

# Dicarbofunctionalization of Unactivated Alkenes by Palladium-Catalyzed Domino Heck/Intermolecular Direct Hetero Arylation with Heteroarenes

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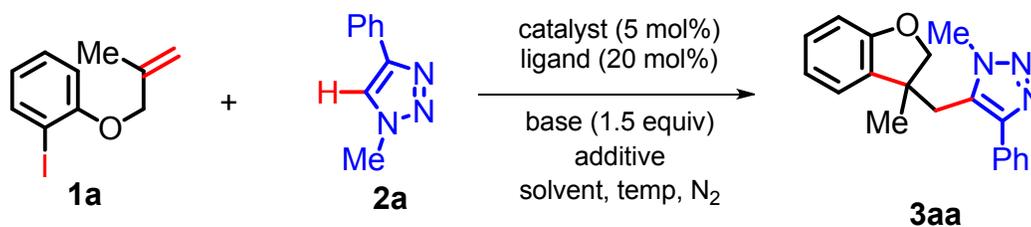
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## 1. Optimization of the Reaction Conditions:

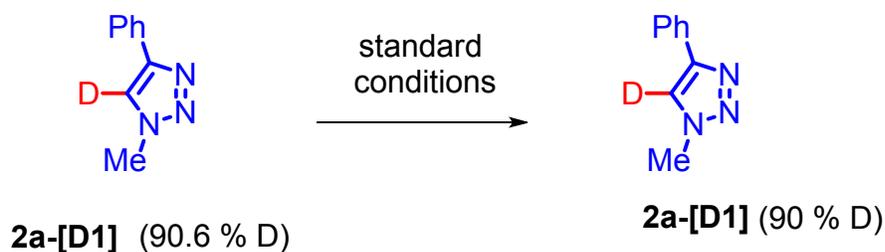


entry	catalyst	ligand	base	additive	solvent	time	Yield (%)
1 <sup>a</sup>	[Pd(allyl)Cl] <sub>2</sub>	BINAP	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	52
2 <sup>a</sup>	[Pd(allyl)Cl] <sub>2</sub>	dppp	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	28
3 <sup>a</sup>	[Pd(allyl)Cl] <sub>2</sub>	Jonphos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	21
4 <sup>a</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	61
5 <sup>a</sup>	[Pd(allyl)Cl] <sub>2</sub>	PPh <sub>3</sub>	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	20
6 <sup>b</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	CsOAc	PivOH	THF	44 h	10
7 <sup>b</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	CsOPiv	PivOH	THF	44 h	11

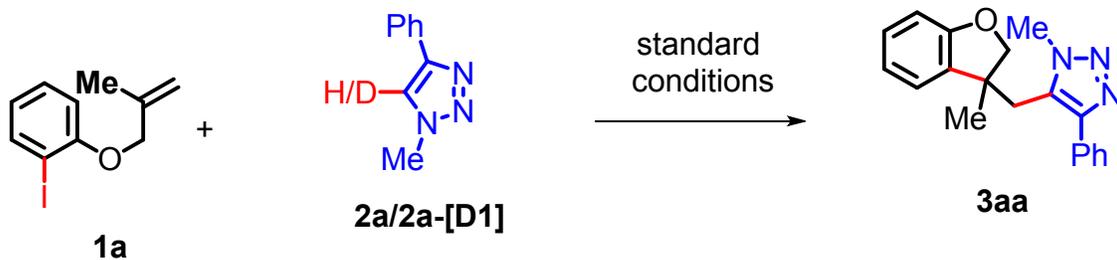
8 <sup>b</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	K <sub>2</sub> OBU	PivOH	THF	44 h	n.d.
9 <sup>b</sup>	Pd(OAc) <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	26
10 <sup>b</sup>	Pd(PPh <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	17
11 <sup>b</sup>	Pd <sub>2</sub> (dba) <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	44 h	36
12 <sup>b</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	CH <sub>3</sub> CN	44 h	21
13 <sup>b</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	Toluene	44 h	29
14 <sup>b</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	Dioxane	44 h	11
15 <sup>b</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	DMF	44 h	n.d.
16 <sup>c</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PTSA.H <sub>2</sub> O	THF	44 h	trace
17 <sup>c</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	<i>p</i> -nitro benzoic acid	THF	44 h	trace
18 <sup>c,d</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	23 h	83
19 <sup>c,d,e</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	41 h	87
20 <sup>c,d,e</sup>	Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	23 h	63
21 <sup>c,d,f</sup>	Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	24 h	9
22 <sup>c,d,g</sup>	[Pd(allyl)Cl] <sub>2</sub>	CycloJohnPhos	Cs <sub>2</sub> CO <sub>3</sub>	PivOH	THF	24 h	42

<sup>a</sup> Reaction conditions: **1a** (1.5 equiv), **2a** (1.0 equiv, 0.06 mmol), catalyst (5 mol%), ligand (5 mol%), PivOH (30 mol%) and base (1.5 equiv) in THF (1 mL) at 80 °C under N<sub>2</sub> for 24 – 44h, <sup>1</sup>H NMR yield using 3,4,5-trichloropyridine as internal standard. n.d. = not detected. <sup>b</sup>ligand (10 mol%). <sup>c</sup> CycloJohnPhos (20 mol%), <sup>d</sup>**1a** (2.0 equiv), <sup>e</sup>PivOH (1.0 equiv), <sup>f</sup>60 °C, <sup>g</sup>70 °C.

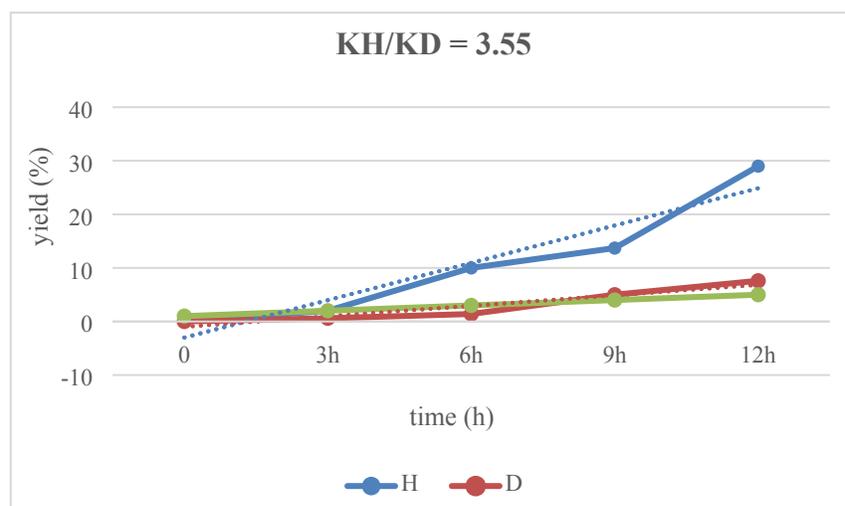
## 2. Deuterium Kinetic Isotope Experiment:



General Procedure for control experiment: **2a-[D1]** was submitted to the standard conditions for 1 h and no loss of deuterium in **2a-[D1]** was observed by <sup>1</sup>H NMR.



General procedure for KIE experiments: Two sets of reactions were carried out in parallel under the same conditions. In each case **1a** (2.0 equiv) was allowed to react with **2a** (1.0 equiv, 0.06 mmol) and **2a-[D1]** (1.0 equiv, 0.06 mmol) respectively, under standard condition. The conversion of the crude reaction mixture was measured carefully at regular time intervals (at 3 h) by  $^1\text{H}$  NMR using 3,4,5-trichloropyridine as an internal standard to compare the initial rates.



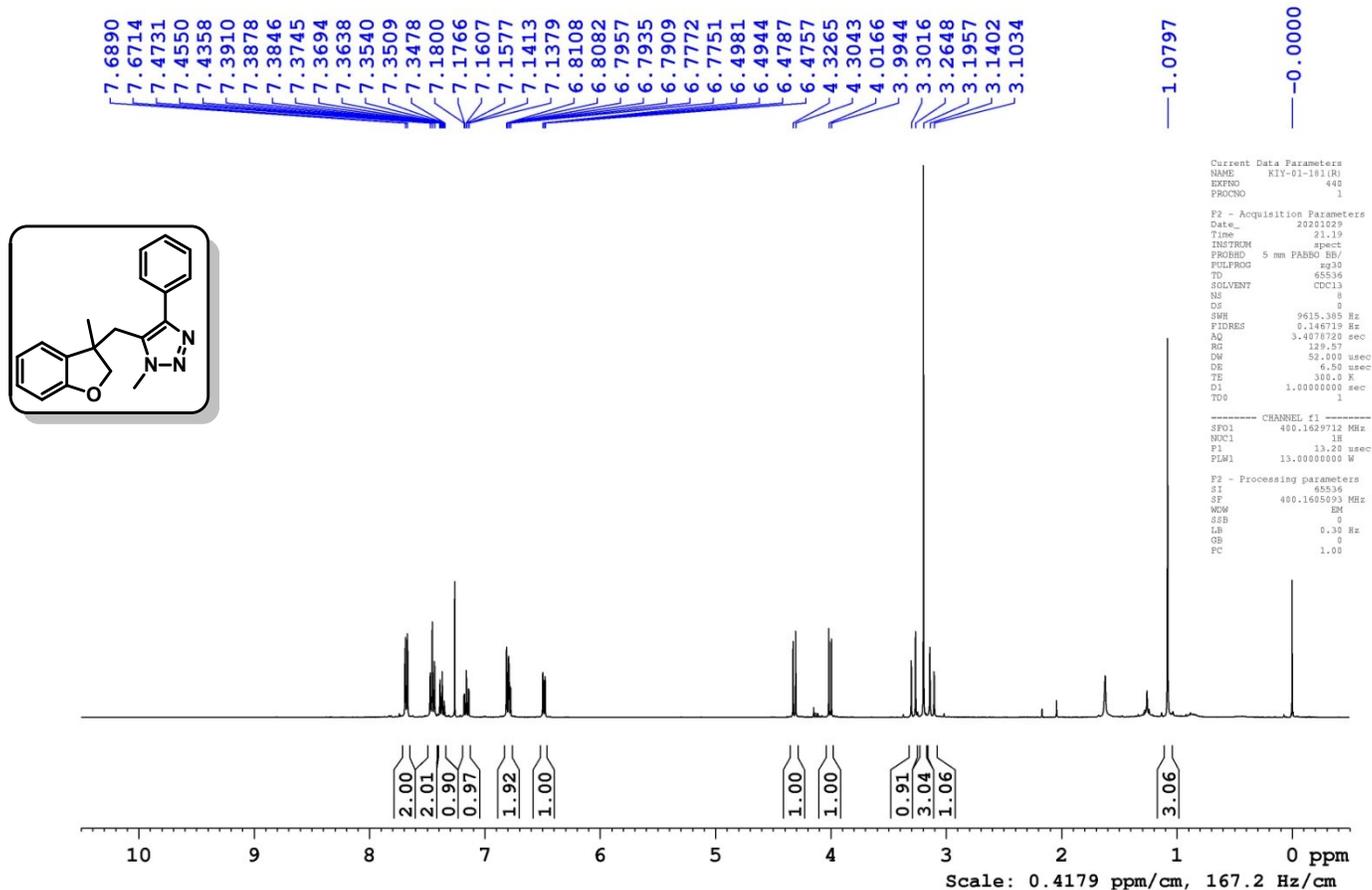


Figure S-1: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3aa

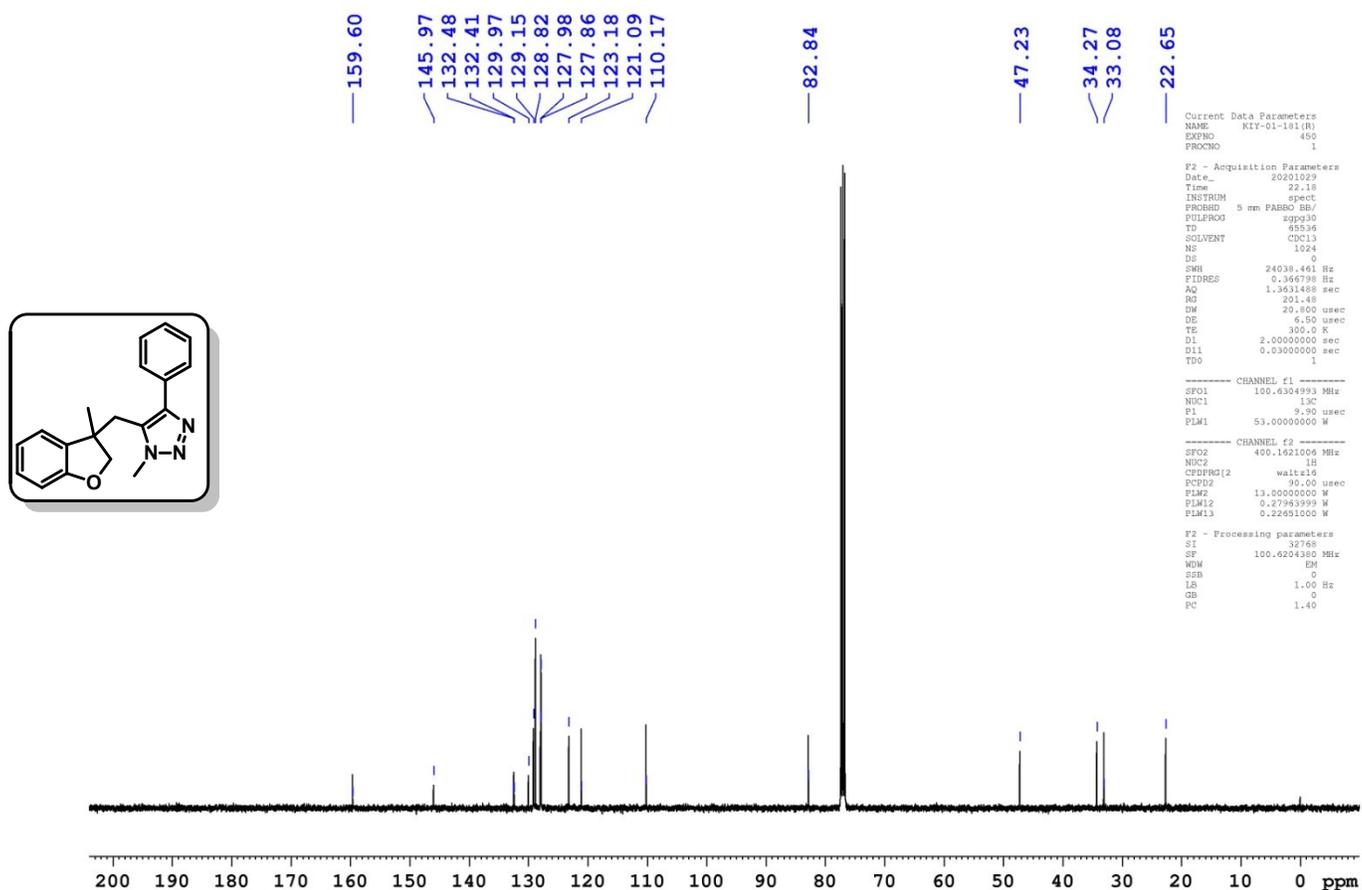


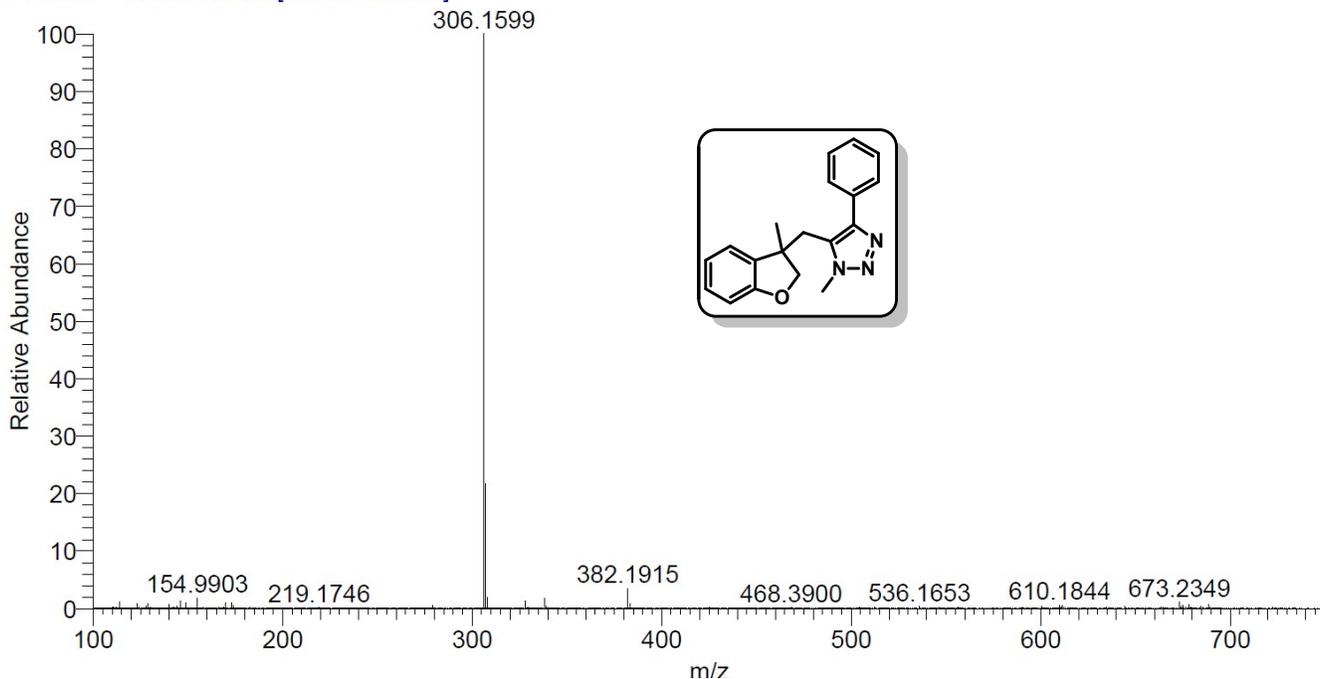
Figure S-2: <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3aa

**SAIF [HRMS Report]**

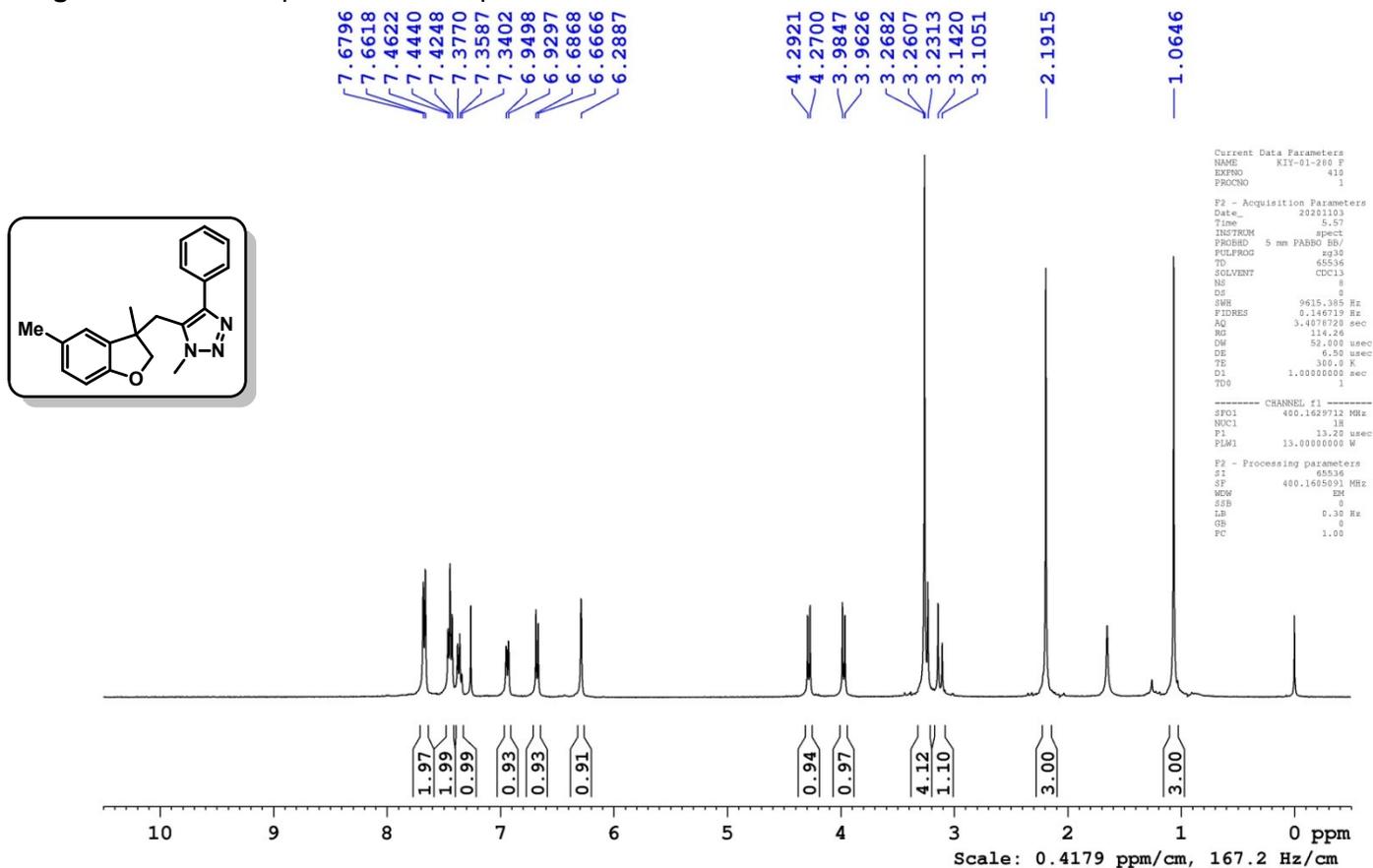
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 2020  
 Sample Name:  
 Run Time(min): 0.00  
 Injection Volume(μl): 1.00

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 T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-3** HRMS spectrum of compound **3aa**



**Figure S-4** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ba**

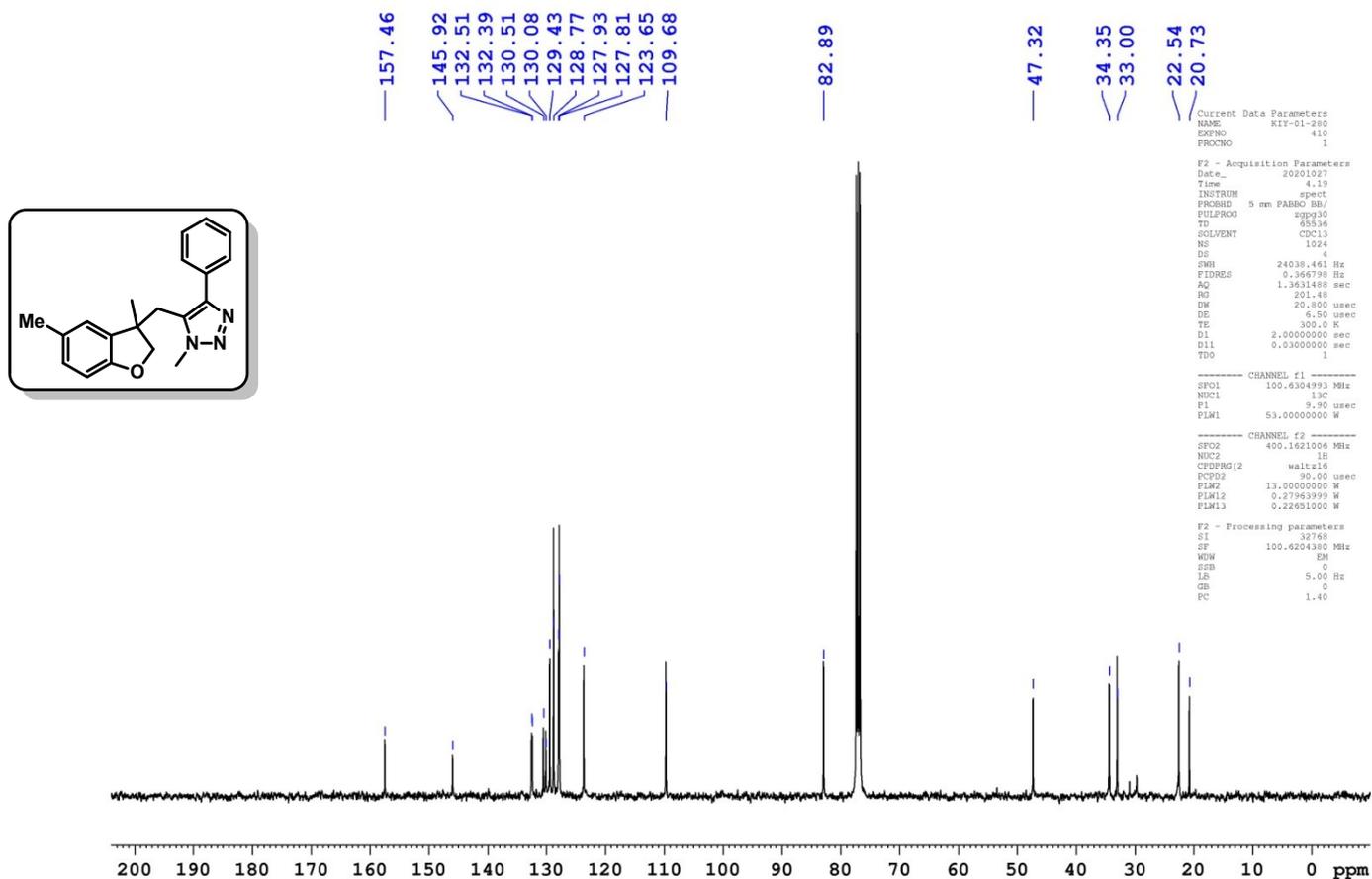


Figure S-5  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) spectrum of compound 3ba

SAIF [HRMS Report]

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Vial:	CStk1-01:17	Injection Volume( $\mu\text{l}$ ):	1.00

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 T: FTMS + c ESI Full ms [100.00-750.00]

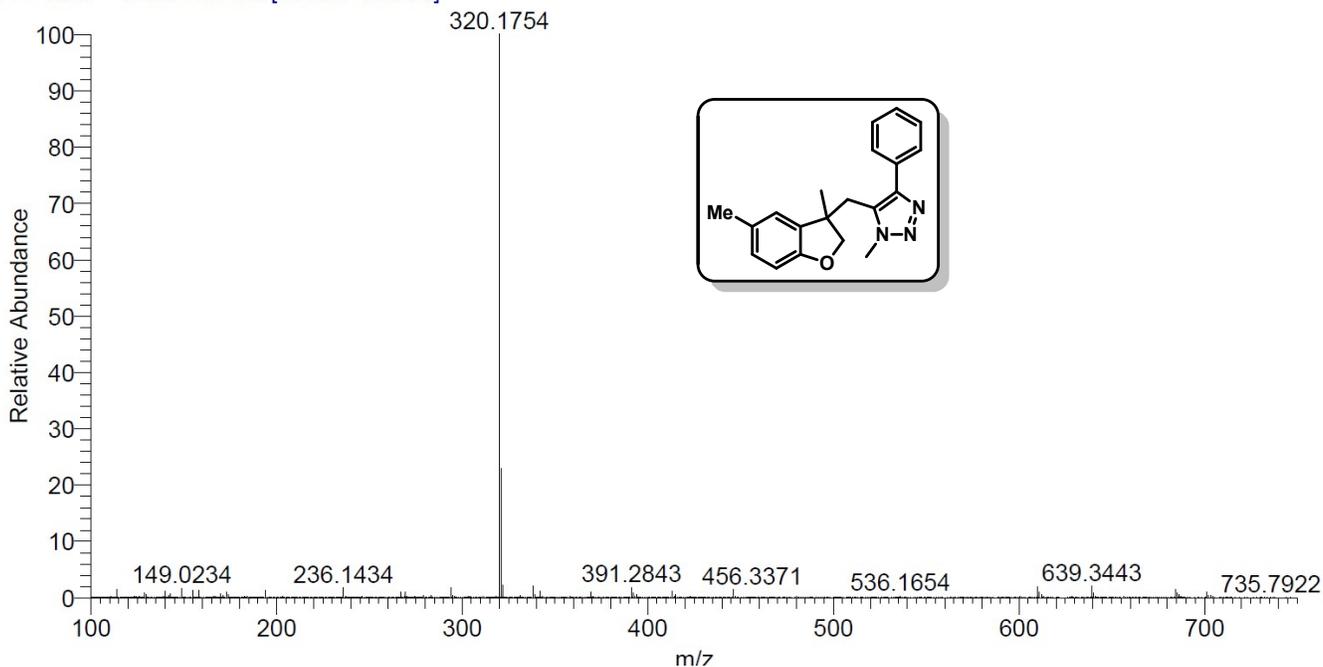


Figure S-6 HRMS spectrum of compound 3ba

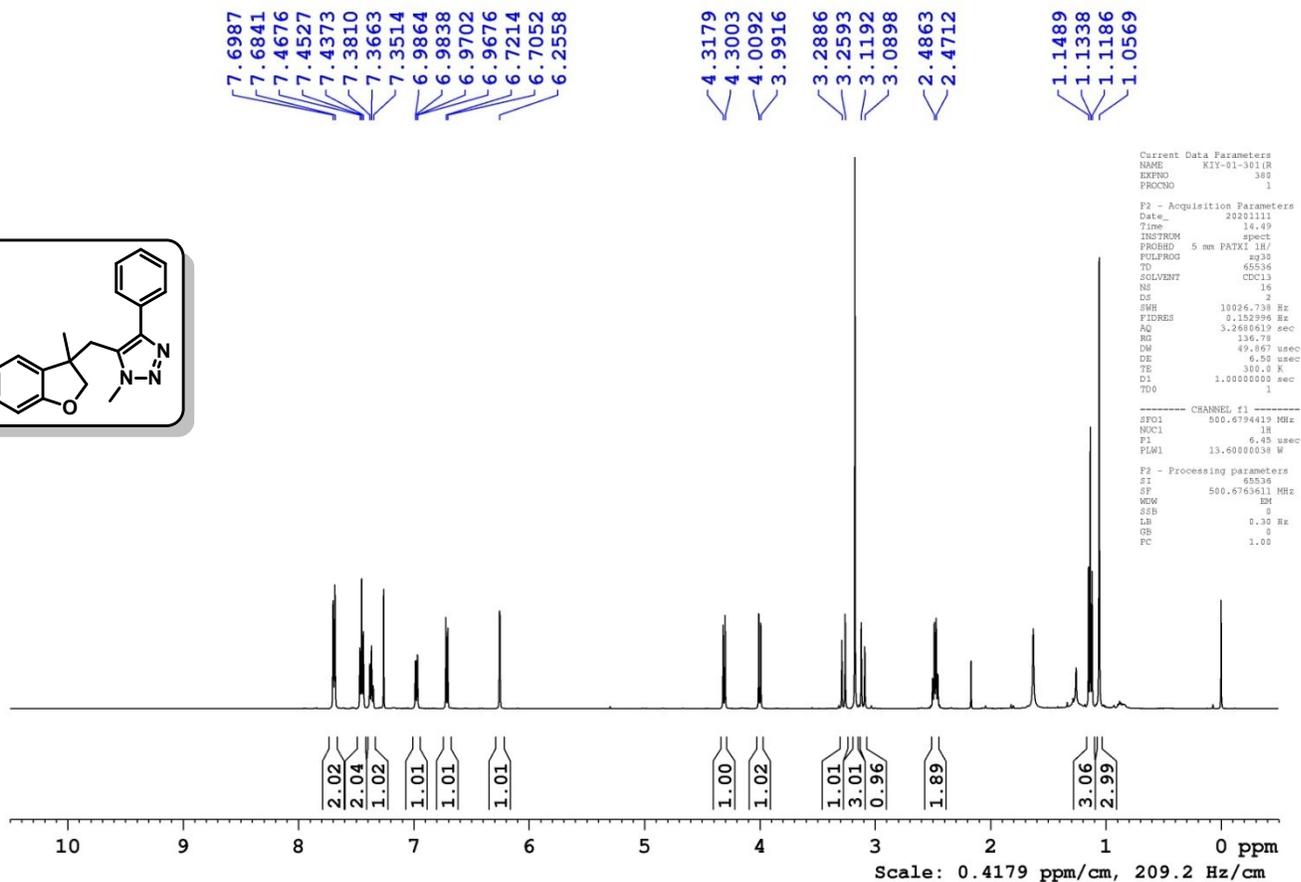
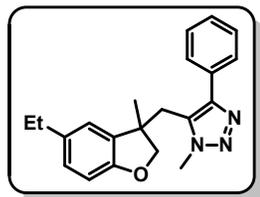


Figure S-7 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3ca

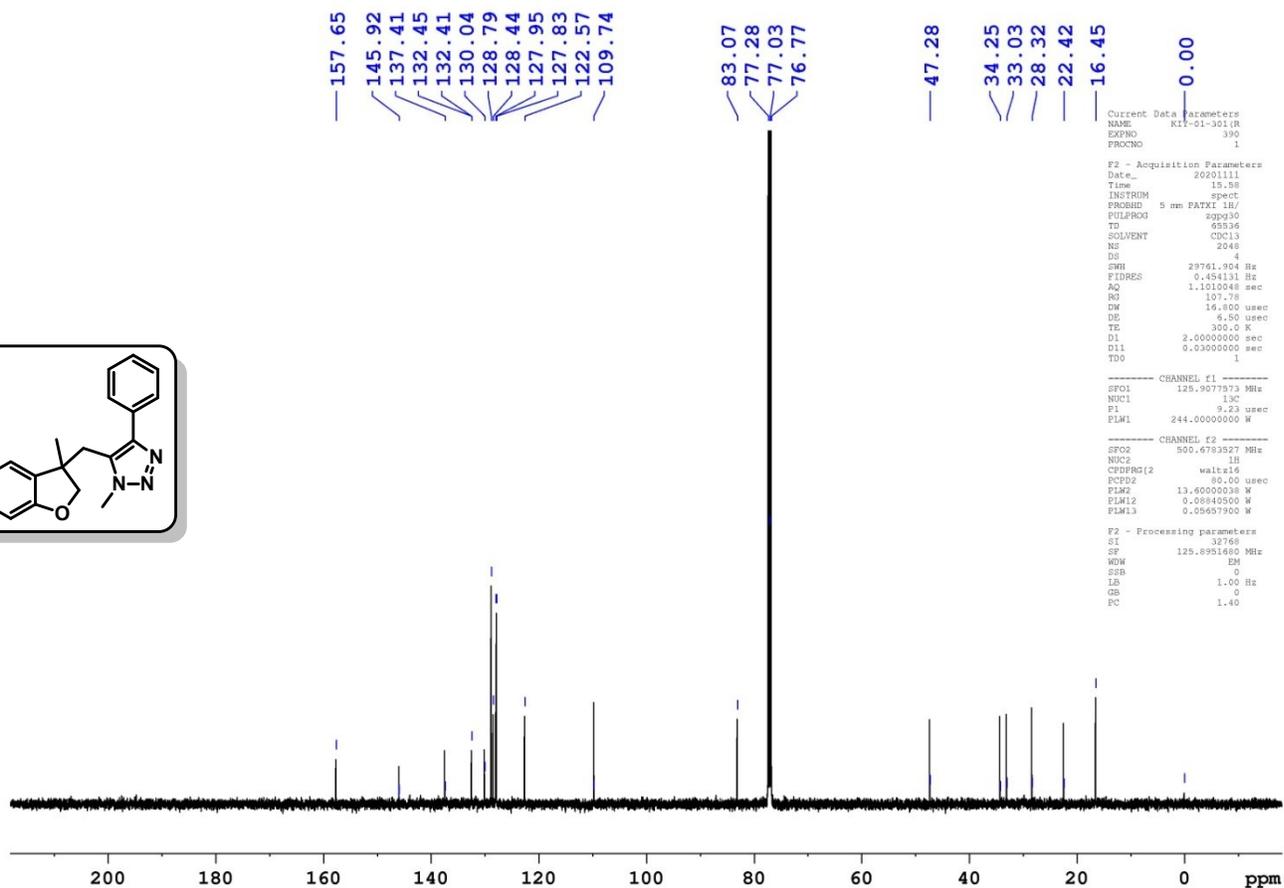
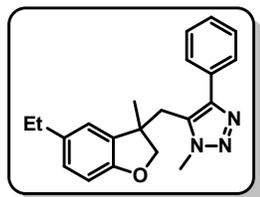
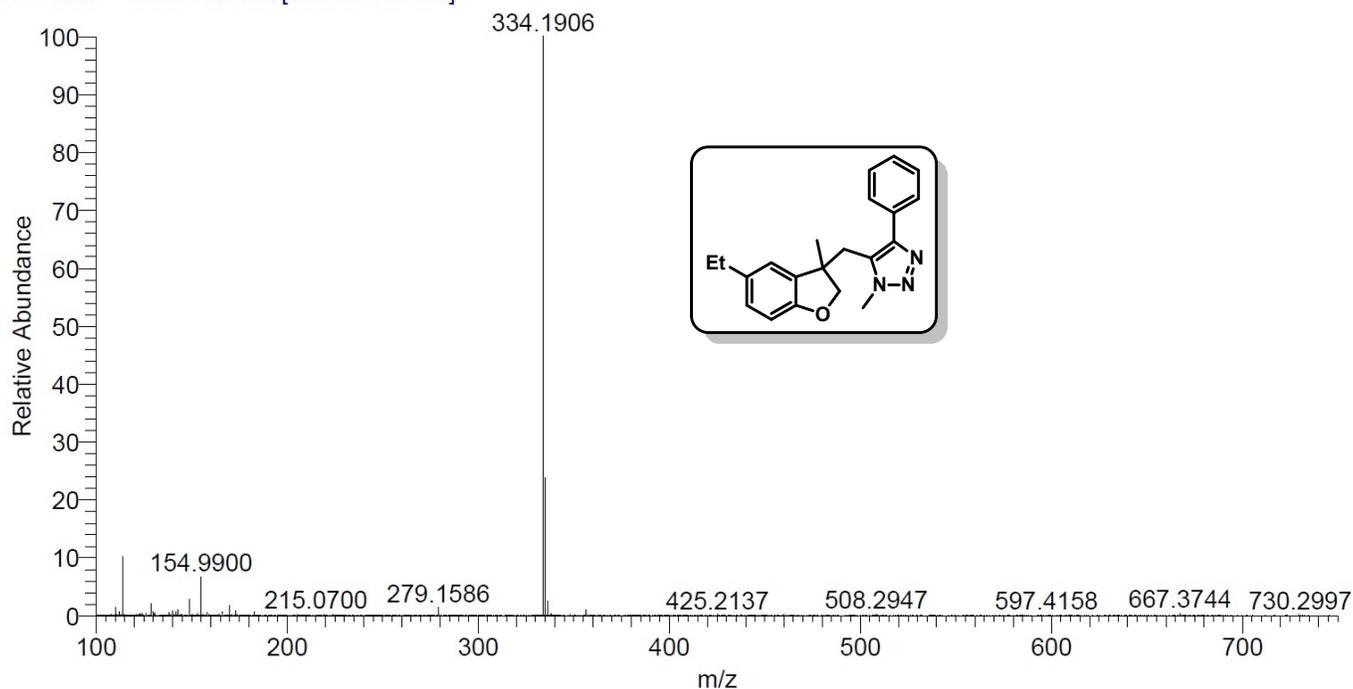


Figure S-8 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ca

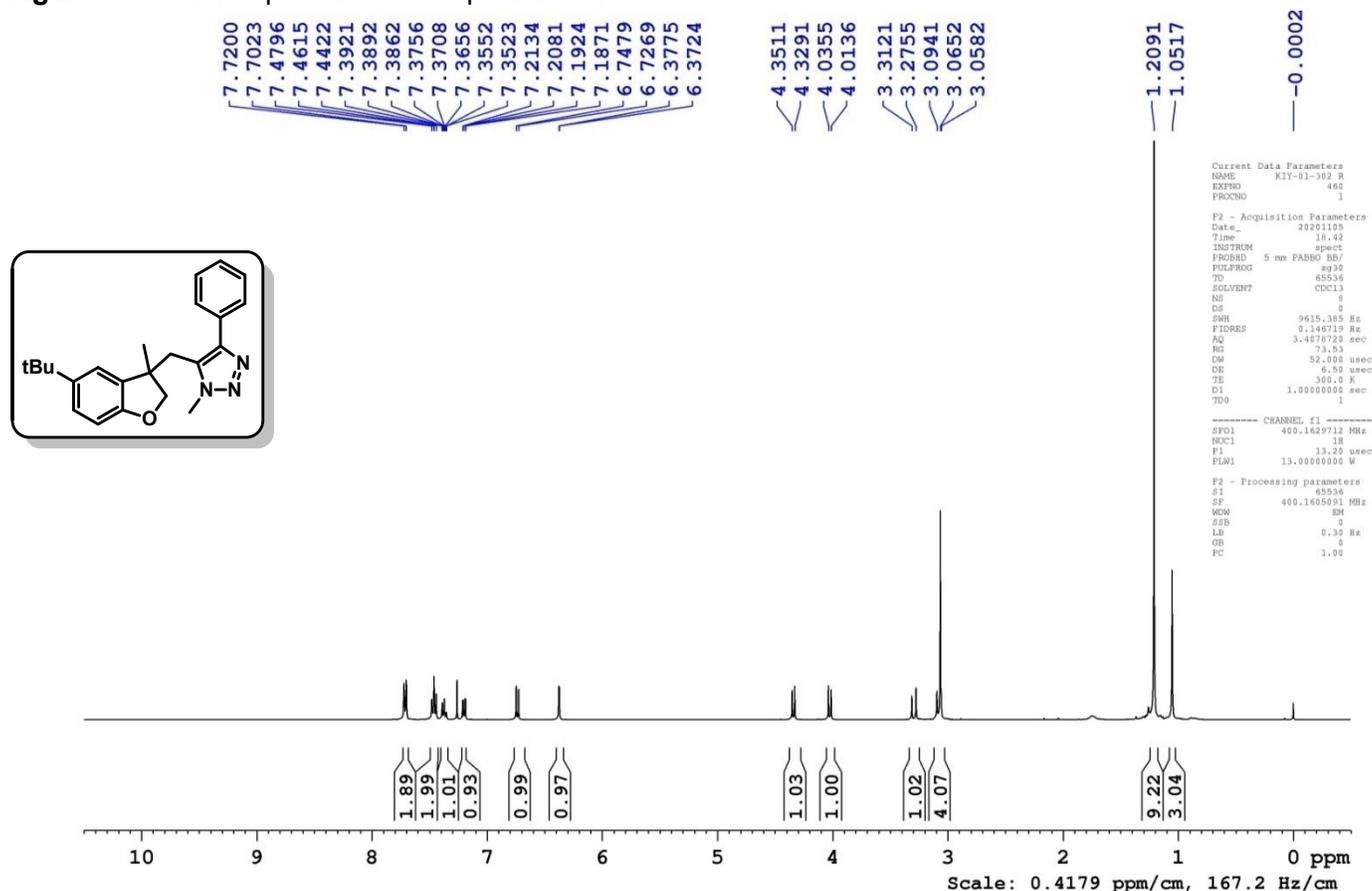
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HRMS20I09NOV25 #13-25 RT: 0.11-0.21 AV: 13 SB: 1 0.01 NL: 2.82E6  
T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-9** HRMS spectrum of compound **3ca**



**Figure S-10** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3da**

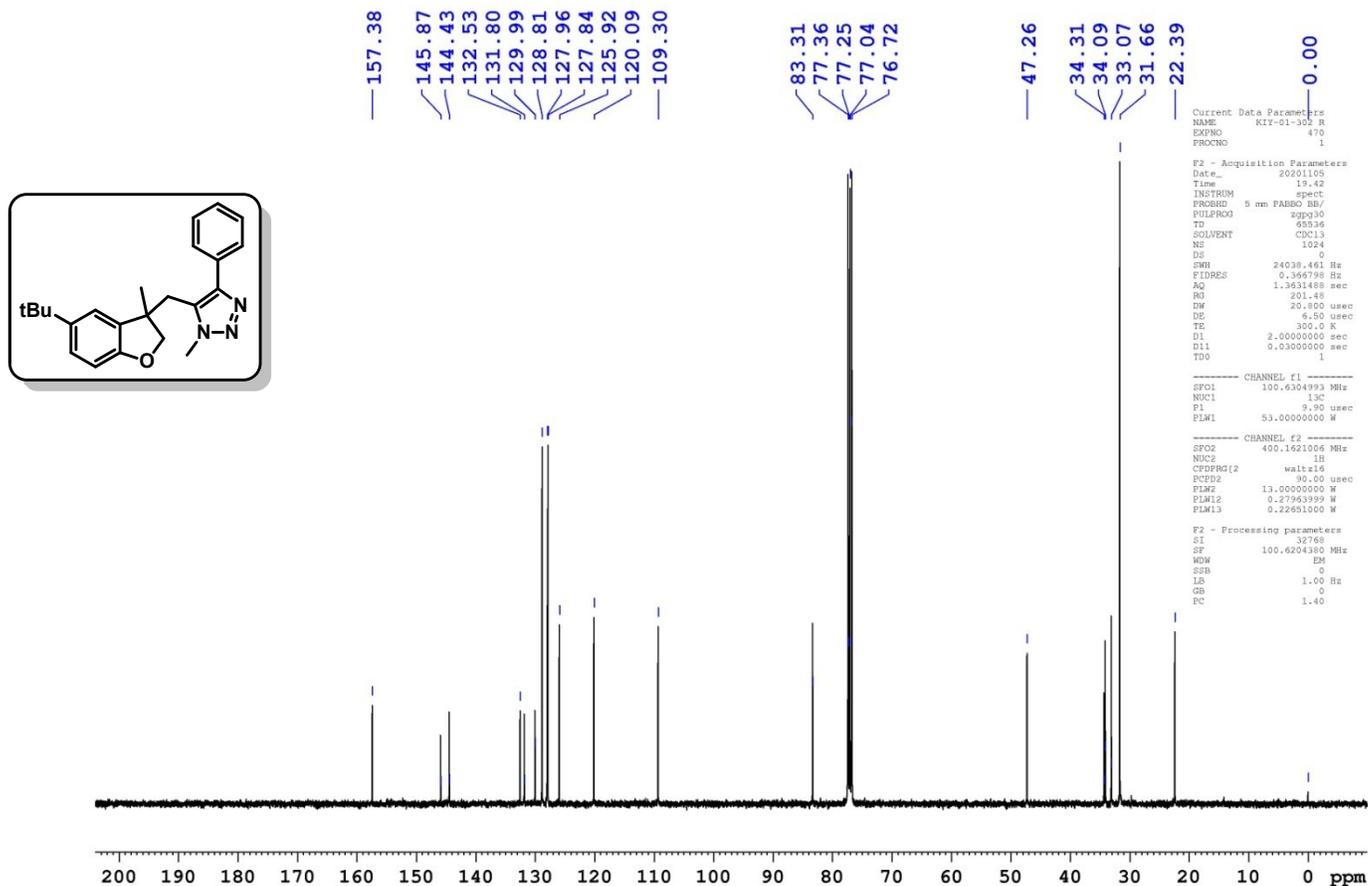


Figure S-11 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3da

SAIF [HRMS Report]

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Vial:	CStk1-01:19	Injection Volume(μl):	1.00

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 T: FTMS + c ESI Full ms [100.00-750.00]

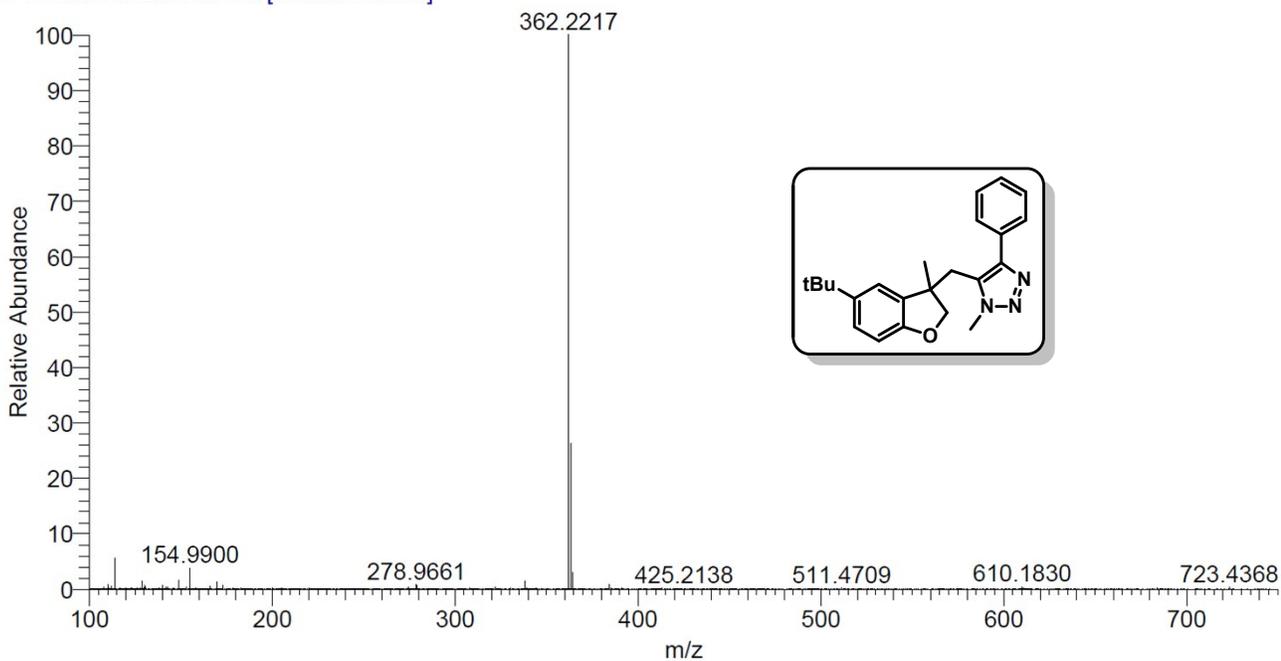


Figure S-12 HRMS spectrum of compound 3da

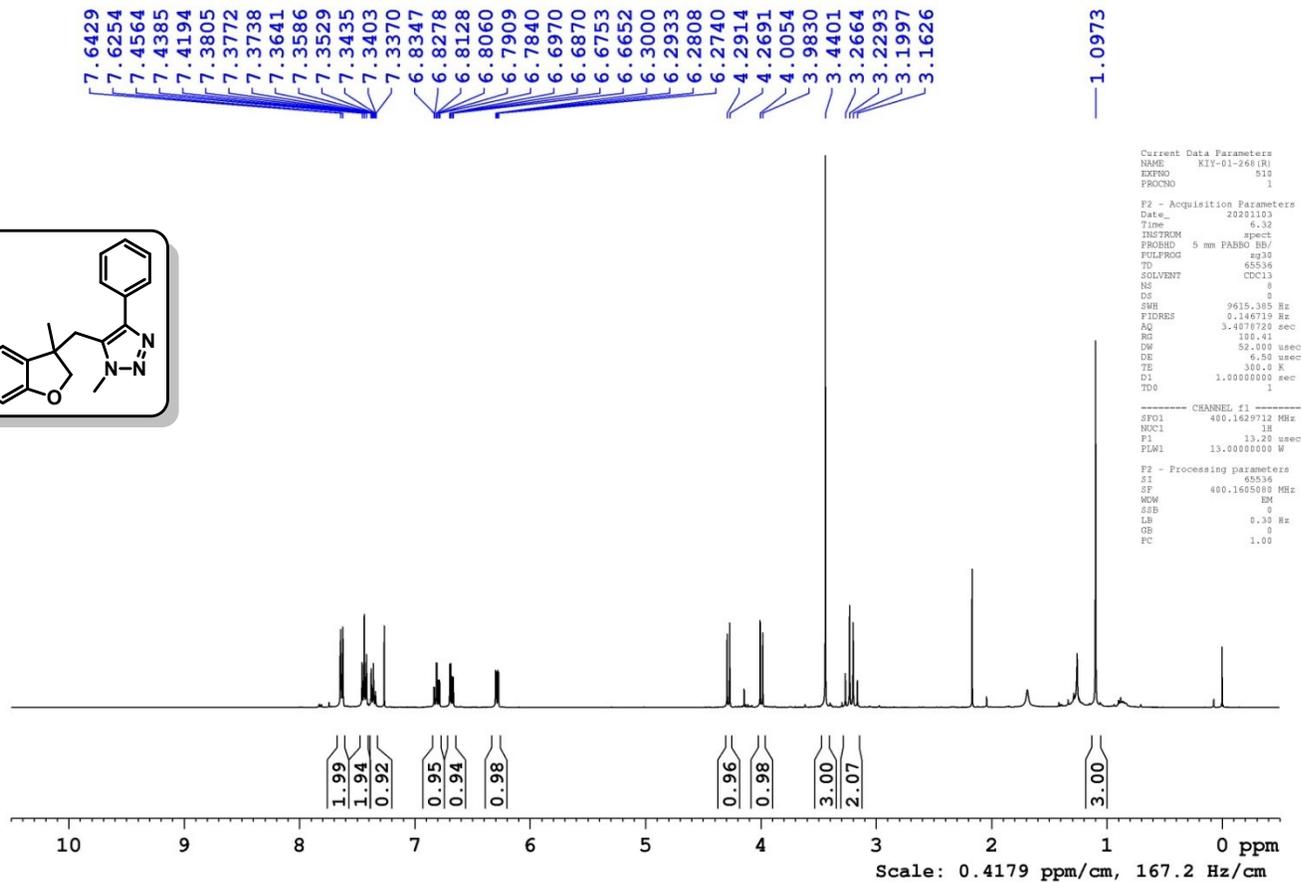
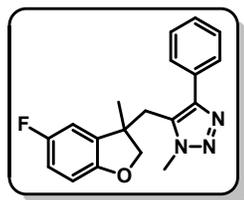


