γ, δ, ε-C(sp^3)–H Functionalization through A Directed Radical H-Abstraction

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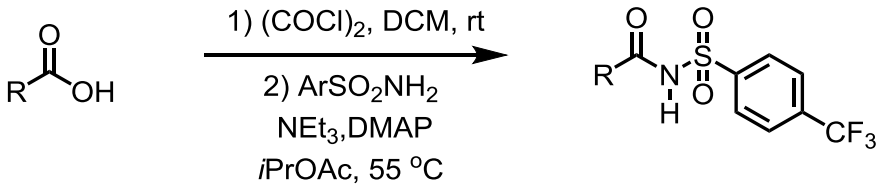
1 General Information

Octafluorotoluene and $TMSN_3$ were obtained from Oakwood Chemical. Other solvents and chemicals were from Sigma-Aldrich, Acros and Alfa Aesar and used directly without further purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. Preparative TLC was performed on 1.0 mm silica gel (Analtech). Columns for flash chromatography (FC) contained silica gel (32–63μ, Dynamic Adsorbents, Inc.). ^{1}H NMR spectra were recorded on Bruker AV-400 instrument (400 MHz) or Varian Inova 400 (400 MHz), Bruker DRX-600 instrument (600 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to 0.0 ppm for tetramethylsilane. ^{13}C NMR spectra were recorded on Bruker DRX-600 instrument (150 MHz), and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-*d*. In the ^{13}C NMR analysis, peaks that correspond to those of the polyfluoroarylamide auxiliary appeared as nearly invisible, complex sets of multiplets; they are omitted in the following spectroscopic analysis. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

2 Experimental Section

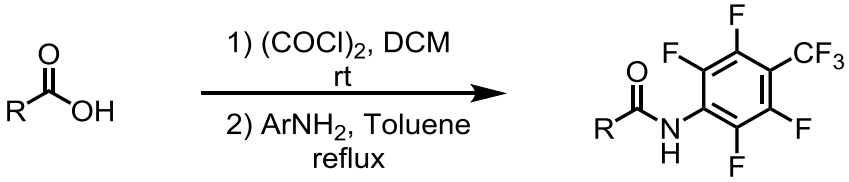
2.1 Synthesis of Starting Materials

General Procedure for the Preparation of Amide Substrates from 4-Trifluoromethyl benzenesulfonamide:

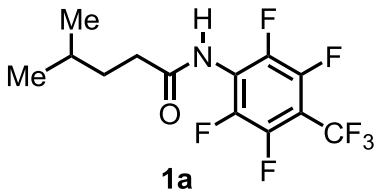


Amide substrates are prepared from benzenesulfonamides according to the literature[1] with minor modifications. 4-Trifluoromethyl benzenesulfonamide (5 mmol), triethylamine (12.5 mmol) and DMAP (0.025 mmol) were added into isopropyl acetate (10 mL) under nitrogen at room temperature. The mixture was heated to 55 °C. A toluene (3 mL) solution of acid chloride (5.5 mmol), prepared from corresponding carboxylic acid and oxalyl chloride, was added slowly over 1h. After the addition was completed, the mixture was maintained at 55 °C for one hour. After cooling to room temperature, the reaction was quenched with water (1.1 mL) and treated with 0.7 M HCl (16.90 mL). Aqueous phase was extracted with ethyl acetate. Combined organic phases were dried with anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by flash column chromatography (silica gel, hexane/EtOAc 10/1 to 5/1).

General Procedure for the Preparation of Amide Substrates from 2,3,5,6-Tetrafluoro-4-(trifluoromethyl)aniline:



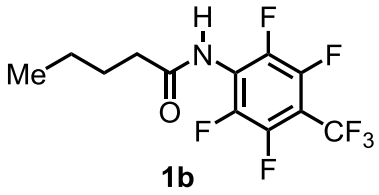
An acid chloride (10 mmol), prepared from the corresponding carboxylic acid and oxalyl chloride, was added to a solution of 2,3,5,6-tetrafluoro-4-(trifluoromethlyl)aniline (10 mmol) in toluene (10 mL). The reaction mixture was stirred for 12 h under reflux. After cooling to room temperature, the product mixture was concentrated in vacuum and was recrystallized from ethyl acetate/hexane to give desired amide.



1a

4-Methyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pentanamide (1a)

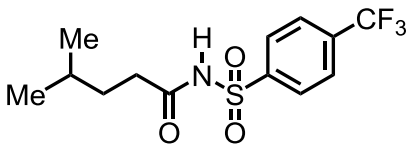
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (s, 1H), 2.30–2.24 (m, 2H), 1.56–1.40 (m, 3H), 0.89 (d, *J* = 6.4 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.15, 34.00, 32.43, 26.99, 21.63. HRMS (ESI-TOF) Calcd for $C_{13}H_{11}F_7NO$ $[M-H]^-$: 330.0734; found: 330.0738.



1b

***N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pentanamide (1b)**

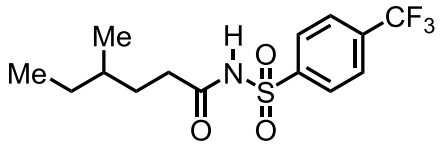
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (s, 1H), 2.30–2.24 (m, 2H), 1.68–1.30 (m, 4H), 0.93 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.93, 33.91, 30.27, 21.90, 19.40. HRMS (ESI-TOF) Calcd for $C_{12}H_9F_7NO$ $[M-H]^-$: 316.0578; found: 316.0581.



1c

4-Methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)pentanamide (1c)

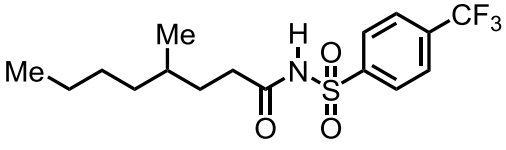
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.21 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 8.0 Hz, 2H), 2.36–2.25 (m, 2H), 1.60–1.43 (m, 3H), 0.87 (d, *J* = 6.4 Hz, 6H).^{13}C NMR (150 MHz, $CDCl_3$) δ 170.22, 141.43, 135.12 (q, *J* = 33.0 Hz), 128.60, 125.68 (q, *J* = 3.6 Hz), 122.60 (q, *J* = 279.0 Hz), 34.00, 32.43, 26.99, 21.63. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}F_3NO_3S$ $[M-H]^-$: 322.0730; found: 322.0726.



1d

4-Methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)hexanamide (1d)

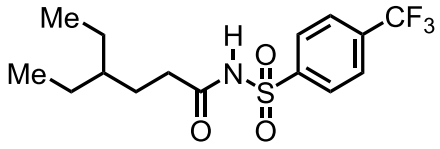
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.23 (d, *J* = 7.6 Hz, 2H), 7.84 (d, *J* = 7.6, 2H), 2.36–2.20 (m, 2H), 1.42–1.38 (m, 1H), 1.32–1.29 (m, 3H), 1.17–1.08 (m, 1H), 0.86–0.82 (m, 6H).^{13}C NMR (150 MHz, $CDCl_3$) δ 170.90, 141.90, 135.81 (q, *J* = 33.3 Hz), 129.11, 126.28 (q, *J* = 3.6 Hz), 122.90 (q, *J* = 271.0 Hz), 33.80, 33.30, 30.24, 28.55, 18.24, 10.72. HRMS (ESI-TOF) Calcd for $C_{14}H_{17}F_3NO_3S$ $[M-H]^-$: 336.0887; found: 336.0871.



1e

4-Methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)octanamide (1e)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.24 (d, *J* = 8.2 Hz, 2H), 7.5 (d, *J* = 8.2 Hz, 2H), 2.36–2.20 (m, 2H), 1.64–1.59 (m, 1H), 1.45–1.32 (m, 2H), 1.30–1.17 (m, 5H), 1.13–1.07 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H), 0.83 (d, *J* = 6.4 Hz, 3H).^{13}C NMR (150 MHz, $CDCl_3$) δ 170.34, 141.43, 134.90 (q, *J* = 33.6 Hz), 128.26, 125.48 (q, *J* = 3.6 Hz), 122.19 (q, *J* = 274.0 Hz), 35.73, 33.76, 31.68, 30.64, 28.57, 22.39, 18.73, 13.58. HRMS (ESI-TOF) Calcd for $C_{16}H_{21}F_3NO_3S$ $[M-H]^-$: 364.1200; found: 364.1196.

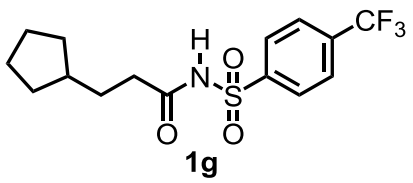


1f

4-Ethyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)hexanamide (1f)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.24 (d, *J* = 8.3 Hz, 2H), 7.85 (d, *J* = 8.3 Hz, 2H), 2.29–2.22 (m, 2H), 1.58–1.50 (m, 2H), 1.28–1.19 (m, 4H), 1.16–1.10 (m, 1H), 0.82 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.35, 141.43, 135.02 (q, *J* = 33.0 Hz), 128.30, 125.48 (q, *J* = 3.7 Hz), 122.20 (q, *J*

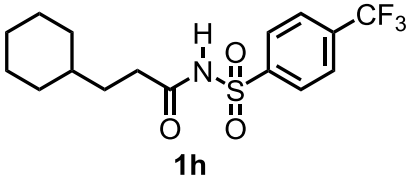
= 278.0 Hz), 39.19, 33.53, 26.63, 24.51, 10.19. HRMS (ESI-TOF) Calcd for $C_{15}H_{19}F_3NO_3S$ $[M-H]^-$: 350.1043; found: 350.1038.



1g

3-Cyclopentyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)propanamide (1g)

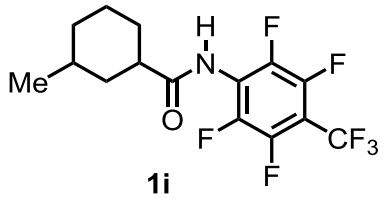
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.24 (d, *J* = 8.1 Hz, 2H), 7.99 (d, *J* = 8.1 Hz, 2H), 2.39–2.20 (m, 2H), 1.76–1.66 (m, 4H), 1.63–1.56 (m, 4H), 1.53–1.46 (m, 2H), 1.08–0.98 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.36, 141.49, 135.22 (q, *J* = 33.5 Hz), 128.58, 125.60 (q, *J* = 3.6 Hz), 122.32 (q, *J* = 280.0 Hz), 38.86, 35.30, 31.85, 29.90, 24.54. HRMS (ESI-TOF) Calcd for $C_{15}H_{17}F_3NO_3S$ $[M-H]^-$: 348.0887; found: 348.0885.



1h

3-Cyclohexyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)propanamide (1h)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.23 (d, *J* = 7.9 Hz, 2H), 7.97 (d, *J* = 7.9 Hz, 2H), 2.34–2.21 (m, 2H), 1.71–1.59 (m, 6H), 1.51–1.45 (m, 2H), 1.19–1.11 (m, 3H), 0.84–0.82 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.49, 141.87, 135.29 (q, *J* = 33.2 Hz), 128.56, 125.78 (q, *J* = 3.6 Hz), 122.60 (q, *J* = 274.80 Hz), 36.46, 33.55, 32.38, 31.07, 25.87, 25.59. HRMS (ESI-TOF) Calcd for $C_{16}H_{19}F_3NO_3S$ $[M-H]^-$: 362.1043; found: 362.1041.

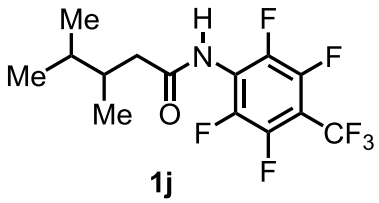


1i

3-Methyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)cyclohexane-1-carboxamide (1i)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (s, 1H), 2.45 (tt, *J* = 12.1, 3.5 Hz, 1H), 2.07–1.95 (m, 2H), 1.93–1.91 (m, 1H), 1.79–1.72 (m, 1H), 1.68–1.60 (m, 1H), 1.52–1.47 (m, 1H), 1.38–1.32 (m, 1H), 1.28–1.17 (m,

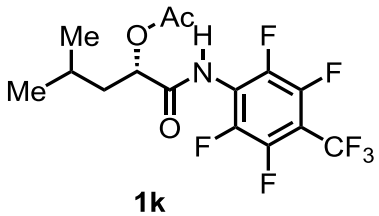
1H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.99–0.94 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 180.19, 45.11, 37.33, 33.72, 31.71, 28.66, 24.99, 22.09. HRMS (ESI-TOF) Calcd for $C_{15}H_{13}F_7NO$ $[M-H]^-$: 356.0891; found: 356.0886.



1j

3,4-Dimethyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pentanamide (1j)

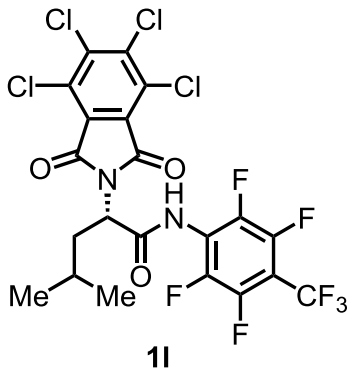
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (s, 1H), 2.56 (dd, *J* = 14.3, 5.1 Hz, 1H), 2.23 (dd, *J* = 14.3, 9.5 Hz, 1H), 2.04–1.96 (m, 1H), 1.72–1.67 (m, 1H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.15, 40.85, 36.01, 31.66, 19.38, 17.83, 15.15. HRMS (ESI-TOF) Calcd for $C_{14}H_{13}F_7NO$ $[M-H]^-$: 344.0891; found: 344.0892.



1k

(*S*)-4-Methyl-1-oxo-1-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)amino)pentan-2-yl acetate (1k)

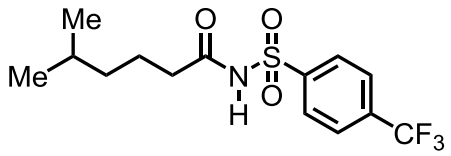
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 5.41 (dd, *J* = 8.8, 4.7 Hz, 1H), 2.24 (s, 3H), 1.92–1.88 (m, 1H), 1.86–1.76 (m, 2H), 1.02 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.53, 167.60, 72.35, 39.93, 24.03, 22.46, 21.45, 20.39. HRMS (ESI-TOF) Calcd for $C_{15}H_{13}F_7NO3$ $[M-H]^-$: 388.0789; found: 388.0784.



1l

(*S*)-4-Methyl-2-(4,5,6,7-tetrachloro-1,3-dioxoisoindolin-2-yl)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pentanamide (1l)

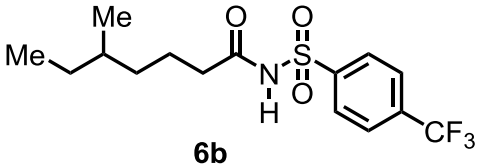
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 5.18 (dd, *J* = 10.9, 5.7 Hz, 1H), 2.47–2.12 (m, 2H), 1.60–1.51 (m, 1H), 1.06–0.95 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.99, 163.08, 140.60, 129.94, 126.44, 53.79, 37.21, 24.86, 22.38, 20.95. HRMS (ESI-TOF) Calcd for $C_{21}H_{10}C_{l4}F_7N_2O_3$ $[M-H]^-$: 610.9339; found:610.9343.



6a

5-Methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)hexanamide (6a)

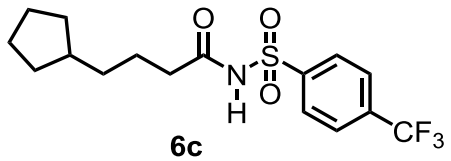
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.24 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 2.31–2.22 (m, 2H), 1.63–1.55 (m, 2H), 1.51–1.46 (m, 1H), 1.17–1.08 (m, 2H), 0.85 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.15, 141.93, 136.00 (q, *J* = 33.0 Hz), 128.21, 125.14 (q, *J* = 3.5 Hz), 121.91 (q, *J* = 276.1 Hz), 37.50, 36.17, 27.22, 21.87, 21.69. HRMS (ESI-TOF) Calcd for $C_{14}H_{17}F_3NO_3S$ $[M-H]^-$: 336.0887; found:336.0885.



6b

5-Methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)heptanamide (6b)

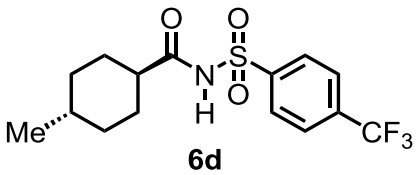
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.24 (d, *J* = 8.1 Hz, 2H), 7.93 (d, *J* = 8.1 Hz, 2H), 2.29–2.23 (m, 2H), 1.59–1.49 (m, 2H), 1.28–1.10 (m, 4H), 1.08–1.04 (m, 1H), 0.84–0.80 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.13, 141.33, 135.78 (q, *J* = 33.2 Hz), 128.91, 125.48 (q, *J* = 3.6 Hz), 121.94 (q, *J* = 279.0 Hz), 36.26, 35.16, 33.59, 28.70, 21.44, 18.47, 10.77. HRMS (ESI-TOF) Calcd for $C_{15}H_{19}F_3NO_3S$ $[M-H]^-$: 350.1043; found: 350.1040.



6c

4-Cyclopentyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)butanamide (6c)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.39 (d, *J* = 8.3 Hz, 2H), 7.85 (d, *J* = 8.3 Hz, 2H), 2.26–2.21 (m, 2H), 1.69–1.60 (m, 2H), 1.54–1.48 (m, 4H), 1.28–1.21 (m, 3H), 1.07–0.93 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.52, 141.72, 135.51 (q, *J* = 33.2 Hz), 128.76, 125.36 (q, *J* = 3.6 Hz), 122.41 (q, *J* = 271.0 Hz), 39.22, 36.17, 34.82, 32.04, 24.62, 23.04. HRMS (ESI-TOF) Calcd for $C_{16}H_{19}F_3NO_3S$ $[M-H]^-$: 362.1043; found: 362.1041.



6d

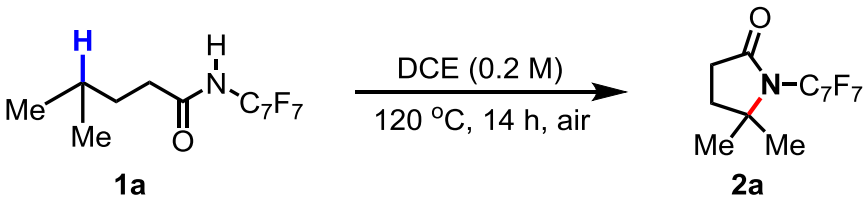
(1*r*,4*r*)-4-Methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)cyclohexane-1-carboxamide (6d)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.23 (d, *J* = 8.2, 2H), 7.84 (d, J = 8.3, 2H), 2.09 (tt, *J* = 12.2, 3.5 Hz, 1H), 1.91–1.82 (m, 2H), 1.81–1.74 (m, 2H), 1.39–1.35 (m, 2H), 1.34–1.29 (m, 2H), 0.89 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.96, 141.12, 135.03 (q, *J* = 33.4 Hz), 128.17, 125.70 (q, *J* = 3.6 Hz), 122.54 (q, *J* = 268.0 Hz), 44.66, 33.39, 31.24, 28.23, 21.79. HRMS (ESI-TOF) Calcd for $C_{15}H_{17}F_3NO_3S$ $[M-H]^-$: 348.0887; found: 348.0890.

2.2 Optimization of Lactamization Reaction

General: The reactions were conducted using 0.1 mmol of substrate in the indicated conditions in solvents. The temperature was detected from oil bath.

Radical Initiator Screening[a,b]

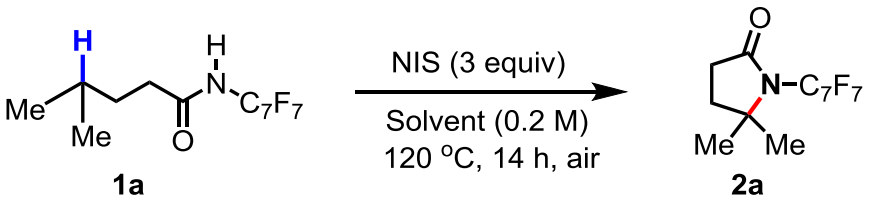


1a **2a**

Entry	Radical Initiator	Amount (equiv)	NMR Yield (%)
1	*t*BuOOH	2.0	0
2	$(t\text{BuO})_2$	2.0	0
3	NIS	2.0	67
4	NBS	2.0	37
5	NCS	2.0	15
6	$PhI(OAc)_2$	2.0	Trace
7	$PhI(OTFA)_2$	2.0	Trace
8	I_2	2.0	0
9	$PhI(OAc)_2+I_2$	1.5 + 1.5	66
10	$PhI(OTFA)_2+I_2$	1.5 + 1.5	43
11	NIS	3.0	76
12	NIS	4.0	56

[a] Conditions: **1a** (0.1 mmol), radical initiator, DCE (0.5 mL), 120 °C, air, 14 h. [b] All yields were determined by ^{1}H NMR using CH_2Br_2 as the internal standard.

Solvent Screening[a,b]

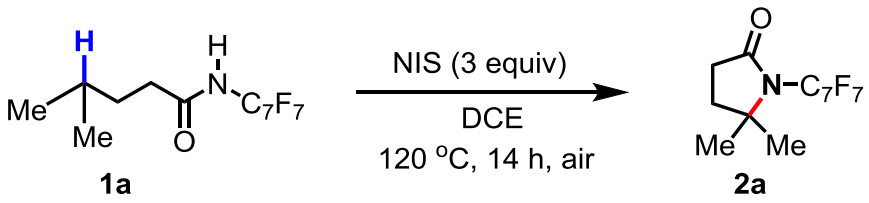


1a **2a**

Entry	Solvent	NMR Yield (%)
1	$C_6F_5CF_3$	62
2	$PhCF_3$	41
3	C_6F_6	57
4	Hexane	20
5	Toluene	15
6	DCE	76
7	HFIP	Trace
8	*t*-BuOH	Trace
9	DMF	12
10	DMSO	14
11	EA	59
12	THF	Trace
13[c]	DCE	74
14[d]	DCE	61

[a] Conditions: **1a** (0.1 mmol), NIS (3 equiv.), solvent (0.5 mL), 120 °C, air, 14 h. [b] All yields were determined by ^1H NMR using CH_2Br_2 as the internal standard. [c] Reaction was carried out in N_2 (1 atm). [d] Reaction was carried out in O_2 (1 atm).

Concentration Screening[a,b]

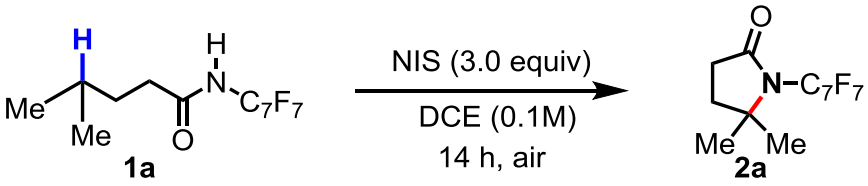


1a **2a**

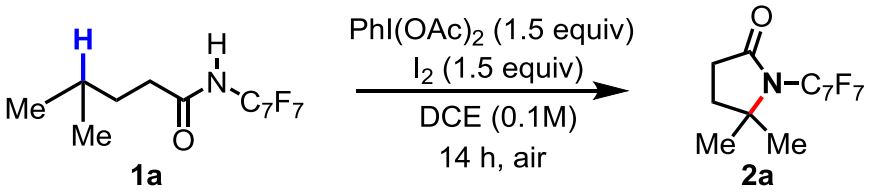
Entry	Concentration (M)	NMR Yield (%)
1	0.2	76
2	0.1	82
3	0.05	54
4	0.025	23

[a] Conditions: **1a** (0.1 mmol), NIS (3 equiv.), DCE, 120 °C, air, 14 h. [b] All yields were determined by ^{1}H NMR using CH_2Br_2 as the internal standard.

Optimization of Temperature [a,b]



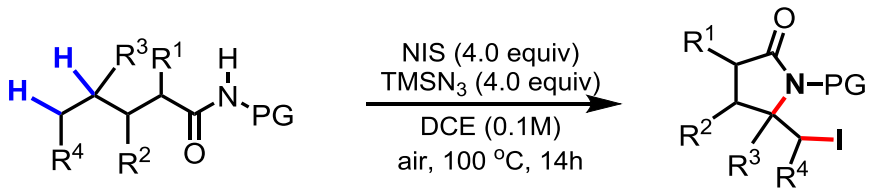
Entry	Temperature (°C)	NMR Yield (%)
1	120	82
2	110	87
3	100	92
4	90	79

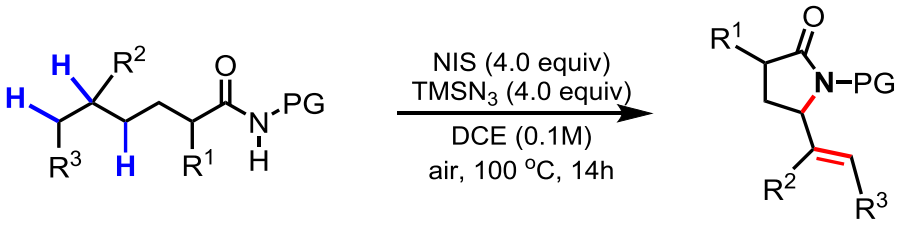


Entry	Temperature (°C)	NMR Yield (%)
1	120	66
2	90	71
3	60	73
4	r.t.	79
5[c]	r.t.	89

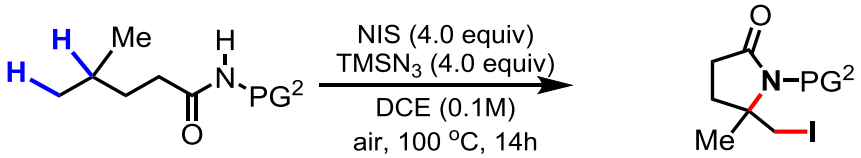
[a] Conditions: **1a** (0.1 mmol), NIS (3 equiv.) or $PhI(OAc)_2$ (1.5 equiv.) and I_2 (1.5 equiv.), DCE (1.0 mL), air, 14 h. [b] All yields were determined by ^1H NMR using CH_2Br_2 as the internal standard. [c] 48 h.

