O−H Bond Activation of β,γ-Unsaturated Oximes via Hydrogen Atom Transfer (HAT) and Photoredox Dual Catalysis

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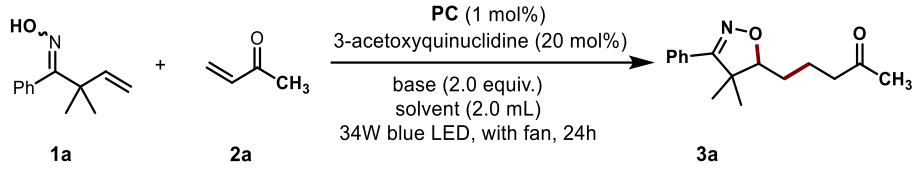
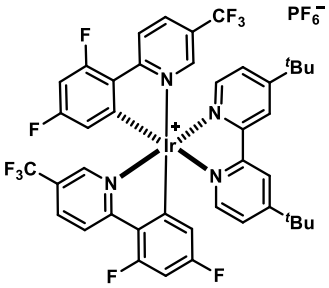
1. General Experimental Details

Unless otherwise noted, all commercially available compounds were used as provided without further purification, $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$[1] and 3-acetoxyquinuclidine[2] were prepared using literature procedures. Solvents for chromatography were technical grade and freshly distilled prior to use. CH_3CN used in reactions was acquired from SPS. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with F-254 indicator, visualised by irradiation with UV light. Column chromatography was performed using silica gel (Macherey Nagel, particle size 0.040-0.063 mm). Preparative Thin Layer Chromatography (PTLC) was performed using glass plates from Macherey-Nagel, Düren, Germany. The eluents for column chromatography and PTLC were presented as ratios of solvent volumes. ^{1}H-NMR and ^{13}C-NMR were recorded on a Varian AV300, AV400 or AV600 spectrometer in $CDCl_3$ and are reported relative to the solvent's residual peaks (^{1}H-signal $CHCl_3$, δ (H) 7.26). Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated s (singlet), bs (broad singlet), d (doublet), t (triplet), m (multiplet); coupling constants (*J*) are in Hertz (Hz). IR spectra were recorded on a Perkin Elmer-100 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Gas chromatography (GC) was performed on a Shimadzu GC-2010 chromatograph. Mass spectra (EI-MS, 70 eV) were conducted on a Finnigan SSQ 7000 spectrometer. HRMS were recorded on a Thermo Scientific LTQ Orbitrap XL spectrometer.

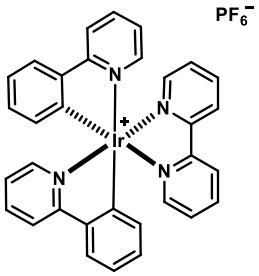
2. Optimization of the Reaction Conditions

Table S1. Optimization of the reaction conditions[a]





PC1



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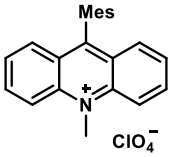
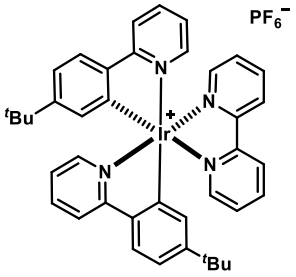
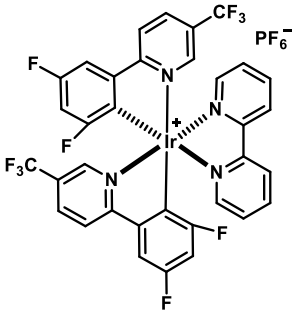


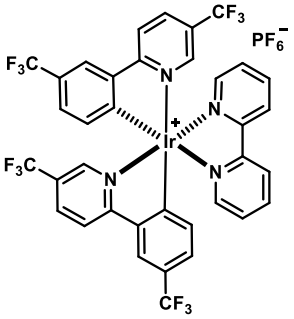
PC3



PC4



PC5



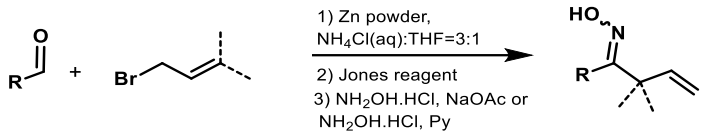
PC6

Entry	**Photocatalysts**	Bases	Solvents	**3a**: Internal Standard[b]
1[a]	**PC1**	DABCO	CH_3CN	30.25: 69.75
2[a]	**PC2**	DABCO	CH_3CN	15.33: 84.67
3[a]	**PC3**	DABCO	CH_3CN	n.d.
4[a]	**PC4**	DABCO	CH_3CN	21.02: 78.98
5[a]	**PC5**	DABCO	CH_3CN	16.45: 83.55
6[a]	**PC6**	DABCO	CH_3CN	27.83: 72.17
7[c]	**PC1**	3-acetoxyquinuclidine	CH_3CN	34.45: 65.55
8[c]	**PC1**	3-acetoxyquinuclidine	DCM	22.63: 77.37
9[c]	**PC1**	3-acetoxyquinuclidine	DMF	3.64: 96.36
10[c]	**PC1**	3-acetoxyquinuclidine	Toluene	25.64: 74.36
11[c]	**PC1**	3-acetoxyquinuclidine	Dioxane	10.83: 89.17
12[c]	**PC1**	3-acetoxyquinuclidine	THF	0.23: 99.77
13[c]	**PC1**	3-acetoxyquinuclidine	DMSO	6.65: 93.35
14[c]	**PC1**	3-acetoxyquinuclidine	DCE	21.62: 78.38
15[c]	**PC1**	3-acetoxyquinuclidine	$PhCF_3$	26.52: 73.48
16[c]	**PC1**	3-acetoxyquinuclidine	Acetone	24.24: 75.76
17[a]	**PC1**	K_3PO_4	CH_3CN	11.87: 88.13
18[a]	**PC1**	2,6-lutidine	CH_3CN	32.20: 67.80 (72%)[d]
19[a]	**PC1**	Cs_2CO_3	CH_3CN	8.41: 91.59
20[a]	**PC1**	$NaHCO_3$	CH_3CN	26.51: 73.49
21[a]	**PC1**	DBU	CH_3CN	trace
22[a]	**PC1**	$KHCO_3$	CH_3CN	25.62: 74.38
23[a]	**PC1**	Na_2CO_3	CH_3CN	27.75: 72.25
24[a]	**PC1**	TMG	CH_3CN	n.d.
25[a]	**PC1**	NaOAc	CH_3CN	31.12: 68.88

[a] reaction condition: 1-(3-methoxyphenyl)-2,2-dimethylbut-3-en-1-one oxime **1a** (0.4 mmol), but-3-en-2-one **2a** (0.2 mmol), photocatalyst (0.002 mmol), base (0.4 mmol), 3-acetoxyquinuclidine (0.04 mmol) in solvent (2.0 mL) at room temperature under irradiation of 34 W blue LED for 24 h. [b] the peak area ratio of product **3a** and n-decane as internal standard measured by GC. [c] 0.4 mmol 3-acetoxyquinuclidine was used. [d] Isolated yield. Note: due to 2, 6-lutidine lower price and is commercially available, compare to 3-acetoxyquinuclidine, instead of entry 7, we chose entry 18 as our optimal conditions.

3. Experiment Procedures

3.1 General procedure for the synthesis of oximes

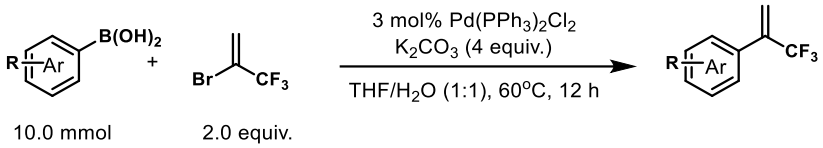


According to a reported procedure,[3] 1) a round bottomed flask charged with a solution of the allybromide (1.5 equiv.) and aldehyde (1.0 equiv.) in saturated NH_4Cl: THF=3:1 was cooled to 0 °C in ice bath. The zinc powder (2.0 equiv.) was added to the solution by portionwise. After siring another 30 min at 0 °C, the ice bath was removed, and the resulting suspension was stirred overnight. Then 1N HCl was added at 0 °C, the THF layer was separated from the aqueous layer, which was extracted with diethyl ether for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuum. The crude homoallylic alcohol product was directly used in the next step without further purification.

2) A solution of the homoallylic alcohol in diethyl ether was stirred at 0 °C while Jones reagent (2.0-4.0 equiv.) was added dropwise. The resulting mixture was allowed to warm to room temperature and stirred for 1 hour. The diethyl ether layer was separated and the aqueous layer was extracted with ethyl acetate for 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude β,γ-unsaturated ketone product was directly used in the next step without further purification.

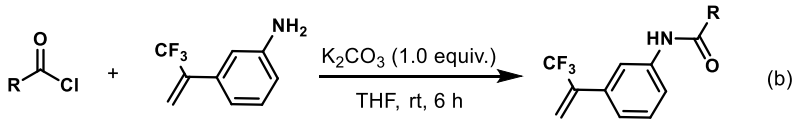
3) To a solution of sodium acetate (7.0 equiv.) in ethanol hydroxylamine hydrochloride (5.0 equiv., dissolved in H_2O) was added. The mixture was stirred at room temperature while the ketone (dissolved in ethanol) was added. The mixture was stirred overnight and then extracted with ethyl acetate 3 times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuum. The crude material was purified by flash chromatography on silica gel to afford the oximes. In the cases of **1m** and **1n**, the procedure was as follows: to a solution of these β,γ-unsaturated ketone (1.0 equiv.) in pyridine was added hydroxylamine hydrochloride (2.0 equiv.). The mixture was stirred at room temperature for 4 h and concentrated in vacuum. Then the mixture was diluted with water and extracted with ethyl acetate, the combined organic layers were dried with $MgSO_4$, filtered, and concentrated in vacuum. The crude material was purified by flash chromatography on silica gel to afford these oximes.

3.2 General procedure for the synthesis of α-trifluoromethyl styrenes



According to the reported procedure,[4] A 100 mL round bottomed flask charged with a magnetic stir bar, boronic acid (10.0 mmol, 1.0 equiv), and $Pd(PPh_3)_2Cl_2$ (126.4 mg, 3 mol%) were added. The vessel was evacuated and filled back with argon (three times), and then THF (40 mL) and aqueous K_2CO_3 (2.0 M, 20 mL, 4.0 equiv) were added. After the addition of 2-bromo-3,3,3-trifluoropropene (2.1 mL, 20 mmol, 2.0 equiv), the reaction mixture was stirred at 60 °C overnight under an argon atmosphere. The reaction mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl, and extracted with EtOAc (3 × 30 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Pentane/EtOAc) to give the desired α-trifluoromethyl styrenes.

3.2.1 Synthetic procedure for **5k**, **5l**, **5m**.

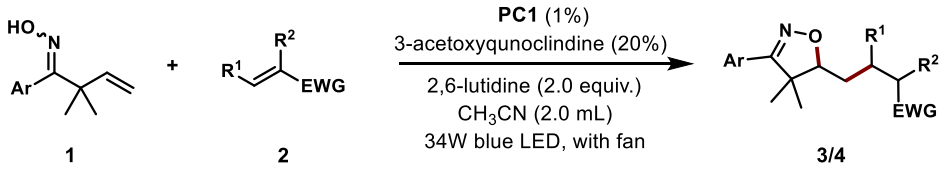


According to the reported procedure,[5] to a mixture of acid (5.0 mmol, 1.0 equiv) and oxalyl chloride (0.85 mL, 10 mmol, 2.0 equiv) in dry CH_2Cl_2 (20 mL) was added dropwise DMF (39 µL, 10 mol%). The reaction mixture was stirred at room temperature for 6 hours. Removal of the solvent in vacuo afforded the desired acid chloride, which was used in the next step without further purification. To a mixture of 3-(3,3,3-trifluoroprop-1-en-2-yl)aniline (0.94 g, 5.0 mmol, 1.0 equiv) and K_2CO_3 (0.69 g, 5.0 mmol, 1.0 equiv) in dry THF (10 mL) was added dropwise a solution of the freshly prepared acid chloride (5.0 mmol, 1.0 equiv) in dry THF (10 mL). This mixture was stirred at room temperature for 6 hours before water was added to quench the reaction. The resulted mixture was extracted with EtOAc (3 X 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The

resulted crude product was purified by column chromatography on silica gel (pentane/EtOAc) to give the desired α-trifluoromethyl styrenes.

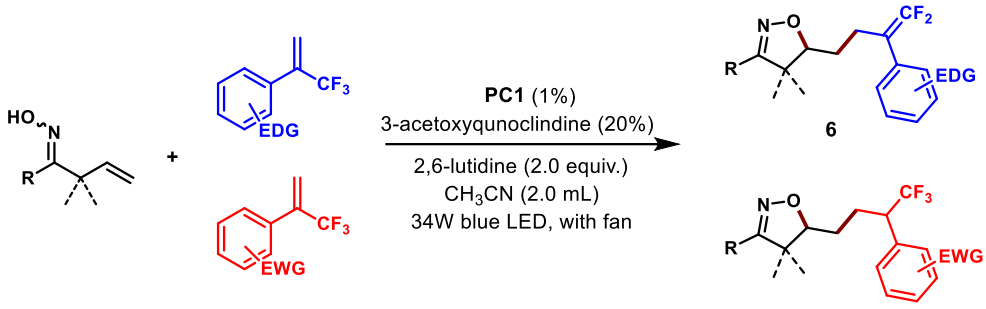
3.3 General procedure for the catalytic reaction

(a) Photoredox/HAT dual catalysis of β,γ–unsaturated oximes and Michael acceptors or styrenes



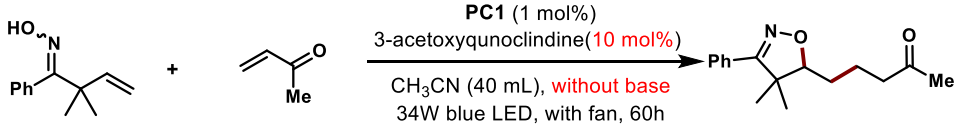
1 2 3/4

(b) Photoredox/HAT dual catalysis of β,γ–unsaturated oximes and α-trifluoromethyl styrenes



1 5 6 7

(c) 20 times scale-up reaction



1a 8.0 mmol **2a** 4.0 mmol **3a** 54%, 0.56g

A dry reaction tube was charged with the oximes **1** (0.4 mmol, 2.0 equiv.), radical acceptors **2** or **5** (0.2 mmol, 1.0 equiv., if solid), 3-acetoxyquinuclidine (0.04 mmol, 0.2 equiv.) and $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.0 mg, 0.02 mmol, 1 mol%). It was capped with a rubber septum, evacuated and backfilled with argon for three times. Then degassed CH_3CN (2.0 mL), radical acceptors **2** or **5** (0.2 mmol, 1.0 equiv., if liquid) and 2,6-lutidine (0.4 mmol, 2.0 equiv.) were added via syringe. The reaction mixture was stirred at room temperature for 24 or 48 h with 34 Watts blue LEDs irradiation under fan cooling. Upon completion, the mixture solution was concentrated under vacuum and purified by column chromatography on silica gel using 25:1-8:1 hexane: EtOAc as eluent to get the corresponding pure products.

Scale-up reaction**:** A dry 100 mL reaction flask charged with 1-(3-methoxyphenyl)-2,2-dimethylbut-3-en-1-one oxime **1a** (1.51 g, 8.0 mmol, 2.0 equiv.), 3-acetoxyquinuclidine (67.6 mg, 0.4 mmol, 0.1 equiv.) and

$Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (**PC1**) (39.2 mg, 0.04 mmol, 1 mol%). It was capped with a rubber septum, evacuated and backfilled with argon for three times. Then degassed CH_3CN (40.0 mL) and but-3-en-2-one **2a** (280 mg, 333ul, 4.0 mmol) were added via syringe. The reaction mixture was stirred for 60 h with two 34 Watts blue LEDs irradiation under fan cooling. Upon completion, the mixture solution was concentrated under vacuum and purified by column chromatography on silica gel using 10:1 hexane: EtOAc as eluent to give the corresponding pure product **3a** in 54% yield (0.56 g).

Figure S1: Catalytic scale reaction set up (left). 20 times scale-up reaction set up (right).

3.4 Cyclic Voltammetry (CV) Measurements

All measurements were performed under anhydrous conditions in an argon-filled glovebox. All supporting electrolytes were dried under dynamic vacuum (less than 0.1 mbar) over 24 h at 100 ^oC and stored inside the glovebox. The cell for the analysis was equipped with a glass vial (working volume is 10 mL) and Teflon cap, equipped with O-ring for tight sealing. Glassy carbon was used as a working electrode (circle, d= 3 mm), platinum wire as a counter electrode, and saturated calomel electrode (SCE) (CHI150 from CH Instruments, Inc.) as a reference electrode. All measurements were conducted in 0.1 M solutions of $^nBu_4NPF_6$ in CH_3CN. The 3-acetoxyquinuclidine concentration was 5 mM, the other two analyte concentrations were 10 mM. The scan rate was 50 mV/s.

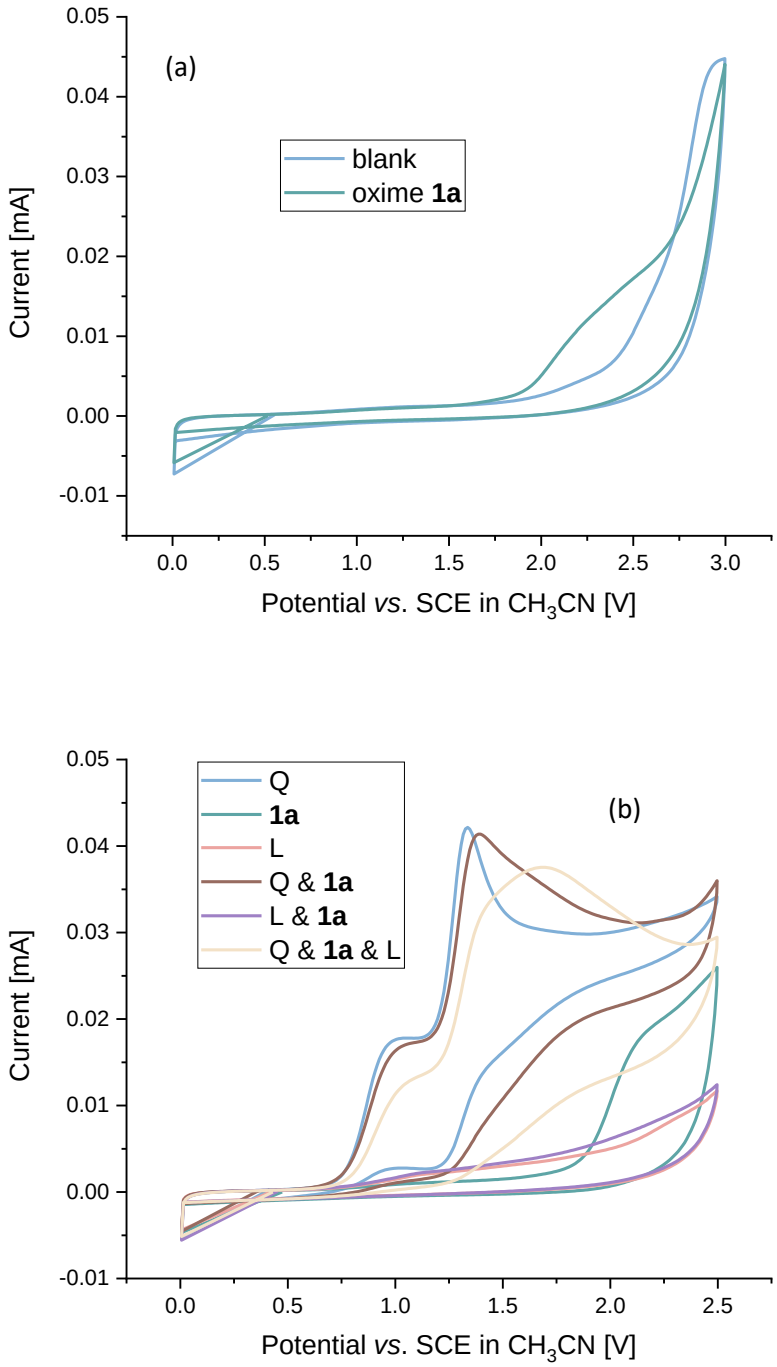
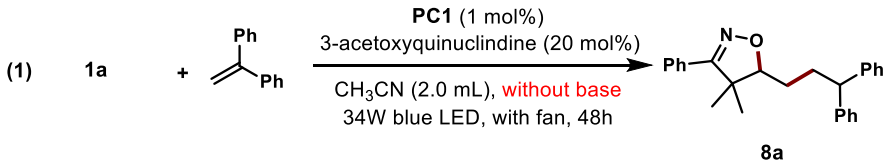
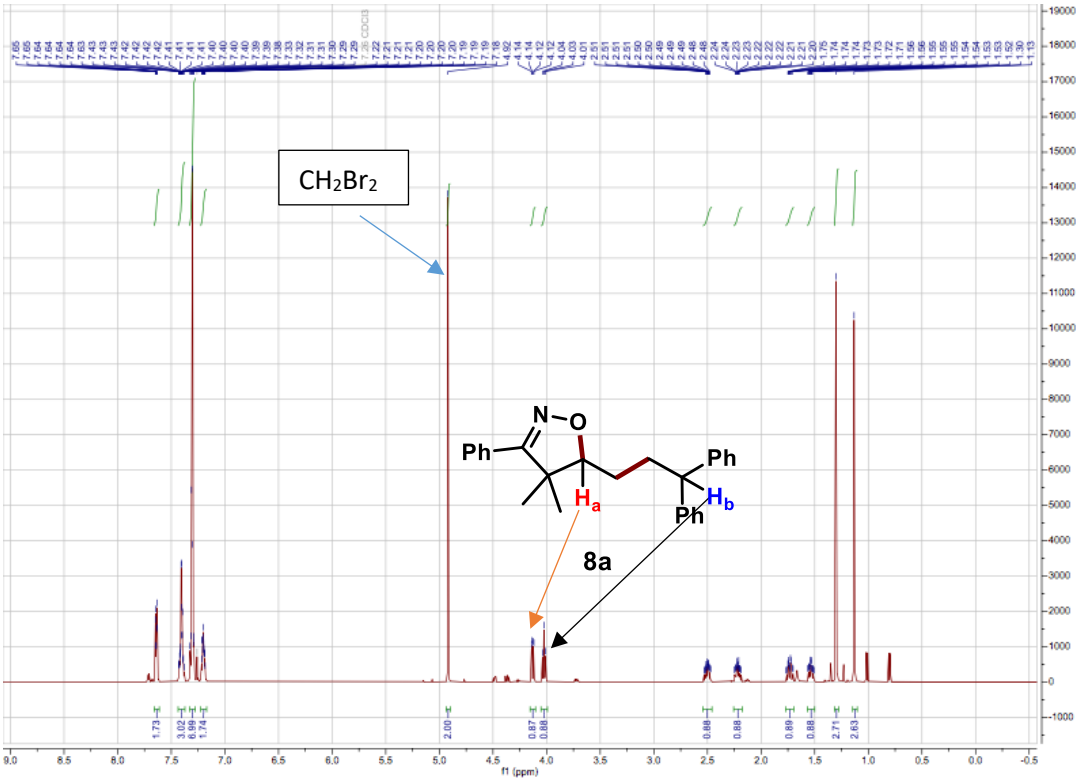
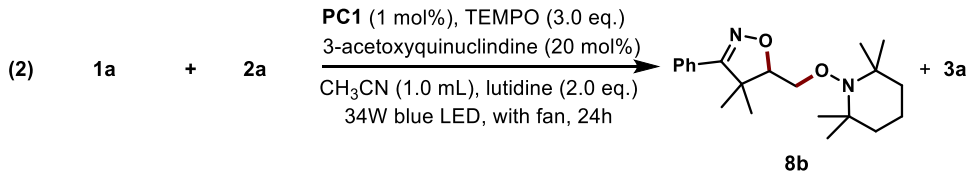


Figure S2: (a) Cyclic voltammetry of oxime **1a**, $E_{p/2}$ = 2.2 V. (b) Cyclic voltammetry of 3-acetoxyquinuclidine (blue line), oxime **1a** (green line), 2,6-lutidine (pink line), mixture of 3-acetoxyquinuclidine and oxime **1a** (brown line), mixture of 2,6-lutidine and oxime **1a** (purple line) and mixture of 3-acetoxyquinuclidine, oxime **1a** and 2,6-lutidine (khaki line).

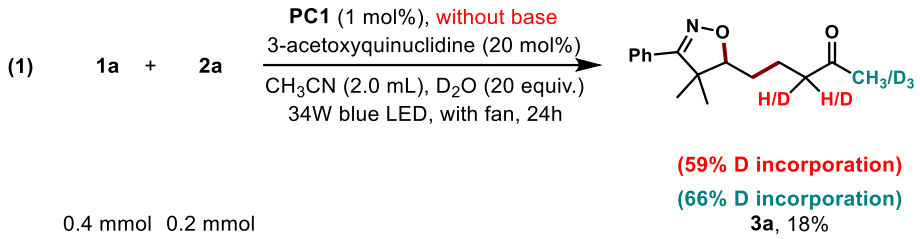
3.5 Radical trap experiments

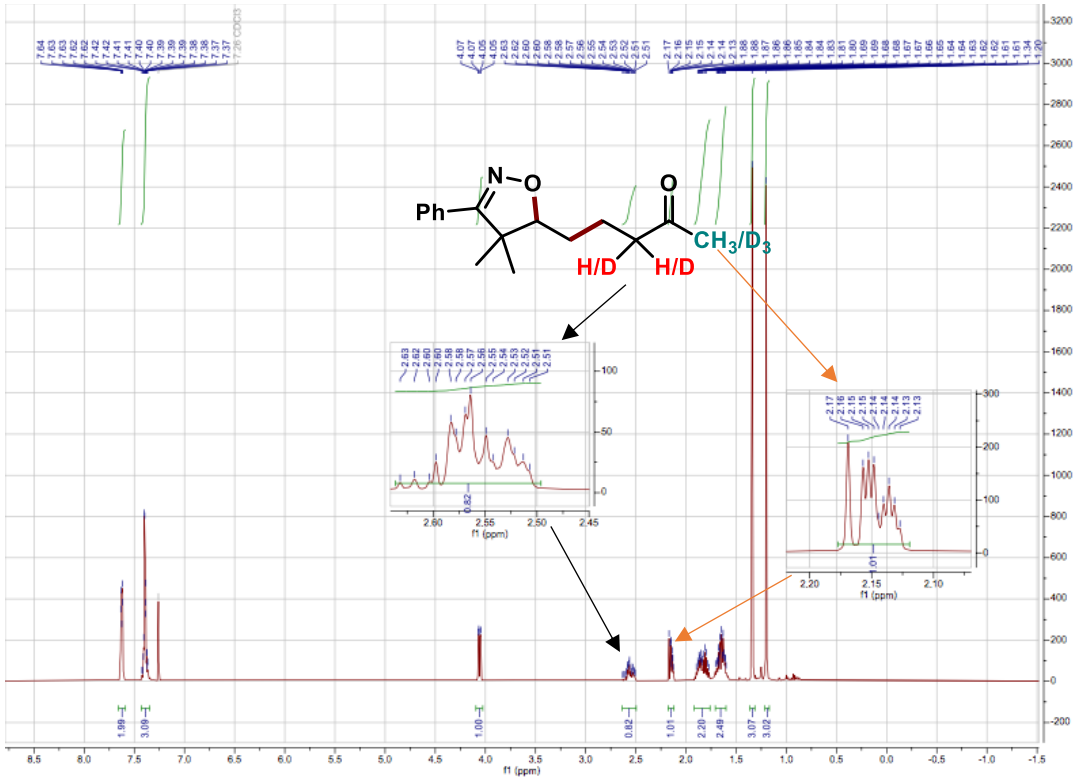


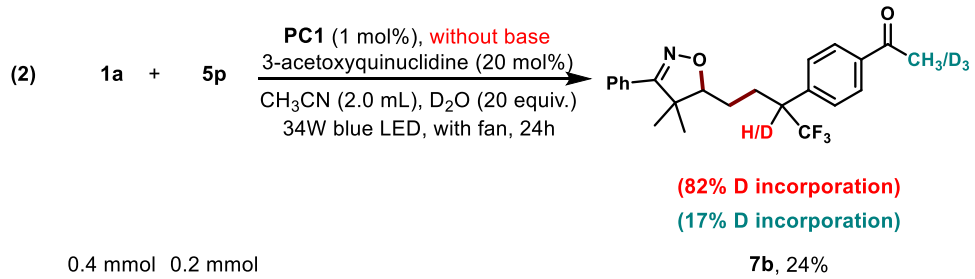


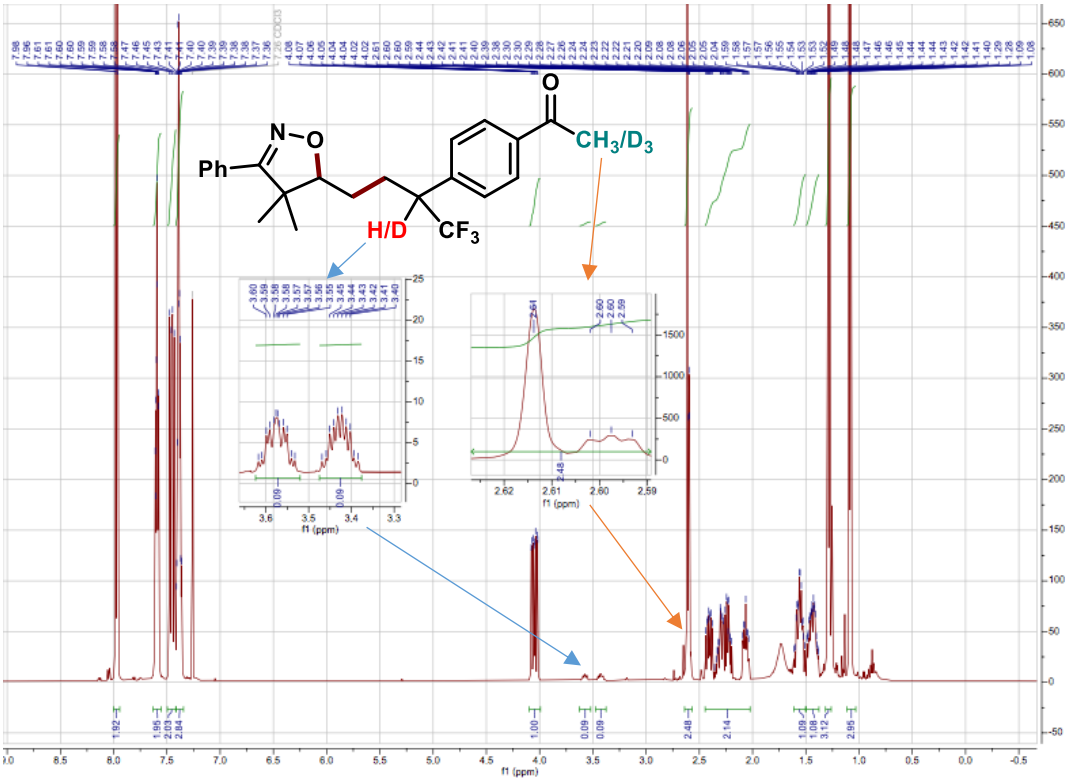


3.6 Isotope-labelling experiments









3.7 Stern–Volmer experiments of **PC1** with various reactants

1) Steady-state Stern-Volmer quenching of PC1 with 3-acetoxyquinuclidine:

Emission spectra were collected on fluoromax-4 spectrophotometer with excitation and emission slit widths of 5 nm. The variable concentrations of quencher (3-acetoxyquinuclidine) were prepared by the serial dilution of 0.01 M stock solution. Quenching experiments were carried out using a 0.01 mM solution of **PC1** in CH_3CN and variable concentrations of quencher (3-acetoxyquinuclidine) (0.2, 0.4, 0.6, 0.8, 1.0 mM) in CH_3CN. The samples were prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S3 and S4).

Inference: At the reaction concentrations (**PC1**:Q, 1:20), we found that 3-acetoxyquinuclidine is a better quencher and the rate of quenching was found to be (k_q = 174.3 $M^{-1}S^{-1}$).

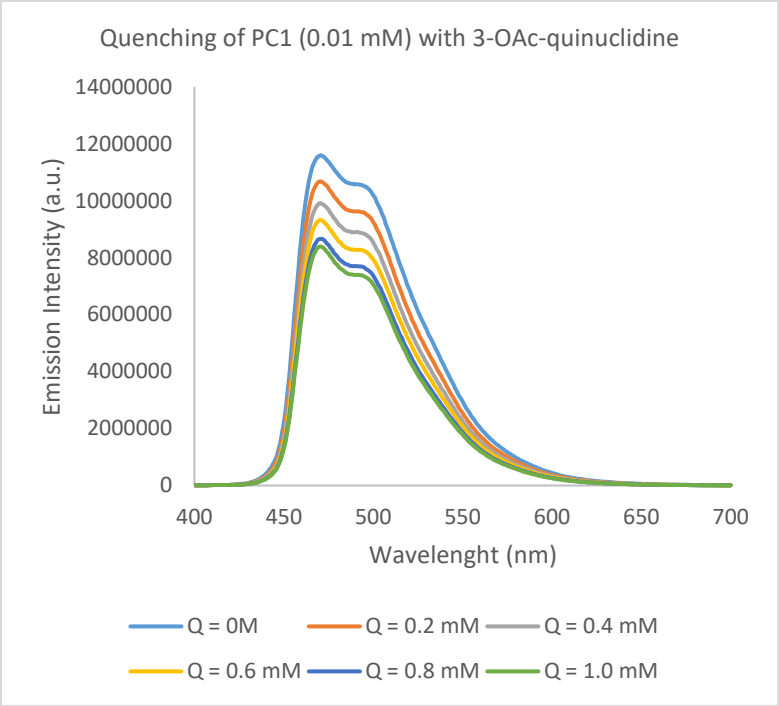


Figure S3. Emission spectra of **PC1** (0.01 mM) at different concentrations of 3-acetoxyquinuclidine.

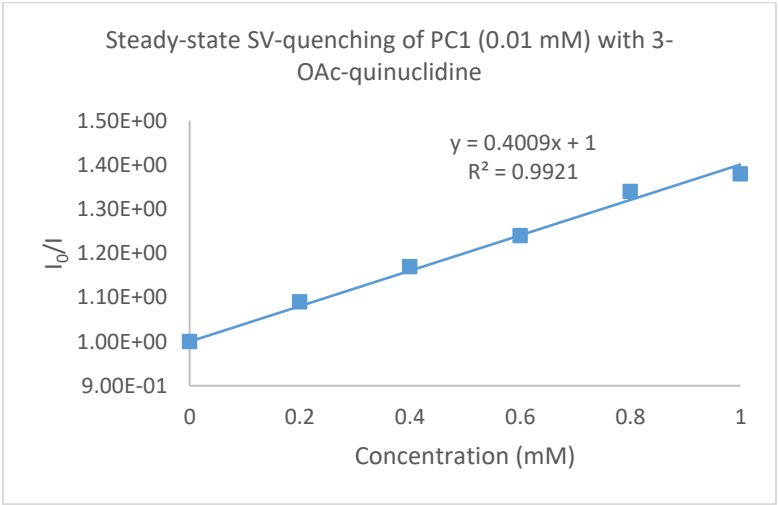


Figure S4. Steady-state Stern-Volmer quenching of **PC1** (0.01 mM) with 3-acetoxyquinuclidine.

2) Steady-state Stern-Volmer quenching of PC1 with oxime 1a:

The variable concentrations of quencher (oxime **1a**) were prepared by the serial dilution of 0.01 M stock solution. Quenching experiments were carried out using a 0.01 mM solution of **PC1** in CH_3CN and variable concentrations of quencher (oxime **1a**) (0.2, 0.6, 1.0, 1.4, 1.8, 2.2 mM) in CH_3CN. The samples were

prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S5 and S6).

Inference: At the reaction concentrations (**PC1**:**1a**, 1:200), we found that oxime **1a** is not a better quencher compared to 3-acetoxyquinuclidine.

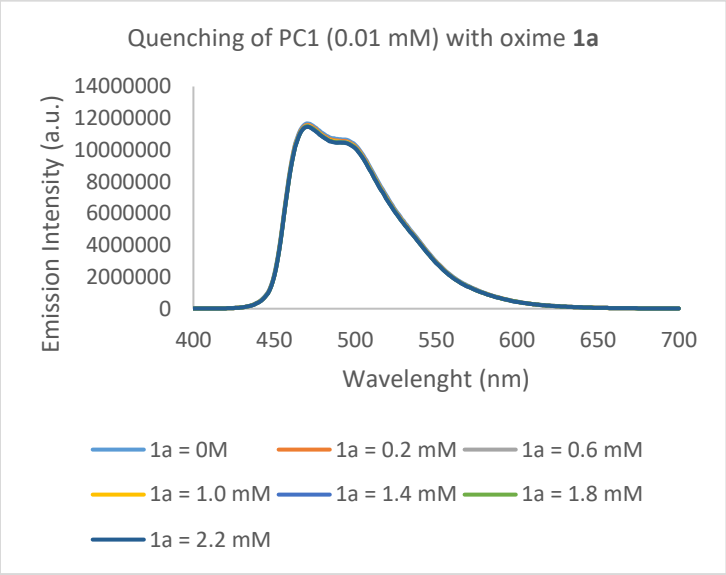


Figure S5. Emission spectra of **PC1** (0.01 mM) at different concentrations of oxime **1a**.

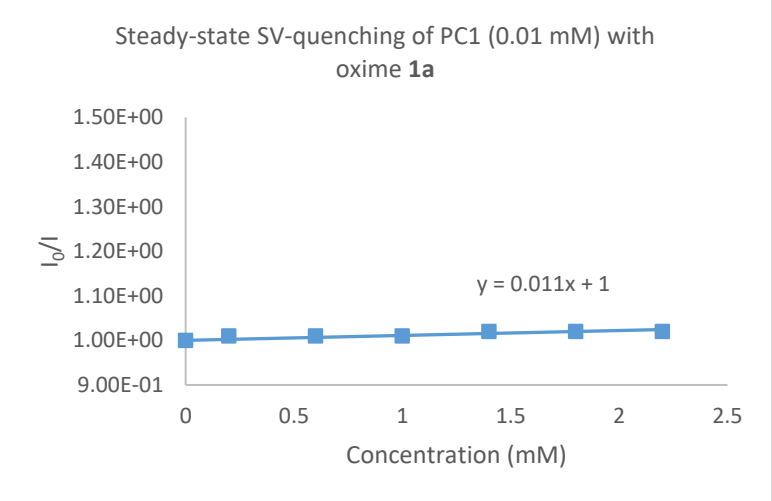


Figure S6. Steady-state Stern-Volmer quenching of **PC1** (0.01 mM) with oxime **1a**.

3) Steady-state Stern-Volmer quenching of PC1 with olefin 2a:

The variable concentrations of quencher (olefin **2a**) were prepared by the serial dilution of 0.01 M stock solution. Quenching experiments were carried out using a 0.01 mM solution of **PC1** in CH_3CN and variable concentrations of quencher (olefin **2a**) (0.2, 0.6, 1.0, 1.4, 1.8, 2.2 mM) in CH_3CN. The samples were prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S7 and S8).

Inference: At the reaction concentrations (**PC1**:**2a**, 1:200), we found that olefin **2a** is not a better quencher compared to 3-acetoxyquinuclidine.

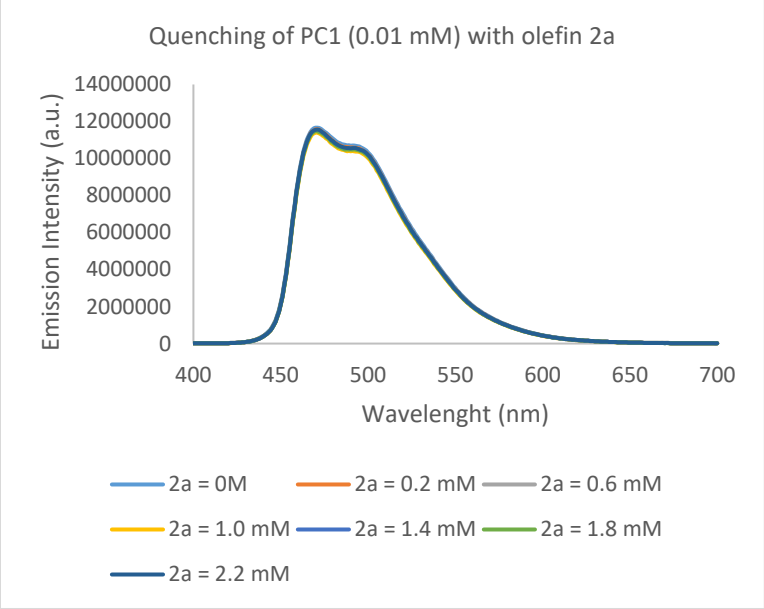


Figure S7. Emission spectra of **PC1** (0.01 mM) at different concentrations of olefin **2a**.

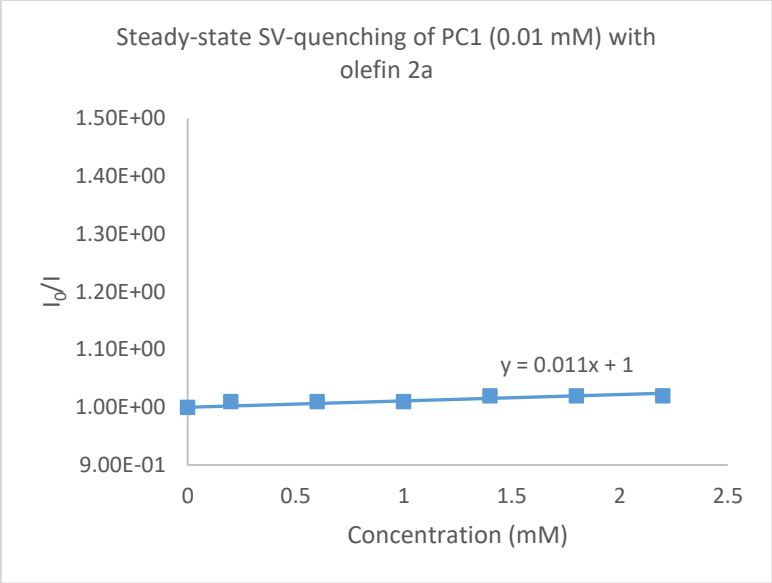


Figure S8. Steady-state Stern-Volmer quenching of **PC1** (0.01 mM) with olefin **2a**.

4) Steady-state Stern-Volmer quenching of PC1 with mixture of oxime 1a and different concentration of 3-acetoxy quinuclidine:

In order to ensure the quenching of **PC1** with oxime **1a** by the interaction with 3-acetoxyquinuclidine, we performed the quenching studies using mixture of oxime **1a** and different concentration of 3-acetoxyquinuclidine. The variable concentrations of quencher (**1a**+3-acetoxyquinuclidine, Q) were prepared by the serial dilution of 0.01 M stock solutions. Quenching experiments were carried out using a 0.01 mM solution of **PC1** in CH_3CN, a fixed concentration of **1a** (0.0022 M), and variable concentrations of quencher (3-acetoxyquinuclidine) (0.2, 0.4, 0.6, 0.8, 1.0 mM) in CH_3CN. The samples were prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S9 and S10).

Inference: The rate of quenching (k_q = 181.8 $M^{-1}S^{-1}$) using the mixture of oxime 1a (0.0022 M) and different concentrations of 3-acetoxyquinuclidineshowed quenching similar to that of 3-acetoxyquinuclidine as quencher (k_q = 174.3 $M^{-1}S^{-1}$).

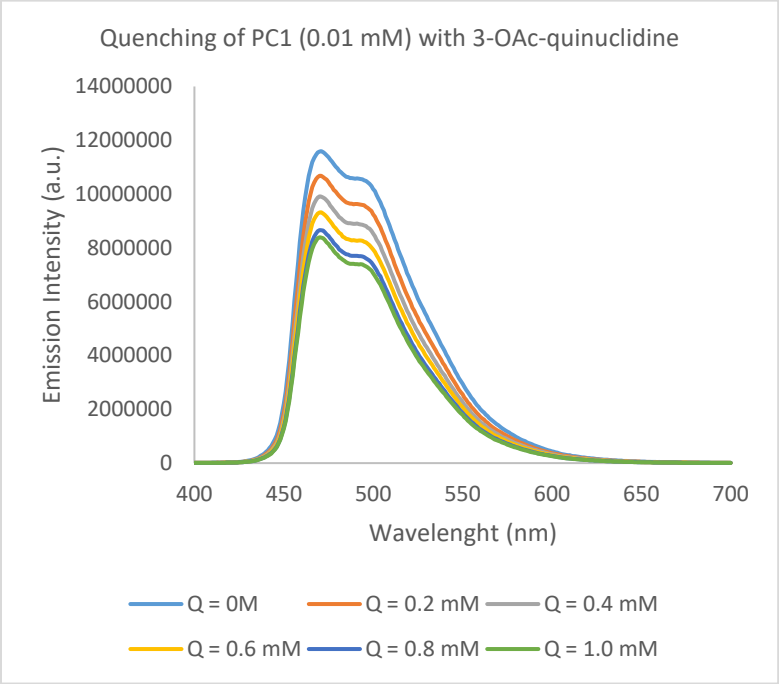


Figure S9. Emission spectra of **PC1** (0.01 mM) at different concentrations of oxime **1a** and 3-acetoxyquinuclidine

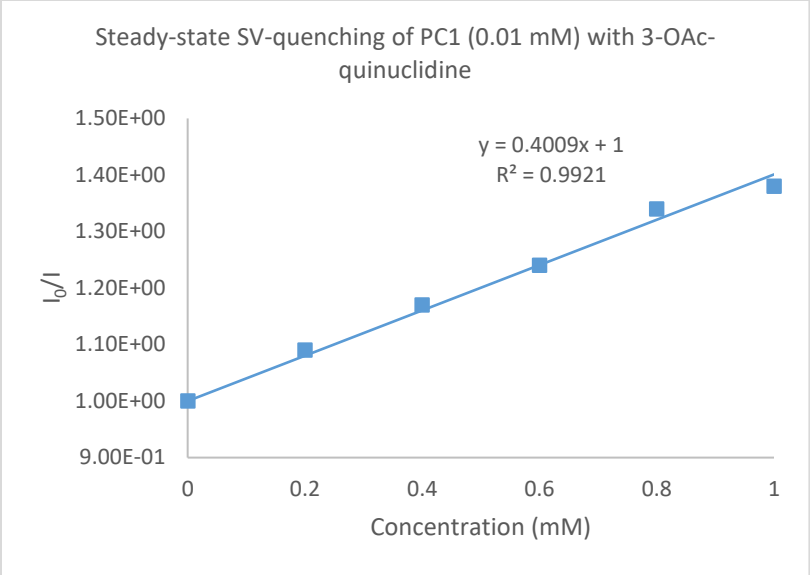


Figure S10. Steady-state Stern-Volmer quenching of **PC1** (0.01 mM) at different concentrations of oxime **1a** and 3-acetoxyquinuclidine.

5) Steady-state Stern-Volmer quenching of PC1 with mixture of 3-acetoxy quinuclidine and different concentration of oxime 1a:

In order to ensure the quenching of PC1 with oxime **1a** by the interaction with 3-acetoxyquinuclidine, we performed the quenching studies using mixture of 3-acetoxyquinuclidineand varied concentrations of oxime **1a**. The variable concentrations of quencher (3-acetoxyquinuclidine, Q+**1a**) were prepared by the serial dilution of 0.01 M stock solutions. Quenching experiments were carried out using a 0.01 mM solution of **PC1** in CH_3CN, a fixed concentration of 3-acetoxyquinuclidine (0.001 M), and variable concentrations of quencher (**1a**) (0.2, 0.6, 1.0, 1.4, 1.8, 2.2 mM) in CH_3CN. The samples were prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S11 and S12).

Inference: The quenching of the mixture of 3-acetoxyquinuclidine (0.001 M) and varied concentrations of oxime **1a** was found to be same to that of the quenching of 3-acetoxyquinuclidine (0.001 M) alone, inferring that the addition of different concentrations of oxime **1a** does not have any effect on the quenching rate.

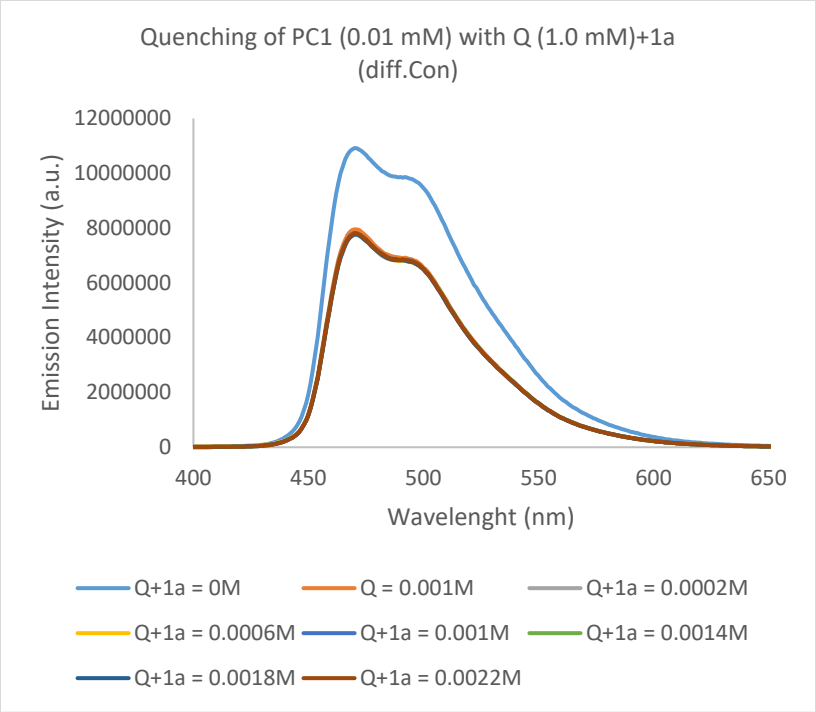


Figure S11. Emission spectra of **PC1** (0.01 mM) at different concentrations of 3-acetoxyquinuclidine and oxime **1a**.

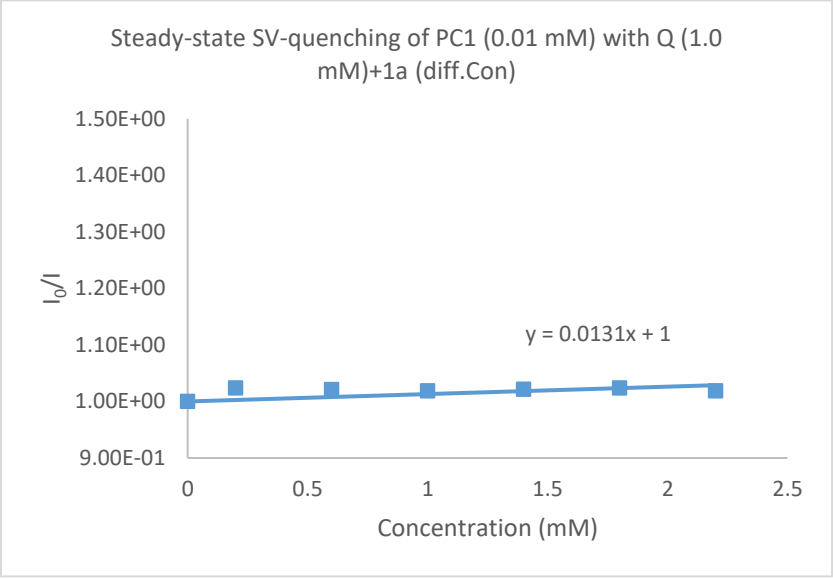


Figure S12. Steady-state Stern-Volmer quenching of **PC1** (0.01 mM) with different concentrations of 3-acetoxyquinuclidine and oxime **1a**.

6) Steady-state Stern-Volmer quenching of PC1 with lutidine:

The variable concentrations of quencher (lutidine) were prepared by the serial dilution of 0.01 M stock solution. Quenching experiments were carried out using a 0.01 mM solution of **PC1** in CH_3CN and variable concentrations of quencher (lutidine) (0.6, 1.2, 1.8, 2.4, 3.0 mM) in CH_3CN. The samples were prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S13 and S14).

Inference: At the reaction concentrations (**PC1**:lutidine, 1:200), we found that lutidine is not a quencher.

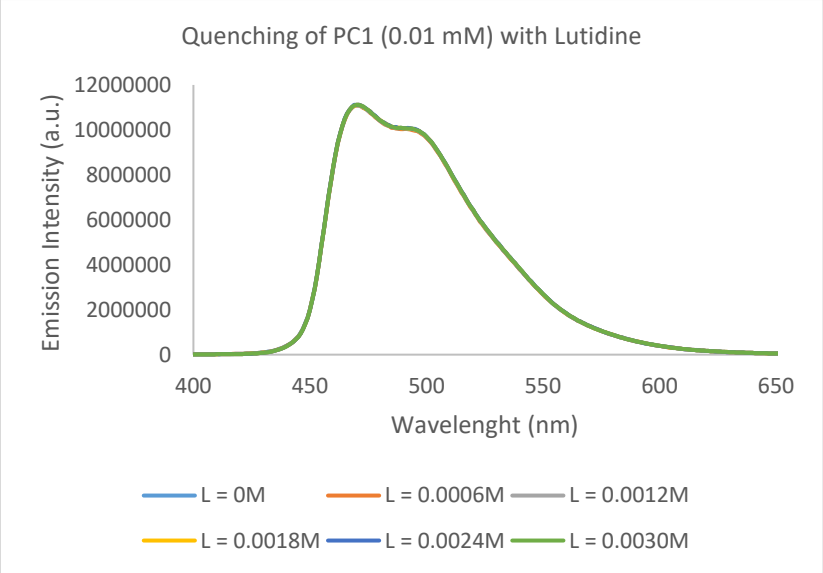


Figure S13. Emission spectra of **PC1** (0.01 mM) at different concentrations of lutidine.

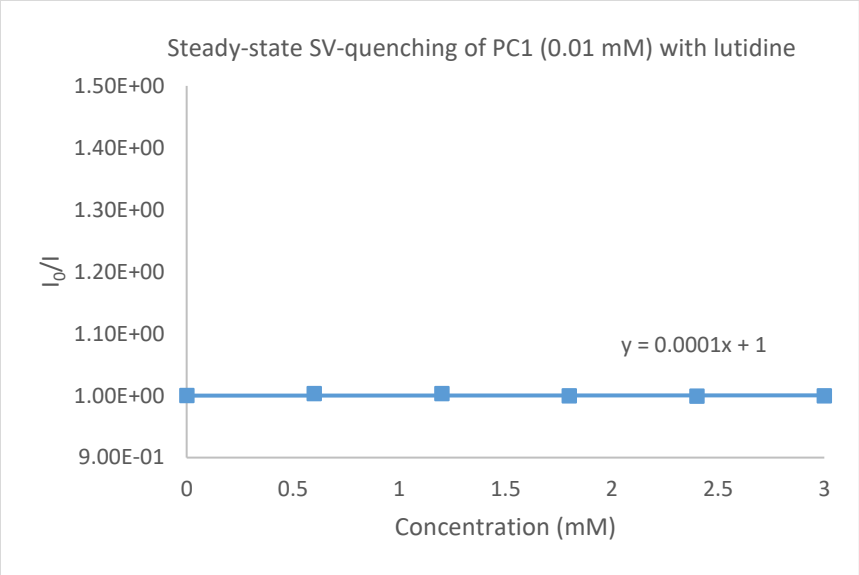


Figure S14. Steady-state Stern-Volmer quenching of **PC1** (0.01 mM) with lutidine.

7) Steady-state Stern-Volmer quenching of PC1 with mixture of oxime 1a and different concentration of lutidine:

In order to ensure the quenching of **PC1** with oxime **1a** by the interaction with lutidine, we performed the quenching studies using mixture of oxime **1a** with varied concentrations of lutidine. The variable concentrations of quencher (**1a**+lutidine) were prepared by the serial dilution of 0.01 M stock solutions. Quenching experiments were carried out using a 0.01 mM solution of PC1 in CH_3CN, a fixed concentration of 1a (0.0022 M), and variable concentrations of quencher (lutidine) (0.6, 1.2, 1.8, 2.4, 3.0 mM) in CH_3CN. The samples were prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S15 and S16).

Inference: We could not see any quenching using the mixture of oxime **1a** and different concentration of lutidine, which infers that there is no interaction between the oxime **1a** and the lutidine.

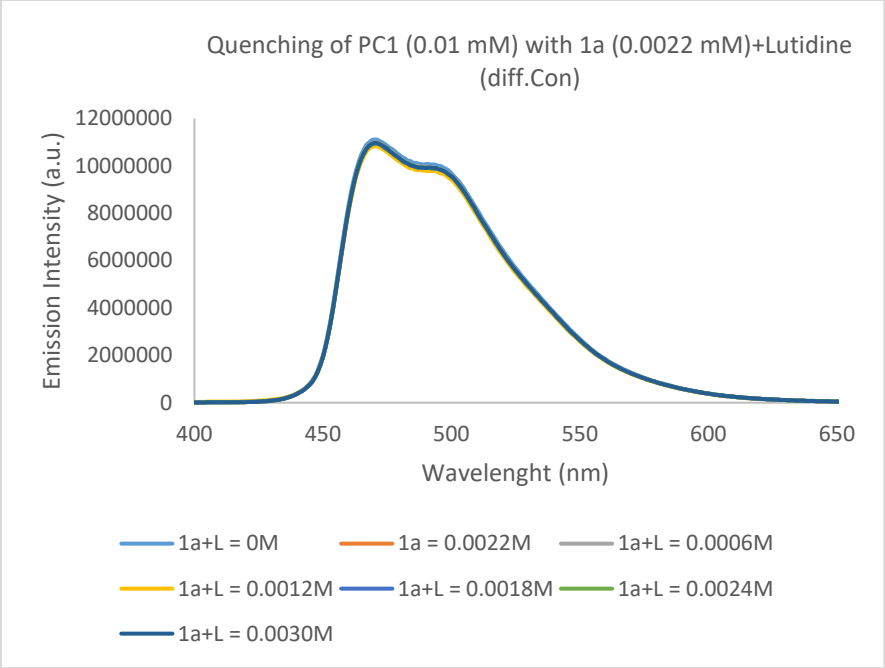


Figure S15. Emission spectra of **PC1** (0.01 mM) at different concentrations of oxime **1a** and lutidine.

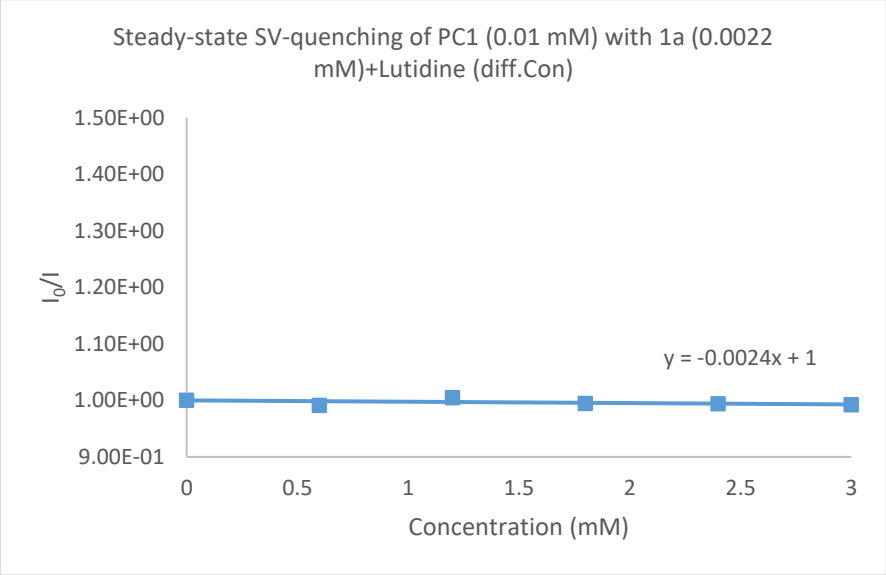


Figure S16. Steady-state Stern-Volmer quenching of **PC1** (0.01 mM) at different concentrations of oxime **1a** and lutidine.

8) Steady-state Stern-Volmer quenching of PC1 with mixture of oxime 1a, 3-acetoxyquinuclidine, and lutidine:

In order to ensure the quenching of **PC1** (0.01 mM) with oxime **1a** by the interaction with 3-acetoxy quinuclidine and lutidine, we performed the quenching studies using mixture of oxime **1a** (2.2 mM), 3-acetoxy quinuclidine (0.2 mM), and lutidine (2.2 mM) similar to the standard reaction condition concentrations. The samples were prepared in 2 mL quartz cuvettes, equipped with PTFE stoppers, and sealed with parafilm inside an argon-filled glove box, removed from the glove box and an emission spectrum was collected. Samples were excited at 390 nm and the intensity of emission was monitored at 471 nm expressed as the ratio I_0/I, where I_0 is the emission intensity of **PC1** at 471 nm in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration was measured (Figure S17). The emission data is correlated with the emission of **PC1** (0.01 mM); PC1 (0.01 mM) and 3-acetoxyquinuclidine (0.2 mM); **PC1** (0.01 mM), **1a** (2.2 mM), and lutidine (2.2 mM)

Inference: We could not see any substantial quenching using the mixture oxime **1a** (2.2 mM), 3-acetoxyquinuclidine (0.2 mM), and lutidine (2.2 mM) which infers that there is no interaction of the oxime **1a** with the other reaction components.

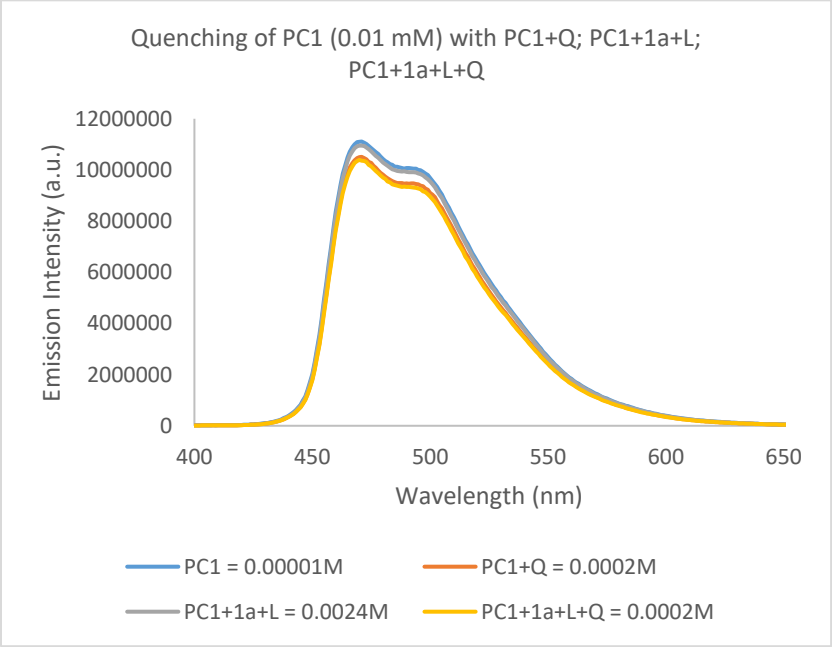
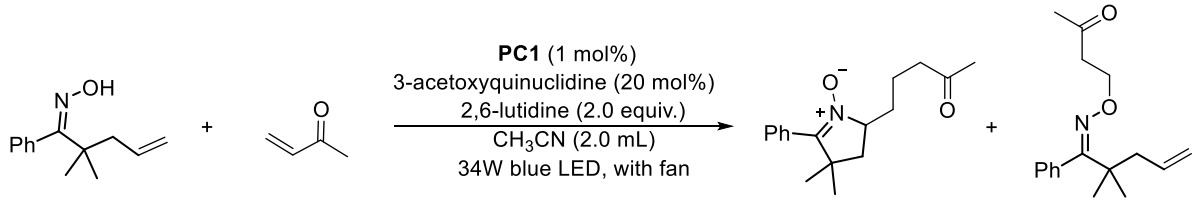


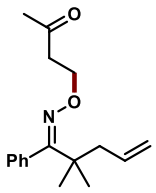
Figure S17. Emission spectra of **PC1** (0.01 mM) at different concentrations of oxime **1a** and lutidine.

3.8 *γ,δ*-unsaturated oxime as substrate under standard reaction condition



1a', 0.4 mmol **2a**, 0.2 mmol not detected **3a'**, 40% yield

Inference: When we using *γ,δ*-unsaturated oxime **1a'** as substrate to perform the model reaction, considering that the generated imidoxy radical has a spin on both the *O* atom and the *N* atom, and according to previous Han's report,[7] a *N*-atom 5-*exo*-*trig* cyclization process would occur and give the cyclic nitrones as the desired product. However, we didn't get the expected product, interestingly, product **3a'** was formed via *O* atom added to the Michael acceptor **2a** instead of adding to the intramolecular double bond first.



3a'

4-(((2,2-dimethyl-1-phenylpent-4-en-1-ylidene)amino)oxy)butan-2-one (3a')

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 3H), 7.06 – 6.95 (m, 2H), 5.86 (ddt, *J* = 17.3, 10.2, 7.2 Hz, 1H), 5.15 – 5.02 (m, 2H), 4.23 (t, *J* = 6.3 Hz, 2H), 2.65 (t, *J* = 6.3 Hz, 2H), 2.23 (dt, *J* = 7.2, 1.3 Hz, 2H), 2.06 (s, 3H), 1.10 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.92, 165.09, 135.13, 134.33, 127.95, 127.74, 127.59, 117.62, 69.12, 44.57, 43.83, 40.36, 30.48, 26.08.

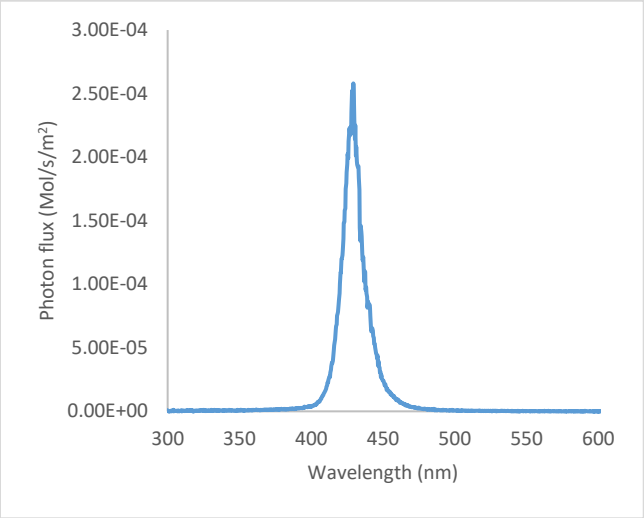
HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{17}H_{24}O_2N$: 274.1802; found: 274.1804.

4. Computational Methods

All DFT-calculations were performed using Gaussian 16, Revision B.01.[8] The geometry optimization and frequency analysis were performed using meta-hybrid-GGA DFT functional ωB97xD.[9] The split-valence plus one polarization function Def2-SVP basis set was used for all atoms.[10] In addition, IEF-PCM implicit solvation model (acetonitrile (MeCN): ε = 35.688) is used for geometry optimization[11]. In all cases, the default integral grid (Ultrafine Grid) was employed. Frequency calculations were performed in order to obtain thermal corrections (298 K) and to confirm the nature of the stationary points (minima with no imaginary frequency or transition states with one imaginary frequency). All transition states were optimized using the default Berny algorithm implemented in the Gaussian 16 code.[8] Moreover, Grimme's quasi-harmonic corrections[12] have been applied to the free energy corrections with a frequency cut-off value of 100.0 cm^{-1} using the GoodVibes[13] program at 298.15 K. Also, GoodVibes applied 1 M standard concentration corrections to all calculations to account for reactions in solution (from 1atm to 1 M). For transition state structures, IRC calculations were undertaken to confirm that the transition states were connected to the correct minima. For further validation of energetics, single-point calculations were performed on the ωB97xD/Def2-SVP optimized geometries using meta-hybrid GGA functional M06-2X[14] employing a valence triple-ζ-type of basis set Def2-TZVPP[10] for all atoms. The solvent effects (acetonitrile (MeCN): ε = 35.688) were evaluated implicitly by a self-consistent reaction field (SCRF) approach for all the intermediates and transition states, using the SMD continuum solvation model.[15] Unless specified otherwise, ΔG was used throughout the text. The ΔG value was obtained by augmenting the E_{el} energy terms at M06-2X(SMD-MeCN)/Def2-TZVPP with the respective free energy corrections at the ωB97xD/Def2-SVP level in 1 M solution.

5. Quantum yield measurement

The quantum yield was measured according to a published procedure.[16,17] The photon flux was measured using the AvaSpec-3648 spectrometer, AvaLight DHS calibration light source, and FC-UV200-2 fiber-optic cable and the Apparent Quantum Efficiency (AQE) measurement was conducted with a 427 nm LEDs. Photon flux of this spectrophotometer was determined as 6.42×10^{-7} Einstein/sec using calibrated light source.



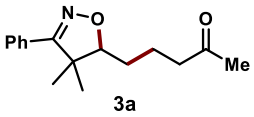
A clean, screw cap reaction tube equipped with a Teflon-coated magnetic stir bar was charged with the oximes **1a** (0.4 mmol, 2.0 equiv.), 3-acetoxyquinuclidine (0.04 mmol, 0.2 equiv.) and $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2.0 mg, 0.02 mmol, 1 mol%). It was capped with a rubber septum, evacuated and backfilled with argon for three times. Then degassed CH_3CN (2.0 mL), methyl vinyl ketone **2a** (0.2 mmol, 1.0 equiv.) and 2,6-lutidine (0.4 mmol, 2.0 equiv.) were added via syringe. The reaction tube was irradiated at 427 nm for 1800 s with fan cooling. After irradiation, the reaction was quenched with air and yield was determined by ^1H NMR analysis using CH_2Br_2 as an internal standard. Finally, the amount of **3a** was measured as 1.38×10^{-5} mol. Essentially all incident light ($f > 0.999$) is absorbed by the **PC1** at the reaction conditions described above.

$$\phi = \frac{\text{moles of product}}{\text{moles of absorbed photons}} = \frac{\text{moles of product}}{\text{flux} \bullet t \bullet f}$$

$$\phi\ (427\ \text{nm}) = \frac{1.38 \times 10^{-5}\ \text{mol}}{6.42 \times 10^{-7}\ \text{Einstein/s} \times 1800\ \text{s} \times 1} = 0.012$$

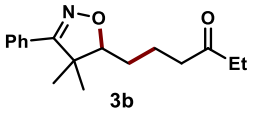
Where Φ is the quantum yield, t is the time (1800 s), and f is the fraction of light absorbed at λ = 427 nm ($f > 0.999$).

6. Compound Characterization Data



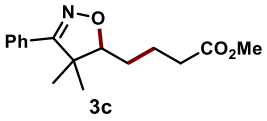
3a

5-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)pentan-2-one (**3a**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol) , the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 10:1 hexane: EtOAc) in 72% yield (37.3 mg). **IR** (neat): 3063, 2958, 1979, 1711, 1458, 1157, 895, 766, 693 cm^{-1}. **^{1}H NMR** (400 MHz, CD_3Cl_3): δ 7.67 – 7.57 (m, 2H), 7.44 – 7.33 (m, 3H), 4.06 (dd, *J* = 9.2, 3.8 Hz, 1H), 2.65 – 2.49 (m, 2H), 2.16 (s, 3H), 1.92 – 1.77 (m, 2H), 1.72 – 1.58 (m, 2H), 1.34 (s, 3H), 1.20 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 208.77, 165.37, 129.73, 129.70, 128.68, 127.45, 90.88, 51.16, 43.41, 30.09, 27.36, 24.15, 21.18, 19.58. **HRMS** (ESI): *m/z* $[M+Na]]^+$ calcd for $C_{16}H_{21}O_2NNa$: 282.14645; found: 282.14636.



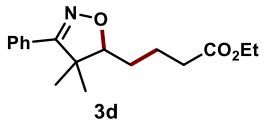
3b

6-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)hexan-3-one (**3b**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2b** (16.8 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 52% yield (28.2 mg). **IR** (neat): 3409, 3060, 2961, 1895, 1710, 1458, 1109, 1017, 893, 762, 691 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.57 (m, 2H), 7.42 – 7.34 (m, 3H), 4.05 (dd, *J* = 9.5, 3.5 Hz, 1H), 2.60 – 2.48 (m, 2H), 2.44 (q, *J* = 7.3 Hz, 2H), 1.91 – 1.77 (m, 2H), 1.69 – 1.58 (m, 2H), 1.33 (s, 3H), 1.19 (s, 3H), 1.06 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 211.43, 165.37, 129.71, 128.67, 127.45, 90.90, 51.14, 42.05, 36.03, 27.45, 24.14, 21.23, 19.57, 7.94. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{23}O_2NNa$: 296.16210; found: 296.16211.



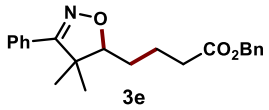
3c

methyl 4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)butanoate (**3c**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2c** (17.2 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 51% yield (28.1 mg). **IR** (neat): 3267, 3061, 2965, 2858, 1730, 1436, 1168, 1004, 973, 895, 764, 693 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 2H), 7.42 – 7.36 (m, 3H), 4.08 (dd, *J* = 9.6, 3.3 Hz, 1H), 3.69 (s, 3H), 2.52 – 2.37 (m, 2H), 2.04 – 1.92 (m, 1H), 1.89 – 1.79 (m, 1H), 1.78 – 1.69 (m, 1H), 1.68 – 1.59 (m, 1H), 1.35 (s, 3H), 1.21 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.91, 165.35, 129.72, 128.69, 128.03, 127.47, 90.60, 51.12, 33.93, 27.50, 25.45, 24.20, 22.29, 19.59. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{21}O_3NNa$: 298.14136; found: 298.14151.



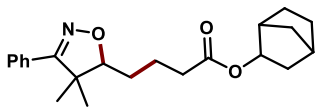
3d

ethyl 4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)butanoate (**3d**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2d** (20.0 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 50% yield (28.4 mg). **IR** (neat): 3449, 3063, 2968, 2329, 1729, 1459, 1174, 1026, 903, 765, 692 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.58 (m, 2H), 7.39 (dd, *J* = 5.3, 2.0 Hz, 3H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.08 (dd, *J* = 9.6, 3.3 Hz, 1H), 2.52 – 2.33 (m, 2H), 2.05 – 1.90 (m, 1H), 1.82 (m, 2H), 1.78 – 1.60 (m, 3H), 1.35 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.21 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.49, 165.37, 129.73, 128.70, 127.48, 90.65, 60.46, 51.12, 34.24, 27.51, 24.21, 22.32, 19.60, 14.39. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{23}O_3NNa$: 312.15701; found: 312.15695.



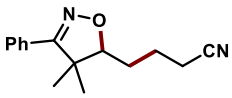
3e

benzyl 4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)butanoate **(3e)**: According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2e** (32.4 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 51% yield (35.7 mg). **IR** (neat): 3050, 2967, 1725, 1458, 1162, 1053, 893, 757, 693 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 – 7.57 (m, 2H), 7.46 – 7.28 (m, 8H), 5.14 (s, 2H), 4.07 (dd, *J* = 9.9, 3.2 Hz, 1H), 2.58 – 2.42 (m, 2H), 2.07 – 1.94 (m, 1H), 1.92 – 1.79 (m, 1H), 1.77 – 1.66 (m, 1H), 1.66 – 1.56 (m, 1H), 1.32 (s, 3H), 1.19 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 173.24, 165.31, 136.14, 129.70, 128.68, 128.34, 127.44, 90.58, 66.30, 51.08, 34.18, 27.44, 24.15, 22.32, 19.55. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{25}O_3NNa$: 374.17266; found: 374.17261.



