Supporting Information for

Catalyst-free Decarboxylative Cross-Coupling of N-hydroxyphthalimide Esters with *tert*-Butyl 2-(trifluoromethyl)acrylate and Its Application

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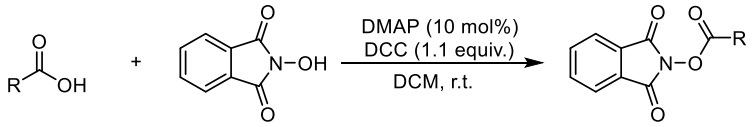
1. General information.

^{1}H NMR and ^{13}C NMR spectra were recorded on an Agilent MR400 spectrometer. ^{19}F NMR was recorded on an Agilent MR400 spectrometer. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. NMR yield was determined by ^{19}F NMR using fluorobenzene as an internal standard before working up the reaction.

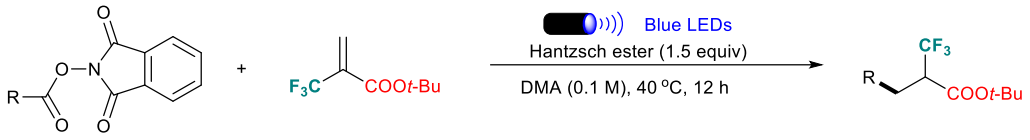
All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature. Anhydrous solvents (DMA, THF, DMSO, MeCN and EA) were purchase from Energy Chemical. Starting compound **2** was purchase from Leyan. These reagents were used without purification. All reagents were weighed and handled in air at room temperature. LEDs (430-490 nm) were bought online (Peak Wavelength: 455.0 nm).

2. Procedure for the synthesis of redox-active ester.



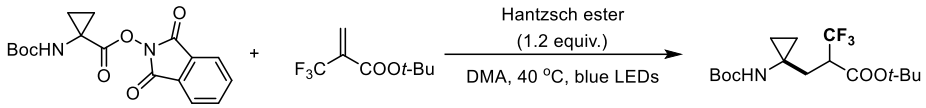
Redox-active ester were prepared according to previous reported procedures[1]. The corresponding alkyl carboxylic acids or N-protected amino acids (2 mmol, 1.0 equiv.), N-hydroxyphthalimide (2 mmol, 1.0 equiv.), and 4-dimethylaminopyridine (0.2 mmol, 10 mol%) were mixed in a flask equipped with a magnetic stirring bar, and DCM (5 mL) was added. Then, a solution of N, N'-dicyclohexylcarbodiimide (454 mg, 2.2 mmol, 1.1 equiv.) in DCM (5 mL) was added slowly at room temperature. After complete conversion of N-hydroxyphthalimide traced by TLC, the white precipitate was filtered off and the solution was concentrated on a rotary evaporator. The residue was purified by silica gel chromatography to give corresponding redox active esters.

3. General procedure for the Cross-Coupling of N-hydroxyphthalimide Esters with *tert*-butyl 2-(trifluoromethyl)acrylate.



A 25 mL oven-dried Schlenk tube equipped with a magnetic stirrer bar was charged with the redox active esters (0.2 mmol, 1.0 equiv.), Hantzsch ester (0.3 mmol, 1.5 equiv.). The tube was evacuated and backfilled with argon for three times, followed by the addition of dry DMA (2.0 mL) and *tert*-Butyl 2-(trifluoromethyl)acrylate (0.3 mmol, 1.5 equiv.). The tube was screw capped and stirred under irradiation of 24 W blue LEDs (40 °C). After stirring for 12 h, the mixtures were diluted with EA (50 mL), washed with brine (30 mL×3) and dried with Na_2SO_4. The organic layer was concentrated and the product was purified with silica gel chromatography to give corresponding pure product.

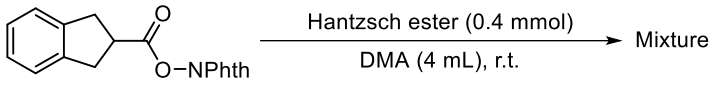
Detailed procedure for the gram scale synthesis of 5o.



A 100 mL oven-dried Schlenk tube equipped with a magnetic stirrer bar was charged with the redox active esters (4.0 mmol, 1.0 equiv.), Hantzsch ester (4.8 mmol, 1.2 equiv.). The tube was evacuated and backfilled with argon for three times, followed by the addition of dry DMA (40.0 mL) and *tert*-butyl 2-(trifluoromethyl)acrylate (6.0 mmol, 1.5 equiv.). The tube was screw capped and stirred under irradiation of 24W blue LEDs (40°C). After stirring for 12 h, the mixtures were diluted with EA (250 mL), washed with brine (50 mL×4) and dried with Na_2SO_4. The organic layer was concentrated and the product was purified with silica gel chromatography (PE:EA=10:1, PE:DCM=1:1) to give corresponding pure product (1324 mg, 93% yield).

4. Mechanism studies.

4.1. UV-vis experiments.



1a

Solution 1: **1a** (112.9 mg, 0.4 mmol) was added in DMA (4 mL). The mixture was stirred for 20 minutes under natural light conditions and then filtered.

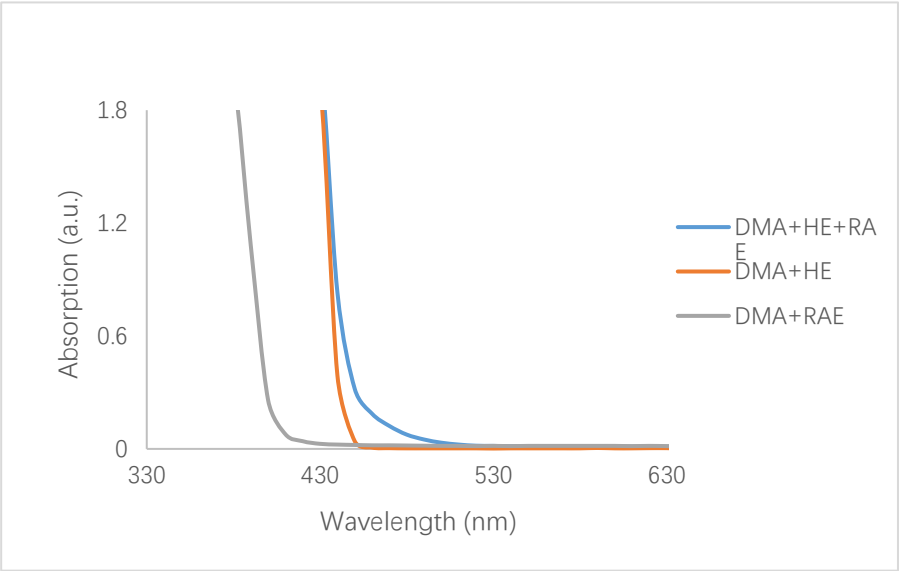
Solution 2: **HE** (101.3 mg, 0.4 mmol) was added in DMA (4 mL). The mixture was stirred for 20 minutes under natural light conditions and then filtered.

Solution 3: **1a** (112.9 mg, 0.4 mmol) and **HE** (101.3 mg, 0.4 mmol) were added in DMA (4 mL). The mixture was stirred for 20 minutes under natural light conditions and then filtered.

Performed on UV visible spectrophotometer, recorded in 1 cm path quartz cuvettes using T6 Xinyue visible spectrophotometer (PERSEE^{TM}).

Wavelength (nm)	1a+DMA	HE+DMA	1a+HE+DMA
330	2.554	2.529	2.527
340	2.748	2.744	2.734
350	2.822	2.784	2.825
360	2.909	2.913	2.896
370	2.038	2.572	2.652
380	1.977	2.674	2.738
390	1.083	2.698	2.765
400	0.26	2.124	2.17
410	0.078	2.01	2.153
420	0.041	2.021	2.18
430	0.027	1.939	2.085
440	0.023	0.391	0.832
450	0.021	0.041	0.319
460	0.019	0.007	0.187
470	0.019	0.004	0.122
480	0.018	0.003	0.076
490	0.017	0.003	0.05
500	0.016	0.003	0.033
510	0.016	0.003	0.023
520	0.015	0.003	0.017
530	0.016	0.002	0.016

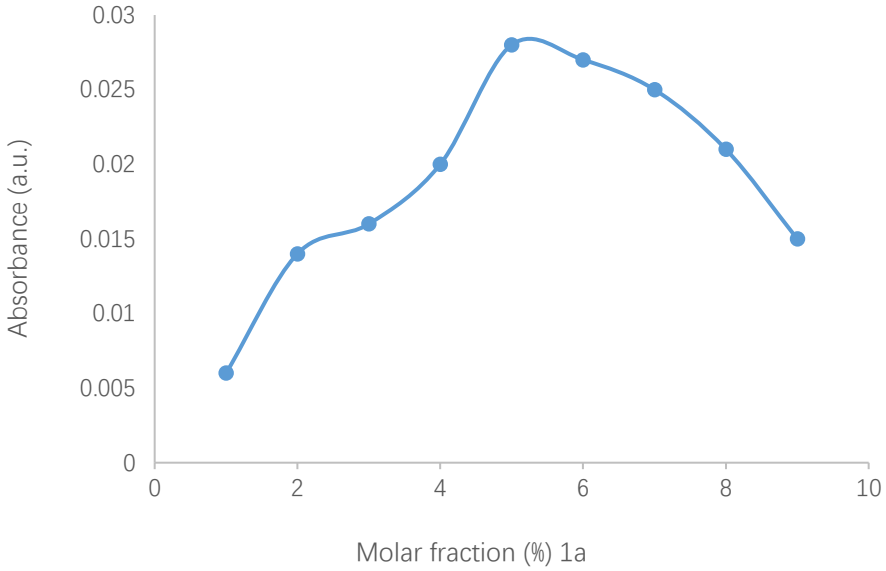
540	0.015	0.003	0.014
550	0.016	0.003	0.014
560	0.016	0.003	0.013
570	0.016	0.003	0.013
580	0.016	0.003	0.012
590	0.016	0.005	0.013
600	0.016	0.003	0.012
610	0.015	0.003	0.012
620	0.016	0.004	0.012
630	0.015	0.004	0.012
640	0.014	0.002	0.012
650	0.014	0.003	0.012



Optical absorption spectra studies.

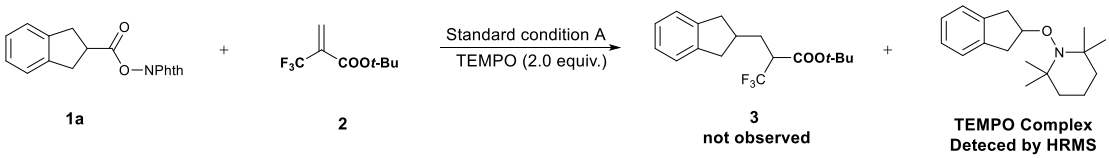
4.2. Stoichiometry of the EDA Complex in Solution.

The Job's plot was constructed to evaluate the stoichiometry of EDA complex between 1a and HE. The absorption of DMA solution at 470 nm with different donor/acceptor ratios with constant concentration (0.05 mol/L) of the two components was tested. All the absorption spectra were recorded in 1 cm path quartz cuvettes using T6 Xinyue visible spectrophotometer (PERSEE^{TM}), which was obtained from Beijing Purkinje General Instrument Co, Ltd. The absorbance values were plotted against the molar fraction (%) of 1a using DMA as blank sample. The maximal absorbance at 50% molar fraction of 1a indicated the 1:1 stoichiometry of the EDA complex in solution.



Job's plots of the EDA complex between 1a and HE.

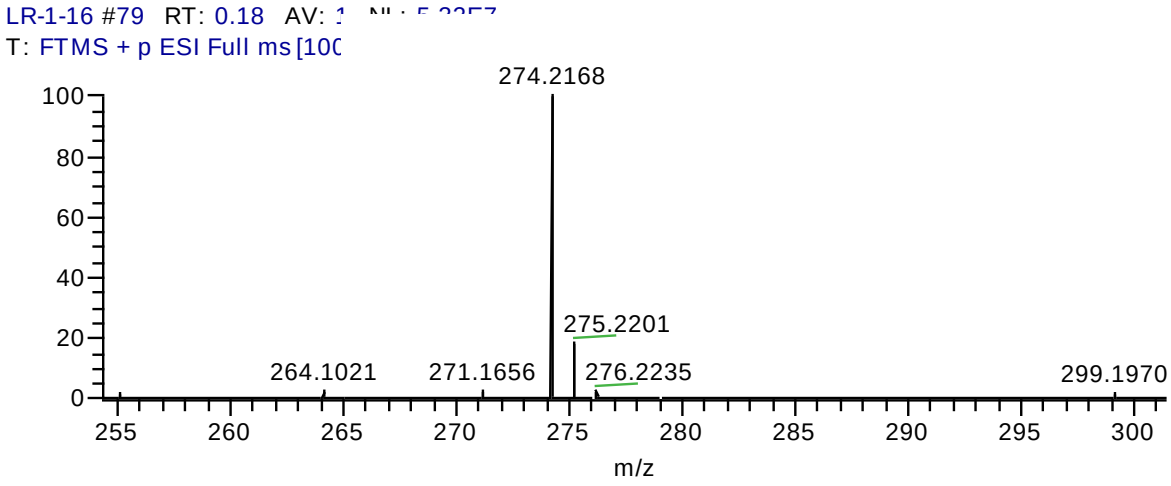
4.3 Addition of radical and SET inhibitors.



Procedure: A 25 mL oven-dried Schlenk tube equipped with a magnetic stirrer bar was charged with the redox active esters (0.2 mmol, 1.0 equiv.), Hantzsch ester (0.3 mmol, 1.5 equiv.) and TEMPO (0.2 mmol, 1.0 equiv.). The tube was evacuated and backfilled with argon three times, followed by the addition of dry DMA (2 mL) and *tert*-butyl 2-(trifluoromethyl)acrylate (0.3 mmol, 1.5 equiv.). The tube was screw capped and heated to 40°C-45°C under irradiation of 24W blue LEDs. After stirring for 12 h, the reaction mixture was cooled to room temperature, monitored by TLC, the reaction solution was diluted with ethyl acetate, and pretreatment and sent to HRMS. The reaction was totally suppressed by the addition of a radical scavenger TEMPO, which suggests that the involvement of radical intermediates is likely during the reaction.

High resolution ESI-MS and MS/MS experiments for detecting TEMPO complex

High resolution ESI-MS and MS/MS spectra were recorded on a Q Exactive HF Orbitrap mass spectrometer (Thermo Fisher Scientific Inc.) equipped with ESI ion source. The ESI conditions were: spray voltage 3500 V; capillary temperature, 275°C; sheath gas flow rate 35 arb. units. Data acquisition and analysis were done with the Thermo Xcalibur (version 4.2.47) software package. The elemental composition analysis of the ion at *m/z* 274.2168 by HRMS supported the proposed structure of TEMPO complex.



High resolution ESI-MS spectrum of TEMPO complex calculated for $C_{18}H_{28}ON$ ($[M+H]^+$): 274.2165; Found: 274.2168.

Elemental composition search on mass 274.2168

m/z= 269.2168-279.2168

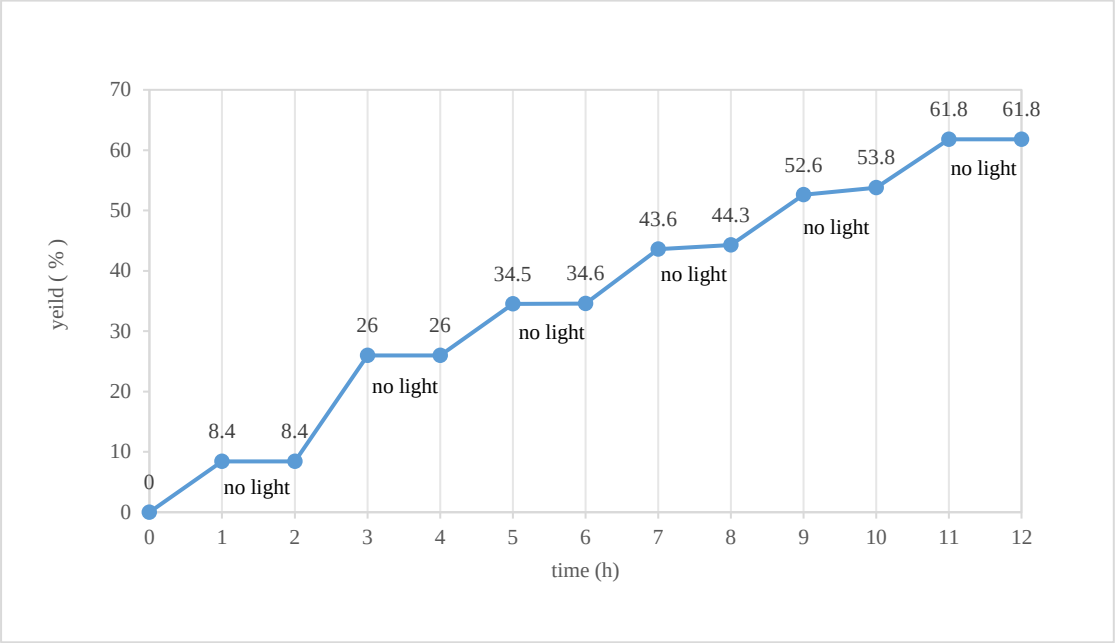
m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
274.2168	274.2165	0.94	5.5	$C_{18}H_{28}ON$

Elemental composition analysis of the ion at *m/z* 274.

4.4 On / off lamp experiments.

Procedure: Twelve 25 mL oven-dried Schlenk tube equipped mixtures according to the standard reaction conditions. After 1 h, one tube was removed from the irradiation setup for analysis. The remaining eleven tubes were stirred in the absence of light for an additional 1 h. Then, one tube was removed for analysis,

and the lamps were turned back on to irradiate the remaining ten reaction mixtures. After an additional 1 h of irradiation, the lamps were turned off, and one tube was removed for analysis. The remaining nine tubes were stirred in the absence of light for an additional 1 h. Then, a tube was removed for analysis, and the lamps were turned back on to irradiate the remaining eight reaction mixtures. After an additional 1 h of irradiation, the lamps were turned off, and one tube was removed for analysis. The remaining seven tubes were stirred in the absence of light for an additional 1 h. Then, a tube was removed for analysis, and the lamps were turned back on to irradiate the remaining six reaction mixtures. After an additional 1 h of irradiation, the lamps were turned off, and one tube was removed for analysis. The remaining five tubes were stirred in the absence of light for an additional 1 h. Then, a tube was removed for analysis, and the lamps were turned back on to irradiate the remaining four reaction mixtures. After an additional 1 h of irradiation, the lamps were turned off, and one tube was removed for analysis. The remaining three tubes were stirred in the absence of light for an additional 1 h. Then, a tube was removed for analysis, and the lamps were turned back on to irradiate the remaining two reaction mixtures. After an additional 1 h of irradiation, the lamps were turned off, and one tube was removed for analysis. The remaining one tube was stirred in the absence light for an additional 1 h. Then it was analyzed. The reaction mixtures were analyzed by ^{19}F NMR with an internal standard.



On / off lamp experiments.

5. Reference.

[1] (*a*) K. Okada, K. Okamoto, M. Oda, *J. Am. Chem. Soc*. 1988, **110**, 8736–8738. (*b*) K. Okada, K. Okamoto, N. Morita, K. Okubo, M. Oda, *J. Am. Chem. Soc*. 1991, **113**, 9401–9402. (*c*) T. Qin, J. Cornella, C. Li, L. R. Malins, J. T. Edwards, S. Kawamura, B. D. Maxwell, M. D. Eastgate, P. S. Baran, *Science*. 2016, **352**, 801-805.

6. Data for compounds.

***tert*-Butyl 2-((2,3-dihydro-1*H*-inden-2-yl)methyl)-3,3,3-trifluoropropanoate (3a).**

The product (59.1 mg, 94% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a white solid. MP 81.9-85.6℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.19 (m, 2H), 7.17 – 7.15 (m, 2H), 3.14 – 3.07 (m, 3H), 2.68 – 2.59 (m, 2H), 2.55 – 2.45 (m, 1H), 2.23 – 2.15 (m, 1H), 1.92 – 1.85 (m, 1H), 1.50 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7 (q, J = 3.0 Hz), 142.7, 142.4, 126.42, 126.38, 124.48, 124.40, 124.9 (q, J = 281.2 Hz), 82.8, 50.6 (q, J = 27.2 Hz), 39.4, 38.5,

37.6, 33.8 (q, J = 1.5 Hz), 27.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.59 (d, J = 8.6 Hz, 3F). HRMS (ESI): Calculated for $C_{17}H_{21}F_3O_2$ ([M-H-C_4H_8]$^-$): 257.0795; Found: 257.0794.

***tert*-Butyl 2-(cycloheptylmethyl)-3,3,3-trifluoropropanoate (3b).** The product (55.9 mg, 95% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 – 3.01 (m, 1H), 1.86 – 1.79 (m, 1H), 1.77 – 1.73 (m, 1H), 1.72 – 1.70 (m, 1H), 1.69 – 1.67 (m, 1H), 1.65 (s, 2H), 1.62 – 1.59 (m, 1H), 1.56 (t, J = 3.6 Hz, 1H), 1.53 (d, J = 3.6 Hz, 1H), 1.51 – 1.50 (m, 2H), 1.47 (s, 9H), 1.44 – 1.38 (m, 2H), 1.27 – 1.10 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0 (q, J = 3.3 Hz), 125.1 (q, J = 281.2 Hz), 82.4, 49.4 (q, J = 26.9 Hz), 36.4, 35.2, 33.9 (q, J = 2.0 Hz), 32.9, 28.4, 28.2, 27.8, 26.2, 26.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.70 (d, J = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{15}H_{25}F_3O_2$ ([M-H-C_4H_8]$^-$): 237.1108; Found: 237.1109.

***tert*-butyl 2-(((3*r*,5*r*,7*r*)-adamantan-1-yl)methyl)-3,3,3-trifluoropropanoate(3c).** The product (61.8 mg, 93% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid.^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 – 3.02 (m, 1H), 1.96 (s, 3H), 1.85 (dd, J = 14.4 Hz, 1H), 1.71 (s, 1H), 1.68 (s, 2H), 1.63 (s, 2H), 1.59 (s, 2H), 1.49 (s, 2H), 1.47 (s, 9H), 1.44 (s, 2H), 1.40 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0 (q, J = 3.4 Hz), 125.0 (q, J = 281.5 Hz), 82.4, 46.3 (q, J = 26.8 Hz), 41.8, 39.5,36.7 31.9, 28.4, 27.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.98

(d, J = 9.0 Hz, 3F). HRMS (ESI): Calculated for $C_{18}H_{27}F_3O_2$ ([M-H-C_4H_8]$^-$): 332.1958; Found: 332.1954.

***tert*-butyl 4-((3*r*,5*r*,7*r*)-adamantan-1-yl)-2-(trifluoromethyl)butanoate(3d)**. The product (65.8 mg, 95% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91 – 2.81 (m, 1H), 1.94 (s, 3H), 1.85 – 1.75 (m, 1H), 1.68 (s, 4H), 1.62 (s, 3H), 1.60 (s, 1H), 1.47 (s, 9H), 1.46 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7 (q, J = 3.43 Hz), 125.0 (q, J = 281.3 Hz), 82.4, 52.0 (q, J = 27.1 Hz), 42.1, 41.1, 37.0, 32.0, 28.5, 27.8, 19.6(q, J = 2.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.42 (d, J = 7.9 Hz, 3F). HRMS (ESI): Calculated for $C_{19}H_{29}F_3O_2$ ([M-H-C_4H_8]$^-$): 346.2114; Found: 346.2118.

***tert*-Butyl 3,3,3-trifluoro-2-((1-(4-methoxyphenyl)cyclopropyl)methyl)propanoate (3e).** The product (59.9 mg, 87% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a white solid. MP 74.8-78.3 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.4 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H), 2.99 – 2.89 (m, 1H), 2.25 (d, J = 13.6 Hz, 1H), 1.85 (dd, J = 14.0, 11.2 Hz, 1H), 1.48 (s, 9H), 0.89 – 0.84 (m, 1H), 0.78 – 0.73 (m, 1H), 0.72 – 0.68 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0 (q, J = 3.1 Hz), 158.3, 134.9, 130.5, 124.9 (q, J = 281.4 Hz), 113.8, 82.4, 55.20 (q, J = 9.8 Hz), 49.7 (q, J = 27.0 Hz), 36.8 (q, J = 1.9 Hz), 27.8, 22.8, 12.9, 12.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.88 (d, J = 8.6 Hz, 3F). HRMS (ESI): Calculated for $C_{18}H_{23}F_3O_3$ ([M-H-C_4H_8]$^-$): 287.0901; Found: 287.0904.

***tert*-Butyl 3,3,3-trifluoro-2-((tetrahydro-2*H*-pyran-4-yl)methyl)propanoate (3f).** The product (42.8 mg, 76% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (td, *J* = 10.8, 4.8 Hz, 2H), 3.38 – 3.30 (m, 2H), 3.13 – 3.03 (m, 1H), 1.93 – 1.86 (m, 1H), 1.66 (d, *J* = 13.6 Hz, 1H), 1.59 (d, *J* = 4.0 Hz, 1H), 1.56 (d, *J* = 3.6 Hz, 1H), 1.47 (s, 9H), 1.38 – 1.29 (m, 1H), 1.27 – 1.20 (m, 1H), 0.85 (q, *J* = 8.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6 (q, *J* = 3.2 Hz), 125.0 (q, *J* = 281.3 Hz), 82.7, 67.7, 67.6, 48.5 (q, *J* = 27.2 Hz), 33.1, 32.8 (q, *J* = 2.0 Hz), 32.6, 32.0, 27.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.65 (d, *J* = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{13}H_{21}F_3O_3$ ($[M\text{-}H\text{-}C_4H_8]^-$): 225.0744; Found: 225.0743.

***tert*-Butyl 4-(2-(*tert*-butoxycarbonyl)-3,3,3-trifluoropropyl)piperidine-1-carboxylate (3g).** The product (74.7 mg, 98% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (t, *J* = 11.6 Hz, 2H), 3.11 – 3.01 (m, 1H), 2.68 – 2.59 (m, 2H), 1.91 – 1.84 (m, 1H), 1.70 (d, *J* = 12.0 Hz, 1H), 1.62 – 1.58 (m, 2H), 1.56 – 1.52 (m, 1H), 1.45 (s, 9H), 1.42 (s, 9H), 1.18 – 1.00 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6 (q, *J* = 3.2 Hz), 154.7, 124.9 (q, *J* = 281.3 Hz), 82.8, 79.4, 48.7 (q, *J* = 27.3 Hz), 43.6, 33.6, 32.5 (q, *J* = 2.0 Hz), 32.2, 31.0, 28.4, 27.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.68 (d, *J* = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{18}H_{30}F_3NO_4$ ($[M+H\text{-}C_4H_8]^+$): 326.1574; Found: 326.1564.

***tert*-Butyl 6-phenyl-2-(trifluoromethyl)hexanoate (3h).** The product (62.0 mg, 98% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 8.8 Hz, 3H), 3.02 – 2.92 (m, 1H), 2.63 (t, *J* = 7.6 Hz, 2H), 1.96 – 1.86 (m, 1H), 1.80 – 1.71 (m, 1H), 1.70 – 1.61 (m, 2H), 1.45 (s, 9H), 1.42 – 1.34 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7 (q, *J* = 3.2 Hz), 142.0, 128.4, 128.3, 125.8, 124.9 (q, *J* = 281.3 Hz), 82.6, 51.2 (q, *J* = 27.2 Hz), 35.5, 30.9, 27.8, 26.2, 26.0 (q, *J* = 2.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.54 (d, *J* = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{17}H_{23}F_3O_2$ ([M-H-C_4H_8]$^-$): 259.0951; Found: 259.0954.

***tert*-Butyl 5-(4-fluorophenyl)-2-(trifluoromethyl)pentanoate (3i).** The product (53.2 mg, 83% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (dd, *J* = 8.0, 5.2 Hz, 2H), 6.96 (t, *J* = 8.8 Hz, 2H), 3.03 – 2.94 (m, 1H), 2.67 – 2.56 (m, 2H), 1.94 – 1.85 (m, 1H), 1.79 – 1.59 (m, 3H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5 (q, *J* = 3.3 Hz), 161.3 (d, *J* = 244.8 Hz), 136.9 (d, *J* = 3.3 Hz), 129.7，129.6，115.3，115.1, 124.8 (q, *J* = 281.2 Hz), 82.7, 51.1 (q, *J* = 27.1 Hz), 34.5, 28.5, 27.8, 25.6 (q, *J* = 2.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.4 (d, *J* = 8.3 Hz, 3F), -117.43 – -117.50 (m, 1F). HRMS (ESI): Calculated for $C_{16}H_{20}F_4O_2$ ([M-H-C_4H_8]$^-$): 263.0701; Found: 263.0699.

***tert*-Butyl 5-(4-chlorophenyl)-2-(trifluoromethyl)pentanoate (3j).** The product (58.9 mg, 87% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 7.6 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 3.03 – 2.93 (m, 1H), 2.67 – 2.55 (m, 2H), 1.94 – 1.84 (m, 1H), 1.79 – 1.59 (m, 3H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5 (q, *J* = 2.7 Hz), 139.7, 131.8, 129.7, 128.5, 124.8 (q, *J* = 281.3 Hz), 82.7, 51.1 (q, *J* = 27.1 Hz), 34.7, 28.3, 27.8, 25.6 (q, *J* = 2.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.40 (d, *J* = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{16}H_{20}ClF_3O_2$ ($[M-H-C_4H_8]^-$): 279.0405; Found: 279.0408.

***tert*-Butyl 5-(4-bromophenyl)-2-(trifluoromethyl)pentanoate (3k).** The product (70.1 mg, 92% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 3.04 – 2.94 (m, 1H),2.66 – 2.54 (m, 2H), 1.94 – 1.85 (m, 1H), 1.79 – 1.75 (m, 1H), 1.72 – 1.61 (m, 2H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5 (q, *J* = 3.1 Hz), 140.2, 131.5, 130.1, 124.8 (q, *J* = 281.2 Hz), 119.8, 82.7, 51.1 (q, *J* = 27.3 Hz), 34.7, 28.3, 27.8, 25.6 (q, *J* = 2.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.39 (d, *J* = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{16}H_{20}BrF_3O_2$ ($[M+NH_4]^+$): 398.0937; Found: 398.0934.

***tert*-Butyl 5-cyclopentyl-2-(trifluoromethyl)pentanoate (3l).** The product (57.7 mg, 98% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate

= 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01 – 2.91 (m, 1H), 1.89 – 1.81 (m, 1H), 1.77 – 1.67 (m, 4H), 1.60 – 1.55 (m, 2H), 1.52 – 1.49 (m, 2H), 1.47 (s, 9H), 1.38 – 1.28 (m, 4H), 1.04 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8 (q, *J* = 3.1 Hz), 124.9 (q, *J* = 281.1 Hz), 82.4, 51.3 (q, *J* = 27.0 Hz), 39.7, 35.5, 32.6, 32.5, 27.8, 26.3 (q, *J* = 1.9 Hz), 25.8, 25.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.60 (d, *J* = 8.6 Hz, 3F). HRMS (ESI): Calculated for $C_{15}H_{25}F_3O_2$ ($[M\text{-}H\text{-}C_4H_8]^-$): 237.1108; Found: 237.1107.

***tert*-Butyl 4-(thiophen-3-yl)-2-(trifluoromethyl)butanoate (3m).** The product (57.7 mg, 98% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 4.8, 2.8 Hz, 1H), 7.00 (s, 1H), 6.95 (d, *J* = 5.2 Hz, 1H), 3.06 – 2.96 (m, 1H), 2.81 – 2.74 (m, 1H), 2.70 – 2.63 (m, 1H), 2.27 – 2.17 (m, 1H), 2.09 – 2.00 (m, 1H), 1.50 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4 (q, *J* = 3.1 Hz), 140.3, 127.8, 125.9, 121.0, 124.9 (q, *J* = 281.7 Hz), 82.8, 50.4 (q, *J* = 27.3 Hz), 27.9, 27.1, 27.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.27 (d, *J* = 8.6 Hz, 3F). HRMS (ESI): Calculated for $C_{13}H_{17}F_3O_2S$ ($[M\text{-}H\text{-}C_4H_8]^-$): 237.0203; Found: 237.0202.

***tert*-Butyl 4-(6-methoxynaphthalen-2-yl)-2-(trifluoromethyl)pentanoate(3n).** The product (63.5 mg, 83% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1, *dr* = 1:0.58) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 2H, minor and major), 7.57 (s, 1H,

major), 7.45 (s, 1H, minor), 7.32 (t, J = 8.4 Hz, 1H, minor and major), 7.20 – 7.14 (m, 2H, minor and major), 3.932 (s, 3H, major), 3.926 (s, 3H, minor), 3.14 – 3.04 (m, 1H, minor), 2.98 – 2.91 (m, 1H, major), 2.89 – 2.86 (m, 1H, minor), 2.81 – 2.71 (m, 1H, major), 2.36 – 2.26 (m, 2H, minor), 2.09 – 2.02 (m, 2H, major), 1.53 (s, 3H, minor and major), 1.40 (s, 9H, minor), 1.39 (s, 9H, major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8 (q, J = 3.1 Hz, minor), 166.6 (q, J = 3.3 Hz, major), 157.5 (minor), 157.4 (major), 140.5 (major), 139.6 (minor), 133.6 (minor), 133.5 (major), 129.13 (minor), 129.07 (major), 129.02 (major), 128.98 (minor), 127.5 (d, J = 6.0 Hz, minor), 127.2 (d, J = 5.6 Hz, major), 125.9 (t, J = 4.4 Hz, minor and major), 125.4 (d, J = 5.6 Hz, minor), 125.2 (d, J = 8.2 Hz, major), 125.18 (q, J = 281.5 Hz, major), 125.0 (q, J = 281.3 Hz, minor), 119.0 (d, J = 4.1 Hz, minor), 118.9 (d, J = 3.8 Hz, major), 105.6 (t, J = 8.9 Hz, minor and major), 82.57 (minor), 82.55 (major), 55.30 (d, J = 10.0 Hz, minor), 55.28 (d, J = 8.8 Hz, major), 49.74 (q, J = 49.7 Hz, major), 49.70 (q, J = 25.9 Hz, minor), 37.4 (minor and major), 34.5 (major), 34.1 (minor), 27.9 (major), 27.68 (minor), 23.2 (q, J = 2.7 Hz, minor), 21.3 (q, J = 2.8 Hz, major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$), δ -68.08 (d, J = 8.6 Hz, 3F, major), 68.68 (d, J = 8.6 Hz, 3F, major); HRMS (ESI): Calculated for $C_{21}H_{25}F_3O_3$ ($[M-H-C_4H_8]^-$): 325.1057; Found: 325.1061.

***tert*-Butyl 4-(4-isobutylphenyl)-2-(trifluoromethyl)pentanoate (3o).** The product (64.5 mg, 90% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1, *dr* = 1:0.64) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 – 7.06 (m, 4H, minor and major), 3.09 – 3.00 (m, 1H,

major), 2.82 – 2.74 (m, 1H, minor and major), 2.72 – 2.66 (m, 1H, minor), 2.47 – 2.45 (m, 2H, minor and major), 2.24 – 2.16 (m, 1H, minor and major), 1.97 – 1.81 (m, 2H, minor and major), 1.51 (s, 9H, minor), 1.45 (s, 9H, major), 1.31 (s, 3H, minor), 1.29 (s, 3H, major), 0.93 (s, 6H, minor), 0.91 (s, 6H, major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7 (q, *J* = 3.1 Hz, minor), 166.6 (q, *J* = 3.4 Hz, major), 142.8 (major), 141.7 (minor), 140.1 (minor), 139.9 (major), 129.4 (minor), 129.3 (major), 126.7 (minor), 126.5 (major), 125.1 (q, *J* = 283.0 Hz, major), 125.0 (q, *J* = 281.2 Hz, minor), 82.49 (major), 82.47 (minor), 49.73 (q, *J* = 27.1 Hz, minor), 49.68 (q, *J* = 27.1 Hz, major), 45.03 (minor), 45.01 (major), 37.0 (minor), 36.8 (major), 34.7 (minor), 34.2 (major), 30.2 (minor and major), 27.84 (minor), 27.80 (major), 23.3 (minor), 22.4 (minor and major), 21.01 (major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$), δ -68.20 (d, *J* = 8.3 Hz, 3F, major), -68.73 (d, *J* = 8.6 Hz, 3F, minor) ; HRMS (ESI): Calculated for $C_{20}H_{29}F_3O_2$ ($[M-H-C_4H_8]^-$): 301.1421; Found: 301.1423.

***tert*-Butyl4-(11-oxo-6,11-dihydrodibenzo[*b,e*]oxepin-2-yl)-2-(trifluoromethyl)butanoate (3p).** The product (62.2 mg, 74% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 2.4 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 7.55 (t, *J* = 8.8 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.31 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.18 (s 1H), 7.00 (s, 2H), 3.04 – 2.94 (m, 1H), 2.80 – 2.72 (m, 1H), 2.67 – 2.59 (m, 1H), 2.27 – 2.17 (m, 1H), 2.09 – 1.99 (m, 1H), 1.52 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 166.4 (q, *J* = 3.1 Hz), 160.0, 140.5, 135.6, 135.5, 133.7, 132.8,

131.3(d, J = 3.0 Hz), 129.4, 129.2, 127.8, 125.2, 121.0, 124.8 (q, J = 281.4 Hz), 82.9, 73.6, 50.4 (q, J = 27.1 Hz), 31.7, 27.9, 27.7 (q, J = 1.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.23 (d, J = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{23}H_{23}F_3O_4$ ($[M+H-C_4H_8]^+$): 365.0995 Found: 365.0985.

***tert*-Butyl4-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)-2-(trifluoromethyl)butanoate (3q).** The product (89.8 mg, 88% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 60:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 2.4 Hz, 1H), 6.89 (d, J = 9.2 Hz, 1H), 6.67 (dd, J = 8.8, 2.4 Hz, 1H), 3.82 (s, 3H), 3.15 – 3.05 (m, 1H), 2.79 – 2.67 (m, 2H), 2.34 (s, 3H), 2.28 – 2.18 (m, 1H), 2.08 – 2.00 (m, 1H), 1.52 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.26, 166.4 (q, J = 3.0 Hz), 156.0, 139.1, 134.5, 134.0, 131.09, 130.96, 130.60, 129.1, 124.9 (q, J = 281.5 Hz), 129.0, 117.8, 115.1, 111.3 (t, J = 2.3 Hz), 101.2, 82.9, 55.7 (d, J = 8.0 Hz), 50.9 (q, J = 27.2 Hz), 27.8, 25.9, 21.3, 13.2 (q, J = 4.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.01 (d, J = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{26}H_{27}ClF_3NO_4$ ($[M+H]^+$): 510.1653; Found: 510.1634.

6-(*tert*-Butyl) 1-methyl (2*S*)-2-((*tert*-butoxycarbonyl)amino)-5-(trifluoromethyl)hexanedioate (5a).

The product (69.5 mg, 87% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* =

1:0.92) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, *J* = 10.8 Hz, 1H, minor and major), 4.39 – 4.30 (m, 1H, minor and major), 3.74 (s, 3H, major), 3.73 (s, 3H, minor), 3.15 – 3.10 (m, 1H, major), 3.03 – 2.93 (m, 1H, minor), 1.94 – 1.79 (m, 2H, minor and major), 1.74 – 1.62 (m, 2H, minor and major), 1.47 (s, 9H, major), 1.46 (s, 9H, minor), 1.43 (s, 9H, minor and major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6 (major), 172.5 (minor), 166.2 (major), 166.0 (minor), 155.4 (major), 155.2 (minor), 124.66 (q, *J* = 281.5 Hz, major), 124.63 (q, *J* = 281.1 Hz, minor), 82.99 (minor), 82.97 (major), 80.2 (major), 80.1 (minor), 52.5 (major), 52.4 (minor), 50.4 (q, *J* = 27.9 Hz, minor and major), 29.8 (minor), 29.7 (major), 28.22 (minor), 28.20 (major), 27.8 (minor and major), 22.1 (minor), 21.9 (major), 18.6 (minor and major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.23 (d, *J* = 8.3 Hz, 3F, minor), -68.48 (d, *J* = 8.5 Hz, 3F, major). HRMS (ESI): Calculated for HRMS (ESI): Calculated for $C_{17}H_{28}F_3NO_6$ ($[M+H]^+$): 400.1941; Found: 400.1940.

1-Benzyl 6-(*tert*-butyl) (2*S*)-2-((*tert*-butoxycarbonyl)amino)-5-(trifluoromethyl)hexanedioate (5b).

The product (71.3 mg, 75% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.97) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.32 (m, 5H, minor and major), 5.23 – 5.16 (m, 2H, minor and major), 5.14 – 5.11 (m, 1H, minor and major), 4.43 – 4.32 (m, 1H, minor and major), 3.15 – 3.07 (m, 1H, major), 2.98 – 2.89 (m, 1H, minor), 1.93 – 1.76 (m, 2H, minor and major), 1.73 –

1.63 (m, 2H, minor and major), 1.44 (s, 9H, minor), 1.43 (s, 9H, minor and major), 1.41 (s, 9H, major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0 (major), 171.8 (minor), 166.2 (minor), 166.0 (major), 155.4 (major), 155.2 (minor), 135.1 (minor and major), 135.0 (minor and major), 128.63 (minor and major), 128.56 (minor and major), 128.4 (minor and major), 128.35 (minor and major), 124.7 (q, *J* = 281.6 Hz, major), 124.6 (q, *J* = 281.6 Hz, minor), 83.0 (minor), 82.9 (major), 80.2 (major), 80.1 (minor), 67.4 (major), 67.3 (minor), 53.0 (minor), 52.4 (major), 50.8 (q, *J* = 27.6 Hz, major), 50.5 (q, *J* = 27.6 Hz, minor), 29.8 (minor), 29.7 (major), 28.23 (minor), 28.21 (major), 27.8 (minor), 27.7 (major), 22.1 (minor), 21.8 (major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.36 (d, *J* = 84.6 Hz, 3F, minor and major). HRMS (ESI): Calculated for $C_{23}H_{32}F_3NO_6$ ($[M+H]^+$): 476.2254; Found: 476.2251.

7-(*tert*-Butyl) 1-methyl (2*S*)-2-((*tert*-butoxycarbonyl)amino)-6-(trifluoromethyl)heptanedioate (5c).