2.3 General Procedure for Directed Radical Reaction





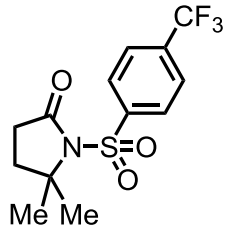
To an oven dried microwave tube (5 mL) equipped with a magnetic stir bar was added substrate (0.1 mmol), NIS (69.2mg, 0.4 mmol) and 1 mL of DCE followed by $TMSN_3$ (53 uL, 0.4 mmol). The mixture was covered with safety shield, then was heated to 100 °C for 14 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with 4 mL dichloromethane and then treated with 5 mL saturated aqueous $Na_2S_2O_3$ solution. Aqueous phase was extracted with 5 mL dichloromethane twice. Combined organic phases were dried with Na_2SO_4. The solvents were removed under reduced pressure and the resulting mixture was purified by preparative TLC using hexane/EtOAc as the eluent.



0.5 g, yield = 64%
1.0 g, yield = 53%

To a 50 mL pressure vessel equipped with a magnetic stir bar was added substrate (0.5 g or 1.0 g), NIS (4 equiv) and DCE (0.1 M) followed by addition of $TMSN_3$ (4 equiv). Pressure vessel was covered with safety shield, then was heated to 100 °C for 14 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with 40 mL dichloromethane and then treated with saturated aqueous $Na_2S_2O_3$ solution. Aqueous phase was extracted with dichloromethane twice. Combined organic phases were dried with Na_2SO_4. The solvents were

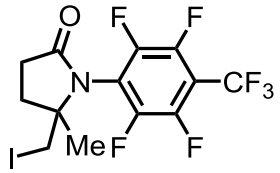
removed under reduced pressure and the resulting mixture was purified by flash column chromatography (silica gel, hexane/EtOAc 10/1 to 3/1).



2c

5,5-Dimethyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (2c)

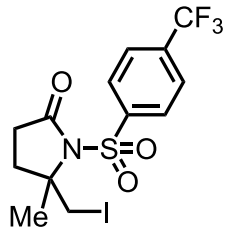
Substrate was treated with standard reagents for 2 hours. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (25.7 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.46 (t, *J* = 7.6 Hz, 2H), 0.81 (s, 3H), 0.81 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ. 171.39, 141.82, 135.59 (q, *J* = 34.2 Hz), 128.96, 126.17 (q, *J* = 3.5 Hz), 123.00 (q, *J* = 275.0 Hz), 34.38, 32.84, 27.42, 22.030, 22.027. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}F_3NO_3S$ $[M+H]^+$: 322.0719; found: 322.0715.



3a

5-(Iodomethyl)-5-methyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidin-2-one (3a)

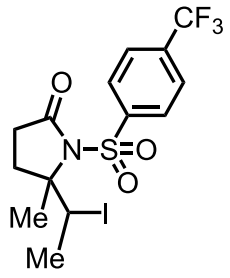
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (37.7 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.43 (d, *J* = 10.2 Hz, 1H), 3.24 (d, *J* = 10.2 Hz, 1H), 2.77–2.60 (m, 2H), 2.50 (ddd, *J* = 13.2, 9.4, 5.5 Hz, 1H), 2.22 (ddd, *J* = 13.2, 9.5, 7.9 Hz, 1H), 1.52 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -56.69 (t, *J* = 21.7 Hz, 3F), -138.81 – -138.97 (m, 2F), -139.33 – -139.48 (m, 2F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.55, 65.70, 33.89, 29.77, 24.77, 12.87. HRMS (ESI-TOF) Calcd for $C_{13}H_{10}F_7INO$ $[M+H]^+$: 455.9690; found: 455.9700.



3c

5-(Iodomethyl)-5-methyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (3c)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (32.1 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 2H), 4.01 (d, *J* = 10.6 Hz, 1H), 3.73 (d, *J* = 10.6 Hz, 1H), 2.59 (ddd, *J* = 18.0, 10.2, 6.6 Hz, 1H), 2.46–2.37 (m, 1H), 2.30 (ddd, *J* = 13.2, 10.2, 6.6 Hz, 1H), 2.00 (ddd, *J* = 13.2, 10.1, 6.7 Hz, 1H), 1.92 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.82, 141.92, 135.51 (q, *J* = 33.6 Hz), 129.90, 125.75 (q, *J* = 3.6 Hz), 122.63 (q, *J* = 274.1 Hz), 68.35, 34.32, 29.68, 26.13, 16.20. HRMS (ESI-TOF) Calcd for $C_{13}H_{14}F_3INO_3S$ $[M+H]^+$: 447.9686; found:447.9690.



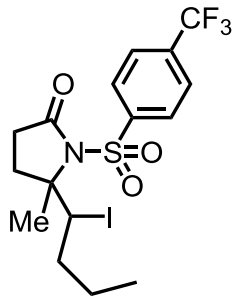
3d

5-(1-Iodoethyl)-5-methyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (3d)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 10/1), two diastereomers were obtained as white solids (15.0 mg, 10.6 mg, 3:2, 71% in total).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 2H), 5.14 (q, *J* = 7.0 Hz, 1H), 2.54–2.47 (m, 1H), 2.46–2.38 (m, 2H), 2.00 (d, *J* = 7.0 Hz, 3H), 1.97–1.92 (m, 4H).^{13}C NMR (150 MHz, $CDCl_3$) δ 174.49, 141.62, 135.58 (q, *J* = 34.1 Hz), 129.75, 125.88 (q, *J* = 3.7 Hz), 123.02 (q, *J* = 279.1 Hz), 72.58, 34.02, 30.73, 30.00, 29.10, 23.67. HRMS (ESI-TOF) Calcd for $C_{14}H_{16}F_3INO_3S$ $[M+H]^+$: 461.9842; found: 461.9848.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.3 Hz, 2H), 7.80 (d, *J* = 8.3 Hz, 2H), 5.38 (q, *J* = 7.1 Hz, 1H), 2.72 – 2.62 (m, 1H), 2.49–2.41 (m, 2H), 2.17 (s, 3H), 1.97 (d, *J* = 7.1 Hz, 3H), 1.94–1.91 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.78, 141.68, 135.44 (q, *J* = 34.1 Hz), 130.42, 125.49 (q, *J* = 3.5 Hz), 123.12 (q, *J* = 279.4 Hz), 73.30, 38.00, 30.63, 29.90, 24.07, 23.87. HRMS (ESI-TOF) Calcd for $C_{14}H_{16}F_3INO_3S$ $[M+H]^+$: 461.9842; found: 461.9844



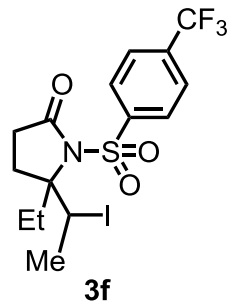
3e

5-(1-Iodobutyl)-5-methyl-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (3e)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 10/1), two diastereomers were obtained as white solids (14.0 mg, 12.0 mg, 7:6, 53% in total).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 2H), 4.97–4.93 (m, 1H), 2.55–2.48 (m, 1H), 2.44–2.39 (m, 2H), 2.02–1.97 (m, 1H), 1.95 (s, 3H), 1.78–1.67 (m, 3H), 1.49–1.41 (m, 1H), 0.98 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.70, 141.81, 135.59 (q, *J* = 32.8 Hz), 129.69, 125.87 (q, *J* = 3.7 Hz), 123.02 (q, *J* = 282.0 Hz), 72.65, 44.84, 36.25, 31.16, 29.90, 29.59, 23.12, 13.05. HRMS (ESI-TOF) Calcd for $C_{16}H_{20}F_3INO_3S$ $[M+H]^+$: 490.0155; found:490.0159.

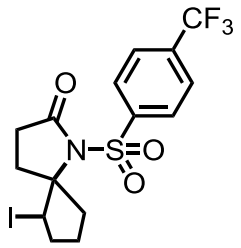
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 5.21–5.18 (m, 1H), 2.71–2.50 (m, 1H), 2.48–2.38 (m, 2H), 1.94 (s, 3H), 1.93-1.89 (m, 1H), 1.80–1.69 (m, 3H), 1.51–1.46 (m, 1H), 1.01 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.89, 141.72, 135.43 (q, *J* = 33.1 Hz), 130.49, 125.44 (q, *J* = 3.6 Hz), 123.14 (q, *J* = 275.0 Hz), 73.24, 49.34, 36.69, 31.15, 29.97, 25.13, 24.18, 13.25. HRMS (ESI-TOF) Calcd for $C_{16}H_{20}F_3INO_3S$ $[M+H]^+$: 490.0155; found:490.0148.



3f

5-Ethyl-5-(1-iodoethyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (3f)

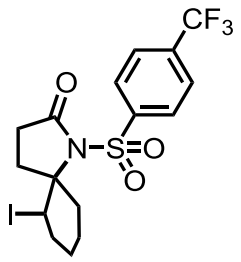
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (29.9 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 5.11 (q, *J* = 7.0 Hz, 1H), 2.46–2.32 (m, 5H), 2.08–1.99 (m, 1H), 1.96 (d, *J* = 7.1 Hz, 3H), 0.83 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.12, 141.03, 135.69 (q, *J* = 33.1 Hz), 130.16, 125.69 (q, *J* = 3.0 Hz), 123.00 (q, *J* = 285.0 Hz), 76.39, 34.68, 33.16, 30.49, 27.31, 23.63, 8.97. HRMS (ESI-TOF) Calcd for $C_{15}H_{18}F_3INO_3S$ $[M+H]^+$: 475.9999; found:475.9994.



3g

(5*R*,6*R*)-6-Iodo-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1-azaspiro[4.4]nonan-2-one (3g)

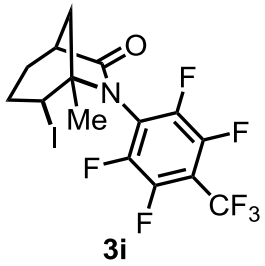
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (22.7 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 2H), 5.25 (dd, *J* = 11.4, 8.0 Hz, 1H), 2.87–2.79 (m, 1H), 2.71–2.64 (m, 1H), 2.48– 2.39 (m, 3H), 2.11–1.88 (m, 4H), 1.84–1.77 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.32, 141.85, 135.45 (q, *J* = 34.0 Hz), 129.92, 125.71 (q, *J* = 3.4 Hz), 122.61 (q, *J* = 283.0 Hz), 76.79, 33.82, 33.08, 33.07, 32.82, 29.45, 21.10. HRMS (ESI-TOF) Calcd for $C_{15}H_{16}F_3INO_3S$ $[M+H]^+$: 473.9842; found: 473.9842.



3h

(5*R*,6*R*)-6-Iodo-1-((4-(trifluoromethyl)phenyl)sulfonyl)-1-azaspiro[4.5]decan-2-one (3h)

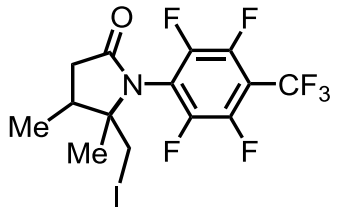
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (34.2 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 5.41 (dd, *J* = 12.8, 4.3 Hz, 1H), 2.84 (td, *J* = 12.6, 4.2 Hz, 1H), 2.71-2.62 (m, 1H), 2.58-2.54 (m, 1H), 2.44-2.36 (m, 2H), 2.18–2.03 (m, 4H), 1.92 (d, J = 10.0 Hz, 1H), 1.54-1.46 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.55, 141.41, 135.42 (q, *J* = 35.1 Hz), 129.95, 125.03 (q, *J* = 3.7 Hz), 122.69 (q, *J* = 279.8 Hz), 73.73, 40.23, 36.99, 36.17, 29.41, 28.22, 27.40, 22.30. HRMS (ESI-TOF) Calcd for $C_{16}H_{18}F_3INO_3S$ $[M+H]^+$: 487.9999; found: 488.0006.



3i

(1*S*,4*R*,5*R*)-4-Iodo-5-methyl-6-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-6-azabicyclo[3.2.1]octan-7-one (3i)

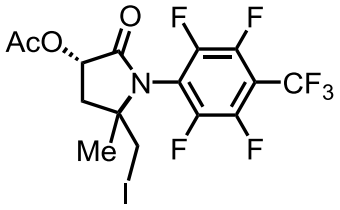
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (34.7 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 (d, *J* = 5.3 Hz, 1H), 2.91 (d, *J* = 11.7 Hz, 1H), 2.84–2.82 (m, 1H), 2.70–2.64 (m, 1H), 2.29 (dd, *J* = 16.3, 5.3 Hz, 1H), 2.24-2.21 (m, 1H), 2.03–1.97 (m, 1H), 1.93–1.88 (m, 1H), 1.38 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -56.62 (t, *J* = 21.7 Hz, 3F), -139.22 – -139.36 (m, 2F), -139.93 – -140.07 (m, 1F), -142.29 (dd, J = 22.6, 7.9 Hz, 1F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.78, 67.70, 41.85, 41.26, 33.25, 31.58, 23.54, 21.02. HRMS (ESI-TOF) Calcd for $C_{15}H_{10}F_7INO$ $[M-H]^-$: 479.9701; found: 479.9693.



3j

(5*S*)-5-(Iodomethyl)-4,5-dimethyl-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidin-2-one (3j)

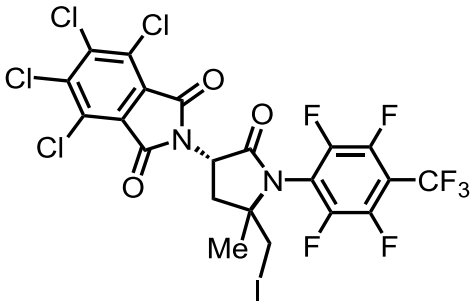
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), a mixture of inseparable diastereomers was obtained as a colorless oil (28.7 mg, 3:2, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.49-3.32 (m, 1H), 3.32-3.20 (m, 1H), 2.91–2.80 (m, 1H), 2.80–2.60 (m, 1H), 2.60-2.27 (m, 1H), 2.55–2.30 (m, 3H), 1.39-1.21 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -56.59 – -56.72 (m, 3F), -138.77 – -138.88 (m, 1F), -139.19 – -140.24 (m, 3F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.81, 173.19, 67.00, 66.58, 39.56, 39.19, 37.51, 37.18, 25.24, 19.80, 15.61, 14.60, 12.78, 7.91. HRMS (ESI-TOF) Calcd for $C_{14}H_{12}F_7INO$ $[M+H]^+$: 469.9846; found: 469.9845



3k

(3*S*,5*S*)-5-(Iodomethyl)-5-methyl-2-oxo-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidin-3-yl acetate (3k)

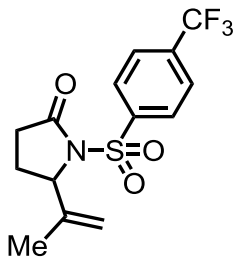
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), a mixture of inseparable mixture of diastereomers was obtained as a white solid (31.8 mg, 3:2, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75–5.52 (m, 1H), 3.52–3.40 (m, 1H), 3.12–3.06 (m, 1H), 2.78-2.72 (m, 1H), 2.40-2.35 (m, 1H), 2.22-2.18 (m, 3H), 1.59-1.58 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -56.62 – -56.75 (m, 3F), -138.42 – -138.94 (m, 4F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.19, 169.83, 69.36, 69.04, 63.76, 63.50, 41.25, 40.57, 25.91, 24.83, 20.72, 13.04, 12.52. HRMS (ESI-TOF) Calcd for $C_{15}H_{12}F_7INO_3$ $[M+H]^+$: 513.9745; found:513.9740



3l

4,5,6,7-Tetrachloro-2-((3*S*,5*S*)-5-(iodomethyl)-5-methyl-2-oxo-1-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pyrrolidin-3-yl)isoindoline-1,3-dione (3l)

One-pot procedure: to an oven dried microwave tube (5 mL) equipped with a magnetic stir bar was added substrate (0.1 mmol), NIS (34.6 mg, 0.2 mmol) and 1 mL of DCE was added. The mixture was covered with safety shield, then was heated to 100 ^{o}C for 8 hours under vigorous stirring. The reaction mixture was then cooled to room temperature. I_2 (76.2 mg, 0.3 mmol) and $TMSN_3$ (53 uL, 0.4 mmol) was added. The mixture was covered with safety shield, then was heated to 100 ^{o}C for 14 hours under vigorous stirring. After workup as described in general procedures, a mixture of inseparable diastereomers was obtained as a yellow solid (53.0 mg, 2:1, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47-5.25 (m, 1H), 3.70–3.52 (m, 1H), 3.40-3.31 (m, 1H), 3.03-2.67 (m, 2H), 1.70-1.69 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -56.62 – -56.75 (m, 3F), -136.37 – -137.63 (m, 1F), -138.54 – -139.01 (m, 3F). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.82, 162.38, 140.74, 130.19, 127.23, 63.72, 63.05, 49.17, 49.10, 38.66, 37.26, 25.72, 24.70, 13.21, 12.29. HRMS (ESI-TOF) Calcd for $C_{21}H_9Cl_4F_7IN_2O_3$ $[M+H]^+$: 736.8295; found:736.8292

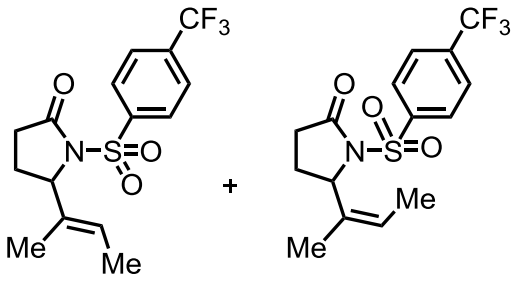


7a

5-(Prop-1-en-2-yl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (7a)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a white solid (23.7 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.2 Hz, 2H), 7.79 (d, *J* = 8.3 Hz, 2H), 4.92 (d, *J* = 26.9 Hz, 2H), 4.86 (d, *J* = 8.5 Hz, 1H), 2.62–2.51 (m, 1H), 2.46–2.29 (m, 2H), 1.92–1.86 (m, 1H), 1.66 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$)

δ 173.11, 142.03, 141.29, 135.00 (q, *J* = 32.4 Hz), 128.76, 125.35 (q, *J* = 3.9 Hz), 120.83 (q, *J* = 289.0 Hz), 113.05, 63.88, 30.10, 24.12, 18.07. HRMS (ESI-TOF) Calcd for $C_{14}H_{15}F_3NO_3S$ $[M+H]^+$: 334.0719; found:334.0717.

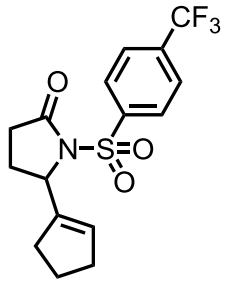


(5:1)

7b

(*E*)-5-(But-2-en-2-yl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (7b)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), a mixture of inseparable region isomers was obtained as a colorless oil (20.2 mg, 5:1, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (m, 2H), 7.78 (d, *J* = 8.3 Hz, 2H), 5.45 (q, *J* = 6.8 Hz, 1H), 4.84 (d, *J* = 9.0 Hz, 1H), 2.57–2.42 (m, 2H), 2.41–2.30 (m, 1H), 1.86–1.80 (m, 1H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.37-1.26 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) Major isomer δ 173.70, 141.93, 135.32 (q, *J* = 34.8 Hz), 132.95, 129.07, 125.76 (q, *J* = 3.7 Hz), 123.18 (q, *J* = 273.0 Hz), 120.38, 66.13, 30.92, 24.29, 13.09, 11.82. HRMS (ESI-TOF) Calcd for $C_{15}H_{17}F_3NO_3S$ $[M+H]^+$: 348.0876; found:348.0876.

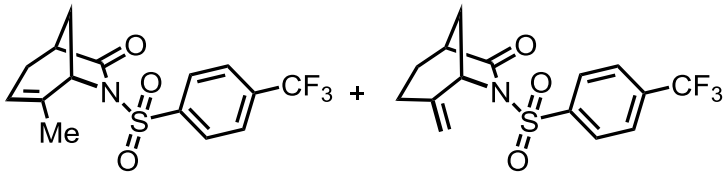


7c

5-(Cyclopent-1-en-1-yl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)pyrrolidin-2-one (7c)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a colorless oil (15.8 mg, 44%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.2 Hz, 2H), 7.78 (d, *J* = 8.3 Hz, 2H), 5.67 (s, 1H), 5.13 (d, *J* = 8.4 Hz, 1H), 2.57–2.52 (m, 1H), 2.48–2.43 (m, 1H), 2.37–2.31 (m, 2H), 2.22–2.17 (m, 1H), 1.92–1.86 (m, 2H), 1.82–1.77 (m, 1H), 1.68–1.63 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.35, 142.01, 141.43, 135.36 (q, *J* = 33.0

Hz), 129.98, 129.04, 125.76 (q, J = 3.6 Hz), 123.00 (q, J = 279.8 Hz), 120.38, 60.11, 32.01, 31.00, 29.69, 24.49, 23.07. HRMS (ESI-TOF) Calcd for $C_{16}H_{17}F_3NO_3S$ $[M+H]^+$: 360.0876; found:360.0877.

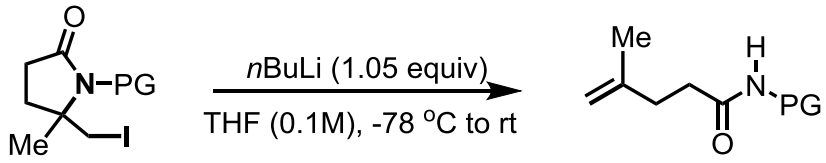


7d (3:1)

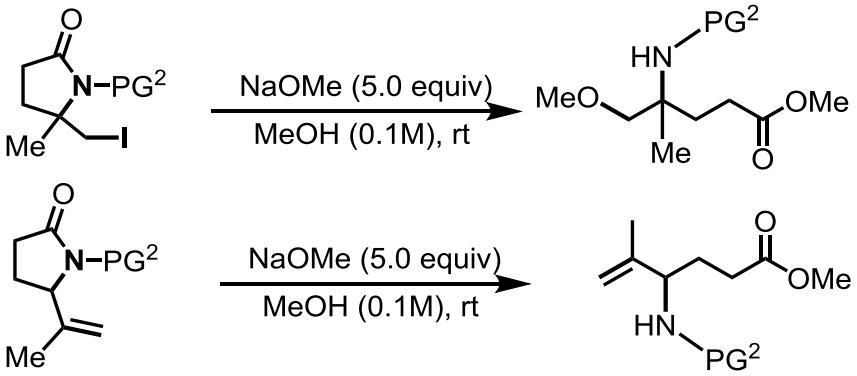
(5*R*)-4-Methyl-6-((4-(trifluoromethyl)phenyl)sulfonyl)-6-azabicyclo[3.2.1]oct-3-en-7-one (7d)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), a mixture of inseparable region isomers was obtained as a colorless oil (18.7 mg, 3:1, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.14 (m, 2H), 7.79–7.77 (d, J = 8.2 Hz, 2H), 5.30–5.10 (m, 1H), 4.94–4.47 (m, 1H), 2.80–2.67 (m, 1H), 2.53–2.35 (m, 2H), 2.26–2.18 (m, 1H), 1.98 (m, 1H), 1.99-1.93 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.53, 174.91, 142.28 (q, J = 42.0 Hz), 137.95, 135.22 (q, J = 32.8 Hz), 128.84, 128.58, 125.94 (q, J = 3.5 Hz), 125.92 (q, J = 3.3 Hz), 122.13 (d, J = 286.0 Hz), 112.00, 64.51, 59.64, 41.72, 40.53, 36.95, 33.44, 27.84, 27.17, 26.31, 21.88. HRMS (ESI-TOF) Calcd for $C_{15}H_{15}F_3NO_3S$ $[M+H]^+$: 346.0719; found:346.0721

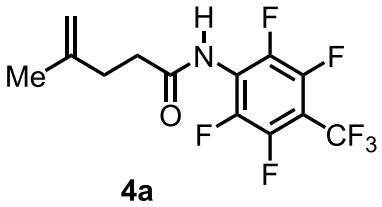
2.4 Procedure for Ring Opening of Lactams



To an oven dried microwave tube (5 mL) equipped with a magnetic stir bar was added substrate (0.1 mmol) and 1 mL of THF. After frozen with a dry ice/acetone bath, the mixture was treated with *n*BuLi (1.05 equiv, 1.6 M in hexane) slowly. The microwave tube was kept in dry ice/acetone bath for 30 min, then was warmed to room temperature. The reaction mixture was diluted with 5 mL ether and quenched with 5 mL saturated ammonium chloride solution. Aqueous phase was extracted with 5 mL ether twice. Combined organic phases are directly dried with Na_2SO_4. The solvents were removed under reduced pressure and the resulting mixture was purified by preparative TLC using hexane/EtOAc (20/1) as the eluent.



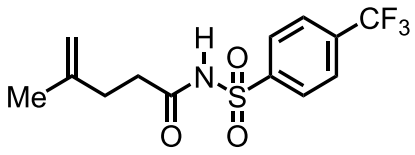
To an oven dried microwave tube (5 mL) equipped with a magnetic stir bar was added substrate (0.1 mmol) and 1 mL of methanol. The mixture was then treated with NaOMe (5.0 equiv, 5.4 M in methanol) slowly. After two hours, reaction mixture was quenched with 5 mL saturated ammonium chloride solution. Aqueous phase was extracted with 10 mL ethyl acetate three times. Combined organic phases were dried with Na_2SO_4. The solvents were removed under reduced pressure and the resulting mixture was purified by preparative TLC using hexane/EtOAc (10/1) as the eluent.



4a

4-Methyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)pent-4-enamide (4a)

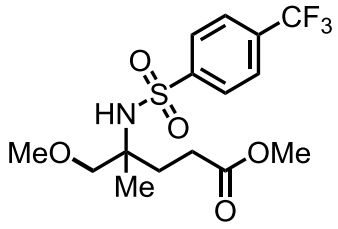
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 10/1), compound was obtained as a white solid (29.8 mg, 91%). ^{1}H NMR (400 MHz, CDCl3) δ 7.24 (s, 1H), 4.85 (s, 1H), 4.79 (s, 1H), 2.65 (t, *J* = 7.5 Hz, 2H), 2.46 (t, *J* = 7.5 Hz, 2H), 1.79 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.26, 143.68, 111.40, 34.42, 32.75, 22.36. HRMS (ESI-TOF) Calcd for $C_{13}H_{11}F_7NO$ $[M+H]^+$: 330.0723; found: 330.0729.



