

Supporting Information  
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# Supporting Information

## Synthesis of Trifluoromethyl Ketone Containing Amino Acid Building Blocks for the Preparation of Peptide-Based Histone Deacetylase (HDAC) Inhibitors

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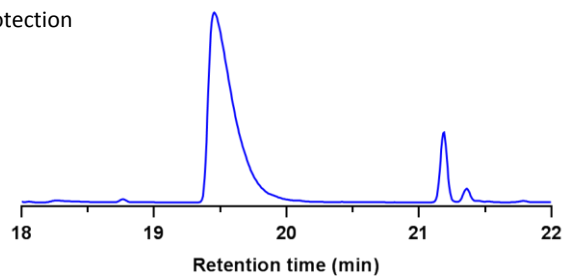
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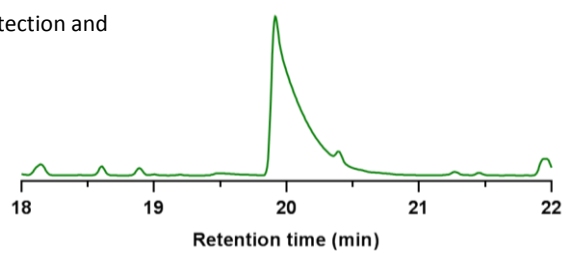
### Table of Contents

|   |   |
|---|---|
| <b>Figure S1</b> Analysis of the enantiomeric purity of amino acid <b>9a</b> using Marfey's method                              | 1 |
| <b>Figure S2</b> Optimization of deprotection conditions for the 1,3-dioxane protecting group of peptide <b>13a</b>             | 2 |
| <b>Figure S3</b> Dose-response curves for the inhibitory potency of peptide <b>13</b> and TSA against class IIa HDACs and HDAC8 | 3 |
| <b>Figures S4–S37</b> NMR spectra   | 4 |

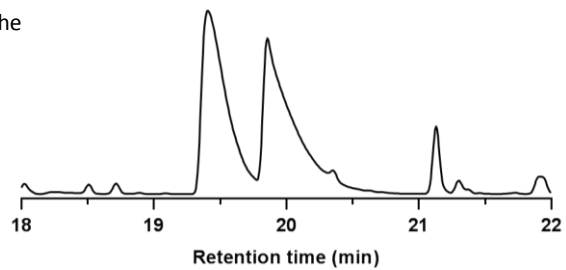
HPLC trace of compound **9a** after Fmoc deprotection and functionalization with Marfey's Reagent:



HPLC trace of compound **8** after acetyl deprotection and functionalization with Marfey's Reagent:

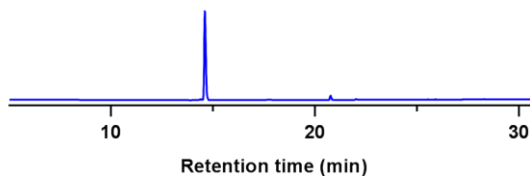


HPLC trace resulting from the coinjection of the previous two samples:

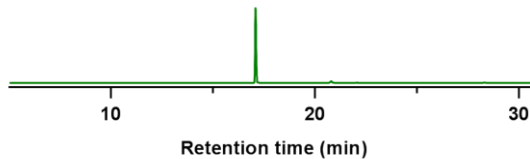


**Figure S1** Analysis of the enantiomeric purity of compounds **8** and **9a** by functionalization with Marfey's Reagent and chromatographic separation. HPLC traces were recorded at 340 nm.

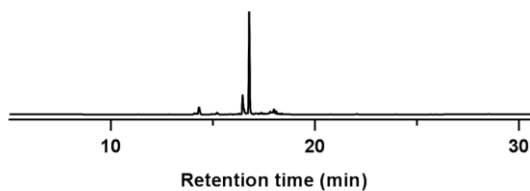
HPLC trace of peptide **13**:



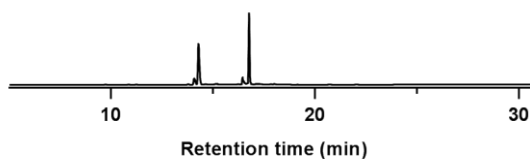
HPLC trace of peptide **13a**:



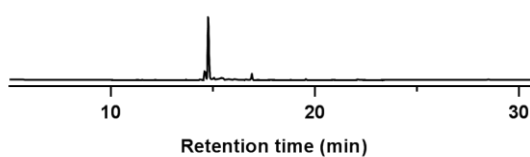
HPLC trace of peptide **13a** after 2 h incubation in TFA-CF<sub>3</sub>SO<sub>3</sub>H-H<sub>2</sub>O-*i*-Pr<sub>3</sub>SiH [88.5:4:5:2.5, (v/v)]:



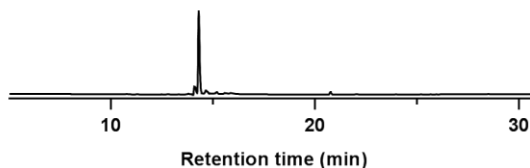
HPLC trace of peptide **13a** after 2 h incubation in TFA-CF<sub>3</sub>SO<sub>3</sub>H-H<sub>2</sub>O-*i*-Pr<sub>3</sub>SiH [84.5:8:5:2.5, (v/v)]:



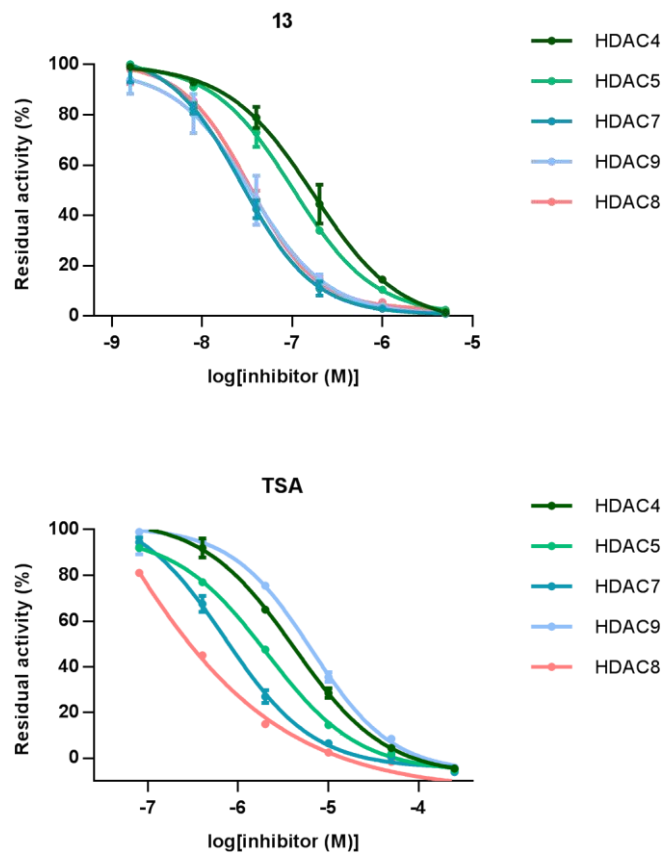
HPLC trace of peptide **13a** after 2 h incubation in TFA-CF<sub>3</sub>SO<sub>3</sub>H-H<sub>2</sub>O-*i*-Pr<sub>3</sub>SiH [80.5:12:5:2.5, (v/v)]:



HPLC trace of peptide **13a** after 2 h incubation in TFA-CF<sub>3</sub>SO<sub>3</sub>H-H<sub>2</sub>O-*i*-Pr<sub>3</sub>SiH [72.5:20:5:2.5, (v/v)]:



**Figure S2** Optimization of CF<sub>3</sub>SO<sub>3</sub>H concentration for the removal of the dioxane protecting group of Atona from peptide **13a** (pre-purified). HPLC traces were recorded at 280 nm.



**Figure S3** Dose-response curves for the inhibitory potency of peptide **13** and trichostatin A (TSA) against class IIa HDACs and HDAC8. Values at each concentration are based on two individual experiments performed in duplicate and represent mean  $\pm$  SD.

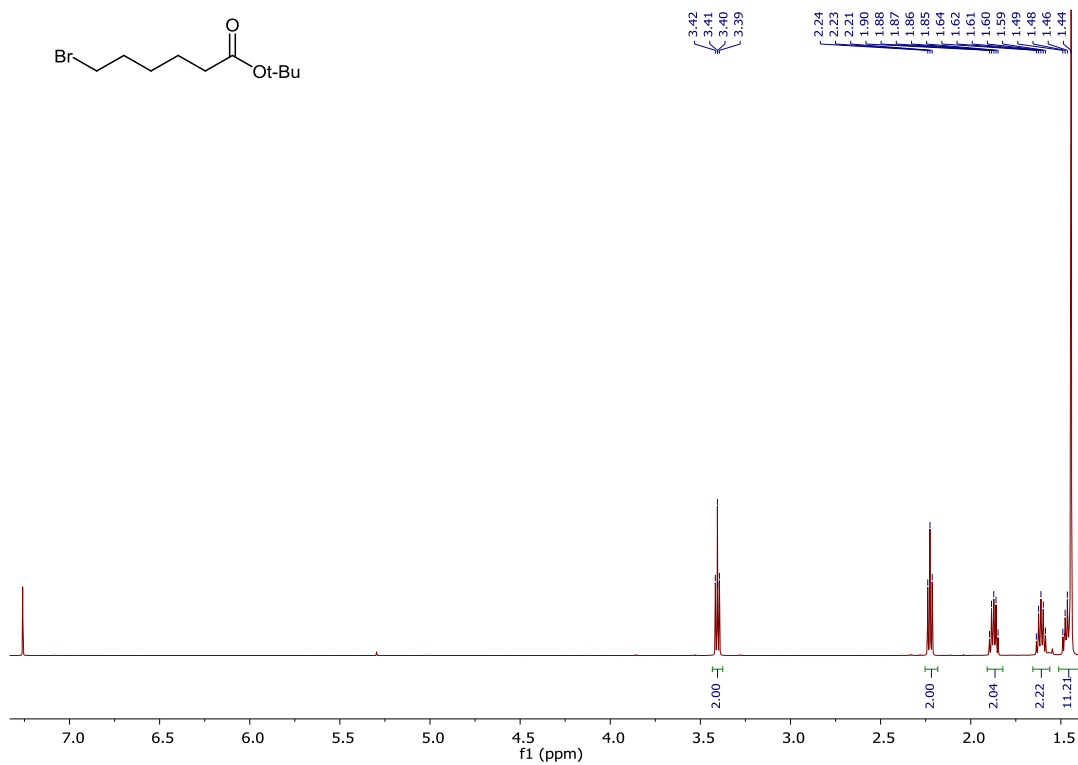


Figure S4 <sup>1</sup>H NMR of compound 4, recorded in CDCl<sub>3</sub>.

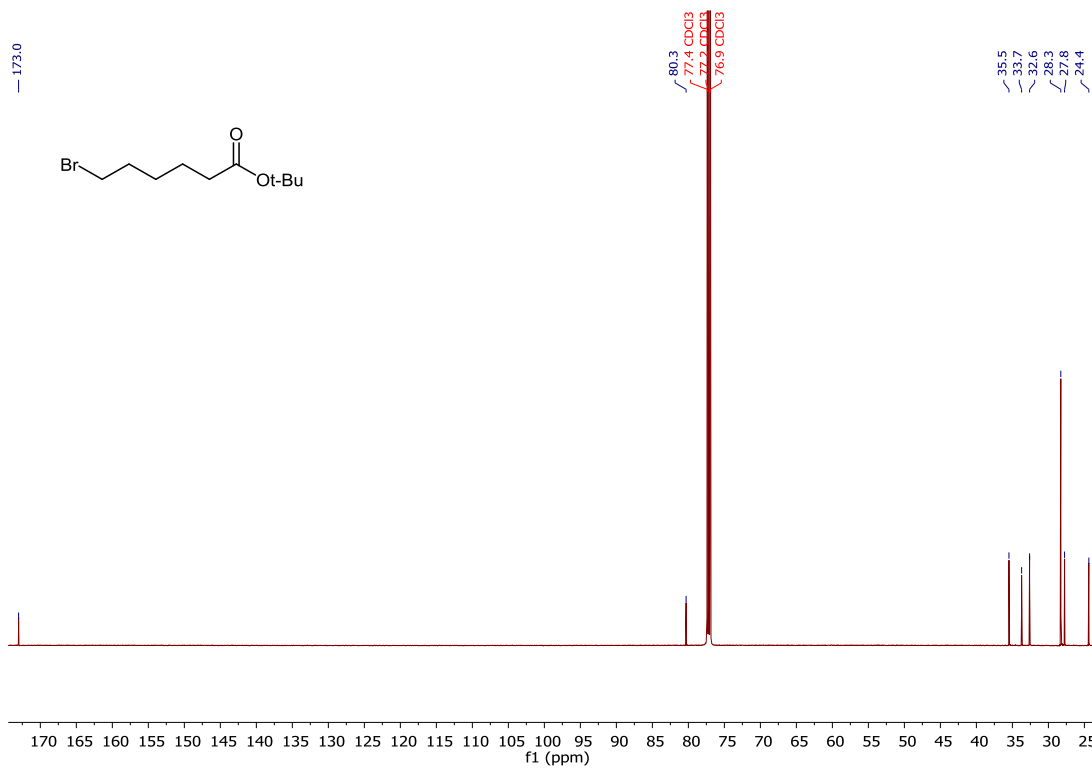


Figure S5 <sup>13</sup>C NMR of compound 4, recorded in CDCl<sub>3</sub>.