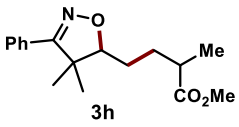
3f

bicyclo[2.2.1]heptan-2-yl 4-((S)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)butanoate (**3f**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2f** (36.0 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 25:1 hexane: EtOAc) in 44% yield (31.0 mg). **IR** (neat): 3066, 2961, 2872, 1718, 1460, 1168, 1070, 978, 889, 765, 694 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.57 (m, 2H), 7.45 – 7.32 (m, 3H), 4.61 (d, *J* = 7.5 Hz, 1H), 4.07 (dd, *J* = 9.6, 3.2 Hz, 1H), 2.46 – 2.31 (m, 2H), 2.30 – 2.25 (m, 2H), 2.00 – 1.89 (m, 1H), 1.84 – 1.68 (m, 3H), 1.67 – 1.60 (m, 1H), 1.56 – 1.47 (m, 2H), 1.46 – 1.38 (m, 2H), 1.34 (s, 3H), 1.20 (s, 3H), 1.17 – 1.10 (m, 2H), 1.10 – 1.05 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.13, 165.36, 129.72, 128.69, 127.46, 90.63, 77.69, 51.09, 41.63, 39.73, 35.53, 35.40, 34.55, 28.26, 27.48, 24.42, 24.18, 22.39, 19.60. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{29}O_3NNa$: 378.20396; found: 378.20398.



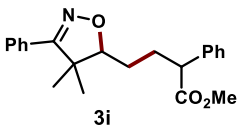
3g

4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)butanenitrile (**3g**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2g** (10.6 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 53% yield (25.6 mg). **IR** (neat): 3060, 2965, 2327, 2090, 1462, 1332, 1070, 902, 766, 695 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 2H), 7.43 – 7.36 (m, 3H), 4.07 (dd, *J* = 10.2, 2.7 Hz, 1H), 2.58 – 2.50 (m, 1H), 2.50 – 2.42 (m, 1H), 2.07 – 1.99 (m, 1H), 1.90 – 1.72 (m, 3H), 1.37 (s, 3H), 1.23 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.35, 129.89, 129.38, 128.74, 127.45, 119.50, 90.00, 51.37, 27.06, 24.22, 23.00, 19.62, 17.31. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{15}H_{18}ON_2Na$: 265.13113; found: 265.13074.



3h

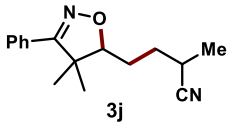
methyl 4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-2-methylbutanoate (**3h**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2h** (20.0 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 70% yield (40.0 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3454, 2968, 2326, 1732, 1460, 1369, 1166, 1002, 894, 765, 694 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.68 – 7.56 (m, 4H), 7.43 – 7.32 (m, 6H), 4.07 (dd, *J* = 8.6, 2.3 Hz, 1H), 4.04 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.76 – 3.60 (m, 6H), 2.63 – 2.48 (m, 2H), 2.05 – 1.71 (m, 4H), 1.71 – 1.51 (m, 4H), 1.33 (s, 6H), 1.26 – 1.14 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 177.00, 176.84, 165.36, 129.69, 128.66, 127.44, 90.81, 90.44, 51.74, 51.64, 51.04, 39.74, 39.14, 30.96, 30.62, 26.11, 25.47, 24.24, 24.17, 19.56, 17.63, 16.99. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{23}O_3NNa$: 312.15701; found: 312.15698.



3i

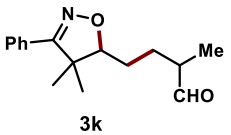
methyl 4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-2-phenylbutanoate (**3i**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2i** (32.4 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 74% yield (51.8 mg, 1.2:1 d.r. inseparable mixture). **IR** (neat): 3452, 3029, 2955, 2329, 1732, 1452, 1162, 1006, 903, 765, 695 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.65 – 7.59 (m, 4.44H), 7.43 – 7.36 (m, 6.66H), 7.36 – 7.30 (m, 8.88H), 7.30 – 7.24 (m, 2.22H), 4.10 (dd, *J* = 9.9, 3.3 Hz, 1H), 4.07 (dd, *J* = 9.9, 3.3 Hz, 1.22H), 3.77 – 3.65 (m, 8.88H), 2.45 – 2.38 (m, 1H), 2.30 – 2.21 (m, 1.22H), 2.16 – 2.10 (m, 1H), 2.05 – 1.96 (m, 1.22H), 1.72 – 1.63 (m, 2.22H), 1.62 – 1.55 (m, 1H), 1.52 – 1.44 (m, 1.22H), 1.33 (s, 3H), 1.30 (s, 3.66H), 1.18 (s, 3H), 1.14 (s, 3.66H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 174.34, 174.30, 165.36, 165.32, 138.89, 138.73, 129.73, 129.66, 128.86, 128.83, 128.68, 128.19,

127.95, 127.50, 127.45, 90.66, 90.47, 52.17, 51.46, 51.43, 51.09, 30.61, 30.55, 26.17, 25.84, 24.21, 24.17, 19.57, 19.52. **HRMS** (EI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{25}O_3NNa$: 374.17266; found: 374.17279.



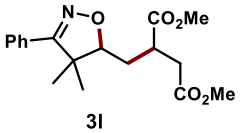
3j

4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-2-methylbutanenitrile (**3j**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2j** (13.4 mg, 0.2 mmol), the title compound was isolated as colourless oil after flash chromatography on silica gel (eluent: 10:1 hexane: EtOAc) in 81% yield (41.4 mg, 1:1 d.r. inseparable mixture). **IR** (neat): 3058, 2972, 2239, 1553, 1461, 1333, 1159, 1004, 898, 769, 696 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.67 – 7.58 (m, 4H), 7.45 – 7.35 (m, 6H), 4.13 – 4.07 (m, 1H), 4.07 – 4.03 (m, 1H), 2.87 – 2.68 (m, 2H), 2.03 – 1.81 (m, 4H), 1.81 – 1.60 (m, 4H), 1.45 – 1.31 (m, 12H), 1.24 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 165.40, 129.88, 129.43, 128.74, 127.47, 122.87, 122.63, 90.56, 89.60, 51.35, 51.31, 31.98, 30.88, 26.32, 26.23, 25.24, 25.15, 24.28, 19.65, 18.49, 17.95. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{20}ON_2Na$: 279.14651; found: 279.14639.



3k

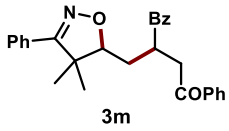
4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-2-methylbutanal (**3k**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2k** (14.0 mg, 0.2 mmol), the title compound was isolated as colourless oil after flash chromatography on silica gel (eluent: 15:1 hexane: EtOAc) in 66% yield (34.4 mg, 1:1 d.r. inseparable mixture). **IR** (neat): 3059, 2970, 2158, 1706, 1462, 1183, 1003, 897, 765, 693 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 9.67 (d, *J* = 1.9 Hz, 1H), 9.65 (d, *J* = 1.9 Hz, 1H), 7.66 – 7.59 (m, 4H), 7.43 – 7.37 (m, 6H), 4.07 (dd, *J* = 2.9, 1.3 Hz, 1H), 4.06 (dd, *J* = 2.8, 1.3 Hz, 1H), 2.52 – 2.44 (m, 2H), 2.15 – 2.07 (m, 1H), 1.91 – 1.82 (m, 1H), 1.81 – 1.67 (m, 4H), 1.64 – 1.51 (m, 4H), 1.37 – 1.33 (m, 6H), 1.21 (d, *J* = 1.1 Hz, 6H), 1.17 (d, *J* = 3.1 Hz, 3H), 1.16 (d, *J* = 3.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 204.92, 204.89, 165.41, 129.81, 129.62, 128.73, 127.48, 90.74, 90.71, 51.20, 51.16, 46.44, 46.24, 27.85, 27.68, 25.73, 25.41, 24.27, 24.25, 19.65, 19.63, 13.80, 13.46. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{21}O_2NNa$: 282.14645; found: 282.14630.



3l

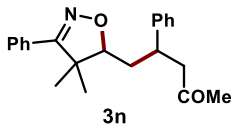
dimethyl 2-((4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)methyl)succinate (**3l**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2l** (28.8 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 15:1 hexane: EtOAc) in 72% yield (47.9 mg, 1.2:1 d.r. inseparable mixture). **IR** (neat): 2956, 1733, 1438, 1165, 1006, 894, 767, 695 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) (mixture

of diastereomers, both isomers quoted) δ 7.68 – 7.55 (m, 4.4 H), 7.43 – 7.32 (m, 6.6 H), 4.14 (dd, *J* = 10.9, 1.9 Hz, 1H), 4.09 (dd, *J* = 10.7, 2.4 Hz, 1.2 H), 3.73 (s, 6.6 H), 3.68 (s, 6.6 H), 3.23 – 3.10 (m, 2.2 H), 2.87 – 2.64 (m, 4.4 H), 2.17 – 1.98 (m, 2.2 H), 1.89 – 1.78 (m, 2.2 H), 1.38 – 1.31 (m, 6.6 H), 1.24 – 1.17 (m, 6.6 H). **^{13}C NMR** (101 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 174.85, 174.82, 172.25, 172.17, 165.21, 129.83, 129.40, 128.70, 128.64, 127.43, 88.94, 87.77, 52.27, 52.21, 51.93, 51.53, 51.48, 39.16, 38.71, 36.54, 34.92, 30.18, 29.50, 23.95, 23.90, 19.43, 19.39. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{18}H_{23}O_5NNa$: 356.14684; found: 356.14676.



3m

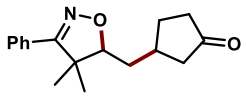
2-((4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)methyl)-1,4-diphenylbutane-1,4-dione (**3m**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2m** (47.2 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 63% yield (53.5 mg, 1.2:1 d.r. inseparable mixture). **IR** (neat): 3353, 3061, 2965, 1984, 1678, 1447, 996, 899, 763, 690 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 8.19 – 8.12 (m, 2H), 8.03 – 7.98 (m, 2H), 7.63 – 7.54 (m, 4H), 7.54 – 7.50 (m, 2H), 7.48 – 7.44 (m, 2H), 7.42 – 7.36 (m, 3H), 4.50 (tt, *J* = 9.2, 3.9 Hz, 1H), 4.25 (dd, *J* = 11.2, 2.0 Hz, 1H), 3.80 (dd, *J* = 17.8, 9.4 Hz, 1H), 3.37 (dd, *J* = 17.9, 4.0 Hz, 1H), 2.22 – 2.15 (m, 1H), 1.79 – 1.71 (m, 1H), 1.33 (s, 3H), 1.17 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 202.47, 198.25, 165.39, 136.76, 136.15, 133.38, 133.30, 129.93, 129.45, 128.95, 128.91, 128.77, 128.73, 128.31, 127.50, 87.83, 51.50, 39.96, 38.61, 30.21, 24.12, 19.49. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{28}H_{27}O_3NNa$: 448.18831; found: 448.18835.



3n

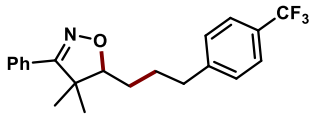
5-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-4-phenylpentan-2-one (**3n**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2n** (29.2 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 53% yield (35.5 mg, 1.4:1 d.r. inseparable mixture). **IR** (neat): 3028, 2929, 2329, 1707, 1601, 1453, 1359, 1167, 900, 759. 696 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.65 – 7.59 (m, 4.72H), 7.41 – 7.28 (m, 11.8H), 7.26 – 7.17 (m, 7.08H), 4.08 (dd, *J* = 11.2, 2.5 Hz, 1.36H), 3.93 (dd, *J* = 11.4, 2.1 Hz, 1H), 3.63 – 3.60 (m, 1H), 3.51 – 3.48 (m, 1.36H), 3.40 – 3.34 (m, 1H), 3.18 – 3.11 (m, 1.36H), 2.91 (dd, *J* = 13.5, 8.6 Hz, 2H), 2.87 – 2.76 (m, 2.72H), 2.08 (s, 3H), 2.06 (s, 4.08H), 1.97 – 1.91 (m, 0.5H), 1.77 – 1.71 (m, 0.5H), 1.65 – 1.59 (m, 2.72H), 1.32 (s, 3H), 1.30 (s, 4.08H), 1.19 (s, 4.08H), 1.18 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 212.91, 211.91, 207.04, 165.39, 165.34, 140.90, 138.97, 138.73, 129.86, 129.84, 129.50, 129.46, 129.14, 129.08, 128.99, 128.93, 128.76, 128.72, 127.46, 127.44,

127.26, 127.21, 126.72, 126.66, 88.79, 88.31, 51.41, 51.38, 51.31, 50.97, 50.60, 48.13, 39.67, 38.15, 32.20, 30.89, 30.09, 29.79, 28.93, 24.21, 24.05, 19.49, 19.39. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{25}O_2NNa$: 358.17775; found: 358.17676.



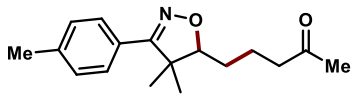
3o

3-((4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)methyl)cyclopentan-1-one (**3o**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **2o** (16.4 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 50% yield (26.9 mg, 1:0.9 d.r. inseparable mixture). **IR** (neat): 3456, 3062, 2962, 2328, 1735, 1460, 1160, 1004, 903, 764, 690 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.66 – 7.61 (m, 3.84H), 7.44 – 7.37 (m, 5.76H), 4.17 (dd, *J* = 11.0, 2.1 Hz, 1H), 4.09 (dd, *J* = 10.9, 2.1 Hz, 0.92H), 2.60 – 2.46 (m, 3.84H), 2.38 – 2.28 (m, 3.84H), 2.25 – 2.16 (m, 1.92H), 1.99 – 1.83 (m, 3.84H), 1.67 – 1.56 (m, 3.84H), 1.38 – 1.33 (m, 5.76H), 1.22 (s, 5.76H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 219.24, 219.03, 165.37, 129.87, 129.56, 128.76, 127.46, 89.61, 88.97, 51.32, 51.25, 45.94, 44.98, 38.82, 38.62, 35.04, 34.98, 33.83, 33.68, 30.42, 29.51, 24.01, 19.66, 19.65. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{21}O_2NNa$: 294.14645; found: 294.14612.



3p

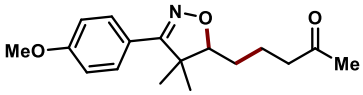
4,4-dimethyl-3-phenyl-5-(3-(4-(trifluoromethyl)phenyl)propyl)-4,5-dihydroisoxazole (**3p**): According to the general procedure, in the absence of 2,6-lutidne, starting from **1a** (75.6 mg, 0.40 mmol) and **2p** (34.4 mg, 0.2 mmol), the title compound was purified by preparative thin layer chromatography (eluent: 20:1 hexane: EtOAc) and isolated as colorless oil in 46% yield (33.0 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 – 7.59 (m, 2H), 7.55 (d, *J* = 7.9 Hz, 2H), 7.40 (dt, *J* = 5.3, 2.6 Hz, 3H), 7.33 (d, *J* = 7.9 Hz, 2H), 4.10 (dd, *J* = 10.0, 2.9 Hz, 1H), 2.79 (h, *J* = 7.2 Hz, 2H), 2.10 – 1.97 (m, 1H), 1.86 – 1.71 (m, 2H), 1.62 – 1.54 (m, 1H), 1.34 (s, 3H), 1.20 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.42, 146.24, 129.78, 129.71, 128.88, 128.72, 128.51, 127.47, 125.43 (q, *J* = 3.8 Hz, CF_3), 124.51 (q, *J* = 272.2 Hz, C*q*-CF_3), 90.74, 51.12, 35.76, 28.31, 27.55, 24.20, 19.63. **^{19}F NMR** (471 MHz, CDCl3) δ -62.27. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{21}H_{22}F_3ONNa$: 384.1546; found: 384.1544.



4a

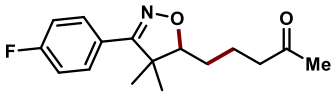
5-(4,4-dimethyl-3-(p-tolyl)-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4a**): According to the general procedure, starting from **1b** (81.2 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as colourless oil after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 61% yield (33.3 mg).

IR (neat): 3089, 2965, 2039, 1710, 1596, 1237, 1028, 902, 786, 698 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 1H), 7.21 – 7.16 (m, 2H), 6.97 – 6.92 (m, 1H), 4.05 (dd, *J* = 9.2, 3.8 Hz, 1H), 3.82 (s, 3H), 2.64 – 2.49 (m, 2H), 2.16 (s, 3H), 1.91 – 1.76 (m, 2H), 1.71 – 1.59 (m, 2H), 1.34 (s, 3H), 1.19 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.77, 165.26, 159.69, 130.91, 129.66, 119.69, 115.68, 112.85, 91.01, 55.47, 55.39, 51.14, 43.40, 30.11, 30.06, 27.34, 24.20, 21.17, 19.63. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{23}O_2NNa$: 296.16210; found: 296.16201.



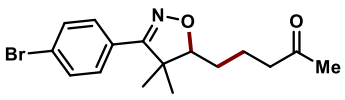
4b

5-(3-(4-methoxyphenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4b**): According to the general procedure, starting from **1c** (87.6 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light yellow solid after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 60% yield (34.5 mg). **IR** (neat): 3408, 2964, 1889, 1710, 1606, 1511, 1248, 1037, 893, 826, 749, 666 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.9 Hz, 2H), 6.96 – 6.85 (m, 2H), 4.02 (dd, *J* = 9.2, 3.8 Hz, 1H), 3.82 (s, 3H), 2.64 – 2.49 (m, 2H), 2.16 (s, 3H), 1.93 – 1.74 (m, 2H), 1.70 – 1.55 (m, 2H), 1.32 (s, 3H), 1.18 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.79, 164.90, 160.77, 128.79, 122.00, 114.12, 90.65, 55.40, 51.03, 43.41, 30.06, 27.31, 24.16, 21.20, 19.59. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{23}O_3NNa$: 312.15701; found: 312.15683.



4c

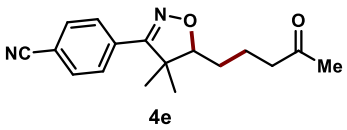
5-(3-(4-fluorophenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4c**): According to the general procedure, starting from **1d** (82.8 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light yellow solid after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 53% yield (29.3 mg). **IR** (neat): 3413, 2957, 1910, 1711, 1507, 1228, 1155, 898, 750, 665 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.57 (m, 2H), 7.12 – 7.03 (m, 2H), 4.05 (dd, *J* = 9.1, 3.9 Hz, 1H), 2.64 – 2.49 (m, 2H), 2.16 (s, 3H), 1.93 – 1.74 (m, 2H), 1.71 – 1.56 (m, 2H), 1.32 (s, 3H), 1.17 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.71, 164.90, 164.47, 162.41, 129.41, 129.32, 125.85, 125.82, 115.94, 115.72, 90.93, 51.04, 43.37, 30.09, 27.34, 24.11, 21.13, 19.53. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{20}O_2NFNa$: 300.13703; found: 300.13684.



4d

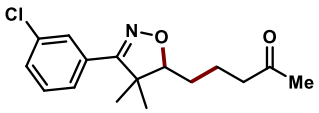
5-(3-(4-bromophenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4d**): According to the general procedure, starting from **1e** (107.2mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light yellow solid after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 42% yield (28.6 mg). **IR** (neat): 3411, 2967, 1919, 1712, 1583, 1463, 1366, 1071, 902, 830, 759, 696 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 – 7.44 (m, 4H), 4.06 (dd, *J* = 8.9, 3.9 Hz, 1H), 2.65 – 2.46 (m, 2H), 2.16 (s, 3H), 1.92 –

1.75 (m, 2H), 1.72 – 1.57 (m, 2H), 1.36 – 1.29 (m, 3H), 1.22 – 1.14 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.73, 164.47, 131.95, 129.74, 128.90, 128.63, 127.46, 124.15, 91.11, 50.94, 43.36, 30.10, 27.31, 24.12, 21.11, 19.56. **HRMS** (EI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{20}O_2NBrNa$: 360.05696; found: 360.05695.



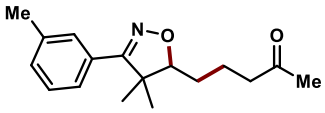
4e

4-(4,4-dimethyl-5-(4-oxopentyl)-4,5-dihydroisoxazol-3-yl)benzonitrile (**4e**): According to the general procedure, starting from **1f** (85.6 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light yellow solid after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 52% yield (29.4 mg). **IR** (neat): 3410, 3069, 2961, 2230, 1711, 1459, 1160, 908, 845, 748, 666 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.71 (m, 2H), 7.71 – 7.63 (m, 2H), 4.10 (dd, *J* = 8.8, 4.2 Hz, 1H), 2.65 – 2.46 (m, 2H), 2.16 (s, 3H), 1.92 – 1.75 (m, 2H), 1.72 – 1.58 (m, 2H), 1.35 (s, 3H), 1.20 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.59, 163.81, 134.25, 132.44, 127.80, 118.43, 113.26, 91.67, 50.72, 43.25, 30.10, 27.21, 24.07, 20.99, 19.56. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{20}O_2N_2Na$: 307.14170; found: 307.14120.



4f

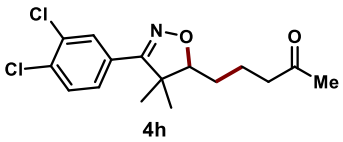
5-(3-(3-chlorophenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)pentan-2-one **(4f)**: According to the general procedure, starting from **1g** (89.4 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as colourless oil after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 51% yield (29.9 mg). **IR** (neat): 3394, 3071, 2956, 2161, 1708, 1463, 1159, 1081, 902, 764, 696 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.59 (m, 1H), 7.55 – 7.49 (m, 1H), 7.40 – 7.35 (m, 1H), 7.34 – 7.30 (m, 1H), 4.07 (dd, 1H), 2.65 – 2.49 (m, 2H), 2.17 (s, 3H), 1.91 – 1.76 (m, 2H), 1.71 – 1.59 (m, 2H), 1.34 (s, 3H), 1.19 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.72, 164.27, 134.70, 131.50, 129.98, 129.80, 127.53, 127.46, 125.51, 51.01, 43.36, 30.14, 27.33, 24.14, 21.11, 19.57. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{20}O_2NClNa$: 316.10748; found: 316.10760.



4g

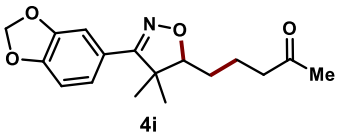
5-(4,4-dimethyl-3-(m-tolyl)-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4g**): According to the general procedure, starting from **1h** (81.2mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light yellow oil after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 50% yield (27.2 mg). **IR** (neat): 3416, 2926, 2119, 1712, 1461, 1365, 1164, 907, 820, 788, 701, 672 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.36 (m, 2H), 7.28 – 7.18 (m, 2H), 4.03 (dd, *J* = 9.2, 3.8 Hz, 1H), 2.60 – 2.50 (m, 2H), 2.35 (s, 3H), 2.15 (s, 3H), 1.90 – 1.76 (m, 2H), 1.68 – 1.58 (m, 2H), 1.32 (s, 3H), 1.18 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.81,

165.57, 138.43, 130.54, 129.61, 128.54, 128.25, 124.45, 90.84, 51.23, 43.44, 30.09, 27.41, 24.22, 21.57, 21.22, 19.61. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{23}O_2NNa$: 296.16210; found: 296.16214.



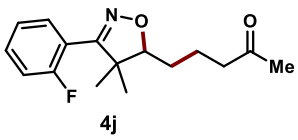
4h

5-(3-(3,4-dichlorophenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4h**): According to the general procedure, starting from **1i** (103.2 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 10:1 hexane: EtOAc) in 41% yield (26.8 mg). **IR** (neat): 3412, 2965, 2878, 1785, 1711, 1467, 1028, 906, 825, 787, 676 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 1.8 Hz, 1H), 7.50 – 7.44 (m, 2H), 4.07 (dd, *J* = 9.4, 3.7 Hz, 1H), 2.62 – 2.51 (m, 2H), 2.17 (s, 3H), 1.90 – 1.83 (m, 1H), 1.83 – 1.77 (m, 1H), 1.69 – 1.60 (m, 2H), 1.34 (s, 3H), 1.18 (s, 3H).**^{13}C NMR** (151 MHz, $CDCl_3$) δ 208.64, 163.44, 134.03, 133.09, 130.76, 129.72, 129.17, 126.51, 91.40, 50.84, 43.33, 30.13, 27.30, 24.14, 21.08, 19.58. HRMS (ESI): m/z $[M+Na]+$ calcd for $C_{16}H_{19}O_2NC_{l2}Na$: 350.06851; found: 350.06857.



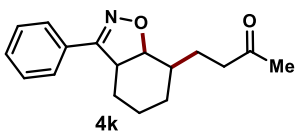
4i

5-(3-(benzo[d][1,3]dioxol-5-yl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4i**): According to the general procedure, starting from **1j** (93.2 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light yellow solid after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 72% yield (43.7 mg). **IR** (neat): 3409, 2964, 2899, 2170, 1712, 1492, 1241, 1105, 1038, 877, 723, 674 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.16 – 7.09 (m, 2H), 6.84 – 6.78 (m, 1H), 5.98 (s, 2H), 4.02 (dd, *J* = 9.1, 3.9 Hz, 1H), 2.63 – 2.48 (m, 2H), 2.16 (s, 3H), 1.90 – 1.75 (m, 2H), 1.68 – 1.55 (m, 2H), 1.32 (s, 3H), 1.16 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 208.80, 164.90, 148.94, 148.00, 123.45, 121.51, 108.38, 108.36, 107.79, 101.53, 101.47, 90.85, 51.00, 43.40, 30.09, 27.29, 24.17, 21.17, 19.62. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{21}O_4NNa$: 326.13628; found: 326.13571.



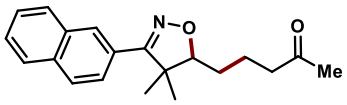
4j

5-(3-(2-fluorophenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4j**): According to the general procedure, starting from **1k** (82.8 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as colourless oil after flash chromatography on silica gel (eluent: 12:1 hexane: EtOAc) in 52% yield (28.8 mg). **IR** (neat): 3416, 2962, 1921, 1712, 1449, 1222, 892, 814, 762, 664 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.30 (m, 2H), 7.22 – 7.09 (m, 2H), 4.12 (dd, *J* = 9.5, 3.5 Hz, 1H), 2.66 – 2.49 (m, 2H), 2.16 (s, 3H), 1.92 – 1.76 (m, 2H), 1.74 – 1.59 (m, 2H), 1.20 (s, 3H), 1.08 (s, 3H). **^{13}C NMR** δ 208.76, 163.25, 161.61, 159.12, 131.54, 131.46, 131.30, 131.27, 124.23, 124.19, 117.71, 117.55, 116.40, 116.18, 90.56, 52.41, 43.40, 30.08, 27.70, 23.53, 23.50, 21.09, 18.69. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{16}H_{20}O_2NFNa$: 300.13703; found: 300.13730.



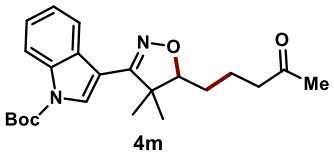
4k

4-((7R,7aS)-3-phenyl-3a,4,5,6,7,7a-hexahydrobenzo[d]isoxazol-7-yl)butan-2-one (**4k**): According to the general procedure, starting from **1l** (80.4 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light brown oil after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 46% yield (25.2 mg, 5:1 d.r. inseparable mixture). **IR** (neat): 3061, 2934, 1900, 1711, 1446, 1161, 1020, 904, 866, 766, 694 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.73 – 7.68 (m, 2H), 7.67 – 7.59 (m, 10H), 7.45 – 7.34 (m, 18H), 4.38 (dd, J = 6.9, 2.8 Hz, 1H), 4.28 (dd, J = 8.5, 5.9 Hz, 5H), 3.49 (td, J = 8.8, 6.2 Hz, 5H), 3.26 (dt, J = 10.5, 6.8 Hz, 1H), 2.69 – 2.54 (m, 12H), 2.18 (s, 15H), 2.17 (s, 3H), 1.90 – 1.78 (m, 14H), 1.78 – 1.66 (m, 15H), 1.60 – 1.52 (m, 5H), 1.52 – 1.34 (m, 11H), 1.34 – 1.15 (m, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.92, 162.36, 130.03, 129.44, 128.87, 127.17, 85.48, 45.00, 41.78, 35.14, 30.20, 27.84, 25.76, 24.25, 19.24. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{21}O_2NNa$: 294.14645; found: 294.14636.



4l

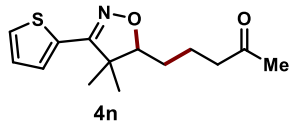
5-(4,4-dimethyl-3-(naphthalen-2-yl)-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4l**): According to the general procedure, starting from **1m** (95.6 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light brown solid after flash chromatography on silica gel (eluent: 10:1 hexane: EtOAc) in 52% yield (32.1 mg). **IR** (neat): 3414, 3060, 2964, 1981, 1711, 1461, 1162, 1055, 884, 802, 741, 661 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 1H), 7.93 – 7.89 (m, 1H), 7.89 – 7.84 (m, 1H), 7.54 – 7.48 (m, 3H), 7.40 (dd, *J* = 7.1, 1.3 Hz, 1H), 4.25 (dd, *J* = 9.4, 3.5 Hz, 1H), 2.71 – 2.54 (m, 2H), 2.20 (s, 3H), 2.00 – 1.85 (m, 2H), 1.84 – 1.68 (m, 2H), 1.20 (s, 3H), 1.10 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.80, 165.02, 133.83, 132.64, 129.75, 128.38, 126.95, 126.92, 126.86, 126.35, 125.85, 124.79, 90.04, 53.78, 43.47, 30.12, 28.05, 24.17, 21.24, 19.24. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{20}H_{23}O_2NNa$: 332.16210; found: 332.16177.



4m

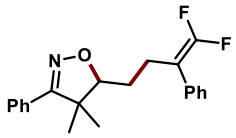
tert-butyl 3-(4,4-dimethyl-5-(3-oxobutyl)-4,5-dihydroisoxazol-3-yl)-1H-indole-1-carboxylate (**4m**): According to the general procedure, starting from **1n** (131.2 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as light yellow oil after flash chromatography on silica gel (eluent: 8:1 hexane: EtOAc) in 75% yield (59.4 mg). **IR** (neat): 3421, 2969, 2931, 1734, 1452, 1363, 1152, 1050, 899, 850, 752, 700 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 – 8.24 (m, 1H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.94 (s, 1H), 7.39 – 7.34 (m, 1H), 7.33 – 7.28 (m, 1H), 4.04 (dd, 1H), 2.68 – 2.52 (m, 2H), 2.18 (s, 3H), 1.94 – 1.82 (m, 2H), 1.71 (s, 9H), 1.45 (s, 3H), 1.24 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.82, 160.90, 149.68, 135.13, 128.62, 125.48, 124.75, 123.77, 123.66, 114.92, 110.31, 89.80, 84.84, 51.57, 43.44, 30.10,

28.29, 27.24, 24.67, 21.32, 19.95. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{23}H_{30}O_4N_2Na$: 421.20978; found:421.20969.



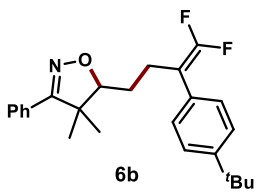
4n

5-(4,4-dimethyl-3-(thiophen-2-yl)-4,5-dihydroisoxazol-5-yl)pentan-2-one (**4n**): According to the general procedure, starting from **1o** (78.0 mg, 0.40 mmol) and **2a** (14.0 mg, 0.2 mmol), the title compound was isolated as brown solid after flash chromatography on silica gel (eluent: 10:1 hexane: EtOAc) in 52% yield (27.8 mg). **IR** (neat): 3405, 3113, 2939, 2161, 1708, 1358, 1160, 1054, 898, 842, 715, 658 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.33 (m, 2H), 7.06 (dd, *J* = 5.1, 3.7 Hz, 1H), 4.11 – 4.05 (m, 1H), 2.66 – 2.49 (m, 2H), 2.16 (s, 3H), 1.92 – 1.75 (m, 2H), 1.69 – 1.60 (m, 2H), 1.41 (s, 3H), 1.22 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.79, 160.87, 131.39, 127.64, 127.47, 126.80, 91.08, 51.17, 43.34, 30.09, 27.36, 24.41, 21.14, 19.64. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{14}H_{19}O_2NNaS$: 288.10287; found: 288.10272.



6a

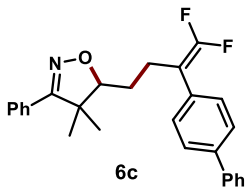
5-(3-(4-(tert-butyl)phenyl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6a**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5a** (34.4 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 80:1–60:1 hexane: EtOAc) in 70% yield (48.0 mg). **IR** (neat): 3448, 3059, 2969, 2870, 2325, 2088, 1888, 1729, 1597, 1496, 1447, 1306, 1232, 1122, 1072, 942, 910, 764, 695 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 2H), 7.43 – 7.34 (m, 7H), 7.32 – 7.27 (m, 1H), 4.09 (dd, *J* = 10.4, 2.7 Hz, 1H), 2.83 – 2.75 (m, 1H), 2.65 – 2.58 (m, 1H), 1.84 – 1.76 (m, 1H), 1.63 – 1.56 (m, 1H), 1.30 (s, 3H), 1.14 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.21, 153.84 (dd, *J* = 291.0, 287.4 Hz), 133.32 (t, *J* = 3.8 Hz), 129.75, 129.62, 128.69, 128.36 (t, *J* = 3.3 Hz), 127.52, 127.45, 91.94 (dd, *J* = 21.4, 13.8 Hz), 90.01, 77.16, 51.06, 26.53 (t, *J* = 3.0 Hz), 25.07, 24.20, 19.58. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -90.46 (dt, *J* = 41.9, 2.6 Hz), -90.78 (d, *J* = 42.9 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{22}ONF_2$: 342.16640; found: 342.16584.



6b

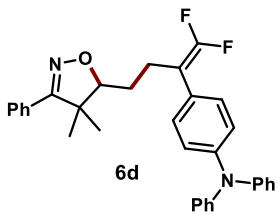
5-(3-(4-(tert-butyl)phenyl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6b**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5b** (45.6 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 80:1–60:1 hexane: EtOAc) in 70% yield (55.8 mg). **IR** (neat): 3449, 3057, 2963, 2869, 1724, 1514, 1463, 1366, 1234, 1106, 943, 911, 835, 764, 693 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.62 (m, 2H), 7.42 – 7.37 (m, 5H), 7.32 – 7.29 (m, 2H), 4.09 (dd, *J* = 10.4, 2.8 Hz, 1H), 2.81 – 2.74 (m, 1H), 2.63 – 2.56 (m, 1H), 1.86 – 1.78 (m, 1H), 1.65

– 1.59 (m, 1H), 1.34 (s, 9H), 1.31 (s, 3H), 1.16 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.24, 153.89 (dd, *J* =306.5, 286.9 Hz), 150.41, 130.23(t, *J* = 3.8 Hz), 129.75, 129.67, 128.70, 127.90 (t, *J* = 3.4 Hz), 127.47, 125.62, 91.68 (dd, *J* = 21.4, 13.1 Hz), 90.13, 51.08, 34.66, 31.40, 26.69 (t, *J* = 2.6 Hz), 25.02, 24.23, 19.63. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -90.54 (dt, *J* = 42.7, 2.7 Hz), -90.83 (d, *J* = 42.7 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{25}H_{30}ONF_2$: 398.22900; found: 398.22845.



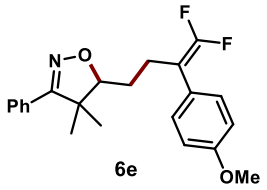
6c

5-(3-([1,1'-biphenyl]-4-yl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6c**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5c** (49.6 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 30:1 hexane: EtOAc) in 54% yield (45.4 mg). **IR** (neat): 3033, 2969, 2931, 1724, 1601, 1488, 1462, 1327, 1235, 1154, 1107, 1004, 910, 840, 763, 693 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 6H), 7.48 – 7.43 (m, 4H), 7.42 – 7.35 (m, 4H), 4.12 (dd, *J* = 10.5, 2.6 Hz, 1H), 2.87 – 2.80 (m, 1H), 2.69 – 2.62 (m, 1H), 1.88 – 1.80 (m, 1H), 1.68 – 1.61 (m, 1H), 1.32 (s, 3H), 1.17 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.24, 153.96 (dd, *J* =291.4, 288.4 Hz), 140.59, 140.28, 132.25 (t, *J* = 4.0 Hz), 129.77, 129.63, 128.96, 128.71, 128.69, 128.66, 127.58, 127.47, 127.37, 127.13, 91.70 (dd, *J* = 21.6, 13.1 Hz), 90.08, 51.12, 26.67 (t, *J* = 2.5 Hz), 24.99, 24.25, 19.63. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -89.76 (dt, *J* = 41.0, 2.6 Hz), -90.14 (d, *J* = 41.1 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{27}H_{26}ONF_2$: 418.19770; found: 418.19724.



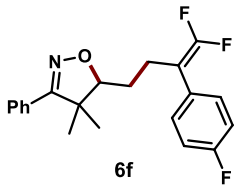
6d

4-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1-difluorobut-1-en-2-yl)-N,N-diphenylaniline (**6d**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5d** (67.8 mg, 0.2 mmol), the title compound was isolated as brown solid after flash chromatography on silica gel (eluent: 80:1–60:1 hexane: EtOAc) in 56% yield (56.7 mg). **IR** (neat): 3037, 2968, 2869, 1723, 1589, 1489, 1321, 1275, 1234, 1176, 1106, 908, 833, 756, 693 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 2H), 7.42 – 7.37 (m, 3H), 7.28 – 7.26 (m, 2H), 7.26 – 7.24 (m, 2H), 7.23 – 7.19 (m, 2H), 7.13 – 7.09 (m, 4H), 7.07 – 7.02 (m, 4H), 4.09 (dd, *J* = 10.3, 2.8 Hz, 1H), 2.77 – 2.70 (m, 1H), 2.57 (dt, *J* = 14.6, 7.9 Hz, 1H), 1.84 (dtd, *J* = 14.8, 10.0, 4.9 Hz, 1H), 1.68 – 1.62 (m, 1H), 1.32 (s, 3H), 1.18 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.27, 153.90 (dd, *J* = 289.9, 288.4 Hz), 147.67, 147.08, 129.78, 129.70, 129.45, 129.00 (t, *J* = 3.6 Hz), 128.73, 127.51, 126.83 (t, *J* = 3.8 Hz), 124.75, 123.27, 123.23, 91.57 (dd, *J* = 20.9, 13.6 Hz), 90.12, 51.13, 26.78, 25.02, 24.31, 19.66. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -90.58 – -90.71 (m), -90.78 (d, *J* = 43.2 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{33}H_{30}ON_2F_2Na$: 531.22184; found: 531.22064.



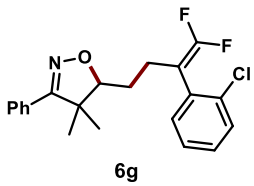
6e

5-(4,4-difluoro-3-(4-methoxyphenyl)but-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6e**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5e** (40.4 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 25:1 pentane: EtOAc) in 64% yield (48.1 mg, 48 h). **IR** (neat): 3454, 3059, 2967, 1728, 1609, 1513, 1462, 1290, 1239, 1181, 1104, 1032, 941, 911, 832, 765, 693 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 7.59 (m, 2H), 7.40 (dt, *J* = 5.4, 2.8 Hz, 3H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.08 (dd, *J* = 10.4, 2.6 Hz, 1H), 3.82 (s, 3H), 2.80 – 2.69 (m, 1H), 2.63 – 2.52 (m, 1H), 1.85 – 1.73 (m, 1H), 1.65 – 1.54 (m, 1H), 1.30 (s, 3H), 1.15 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.22, δ 156.92 – 150.58 (m), 156.57, 153.72, 150.84, 129.75, 129.67, 129.49 (t, *J* = 3.4 Hz), 128.69, 127.47, 114.16, 91.61 – 91.17 (m), 90.07, 55.38, 51.08, 26.53, 25.14, 24.23, 19.60. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -91.49 (d, *J* = 44.6 Hz), -91.76 (d, *J* = 44.6 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{24}O_2NF_2$: 372.17696; found: 372.17624.



6f

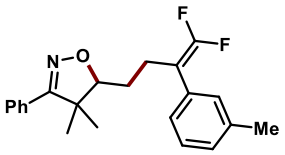
5-(4,4-difluoro-3-(4-fluorophenyl)but-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6f**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5f** (38.0 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 50:1 hexane: EtOAc) in 68% yield (48.7 mg). **IR** (neat): 3451, 3061, 2970, 2871, 2326, 1730, 1602, 1510, 1463, 1235, 1158, 1094, 943, 909, 837, 765, 693 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.59 (m, 2H), 7.44 – 7.36 (m, 3H), 7.36 – 7.30 (m, 2H), 7.07 (td, *J* = 8.6, 1.7 Hz, 2H), 4.07 (dd, *J* = 10.5, 2.5 Hz, 1H), 2.81 – 2.69 (m, 1H), 2.65 – 2.53 (m, 1H), 1.85 – 1.70 (m, 1H), 1.63 – 1.53 (m, 1H), 1.30 (s, 3H), 1.14 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.23, 162.06 (d, *J* = 247.0 Hz), 153.84 (t, *J* = 289.2 Hz), 130.08 (dt, *J* = 7.8, 3.5 Hz), 129.80, 129.60, 129.24 (q, *J* = 3.6 Hz), 128.72, 127.47, 115.72 (d, *J* = 21.4 Hz), 91.20 (dd, *J* = 22.2, 13.6 Hz), 89.98, 51.13, 26.51, 25.24, 24.26, 19.59. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -90.52 (d, *J* = 42.1 Hz), -90.90 (d, *J* = 42.2 Hz), -114.47. **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{21}ONF_3$: 360.15698; found: 360.15695.



6g

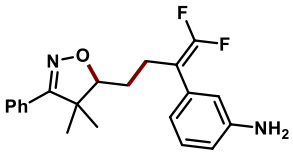
5-(3-(2-chlorophenyl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6g**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5g** (41.3 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 65% yield (48.7 mg). **IR** (neat): 3483, 3061, 2968, 2868, 1743, 1467, 1440, 1315, 1238, 1118, 1040, 945, 888, 760, 693 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 2H), 7.47 – 7.43 (m, 1H), 7.43 – 7.37 (m, 3H), 7.31 – 7.25 (m, 3H), 4.10 (dd, *J* = 10.4, 2.8 Hz, 1H), 2.76 – 2.69 (m, 1H), 2.65 – 2.57 (m, 1H), 1.82 –

1.73 (m, 1H), 1.60 – 1.53 (m, 1H), 1.32 (s, 3H), 1.16 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.21, 153.42 (t, *J* = 289.2 Hz), 134.42, 132.46 (dd, *J* = 5.6, 1.7 Hz) , 131.58 (t, *J* = 1.9 Hz), 129.96, 129.74, 129.62, 129.49, 128.68, 127.46, 127.02, 89.90, 89.81 (dd, *J* = 24.4, 17.1 Hz), 51.09, 26.07 (t, *J* = 2.7 Hz), 25.75, 24.30, 19.59. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -87.21 (d, *J* = 38.8 Hz), -92.25 (dt, *J* = 39.0, 2.5 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{21}ONClF_2$: 376.12742; found: 376.12729.



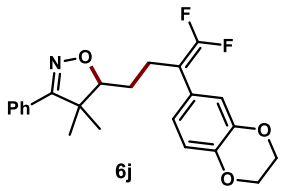
6h

5-(4,4-difluoro-3-(m-tolyl)but-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6h**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5h** (37.2 mg, 0.2 mmol), the title compound was isolated as brown solid after flash chromatography on silica gel (eluent: 10:1 hexane: EtOAc) in 72% yield (51.4 mg). **IR** (neat): 3451, 3054, 2968, 1730, 1604, 1491, 1461, 1054, 1371, 1327, 1240, 1206, 1119, 1003, 962, 891, 786, 765, 695 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 2H), 7.43 – 7.37 (m, 3H), 7.29 – 7.25 (m, 1H), 7.18 – 7.13 (m, 2H), 7.11 (d, *J* = 7.1 Hz, 1H), 4.09 (dd, *J* = 10.4, 2.7 Hz, 1H), 2.81 – 2.73 (m, 1H), 2.63 – 2.56 (m, 1H), 2.38 (s, 3H), 1.84 – 1.76 (m, 1H), 1.62 – 1.56 (m, 1H), 1.30 (s, 3H), 1.15 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.23, 153.80 (dd, *J* = 290.2, 287.6 Hz), 138.29, 133.25 (t, *J* = 3.0 Hz), 129.75, 129.65, 129.08 (t, *J* = 3.1 Hz), 128.69, 128.56, 128.33, 127.46, 125.45 (t, *J* = 3.0 Hz), 91.97 (dd, *J* = 20.4, 14.5 Hz), 90.05, 51.06, 26.55 (t, *J* = 2.3 Hz), 25.14, 24.20, 21.60, 19.60. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -90.77 (dt, *J* = 42.6, 2.9 Hz), -90.89 (d, *J* = 44.7 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{24}ONF_2$: 356.18205; found: 356.18158.



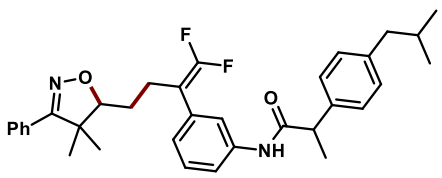
6i

3-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1-difluorobut-1-en-2-yl)aniline (**6i**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5i** (37.4 mg, 0.2 mmol), the title compound was isolated as light brown oil after flash chromatography on silica gel (eluent: 10:1 pentane: EtOH) in 73% yield (52.1 mg). **IR** (neat): 3460, 3369, 3057, 2969, 2872, 1730, 1607, 1494, 1454, 1330, 1259, 1220, 1151, 1116, 988, 894, 767, 694 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 2H), 7.42 – 7.37 (m, 3H), 7.15 (t, *J* = 7.8 Hz, 1H), 6.74 (dq, *J* = 7.7, 1.3 Hz, 1H), 6.68 (dt, *J* = 2.7, 1.5 Hz, 1H), 6.61 (ddd, *J* = 8.1, 2.4, 0.9 Hz, 1H), 4.07 (dd, *J* = 10.4, 2.7 Hz, 1H), 3.70 (s, 2H), 2.77 – 2.69 (m, 1H), 2.59 – 2.51 (m, 1H), 1.83 – 1.75 (m, 1H), 1.63 – 1.56 (m, 1H), 1.30 (s, 3H), 1.15 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.24, 153.74 (dd, *J* = 291.0, 287.3 Hz), 146.66, 134.32 (t, *J* = 3.8 Hz), 129.73, 129.64, 129.54, 128.67, 127.45, 118.64 (t, *J* = 3.3 Hz), 115.00 (t, *J* = 3.4 Hz),, 114.37, 92.00 (dd, *J* = 21.4, 13.6 Hz), 90.08, 51.06, 26.54 (t, *J* = 2.6 Hz), 25.06, 24.20, 19.58, 19.52. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -90.36 (d, *J* = 42.2 Hz), -90.70 (dt, *J* = 42.4, 2.7 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{23}ON_2F_2$: 357.17730; found: 357.17679.



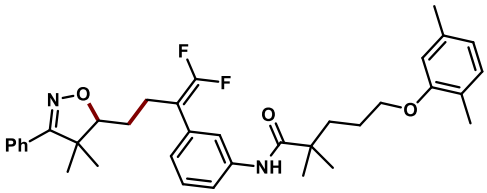
6j

5-(3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6j**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5j** (46.0 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 72% yield (57.8 mg). **IR** (neat): 3059, 2971, 2876, 1727, 1582, 1507, 1461, 1318, 1282, 1250, 1113, 1066, 975, 891, 815, 764, 694 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 2H), 7.42 – 7.35 (m, 3H), 6.88 – 6.85 (m, 2H), 6.83 (dd, *J* = 8.5, 2.1 Hz, 1H), 4.26 (s, 4H), 4.07 (dd, *J* = 10.4, 2.7 Hz, 1H), 2.75 – 2.66 (m, 1H), 2.57 – 2.49 (m, 1H), 1.83 – 1.75 (m, 1H), 1.63 – 1.55 (m, 1H), 1.30 (s, 3H), 1.15 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.20, 153.73 (t, *J* = 288.8 Hz), 143.27 (d, *J* = 83.1 Hz), 129.73, 129.65, 128.67, 127.45, 126.41, 121.48 (t, *J* = 3.3 Hz), 117.25 (t, *J* = 3.5 Hz), 91.36 (t, *J* = 18.1 Hz), 90.04, 64.50, 64.44, 51.05, 26.53, 25.11, 24.21, 19.60. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -91.09. **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{23}H_{24}O_3NF_2$: 400.17188; found: 400.17129.



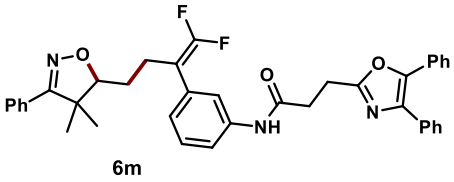
6k

N-(3-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1-difluorobut-1-en-2-yl)phenyl)-2-(4-isobutylphenyl)propanamide (**6k**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5k** (75.0 mg, 0.2 mmol), the title compound was isolated as light brown oil after flash chromatography on silica gel (eluent: 10:1–5:1 hexane: EtOAc) in 83% yield (90.2 mg). **IR** (neat): 3309, 3059, 2961, 2870, 1731, 1667, 1608, 1590, 1546, 1488, 1431, 1328, 1247, 1166, 1119, 1081, 997, 906, 791, 765, 730, 695 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.55 (m, 2H), 7.49 – 7.35 (m, 5H), 7.33 (s, 1H), 7.28 (d, *J* = 7.8 Hz, 3H), 7.15 (d, *J* = 7.7 Hz, 2H), 7.05 (d, *J* = 7.7 Hz, 1H), 4.07 (dd, *J* = 10.3, 2.6 Hz, 1H), 3.71 (q, *J* = 7.2 Hz, 1H), 2.78 – 2.66 (m, 1H), 2.62 – 2.50 (m, 1H), 2.47 (d, *J* = 7.2 Hz, 2H), 1.92 – 1.82 (m, 1H), 1.82 – 1.69 (m, 1H), 1.63 – 1.49 (m, 4H), 1.29 (s, 3H), 1.13 (s, 3H), 0.91 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.87, 165.32, 153.80 (t, *J* = 290.8 Hz), 141.16, 138.40, 138.13 (d, *J* = 2.8 Hz), 134.06 (d, *J* = 3.4 Hz), 129.93, 129.76, 129.57, 129.18, 128.68, 127.50, 127.45, 124.15, 119.59, 118.93, 91.72 (dd, *J* = 21.1, 14.3 Hz), 90.00, 51.11, 47.81, 45.12, 30.26, 26.45, 25.02, 24.18, 22.47, 19.54, 18.65. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -90.06 (dd, *J* = 41.0, 10.5 Hz), -90.20 (dd, *J* = 41.0, 17.0 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{34}H_{39}O_2N_2F_2$: 545.29741; found: 545.29558.



6l

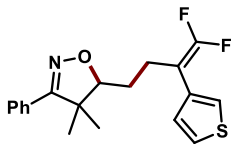
N-(3-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1-difluorobut-1-en-2-yl)phenyl)-5-(2,5-dimethylphenoxy)-2,2-dimethylpentanamide (**6l**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5l** (83.8 mg, 0.2 mmol), the title compound was isolated as light brown oil after flash chromatography on silica gel (eluent: 10:1–5:1 hexane: EtOAc) in 74% yield (86.9 mg). **IR** (neat): 3349, 3054, 2962, 2870, 1731, 1666, 1608, 1588, 1533, 1483, 1425, 1249, 1154, 1127, 1043, 996, 906, 796, 765, 731, 695 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 – 7.59 (m, 2H), 7.53 – 7.50 (m, 2H), 7.47 (s, 1H), 7.42 – 7.36 (m, 3H), 7.33 (dd, *J* = 8.8, 7.7 Hz, 1H), 7.10 (dq, *J* = 7.8, 1.3 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.6 Hz, 1H), 6.61 (s, 1H), 4.09 (dd, *J* = 10.5, 2.7 Hz, 1H), 3.96 – 3.92 (m, 2H), 2.80 – 2.72 (m, 1H), 2.64 – 2.56 (m, 1H), 2.29 (s, 3H), 2.17 (s, 3H), 1.86 – 1.80 (m, 4H), 1.80 – 1.74 (m, 1H), 1.63 – 1.57 (m, 1H), 1.35 (s, 6H), 1.30 (s, 3H), 1.14 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.96, 165.30, 156.95, δ 153.84 (dd, *J* = 291.2, 287.9 Hz), 138.33, 136.63, 134.12 (t, *J* = 3.6 Hz), 130.43, 129.74, 129.58, 129.26, 128.67, 127.44, 124.29 (t, *J* = 3.3 Hz), 123.59, 120.96, 120.05 (t, *J* = 3.7 Hz), 119.40, 112.26, 91.75 (dd, *J* = 21.7, 13.6 Hz), 90.01, 67.97, 51.12, 42.97, 37.76, 26.5126.50 (t, *J* = 2.3 Hz), 25.73, 25.69, 25.26, 25.00, 24.23, 21.48, 19.55, 15.93. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -89.99 (d, *J* = 41.3 Hz), -90.16 (dt, *J* = 40.9, 2.7 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{36}H_{43}O_3N_2F_2$: 589.32363; found: 589.32217.



6m

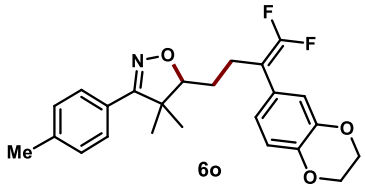
N-(3-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1-difluorobut-1-en-2-yl)phenyl)-3-(4,5-diphenyloxazol-2-yl)propanamide (**6m**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5m** (92.4 mg, 0.2 mmol), the title compound was isolated as light yellow oil after flash chromatography on silica gel (eluent: 8:1–4:1 hexane: EtOAc) in 54% yield (68.1 mg). **IR** (neat): 3341, 3061, 2968, 1729, 1686, 1589, 1550, 1490, 1436, 1327, 1246, 1154, 964, 906, 764, 693 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.63 (dt, *J* = 6.0, 1.6 Hz, 2H), 7.60 – 7.57 (m, 2H), 7.56 – 7.53 (m, 3H), 7.38 – 7.31 (m, 10H), 7.29 – 7.25 (m, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 4.01 (dd, *J* = 10.4, 2.7 Hz, 1H), 3.26 (t, *J* = 6.8 Hz, 2H), 2.95 (t, *J* = 6.9 Hz, 2H), 2.66 (dddt, *J* = 14.8, 10.1, 5.1, 2.7 Hz, 1H), 2.55 – 2.46 (m, 1H), 1.71 (dtd, *J* = 14.6, 9.9, 4.9 Hz, 1H), 1.52 (dddd, *J* = 13.9, 9.7, 6.7, 2.7 Hz, 1H), 1.24 (s, 3H), 1.09 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.08, 165.28, 162.65, 153.80 (dd, *J* = 289.9, 288.4 Hz), 145.87, 138.60, 134.86, 134.09, 132.28, 129.75, 129.61, 129.33, 128.82, 128.79, 128.75, 128.70, 128.69, 128.46, 127.98, 127.46, 126.61, 124.06 (d, *J* = 4.0 Hz), 119.56 (d, *J* = 3.6 Hz), 118.96, 91.71 (dd, *J* = 21.4, 13.9 Hz), 89.95, 51.10, 34.24, 26.41, 24.99, 24.18, 24.16, 19.57. **^{19}F NMR** (565 MHz,

$CDCl_3$) δ -90.14 (d, *J* = 41.2 Hz), -90.30 (d, *J* = 41.1 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{39}H_{36}O_3N_3F_2$: 632.27192; found: 632.27105.



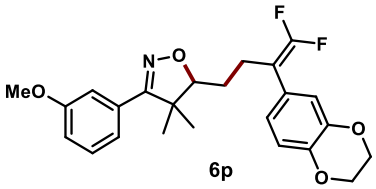
6n

5-(4,4-difluoro-3-(thiophen-3-yl)but-3-en-1-yl)-4,4-dimethyl-3-phenyl-4,5-dihydroisoxazole (**6n**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5n** (35.6 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 60:1-30:1 hexane: EtOAc) in 54% yield (37.3 mg). **IR** (neat): 3452, 3107, 2970, 2873, 1722, 1462, 1372, 1227, 1114, 997, 970, 893, 855, 766, 692 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.65 – 7.62 (m, 2H), 7.42 – 7.38 (m, 3H), 7.35 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.31 (dd, *J* = 3.0, 1.4 Hz, 1H), 7.23 (ddd, *J* = 5.1, 2.3, 1.3 Hz, 1H), 4.11 (dd, *J* = 10.7, 2.5 Hz, 1H), 2.81 – 2.74 (m, 1H), 2.63 – 2.56 (m, 1H), 1.93 – 1.85 (m, 1H), 1.72 – 1.66 (m, 1H), 1.33 (s, 3H), 1.18 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.31, 154.23 (dd, *J* = 293.9, 287.2 Hz), 133.46 (t, *J* = 4.5 Hz), 129.82, 129.55, 128.72, 127.48, 127.01 (dd, *J* = 6.7, 2.5 Hz), 125.91, 122.14 (t, *J* = 5.5 Hz), 90.09, 88.38 (dd, *J* = 23.7, 12.2 Hz), 51.15, 27.14, 27.12, 27.10, 24.69, 24.29, 19.61. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -86.71 (dt, *J* = 39.8, 2.8 Hz), -91.09 (dt, *J* = 40.1, 2.9 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{20}ONF_2S$: 348.12282; found: 348.12219.

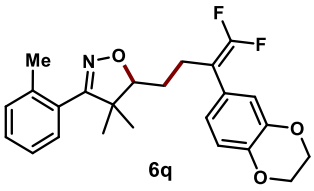


6o

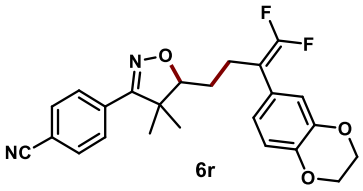
5-(3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-(p-tolyl)-4,5-dihydroisoxazole (**6o**): According to the general procedure, starting from **1b** (81.2 mg, 0.40 mmol) and **5j** (46.0 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 20:1–10:1 hexane: EtOAc) in 71% yield (58.8 mg). **IR** (neat): 2969, 2876, 1728, 1584, 1507, 1461, 1425, 1322, 1283, 1247, 1173, 1113, 1064, 892, 816, 786, 732, 698 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 1H), 7.21 – 7.17 (m, 2H), 6.96 – 6.92 (m, 1H), 6.88 – 6.84 (m, 2H), 6.82 (dd, *J* = 8.5, 2.1 Hz, 1H), 4.26 (s, 4H), 4.06 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.82 (s, 3H), 2.74 – 2.66 (m, 1H), 2.57 – 2.49 (m, 1H), 1.82 – 1.73 (m, 1H), 1.61 – 1.55 (m, 1H), 1.30 (s, 3H), 1.15 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.09, 159.69, 153.75 (t, *J* = 288.6 Hz), 143.56, 143.01, 130.89, 129.66, 126.43, 121.50 (t, *J* = 3.6 Hz), 119.70, 117.45, 117.26 (t, *J* = 3.6 Hz), 115.70, 112.85, 91.36 (dd, *J* = 36.2, 15.1 Hz), 90.15, 64.52, 64.46, 55.44, 51.05, 26.52, 25.11, 24.29, 19.67. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -65.74. **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{26}O_3NF_2$: 414.18753; found: 414.18644.



5-(3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4,4-difluorobut-3-en-1-yl)-3-(3-methoxyphenyl)-4,4-dimethyl-4,5-dihydroisoxazole (**6p**): According to the general procedure, starting from **1p** (87.6 mg, 0.40 mmol) and **5j** (46.0 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 62% yield (53.4 mg). **IR** (neat): 2970, 2931, 2875, 1728, 1582, 1508, 1460, 1424, 1318, 1282, 1251, 1113, 1066, 976, 891, 816, 728 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.55 – 7.49 (m, 2H), 7.22 – 7.17 (m, 2H), 6.87 – 6.81 (m, 3H), 4.26 (s, 4H), 4.05 (dd, *J* = 10.4, 2.8 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.56 – 2.50 (m, 1H), 2.37 (s, 3H), 1.81 – 1.73 (m, 1H), 1.61 – 1.54 (m, 1H), 1.29 (s, 3H), 1.14 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.12, δ 153.72 (t, *J* = 288.6 Hz), 143.55, 142.99, 139.86, 129.39, 127.33, 126.71, 126.43, 121.48 (t, *J* = 3.3 Hz), 117.43, 117.25 (t, *J* = 3.6 Hz), 91.39 (t, *J* = 17.7 Hz), 89.92, 64.50, 64.44, 64.42, 51.01, 26.53 (t, *J* = 2.5 Hz), 25.12, 24.24, 21.44, 19.62. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -91.12 (t, *J* = 2.4 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{26}O_4NF_2$: 430.18244; found: 430.18313.

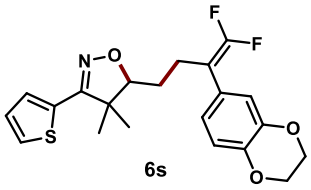


5-(3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-(o-tolyl)-4,5-dihydroisoxazole (**6q**): According to the general procedure, starting from **1q** (81.2 mg, 0.40 mmol) and **5j** (46.0 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 20:1–10:1 hexane: EtOAc) in 58% yield (48.1 mg). **IR** (neat): 2970, 2932, 2875, 1728, 1582, 1508, 1461, 1424, 1319, 1282, 1251, 1112, 1066, 977, 893, 816, 789, 732, 700 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 1H), 7.41 – 7.37 (m, 1H), 7.30 – 7.25 (m, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.88 – 6.81 (m, 3H), 4.26 (s, 4H), 4.05 (dd, *J* = 10.4, 2.8 Hz, 1H), 2.74 – 2.66 (m, 1H), 2.57 – 2.50 (m, 1H), 2.37 (s, 3H), 1.82 – 1.74 (m, 1H), 1.62 – 1.54 (m, 1H), 1.29 (s, 3H), 1.15 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.38, δ 153.73 (t, *J* = 288.7 Hz), 143.55, 143.00, 138.41, 130.52, 129.54, 128.51, 128.23, 126.44, 124.43, 121.49 (t, *J* = 3.4 Hz), 117.44, 117.26 (t, *J* = 3.6 Hz), 91.38 (t, *J* = 17.8 Hz), 90.00, 64.51, 64.45, 51.09, 26.56 (t, *J* = 2.5 Hz), 25.12, 24.27, 21.55, 19.63. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -91.12. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{24}H_{26}O_3NF_2$: 414.18753; found: 414.18653.



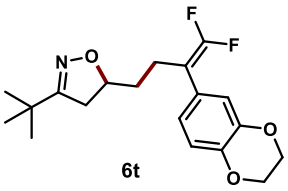
4-(5-(3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-4,5-dihydroisoxazol-3-yl)benzonitrile (**6r**): According to the general procedure, starting from **1f** (85.6 mg, 0.40 mmol) and **5j** (46.0 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 10:1 – 6:1 pentane: EtOAc) in 34% yield (28.5 mg). **IR** (neat): 3062,

2972, 2877, 2229, 1727, 1609, 1581, 1508, 1462, 1423, 1282, 1251, 1113, 1066, 972, 892, 841, 731 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.77 – 7.75 (m, 2H), 7.69 – 7.66 (m, 2H), 6.87 – 6.84 (m, 2H), 6.82 – 6.80 (m, 1H), 4.26 (s, 4H), 4.10 (dd, *J* = 10.5, 2.7 Hz, 1H), 2.73 – 2.66 (m, 1H), 2.57 – 2.50 (m, 1H), 1.82 – 1.74 (m, 1H), 1.62 – 1.56 (m, 1H), 1.31 (s, 3H), 1.16 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.67, 153.76 (t, *J* = 288.4 Hz), 143.58, 143.05, 134.22, 132.46, 127.82, 126.26, 121.46 (t, *J* = 3.3 Hz), 118.47, 117.49, 117.22 (t, *J* = 3.3 Hz), 113.28, 91.17 (dd, *J* = 36.2, 15.1 Hz), 90.81, 64.51, 64.46, 50.64, 26.34, 25.01, 24.15, 19.63. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -90.87 (dd, *J* = 43.3, 2.7 Hz), -91.00 (dt, *J* = 43.0, 2.8 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{24}H_{22}O_3N_2F_2Na$: 447.14907; found: 447.14850.



6s

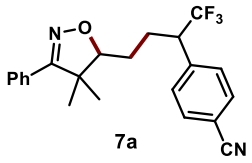
5-(3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4,4-difluorobut-3-en-1-yl)-4,4-dimethyl-3-(thiophen-2-yl)-4,5-dihydroisoxazole (**6s**): According to the general procedure, starting from **1o** (78.0 mg, 0.40 mmol) and **5j** (46.0 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 20:1–10:1 hexane: EtOAc) in 33% yield (26.9 mg). **IR** (neat): 3105, 2971, 2934, 2875, 1730, 1581, 1508, 1460, 1426, 1317, 1281, 1250, 1114, 1064, 977, 892, 846, 710, 658 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 – 7.35 (m, 2H), 7.07 – 7.04 (m, 1H), 6.87 – 6.83 (m, 2H), 6.81 (dd, *J* = 8.4, 2.2 Hz, 1H), 4.26 (s, 4H), 4.08 (dd, *J* = 10.4, 2.8 Hz, 1H), 2.72 – 2.65 (m, 1H), 2.56 – 2.48 (m, 1H), 1.81 – 1.72 (m, 1H), 1.61 – 1.55 (m, 1H), 1.37 (s, 3H), 1.17 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.75, δ 153.75 (t, *J* = 288.8 Hz), 143.57, 143.02, 131.38, 127.67, 127.47, 126.80, 126.40, 121.50 (t, *J* = 3.5 Hz), 117.46, 117.25 (t, *J* = 3.4 Hz), 91.46 – 91.12 (m), 90.23, 64.52, 64.46, 51.08, 26.55, 25.10, 24.48, 19.71. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -91.06 (q, *J* = 2.8 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{22}O_3NF_2S$: 406.12830; found: 406.12703.



6t

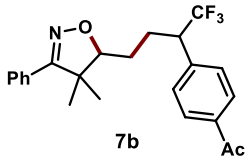
3-(tert-butyl)-5-(3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4,4-difluorobut-3-en-1-yl)-4,5-dihydroisoxazole (**6t**): According to the general procedure, starting from **1r** (56.4 mg, 0.40 mmol) and **5j** (46.0 mg, 0.2 mmol), the title compound was isolated as colorless oil after flash chromatography on silica gel (eluent: 20:1–10:1 hexane: EtOAc) in 54% yield (38.1 mg). **IR** (neat): 2965, 2875, 1727, 1582, 1508, 1459, 1317, 1282, 1250, 1112, 1066, 977, 927, 883, 813, 748 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.85 – 6.80 (m, 2H), 6.80 – 6.76 (m, 1H), 4.48 (dtd, *J* = 10.1, 7.6, 5.3 Hz, 1H), 4.25 (s, 4H), 2.98 (dd, *J* = 16.6, 10.1 Hz, 1H), 2.53 (dd, *J* = 16.6, 7.8 Hz, 1H), 2.51 – 2.39 (m, 2H), 1.72 (dddd, *J* = 13.5, 9.5, 7.5, 5.9 Hz, 1H), 1.56 (ddt, *J* = 13.7, 9.6, 5.8 Hz, 1H), 1.17 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 165.94, 155.59 – 151.58 (m), 143.52, 142.99, 126.41, 121.44 (t, *J* = 3.4 Hz), 117.42, 117.23 (t, *J* = 3.4 Hz), 91.36 – 90.99 (m), 79.51, 64.51, 64.45, 39.38,

33.34, 33.09, 28.17, 24.03. **^{19}F NMR** (564 MHz, Chloroform-*d*) δ -91.29 (d, *J* = 43.9 Hz), -91.49 (d, *J* = 43.7 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{19}H_{24}O_3NF_2$: 352.17188; found: 352.17076.



7a

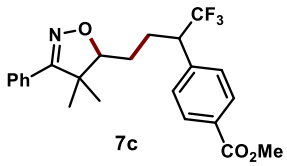
4-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1,1-trifluorobutan-2-yl)benzonitrile (**7a**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5o** (39.4 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 10:1-8:1 pentane: EtOAc) in 70% yield (54.3 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3069, 2964, 2926, 2856, 2229, 1611, 1499, 1463, 1372, 1331, 1255, 1161, 1116, 909, 831, 772, 695 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.69 (d, *J* = 1.9 Hz, 2H), 7.68 (d, *J* = 1.8 Hz, 2H), 7.61 – 7.57 (m, 4H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.43 – 7.35 (m, 6H), 4.07 – 4.02 (m, 2H), 3.63 (dddd, *J* = 13.1, 11.1, 9.0, 4.1 Hz, 1H), 3.43 (ddt, *J* = 17.4, 9.0, 5.1 Hz, 1H), 2.40 (dddd, *J* = 13.9, 8.8, 7.2, 4.1 Hz, 1H), 2.32 – 2.20 (m, 2H), 2.06 (dddd, *J* = 13.8, 11.2, 8.3, 5.4 Hz, 1H), 1.58 – 1.50 (m, 2H), 1.50 – 1.46 (m, 1H), 1.46 – 1.40 (m, 1H), 1.30 (s, 3H), 1.29 (s, 3H), 1.10 (s, 3H), 1.08 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 165.32, 165.28, 140.02, 139.78, 132.71, 132.65, 130.19, 130.01, 129.93, 129.90, 129.29, 129.27, 128.75, 128.73, 127.41, 127.38, 118.47, 118.41, 112.65, 112.52, 90.99, 89.68, 51.41, 51.16, 50.29, 50.11, 49.95, 49.93, 49.77, 49.75, 49.59, 26.77, 25.83, 25.46, 24.84, 24.23, 24.04, 19.48, 19.45. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.33, -69.35 (d, *J* = 4.0 Hz), -69.37. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{22}H_{21}ON_2F_3Na$: 409.14982; found: 409.14913.



7b

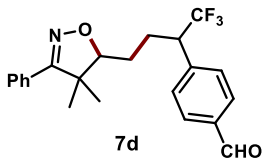
1-(4-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1,1-trifluorobutan-2-yl)phenyl)ethan-1-one (**7b**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5p** (42.8 mg, 0.20 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 12:1 – 10:1 hexane: EtOAc) in 78% yield (62.8 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3061, 2968, 2875, 1685, 1609, 1463, 1422, 1362, 1332, 1260, 1158, 1112, 957, 905, 829, 766, 690 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 7.99 – 7.94 (m, 2H), 7.62 – 7.56 (m, 2H), 7.45 (dd, *J* = 15.8, 8.2 Hz, 2H), 7.41 – 7.34 (m, 3H), 4.08 – 4.01 (m, 1H), 3.62 – 3.52 (m, 0.5H), 3.47 – 3.38 (m, 0.5H), 2.60 (d, *J* = 1.0 Hz, 3H), 2.45 – 2.37 (m, 0.5H), 2.35 – 2.19 (m, 1H), 2.10 – 2.02 (m, 0.5H), 1.61 – 1.51 (m, 1H), 1.49 – 1.37 (m, 1H), 1.28 (d, *J* = 8.4 Hz, 3H), 1.08 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (mixture of diastereomers, both isomers quoted) (151 MHz, $CDCl_3$) δ 197.73, 197.68, 165.29, 165.26, 139.88, 139.62, 137.19, 137.14, 129.86, 129.84, 129.58, 129.46, 129.38, 129.37, 128.89, 128.84, 128.71, 128.71, 127.52 (d, *J* = 5.1 Hz), 127.41, 127.39, 125.67 (d, *J* = 5.2 Hz), 90.97, 89.71, 51.30, 51.10, 50.09 (dd, *J* = 26.8, 3.0 Hz), 49.74 (dd, *J*

= 26.8, 3.0 Hz), 26.73, 26.69, 25.82, 25.40, 25.08, 24.20, 24.06, 19.48, 19.46. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.37 (dd, *J* = 14.1, 9.1 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{23}H_{24}O_2NF_3Na$: 426.16513; found: 426.16418.



7c

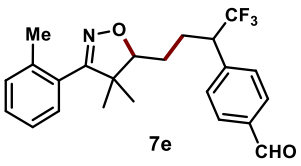
4-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1,1-trifluorobutan-2-yl)benzoate (**7c**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5q** (46.0 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 15:1 pentane: EtOAc) in 71% yield (59.6 mg, 1:1.2 d.r., inseparable mixture). **IR** (neat): 2960, 2877, 1722, 1613, 1461, 1437, 1278, 1158, 1110, 1018, 905, 849, 766, 694 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 8.05 (d, *J* = 7.9 Hz, 2H), 7.59 (tt, *J* = 6.3, 1.8 Hz, 2H), 7.47 – 7.33 (m, 5H), 4.08 – 4.00 (m, 1H), 3.92 (s, 3H), 3.60 – 3.51 (m, 0.5H), 3.47 – 3.38 (m, 0.5H), 2.45 – 2.38 (m, 0.5H), 2.34 – 2.19 (m, 1H), 2.10 – 2.02 (m, 0.5H), 1.61 – 1.51 (m, 1H), 1.48 – 1.36 (m, 1H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 166.77, 166.73, 165.29, 165.27, 139.72, 139.45, 130.41, 130.34, 130.17, 130.12, 129.86, 129.84, 129.41, 129.38, 129.27, 128.72, 128.71, 127.56 (d, *J* = 3.3 Hz), 127.43, 127.41, 125.70 (d, *J* = 3.2 Hz), 90.97, 89.67, 52.32, 51.29, 51.11, 50.14 (dd, *J* = 26.9, 13.1 Hz), 49.78 (dd, *J* = 26.8, 13.2 Hz), 26.71, 25.80, 25.36, 25.12, 24.19, 24.08, 19.48, 19.46. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.41 (t, *J* = 9.4 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{23}H_{24}O_3NF_3Na$: 442.16005; found: 442.15930.



7d

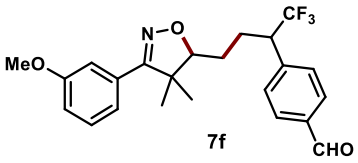
4-(4-(4,4-dimethyl-3-phenyl-4,5-dihydroisoxazol-5-yl)-1,1,1-trifluorobutan-2-yl)benzaldehyde (**7d**): According to the general procedure, starting from **1a** (75.6 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 66% yield (51.4 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3067, 2924, 2853, 1700, 1607, 1462, 1374, 1333, 1260, 1162, 1110, 912, 827, 771, 726, 694 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.05 – 10.01 (m, 2H), 7.91 (s, 2H), 7.90 (s, 2H), 7.62 – 7.57 (m, 4H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.43 – 7.34 (m, 6H), 4.07 (dd, *J* = 10.5, 2.7 Hz, 1H), 4.04 (dd, *J* = 10.4, 2.6 Hz, 1H), 3.67 – 3.58 (m, 1H), 3.50 – 3.42 (m, 1H), 2.43 (dddd, *J* = 13.6, 9.2, 6.7, 4.1 Hz, 1H), 2.36 – 2.28 (m, 1H), 2.25 (dddd, *J* = 13.9, 10.0, 6.3, 4.9 Hz, 1H), 2.09 (dddd, *J* = 14.0, 11.2, 8.8, 5.3 Hz, 1H), 1.61 – 1.56 (m, 1H), 1.56 – 1.51 (m, 1H), 1.51 – 1.45 (m, 1H), 1.42 (dddd, *J* = 12.1, 9.5, 5.2, 2.6 Hz, 1H), 1.29 (s, 3H), 1.28 (s, 3H), 1.09 (s, 3H), 1.08 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.83, 191.78, 165.31, 165.28, 141.42, 141.16, 136.45, 136.39, 130.23, 130.18, 130.06, 129.93,

129.90, 129.88, 129.36, 128.74, 128.73, 127.42, 127.40, 90.98, 89.71, 51.35, 51.14, 50.26 (dd, *J* = 26.9, 5.1 Hz), 49.91 (dd, *J* = 26.9, 5.2 Hz), 26.78, 25.90, 25.45, 25.03, 24.22, 24.07, 19.49, 19.47. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.24, -69.25, -69.27. **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}O_2NF_3$: 390.16754; found: 390.16802.