4b

4-Methyl-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)pent-4-enamide (4b)

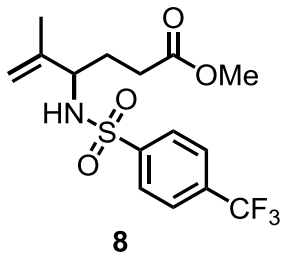
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 10/1), compound was obtained as a white solid (29.9 mg, 93%). ^{1}H NMR (400 MHz, CDCl3) δ 8.21 (d, *J* = 8.5 Hz, 2H), 7.82 (d, *J* = 8.5 Hz, 2H), 4.74 (s, 1H), 4.61 (s, 1H), 2.42 (t, *J* = 7.5 Hz, 2H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.68 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.84, 143.09, 141.83, 135.63 (q, *J* = 33.6 Hz), 129.10, 126.15 (q, *J* = 3.1 Hz), 123.25 (q, *J* = 294.0 Hz), 111.42, 34.56, 31.76, 22.33. HRMS (ESI-TOF) Calcd for $C_{13}H_{15}F_3NO_3S$ $[M+H]^+$: 322.0719; found: 322.0719.



5

Methyl 5-methoxy-4-methyl-4-((4-(trifluoromethyl)phenyl)sulfonamido)pentanoate (5)

Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a colorless oil (31.4 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.2 Hz, 2H), 7.76 (d, J = 8.3 Hz, 2H), 5.23 (s, 1H), 3.67 (s, 3H), 3.19 (s, 3H), 3.17–3.09 (m, 2H), 2.42–2.33 (m, 2H), 2.03–1.97 (m, 1H), 1.85 (ddd, *J* = 14.8, 9.1, 6.3 Hz, 1H), 1.15 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.83, 146.61, 134.02 (q, *J* = 32.0 Hz), 127.46, 126.04 (q, *J* = 3.4 Hz), 123.24 (q, *J* = 279.0 Hz), 78.03, 58.90, 58.80, 51.79, 33.29, 28.64, 21.30. HRMS (ESI-TOF) Calcd for $C_{15}H_{19}F_3NO_5S$ $[M-H]^-$: 382.0942; found: 382.0946.



8

Methyl 5-methyl-4-((4-(trifluoromethyl)phenyl)sulfonamido)hex-5-enoate (8)

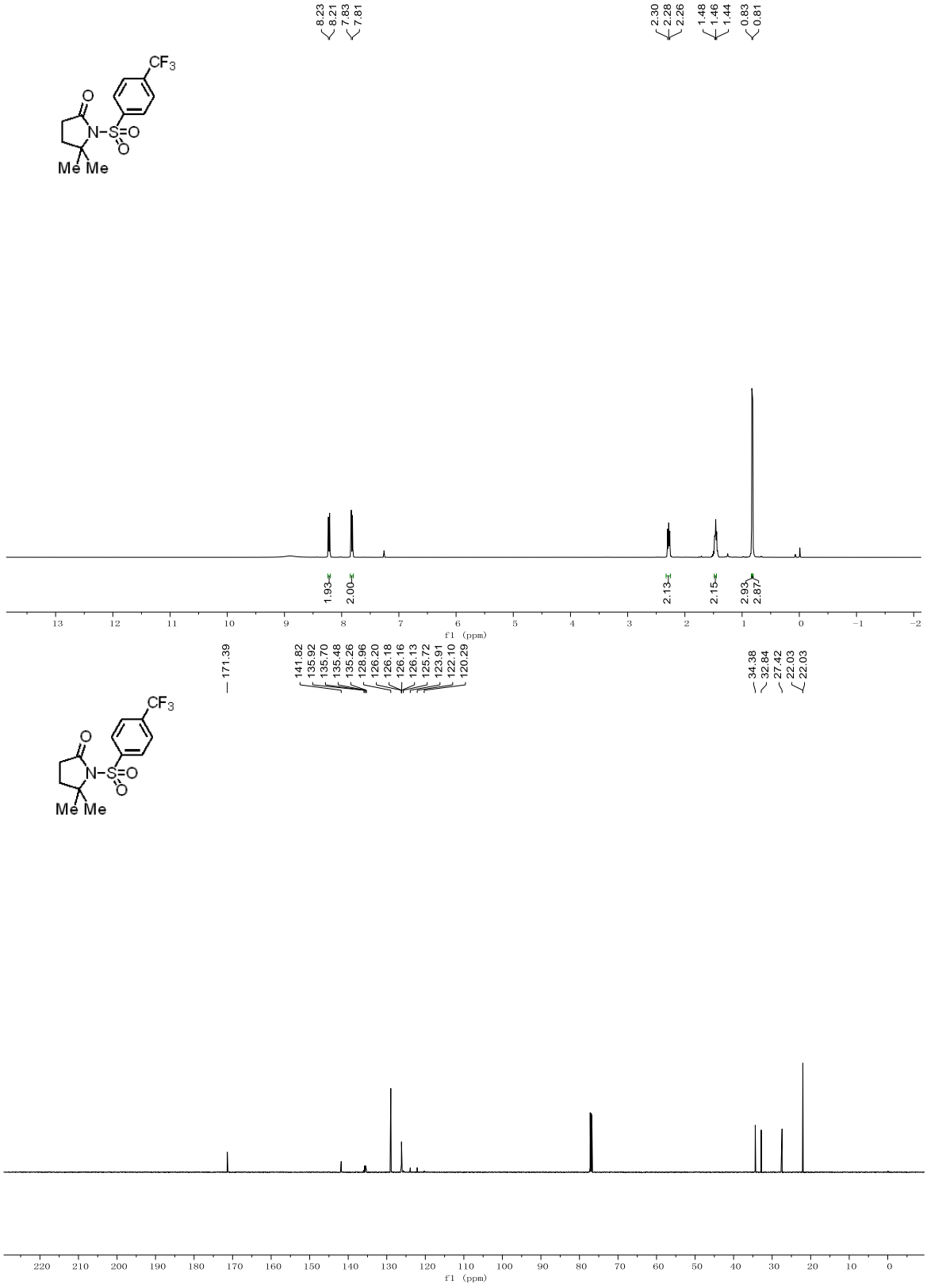
Substrate was treated with standard condition. After purification by preparative TLC (eluent: hexane/EtOAc = 5/1), compound was obtained as a colorless oil (32.1 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 2H), 5.20–5.19 (m, 1H), 4.75–4.72 (m, 2H), 3.87 (q, *J* = 7.5 Hz, 1H), 3.67 (s, 3H), 2.36–2.32 (m, 2H), 1.86–1.49 (m, 2H), 1.49 (d, *J* = 1.5 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.75, 144.43, 142.38, 134.16 (q, *J* = 33.9 Hz), 127.62, 125.94 (q, *J* = 4.0

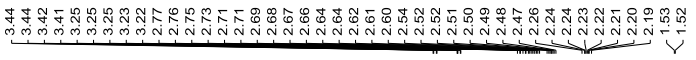
Hz), 123.22 (q, *J* = 269.6 Hz), 114.04, 59.42, 51.87, 30.23, 28.58, 17.54. HRMS (ESI-TOF) Calcd for $C_{15}H_{17}F_3NO_4S$ $[M-H]^-$: 364.0836; found: 364.0841.

3 Reference

1. Yates, M.; Kallman, N.; Ley, C.; Wei, J. *Org. Process Res. Dev.*, **2009**, *13*, 255.

4 NMR Spectra of New Compounds

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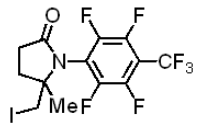
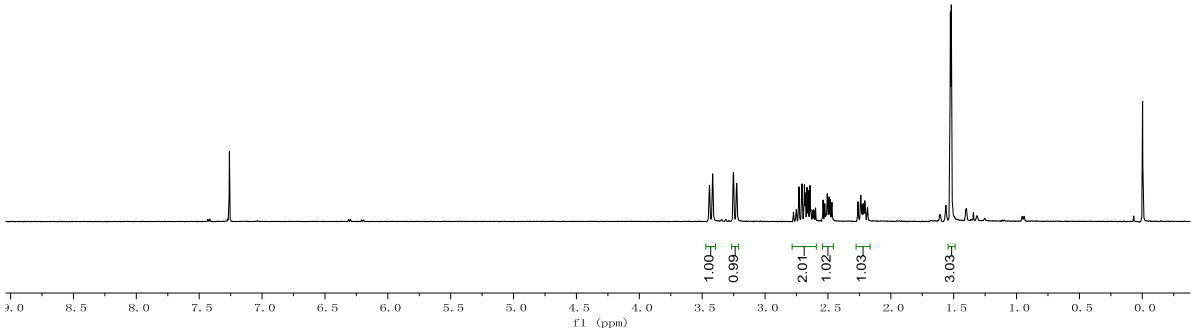
1.52


O
F
F
N
CF3
MeF
F
I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2.01
1.02
1.03
3.03
f1 (ppm)


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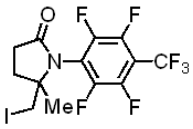
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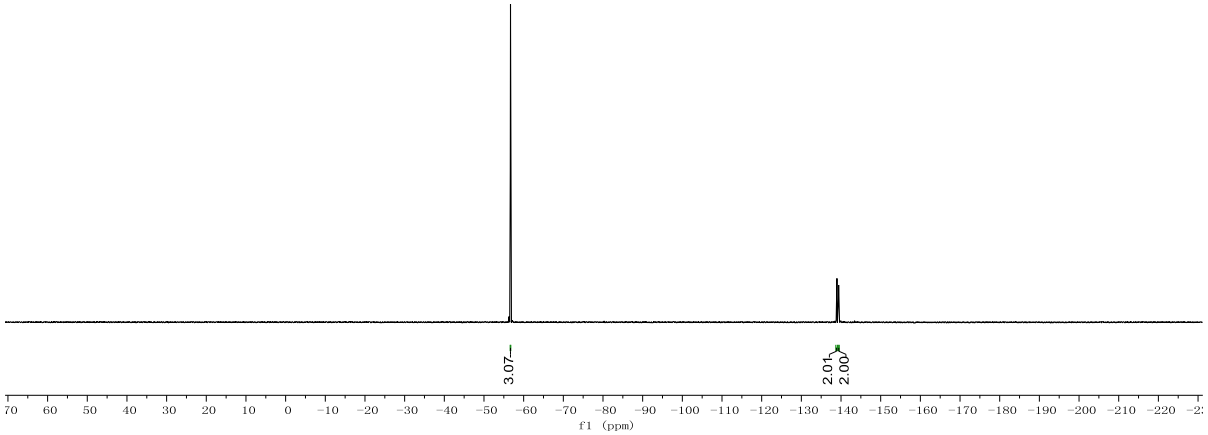
F
F
N
CF3
MeF
F
I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2.00
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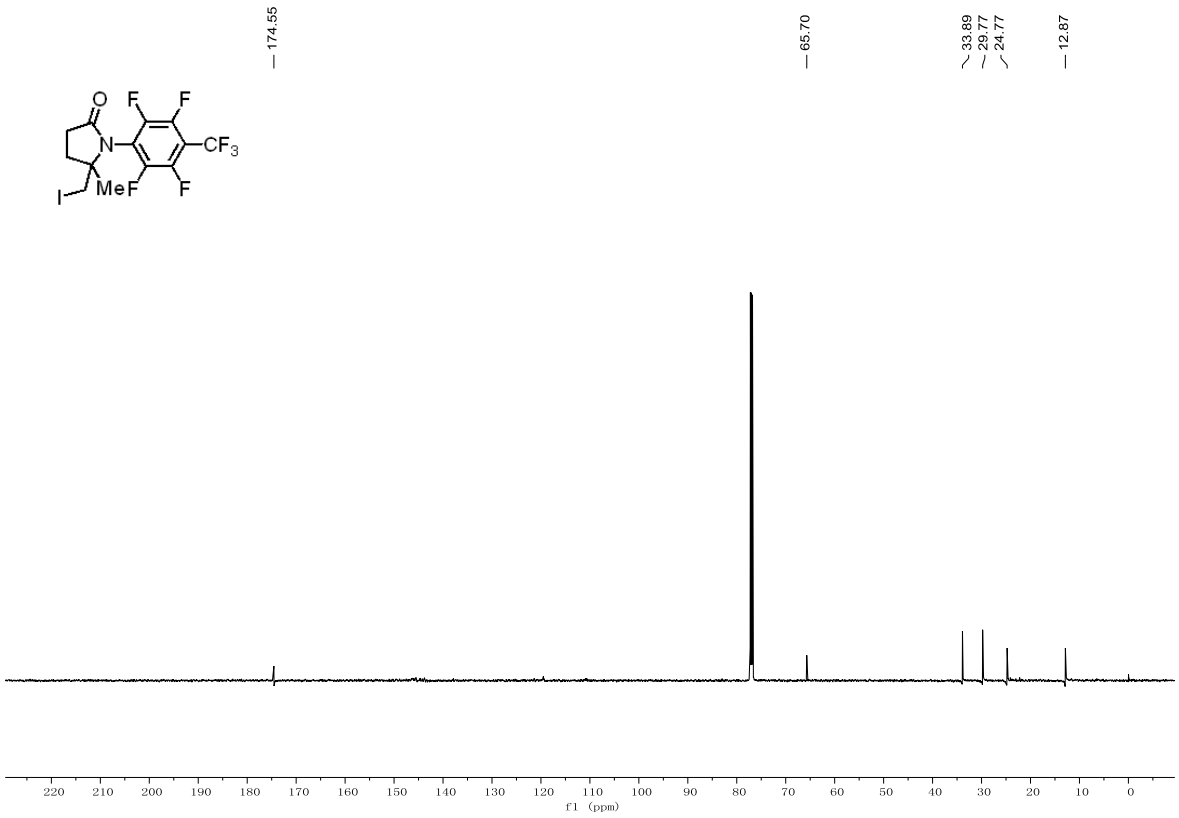
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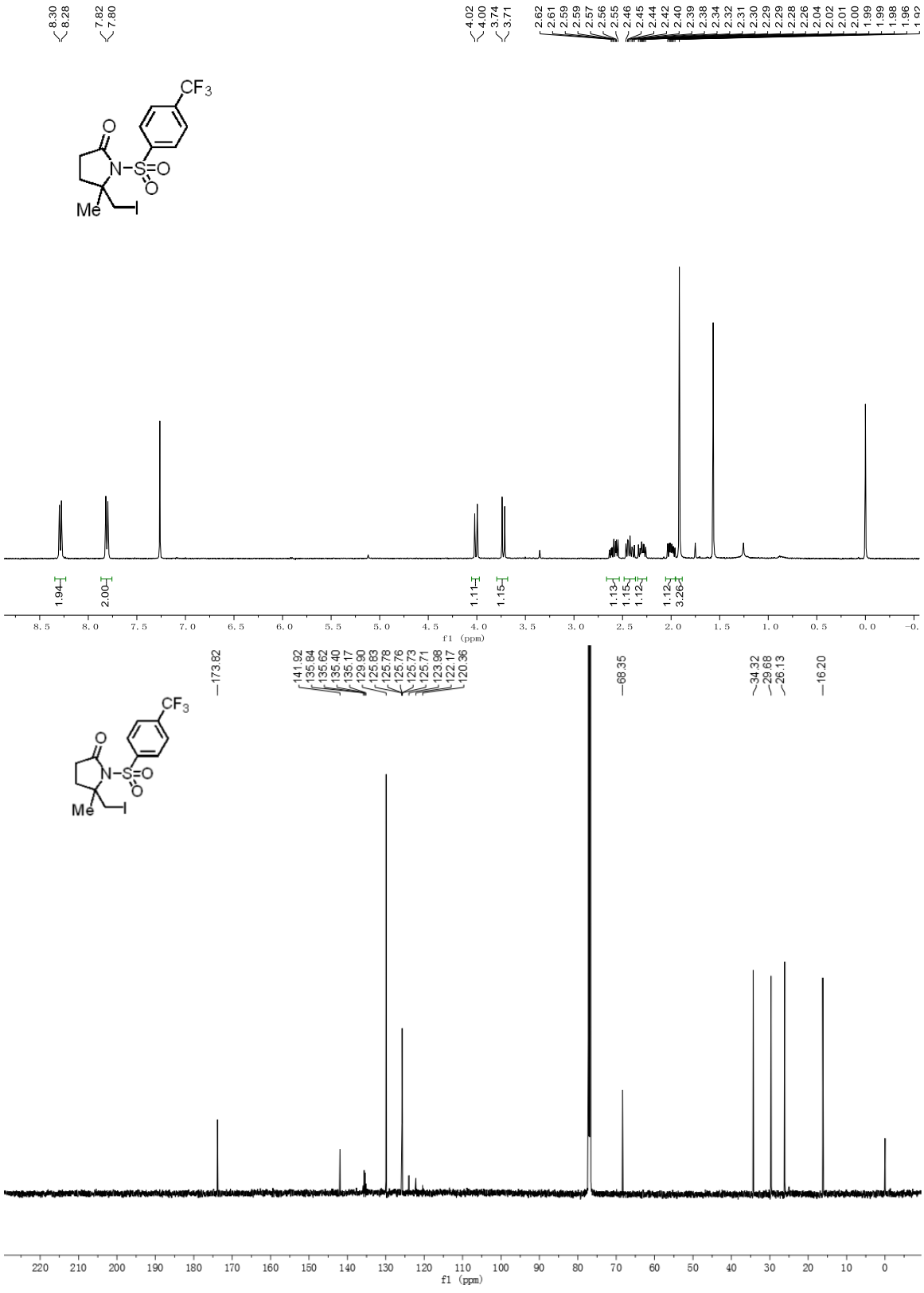
f1 (ppm)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2.01
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S
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1.13
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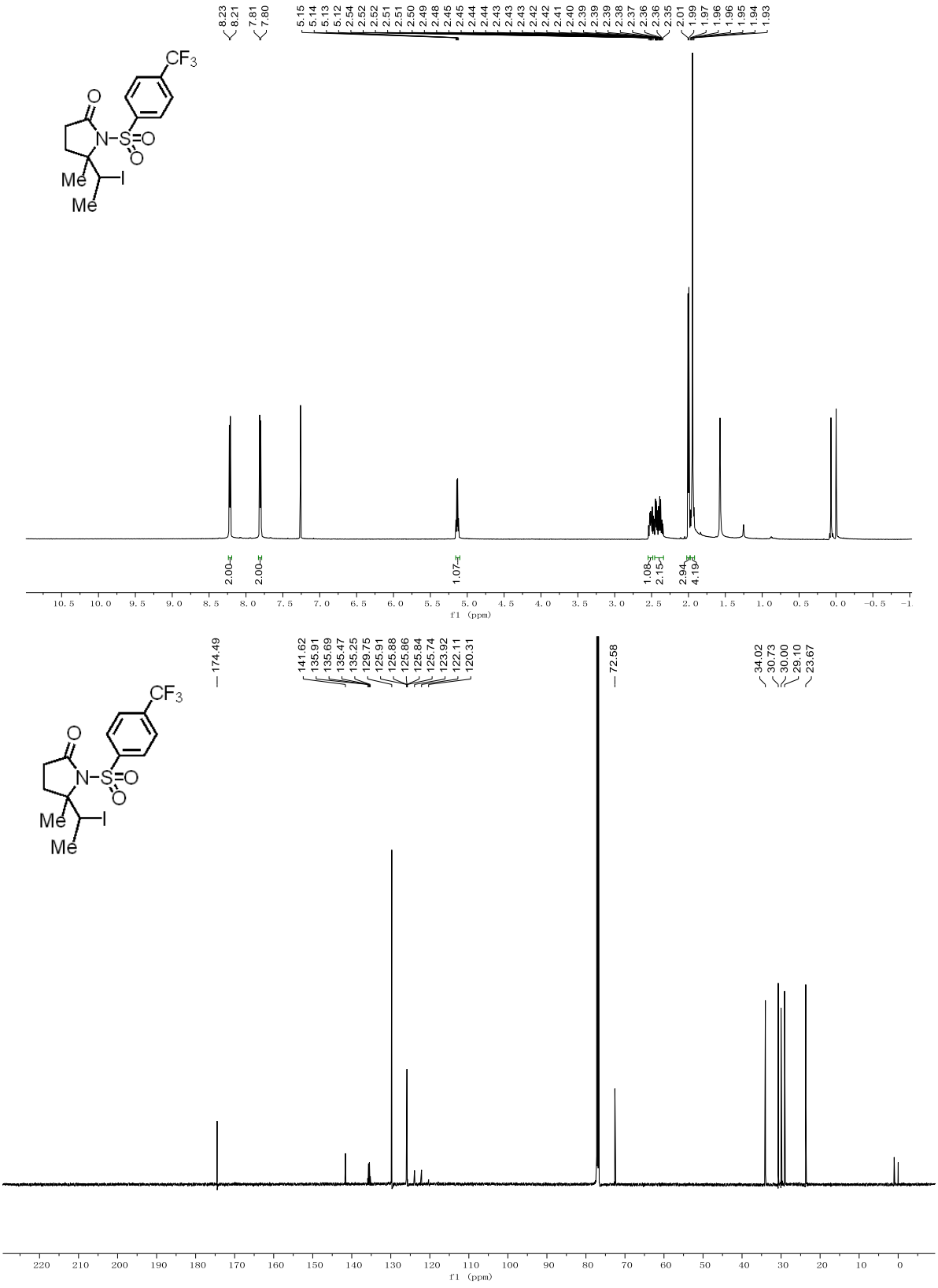
f1 (ppm)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2.36
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2.35
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1.97
1.96
1.96
1.95
1.94
1.93
CF3
O
N
S
O
O
Me
I
Me
2.00
2.00
1.07
1.08
2.15
2.94
4.19
f1 (ppm)
174.49
141.62
135.91
135.69
135.47
135.25
129.75
125.91
125.88
125.86
125.84
125.74
123.92
122.11
120.31
72.58
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29.10
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CF3
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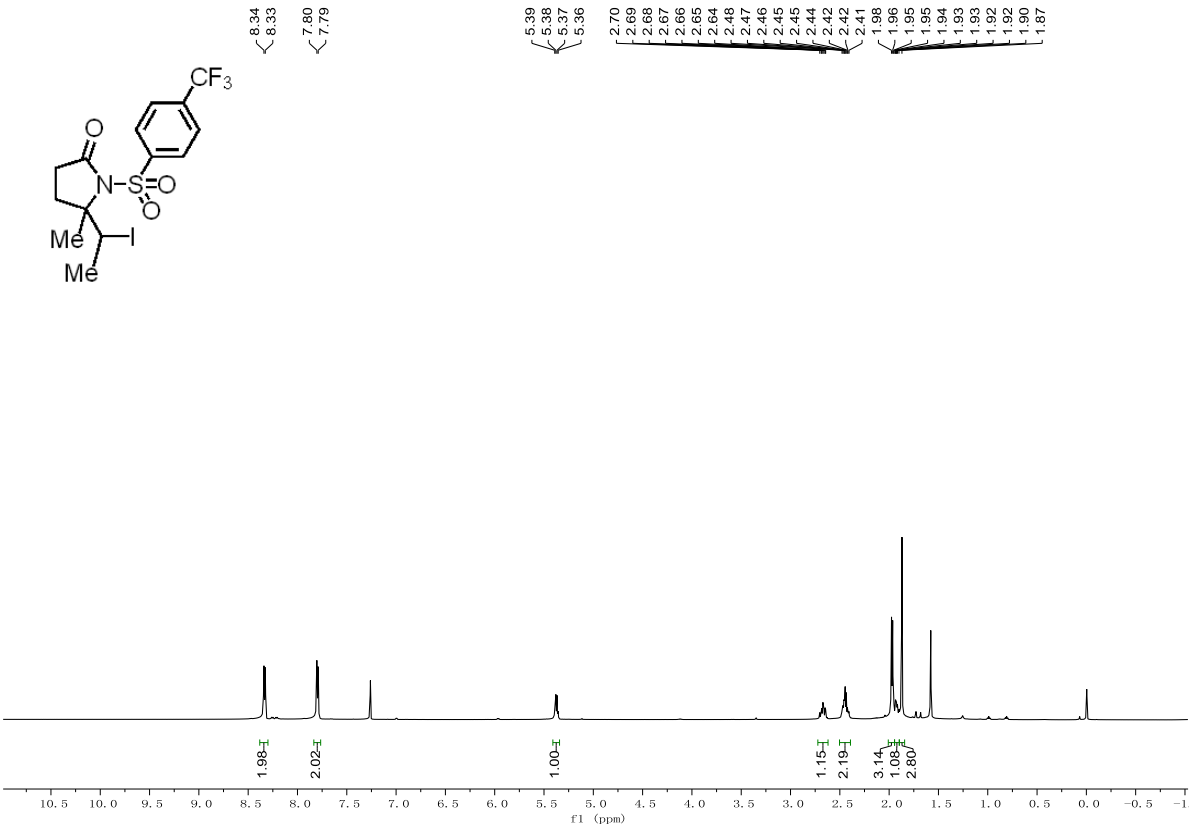
S
O
O
Me
I
Me
f1 (ppm)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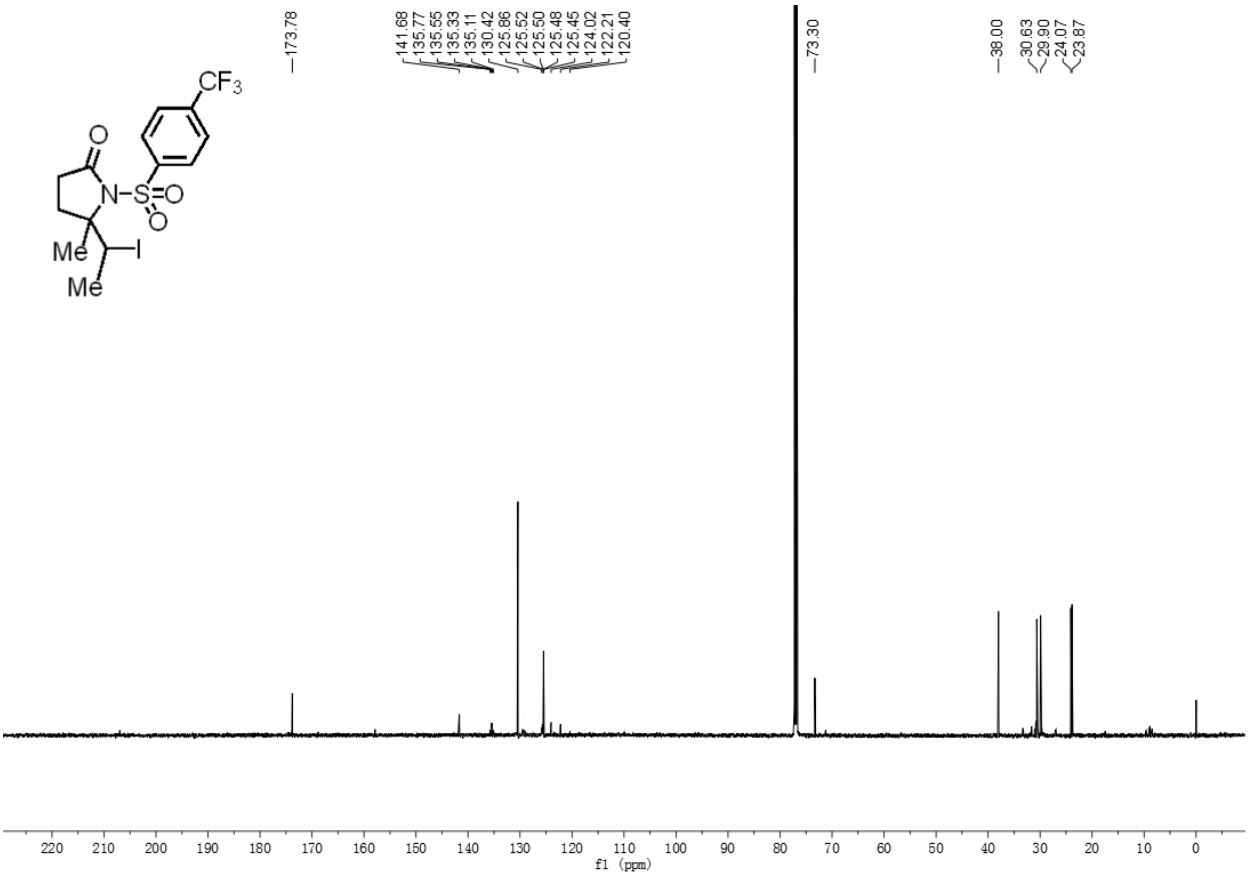
2.66
2.65
2.64
2.48
2.47
2.46
2.45
2.45
2.44
2.42
2.42
2.41
1.98
1.96
1.95
1.95
1.94
1.93
1.93
1.92
1.92
1.90
1.87
CF3
O
N
S
O
O
Me
I
Me
1.98
2.02
1.00
1.15
2.19
3.14
1.08
2.80
f1 (ppm)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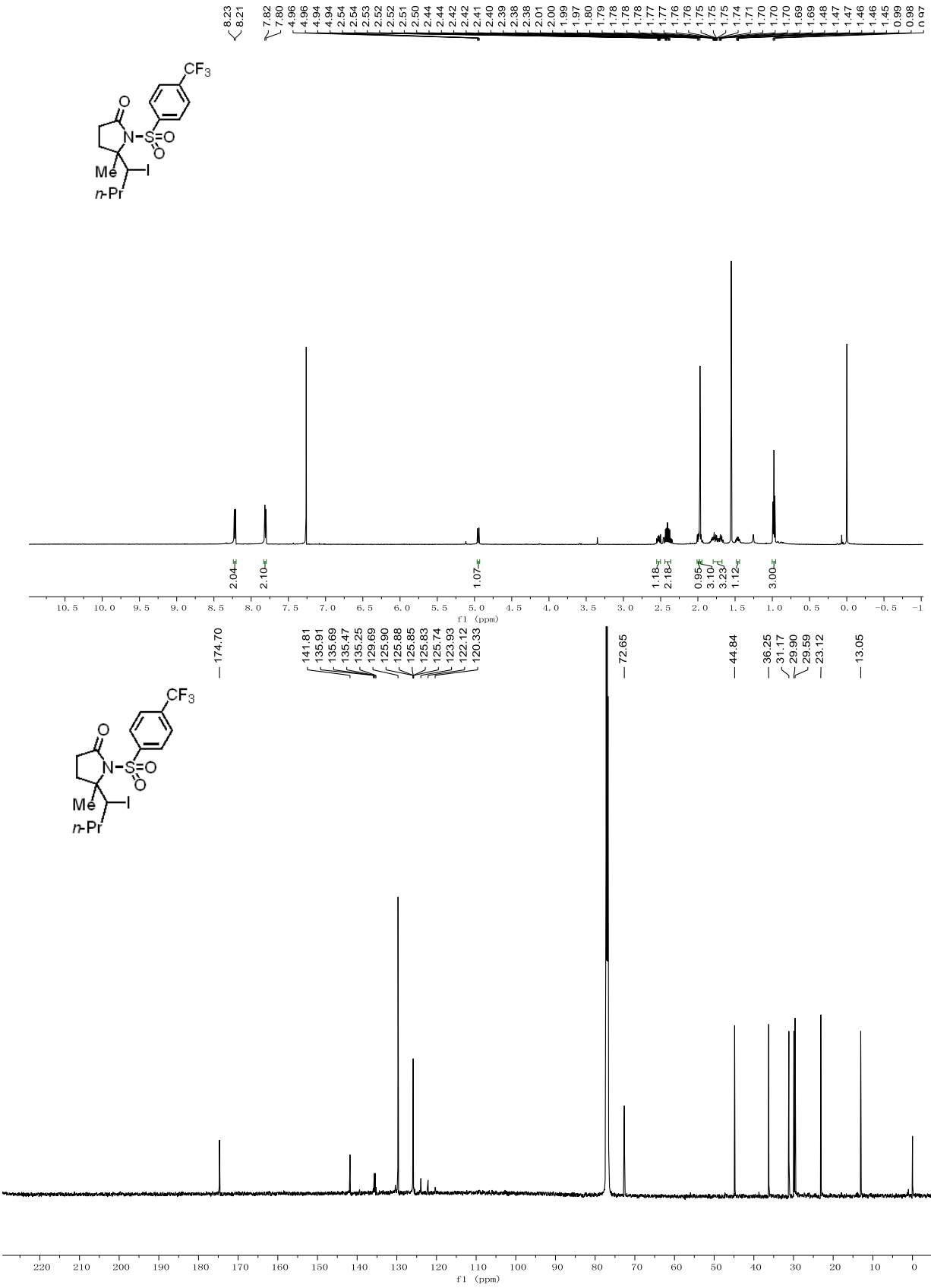
135.55
135.33
135.11
130.42
125.86
125.52
125.50
125.48
125.45
124.02
122.21
120.40
73.30
38.00
30.63
29.90
24.07
23.87
CF3
O
N
S
O
O
Me
I
Me
f1 (ppm)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8.21
7.82
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4.94
4.94
2.54
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2.52
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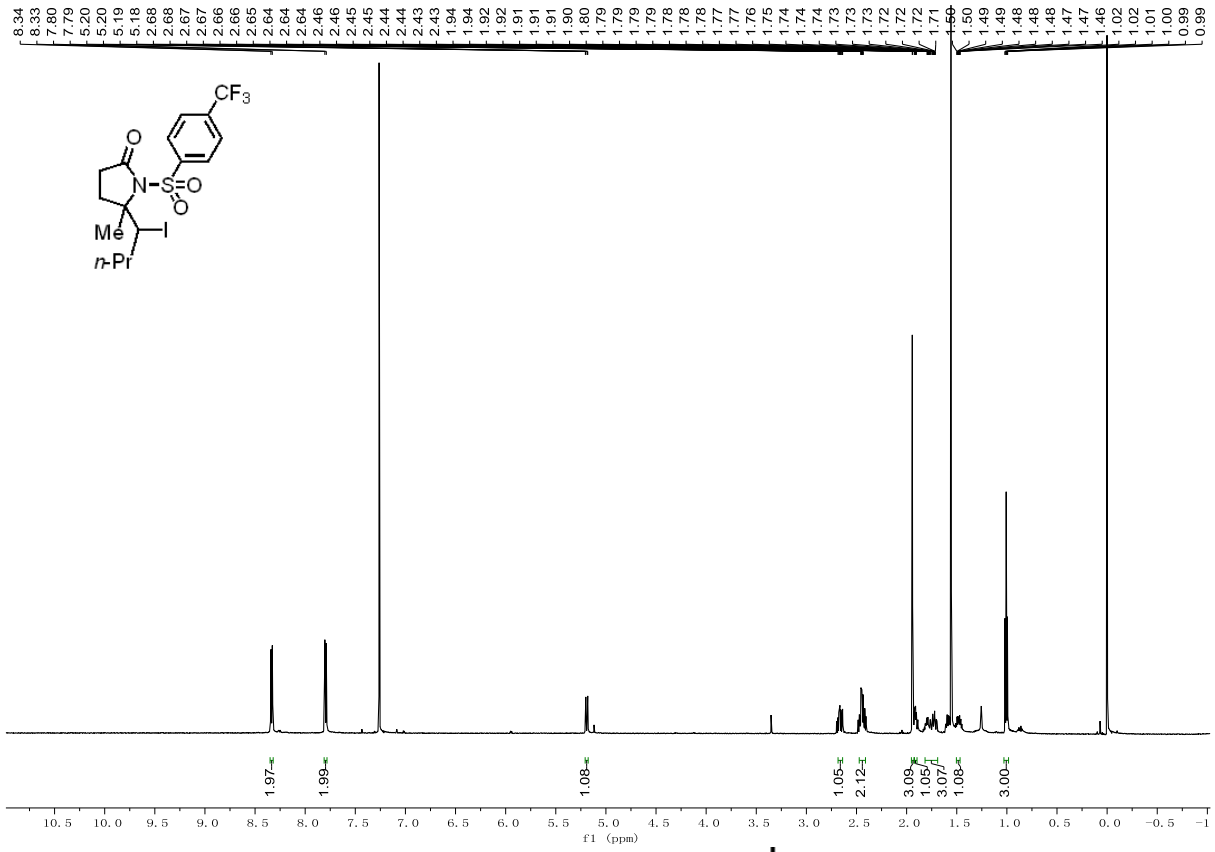
2.44
2.44
2.42
2.42
2.41
2.40
2.39
2.38
2.38
2.01
2.00
1.99
1.97
1.80
1.79
1.78
1.78
1.78
1.77
1.77
1.76
1.76
1.75
1.75
1.75
1.74
1.71
1.70
1.70
1.70
1.69
1.69
1.48
1.47
1.47
1.46
1.46
1.45
0.99
0.98
CF3
O
N
S
O
O
Me
I
n-Pr
2.04
2.10
1.07
1.18
2.18
0.95
3.10
3.23
1.12
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)
174.70
141.81
135.91
135.69
135.47
135.25
129.69
125.90
125.88
125.85
125.83
125.74
123.93
122.12
120.33
72.65
44.84
36.25
31.17
29.90
29.59
23.12
13.05
CF3
O
N
S
O
O
Me
I
n-Pr
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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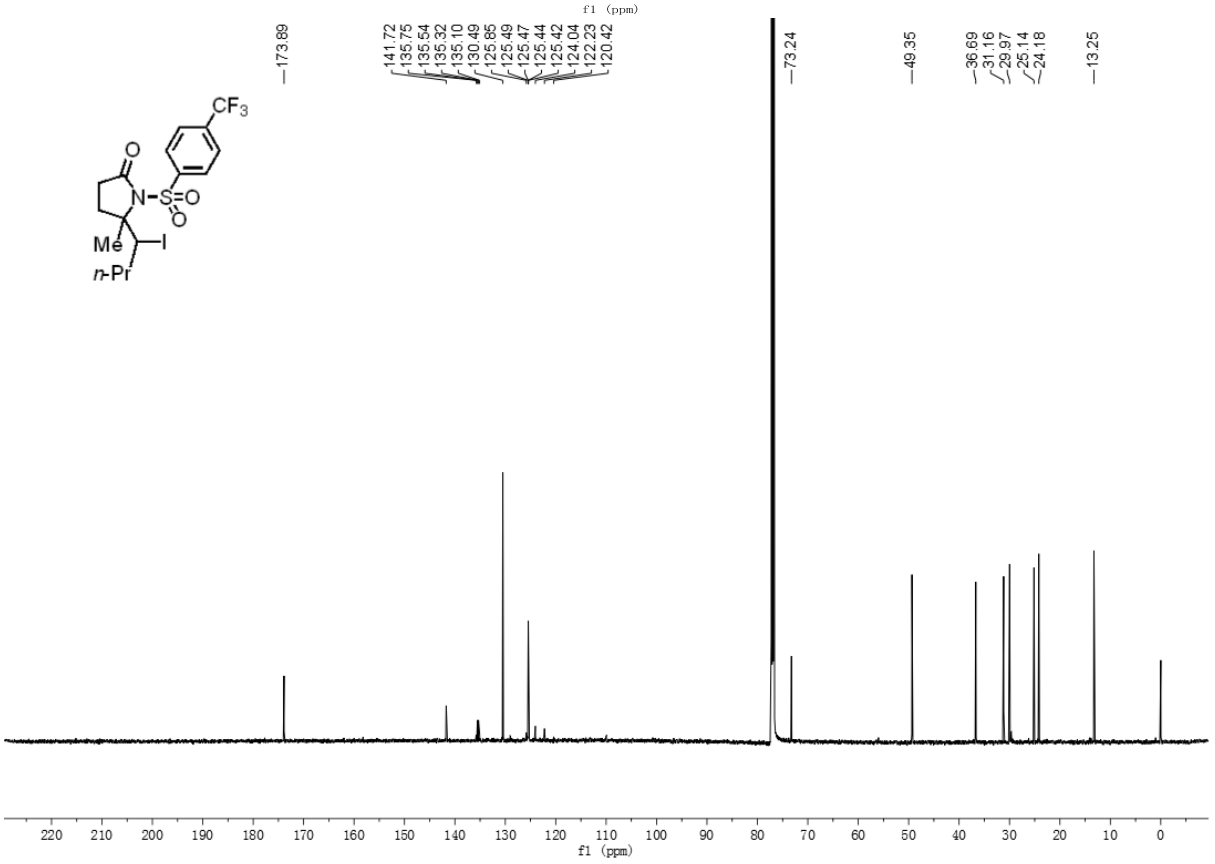
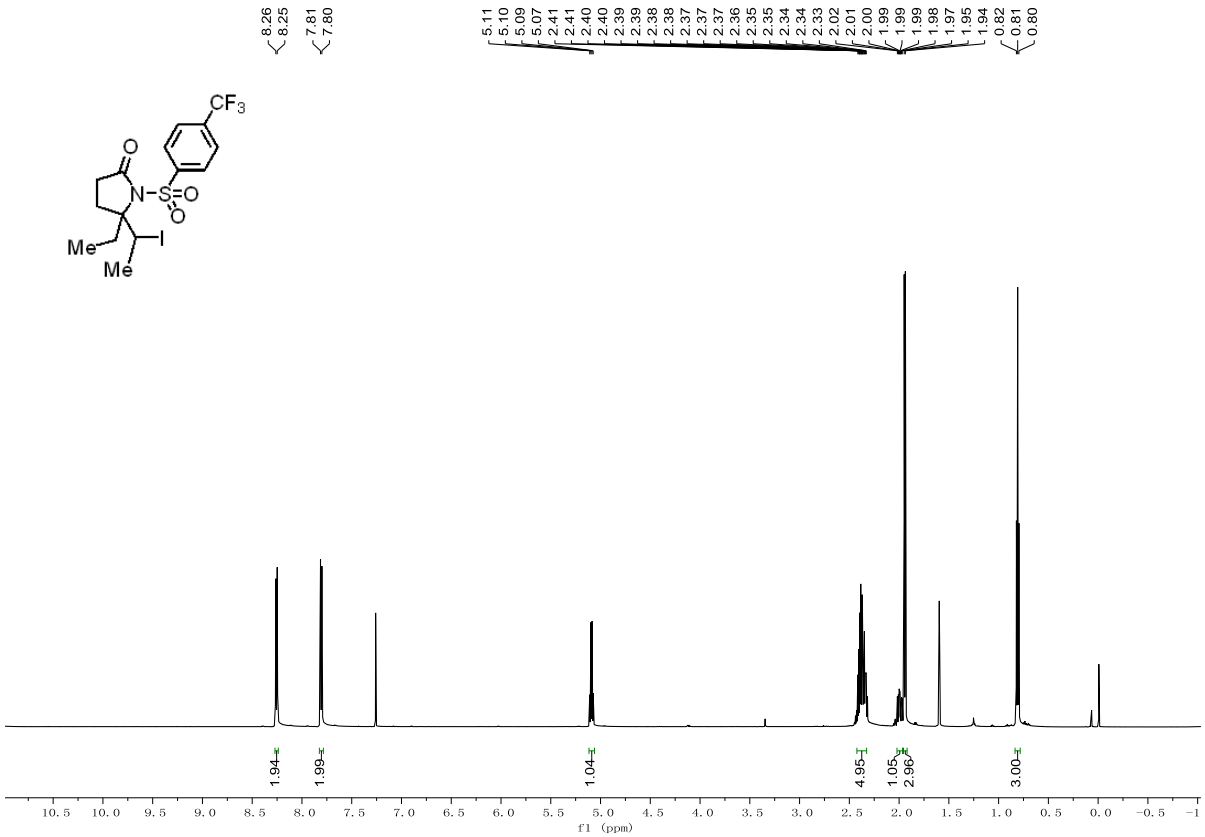
O
N
S
O
O
Me
I
n-Pr
f1 (ppm)


