Supporting Information

A Three-Component Difunctionalization of *N*-Alkenyl Amides *via* Organophotoredox Radical-Polar Crossover

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1. General Considerations

1.1 General: For irradiation, blue LED strips (light-emitting diode, λ_{max} = 456 nm) were placed 1.5 inches away from the reaction vials. NMR spectra (^{1}H, ^{13}C, ^{19}F {^{1}H decoupled}) were obtained at 298 K using 400, 500, and 600 MHz spectrometers. Chemical shifts are referenced to residual, nondeuterated $CHCl_3$ (δ 7.26 in ^{1}H NMR and 77.2 in ^{13}C NMR), CD_3CN (δ 1.93 in ^{1}H NMR and 1.3 in ^{13}C NMR), and trifluorotoluene (δ 63.72 in ^{19}F NMR) was used as internal standard for ^{19}F NMR. The following conventions are used for multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; ddd, doublet of doublet of doublets; td, triplet of doublets; br, broad. Reactions were monitored by GC/MS, ^{1}H NMR, and/or TLC on silica gel plates (60 Å porosity, 250 μm thickness). TLC analysis was performed using hexanes/EtOAc as the eluent and visualized using phosphomolybdic acid, ninhydrin, *p*-anisaldehyde stain, and/or UV light. Flash chromatography was accomplished using an automated system (CombiFlash®, UV detector, λ = 254 nm and 280 nm) with RediSep® R_f silica gel disposable flash columns (60 Å porosity, 40–60 μm) or RediSep R_f Gold® silica gel disposable flash columns (60 Å porosity, 20–40 μm). Accurate mass measurement analyses were conducted using electrospray ionization (ESI). The signals were mass measured against an internal lock mass reference of leucine enkephalin for ESI-LC/MS. The utilized software calibrates the instruments and reports measurements by use of neutral atomic masses. The mass of the electron is not included. IR spectra were recorded on an FT-IR using either neat oil or solid products. UV/vis studies were measured in a 1 cm quartz cuvette using a Genesys 150 UV/vis spectrophotometer from Thermo Scientific.

1.2 Chemicals: Deuterated NMR solvents were purchased from Cambridge Isotopes and stored over 4 Å molecular sieves. Anhydrous DMF was obtained from Acros Organics and used as received. Bulk solvents were obtained from Fisher. Enamides, α-bromocarbonyl compounds, thiols, alcohols, and sodium azide were purchased from commercial suppliers and used as received. (*E*)-1-(Prop-1-en-1-yl)pyrrolidin-2-one[1] and 2-bromo-*N*,*N*-diethyl-2,2-difluoroacetamide[2] were prepared according to the literature. Photoredox-catalyzed reactions were performed using 8 mL Chemglass vials (2-dram, 17 x 60 mm, 15-425 Green Open Top Cap, TFE Septa).

[1] Thullen, M. S.; Rubush, D. M.; Rovis, T. *Synlett* 2017, **28**, 2755-2758.
[2] Engel-Andreasen, J.; Wellhöfer, I.; Wich, K.; Olsen, C. A. *J. Org. Chem.* 2017, **82**, 11613-11619.

2. Difunctionalization of *N*-Alkenyl Amides: Reaction Workflow and Compound Characterization

A. Reaction Workflow

All photoredox reactions were performed with blue LED strips (light-emitting diode, λ_{max} = 456 nm). The LEDs were placed 1.5 inches away from the reaction vials within a ventilated fume hood. A typical reaction setup is shown below.

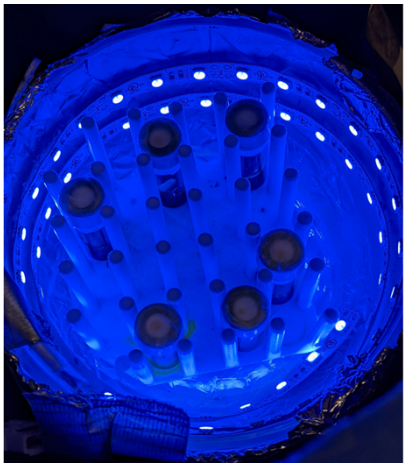


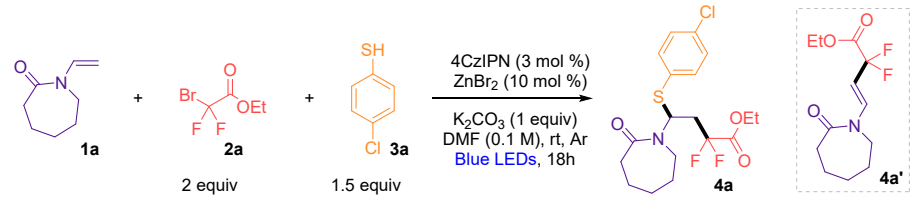
Figure 1: Reaction setup for the difunctionalization of *N*-alkenyl amides

B. *Reaction Optimization*

To evaluate the feasibility of the designed organophotoredox difunctionalization, *N*-vinyl caprolactam (**1a**), ethyl bromodifluoroacetate (**2a**), and 4-chlorothiophenol (**3a**) were selected as model substrates (Table 1) to scrutinize various reaction parameters. First, considering that the choice of photocatalyst significantly impacts the product distributions, we selected 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN) as the photocatalyst ($E_{1/2}$ PC^+/PC^* = -1.04 V vs SCE). Under these reaction conditions, product **4a** was formed in a trace amount (Table 1, entry 2). As thiophenols are not strong nucleophiles, we reasoned that only a trace amount of product **4a** was observed because of the low nucleophilicity of **3a**. Therefore, to increase the propensity of nucleophilic attack of thiophenols on the *N*-vinyl caprolactam (**1a**), Lewis acids were screened to increase the electrophilicity of **1a**. After examining several Lewis acids (see Table 1, entries 3-4 and Supporting Information), we observed the formation of product **4a** in 80% yield when 10 mol % of $ZnBr_2$ was used. The viability of this transformation was also evaluated in the presence of a more strongly reducing photocatalyst [$Ir(ppy)_3$]. The use of $Ir(ppy)_3$ provided the desired compound in low yield (Table 1, entry 5) because of the formation of the elimination product **4a'**. In this case, the rate of single-electron oxidation of the α- amidoalkyl

radical may be faster compared to that when 4CzIPN is used or this photocatalyst promotes the oxidation of the thiol to the corresponding disulfide. Also, the rate of nucleophilic addition of thiolate to the α-amide carbocation may not be taking place preferentially, thus providing the elimination product. The difunctionalized amide **4a** was obtained in good yield when using the less reducing 4-ClCzIPN [2,4,5,6-tetrakis(3,6-dichloro-9*H*-carbazol-9-yl)isophthalonitrile] photocatalyst (Table 1, entry 6, $E_{1/2}$ PC^+/PC^* = -0.63 V vs SCE). Given these observations, we selected the more accessible 4CzIPN as the most suitable organophotocatalyst for the desired transformation. Also, the exploration of other solvents resulted in the formation of product **4a** in lower yields. Finally, control experiments, avoiding light irradiation as well as a photocatalyst, validated the necessity of all reaction components to obtain the difunctionalized amide **4a** (Table 1, entries 11 and 12).

Table S1. Optimization of Reaction Conditions



Entry	Deviation from above	Yield (%)[a]
1	none	80 (74)[b]
2	without $ZnBr_2$	traces
3	w/ $ZnCl_2$ instead of $ZnBr_2$	66
4	w/ $Zn(OTf)_2$ instead of $ZnBr_2$	20
5	w/ $Ir(ppy)_3$ instead of 4CzIPN	15
6	w/ 4-ClCzIPN instead of 4CzIPN	76
7	DMA as solvent	40
8	DMSO as solvent	15
9	MeCN as solvent	35
10	Acetone as solvent	traces
11	without 4CzIPN	0
12	without light irradiation	0
13	without argon	20

Optimization of reactions were performed using **1a** (0.10 mmol), **2a** (0.20 mmol), **3a** (0.15 mmol), photocatalyst (0.003 mmol), $ZnBr_2$ (0.01 mmol) and K_2CO_3 (0.15 mmol), in dry degassed solvent (1.0 mL, c = 0.1 M) under blue LED strip irradiation (λ_{max} = 456 nm) for 18 h at rt. Measured by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard from the crude mixture. [b]Isolated yield of **4a** on 0.5 mmol scale.

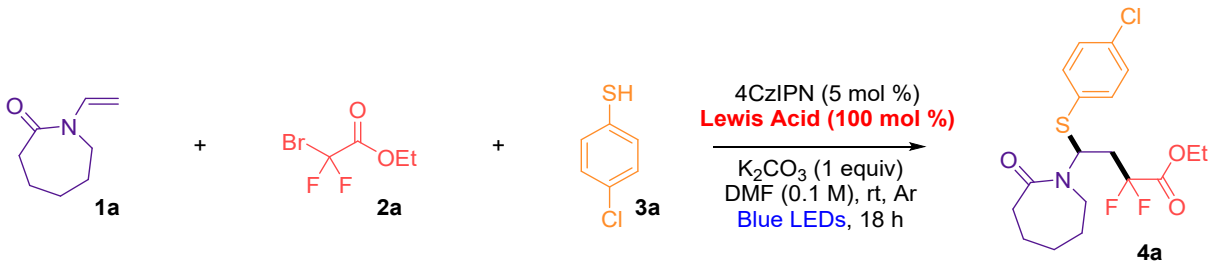


Table S2. Lewis acid screening[a]

Entry	Lewis Acid	Yield 4a (%)[b]
1	**$ZnBr_2$**	**81**
2	$ZnBr_2$ (20 mol %)	80
3	$ZnBr_2$ (10 mol %)	80
4	$ZnCl_2$	66
5	ZnI_2	25
6	$Zn(OTf)_2$	20
7	$Cu(OAc)_2$	55
8	CuI	70

[a]Optimization reactions were performed using **1a** (0.10 mmol), **2a** (0.20 mmol), **3a** (0.15 mmol), photocatalyst (0.005 mmol), LA (0.1 mmol) and K_2CO_3 (0.15 mmol), in dry degassed solvent (1.0 mL, c = 0.1 M) under blue LED strip irradiation (λ_{max} = 456 nm) for 18 h at rt. [b] ^1H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

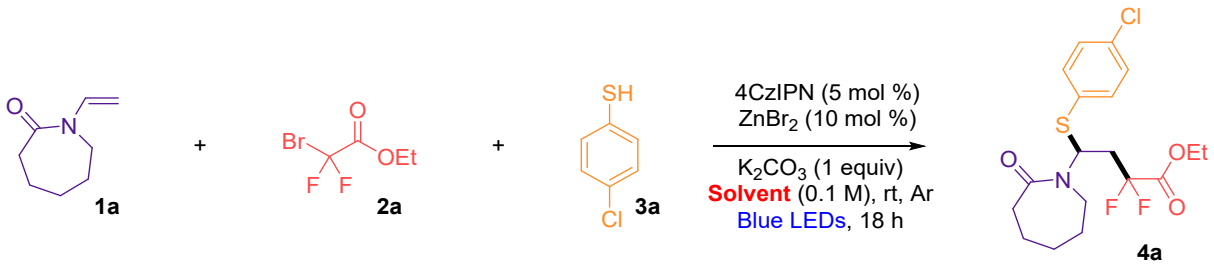


Table S3. Solvent screening[a]

Entry	Solvent	Yield 4a (%)[b]
1	**DMF**	**80**
2	DMA	40
3	DMSO	15
4	Acetone	traces
5	MeCN	35

[a]Optimization reactions were performed using **1a** (0.10 mmol), **2a** (0.20 mmol), **3a** (0.15 mmol), photocatalyst (0.005 mmol), Zn^{+2} (0.01 mmol) and K_2CO_3 (0.15 mmol), in dry degassed solvent (1.0 mL, c = 0.1 M) under blue LED strip irradiation (λ_{max} = 456 nm) for 18 h at rt. [b] ^1H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

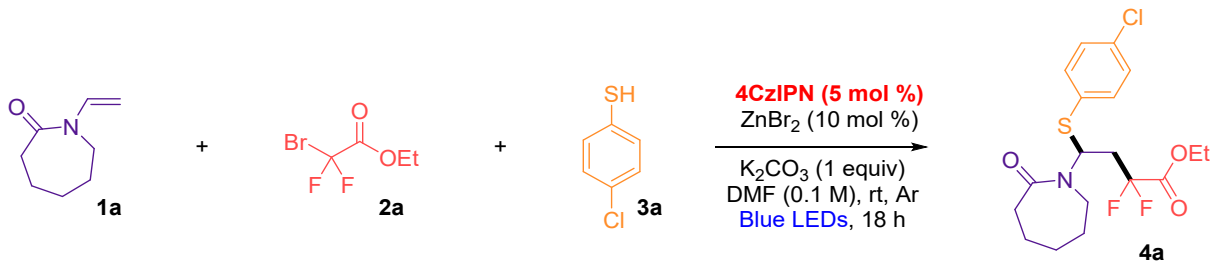


Table S4. Photocatalyst screening[a]

Entry	Solvent	Yield 4a (%)[b]
1	4CzIPN	80
2	**4CzIPN (3 mol %)**	**80**
3	4CzIPN (2 mol %)	70
4	4-ClCzIPN	76
5	$Ir(ppy)_3$	15

[a]Optimization reactions were performed using **1a** (0.10 mmol), **2a** (0.20 mmol), **3a** (0.15 mmol), photocatalyst (x mol %), Zn^{+2} (0.01 mmol) and K_2CO_3 (0.15 mmol), in dry degassed solvent (1.0 mL, c = 0.1 M) under blue LED strip irradiation (λ_{max} = 456 nm) for 18 h at rt. [b] ^1H NMR yield using 1,3,5-trimethoxybenzene as internal standard.

C. General Procedure

General Procedure for Table S1–S4

To an oven-dried 1 dram vial equipped with a magnetic stir bar 4CzIPN (2.4 mg, 0.003 mmol, 3 mol %), $ZnBr_2$ (2.2 mg, 0.01 mmol, 10 mol %), *N*-vinyl caprolactam **1a** (13.9 mg, 0.1 mmol, 1.0 equiv), 4-chlorothiophenol **3a** (21.6 mg, 0.15 mmol, 1.5 equiv), and K_2CO_3 (13.8 mg, 0.1 mmol, 1.0 equiv) were added, and the vial was subjected to 3 cycles of vacuum/argon degassing. Subsequently, DMF (1 mL, 0.1 M) and ethyl 2-bromo-2,2-difluoroacetate **2a** were added via syringe (0.2 mmol, 2 equiv). The reaction mixture was irradiated for 18 h with blue LED strips (light-emitting diode, λ_{max} = 456 nm) as described in the "Workflow" section. The temperature of the reaction was maintained at approximately 25 °C via a fan. Upon completion, 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol, 1 equiv) was added to the reaction mixture, which was then diluted with EtOAc (1 mL) and washed with H_2O (1 mL × 3). The organic layer was dried (Na_2SO_4) and then subjected to rotary evaporation to remove the solvent. The residue obtained was dissolved in $CDCl_3$ and analyzed by ^{1}HNMR.

General Procedure for Table 1 in Manuscript

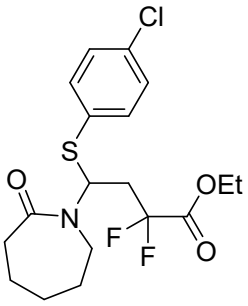
To an oven-dried 8 mL vial equipped with a magnetic stir bar, 4CzIPN (7.2 mg, 0.015 mmol, 3 mol %), $ZnBr_2$ (11 mg, 0.25 mmol, 10 mol %), K_2CO_3 (69 mg, 0.5 mmol, 1.0 equiv), and, if solids, *N*-alkenyl amide (0.5 mmol, 1.0 equiv) and/or arylthiol (0.75 mmol, 1.5 equiv), were added, and the vial was subjected to 3 cycles of vacuum/argon degassing. Subsequently, DMF (5 mL, 0.1 M) and the α-bromocarbonyl compound were added via syringe (0.2 mmol, 2 equiv). If liquids, the *N*-alkenyl amide (0.5 mmol, 1.0 equiv) and/or arylthiol (0.75 mmol, 1.5 equiv), were added via syringe after the addition of the α-bromocarbonyl compound. The reaction mixture was irradiated for 18 h with blue LED strips (light-emitting diode, λ_{max} = 456 nm) as described in the "Workflow" section. The temperature of the reaction was maintained at approximately 25 °C via a fan. Upon completion, the reaction mixture was poured into a separatory funnel and diluted with EtOAc (5 mL) and washed with H_2O (5 mL × 3) followed by brine (5 mL). The organic layer was dried (anhyd Na_2SO_4) and then subjected to rotary evaporation to remove the solvent. Purification of the desired compound was achieved by automated flash column chromatography using hexanes/EtOAc mixtures.

General Procedure for Table 2 in Manuscript

To an oven-dried 8 mL vial equipped with a magnetic stir bar, 4CzIPN (7.2 mg, 0.015 mmol, 3 mol %), K_2CO_3 (69 mg, 0.5 mmol, 1.0 equiv), and, if solids, *N*-alkenyl amide (0.5 mmol, 1.0 equiv), and/or the corresponding nucleophile (for the amount see below this procedure), were added, and the vial was subjected to 3 cycles of vacuum/argon degassing. Subsequently, DMF (5 mL, 0.1 M) and the α-bromocarbonyl compound were added via syringe (0.2 mmol, 2 equiv). If liquids, the *N*-alkenyl amide (0.5 mmol, 1.0 equiv) and/or the corresponding nucleophile (for the amount see below this procedure), were added via syringe after the addition of the α-bromocarbonyl compound. The reaction mixture was irradiated for 18 h with blue LED strips (light-emitting diode, λ_{max} = 456 nm) as described in the "Workflow" section. The temperature of the reaction was maintained at approximately 25 °C via a fan. Upon completion, the reaction mixture was poured into a separatory funnel and diluted with EtOAc (5 mL) and washed with H_2O (5 mL × 3) followed by brine (5 mL). The organic layer was dried (anhyd Na_2SO_4) and then subjected to rotary evaporation to remove the solvent. Purification of the desired compound was achieved by automated flash column chromatography using hexanes/EtOAc mixtures.

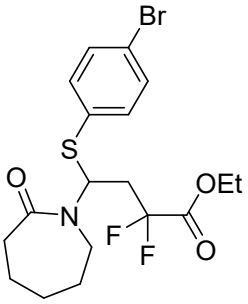
Nucleophiles used: MeOH or EtOH (2.5 mmol, 5 equiv), H_2O (1.0 mmol, 2 equiv), and NaN_3 (0.75 mmol, 1.5 equiv)

D. Characterization Data for New Compounds



Ethyl 4-((4-Chlorophenyl)thio)-2,2-difluoro-4-(2-oxoazepan-1-yl)butanoate (4a): The title compound **4a** was obtained as a yellow oil (150.0 mg, 74% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

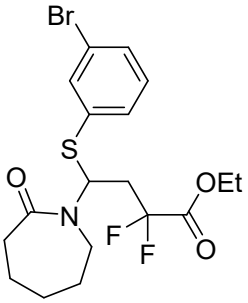
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.32 (m, 2H), 7.29 – 7.24 (m, 2H), 6.60 (br, 1H), 4.35 (q, J = 7.2 Hz, 2H), 3.43 – 3.30 (m, 2H), 2.61 – 2.52 (m, 2H), 2.44 – 2.37 (m, 2H), 1.69 – 1.55 (m, 4H), 1.49 – 1.31 (m, 5H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 176.0, 163.3 (t, $J_{C\text{-}F}$ = 31.8 Hz), 133.6, 132.3, 131.5, 129.3, 114.4 (t, $J_{C\text{-}F}$ = 254.0 Hz), 63.5, 55.5, 44.2, 37.5, 37.4 (t, $J_{C\text{-}F}$ = 23.7 Hz), 29.9, 28.8, 23.1, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -102.7 (d, J = 270.9 Hz), -106.2 (d, J = 270.7 Hz); **IR (neat)** cm^{-1}: 2925, 1756, 1648, 1587, 1093; **HRMS (ESI)**: Calcd. for $C_{18}H_{22}ClF_2NNaO_3S$ $(M+Na)^+$ 428.0875, found 428.0880.



Ethyl 4-((4-Bromophenyl)thio)-2,2-difluoro-4-(2-oxoazepan-1-yl)butanoate (4b): The title compound **4b** was obtained as a yellow oil (153.0 mg, 68% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

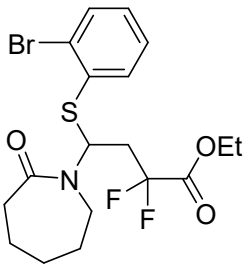
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 – 7.39 (m, 2H), 7.26 – 7.23 (m, 2H), 6.59 (br, 1H), 4.36 – 4.31 (m, 2H), 3.38 – 3.31 (m, 2H), 2.58 – 2.50 (m, 2H), 2.41 – 2.36 (m, 2H), 1.72 – 1.52 (m, 4H), 1.44 – 1.29 (m, 5H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.0, 163.3 (t, $J_{C\text{-}F}$ = 31.7 Hz), 132.3, 132.2, 132.1, 121.5, 114.4 (t, $J_{C\text{-}F}$ = 253.7 Hz), 63.4, 55.2, 44.1, 37.5, 37.4 (t, $J_{C\text{-}F}$ = 23.4 Hz), 29.9, 28.8, 23.1, 14.0; **^{19}F NMR (376**

MHz, $CDCl_3$): δ -102.7 (d, *J* = 270.9 Hz), -106.2 (d, *J* = 270.9 Hz); **IR (neat)** cm^{-1}: 2925, 1749, 1580, 1194, 1086; **HRMS (ESI)**: Calcd. for $C_{18}H_{22}BrF_2NNaO_3S$ $(M+Na)^+$ 472.0370, found 472.0399.



Ethyl 4-((3-Bromophenyl)thio)-2,2-difluoro-4-(2-oxoazepan-1-yl)butanoate (4c): The title compound **4c** was obtained as a yellow oil (144.0 mg, 64% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

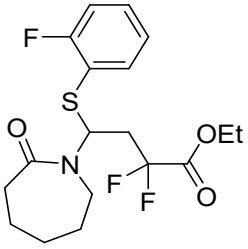
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41 – 7.39 (m, 2H), 7.26 – 7.23 (m, 2H), 6.59 (br, 1H), 4.36 – 4.31 (m, 2H), 3.38 – 3.31 (m, 2H), 2.58 – 2.50 (m, 2H), 2.41 – 2.36 (m, 2H), 1.72 – 1.52 (m, 4H), 1.44 – 1.29 (m, 5H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.6, 163.9 (t, J_{C-F} = 31.7 Hz), 136.8, 133.9, 131.6, 131.2, 130.4, 123.2, 115.8 (t, J_{C-F} = 253.7 Hz), 64.4, 56.1, 44.6, 38.8, 38.0 (t, J_{C-F} = 23.4 Hz), 30.2, 29.5, 23.8, 14.1; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -102.7 (d, *J* = 270.9 Hz), -106.2 (d, *J* = 270.9 Hz); **IR (neat)** cm^{-1}: 2929, 1755, 1575, 1442, 1190; **HRMS (ESI)**: Calcd. for $C_{18}H_{22}BrF_2NNaO_3S$ $(M+Na)^+$ 472.0370, found 472.0372.



Ethyl 4-((2-Bromophenyl)thio)-2,2-difluoro-4-(2-oxoazepan-1-yl)butanoate (4d): The title compound **4d** was obtained as a yellow oil (112.0 mg, 50% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

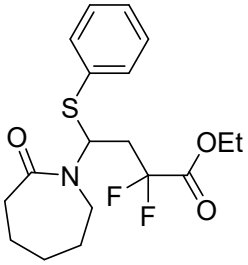
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.56 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.47 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.31 – 7.28 (m, 1H), 7.08 (td, *J* = 7.5, 1.5 Hz, 1H), 6.66 (br, 1H), 4.40 – 4.32 (m, 2H), 3.49 – 3.35 (m, 2H), 2.70 – 2.60 (m, 2H), 2.50 – 2.41 (m, 2H), 1.72 – 1.55 (m, 5H), 1.38 (t, *J* = 1.5 Hz, 3H), 1.33 – 1.29 (m, 1H); **^{13}C**

NMR (151 MHz, $CDCl_3$): δ 176.3, 163.3 (t, J_{C-F} = 31.7 Hz), 134.8, 133.3, 131.0, 128.2, 128.1, 123.9, 114.5 (t, J_{C-F} = 252.9 Hz), 63.5, 54.5, 44.4, 37.6, 37.4 (t, J_{C-F} = 23.4 Hz), 29.9, 28.6, 23.1, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -101.2 (d, J = 271.9 Hz), -105.1 (d, J = 271.5 Hz); **IR (neat)** cm^{-1}: 2946, 1758, 1649, 1591, 1178; **HRMS (ESI)**: Calcd. for $C_{18}H_{23}BrF_2NO_3S$ $(M+H)^+$ 450.0550, found 450.0555.



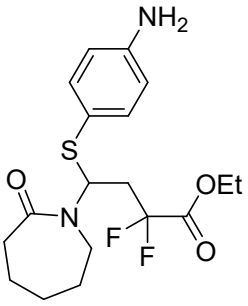
Ethyl 2,2-Difluoro-4-((2-fluorophenyl)thio)-4-(2-oxoazepan-1-yl)butanoate (4e): The title compound **4e** was obtained as a yellow oil (132.0 mg, 68% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (400 MHz, CD_3CN): δ 7.47 (td, J = 7.8, 1.8 Hz, 1H), 7.36 – 7.32 (m, 1H), 7.15 – 7.10 (m, 2H), 6.46 (br, 1H), 4.32 – 4.26 (m, 2H), 3.45 – 3.34 (m, 2H), 2.76 – 2.49 (m, 2H), 2.32 – 2.23 (m, 2H), 1.66 – 1.45 (m, 6H), 1.30 (t, J = 7.1 Hz, 3H); **^{13}C NMR (101 MHz, CD_3CN)**: δ 176.4, 164.0 (t, J_{C-F} = 31.8 Hz), 162.9 (d, J_{C-F} = 245.4 Hz), 136.0, 131.6 (d, J_{C-F} = 8.1 Hz), 125.7 (d, J_{C-F} = 3.0 Hz), 120.6 (d, J_{C-F} = 18.2 Hz), 116.7 (d, J_{C-F} = 23.2 Hz), 115.8 (d, J_{C-F} = 251.5 Hz), 63.4, 55.4, 43.8, 37.2 (t, J_{C-F} = 23.7 Hz), 36.8, 29.3, 28.6, 22.9, 13.1; **^{19}F NMR (376 MHz, CD_3CN)**: δ -98.5 (d, J = 278.8 Hz), -101.0 (d, J = 278.9 Hz), -109.2; **IR (neat)** cm^{-1}: 2945, 1758, 1648, 1191, 1182; **HRMS (ESI)**: Calcd. for $C_{18}H_{22}F_3NNaO_3S$ $(M+Na)^+$ 412.1170, found 412.1178.



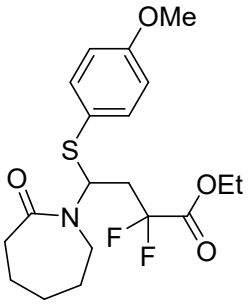
***Ethyl 2,2-Difluoro-4-(2-oxoazepan-1-yl)-4-(phenylthio)butanoate (4f)*:** The title compound **4f** was obtained as a yellow oil (149.0 mg, 80% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 – 7.37 (m, 2H), 7.29 – 7.27 (m, 2H), 7.23 – 7.20 (m, 1H), 6.59 (br, 1H), 4.36 – 4.29 (m, 2H), 3.39 – 3.33 (m, 2H), 2.59 – 2.53 (m, 2H), 2.40 – 2.34 (m, 2H), 1.69 – 1.52 (m, 4H), 1.46 – 1.28 (m, 5H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.0, 163.4 (t, J_{C-F} = 31.7 Hz), 132.9, 131.0, 129.2, 127.5, 114.6 (t, J_{C-F} = 252.9 Hz), 63.4, 55.5, 44.2, 37.6, 37.5 (t, J_{C-F} = 23.4 Hz), 29.9, 28.7, 23.1, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -102.4 (d, J = 281.7 Hz), -106.3 (d, J = 270.8 Hz); **IR (neat)** cm^{-1}: 2930, 1747, 1579, 1198; **HRMS (ESI)**: Calcd. for $C_{18}H_{23}F_2NNaO_3S$ $(M+Na)^+$ 394.1264, found 394.1249.



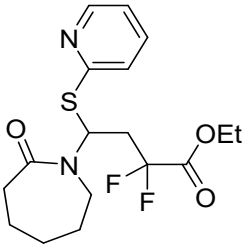
Ethyl 4-((4-Aminophenyl)thio)-2,2-difluoro-4-(2-oxoazepan-1-yl)butanoate (4g): The title compound **4g** was obtained as a dark yellow oil (58.0 mg, 30% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1). This compound is formed as rotamers in the ratio 3:1 as determined by crude ^{1}HNMR.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 – 7.34 (m, 0.4 × 2, 2H), 7.29 – 7.18 (m, 1.6 × 2, 2H), 6.65 – 6.50 (m, 2H), 6.31 (br, 0.6 × 1, 1H), 6.12 (br, 0.2 × 1, 1H), 4.34 – 4.22 (m, 2H), 4.09 – 2.99 (m, overlapped with two active protons, 4H), 2.72 – 2.31 (m, 4H), 1.79 – 1.40 (m, 6H), 1.37 – 1.33 (m, 2.2 × 3, 3H), 1.29 – 1.25 (m, 1.0 × 3, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.1, 175.8, 163.5 (t, J_{C-F} = 32.4 Hz), 162.0 (t, J_{C-F} = 32.5 Hz), 147.6, 147.0, 138.6, 135.1, 135.1, 115.6, 114.7 (t, J_{C-F} = 252.9 Hz), 113.9, 63.5, 63.3, 58.8, 57.2, 44.1, 41.5, 38.1, 37.5, 37.4 (t, J_{C-F} = 23.4 Hz), 30.2, 30.1, 29.1, 28.8, 23.5, 23.2, 19.8, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -101.7 (d, J = 265.9 Hz), -105.5 (d, J = 268.2 Hz); **IR (neat)** cm^{-1}: 3345, 2928, 1759, 1626, 1595, 1177; **HRMS (ESI)**: Calcd. for $C_{18}H_{25}F_2N_2O_3S$ $(M+H)^+$ 387.1554, found 387.1569.



Ethyl 2,2-Difluoro-4-((4-methoxyphenyl)thio)-4-(2-oxoazepan-1-yl)butanoate (4h): The title compound **4h** was obtained as a yellow oil (150.0 mg, 75% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

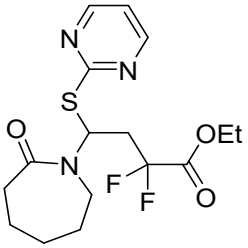
^{1}H NMR (400 MHz, CD_3CN): δ 7.38 – 7.35 (m, 2H), 6.88 – 6.85 (m, 2H), 6.26 (br, 1H), 4.32 – 4.26 (m, 2H), 3.76 (s, 3H), 3.41 – 3.36 (m, 2H), 2.64 – 2.48 (m, 2H), 2.29 – 2.27 (m, 2H), 1.67 – 1.58 (m, 4H), 1.52 – 1.37 (m, 2H), 1.30 (t, J = 7.2 Hz, 3H); **^{13}C NMR (101 MHz, CD_3CN)**: δ 175.2, 163.1 (t, $J_{C\text{-}F}$ = 31.8 Hz), 160.0, 135.0, 123.1, 115.0 (t, $J_{C\text{-}F}$ = 250.5 Hz), 114.5, 63.4, 57.0, 55.1, 43.8, 37.2 (t, $J_{C\text{-}F}$ = 47.5 Hz), 36.8, 29.4, 28.6, 23.0, 13.1; **^{19}F NMR (376 MHz, CD_3CN)**: δ = -103.3 (d, J = 264.2 Hz), -105.8 (d, J = 264.4 Hz); **IR (neat)** cm^{-1}: 2944, 1757, 1649, 1591, 1178; **HRMS (ESI)**: Calcd. for $C_{19}H_{26}F_2NO_4S$ $(M+H)^+$ 402.1551, found 402.1553.



Ethyl 2,2-Difluoro-4-(2-oxoazepan-1-yl)-4-(pyridin-2-ylthio)butanoate (4i): The title compound **4i** was obtained as a yellow oil (119.0 mg, 64% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

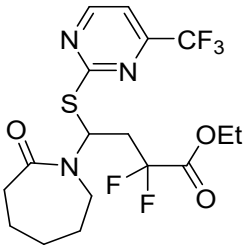
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (dd, J = 4.8, 1.8 Hz, 1H), 7.51 (td, J = 7.7, 1.9 Hz, 1H), 7.21 (d, J = 8.1 Hz, 1H), 7.01 (dd, J = 7.4, 4.9 Hz, 1H), 6.54 (br, 1H), 4.35 – 4.27 (m, 2H), 3.59 – 3.43 (m, 2H), 3.06 (s, 1H), 2.76 – 2.61 (m, 1H), 2.52 – 2.42 (m, 2H), 1.66 – 1.50 (m, 6H), 1.34 (t, J = 7.1 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 176.5, 163.6 (t, $J_{C\text{-}F}$ = 32.8 Hz), 157.5, 149.6, 136.7, 122.6, 120.3, 114.8 (t, $J_{C\text{-}F}$ = 253.0 Hz), 63.3, 56.5, 48.9, 38.4 (t, $J_{C\text{-}F}$ = 23.2 Hz), 37.8, 29.9, 28.6, 23.1, 14.0; **^{19}F NMR (376**

MHz, $CDCl_3$): δ -103.6 (br), -105.6 (d, *J* = 263.5 Hz); **IR (neat)** cm^{-1}: 2928, 1724, 1611, 1561, 1416; **HRMS (ESI)**: Calcd. for $C_{17}H_{22}F_2N_2NaO_3S$ $(M+Na)^+$ 395.1217, found 395.1221.



Ethyl 2,2-Difluoro-4-(2-oxoazepan-1-yl)-4-(pyrimidin-2-ylthio)butanoate (4j): The title compound **4j** was obtained as a yellow oil (114.0 mg, 61% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

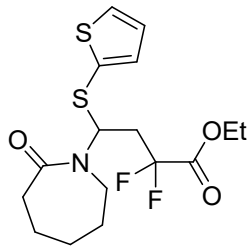
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (dd, *J* = 4.9, 1.5 Hz, 2H), 6.98 (td, *J* = 4.9, 1.4 Hz, 1H), 6.37 (br, 1H), 4.35 – 4.24 (m, 2H), 3.59 – 3.46 (m, 2H), 3.20 (br, 1H), 2.79 – 2.68 (m, 1H), 2.53 – 2.43 (m, 2H), 1.64 (br, 6H), 1.33 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 176.3, 171.2, 163.6 (t, J_{C-F} = 32.3 Hz), 157.6, 117.0, 114.8 (t, J_{C-F} = 253.0 Hz), 63.2, 58.2, 50.6, 39.1 (t, J_{C-F} = 22.7 Hz), 37.6, 29.8, 28.6, 23.0, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -106.5 (d, *J* = 255.7 Hz), -106.7 (d, *J* = 267.0 Hz); **IR (neat)** cm^{-1}: 2930, 1755, 1695, 1475, 1185; **HRMS (ESI)**: Calcd. for $C_{16}H_{21}F_2N_3NaO_3S$ $(M+Na)^+$ 396.1169, found 396.1171.



Ethyl 2,2-Difluoro-4-(2-oxoazepan-1-yl)-4-((4-(trifluoromethyl)pyrimidin-2-yl)thio)butanoate (4k): The title compound **4k** was obtained as a yellow oil (88.0 mg, 40% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

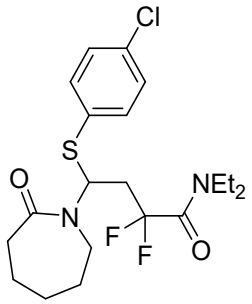
^{1}H NMR (400 MHz, CD_3CN): δ 8.85 (d, *J* = 5.0 Hz, 1H), 7.48 (d, *J* = 5.0 Hz, 1H), 6.36 (br, 1H), 4.31 – 4.25 (m, 2H), 3.61 – 3.44 (m, 2H), 3.30 – 3.10 (m, 1H), 2.84 – 2.70 (m, 1H), 2.46 – 2.40 (m, 2H), 1.64 – 1.54 (m, 6H), 1.28 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (101 MHz, CD_3CN)**: δ 176.9, 172.9, 164.2 (t, J_{C-F} = 32.3 Hz), 161.7, 156.1 (q, J_{C-F} = 36.4 Hz), 121.4 (q, J_{C-F} = 275.7 Hz), 115.9 (t, J_{C-F} = 251.5 Hz), 114.1 (q, J_{C-F} = 3.0 Hz), 64.3 59.2, 50.4, 39.7, 38.5 (t, J_{C-F} = 22.7 Hz), 37.9, 30.2, 29.4, 23.7, 14.1; **^{19}F NMR**

(376 MHz, CD_3CN): δ -70.9, -105.5 (br); **IR (neat)** cm^{-1}: 2935, 1763, 1651, 1563, 1332; **HRMS (ESI)**: Calcd. for $C_{17}H_{20}F_5N_3NaO_3S$ $(M+Na)^+$ 464.1043, found 464.1036.



Ethyl 2,2-Difluoro-4-(2-oxoazepan-1-yl)-4-(thiophen-2-ylthio)butanoate (4l): The title compound **4l** was obtained as a brown oil (83.0 mg, 44% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

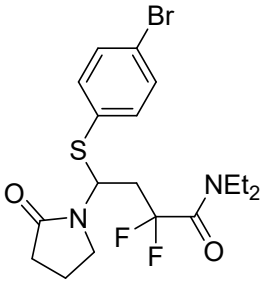
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 (dd, *J* = 5.4, 1.2 Hz, 1H), 7.17 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.98 (dd, *J* = 5.4, 3.6 Hz, 1H), 6.19 (br, 1H), 4.35 – 4.29 (m, 2H), 3.45 – 3.35 (m, 2H), 2.66 – 2.51 (m, 2H), 2.43 – 2.39 (m, 2H), 1.82 – 1.58 (m, 6H), 1.35 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 175.8, 163.4 (t, J_{C-F} = 31.7 Hz), 135.7, 130.9, 130.5, 127.9, 114.5 (t, J_{C-F} = 252.9 Hz), 63.4, 60.5, 45.4, 37.5, 37.3 (t, J_{C-F} = 24.2 Hz), 30.0, 28.9, 23.2, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -94.8 (d, *J* = 37.5 Hz), -106.3 (d, *J* = 268.6 Hz); **IR (neat)** cm^{-1}: 2925, 1758, 1650, 1146, 1079; **HRMS (ESI)**: Calcd. for $C_{16}H_{21}F_2NNaO_3S_2$ $(M+Na)^+$ 400.0829, found 400.0817.



4-((4-Chlorophenyl)thio)-N,N-diethyl-2,2-difluoro-4-(2-oxoazepan-1-yl)butanamide (4m): The title compound **4m** was obtained as a colorless oil (156.0 mg, 72% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

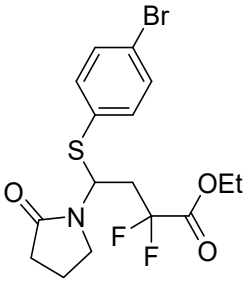
^{1}H NMR (500 MHz, CD_3CN): δ 7.37 (d, *J* = 8.2 Hz, 2H), 7.32 – 7.27 (m, 2H), 6.58 (br, 1H), 3.50 – 3.30 (m, 6H), 2.65 – 2.50 (m, 2H), 2.34 – 2.26 (m, 2H), 1.64 – 1.44 (m, 5H), 1.35 – 1.25 (m, 1H), 1.14 (t, *J* = 7.0 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (151 MHz, CD_3CN)**: δ 176.4, 162.6 (t, J_{C-F} = 42.3 Hz), 133.7, 133.4, 129.9, 129.8, 119.3 (t, J_{C-F} = 257.5 Hz), 56.8, 44.6, 42.8 (t, J_{C-F} = 6.6 Hz), 42.5, 38.2 (t, J_{C-F}

= 24.7 Hz), 37.9, 30.3, 29.5, 23.9, 14.6, 12.6; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -98.48 (d, *J* = 278.8 Hz), -100.97 (d, *J* = 278.9 Hz); **IR (neat)** cm^{-1}: 2925, 1650, 1477, 1192, 1183; **HRMS (ESI)**: Calcd. for $C_{20}H_{27}ClF_2N_2NaO_2S$ $(M+Na)^+$ 455.1348, found 455.1358.



4-((4-Bromophenyl)thio)-N,N-diethyl-2,2-difluoro-4-(2-oxopyrrolidin-1-yl)butanamide (4n): The title compound **4n** was obtained as a yellow oil (164.0 mg, 73% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

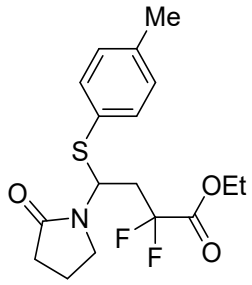
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.37 (m, 2H), 7.32 – 7.26 (m, 2H), 6.15 (dd, *J* = 10.2, 3.5 Hz, 1H), 3.58 – 3.31 (m, 6H), 2.83 – 2.49 (m, 2H), 2.28 – 2.20 (m, 1H), 2.16 – 2.04 (m, 1H), 1.96 – 1.87(m, 1H), 1.83 – 1.70 (m, 1H), 1.19 – 1.12 (m, 6H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 174.9, 162.0 (t, J_{C-F} = 28.3 Hz), 134.1, 132.2, 131.3, 122.3, 118.1 (t, J_{C-F} = 259.6 Hz), 53.3 (t, J_{C-F} = 4.0 Hz), 42.0 (t, J_{C-F} = 6.6 Hz), 41.9, 41.7, 36.3 (t, J_{C-F} = 23.2 Hz), 31.2, 18.0, 14.4, 12.4; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -100.7 (d, *J* = 285.0 Hz), -101.9 (d, *J* = 285.2 Hz); **IR (neat)** cm^{-1}: 2975, 1693, 1656, 1265, 1192; **HRMS (ESI)**: Calcd. for $C_{18}H_{23}BrF_2N_2NaO_2S$ $(M+Na)^+$ 471.0529, found 471.0524.



Ethyl 4-((4-Bromophenyl)thio)-2,2-difluoro-4-(2-oxopyrrolidin-1-yl)butanoate (4o): The title compound **4o** was obtained as a yellow oil (131.0 mg, 62% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

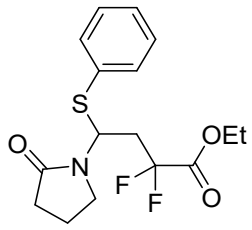
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45 – 7.39 (m, 2H), 7.30 – 7.26 (m, 2H), 6.00 (dd, *J* = 10.2, 4.2 Hz, 1H), 4.34 – 4.29 (m, 2H), 3.50 – 3.46 (m, 1H), 3.34 – 3.30 (m, 1H), 2.72 – 2.51 (m, 2H), 2.28 – 2.23 (m, 1H),

2.12 – 2.06 (m, 1H), 1.99 – 1.89 (m, 1H), 1.84 – 1.75 (m, 1H), 1.35 (t, J = 7.2 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 174.9, 163.3 (t, J_{C-F} = 31.9 Hz), 134.4, 132.4, 130.8, 122.7, 114.3 (t, J_{C-F} = 253.7 Hz), 63.5, 53.4 (t, J_{C-F} = 4.7 Hz), 41.8, 36.7 (t, J_{C-F} = 23.8 Hz), 31.0, 18.0, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -103.8 (d, J = 269.8 Hz), -105.3 (d, J = 269.7 Hz); **IR (neat)** cm^{-1}: 2983, 1759, 1696, 1190, 1091; **HRMS (ESI)**: Calcd. for $C_{16}H_{18}BrF_2NNaO_3S$ $(M+Na)^+$ 444.0057, found 444.0065.



Ethyl 2,2-Difluoro-4-(2-oxopyrrolidin-1-yl)-4-(p-tolylthio)butanoate (4p): The title compound **4p** was obtained as a yellow oil (107.0 mg, 60% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

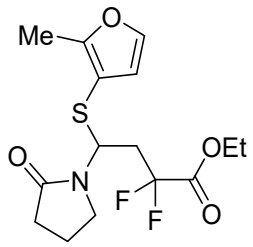
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H), 5.92 (dd, J = 10.2, 4.2 Hz, 1H), 4.33 – 4.28 (m, 2H), 3.56 – 3.52 (m, 1H), 3.32 – 3.28 (m, 1H), 2.71 – 2.53 (m, 2H), 2.31 (s, 3H), 2.26 – 2.18 (m, 1H), 2.08 – 2.02 (m, 1H), 1.96 – 1.88 (m, 1H), 1.84 – 1.77 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 174.8, 163.4 (t, J_{C-F} = 32.0 Hz), 138.9, 133.7, 130.0, 127.8, 114.5 (t, J_{C-F} = 252.9 Hz), 63.5, 53.9 (t, J_{C-F} = 4.6 Hz), 41.9, 36.7 (t, J_{C-F} = 23.7 Hz), 31.1, 21.4, 18.0, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -103.8 (d, J = 268.3 Hz), -105.3 (d, J = 268.5 Hz).; **IR (neat)** cm^{-1}: 2983, 1759, 1696, 1190, 1084; **HRMS (ESI)**: Calcd. for $C_{17}H_{22}F_2NO_3S$ $(M+H)^+$ 358.1288, found 358.1276.



Ethyl 2,2-Difluoro-4-(2-oxopyrrolidin-1-yl)-4-(phenylthio)butanoate (4q): The title compound **4q** was obtained as a yellow oil (111.0 mg, 65% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

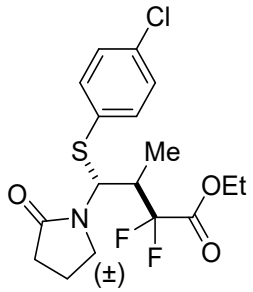
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 – 7.42 (m, 2H), 7.30 – 7.26 (m, 3H), 6.00 (dd, J = 10.3, 4.2 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 3.54 – 3.49 (m, 1H), 3.33 – 3.29 (m, 1H), 2.73 – 2.54 (m, 2H), 2.26 – 2.19 (m,

1H), 2.07 – 2.01 (m, 1H), 1.96 – 1.87 (m, 1H), 1.84 – 1.74 (m, 1H), 1.35 (td, J = 7.2, 1.4 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 174.7, 163.2 (t, J_{C-F} = 31.8 Hz), 133.1, 131.4, 129.1, 128.3, 114.3 (t, J_{C-F} = 254.0 Hz), 63.3, 53.5 (t, J_{C-F} = 5.0 Hz), 41.8, 36.7 (t, J_{C-F} = 23.7 Hz), 30.9, 17.8, 13.8; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -104.72 (d, J = 268.8 Hz), -106.22 (d, J = 268.8 Hz); **IR (neat)** cm^{-1}: 2932, 1765, 1728, 1443, 1183; **HRMS (ESI)**: Calcd. for $C_{16}H_{19}F_2NNaO_3S$ $(M+Na)^+$ 366.0951, found 366.0960.



Ethyl 2,2-Difluoro-4-((2-methylfuran-3-yl)thio)-4-(2-oxopyrrolidin-1-yl)butanoate (4r): The title compound **4r** was obtained as a yellow oil (69.0 mg, 40% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

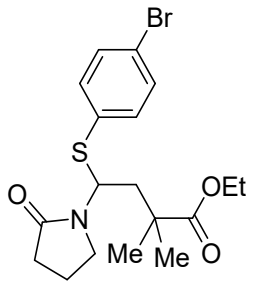
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.24 (d, J = 2.0 Hz, 1H), 6.28 (d, J = 2.0 Hz, 1H), 5.67 (dd, J = 10.4, 4.1 Hz, 1H), 4.37 – 4.24 (m, 2H), 3.52 (td, J = 8.8, 6.0 Hz, 1H), 3.31 (td, J = 8.8, 5.4 Hz, 1H), 2.67 – 2.43 (m, 2H), 2.32 (s, 3H), 2.29 – 2.23 (m, 1H), 2.16 – 2.11 (m, 1H), 2.00 – 1.84 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 174.7, 163.4 (t, J_{C-F} = 32.1 Hz), 156.7, 141.0, 115.4, 114.4 (t, J_{C-F} = 252.9 Hz), 107.0, 63.4, 53.5 (t, J_{C-F} = 4.5 Hz), 41.8, 36.5 (t, J_{C-F} = 23.8 Hz), 31.0, 17.9, 13.9, 11.9; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -104.1 (d, J = 267.8 Hz), -105.4 (d, J = 268.1 Hz).; **IR (neat)** cm^{-1}: 2983, 1808, 1759, 1695, 1190; **HRMS (ESI)**: Calcd. for $C_{15}H_{20}F_2NO_4S$ $(M+H)^+$ 348.1081, found 348.1086.



Ethyl (3R*,4S*)-4-((4-Chlorophenyl)thio)-2,2-difluoro-3-methyl-4-(2-oxopyrrolidin-1-yl)butanoate (4s): The title compound **4s** was obtained as a yellow oil (137.0 mg, 70% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1). The compound **4s** was formed as a mixture of partially separable diastereomers in a 3.5:1 ratio as determined in a crude reaction mixture by

^{1}H NMR. The observed coupling constant value ($^3J_{HH}$ = 9.8 Hz) for vicinal ^{1}H-^{1}H coupling for major diastereomer provides the support that the product is the *syn* isomer.[3,4]

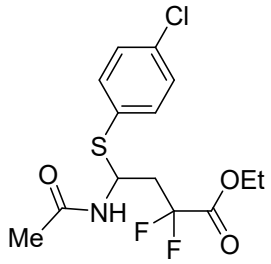
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35 – 7.31 (m, 2H), 7.25 – 7.22 (m, 2H), 5.82 (d, *J* = 9.8 Hz, 0.9 × 1, 1H), 5.77 (d, *J* = 9.8 Hz, 0.1 × 1, 1H), 4.38 – 4.24 (m, 2H), 3.67 – 3.63 (m, 0.1 × 1, 1H), 3.51 – 3.46 (m, 0.9 × 1, 1H), 3.35 – 3.30 (m, 0.9 × 1, 1H), 3.28 – 3.25 (m, 0.1 × 1, 1H), 2.91 – 2.73 (m, 1H), 2.32 – 2.25 (m, 0.1 × 1, 1H), 2.22 – 2.14 (m, 0.9 × 1, 1H), 2.13 – 2.08 (m, 0.1 × 1, 1H), 1.99 – 1.93 (m, 0.9 × 1, 1H), 1.91 – 1.82 (m, 1H), 1.75 – 1.66 (m, 1H), 1.37 – 1.30 (m, 6H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 175.2, 175.1, 163.7 (t, $J_{C\text{-}F}$ = 32.5 Hz), 163.4 (t, $J_{C\text{-}F}$ = 32.5 Hz), 134.5, 134.4, 134.3, 133.8, 130.6, 130.1, 129.4, 129.3, 116.0 (t, $J_{C\text{-}F}$ = 255.9 Hz), 115.8 (t, $J_{C\text{-}F}$ = 255.9 Hz), 63.3, 63.3, 60.2 (t, $J_{C\text{-}F}$ = 3.0 Hz), 59.3 (br), 43.1, 42.7, 41.4 (t, $J_{C\text{-}F}$ = 21.9 Hz), 40.8 (t, $J_{C\text{-}F}$ = 21.9 Hz), 30.8, 30.7, 18.3, 17.9, 13.9, 12.2 (t, $J_{C\text{-}F}$ = 4.5 Hz), 10.23 (t, $J_{C\text{-}F}$ = 4.5 Hz); **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -105.7 (d, *J* = 270.7 Hz), -110.0 (d, *J* = 263.2 Hz), -110.8 (d, *J* = 263.2 Hz), -116.1 (d, *J* = 267.0 Hz); **IR (neat)** cm^{-1}: 2978, 1755, 1693, 1191, 1093; **HRMS (ESI)**: Calcd. for $C_{17}H_{20}ClF_2NNaO_3S$ $(M+Na)^+$ 414.0718, found 414.0724.



Ethyl 4-((4-Bromophenyl)thio)-2,2-dimethyl-4-(2-oxopyrrolidin-1-yl)butanoate (4t): The title compound **4t** was obtained as a yellow oil (87.0 mg, 42% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

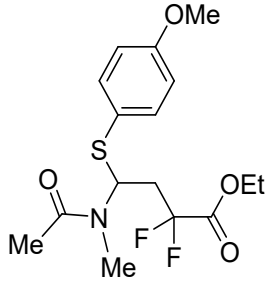
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.35 (m, 2H), 7.26 – 7.21 (m, 2H), 5.89 (dd, *J* = 9.6, 4.0 Hz, 1H), 4.14 – 4.02 (m, 2H), 3.46 – 3.29 (m, 2H), 2.24 – 2.14 (m, 2H), 2.06 – 1.97 (m, 1H), 1.90 – 1.79 (m, 2H), 1.77 – 1.67 (m, 1H), 1.28 – 1.23 (m, 9H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 176.9, 175.0, 133.7, 132.1, 132.1, 121.8, 60.9, 56.3, 41.8, 41.7, 41.6, 31.2, 26.6, 24.3, 17.8, 14.21; **IR (neat)** cm^{-1}: 2975, 1717, 1688, 1473, 1185; **HRMS (ESI)**: Calcd. for $C_{18}H_{24}BrNNaO_3S$ $(M+Na)^+$ 436.0558, found 436.0584.

[3] Karplus, M. *J. Chem. Phys*. 1959, **30**, 11-15.
[4] Karplus, M. *J. Am. Chem. Soc.* 1963, **85**, 2870-2871.



Ethyl 4-Acetamido-4-((4-chlorophenyl)thio)-2,2-difluorobutanoate (4u): The title compound **4u** was obtained as a yellow oil (72.0 mg, 41% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

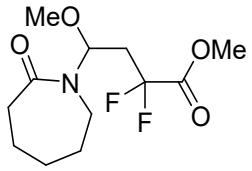
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.36 (m, 2H), 7.36 – 7.28 (m, 2H), 5.73 (d, J = 9.7 Hz, 1H), 5.65 – 5.60 (m, 1H), 4.32 (q, J = 7.1 Hz, 2H), 2.74 – 2.49 (m, 2H), 1.89 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 169.0, 163.6 (t, $J_{C\text{-}F}$ = 32.1 Hz), 135.2, 135.2, 130.0, 129.6, 114.4 (t, $J_{C\text{-}F}$ = 252.9 Hz), 63.6, 51.6 (t, $J_{C\text{-}F}$ = 4.7 Hz), 40.0 (t, $J_{C\text{-}F}$ = 23.5 Hz), 23.2, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -103.0 (d, J = 101.5 Hz), -103.3 (d, J = 97.6 Hz); **IR (neat)** cm^{-1}: 3250, 1767, 1659, 1543, 1132; **HRMS (ESI)**: Calcd. for $C_{14}H_{17}ClF_2NO_3S$ $(M+H)^+$ 352.0586, found 352.0577.



Ethyl 2,2-Difluoro-4-((4-methoxyphenyl)thio)-4-(N-methylacetamido)butanoate (4v): The title compound **4v** was obtained as a yellow oil (90.0 mg, 50% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1). The compounds are formed as rotamers in the ratio 1.5:1 as determined by crude ^{1}HNMR.

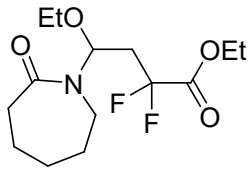
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38 – 7.31 (m, 2H), 6.88 – 6.83 (m, 1.2 × 2, 2H), 6.83 – 6.78 (m, 0.8 × 2, 2H), 6.38 (br, 0.4 × 1, 1H), 5.29 (dd, J = 9.9, 3.8 Hz, 0.6 × 1, 1H), 4.33 – 4.25 (m, 2H), 3.79 (s, 1.9 × 3, 3H), 3.77 (s, 1.1 × 3, 3H), 2.92 (s, 1.8 × 3, 3H), 2.91 (s, 1.2 × 3, 3H), 2.76 – 2.65 (m, 0.7 × 2, 2H), 2.59 – 2.47 (m, 1.4 × 2, 2H), 1.86 (s, 1.1 × 3, 3H), 1.49 (s, 1.9 × 3, 3H), 1.35 – 1.33 (m, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 170.9, 170.8, 163.4 (t, $J_{C\text{-}F}$ = 31.7 Hz), 163.3 (t, $J_{C\text{-}F}$ = 31.7 Hz), 161.2 160.2, 137.6, 135.8, 122.1, 121.6, 114.6 (t, $J_{C\text{-}F}$ = 252.9 Hz), 114.3 (dd, $J_{C\text{-}F}$ = 252.9, 4.5 Hz), 63.7, 63.4, 63.3 (dd, $J_{C\text{-}F}$

= 5.3, 4.5 Hz), 55.5, 55.4, 37.6 (t, $J_{C\text{-}F}$ = 24.2 Hz), 36.6 (t, $J_{C\text{-}F}$ = 24.2 Hz), 27.0, 22.0, 20.6, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -104.53 (d, *J* = 264.3 Hz), -105.97 (d, *J* = 264.3 Hz); **IR (neat)** cm^{-1}: 2942 1765, 1648, 1098; **HRMS (ESI)**: Calcd. for $C_{16}H_{22}F_2NO_4S$ $(M+H)^+$ 362.1238, found 362.1264.