7e

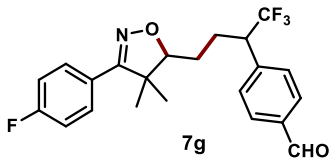
4-(4-(4,4-dimethyl-3-(o-tolyl)-4,5-dihydroisoxazol-5-yl)-1,1,1-trifluorobutan-2-yl)benzaldehyde (**7e**): According to the general procedure, starting from **1q** (81.2 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 20:1–10:1 hexane: EtOAc) in 71% yield (57.4 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3040, 2964, 2927, 2855, 1703, 1608, 1463, 1373, 1329, 1256, 1211, 1161, 1113, 1040, 912, 820, 792, 726, 700 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.04 (d, *J* = 1.4 Hz, 1H), 7.94 – 7.89 (m, 2H), 7.54 (dd, *J* = 17.8, 8.0 Hz, 2H), 7.42 (d, *J* = 9.1 Hz, 1H), 7.37 (dd, *J* = 7.7, 6.0 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.24 – 7.20 (m, 1H), 4.08 – 4.01 (m, 1H), 3.67 – 3.59 (m, 0.5 H), 3.52 – 3.41 (m, 0.5 H), 2.48 – 2.40 (m, 0.5 H), 2.37 (d, *J* = 4.3 Hz, 3H), 2.35 – 2.21 (m, 1H), 2.13 – 2.06 (m, 0.5 H), 1.61 – 1.51 (m, 1H), 1.51 – 1.39 (m, 1H), 1.29 (d, *J* = 8.0 Hz, 3H), 1.08 (d, *J* = 9.0 Hz, 3H). **^{13}C NMR** (mixture of diastereomers, both isomers quoted) (151 MHz, $CDCl_3$) δ 191.84, 191.79, 165.48, 165.45, 141.44, 141.17, 138.49, 138.48, 136.44, 136.38, 130.69, 130.67, 130.23, 130.17, 130.08, 129.94, 129.25, 129.23, 128.57, 128.56, 128.19, 128.17, 127.47 (d, *J* = 5.7 Hz), 125.61 (d, *J* = 5.9 Hz), 124.40, 124.38, 90.92, 89.65, 51.39, 51.18, 50.27 (dd, *J* = 26.9, 6.8 Hz), 49.92 (dd, *J* = 26.6, 6.9 Hz), 26.79, 25.93, 25.48, 25.04, 24.26, 24.12, 21.54, 19.51, 19.49. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.26 (dd, *J* = 9.0, 5.0 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{23}H_{24}O_2NF_3Na$: 426.16513; found: 426.16375.



7f

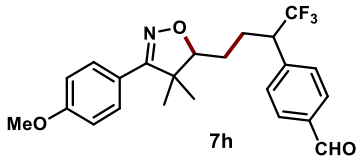
4-(1,1,1-trifluoro-4-(3-(3-methoxyphenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)butan-2-yl)benzaldehyde (**7f**): According to the general procedure, starting from **1p** (87.6 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as light brown oil after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 77% yield (64.8 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 2966, 2868, 1702, 1609, 1463, 1332, 1256, 1161, 1113, 910, 822, 729, 686 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.03 (d, *J* = 1.6 Hz, 1H), 7.90 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.47 (m, 4H), 7.19 (dd, *J* = 8.0, 4.8 Hz, 2H), 4.07 – 4.00 (m, 1H), 3.67 – 3.58 (m, 0.5 H), 3.50 – 3.41 (m, 0.5 H), 2.45 – 2.38 (m, 0.5 H), 2.36 (d, *J* = 3.2 Hz, 3H), 2.34 – 2.20 (m, 1H), 2.12 – 2.03 (m, 0.5 H), 1.60 – 1.50 (m, 1H), 1.50 – 1.38 (m, 1H), 1.28 (d, *J* = 7.9 Hz, 3H), 1.07 (d, *J* = 8.0 Hz, 3H). **^{13}C**

NMR (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.84, 191.79, 165.23, 165.20, 141.45, 141.18, 140.07, 140.04, 136.43, 136.36, 130.21, 130.16, 130.07, 129.93, 129.45, 129.43, 127.46 (d, *J* = 6.1 Hz), 127.30, 127.28, 126.41, 126.39, 125.61 (d, *J* = 6.1 Hz), 90.87, 89.56, 51.30, 51.09, 50.25 (dd, *J* = 27.1, 6.0 Hz), 49.89 (dd, *J* = 27.0, 6.2 Hz), 26.80, 25.90, 25.43, 25.00, 24.23, 24.08, 21.44, 19.50, 19.47. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.26 (t, *J* = 9.5 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{23}H_{25}O_3NF_3$: 420.17810; found: 420.17712.



7g

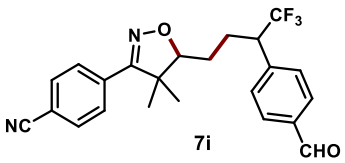
4-(1,1,1-trifluoro-4-(3-(4-fluorophenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)butan-2-yl)benzaldehyde (**7g**): According to the general procedure, starting from **1d** (82.8 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as light brown oil after flash chromatography on silica gel (eluent: 30:1 hexane: EtOAc) in 75% yield (60.7 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3068, 2968, 1702, 1605, 1510, 1464, 1329, 1256, 1159, 1113, 906, 834, 730, 686 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.03 (s, 2H), 7.90 (d, *J* = 8.2 Hz, 4H), 7.61 – 7.56 (m, 4H), 7.52 (dd, *J* = 16.5, 8.0 Hz, 4H), 7.10 – 7.04 (m, 4H), 4.06 (dd, *J* = 10.5, 2.7 Hz, 1H), 4.03 (dd, *J* = 10.4, 2.6 Hz, 1H), 3.65 – 3.56 (m, 1H), 3.50 – 3.40 (m, 1H), 2.42 (dddd, *J* = 13.7, 9.3, 6.7, 4.1 Hz, 1H), 2.35 – 2.20 (m, 2H), 2.08 (dddd, *J* = 14.0, 11.2, 8.9, 5.3 Hz, 1H), 1.60 – 1.51 (m, 2H), 1.50 – 1.39 (m, 2H), 1.28 (s, 3H), 1.26 (s, 3H), 1.07 (s, 3H), 1.06 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.82, 191.78, 164.55, 164.42, 164.39, 162.89, 141.38, 141.12, 136.46, 136.40, 130.23, 130.18, 130.05, 129.92, 129.39, 129.37, 129.34, 129.32, 127.46, 127.43, 125.61, 125.57, 125.50, 125.48, 115.98, 115.96, 115.83, 115.81, 91.02, 89.76, 51.22, 51.02, 50.34, 50.19, 50.16, 50.01, 49.98, 49.83, 49.80, 26.77, 25.91, 25.42, 25.02, 24.16, 24.03, 19.46, 19.43. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.27 (t, *J* = 8.6 Hz), -110.57 (dtt, *J* = 22.6, 8.5, 5.3 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{22}O_2NF_4$: 408.15812; found: 408.15706.



7h

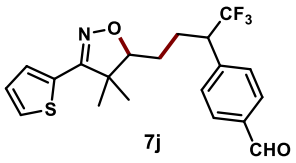
4-(1,1,1-trifluoro-4-(3-(4-methoxyphenyl)-4,4-dimethyl-4,5-dihydroisoxazol-5-yl)butan-2-yl)benzaldehyde (**7h**): According to the general procedure, starting from **1c** (87.6 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as light brown solid after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 75% yield (62.9 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 2964, 2843, 1703, 1608, 1513, 1462, 1332, 1303, 1250, 1165, 1112, 1035, 910, 833, 730, 685 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.03 (d, *J* = 1.7 Hz, 1H), 7.92 – 7.87 (m, 2H), 7.58 – 7.53 (m, 3H), 7.51 (d, *J* = 8.0 Hz, 1H), 6.92 – 6.88 (m, 2H), 4.05 – 3.98 (m, 1H), 3.81 (d, *J* = 2.9 Hz, 3H), 3.66 – 3.58 (m, 0.5H), 3.49 – 3.41 (m, 0.5H), 2.44 – 2.37 (m, 0.5H),

2.35 – 2.19 (m, 1H), 2.11 – 2.04 (m, 0.5H), 1.60 – 1.49 (m, 1H), 1.49 – 1.38 (m, 1H), 1.27 (d, *J* = 7.6 Hz, 3H), 1.07 (d, *J* = 7.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.84, 191.80, 164.85, 164.82, 160.90, 160.89, 141.46, 141.18, 136.43, 136.36, 130.21, 130.16, 130.07, 129.93, 128.80, 128.78, 127.47 (d, *J* = 6.4 Hz), 125.61 (d, *J* = 6.1 Hz), 121.65, 121.63, 114.18, 114.17, 90.80, 89.48, 55.41, 51.23, 51.02, 50.24 (dd, *J* = 27.0, 5.4 Hz), 49.89 (dd, *J* = 27.0, 5.4 Hz), 26.80, 25.89, 25.40, 24.97, 24.24, 24.10, 19.53, 19.50. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.26 (t, *J* = 9.5 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{23}H_{25}O_3NF_3$: 420.17810; found: 420.17745.



7i

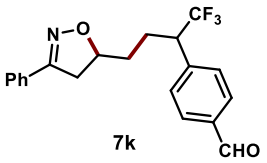
5-(4,4-dimethyl-3-(thiophen-2-yl)-4,5-dihydroisoxazol-5-yl)pentan-2-one (**7i**): According to the general procedure, starting from **1f** (75.6 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as light brown oil after flash chromatography on silica gel (eluent: 10:1 hexane: EtOAc) in 69% yield (57.5 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3405, 3065, 2969, 2875, 2229, 1701, 1609, 1578, 1464, 1332, 1257, 1208, 1160, 1112, 909, 835, 730, 687 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.03 (s, 1H), 7.90 (d, *J* = 7.9 Hz, 2H), 7.73 (dd, *J* = 8.5, 4.2 Hz, 2H), 7.66 (dd, *J* = 8.5, 3.0 Hz, 2H), 7.52 (t, *J* = 8.6 Hz, 2H), 4.15 – 4.03 (m, 1H), 3.65 – 3.52 (m, 0.5 H), 3.52 – 3.38 (m, 0.5 H), 2.48 – 2.36 (m, 0.5 H), 2.36 – 2.17 (m, 1H), 2.14 – 2.02 (m, 0.5 H), 1.64 – 1.39 (m, 2H), 1.30 (d, *J* = 7.0 Hz, 3H), 1.09 (d, *J* = 4.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.79, 191.75, 163.78, 163.74, 141.20, 140.97, 136.47, 136.42, 133.89, 132.49, 132.47, 130.24, 130.20, 129.99, 129.87, 127.79, 127.37 (d, *J* = 4.7 Hz), 125.51 (d, *J* = 4.7 Hz), 118.36, 113.43, 113.41, 91.67, 90.49, 50.91, 50.71, 50.22 (d, *J* = 27.1 Hz), 49.87 (d, *J* = 27.0 Hz), 26.66, 25.85, 25.30, 24.95, 24.11, 23.98, 19.49, 19.46. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -69.28 (dd, *J* = 9.1, 4.3 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{23}H_{21}O_2N_2F_3Na$: 437.14473; found: 437.14407.



7j

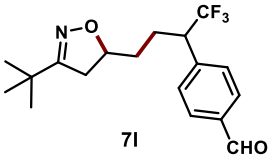
4-(4,4-dimethyl-5-(4,4,4-trifluoro-3-(4-formylphenyl)butyl)-4,5-dihydroisoxazol-3-yl)benzonitrile (**7j**): According to the general procedure, starting from **1o** (78.0 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as white solid after flash chromatography on silica gel (eluent: 30:1–20:1 hexane: EtOAc) in 72% yield (57.2 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3384, 3104, 2925, 2852, 1702, 1608, 1462, 1431, 1310, 1260, 1162, 1110, 943, 904, 829, 718, 658 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.03 (d, *J* = 2.3 Hz, 1H), 7.93 – 7.87 (m, 2H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.05 (dt, *J* = 5.1, 3.8 Hz, 1H), 4.11 – 4.03 (m, 1H), 3.66 – 3.57 (m, 0.5 H), 3.50 – 3.40 (m, 0.5 H), 2.44 – 2.36 (m, 0.5 H), 2.34 – 2.19 (m,

1H), 2.12 – 2.04 (m, 0.5 H), 1.60 – 1.40 (m, 2H), 1.35 (d, *J* = 7.0 Hz, 3H), 1.10 (d, *J* = 12.8 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.84, 191.78, 160.83, 160.78, 141.36, 141.10, 136.44, 136.37, 130.99, 130.23, 130.18, 130.06, 129.91, 127.86, 127.84, 127.54, 127.51, 127.44 (d, *J* = 5.9 Hz), 126.96, 126.94, 125.58 (d, *J* = 6.2 Hz), 91.17, 89.88, 51.37, 51.14, 50.20 (dd, *J* = 27.0, 8.3 Hz), 49.84 (dd, *J* = 27.0, 8.1 Hz), 26.77, 25.88, 25.47, 24.99, 24.46, 24.30, 19.58, 19.53. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.26 (d, *J* = 9.1 Hz). **HRMS** (ESI): *m/z* $[M+H]^+$ calcd for $C_{20}H_{21}O_2NF_3S$: 396.12396; found: 396.12337.



7k

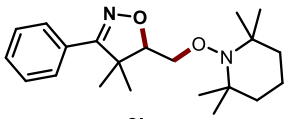
4-(1,1,1-trifluoro-4-(3-phenyl-4,5-dihydroisoxazol-5-yl)butan-2-yl)benzaldehyde (**7k**): According to the general procedure, starting from **1s** (64.4 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 15:1 – 10:1 hexane: EtOAc) in 63% yield (45.4 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 3061, 2941, 2844, 1701, 1608, 1447, 1356, 1256, 1209, 1163, 1111, 906, 823, 759, 690 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.01 (s, 1H), 7.91 – 7.86 (m, 2H), 7.64 – 7.59 (m, 2H), 7.49 (dd, *J* = 8.0, 5.7 Hz, 2H), 7.42 – 7.35 (m, 3H), 4.73 – 4.66 (m, 1H), 3.53 – 3.36 (m, 2H), 2.93 – 2.88 (m, 0.5H), 2.88 – 2.84 (m, 0.5H), 2.38 – 2.30 (m, 0.5H), 2.25 – 2.12 (m, 1H), 2.07 – 1.98 (m, 0.5H), 1.67 – 1.61 (m, 0.5H), 1.61 – 1.53 (m, 1H), 1.50 – 1.43 (m, 0.5H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.76, 191.75, 156.55, 156.51, 141.29, 141.11, 136.44, 136.40, 130.28, 130.24, 130.21, 129.95, 129.88, 129.51, 128.84, 127.39 (d, *J* = 3.3 Hz), 126.70, 125.53 (d, *J* = 3.2 Hz), 80.92, 80.23, 50.36 – 50.17 (m), 50.01 – 49.82 (m), 40.34, 40.14, 32.65, 32.55, 25.48, 24.89. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.33 (dd, *J* = 17.4, 8.9 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{20}H_{18}O_2NF_3Na$: 384.11818; found: 384.11765.



7l

4-(4-(3-(tert-butyl)-4,5-dihydroisoxazol-5-yl)-1,1,1-trifluorobutan-2-yl)benzaldehyde (**7l**): According to the general procedure, starting from **1r** (56.4 mg, 0.40 mmol) and **5r** (40.0 mg, 0.2 mmol), the title compound was isolated as milky oil after flash chromatography on silica gel (eluent: 20:1–10:1 hexane: EtOAc) in 68% yield (46.2 mg, 1:1 d.r., inseparable mixture). **IR** (neat): 2965, 2873, 1702, 1610, 1462, 1367, 1255, 1210, 1163, 1112, 874, 821, 730, 687 cm^{-1}. **^{1}H NMR** (600 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 10.01 (s, 2H), 7.90 – 7.84 (m, 4H), 7.47 (dd, *J* = 8.0, 6.0 Hz, 4H), 4.51 – 4.44 (m, 2H), 3.48 – 3.35 (m, 2H), 3.02 – 2.95 (m, 2H), 2.53 – 2.42 (m, 2H), 2.29 – 2.21 (m, 1H), 2.17 – 2.03 (m, 2H), 1.98 – 1.90 (m, 1H), 1.52 – 1.43 (m, 3H), 1.36 – 1.29 (m, 1H), 1.15 (s, 9H), 1.14 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) (mixture of diastereomers, both isomers quoted) δ 191.77, 166.06, 141.38, 141.25, 136.39, 136.37, 130.18,

130.14, 129.97, 129.90, 127.41, 125.55, 79.85, 79.21, δ 50.20 (dd, *J* = 27.0, 8.3 Hz), 49.84 (dd, *J* = 26.8, 8.2 Hz) 39.64, 39.45, 33.09, 33.07, 32.29, 32.22, 28.12, 28.10, 25.38, 24.85. **^{19}F NMR** (564 MHz, $CDCl_3$) δ -69.38 (dd, *J* = 22.1, 9.1 Hz). **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{18}H_{23}O_2NF_3$: 342.16754; found: 342.16650.



8b

***4,4-dimethyl-3-phenyl-5-(((2,2,6,6-tetramethylpiperidin-1-yl)oxy)methyl)-4,5-dihydroisoxazole* (8b)**: According to the general procedure, starting from **1a** (36.8 mg, 0.20 mmol) and **2a** (7.0 mg, 0.1 mmol), and TEMPO (46.8 mg, 0.3 mmol) was added, the title compound was isolated as gray-white solid after flash chromatography on silica gel (eluent: 20:1 hexane: EtOAc) in 25% yield (16.9 mg). **IR** (eat): 3421, 2929, 1734, 1461, 1243, 1043, 894, 765, 695 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 – 7.59 (m, 2H), 7.47 – 7.35 (m, 3H), 4.34 (dd, *J* = 6.2, 5.1 Hz, 1H), 4.13 (dd, *J* = 10.2, 6.2 Hz, 1H), 4.07 (dd, *J* = 10.2, 5.1 Hz, 1H), 1.63 – 1.45 (m, 5H), 1.45 (s, 3H), 1.38 – 1.33 (m, 1H), 1.31 (s, 3H), 1.24 (s, 3H), 1.22 (s, 3H), 1.13 (s, 3H), 1.12 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.50, 129.54, 128.53, 127.43, 88.40, 74.72, 59.99, 59.93, 50.88, 39.66, 33.16, 32.82, 24.70, 20.15, 20.04, 19.57, 17.04. **HRMS** (ESI): *m/z* $[M+Na]^+$ calcd for $C_{21}H_{32}O_2N_2Na$: 367.23560; found: 367.23584.

7. Thermochemical Data and Cartesian Coordinates

Name	E / a.u.	ZPE / a.u.	H / a.u.	T·S / a.u.	G / a.u.	ν_{imag} / cm^{-1}
VII	-595.549	0.232976	-595.302	0.049481	-595.352	
TS2	-595.523	0.232206	-595.277	0.048527	-595.326	-631.8
1a	-596.188	0.245861	-595.927	0.050427	-595.978	
TS1	-1153.16	0.482296	-1152.65	0.077179	-1152.73	-1301.21
VI	-595.546	0.233322	-595.298	0.051136	-595.349	
V	-556.986	0.239186	-556.735	0.045788	-556.781	
X	-557.659	0.255372	-557.392	0.044834	-557.437	

VII:

C	3.41934100	-1.10279600	-0.21021700
C	2.04077600	-1.28759700	-0.19577400
C	1.17403000	-0.20628100	0.03763100
C	1.72860800	1.06437300	0.24597500
C	3.11087400	1.24780500	0.22931500
C	3.96060300	0.16694900	0.00186700
H	4.07705700	-1.95472200	-0.39553700
H	1.61653900	-2.27708200	-0.37273100
H	1.08649700	1.92413800	0.43636400
H	3.52344600	2.24470100	0.39732700
H	5.04275900	0.31284100	-0.01438800
C	-0.28548200	-0.43877100	0.06095500
N	-0.73441900	-1.61697400	0.29948100
O	-2.10465000	-1.62756900	0.23632600
C	-1.40021900	0.58874000	-0.11998200
C	-1.64337100	1.33100400	1.20356100
H	-1.84179100	0.62421000	2.02255500
H	-0.77803900	1.94585000	1.48653000
H	-2.51348900	1.99761000	1.10527700
C	-1.21880600	1.55844100	-1.28577100
H	-0.45345300	2.31753200	-1.07526800
H	-0.93359700	1.02941500	-2.20703500
H	-2.16540900	2.08849900	-1.47354600
C	-2.54061700	-0.42953600	-0.42533700
H	-2.52218100	-0.62654100	-1.51624400
C	-3.90816900	-0.07686900	0.00115900
H	-4.22672200	-0.26710600	1.02783900
H	-4.55889600	0.48725000	-0.66840400

TS2:

C	3.38274100	1.09598800	0.30150600
C	2.00199700	1.26502500	0.26400400
C	1.15087100	0.19570200	-0.06491100
C	1.73052000	-1.05080400	-0.34488700
C	3.11393400	-1.22075700	-0.30042800
C	3.94606400	-0.15010900	0.02151900
H	4.02345700	1.94175700	0.56056900
H	1.56360800	2.23688200	0.49761200
H	1.10879500	-1.90370500	-0.61629100
H	3.54179200	-2.19999200	-0.52535700
H	5.02907600	-0.28583900	0.05704800
C	-0.31022000	0.43254800	-0.11243700
N	-0.73638800	1.60260700	-0.42836900
O	-2.00074700	1.82264800	-0.38696100
C	-1.42478600	-0.59764700	0.15153400
C	-1.67142100	-1.41759800	-1.12588600
H	-1.96641400	-0.76570900	-1.96122300
H	-0.76853200	-1.96313200	-1.42845300
H	-2.46543700	-2.16159200	-0.96352600
C	-1.10002600	-1.51327800	1.34399600
H	-0.23984800	-2.16233600	1.13417900
H	-0.87036900	-0.92517500	2.24497100
H	-1.96167000	-2.16032100	1.56444200
C	-2.63215200	0.25030800	0.52319900
H	-2.54825700	0.72793500	1.50627800
C	-3.92002400	0.02426000	0.06135100
H	-4.12262300	-0.58225500	-0.82299500
H	-4.76788600	0.52221800	0.53566600

1a:

C	2.92803000	-0.39238400	-1.28095400
C	1.57799700	-0.04722400	-1.22792300
C	0.94225900	0.13573200	0.00541000
C	1.68053800	-0.02051500	1.18414400
C	3.03035400	-0.36525100	1.13023700
C	3.65627100	-0.55434800	-0.10225800
H	3.41333200	-0.53375000	-2.24911800
H	1.01184400	0.08599800	-2.15248400
H	1.19412000	0.13099200	2.15028700
H	3.59613600	-0.48583600	2.05661700
H	4.71335000	-0.82580500	-0.14408800
C	-0.50282300	0.51388300	0.06281500

N	-0.89061800	1.73107300	0.04785700
O	0.13720200	2.63631500	-0.02108400
H	-0.31265100	3.48837600	-0.02197300
C	-1.57607900	-0.57756900	0.11955900
C	-1.53869300	-1.37871000	-1.19025000
H	-1.73923300	-0.73631500	-2.06080200
H	-0.55562500	-1.85063100	-1.32954800
H	-2.29166700	-2.18060600	-1.16912200
C	-1.28027400	-1.52669600	1.30064200
H	-0.30648600	-2.02340100	1.17964000
H	-1.27399900	-0.98410100	2.25844100
H	-2.05695400	-2.30400400	1.35225400
C	-2.93038300	0.05451200	0.37326100
H	-2.98585300	0.64228600	1.29644500
C	-4.02956300	-0.07310300	-0.36916500
H	-4.04849000	-0.63886600	-1.30431800
H	-4.96692200	0.39766700	-0.06167800

TS1:

C	4.90562700	-2.34133800	1.29994100
C	3.91248300	-1.36348300	1.26920200
C	3.64723100	-0.67324300	0.08134500
C	4.37331700	-0.97558500	-1.07569300
C	5.36378500	-1.95567600	-1.04021300
C	5.63268300	-2.63732600	0.14691800
H	5.11035300	-2.87527700	2.23007100
H	3.33893500	-1.13604200	2.17034400
H	4.16200100	-0.44408300	-2.00588900
H	5.92778900	-2.18756900	-1.94589600
H	6.41032700	-3.40351500	0.17291400
C	2.57435100	0.36403800	0.04699400
N	1.35569100	0.04819700	-0.15207800
O	0.99561300	-1.20486300	-0.34098900
H	-0.02413400	-1.18581700	-0.44986300
C	2.88083500	1.83949500	0.30907700
C	3.24435000	1.98736700	1.79464300
H	2.41923300	1.66377700	2.44619200
H	4.13207700	1.38624600	2.03807900
H	3.47858400	3.03752300	2.02237200
C	4.07409500	2.28547200	-0.55874800
H	4.98075600	1.71257000	-0.31680500
H	3.86068000	2.16112400	-1.63111700

H	4.28080000	3.34924000	-0.37243700
C	1.67719100	2.67344500	-0.08722000
H	1.42951500	2.62479000	-1.15462200
C	0.94203000	3.45439300	0.70375600
H	1.12907200	3.55161400	1.77613300
H	0.11140300	4.03459900	0.29407200
C	-2.52232400	-1.55025500	-0.61099200
C	-3.86428100	-0.75437400	-0.61904600
C	-3.55594700	0.71925900	-0.91801100
C	-2.73632700	1.31594200	0.23012000
C	-1.52558500	0.36099900	0.49249900
H	-4.53935100	-1.16795400	-1.38038300
H	-2.45945700	-2.15761900	0.30002100
H	-2.42783200	-2.19515100	-1.49161300
H	-2.38696200	2.32152700	-0.03899800
H	-3.32145200	1.39598600	1.15473000
H	-0.57577900	0.92424200	0.54360800
H	-1.66064400	-0.22356100	1.41031300
H	-4.49920100	1.26810300	-1.04561400
N	-1.45174600	-0.56078900	-0.62589500
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H	-0.53740600	0.86580600	-1.83072700
H	-1.07047800	-0.61531000	-2.68160200
C	-2.72617700	0.77869800	-2.20157000
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H	-3.22992600	0.24736300	-3.02099400
O	-4.45013600	-0.91417300	0.66438600
C	-5.77983600	-0.72142300	0.77472000
O	-6.47191200	-0.42489100	-0.16441800
C	-6.23847300	-0.91700900	2.18780400
H	-5.92239900	-1.90408100	2.55155300
H	-5.76756500	-0.15976700	2.83080800
H	-7.32799100	-0.82306500	2.23998100

VI:

C	-2.98090000	-0.12416000	1.29879200
C	-1.61909500	0.16255900	1.21351700
C	-0.97251200	0.15213100	-0.02838700
C	-1.70715200	-0.14039000	-1.18368200
C	-3.06887700	-0.42646100	-1.09578800
C	-3.70681200	-0.42068600	0.14495800
H	-3.47682800	-0.11489000	2.27167400

H	-1.05090400	0.39767200	2.11639000
H	-1.20945200	-0.14133300	-2.15580300
H	-3.63431500	-0.65346400	-2.00202000
H	-4.77338000	-0.64562100	0.21250400
C	0.48556600	0.47297600	-0.11655700
N	0.84825500	1.70074400	-0.18341800
O	0.27405100	2.77444500	-0.21133200
C	1.55841100	-0.61504400	-0.07537200
C	1.52048000	-1.29124600	1.30286600
H	1.72109500	-0.57101500	2.10994900
H	0.53392400	-1.74224600	1.48346600
H	2.27028100	-2.09456100	1.35708800
C	1.26722400	-1.66657300	-1.16586200
H	0.29217900	-2.14891400	-1.00313000
H	1.26538100	-1.21334000	-2.16887000
H	2.04225300	-2.44673200	-1.14257000
C	2.90392100	0.01293600	-0.38256600
H	2.96389500	0.48937000	-1.36881100
C	3.98771000	0.01005200	0.39258200
H	4.00113100	-0.44625100	1.38573900
H	4.91675700	0.47400200	0.05196400

V:

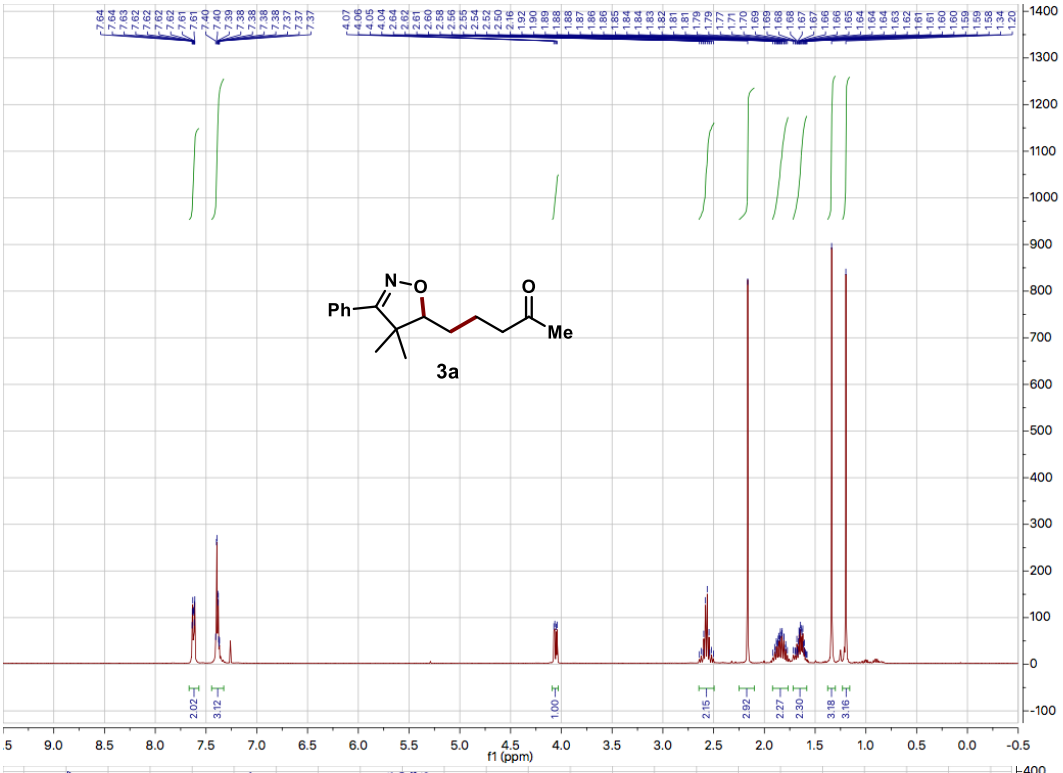
C	-0.79334500	-0.45083200	1.45981600
C	0.20202600	0.37839100	0.56035000
C	-0.52033100	0.71034900	-0.75131300
C	-0.85285000	-0.58907000	-1.48805700
C	-1.71760500	-1.49888500	-0.52263100
H	0.49476900	1.29671100	1.08636100
H	-0.32674600	-1.40420100	1.73305800
H	-1.08189100	0.10812400	2.35619400
H	-1.42665700	-0.37967800	-2.39933400
H	0.05608500	-1.13578600	-1.76547800
H	-2.67665200	-1.77068500	-0.97833700
H	-1.17191300	-2.40113800	-0.22473500
H	0.13161300	1.34605900	-1.36652200
N	-1.94841200	-0.67773900	0.63464500
C	-2.75759400	0.48946700	0.40434900
H	-3.64524400	0.20844700	-0.17257900
H	-3.05550300	0.92733800	1.36409100
C	-1.81014100	1.45984400	-0.40863500
H	-2.33061500	1.77206700	-1.32233300

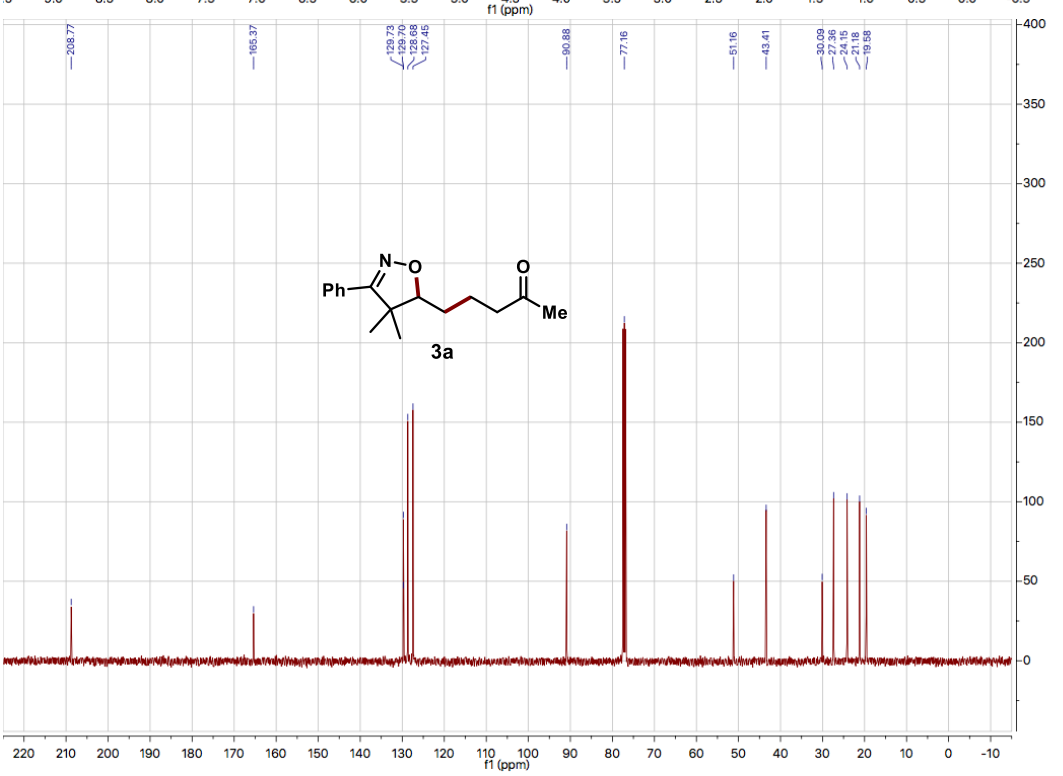
H	-1.60036300	2.35497600	0.19110100
O	1.34043600	-0.43175300	0.34960600
C	2.50466900	0.19060200	0.05663600
O	2.58827300	1.38630500	-0.04131600
C	3.61329100	-0.79925400	-0.12579600
H	3.69986200	-1.43201600	0.76792600
H	3.37972500	-1.45546200	-0.97621000
H	4.55402400	-0.27066800	-0.31034900

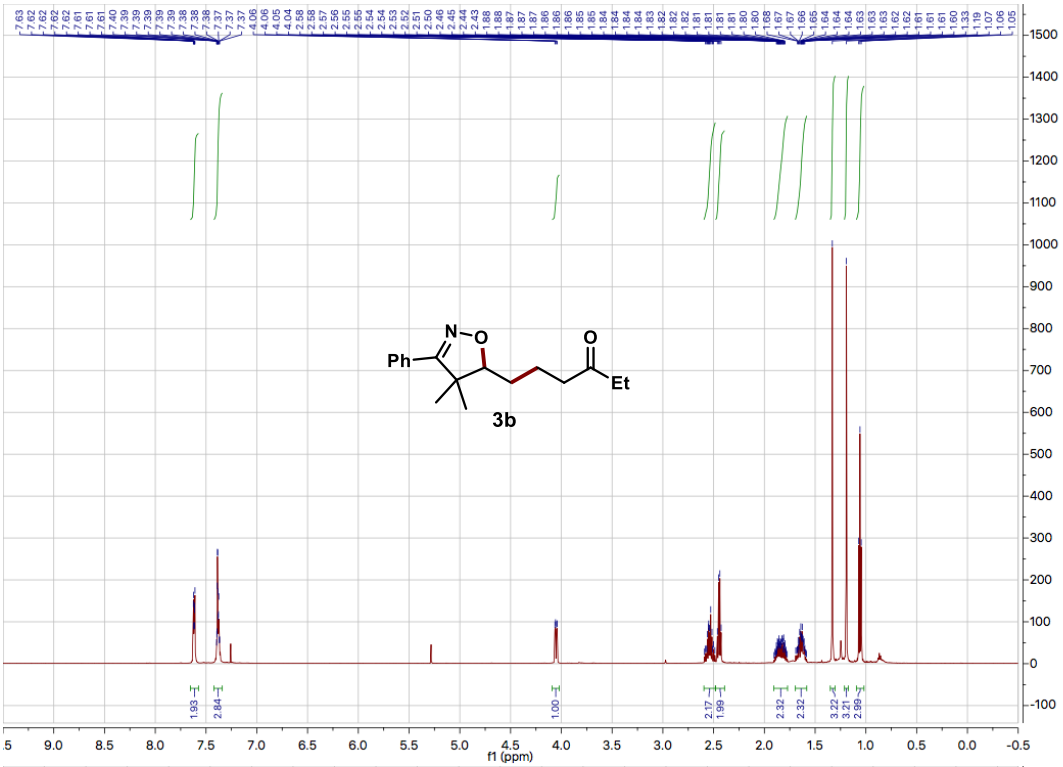
X:

C	0.79795400	-0.46123600	-1.44049000
C	-0.19766300	0.38576700	-0.63945600
C	0.47816200	0.84458700	0.65998000
C	0.74758800	-0.37689600	1.54745300
C	1.47798500	-1.44382000	0.71764900
H	-0.51932300	1.25592200	-1.22671500
H	0.32981900	-1.39058200	-1.78405900
H	1.19901000	0.07547100	-2.30771900
H	1.35646800	-0.07207100	2.40926700
H	-0.18826500	-0.79356100	1.93884000
H	2.35799700	-1.85626600	1.22403200
H	0.82170600	-2.27333300	0.42779900
H	-0.16937900	1.56475700	1.17411400
N	1.95637600	-0.81096200	-0.55931600
C	2.76471000	0.42072300	-0.26230100
H	3.53448000	0.12417400	0.46019600
H	3.26151300	0.71884800	-1.19282800
C	1.81390300	1.49887200	0.28437400
H	2.26058900	1.97239800	1.16775800
H	1.65502300	2.28961000	-0.46239900
O	-1.33016600	-0.43705300	-0.37440400
C	-2.49362600	0.17461500	-0.08436900
O	-2.60725400	1.37299900	-0.05117000
C	-3.57797100	-0.82540700	0.18278500
H	-3.67818100	-1.50547500	-0.67417000
H	-3.30708100	-1.43279700	1.05812300
H	-4.52399800	-0.30634200	0.36773500
H	2.54809800	-1.48481400	-1.05391100

8. NMR spectra



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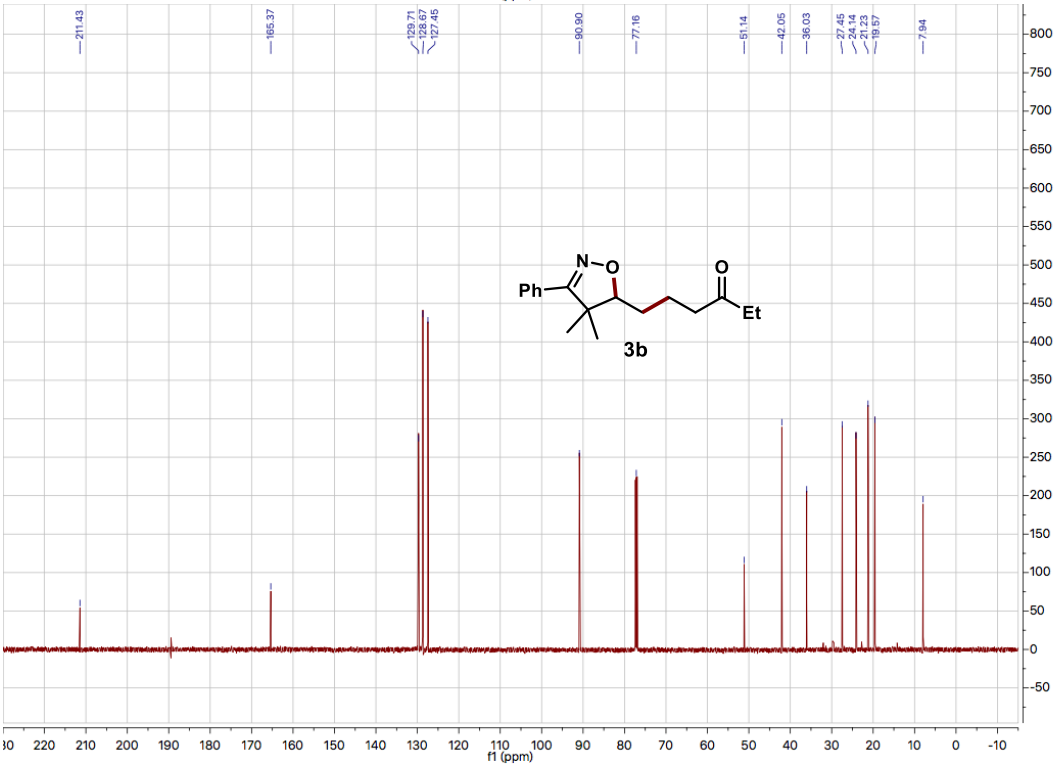
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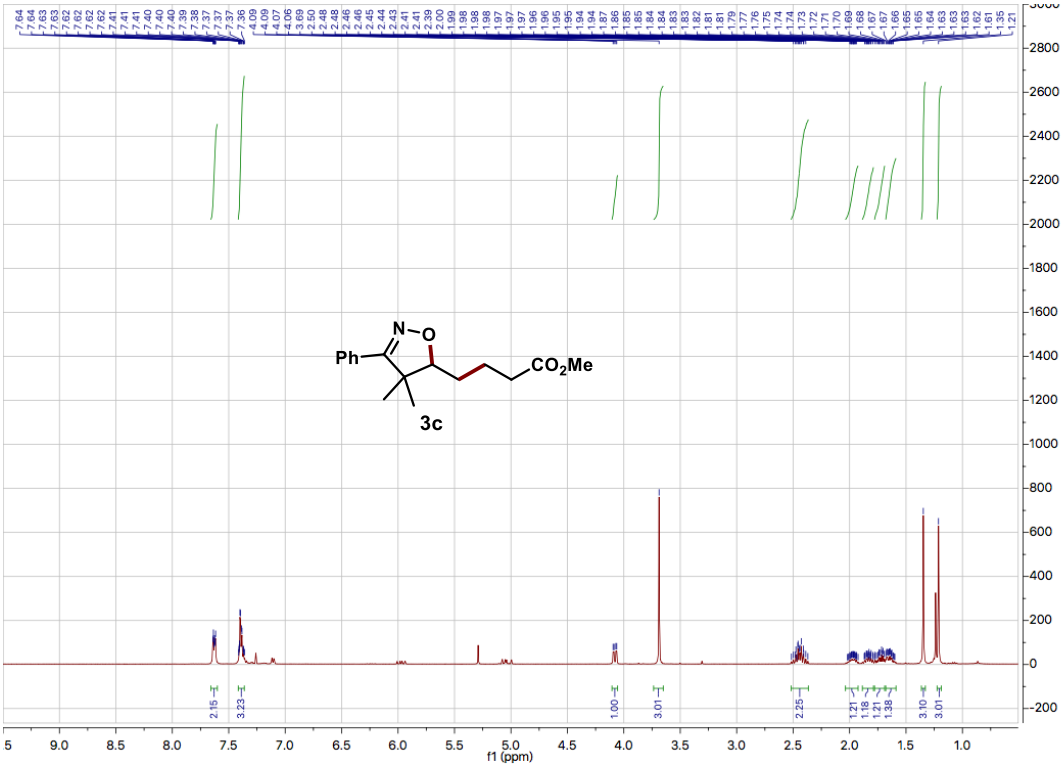
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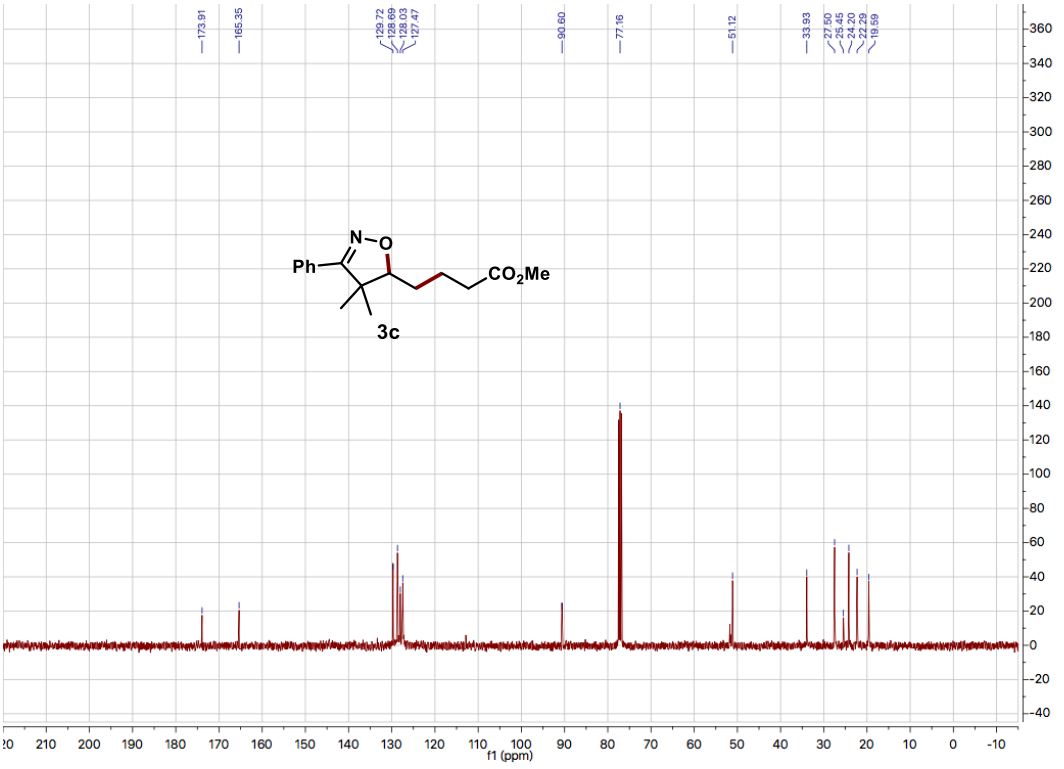
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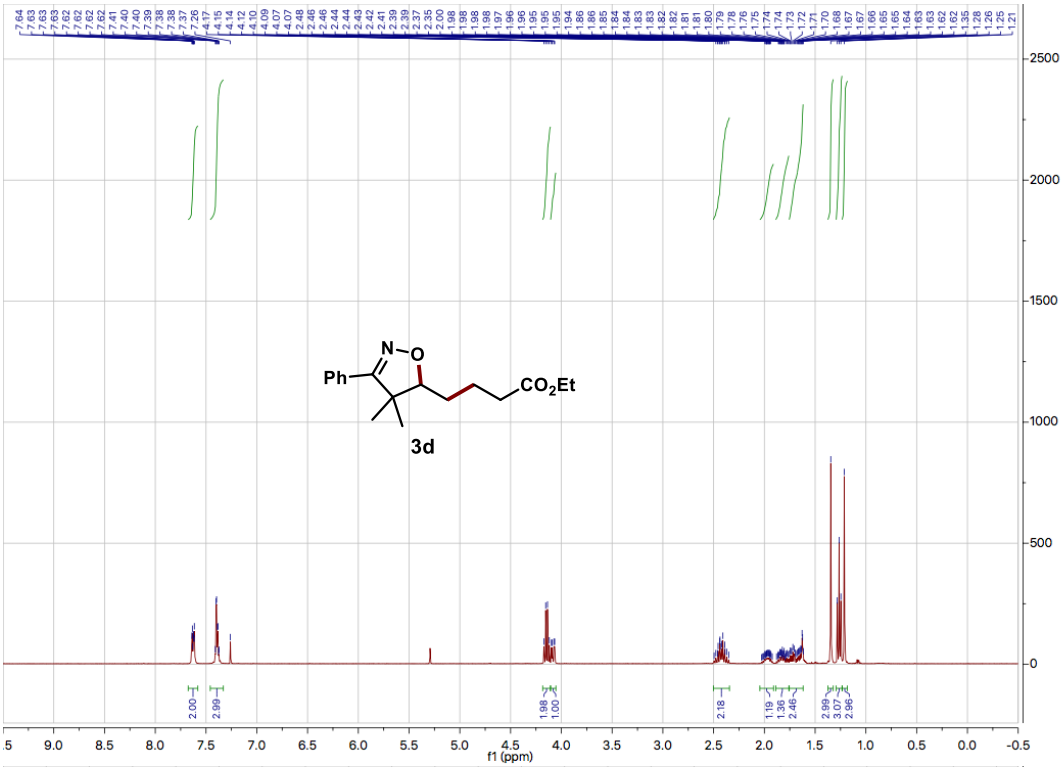
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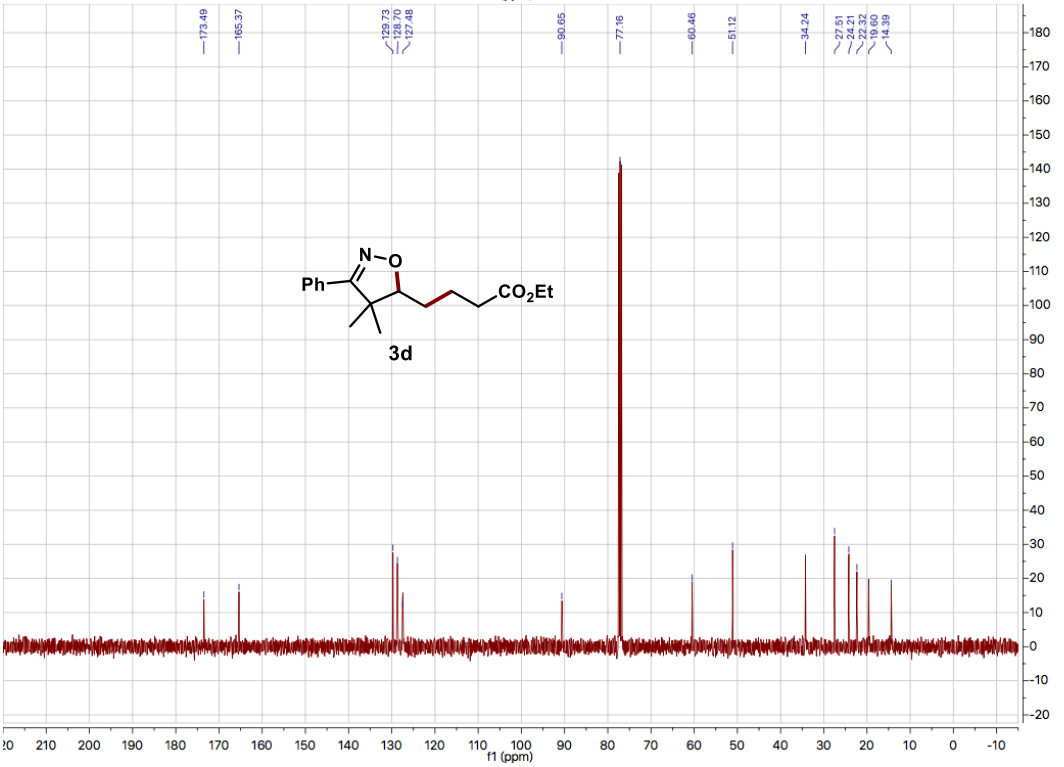
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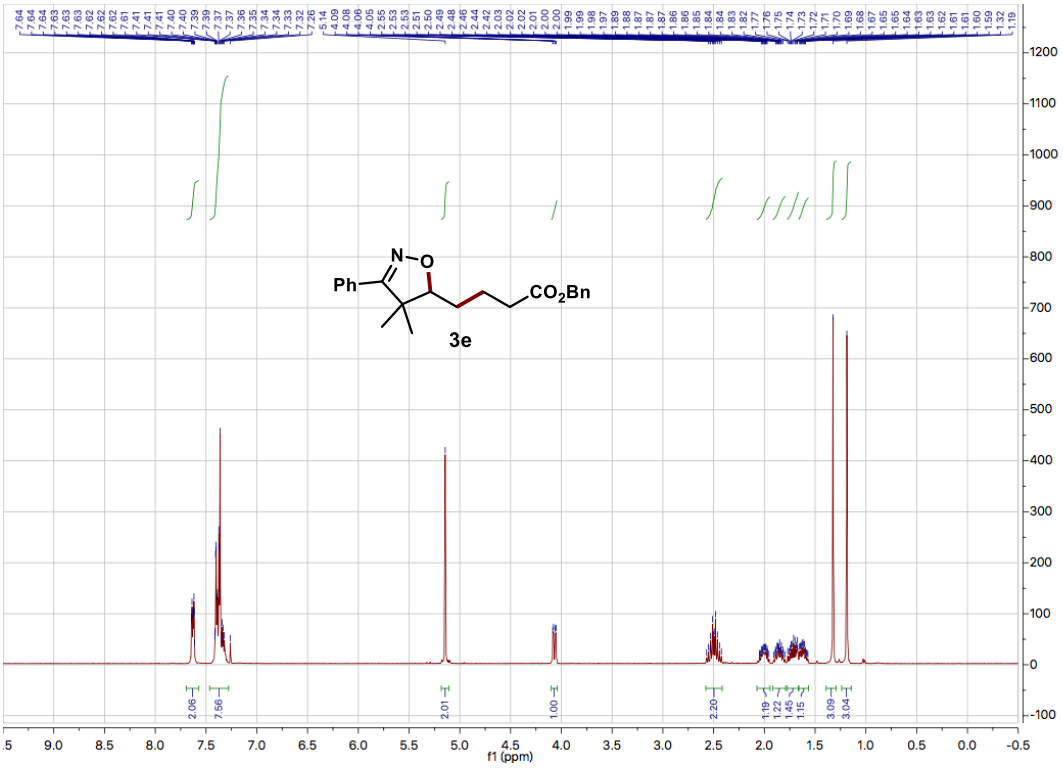
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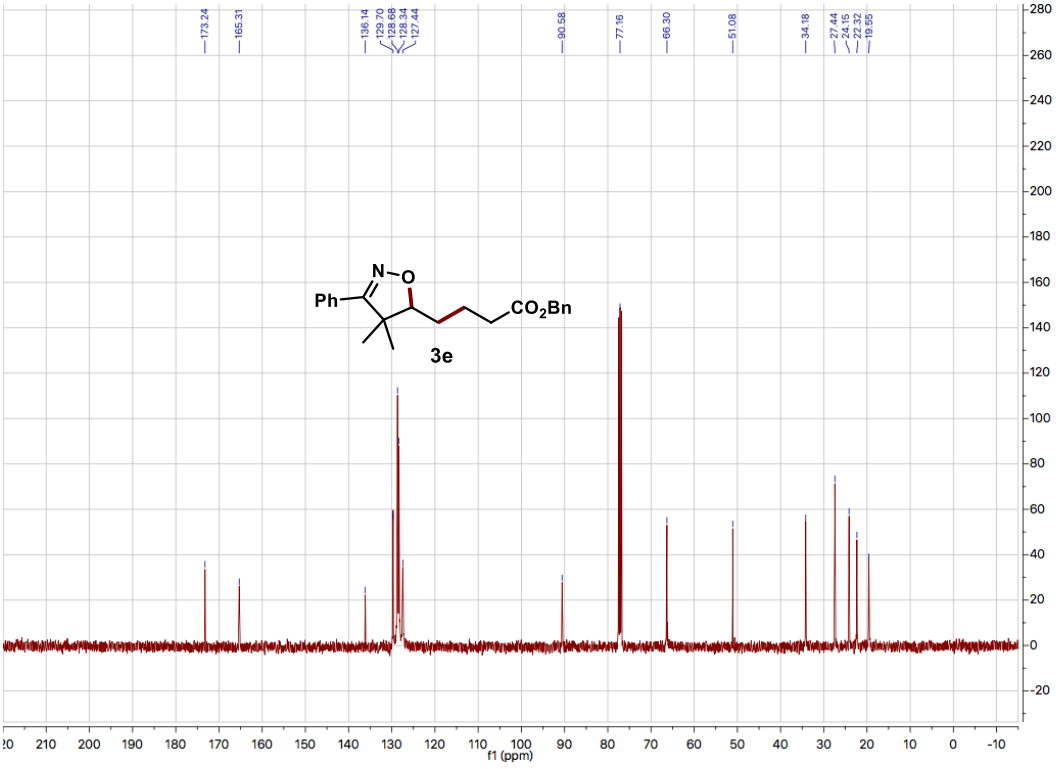
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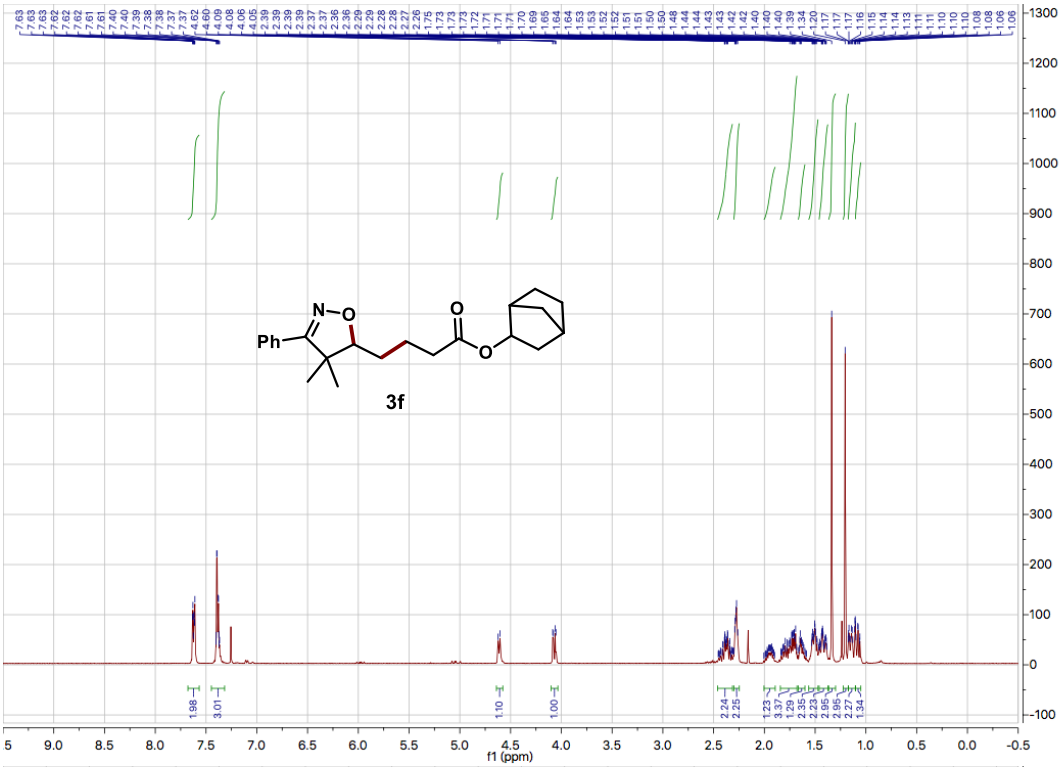
f1 (ppm)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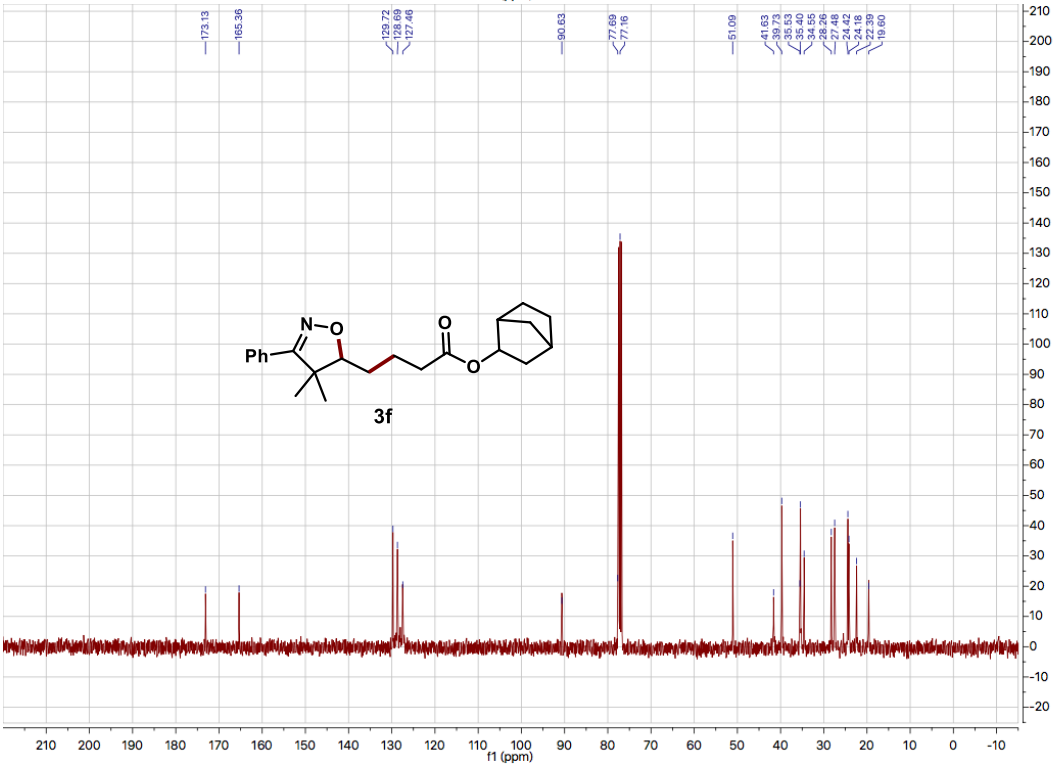
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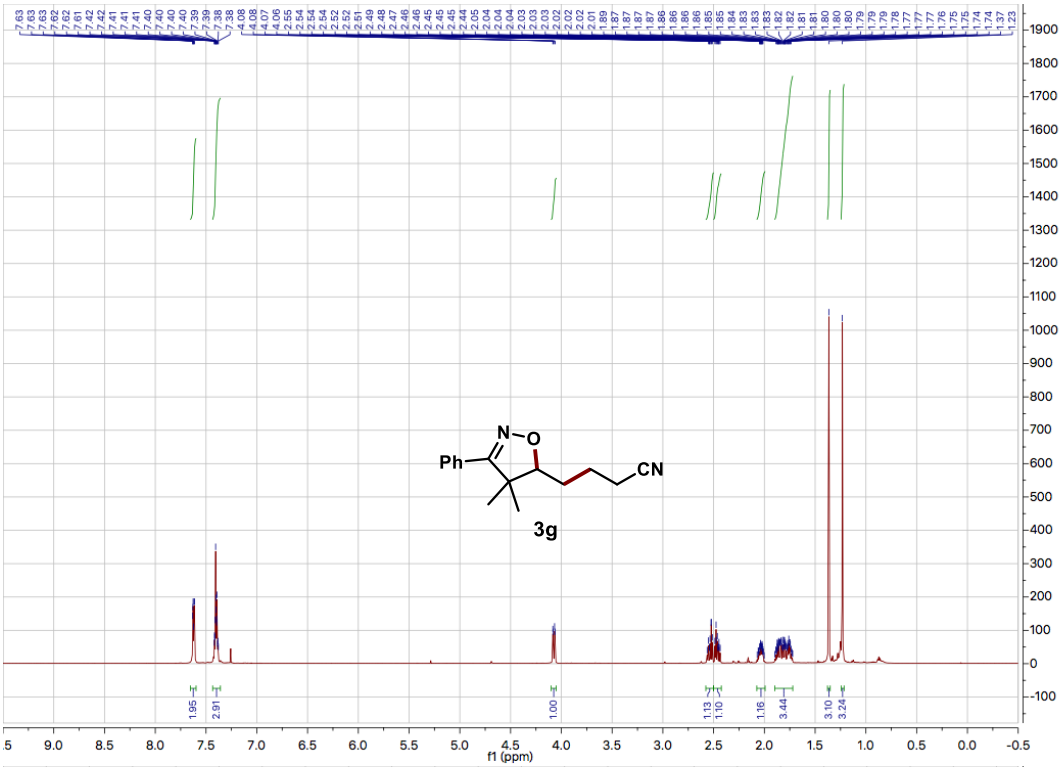
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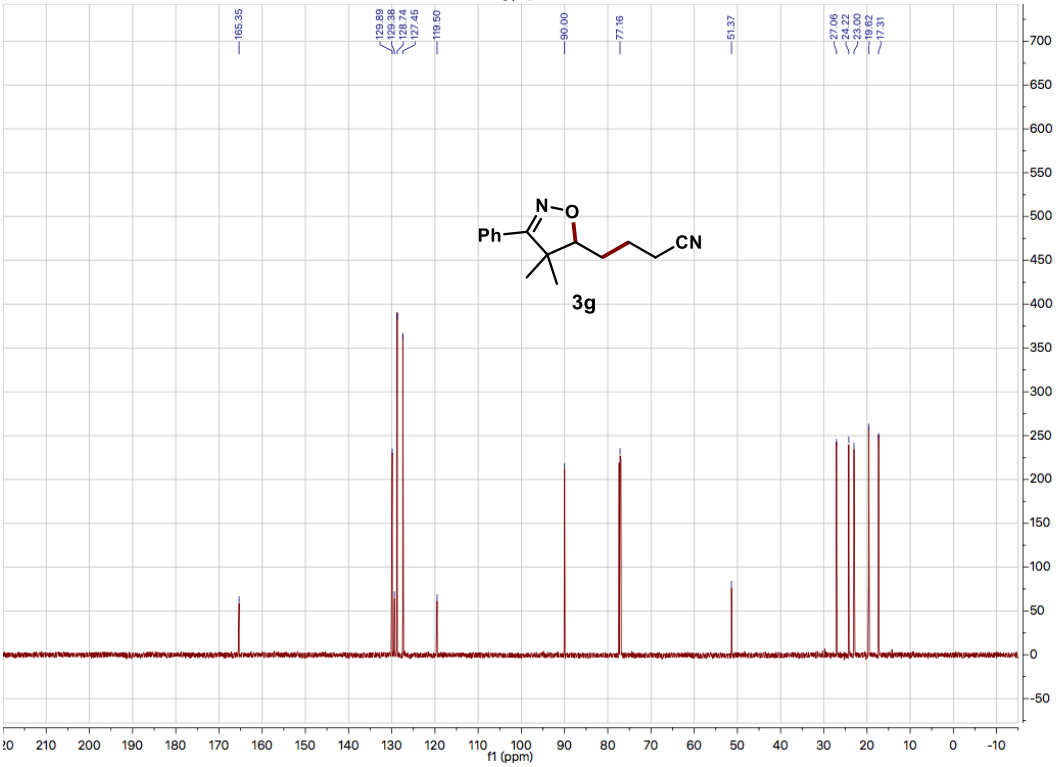
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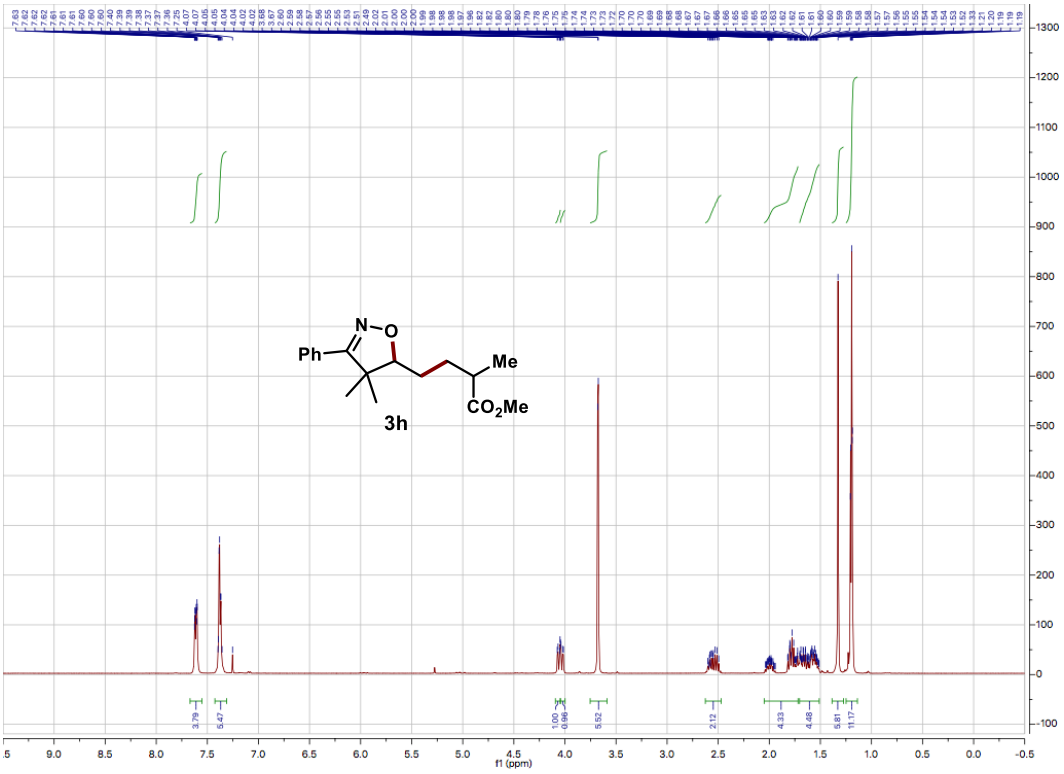
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CO2Me
3h
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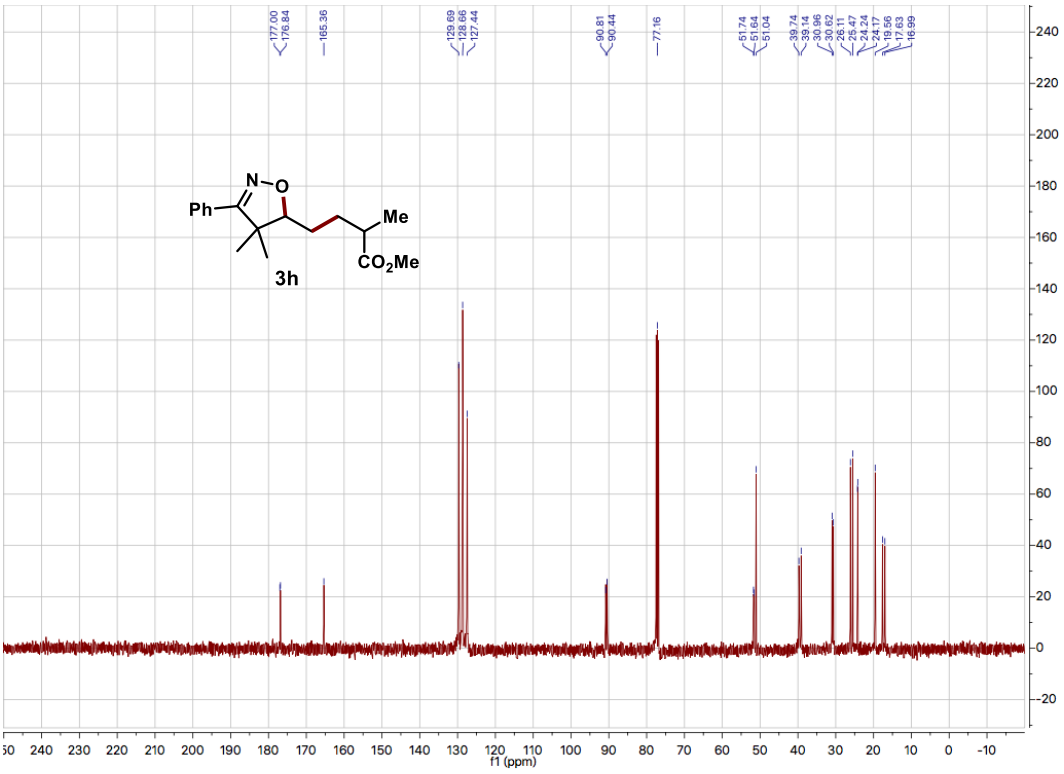
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39.14
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30.62
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Me
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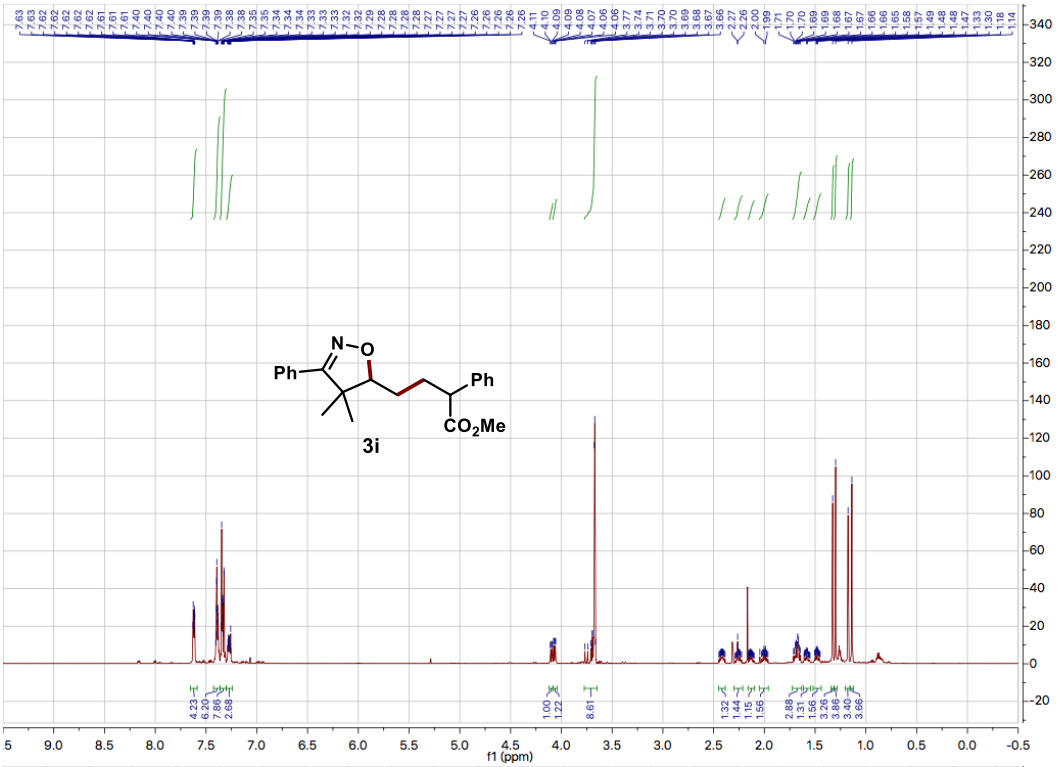
3h
f1 (ppm)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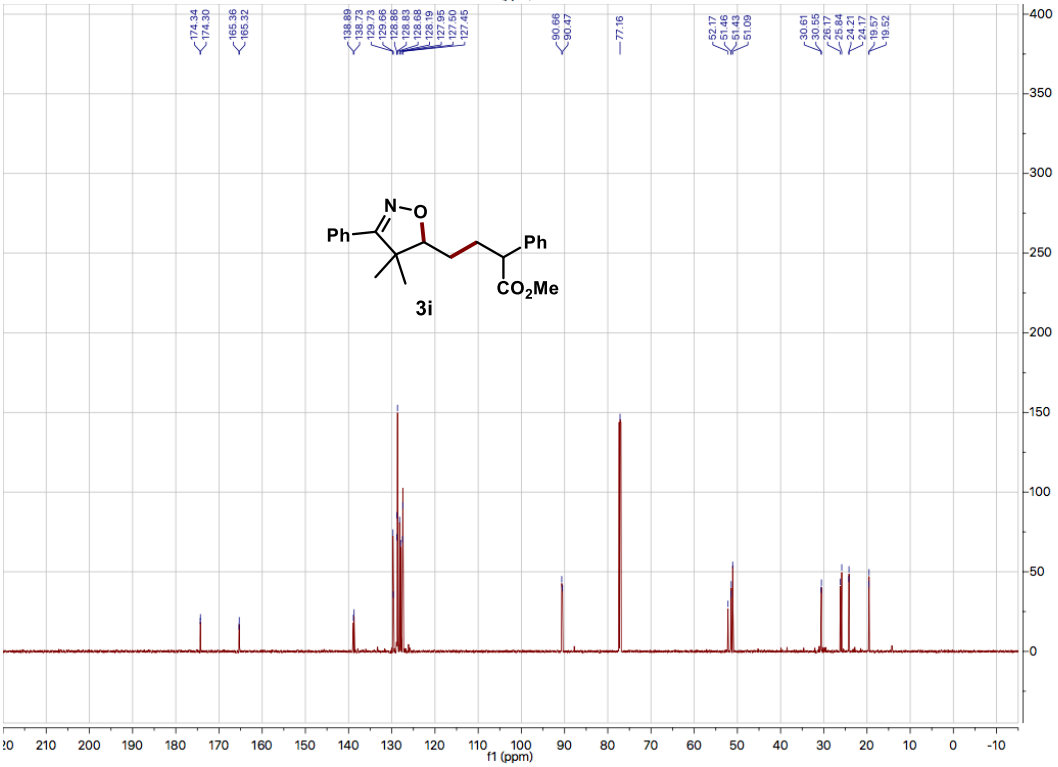
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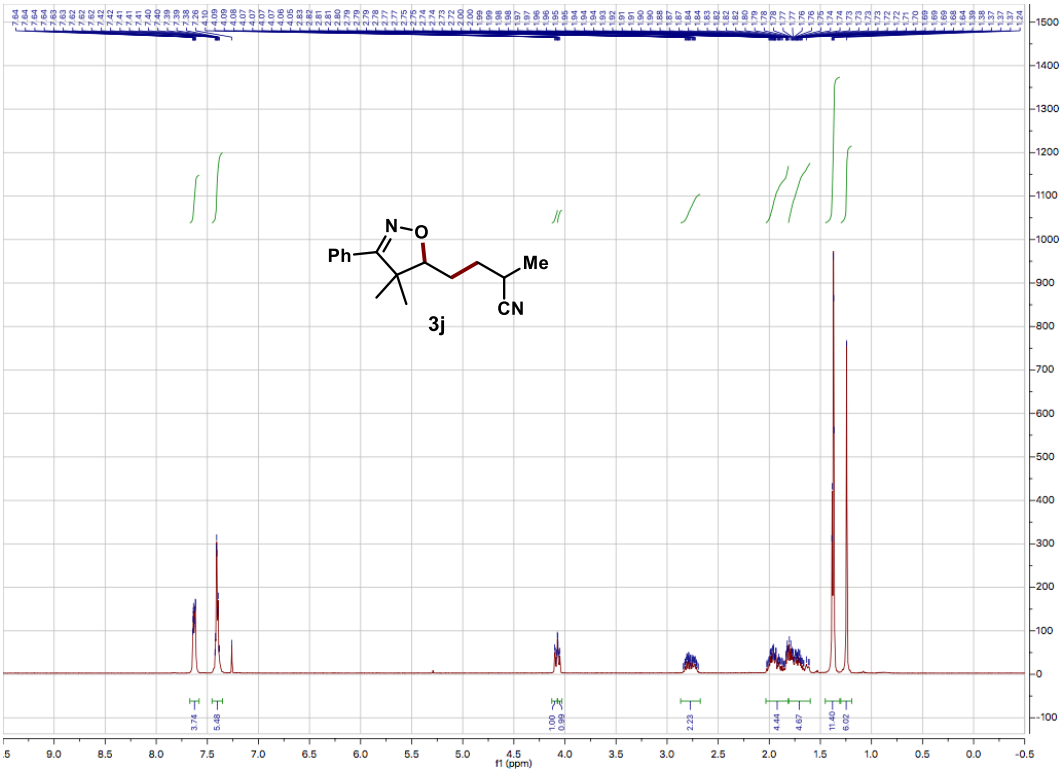
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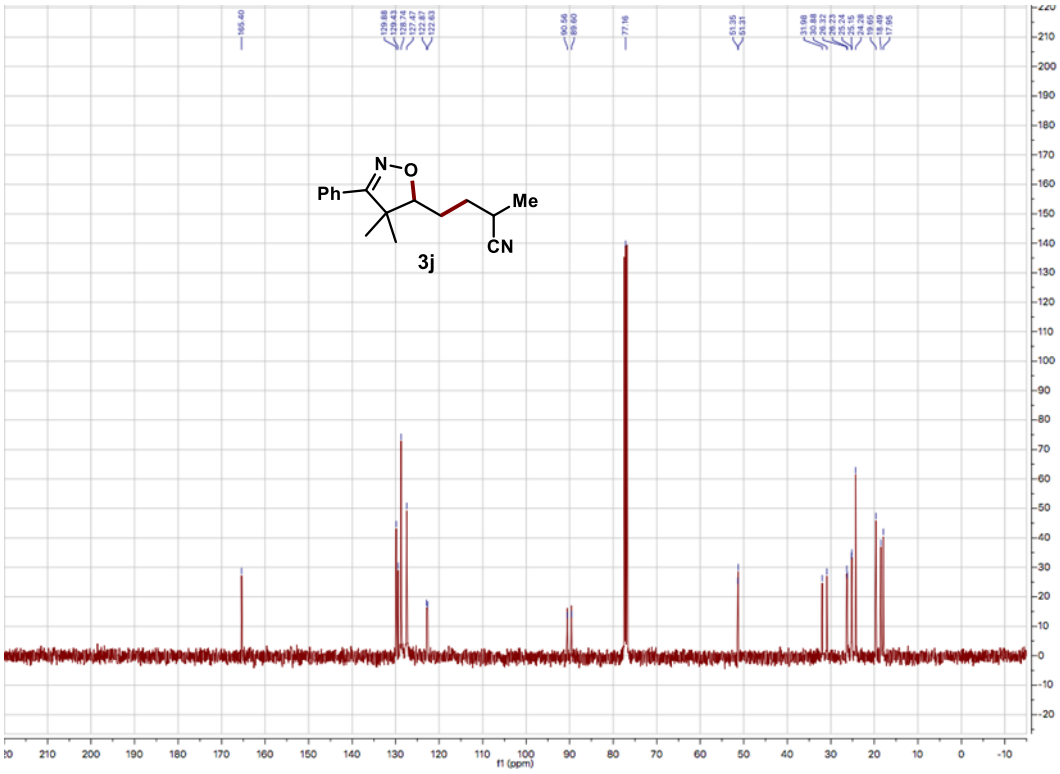
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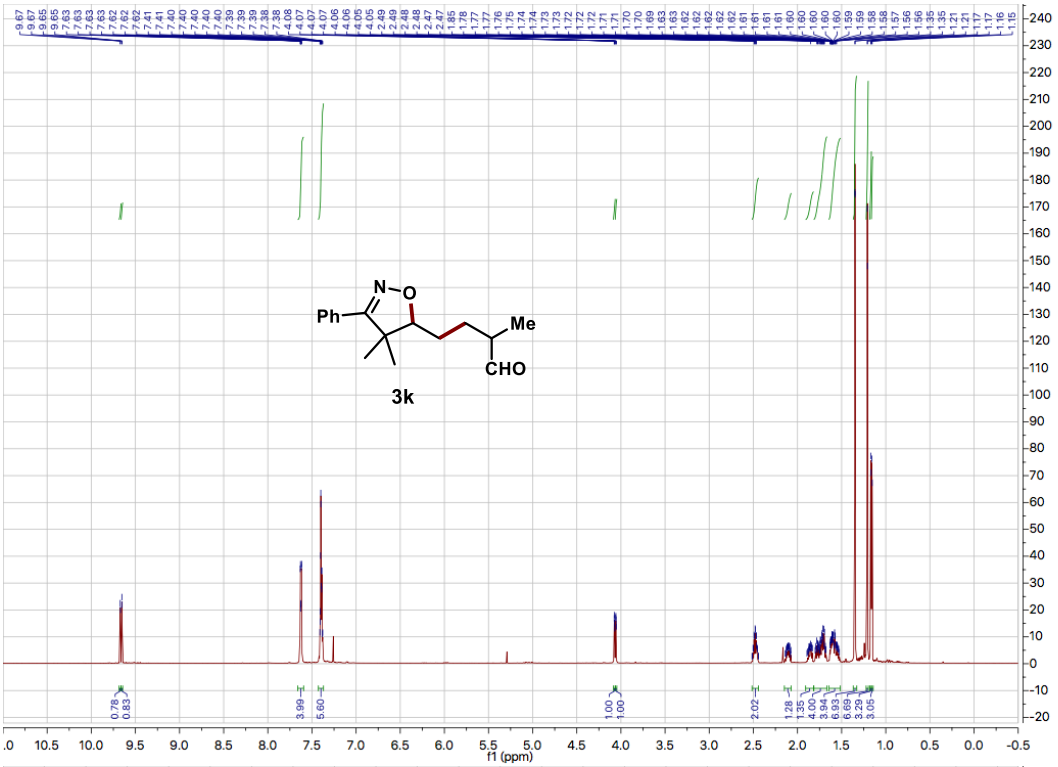
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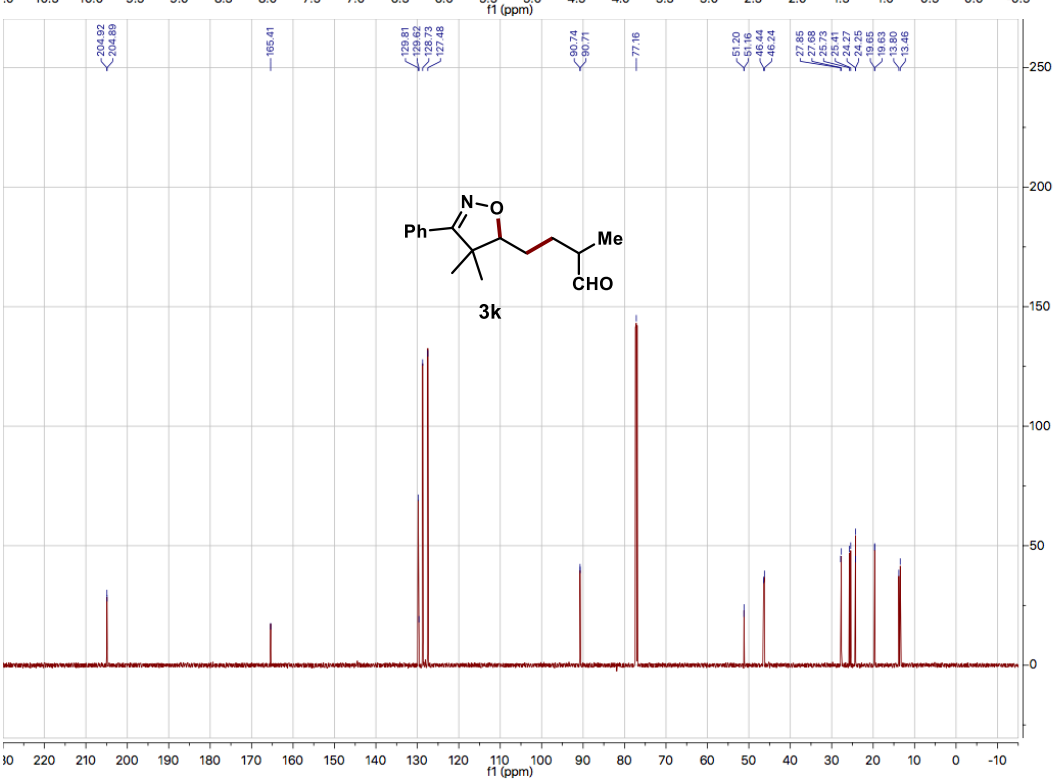
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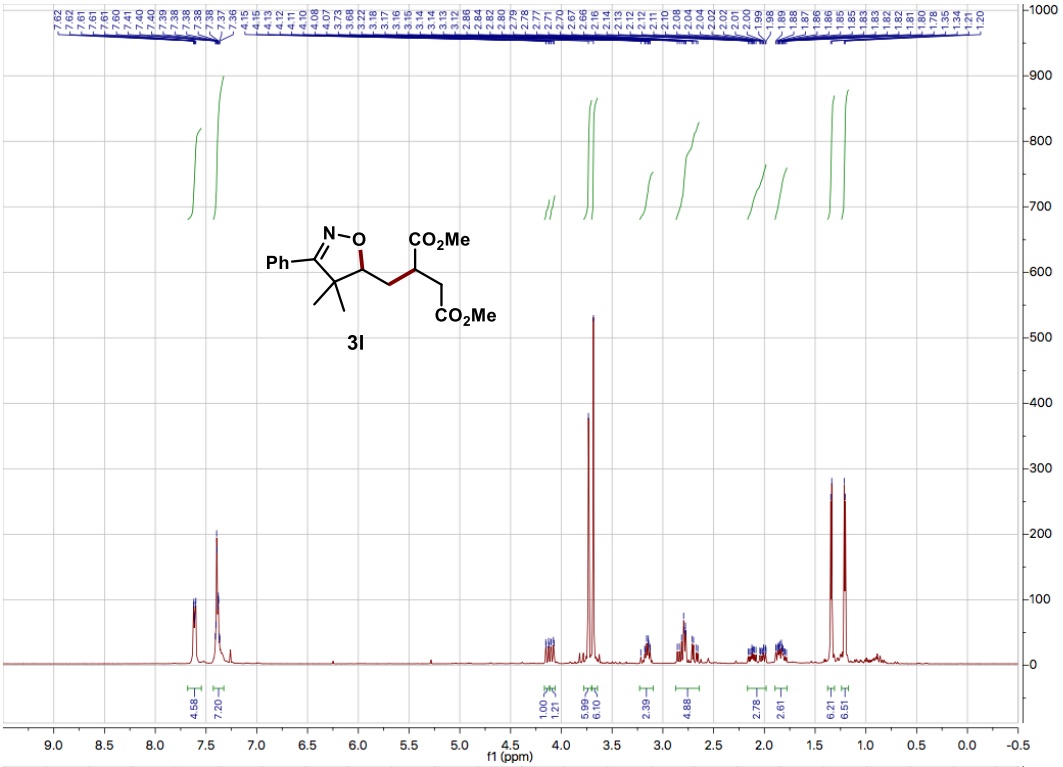
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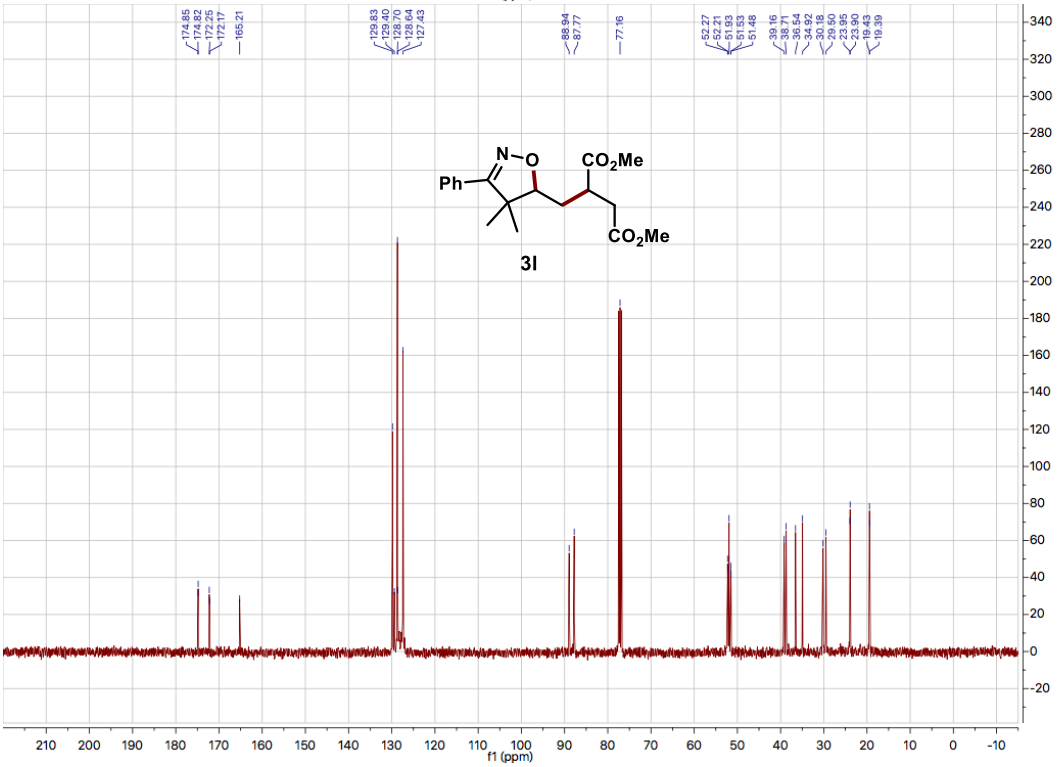
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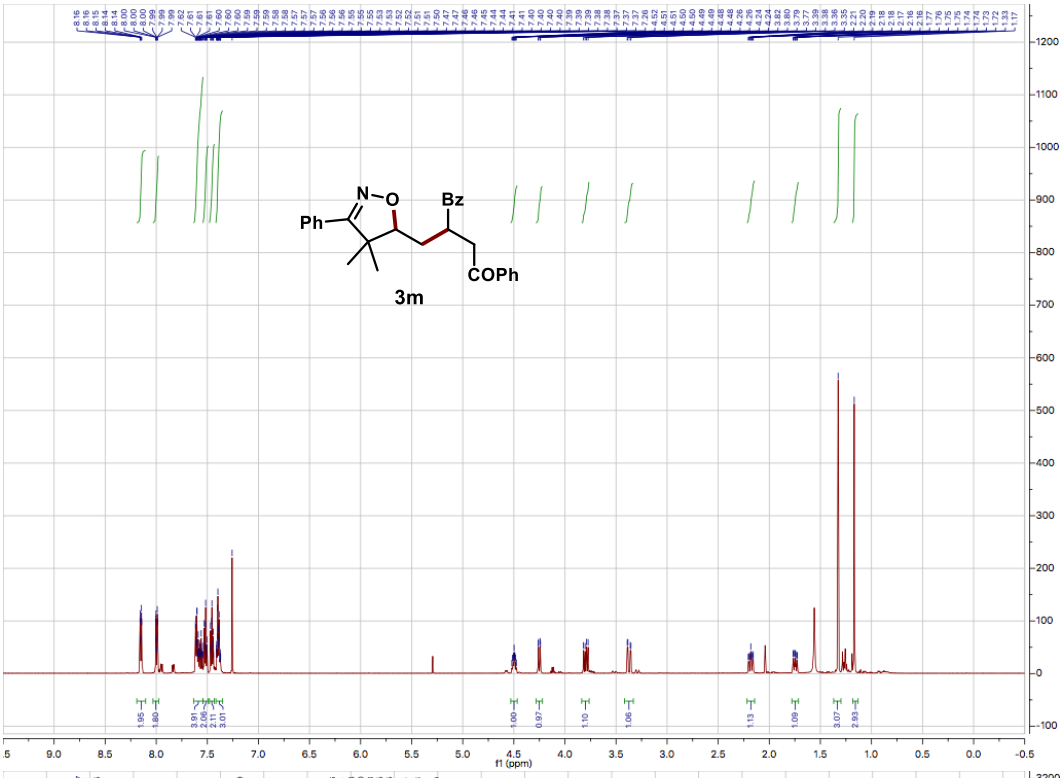
f1 (ppm)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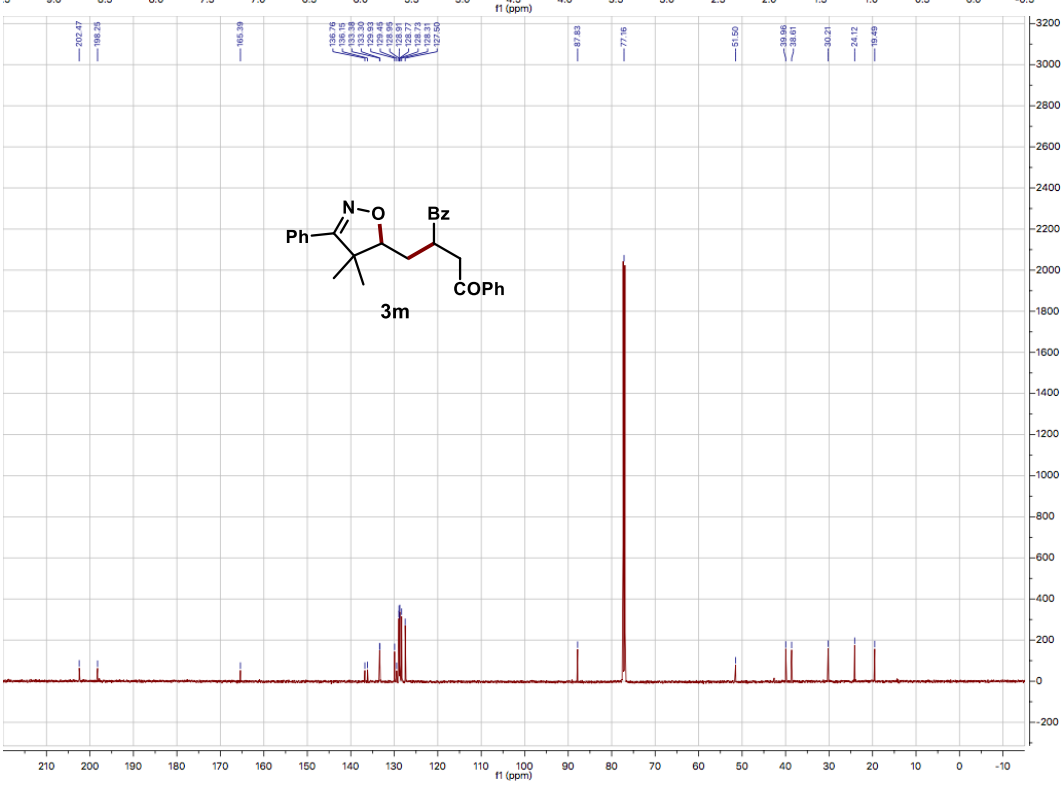
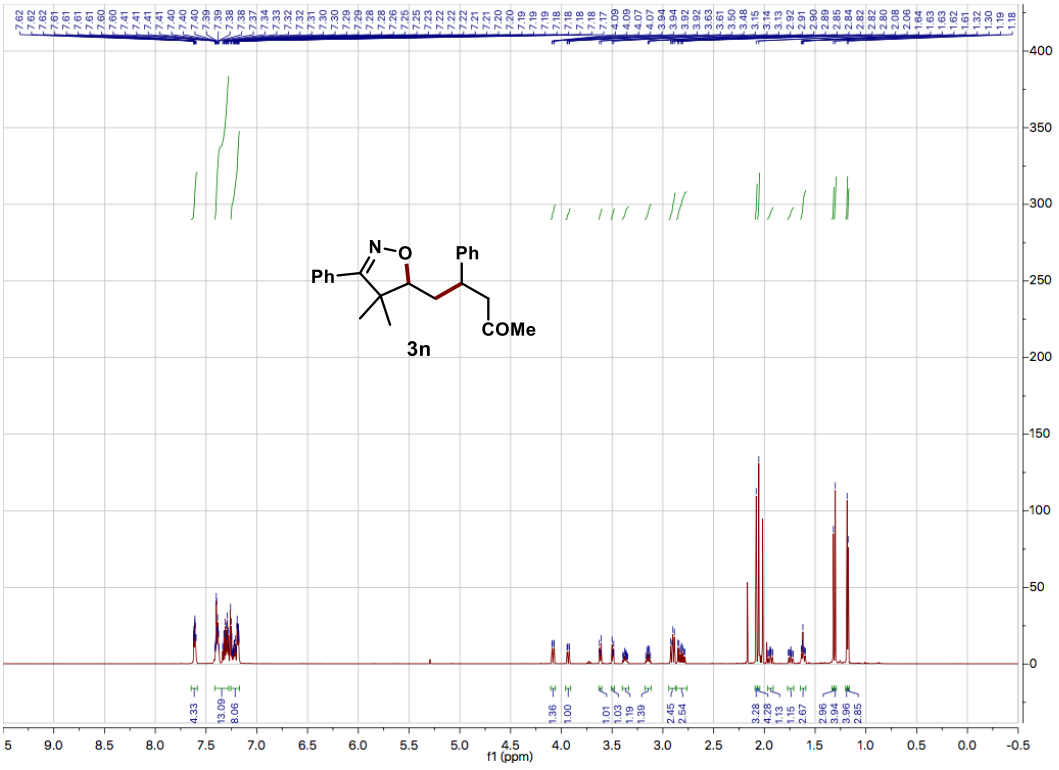
O
Bz
COPh
3m
f1 (ppm)


