2 of the paper. After completion, the solvent was evaporated, and the crude mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 100/0 to 80/20) to afford products **5a-c** in 78-83% yield.

### Methyl 2-(4-nitrophenyl)-2-((trifluoromethyl)thio)acetate (**5a**)



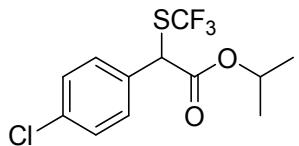
Pale yellow solid, 47.2 mg, 80% yield. **mp** 60.2-61.7 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3460, 1652, 1549, 1508, 1152, 1113, 767, 696, 419. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  8.25 (d, 2H,  $J$  = 8.7 Hz), 7.66 (d, 2H,  $J$  = 8.7 Hz), 5.15 (s, 1H), 3.79, (s, 3H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  168.1, 148.2, 141.4, 129.4 ( $\text{q}, ^1J_{\text{CF}} = 308.6$  Hz), 129.3, 124.3, 53.9, 50.8. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.8. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{10}\text{H}_8\text{F}_3\text{NO}_4\text{S}$ : 296.0126, found: 296.0173.

### Ethyl 2-(4-bromophenyl)-2-((trifluoromethyl)thio)acetate (**5b**)



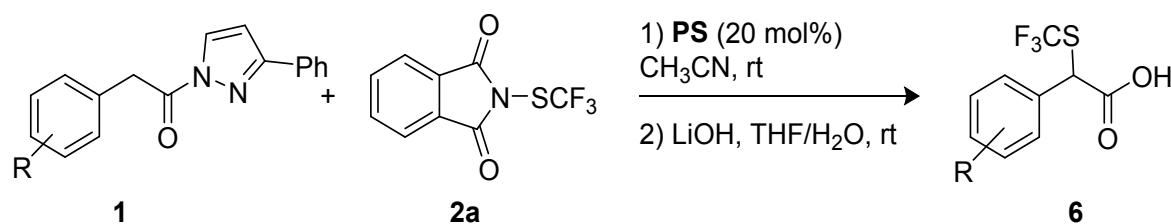
Yellow oil, 53.5 mg, 78% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3454, 2986, 1654, 1489, 1299, 1274, 1157, 1113, 1013, 757, 508. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz): 7.51 (d, 2H,  $J$  = 8.3 Hz), 7.33 (d, 2H,  $J$  = 8.3 Hz), 4.9, (s, 1H), 4.25 (dq, 1H,  $J$  = 15.8 Hz,  $J$  = 7.1 Hz), 4.19 (dq, 1H,  $J$  = 15.8 Hz,  $J$  = 7.1 Hz), 1.25 (t, 3H,  $J$  = 7.1 Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  168.4, 133.3, 132.2, 129.8, 129.6 ( $\text{q}, ^1J_{\text{CF}} = 306.9$  Hz), 123.3, 62.8, 50.9, 13.8. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.4. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{Na}]^+$  calculated for  $\text{C}_{11}\text{H}_{10}\text{BrF}_3\text{O}_2\text{S}$ : 366.9409, found: 366.9407.

### Isopropyl 2-(4-chlorophenyl)-2-((trifluoromethyl)thio)acetate (**5c**)



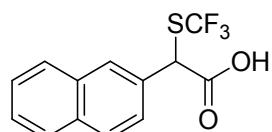
Brown oil, 51.9 mg, 83% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3440, 2987, 1733, 1652, 1493, 1377, 1280, 1116, 1098, 1016, 767. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.39 (d, 2H,  $J$  = 8.6 Hz), 7.34 (d, 2H,  $J$  = 8.6 Hz), 5.04 (sept, 1H,  $J$  = 6.3 Hz), 4.97 (s, 1H), 1.26 (d, 3H,  $J$  = 6.3 Hz), 1.17 (d, 3H,  $J$  = 6.3 Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  168.0, 135.1, 132.8, 129.7 ( $\text{q}, ^1J_{\text{CF}} = 308.3$  Hz), 129.5, 129.3, 70.8, 51.1, 21.4, 21.3. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.9. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_{12}\text{ClF}_3\text{O}_2\text{S}$ : 313.0199, found: 313.0146.

## General procedure for one-pot synthesis of $\alpha$ -trifluoromethylthio carboxylic acids



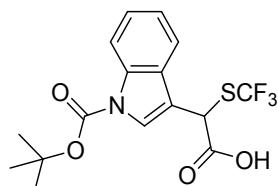
In an oven-dried vial, under nitrogen atmosphere, **PS** (0.02 mmol) was added to a mixture of *N*-acylpyrazole **1** (0.2 mmol) and *N*-(trifluoromethylthio)phthalimide **2a** (0.24 mmol) in anhydrous acetonitrile (1 mL). The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the first step, acetonitrile was evaporated, then  $\text{LiOH} \cdot \text{H}_2\text{O}$  (0.4 mmol) and  $\text{THF}/\text{H}_2\text{O}$  (2:1, 1.5 mL) were added. The mixture was stirred for 16 h at room temperature. After completion,  $\text{LiOH}$  was quenched with acetic acid, then the reaction mixture was diluted with  $\text{H}_2\text{O}$  and the aqueous phase was extracted with EtOAc (50 mL x 3). The organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered and evaporated. The crude mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 100/0 to 90/10 + 1% of acetic acid) to afford product **6a** and **6b** in 70-90% yield.

### **2-(naphthalen-2-yl)-2-((trifluoromethyl)thio)acetic acid (6a)**



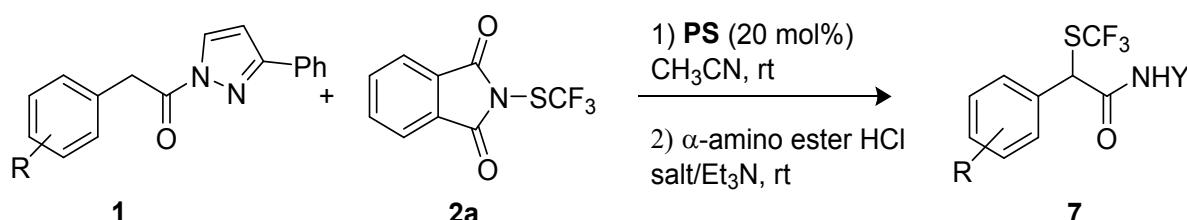
White solid, 51.5 mg, 90% yield. **mp** 103.0-105.4 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3460, 2925, 2852, 1719, 1273, 1159, 1110, 811, 748, 482. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$ , 8.49 (bs, 1H), 7.91 (s, 1H), 7.87-7.82 (m 3H), 7.54-7.51 (m, 3H), 5.25 (s, 1H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  173.7, 134.2, 133.1, 130.5, 129.6 (q,  $^1J_{\text{CF}} = 307.8$  Hz), 129.3, 128.1, 127.9, 127.7, 127.1, 126.8, 125.0, 51.4. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.7. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{Na}]^+$  calculated for  $\text{C}_{26}\text{H}_{18}\text{F}_6\text{O}_4\text{S}_2$ : 595.0448, found: 595.0450

### **2-(1-(tert-butoxycarbonyl)-1*H*-indol-3-yl)-2-((trifluoromethyl)thio)acetic acid (6b)**



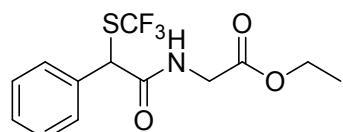
Pale yellow solid, 52.5 mg, 70% yield. **mp** 129.0-131.2°C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3450, 2915, 2851, 1705, 1265, 1139, 1110, 821, 750. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz):  $\delta$ , 9.0 (bs, 1H), 8.16 (d, 1H,  $J$  = 7.8 Hz), 7.78 (s, 1H), 7.68 (d, 1H,  $J$  = 7.4 Hz), 7.38 (dd, 1H,  $J$  = 7.1 Hz,  $J$  = 7.8 Hz), 7.31 (dd, 1H,  $J$  = 7.1 Hz,  $J$  = 7.4 Hz), 5.35 (s, 1H), 1.67 (s, 9H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  174.3, 149.2, 135.5, 129.6 (q,  $^1J_{\text{CF}}$  = 308.8 Hz), 127.6, 125.7, 125.3, 123.2, 119.1, 115.6, 111.6, 84.7, 43.1, 28.1. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -41.0. **HRMS (MALDI-FT ICR)** exact mass [M+Na]<sup>+</sup> calculated for  $\text{C}_{32}\text{H}_{32}\text{F}_6\text{N}_2\text{O}_8\text{S}_2$ : 773.1397, found: 773.1460.

### General procedure for one-pot synthesis of functionalized $\alpha$ -trifluoromethylthio amides



In an oven-dried vial *N*-acylpyrazole **1** (0.2 mmol), *N*-(trifluoromethylthio)phthalimide **2a** (0.24 mmol) and anhydrous acetonitrile (1 mL) were introduced. Under nitrogen atmosphere, **PS** (0.02 mmol) was added to this solution. The reaction mixture was stirred at room temperature for the time indicated in Table 3 and monitored by TLC. After completion,  $\alpha$ -amino ester hydrochloride (0.26 mmol) and triethylamine (0.26 mmol) were added and the mixture was stirred at room temperature for 2 hours. After completion, the solvent was evaporated, and the crude mixture was purified by flash chromatography (eluent: hexane/diethyl ether 100/0 to 70/30) to afford products **7a-d** in 76-95% yield.

### Ethyl 2-(2-phenyl-2-((trifluoromethyl)thio)acetamido)acetate (7a)



White solid, 61.0 mg, 95% yield. **mp** 90.7-93.9 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3304, 3216, 1750, 1661, 1539, 1377, 1307, 1201, 1163, 1112, 1053, 1023, 713. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.44-7.34 (m, 5H), 6.70 (bs, 1H), 5.09 (s, 1H), 4.20 (q, 2H,  $J$  = 7.1 Hz), 4.09 (dd, 1H,  $J$  = 18.3 Hz,  $J$  = 5.2 Hz), 3.98 (dd, 1H,  $J$  = 18.3 Hz,  $J$  = 5.2 Hz), 1.26 (t, 3H,  $J$  = 7.1 Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  169.2, 167.8, 134.3, 129.8 (q,  $^1J_{\text{CF}}$  = 309.4 Hz), 129.2, 129.1, 128.2, 61.8, 53.3, 41.9, 14.0. **<sup>19</sup>F NMR**

**NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.8. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for:  $\text{C}_{13}\text{H}_{14}\text{F}_3\text{NO}_3\text{S}$ : 322.0646, found: 322.0617.

**Methyl 2-(2-(3,4-dichlorophenyl)-2-((trifluoromethyl)thio)acetamido)propanoate (7b)**



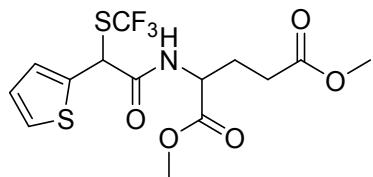
White solid, 60.9 mg, 78% yield, dr 1/1. **mp** 75.5-79.4 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3309, 2959, 1747, 1658, 1543, 1484, 1455, 1397, 1353, 1219, 1154, 1113, 767.  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (diastereoisomers A+B) 7.55 (m, 1H+1H,  $J = 2.6$  Hz), 7.47 (s, 1H), 7.45 (s, 1H), 7.30 (m, 1H,  $J = 2.6$  Hz), 7.28 (m, 1H,  $J = 2.6$  Hz), 6.73 (d, 1H,  $J = 5.6$  Hz), 6.62 (d, 1H,  $J = 5.6$  Hz), 4.96 (s, 1H), 4.92 (s, 1H), 4.60 (q, 1H,  $J = 7.2$  Hz), overlapped with 4.55 (q, 1H,  $J = 7.1$  Hz), 3.78 (s, 3H), 3.74 (s, 3H), 1.45 (d, 3H,  $J = 7.2$  Hz), 1.40 (d, 3H,  $J = 7.1$  Hz).  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  (diastereoisomers A+B) 172.7, 172.6, 166.2, 166.1, 135.0, 133.5, 133.4, 133.3, 131.2, 131.1, 130.1, 129.6 (q,  $^1J_{\text{CF}} = 308.5$  Hz), 127.4, 52.8, 52.7, 52.0, 48.9, 48.7, 18.1, 17.9.  **$^{19}\text{F NMR}$**  ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.6. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{F}_3\text{NO}_3\text{S}$ : 389.9867, found: 389.9821.

**Methyl 2-(2-(4-fluorophenyl)-2-((trifluoromethyl)thio)acetamido)-3-methylbutanoate (7c)**



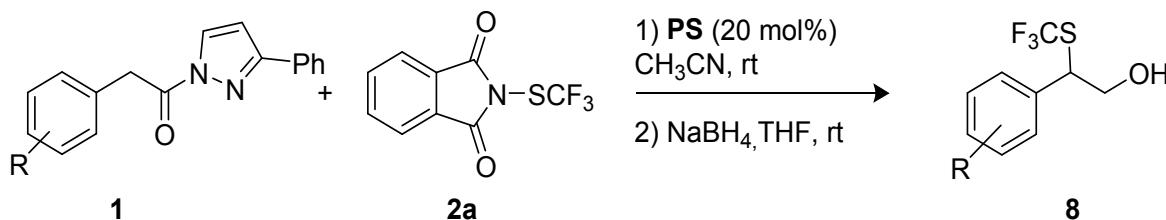
White solid, 55.8 mg, 76% yield, dr 1/1. **mp** 75.5-79.4 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3836, 3676, 3600, 3525, 2957, 1748, 1650, 1558, 1509, 1227, 1114, 669.  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (diastereoisomers A+B) 7.44-7.39 (m, 2H+2H), 7.09-7.04 (m, 2H+2H), 6.63 (bs, 1H+1H), 5.08 (s, 1H), 5.04 (s, 1H), 4.56 (q, 1H,  $J = 4.3$  Hz) overlapped with 4.52 (q, 1H,  $J = 4.3$  Hz), 3.75 (s, 3H), 3.71 (s, 3H), 2.17 (sept, 1H+1H,  $J = 6.6$  Hz), 0.92 (d, 3H,  $J = 6.6$  Hz), 0.89 (d, 3H,  $J = 6.6$  Hz), 0.83 (d, 3H,  $J = 6.6$  Hz), 0.79 (d, 3H,  $J = 6.6$  Hz).  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  (diastereoisomers A+B) 171.9, 171.7, 167.5, 167.3, 162.8 (d,  $^1J_{\text{CF}} = 249.6$  Hz), 131.8, 131.2 (d,  $^4J_{\text{CF}} = 2.9$  Hz), 130.7 (d,  $^4J_{\text{CF}} = 2.9$  Hz), 129.9 (d,  $^3J_{\text{CF}} = 8.4$  Hz), 129.7 (q,  $^1J_{\text{CF}} = 308.6$  Hz), 129.6 (q,  $^1J_{\text{CF}} = 308.6$  Hz), 116.3 (d,  $^2J_{\text{CF}} = 21.8$  Hz), 116.2 (d,  $^2J_{\text{CF}} = 21.8$  Hz), 57.7, 57.6, 52.9, 52.5, 52.4, 52.3, 31.8, 31.2, 18.7, 17.7, 17.3.  **$^{19}\text{F NMR}$**  ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.6, -40.7, -111.9. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{15}\text{H}_{17}\text{F}_4\text{NO}_3\text{S}$ : 368.0865, found: 368.0842.

**Dimethyl 2-(2-(thiophen-2-yl)-2-((trifluoromethyl)thio)acetamido)malonate (7d)**



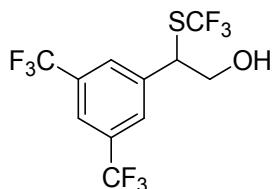
Colorless oil, 61.6 mg, 83% yield, dr 1/1. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3348, 1734, 1675, 1457, 1441, 1115, 1110.  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  (diastereoisomers A+B) 7.34 (d, 2H,  $J = 5.2$  Hz), 7.18 (d, 1H,  $J = 3.4$  Hz), 7.15 (d, 2H,  $J = 3.5$  Hz), 7.01-6.97 (m, 4H), 5.35 (s, 1H), 5.32 (s, 1H), 4.65-4.58 (m, 2H), 2.76 (s, 3H), 3.74 (s, 3H), 3.68 (s, 3H), 3.65 (s, 3H), 2.46-2.19 (m, 6H), 2.11-1.99 (m, 2H).  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 75 MHz): (diastereoisomers A+B)  $\delta$  173.3, 173.2, 171.5, 171.4, 167.1, 167.0, 136.2, 136.0, 129.5 ( $q, ^1J_{\text{CF}} = 308.6$  Hz), 128.1, 127.5, 127.2, 127.2, 52.7, 52.44, 52.42, 51.9, 48.6, 29.8, 29.7, 26.8, 26.7.  **$^{19}\text{F NMR}$**  ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -40.9, -41.0. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{12}\text{H}_{12}\text{F}_3\text{NO}_5\text{S}_2$ : 400.0042, found: 400.0028.

**General procedure for one-pot synthesis of  $\beta$ -trifluoromethylthio alcohols**



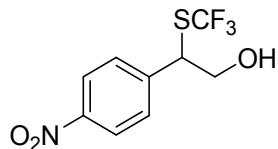
In an oven-dried vial, under nitrogen atmosphere, **PS** (0.02 mmol) was added to a mixture of *N*-acylpyrazole **1** (0.2 mmol) and *N*-(trifluoromethylthio)phthalimide **2a** (0.24 mmol) in anhydrous acetonitrile (1 mL). The reaction mixture was stirred at room temperature and monitored by TLC. After completion acetonitrile was evaporated and then THF (1 mL) and  $\text{NaBH}_4$  (0.2 mmol) were added. The mixture was stirred at room temperature for the time reported in Scheme 2 of the paper. After completion,  $\text{NaBH}_4$  was quenched with water and the aqueous phase was extracted with  $\text{EtOAc}$  (50 mL x3). The organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered and evaporated. The crude mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 100/0 to 70/30) to afford products **8a-d** in 75-80% yield.

**2-(3,5-bis(trifluoromethyl)phenyl)-2-((trifluoromethyl)thio)ethanol (8a)**



Colorless oil, 57.9 mg, 75% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3435, 3221, 1959, 1774, 1754, 1634, 1328, 1308, 1280, 1175, 1139, 1054, 1037, 926. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.86 (s, 3H), 4.57 (t, 1H,  $J = 5.9$  Hz), 4.11 (dd, 1H,  $J = 11.4$  Hz,  $J = 5.8$  Hz), 4.07 (dd, 1H,  $J = 11.4$  Hz,  $J = 5.8$  Hz), 1.96 (bs, 1H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 150 MHz):  $\delta$  140.9, 132.3 (q,  $^2J_{\text{CF}} = 34.1$  Hz), 130.1 (q,  $^1J_{\text{CF}} = 308.0$  Hz), 128.3, 123.0 (q,  $^1J_{\text{CF}} = 272.1$  Hz), 122.4 (q,  $^3J_{\text{CF}} = 3.6$  Hz), 65.2, 50.4. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -39.7, -62.9. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{11}\text{H}_7\text{F}_9\text{OS}$ : 359.0074, found: 359.0029.

### 2-(4-nitrophenyl)-2-((trifluoromethyl)thio)ethanol (8b)



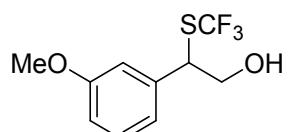
Colorless oil, 45.5 mg, 77% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3435, 2929, 1773, 1726, 1608, 1592, 1350, 1163, 1124, 1066, 862. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  8.24 (d, 2H,  $J = 8.4$  Hz), 7.58 (d, 2H,  $J = 8.4$  Hz), 4.55 (t, 1H,  $J = 5.9$  Hz), 4.07 (m, 2H), 1.98 (dd, 1H,  $J = J = 5.9$  Hz). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  147.7, 145.3, 130.1 (q,  $^1J_{\text{CF}} = 307.7$  Hz), 129.0, 128.0, 124.1, 65.2, 50.5. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -39.7. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_9\text{H}_8\text{F}_3\text{NO}_3\text{S}$ : 268.0177, found: 268.0138.

### 2-(*p*-tolyl)-2-((trifluoromethyl)thio)ethanol (8c)



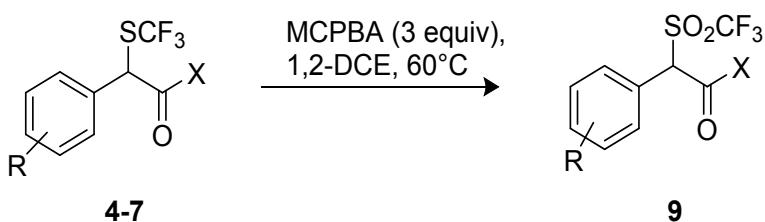
Brown oil, 42.3 mg, 80% yield. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3455, 2924, 1645, 1515, 1112, 756. **<sup>1</sup>H NMR** ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.24 (d, 2H,  $J = 8.7$  Hz), 7.21 (d, 2H,  $J = 8.7$  Hz), 4.44 (t, 1H,  $J = 6.6$  Hz), 4.00 (d, 2H,  $J = 6.6$  Hz), 2.35 (s, 3H), 1.78 (bs, 1H). **<sup>13</sup>C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  138.4, 134.1, 130.4 (q,  $^1J_{\text{CF}} = 307.4$  Hz), 129.8, 127.7, 65.7, 50.9, 21.1. **<sup>19</sup>F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -39.6. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{10}\text{H}_{11}\text{F}_3\text{OS}$ : 237.0483, found: 237.0416.

### 2-(3-methoxyphenyl)-2-((trifluoromethyl)thio)ethanol (8d)



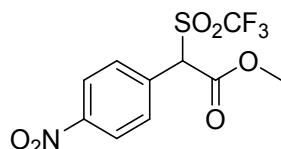
Brown oil, 42.6 mg, 76% yield. **FTIR** $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3416, 2924, 1602, 1587, 1493, 1438, 1264, 1148, 1112, 1051, 757, 700.  **$^1\text{H NMR}$**  ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.29 (t, 1H,  $J$  = 7.9 Hz), 6.93 (d, 1H,  $J$  = 7.9 Hz), 6.87 (m, 2H), 4.42 (t, 1H,  $J$  = 6.4 Hz), 4.01 (m, 2H), 3.82 (s, 3H), 1.86 (bs, 1H).  **$^{13}\text{C NMR}$**  ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  161.0, 139.7, 131.3 (q,  $^1J_{\text{CF}}$  = 305.9 Hz), 131.2, 120.9, 114.8, 114.7, 66.7, 56.3, 52.1.  **$^{19}\text{F NMR}$**  ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -39.7. **HRMS (MALDI-FT ICR)** exact mass [M+H] $^+$  calculated for  $\text{C}_{10}\text{H}_{11}\text{F}_3\text{O}_2\text{S}$ : 253.0432, found: 253.0498.

## General procedure for oxidation of $\alpha$ -trifluoromethylthio derivates



In an oven-dried vial  $\alpha$ -trifluoromethylthio derivate **4-7** (0.2 mmol), MCPBA (0.6 mmol) and anhydrous 1,2-dichlorethane (1 mL) were introduced. The reaction mixture was stirred at 60°C for 16 hours as reported in Scheme 3 of the paper. After completion of the reaction, PPh<sub>3</sub> (0.2 mmol) was added and the mixture was stirred for 30 min and then extracted with EtOAc (50 mL x 3) washed with NaHCO<sub>3</sub> and brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated. The crude mixture was purified by flash chromatography (eluent: hexane/ethyl acetate 100/0 to 70/30) to afford products **9a-e** in 72-85% yield.

### Methyl 2-(4-nitrophenyl)-2-((trifluoromethyl)sulfonyl)acetate (9a)



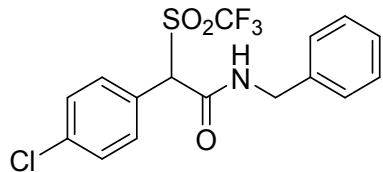
Yellow solid, 47.1 mg, 72% yield. **mp** 200.6-204.6 °C. **FTIR**  $\nu_{\text{max}}$ (KBr)/cm<sup>-1</sup>: 3435, 2950, 2919, 2850, 1752, 1654, 1529, 1376, 1352, 1209, 1114. **<sup>1</sup>H NMR** (CDCl<sub>3</sub>, 300 MHz):  $\delta$  8.32 (d, 2H, *J* = 8.8 Hz), 7.84 (d, 2H, *J* = 8.8 Hz), 5.43 (s, 1H), 3.92 (s, 3H). **<sup>13</sup>C NMR** (CDCl<sub>3</sub>, 75 MHz):  $\delta$  161.8, 149.4, 131.9, 130.9, 124.2, 119.6 (q, <sup>1</sup>*J*<sub>CF</sub> = 327.8 Hz), 69.2, 54.5. **<sup>19</sup>F NMR** (CDCl<sub>3</sub>, 376 MHz):  $\delta$  -73.4. **HRMS (MALDI-FT ICR)** exact mass [M+H]<sup>+</sup> calculated for C<sub>10</sub>H<sub>8</sub>F<sub>3</sub>NO<sub>6</sub>S: 328.0024, found: 328.0059.

**Ethyl 2-(4-bromophenyl)-2-((trifluoromethyl)sulfonyl)acetate (9b)**



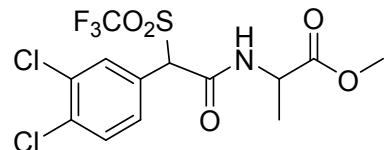
White solid, 63.8 mg, 80% yield. **mp** 60.2-61.7 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3328, 1747, 1658, 1540, 1484, 1455, 1397, 1353, 1219, 1163, 1113, 757. **1H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.61 (d, 2H,  $J$  = 8.5 Hz), 7.49 (d, 2H,  $J$  = 8.5 Hz), 5.26 (s, 1H), 4.37 (dq, 1H,  $J$  = 14.3 Hz,  $J$  = 7.2 Hz), 4.31 (dq, 1H,  $J$  = 14.3 Hz,  $J$  = 7.2 Hz), 1.33 (t, 3H,  $J$  = 7.2 Hz). **13C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  161.2, 132.6, 132.2, 125.7, 124.6, 119.6 ( $q, ^1J_{\text{CF}} = 329.9$  Hz), 69.6, 63.9, 13.8. **19F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -73.4. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{11}\text{H}_{10}\text{BrF}_3\text{O}_4\text{S}$ : 374.9435, found: 374.9416.

**N-benzyl-2-(4-chlorophenyl)-2-((trifluoromethyl)sulfonyl)acetamide (9c)**



White solid, 58.8 mg, 75% yield. **mp** 162.8-164.1 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3462, 2960, 2376, 2045, 1652, 1558, 1539, 1504, 1373, 1215, 1129, 701. **1H NMR** ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.52 (d, 2H,  $J$  = 8.4 Hz), 7.42 (d, 2H,  $J$  = 8.4 Hz), 7.35-7.30 (m, 3H), 7.24 (d, 2H,  $J$  = 7.7 Hz), 6.72 (bs, 1H), 5.21 (s, 1H), 4.54 (dd, 1H,  $J$  = 14.7 Hz,  $J$  = 5.3 Hz), 4.46 (dd, 1H,  $J$  = 14.7 Hz,  $J$  = 5.3 Hz). **13C NMR** ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  160.0, 137.3, 136.4, 131.8, 129.6, 128.9, 128.1, 127.8, 123.4, 119.6 ( $q, ^1J_{\text{CF}} = 330.0$  Hz), 70.4, 44.6. **19F NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -73.1. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{16}\text{H}_{13}\text{ClF}_3\text{NO}_3\text{S}$ : 392.0257, found: 392.0249.

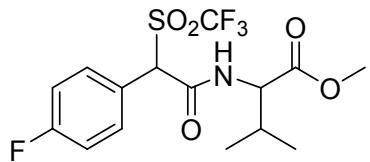
**Methyl 2-(2-(3,4-dichlorophenyl)-2-((trifluoromethyl)sulfonyl)acetamido)propanoate (9d)**



Pale yellow oil, 65.9 mg, 78% yield, dr 1/1. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3343, 2956, 2921, 2850, 1743, 1674, 1538, 1471, 1375, 1213, 1116. **1H NMR** ( $\text{CDCl}_3$ , 300 MHz): (diastereoisomers A+B)  $\delta$  7.73 (s, 1H+1H), 7.56-7.46 (m, 2H+2H), 7.28 (bs, 1H), 7.13 (bs, 1H), 5.32 (s, 1H) overlapped with 5.30

(s, 1H), 4.63 (q, 1H+1H,  $J = 7.2$  Hz), 3.79 (s, 3H), 3.76 (s, 3H), 1.48 (d, 3H,  $J = 7.2$  Hz), 1.43 (d, 3H,  $J = 7.2$  Hz).  **$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 75 MHz): (diastereoisomers A+B)  $\delta$  172.5, 172.4, 159.4, 159.3, 135.7, 135.6, 133.7, 133.5, 132.45, 132.39, 131.2, 131.1, 129.8, 129.7, 124.8, 124.7, 121.6 (q,  $^1J_{\text{CF}} = 331.7$  Hz), 69.4, 69.3, 52.93, 52.90, 49.2, 49.1, 17.9, 17.8.  **$^{19}\text{F}$  NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -72.9, -73.2. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{Na}]^+$  calculated for  $\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{F}_3\text{NO}_5\text{S}$ : 443.9658, found: 443.9669.

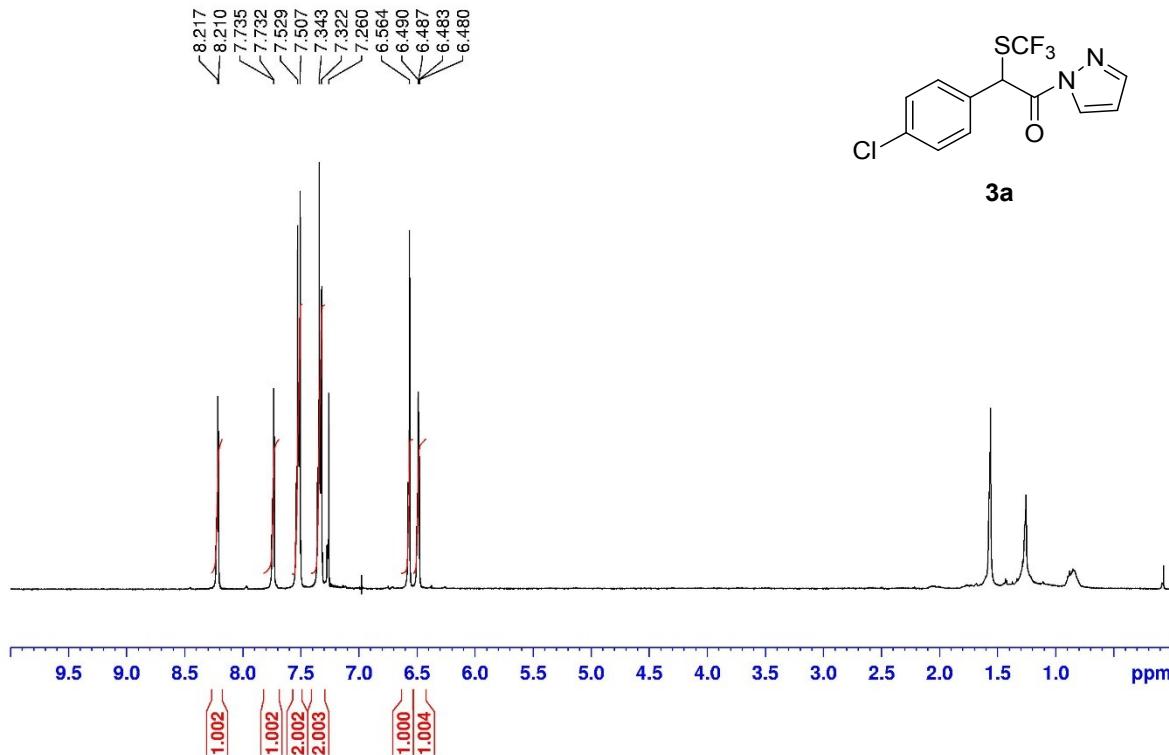
### Methyl 2-(2-(4-fluorophenyl)-2-((trifluoromethyl)sulfonyl)acetamido)-3-methylbutanoate (9e)



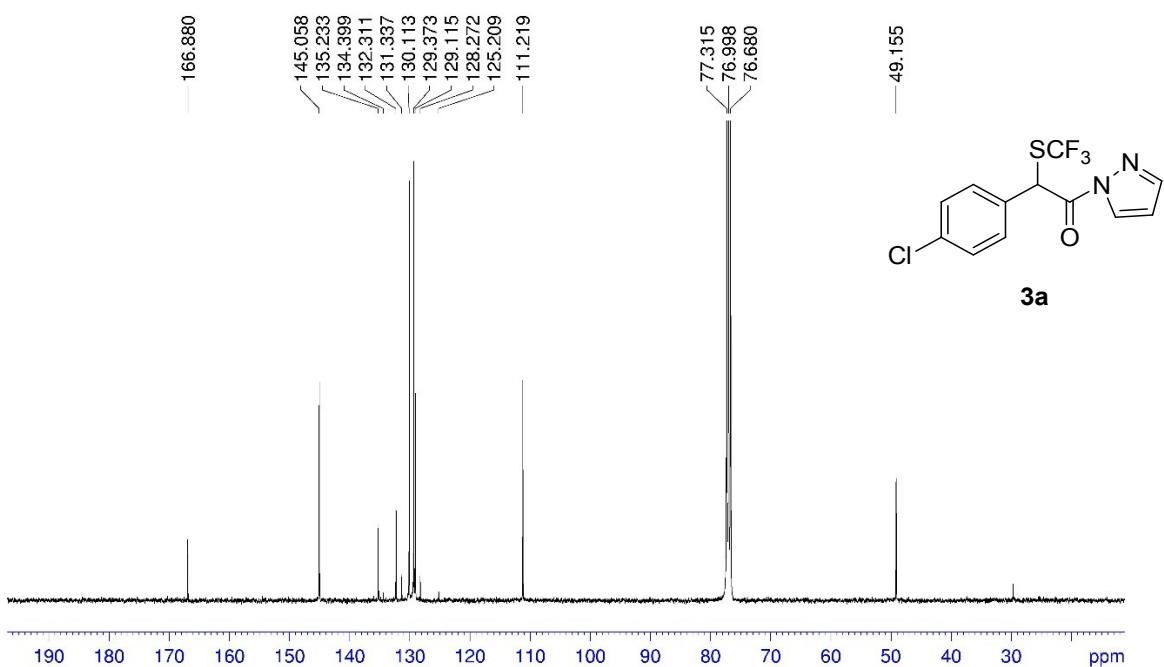
White solid, 58.3 mg, 73% yield, dr 1/1. **mp** 100.9-102.4 °C. **FTIR**  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ : 3343, 2970, 1747, 1668, 1607, 1539, 1509, 1440, 1373, 1211, 1116.  **$^1\text{H}$  NMR** ( $\text{CDCl}_3$ , 300 MHz): (diastereoisomers A+B)  $\delta$  7.65-7.57 (m, 2H+2H), 7.20-7.10 (m, 2H+2H), 7.03 (d, 1H,  $J = 8.4$  Hz), 6.94 (d, 1H,  $J = 7.8$  Hz), 5.29 (s, 1H+1H), 4.63-4.58 (m, 1H+1H), 3.76 (s, 3H), 3.75 (s, 3H), 2.25 (sept, 1H+1H,  $J = 6.4$  Hz), 0.99 (d, 3H,  $J = 6.4$  Hz), 0.94 (d, 3H,  $J = 6.4$  Hz), 0.93 (d, 3H,  $J = 6.4$  Hz), 0.89 (d, 3H,  $J = 6.4$  Hz).  **$^{13}\text{C}$  NMR** ( $\text{CDCl}_3$ , 75 MHz): (diastereoisomers A+B)  $\delta$  171.6, 171.4, 164.2 (d,  $^1J_{\text{CF}} = 252.4$  Hz), 164.1 (d,  $^1J_{\text{CF}} = 252.3$  Hz), 160.6, 159.8, 132.8 (d,  $^3J_{\text{CF}} = 8.7$  Hz), 132.6 (d,  $^3J_{\text{CF}} = 8.7$  Hz), 120.7 (d,  $^4J_{\text{CF}} = 2.9$  Hz), 120.6 (d,  $^4J_{\text{CF}} = 2.6$  Hz), 119.7 (q,  $^1J_{\text{CF}} = 329.8$  Hz), 119.6 (q,  $^1J_{\text{CF}} = 329.9$  Hz), 116.7 (d,  $^2J_{\text{CF}} = 22.4$  Hz), 116.4 (d,  $^2J_{\text{CF}} = 22.4$  Hz), 70.2, 70.1, 58.1, 57.9, 52.5, 31.5, 31.1, 18.8, 17.5, 17.4.  **$^{19}\text{F}$  NMR** ( $\text{CDCl}_3$ , 376 MHz):  $\delta$  -73.2, -73.5, -109.3, -109.8. **HRMS (MALDI-FT ICR)** exact mass  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{15}\text{H}_{17}\text{F}_4\text{NO}_5\text{S}$ : 400.0764, found: 400.0725.

