Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Photoredox initiated azole-Nucleophilic Addition: oxo-azolation of *gem*-Difluoroalkenes.

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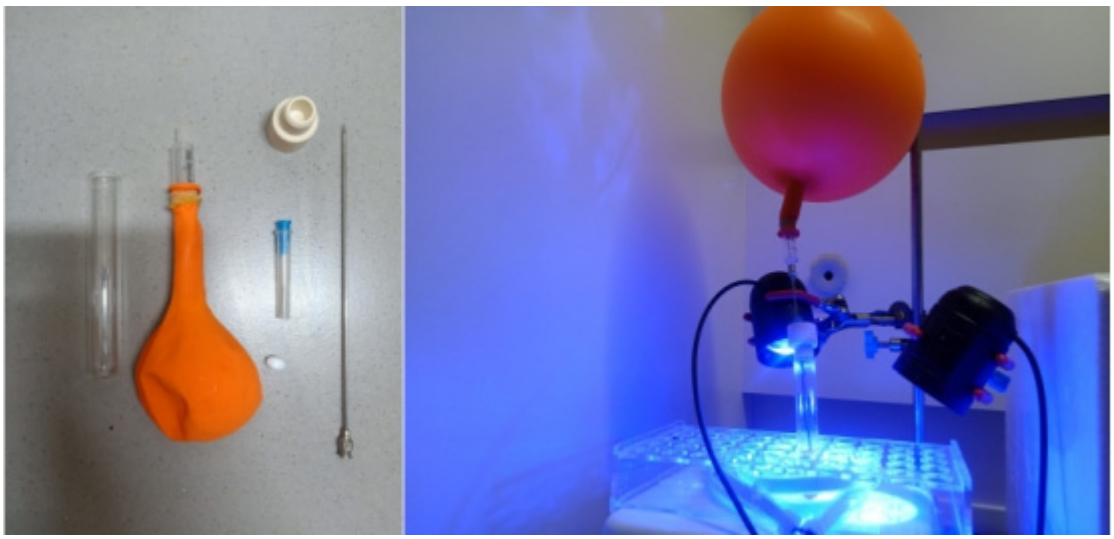
1. Materials and Methods:

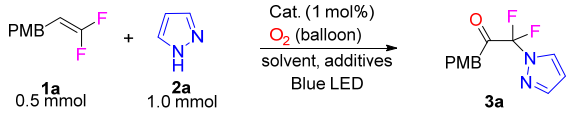
All commercially available reagents were used without further purification. Ananlytical grade solvents were bought from Energy Chemical Co., LTD and used without processed. The reactions were carried out under blue light, an oxygen atmosphere (realized by inserting a balloon), magnetically stirred, and monitored by thin layer chromatography (TLC), visualized by fluorescence quenching under UV light. Flash chromatography was performed on silica gel (200-300 mesh). All deuterated solvents were purchased from Meryer (Shanghai) chemical technology Co., LTD. NMR spectra were recorded on a Bruker Ascend 300 spectrometer operating at 300 MHz for ^{1}H acquisitions, 75 MHz for ^{13}C acquisitions and 282 MHz for ^{19}F acquisitions. Chemical shifts were referenced to the residual proton solvent peaks (^{1}H: $CDCl_3$, δ 7.26; $(CD_3)_2SO$, δ 2.50; CD_3OD, δ 3.31; CD_3CN, δ 1.94), solvent ^{13}C signals ($CDCl_3$, δ 77.16; $(CD_3)_2SO$, δ 39.52; CD_3OD, δ 49.00), dissolved or external neat $PhCF_3$ (^{19}F, δ –63.3 relative to $CFCl_3$). Signals are listed in ppm, and multiplicity identified as s = singlet, br = broad, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants in Hz; integration. High-resolution mass spectra were obtained using Agilent LC-UV-TOFmass spectrometer. Yields refer to purified and spectroscopically pure compounds.

2. Information for reaction set up:



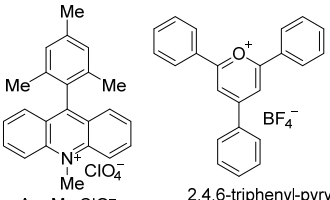
3. Optimization of the reaction

3.1 Screen different photoredox catalyst



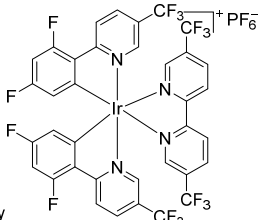
1a 0.5 mmol　　**2a** 1.0 mmol　　**3a**

Entry	Catalyst (1 mol%)	Solvent (0.25 M)	Additives (10 mol%)	Yield[a]
1	PC-I	o-DCB	TEMPO, O_2	64%
2	[Ir]-2	o-DCB	TEMPO, O_2	NR
3	[Ru]-1	o-DCB	TEMPO, O_2	NR
4	PC-II	o-DCB	TEMPO, O_2	<5%
5	PC-III	o-DCB	TEMPO, O_2	83%

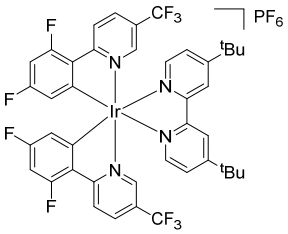


Acr-Me ClO_4^-
PC-I
E*red = +2.20 V

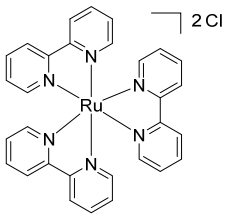
2,4,6-triphenyl-pyrylium fluoroborate
PC-II
E*red = +2.55 V



$[Ir(dF)(CF_3)(ppy)_2(5,5'\text{-}dCF_3)bpy]PF_6$
PC-III
E*red = +1.94 V



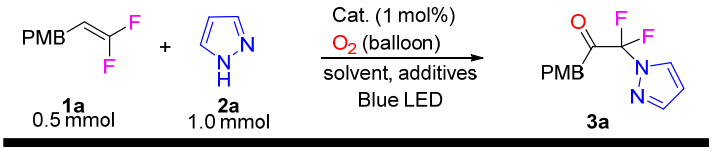
$Ir(dF\text{-}CF_3\text{-}ppy)_2(dtbpy)PF_6$
PC-IV
E*red = +1.69 V



$Ru(bpy)_3Cl_2\,6H_2O$
PC-V
E*red = +1.29 V

[a]NMR yield using trifluorotoluene as an internal standard.

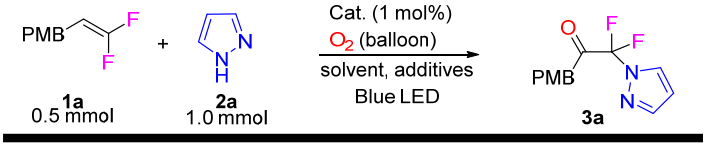
3.2 Screen different solvent.



Entry	Catalyst (1 mol%)	Solvent (0.25 M)	Additives (10 mol%)	Yield[a]
1	PC-I	THF	TEMPO, O_2	16%
2	PC-I	DMF	TEMPO, O_2	NR
3	PC-I	DCM	TEMPO, O_2	35%
4	PC-I	DMSO	TEMPO, O_2	NR
5	PC-I	MeCN	TEMPO, O_2	18%
6	PC-I	tBuOMe	TEMPO, O_2	NR
7	PC-I	$CHCl_3$	TEMPO, O_2	55%
8	PC-I	HFIP	TEMPO, O_2	NR
9	PC-I	NMP	TEMPO, O_2	NR
10	PC-I	o-DCB	TEMPO, O_2	64%
11	PC-I	o-DCB/DCE (1:1)	TEMPO, O_2	53%
12	PC-III	m-DCB	TEMPO, O_2	72%

[a]NMR yield using trifluorotoluene as an internal standard.

3.3 Screen different additives.

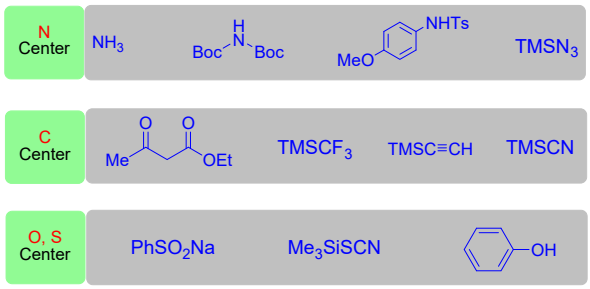


Entry	Catalyst (1 mol%)	Solvent (0.25 M)	Additives (10 mol%)	Yield[a]
1	PC-I	o-DCB	TEMPO, $NaCO_3$	48%
2	PC-I	o-DCB	TEMPO, t-BuONa	33%
3	PC-I	o-DCB	TEMPO, 2,6-Lutidine	28%
4	PC-III	o-DCB	TEMPO	70%
5	PC-III	o-DCB	TEMPO, LiCl	83%
6	PC-III	o-DCB	TEMPO, Li_2CO_3	80%
7	PC-III	o-DCB	TEMPO, AcOONa	75%
8	PC-III	o-DCB	TEMPO, 4 Å	94% (88%)
9	PC-III	o-DCB	TEMPO, KI	NR
10	PC-III	o-DCB	4 Å	64%
11	PC-III	o-DCB	$Sc(OTf)_3$	35%
12	PC-III	o-DCB	$Zn(OTf)_3$	28%

[a]NMR yield using trifluorotoluene as an internal standard. Isolated yield shows in bracket

3.4 Screen different nucleophile.

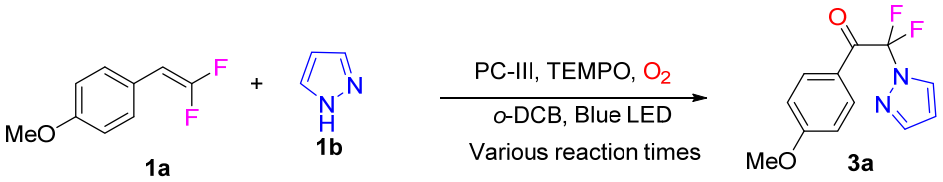
A messy mixture was formed when we use other nucleophiles (as shown in the table below) to react with *gem*-difluoroalkene (**1a**) under optimal conditions.



The table of nucleophiles

4. Mechanistic studies

4.1 The effect of irradiation time on the experiment



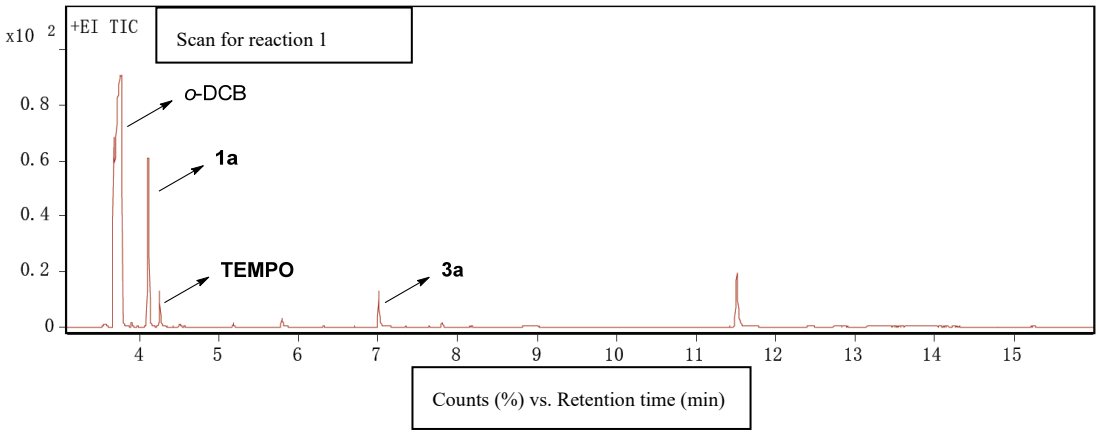
To gain insights into the reaction mechanism, intermittent light illumination of the reaction was carried out and results indicated that continuous irradiation is necessary to maintain conversion. The reaction was conducted under standard condition with light illumination for different time. The reaction was monitored by GC-Ms.

Reaction 1: After 1 hour light irradiation, the reaction was carried out in dark environment for 11 h.

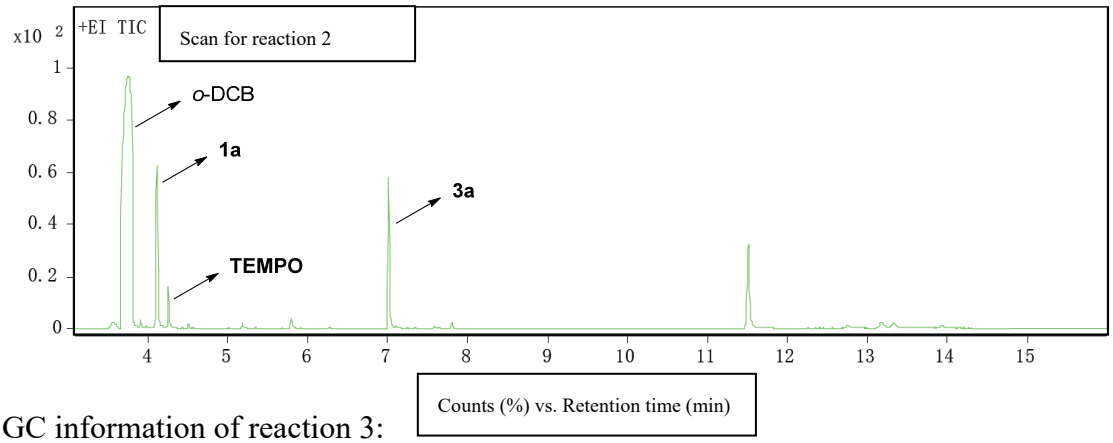
Reaction 2: The reaction was conducted under light irradiation for 5h, and then, stir at dark environment.

Reaction 3: The reaction was performed under 12 hour continued light irradiation, and the reaction was monitored by GC-MS per 2 h.

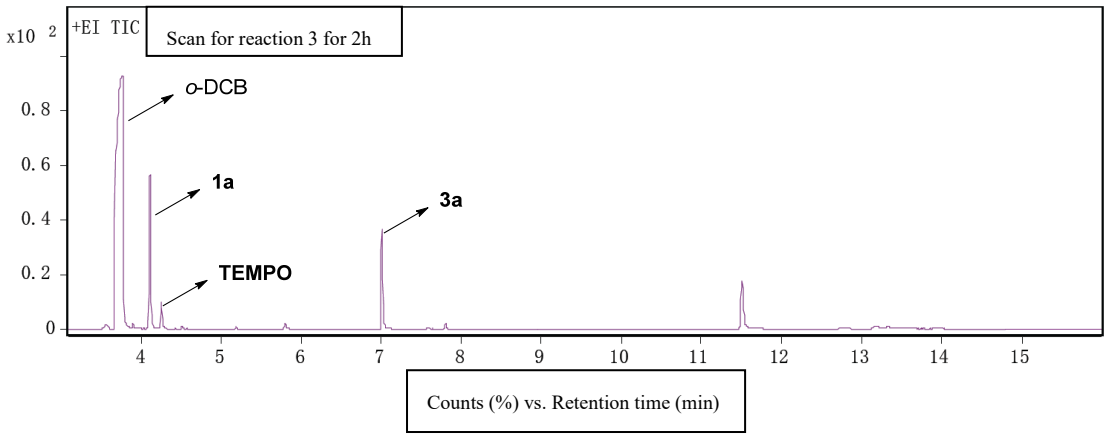
GC information of reaction 1:

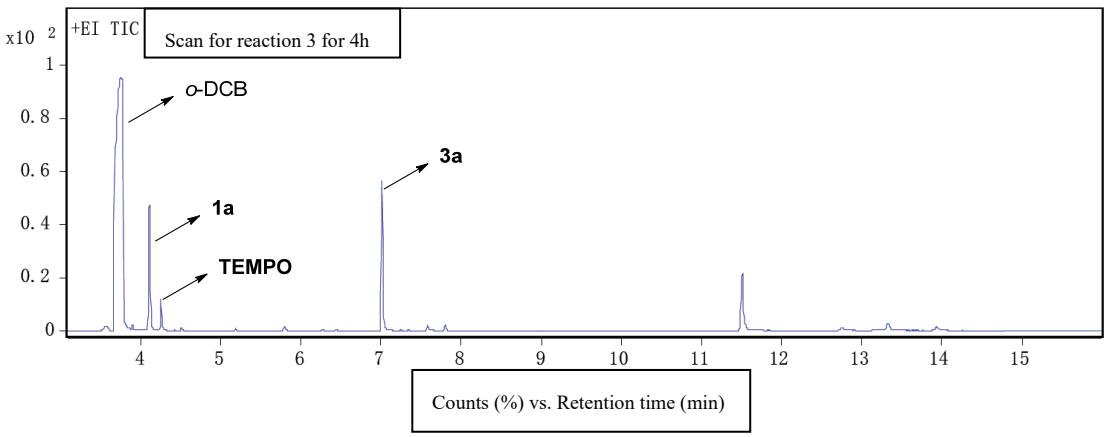


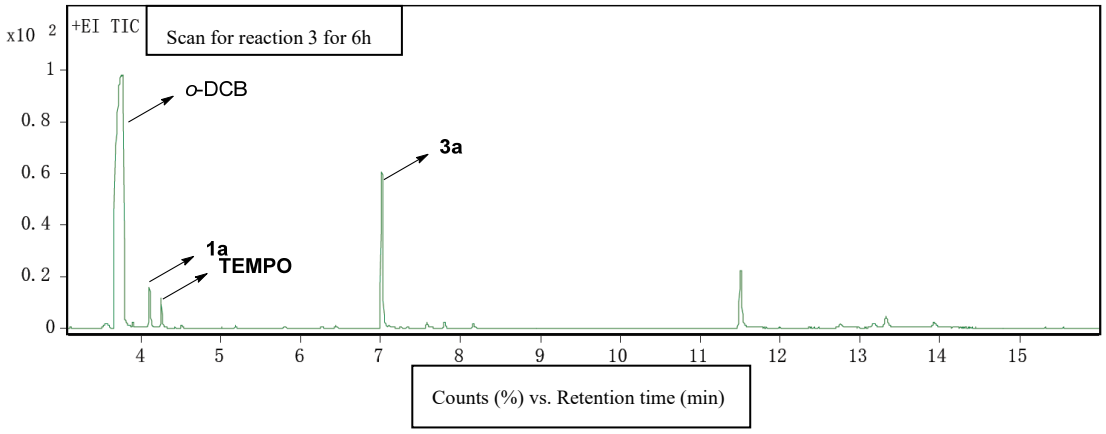
GC information of reaction 2:

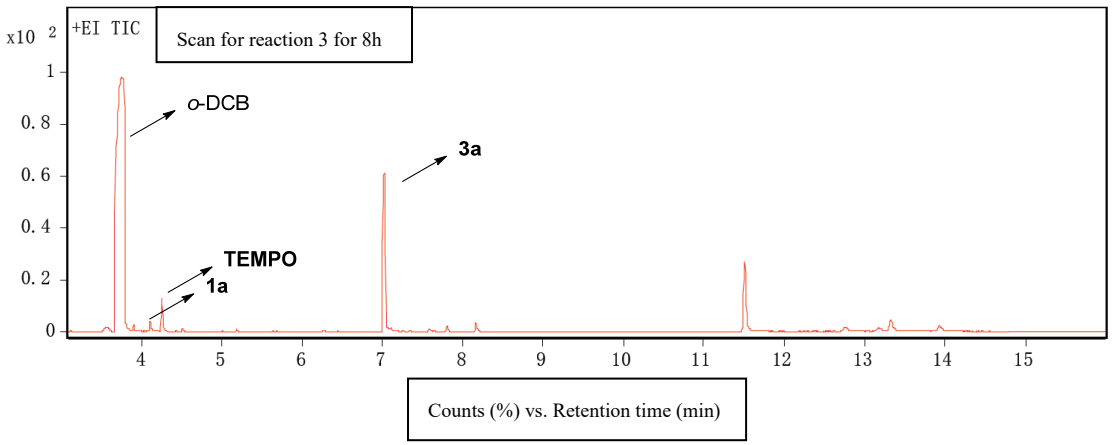


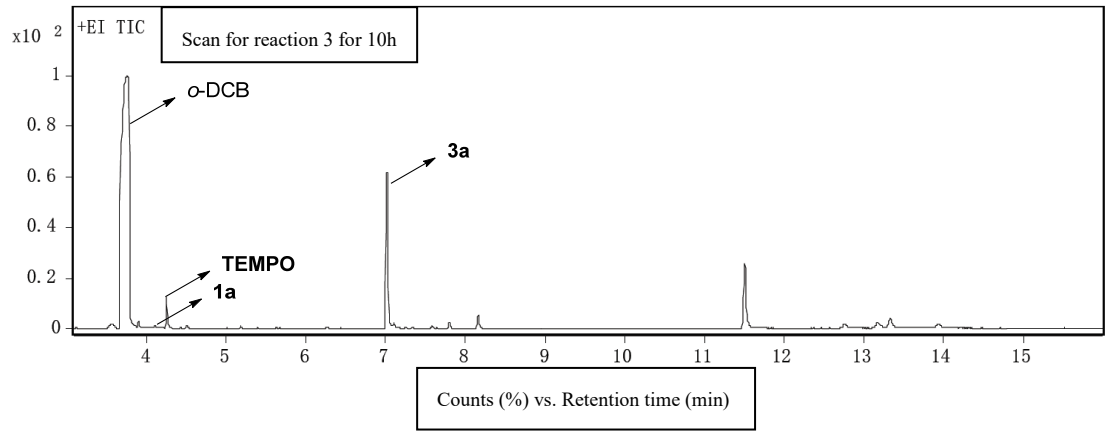
GC information of reaction 3:

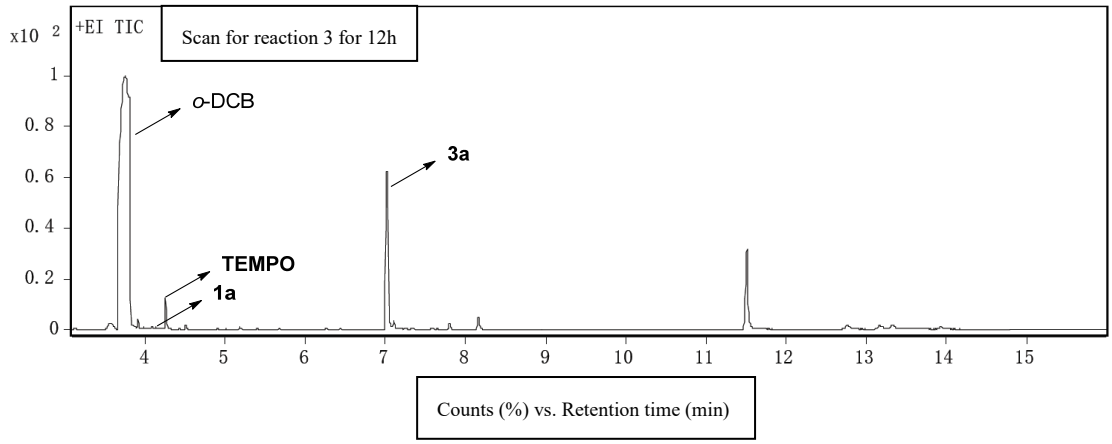






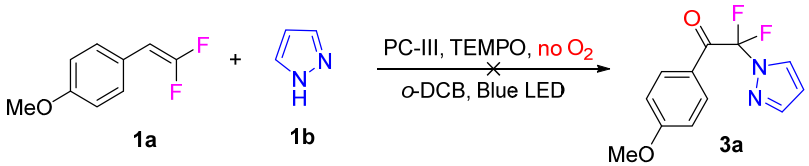






4.2. Reaction without O_2

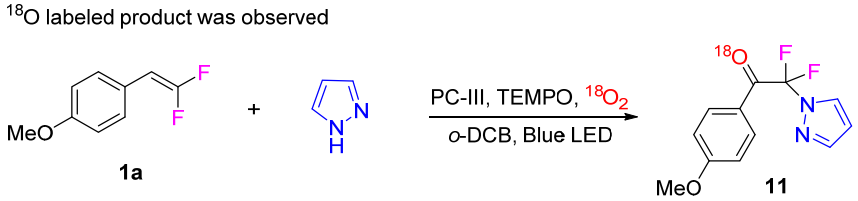
The reaction runs without O_2



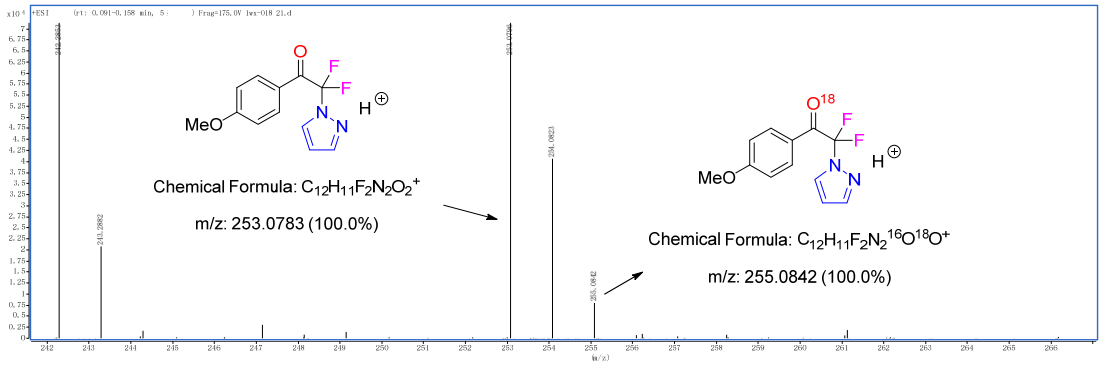
Recovery of **1a** in 88%

The reaction was conducted under the optimized condition without O_2. After 8 hours light irradiation, the product of **3a** was not observed. The starting material of 1a could be recovered in 88% yield after column chromatography.

4.3. Reaction with $^{18}O_2$

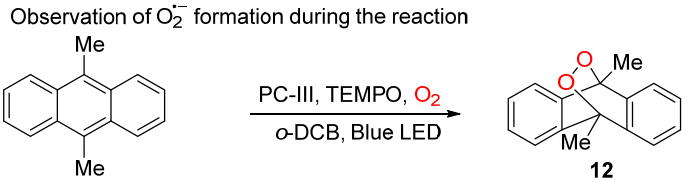


The reaction was conducted under the optimized condition, and a 10% purity of $^{18}O_2$ was used instead of pure normal oxygen. The product was isolated. Further HRMS analysis was confirmed the formation of product **11**. The result indicated the oxygen atom of product comes from O_2.

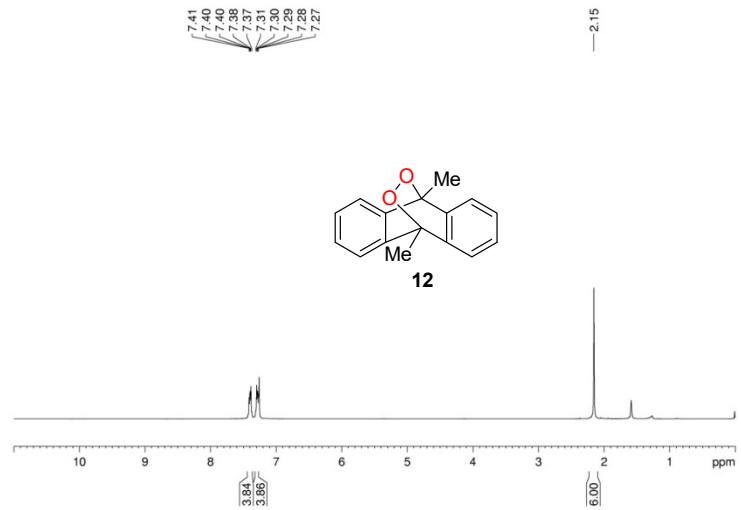


HMRS of compound **11** mixed with compound **3a**

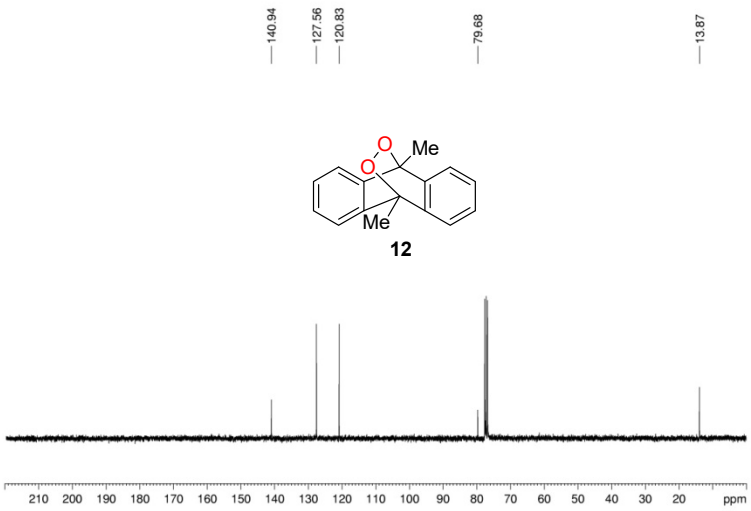
4.4. Investigation the formation of $O_2^{\bullet-}$ species



It is well known that singlet oxygen or $O_2^{\bullet-}$ species could be generated by the energy transfer from photosensitizer to molecular oxygen under light. It is confirmed that oxygen and photoredox are necessary for this transformation. However, it is not clear how oxygen participate in the reaction. One possibility is that $O_2^{\bullet-}$ species is produced, which is responsible for the oxidative procedure coupling process under standard reaction condition. Trapping experiments using 9,10-dimethylanthracene under the standard conditions afforded **12** formed. The result supported the generation of $O_2^{\bullet-}$ species (*J. Am. Chem. Soc.* **2004**, *126*, 15999-16006). Compound **12** (white solid), NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25ºC, δ): 7.41-7.37 (m, 4H), 7.31-7.27 (m, 4H), 2.15 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ):140.9, 127.6, 120.8, 79.7, 13.9. The data is consistent with the published literature (*J. Am. Chem. Soc.* **2004**, *126*, 15999-16006).



^{1}H NMR spectrum of compound **12**

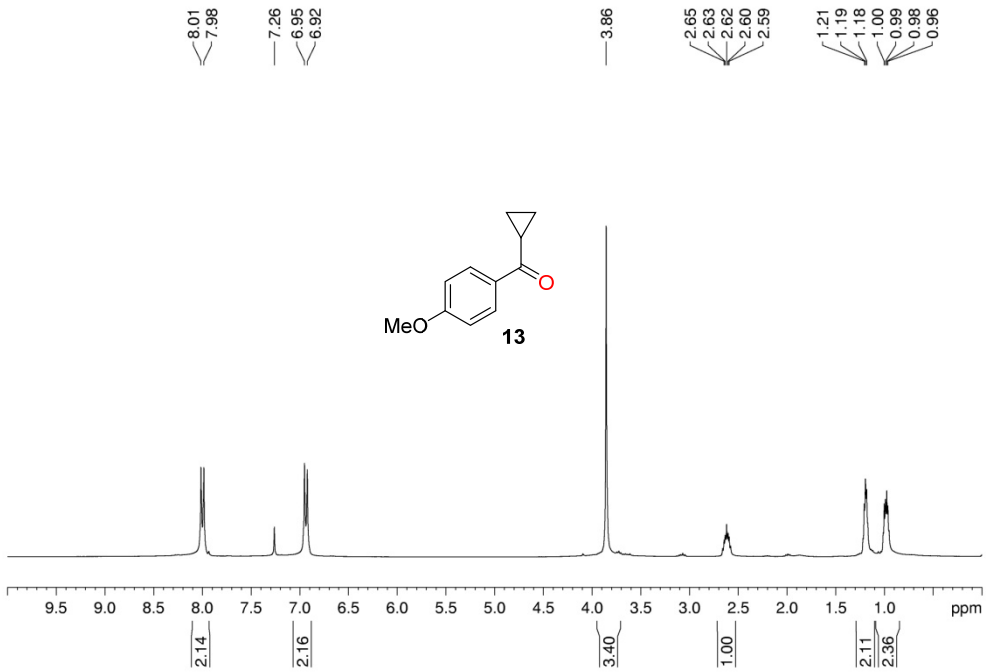


^{13}C NMR spectrum of compound **12**

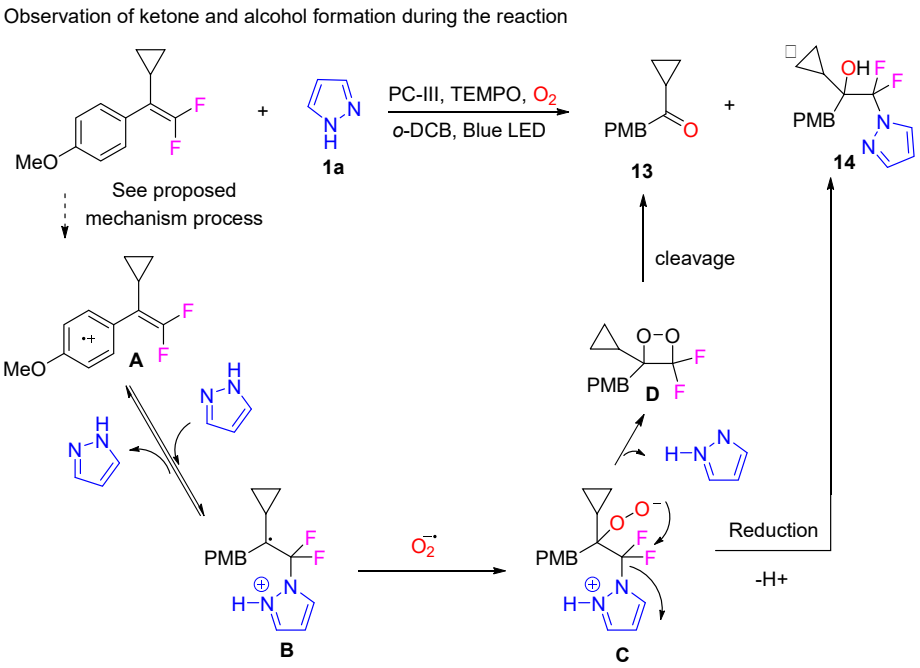
4.5. Observation of ketone and alcohol formation

Next, cyclopropane substituted *gem*-difluoroalkene and pyrazole were mixed in the standard condition. The result turned out that ketone **13** was separated in 51% yield and tertiary alcohol was detected by HRMS, without identifying any cyclopropane ring cleavage product. These implicate the involvement of long live benzylic radicals in the transformation is not possible. It is proposed that the reversible intermediate **B** could readily trapped by $O_2^{\bullet-}$ species to gain intermediate **C** which could undergo a fast intramolecular substation reaction to form dioxetane intermediate **D**. Trace amount of

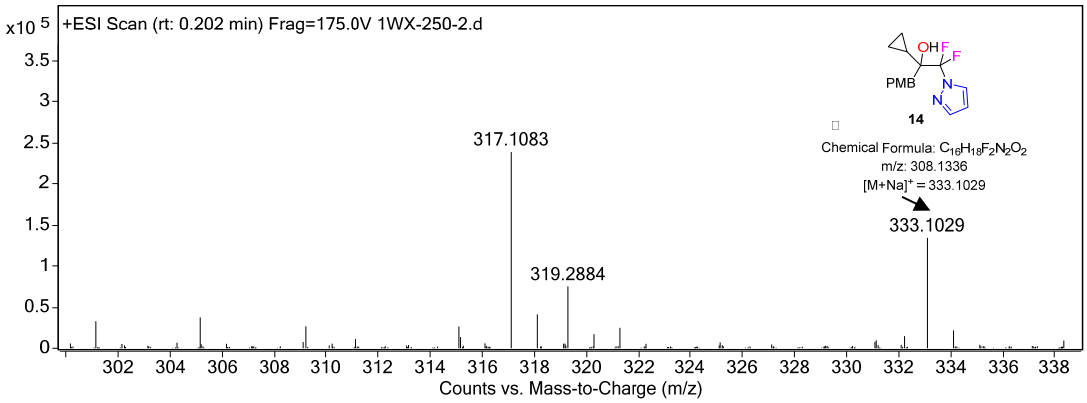
14 was possibly formed by reduction of C. Intermediate **D** could proceed a ring cleavage process to gain product **13**.



^{1}H NMR spectrum of compound **13**



Proposed pathway to gain compound **13** and **14**



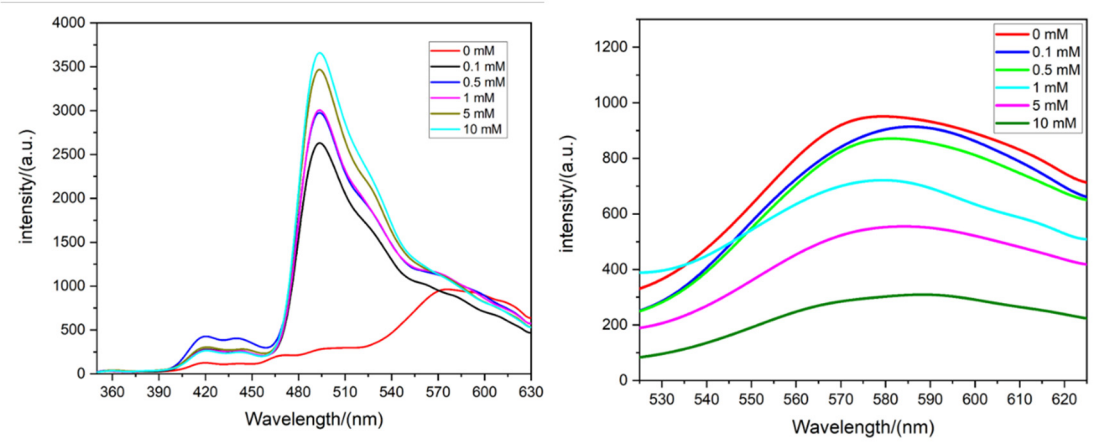
HRMS of track compound **14**

4.6. Luminescence Quenching Studies

Visible light luminescence intensities were recorded using an Thermo Scientific Lumina spectrophotometer. All luminescence measurements were recorded using a fluorescence glass cuvette (10 x 10 mm, 3.5 mL).

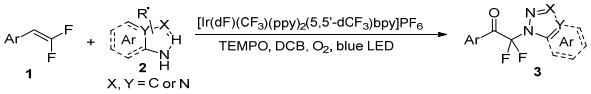
In a typical procedure, pyrazole (6.8 mg, 0.1 mmol) was dissolved and diluted to a final volume of 10 mL (c = 10 mM) with a stock solution of Ir[(dF)(CF_3)(ppy)$_2$(5,5-dCF_3)bpy]PF_6 in *o*-DCB (c = 10 µM). Serial dilution of this 10 mM pyrazole solution was carried out by dilution of 5 mL of the 10 mM pyrazole solution to 10 mL (5 mM) with the 10 µM stock solution of Ir[(dF)(CF_3)(ppy)$_2$(5,5'-dCF_3)bpy]PF_6. All subsequent solutions were prepared by dilution of preceding pyrazole solution to a final volume of 10 mL. All solutions were excited at 320 nm and the emission was measured from 330 to 650 nm.

Fluorescence quenching experiments revealed that the excited state Ir(III) compound was quenched by gem-difluoroalkenes rather than pyrazole, thus indicating a possible SET process between gem-difluoroalkenes and the excited state Ir(III) compound.



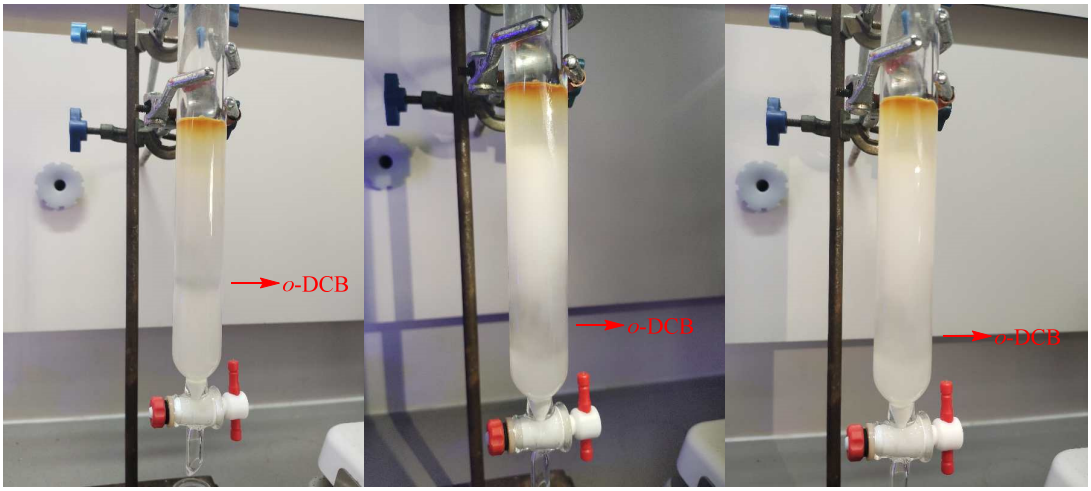
Emission spectra for Ir[(dF)(CF_3)(ppy)$_2$(5,5'-dCF_3)bpy]PF_6 luminescence quenching by pyrazole (left) and *gem*-difluoroalkenes (right).

5. General Procedure for Photoredox initiated azole-Nucleophilic Addition



A solution of *gem*-difluoroalkenes **1** (0.5 mmol), azoles **2** (1.0 mmol), TEMPO (10% mmol) and Ir[(dF)(CF_3)(ppy)$_2$(5,5'-dCF_3)bpy]PF_6 (PC-III)(1% mmol) in *o*-DCB (2.0 mL, 0.25 M of **1**) was stirred at room temperature under O_2 atmosphere in a test tube with rubber plug. The tube was sealed with an oxygen balloon and then the mixture was allowed to stir at room temperature with the irradiation of blue LED for 8 h or until the totally consumption of **1** which was detected by TLC. Upon completion of the reaction, the mixture was directly purified column chromatography on silica gel, using petroleum ether/ethyl acetate as eluent to get pure product.

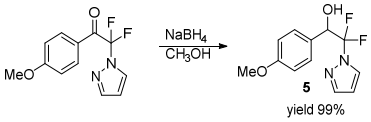
The solvent of *o*-DCB could be easily recovered by column chromatography (see the following pictures). It will firstly come down from the column and it can be recovered by concentration via vacuum. The solvent was reused for 5 times and the reaction efficiency was maintained.



Recover the solvent of *o*-DCB

6. Product Transformation

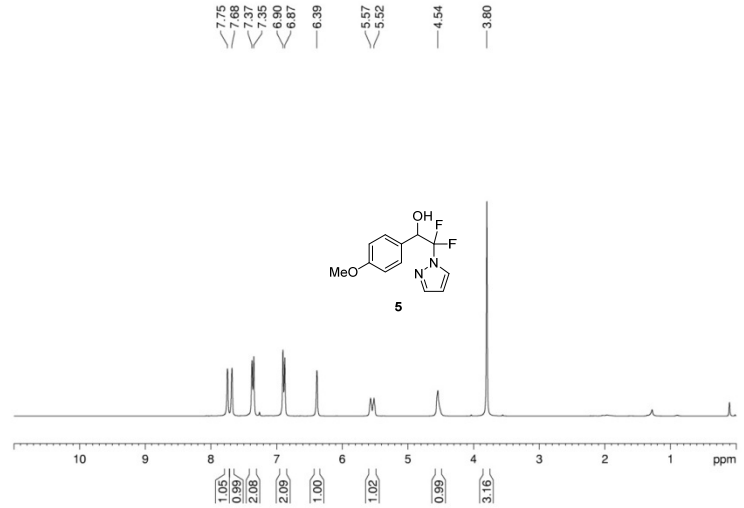
Synthesis of 2,2-difluoro-1-(4-methoxyphenyl)-2-(1H-pyrazol-1-yl)ethan-1-ol (5)



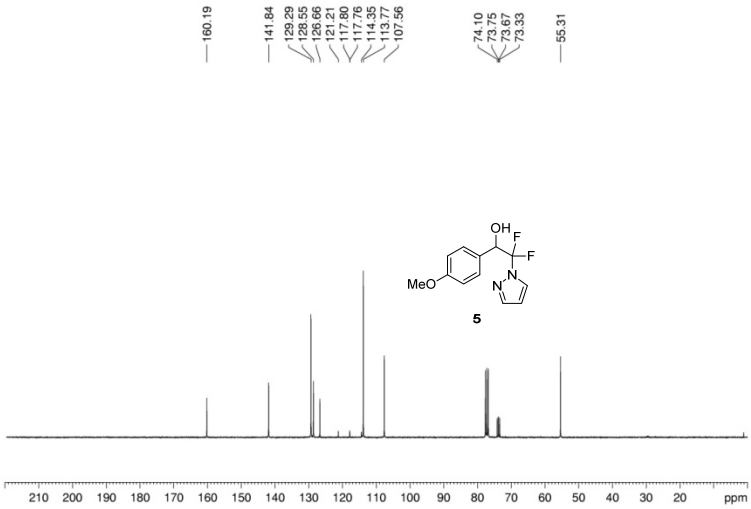
yield 99%

Under the temperature of 0 ºC, to a solution of 2,2-difluoro-1-(4-methoxyphenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (1.0 mmol, 252 mg) in methanol (3.0 mL), sodium borohydride (1.0 mmol, 38 mg) was added. The reaction mixture was stirred for 3 h at 0 ºC. The mixture was quenched by adding a few drops of 1.0 M HCl and then the solvent was evaporated under reduced pressure. Finally, the mixture was extracted by

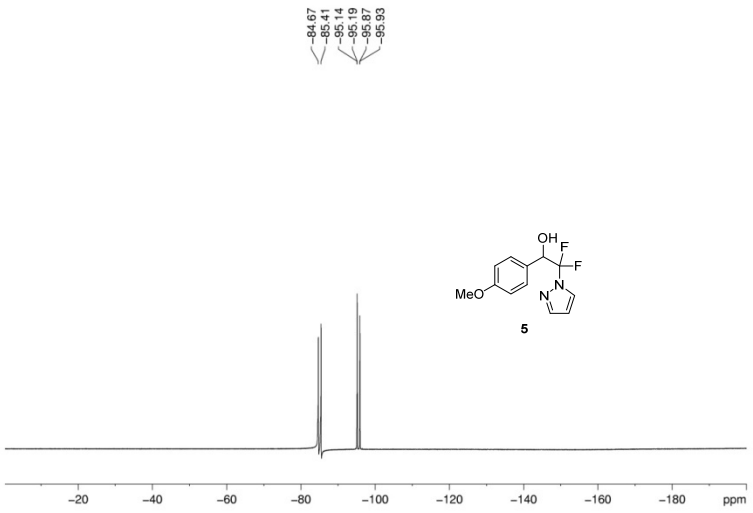
CH_2Cl_2 (8 mL ð 3). The organic phase was combined and dried over $MgSO_4$, concentrated and purified by chromatography on silica gel, eluting with Petroleum ether:EtOAc = 10:1 (v/v), to afford the title product as a white solid. (250 mg, 99%). R_f = 0.17 (petroleum ether/ethyl acetate = 10 : 1 (v/v)). NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.75 (s, 1H), 7.68 (s, 1H), 7.36 (d, *J* = 8.22 Hz, 2H), 6.89 (d, *J* = 8.49 Hz, 2H), 6.39 (s, 1H), 5.55 (d, *J* = 15 Hz, 1H), 4.54 (s, 1H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 160.2, 141.8, 129.3, 128.6, 126.7, 117.8, (dd, $J_{1\ C\text{-}F}$ = 255.8, 258.5 Hz), 113.8, 107.6, 73.7 (dd, $J_{2\ C\text{-}F}$ = 25.9, 31.7 Hz), 55.3. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -85.0 (d, *J* = 207.4 Hz), -95.5 (d, *J* = 16.5, 207.2 Hz), Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{12}F_2N_2NaO_2^+$ ([M + Na]$^+$), 277.0759, found, 277.0758.



^{1}H NMR spectrum of compound **5**

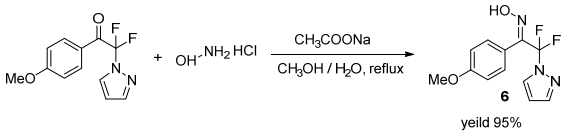


^{13}C NMR spectrum of compound **5**



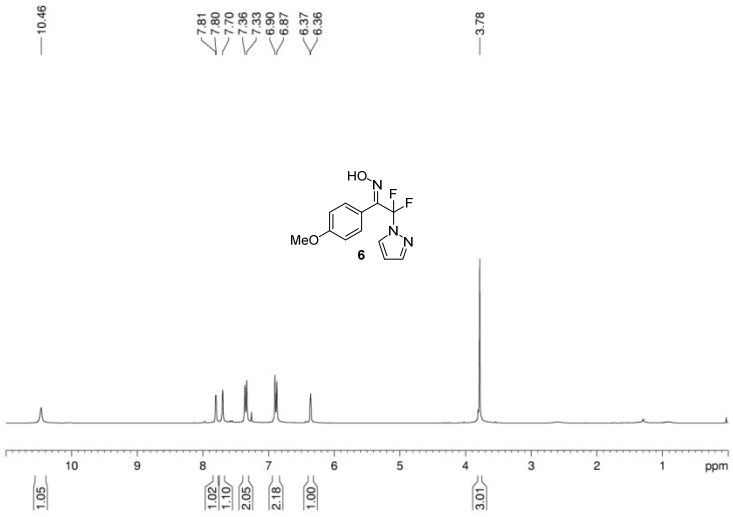
^{19}F NMR spectrum of compound **5**

Synthesis of (E)-2,2-difluoro-1-(4-methoxyphenyl)-2-(1H-pyrazol-l-yl)ethan-l-one oxime

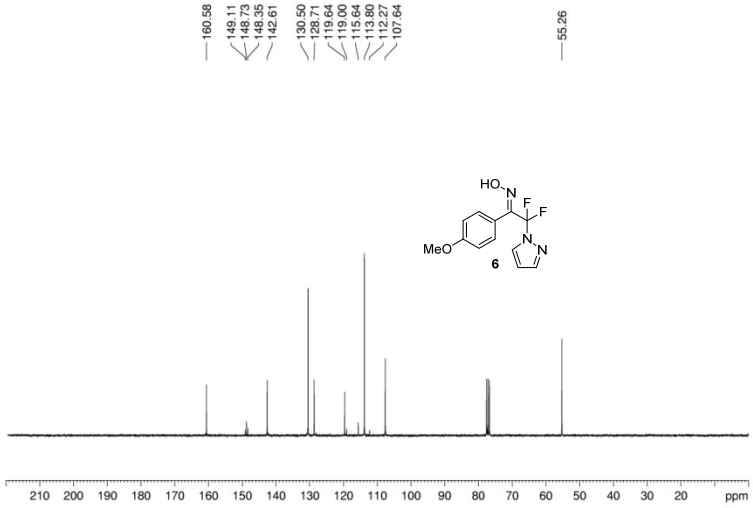


yeild 95%

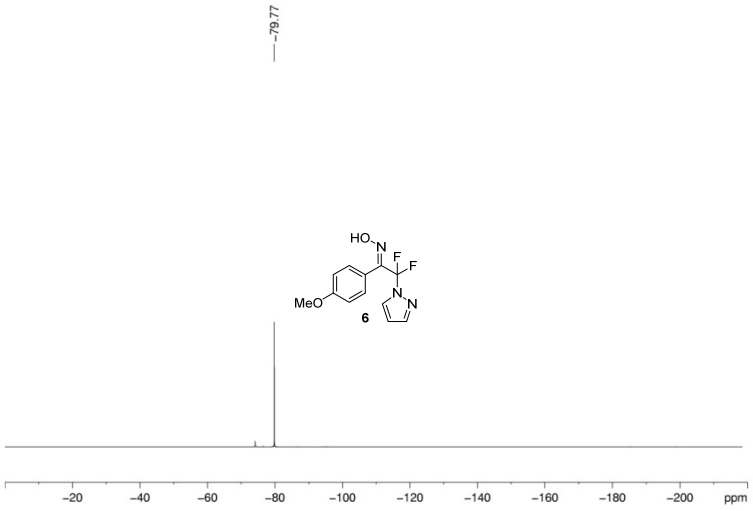
To a solution of ketone (0.6 mmol, 150 mg) and 2.3 equiv of hydrochloride (1.38 mmol, 95 mg) in 4 mL of MeOH, 2.5 equiv of sodium acetate (1.5 mmol, 123 mg) in 2 mL of water was added at room temperature, and the mixture was refluxed for 2.5 h. After completion of the reaction, the sulotion was evaporated under reduced pressure directly, and then, the mixture was extracted by EtOAc (6 mL ð 3). The organic phase was combined and dried over $MgSO_4$, concentrated and purified by chromatography on silica gel, eluting with Petroleum ether: EtOAc 10:1 (v/v), to afford the title product as a colorless oil (152 mg, 95%). R_f = 0.28 (petroleum ether/ethyl acetate = 5 : 1 (v/v)). NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 10.46 (s, 1H), 7.81 (d, J = 1.92 Hz, 1H), 7.70 (s, 1H), 7.35 (d, J = 8.67 Hz, 2H), 6.89 (d, J = 8.79 Hz, 2H), 6.37 (d, J = 1.89 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 160.6, 148.7(t, $J_{2\ C\text{-}F}$ = 28.5 Hz), 142.6, 130.5, 128.7, 119.6, 115.6 (t, $J_{1\ C\text{-}F}$ = 252 Hz), 113.8, 107.6, 55.3. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -79.8, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{12}F_2N_3O_2^+$ ([M + H]$^+$), 268.0892, found, 268.0885.