Figure S-13 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3ea

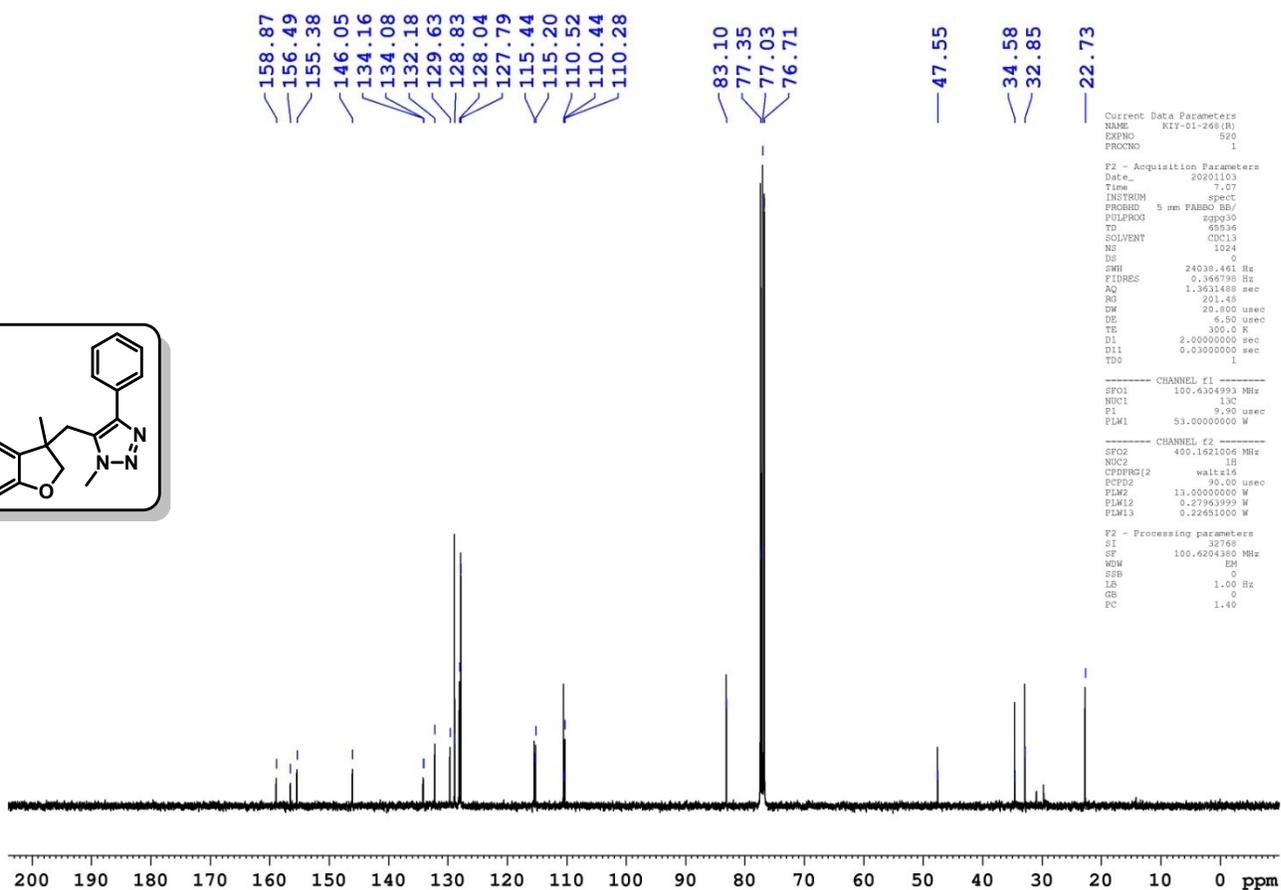
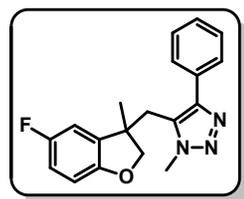
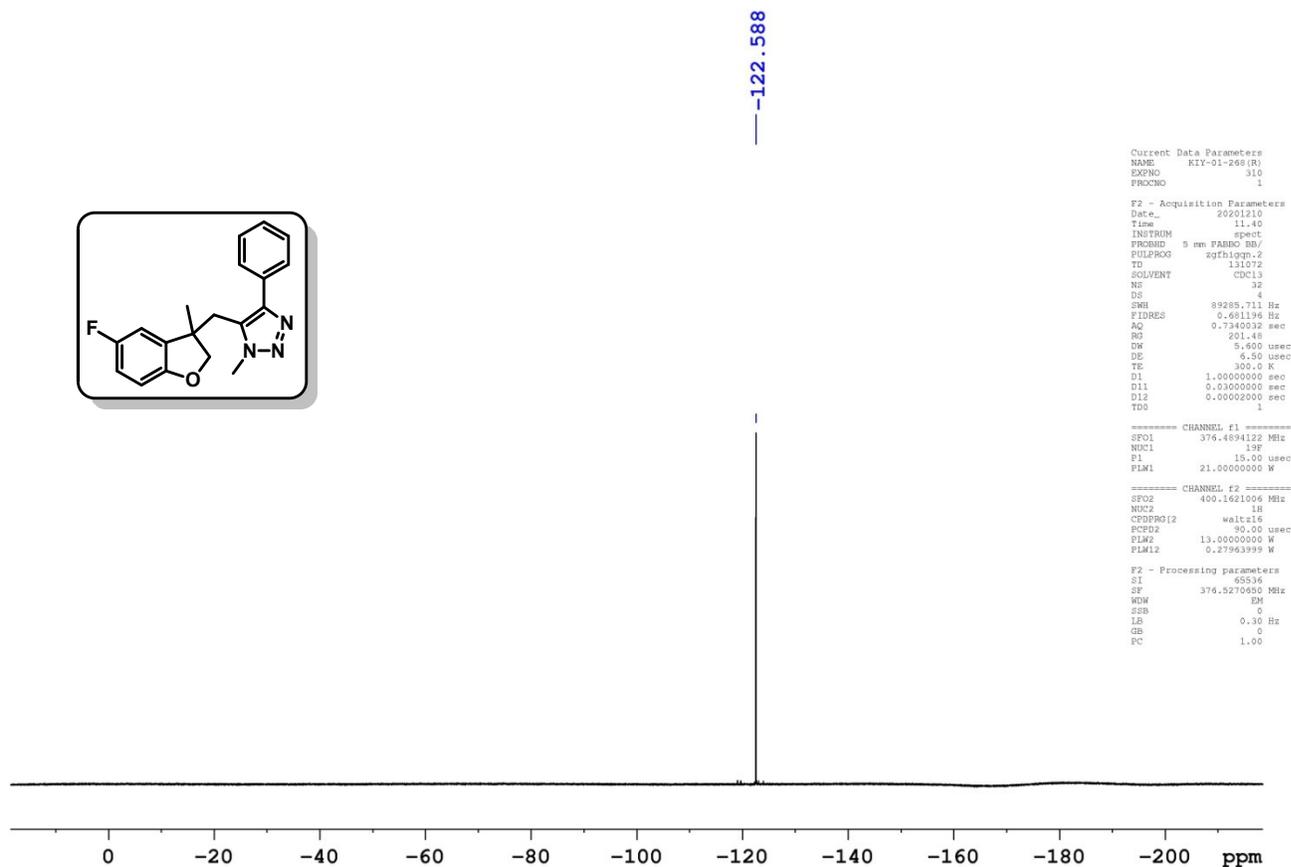


Figure S-14 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ea

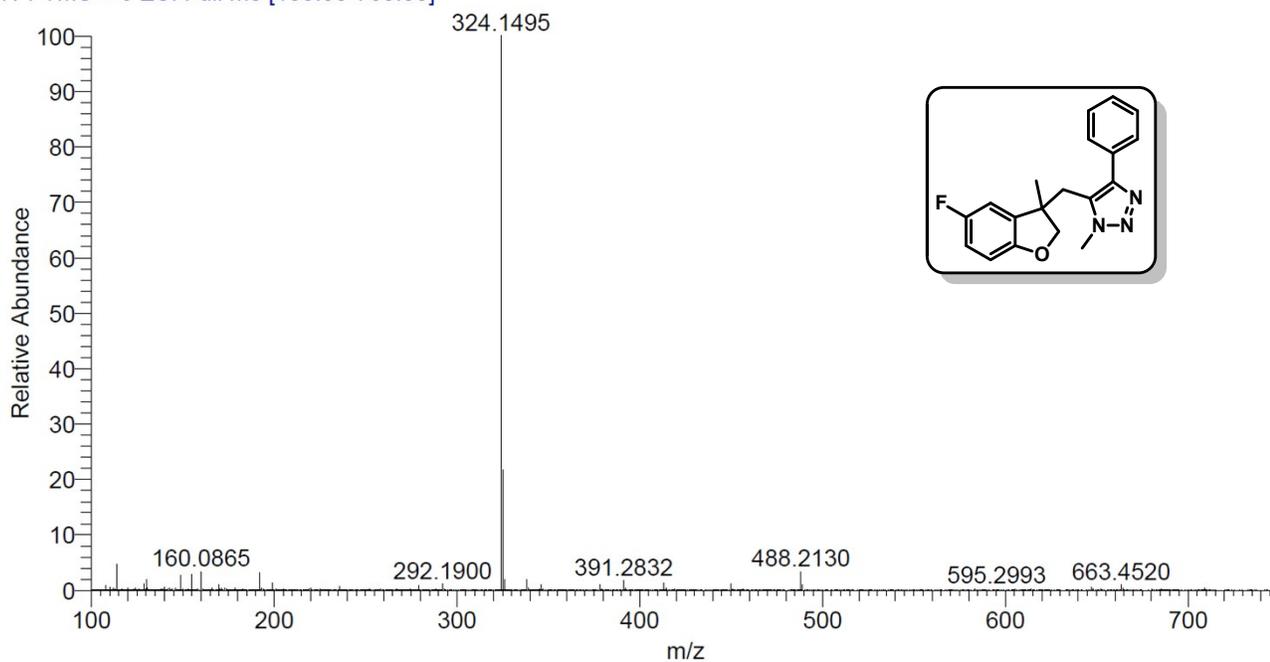


**Figure S-15**  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of compound **3ea**

**SAIF [HRMS Report]**

Data File:	HRMS20I05NOV20	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
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Vial:	CStk1-01:20	Injection Volume( $\mu\text{l}$ ):	1.00

HRMS20I05NOV20 #13-25 RT: 0.11-0.21 AV: 13 SB: 1 0.01 NL: 4.62E6  
T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-16** HRMS spectrum of compound **3ea**

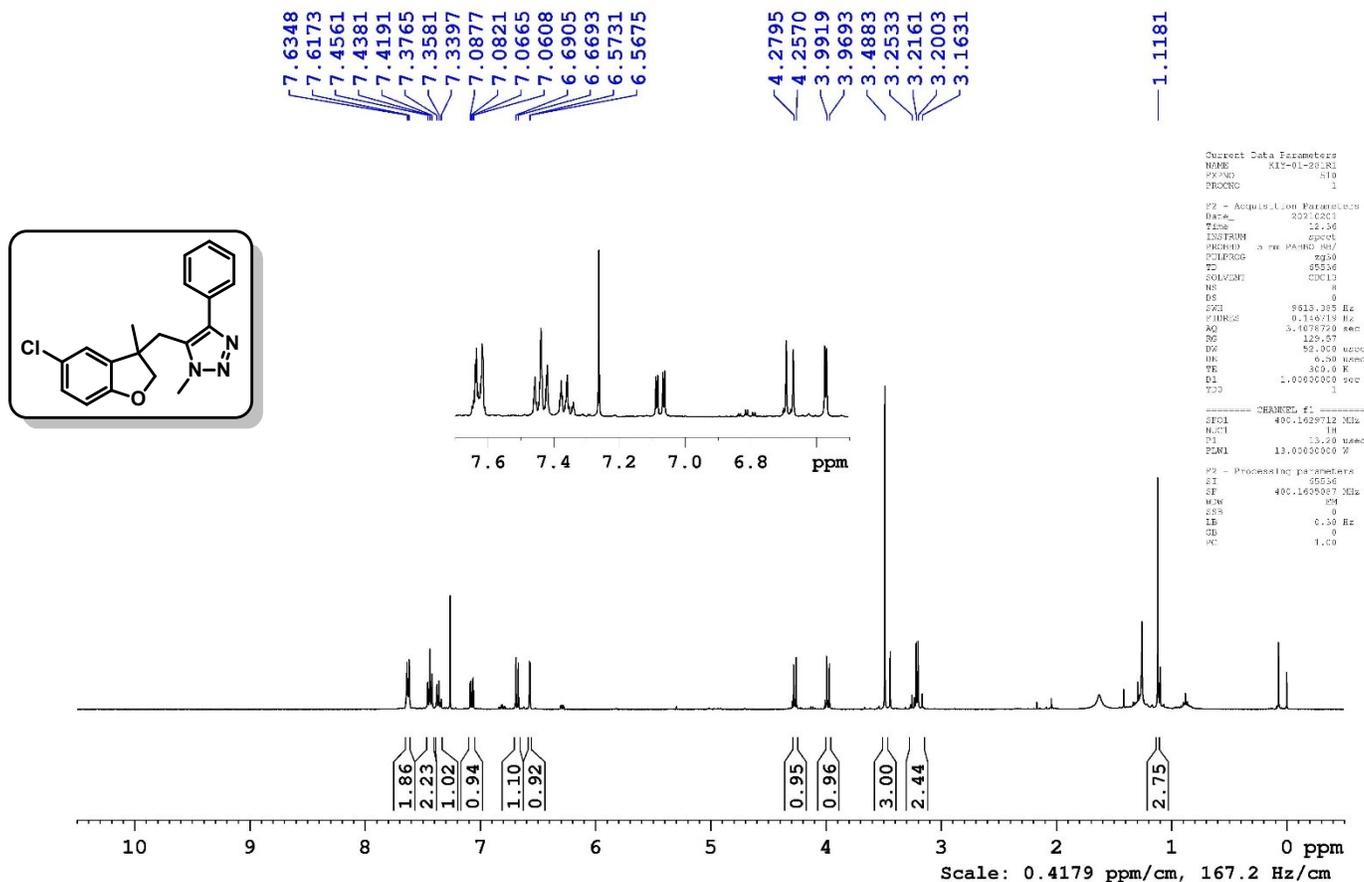


Figure S-17 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3fa

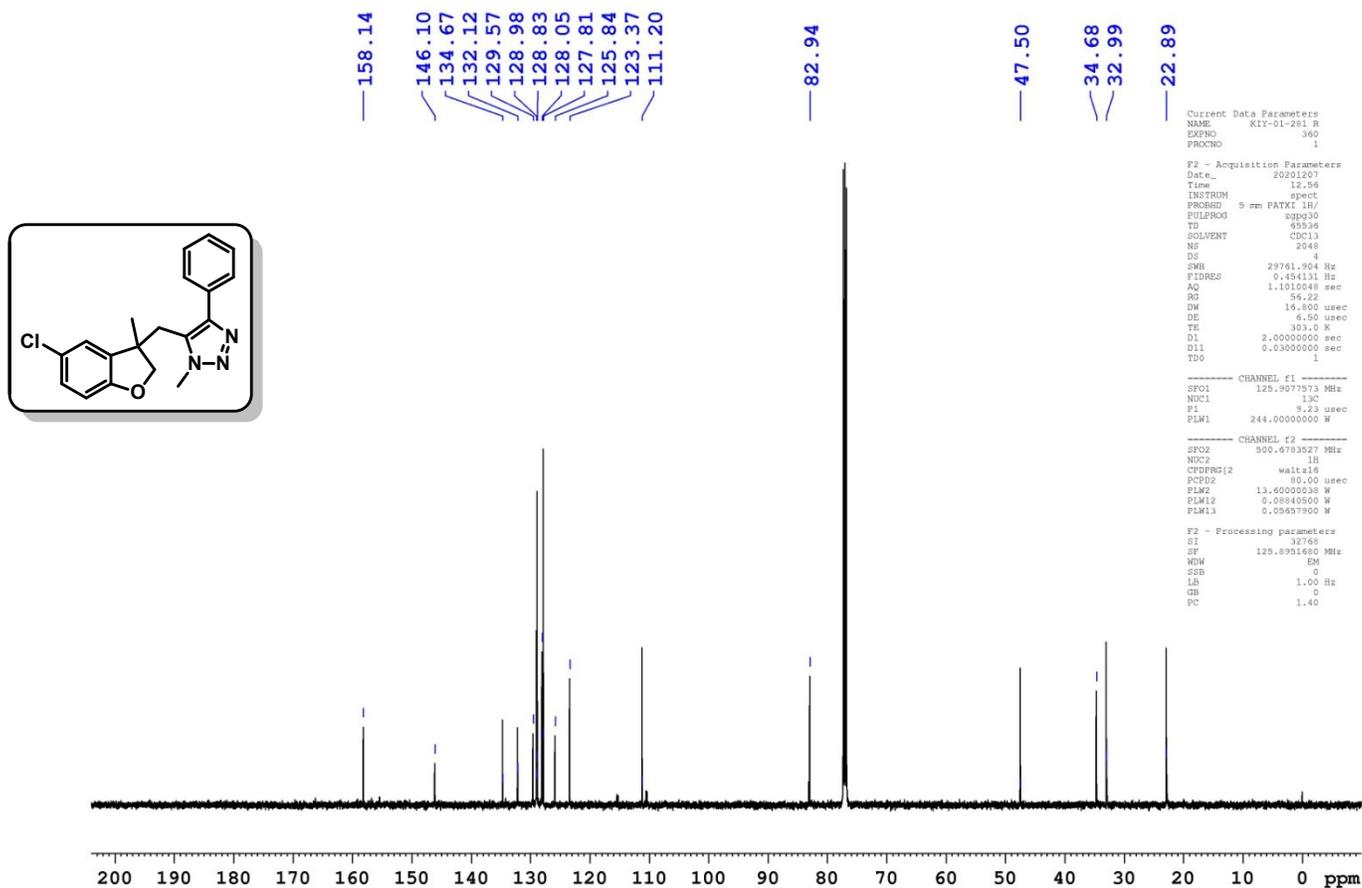
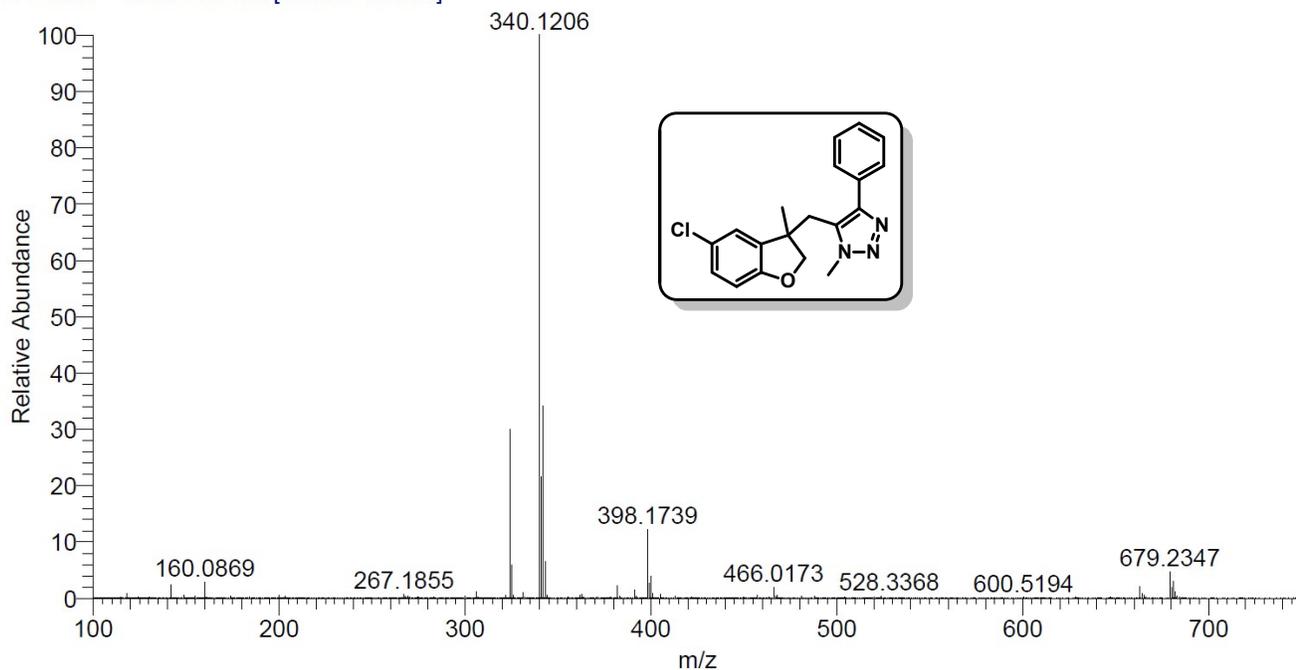


Figure S-18 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3fa

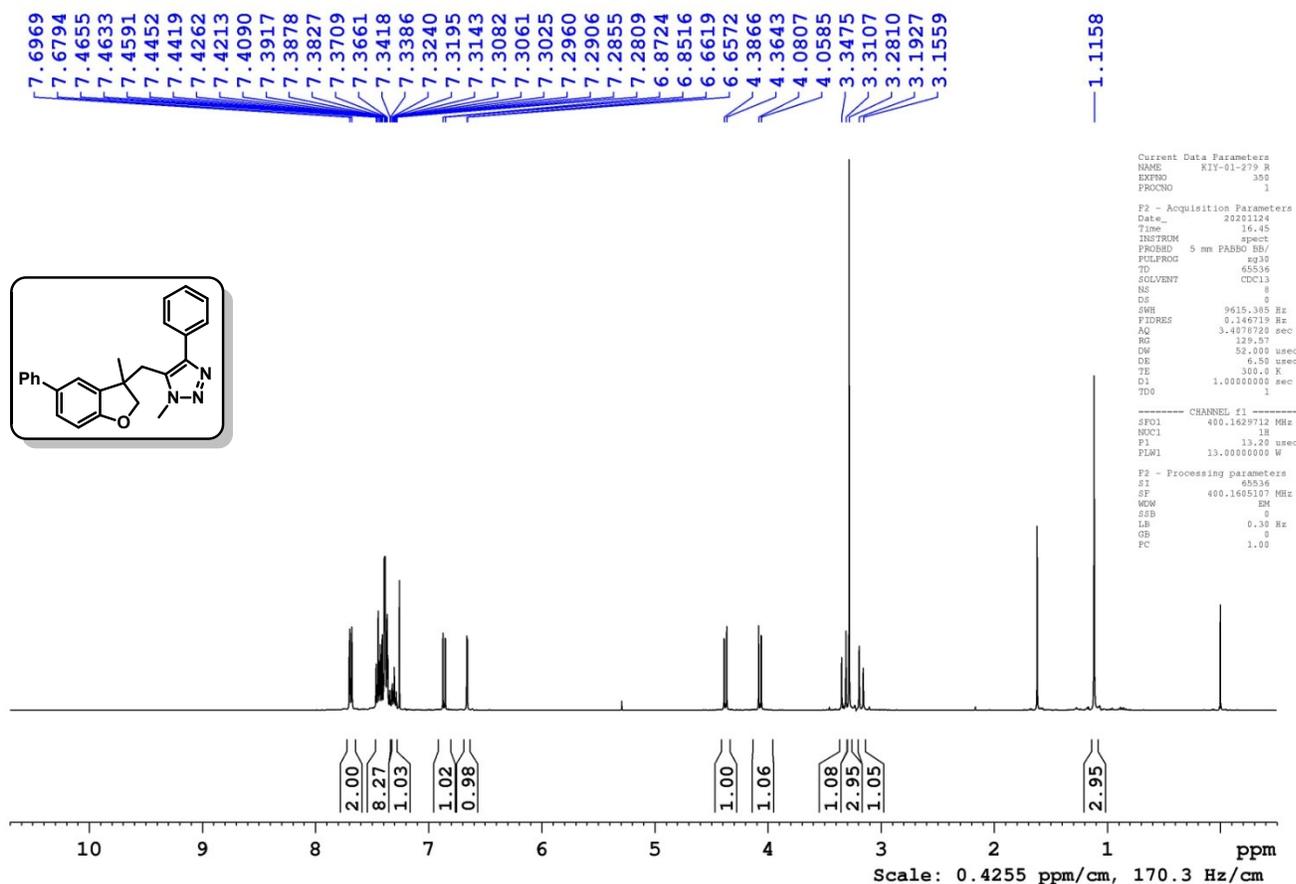
**SAIF [HRMS Report]**

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HRMS20I23OCT22 #11-23 RT: 0.11-0.21 AV: 13 SB: 1 0.01 NL: 4.20E6  
T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-19** HRMS spectrum of compound **3fa**



**Figure S-20** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ga**

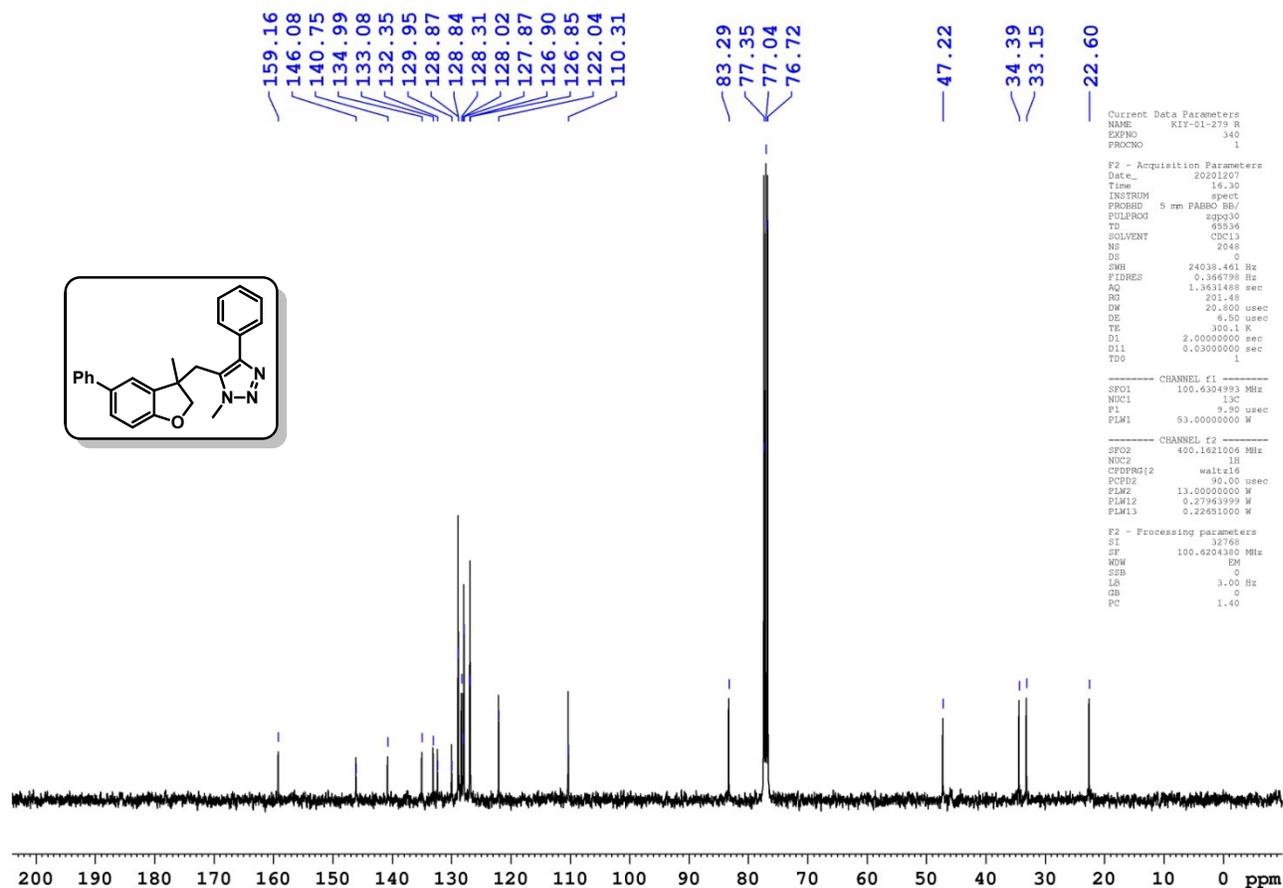


Figure S-21 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ga

SAIF [HRMS Report]

Data File:	HRMS20I21OCT17	Original Data Path:	D:\INTERNAL NEW\2020\OCT 2020
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Vial:	CStk1-01:17	Injection Volume(μl):	1.00

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 T: FTMS + c ESI Full ms [100.00-750.00]

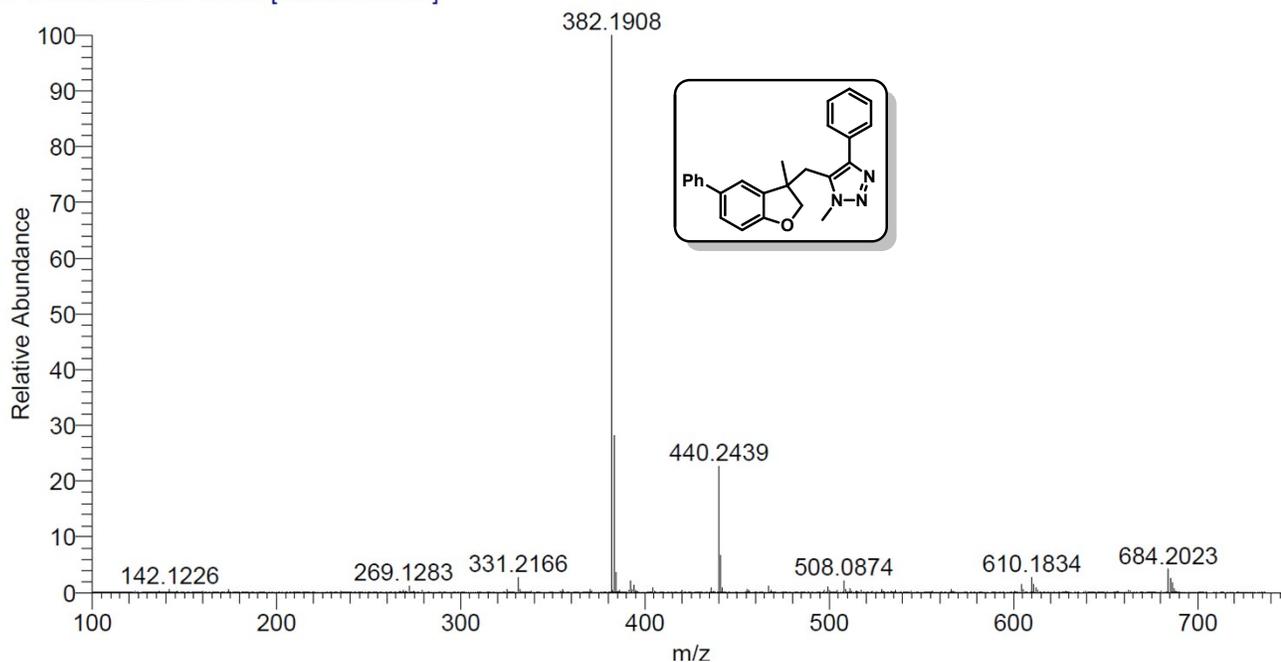


Figure S-22 HRMS spectrum of compound 3ga

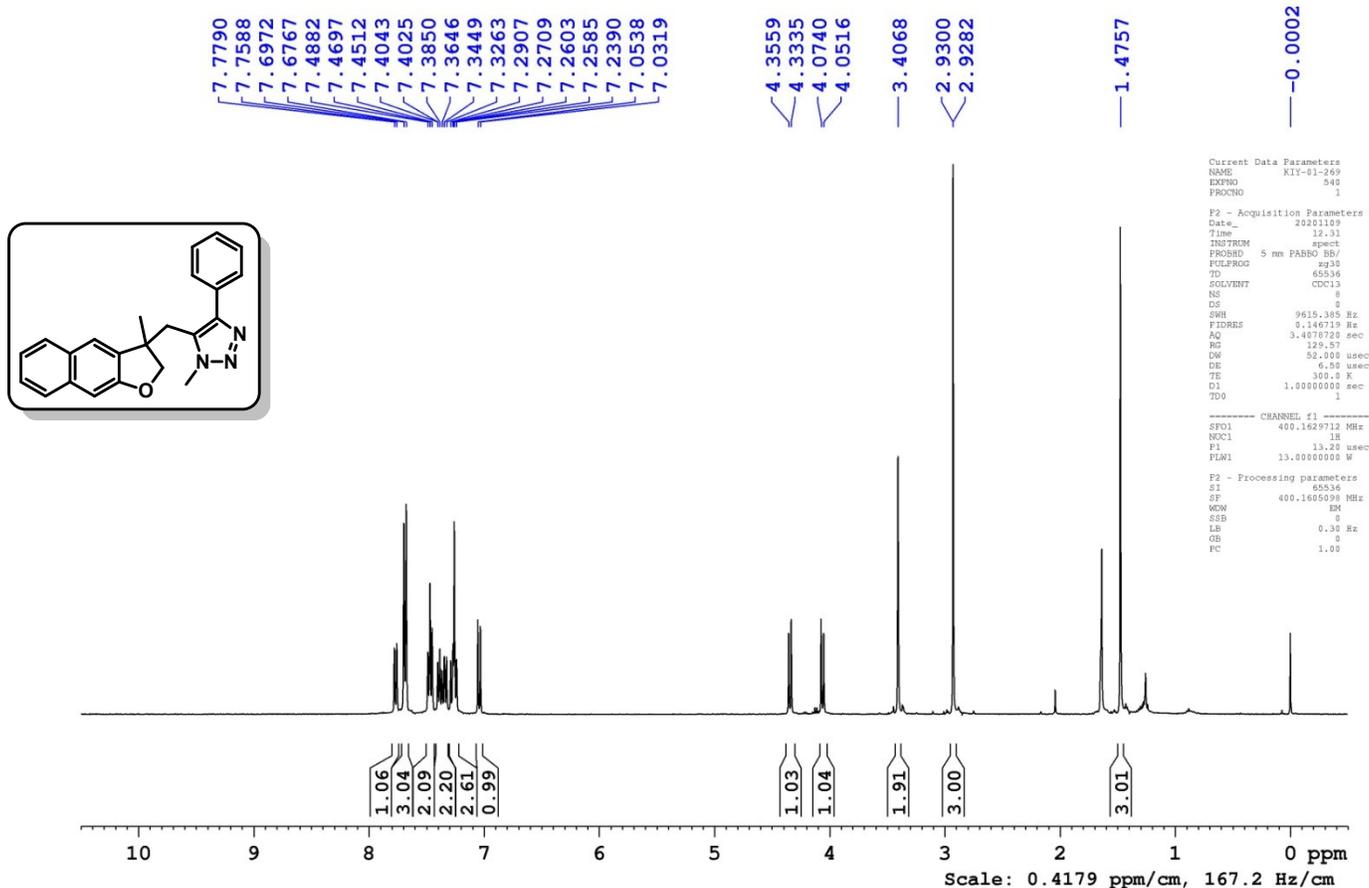


Figure S-23 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3ia

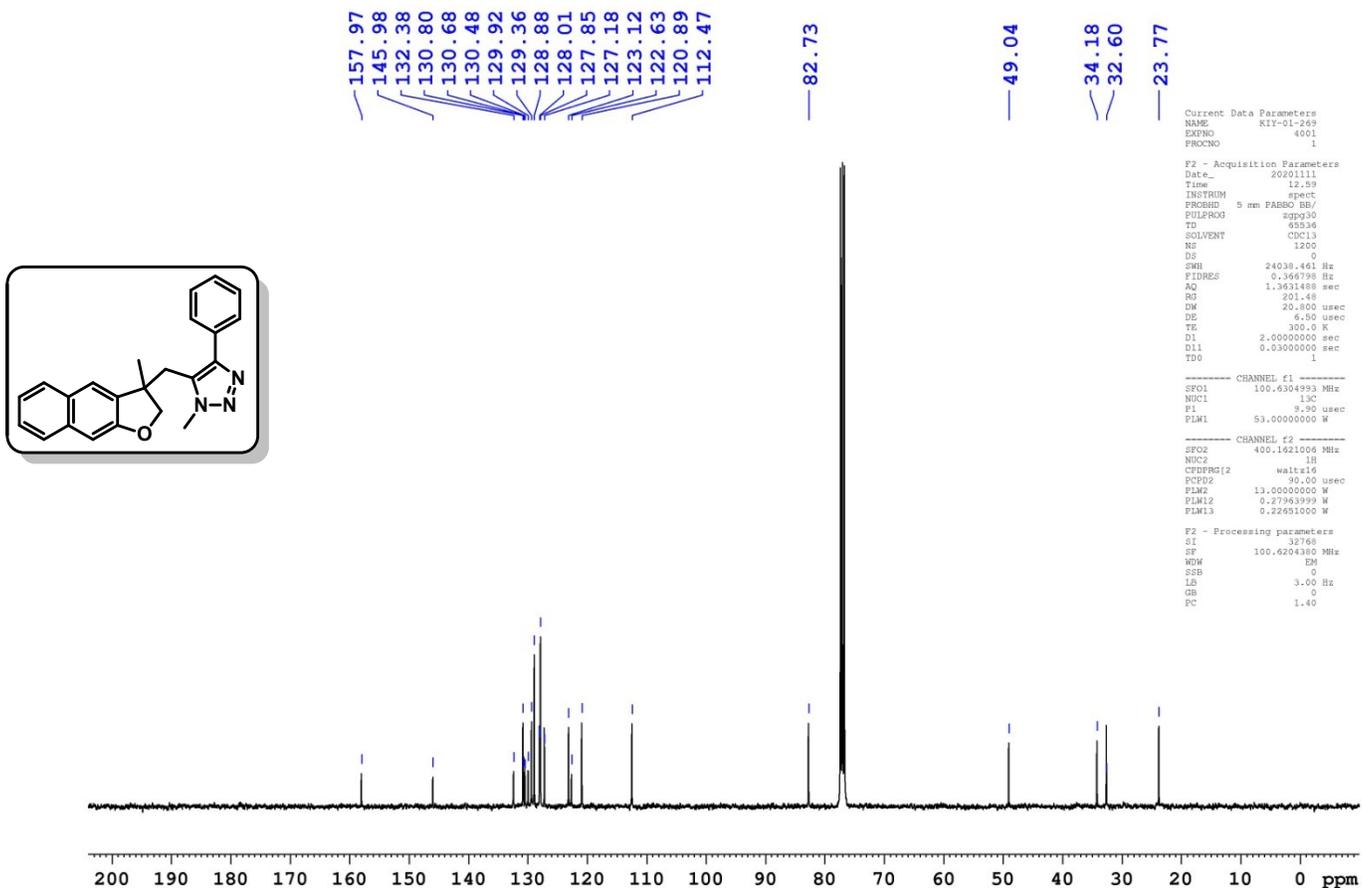
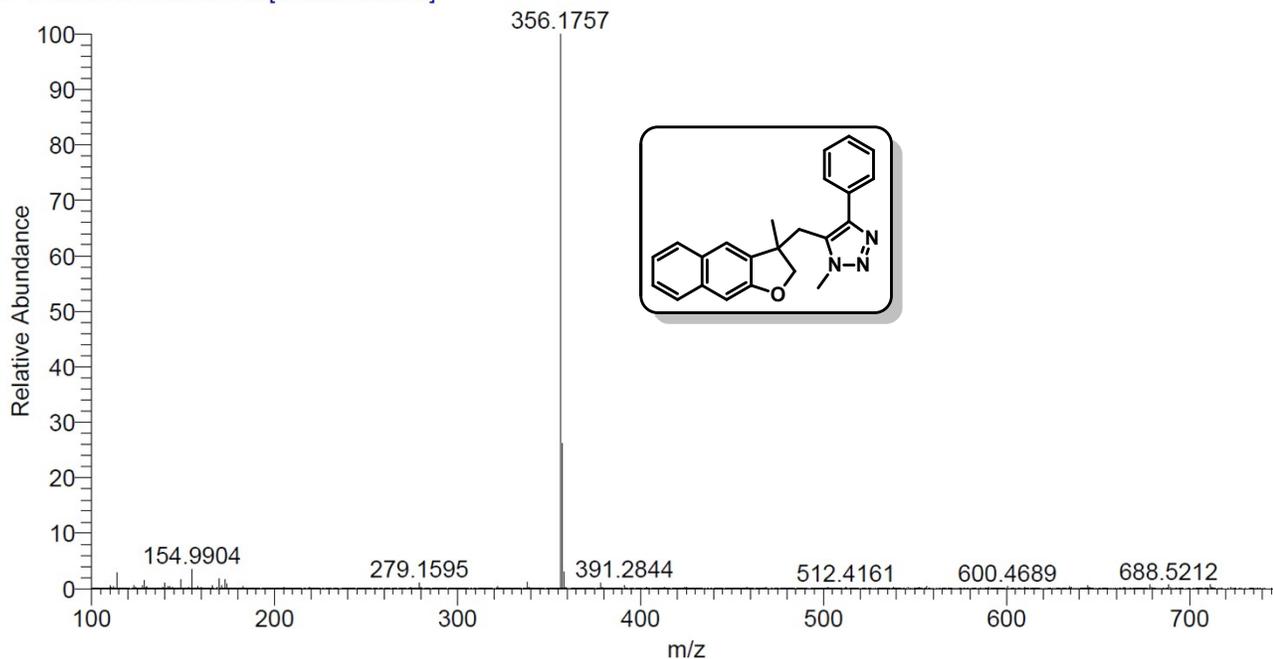


Figure S-24 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ia

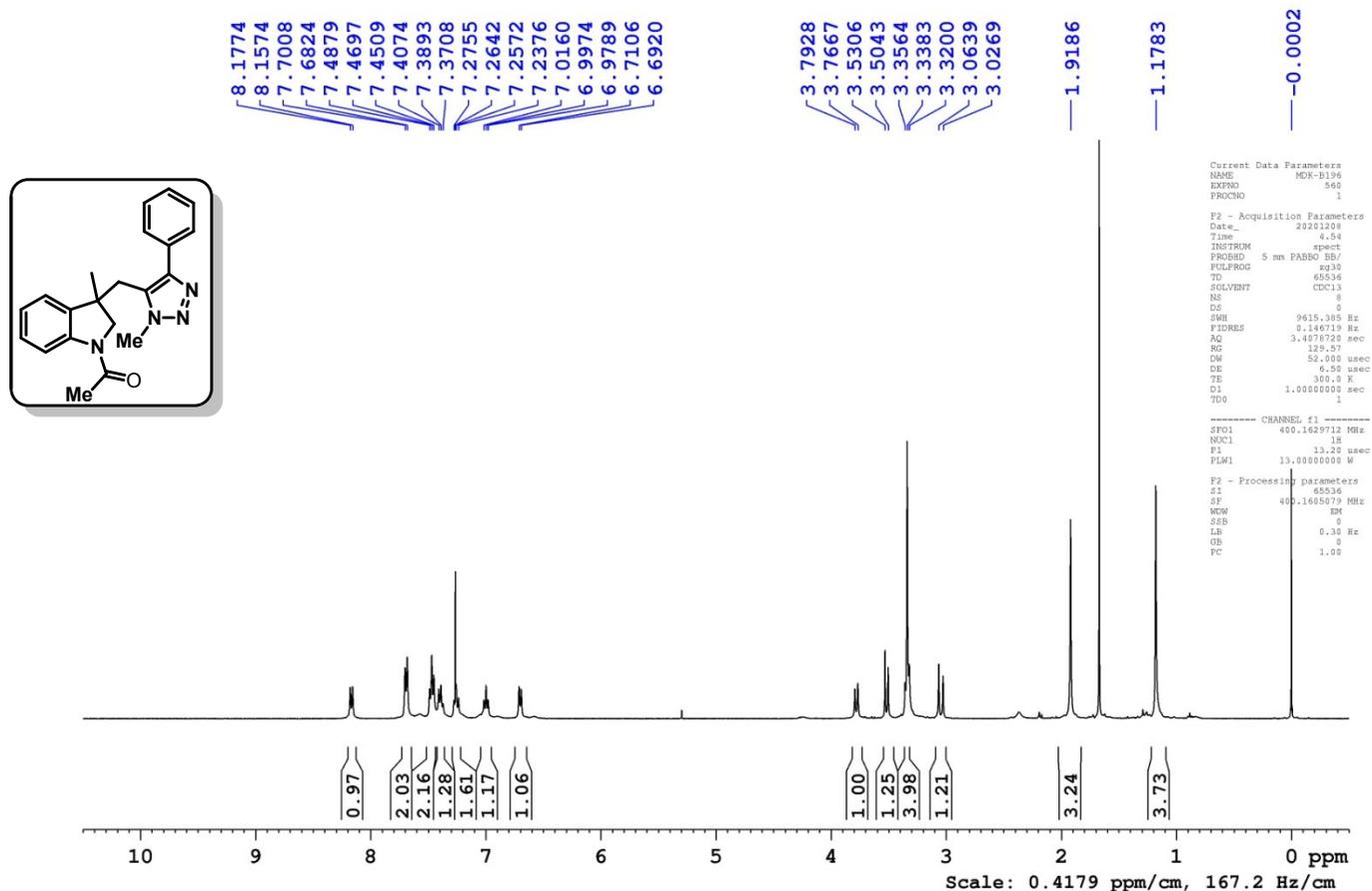
**SAIF [HRMS Report]**

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 Vial: CStk1-01:20 Injection Volume(μl): 1.00

HRMS20I08DEC20 #30-61 RT: 0.25-0.50 AV: 32 SB: 1 0.01 NL: 3.92E6  
 T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-25** HRMS spectrum of compound 3ia



**Figure S-26** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3ka

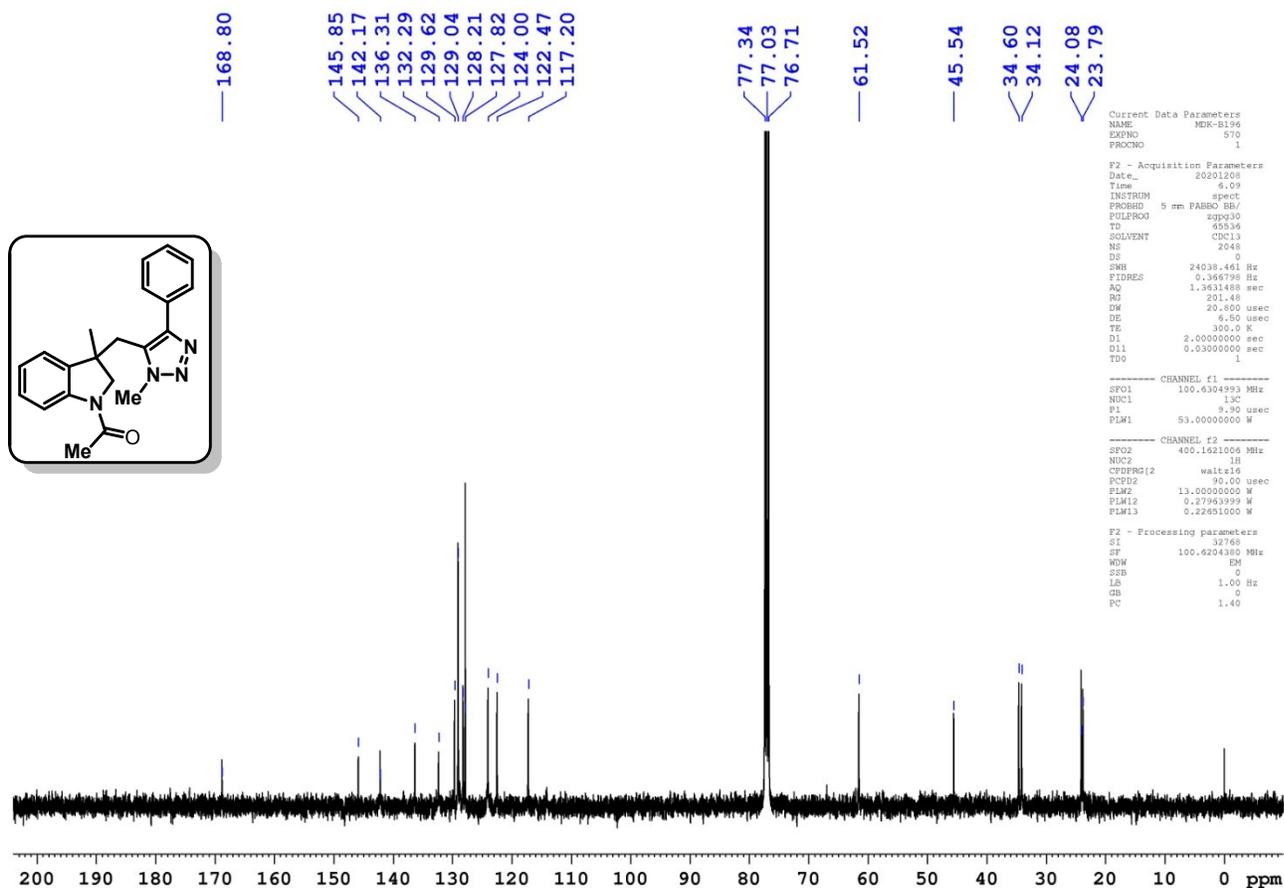


Figure S-27 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ka

**SAIF [HRMS Report]**

Data File:	HRMS20I02NOV20	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
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Vial:	CStk1-01:20	Injection Volume(μl):	1.00

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T: FTMS + p ESI Full ms [100.00-1000.00]