Ph
N
O
Bz
COPh
3m
f1 (ppm)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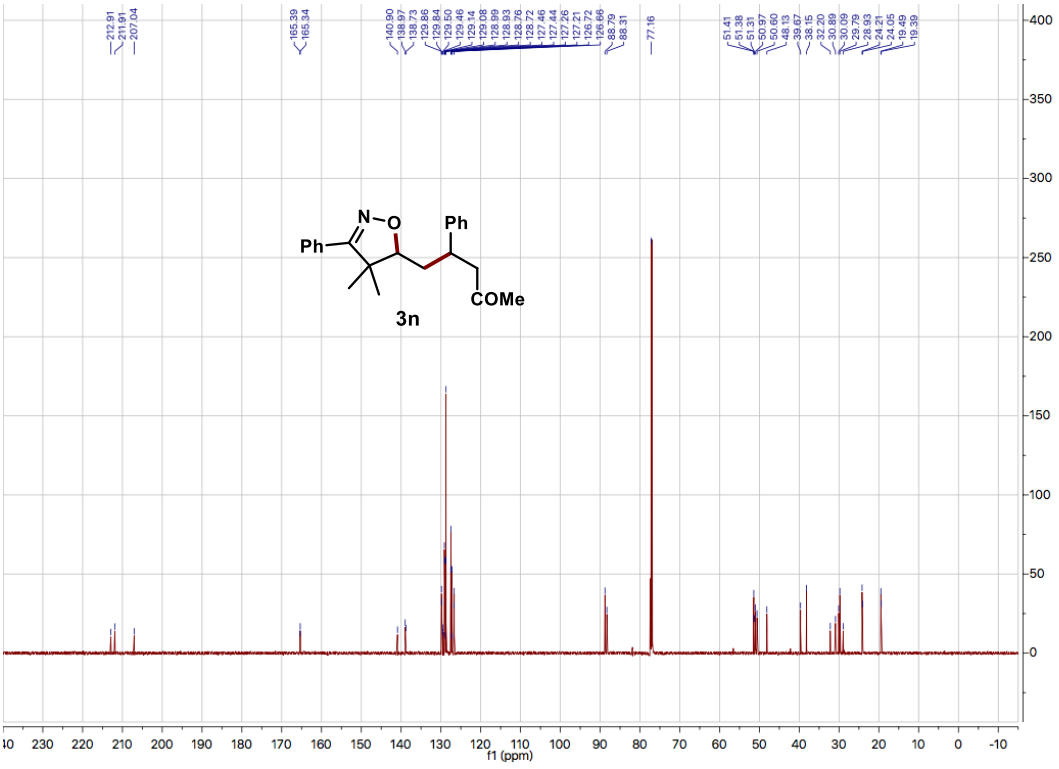
O
Ph
COMe
3n
f1 (ppm)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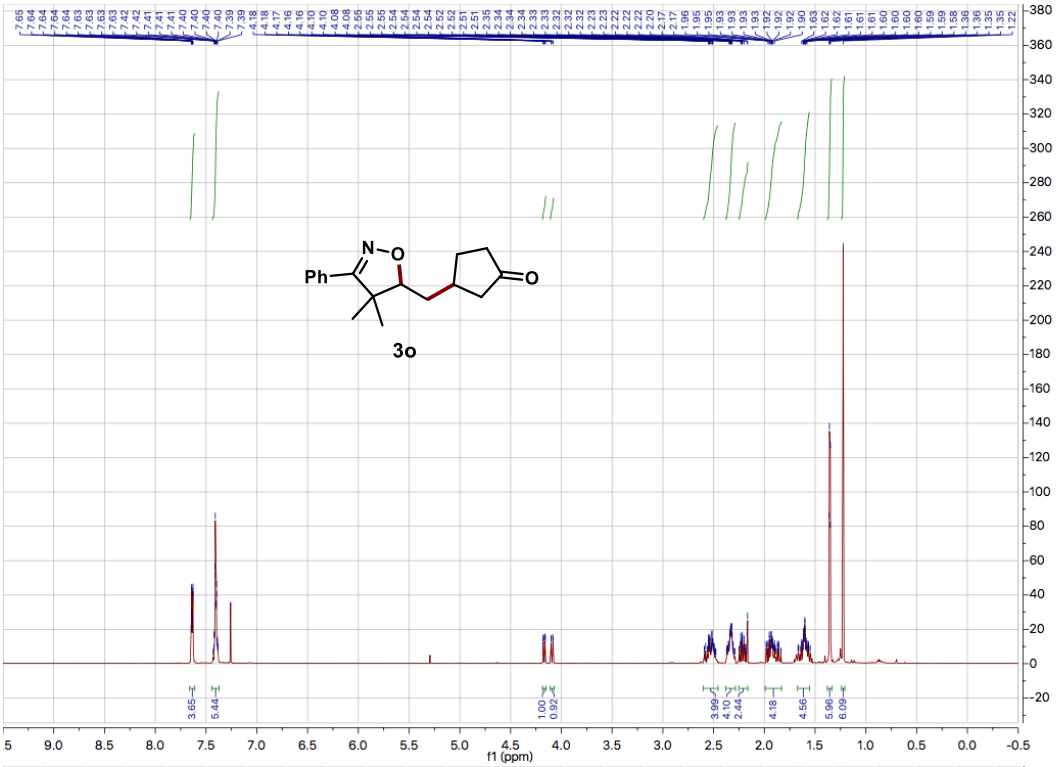
N
O
Ph
COMe
3n
f1 (ppm)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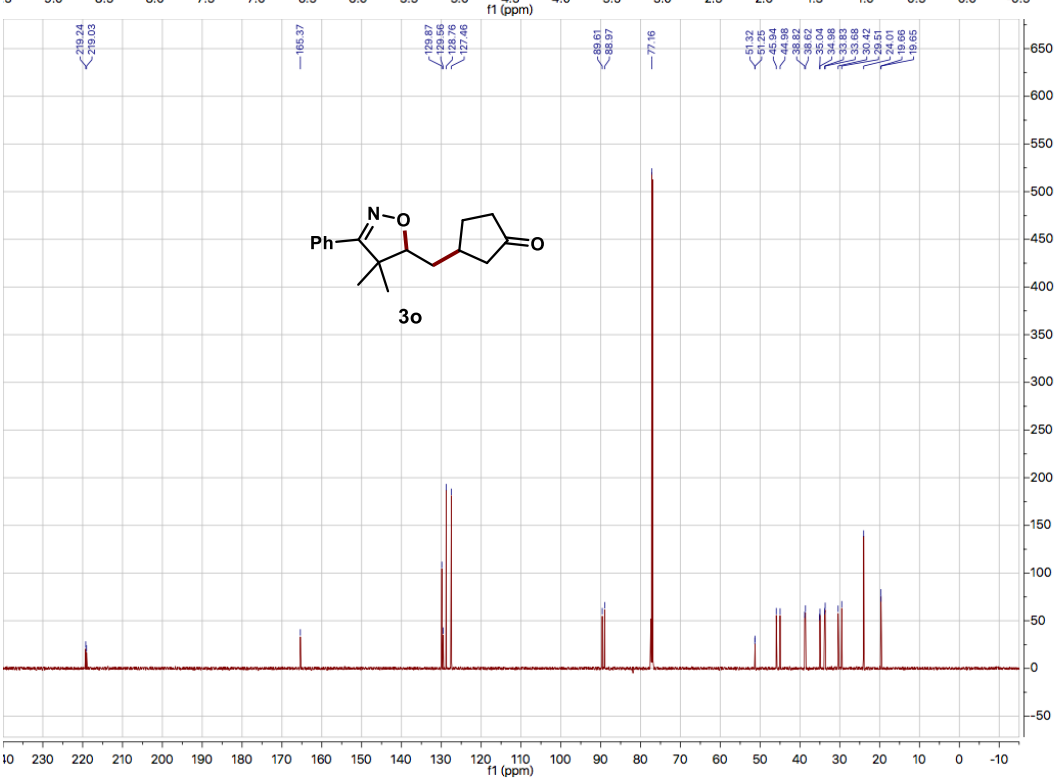
O
O
3o
f1 (ppm)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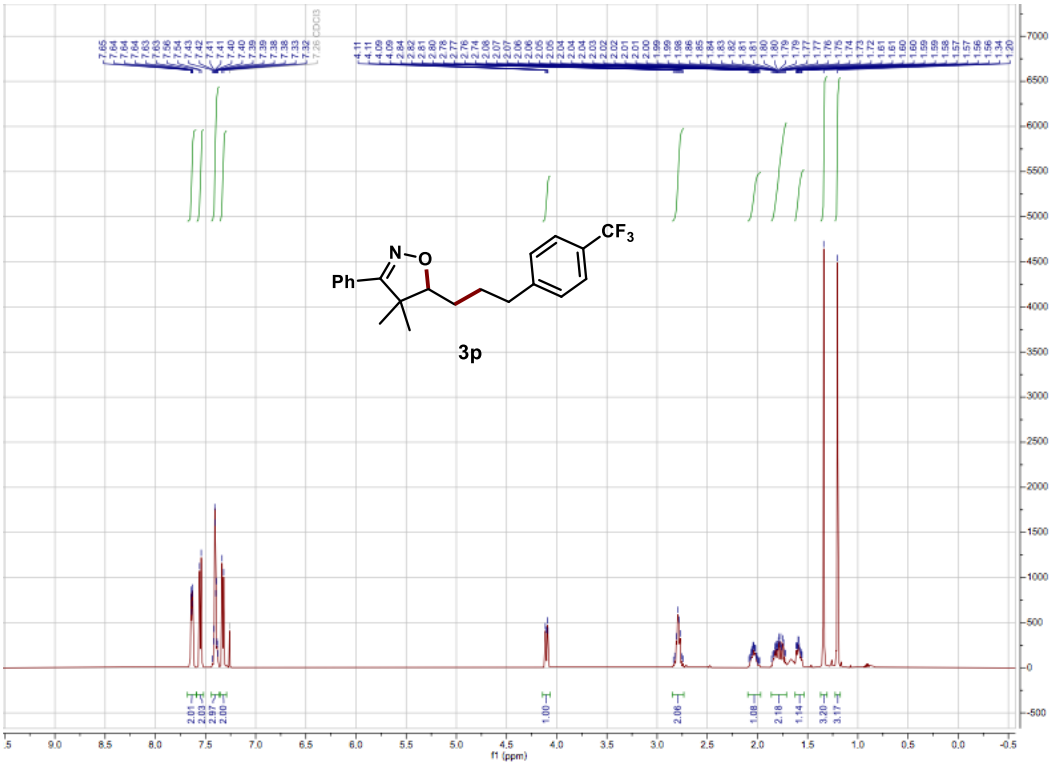
O
O
3o
f1 (ppm)


Ph
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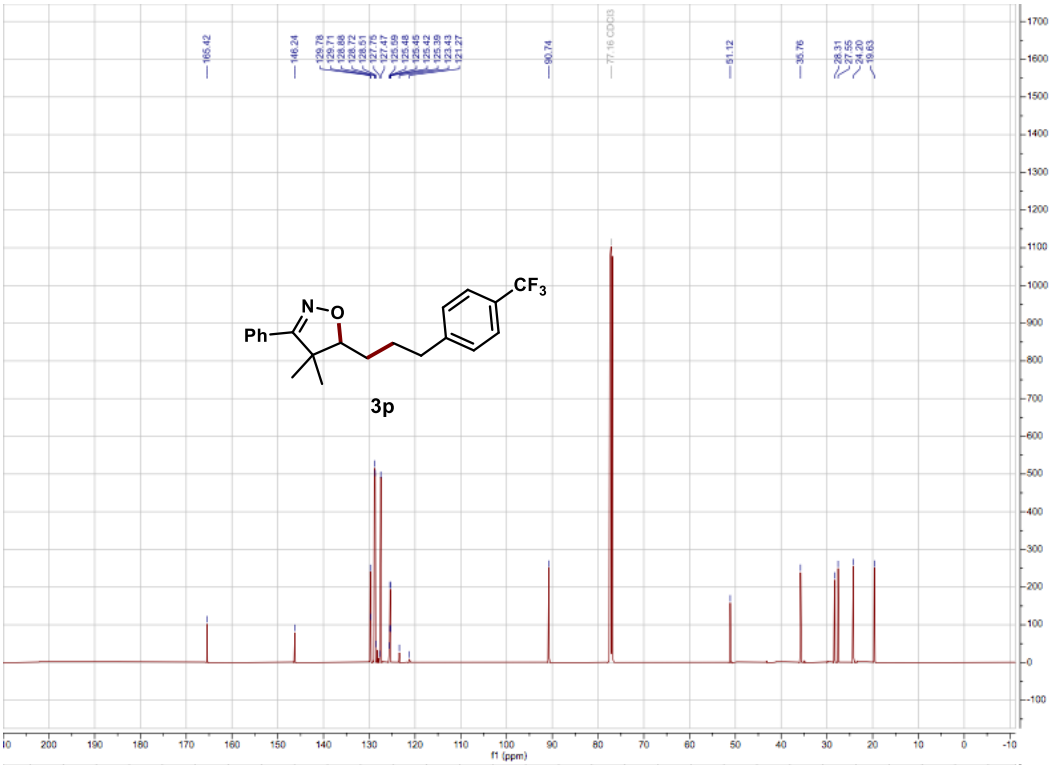
O
CF3
3p
f1 (ppm)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128.72
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127.75
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125.59
125.48
125.45
125.43
125.39
123.43
121.27
90.74
77.16 CDCl3
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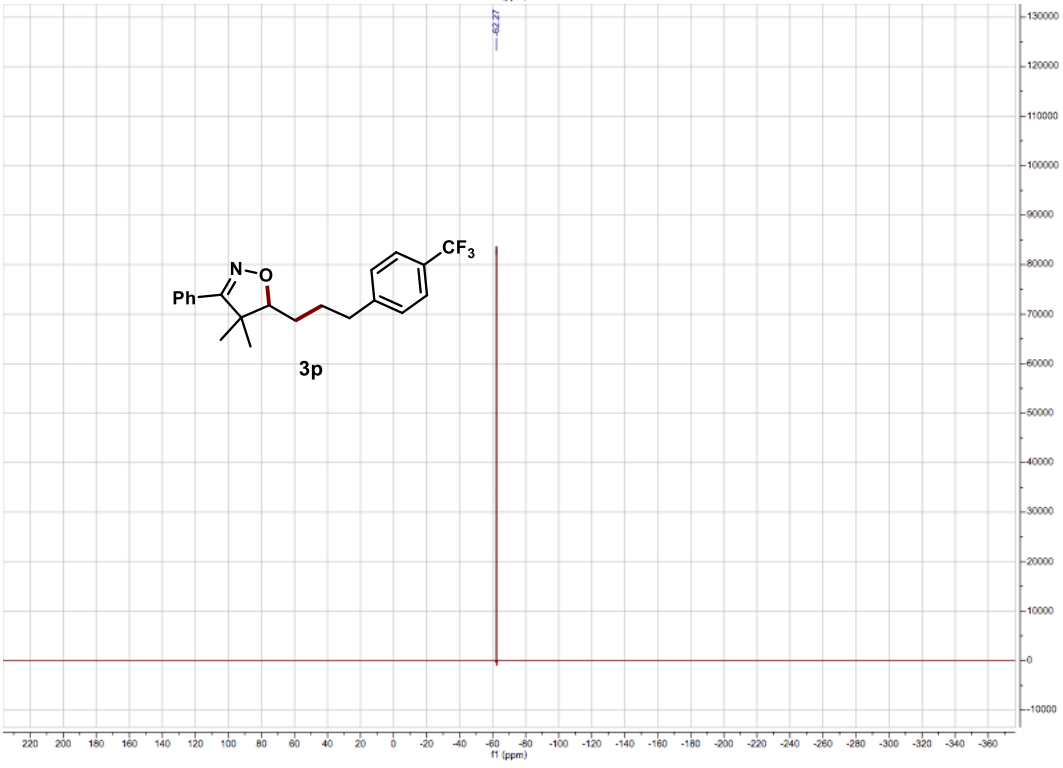
35.76
28.31
27.55
24.20
19.63
CF3
N
O
Ph
3p
f1 (ppm)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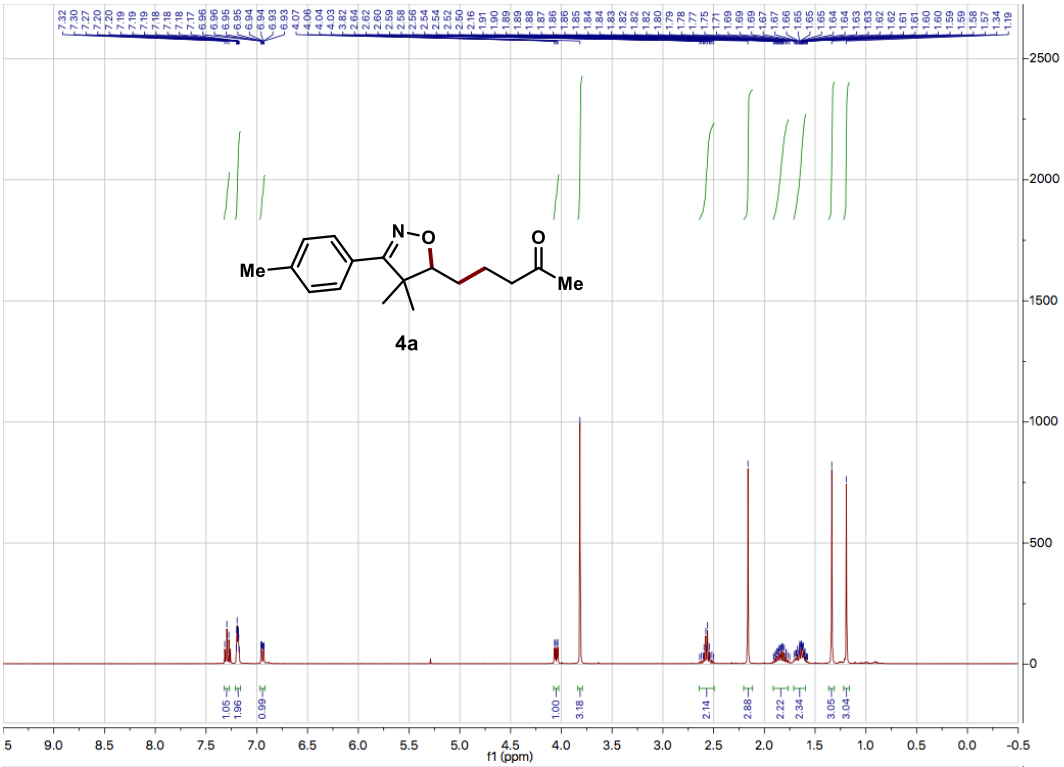
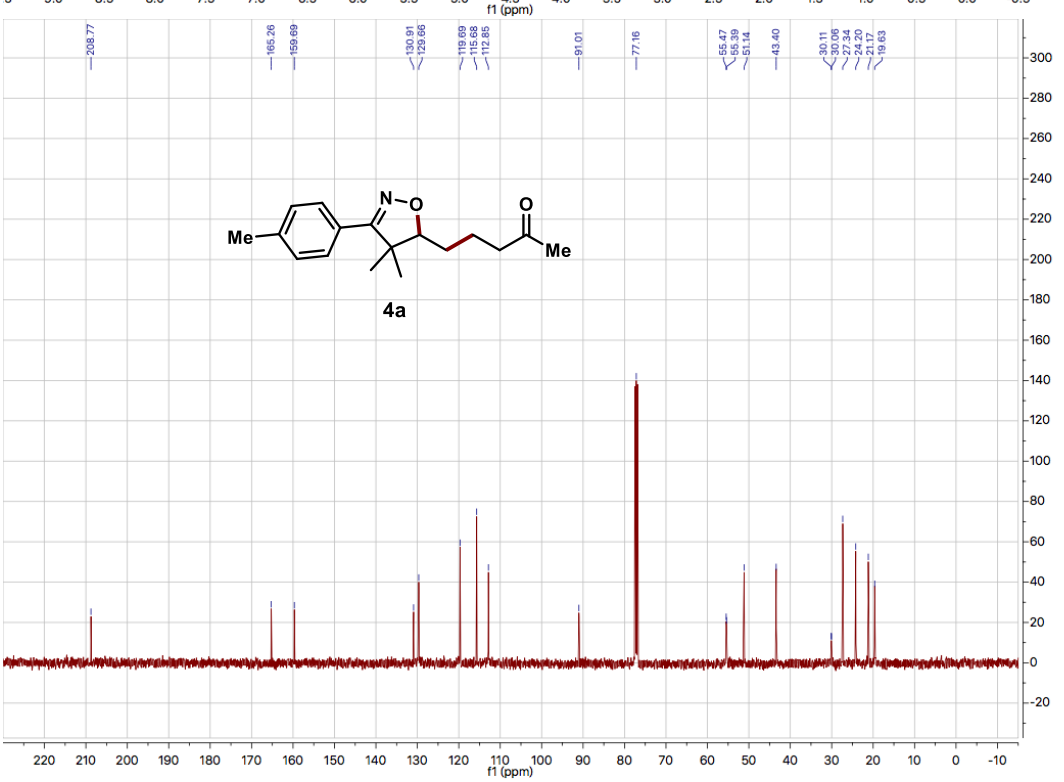
3p
f1 (ppm)


Me
N
O
O
Me
4a
f1 (ppm)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O
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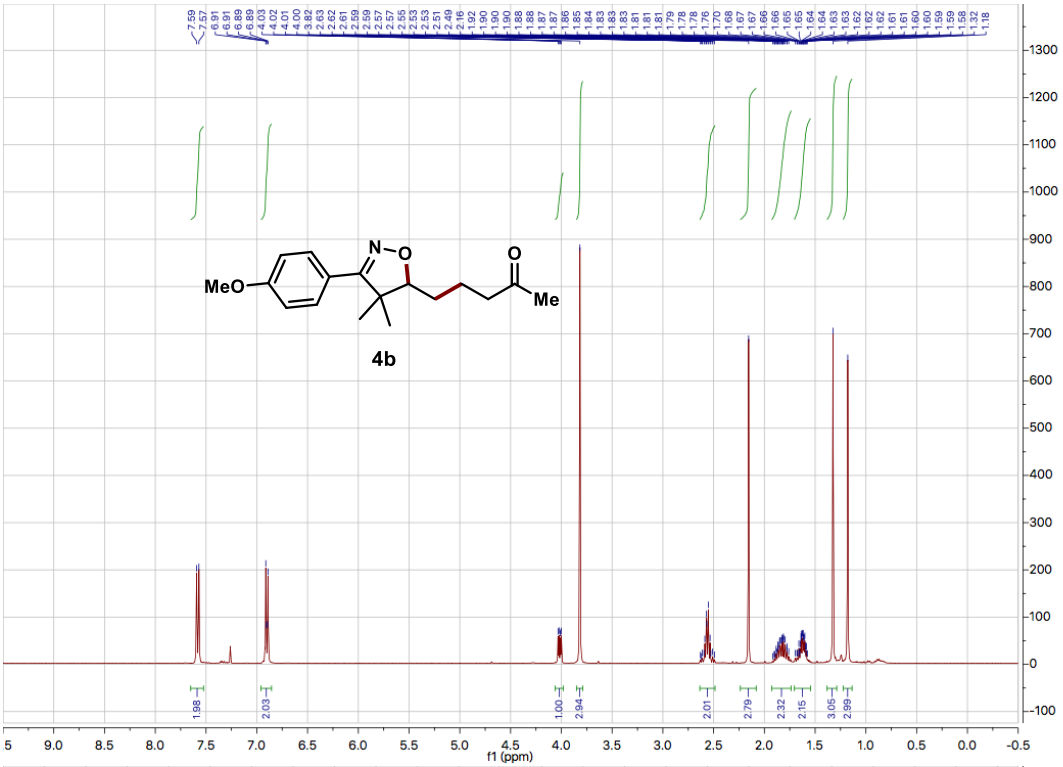
4a
f1 (ppm)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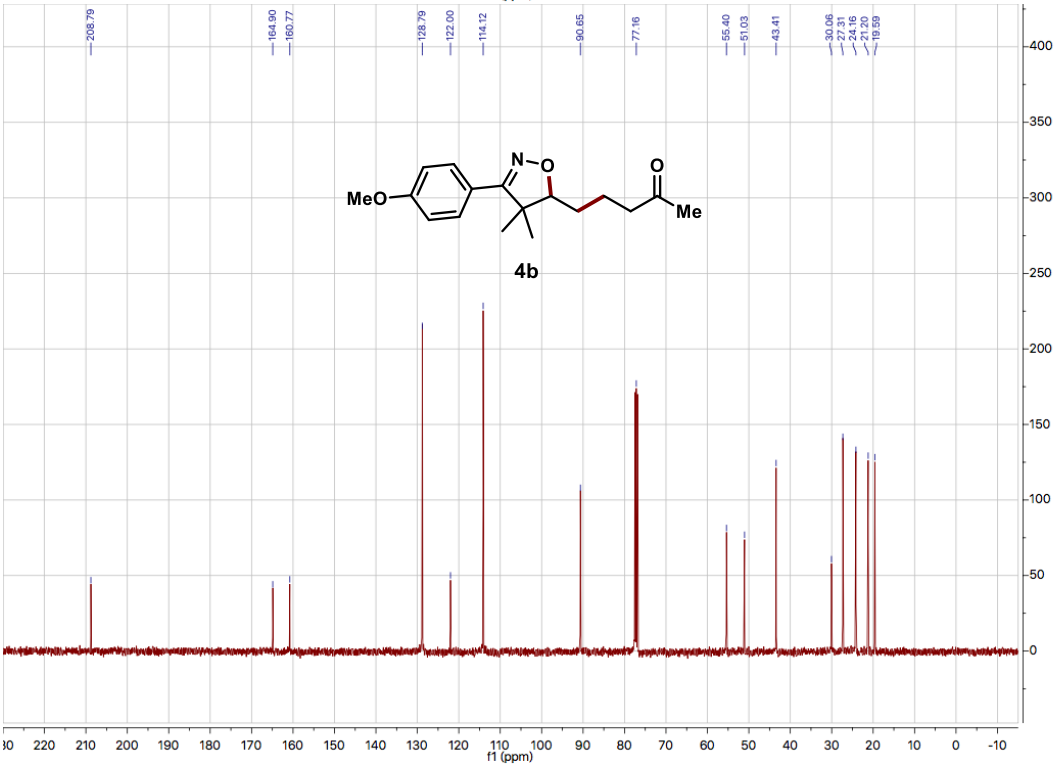
N
O
O
Me
4b
f1 (ppm)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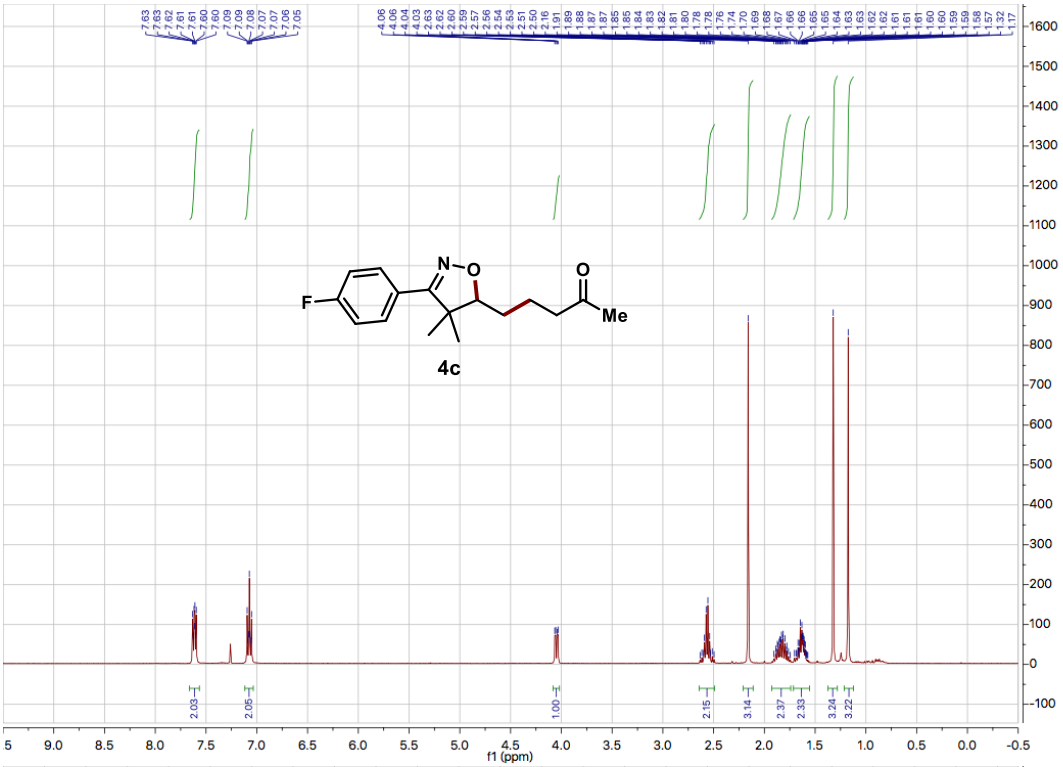
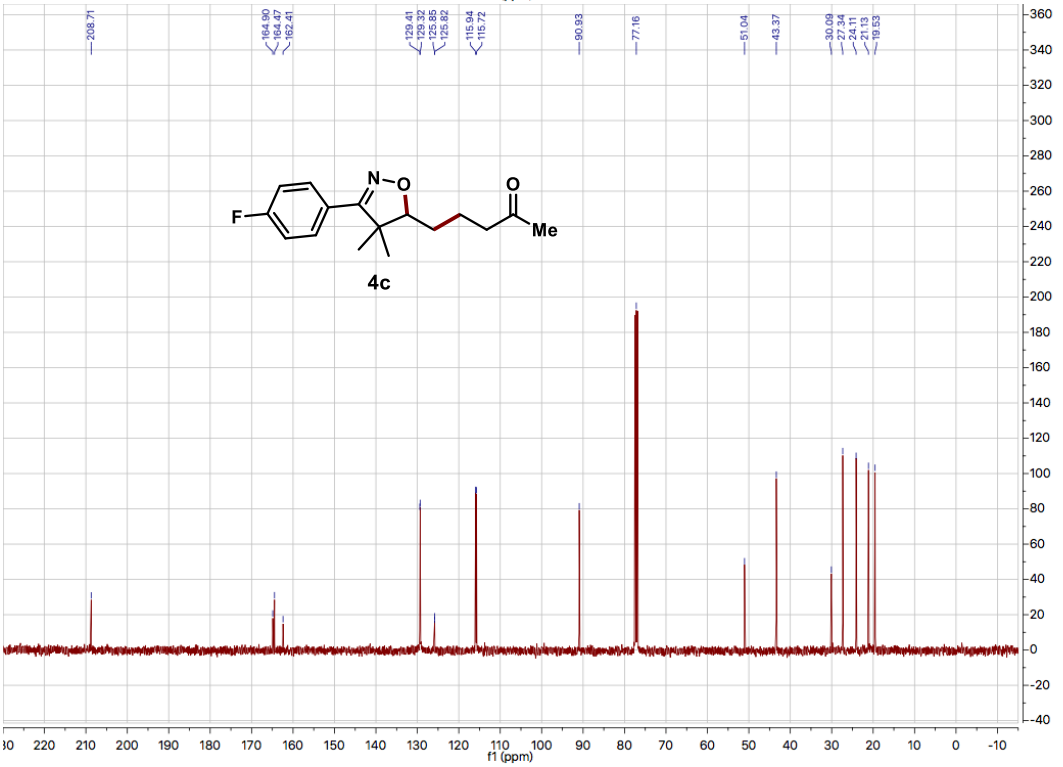
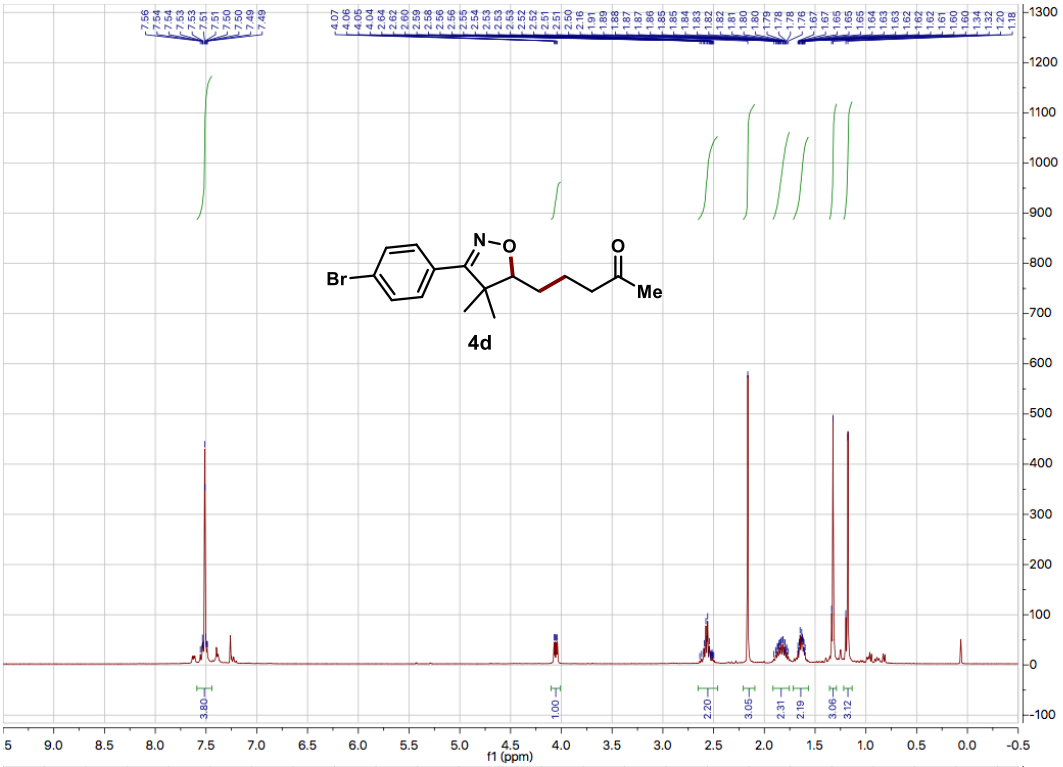
N
O
O
Me
4b
f1 (ppm)


F
N
O
O
Me
4c
f1 (ppm)


F
N
O
O
Me
4c
f1 (ppm)


Br
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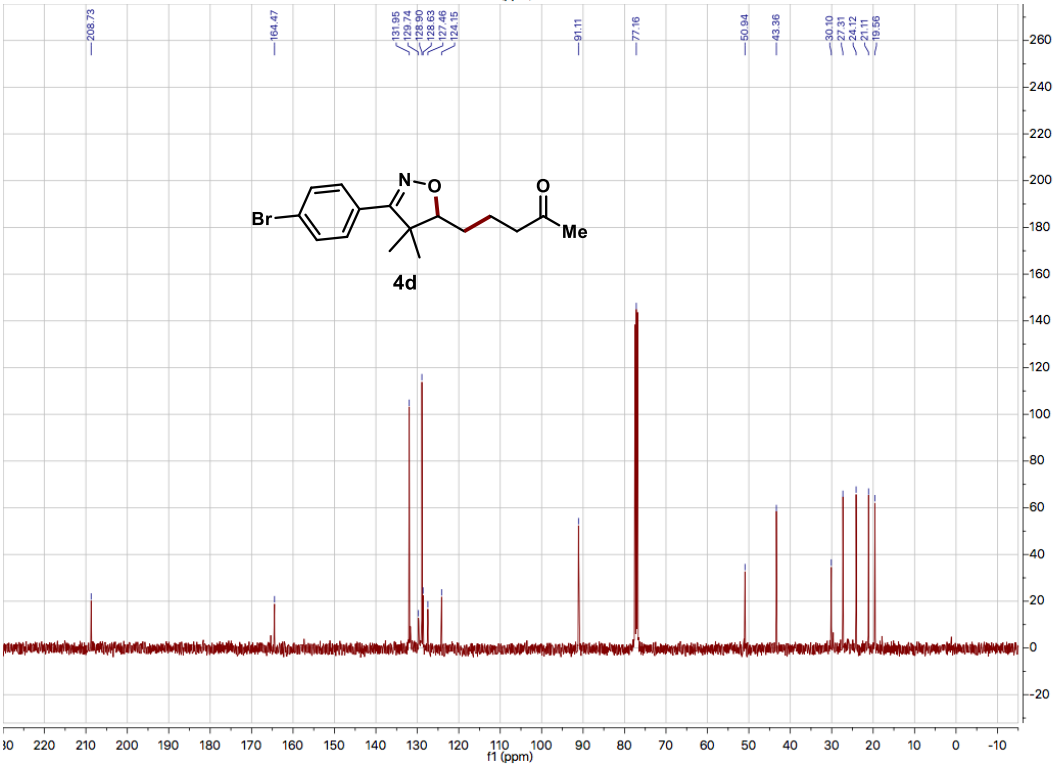
O
O
Me
4d
f1 (ppm)


Br
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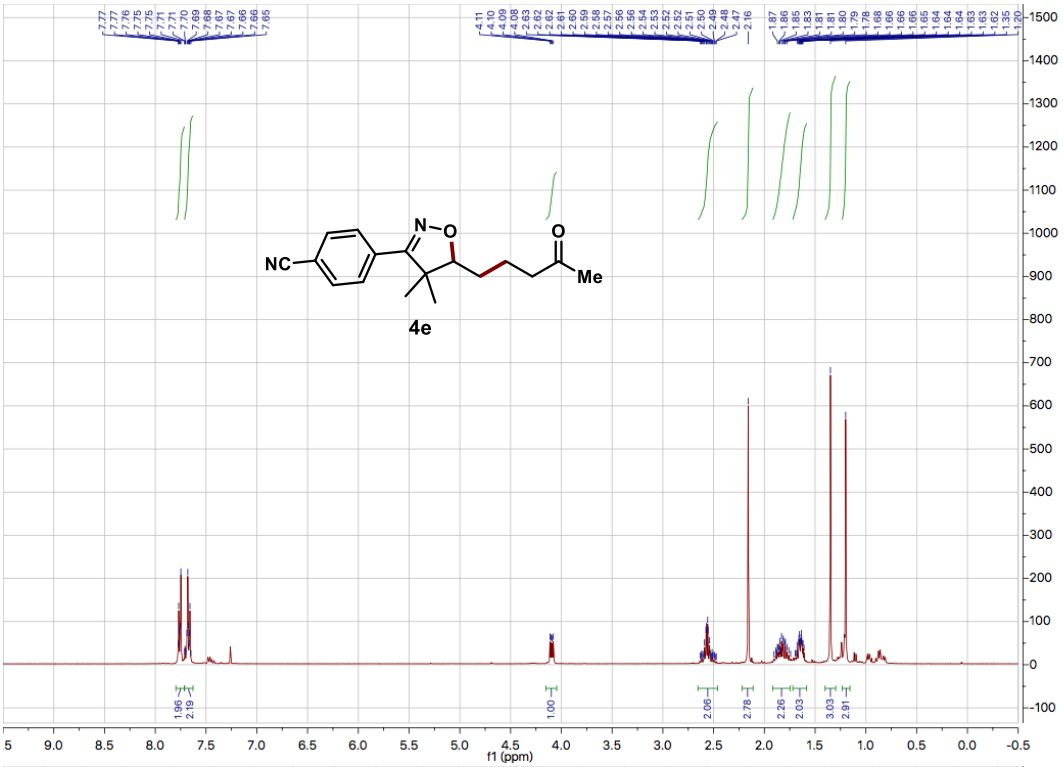
O
O
Me
4d
f1 (ppm)


NC
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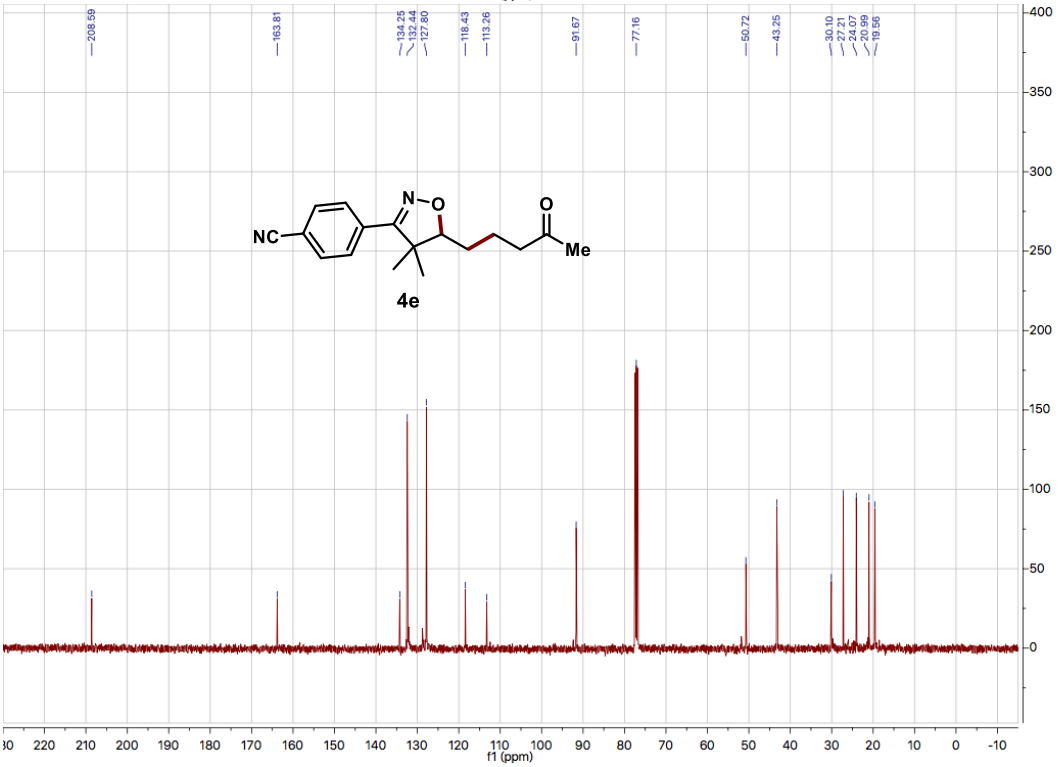
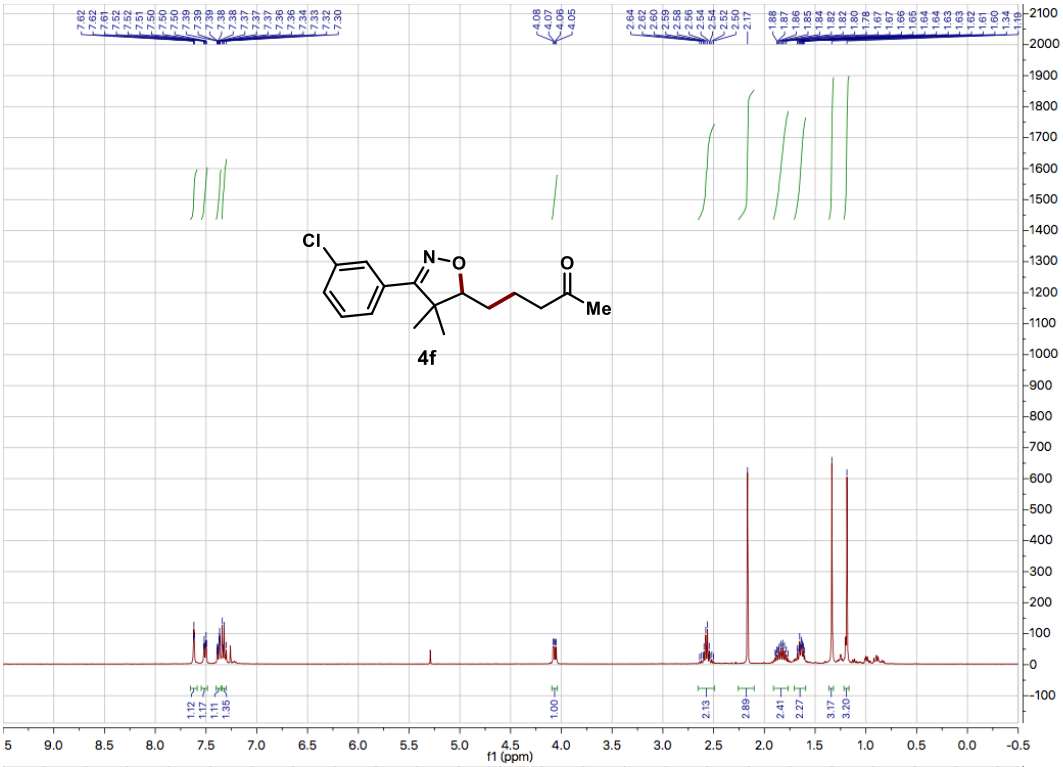
O
O
Me
4e
f1 (ppm)


NC
N
O
O
Me
4e
f1 (ppm)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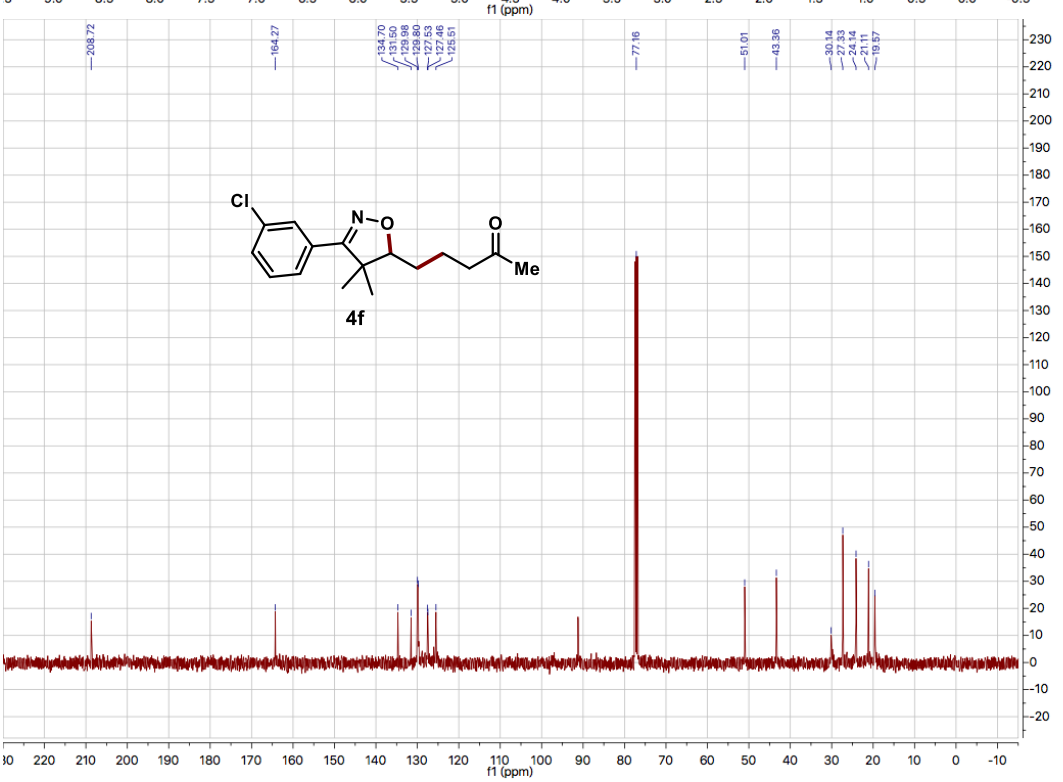
O
O
Me
4f
f1 (ppm)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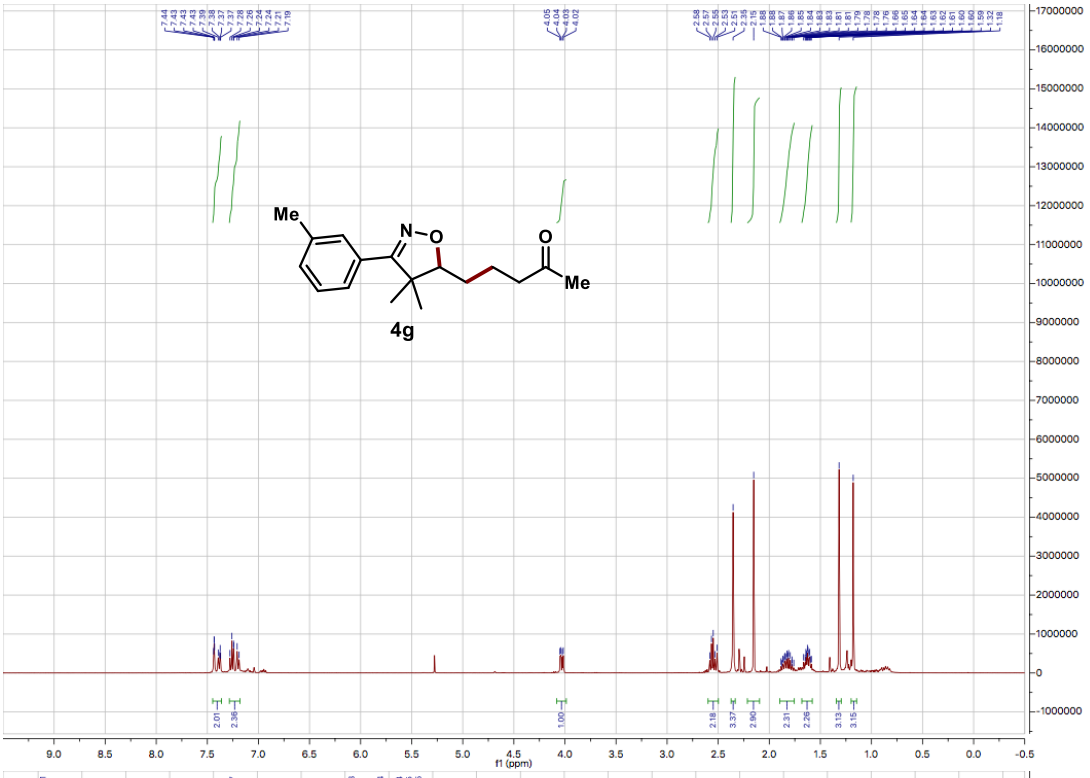
O
Me
4f
f1 (ppm)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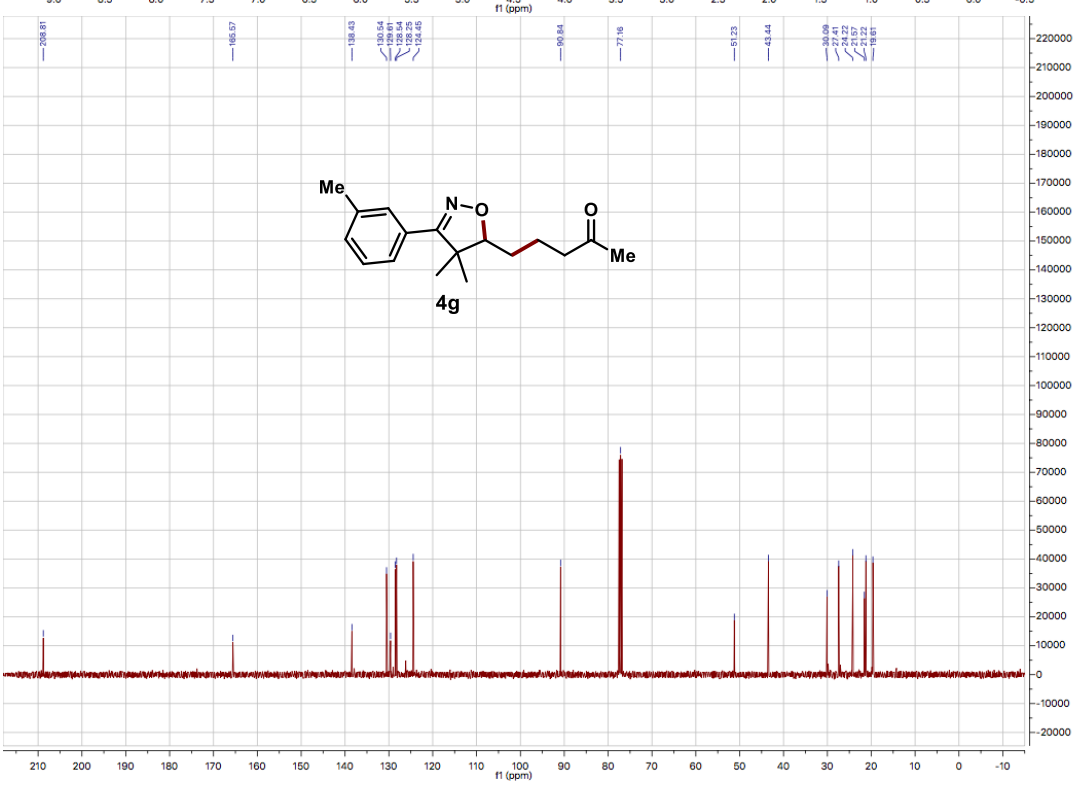
Me
4g
f1 (ppm)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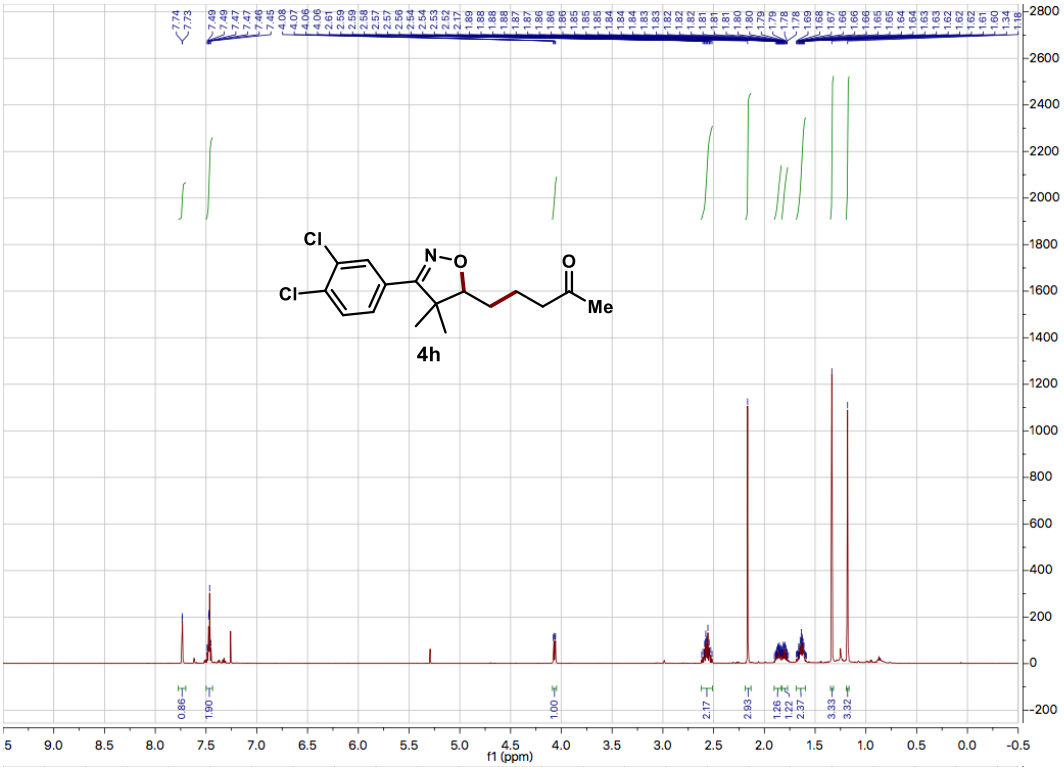
O
O
Me
4g
f1 (ppm)