^{1}H NMR spectrum of compound **6**

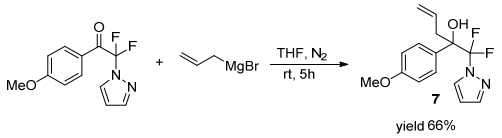


^{13}C NMR spectrum of compound **6**

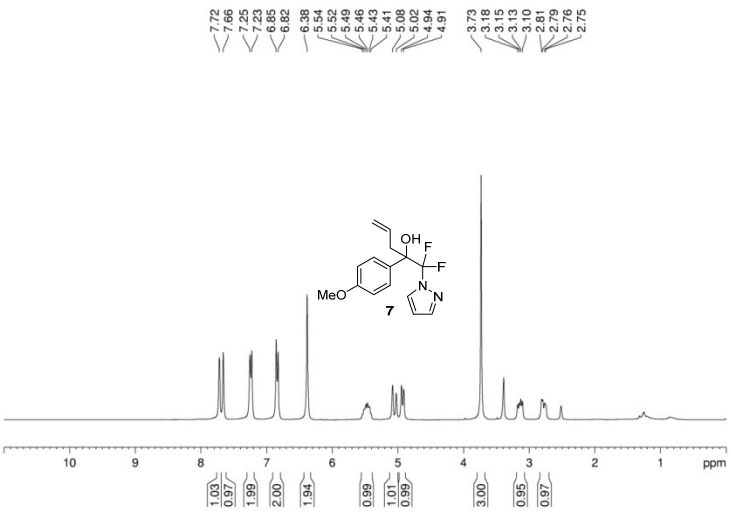


^{19}F NMR spectrum of compound **6**

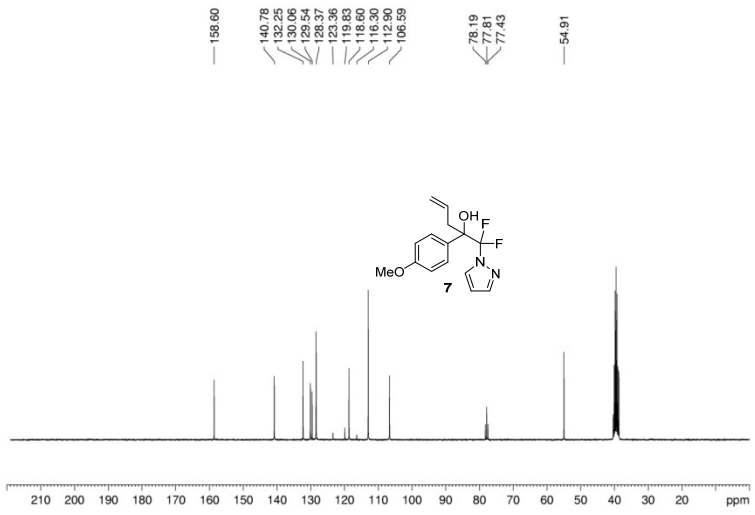
Synthesis of 1,1-difluoro-2-(4-methoxyphenyl)-1-(1H-pyrazol-1-yl)pent-4-en-2-ol



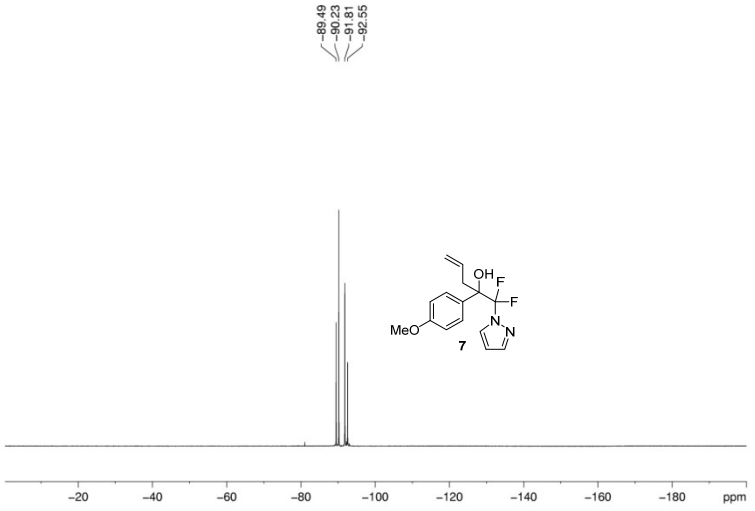
In a oven-dry round flask, 2,2-difluoro-1-(4-methoxyphenyl)-2- (1H-pyrazol-1-yl)ethan-1- one (0.5 mmol, 126 mg) was dissolved in dry THF (5 mL) under argon atmosphere. Allylmagnesium bromide (0.6 mmol 87 mg) was added at 0 ºC, and then the reaction mixture was stirred at room temperature for 5 h. When reaction finished, 1.0 M HCl was added to quenched the mixture and then extracted by ethyl acetate. The combined organic phases were dried over $MgSO_4$, and the solvent was removed. Purified by column chromatography (R_f = 0.26, petroleum ether/EtOAc = 10:1) to give product as a white solid (97 mg, 66 %). NMR Spectroscopy: ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 25 ºC, δ): 7.72 (s, 1H), 7.66 (s, 1H), 7.24 (d, J = 8.16 Hz, 2H), 6.84 (d, J = 8.49 Hz, 2H), 6.38 (s, 2H), 5.54-5.41 (m, 1H), 5.05 (d, J = 18 Hz, 1H), 4.93 (d, J = 10.05 Hz, 1H), 3.73 (s, 3H), 3.18-3.10 (m, 1H), 2.78 (dd, J = 4.89, 9.45 Hz, 1H). ^{13}C NMR (75 MHz, $(CD_3)_2SO$, 25 ºC, δ): 158.6, 140.8, 132.3, 130.1, 129.5, 128.4, 119.8 (t, $J_{1\ C\text{-}F}$ = 265.0 Hz), 118.6, 112.9, 106.6, 77.8 (t, $J_{2\ C\text{-}F}$ = 28.4 Hz), 54.9. ^{19}F NMR (282 MHz, $(CD_3)_2SO$, 25 ºC, δ): -89.9 (d, J = 207.8 Hz), -92.2 (d, J = 207.8 Hz), Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{15}H_{17}F_2N_2O_2^+$ ([M + H]$^+$), 295.1253, found, 295.1258.



^{1}H NMR spectrum of compound **7**

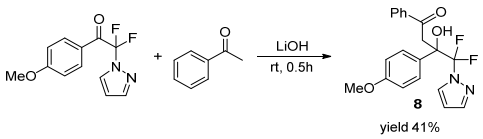


^{13}C NMR spectrum of compound **7**



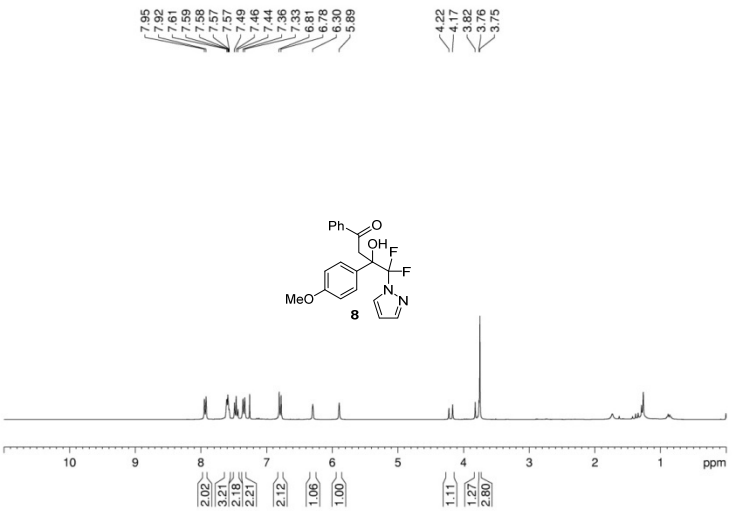
^{19}F NMR spectrum of compound **7**

Synthesis of 4,4-difluoro-3-hydroxy-3-(4-methoxyphenyl)-1-phenyl-4-(1H-pyrazol-1-yl)butan-1-one 8

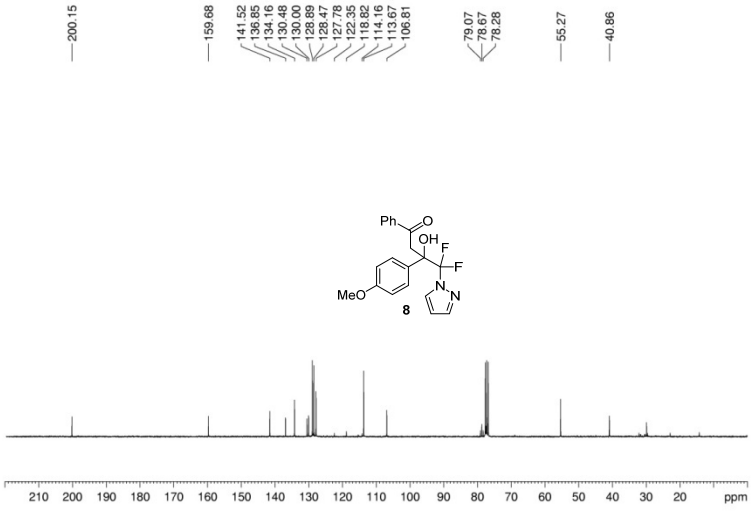


In a test tube, 2,2-difluoro-1-(4-methoxyphenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (0.55 mmol, 138 mg), acetophenone (0.5 mL), lithium hydroxide (0.66 mmol, 29 mg) were mixed together. This mixture was allowed to stir at room temperature for 30 min. When the reaction was completed (according to the TLC), the mixture was directly purified by column chromatography (R_f = 0.15, petroleum ether/EtOAc = 10:1) to give product as a light yellow oil (85 mg, 41%). NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$,

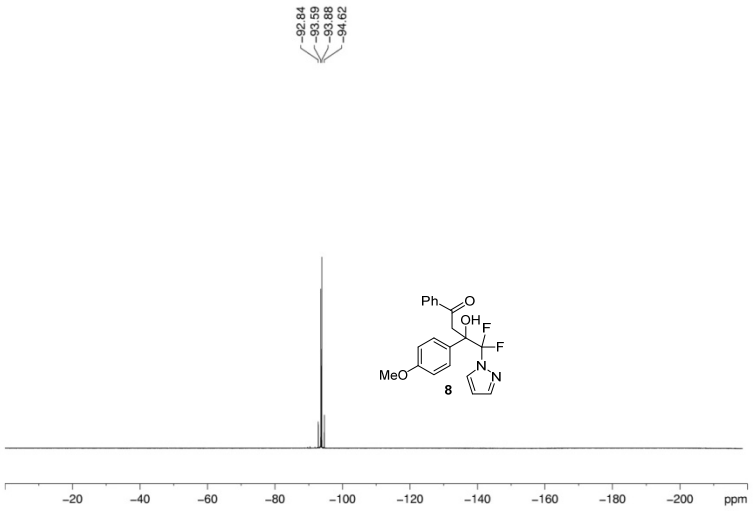
25 ºC, δ): 7.94 (d, J = 7.32 Hz, 2H), 7.61-7.57 (m, 3H), 7.49-7.44 (m, 2H), 7.35 (d, J = 8.73 Hz, 2H), 6.79 (d, J = 8.88 Hz, 2H), 6.30 (s, 1H), 5.89 (s, 1H), 4.20 (d, J = 17.31 Hz, 1H), 3.79 (d, J = 17.43 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 200.2, 159.7, 141.5, 136.9, 134.2, 130.5, 130.0, 128.9, 128.5, 127.8, 118.8 (t, $J_{1\ C\text{-}F}$ = 264.8 Hz), 113.7, 106.8, 78.7 (t, $J_{2\ C\text{-}F}$ = 30 Hz), 55.3, 40.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -93.2 (d, J = 211.5 Hz), -94.3 (d, J = 208.7 Hz), Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{20}H_{19}F_2N_2O_3^+$ ([M + H]$^+$), 373.1358, found, 373.1355.



^{1}H NMR spectrum of compound **8**

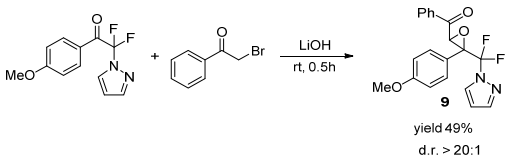


^{13}C NMR spectrum of compound **8**

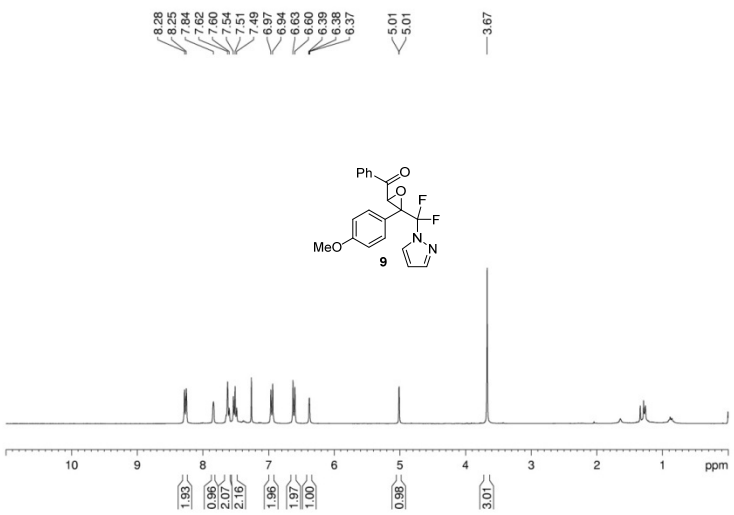


^{19}F NMR spectrum of compound **8**

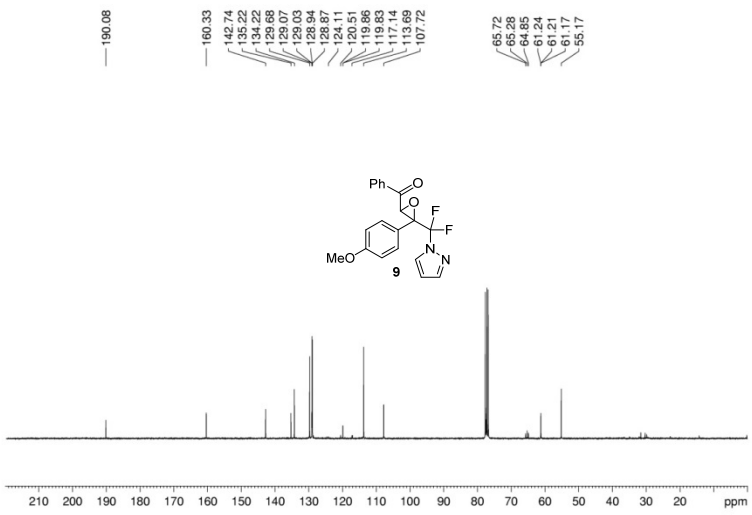
Synthesis of 2-bromo-4,4-difluoro-3-hydroxy-3-(4-methoxyphenyl)-1-phenyl-4-(1H-pyrazol-1-yl)butan-1-one



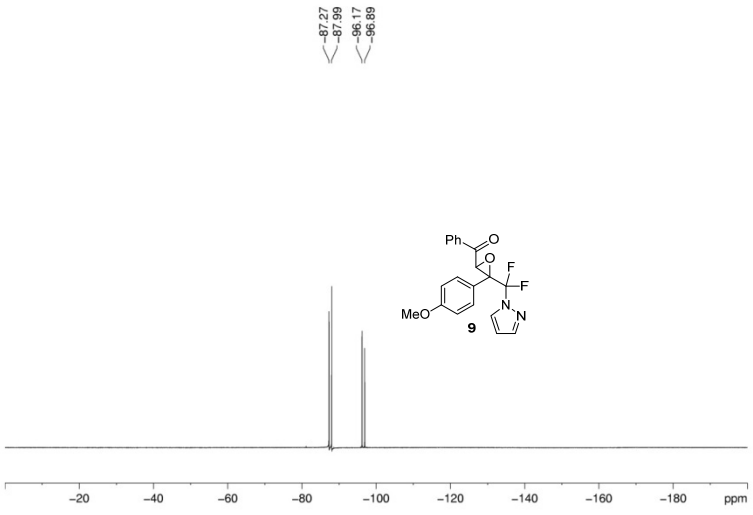
In a test tube, 2,2-difluoro-1-(4-methoxyphenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (0.6 mmol 150 mg), benzoyl bromide (0.6 mmol, 120 mg), lithium hydroxide (0.72 mmol, 29 mg) were directly mixed together, and then CH_2Cl_2 was added to dissolve those solid compound. This mixture was allowed to stir at room temperature for 30 min. When the reaction was completed according to the TLC of **3a**, water was added and the reaction mixture was extracted with CH_2Cl_2. The organic layers were combined and dried over $MgSO_4$, and the solvent was removed. Purified by column chromatography (R_f = 0.19, petroleum ether/EtOAc = 10:1) to give product as a white solid (109 mg, 49 %). NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.27 (d, J = 7.32 Hz, 2H), 7.84 (s, 1H), 7.61 (d, J = 7.56 Hz, 2H), 7.51 (t, J = 7.71 Hz, 2H), 6.96 (d, J = 8.64 Hz, 2H), 6.62 (d, J = 8.76 Hz, 2H), 6.38 (t, J = 2.13 Hz, 1H), 5.01 (d, J = 0.81 Hz, 1H), 3.67 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 190.1, 160.3, 142.7, 135.2, 134.2, 129.7, 129.1 (d, J = 3.2 Hz), 128.9 (d, J = 5.4 Hz), 124.1, 120.5, 119.9 (d, J = 2.0 Hz), 117.1 (dd, $J_{1\ C\text{-}F}$ = 252.6, 264.7 Hz), 113.7, 107.7, 65.3 (t, $J_{2\ C\text{-}F}$ = 32.3 Hz), 61.2 (t, J = 2.61 Hz), 55.2. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -87.6 (d, J = 203.0 Hz), -96.5 (d, J = 203.0 Hz), Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{20}H_{17}F_2N_2O_3^+$ ([M + H]$^+$), 371.1202, found, 371.1193.



^{1}H NMR spectrum of compound **9**



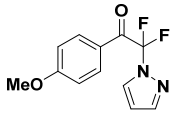
^{13}C NMR spectrum of compound **9**



^{19}F NMR spectrum of compound **9**

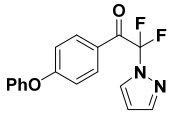
Characterization of product

2,2-difluoro-1-(4-methoxyphenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (3a)



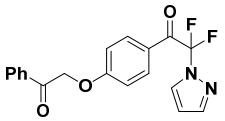
Yellow oil (110 mg, 88 % yield, R_f = 0.30 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25ºC, δ): 7.99 (d, *J* = 2.16 Hz, 1H), 7.89 (d, *J* = 8.82 Hz, 2H), 7.60 (s, 1H), 6.89 (d, *J* = 8.97 Hz, 2H), 6.48 (s, 1H), 3.81 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 181.3 (t, $J_{2\ C\text{-}F}$ = 29.8 Hz), 164.8, 142.3, 132.8, 132.7, 132.7, 127.7, 124.3, 114.1, 112.1 (t, $J_{1\ C\text{-}F}$ = 261.1 Hz), 108.7, 55.6. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.1, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{11}F_2N_2O_2^+$ ([M + H]$^+$), 253.0783, found, 253.0778.

2,2-difluoro-1-(4-phenoxyphenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (3b)



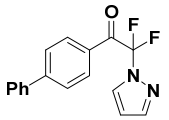
White solid (123 mg, 78 % yield, R_f = 0.53 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.06 (d, *J* = 2.13 Hz, 1H), 7.97 (d, *J* = 8.55 Hz, 2H), 7.70 (s, 1H), 7.46 (t, *J* = 7.77 Hz, 2H), 7.32-7.28 (m, 1H), 7.13 (d, *J* = 7.79 Hz, 2H), 7.02 (d, *J* = 8.82 Hz, 2H), 6.57 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 181.5 (t, $J_{2\ C\text{-}F}$ = 30.0 Hz), 163.7, 154.8, 142.5, 132.9 (d, $J_{3\ C\text{-}F}$ = 2.0 Hz), 130.3, 127.8, 125.9, 125.3, 120.8, 117.1, 112.1 (t, $J_{1\ C\text{-}F}$ = 260.8 Hz), 108.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.1, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{17}H_{13}F_2N_2O_2^+$ ([M + H]$^+$), 315.0940, found, 315.0947.

2,2-difluoro-1-(4-(2-oxo-2-phenylethoxy)phenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (3c)



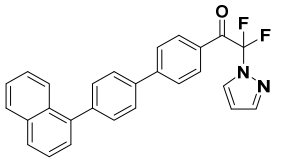
White solid (112 mg, 63 % yield, R_f = 0.14 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 25 ºC, δ): 8.58 (s, 1H), 8.02 (s, 2H), 7.77 (s, 3H), 7.70 (s, 1H), 7.57 (s, 2H), 7.13 (d, *J* = 5.7 Hz, 2H), 6.69 (s, 1H), 5.79 (s, 2H). ^{13}C NMR (75 MHz, $(CD_3)_2SO$, 25 ºC, δ): 193.6, 180.5 (t, $J_{2\ C\text{-}F}$ = 29.1 Hz), 163.4, 142.8, 134.1, 134.0, 132.1, 131.7, 128.9, 128.8, 127.9, 123.8, 115.3, 111.6 (t, $J_{1\ C\text{-}F}$ = 258.9 Hz), 109.4, 70.4. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -79.9, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{19}H_{15}F_2N_2O_3^+$ ([M + H]$^+$), 357.1045, found, 357.1046.

1-([1,1'-biphenyl]-4-yl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3d)



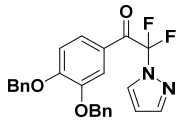
White solid (121 mg, 81 % yield, R_f = 0.52 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.05-7.99 (m, 3H), 6.68 (d, *J* = 6.93 Hz, 3H), 7.61 (d, *J* = 5.1 Hz, 2H), 7.46 (d, *J* = 7.26 Hz, 3H), 6.55 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.6 (t, $J_{2\ C\text{-}F}$ = 30.2 Hz), 147.5, 142.5, 139.5, 130.9, 130.3, 129.2, 128.8, 127.8, 127.5, 127.4, 112.1 (t, $J_{1\ C\text{-}F}$ = 261.0 Hz), 109.0. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.2, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{17}H_{13}F_2N_2O^+$ ($[M + H]^+$), 299.0990, found, 299.0998.

2,2-difluoro-1-(4'-(naphthalen-1-yl)-[1,1'-biphenyl]-4-yl)-2-(1H-pyrazol-1-yl)ethan-1-one (3e)



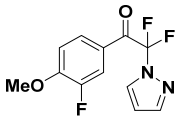
White solid (162 mg, 76 % yield, R_f = 0.35 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.10 (d, *J* = 6.78 Hz, 3H), 8.02-7.92 (m, 3H), 7.80-7.71 (m, 5H), 7.64 (d, *J* = 7.95 Hz, 2H), 7.57 (d, *J* = 7.50 Hz, 1H), 7.52 (d, *J* = 5.25 Hz, 3H), 6.57 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.5 (t, $J_{2\ C\text{-}F}$ = 30.2 Hz), 146.9, 142.5, 141.3, 139.4, 138.2, 133.9, 131.5, 131.0, 130.8, 130.4, 128.5, 128.1, 127.7, 127.3, 127.3, 127.1, 126.3, 126.0, 125.9, 125.5, 112.1 (t, $J_{1\ C\text{-}F}$ = 261.0 Hz), 108.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.0, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{27}H_{19}F_2N_2O^+$ ($[M + H]^+$), 425.1460, found, 425.1464.

1-(3,4-bis(phenoxymethyl)phenyl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3f)



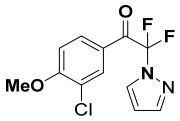
White solid (167 mg, 77 % yield, R_f = 0.24 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.96 (s, 1H), 7.63 (s, 2H), 7.51-7.33 (m, 11H), 6.91 (d, *J* = 8.58 Hz, 1H), 6.50 (s, 1H), 5.23 (s, 2H), 5.16 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 181.3 (t, $J_{2\ C\text{-}F}$ = 29.9 Hz), 154.7, 148.6, 142.4, 136.5, 136.1, 128.8, 128.7, 128.3, 128.1, 127.7, 127.4, 127.1, 125.9, 125.9, 125.8, 124.6, 115.4, 112.8, 112.1 (t, $J_{1\ C\text{-}F}$ = 209.9 Hz), 108.7, 71.2, 70.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -80.6, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{25}H_{21}F_2N_2O_3^+$ ($[M + H]^+$), 435.1515, found, 435.1521.

2,2-difluoro-1-(3-fluoro-4-methoxyphenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (3g)



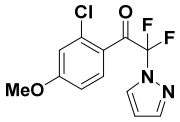
Colorless oil (68 mg, 50 % yield, R_f = 0.28 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.00 (d, J = 2.1 Hz, 1H), 7.72-7.68 (m, 2H), 7.63 (d, J = 7.74 Hz, 1H), 6.97 (t, J = 8.28 Hz, 1H), 6.51 (s, 1H), 3.93 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.8 (dd, $J_{2\ C\text{-}F}$ = 30.2, 2.2 Hz), 153.5 (t, J = 3.18 Hz), 150.2, 142.5, 128.3 (q, J = 2.7 Hz), 127.7, 124.5 (d, J = 5.9 Hz), 117.9 (t, J = 2.0 Hz), 117.6 (t, J = 2.1 Hz), 112.6 (d, J = 1.4 Hz), 112.0 (t, $J_{1\ C\text{-}F}$ = 260.7 Hz), 109.0, 56.4. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.0, -133.5 (t, J = 11.7 Hz), Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{10}F_3N_2O_2^+$ ($[M + H]^+$), 271.0689, found, 271.0700.

1-(3-chloro-4-methoxyphenyl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3h)



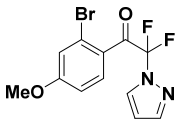
Colorless oil (102 mg, 71 % yield, R_f = 0.2 (petroleum ether/ethyl acetate = 20 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.99 (d, J = 2.22 Hz, 1H), 7.94 (s, 1H), 7.76 (d, J = 8.61 Hz, 1H), 7.58 (s, 1H), 6.90 (d, J = 8.79 Hz, 1H), 6.48 (s, 1H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.6 (t, $J_{2\ C\text{-}F}$ = 30.2 Hz), 160.0, 142.4, 132.1, 131.1 (t, $J_{3\ C\text{-}F}$ = 2.6 Hz), 127.6, 124.8, 123.2, 111.9 (t, $J_{1\ C\text{-}F}$ = 260.6 Hz), 111.5, 108.9, 56.5. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.0, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{10}ClF_2N_2O_2^+$ ($[M + H]^+$), 287.0393, found, 287.0400.

1-(2-chloro-4-methoxyphenyl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3i)



White solid (87 mg, 60 % yield, R_f = 0.26 (petroleum ether/ethyl acetate = 20 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.95 (d, J = 2.55 Hz, 1H), 7.67 (s, 1H), 7.62 (d, J = 8.91 Hz, 1H), 7.02 (d, J = 2.46 Hz, 1H), 6.78 (dd, J = 2.49, 8.91 Hz, 1H), 6.50-6.48 (m, 1H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.5 (t, $J_{2\ C\text{-}F}$ = 32.2 Hz), 163.3, 142.7, 136.8, 133.2 (t, $J_{3\ C\text{-}F}$ = 3.0 Hz), 128.2, 123.6, 117.3, 112.4. 111.8 (t, $J_{1\ C\text{-}F}$ = 262.5 Hz), 108.7, 55.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.5, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{10}ClF_2N_2O_2^+$ ($[M + H]^+$), 287.0393, found, 287.0386.

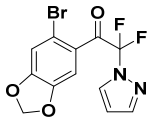
1-(2-bromo-4-methoxyphenyl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3j)



White solid (84 mg, 51 % yield, R_f = 0.41 (petroleum ether/ethyl acetate = 10 : 1 (v/v));

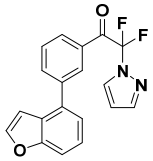
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.95 (d, J = 2.04 Hz, 1H), 7.68 (s, 1H), 7.61 (d, J = 8.88 Hz, 1H), 7.25 (d, J = 2.4 Hz, 1H), 6.83 (dd, J = 8.85, 2.28 Hz, 1H), 6.49 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 183.1 (t, $J_{2\ C\text{-}F}$ = 31.9 Hz), 163.0, 142.7, 133.1 (t, $J_{3\ C\text{-}F}$ = 3.7 Hz), 128.3, 125.1, 124.5, 120.8, 112.8, 111.6 (t, $J_{1\ C\text{-}F}$ = 263.6 Hz), 108.7, 56.0. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.4, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{10}BrF_2N_2O_2^+$ ($[M + H]^+$), 330.9888, found, 330.9889.

(6-bromobenzo[d][1,3]dioxol-5-yl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3k)



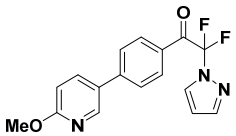
White solid (77 mg, 45 % yield, R_f = 0.30 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.94 (d, J = 2.4 Hz, 1H), 7.70 (s, 1H), 7.14 (s, 1H), 7.11 (s, 1H), 6.51-6.49 (m, 1H), 6.05 (s, 2H),. ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 184.0 (t, $J_{2\ C\text{-}F}$ = 33.0 Hz), 151.6, 147.1, 142.8, 128.3, 126.6, 115.4, 114.9, 111.5 (t, $J_{1\ C\text{-}F}$ = 263.3 Hz), 110.4 (t, $J_{3\ C\text{-}F}$ = 3.0 Hz), 108.7, 102.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -83.4, Mass Spectr-ometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_8BrF_2N_2O_3^+$ ($[M + H]^+$), 344.9681, found, 344.9686.

1-(3-(benzofuran-4-yl)phenyl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3l)



White solid (149 mg, 88 % yield, R_f = 0.38 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.07 (s, 1H), 8.02 (d, J = 8.04 Hz, 2H), 7.81 (s, 1H), 7.68 (d, J = 6.93 Hz, 4H), 7.55 (dd, J = 17.67, 8.46 Hz, 2H), 6.81 (s, 1H), 6.54 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.5 (t, $J_{2\ C\text{-}F}$ = 30.1 Hz), 155.2, 147.8, 146.0, 142.4, 134.5, 130.8, 129.9, 128.2, 127.7, 127.5, 123.9, 120.2, 112.1 (t, $J_{1\ C\text{-}F}$ = 261.0 Hz), 111.9, 108.9, 106.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.2, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{19}H_{13}F_2N_2O_2^+$ ($[M + H]^+$), 339.0940, found, 339.0948.

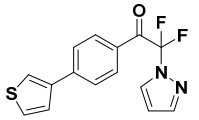
2,2-difluoro-1-(4-(6-methoxypyridin-3-yl)phenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (3m)



White solid (86 mg, 52 % yield, R_f = 0.24 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.40 (d, J = 2.37 Hz, 1H), 8.03-7.96 (m, 5H), 7.71 (d, J = 8.73 Hz, 1H), 7.62 (s, 1H), 7.25 (dd, J = 8.64, 2.79 Hz,

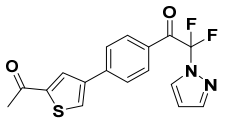
1H), 6.52 (s, 1H), 3.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.5 (t, $J_{2\ C\text{-}F}$ = 30.1 Hz), 155.8, 147.9, 144.9, 142.5, 138.0, 130.9, 130.8, 127.7, 126.5, 121.7, 121.0, 112.1 (t, $J_{1\ C\text{-}F}$ = 261.0 Hz), 108.9, 55.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.4, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{17}H_{14}F_2N_3O_2^+$ ($[M + H]^+$), 330.1049, found, 330.1055.

2,2-difluoro-2-(1H-pyrazol-1-yl)-1-(4-(thiophen-3-yl)phenyl)ethan-1-one (3n)



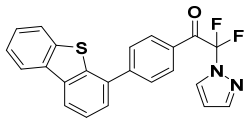
White solid (143 mg, 94 % yield, R_f = 0.43 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.04 (s, 1H), 7.96 (d, J = 8.1 Hz, 2H), 7.66 (d, J = 7.98 Hz, 3H), 7.59 (s, 1H), 7.41 (s, 2H), 6.53 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.3 (t, $J_{2\ C\text{-}F}$ = 30.1 Hz), 142.5, 141.7, 140.7, 131.1(t, $J_{3\ C\text{-}F}$ = 2.0 Hz), 130.0, 127.7, 127.1, 126.5, 126.1, 123.0, 112.1 (t, $J_{1\ C\text{-}F}$ = 261.0 Hz), 108.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.2, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{15}H_{11}F_2N_2OS^+$ ($[M + H]^+$), 305.0555, found, 305.0563.

1-(4-(5-acetylthiophen-2-yl)phenyl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3o)



White solid (104 mg, 60 % yield, R_f = 0.19 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.04 (d, J = 1.95 Hz, 1H), 7.98 (d, J = 8.01 Hz, 3H), 7.85 (d, J = 3.15 Hz, 1H), 7.67 (d, J = 8.7 Hz, 3H), 6.54 (s, 1H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 190.6, 182.3 (t, $J_{2\ C\text{-}F}$ = 30.3 Hz), 145.8, 142.5, 141.6, 140.6, 131.2, 130.7, 130.4, 127.8, 126.5, 112.0 (t, $J_{1\ C\text{-}F}$ = 261.0 Hz), 109.0, 27.0. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.3, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{17}H_{13}F_2N_2O_2S^+$ ($[M + H]^+$), 347.0660, found, 347.0657.

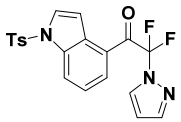
1-(4-(dibenzo[b,d]thiophen-4-yl)phenyl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3p)



Yellow oil (111 mg, 55 % yield, R_f = 0.27 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.19 (d, J = 7.02 Hz, 2H), 8.09 (d, J = 7.47 Hz, 3H), 7.85 (d, J = 7.77 Hz, 3H), 7.70 (s, 1H), 7.56 (t, J = 7.41 Hz, 1H), 7.48 (d, J = 4.98 Hz, 3H), 6.57 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.6 (t, $J_{2\ C\text{-}F}$ = 30.1 Hz), 147.0, 142.6, 139.4, 138.4, 136.7, 135.6, 135.3, 131.0, 128.7, 127.8, 127.2, 127.2, 125.4, 124.8, 122.8, 121.9, 121.7, 112.1 (t, $J_{1\ C\text{-}F}$ = 261.4 Hz), 109.0. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.1, Mass Spectrometry: HRMS (ESI-TOF)

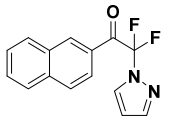
(m/z): calcd for $C_{23}H_{15}F_2N_2OS^+$ ([M + H]$^+$), 405.0868, found, 405.0878.

2,2-difluoro-2-(1H-pyrazol-1-yl)-1-(1-tosyl-1H-indol-4-yl)ethan-1-one (3q)



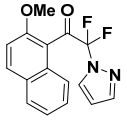
White solid (109 mg, 52 % yield, R_f = 0.17 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.28 (d, *J* = 8.28 Hz, 1H), 8.03 (d, *J* = 2.16 Hz, 1H), 7.80-7.74 (m, 3H), 7.58 (t, *J* = 4.80 Hz, 3H), 7.31 (d, *J* = 8.07 Hz, 1H), 7.24 (d, *J* = 8.07 Hz, 2H), 6.51 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.8 (t, $J_{2\ C\text{-}F}$ = 29.9 Hz), 145.7, 142.5, 135.6, 135.0, 131.3, 130.2, 129.9, 127.8, 127.4 (t, $J_{3\ C\text{-}F}$ = 4.2 Hz), 127.0, 123.9, 123.7, 120.0, 111.9 (t, $J_{1\ C\text{-}F}$ = 261.5 Hz), 109.7, 108.9, 21.7. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -80.2, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{20}H_{16}F_2N_3O_3S^+$ ([M + H]$^+$), 416.0875, found, 416.0879.

2,2-difluoro-1-(naphthalen-2-yl)-2-(1H-pyrazol-1-yl)ethan-1-one (3r)



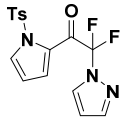
White solid (99 mg, 72 % yield, R_f = 0.45 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.47 (s, 1H), 8.08 (d, *J* = 2.13 Hz, 1H), 7.97-7.85 (m, 4H), 7.63 (t, *J* = 5.82 Hz, 2H), 7.54 (t, *J* = 5.82 Hz, 1H), 6.54 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 183.0 (t, $J_{2\ C\text{-}F}$ = 30.2 Hz), 142.6, 136.2, 133.1 (t, $J_{3\ C\text{-}F}$ = 2.9 Hz), 132.3, 130.2, 129.7, 129.0, 128.8, 127.9, 127.8, 127.2, 124.8, 112.2 (t, $J_{1\ C\text{-}F}$ = 261.2 Hz), 108.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -80.9, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{15}H_{11}F_2N_2O^+$ ([M + H]$^+$), 273.0834, found, 273.0840.

2,2-difluoro-1-(2-methoxynaphthalen-1-yl)-2-(1H-pyrazol-1-yl)ethan-1-one (3s)



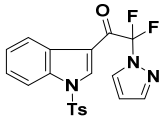
White solid (77 mg, 51 % yield, R_f = 0.37 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.99 (d, *J* = 9.12 Hz, 1H), 7.92 (d, *J* = 1.56 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 9.03 Hz, 2H), 7.51 (t, *J* = 7.29 Hz, 1H), 7.39 (t, *J* = 7.47 Hz, 1H), 7.27 (d, *J* = 9.09 Hz, 1H), 6.45 (s, 1H), 3.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 191.3 (t, $J_{2\ C\text{-}F}$ = 36.5 Hz), 156.9, 142.8, 134.2, 131.4, 129.0, 128.8, 128.6, 128.4, 124.7, 123.5, 117.7, 112.4, 111.4 (t, $J_{1\ C\text{-}F}$ = 267.0 Hz), 107.6, 56.7. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -89.5, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{16}H_{13}F_2N_2O_2^+$ ([M + H]$^+$), 303.0940, found, 303.0947.

2,2-difluoro-2-(1H-pyrazol-1-yl)-1-(1-tosyl-1H-pyrrol-2-yl)ethan-1-one (3t)



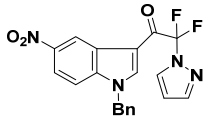
Colorless oil (88 mg, 48 % yield, R_f = 0.2 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.94 (d, *J* = 8.19 Hz, 3H), 7.85 (d, *J* = 1.92 Hz 1H), 7.59 (s, 1H), 7.33 (d, *J* = 8.10 Hz, 2H), 7.10 (d, *J* = 1.77 Hz, 1H), 6.42 (s, 1H), 6.37 (t, *J* = 3.24 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 171.2 (t, $J_{2\ C\text{-}F}$ = 32.3 Hz), 145.6, 142.6, 135.0, 133.0, 129.7, 128.8, 128.2 (t, $J_{3\ C\text{-}F}$ = 5.0 Hz), 128.1, 127.6, 111.8 (t, $J_{1\ C\text{-}F}$ = 261.8 Hz), 111.5, 108.5, 21.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.5, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{16}H_{14}F_2N_3O_3S^+$ ($[M + H]^+$), 366.0718, found, 366.0727.

2,2-difluoro-2-(1H-pyrazol-1-yl)-1-(1-tosyl-1H-indol-3-yl)ethan-1-one (3u)



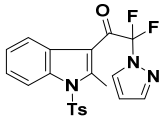
White solid (127 mg, 61 % yield, R_f = 0.75 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.37 (d, *J* = 7.83 Hz, 1H), 8.33 (s, 1H), 8.03 (s, 1H), 7.95 (d, *J* = 7.44 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.67 (s, 1H), 7.44-7.36 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 6.53 (s, 1H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 178.8 (t, $J_{2\ C\text{-}F}$ = 32.6 Hz), 146.5, 142.7, 135.6 (t, $J_{3\ C\text{-}F}$ = 7.2 Hz), 134.4, 134.1, 130.5, 128.3, 128.0, 127.4, 126.5, 125.6, 123.1, 115.1, 113.3, 112.0 (t, $J_{1\ C\text{-}F}$ = 262.5 Hz), 168.6, 21.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -84.1, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{20}H_{16}F_2N_3O_3S^+$ ($[M + H]^+$), 416.0875, found, 416.0879.

1-(1-benzyl-5-nitro-1H-indol-3-yl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3v)



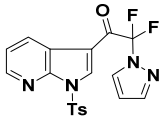
Yellow oil (59 mg, 30 % yield, R_f = 0.13 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 9.31 (d, *J* = 1.53 Hz, 1H), 8.17-8.11 (m, 2H), 7.97 (d, *J* = 1.53 Hz, 1H), 7.64 (s, 1H), 7.38-7.35 (m, 4H), 7.15 (d, *J* = 4.2 Hz, 2H), 6.47 (s, 1H), 5.42 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 177.8 (t, $J_{2\ C\text{-}F}$ = 32.8 Hz), 144.6, 142.7, 140.8 (t, $J_{3\ C\text{-}F}$ = 7.4 Hz), 139.3, 134.0, 129.4, 128.9, 128.4, 127.1, 127.0, 119.9, 119.5, 112.1, 112.2 (t, $J_{1\ C\text{-}F}$ = 263.2 Hz), 111.0, 108.3, 51.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -84.8, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{20}H_{14}F_2N_4NaO_3^+$ ($[M + Na]^+$), 419.0926, found, 419.0924.

2,2-difluoro-1-(2-methyl-1-tosyl-1H-indol-3-yl)-2-(1H-pyrazol-1-yl)ethan-1-one (3w)



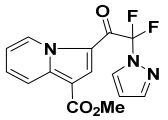
Light yellow oil (174 mg, 81 % yield, R_f = 0.2 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.33 (d, J = 8.67 Hz, 1H), 8.04 (d, J = 2.22 Hz, 1H), 7.80 (d, J = 8.25 Hz, 2H), 7.67 (s, 1H), 7.37-7.21 (m, 5H), 6.56 (s, 1H), 2.89 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.0 (t, $J_{2\ C\text{-}F}$ = 32.7 Hz), 147.3, 146.1, 142.4, 135.8, 135.5, 130.4, 128.3, 126.8, 125.9, 125.2, 124.6, 120.9 (t, $J_{3\ C\text{-}F}$ = 3.3 Hz), 115.8, 114.4, 111.8 (t, $J_{1\ C\text{-}F}$ = 260.2 Hz), 109.0, 21.7, 14.6. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.4, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{21}H_{18}F_2N_3O_3S^+$ ([M + H]$^+$), 430.1031, found, 430.1037.

2,2-difluoro-2-(1H-pyrazol-1-yl)-1-(1-tosyl-1H-pyrrolo[2,3-b]pyridin-3-yl)ethan-1-one(3x)



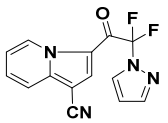
White solid (75 mg, 36 % yield, R_f = 0.22 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.61-8.58 (m, 1H), 8.50 (d, J = 3.69 Hz, 1H), 8.43 (s, 1H), 8.13 (d, J = 8.31 Hz, 2H), 8.03 (d, J = 2.31 Hz, 1H), 7.65 (s, 1H), 7.35-7.30 (m, 3H), 6.53 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 178.8 (t, $J_{2\ C\text{-}F}$ = 32.7 Hz), 146.8, 146.7, 146.6, 142.8, 135.1 (t, $J_{3\ C\text{-}F}$ = 7.2 Hz), 134.0, 131.7, 130.1, 128.9, 128.3, 121.0, 120.7, 112.5, 111.9 (t, $J_{1\ C\text{-}F}$ = 261.8 Hz), 108.8, 21.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -83.9, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{19}H_{15}F_2N_4O_3S^+$ ([M + H]$^+$), 417.0827, found, 417.0838.

methyl 3-(2,2-difluoro-2-(1H-pyrazol-1-yl)acetyl)indolizine-1-carboxylate (3y)



White solid (65 mg, 41 % yield, R_f = 0.28 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 9.96 (d, J = 7.02 Hz, 1H), 8.44 (d, J = 8.85 Hz, 1H), 8.03 (s, 2H), 7.65 (s, 1H), 7.56 (t, J = 7.35 Hz, 1H), 7.18 (t, J = 7.35 Hz, 1H), 6.50 (t, J = 2.19 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 172.0 (t, $J_{2\ C\text{-}F}$ = 31.4 Hz), 164.0, 142.7, 140.9, 129.9, 129.7, 129.1 (t, $J_{3\ C\text{-}F}$ = 5.6 Hz), 128.3, 119.9, 118.6, 116.7, 112.6 (t, $J_{1\ C\text{-}F}$ = 261.8 Hz), 108.5, 108.3, 51.6. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.9, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{15}H_{12}F_2N_3O_3^+$ ([M + H]$^+$), 320.0841, found, 320.0843.

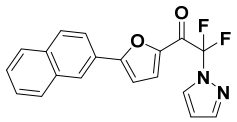
3-(2,2-difluoro-2-(1H-pyrazol-1-yl)acetyl)indolizine-1-carbonitrile (3z)



White solid (66 mg, 46 % yield, R_f = 0.12 (petroleum ether/ethyl acetate = 5 : 1 (v/v));

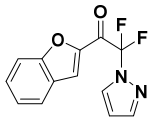
NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 9.96 (d, J = 6.99 Hz, 1H), 8.07 (d, J = 2.04 Hz, 1H), 7.89 (d, J = 8.76 Hz, 1H), 7.82 (s, 1H), 7.67-7.61 (m, 2H), 7.29 (d, J = 4.29 Hz, 1H), 6.55 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 171.9 (t, $J_{2\ C\text{-}F}$ = 32.0 Hz), 142.8, 141.8, 130.1, 129.8 (t, $J_{3\ C\text{-}F}$ = 5.4 Hz), 128.2, 118.9, 117.9, 117.3, 114.3, 112.2 (t, $J_{1\ C\text{-}F}$ = 261.3 Hz), 108.8, 87.5. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.1, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_9F_2N_4O^+$ ([M + H]$^+$), 287.0739, found, 287.0742.

2,2-difluoro-1-(5-(naphthalen-2-yl)furan-2-yl)-2-(1H-pyrazol-1-yl)ethan-1-one (3aa)



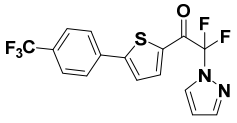
Yellow oil (51 mg, 30 % yield, R_f = 0.58 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.29 (s, 1H), 8.03 (s, 1H), 7.89-7.78 (m, 4H), 7.68 (s, 1H), 7.53 (d, J = 9.02 Hz, 3H), 6.94 (d, J = 3.69 Hz, 1H), 6.51 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 170.7 (t, $J_{2\ C\text{-}F}$ = 33.0 Hz), 161.0, 147.3, 142.8, 134.1, 133.3, 129.0, 128.8, 128.1, 128.0, 127.6, 127.1, 126.3 (t, $J_{3\ C\text{-}F}$ = 4.2 Hz), 125.9, 125.6, 122.7, 112.0 (t, $J_{1\ C\text{-}F}$ = 261.6 Hz), 108.8, 108.5. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -84.7, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{19}H_{13}F_2N_2O_2^+$([M + H]$^+$), 339.0940, found, 339.0941.

1-(benzofuran-2-yl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3ab)



White solid (79 mg, 60 % yield, R_f = 0.32 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.03 (s, 1H), 7.72 (d, J = 12 Hz, 2H), 7.64 (s, 1H), 7.61-7.51 (m, 2H), 7.36-7.31 (m, 1H), 6.52 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 173.4 (t, $J_{2\ C\text{-}F}$ = 33.2 Hz), 156.6, 147.9, 142.8, 130.1, 128.1, 126.8, 124.6, 124.2, 119.6 (t, $J_{3\ C\text{-}F}$ = 4.2 Hz), 112.8, 111.7 (t, $J_{1\ C\text{-}F}$ = 261.1 Hz), 108.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -84.5, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_9F_2N_2O_2^+$ ([M + H]$^+$), 263.0627, found, 263.0629.

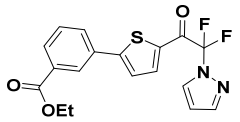
2,2-difluoro-2-(1H-pyrazol-1-yl)-1-(5-(4-(trifluoromethyl)phenyl)thiophen-2-yl)ethan-1-one (3ac)



White solid (106 mg, 57 % yield, R_f = 0.38 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.05 (d, J = 8.04 Hz, 2H), 7.95 (s, 1H), 7.75 (s, 1H), 7.70 (d, J = 9.57 Hz, 2H), 7.61-7.51 (m, 2H), 6.53 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 176.4 (t, $J_{2\ C\text{-}F}$ = 32.9 Hz), 142.9, 142.6, 138.4, 135.0, 134.5 (t, $J_{3\ C\text{-}F}$ = 3.5 Hz), 132.6, 131.6 (q, J = 32.3 Hz), 129.8 (d, J = 4.8

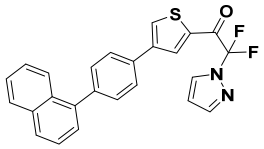
Hz), 128.1, 125.8, 124.8 (q, J = 3.7 Hz), 123.2 (q, J = 3.7 Hz), 122.2, 112.0 (t, $J_{1\ C\text{-}F}$ = 261.8 Hz), 108.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -62.8, -83.3, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{16}H_{10}F_5N_2OS^+$ ([M + H]$^+$), 373.0429, found, 373.0431.

ethyl 3-(5-(2,2-difluoro-2-(1H-pyrazol-1-yl)acetyl)thiophen-2-yl)benzoate (3ad)



Light yellow oil (86 mg, 46 % yield, R_f = 0.20 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.19 (s, 1H), 8.08 (s, 1H), 8.01 (d, J = 7.11 Hz, 2H), 7.96 (d, J = 0.96 Hz, 1H), 7.69 (d, J = 11.61 Hz, 2H), 7.48 (t, J = 7.71 Hz, 1H), 6.52 (d, J = 0.6 Hz, 1H), 4.41 (q, J = 7.11 Hz, 2H), 1.41 (t, J = 7.11 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 176.4 (t, $J_{2\ C\text{-}F}$ = 32.8 Hz), 166.3, 143.2, 142.9, 138.2, 134.7 (t, $J_{3\ C\text{-}F}$ = 3.6 Hz), 134.5, 132.4, 131.5, 130.7, 130.6, 130.3, 129.2 (d, $J_{4\ C\text{-}F}$ = 3.3 Hz), 128.1, 127.6, 112.0 (t, $J_{1\ C\text{-}F}$ = 261.9 Hz), 108.8, 61.4, 14.4. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -83.2, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{18}H_{15}F_2N_2O_3S^+$ ([M + H]$^+$), 377.0766, found, 377.0775.

2,2-difluoro-1-(4-(4-(naphthalen-1-yl)phenyl)thiophen-2-yl)-2-(1H-pyrazol-1-yl)ethan-1-one (3ae)



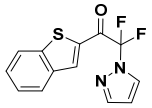
Yellow oil (77 mg, 36 % yield, R_f = 0.25 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.16 (s, 1H), 8.05 (s, 1H), 7.97-7.89 (m, 4H), 7.72 (s, 1H), 7.66 (d, J = 8.1 Hz, 2H), 7.58-7.53 (m, 4H), 7.50-7.45 (m, 2H), 6.54 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 176.4 (t, $J_{2\ C\text{-}F}$ = 32.8 Hz), 144.0, 142.8, 140.8, 139.5, 138.1, 134.8 (t, $J_{3\ C\text{-}F}$ = 3.9 Hz), 133.9, 133.2, 131.9, 131.5, 130.8, 128.5, 128.1 (d, J = 3.3 Hz), 127.0, 126.4, 126.3, 126.0, 125.9, 125.5, 112.0 (t, $J_{1\ C\text{-}F}$ = 261.9 Hz), 108.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -83.1, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{25}H_{17}F_2N_2OS^+$ ([M + H]$^+$), 431.1024, found, 431.1031.

2,2-difluoro-1-(4-(furan-3-yl)thiophen-2-yl)-2-(1H-pyrazol-1-yl)ethan-1-one (3af)

Yellow oil (41 mg, 28 % yield, R_f = 0.48 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.00 (d, J = 2.49 Hz, 1H), 7.88 (d, J = 1.02 Hz, 1H), 7.71 (d, J = 0.93 Hz, 1H), 7.67 (s, 2H), 7.46 (s, 1H), 6.58 (s, 1H), 6.52-6.51(m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 176.4 (t, $J_{2\ C\text{-}F}$ = 32.8

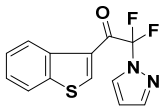
Hz), 144.0, 142.9, 139.2, 137.8, 135.5, 134.5 (t, $J_{3\ C\text{-}F}$ = 3.6 Hz), 131.0, 128.1, 120.6, 112.0 (t, $J_{1\ C\text{-}F}$ = 262.3 Hz), 109.1, 108.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -83.3, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_9F_2N_2O_2S^+$ ($[M + H]^+$), 295.0347, found, 295.0349.

1-(benzo[b]thiophen-2-yl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3ag)



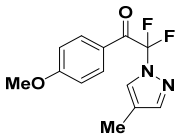
White solid (105 mg, 75 % yield, R_f = 0.45 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.06 (s, 1H), 8.03 (d, *J* = 2.1 Hz, 1H), 7.88 (dd, *J* = 4.5, 3.36 Hz, 2H), 7.66 (s, 1H), 7.51 (t, *J* = 7.05 Hz, 1H), 7.41 (t, *J* = 7.56 Hz, 1H), 6.52 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 177.9 (t, $J_{2\ C\text{-}F}$ = 32.7 Hz), 143.5, 142.9, 139.0, 137.0, 134.1 (t, $J_{3\ C\text{-}F}$ = 4.2 Hz), 128.9, 128.1, 127.1, 125.6, 122.9, 112.0 (t, $J_{1\ C\text{-}F}$ = 262.0 Hz), 108.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.7, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_9F_2N_2OS^+$ ($[M + H]^+$), 279.0398, found, 279.0403.

1-(benzo[b]thiophen-3-yl)-2,2-difluoro-2-(1H-pyrazol-1-yl)ethan-1-one (3ah)



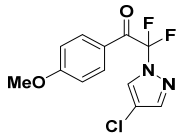
Yellow oil (92 mg, 66 % yield, R_f = 0.53 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.91 (d, *J* = 7.80 Hz, 1H), 8.51 (s, 1H), 8.12 (s, 1H), 7.97 (d, *J* = 7.53 Hz, 1H), 7.76 (s, 1H), 7.65 (t, *J* = 6.78 Hz, 1H), 7.56 (t, *J* = 7.11 Hz, 1H), 6.61 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 175.5 (t, $J_{2\ C\text{-}F}$ = 31.2 Hz), 140.8, 140.5 (t, $J_{3\ C\text{-}F}$ = 5.7 Hz), 137.1, 135.1, 126.5, 126.4, 124.7, 124.3, 123.4, 120.5, 110.1 (t, $J_{1\ C\text{-}F}$ = 262.4 Hz), 106.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.0, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_9F_2N_2OS^+$ ($[M + H]^+$), 279.0398, found, 279.0403.

(4-methoxyphenyl)(4-methyl-1H-pyrazol-1-yl)methanone (4a)



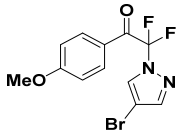
Colorless oil (81 mg, 61 % yield, R_f = 0.41 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.90 (d, *J* = 8.46 Hz, 2H), 7.73 (s, 1H), 7.42 (s, 1H), 6.90 (d, *J* = 8.82 Hz, 2H), 3.84 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 181.5 (t, $J_{2\ C\text{-}F}$ = 29.7 Hz), 164.7, 143.4, 132.8, 125.7, 124.5, 119.5, 114.1, 112.1 (t, $J_{1\ C\text{-}F}$ = 259.9 Hz), 55.6, 8.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -80.8, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_{13}F_2N_2O_2^+$ ($[M + H]^+$), 267.0940, found, 267.0949.