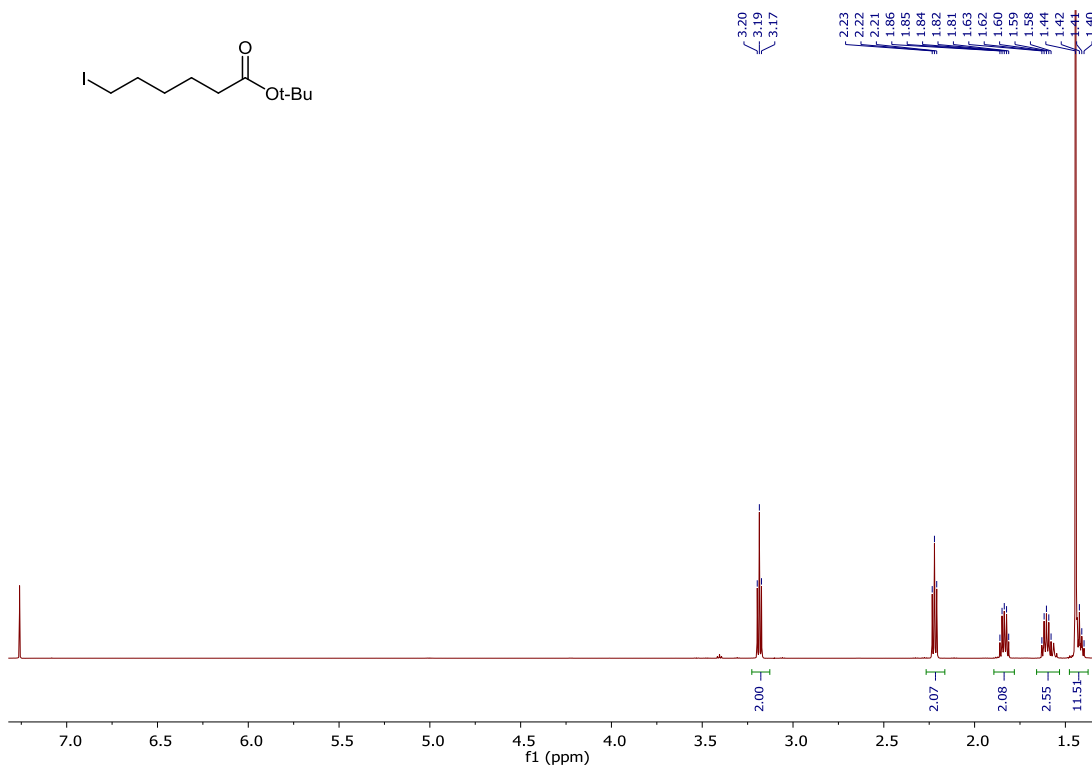


Figure S6 <sup>1</sup>H NMR of *tert*-butyl 6-iodohexanoate, recorded in CDCl<sub>3</sub>.

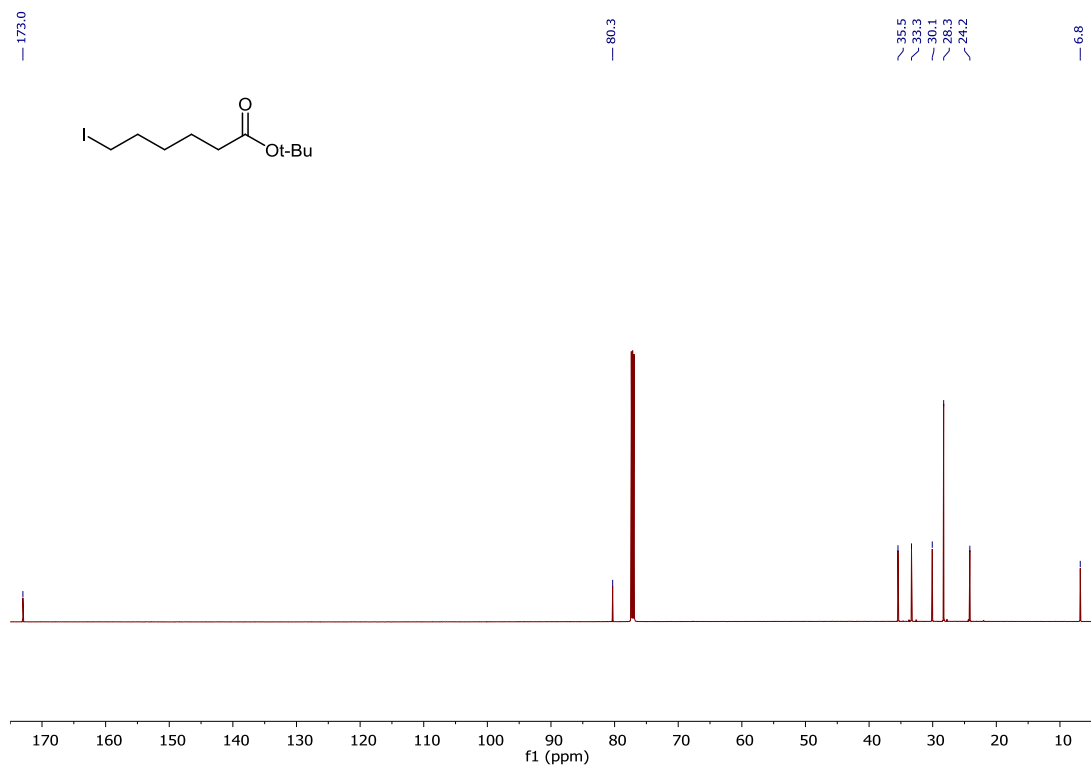


Figure S7 <sup>13</sup>C NMR of *tert*-butyl 6-iodohexanoate, recorded in CDCl<sub>3</sub>.

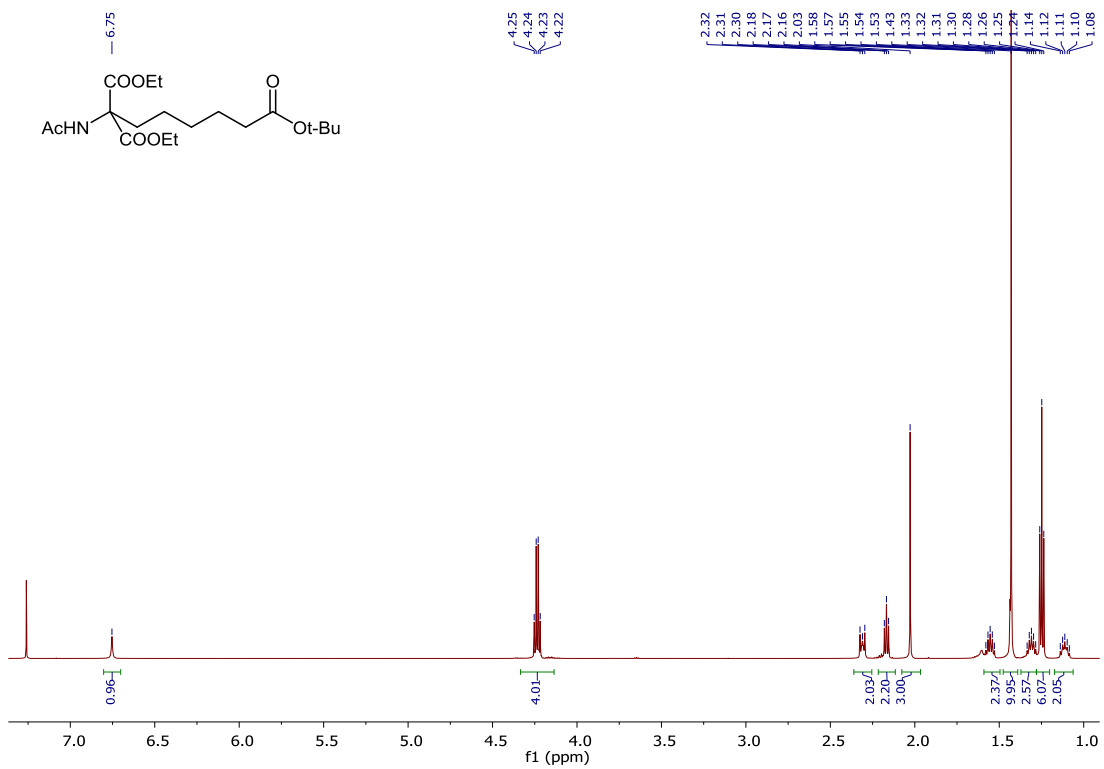


Figure S8 <sup>1</sup>H NMR of compound 5, recorded in CDCl<sub>3</sub>.

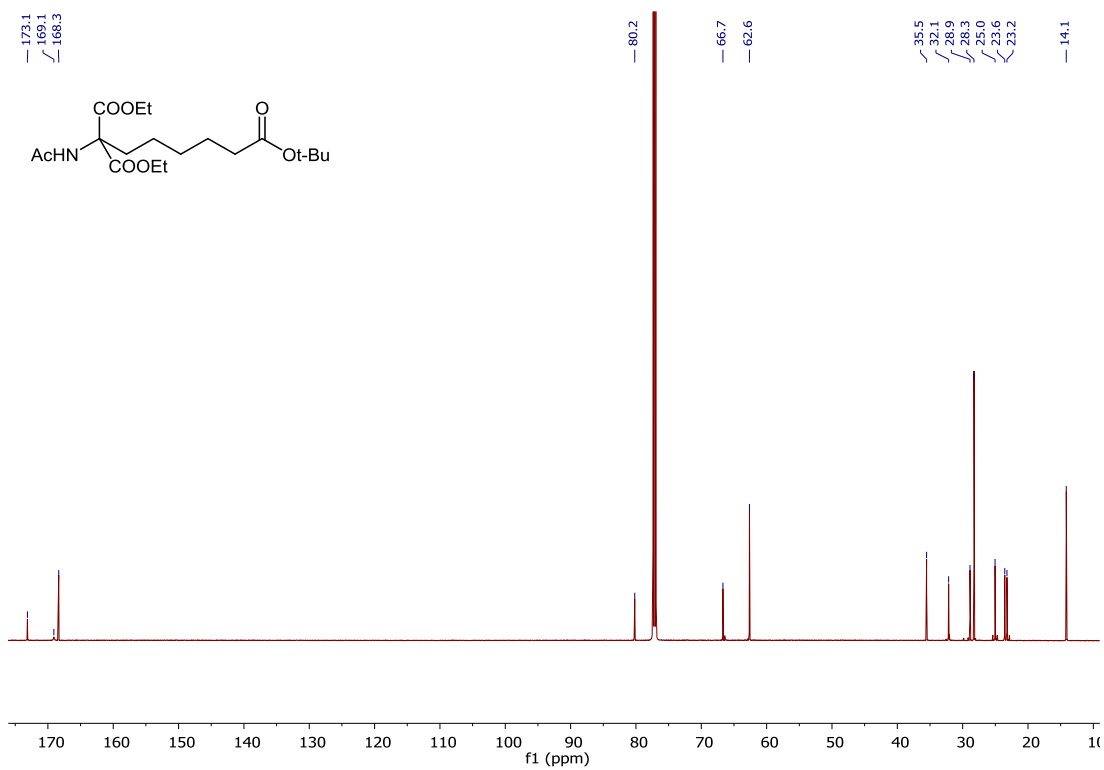


Figure S9 <sup>13</sup>C NMR of compound 5, recorded in CDCl<sub>3</sub>.