The product (69.5 mg, 84% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.84) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (t, *J* = 6.8 Hz, 1H, minor and major), 4.32 – 4.25 (m, 1H, minor and major), 3.714 (s, 3H, major), 3.710 (s, 3H, major), 2.99 – 2.89 (m, 1H, minor and major), 1.92 – 1.79 (m, 2H, minor and major), 1.77 – 1.67 (m, 2H, minor and major), 1.66 – 1.57 (m, 2H, major), 1.450 (s, 9H, minor), 1.446 (s, 9H, major), 1.41 (s, 9H, minor and major), 1.38 – 1.36 (m, 2H, minor); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0 (minor

and major), 166.39 (major), 166.35 (minor), 155.27 (minor), 155.26 (major), 124.71 (q, J = 283.3 Hz, minor), 124.69 (q, J = 283.3 Hz, major), 82.8 (minor), 82.7 (major), 79.9 (minor and major), 53.04 (minor), 52.97 (major), 52.30 (minor and major), 51.0 (q, J = 27.3 Hz, minor and major), 32.4 (major), 32.2 (minor), 28.2 (minor and major), 27.8 (minor and major), 25.6 (minor and major), 22.53 (minor), 25.50 (major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.47 (d, J = 8.3 Hz, 3F, major), -68.53 (d, J = 8.3 Hz, 3F, minor). HRMS (ESI): Calculated for $C_{18}H_{30}F_3NO_6$ ($[M+Na]^+$): 436.1917; Found: 436.1916.

di-*tert*-Butyl(2*S*)-2-((*tert*-butoxycarbonyl)amino)-6-(trifluoromethyl)heptanedioate (5d). The product (78.3 mg, 86% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.94) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (t, J = 9.2 Hz, 1H, minor and major), 4.18 – 4.10 (m, 1H, minor and major), 2.98 – 2.88 (m, 1H, minor and major), 1.91 – 1.79 (m, 2H, minor and major), 1.77 – 1.66 (m, 2H, minor and major), 1.64 – 1.55 (m, 2H, minor and major), 1.44 (s, 9H, minor), 1.431 (s, 9H, major), 1.426 (s, 9H, minor), 1.423 (s, 9H, major), 1.40 (s, 9H, minor and major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6 (minor), 171.3 (major), 166.44 (minor), 166.41 (major), 155.3 (minor and major), 124.8 (q, J = 281.3 Hz, minor), 124.7 (q, J = 281.3 Hz, major), 82.7 (minor), 82.6 (major), 81.98 (major), 81.96 (minor), 79.6 (minor and major)， 53.6 (minor)，

53.5 (major)， 51.05 (q, J = 27.2 Hz, minor), 51.03 (q, J = 27.3 Hz, major), 32.6 (major), 32.5 (minor), 28.2 (minor and major), 27.9 (minor and major), 27.8 (minor and major), 25.78 (d, J = 1.9 Hz minor and major), 22.5 (minor), 22.3 (major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.24 (s, 3F， minor and major). HRMS (ESI): Calculated for $C_{21}H_{36}F_3NO_6$ ($[M+H]^+$): 456.2567; Found: 456.2564.

1-Benzyl7-(*tert*-butyl)(2*S*)-2-((*tert*-butoxycarbonyl)amino)-6-(trifluoromethyl)heptanedioate (5e). The product (78.3 mg, 80% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.96) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 5H, minor and major), 5.20 – 5.14 (m, 2H, minor and major), 5.11 – 5.06 (m, 1H, minor and major), 4.37 – 4.30 (m, 1H, minor and major), 2.97 – 2.86 (m, 1H, minor and major), 189 – 1.80 (m, 2H, minor and major), 1.74 – 1.58 (m, 2H, minor and major), 1.451 (s, 9H, major), 1.447 (s, 9H, minor), 1.42 (s, 9H, minor and major), 1.39 – 1.29 (m, 2H, minor and major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4 (minor and major), 166.4 (minor and major), 155.3 (minor and major), 135.24 (minor and major), 135.22 (minor and major), 128.6 (minor and major), 128.5 (minor and major), 128.3 (minor and major), 128.27 (minor and major), 124.7 (q, J = 281.2 Hz, minor and major), 82.74 (major), 82.71 (minor), 79.9 (minor and major), 67.1 (minor and major), 53.1 (minor and major), 51.0 (q, J = 27.4 Hz, minor), 50.96 (q, J = 27.2 Hz, major), 32.3 (major), 32.2 (minor), 28.2 (minor and major), 27.8 (minor and major), 25.6 (q, J = 2.1 Hz, minor and major), 22.6 (minor and

major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.40 (d, *J* = 8.3 Hz, 3F, minor and major). HRMS (ESI): Calculated for $C_{24}H_{34}F_3NO_6$ ($[M+Na]^+$): 512.2230; Found: 512.2214.

di-*tert*-Butyl(2*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-5-(trifluoromethyl)hexanedioate (5f). The product (93.5 mg, 83% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.85) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 5.51 (t, *J* = 8.0 Hz, 1H), 4.44 – 4.39 (m, 2H), 4.36 – 4.28 (m, 1H), 4.23 (t, *J* = 6.8 Hz, 1H), 3.13 – 2.97 (m, 1H), 1.91 – 1.83 (m, 2H), 1.78 – 1.71 (m, 2H), 1.50 (s, 18H); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9 (minor), 170.8 (major), 166.2 (major), 166.1 (minor), 155.9 (major), 155.8 (minor), 143.8 (d, *J* = 12.9 Hz, minor and major), 141.3 (d, *J* = 1.0 Hz, minor and major), 127.7 (minor and major), 127.1 (minor and major), 125.1 (d, *J* = 3.6 Hz, minor and major), 124.8 (q, *J* = 291.1 Hz, minor and major), 120.0 (d, *J* = 1.5 Hz, minor and major), 83.0 (minor), 82.9 (major), 82.81 (major), 82.75 (minor), 67.1 (minor and major), 53.8 (minor), 53.4 (major), 50.9 (q, *J* = 27.7 Hz, minor), 50.3 (q, *J* = 27.2 Hz, major), 47.1(minor and major), 30.0 (minor), 29.6 (major), 27.9 (minor and major), 27.84 (major), 27.79 (minor), 22.1 (d, *J* = 1.9 Hz, minor), 21.5 (d, *J* = 2.4 Hz, major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.14 (d, *J* = 8.3 Hz, 3F, minor), -68.36 (d, *J* = 8.6 Hz, 3F, major). HRMS (ESI): Calculated for $C_{30}H_{36}F_3NO_6$ ($[M+H]^+$):

564.2567; Found: 564.2565.

6-(*tert*-Butyl) 1-methyl (2*S*)-2-(((benzyloxy)carbonyl)amino)-5-(trifluoromethyl)hexanedioate (5g).

The product (53.7 mg, 62% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.84) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 5H, minor and major), 5.38 (t, *J* = 7.2 Hz, 1H, minor and major), 5.11 (s, 2H, minor and major), 4.47 – 4.38 (m, 1H, minor and major), 3.76 (s, 3H, minor and major), 3.11 – 3.03 (m, 1H, major), 3.01 – 2.94 (m, 1H, minor), 1.97 – 1.90 (m, 2H, minor), 1.88 – 1.82 (m, 2H, major), 1.82 – 1.69 (m, 2H, minor and major), 1.47 (s, 9H, major), 1.47 (s, 9H, minor); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2 (major), 172.1 (minor), 166.1 (major), 166.0 (minor), 155.9 (major), 155.8 (minor), 128.6 (minor and major), 128.3 (minor and major), 128.1 (minor and major), 124.6 (q, *J* = 282.0 Hz, minor and major), 83.08 (minor), 83.06 (major), 67.2 (major), 67.1 (minor), 53.4 (minor), 53.0 (major), 52.7 (minor and major), 50.7 (q, *J* = 27.4 Hz, minor), 50.3 (q, *J* = 27.4 Hz, major), 29.7 (minor), 29.5 (major), 27.79 (major), 27.78 (minor), 22.0 (d, *J* = 2.3 Hz, minor), 21.7 (d, *J* = 2.4 Hz, major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.16 (d, *J* = 8.3 Hz, 3F, minor), -68.38 (d, *J* = 8.7 Hz, 3F, major). HRMS (ESI): Calculated for $C_{20}H_{26}F_3NO_6$ ($[M+H]^+$): 434.1785; Found: 434.1782.

7-(*tert*-Butyl) 1-methyl (2*S*)-2-(((benzyloxy)carbonyl)amino)-6-(trifluoromethyl)heptanedioate (5h).

The product (37.6 mg, 42% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.97) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 5H, minor and major), 5.23 (t, *J* = 8.0 Hz, 1H, minor and major), 5.10 (s, 2H, minor and major), 4.42 – 4.35 (m, 1H, minor and major), 3.74 (s, 3H, minor and major), 3.00 – 2.90 (m, 1H, minor and major), 1.95 – 1.84 (m, 2H, minor and major), 1.77 – 1.67 (m, 2H, minor and major), 1.458 (s, 9H, minor), 1.457 (s, 9H, major), 1.42 – 1.33 (m, 2H, minor and major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6 (minor and major), 166.4 (q, *J* = 3.9 Hz, minor and major), 155.79 (minor and major), 136.09 (minor and major), 128.5 (minor and major), 128.2 (minor and major), 128.1 (minor and major), 124.7 (q, *J* = 281.4 Hz, minor and major), 82.84 (minor), 82.81 (major), 67.0 (minor and major), 53.5 (minor), 53.4 (major), 52.5 (minor and major), 51.0 (q, *J* = 27.4 Hz, minor), 50.9 (q, *J* = 27.3 Hz, major), 32.24 (major), 32.18 (minor), 27.78 (minor and major), 25.7 (d, *J* = 2.3 Hz, minor and major), 22.44 (minor), 22.35 (major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.42 (d, *J* = 8.3 Hz, 3F，minor), -68.48 (d, *J* = 8.3 Hz, 3F, major). HRMS (ESI): Calculated for $C_{21}H_{28}F_3NO_6$ ($[M+Na]^+$): 470.1761; Found: 470.1757.

***tert*-Butyl4-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-6-methyl-2-(trifluoromethyl)heptanoate (5i).** The product (75.8 mg, 75% yield) was purified with

silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.39) as a colorless liquid. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.2 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 2H), 4.48 (d, *J* = 6.4 Hz, 2H), 4.34 (d, *J* = 9.6 Hz, 1H), 4.21 (t, *J* = 6.8 Hz, 1H), 3.75 – 3.67 (m, 1H), 3.13 – 3.03 (m, 1H), 2.15 – 2.08 (m, 1H), 1.62 – 1.57 (m, 2H), 1.49 (s, 9H), 1.40 – 1.23 (m, 2H), 0.91 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 155.9, 143.9(d, *J* = 9.6 Hz,), 141.4, 127.7 (d, *J* = 2.7 Hz), 127.1 (d, *J* = 2.7 Hz), 124.9 (d, *J* = 1.8 Hz), 120.0, 124.9 (q, *J* = 281.1 Hz), 83.0, 66.1, 48.1 (q, *J* = 27.2 Hz), 47.4, 47.0, 45.4, 32.2, 27.7, 24.8, 22.8, 22.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.40 (d, *J* = 8.3 Hz, 3F). HRMS (ESI): Calculated for $C_{28}H_{34}F_3NO_4$ ($[M+H]^+$): 506.2513; Found: 506.2499.

***tert*-Butyl 4-((*tert*-butoxycarbonyl)amino)-5-methyl-2-(trifluoromethyl)hexanoate (5j).** The product (33.9 mg, 54% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.46) as a white solid. MP 68.9-70.1℃. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.37 – 4.23 (m, 1H, minor and major), 3.58 – 3.50 (m, 1H, minor), 3.48 – 3.41 (m, 1H, major), 3.17 – 3.07 (m, 1H, major), 3.07 – 2.97 (m, 1H, minor), 2.14 – 1.86 (m, 2H, major), 1.75 – 1.67 (m, 2H, minor), 1.54 – 1.50 (m, 1H, minor and major), 1.474 (s, 9H, major), 1.466 (s, 9H, minor), 1.42 (s, 9H, major), 1.41 (s, 9H, minor), 0.89 (t, *J* = 6.8 Hz, 6H, minor and major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.12 (q, *J* = 2.5 Hz, minor and major), 155.7 (minor), 155.5 (major), 125.8 (q, *J* =

281.2 Hz, major), 125.05 (q, J = 281.7 Hz, minor), 82.9 (major), 82.7 (minor), 79.3 (minor), 79.2 (major), 54.9 (minor),52.7 (major), 49.5 (q, J = 26.8 Hz, minor), 48.2 (q, J = 27.0 Hz, major), 32.9 (major), 32.8 (minor), 28.7 (minor and major), 28.32 (minor), 28.28 (major), 27.8 (minor), 27.7 (major), 18.73 (major), 18.66 (minor), 17.87 (major), 17.66 (minor); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.14 (d, J = 9.0 Hz, 3F, minor and major). HRMS (ESI): Calculated for $C_{17}H_{30}F_3NO_4$ ($[M+Na]^+$): 392.2019; Found: 392.2016.

***tert*-Butyl 4-((*tert*-butoxycarbonyl)amino)-5-phenyl-2-(trifluoromethyl)pentanoate (5k).** The product (77.6 mg, 93% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.45) as a white solid. MP 70.2-71.7 °C. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (m, 2H, minor and major), 7.22 (t, J = 7.2 Hz, 1H, minor and major), 7.16 (d, J = 7.2 Hz, 2H, minor and major), 4.35 (t, J = 10.4 Hz, 1H, minor and major), 3.94 – 3.85 (m, 1H, minor and major), 3.21 – 3.14 (m, 1H, minor), 3.09 – 3.00 (m,1H, major), 2.86 – 2.74 (m, 2H, minor and major), 2.16 – 1.89 (m, 2H, minor and major), 1.47 (s, 9H, major), 1.44 (s, 9H, minor), 1.40 (s, 9H, minor), 1.37 (s, 9H, major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0 (major), 166.0 (minor), 155.2 (major), 155.1 (minor), 137.2 (minor and major), 129.41 (minor and major), 129.37 (minor and major), 128.5 (minor and major), 126.6 (minor and major), 124.9 (q, J = 281.9 Hz, minor and major), 82.9 (minor and major), 79.5 (major), 79.4 (minor), 51.2 (minor and major), 49.5 (q, J = 27.2 Hz, major), 48.1 (q, J

= 27.2 Hz, minor), 41.93 (major), 41.89 (minor), 30.5 (minor), 29.7 (major), 28.4 (minor), 28.3 (major), 27.75 (major), 27.68 (minor); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.41 (d, *J* = 29.3 Hz, 3F, minor and major). HRMS (ESI): Calculated for $C_{21}H_{30}F_3NO_4$ ($[M+Na]^+$): 440.2019; Found: 440.2015.

***tert*-Butyl4-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-7-((*tert*-butoxycarbonyl)amino)-2-(trifluoromethyl)heptanoate (5l).** The product (91.0 mg, 75% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.38) as a white solid. MP 112.4-113.7 ℃. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H, minor and major), 7.58 (q, *J* = 3.6 Hz, 2H, minor and major), 7.40 (t, *J* = 7.6 Hz, 2H, minor and major), 7.31 (t, *J* = 7.6 Hz, 2H, minor and major), 4.70 (d, *J* = 9.2 Hz, 1H, minor and major), 4.59 (dd, *J* = 6.4, 10.8 Hz, 2H, minor and major), 4.30 (dd, *J* = 6.8, 10.8 Hz, 1H, minor and major), 4.17 (t, *J* = 6.4 Hz, 1H, minor and major), 3.77 – 3.66 (m, 1H, minor and major), 3.14 – 2.87 (m, 3H, minor and major), 2.07 – 1.99 (m, 2H, major), 1.91 – 1.86 (m, 2H, minor), 1.60 – 1.52 (m, 2H, major), 1.45 (s, 9H, minor and major), 1.43 (s, 9H, minor and major), 1.40 – 1.35 (m, 2H, minor), 1.29 – 1.26 (s, 2H, major), 0.97 – 0.83 (m, 2H, minor); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 156.0, 143.8, 143.7, 141.33, 141.31, 127.72, 127.69, 127.1, 127.0, 125.1, 124.9, 124.8 (q, *J* = 281.4 Hz), 120.0, 119.95, 83.1, 79.2, 66.4, 50.2, 49.0 (q, *J* = 27.2 Hz), 47.3, 40.1, 32.6, 31.2, 28.4, 27.7, 26.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.34 (d, *J* = 8.6 Hz, 3F). HRMS (ESI): Calculated for $C_{32}H_{41}F_3N_2O_6$ ($[M+H]^+$): 607.2989; Found: 607.2971.

***tert*-Butyl4-((*tert*-butoxycarbonyl)amino)-6-(methylthio)-2-(trifluoromethyl)hexanoate (5m).** The product (53.0 mg, 75% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.72) as a white solid. m.p 67.7-69.5 ºC. Mixture of diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (t, *J* = 9.2 Hz, 1H, minor and major), 3.82 – 3.72 (m, 1H, major), 3.72 – 3.65 (m, 1H, minor), 3.19 – 3.12 (m, 1H, minor), 3.10 – 3.00 (m, 1H, major), 2.50 (q, *J* = 8.0 Hz, 2H, minor and major), 2.08 (s, 3H, minor and major), 2.04 – 1.63 (m, 4H, minor and major), 1.48 (s, 9H, minor), 1.47 (s, 9H, major), 1.42 (s, 9H, minor), 1.41 (s, 9H, major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9 (major), 166.0 (minor), 155.4 (major), 155.3 (minor), 124.9 (q, *J* = 281.9 Hz, minor and major), 83.1 (minor), 83.0 (major), 79.6 (major), 79.5 (minor), 49.3 (minor and major), 48.3 (q, *J* = 25.8 Hz, minor and major), 35.7 (minor), 35.5 (major), 31.5 (minor),31.4 (major), 30.5 (minor), 30.3 (major), 28.3 (major), 28.27 (minor), 27.8 (major), 27.7 (minor), 15.6 (minor and major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.3 (s, 3F, minor), -68.42 (d, *J* = 6.8 Hz, 3F, major). HRMS (ESI): Calculated for $C_{17}H_{30}F_3NO_4S$ ($[M+Na]^+$): 424.1740; Found: 424.1739.

***tert*-Butyl4-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-4-cyclohexyl-2-(trifluoromethyl)butanoate (5n).** The product (80.8 mg, 76% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1, *dr* = 1:0.35) as a white solid. m.p 98.3-99.1 ºC. Mixture of

diastereomers: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 2H, minor and major), 7.60 – 7.57 (m, 2H, minor and major), 7.40 (td, *J* = 2.4, 7.2 Hz, 2H, minor and major), 7.34 – 7.29 (m, 2H, minor and major), 4.66 (dd, *J* = 6.0, 10.4 Hz, 1H, minor and major), 4.48 (d, *J* = 10.0 Hz, 1H, minor and major), 4.28 – 4.17 (m, 2H, minor and major), 3.64 – 3.57 (m, 1H, minor and major), 3.07 – 3.00 (m, 1H, minor and major), 2.04 – 1.92 (m, 2H, minor and major), 1.75 (d, *J* = 12.0 Hz, 2H, minor and major), 1.65 (t, *J* = 11.6 Hz, 3H, minor and major), 1.43(s, 1H, minor and major), 1.42 (s, 9H, major), 1.40 (s, 9H, minor), 1.26 – 1.04 (m, 3H, minor and major), 1.00 – 0.88 (m, 2H, minor and major); For the mixture: ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4 (minor and major), 167.1 (q, *J* = 2.7 Hz, minor and major), 156.2 (minor and major), 143.82 (major), 143.78 (minor), 141.35 (minor), 141.324 (major), 134.319 (minor and major), 131.7(minor and major), 127.71 (minor), 127.66 (major), 127.01 (major), 127.00 (minor), 125.15 (minor and major), 125.06 (minor and major), 124.6 (minor), 124.5 (major), 124.4 (q, *J* = 154.7 Hz, minor and major), 123.6 (minor and major), 120.0 (minor), 119.9 (major), 83.6 (minor), 82.9 (major), 66.6 (minor), 66.4 (major), 56.1 (minor), 55.0 (major), 49.3 (q, *J* = 27.0 Hz, major), 49.2 (q, *J* = 27.6 Hz, minor), 47.3 (major), 47.2 (minor), 42.74 (minor), 42.66 (major), 34.42 (minor), 34.39 (major), 29.4 (major), 29.1 (minor), 28.5 (minor), 28.2 (major), 28.0 (minor and major), 27.7 (major), 27.6 (minor), 26.2 (minor and major), 26.0 (d, *J* = 3.2 Hz, minor and major); For the mixture: ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.62 (d, *J* = 8.3 Hz, 3F, minor), -68.27 (d, *J* = 9.0 Hz, 3F, major). HRMS (ESI): Calculated for $C_{30}H_{36}F_3NO_4$ ($[M+NH_4]^+$): 549.2935; Found: 549.2919.

***tert*-Butyl2-((1-((*tert*-butoxycarbonyl)amino)cyclopropyl)methyl)-3,3,3-trifluoropropanoate (5o).** The product (65.7 mg, 93% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1) as a white solid. MP 46.8-47.9 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.88 (s, 1H), 3.22 (s, 1H), 2.18 (d, *J* = 13.2 Hz, 1H), 1.90 (t, *J* = 12.0 Hz, 1H), 1.46 (s, 9H), 1.40 (s, 9H), 0.80 (d, *J* = 10.8 Hz, 1H), 0.71 (d, *J* = 11.2 Hz, 1H), 0.66 (s, 2H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8 (q, *J* = 3.2 Hz), 155.1, 124.8 (q, *J* = 281.0 Hz), 82.7, 79.6, 49.5 (q, *J* = 27.7 Hz), 32.7, 31.1, 28.2, 27.7, 14.6, 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.44 (s, 3F). HRMS (ESI): Calculated for $C_{16}H_{26}F_3NO_4$ ($[M+Na]^+$): 376.1706; Found: 376.1705.

***tert*-Butyl-4-((*tert*-butoxycarbonyl)amino)-4-methyl-2-(trifluoromethyl)pentanoate (5p).** The product (66.8 mg, 94% yield) was purified with silica gel chromatography (Petroleum ether / Ethyl acetate = 10:1, Petroleum ether / Dichloromethane = 1:1) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.45 (s, 1H), 3.12 – 3.02 (m, 1H), 2.27 – 2.12 (m, 2H), 1.45 (s, 9H), 1.39 (s, 9H), 1.33 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3 (q, *J* = 3.2 Hz), 154.1, 125.2 (q, *J* = 281.6 Hz), 83.0, 79.0, 51.6, 47.7(q, *J* = 27.3 Hz), 35.3 (q, *J* = 1.9 Hz), 28.3, 27.7, 27.3, 26.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.64 (d, *J* = 8.6 Hz, 3F). HRMS (ESI): Calculated for $C_{16}H_{28}F_3NO_4$ ($[M+Na]^+$): 378.1863; Found: 378.1862.

7. Copies of NMR spectra

tert-butyl 2-((2,3-dihydro-1*H*-inden-2-yl)methyl)-3,3,3-trifluoropropanoate (3a)

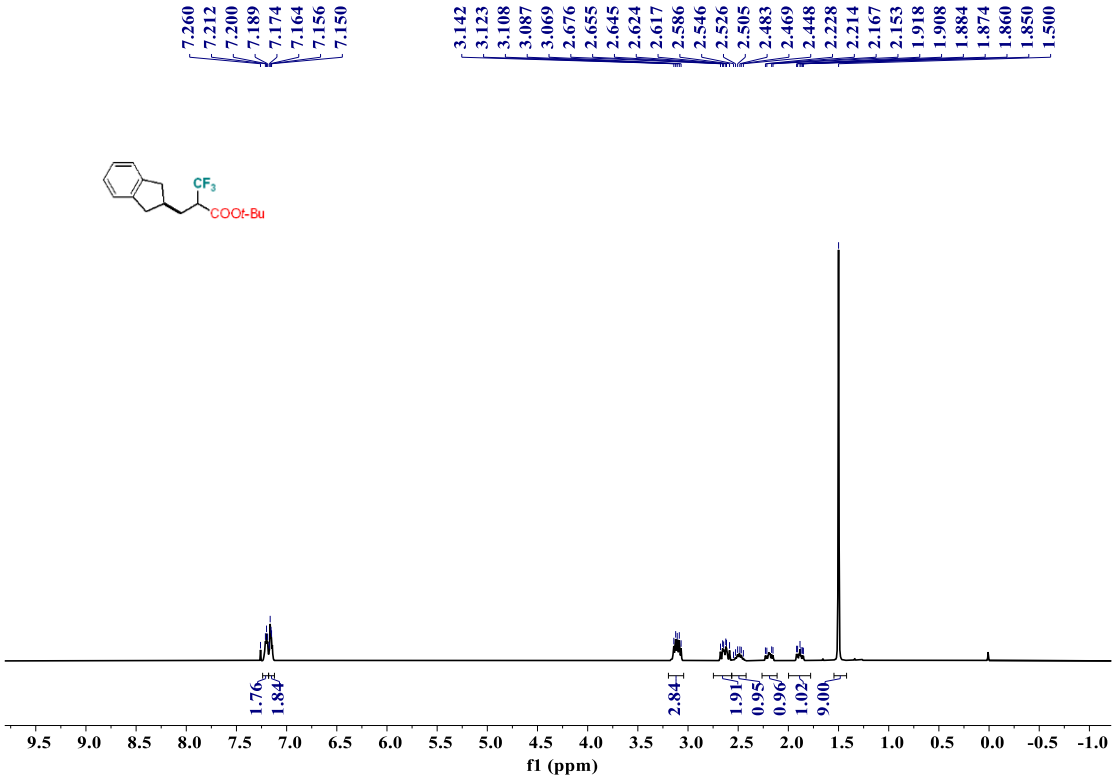


Figure S1. ^{1}H NMR of Compound **3a** (400 MHz, $CDCl_3$)

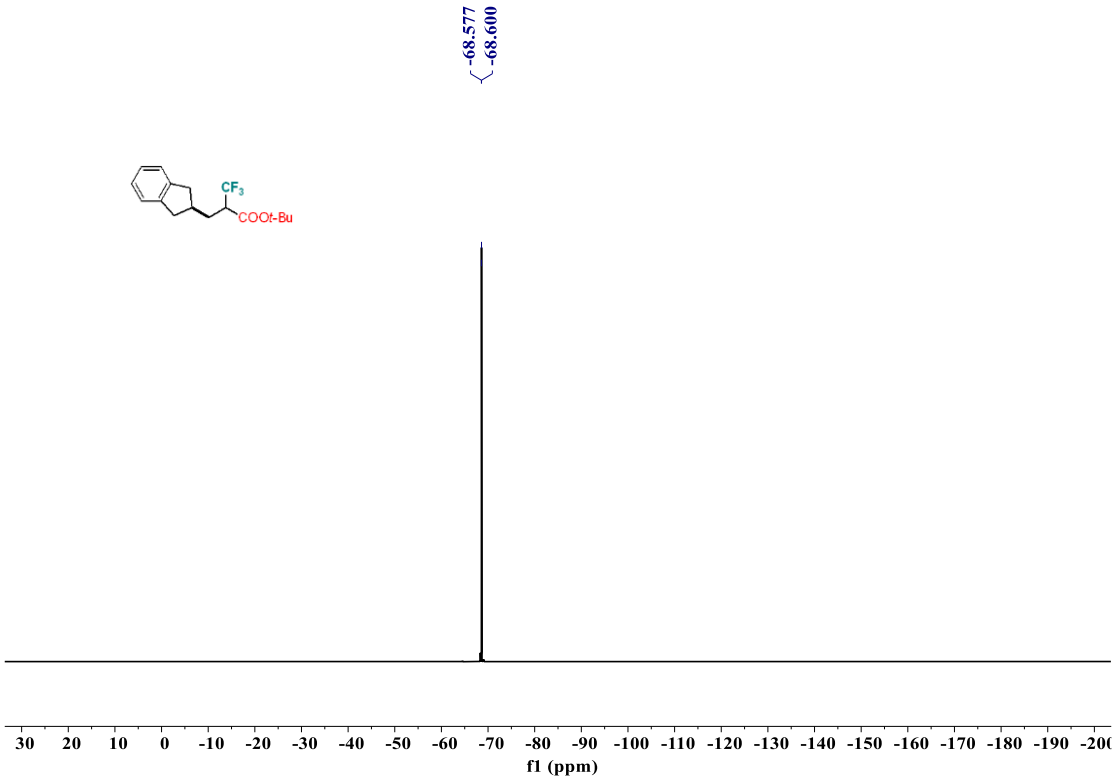


Figure S2. ^{19}F NMR of Compound **3a** (376 MHz, $CDCl_3$)

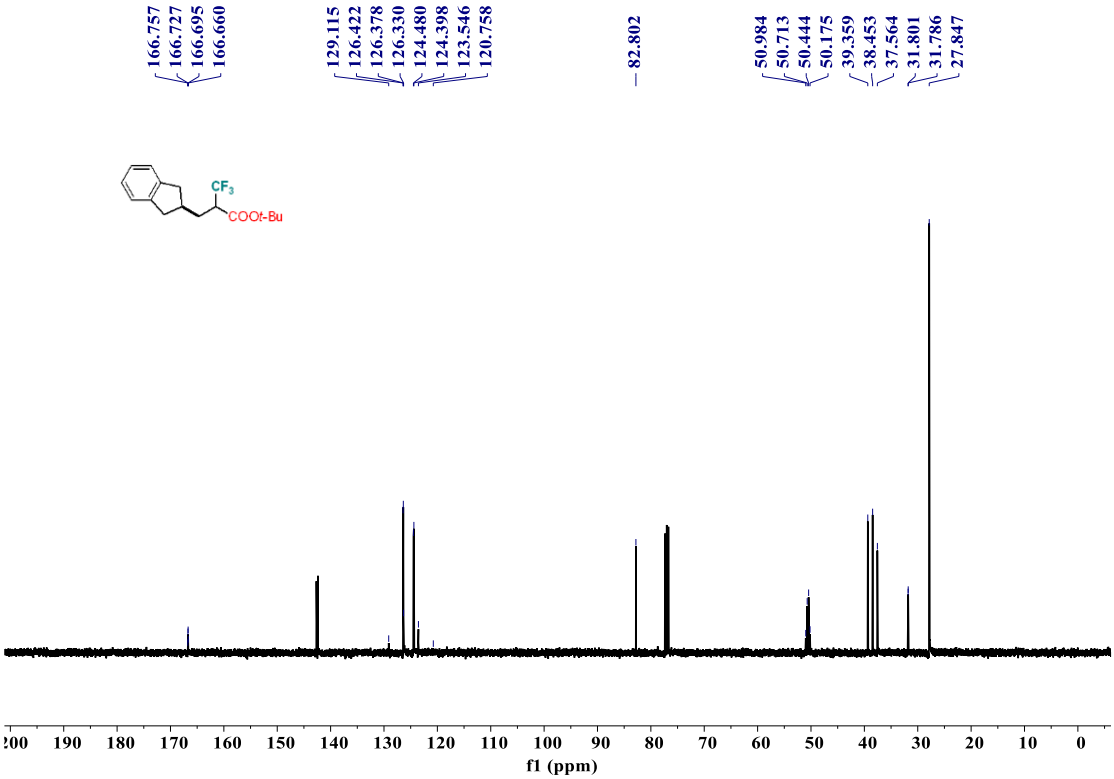


Figure S3. ^{13}C NMR of Compound **3a** (101 MHz, $CDCl_3$)

***tert*-butyl 2-(cycloheptylmethyl)-3,3,3-trifluoropropanoate (3b)**

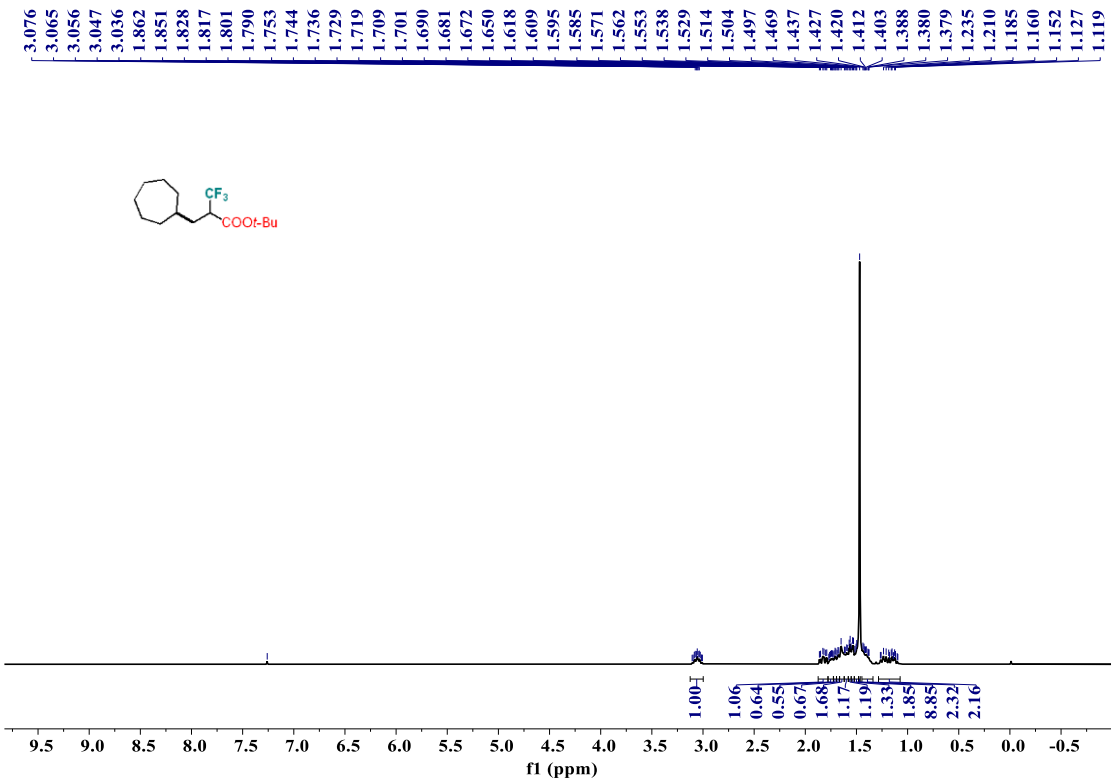


Figure S4. ^{1}H NMR of Compound **3b** (400 MHz, $CDCl_3$)

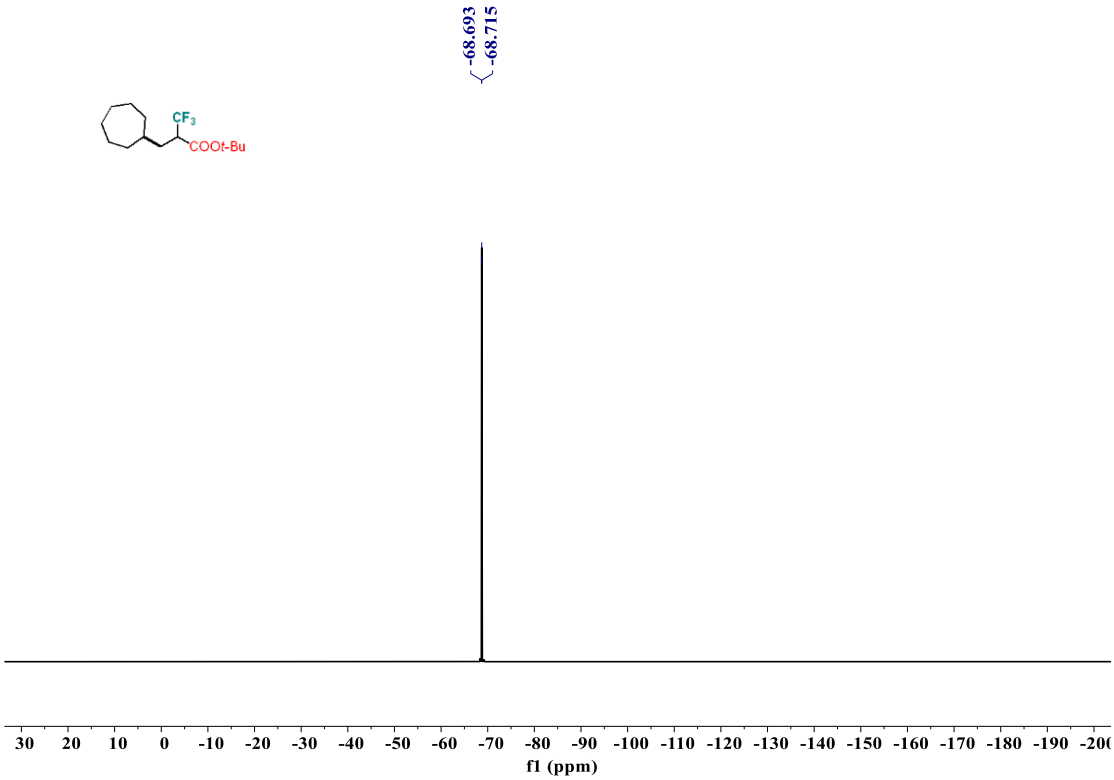


Figure S5. ^{19}F NMR of Compound **3b** (376 MHz, $CDCl_3$)

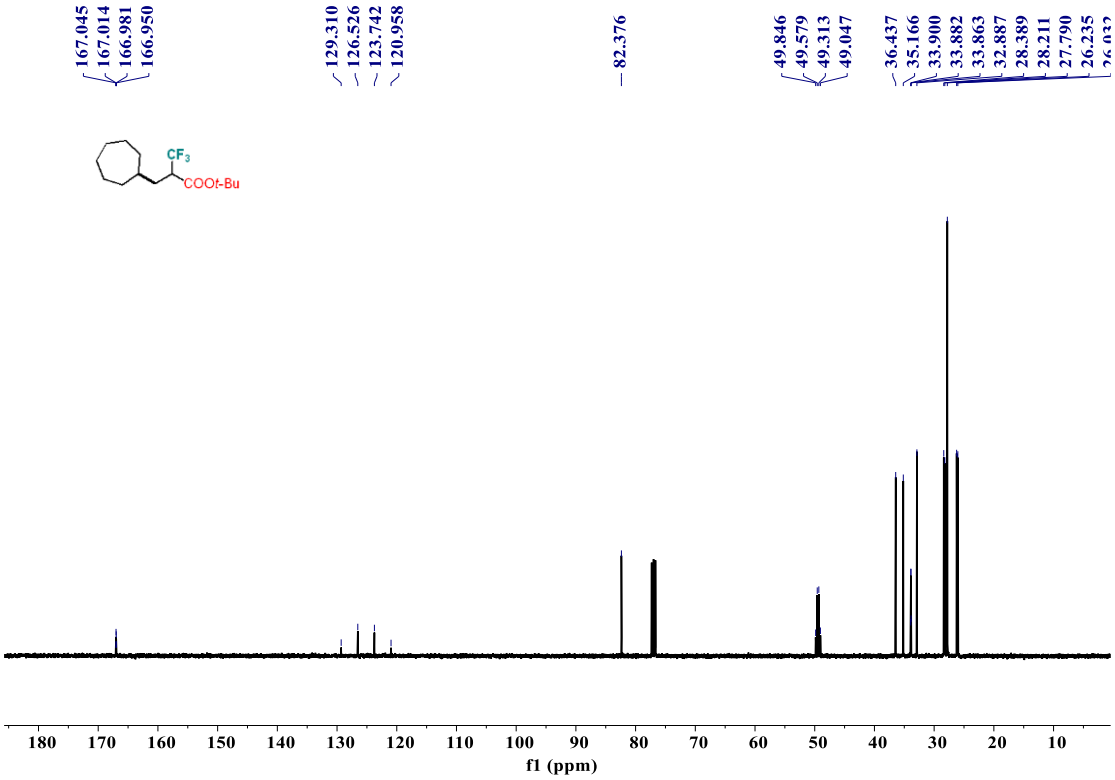


Figure S6. ^{13}C NMR of Compound **3b** (101 MHz, $CDCl_3$)

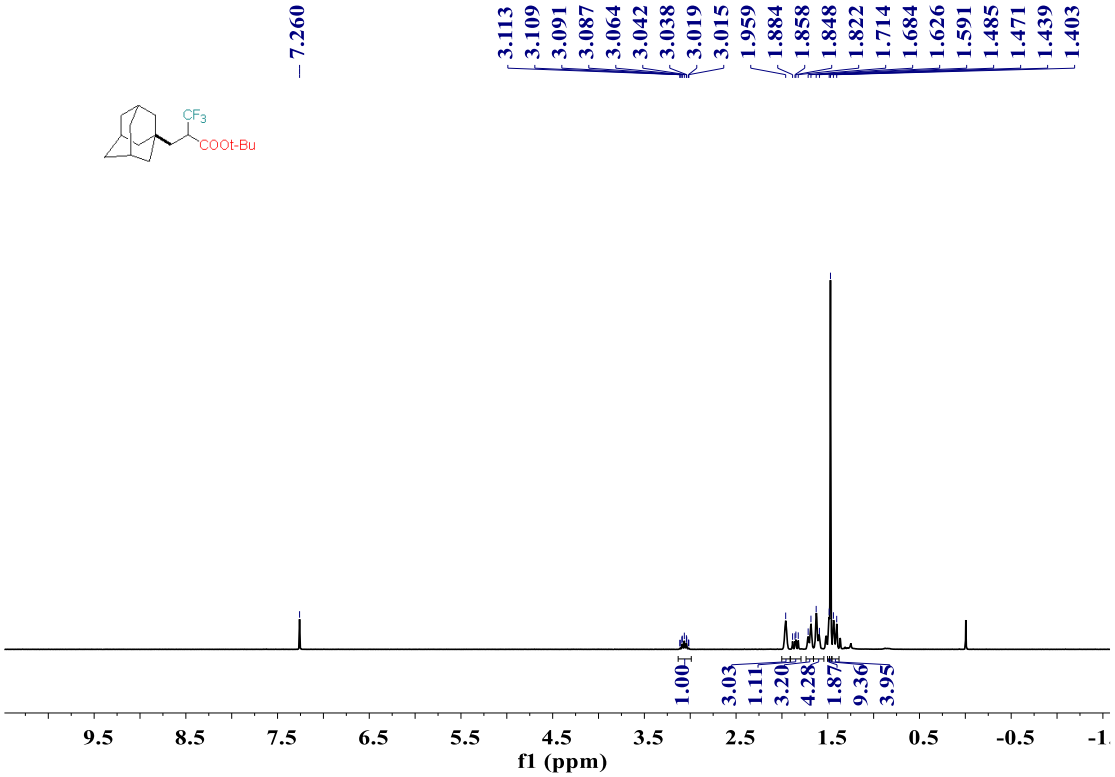


Figure S7. ^{1}H NMR of Compound **3c** (400 MHz, $CDCl_3$)

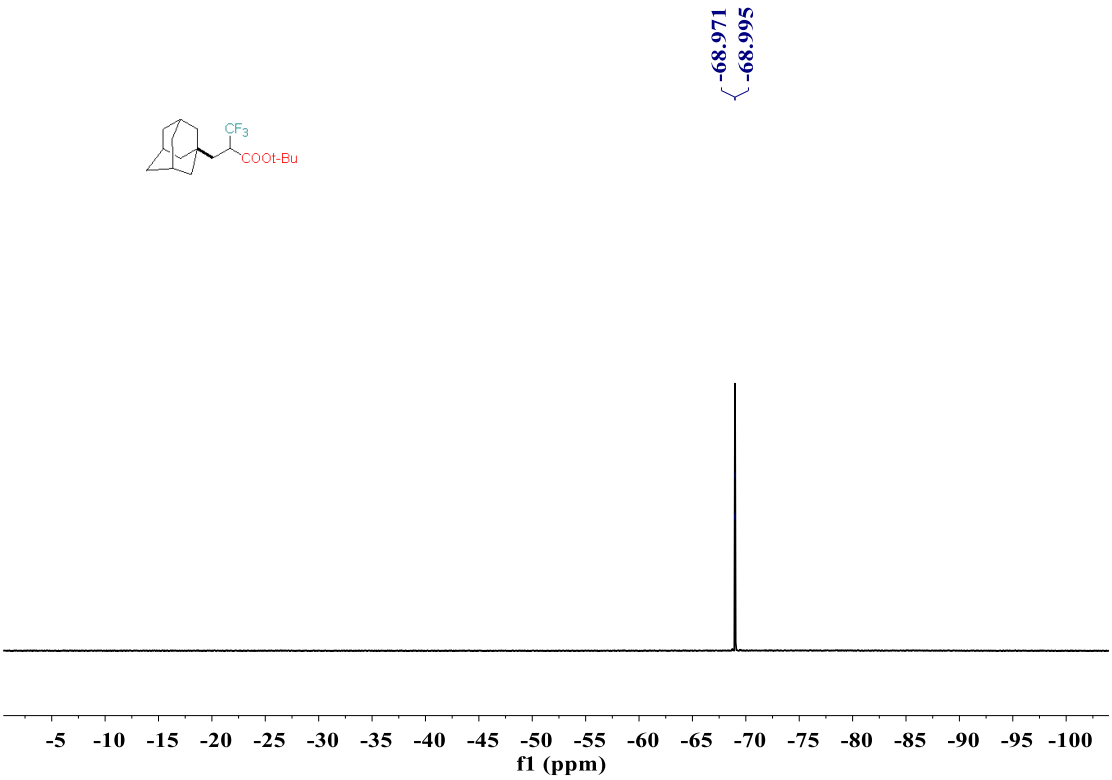


Figure S8. ^{19}F NMR of Compound **3c** (376 MHz, $CDCl_3$)