## NMR Spectra

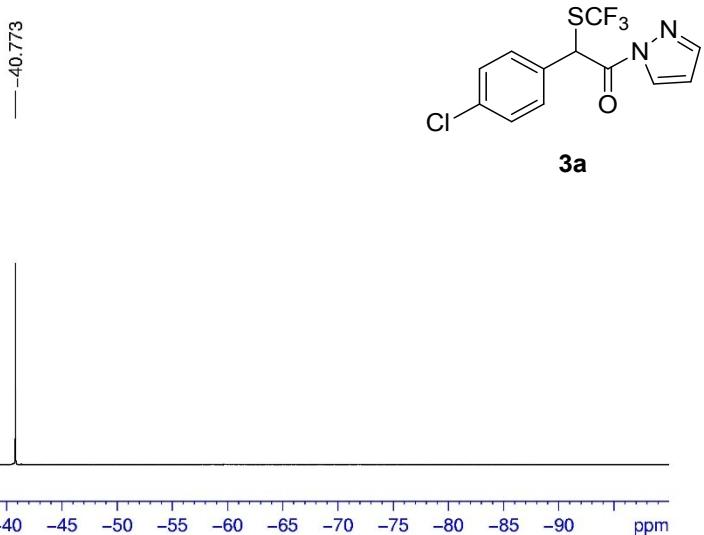
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



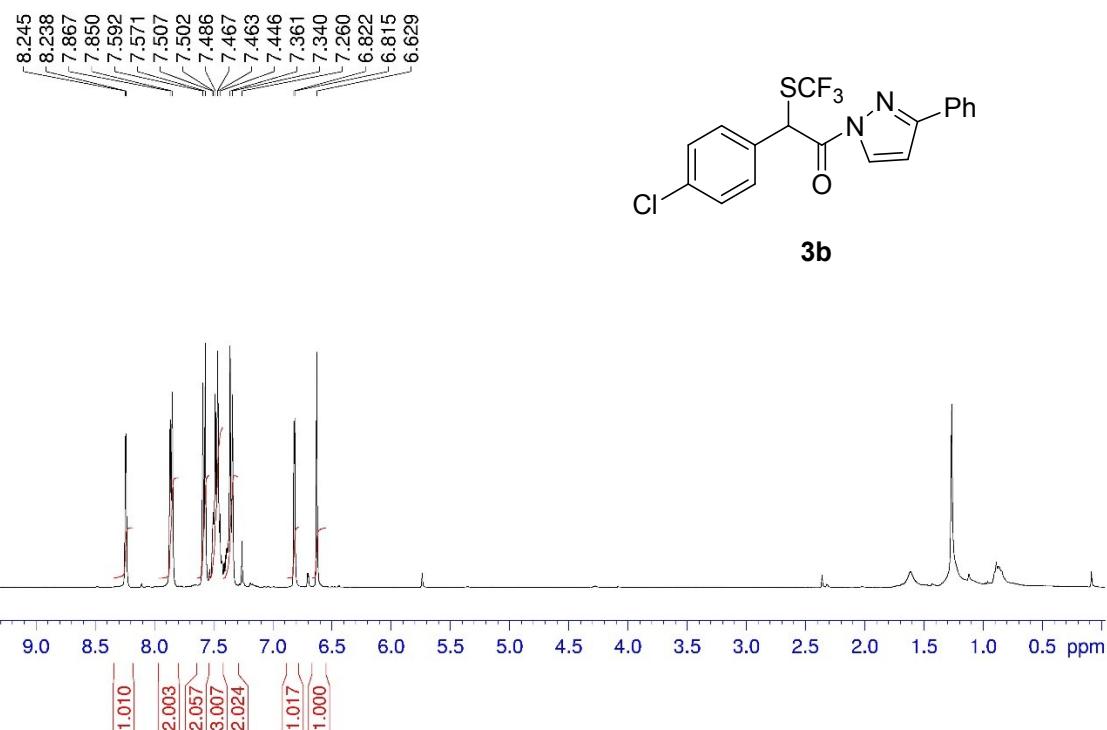
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



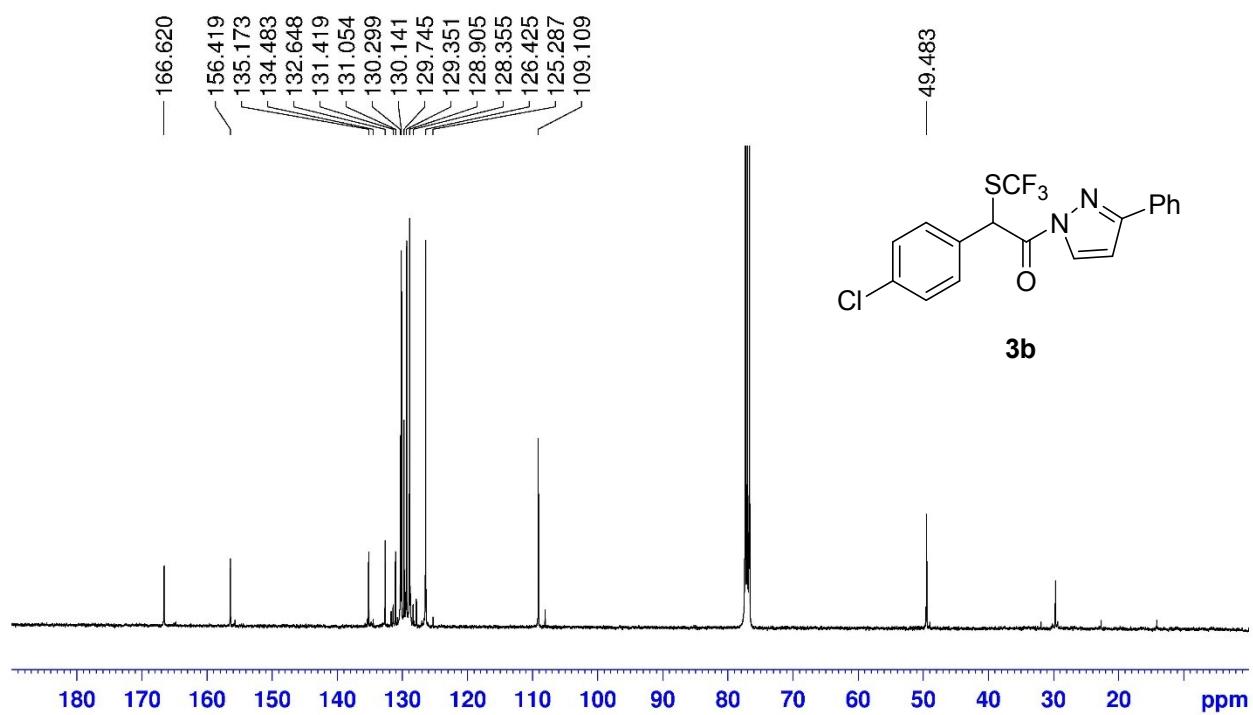
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



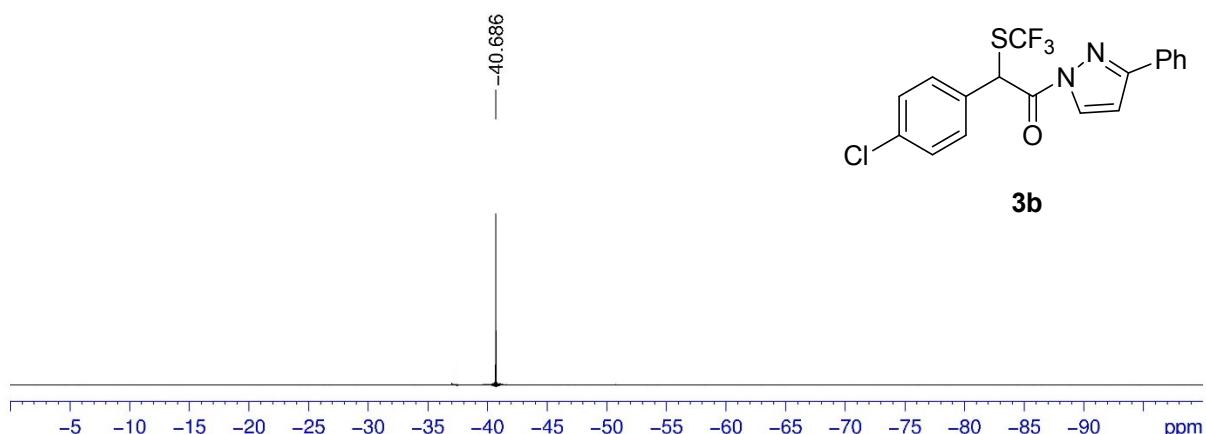
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



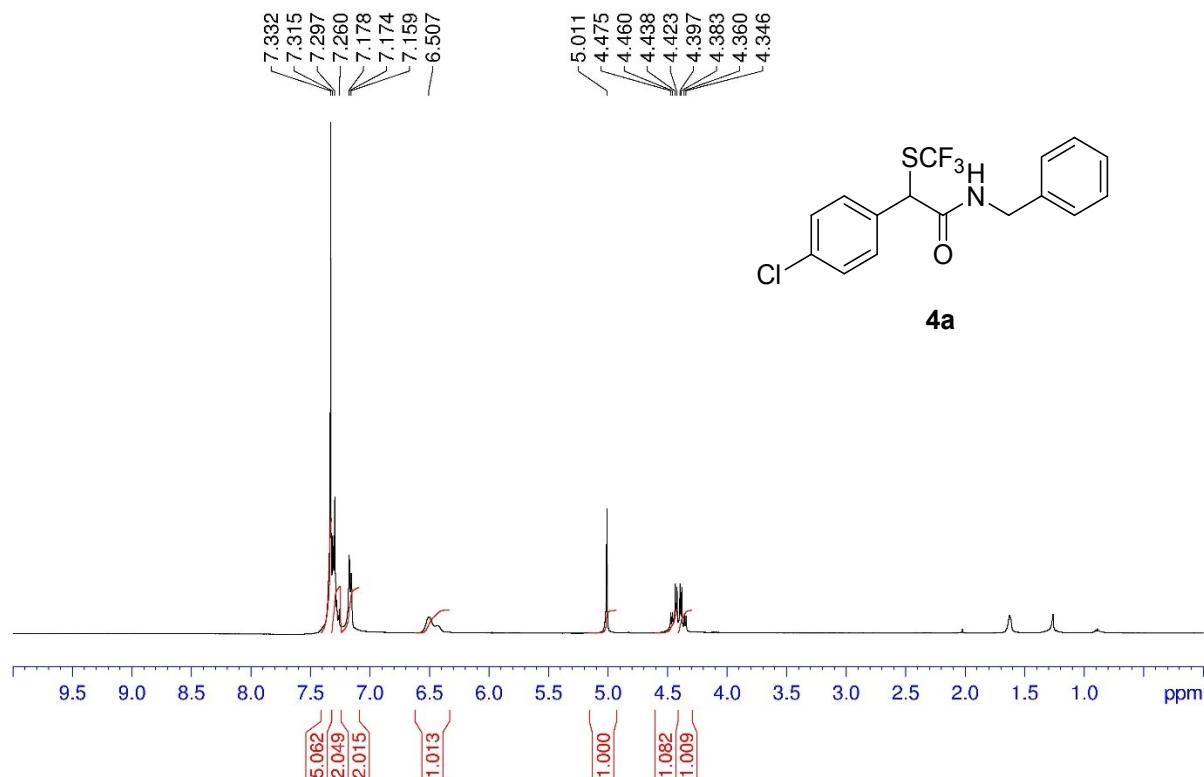
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



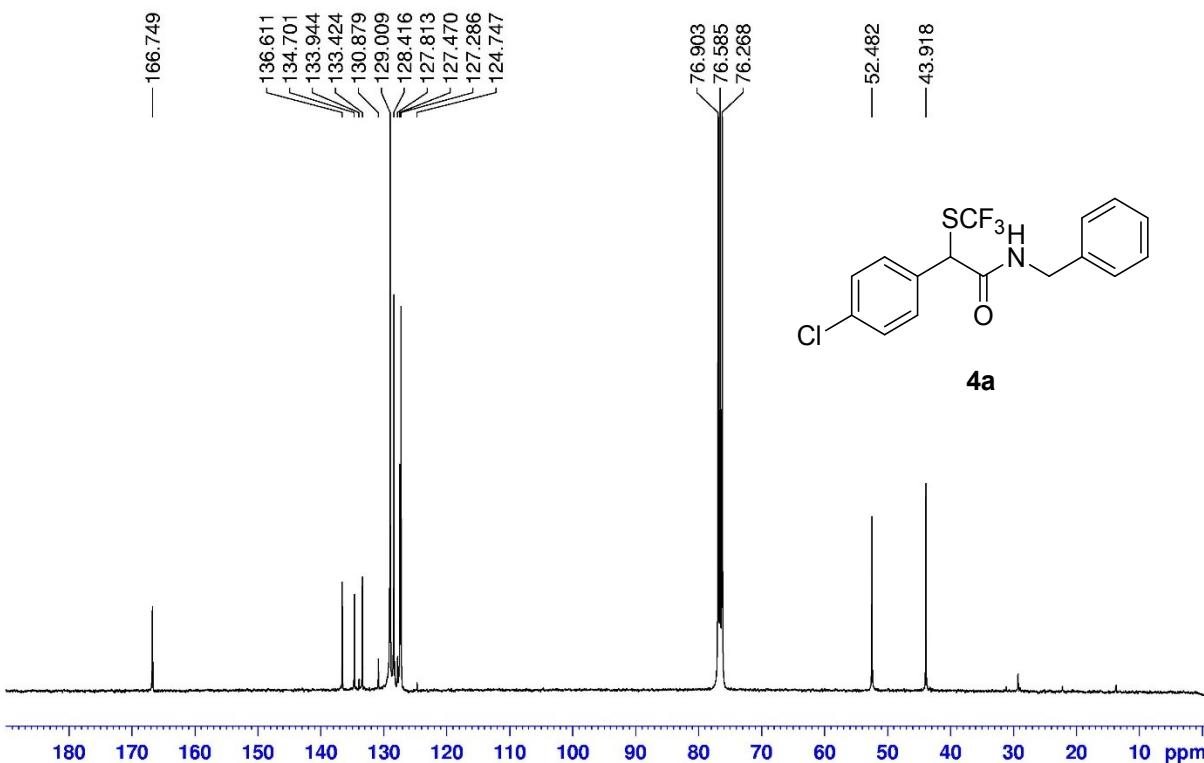
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



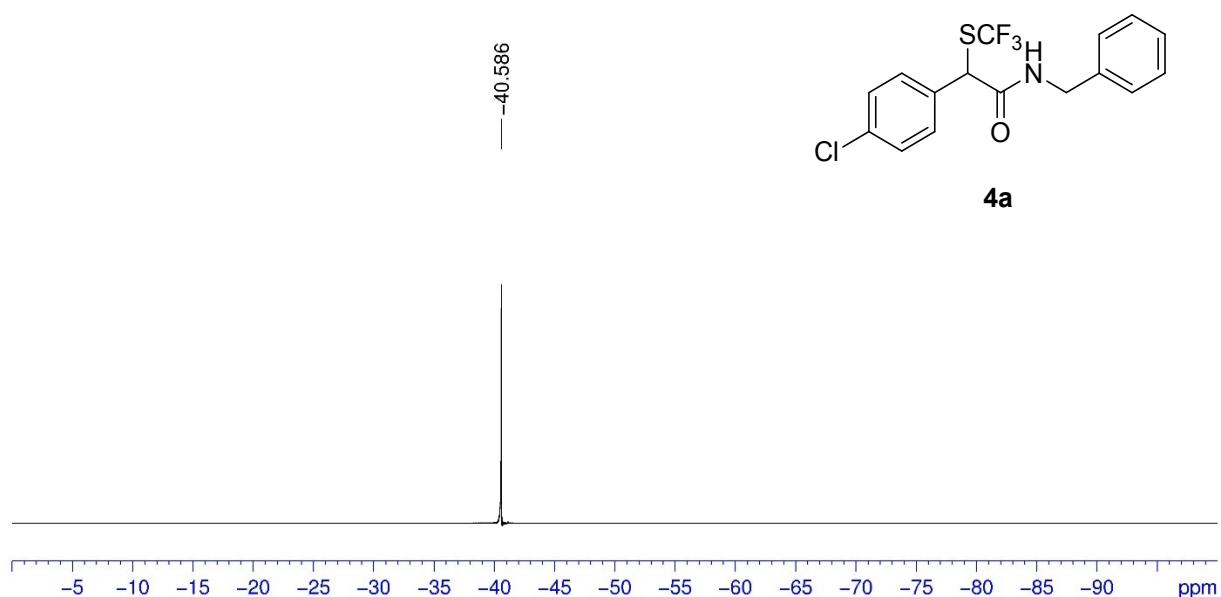
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



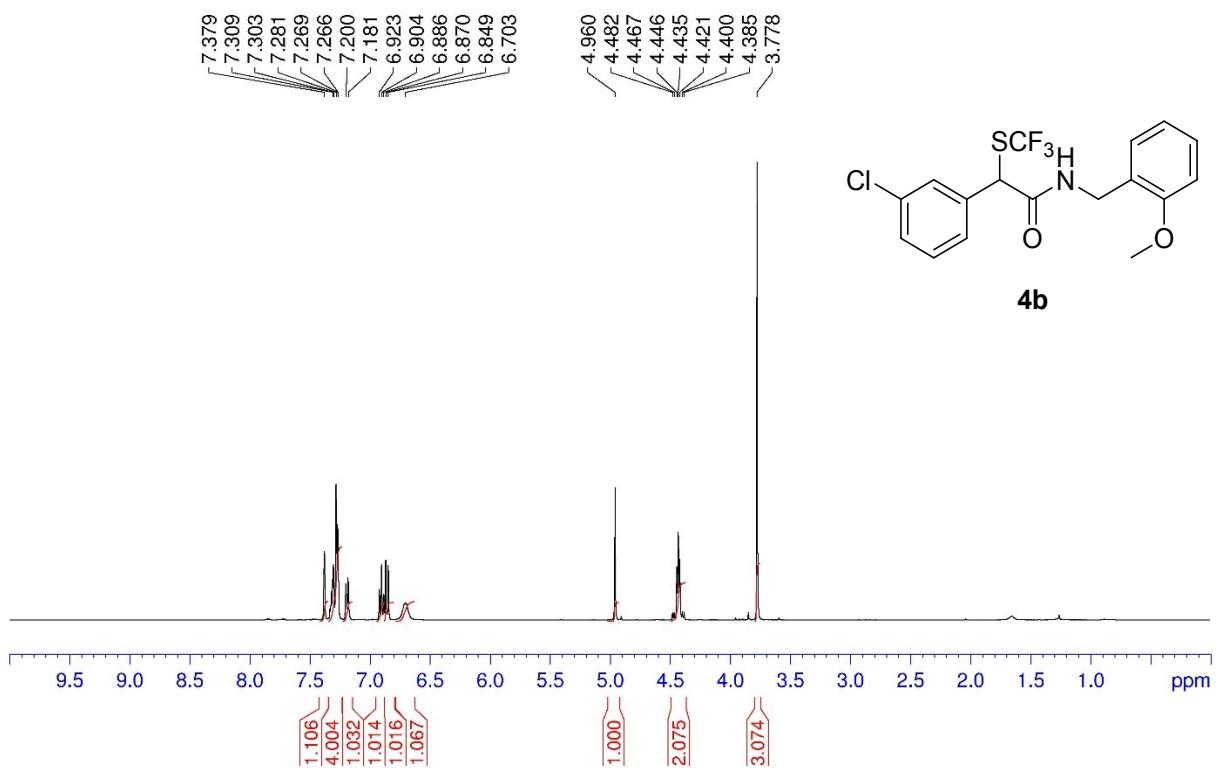
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



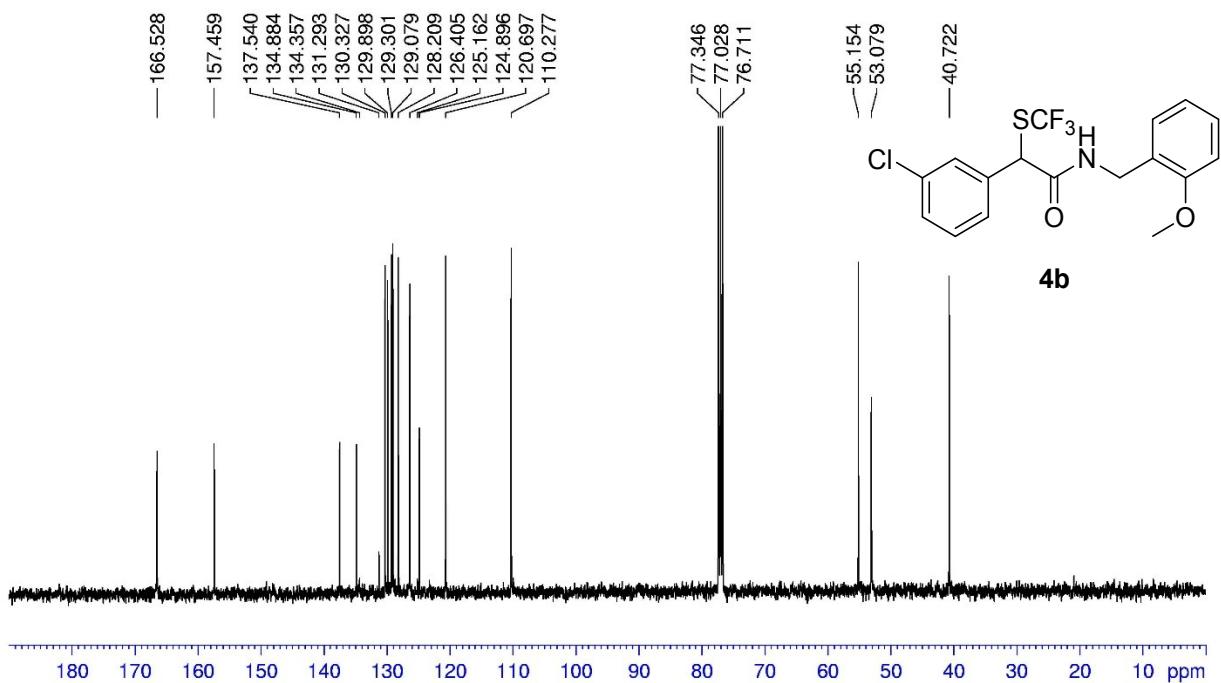
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



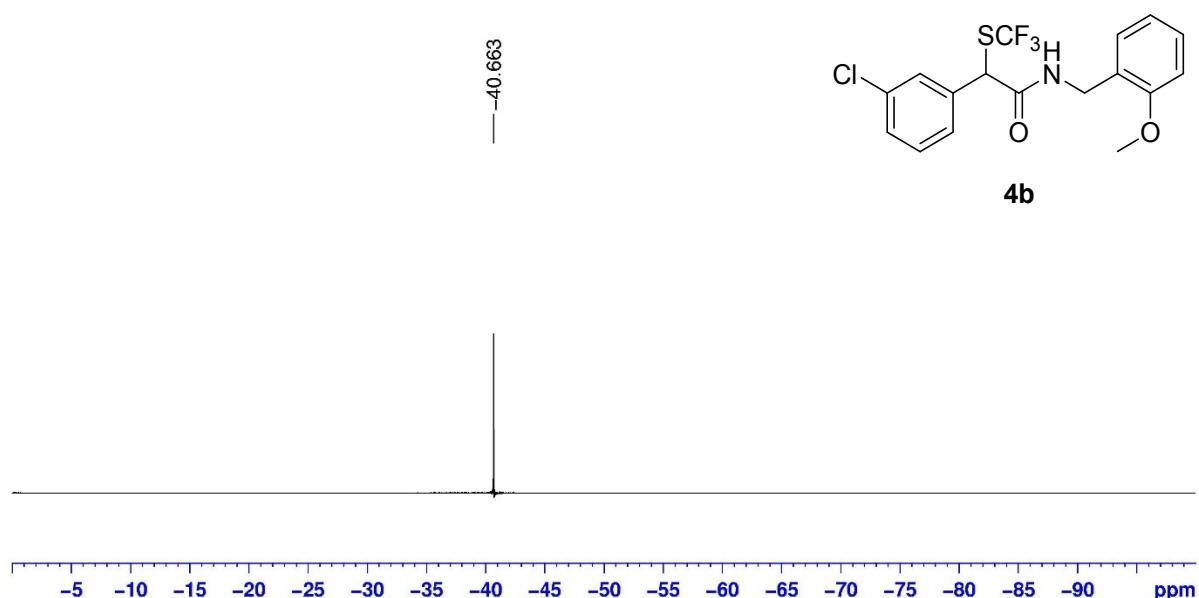
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



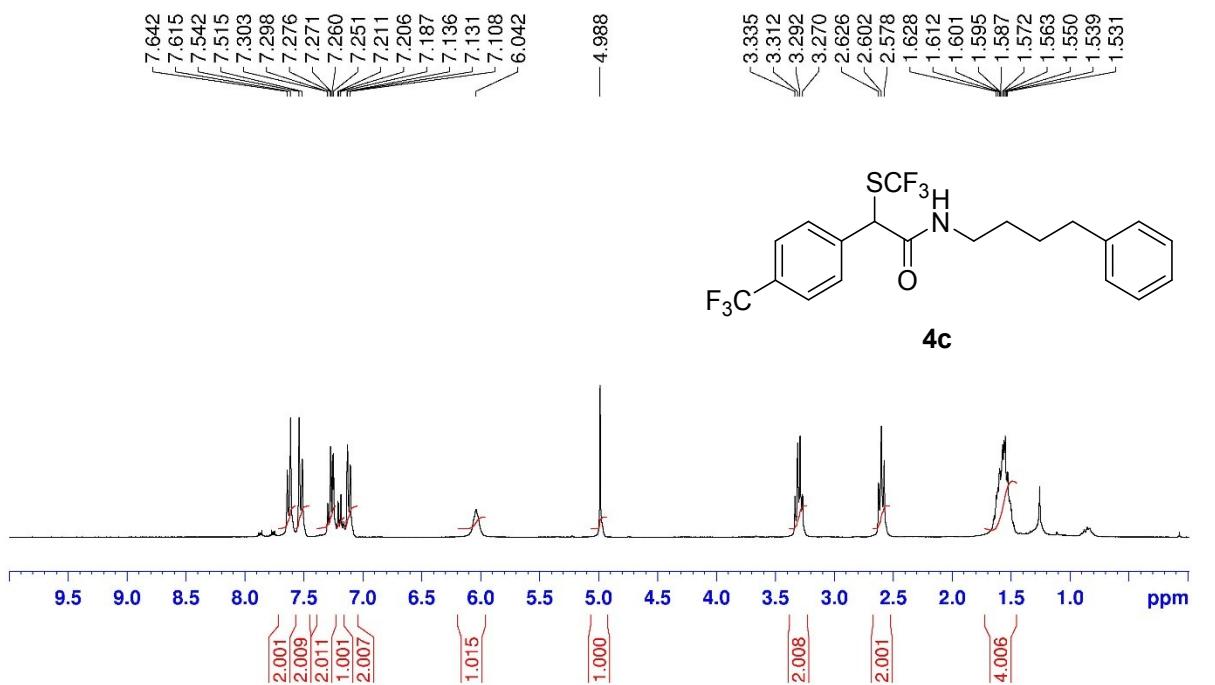
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



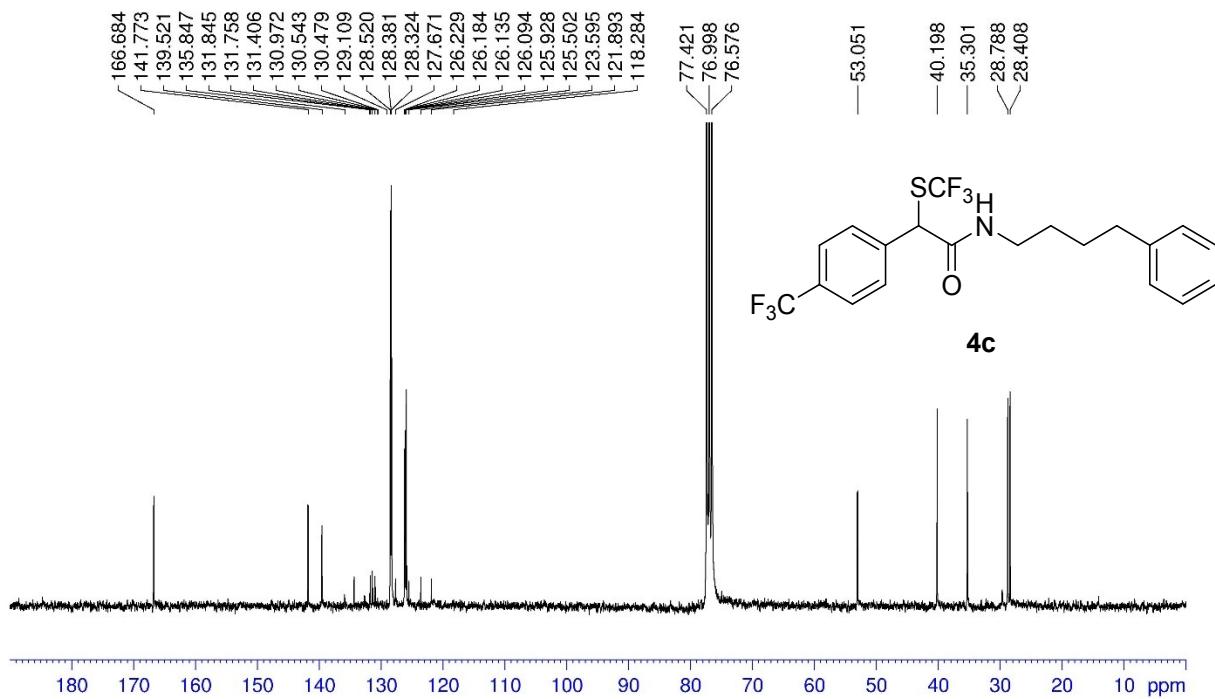
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



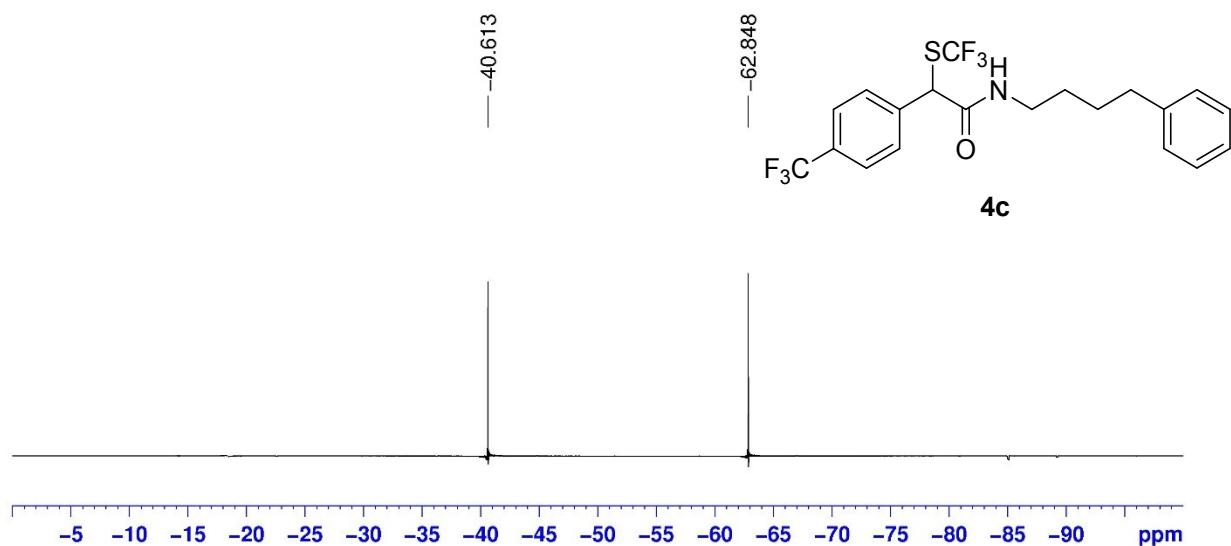
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



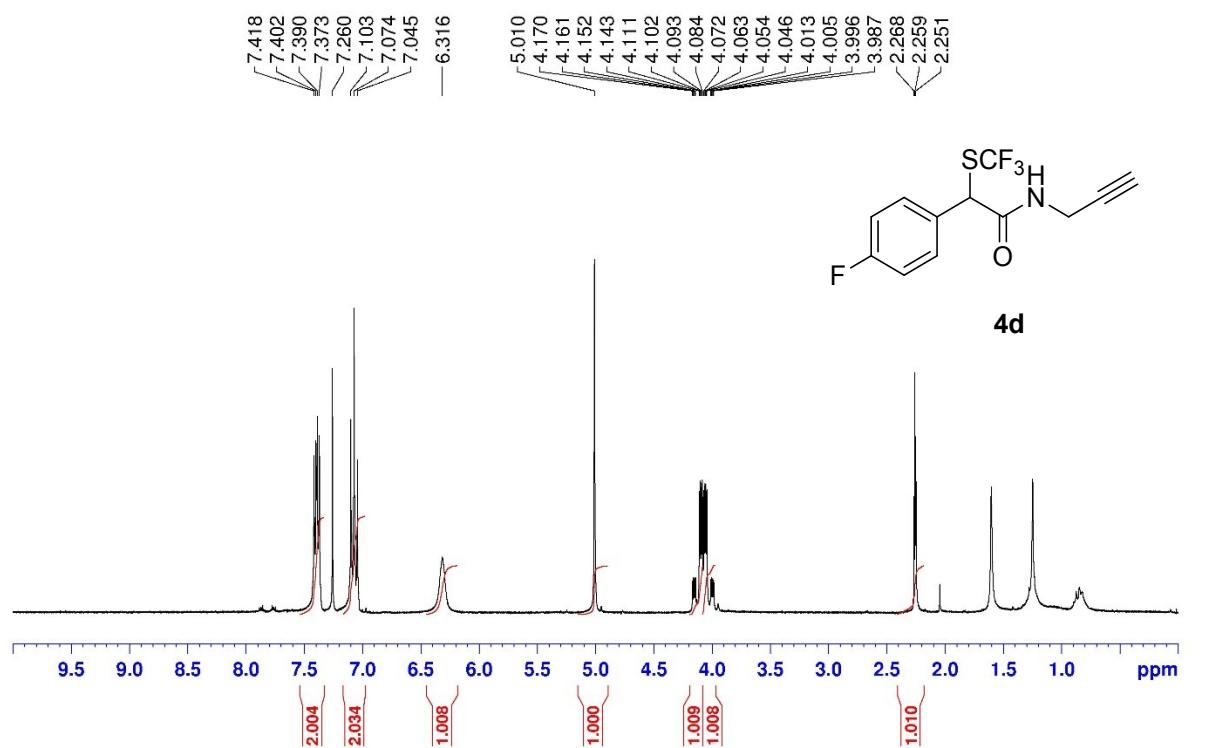
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



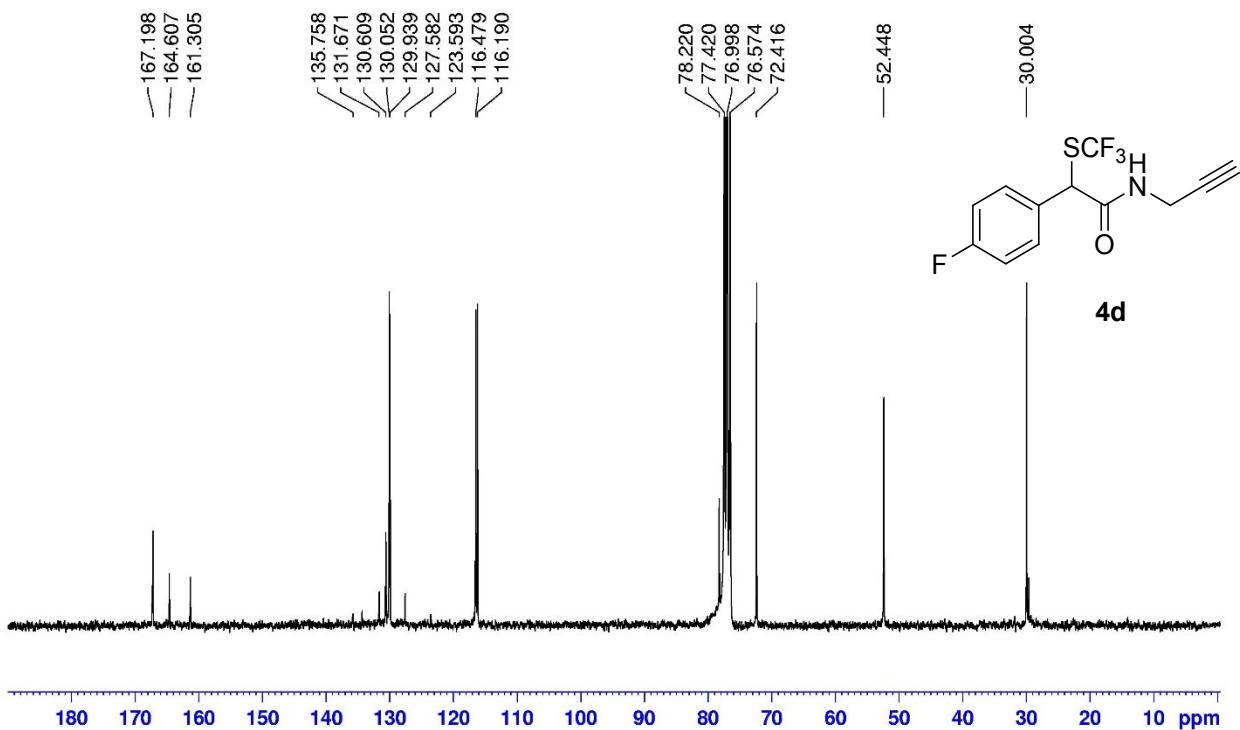
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