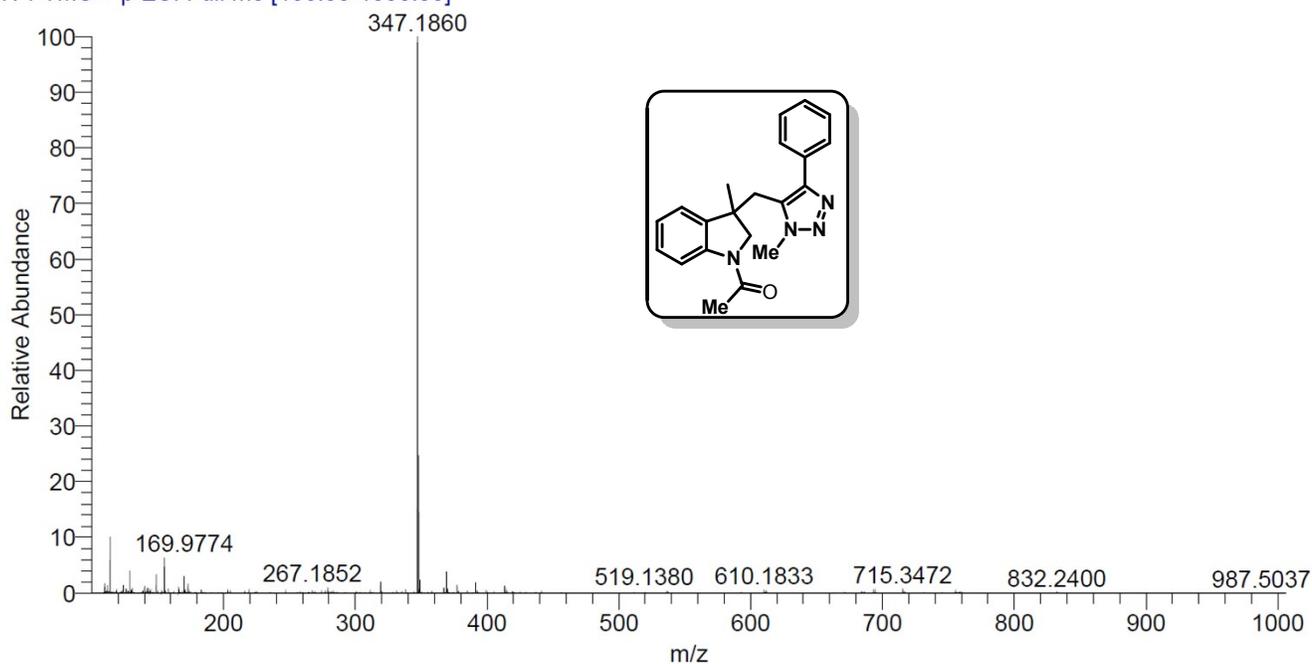


Figure S-28 HRMS spectrum of compound 3ka

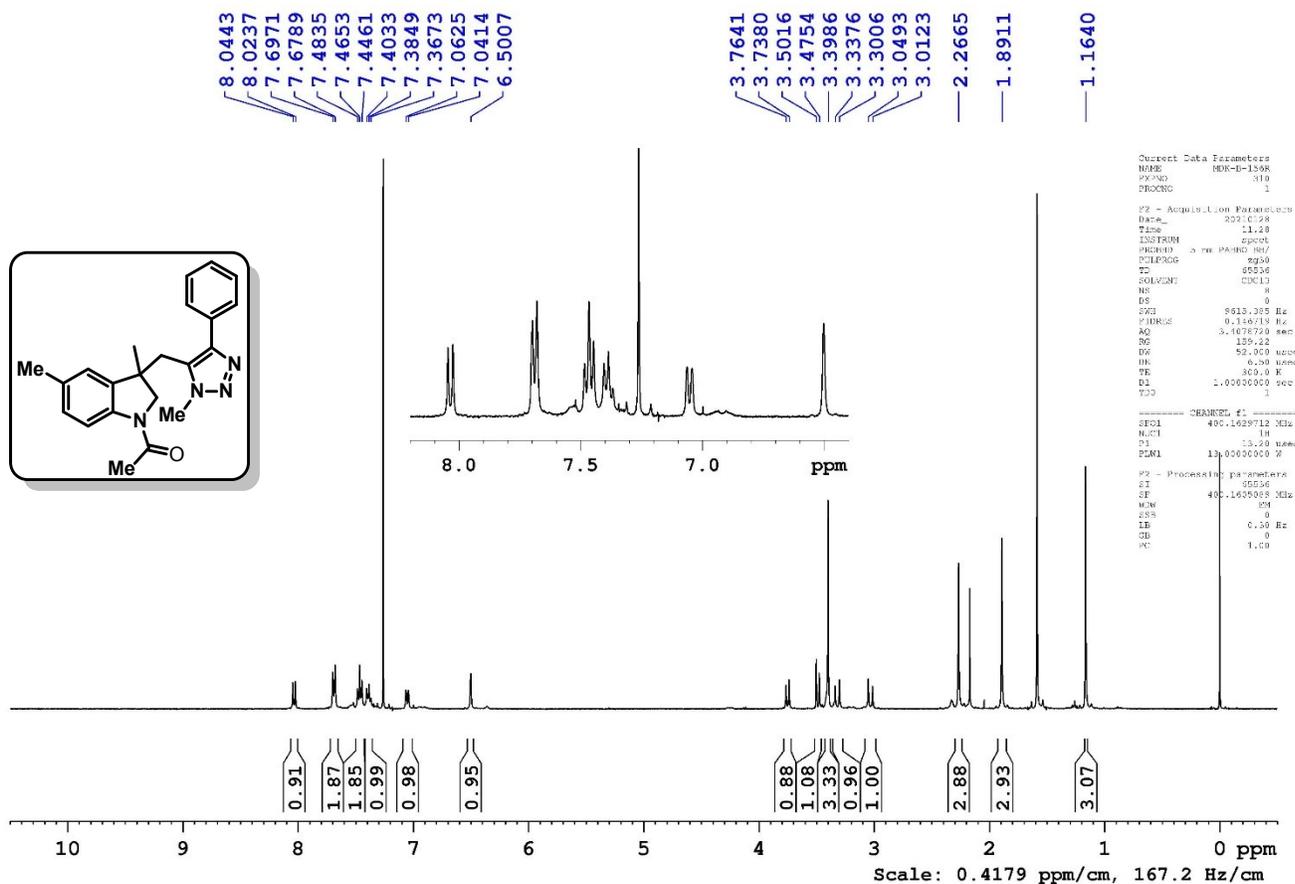


Figure S-29 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3la

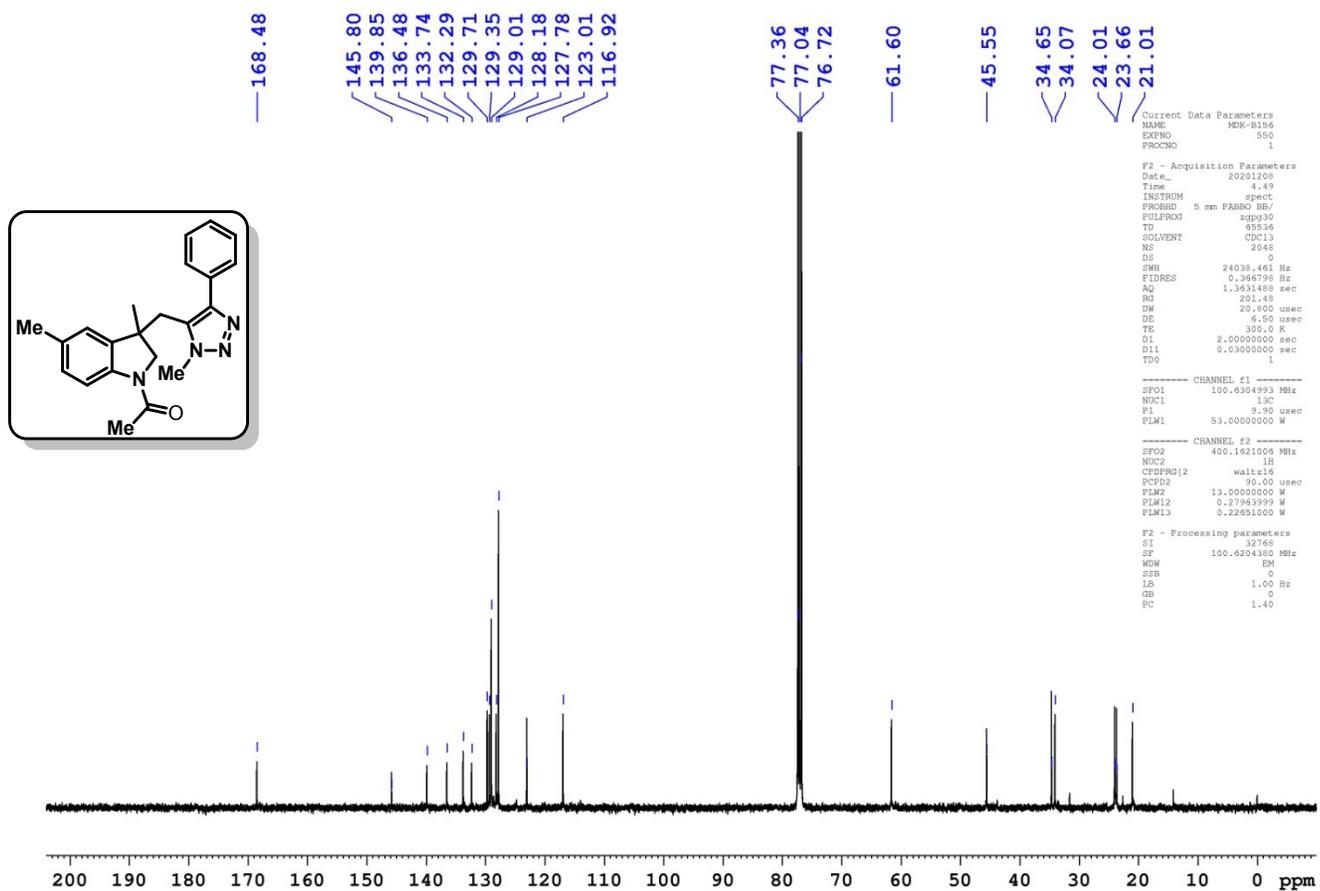
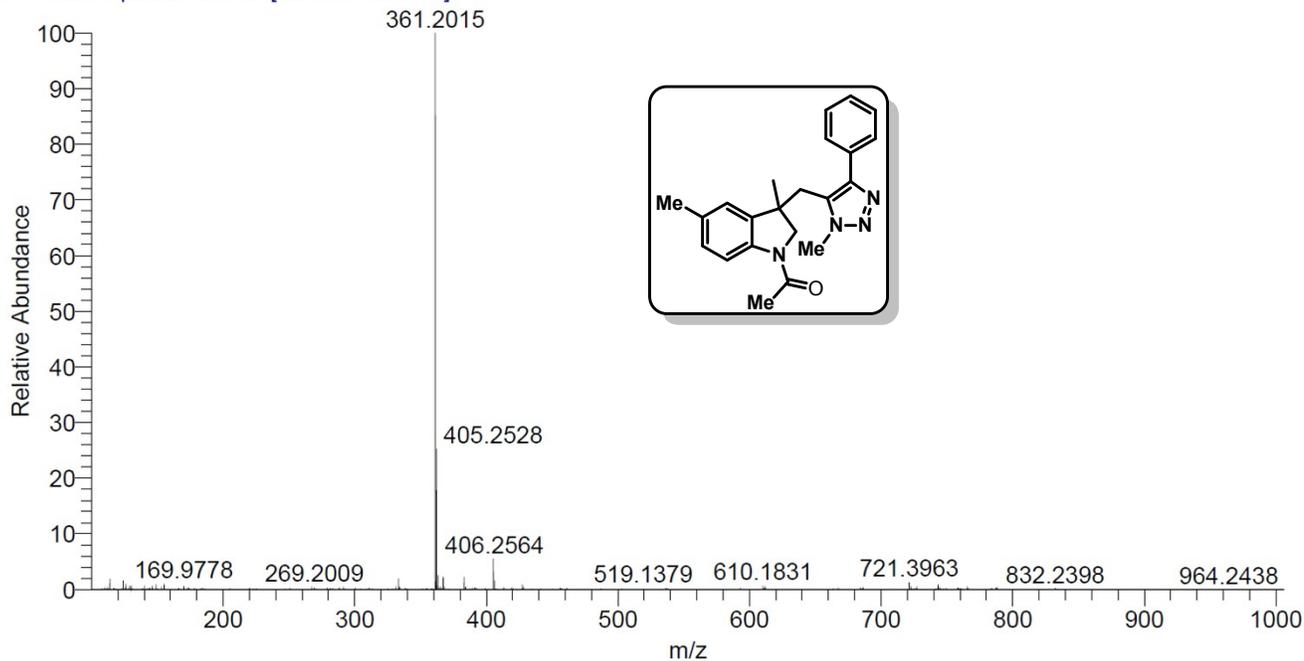


Figure S-30 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3la

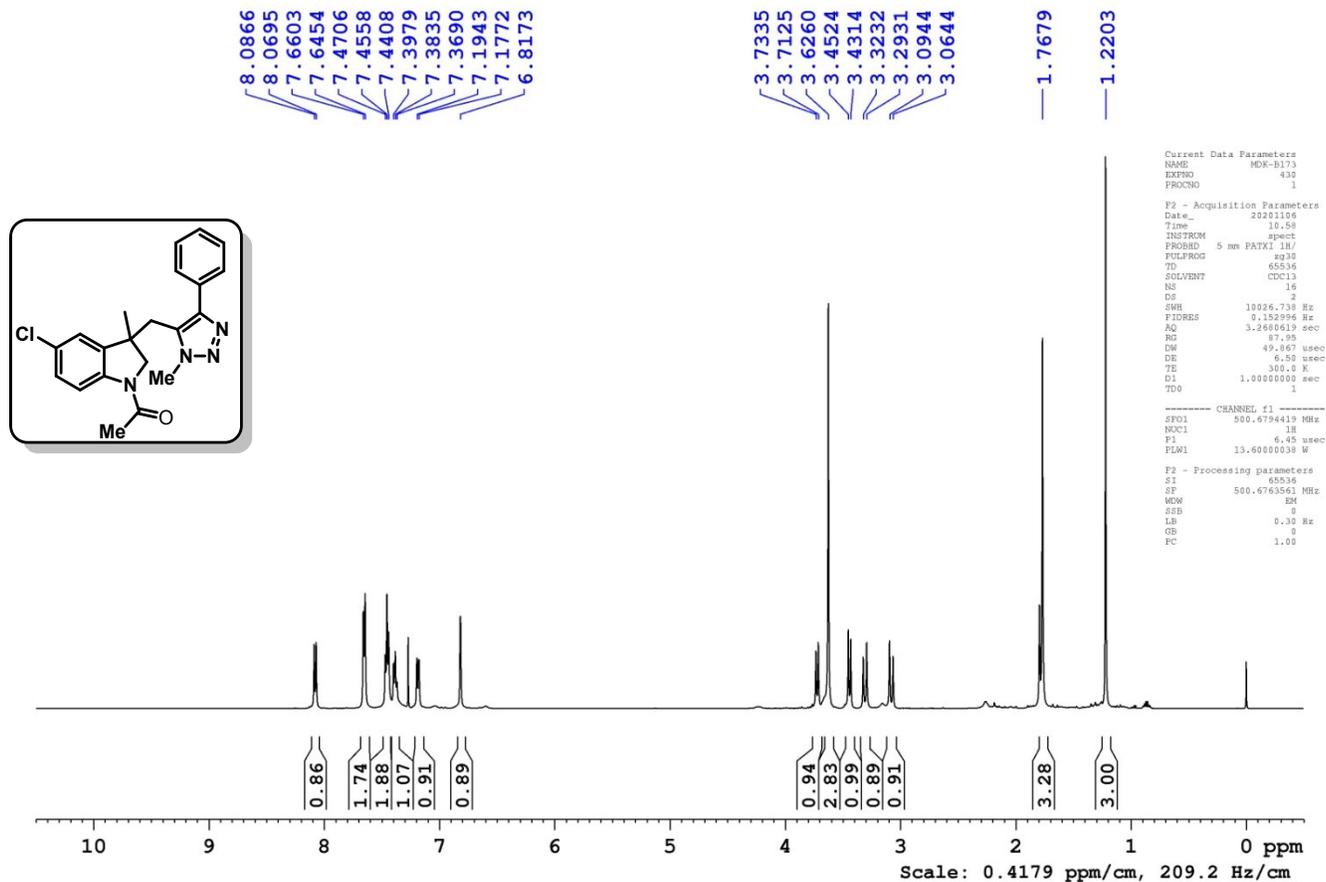
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Vial:	CStk1-01:23	Injection Volume(μl):	1.00

HRMS20I02NOV23 #13-26 RT: 0.11-0.21 AV: 14 SB: 1 0.01 NL: 8.84E6  
T: FTMS + p ESI Full ms [100.00-1000.00]



**Figure S-31** HRMS spectrum of compound **31a**



**Figure S-32** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ma**

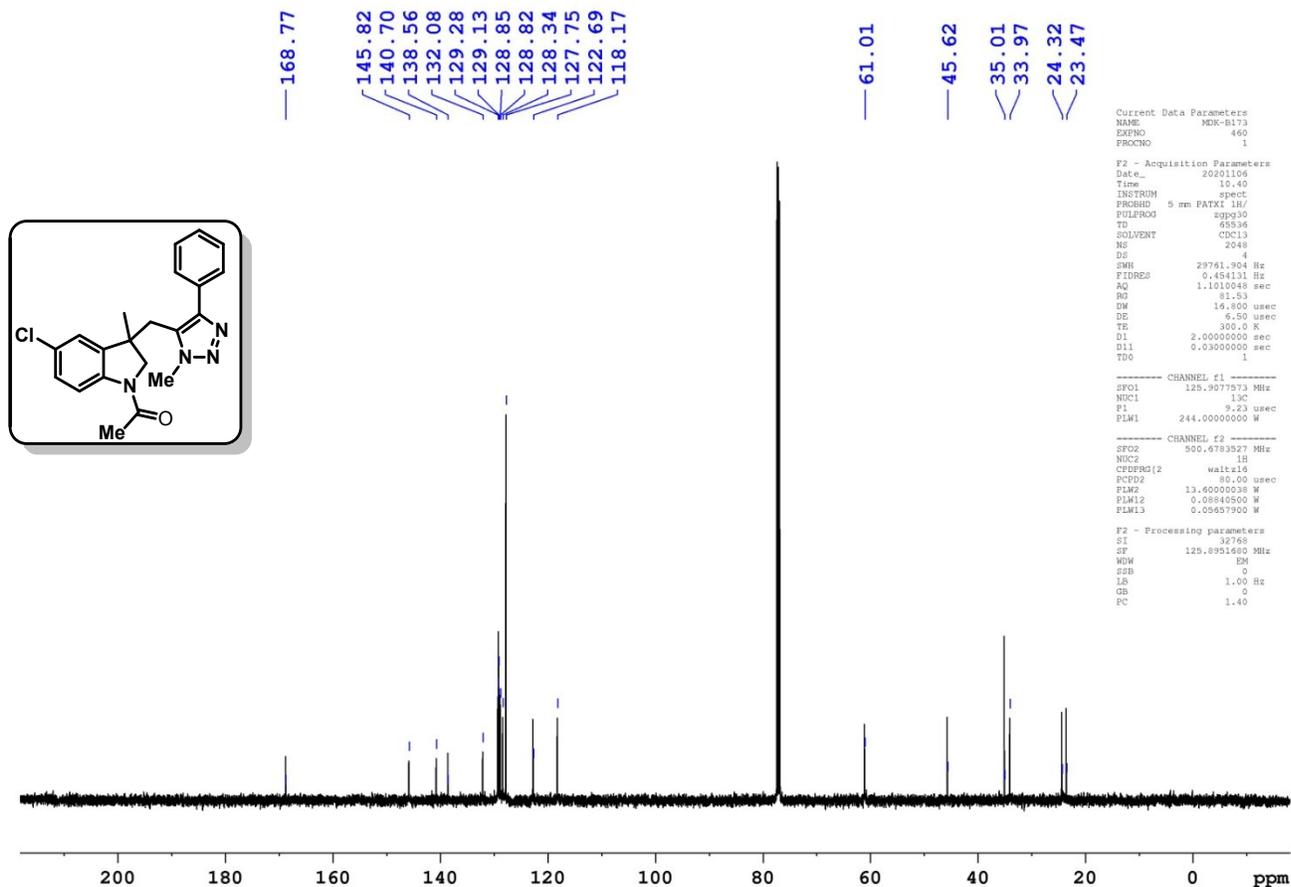


Figure S-33  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) spectrum of compound **3ma**

SAIF [HRMS Report]

Data File:	HRMS20110NOV36	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
Sample ID:	MDK-B173	Sample Name:	
Acquisition Date:	11/10/20 01:59:07 PM	Run Time(min):	0.00
Vial:	CStk1-01:36	Injection Volume( $\mu\text{l}$ ):	1.00

HRMS20110NOV36 #12-23 RT: 0.11-0.21 AV: 12 SB: 1 0.00 NL: 1.01E6  
 T: FTMS + p ESI Full ms [150.00-1000.00]

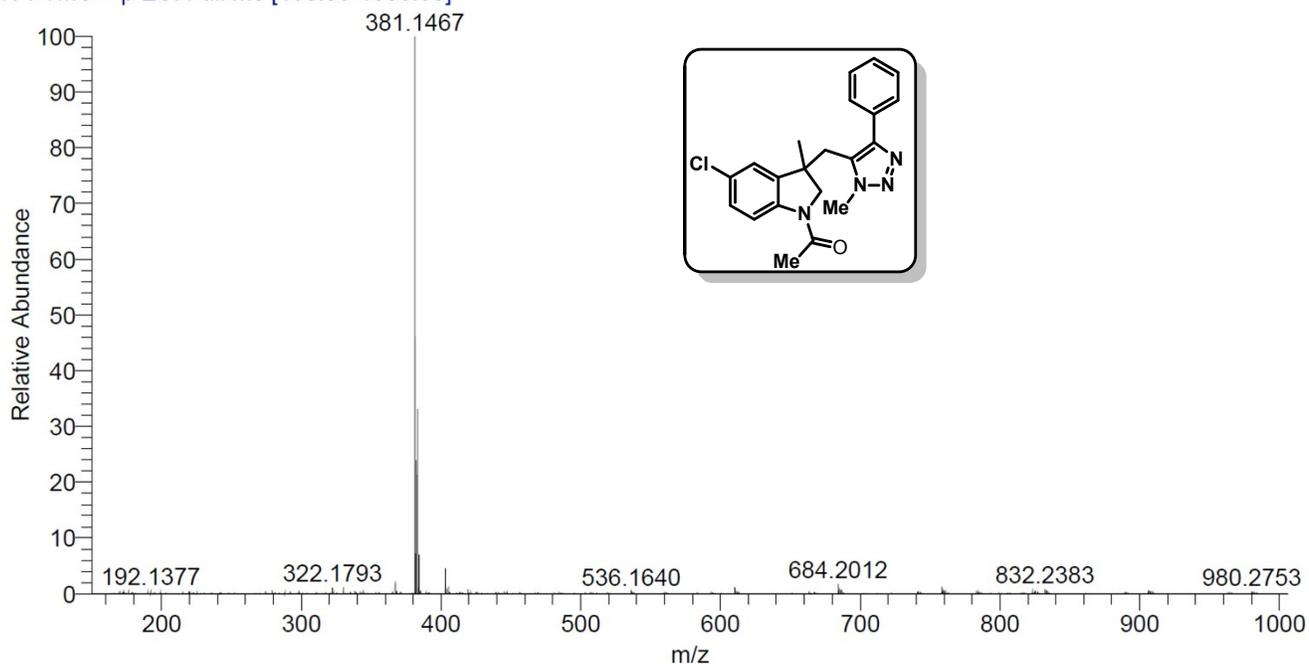


Figure S-34 HRMS spectrum of compound **3ma**

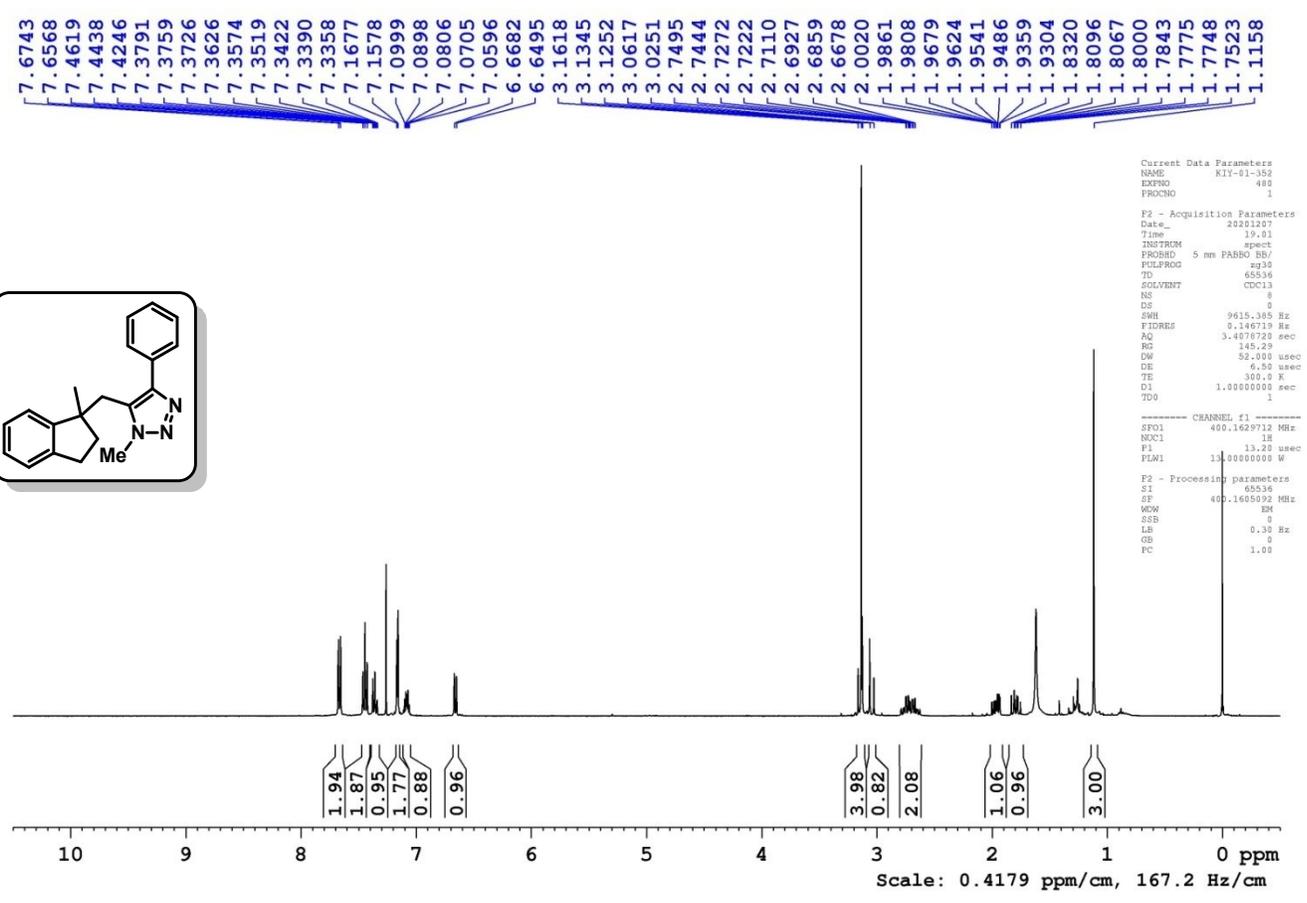
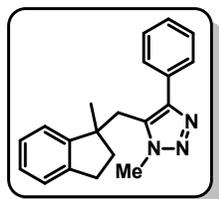


Figure S-35 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3na

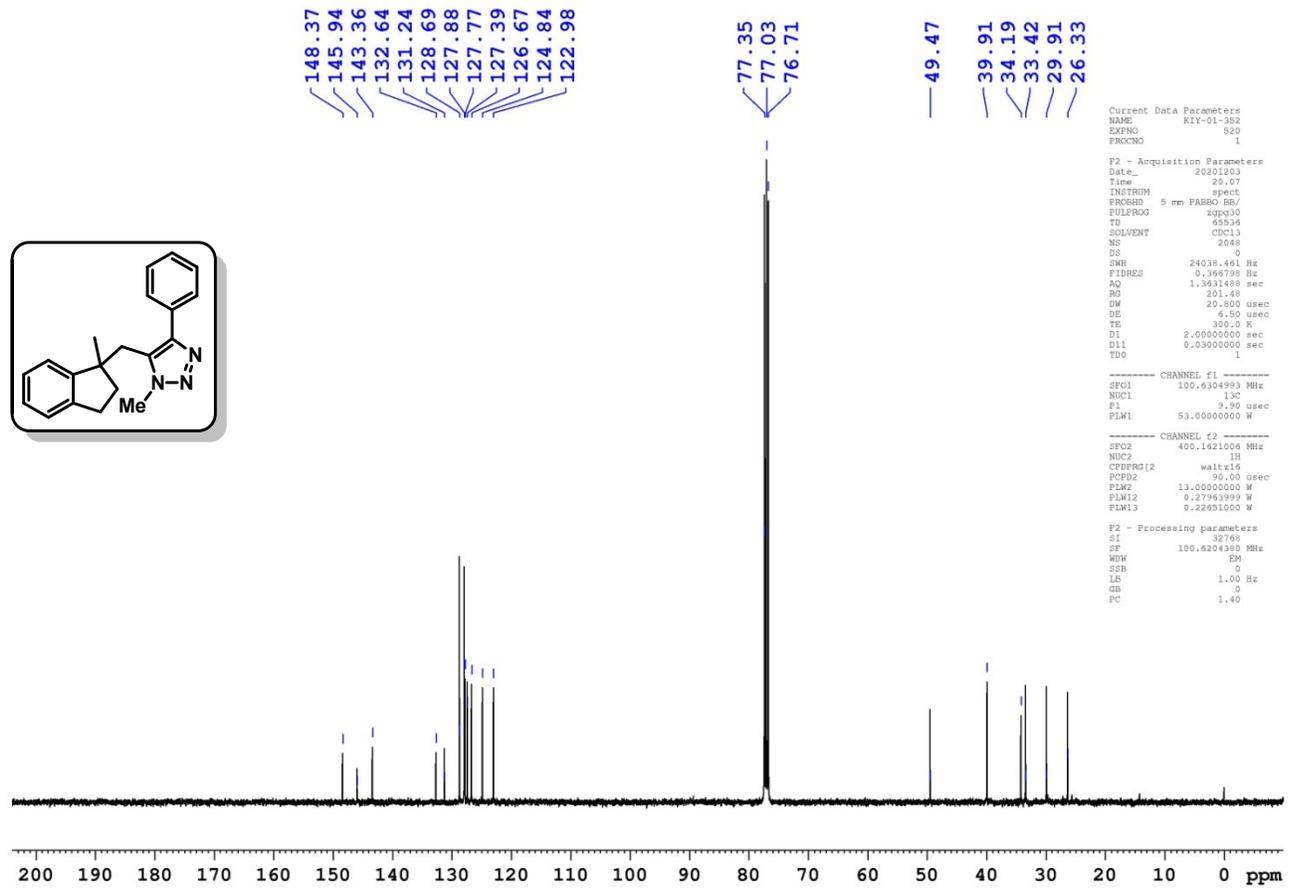
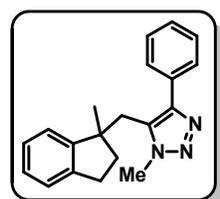
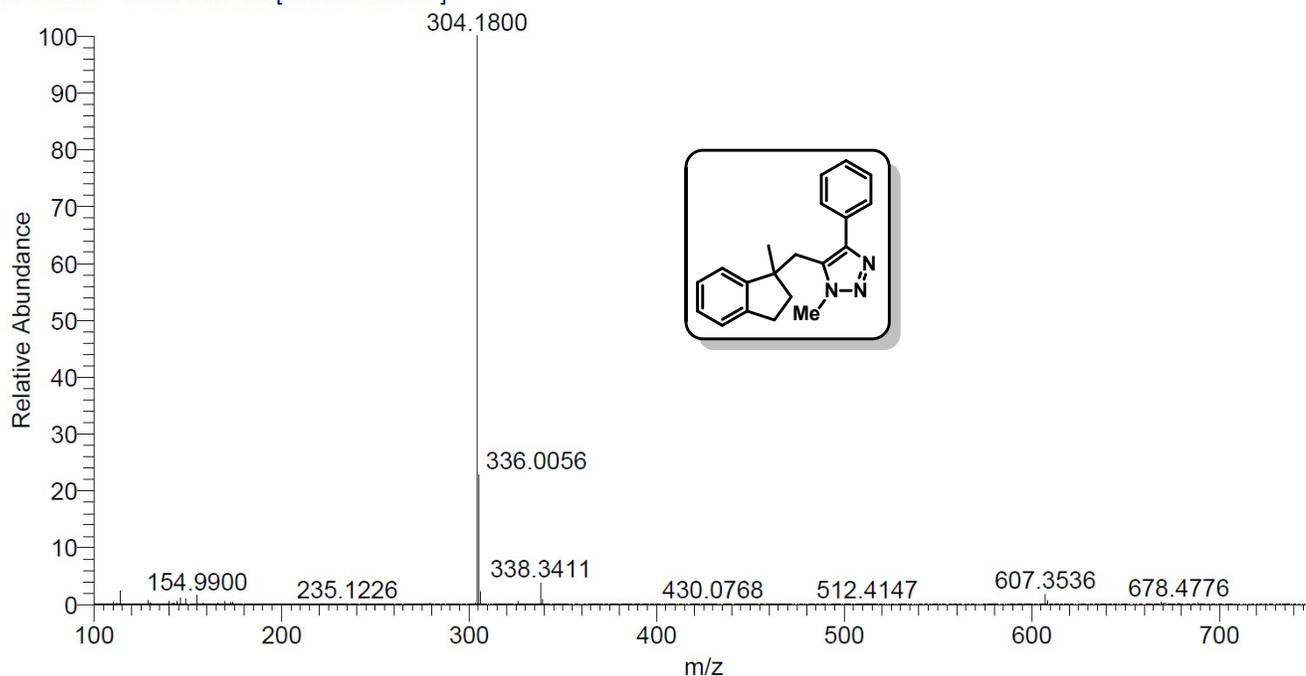


Figure S-36 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3na

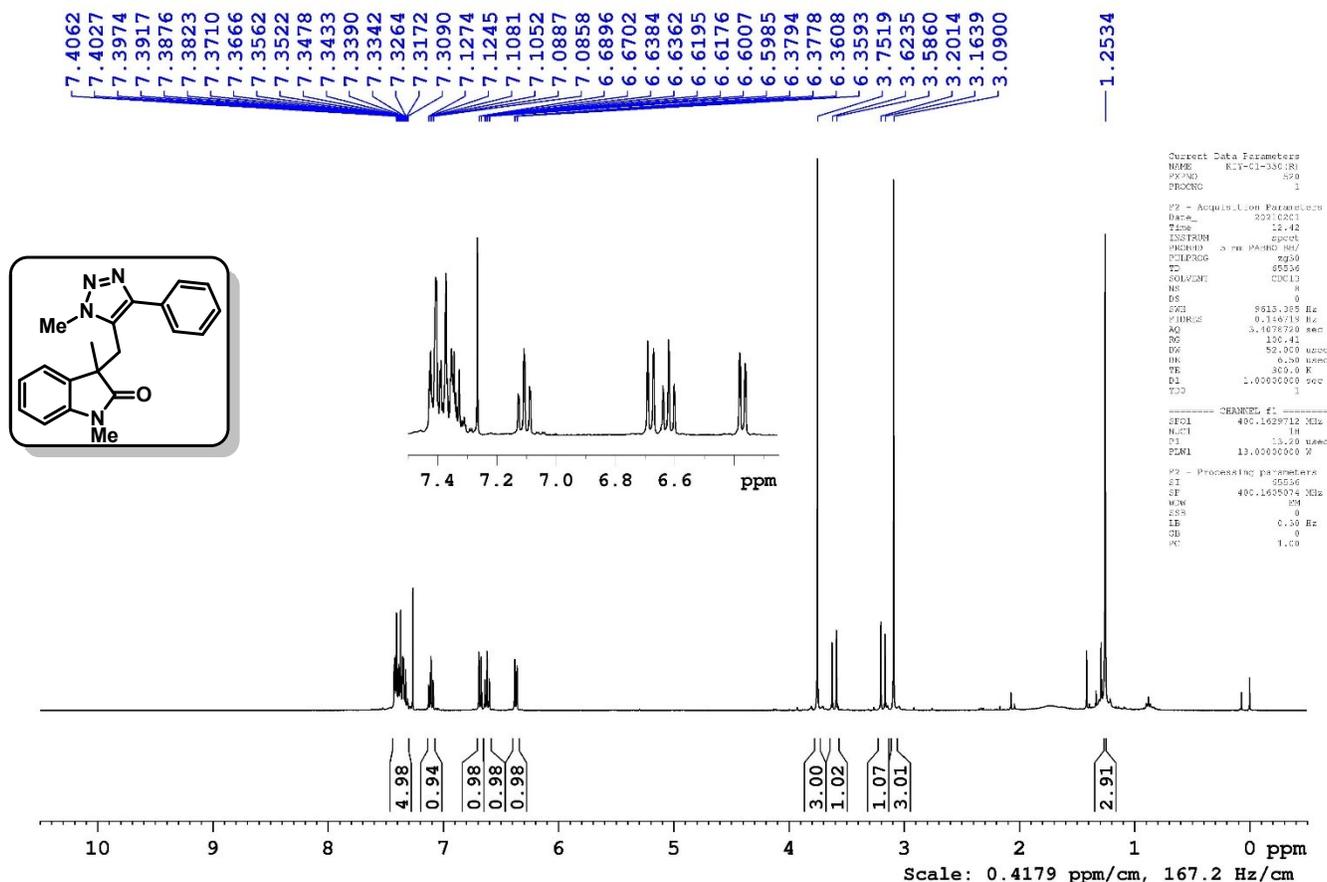
# SAIF [HRMS Report]

Data File:	HRMS20I02DEC24	Original Data Path:	D:\INTERNAL NEW\2020\DEC 2020
Sample ID:	KIY-01-352	Sample Name:	
Acquisition Date:	12/02/20 01:51:53 PM	Run Time(min):	0.00
Vial:	CStk1-01:24	Injection Volume(μl):	1.00

HRMS20I02DEC24 #30-63 RT: 0.25-0.50 AV: 34 SB: 1 0.01 NL: 1.05E7  
 T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-37** HRMS spectrum of compound **3na**



**Figure S-38** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3oa**

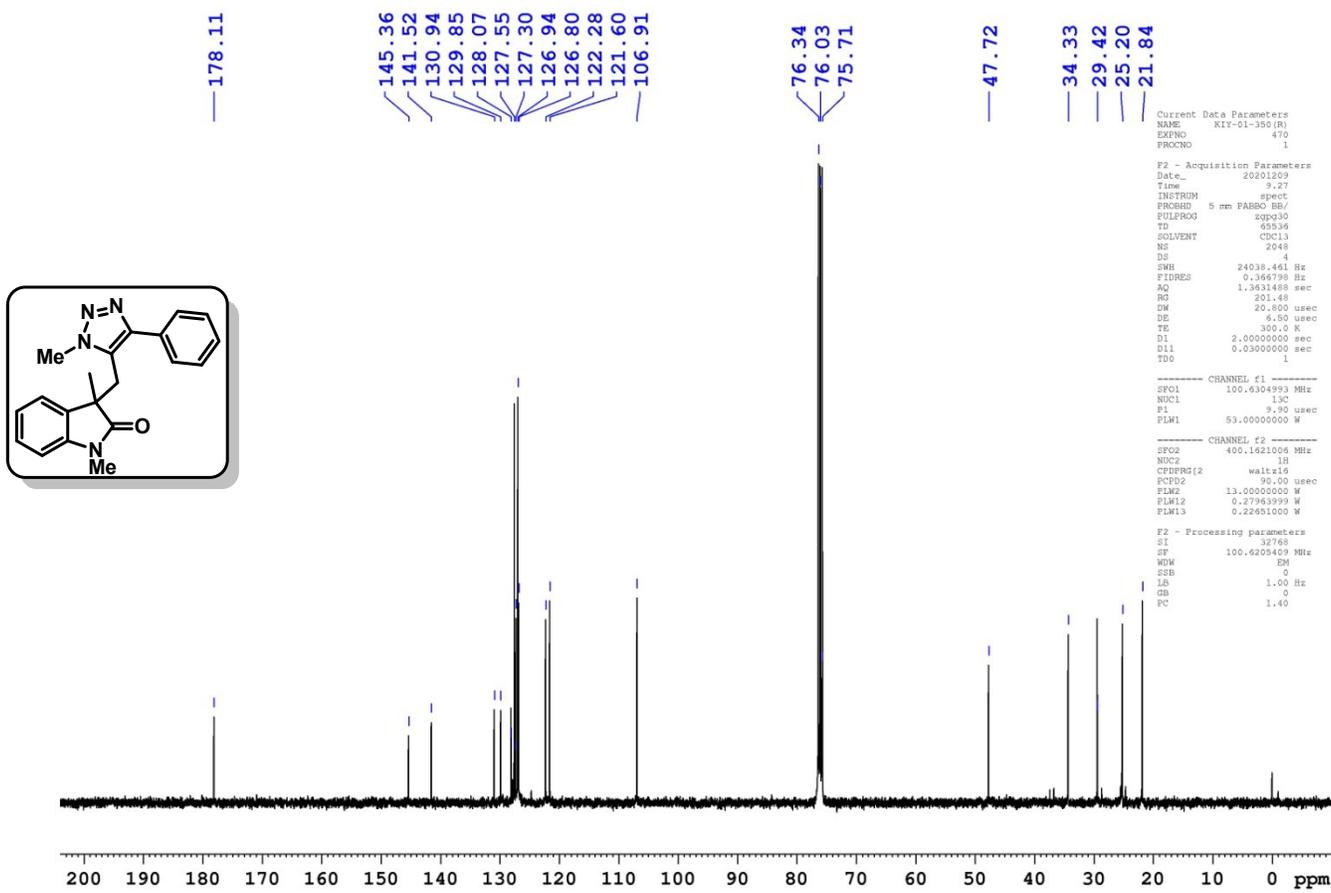


Figure S-39 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 30a

SAIF [HRMS Report]

Data File:	HRMS20I03DEC37	Original Data Path:	D:\INTERNAL NEW\2020\DEC 2020
Sample ID:	KIY-01-350	Sample Name:	
Acquisition Date:	12/03/20 01:44:28 PM	Run Time(min):	0.00
Vial:	CSfk1-01:37	Injection Volume(μl):	1.00

HRMS20I03DEC37 #30-62 RT: 0.25-0.50 AV: 33 SB: 1 0.01 NL: 6.16E6  
 T: FTMS + c ESI Full ms [100.00-750.00]

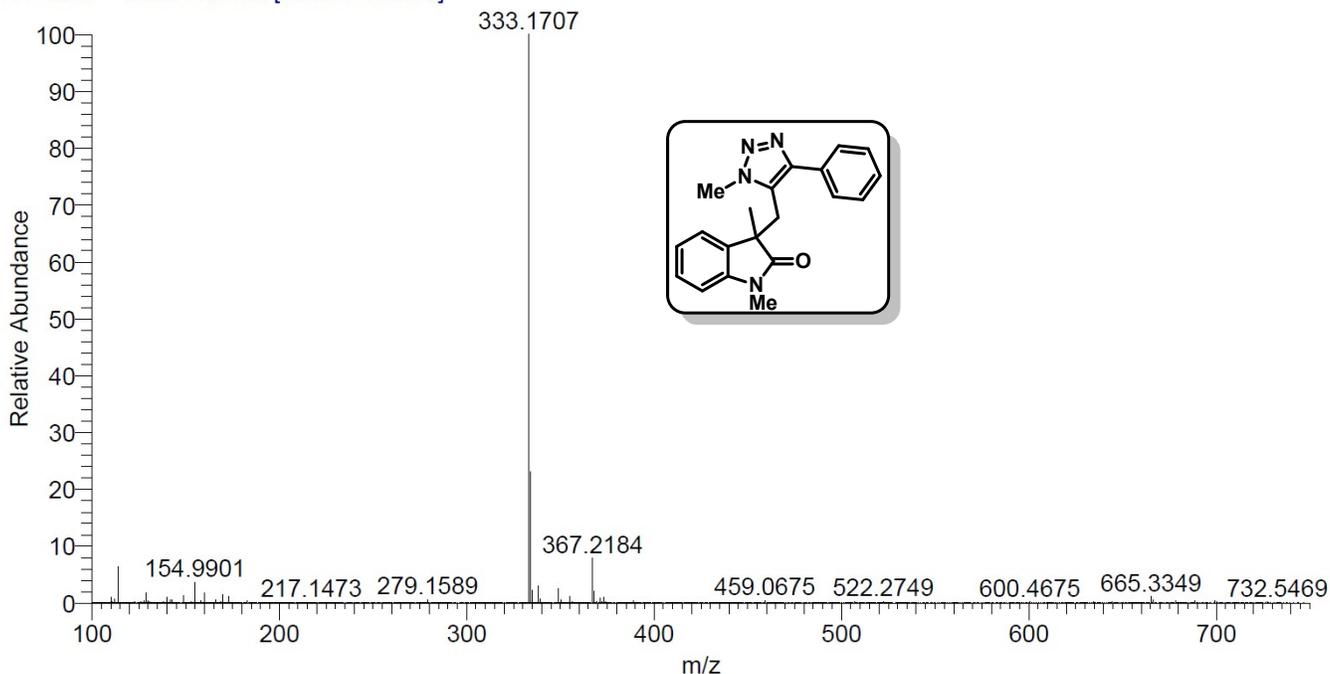


Figure S-40 HRMS spectrum of compound 30a

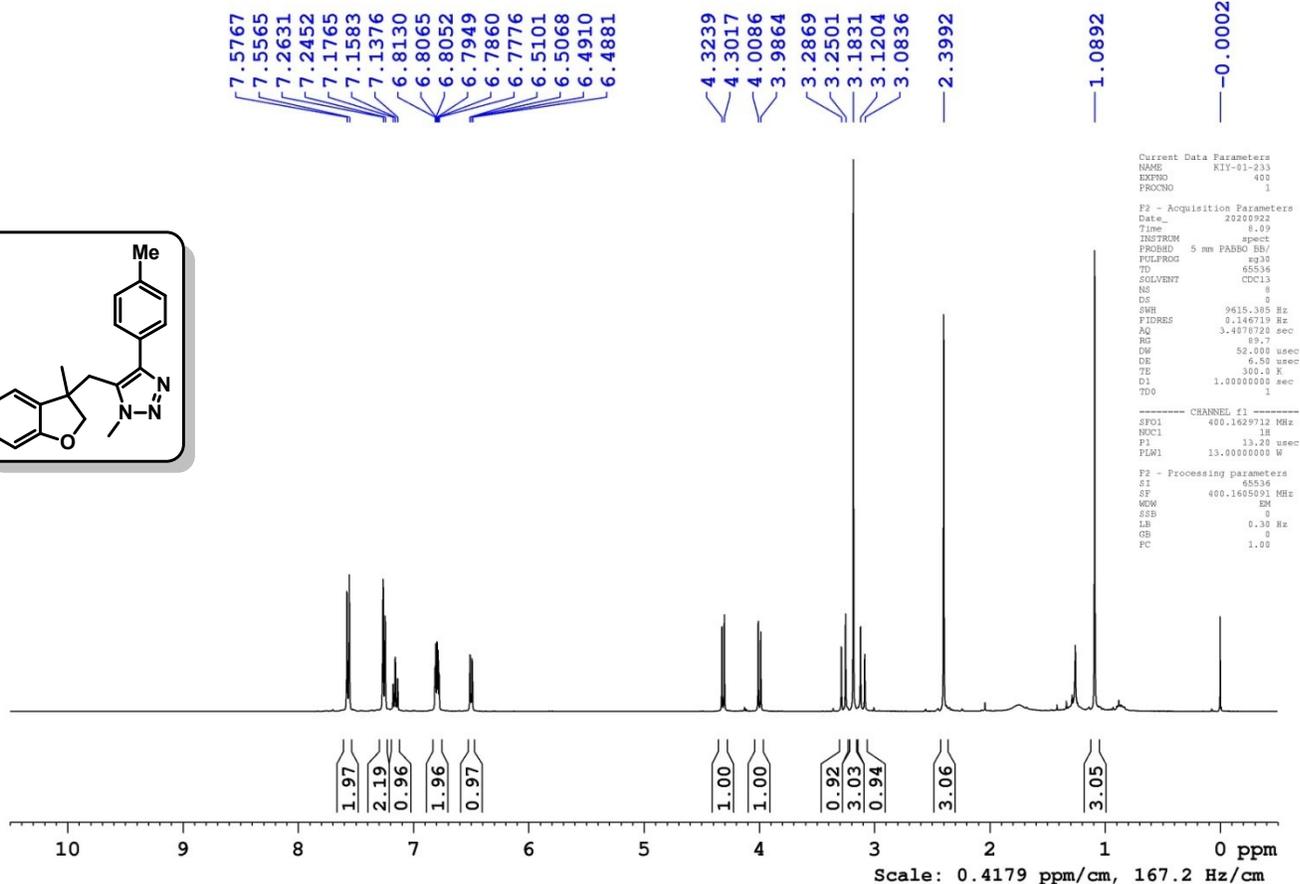
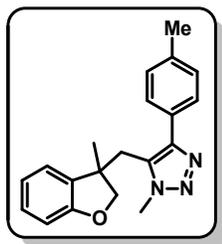


Figure S-41 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ab**

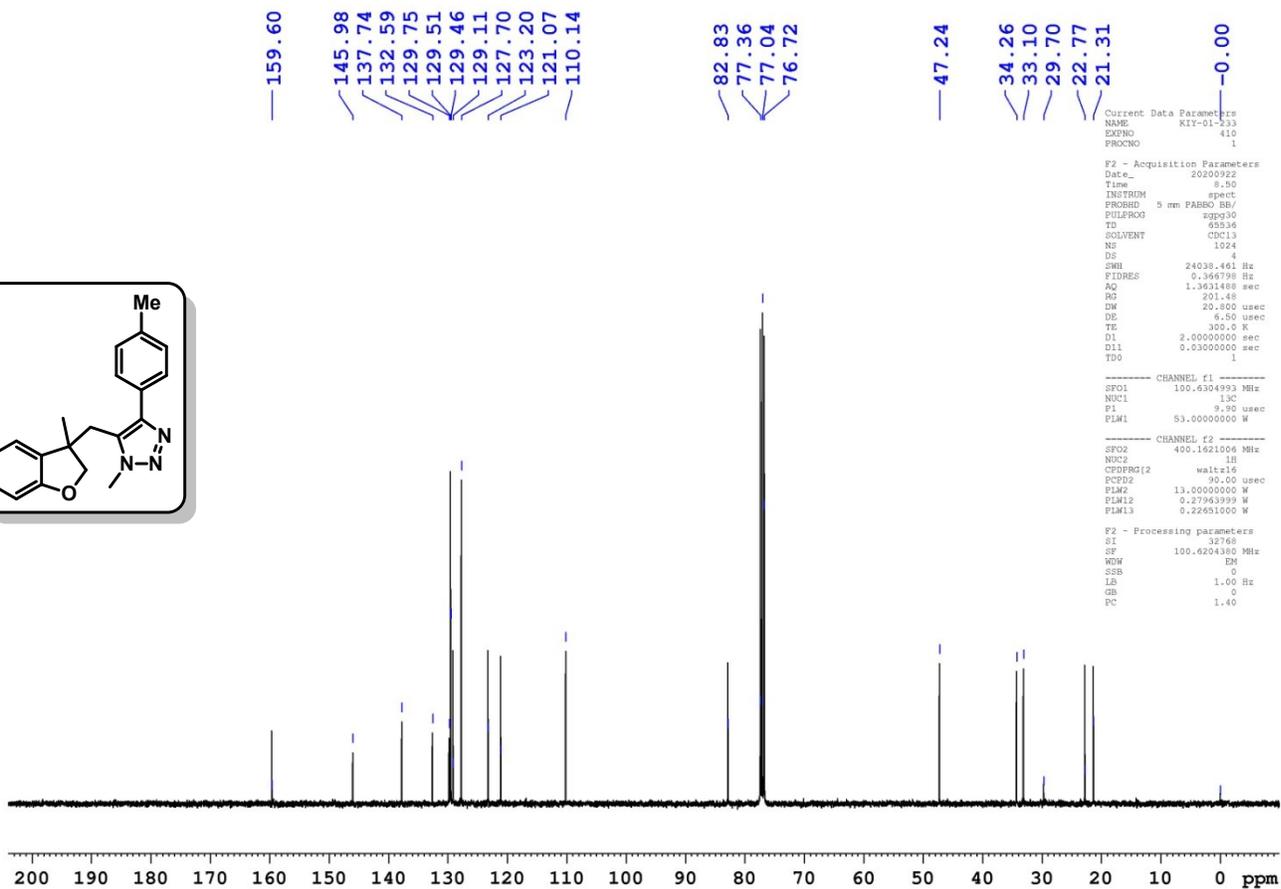
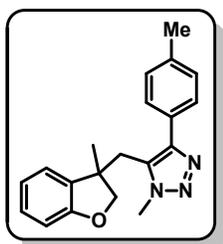