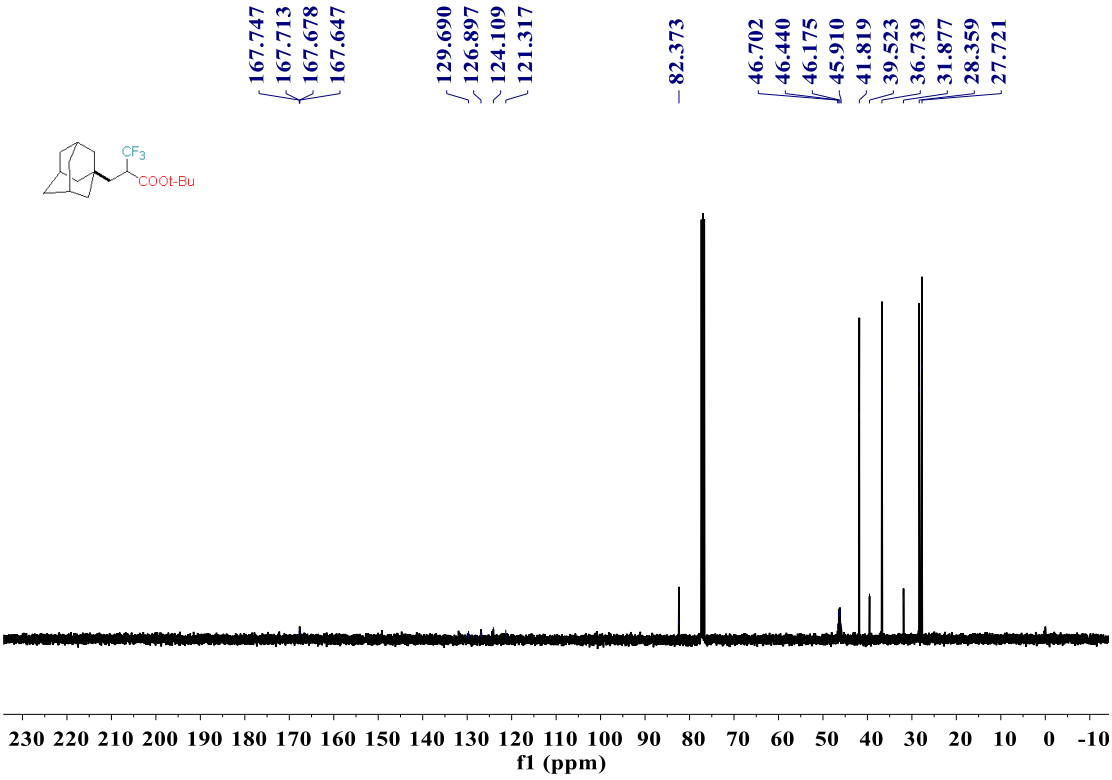


Figure S9. ^{13}C NMR of Compound **3c** (101 MHz, $CDCl_3$)

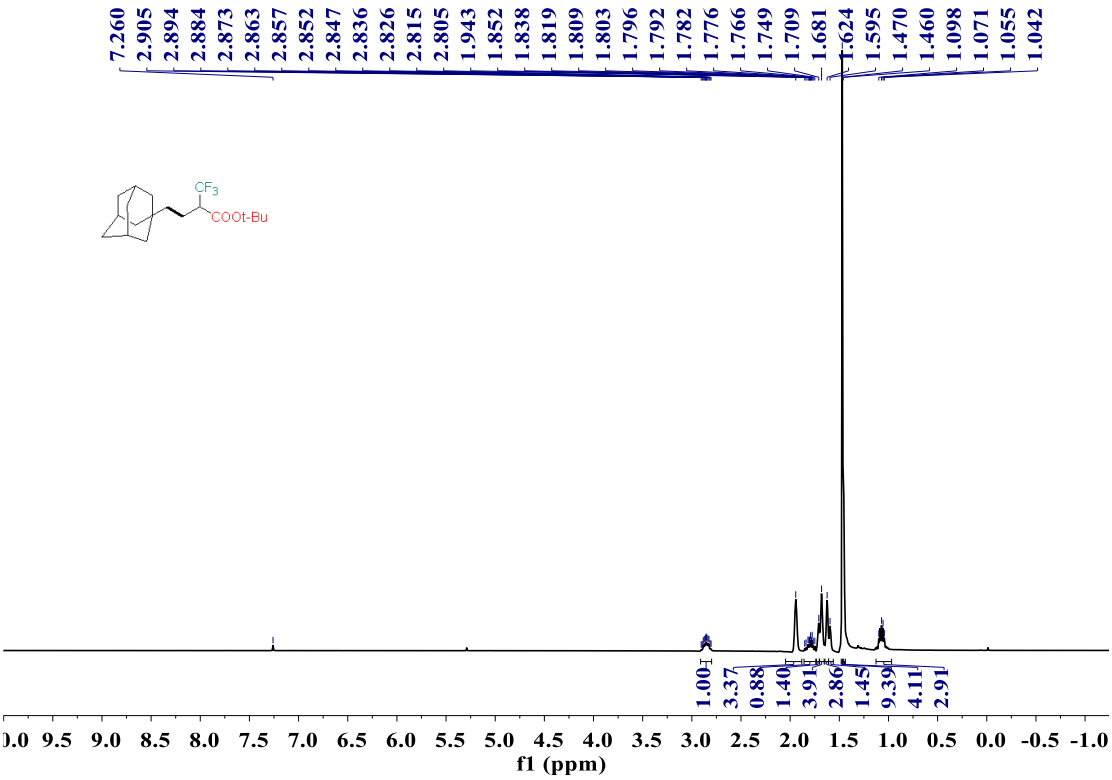


Figure S10. ^{1}H NMR of Compound **3d** (400 MHz, $CDCl_3$)

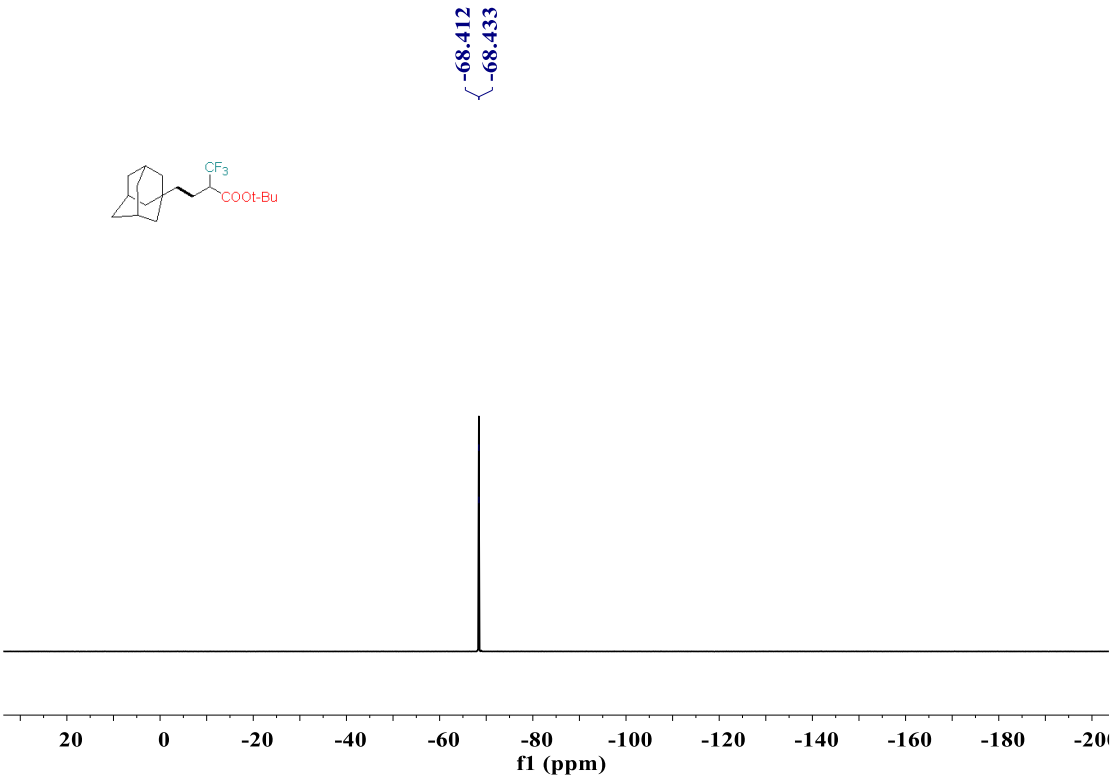


Figure S11. ^{19}F NMR of Compound **3d** (376 MHz, $CDCl_3$)

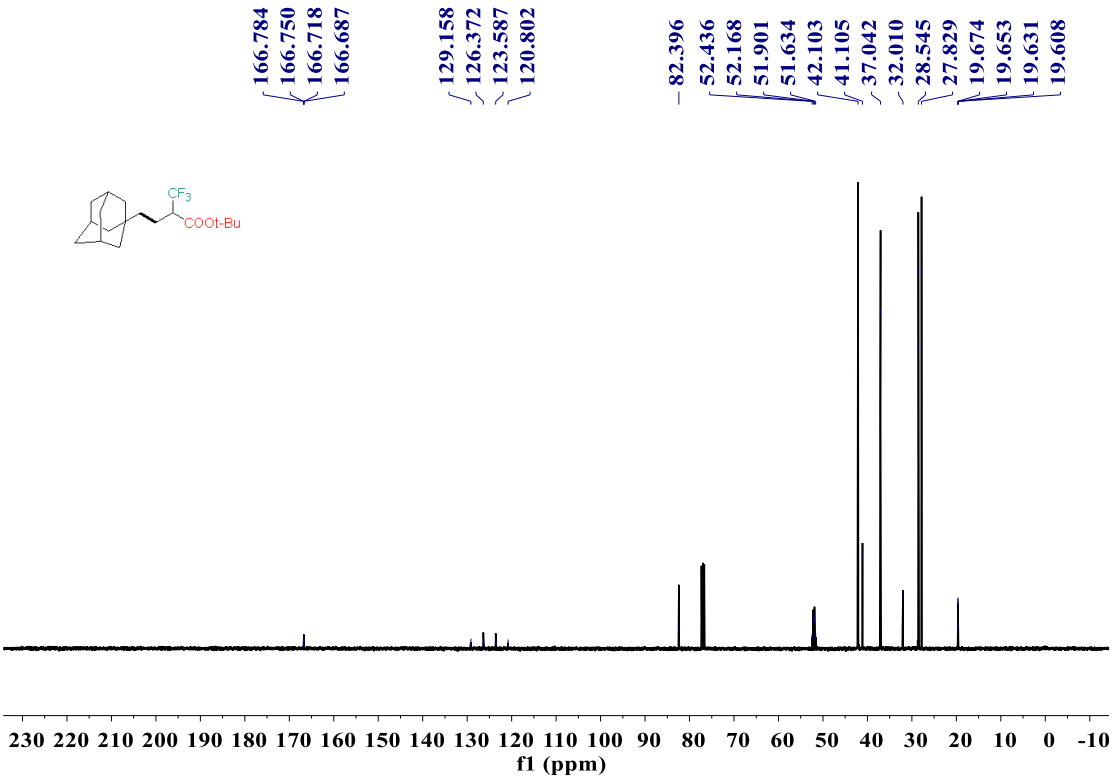


Figure S12. ^{13}C NMR of Compound **3d** (101 MHz, $CDCl_3$)

tert-butyl 3,3,3-trifluoro-2-((1-(4-methoxyphenyl)cyclopropyl)methyl)propanoate (3e)

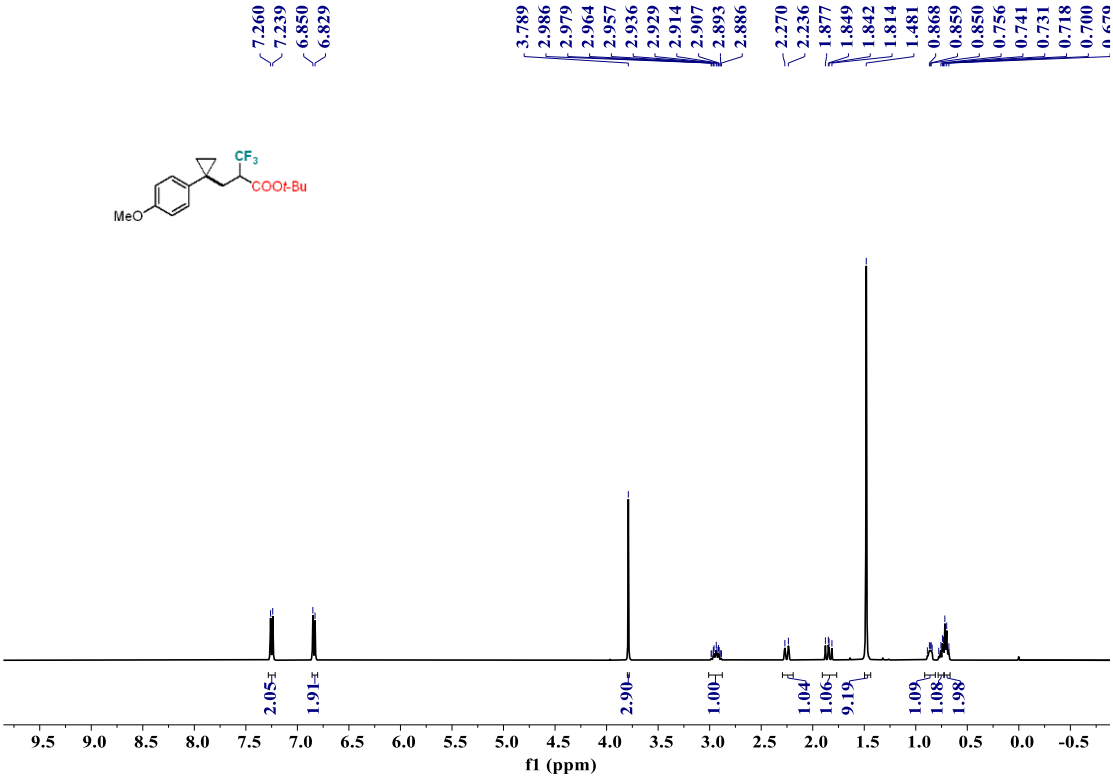


Figure S13. ^{1}H NMR of Compound **3e** (400 MHz, $CDCl_3$)

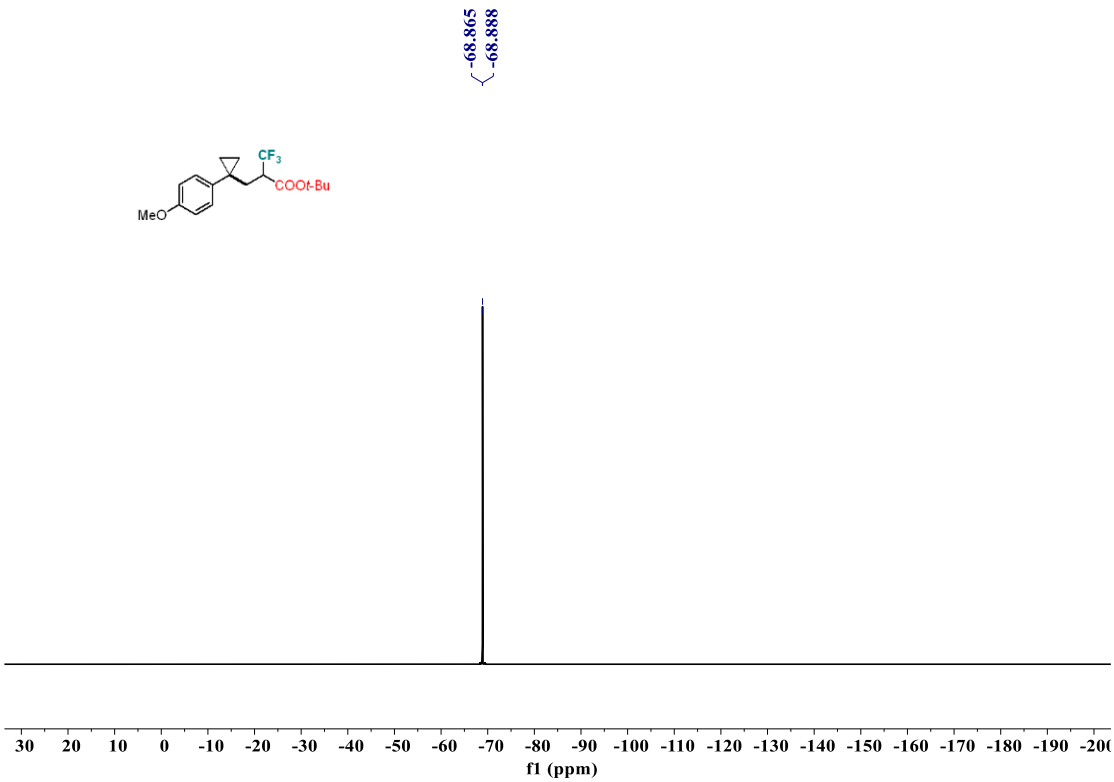


Figure S14. ^{19}F NMR of Compound **3e** (376 MHz, $CDCl_3$)

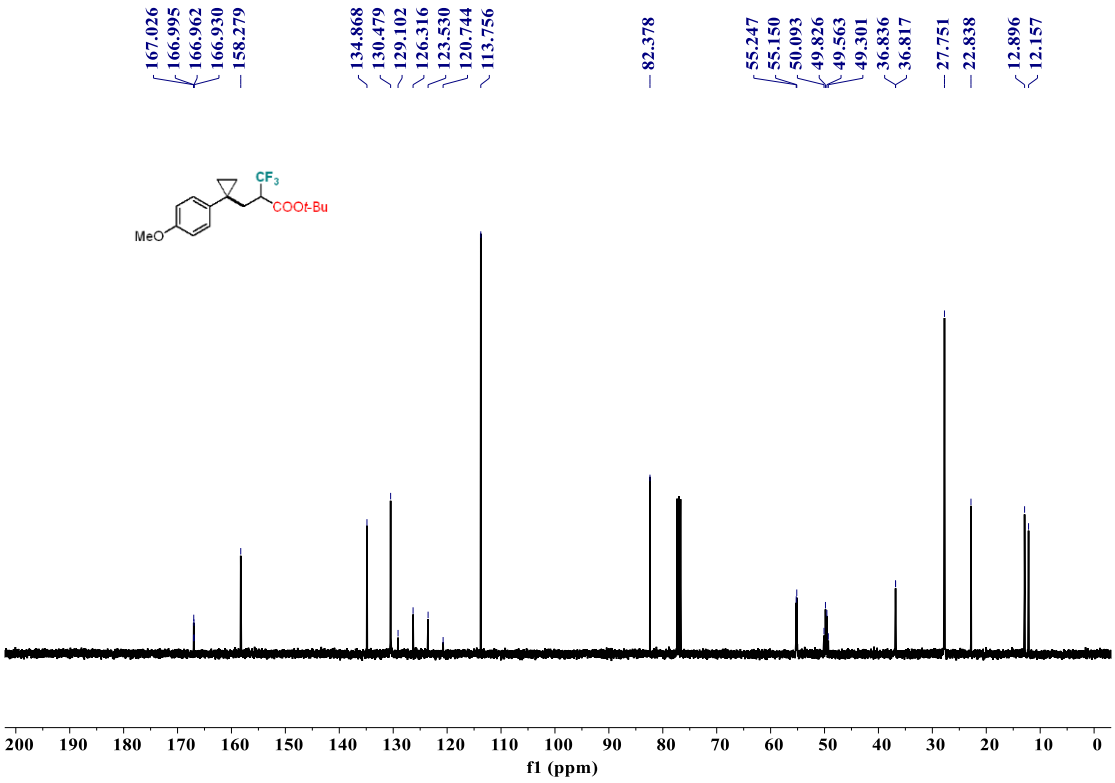


Figure S15. ^{13}C NMR of Compound **3e** (101 MHz, $CDCl_3$)

***tert*-butyl 3,3,3-trifluoro-2-((tetrahydro-2*H*-pyran-4-yl)methyl)propanoate (3f)**

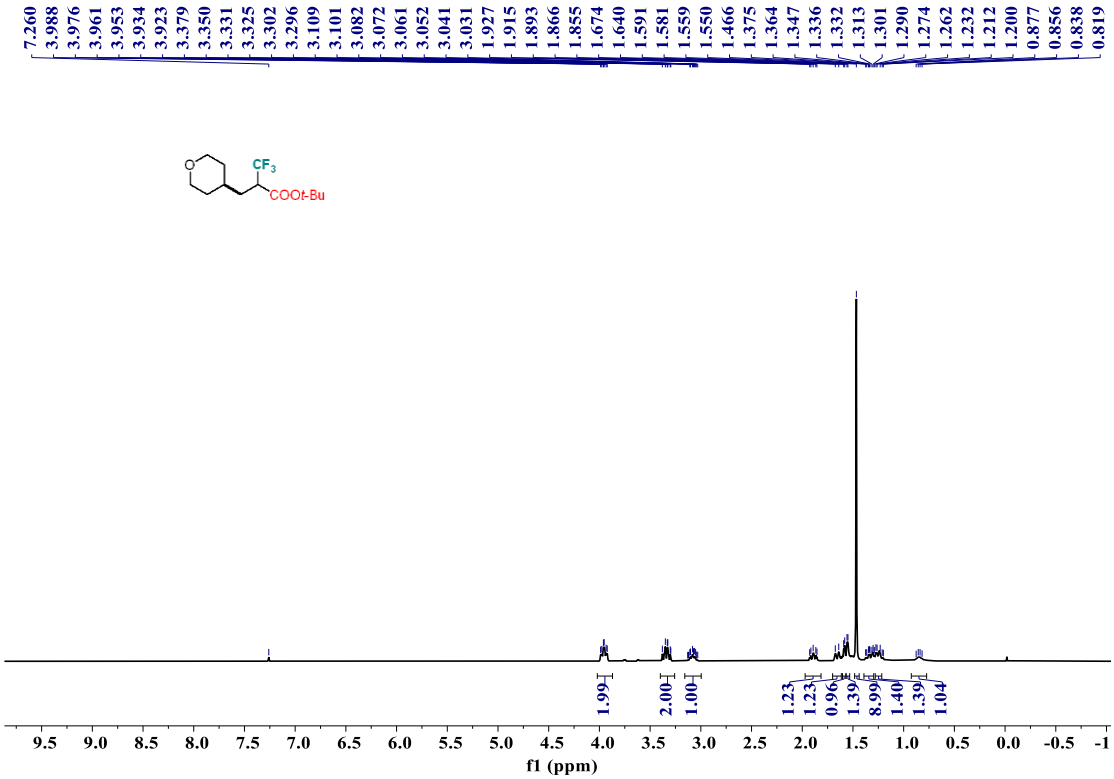


Figure S16. ^{1}H NMR of Compound **3f** (400 MHz, $CDCl_3$)

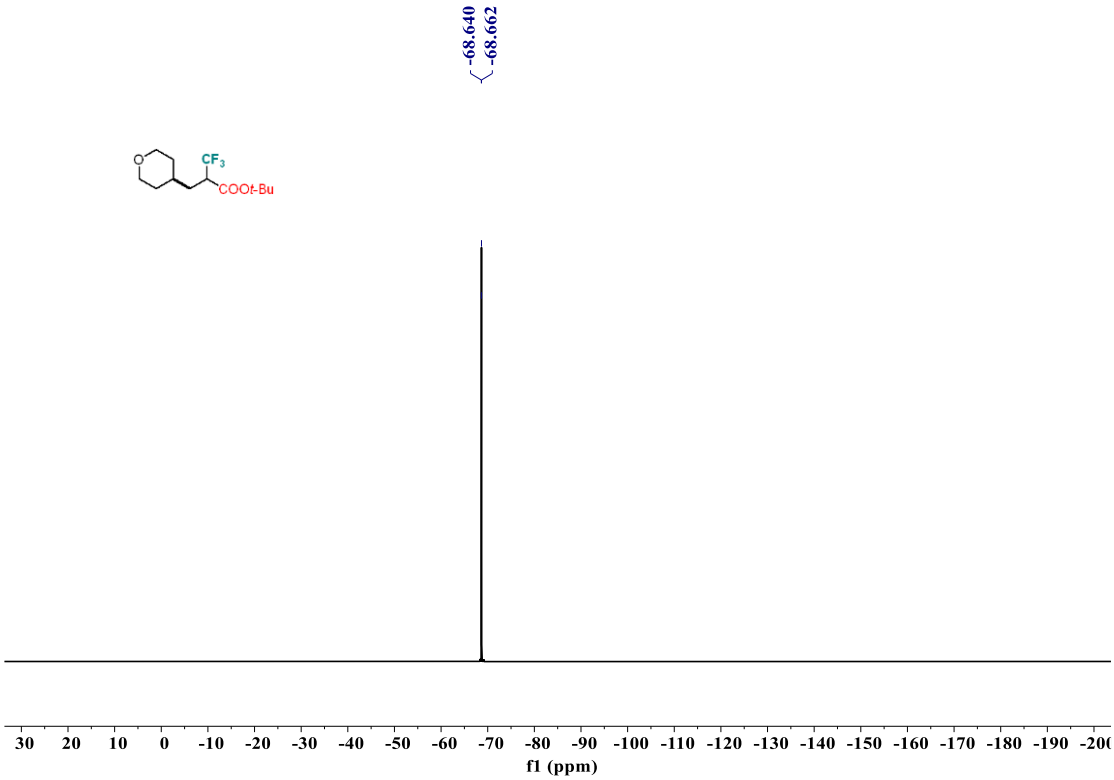


Figure S17. ^{19}F NMR of Compound **3f** (376 MHz, $CDCl_3$)

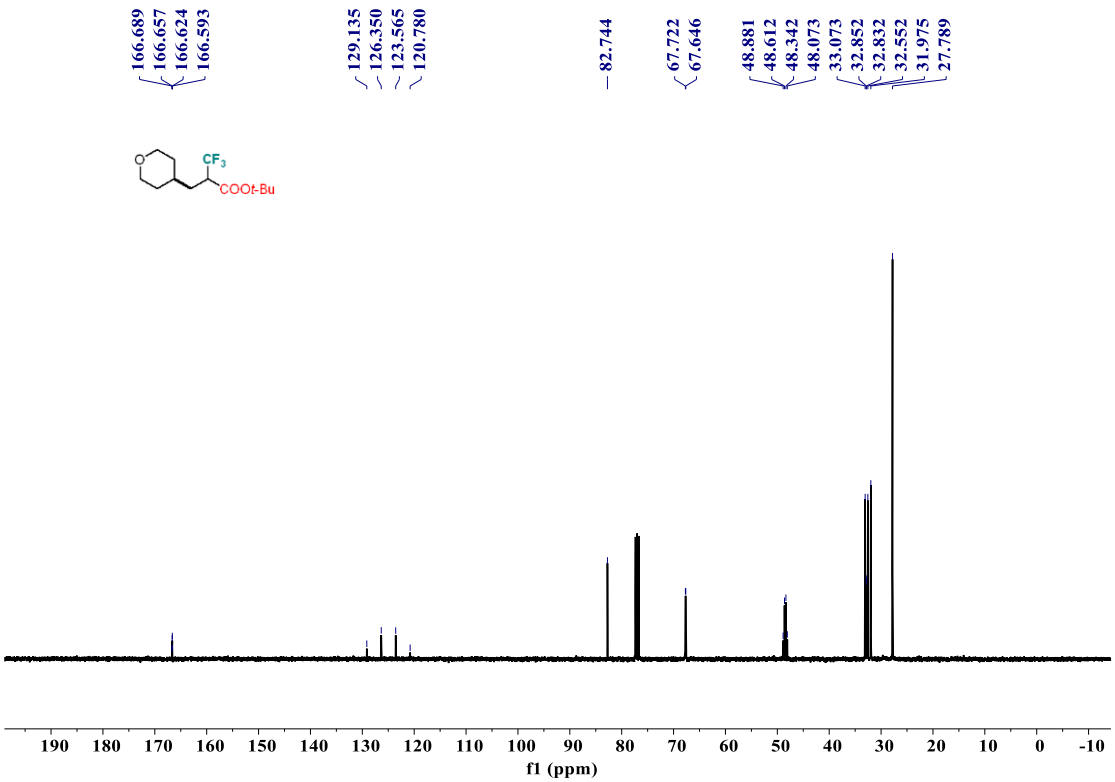


Figure S18. ^{13}C NMR of Compound **3f** (101 MHz, $CDCl_3$)

***tert*-butyl 4-(2-(*tert*-butoxycarbonyl)-3,3,3-trifluoropropyl)piperidine-1-carboxylate (3g)**

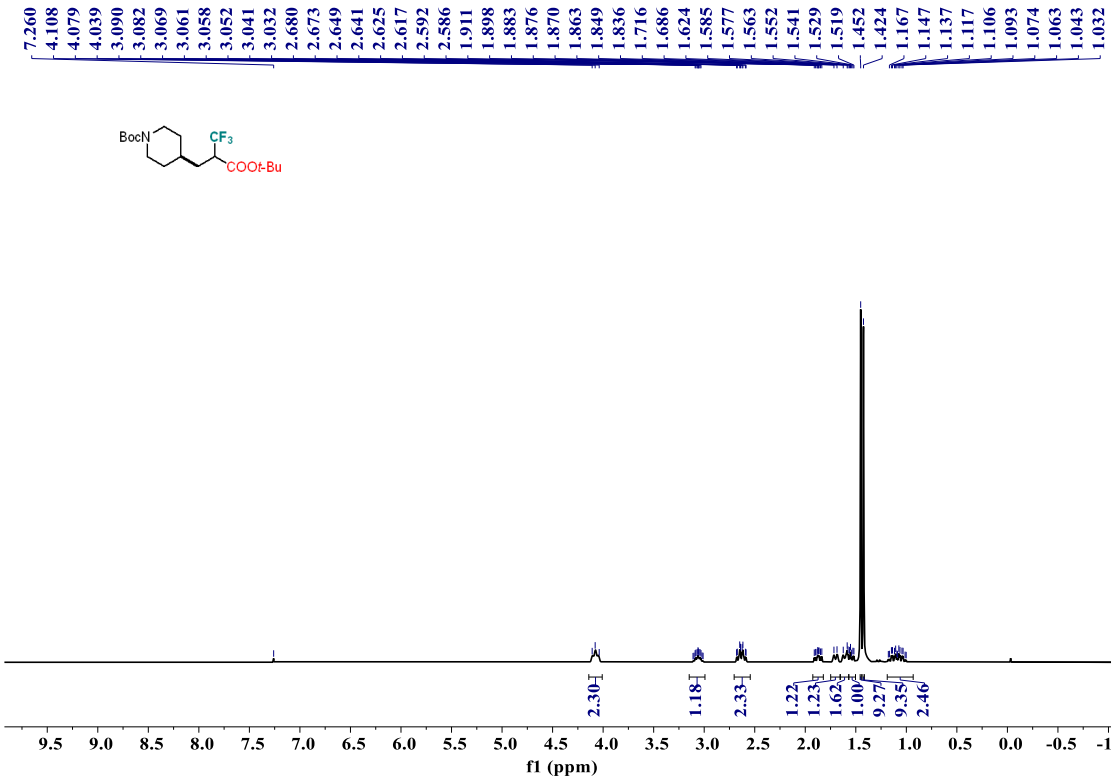


Figure S19. ^{1}H NMR of Compound **3g** (400 MHz, $CDCl_3$)

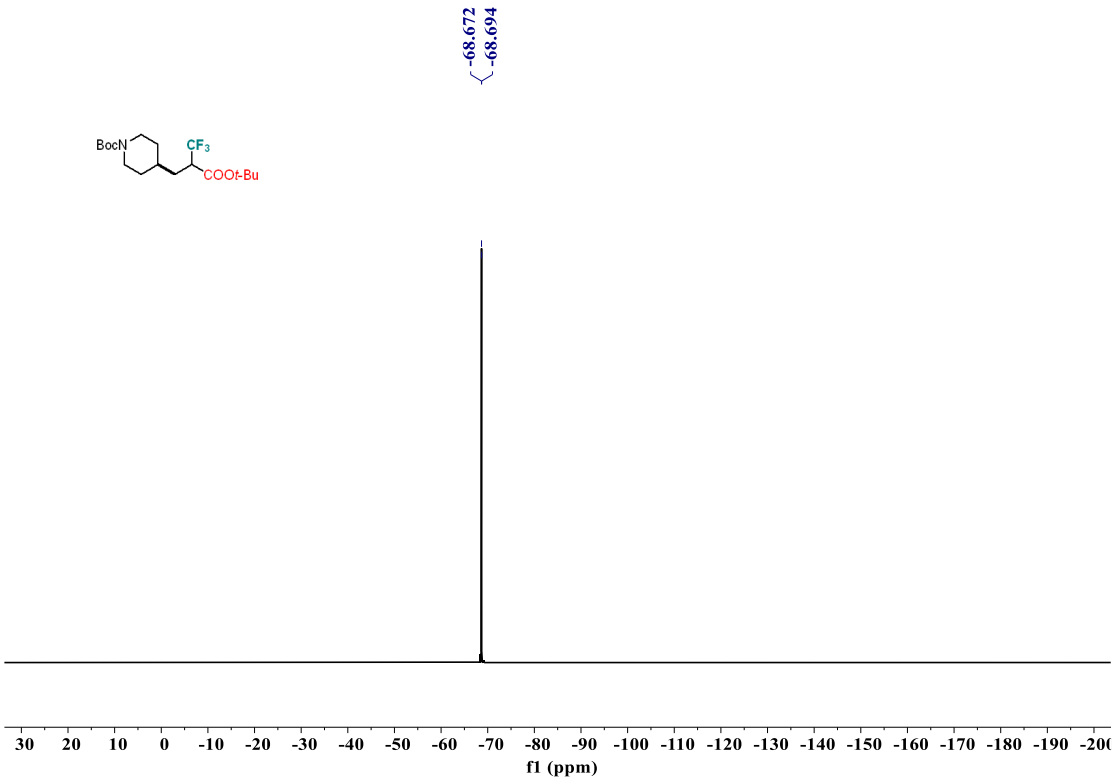


Figure S20. ^{19}F NMR of Compound **3g** (376 MHz, $CDCl_3$)

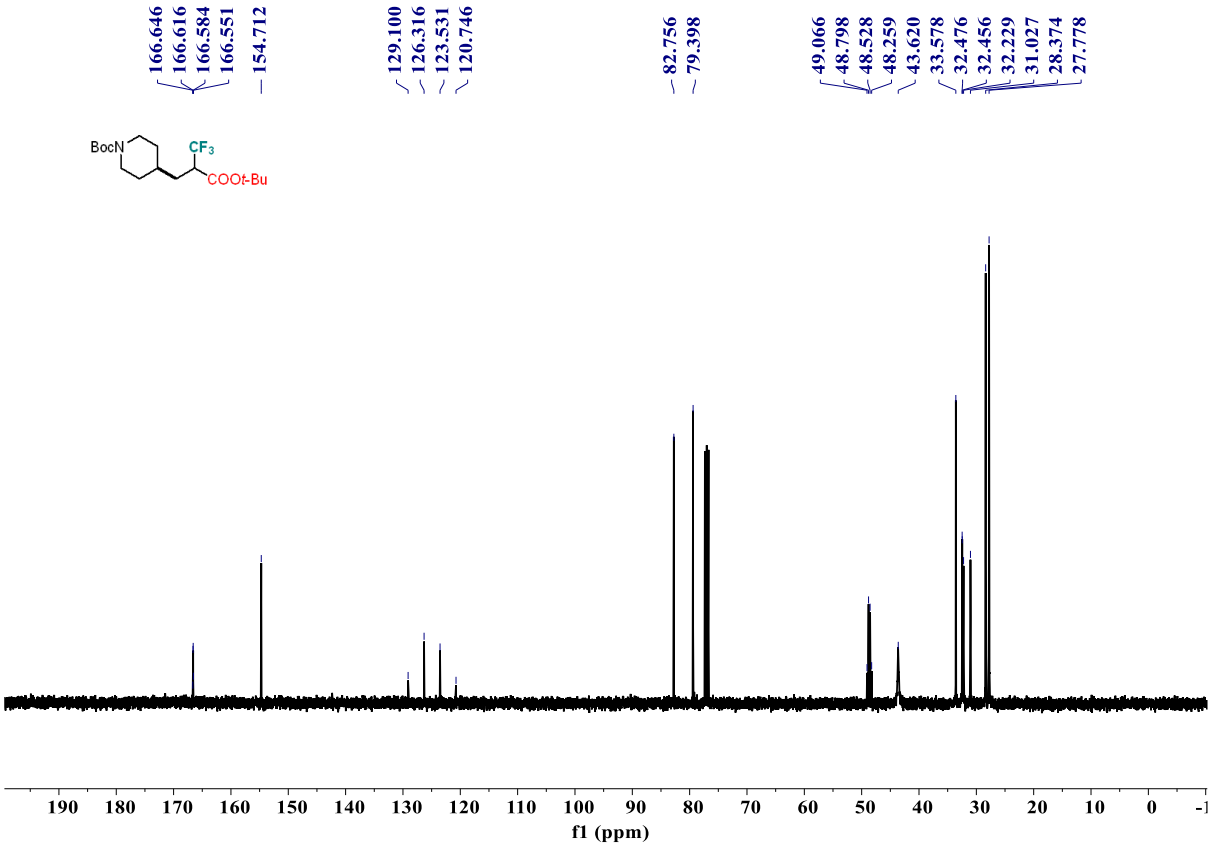


Figure S21. ^{13}C NMR of Compound **3g** (101 MHz, $CDCl_3$)

***tert*-butyl 6-phenyl-2-(trifluoromethyl)hexanoate (3h)**

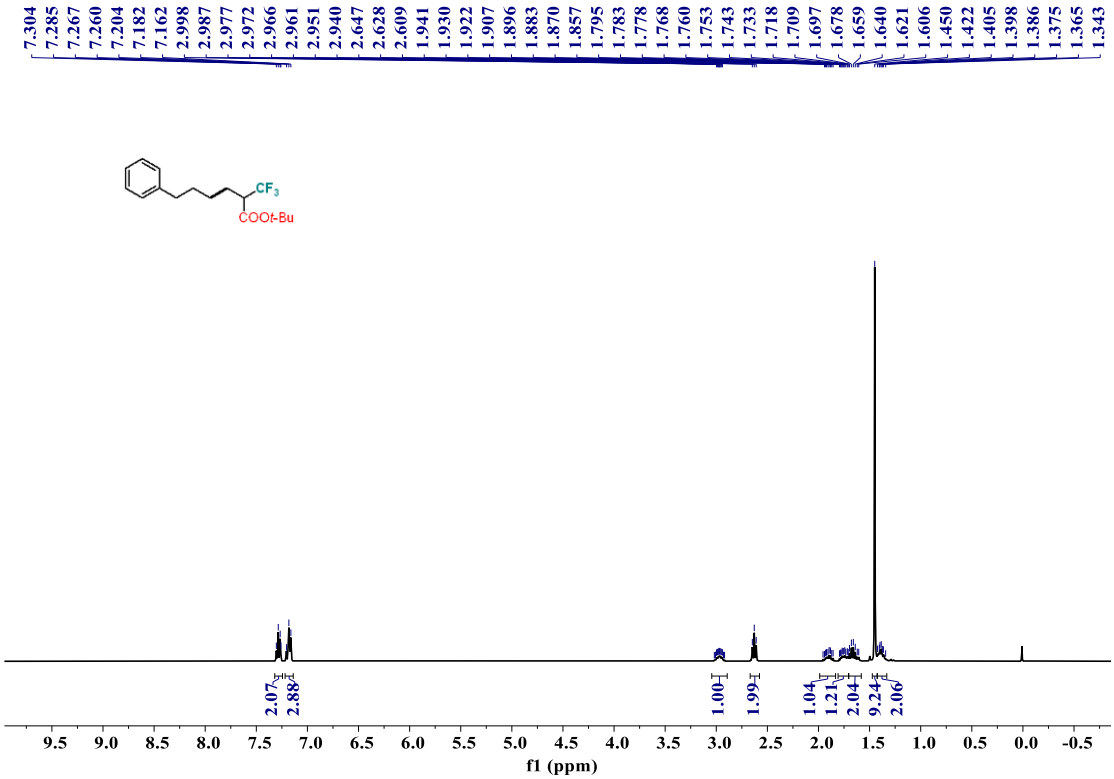


Figure S22. ^{1}H NMR of Compound **3h** (400 MHz, $CDCl_3$)

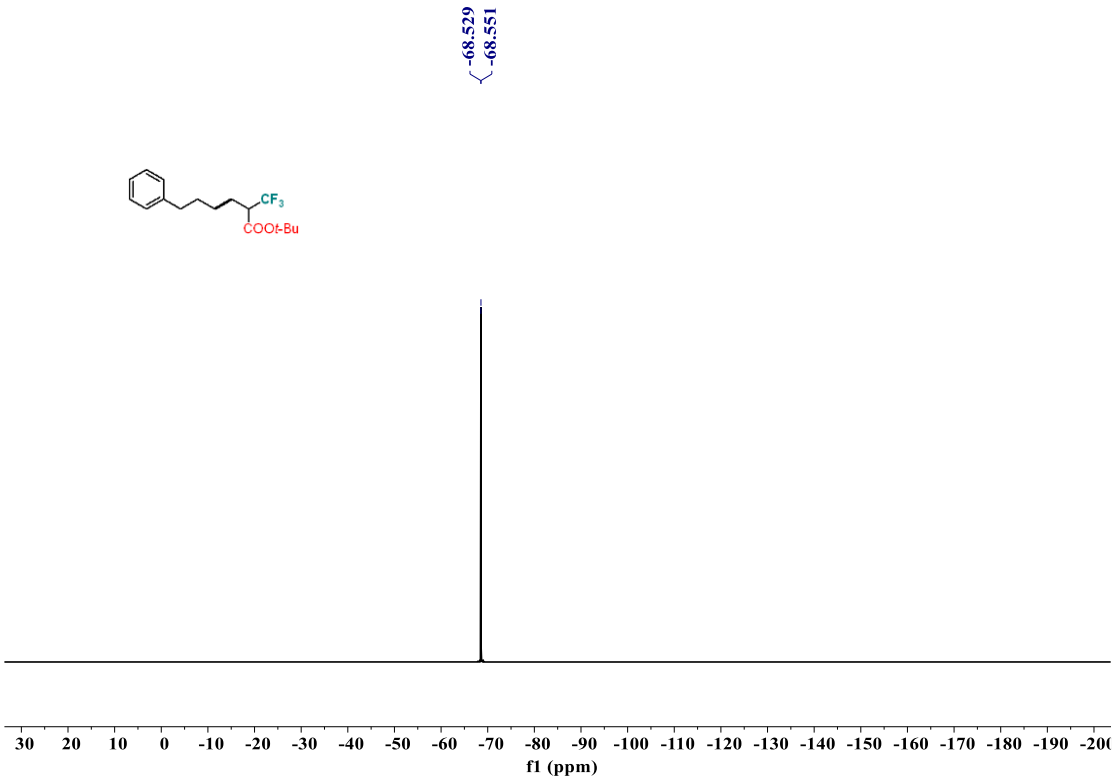


Figure S23. ^{19}F NMR of Compound **3h** (376 MHz, $CDCl_3$)