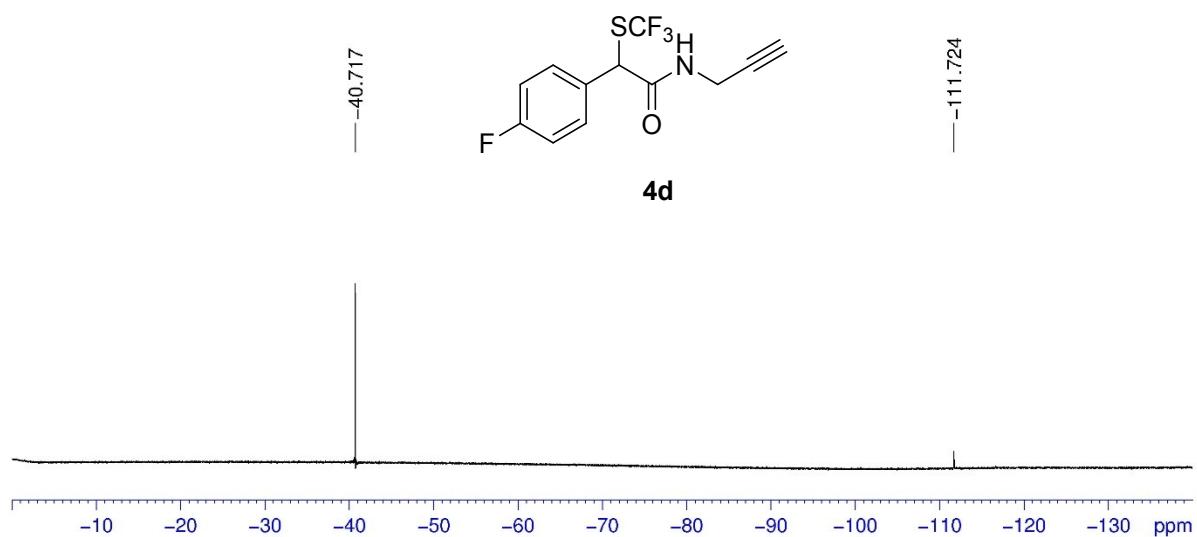
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



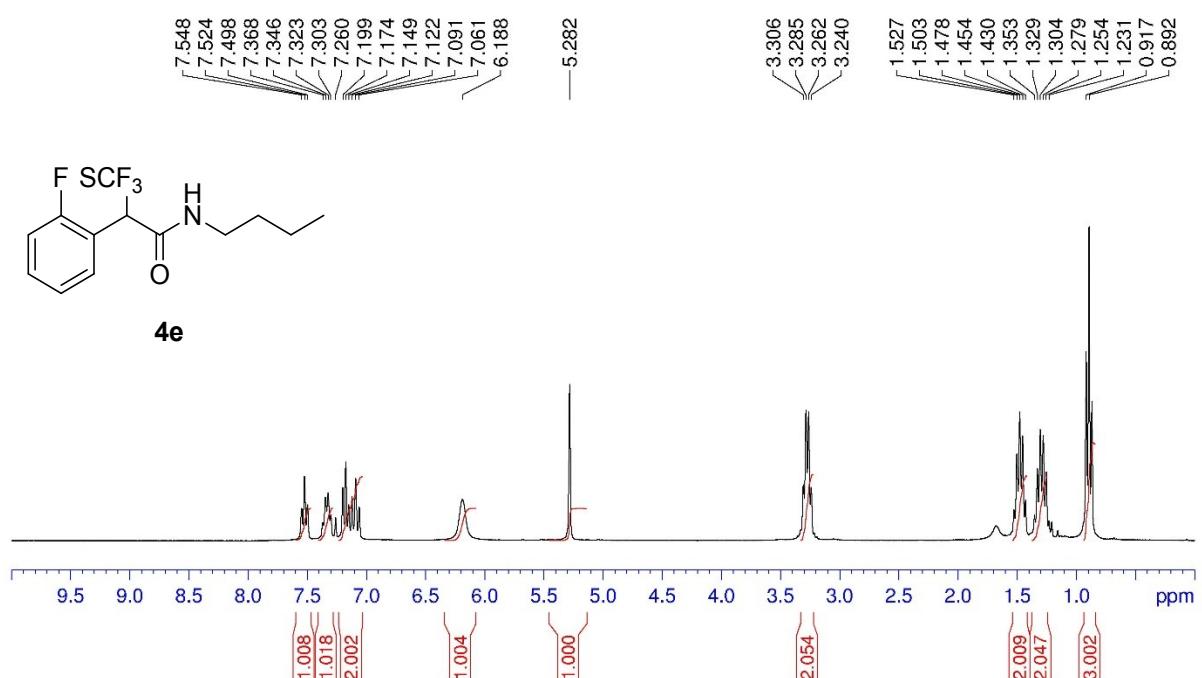
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



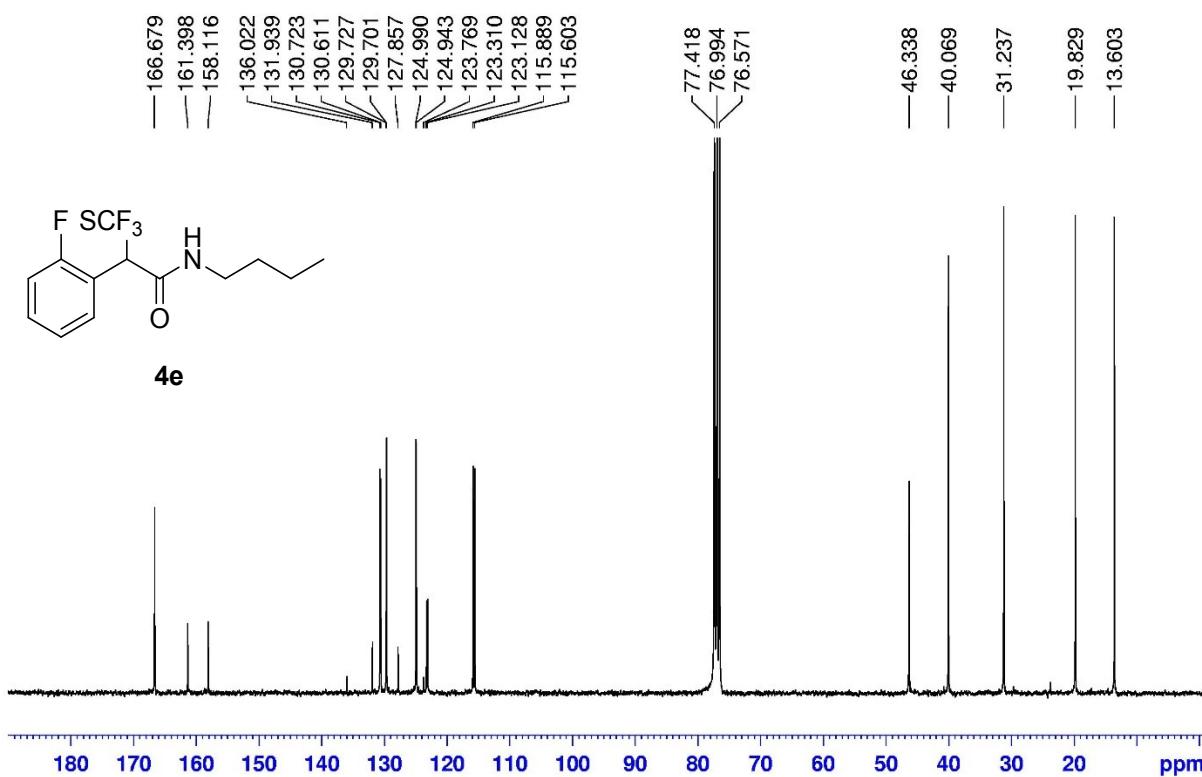
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



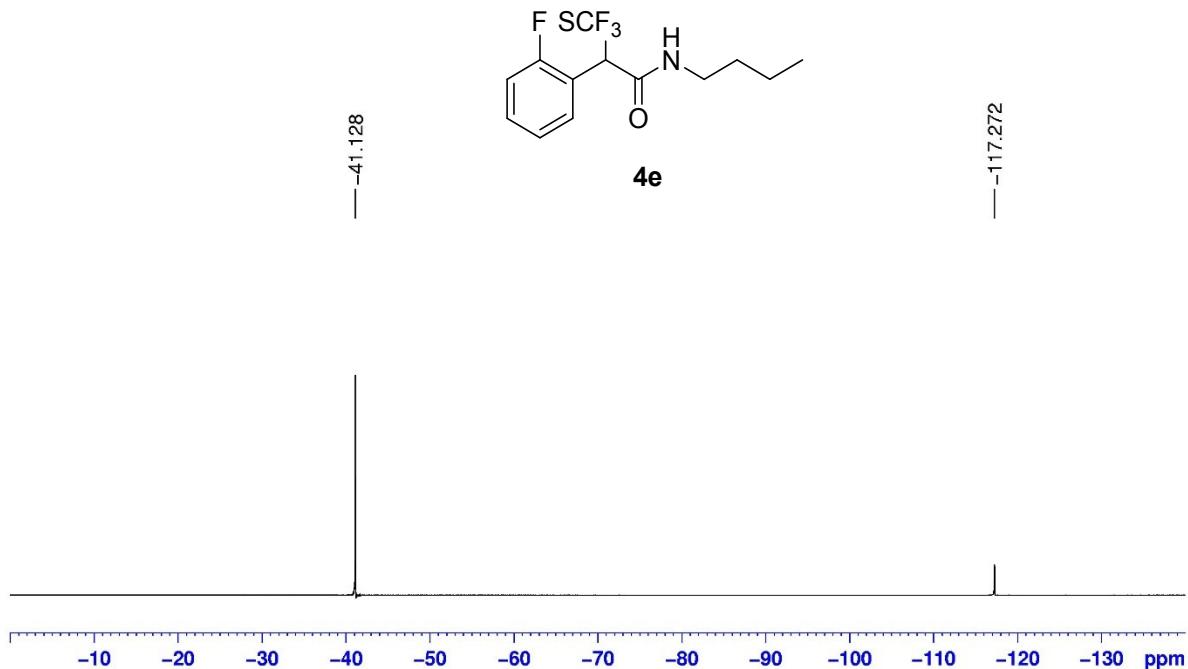
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



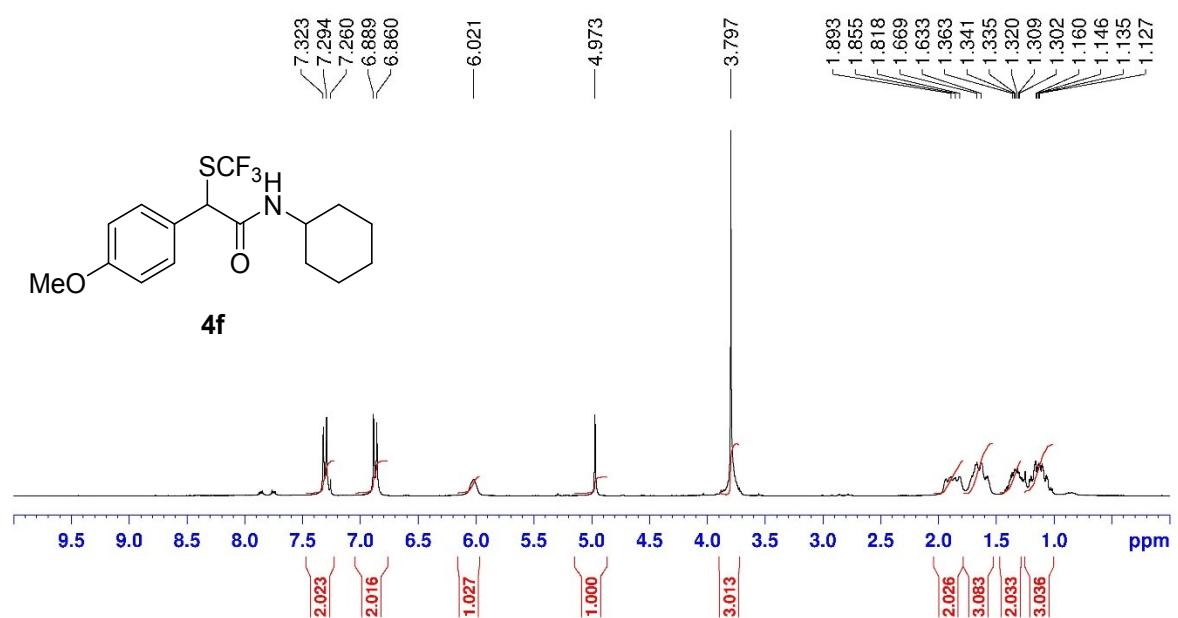
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



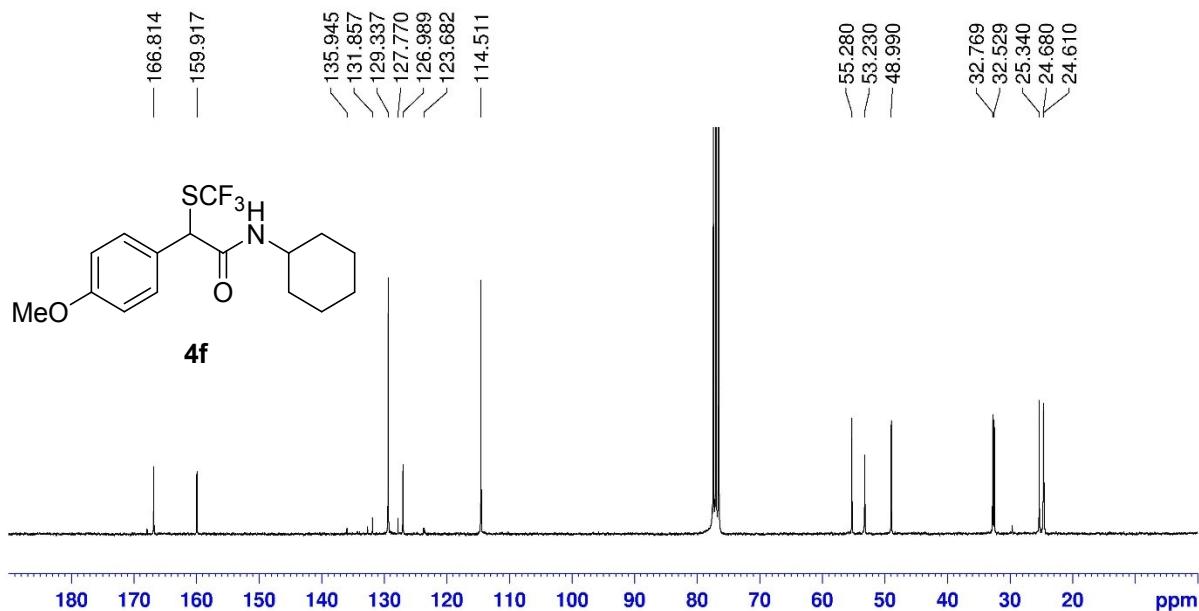
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



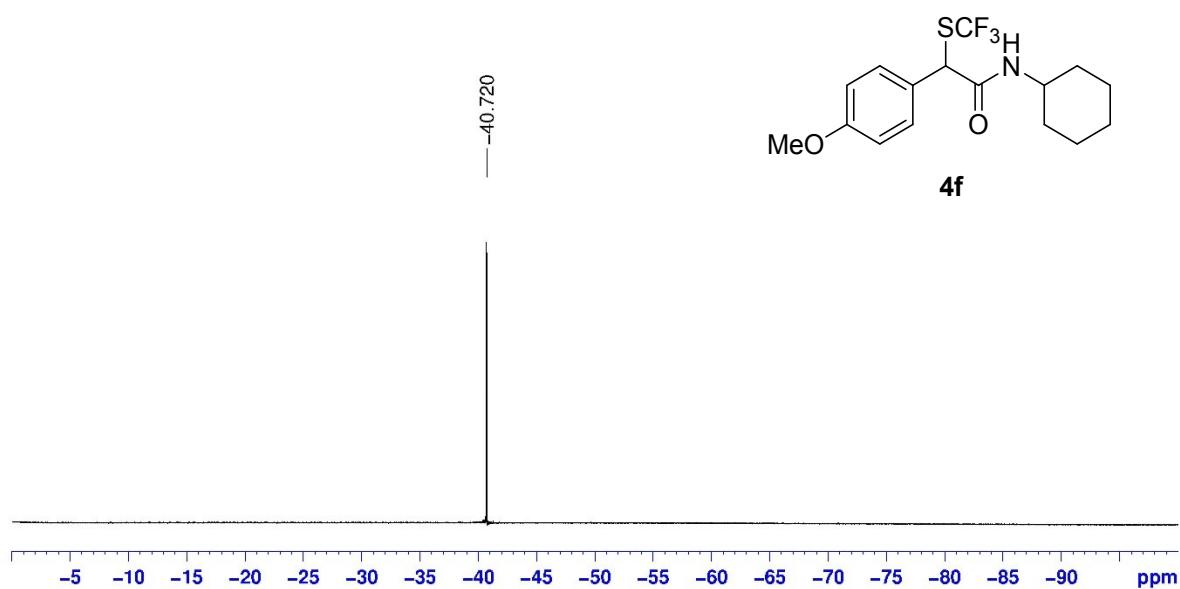
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



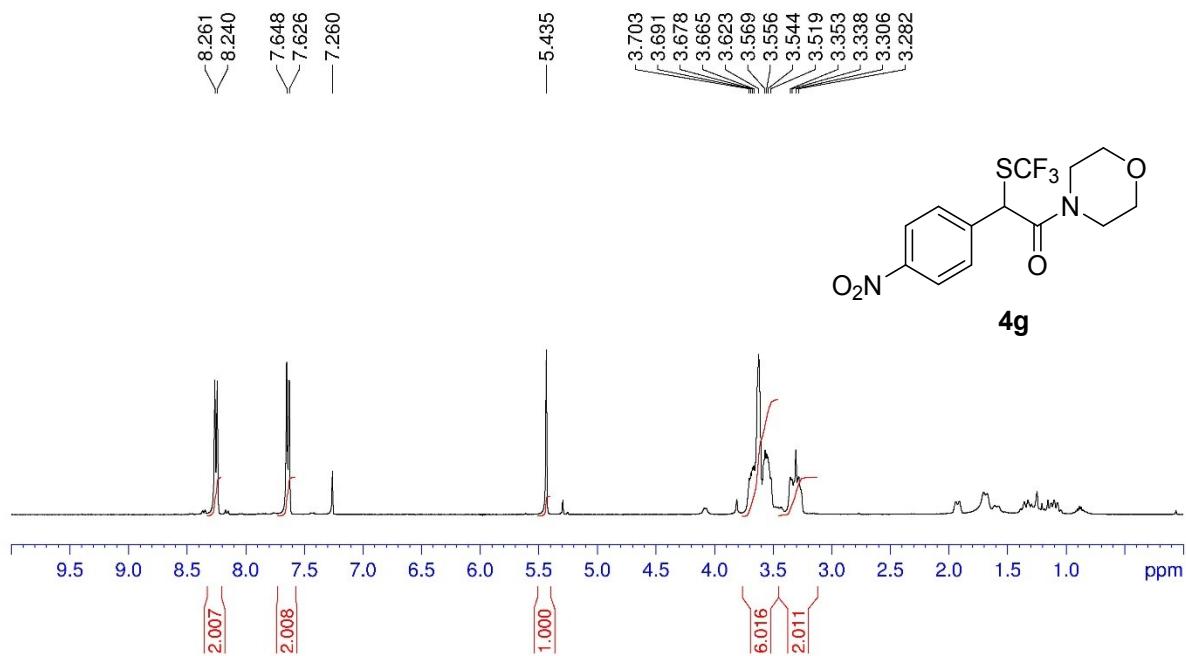
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



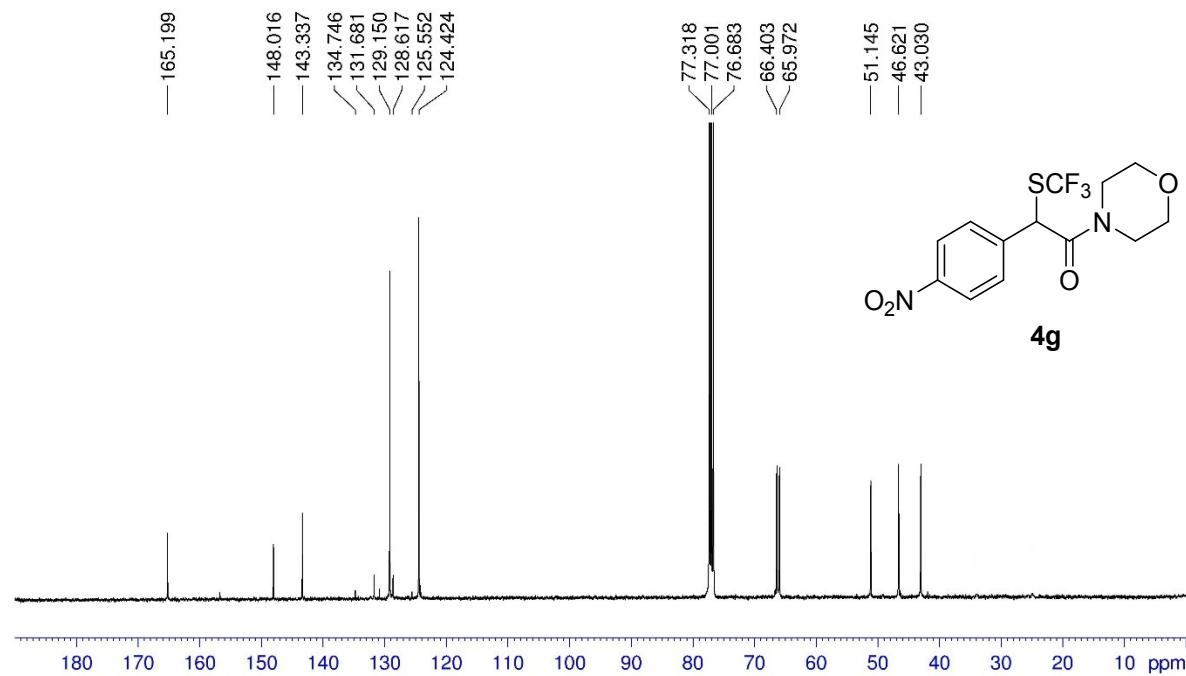
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



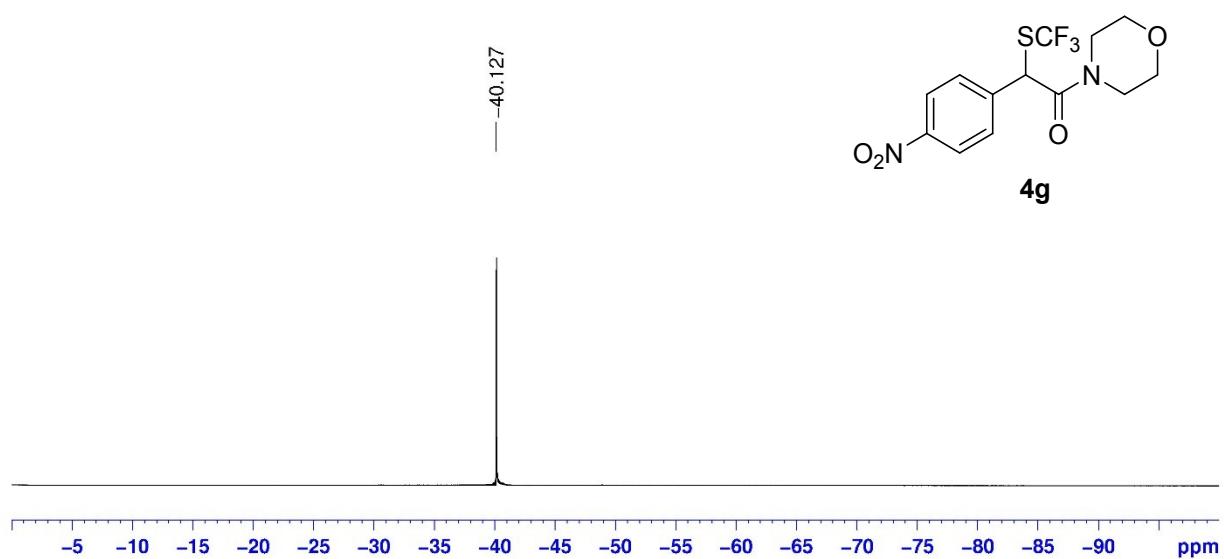
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



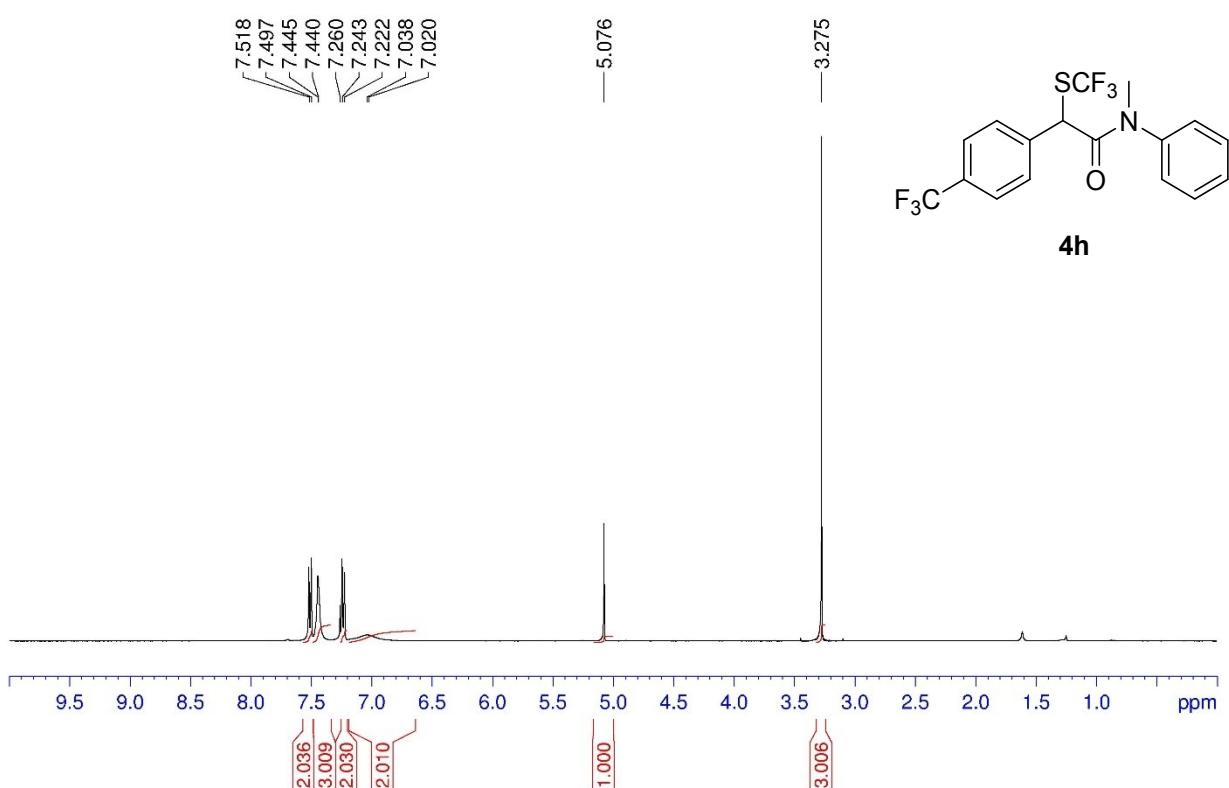
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



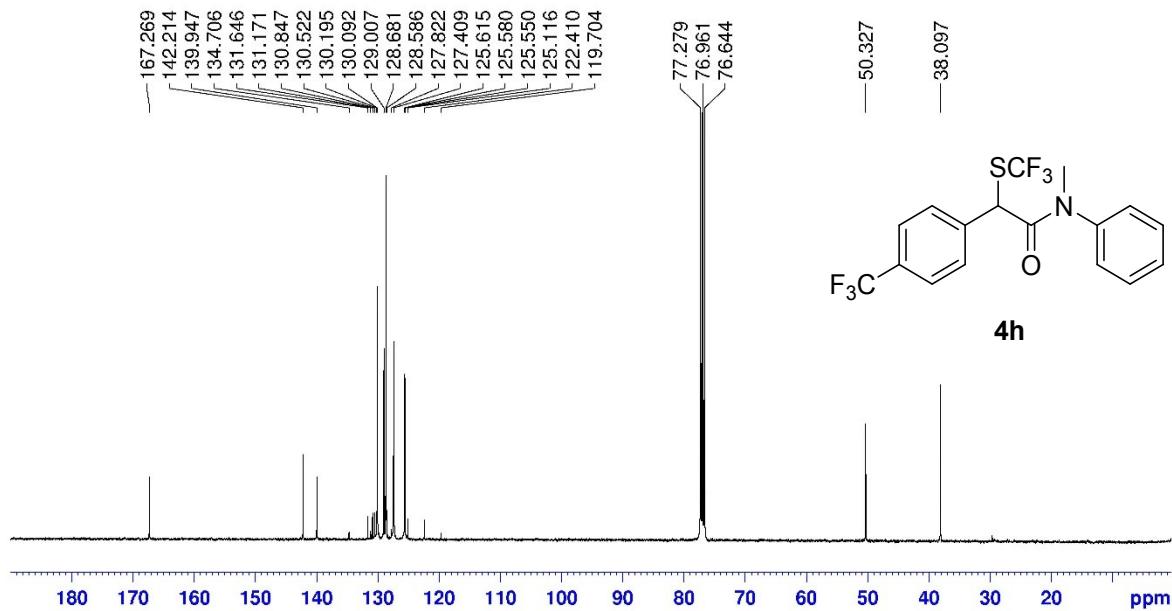
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



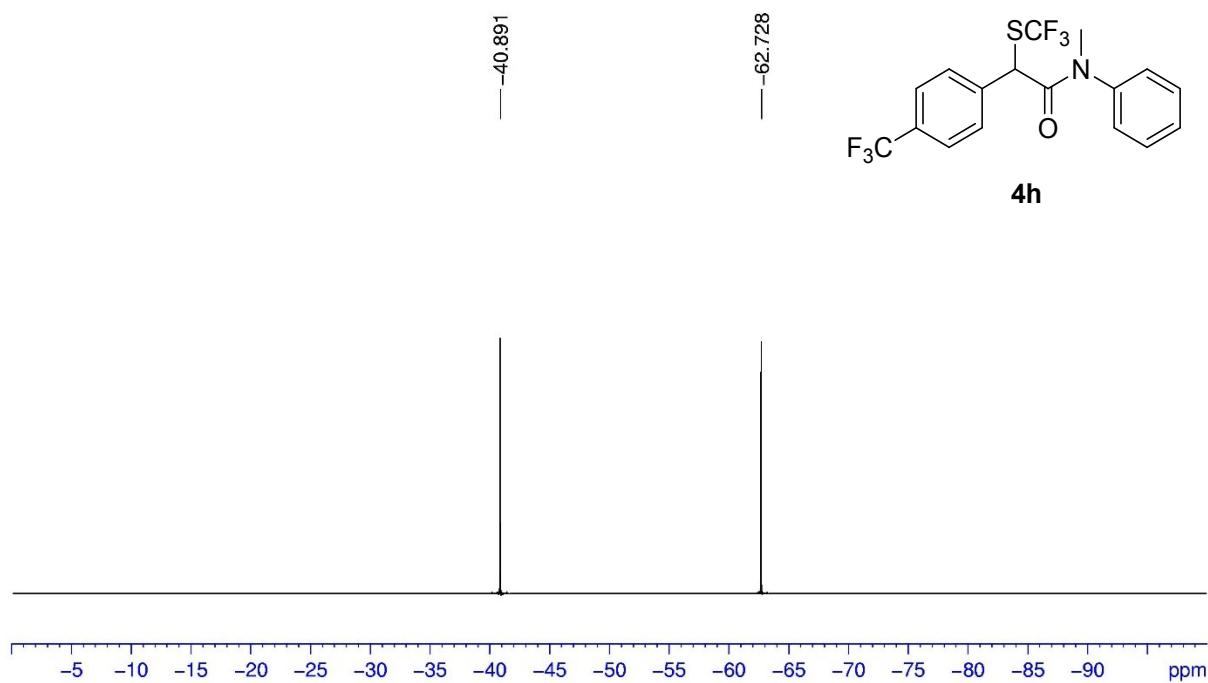
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



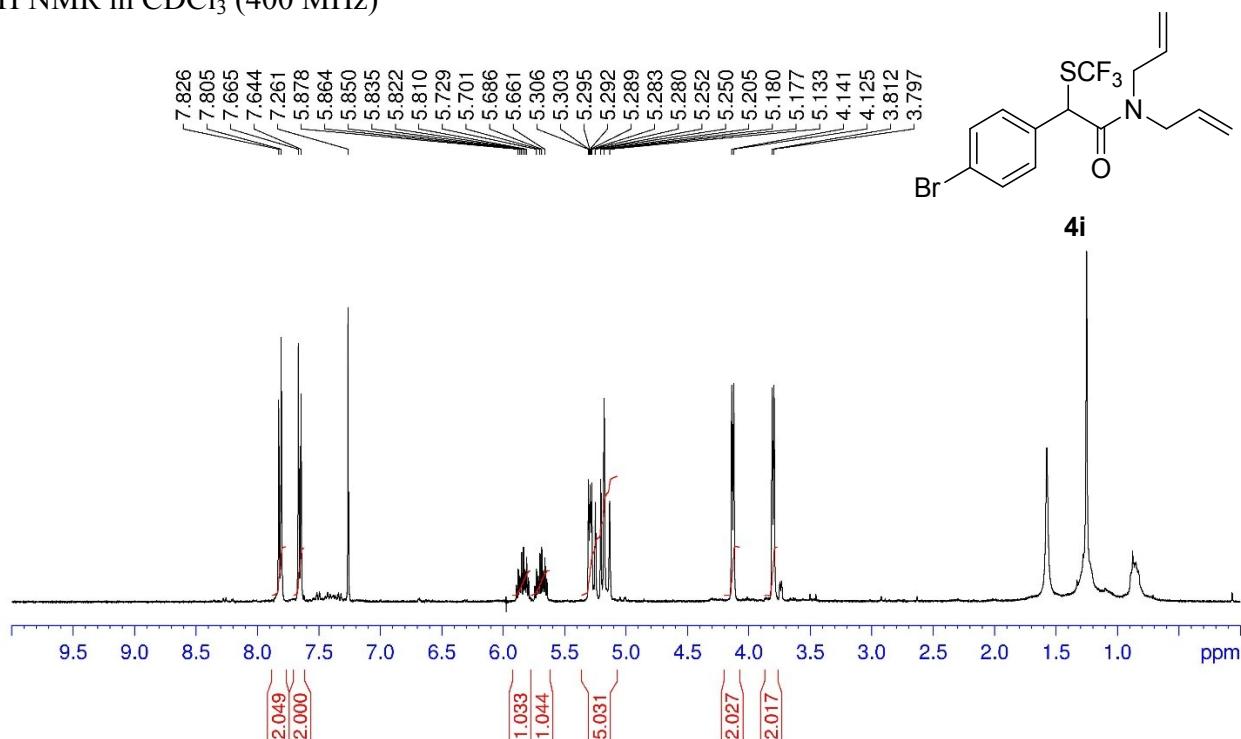
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



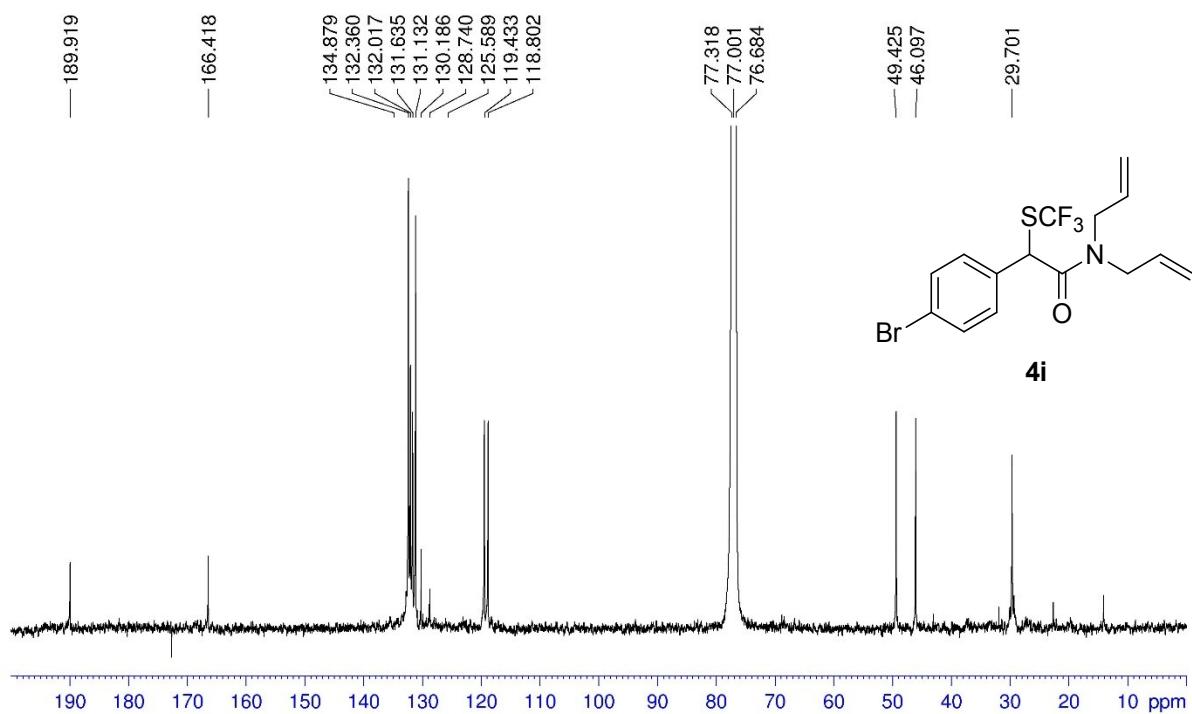
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