CF3
O
N
S
O
O
Me
I
n-Pr
f1 (ppm)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8.25
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7.80
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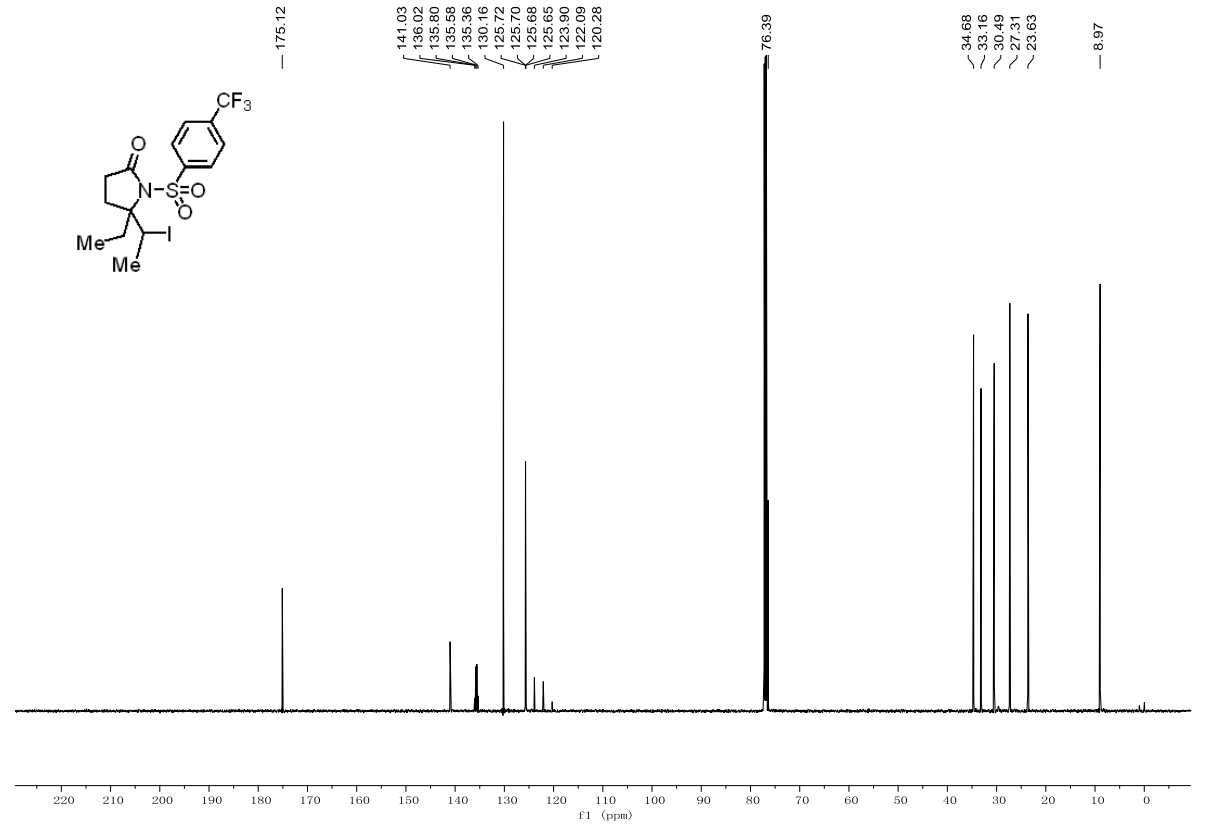
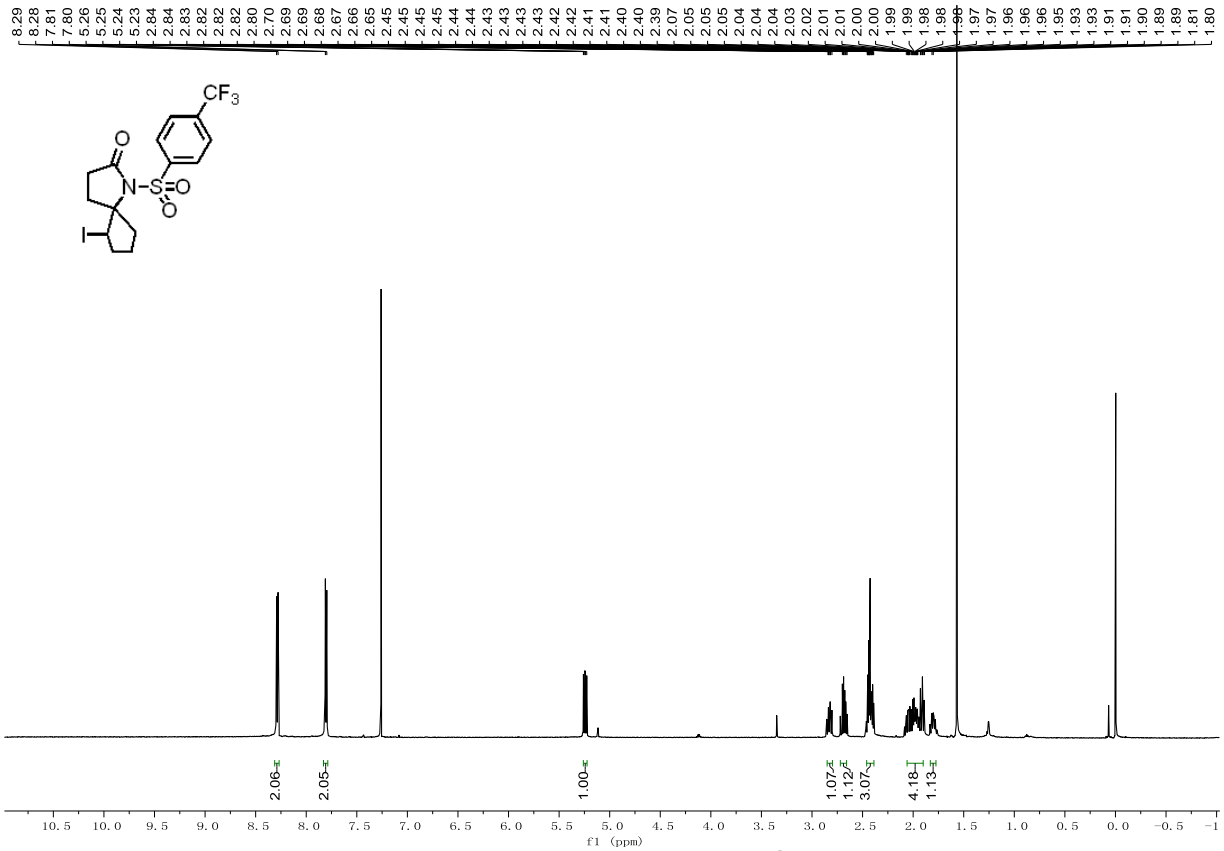
5.10
5.09
5.07
2.41
2.41
2.40
2.40
2.39
2.39
2.38
2.38
2.37
2.37
2.37
2.36
2.35
2.35
2.34
2.34
2.33
2.02
2.01
2.00
1.99
1.99
1.99
1.98
1.97
1.95
1.94
0.82
0.81
0.80
CF3
O
N
S
O
O
Me
I
Me
1.94
1.99
1.04
4.95
1.05
2.96
3.00
f1 (ppm)