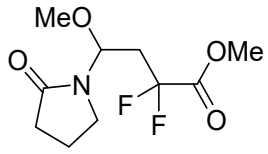
Methyl 2,2-Difluoro-4-methoxy-4-(2-oxoazepan-1-yl)butanoate (5a): The title compound **5a** was obtained as a yellow oil (102.0 mg, 73% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.85 (dd, *J* = 9.5, 3.8 Hz, 1H), 3.86 (s, 3H), 3.32 – 3.19 (m, 5H, overlapped with three methyl protons), 2.62 – 2.47 (m, 3H), 2.23 – 2.16 (m, 1H), 1.78 – 1.55 (m, 6H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.8, 164.4 (dd, $J_{C\text{-}F}$ = 33.2, 31.1 Hz), 114.7 (dd, $J_{C\text{-}F}$ = 254.6, 247.2 Hz), 79.4 (dd, J $J_{C\text{-}F}$ = 11.5, 3.2 Hz), 56.2, 53.3, 41.5, 38.8 (t, $J_{C\text{-}F}$ = 23.7 Hz), 37.7, 30.1, 29.4, 23.6; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -101.4 (d, *J* = 265.2 Hz), -109.8 (d, *J* = 265.4 Hz); **IR (neat)** cm^{-1}: 2922, 1769, 1620, 1437, 1198; **HRMS (ESI)**: Calcd. for $C_{12}H_{19}F_2NNaO_4$ $(M+Na)^+$ 302.1180, found 302.1152.



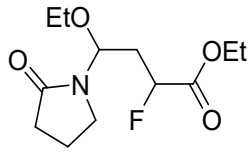
Ethyl 4-Ethoxy-2,2-difluoro-4-(2-oxoazepan-1-yl)butanoate (5b): The title compound **5b** was obtained as a yellow oil (104.0 mg, 68% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.95 (dd, *J* = 9.5, 4.0 Hz, 1H), 4.29 (m, 2H), 3.45 – 3.20 (m, 4H), 2.63 – 2.46 (m, 3H), 2.23 – 2.13 (m, 1H), 1.76 – 1.58 (m, 6H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.6, 163.8 (t, $J_{C\text{-}F}$ = 32.3 Hz), 114.7 (dd, $J_{C\text{-}F}$ = 254.3, 246.7 Hz), 77.8 (dd, $J_{C\text{-}F}$ = 11.4, 3.4 Hz), 64.0, 62.7, 41.6, 38.5 (t, $J_{C\text{-}F}$ = 23.5 Hz), 37.8, 30.2, 29.4, 23.6, 14.6, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -100.9 (d, *J* = 266.5 Hz), -110.4 (d, *J* = 266.5 Hz); **IR (neat)** cm^{-1}: 2926, 1770, 1649, 1467, 1098; **HRMS (ESI)**: Calcd. for $C_{14}H_{23}F_2NNaO_4$ $(M+Na)^+$ 330.1493, found 330.1498.



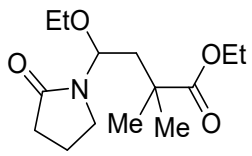
Methyl 2,2-Difluoro-4-methoxy-4-(2-oxopyrrolidin-1-yl)butanoate (5c): The title compound **5c** was obtained as a yellow oil (88.0 mg, 70% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.43 (dd, J = 8.8, 4.4 Hz, 1H), 3.85 (s, 3H), 3.38 – 3.26 (m, 2H), 3.19 (s, 3H), 2.70 – 2.60 (m, 1H), 2.49 – 2.39 (m, 2H), 2.31 – 2.23 (m, 1H), 2.07 – 2.02 (m, 2H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.0, 164.2 (t, $J_{C\text{-}F}$ = 32.4 Hz), 114.6 (dd, $J_{C\text{-}F}$ = 253.7, 247.8 Hz), 77.4, 56.0, 53.4, 41.2, 38.4 (t, $J_{C\text{-}F}$ = 24.0 Hz), 31.5, 18.3; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -102.4 (d, J = 265.3 Hz), -109.2 (d, J = 265.4 Hz); **IR (neat)** cm^{-1}: 2924, 1770, 1731, 1286, 1092; **HRMS (ESI)**: Calcd. for $C_{10}H_{15}F_2NNaO_4$ $(M+Na)^+$ 274.0867, found 274.0875.



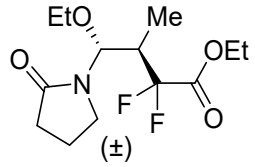
Ethyl 4-Ethoxy-2-fluoro-4-(2-oxopyrrolidin-1-yl)butanoate (5d): The title compound **5d** was obtained as a yellow oil (91.0 mg, 70% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1). The diastereomers were obtained in 1:1 ratio as determined by crude ^{1}HNMR.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.51 – 5.48 (m, 1H), 5.08 – 4.97 (m, 0.6 × 1, 1H), 4.93 – 4.83 (m, 0.4 × 1, 1H), 4.25 – 4.16 (m, 2H), 3.48 – 3.27 (m, 4H), 2.43 – 2.37 (m, 2H), 2.37 – 2.21 (m, 1H), 2.15 – 2.07 (m, 0.4 × 3, 3H), 2.04 – 1.94 (m, 2.7 × 3, 3H), 1.29 – 1.26 (m, 3H), 1.15 (t, J = 7.0 Hz, 1.9 × 3, 3H), 1.11 (t, J = 7.1 Hz, 1.1 × 3, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 175.9, 169.4 (d, $J_{C\text{-}F}$ = 23.1 Hz), 169.2 (d, $J_{C\text{-}F}$ = 23.6 Hz), 86.2 (d, $J_{C\text{-}F}$ = 184.8 Hz), 85.7 (d, $J_{C\text{-}F}$ = 185.7 Hz), 77.1 (d, $J_{C\text{-}F}$ = 2.8 Hz), 76.9 (d, $J_{C\text{-}F}$ = 5.1 Hz), 63.7, 63.6, 61.8, 61.6, 41.3, 41.1, 35.8 (d, $J_{C\text{-}F}$ = 20.8 Hz), 35.6 (d, $J_{C\text{-}F}$ = 21.0 Hz), 31.6, 31.6, 18.3, 18.3, 14.9, 14.8, 14.2; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -194.0, -195.0 ; **IR (neat)** cm^{-1}: 2925, 1790, 1759, 1681, 1266; **HRMS (ESI)**: Calcd. for $C_{12}H_{20}FNNaO_4$ $(M+Na)^+$ 284.1274, found 284.1280.



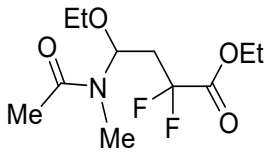
Ethyl 4-Ethoxy-2,2-dimethyl-4-(2-oxopyrrolidin-1-yl)butanoate (5e): The title compound **5e** was obtained as a yellow oil (61.0 mg, 45% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.34 (dd, *J* = 8.5, 4.6 Hz, 1H), 4.13 – 4.05 (m, 2H), 3.39 – 3.31 (m, 4H), 2.45 – 2.35 (m, 2H), 2.14 (dd, *J* = 13.9, 8.5 Hz, 1H), 2.02 – 1.96 (m, 2H), 1.64 (dd, *J* = 13.9, 4.7 Hz, 1H), 1.26 – 1.19 (m, 9H), 1.12 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 177.4, 175.6, 78.8, 63.5, 60.5, 42.7, 41.4, 40.4, 31.8, 26.5, 24.7, 18.4, 15.0, 14.3; **IR (neat)** cm^{-1}: 2976, 1726, 1694, 1146; **HRMS (ESI)**: Calcd. for $C_{14}H_{25}NNaO_4$ $(M+Na)^+$ 294.1681, found 294.1684.



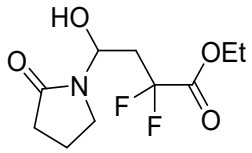
Ethyl (3R,4R)-4-Ethoxy-2,2-difluoro-3-methyl-4-(2-oxopyrrolidin-1-yl)butanoate (5f): The title compound **5f** was obtained as a yellow oil (97.0 mg, 66% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 4:1). The compound **5f** was formed as a mixture of partially separable diastereomers in a 1.3:1 ratio as determined in a crude reaction mixture by ^{1}H NMR. The observed coupling constant value ($^3J_{HH}$ = 10.1 Hz) for vicinal ^{1}H-^{1}H coupling for major diastereomer provides the support that two groups remain *anti* to each other.[3,4]

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.27 (d, *J* = 8.0 Hz, 0.2 × 1, 1H), 5.17 (d, *J* = 10.1 Hz, 0.8 × 1, 1H), 4.33 – 4.20 (m, 2H), 3.42 – 3.28 (m, 3.1 × 4, 4H), 3.24 – 3.20 (m, 0.8 × 4, 4H), 2.80 – 2.62 (m, 1H), 2.46 – 2.36 (m, 2H), 2.06 – 1.95 (m, 2H), 1.36 – 1.30 (m, 3H), 1.17 (d, *J* = 7.0 Hz, 0.6 × 3, 3H), 1.15 (t, *J* = 7.0 Hz, 0.6 × 3, 3H), 1.07 (t, *J* = 7.1 Hz, 2.3 × 3, 3H), 0.98 (dd, *J* = 7.1, 1.5 Hz, 2.3 × 3, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.4, 176.2, 164.2 (dd, $J_{C\text{-}F}$ = 32.4, 3.0 Hz), 163.8 (t, $J_{C\text{-}F}$ = 33.0 Hz), 116.0 (dd, $J_{C\text{-}F}$ = 253.7, 253.7 Hz), 115.7 (dd, $J_{C\text{-}F}$ = 246.4, 246.4 Hz), 80.76 (dd, $J_{C\text{-}F}$ = 9.1, 2.8 Hz), 79.7 (t, $J_{C\text{-}F}$ = 4.5 Hz), 64.1, 63.8, 62.9, 62.4, 41.0 (t, $J_{C\text{-}F}$ = 21.1 Hz), 41.0, 40.1 (t, $J_{C\text{-}F}$ = 22.6 Hz), 31.6, 31.5, 18.4, 14.8, 14.4, 14.0, 14.0, 10.0 (t, $J_{C\text{-}F}$ = 4.7 Hz), 7.79 (dd, $J_{C\text{-}F}$ = 6.6, 2.4 Hz); **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -105.4 (d, *J* = 265.3 Hz), -109.9 (d, *J* = 263.1 Hz), -111.9 (d, *J* = 264.0 Hz), -125.0 (d, *J* = 265.4 Hz); **IR (neat)** cm^{-1}: 2980, 1770, 1694, 1172, 1068; **HRMS (ESI)**: Calcd. for $C_{13}H_{21}F_2NNaO_4$ $(M+Na)^+$ 316.1336, found 316.1339.



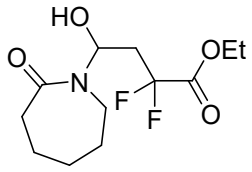
Ethyl 4-Ethoxy-2,2-difluoro-4-(N-methylacetamido)butanoate (5g): The title compound **5g** was obtained as a yellow oil (60.0 mg, 45% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1). This compound was formed as rotamers in the ratio 1.2:1 as determined by crude ^{1}HNMR.

^{1}H NMR (600 MHz, $CDCl_3$): δ 5.99 – 5.97 (m, 0.6 × 1, 1H), 5.15 – 5.13 (m, 0.4 × 1, 1H), 4.36 – 4.23 (m, 2H), 3.44 – 3.23 (m, 2H), 2.82 (s, 1.8 × 3, 3H), 2.74 (s, 1.2 × 3, 3H), 2.71 – 2.51 (m, 1H), 2.36 – 2.28 (m, 0.4 × 1, 1H), 2.22 – 2.15 (m, 0.6 × 1, 1H), 2.14 (s, 1.2 × 3, 3H), 2.09 (s, 1.8 × 3, 3H), 1.36 – 1.33 (m, 3H), 1.14 (t, J = 7.0 Hz, 1.2 × 3, 3H), 1.10 (t, J = 7.1 Hz, 1.7 × 3, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 171.6, 170.2, 163.7 (dd, $J_{C\text{-}F}$ = 32.5, 32.5 Hz), 163.4 (dd, $J_{C\text{-}F}$ = 32.5, 32.5 Hz), 114.7 (t, $J_{C\text{-}F}$ = 250.7 Hz), 114.5 (dd, $J_{C\text{-}F}$ = 250.7, 250.7 Hz), 82.2 (dd, $J_{C\text{-}F}$ = 6.8, 6.8 Hz), 63.7, 63.1, 63.1, 62.8, 39.1 (t, $J_{C\text{-}F}$ = 23.4 Hz), 37.8 (t, $J_{C\text{-}F}$ = 23.4 Hz), 28.4, 22.4, 21.8, 14.6, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -100.4 (d, J = 267.0 Hz), -102.8 (d, J = 265.5 Hz), -107.2 (d, J = 265.5 Hz), -108.8 (d, J = 267.0 Hz); **IR (neat)** cm^{-1}: 2988, 1768, 1653, 1092; **HRMS (ESI)**: Calcd. for $C_{11}H_{20}F_2NO_4$ $(M+H)^+$ 268.1360, found 268.1370.



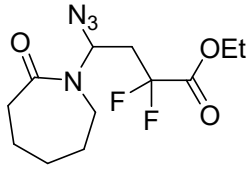
Ethyl 2,2-Difluoro-4-hydroxy-4-(2-oxopyrrolidin-1-yl)butanoate (5h): The title compound **5h** was obtained as a yellow oil (44.0 mg, 35% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.70 (dd, J = 8.3, 4.8 Hz, 1H), 4.46 (s, 1H), 4.31 (q, J = 7.1 Hz, 2H), 3.55 – 3.61 (m, 1H), 3.41 – 3.34 (m, 1H), 2.75 – 2.60 (m, 1H), 2.42 – 2.25 (m, 3H), 2.09 – 1.98 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 176.3, 163.8 (t, $J_{C\text{-}F}$ = 32.3 Hz), 114.7 (dd, $J_{C\text{-}F}$ = 248.4, 248.3 Hz), 70.6 (dd, $J_{C\text{-}F}$ = 9.8, 4.4 Hz), 63.1, 42.2, 38.8 (t, $J_{C\text{-}F}$ = 23.5 Hz), 31.7, 18.2, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -102.2 (d, J = 265.7 Hz), -108.1 (d, J = 265.7 Hz); **IR (neat)** cm^{-1}: 3075, 2923, 1716, 1651, 1193; **HRMS (ESI)**: Calcd. for $C_{10}H_{16}F_2NO_4$ $(M+H)^+$ 252.1047, found 252.1055.



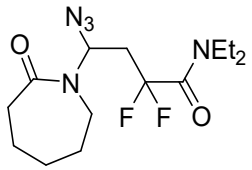
Ethyl 2,2-Difluoro-4-hydroxy-4-(2-oxoazepan-1-yl)butanoate (5i): The title compound **5i** was obtained as a yellow oil (56.0 mg, 40% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1). This compound was formed as rotamers in the ratio 3.5:1 as determined by crude ^{1}HNMR.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.08 (br, 0.2 × 1, 1H), 5.83 (dd, J = 8.5, 4.6 Hz, 0.8 × 1, 1H), 4.40 – 4.27 (m, 2H), 3.45 – 3.15 (m, 2H), 2.78 – 2.60 (m, 1H), 2.56 – 2.29 (m, 3H), 1.82 – 1.60 (m, 6H), 1.38 – 1.33 (m, 3H); **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 179.5, 176.7, 163.9 (t, $J_{C\text{-}F}$ = 32.3 Hz), 114.8 (dd, $J_{C\text{-}F}$ = 245.6, 247.2 Hz), 73.0 (dd, $J_{C\text{-}F}$ = 10.5, 10.5 Hz), 62.8, 47.8 (t, $J_{C\text{-}F}$ = 22.9 Hz), 43.0, 42.8, 39.2 (t, $J_{C\text{-}F}$ = 22.9 Hz), 37.6, 36.6, 30.6, 29.9, 29.6, 29.3, 23.2, 13.8; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -101.1 (d, J = 265.0 Hz), -108.5 (d, J = 265.3 Hz); **IR (neat)** cm^{-1}: 3287, 2928, 1659, 1481, 1198; **HRMS (ESI)**: Calcd. for $C_{12}H_{20}F_2NO_4$ $(M+H)^+$ 280.1360, found 280.1369.



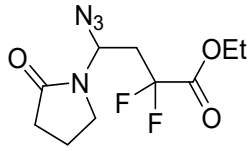
Ethyl 4-Azido-2,2-difluoro-4-(2-oxoazepan-1-yl)butanoate (5j): The title compound **5j** was obtained as a colorless oil (100.0 mg, 66% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.50 – 6.47 (m, 1H), 4.34 (q, J = 7.1 Hz, 2H), 3.39 – 3.28 (m, 2H), 2.62 – 2.58 (m, 1H), 2.55 – 2.40 (m, 2H), 2.32 – 2.24 (m, 1H), 1.83 – 1.62 (m, 6H), 1.36 (t, J = 7.1 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.5, 163.4 (t, $J_{C\text{-}F}$ = 31.6 Hz), 114.1 (dd, $J_{C\text{-}F}$ = 252.1, 252.4 Hz), 65.3 (dd, $J_{C\text{-}F}$ = 8.7, 3.8 Hz), 63.4, 43.6, 37.6 (t, $J_{C\text{-}F}$ = 23.4 Hz), 37.4, 30.0, 29.4, 23.5, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -102.7 (d, J = 268.7 Hz), -108.0 (d, J = 269.9 Hz); **IR (neat)** cm^{-1}: 2925, 2106, 1764, 1654, 1185; **HRMS (ESI)**: Calcd. for $C_{12}H_{19}F_2N_4O_3$ $(M+H)^+$ 305.1425, found 305.1428.



4-Azido-N,N-diethyl-2,2-difluoro-4-(2-oxoazepan-1-yl)butanamide (5k): The title compound **5k** was obtained as a colorless oil (129.0 mg, 78% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

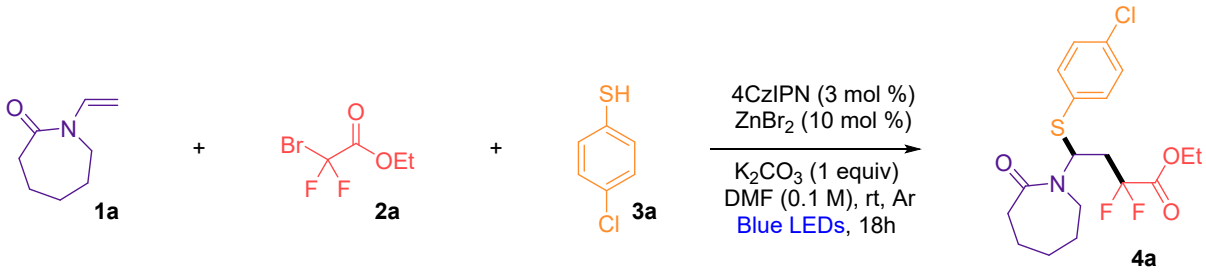
^{1}H NMR (600 MHz, $CDCl_3$): δ 6.59 (t, *J* = 6.4 Hz, 1H), 3.55 – 3.44 (m, 2H), 3.40 – 3.32 (m, 4H), 2.65 – 2.41 (m, 4H), 1.84 – 1.61 (m, 6H), 1.18 (t, *J* = 12.0 Hz, 3H), 1.14 (t, *J* = 12.0 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 176.3, 161.9 (t, $J_{C\text{-}F}$ = 28.3 Hz), 118.0 (t, $J_{C\text{-}F}$ = 257.4 Hz), 65.6 (t, $J_{C\text{-}F}$ = 4.5 Hz), 43.7, 42.0 (t, $J_{C\text{-}F}$ = 6.0 Hz), 41.8, 37.5, 37.4 (t, $J_{C\text{-}F}$ = 21.9 Hz), 30.0, 29.2, 23.5, 14.4, 12.4; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -99.2 (d, *J* = 285.3 Hz), -100.3 (d, *J* = 285.4 Hz); **IR (neat)** cm^{-1}: 2934, 2106, 1652, 1187, 1066; **HRMS (ESI)**: Calcd. for $C_{14}H_{24}F_2N_5O_2$ $(M+H)^+$ 332.1898, found 333.1905.

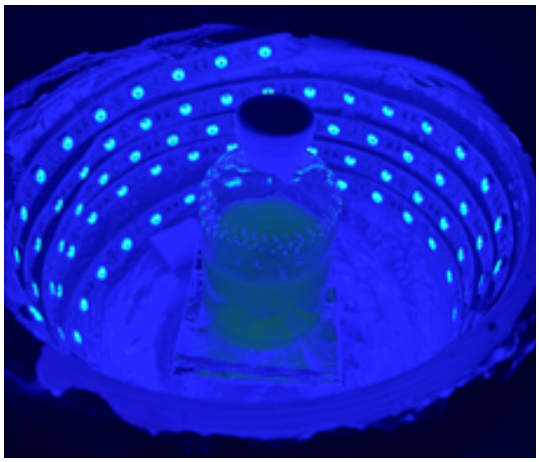


Ethyl 4-Azido-2,2-difluoro-4-(2-oxopyrrolidin-1-yl)butanoate (5l): The title compound **5l** was obtained as a yellow oil (72.0 mg, 52% yield) after purification by automated flash column chromatography (hexanes/EtOAc = 3:1).

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.02 (t, *J* = 7.0 Hz, 1H), 4.34 (q, *J* = 7.2 Hz, 2H), 3.49 – 3.45 (m, 1H), 3.41 – 3.47 (m, 1H), 2.56 – 2.35 (m, 4H), 2.15 – 2.04 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR (151 MHz, $CDCl_3$)**: δ 175.5, 163.3 (t, $J_{C\text{-}F}$ = 31.9 Hz), 114.0 (dd, $J_{C\text{-}F}$ = 250.7, 250.7 Hz), 63.5, 63.2 (dd, $J_{C\text{-}F}$ = 7.6, 4.4 Hz), 42.1, 37.1 (t, $J_{C\text{-}F}$ = 24.0 Hz), 30.8, 18.2, 14.0; **^{19}F NMR (376 MHz, $CDCl_3$)**: δ -103.9 (d, *J* = 269.9 Hz), -108.0 (d, *J* = 268.7 Hz); **IR (neat)** cm^{-1}: 2987, 2108, 1763, 1701, 1211; **HRMS (ESI)**: Calcd. for $C_{10}H_{15}F_2N_4O_3$ $(M+H)^+$ 277.1112, found 277.1120.

3. General Procedure for Large-scale Reaction of 4a



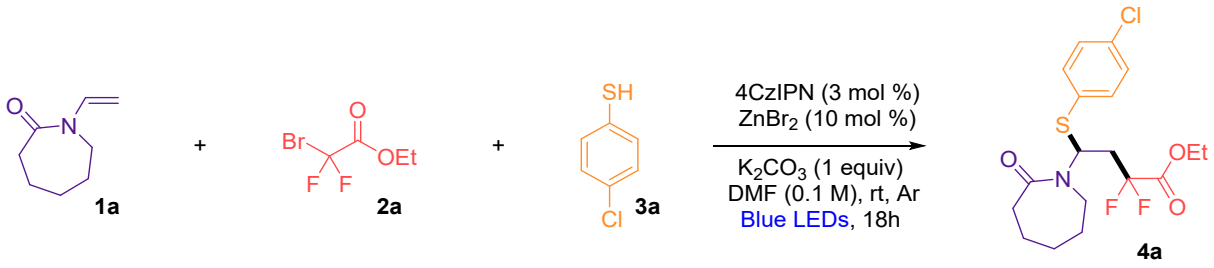


To an oven-dried 100 mL flaks equipped with a magnetic stir bar, 4CzIPN (59 mg, 0.075 mmol, 3 mol %), $ZnBr_2$ (56 mg, 0.25 mmol, 10 mol %), *N*-vinyl caprolactam (2.5 mmol, 1.0 equiv), 4-chlorobenzenethiol (542 mg, 3.75 mmol, 1.5 equiv), K_2CO_3 (345 mg, 2.5 mmol, 1.0 equiv) were added, and the vial was subjected to 3 cycles of vacuum/argon degassing. Subsequently, DMF (25 mL, 0.1 M) and ethyl 2-bromo-2-difluoroacetate was added via syringe (641 µL, 1.01 g, 5.0 mmol, 2 equiv). The reaction mixture was irradiated for 36 hours with blue LED strip (light-emitting diode, λ_{max} = 456 nm) as described in the "Workflow" section. The temperature of the reaction was maintained at approximately 25 °C via a fan. Upon completion, the reaction mixture was poured into a separatory funnel and diluted with EtOAc (20 mL) and washed with H_2O (25 mL × 3) followed by brine (25 mL). The organic layer was dried (anhyd Na_2SO_4) and then subjected to rotary evaporation to remove the solvent. Purification of compound **4a** by automated flash column chromatography using hexanes/EtOAc mixture gave the pure compound in 60% yield (601 mg, 1.48 mmol).

4. Mechanistic Investigations

A. Quantum yield

The quantum yield of the reaction was determined using the procedure reported previously:[5] *N*-Vinyl amide **1a**, ethyl bromodifluoroacetate **2a**, and 4-chlorothiophenol **3a** were used as model substrates to determinate the quantum yield of this transformation, using 1,3,5-trimethoxybenzene as an internal standard in a proportion 1:1 with **1a**.



The quantum yield of the reaction is defined as:

$$\Phi(reaction\ at\ 456\ nm) = \frac{mol\ of\ formed\ product}{mol\ of\ photon\ flux \cdot t \cdot f} \qquad (1)$$

where Φ is the quantum yield of the reaction, t is the time of the reaction (s), and f is the incident light absorbed by the 4CzIPN photocatalyst at 458 nm. The photon flux is calculated by standard ferrioxalate actinometry[6] (see Section *B.3*).

B.1. Incident light absorbed by 4CzIPN

The fraction of light, f, absorbed was determined according to equation 2:

$$F = 1 - 10^{-A} \qquad (2)$$

where A is the absorbance of the 4CzIPN photocatalyst in DMF at 458 nm. The wavelength of 458 nm was chosen based on the known absolute $\Phi(Fe^{+2})$ value[6] and is where the photocatalyst absorbs most. The absorbance of 4CzIPN was measured (0.005 M) in DMF (1 mL) to a cuvette equipped with a Teflon-coated magnetic stir bar and stirred for 30 seconds. The absorbance was recorded. The absorbance (A) at 458 nm was determined to be >3, thus indicating the fraction of light absorbed is ~1 according to equation 2.

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[5] M. El Khatib, R. A. M. Serafim, G. A. Molander, *Angew. Chem. Int. Ed.* 2016, **55**, 254.

[6] J. N. Demas, W. D. Bowman, E. F. Zalewski, R. Velapoidl, *J. Phys. Chem*. 1981, **85**, 2766.

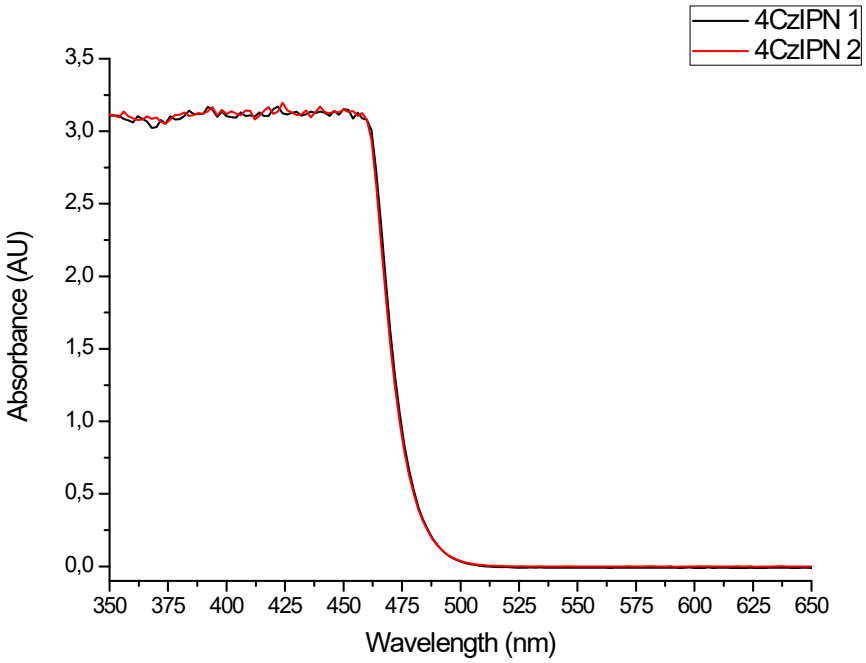


Figure S2. *UV-Vis spectra of all reaction components (**1a**: 0.1 M, **2a**: 0.2 M, **3a**: 0.15 M and 4CzIPN: 0.2 mM) in DMF*

B.2. The photoredox reaction

The photoredox transformation was developed using the general procedure for 360 min. Afterwards, 1,3,5-trimethoxybenzene was added as an internal standard, and the solvent was evaporated. The yield of the reaction was determined by ^{1}H NMR (Figure S3), where the desired compound was obtained in 16% yield.

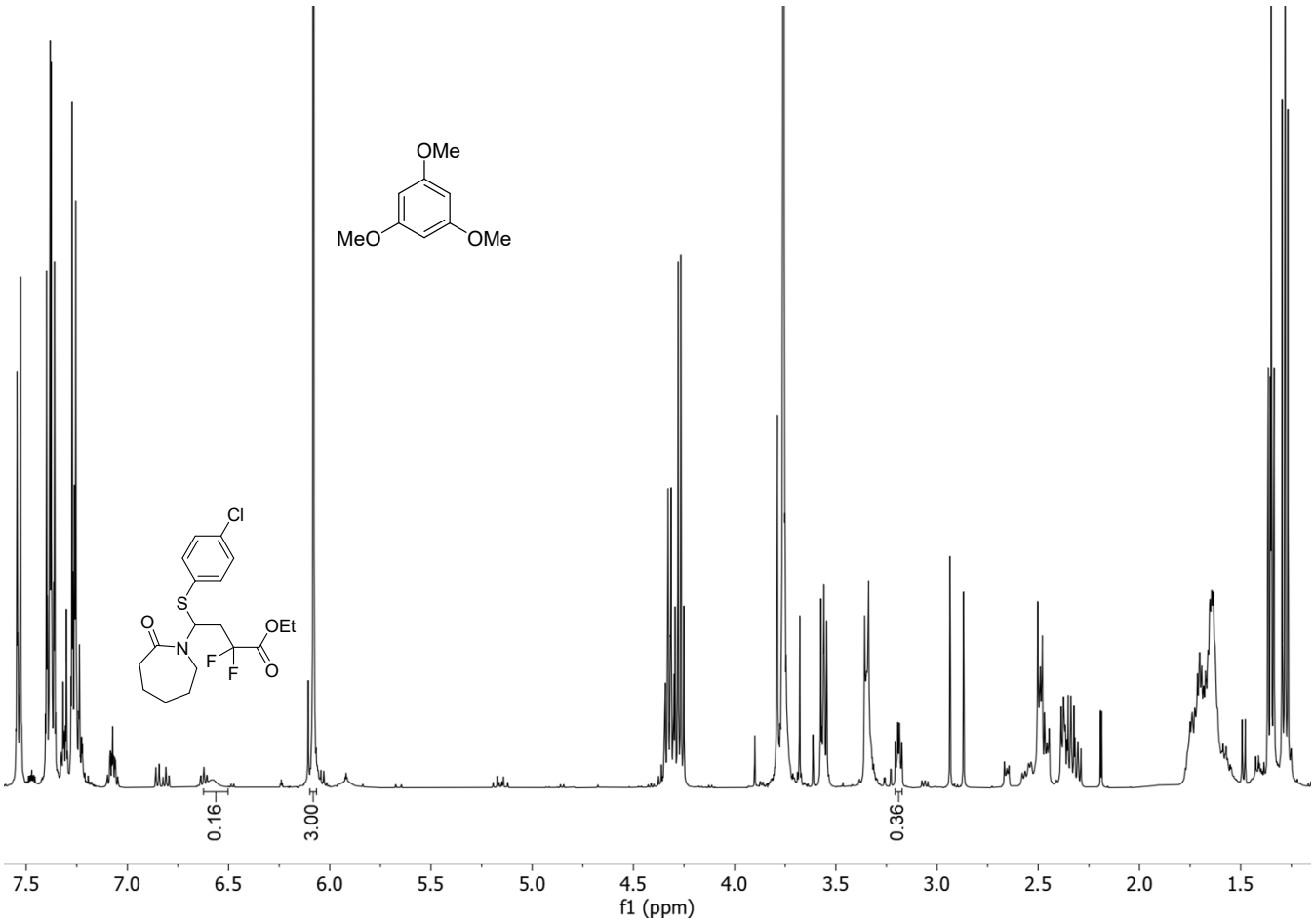


Figure S3. ^{1}H NMR (500 MHz, $CDCl_3$) of the reaction after 360 min in the presence of 1,3,5-trimethoxybenzene

B.3. Photon flux at 458 nm

Standard ferrioxalate actinometry was used to determine the photon flux of the spectrophotometer using equations 3 and 4. For the ferrioxalate actinometer, the production of iron(II) ions proceeds by the following reactions:[5]

$$[Fe(C_2O_4)n]^{+(3-2n)} \xrightarrow{\text{light}} Fe^{+2} + (n-1)(C_2O_4)^{-2} + C_2O_4^{-}$$

$$[Fe(C_2O_4)n]^{+(3-2n)} + C_2O_4^{-} \longrightarrow Fe^{+2} + n(C_2O_4)^{-2} + 2\,CO_2$$

The moles of Fe^{+2} formed are determined spectrophotometrically by development with 1,10-phenanthroline (phen) to form the red $[Fe(phen)_3]^{+2}$ moiety (λ = 510 nm).[5] The photon flux is defined as shown in equation 3:

$$Photon\ flux = \frac{mol\ Fe^{+2}}{\Phi\left(Fe^{+2}\right)\cdot t\cdot f} \qquad (3)$$

where Φ is the quantum yield for the ferrioxalate actinometer (0.84 at λ = 458 nm),[6] t is the time (s), f ~1, and the mol of Fe^{+2} are calculated according to equation 4.

$$mol\left(Fe^{+2}\right) = \frac{V \cdot \Delta A}{l \cdot \epsilon} \qquad (4)$$

where V is the total volume of the solution, ΔA is the difference in absorbance between irradiated and nonirradiated solutions, l is the path length (1.0 cm), and ε is the molar absorptivity at 510 nm (11110 L mol^{-1} cm^{-1}).[3]

B.4. Experimental

The following solutions were prepared in the dark (flasks were wrapped in aluminum foil) and stored in the dark at room temperature:

– Ferrioxalate solution (0.15 M): Potassium ferrioxalate hydrate (1.312 g) was added to a flask wrapped in aluminum foil containing H_2SO_4 (20 mL, 0.05 M). The flask was stirred for complete solvation of the green solid in complete darkness. It is noteworthy that the solution should not be exposed to any incident light.

– Developer solution: 1,10-Phenanthroline (50 mg) and NaOAc (11.25 g) was added to a flask containing H_2SO_4 (50 mL, 0.5 M) and sonicated until completely solvated.

The absorbance of the non-irradiated sample. The buffered solution of phen (350 μL) was added to a ferrioxalate solution (2.0 mL) in a vial that had been covered with aluminum foil and with the lights of the laboratory switched off. The vial was capped and allowed to rest for 1 h and then transferred to a cuvette. The absorbance of the non-irradiated solution was measured at 510 nm to be 0.32 (average of two determinations, see *Figure S4*).

The absorbance of the irradiated sample. In a cuvette equipped with a stir bar was added the ferrioxalate solution (2.0 mL), and the stirred solution was irradiated for 90 s at λ = 427 nm with an excitation slit width = 10.0 nm. After irradiation, the buffered phen solution (350 μL) was added to the cuvette and allowed to rest for 1 h in the dark to allow the ferrous ions to coordinate completely to phen. The absorbance was measured at 510 nm to be 1.80 (average of two determinations, *Figure S4*).

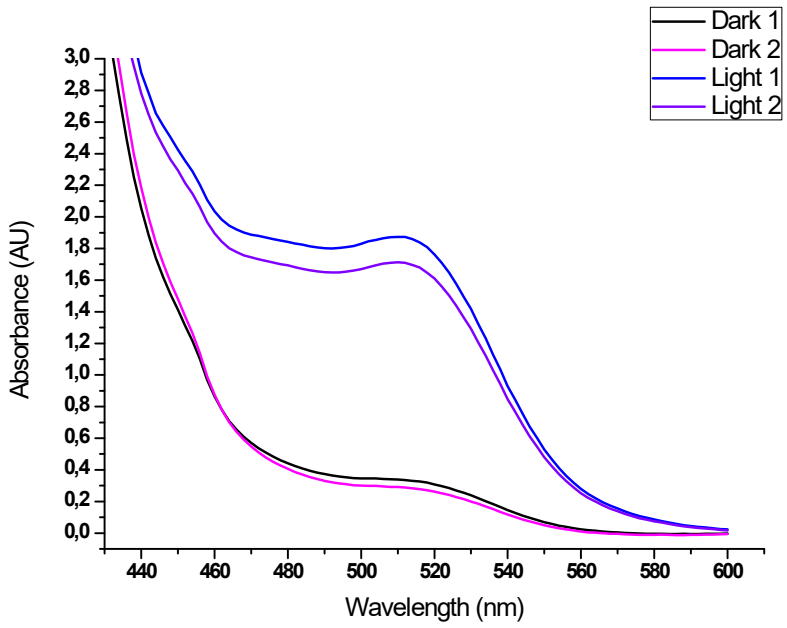


Figure S4. Absorption spectra for irradiated and non-irradiated samples of red $[Fe(phen)_3]^{+2}$

Photon flux sample calculation. Sample calculation:

$$mol\left(Fe^{+2}\right) = \frac{V \cdot \Delta A}{l \cdot \epsilon} \qquad (4)$$

$$mol\left(Fe^{+2}\right) = \frac{0.00235\ L \cdot 1.48}{1.0\ cm \cdot 11100\ L \cdot mol^{-1} cm^{-1}} = 3.13x10^{-7} mol$$

$$Photon\ flux = \frac{mol\ Fe^{+2}}{\Phi\left(Fe^{+2}\right) \cdot t \cdot f} \qquad (3)$$

$$Photon\ flux = \frac{3.13x10^{-7} mol}{0.84 \cdot 90\ s \cdot 1} = 4.14x10^{-9}\ einstein\ s^{-1}$$

B.5. Quantum yield of the photoinduced transformation

Therefore, the quantum yield of the reaction was determined to be:

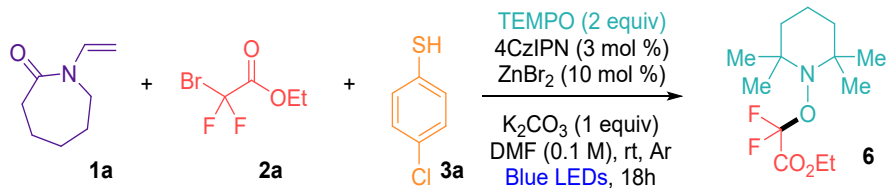
$$\Phi(reaction\ at\ 458\ nm) = mol\ of\ formed \frac{product}{mol\ of\ photon\ flux \cdot t \cdot f} \qquad (1)$$

$$\Phi(reaction\ at\ 458\ nm) = \frac{1.6x10^{-5}\ mol}{4.14x10^{-9}\ einstein\ s^{-1} \cdot 21600\ s \cdot 0.91} = 0.18$$

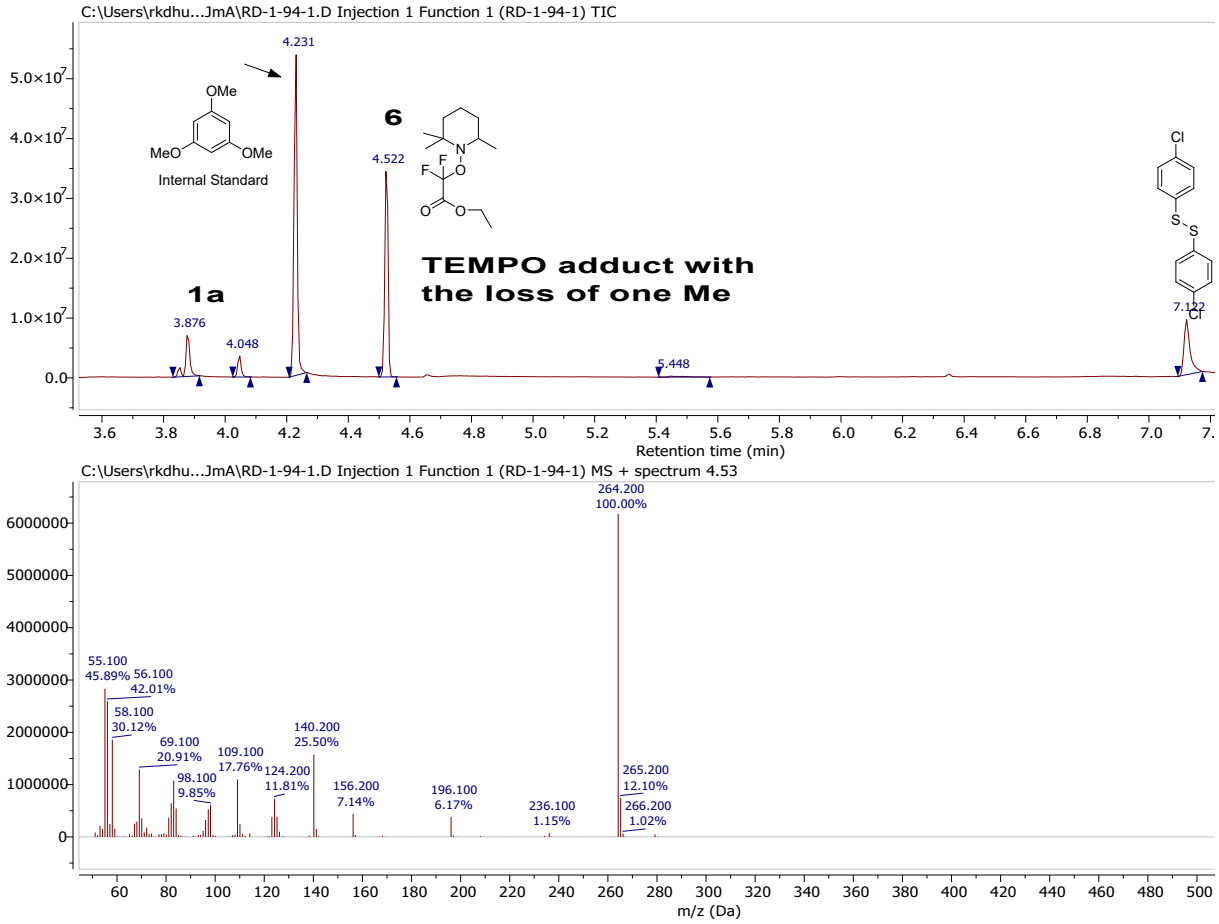
The quantum yield studies indicate that this is not a radical-chain process as evidenced by the Φ value. In other words, the quantum yield value indicated that 0.18 equivalents of product are formed for every photon absorbed, which is a result that implies the reaction is most likely going through radical-polar crossover and is unlikely to go through radical chain mechanism.

B. TEMPO Experiment

Radical trapping studies were performed under the standard conditions. Addition of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) inhibited the product formation. Specifically, the difluoroalkylated TEMPO adduct **6** (with the loss of one methyl group from the six-membered ring) was detected as a major reaction product by GC/MS. GC/MS shows the mass of the product with the loss of one methyl group.

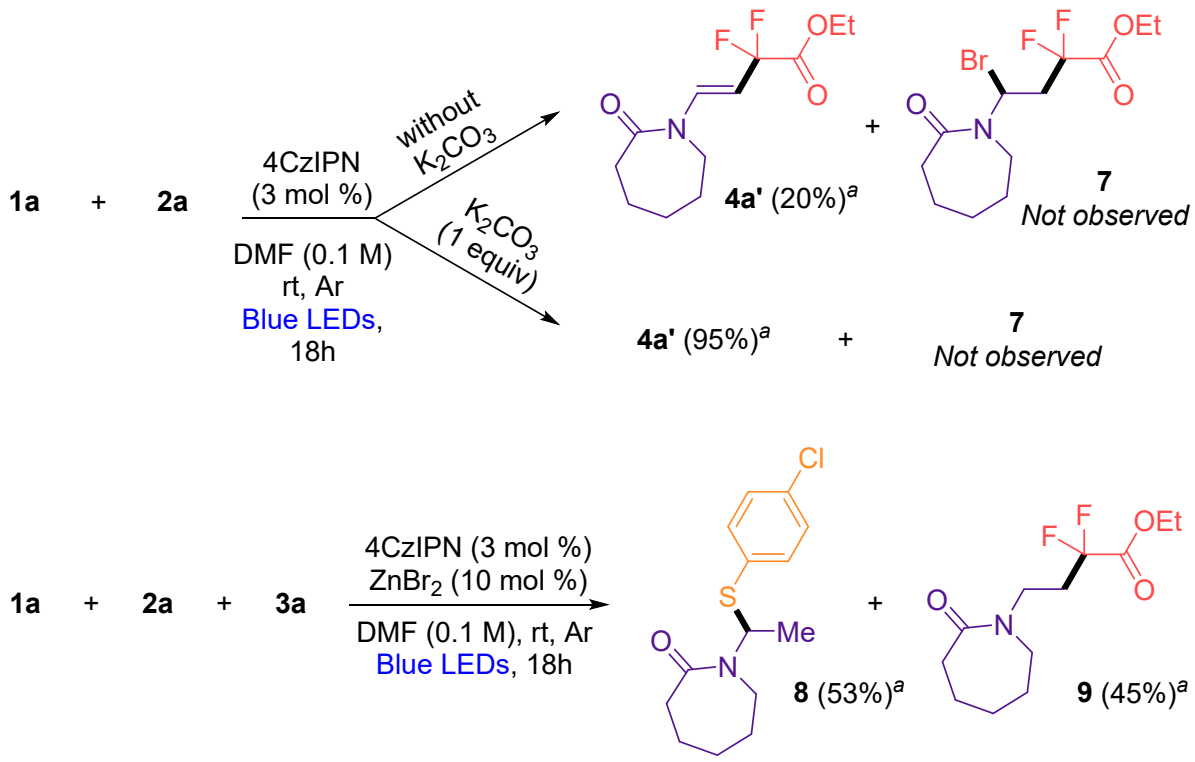


1a **2a** **3a** **6**



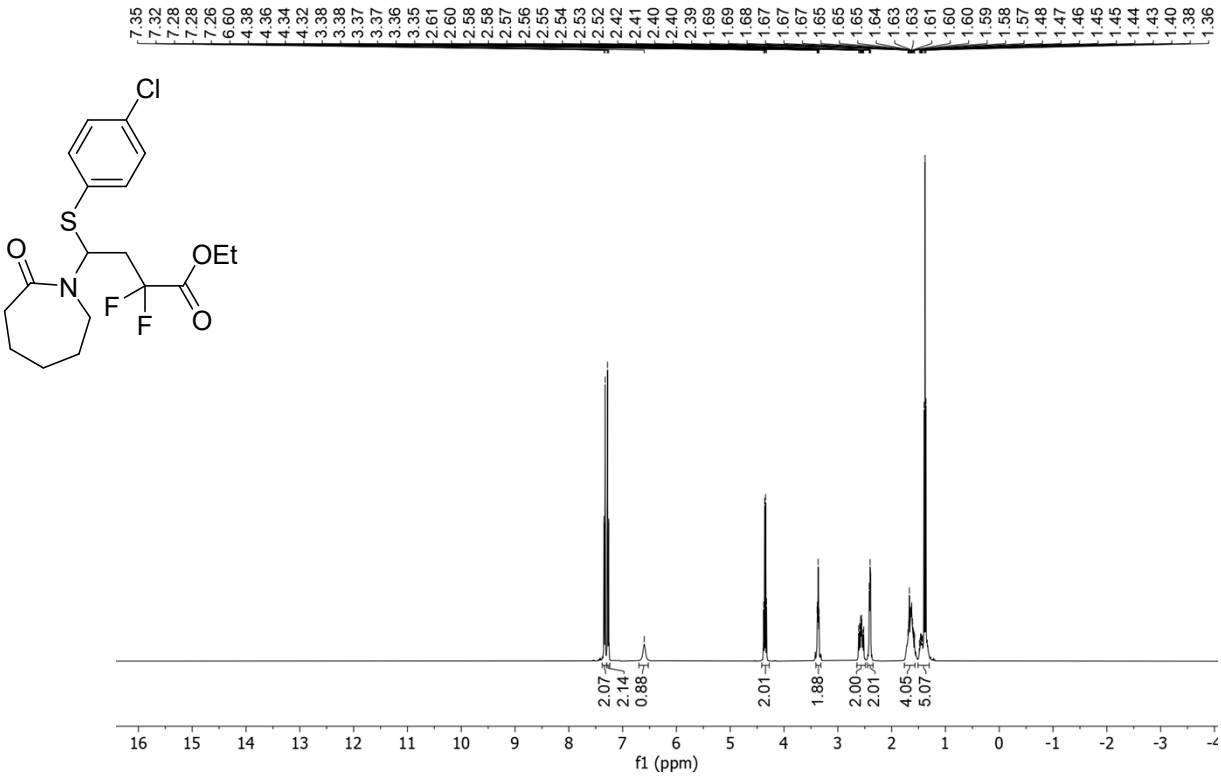
C. Control Experiments

When the reaction was carried out in the absence of K_2CO_3 and thiol **3a**, bromination product **7** was expected if the reaction transpired via an ATRA process. However, under these conditions most of the starting material **1a** remained along with the formation of elimination product **4a'** in small amount (20%). Importantly, no trace of compound **7** was detected (Scheme 2). When the same reaction was carried out in the presence of base, the elimination product was formed exclusively. These two control experiments indicate that the sequential C–C and C–S/O/N bonds are not formed *via* intermediate **7**. As expected, the use of base was crucial to achieve the desired difunctionalized product, because when the base was omitted in the reaction mixture, we observed the thiol Markovnikov addition to the alkene (**8**) as well as compound **9**.

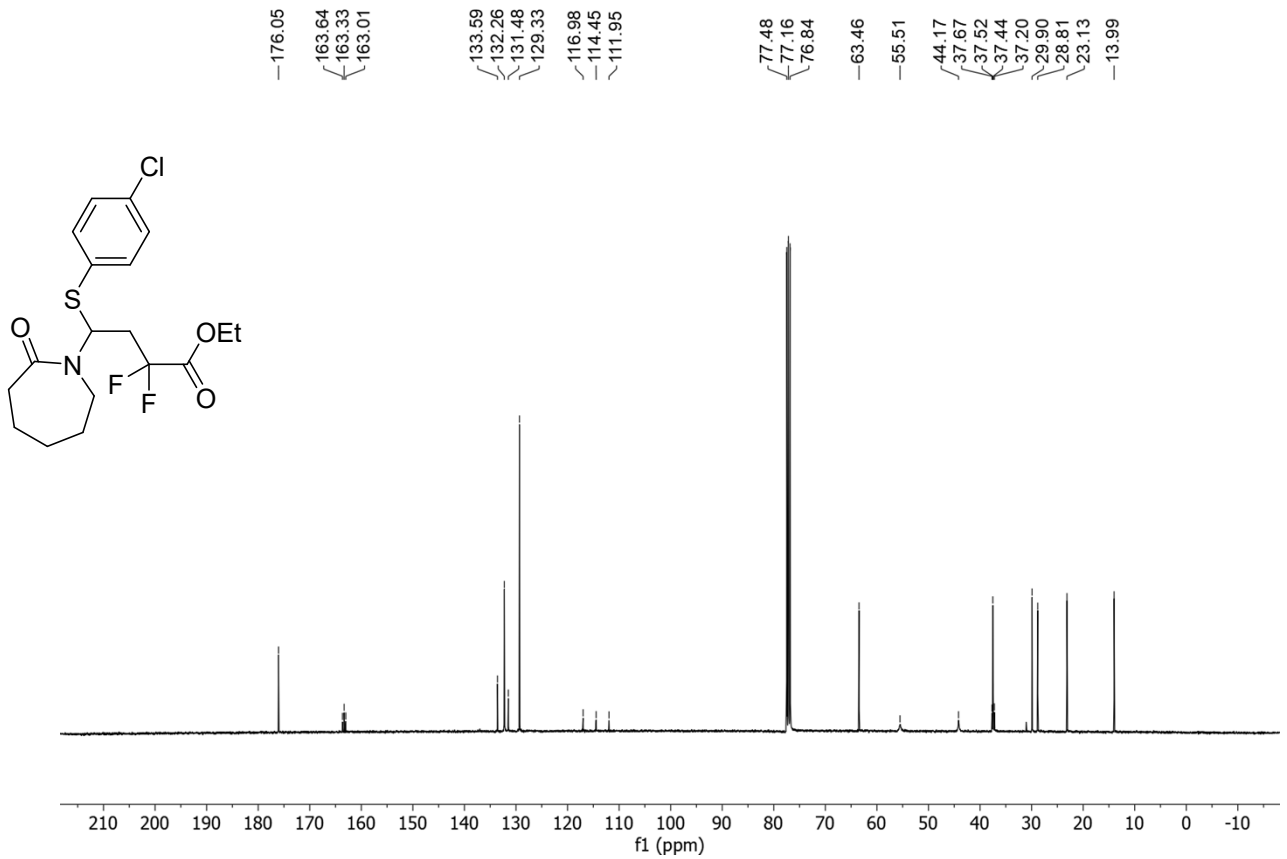


Scheme S1. Control experiments

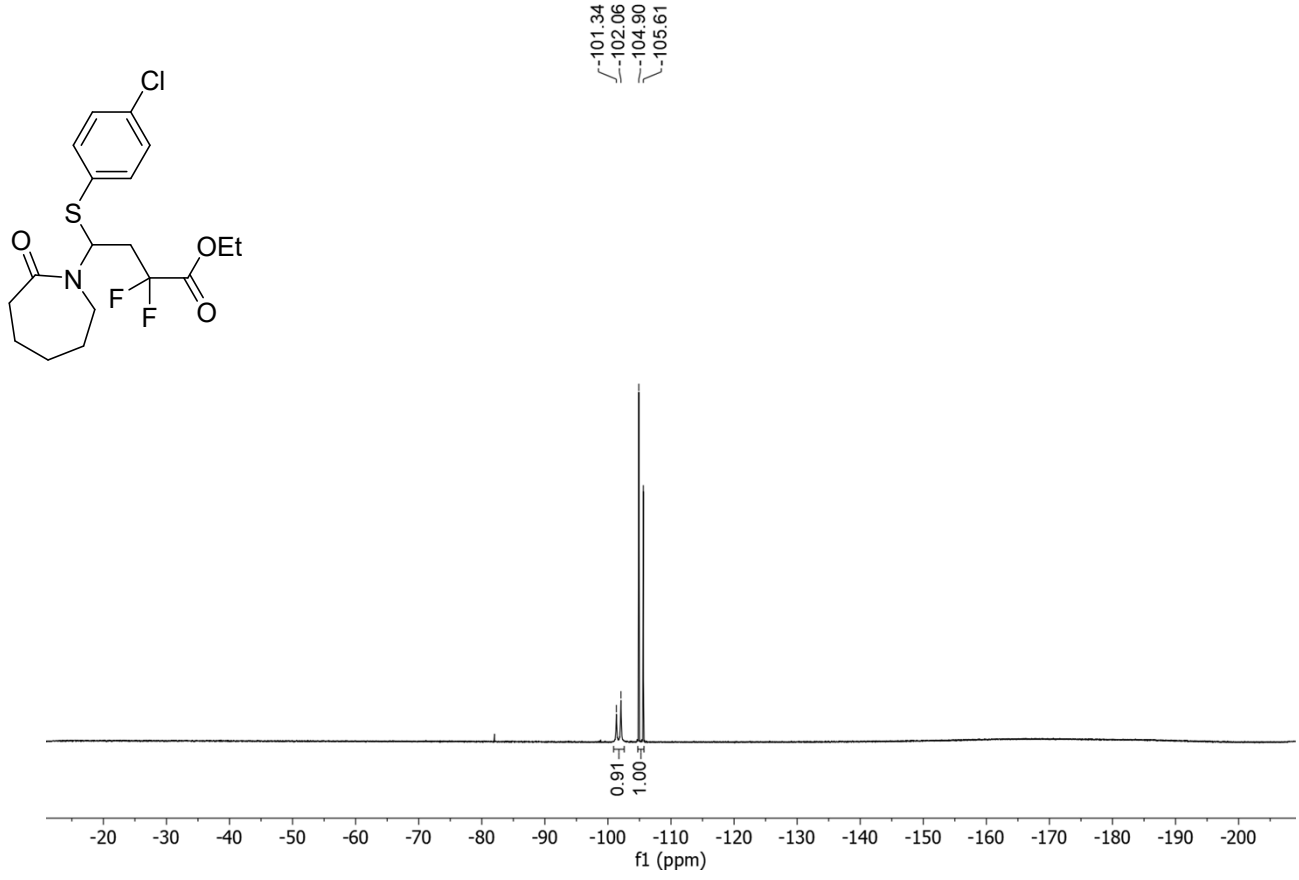
5. NMR spectra



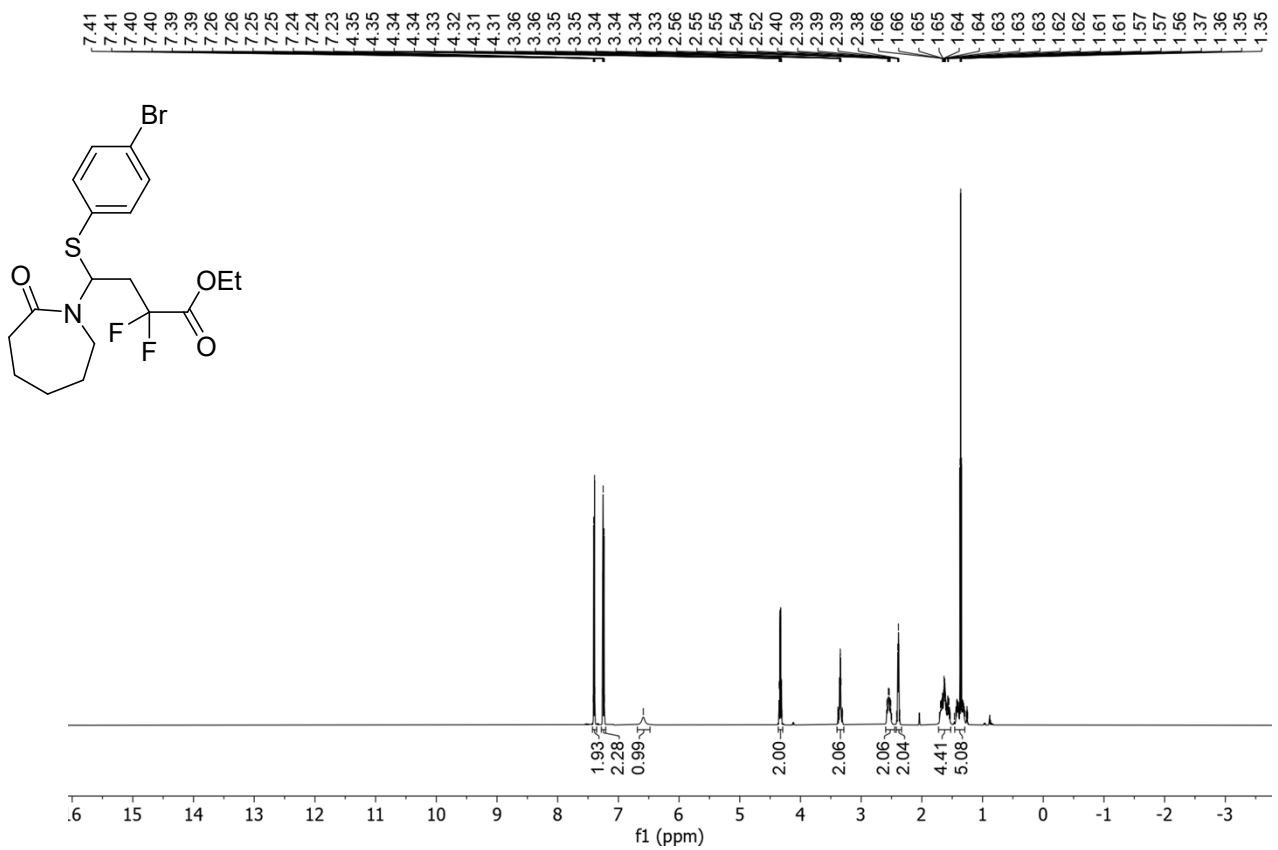
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4a**.