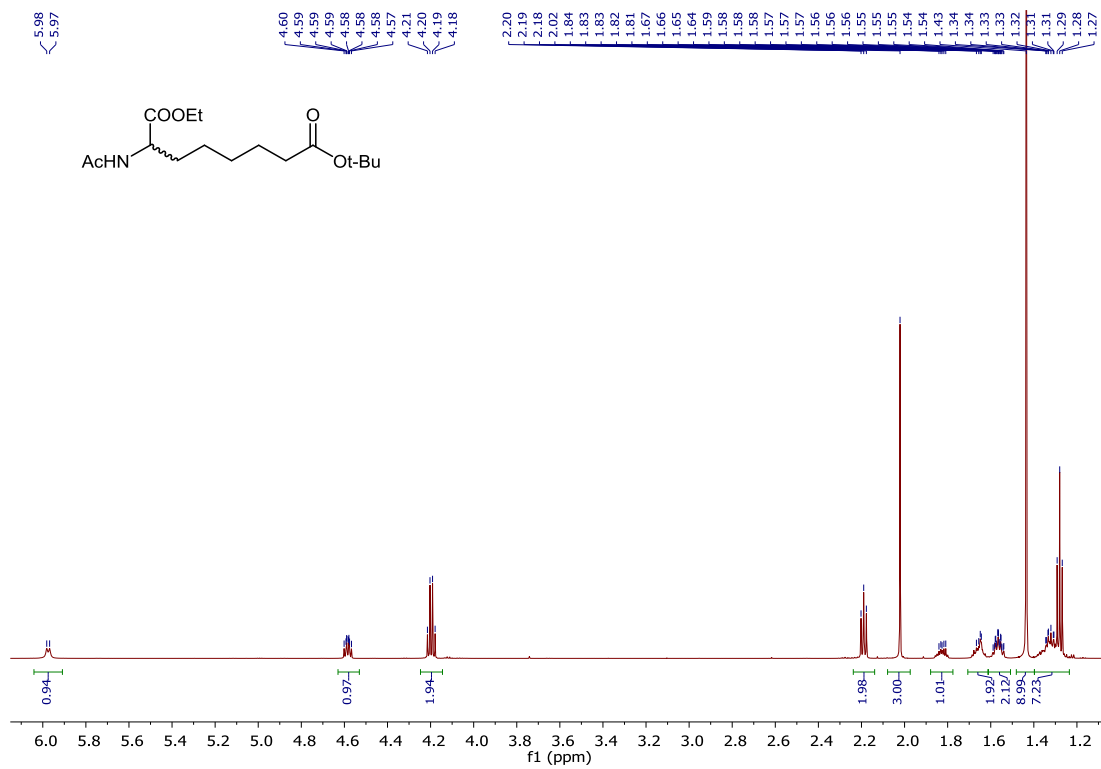


Figure S10  $^1\text{H}$  NMR of compound **6**, recorded in CDCl<sub>3</sub>.

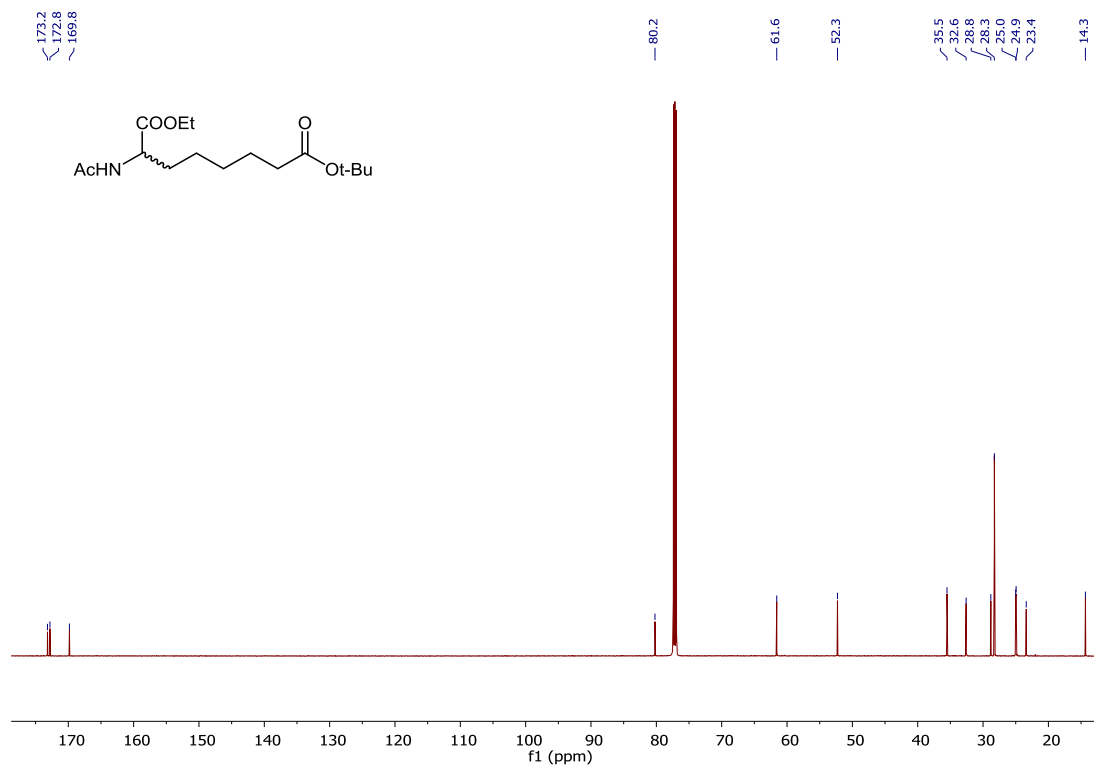


Figure S11  $^{13}\text{C}$  NMR of compound **6**, recorded in CDCl<sub>3</sub>.

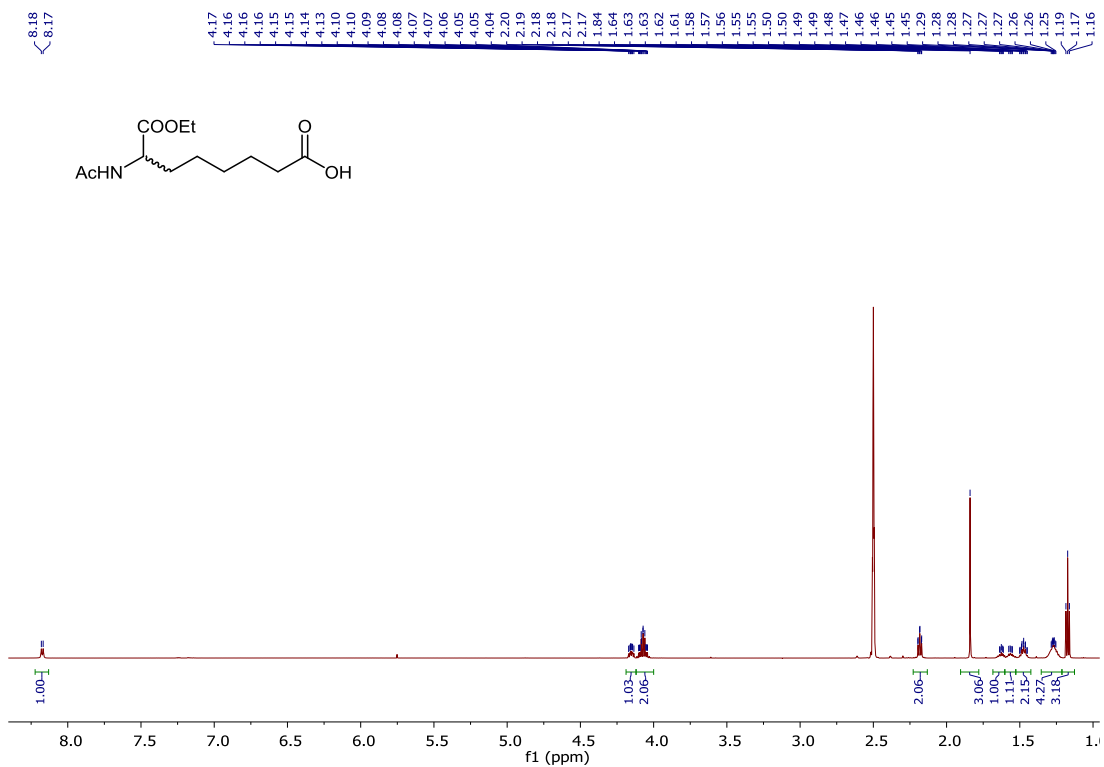


Figure S12 <sup>1</sup>H NMR of 7-acetamido-8-ethoxy-8-oxooctanoic acid, recorded in DMSO-*d*<sub>6</sub>.

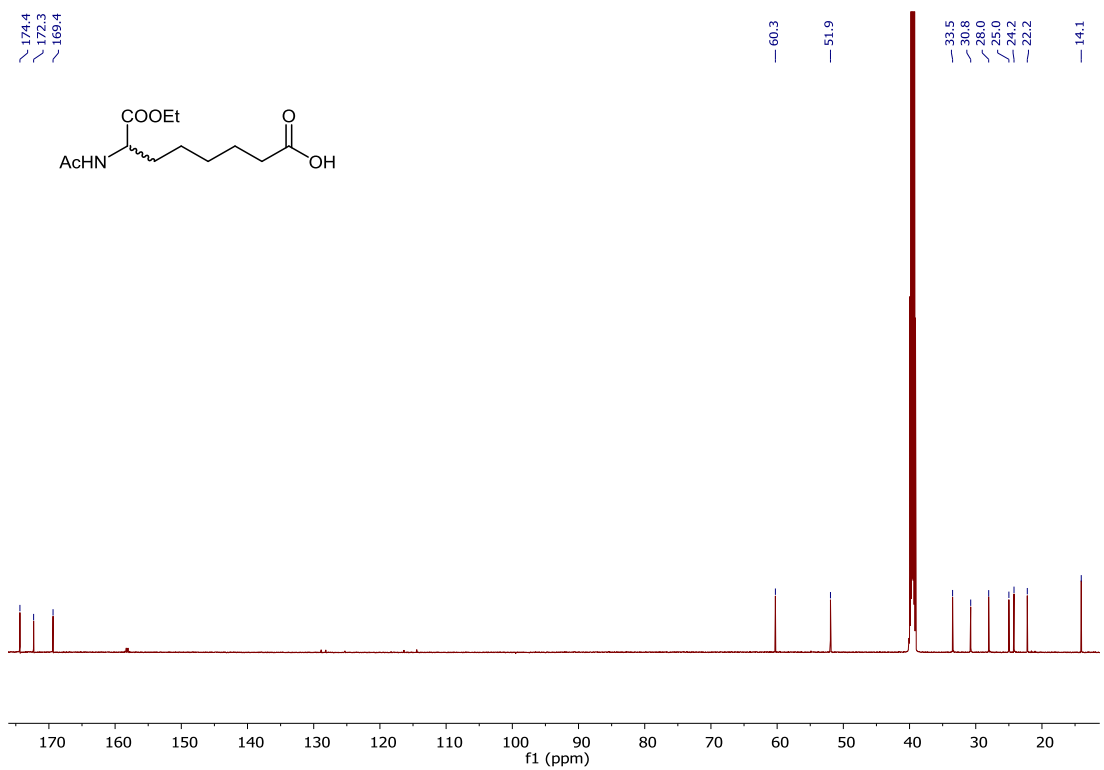


Figure S13 <sup>13</sup>C NMR of 7-acetamido-8-ethoxy-8-oxooctanoic acid, recorded in DMSO-*d*<sub>6</sub>.

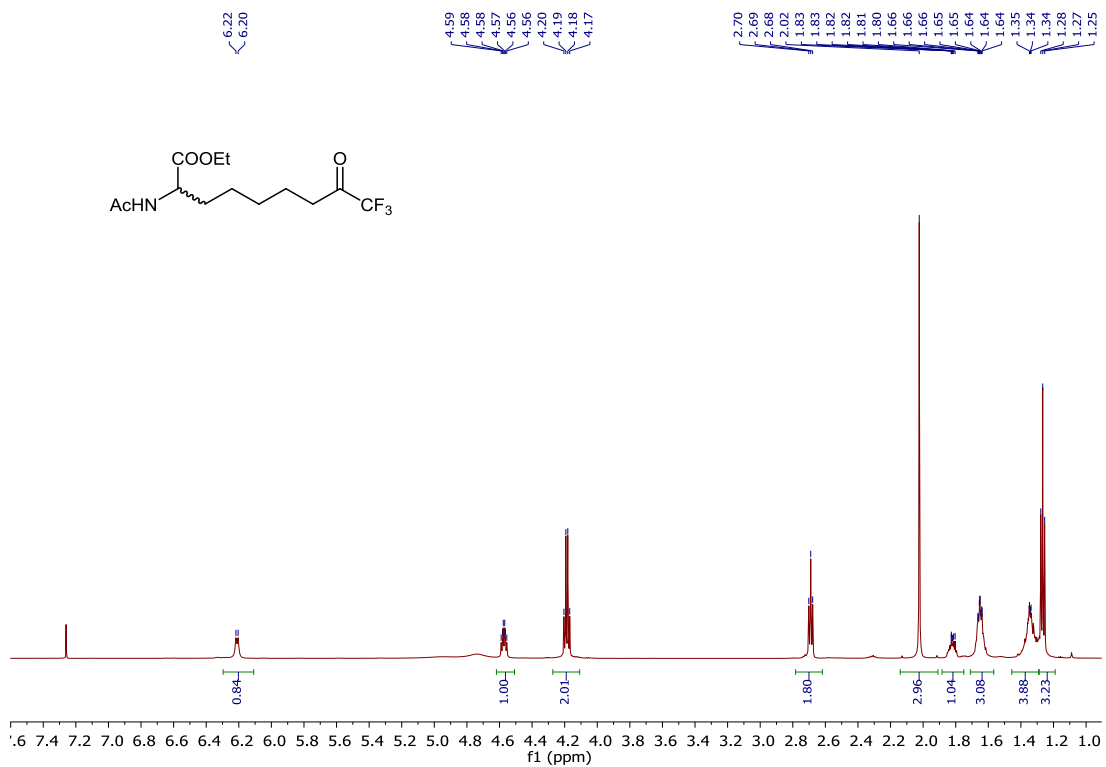


Figure S14 <sup>1</sup>H NMR of compound 7, recorded in CDCl<sub>3</sub>.