Figure S-42 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound **3ab**

HRMS20124SEP11\_200924120942 #53 RT: 0.43 AV: 1 SB: 7 0.02-0.08 NL: 3.05E6  
T: FTMS + c ESI Full ms [100.00-750.00]

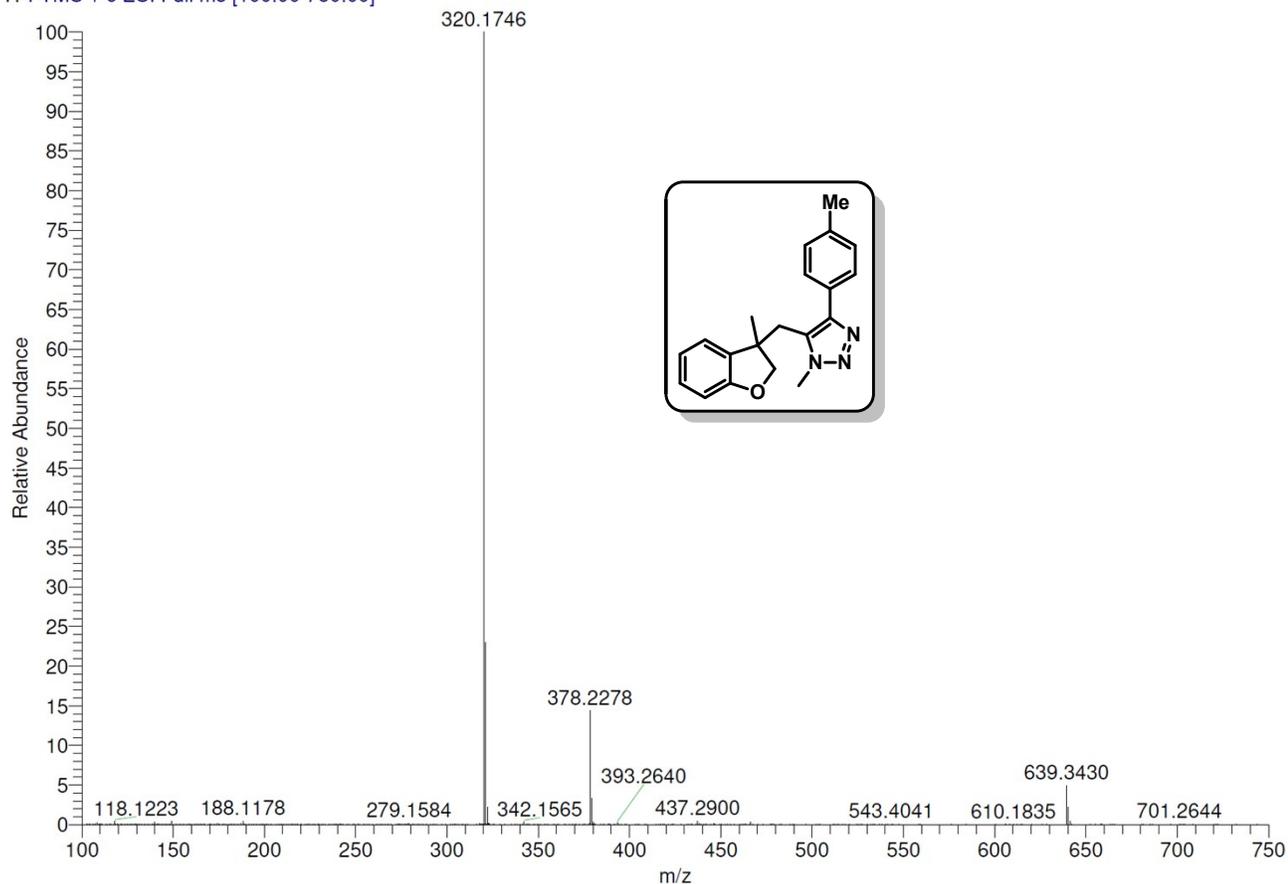


Figure S-43 HRMS spectrum of compound **3ab**

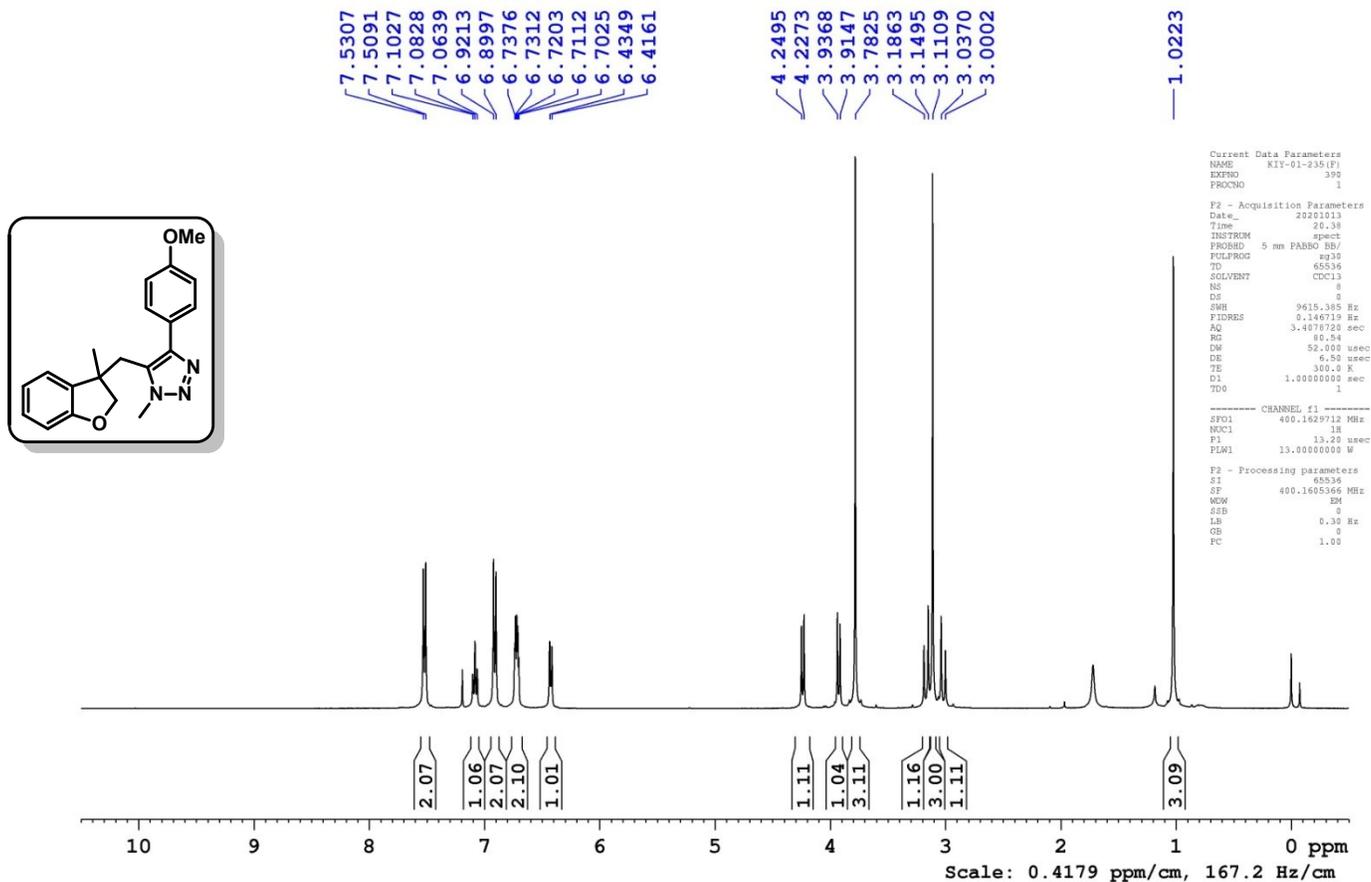


Figure S-44 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ac**

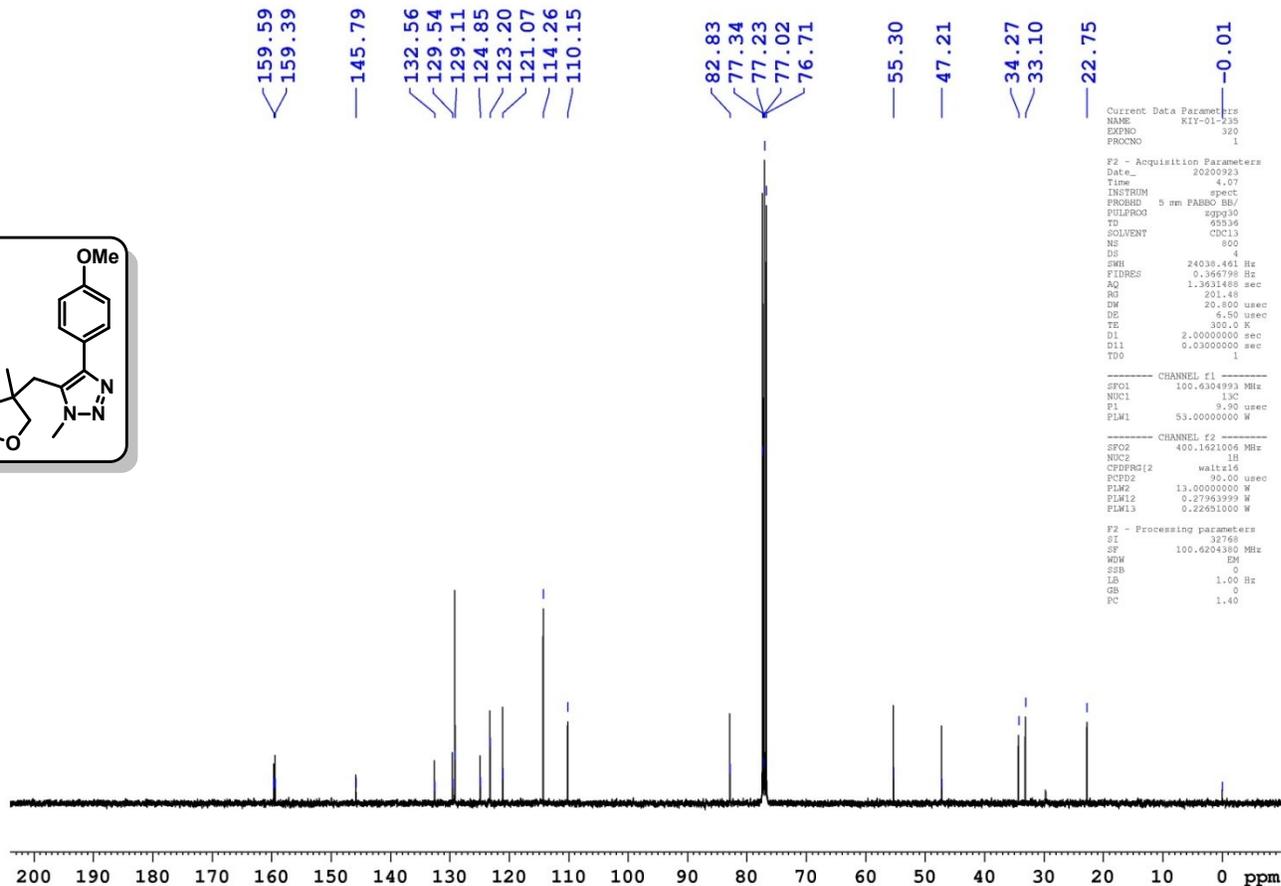
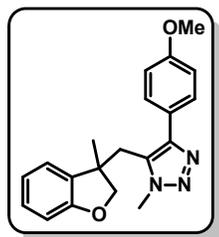


Figure S-45 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ac

**SAIF [HRMS Report]**

Data File:	HRMS20I28SEP13	Original Data Path:	D:\INTERNAL NEW\2020\Sep 2020
Sample ID:	KIY-01-235	Sample Name:	
Acquisition Date:	09/28/20 11:13:57 AM	Run Time(min):	0.00
Vial:	CStk1-01:13	Injection Volume(μl):	1.00

HRMS20I28SEP13 #12-24 RT: 0.11-0.21 AV: 13 SB: 1 0.01 NL: 6.41E6  
T: FTMS + c ESI Full ms [100.00-750.00]

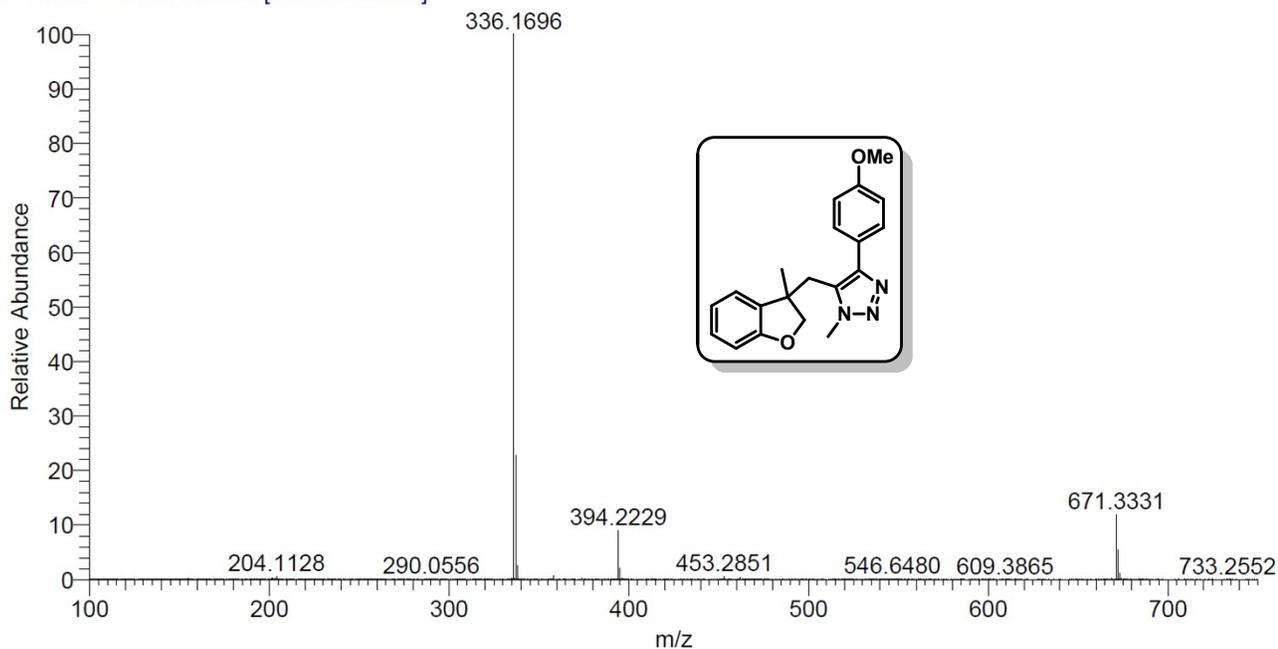


Figure S-46 HRMS spectrum of compound 3ac

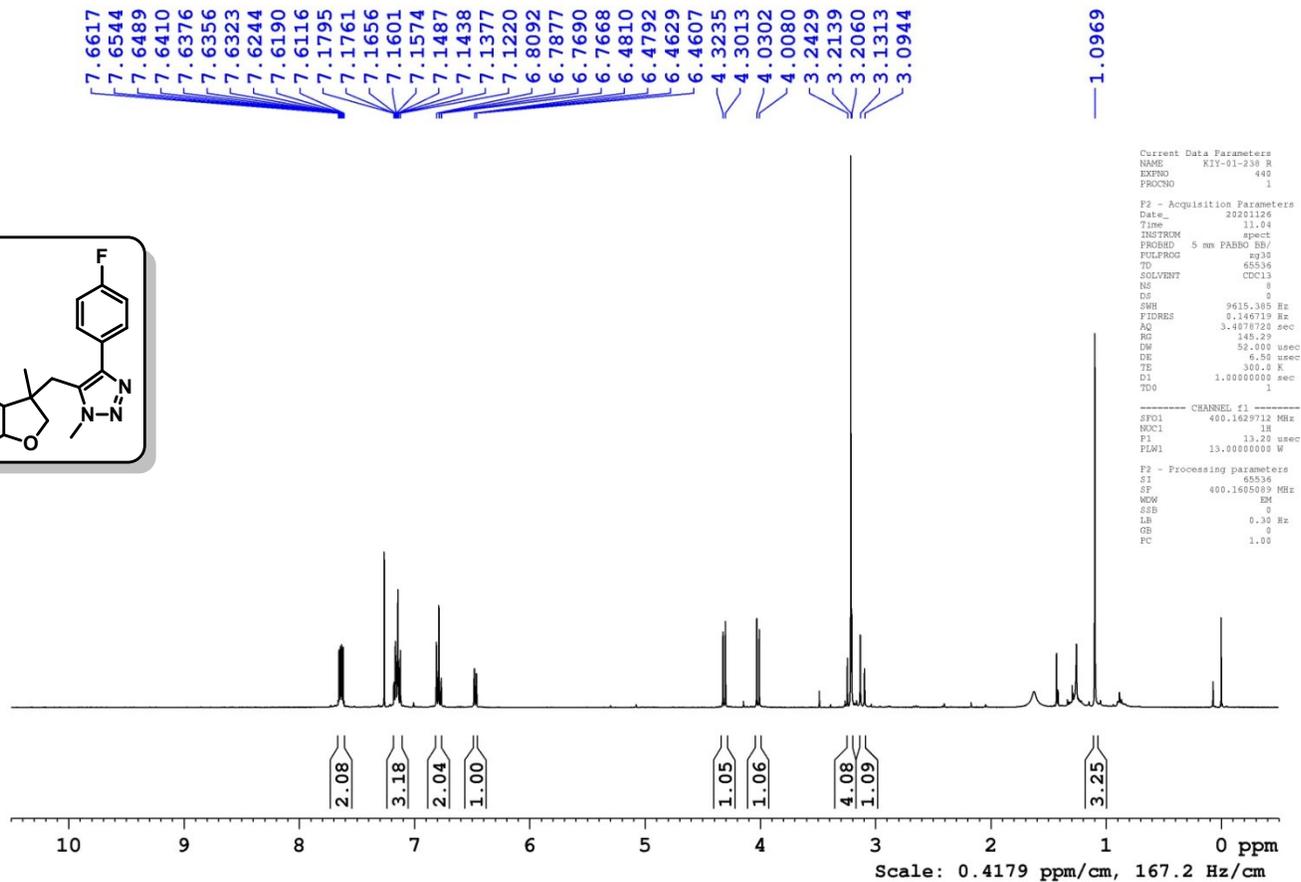
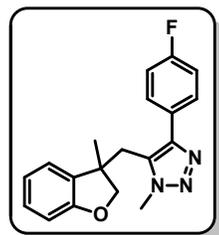


Figure S-47 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3ad

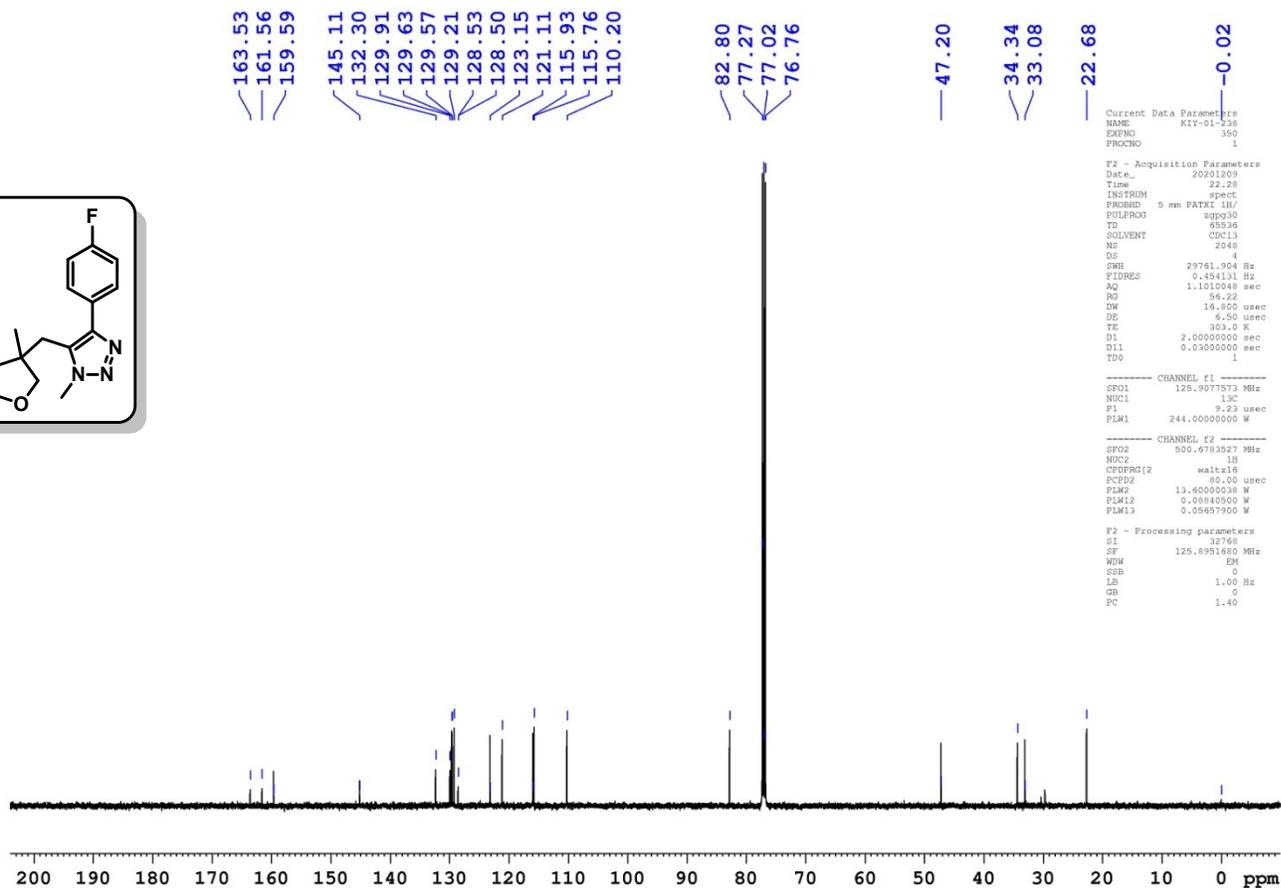
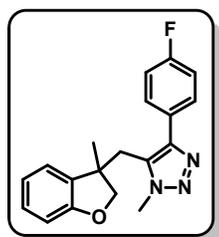
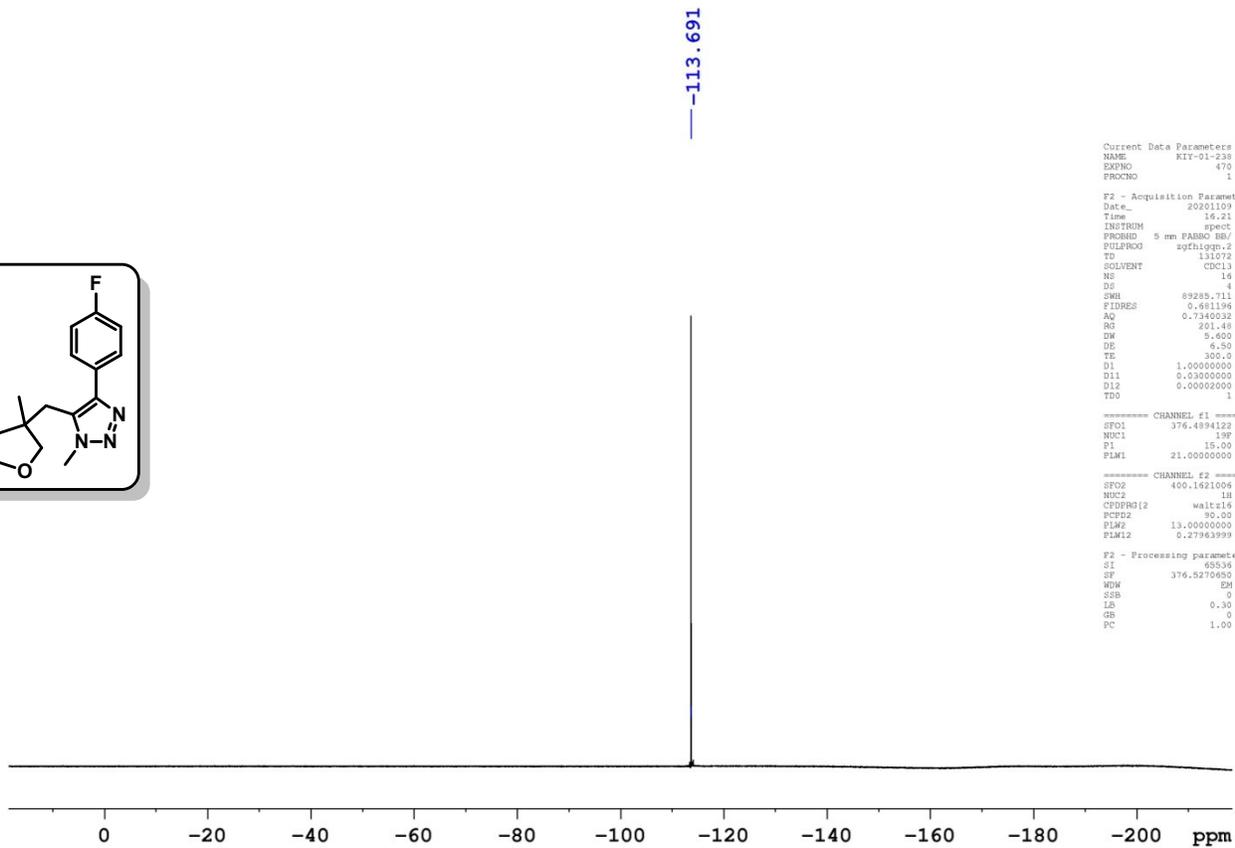
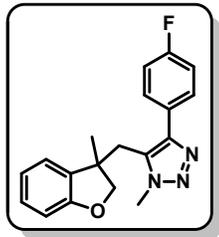


Figure S-48 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ad



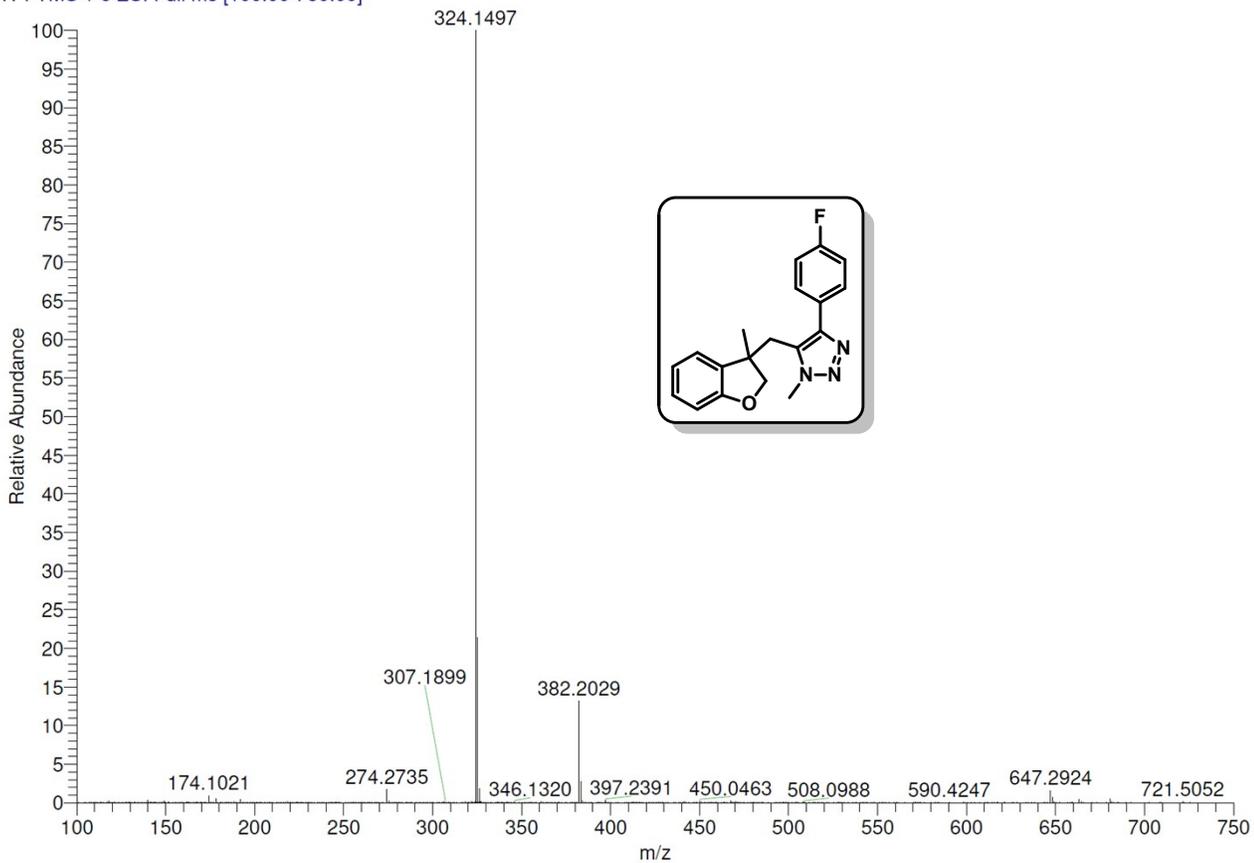
**Figure S-49** <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) spectrum of compound **3ad**

HRMS20I24SEP12\_200924121139

9/24/2020 12:11:39 PM

K1Y-01-238

HRMS20I24SEP12\_200924121139 #47 RT: 0.39 AV: 1 SB: 7 0.02-0.08 NL: 1.05E6  
 T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-50** HRMS spectrum of compound **3ad**

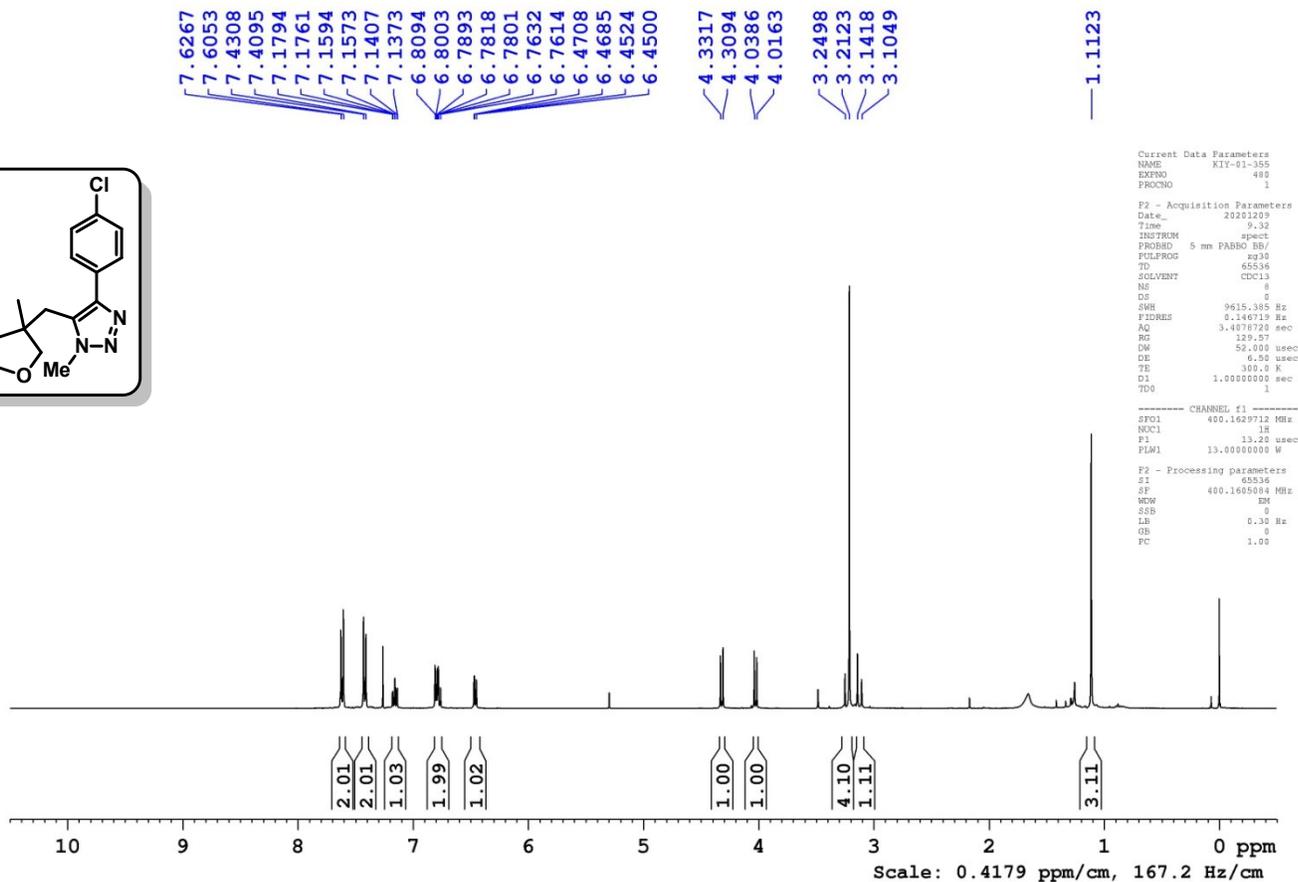
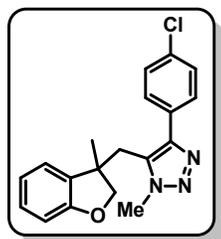


Figure S-51 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3ae

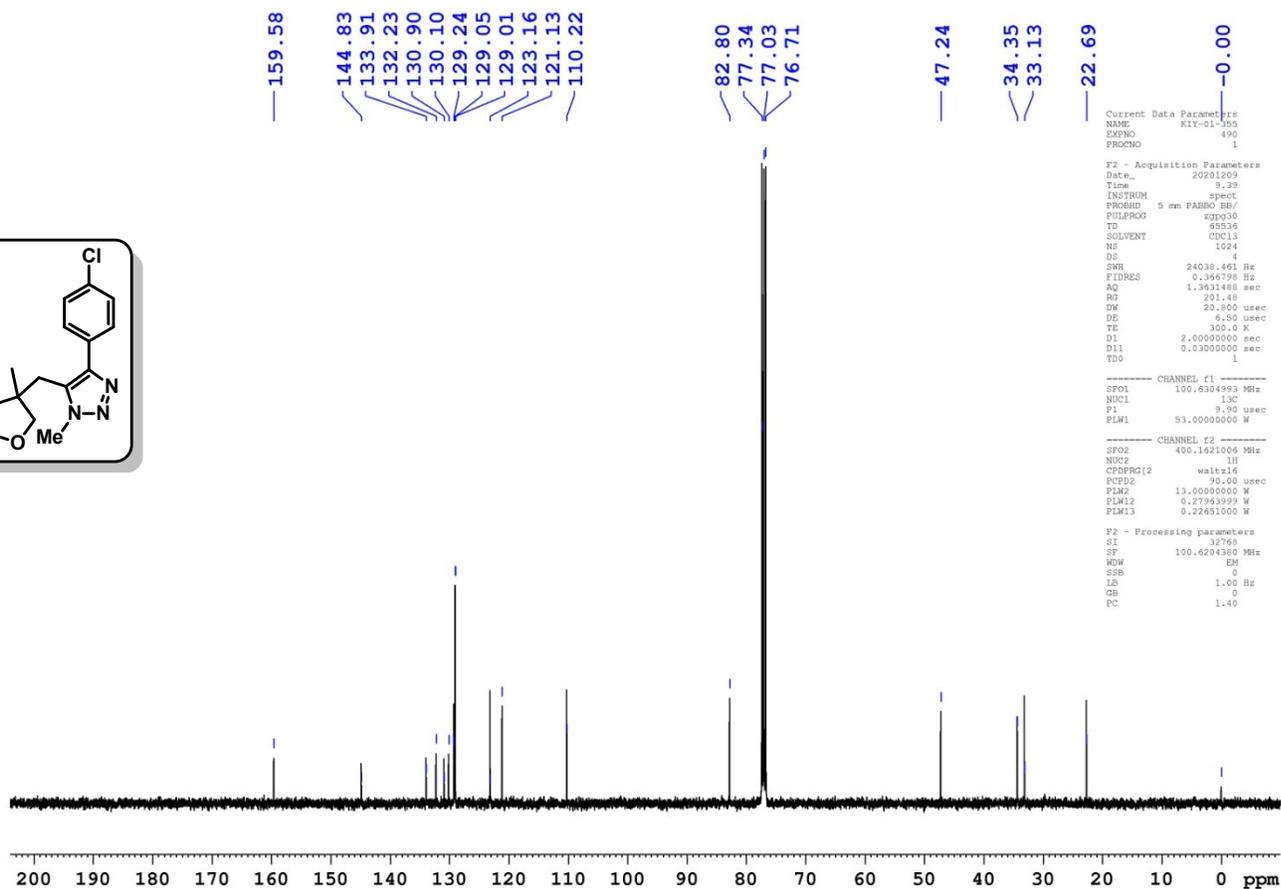
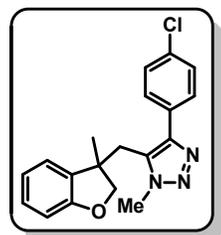
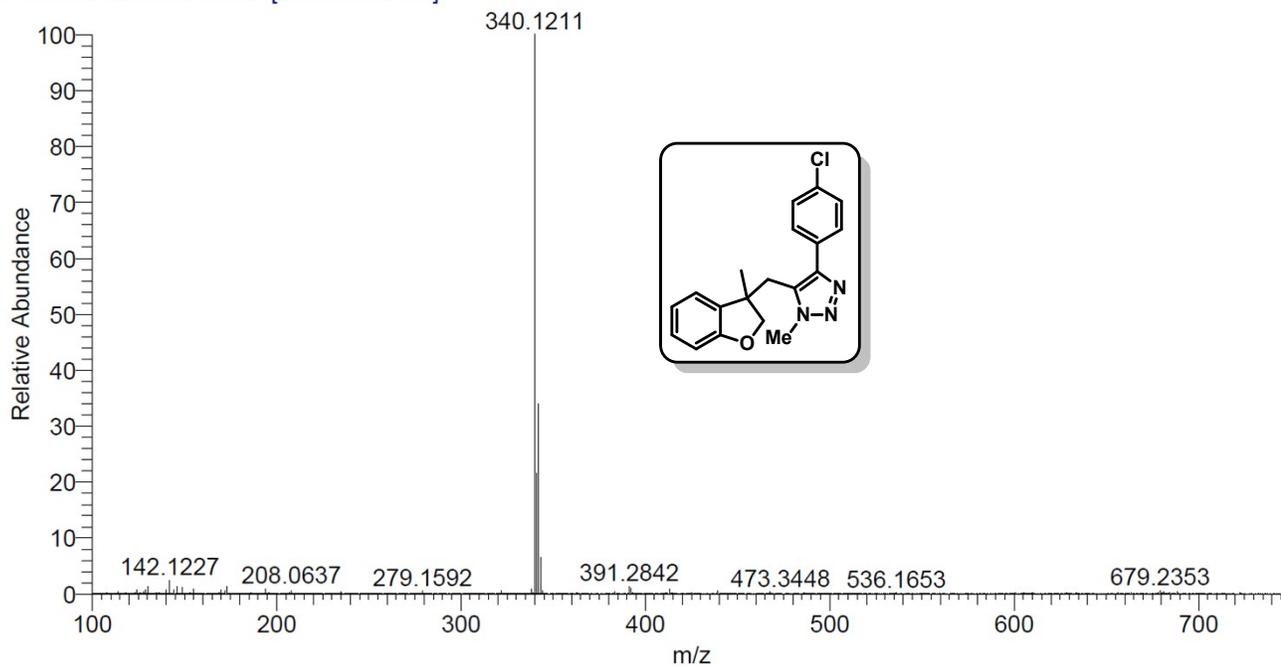


Figure S-52 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ae

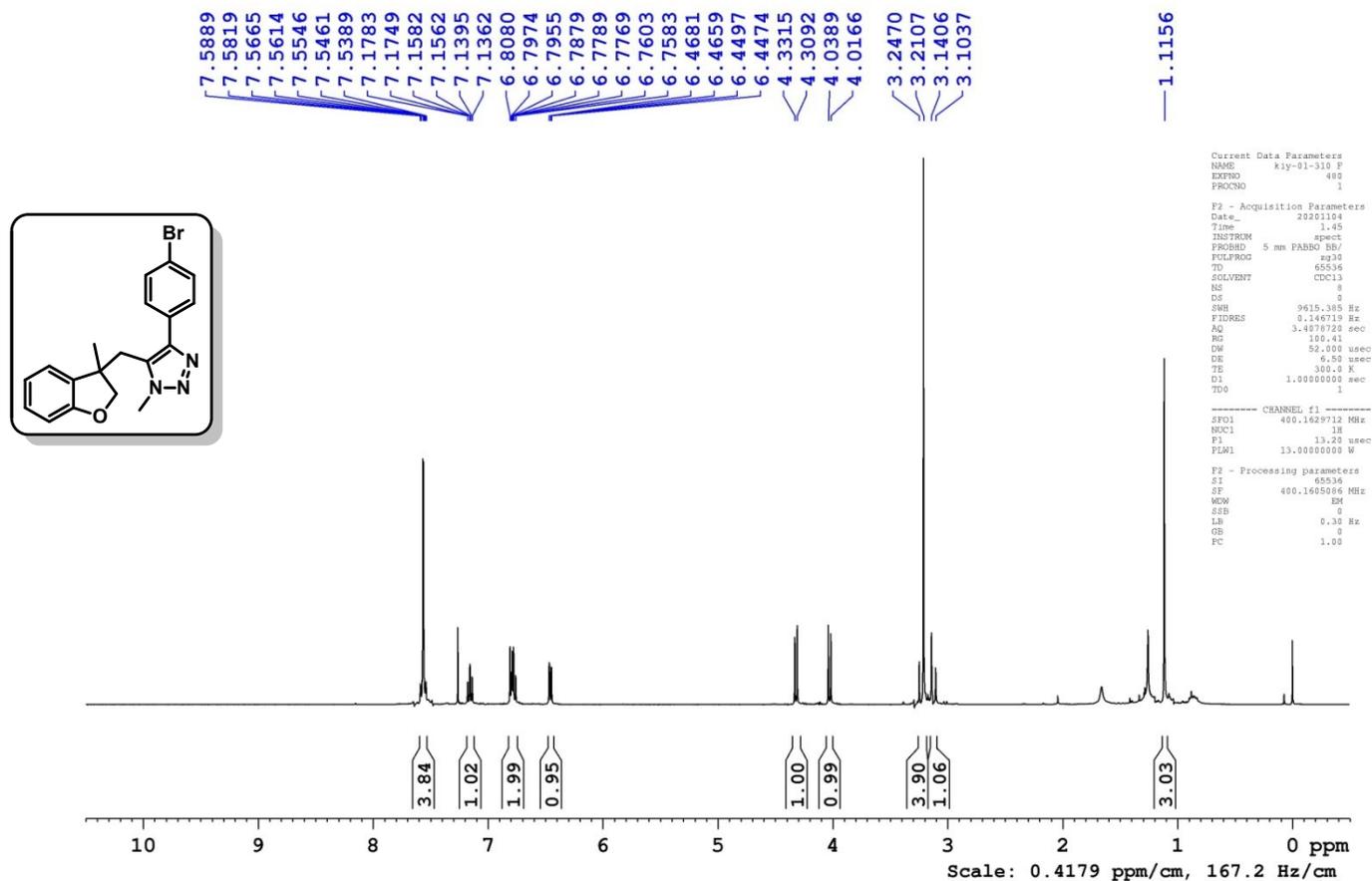
**SAIF [HRMS Report]**

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Sample ID:	KIY-01-355	Sample Name:	
Acquisition Date:	12/08/20 12:01:11 PM	Run Time(min):	0.00
Vial:	CStk1-01:19	Injection Volume(μl):	1.00

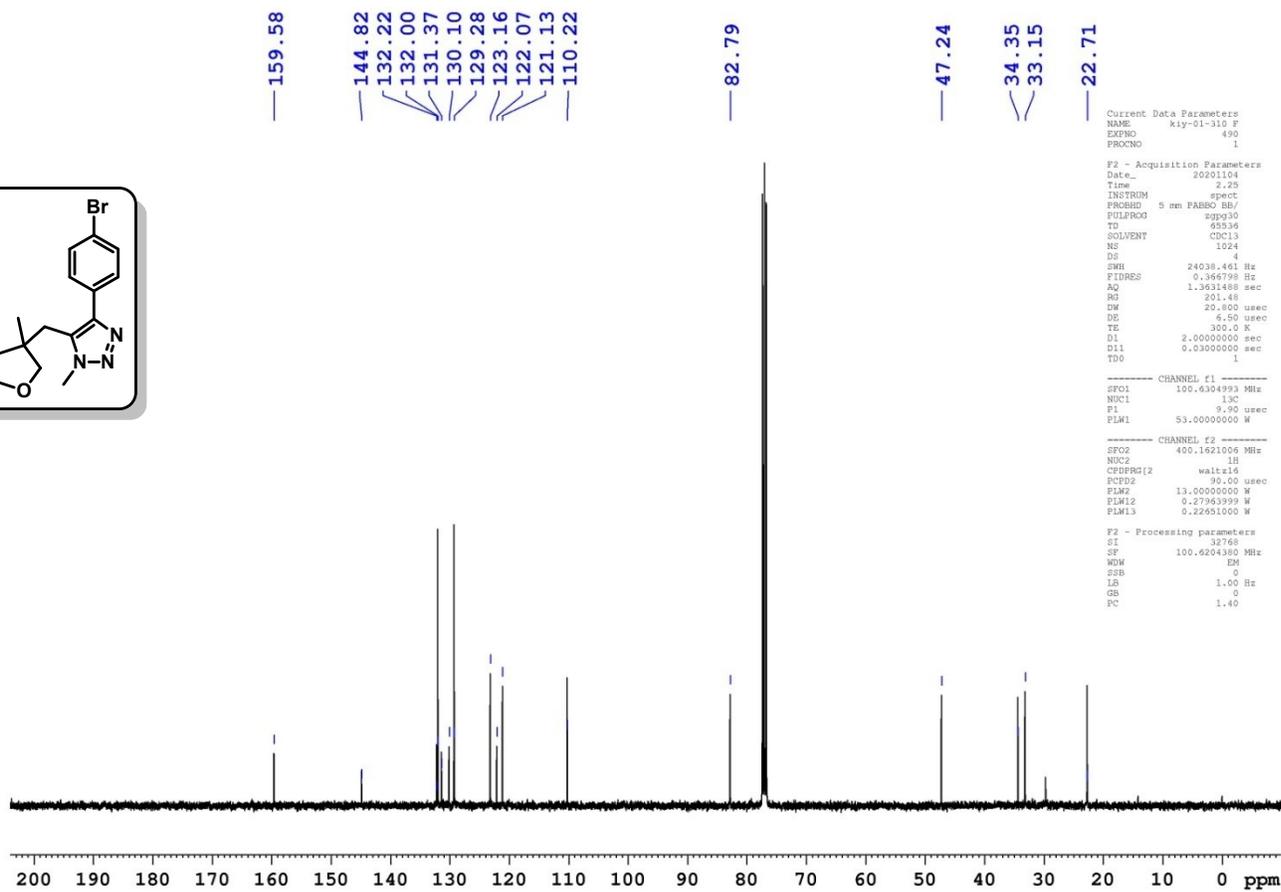
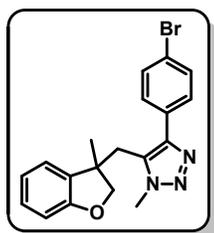
HRMS20I08DEC19 #30-62 RT: 0.25-0.50 AV: 33 SB: 1 0.01 NL: 4.39E6  
T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-53** HRMS spectrum of compound 3ae



**Figure S-54** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3af



```

Current Data Parameters
NAME      k1y-01-310 F
EXPNO    490
PROCNO   1

F2 - Acquisition Parameters
Date_    20201104
Time     2.25
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zgpg30
TD        65536
SOLVENT  CDCl3
NS        1024
DS        4
SWH       24038.461 Hz
FIDRES    0.356798 Hz
AQ        1.3631488 sec
RG        201.48
DM        20.600 usec
DE        6.50 usec
TE        300.0 K
D1        2.00000000 sec
D11       0.03000000 sec
TD0       1

----- CHANNEL f1 -----
SFO1     100.6304993 MHz
NUC1      13C
P1        9.90 usec
PLM1      53.00000000 W

----- CHANNEL f2 -----
SFO2     400.1621006 MHz
NUC2      1H
PCPD2     wait16
PCPD2     90.00 usec
PLM2      13.00000000 W
PLM12     0.27953939 W
PLM13     0.22651000 W

F2 - Processing parameters
SI        32768
SF        100.6204360 MHz
WDW       EM
SSB       0
LB        1.00 Hz
GB        0
PC        1.40

```

Figure S-55 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3af

Fig

HRMS20103NOV04 #22-36 RT: 0.19-0.29 AV: 15 SB: 7 0.02-0.07 NL: 5.07E6  
T: FTMS + c ESI Full ms [100.00-750.00]