2-(4-chloro-1H-pyrazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4b)



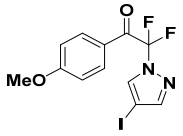
Yellow oil (116 mg, 81 % yield, R_f = 0.47 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.03 (d, *J* = 8.58 Hz, 3H), 7.64 (s, 1H), 7.03 (d, *J* = 8.16 Hz, 2H), 3.97 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 179.7 (t, $J_{2\ C\text{-}F}$ = 29.8 Hz), 163.9, 140.1, 131.8, 124.8, 123.1, 113.3, 113.0, 110.9 (t, $J_{1\ C\text{-}F}$ = 263.4 Hz), 54.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.5, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{10}ClF_2N_2O_2^+$ ([M + H]$^+$), 287.0393, found, 287.0395.

2-(4-bromo-1H-pyrazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4c)



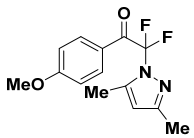
Colorless oil (125 mg, 76 % yield, R_f = 0.45 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.01 (s,1H), 7.93 (d, *J* = 8.79 Hz, 2H), 7.58 (s, 1H), 6.93 (d, *J* = 8.94 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.8 (t, $J_{2\ C\text{-}F}$ = 29.5 Hz), 165.1, 143.1, 132.9 (t, $J_{3\ C\text{-}F}$ = 2.3 Hz), 127.9, 124.2, 114.3, 111.9 (t, $J_{1\ C\text{-}F}$ = 263.8 Hz), 97.4, 55.7. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.5, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_{10}BrF_2N_2O_2^+$ ([M + H]$^+$), 330.9888, found, 330.9884.

(4-iodo-1H-pyrazol-1-yl)(4-methoxyphenyl)methanone (4d)



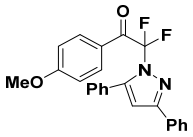
Colorless oil (119 mg, 63 % yield, R_f = 0.5 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.05 (s, 1H), 7.93 (d, *J* = 8.67 Hz, 2H), 7.62 (s, 1H), 6.94 (d, *J* = 8.85 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.8 (t, $J_{2\ C\text{-}F}$ = 29.6 Hz), 165.0, 147.3, 132.9 (t, $J_{3\ C\text{-}F}$ = 2.5 Hz), 132.2, 124.2, 114.3, 111.7 (t, $J_{1\ C\text{-}F}$ = 263.7 Hz), 60.9, 55.7. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.3, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{12}H_9F_2IN_2O_2^+$ ([M + H]$^+$), 378.9750, found, 378.9753.

(3,5-dimethyl-1H-pyrazol-1-yl)(4-methoxyphenyl)methanone (4e)



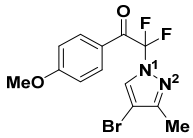
Colorless oil (57 mg, 41 % yield, R_f = 0.45 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.90 (d, J = 8.70 Hz, 2H), 6.91 (d, J = 8.88 Hz, 2H), 5.98 (s,1H), 3.86 (s, 3H), 2.51 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 182.0 (t, $J_{2\ C\text{-}F}$ = 29.5 Hz), 164.5, 150.9, 141.5, 133.0, 125.1, 113.9, 113.5 (t, $J_{1\ C\text{-}F}$ = 257.3 Hz), 109.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -79.4, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_{15}F_2N_2O_2^+$ ([M + H]$^+$), 281.1096, found, 281.1111.

2-(3,5-diphenyl-1H-pyrazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4f)



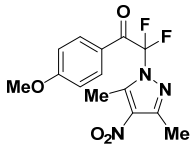
Colorless oil (105 mg, 52 % yield, R_f = 0.38 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.88 (d, J = 8.64 Hz, 2H), 7.66-7.69 (m, 4H), 7.49-7.51 (m, 3H), 7.34 (d, J = 5.97 Hz, 3H), 6.90 (d, J = 9.00 Hz, 2H), 6.79 (s, 1H), 3.84 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 181.4 (t, $J_{2\ C\text{-}F}$ = 29.3 Hz), 164.3, 152.7, 146.4, 132.7, 131.7, 129.6, 129.4 (d, $J_{3\ C\text{-}F}$ = 6.6 Hz), 128.9, 128.7, 128.6, 126.2, 125.1, 114.0, 113.5 (t, $J_{1\ C\text{-}F}$ = 260.6 Hz), 107.8, 55.6. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -76.7, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{24}H_{19}F_2N_2O_2^+$ ([M + H]$^+$), 405.1409, found, 405.1411.

2-(4-bromo-3-methyl-1H-pyrazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4g)



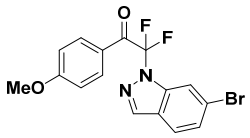
Light yellow oil (115mg, 67% yield, R_f = 0.45 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); isomers (N_1 : N_2 = 4:1 based on NMR), NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.71-7.78 (m, 3H), 6.76 (d, J = 8.70 Hz, 2H), 3.70 (s, 3.7H), 2.39 (s, 0.8H), 2.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.9 (t, $J_{2\ C\text{-}F}$ = 30.2 Hz), 164.6, 151.0, 141.4, 132.7 (d, $J_{3\ C\text{-}F}$ = 2.1 Hz), 127.9, 124.0, 111.6 (t, $J_{1\ C\text{-}F}$ = 263.1 Hz), 98.4, 55.4, 11.9. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -79.9, -81.8, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_{12}BrF_2N_2NaO_2^+$ ([M + Na]$^+$), 366.9864, found, 366.9873.

2-(3,5-dimethyl-4-nitro-1H-pyrazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4h)



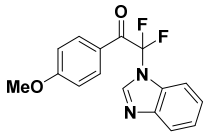
White solid (86 mg, 52 % yield, R_f = 0.7 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.90 (d, *J* = 8.76 Hz, 2H), 6.94 (d, *J* = 8.91 Hz, 2H), 3.88 (s, 3H), 2.90 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.4 (t, $J_{2\ C\text{-}F}$ = 28.7 Hz), 165.0, 147.3, 143.0, 133.0 (t, $J_{3\ C\text{-}F}$ = 2.2 Hz), 124.3, 114.3, 113.8 (t, $J_{1\ C\text{-}F}$ = 264.6 Hz), 55.8, 14.1, 11.7 (t, *J* = 3.2 Hz). ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -80.3, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_{14}F_2N_3O_4^+$ ([M + H]$^+$), 326.0947, found, 326.0949.

2-(6-bromo-1H-indazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4i)



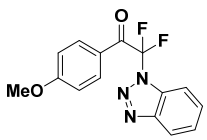
Yellow oil (82 mg, 43 % yield, R_f = 0.35 (petroleum ether/ethyl acetate = 10 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.52 (s, 1H), 7.97 (d, *J* = 8.34 Hz, 2H), 7.88 (s, 1H), 7.62 (d, *J* = 9.00 Hz, 1H), 7.26 (t, *J* = 7.95 Hz, 1H), 6.94 (d, *J* = 8.88 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.8 (t, $J_{2\ C\text{-}F}$ = 29.6 Hz), 165.1, 150.4, 133.0, 128.0, 124.1, 122.5, 122.3, 122.0, 121.1, 120.4, 114.4, 112.8 (t, $J_{1\ C\text{-}F}$ = 266.4 Hz), 55.7. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.4, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{16}H_{12}BrF_2N_2O_2^+$ ([M + H]$^+$), 381.0045, found, 381.0042.

2-(1H-benzo[d]imidazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4j)



Light yellow oil (68 mg, 45 % yield, R_f = 0.58 (petroleum ether/ethyl acetate = 2 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.07 (t, *J* = 6.6 Hz, 3H), 7.83 (t, *J* = 3.90 Hz, 1H), 7.55 - 7.52 (m, 1H), 7.34 (t, *J* = 4.26 Hz, 2H), 6.95 (d, *J* = 8.97 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 181.4 (t, $J_{2\ C\text{-}F}$ = 33.4 Hz), 165.5, 143.8 139.3, 133.1 (t, $J_{3\ C\text{-}F}$ = 2.6 Hz), 131.3, 125.0, 124.1, 123.3, 121.0, 114.6, 113.5 (t, $J_{1\ C\text{-}F}$ = 266.0 Hz), 112.2 (t, *J* = 2.5 Hz), 55.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -81.0, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{16}H_{13}F_2N_2O_2^+$ ([M + H]$^+$), 303.0940, found, 303.0943.

2-(1H-benzo[d][1,2,3]triazol-1-yl)-2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (4k)

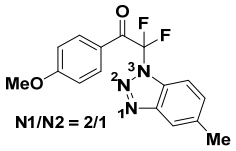


Yellow oil (61 mg, 40 % yield, R_f = 0.46 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 8.13 (dd, *J* = 6.3, 0.54 Hz,

1H), 7.99-7.97 (m, 2H), 7.90-7.88 (m, 1H), 7.68-7.64 (m, 1H), 7.53-7.49 (m, 1H), 6.93-6.90 (m, 2H), 3.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.4 (t, $J_{2\ C\text{-}F}$ = 28.6 Hz), 165.2, 146.1, 133.2, 131.1, 129.9, 125.8, 124.1, 120.7, 114.4, 113.3 (t, $J_{1\ C\text{-}F}$ = 263.6 Hz), 111.3, 55.8. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.9, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{15}H_{12}F_2N_3O_2^+$ ([M + H]$^+$), 304.0892, found, 304.0886.

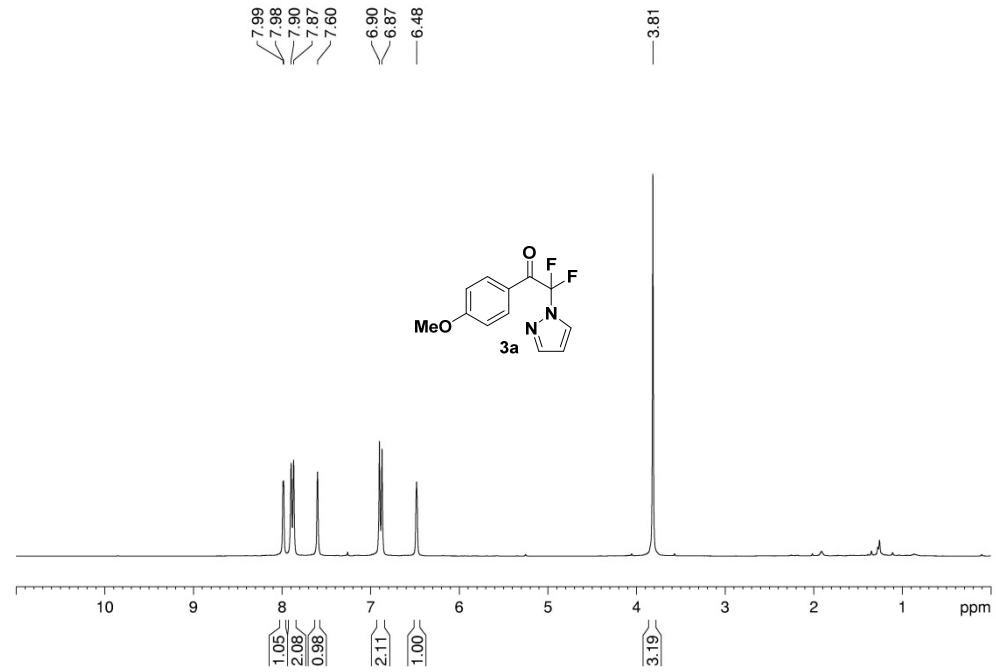
2,2-difluoro-1-(4-methoxyphenyl)-2-(5-methyl-1H-benzo[d][1,2,3]triazol-1-yl)ethan-1-one (4l)

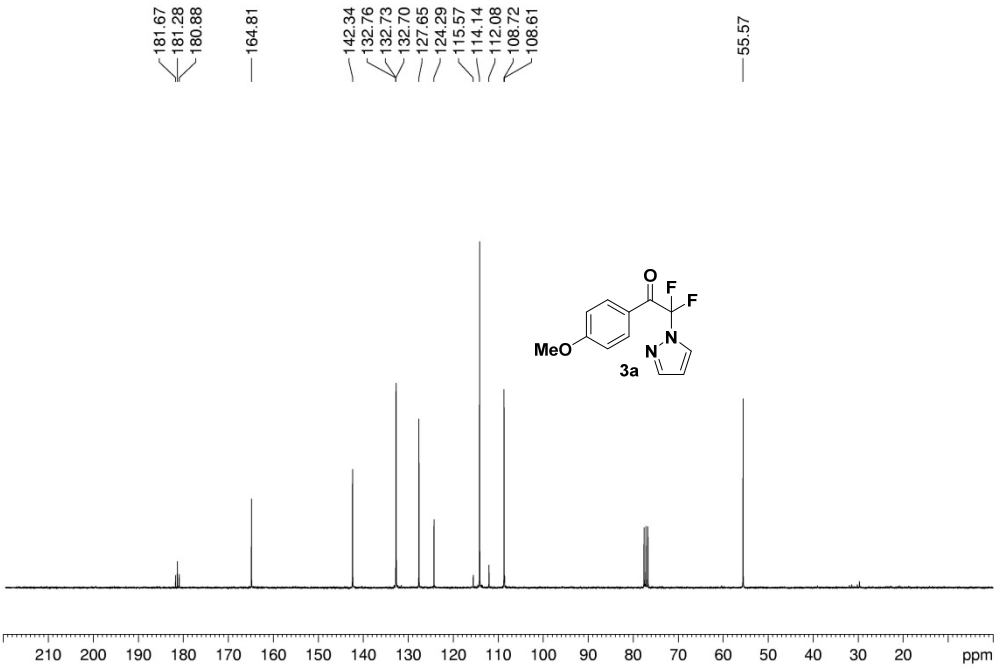
2,2-difluoro-1-(4-methoxyphenyl)-2-(5-methyl-2H-benzo[d][1,2,3]triazol-2-yl)ethan-1-one (4l')

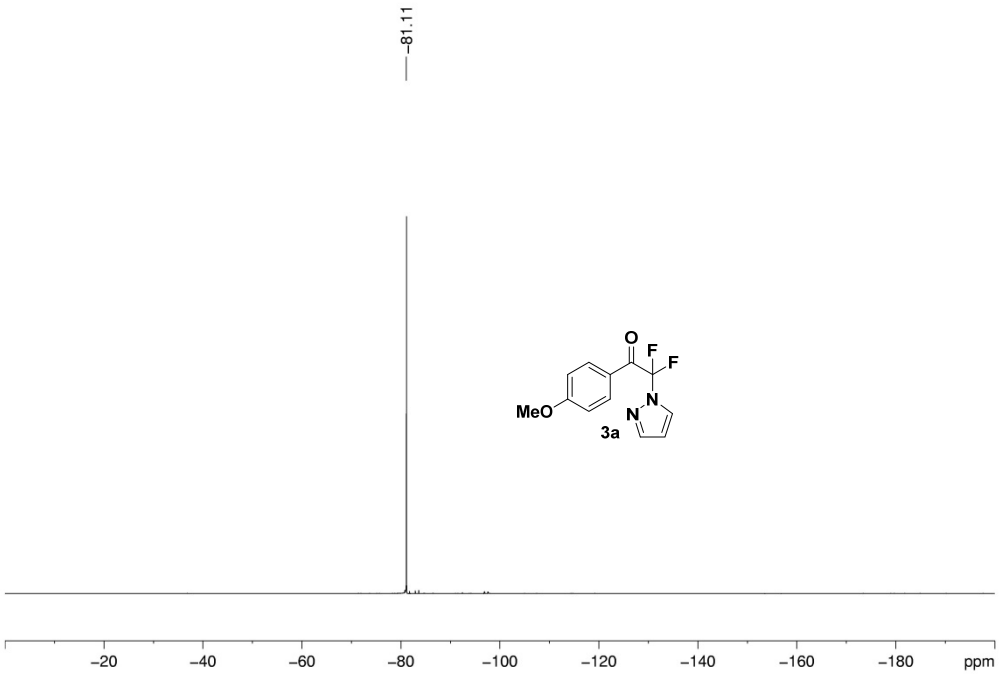


Colorless oil (68 mg, 43 % yield, R_f = 0.46 (petroleum ether/ethyl acetate = 5 : 1 (v/v)); isomers (N_1 : N_2 = 2:1 based on NMR), NMR Spectroscopy: ^{1}H NMR (300 MHz, $CDCl_3$, 25 ºC, δ): 7.96 (t, *J* = 5.28 Hz, 2H), 7.87 (s, 0.6H), 7.76 (d, *J* = 8.43 Hz, 0.6H), 7.66 (s, 0.4H), 7.47 (d, *J* = 8.34 Hz, 0.6H), 7.31 (d, *J* = 8.49 Hz, 0.4H), 6.89 (d, *J* = 8.70 Hz, 2H), 3.83 (s, 3H), 2.57 (s, 1H), 2.52 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 ºC, δ): 180.4 (t, $J_{2\ C\text{-}F}$ = 28.7 Hz), 165.1, 146.6, 144.6, 141.0, 136.1, 133.0, 131.9, 131.4, 129.4, 127.9, 124.1, 120.0, 119.6, 114.3, 113.2 (t, $J_{1\ C\text{-}F}$ = 263.2 Hz), 110.6 (t, $J_{3\ C\text{-}F}$ = 7.4 Hz), 55.7, 22.1, 21.5. ^{19}F NMR (282 MHz, $CDCl_3$, 25 ºC, δ): -82.9, -83.0, Mass Spectrometry: HRMS (ESI-TOF) (m/z): calcd for $C_{16}H_{14}F_2N_3O_2^+$ ([M + H]$^+$), 318.1049, found, 318.1053.

NMR Spectrum



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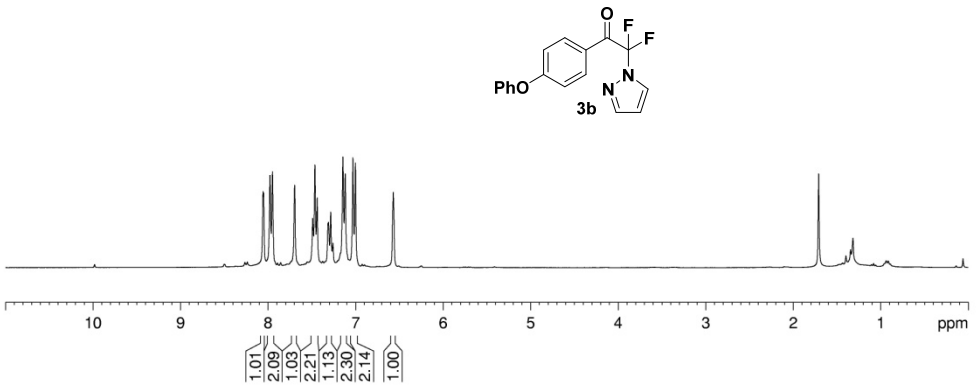
6.57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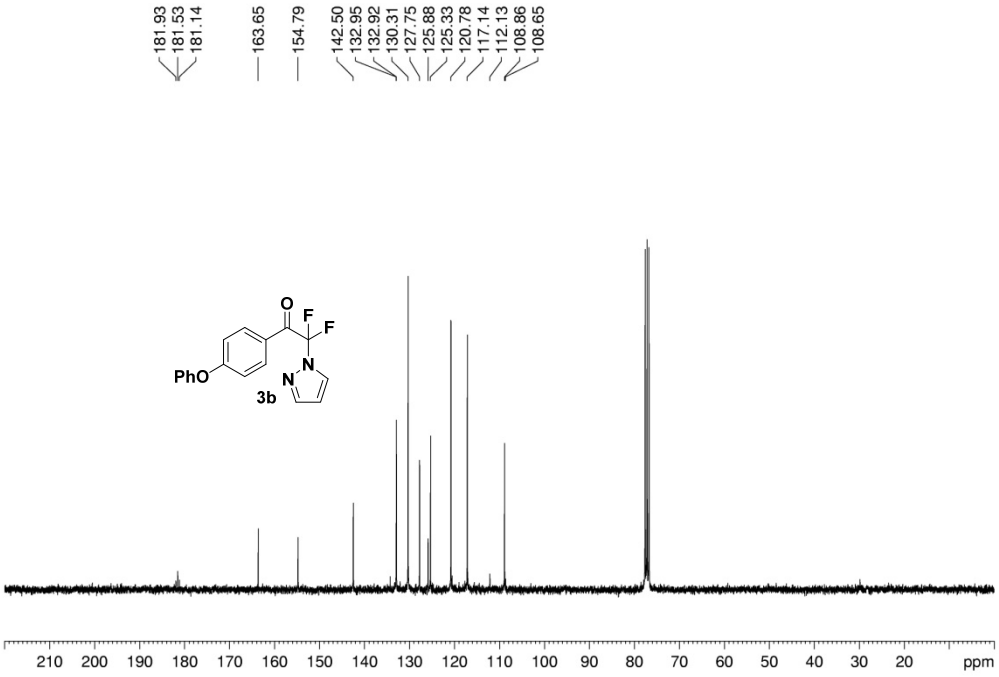
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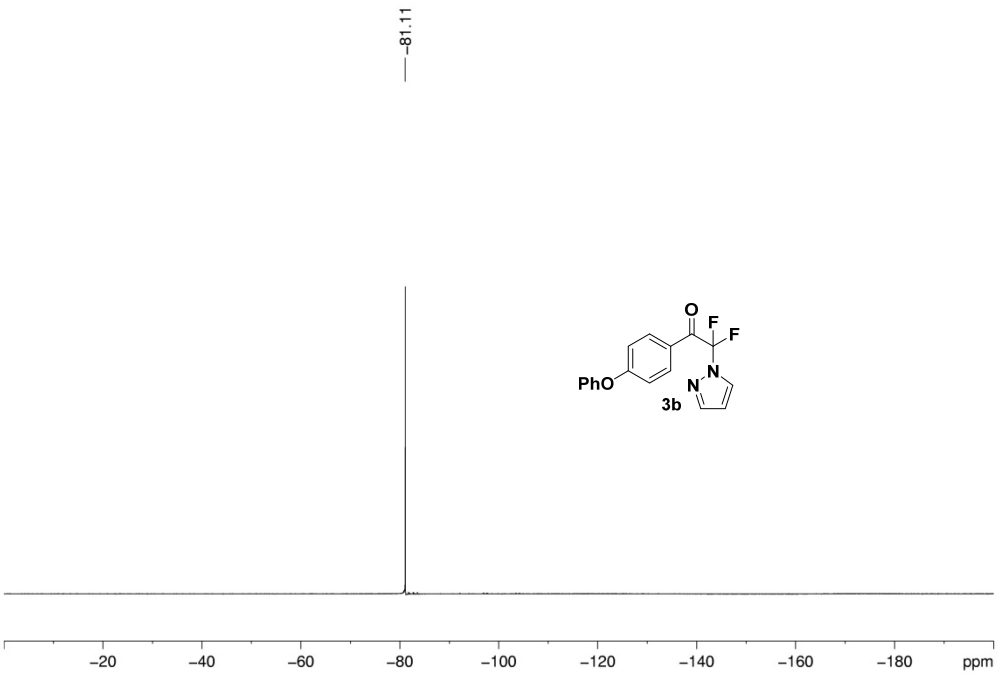
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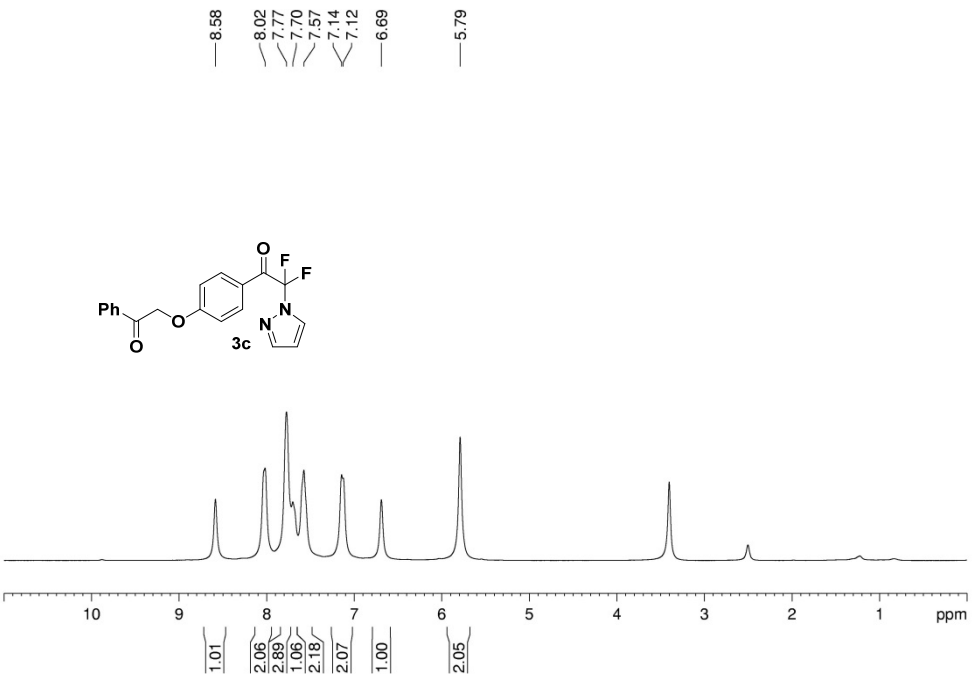
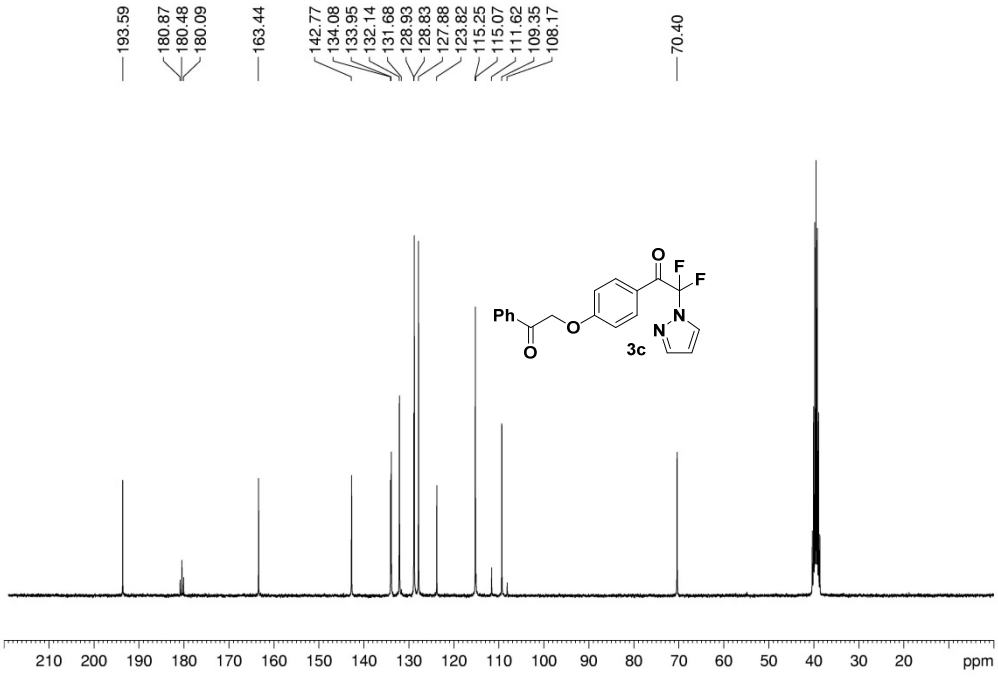
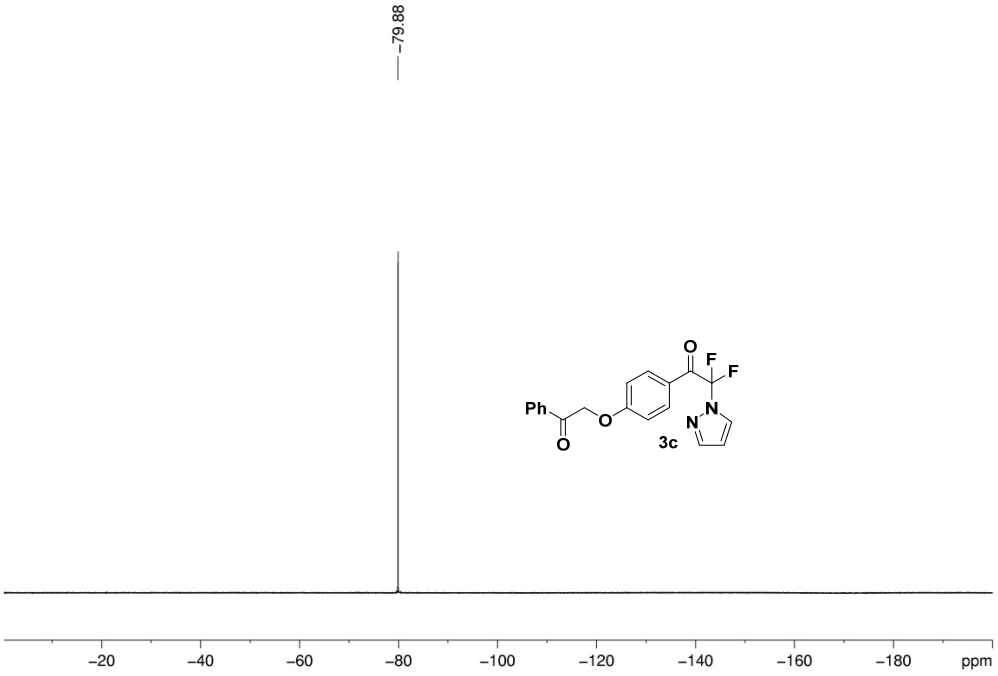
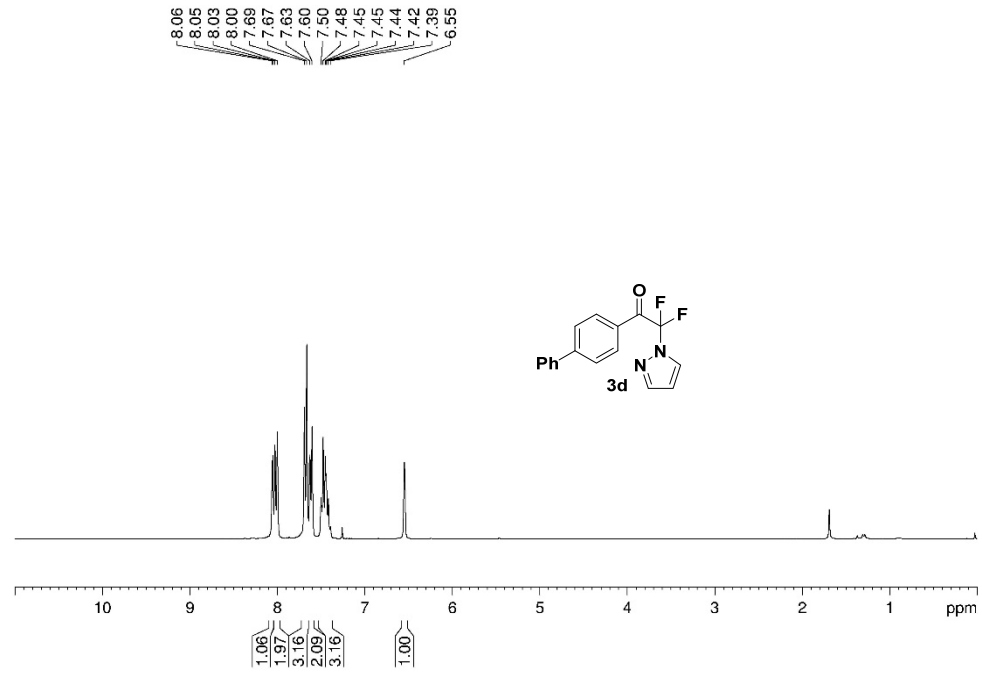
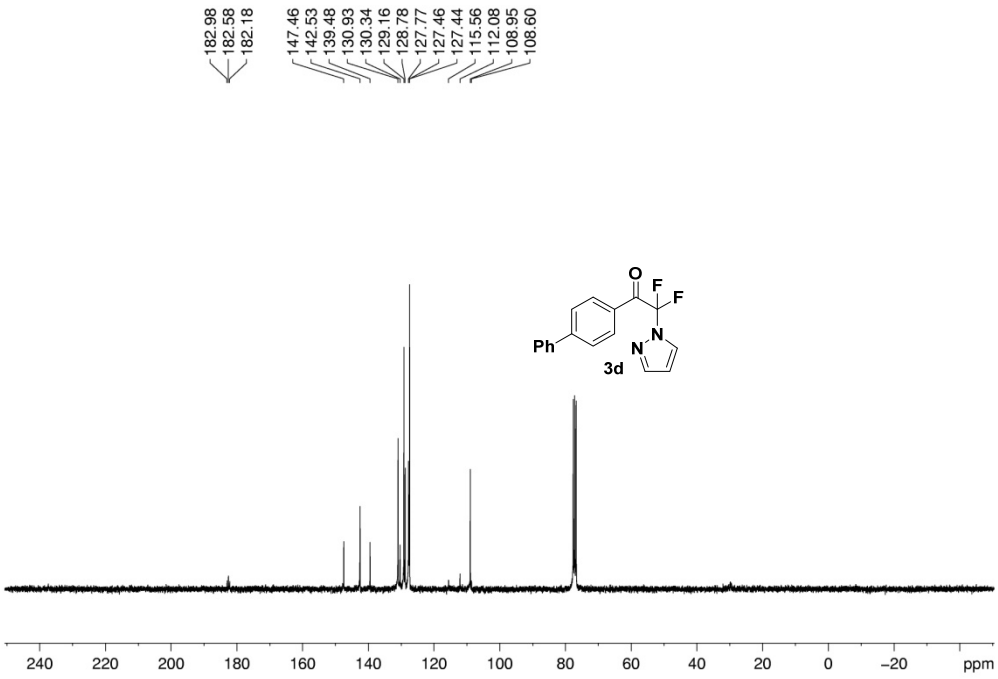
F
F
PhO
N
N
3b
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm

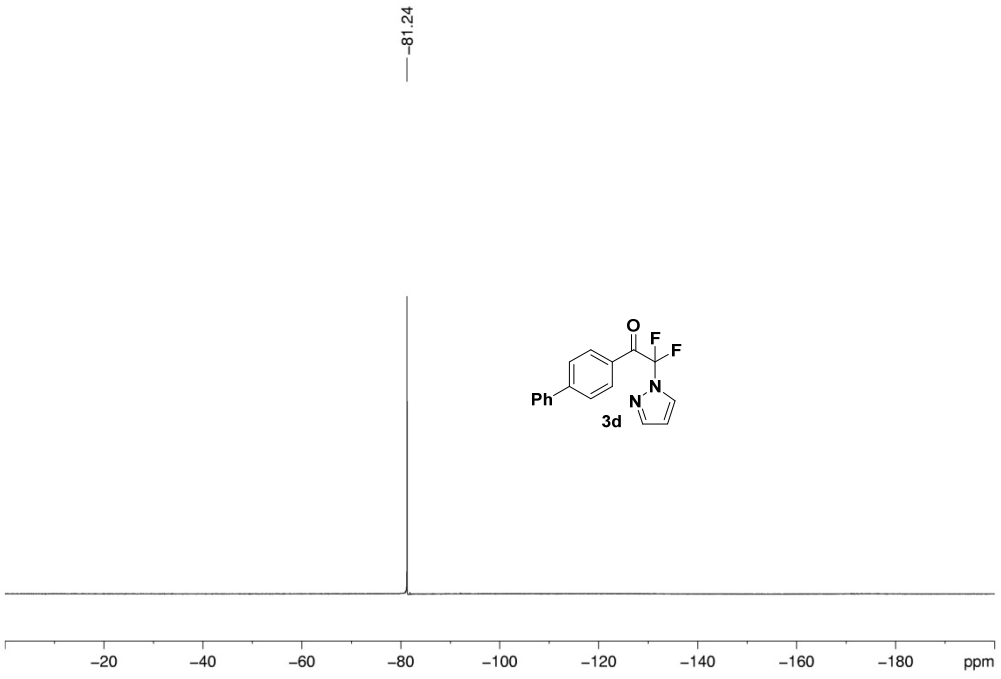

8.58
8.02
7.77
7.70
7.57
7.14
7.12
6.69
5.79
O
F
F
Ph
O
N
N
O
3c
10
9
8
7
6
5
4
3
2
1
ppm
1.01
2.06
2.89
1.06
2.18
2.07
1.00
2.05

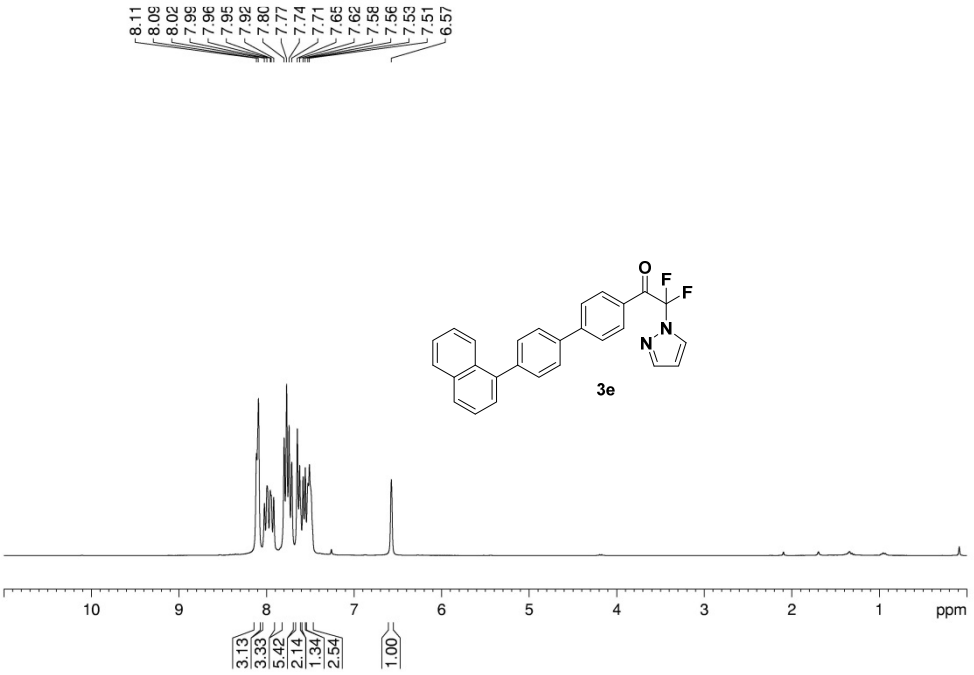

193.59
180.87
180.48
180.09
163.44
142.77
134.08
133.95
132.14
131.68
128.93
128.83
127.88
123.82
115.25
115.07
111.62
109.35
108.17
70.40
O
F
F
Ph
O
N
N
O
3c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

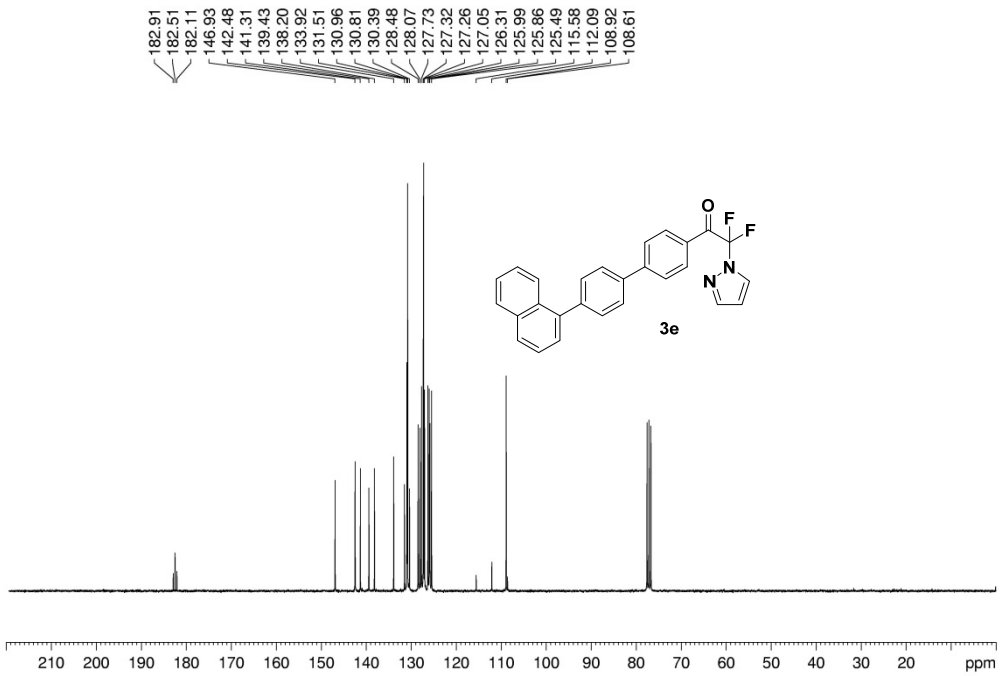

−79.88
Ph
O
O
O
F
F
N
N
3c
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm

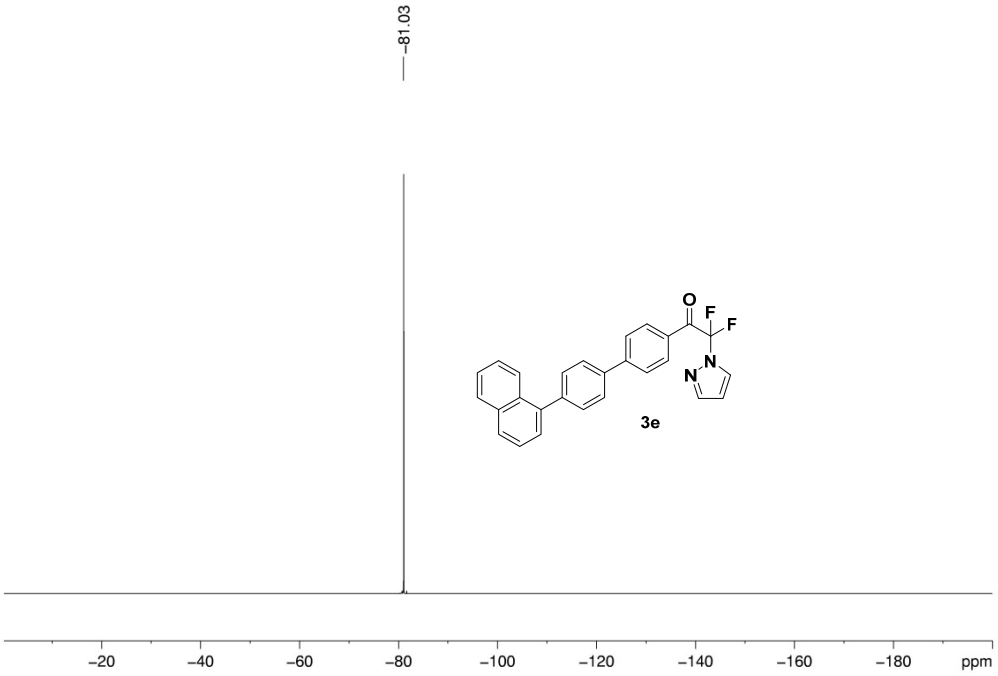

8.06
8.05
8.03
8.00
7.69
7.67
7.63
7.60
7.50
7.48
7.45
7.45
7.44
7.42
7.39
6.55
O
F
F
Ph
N
N
3d
10
9
8
7
6
5
4
3
2
1
ppm
1.06
1.97
3.16
2.09
3.16
1.00

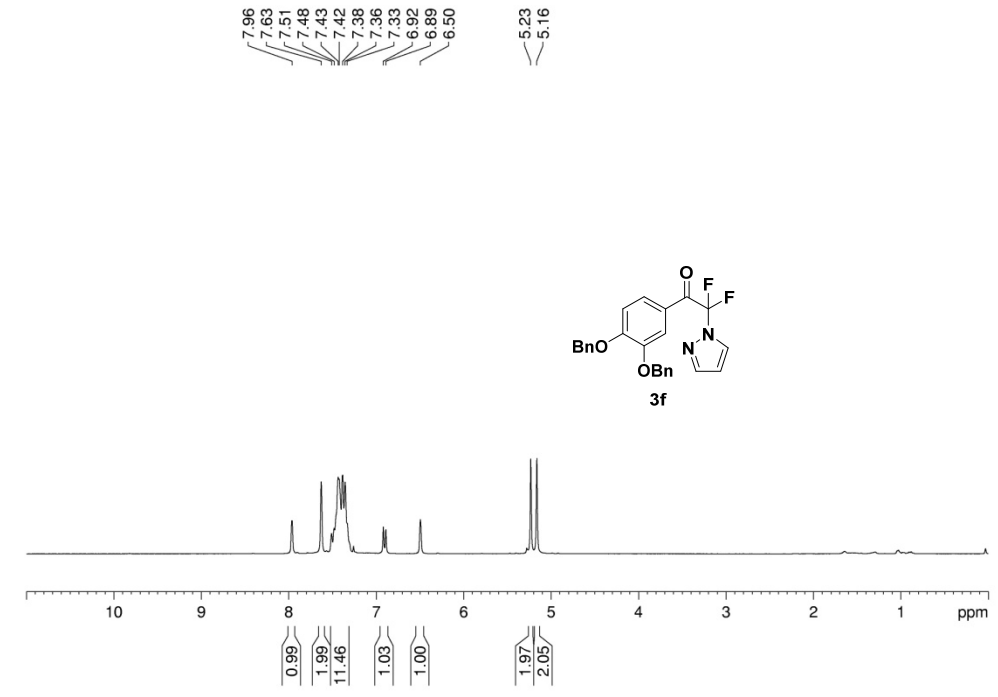

182.98
182.58
182.18
147.46
142.53
139.48
130.93
130.34
129.16
128.78
127.77
127.46
127.44
115.56
112.08
108.95
108.60
O
F
F
Ph
N
N
3d
240
220
200
180
160
140
120
100
80
60
40
20
0
−20
ppm

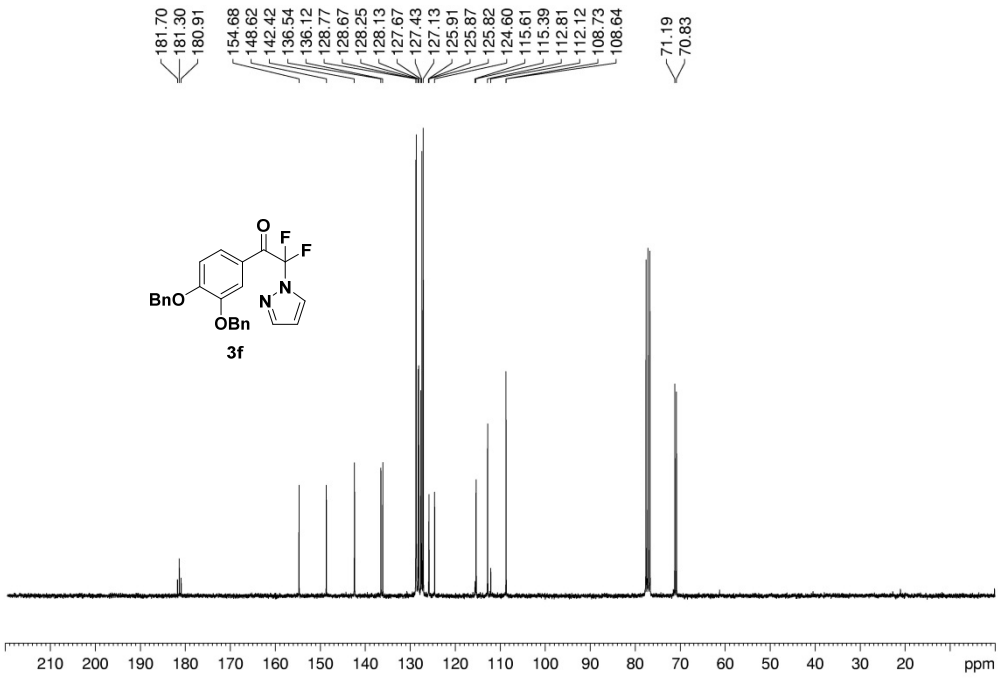

−81.24
O
F
F
Ph
N
N
3d
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm

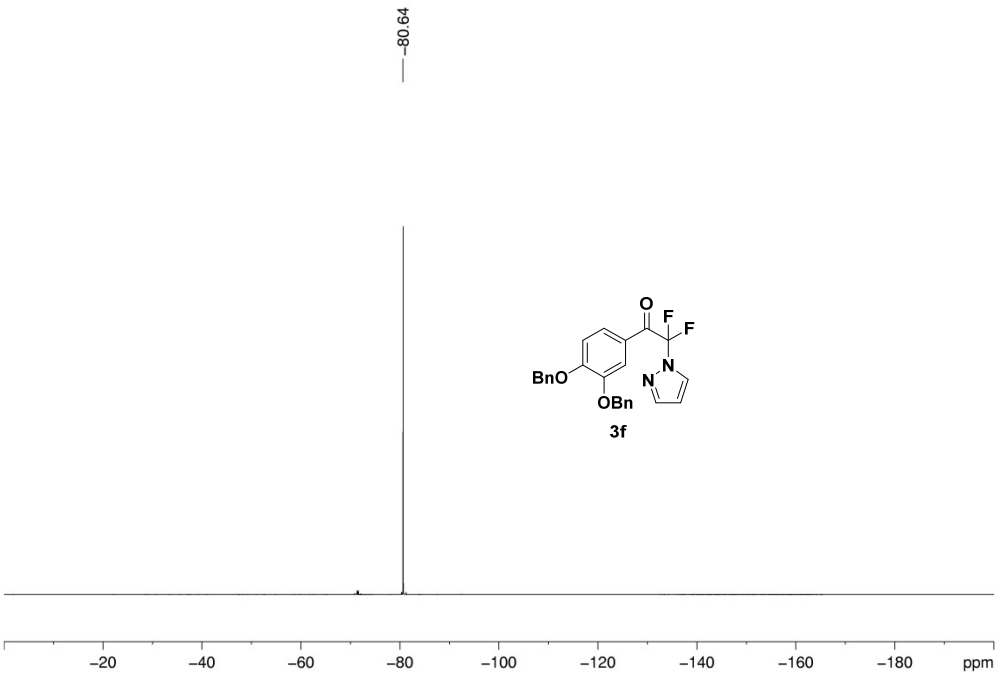

8.11
8.05
8.02
7.99
7.96
7.95
7.92
7.80
7.77
7.74
7.71
7.65
7.62
7.58
7.56
7.53
7.51
6.57
O
F
F
N
N
3e
10
9
8
7
6
5
4
3
2
1
ppm
3.13
3.33
5.42
2.14
1.34
2.54
1.00

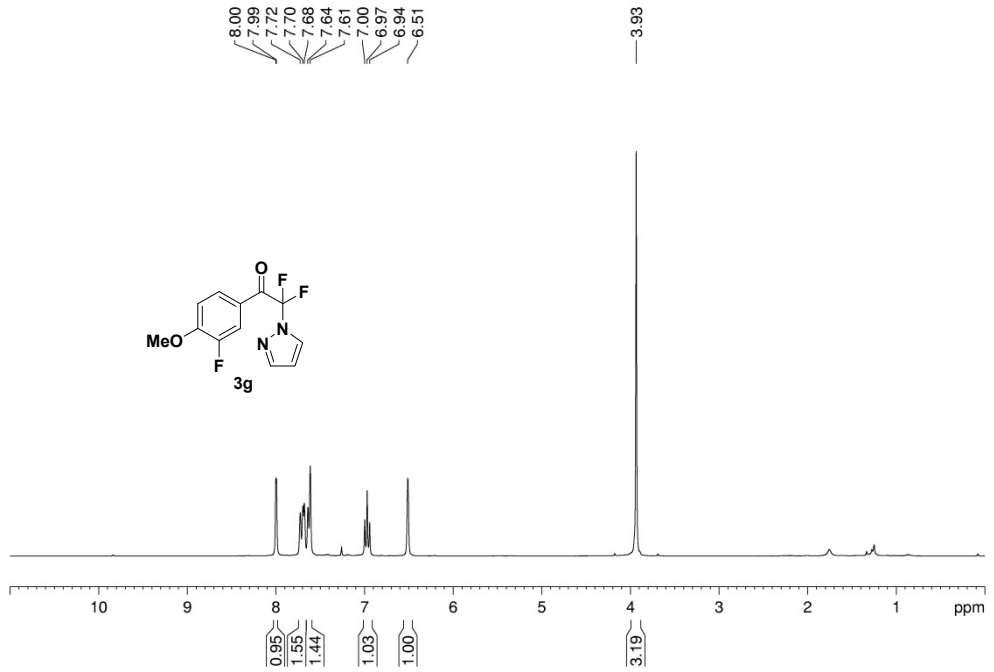

182.91
182.51
182.11
146.93
142.48
141.31
139.43
138.20
133.92
131.51
130.96
130.81
130.39
128.48
128.07
127.73
127.32
127.26
127.05
126.31
125.99
125.86
125.49
115.58
112.09
108.92
108.61
O
F
F
N
N
3e
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