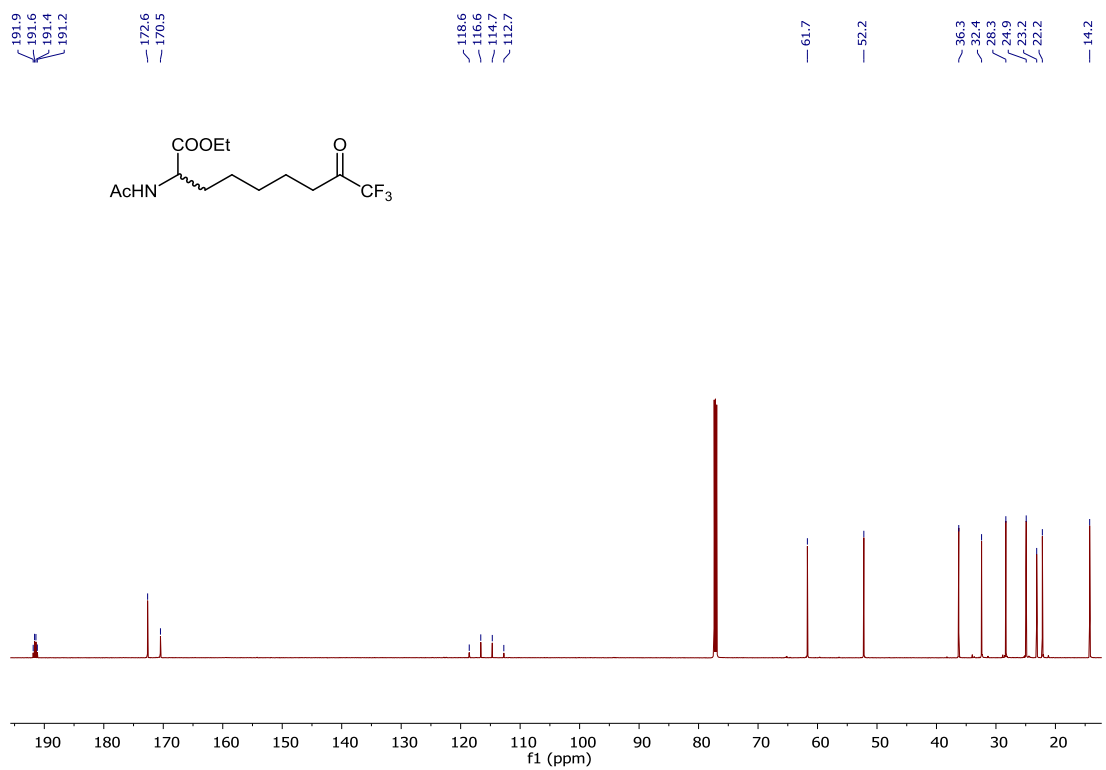


Figure S15 <sup>13</sup>C NMR of compound 7, recorded in CDCl<sub>3</sub>.

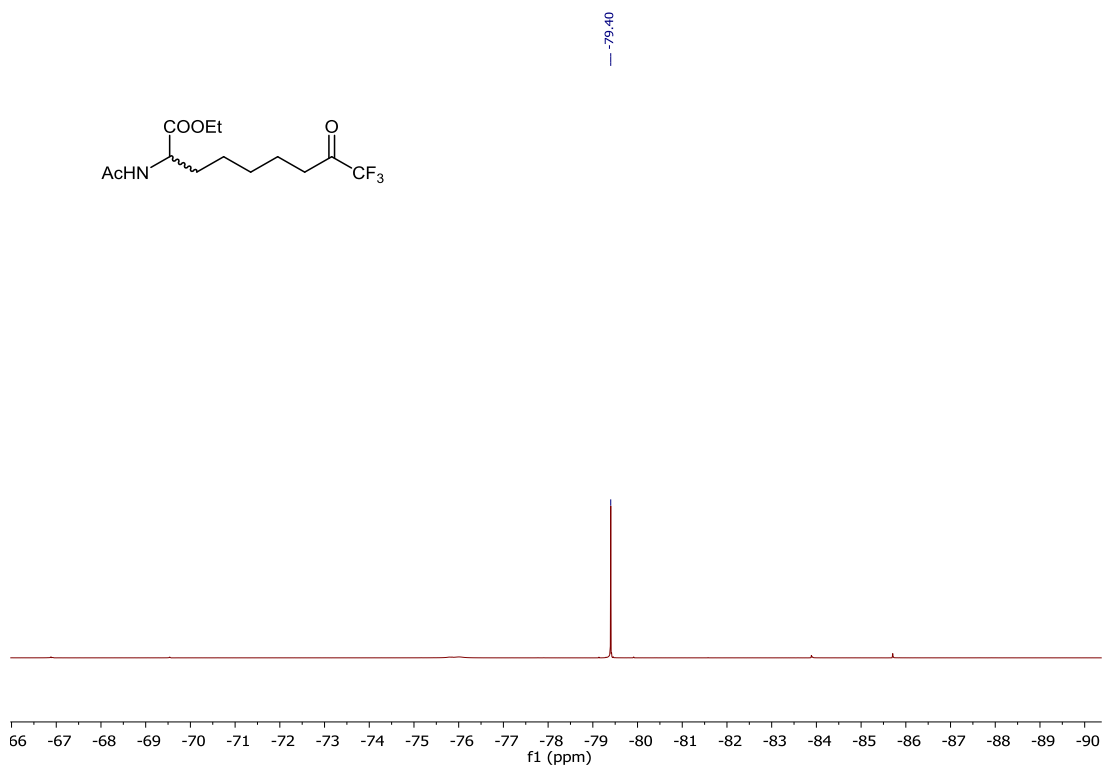


Figure S16 <sup>19</sup>F NMR of compound **7**, recorded in CDCl<sub>3</sub>.

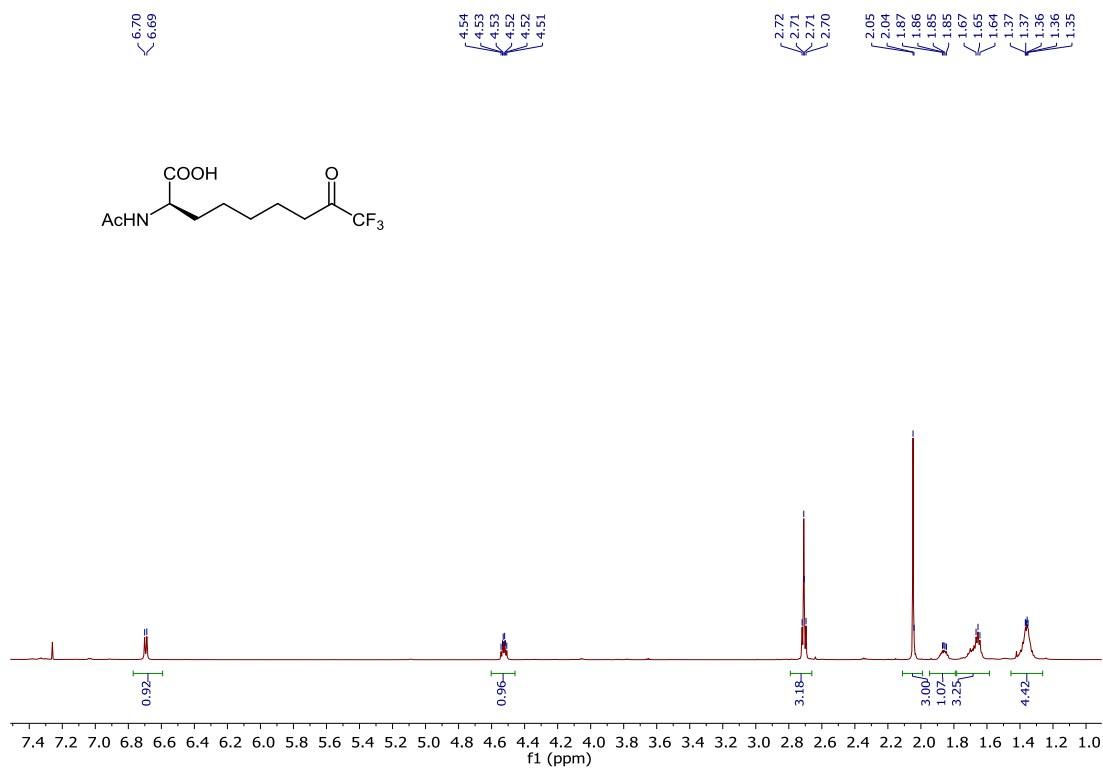


Figure S17 <sup>1</sup>H NMR of compound **8**, recorded in CDCl<sub>3</sub>.

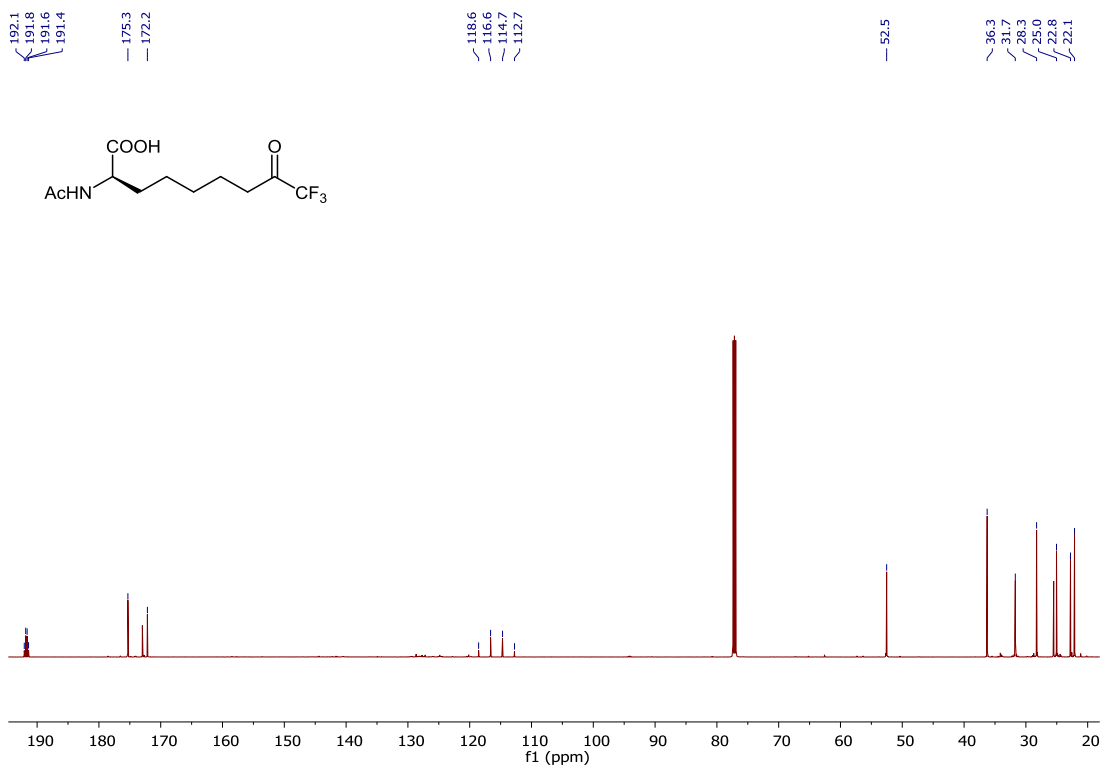


Figure S18  $^{13}\text{C}$  NMR of compound **8**, recorded in  $\text{CDCl}_3$ .

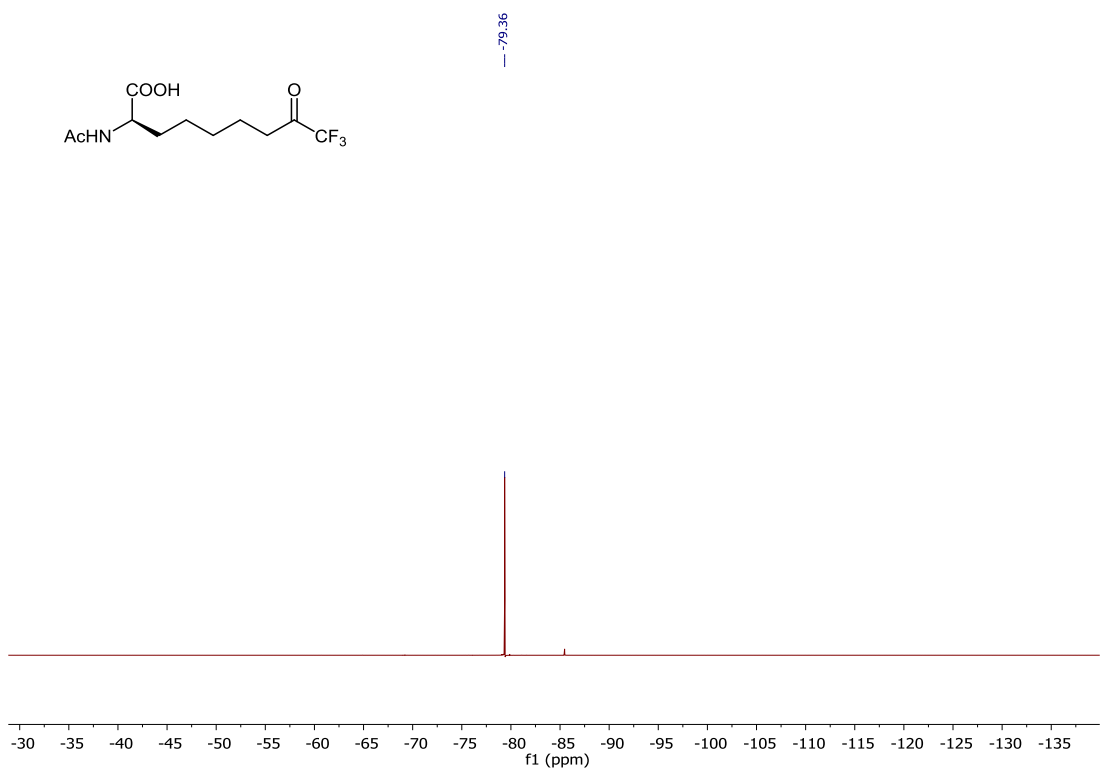


Figure S19  $^{19}\text{F}$  NMR of compound **6**, recorded in  $\text{CDCl}_3$ .