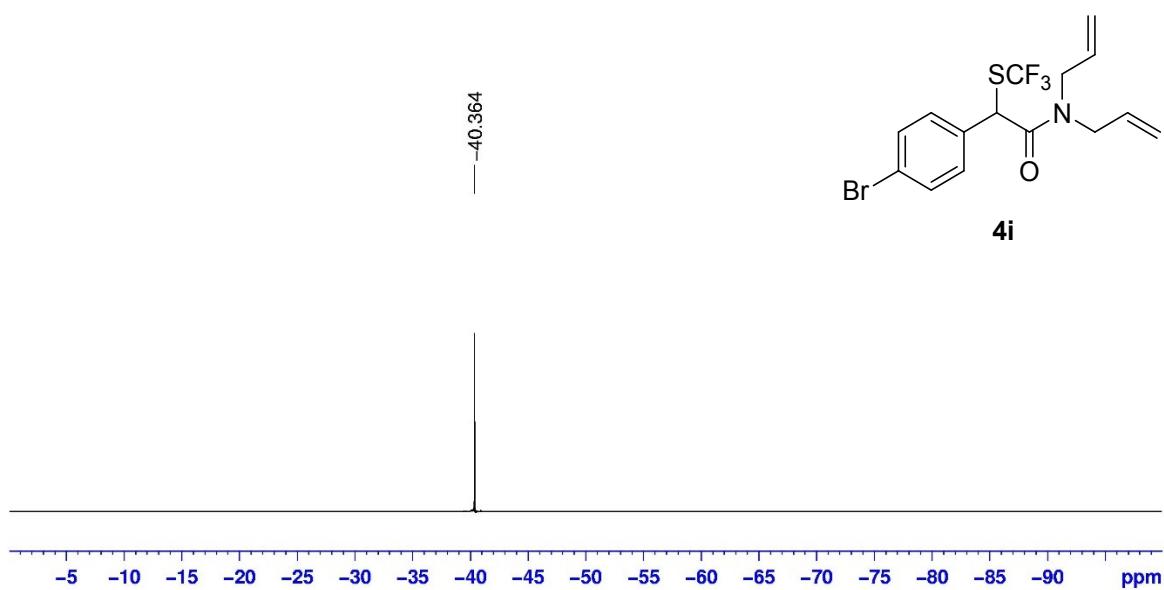
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



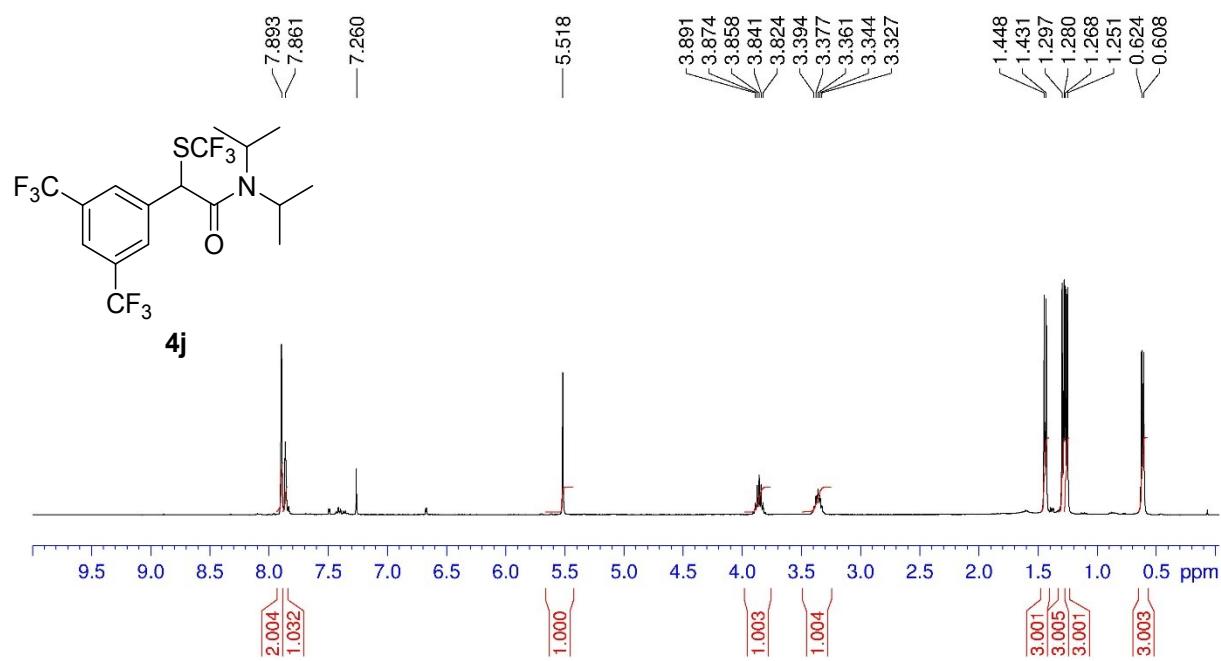
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



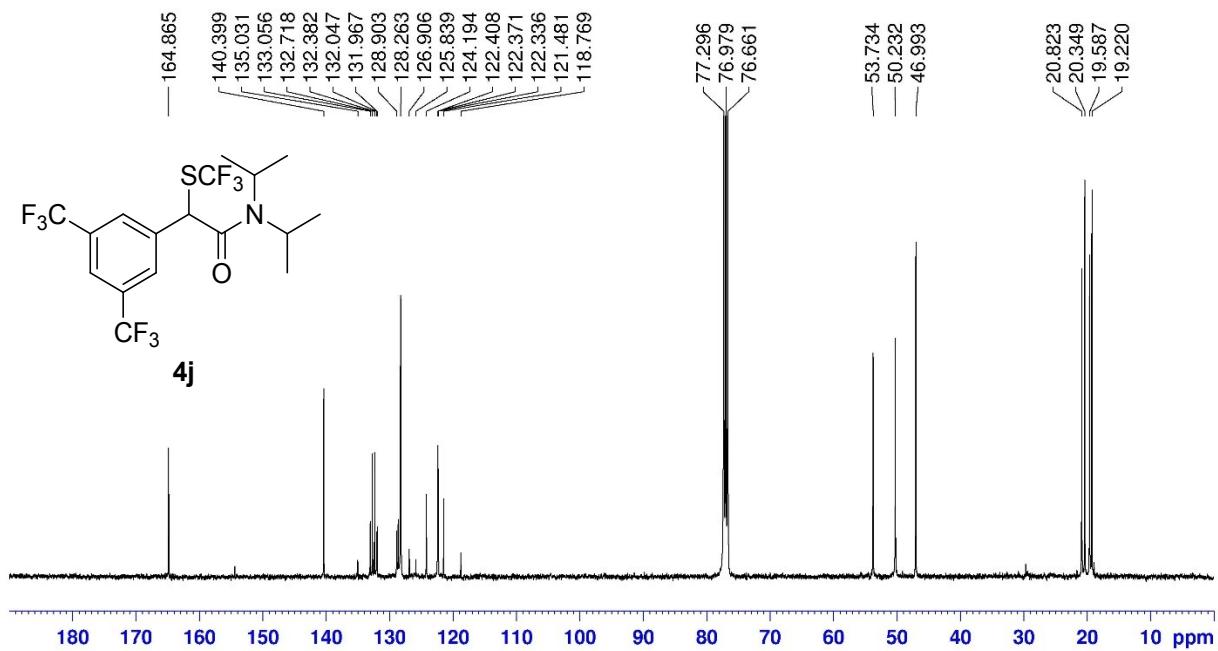
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



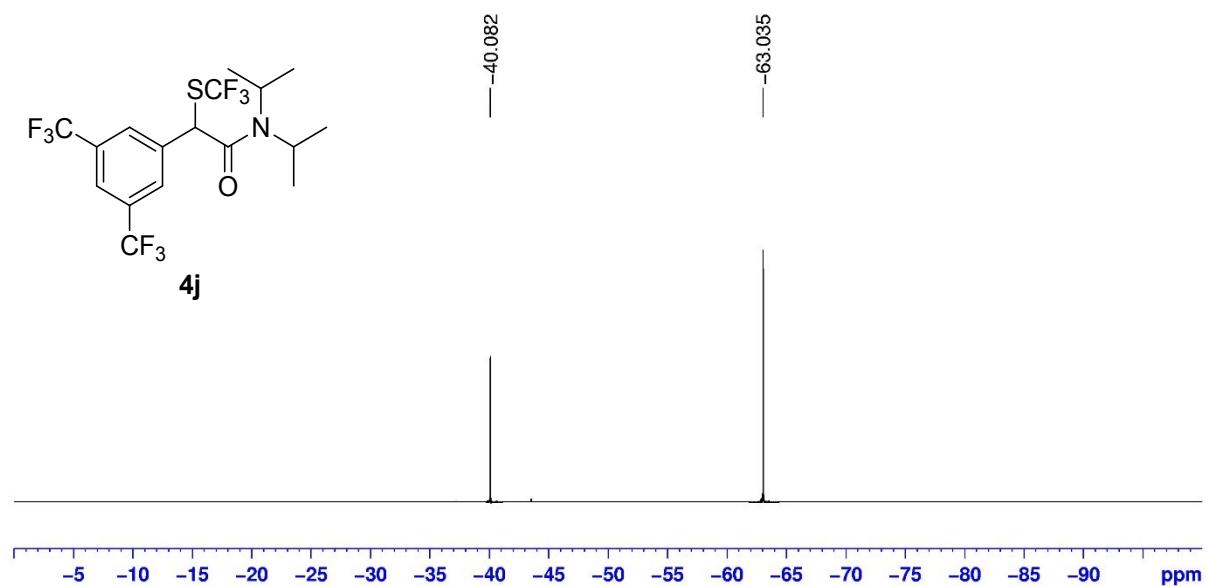
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



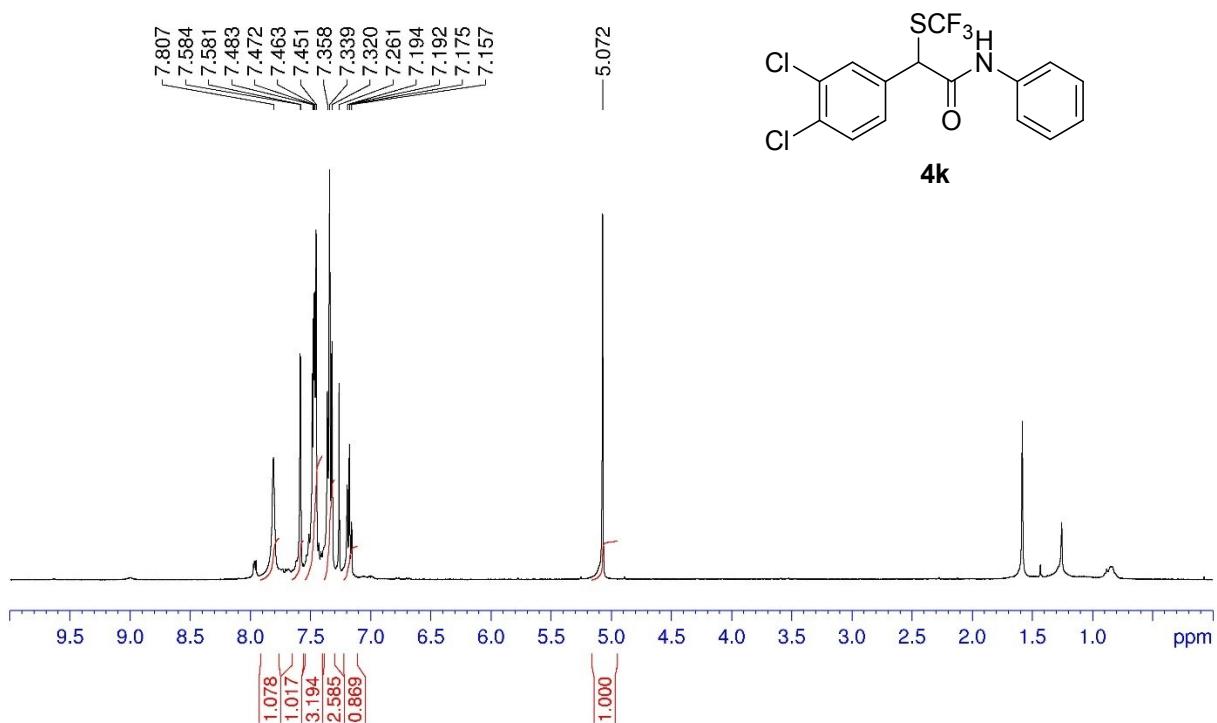
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



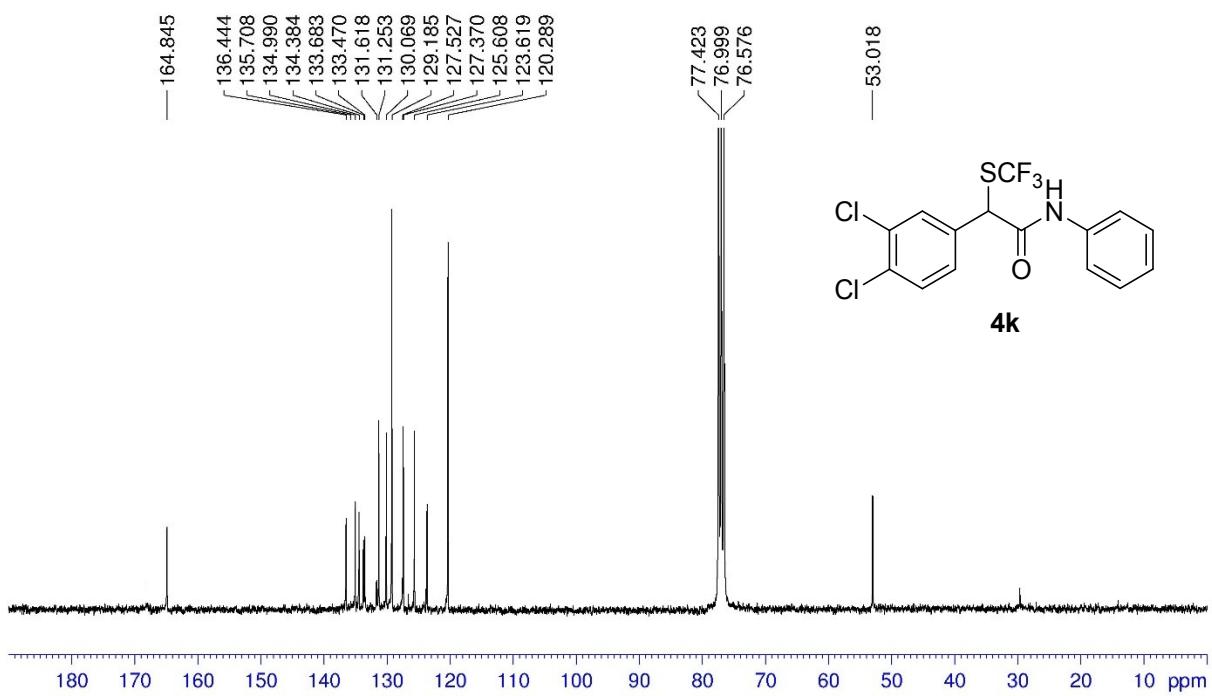
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



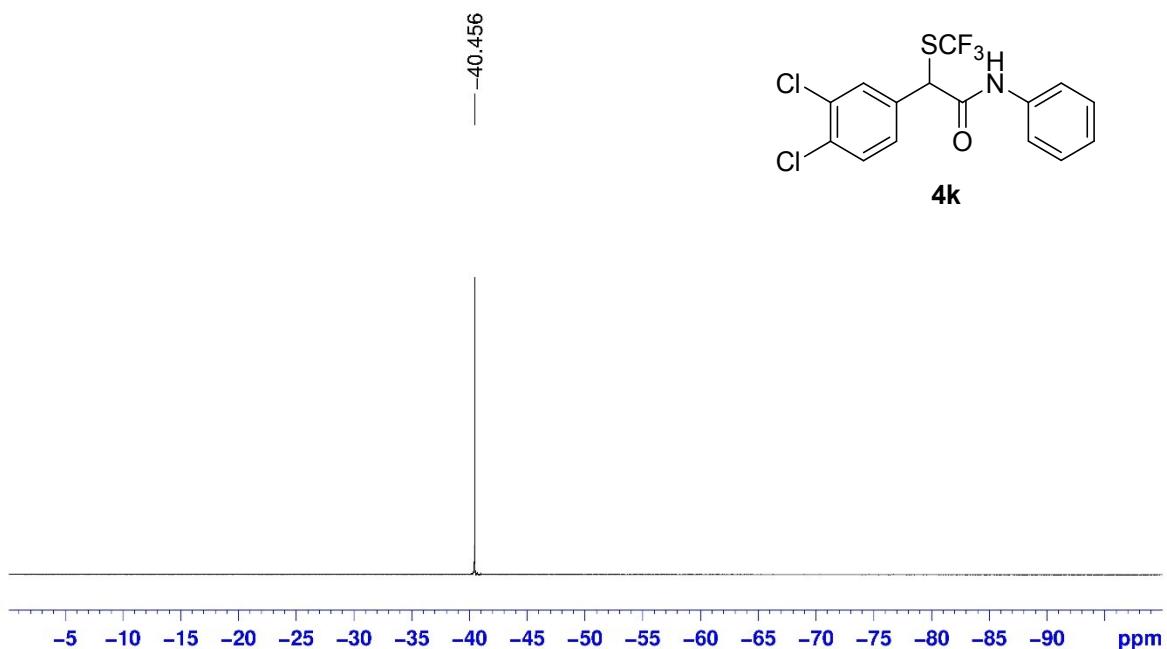
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



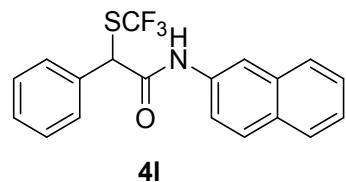
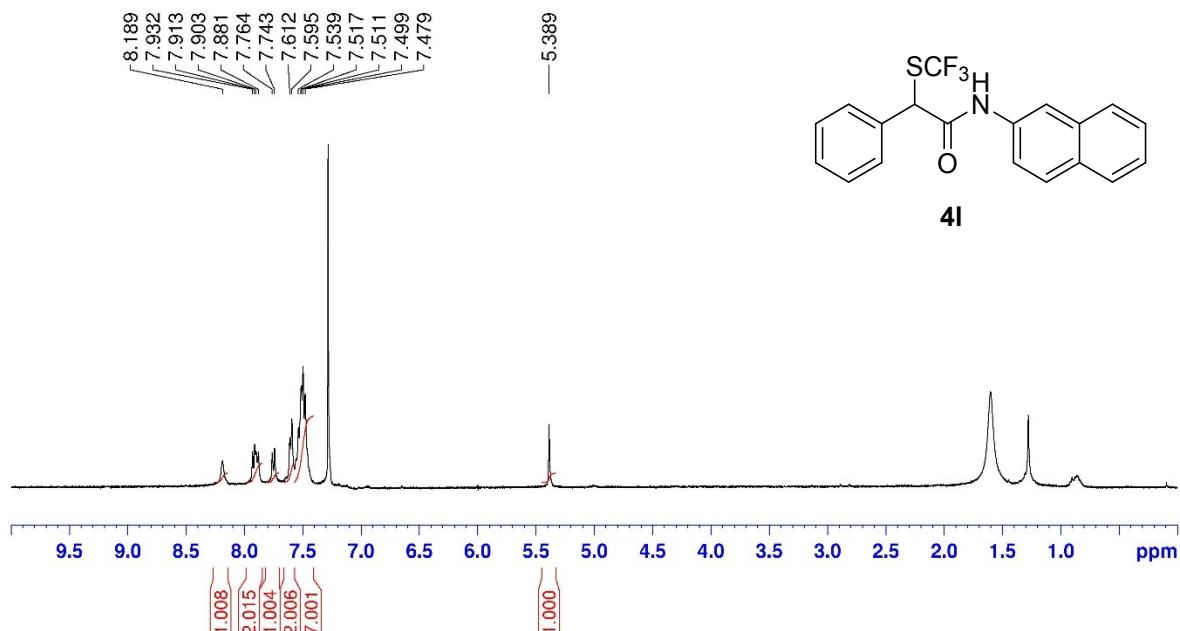
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



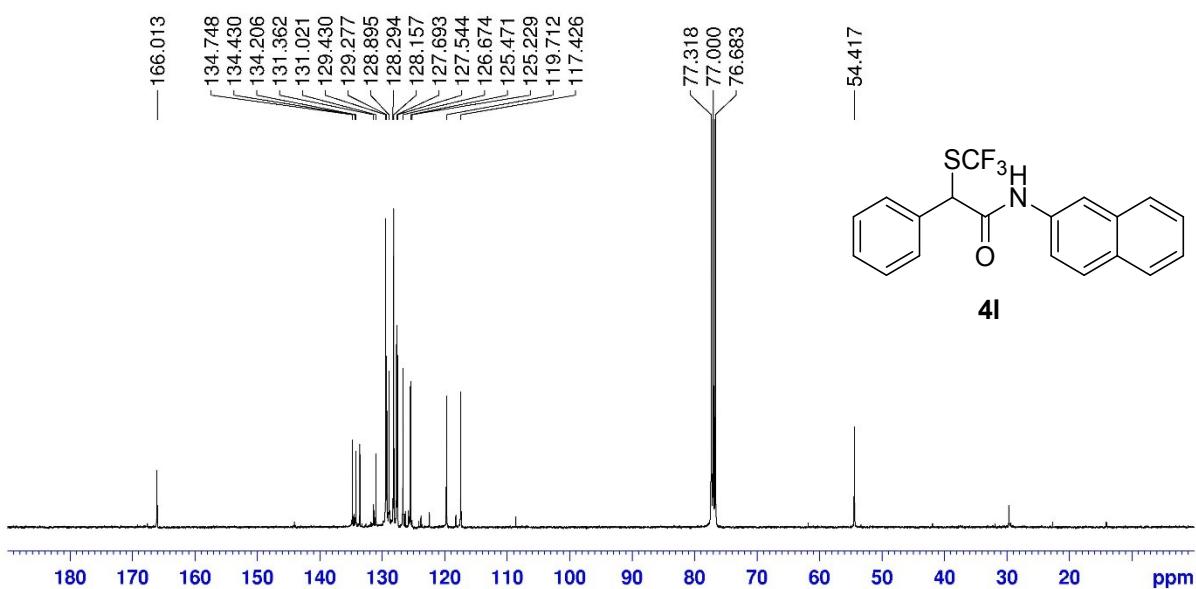
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



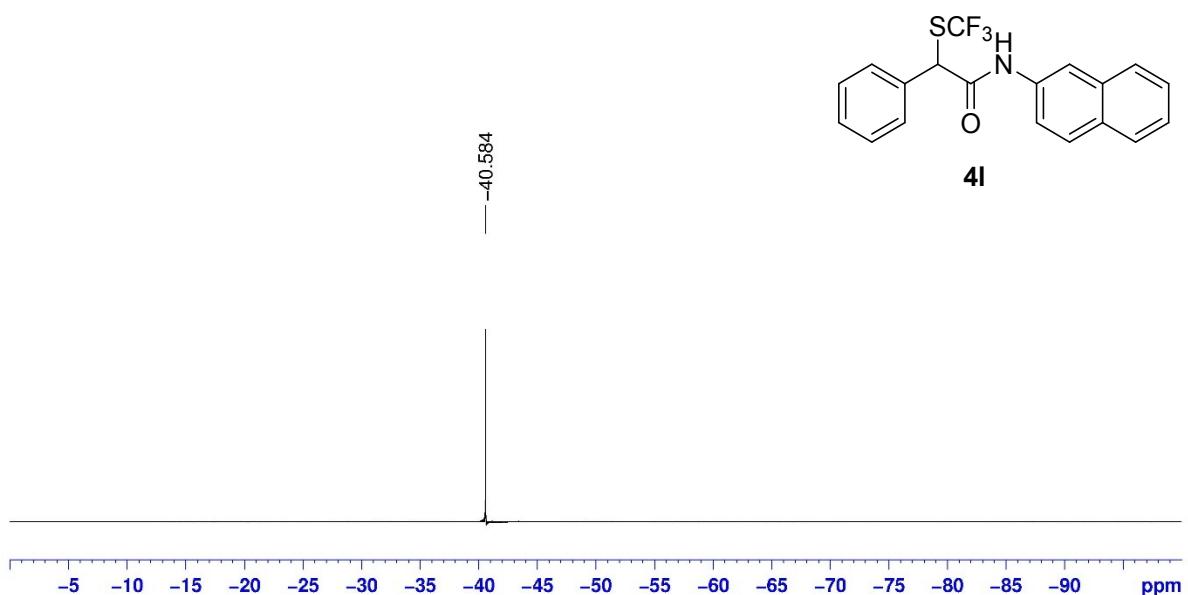
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



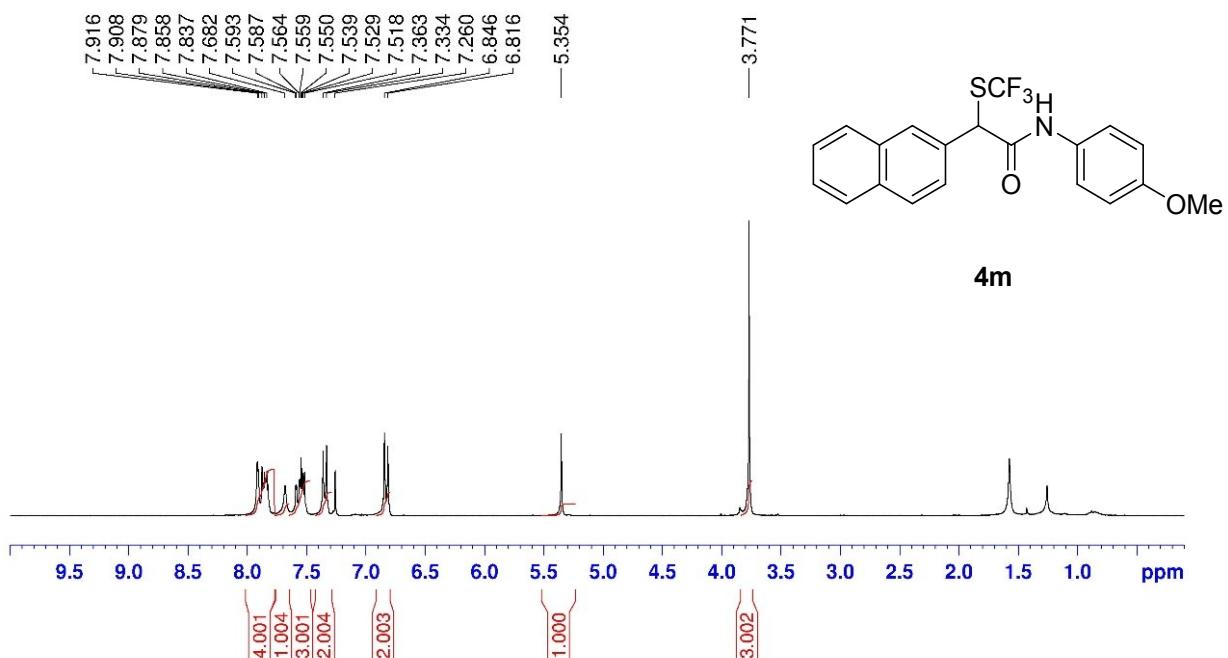
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



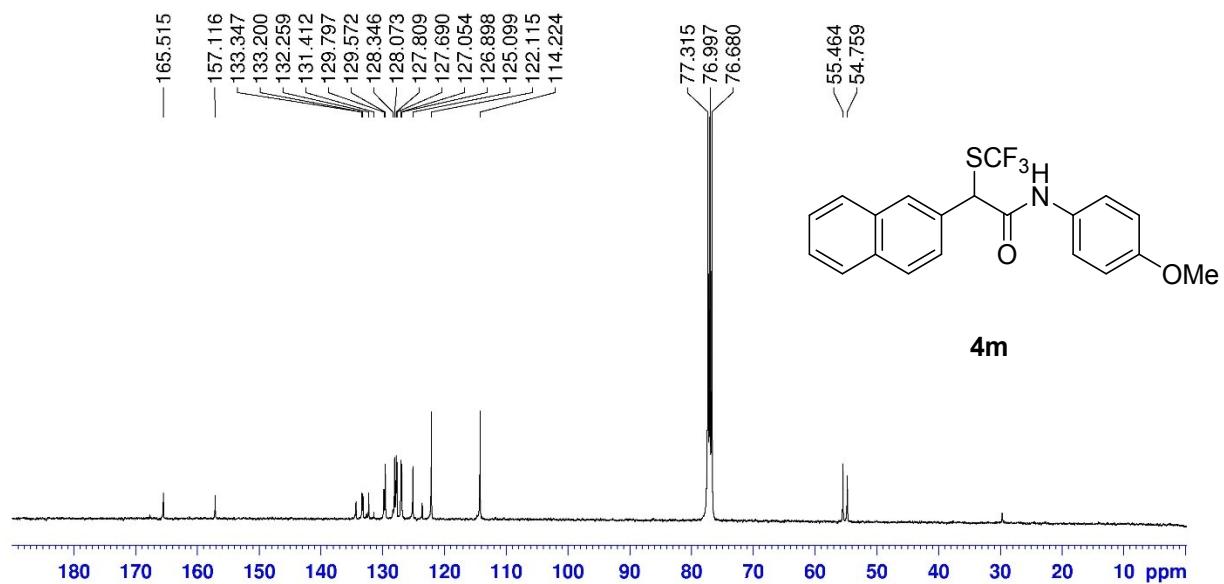
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)

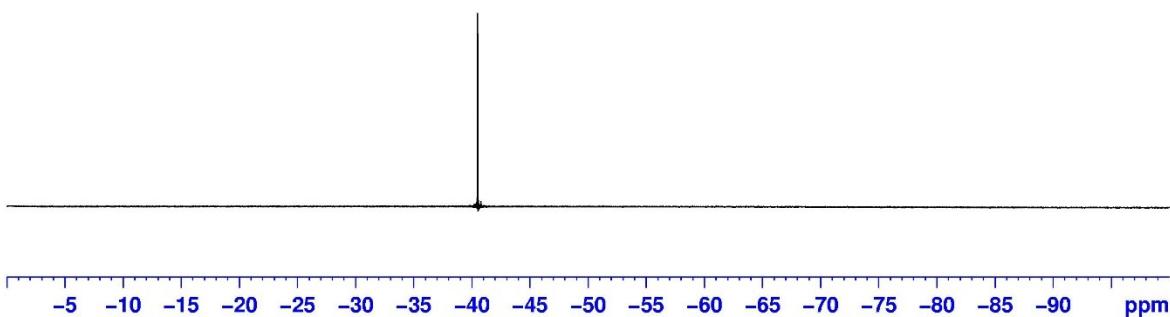


<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)

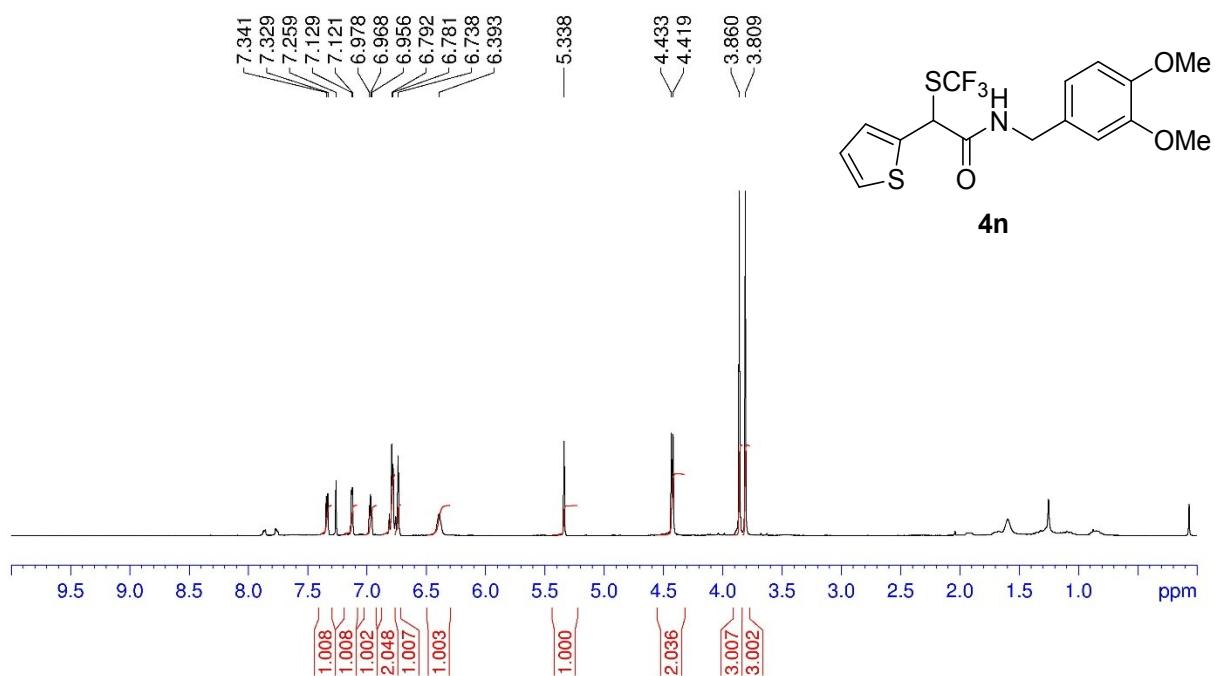
—40.474



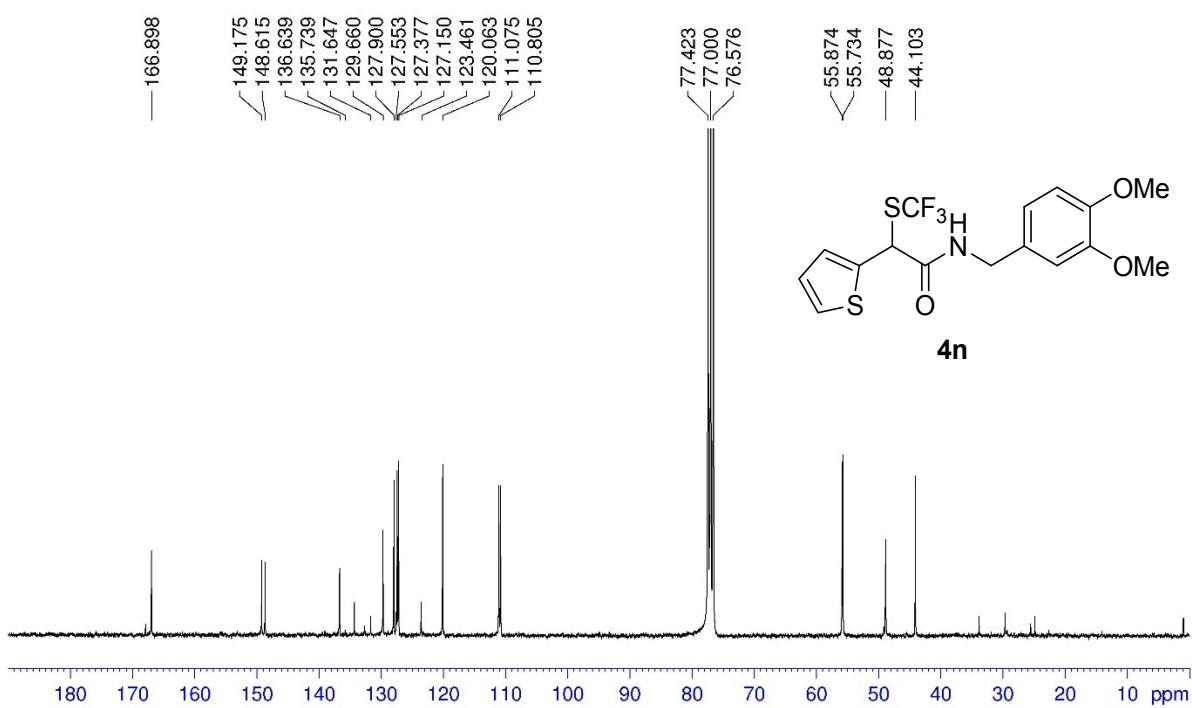
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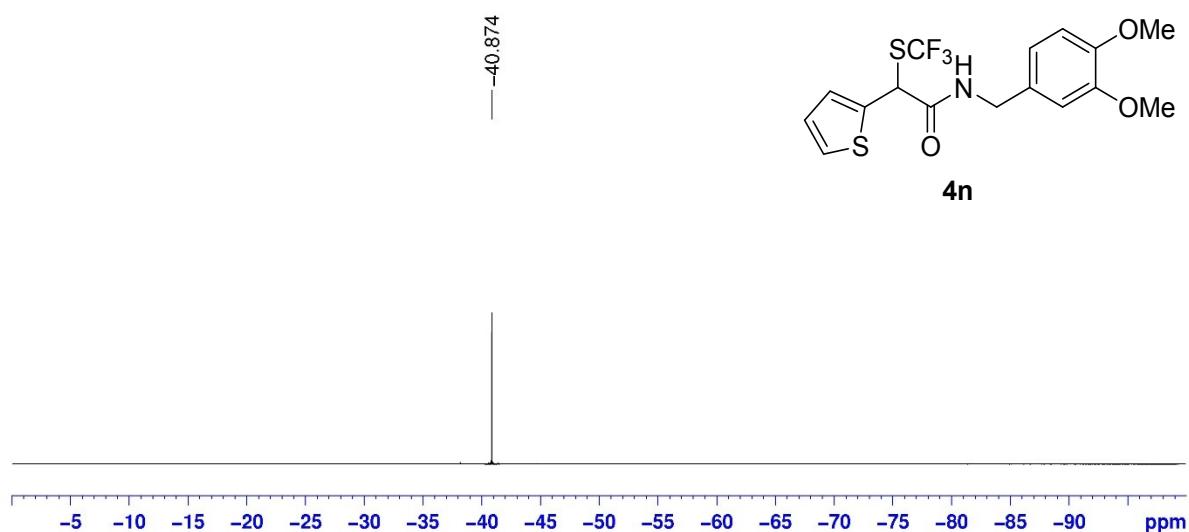
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