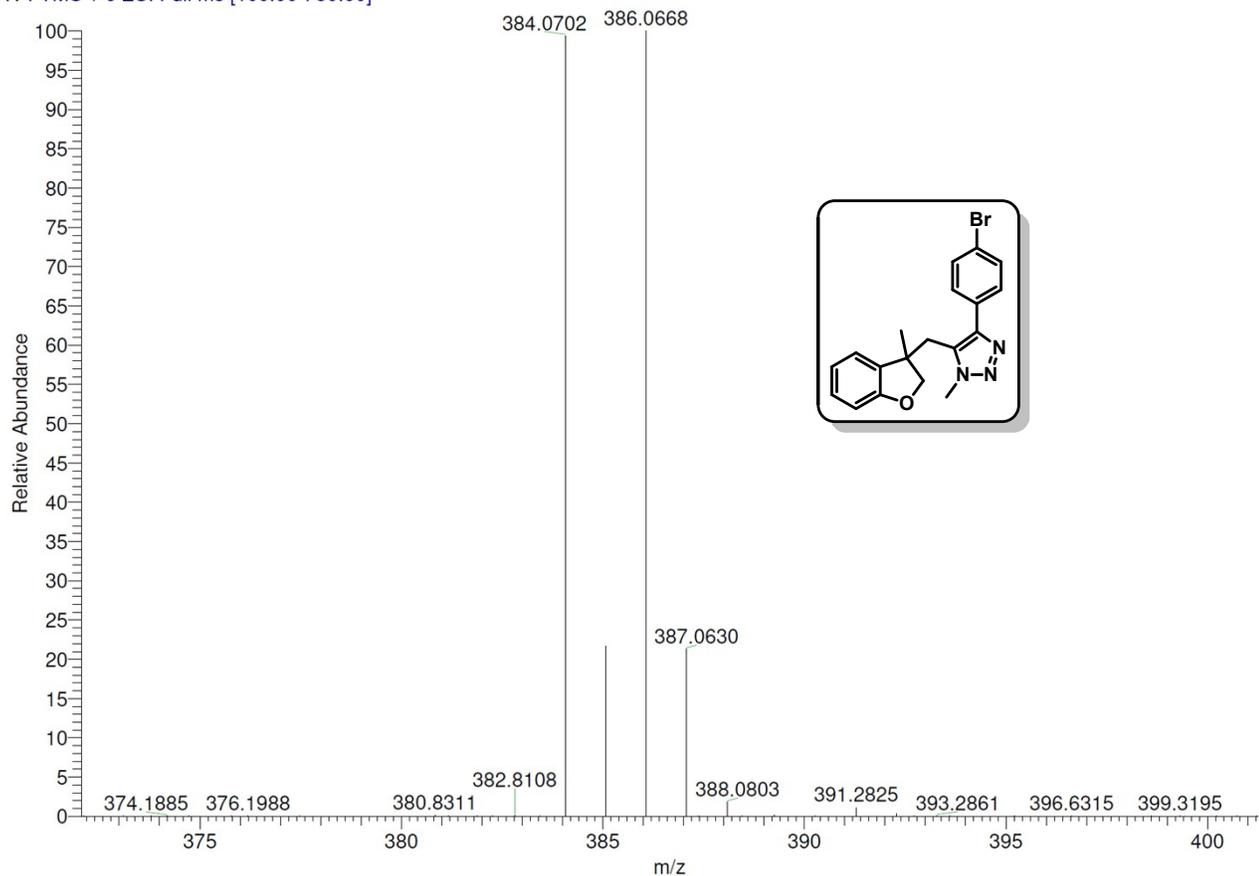


Figure S-56 HRMS spectrum of compound **3af**

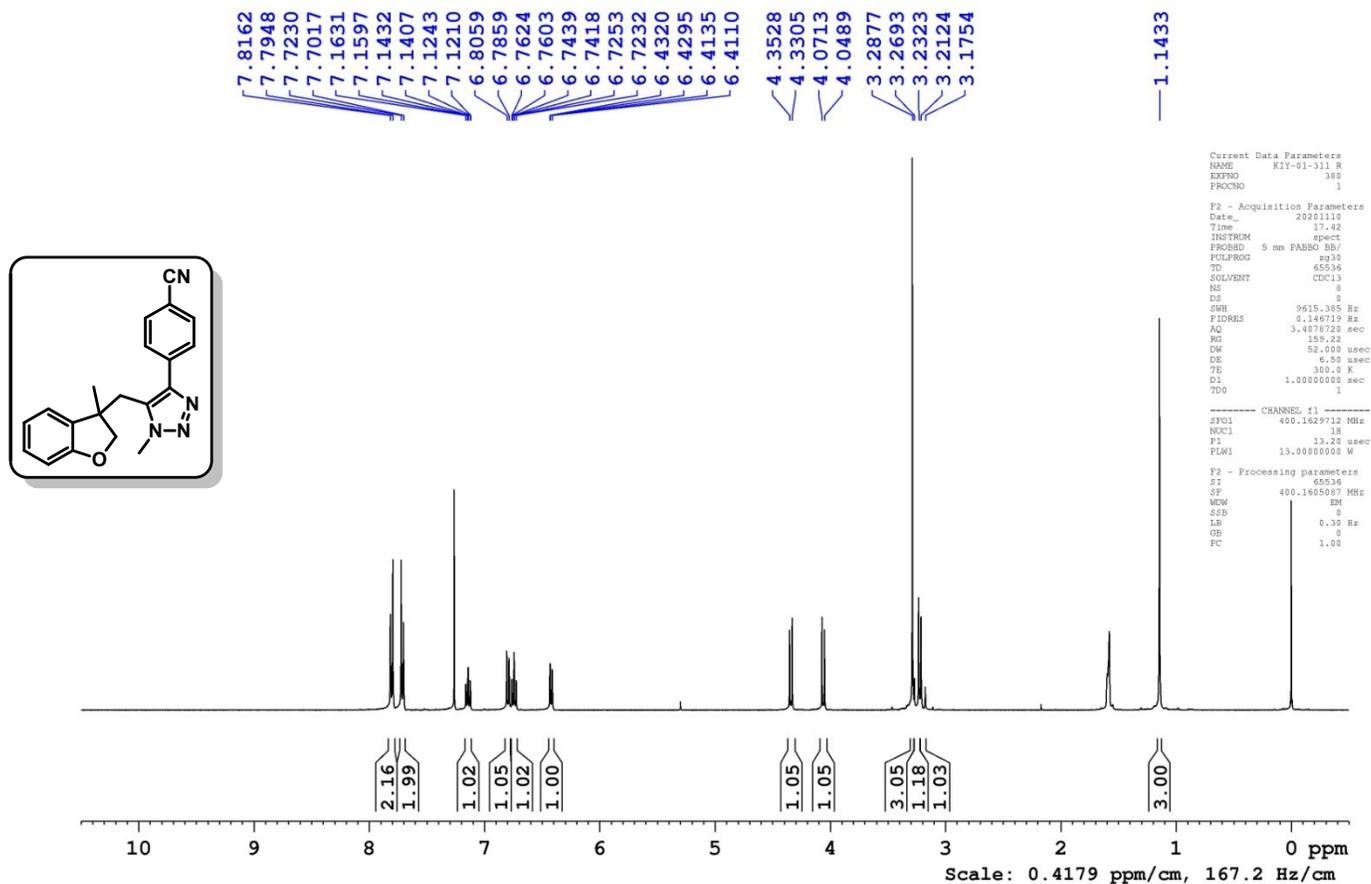


Figure S-57 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ag**

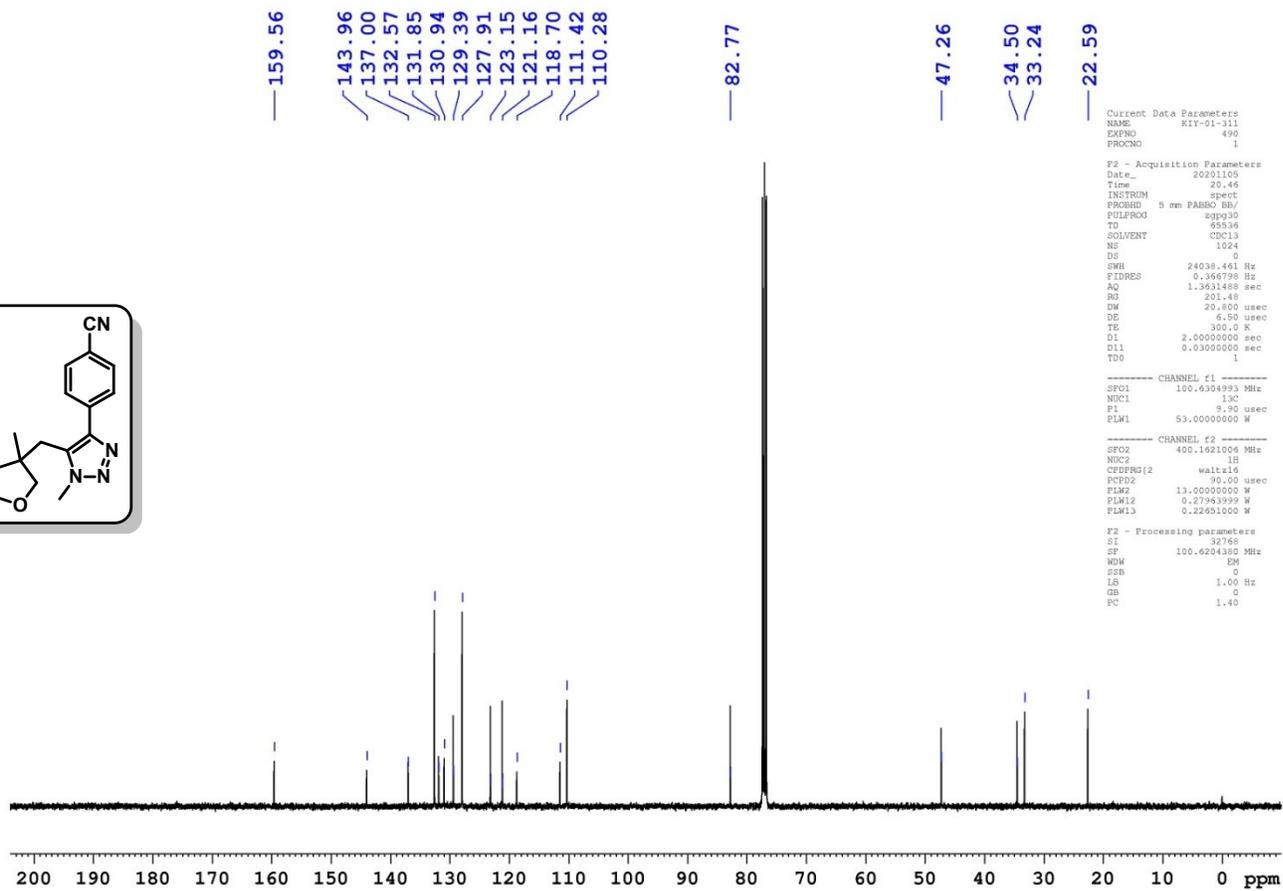
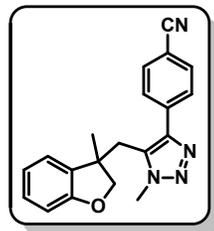
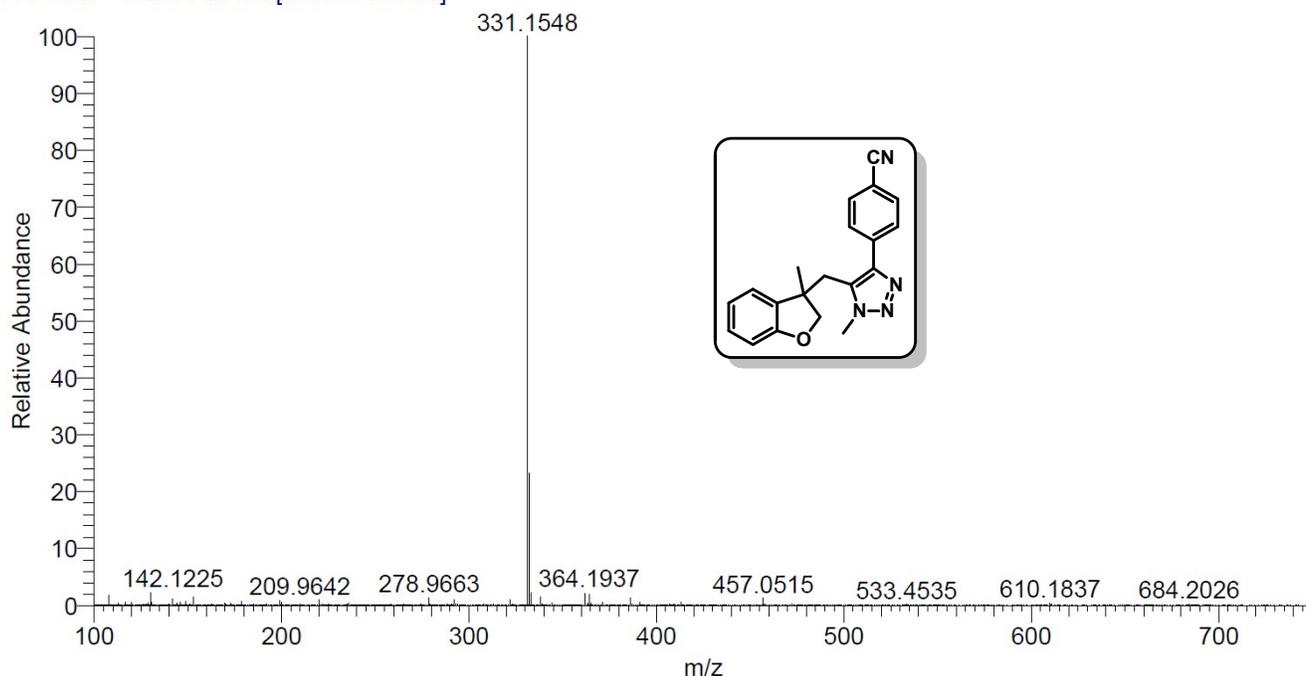


Figure S-58 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ag

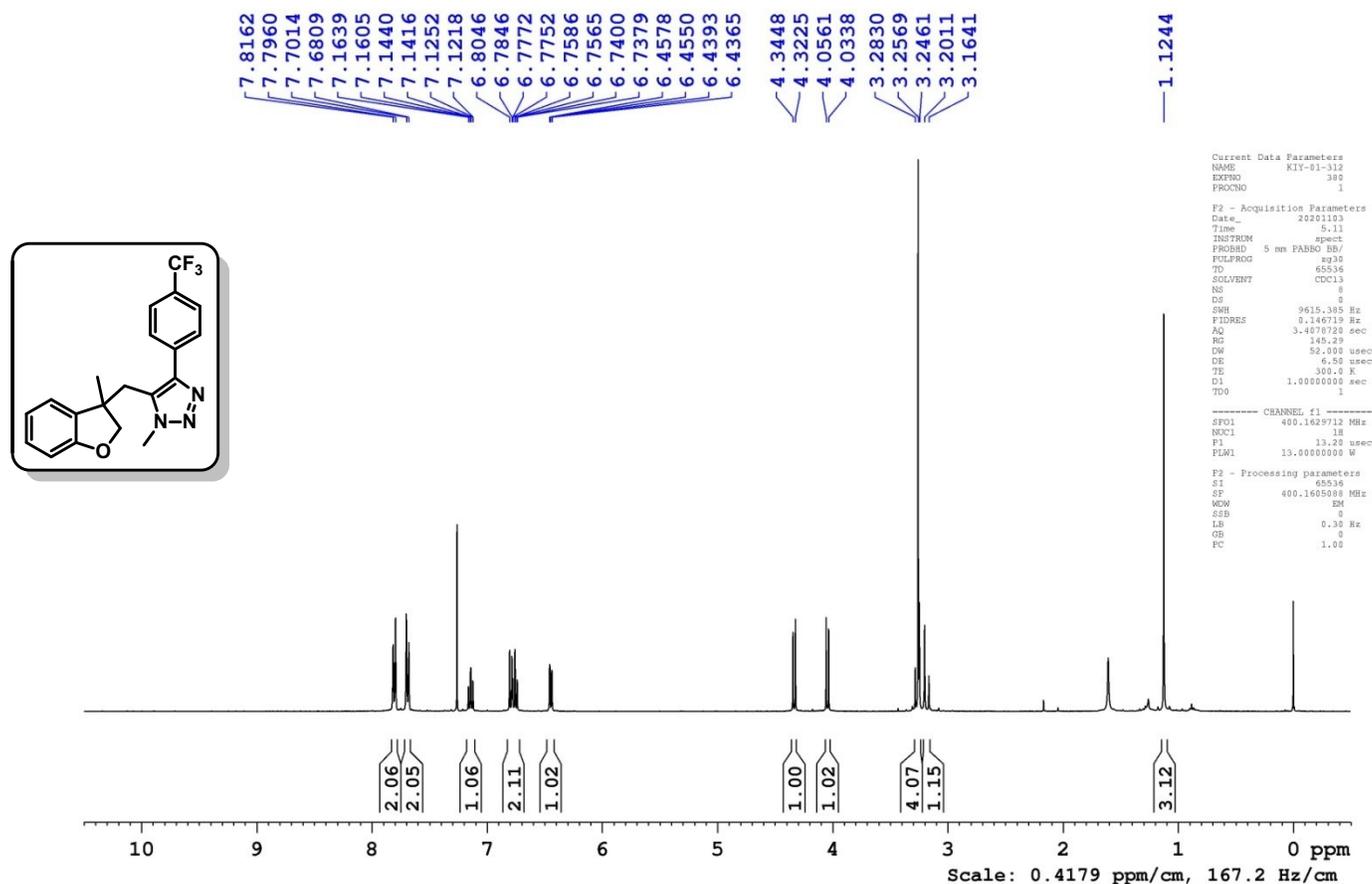
**SAIF [HRMS Report]**

Data File: HRMS20I04NOV21 Original Data Path: D:\INTERNAL NEW\2020\NOV  
 Sample ID: KIY-01-311 Sample Name: 2020  
 Acquisition Date: 11/04/20 04:49:28 PM Run Time(min): 0.00  
 Vial: CStk1-01:21 Injection Volume(μl): 1.00

HRMS20I04NOV21 #13-26 RT: 0.11-0.21 AV: 14 SB: 1 0.01 NL: 4.40E6  
 T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-59** HRMS spectrum of compound **3ag**



**Figure S-60** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ah**

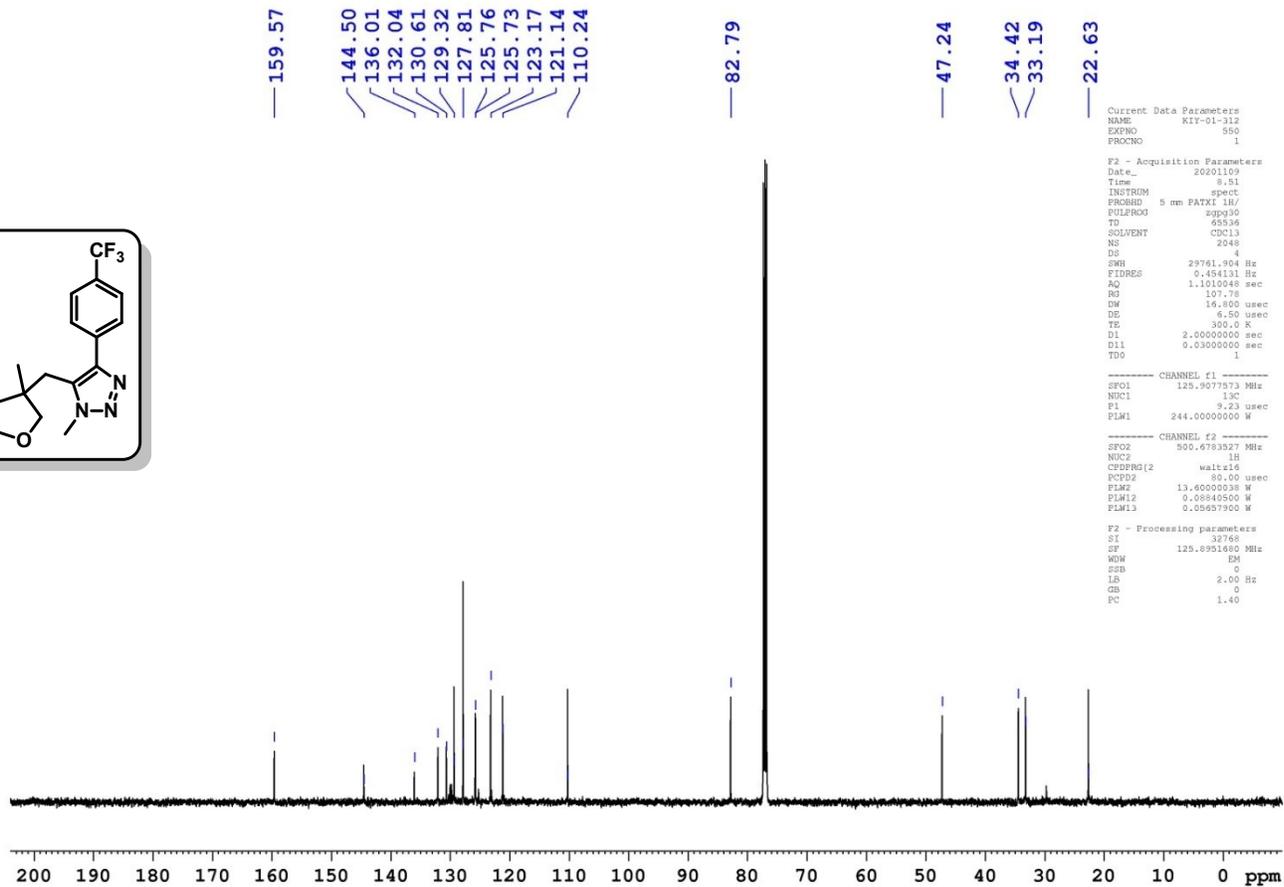
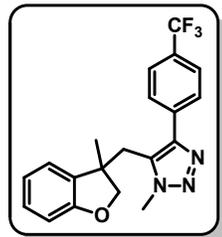


Figure S-61  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) spectrum of compound **3ah**

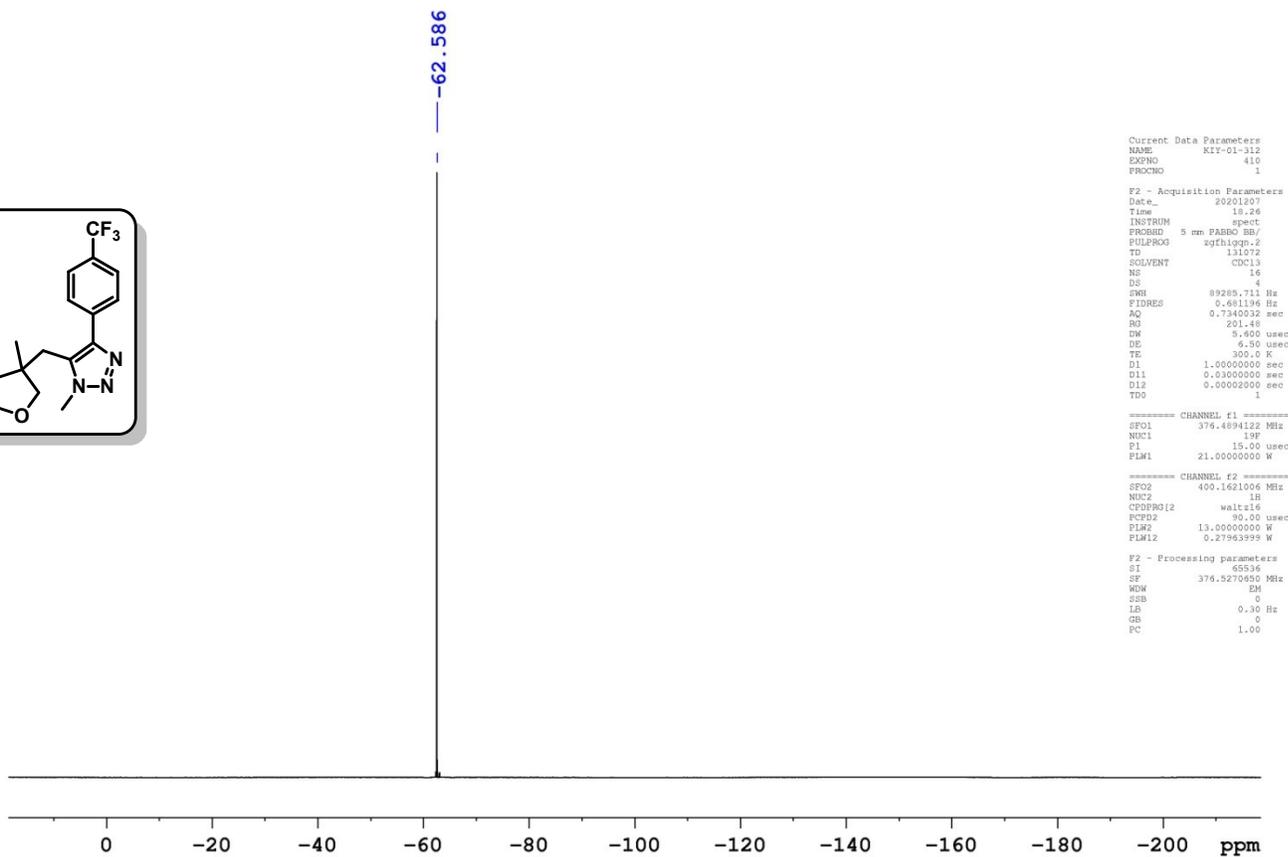
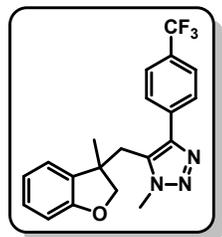
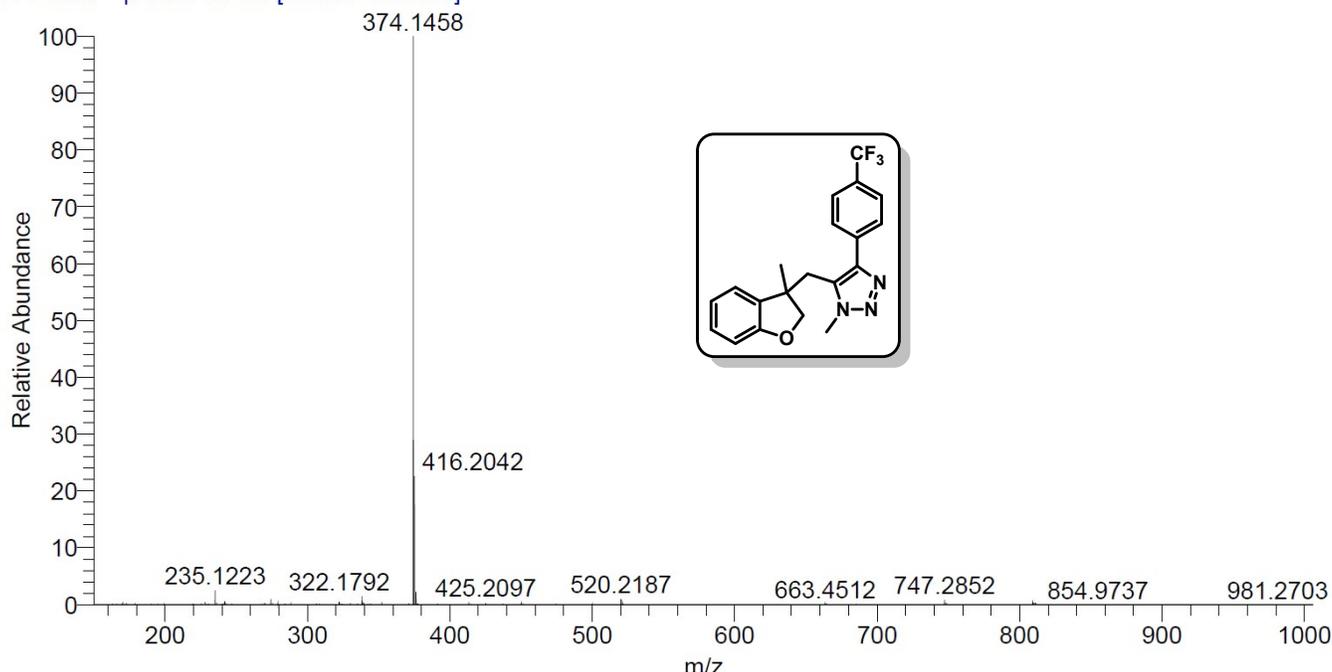


Figure S-62  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of compound **3ah**

**SAIF [HRMS Report]**

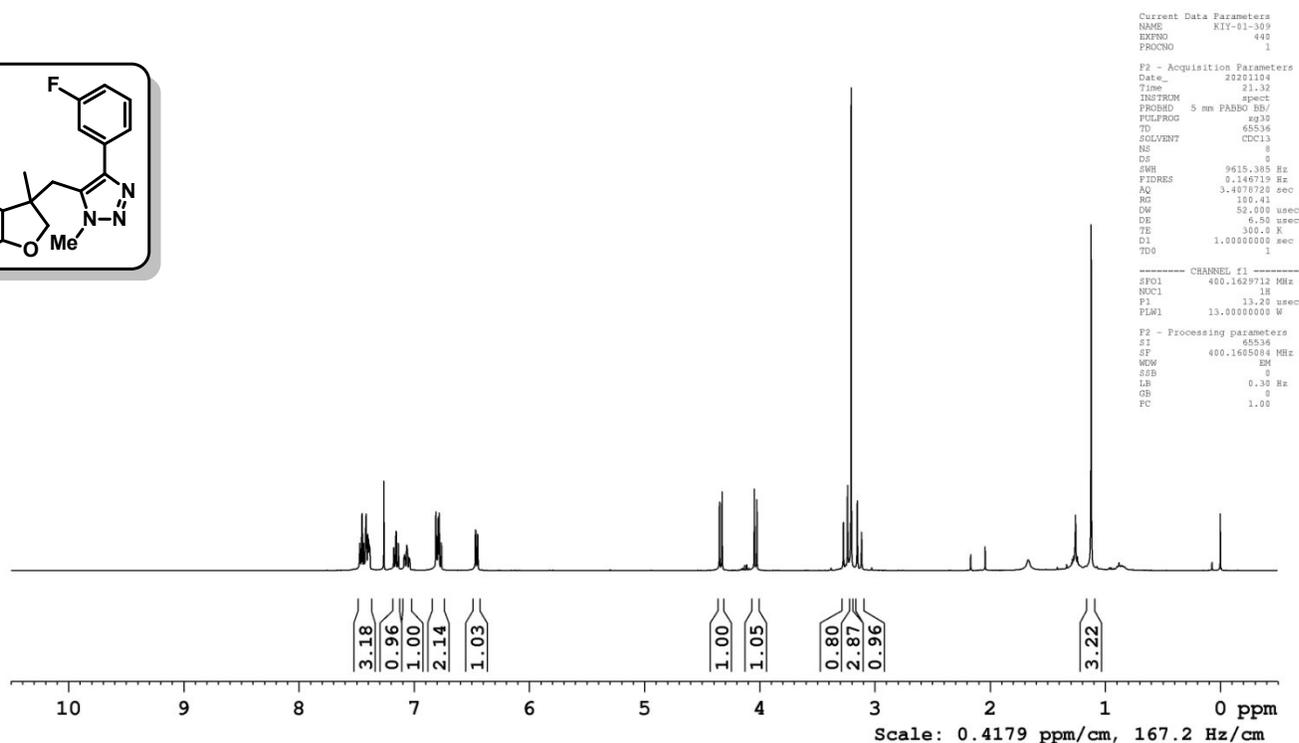
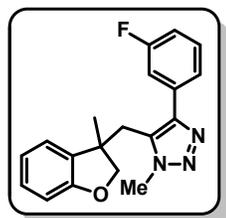
Data File: HRMS20I05NOV08 Original Data Path: D:\INTERNAL NEW\2020\NOV 2020  
 Sample ID: KIY-01-312 Sample Name:  
 Acquisition Date: 11/05/20 11:08:06 AM Run Time(min): 0.00  
 Vial: CStk1-01:8 Injection Volume(μl): 1.00

HRMS20I05NOV08 #12-24 RT: 0.11-0.21 AV: 13 SB: 1 0.00 NL: 6.03E6  
 T: FTMS + p ESI Full ms [150.00-1000.00]



**Figure S-63** HRMS spectrum of compound **3ah**

7.4720 7.4689 7.4556 7.4526 7.4494 7.4364 7.4217 7.4166 7.4110 7.4024 7.3967 7.3919 7.3901 7.3855 7.3836 7.1777 7.1743 7.1576 7.1557 7.1390 7.1356 7.0874 7.0842 7.0806 7.0777 7.0634 7.0611 7.0595 7.0579 7.0456 7.0428 7.0391 7.0391 6.8019 6.7999 6.7907 6.7833 6.7813 6.7648 6.7627 6.4676 6.4655 6.4492 6.4471 4.3483 4.3260 4.0462 4.0240 3.2727 3.2358 3.2054 3.1518 3.1149 1.1216



**Figure S-64** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ai**

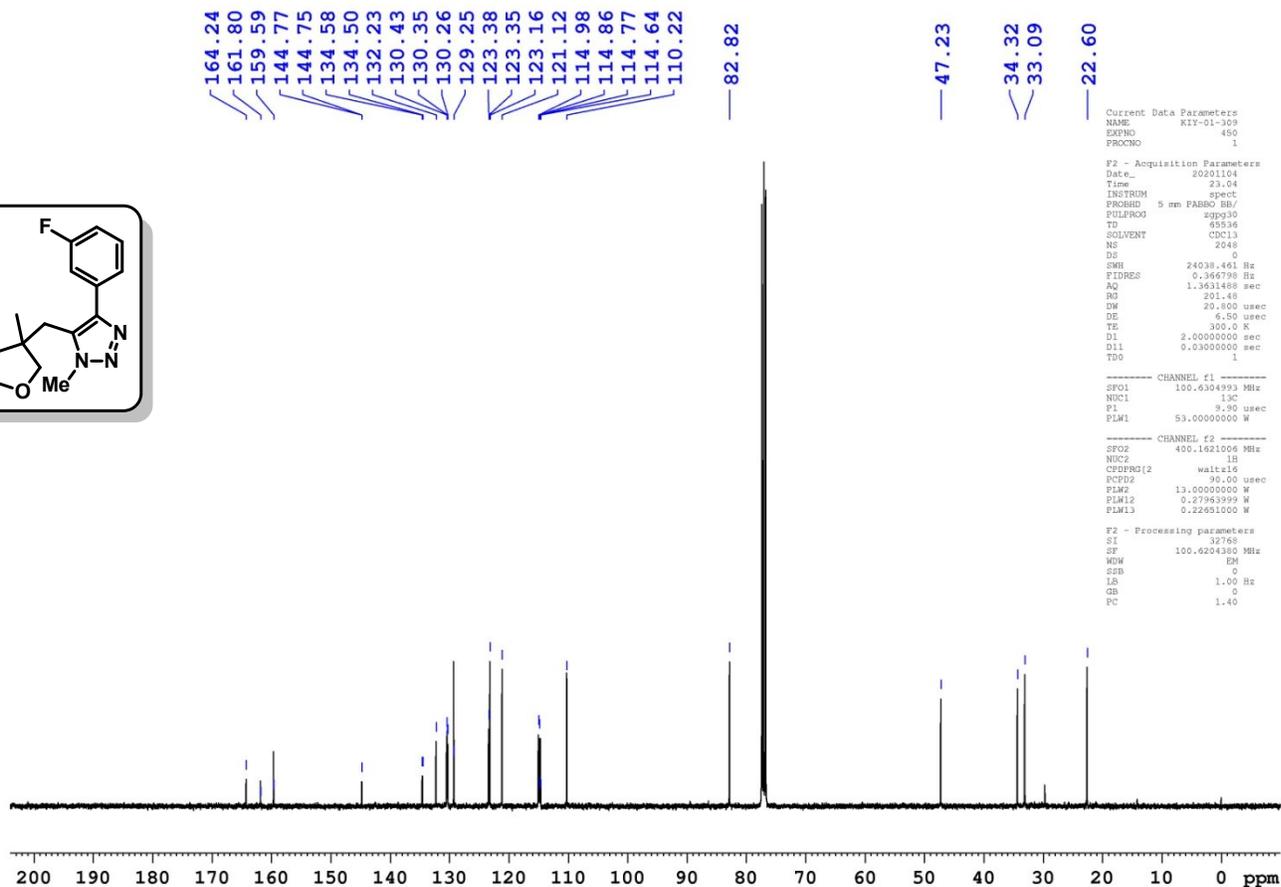
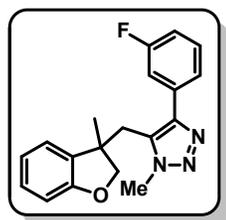


Figure S-65 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ai

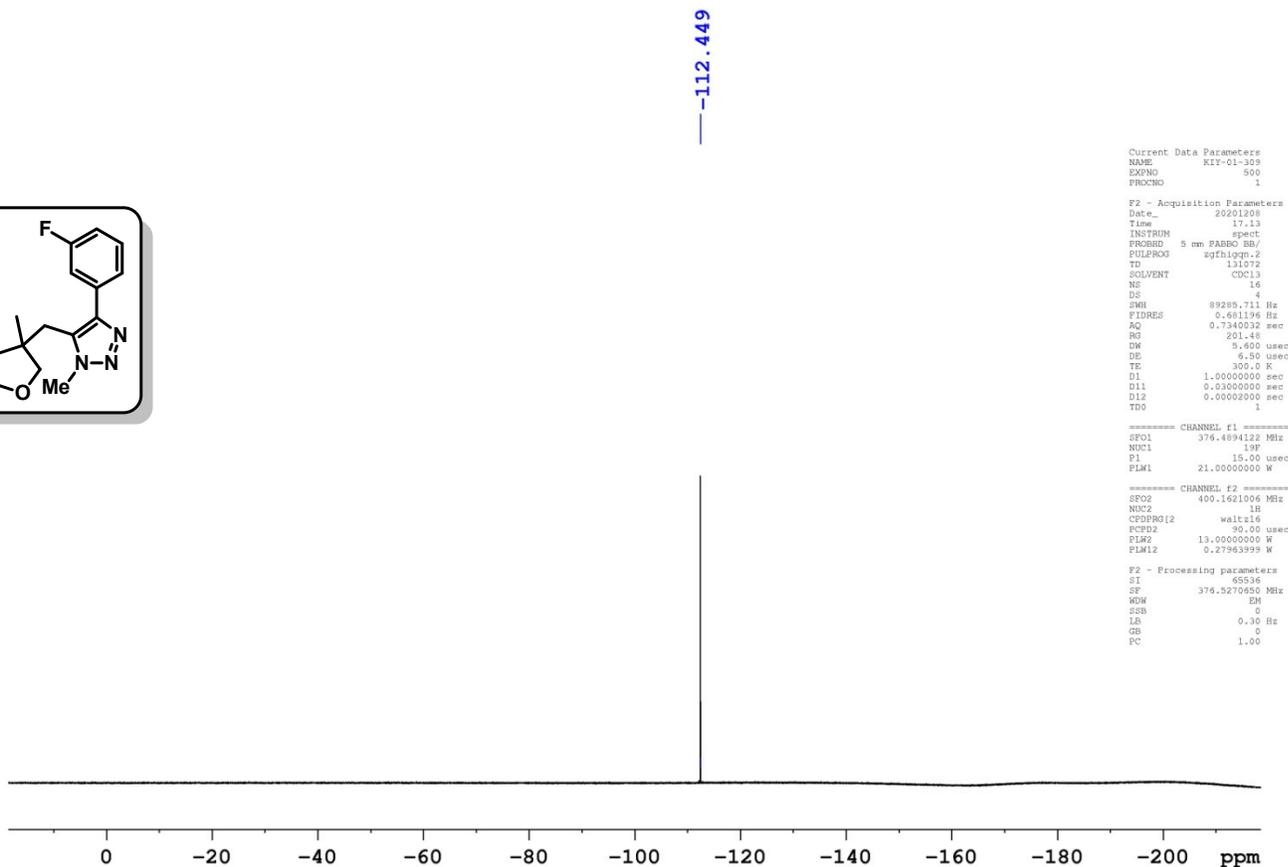
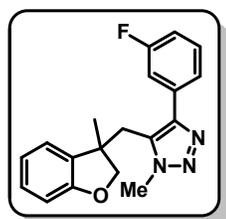
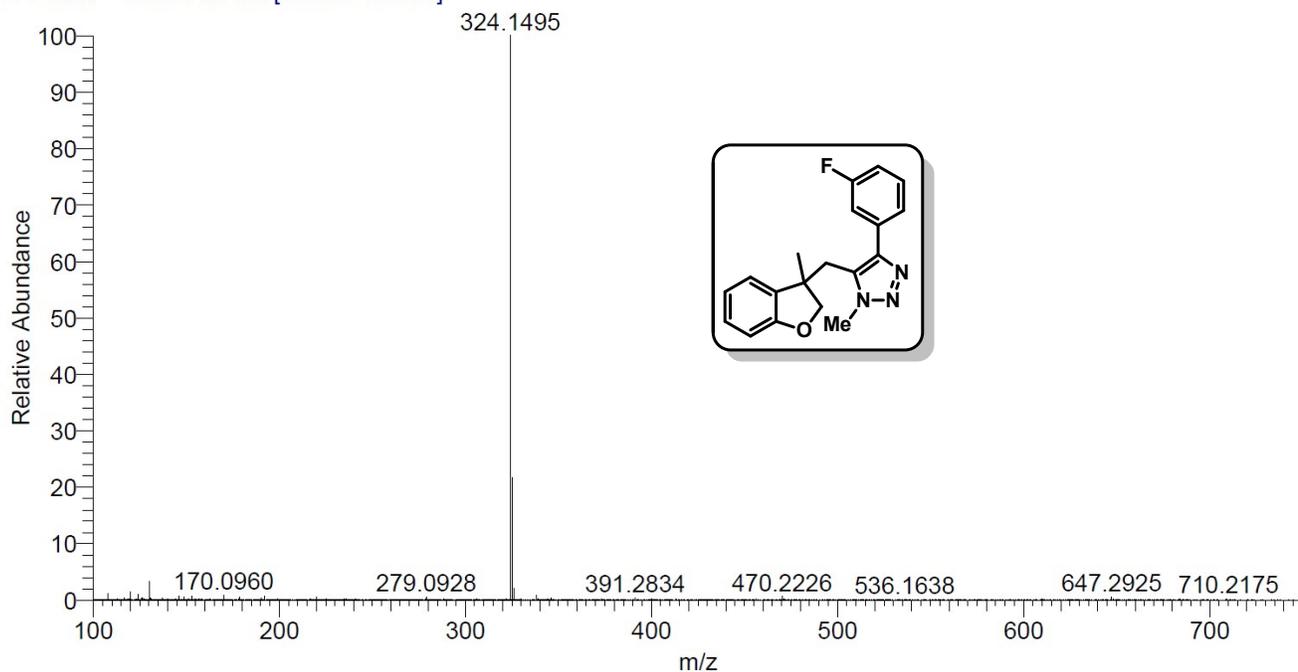


Figure S-66 <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) spectrum of compound 3ai

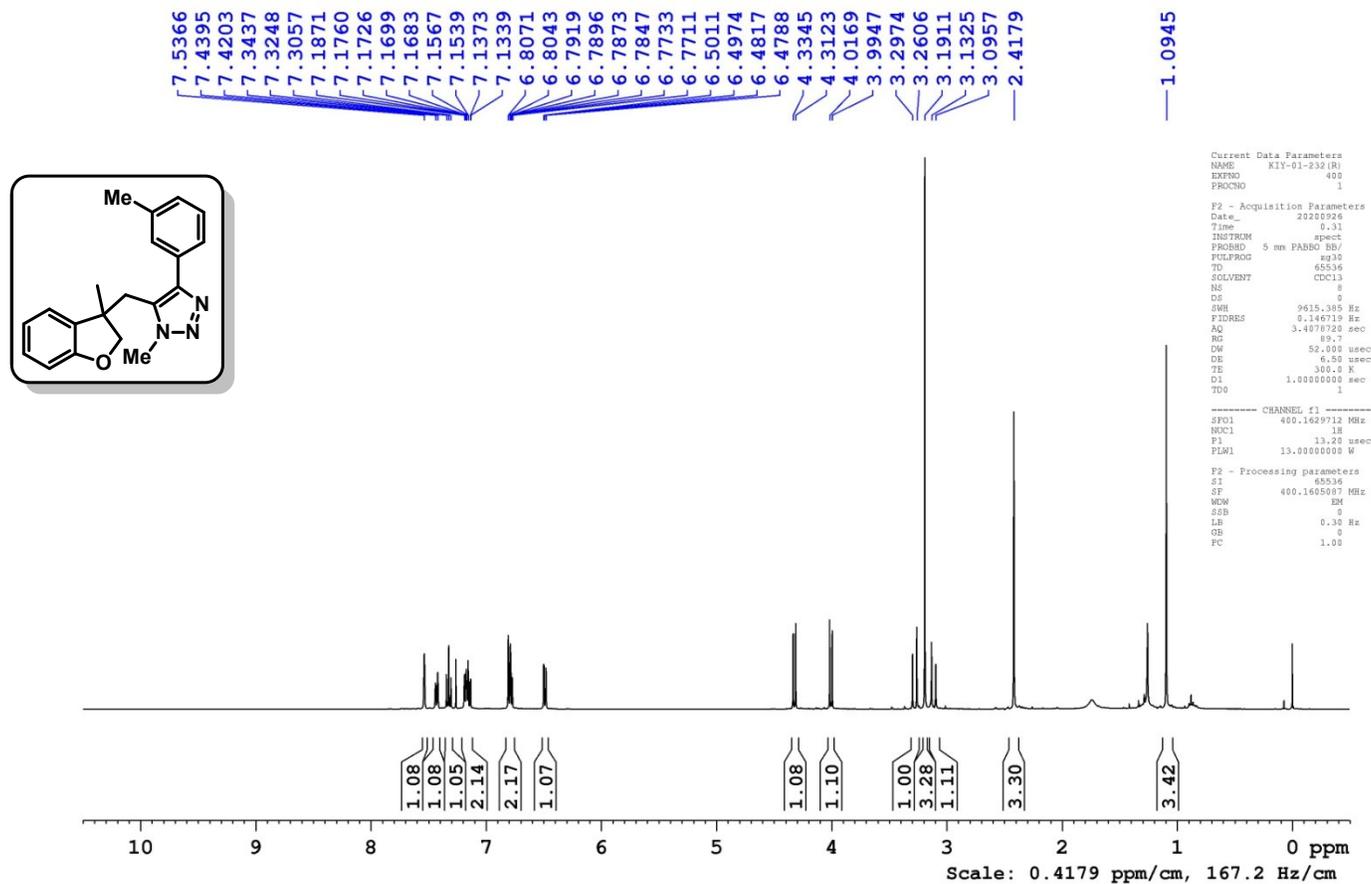
**SAIF [HRMS Report]**

Data File: HRMS20I05NOV21 Original Data Path: D:\INTERNAL NEW\2020\NOV 2020  
 Sample ID: KIY-01-309 Sample Name:  
 Acquisition Date: 11/05/20 11:33:48 AM Run Time(min): 0.00  
 Vial: CStk1-01:21 Injection Volume(μl): 1.00

HRMS20I05NOV21 #13-25 RT: 0.11-0.21 AV: 13 SB: 1 0.01 NL: 7.90E6  
 T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-67** HRMS spectrum of compound **3ai**



**Figure S-68** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3aj**

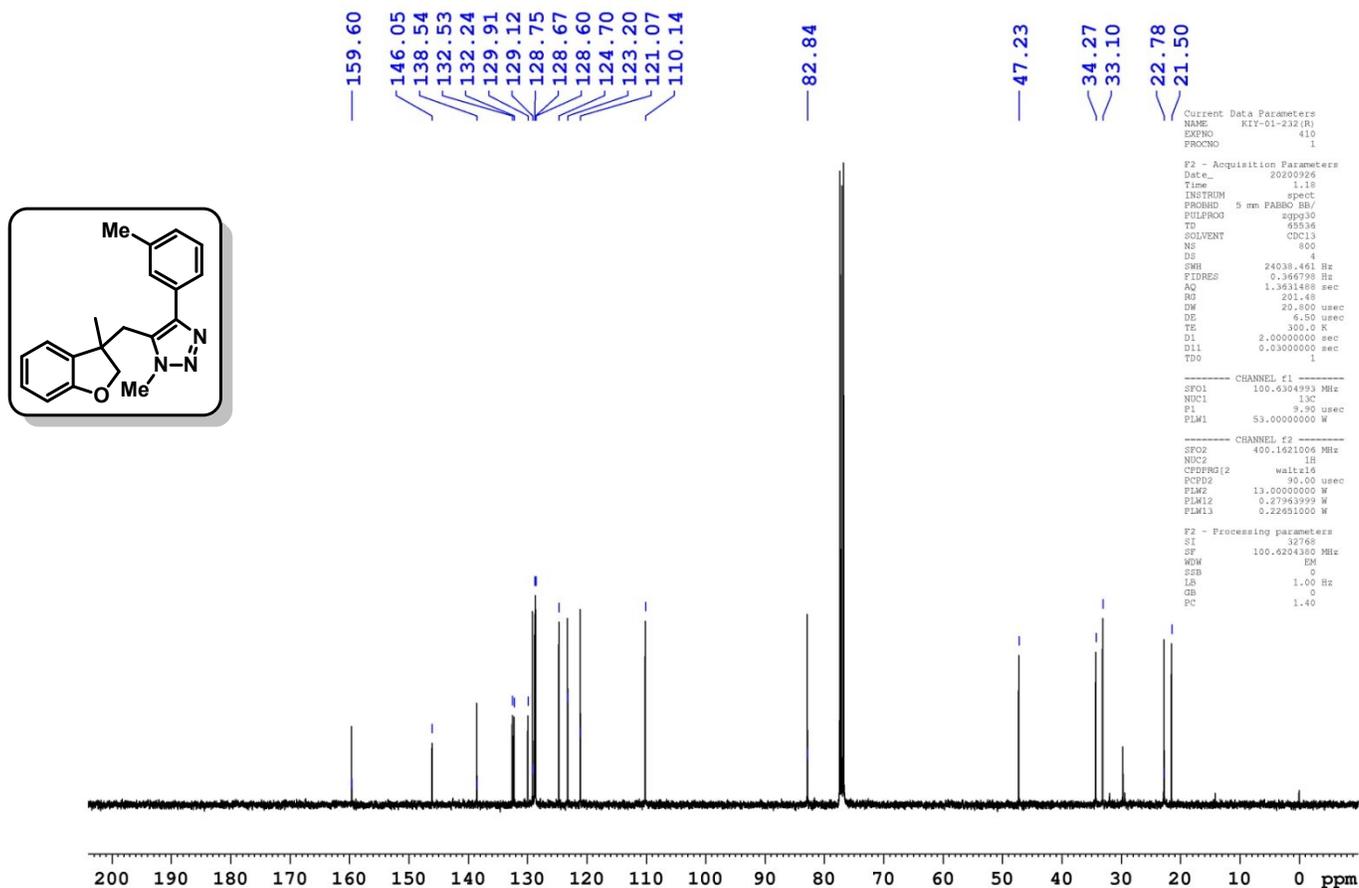


Figure S-69 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3aj

**SAIF [HRMS Report]**

Data File:	HRMS20I28SEP04	Original Data Path:	D:\INTERNAL NEW\2020\Sep 2020
Sample ID:	KIY-01-232	Sample Name:	
Acquisition Date:	09/28/20 10:56:10 AM	Run Time(min):	0.00
Vial:	CStk1-01:4	Injection Volume(μl):	1.00

HRMS20I28SEP04 #12-25 RT: 0.11-0.21 AV: 14 SB: 1 0.01 NL: 1.10E7  
 T: FTMS + c ESI Full ms [100.00-750.00]