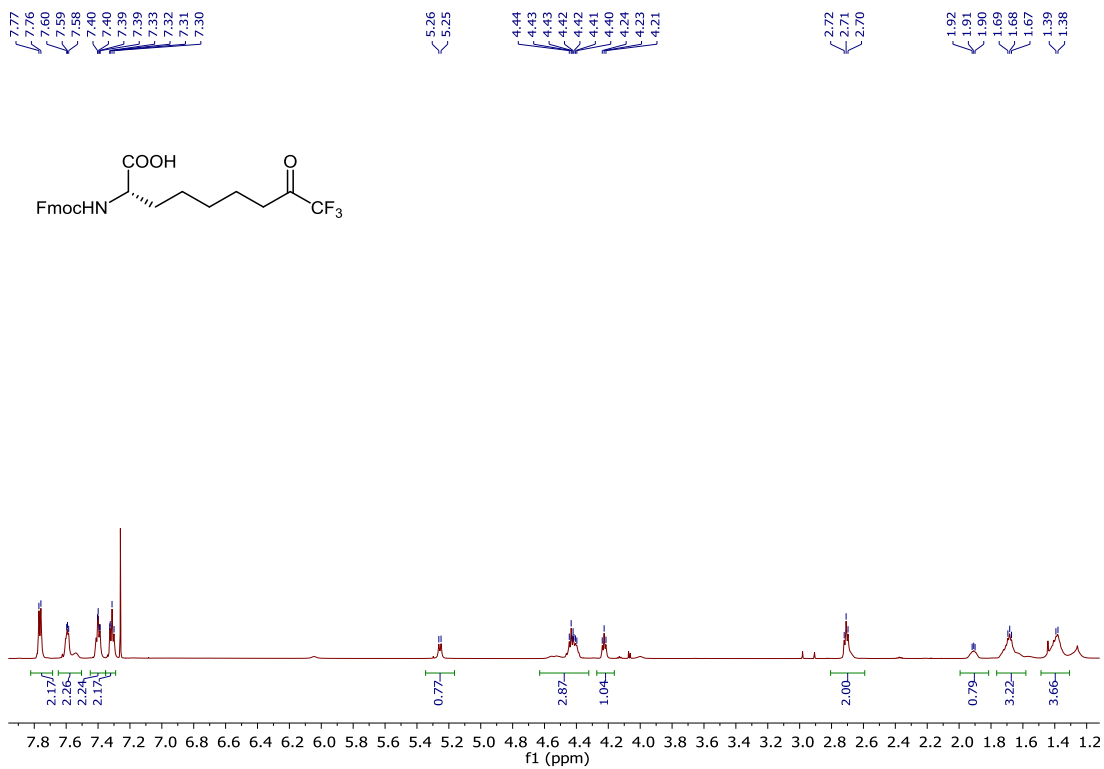


Figure S20 <sup>1</sup>H NMR of compound **9a**, recorded in CDCl<sub>3</sub>.

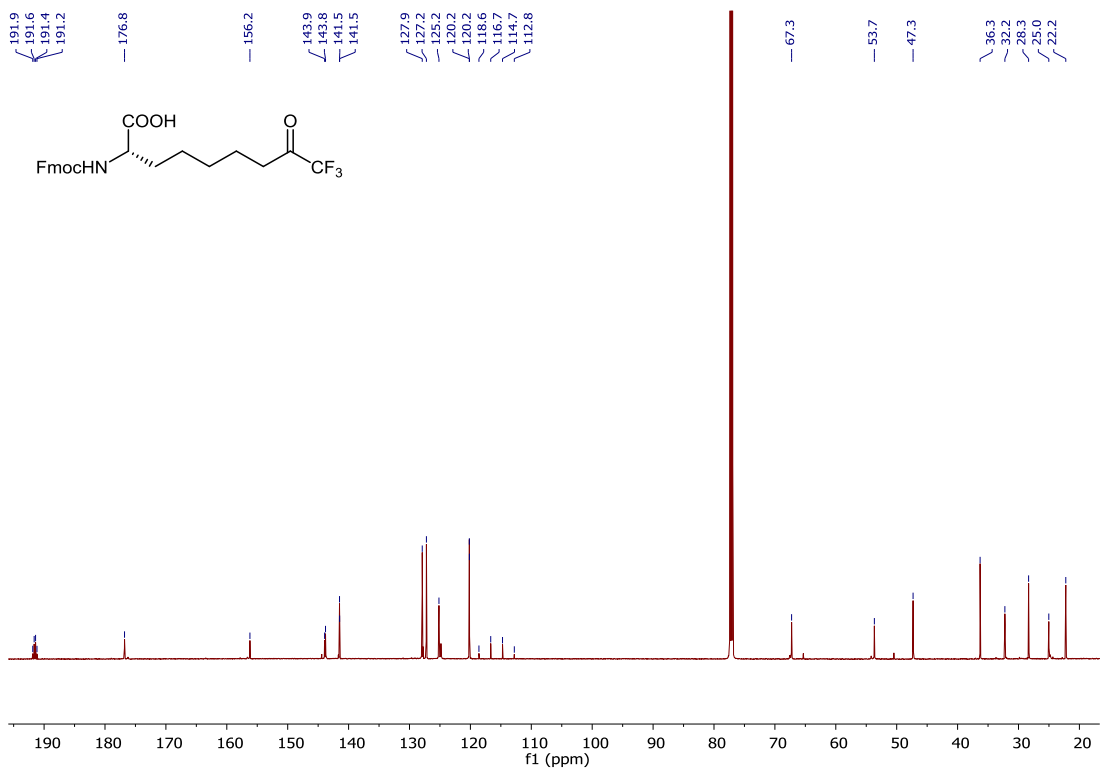


Figure S21 <sup>13</sup>C NMR of compound **9a**, recorded in CDCl<sub>3</sub>.

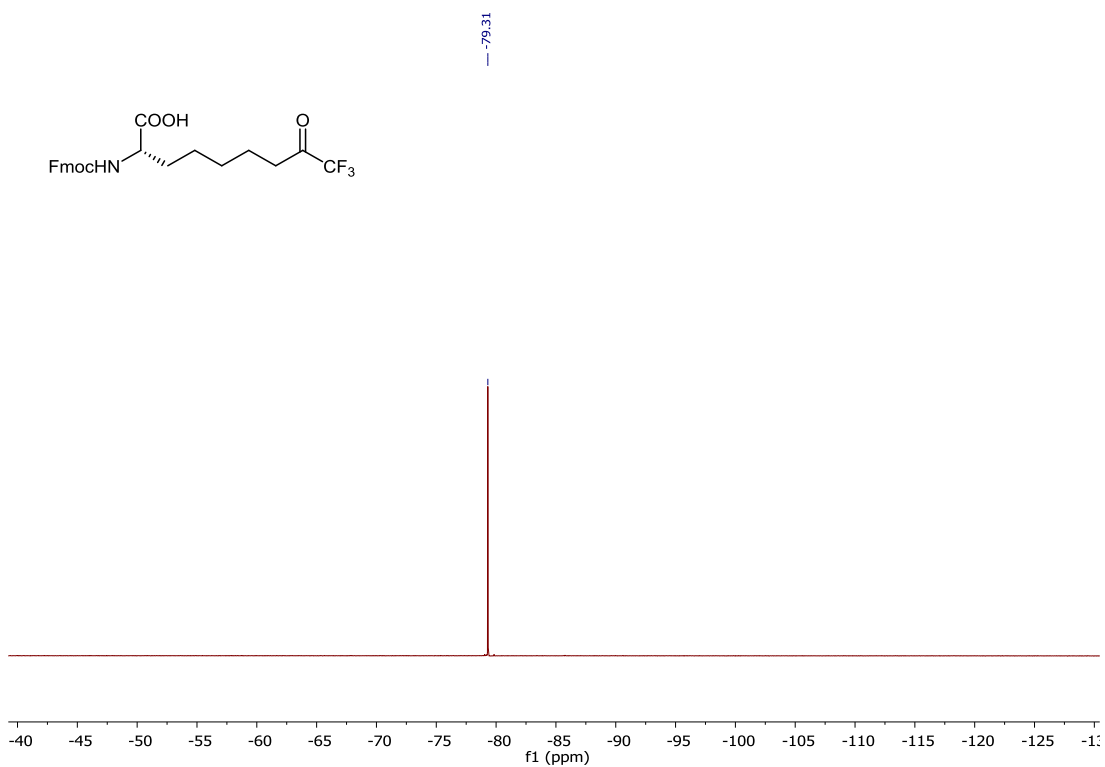


Figure S22  $^{19}\text{F}$  NMR of compound **9a**, recorded in  $\text{CDCl}_3$ .

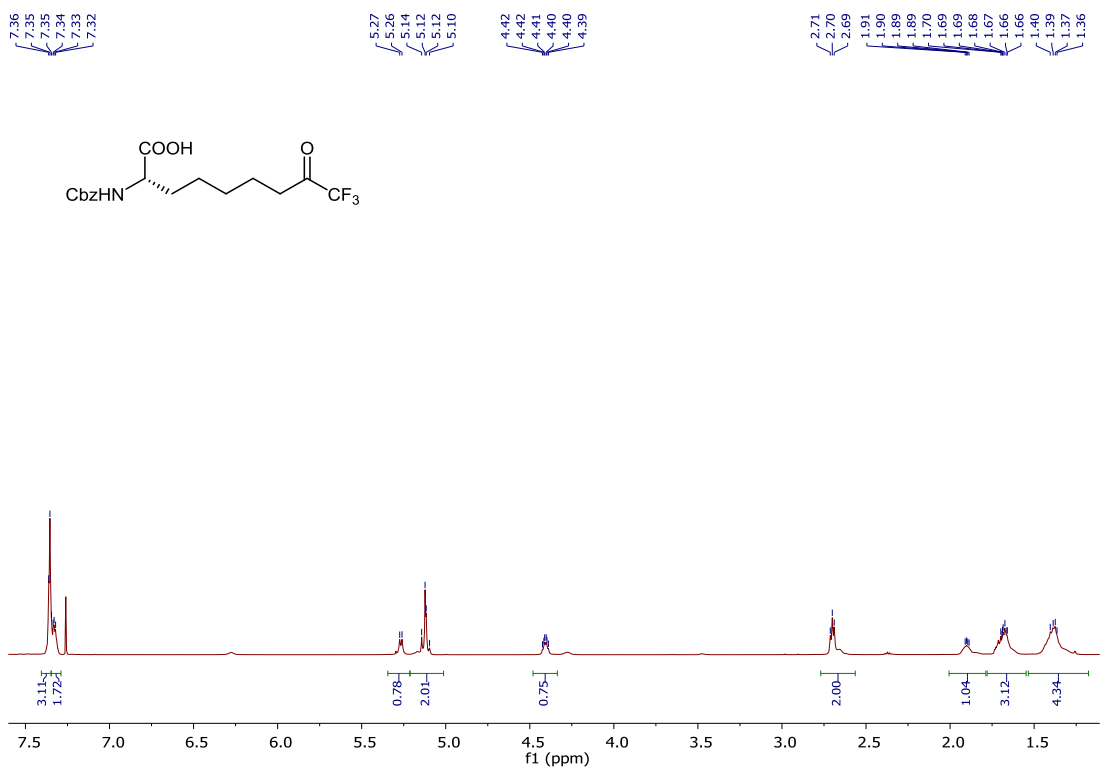


Figure S23  $^1\text{H}$  NMR of compound **9b**, recorded in  $\text{CDCl}_3$ .