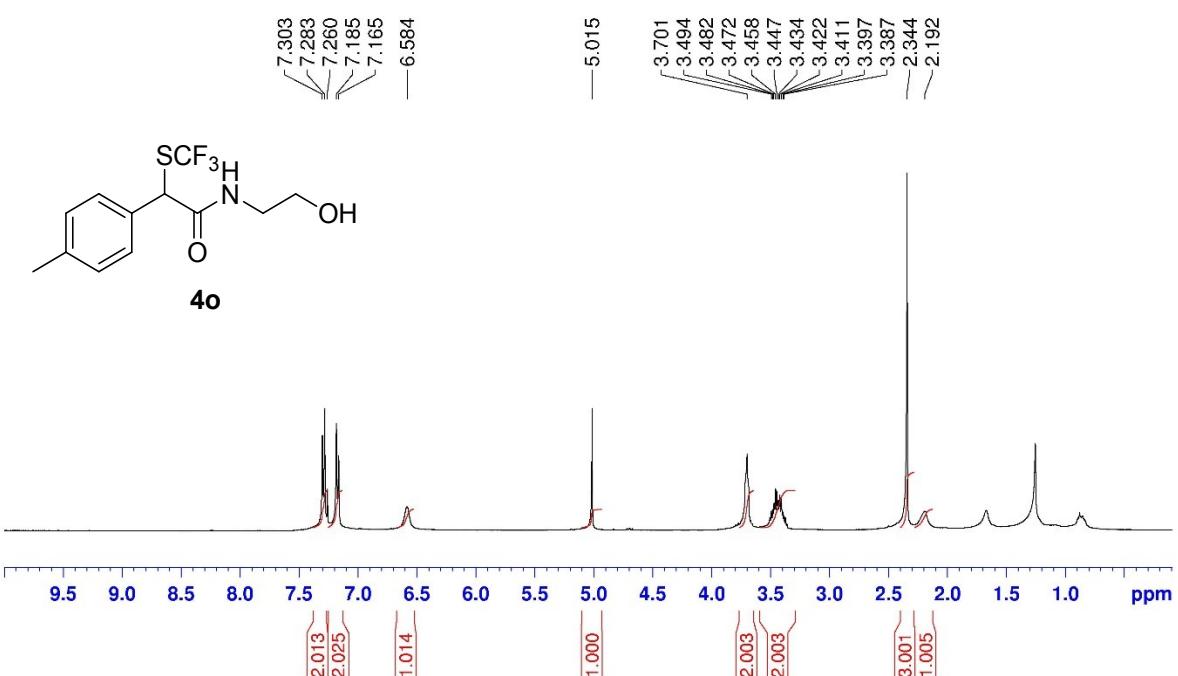
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



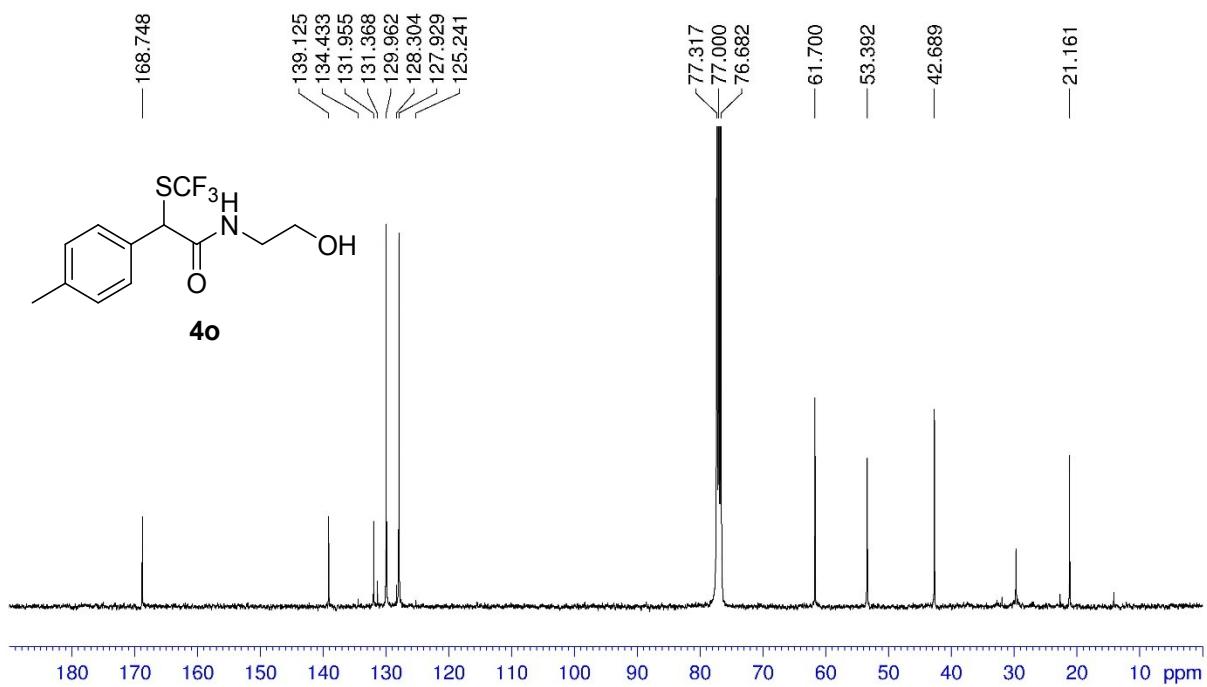
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



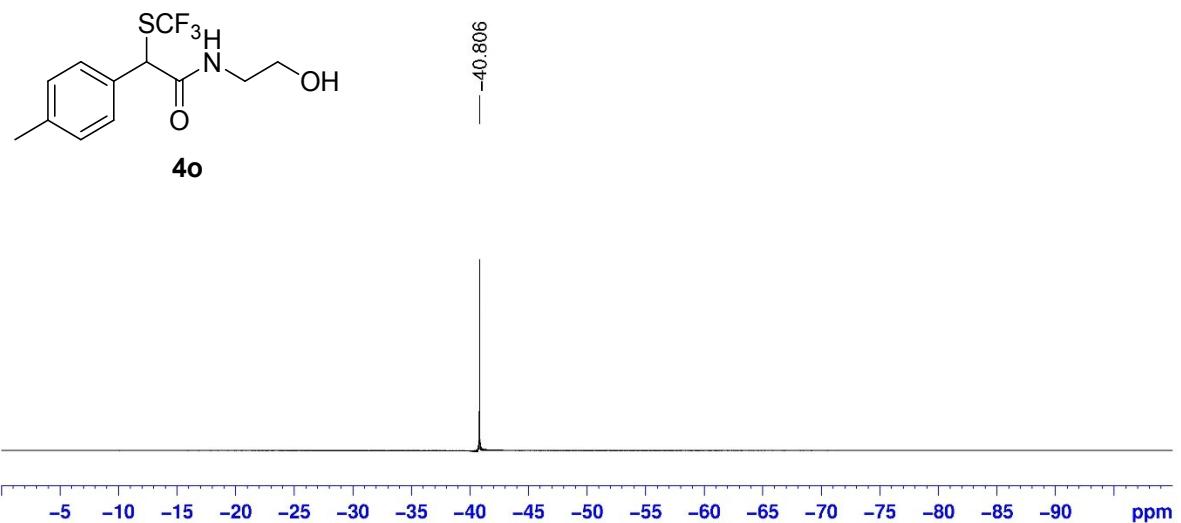
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



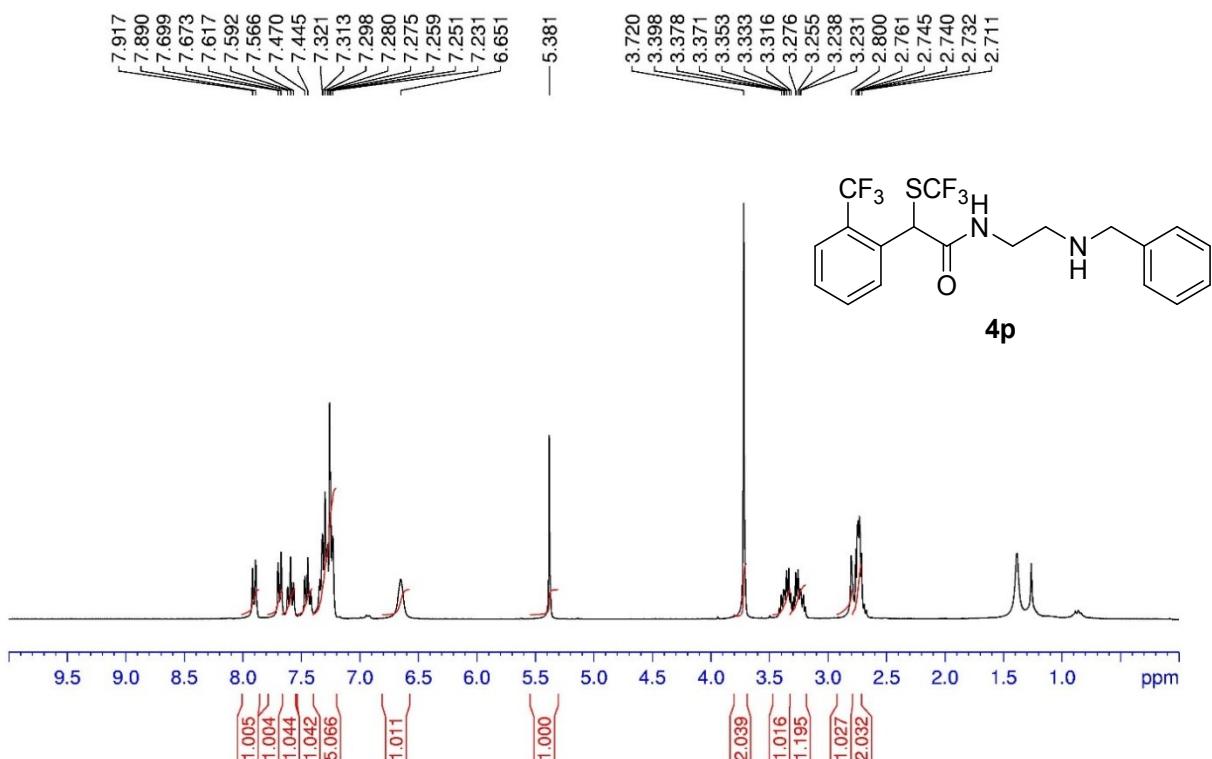
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



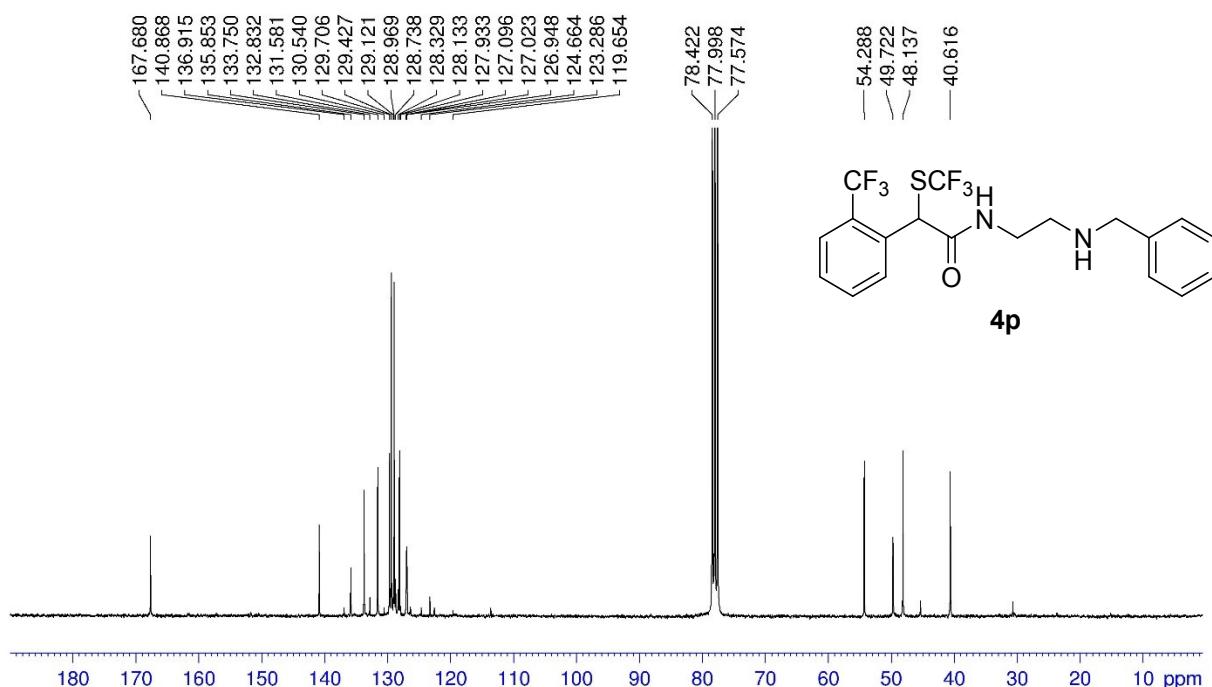
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



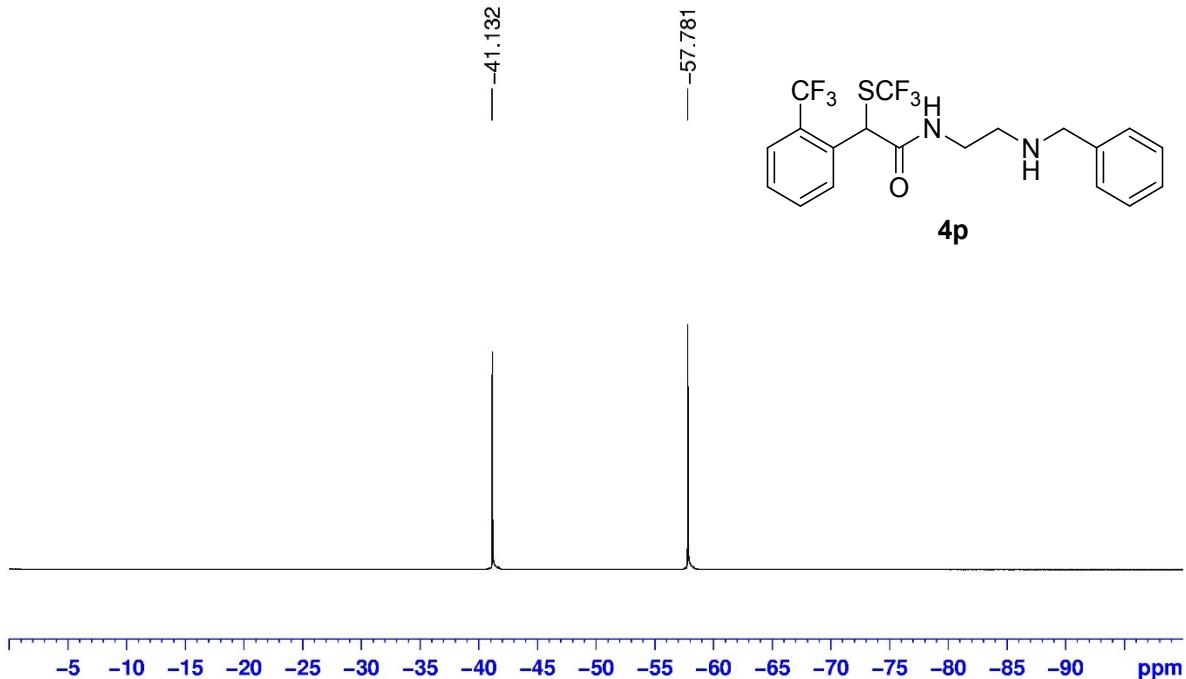
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



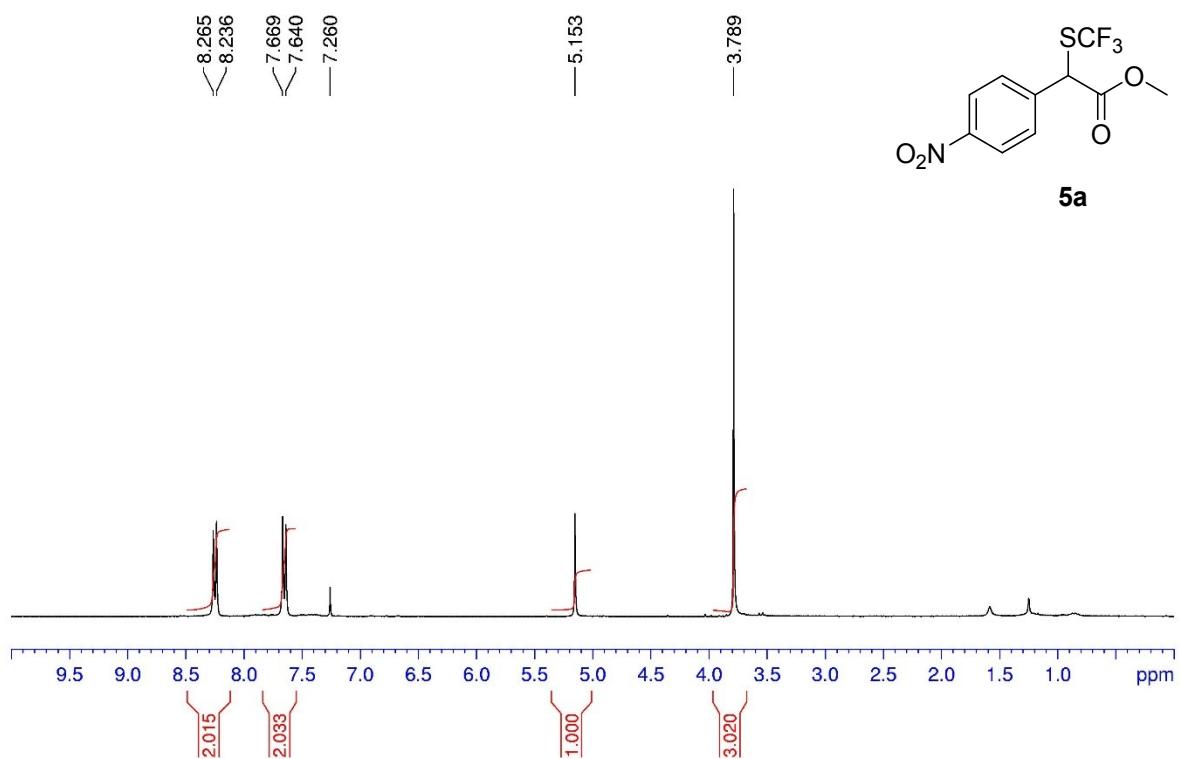
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



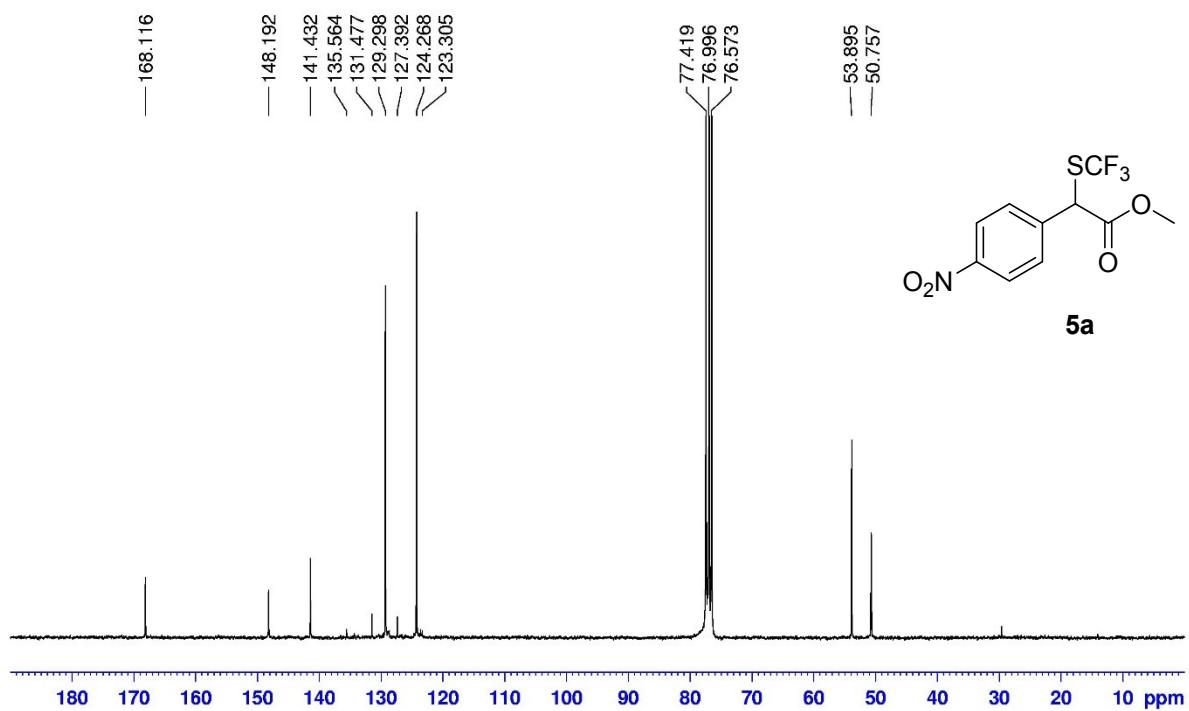
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



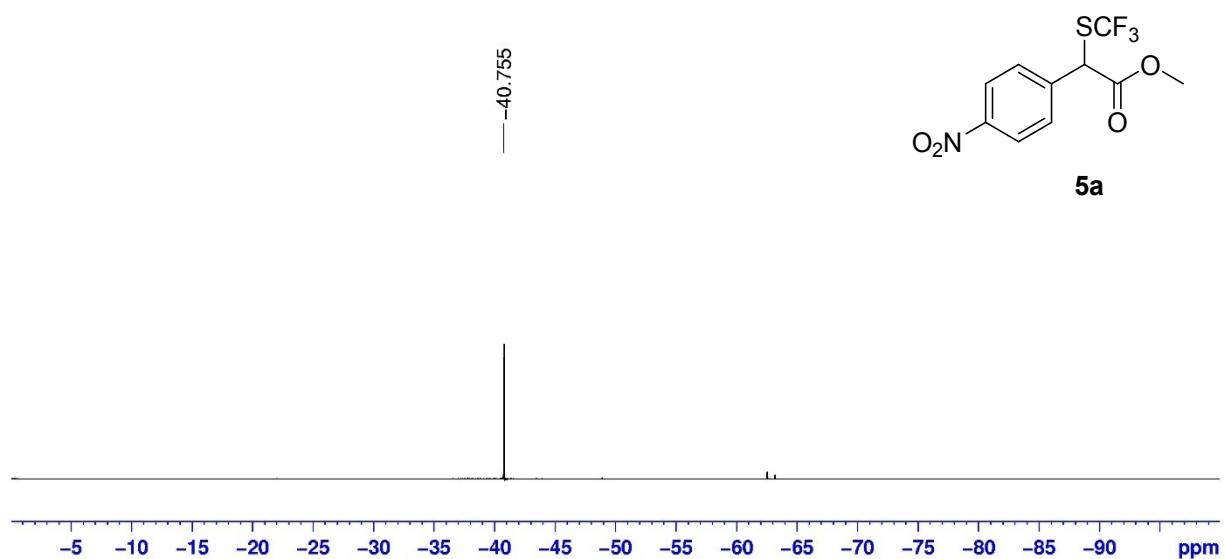
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



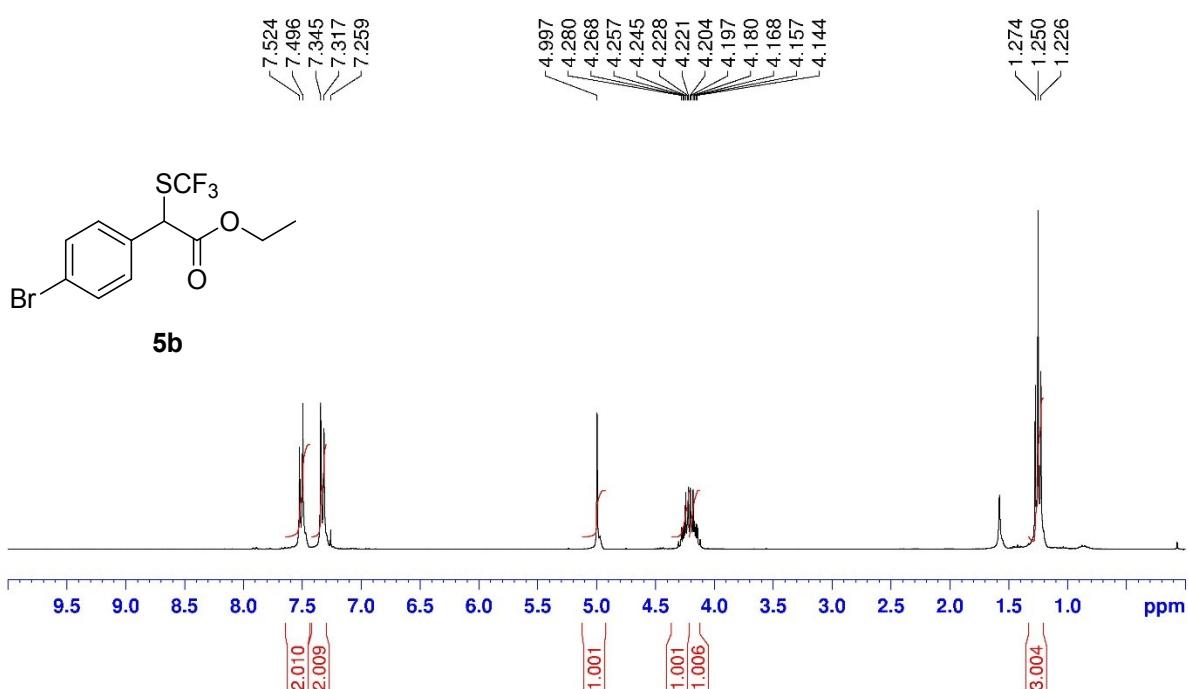
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



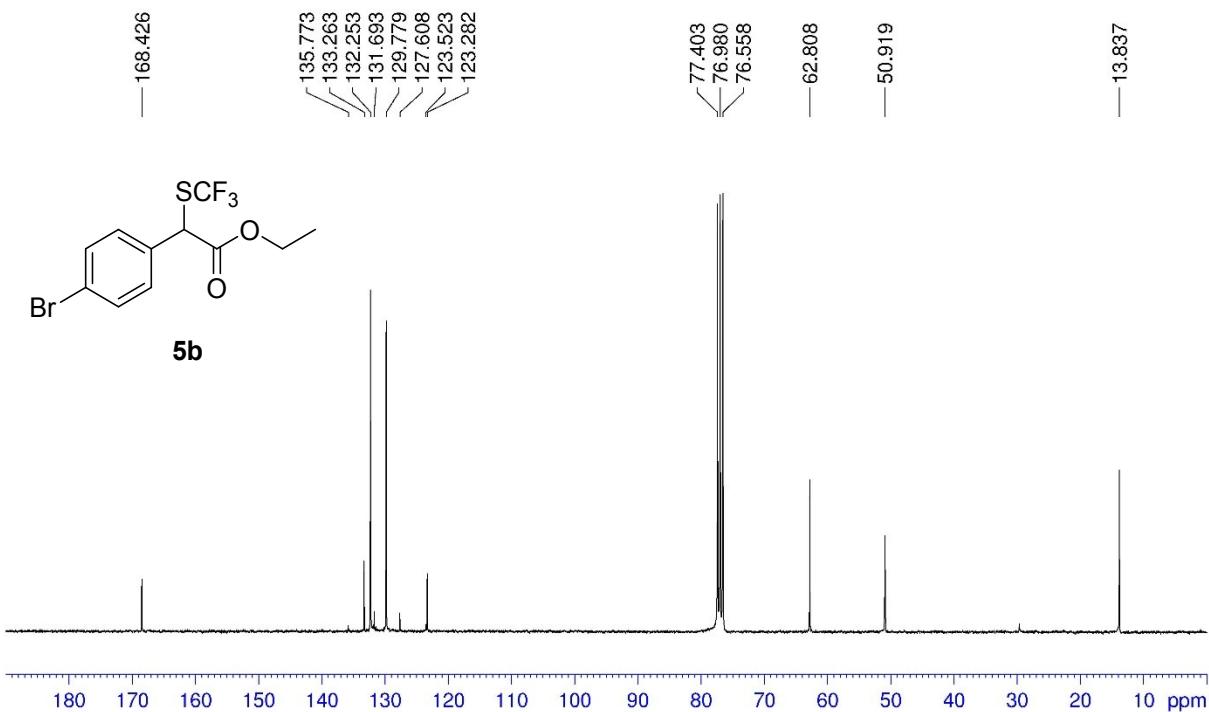
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



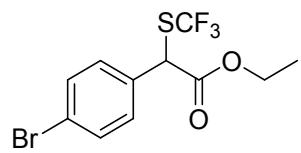
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



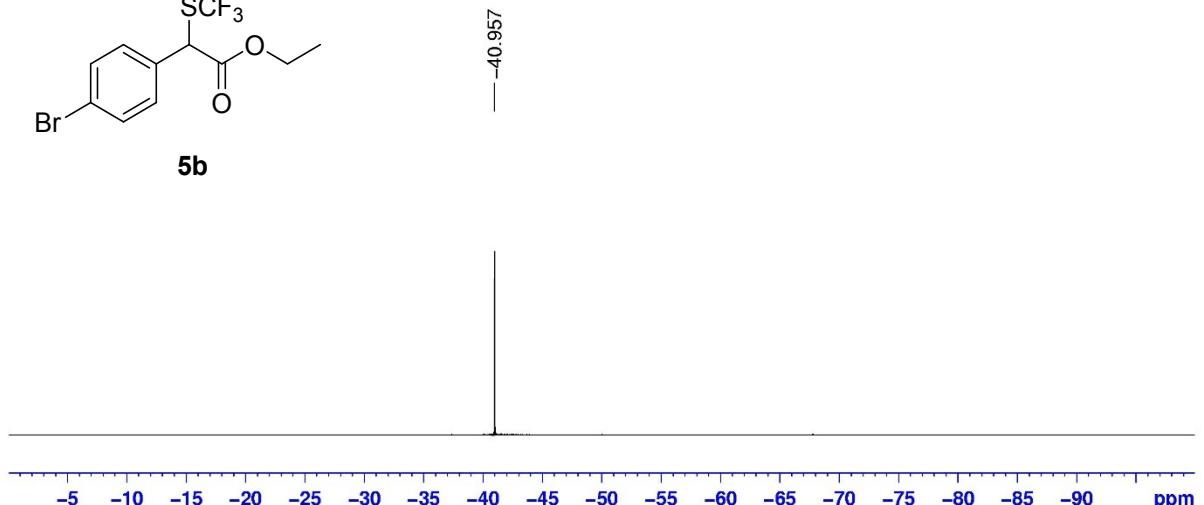
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



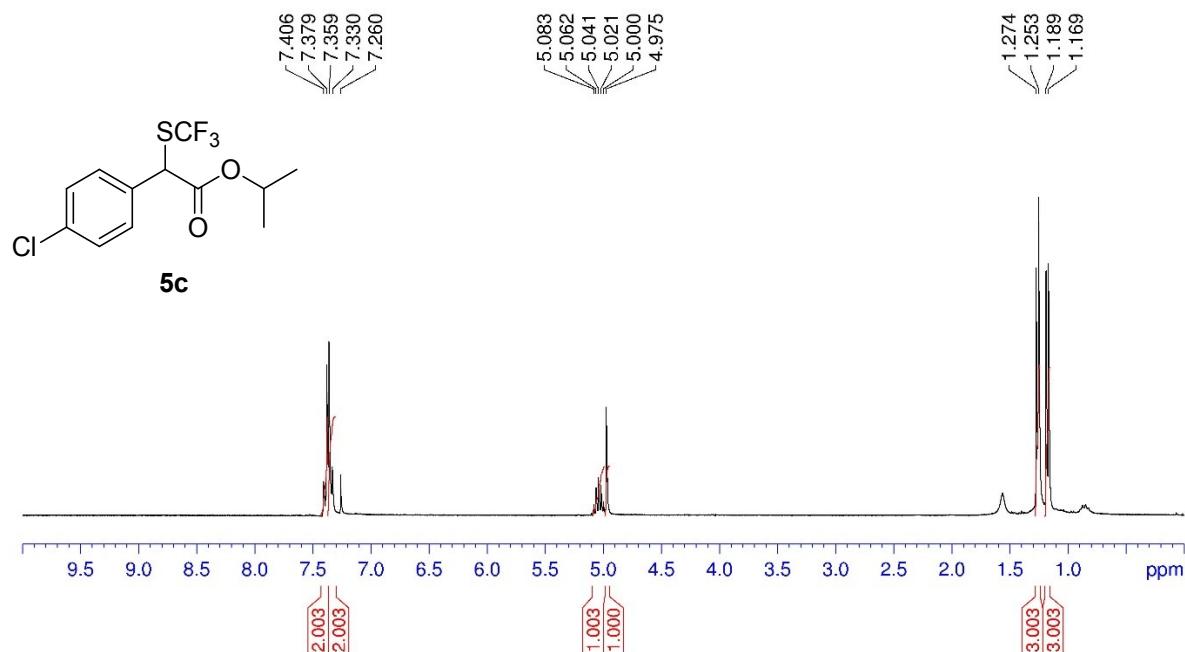
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



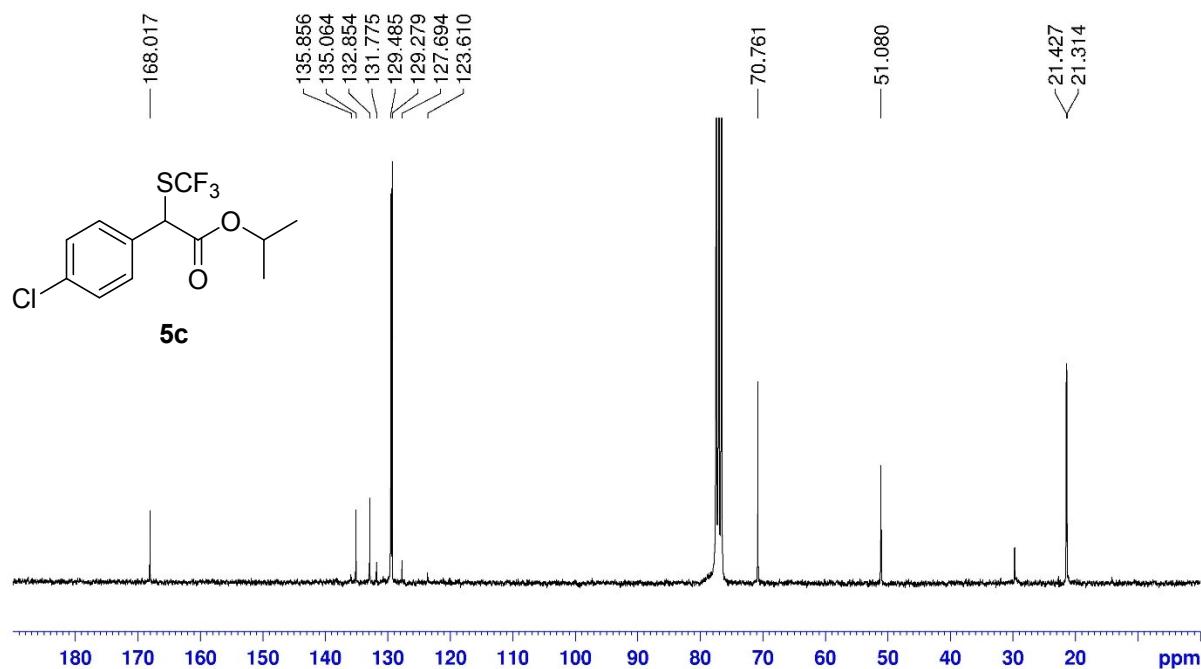
**5b**



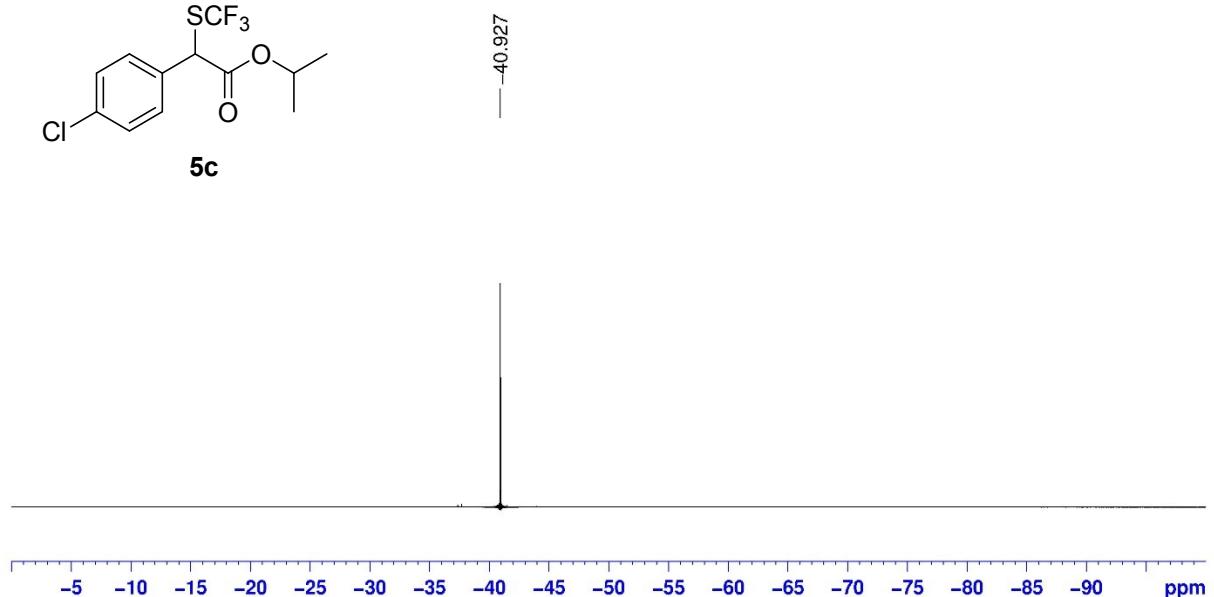
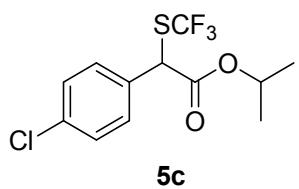
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