175.12
141.03
136.02
135.80
135.58
135.36
130.16
125.72
125.70
125.68
125.65
123.90
122.09
120.28
76.39
34.68
33.16
30.49
27.31
23.63
8.97
CF3
O
N
S
O
O
Me
I
Me
f1 (ppm)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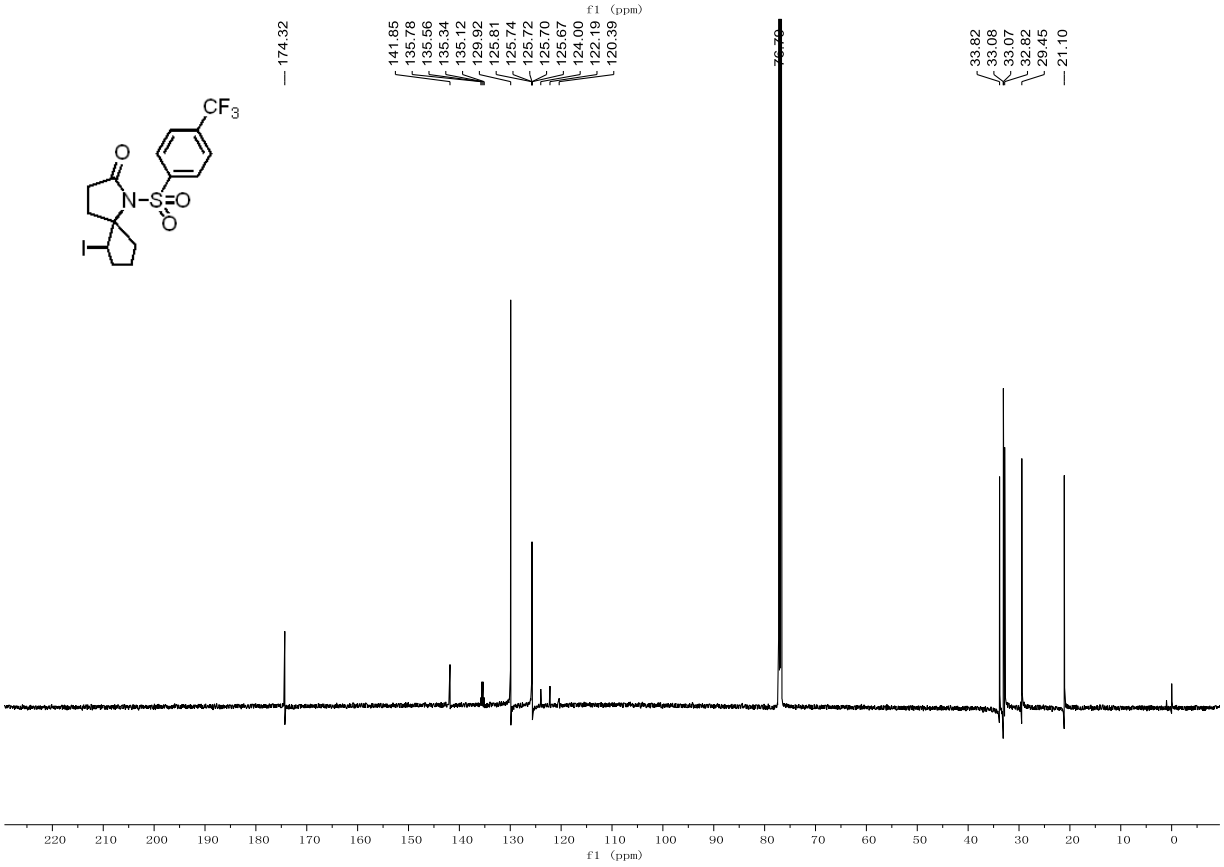
CF3
O
N
S
O
O
I
2.06
2.05
1.00
1.07
1.12
3.07
4.18
1.13
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1
f1 (ppm)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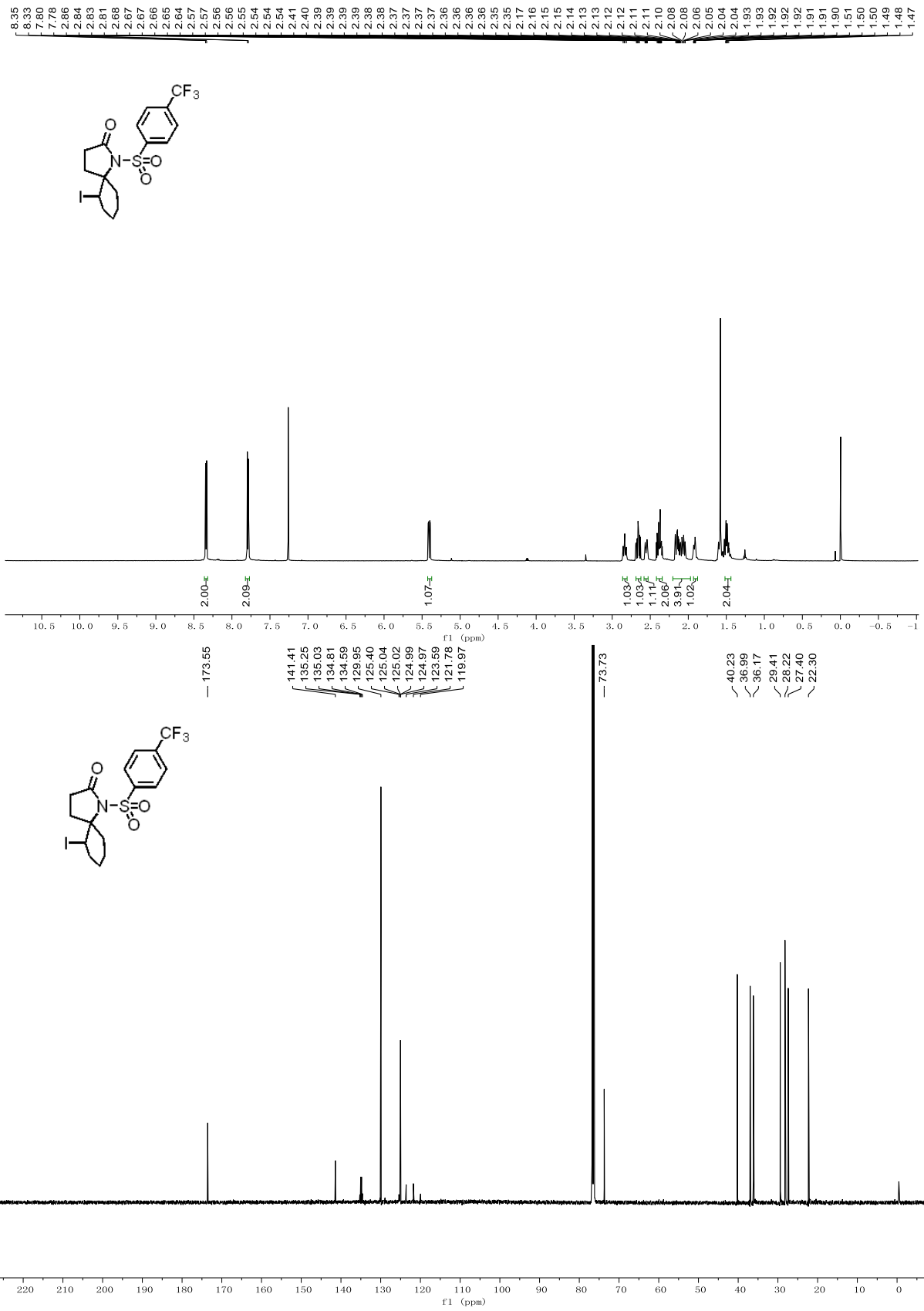
135.12
129.92
125.81
125.74
125.72
125.70
125.67
124.00
122.19
120.39
76.70
33.82
33.08
33.07
32.82
29.45
21.10
CF3
O
N
S
O
O
I
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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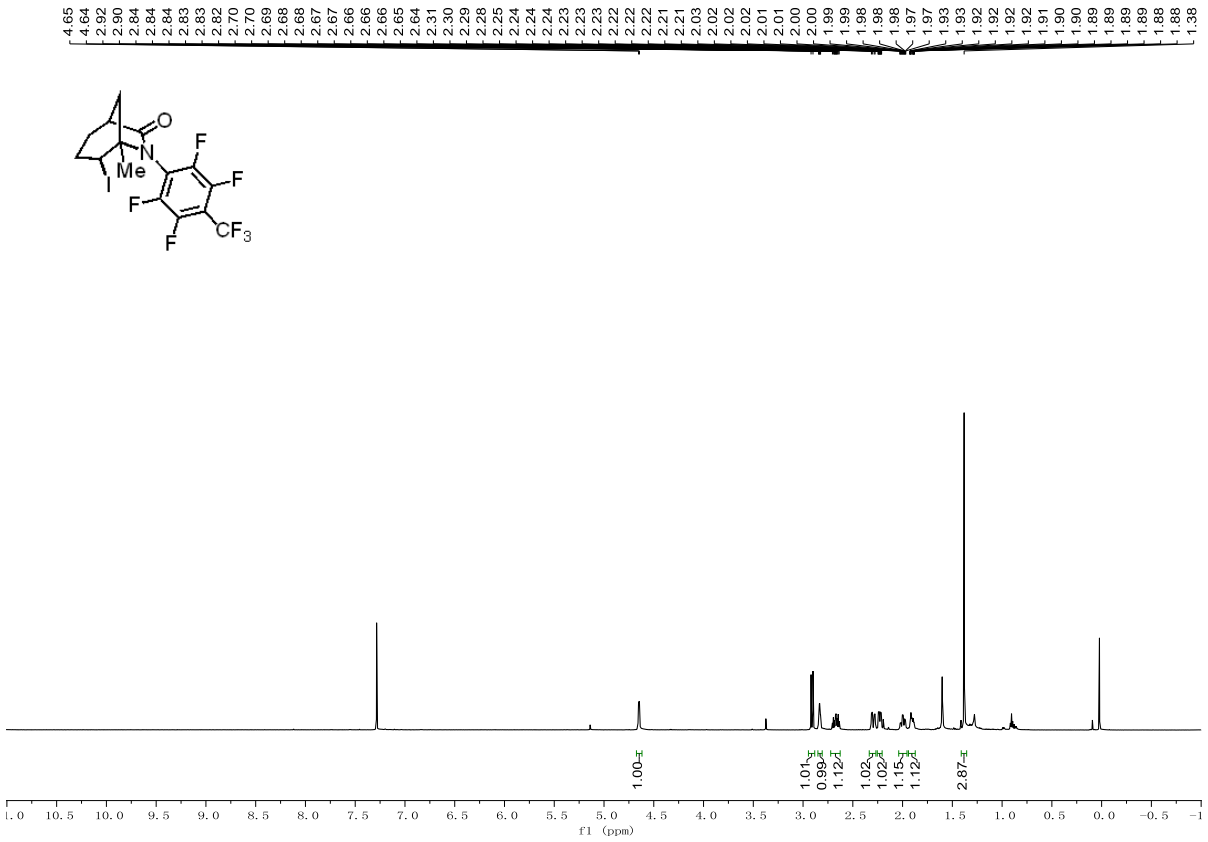
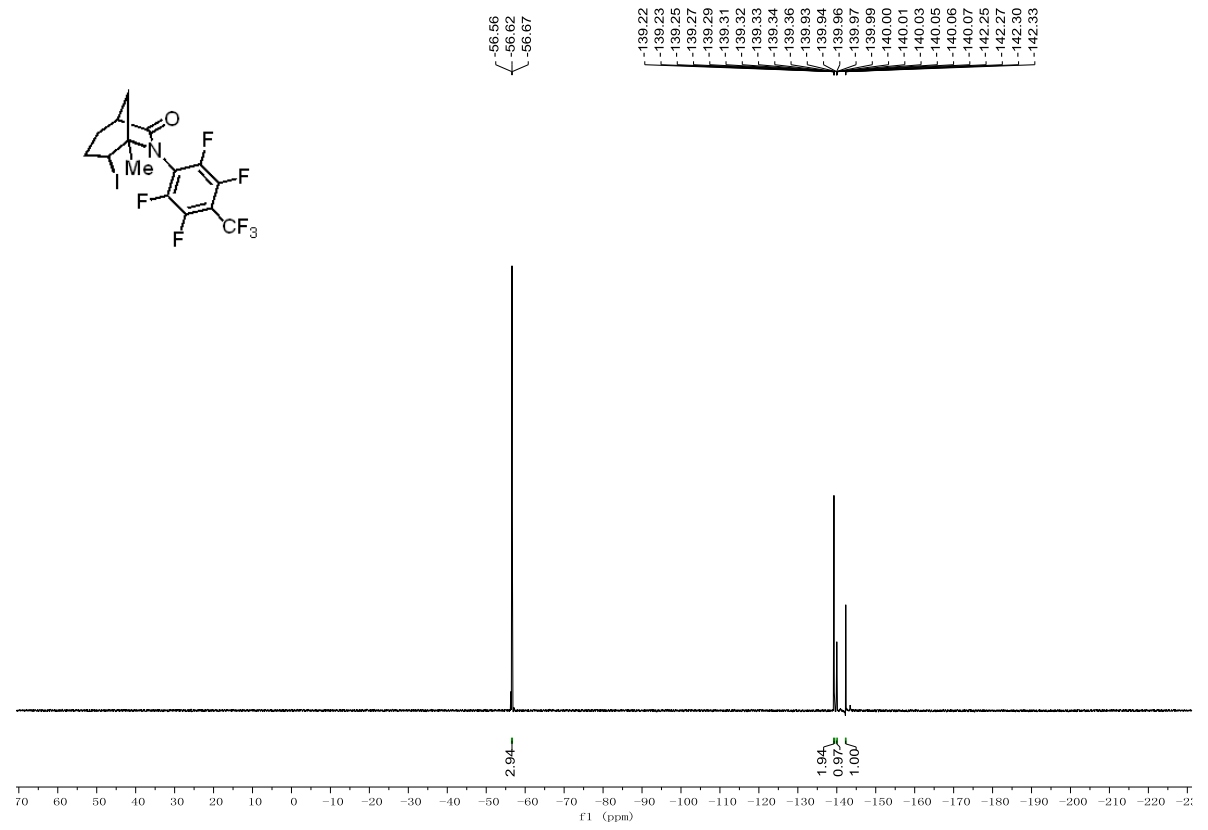
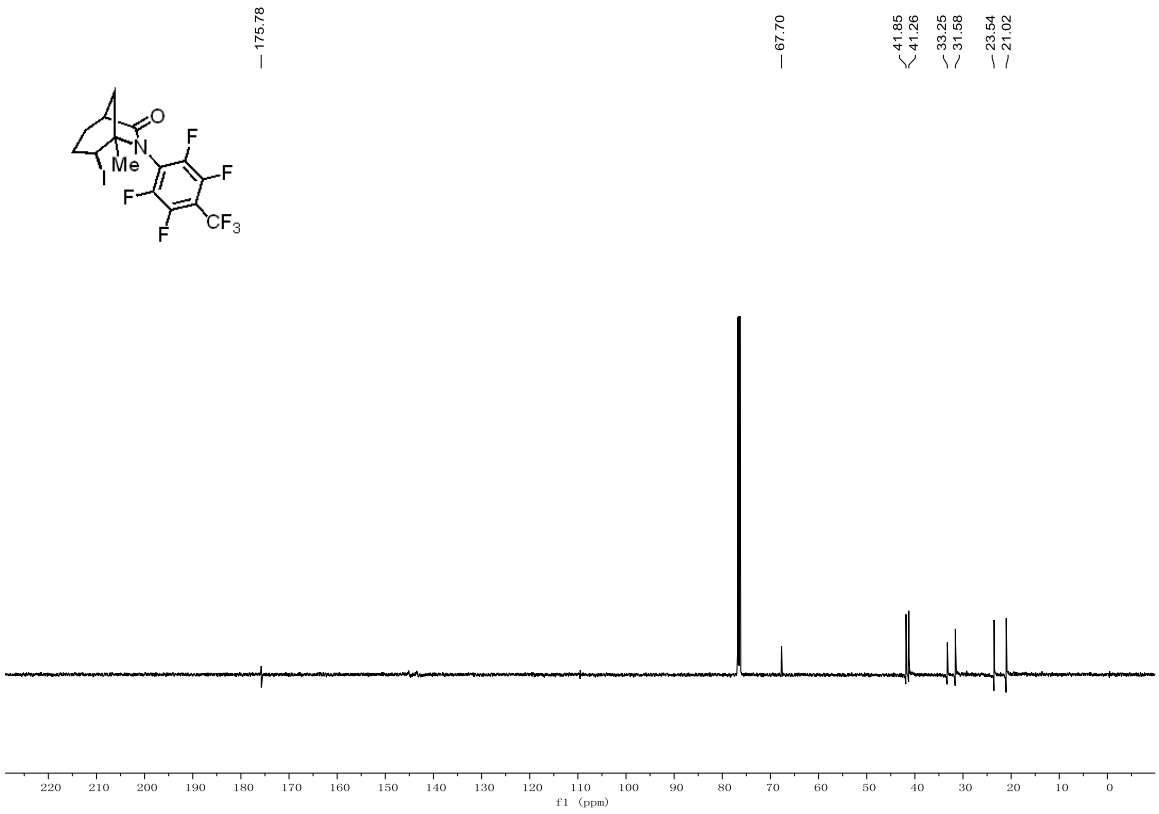
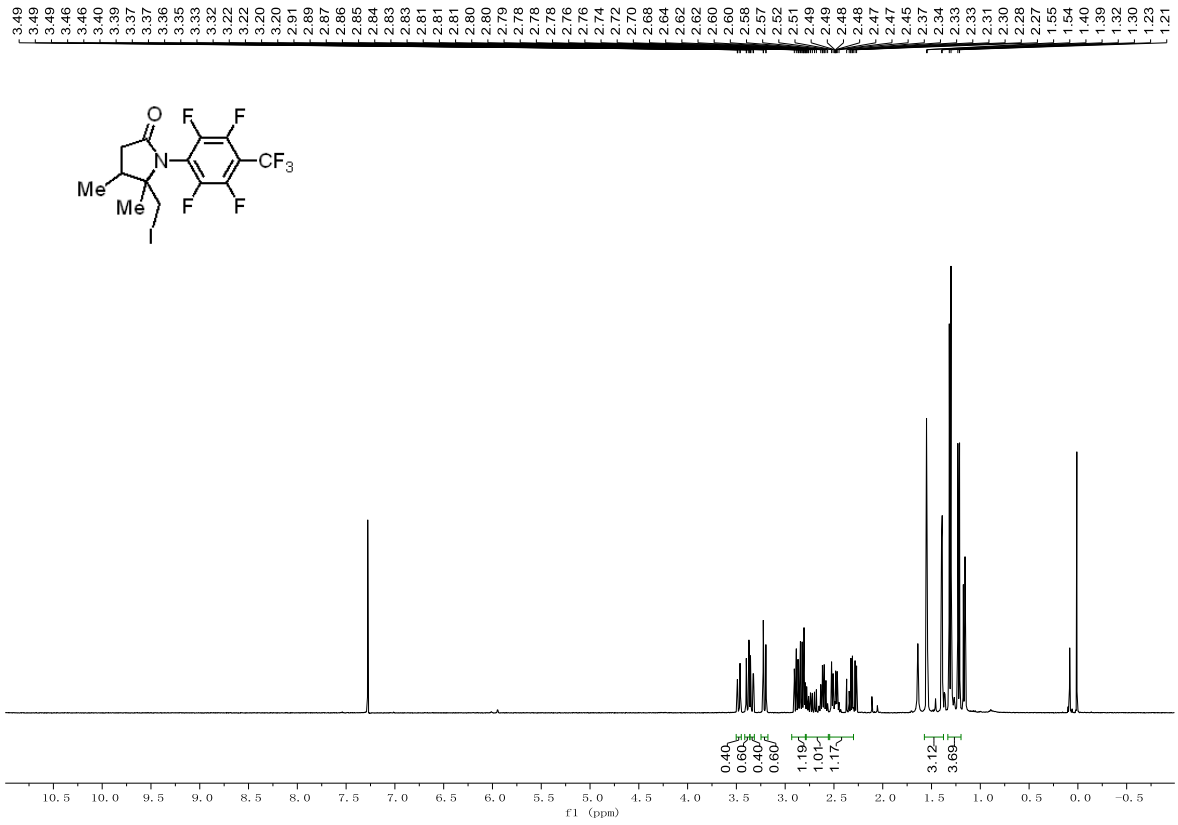
CF3
O
N
S
O
O
I
2.00
2.09
1.07
1.03
1.03
1.11
2.06
3.91
1.02
2.04
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1
f1 (ppm)
173.55
141.41
135.25
135.03
134.81
134.59
129.95
125.40
125.04
125.02
124.99
124.97
123.59
121.78
119.97
73.73
40.23
36.99
36.17
29.41
28.22
27.40
22.30
CF3
O
N
S
O
O
I
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


4.65 4.64 2.92 2.90 2.84 2.84 2.84 2.83 2.83 2.82 2.70 2.70 2.69 2.68 2.68 2.67 2.67 2.66 2.66 2.66 2.65 2.64 2.31 2.30 2.29 2.28 2.25 2.24 2.24 2.23 2.23 2.23 2.22 2.22 2.22 2.21 2.21 2.03 2.02 2.02 2.02 2.01 2.01 2.00 2.00 1.99 1.99 1.98 1.98 1.98 1.97 1.97 1.93 1.93 1.92 1.92 1.92 1.92 1.91 1.90 1.90 1.89 1.89 1.89 1.89 1.88 1.88 1.38
O
N
Me
I
F
F
F
F
CF3
1.00
1.01
0.99
1.12
1.02
1.02
1.15
1.12
2.87
f1 (ppm)


-56.56 -56.62 -56.67
-139.22 -139.23 -139.25 -139.27 -139.29 -139.31 -139.32 -139.33 -139.34 -139.36 -139.93 -139.94 -139.96 -139.97 -139.99 -140.00 -140.01 -140.03 -140.05 -140.06 -140.07 -142.25 -142.27 -142.30 -142.33
O
N
Me
I
F
F
F
F
CF3
2.94
1.94
0.97
1.00
f1 (ppm)


175.78
67.70
41.85
41.26
33.25
31.58
23.54
21.02
O
N
Me
I
F
F
F
F
CF3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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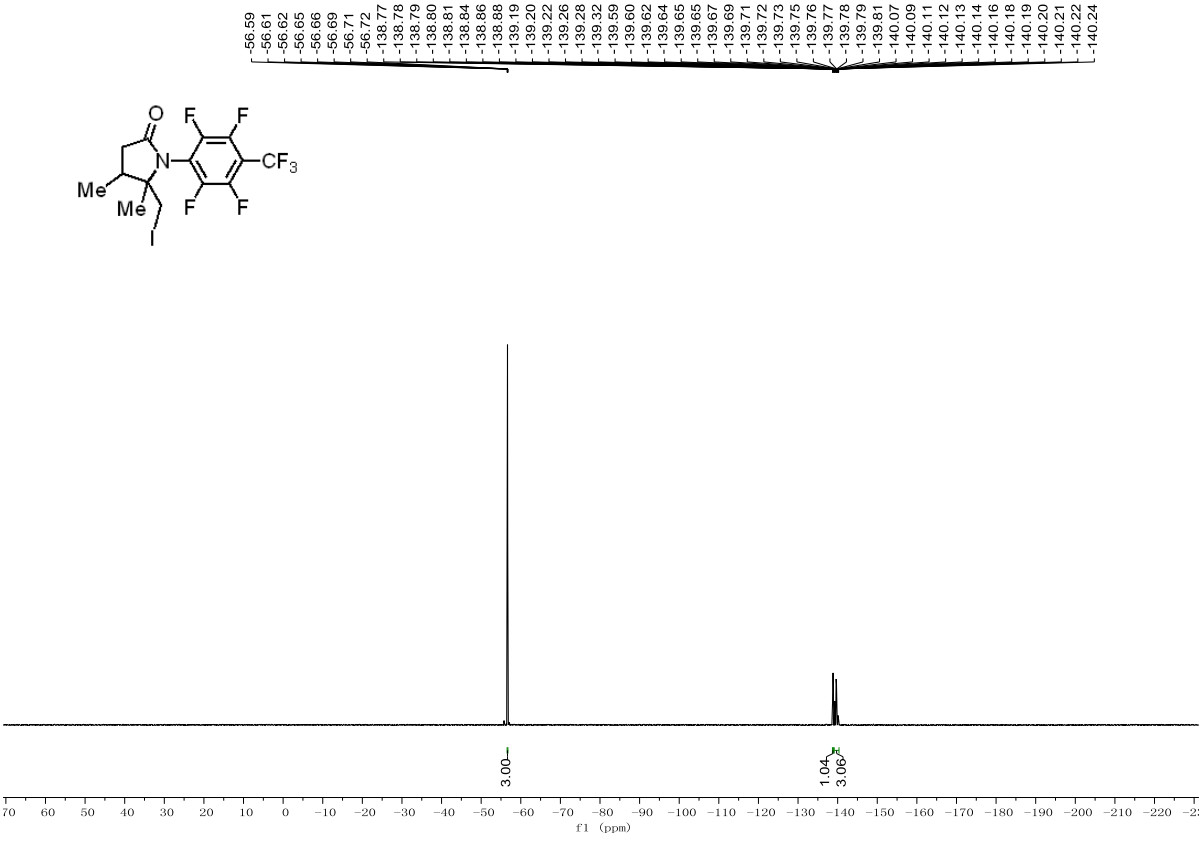
O
F
F
N
CF3
Me
Me
F
F
I
0.40
0.60
0.40
0.60
1.19
1.01
1.17
3.12
3.69
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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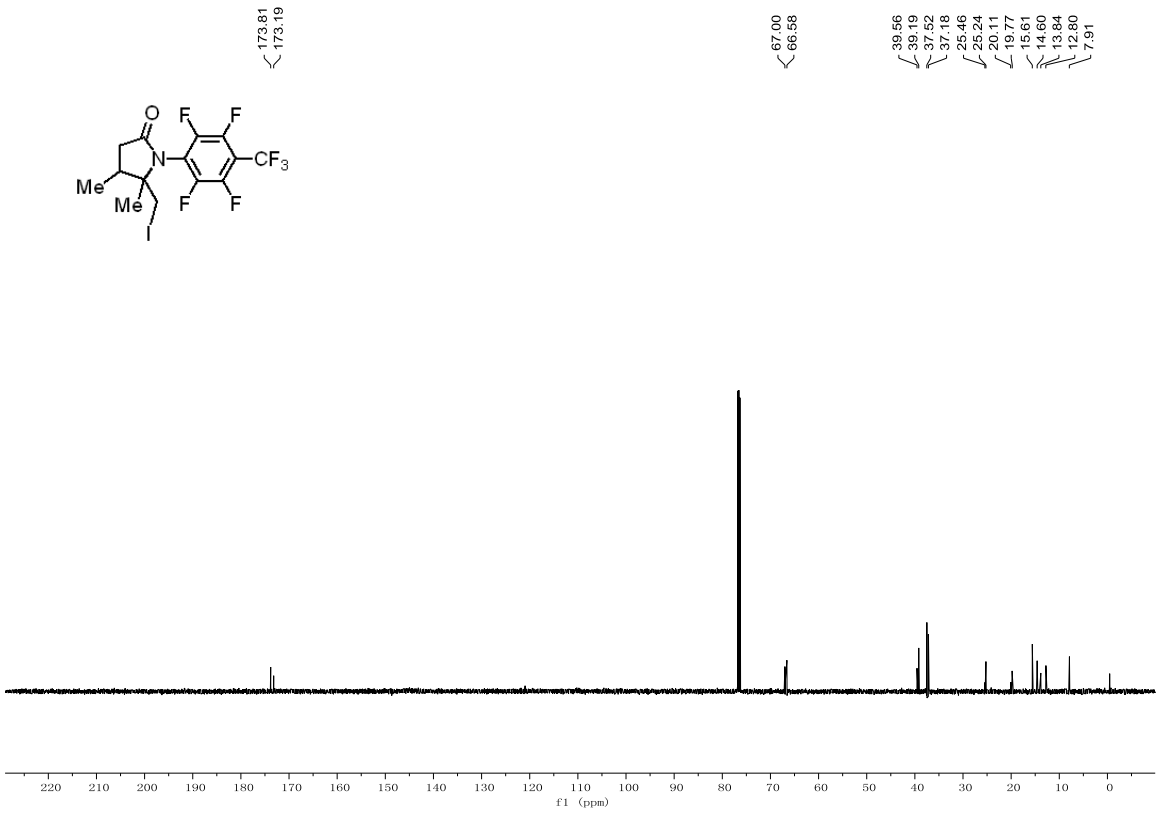
O
F
F
N
CF3
Me
Me
F
F
I
3.00
1.04
3.06
70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220
f1 (ppm)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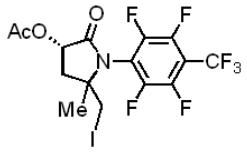
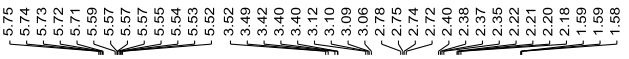
173.19
67.00
66.58
39.56
39.19
37.52
37.18
25.46
25.24
20.11
19.77
15.61
14.60
13.84
12.80
7.91
O
F
F
N
CF3
Me
Me
I
F
F
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