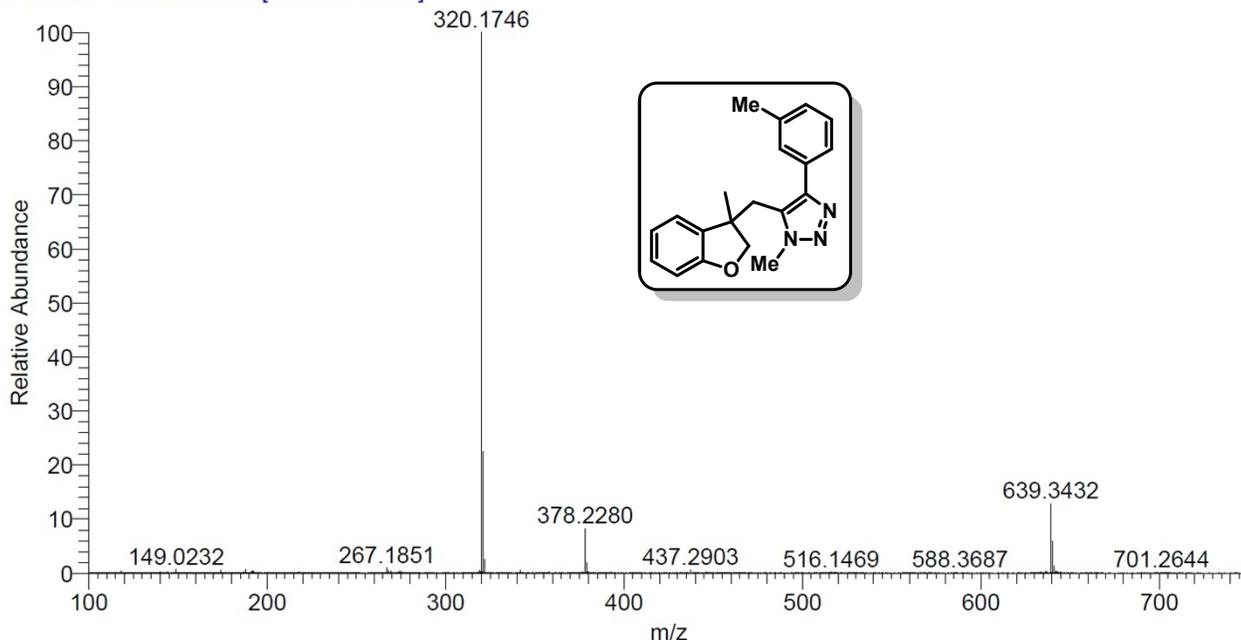


Figure S-70 HRMS spectrum of compound 3aj

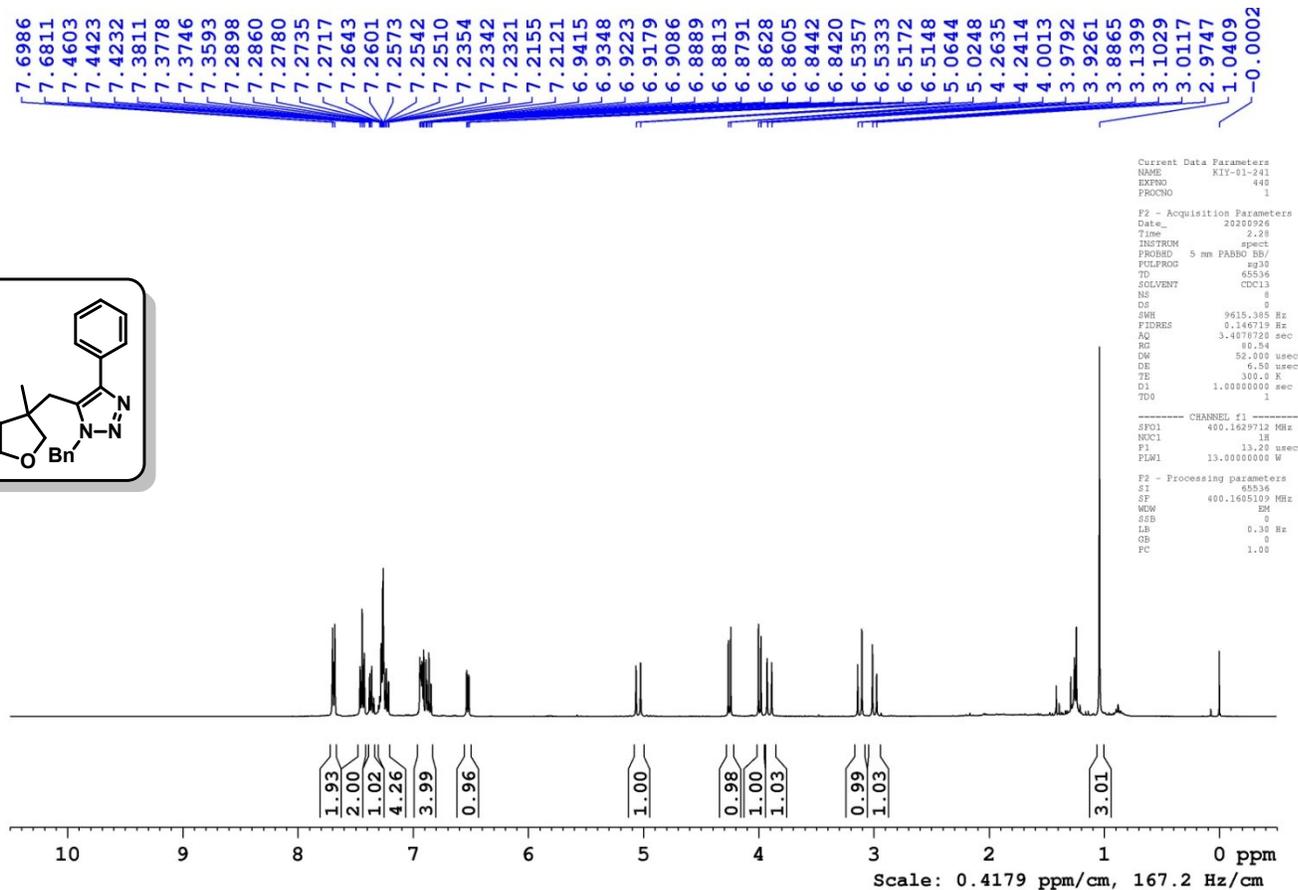
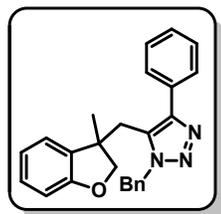


Figure S-71 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3a1

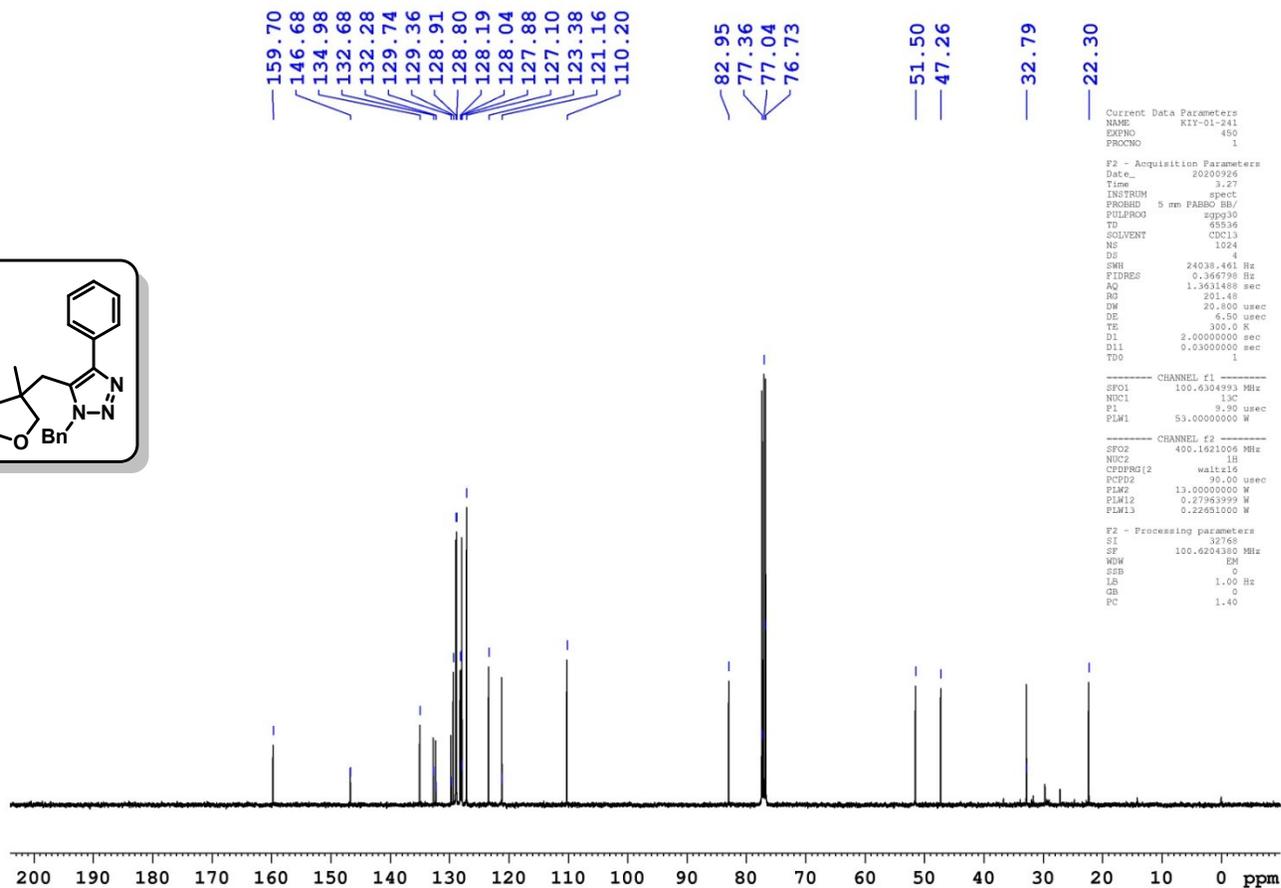
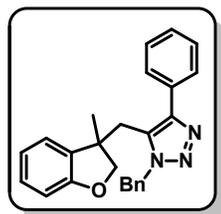
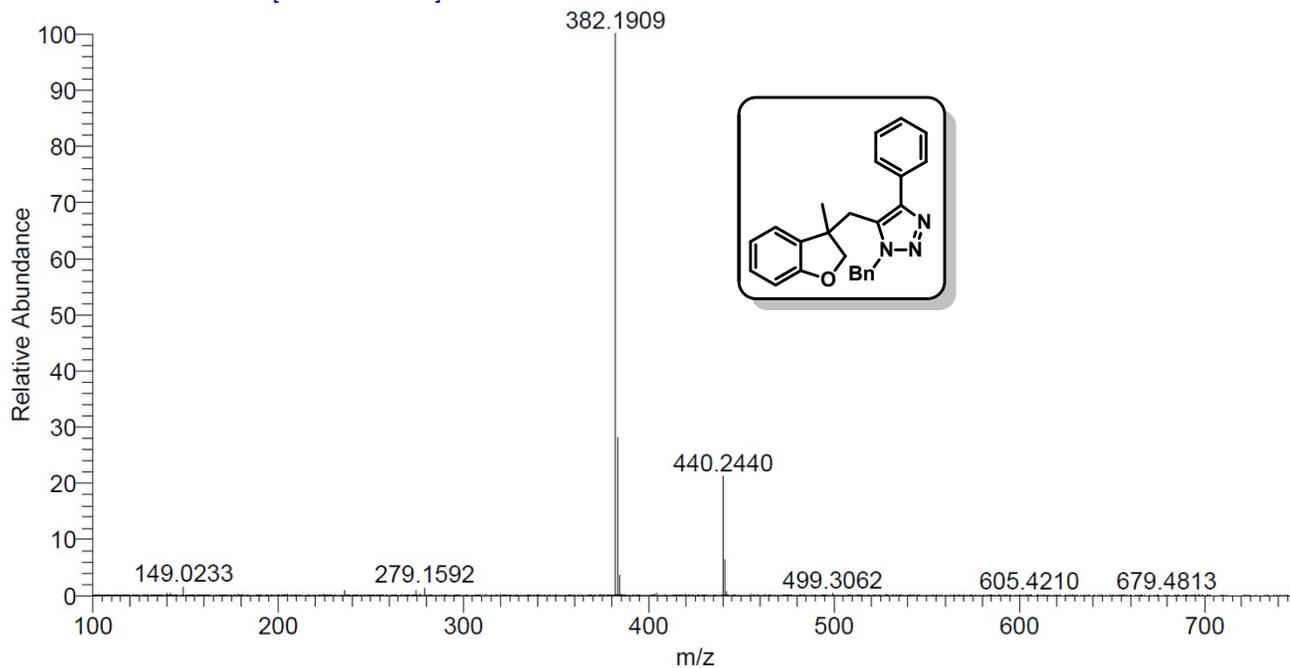


Figure S-72 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3a1

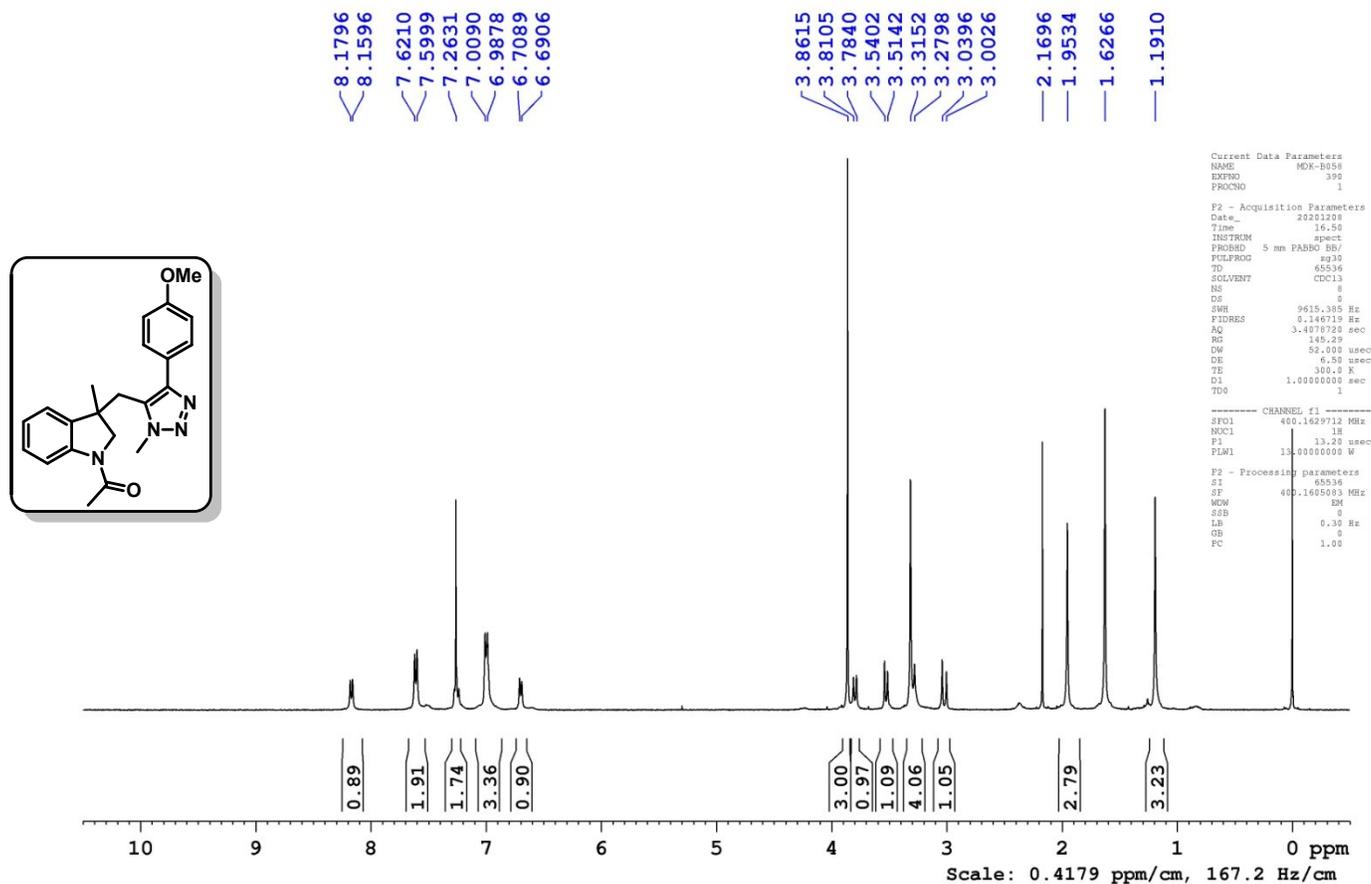
**SAIF [HRMS Report]**

Data File: HRMS20I28SEP06 Original Data Path: D:\INTERNAL NEW\2020\Sep 2020  
 Sample ID: KIY-01-241 Sample Name:  
 Acquisition Date: 09/28/20 11:00:07 AM Run Time(min): 0.00  
 Vial: CStk1-01:6 Injection Volume(μl): 1.00

HRMS20I28SEP06 #12-23 RT: 0.11-0.21 AV: 12 SB: 1 0.01 NL: 1.39E6  
 T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-73** HRMS spectrum of compound **3a**



**Figure S-74** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3kc**

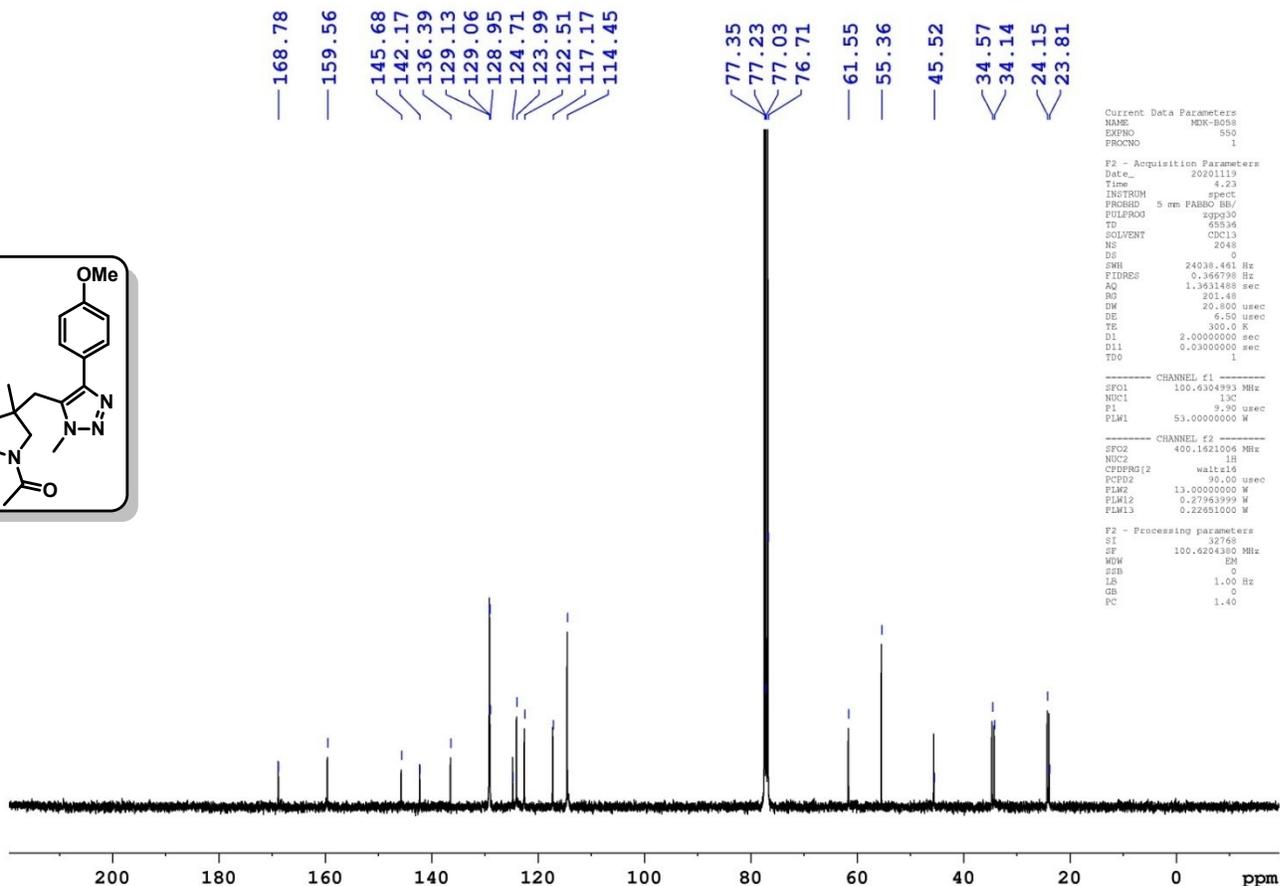
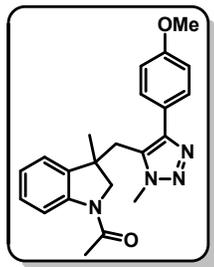


Figure S-75 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound **3kc**

**SAIF [HRMS Report]**

Data File:	HRMS20I02NOV22	Original Data Path:	D:\INTERNAL NEW\2020\NOV
Sample ID:	MDK-B058	Sample Name:	2020
Acquisition Date:	11/02/20 11:59:49 AM	Run Time(min):	0.00
Vial:	CStk1-01:22	Injection Volume(μl):	1.00

HRMS20I02NOV22 #13-26 RT: 0.11-0.21 AV: 14 SB: 1 0.01 NL: 2.80E6  
T: FTMS + p ESI Full ms [100.00-1000.00]

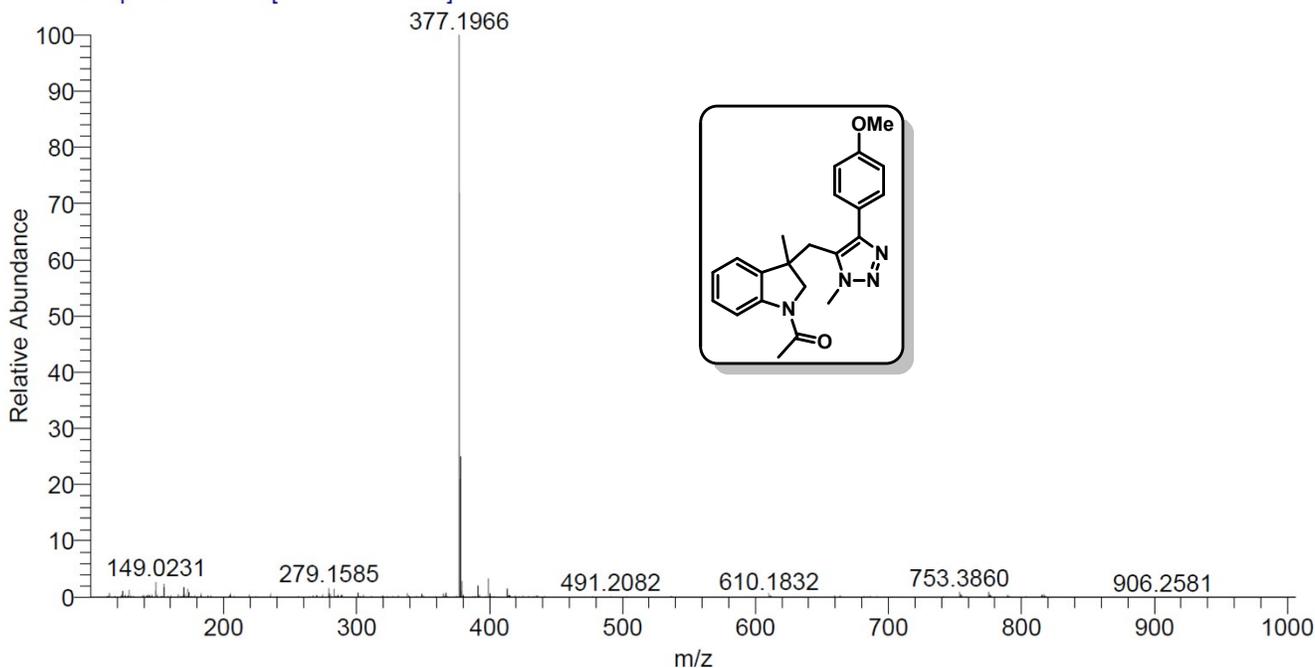


Figure S-76 HRMS spectrum of compound **3kc**

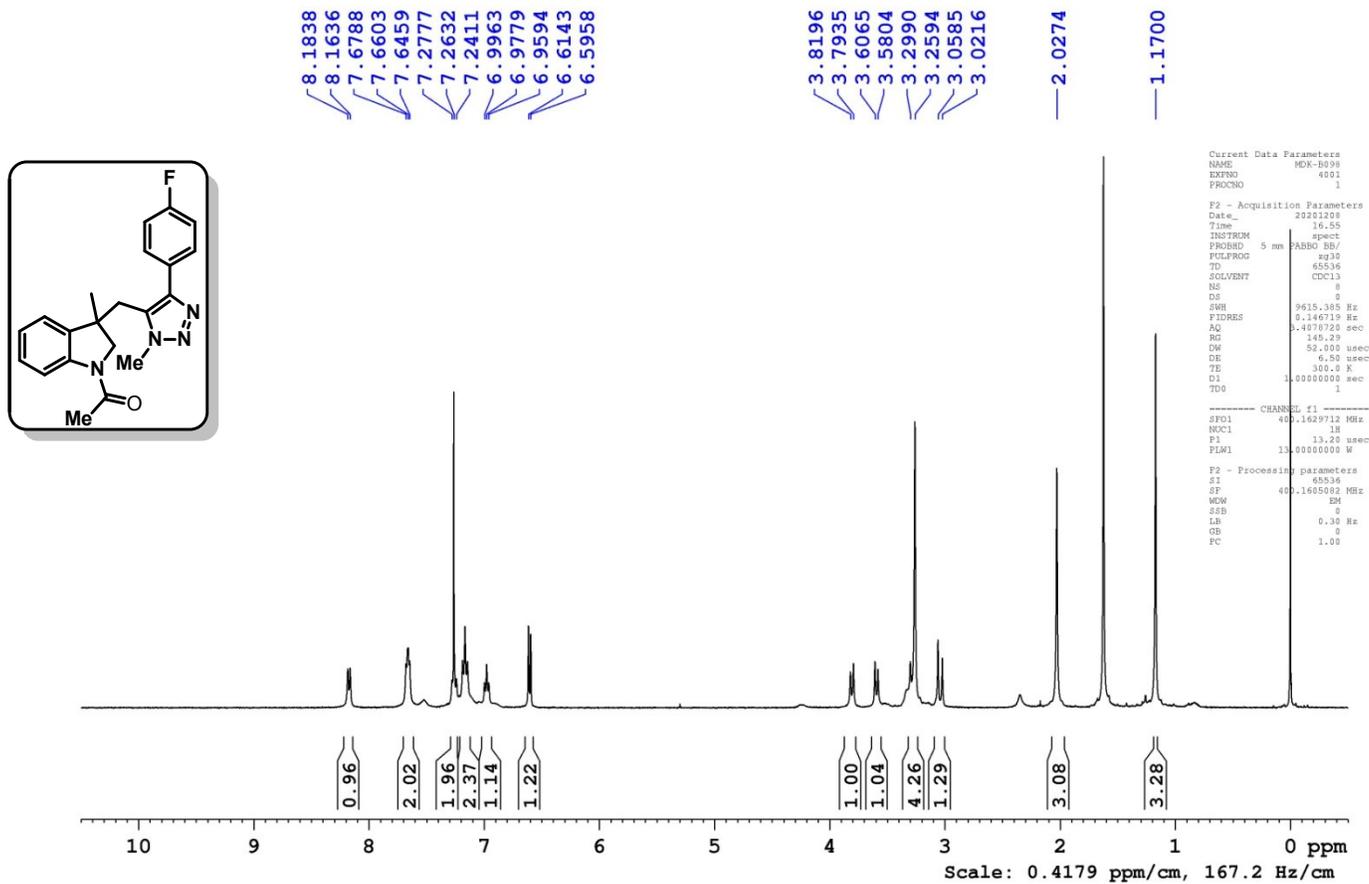


Figure S-77  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ) spectrum of compound 3kd

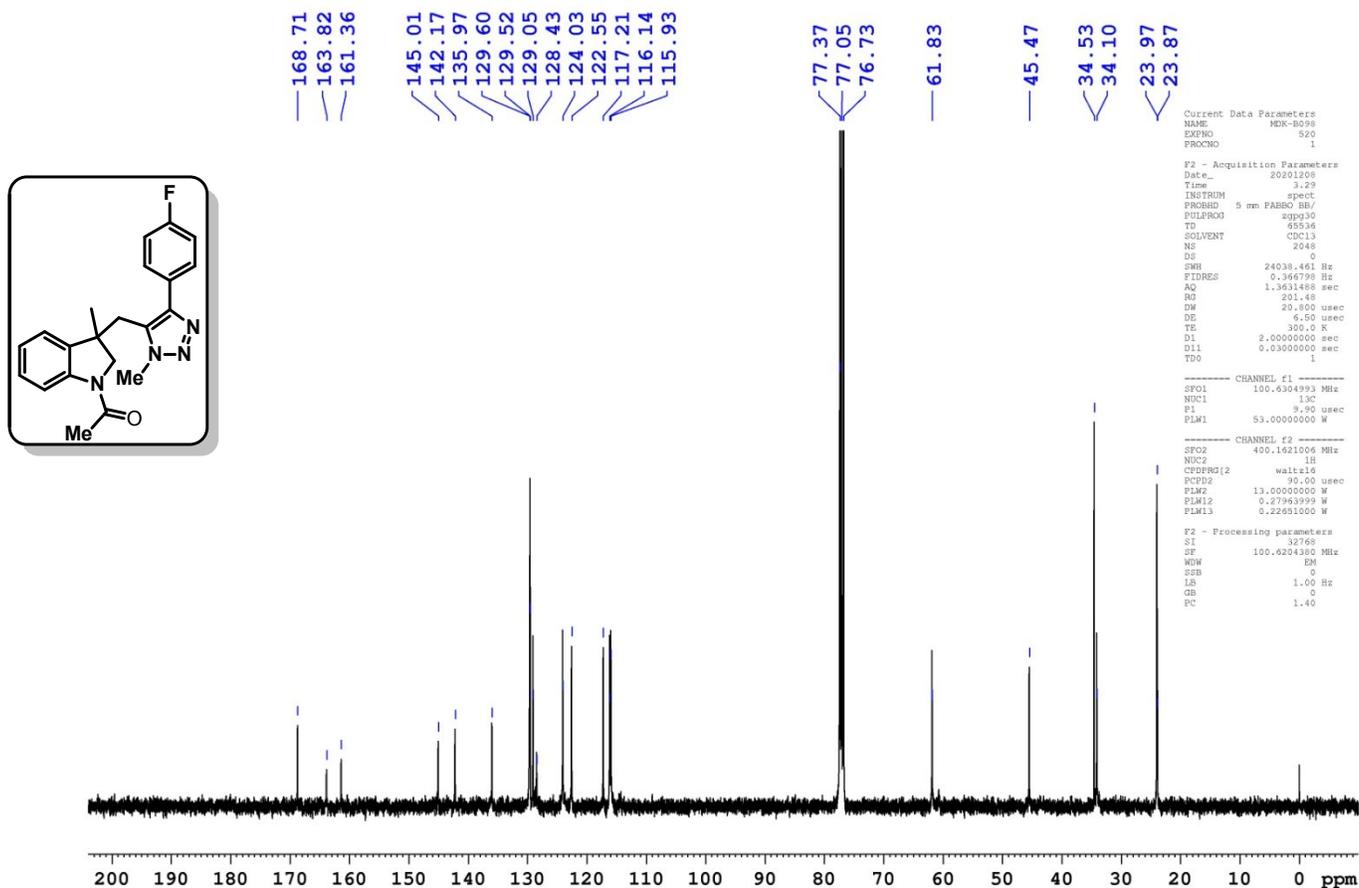
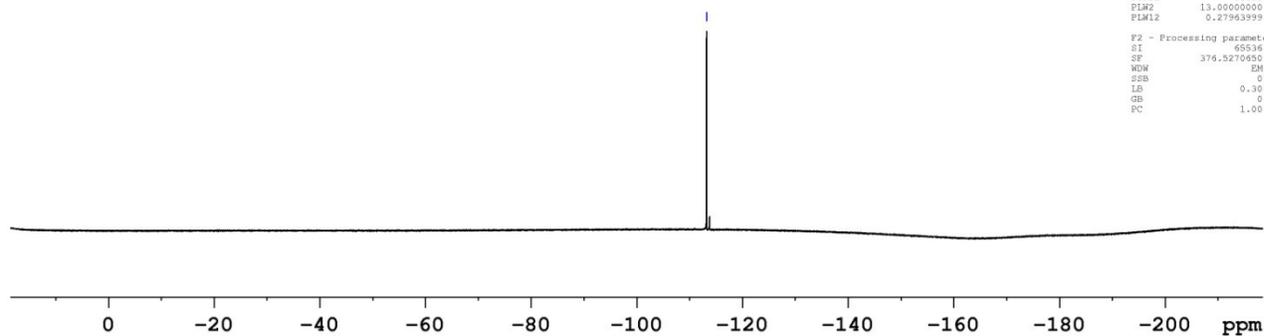
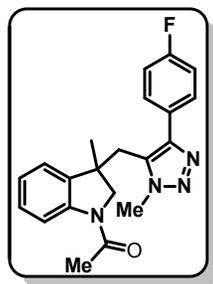


Figure S-78  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) spectrum of compound 3kd

---113.239



Current Data Parameters  
NAME MDK-B098  
EXPMO 400  
PROCNO 1  
F2 - Acquisition Parameters  
Date\_ 20201209  
Time 17.26  
INSTRUM spect  
PROBHD 5 mm F4BBO BB/  
PULPROG zgpg30  
TD 131072  
SOLVENT CDCl3  
NS 32  
DS 4  
SWH 89285.711 Hz  
FIDRES 0.481196 Hz  
AQ 0.7340032 sec  
RG 201.48  
DM 9.400 usec  
DE 6.50 usec  
TE 300.0 K  
D1 1.00000000 sec  
D11 0.03000000 sec  
D12 0.00020000 sec  
TD0 1

===== CHANNEL f1 =====  
SFO1 374.4694122 MHz  
NUC1 19F  
P1 15.00 usec  
PLM1 21.00000000 W

===== CHANNEL f2 =====  
SFO2 400.1621006 MHz  
NUC2 1H  
CPCPRG2 waltz16  
PCPD2 90.00 usec  
PLM2 13.00000000 W  
PLM12 0.2796399 W

F2 - Processing parameters  
SI 65536  
SF 374.5270950 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

Figure S-79 <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) spectrum of compound 3kd

### SAIF [HRMS Report]

Data File:	HRMS20110NOV35	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
Sample ID:	MDK-B098	Sample Name:	
Acquisition Date:	11/10/20 01:57:08 PM	Run Time(min):	0.00
Vial:	CStk1-01:35	Injection Volume(μl):	1.00

HRMS20110NOV35 #12-23 RT: 0.11-0.21 AV: 12 SB: 1 0.00 NL: 1.21E6  
T: FTMS + p ESI Full ms [150.00-1000.00]

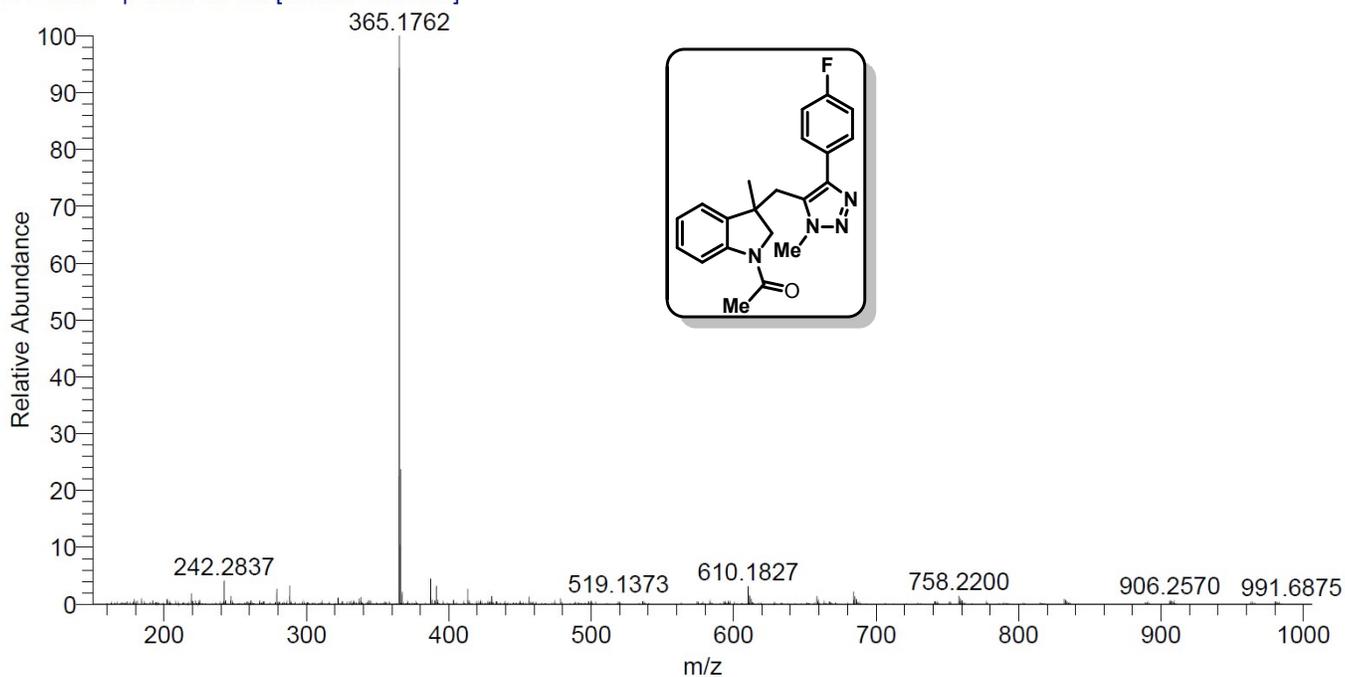


Figure S-80 HRMS spectrum of compound 3kd

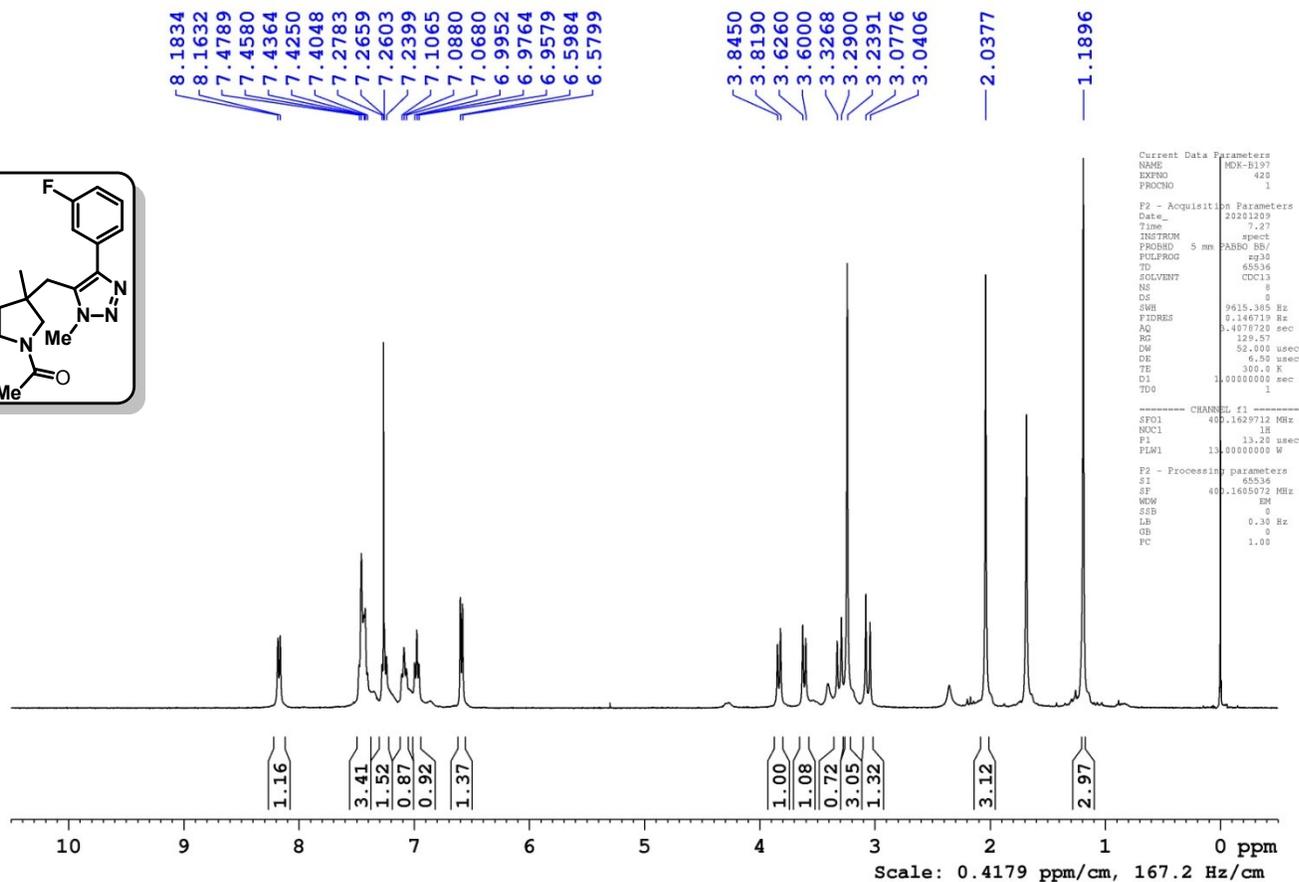
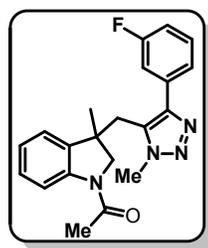


Figure S-81 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3ki

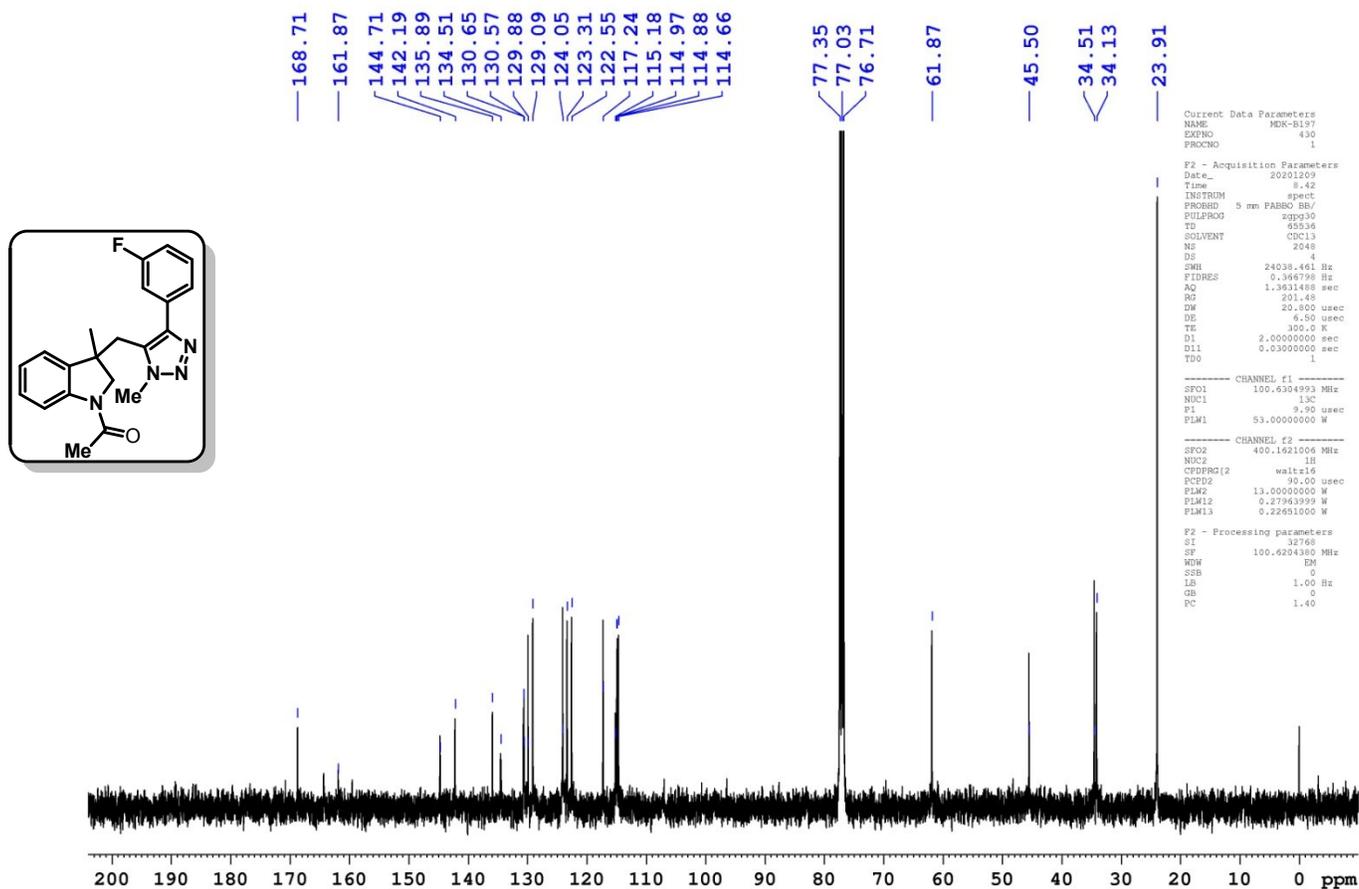
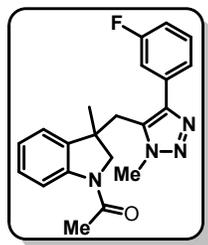
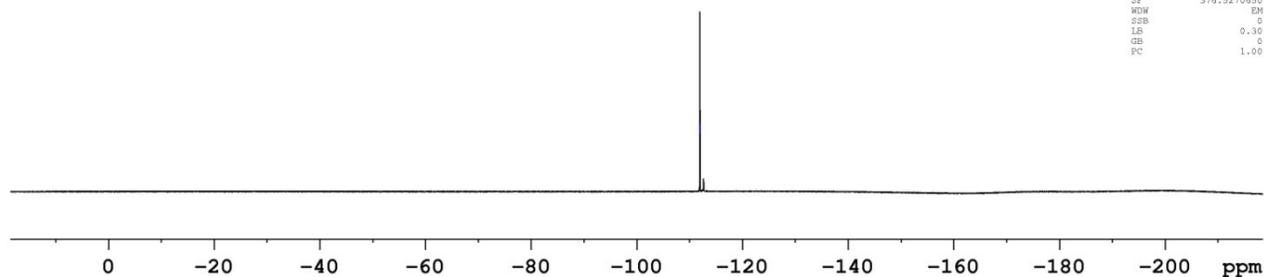


Figure S-82 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3ki



-111.987



```

Current Data Parameters
NAME      MDK-B197F
EXPNO    360
PROCNO   1

F2 - Acquisition Parameters
Date_    20201209
Time     17.21
INSTRUM  spect
PROBHD   5 mm PABBO BB/
PULPROG  zgpg30m.2
TD       131072
SOLVENT  CDCl3
NS       32
DS       4
SWH      89285.711 Hz
FIDRES   0.481196 Hz
AQ       0.7340032 sec
RG       201.48
DM       5.500 usec
DE       6.50 usec
TE       303.1 K
D1       1.00000000 sec
D11      0.03000000 sec
D12      0.00002000 sec
TD0      1

===== CHANNEL F1 =====
SFO1     376.4894122 MHz
NUC1     19F
P1       15.00 usec
PLM1     21.00000000 W

===== CHANNEL F2 =====
SFO2     400.1621006 MHz
NUC2     1H
CPDPRG2  waltz16
PCPD2    90.00 usec
PLM2     13.00000000 W
PLM12    0.27963999 W

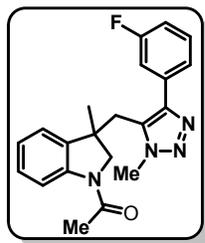
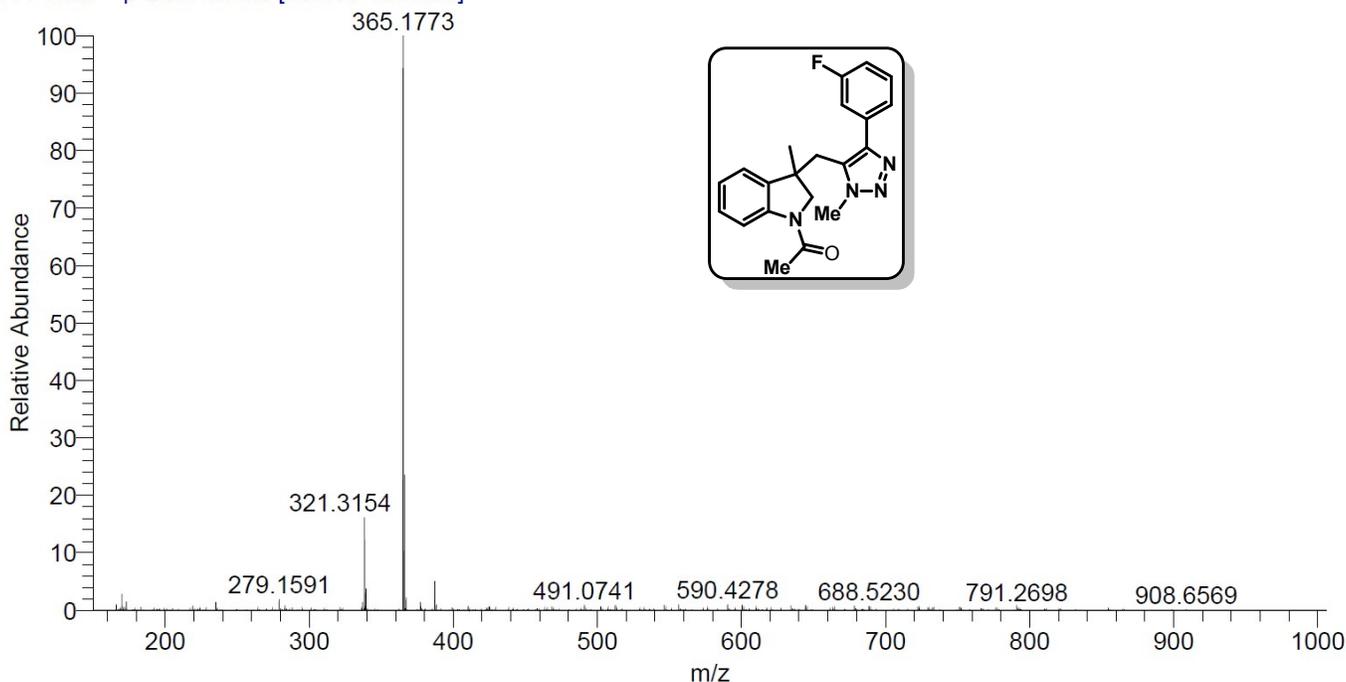
F2 - Processing parameters
SI       65536
SF       376.5270650 MHz
WDW      EM
SSB      0
LB       0.30 Hz
GB       0
PC       1.00
  
```

**Figure S-83**  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ ) spectrum of compound **3ki**

**SAIF [HRMS Report]**

Data File:	HRMS20I03DEC25	Original Data Path:	D:\INTERNAL NEW\2020\DEC 2020
Sample ID:	MDK-B197	Sample Name:	
Acquisition Date:	12/03/20 01:20:45 PM	Run Time(min):	0.00
Vial:	CStk1-01:25	Injection Volume( $\mu\text{l}$ ):	1.00

HRMS20I03DEC25 #29-59 RT: 0.25-0.50 AV: 31 SB: 1 0.00 NL: 1.76E6  
 T: FTMS + p ESI Full ms [150.00-1000.00]



**Figure S-84** HRMS spectrum of compound **3ki**

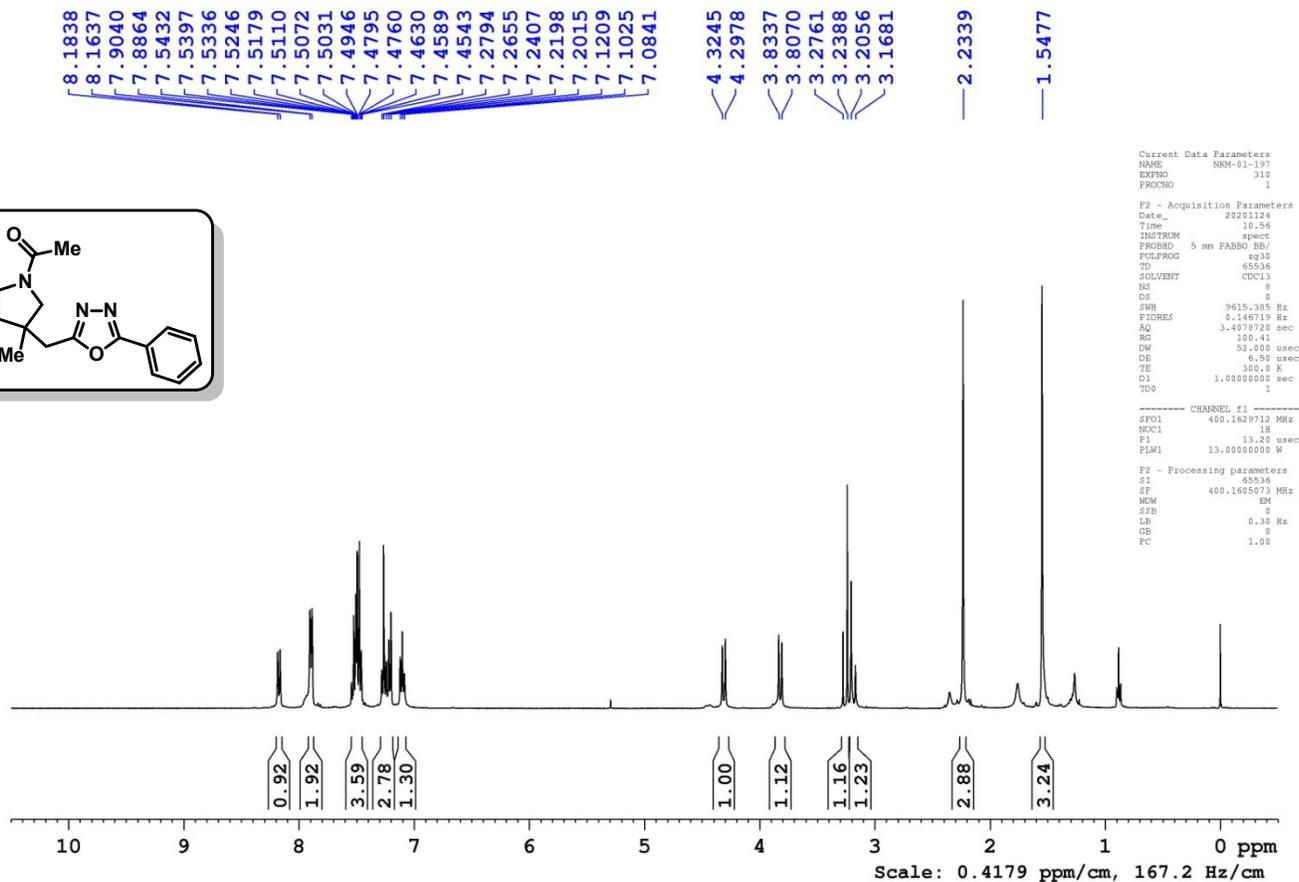
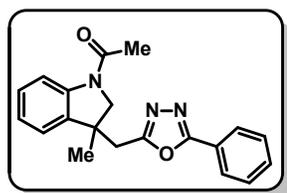