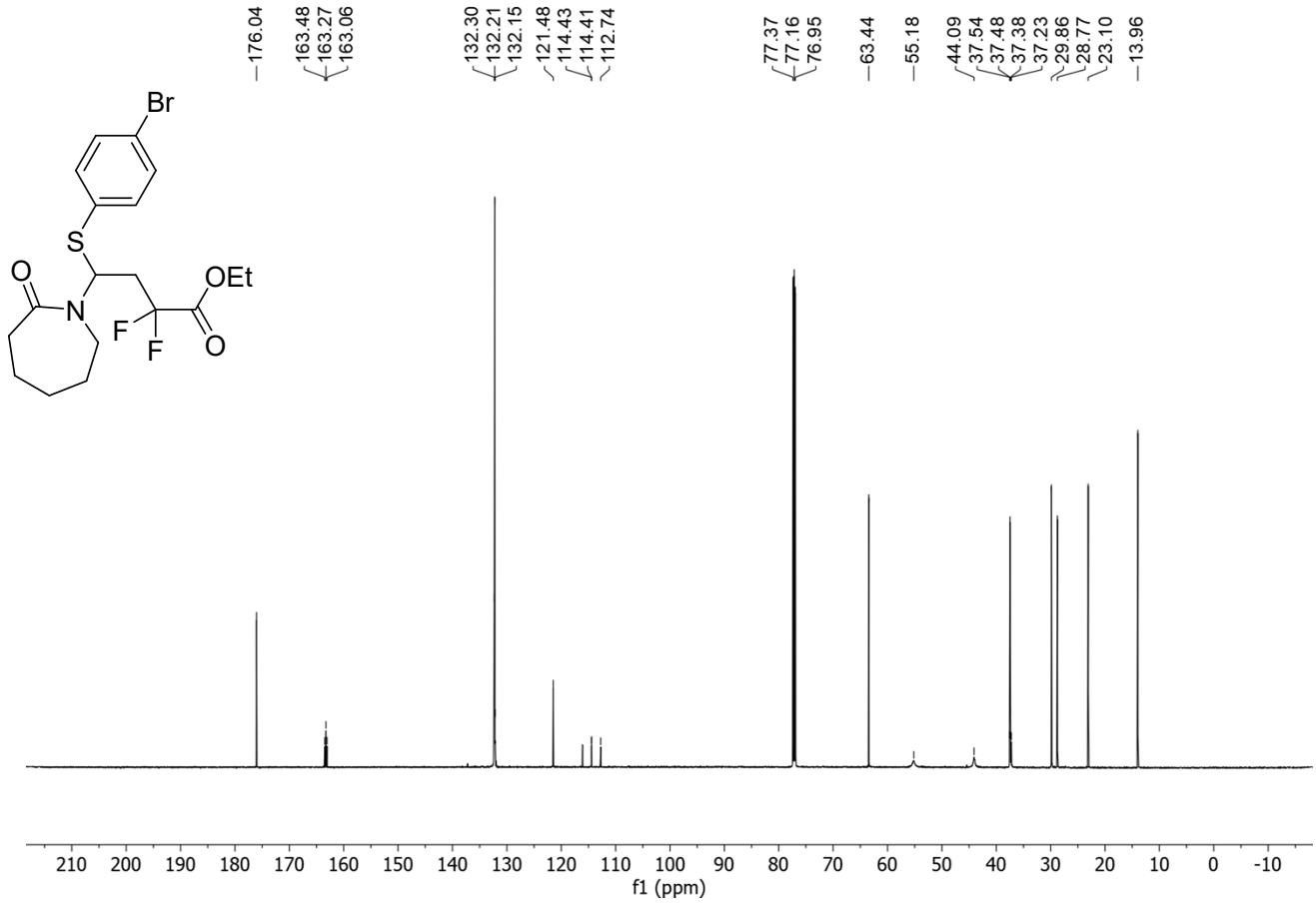
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4a**.



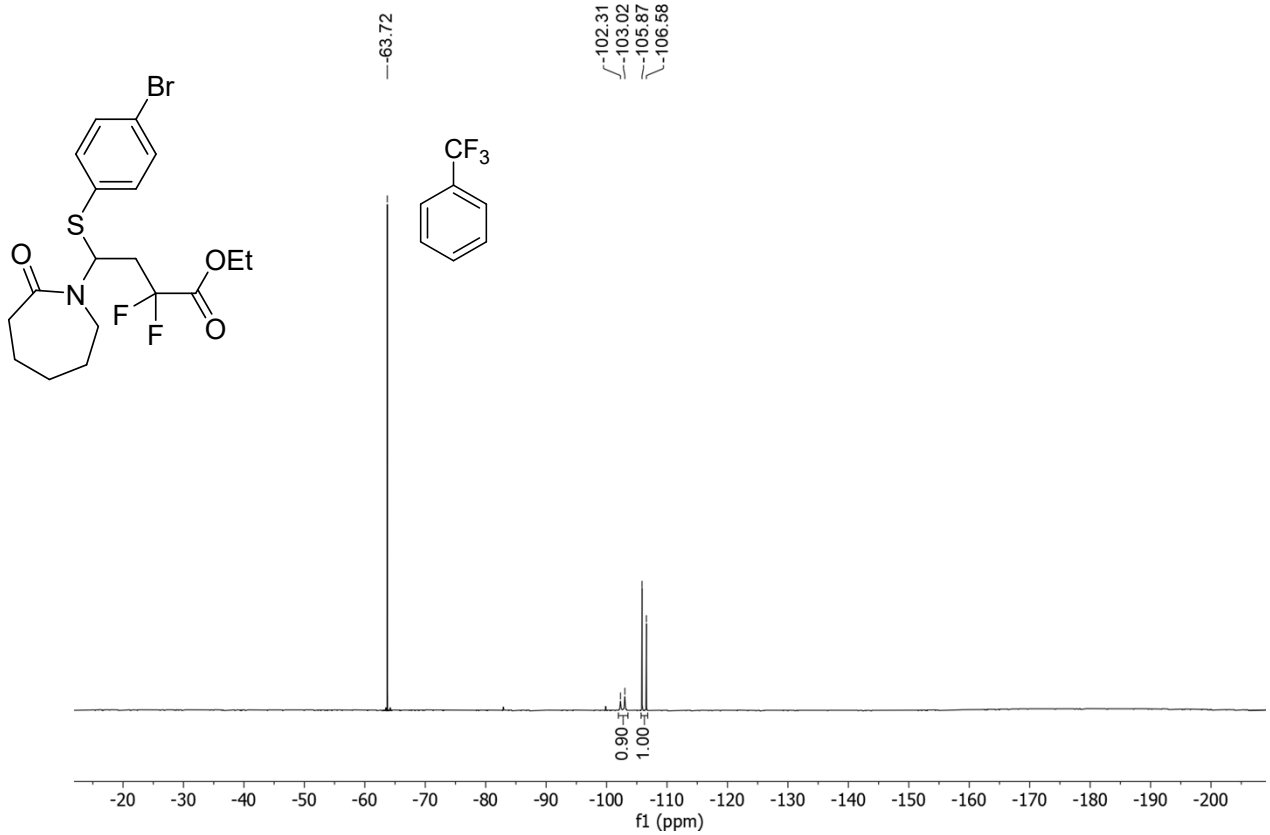
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4a**.



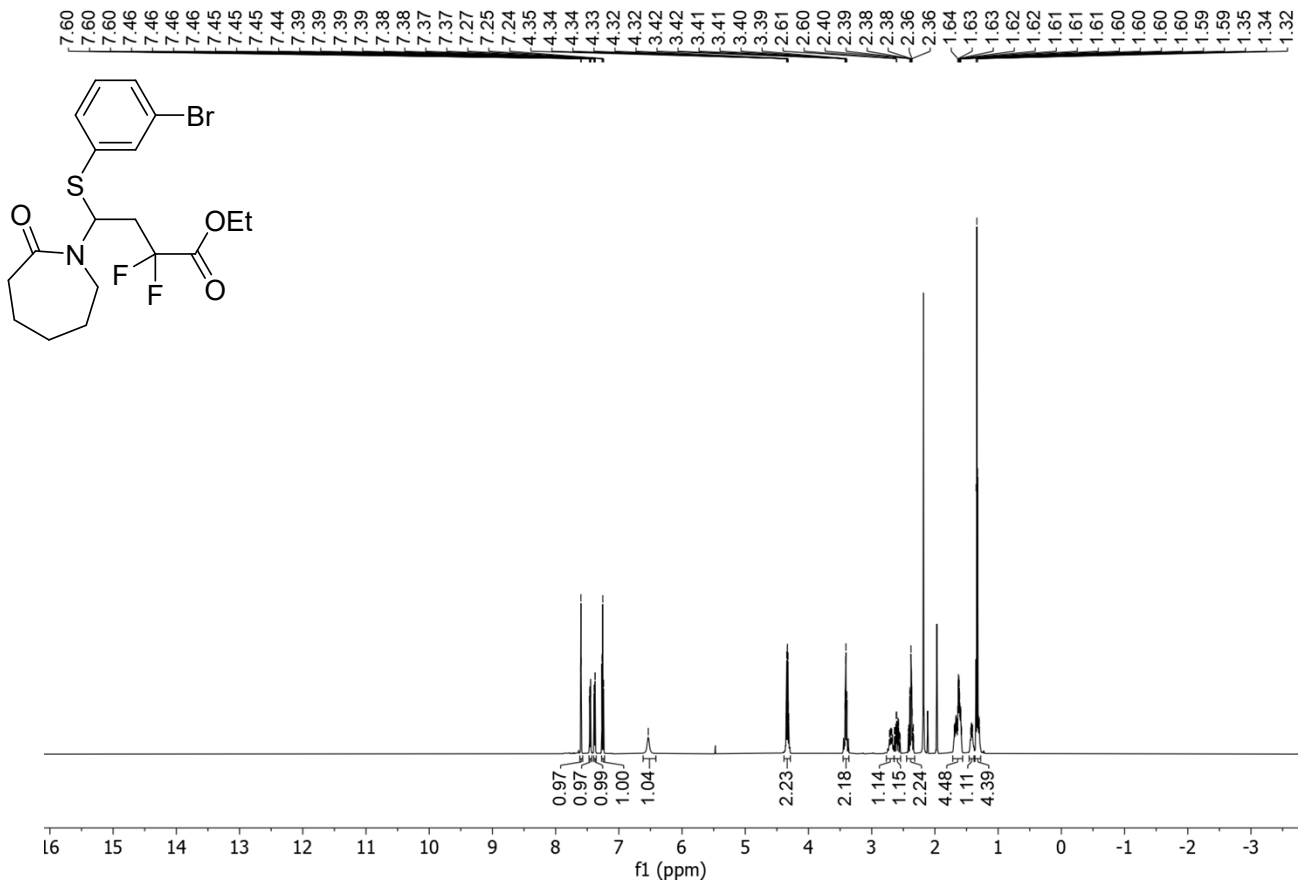
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4b.**



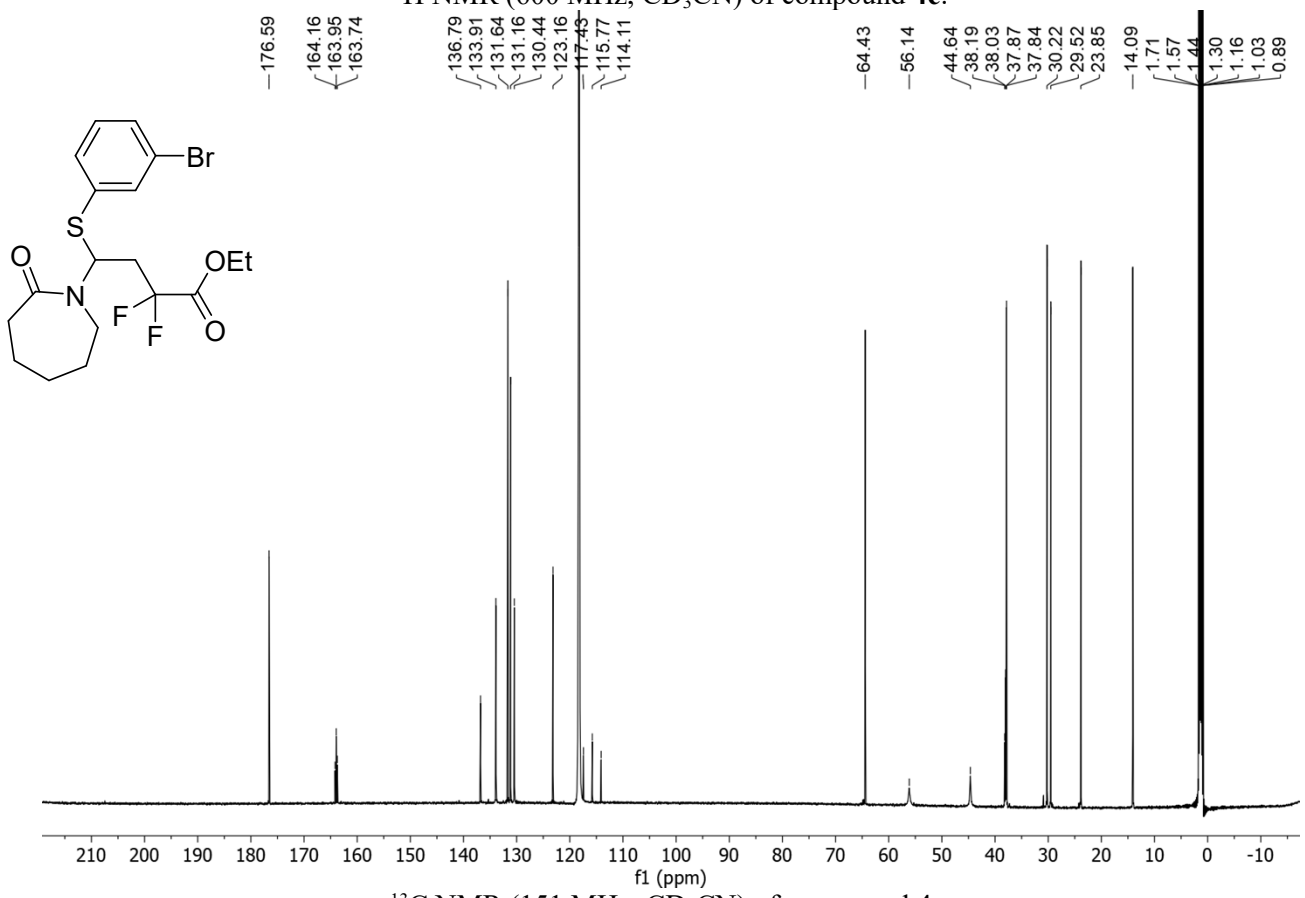
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4b**.



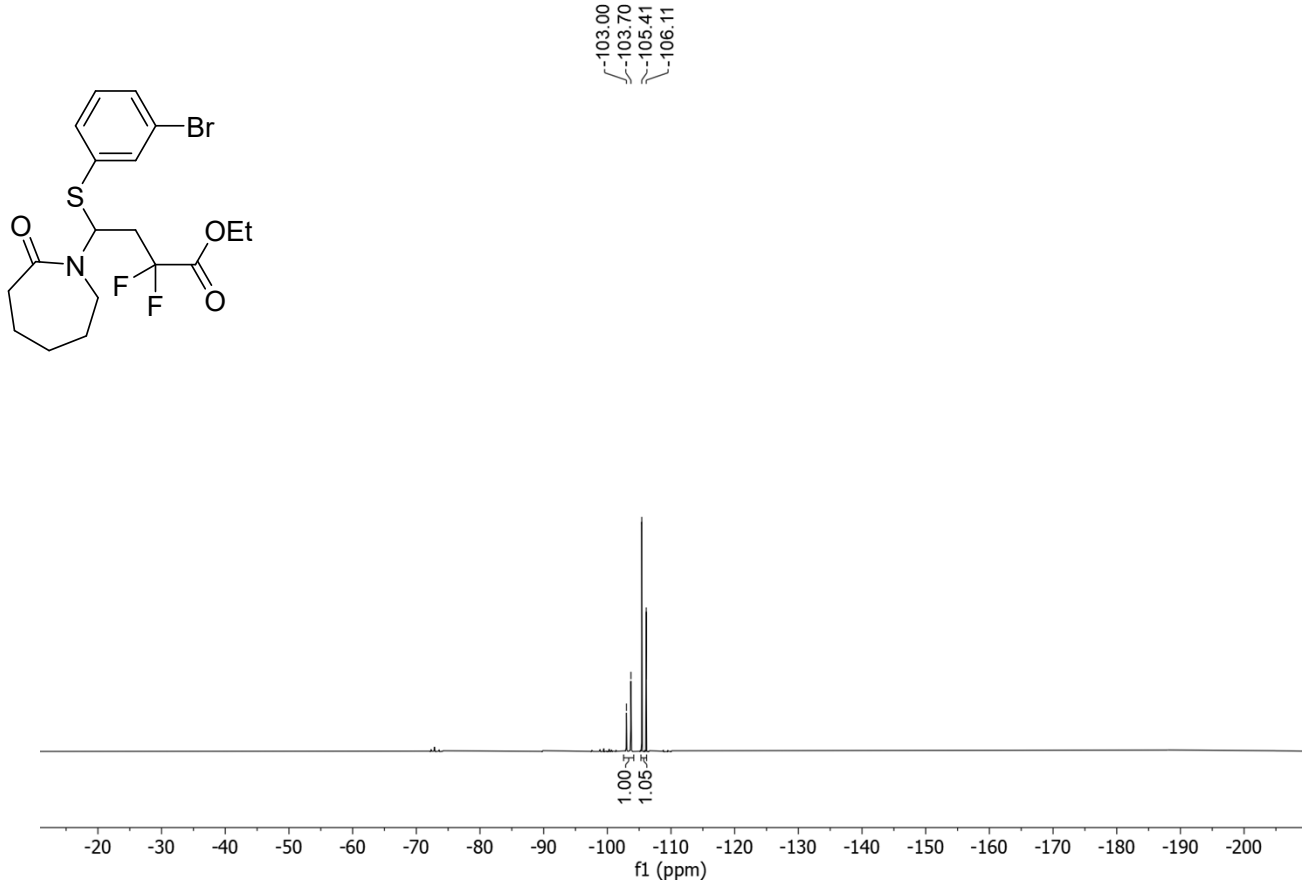
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4b**.



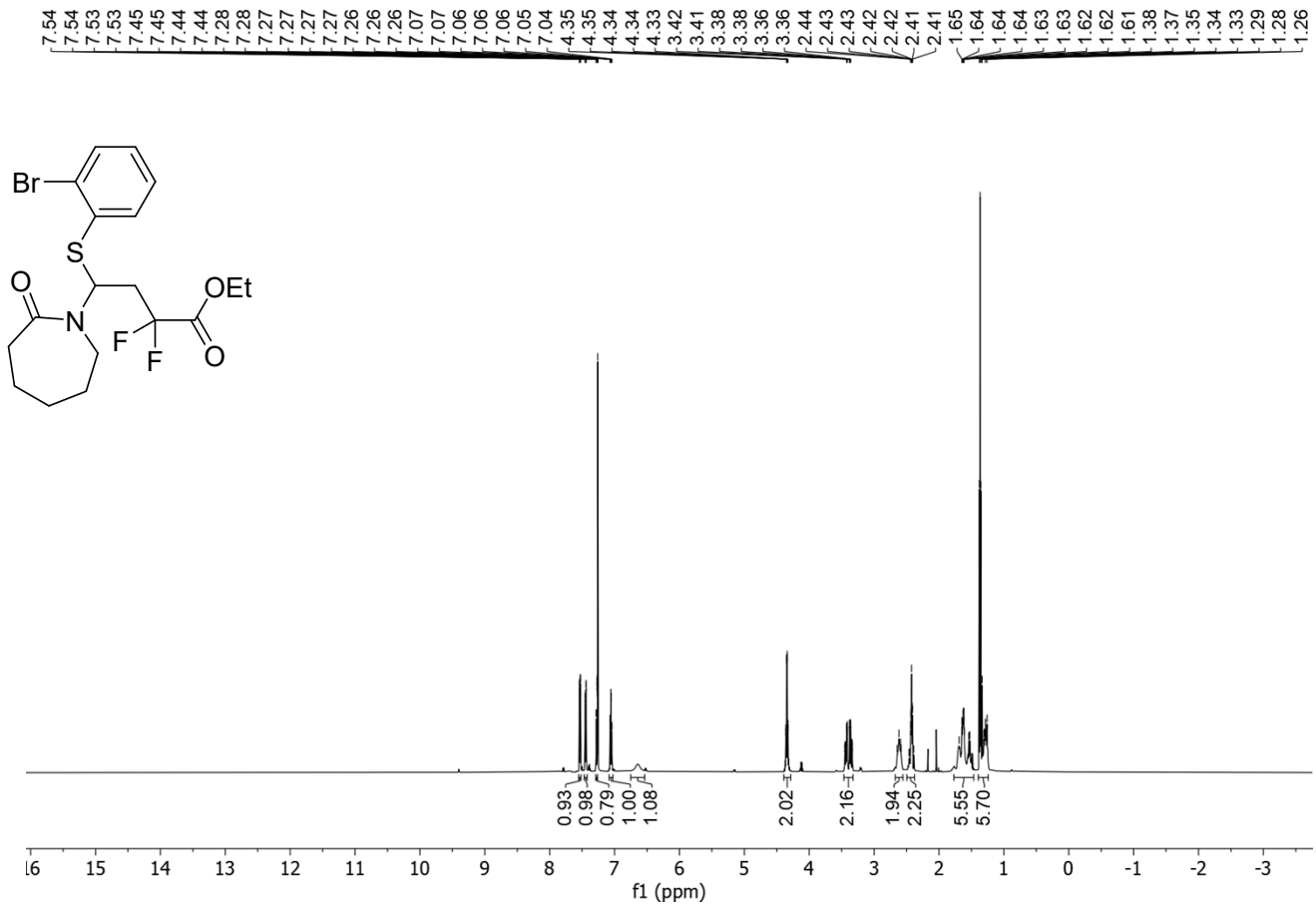
^{1}H NMR (600 MHz, CD_3CN) of compound **4c**.



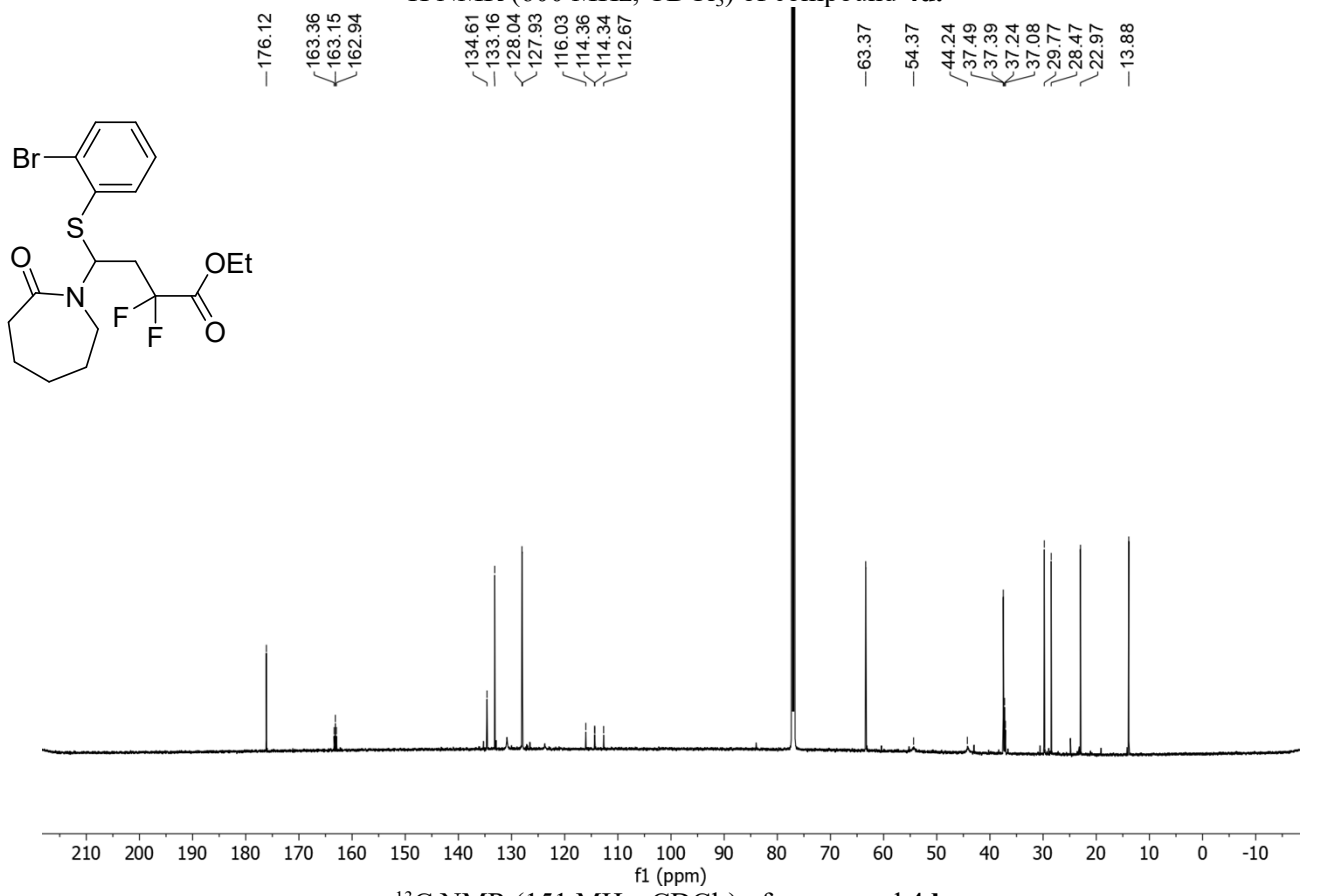
^{13}C NMR (151 MHz, CD_3CN) of compound **4c.**



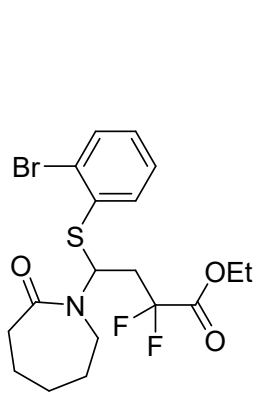
^{19}F NMR (376 MHz, CD_3CN) of compound **4c**.



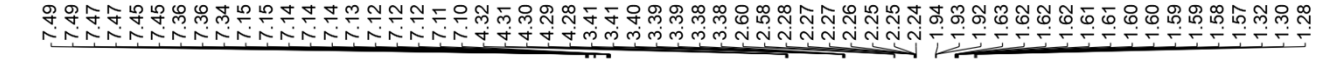
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4d.**

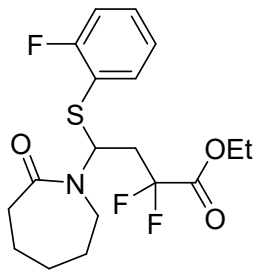


^{13}C NMR (151 MHz, $CDCl_3$) of compound **4d**.

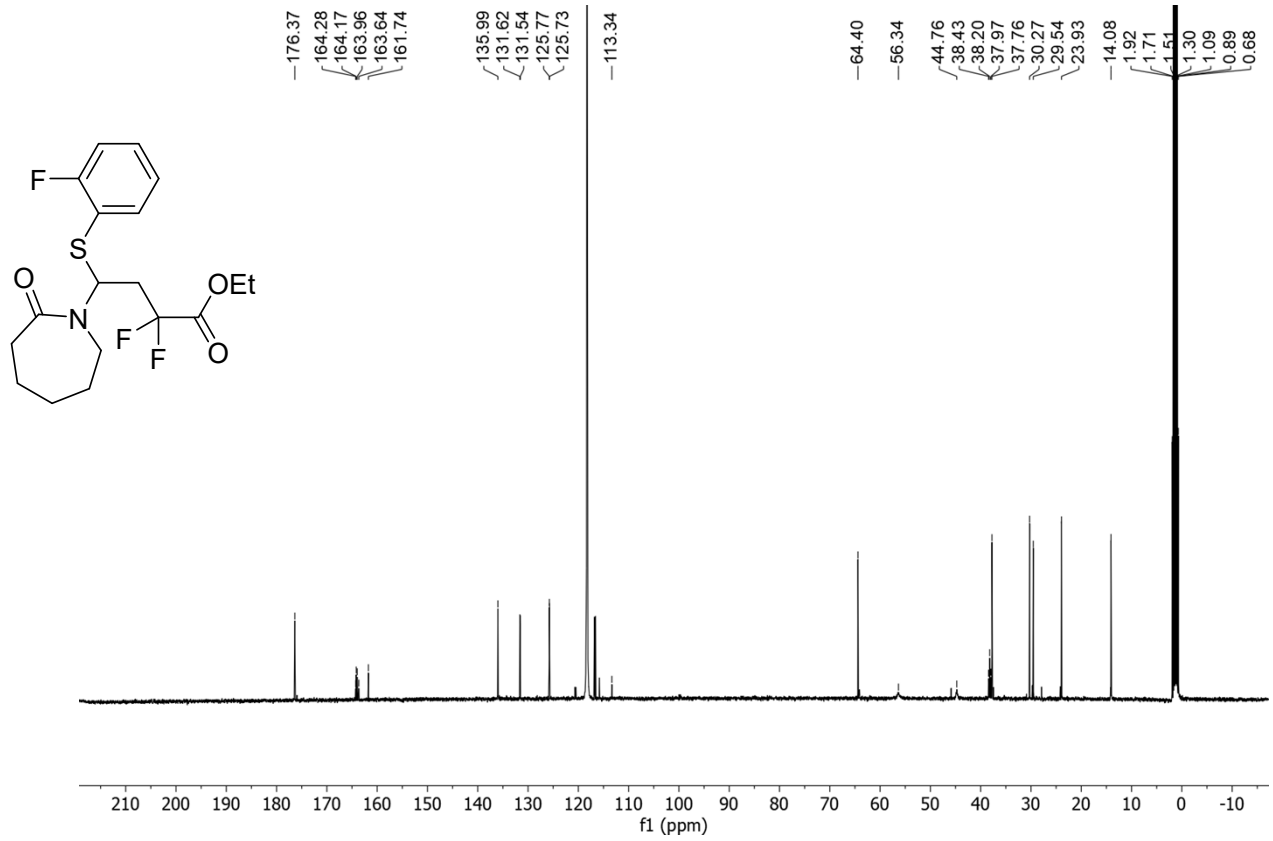


^{19}F NMR (376 MHz, $CDCl_3$) of compound **4d**.

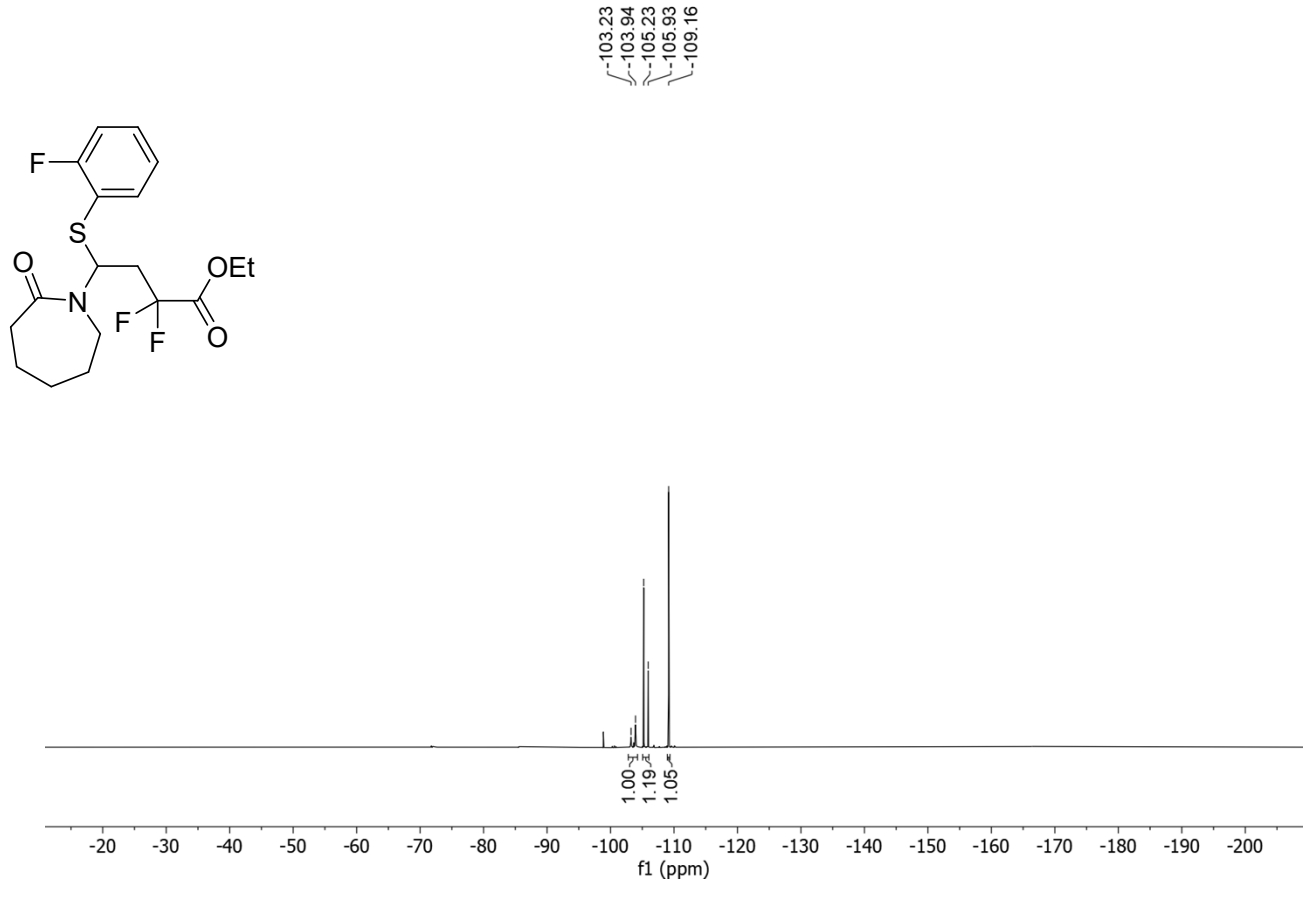




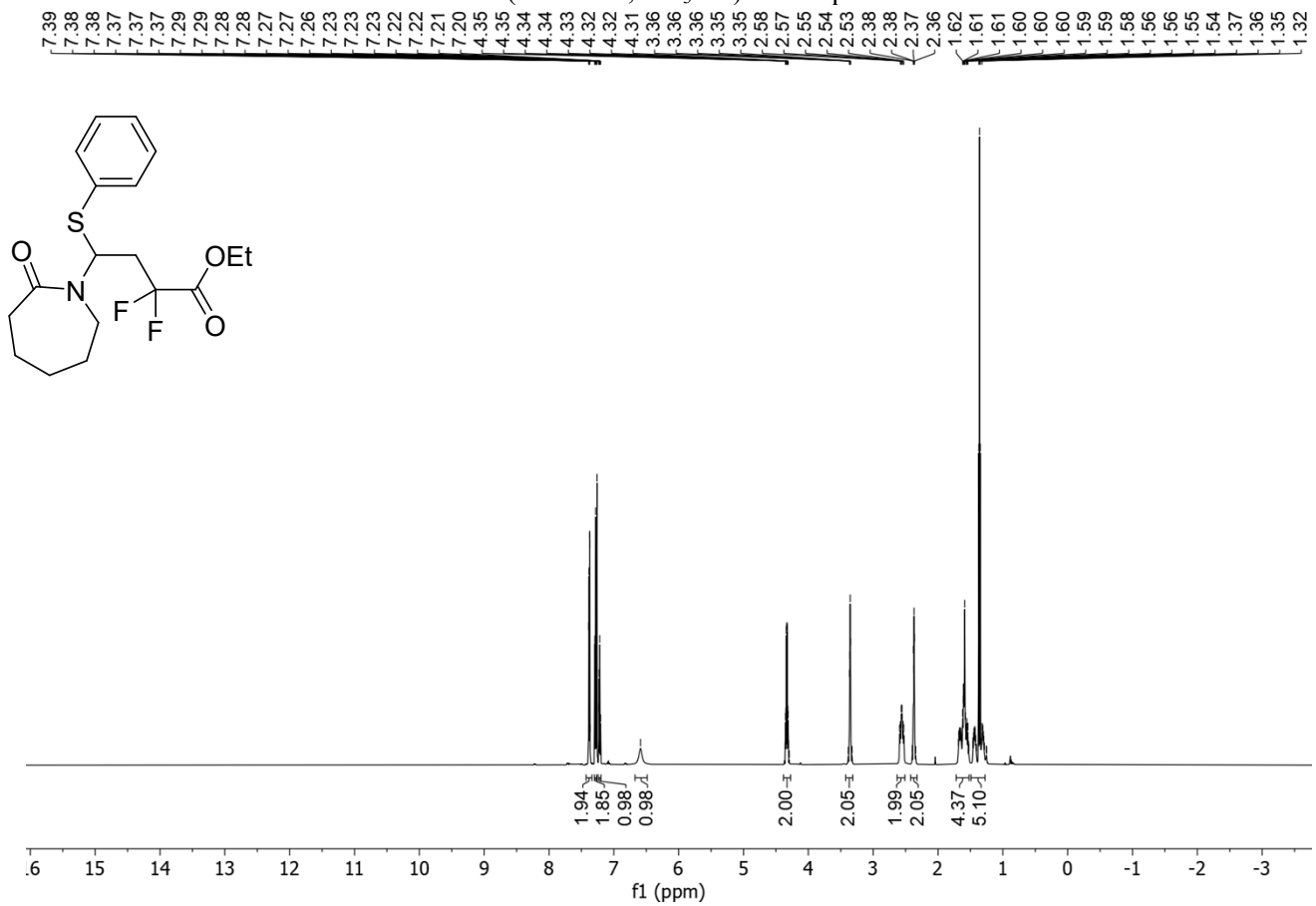
^{1}H NMR (400 MHz, CD_3CN) of compound **4e.**



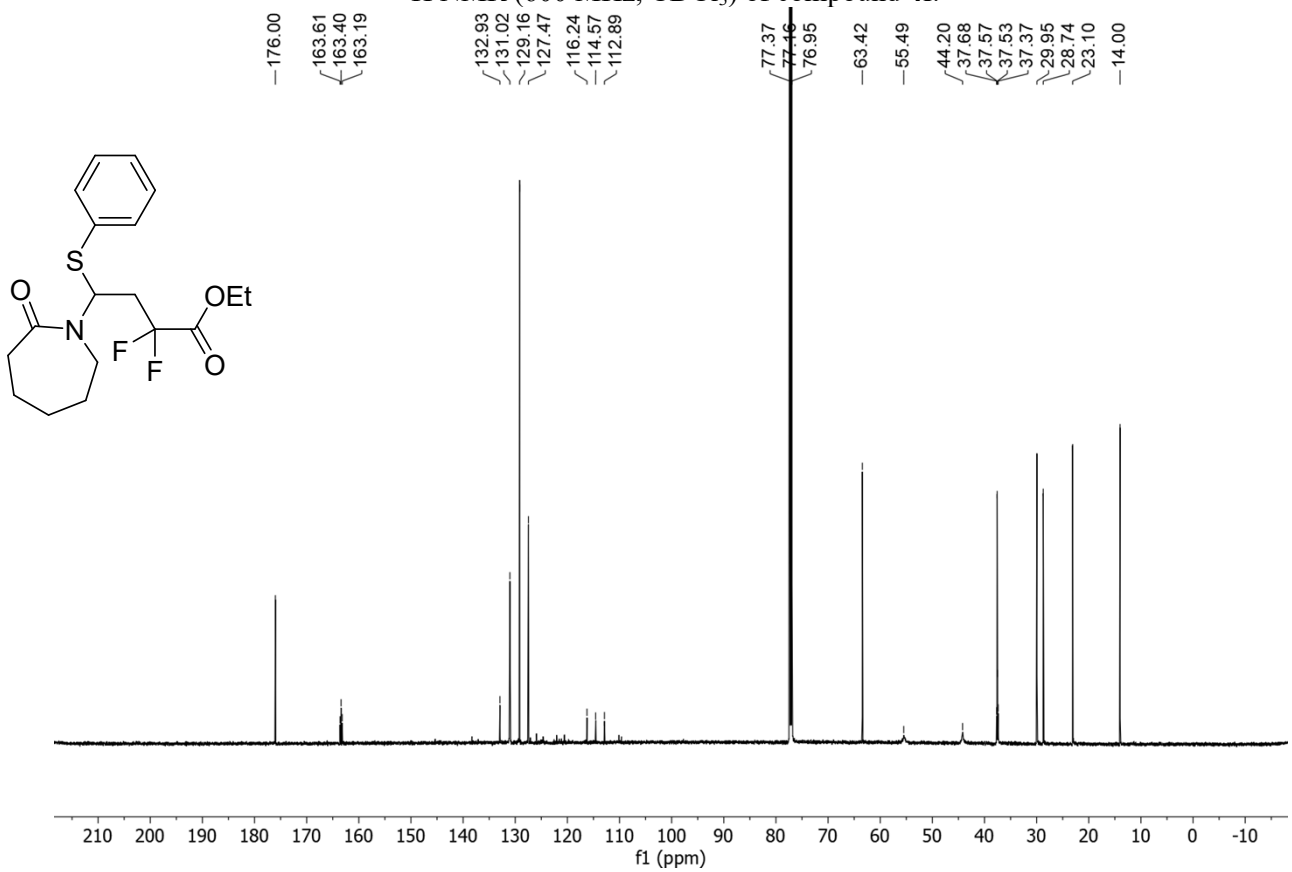
^{13}C NMR (101 MHz, CD_3CN) of compound **4e**.



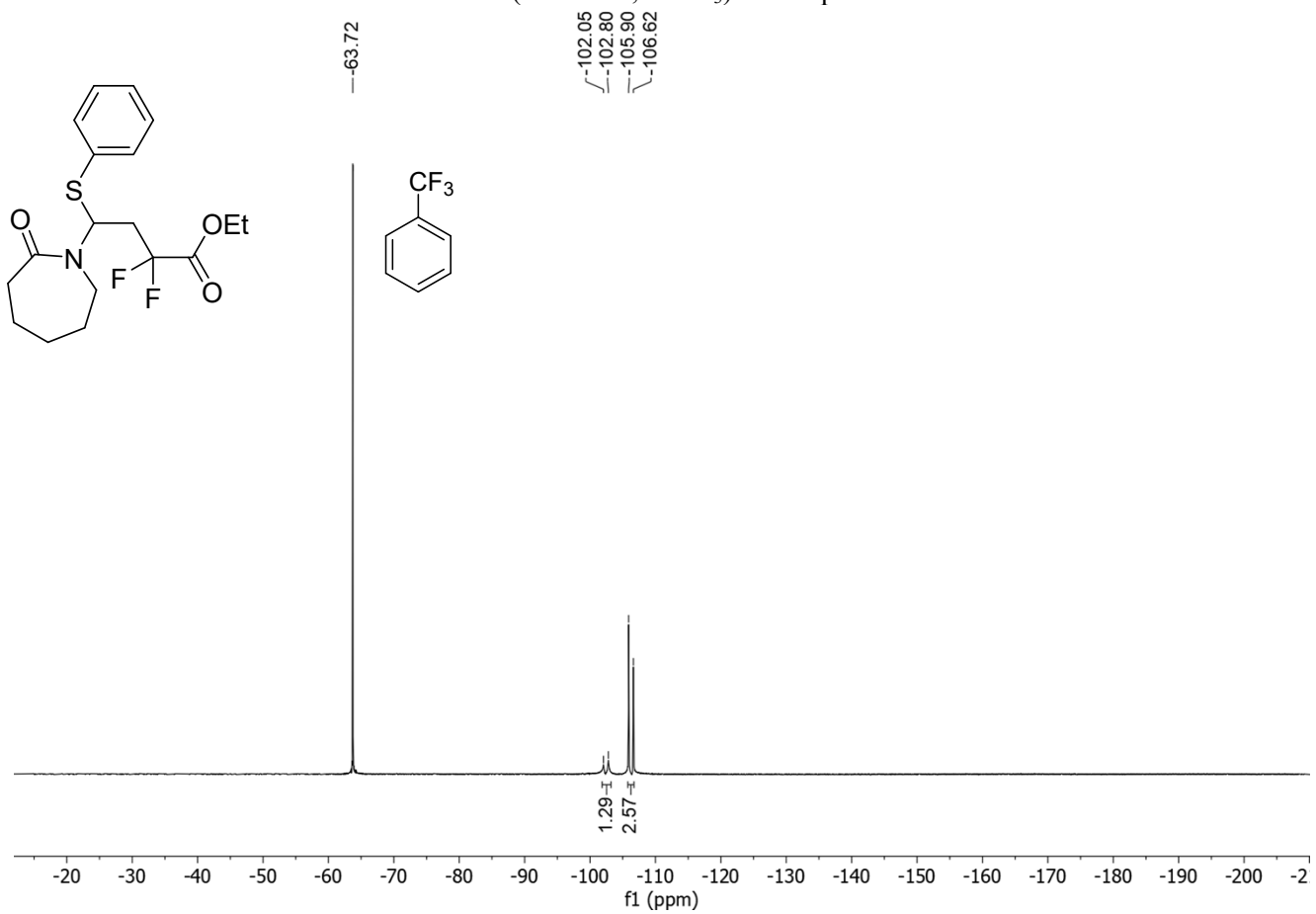
^{19}F NMR (376 MHz, CD_3CN) of compound **4e.**



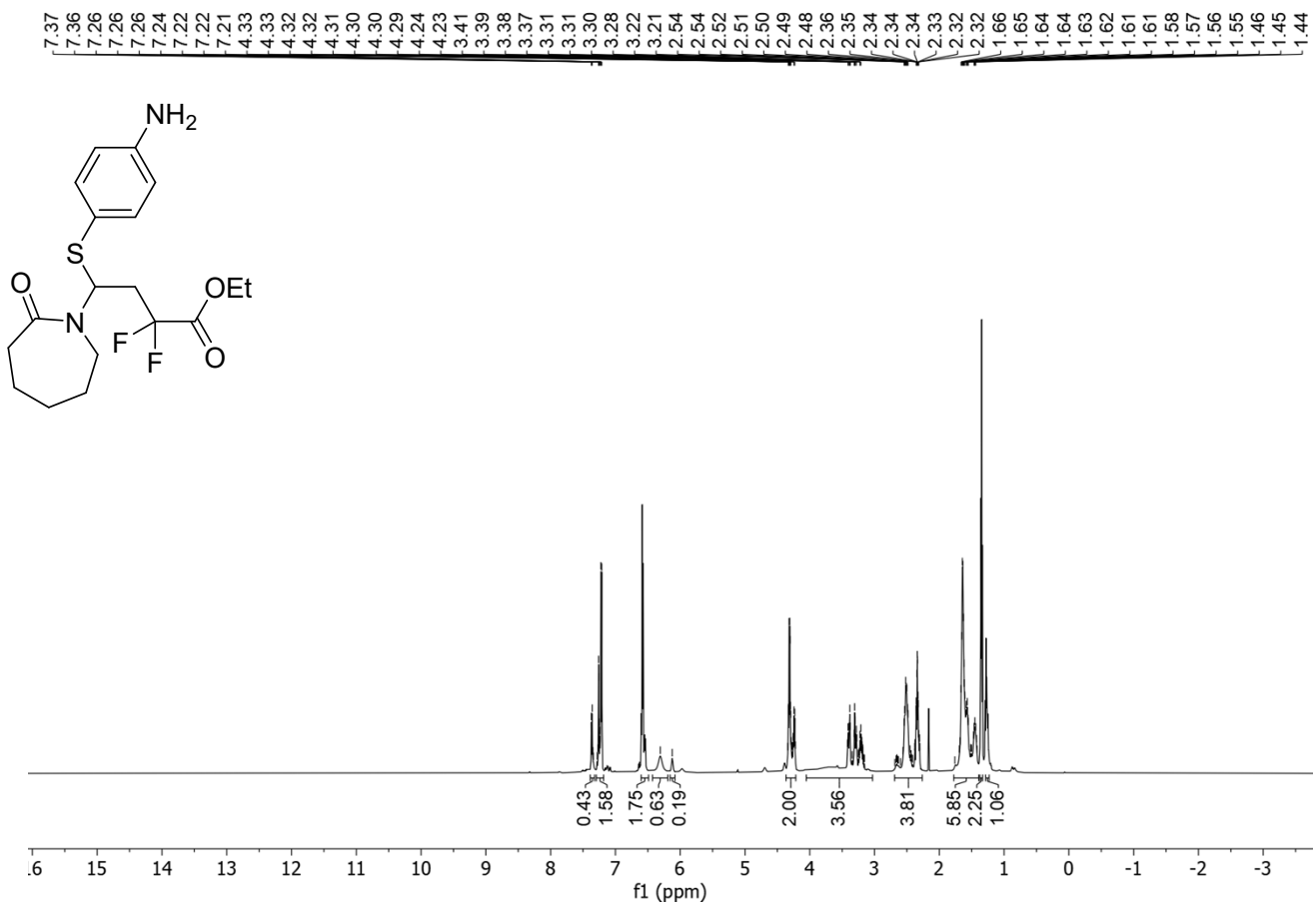
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4f**.



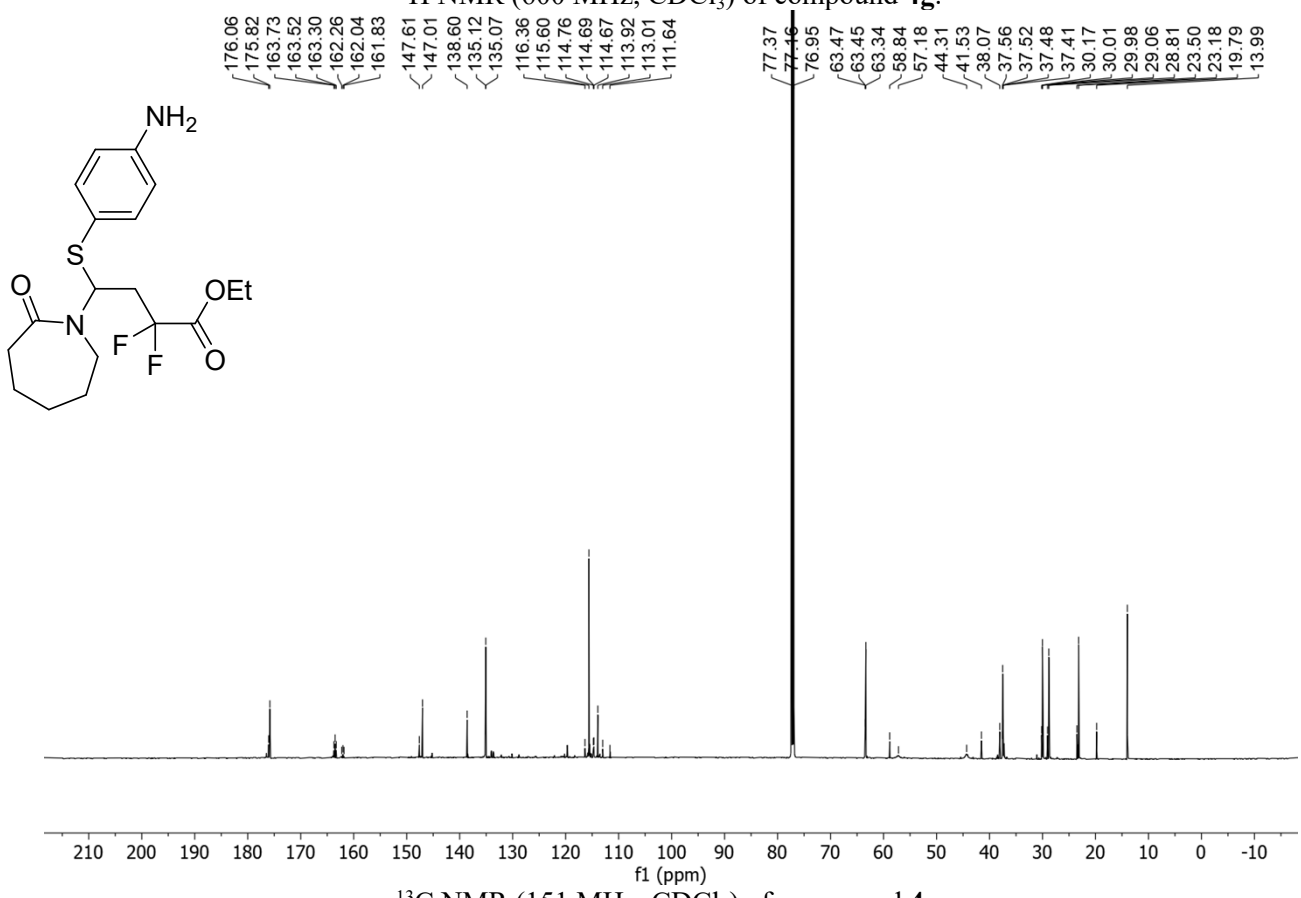
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4f**.