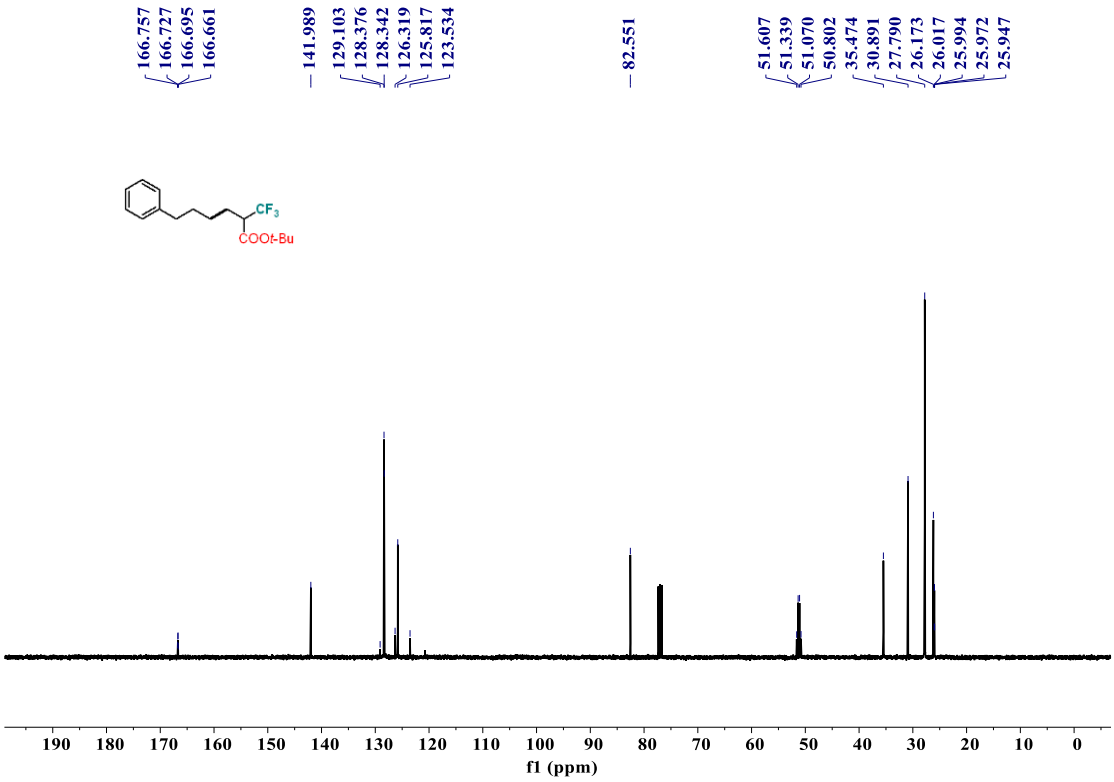


Figure S24. ^{13}C NMR of Compound **3h** (101 MHz, $CDCl_3$)

tert-butyl 5-(4-fluorophenyl)-2-(trifluoromethyl)pentanoate (3i)

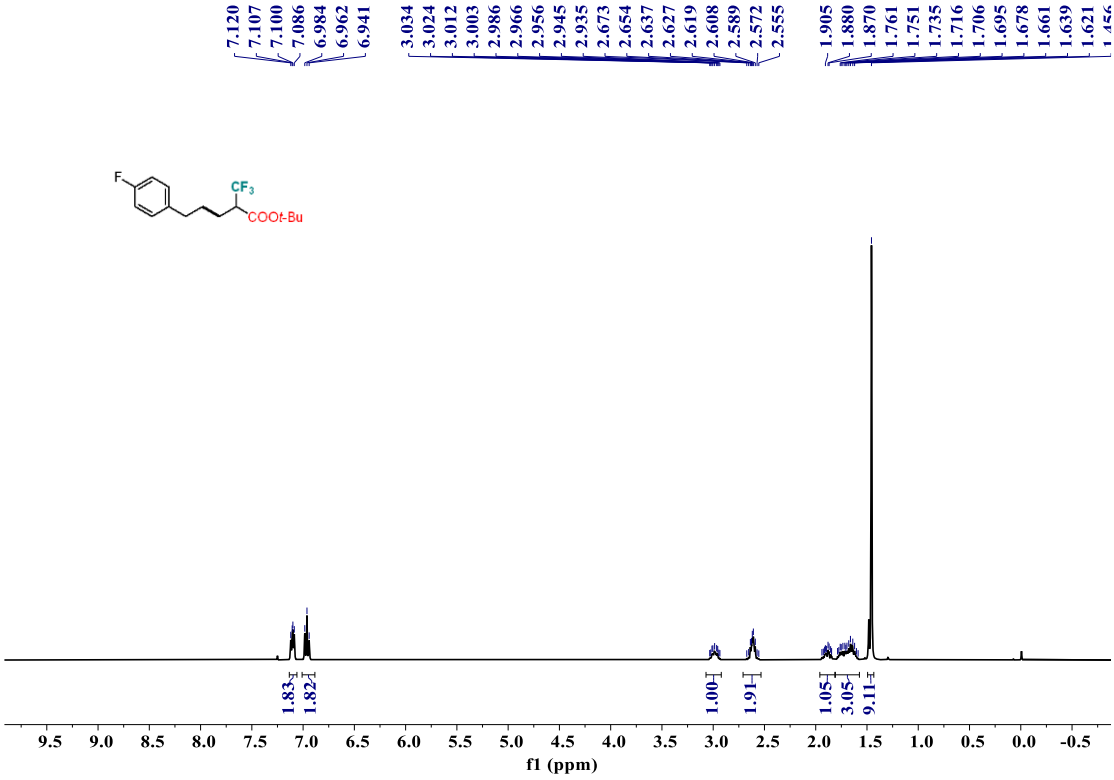


Figure S25. ^{1}H NMR of Compound **3i** (400 MHz, $CDCl_3$)

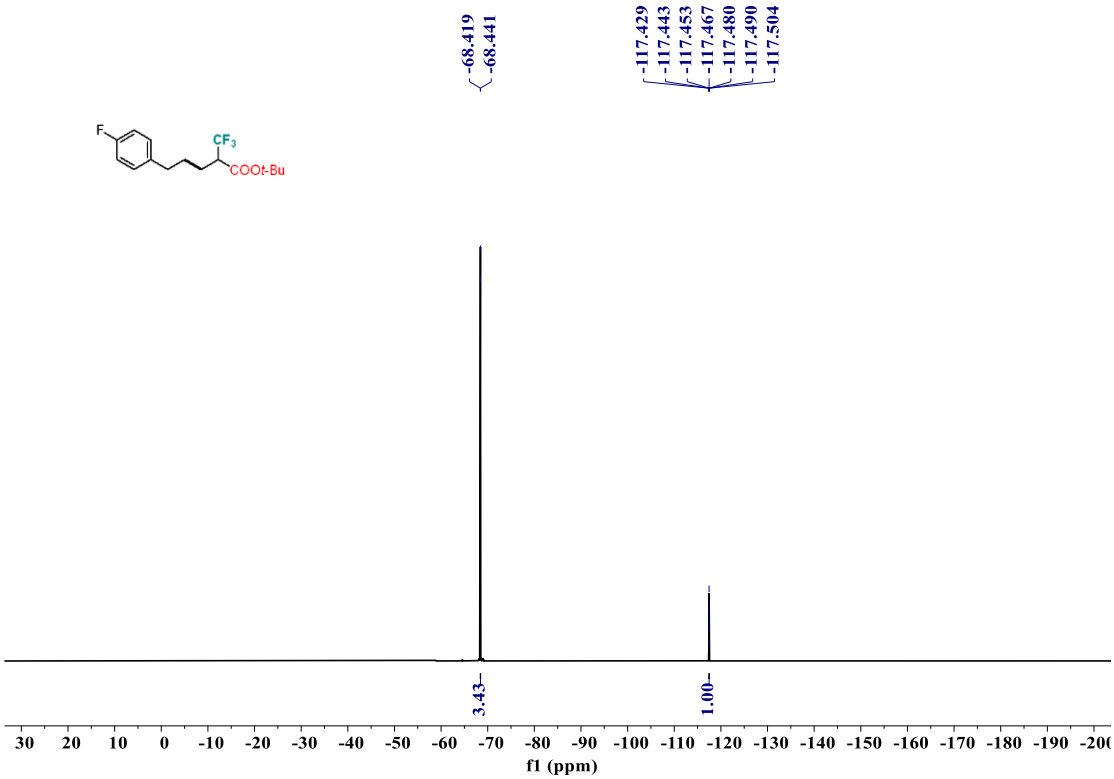


Figure S26. ^{19}F NMR of Compound **3i** (376 MHz, $CDCl_3$)

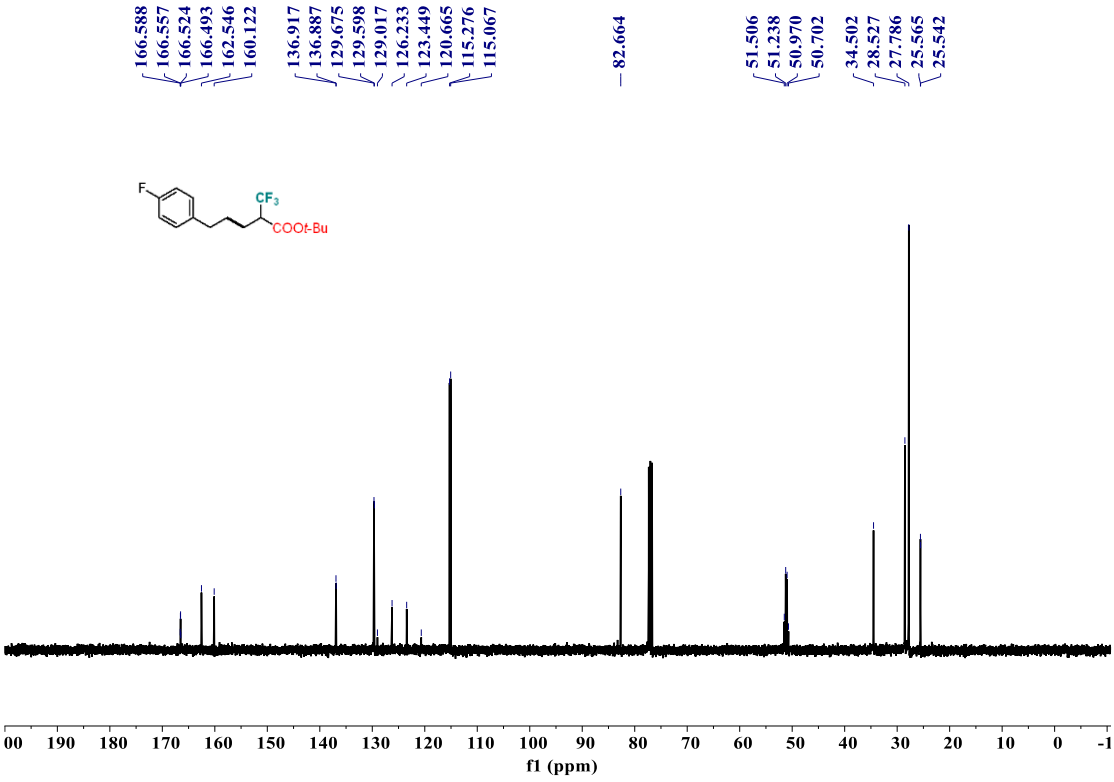


Figure S27. ^{13}C NMR of Compound **3i** (101 MHz, $CDCl_3$)

***tert*-butyl 5-(4-chlorophenyl)-2-(trifluoromethyl)pentanoate (3j)**

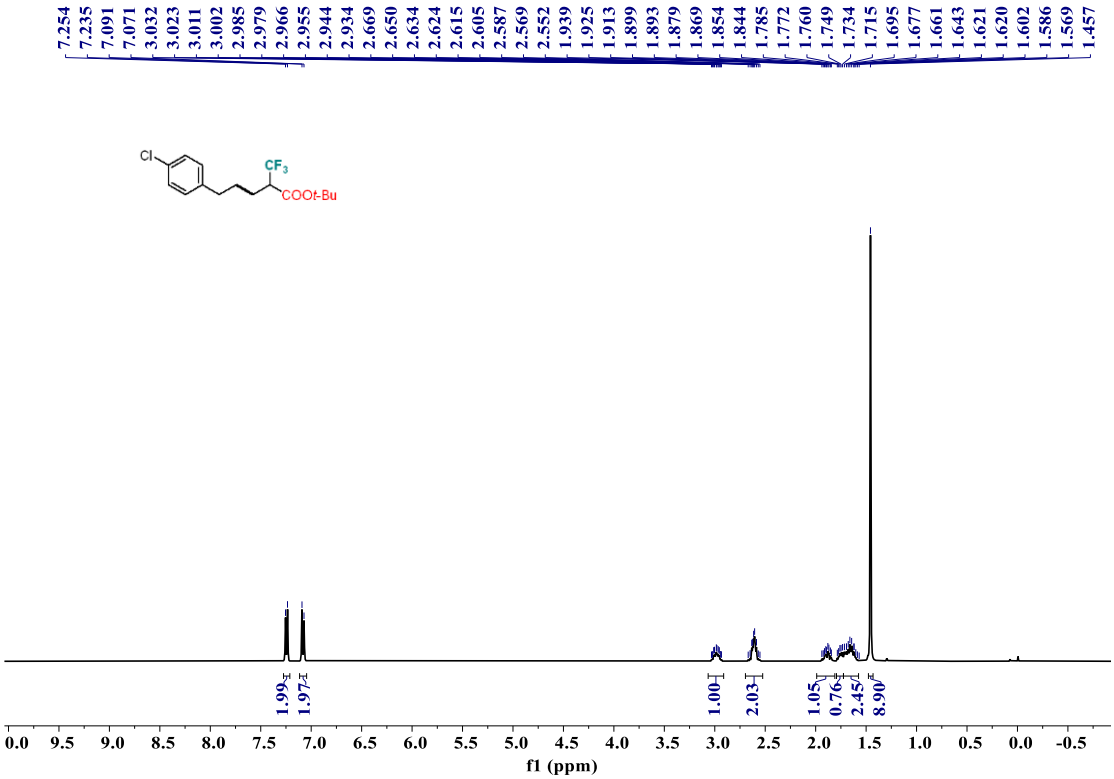


Figure S28. ^{1}H NMR of Compound **3j** (400 MHz, $CDCl_3$)

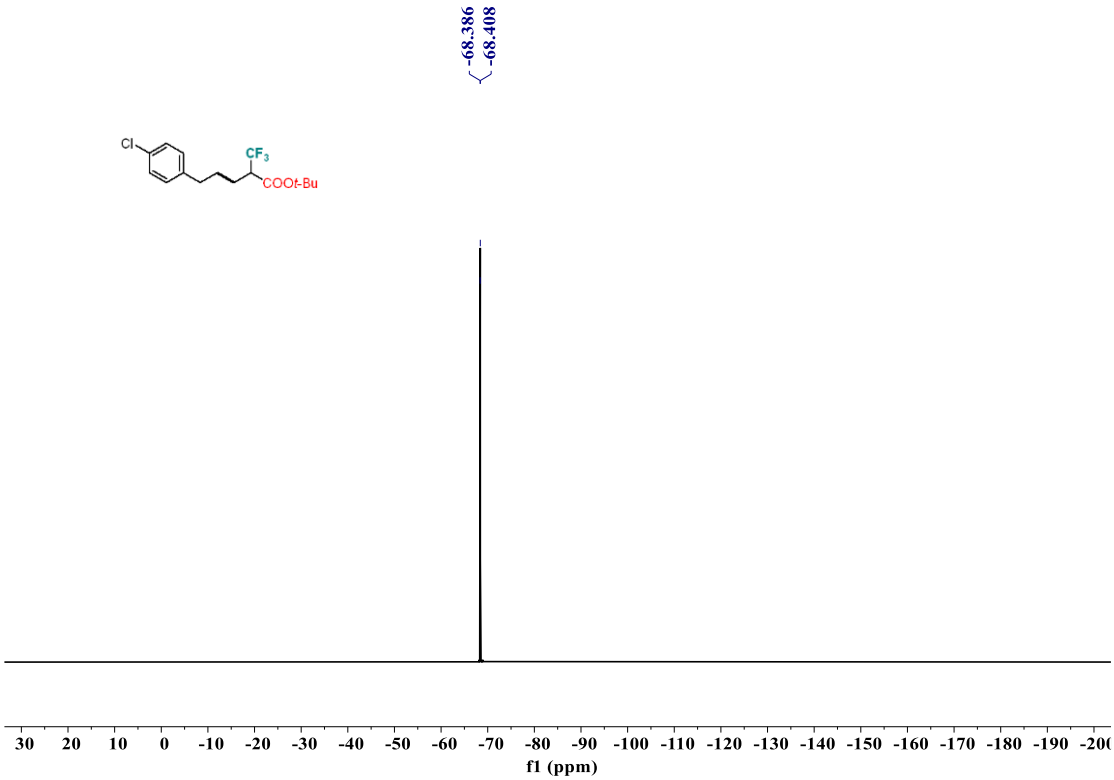


Figure S29. ^{19}F NMR of Compound **3j** (376 MHz, $CDCl_3$)

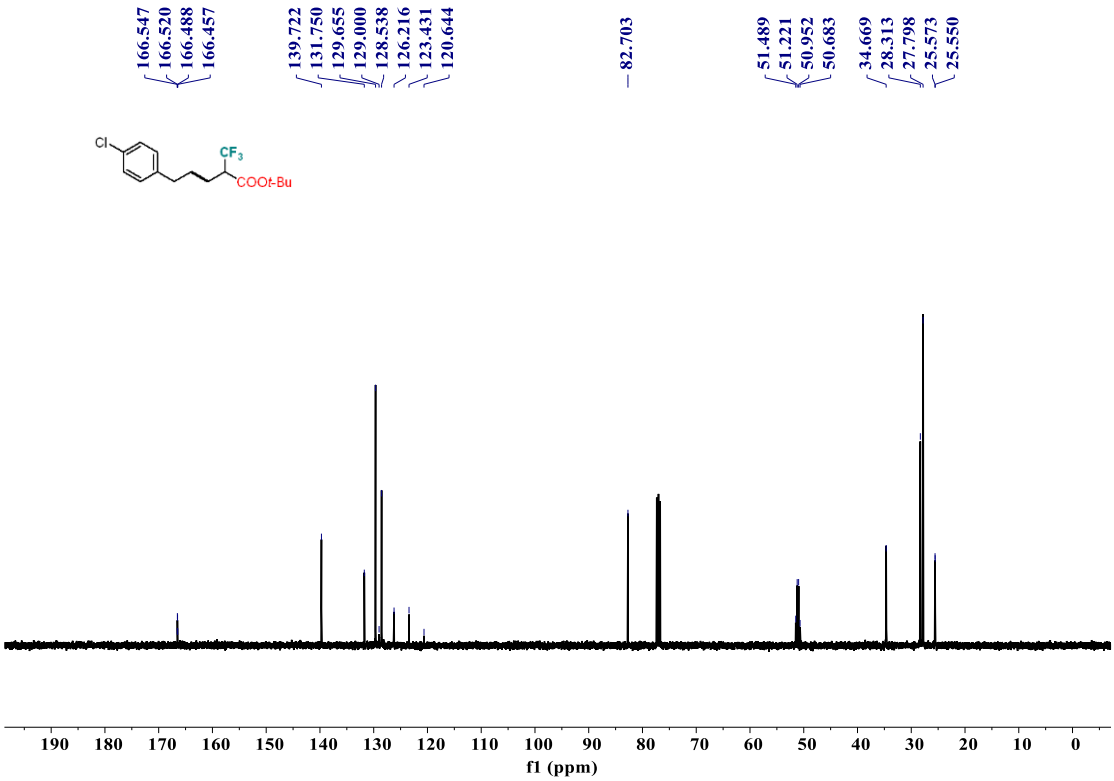


Figure S30. ^{13}C NMR of Compound **3j** (101 MHz, $CDCl_3$)

tert-butyl 5-(4-bromophenyl)-2-(trifluoromethyl)pentanoate (3k)

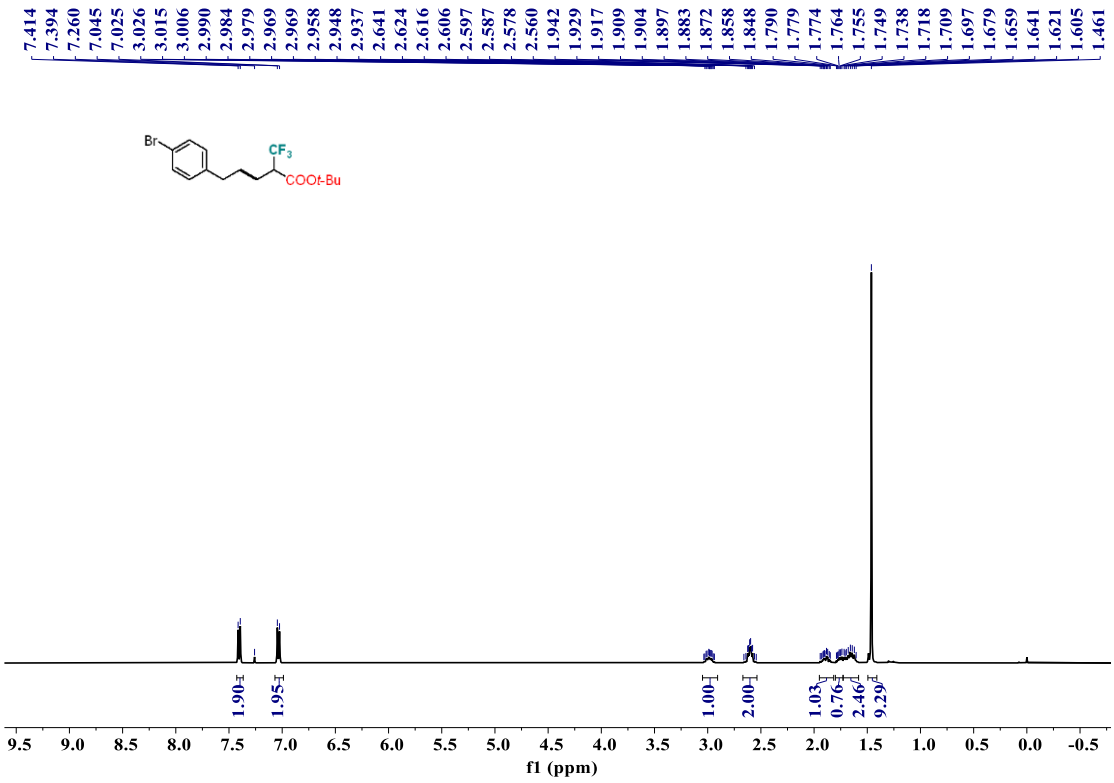


Figure S31. ^{1}H NMR of Compound **3k** (400 MHz, $CDCl_3$)

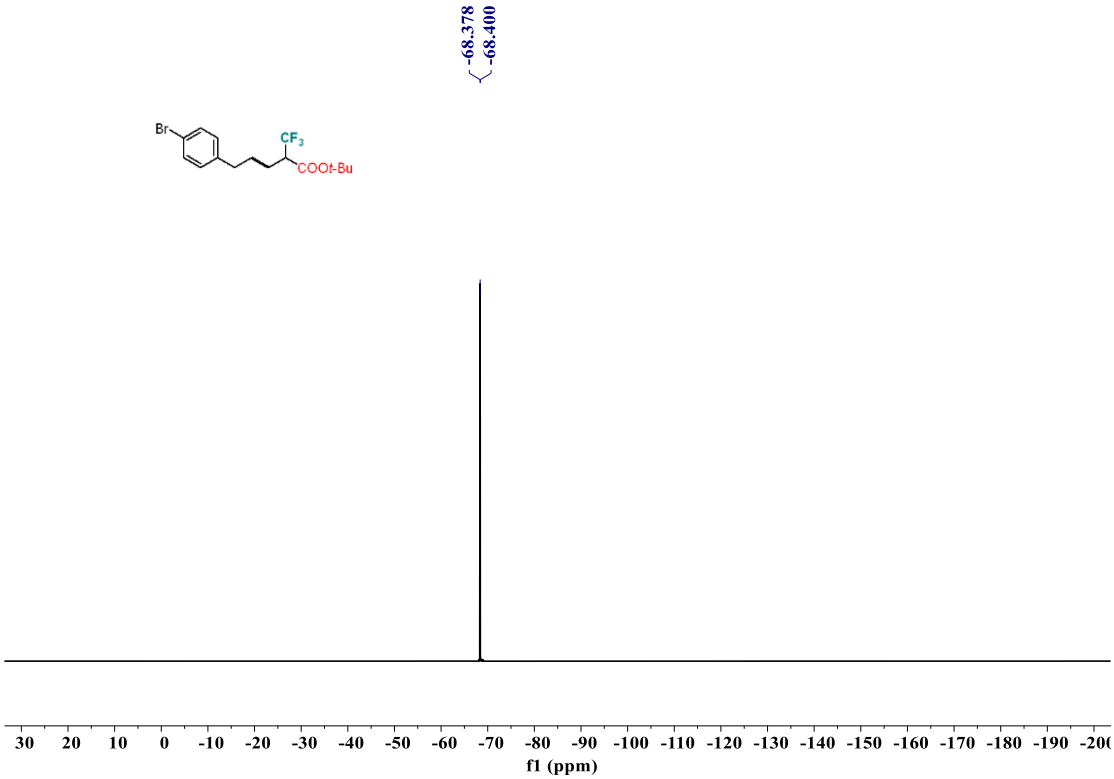


Figure S32. ^{19}F NMR of Compound **3k** (376 MHz, $CDCl_3$)

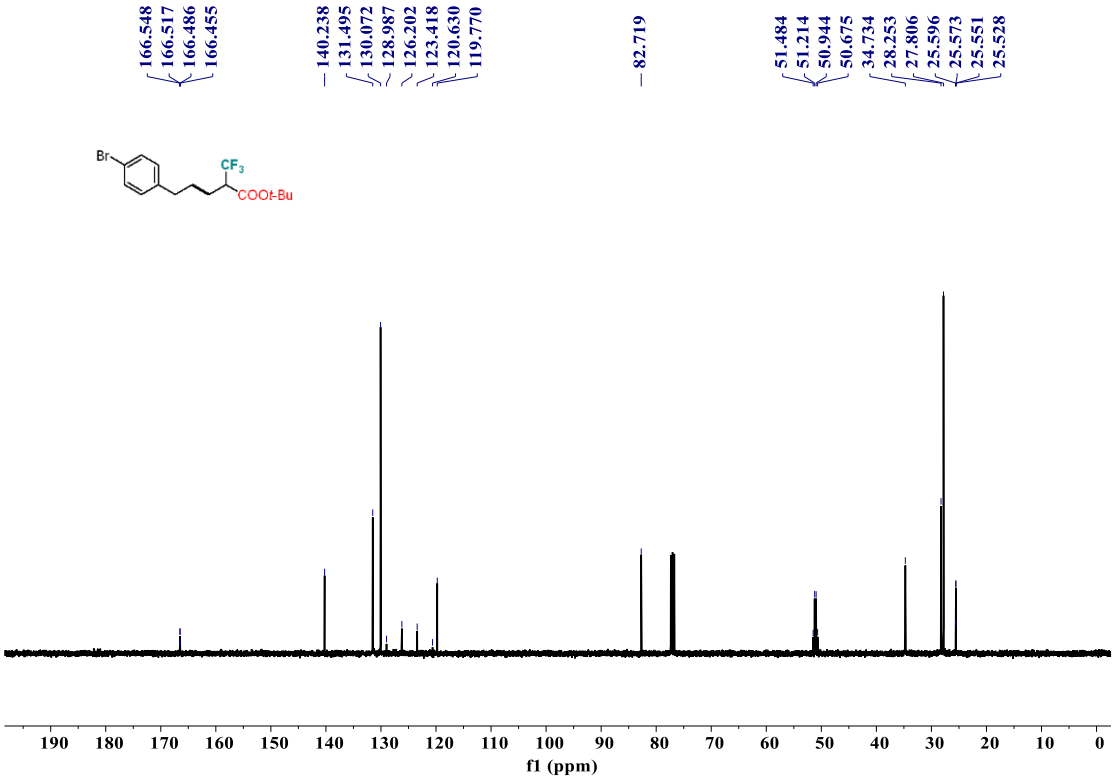


Figure S33. ^{13}C NMR of Compound **3k** (101 MHz, $CDCl_3$)

tert-butyl 5-cyclopentyl-2-(trifluoromethyl)pentanoate (3l)

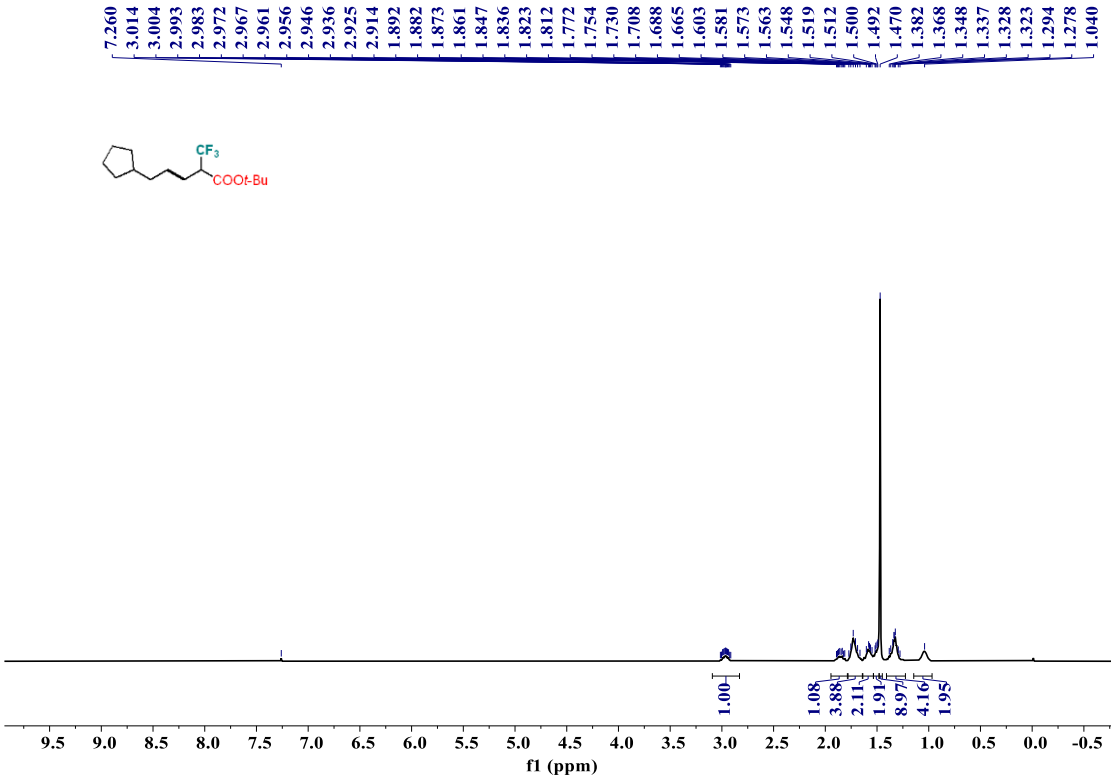


Figure S34. ^{1}H NMR of Compound **3l** (400 MHz, $CDCl_3$)

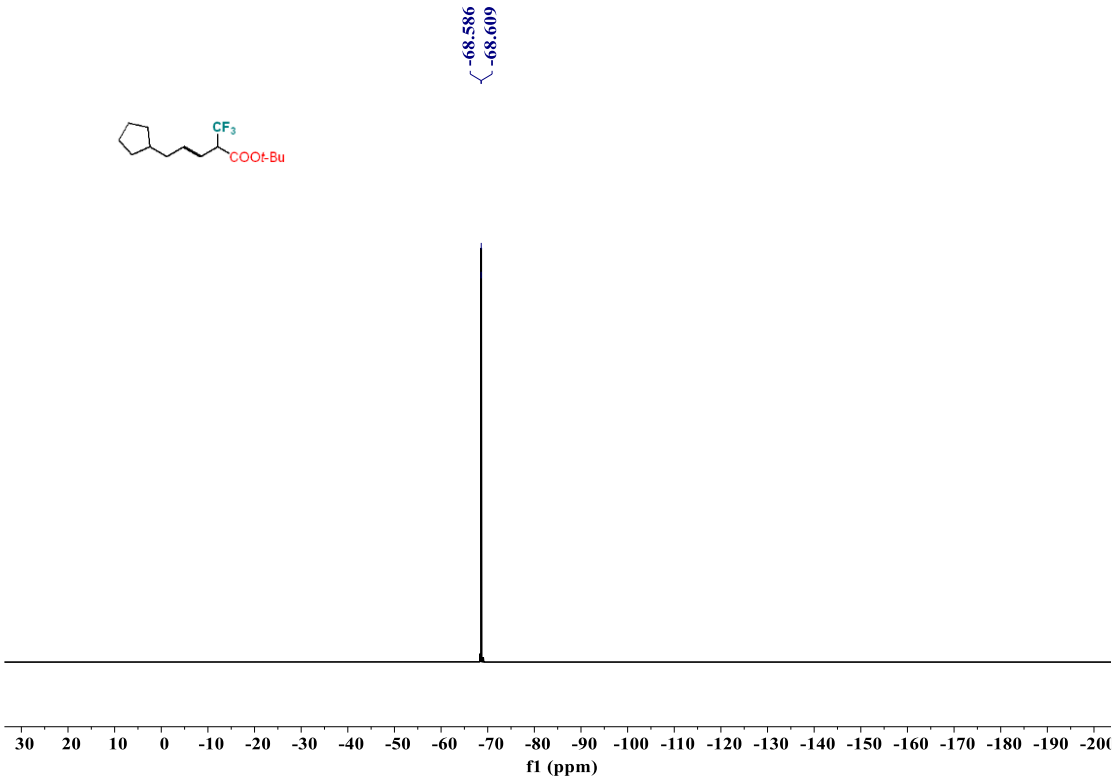


Figure S35. ^{19}F NMR of Compound **3l** (376 MHz, $CDCl_3$)

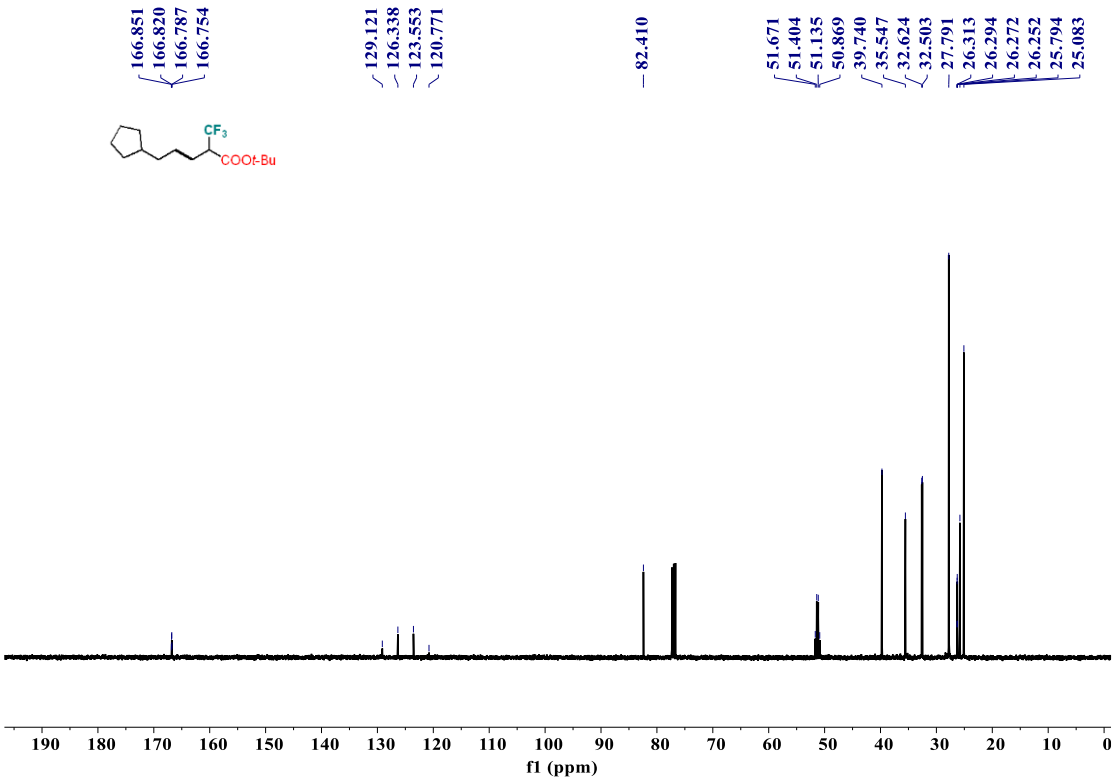


Figure S36. ^{13}C NMR of Compound **3l** (101 MHz, $CDCl_3$)

tert-butyl 4-(thiophen-3-yl)-2-(trifluoromethyl)butanoate (3m)

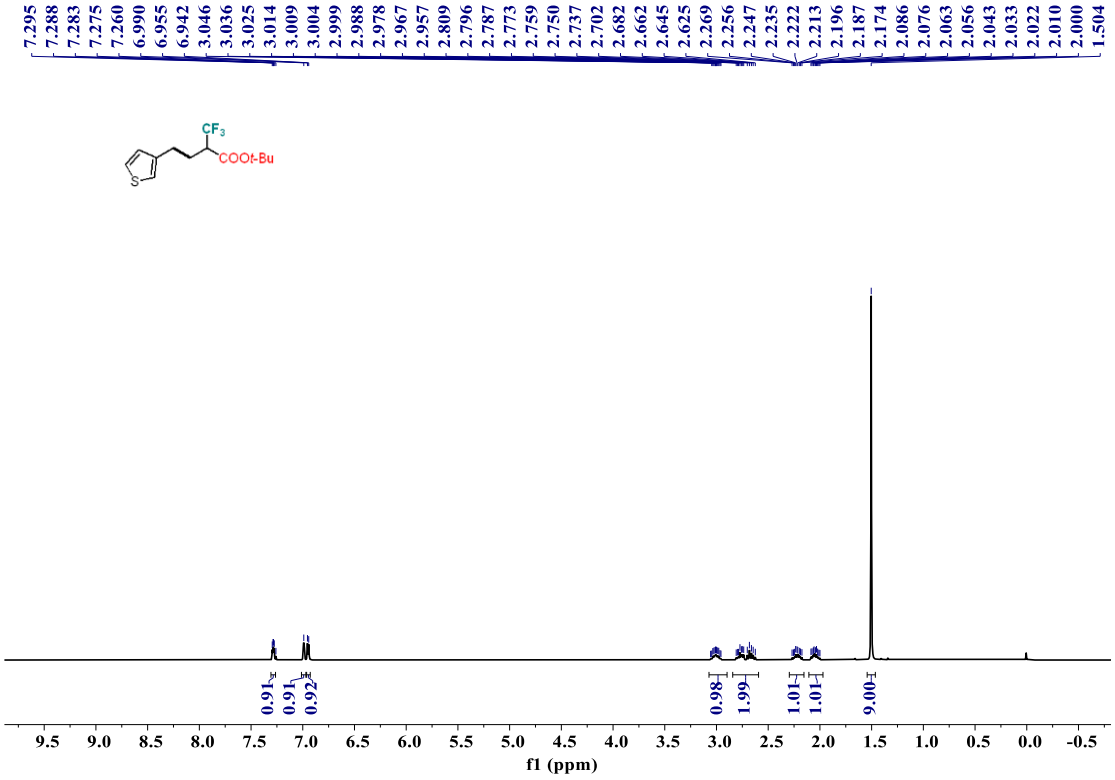


Figure S37. ^{1}H NMR of Compound **3m** (400 MHz, $CDCl_3$)

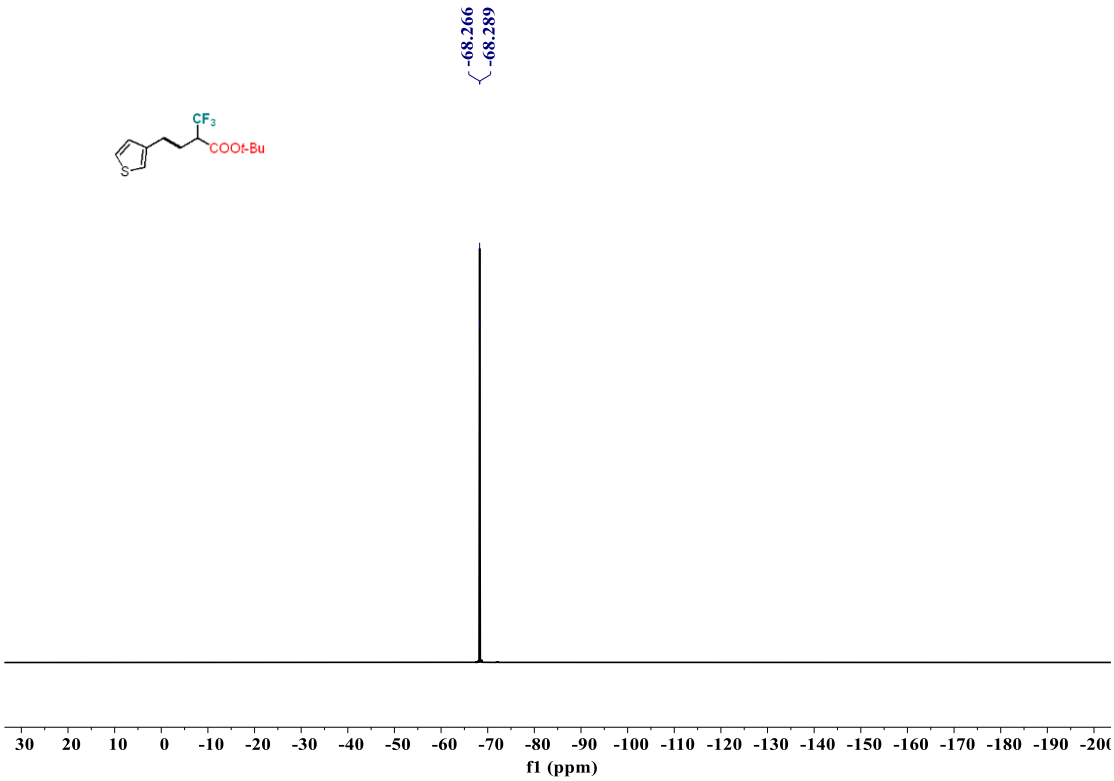


Figure S38. ^{19}F NMR of Compound **3m** (376 MHz, $CDCl_3$)