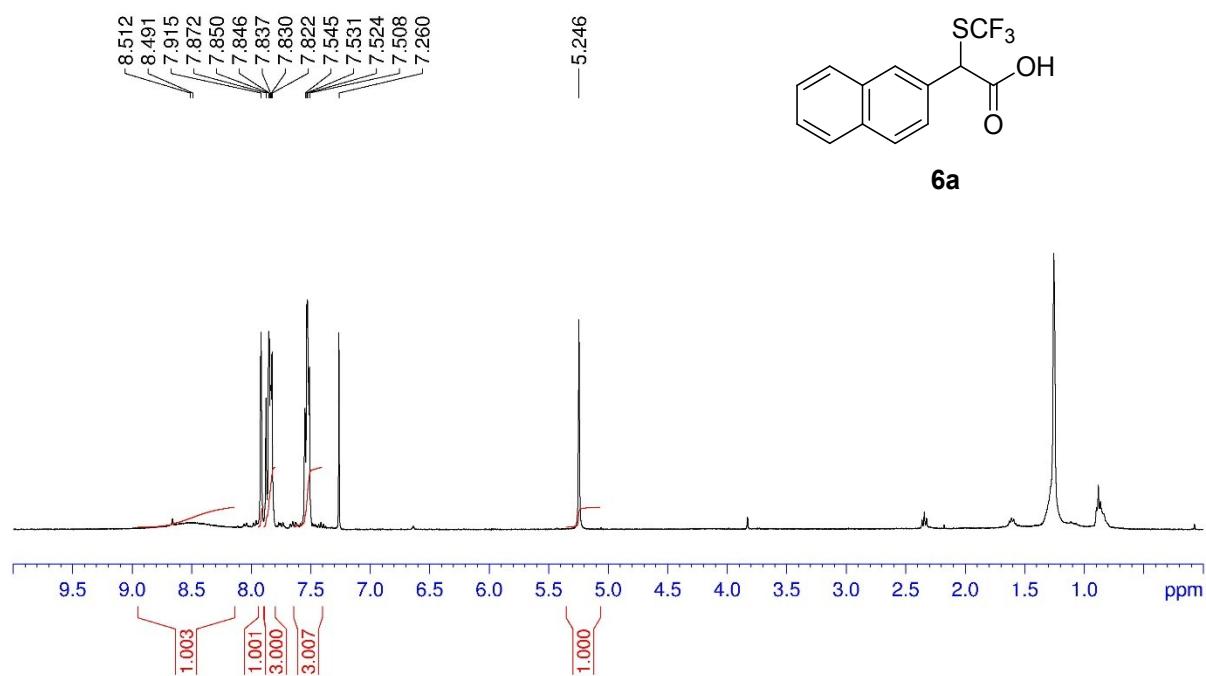
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



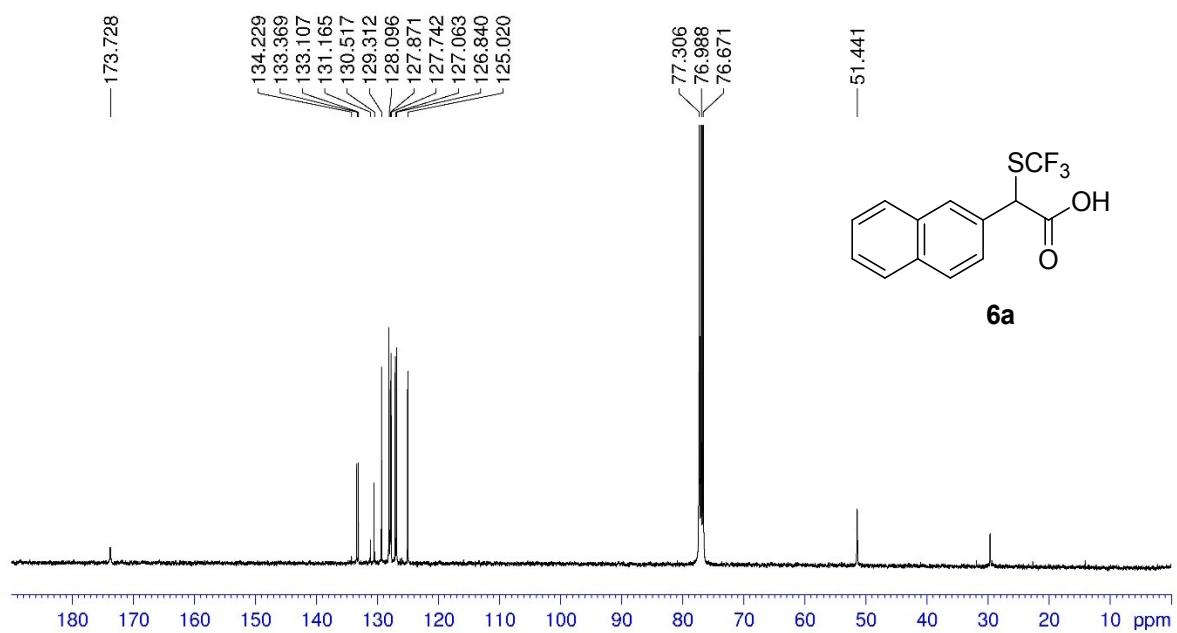
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



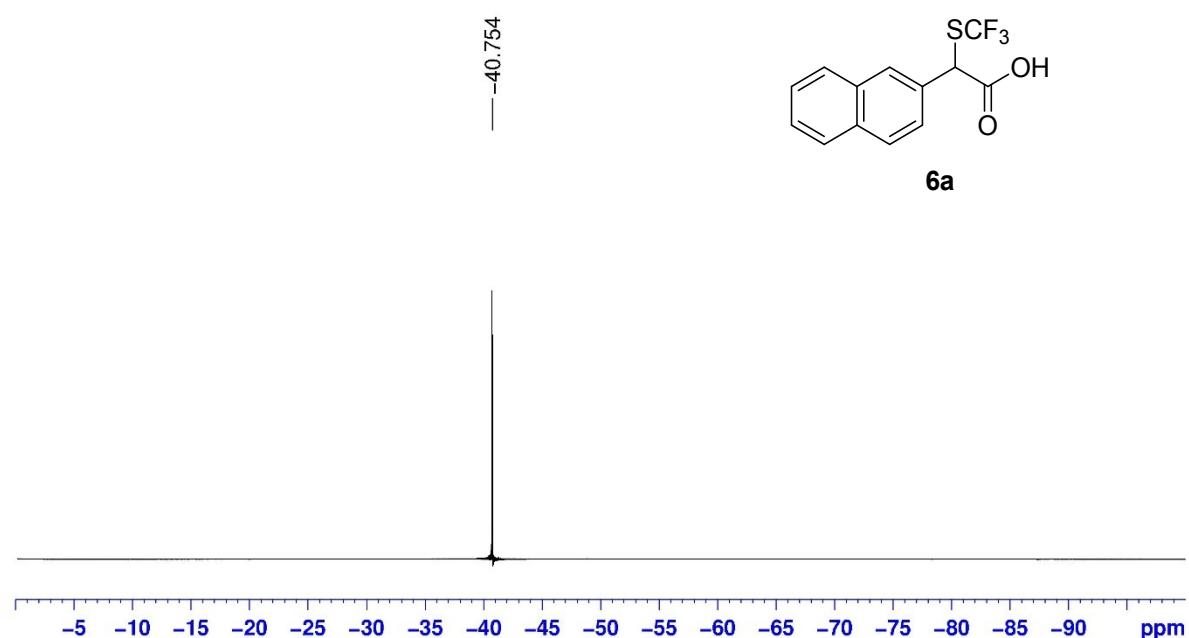
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



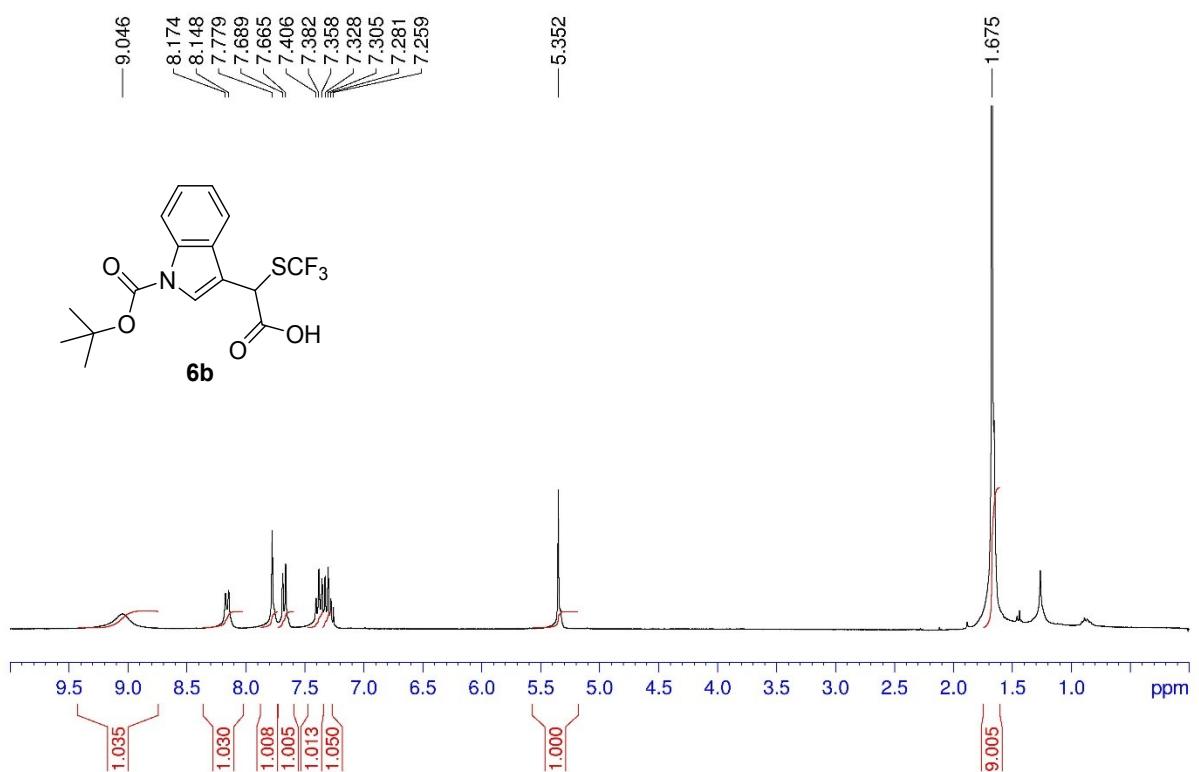
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



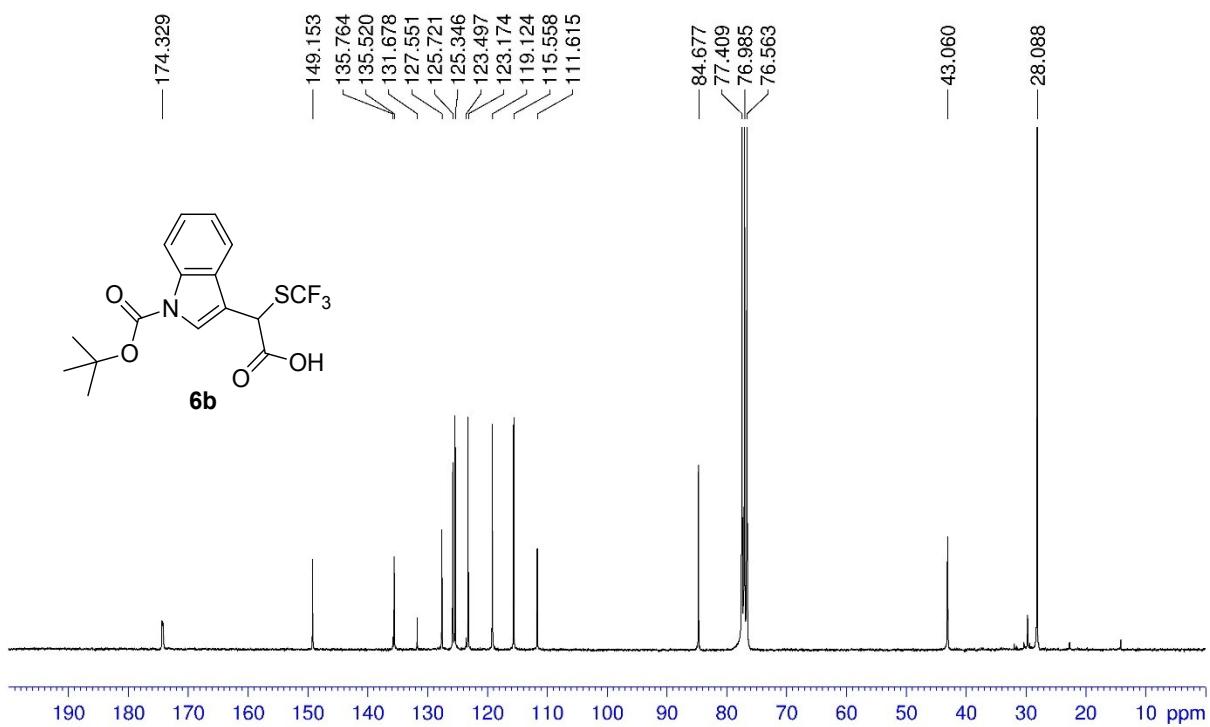
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



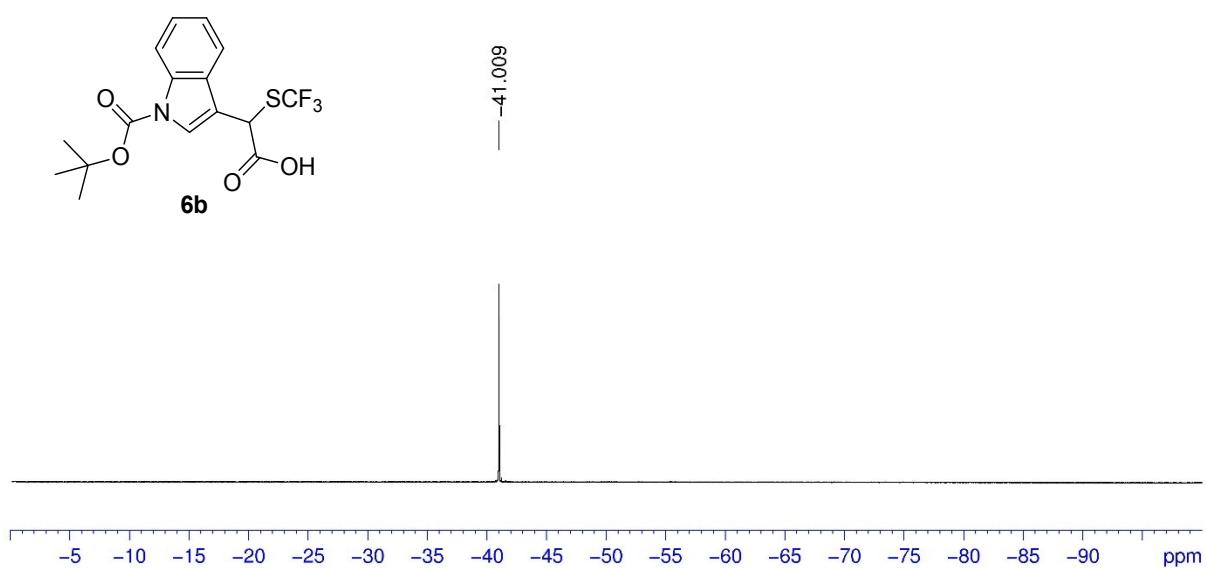
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



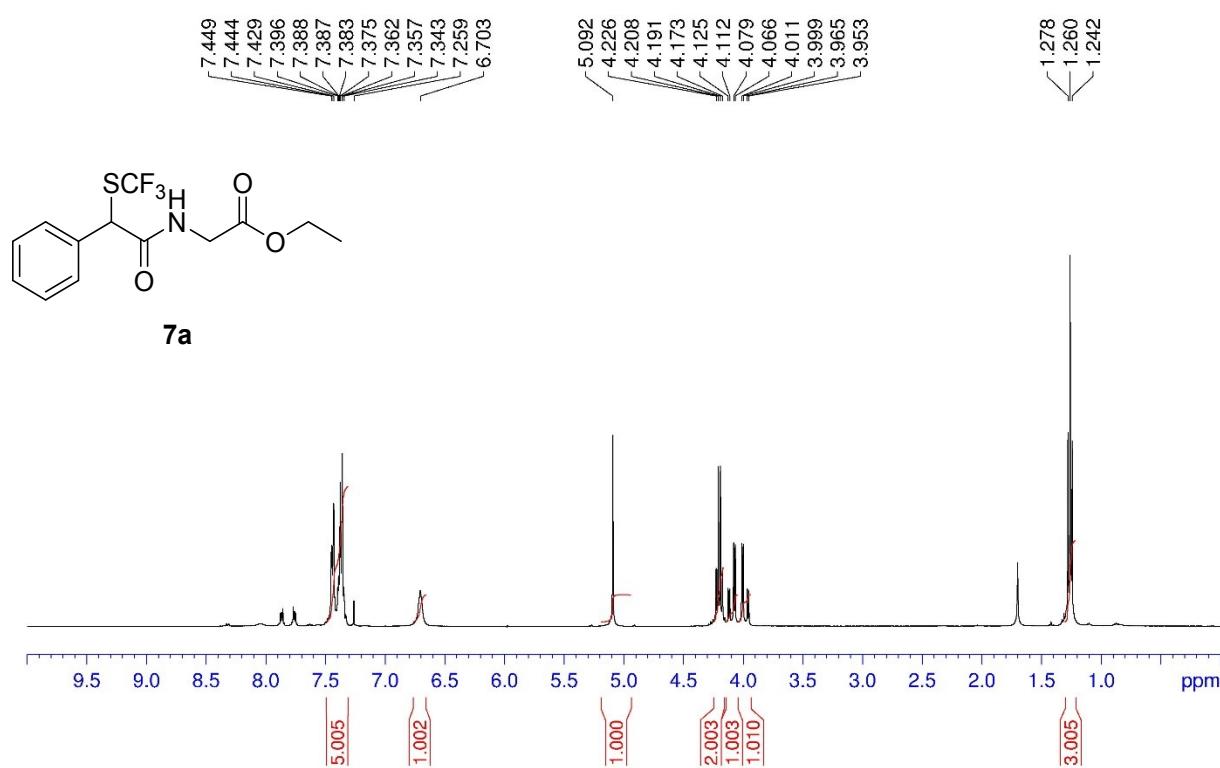
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



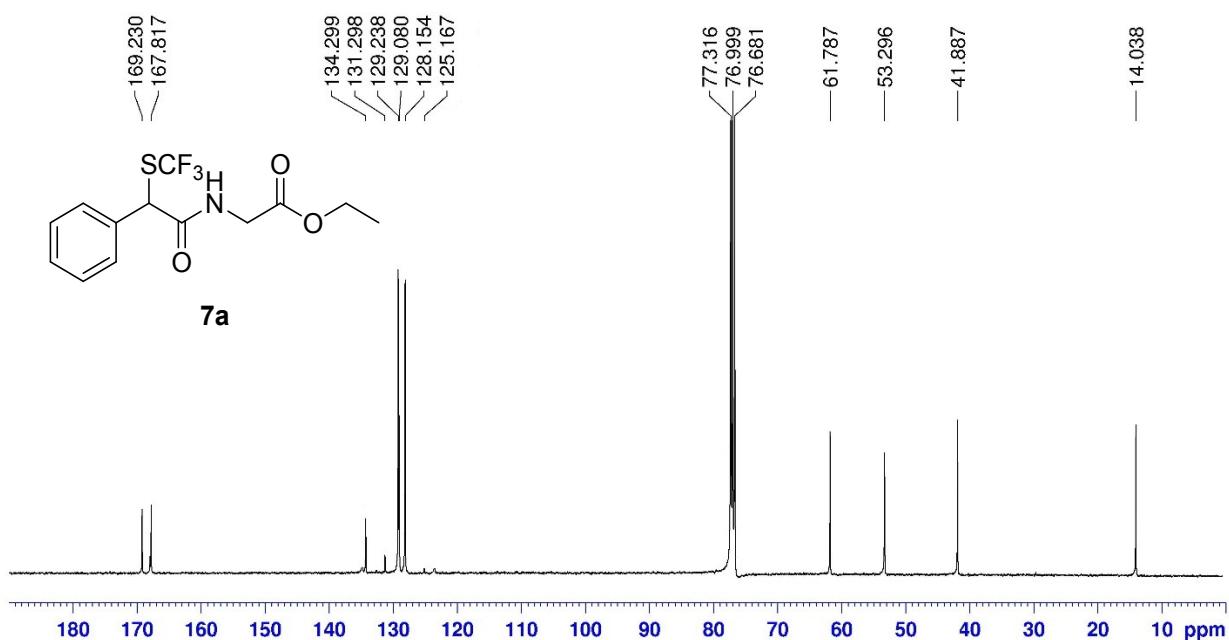
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



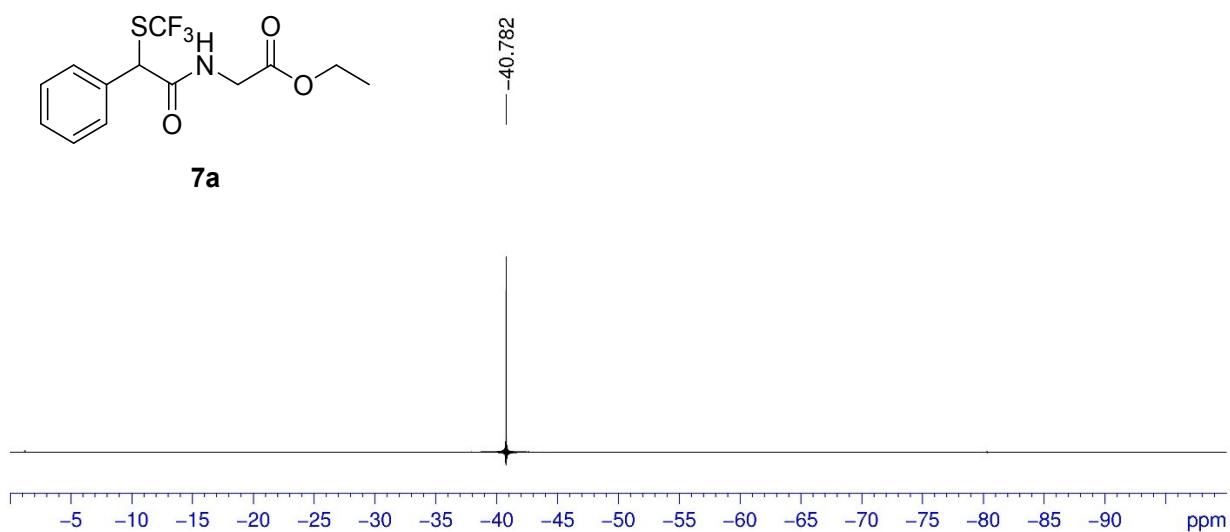
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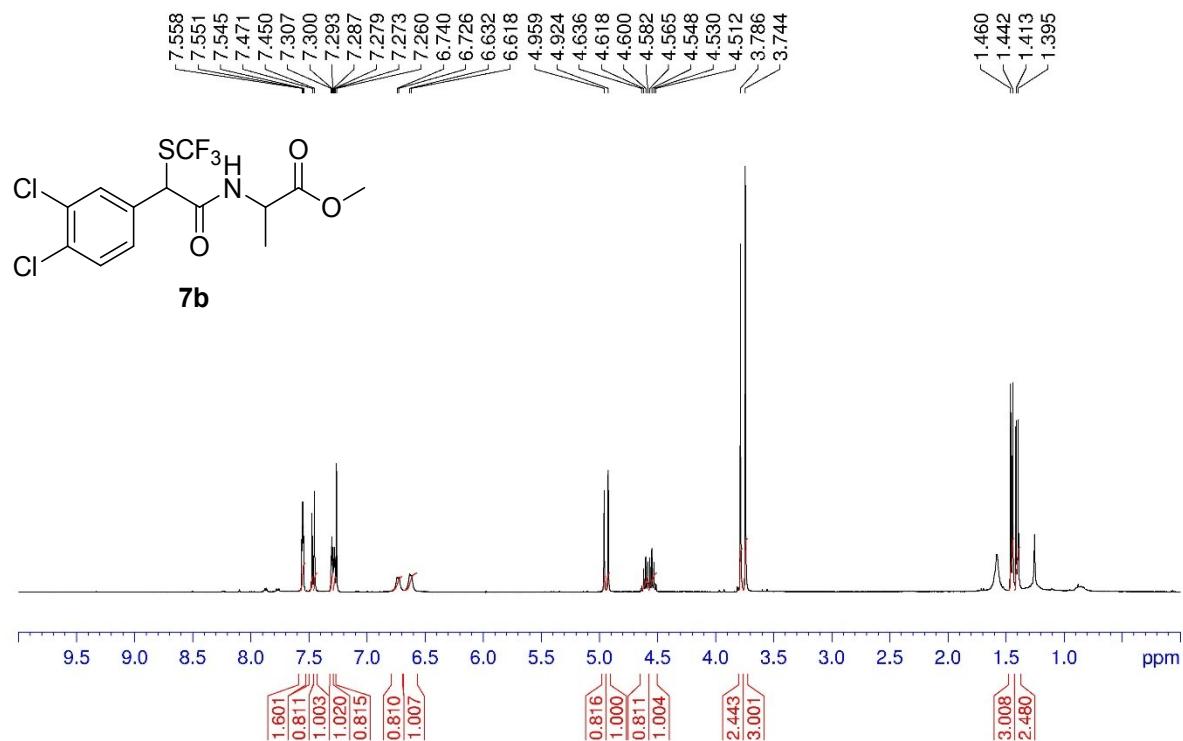
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



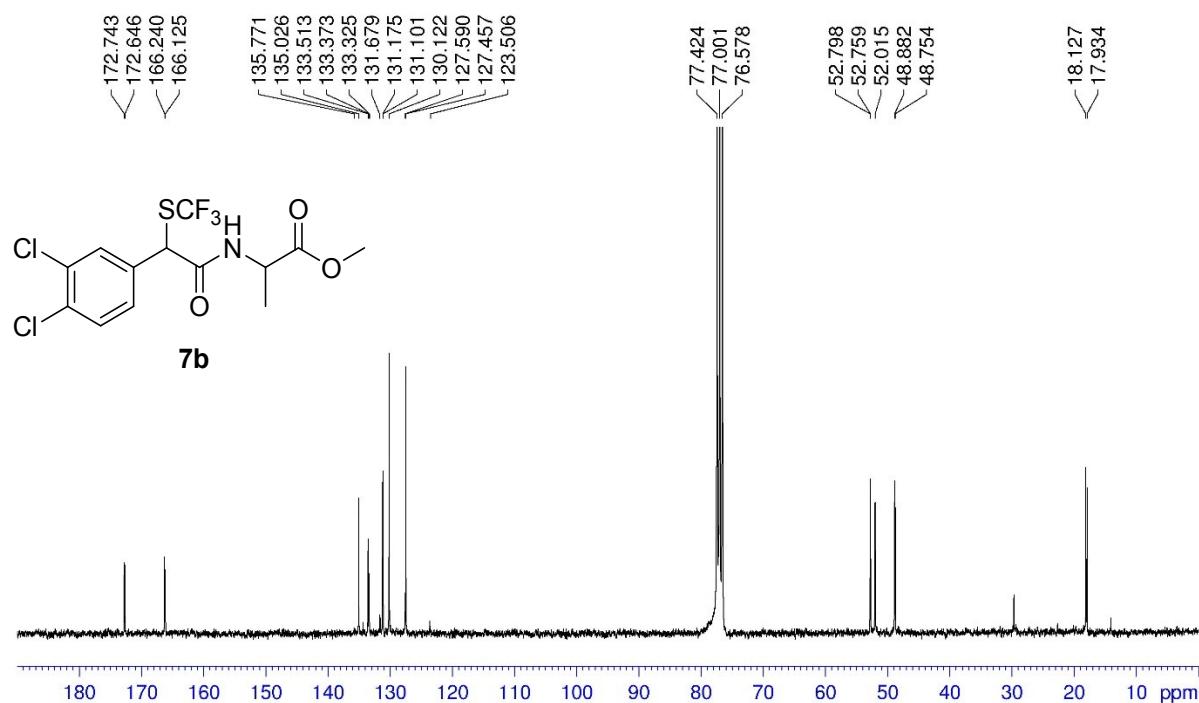
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



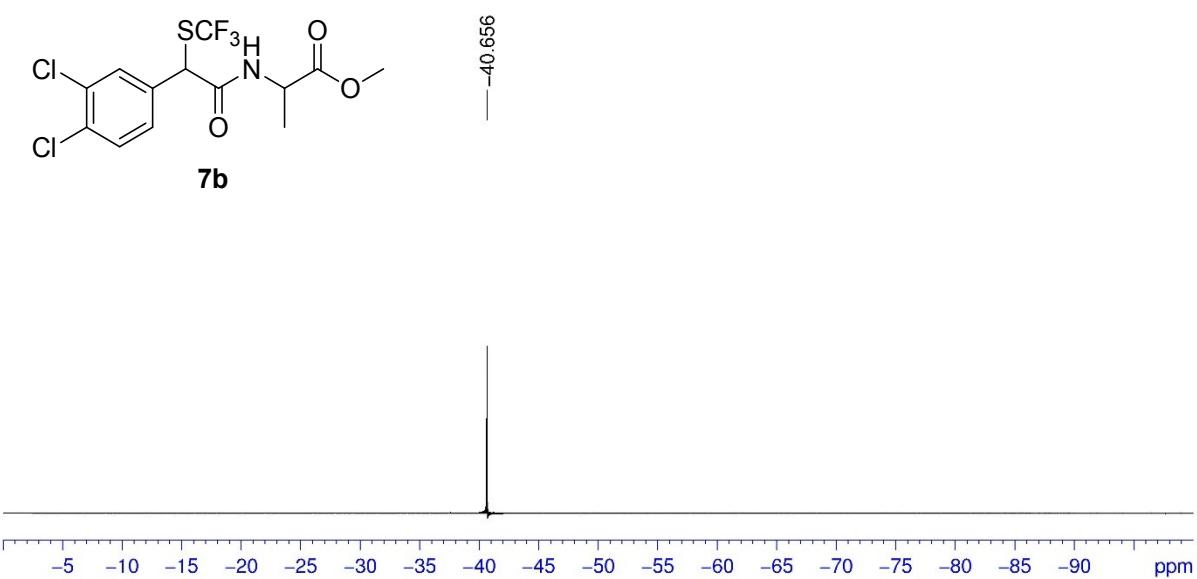
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



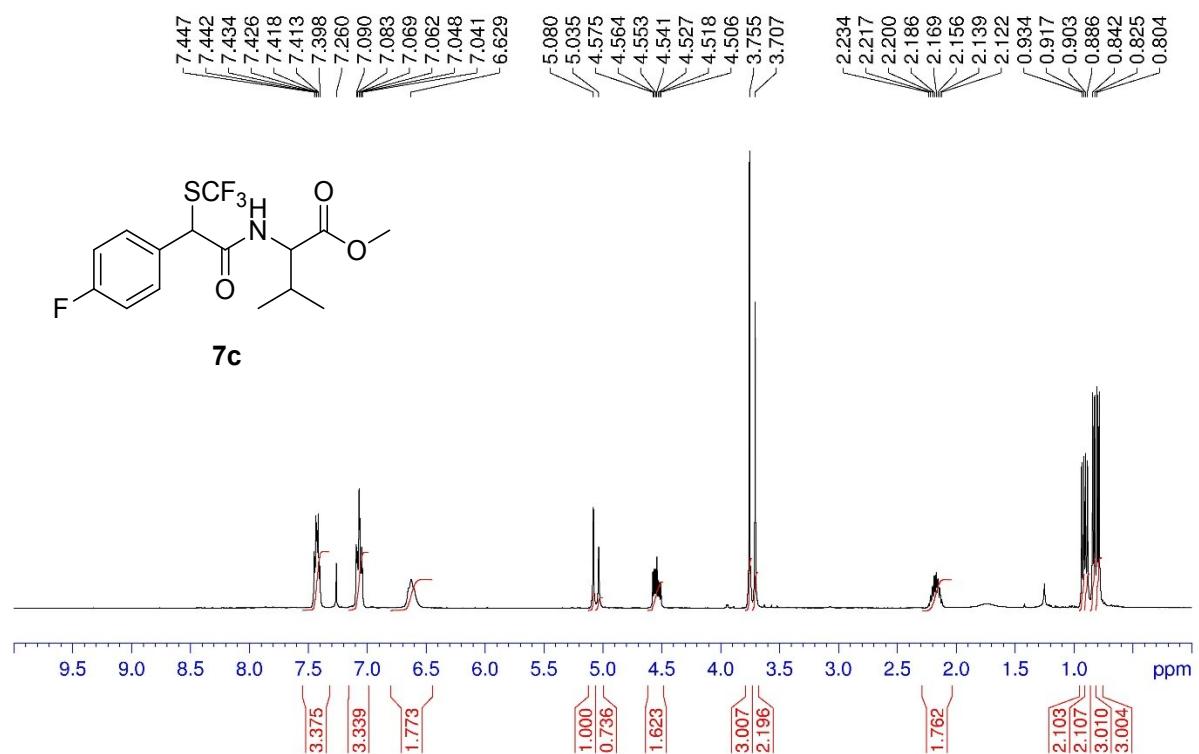
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



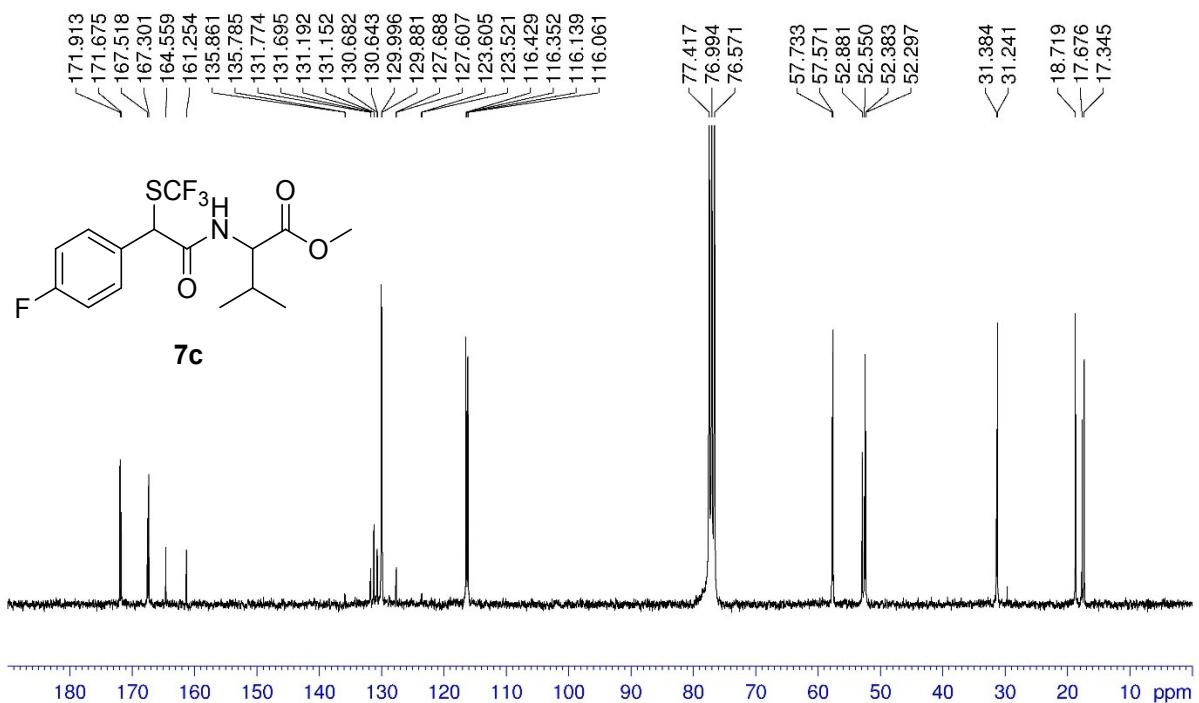
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