Figure S-85 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3km**

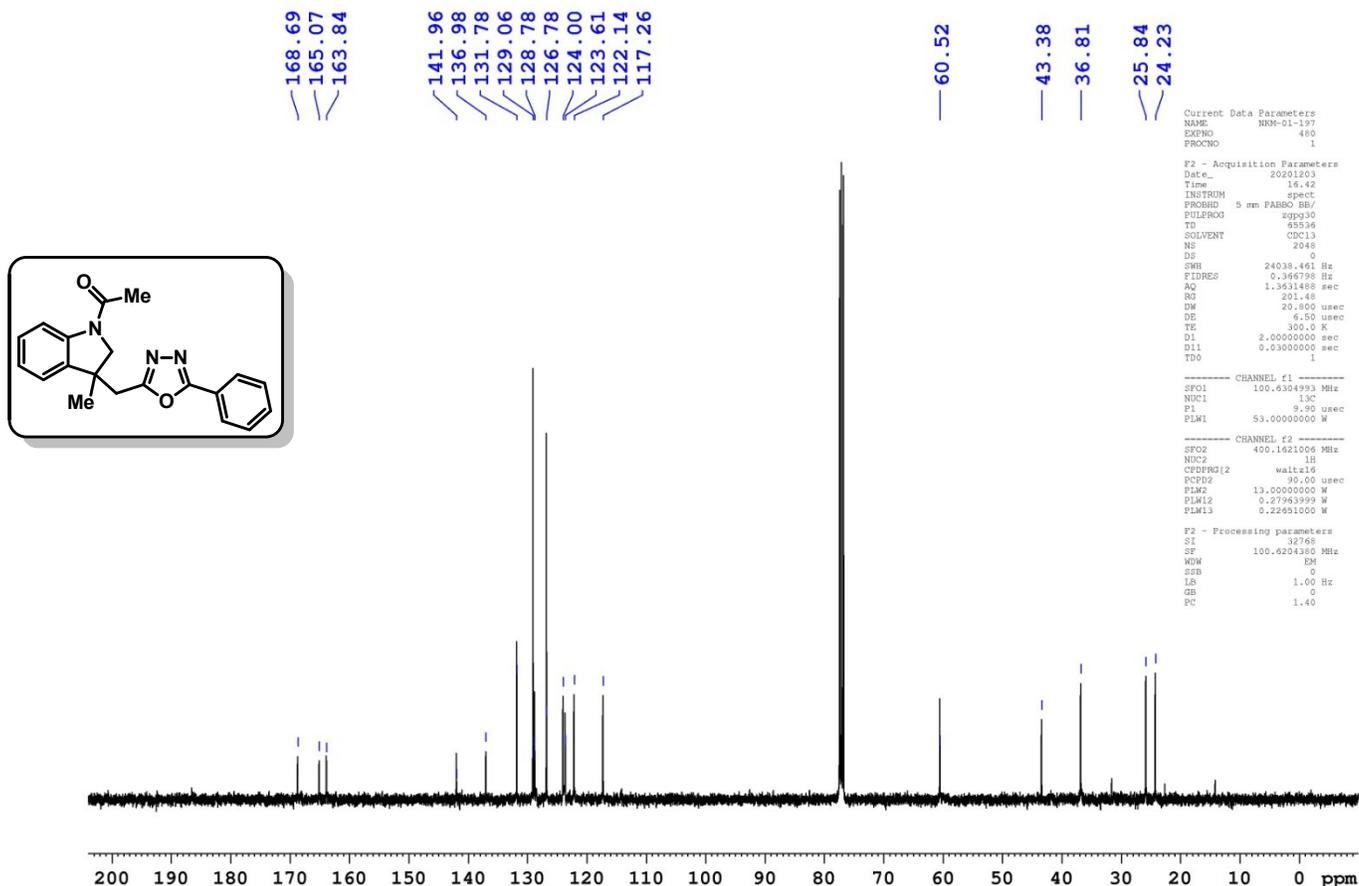
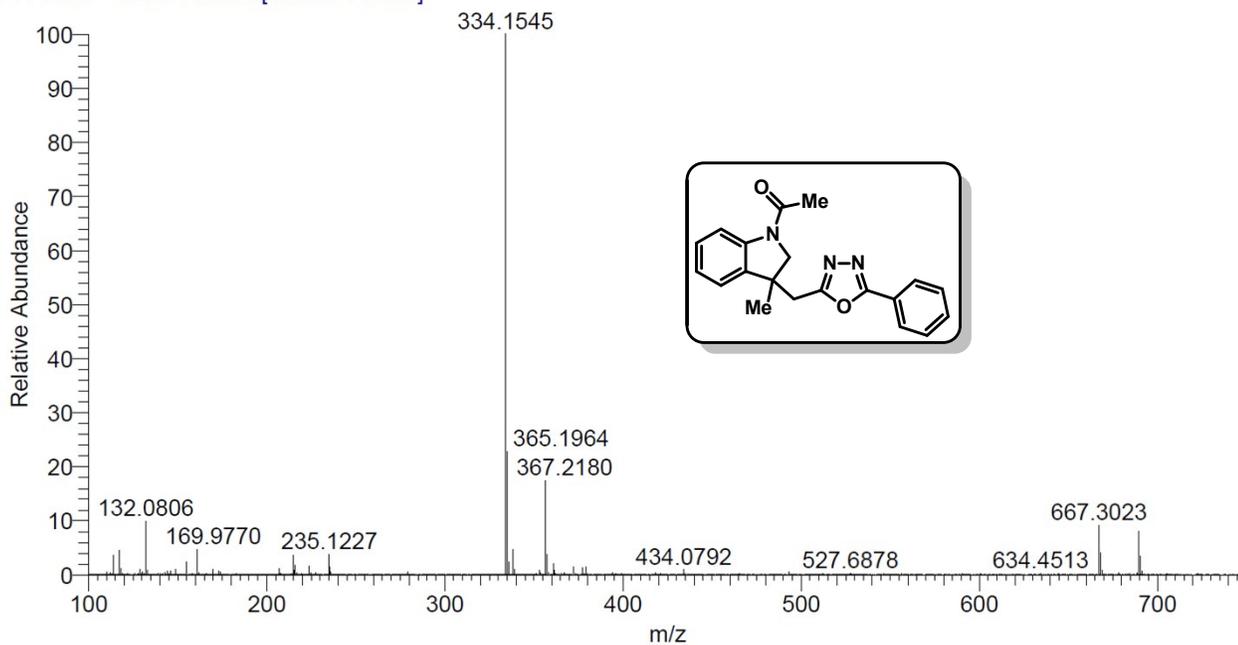


Figure S-86 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound **3km**

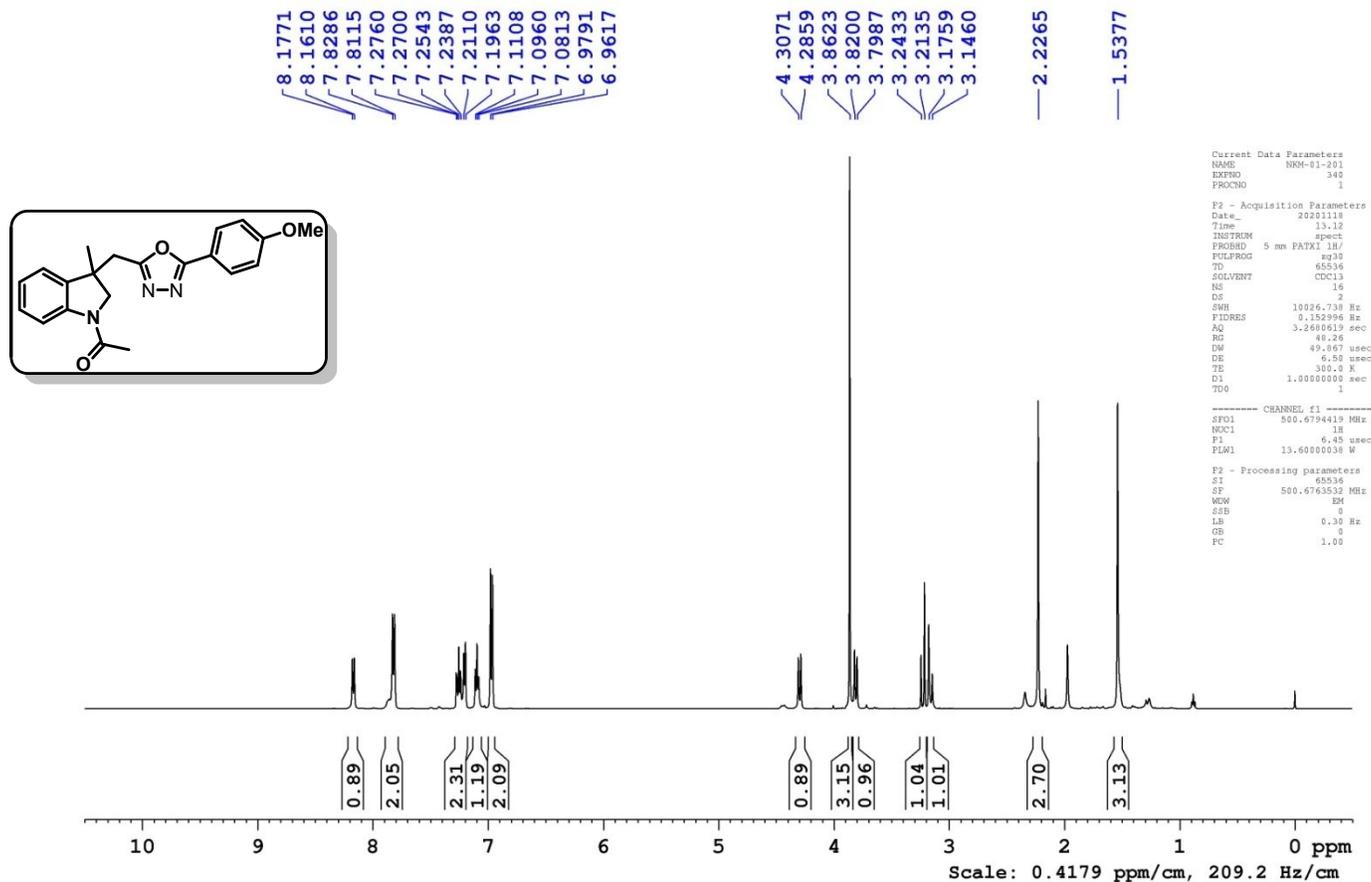
**SAIF [HRMS Report]**

Data File:	HRMS25I20NOV01	Original Data Path:	D:\INTERNAL NEW\2020\NOV
			2020
Sample ID:	NKM-01-197	Sample Name:	
Acquisition Date:	11/25/20 12:56:23 PM	Run Time(min):	0.00
Vial:	CStk1-01:1	Injection Volume(μl):	1.00

HRMS25I20NOV01 #30-63 RT: 0.25-0.50 AV: 34 SB: 1 0.01 NL: 5.73E6  
T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-87** HRMS spectrum of compound **3km**



**Figure S-88** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3kn**

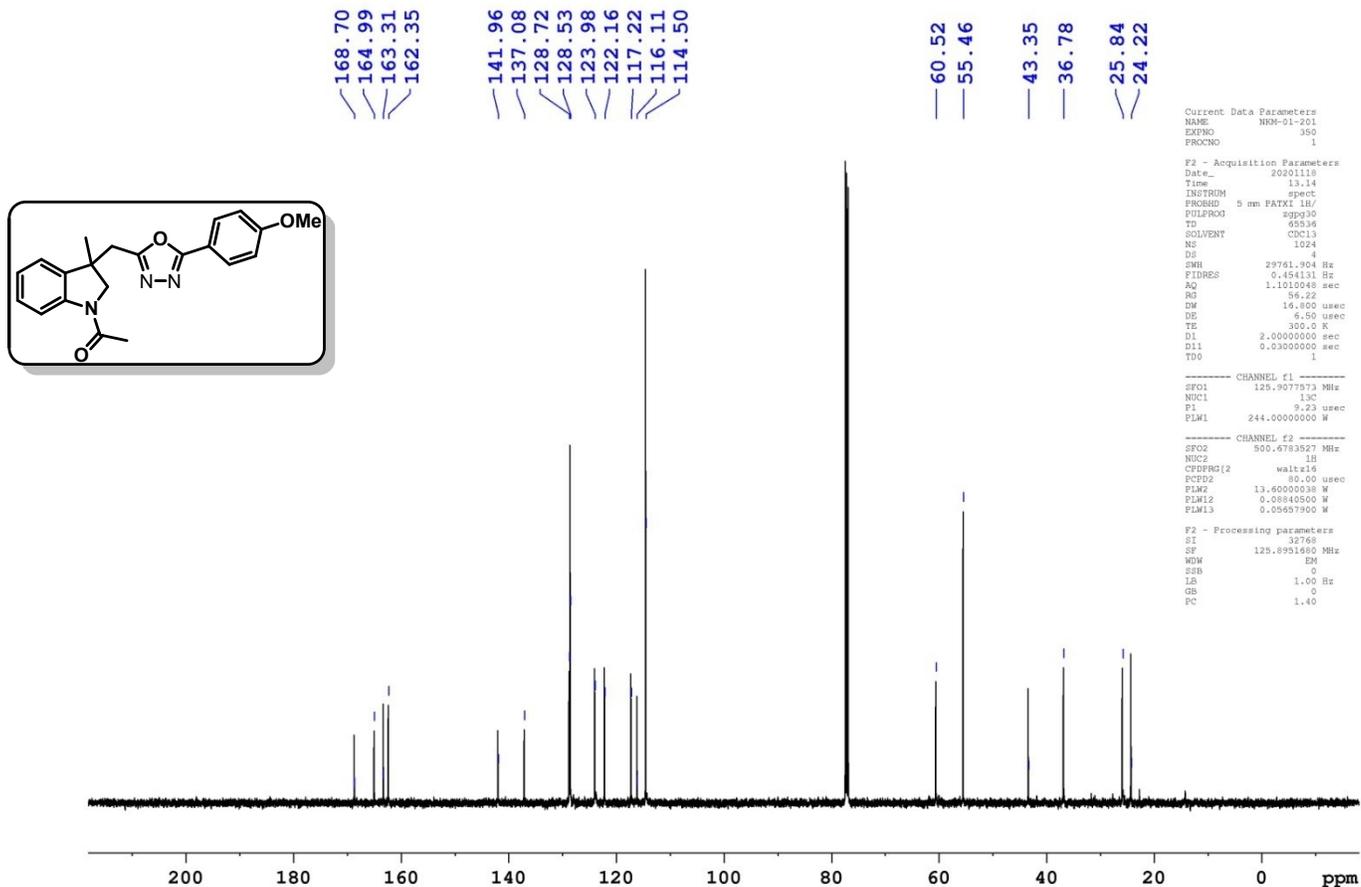


Figure S-89 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3kn

**SAIF [HRMS Report]**

Data File:	HRMS20118NOV25	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
Sample ID:	NKM-01-201	Sample Name:	
Acquisition Date:	11/18/20 03:25:49 PM	Run Time(min):	0.00
Vial:	CStk1-01:25	Injection Volume(μl):	1.00

HRMS20118NOV25 #13-25 RT: 0.11-0.21 AV: 13 SB: 1 0.01 NL: 1.16E6  
 T: FTMS + c ESI Full ms [100.00-750.00]

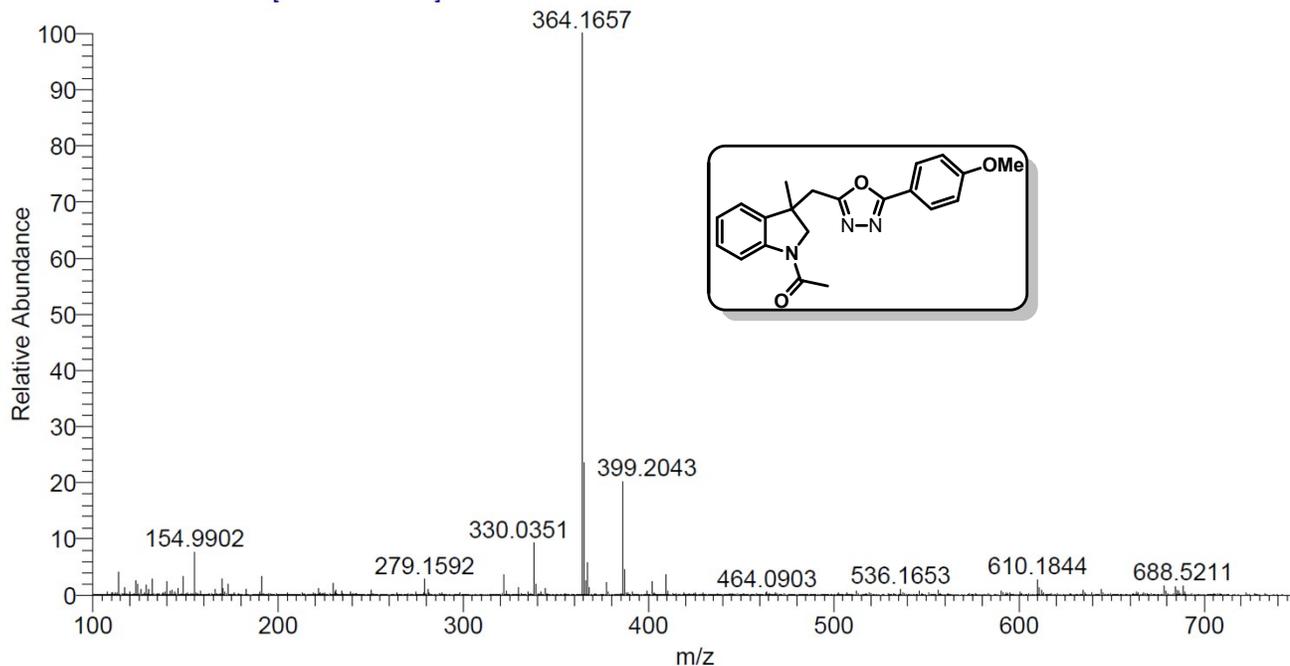


Figure S-90 HRMS spectrum of compound 3kn

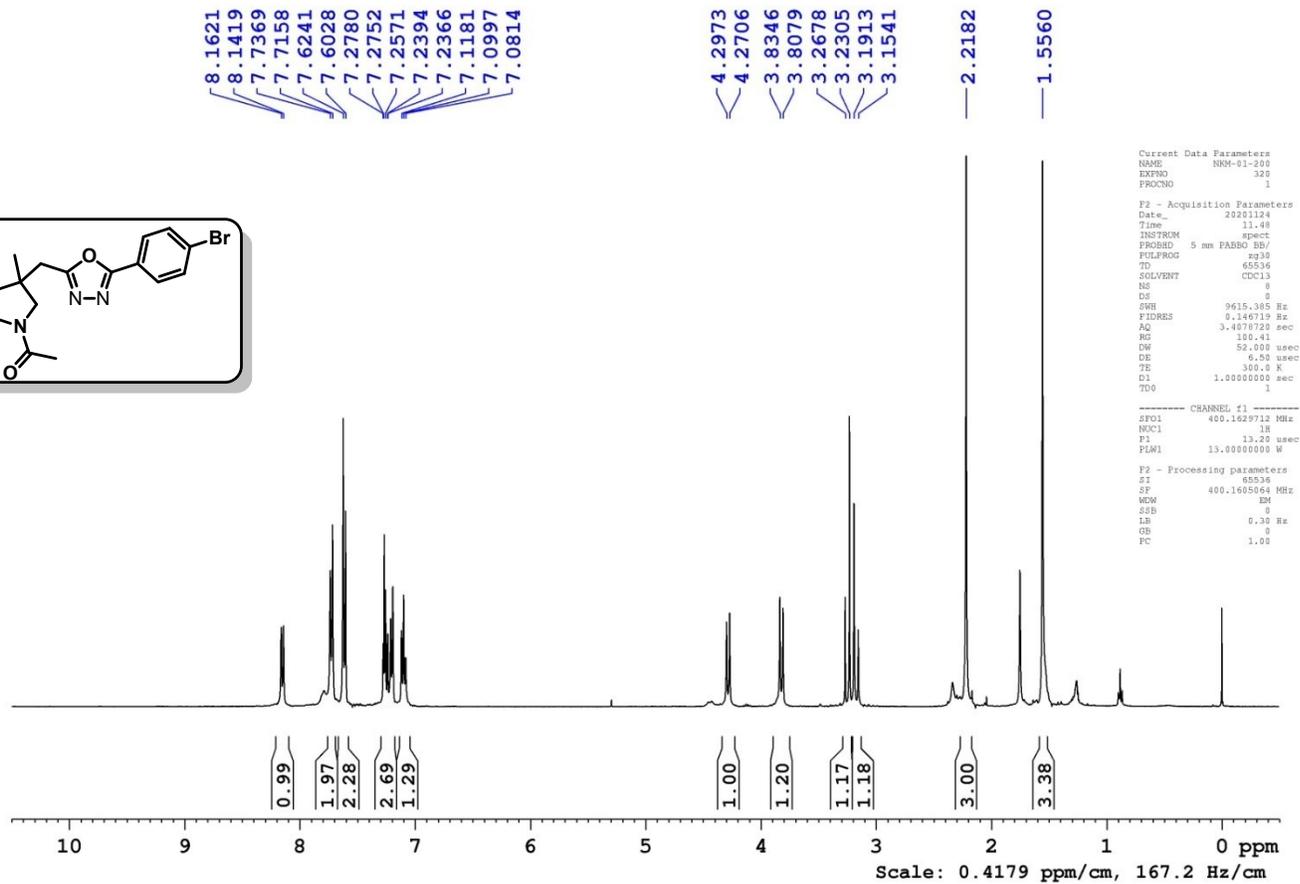
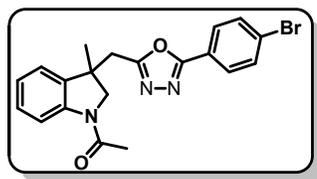


Figure S-91 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ko**

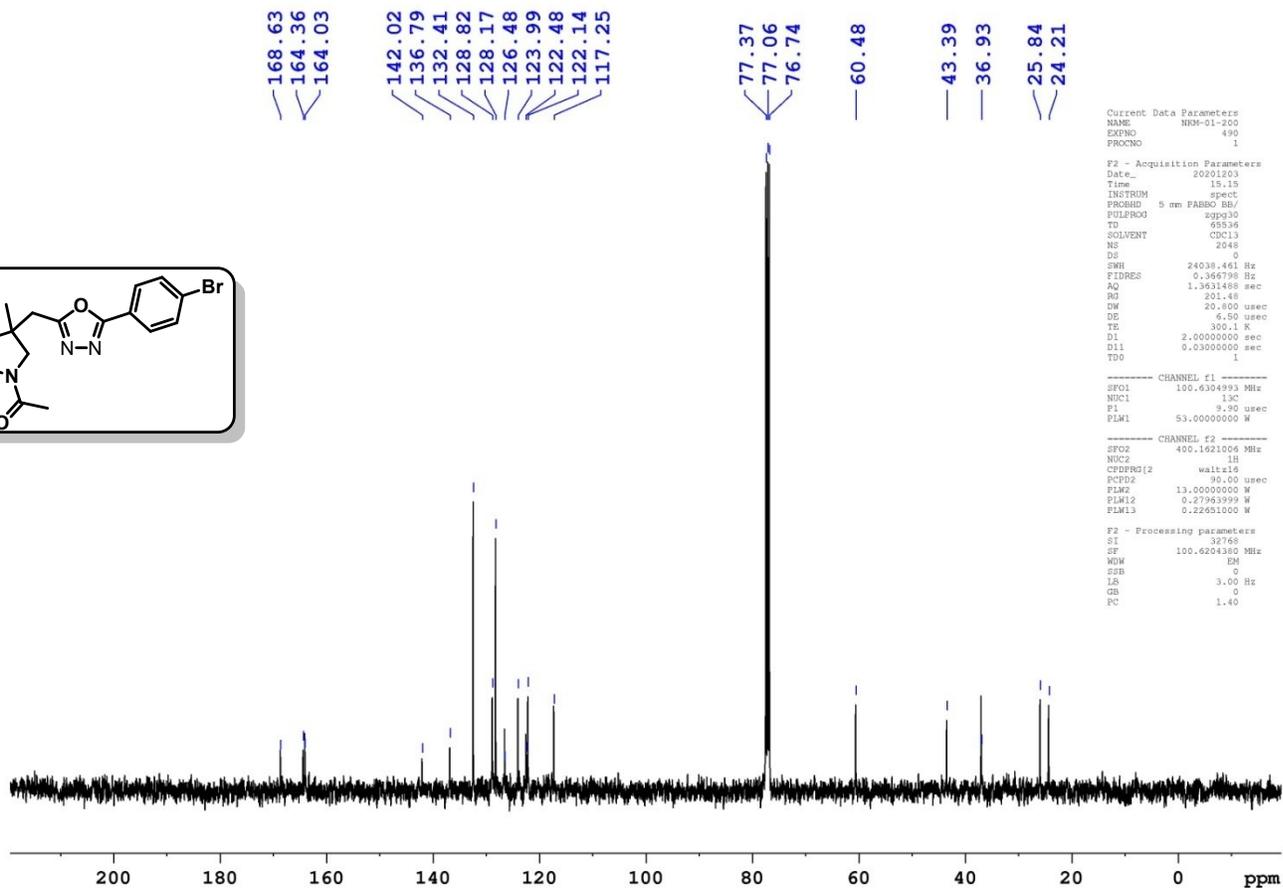
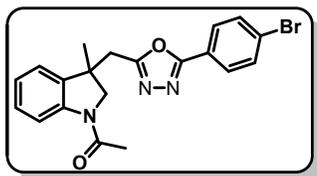


Figure S-92 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound **3ko**

SAIF [HRMS Report]

Data File: HRMS25I20NOV02 Original Data Path: D:\INTERNAL NEW\2020\NOV 2020  
 Sample ID: NKM-01-200 Sample Name:  
 Acquisition Date: 11/25/20 12:58:21 PM Run Time(min): 0.00  
 Vial: CStk1-01:2 Injection Volume(μl): 1.00

HRMS25I20NOV02 #30-62 RT: 0.25-0.50 AV: 33 SB: 1 0.01 NL: 1.73E6  
 T: FTMS + c ESI Full ms [100.00-750.00]

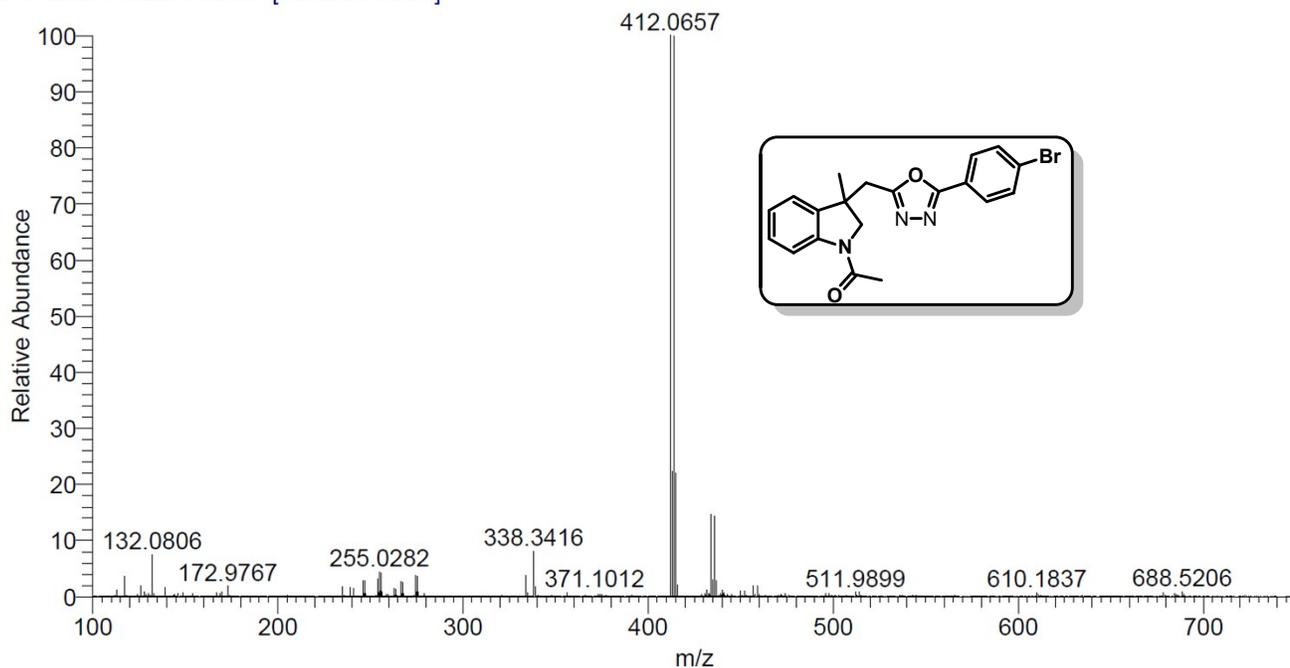


Figure S-93 HRMS spectrum of compound 3ko

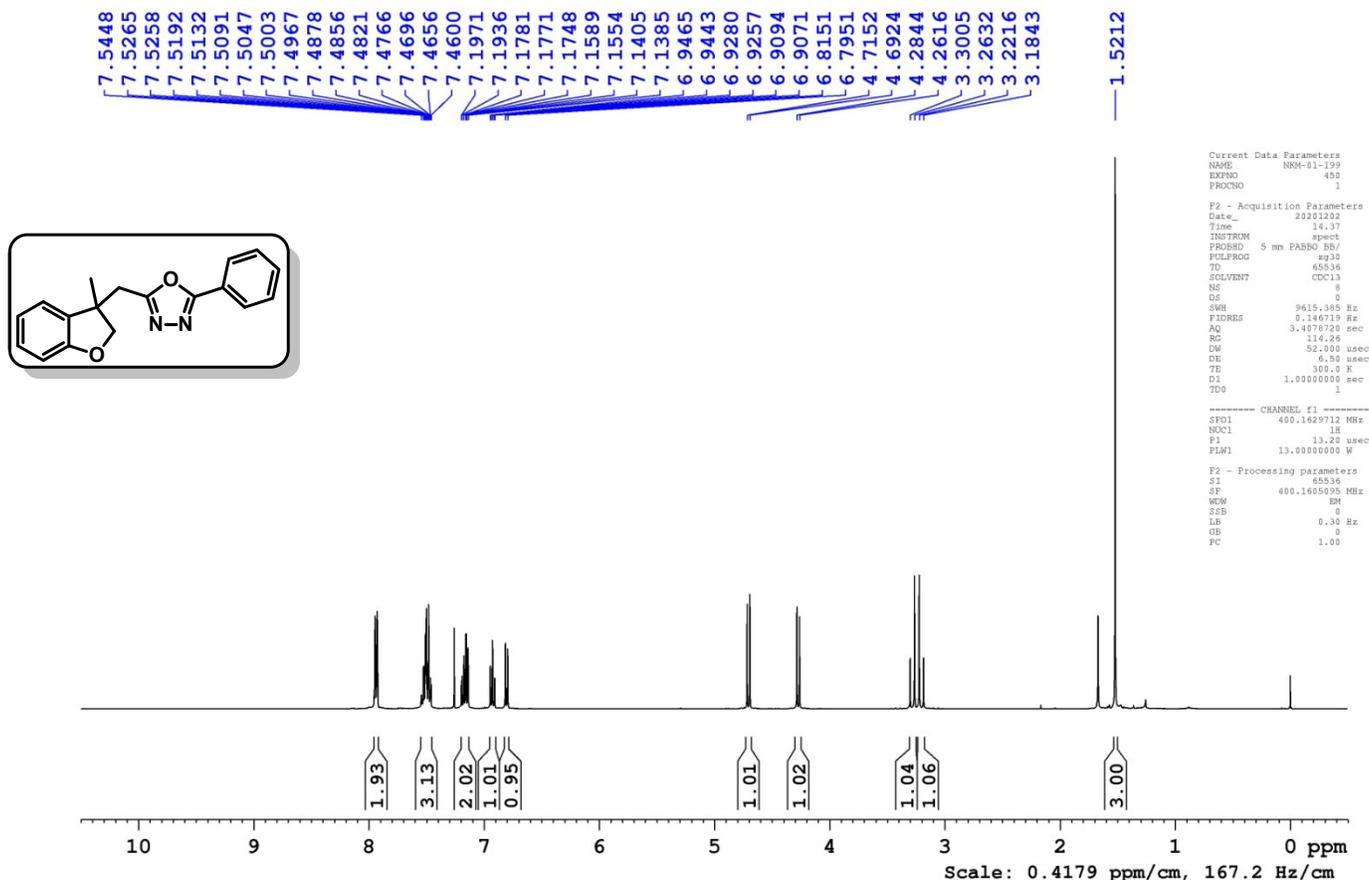


Figure S-94 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 3am

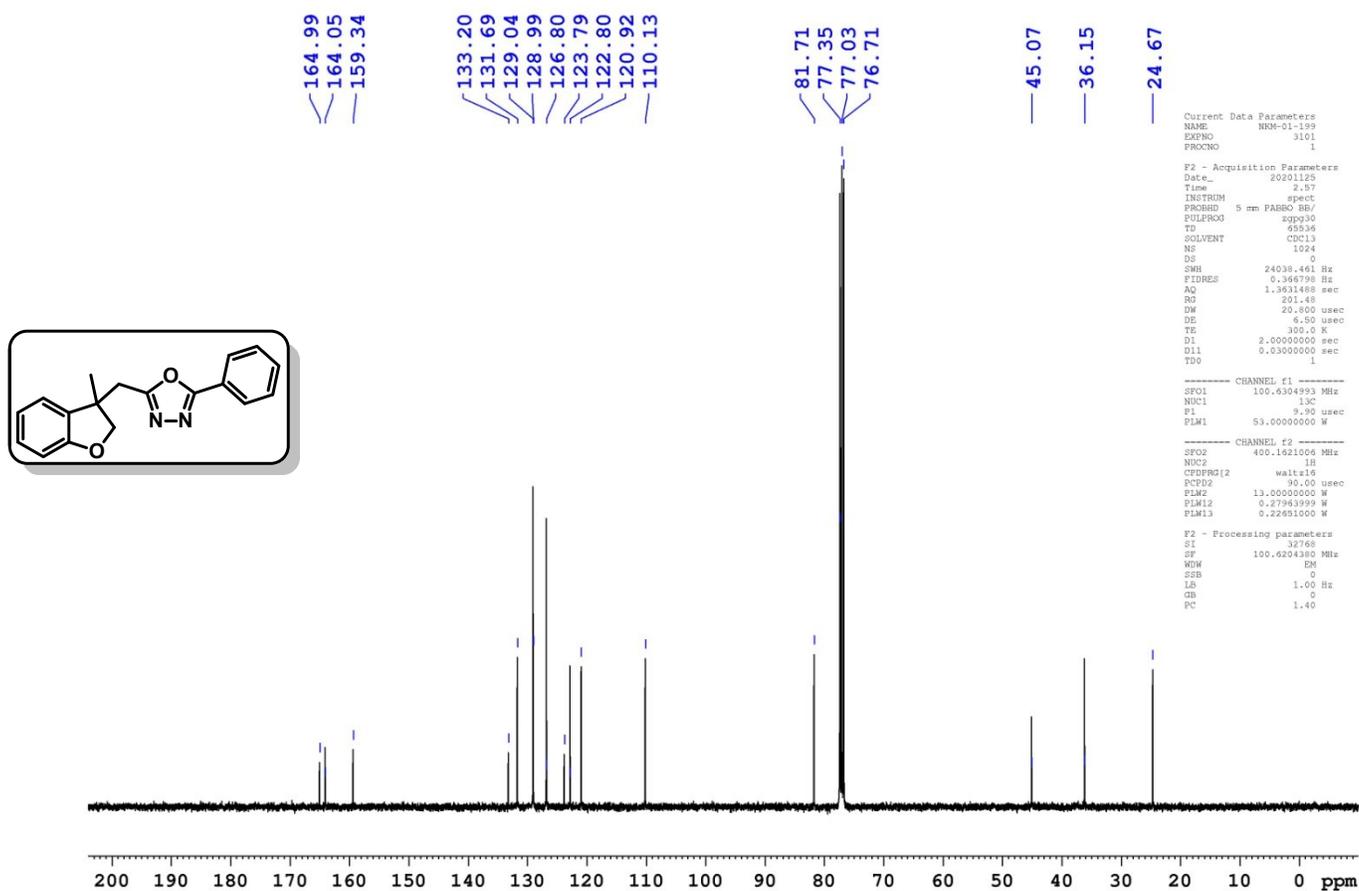


Figure S-95 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 3am

**SAIF [HRMS Report]**

Data File:	HRMS23I20NOV07	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
Sample ID:	NKM-01-199	Sample Name:	
Acquisition Date:	11/23/20 12:40:06 PM	Run Time(min):	0.00
Vial:	CStk1-01:7	Injection Volume(μl):	1.00

HRMS23I20NOV07 #31-62 RT: 0.25-0.50 AV: 32 SB: 1 0.01 NL: 5.64E5  
T: FTMS + c ESI Full ms [100.00-750.00]

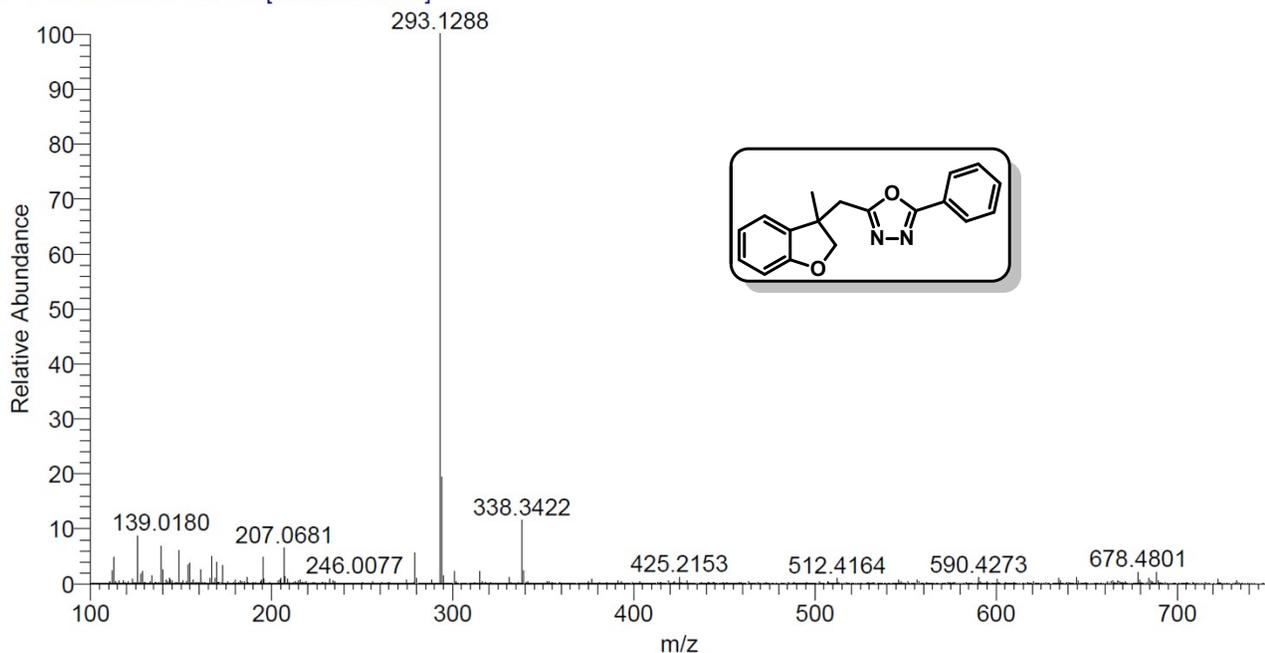


Figure S-96 HRMS spectrum of compound 3am

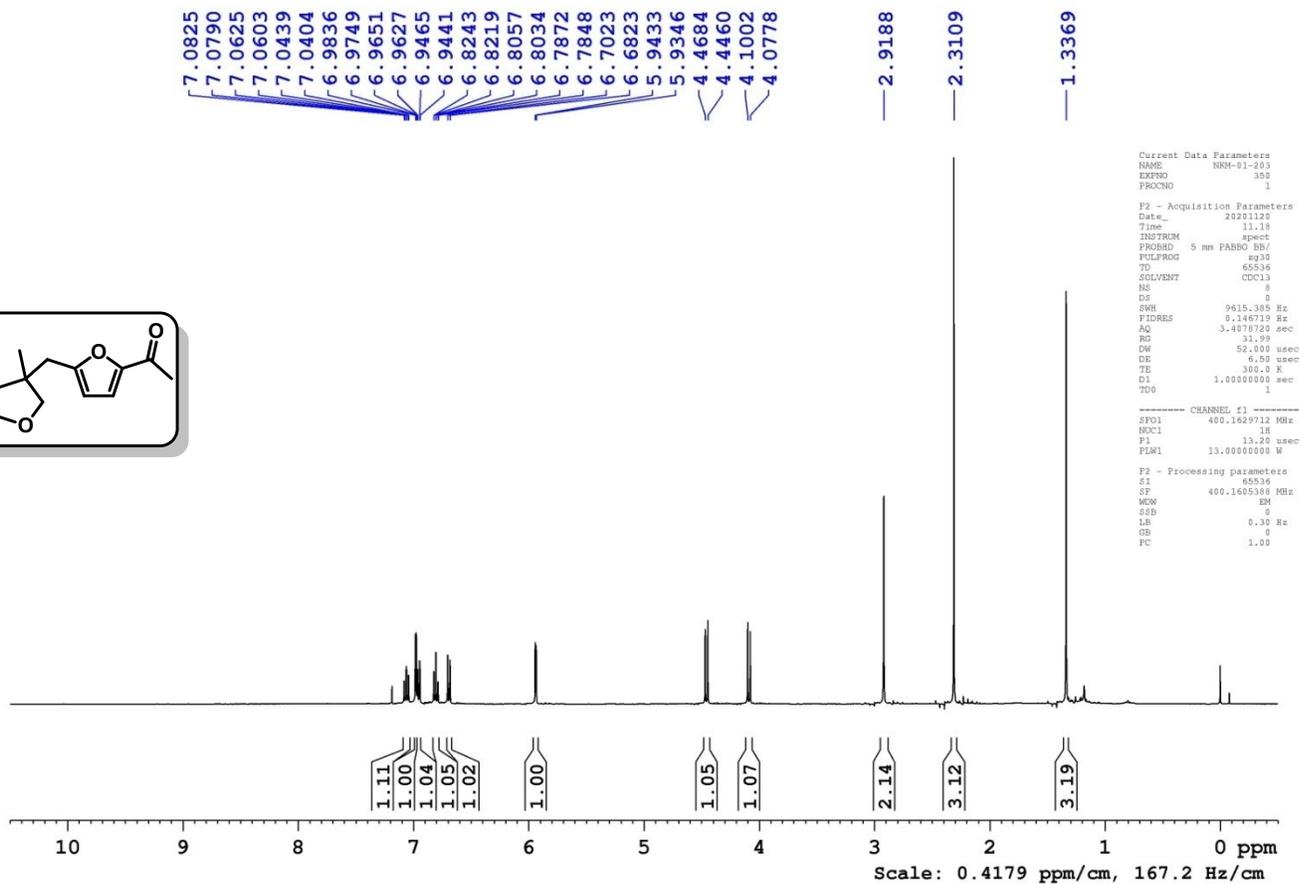
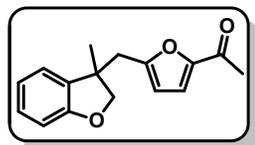


Figure S-97 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3ap**

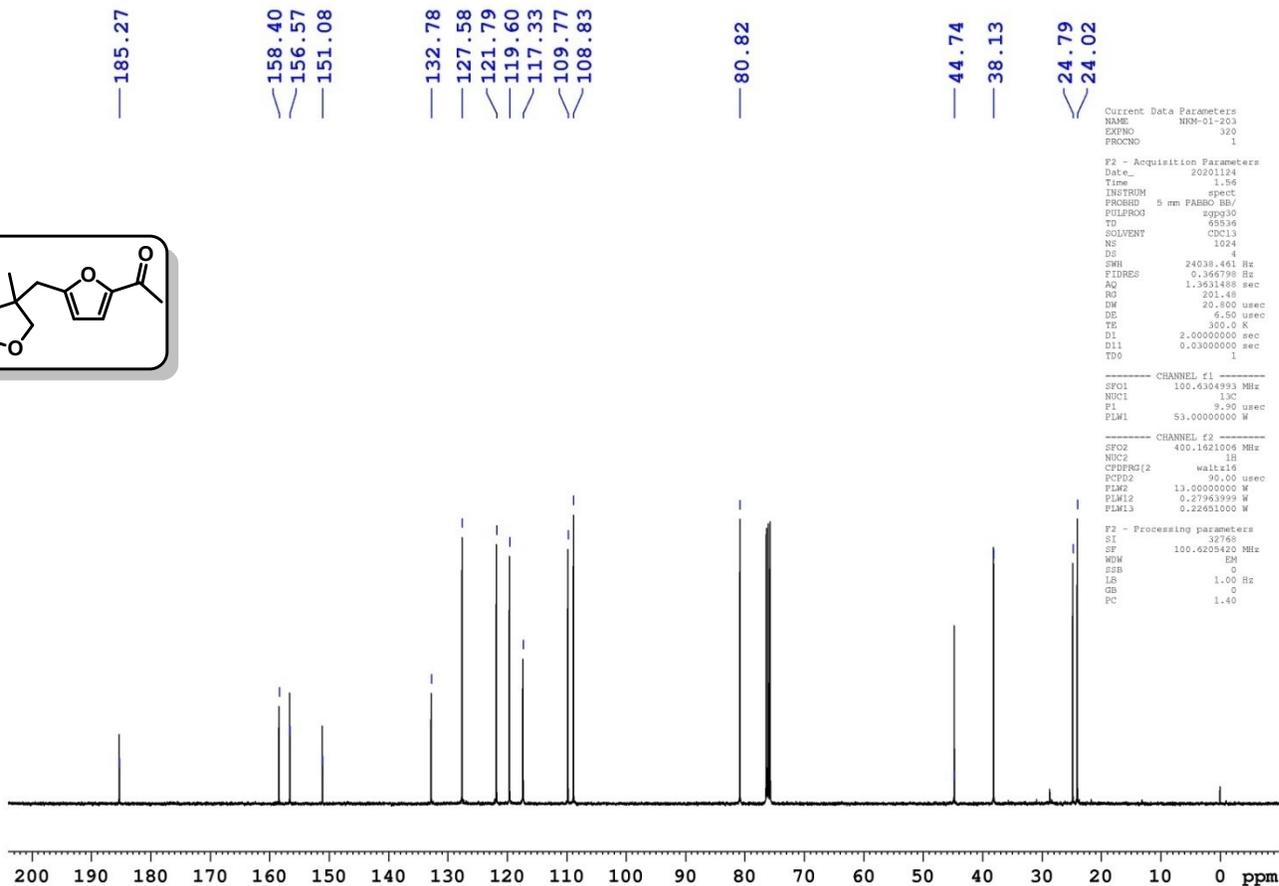
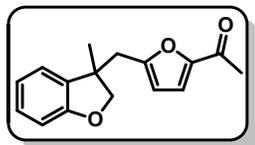
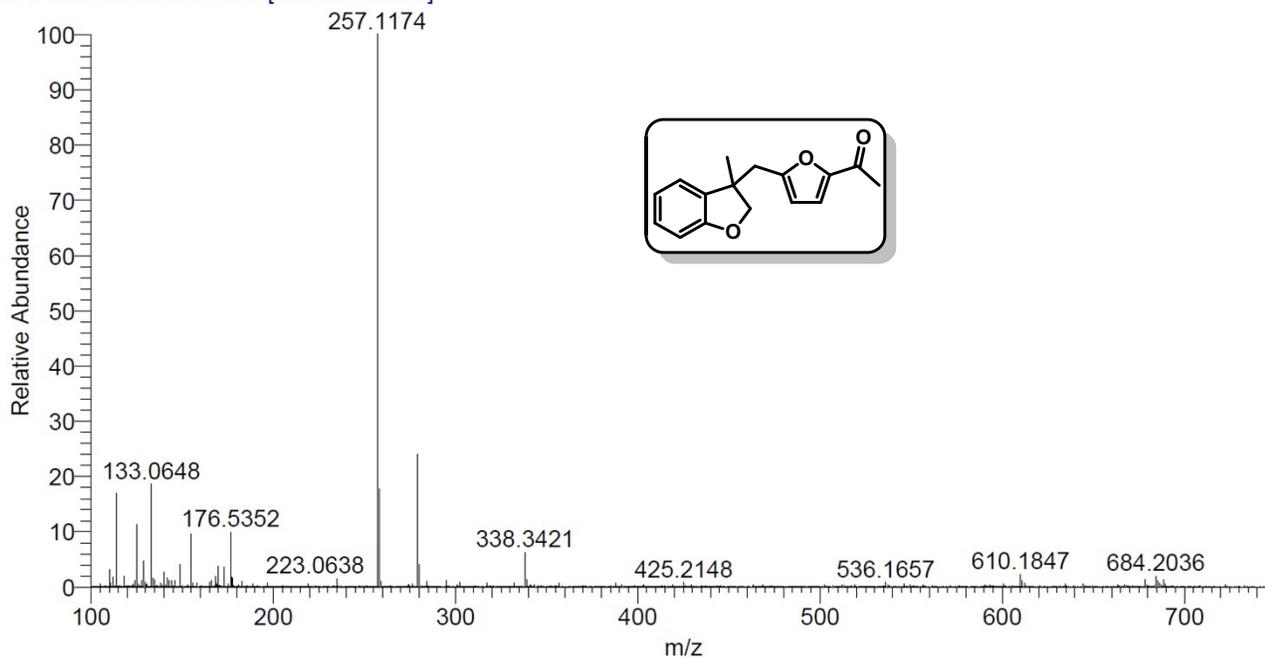