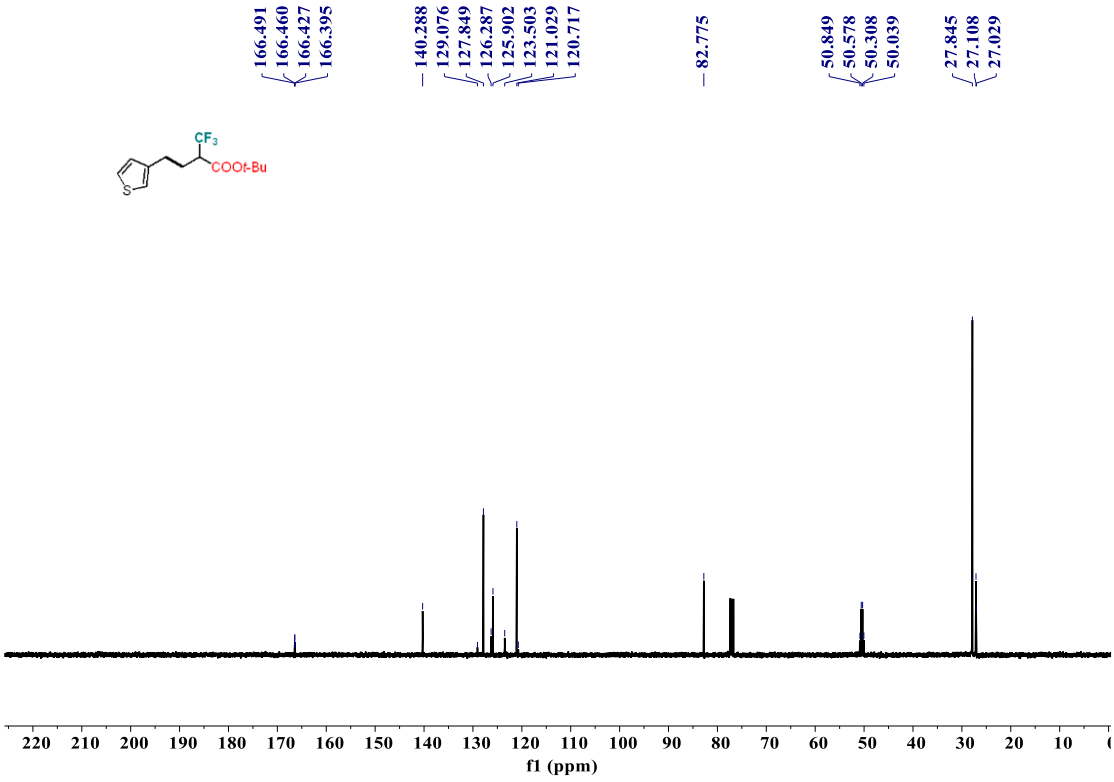


Figure S39. ^{13}C NMR of Compound **3m** (101 MHz, $CDCl_3$)

***tert*-butyl 4-(6-methoxynaphthalen-2-yl)-2-(trifluoromethyl)pentanoate (3nl)**

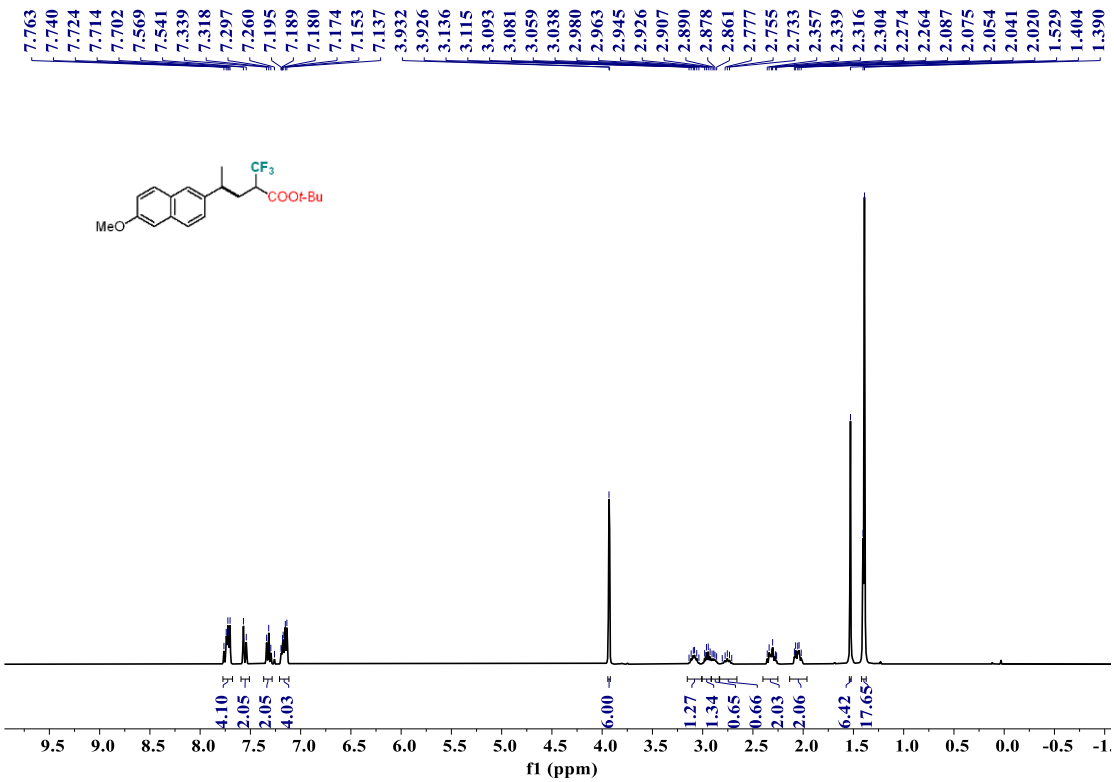


Figure S40. ^{1}H NMR of Compound **3n** (400 MHz, $CDCl_3$)

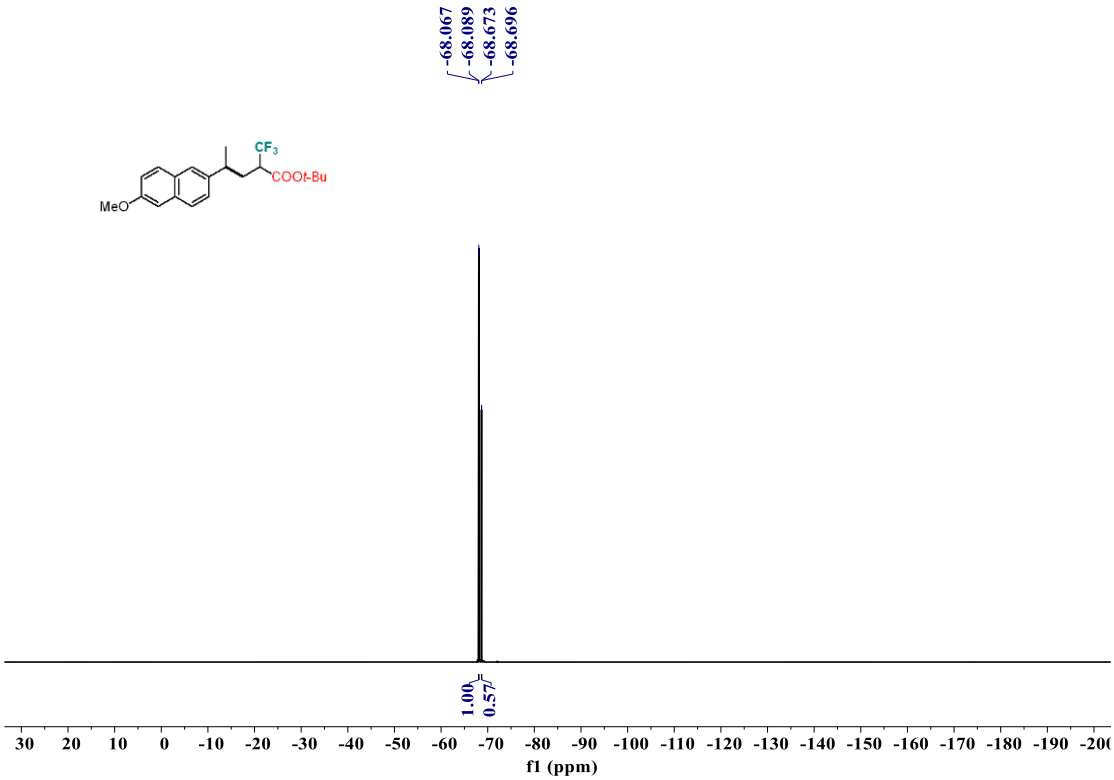


Figure S41. ^{19}F NMR of Compound **3n** (376 MHz, $CDCl_3$)

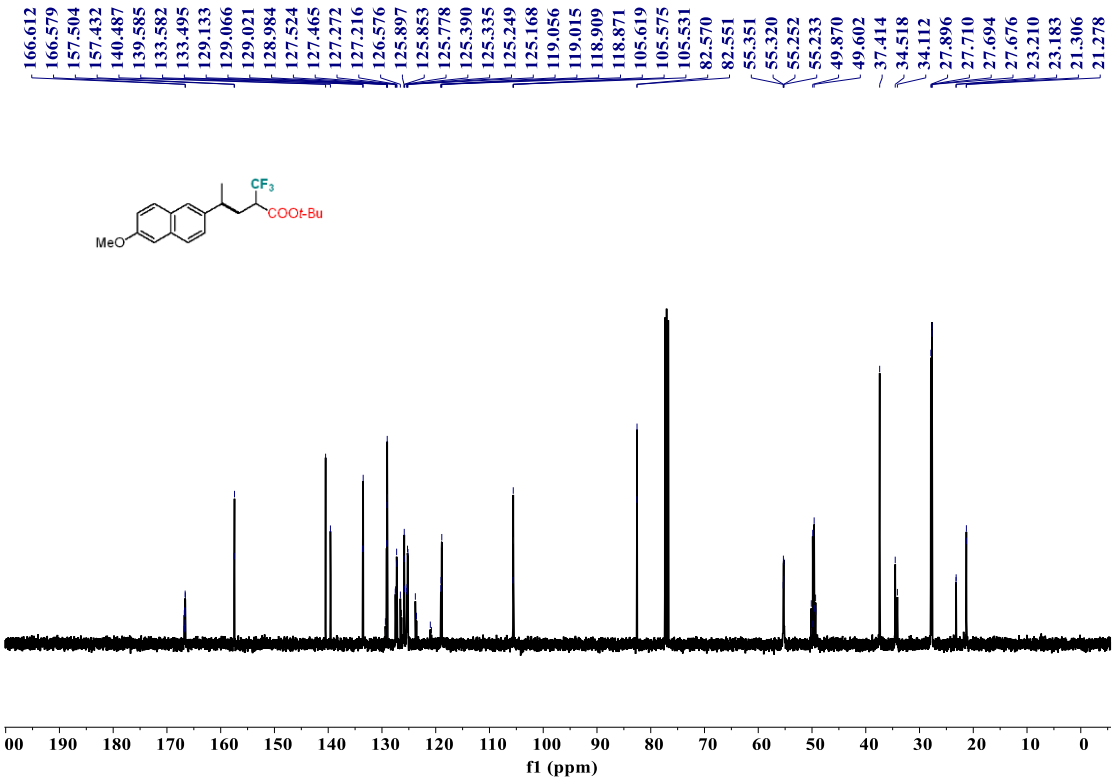


Figure S42. ^{13}C NMR of Compound **3n** (101 MHz, $CDCl_3$)

tert-butyl 4-(4-isobutylphenyl)-2-(trifluoromethyl)pentanoate (3o)

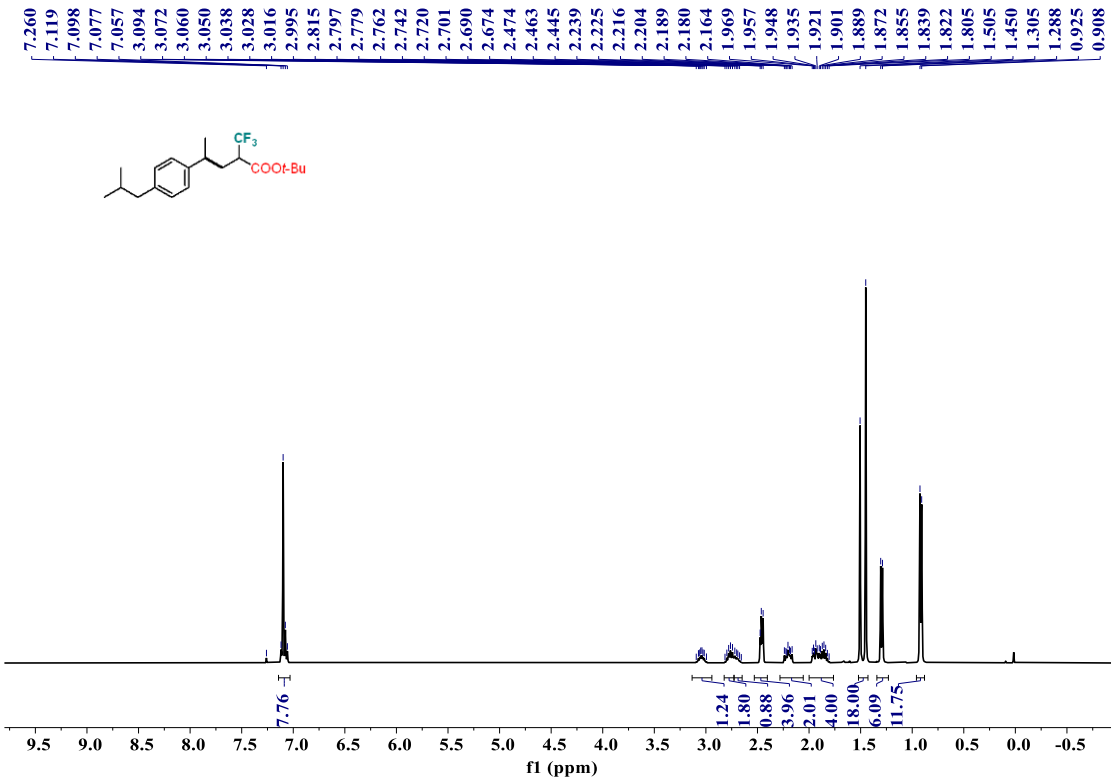


Figure S43. ^{1}H NMR of Compound **3o** (400 MHz, $CDCl_3$)

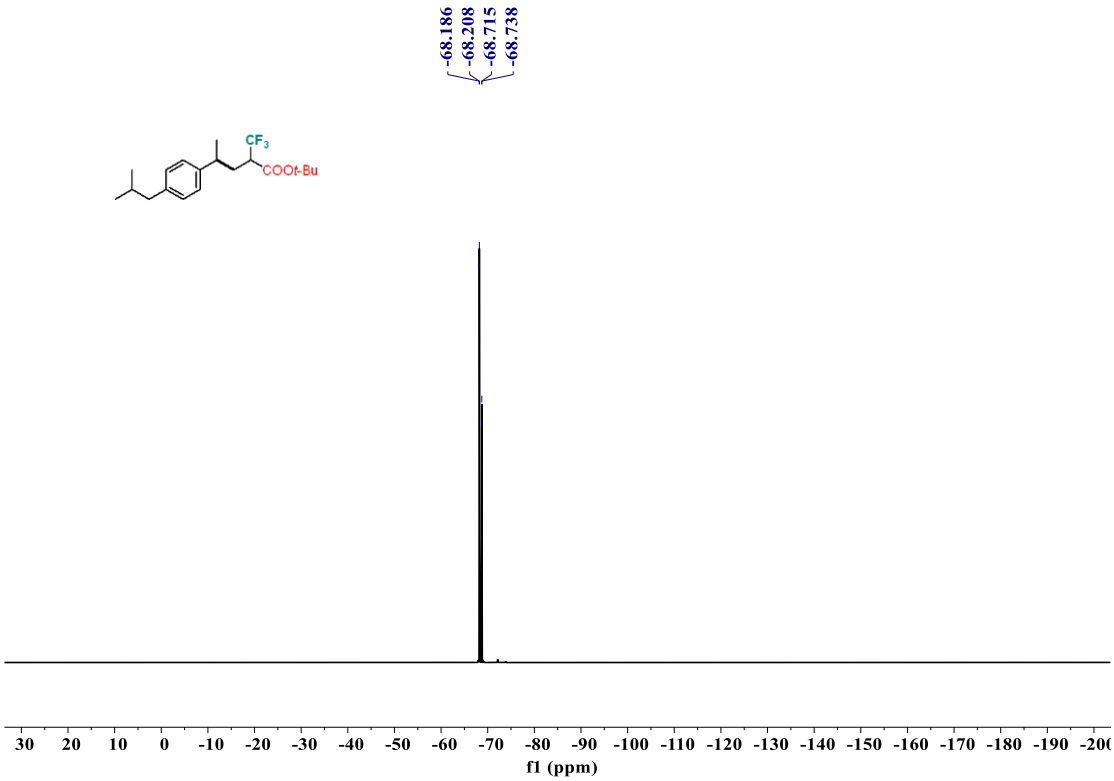


Figure S44. ^{19}F NMR of Compound **3o** (376 MHz, $CDCl_3$)

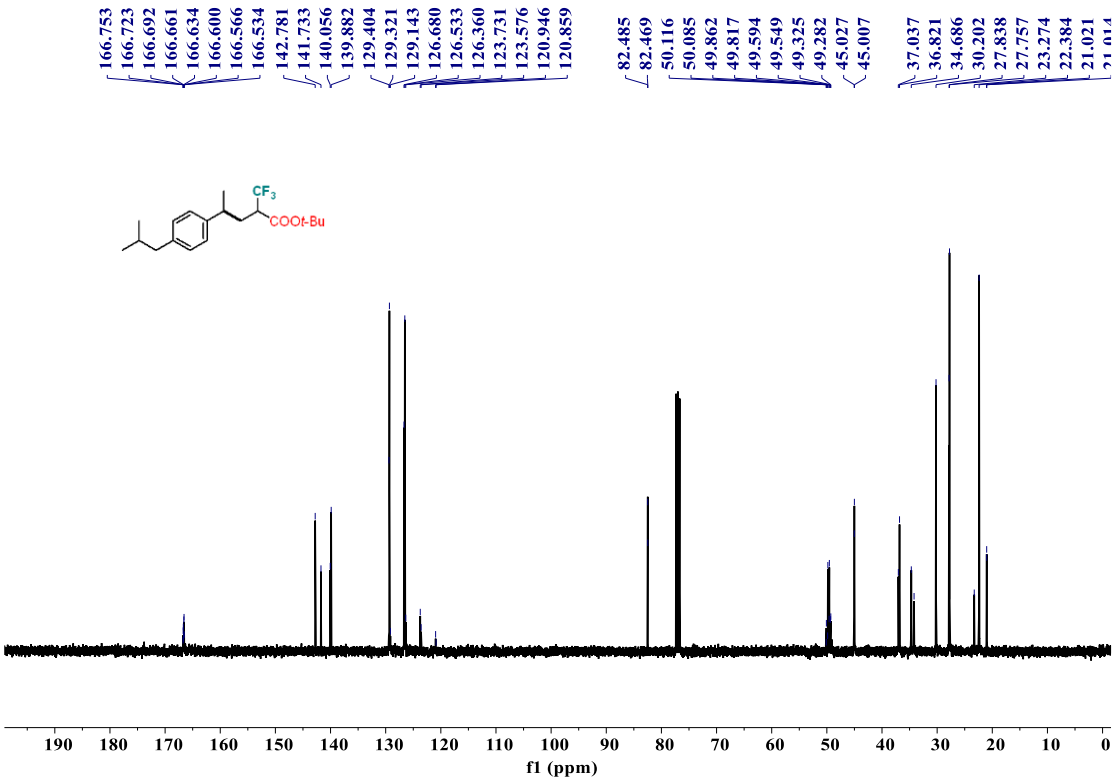


Figure S45. ^{13}C NMR of Compound **3o** (101 MHz, $CDCl_3$)

***tert*-butyl**
4-(11-oxo-6,11-dihydrodibenzo[b,e]oxepin-2-yl)-2-(trifluoromethyl)butanoate (3p)

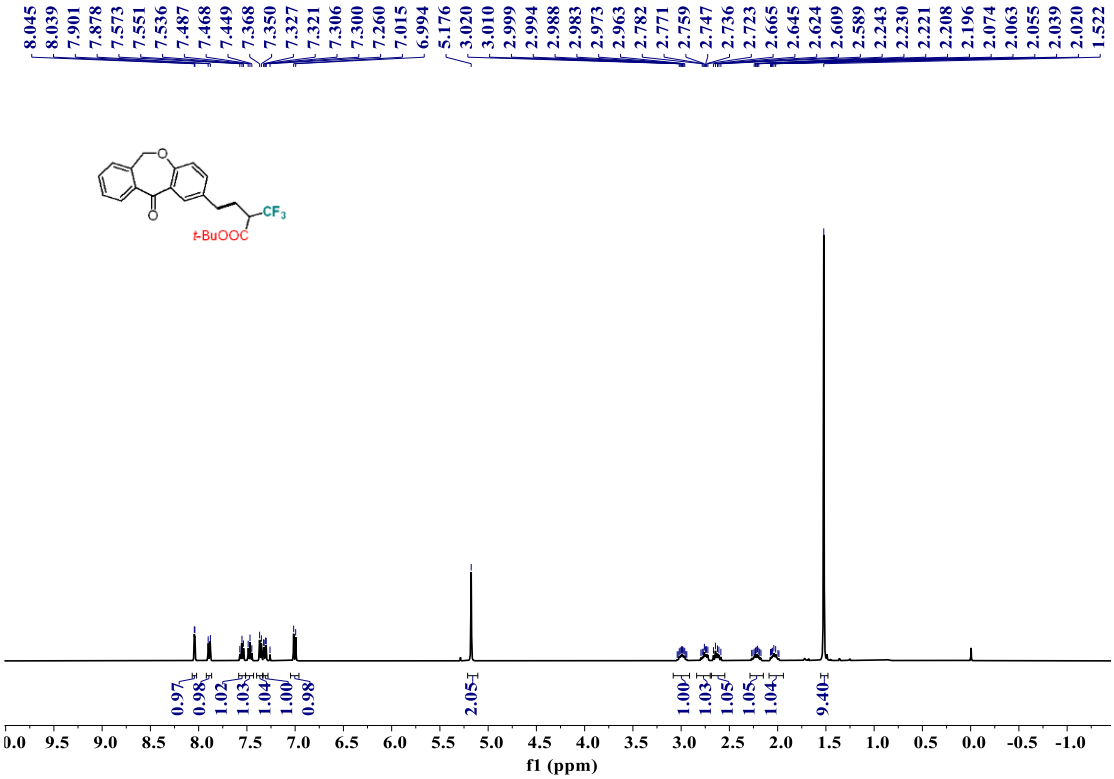


Figure S46. ^{1}H NMR of Compound **3p** (400 MHz, $CDCl_3$)

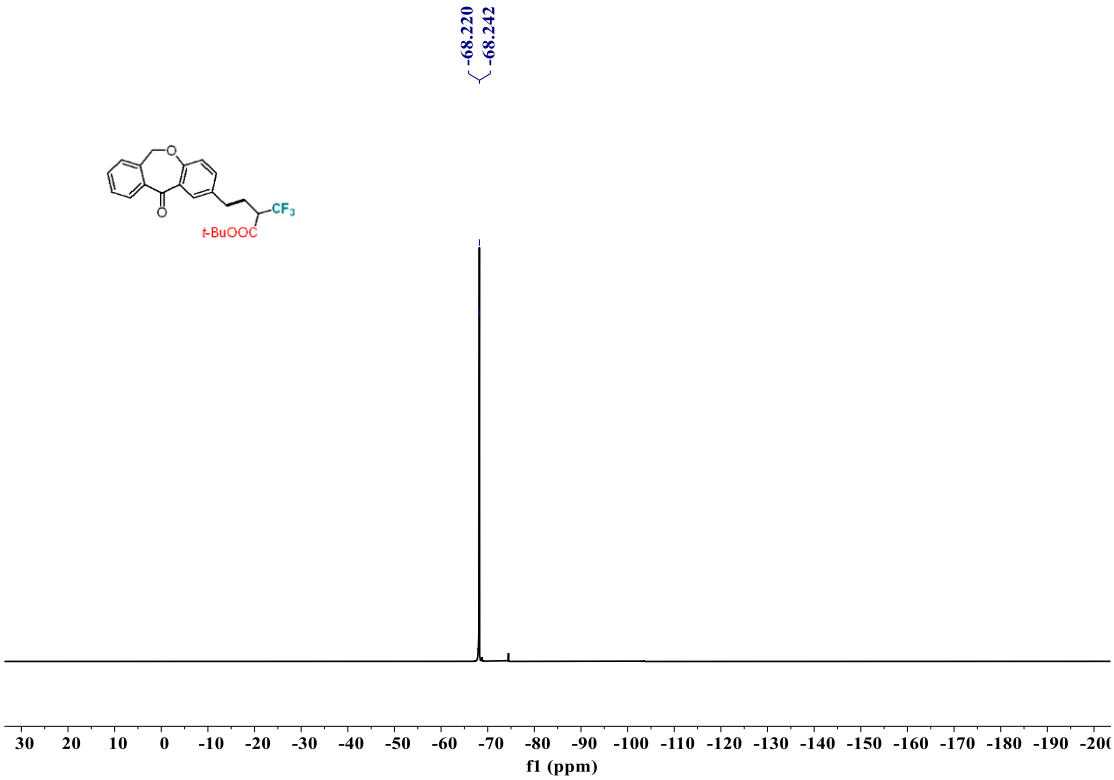


Figure S47. ^{19}F NMR of Compound **3p** (376 MHz, $CDCl_3$)

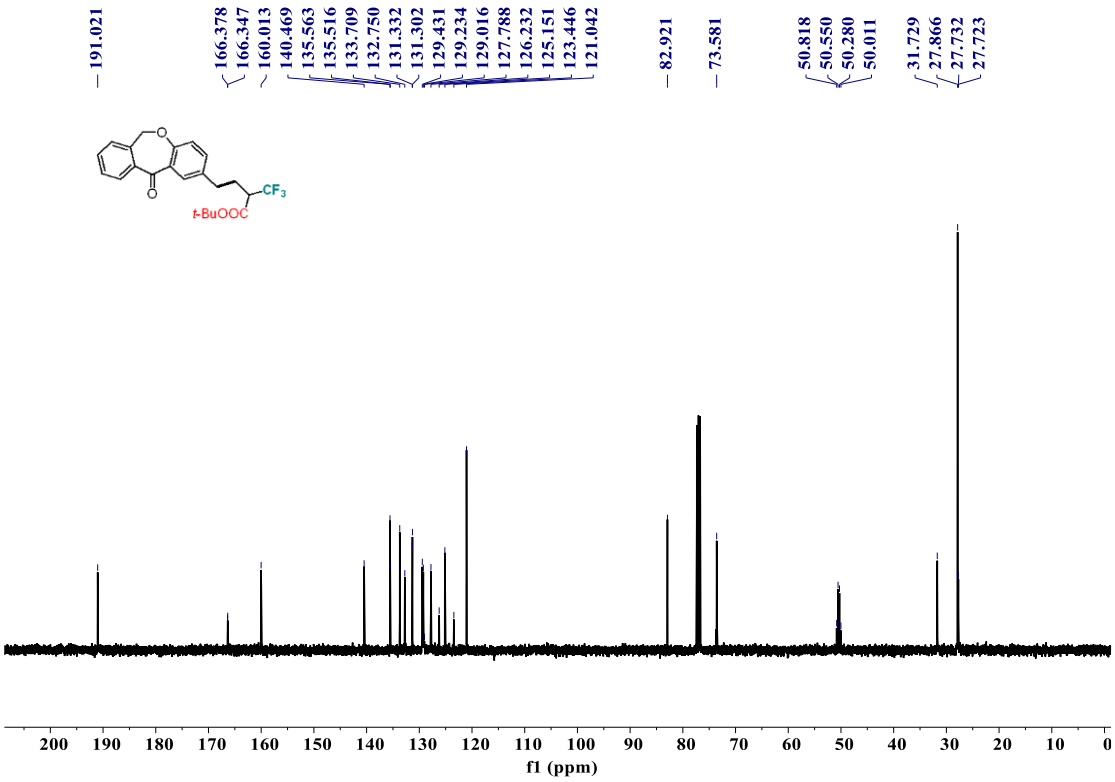


Figure S48. ^{13}C NMR of Compound **3p** (101 MHz, $CDCl_3$)

tert-butyl-4-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)-2-(trifluoromethyl)butanoate(3q)

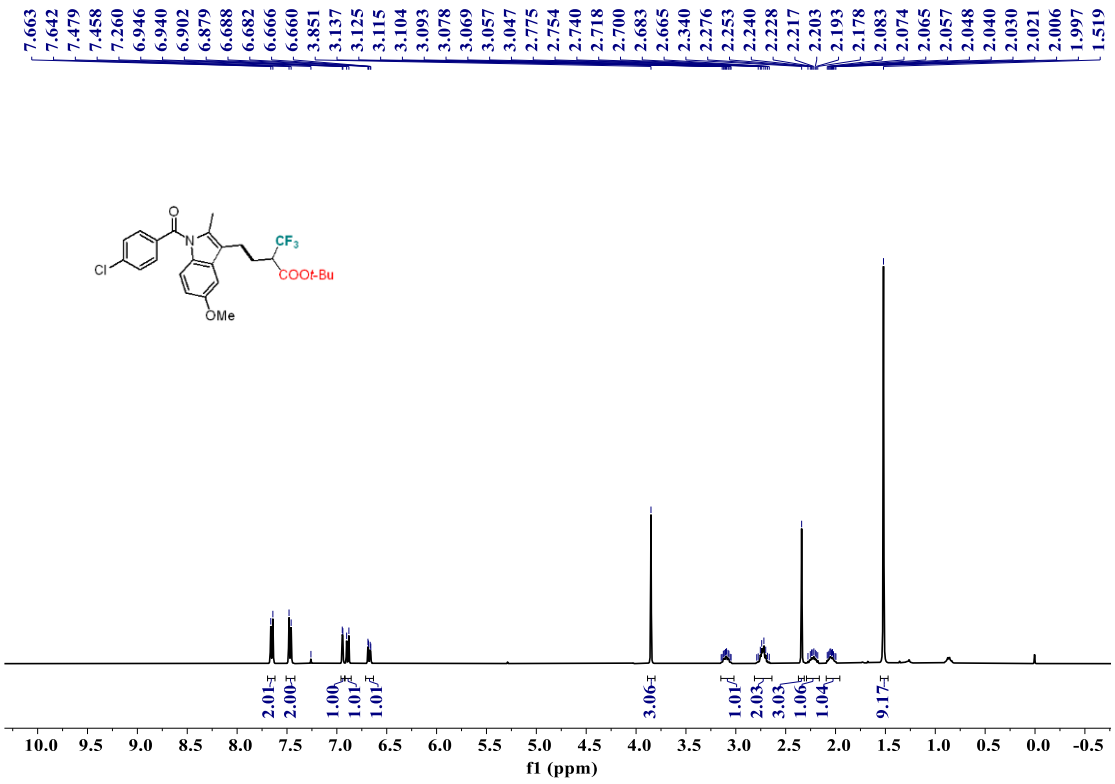


Figure S49. ^{1}H NMR of Compound **3q** (400 MHz, $CDCl_3$)

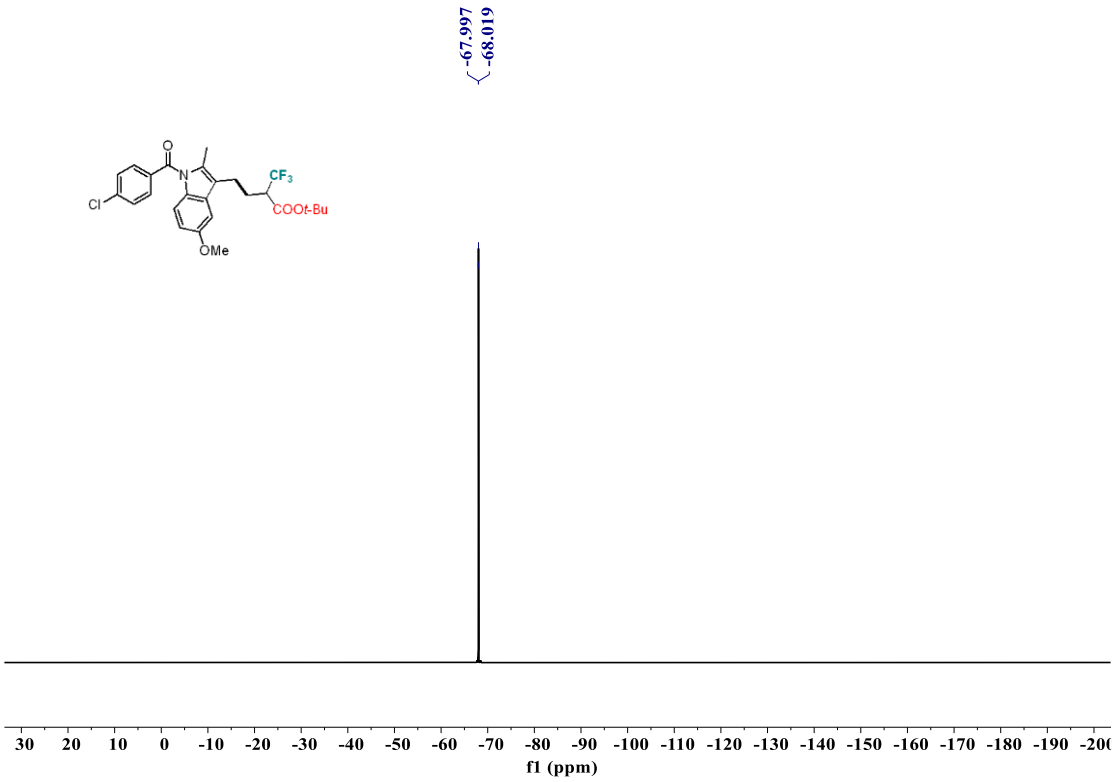


Figure S50. ^{19}F NMR of Compound **3q** (376 MHz, $CDCl_3$)

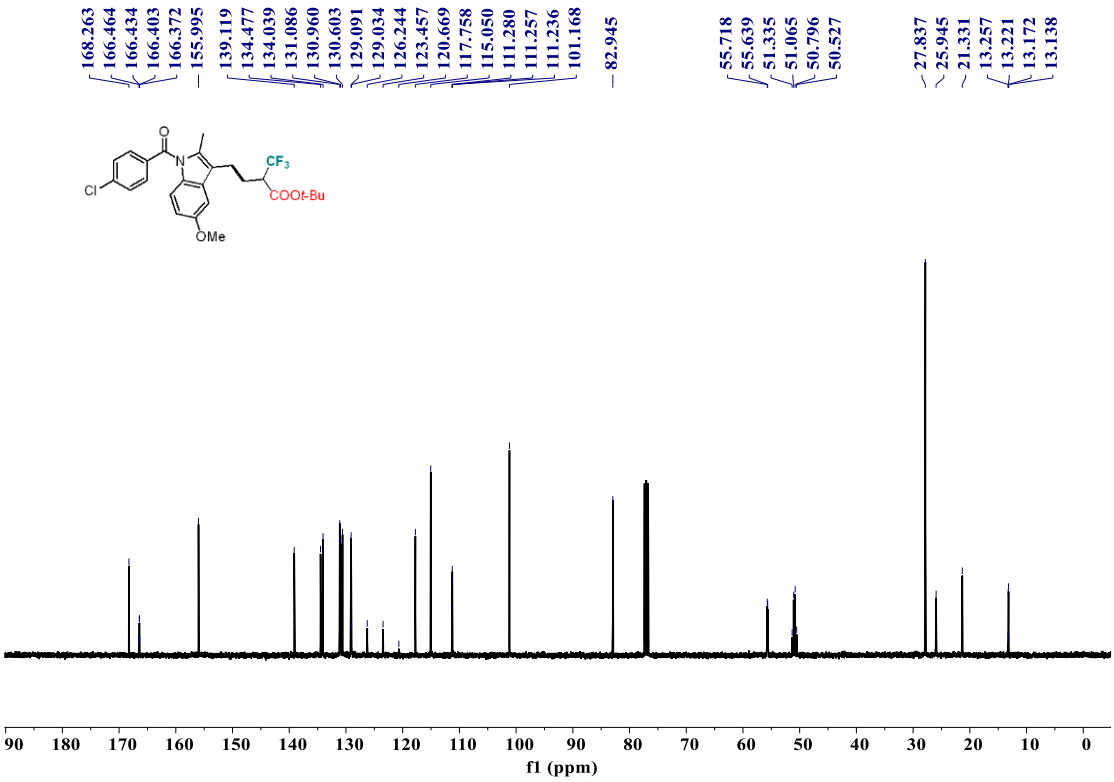


Figure S51. ^{13}C NMR of Compound **3q** (101 MHz, $CDCl_3$)

6-(*tert*-butyl) 1-methyl (2*S*)-2-((*tert*-butoxycarbonyl)amino)-5-(trifluoromethyl)hexanedioate (5a)

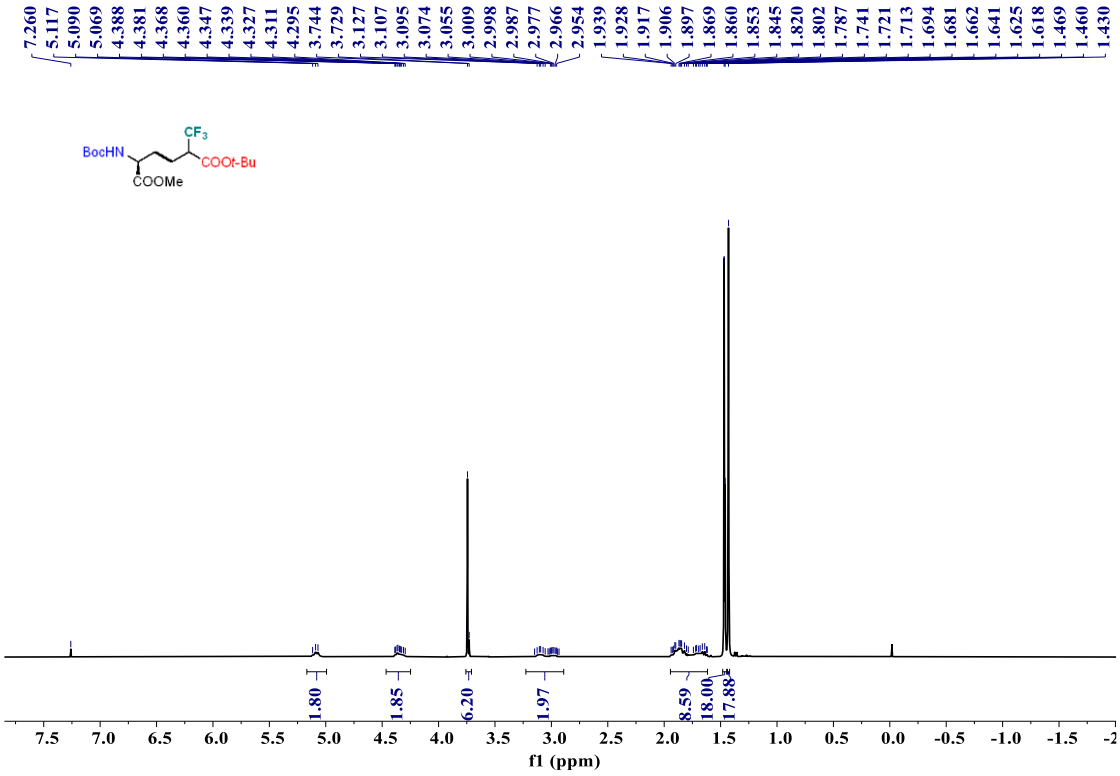


Figure S52. ^{1}H NMR of Compound **5a** (400 MHz, $CDCl_3$)

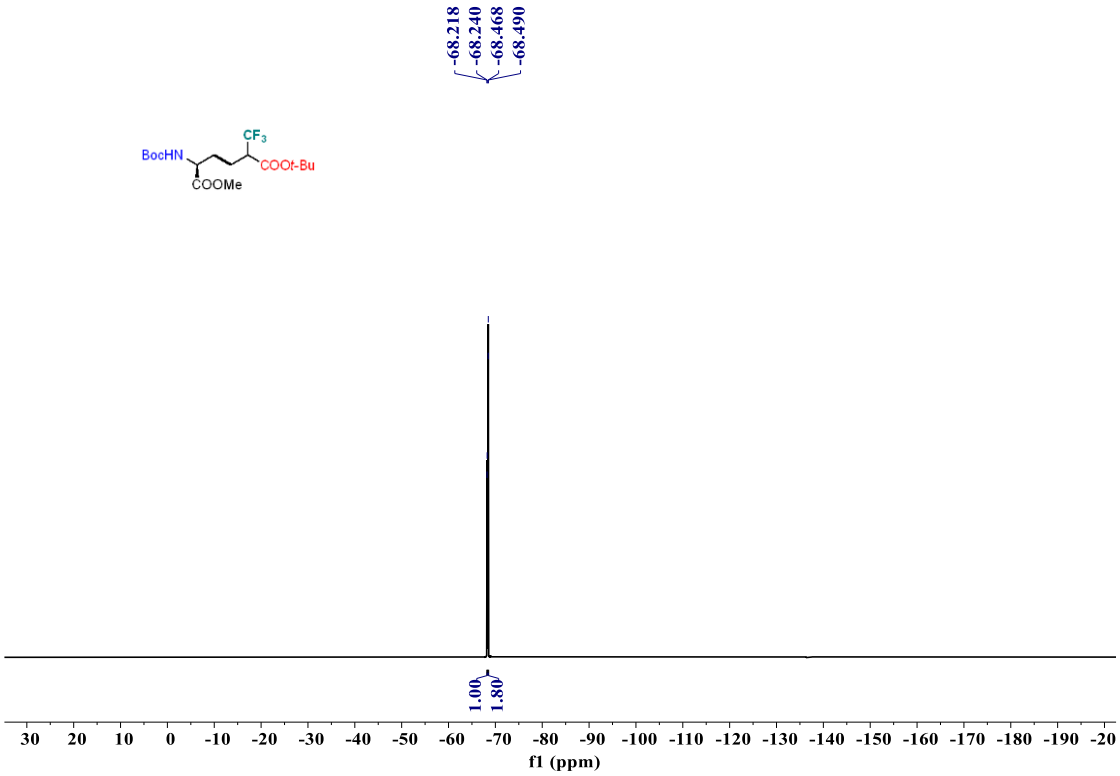


Figure S53. ^{19}F NMR of Compound **5a** (376 MHz, $CDCl_3$)