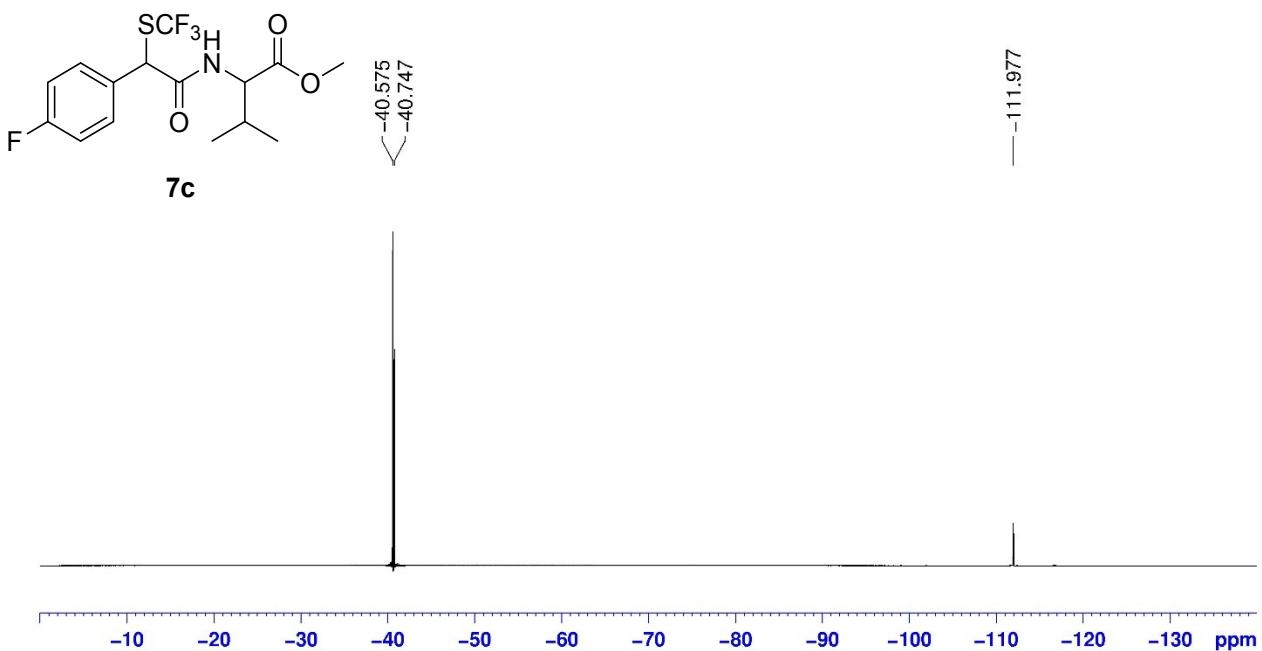
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



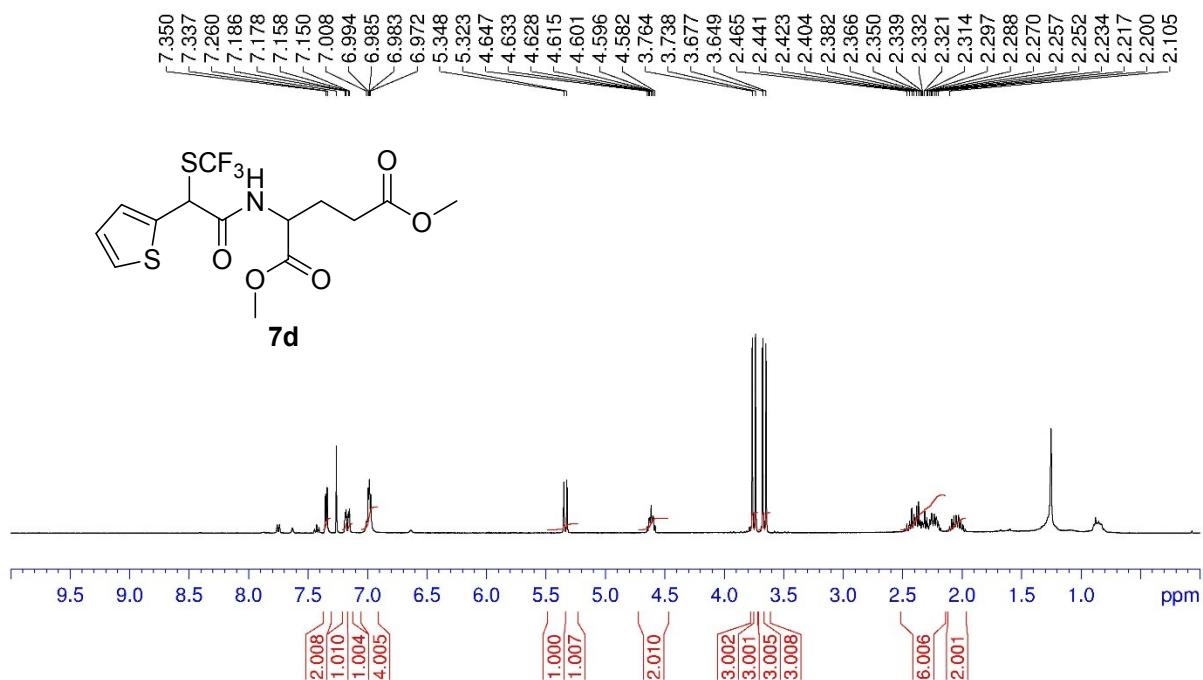
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



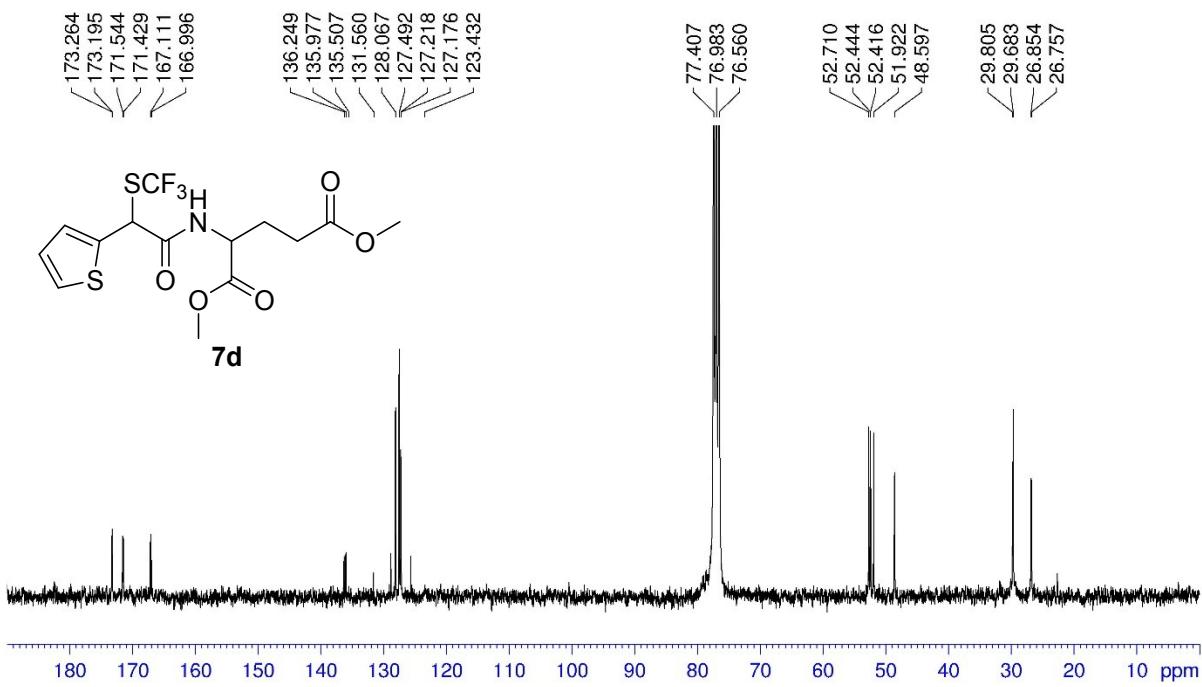
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



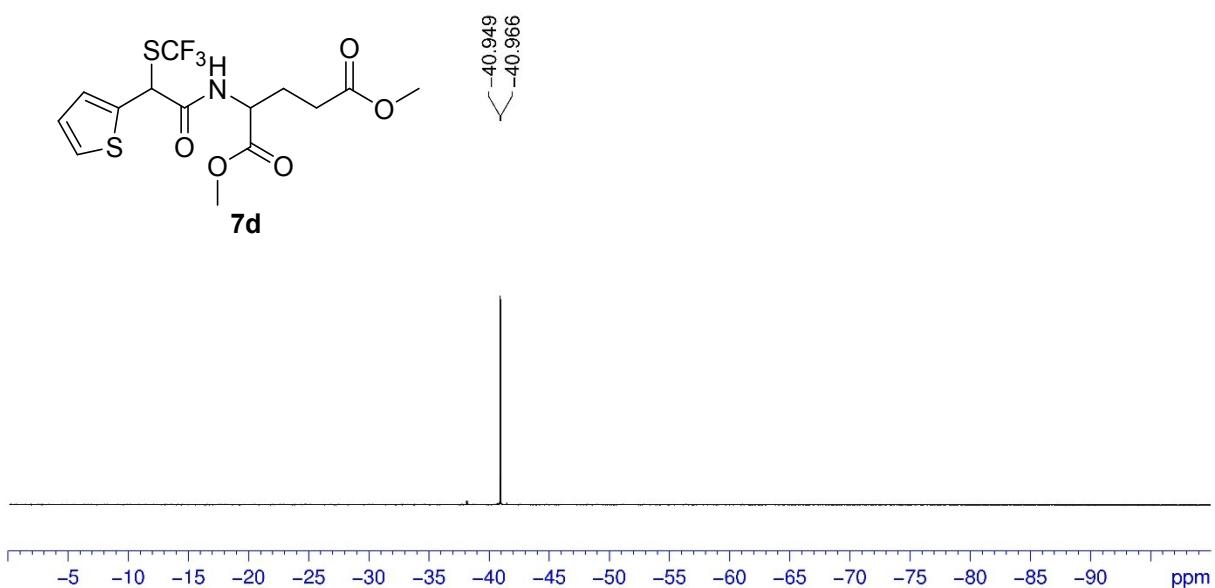
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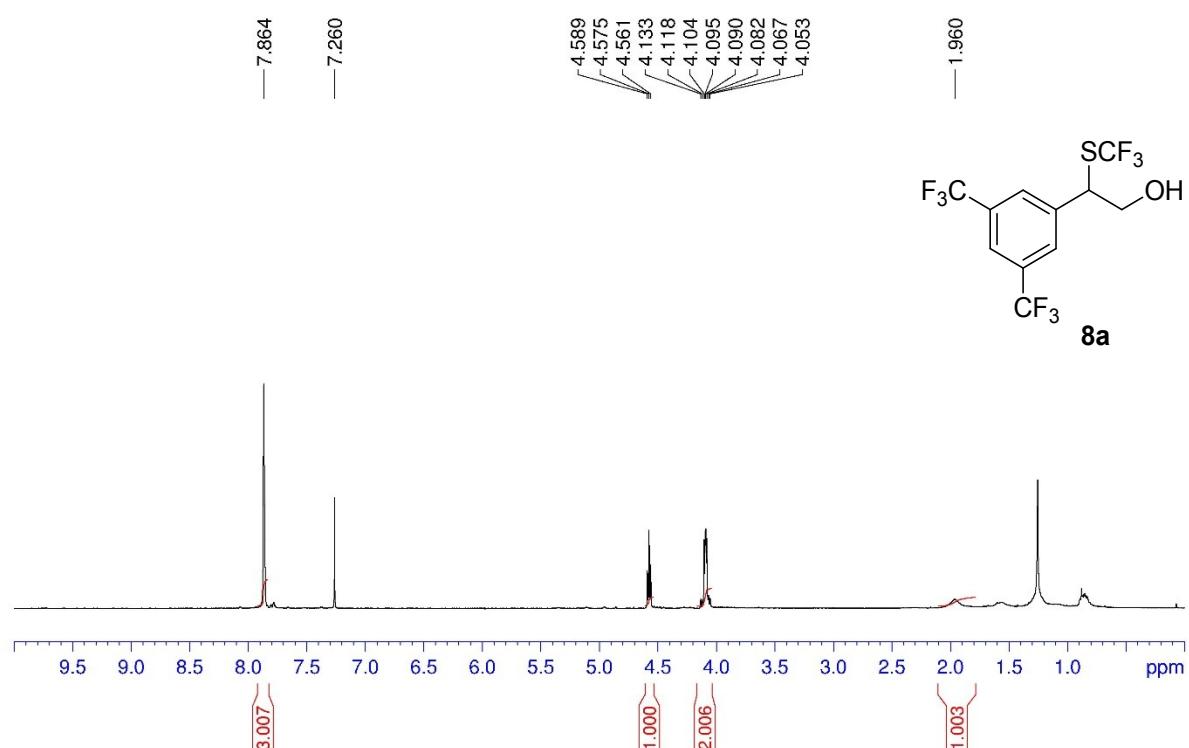
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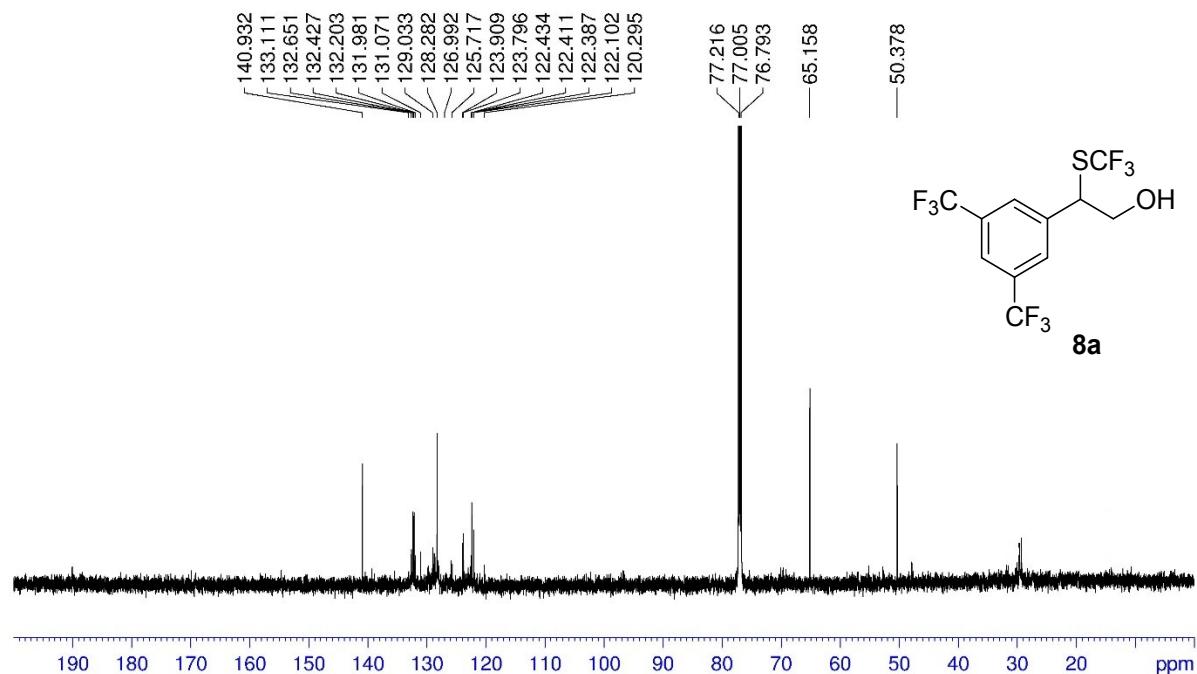
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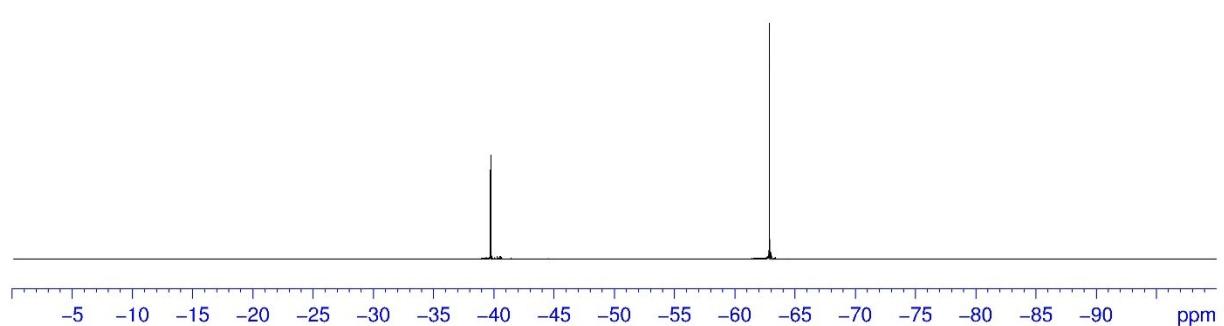
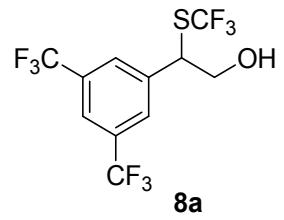
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



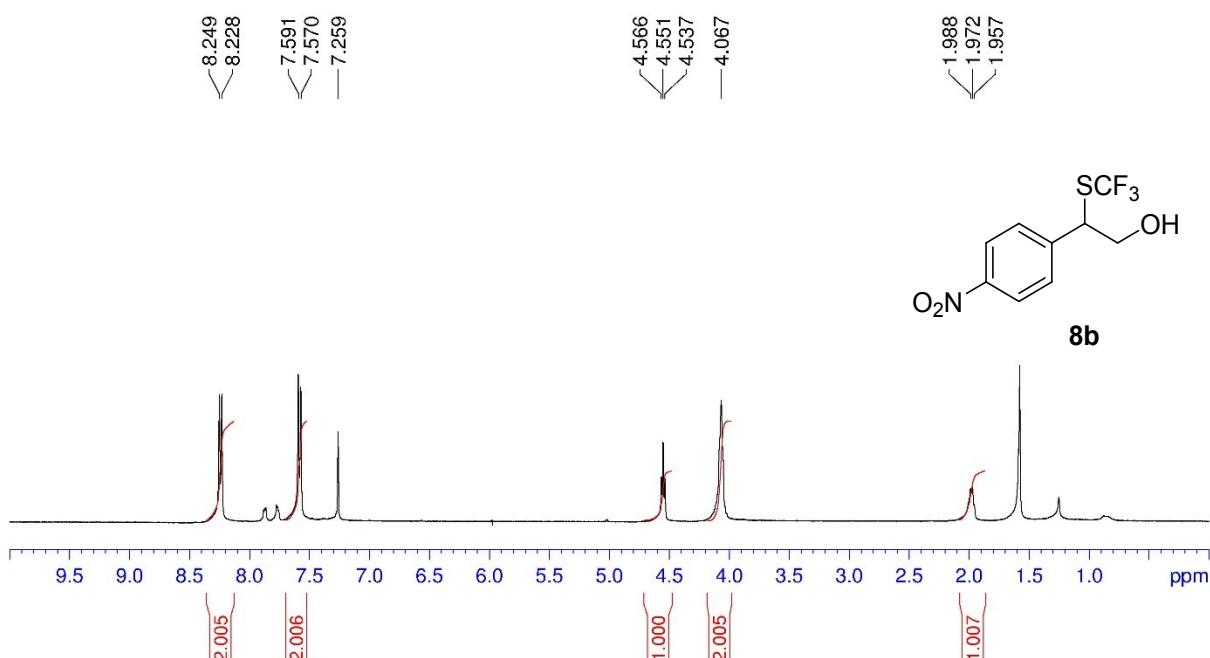
<sup>13</sup>C NMR in CDCl<sub>3</sub> (150 MHz)



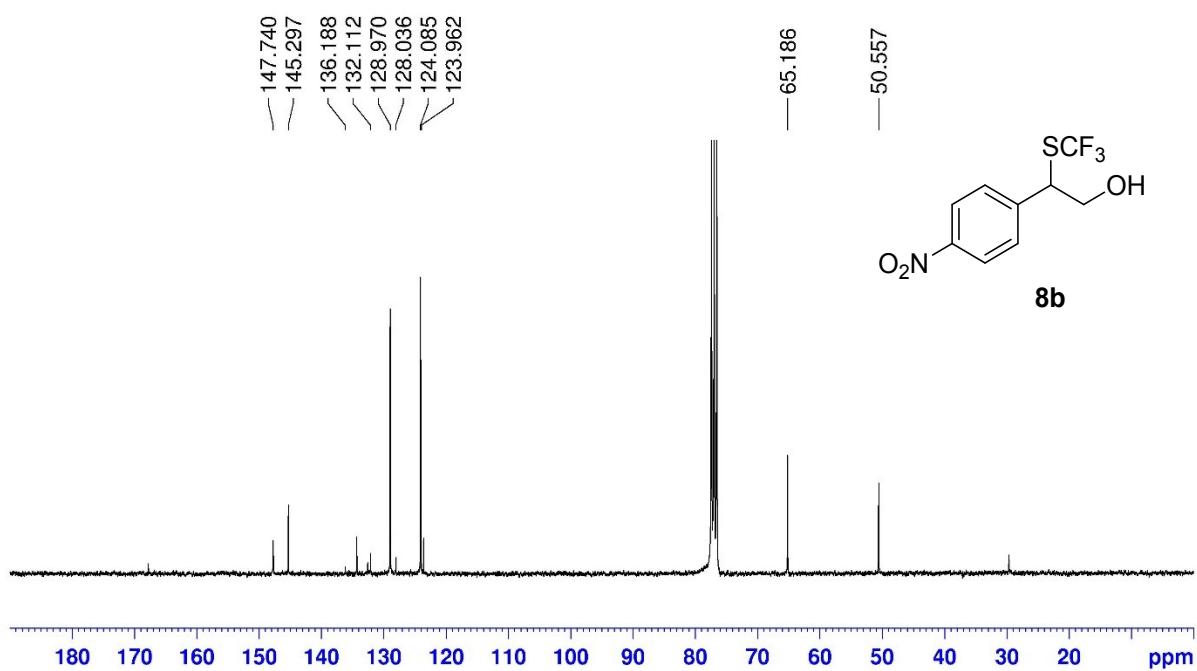
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



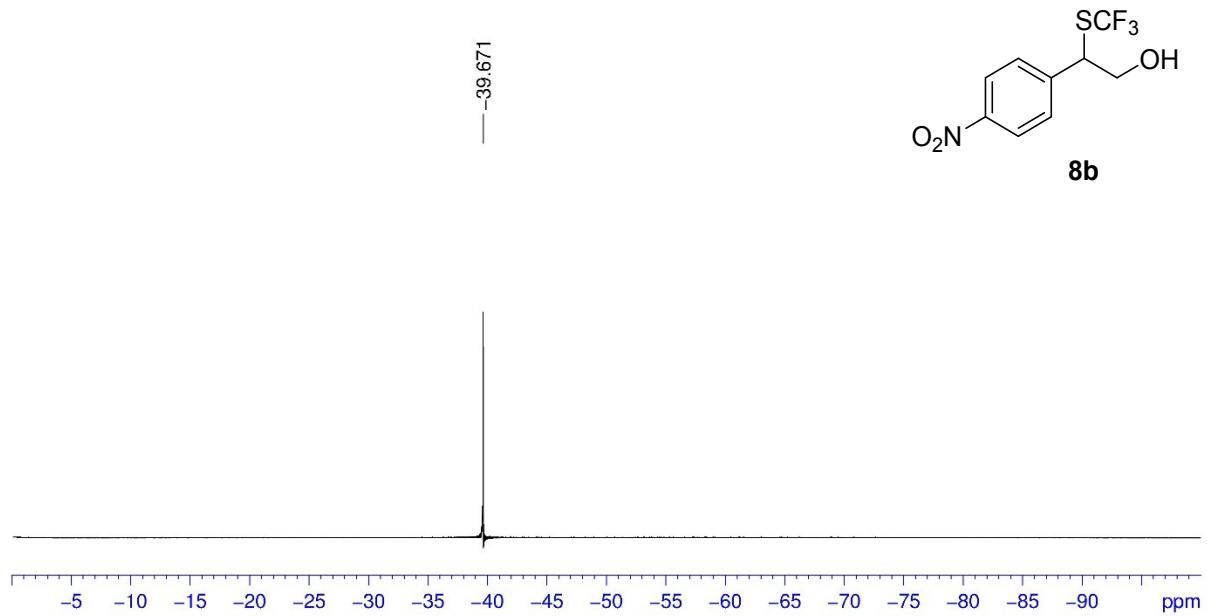
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



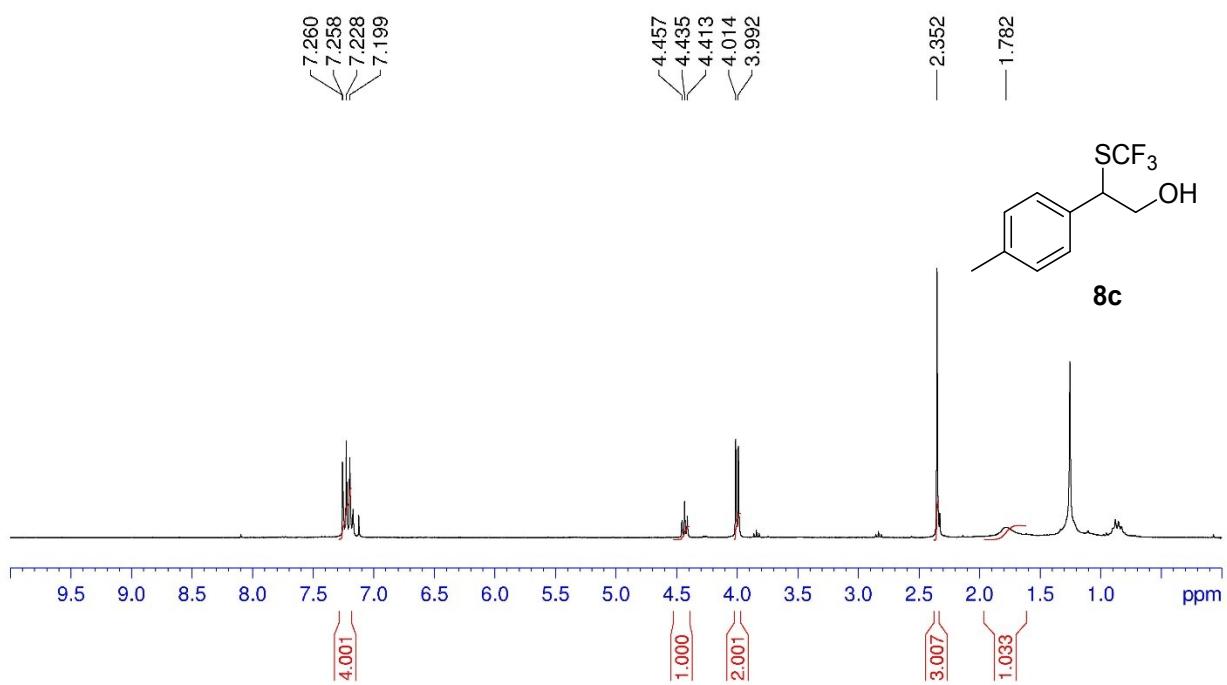
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



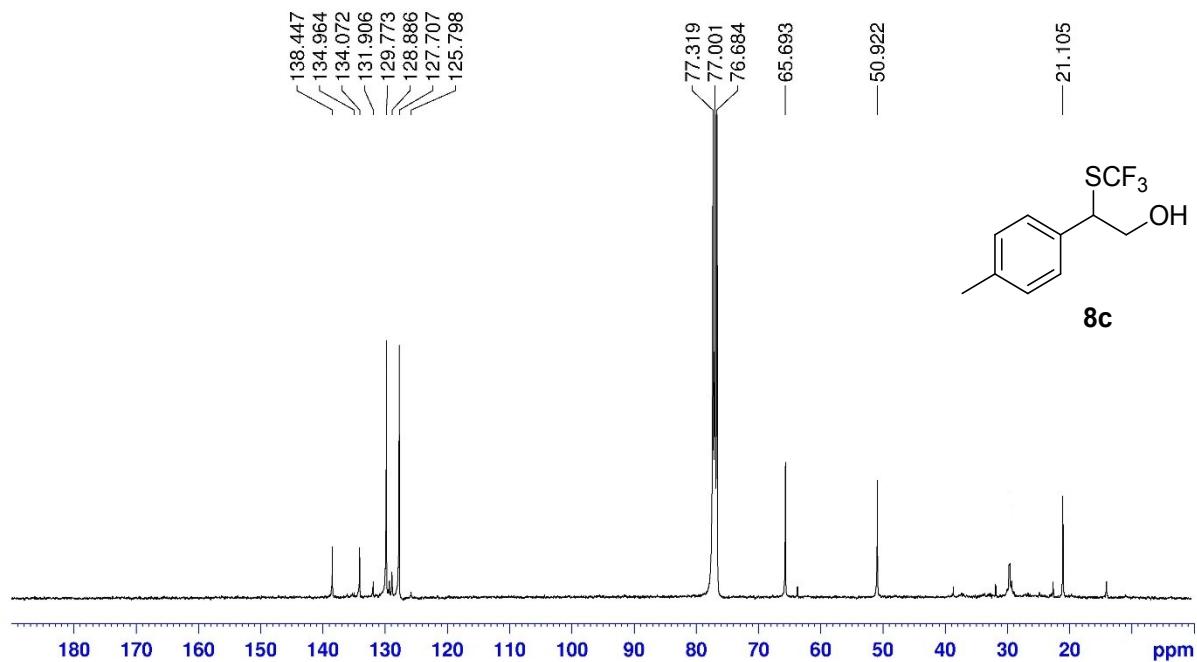
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



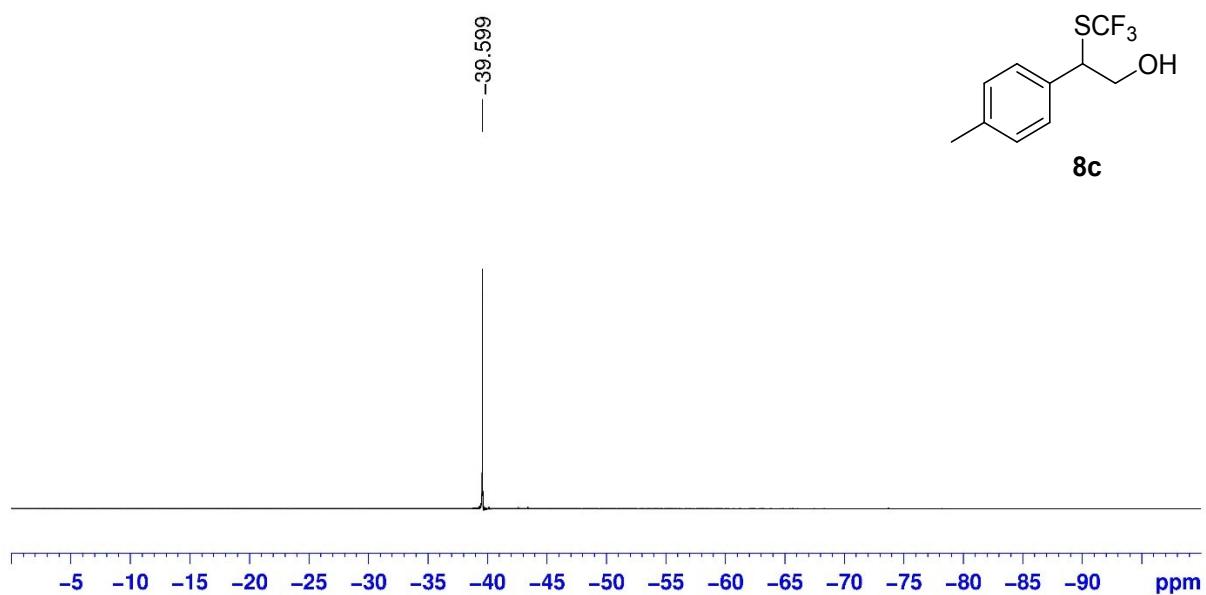
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



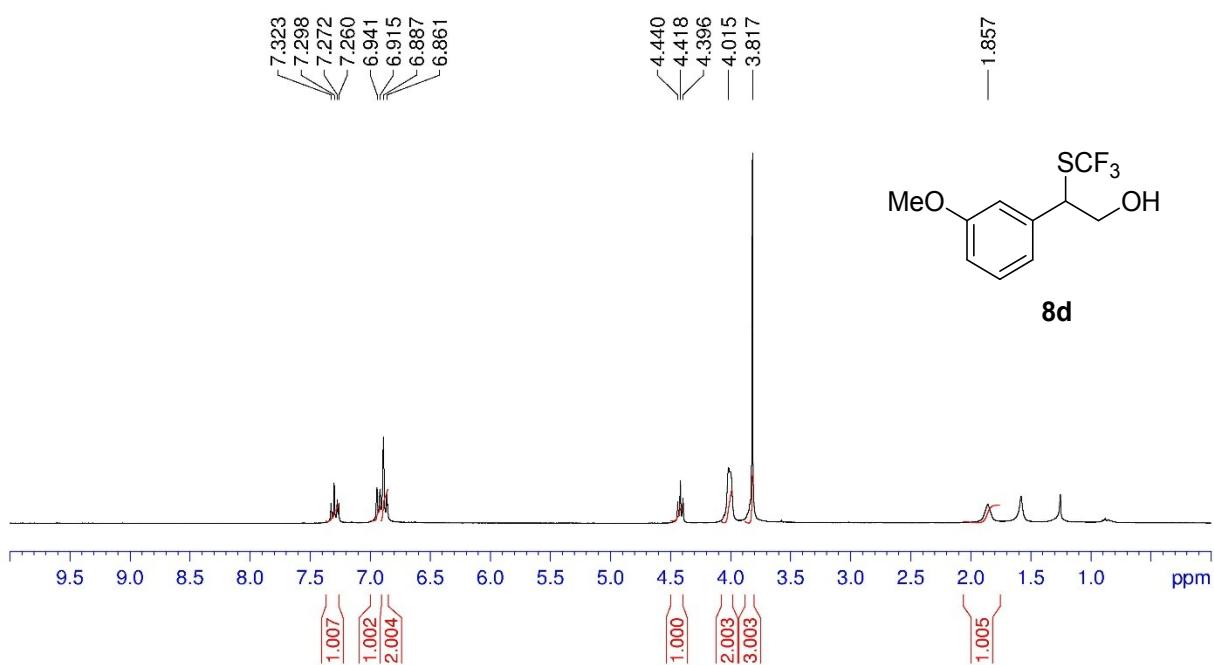
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



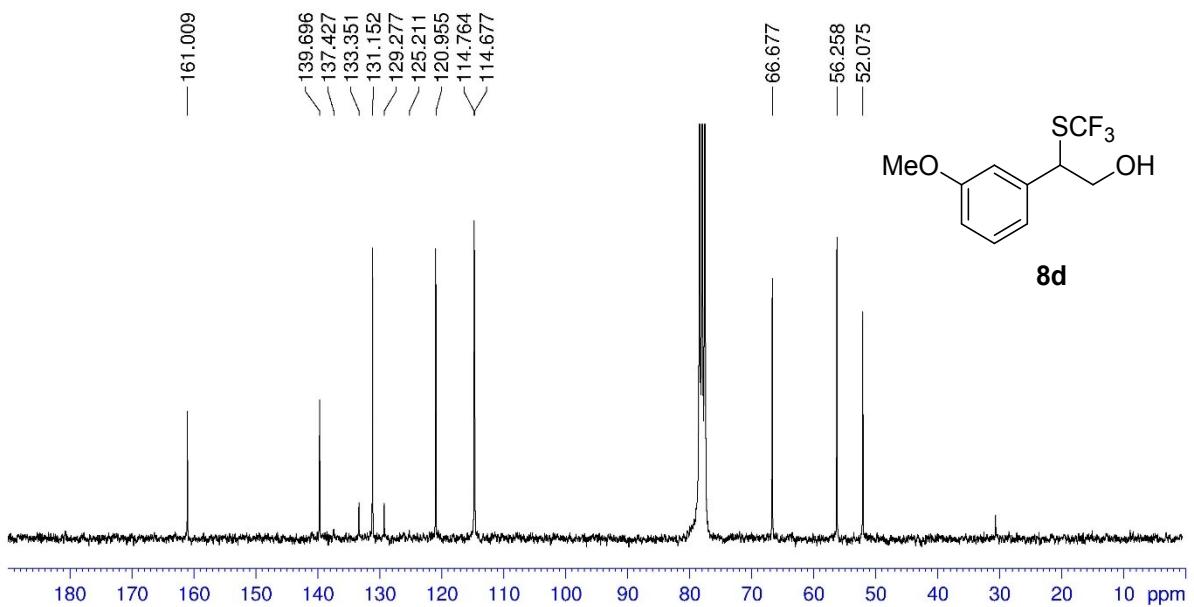
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