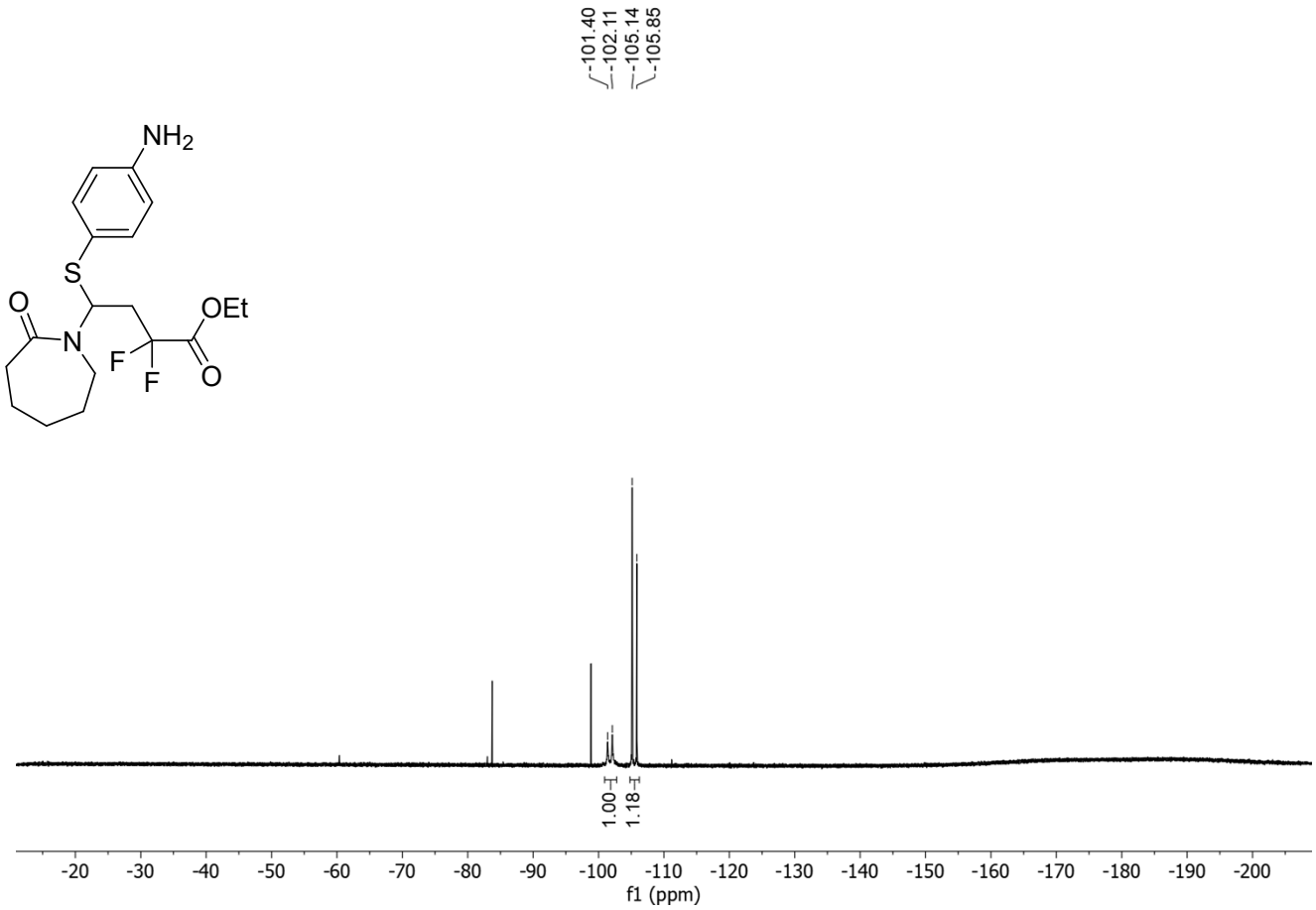
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4f.**



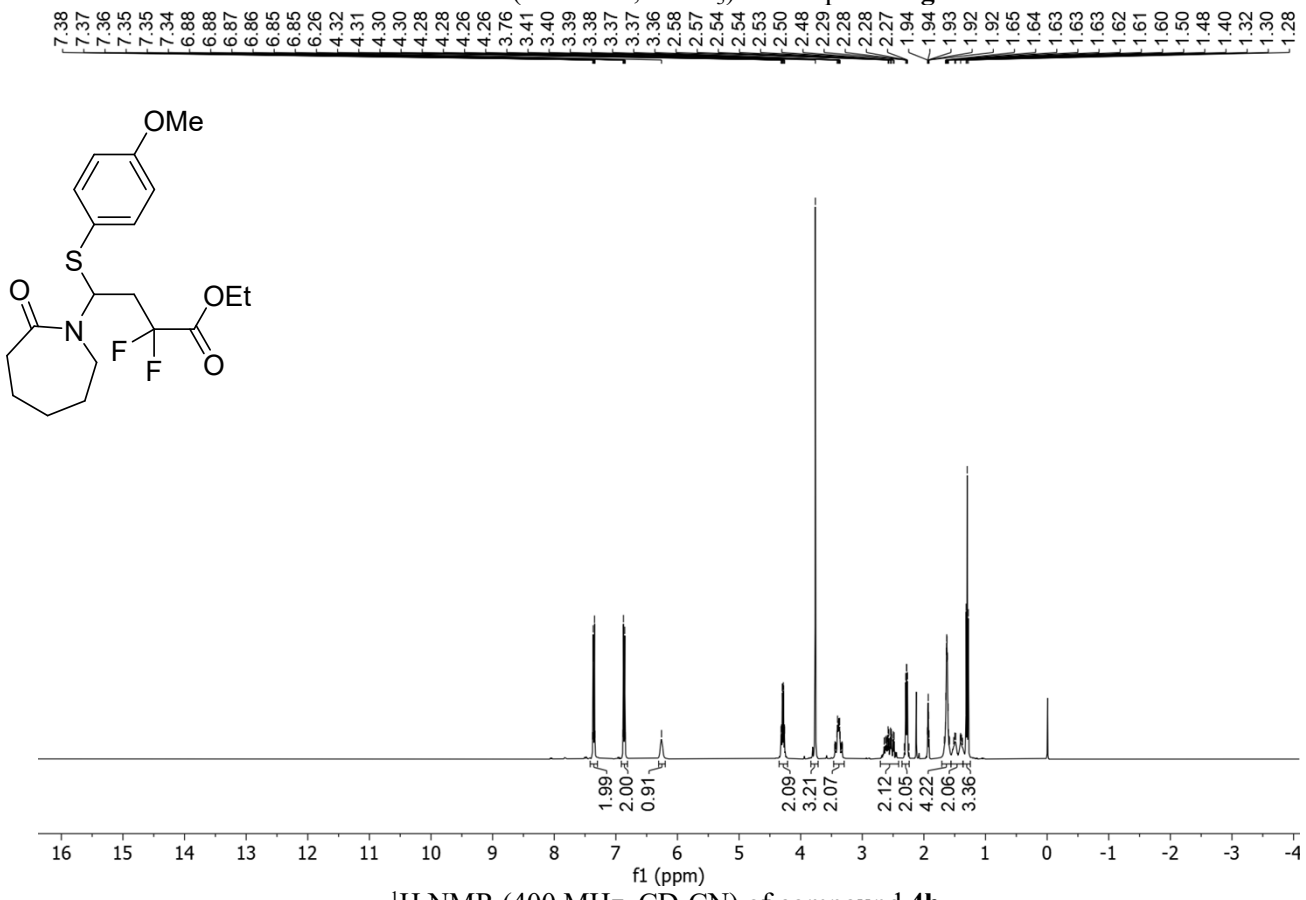
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4g**.



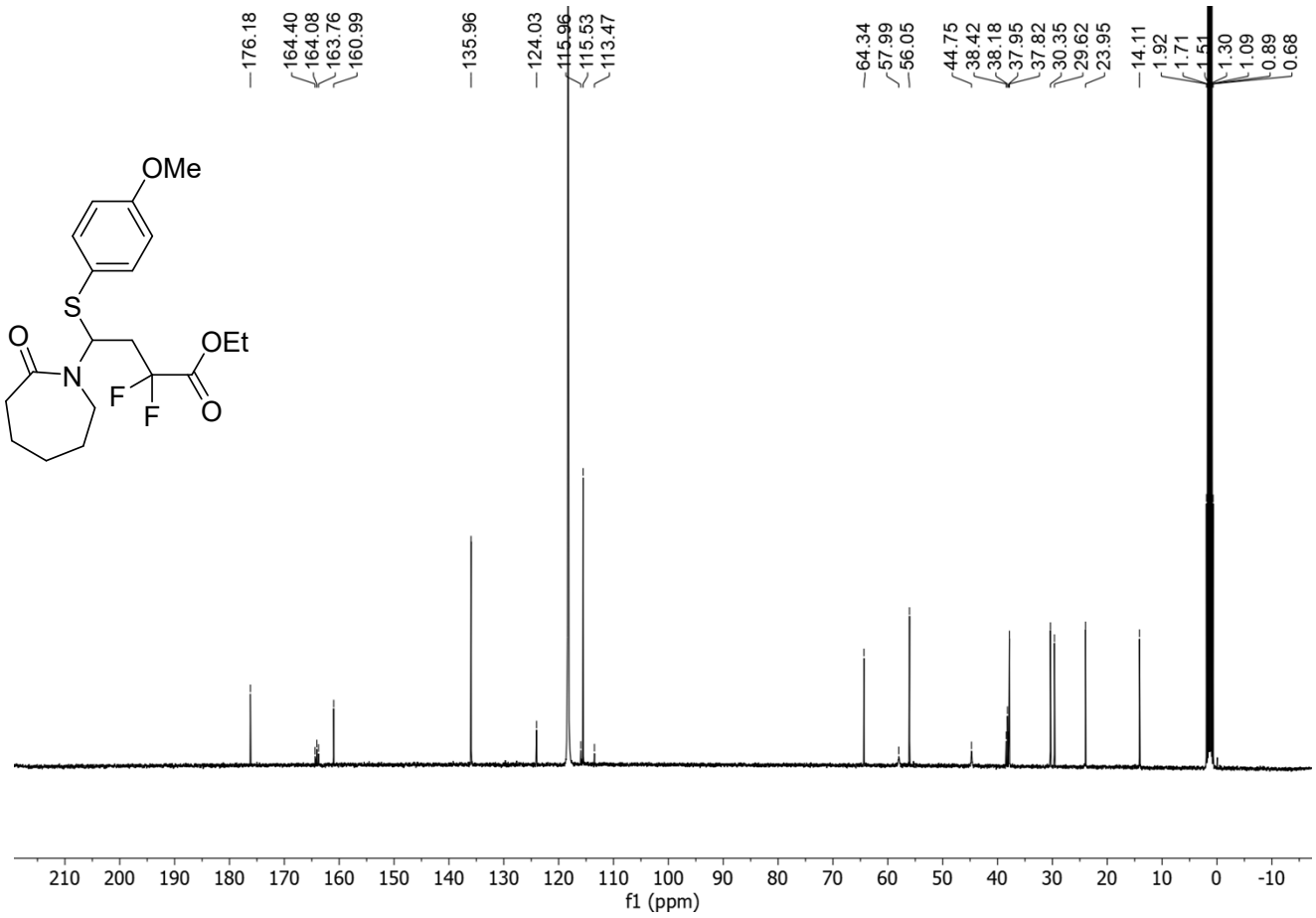
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4g.**



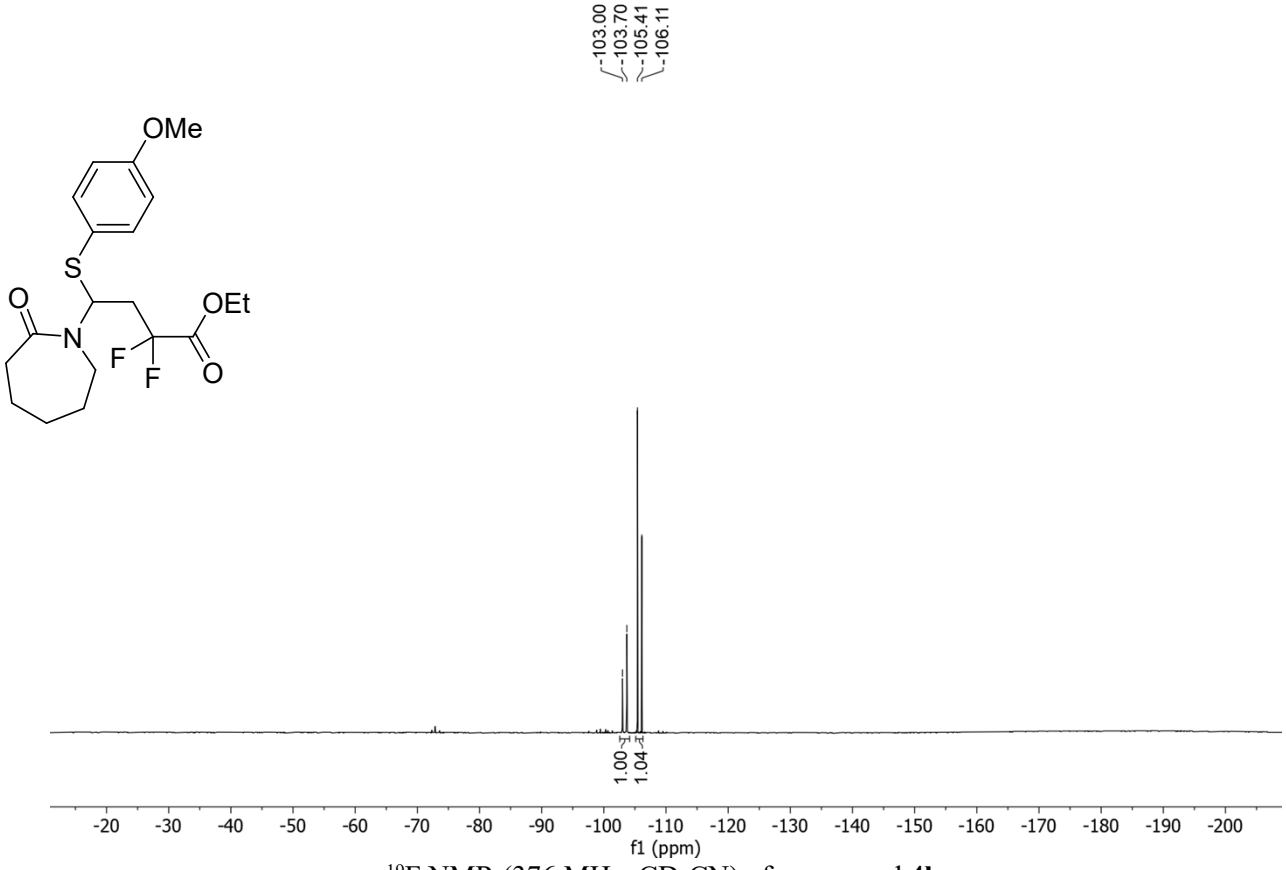
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4g**.



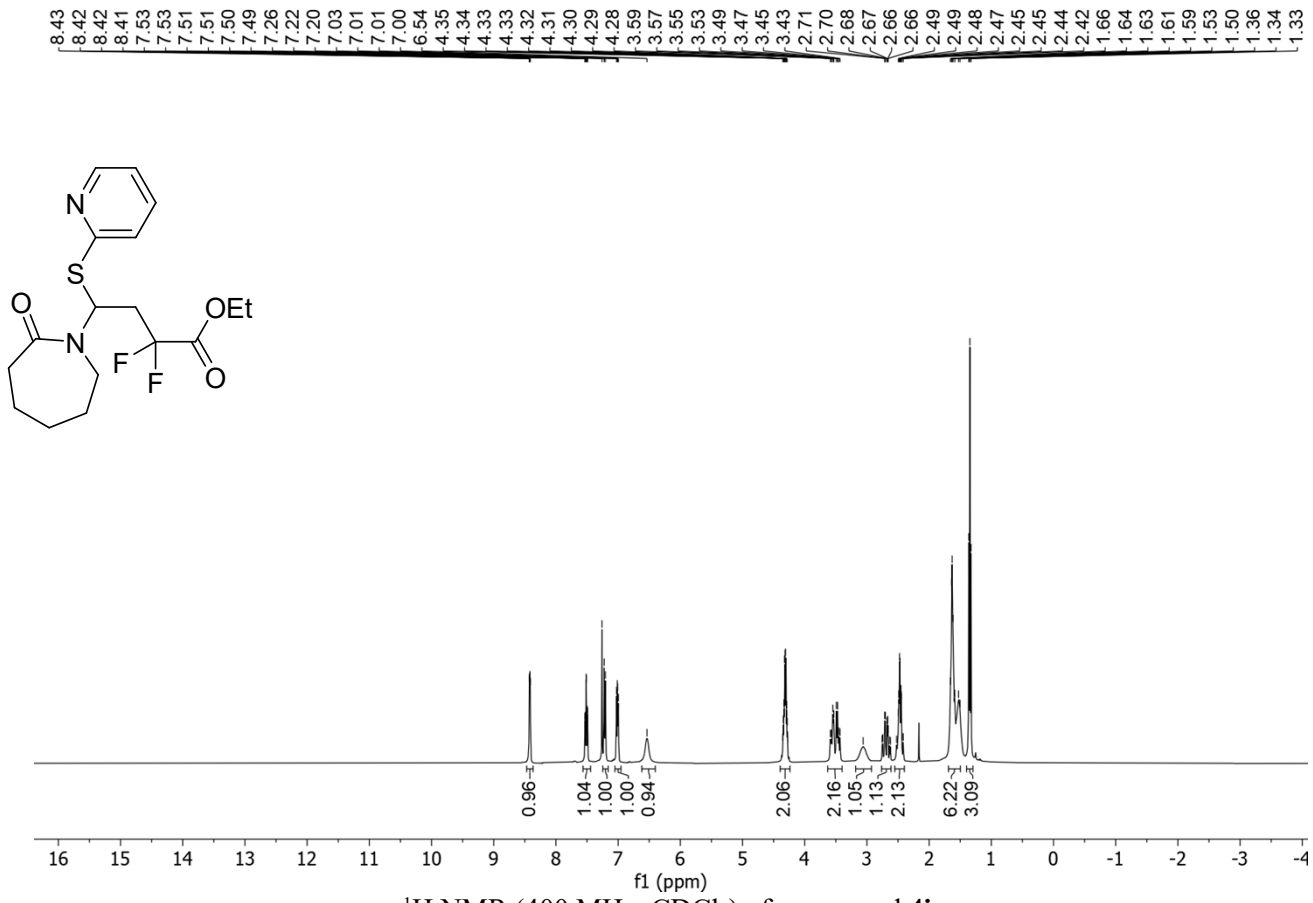
^{1}H NMR (400 MHz, CD_3CN) of compound **4h**.



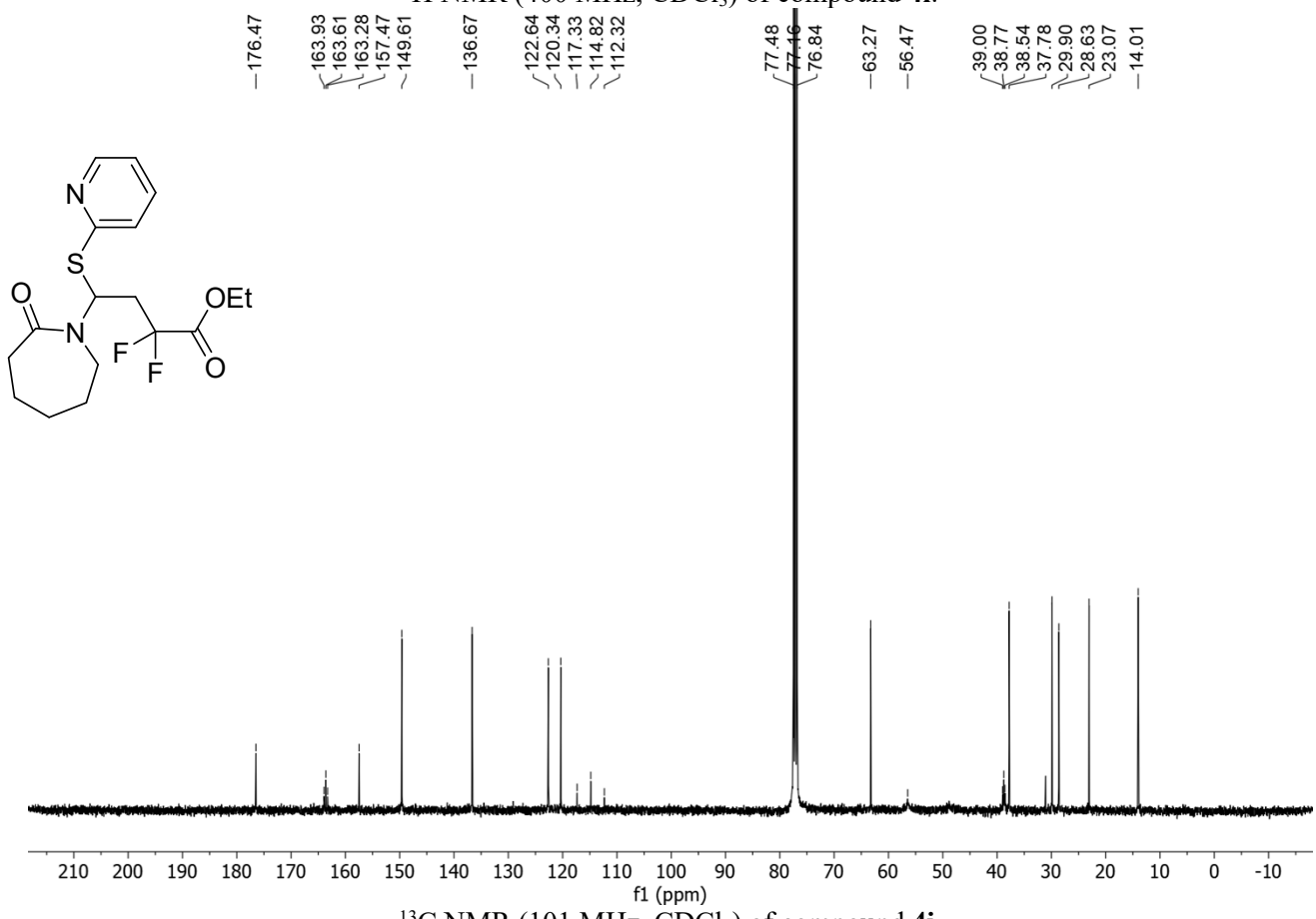
^{13}C NMR (101 MHz, CD_3CN) of compound **4h**.



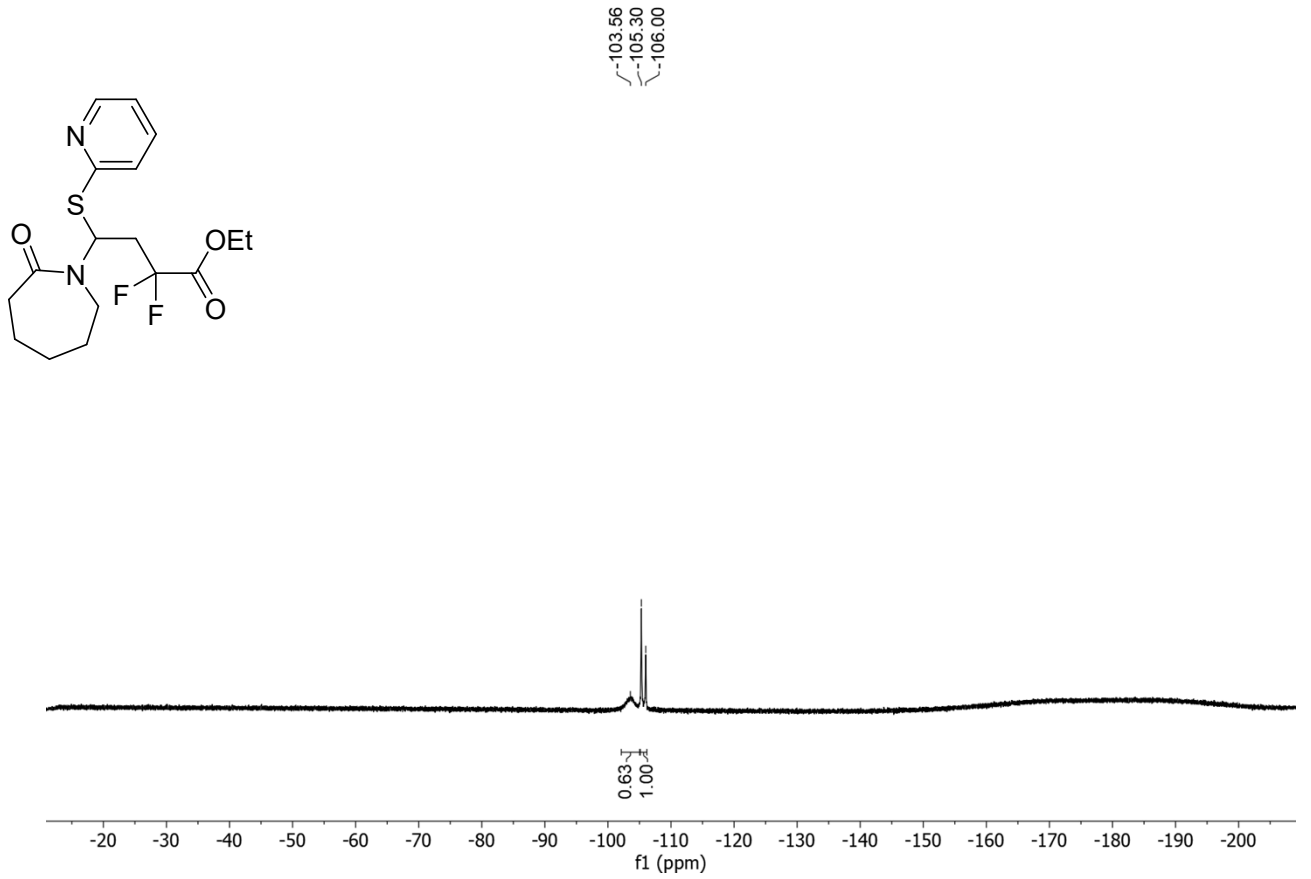
^{19}F NMR (376 MHz, CD_3CN) of compound **4h**.



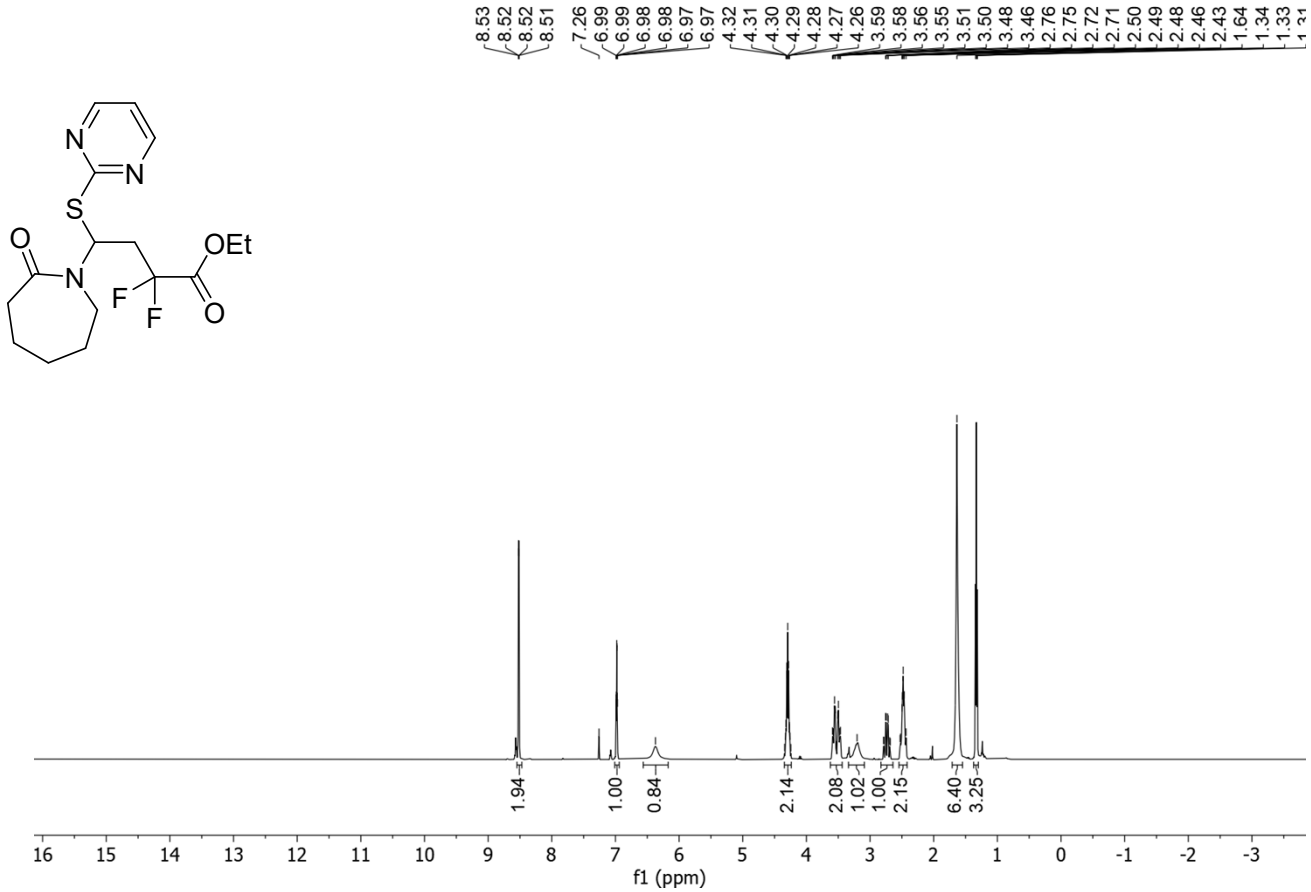
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4i**.



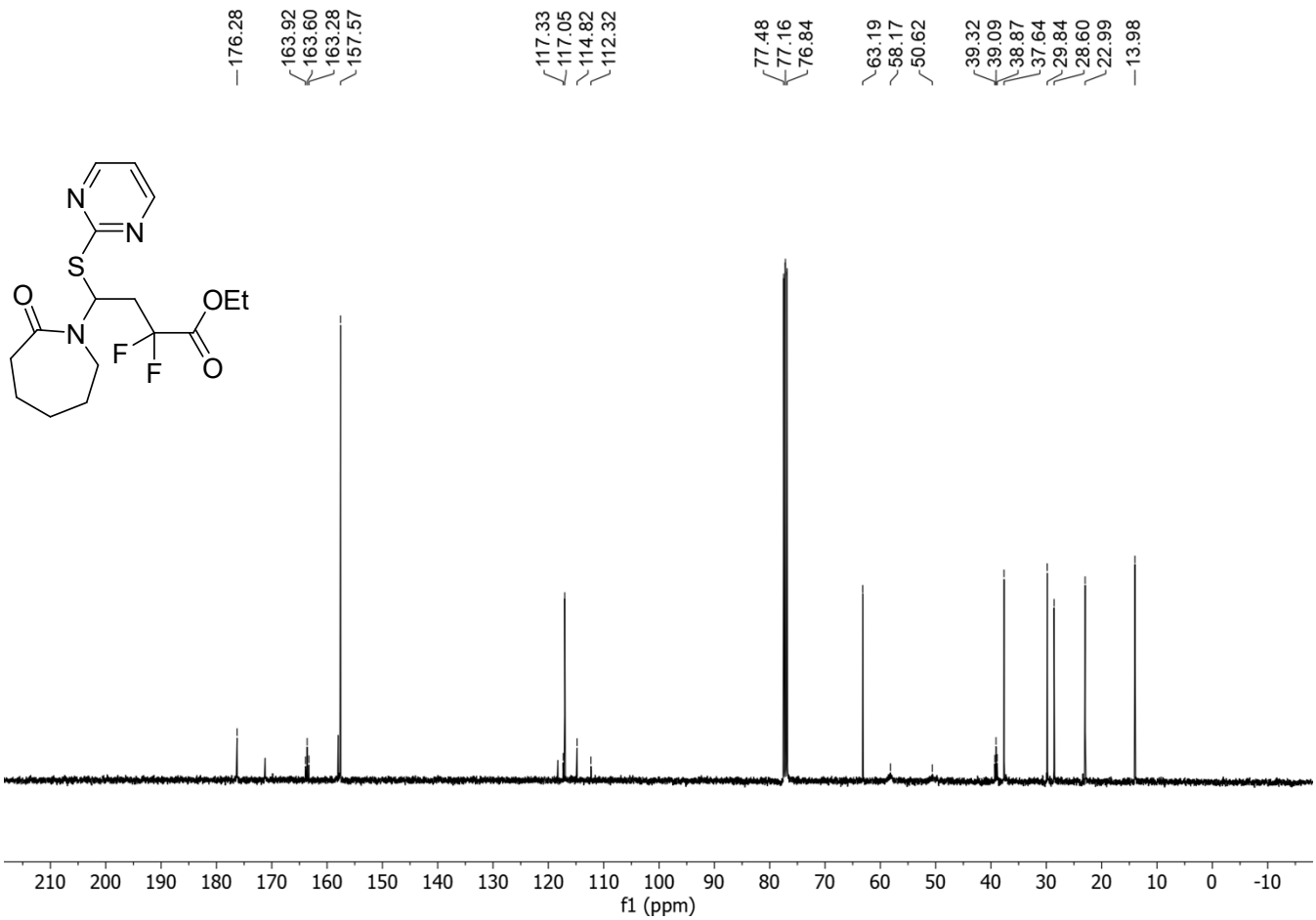
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4i**.



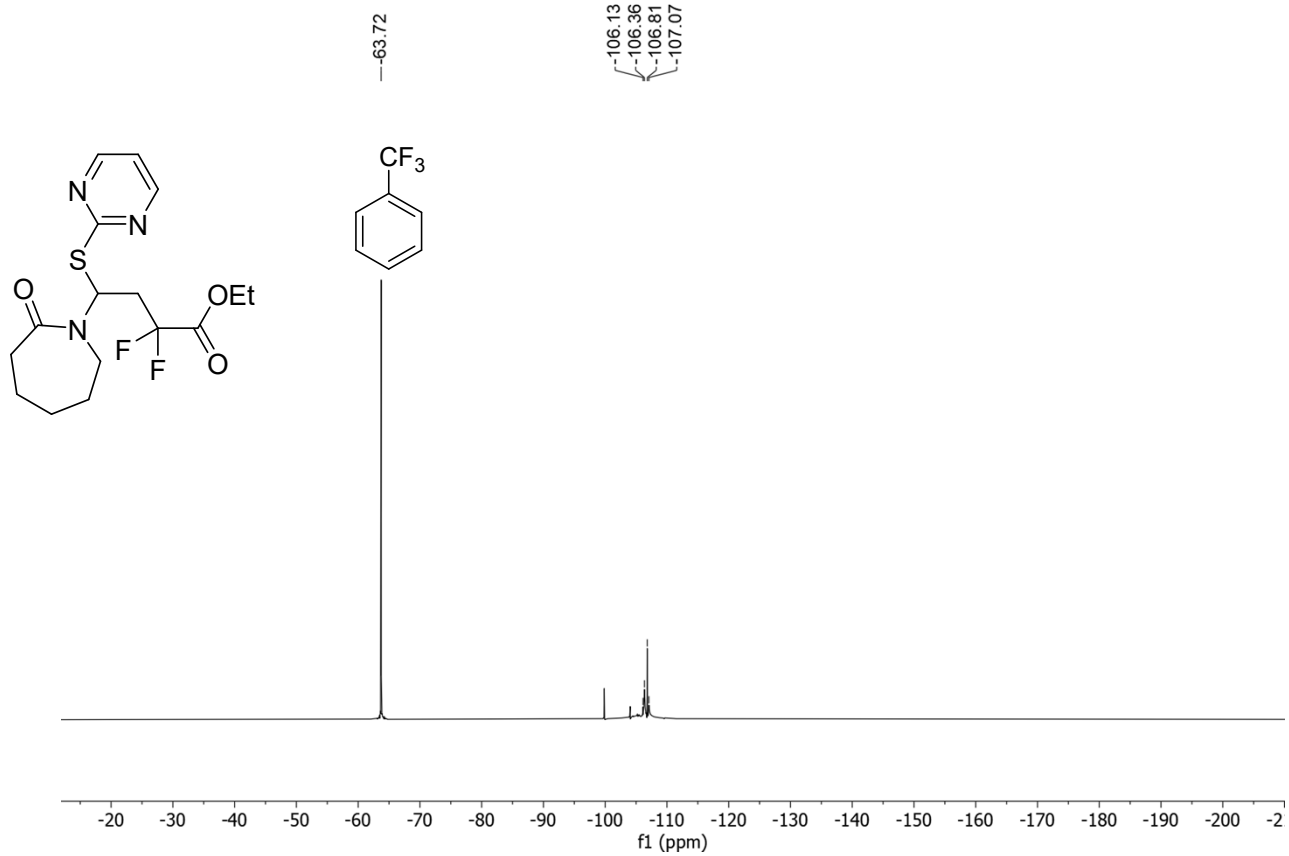
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4i**.



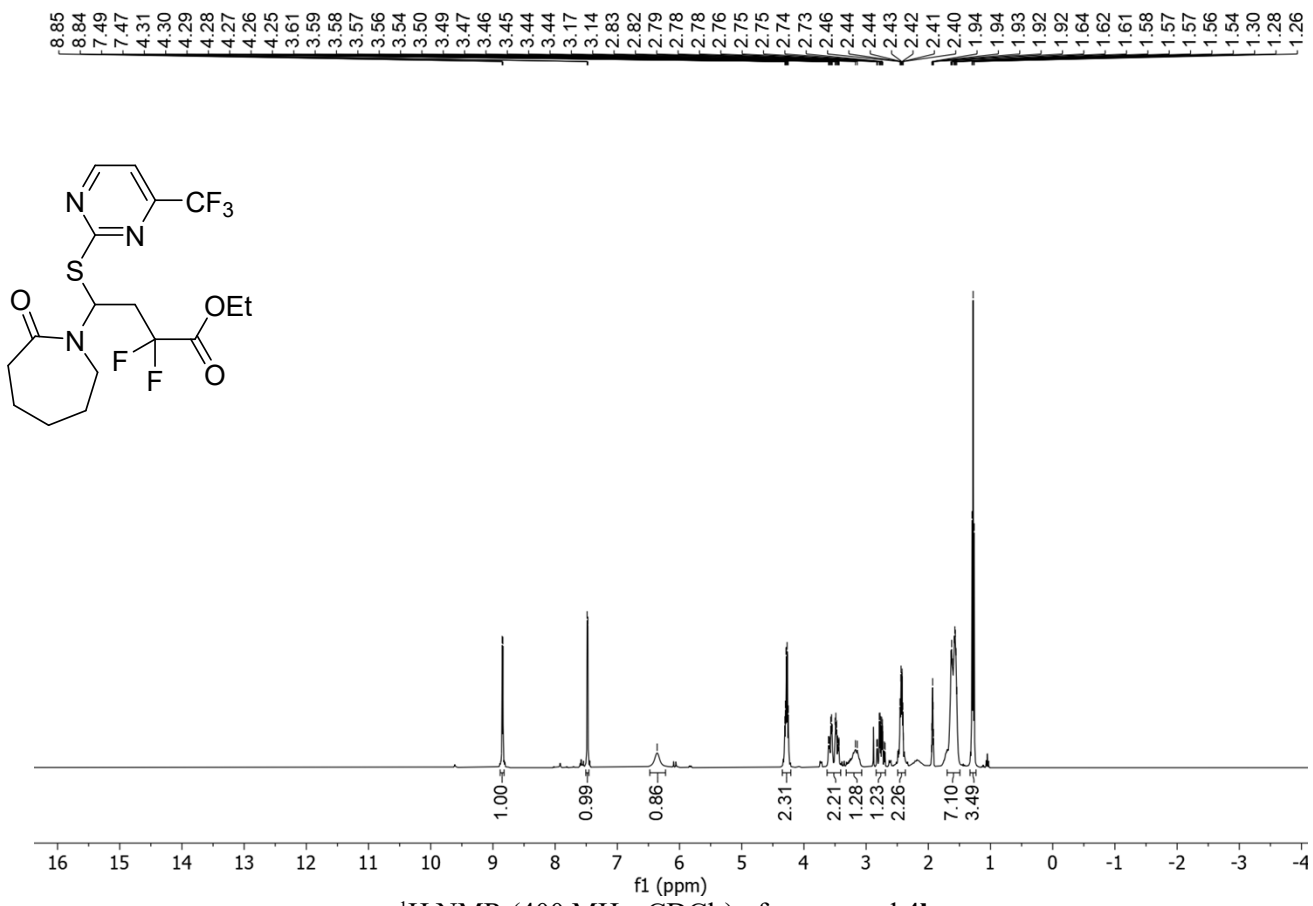
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4j**.



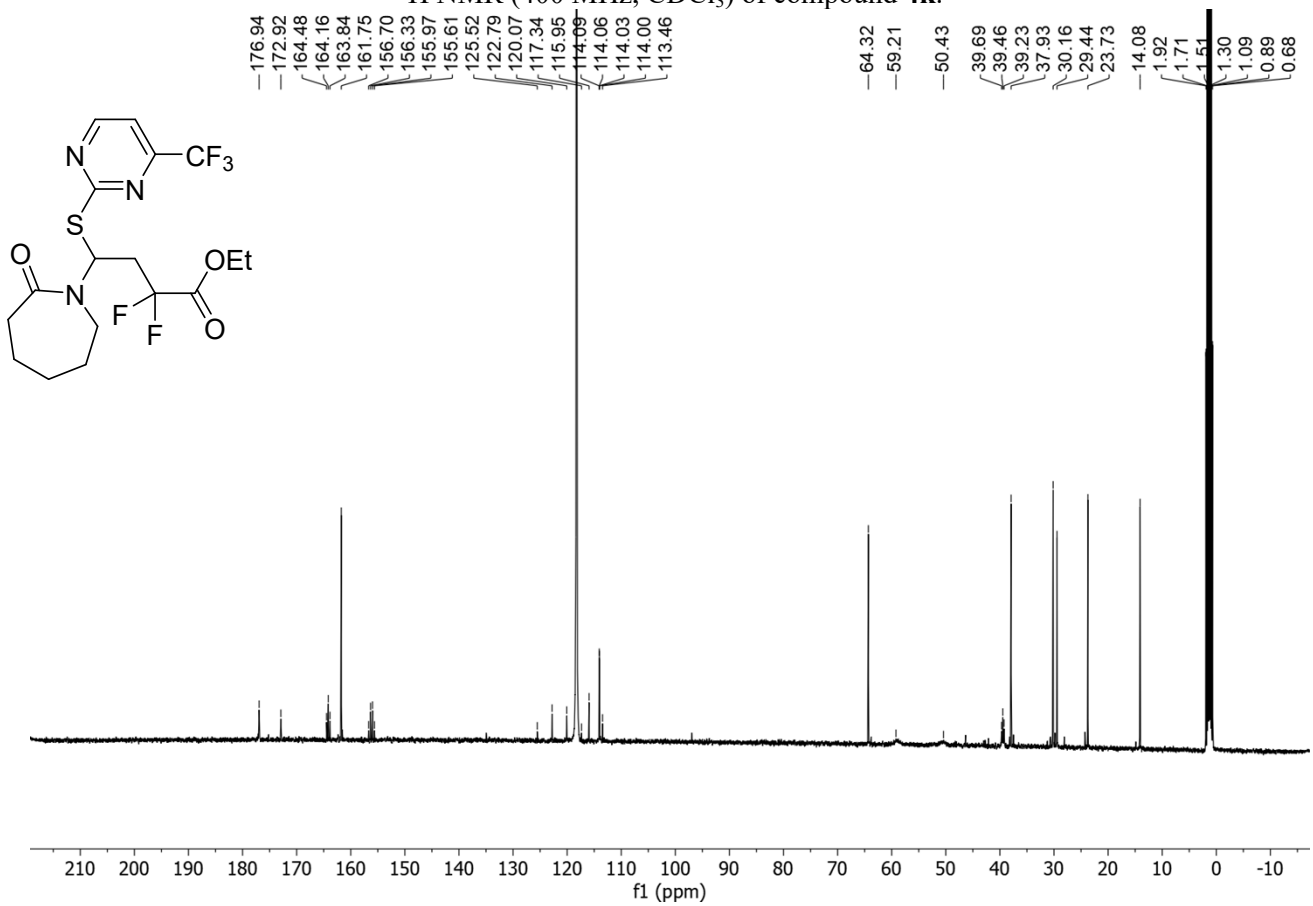
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4j**.



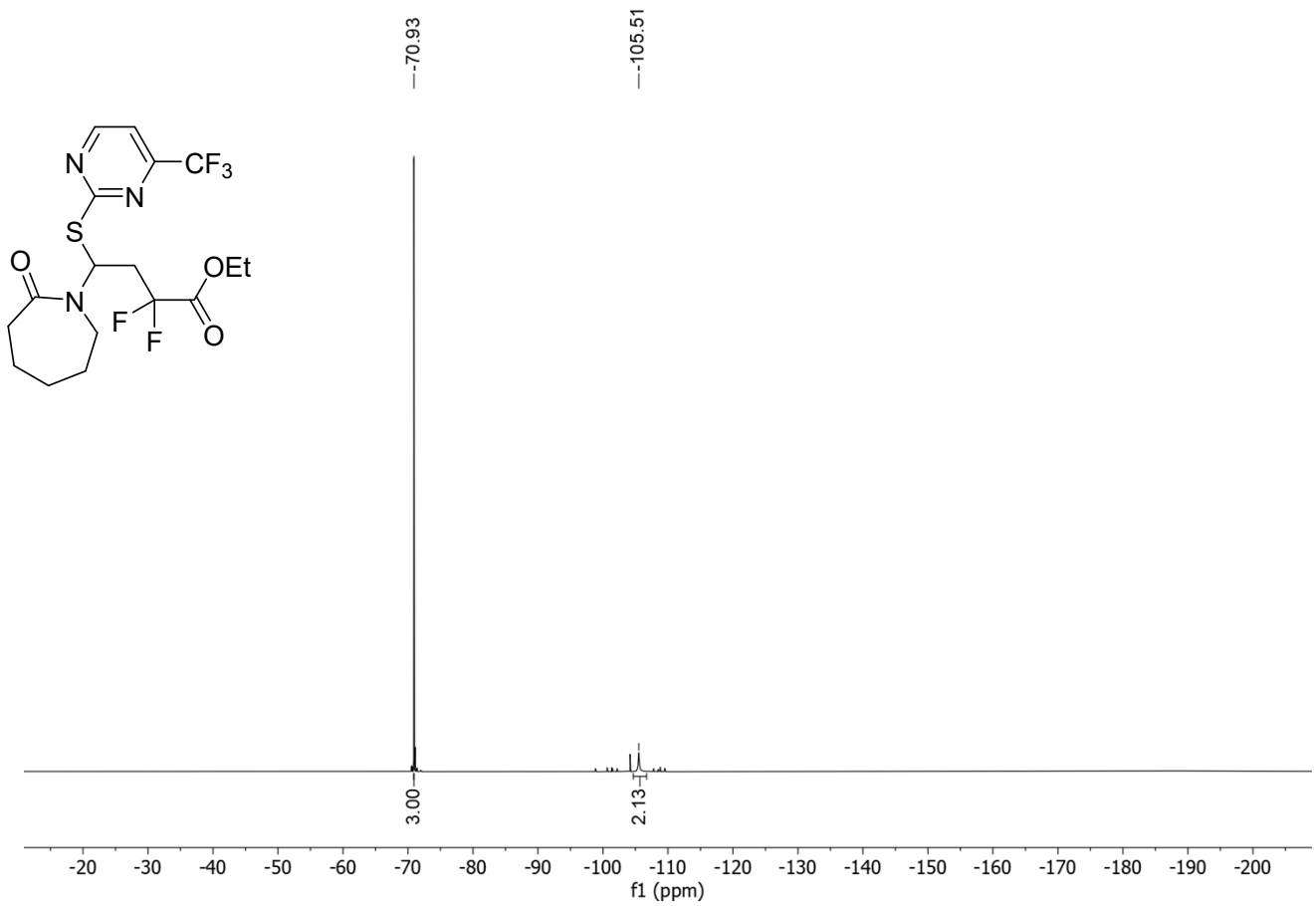
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4j**.



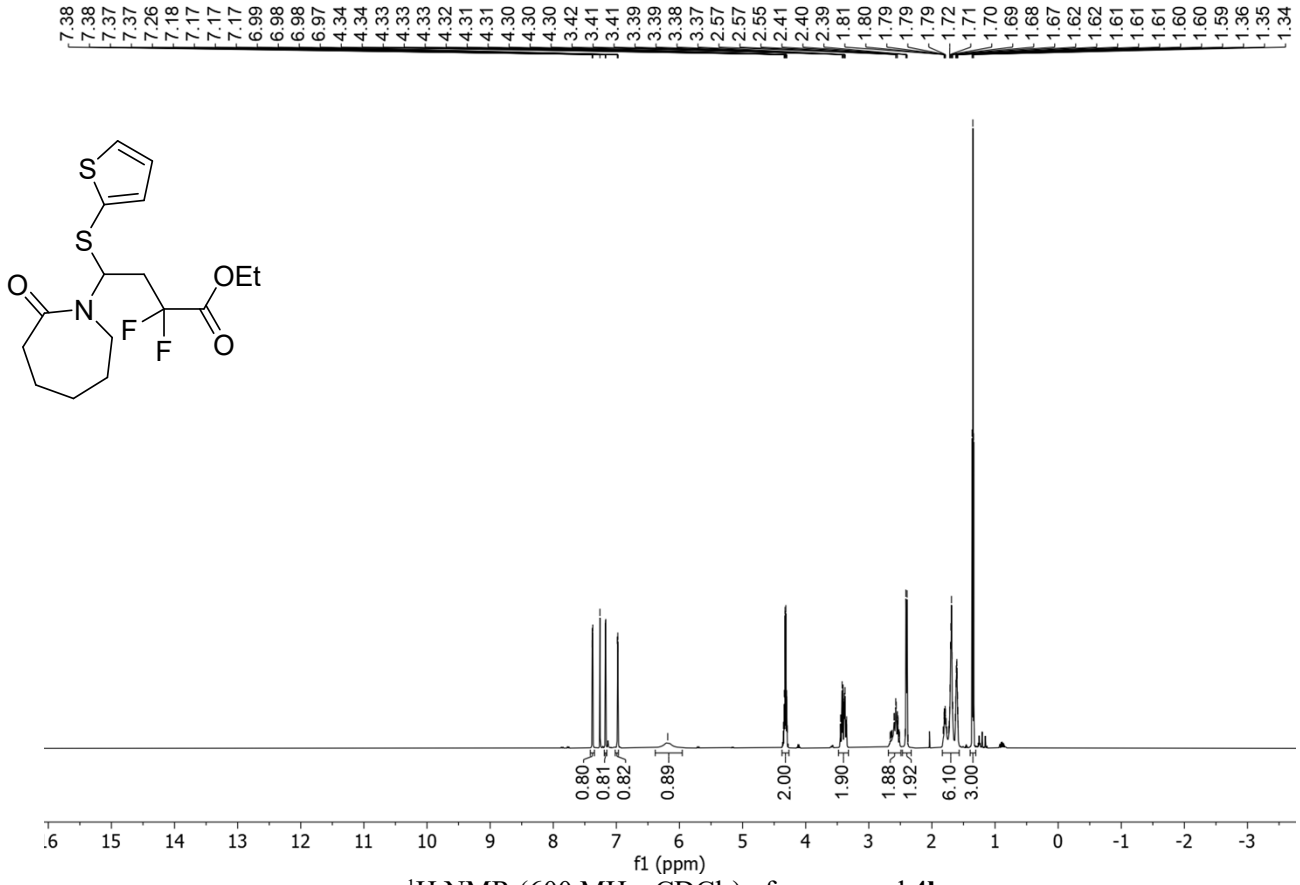
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4k**.



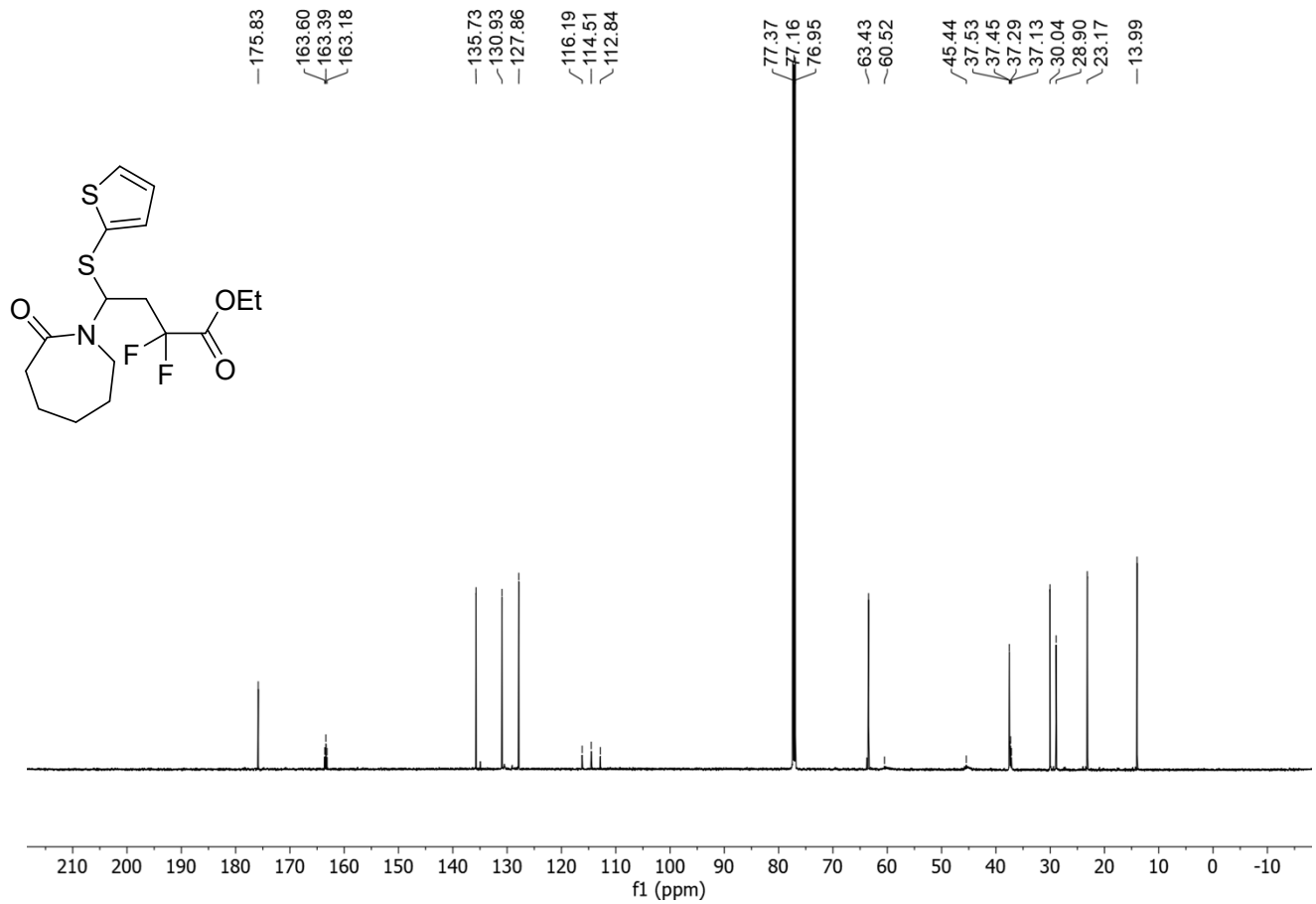
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4k**.



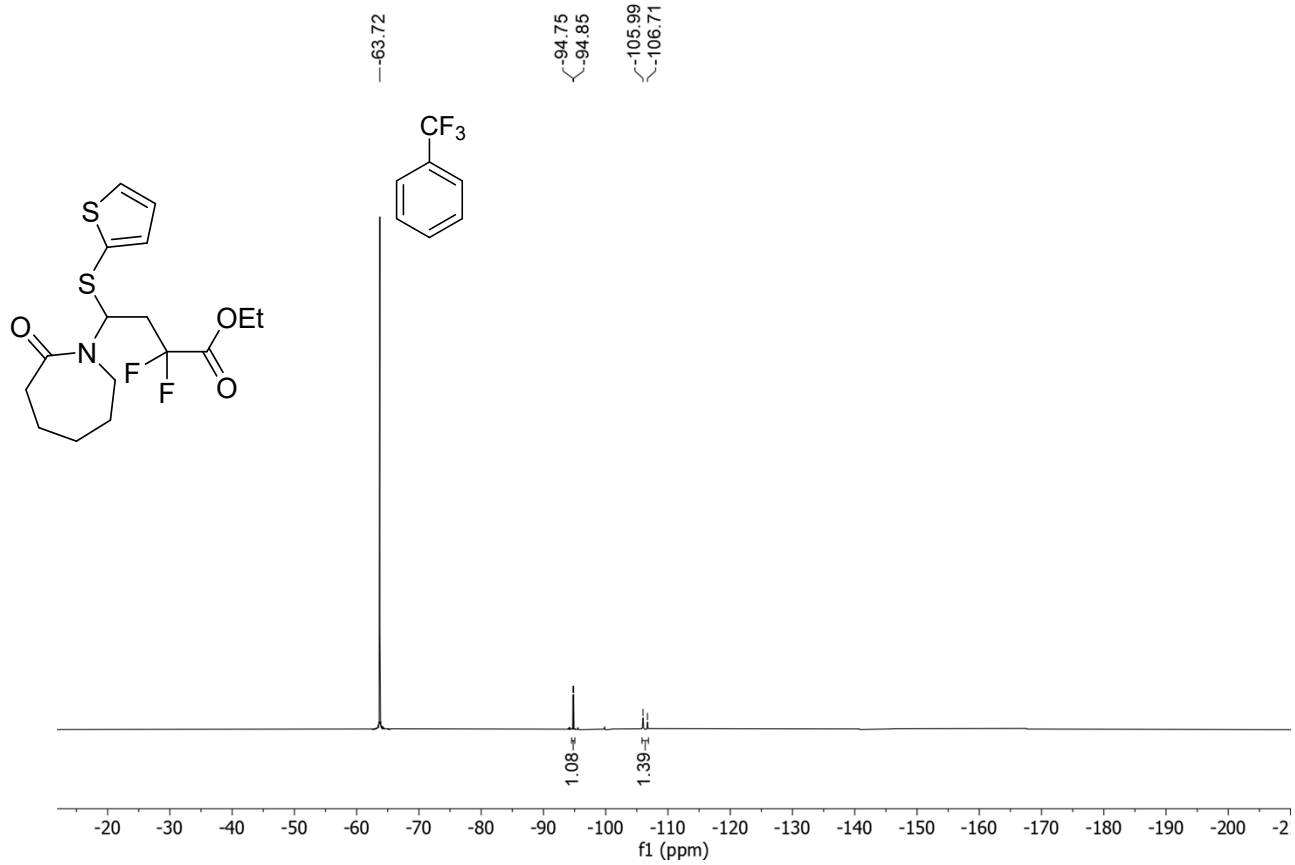
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4k**.



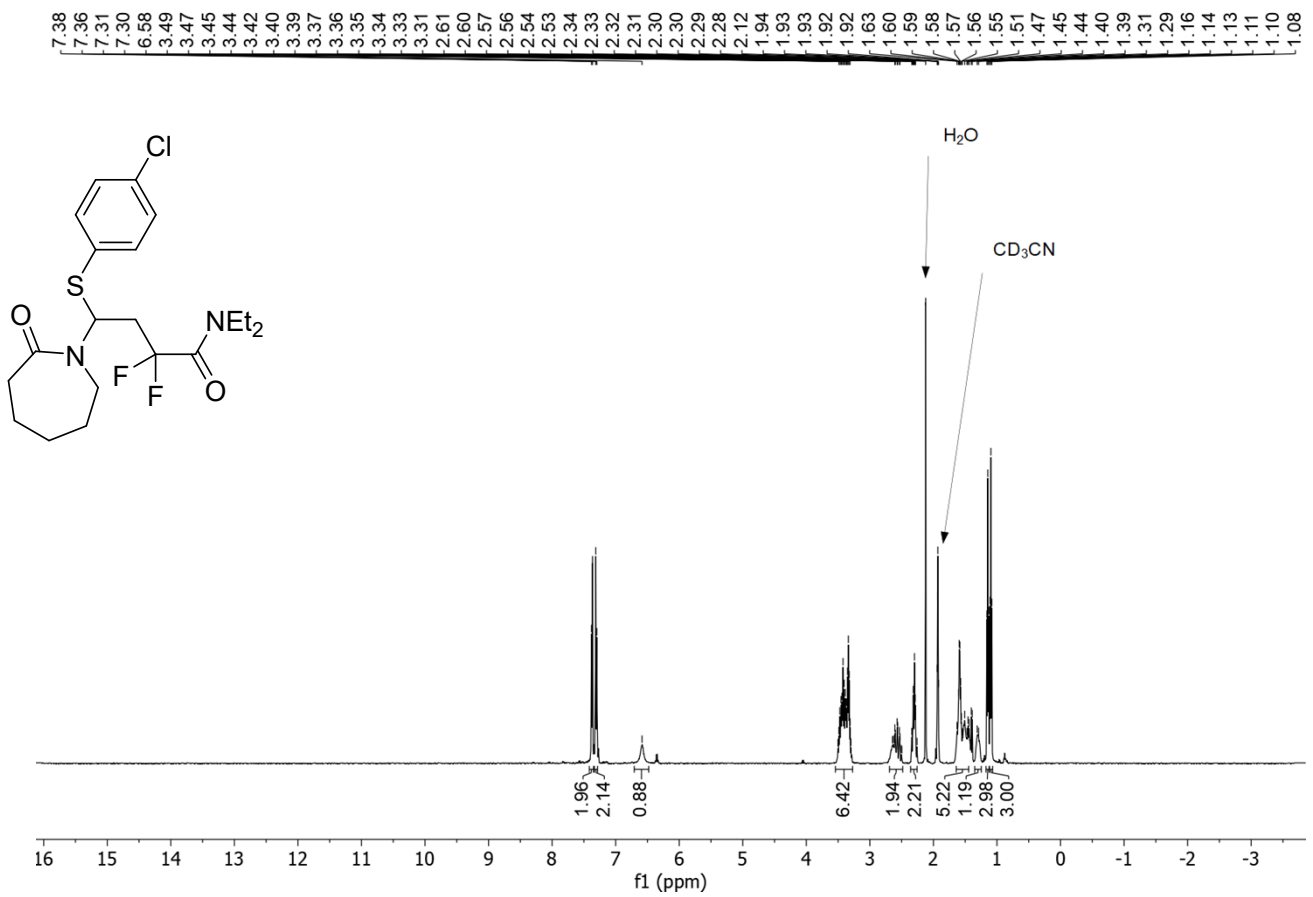
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4l**.