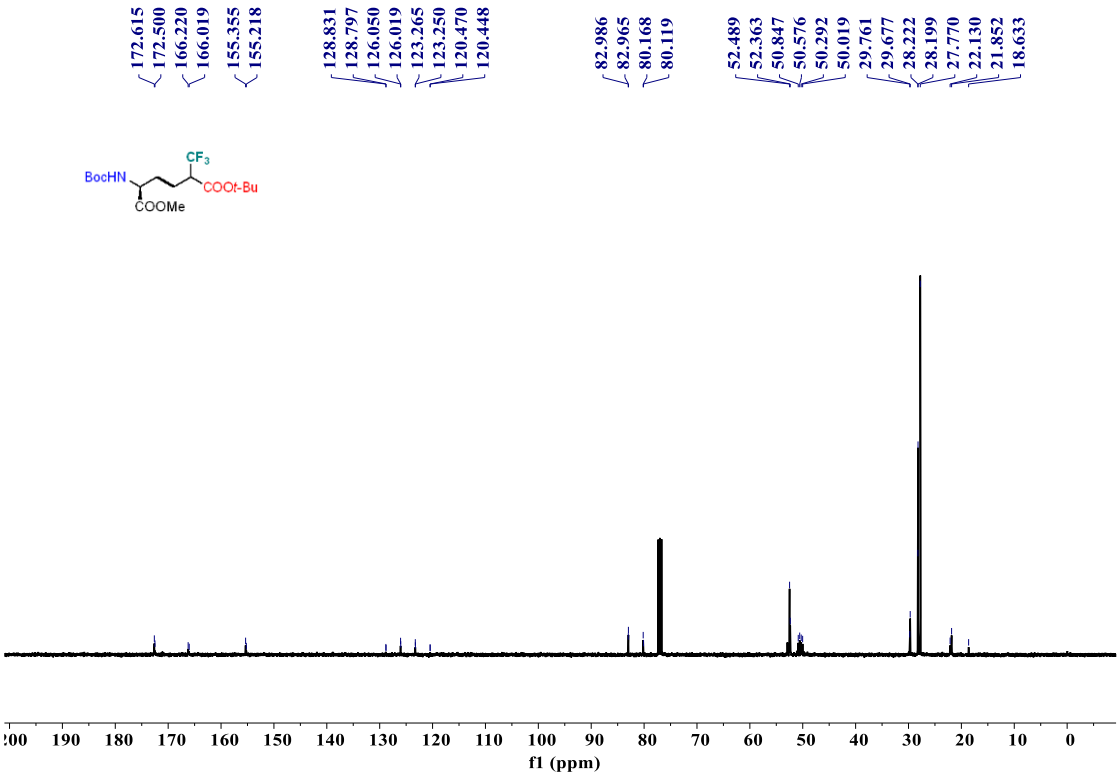


Figure S54. ^{13}C NMR of Compound **5a** (101 MHz, $CDCl_3$)

1-benzyl 6-(*tert*-butyl) (2*S*)-2-((*tert*-butoxycarbonyl)amino)-5-(trifluoromethyl)hexanedioate (5b)

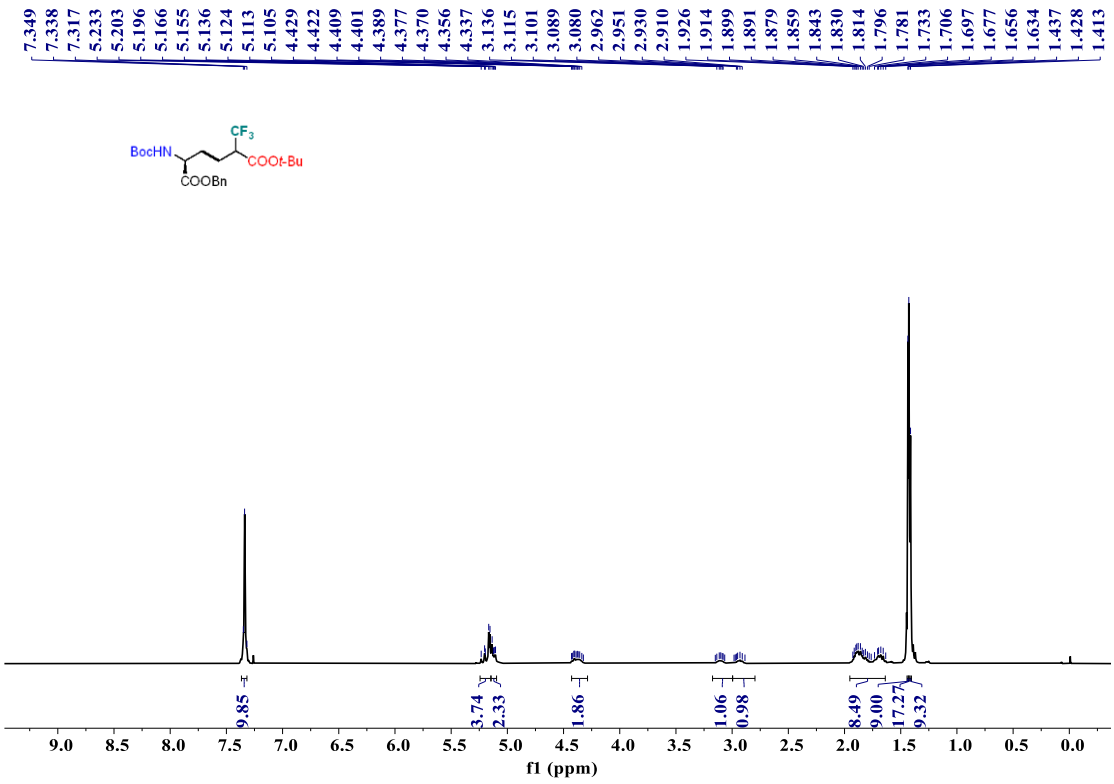


Figure S55. ^{1}H NMR of Compound **5b** (400 MHz, $CDCl_3$)

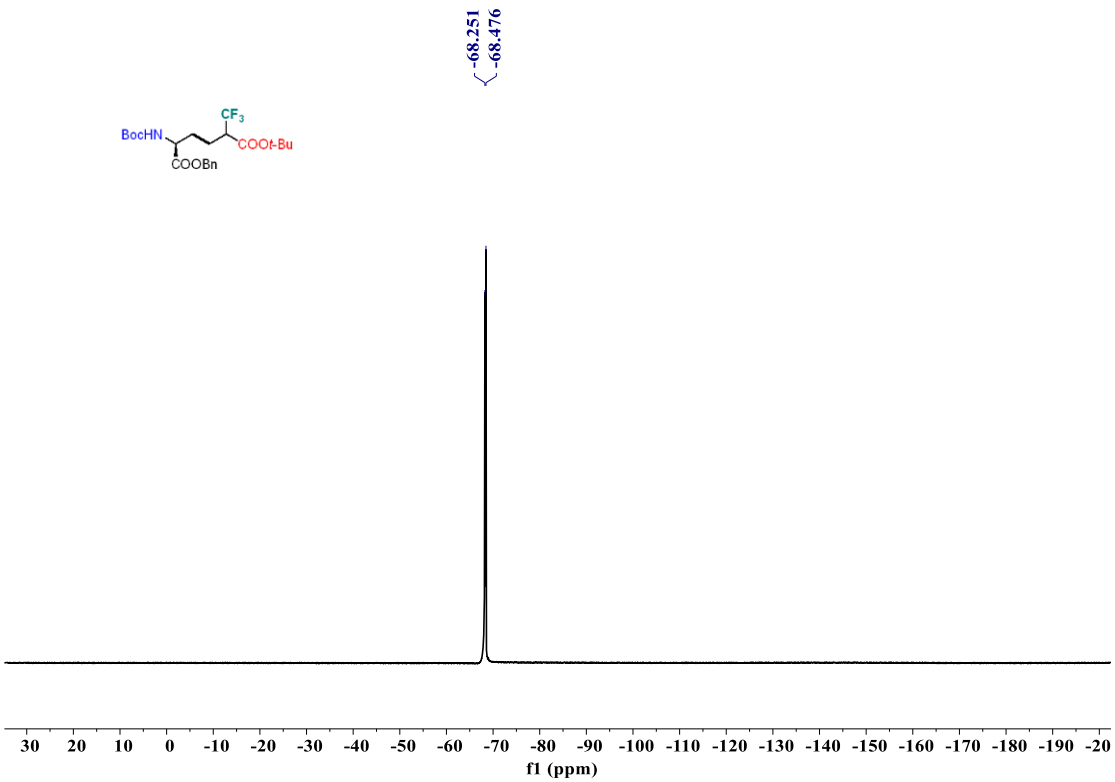


Figure S56. ^{19}F NMR of Compound **5b** (376 MHz, $CDCl_3$)

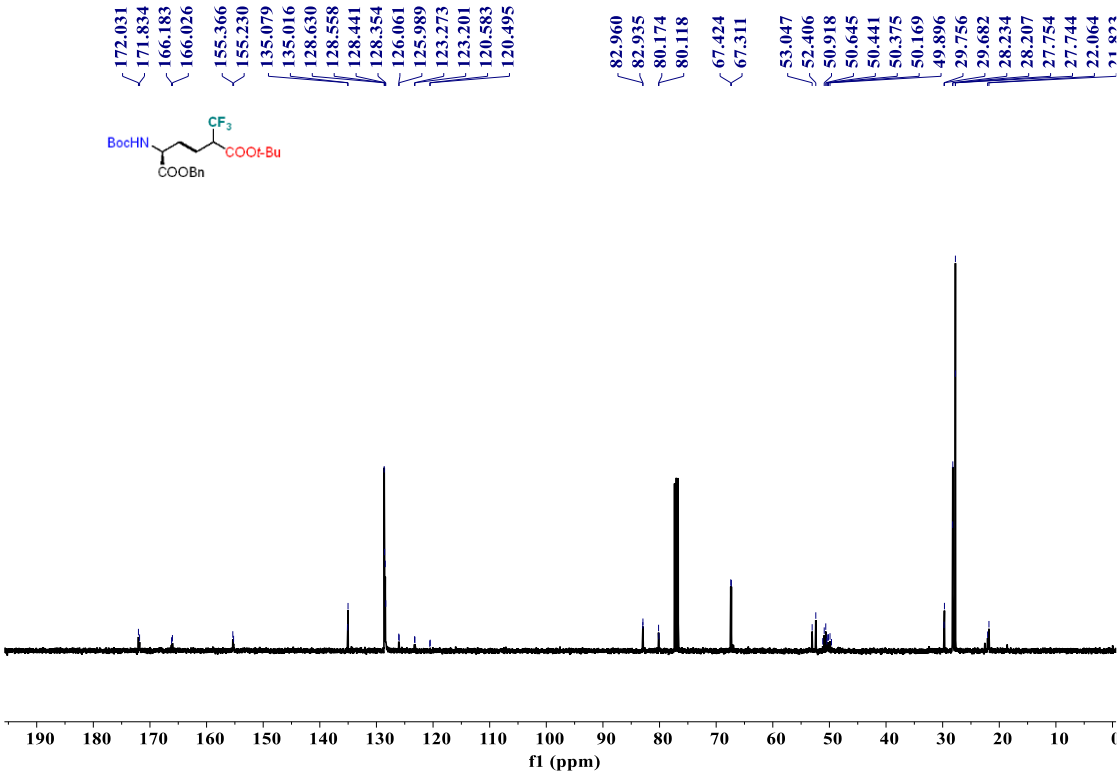


Figure S57. ^{13}C NMR of Compound **5b** (101 MHz, $CDCl_3$)

7-(*tert*-butyl) 1-methyl (2*S*)-2-((*tert*-butoxycarbonyl)amino)-6-(trifluoromethyl)heptanedioate (5c)

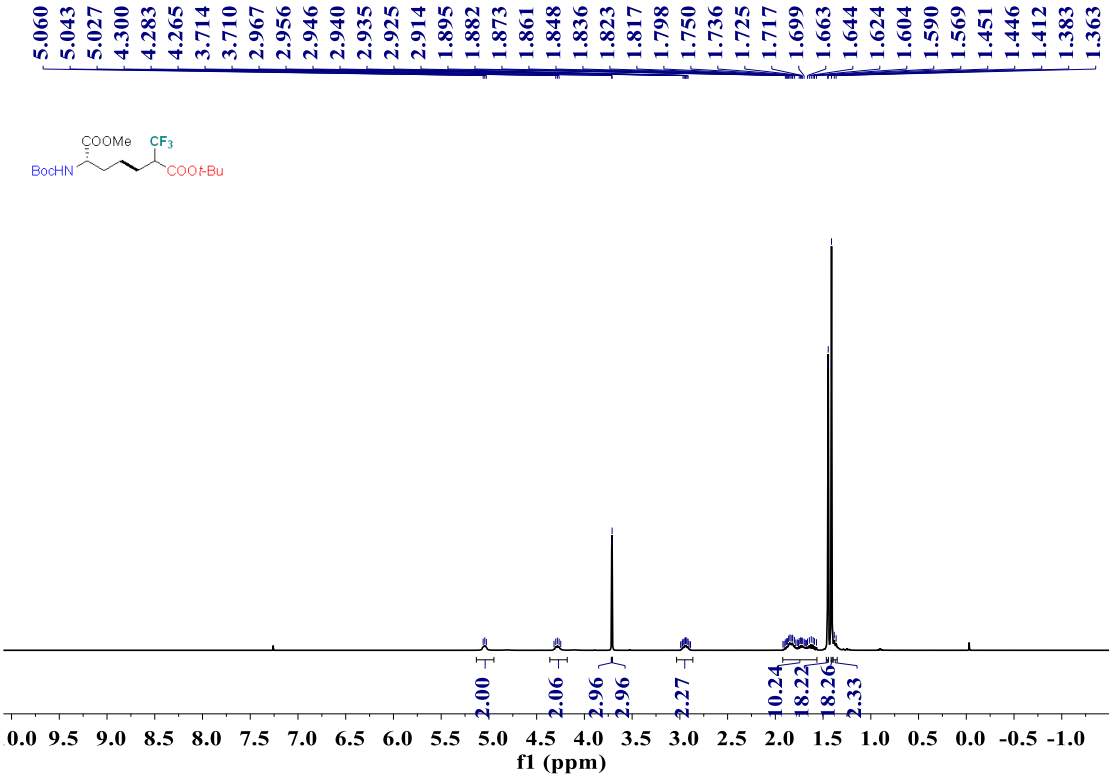


Figure S58. ^{1}H NMR of Compound **5c** (400 MHz, $CDCl_3$)

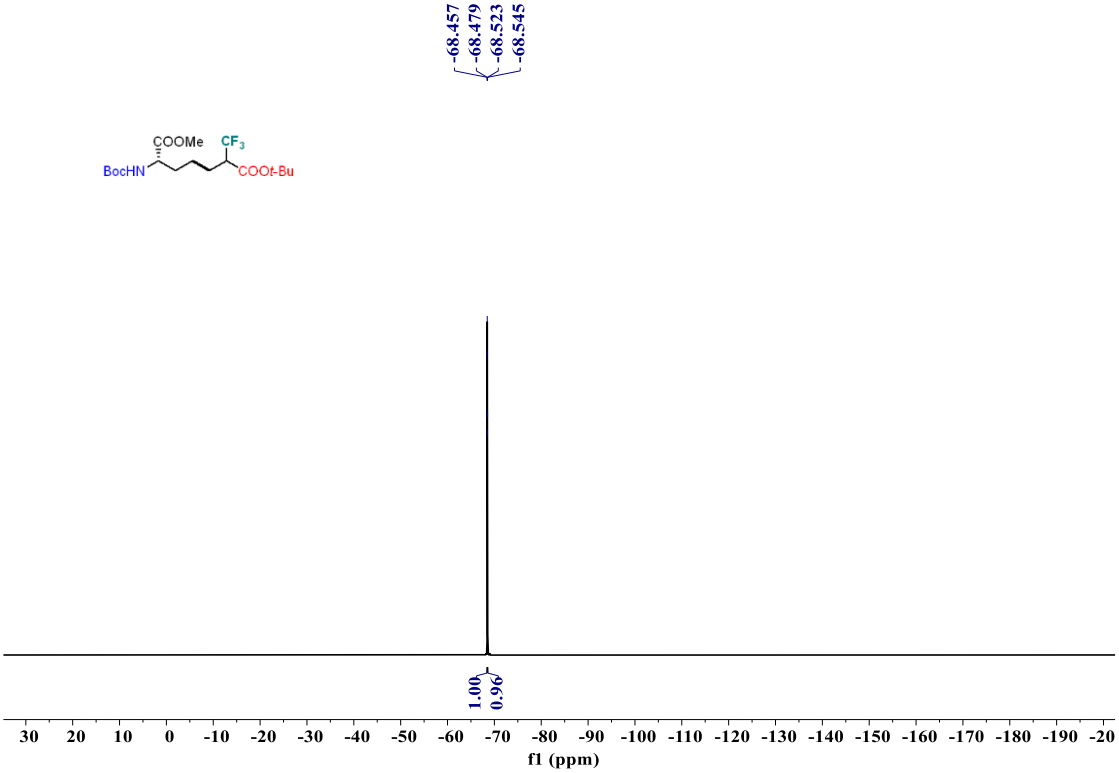


Figure S59. ^{19}F NMR of Compound **5c** (376 MHz, $CDCl_3$)

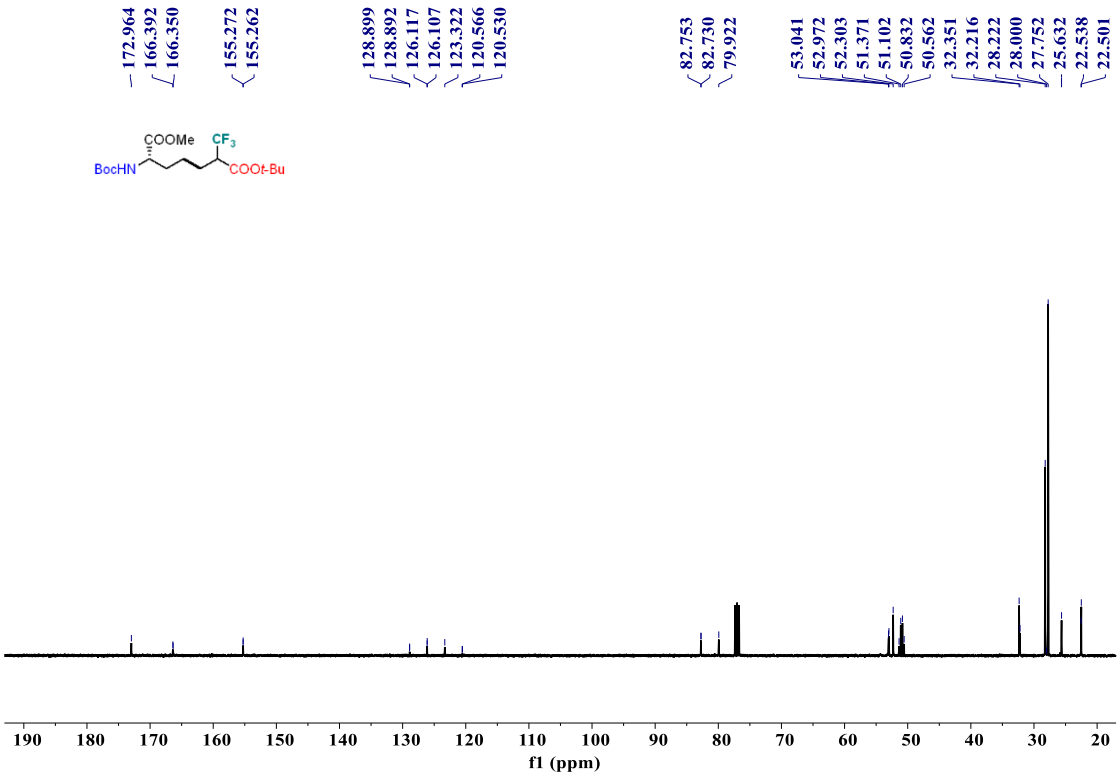


Figure S60. ^{13}C NMR of Compound **5c** (101 MHz, $CDCl_3$)

di-*tert*-butyl (2*S*)-2-((*tert*-butoxycarbonyl)amino)-6-(trifluoromethyl)heptanedioate (5d)

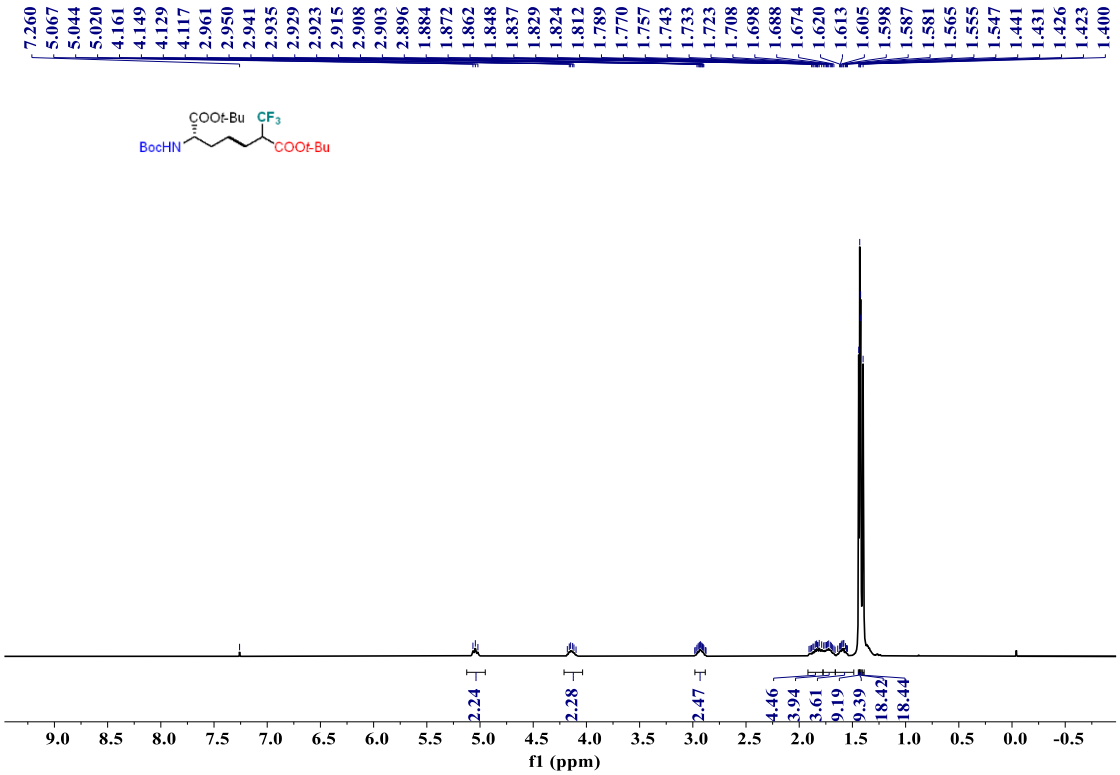


Figure S61. ^{1}H NMR of Compound **5d** (400 MHz, $CDCl_3$)

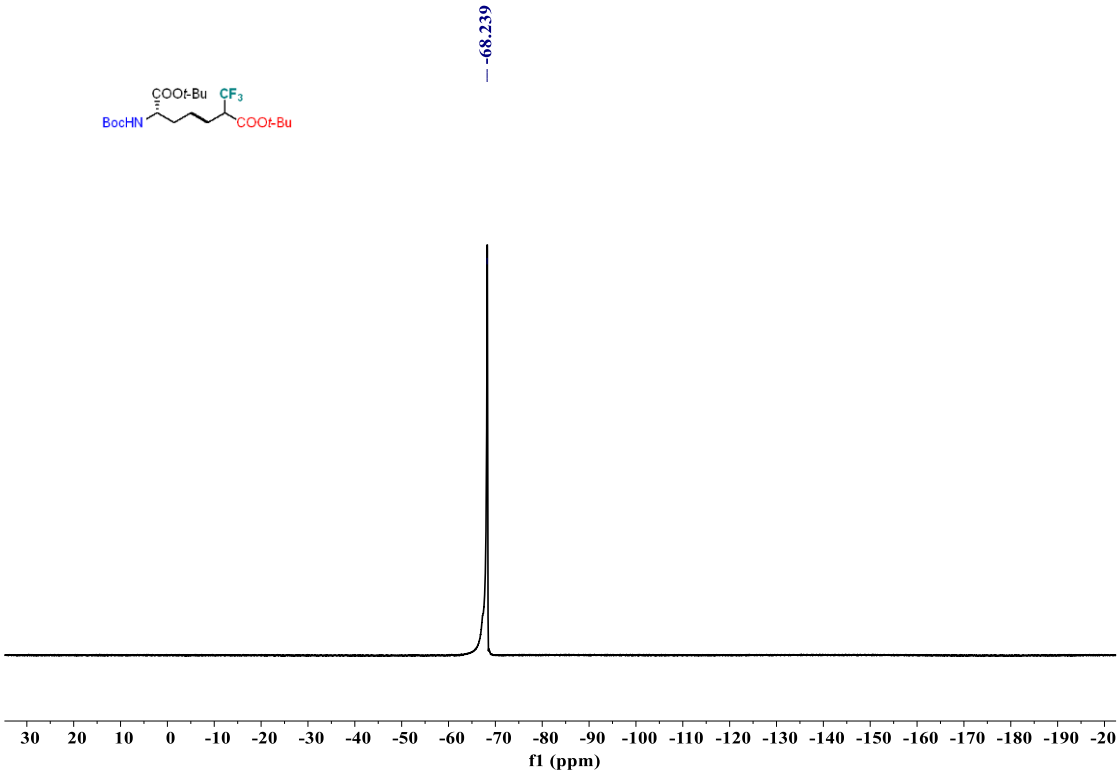


Figure S62. ^{19}F NMR of Compound **5d** (376 MHz, $CDCl_3$)

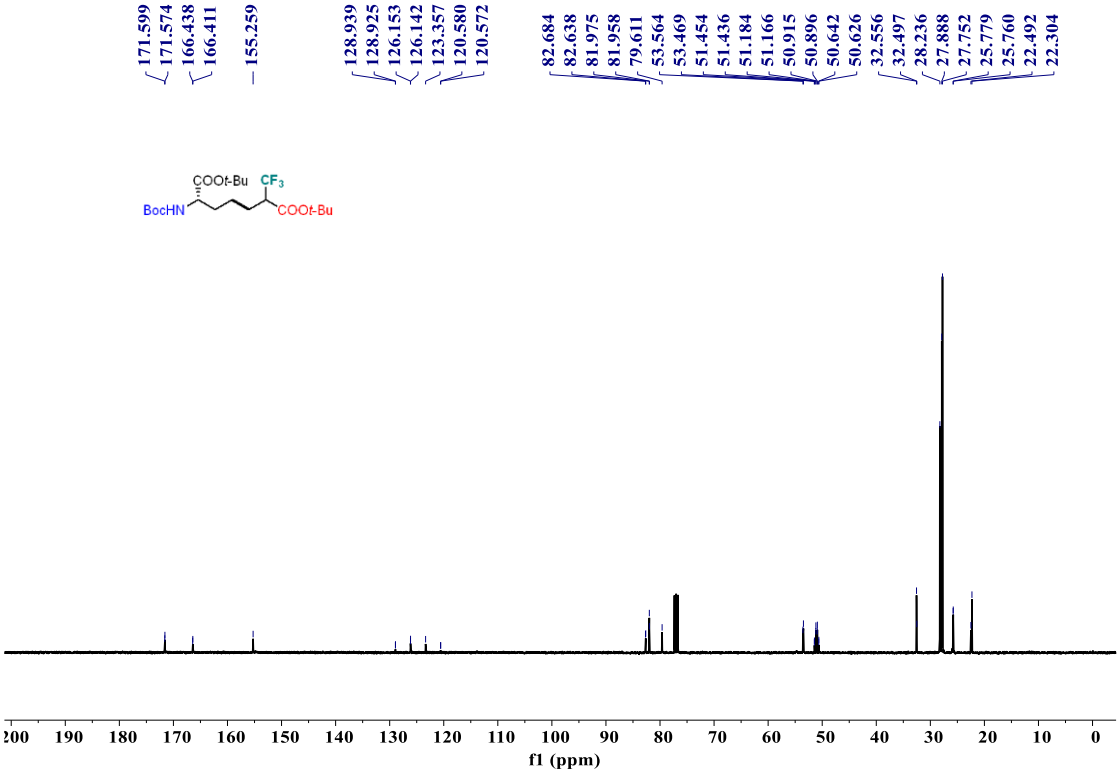


Figure S63. ^{13}C NMR of Compound **5d** (101 MHz, $CDCl_3$)

1-benzyl 7-(*tert*-butyl) (2*S*)-2-((*tert*-butoxycarbonyl)amino)-6-(trifluoromethyl)heptanedioate (5e)

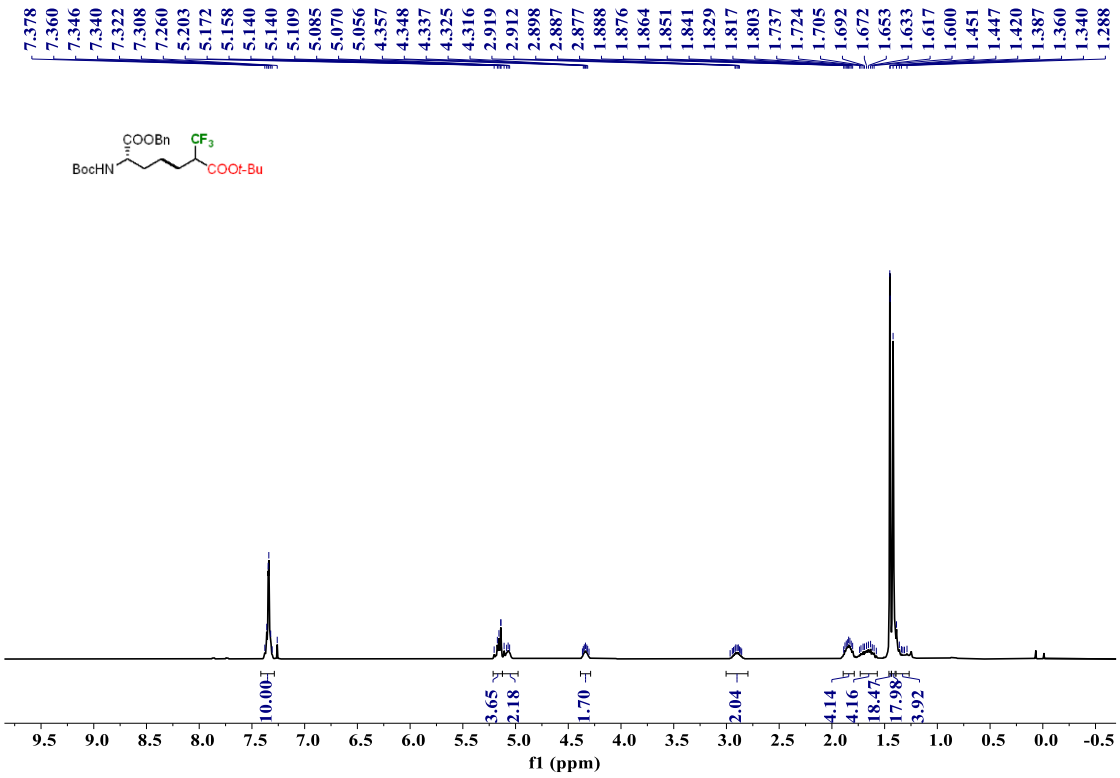


Figure S64. ^{1}H NMR of Compound **5e** (400 MHz, $CDCl_3$)

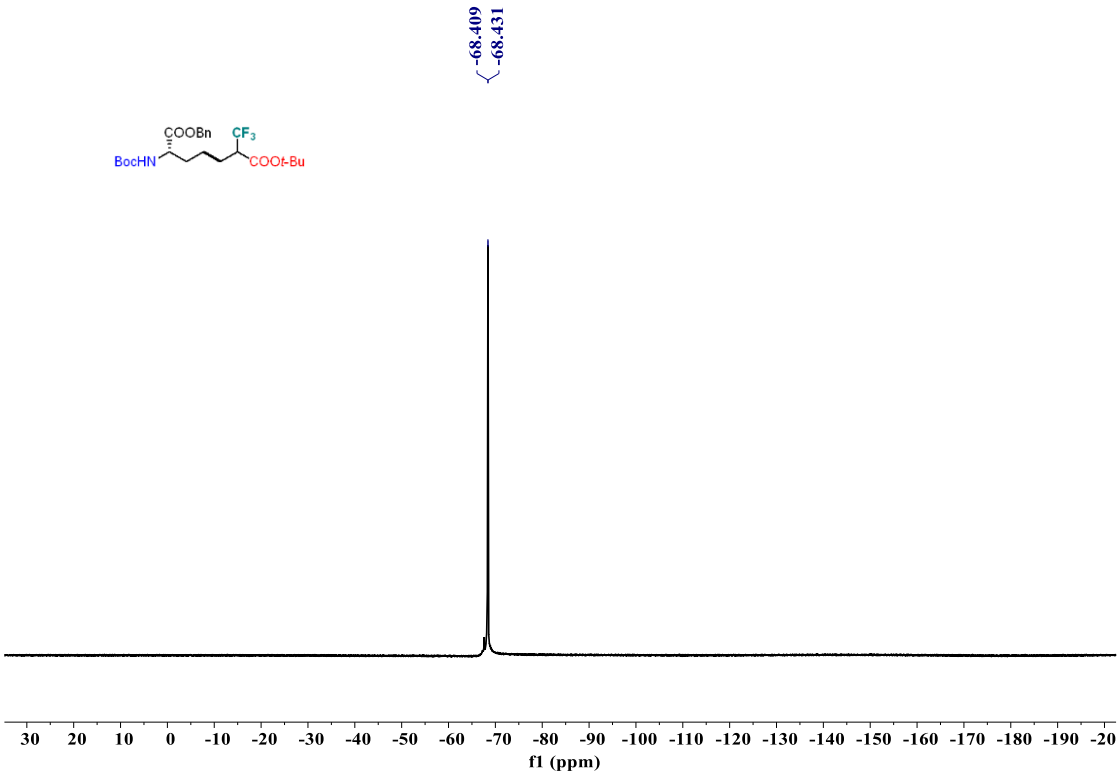


Figure S65. ^{19}F NMR of Compound **5e** (376 MHz, $CDCl_3$)

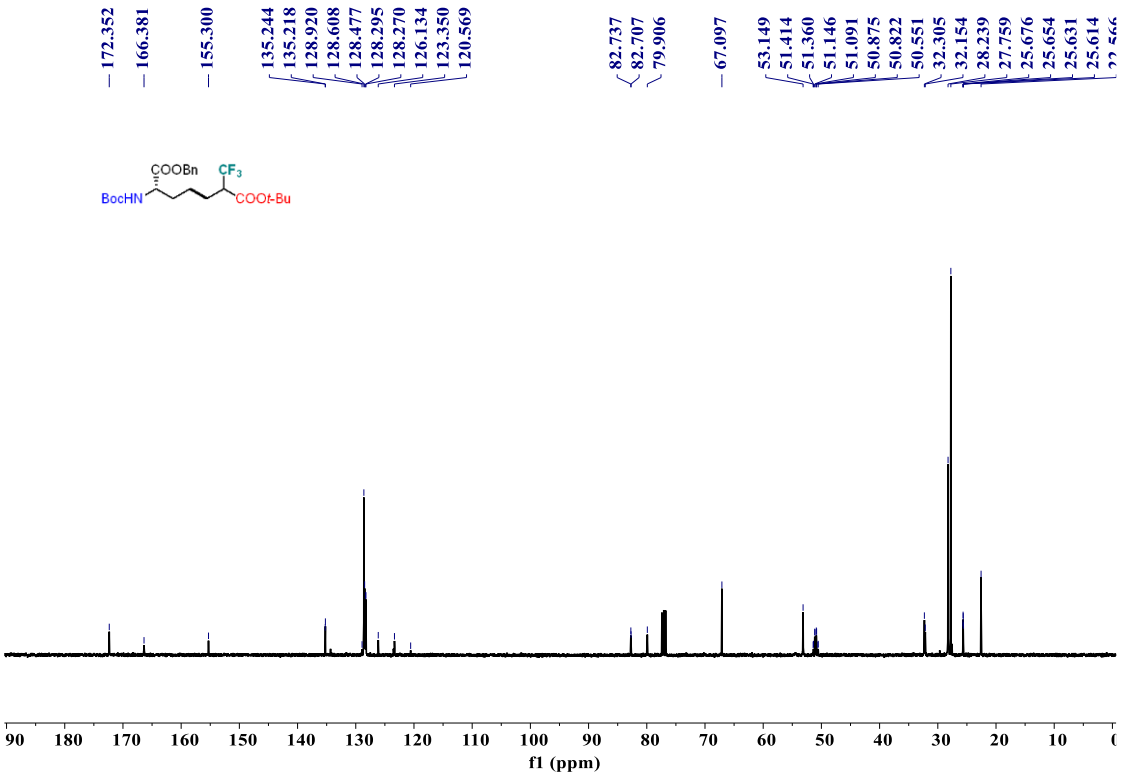


Figure S66. ^{13}C NMR of Compound **5e** (101 MHz, $CDCl_3$)

di-*tert*-butyl (2*S*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-5-(trifluoromethyl)hexanedioate (5f)

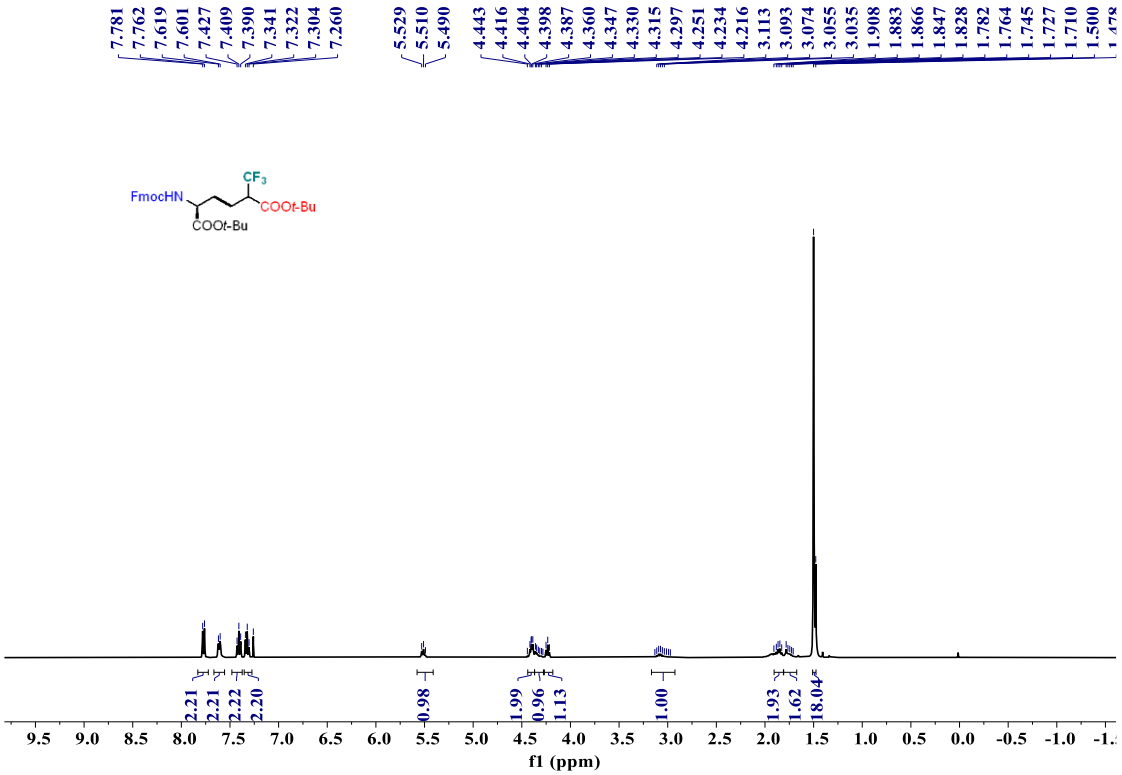


Figure S67. ^{1}H NMR of Compound **5f** (400 MHz, $CDCl_3$)

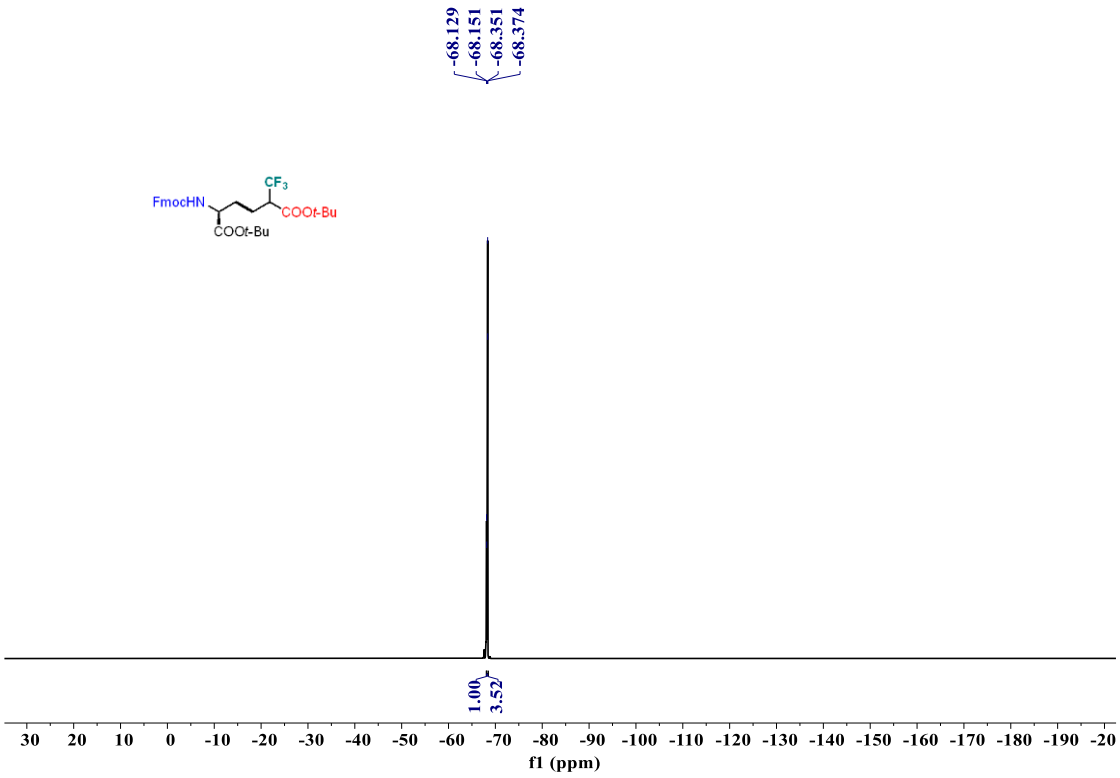


Figure S68. ^{19}F NMR of Compound **5f** (376 MHz, $CDCl_3$)