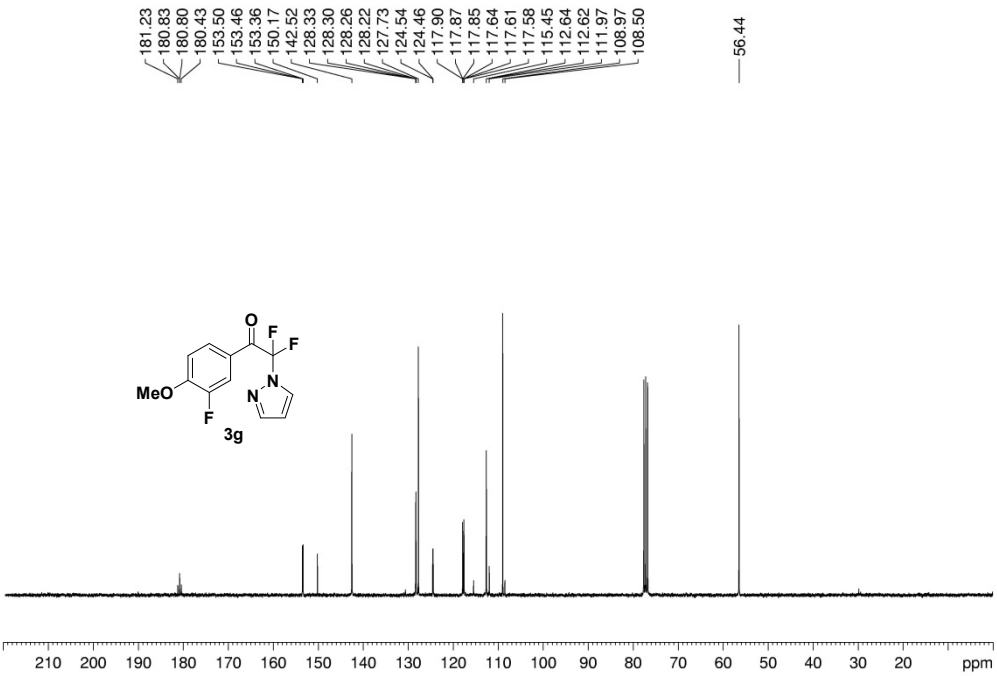

−81.03
O
F
F
N
N
3e
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm

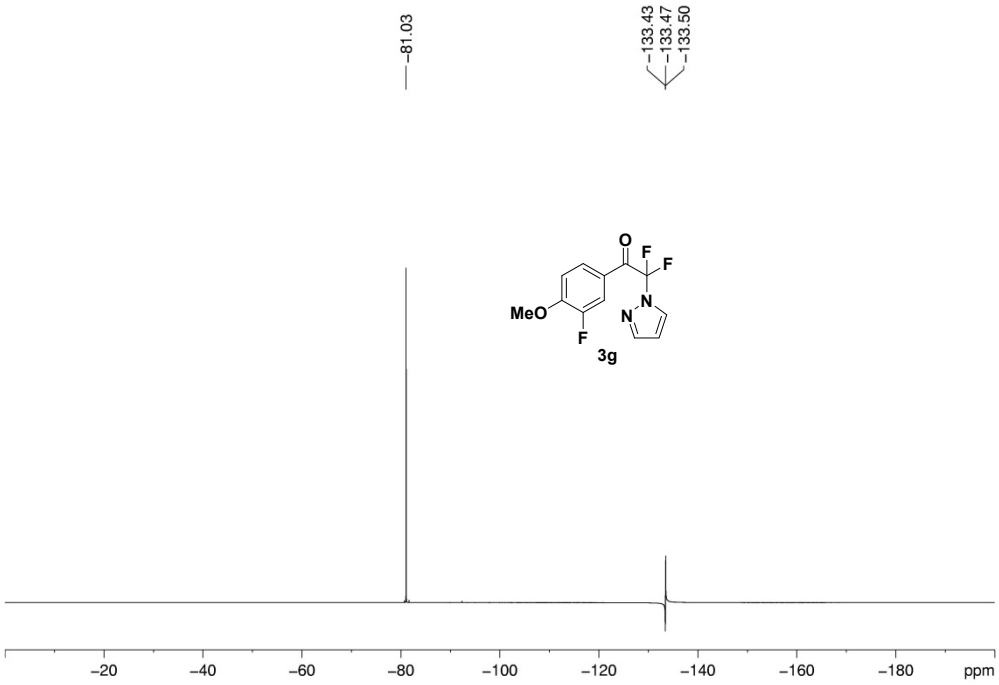

7.96
7.63
7.51
7.48
7.43
7.42
7.38
7.36
7.33
6.92
6.89
6.50
5.23
5.16
O
F
F
BnO
OBn
N
N
3f
10
9
8
7
6
5
4
3
2
1
ppm
0.99
1.99
11.46
1.03
1.00
1.97
2.05

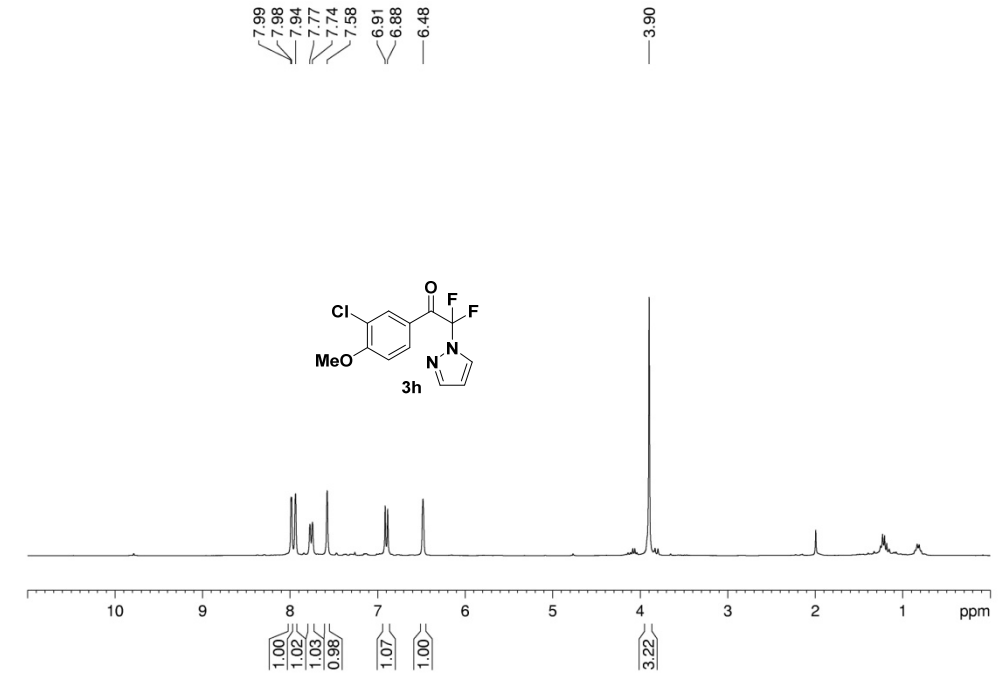

181.70
181.30
180.91
154.68
148.62
142.42
136.54
136.12
128.77
128.67
128.25
128.13
127.67
127.43
127.13
125.91
125.87
125.82
124.60
115.61
115.39
112.81
112.12
108.73
108.64
71.19
70.83
O
F
F
N
N
BnO
OBn
3f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

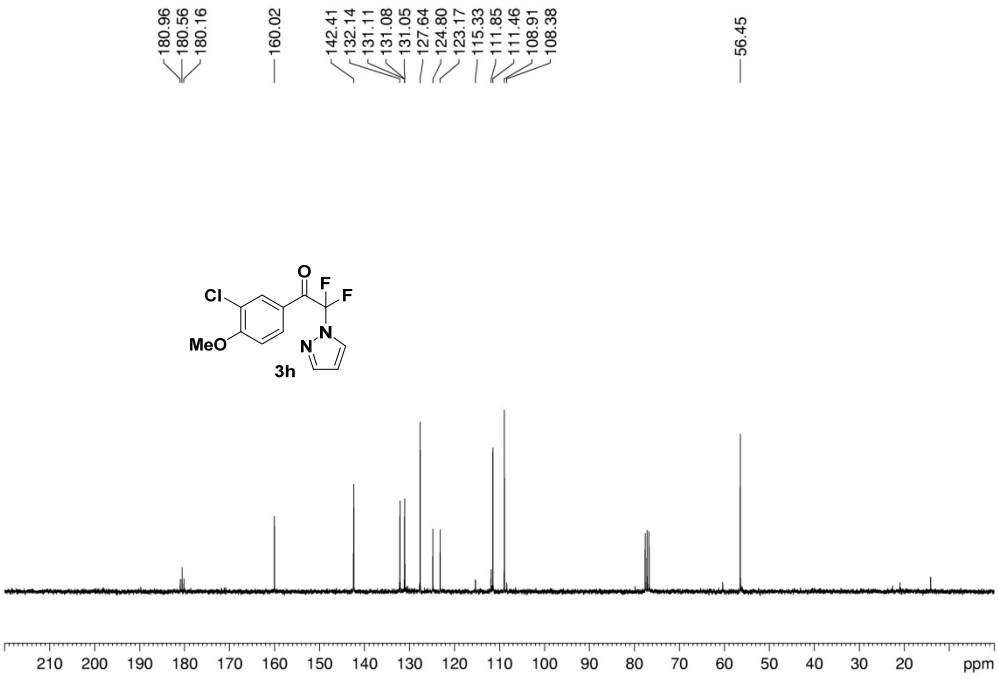

−80.64
O
F
F
N
N
BnO
OBn
3f
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm

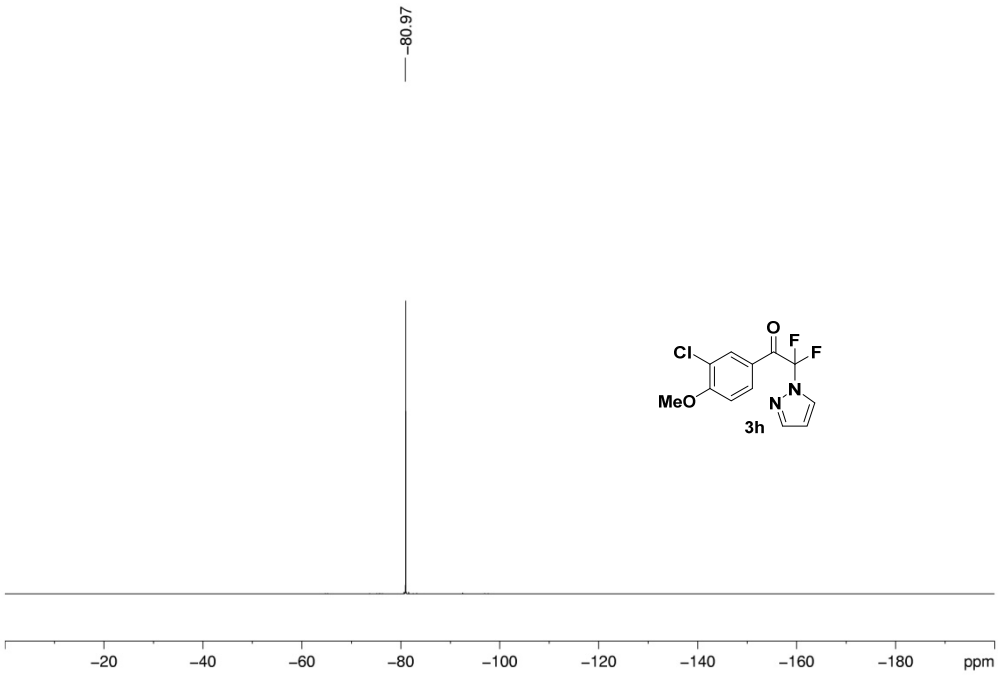

8.00
7.99
7.72
7.70
7.68
7.64
7.61
7.00
6.97
6.94
6.51
3.93
O
F
F
MeO
N
N
F
3g
10
9
8
7
6
5
4
3
2
1
ppm
0.95
1.55
1.44
1.03
1.00
3.19

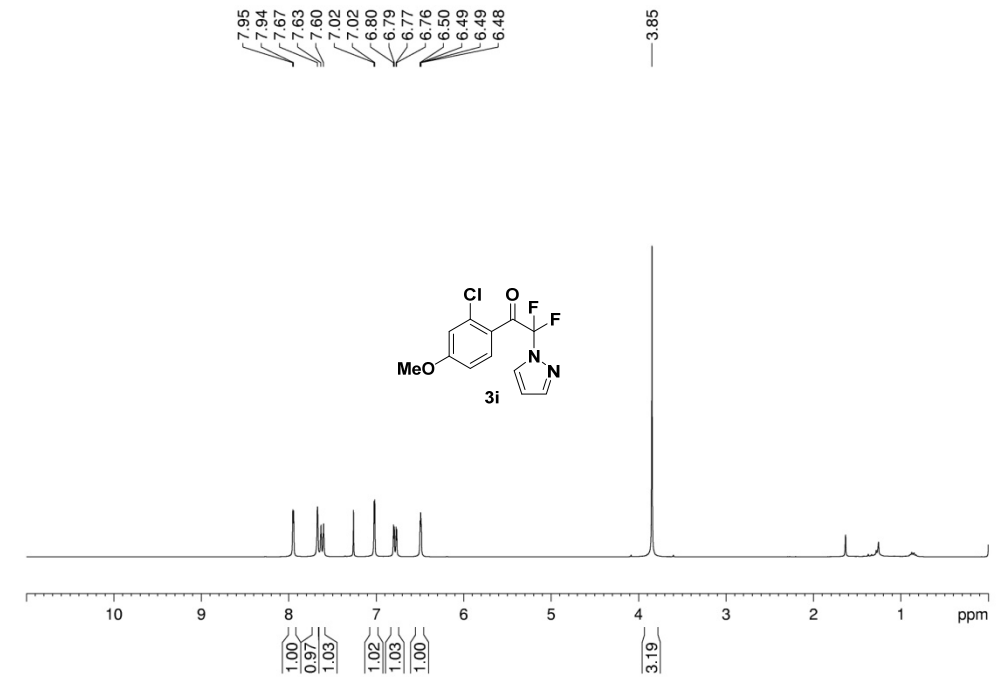

181.23
180.83
180.80
180.43
153.50
153.46
153.36
150.17
142.52
128.33
128.30
128.26
128.22
127.73
124.54
124.46
117.90
117.87
117.85
117.64
117.61
117.58
115.45
112.64
112.62
111.97
108.97
108.50
56.44
O
F
F
MeO
N
N
F
3g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

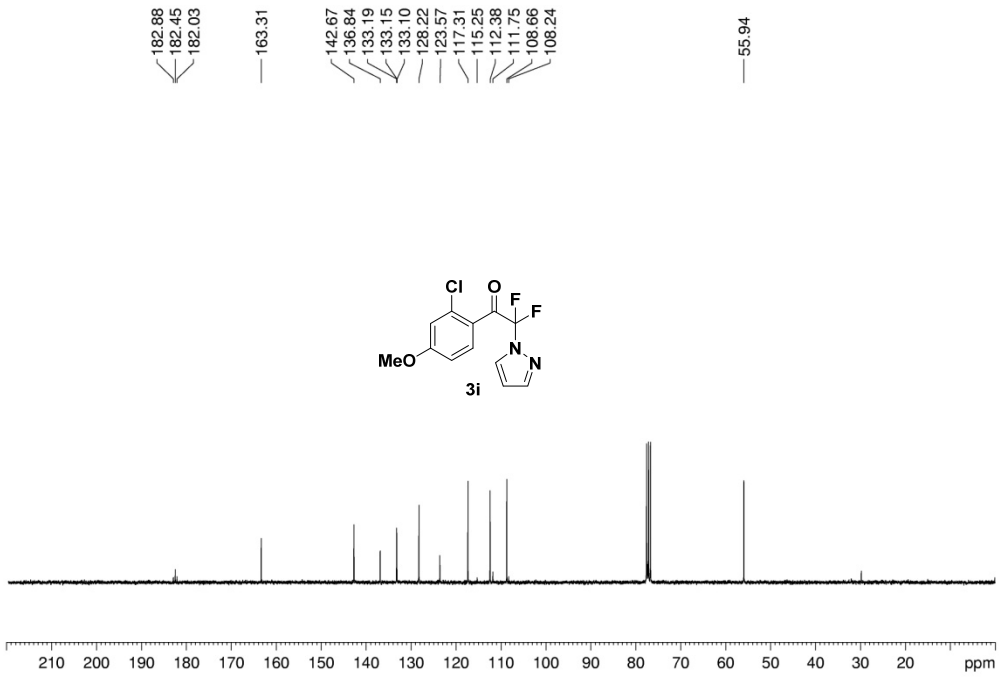

-81.03
-133.43
-133.47
-133.50
O
F
F
MeO
F
N
N
3g
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

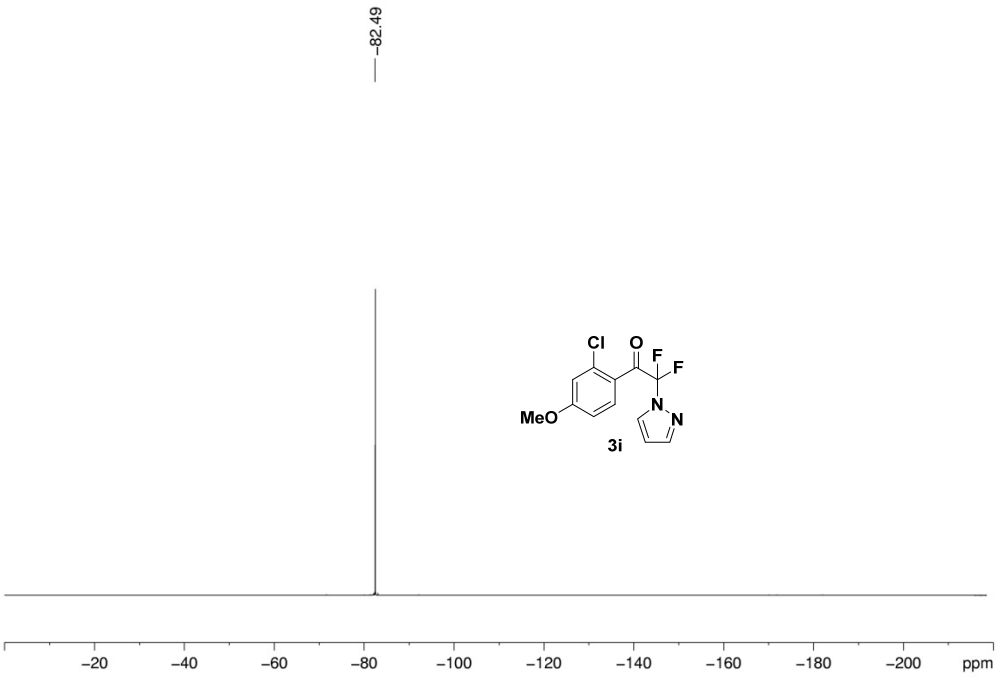

7.99
7.98
7.94
7.77
7.74
7.58
6.91
6.88
6.48
3.90
O
F
F
Cl
MeO
N
N
3h
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.02
1.03
0.98
1.07
1.00
3.22

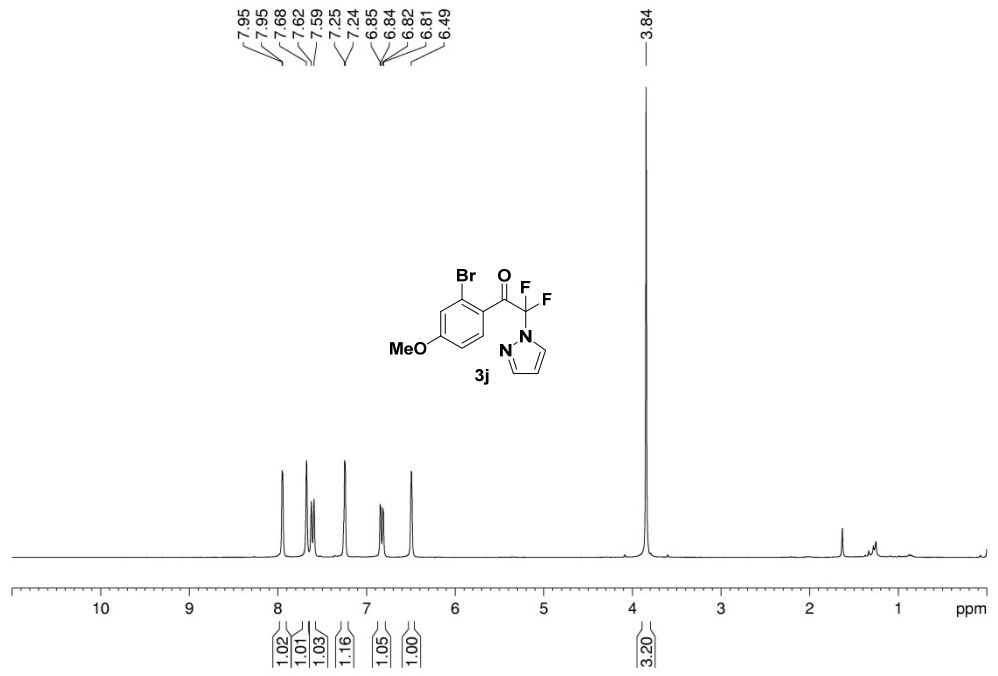

180.96
180.56
180.16
160.02
142.41
132.14
131.11
131.08
131.05
127.64
124.80
123.17
115.33
111.85
111.46
108.91
108.38
56.45
Cl
MeO
O
F
F
N
N
3h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

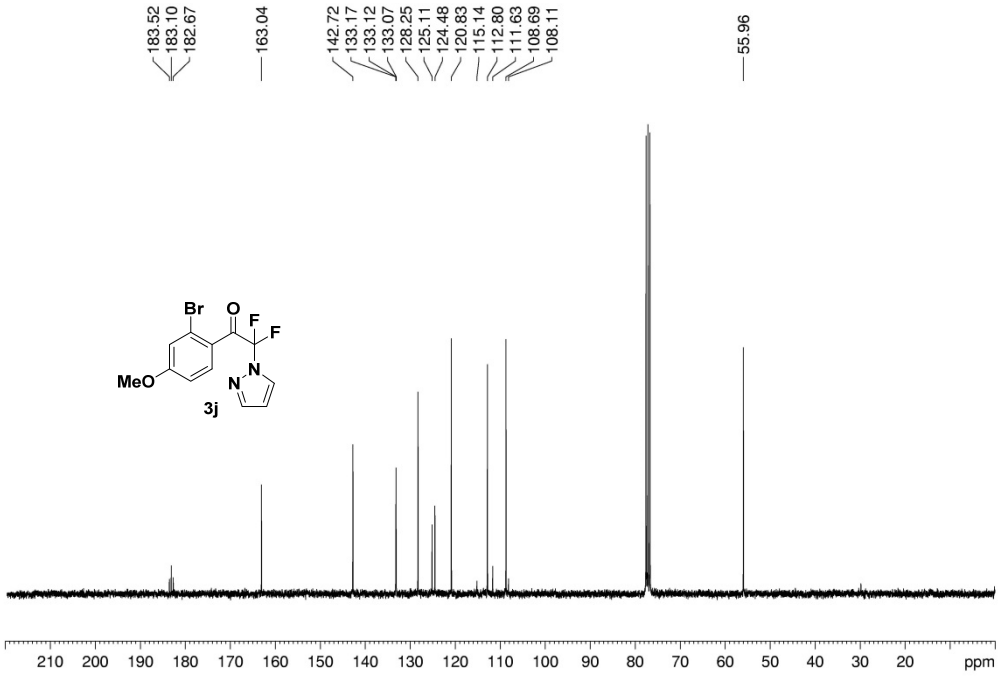

−80.97
Cl
MeO
O
F
F
N
N
3h
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm

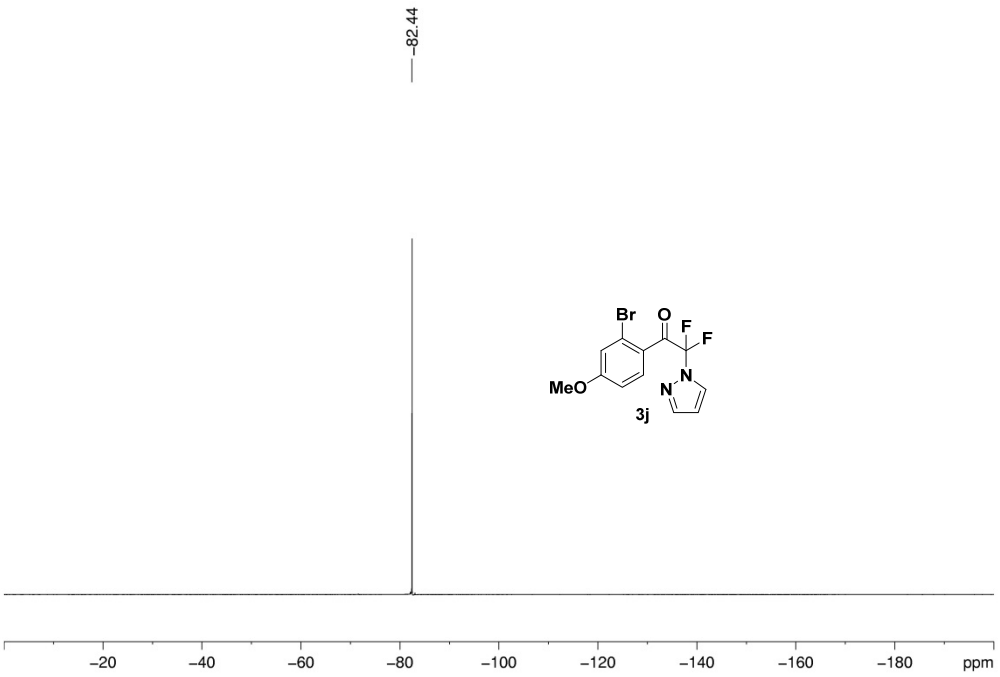

7.95
7.94
7.67
7.63
7.60
7.02
7.02
6.80
6.79
6.77
6.76
6.50
6.49
6.49
6.48
3.85
Cl
O
F
F
MeO
N
N
3i
10
9
8
7
6
5
4
3
2
1
ppm
1.00
0.97
1.03
1.02
1.03
1.00
3.19


182.88
182.45
182.03
163.31
142.67
136.84
133.19
133.15
133.10
128.22
123.57
117.31
115.25
112.38
111.75
108.66
108.24
55.94
Cl
O
F
F
MeO
N
N
3i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-82.49
Cl
O
F
F
N
N
MeO
3i
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


7.95
7.95
7.68
7.62
7.59
7.25
7.24
6.85
6.84
6.82
6.81
6.49
3.84
Br
O
F
F
N
N
MeO
3j
10
9
8
7
6
5
4
3
2
1
ppm
1.02
1.01
1.03
1.16
1.05
1.00
3.20


183.52
183.10
182.67
163.04
142.72
133.17
133.12
133.07
128.25
125.11
124.48
120.83
115.14
112.80
111.63
108.69
108.11
55.96
Br
O
F
F
MeO
N
N
3j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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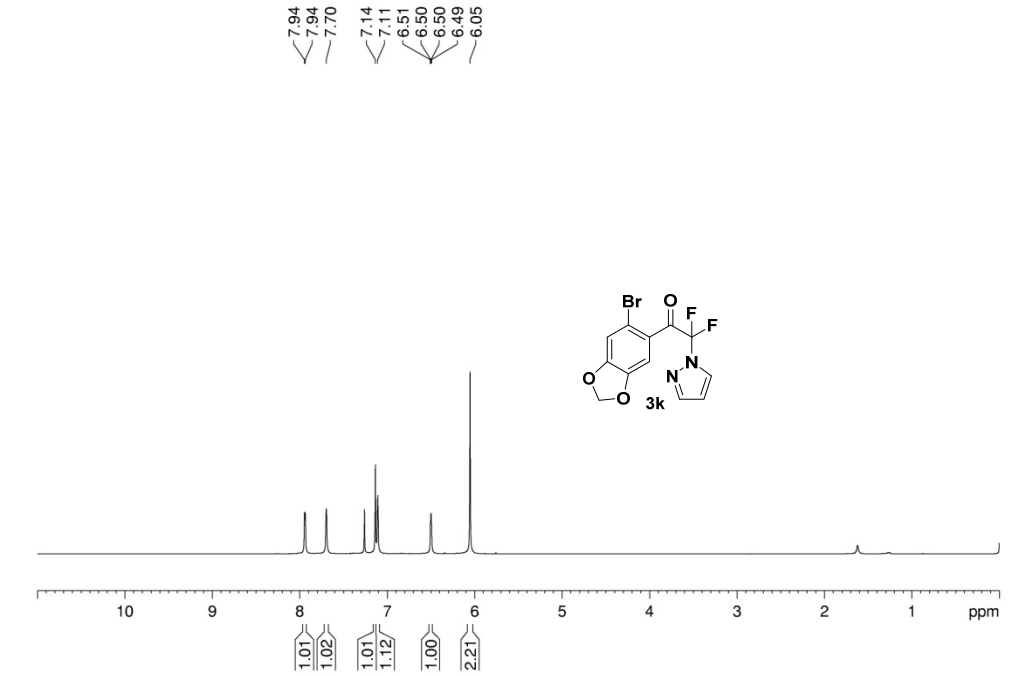
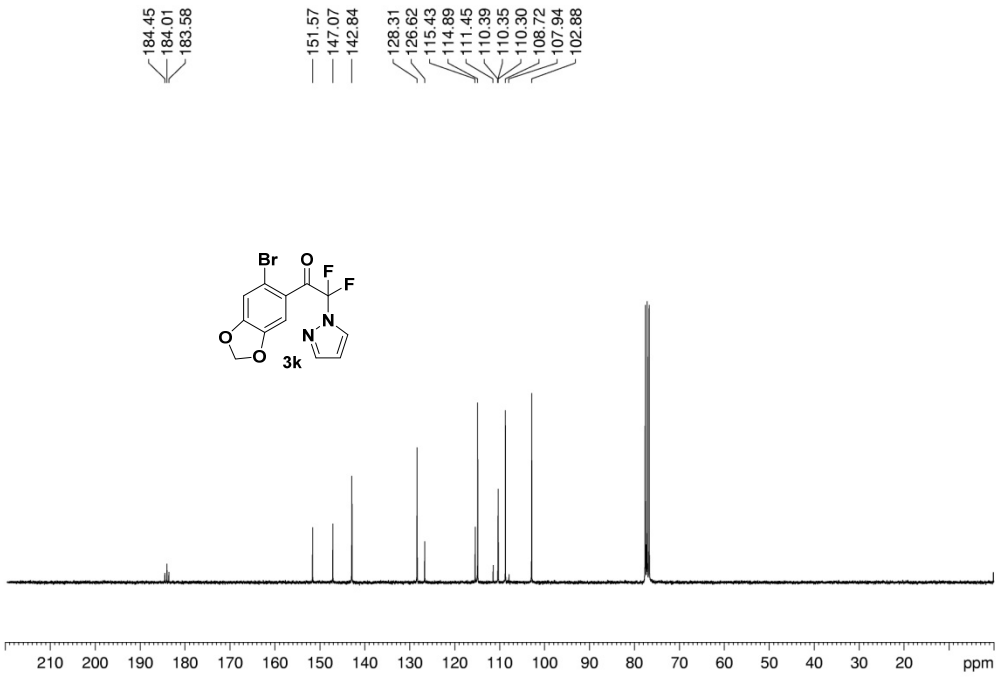
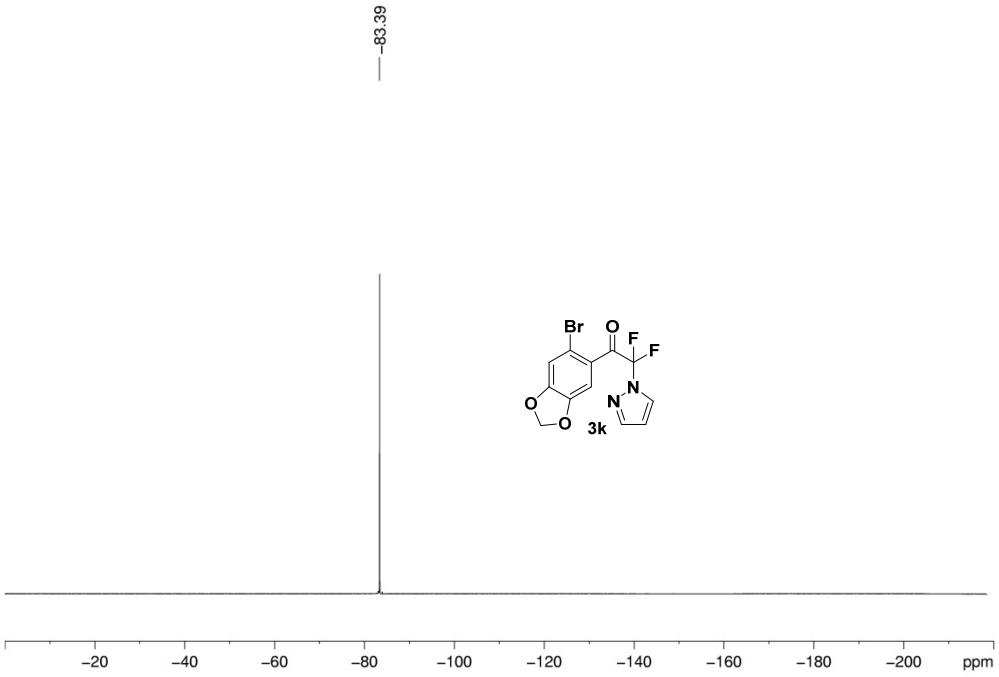
Br
O
F
F
MeO
N
N
3j
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm


7.94
7.94
7.70
7.14
7.11
6.51
6.50
6.50
6.49
6.05
Br
O
F
F
N
N
O
O
3k
10
9
8
7
6
5
4
3
2
1
ppm
1.01
1.02
1.01
1.12
1.00
2.21


184.45
184.01
183.58
151.57
147.07
142.84
128.31
126.62
115.43
114.89
111.45
110.39
110.35
110.30
108.72
107.94
102.88
Br
O
F
F
N
N
O
O
3k
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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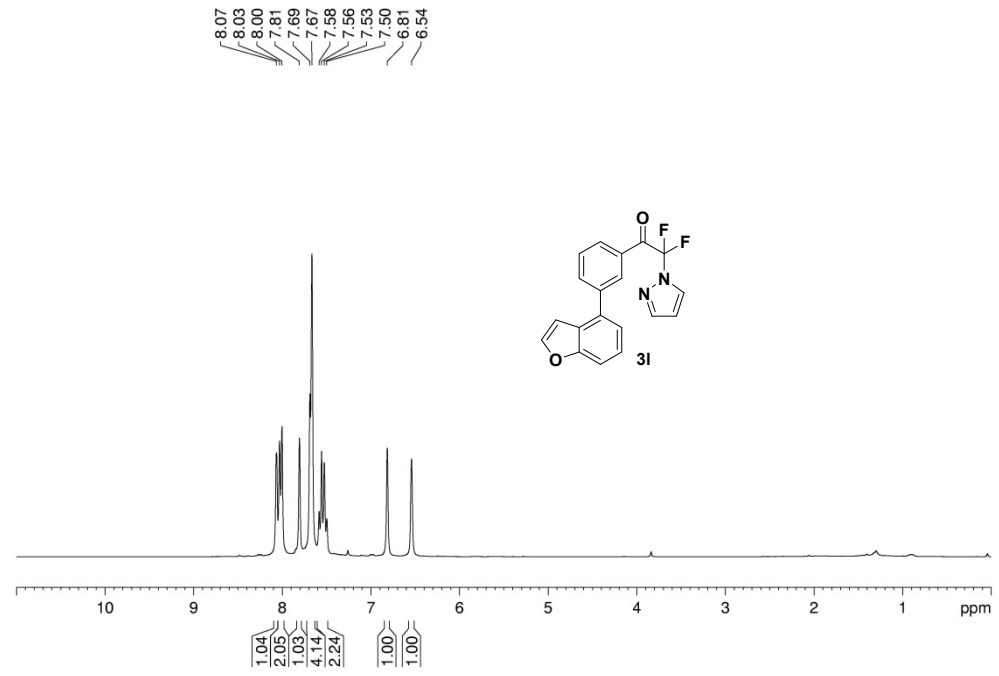
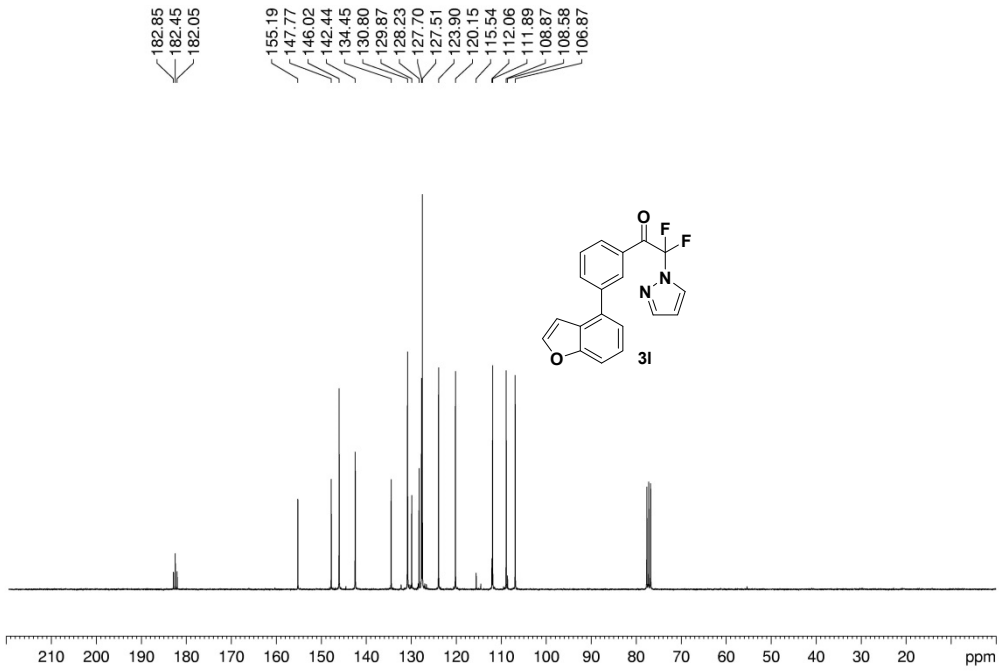
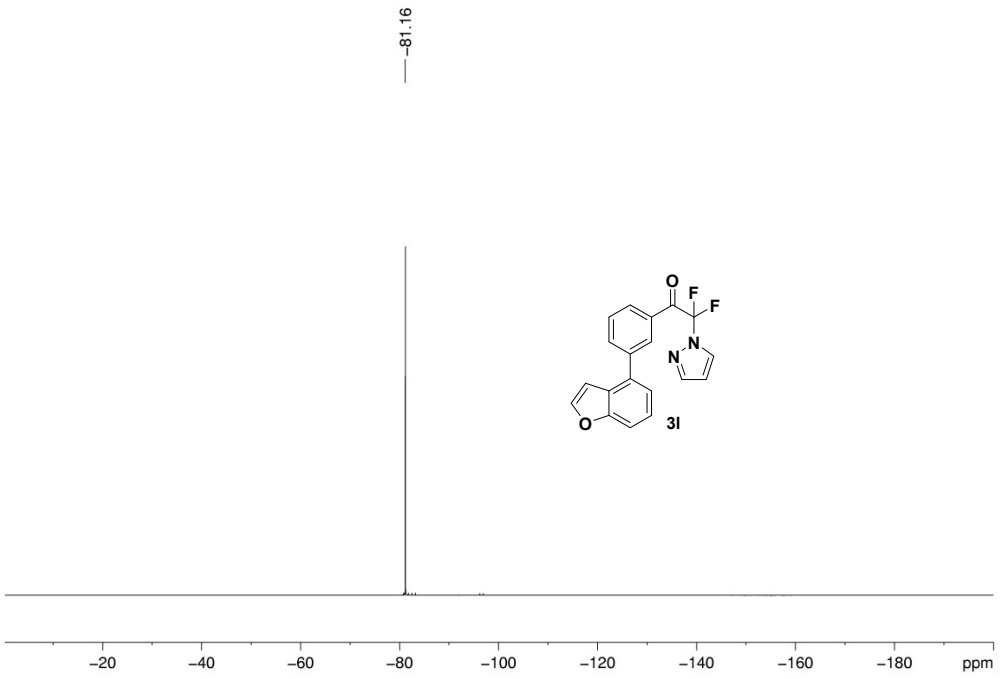
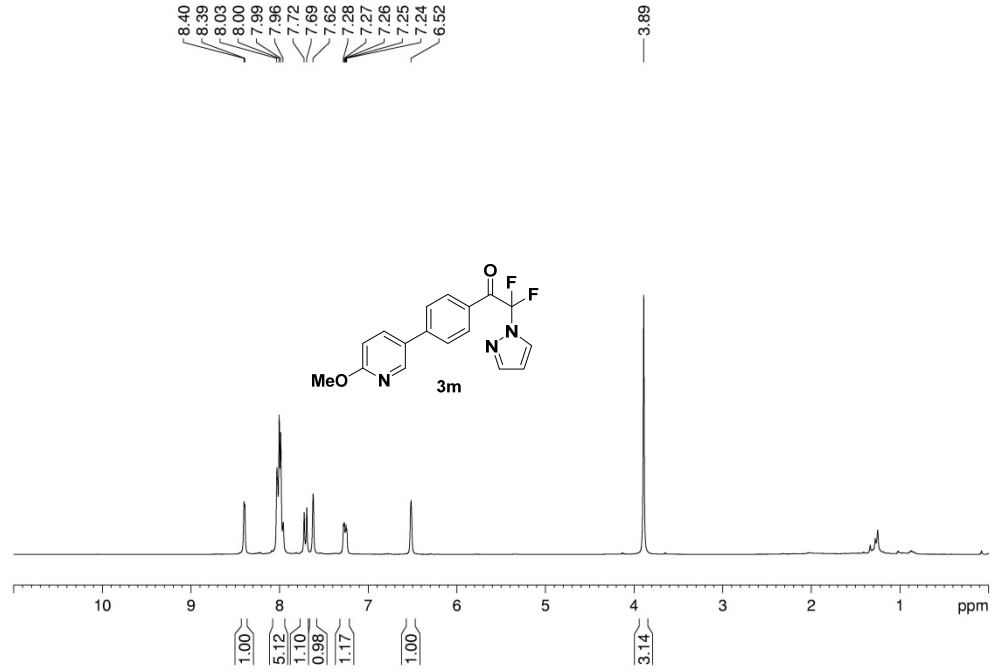
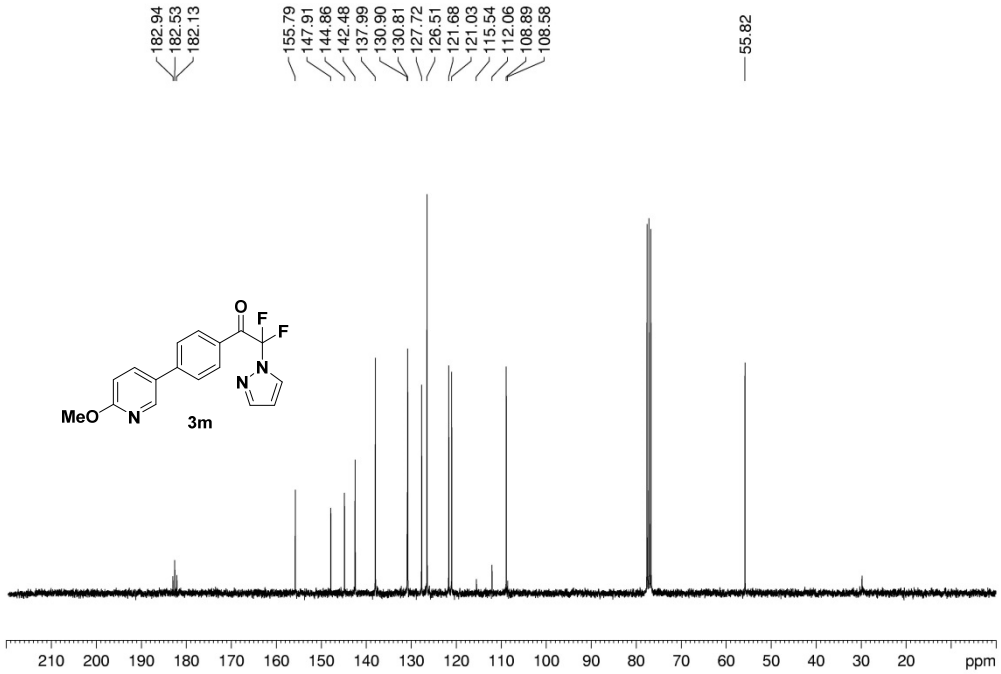
Br
O
F
F
O
O
N
N
3k
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
ppm


8.07
8.03
8.00
7.81
7.69
7.67
7.58
7.56
7.53
7.50
6.81
6.54
O
F
F
N
N
O
3l
10
9
8
7
6
5
4
3
2
1
ppm
1.04
2.05
1.03
4.14
2.24
1.00
1.00


182.85
182.45
182.05
155.19
147.77
146.02
142.44
134.45
130.80
129.87
128.23
127.70
127.51
123.90
120.15
115.54
112.06
111.89
108.87
108.58
106.87
O
F
F
N
N
O
3l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


−81.16
O
F
F
N
N
O
3l
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm


8.40
8.39
8.03
8.00
7.99
7.96
7.72
7.69
7.62
7.28
7.27
7.26
7.25
7.24
6.52
3.89
O
F
F
N
N
MeO
N
3m
10
9
8
7
6
5
4
3
2
1
ppm
1.00
5.12
1.10
0.98
1.17
1.00
3.14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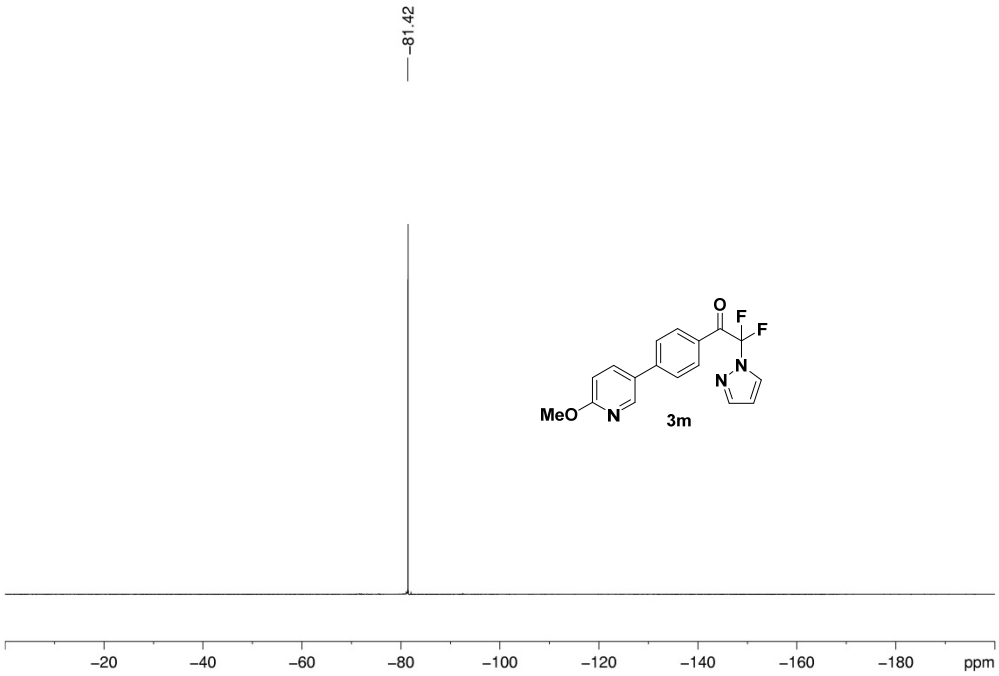
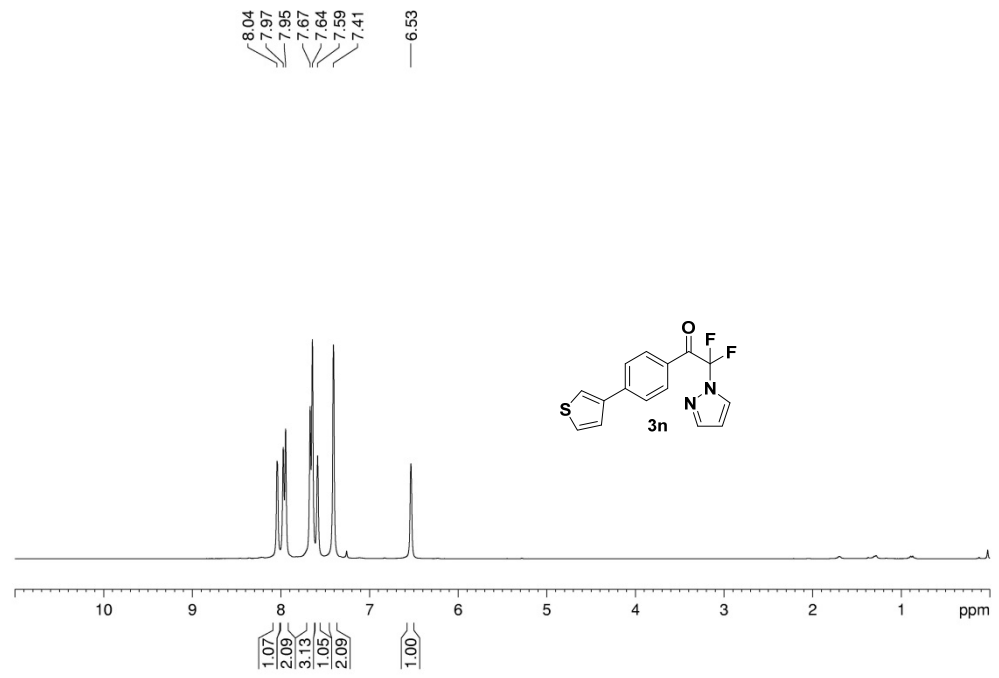
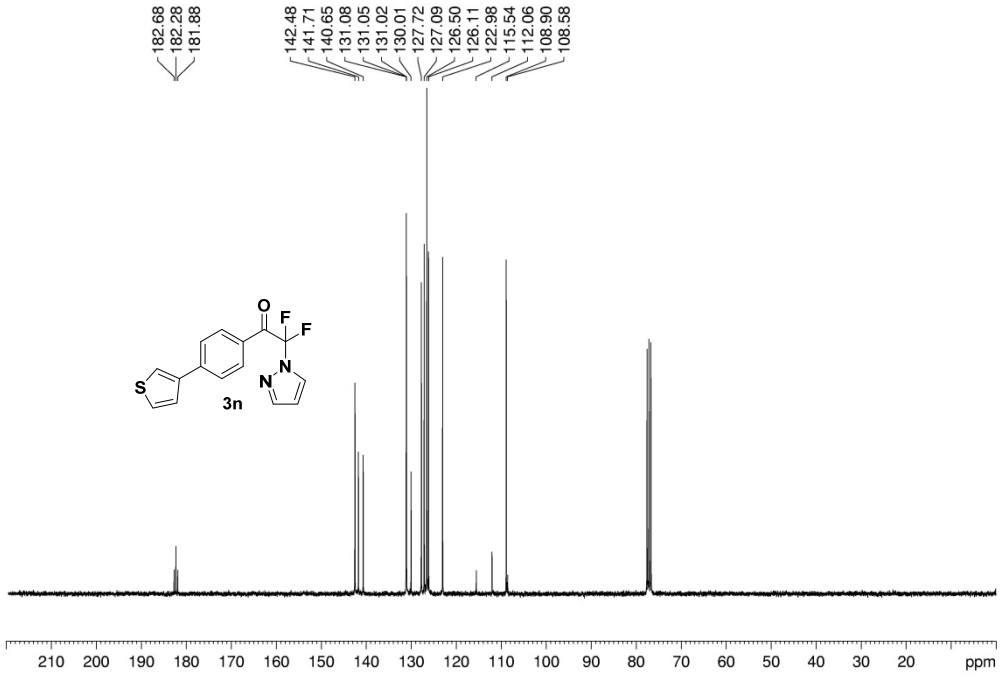
182.53
182.13
155.79
147.91
144.86
142.48
137.99
130.90
130.81
127.72
126.51
121.68
121.03
115.54
112.06
108.89
108.58
55.82
O
F
F
N
N
MeO
N
3m
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