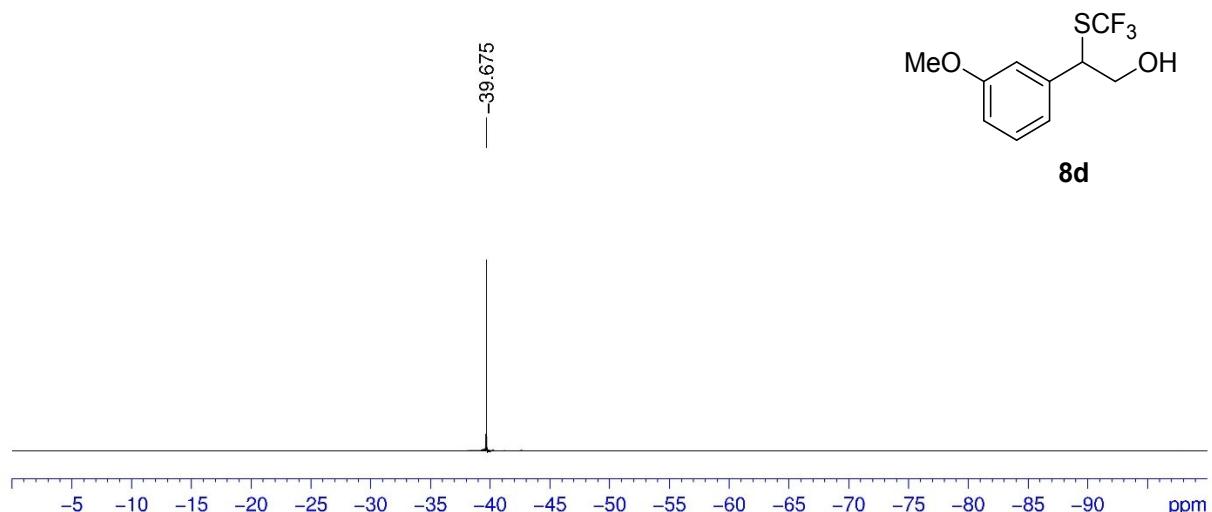
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



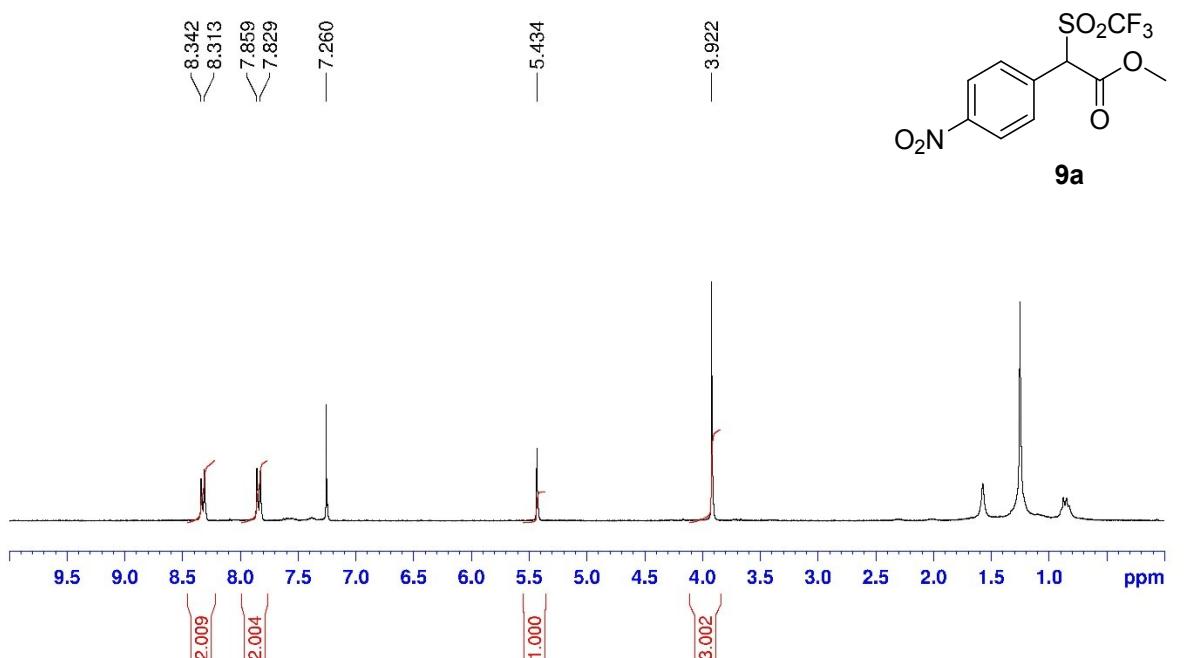
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



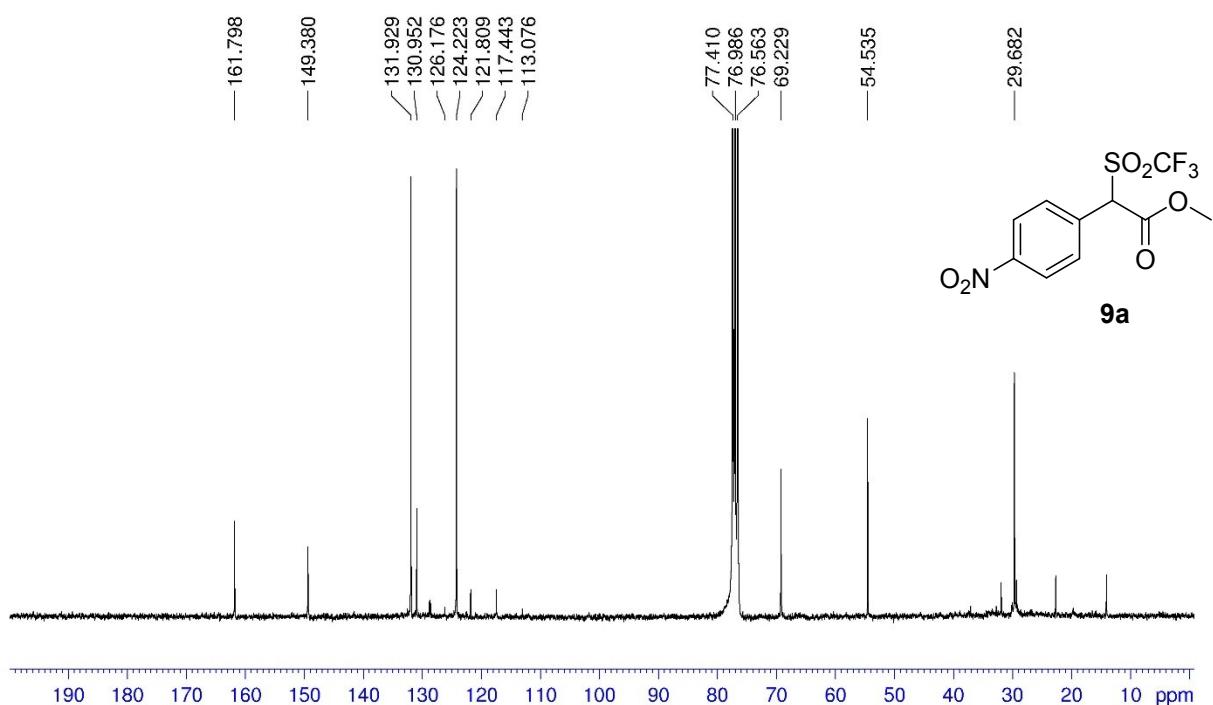
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



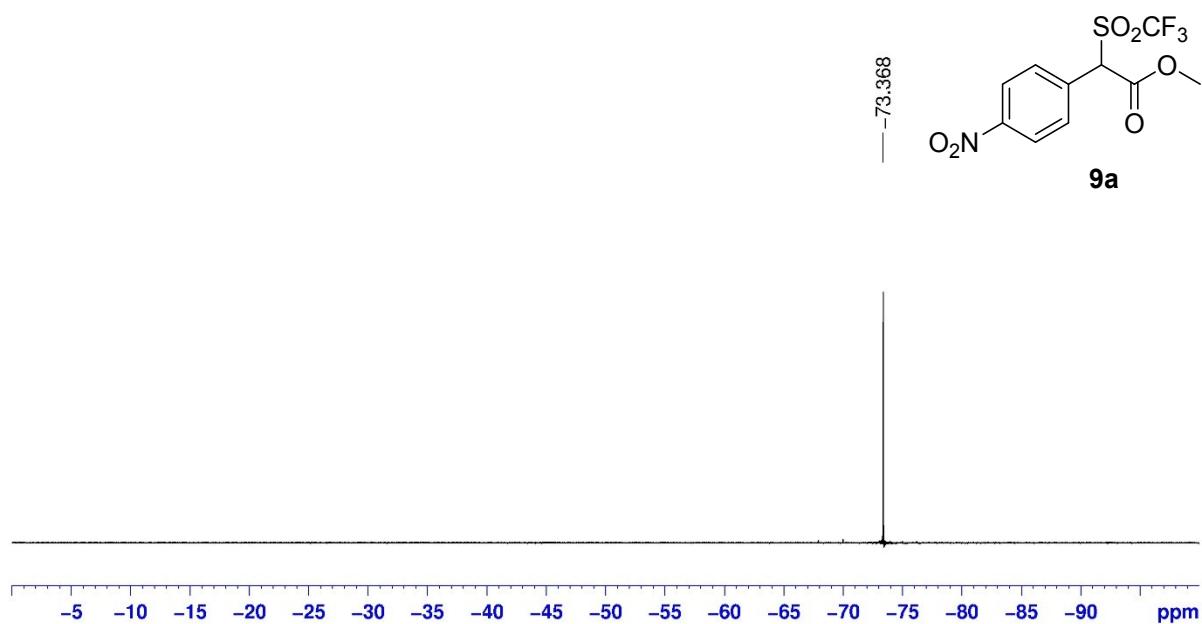
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



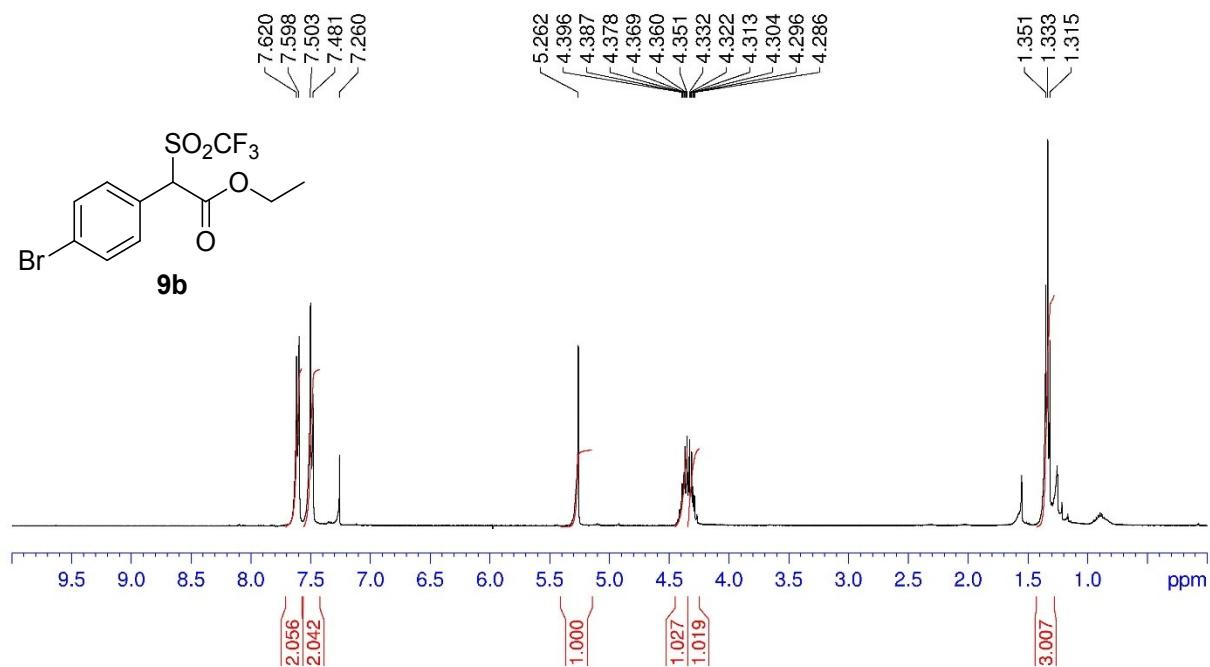
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



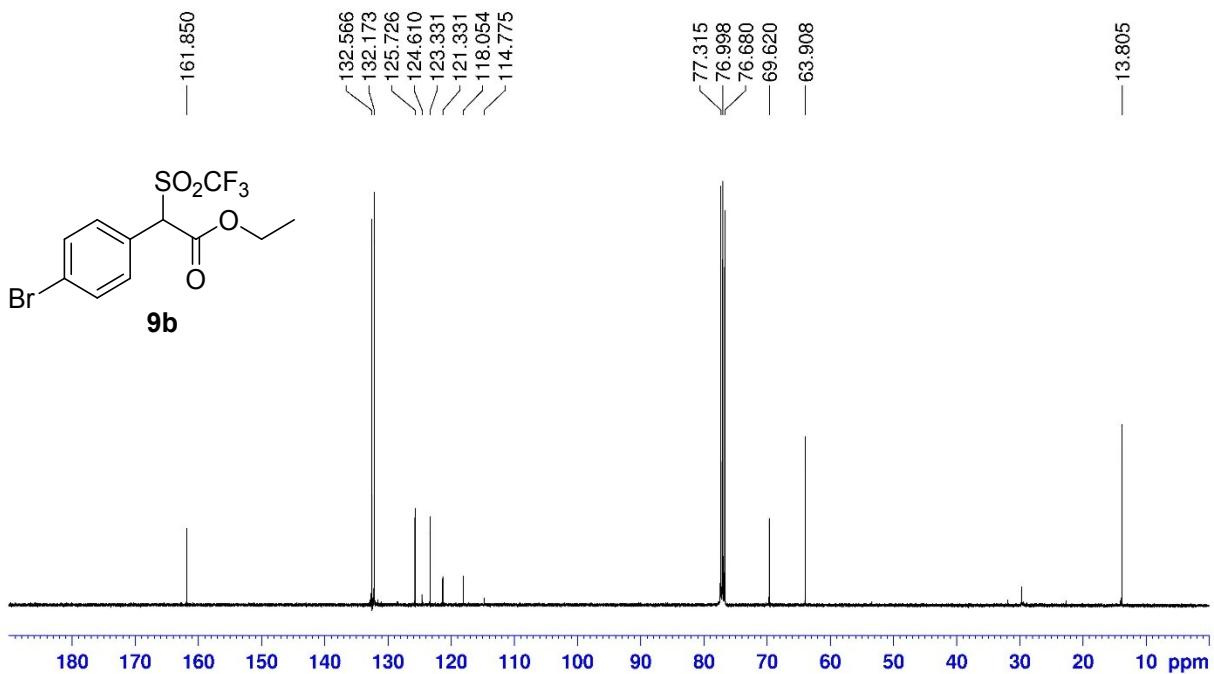
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



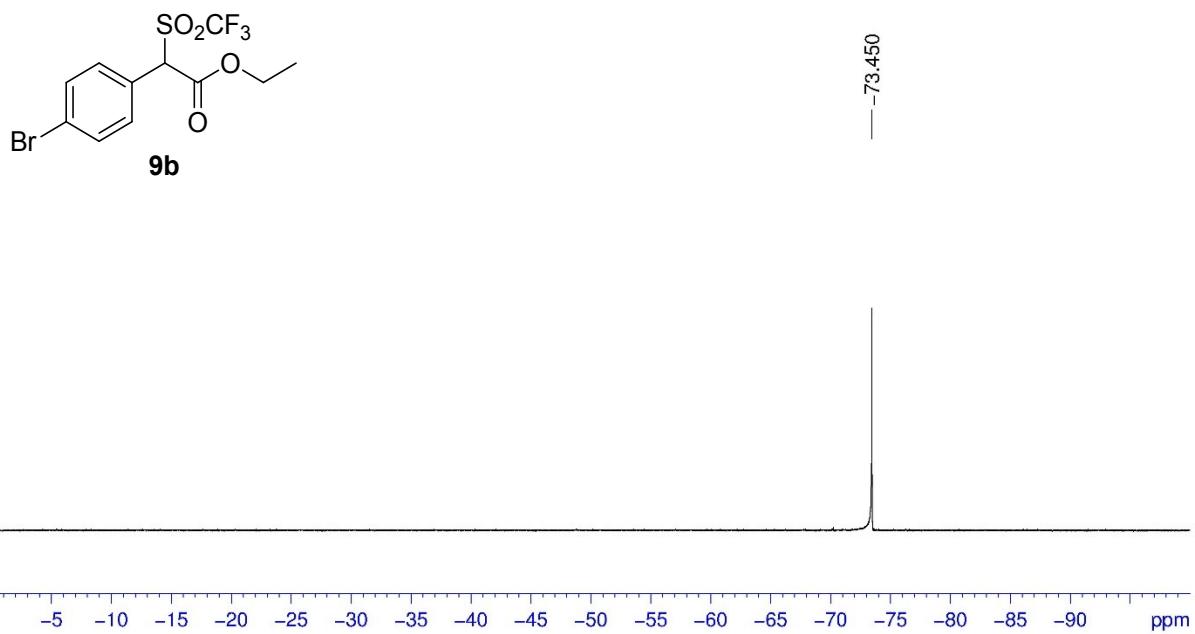
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



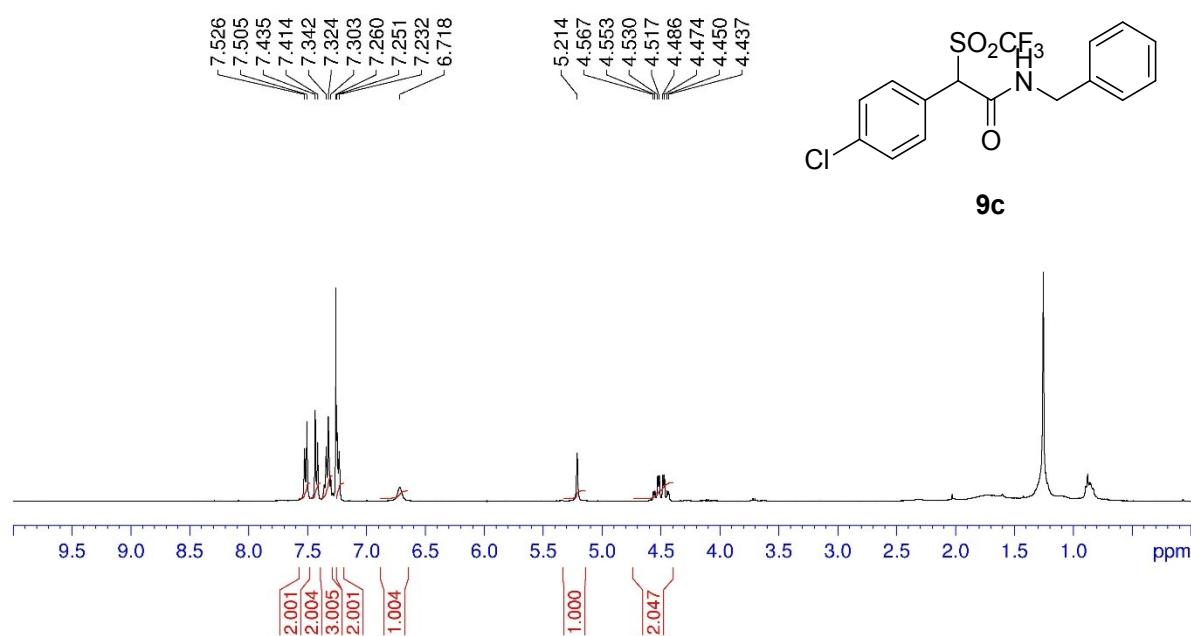
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



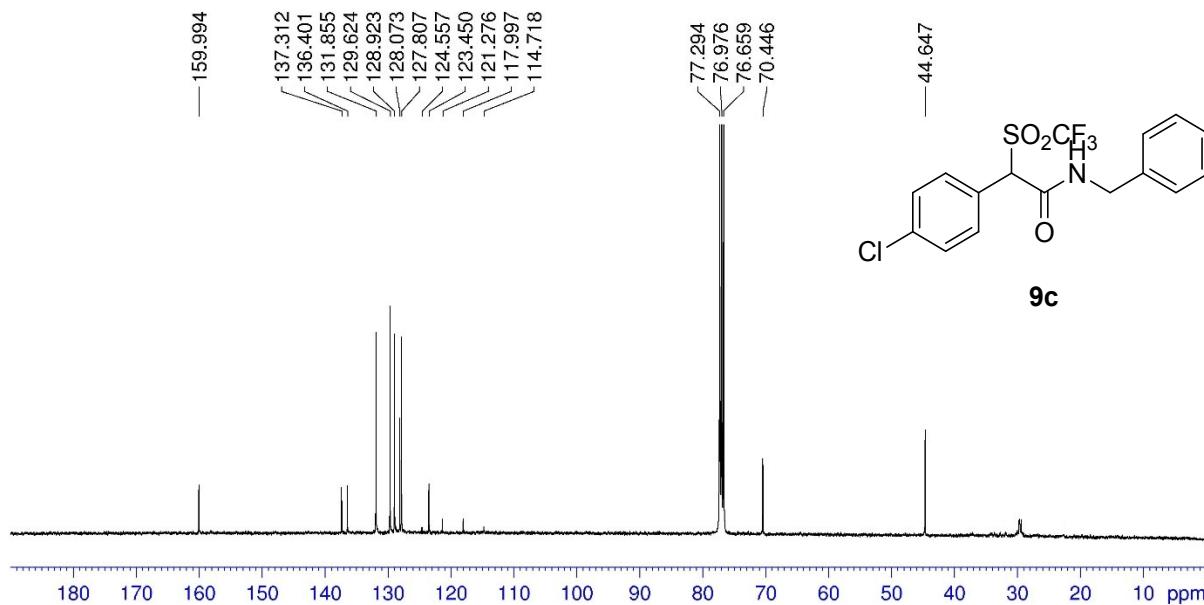
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



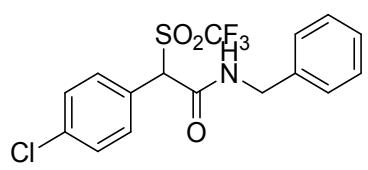
<sup>1</sup>H NMR in CDCl<sub>3</sub> (400 MHz)



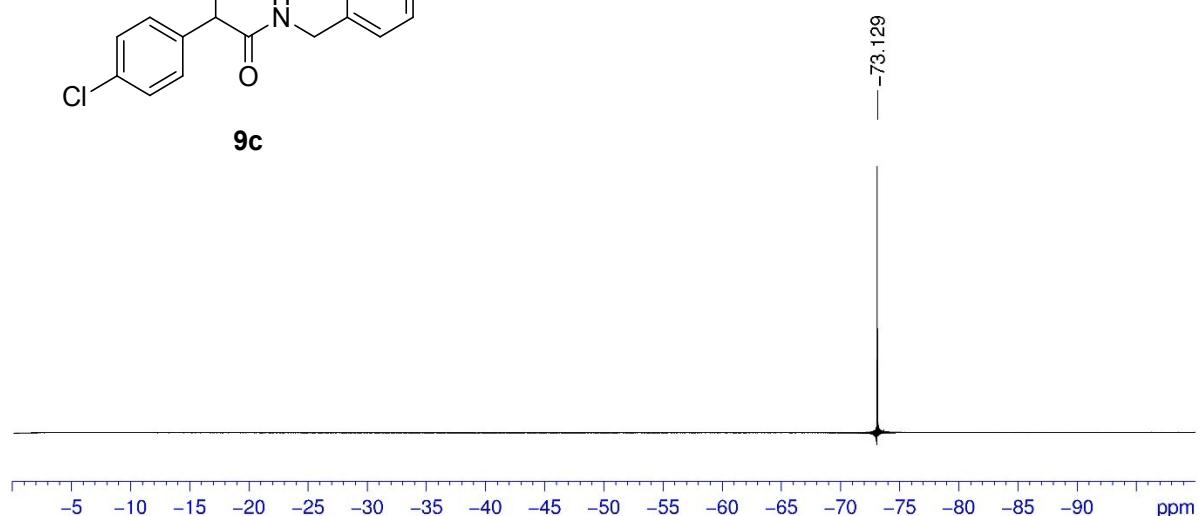
<sup>13</sup>C NMR in CDCl<sub>3</sub> (100 MHz)



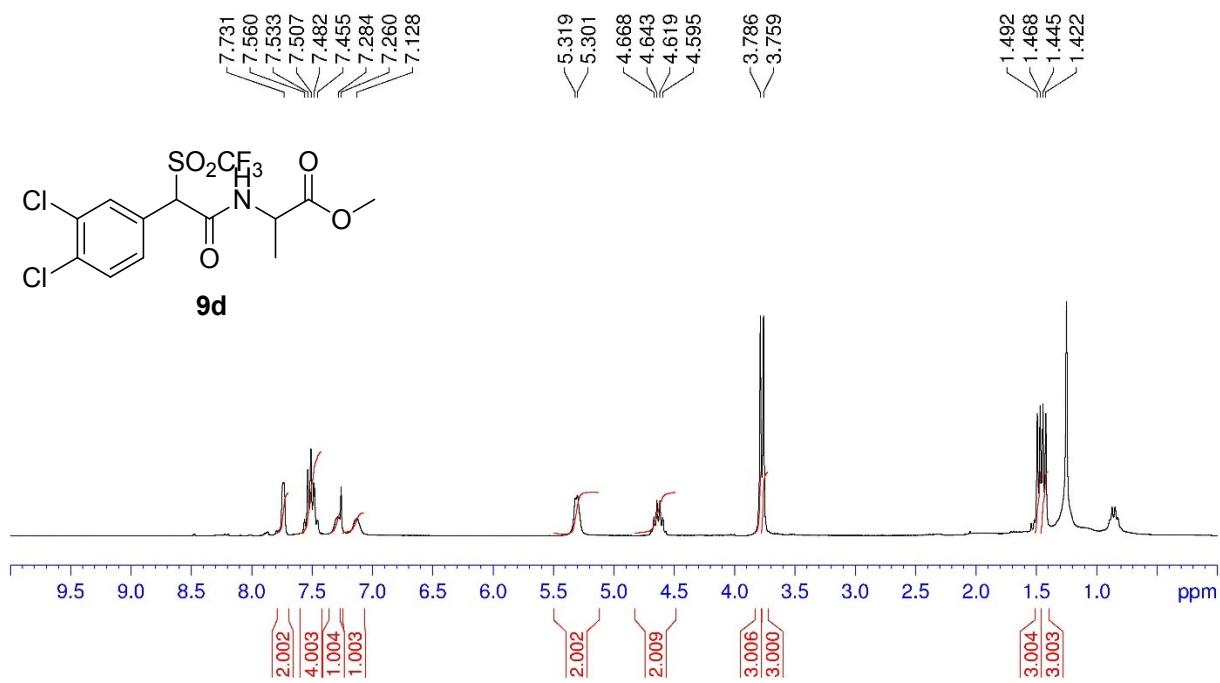
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



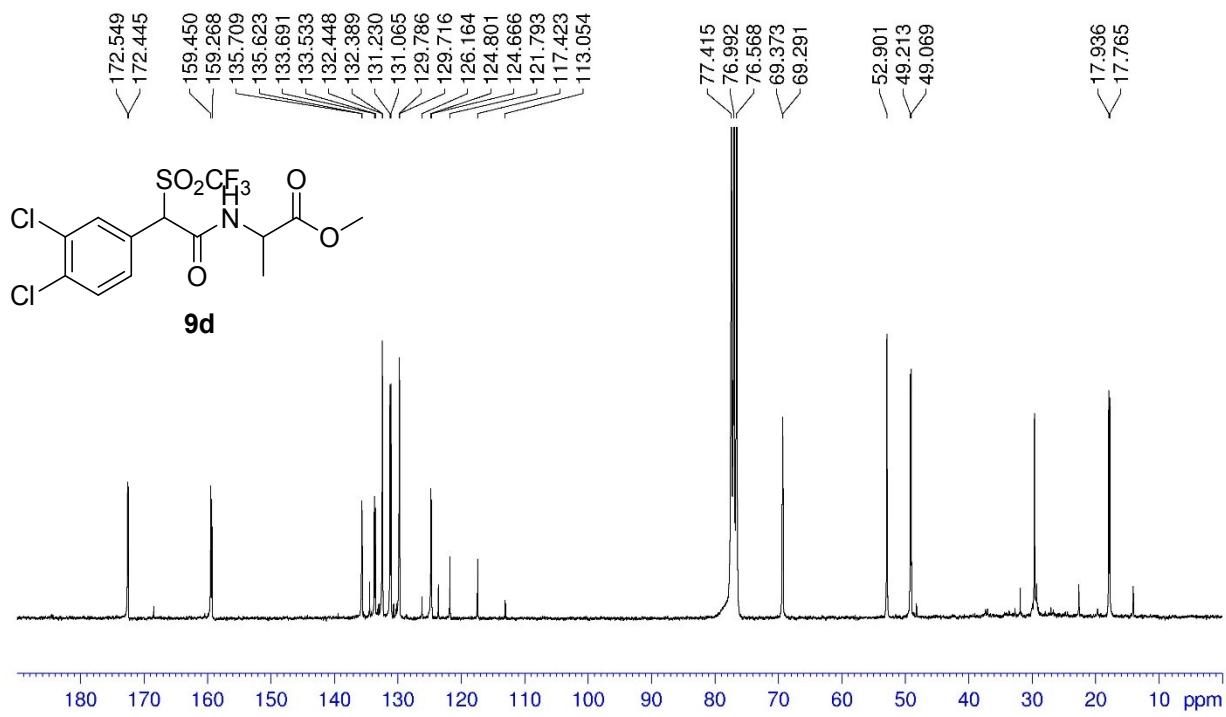
**9c**



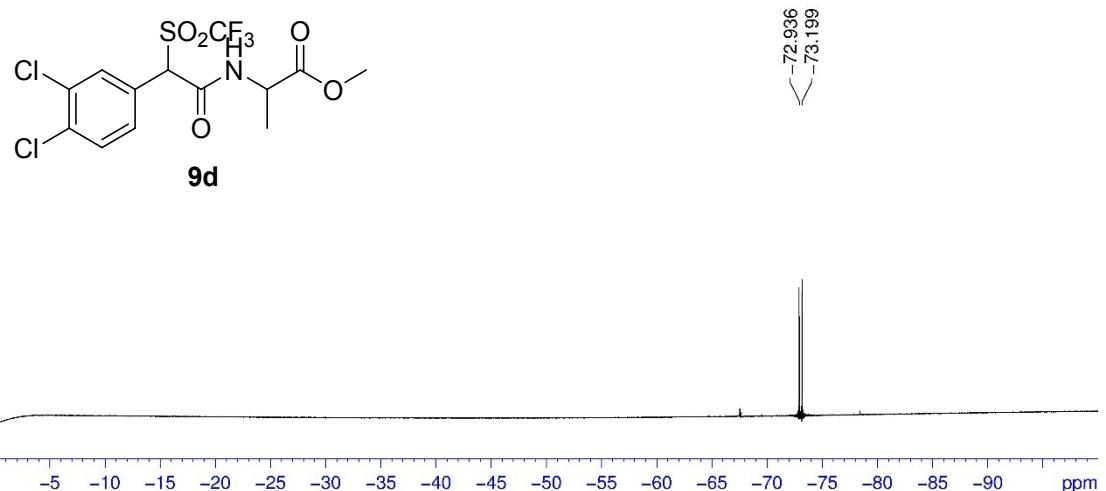
<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



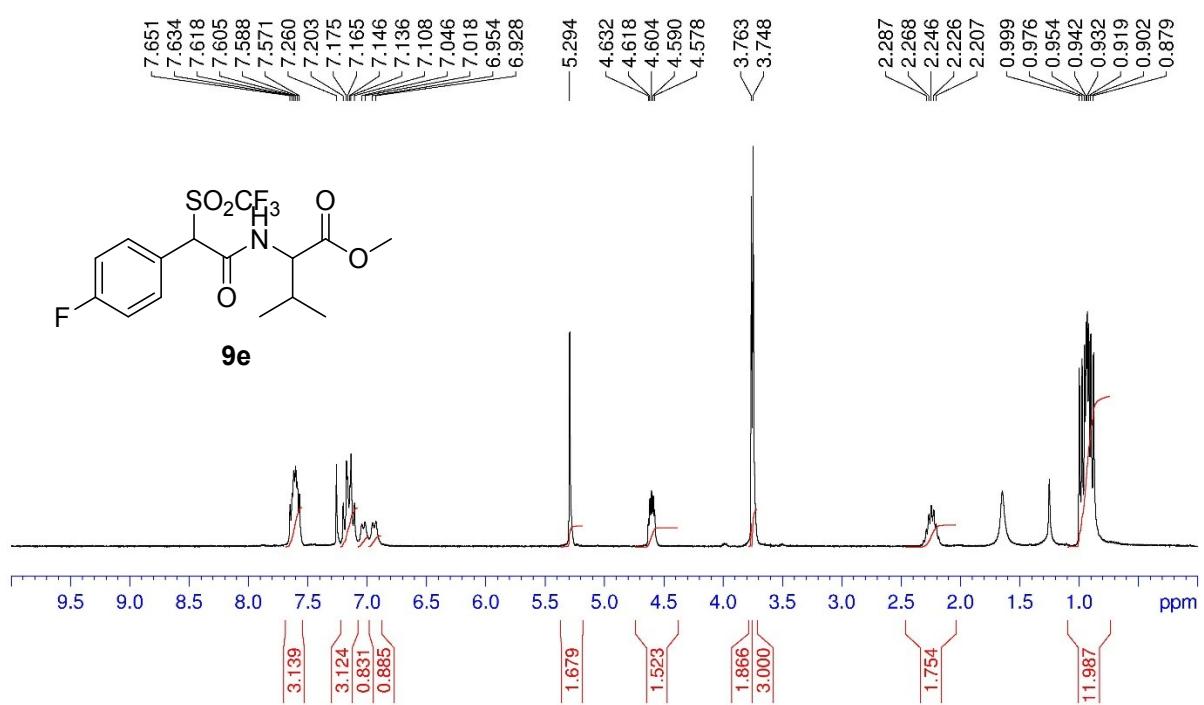
<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



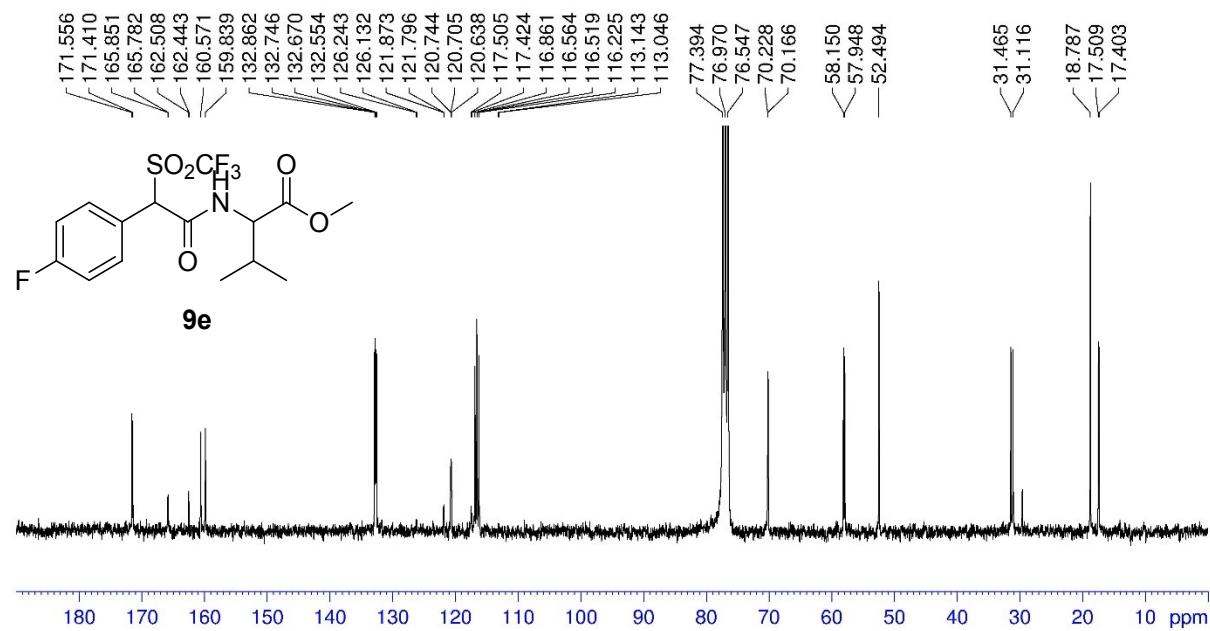
<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)



<sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz)



<sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz)



<sup>19</sup>F NMR in CDCl<sub>3</sub> (376 MHz)