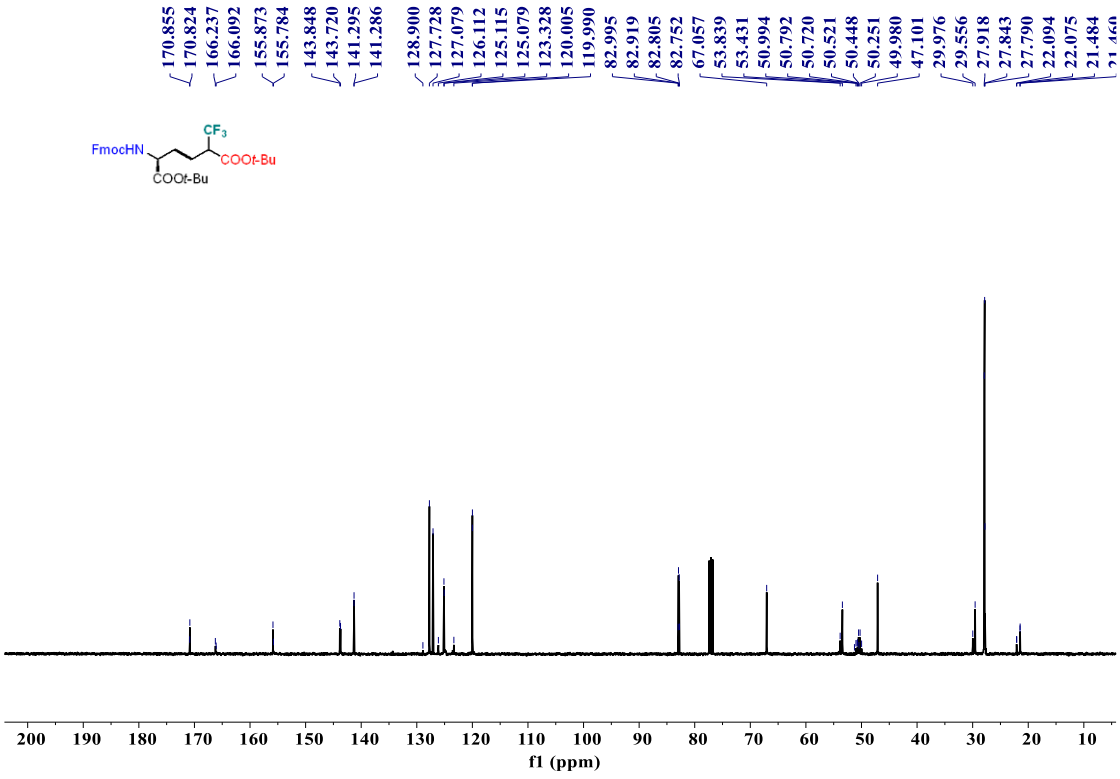


Figure S69. ^{13}C NMR of Compound **5f** (101 MHz, $CDCl_3$)

6-(*tert*-butyl) 1-methyl (2*S*)-2-(((benzyloxy)carbonyl)amino)-5-(trifluoromethyl)hexanedioate (5g)

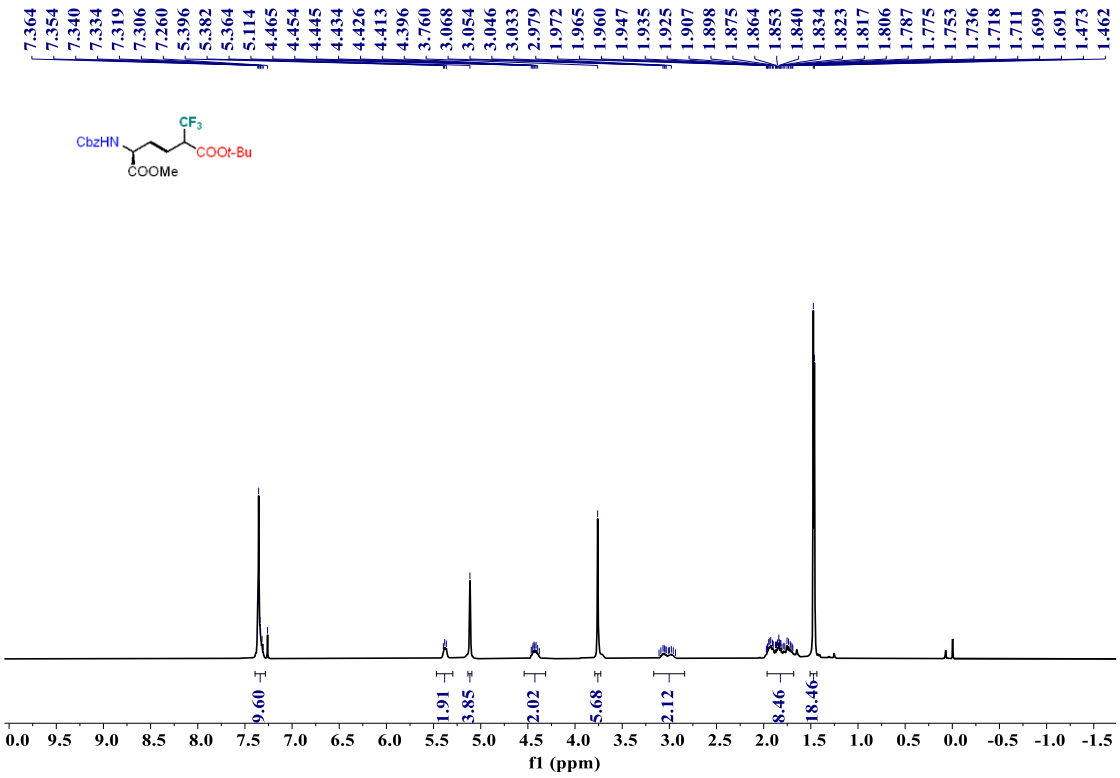


Figure S70. ^{1}H NMR of Compound **5g** (400 MHz, $CDCl_3$)

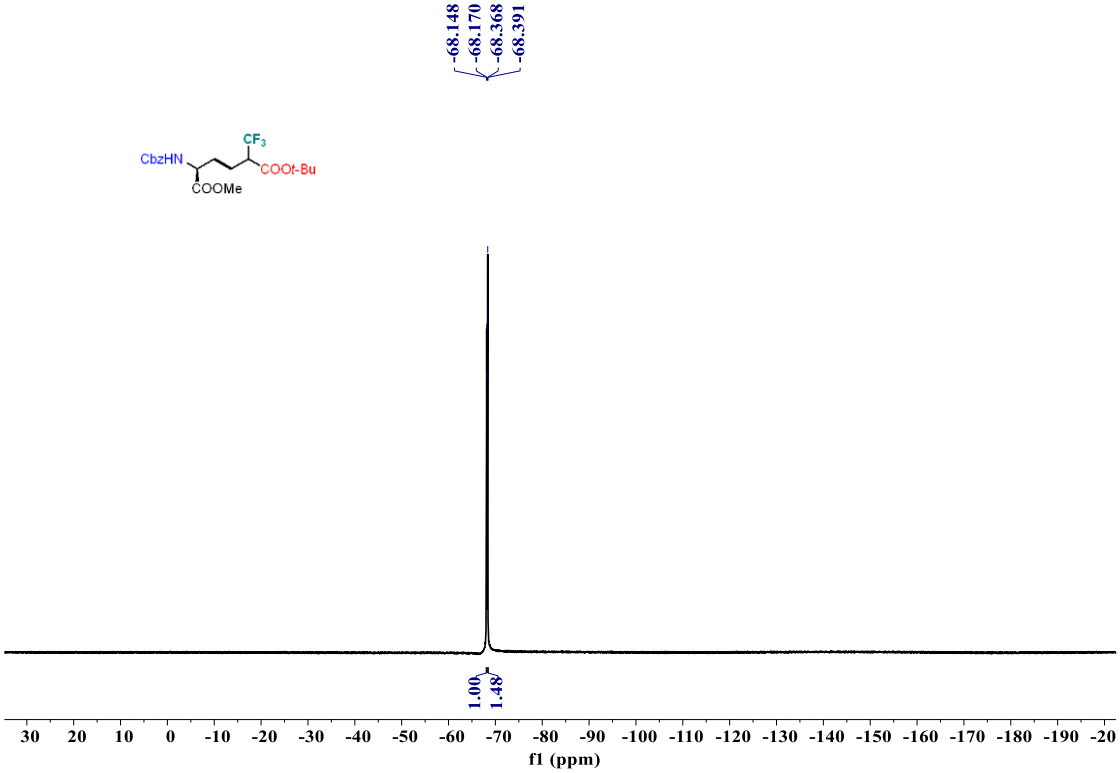


Figure S71. ^{19}F NMR of Compound **5g** (376 MHz, $CDCl_3$)

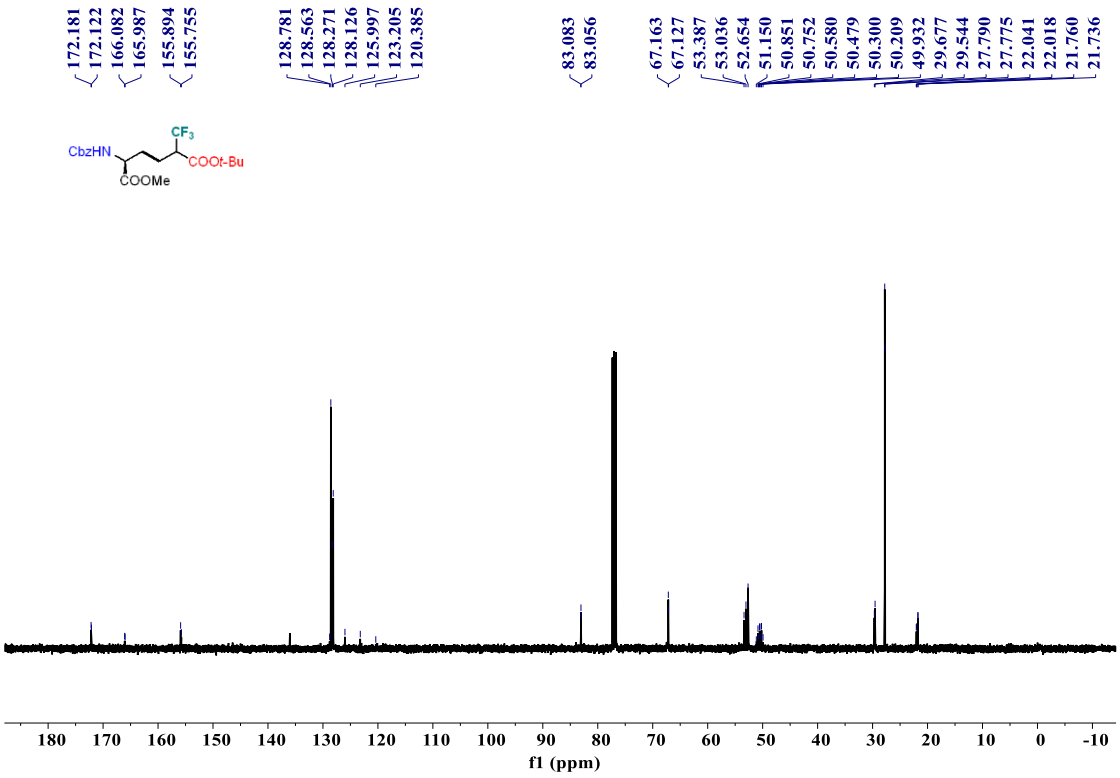


Figure S72. ^{13}C NMR of Compound **5g (**101 MHz, $CDCl_3$)

7-(*tert*-butyl) 1-methyl (2*S*)-2-(((benzyloxy)carbonyl)amino)-6-(trifluoromethyl)heptanedioate (5h)

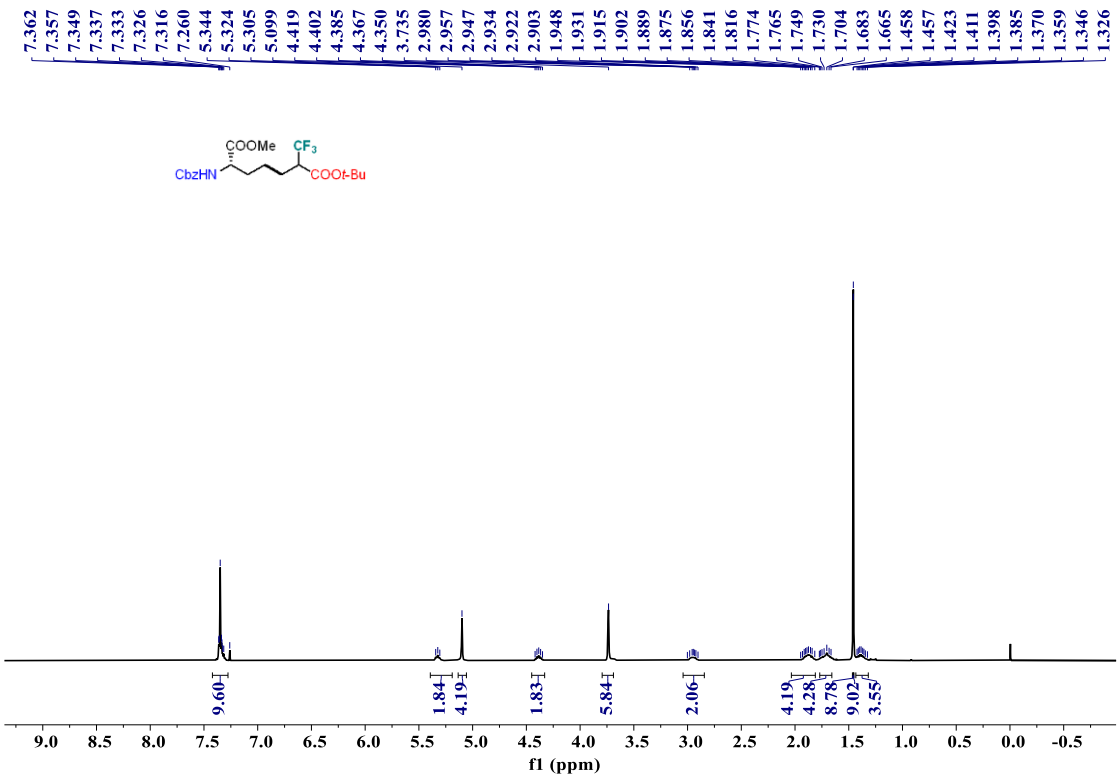


Figure S73. ^{1}H NMR of Compound **5h** (400 MHz, $CDCl_3$)

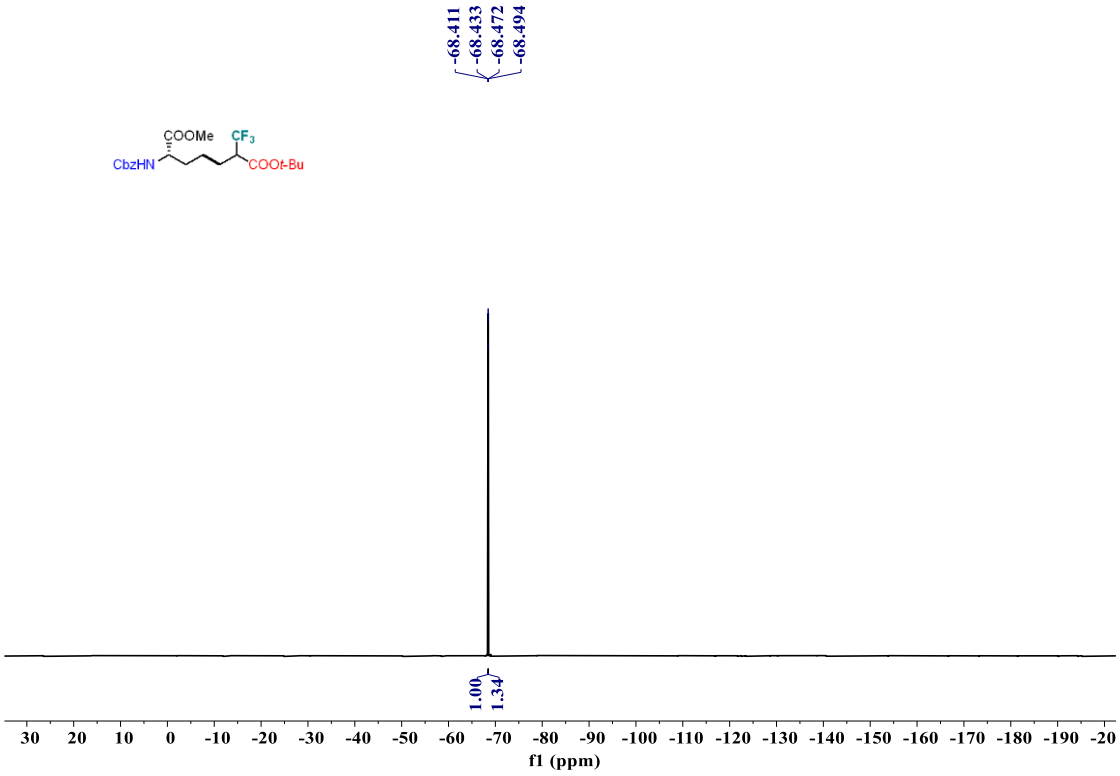


Figure S74. ^{19}F NMR of Compound **5h** (376 MHz, $CDCl_3$)

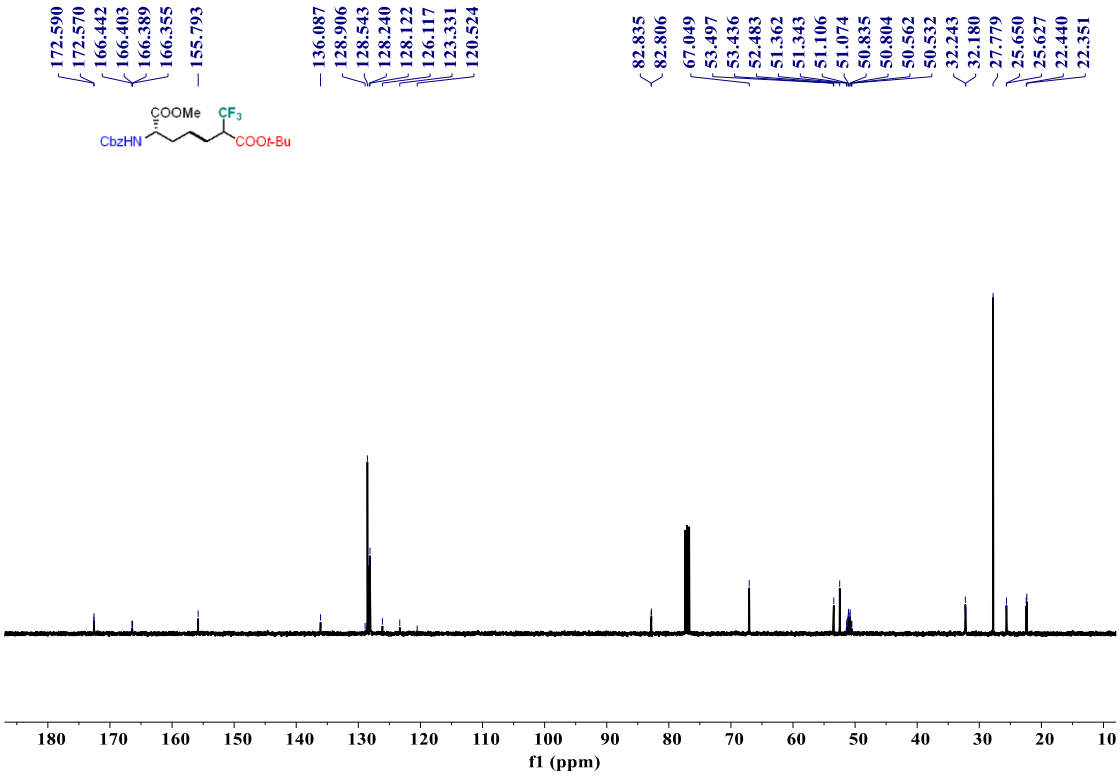


Figure S75. ^{13}C NMR of Compound **5h** (101 MHz, $CDCl_3$)

***tert*-butyl (4-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-6-methyl-2-(trifluoromethyl)heptanoate (5i)**

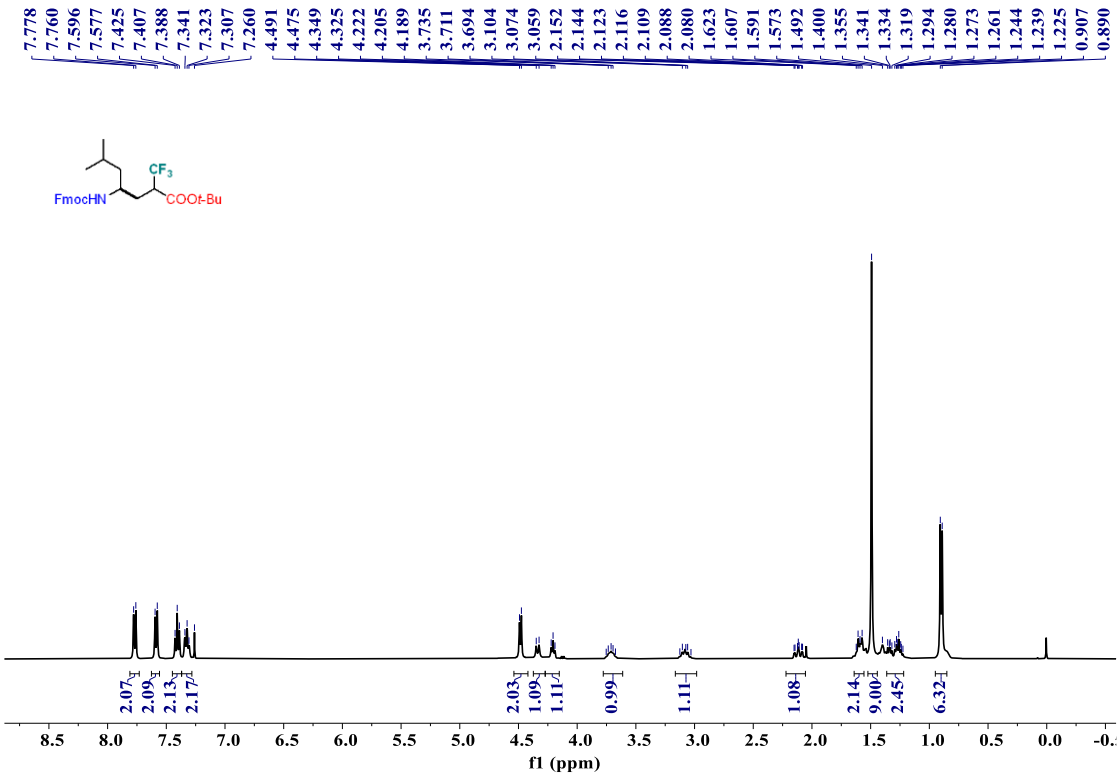


Figure S76. ^{1}H NMR of Compound **5i** (400 MHz, $CDCl_3$)

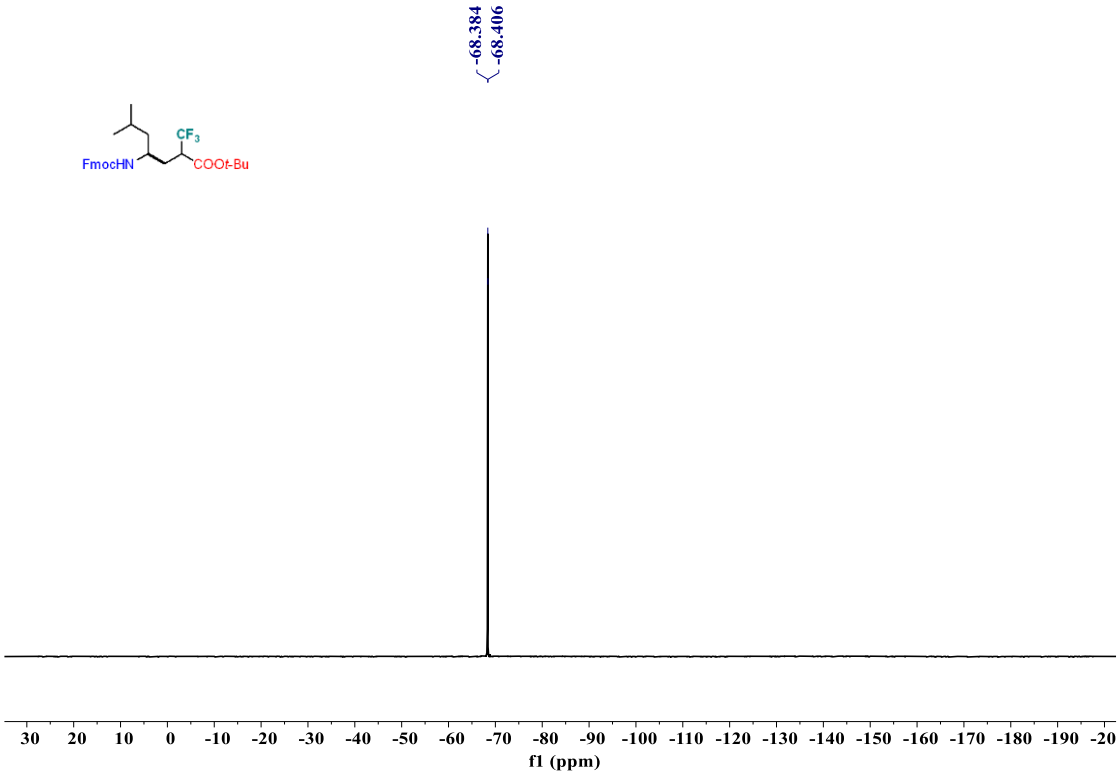


Figure S77. ^{19}F NMR of Compound **5i** (376 MHz, $CDCl_3$)

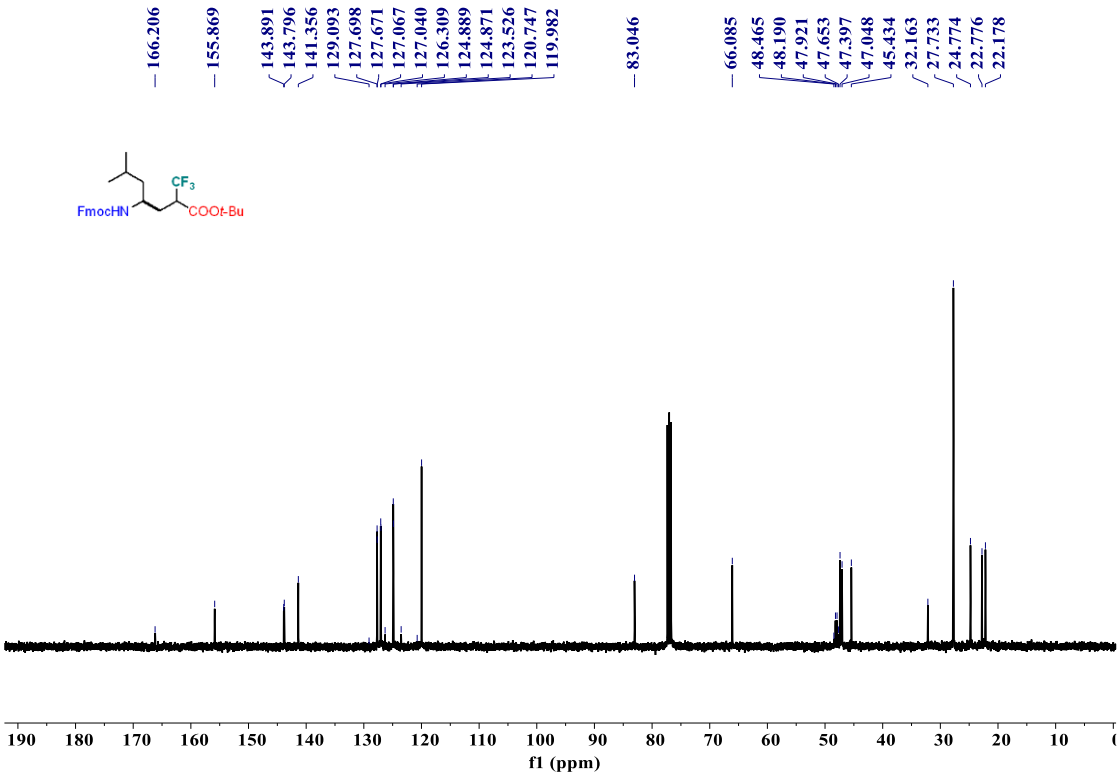


Figure S78. ^{13}C NMR of Compound **5i** (101 MHz, $CDCl_3$)

tert-butyl 4-((*tert*-butoxycarbonyl)amino)-5-methyl-2-(trifluoromethyl)hexanoate (5j)

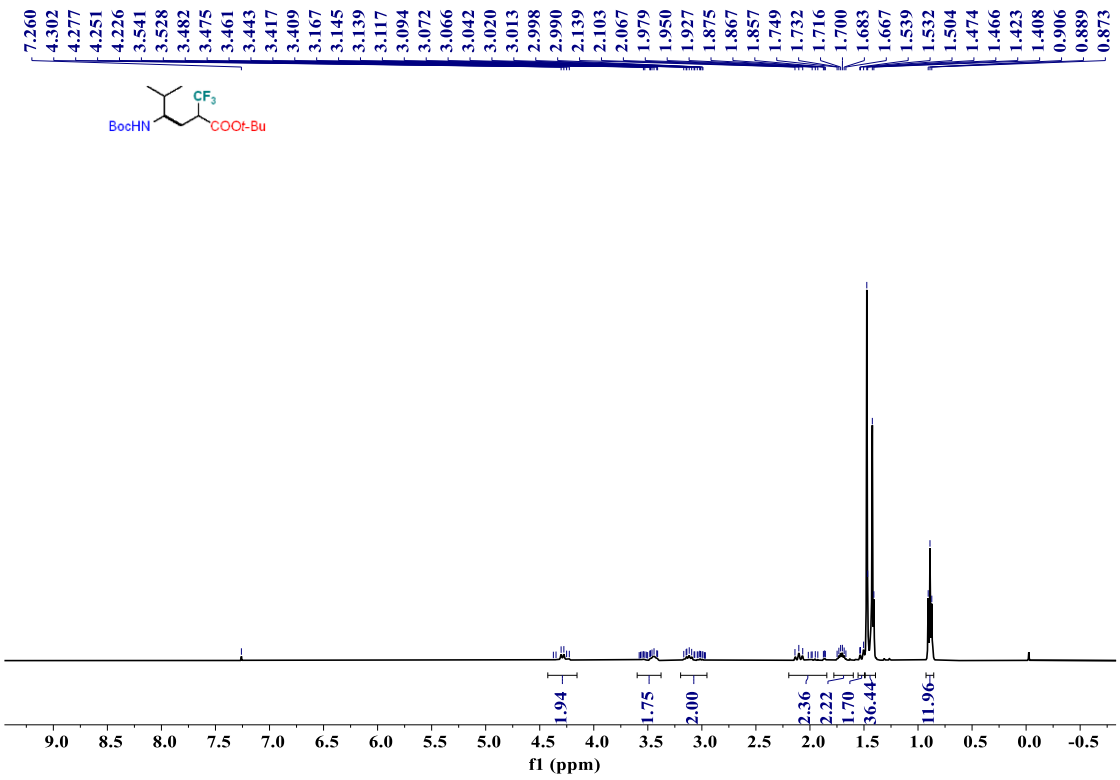


Figure S79. ^{1}H NMR of Compound **5j** (400 MHz, $CDCl_3$)

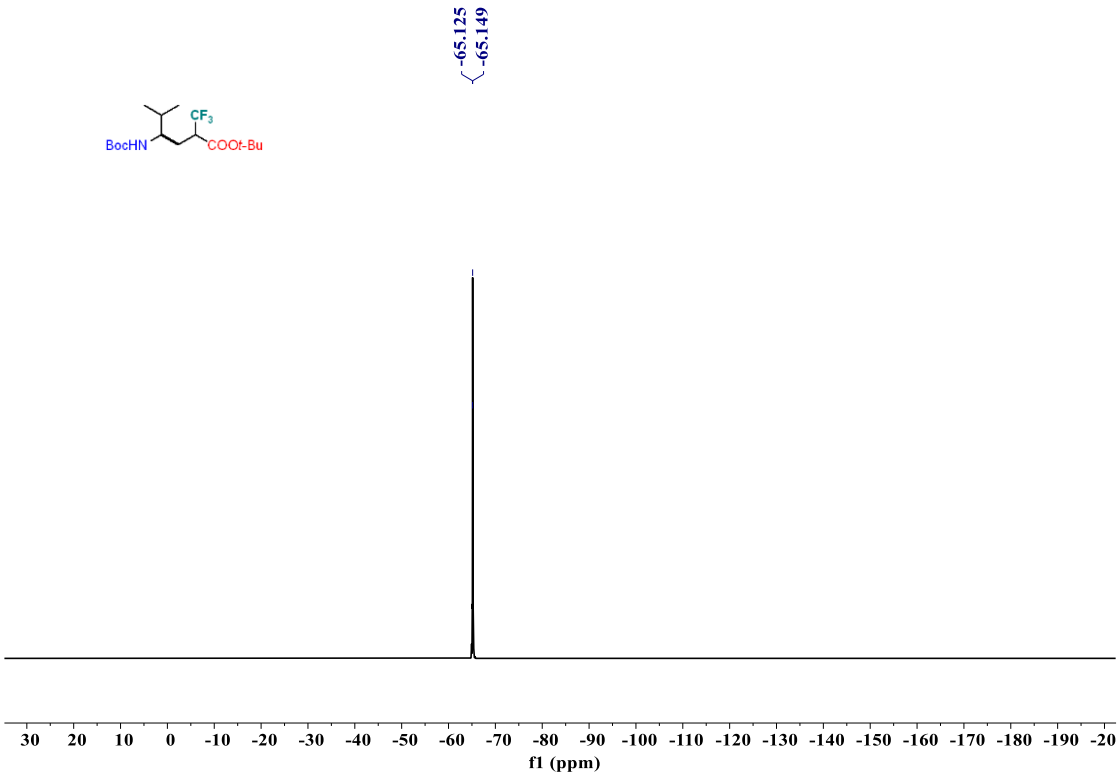


Figure S80. ^{19}F NMR of Compound **5j** (376 MHz, $CDCl_3$)

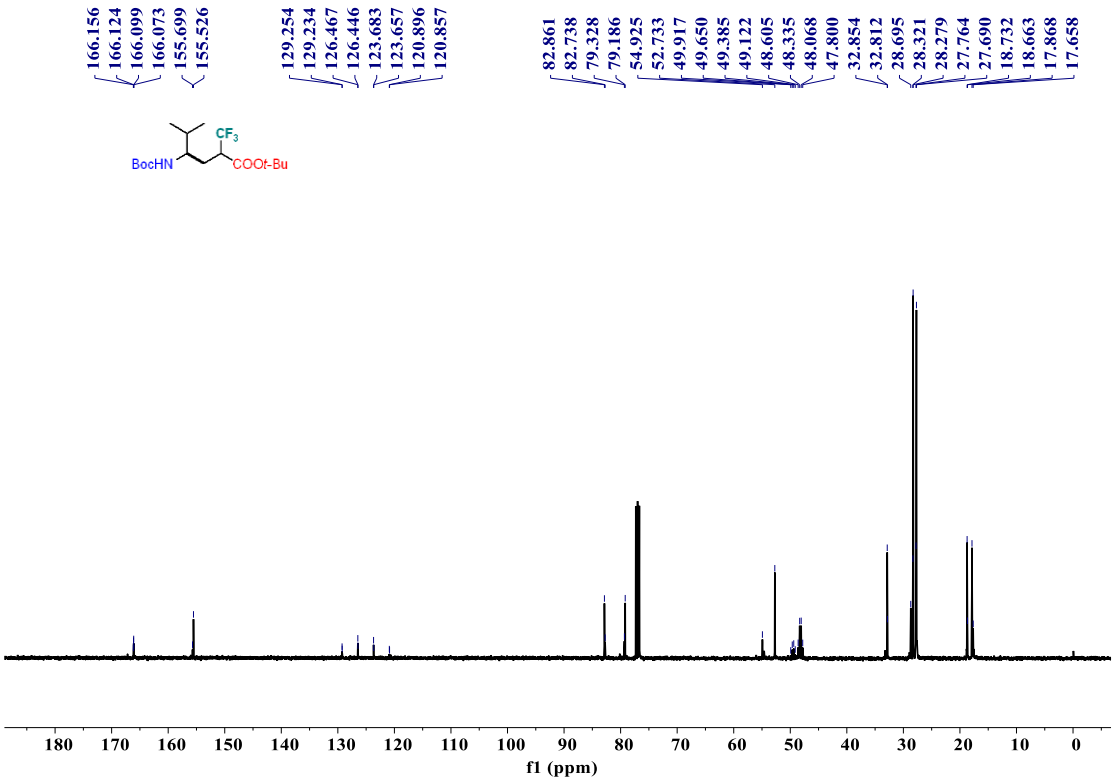


Figure S81. ^{13}C NMR of Compound **5j** (101 MHz, $CDCl_3$)

***tert*-butyl 4-((*tert*-butoxycarbonyl)amino)-5-phenyl-2-(trifluoromethyl)pentanoate (5k)**

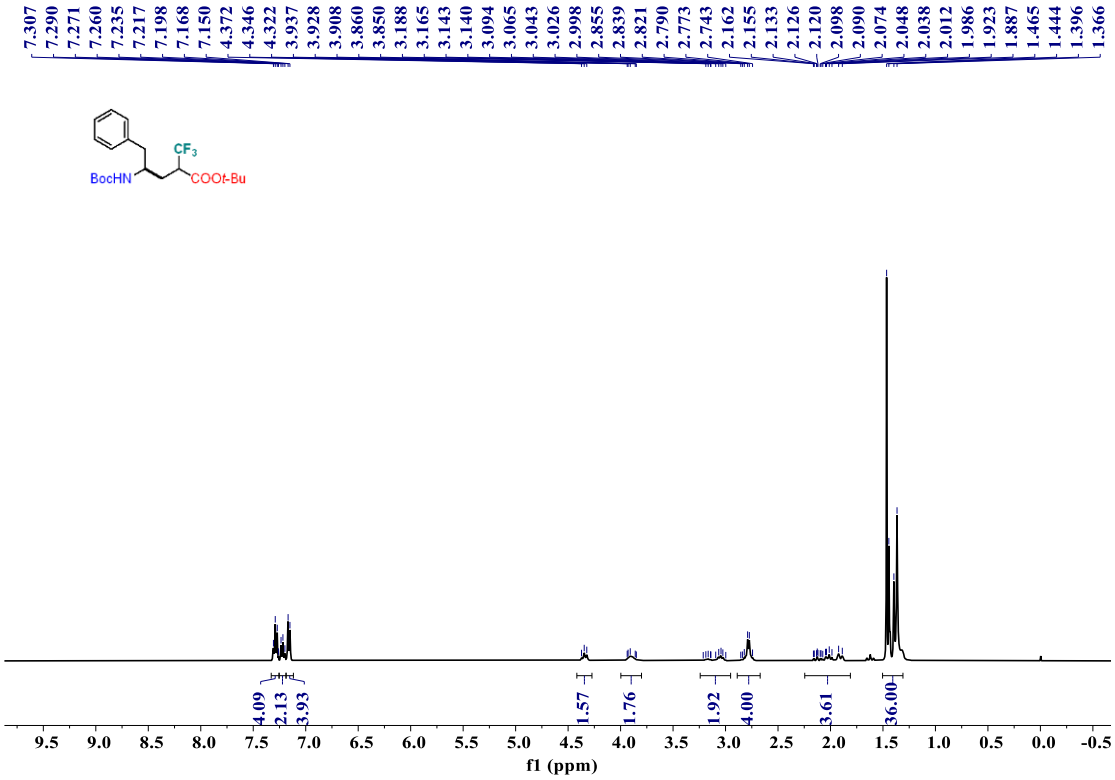


Figure S82. ^{1}H NMR of Compound **5k** (400 MHz, $CDCl_3$)

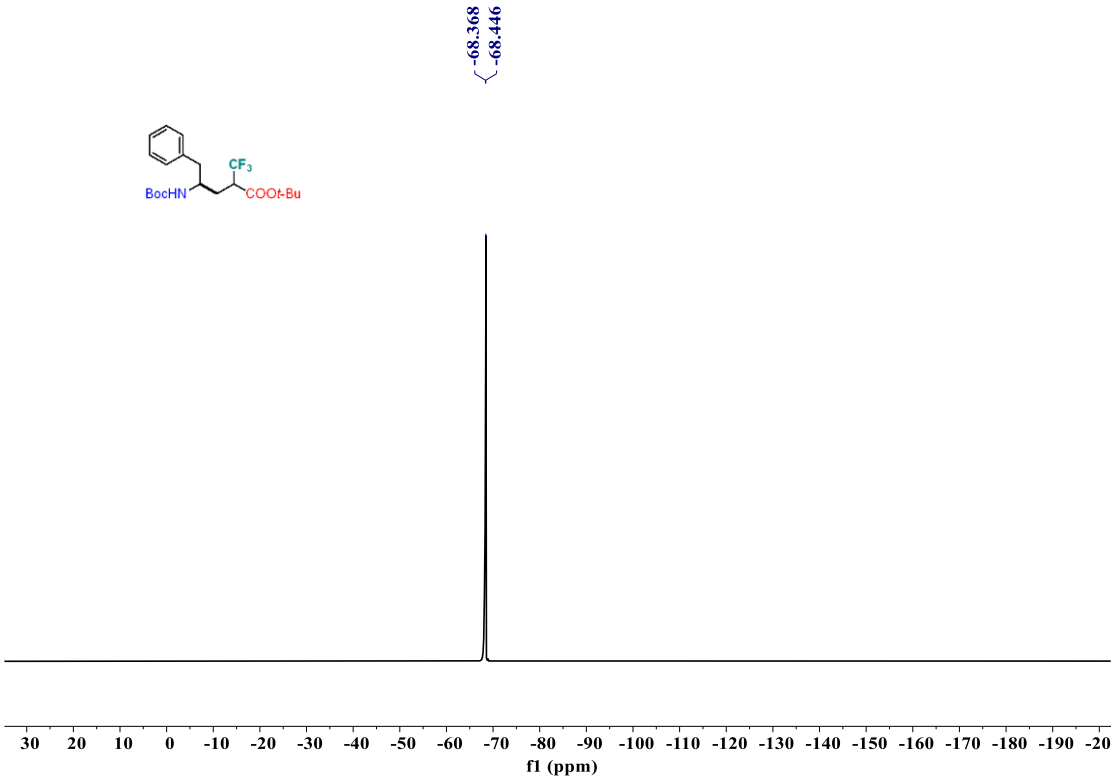


Figure S83. ^{19}F NMR of Compound **5k** (376 MHz, $CDCl_3$)

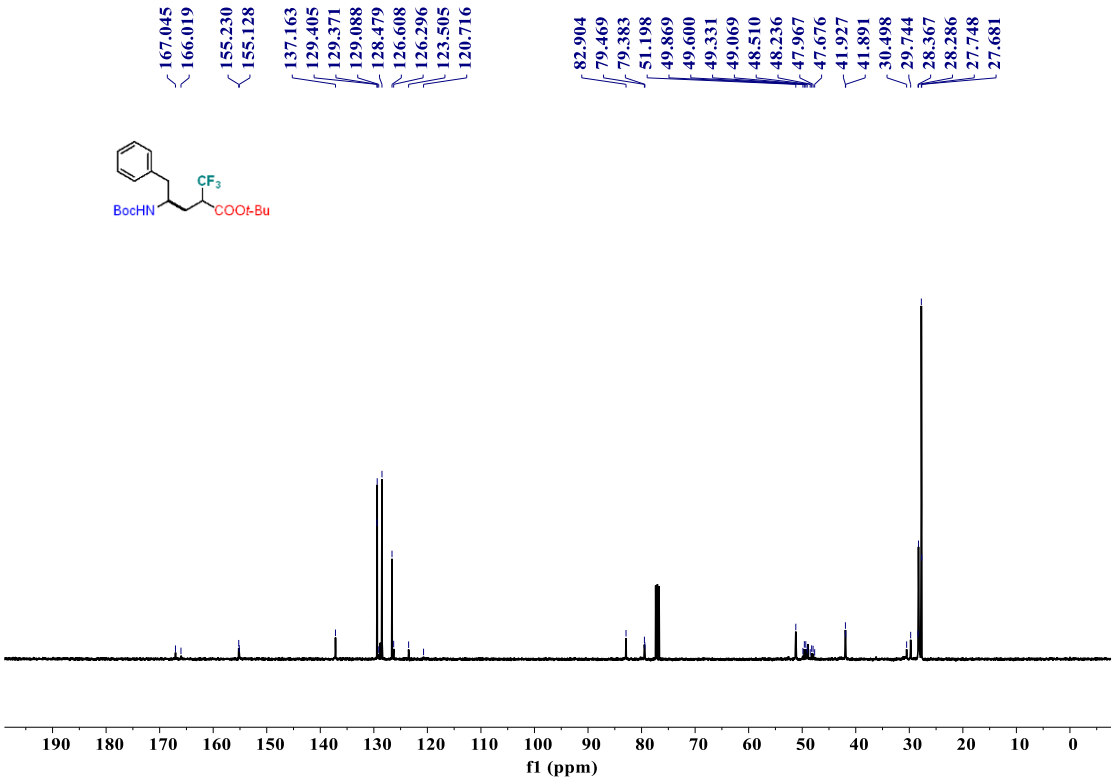


Figure S84. ^{13}C NMR of Compound **5k** (101 MHz, $CDCl_3$)

tert-butyl 4-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-7-((_tert_-butoxycarbonyl)amino)-2-(trifluoromethyl)heptanoate (5l)