−81.42
O
F
F
N
N
MeO
N
3m
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm


8.04
7.97
7.95
7.67
7.64
7.59
7.41
6.53
O
F
F
N
N
S
3n
10
9
8
7
6
5
4
3
2
1
ppm
1.07
2.09
3.13
1.05
2.09
1.00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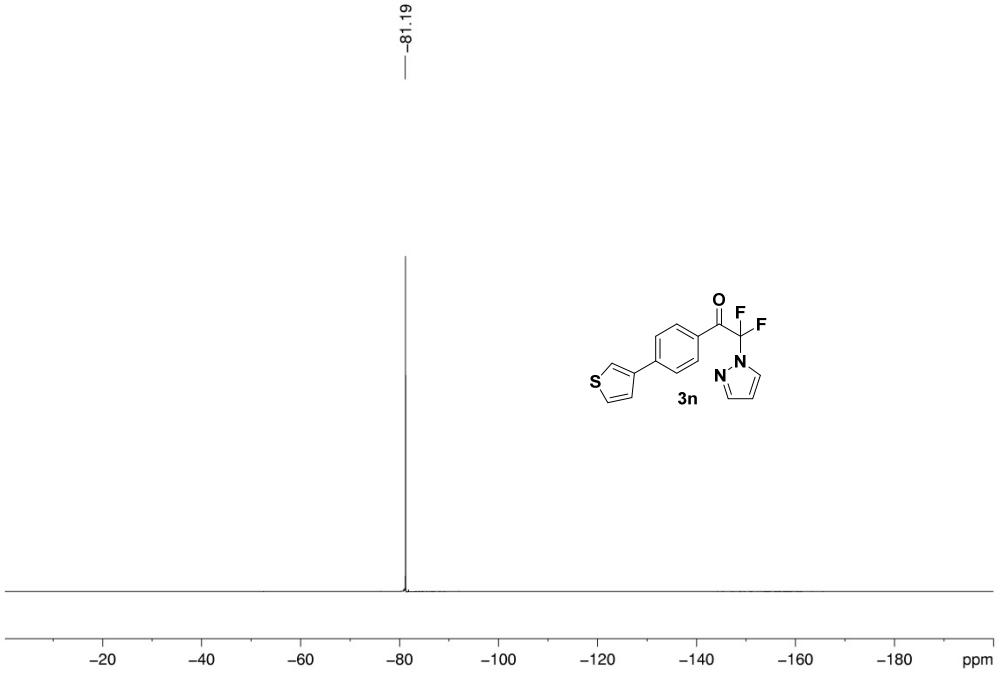
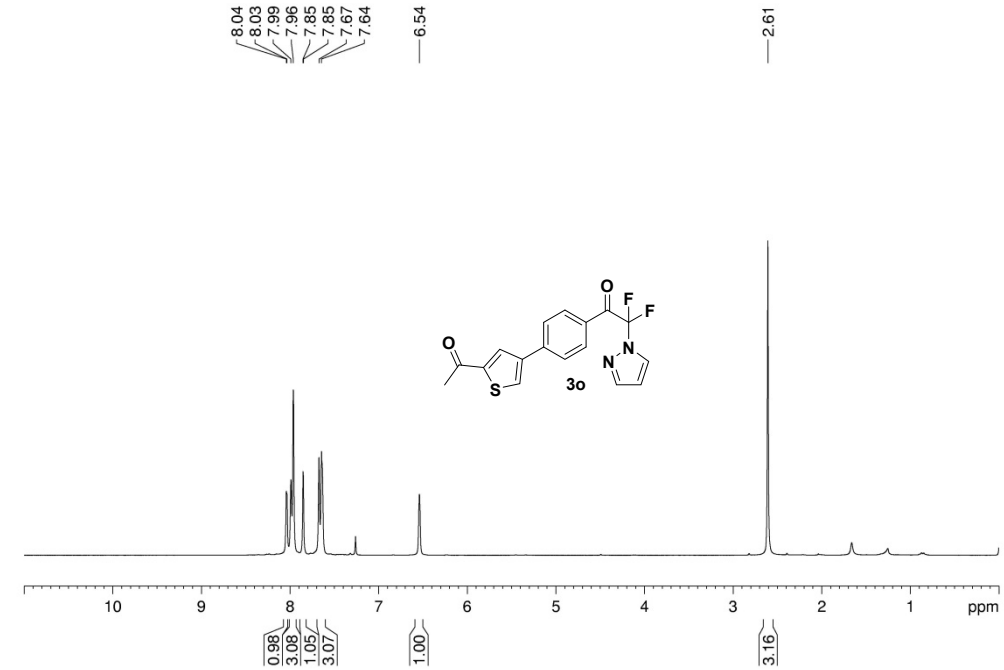
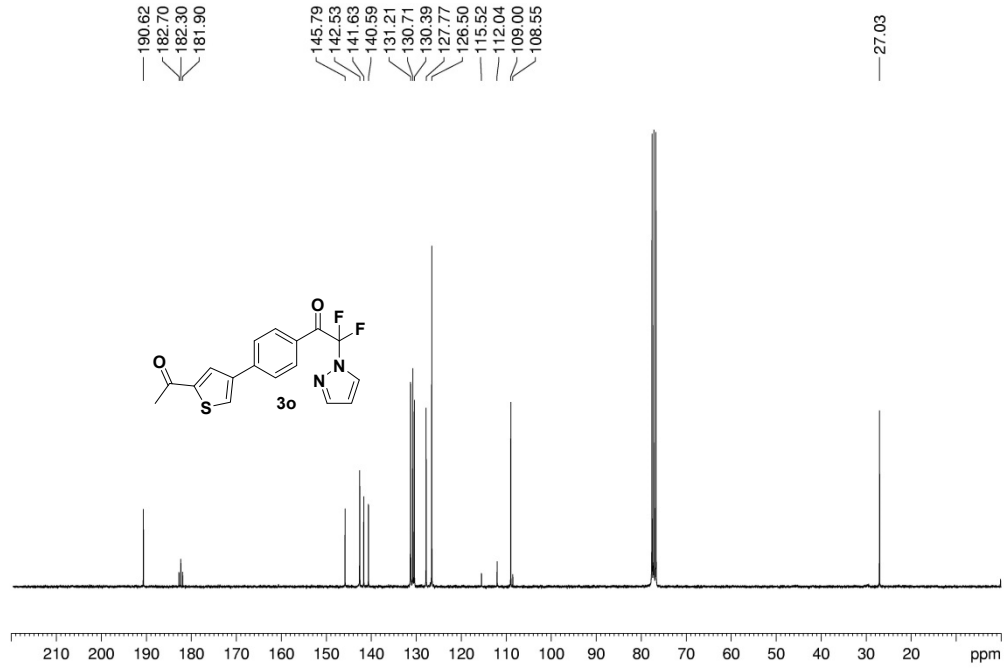
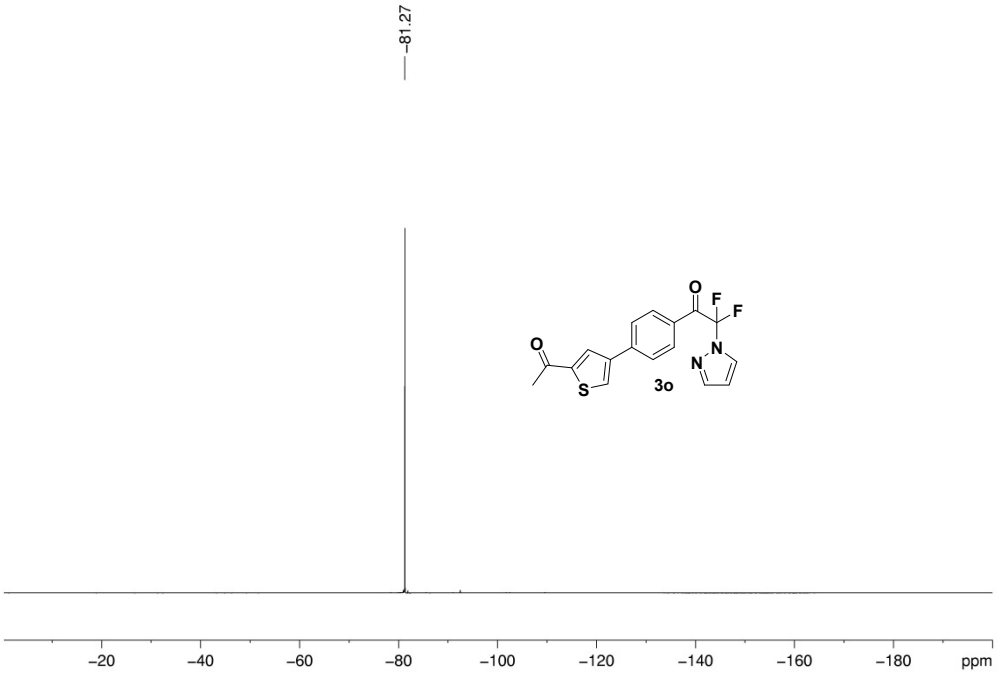
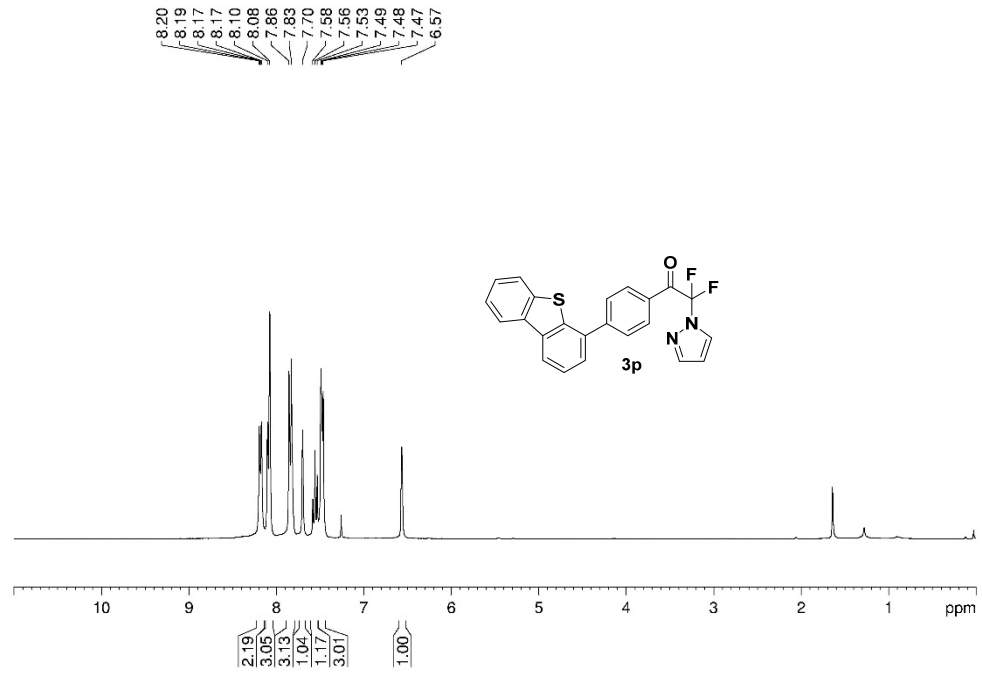
182.28
181.88
142.48
141.71
140.65
131.08
131.05
131.02
130.01
127.72
127.09
126.50
126.11
122.98
115.54
112.06
108.90
108.58
O
F
F
N
N
S
3n
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

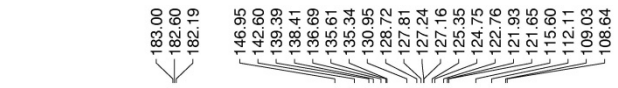

−81.19
O
F
F
N
N
S
3n
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm


8.04
8.03
7.99
7.96
7.85
7.85
7.67
7.64
6.54
2.61
O
F
F
O
N
N
S
3o
10
9
8
7
6
5
4
3
2
1
ppm
0.98
3.08
1.05
3.07
1.00
3.16


190.62
182.70
182.30
181.90
145.79
142.53
141.63
140.59
131.21
130.71
130.39
127.77
126.50
115.52
112.04
109.00
108.55
27.03
O
F
F
O
N
N
S
3o
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-81.27
O
F
F
O
N
N
S
3o
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


8.20
8.19
8.17
8.17
8.10
8.08
7.86
7.83
7.70
7.58
7.56
7.53
7.49
7.48
7.47
6.57
O
F
F
S
N
N
3p
10
9
8
7
6
5
4
3
2
1
ppm
2.19
3.05
3.13
1.04
1.17
3.01
1.00


183.00
182.60
182.19
146.95
142.60
139.39
138.41
136.69
135.61
135.34
130.95
128.72
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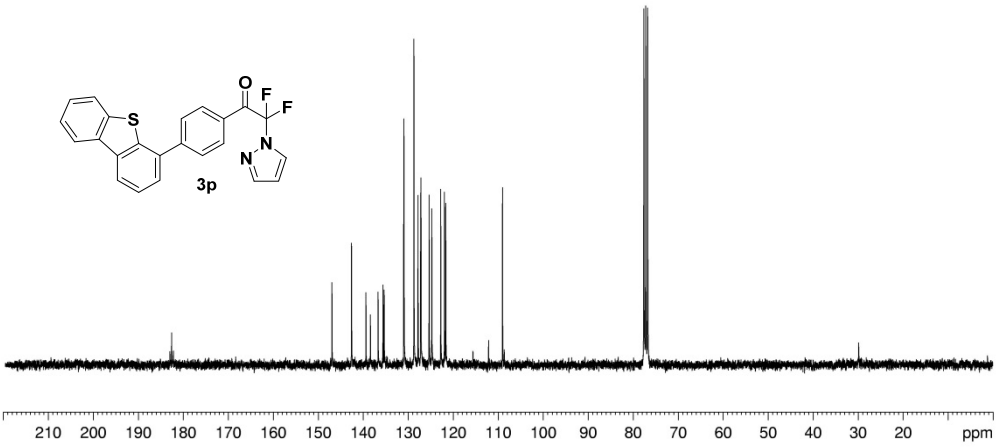
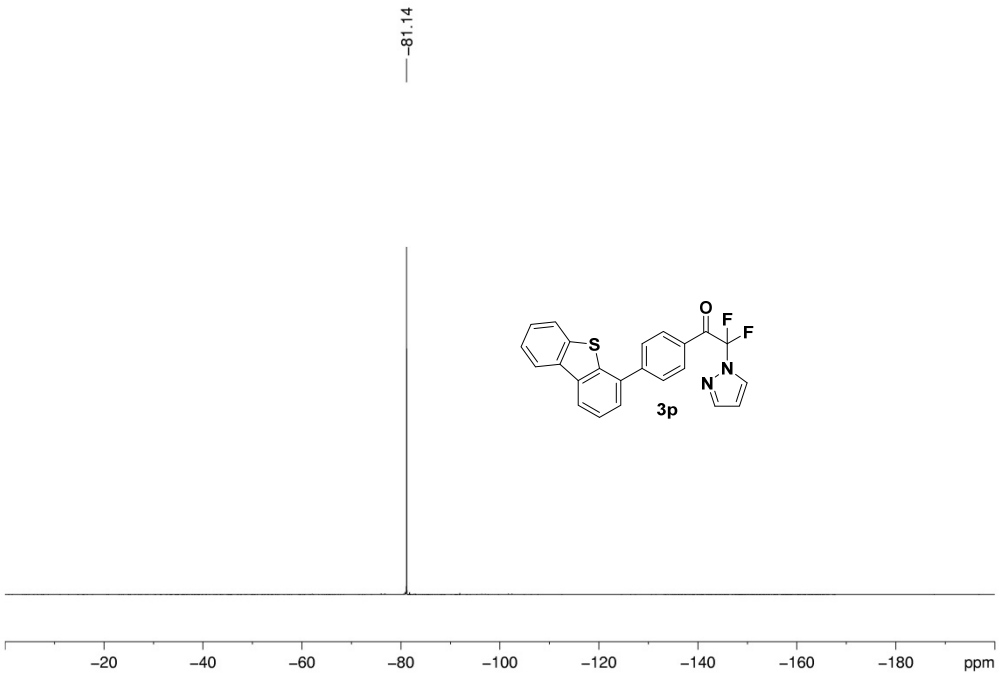
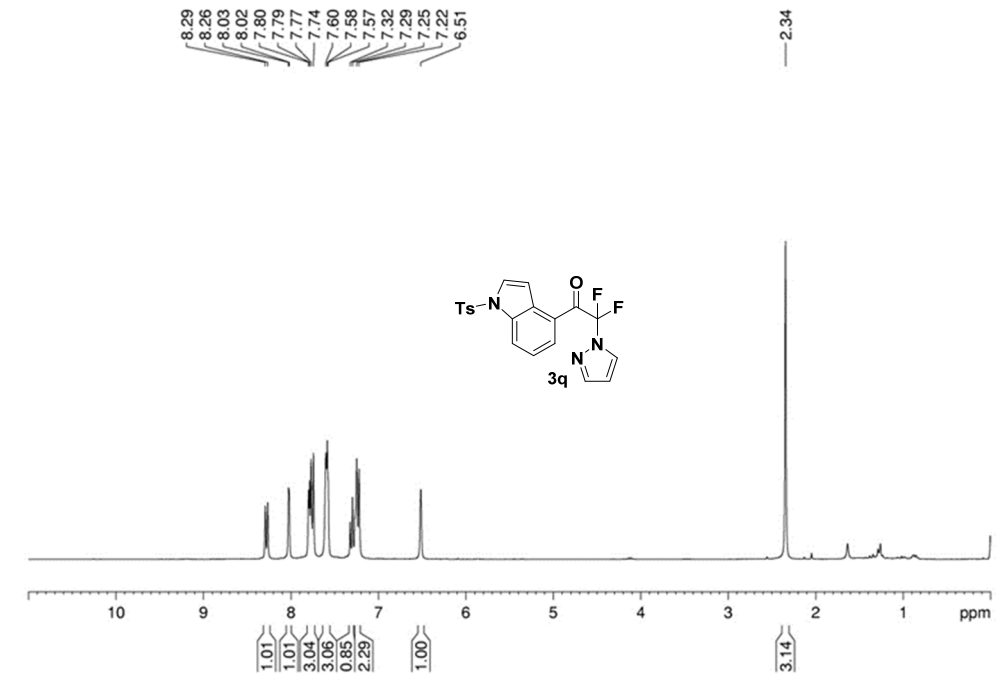
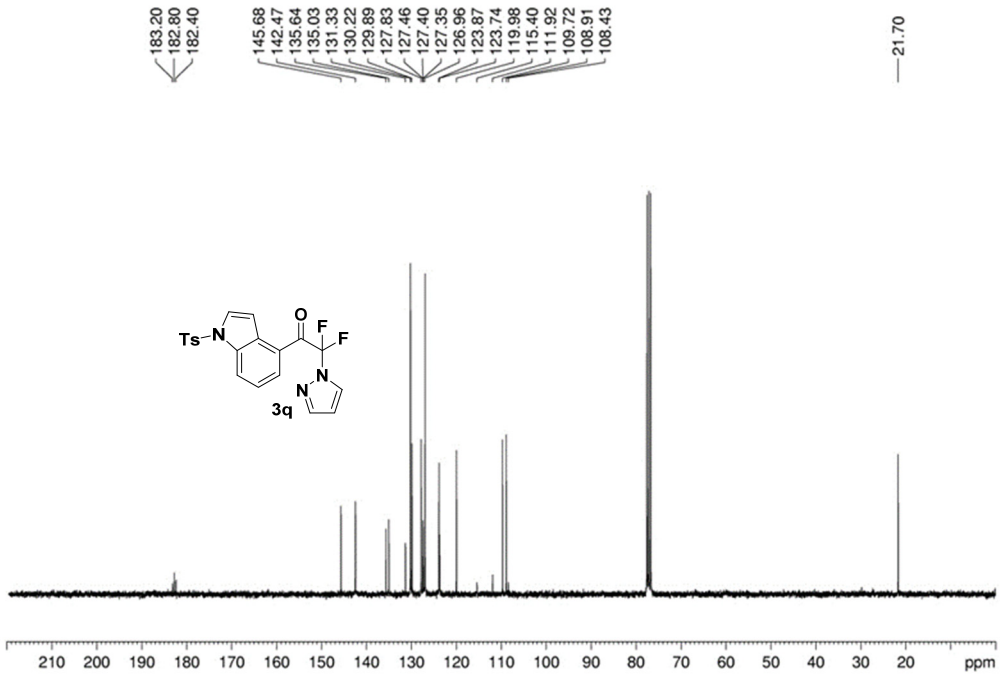
121.93
121.65
115.60
112.11
109.03
108.64


O
F
F
S
N
N
3p
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


−81.14
O
F
F
S
N
N
3p
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm


8.29
8.26
8.03
8.02
7.80
7.79
7.77
7.74
7.60
7.58
7.57
7.32
7.29
7.25
7.22
6.51
2.34
Ts
N
O
F
F
N
N
3q
10
9
8
7
6
5
4
3
2
1
ppm
1.01
1.01
3.04
3.06
0.85
2.29
1.00
3.14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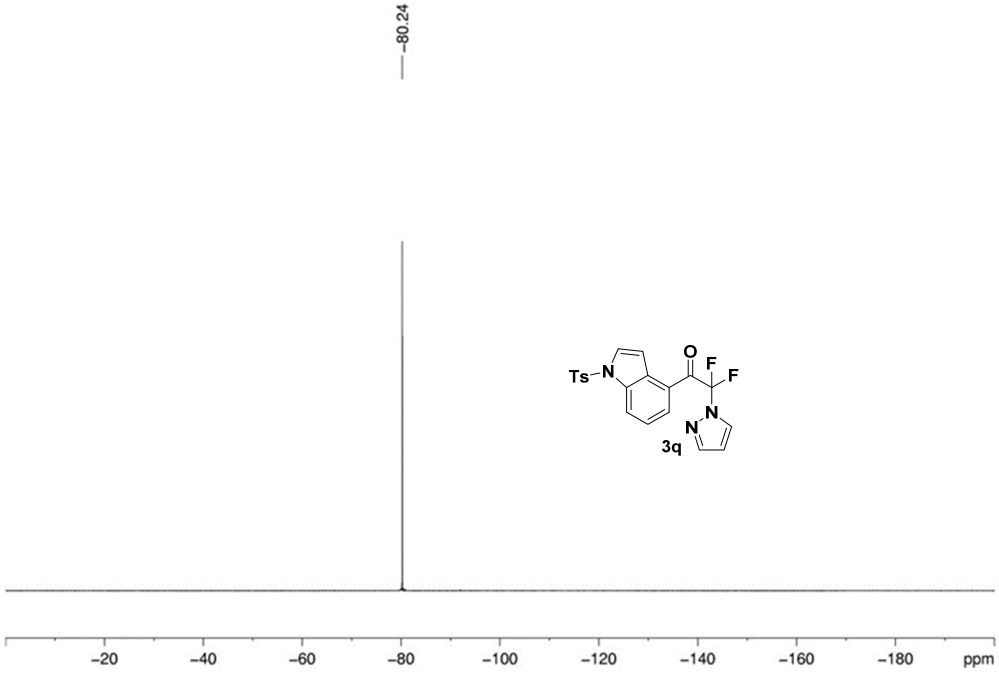
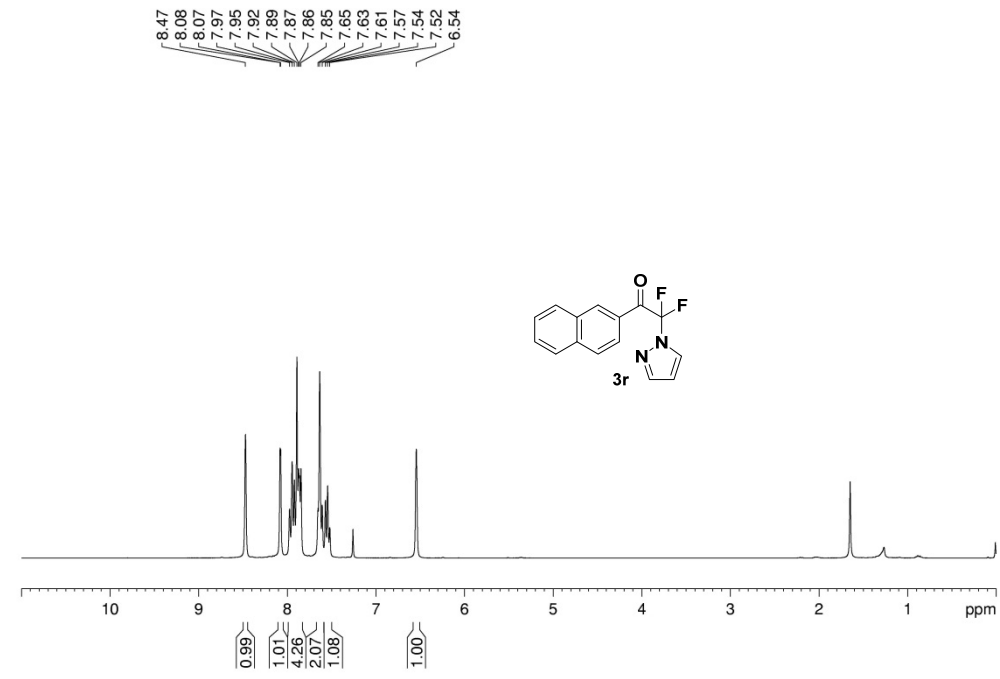
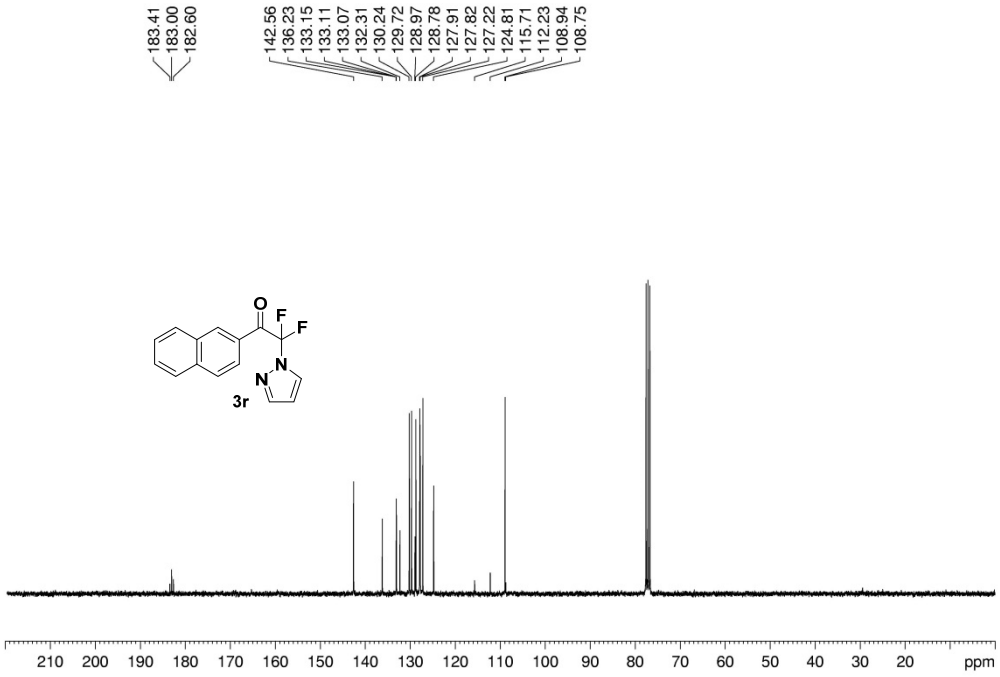
182.80
182.40
145.68
142.47
135.64
135.03
131.33
130.22
129.89
127.83
127.46
127.40
127.35
126.96
123.87
123.74
119.98
115.40
111.92
109.72
108.91
108.43
21.70
Ts
N
O
F
F
N
N
3q
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


−80.24
Ts
N
O
F
F
N
N
3q
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm


8.47
8.08
8.07
7.97
7.95
7.92
7.89
7.87
7.86
7.85
7.65
7.63
7.61
7.57
7.54
7.52
6.54
O
F
F
N
N
3r
10
9
8
7
6
5
4
3
2
1
ppm
0.99
1.01
4.26
2.07
1.08
1.00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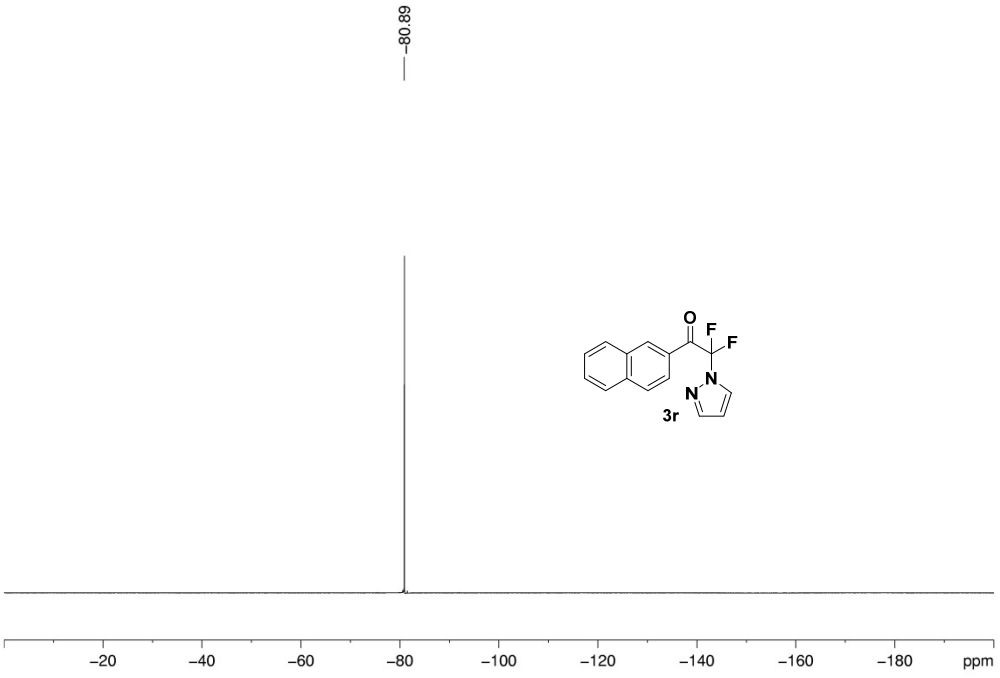
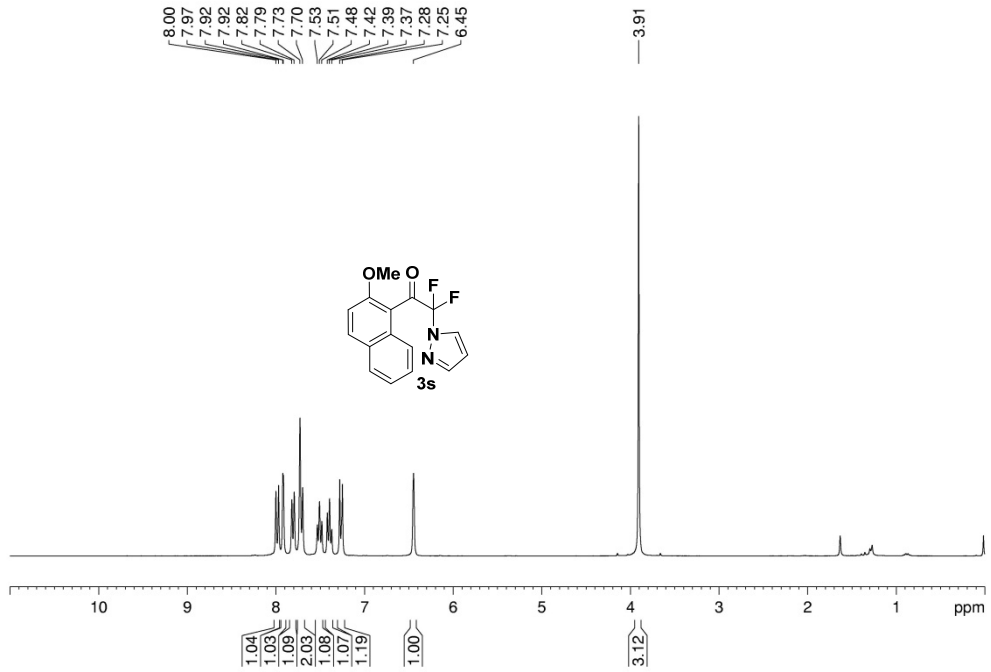
183.00
182.60
142.56
136.23
133.15
133.11
133.07
132.31
130.24
129.72
128.97
128.78
127.91
127.82
127.22
124.81
115.71
112.23
108.94
108.75
O
F
F
N
N
3r
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


−80.89
O
F
F
N
N
3r
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm


8.00
7.97
7.92
7.92
7.82
7.79
7.73
7.70
7.53
7.51
7.48
7.42
7.39
7.37
7.28
7.25
6.45
3.91
OMe O
F
F
N
N
3s
10
9
8
7
6
5
4
3
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ppm
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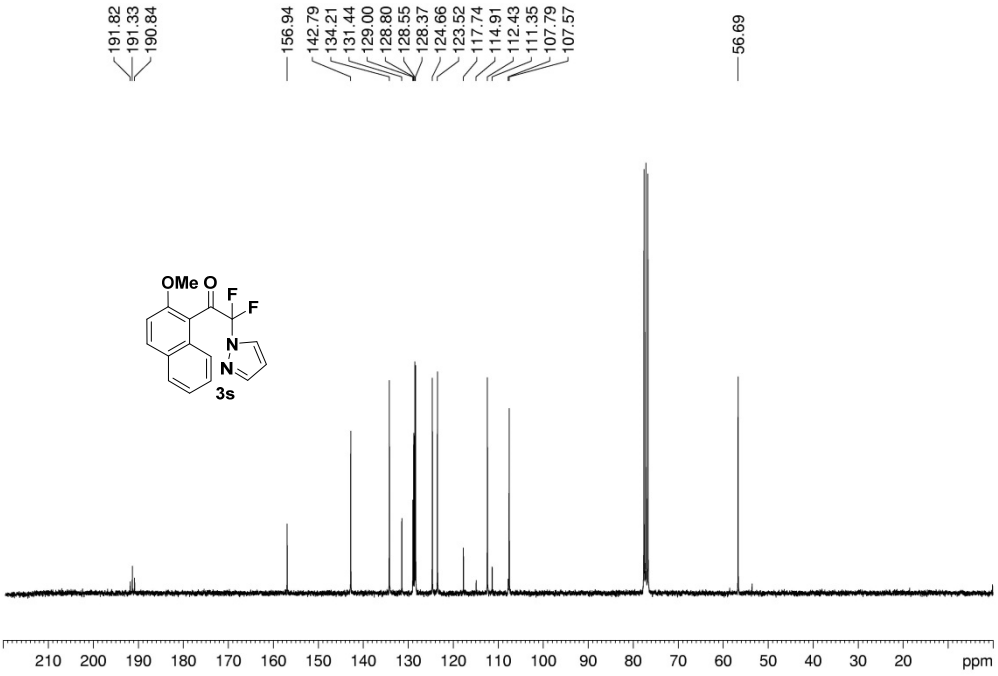
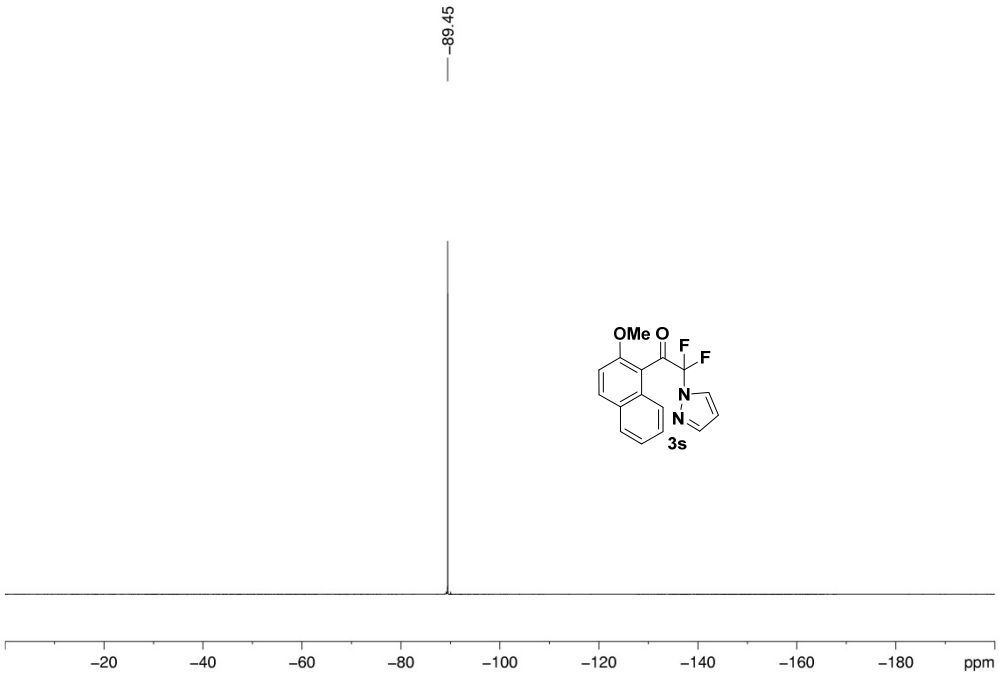
1.03
1.09
2.03
1.08
1.07
1.19
1.00
3.12


191.82
191.33
190.84
156.94
142.79
134.21
131.44
129.00
128.80
128.55
128.37
124.66
123.52
117.74
114.91
112.43
111.35
107.79
107.57
56.69
OMe O
F
F
N
N
3s
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


−89.45
OMe O
F
F
N
N
3s
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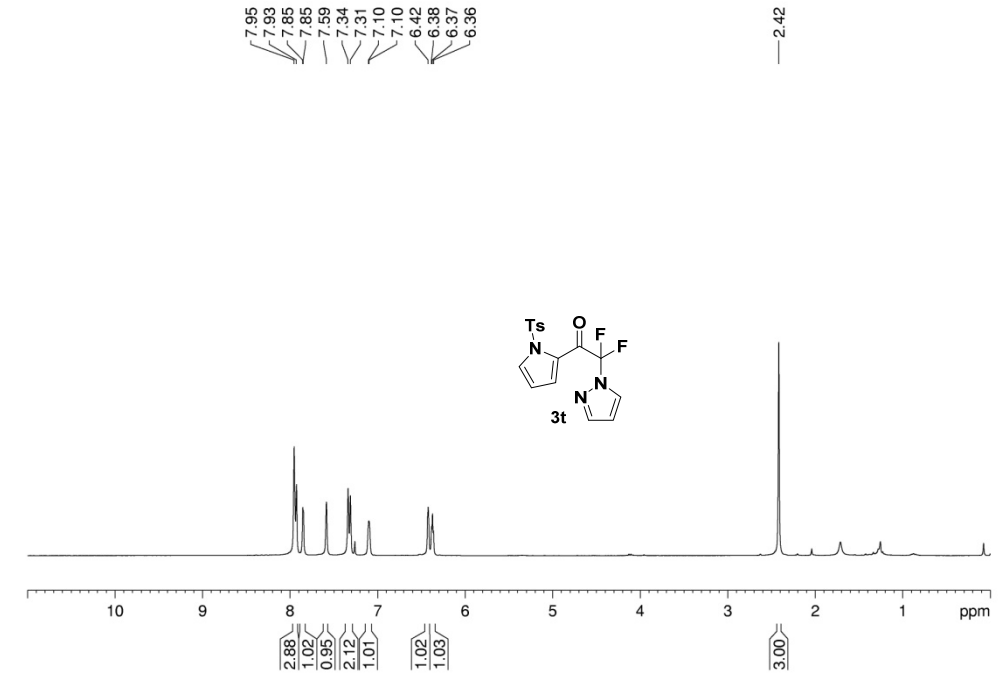
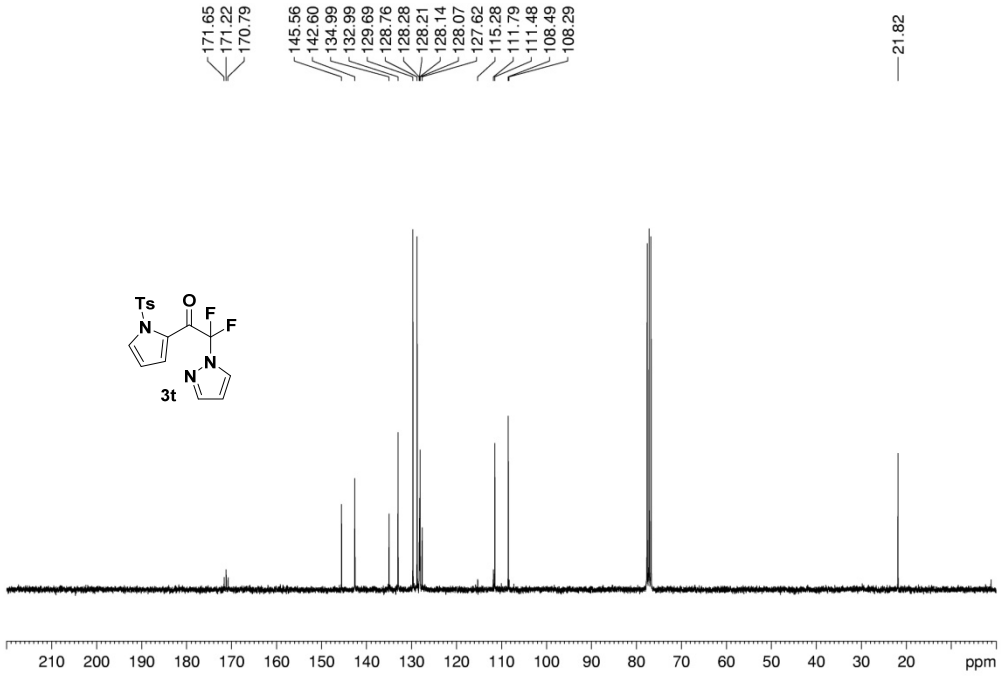
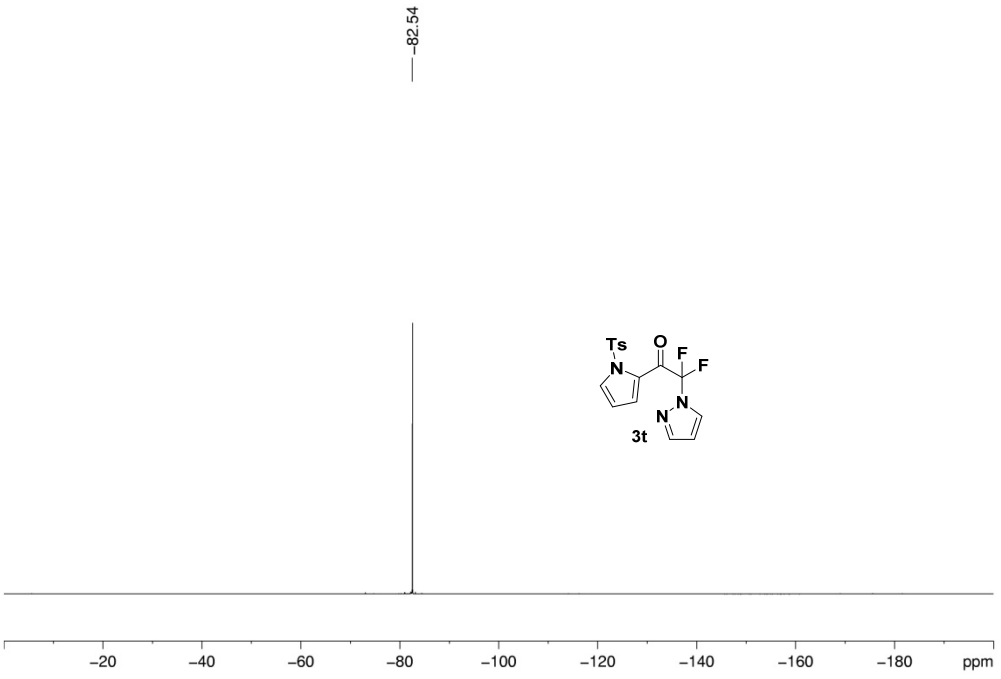
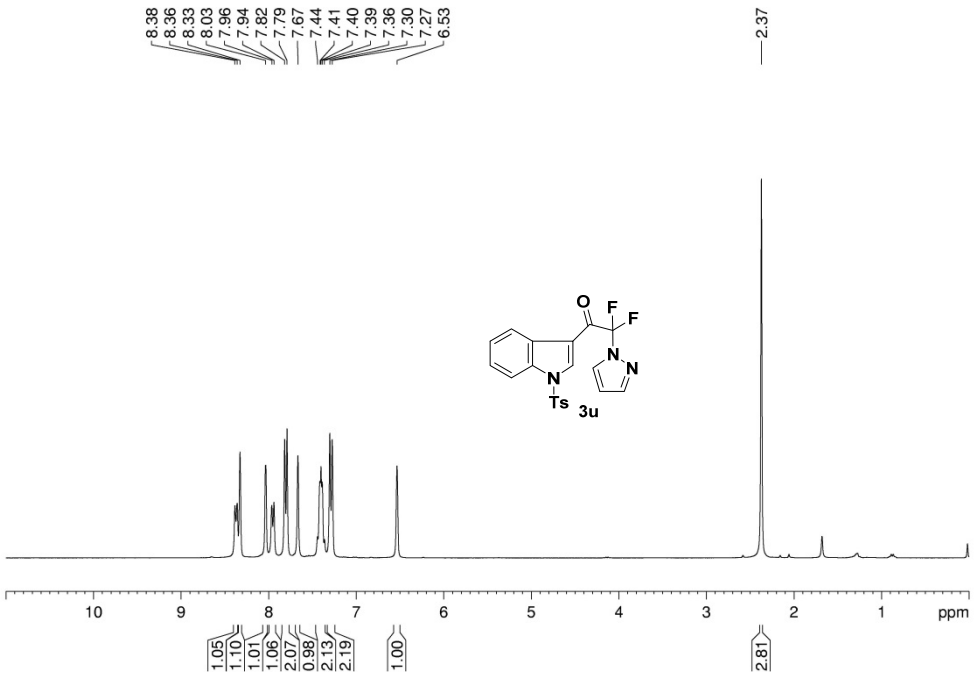
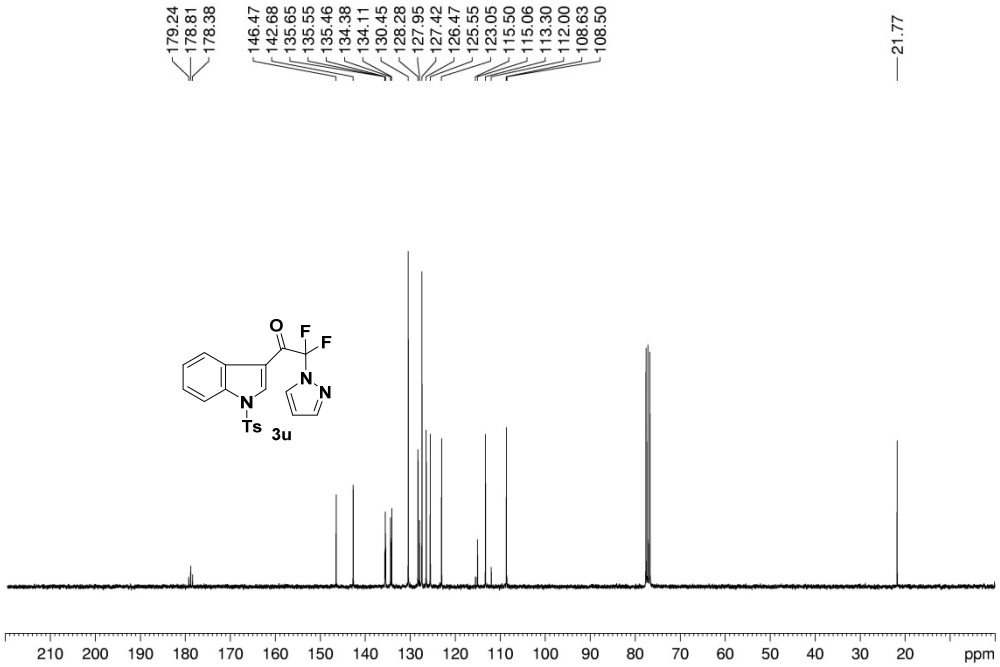
−40
−60
−80
−100
−120
−140
−160
−180
ppm


7.95
7.93
7.85
7.85
7.59
7.34
7.31
7.10
7.10
6.42
6.38
6.37
6.36
2.42
Ts
O
F
F
N
N
3t
10
9
8
7
6
5
4
3
2
1
ppm
2.88
1.02
0.95
2.12
1.01
1.02
1.03
3.00


171.65
171.22
170.79
145.56
142.60
134.99
132.99
129.69
128.76
128.28
128.21
128.14
128.07
127.62
115.28
111.79
111.48
108.49
108.29
21.82
Ts
O
F
F
N
N
3t
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


-82.54
Ts
O
F
F
N
N
3t
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm


8.38
8.36
8.33
8.03
7.96
7.94
7.82
7.79
7.67
7.44
7.41
7.40
7.39
7.36
7.30
7.27
6.53
2.37
O
F
F
N
N
N
Ts
3u
10
9
8
7
6
5
4
3
2
1
ppm
1.05
1.10
1.01
1.06
2.07
0.98
2.13
2.19
1.00
2.81


179.24
178.81
178.38
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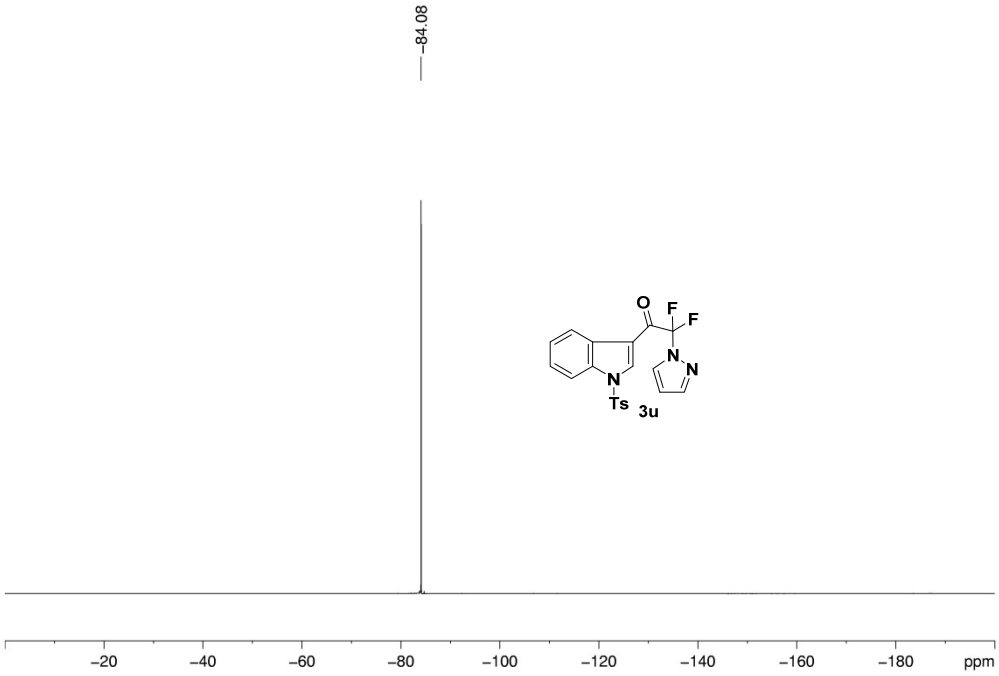
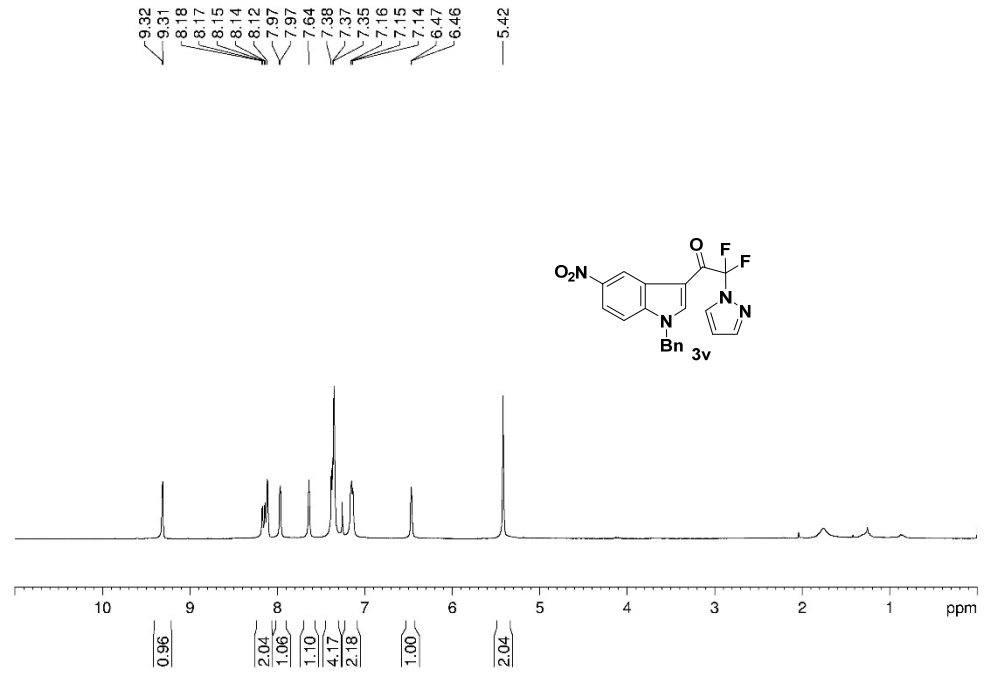
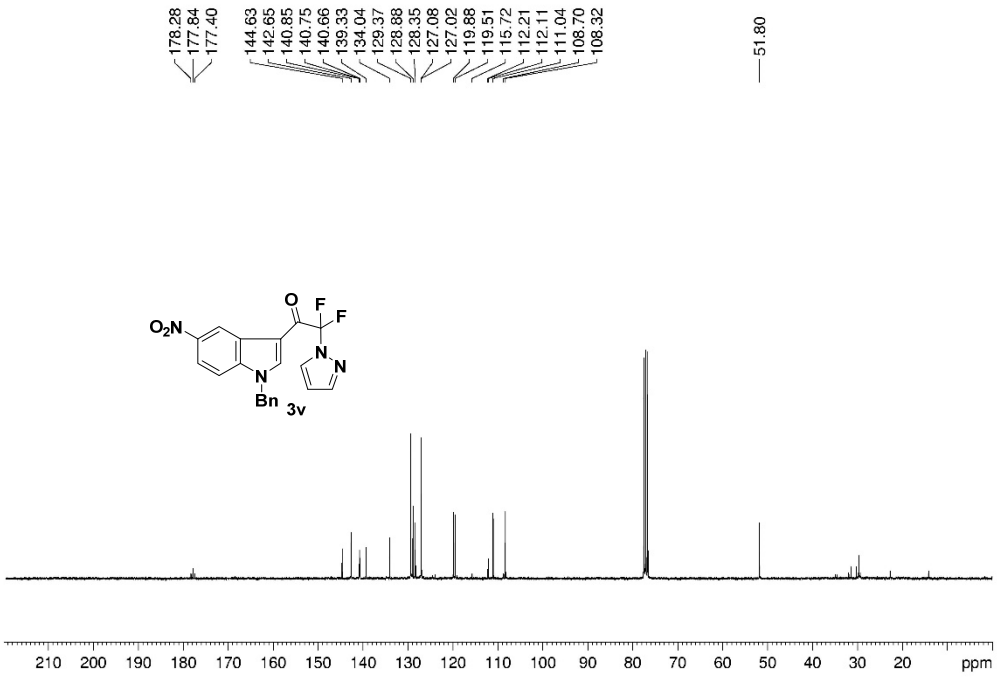
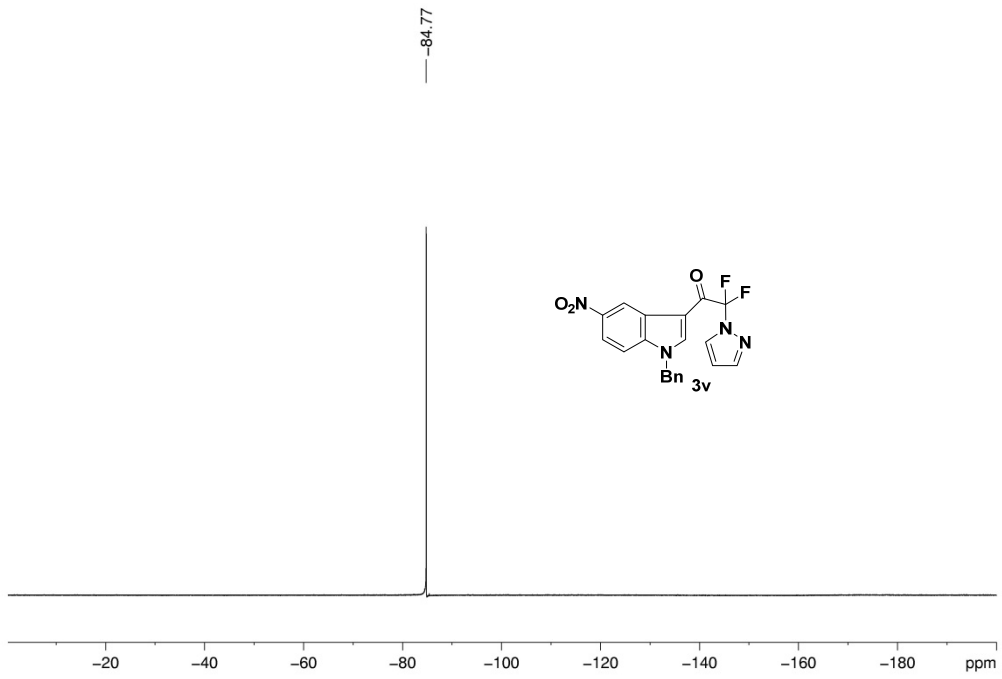
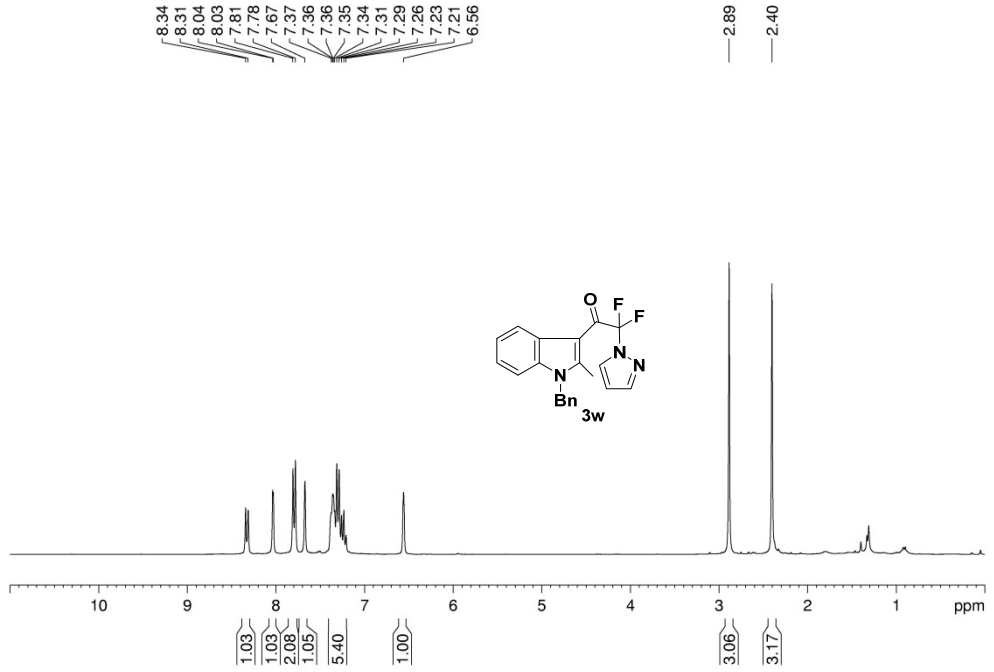
142.68
135.65
135.55
135.46
134.38
134.11
130.45
128.28
127.95
127.42
126.47
125.55
123.05
115.50
115.06
113.30
112.00
108.63
108.50
21.77
O
F
F
N
N
N
Ts
3u
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