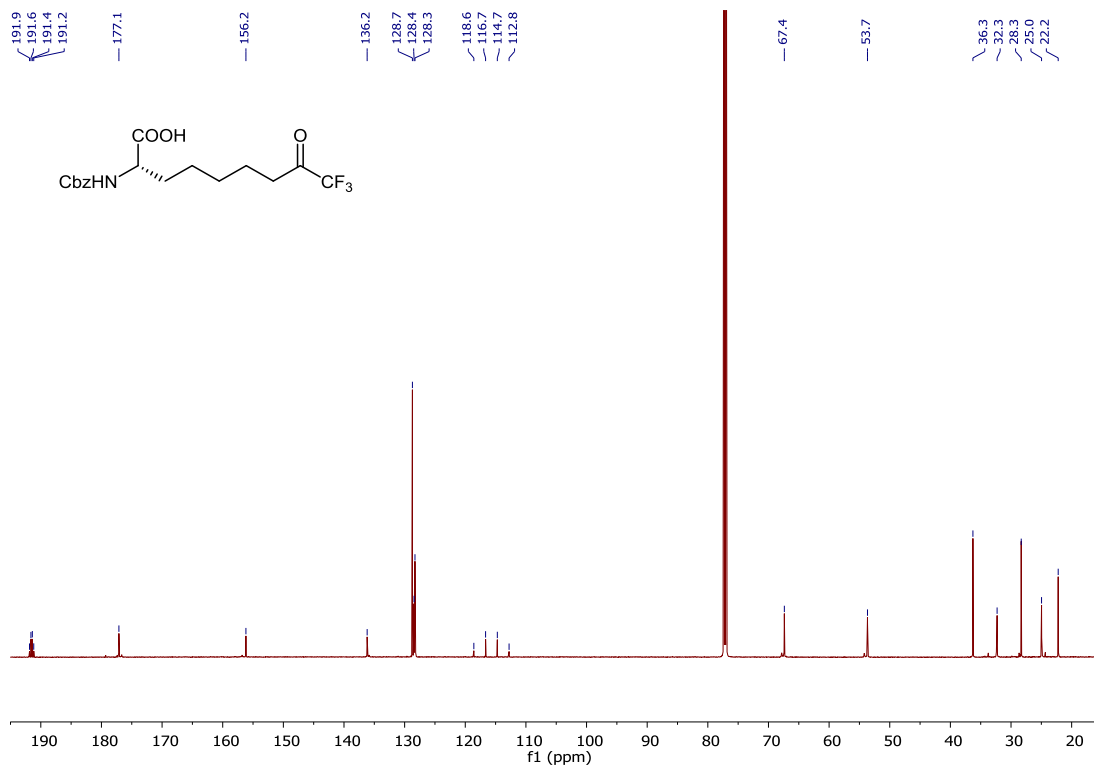


Figure S24 <sup>13</sup>C NMR of compound **9b**, recorded in CDCl<sub>3</sub>.

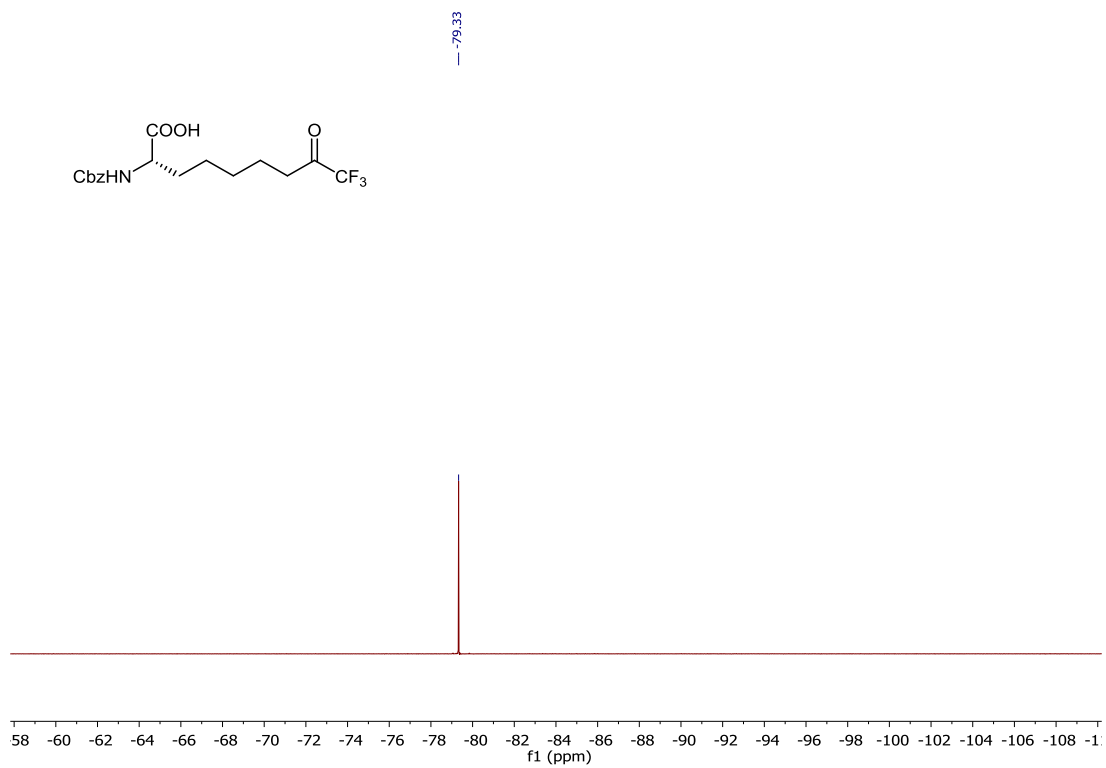


Figure S25 <sup>19</sup>F NMR of compound **9b**, recorded in CDCl<sub>3</sub>.

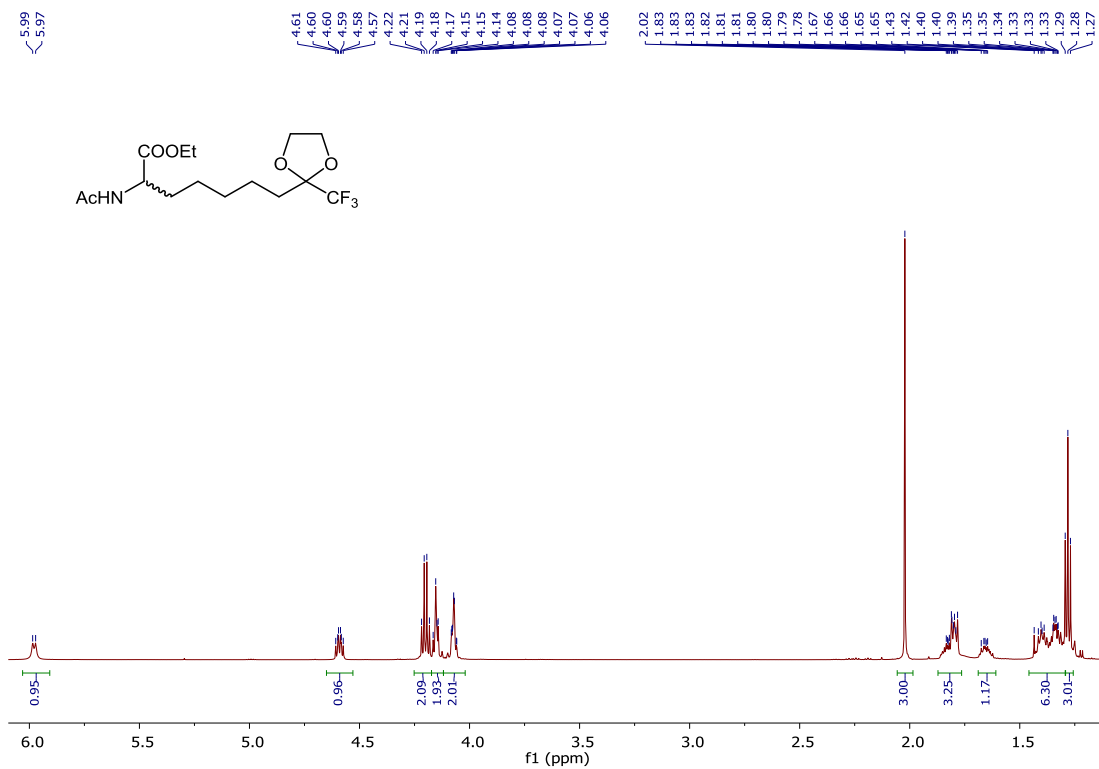


Figure S26 <sup>1</sup>H NMR of compound 10a, recorded in CDCl<sub>3</sub>.

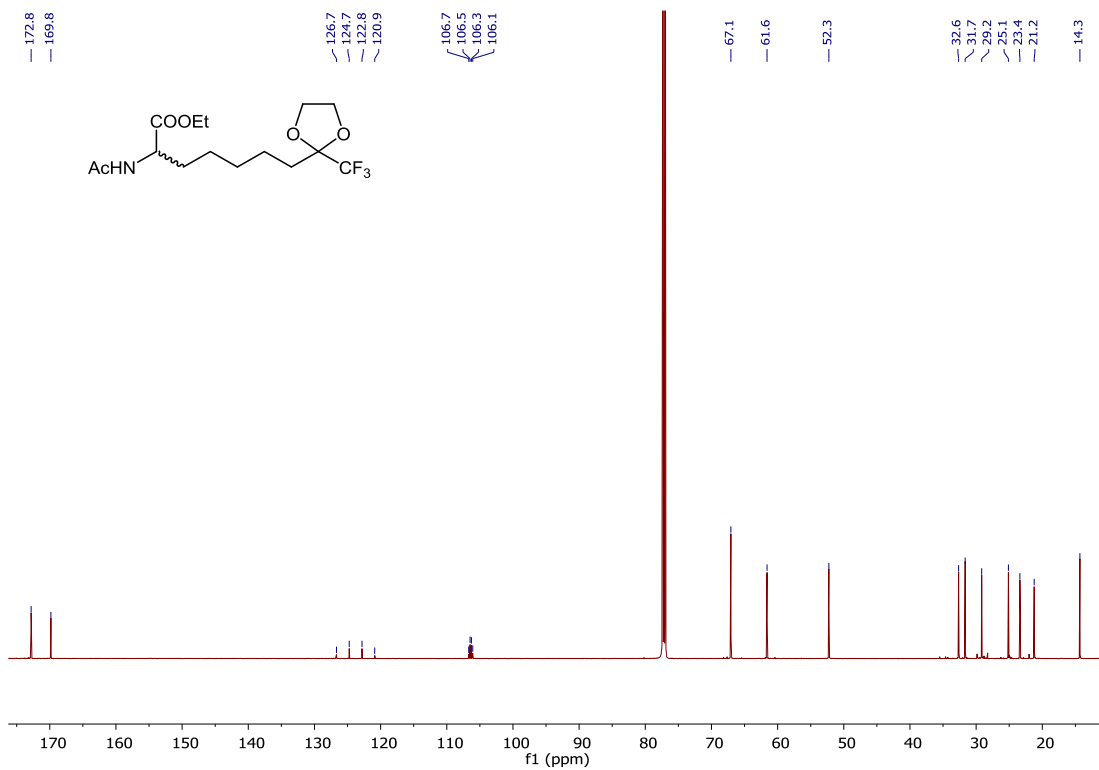


Figure S27 <sup>13</sup>C NMR of compound 10a, recorded in CDCl<sub>3</sub>.

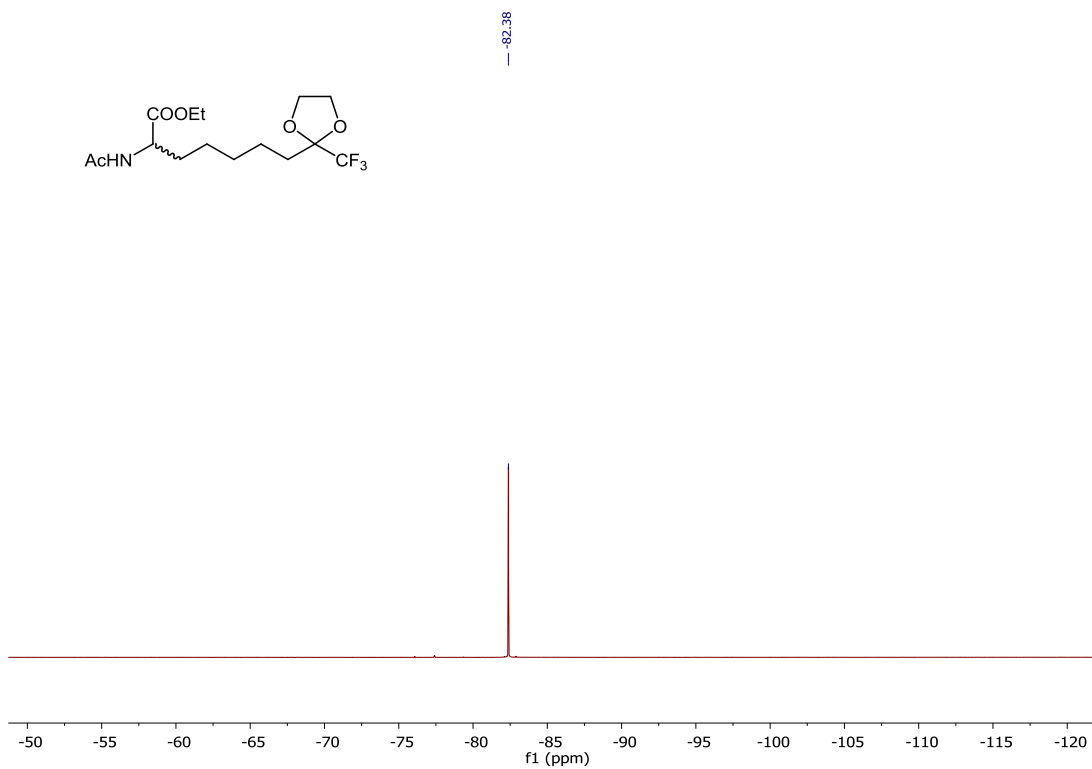


Figure S28 <sup>19</sup>F NMR of compound 10a, recorded in CDCl<sub>3</sub>.