AcO
O
F
F
N
CF3
Me
F
F
I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5.52
3.52
3.49
3.42
3.40
3.40
3.12
3.10
3.09
3.06
2.78
2.75
2.74
2.72
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2.18
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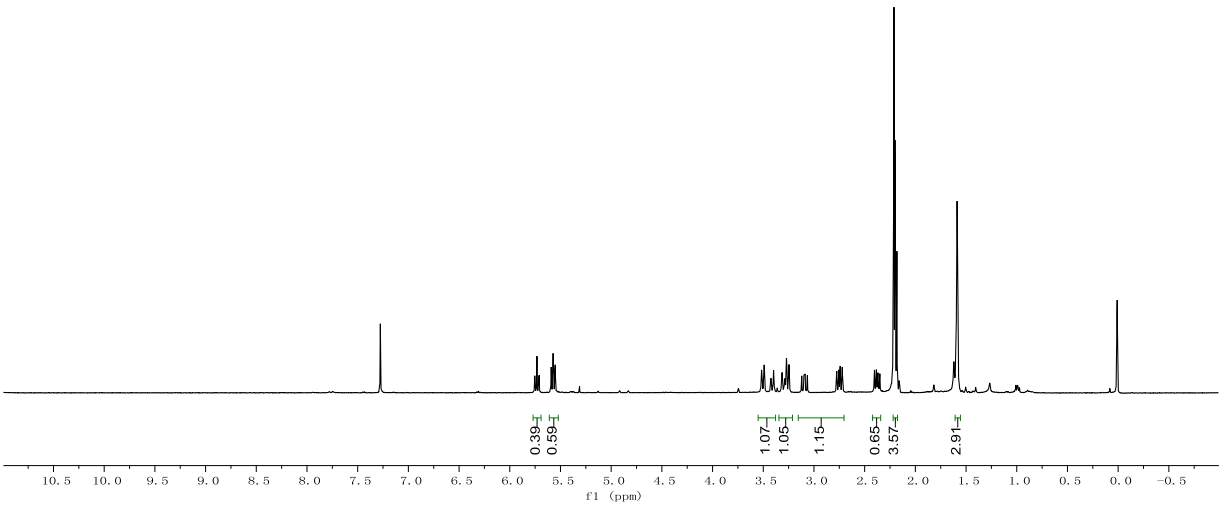
1.59
1.59
1.58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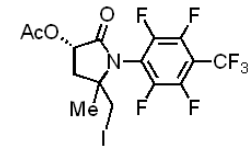
1.07
1.05
1.15
0.65
3.57
2.91
f1 (ppm)


AcO
O
F
F
N
CF3
Me
F
F
I


-56.62
-56.64
-56.68
-56.69
-56.74
-56.75
-138.42
-138.43
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-138.46
-138.48
-138.49
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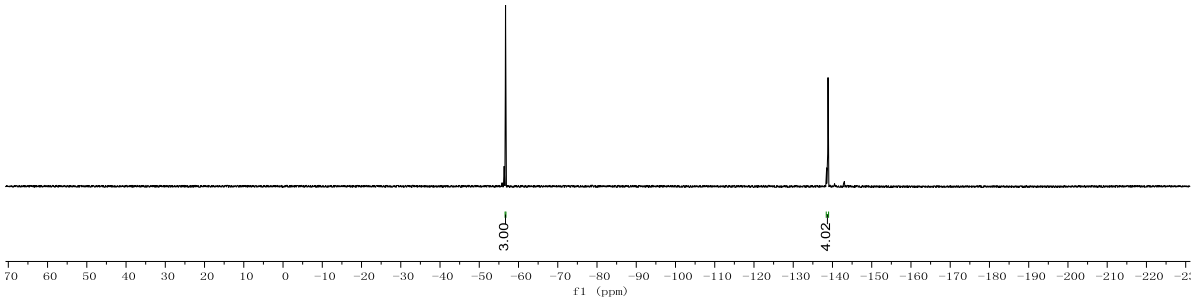
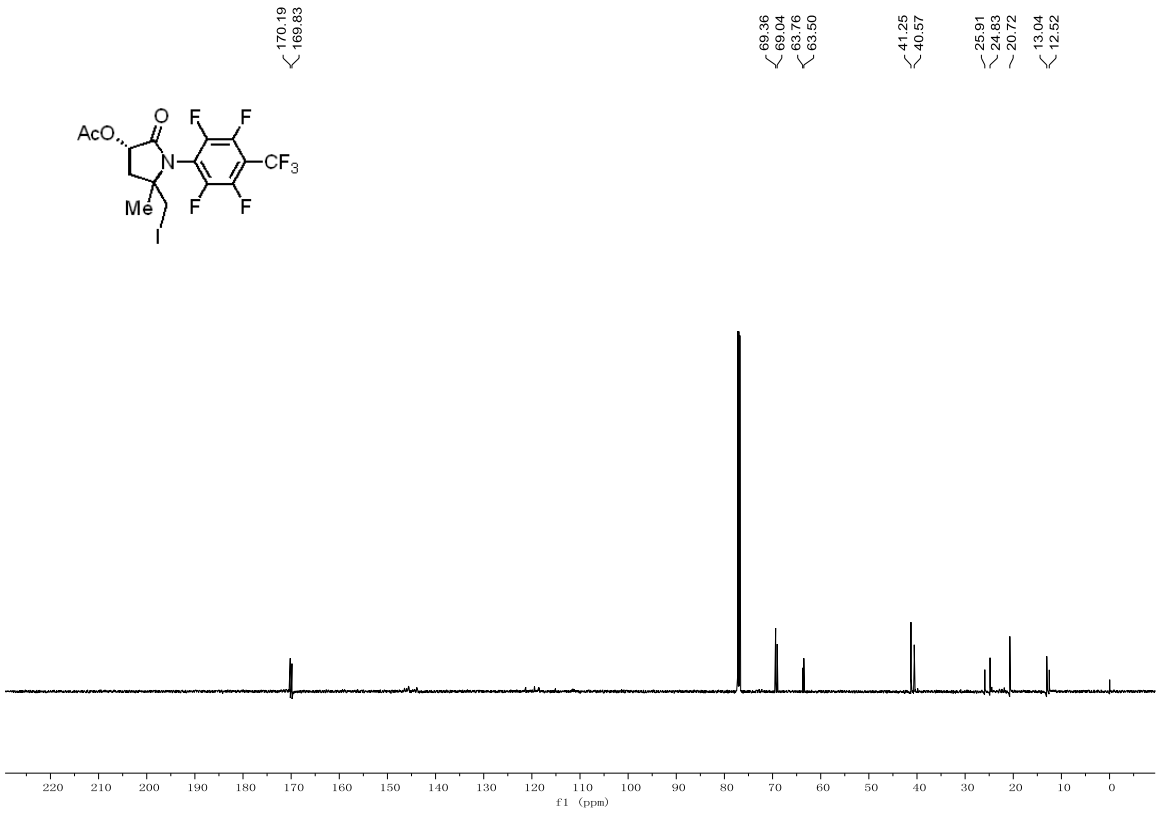
-138.92
-138.94


3.00
4.02
f1 (ppm)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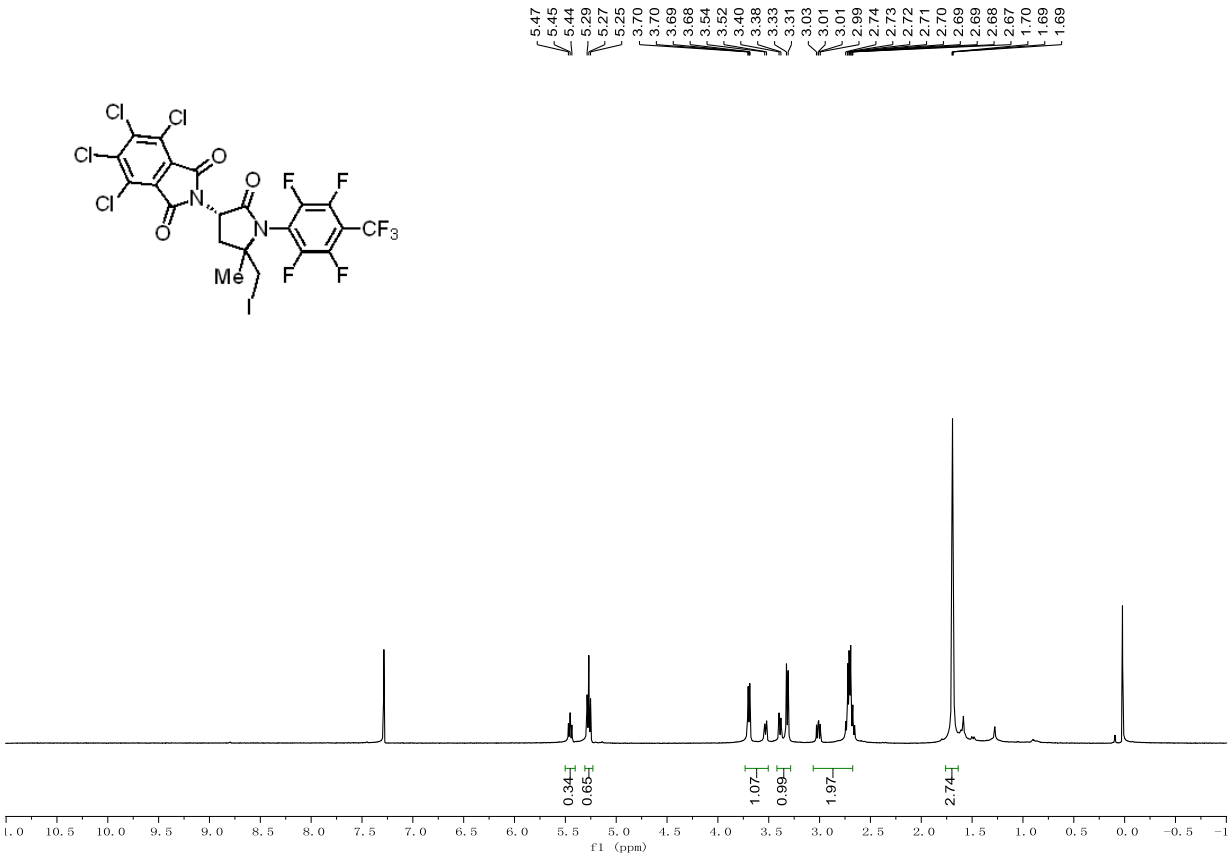
63.76
63.50
41.25
40.57
25.91
24.83
20.72
13.04
12.52
AcO
O
N
F
F
F
F
CF3
Me
I
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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5.25
3.70
3.70
3.69
3.68
3.54
3.52
3.40
3.38
3.33
3.31
3.03
3.01
3.01
2.99
2.74
2.73
2.72
2.71
2.70
2.69
2.69
2.68
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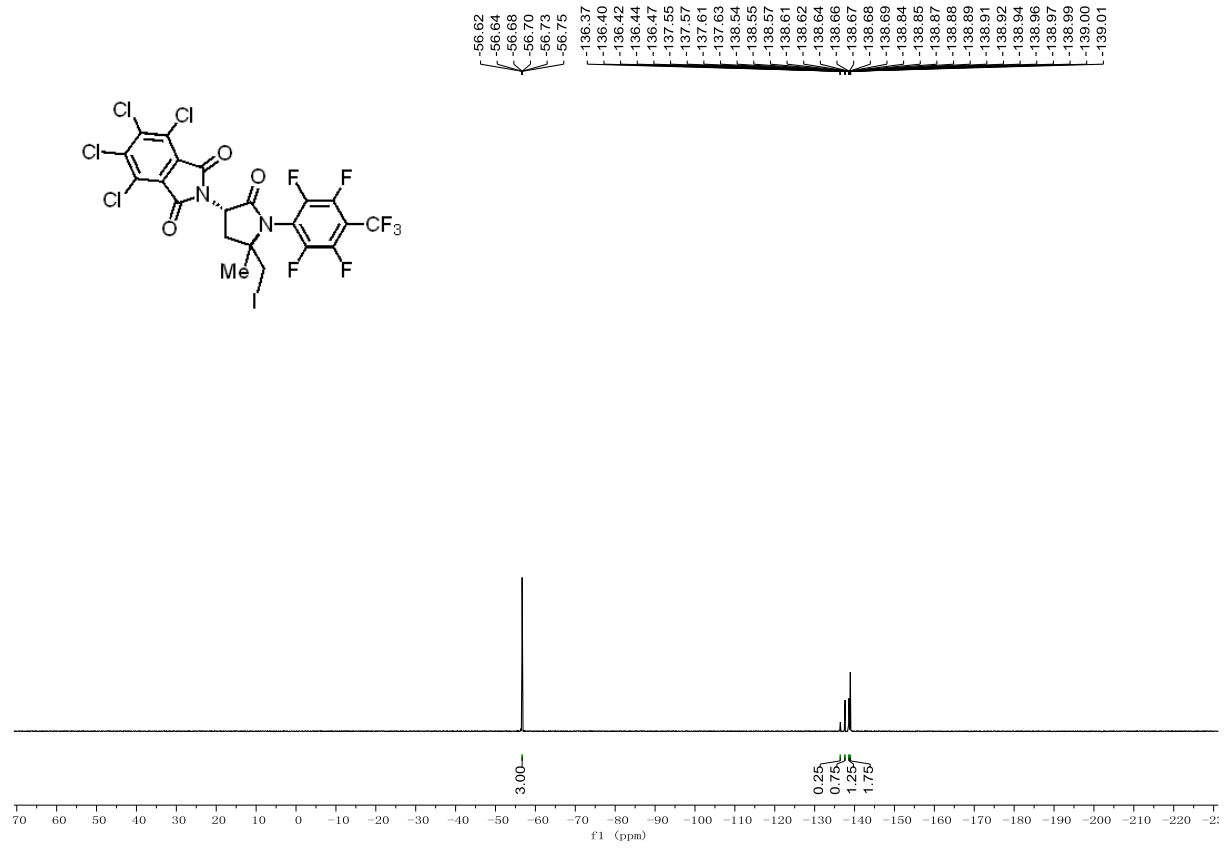
1.69
1.69
Cl
Cl
Cl
Cl
O
O
O
O
N
N
F
F
F
F
CF3
Me
I
0.34
0.65
1.07
0.99
1.97
2.74
f1 (ppm)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-137.55
-137.57
-137.61
-137.63
-138.54
-138.55
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-138.61
-138.62
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-138.66
-138.67
-138.68
-138.69
-138.84
-138.85
-138.87
-138.88
-138.89
-138.91
-138.92
-138.94
-138.96
-138.97
-138.99
-139.00
-139.01
Cl
Cl
Cl
Cl
O
O
O
O
N
N
F
F
F
F
CF3
Me
I
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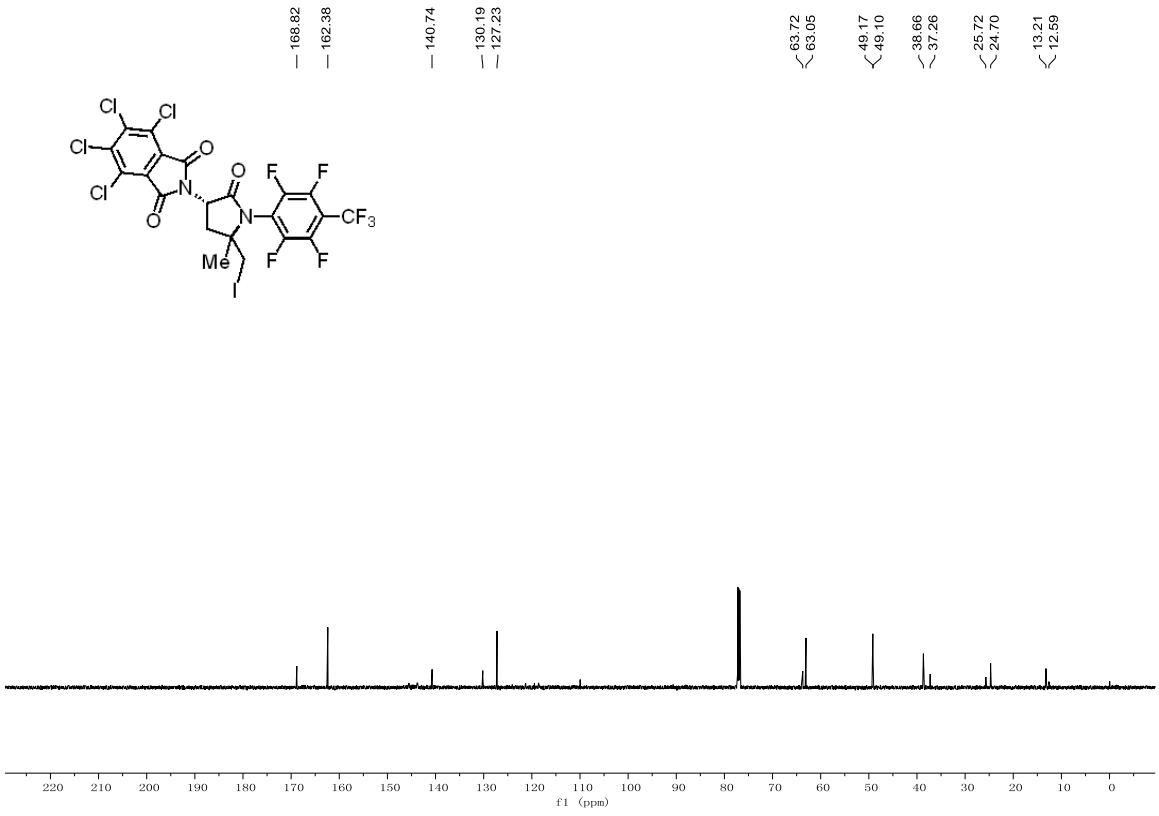
0.75
1.25
1.75
f1 (ppm)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140.74
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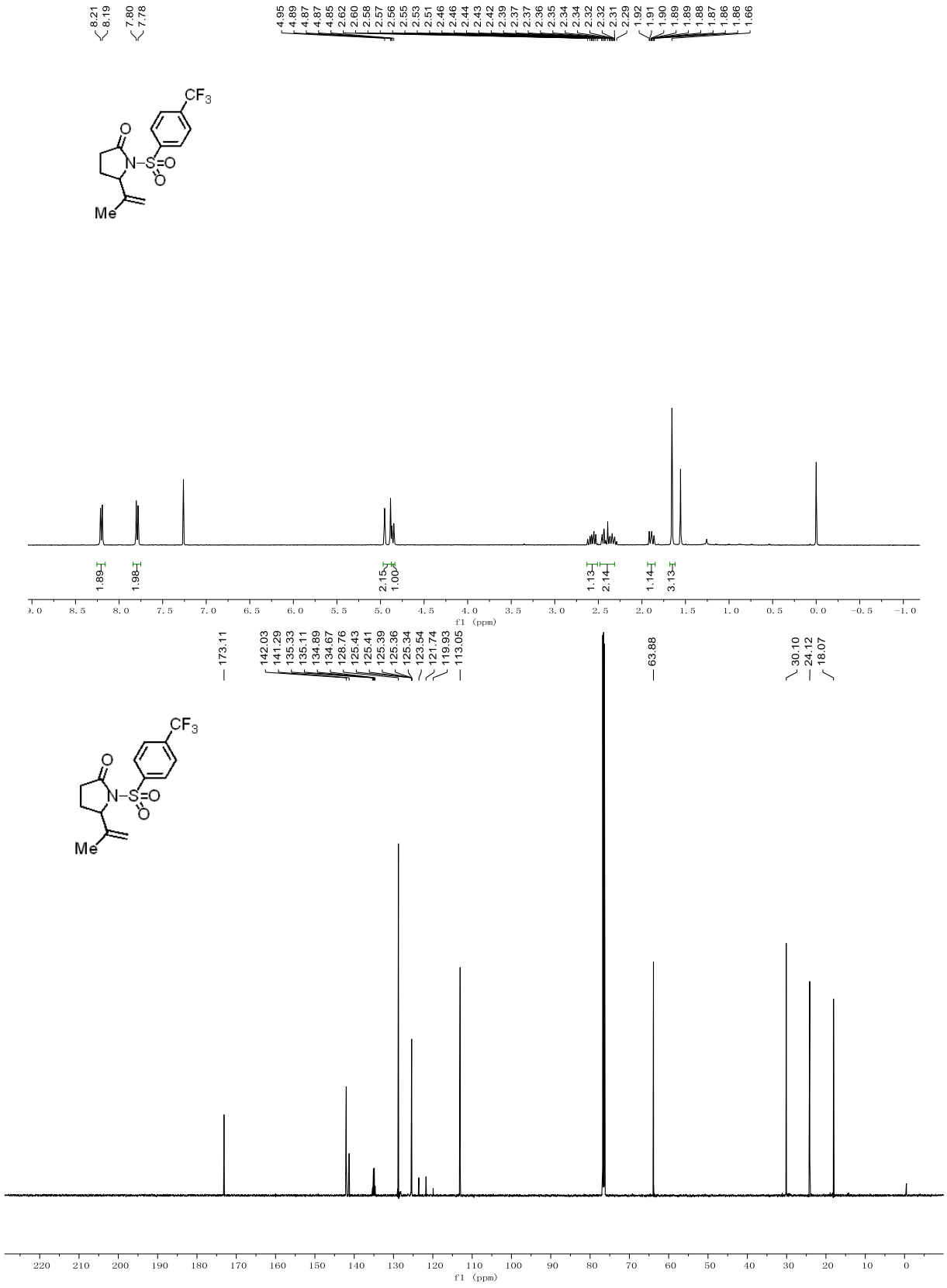
63.05
49.17
49.10
38.66
37.26
25.72
24.70
13.21
12.59
Cl
Cl
Cl
Cl
O
O
O
N
N
F
F
F
F
CF3
Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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2.57
2.56
2.55
2.53
2.51
2.46
2.46
2.44
2.43
2.42
2.39
2.37
2.37
2.36
2.35
2.34
2.34
2.32
2.32
2.31
2.29
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1.91
1.90
1.89
1.89
1.88
1.87
1.86
1.86
1.66
CF3
O
N
S
O
O
Me
1.89
1.98
2.15
1.00
1.13
2.14
1.14
3.13
f1 (ppm)
173.11
142.03
141.29
135.33
135.11
134.89
134.67
128.76
125.43
125.41
125.39
125.36
125.34
123.54
121.74
119.93
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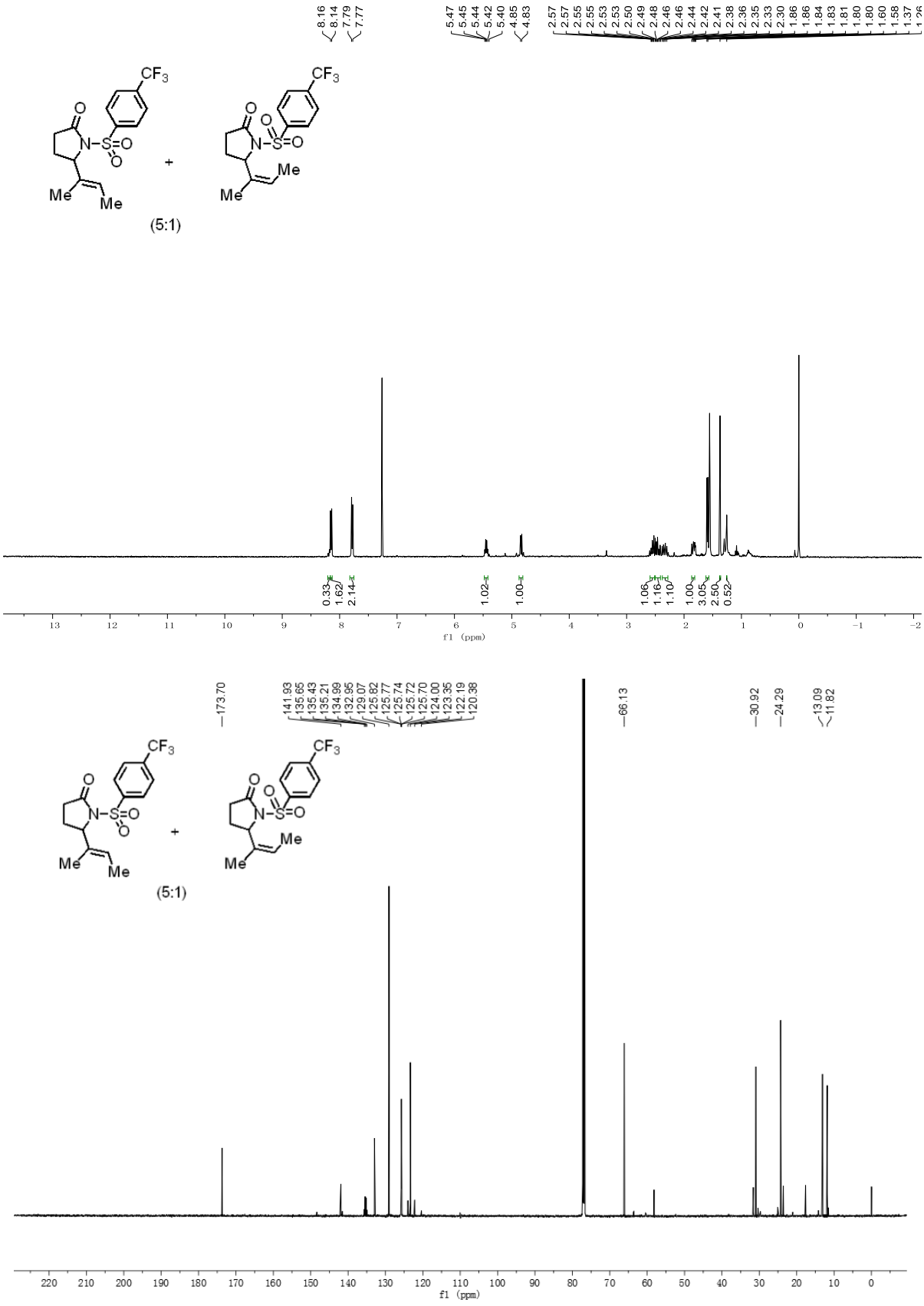
63.88
30.10
24.12
18.07
CF3
O
N
S
O
O
Me
f1 (ppm)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5.42
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4.83
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2.57
2.55
2.55
2.53
2.53
2.50
2.49
2.48
2.46
2.46
2.44
2.42
2.41
2.38
2.36
2.35
2.33
2.30
1.86
1.84
1.83
1.81
1.80
1.80
1.60
1.58
1.37
CF3
O
N–S=O
O
Me
Me
+
(5:1)
0.33
1.62
2.14
1.02
1.00
1.06
1.16
1.10
1.00
3.05
2.50
0.52
f1 (ppm)
173.70
141.93
135.65
135.43
135.21
134.99
132.95
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125.82
125.77
125.74
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24.29
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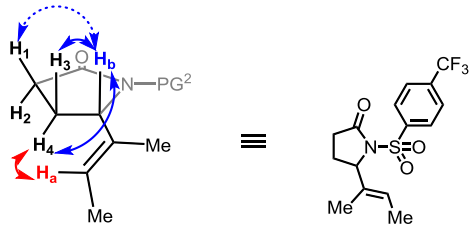
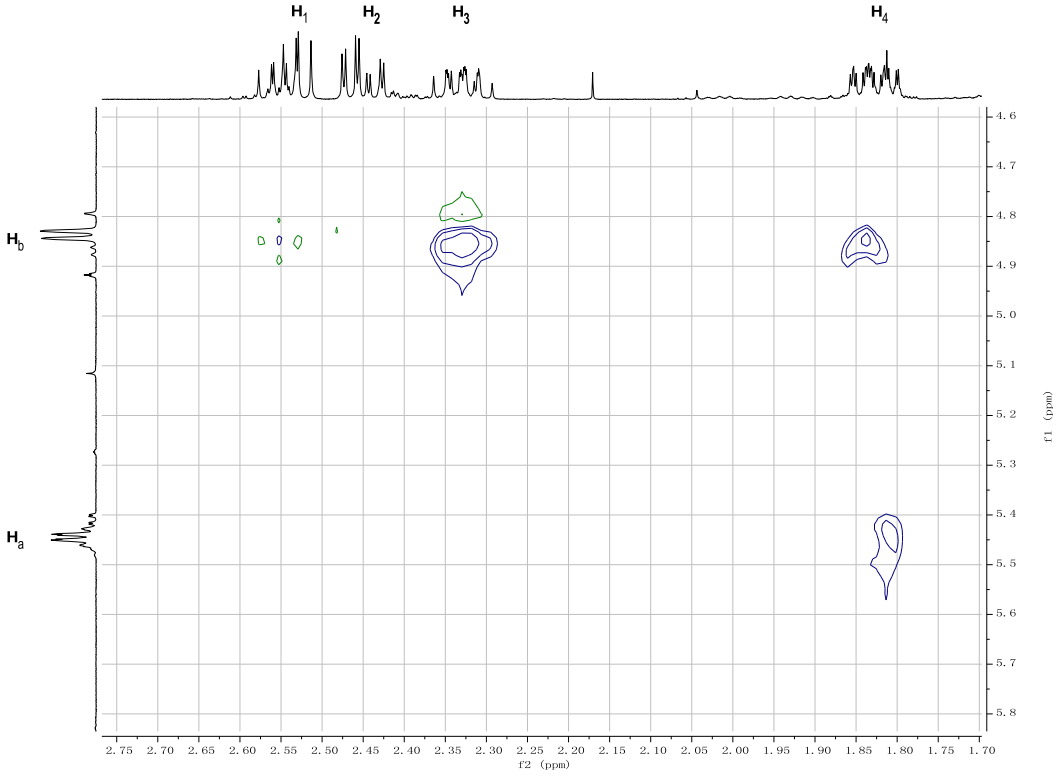
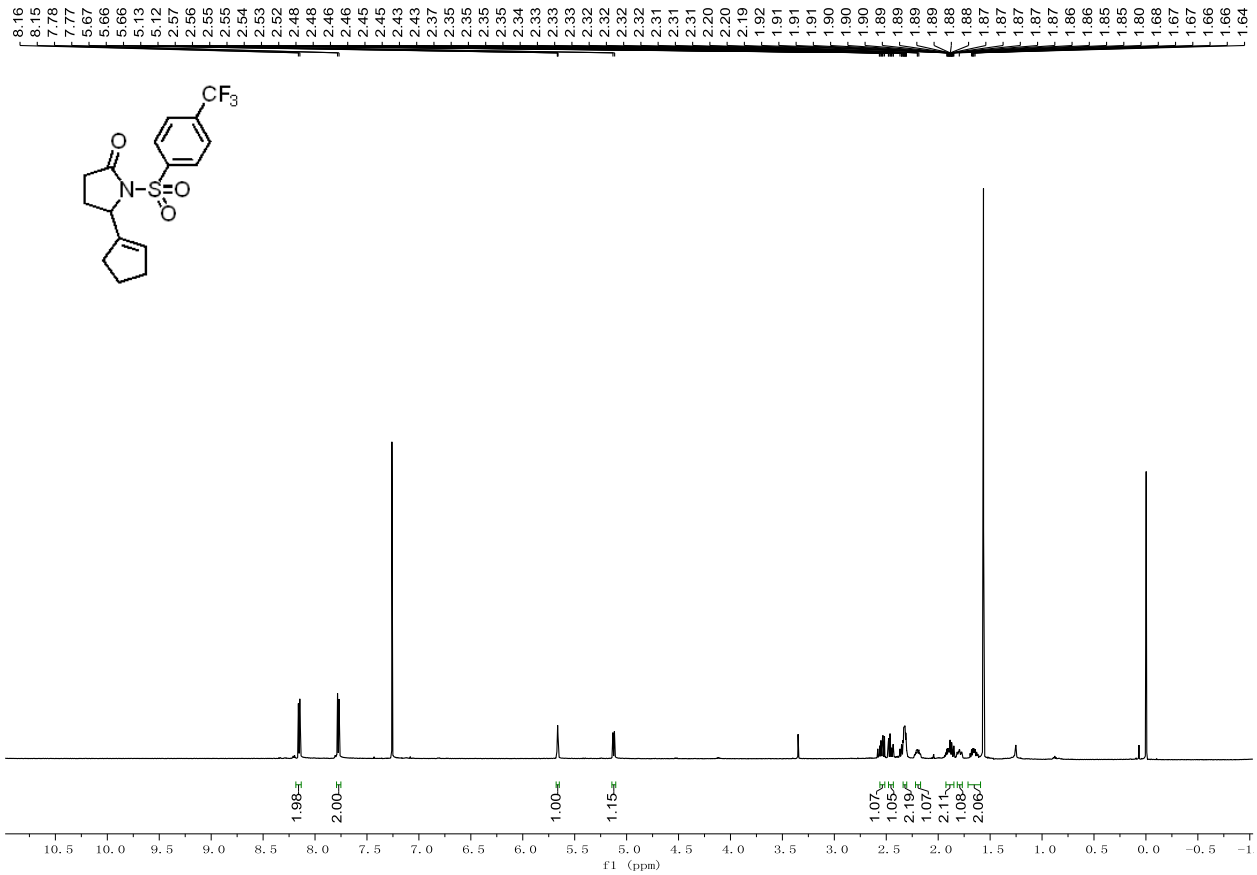
11.82
f1 (ppm)