Cl
Cl
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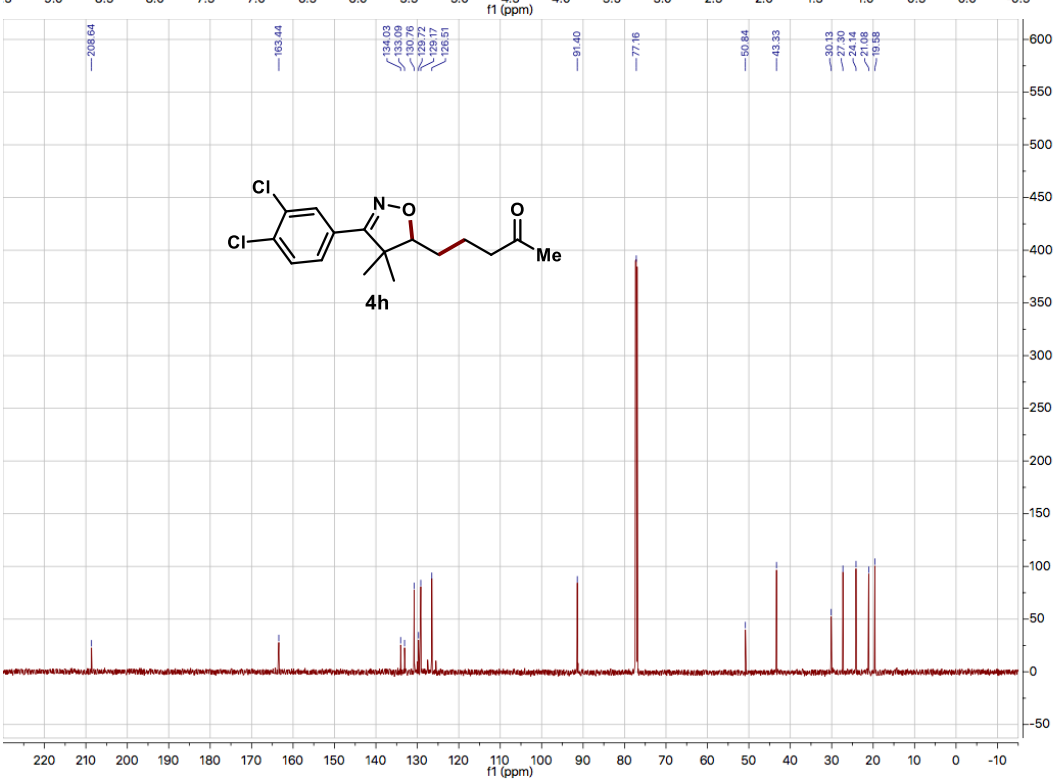
O
O
Me
4h
f1 (ppm)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129.17
126.51
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77.16
50.84
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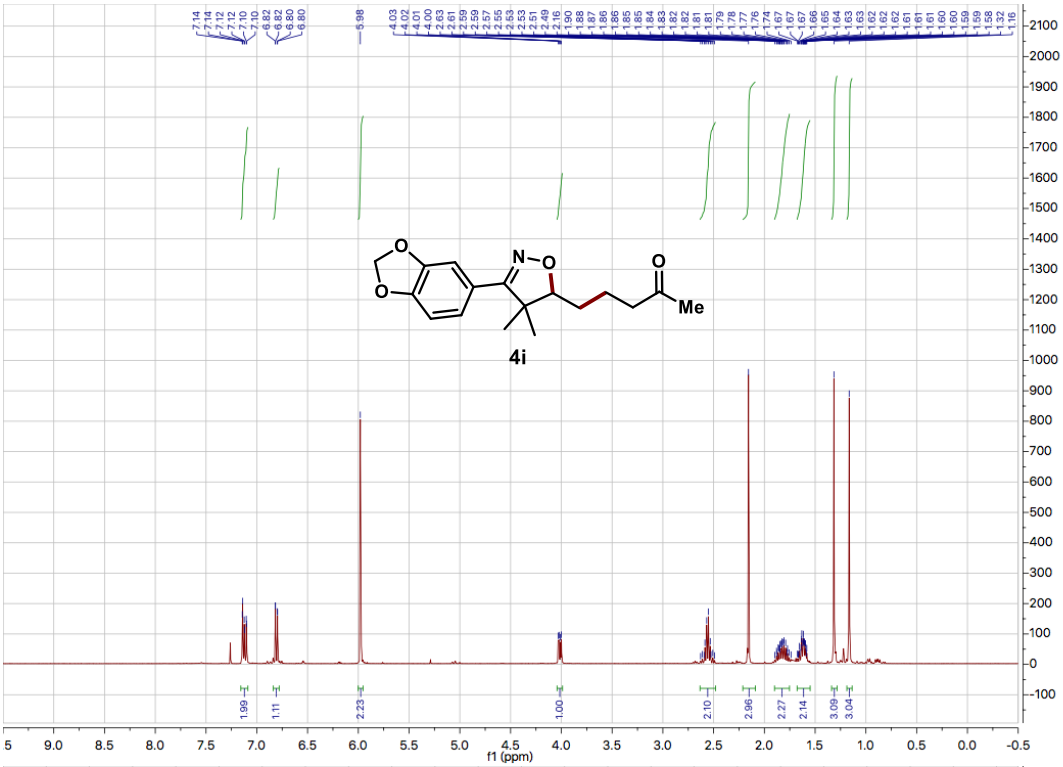
27.30
24.14
21.08
19.58
Cl
Cl
N
O
O
Me
4h
f1 (ppm)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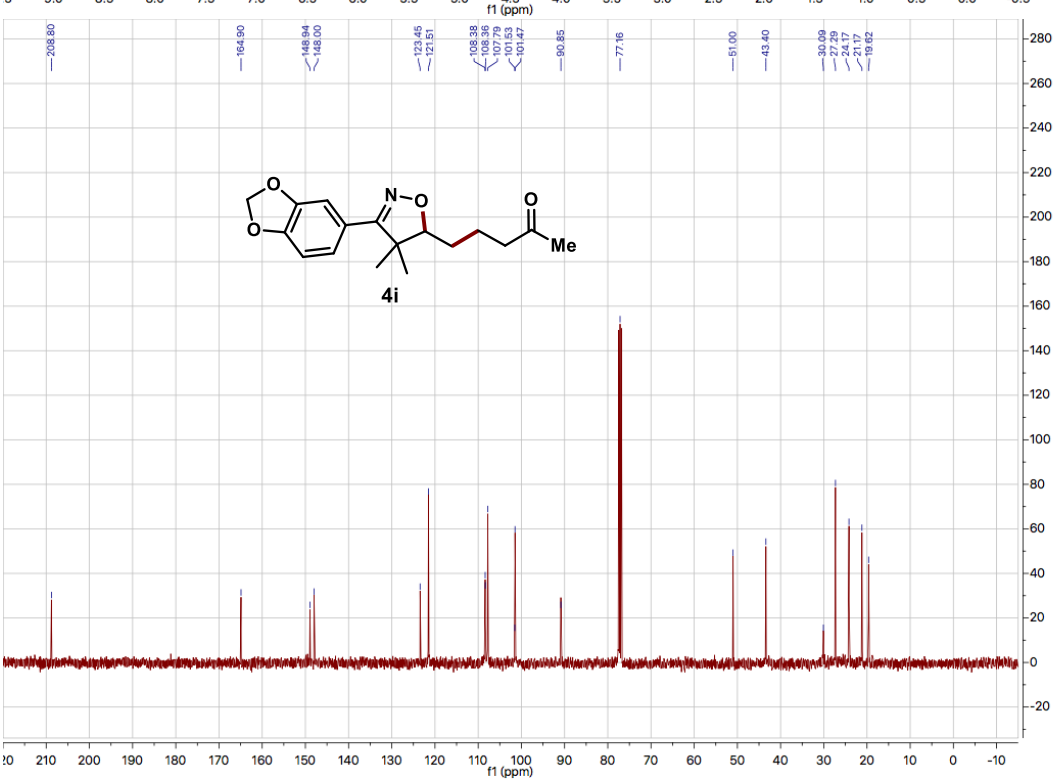
f1 (ppm)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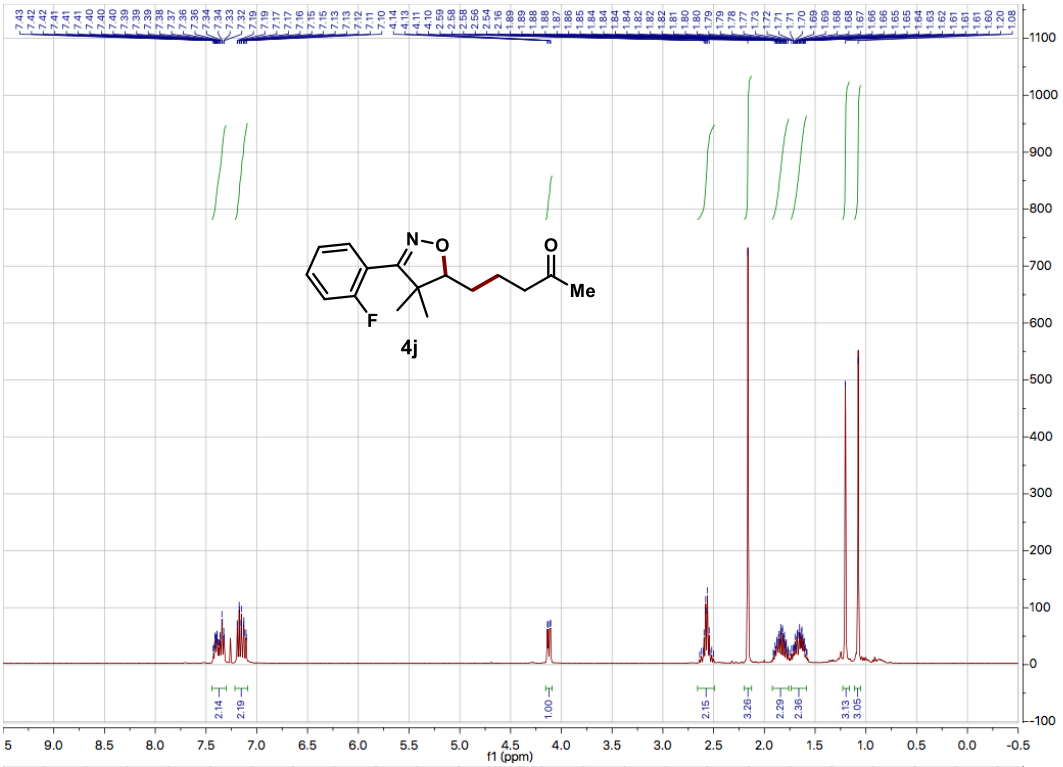
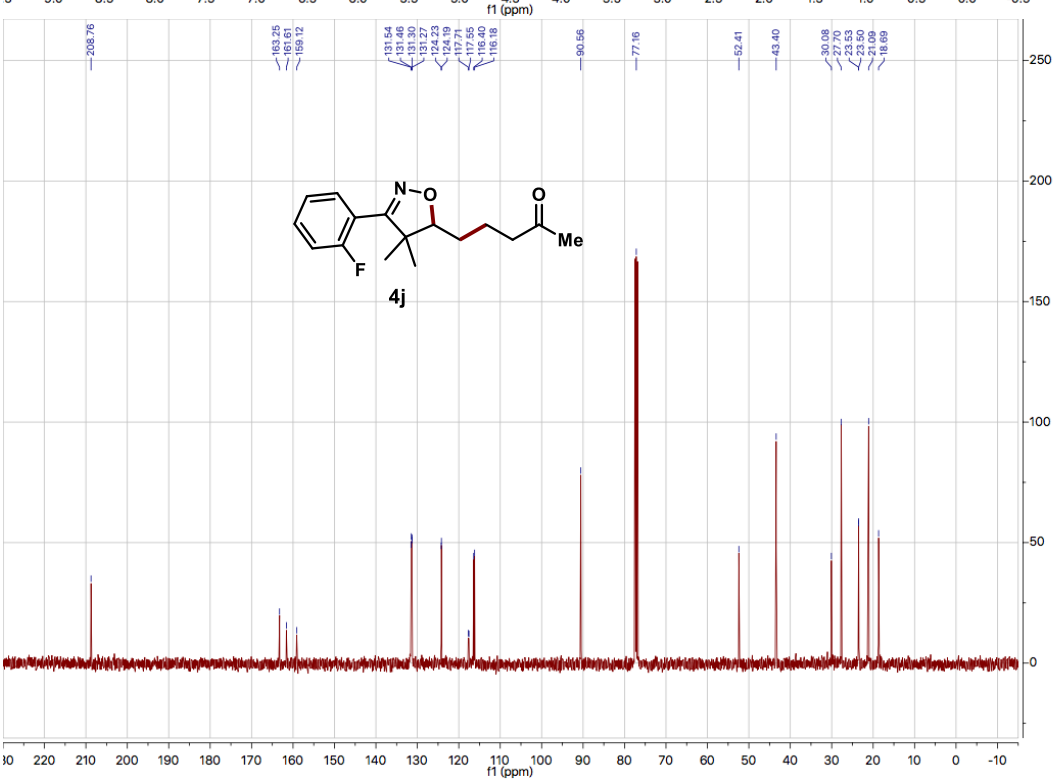
f1 (ppm)


N
O
O
Me
F
4j
f1 (ppm)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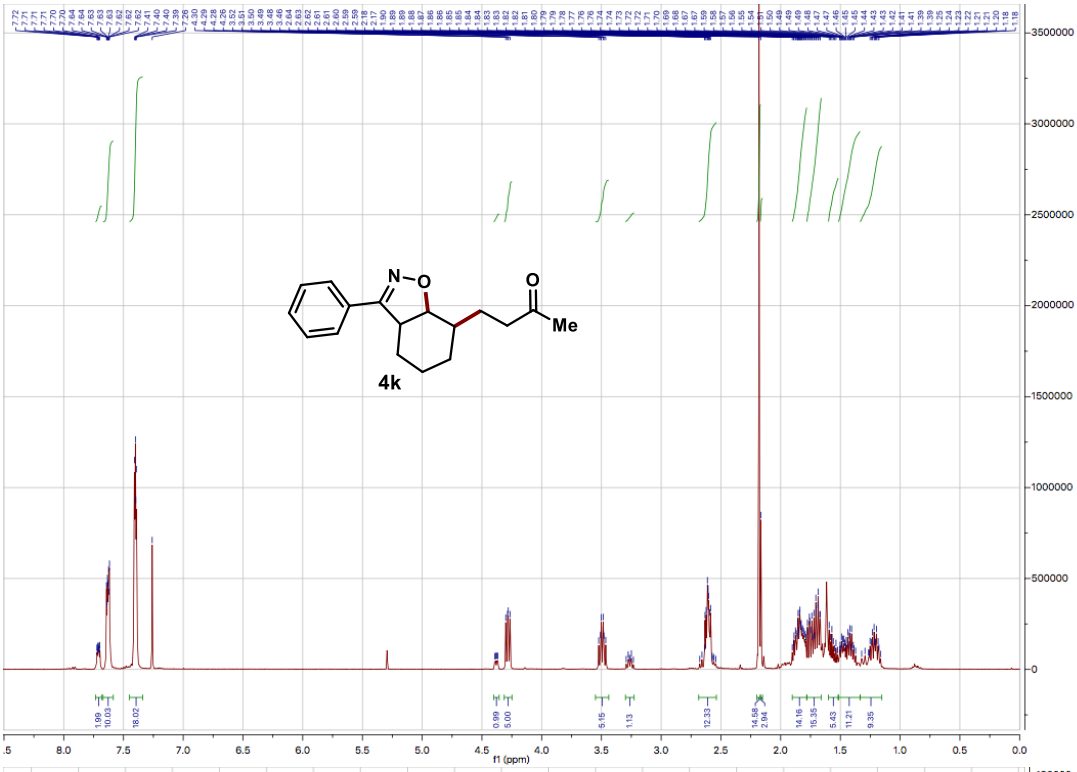
O
O
Me
F
4j
f1 (ppm)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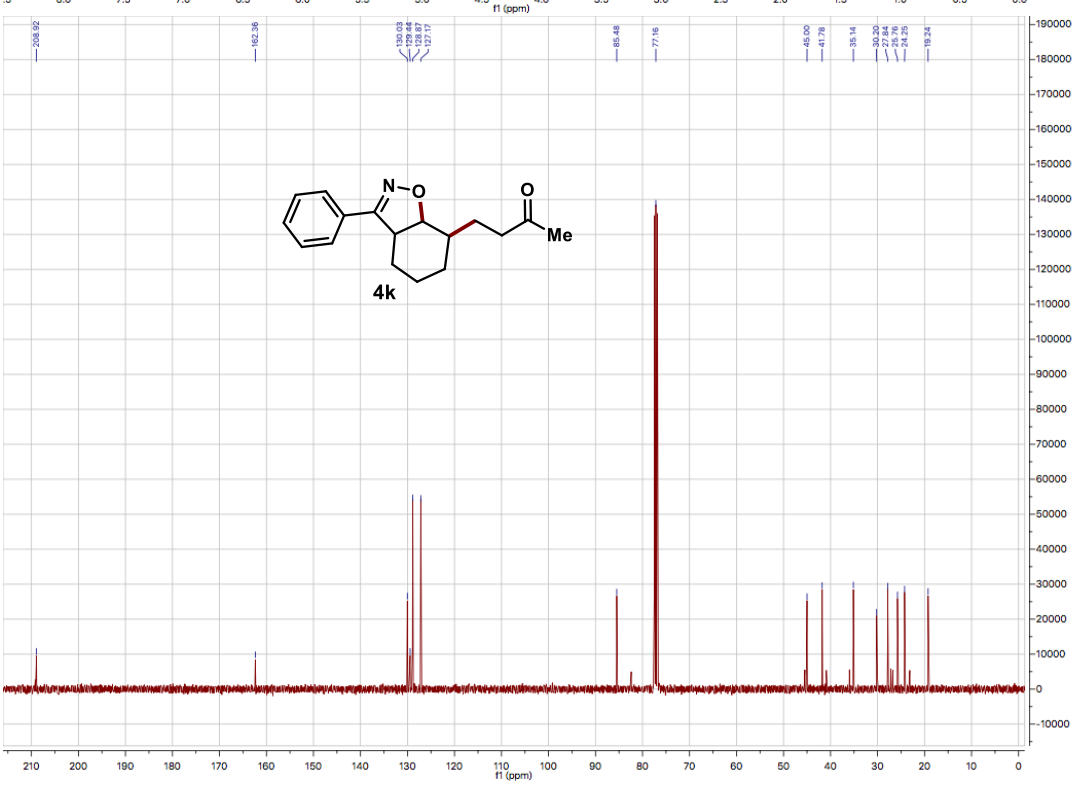
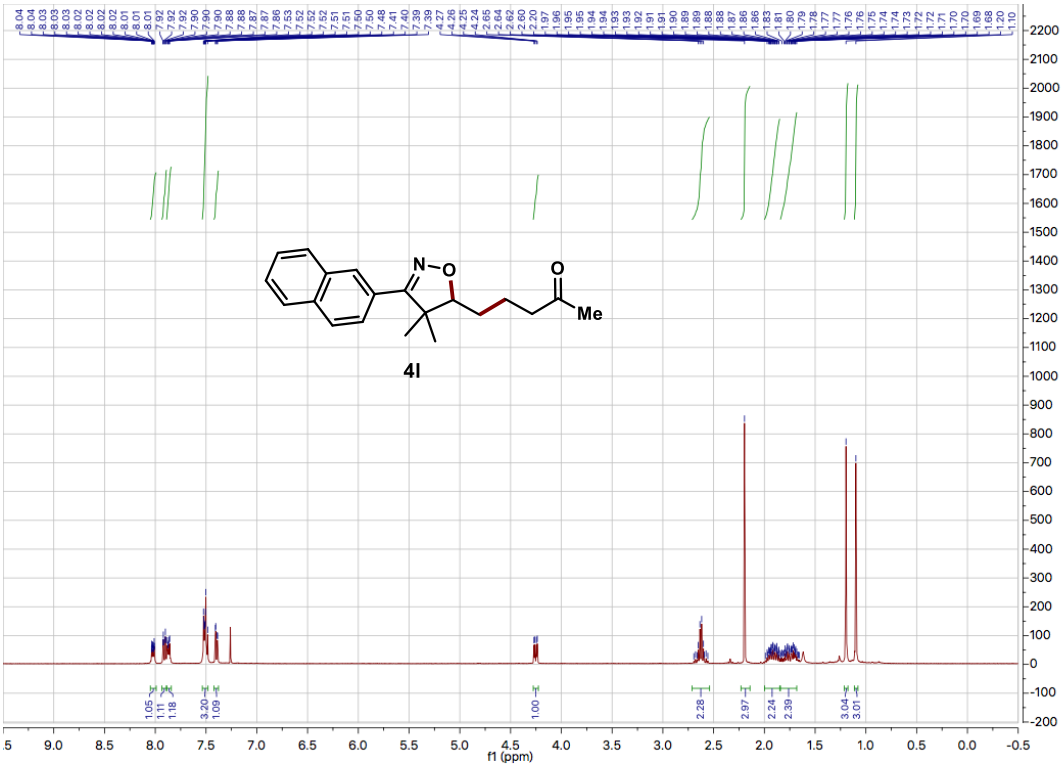
O
O
Me
4k
f1 (ppm)


N
O
O
Me
4k
f1 (ppm)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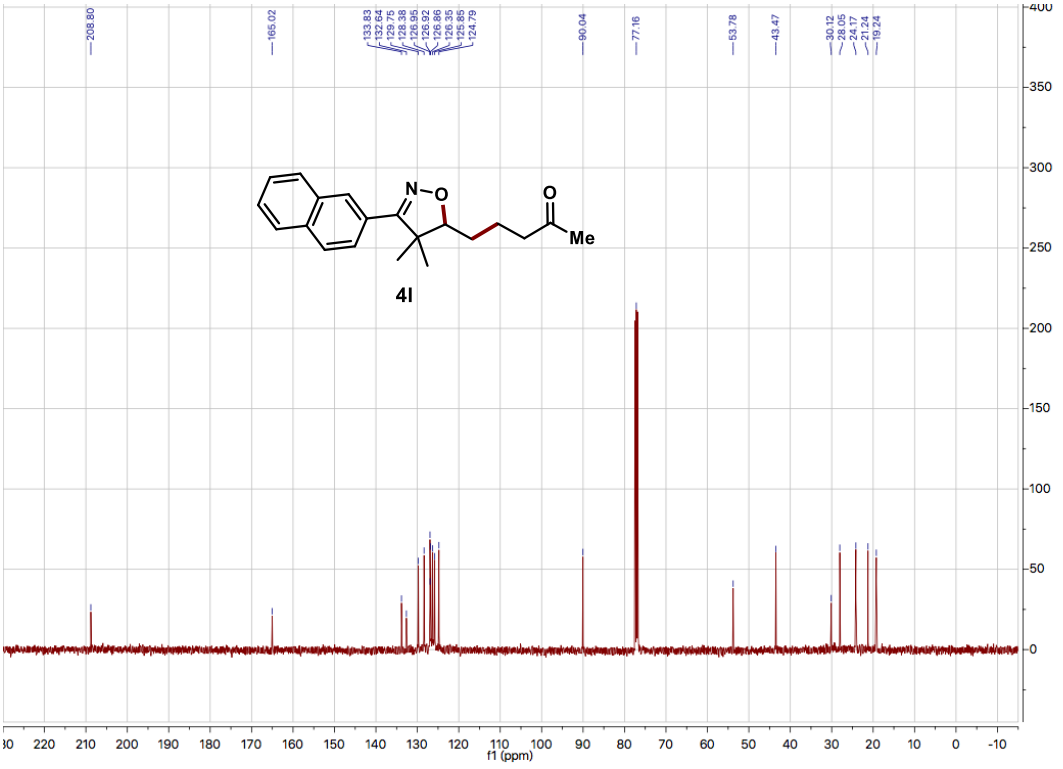
O
O
Me
4l
f1 (ppm)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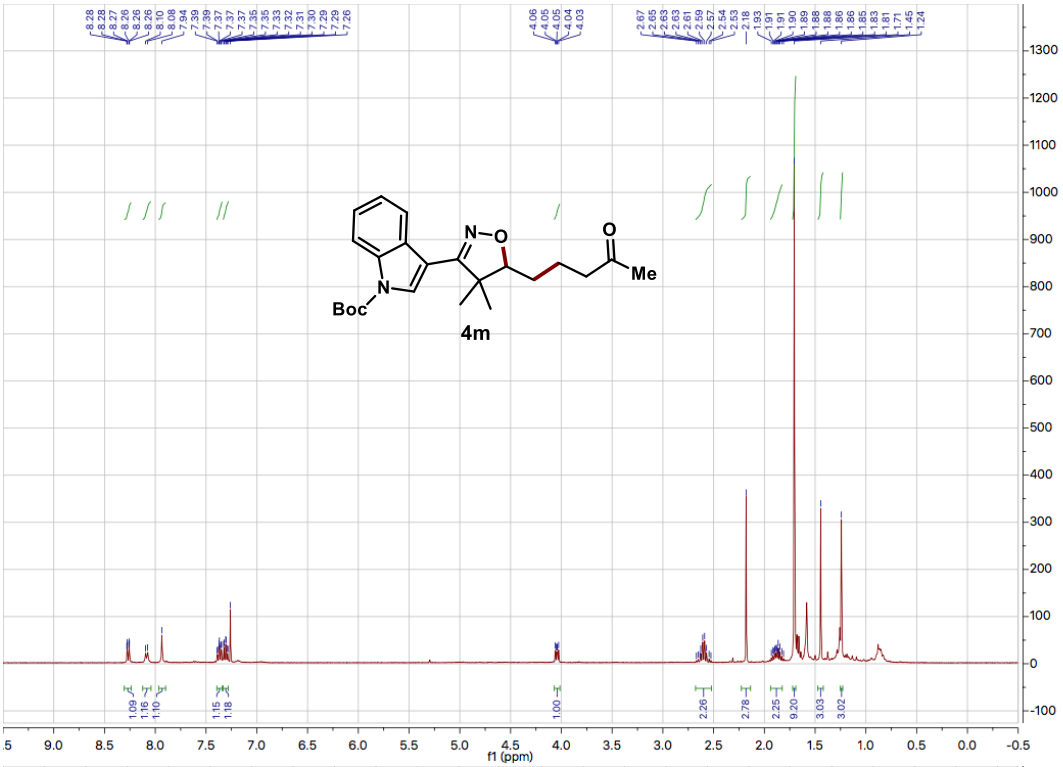
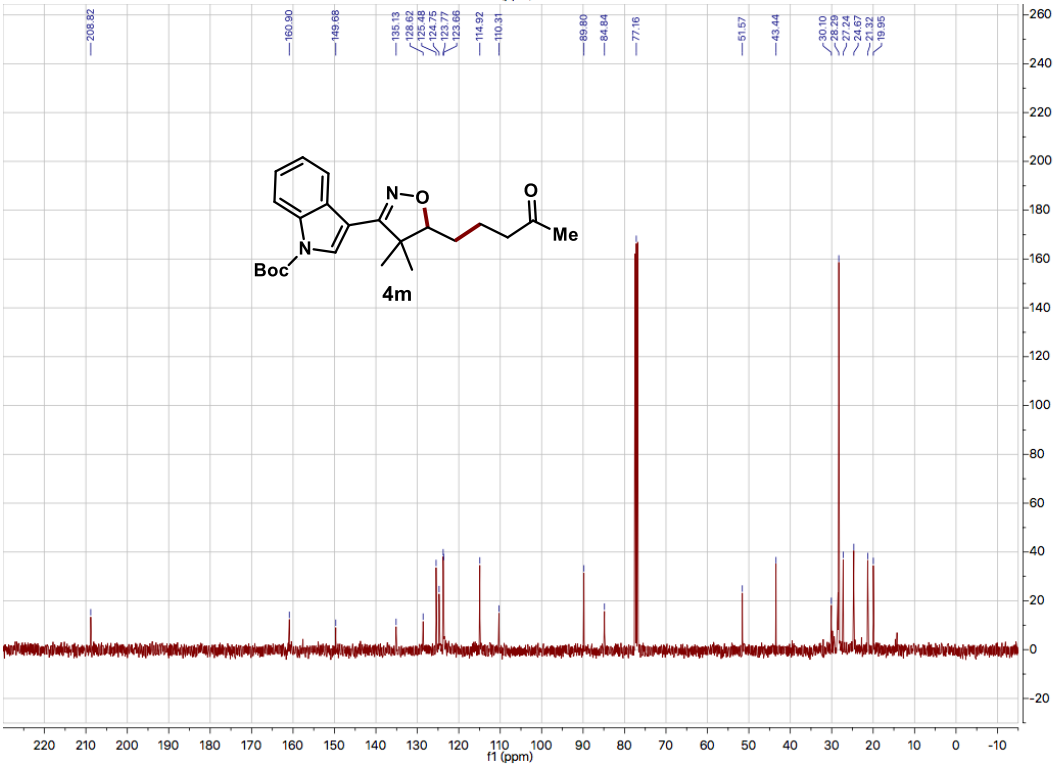
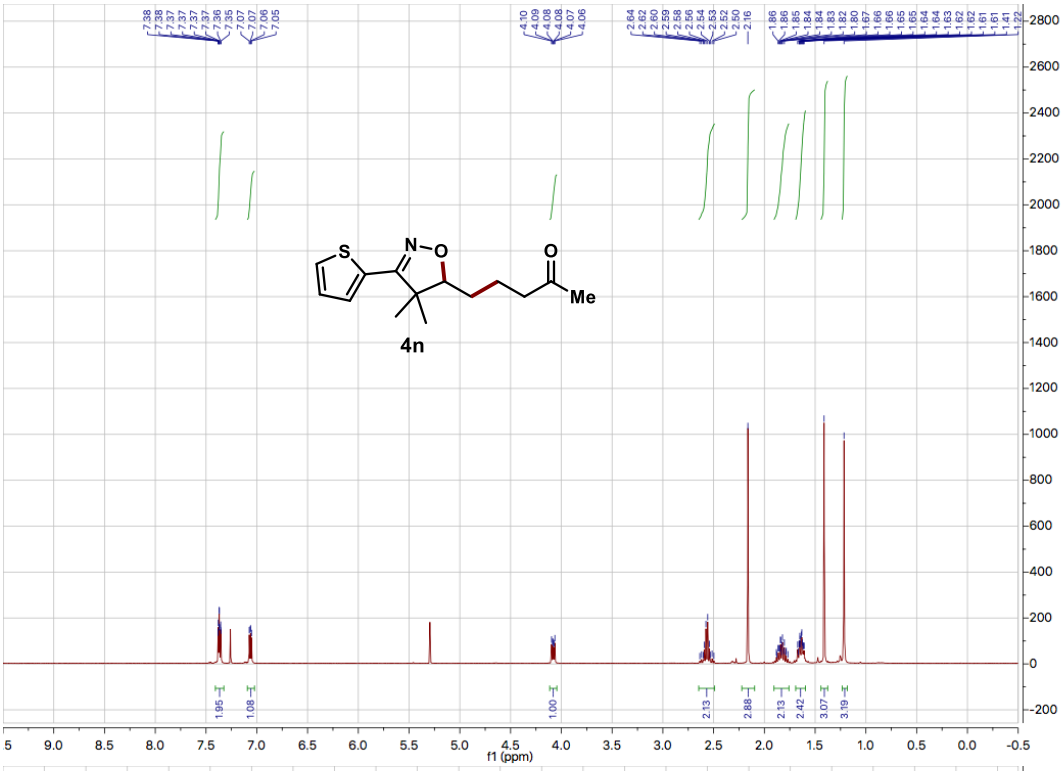
O
O
Me
4l
f1 (ppm)


Boc
N
O
O
Me
4m
f1 (ppm)


Boc
N
O
O
Me
4m
f1 (ppm)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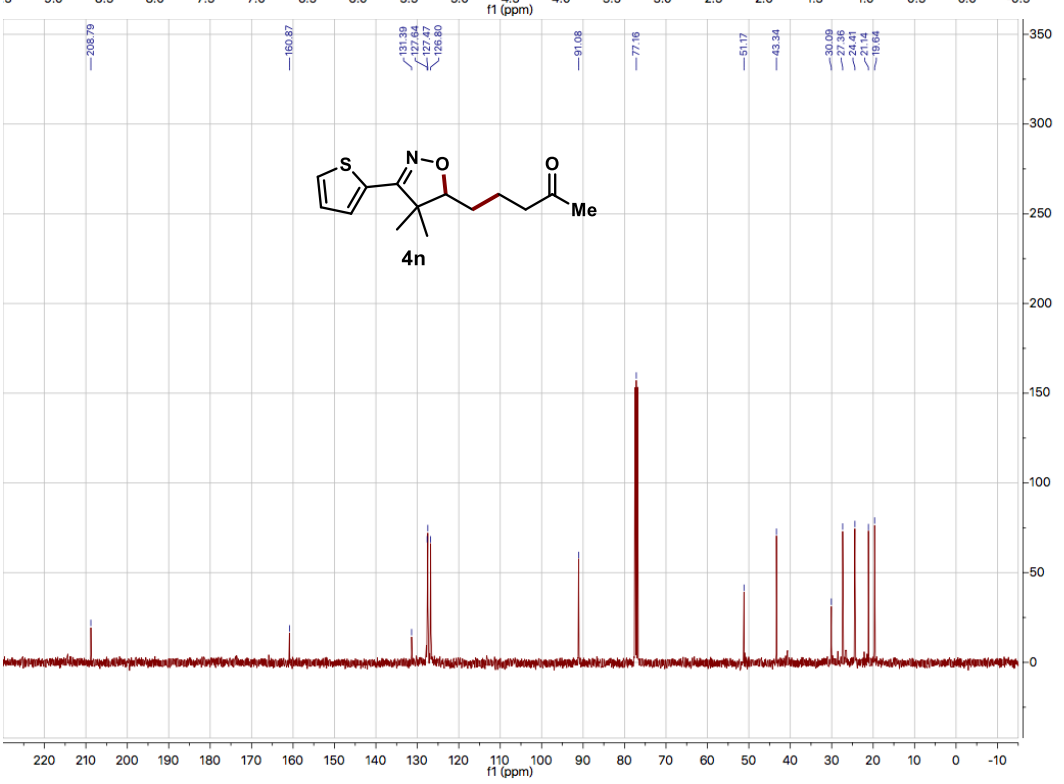
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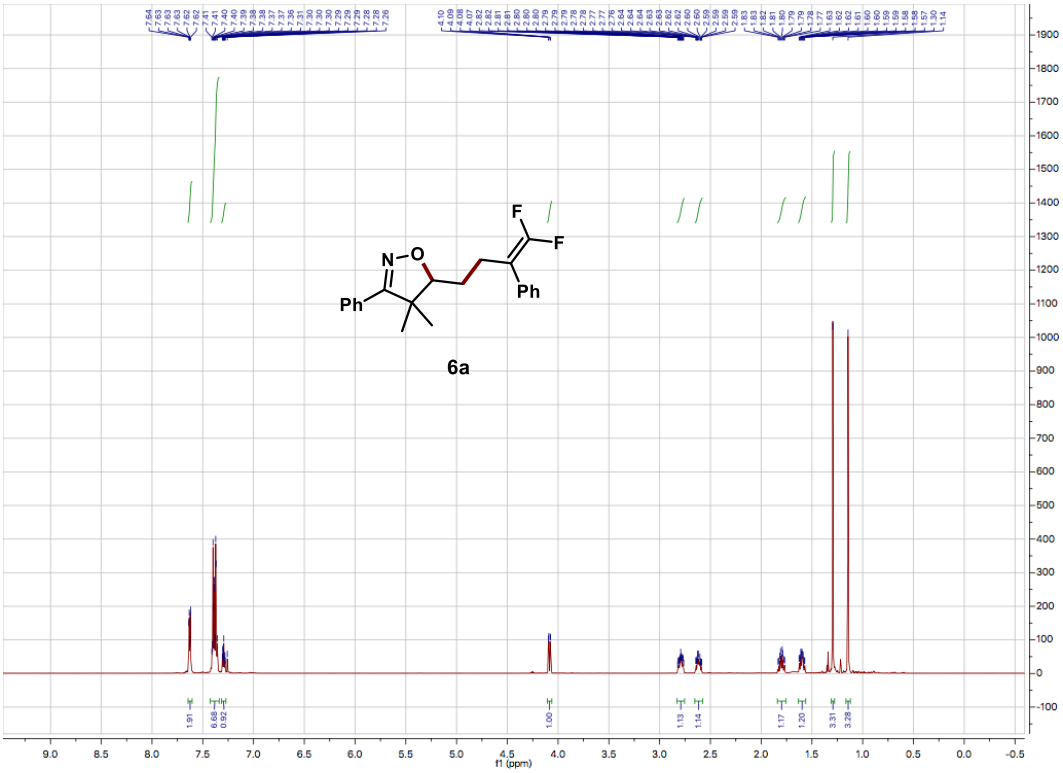
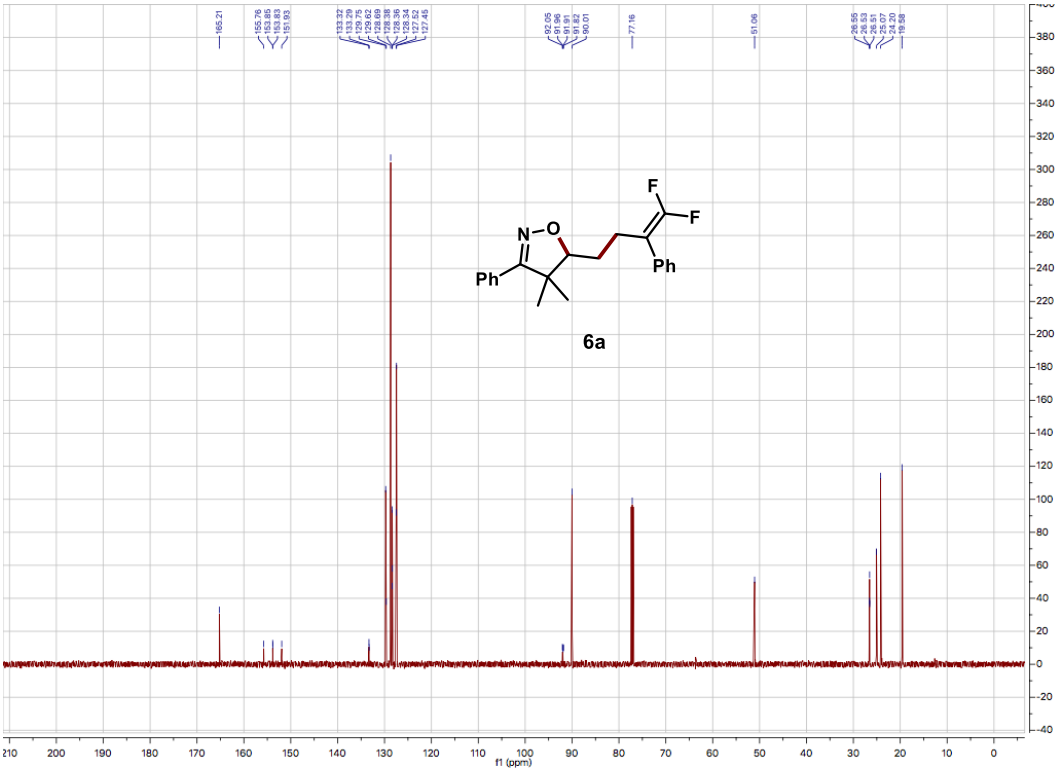

F
F
N
O
Ph
Ph
6a
f1 (ppm)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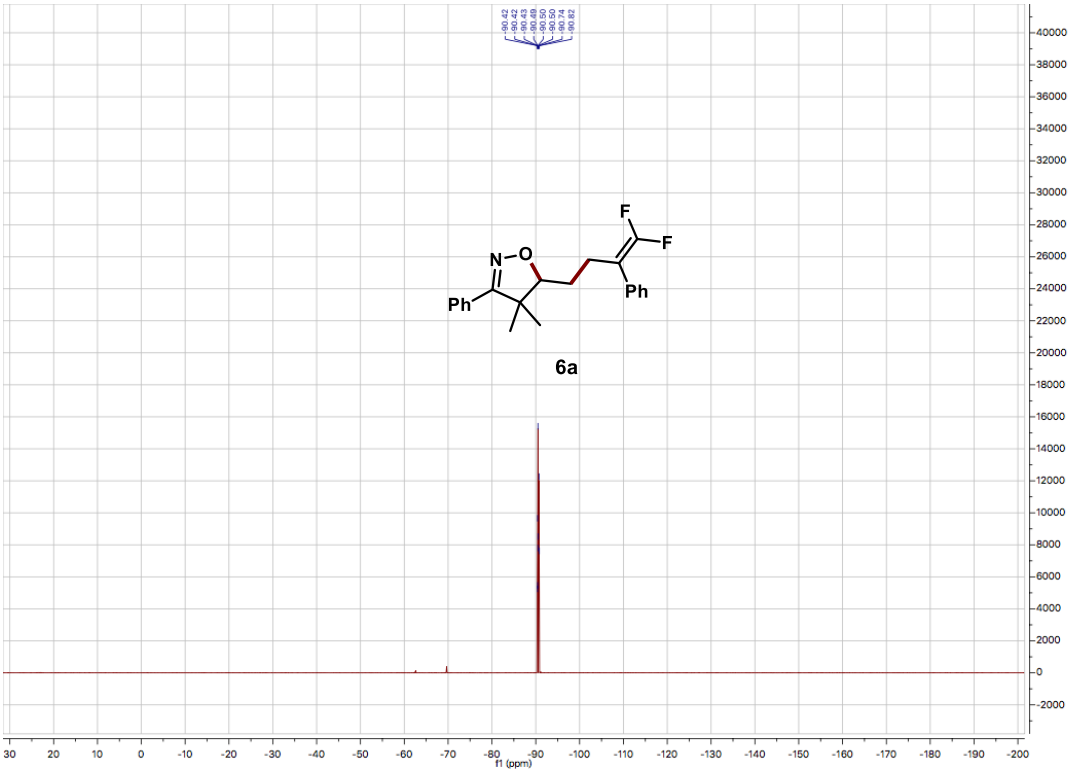
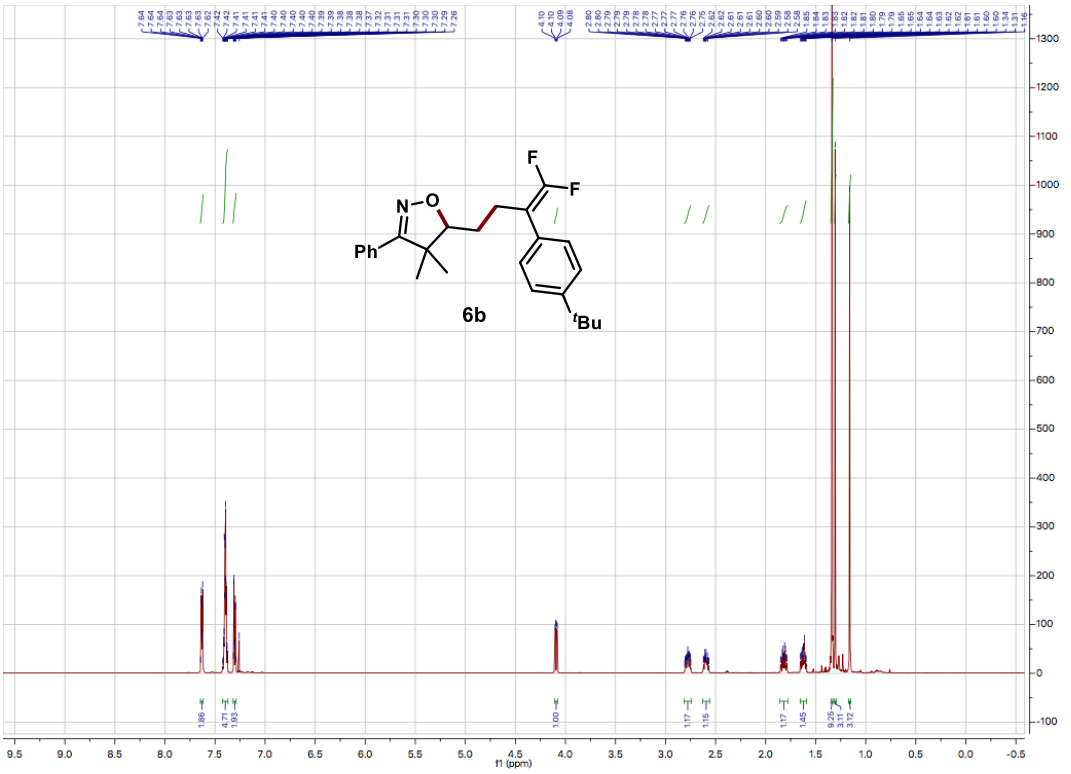
F
N
O
Ph
Ph
6a
f1 (ppm)


F
F
N
O
Ph
Ph
6a
f1 (ppm)


F
F
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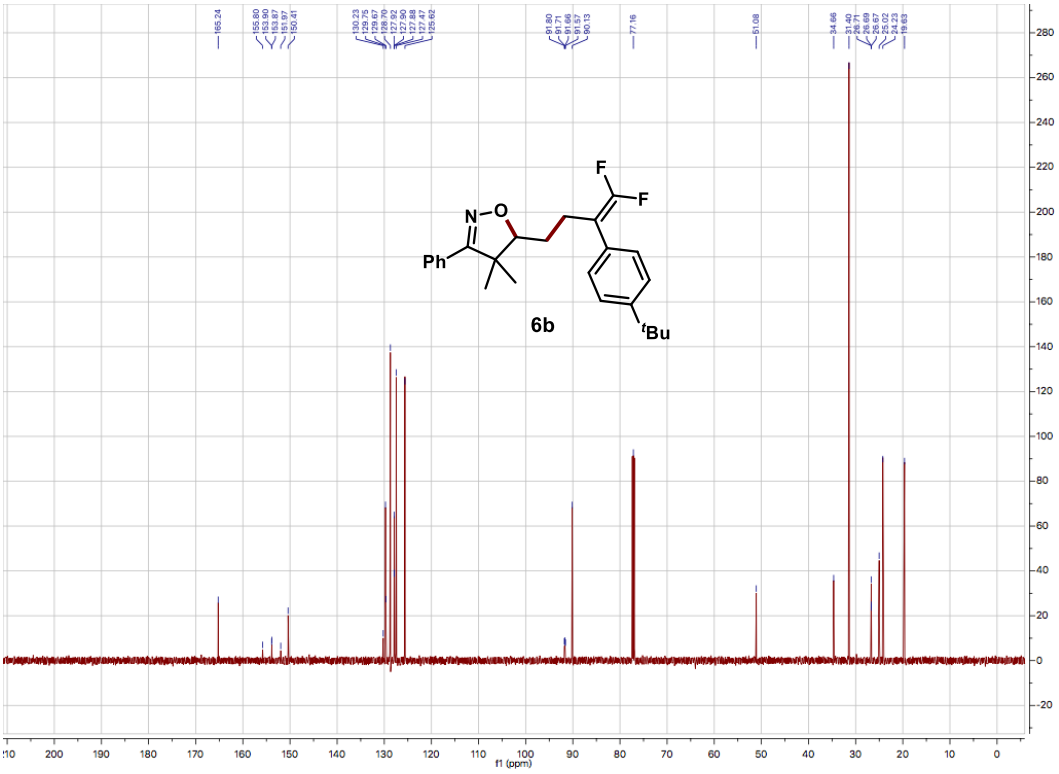
O
Ph
6b
tBu
f1 (ppm)


F
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Ph
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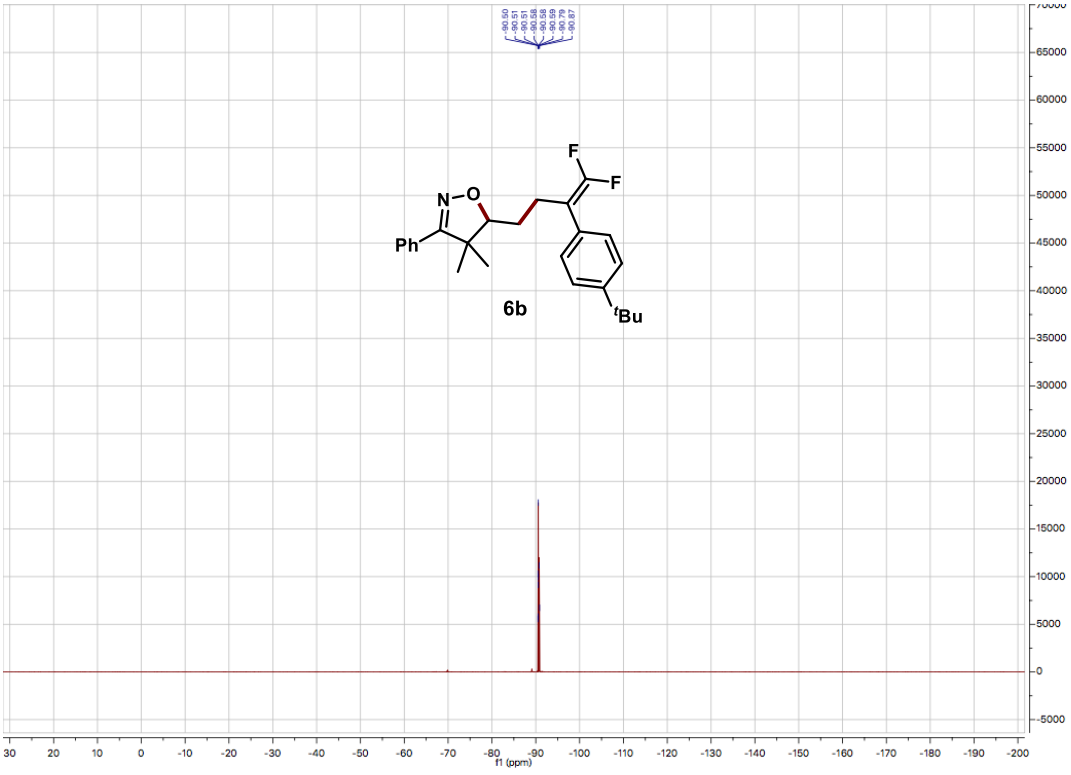
tBu
f1 (ppm)


F
F
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Ph
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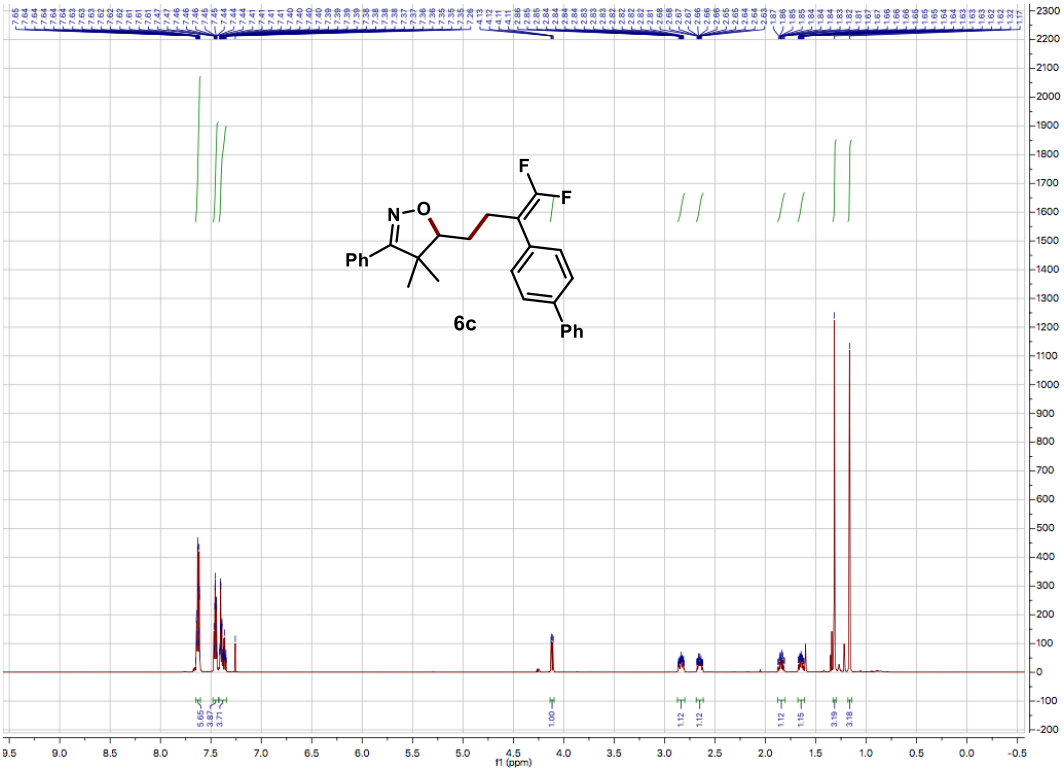
tBu
f1 (ppm)


F
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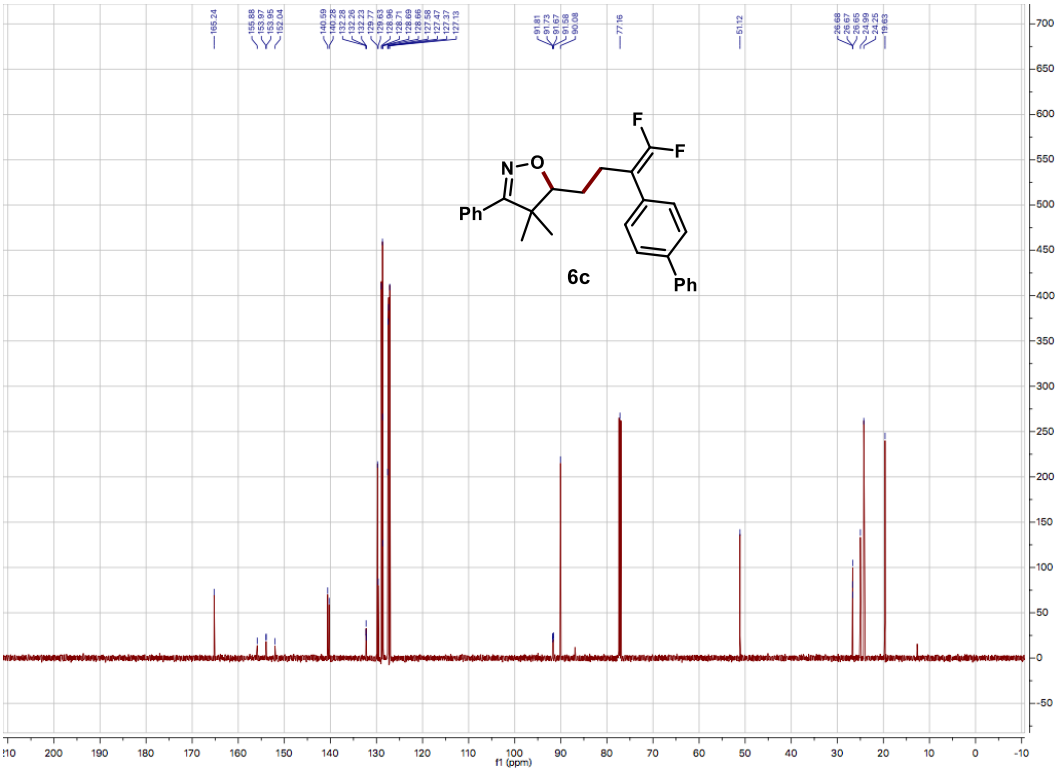
N
O
Ph
6c
Ph
f1 (ppm)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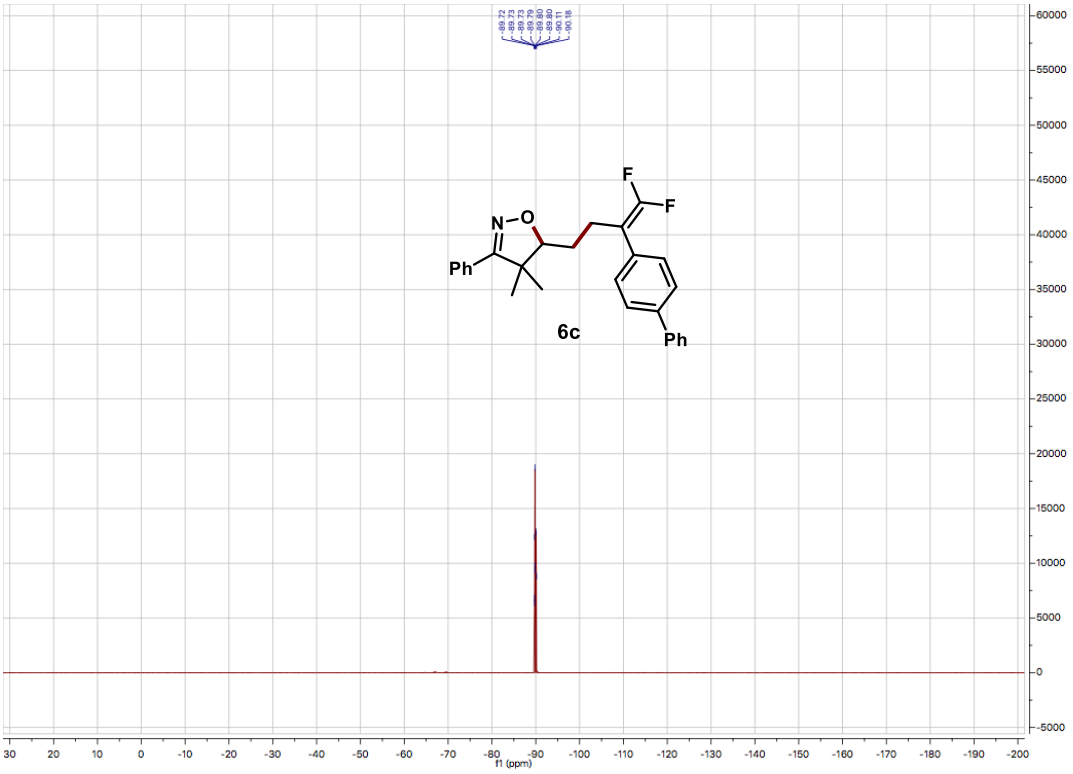
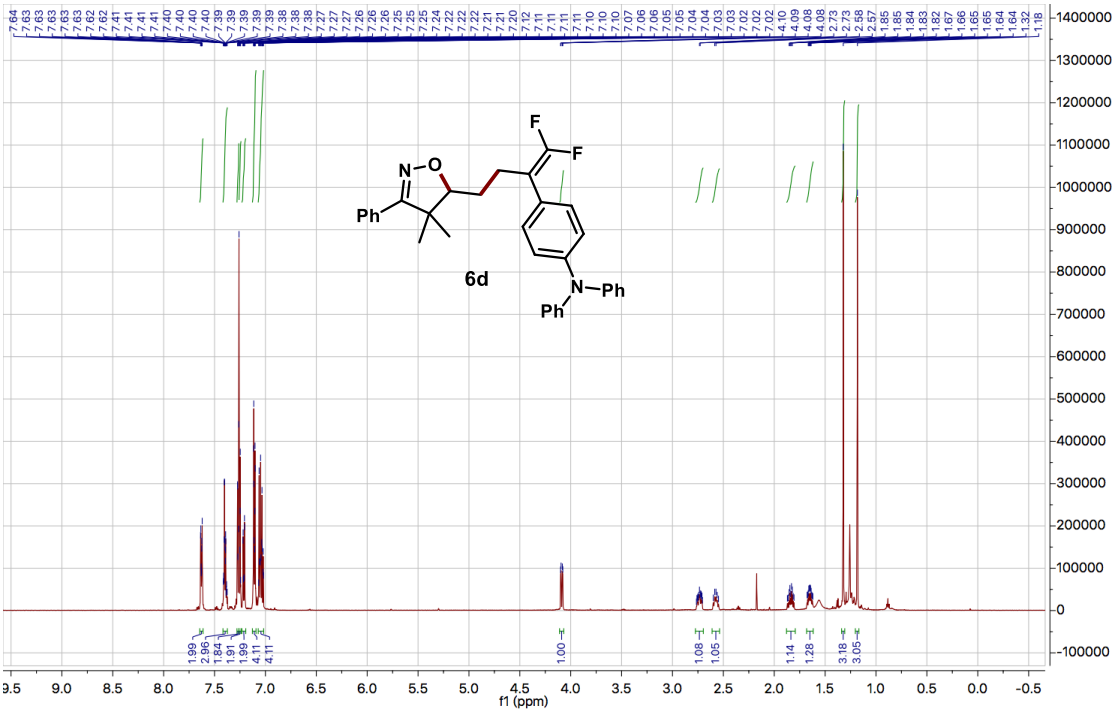
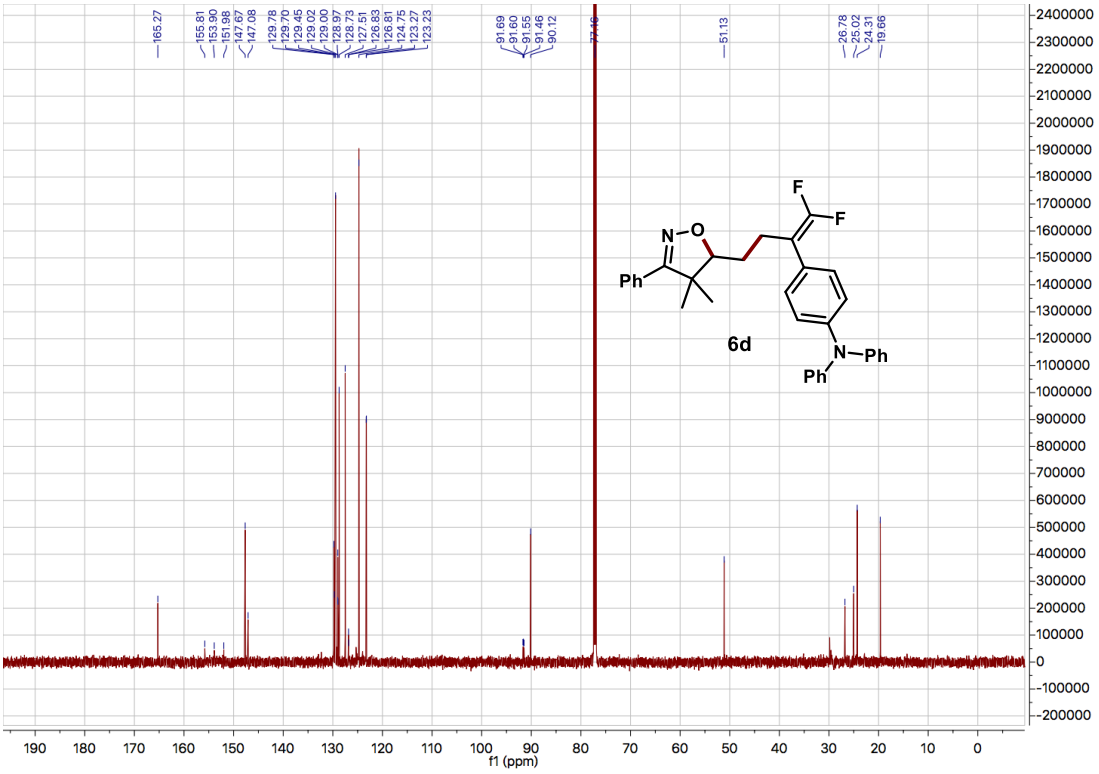
Ph
6c
Ph
f1 (ppm)


F
F
N
O
Ph
6c
Ph
f1 (ppm)


F
F
N
O
Ph
6d
N
Ph
Ph
f1 (ppm)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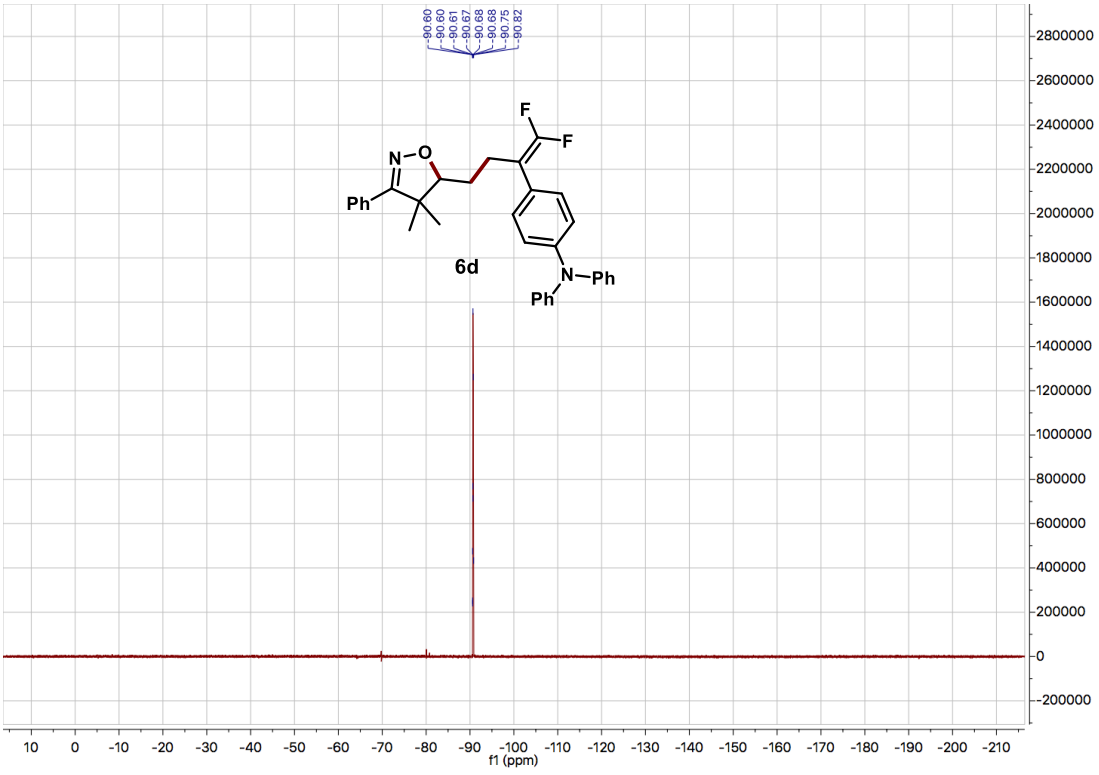
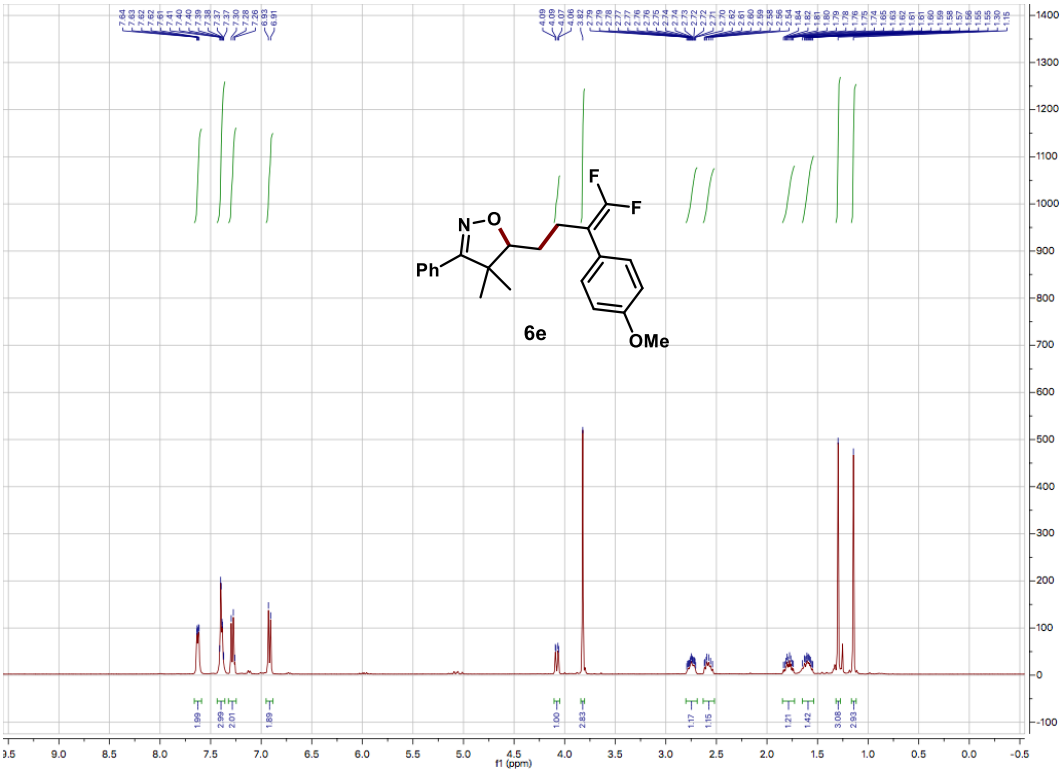
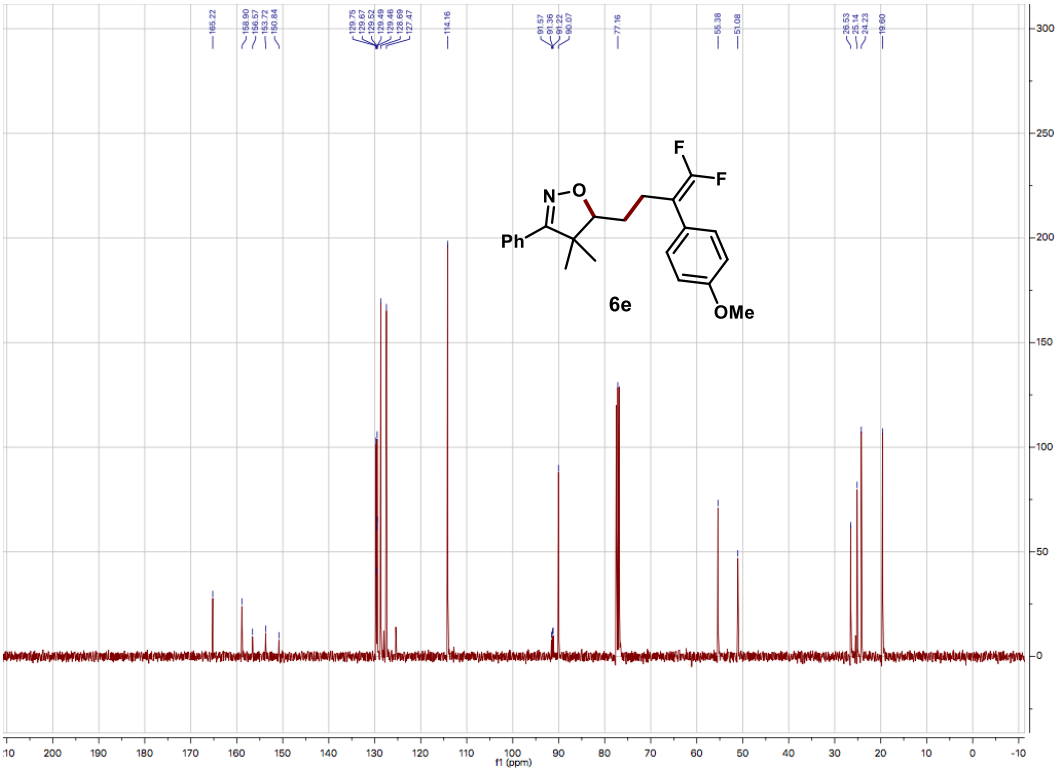
129.70
129.45
129.02
129.00
128.97
128.73
127.51
126.83
126.81
124.75
123.27
123.23
91.69
91.60
91.55
91.46
90.12
77.16
51.13
26.78
25.02
24.31
19.66
F
F
N
O
Ph
6d
N
Ph
Ph
f1 (ppm)