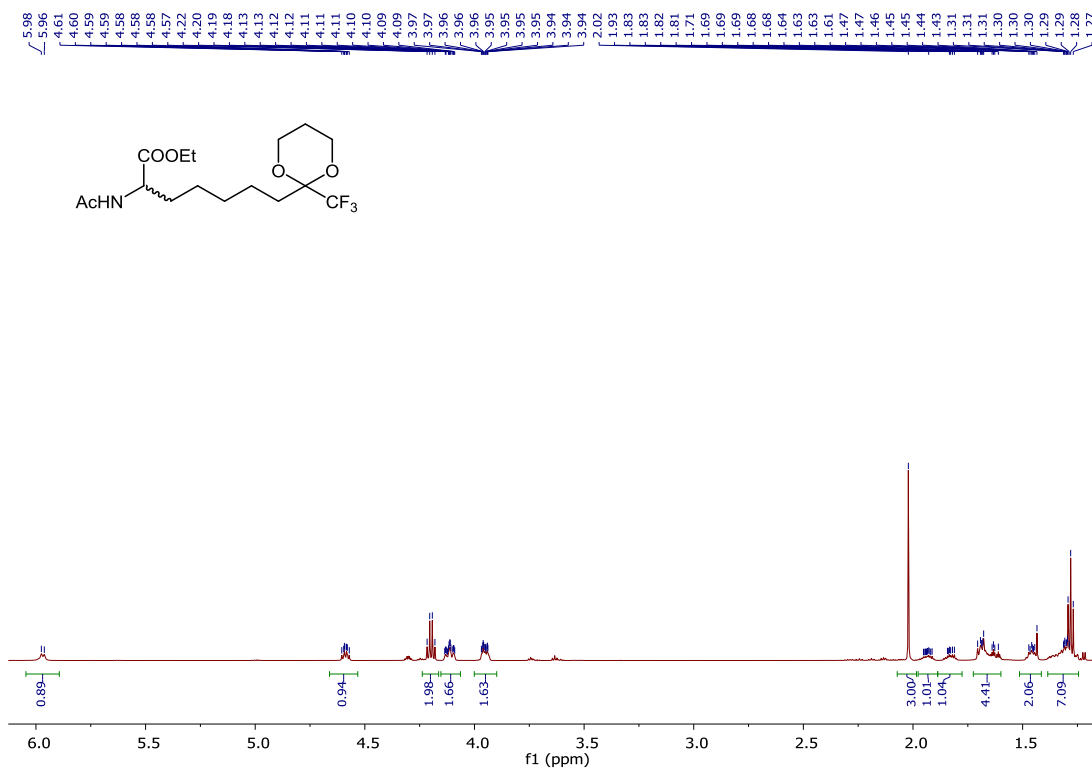


Figure S29 <sup>1</sup>H NMR of compound 10b, recorded in CDCl<sub>3</sub>.

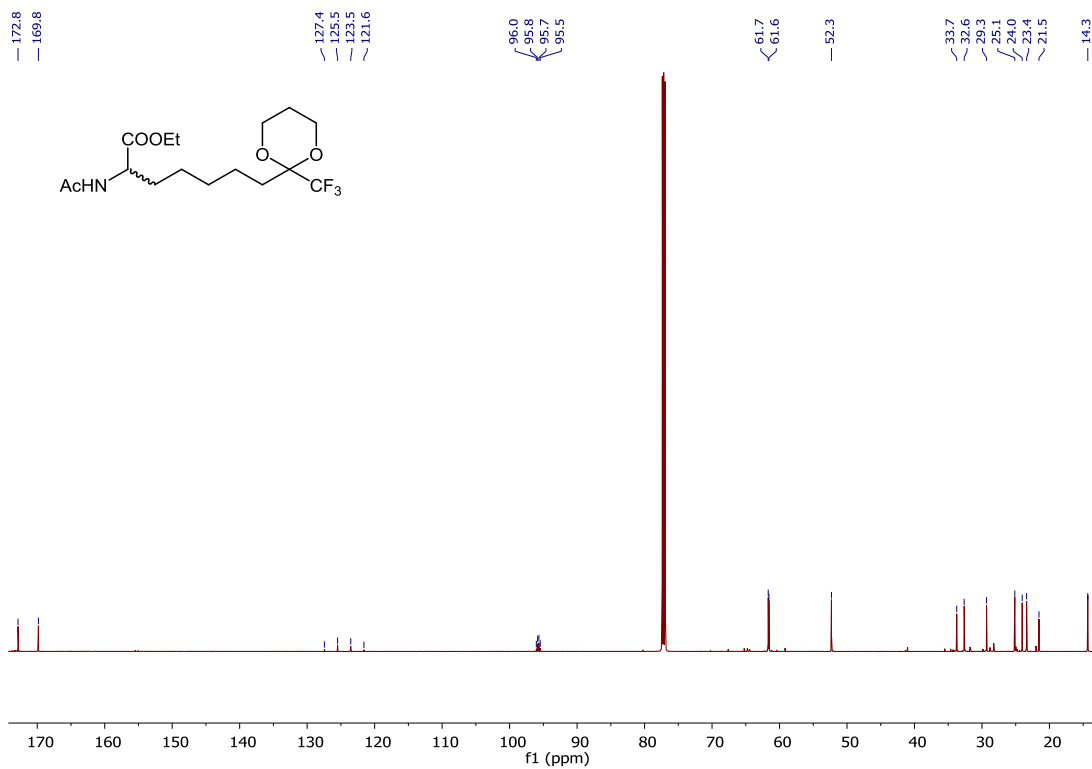


Figure S30  $^{13}\text{C}$  NMR of compound **10b**, recorded in  $\text{CDCl}_3$ .

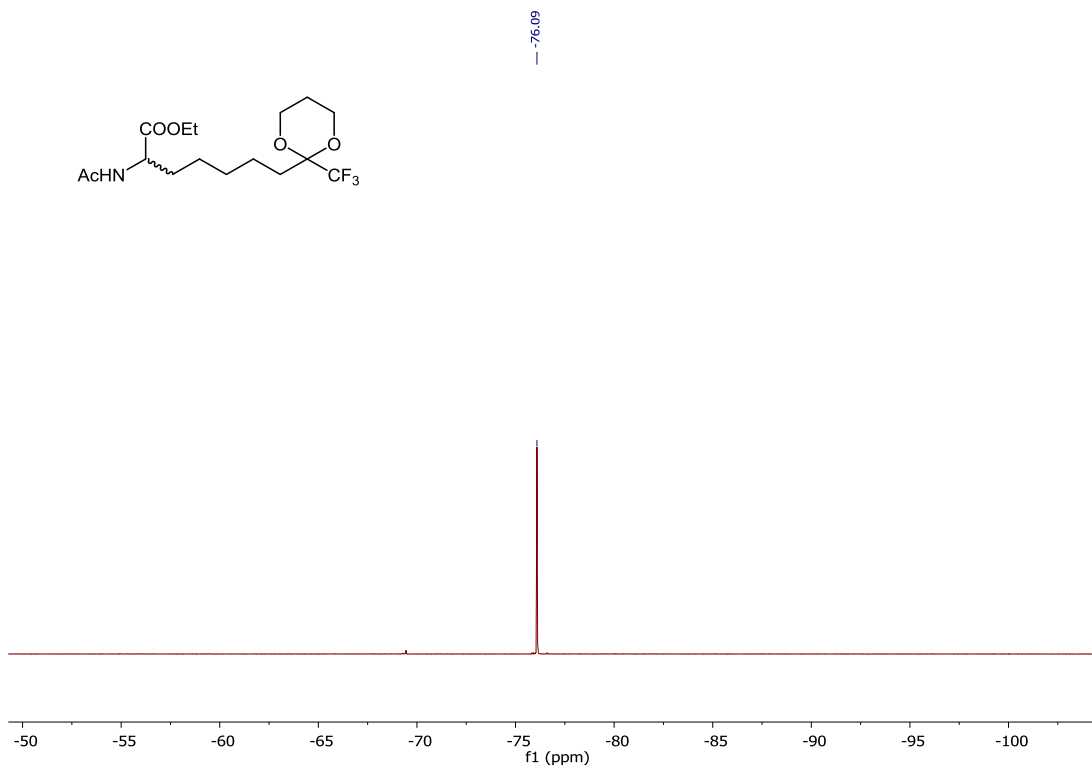


Figure S31  $^{19}\text{F}$  NMR of compound **10b**, recorded in  $\text{CDCl}_3$ .

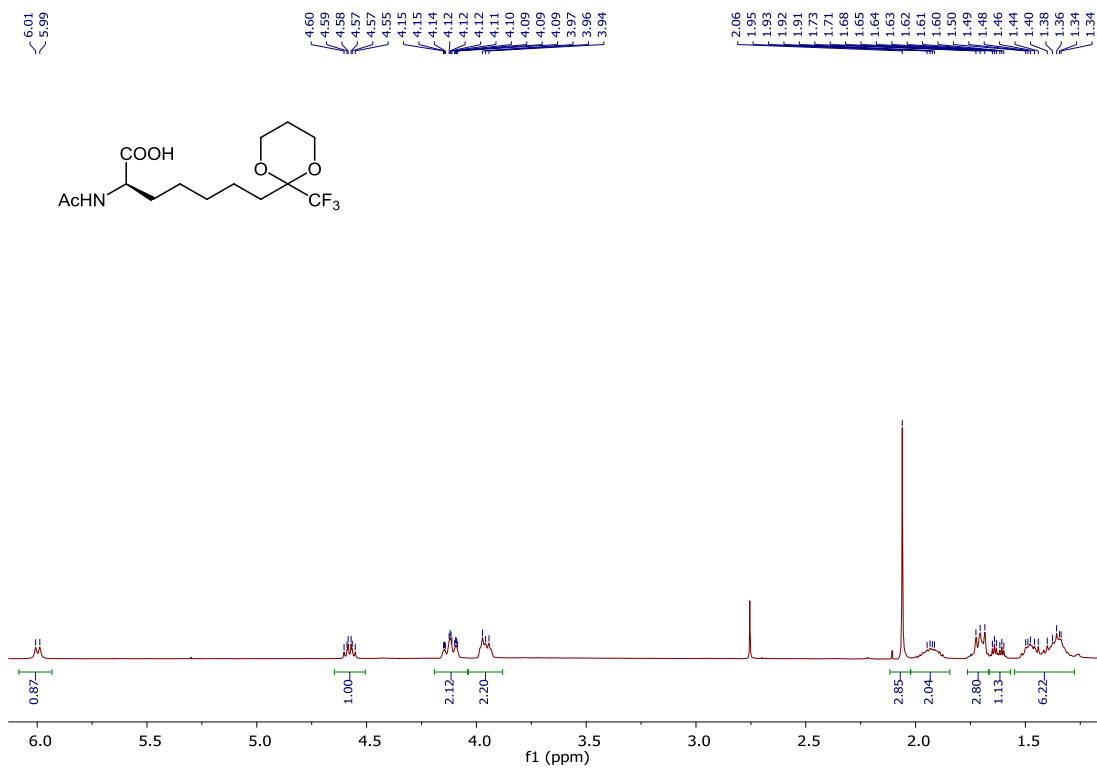


Figure S32 <sup>1</sup>H NMR of compound **11**, recorded in CDCl<sub>3</sub>.