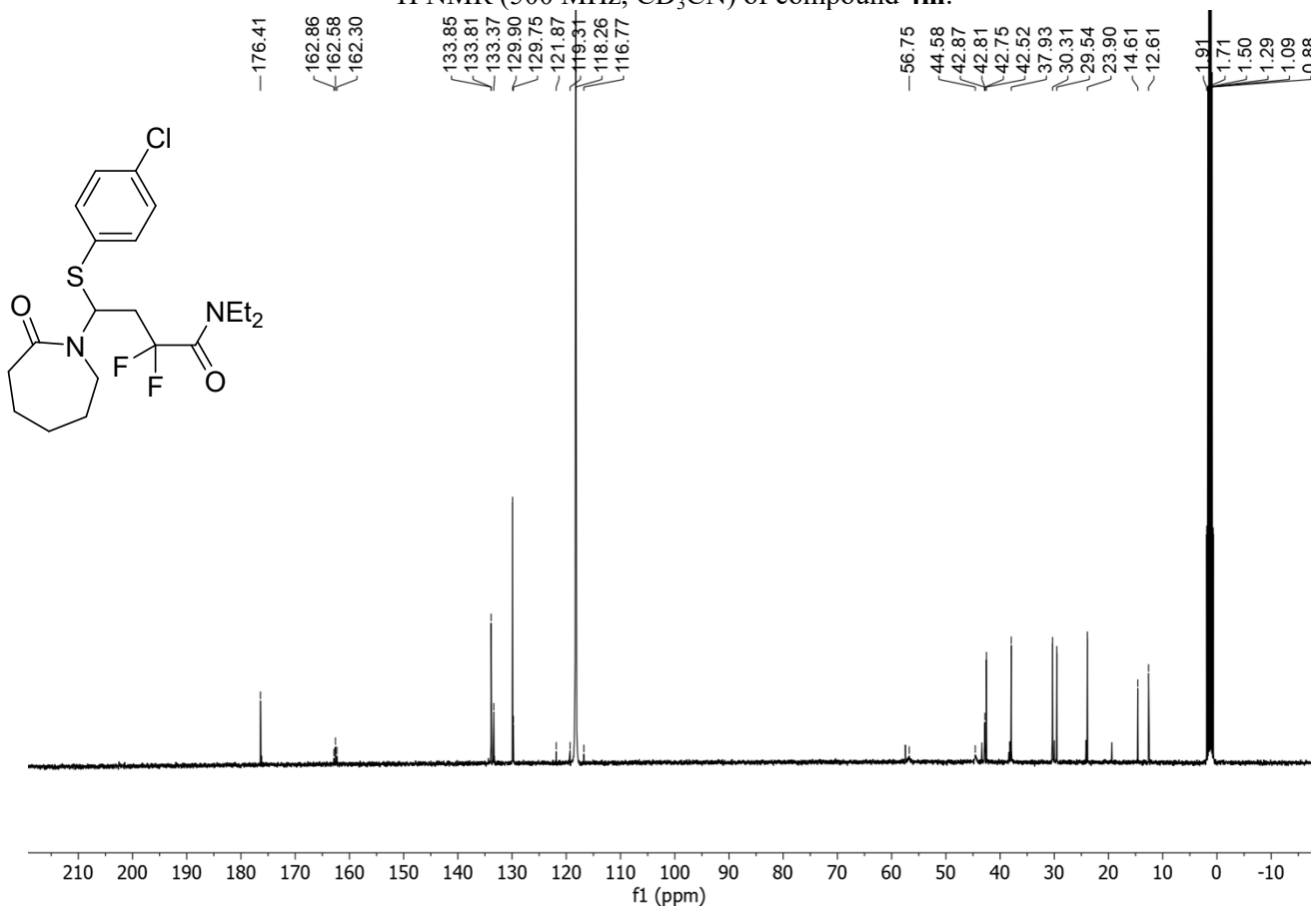
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4l**.



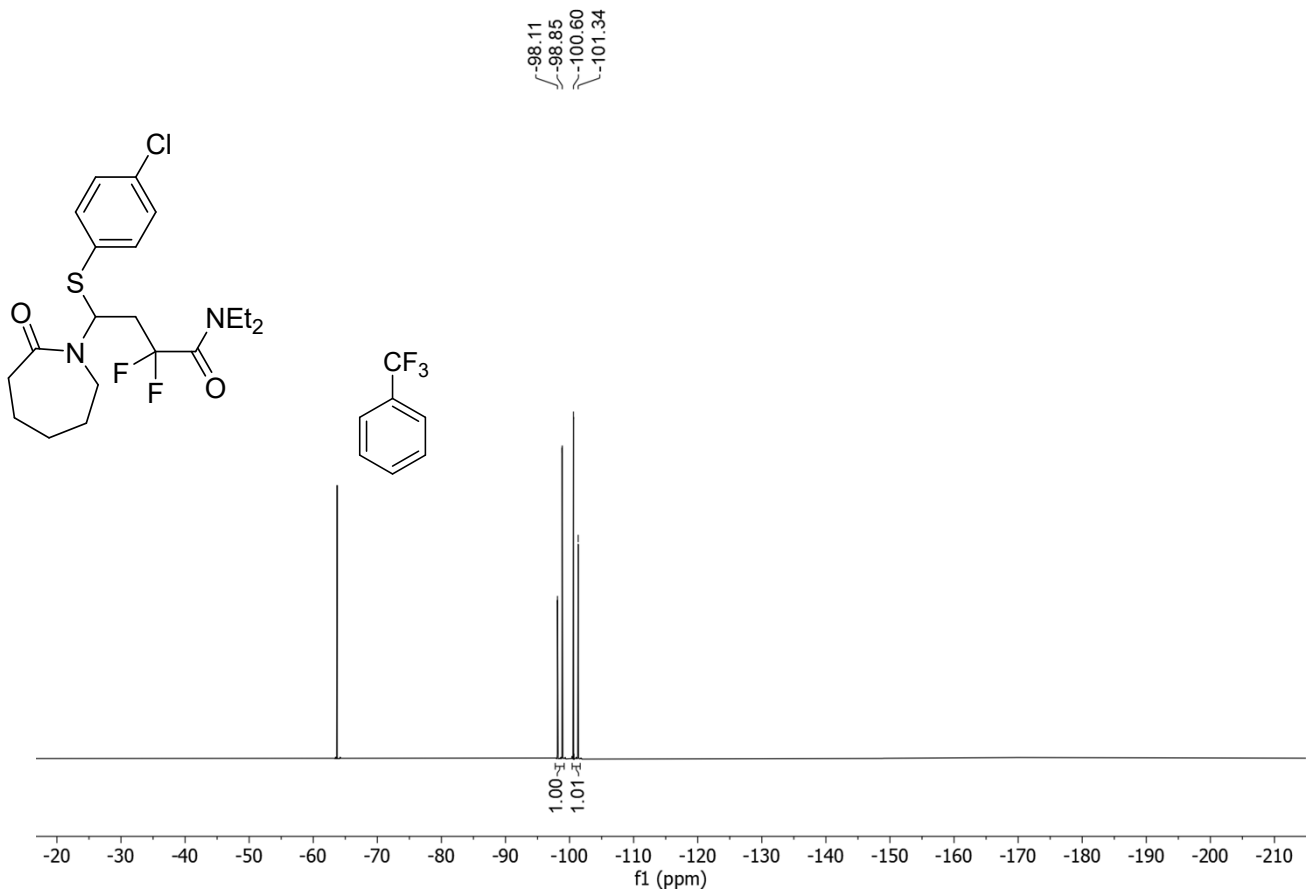
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4l**.



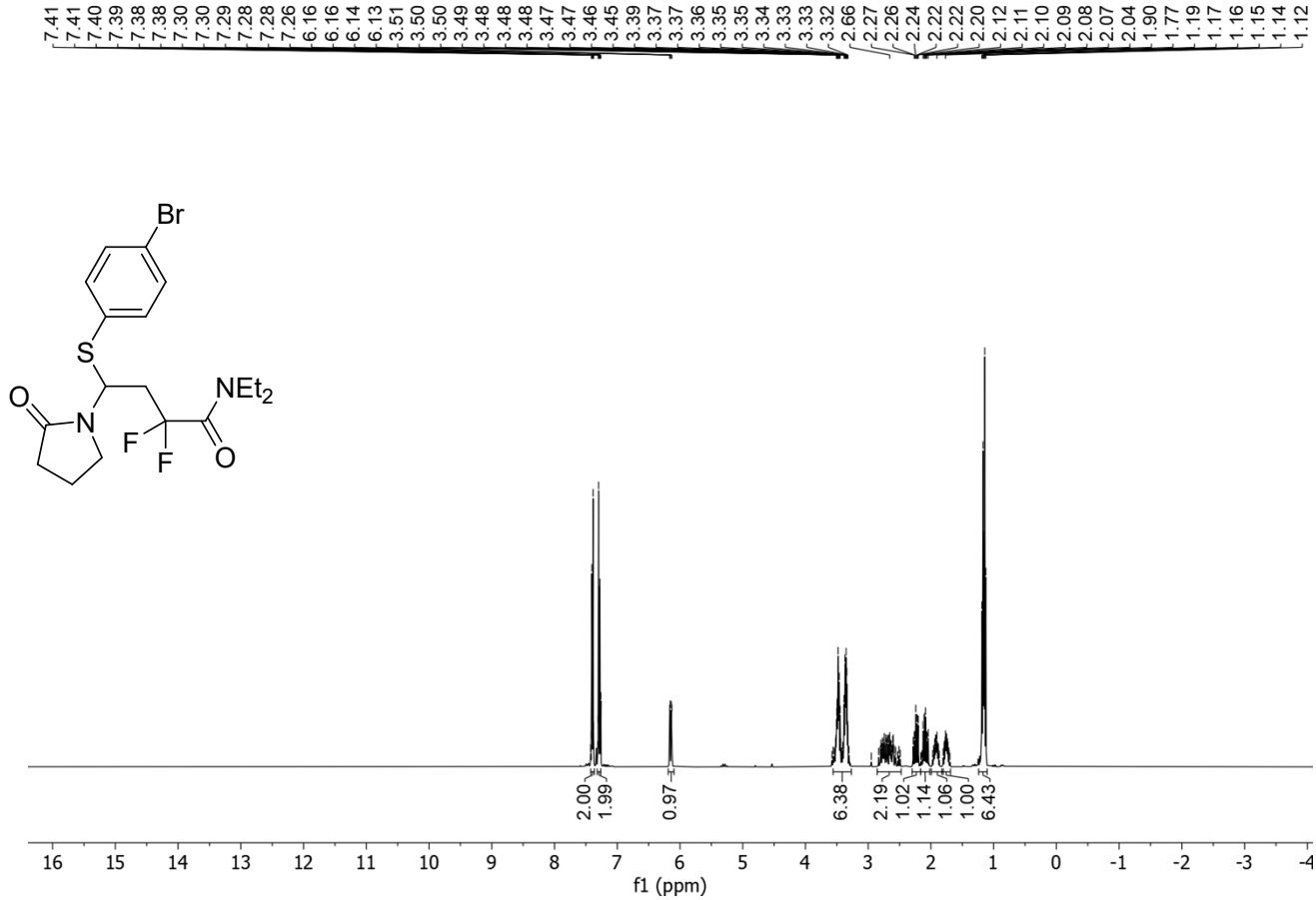
^{1}H NMR (500 MHz, CD_3CN) of compound **4m**.



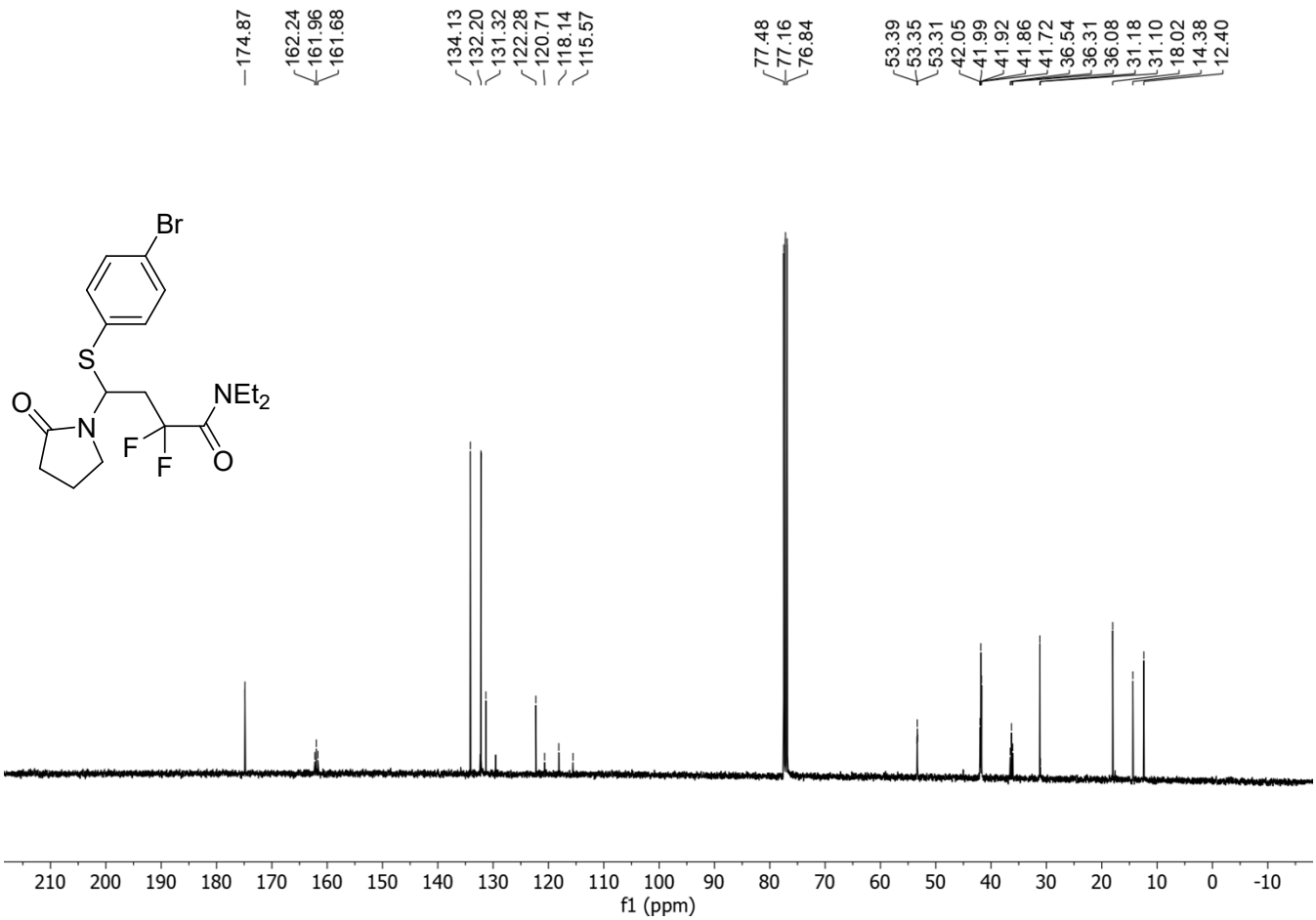
^{13}C NMR (101 MHz, CD_3CN) of compound **4m**.



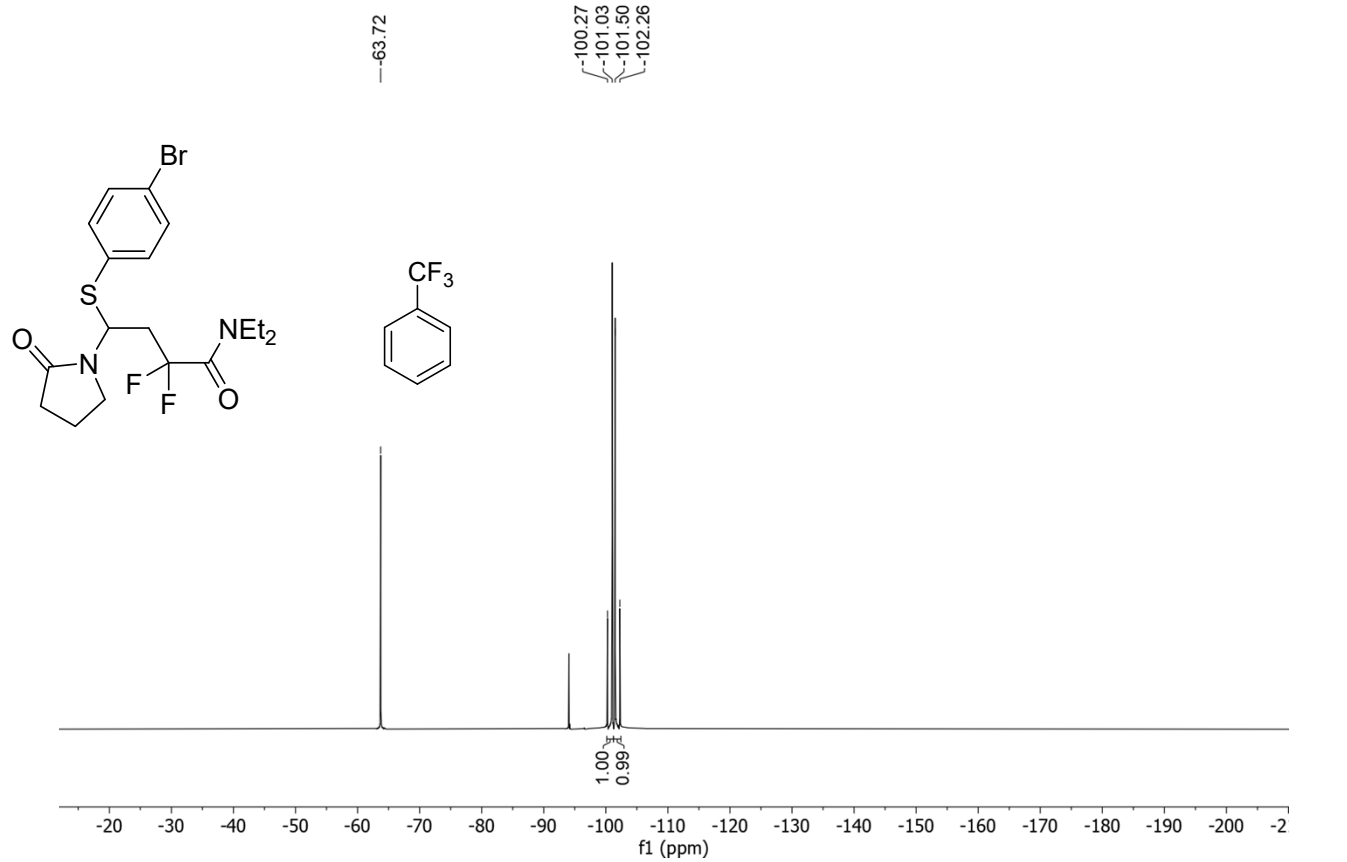
^{19}F NMR (376 MHz, CD_3CN) of compound **4m**.



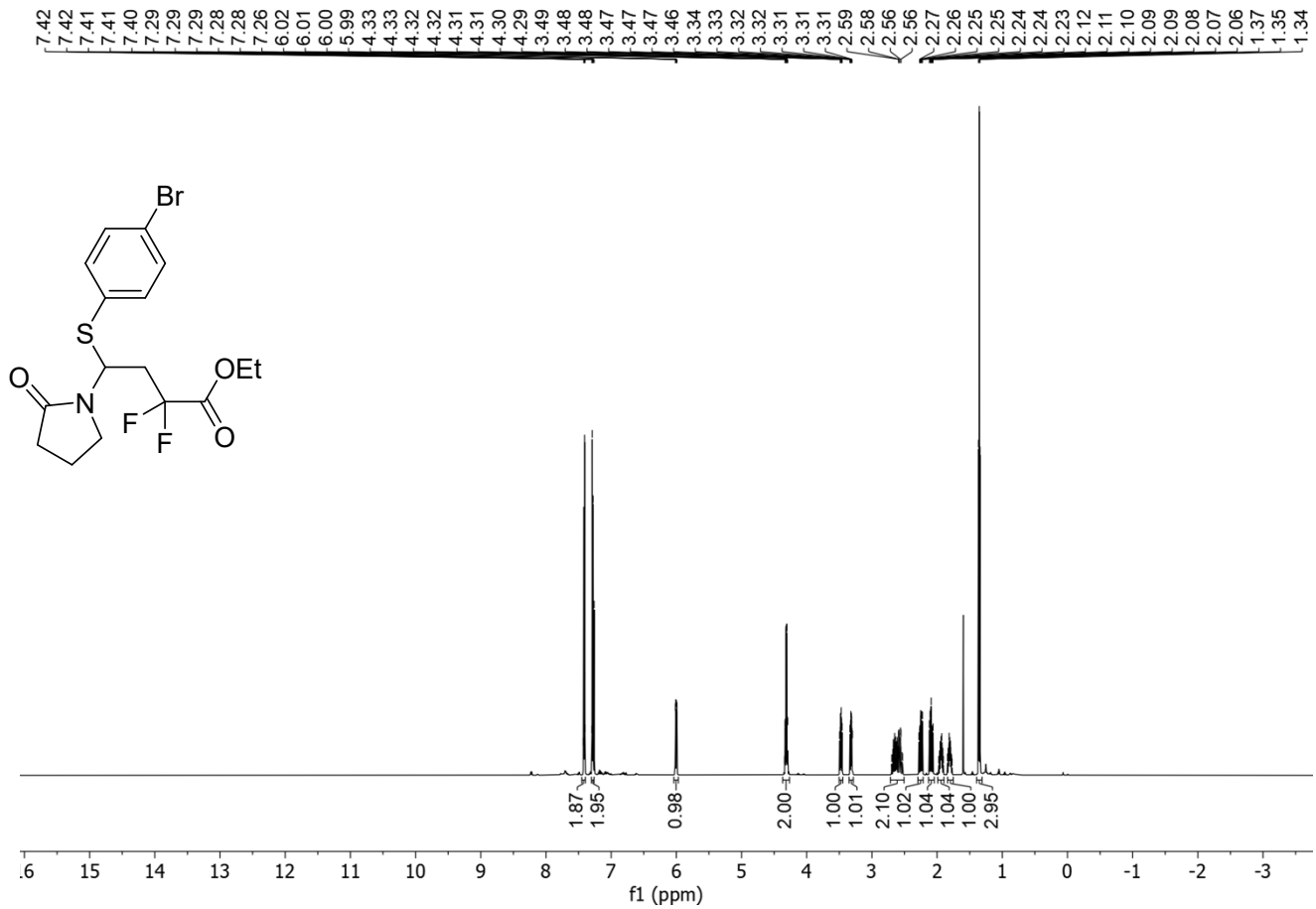
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4n**.



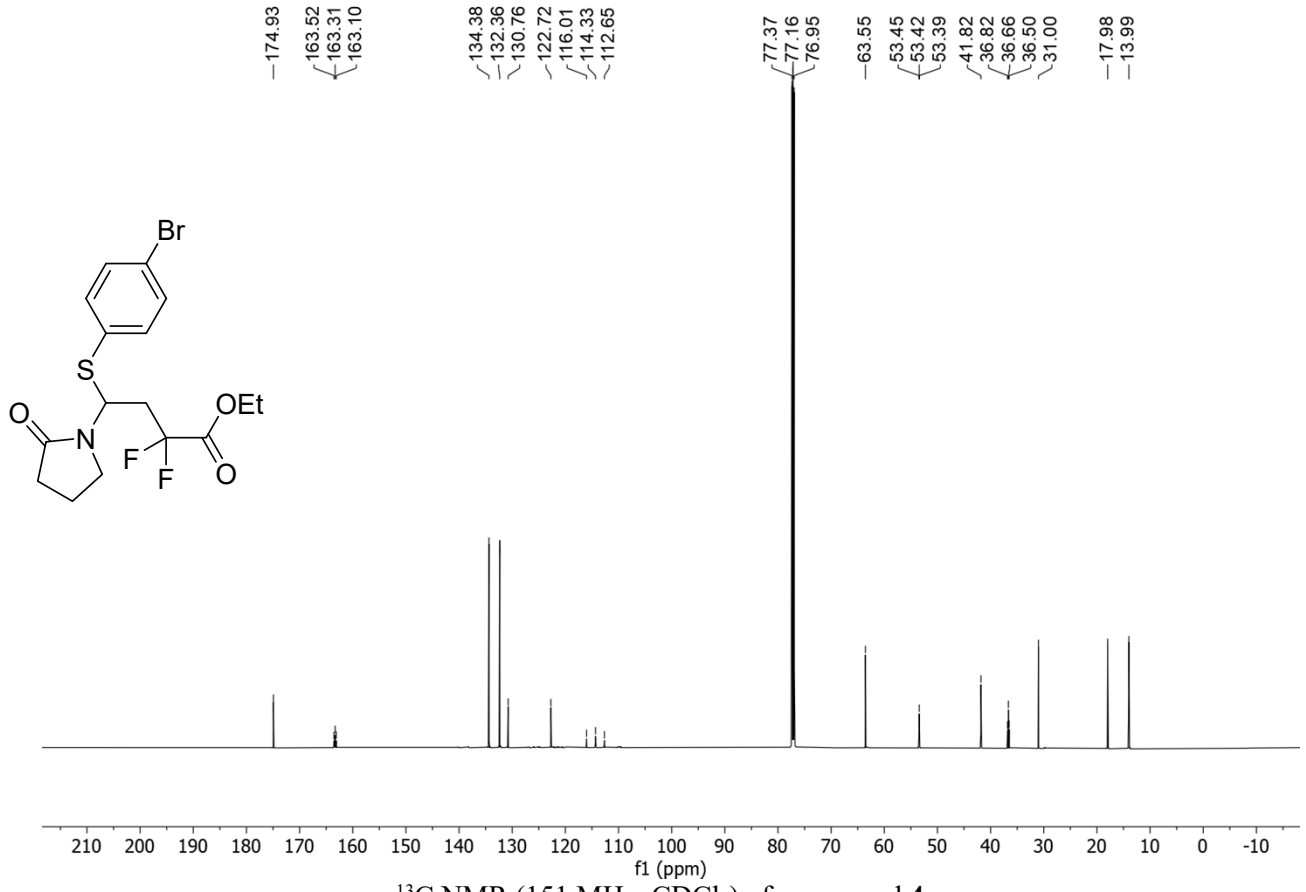
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4n**.



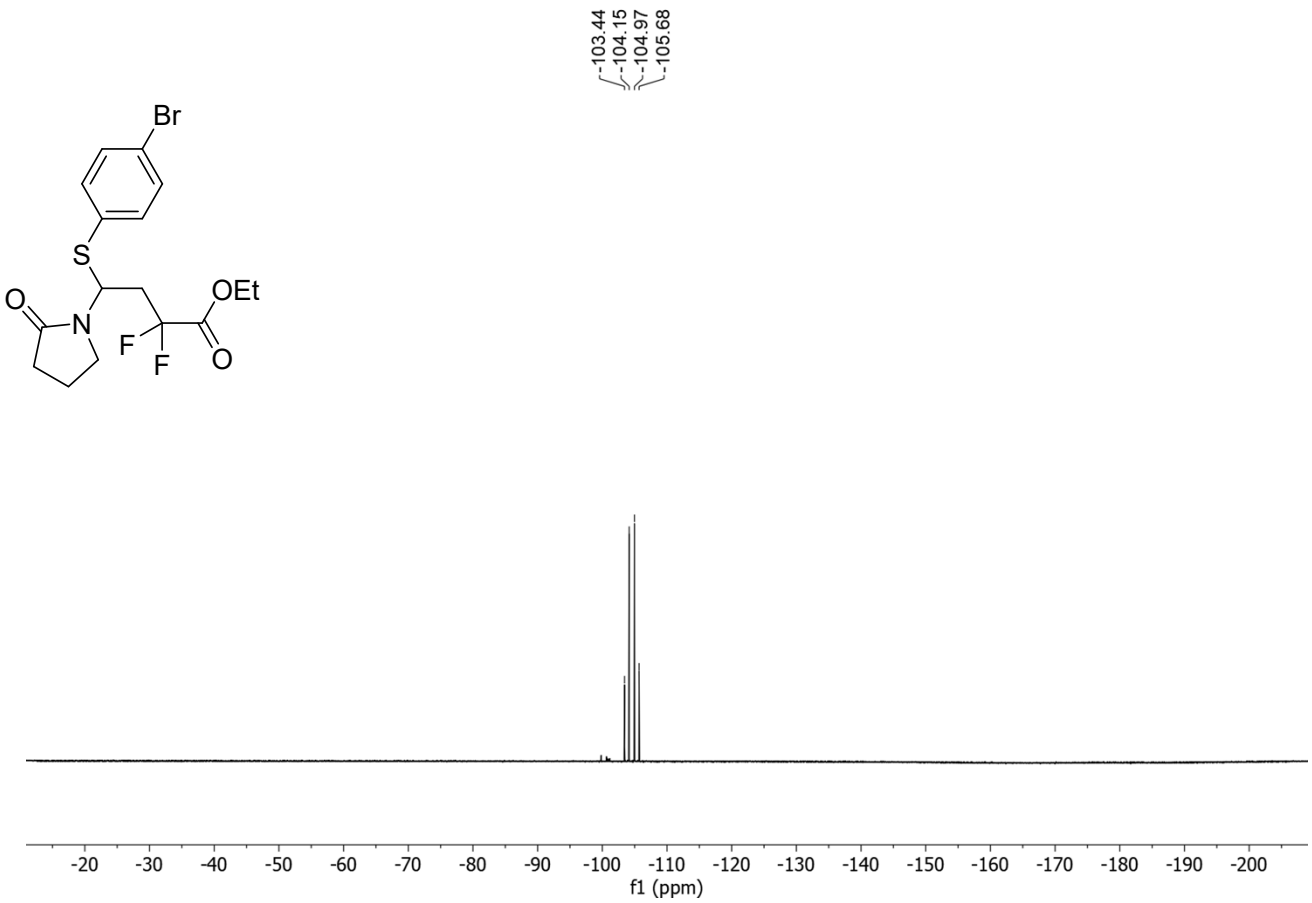
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4n**.



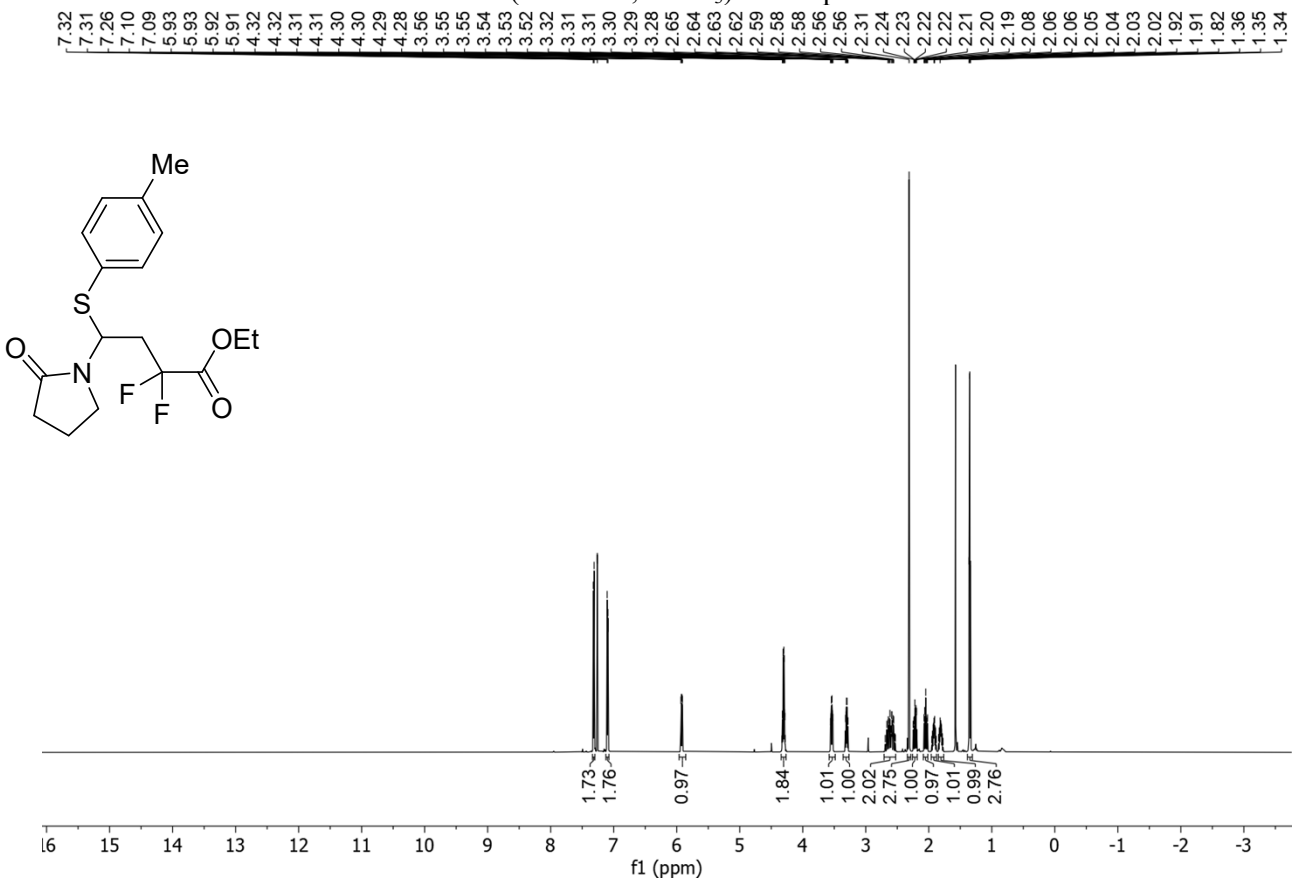
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4o**.



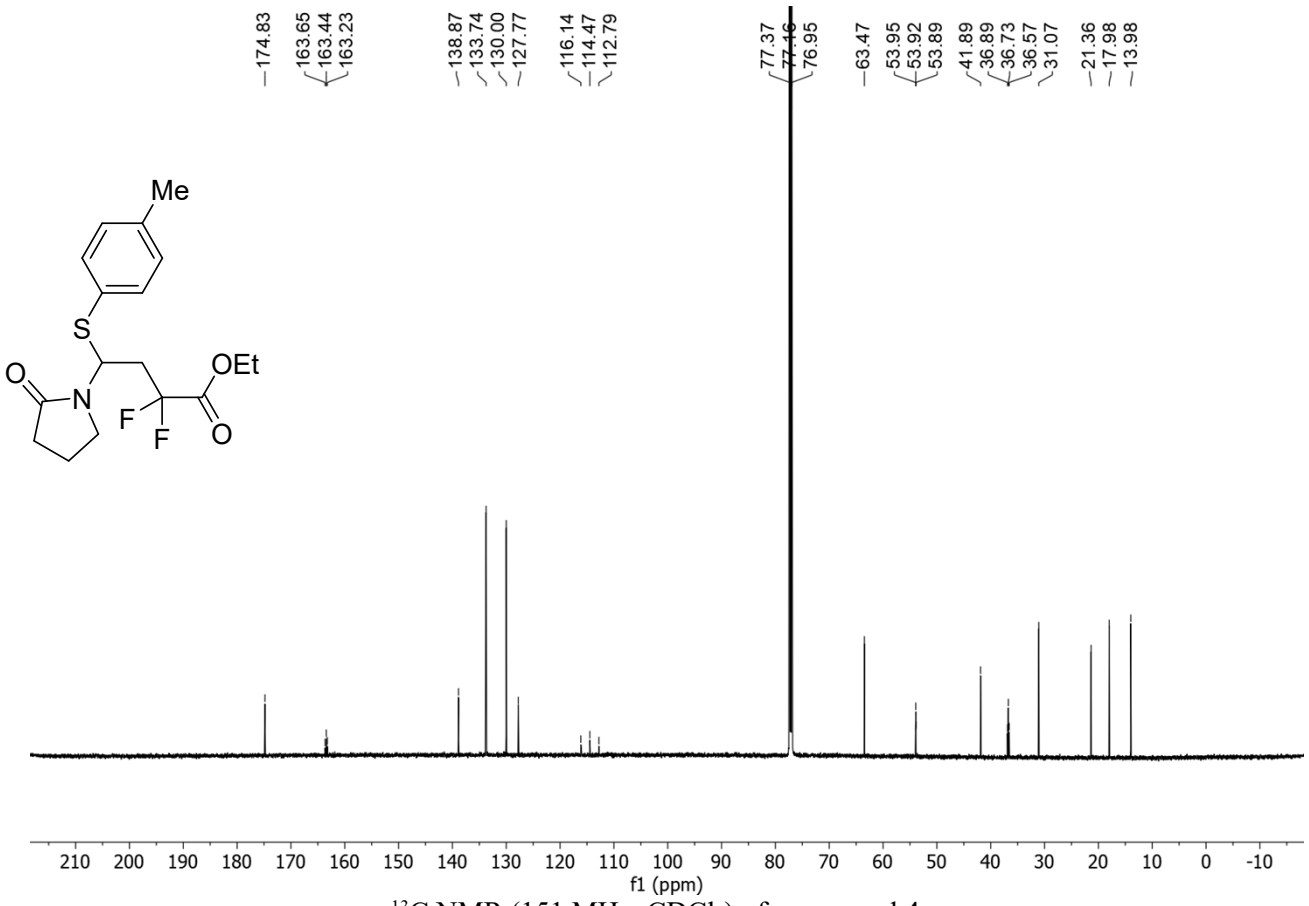
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4o**.



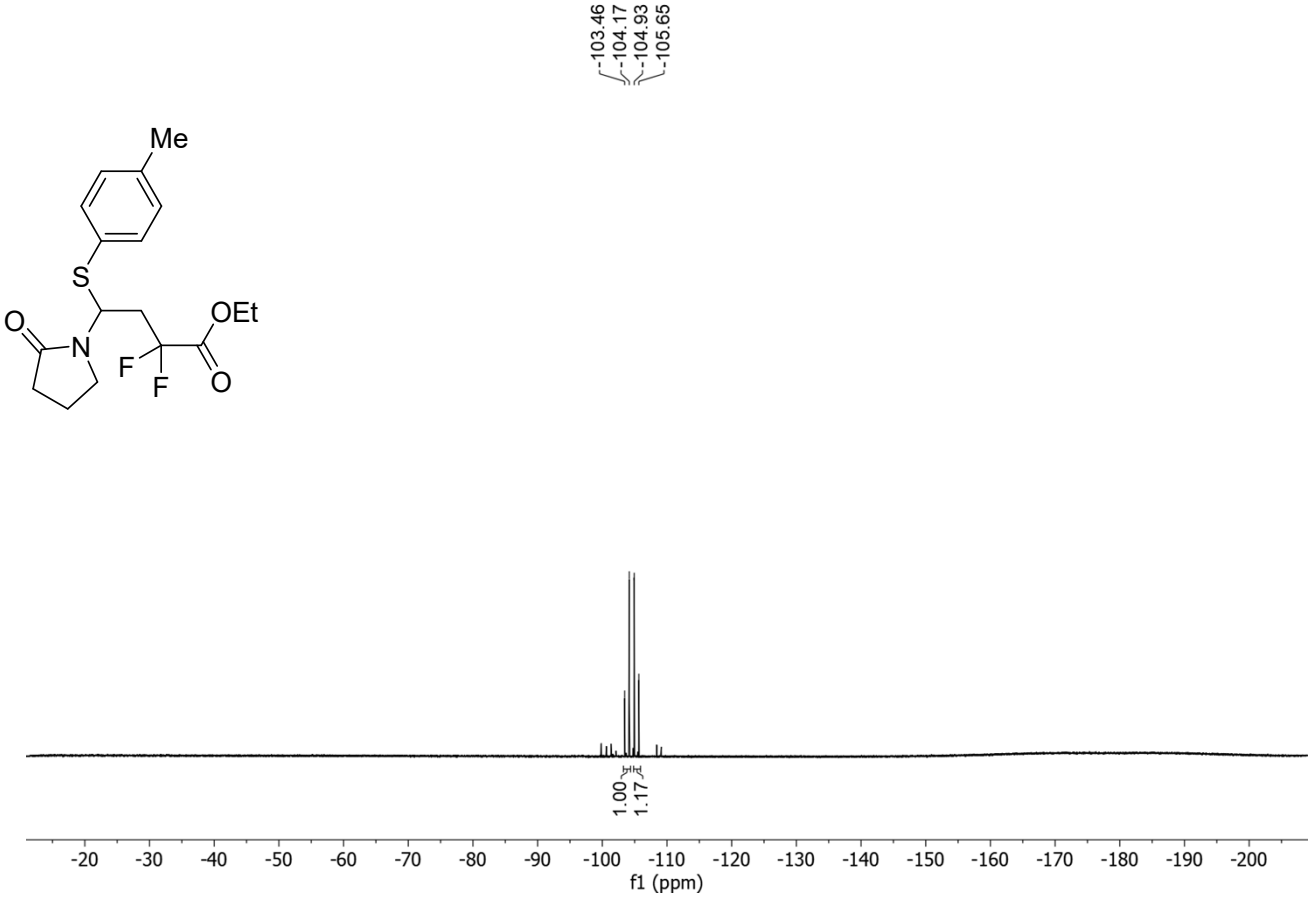
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4o**.



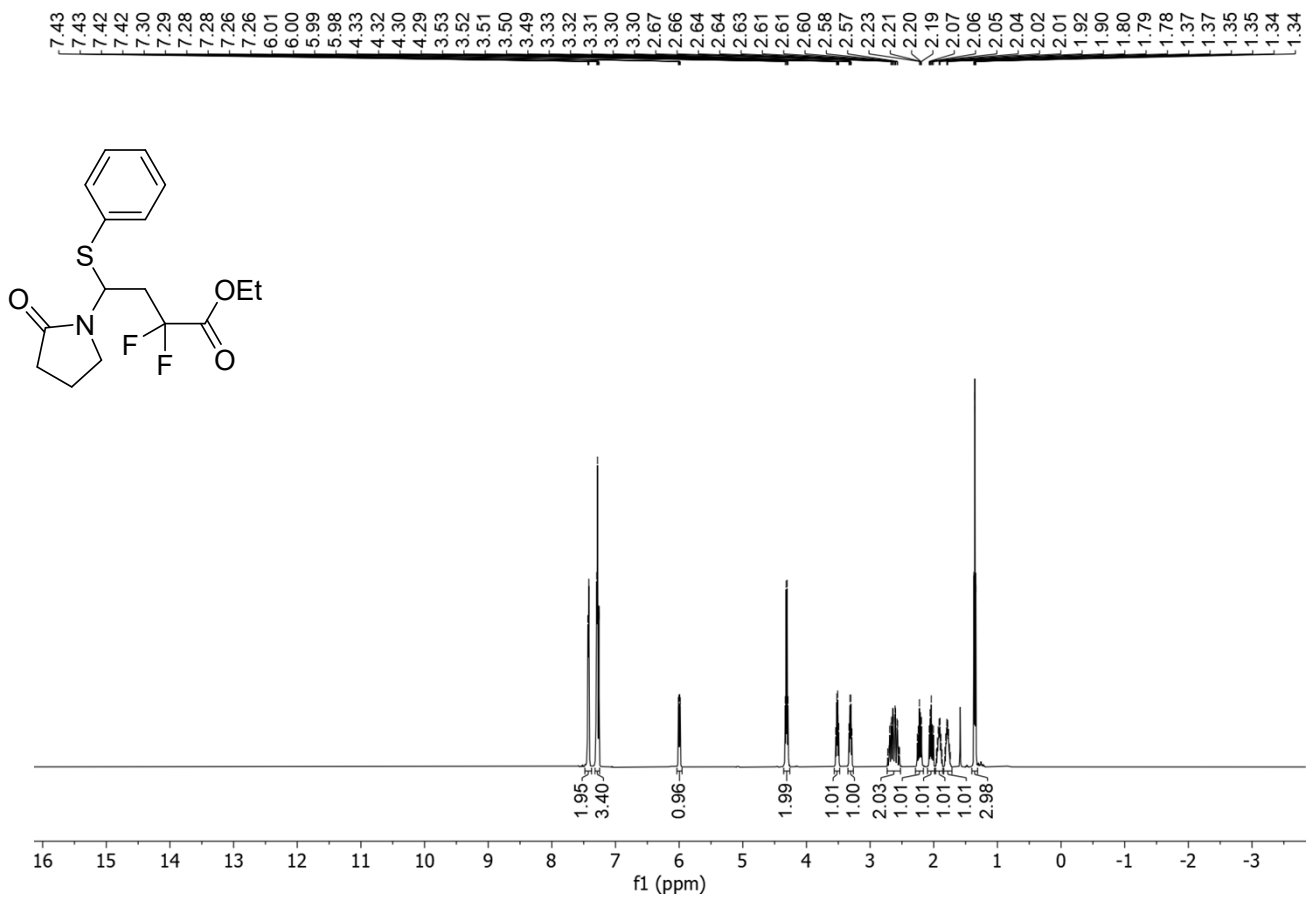
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4p**.



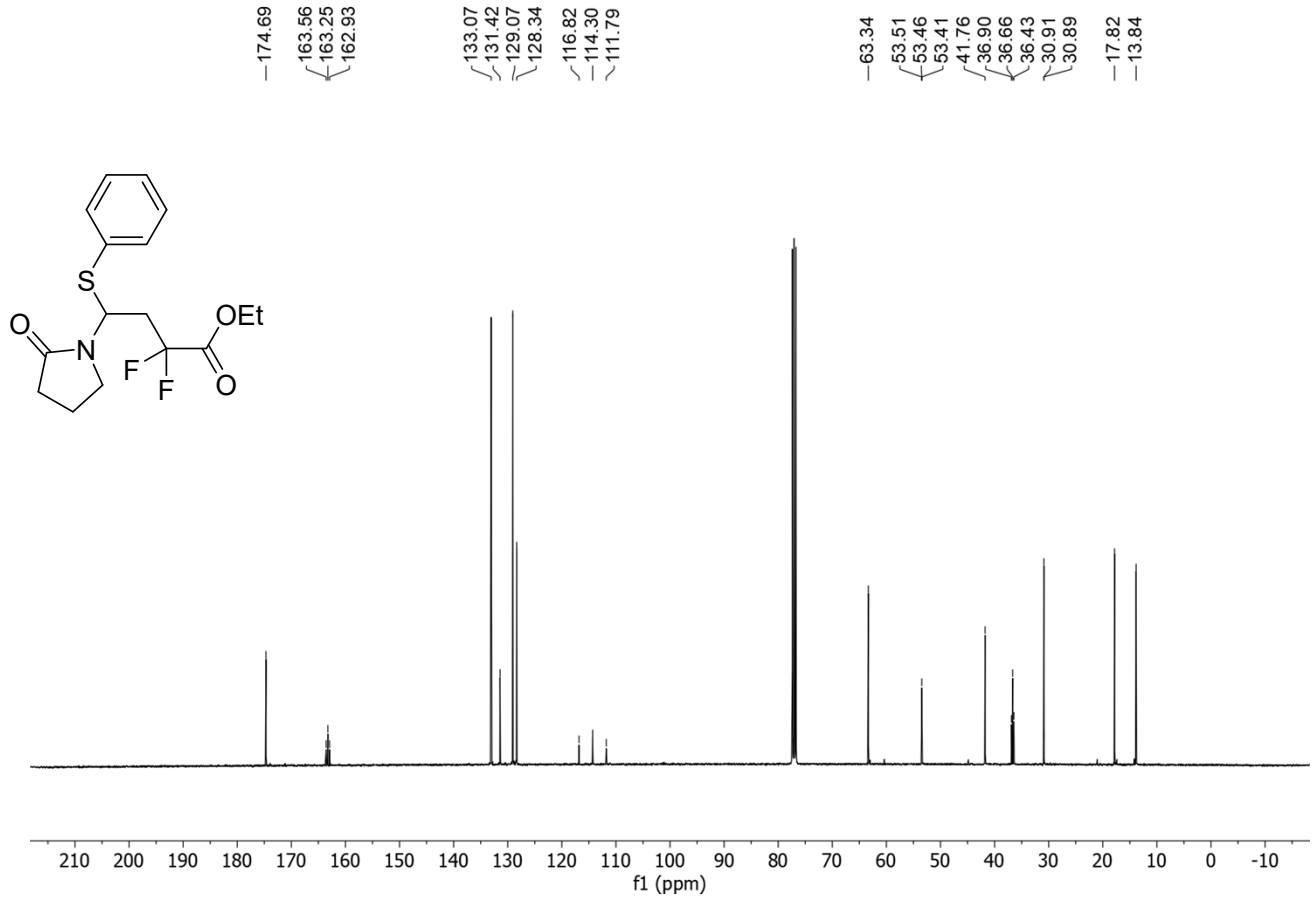
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4p**.



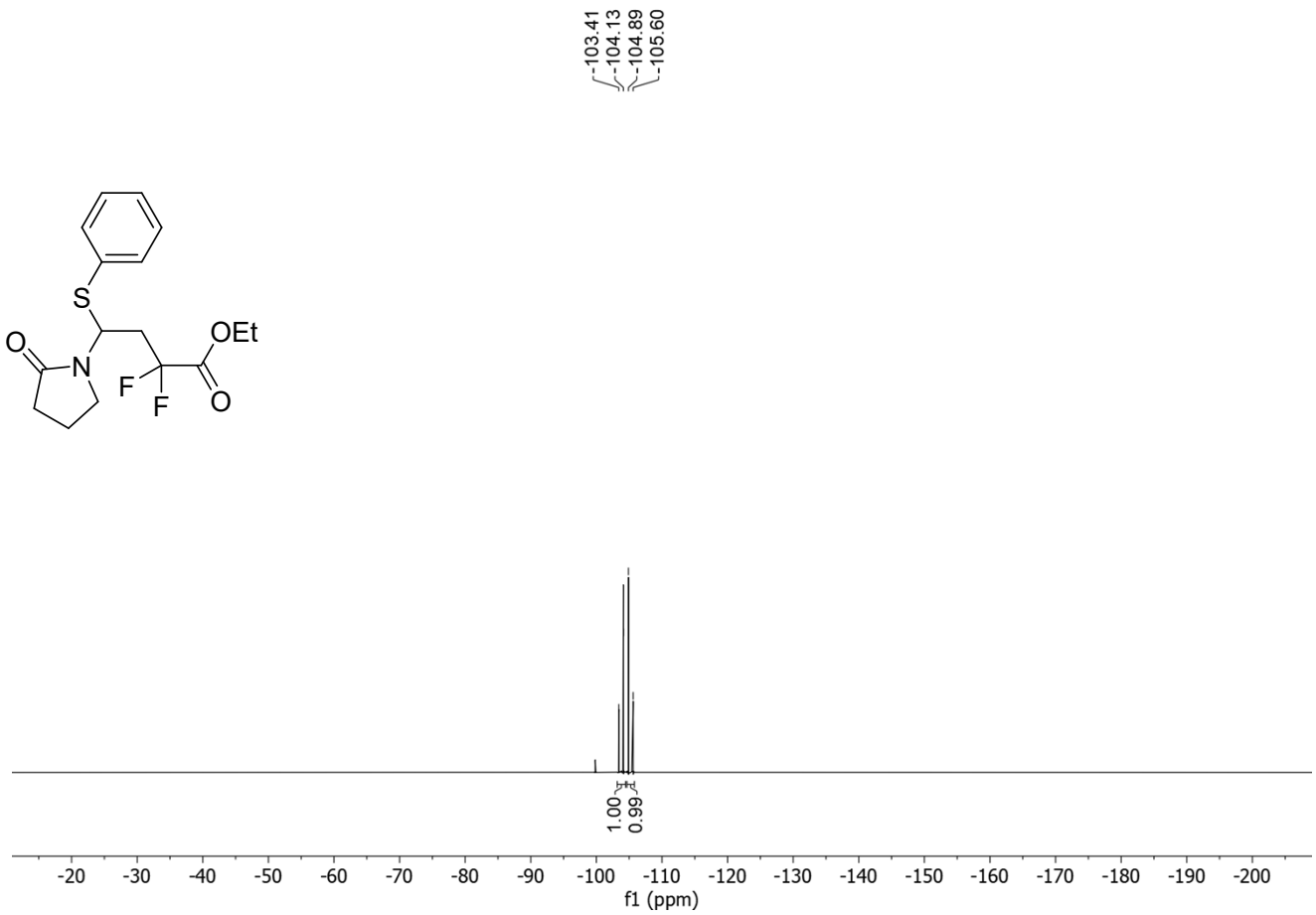
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4p**.



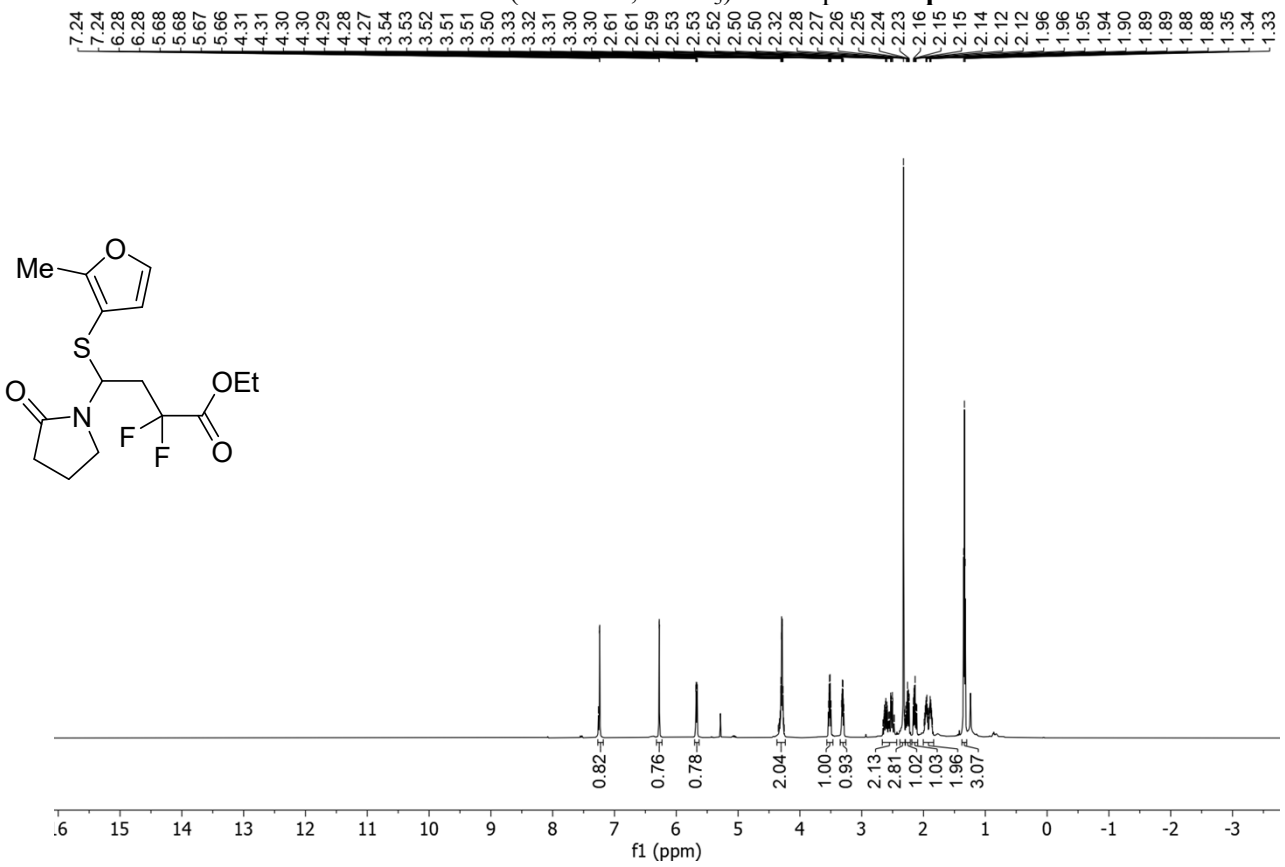
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4q**.