Major isomer

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CF3
O
N
S
O
O
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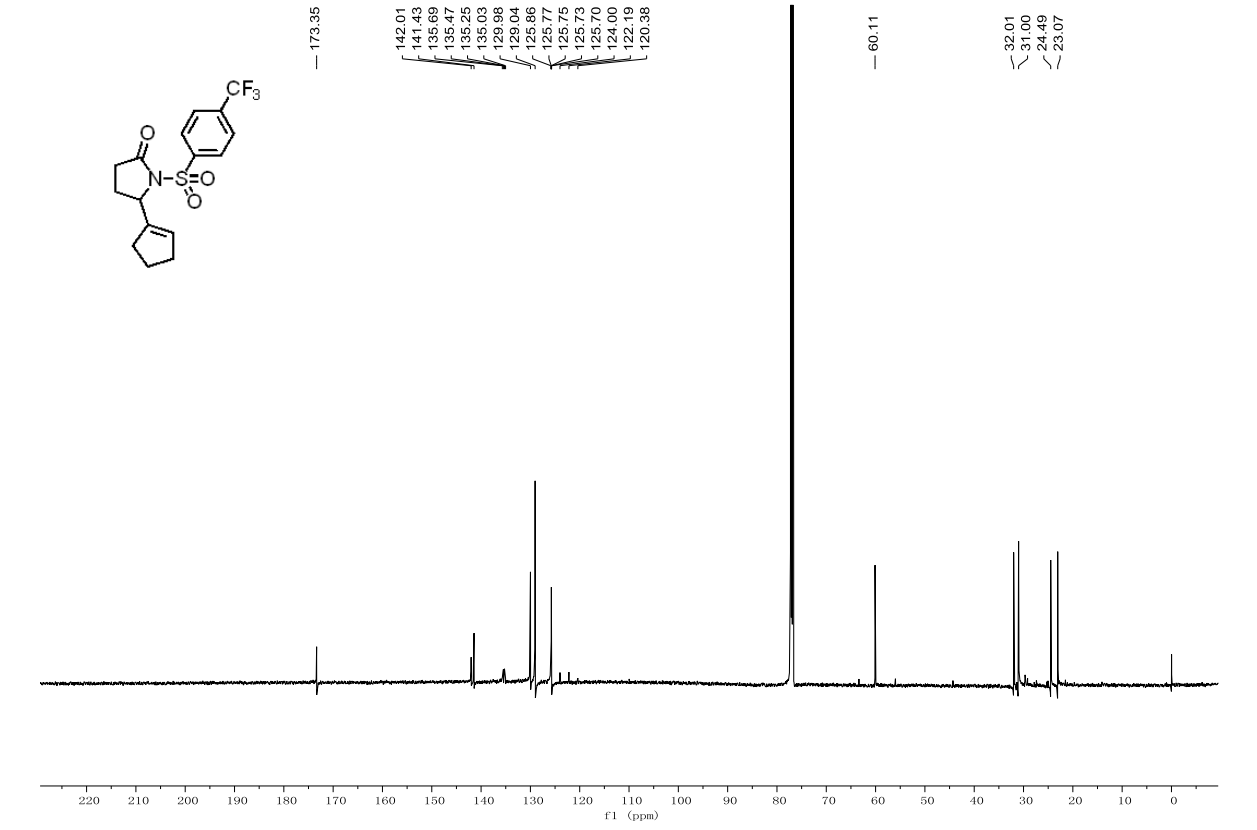
1.15
1.07
1.05
2.19
1.07
2.11
1.08
2.06
f1 (ppm)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129.98
129.04
125.86
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125.75
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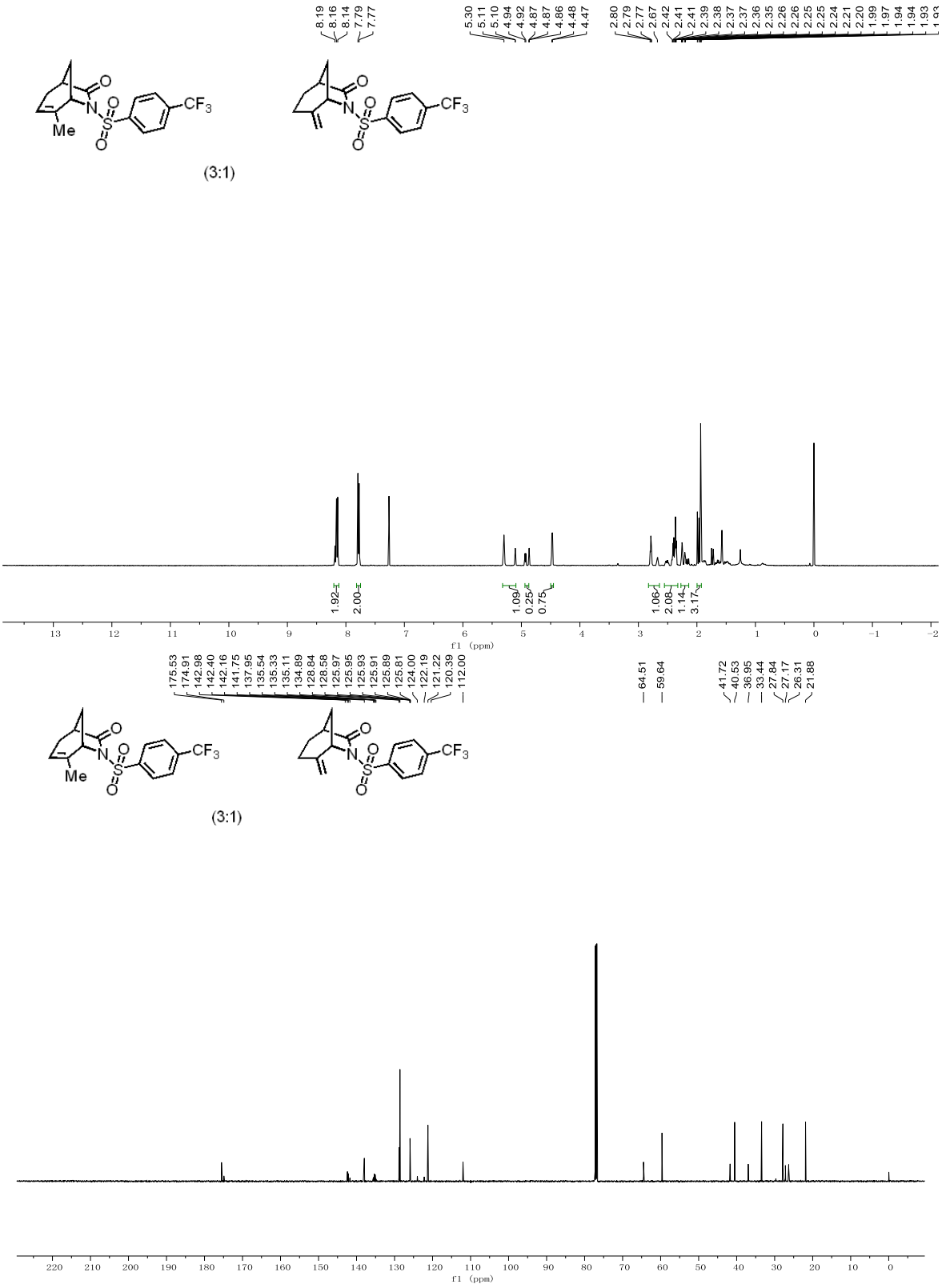
125.70
124.00
122.19
120.38
60.11
32.01
31.00
24.49
23.07
CF3
O
N
S
O
O
f1 (ppm)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5.10
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4.92
4.87
4.87
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2.41
2.41
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2.36
2.35
2.26
2.26
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2.25
2.24
2.21
2.20
1.99
1.97
1.94
1.94
1.93
Me
CF3
(3:1)
1.92
2.00
1.09
0.25
0.75
1.06
2.08
1.14
3.17
f1 (ppm)
175.53
174.91
142.98
142.40
142.16
141.75
137.95
135.54
135.33
135.11
134.89
128.84
128.58
125.97
125.95
125.93
125.91
125.89
125.81
124.00
122.19
121.22
120.39
112.00
64.51
59.64
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33.44
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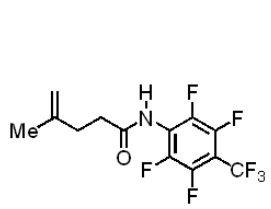
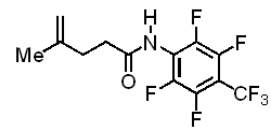
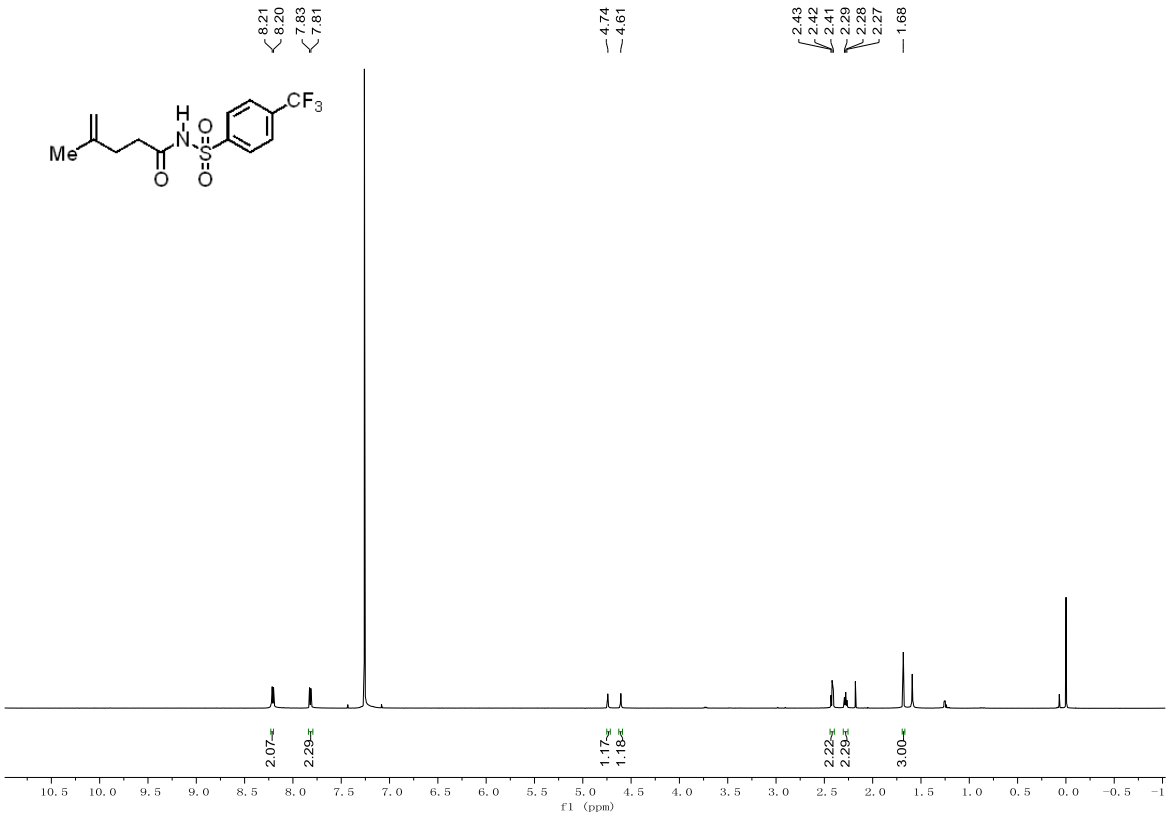
27.17
26.31
21.88
Me
CF3
(3:1)
f1 (ppm)


Me
O
H
N
F
F
F
F
CF3

7.24
4.85
4.79
2.67
2.65
2.63
2.48
2.46
2.44
1.79
0.78
1.05
1.06
2.23
2.13
3.00
f1 (ppm)


Me
O
H
N
F
F
F
F
CF3

170.26
143.68
111.40
34.42
32.75
22.36
f1 (ppm)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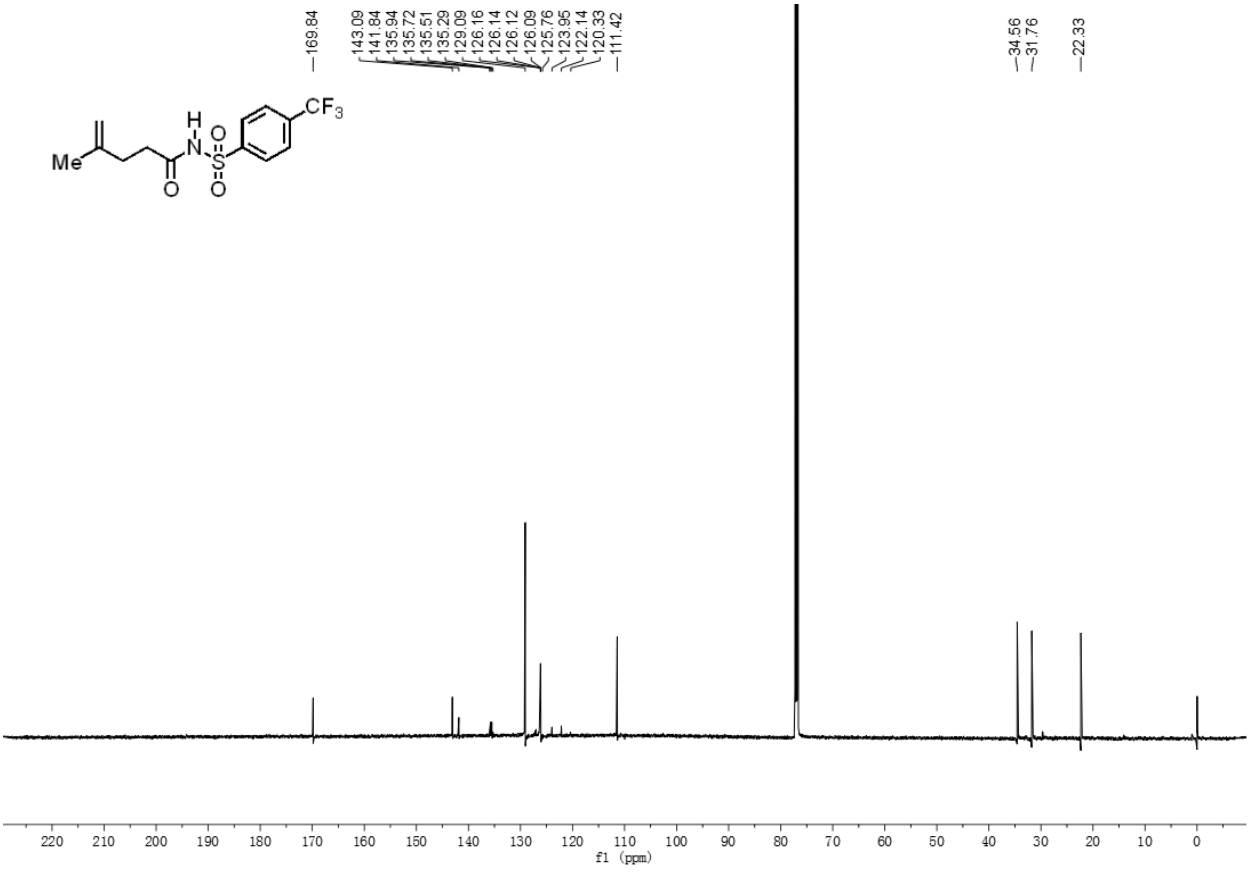
7.83
7.81
4.74
4.61
2.43
2.42
2.41
2.29
2.28
2.27
1.68
CF3
Me
H
N
O
S
O
O
2.07
2.29
1.17
1.18
2.22
2.29
3.00
f1 (ppm)