Figure S-98 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound **3ap**

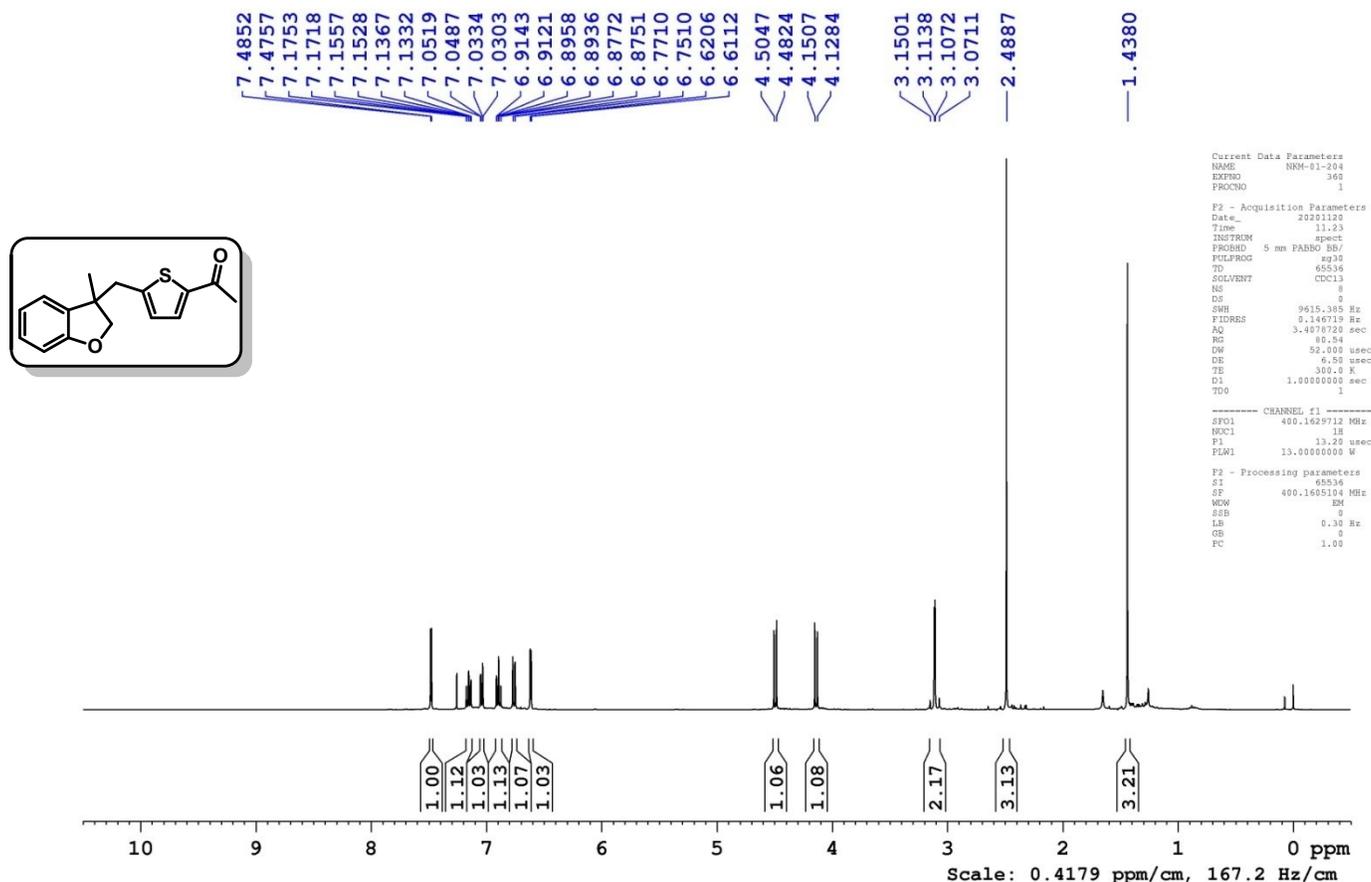
**SAIF [HRMS Report]**

Data File:	HRMS20I20NOV33	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
Sample ID:	NKM-01-203	Sample Name:	
Acquisition Date:	11/20/20 04:25:05 PM	Run Time(min):	0.00
Vial:	CStk1-01:33	Injection Volume(μl):	1.00

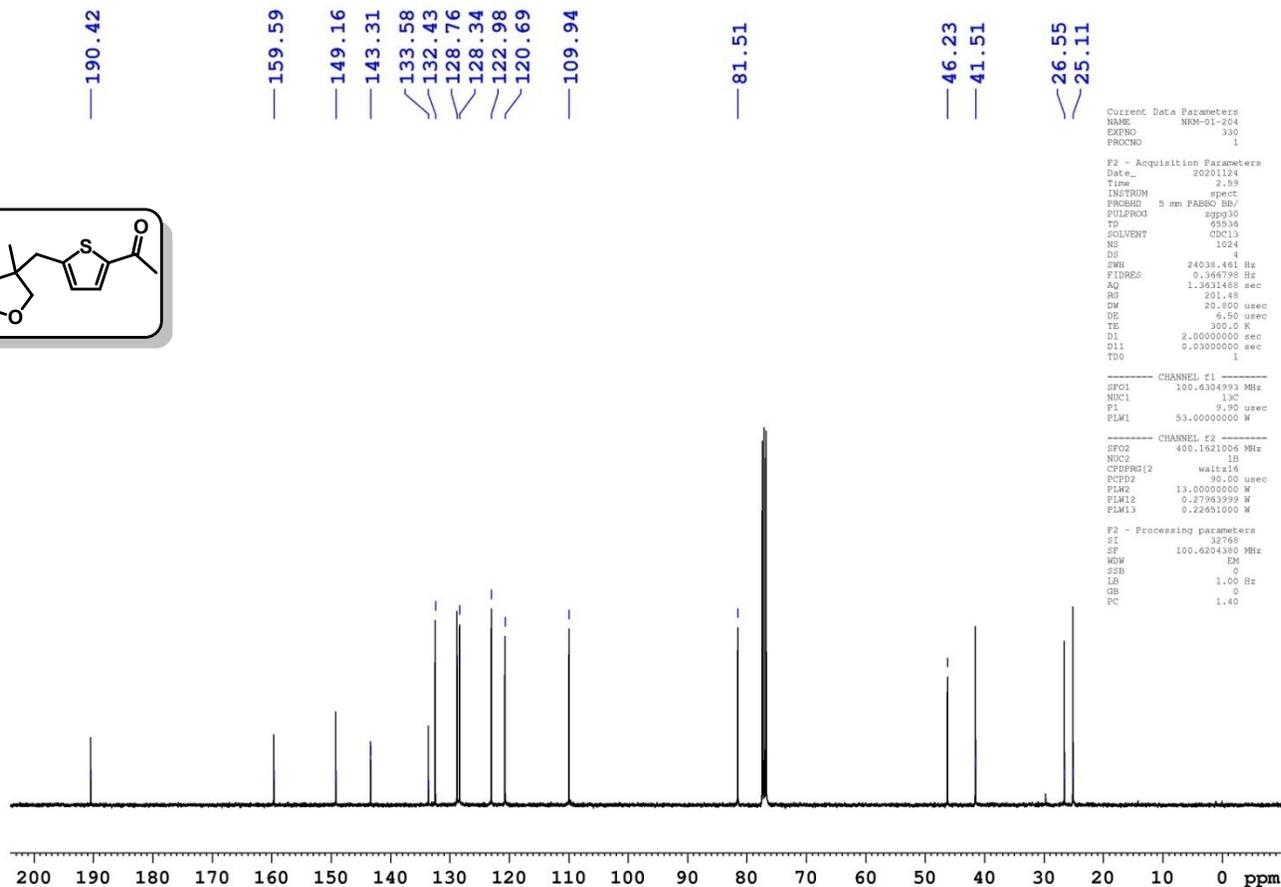
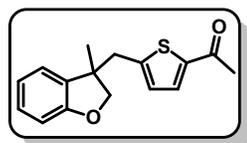
HRMS20I20NOV33 #29-60 RT: 0.25-0.50 AV: 32 SB: 1 0.01 NL: 1.13E6  
T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-99** HRMS spectrum of compound **3ap**



**Figure S-100** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound **3aq**

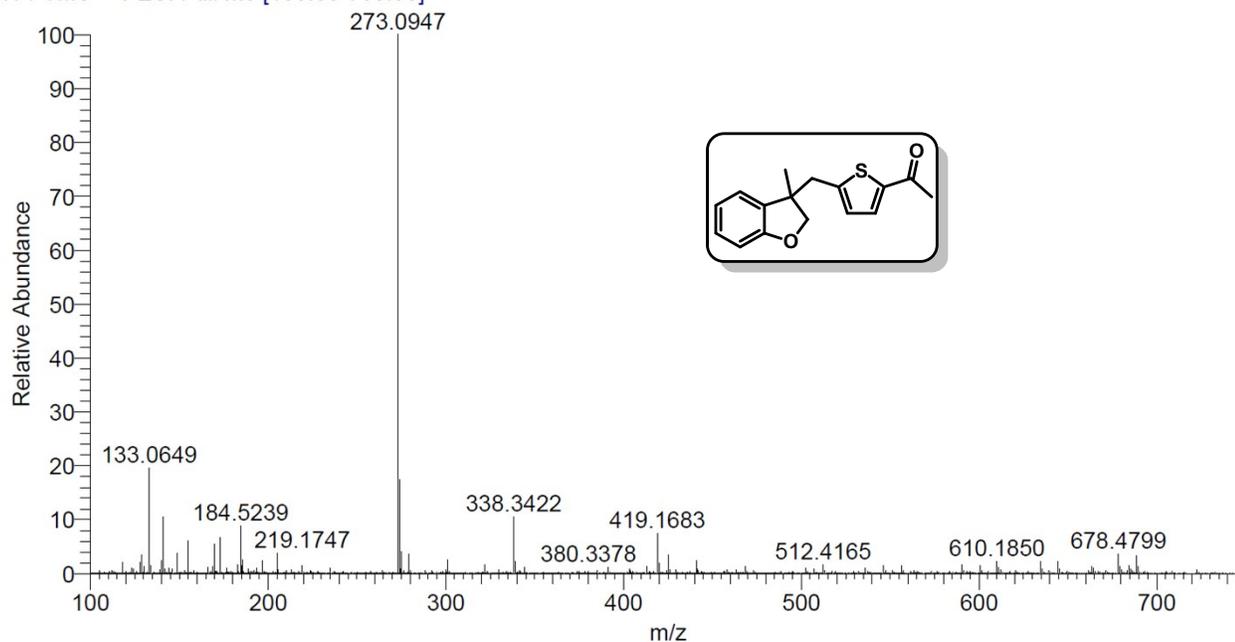


**Figure S-101** <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound **3aq**

**SAIF [HRMS Report]**

Data File:	HRMS20I20NOV34	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
Sample ID:	NKM-01-204	Sample Name:	
Acquisition Date:	11/20/20 04:27:03 PM	Run Time(min):	0.00
Vial:	CStk1-01:34	Injection Volume(μl):	1.00

HRMS20I20NOV34 #29-59 RT: 0.25-0.50 AV: 31 SB: 1 0.01 NL: 6.18E5  
T: FTMS + c ESI Full ms [100.00-750.00]



**Figure S-102** HRMS spectrum of compound **3aq**

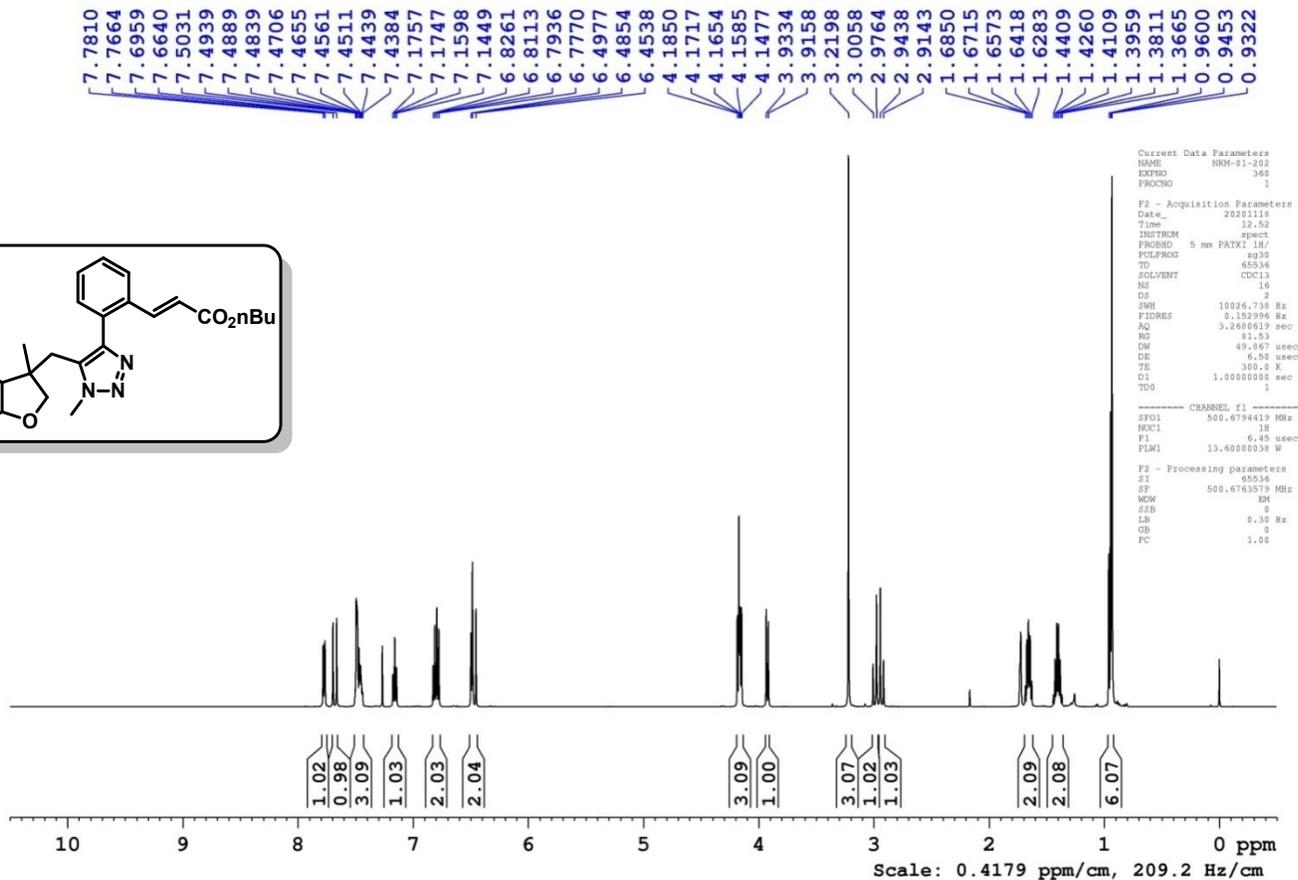
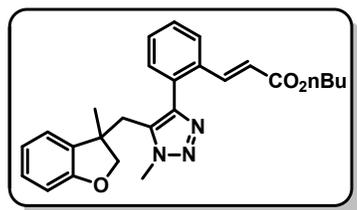


Figure S-103 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 4

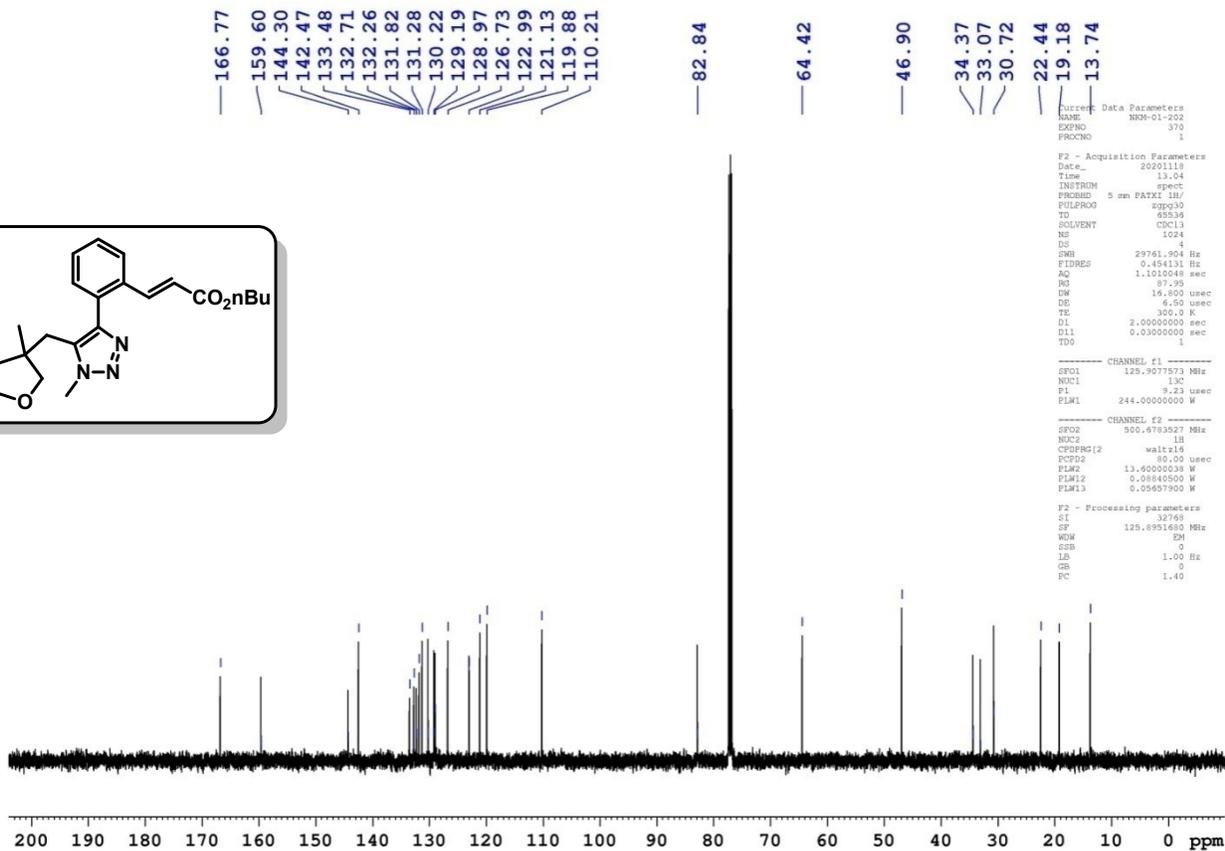
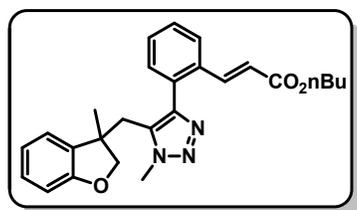


Figure S-104 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 4

SAIF [HRMS Report]

Data File: HRMS20I18NOV26 Original Data Path: D:\INTERNAL NEW\2020\NOV 2020  
 Sample ID: NKM-01-202 Sample Name:  
 Acquisition Date: 11/18/20 03:27:48 PM Run Time(min): 0.00  
 Vial: CStk1-01:26 Injection Volume(μl): 1.00

HRMS20I18NOV26 #13-26 RT: 0.11-0.21 AV: 14 SB: 1 0.01 NL: 4.51E6  
 T: FTMS + c ESI Full ms [100.00-750.00]

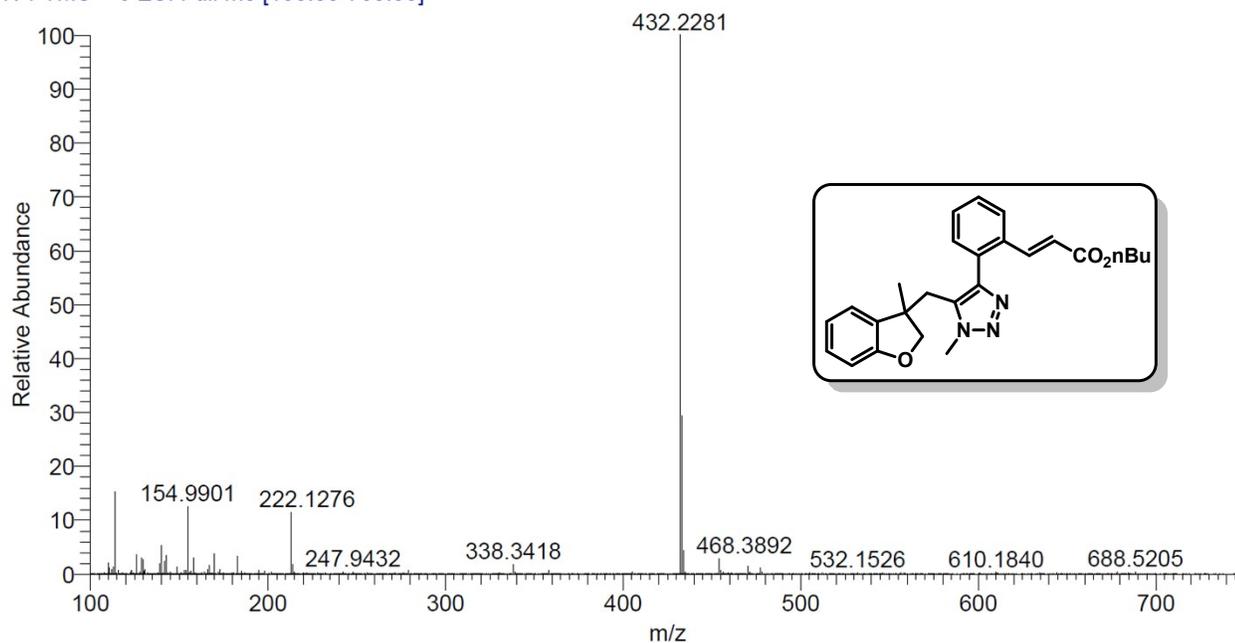


Figure S-105 HRMS spectrum of compound 4

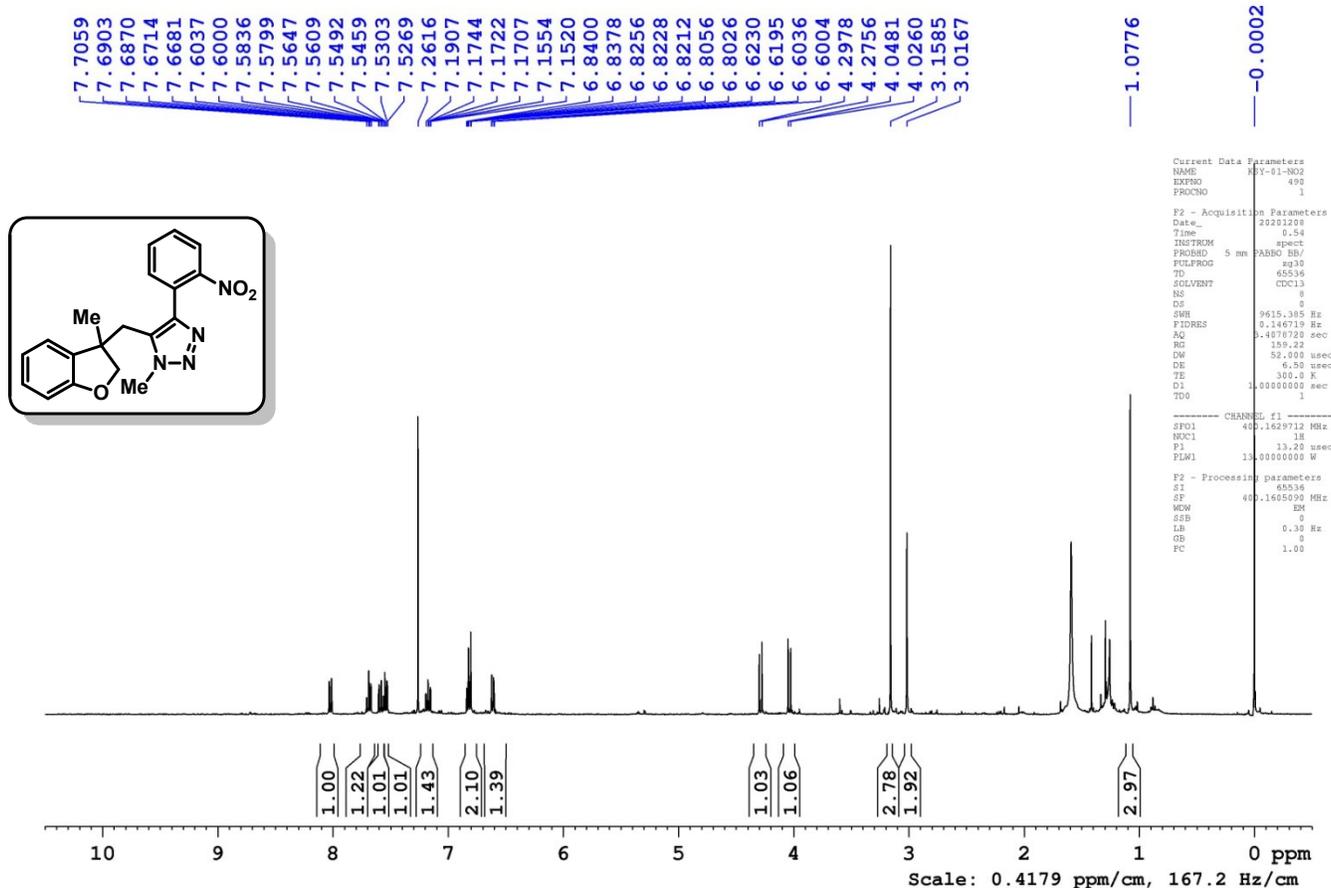


Figure S-106 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 5

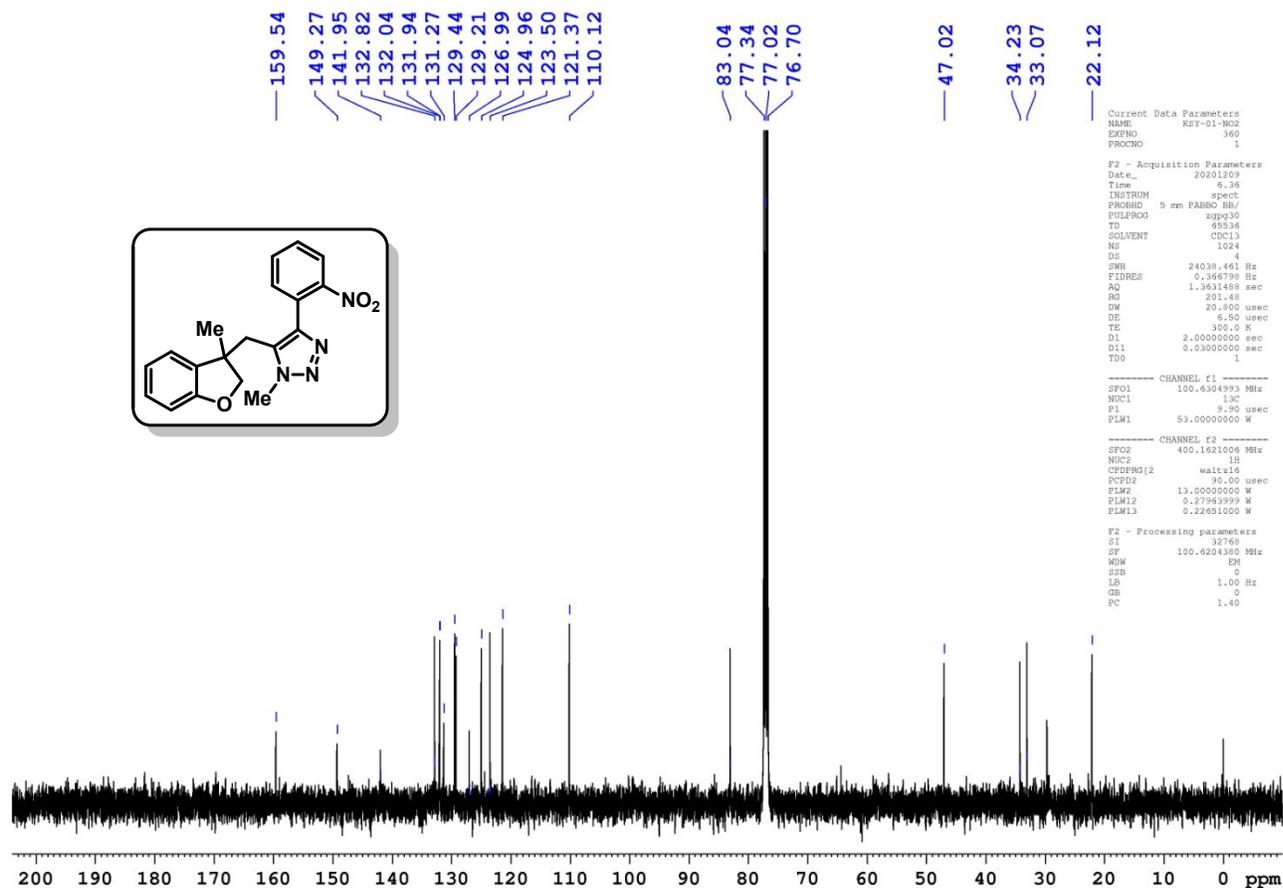


Figure S-107 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 5

SAIF [HRMS Report]

Data File:	HRMS20107DEC17	Original Data Path:	D:\INTERNAL NEW\2020\DEC 2020
Sample ID:	KSY-01-NO2	Sample Name:	
Acquisition Date:	12/07/20 01:08:02 PM	Run Time(min):	0.00
Vial:	CStk1-01:17	Injection Volume(μl):	1.00

HRMS20107DEC17 #31-63 RT: 0.25-0.50 AV: 33 SB: 1 0.01 NL: 4.42E6  
 T: FTMS + c ESI Full ms [100.00-750.00]

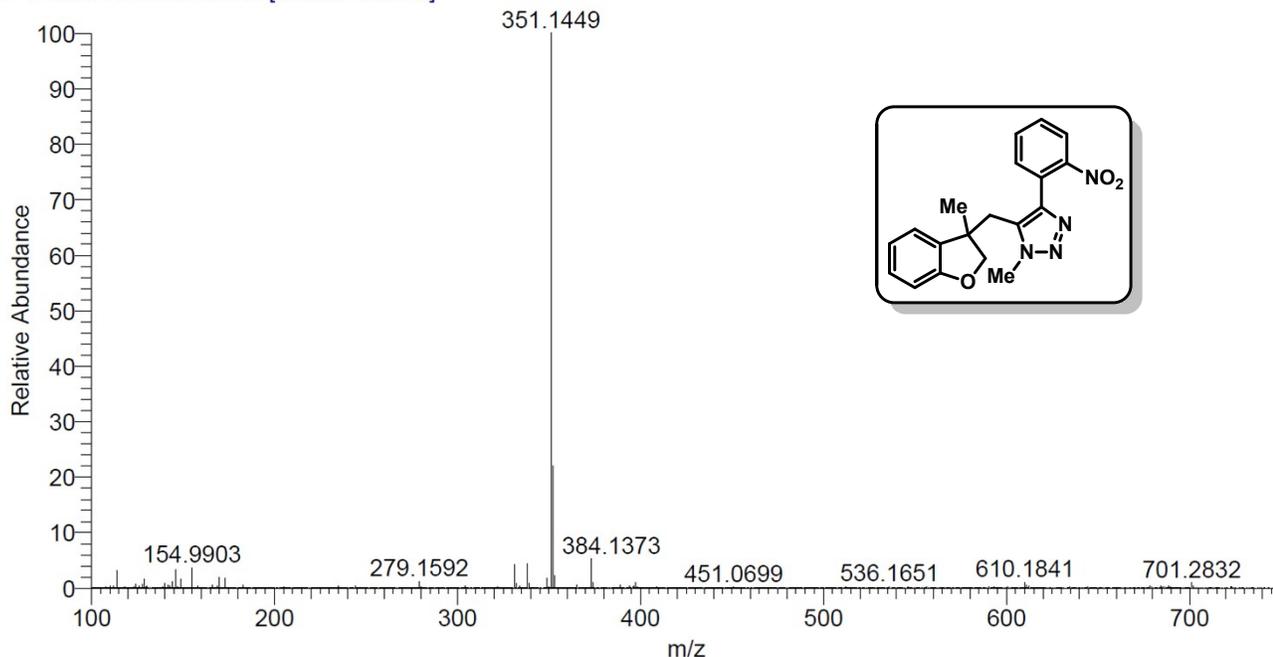


Figure S-108 HRMS spectrum of compound 5

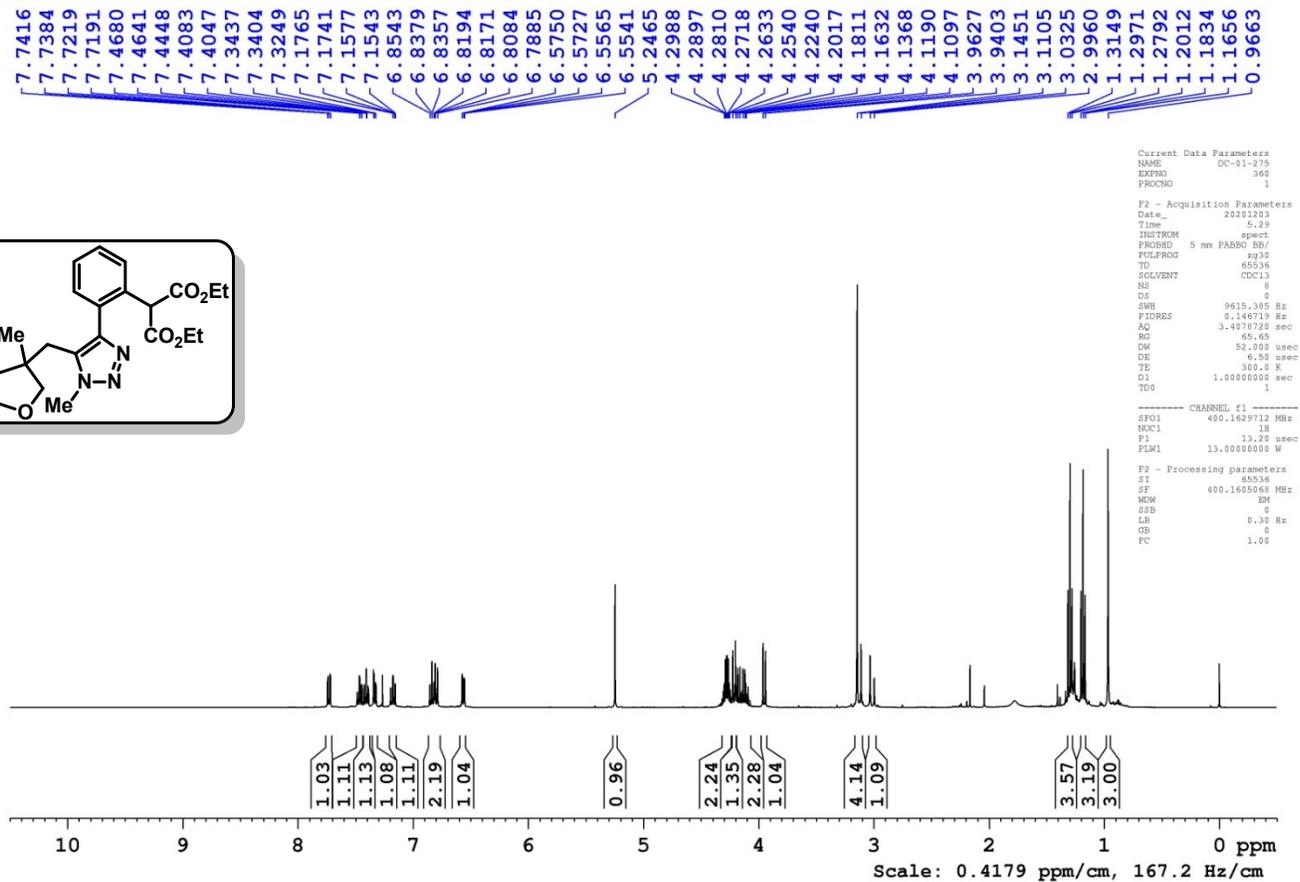
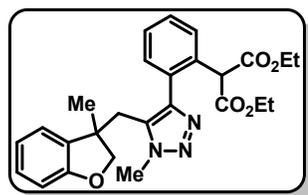


Figure S-109 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 6

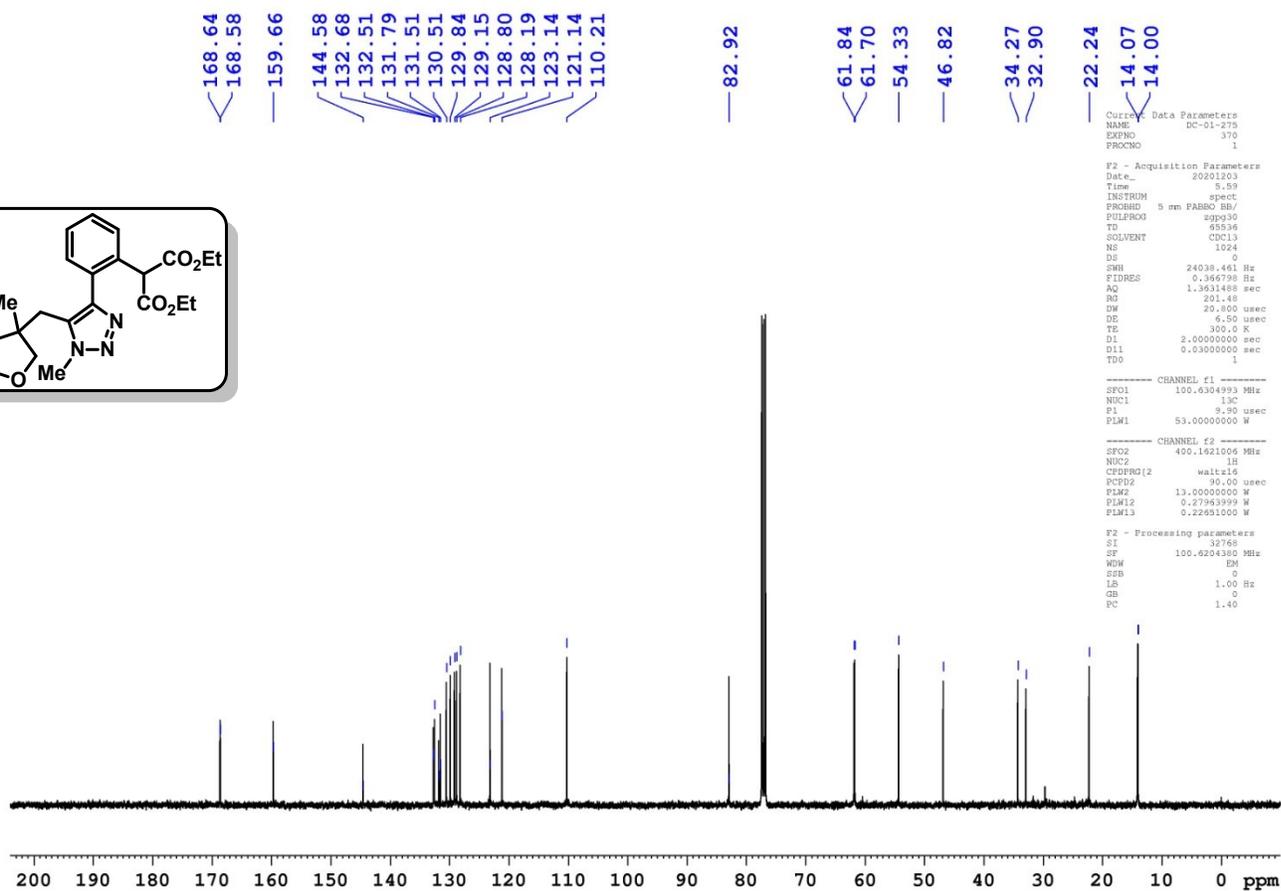
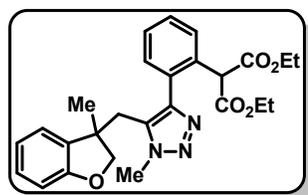


Figure S-110 <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) spectrum of compound 6

SAIF [HRMS Report]

Data File: HRMS20102DEC26 Original Data Path: D:\INTERNAL NEW\2020\DEC  
 Sample ID: DC-01-275 Sample Name: 2020  
 Acquisition Date: 12/02/20 01:55:51 PM Run Time(min): 0.00  
 Vial: CStk1-01:26 Injection Volume(μl): 1.00

HRMS20102DEC26 #30-63 RT: 0.25-0.50 AV: 34 SB: 1 0.01 NL: 8.18E6  
 T: FTMS + c ESI Full ms [100.00-750.00]

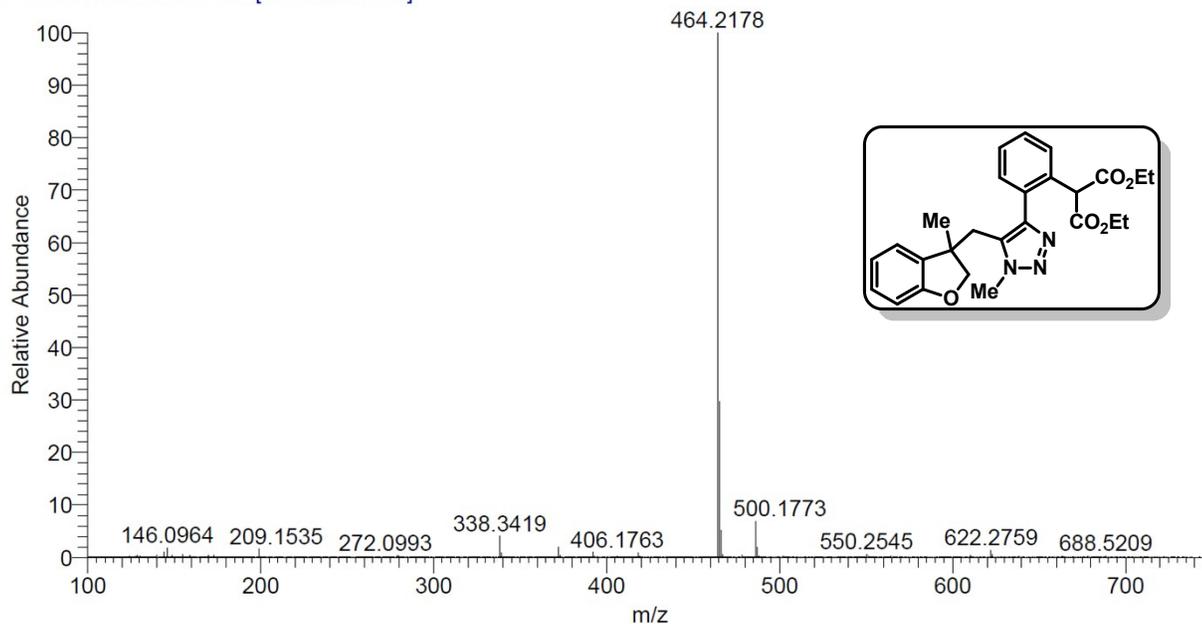


Figure S-111 HRMS spectrum of compound 6

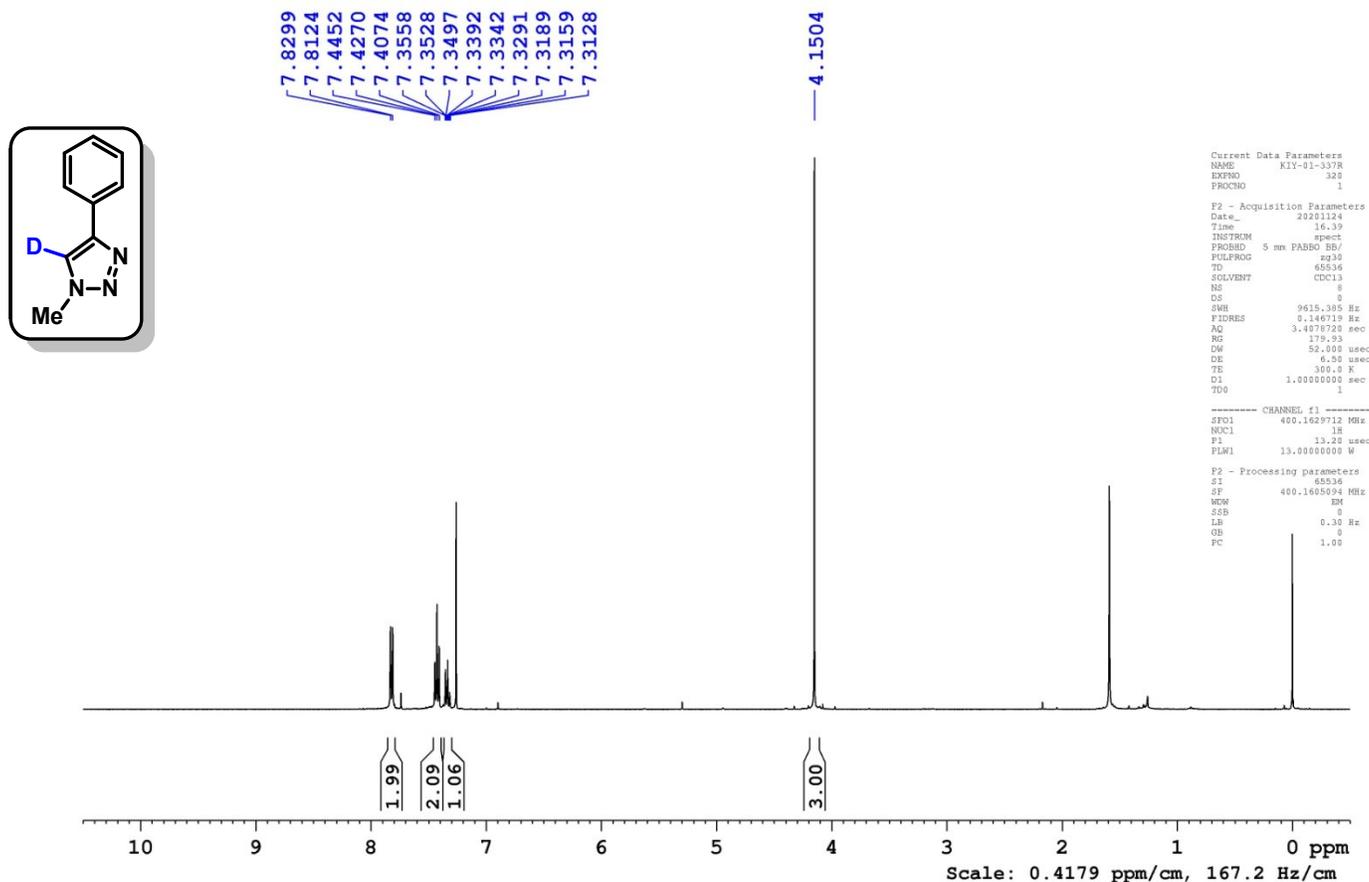


Figure S-112 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of compound 2a-[D1]

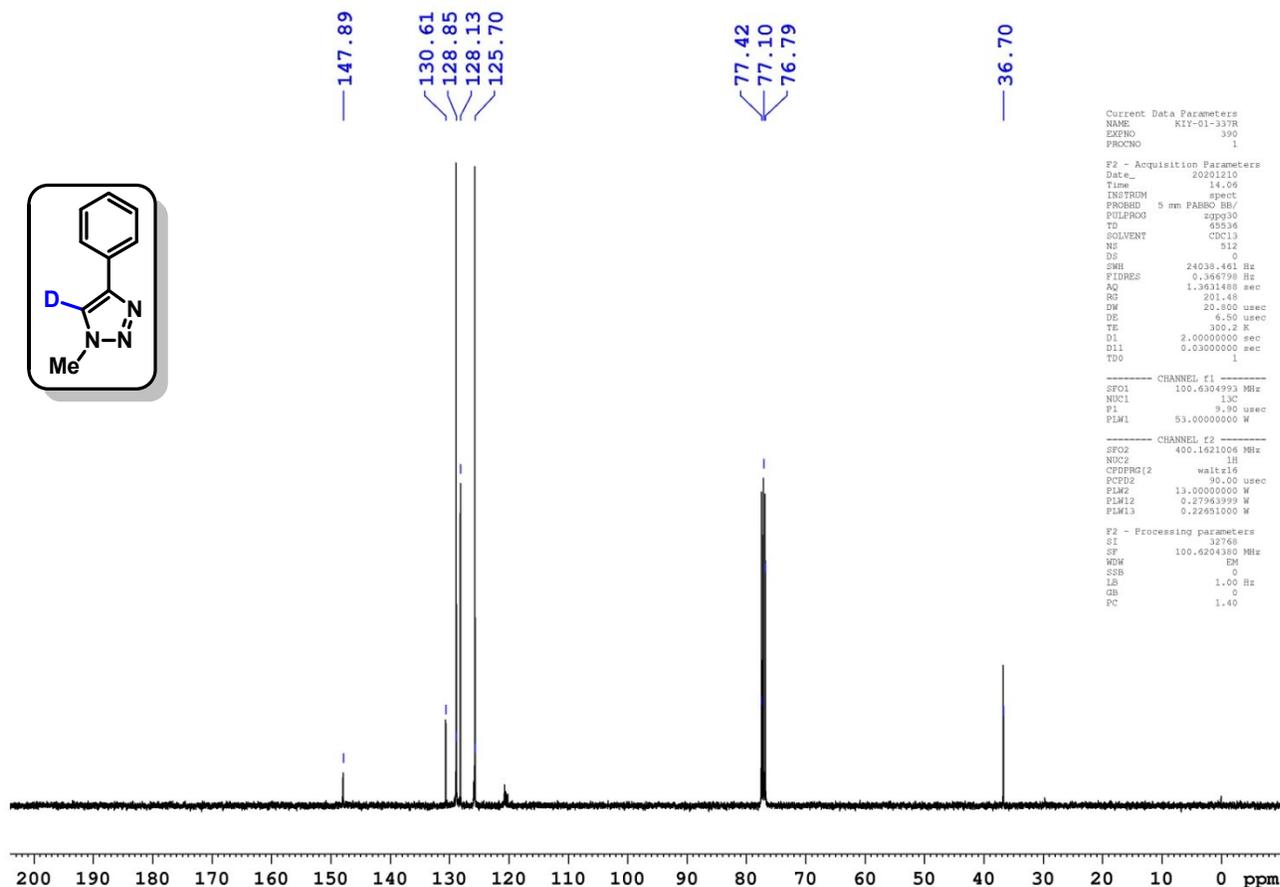


Figure S-113  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ) spectrum of compound 2a-[D1]

**SAIF [HRMS Report]**

Data File:	HRMS24I20NOV14	Original Data Path:	D:\INTERNAL NEW\2020\NOV 2020
Sample ID:	KIY-01-337	Sample Name:	
Acquisition Date:	11/24/20 03:35:10 PM	Run Time(min):	0.00
Vial:	CStk1-01:14	Injection Volume( $\mu\text{l}$ ):	1.00

HRMS24I20NOV14 #29-62 RT: 0.25-0.50 AV: 34 SB: 1 0.01 NL: 7.56E6  
T: FTMS + c ESI Full ms [100.00-750.00]

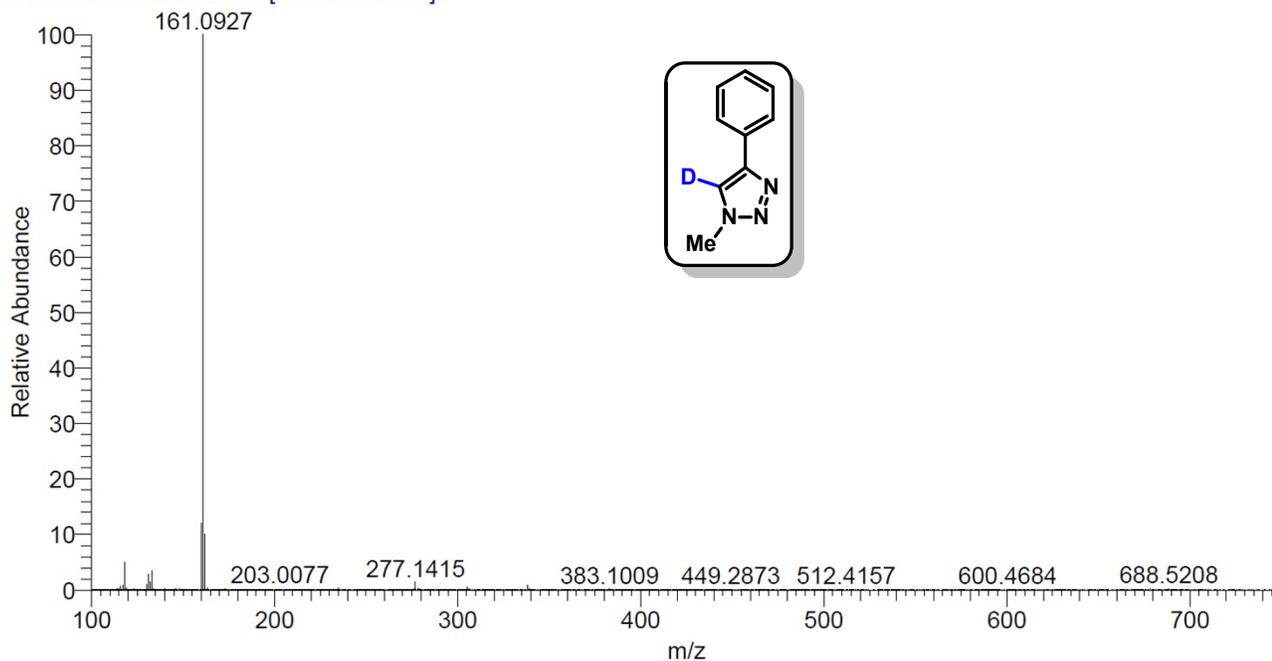


Figure S-114 HRMS spectrum of compound 2a-[D1]