90.60
90.60
90.61
90.67
90.68
90.68
90.75
90.82
F
F
N
O
Ph
6d
N
Ph
Ph
f1 (ppm)


F
F
N
O
Ph
6e
OMe
f1 (ppm)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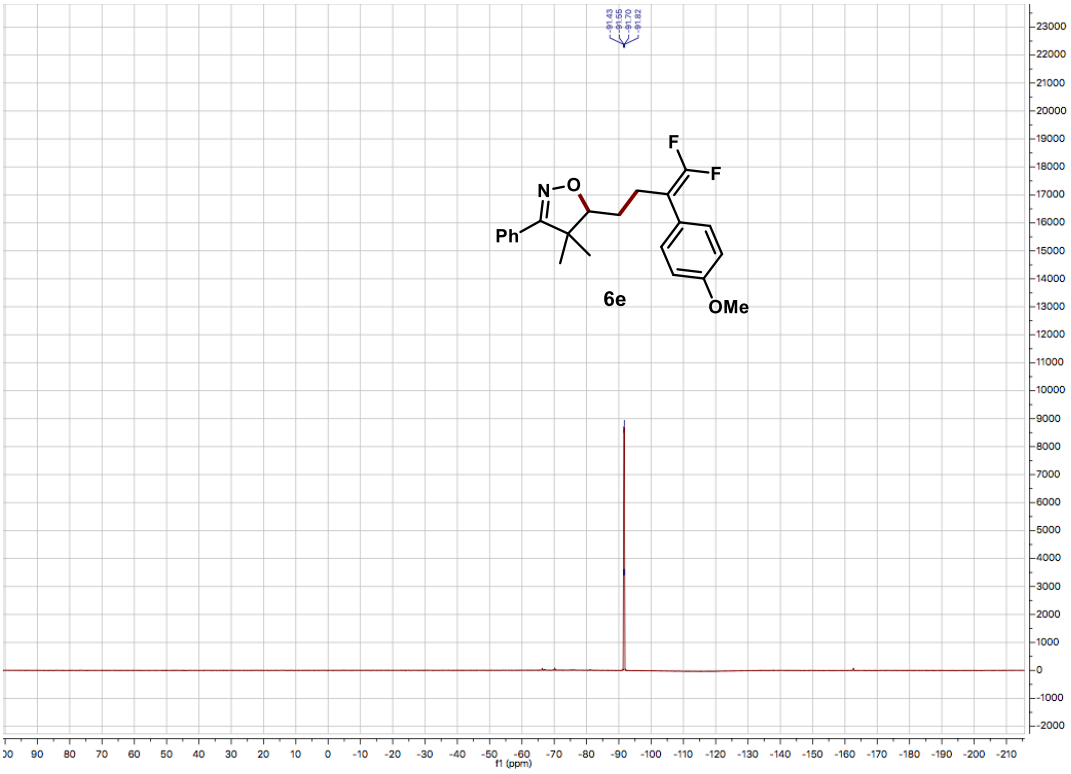
F
N
O
Ph
6e
OMe
f1 (ppm)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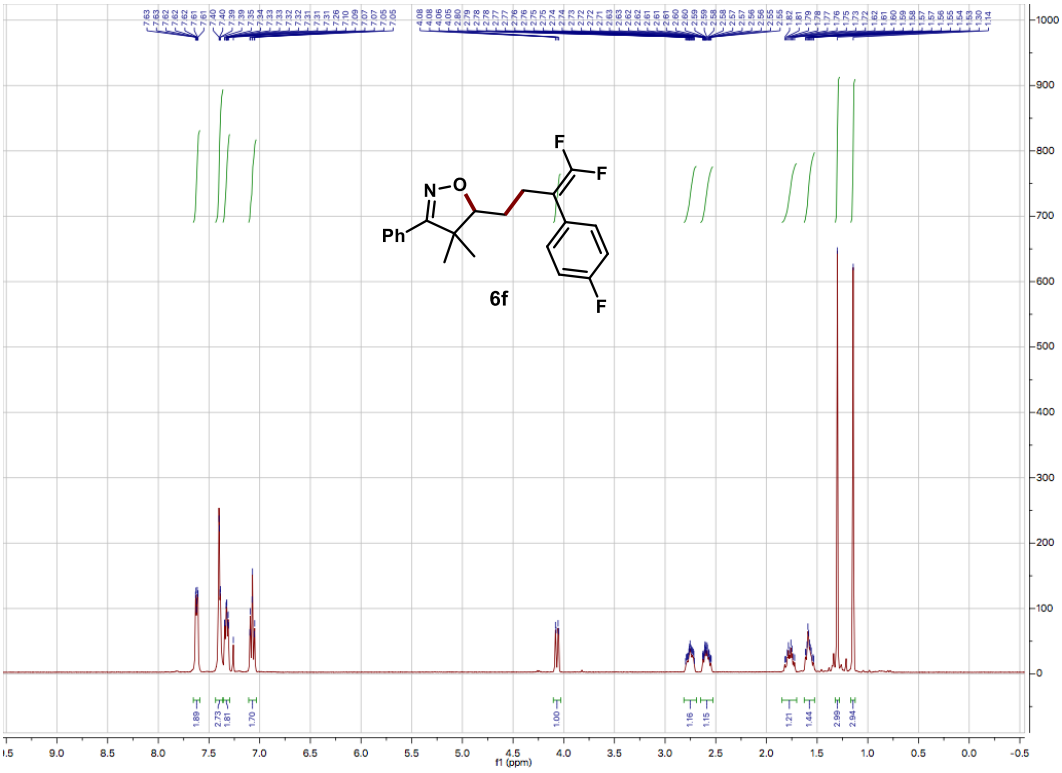
F
N
O
Ph
6e
OMe
f1 (ppm)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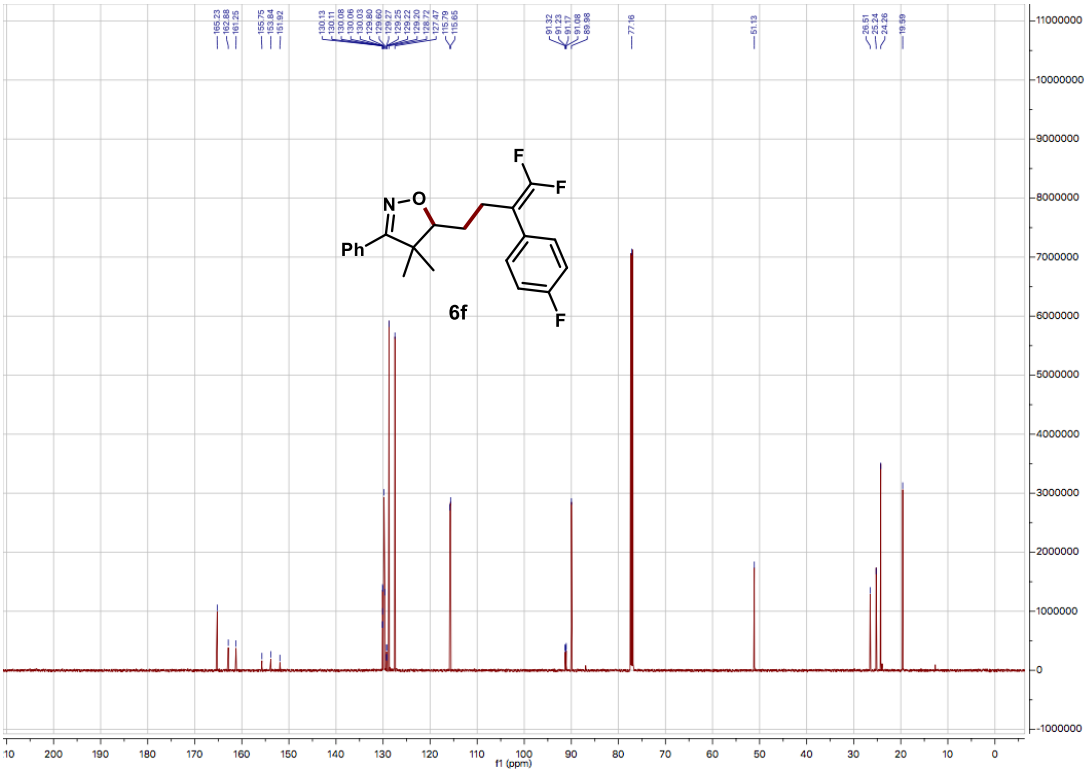
F
N
O
Ph
6f
F
f1 (ppm)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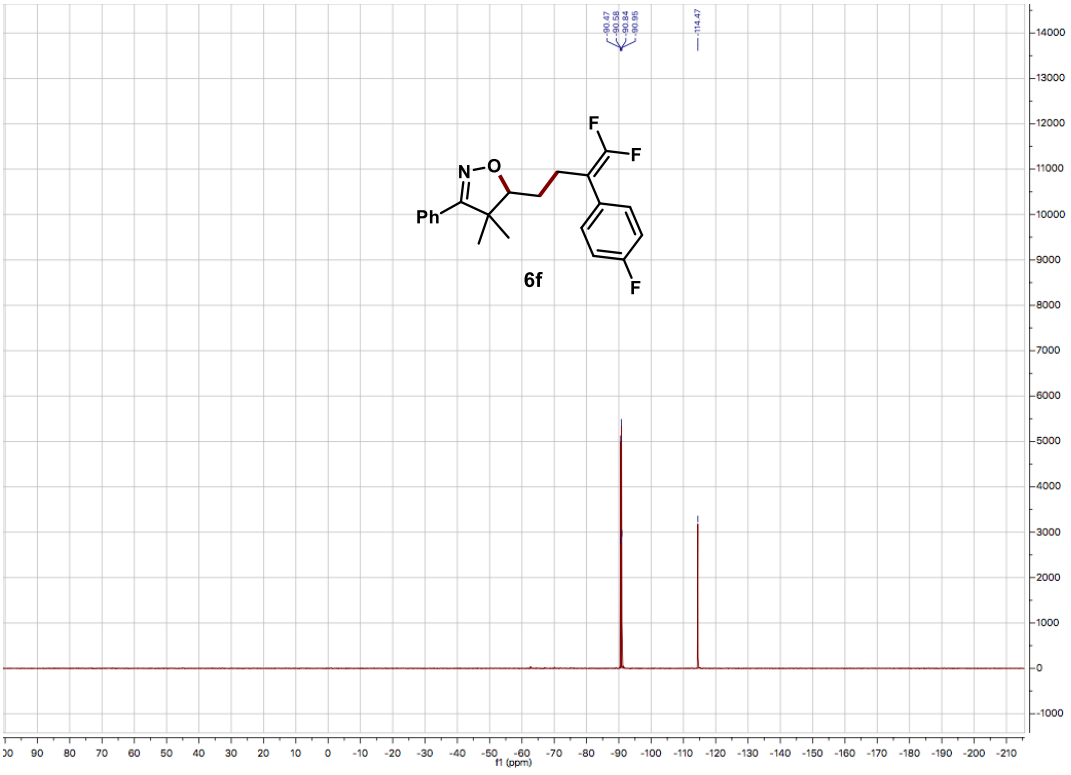
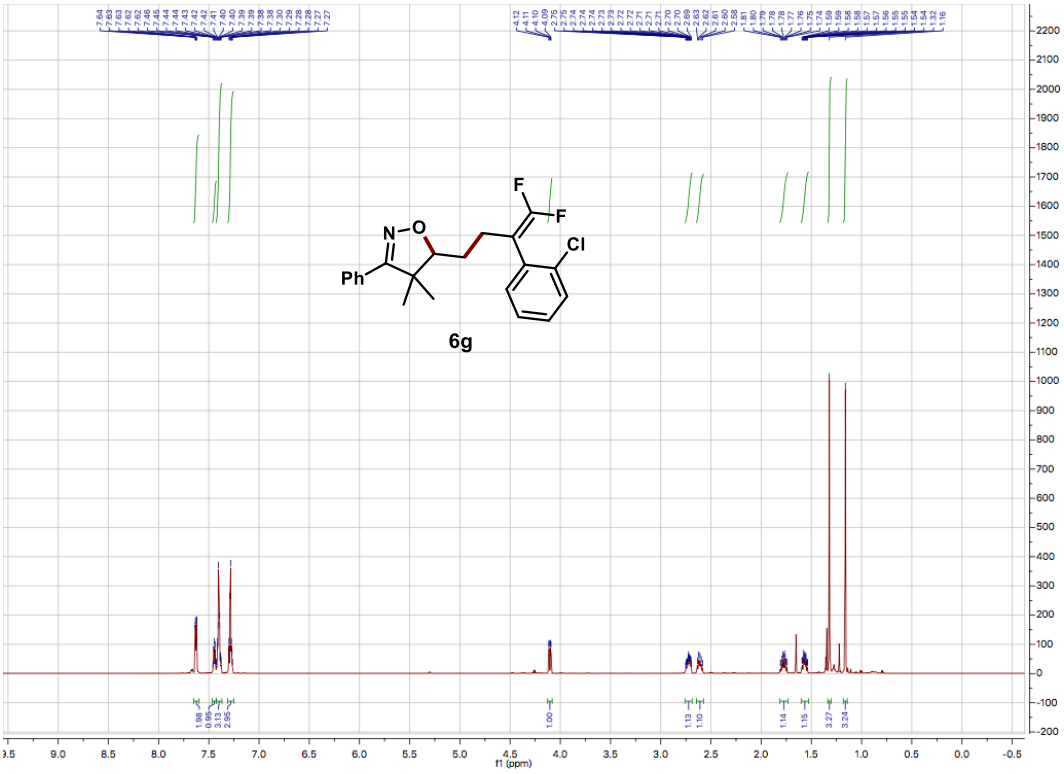
F
N
O
Ph
F
6f
f1 (ppm)


F
F
N
O
Ph
F
6f
f1 (ppm)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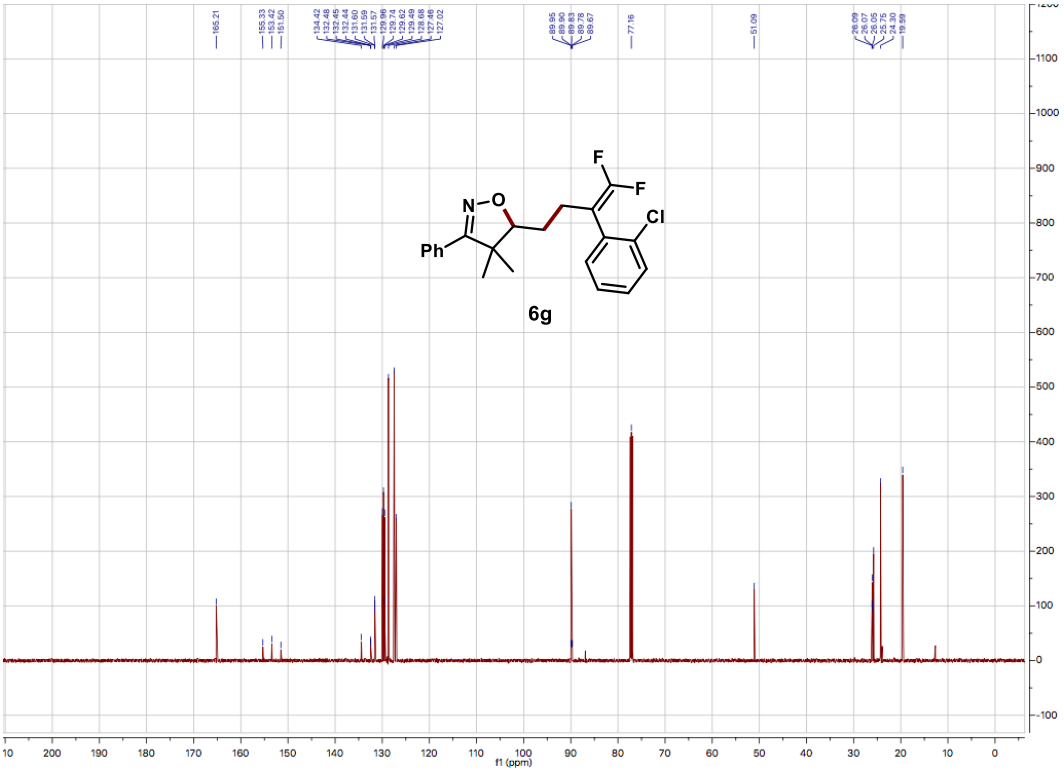
F
Cl
N
O
Ph
6g
f1 (ppm)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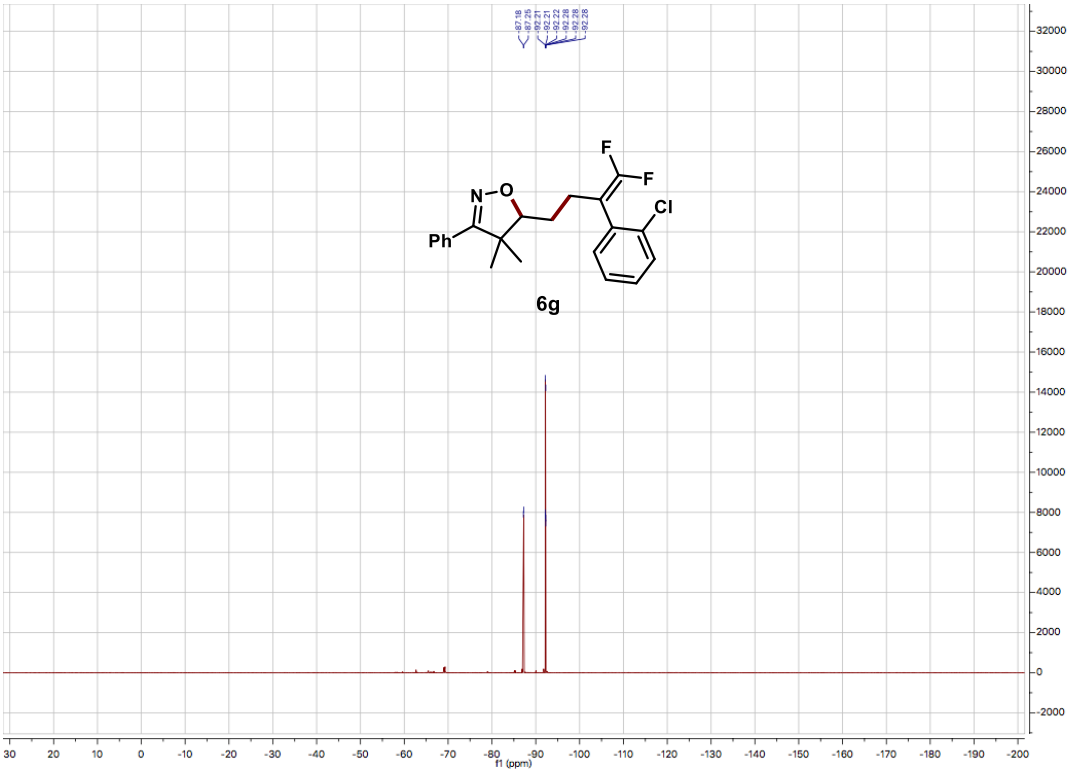
F
Cl
N
O
Ph
6g
f1 (ppm)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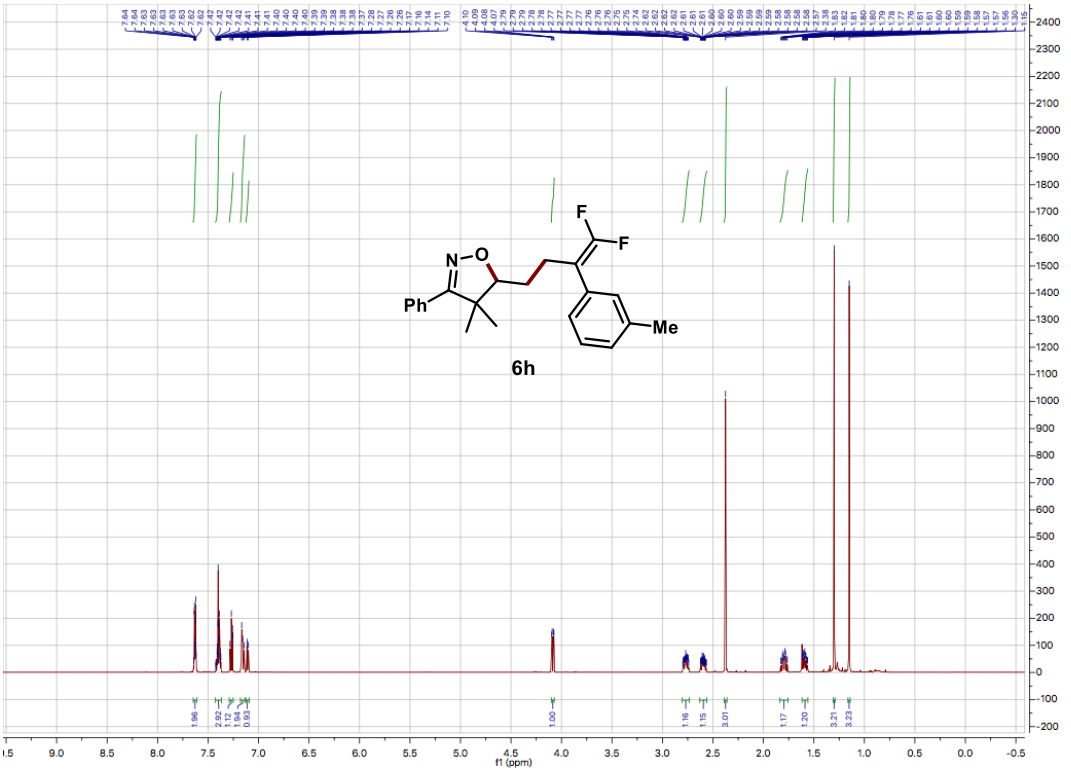
F
N
O
Ph
Cl
6g
f1 (ppm)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F
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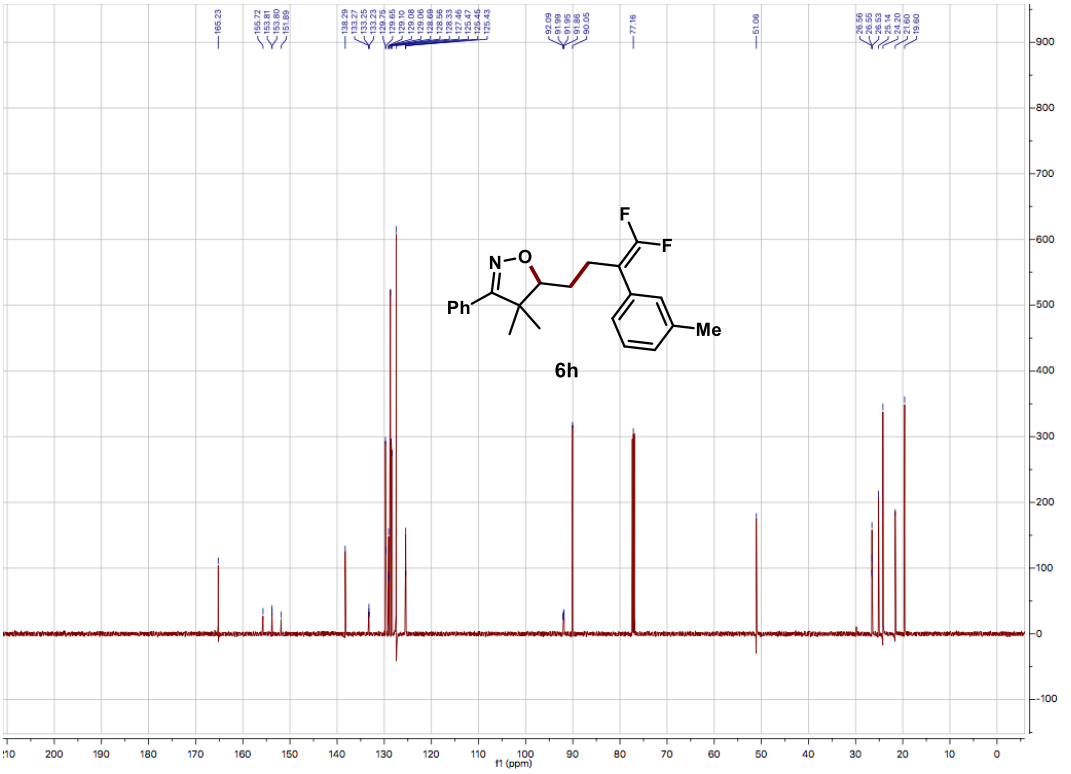
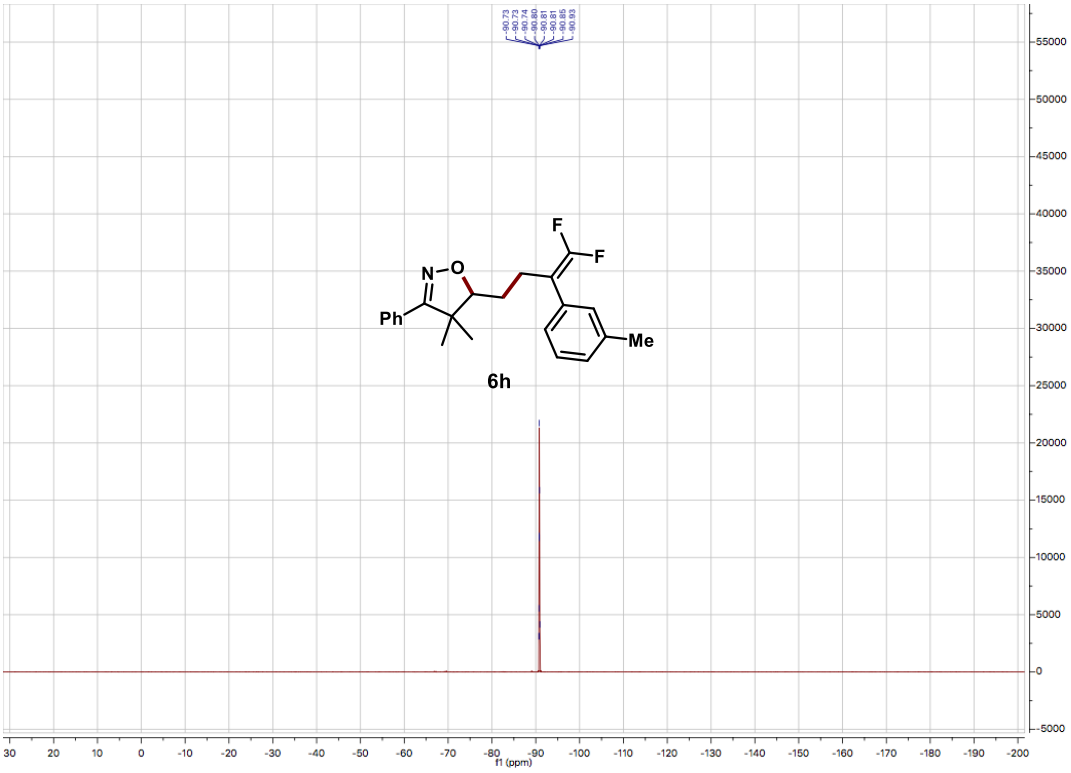
O
Ph
Me
6h
f1 (ppm)


F
F
N
O
Ph
Me
6h
f1 (ppm)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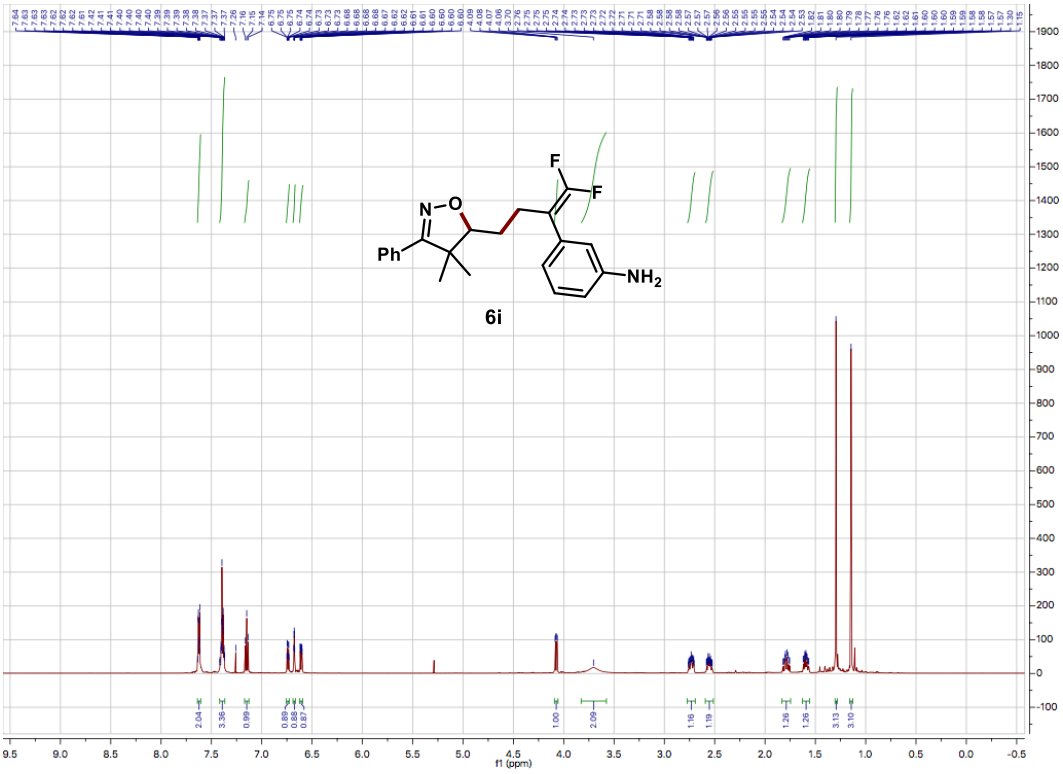
F
N
O
Ph
Me
6h
f1 (ppm)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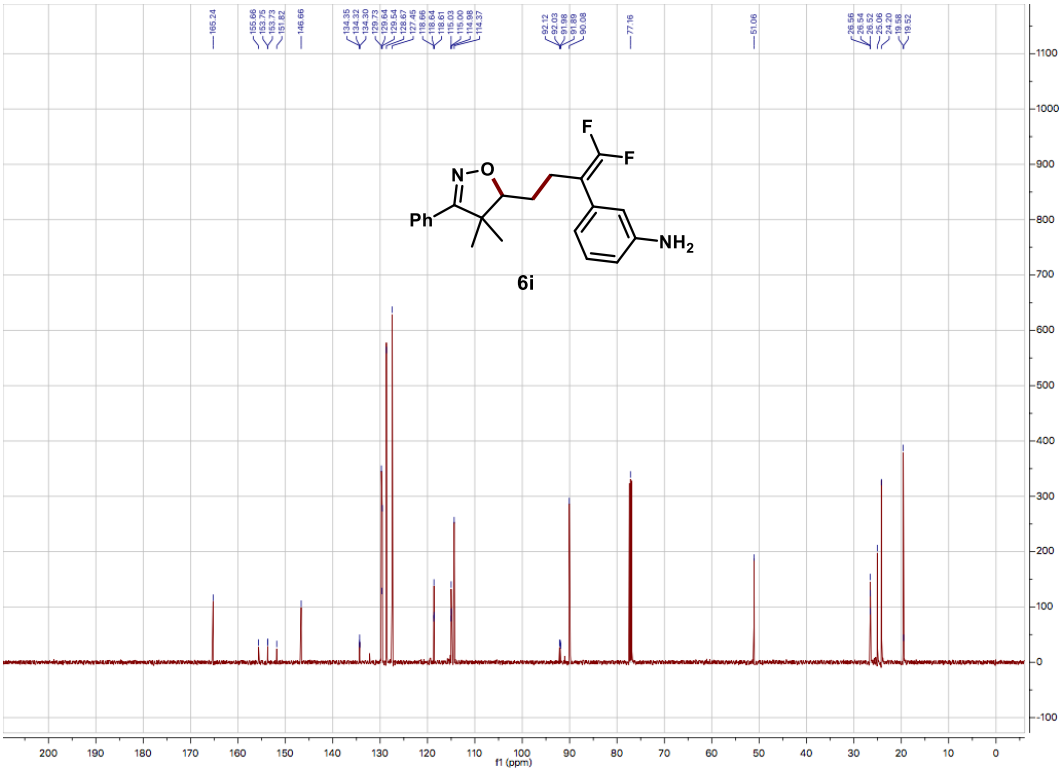
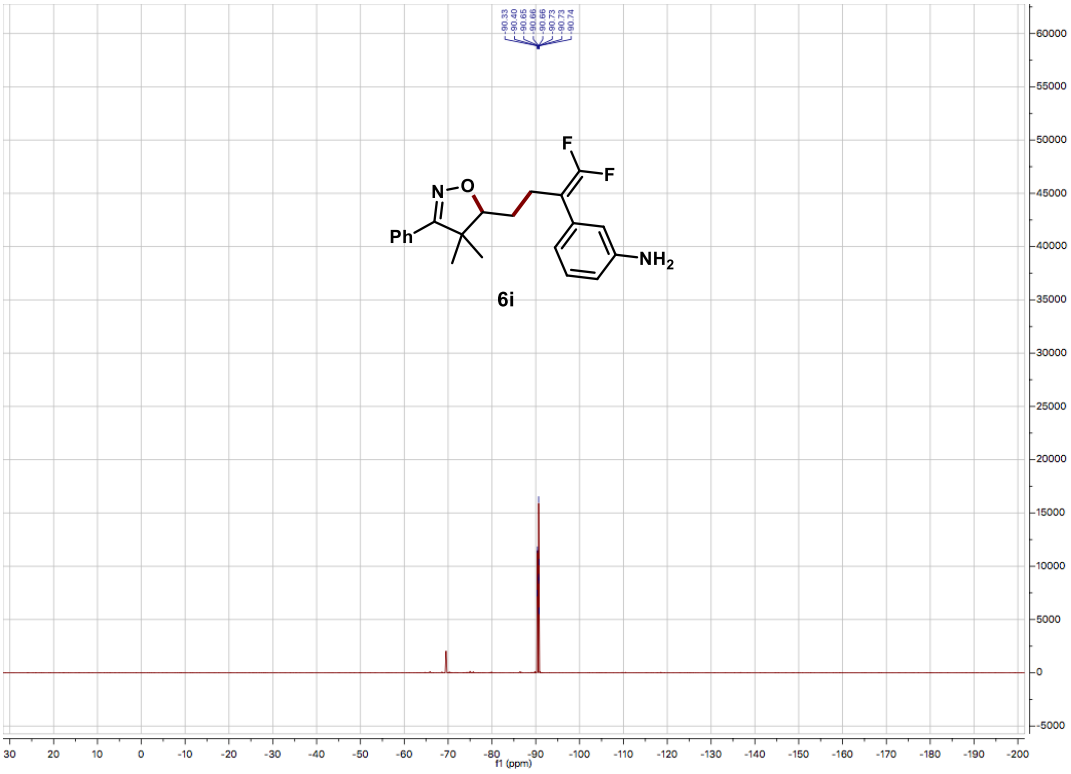
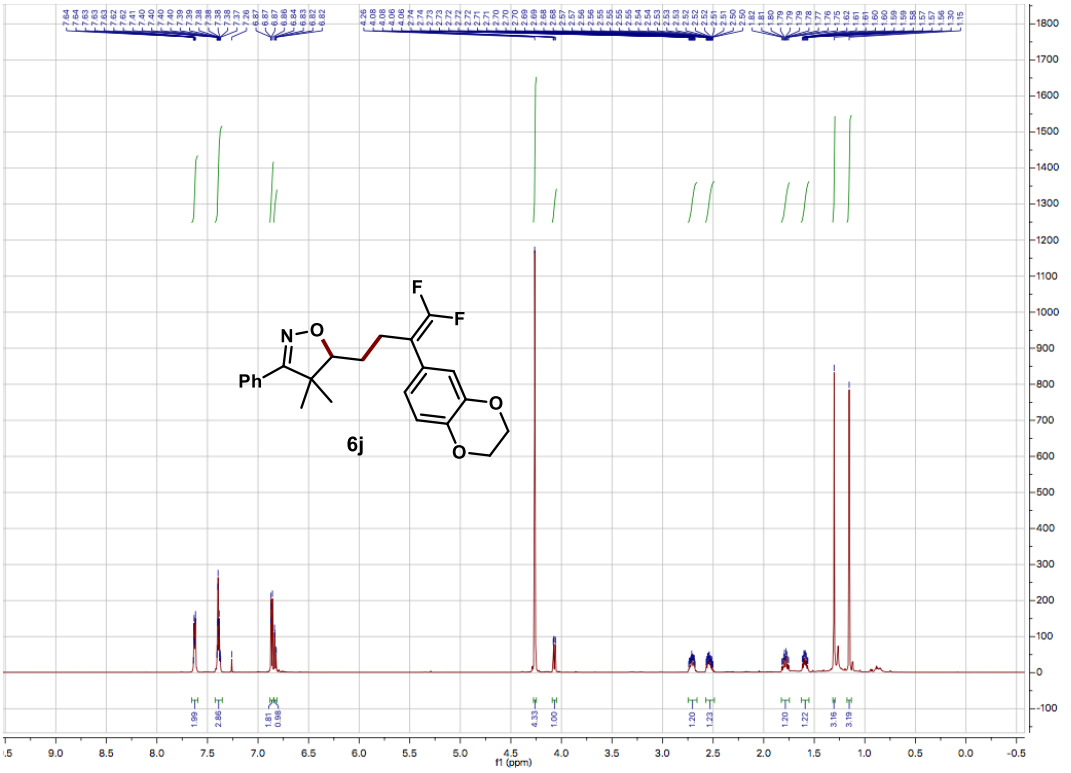
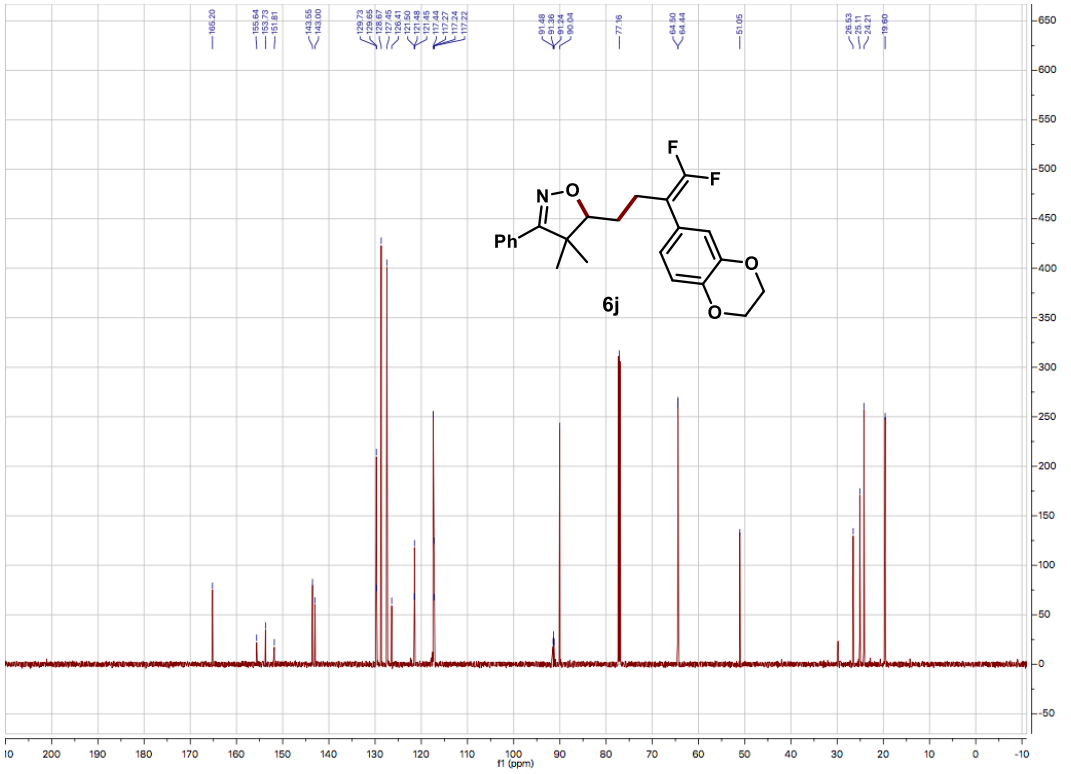
F
N
O
Ph
NH2
6i
f1 (ppm)


F
F
N
O
Ph
NH2
6i
f1 (ppm)


F
F
N
O
Ph
NH2
6i
f1 (ppm)


F
F
N
O
Ph
O
O
6j
f1 (ppm)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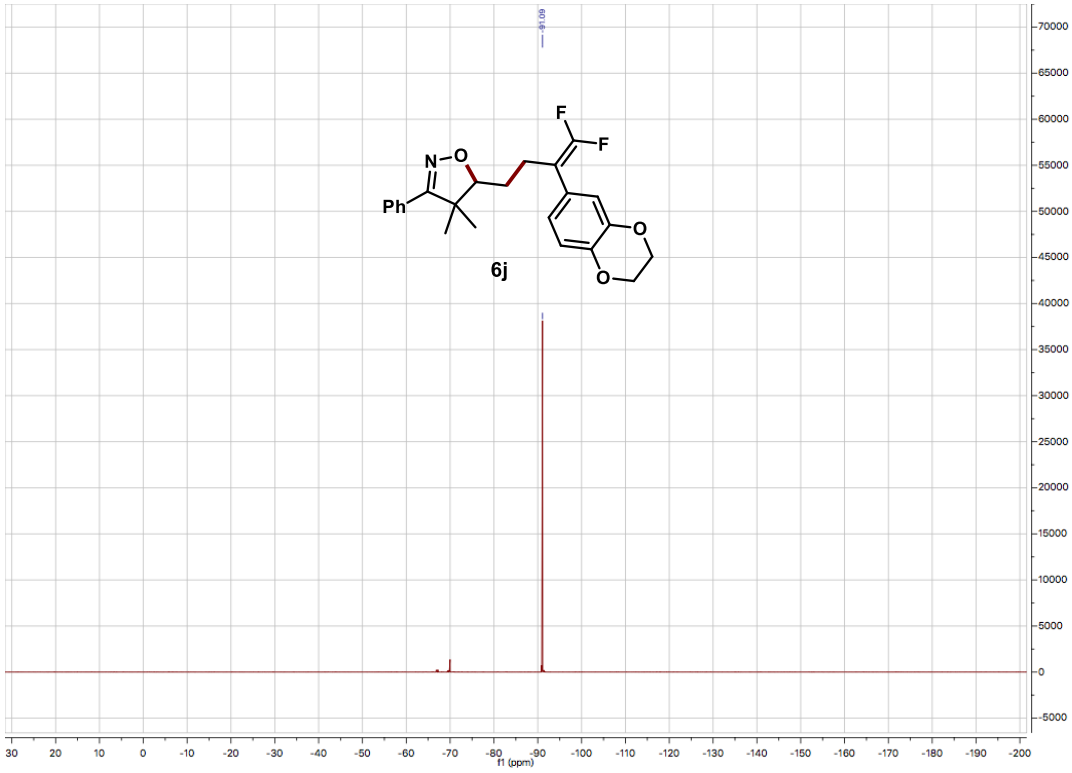
F
N
O
Ph
O
O
6j
f1 (ppm)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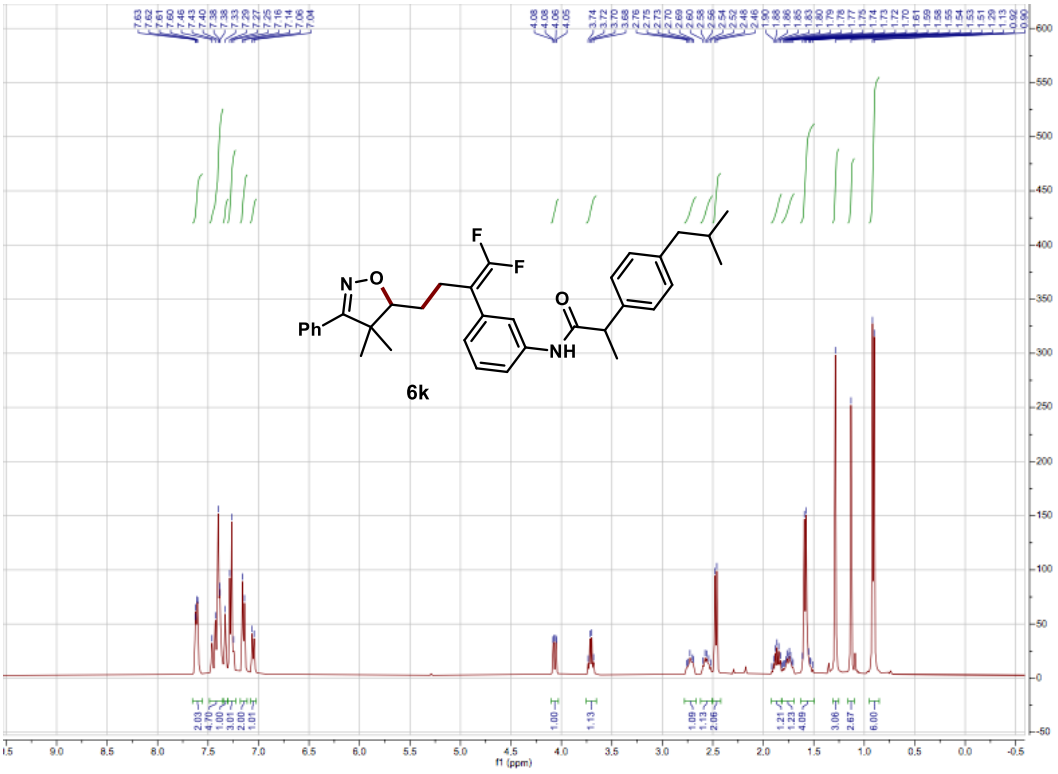
N
O
Ph
O
O
6j
f1 (ppm)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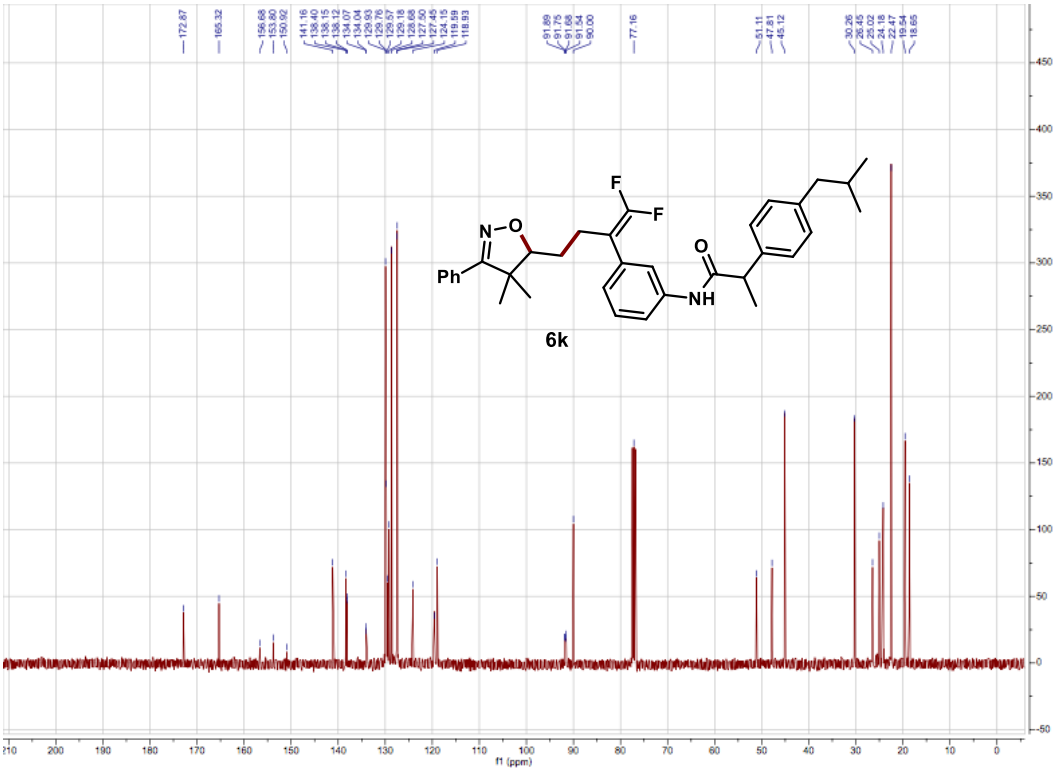
N
O
Ph
O
NH
6k
f1 (ppm)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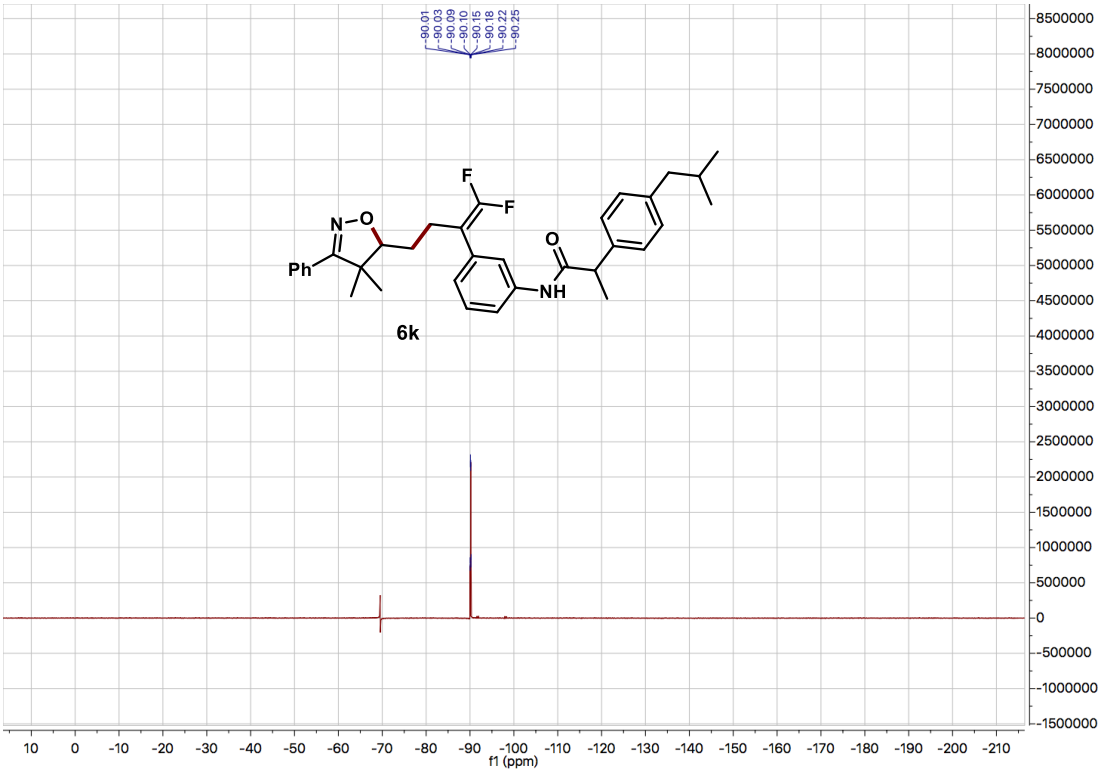
F
N
O
Ph
O
NH
6k
f1 (ppm)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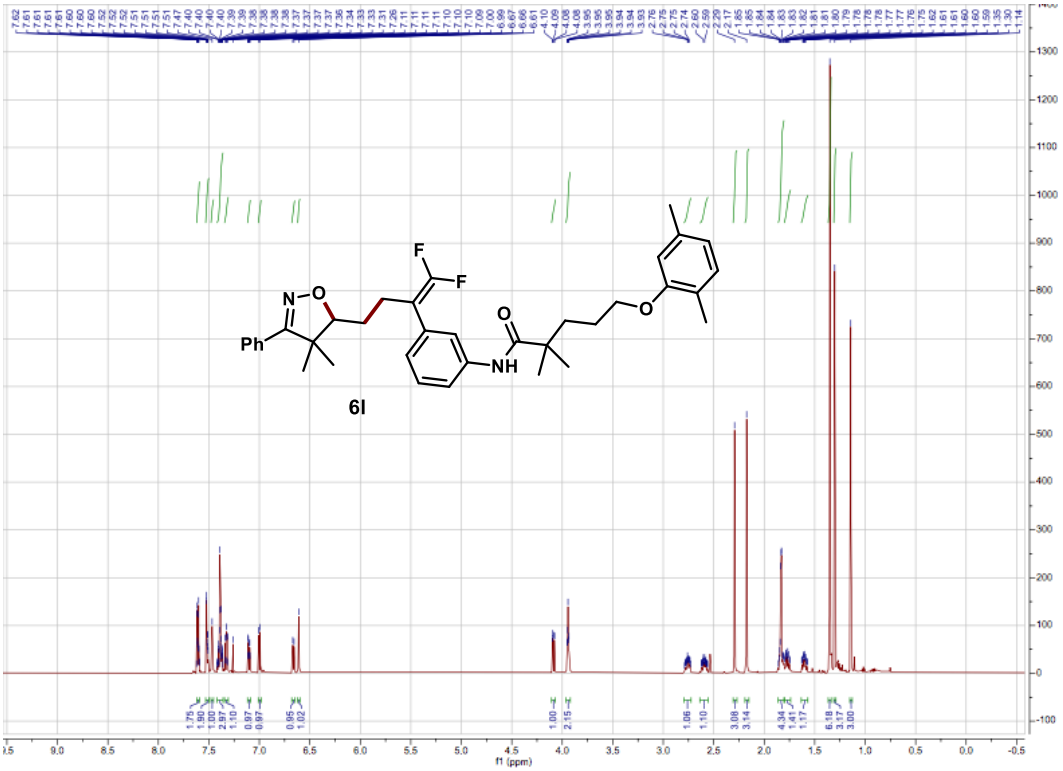
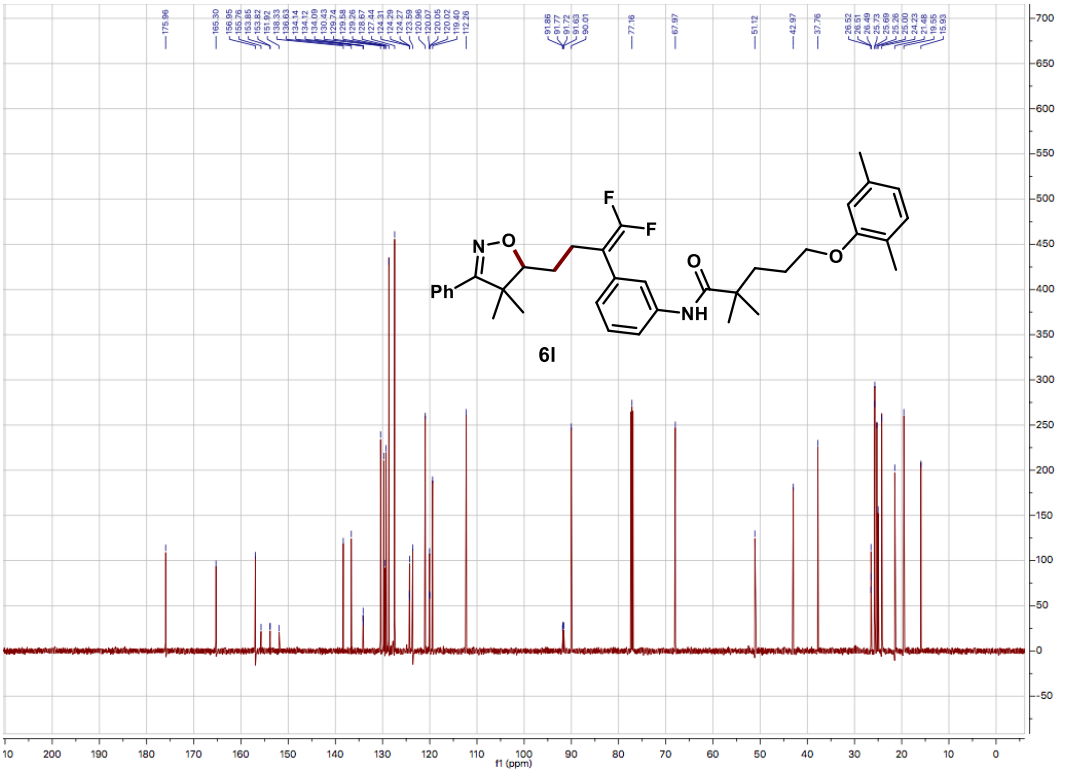
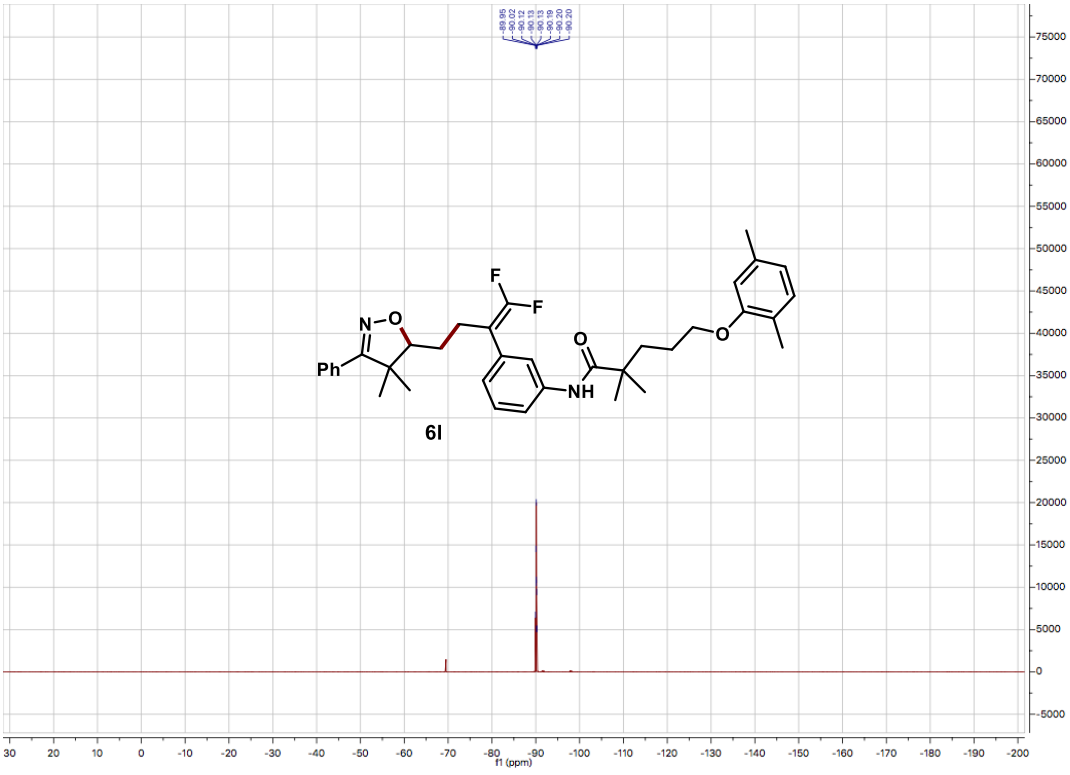
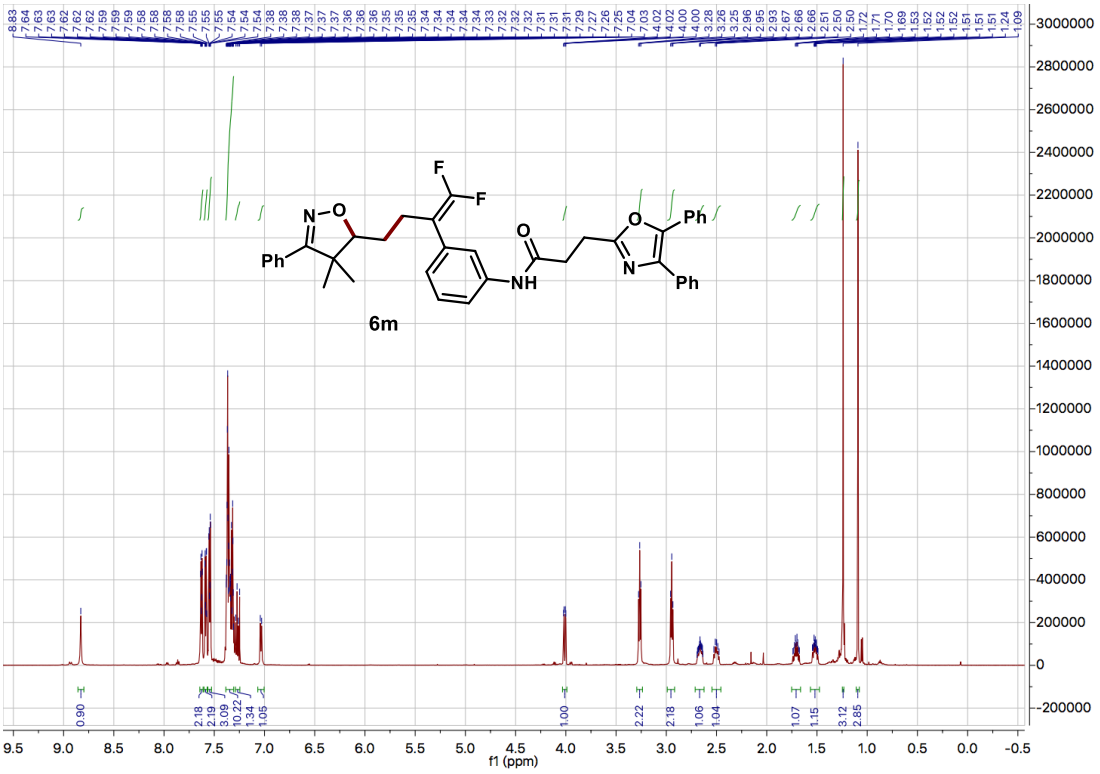
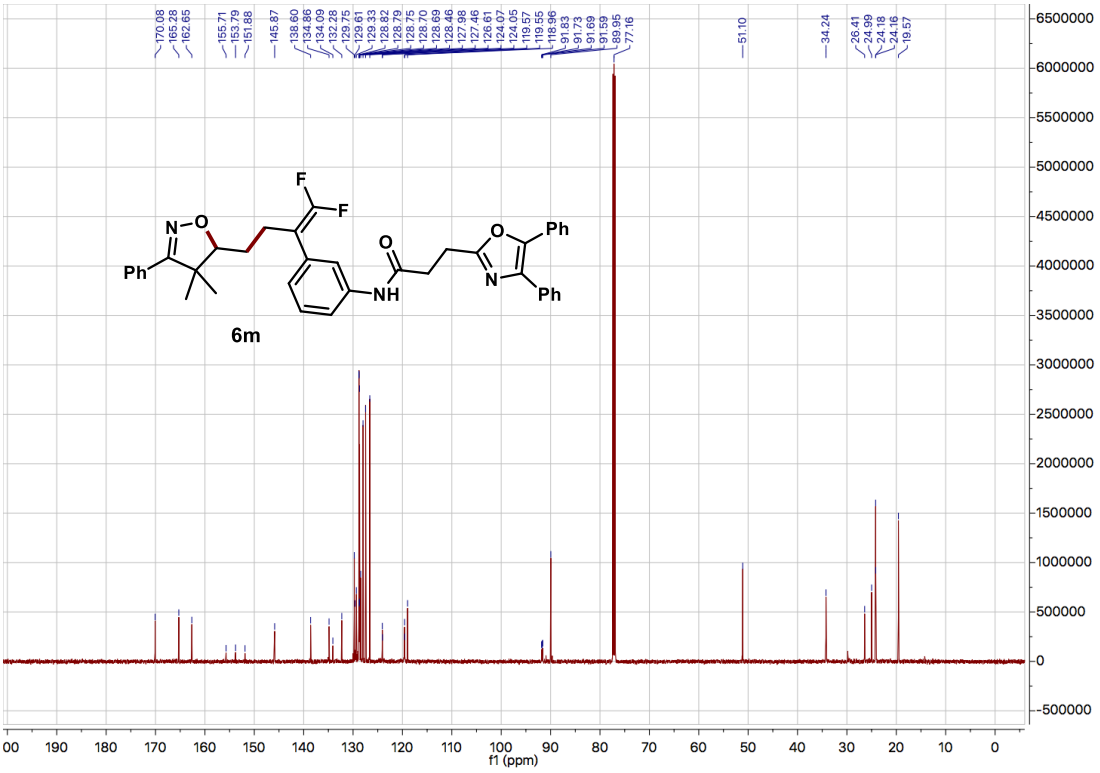
N
O
Ph
O
NH
6k
f1 (ppm)

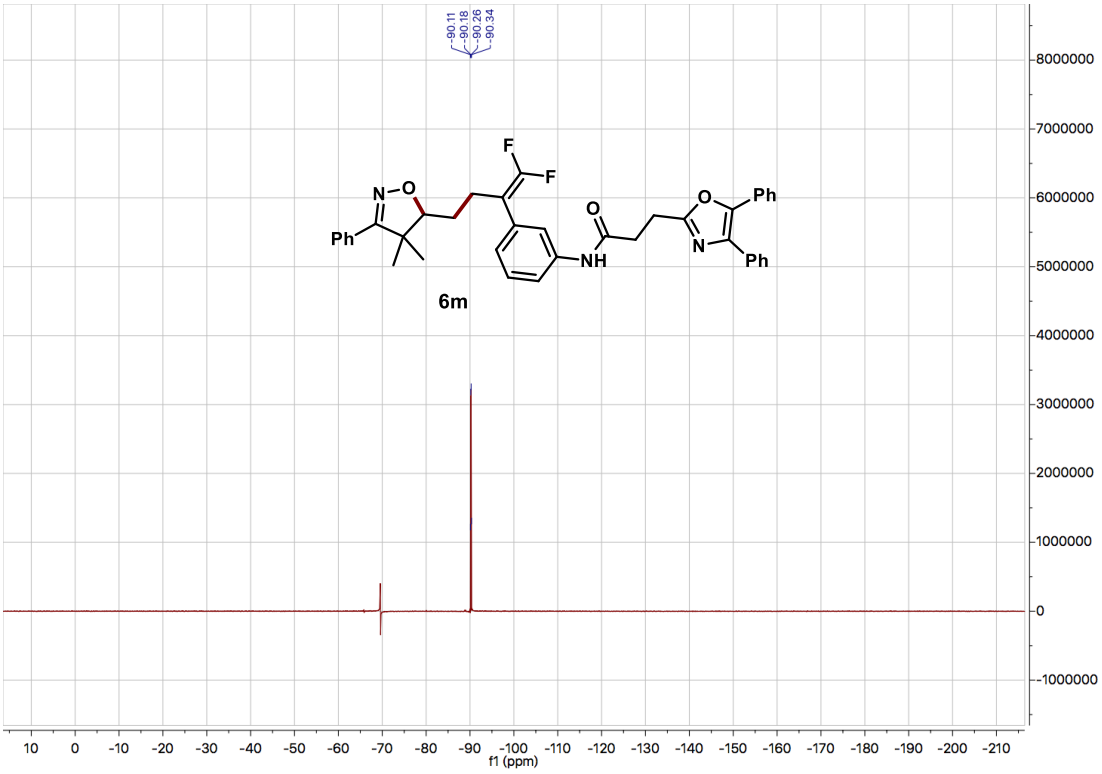

F
F
N
O
Ph
O
NH
O
6l
f1 (ppm)

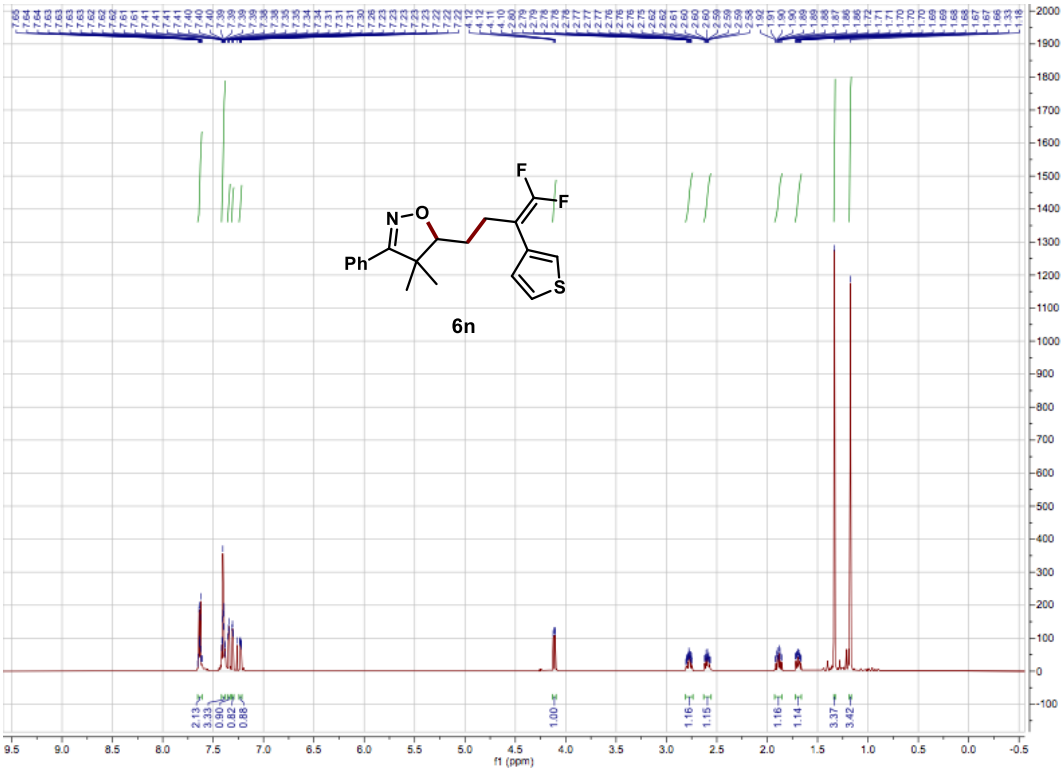

F
F
N
O
Ph
O
NH
O
6l
f1 (ppm)

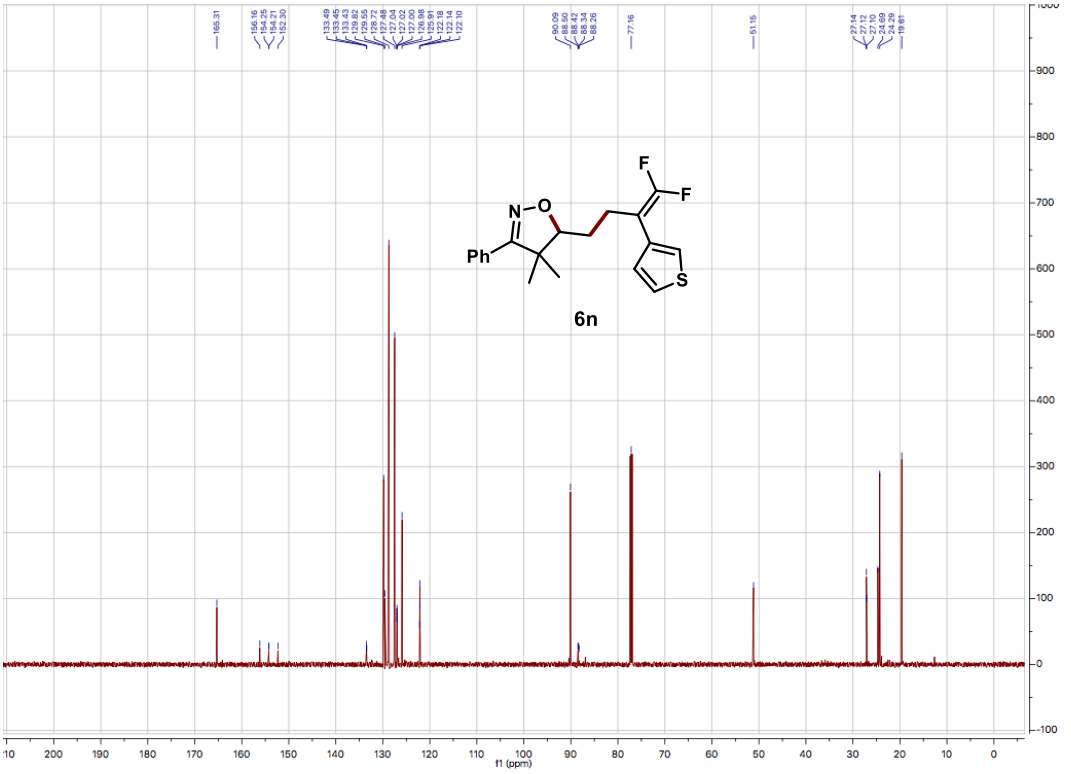

F
F
N
O
Ph
O
NH
O
6l
f1 (ppm)

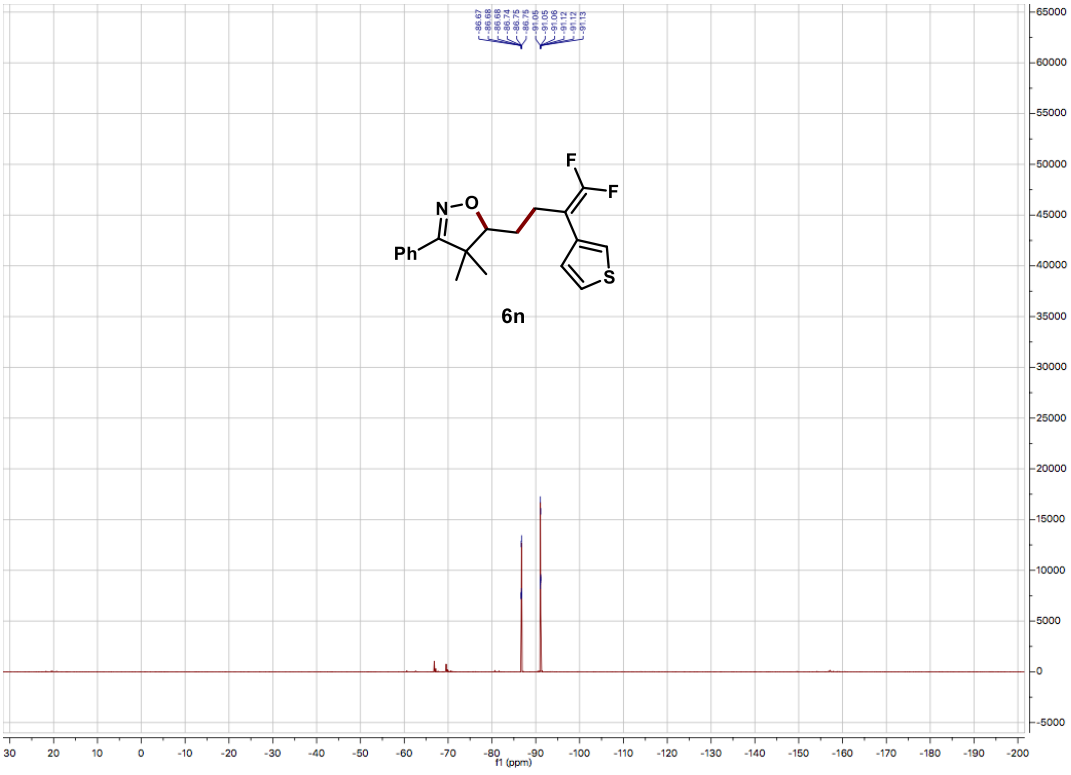

F
F
N
O
Ph
O
NH
O
N
Ph
Ph
6m
f1 (ppm)