169.84
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135.72
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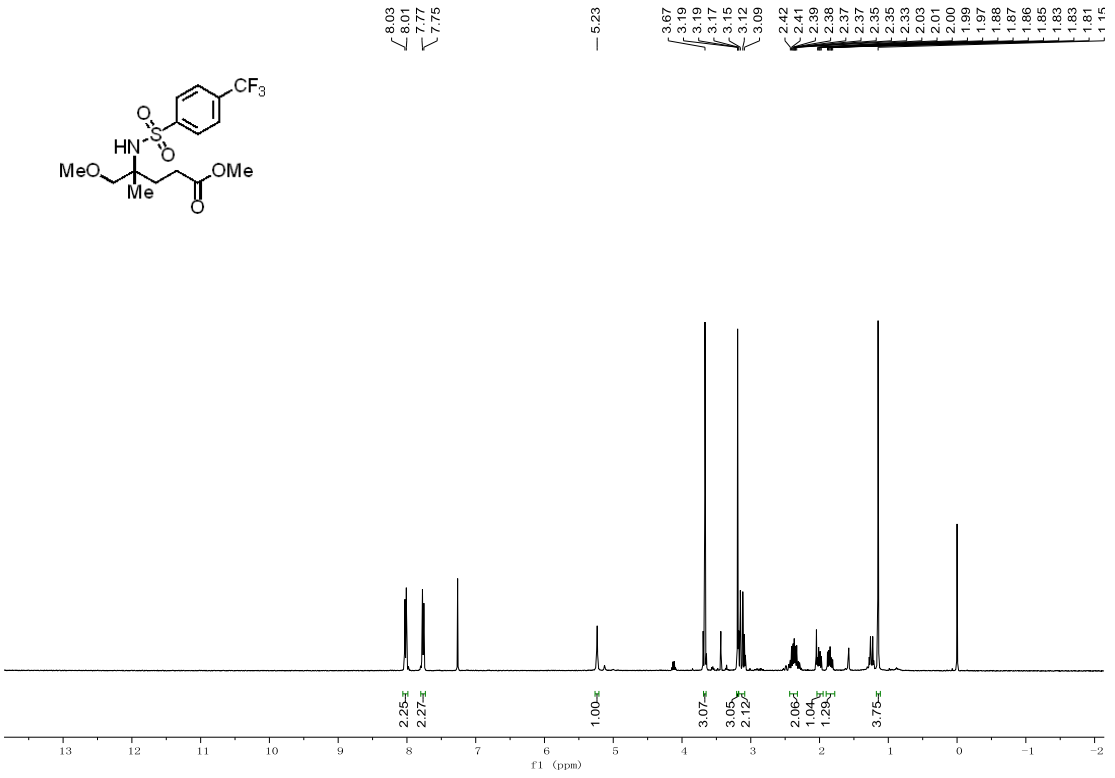
135.29
129.09
126.16
126.14
126.12
126.09
125.76
123.95
122.14
120.33
111.42
34.56
31.76
22.33
CF3
Me
H
N
O
S
O
O
f1 (ppm)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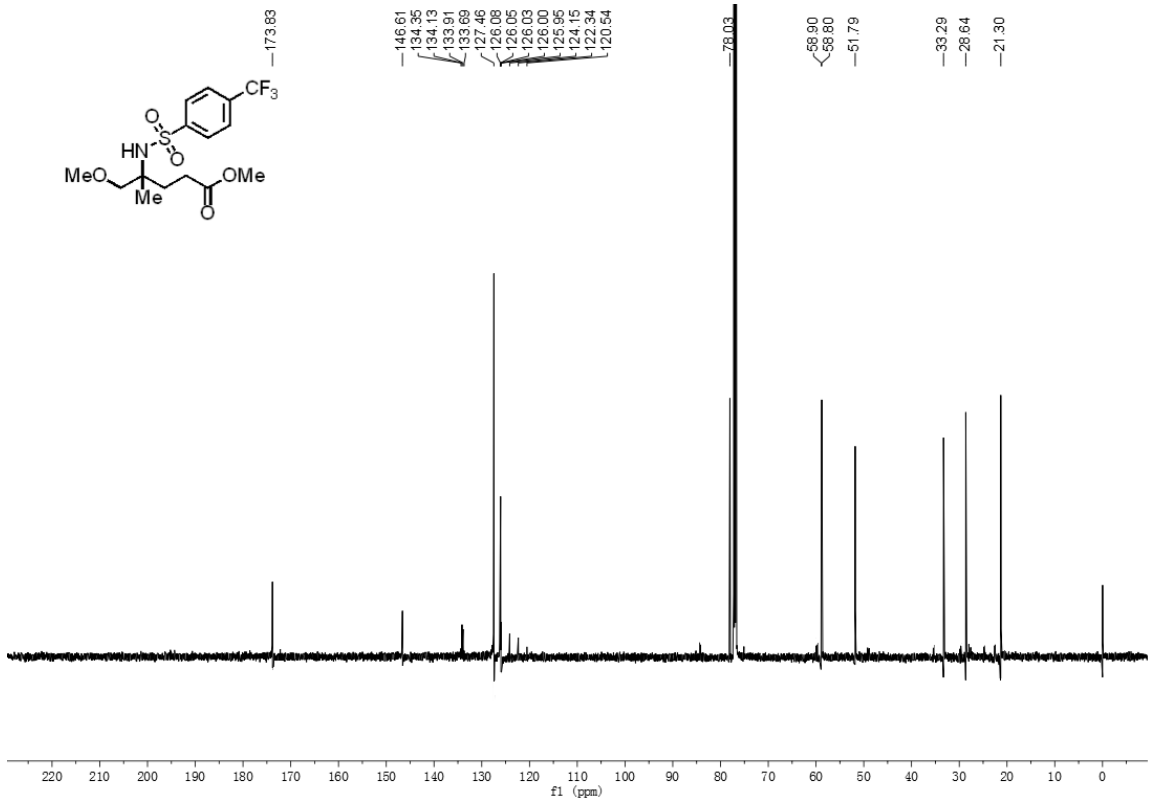
8.01
7.77
7.75
5.23
3.67
3.19
3.17
3.15
3.12
3.09
2.42
2.41
2.39
2.38
2.37
2.37
2.35
2.33
2.03
2.01
2.00
1.99
1.97
1.88
1.87
1.86
1.85
1.83
1.83
1.81
CF3
HN
MeO
Me
OMe
2.25
2.27
1.00
3.07
3.05
2.12
2.06
1.04
1.29
3.75
f1 (ppm)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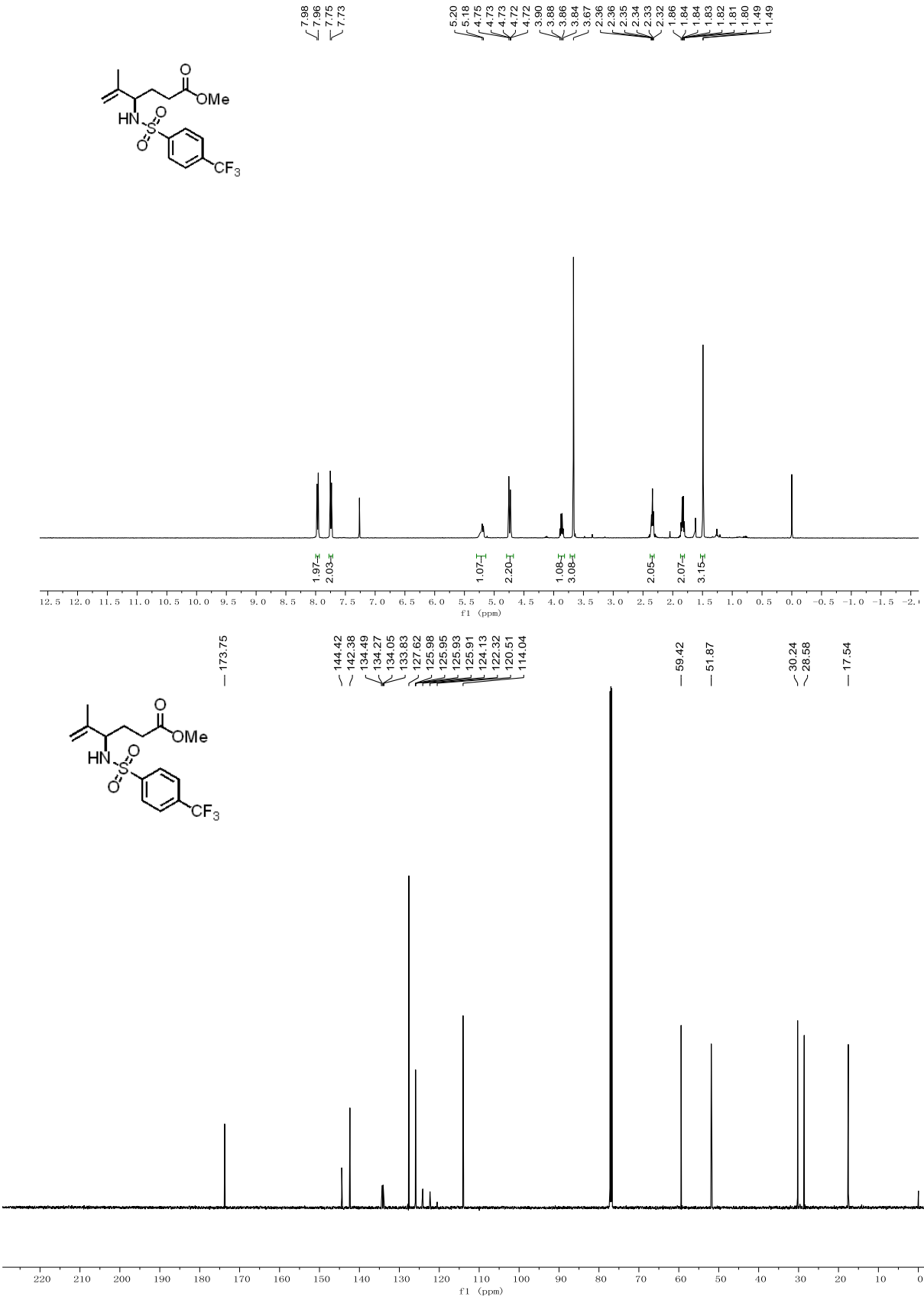
133.91
133.69
127.46
126.08
126.05
126.03
126.00
125.95
124.15
122.34
120.54
78.03
58.90
58.80
51.79
33.29
28.64
21.30
CF3
HN
MeO
Me
OMe
f1 (ppm)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5.18
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4.73
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4.72
4.72
3.90
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1.81
1.80
1.49
1.49
O
OMe
HN
O
O
S
O
CF3
1.97
2.03
1.07
2.20
1.08
3.08
2.05
2.07
3.15
f1 (ppm)
173.75
144.42
142.38
134.49
134.27
134.05
133.83
127.62
125.98
125.95
125.93
125.91
124.13
122.32
120.51
114.04
59.42
51.87
30.24
28.58
17.54
f1 (ppm)

5 X-Ray Crystallographic Analysis

5.1 X-Ray Crystallographic Analysis of Iodo Lactam 3a

Experimental Summary

A colorless crystal was affixed to a Cryo-Loop and cooled to 100K. Data were collected and refined as given in Table S1-S5. A Bruker D8 platform diffractometer with an Ultra rotating-anode source equipped with microfocus optics was used to collect the data. All processing of the data was by standard routines and proceeded without complication. H atoms were idealized as isotropic contributions. All software is contained in the current SHELXTL library maintained by Bruker XRD (Madison, WI).

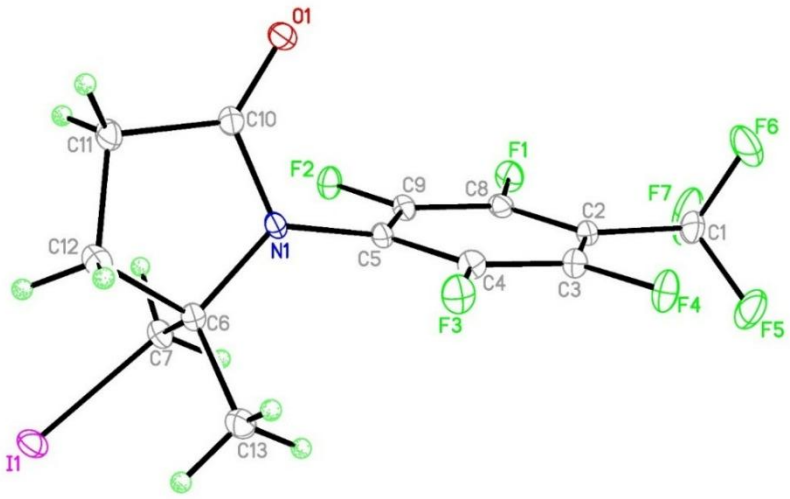

Table S1. Crystal data and structure refinement for yu33.

Identification code	yu33	
Empirical formula	C13 H9 F7 I N O	
Formula weight	455.11	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 6.1326(4) Å	α= 90°.
	b = 27.1761(14) Å	β= 103.6510(10)°.
	c = 8.9213(5) Å	γ = 90°.
Volume	1444.82(14) $Å^3$	
Z	4	
Density (calculated)	2.092 Mg/m^3	
Absorption coefficient	2.297 mm^{-1}	
F(000)	872	
Crystal size	0.290 x 0.230 x 0.080 mm^3	
Theta range for data collection	2.466 to 28.295°.	
Index ranges	-7<=h<=8, -36<=k<=36, -11<=l<=11	
Reflections collected	19340	
Independent reflections	3580 [R(int) = 0.0282]	
Completeness to theta = 25.000°	99.9 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3580 / 0 / 209	
Goodness-of-fit on F^2	1.224	
Final R indices [I>2sigma(I)]	R1 = 0.0493, wR2 = 0.1166	
R indices (all data)	R1 = 0.0498, wR2 = 0.1168	
Extinction coefficient	n/a	
Largest diff. peak and hole	4.310 and -1.099 $e.Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for yu33. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
I(1)	4410(1)	4262(1)	-817(1)	26(1)
F(1)	9448(5)	3501(1)	7387(3)	27(1)
F(2)	7559(5)	4127(1)	5178(3)	24(1)
F(3)	606(5)	3319(1)	4597(3)	26(1)
F(4)	2510(6)	2664(1)	6736(4)	32(1)
F(5)	6428(7)	2229(1)	7982(4)	43(1)
F(6)	6306(10)	2787(2)	9624(4)	68(2)
F(7)	9219(7)	2705(2)	8808(6)	61(1)
O(1)	3069(6)	4670(1)	5737(4)	23(1)
N(1)	2972(6)	4111(1)	3792(4)	17(1)
C(1)	7033(10)	2690(2)	8363(6)	31(1)
C(2)	6034(9)	3049(2)	7090(5)	22(1)
C(3)	3785(9)	3018(2)	6345(6)	23(1)
C(4)	2810(8)	3355(2)	5240(5)	20(1)
C(5)	4037(8)	3739(2)	4806(5)	17(1)
C(6)	2515(8)	4092(2)	2070(5)	19(1)
C(7)	4761(8)	4182(2)	1640(5)	22(1)
C(8)	7279(8)	3433(2)	6676(5)	20(1)
C(9)	6304(8)	3766(2)	5547(5)	20(1)
C(10)	2605(7)	4567(2)	4371(5)	18(1)
C(11)	1552(8)	4889(2)	3017(5)	23(1)
C(12)	909(8)	4535(2)	1666(6)	24(1)
C(13)	1457(9)	3609(2)	1438(6)	27(1)

Table S3. Bond lengths [Å] and angles [°] for yu33.

I(1)-C(7)	2.162(5)	C(1)-C(2)	1.512(7)
F(1)-C(8)	1.345(5)	C(2)-C(3)	1.385(7)
F(2)-C(9)	1.335(5)	C(2)-C(8)	1.395(7)
F(3)-C(4)	1.342(5)	C(3)-C(4)	1.374(7)
F(4)-C(3)	1.337(5)	C(4)-C(5)	1.394(6)
F(5)-C(1)	1.328(6)	C(5)-C(9)	1.393(6)
F(6)-C(1)	1.330(7)	C(6)-C(13)	1.514(7)
F(7)-C(1)	1.306(7)	C(6)-C(7)	1.534(7)
O(1)-C(10)	1.216(6)	C(6)-C(12)	1.544(7)
N(1)-C(10)	1.382(6)	C(8)-C(9)	1.379(6)
N(1)-C(5)	1.410(5)	C(10)-C(11)	1.508(6)
N(1)-C(6)	1.496(6)	C(11)-C(12)	1.520(7)

C(10)-N(1)-C(5)	119.7(4)	N(1)-C(6)-C(13)	111.9(4)
C(10)-N(1)-C(6)	114.0(4)	N(1)-C(6)-C(7)	106.9(4)
C(5)-N(1)-C(6)	125.5(4)	C(13)-C(6)-C(7)	112.1(4)
F(7)-C(1)-F(5)	108.2(5)	N(1)-C(6)-C(12)	99.6(3)
F(7)-C(1)-F(6)	105.2(5)	C(13)-C(6)-C(12)	113.3(4)
F(5)-C(1)-F(6)	105.9(5)	C(7)-C(6)-C(12)	112.3(4)
F(7)-C(1)-C(2)	114.4(5)	C(6)-C(7)-I(1)	112.9(3)
F(5)-C(1)-C(2)	112.1(4)	F(1)-C(8)-C(9)	117.7(4)
F(6)-C(1)-C(2)	110.5(5)	F(1)-C(8)-C(2)	121.4(4)
C(3)-C(2)-C(8)	117.6(4)	C(9)-C(8)-C(2)	121.0(4)
C(3)-C(2)-C(1)	120.2(5)	F(2)-C(9)-C(8)	119.1(4)
C(8)-C(2)-C(1)	122.1(5)	F(2)-C(9)-C(5)	119.3(4)
F(4)-C(3)-C(4)	119.0(5)	C(8)-C(9)-C(5)	121.6(4)
F(4)-C(3)-C(2)	119.7(4)	O(1)-C(10)-N(1)	124.0(4)
C(4)-C(3)-C(2)	121.3(4)	O(1)-C(10)-C(11)	128.6(4)
F(3)-C(4)-C(3)	118.8(4)	N(1)-C(10)-C(11)	107.3(4)
F(3)-C(4)-C(5)	119.4(4)	C(10)-C(11)-C(12)	104.4(4)
C(3)-C(4)-C(5)	121.7(4)	C(11)-C(12)-C(6)	106.1(4)
C(9)-C(5)-C(4)	116.8(4)		
C(9)-C(5)-N(1)	121.8(4)		
C(4)-C(5)-N(1)	121.1(4)		

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for yu33. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
I(1)	30(1)	30(1)	18(1)	-2(1)	8(1)	-2(1)
F(1)	22(1)	30(2)	24(1)	3(1)	-4(1)	0(1)
F(2)	22(1)	23(1)	27(1)	7(1)	4(1)	-4(1)
F(3)	20(1)	30(2)	29(2)	4(1)	4(1)	-5(1)
F(4)	33(2)	25(2)	38(2)	11(1)	11(1)	-6(1)
F(5)	56(2)	22(2)	43(2)	9(1)	-6(2)	-1(2)
F(6)	132(5)	52(2)	26(2)	17(2)	27(2)	26(3)
F(7)	44(2)	49(2)	74(3)	37(2)	-18(2)	-4(2)
O(1)	28(2)	24(2)	17(2)	0(1)	6(1)	6(1)
N(1)	21(2)	18(2)	12(2)	3(1)	4(1)	2(1)
C(1)	43(3)	22(2)	24(2)	8(2)	3(2)	2(2)
C(2)	34(3)	17(2)	15(2)	3(2)	6(2)	4(2)
C(3)	30(3)	19(2)	21(2)	2(2)	9(2)	-2(2)
C(4)	18(2)	22(2)	20(2)	0(2)	4(2)	-1(2)
C(5)	21(2)	17(2)	13(2)	2(2)	2(2)	3(2)
C(6)	21(2)	19(2)	16(2)	2(2)	4(2)	1(2)
C(7)	23(2)	25(2)	18(2)	2(2)	6(2)	0(2)
C(8)	21(2)	20(2)	15(2)	-1(2)	1(2)	3(2)
C(9)	23(2)	21(2)	16(2)	2(2)	6(2)	-1(2)
C(10)	17(2)	21(2)	18(2)	3(2)	7(2)	4(2)
C(11)	26(2)	26(2)	19(2)	4(2)	5(2)	10(2)
C(12)	23(2)	31(2)	19(2)	2(2)	5(2)	5(2)
C(13)	35(3)	26(2)	19(2)	-1(2)	2(2)	-8(2)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for yu33.

	x	y	z	U(eq)
H(9)	5780	3902	2016	26
H(8)	5459	4483	2166	26
H(1)	2634	5138	2828	28
H(4)	211	5060	3199	28
H(3)	1081	4694	703	29
H(2)	-669	4428	1525	29
H(5)	2519	3340	1790	41
H(7)	1073	3620	308	41
H(6)	92	3554	1807	41

5.2 X-Ray Crystallographic Analysis of Vinyl Lactam 7a

Experimental Summary

A colorless crystal was affixed to a Cryo-Loop and cooled to 100K. Data were collected and refined as given in Table S6-S10. A Bruker D8 platform diffractometer with an Ultra rotating-anode source equipped with microfocus optics was used to collect the data. All processing of the data was by standard routines and proceeded without complication. H atoms were idealized as isotropic contributions. All software is contained in the current SHELXTL library maintained by Bruker XRD (Madison, WI).

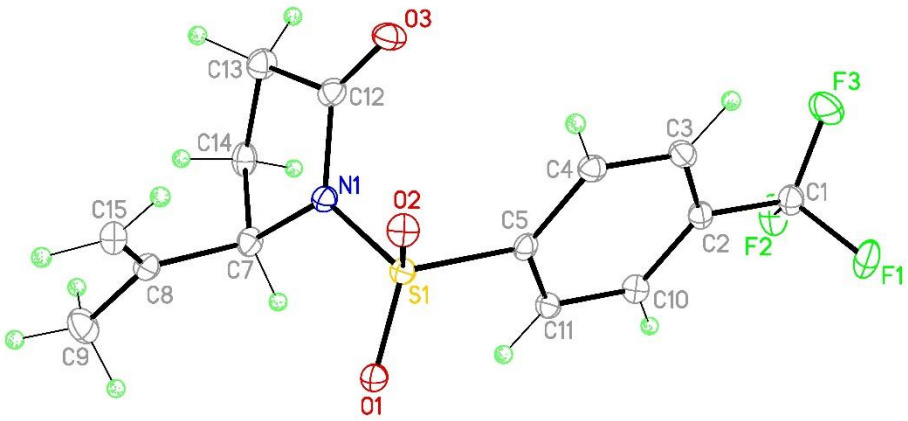
O3
C13
C12
F3
C3
C14
C4
N1
O2
C1
C15
C5
C2
F2
C7
S1
C8
C10
F1
C11
C9
O1

Table S6. Crystal data and structure refinement for yu37.

Identification code	yu37	
Empirical formula	C15 H14 F3 N O3 S	
Formula weight	345.33	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 8.2394(5) Å	α= 90°.
	b = 16.8092(7) Å	β= 106.356(2)°.
	c = 10.9777(5) Å	γ = 90°.
Volume	1458.86(13) $Å^3$	
Z	4	
Density (calculated)	1.572 Mg/m^3	
Absorption coefficient	0.270 mm^{-1}	
F(000)	712	
Crystal size	0.300 x 0.270 x 0.240 mm^3	
Theta range for data collection	2.282 to 25.344°.	
Index ranges	-6<=h<=9, -20<=k<=18, -12<=l<=13	
Reflections collected	8451	
Independent reflections	2664 [R(int) = 0.0215]	
Completeness to theta = 25.000°	99.7 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2664 / 0 / 200	
Goodness-of-fit on F^2	1.095	
Final R indices [I>2sigma(I)]	R1 = 0.0382, wR2 = 0.0915	
R indices (all data)	R1 = 0.0434, wR2 = 0.0944	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.667 and -0.412 $e.Å^{-3}$	

Table S7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for yu37. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	6773(1)	7063(1)	206(1)	19(1)
F(1)	7762(2)	10693(1)	-1845(1)	35(1)
F(2)	5378(2)	10860(1)	-1454(1)	37(1)
F(3)	7692(2)	10991(1)	37(1)	42(1)
O(1)	5954(2)	6663(1)	-947(1)	24(1)
O(2)	8404(2)	6812(1)	955(1)	24(1)
O(3)	7071(2)	7715(1)	2809(1)	27(1)
N(1)	5423(2)	7026(1)	1082(2)	21(1)
C(1)	6921(3)	10550(1)	-988(2)	26(1)
C(2)	6883(3)	9683(1)	-676(2)	22(1)
C(3)	8106(3)	9374(1)	363(2)	23(1)
C(4)	8098(3)	8569(1)	651(2)	22(1)
C(5)	6851(2)	8093(1)	-121(2)	19(1)
C(7)	3728(2)	6652(1)	664(2)	23(1)
C(8)	3782(3)	5763(1)	887(2)	24(1)
C(9)	2133(3)	5357(2)	246(2)	36(1)
C(10)	5646(3)	9197(1)	-1450(2)	24(1)
C(11)	5625(3)	8391(1)	-1162(2)	22(1)
C(12)	5749(3)	7393(1)	2270(2)	24(1)
C(13)	4169(3)	7300(1)	2695(2)	29(1)
C(14)	2784(3)	7107(1)	1479(2)	28(1)
C(15)	5132(3)	5377(1)	1573(2)	29(1)

Table S8. Bond lengths [Å] and angles [°] for yu37.

S(1)-O(1)	1.4236(15)	C(2)-C(3)	1.392(3)
S(1)-O(2)	1.4279(15)	C(3)-C(4)	1.389(3)
S(1)-N(1)	1.6640(17)	C(4)-C(5)	1.387(3)
S(1)-C(5)	1.773(2)	C(5)-C(11)	1.388(3)
F(1)-C(1)	1.338(2)	C(7)-C(8)	1.513(3)
F(2)-C(1)	1.335(3)	C(7)-C(14)	1.543(3)
F(3)-C(1)	1.348(3)	C(8)-C(15)	1.324(3)
O(3)-C(12)	1.211(3)	C(8)-C(9)	1.506(3)
N(1)-C(12)	1.398(3)	C(10)-C(11)	1.394(3)
N(1)-C(7)	1.482(2)	C(12)-C(13)	1.509(3)
C(1)-C(2)	1.500(3)	C(13)-C(14)	1.527(3)
C(2)-C(10)	1.392(3)		

O(1)-S(1)-O(2)	120.43(9)	C(4)-C(5)-S(1)	120.20(16)
O(1)-S(1)-N(1)	105.68(9)	C(11)-C(5)-S(1)	117.34(15)
O(2)-S(1)-N(1)	109.27(9)	N(1)-C(7)-C(8)	112.72(17)
O(1)-S(1)-C(5)	108.39(9)	N(1)-C(7)-C(14)	101.26(16)
O(2)-S(1)-C(5)	108.82(9)	C(8)-C(7)-C(14)	113.12(17)
N(1)-S(1)-C(5)	102.82(9)	C(15)-C(8)-C(9)	123.1(2)
C(12)-N(1)-C(7)	113.12(17)	C(15)-C(8)-C(7)	123.89(19)
C(12)-N(1)-S(1)	122.58(14)	C(9)-C(8)-C(7)	112.98(19)
C(7)-N(1)-S(1)	124.19(14)	C(2)-C(10)-C(11)	119.1(2)
F(2)-C(1)-F(1)	106.72(18)	C(5)-C(11)-C(10)	119.00(19)
F(2)-C(1)-F(3)	106.20(18)	O(3)-C(12)-N(1)	124.2(2)
F(1)-C(1)-F(3)	105.86(17)	O(3)-C(12)-C(13)	129.1(2)
F(2)-C(1)-C(2)	112.76(18)	N(1)-C(12)-C(13)	106.65(18)
F(1)-C(1)-C(2)	112.54(18)	C(12)-C(13)-C(14)	104.42(18)
F(3)-C(1)-C(2)	112.25(18)	C(13)-C(14)-C(7)	103.75(17)
C(10)-C(2)-C(3)	121.16(19)		
C(10)-C(2)-C(1)	119.27(19)		
C(3)-C(2)-C(1)	119.55(19)		
C(4)-C(3)-C(2)	120.08(19)		
C(5)-C(4)-C(3)	118.23(19)		
C(4)-C(5)-C(11)	122.47(19)		

Symmetry transformations used to generate equivalent atoms:

Table S9. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for yu37. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	19(1)	20(1)	19(1)	0(1)	6(1)	-1(1)
F(1)	43(1)	26(1)	47(1)	7(1)	29(1)	1(1)
F(2)	30(1)	25(1)	60(1)	9(1)	17(1)	6(1)
F(3)	62(1)	23(1)	39(1)	-6(1)	10(1)	-8(1)
O(1)	26(1)	26(1)	20(1)	0(1)	6(1)	-6(1)
O(2)	22(1)	25(1)	27(1)	1(1)	7(1)	2(1)
O(3)	24(1)	34(1)	23(1)	-6(1)	4(1)	-4(1)
N(1)	20(1)	23(1)	19(1)	0(1)	6(1)	-3(1)
C(1)	26(1)	24(1)	31(1)	0(1)	13(1)	-1(1)
C(2)	23(1)	19(1)	27(1)	-2(1)	13(1)	0(1)
C(3)	22(1)	24(1)	26(1)	-5(1)	9(1)	-4(1)
C(4)	21(1)	25(1)	21(1)	-1(1)	7(1)	0(1)
C(5)	19(1)	21(1)	21(1)	1(1)	11(1)	0(1)
C(7)	16(1)	27(1)	24(1)	3(1)	4(1)	-3(1)
C(8)	26(1)	26(1)	22(1)	-1(1)	11(1)	-5(1)
C(9)	32(1)	33(1)	43(1)	-5(1)	10(1)	-11(1)
C(10)	23(1)	24(1)	26(1)	1(1)	7(1)	1(1)
C(11)	21(1)	24(1)	23(1)	-3(1)	9(1)	-4(1)
C(12)	27(1)	23(1)	21(1)	3(1)	7(1)	3(1)
C(13)	30(1)	30(1)	30(1)	0(1)	15(1)	1(1)
C(14)	24(1)	24(1)	38(1)	5(1)	14(1)	1(1)
C(15)	35(1)	23(1)	28(1)	2(1)	9(1)	-5(1)

Table S10. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for yu37.

	x	y	z	U(eq)
H(5)	8946	9713	875	28
H(6)	8924	8351	1358	26
H(11)	3194	6768	-255	27
H(14)	2231	4787	440	54
H(2)	1866	5434	-674	54
H(1)	1230	5586	555	54
H(3)	4828	9413	-2164	29
H(4)	4785	8049	-1671	26
H(7)	3908	7798	3083	35
H(8)	4300	6863	3319	35
H(10)	2262	7599	1047	33
H(9)	1893	6772	1661	33
H(12)	5088	4818	1679	34
H(13)	6145	5660	1959	34