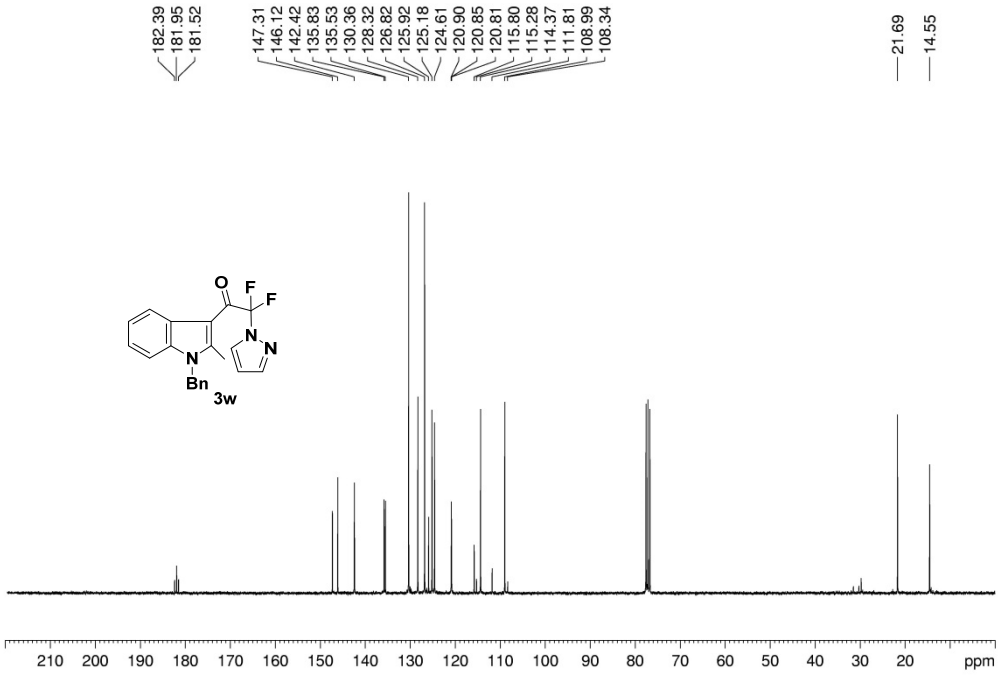

-84.08
O
F
F
N
N
N
Ts
3u
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


9.32
9.31
8.18
8.17
8.15
8.14
8.12
7.97
7.97
7.64
7.38
7.37
7.35
7.16
7.15
7.14
6.47
6.46
5.42
O2N
O
F
F
N
N
N
Bn
3v
10
9
8
7
6
5
4
3
2
1
ppm
0.96
2.04
1.06
1.10
4.17
2.18
1.00
2.04


178.28
177.84
177.40
144.63
142.65
140.85
140.75
140.66
139.33
134.04
129.37
128.88
128.35
127.08
127.02
119.88
119.51
115.72
112.21
112.11
111.04
108.70
108.32
51.80
O
F
F
O2N
N
N
N
Bn
3v
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-84.77
O
F
F
O2N
N
N
N
Bn
3v
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


8.34
8.31
8.04
8.03
7.81
7.78
7.67
7.37
7.36
7.36
7.35
7.34
7.31
7.29
7.26
7.23
7.21
6.56
2.89
2.40
O
F
F
N
N
N
Bn
3w
10
9
8
7
6
5
4
3
2
1
ppm
1.03
1.03
2.08
1.05
5.40
1.00
3.06
3.17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181.52
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146.12
142.42
135.83
135.53
130.36
128.32
126.82
125.92
125.18
124.61
120.90
120.85
120.81
115.80
115.28
114.37
111.81
108.99
108.34
21.69
14.55
O
F
F
N
N
N
Bn
3w
210
200
190
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170
160
150
140
130
120
110
100
90
80
70
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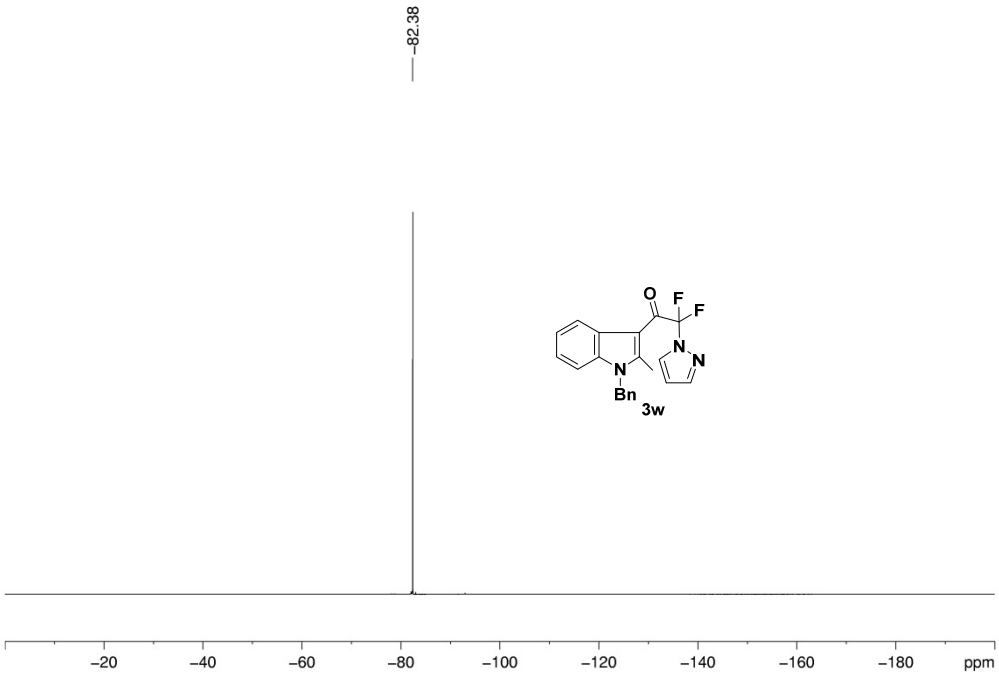
50
40
30
20
ppm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F
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N
Bn
3w
-20
-40
-60
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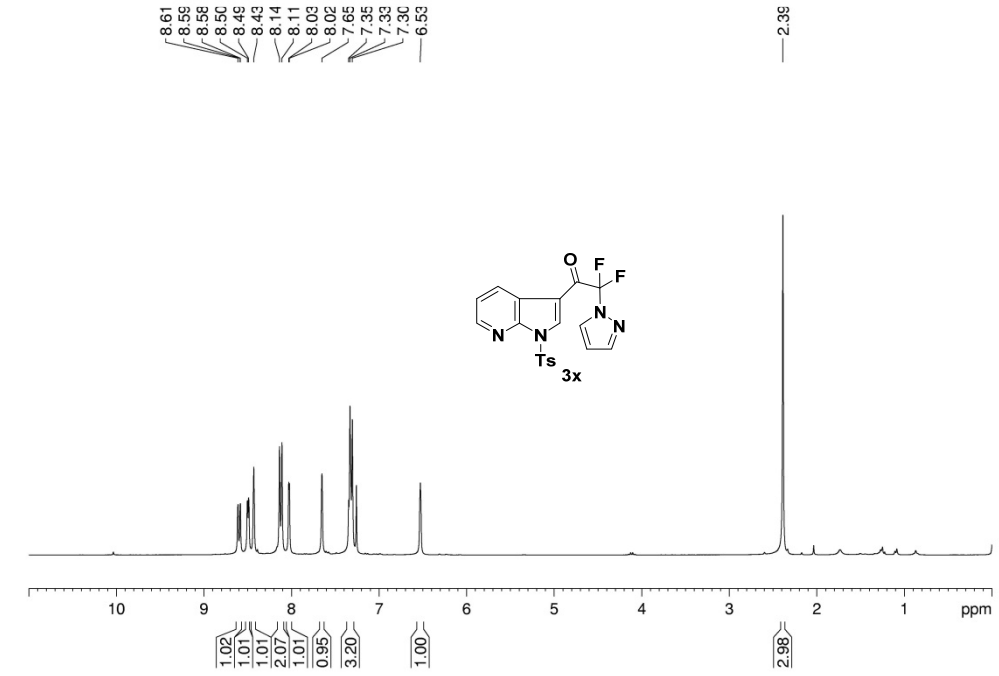
-100
-120
-140
-160
-180
ppm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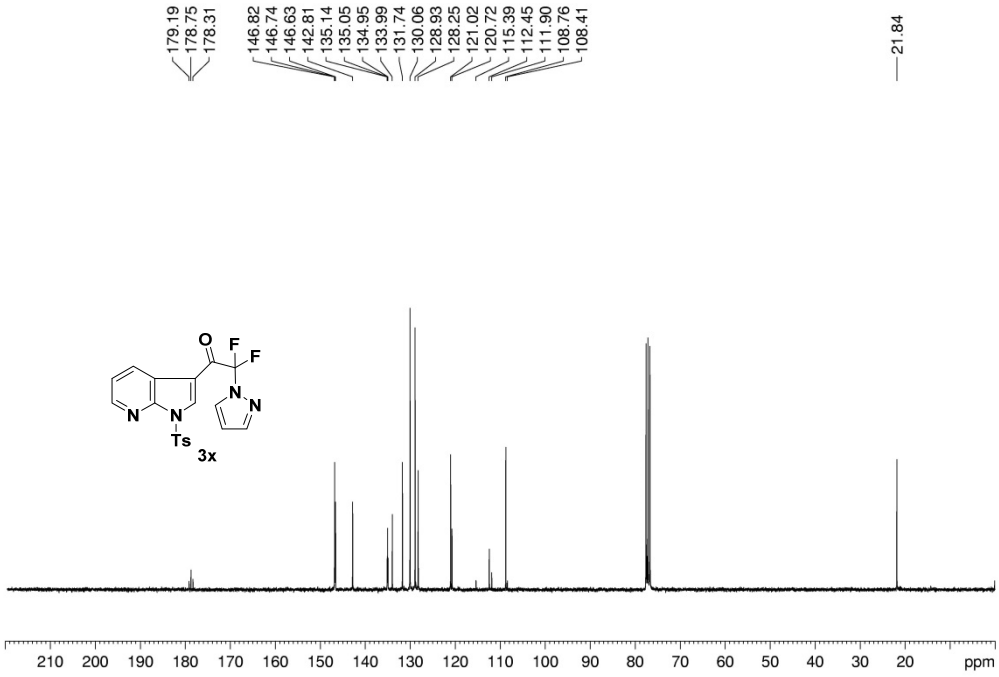
8.59
8.58
8.50
8.48
8.43
8.14
8.11
8.03
8.02
7.65
7.35
7.33
7.30
6.53
2.39
O
F
F
N
N
N
Ts
3x
10
9
8
7
6
5
4
3
2
1
ppm
1.02
1.01
1.01
2.07
1.01
0.95
3.20
1.00
2.98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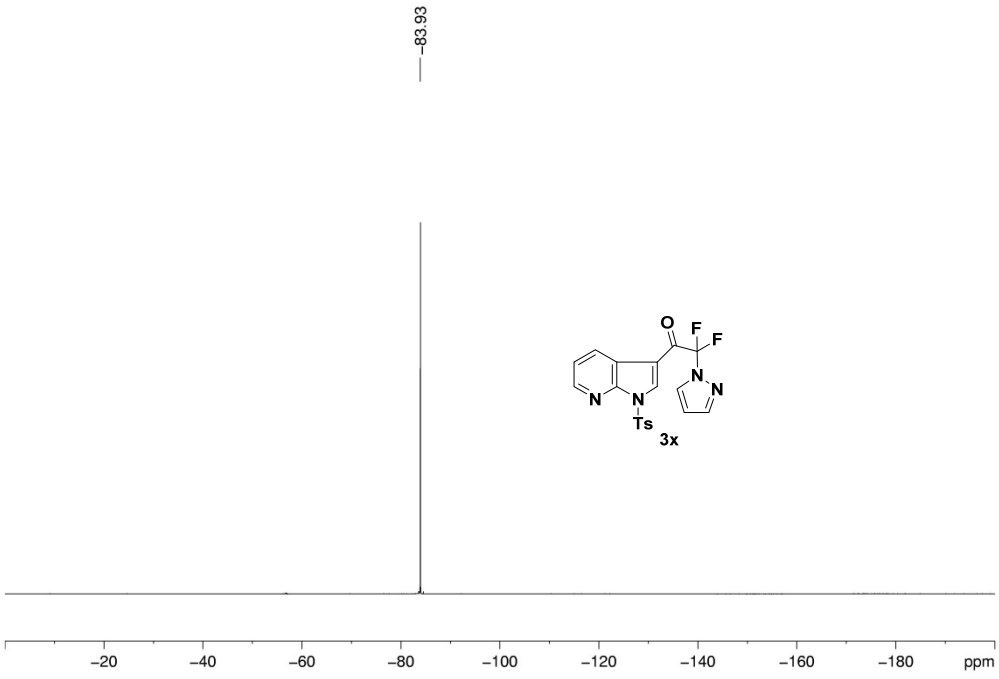
135.14
135.05
134.95
133.99
131.74
130.06
128.93
128.25
121.02
120.72
115.39
112.45
111.90
108.76
108.41
21.84
O
F
F
N
N
N
Ts
3x
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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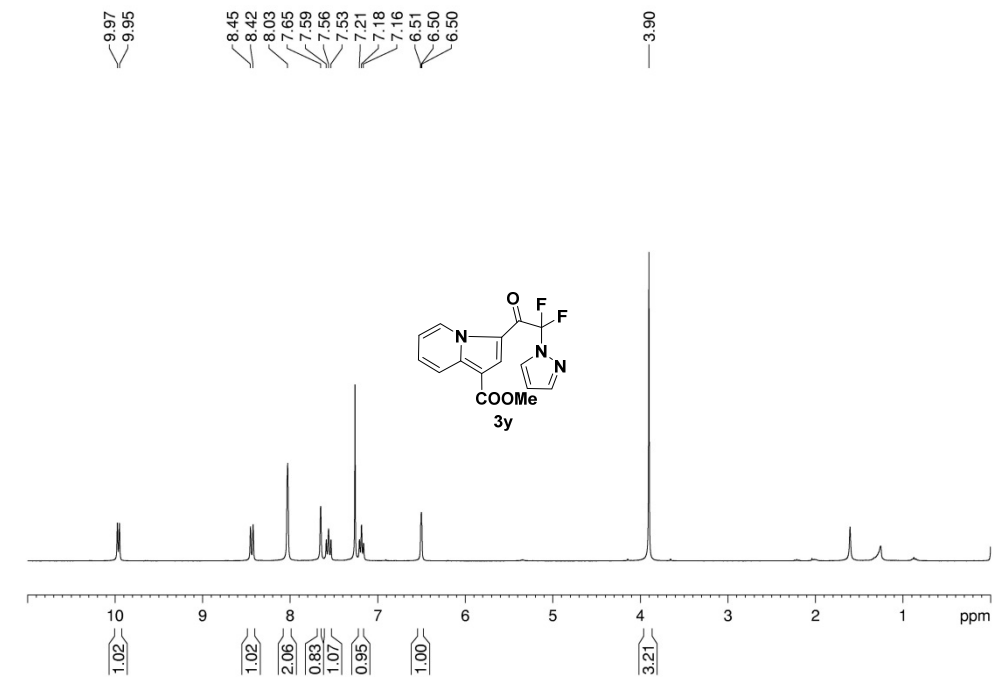
O
F
F
N
N
N
Ts
3x
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm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9.95
8.45
8.42
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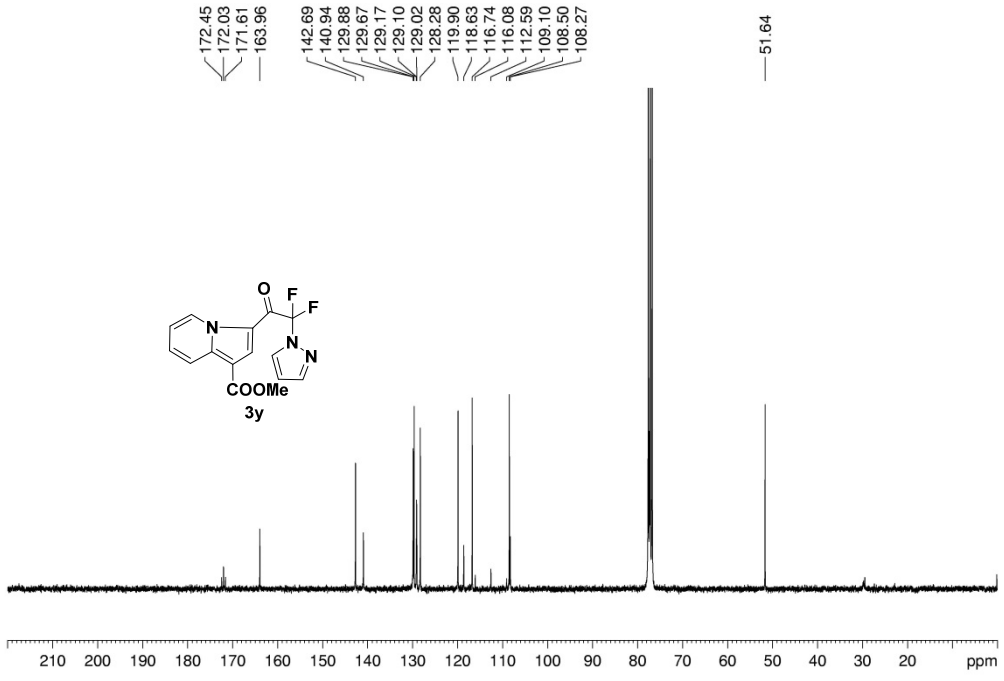
7.65
7.59
7.56
7.53
7.21
7.18
7.16
6.51
6.50
6.50
3.90
O
F
F
N
N
N
COOMe
3y
10
9
8
7
6
5
4
3
2
1
ppm
1.02
1.02
2.06
0.83
1.07
0.95
1.00
3.21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172.03
171.61
163.96
142.69
140.94
129.88
129.67
129.17
129.10
129.02
128.28
119.90
118.63
116.74
116.08
112.59
109.10
108.50
108.27
51.64
O
F
F
N
N
N
COOMe
3y
210
200
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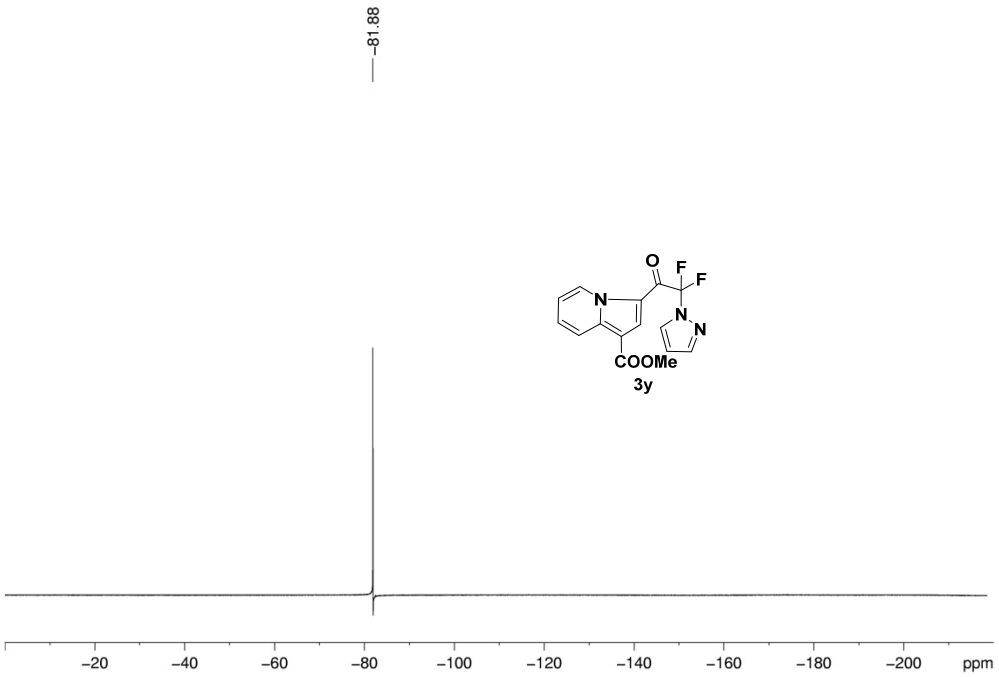
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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F
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N
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3y
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-40
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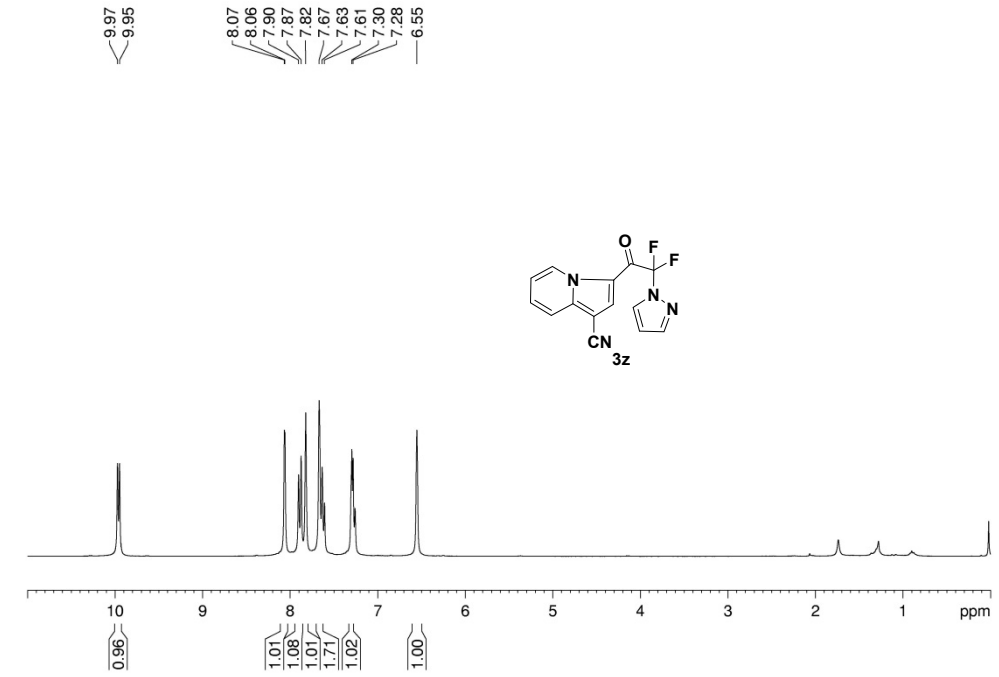
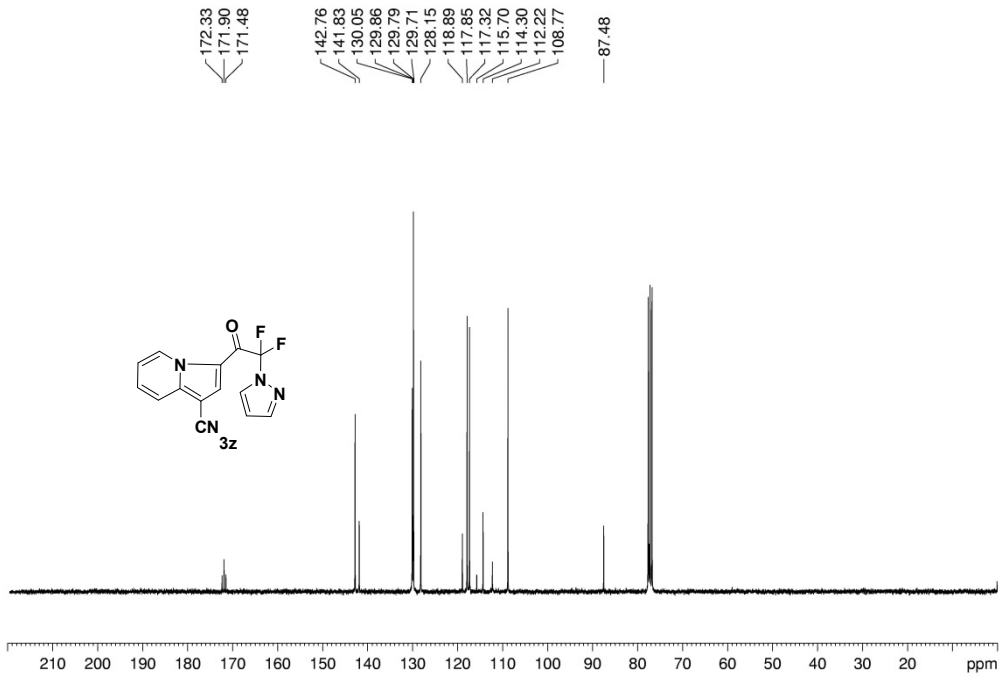
-80
-100
-120
-140
-160
-180
-200
ppm


9.97
9.95
8.07
8.06
7.90
7.87
7.82
7.67
7.63
7.61
7.30
7.28
6.55
O
F
F
N
N
N
CN
3z
10
9
8
7
6
5
4
3
2
1
ppm
0.96
1.01
1.08
1.01
1.71
1.02
1.00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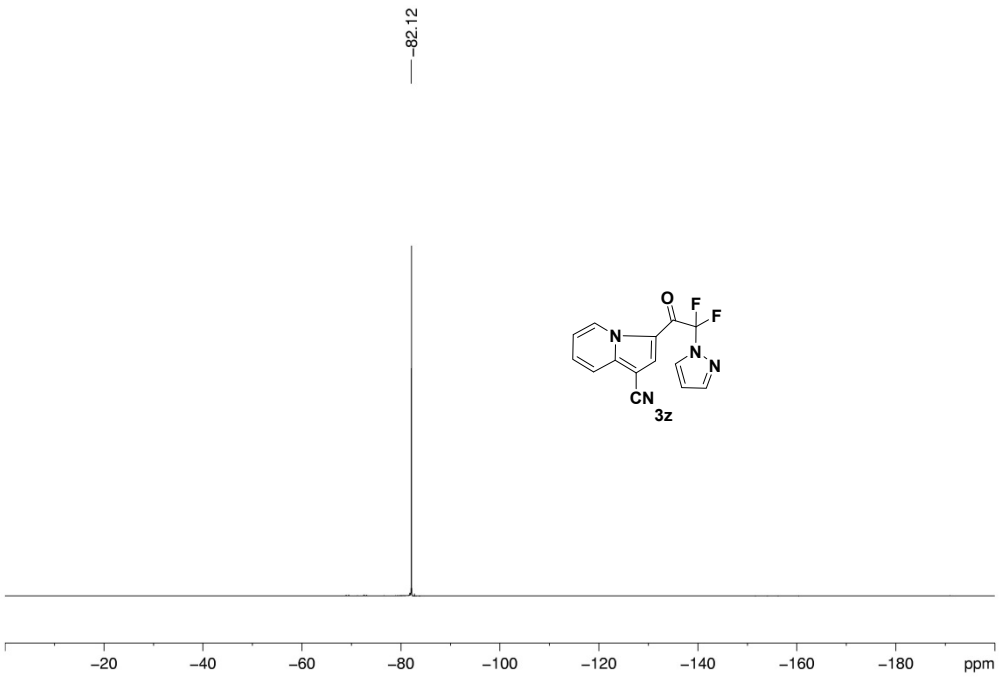
171.48
142.76
141.83
130.05
129.86
129.79
129.71
128.15
118.89
117.85
117.32
115.70
114.30
112.22
108.77
87.48
O
F
F
N
N
N
CN
3z
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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O
F
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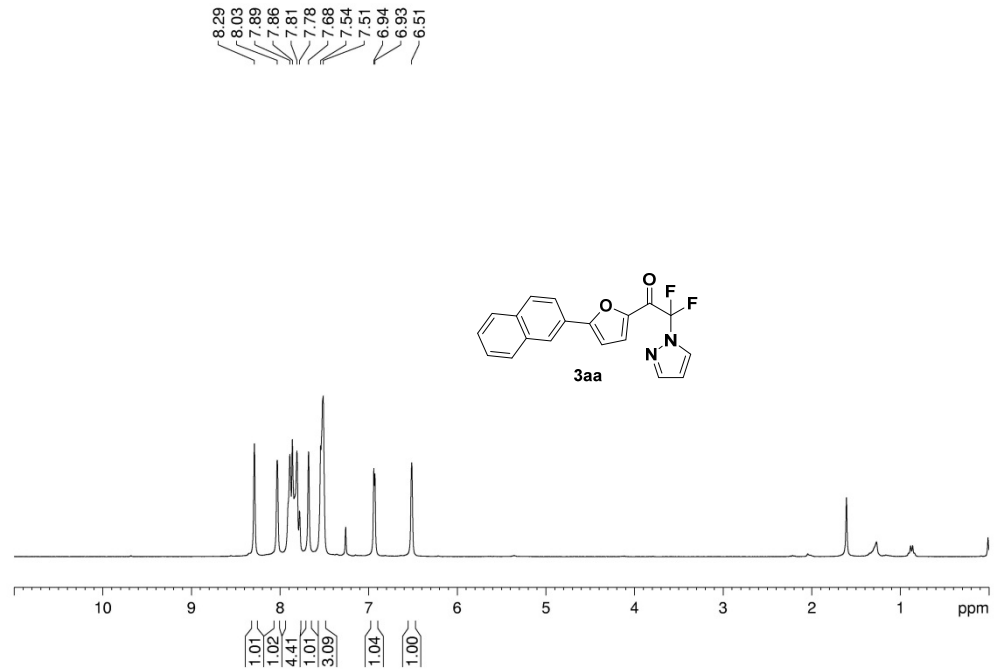
N
N
N
CN
3z
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


8.29
8.03
7.89
7.86
7.81
7.78
7.68
7.54
7.51
6.94
6.93
6.51
3aa
10
9
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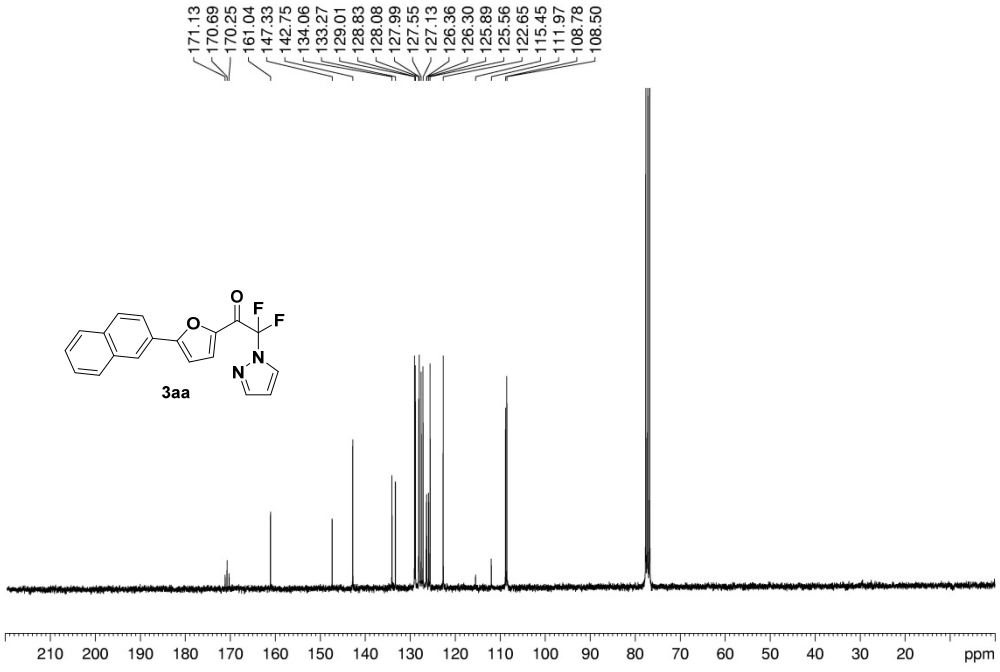
1.02
4.41
1.01
3.09
1.04
1.00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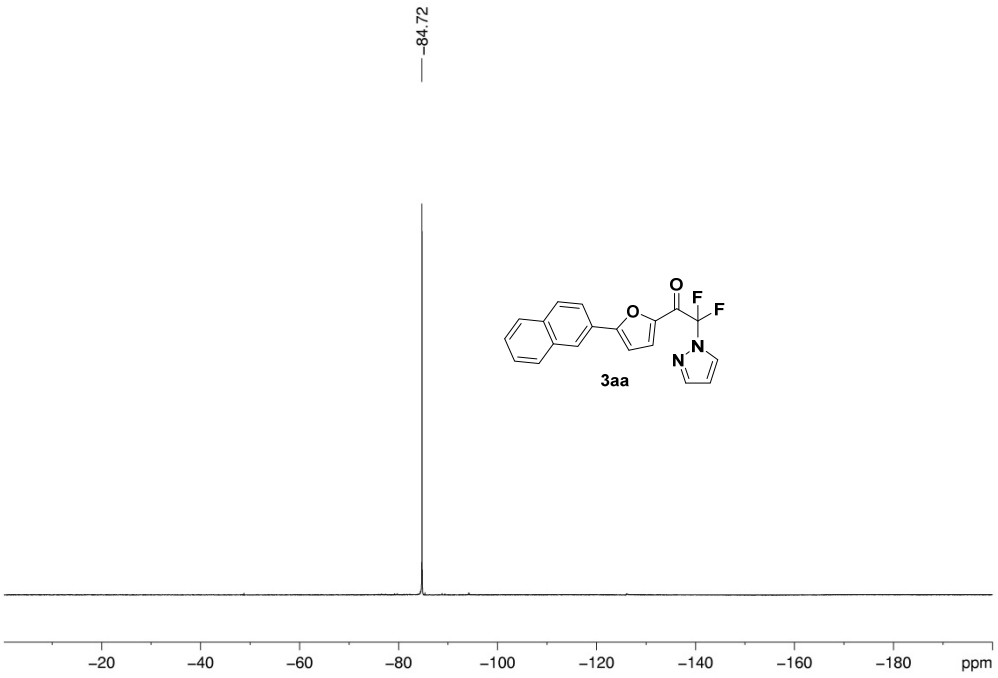
170.69
170.25
161.04
147.33
142.75
134.06
133.27
129.01
128.83
128.08
127.99
127.55
127.13
126.36
126.30
125.89
125.56
122.65
115.45
111.97
108.78
108.50
3aa
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


−84.72
O
F
F
O
N
N
3aa
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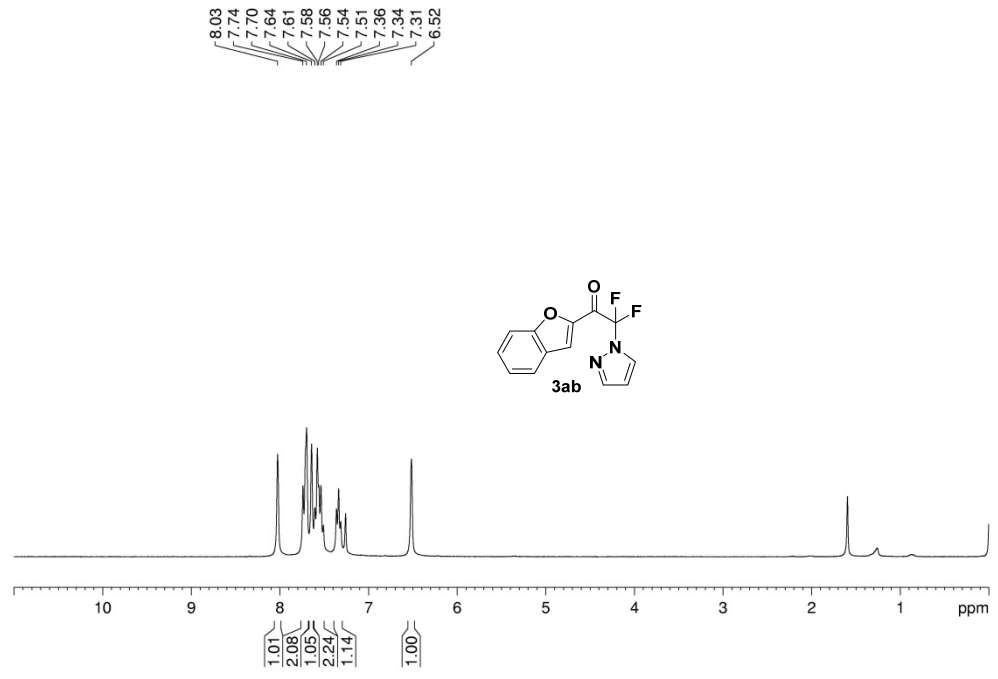
−40
−60
−80
−100
−120
−140
−160
−180
ppm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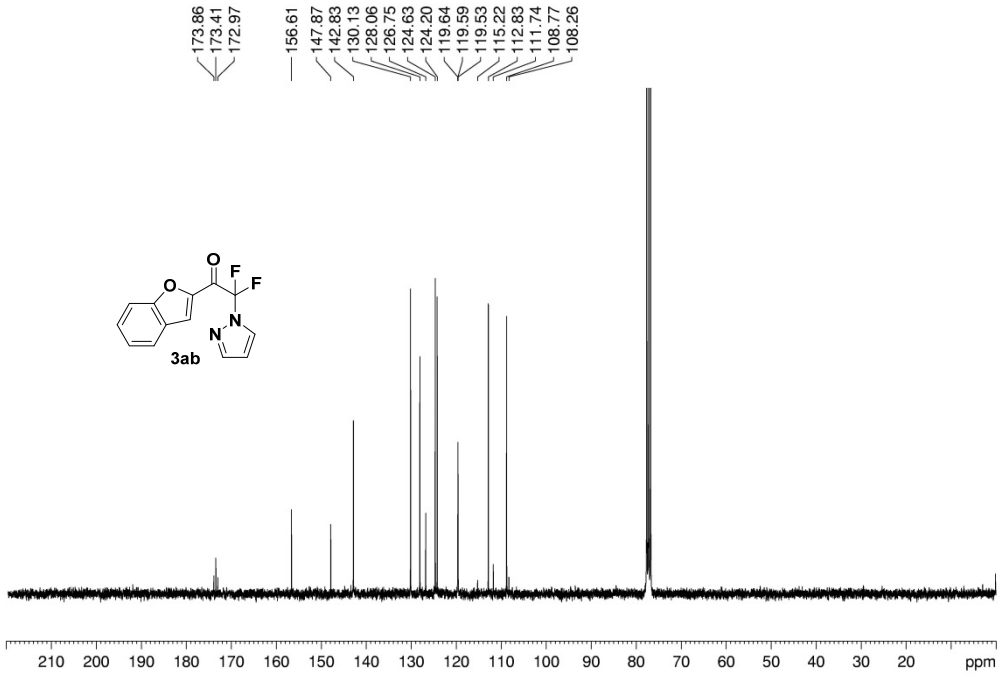
7.74
7.70
7.64
7.61
7.58
7.56
7.54
7.51
7.36
7.34
7.31
6.52
O
F
F
O
N
N
3ab
10
9
8
7
6
5
4
3
2
1
ppm
1.01
2.08
1.05
2.24
1.14
1.00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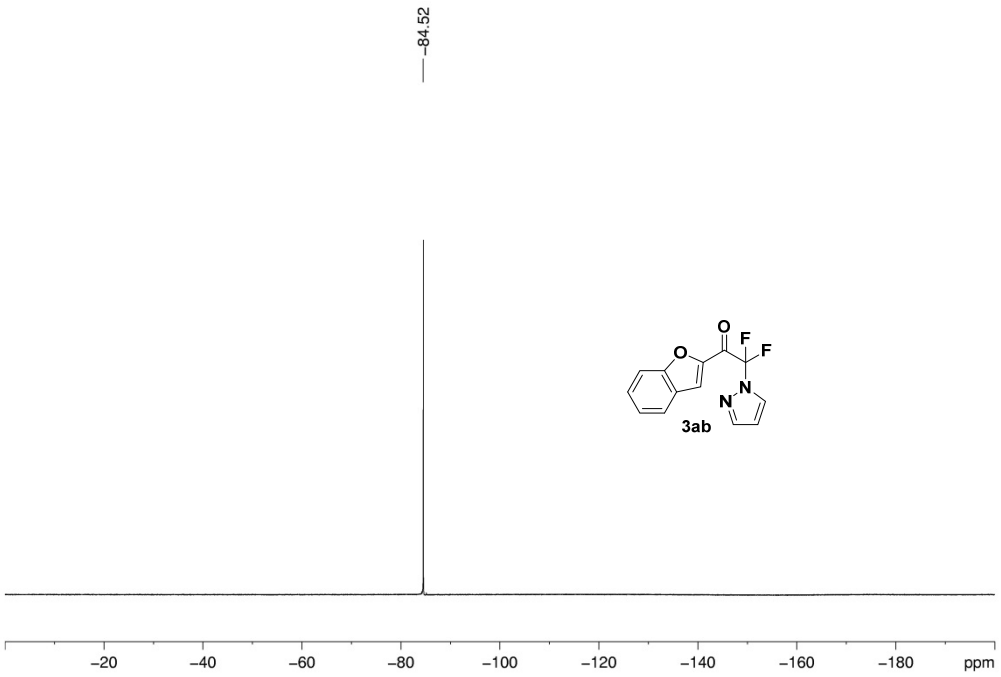
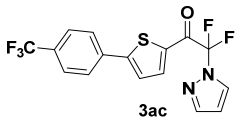
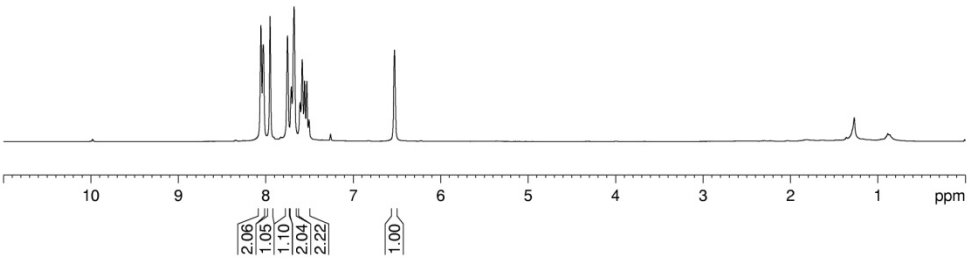
173.41
172.97
156.61
147.87
142.83
130.13
128.06
126.75
124.63
124.20
119.64
119.59
119.53
115.22
112.83
111.74
108.77
108.26
O
F
F
O
N
N
3ab
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


-84.52
O
F
F
O
N
N
3ab
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm


8.06
8.03
7.95
7.75
7.71
7.68
7.61
7.58
7.56
7.53
7.51
6.53


O
F
F
S
F3C
N
N

3ac


10
9
8
7
6
5
4
3
2
1
ppm
2.06
1.05
1.10
2.04
2.22
1.00


176.83
176.39
175.95
142.87
142.62
138.43
135.00
134.50
134.46
134.41
132.58
132.20
131.77
131.34
130.91
129.80
129.74
129.43
128.12
125.82
124.92
124.87
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123.30
123.25
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123.15
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118.60
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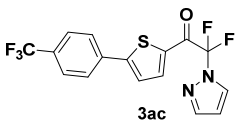
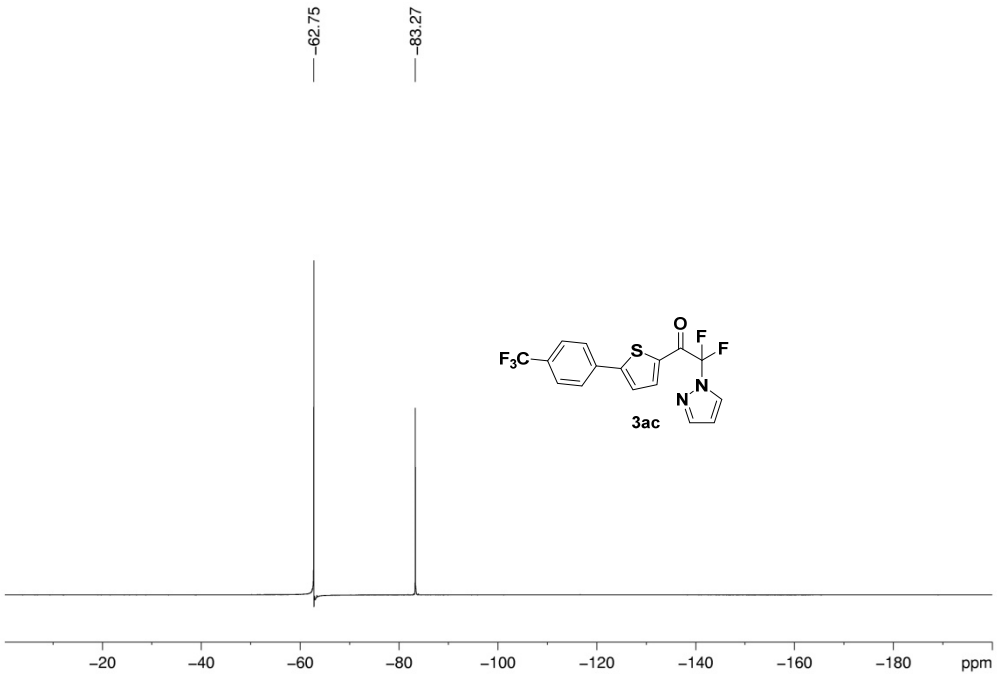
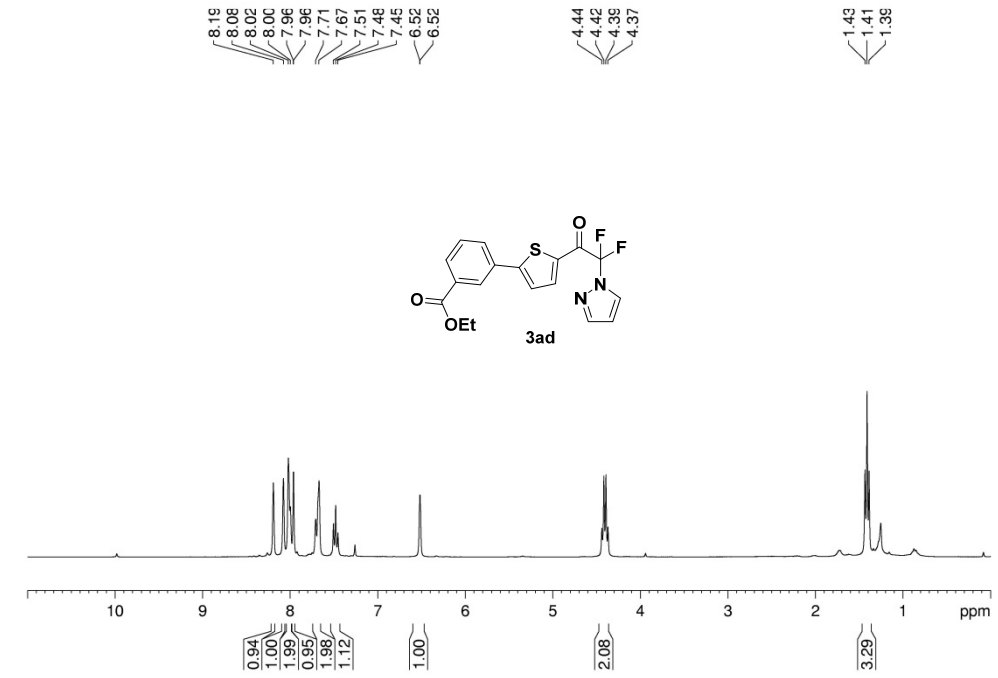
111.97
108.85
108.48


O
F
F
S
F3C
N
N

3ac

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


−62.75
−83.27
O
F
F
S
F3C
N
N
3ac
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm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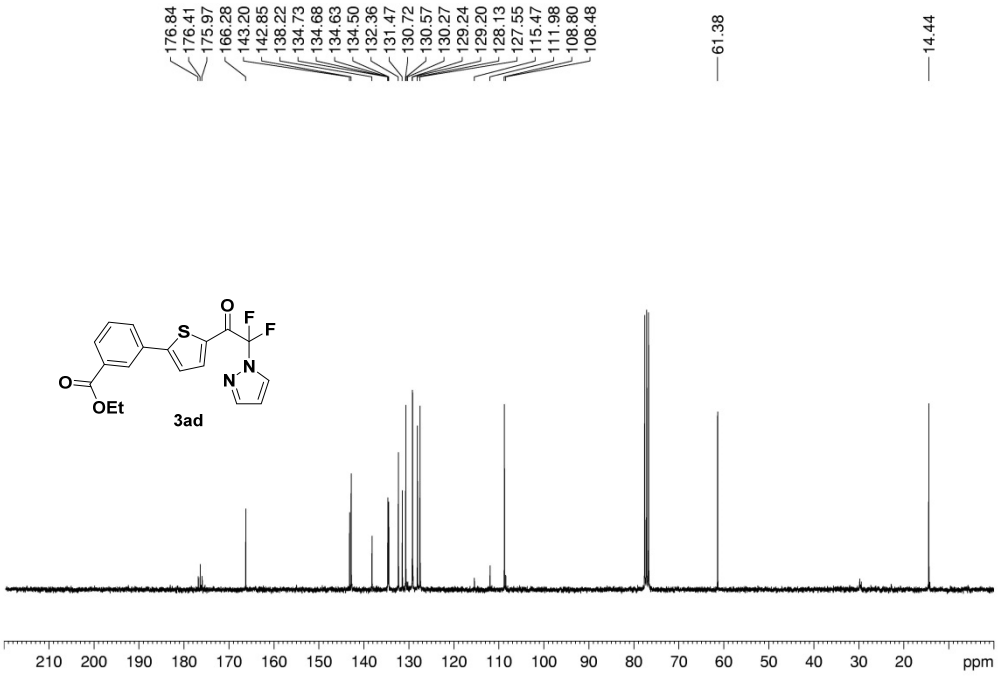
8.08
8.02
8.00
7.96
7.96
7.71
7.67
7.51
7.48
7.45
6.52
6.52
4.44
4.42
4.39
4.37
1.43
1.41
1.39
O
F
F
S
O
OEt
N
N
3ad
10
9
8
7
6
5
4
3
2
1
ppm
0.94
1.00
1.99
0.95
1.98
1.12
1.00
2.08
3.29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142.85
138.22
134.73
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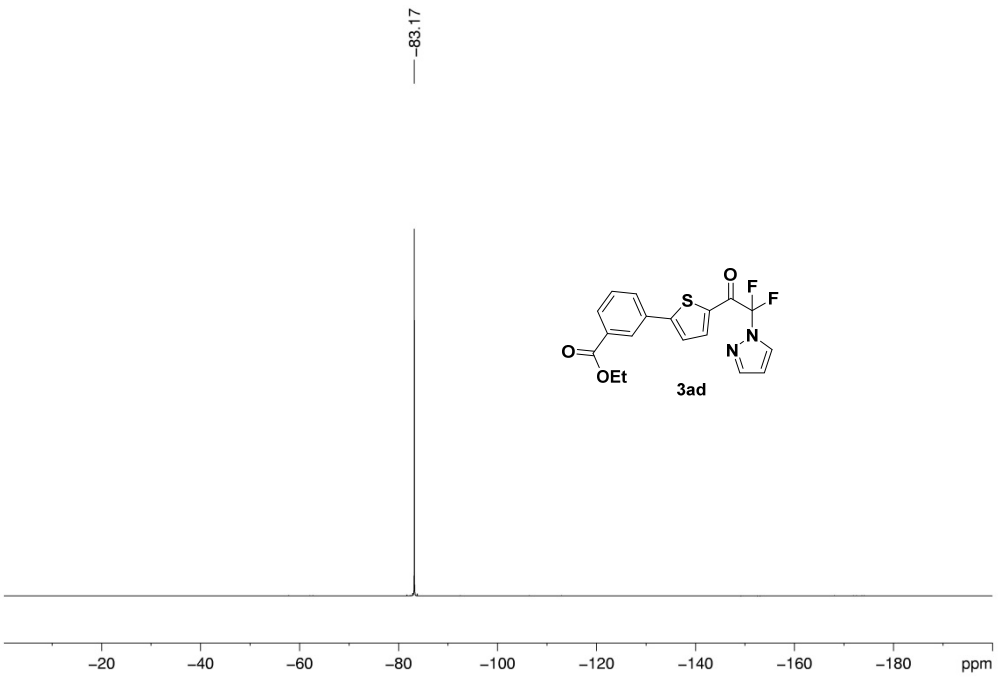
134.63
134.50
132.36
131.47
130.72
130.57
130.27
129.24
129.20
128.13
127.55
115.47
111.98
108.80
108.48
61.38
14.44
O
F
F
S
N
N
O
OEt
3ad
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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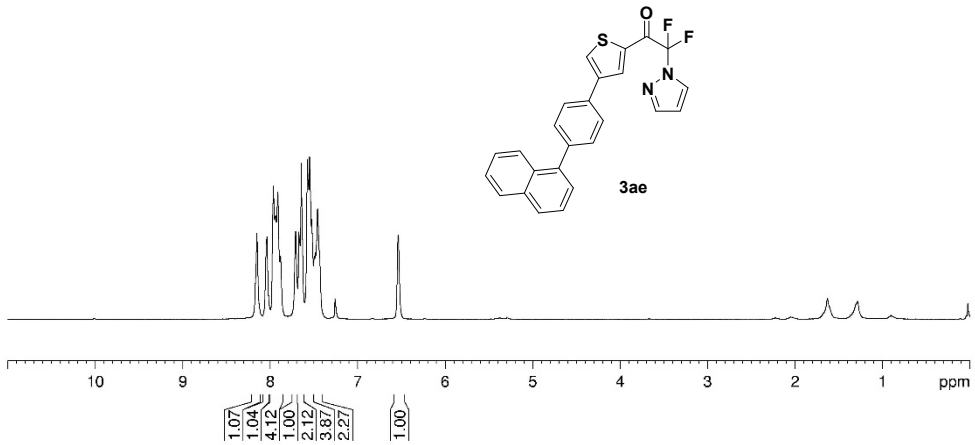
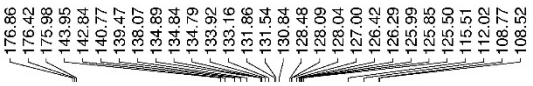
O
F
F
S
N
N
O
OEt
3ad
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