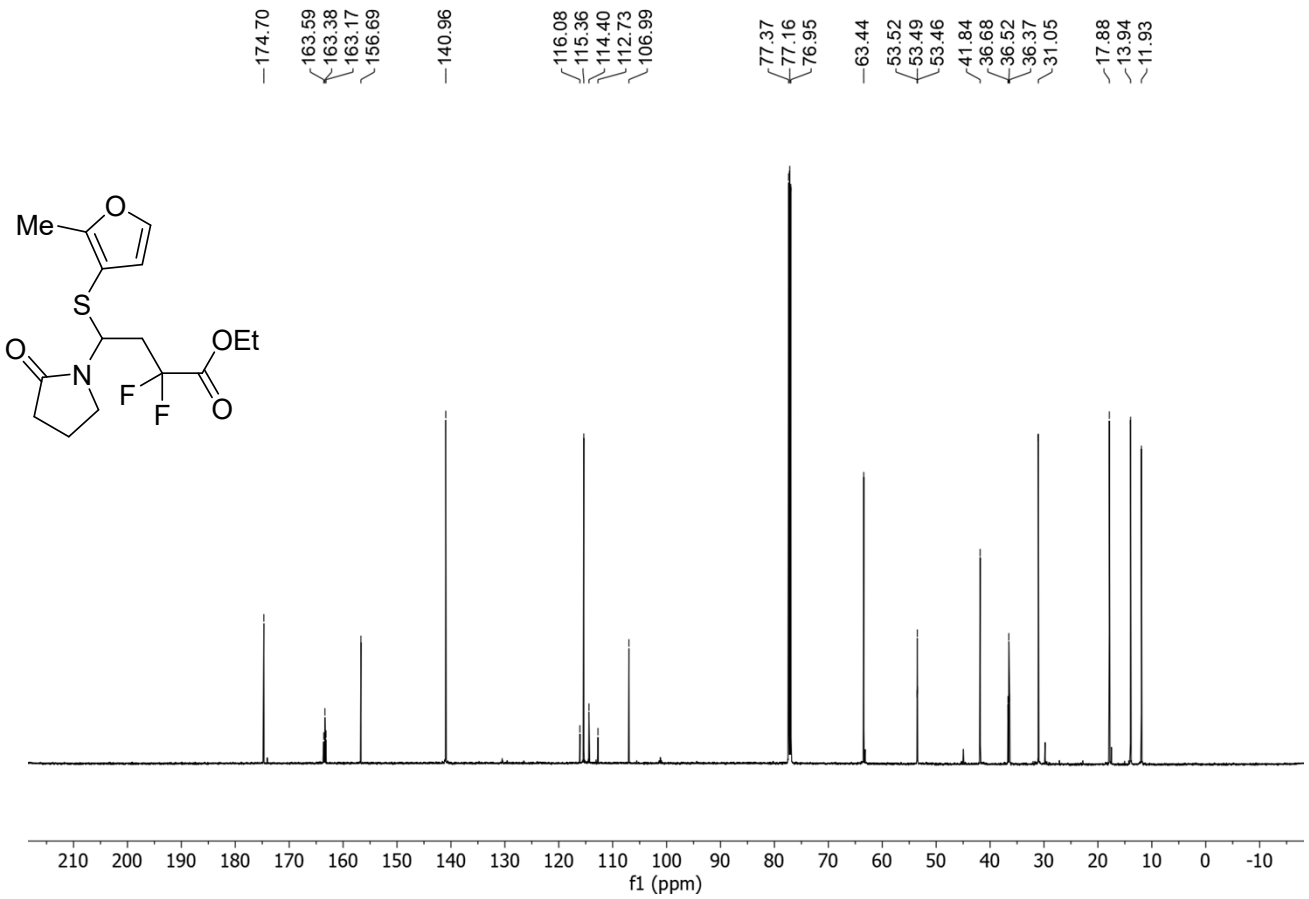
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4q**.



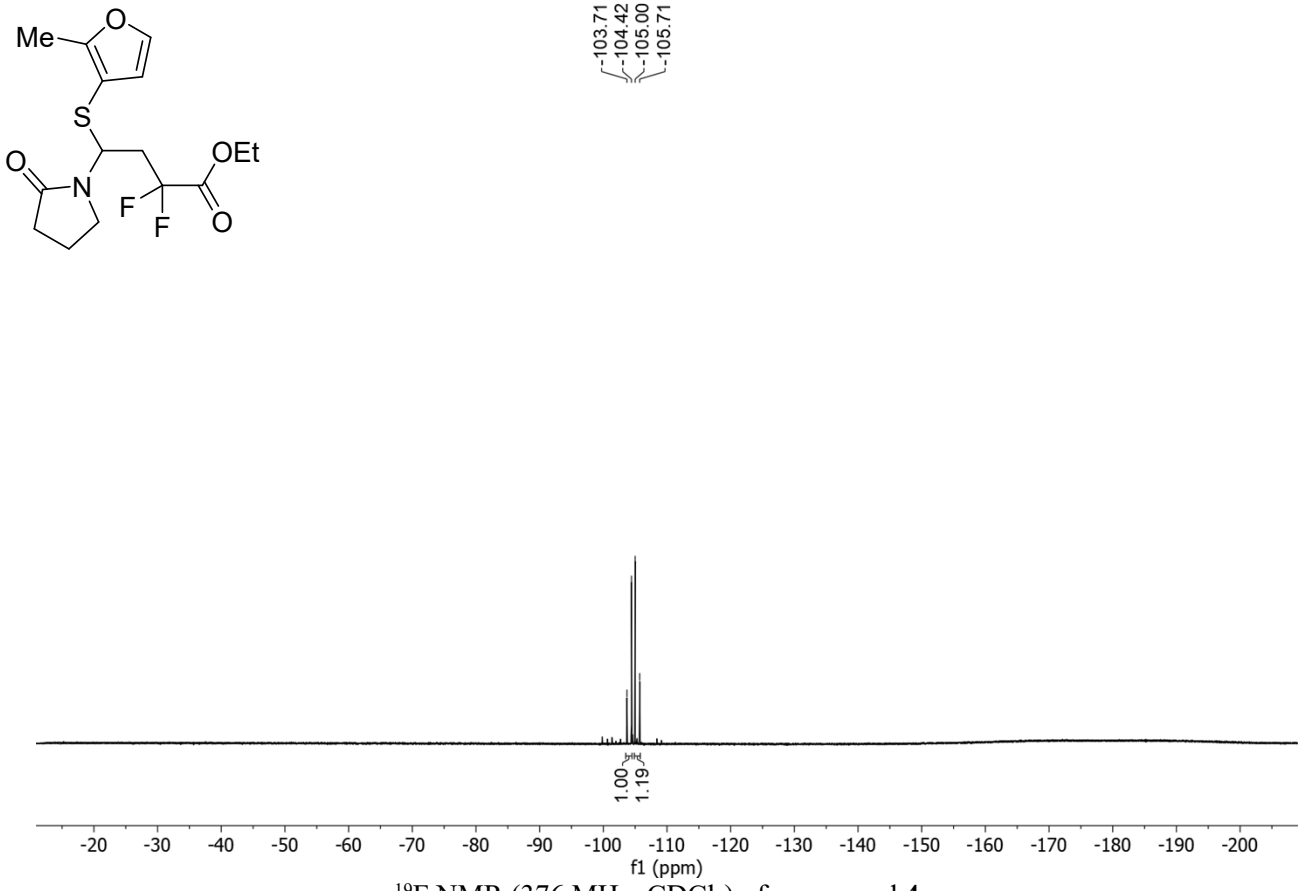
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4q**.



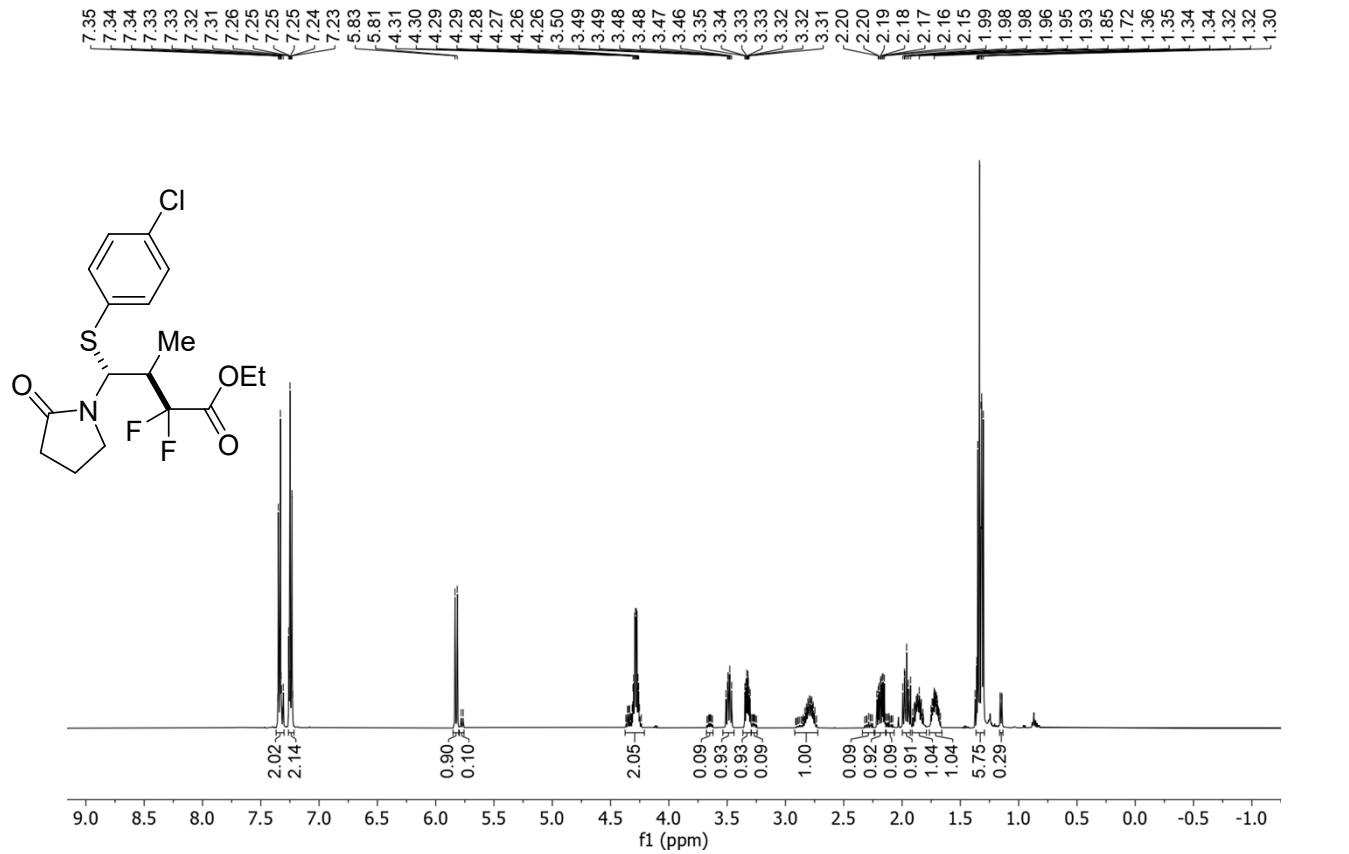
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4r**.



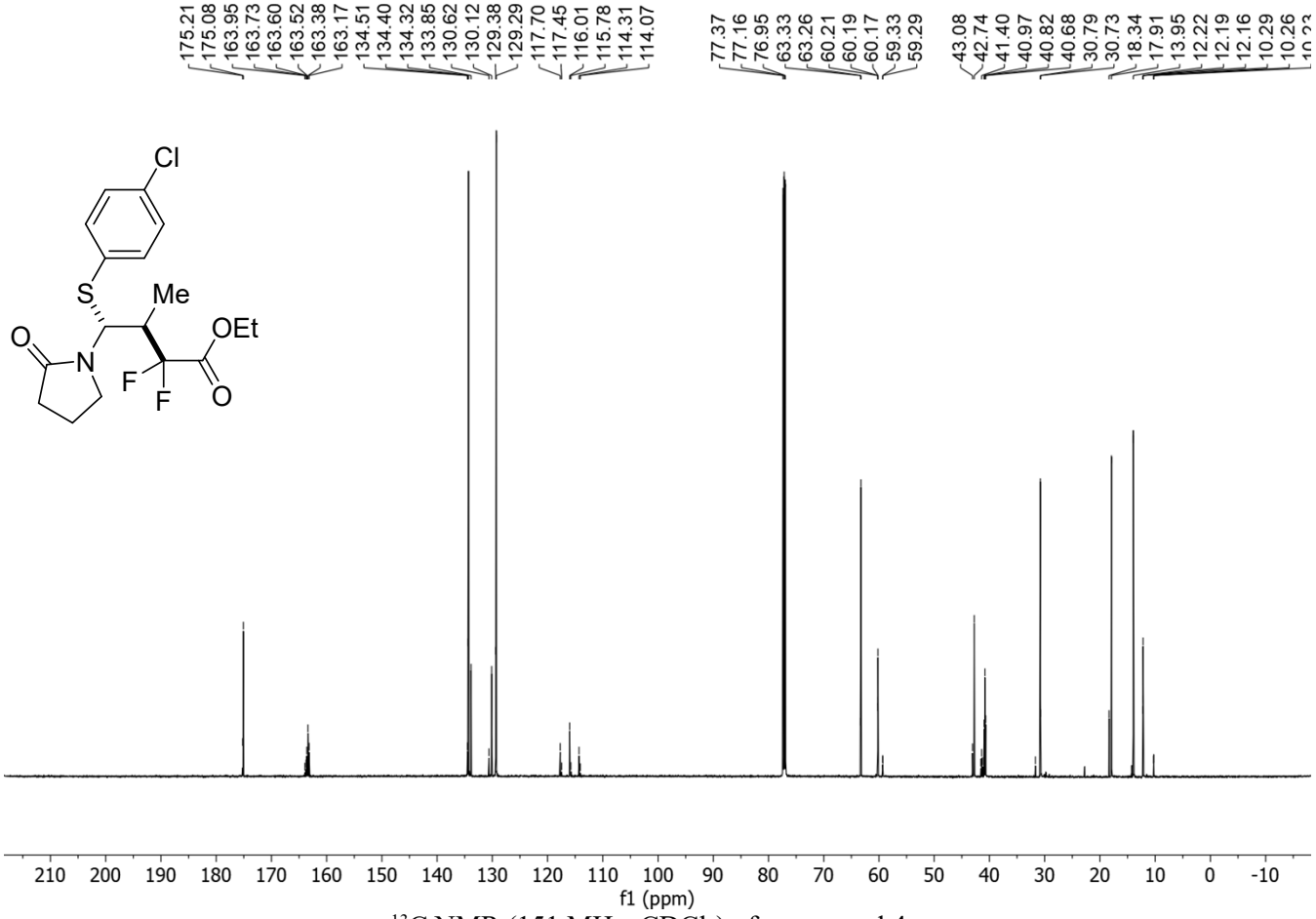
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4r**.



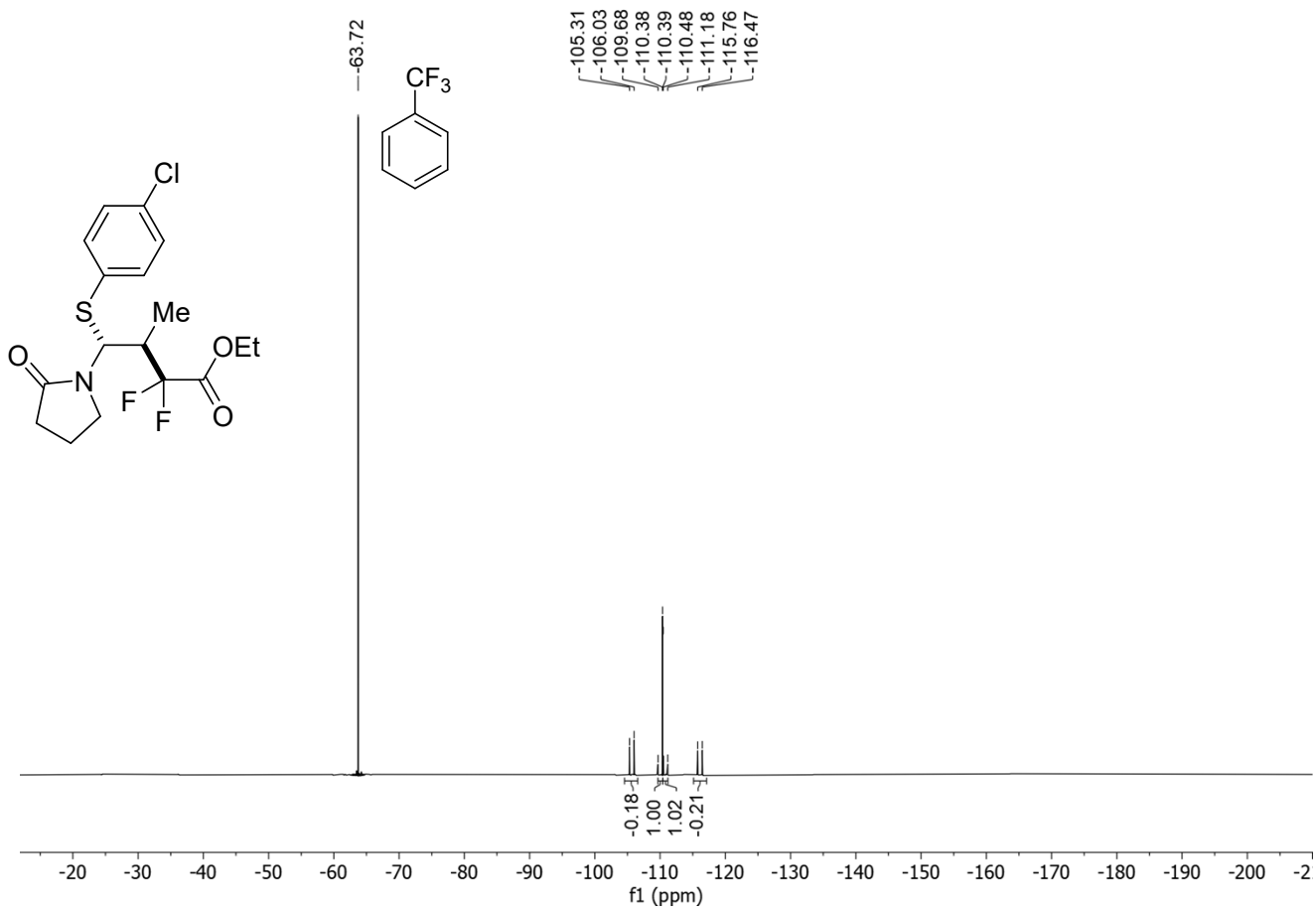
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4r**.



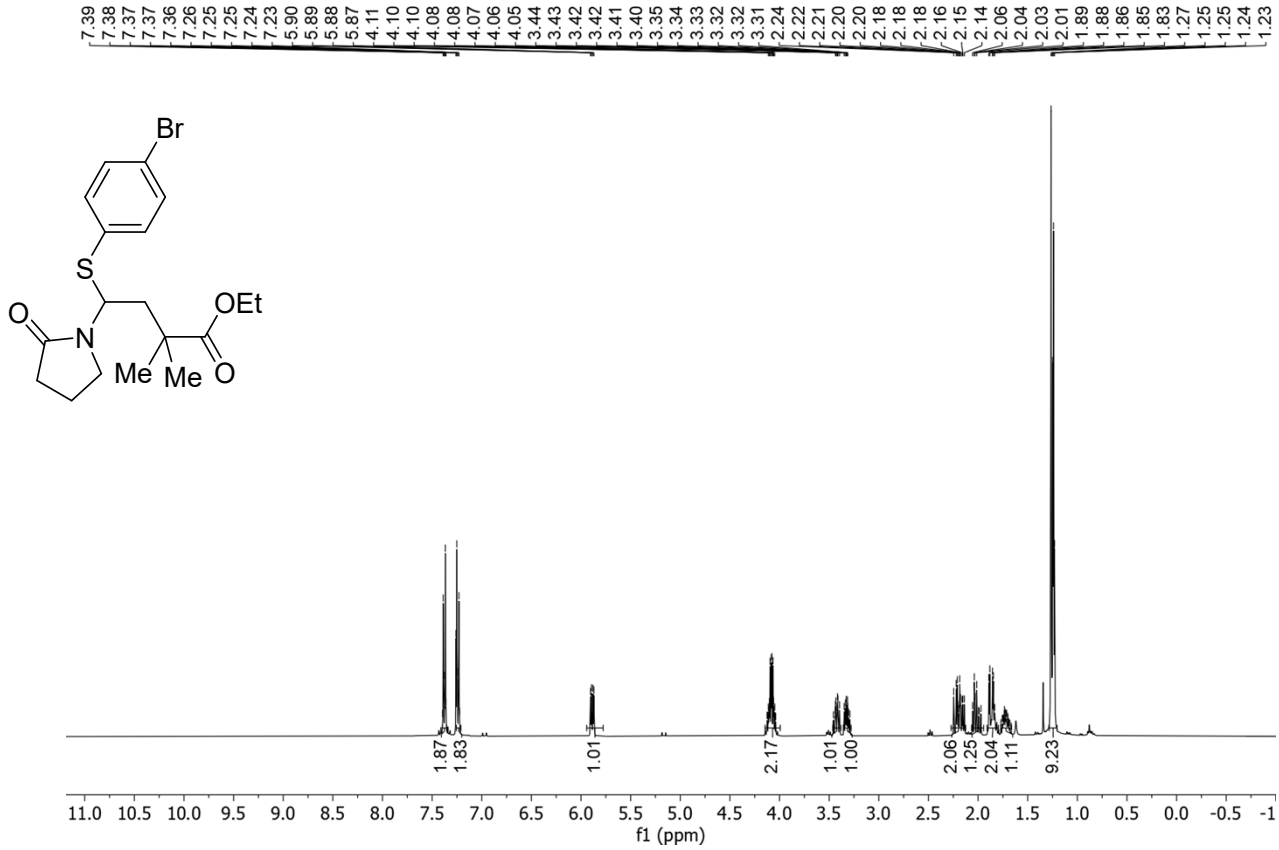
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4s.**



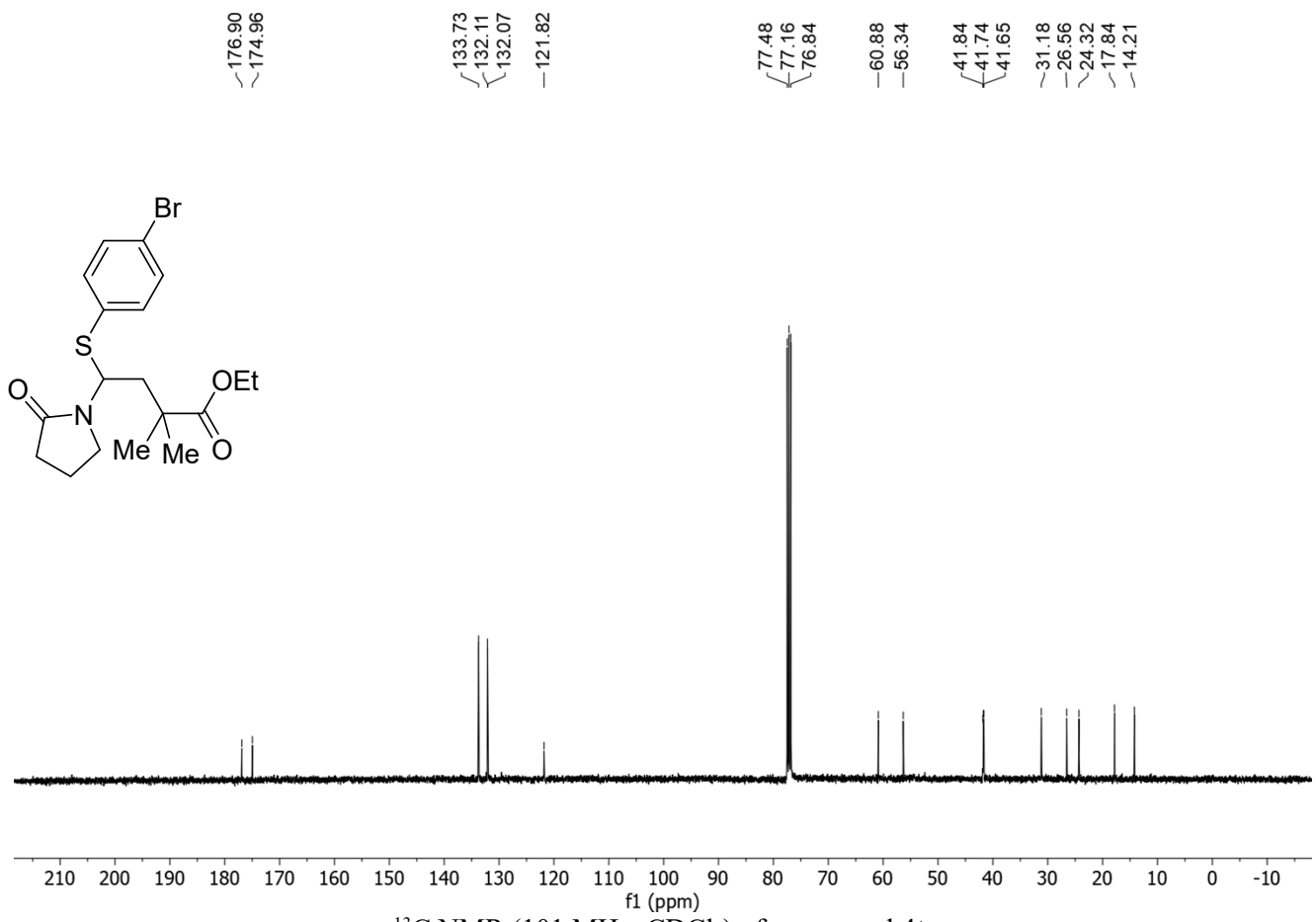
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4s**.



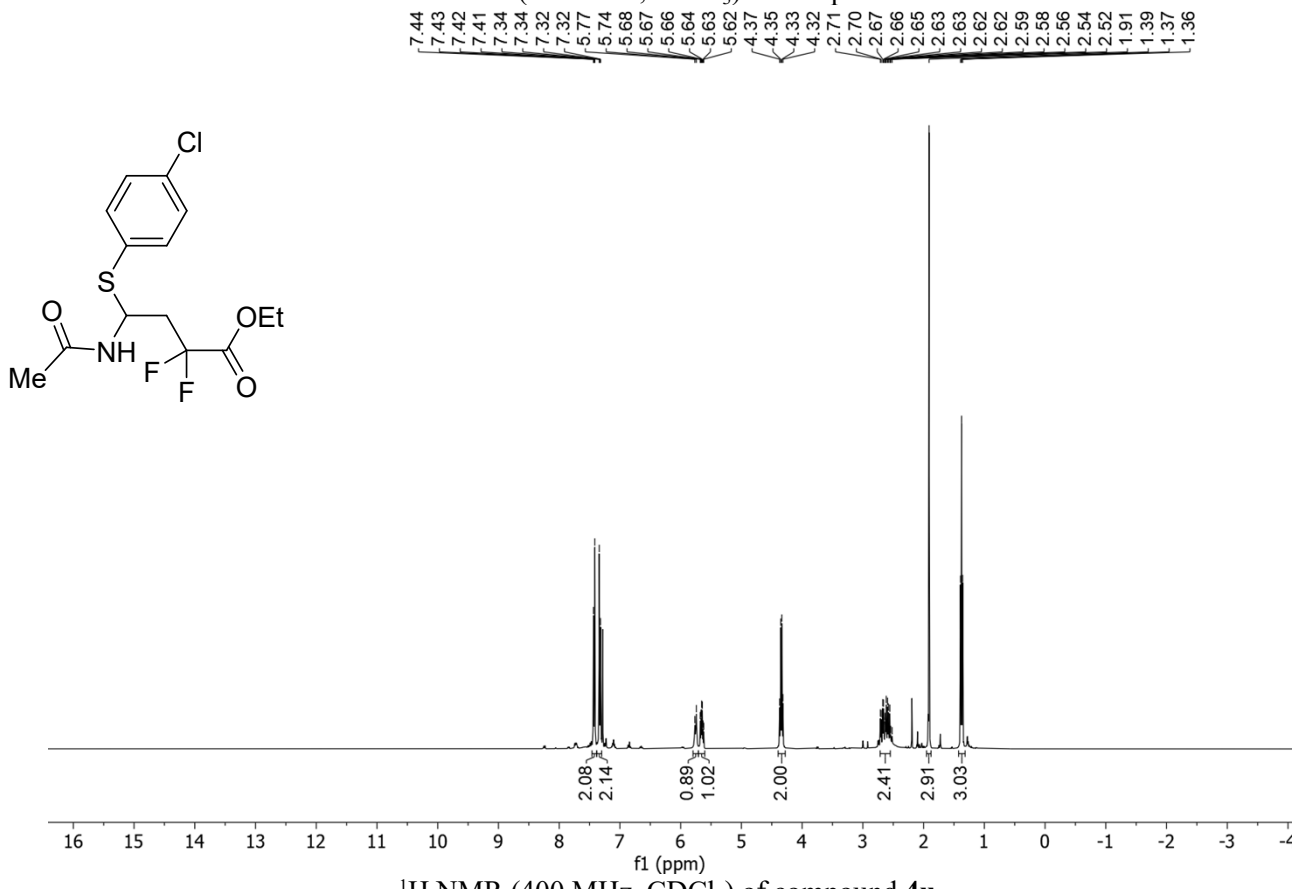
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4s**.



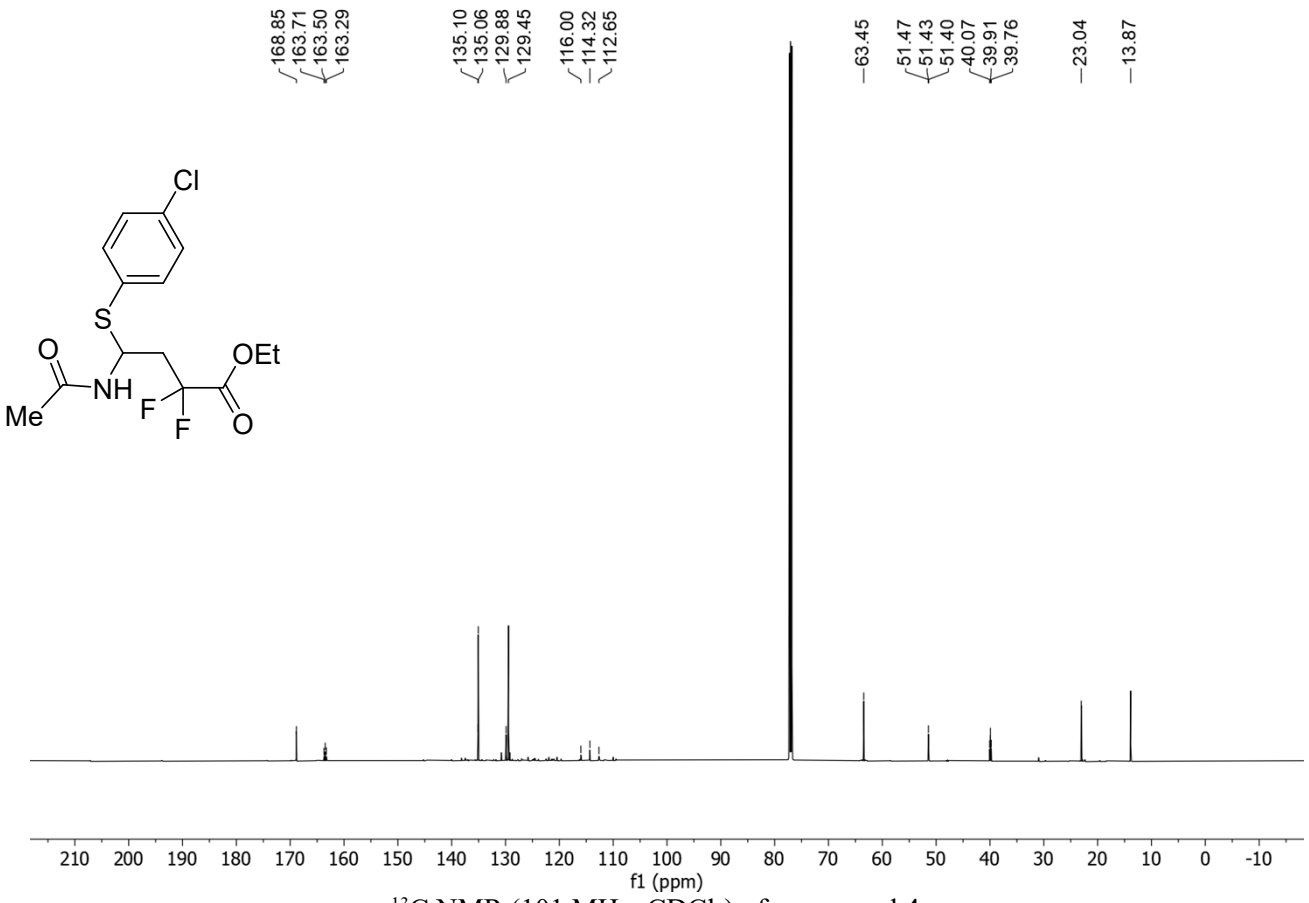
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4t**.



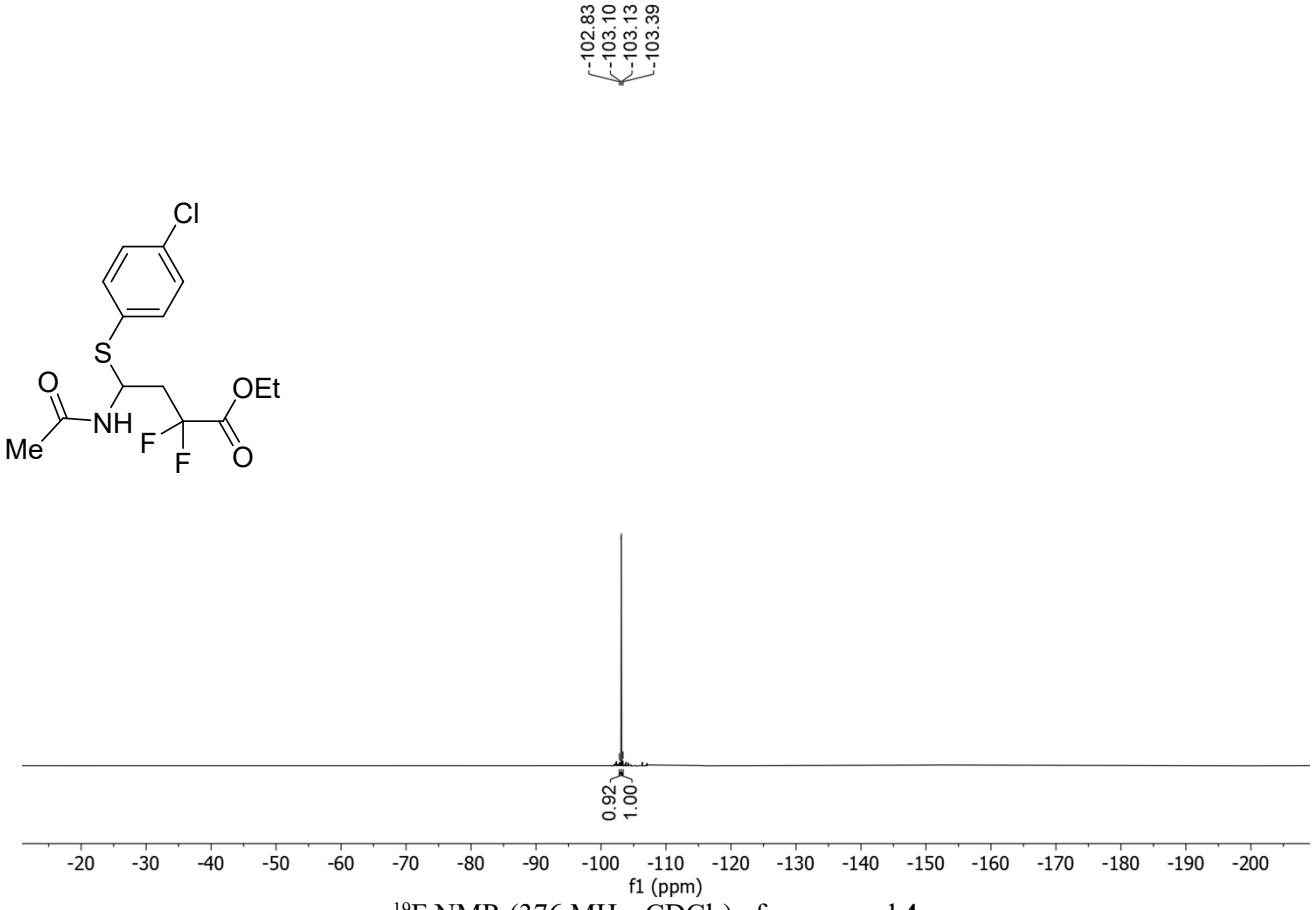
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4t**.



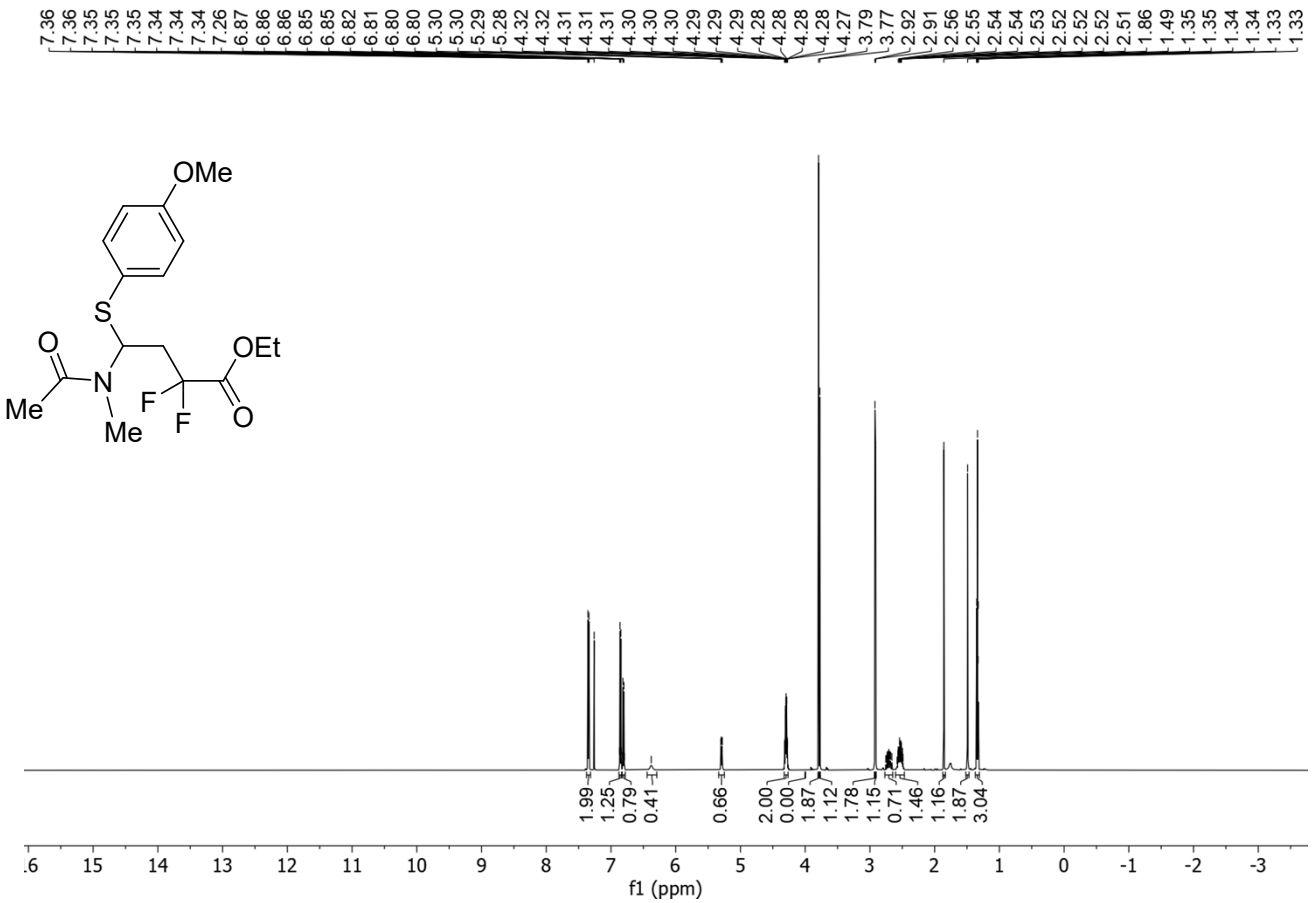
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4u**.



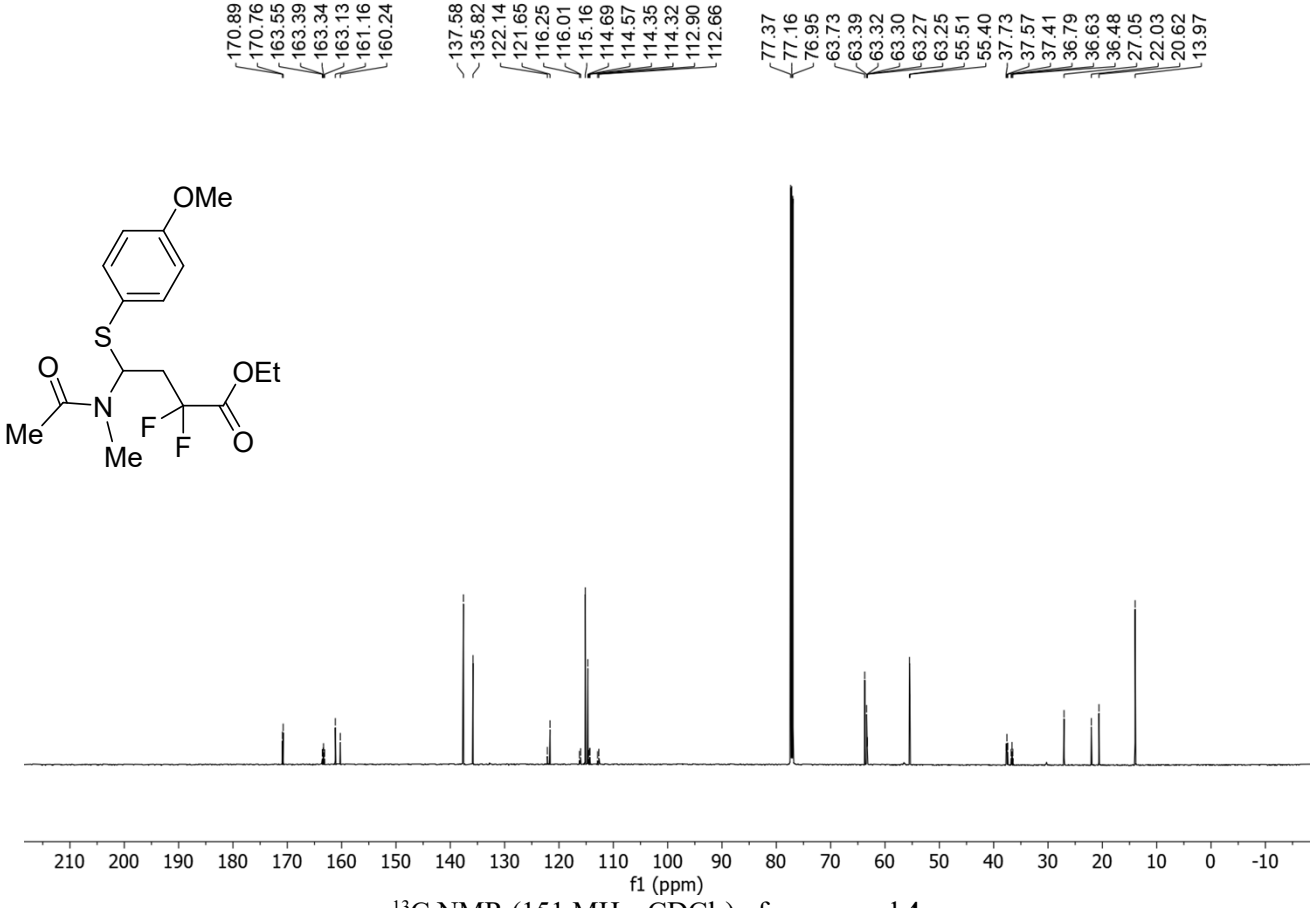
^{13}C NMR (101 MHz, $CDCl_3$) of compound **4u**.



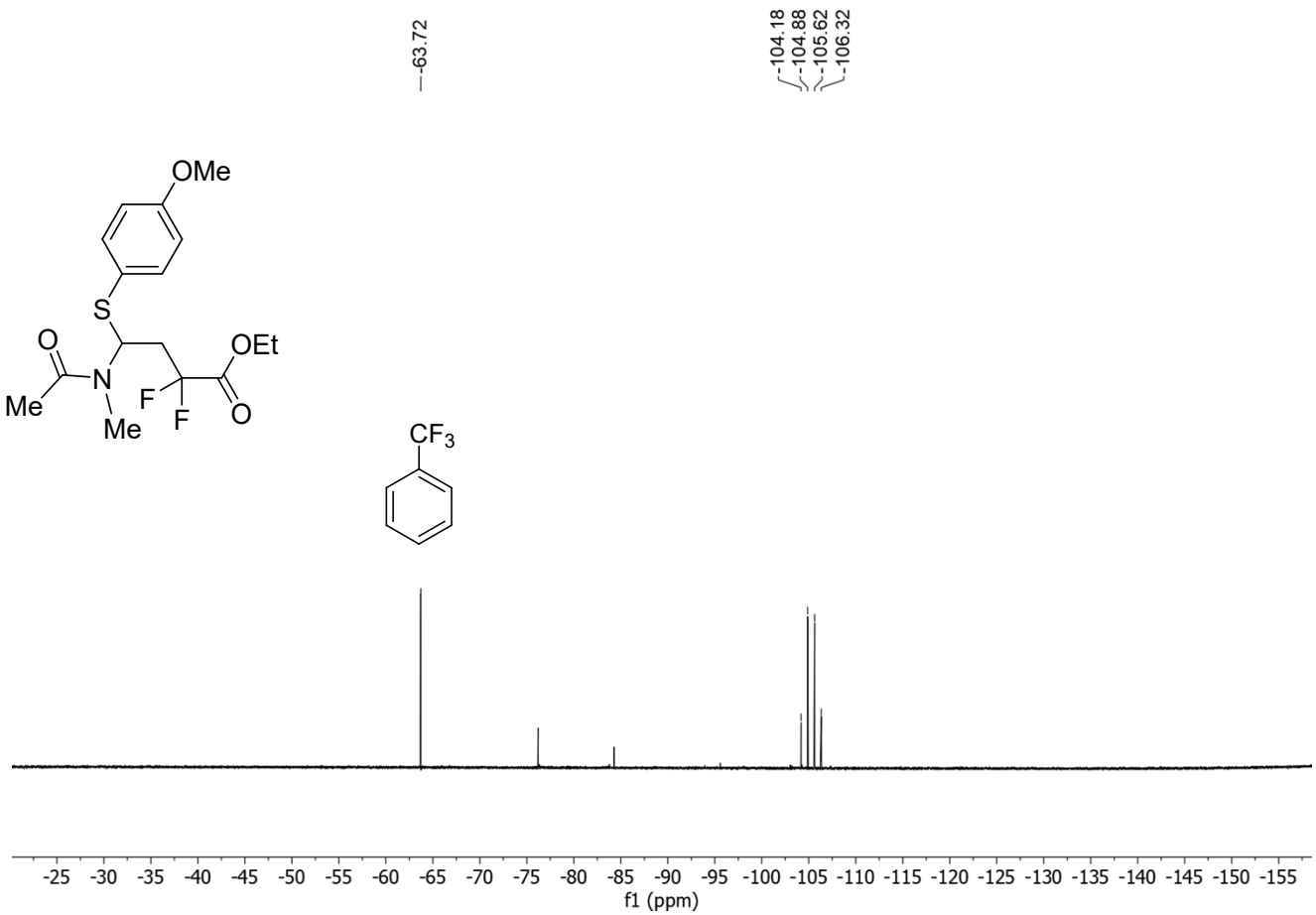
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4u**.



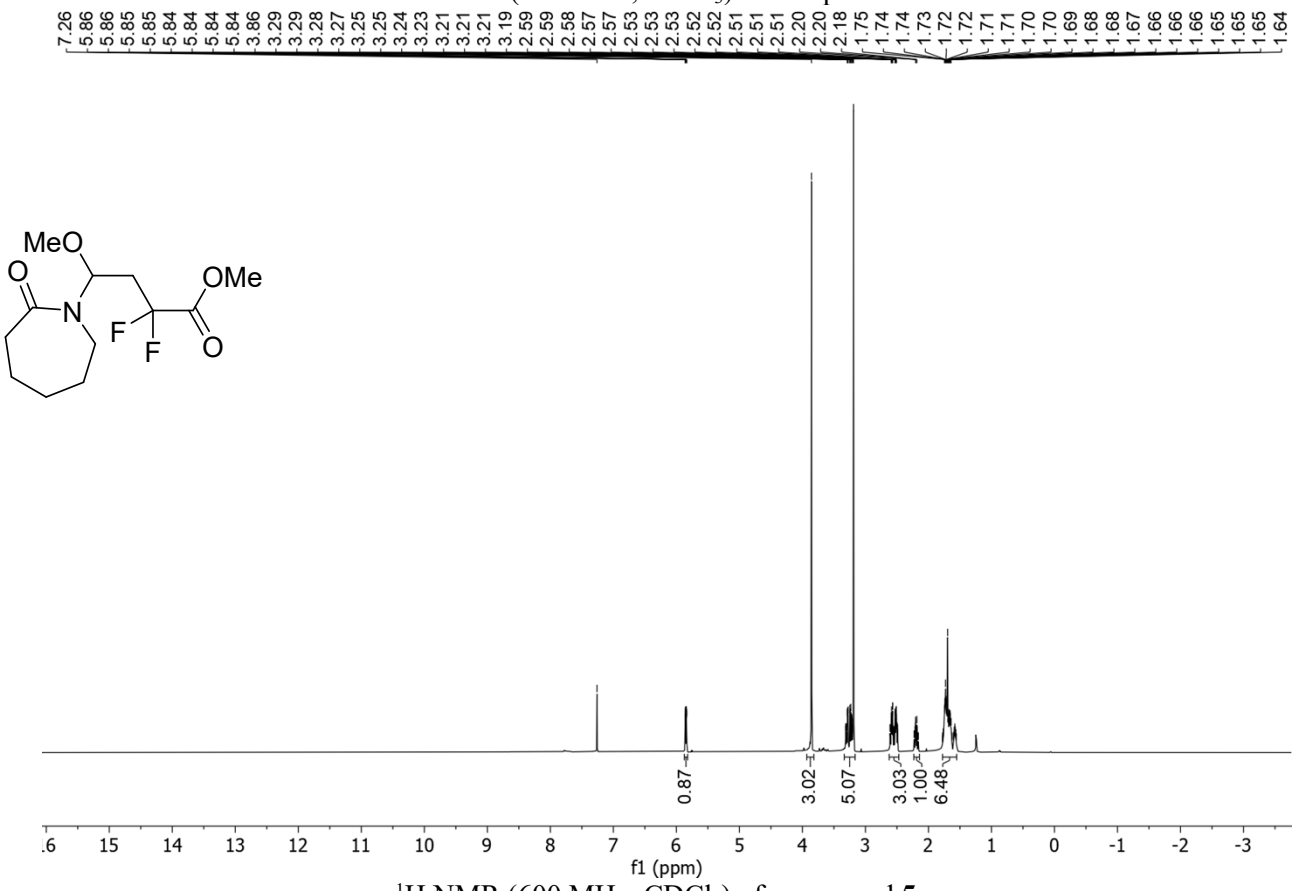
^{1}H NMR (600 MHz, $CDCl_3$) of compound **4v**.



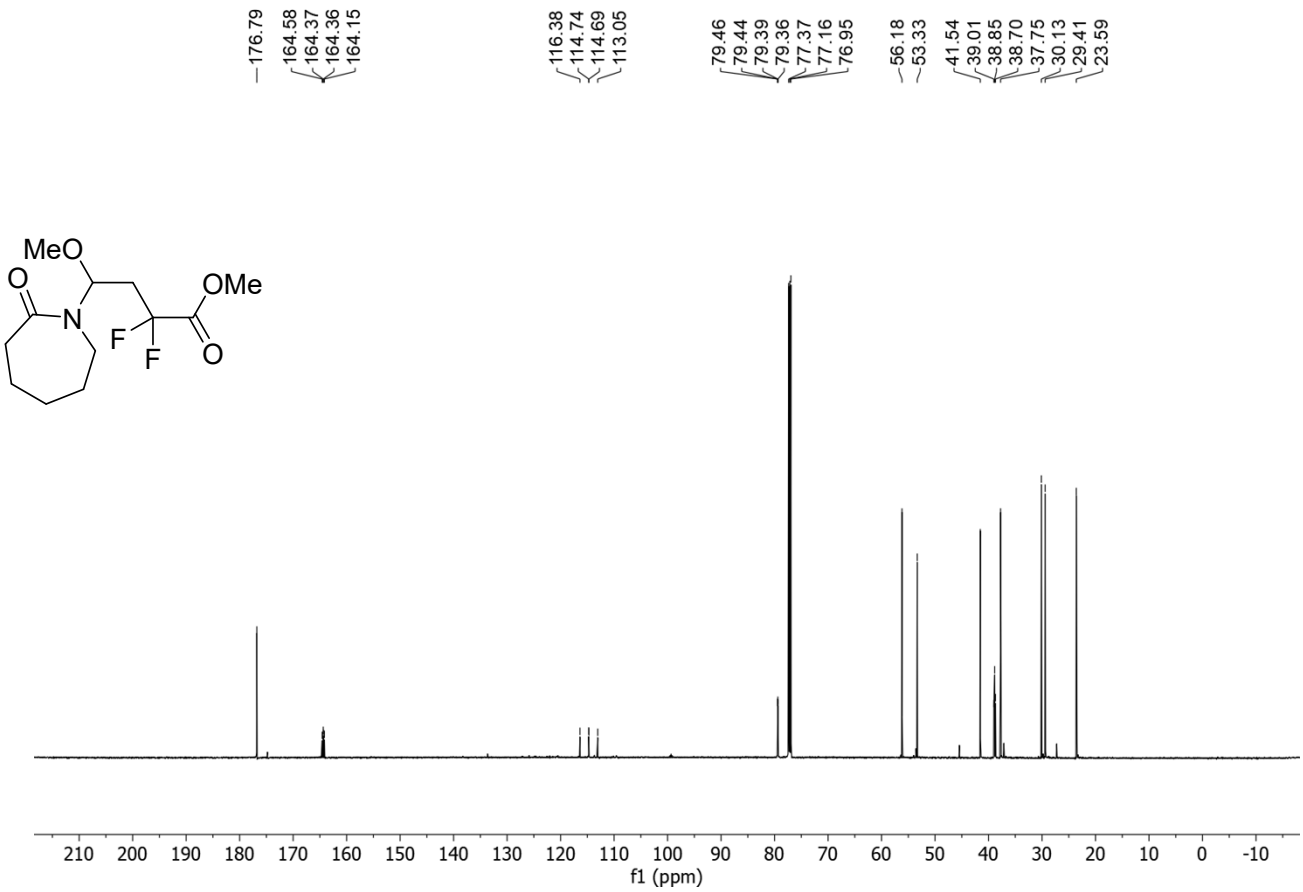
^{13}C NMR (151 MHz, $CDCl_3$) of compound **4v**.



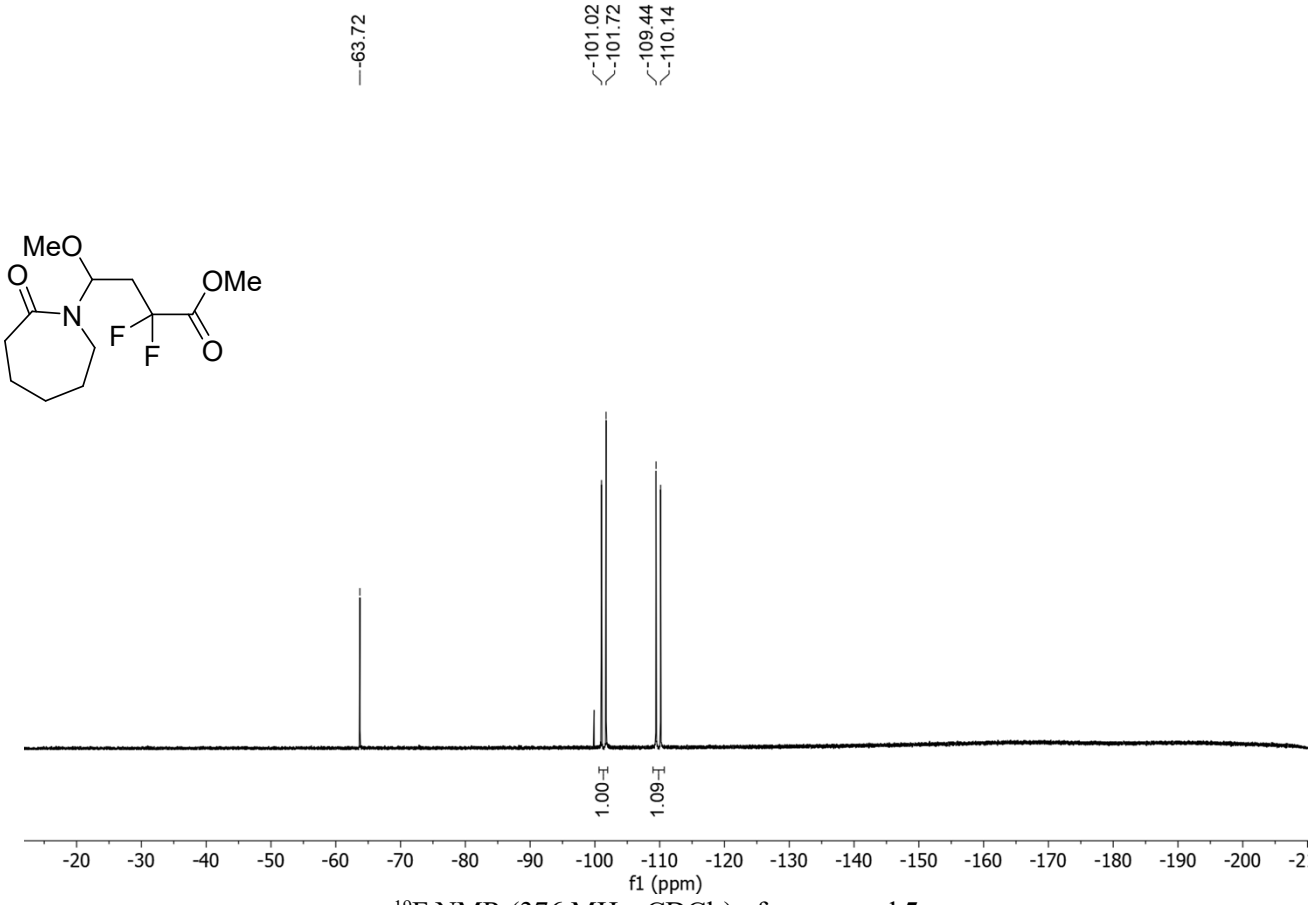
^{19}F NMR (376 MHz, $CDCl_3$) of compound **4v**.