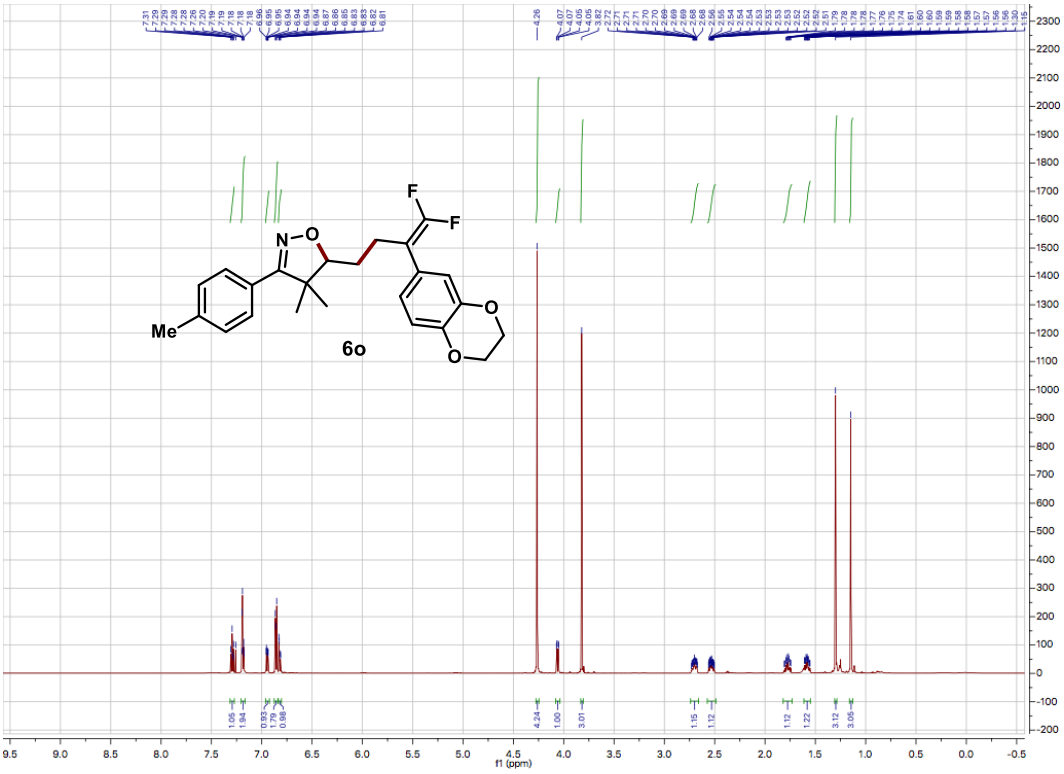

F
F
N
O
Ph
O
NH
O
N
Ph
Ph
6m
f1 (ppm)

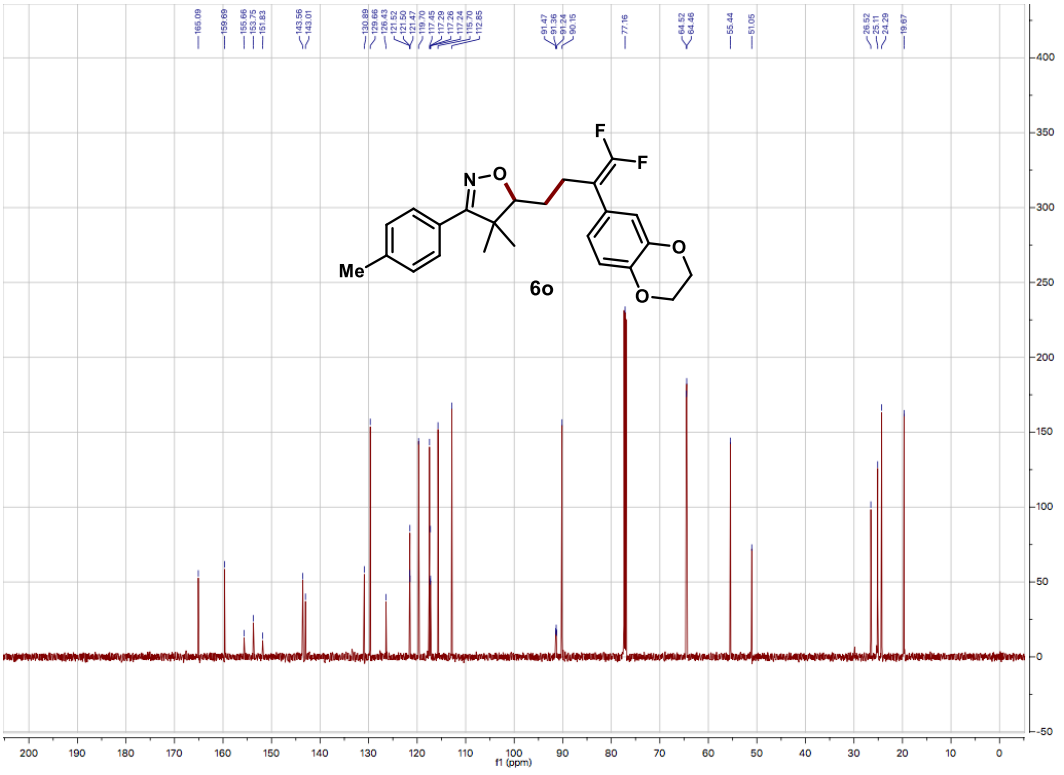

90.11
90.18
90.26
90.34
F
F
N
O
Ph
O
NH
O
N
Ph
Ph
6m
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
-1000000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

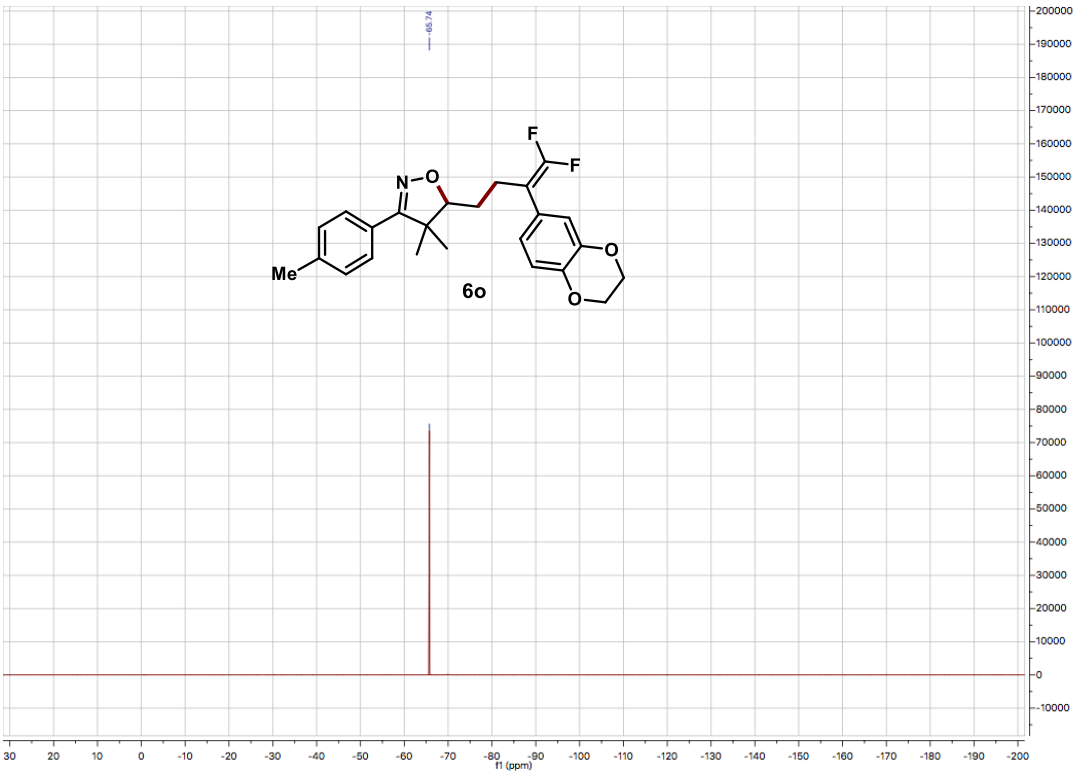

F
F
N
O
Ph
S
6n
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

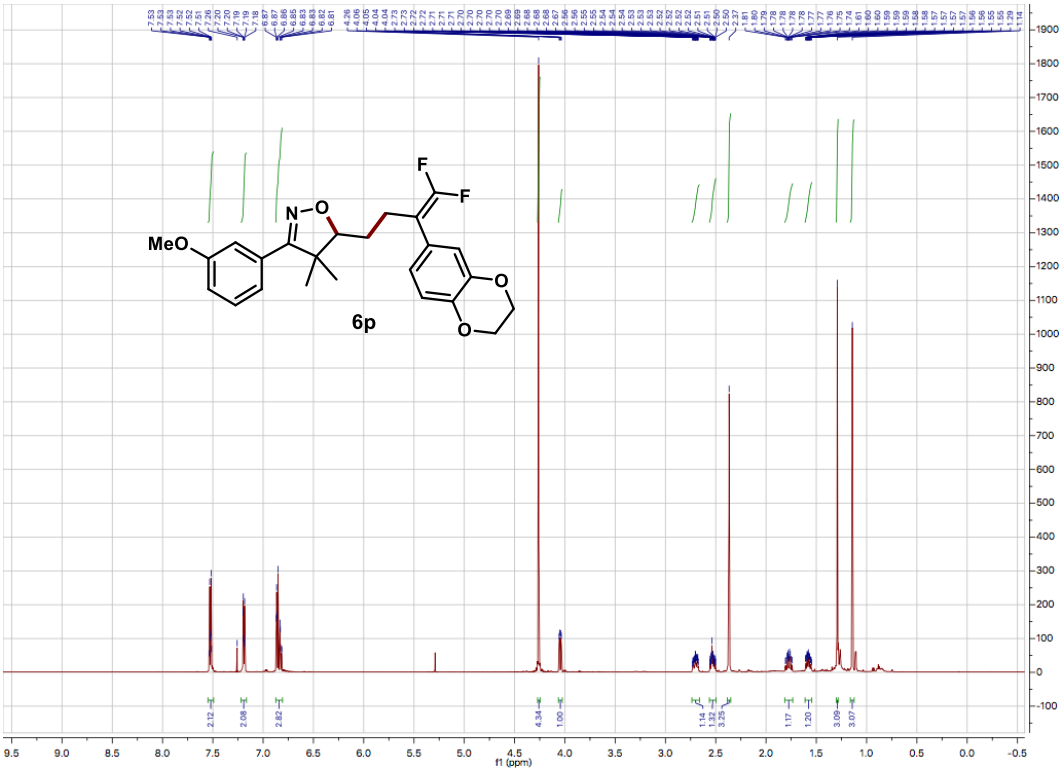

F
F
N
O
Ph
S
6n
f1 (ppm)

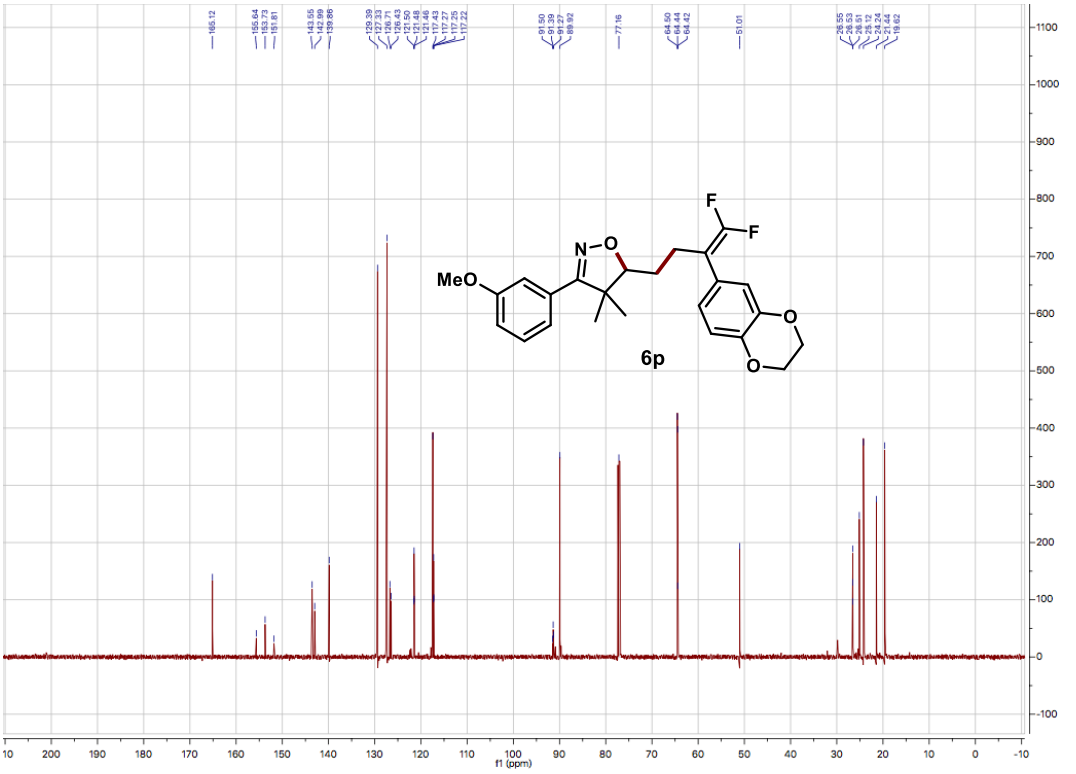

F
F
N
O
Ph
S
6n
f1 (ppm)

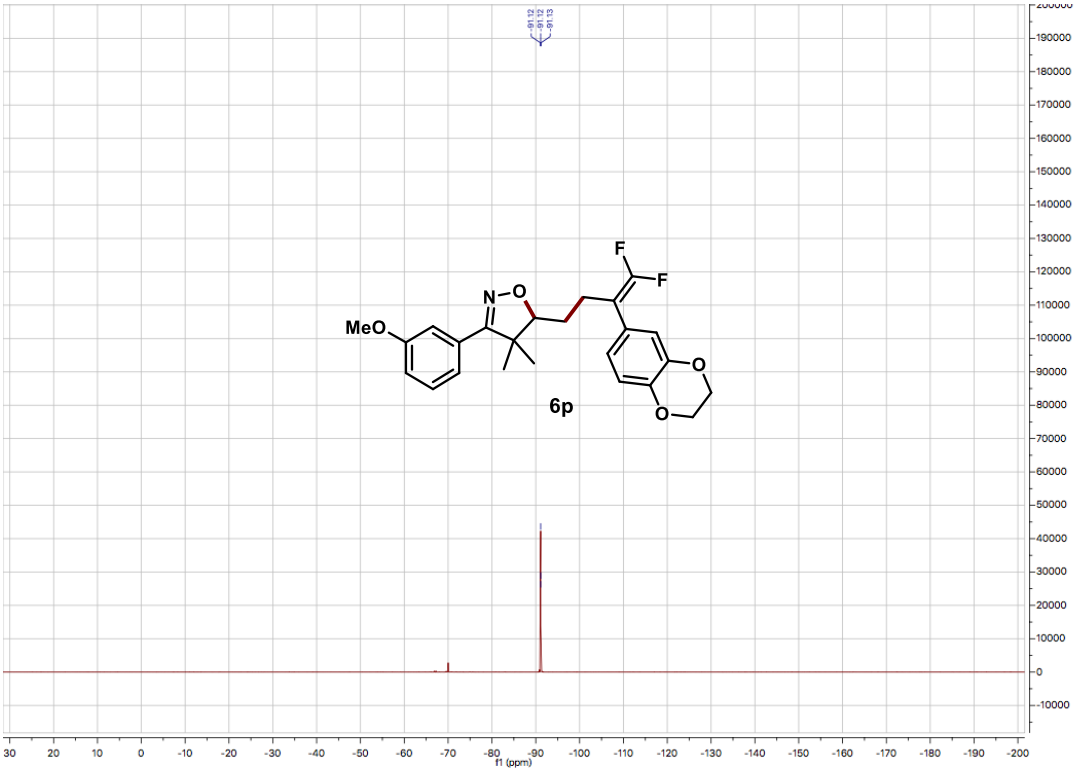

F
F
N
O
Me
O
O
6o
f1 (ppm)


F
F
N
O
Me
O
O
6o
f1 (ppm)


F
F
N
O
Me
O
O
6o
f1 (ppm)


F
F
N
O
MeO
O
O
6p
f1 (ppm)


F
F
N
O
MeO
O
O
6p
f1 (ppm)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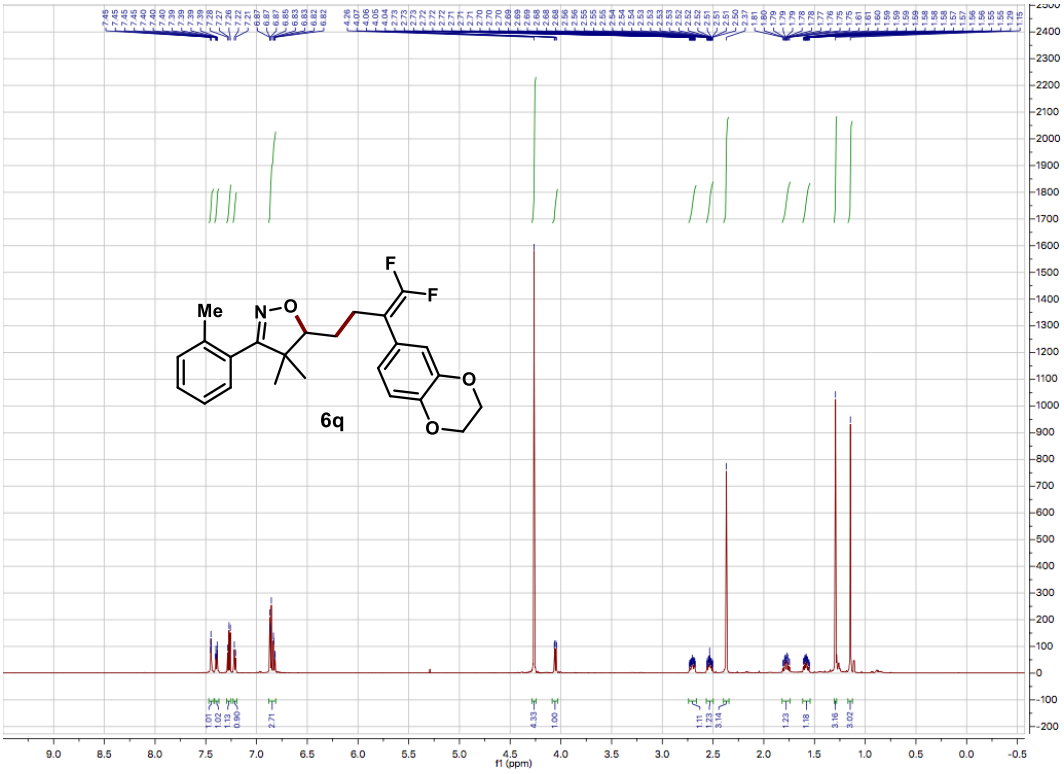
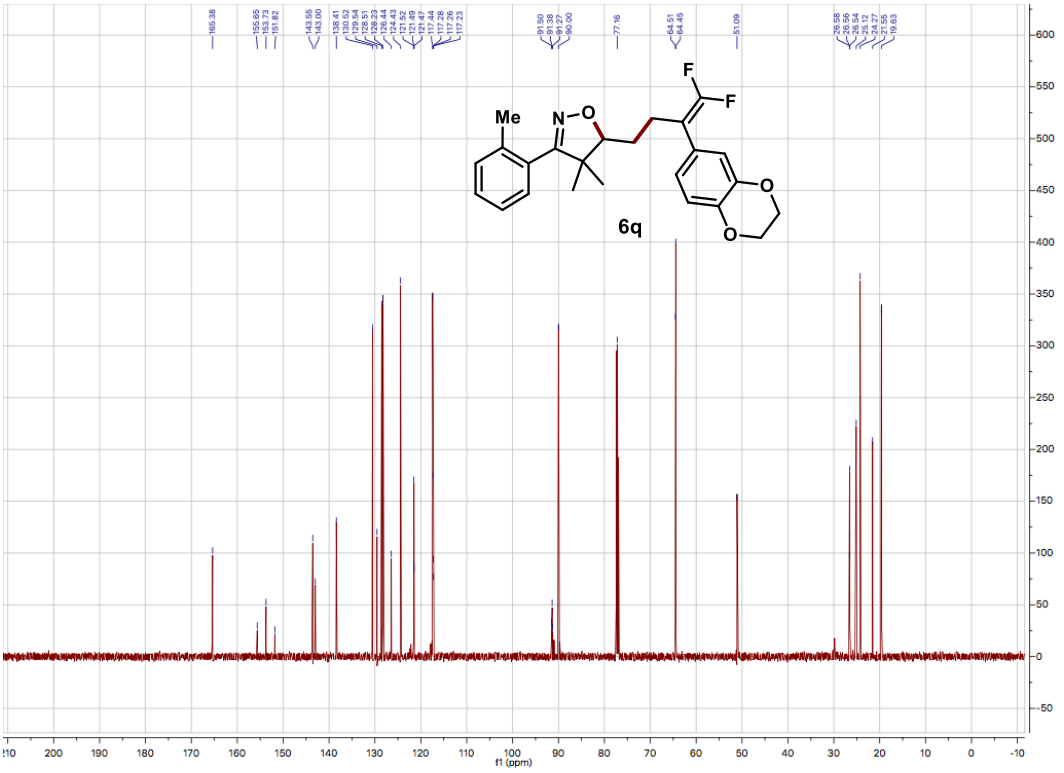
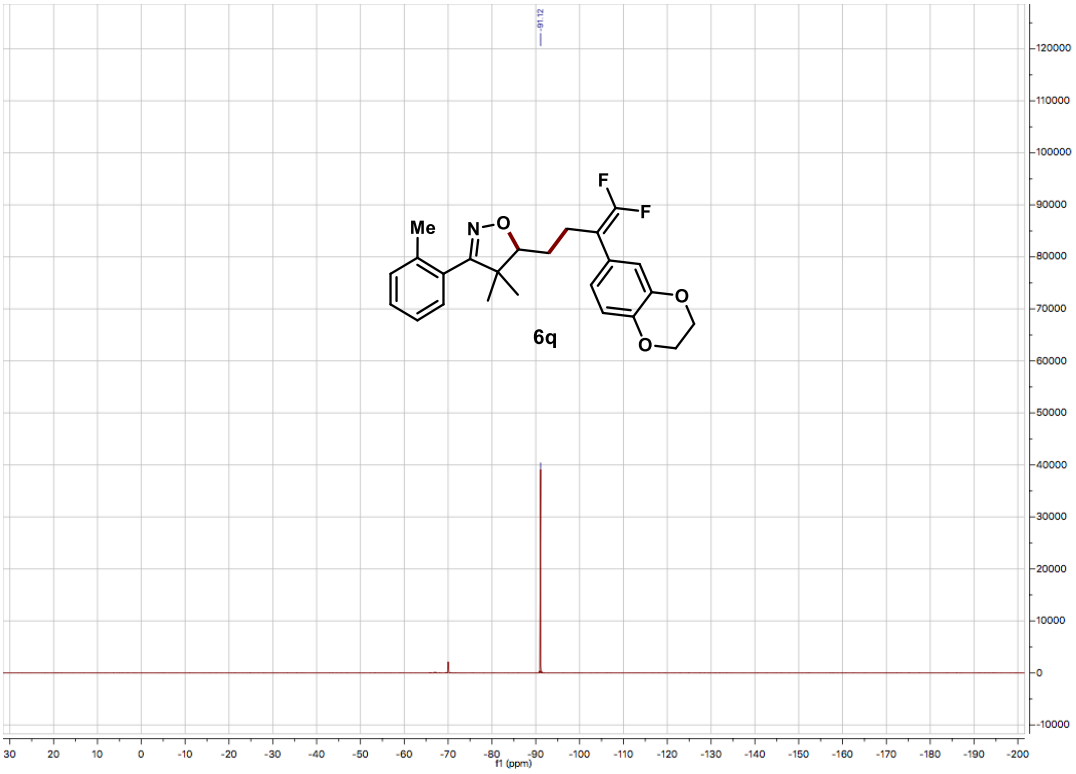
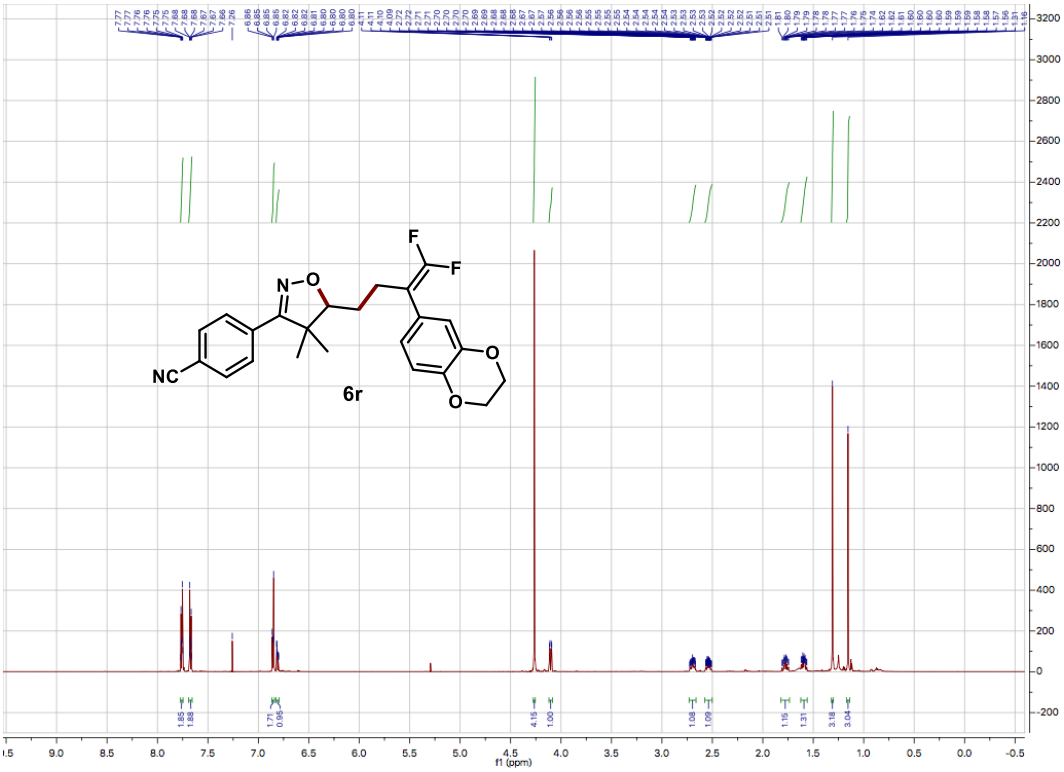
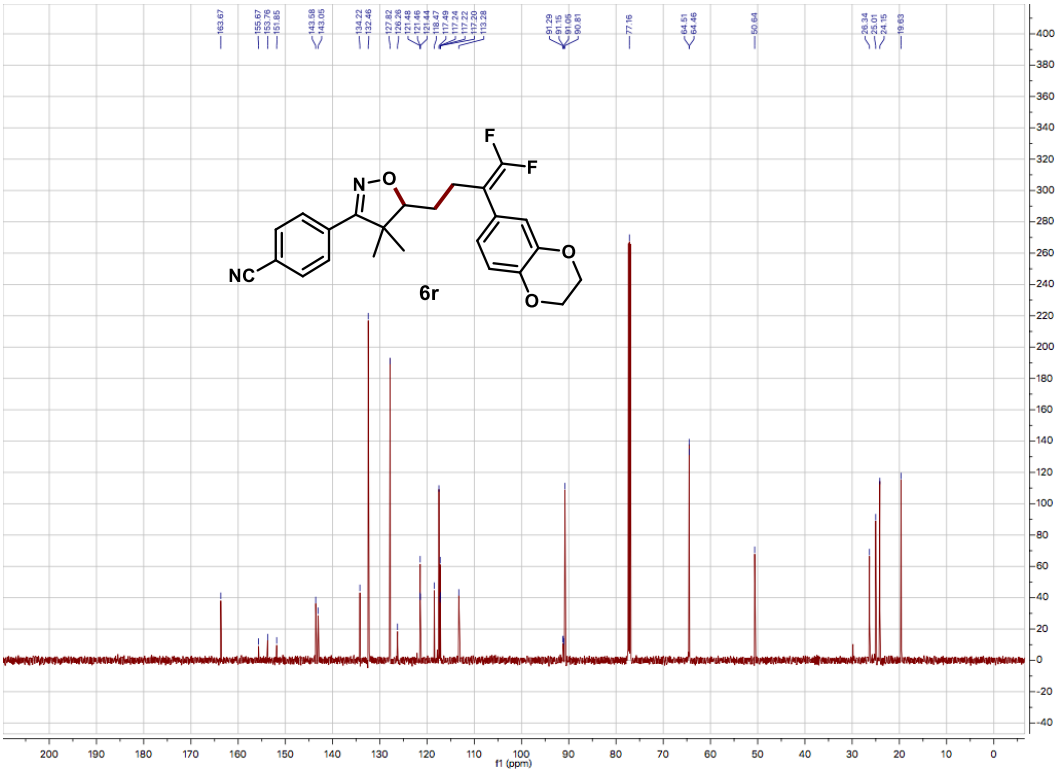
F
N
O
MeO
O
O
6p
f1 (ppm)

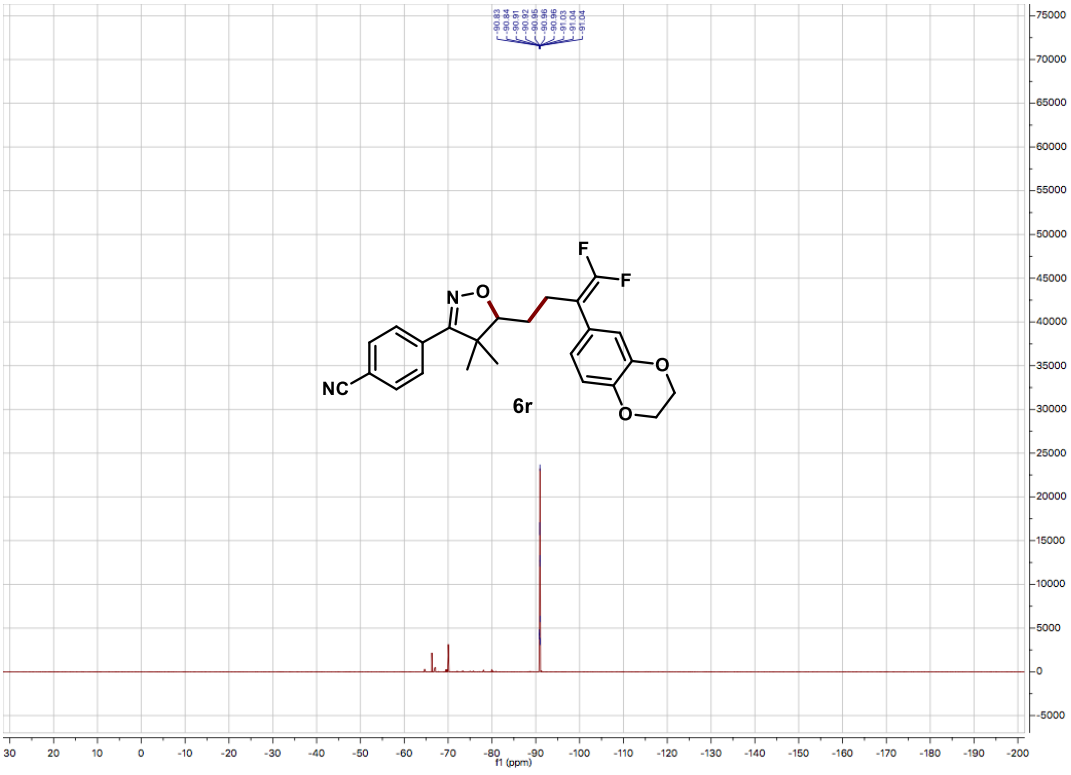

Me
N
O
F
F
O
O
6q
f1 (ppm)

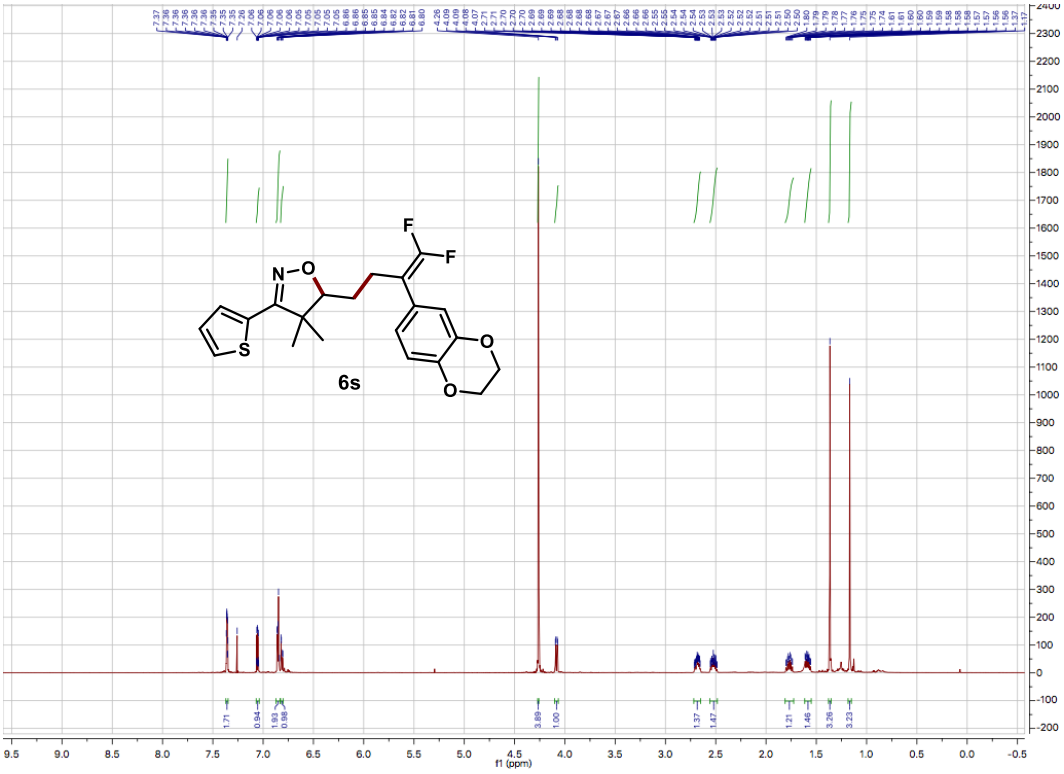

Me
N
O
F
F
O
O
6q
f1 (ppm)

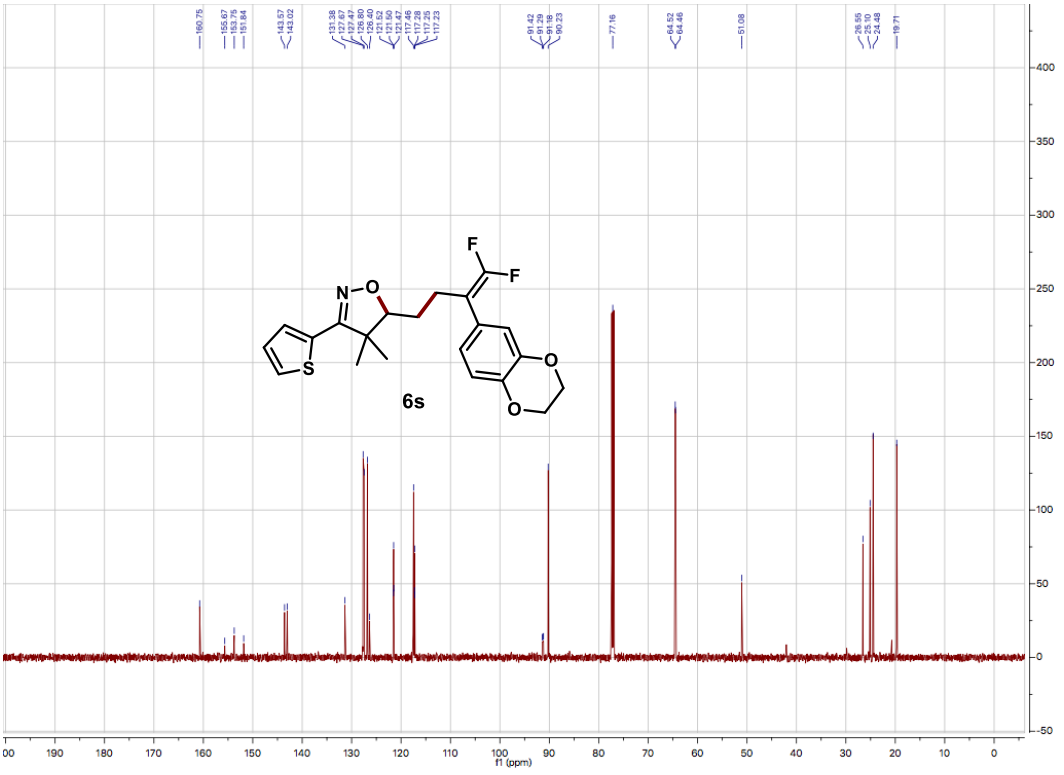

Me
N
O
F
F
O
O
6q
f1 (ppm)

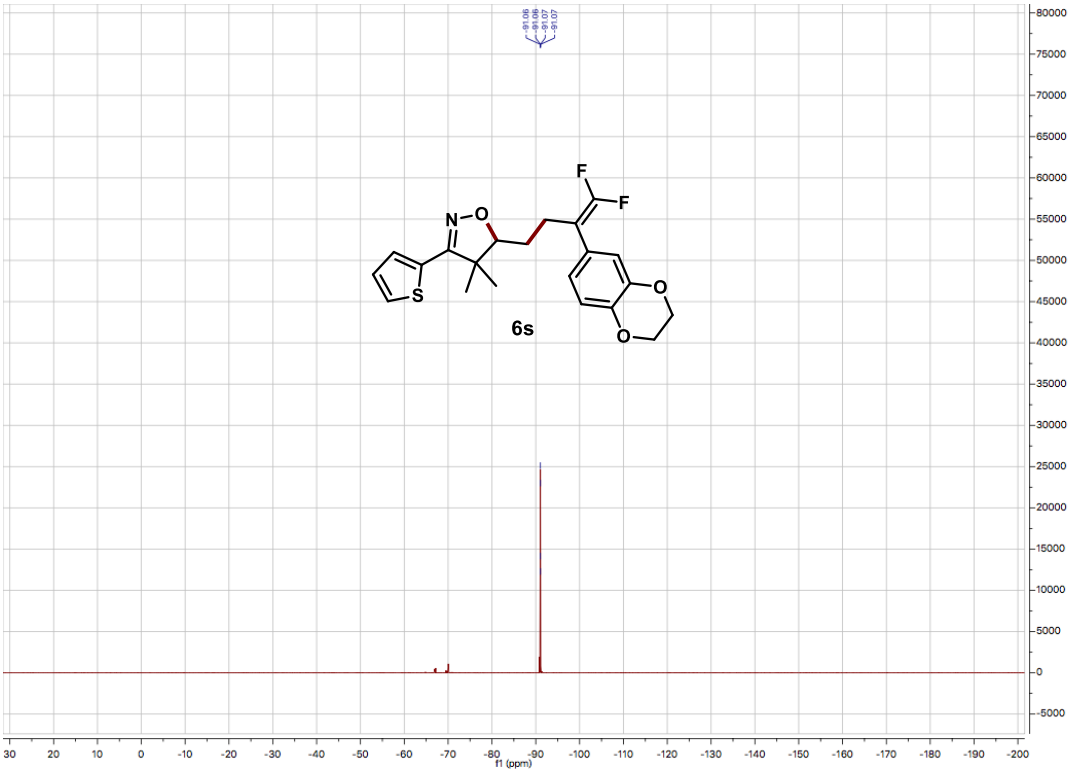

NC
N
O
F
F
O
O
6r
f1 (ppm)

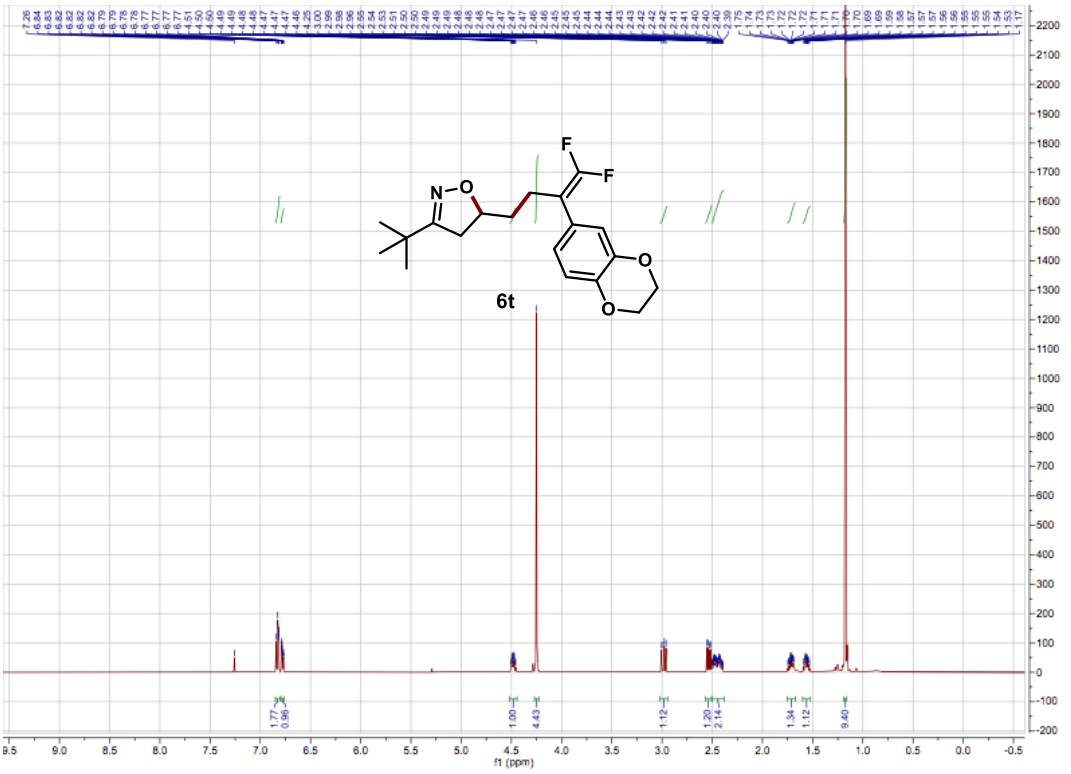

F
F
N
O
NC
O
O
6r
f1 (ppm)


F
F
N
O
NC
O
O
6r
f1 (ppm)


F
F
N
O
S
O
O
6s


F
F
N
O
S
O
O
6s


F
F
N
O
S
O
O
6s
f1 (ppm)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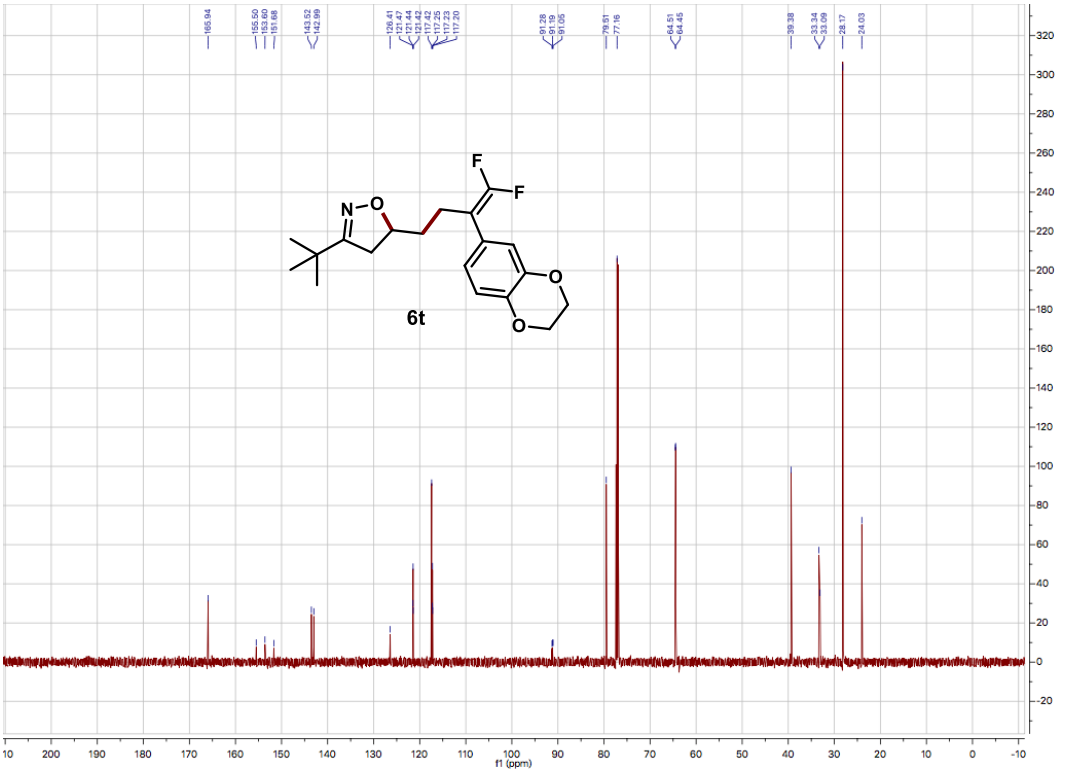
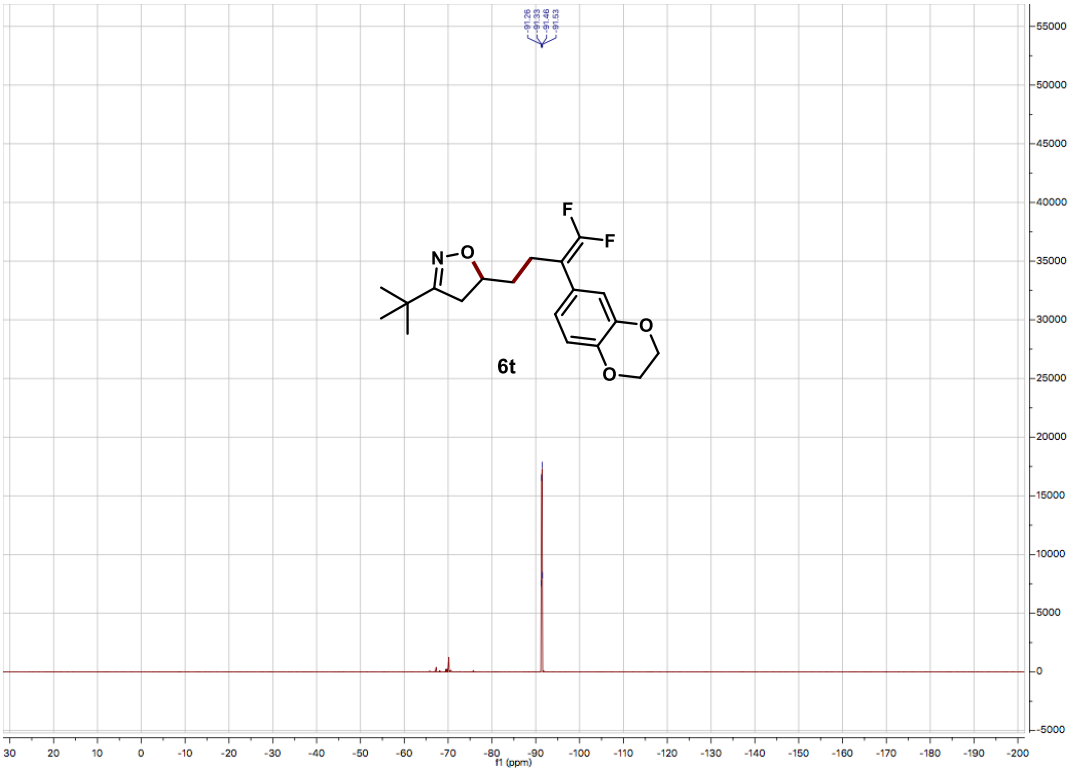
F
N
O
O
O
6t
f1 (ppm)


F
F
N
O
O
O
O
6t
f1 (ppm)