8.15
8.05
8.04
7.96
7.94
7.91
7.88
7.71
7.67
7.65
7.58
7.57
7.56
7.55
7.53
7.50
7.49
7.48
7.46
7.44
6.54
6.53


O
F
F
S
N
N
3ae
10
9
8
7
6
5
4
3
2
1
ppm
1.07
1.04
4.12
1.00
2.12
3.87
2.27
1.00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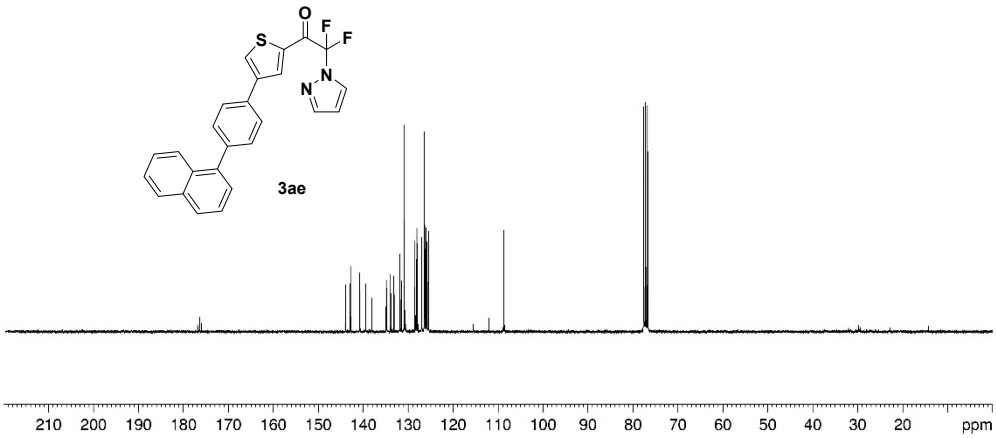
176.42
175.98
143.95
142.84
140.77
139.47
138.07
134.89
134.84
134.79
133.92
133.16
131.86
131.54
130.84
128.48
128.09
128.04
127.00
126.42
126.29
125.99
125.85
125.50
115.51
112.02
108.77
108.52


O
F
F
S
N
N
3ae
210
200
190
180
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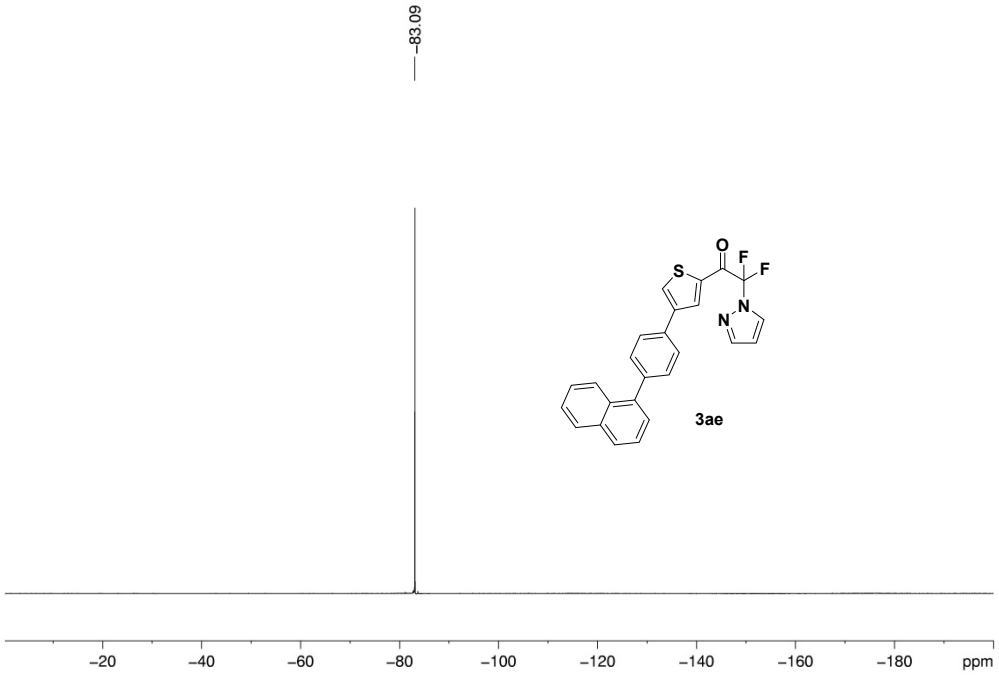
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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O
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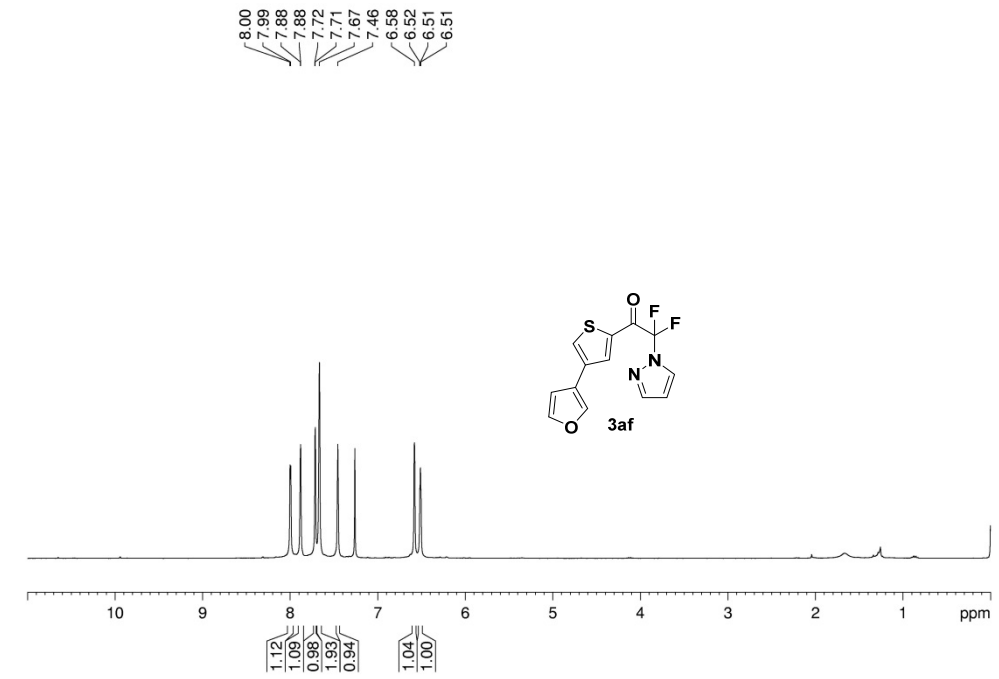
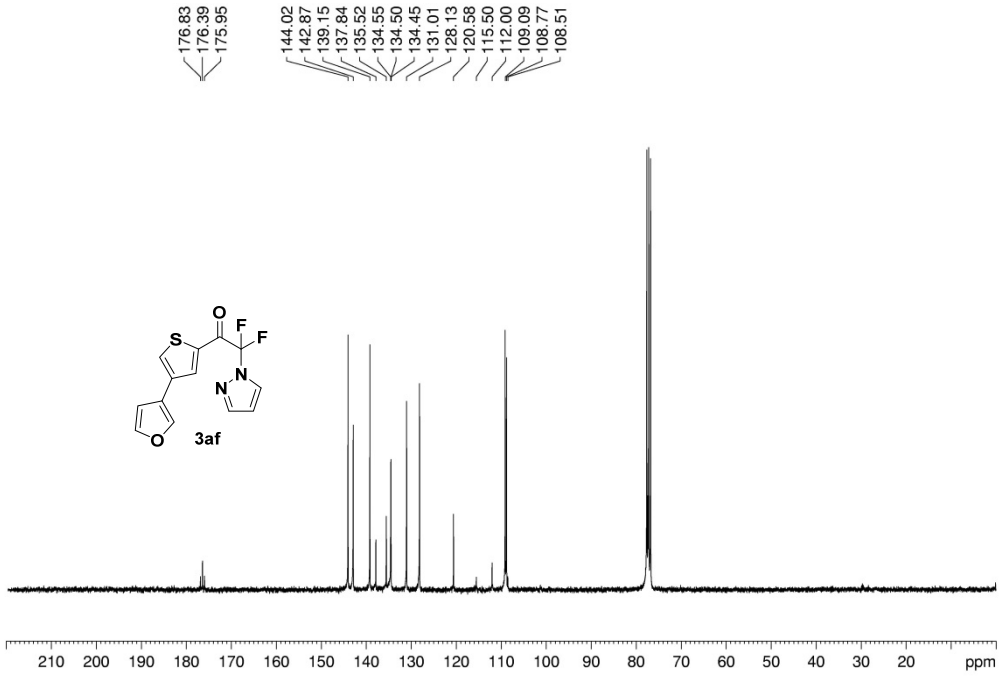
F
S
N
N
3ae
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


8.00
7.99
7.88
7.88
7.72
7.71
7.67
7.46
6.58
6.52
6.51
6.51
O
F
F
S
N
N
O
3af
10
9
8
7
6
5
4
3
2
1
ppm
1.12
1.09
0.98
1.93
0.94
1.04
1.00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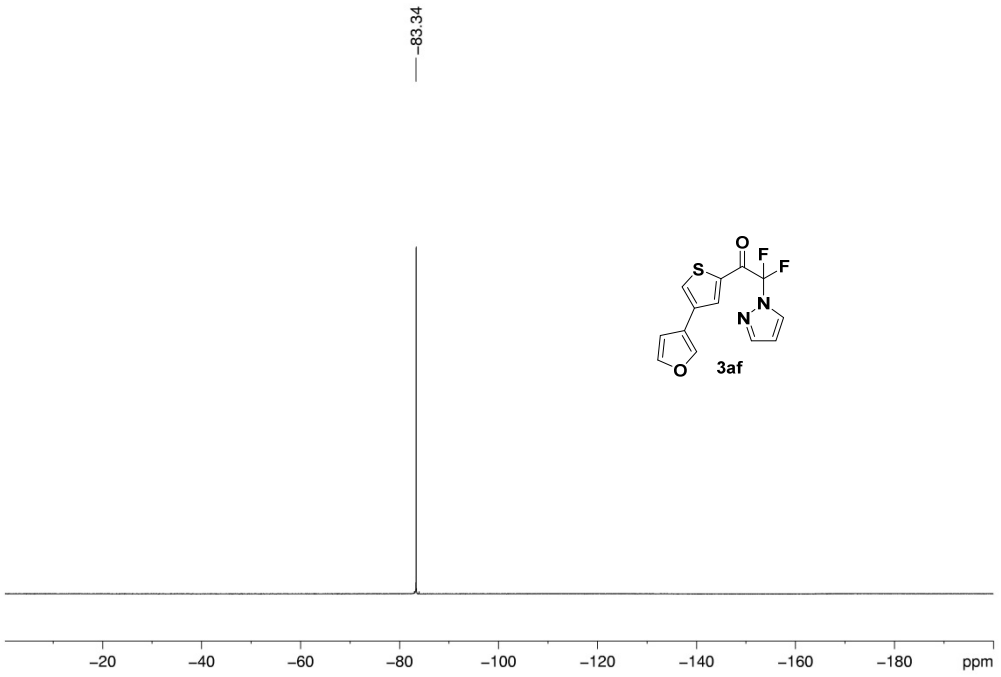
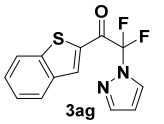
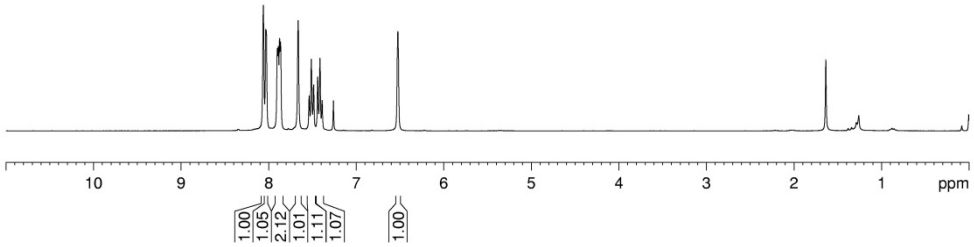
176.39
175.95
144.02
142.87
139.15
137.84
135.52
134.55
134.50
134.45
131.01
128.13
120.58
115.50
112.00
109.09
108.77
108.51
O
F
F
S
N
N
O
3af
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


−83.34
O
F
F
S
N
N
O
3af
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm


8.06
8.03
8.03
7.90
7.89
7.87
7.86
7.66
7.54
7.51
7.49
7.44
7.41
7.39
6.52


O
F
F
S
N
N
3ag


10
9
8
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6
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4
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2
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ppm
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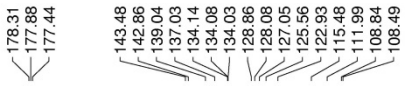
1.05
2.12
1.01
1.11
1.07
1.00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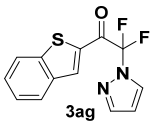
177.88
177.44

143.48
142.86
139.04
137.03
134.14
134.08
134.03
128.86
128.08
127.05
125.56
122.93
115.48
111.99
108.84
108.49


O
F
F
S
N
N
3ag

210
200
190
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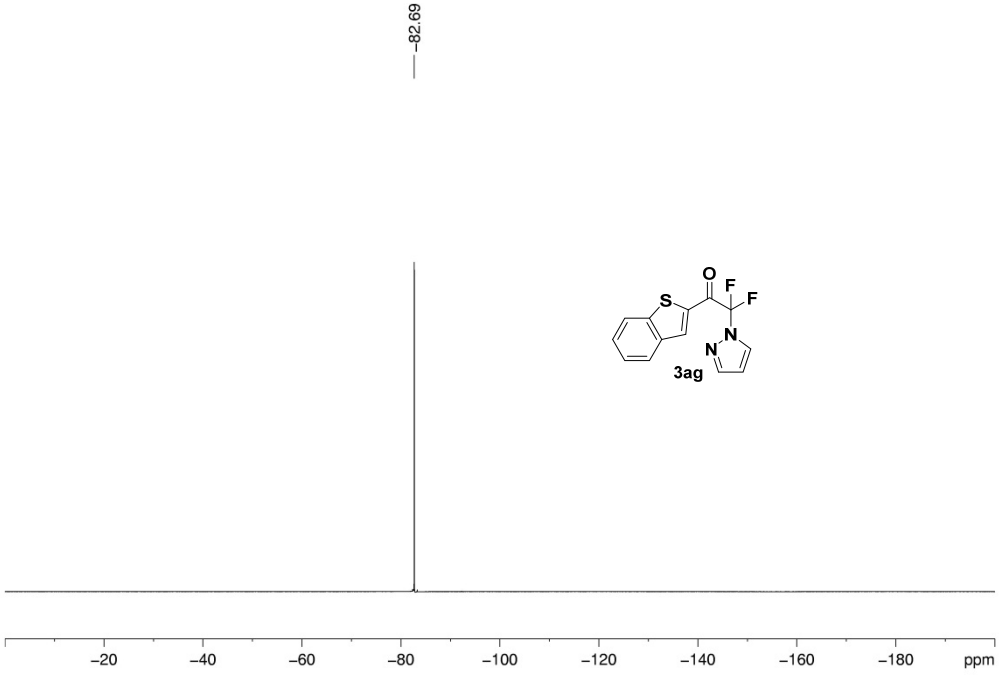
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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3ag
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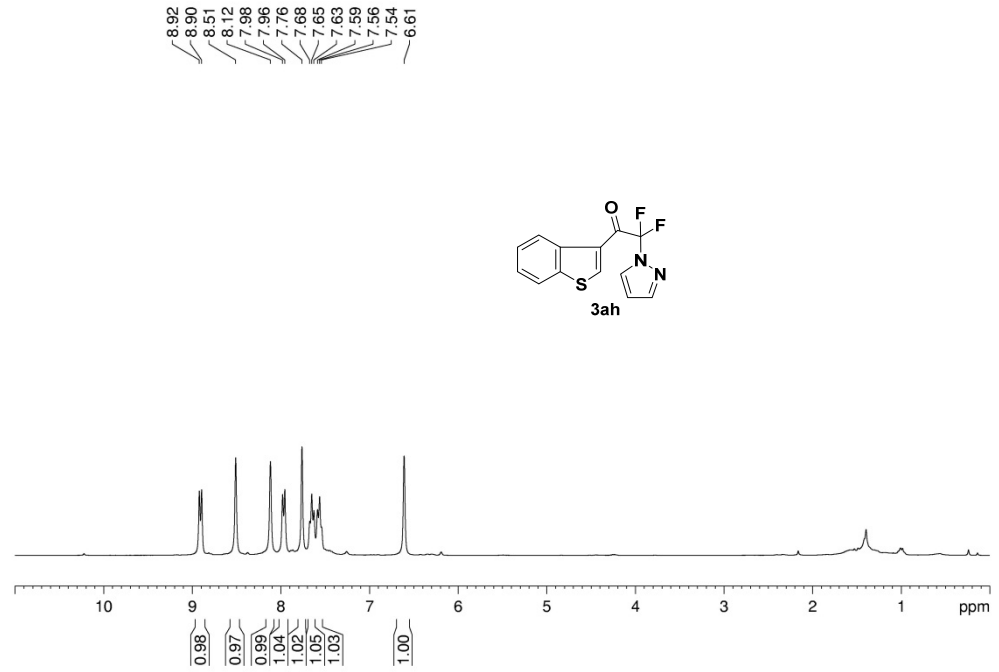
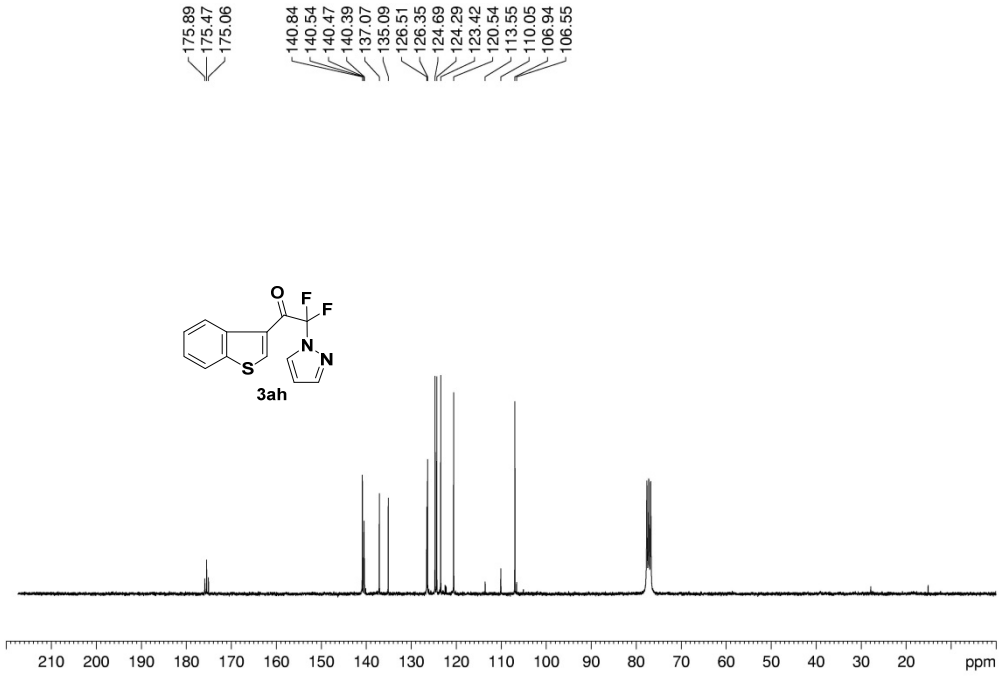
-160
-180
ppm


8.92
8.90
8.51
8.12
7.98
7.96
7.76
7.68
7.65
7.63
7.59
7.56
7.54
6.61
O
F
F
N
N
S
3ah
10
9
8
7
6
5
4
3
2
1
ppm
0.98
0.97
0.99
1.04
1.02
1.05
1.03
1.00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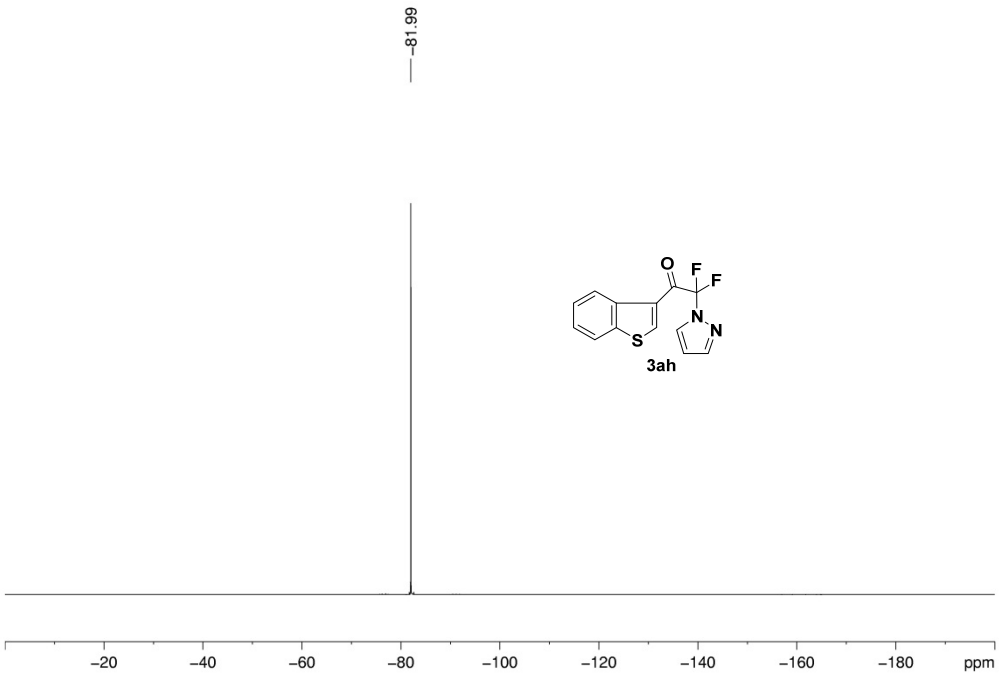
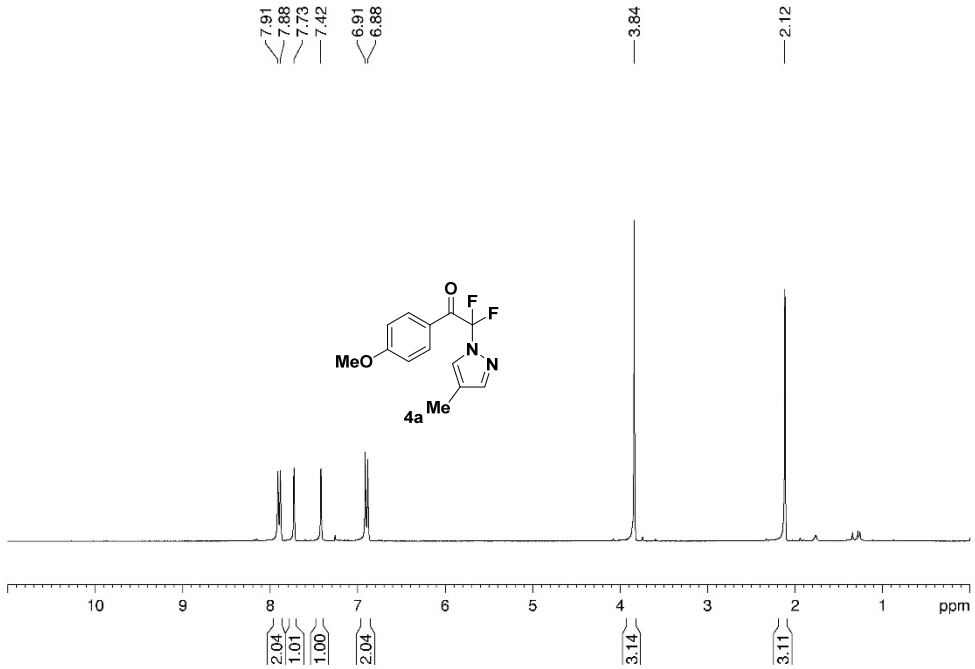
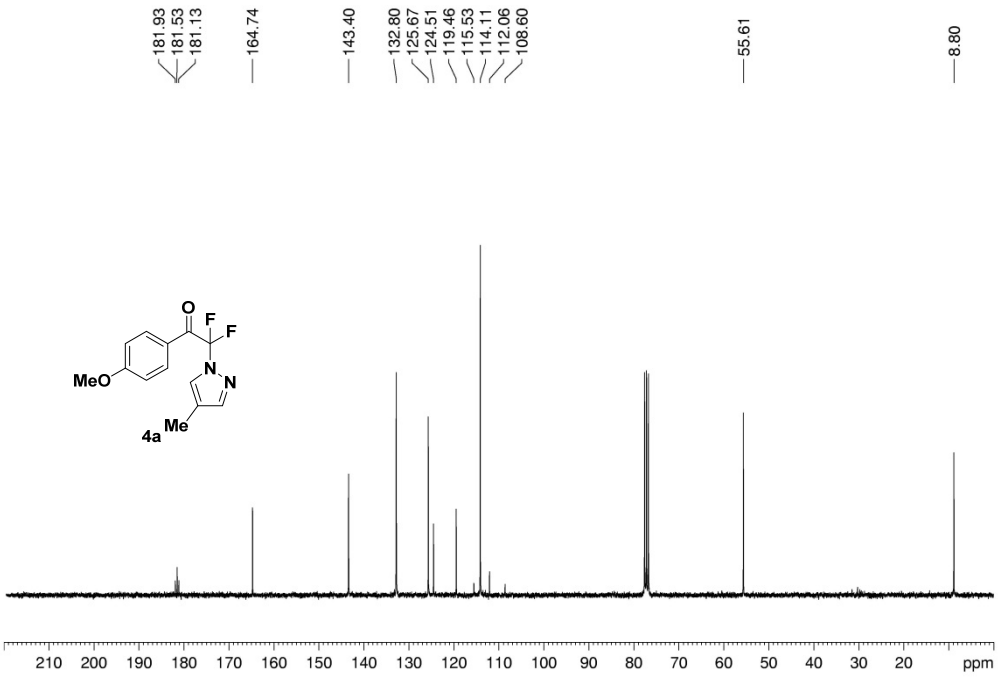
175.47
175.06
140.84
140.54
140.47
140.39
137.07
135.09
126.51
126.35
124.69
124.29
123.42
120.54
113.55
110.05
106.94
106.55
O
F
F
N
N
S
3ah
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


-81.99
O
F
F
N
N
S
3ah
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm


7.91
7.88
7.73
7.42
6.91
6.88
3.84
2.12
O
F
F
MeO
N
N
4a
Me
10
9
8
7
6
5
4
3
2
1
ppm
2.04
1.01
1.00
2.04
3.14
3.11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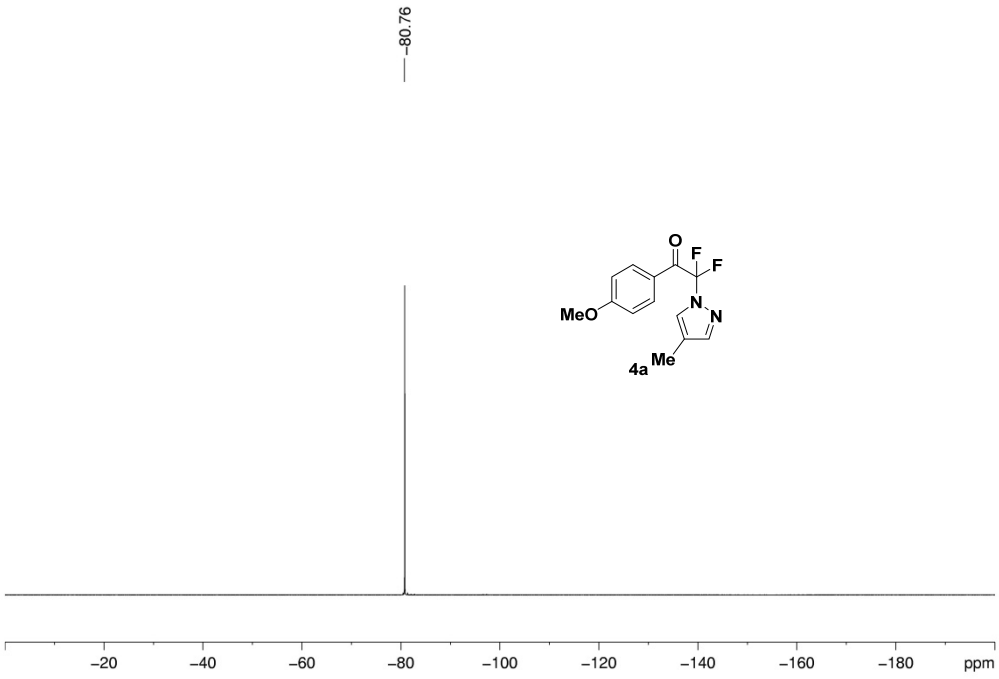
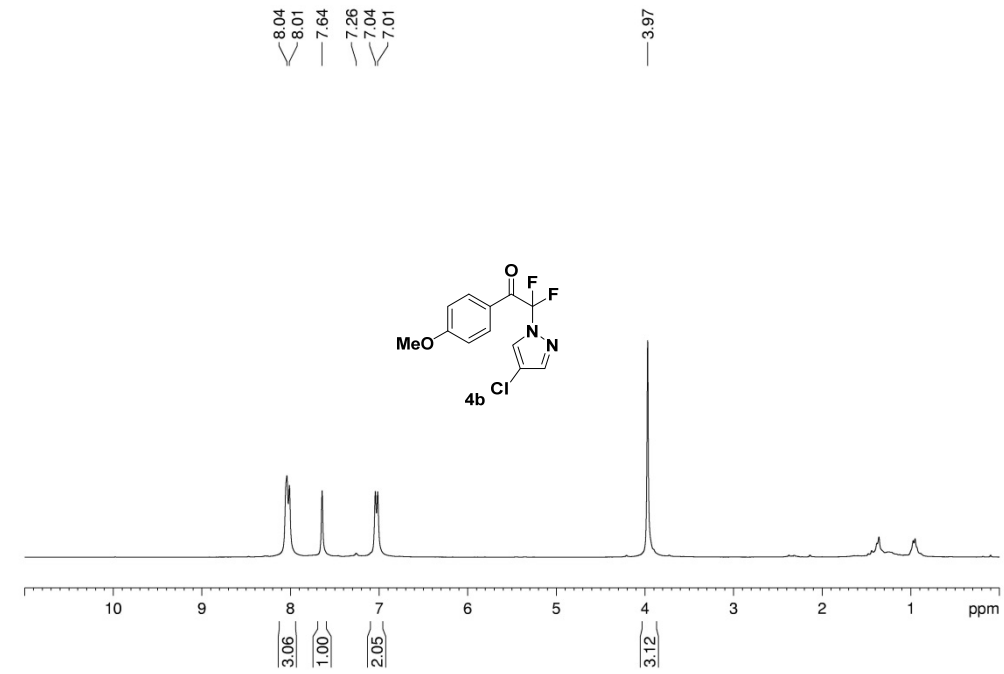
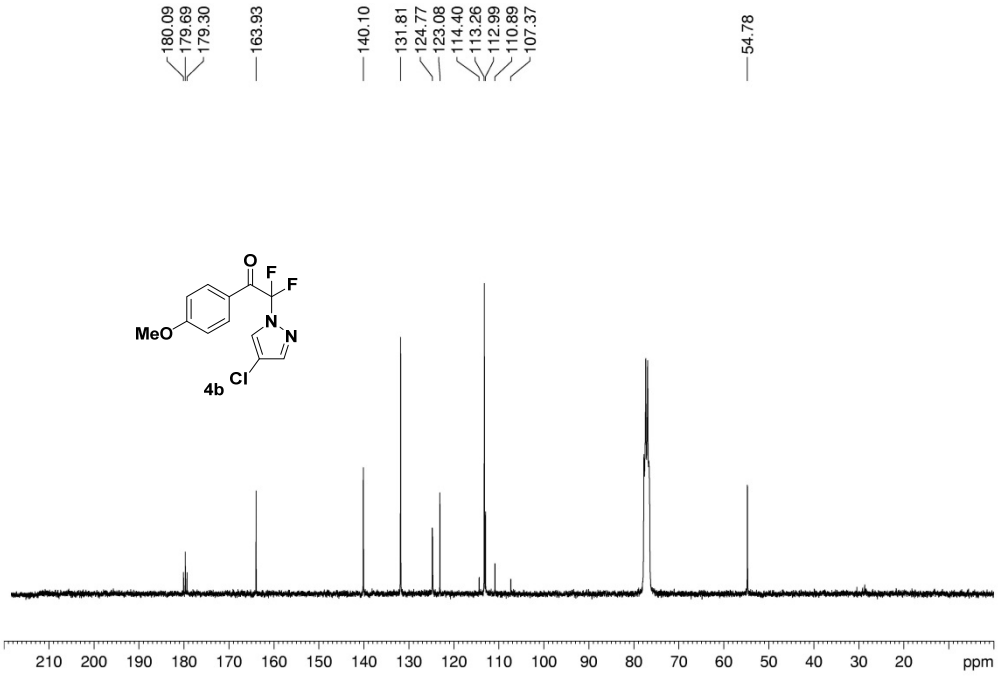
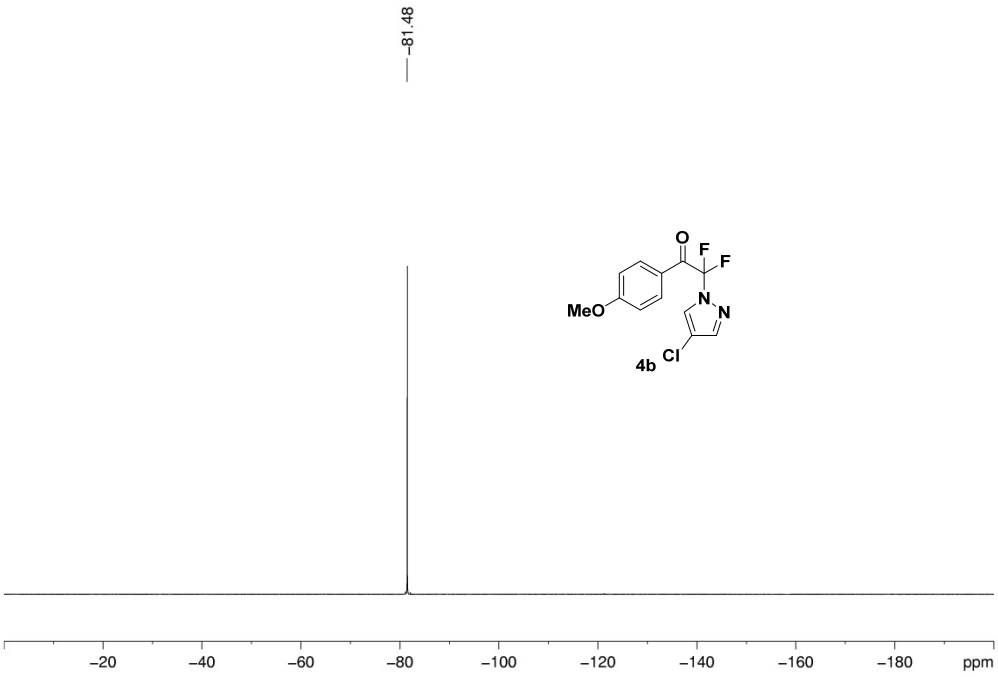
181.53
181.13
164.74
143.40
132.80
125.67
124.51
119.46
115.53
114.11
112.06
108.60
55.61
8.80
O
F
F
MeO
N
N
4a
Me
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


−80.76
O
F
F
MeO
N
N
Me
4a
−20
−40
−60
−80
−100
−120
−140
−160
−180
ppm


8.04
8.01
7.64
7.26
7.04
7.01
3.97
O
F
F
MeO
N
N
Cl
4b
10
9
8
7
6
5
4
3
2
1
ppm
3.06
1.00
2.05
3.12


180.09
179.69
179.30
163.93
140.10
131.81
124.77
123.08
114.40
113.26
112.99
110.89
107.37
54.78
O
F
F
N
N
MeO
Cl
4b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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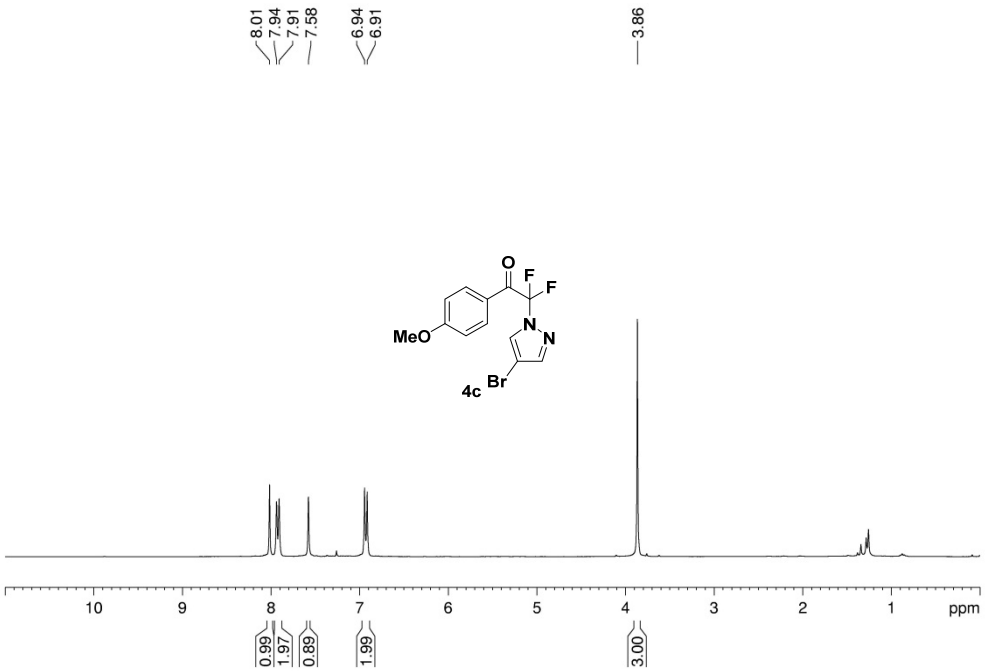
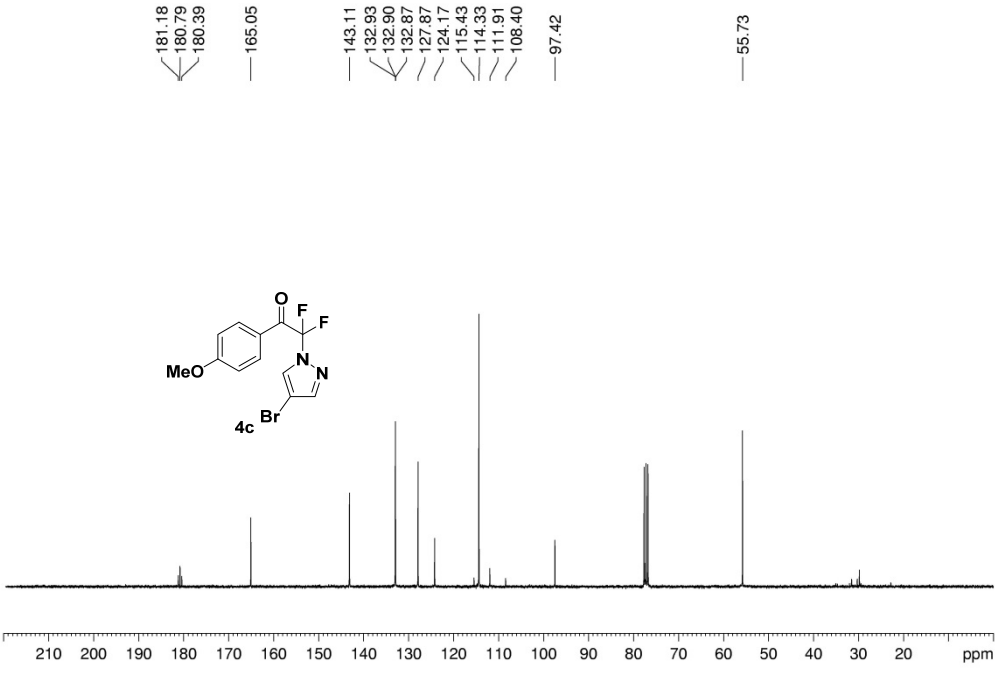
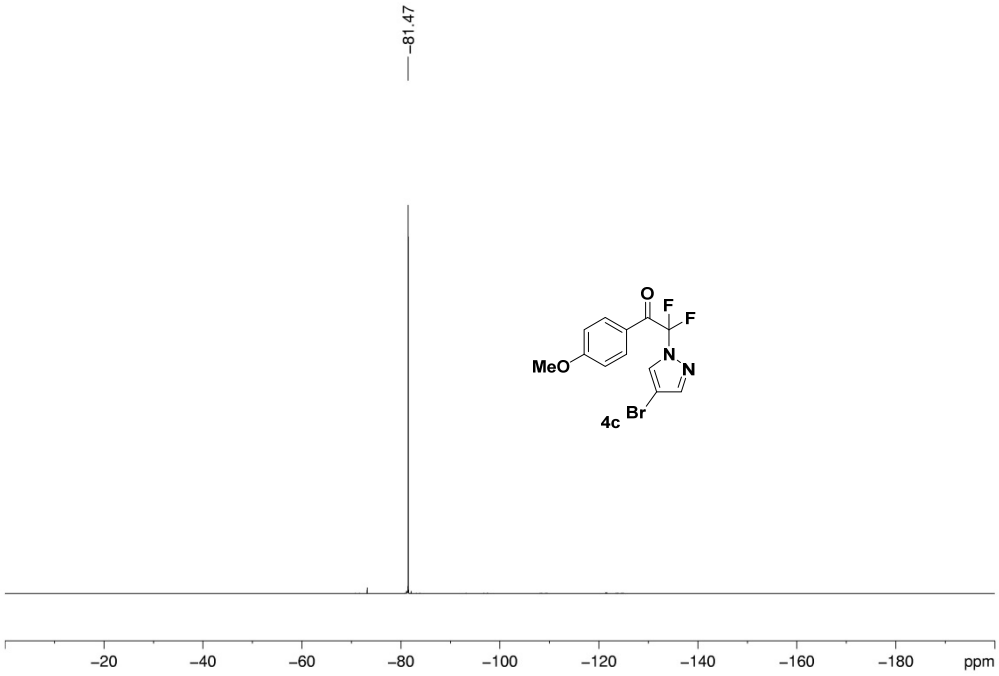
O
F
F
N
N
MeO
Cl
4b
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm


8.01
7.94
7.91
7.58
6.94
6.91
3.86
O
F
F
MeO
N
N
Br
4c
10
9
8
7
6
5
4
3
2
1
ppm
0.99
1.97
0.89
1.99
3.00


181.18
180.79
180.39
165.05
143.11
132.93
132.90
132.87
127.87
124.17
115.43
114.33
111.91
108.40
97.42
55.73
O
F
F
MeO
N
N
Br
4c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-81.47
O
F
F
N
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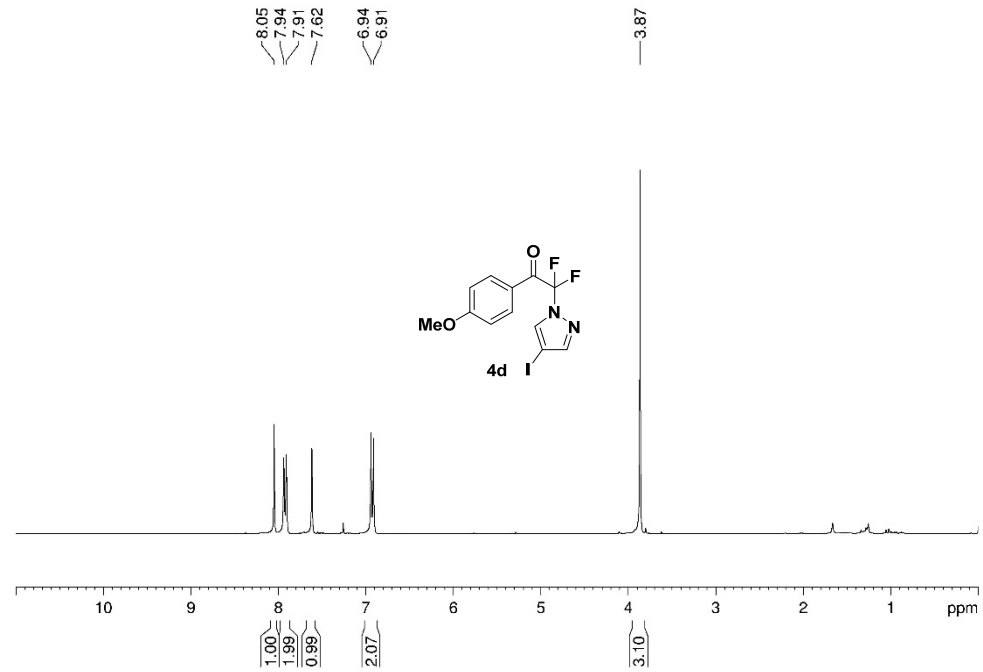
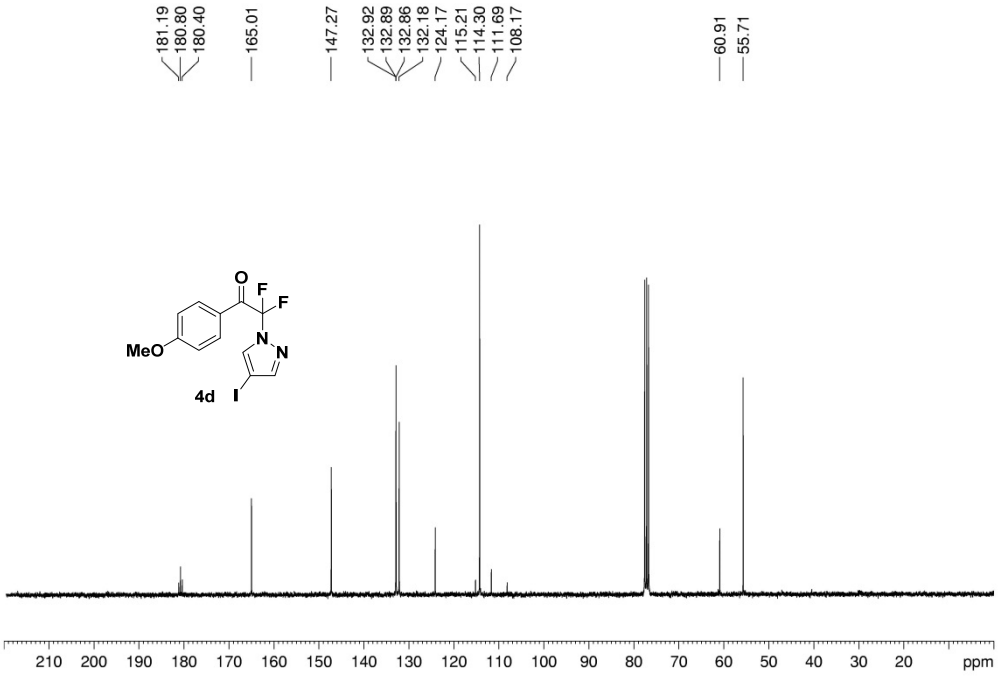
MeO
Br
4c
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


8.05
7.94
7.91
7.62
6.94
6.91
3.87
O
F
F
N
N
MeO
I
4d
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.99
0.99
2.07
3.10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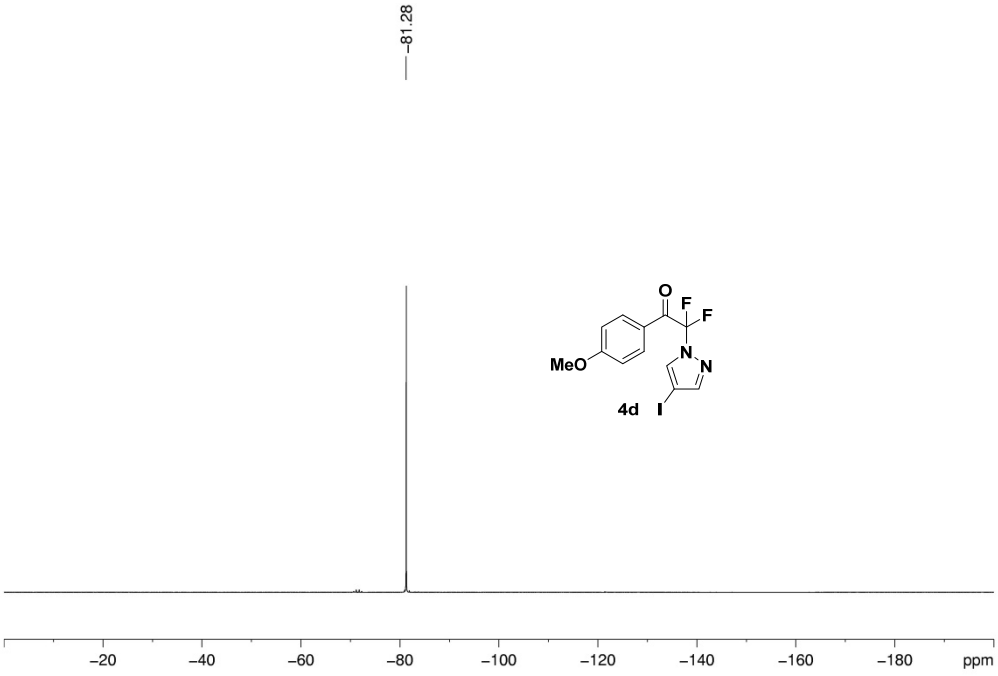
180.80
180.40
165.01
147.27
132.92
132.89
132.86
132.18
124.17
115.21
114.30
111.69
108.17
60.91
55.71
O
F
F
N
N
MeO
4d
I
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm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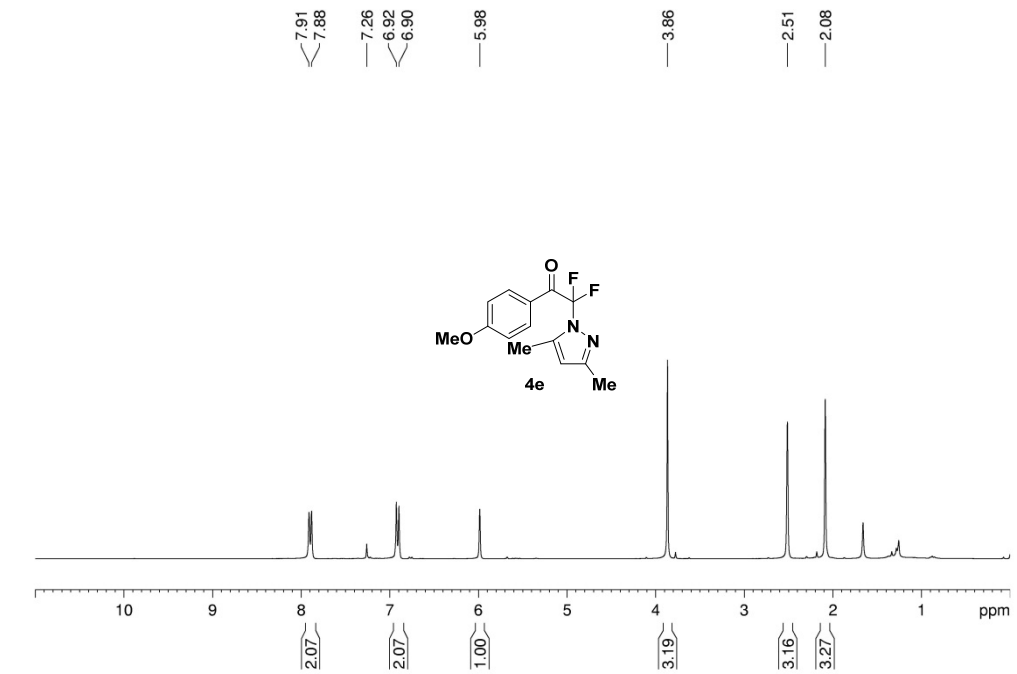
O
F
F
N
N
MeO
4d
I
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm