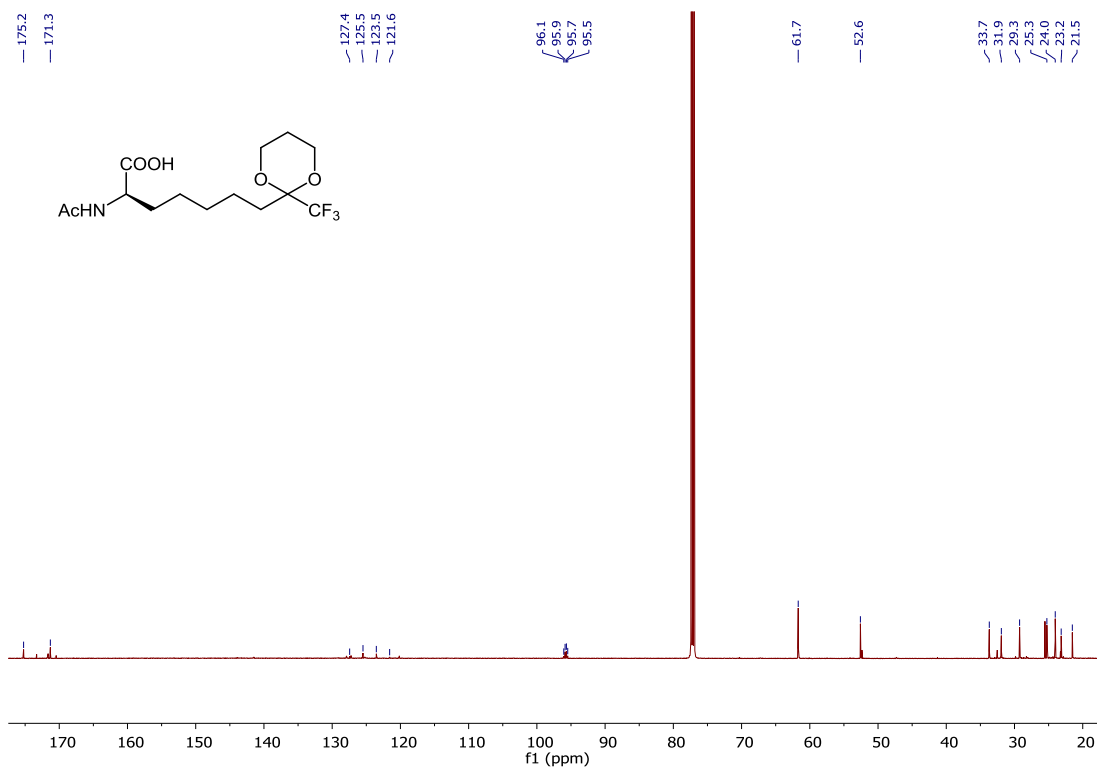


Figure S33 <sup>13</sup>C NMR of compound **11**, recorded in CDCl<sub>3</sub>.

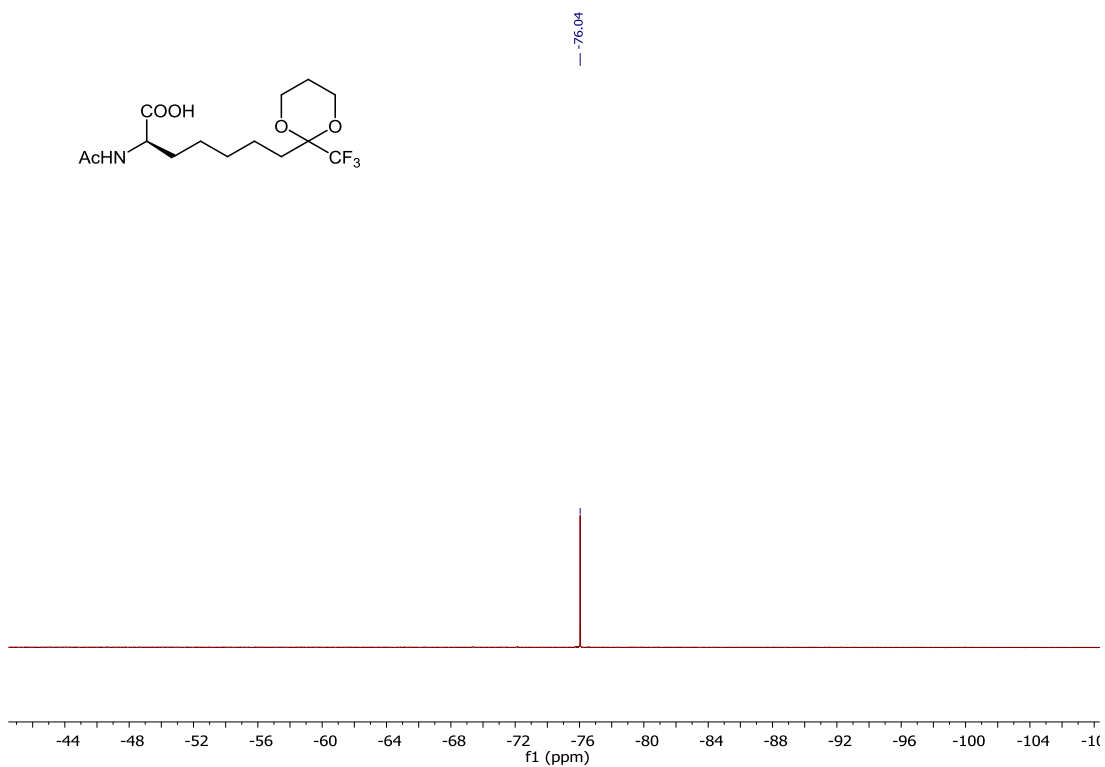


Figure S34  $^{19}\text{F}$  NMR of compound **11**, recorded in  $\text{CDCl}_3$ .

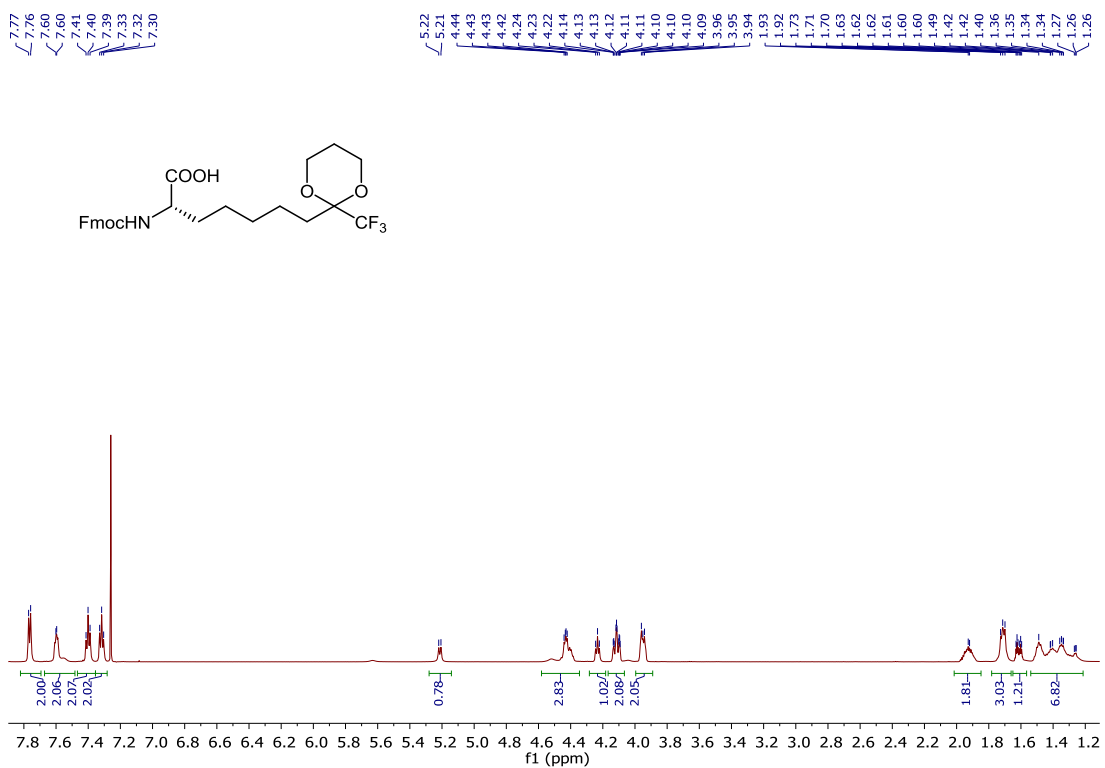


Figure S35  $^{13}\text{C}$  NMR of compound **12**, recorded in  $\text{CDCl}_3$ .

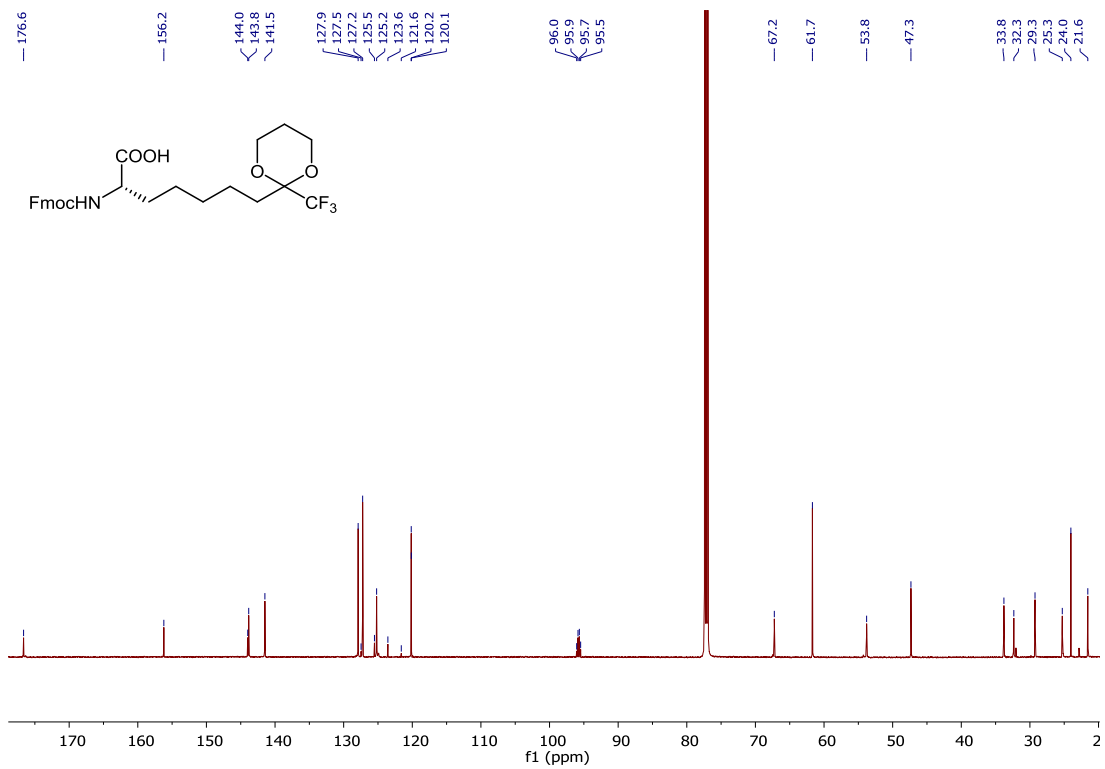


Figure S36 <sup>13</sup>C NMR of compound **12**, recorded in CDCl<sub>3</sub>.

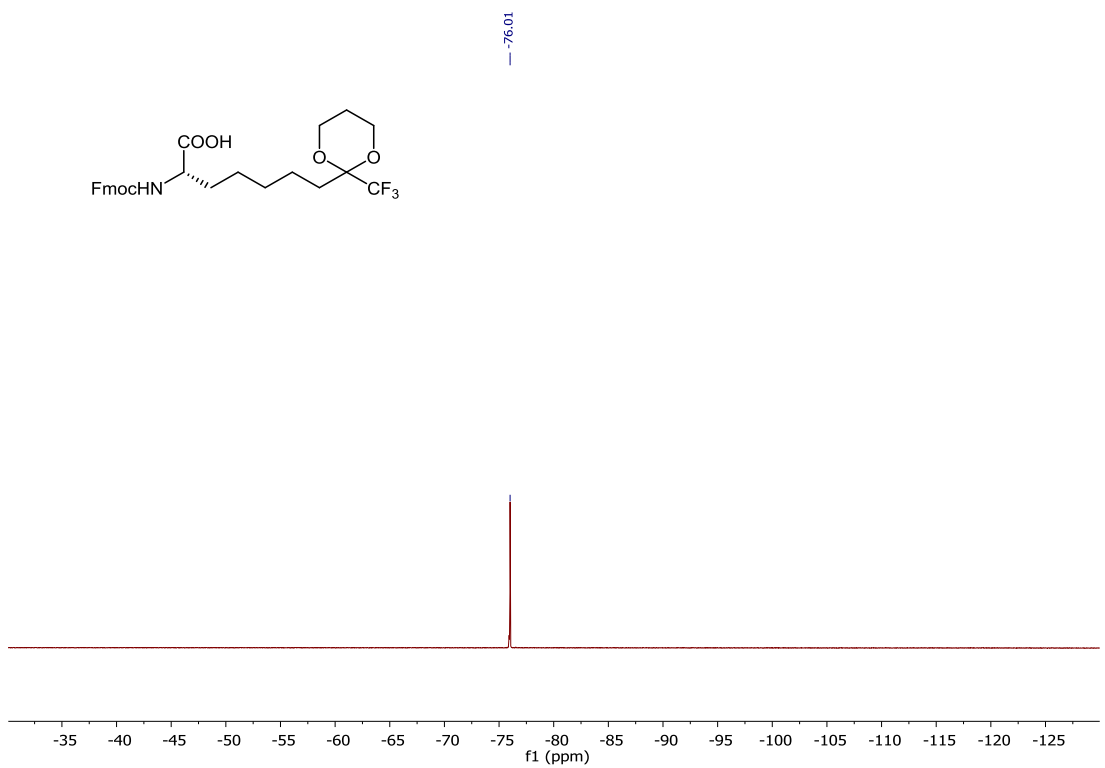


Figure S37 <sup>19</sup>F NMR of compound **12**, recorded in CDCl<sub>3</sub>.