F
F
N
O
O
O
O
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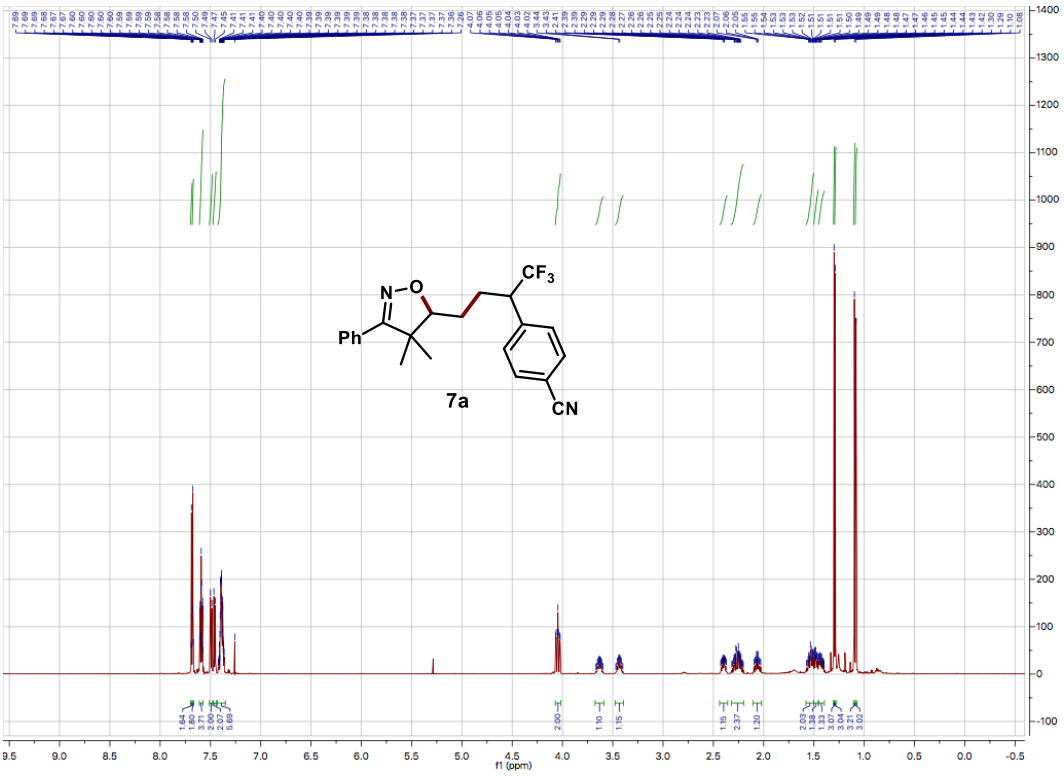
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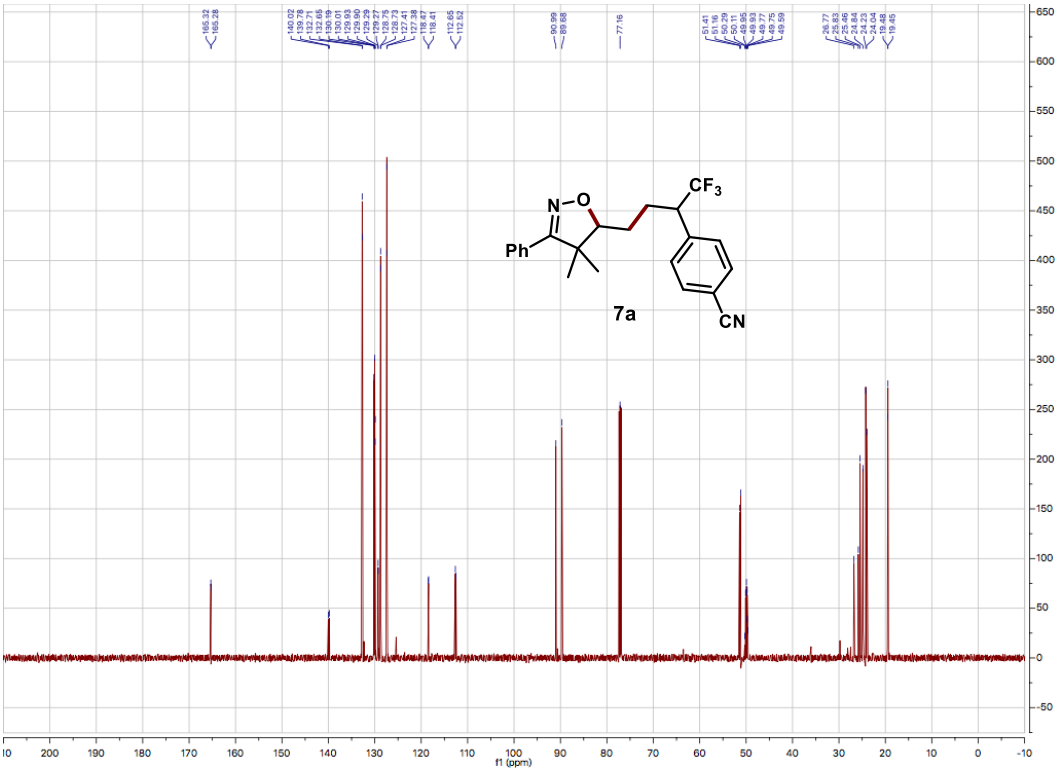
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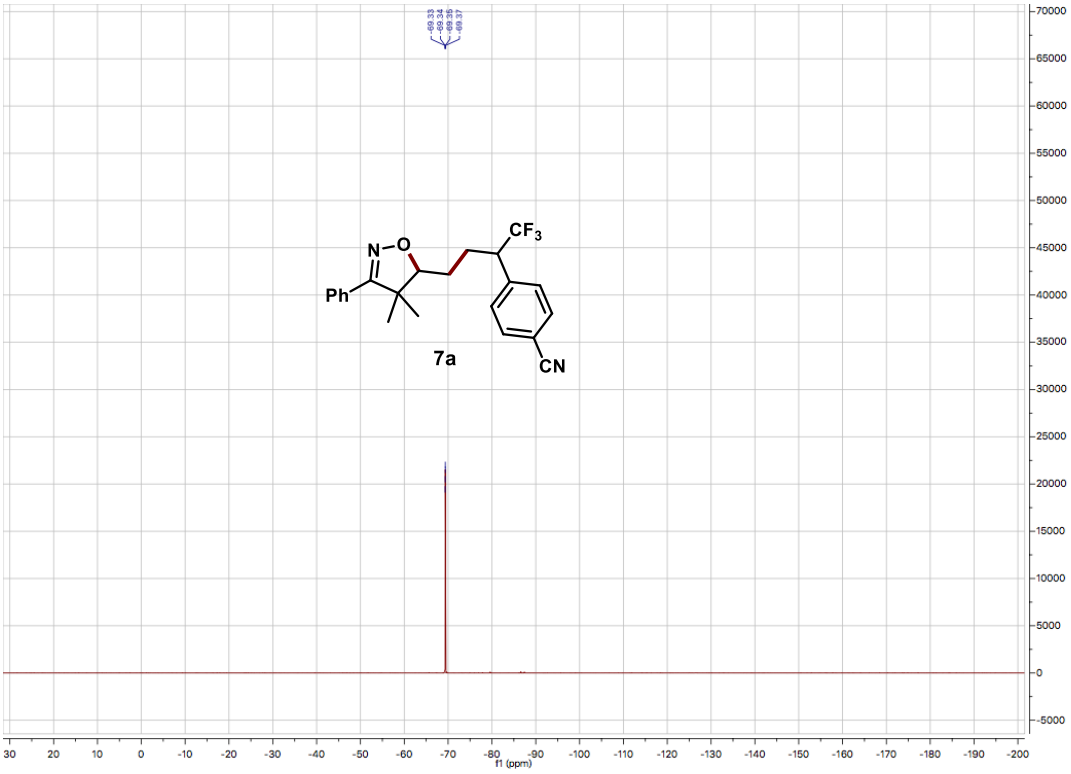
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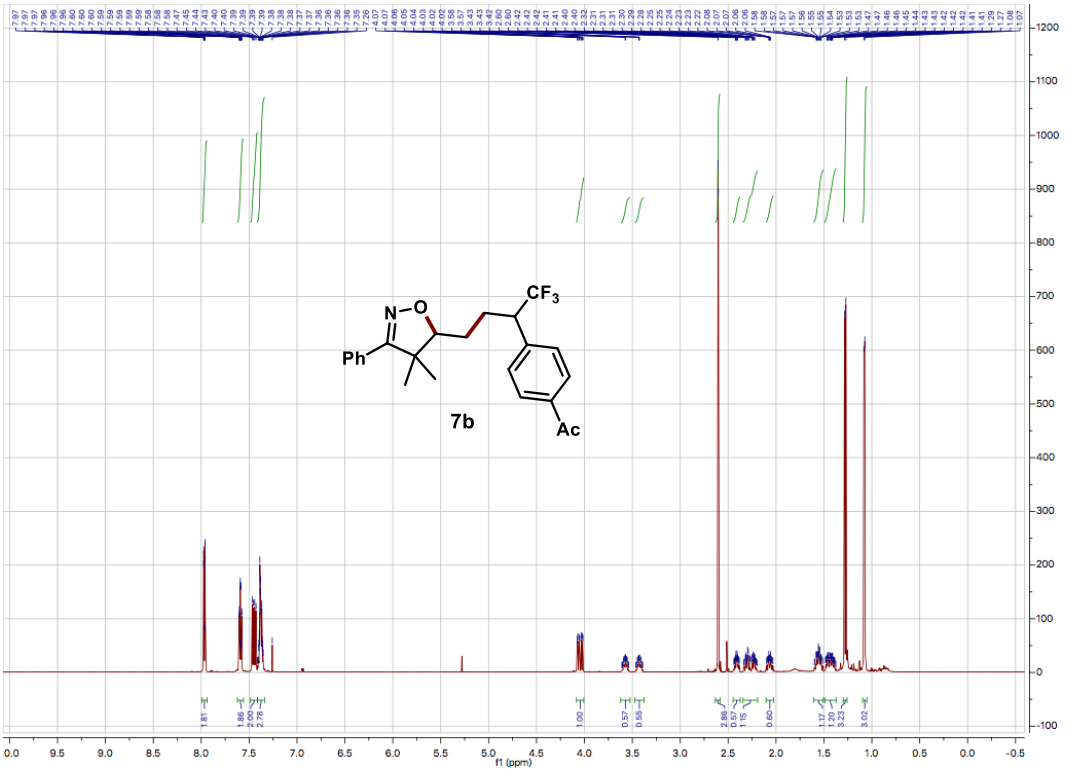
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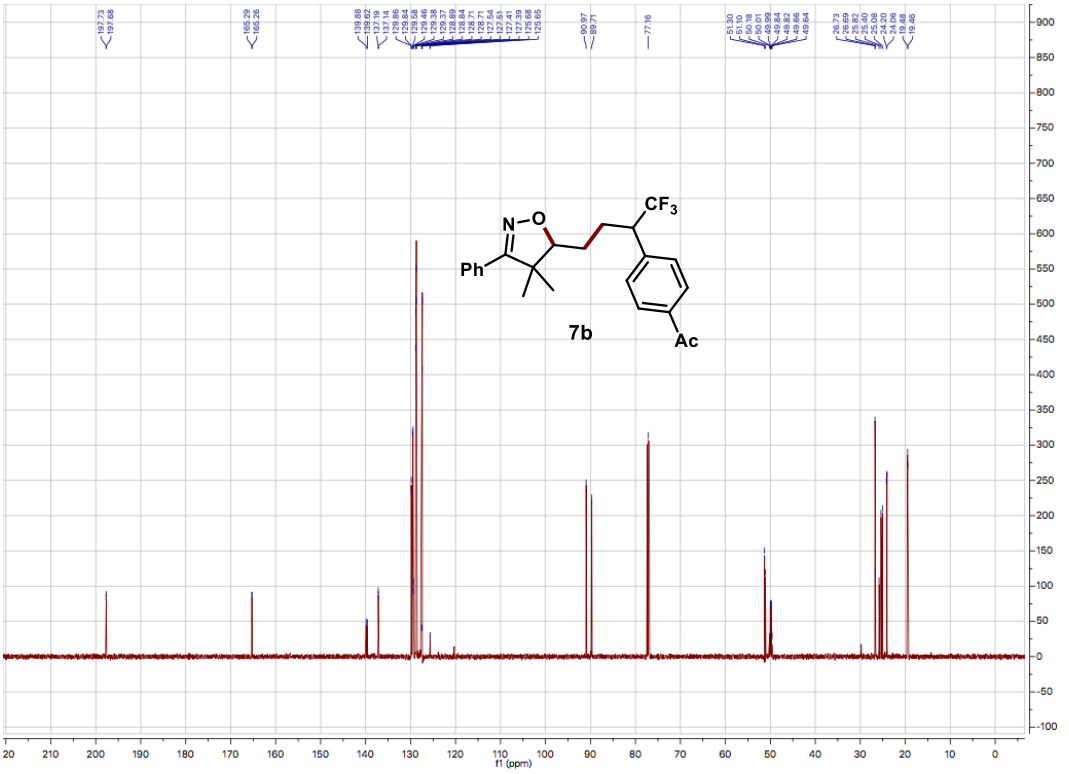
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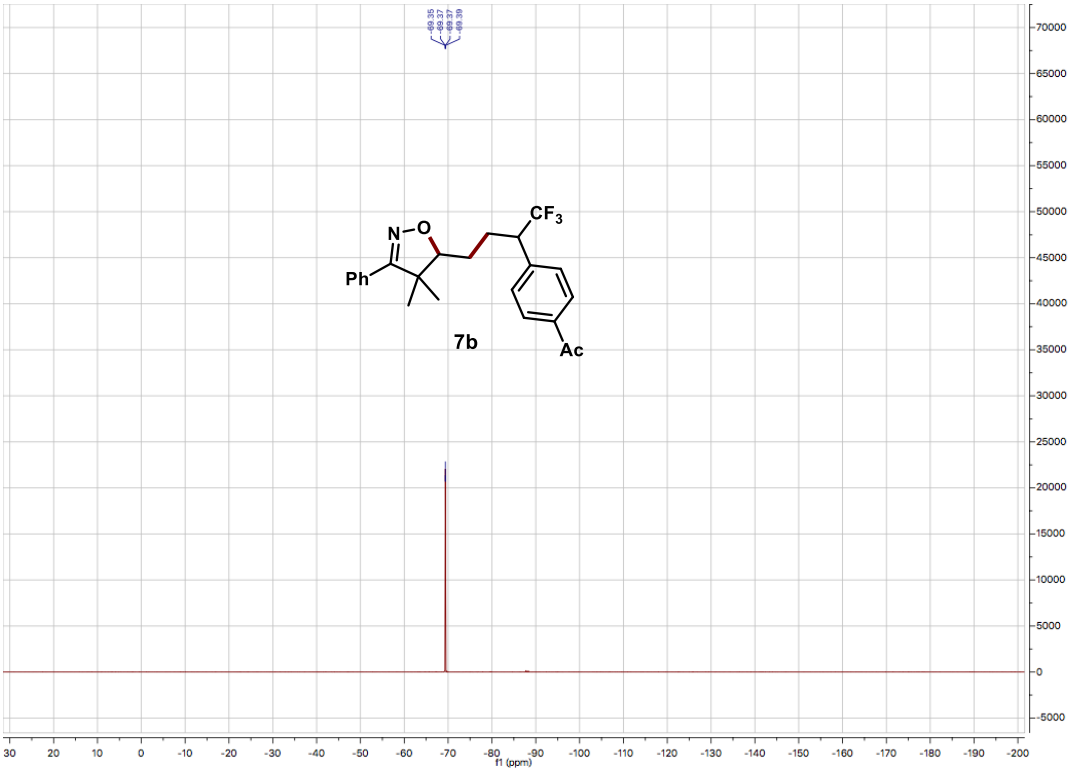
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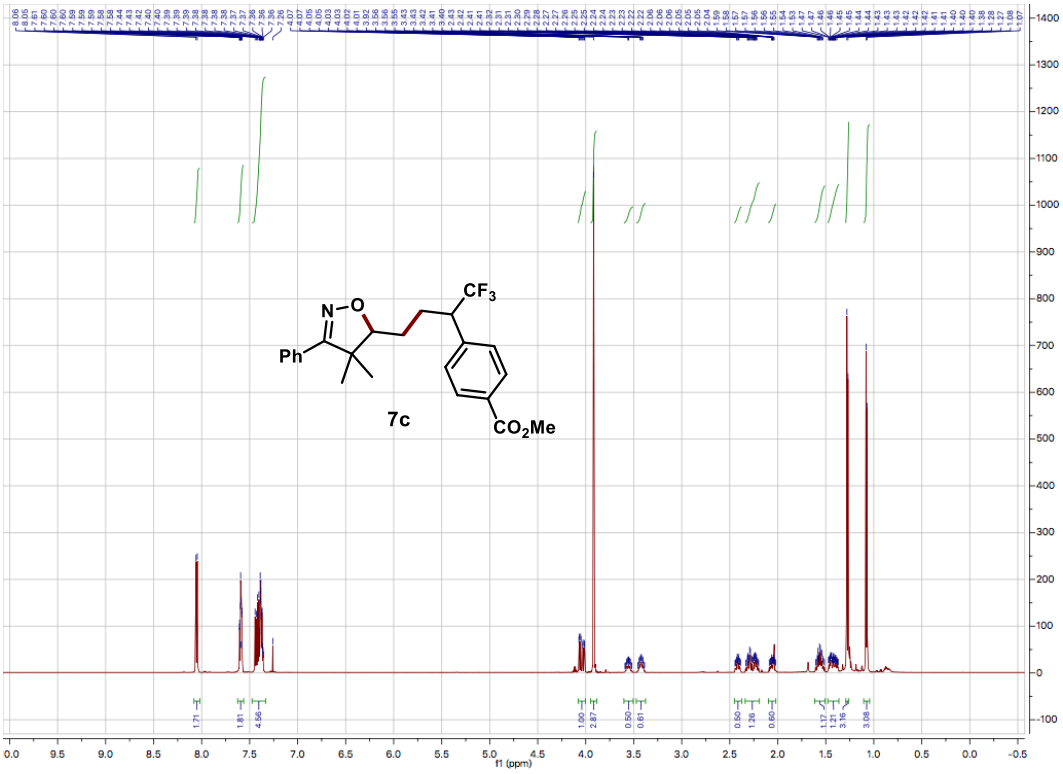
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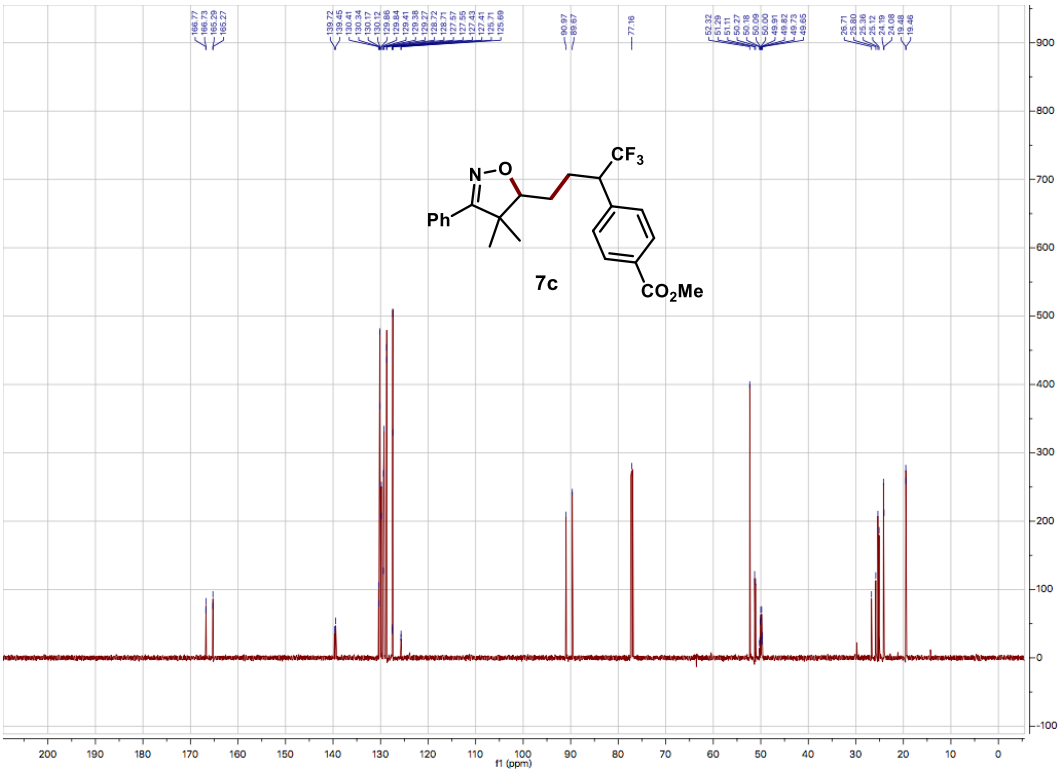
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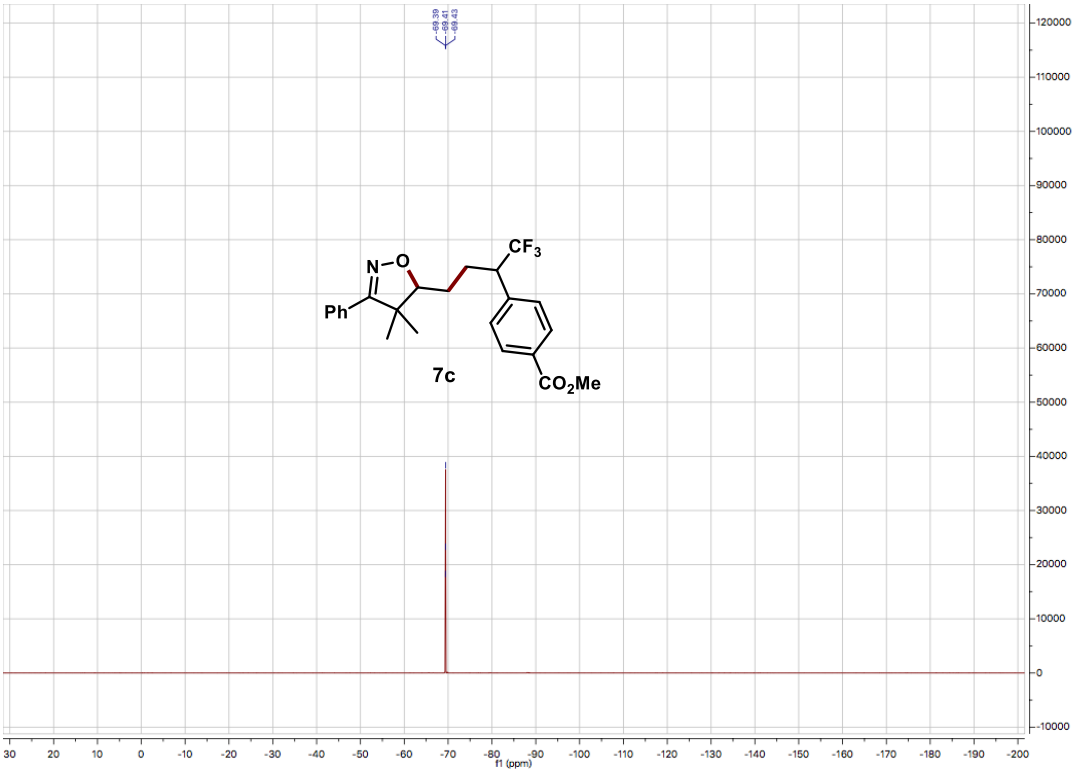
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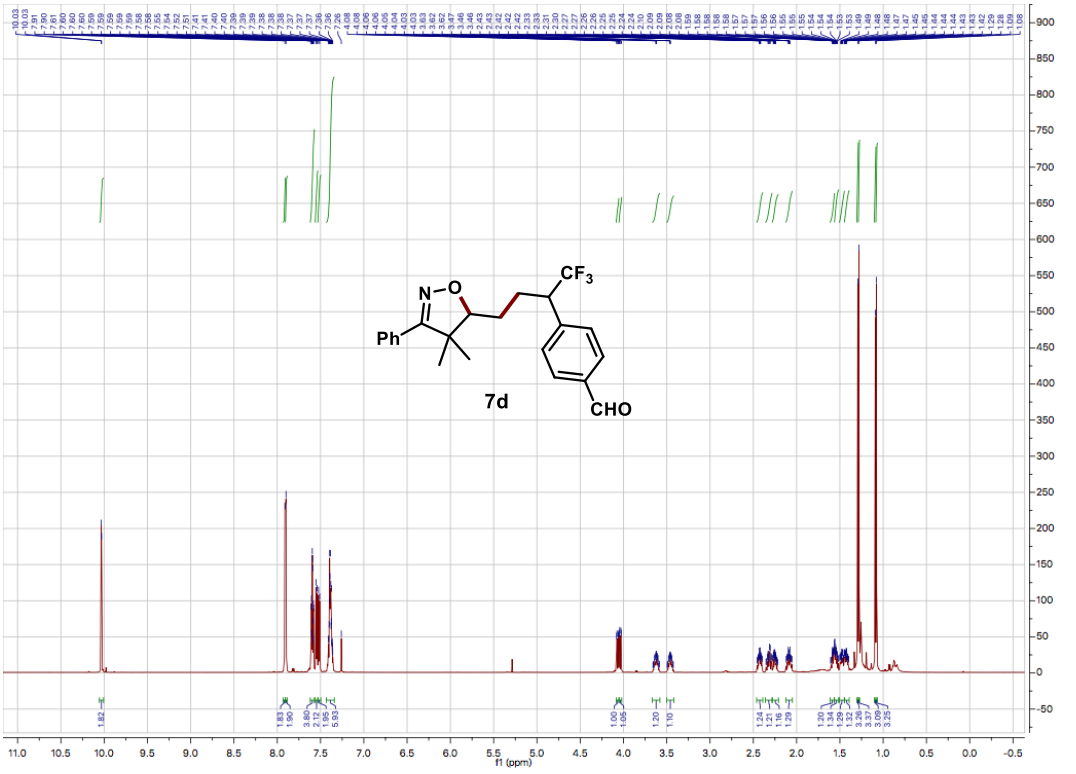
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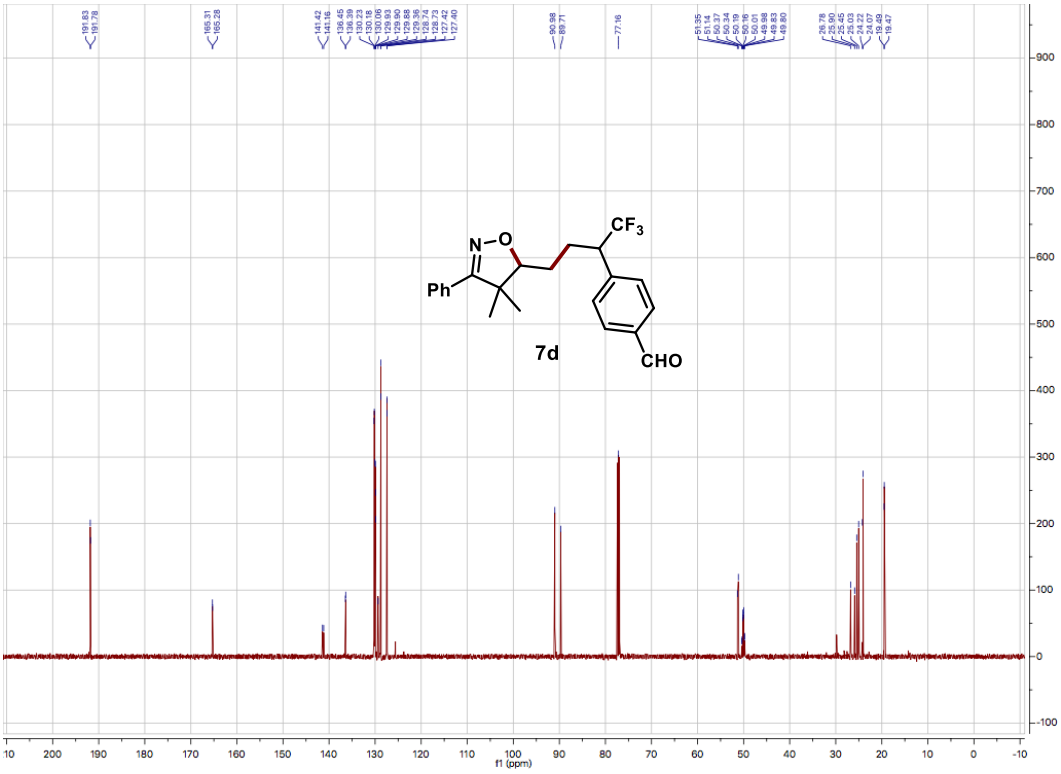
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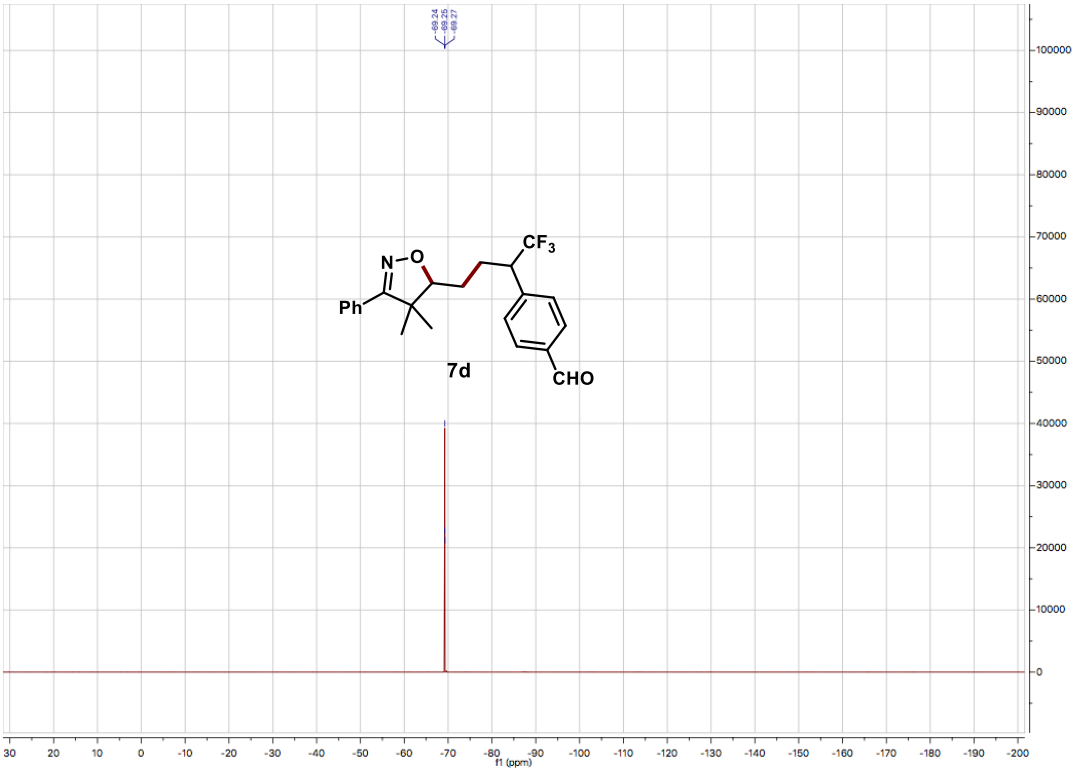
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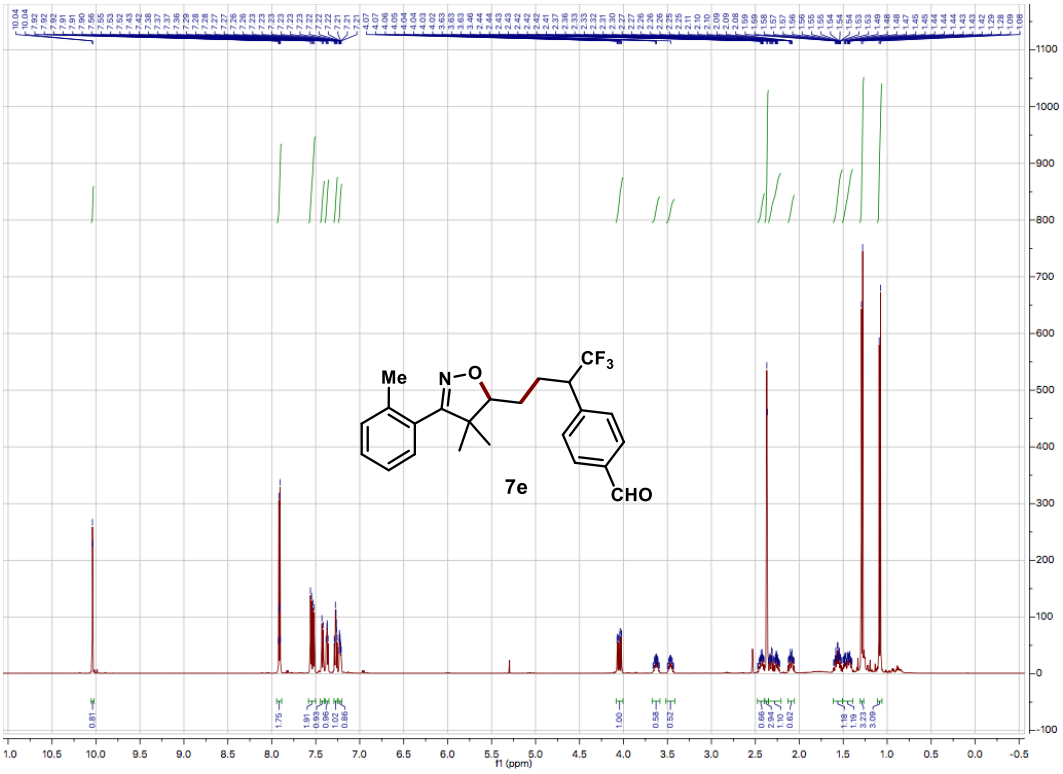
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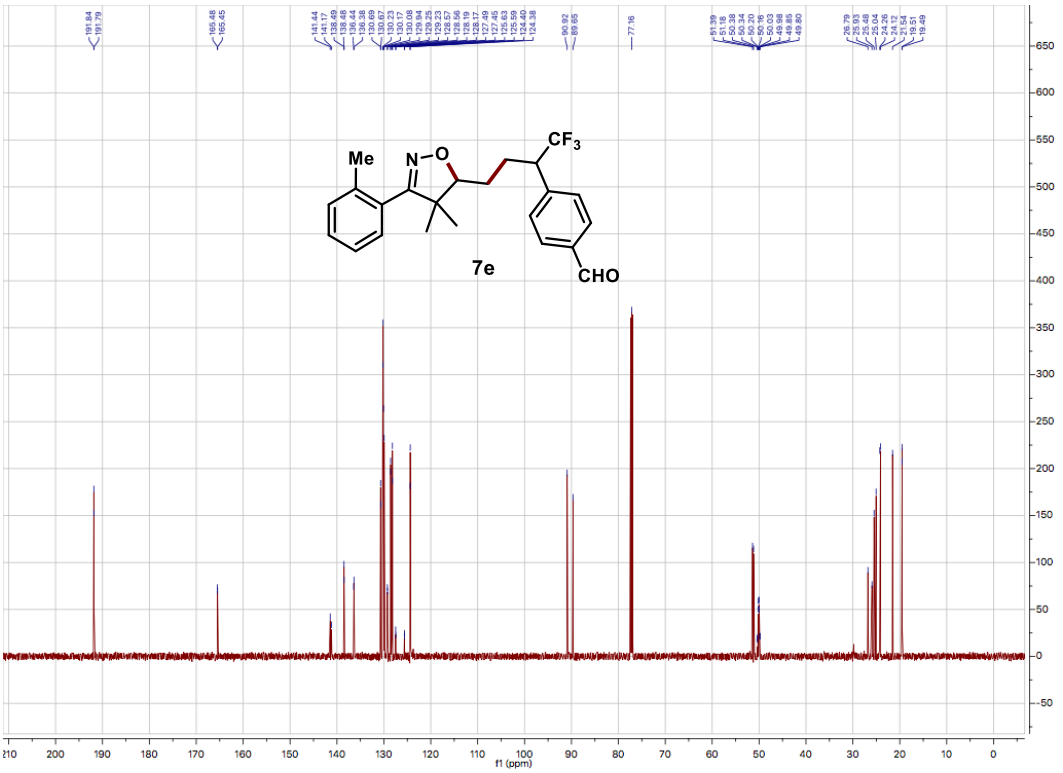
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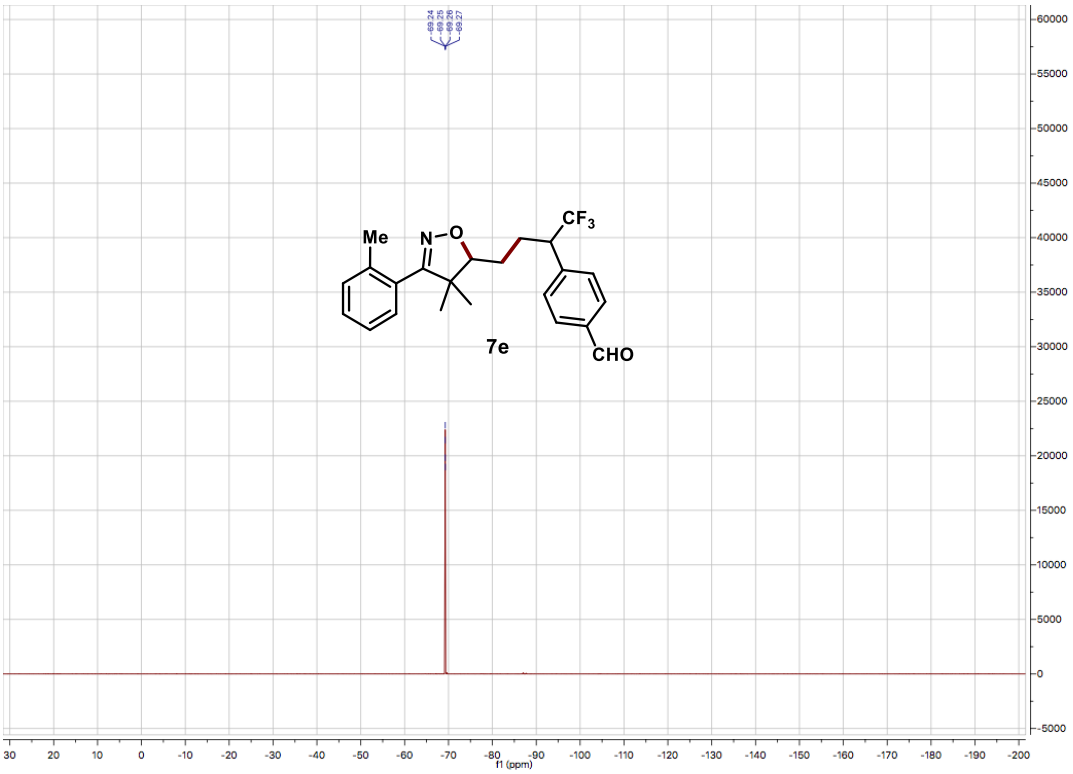
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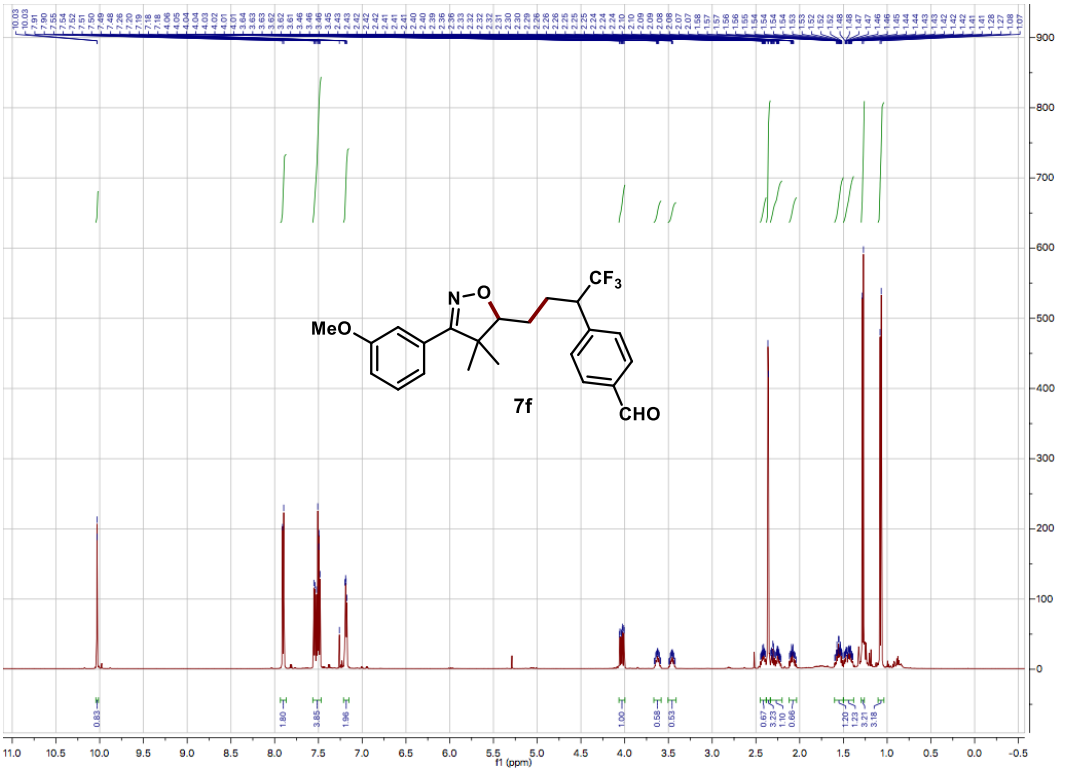
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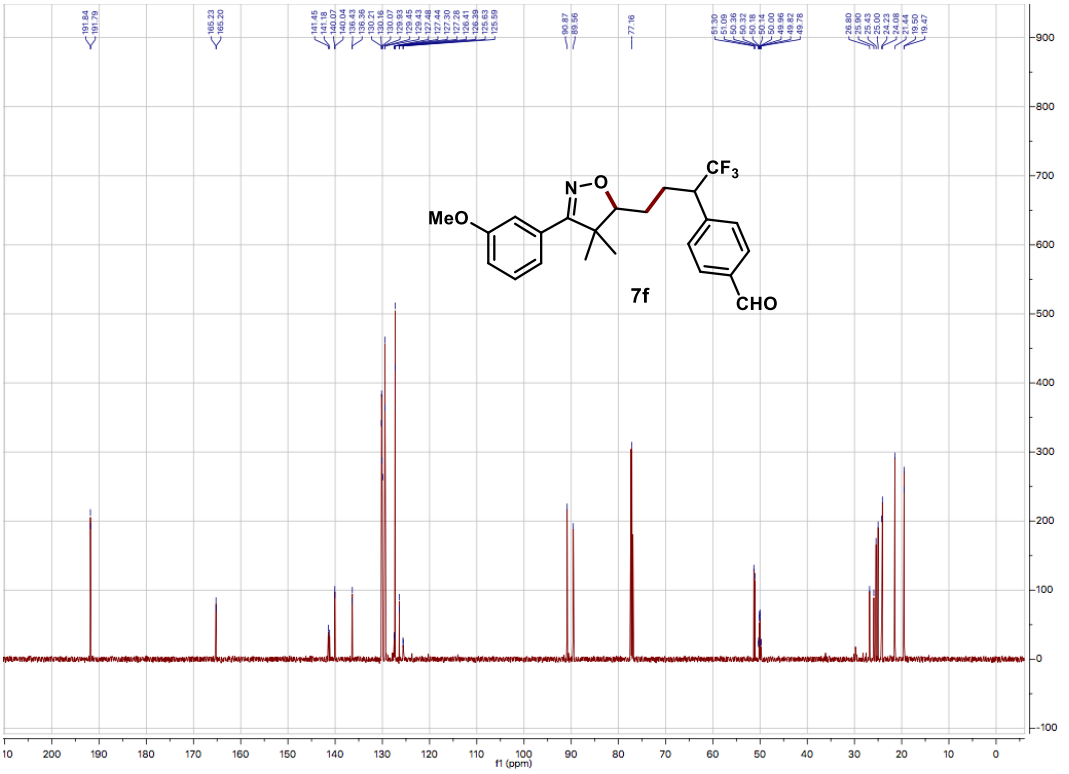
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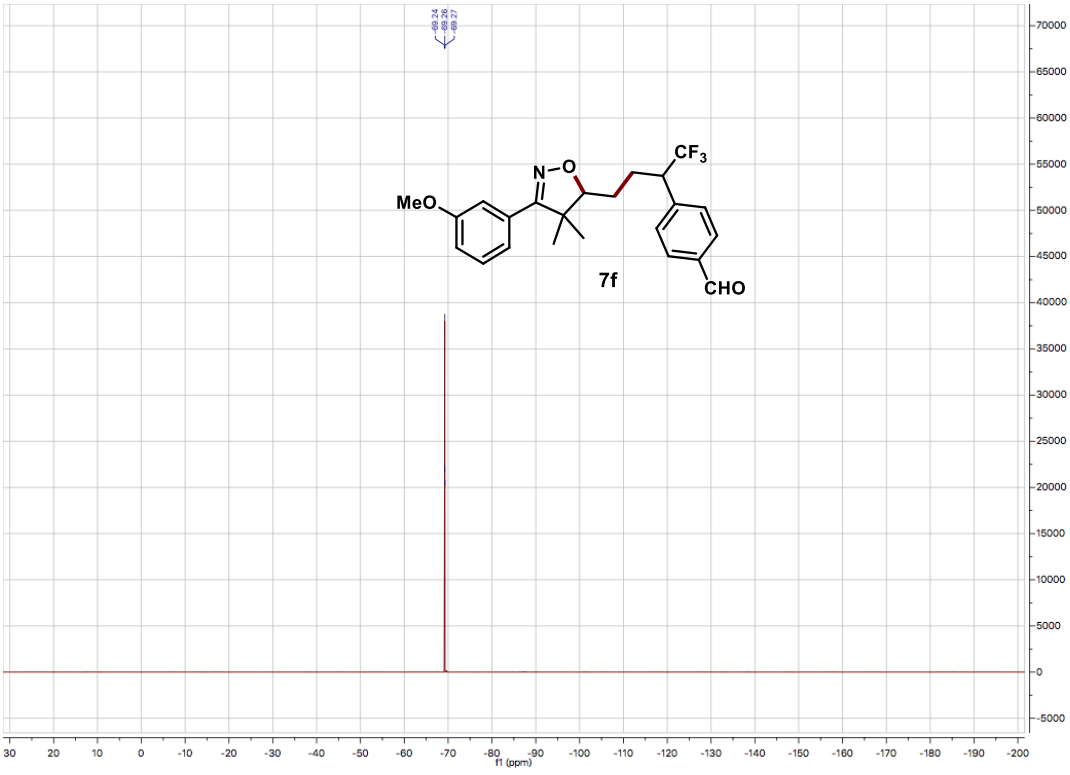
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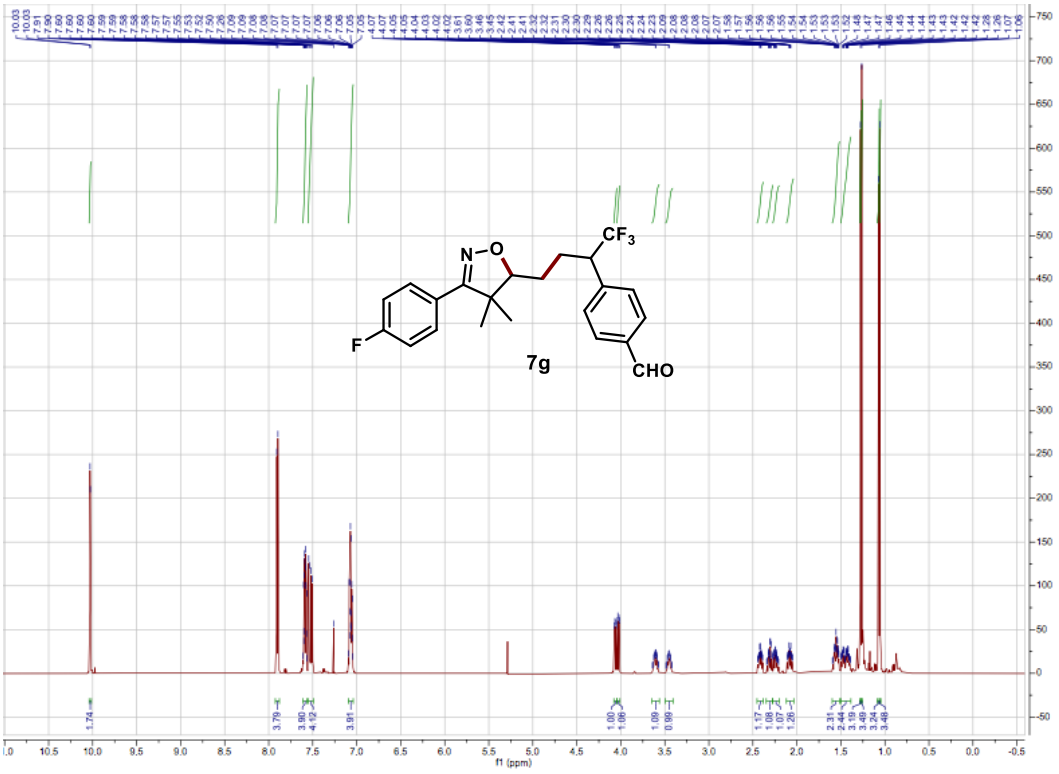
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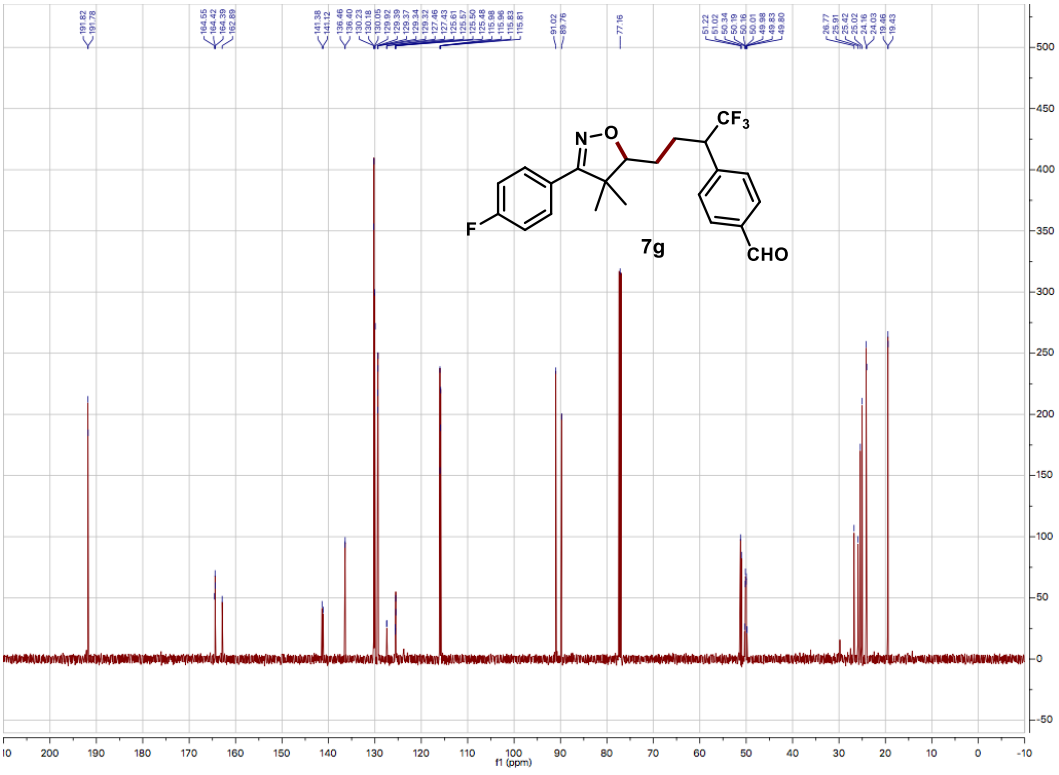
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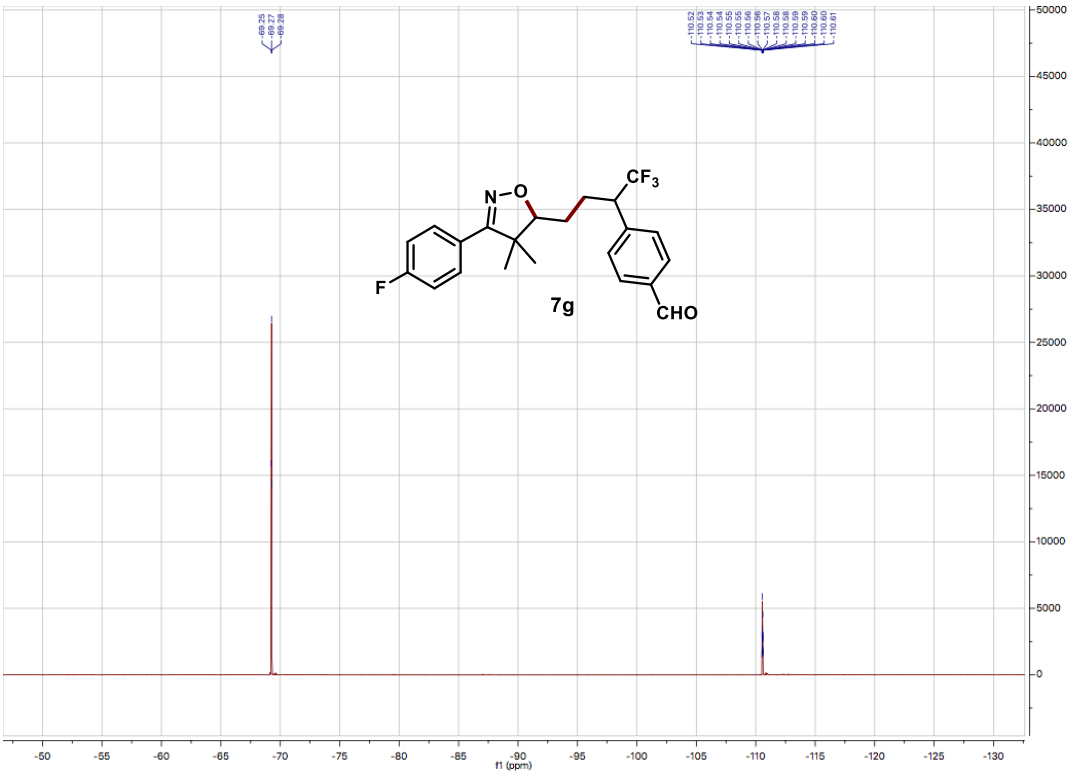
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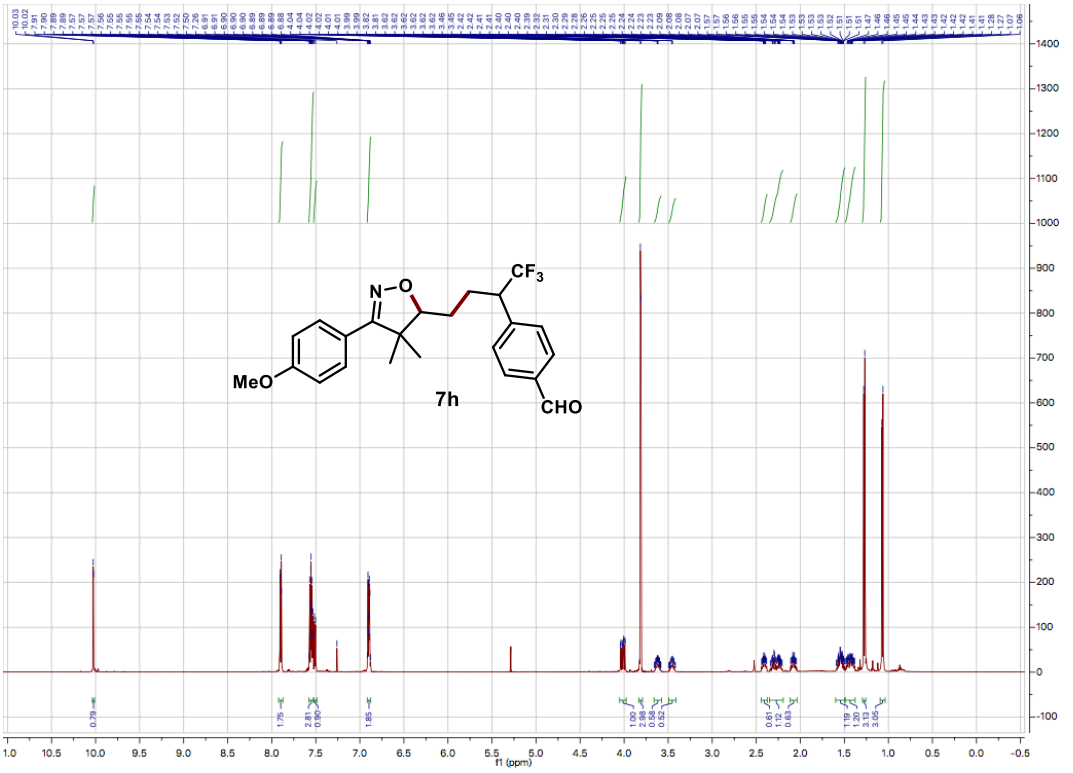
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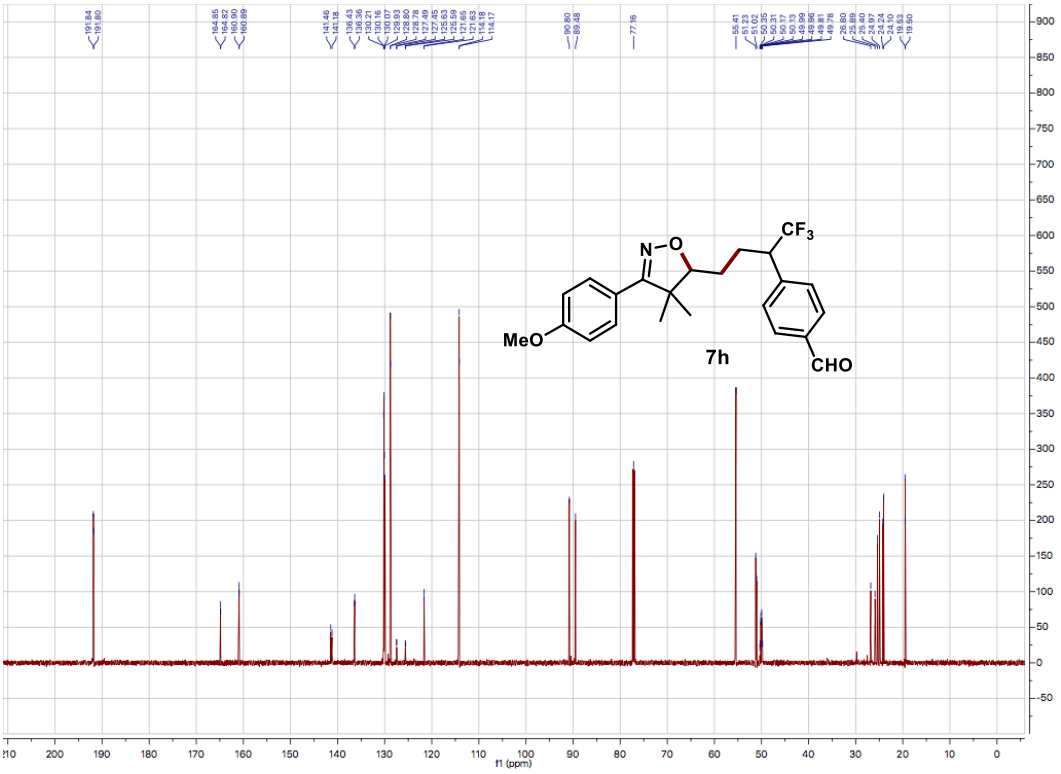
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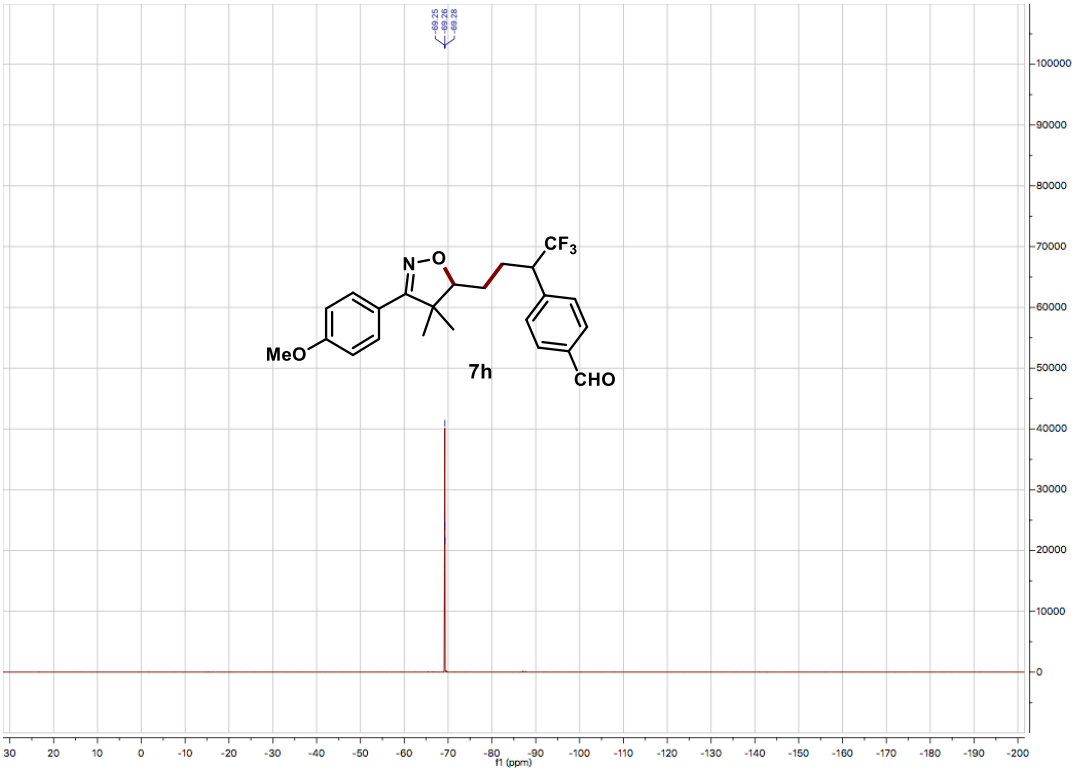
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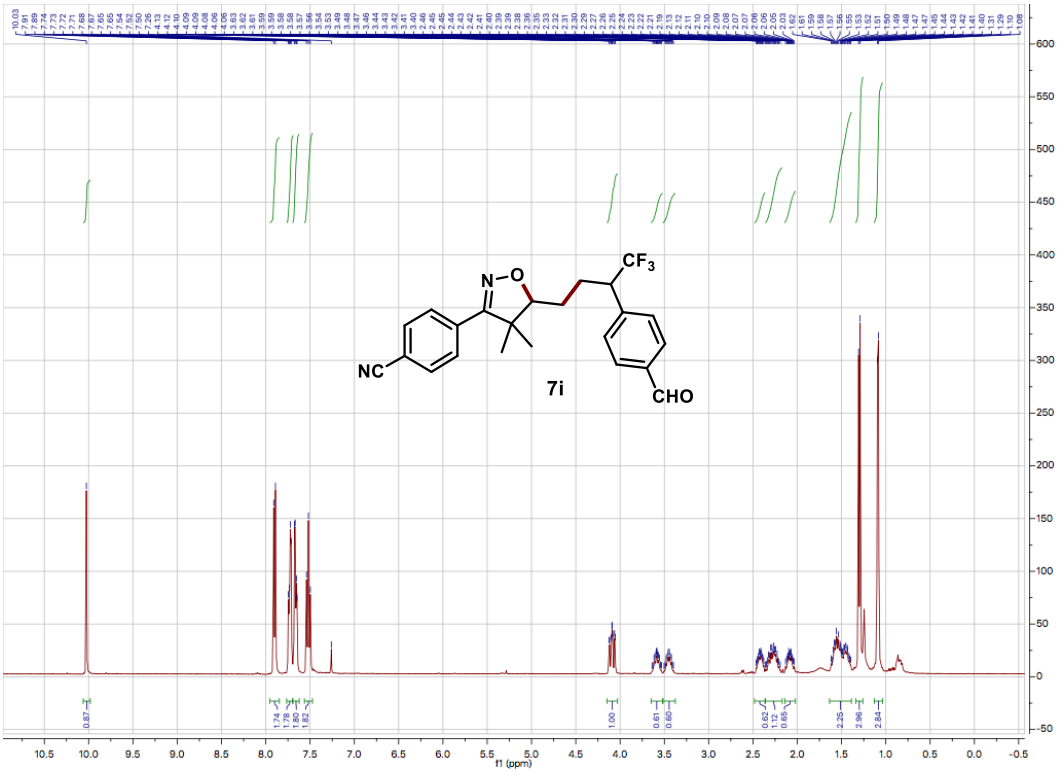
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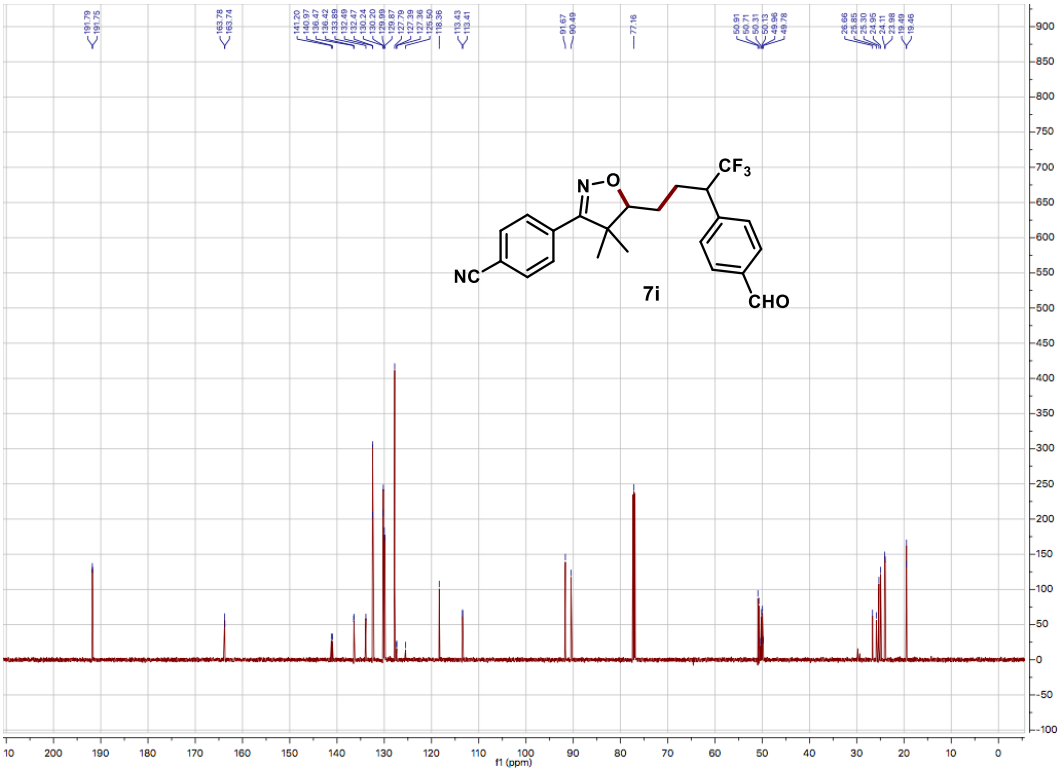
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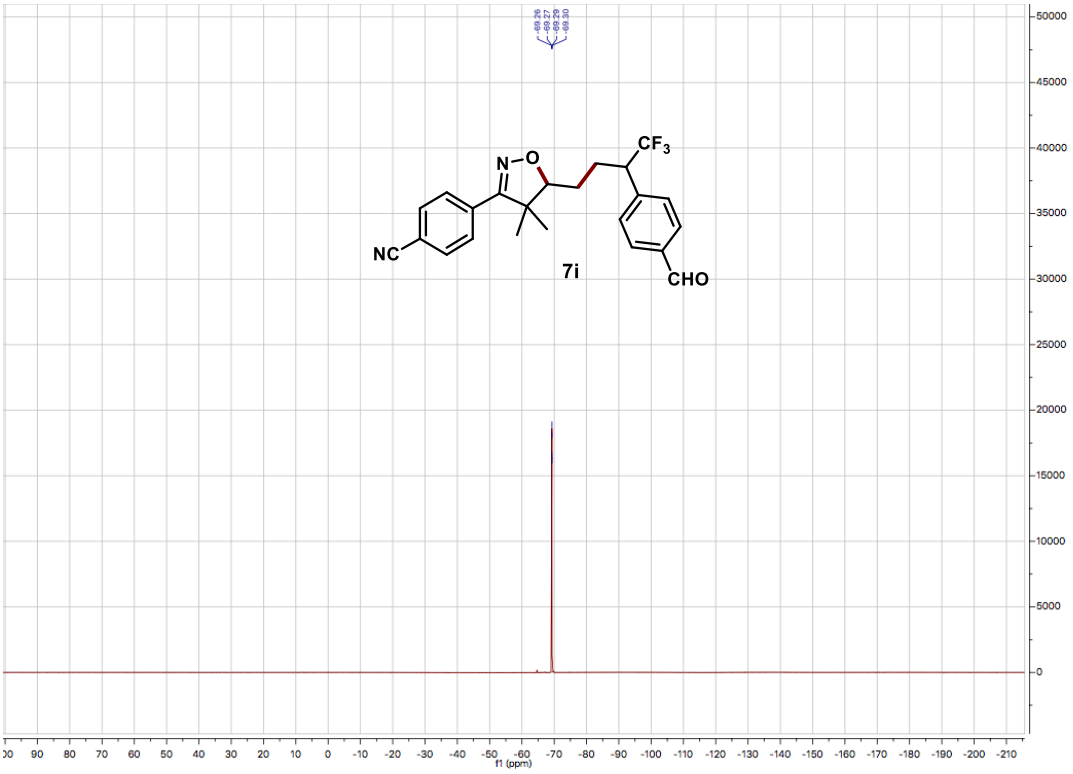
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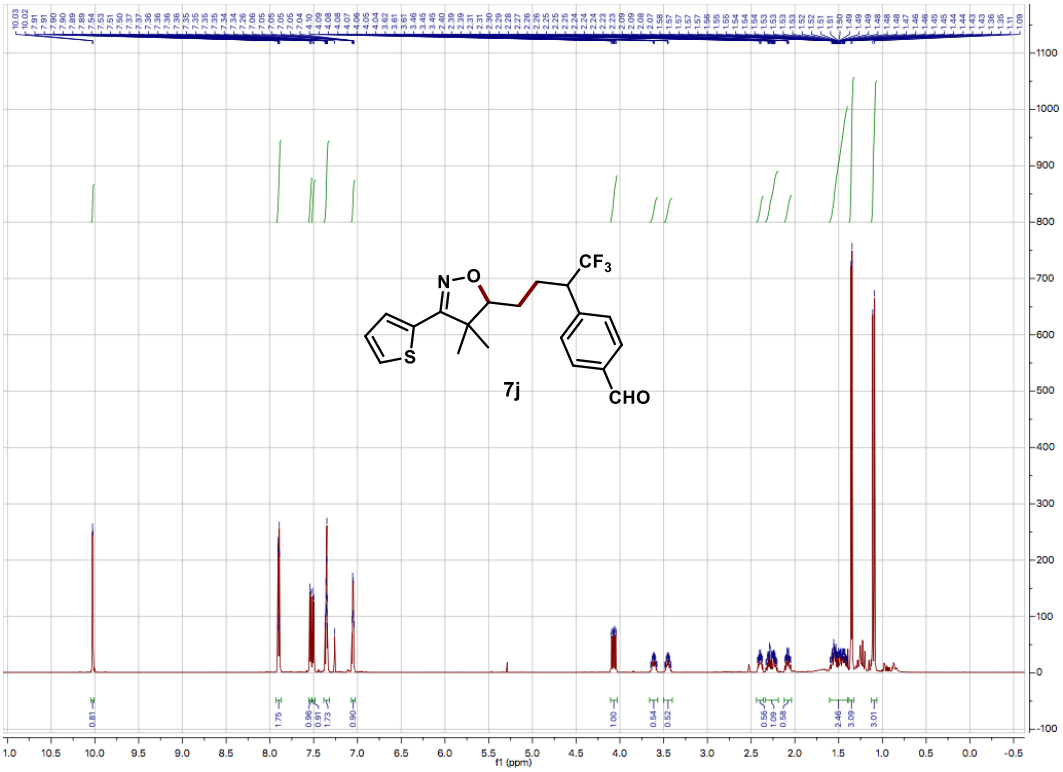
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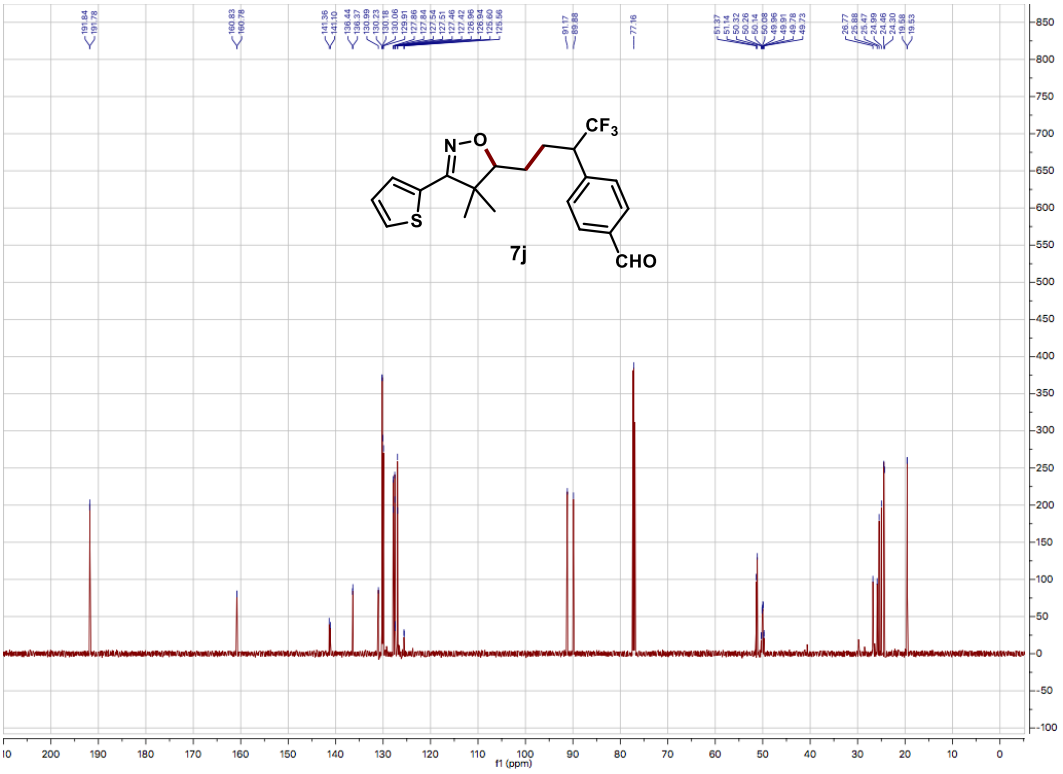
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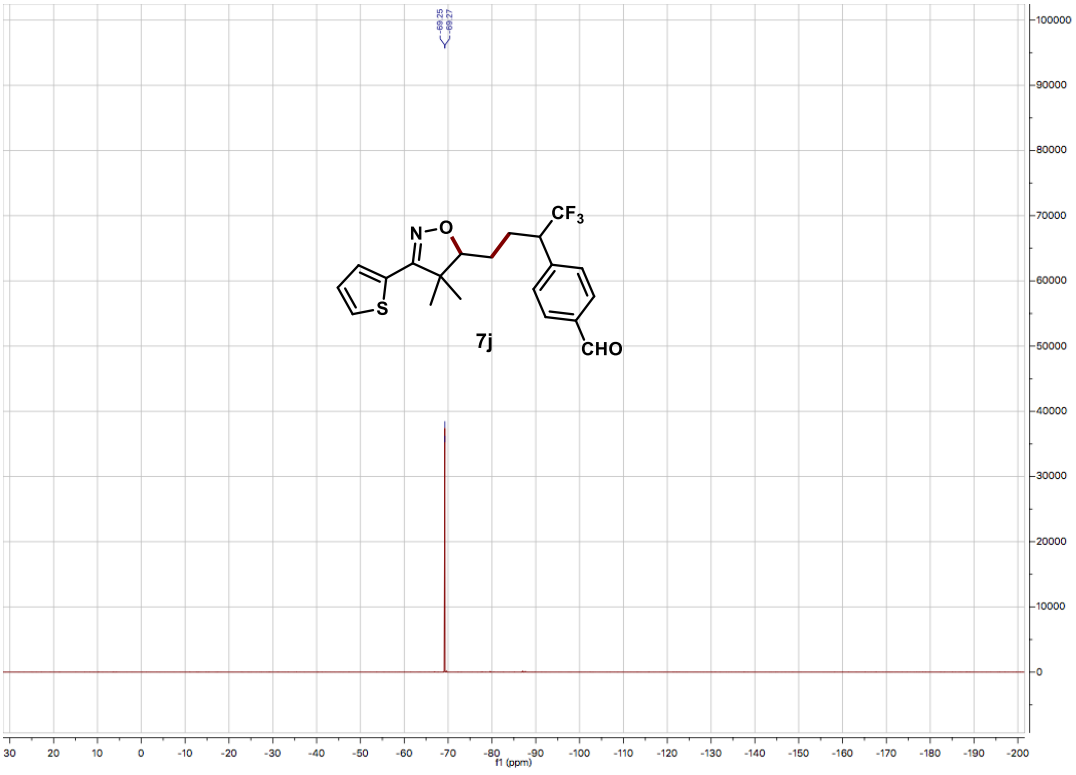
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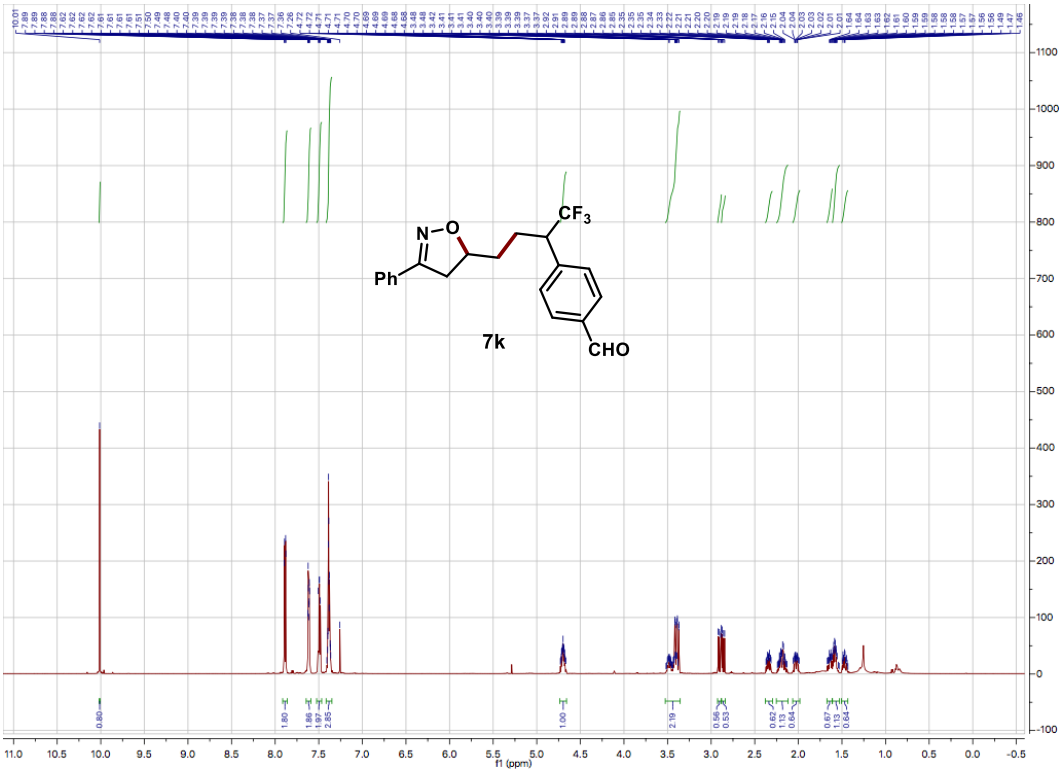
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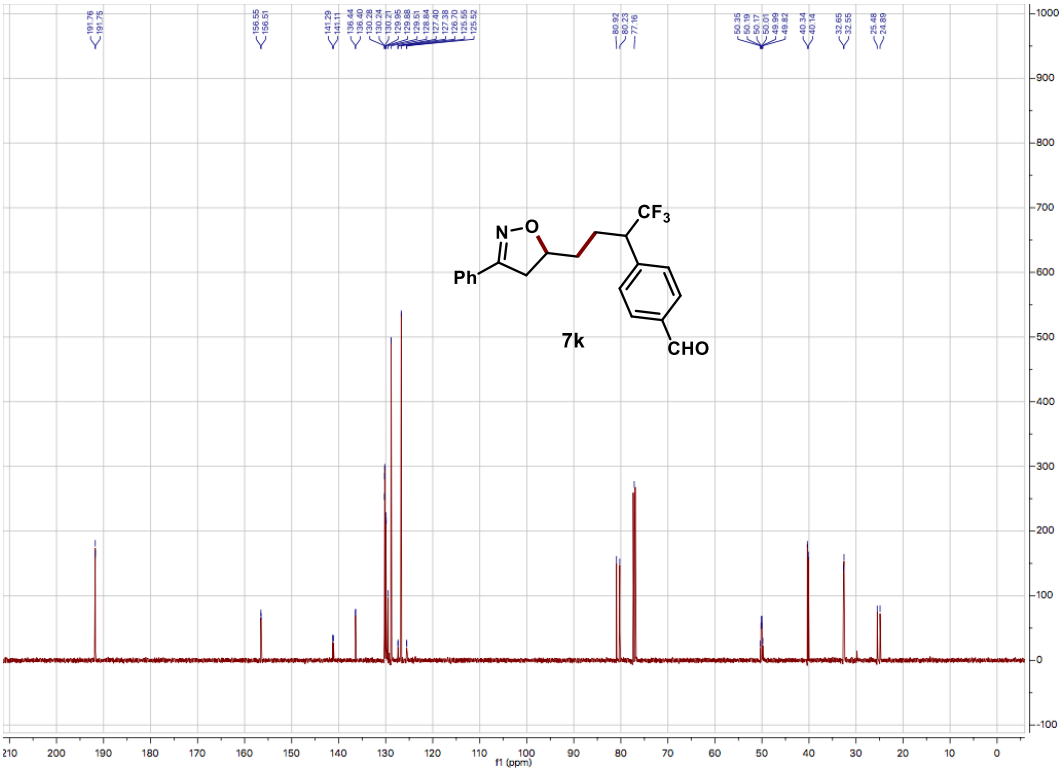
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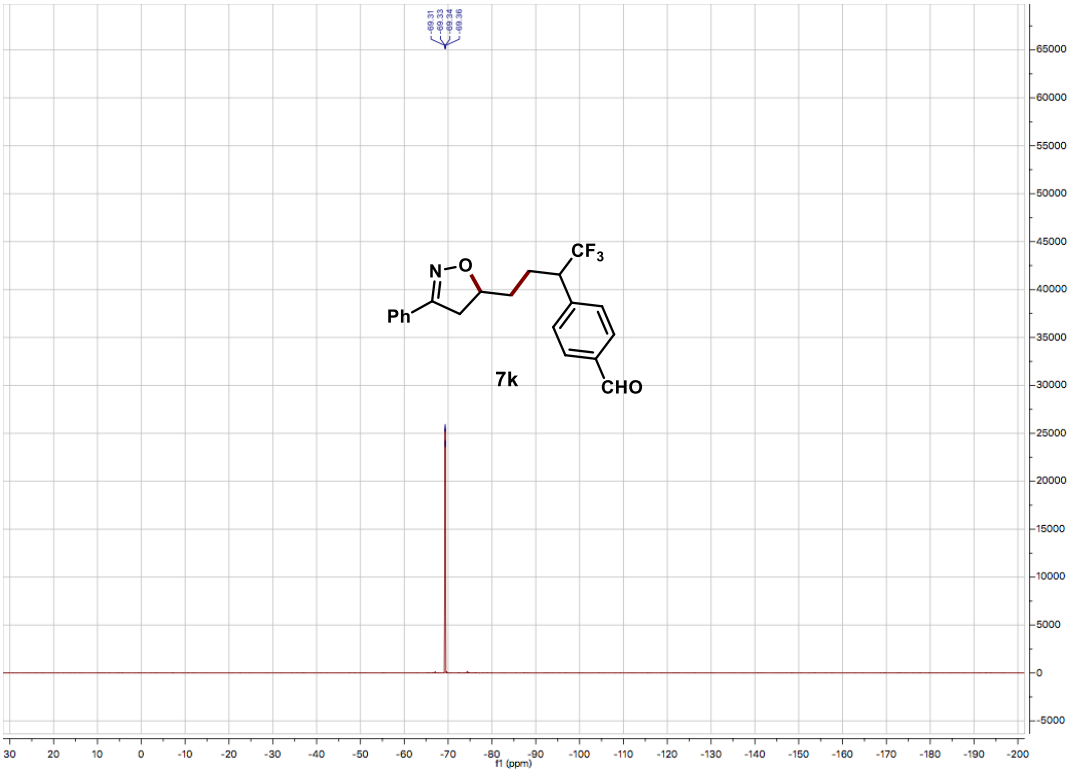
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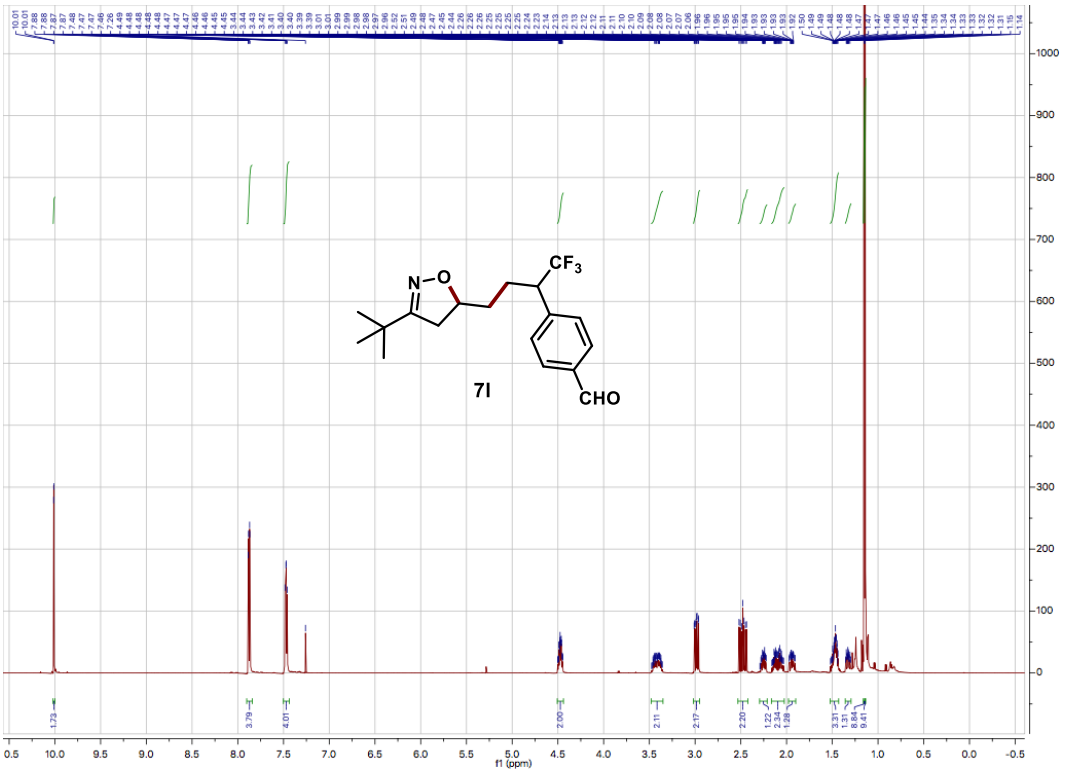
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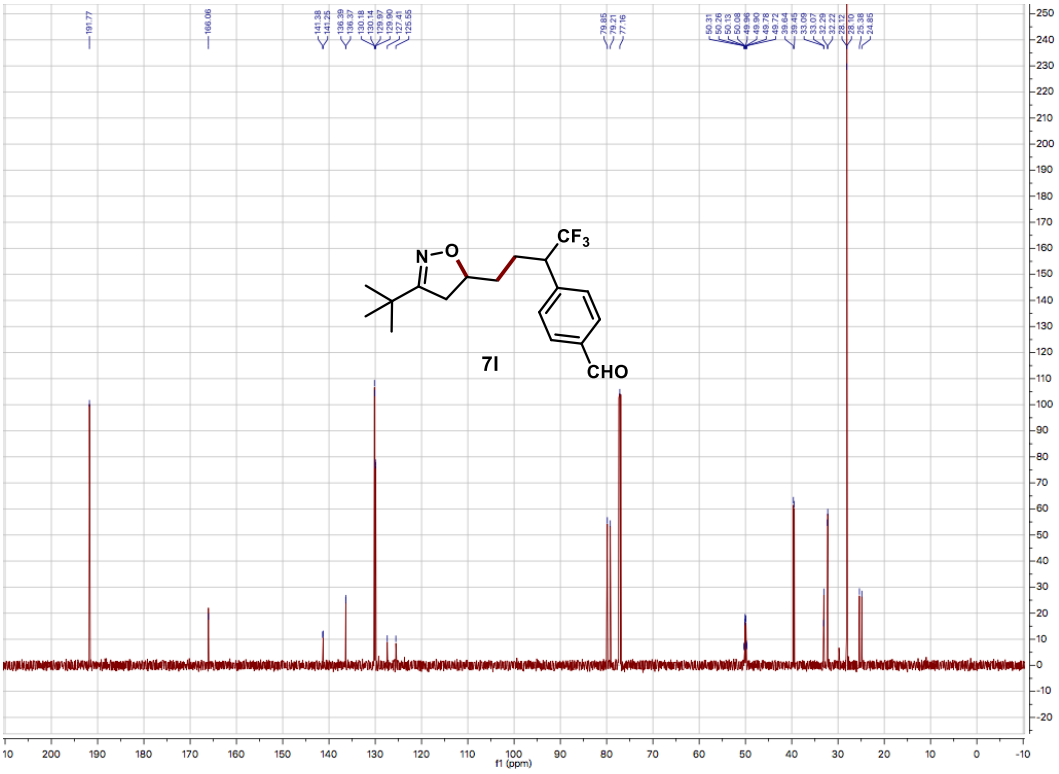
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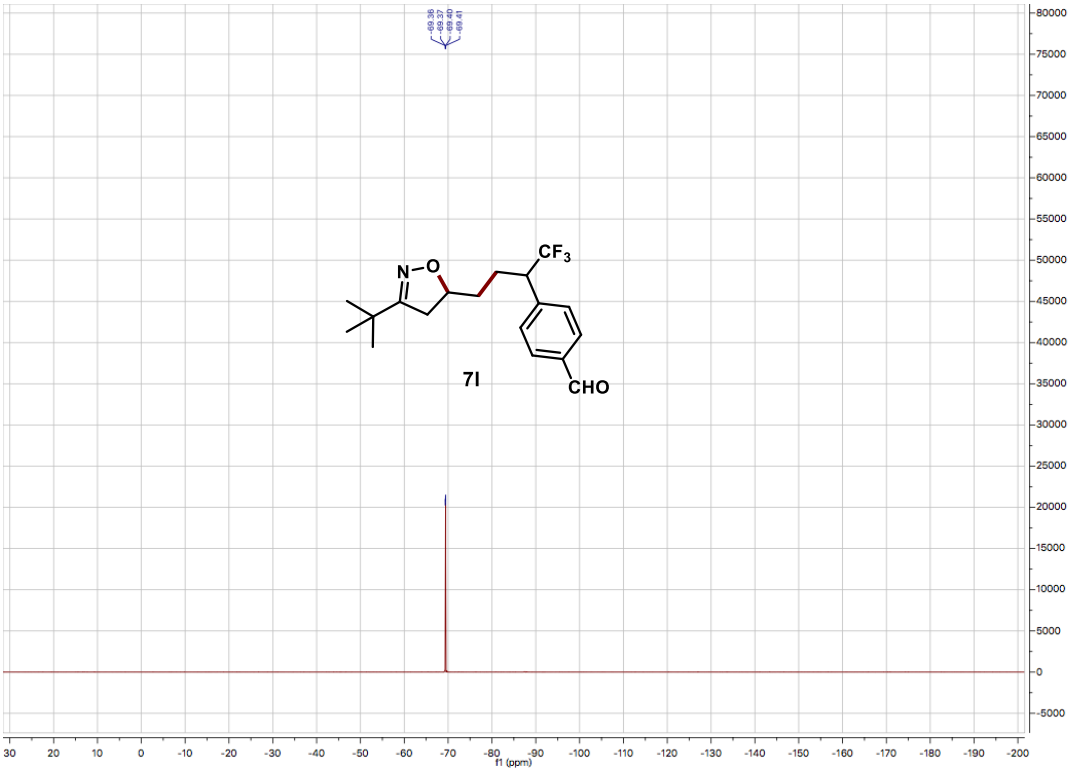
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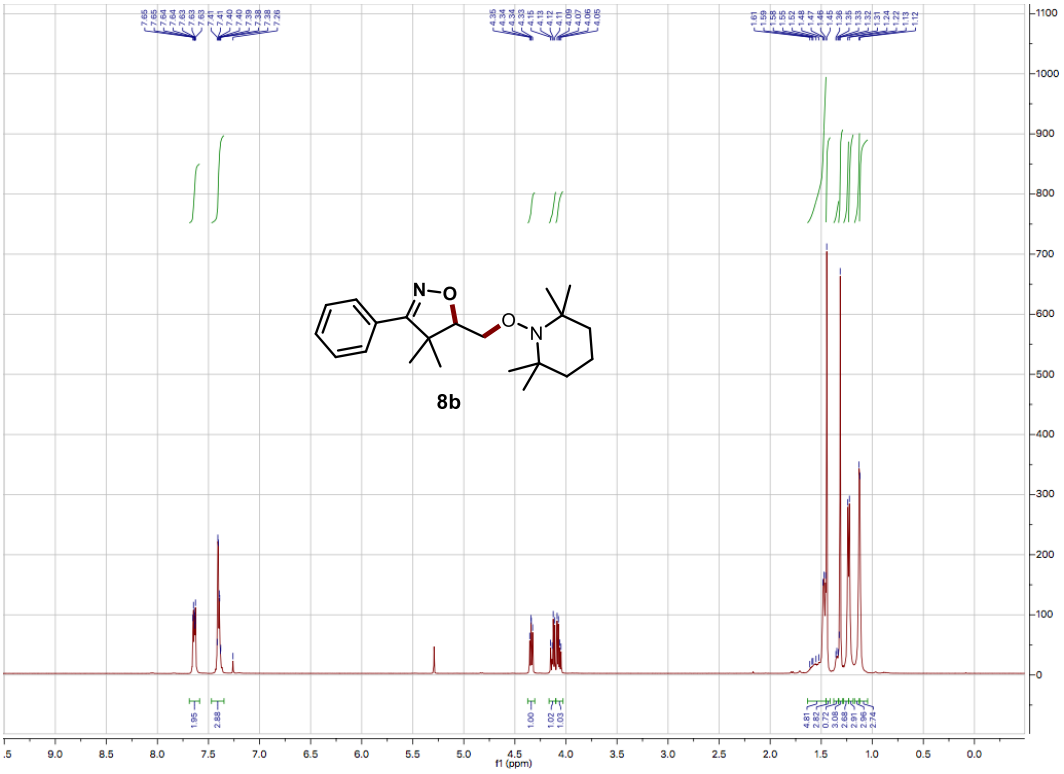
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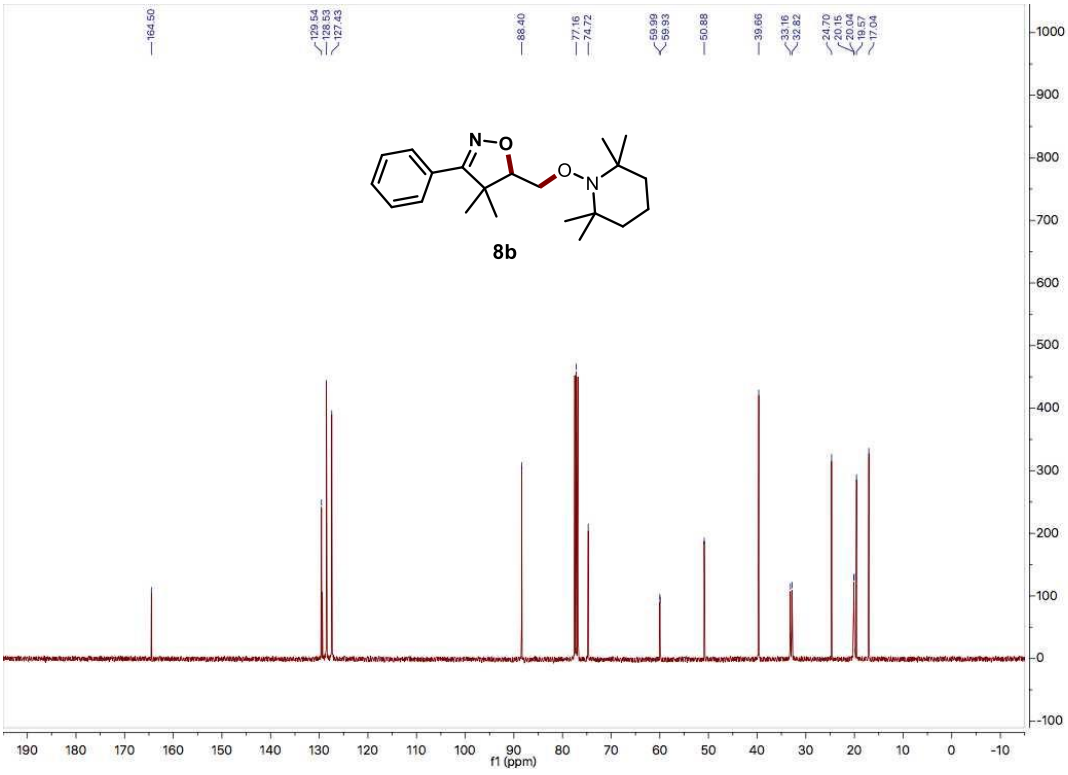
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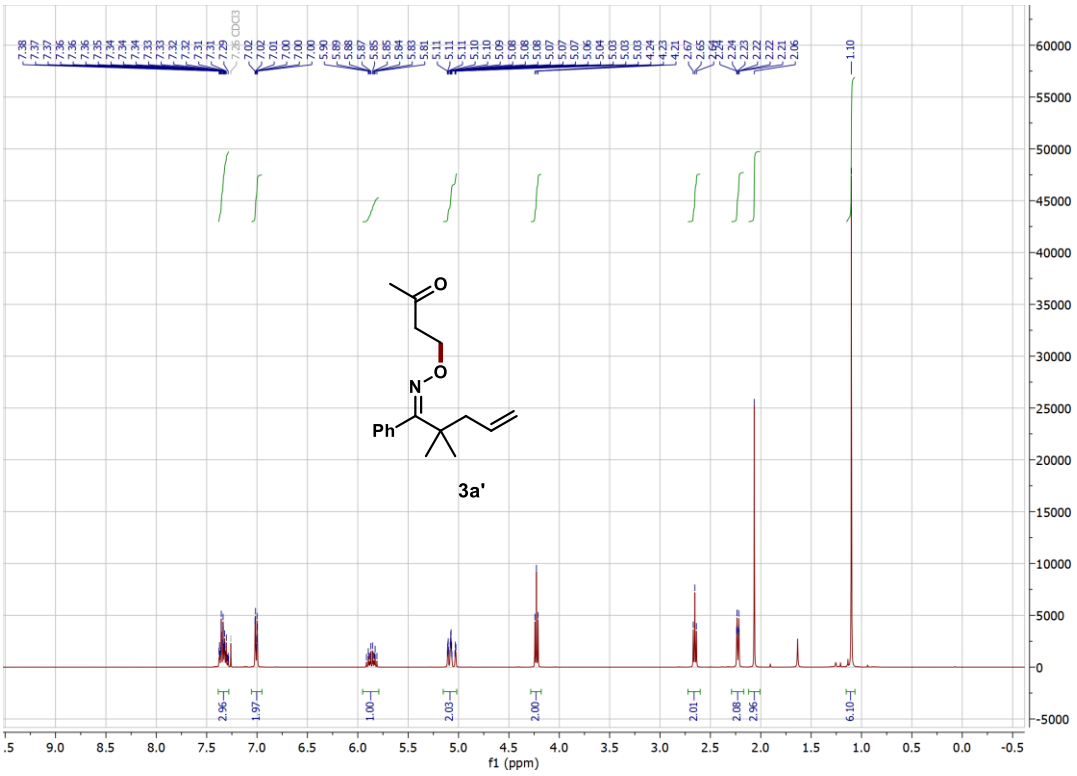
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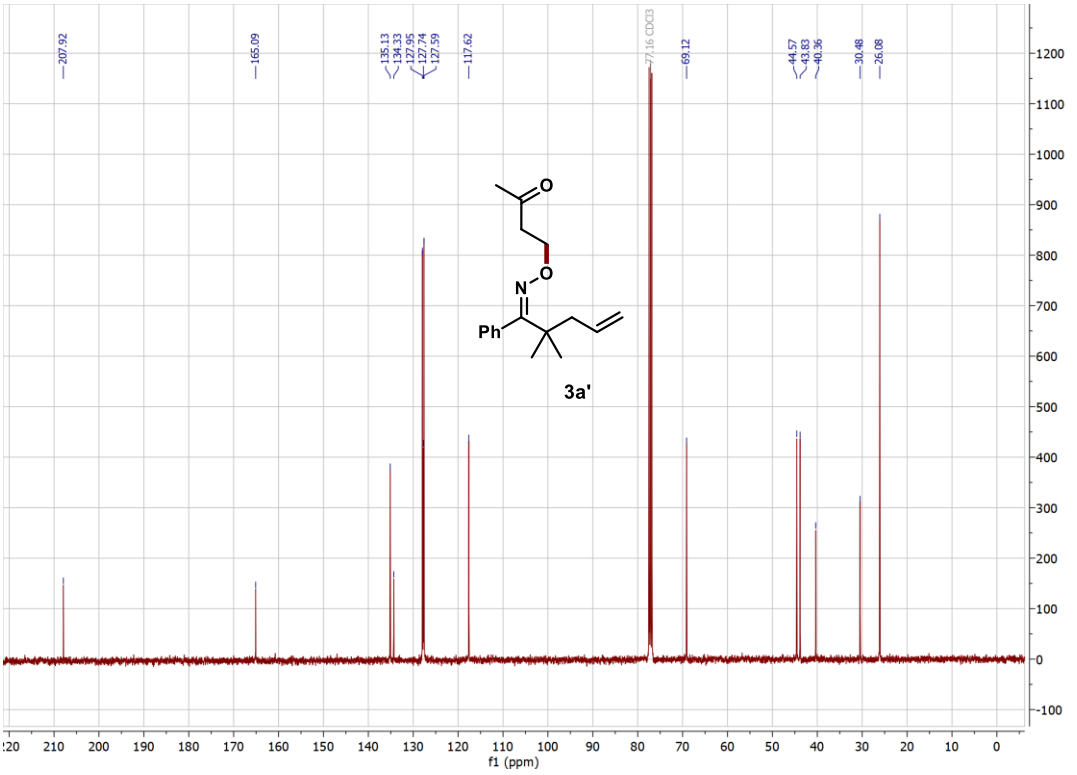
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3a'
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9. References

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