7.91
7.88
7.26
6.92
6.90
5.98
3.86
2.51
2.08
O
F
F
N
N
MeO
Me
4e
Me
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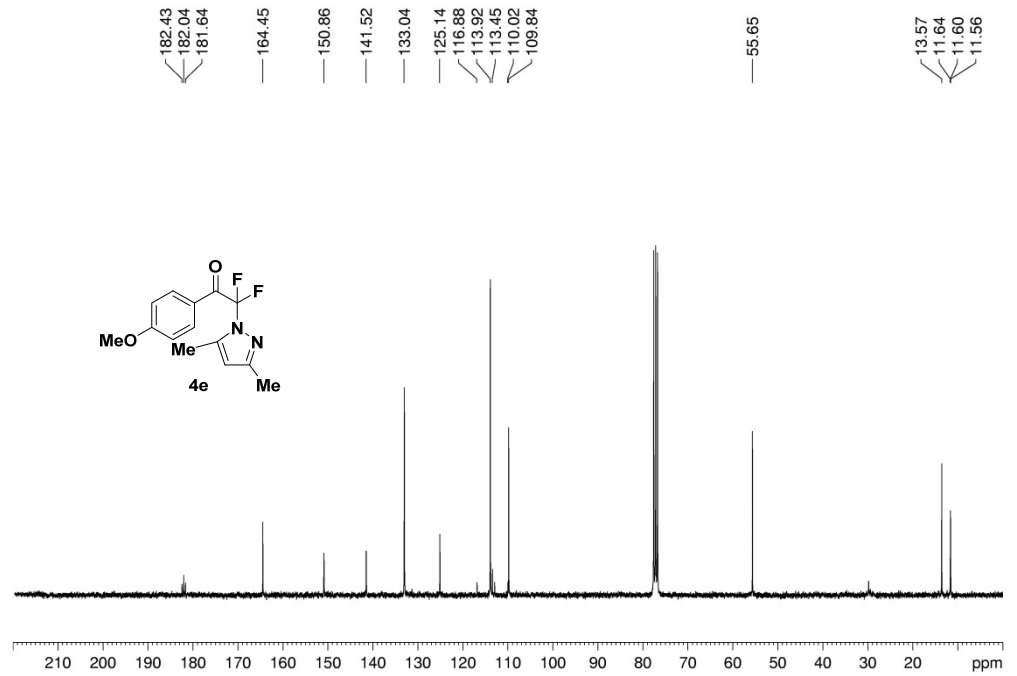
2.07
2.07
1.00
3.19
3.16
3.27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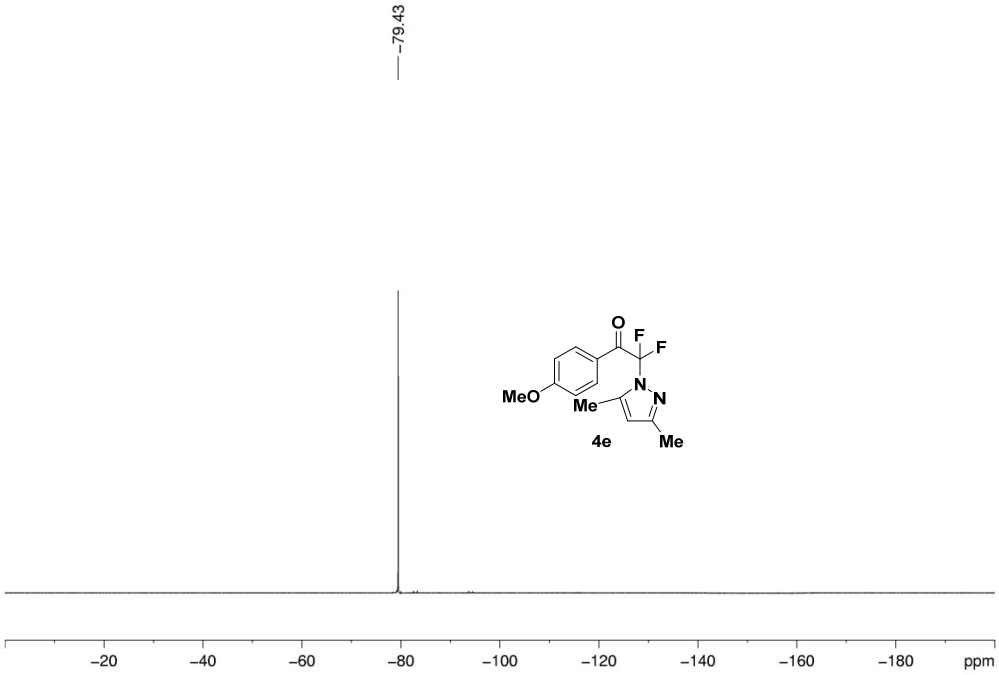
182.04
181.64
164.45
150.86
141.52
133.04
125.14
116.88
113.92
113.45
110.02
109.84
55.65
13.57
11.64
11.60
11.56
O
F
F
N
N
MeO
Me
4e
Me
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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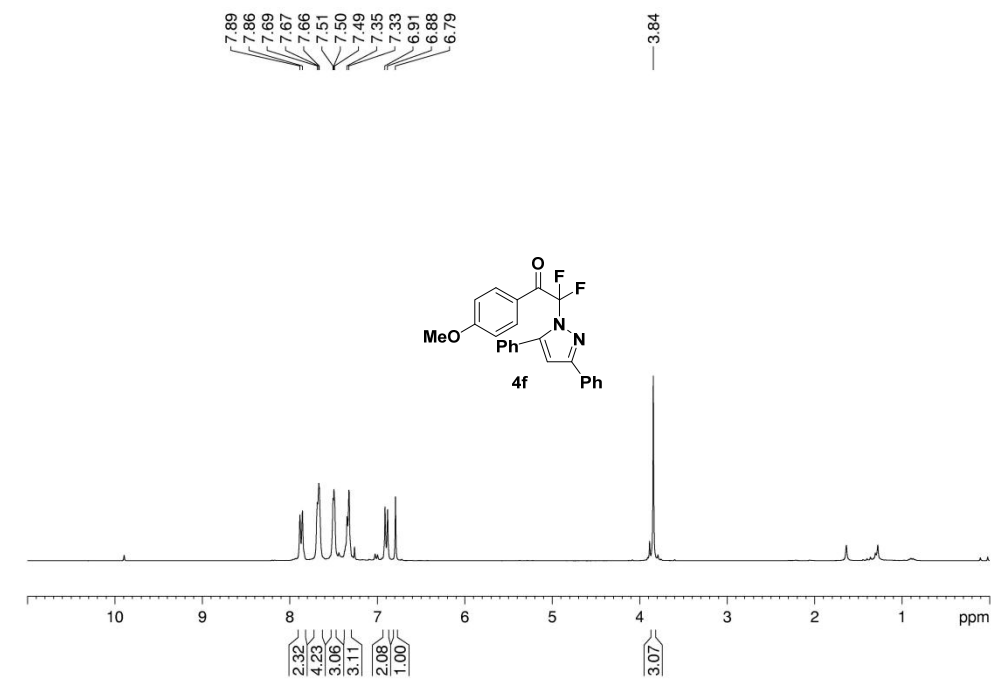
O
F
F
MeO
Me
N
N
Me
4e
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm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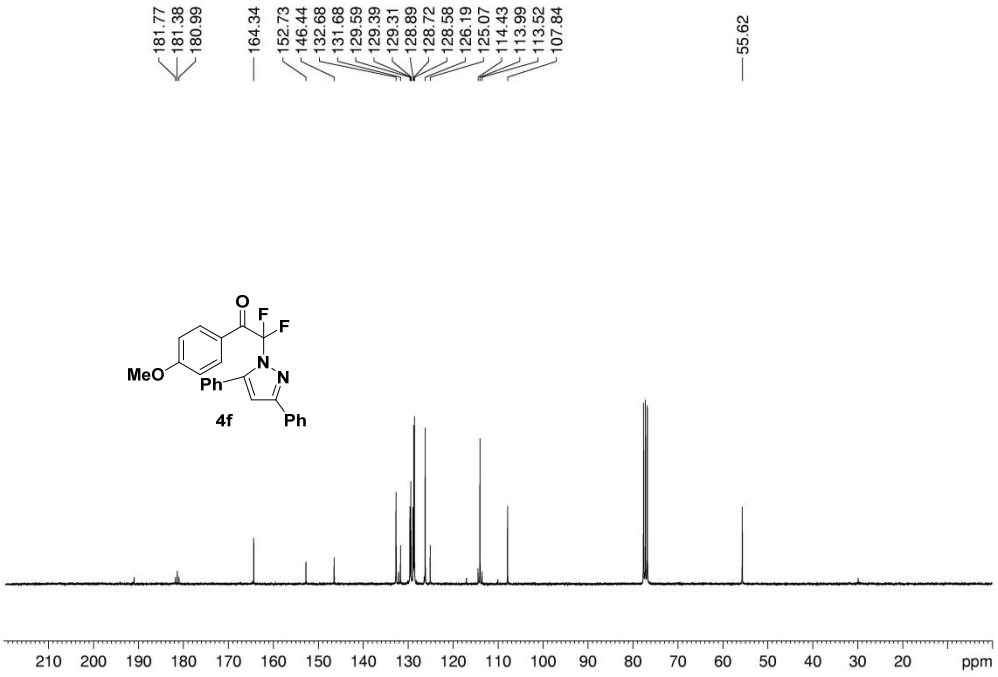
7.86
7.69
7.67
7.66
7.51
7.50
7.49
7.35
7.33
6.91
6.88
6.79
3.84
O
F
F
MeO
Ph
N
N
4f
Ph
10
9
8
7
6
5
4
3
2
1
ppm
2.32
4.23
3.06
3.11
2.08
1.00
3.07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181.38
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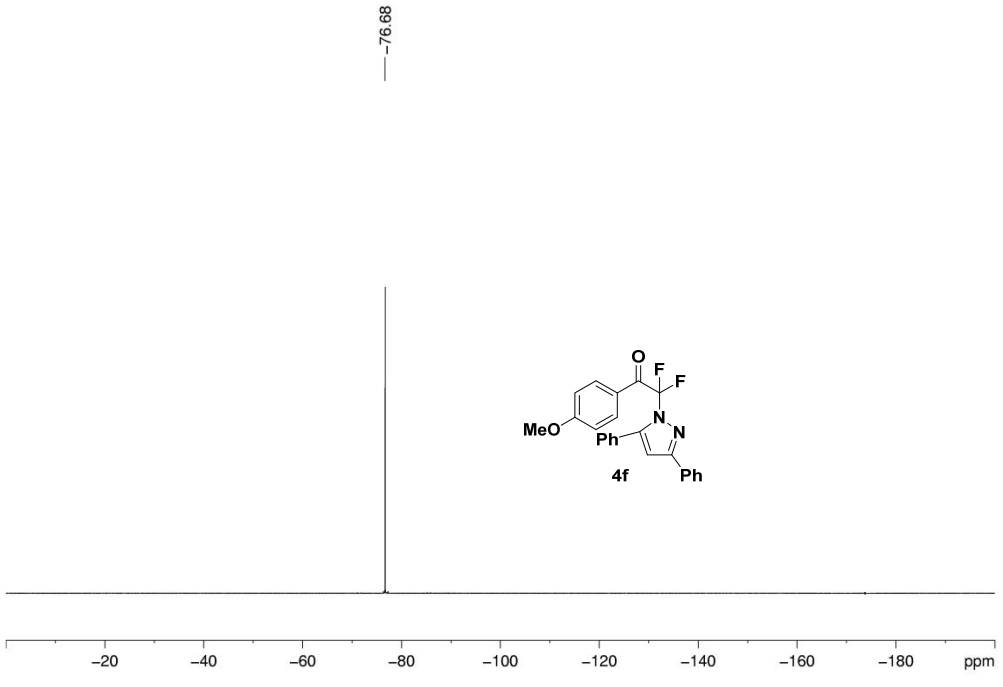
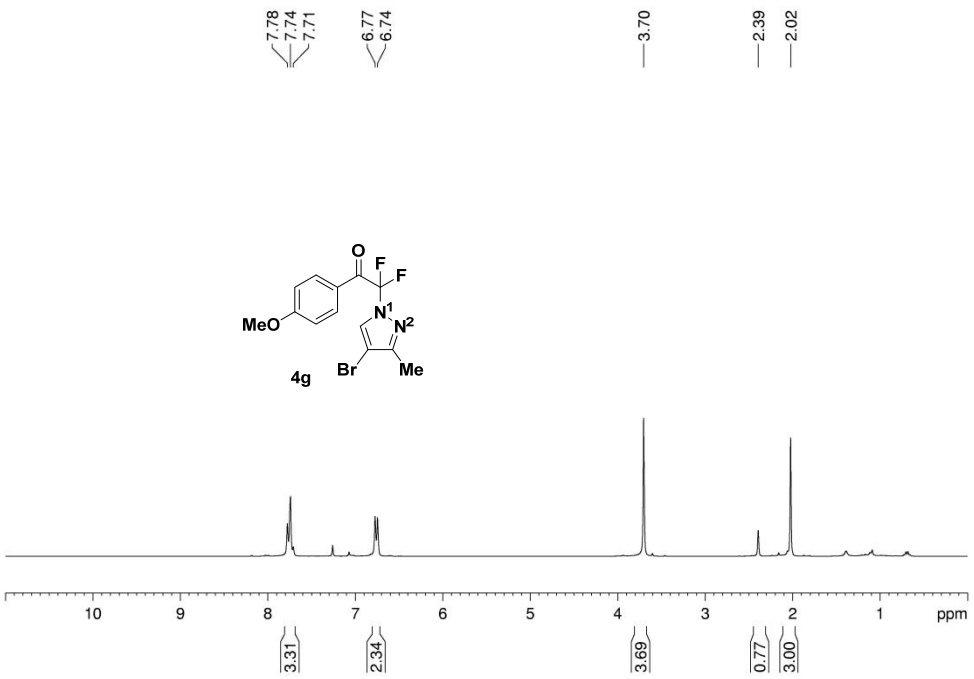
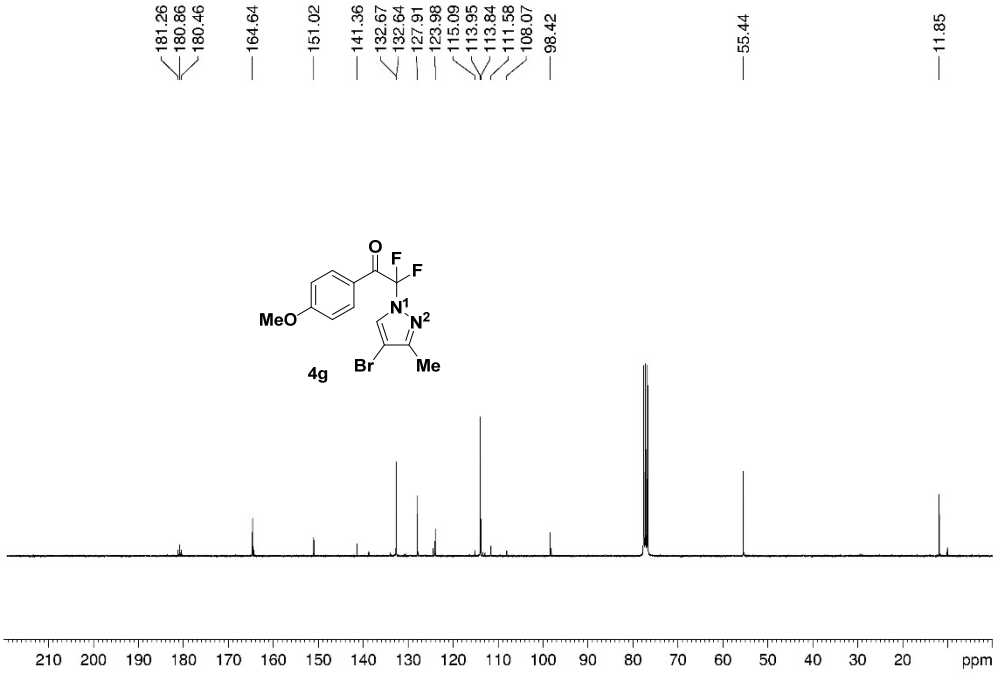
152.73
146.44
132.68
131.68
129.59
129.39
129.31
128.89
128.72
128.58
126.19
125.07
114.43
113.99
113.52
107.84
55.62
O
F
F
N
N
MeO
Ph
Ph
4f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


-76.68
O
F
F
N
N
MeO
Ph
Ph
4f
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm


7.78
7.74
7.71
6.77
6.74
3.70
2.39
2.02
O
F
F
MeO
N1
N2
Br
Me
4g
10
9
8
7
6
5
4
3
2
1
ppm
3.31
2.34
3.69
0.77
3.00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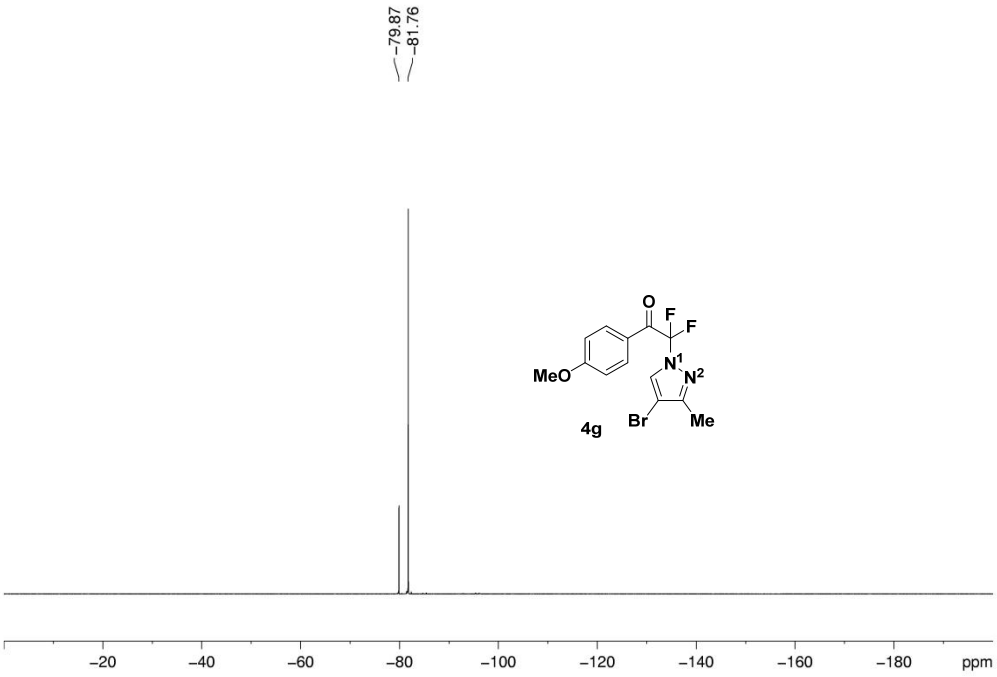
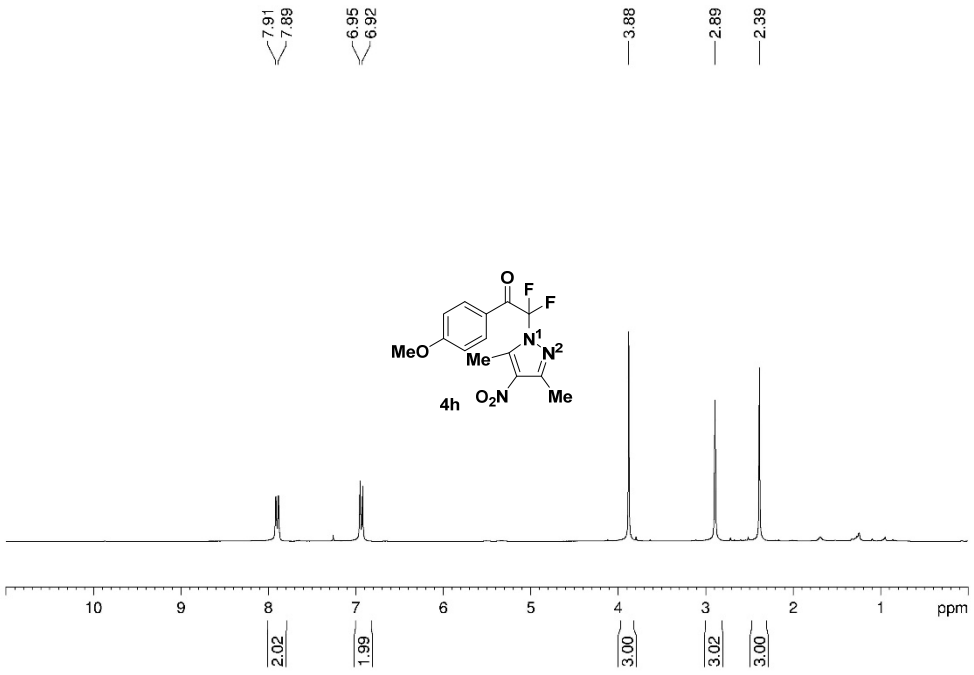
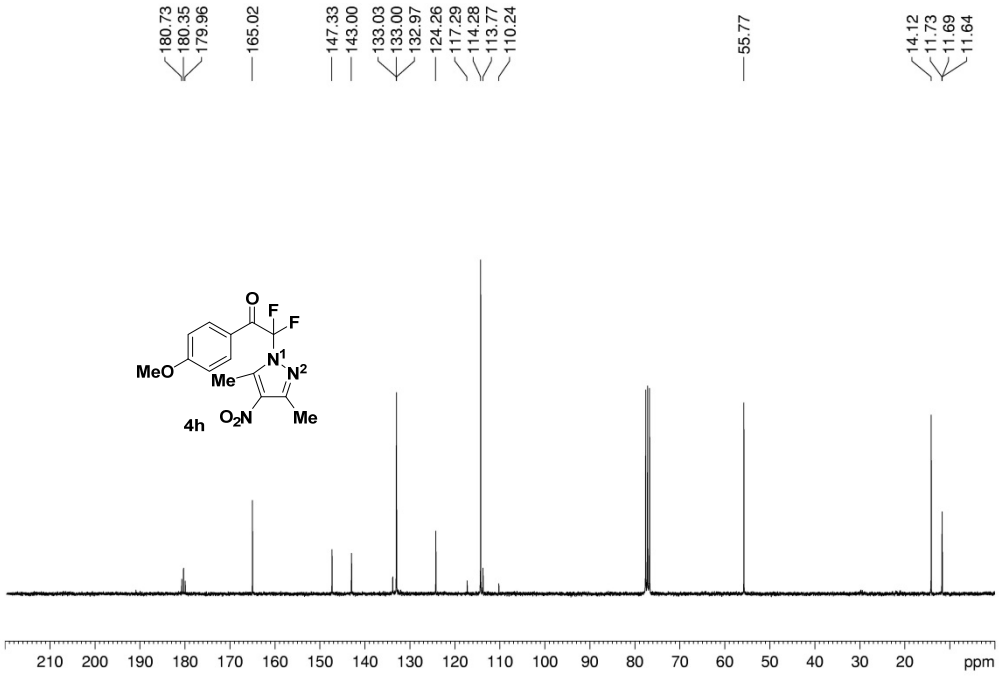
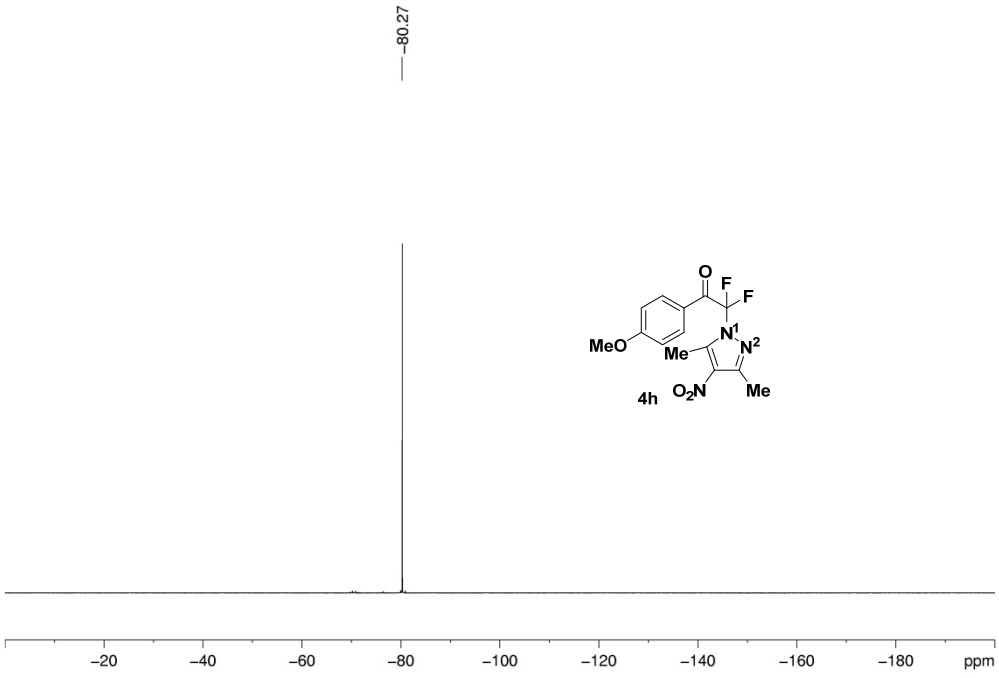
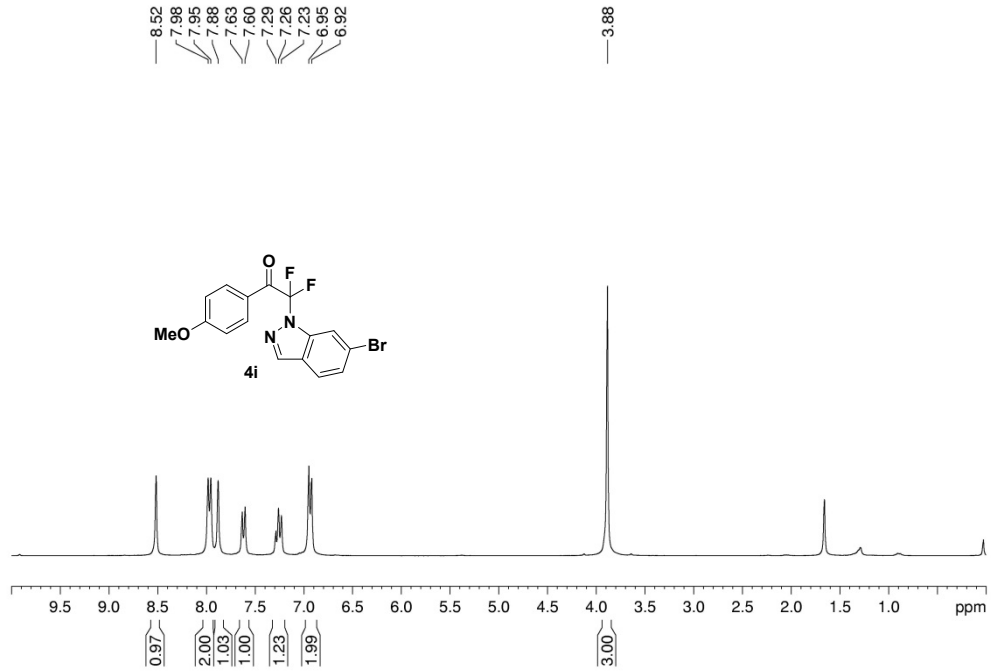
151.02
141.36
132.67
132.64
127.91
123.98
115.09
113.95
113.84
111.58
108.07
98.42
55.44
11.85
O
F
F
MeO
N1
N2
Br
Me
4g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

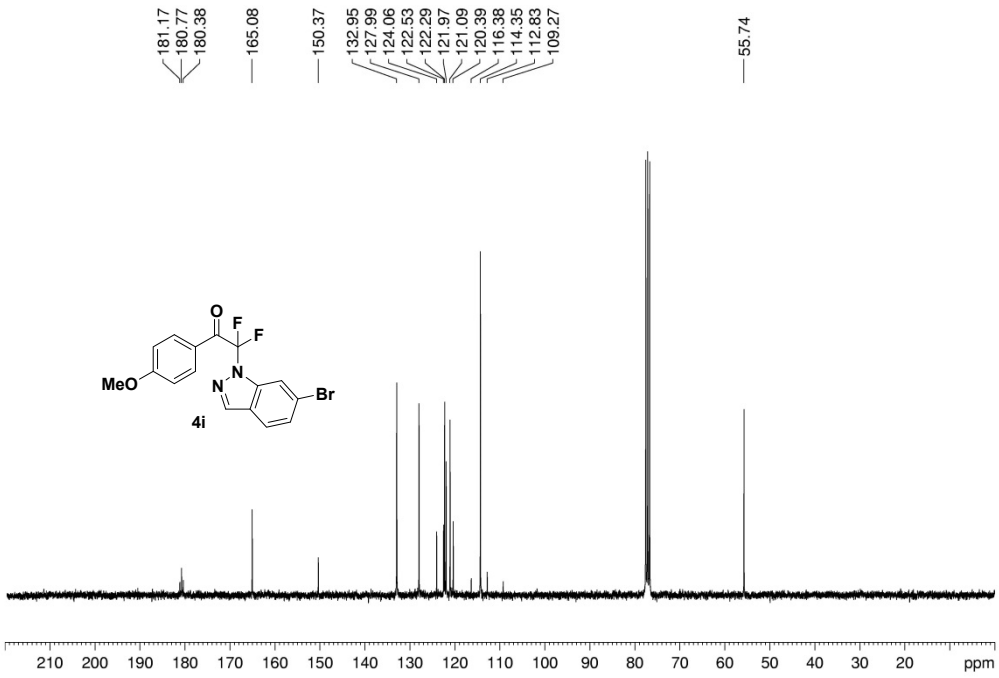

-79.87
-81.76
O
F
F
MeO
N1
N2
Br
Me
4g
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


7.91
7.89
6.95
6.92
3.88
2.89
2.39
O
F
F
MeO
Me
N1
N2
O2N
Me
4h
10
9
8
7
6
5
4
3
2
1
ppm
2.02
1.99
3.00
3.02
3.00


180.73
180.35
179.96
165.02
147.33
143.00
133.03
133.00
132.97
124.26
117.29
114.28
113.77
110.24
55.77
14.12
11.73
11.69
11.64
O
F
F
MeO
N1
N2
Me
O2N
Me
4h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


-80.27
O
F
F
MeO
N1
N2
Me
O2N
Me
4h
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm


8.52
7.98
7.95
7.88
7.63
7.60
7.29
7.26
7.23
6.95
6.92
3.88
O
F
F
MeO
N
N
Br
4i
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
ppm
0.97
2.00
1.03
1.00
1.23
1.99
3.00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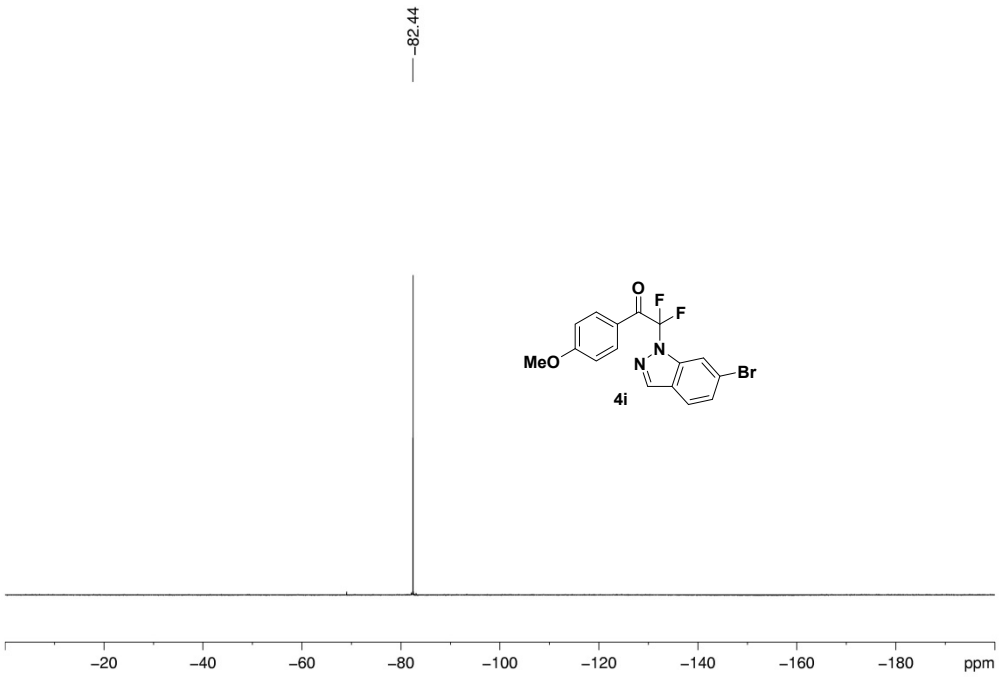
150.37
132.95
127.99
124.06
122.53
122.29
121.97
121.09
120.39
116.38
114.35
112.83
109.27
55.74
O
F
F
MeO
N
N
Br
4i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm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O
F
F
N
N
MeO
Br
4i
-20
-40
-60
-80
-100
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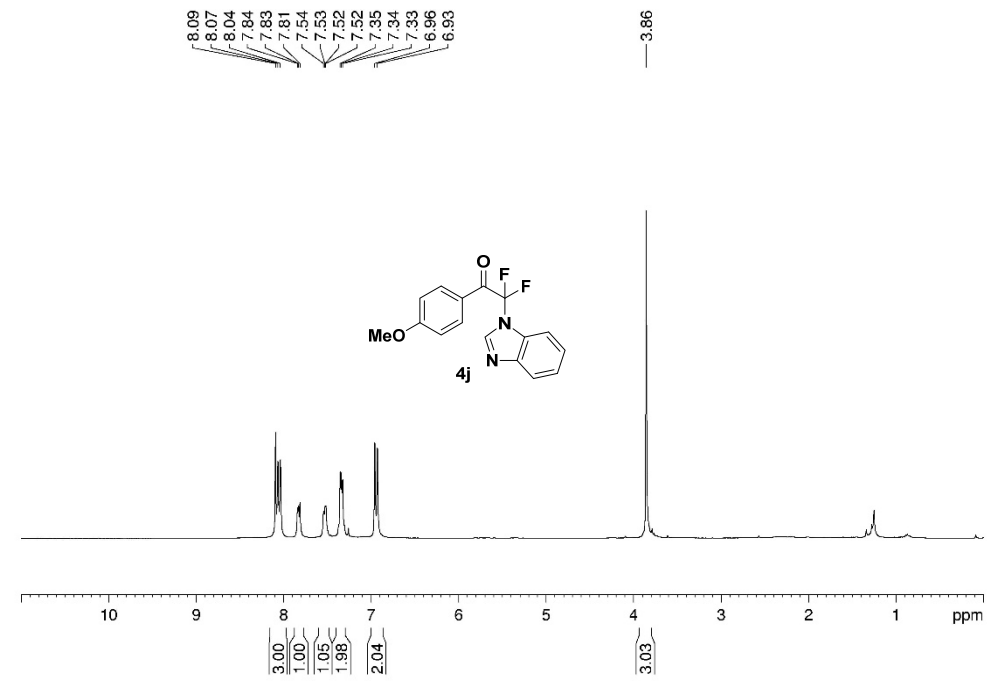
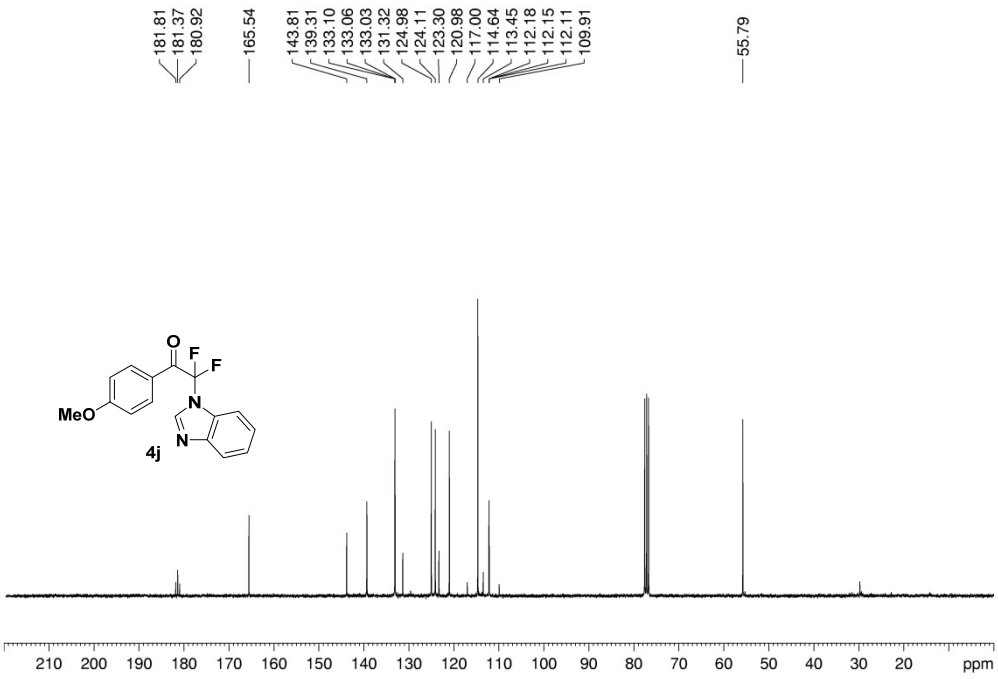
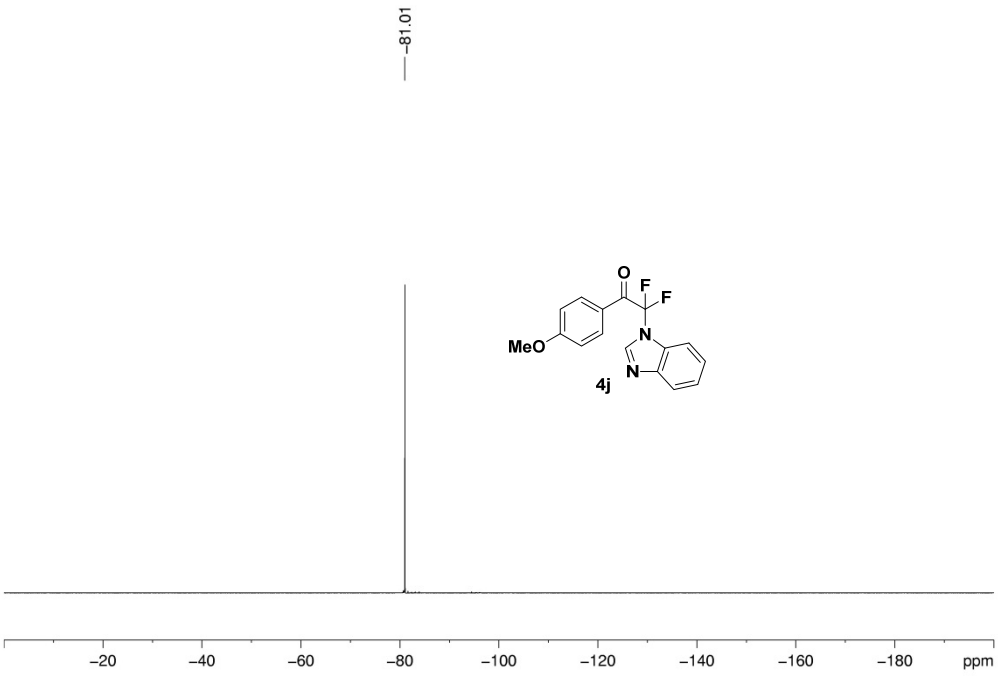
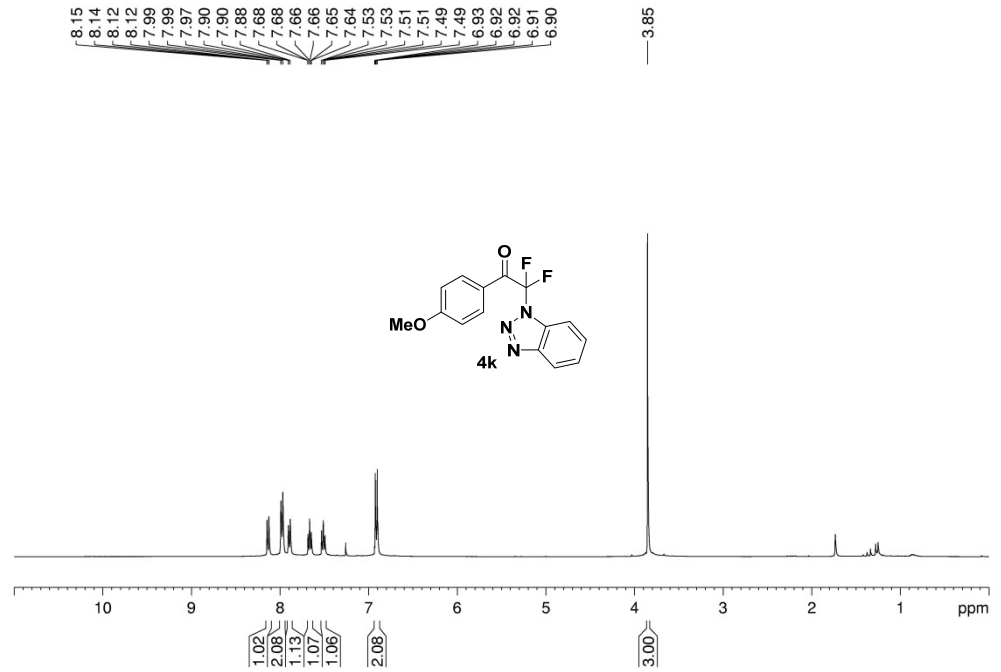
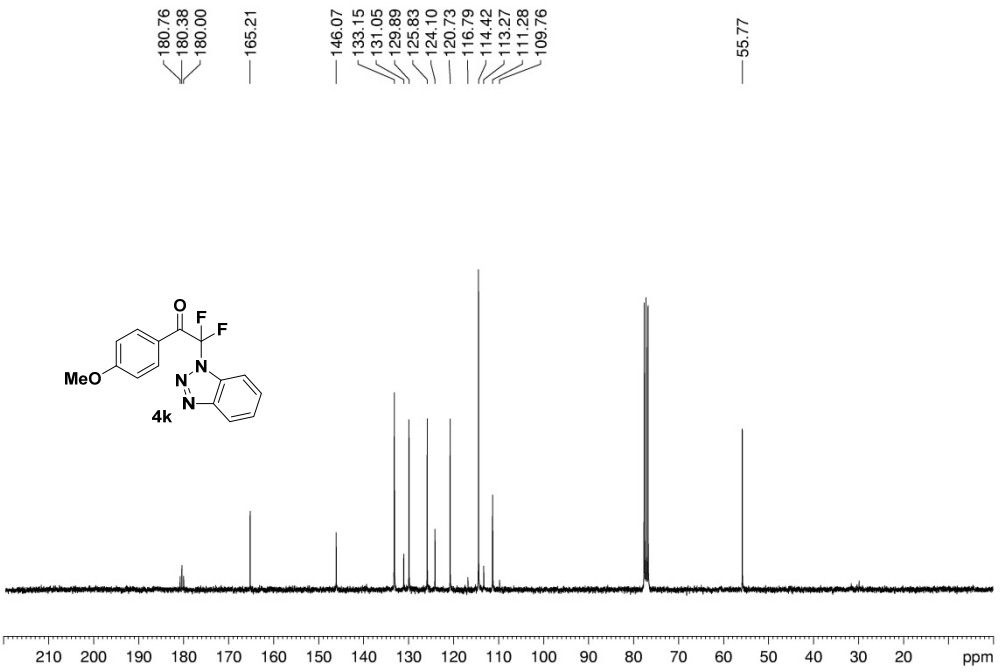
-140
-160
-180
ppm

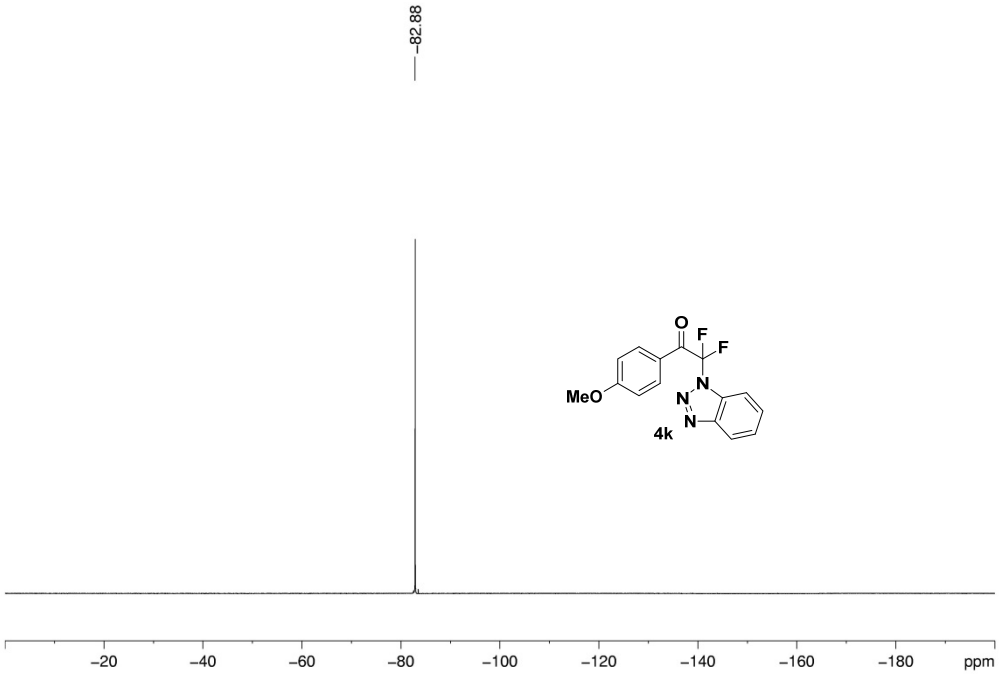

8.09
8.07
8.04
7.84
7.83
7.81
7.54
7.53
7.52
7.52
7.35
7.34
7.33
6.96
6.93
3.86
O
F
F
N
N
MeO
4j
10
9
8
7
6
5
4
3
2
1
ppm
3.00
1.00
1.05
1.98
2.04
3.03

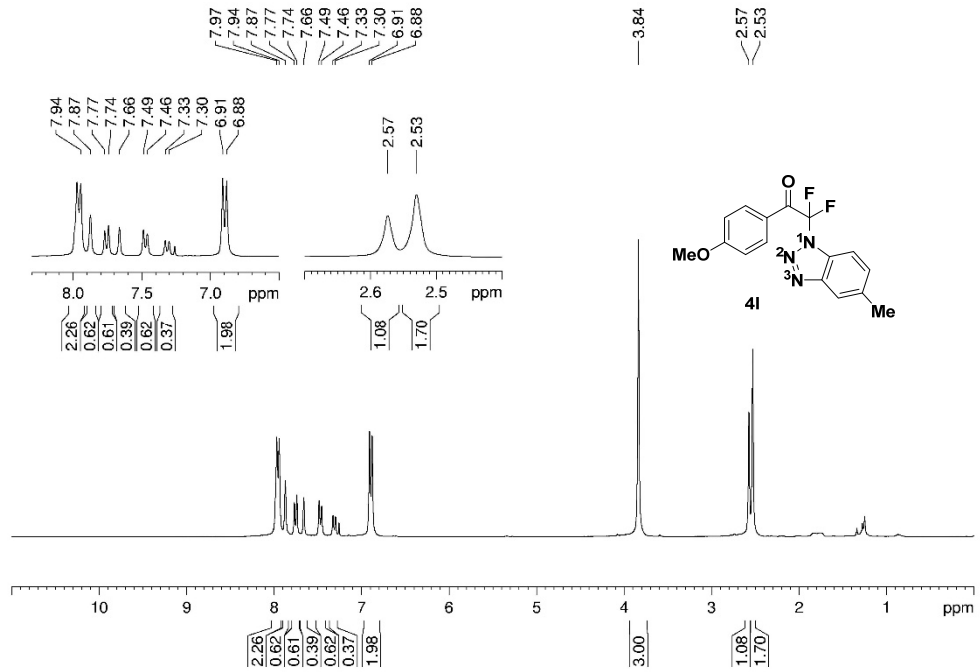

181.81
181.37
180.92
165.54
143.81
139.31
133.10
133.06
133.03
131.32
124.98
124.11
123.30
120.98
117.00
114.64
113.45
112.18
112.15
112.11
109.91
55.79
O
F
F
N
MeO
N
4j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

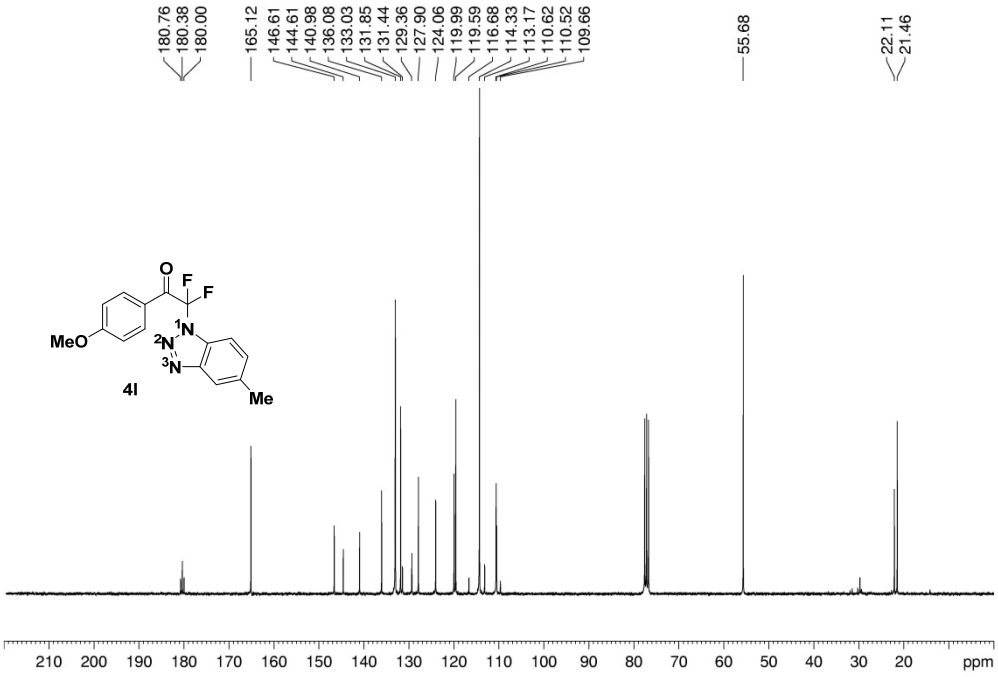

-81.01
O
F
F
N
MeO
N
4j
-20 -40 -60 -80 -100 -120 -140 -160 -180 ppm

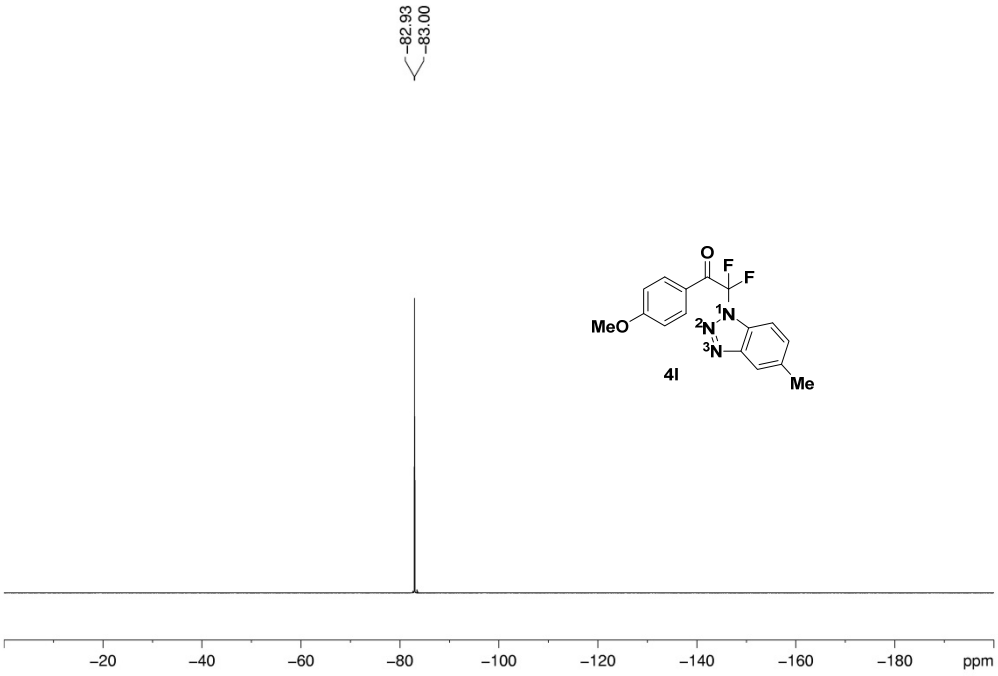

8.15
8.14
8.12
8.12
7.99
7.99
7.97
7.90
7.90
7.88
7.68
7.68
7.66
7.66
7.65
7.64
7.53
7.53
7.51
7.51
7.49
7.49
6.93
6.92
6.92
6.91
6.90
3.85
O
F
F
N
N
N
MeO
4k
10
9
8
7
6
5
4
3
2
1
ppm
1.02
2.08
1.13
1.07
1.06
2.08
3.00


180.76
180.38
180.00
165.21
146.07
133.15
131.05
129.89
125.83
124.10
120.73
116.79
114.42
113.27
111.28
109.76
55.77
O
F
F
N
N
N
MeO
4k
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


-82.88
O
F
F
N
N
N
MeO
4k
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


7.97
7.94
7.87
7.77
7.74
7.66
7.49
7.46
7.33
7.30
6.91
6.88
3.84
2.57
2.53
O
F
F
MeO
N
N
N
Me
4l
8.0
7.5
7.0
ppm
2.6
2.5
ppm
2.26
0.62
0.61
0.39
0.62
0.37
1.98
1.08
1.70
10
9
8
7
6
5
4
3
2
1
ppm
3.00


180.76
180.38
180.00
165.12
146.61
144.61
140.98
136.08
133.03
131.85
131.44
129.36
127.90
124.06
119.99
119.59
116.68
114.33
113.17
110.62
110.52
109.66
55.68
22.11
21.46
O
F
F
MeO
1N
2N
3N
Me
4l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


82.93
83.00
O
F
F
MeO
1N
2N
3N
Me
4l
−20 −40 −60 −80 −100 −120 −140 −160 −180 ppm