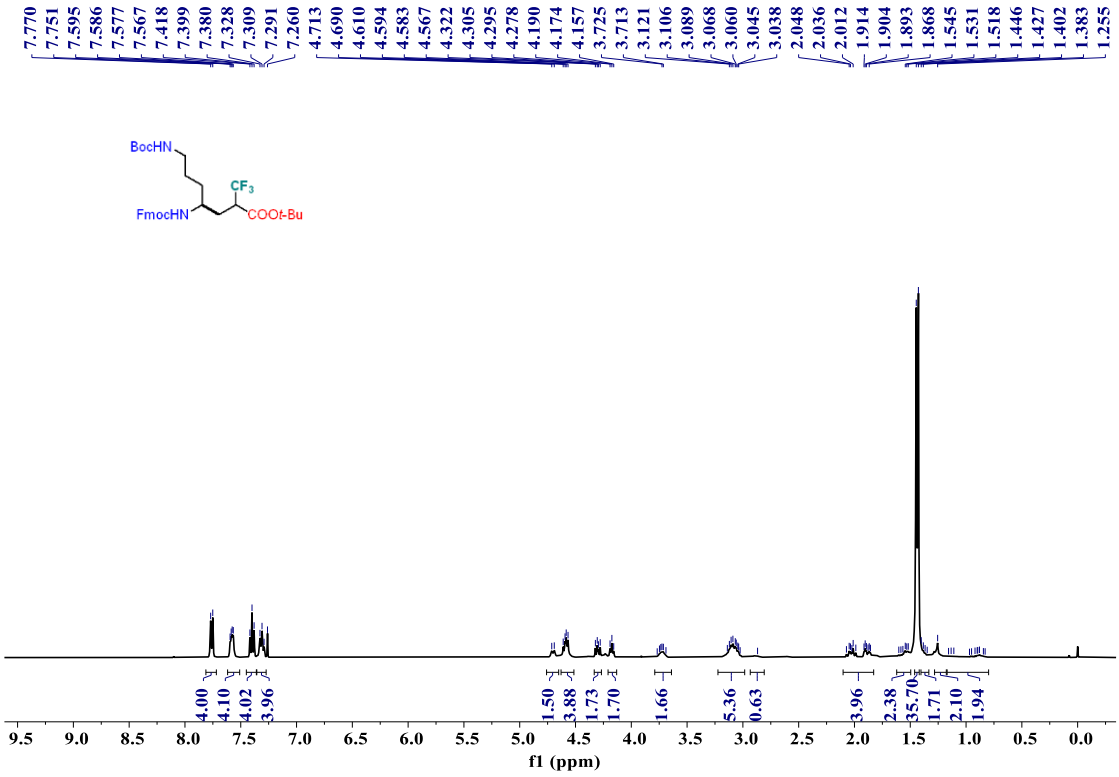


Figure S85. ^{1}H NMR of Compound **5l** (400 MHz, $CDCl_3$)

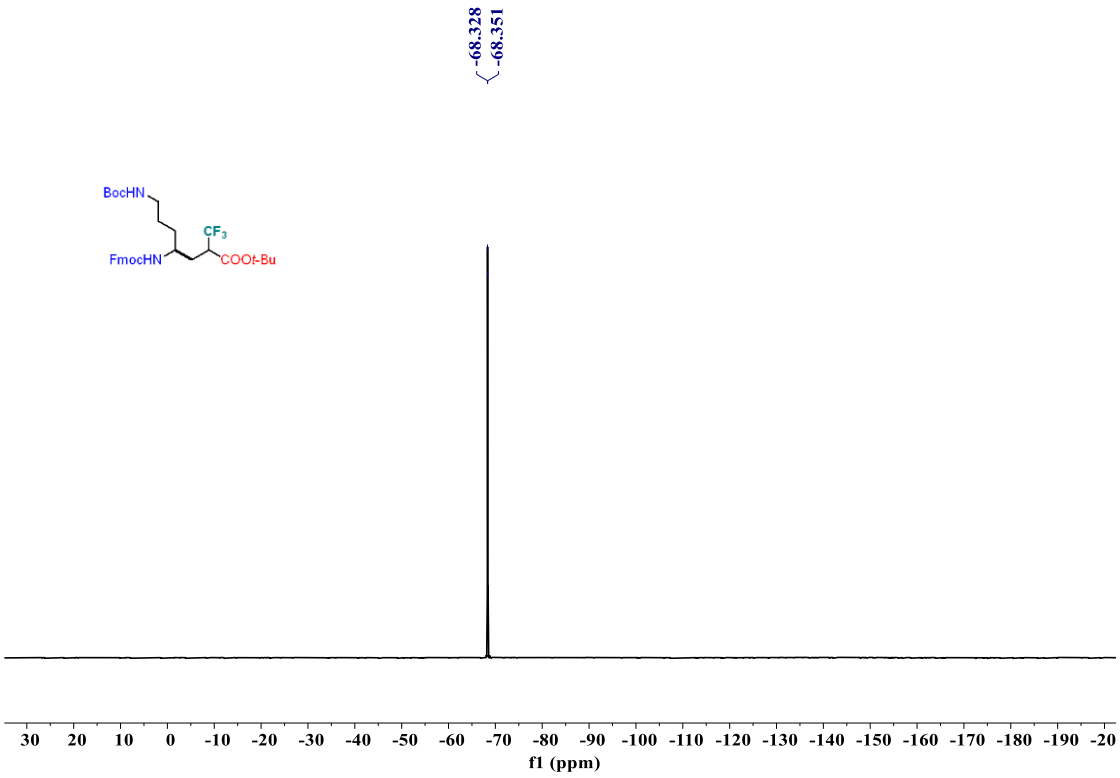


Figure S86. ^{19}F NMR of Compound **5l** (376 MHz, $CDCl_3$)

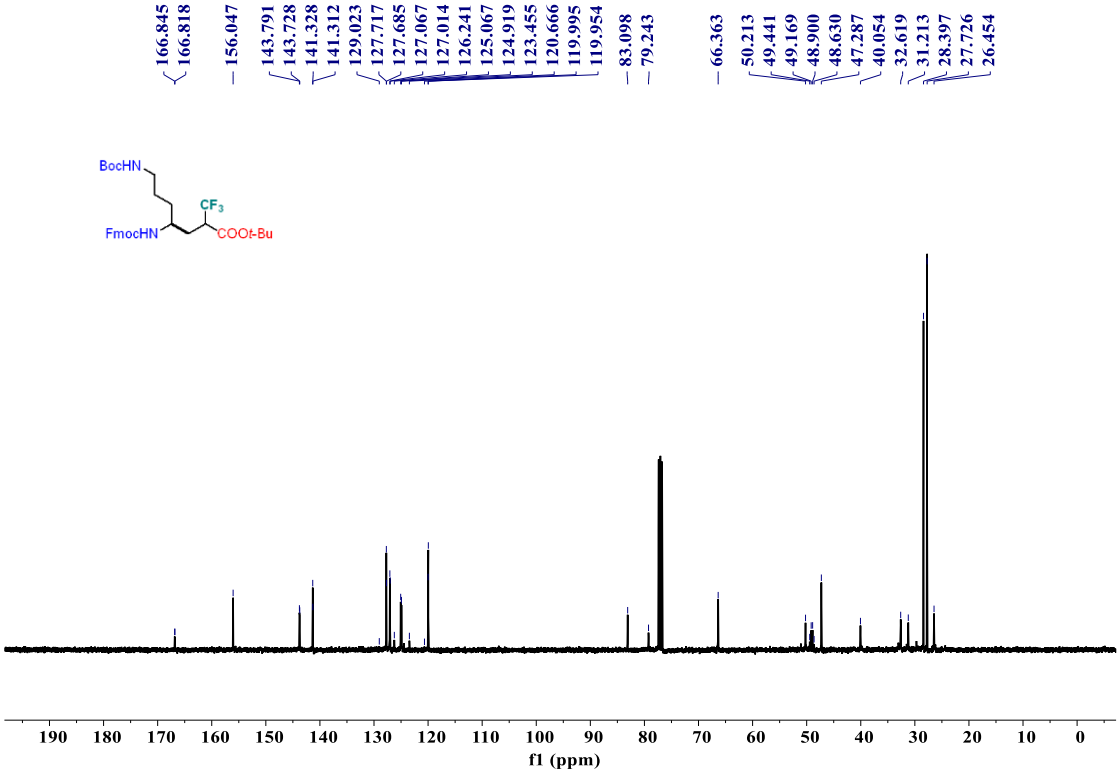


Figure S87. ^{13}C NMR of Compound **5l** (101 MHz, $CDCl_3$)

tert-butyl 4-((_tert_-butoxycarbonyl)amino)-6-(methylthio)-2-(trifluoromethyl)hexanoate (5m)

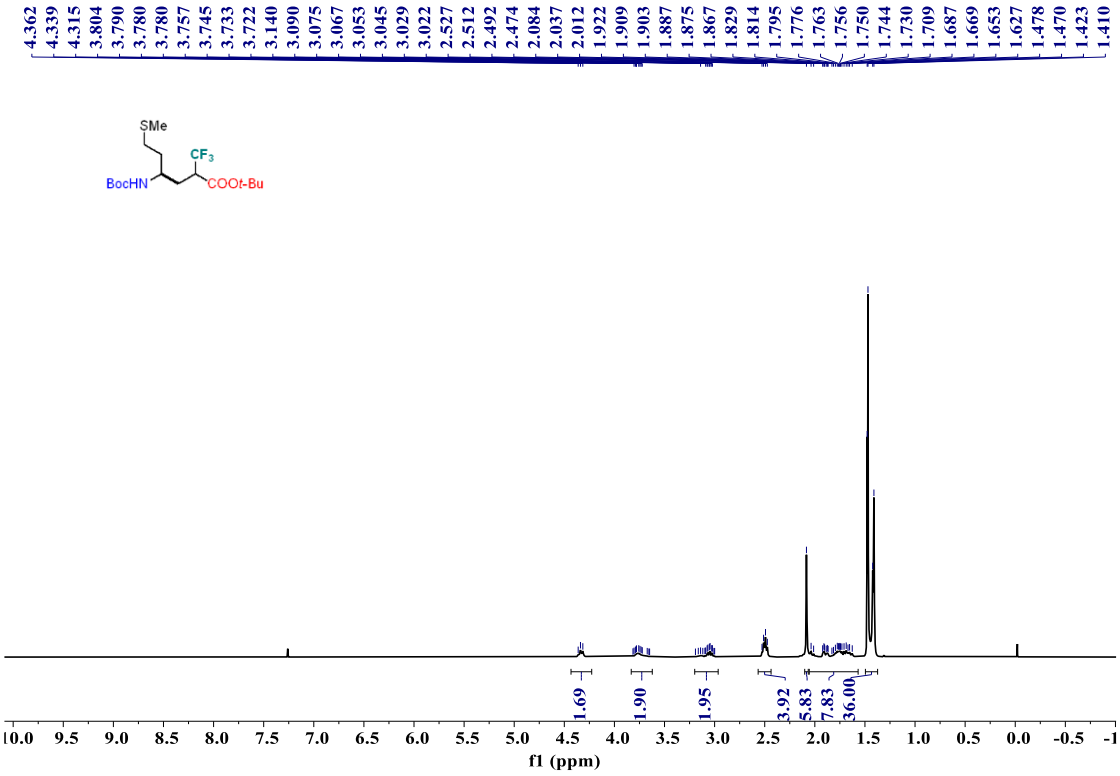


Figure S88. ^{1}H NMR of Compound **5m** (400 MHz, $CDCl_3$)

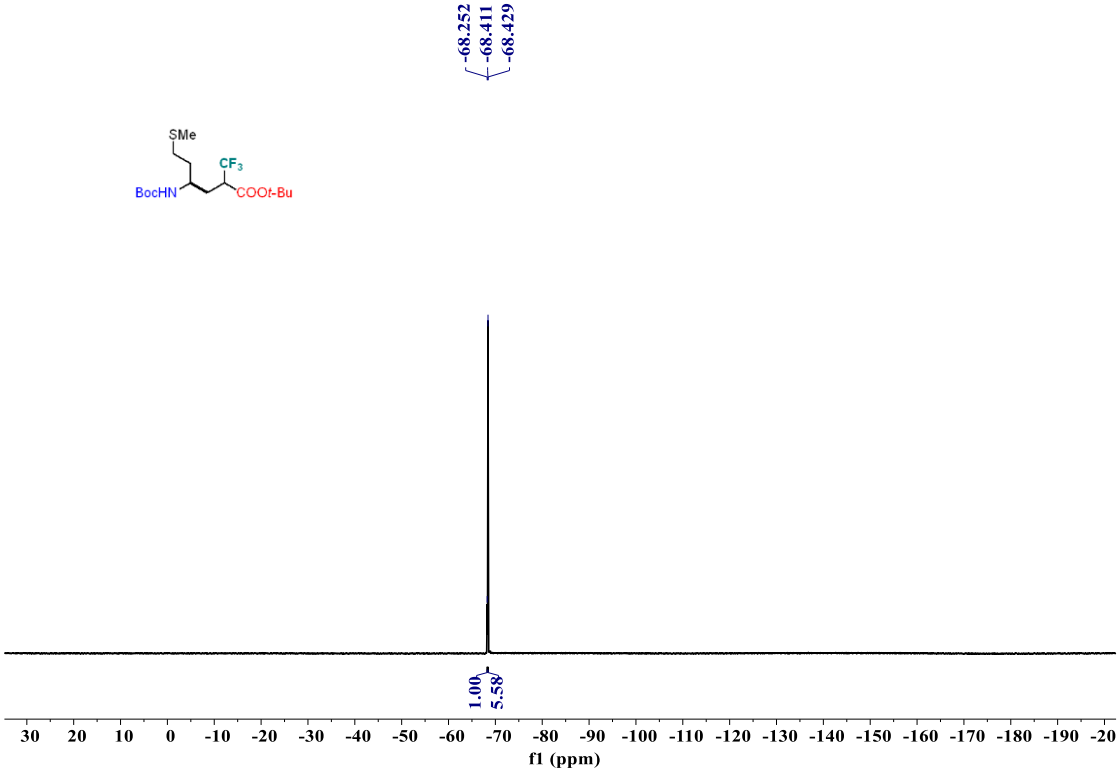


Figure S89. ^{19}F NMR of Compound **5m** (376 MHz, $CDCl_3$)

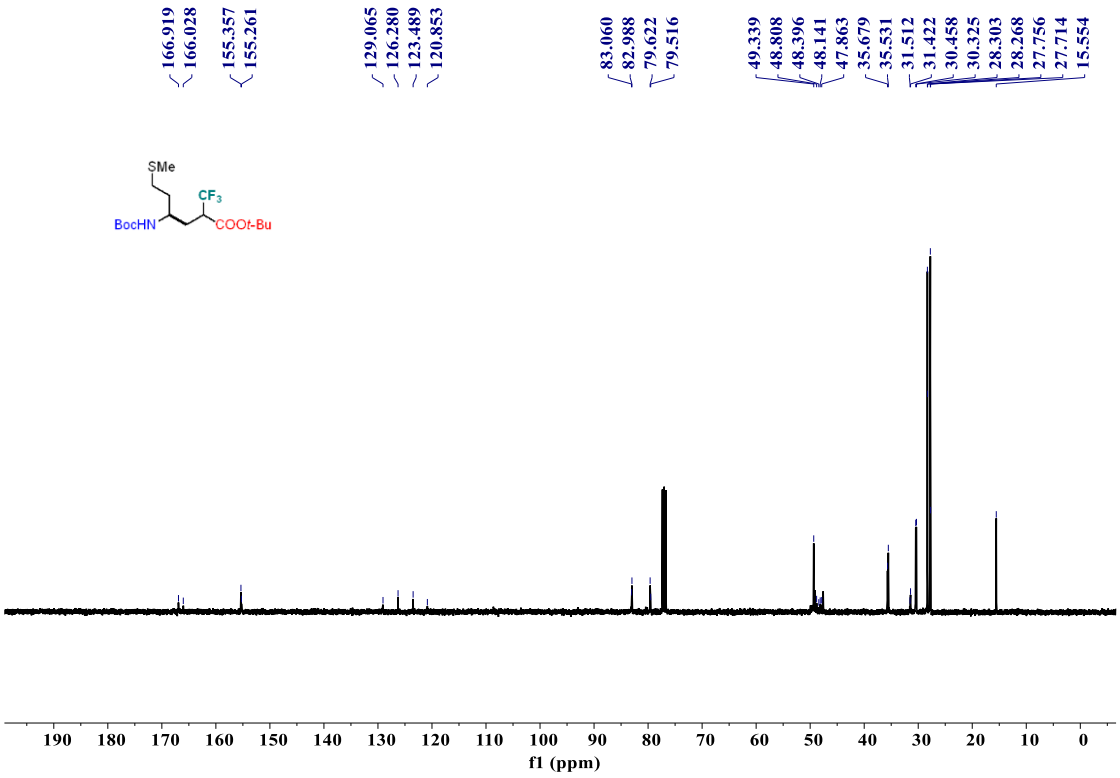


Figure S90. ^{13}C NMR of Compound **5m** (101 MHz, $CDCl_3$)

tert-butyl 4-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)-4-cyclohexyl-2-(trifluoromethyl)butanoate (5n)

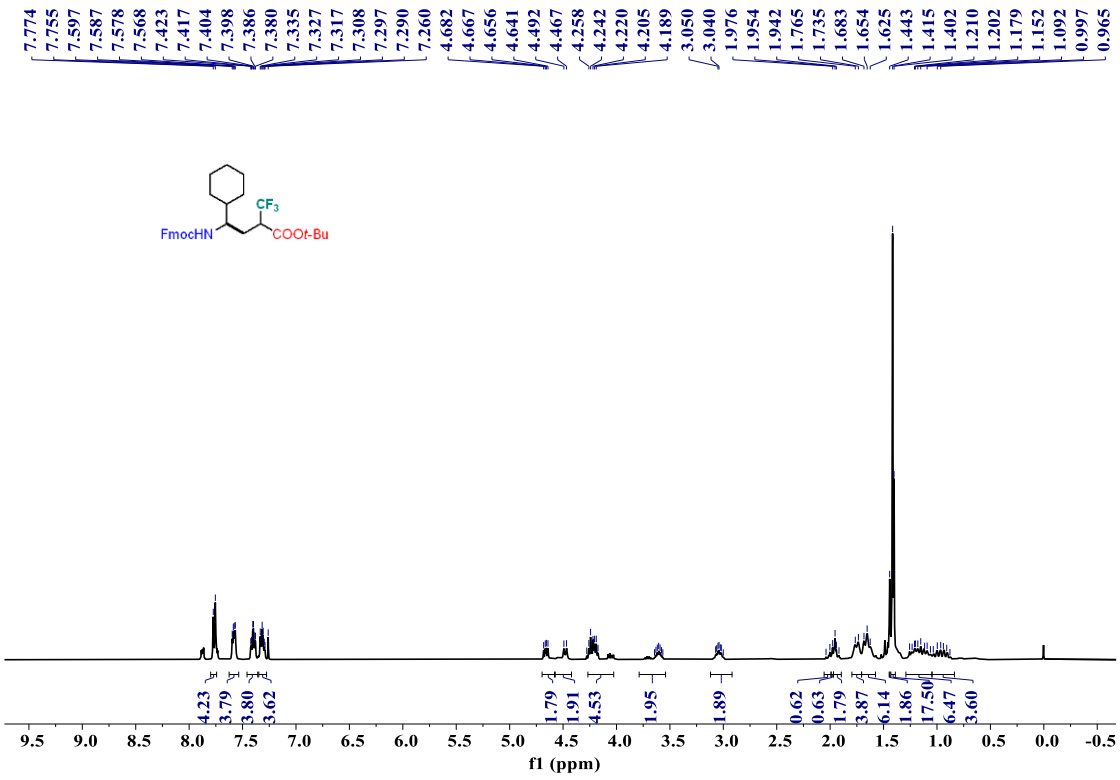


Figure S91. ^{1}H NMR of Compound **5n** (400 MHz, $CDCl_3$)

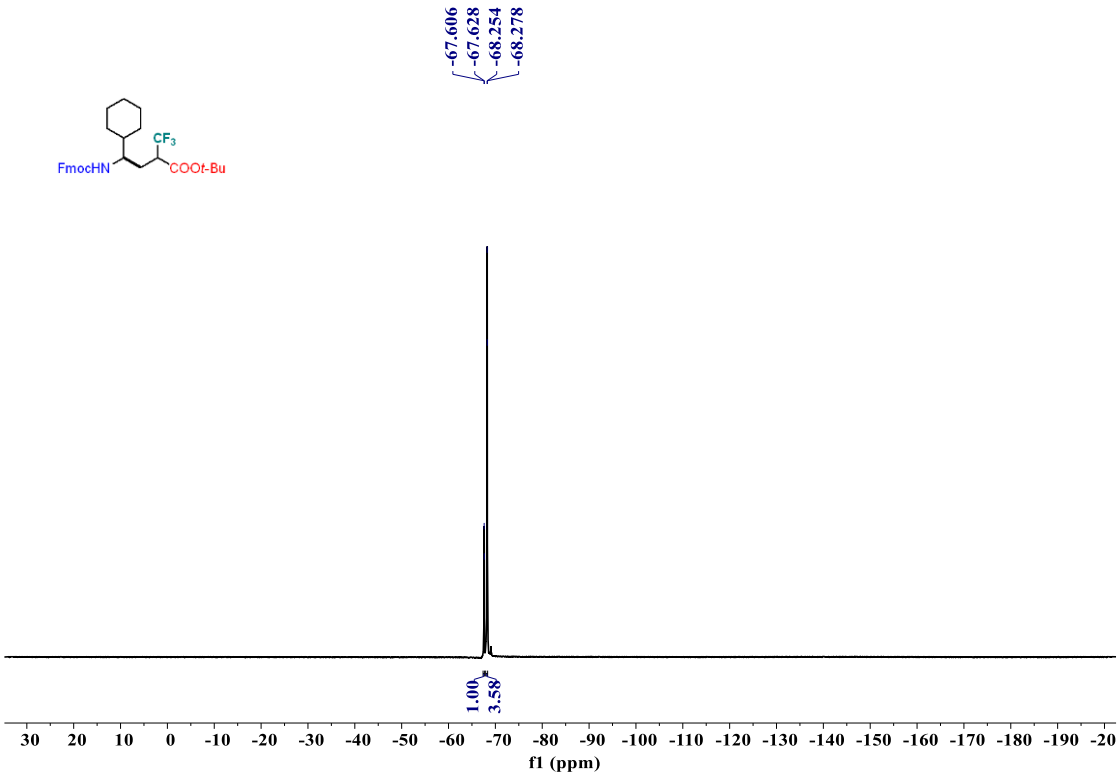


Figure S92. ^{19}F NMR of Compound **5n** (376 MHz, $CDCl_3$)

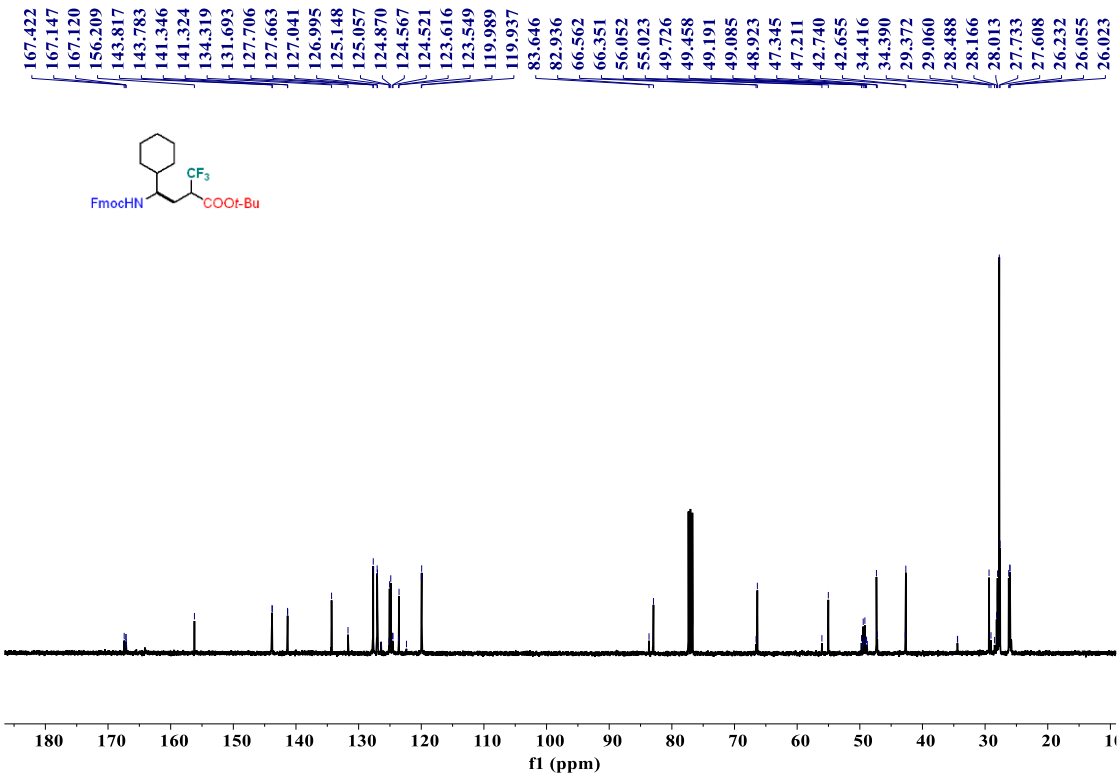


Figure S93. ^{13}C NMR of Compound **5n** (101 MHz, $CDCl_3$)

tert-butyl 2-((1-((_tert_-butoxycarbonyl)amino)cyclopropyl)methyl)-3,3,3-trifluoropropanoate (5o)

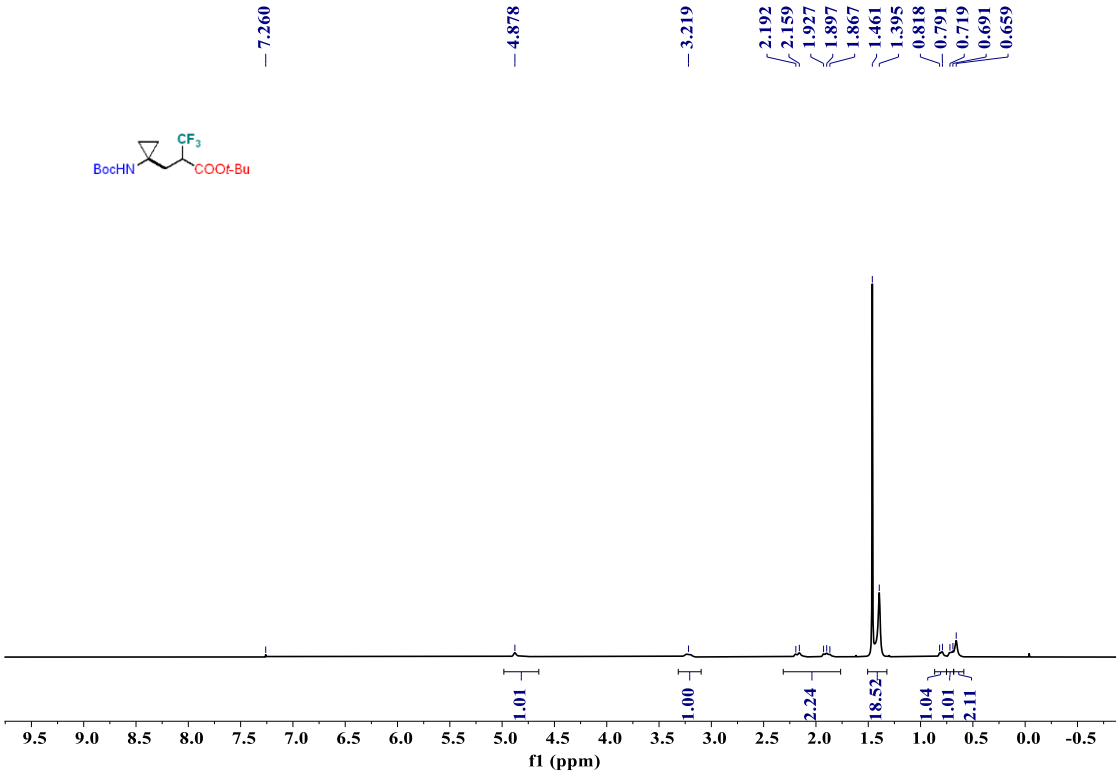


Figure S94. ^{1}H NMR of Compound **5o** (400 MHz, $CDCl_3$)

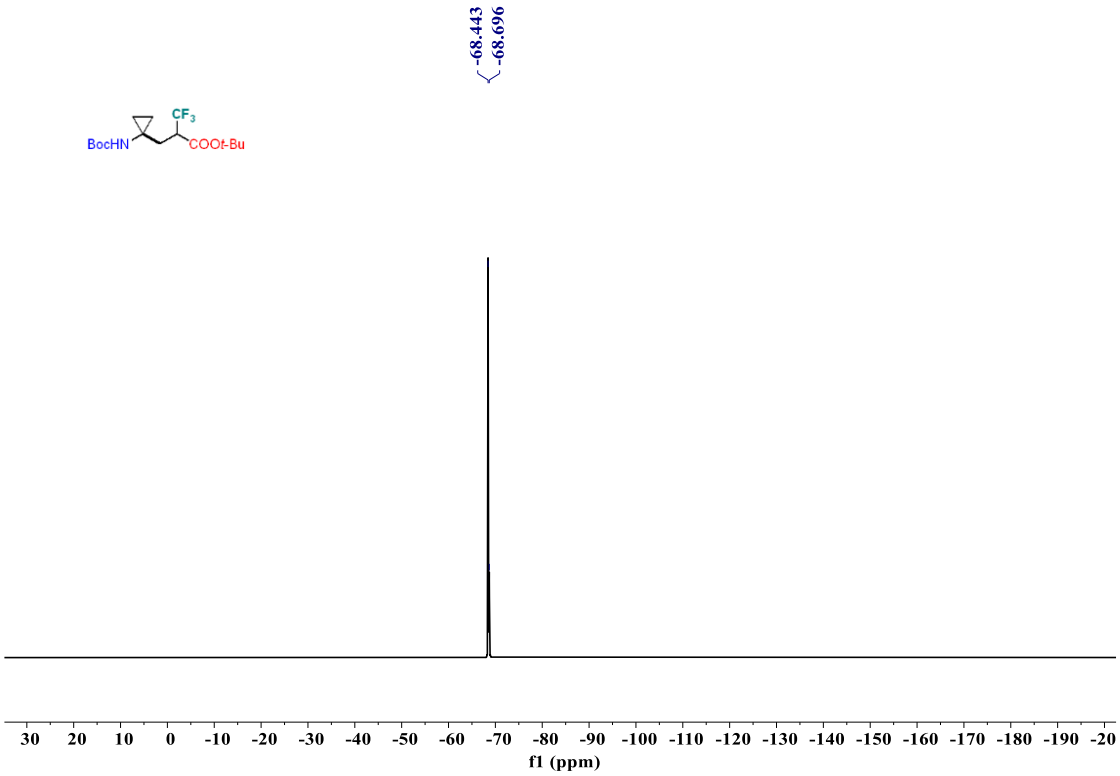


Figure S95. ^{19}F NMR of Compound **5o** (376 MHz, $CDCl_3$)

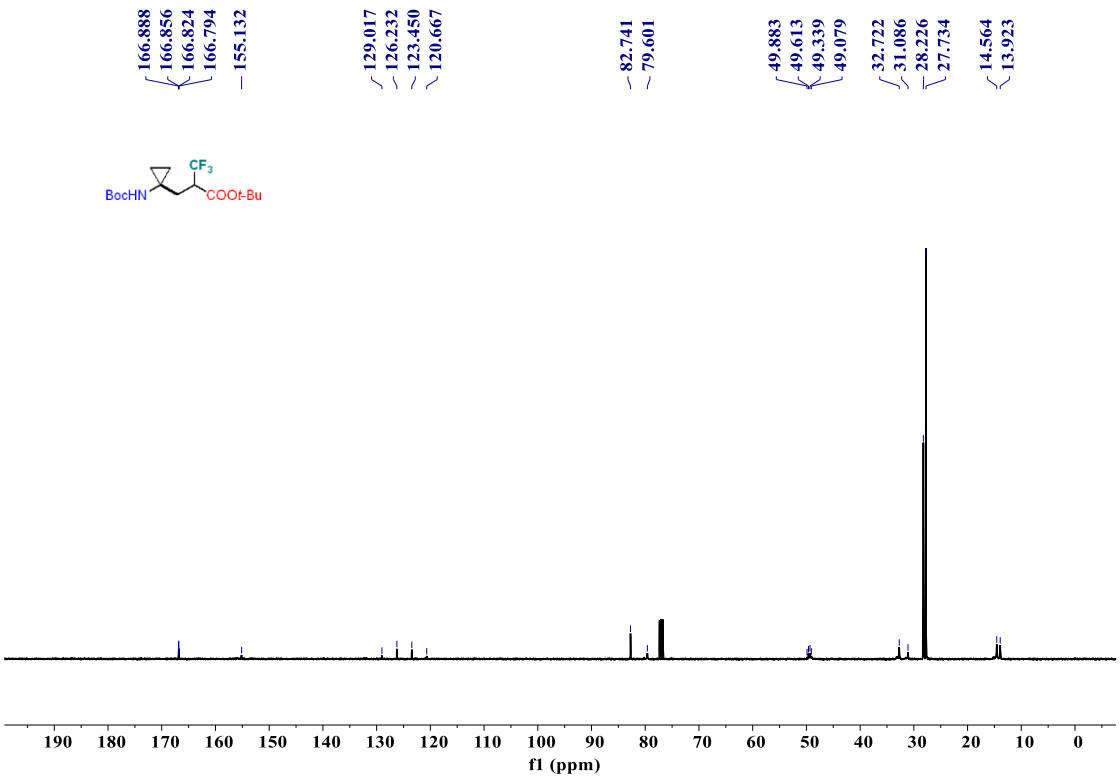


Figure S96. ^{13}C NMR of Compound **5o** (101 MHz, $CDCl_3$)

4-((*tert*-butoxycarbonyl)amino)-4-methyl-2-(trifluoromethyl)pentanoate (5p)

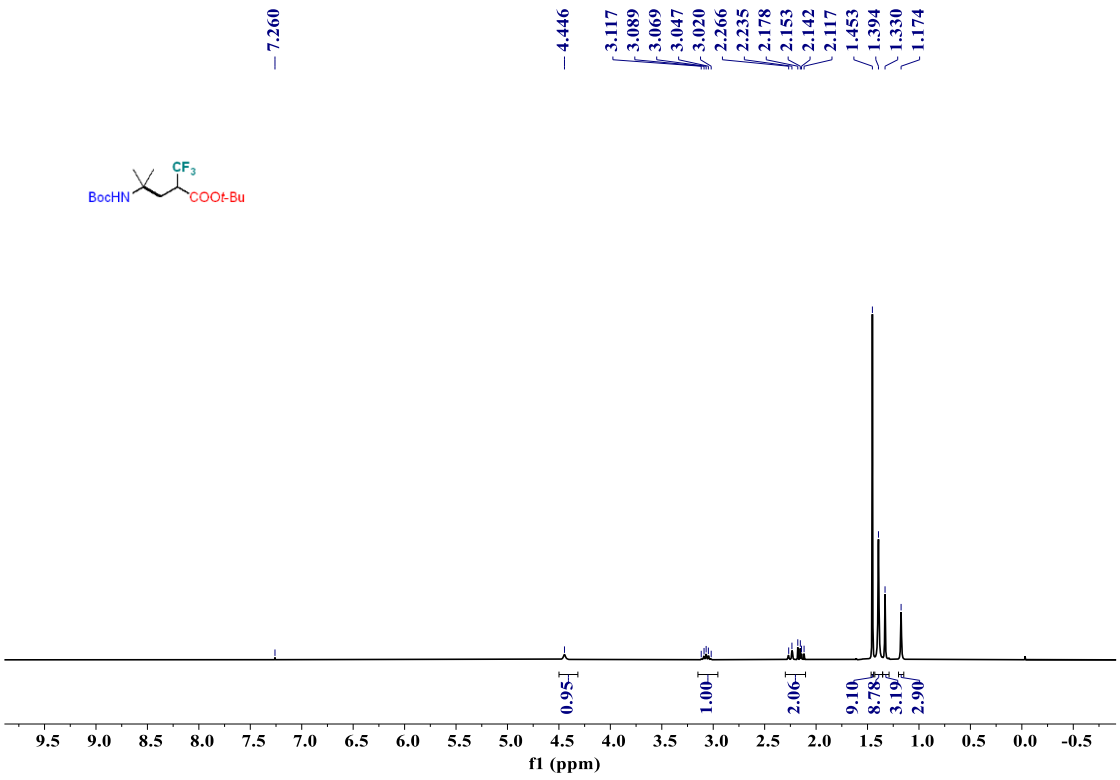


Figure S97. ^{1}H NMR of Compound **5p** (400 MHz, $CDCl_3$)

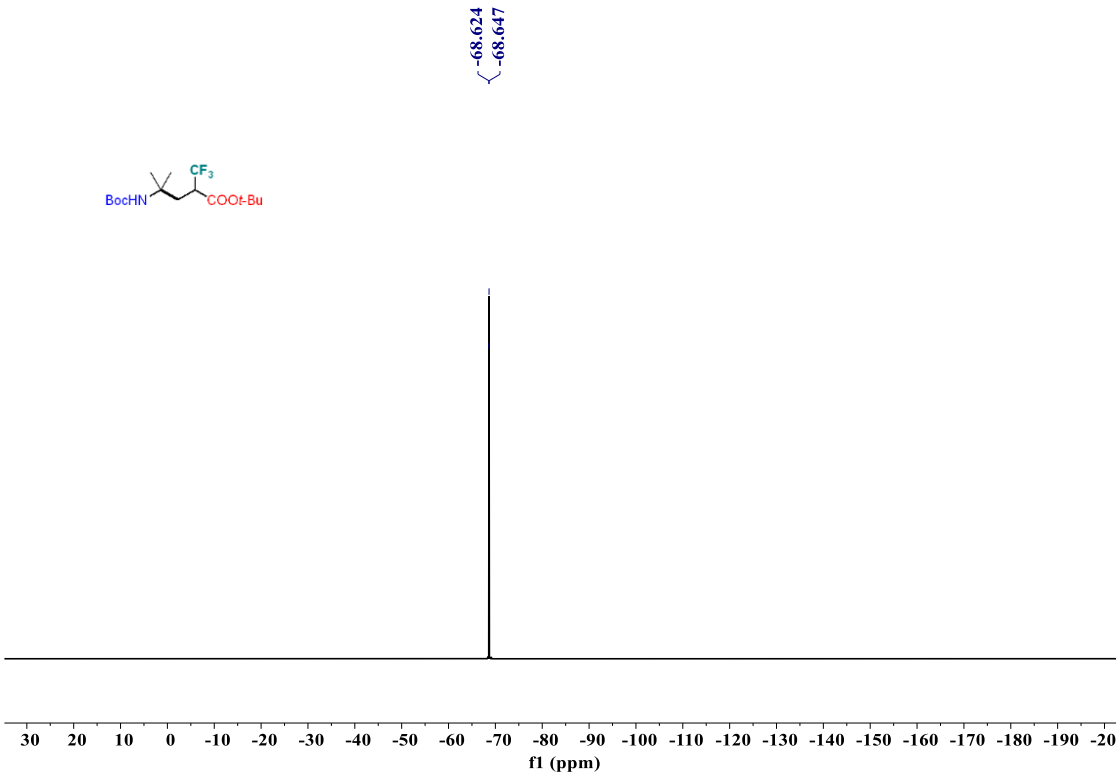


Figure S98. ^{19}F NMR of Compound **5p** (376 MHz, $CDCl_3$)

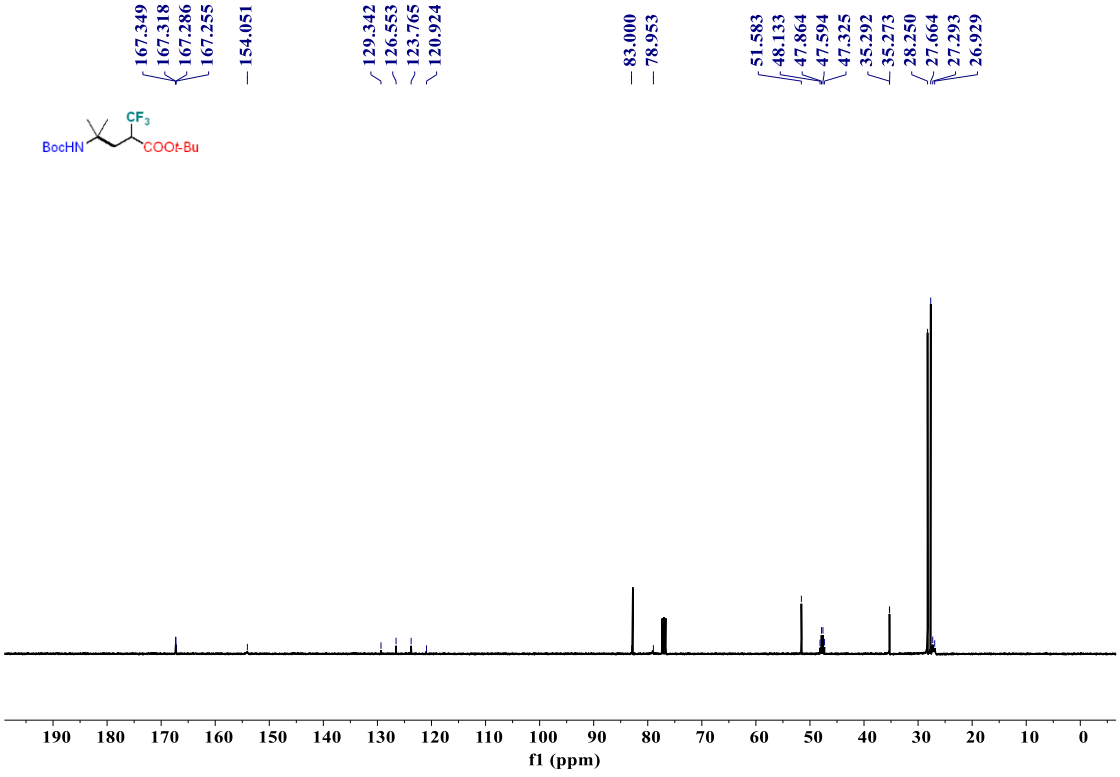


Figure S99. ^{13}C NMR of Compound **5p** (101 MHz, $CDCl_3$)