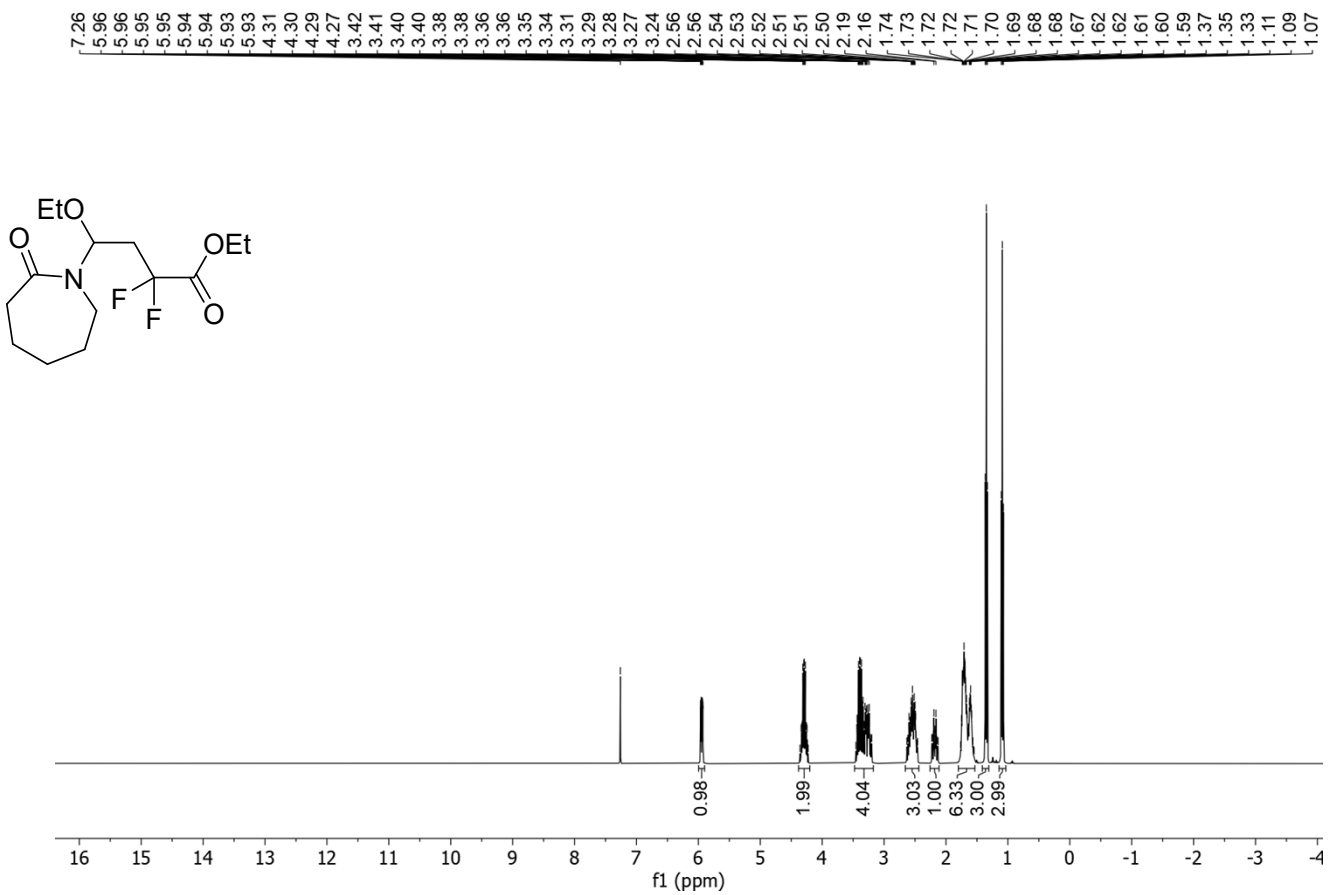
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5a**.



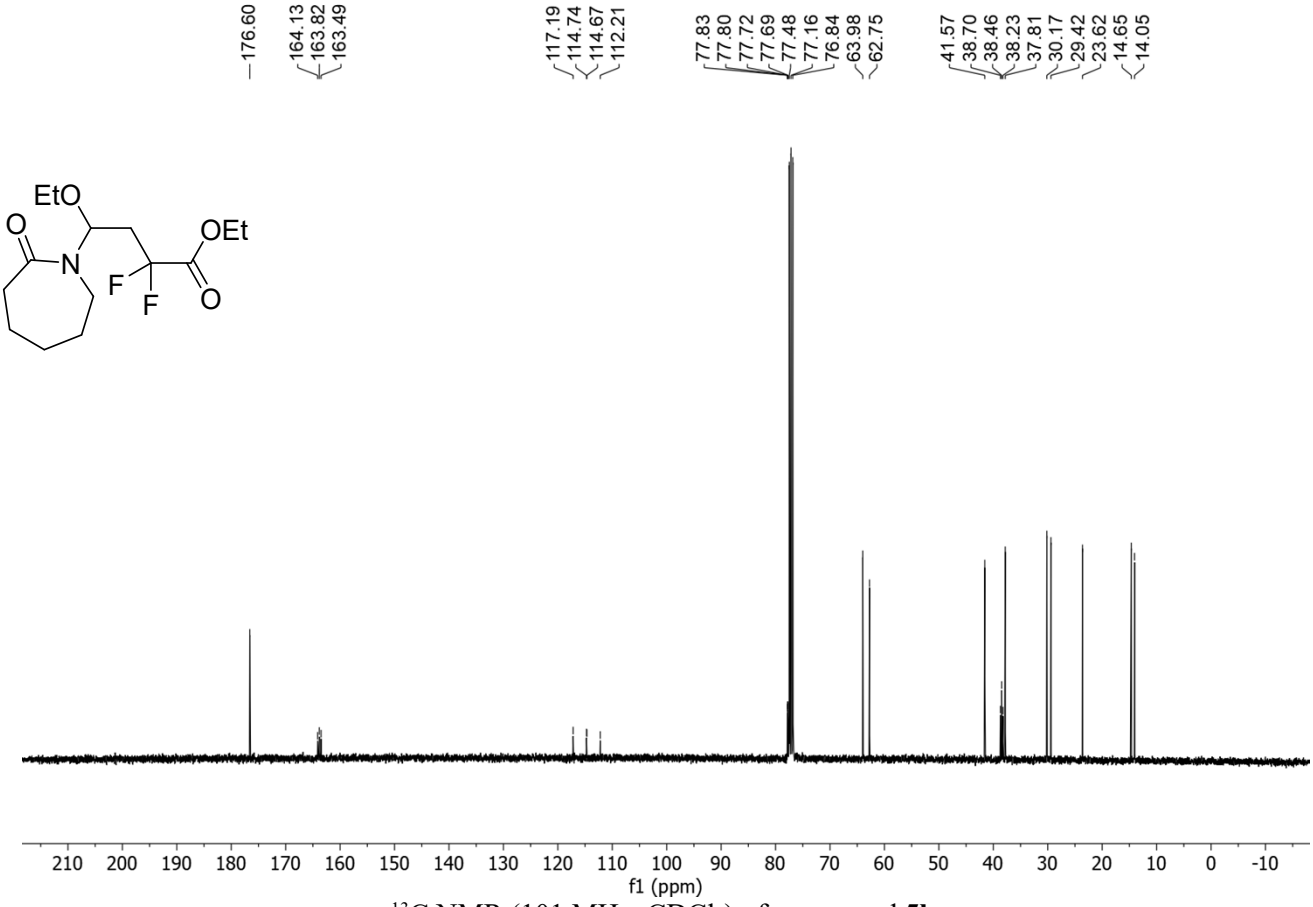
^{13}C NMR (151 MHz, $CDCl_3$) of compound **5a.**



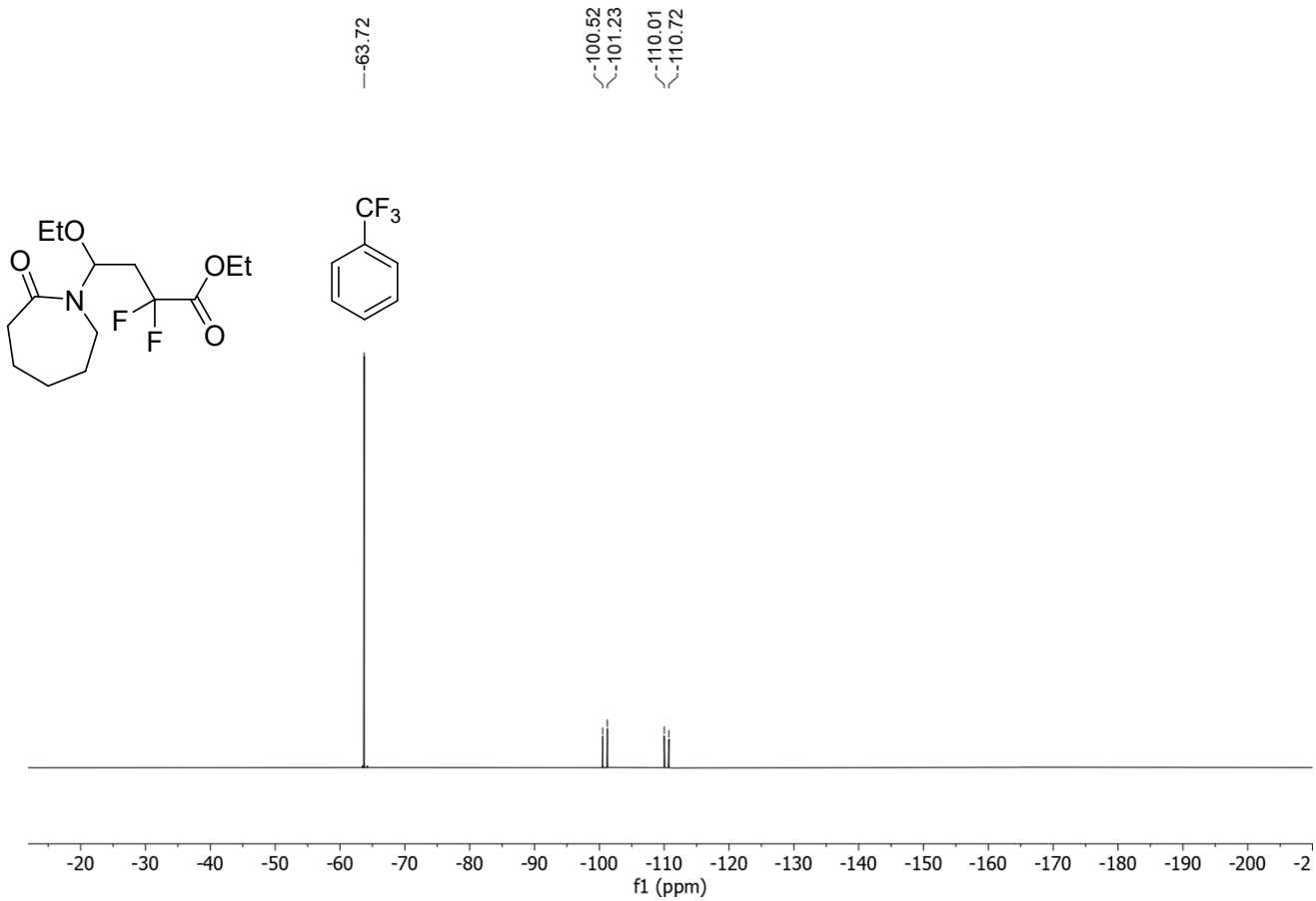
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5a**.



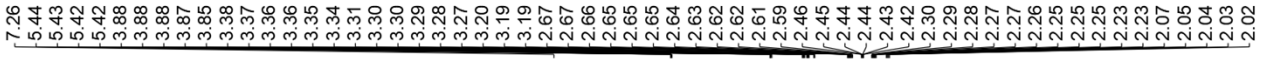
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5b**.

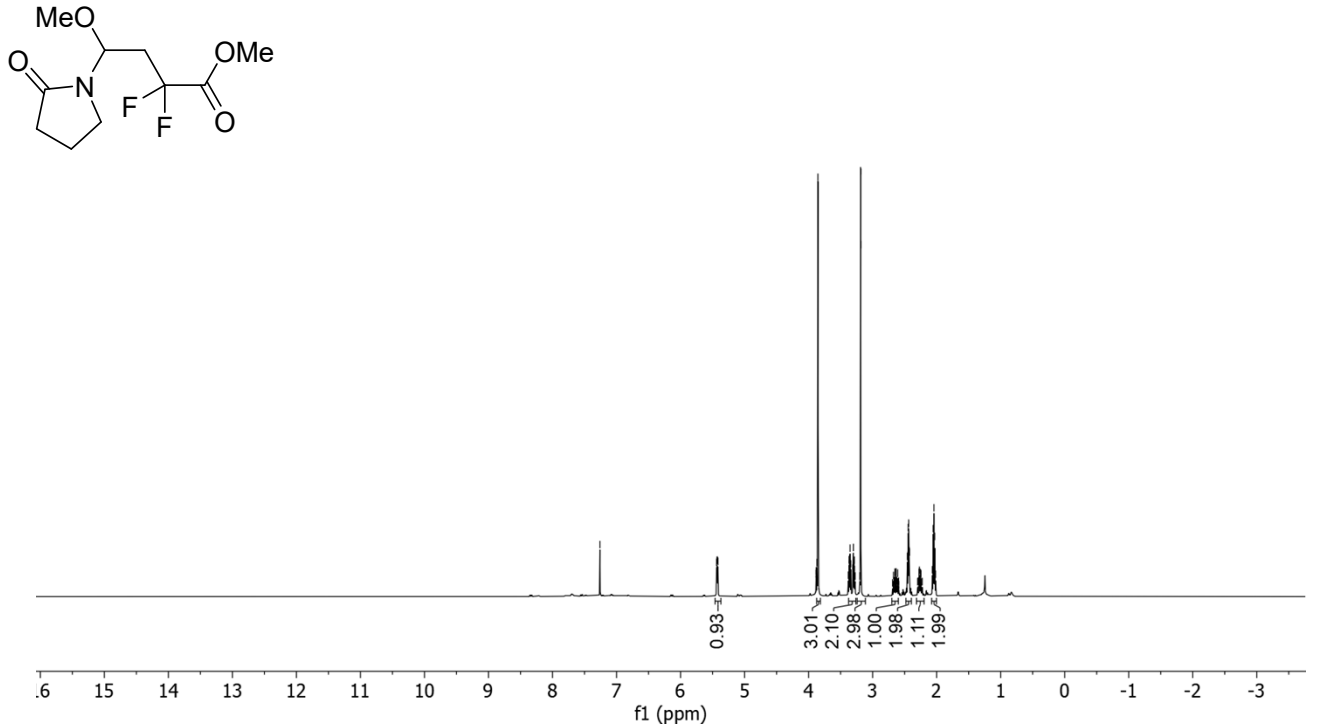


^{13}C NMR (101 MHz, $CDCl_3$) of compound **5b**.

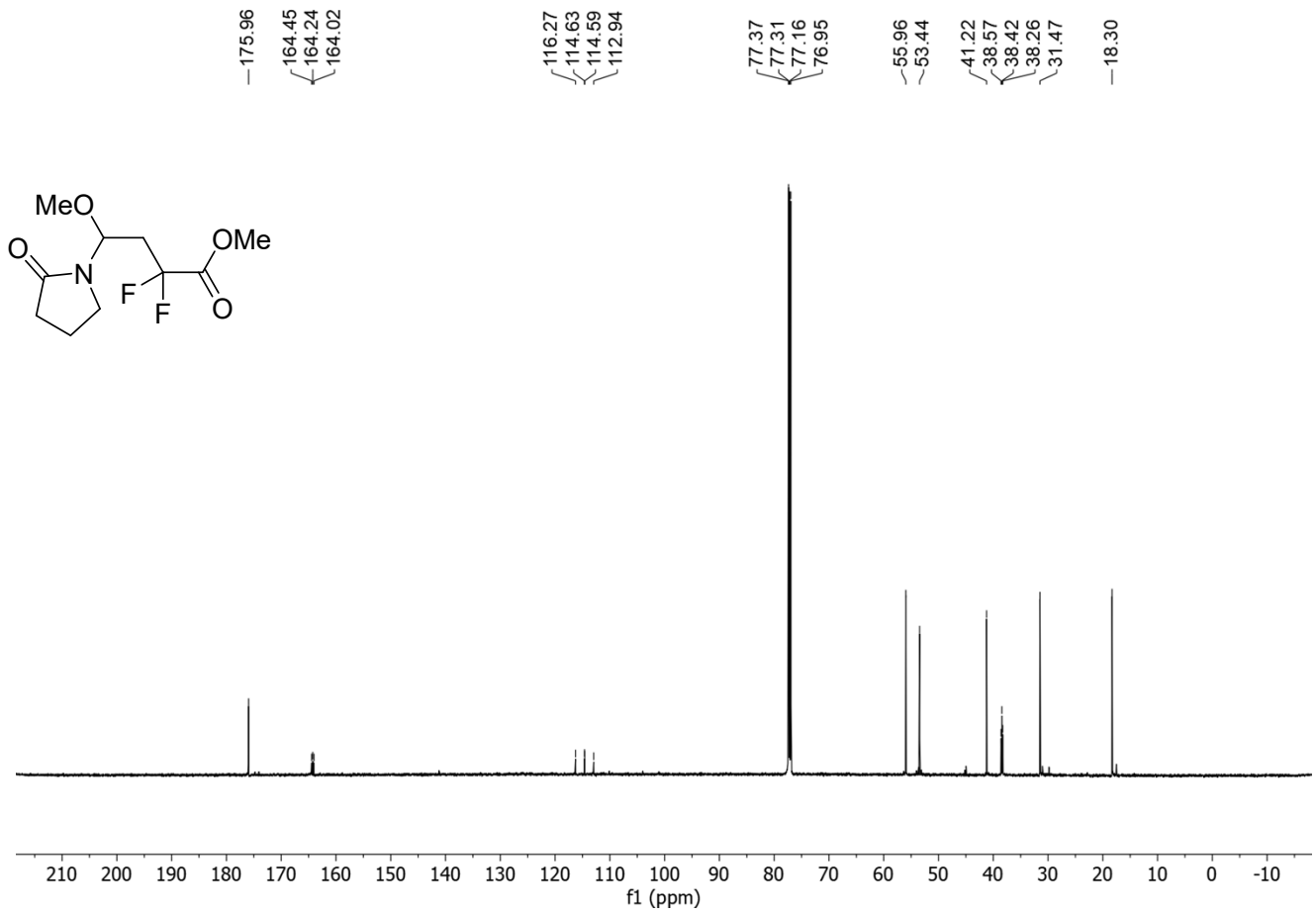


^{19}F NMR (376 MHz, $CDCl_3$) of compound **5b**.

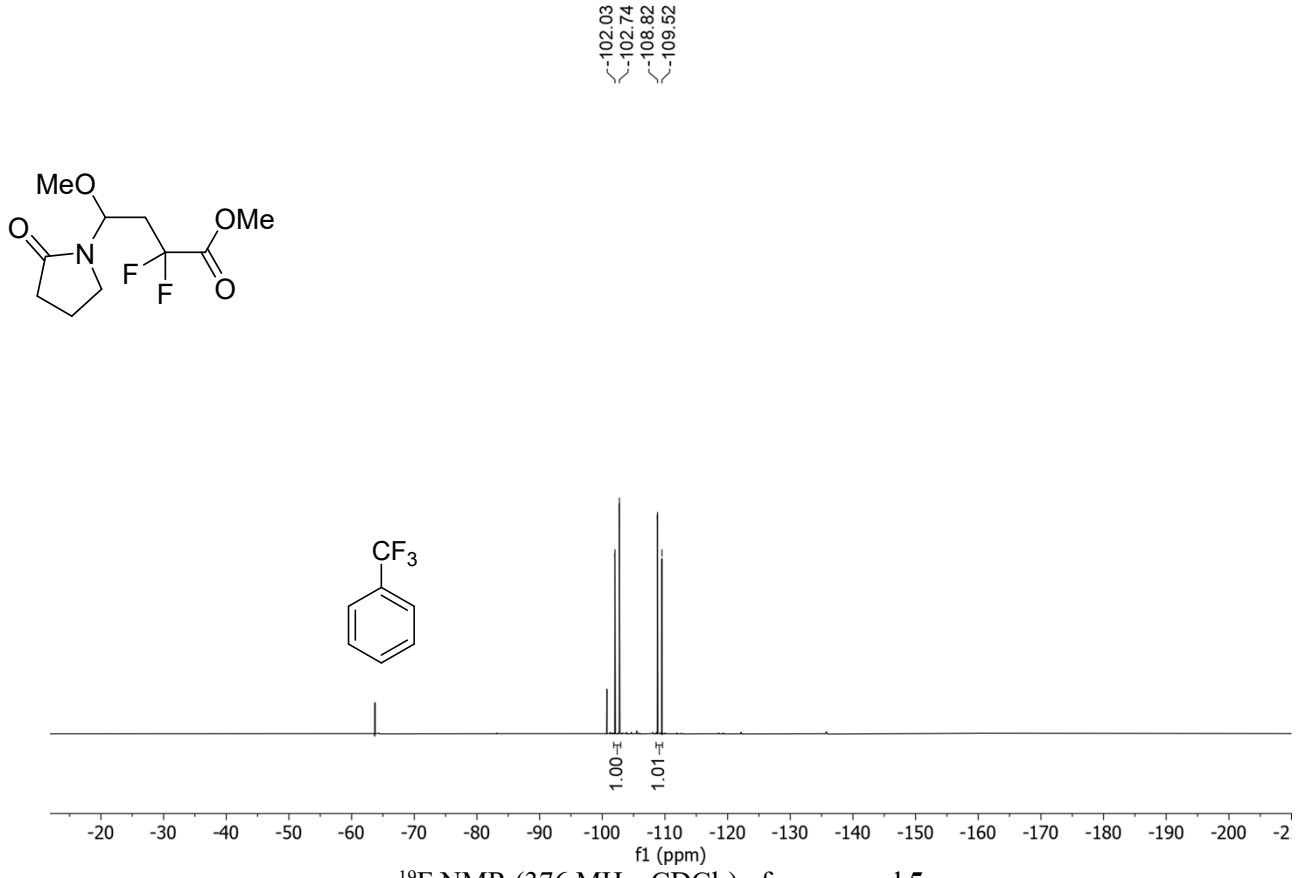




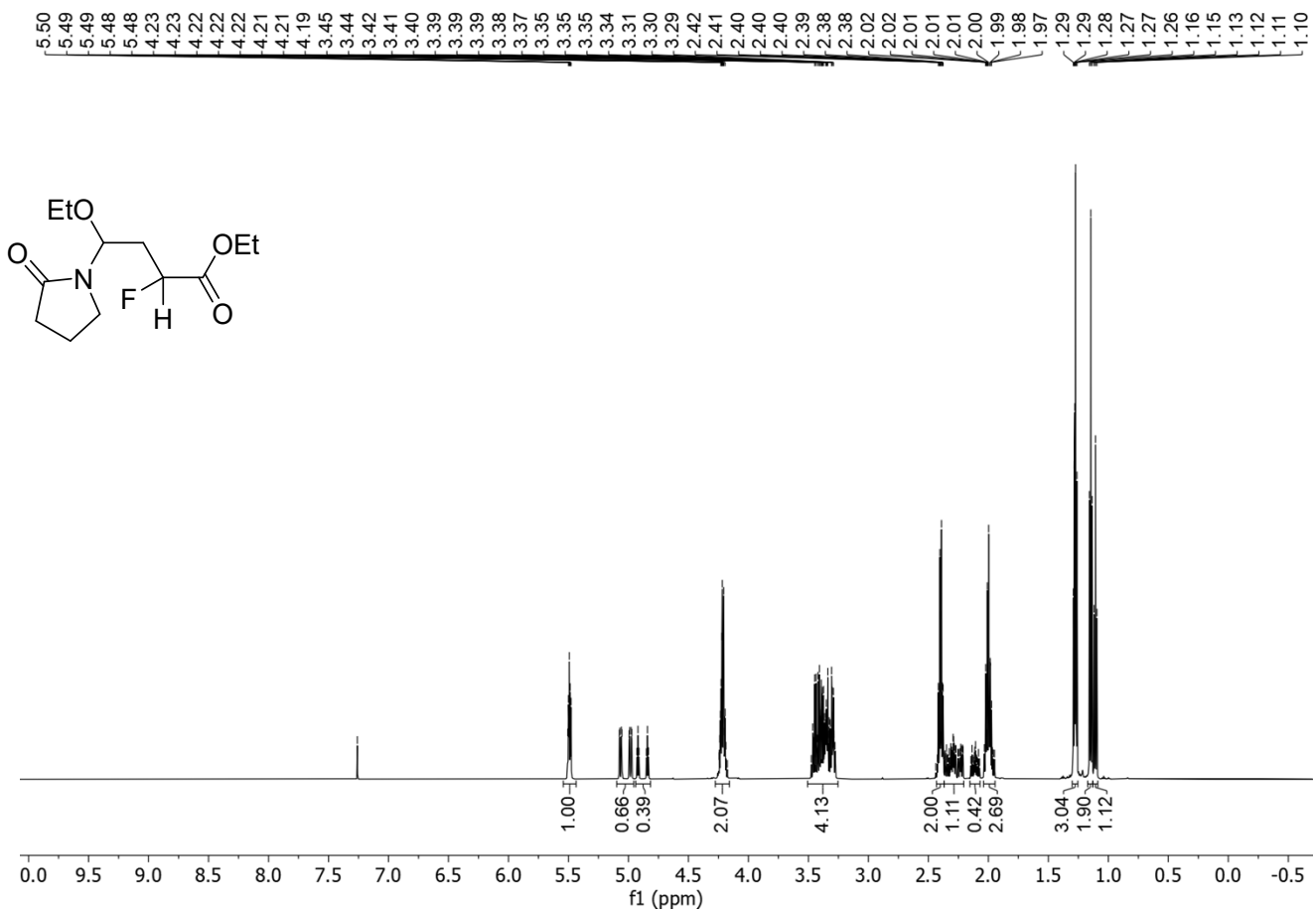
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5c**.



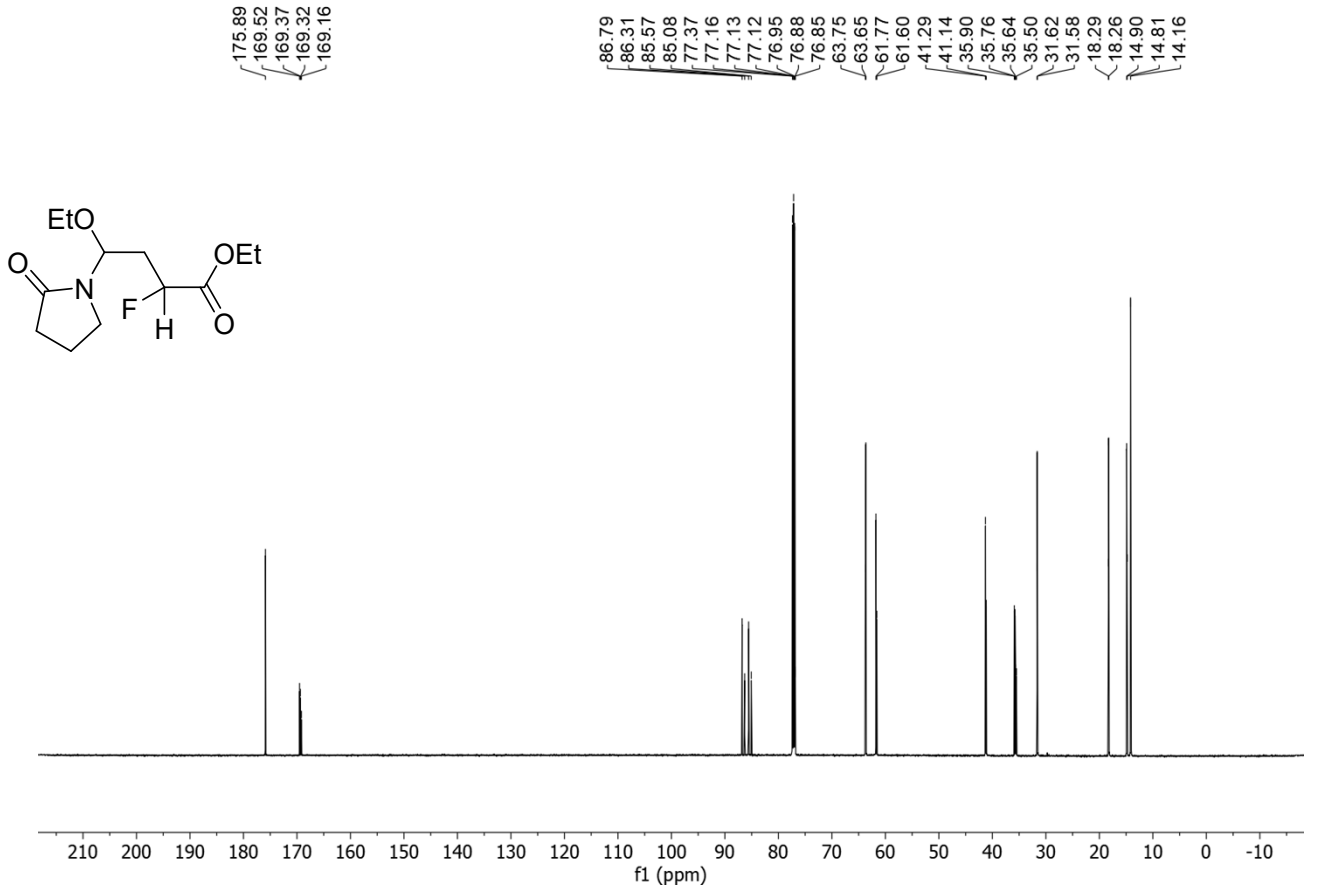
^{13}C NMR (151 MHz, $CDCl_3$) of compound **5c**.



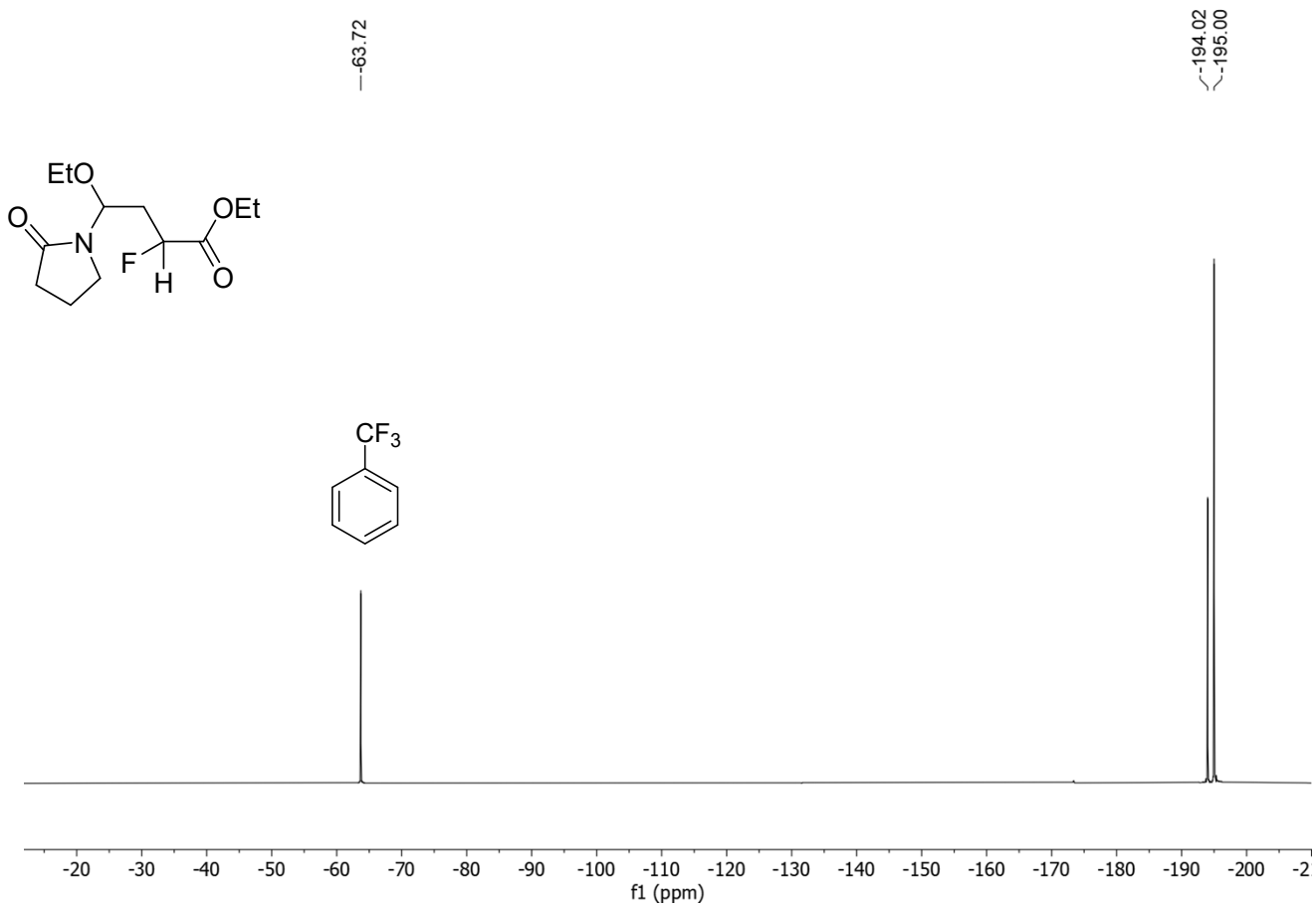
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5c**.



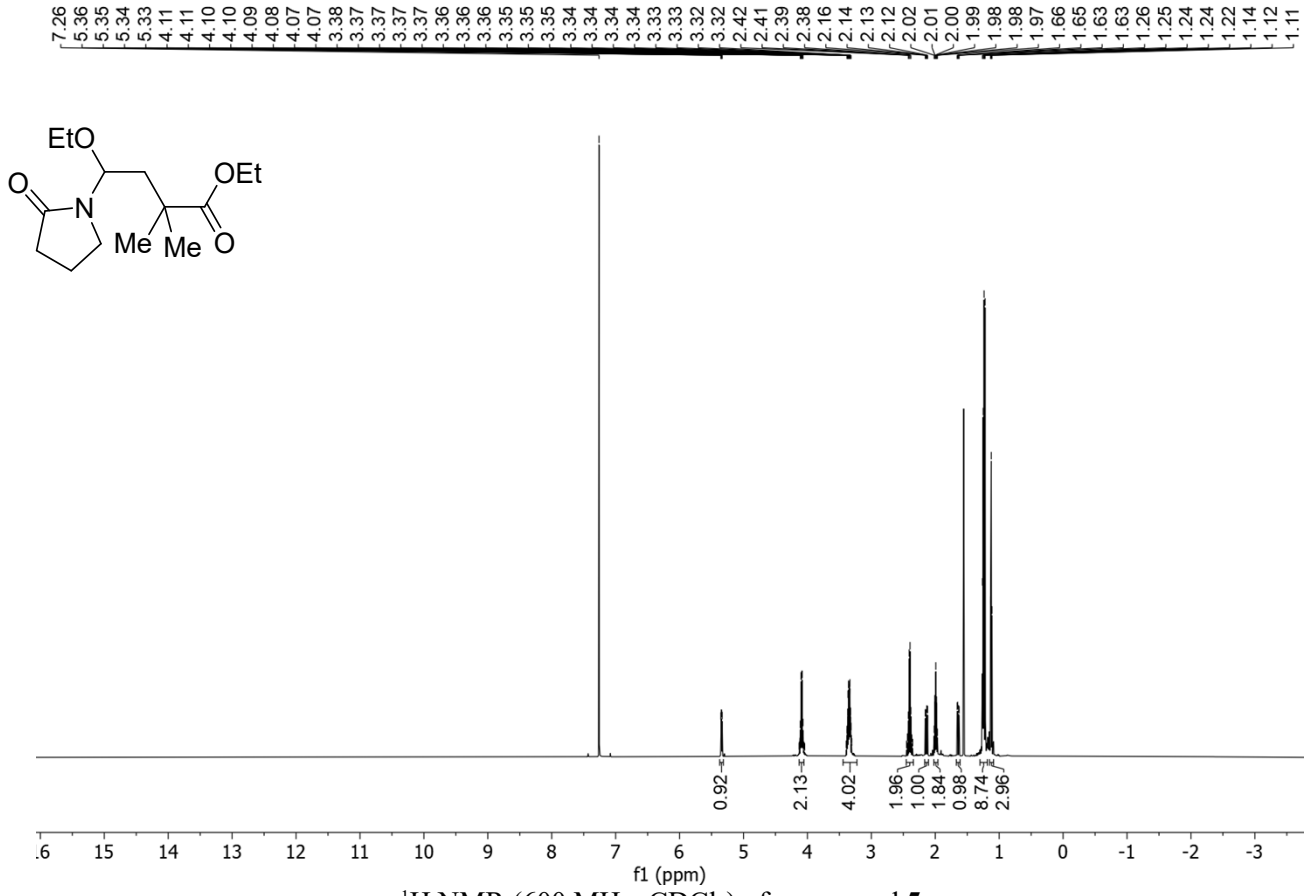
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5d**.



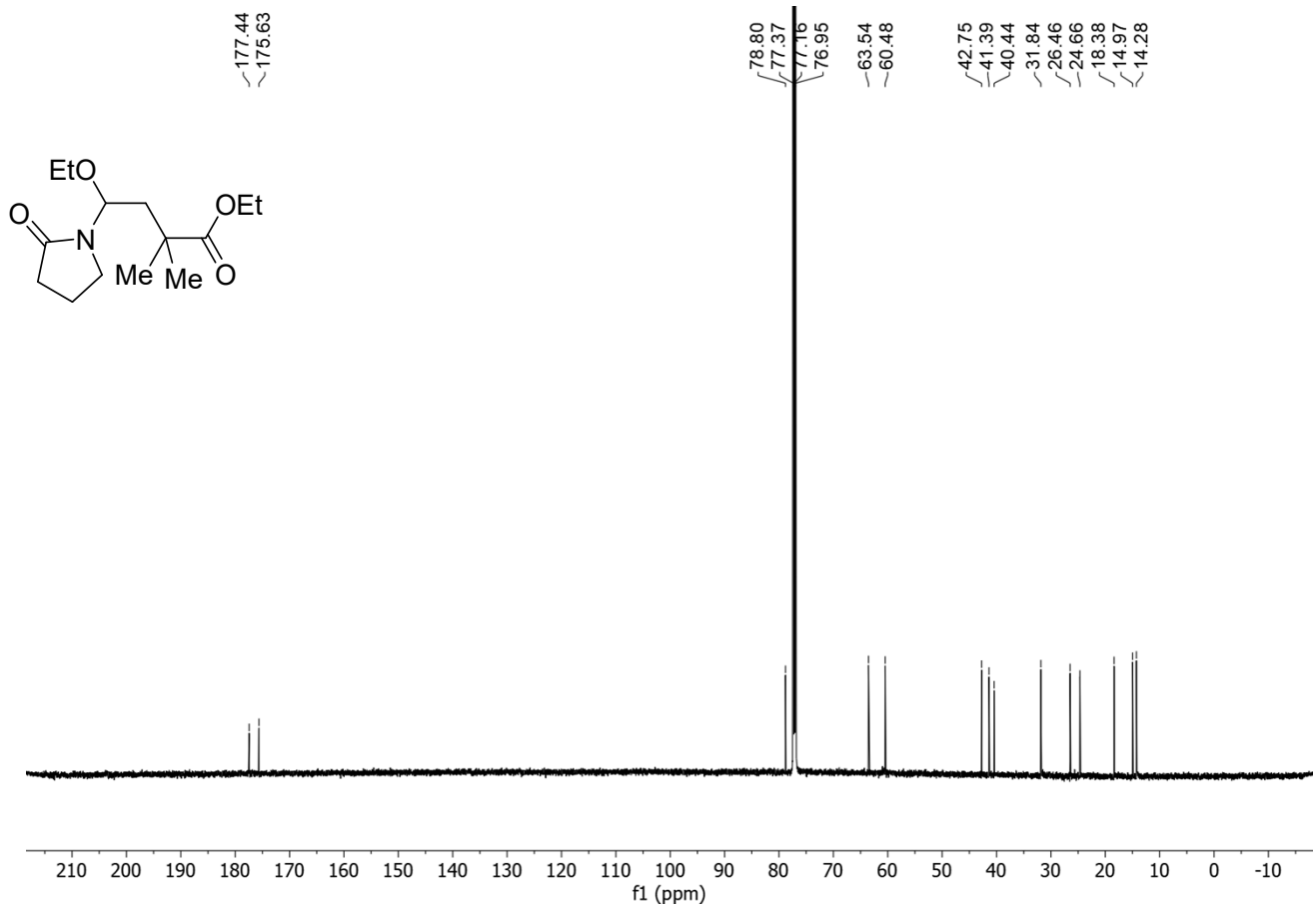
^{13}C NMR (151 MHz, $CDCl_3$) of compound **5d**.



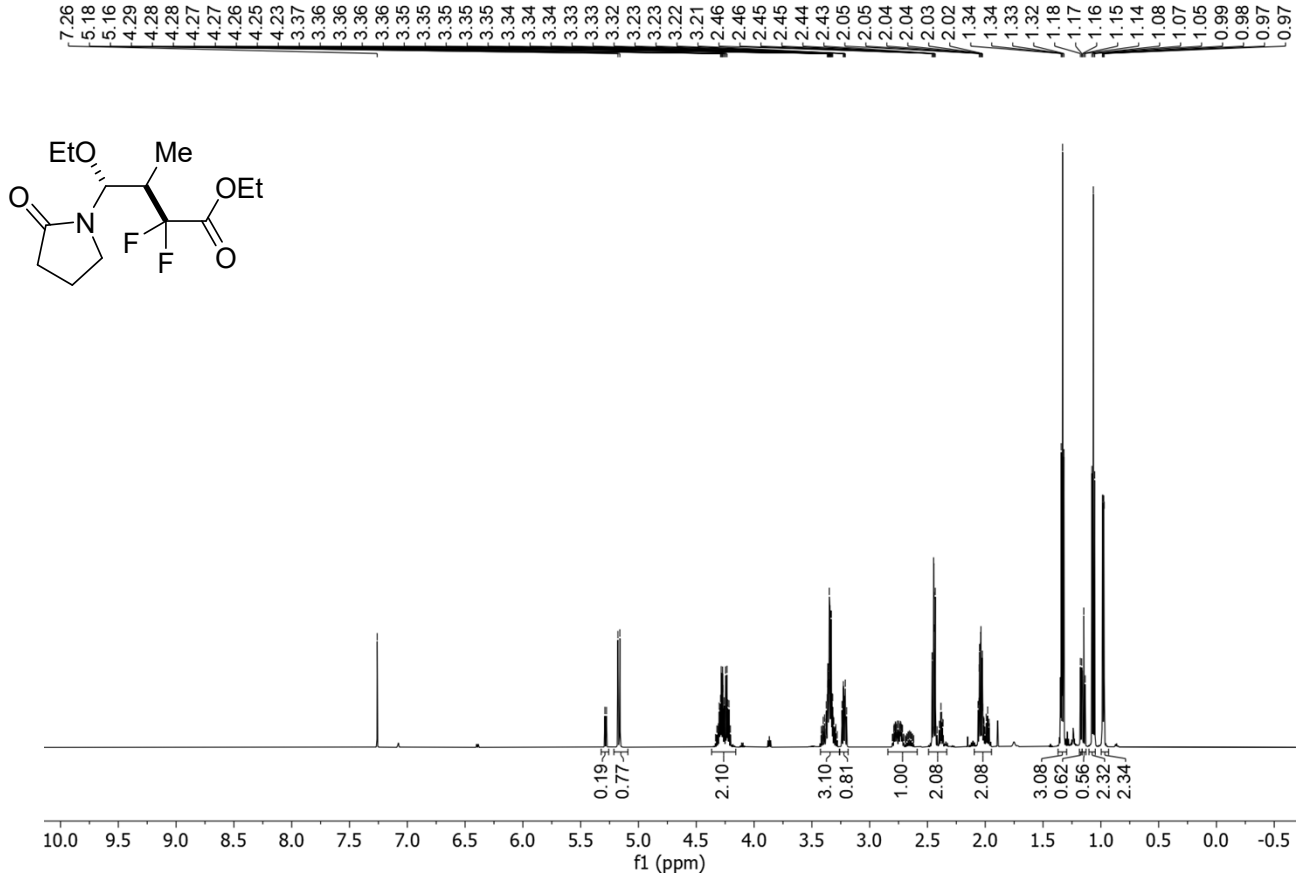
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5d**.



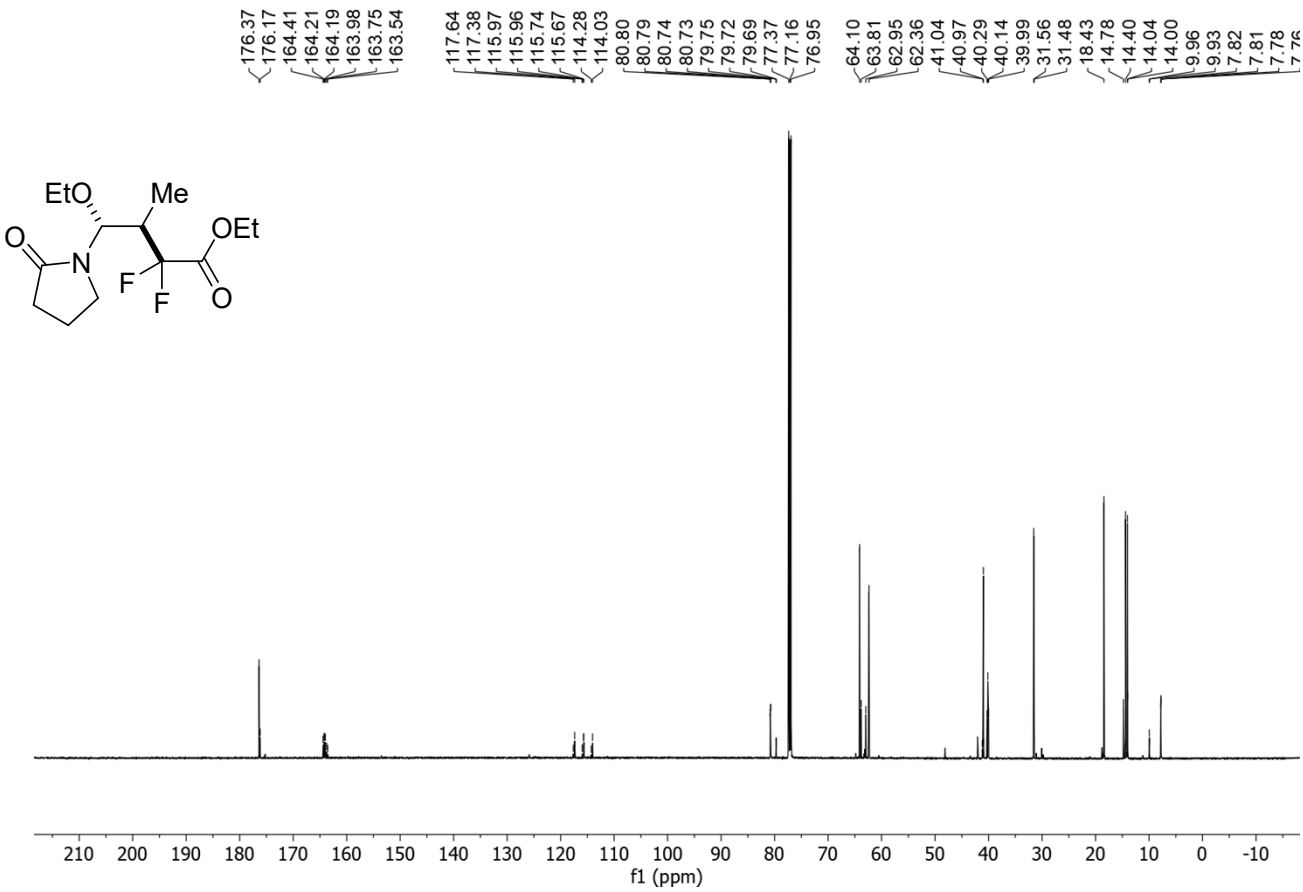
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5e**.



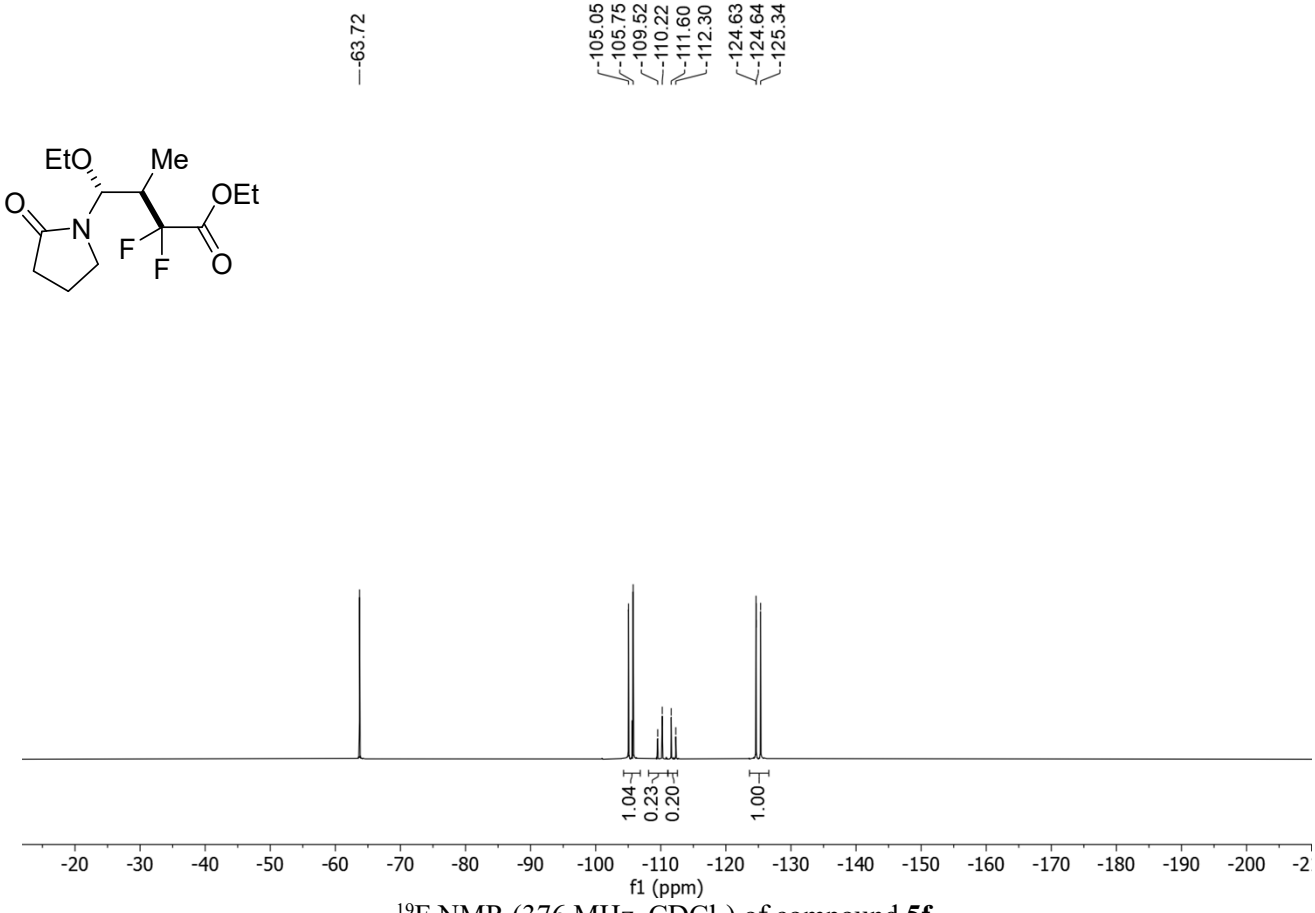
^{13}C NMR (151 MHz, $CDCl_3$) of compound **5e**.



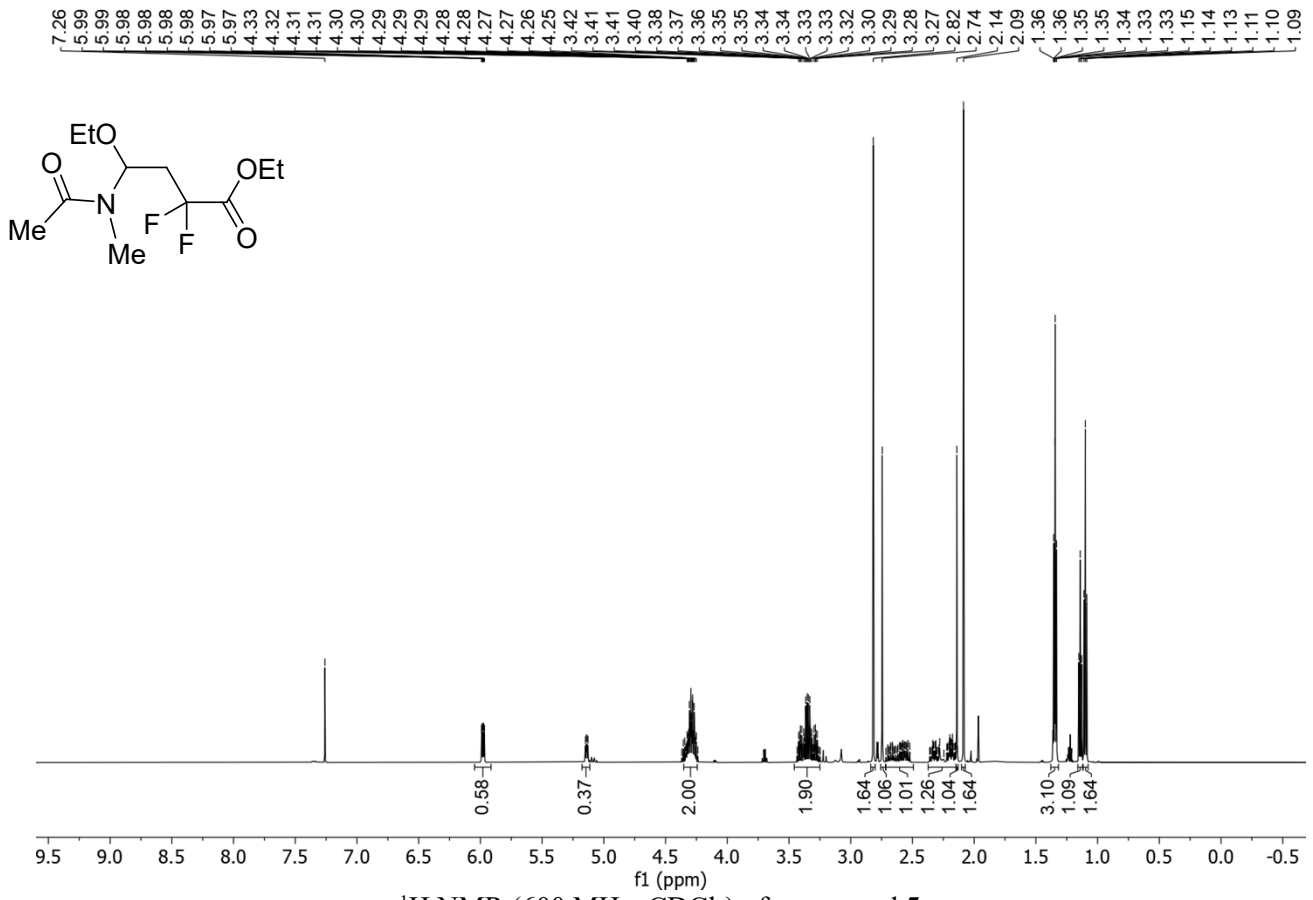
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5f.**



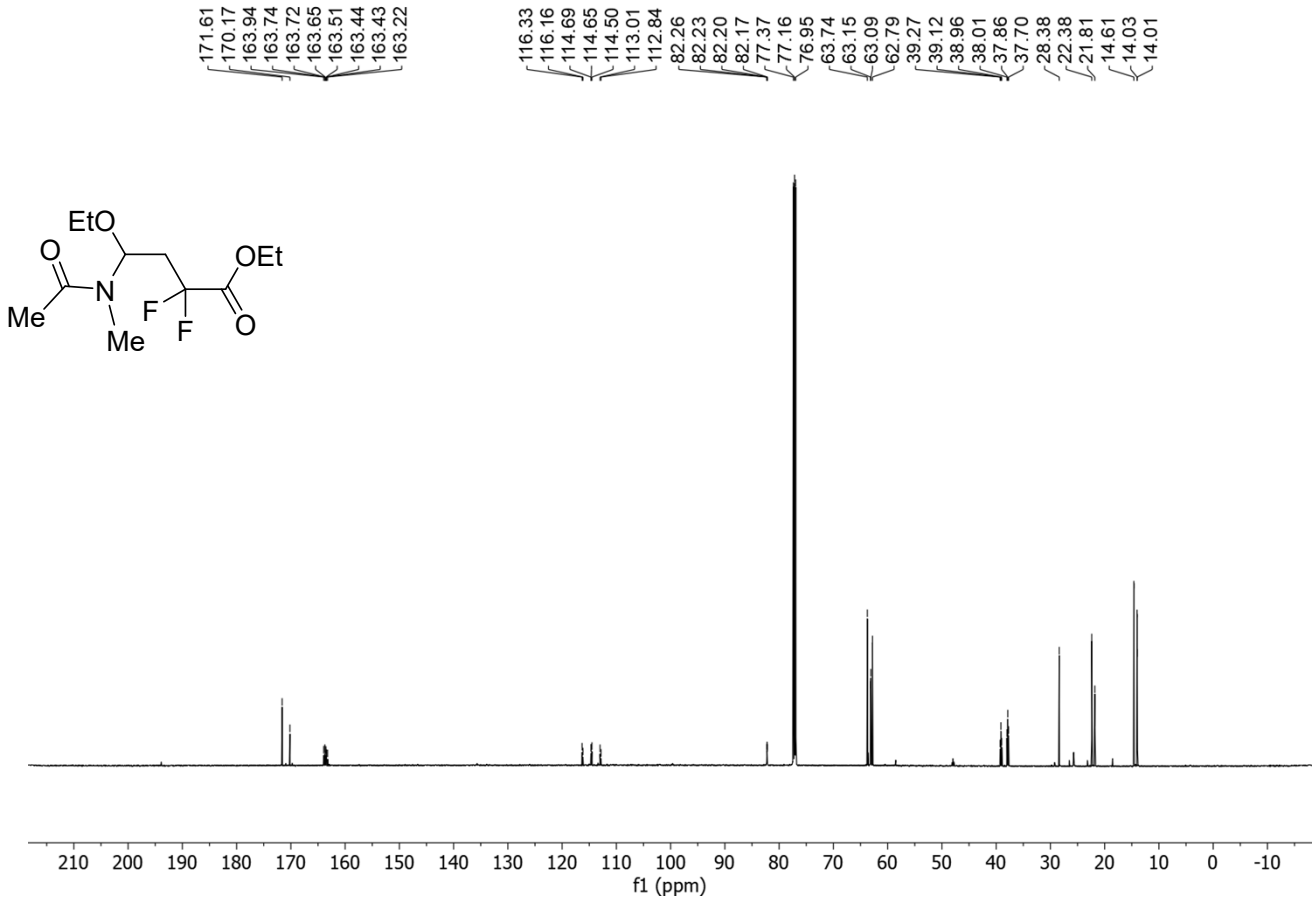
^{13}C NMR (151 MHz, $CDCl_3$) of compound **5f**.



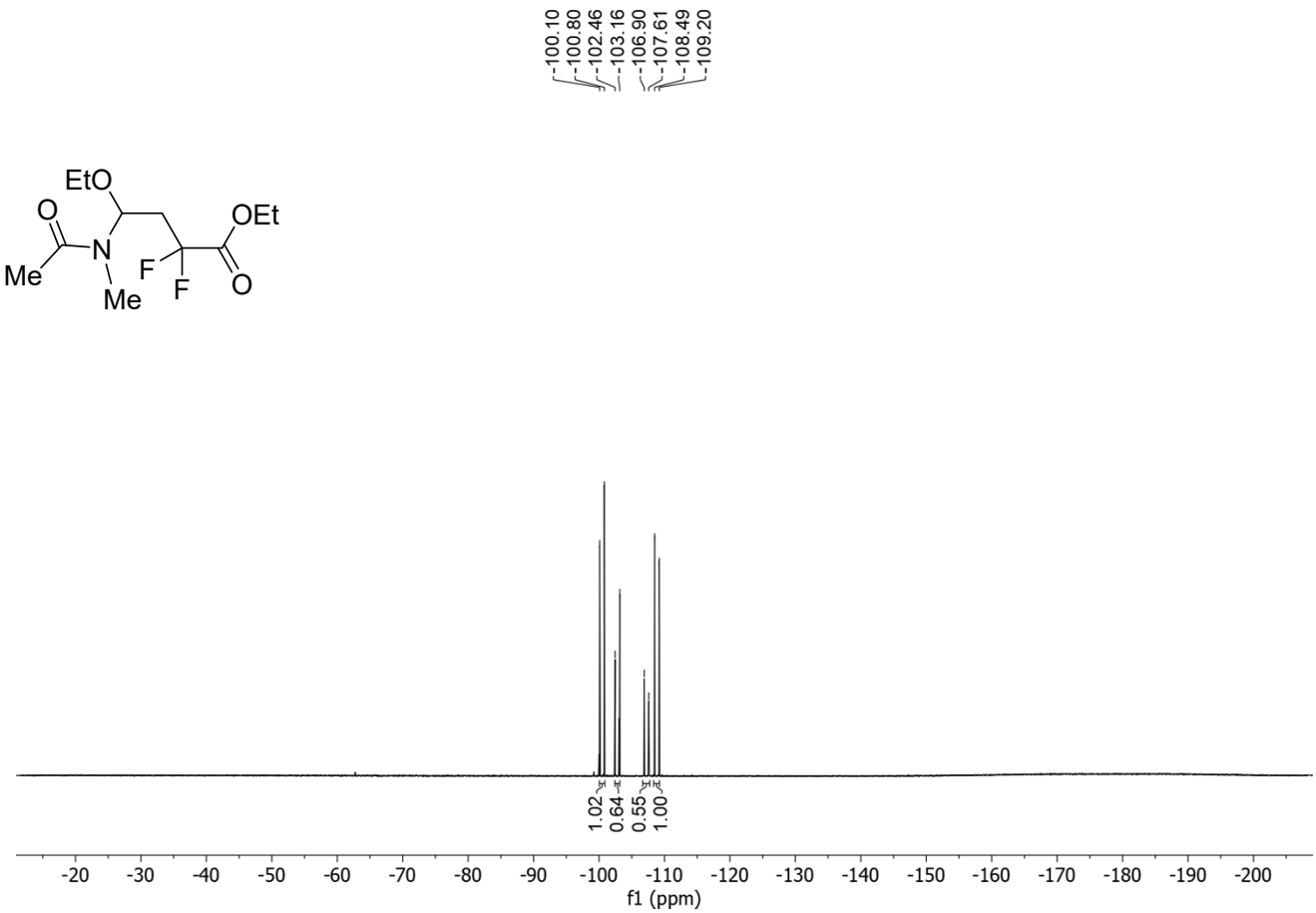
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5f**.



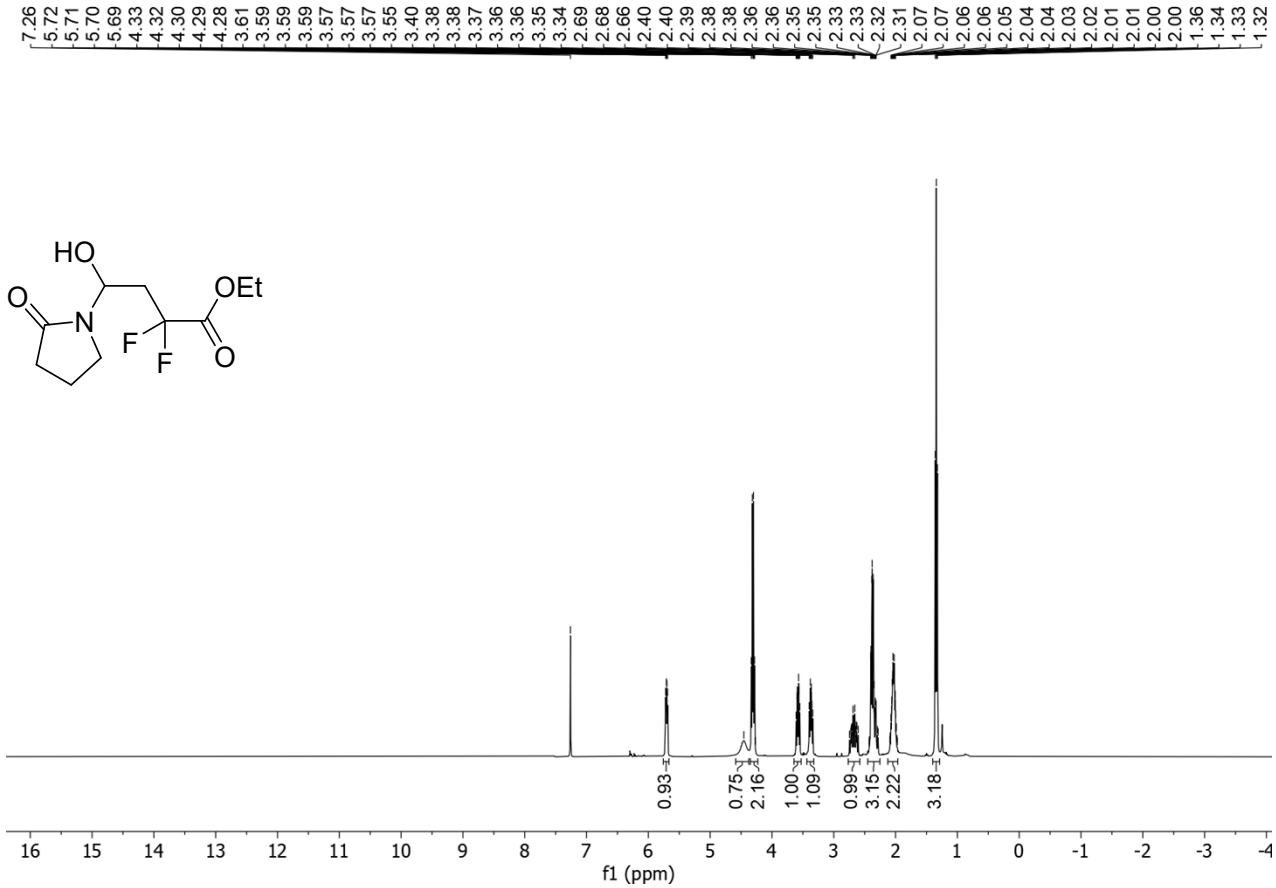
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5g**.



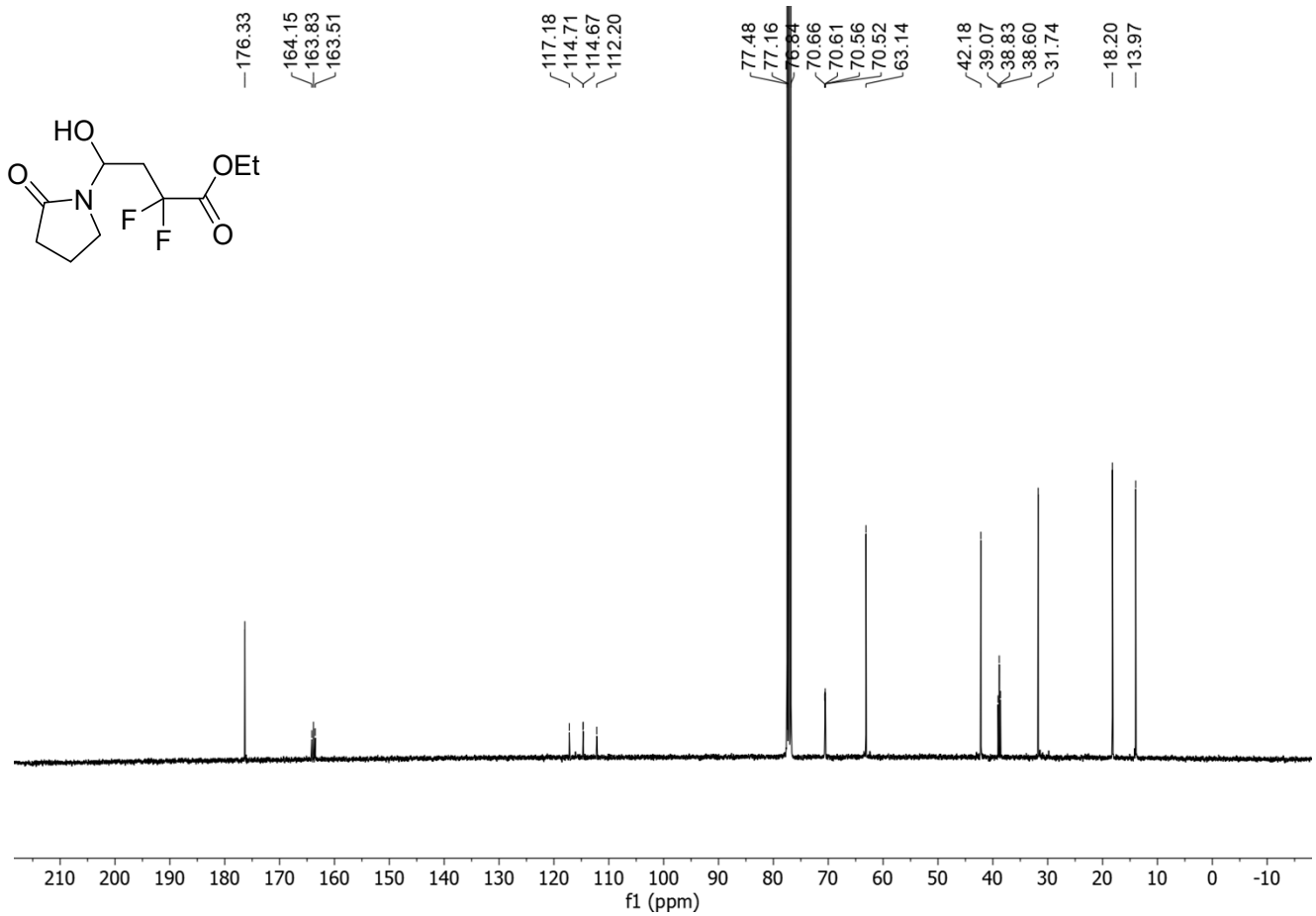
^{13}C NMR (151 MHz, $CDCl_3$) of compound **5g**.



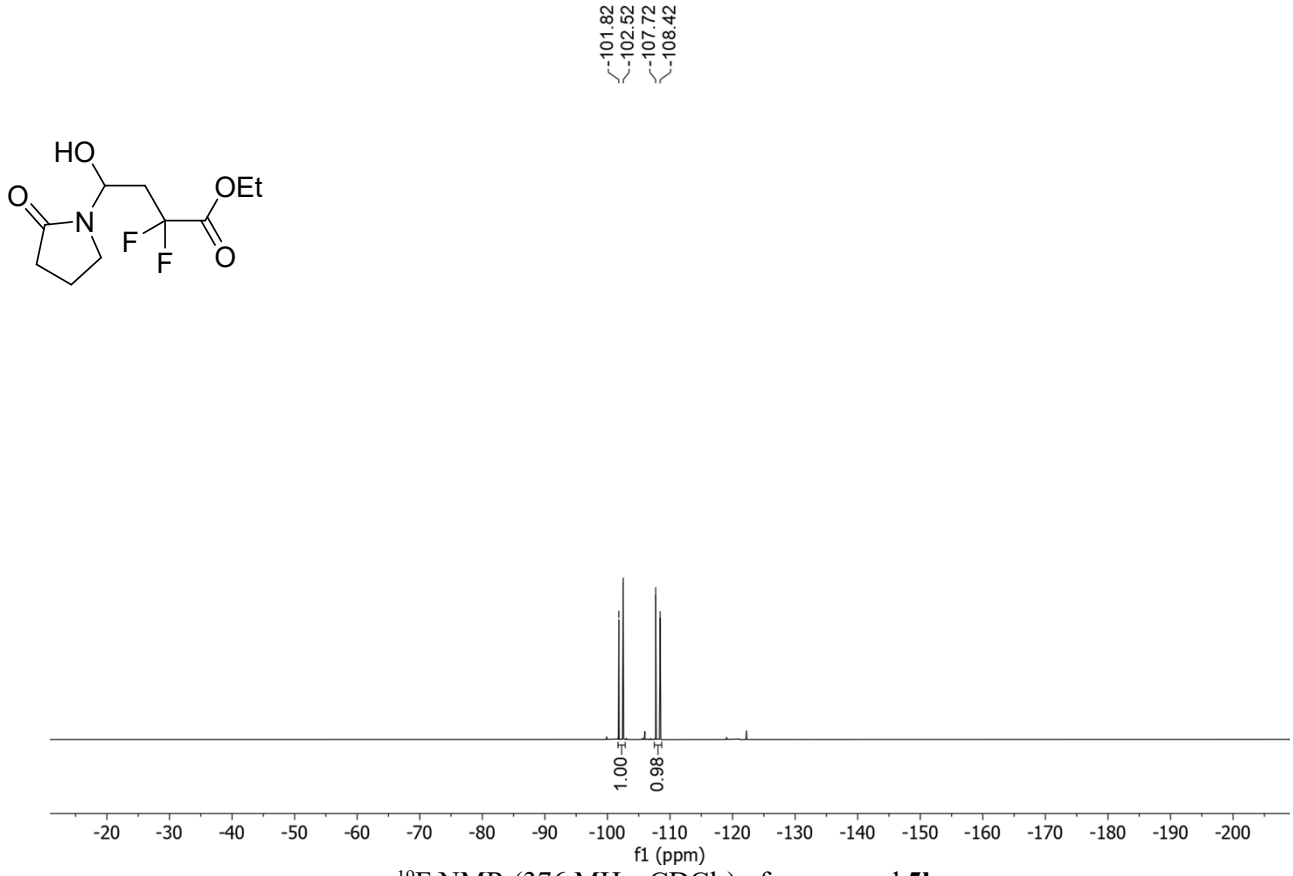
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5g**.



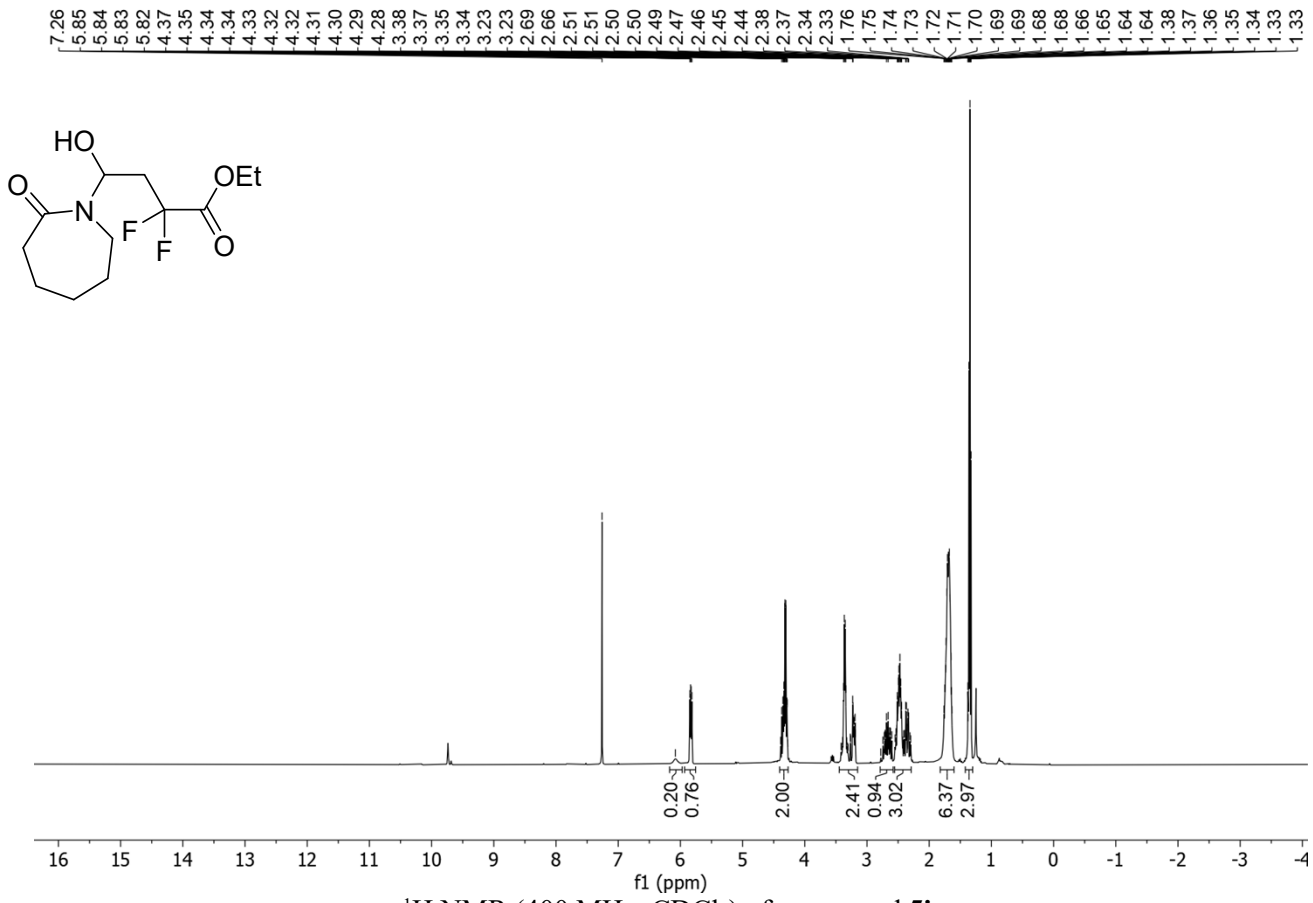
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5h**.



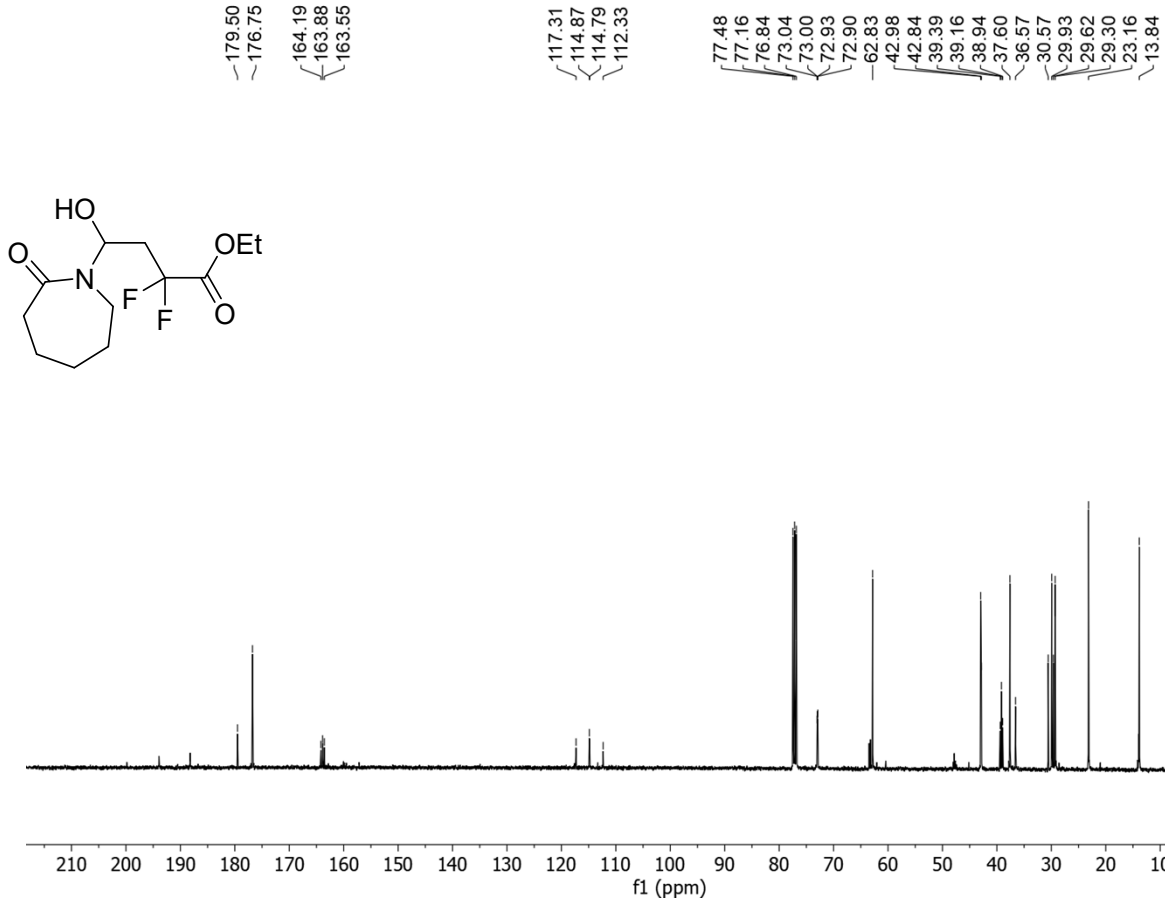
^{13}C NMR (400 MHz, $CDCl_3$) of compound **5h**.



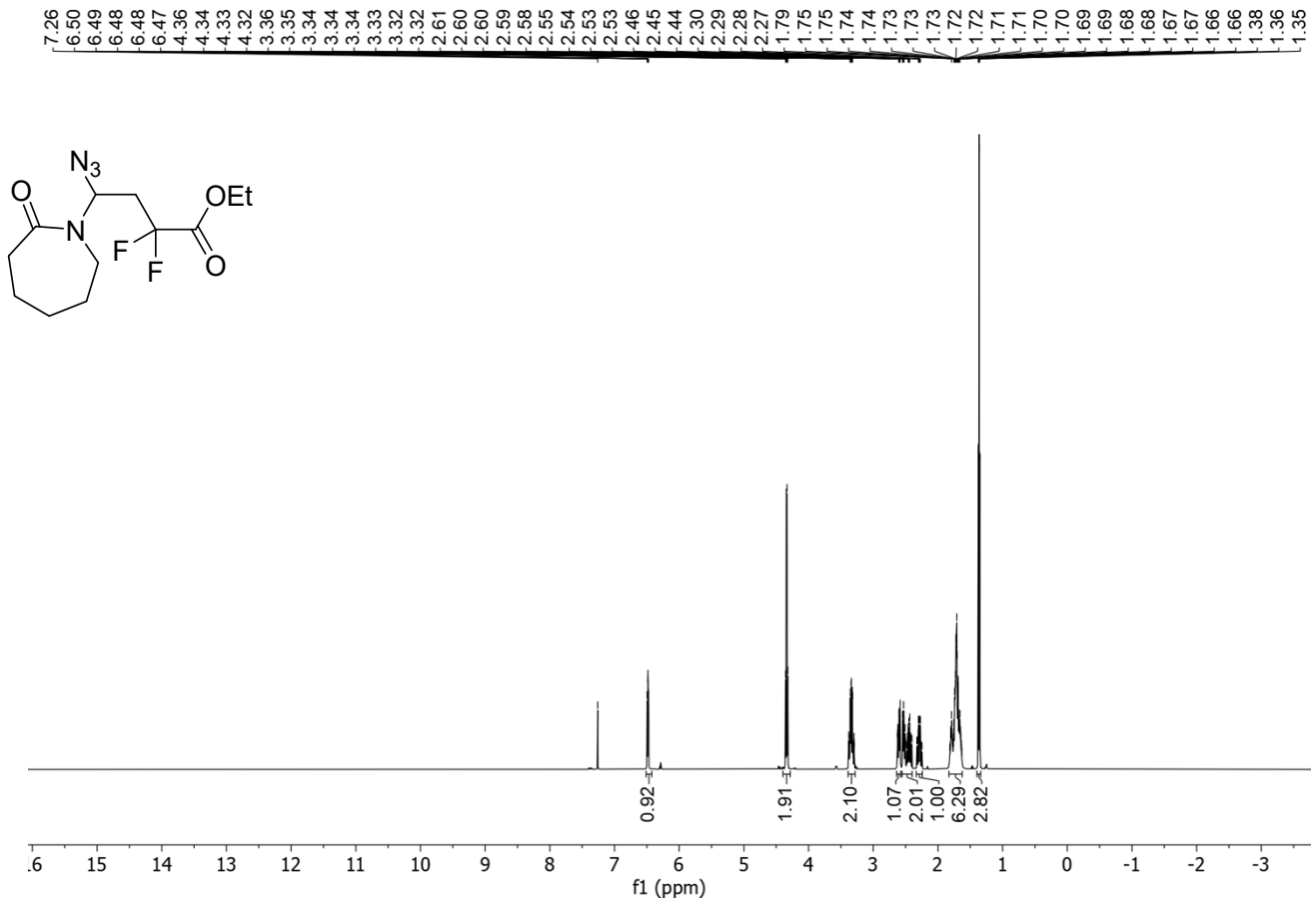
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5h**.



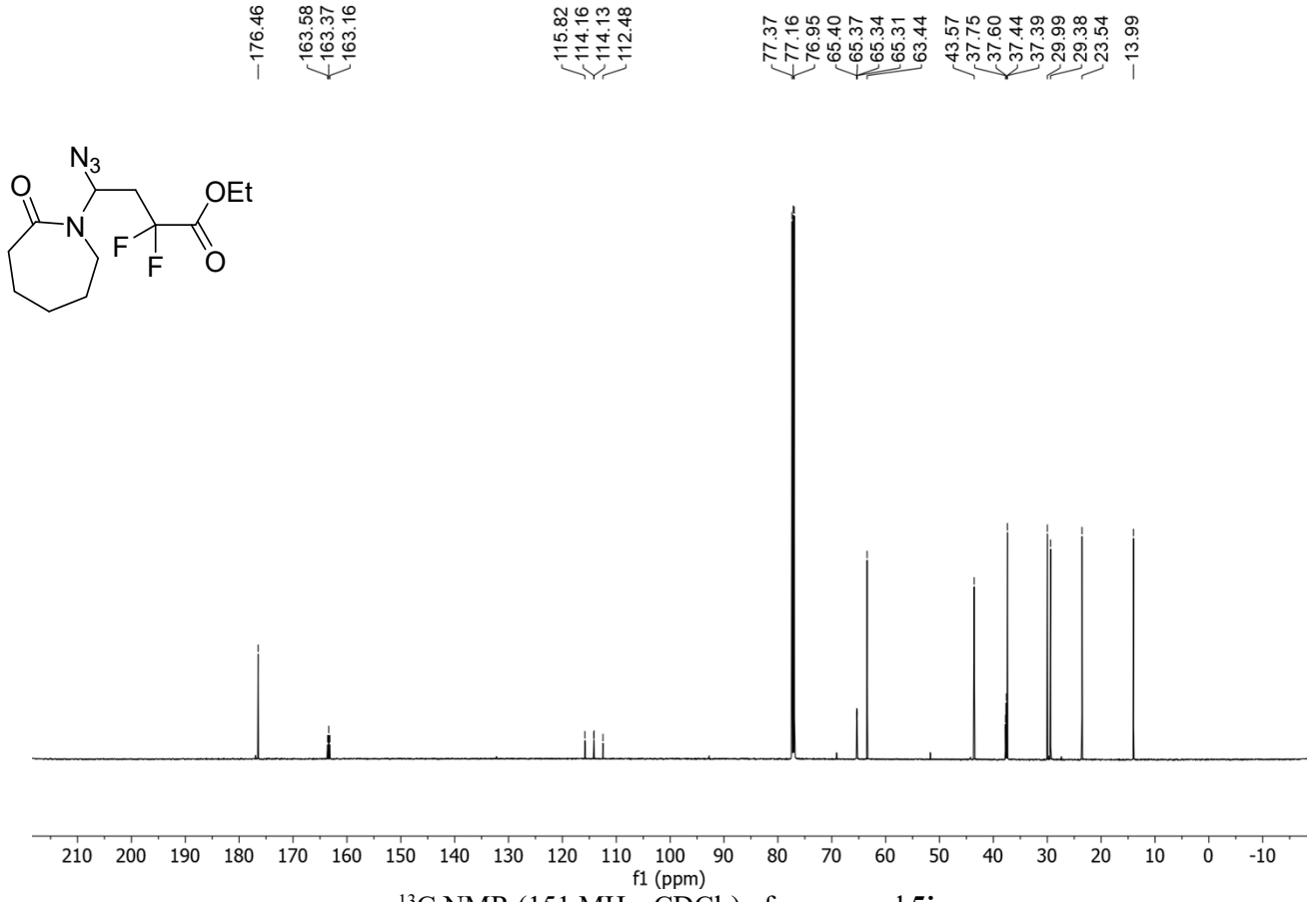
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5i**.



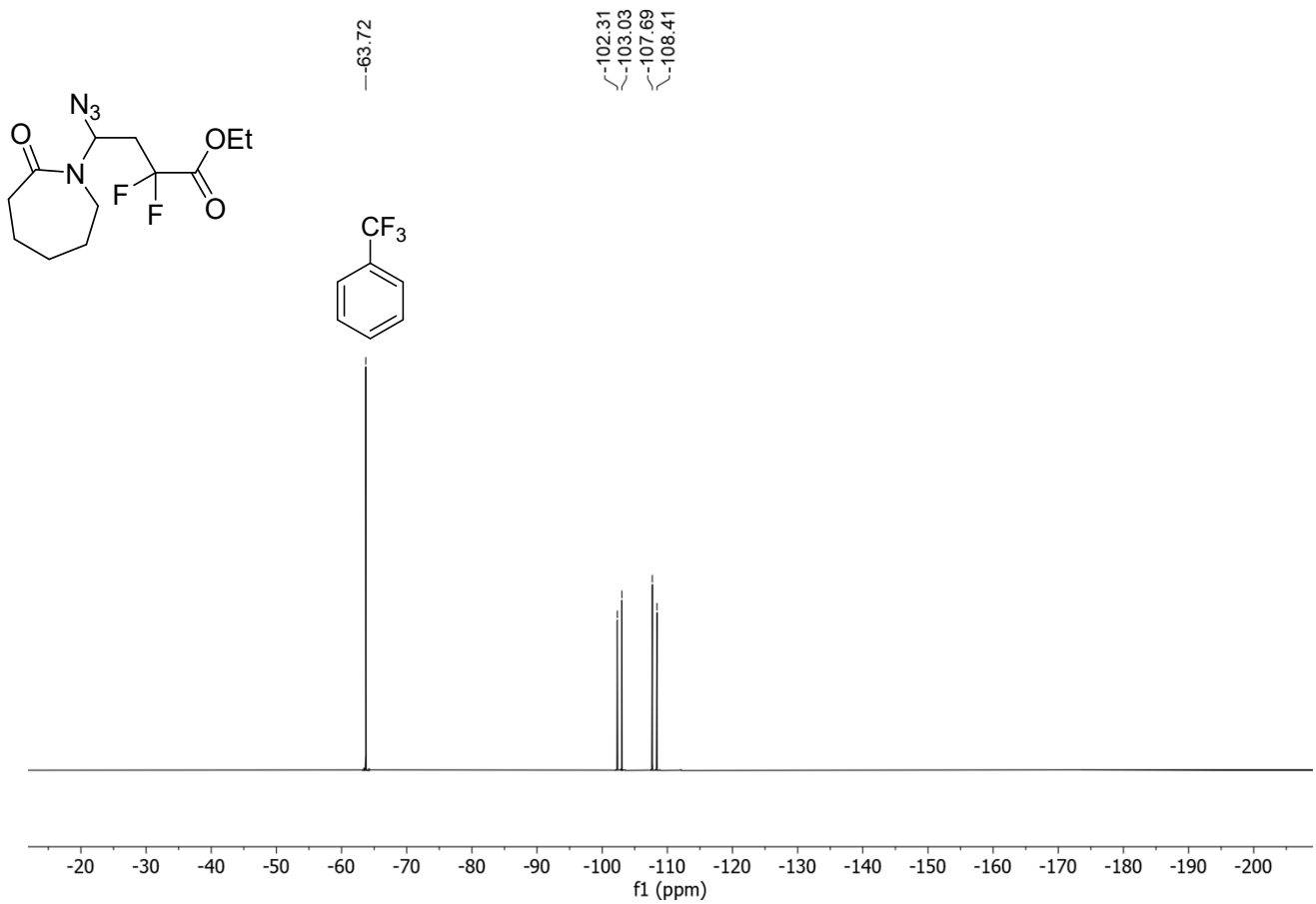
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5i**.



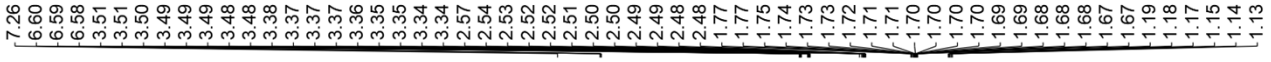
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5j**.

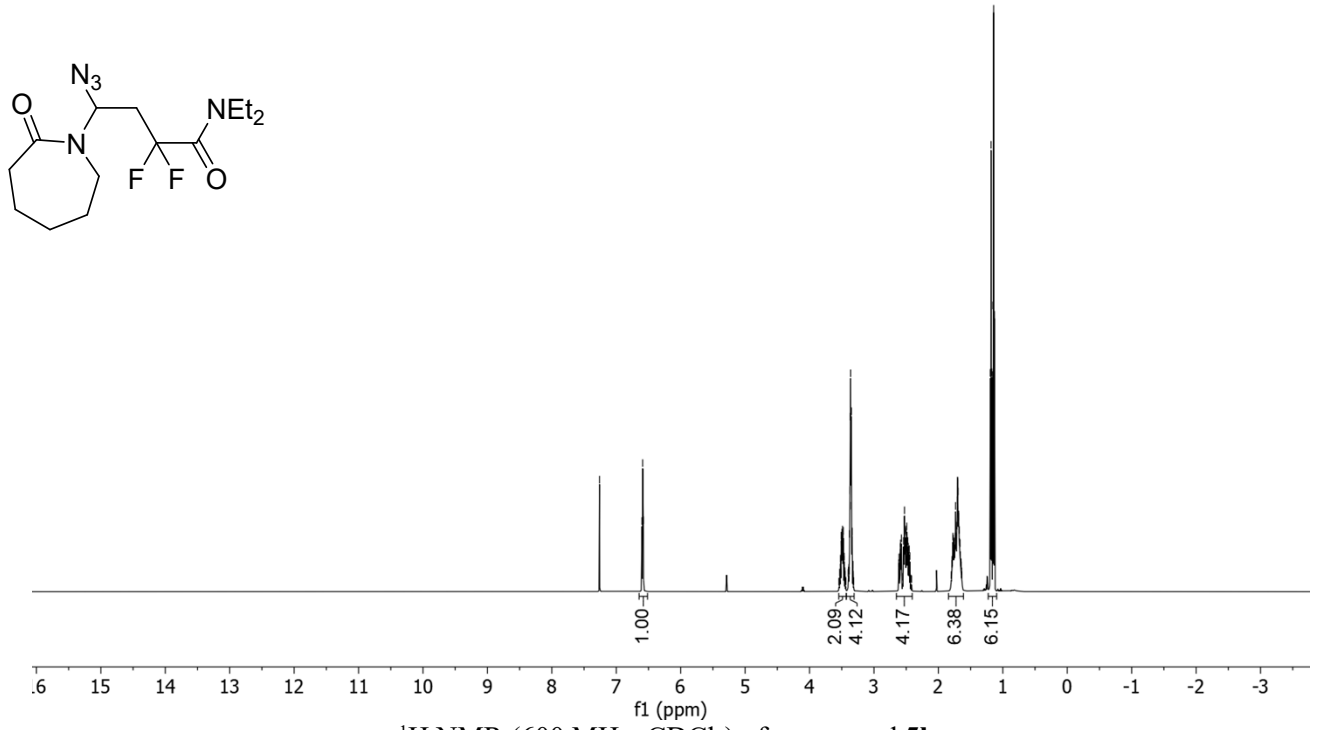


^{13}C NMR (151 MHz, $CDCl_3$) of compound **5j**.

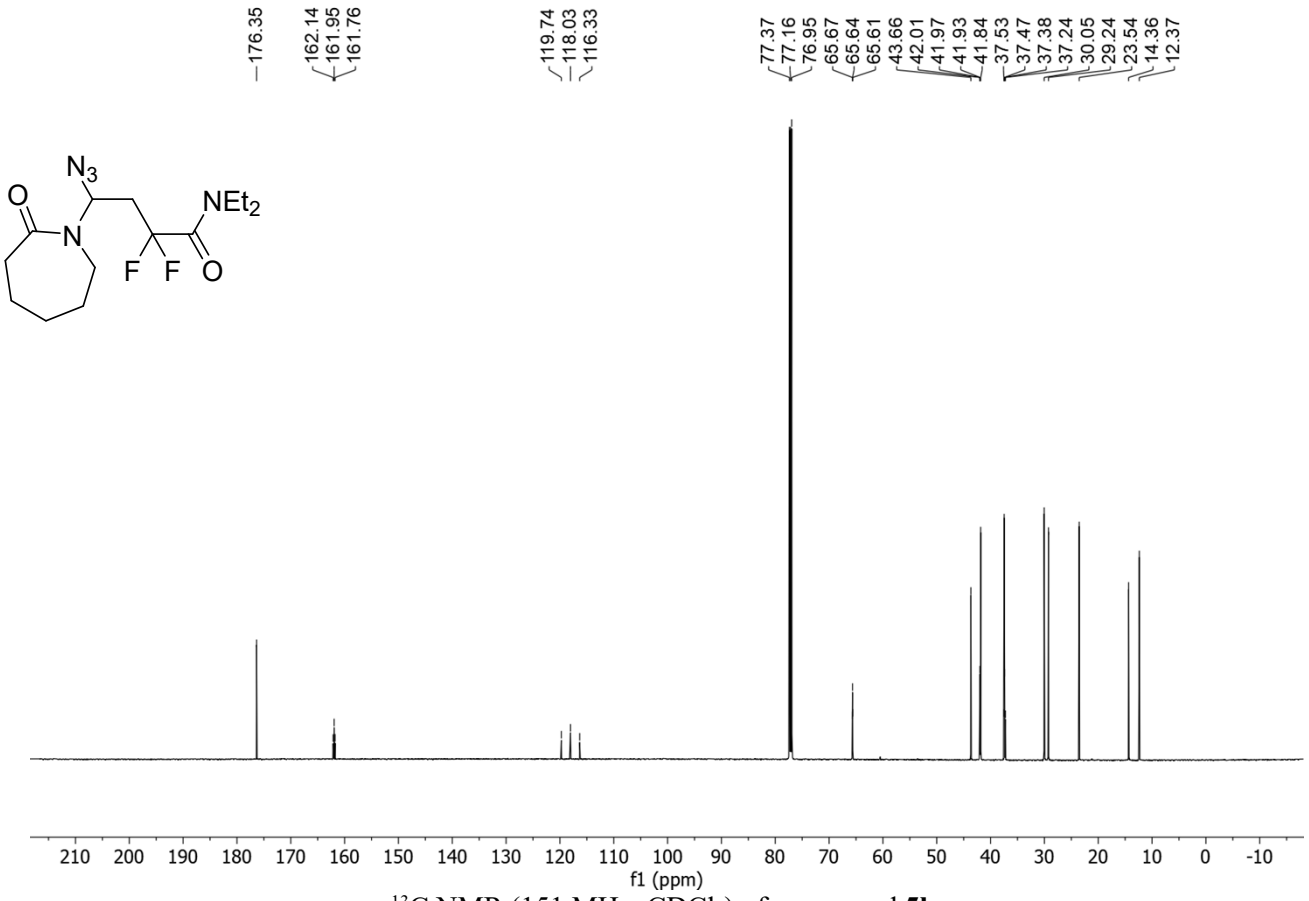


^{19}F NMR (376 MHz, $CDCl_3$) of compound **5j**.

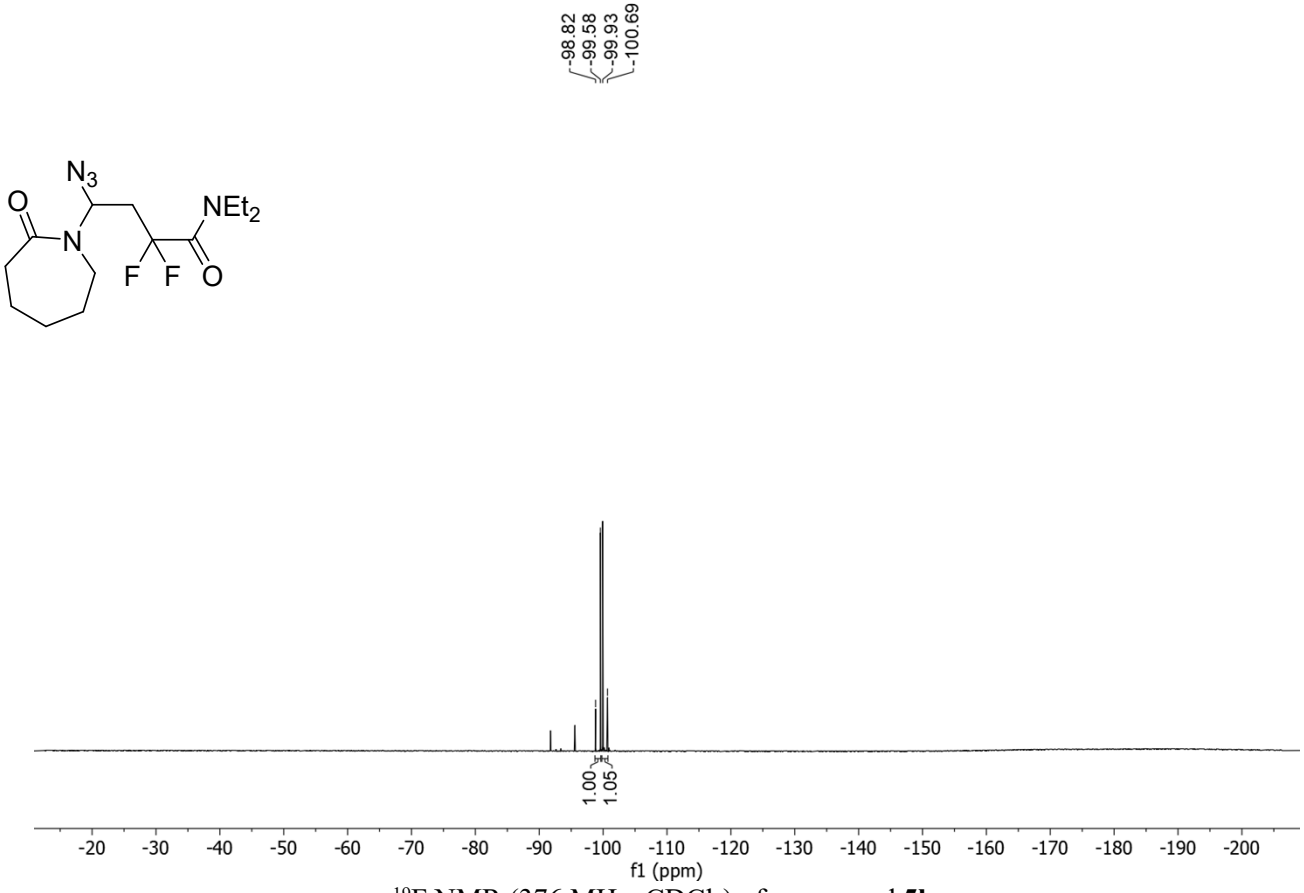




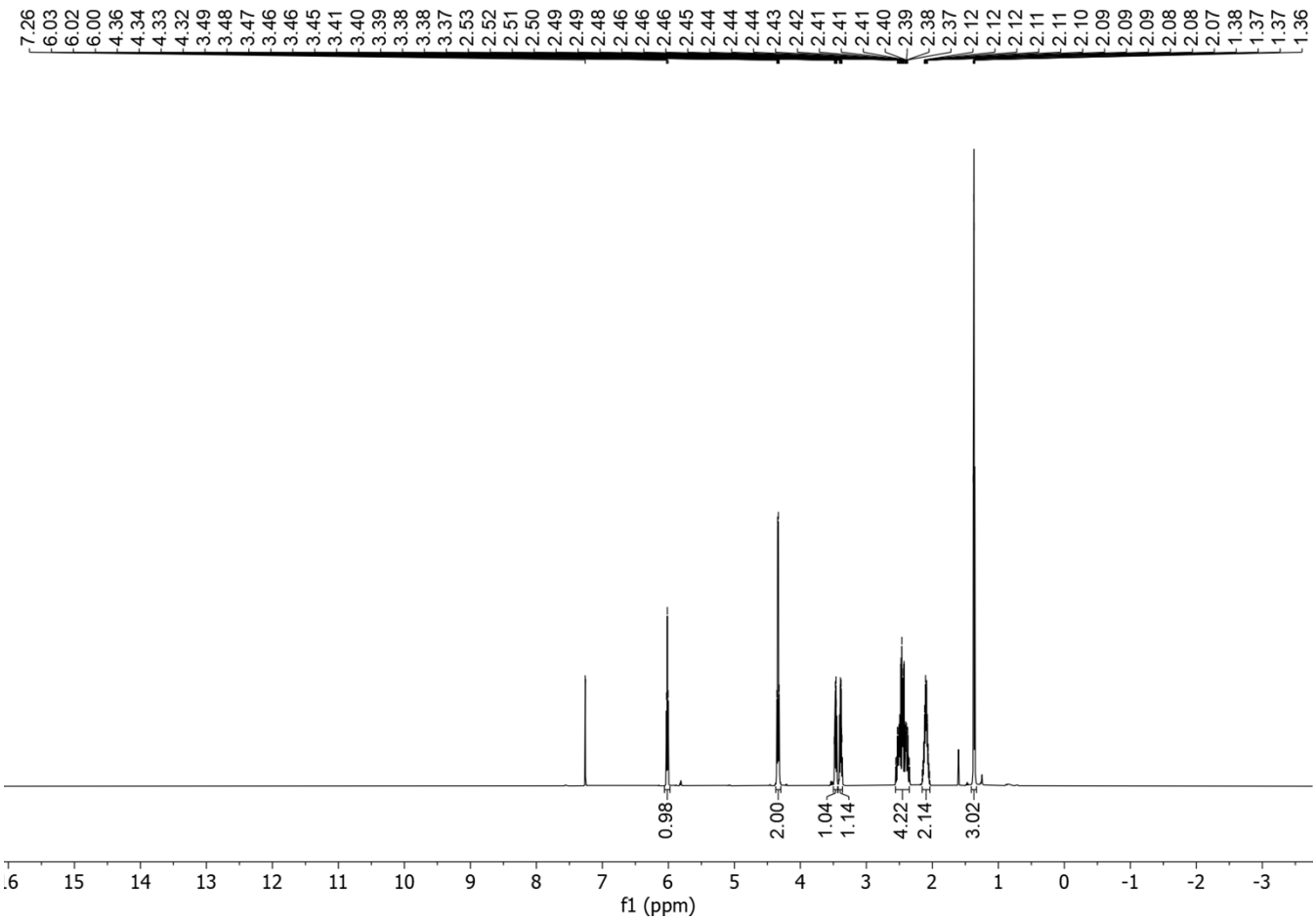
^{1}H NMR (600 MHz, $CDCl_3$) of compound **5k**.



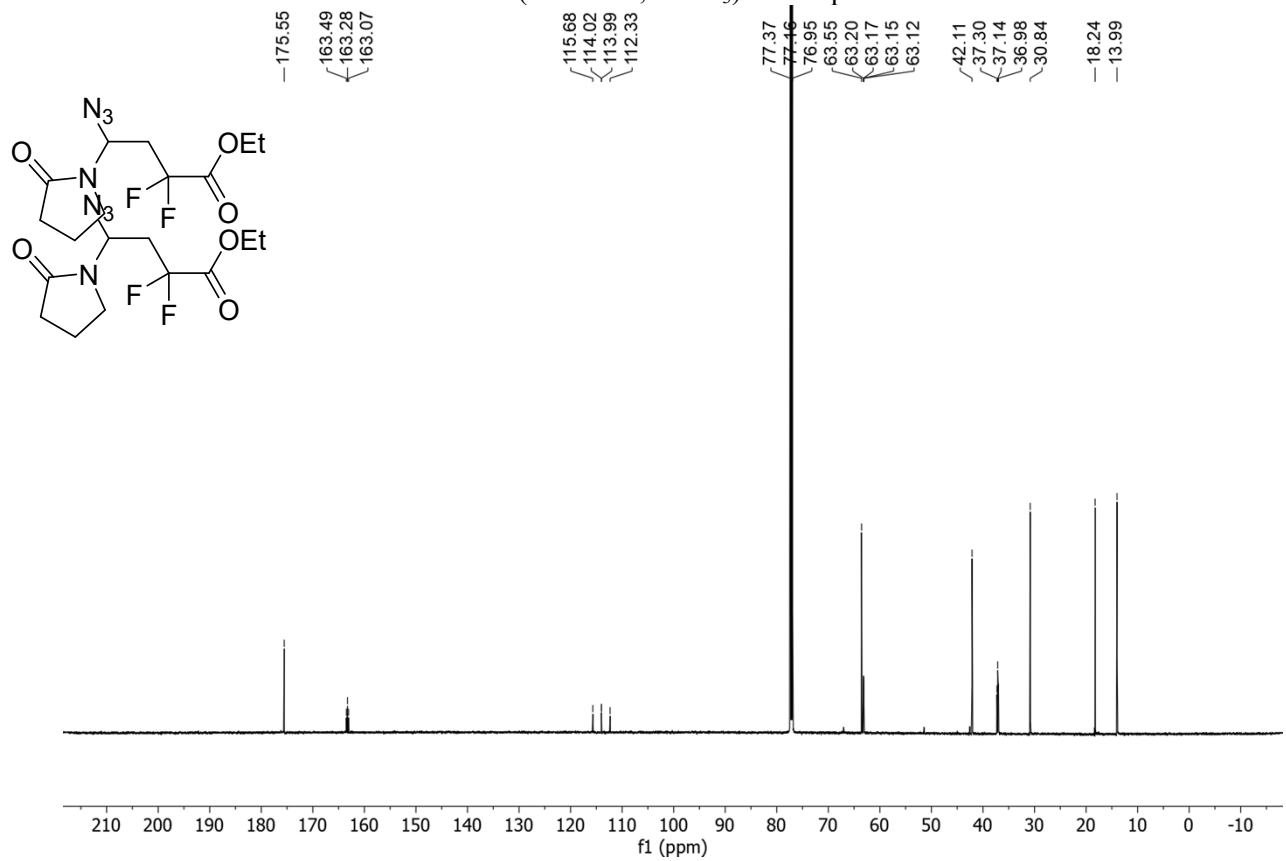
^{13}C NMR (151 MHz, $CDCl_3$) of compound **5k**.



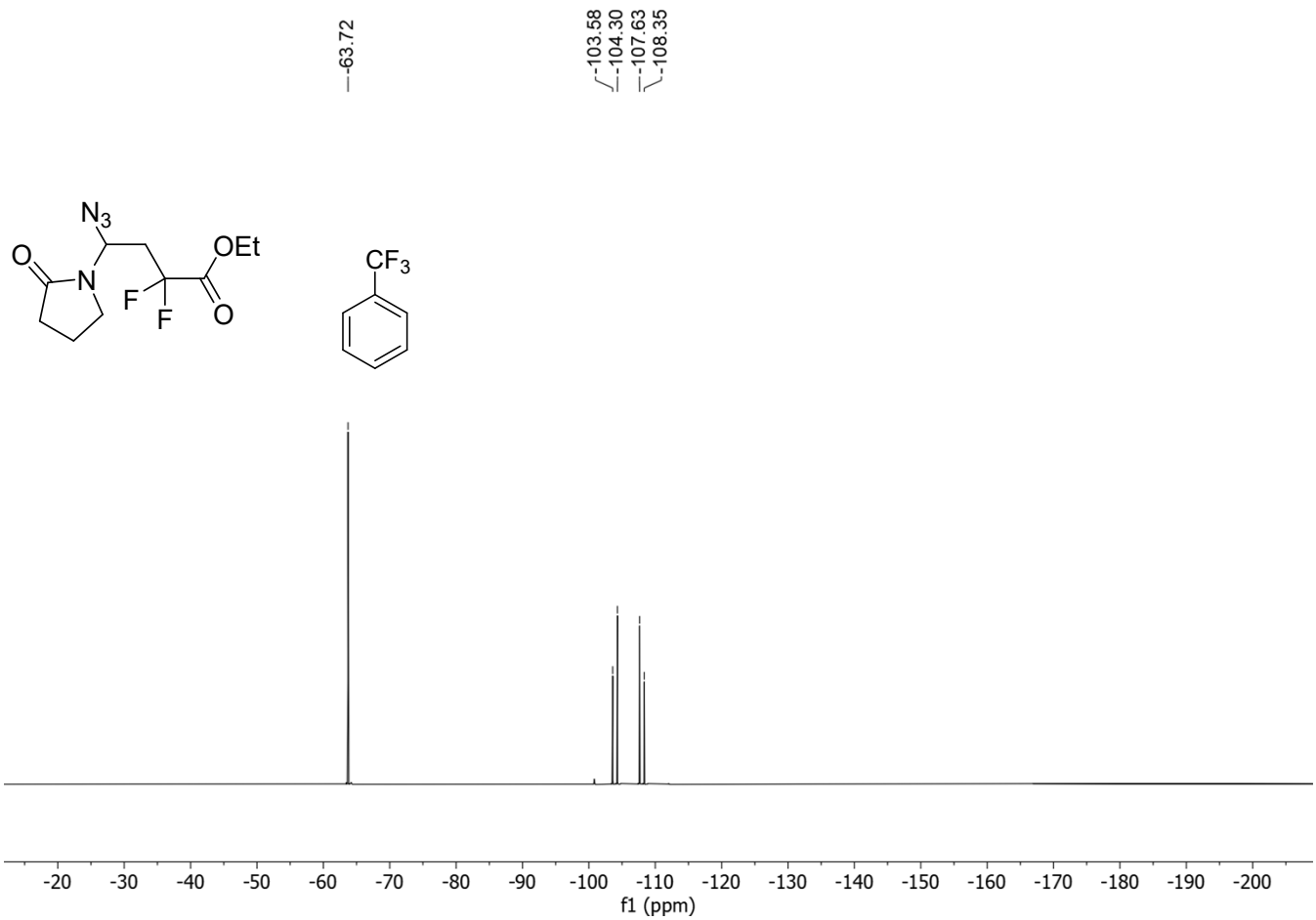
^{19}F NMR (376 MHz, $CDCl_3$) of compound **5k**.



^{1}H NMR (600 MHz, $CDCl_3$) of compound **5l**.



^{13}C NMR (151 MHz, $CDCl_3$) of compound **5l**.



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