Supporting Information

NBS-induced intramolecular annulation reactions for the divergent synthesis of fused- and spirocyclic indolines

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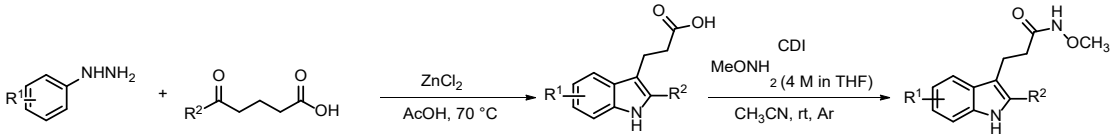
General Methods. Unless otherwise noted, all solvents were used directly without further purification. 3-indolepropionic acid were obtained from Bide Pharmatech, and used directly without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker instrument (400 MHz and 100 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protic solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant (s) in Hz, integration). Data for ^{13}C NMR and ^{19}F NMR are reported in terms of chemical shift (δ, ppm).

General procedure for the synthesis of substrates[1]

Procedure A



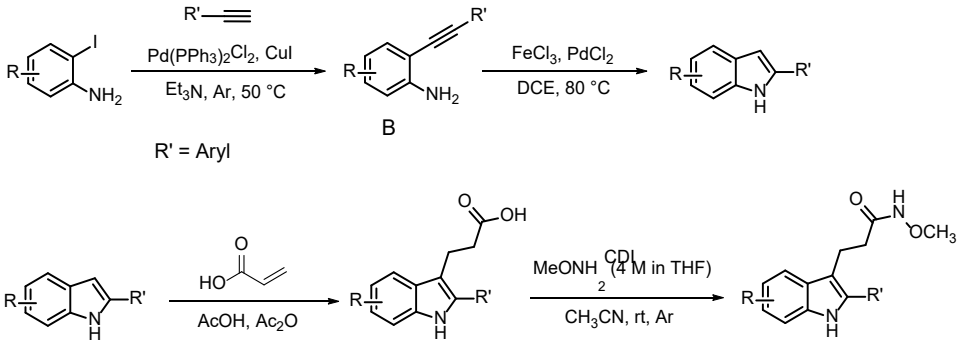
Step 1: To a stirring solution of 5-oxohexanoic acid (6.1 mmol, 1.0 equiv.) and phenylhydrazine (6.1 mmol, 1.0 equiv.) in AcOH (15 mL) was added zinc chloride (6.1 mmol, 1.0 equiv.) and the mixture was heated to 70 °C. After 16 h, the mixture was cooled to rt, diluted with EtOAc (100 mL), washed with water (50 mL), dried (Na_2SO_4), and concentrated under reduced pressure, which was used without further purification.

Preparation of $MeONH_2$ solution: To a 100 mL round bottle charged with a stirring bar was added $MeONH_2 \cdot HCl$ (80.0 mmol) and 20 mL THF. Sodium hydroxide (powder, 1.0 equiv.) was then added and the reaction was stirred at room temperature for another 3 h until the system became clear which was ready to use for **Step 2** reaction.

Step 2: To a Schlenk tube charged with stirring bar was added 1*H*-indole-carboxylic acid (5.0 mmol, 1.0 equiv.) and 1,1'-carbonyldiimidazole (CDI, 5.0 mmol, 1.0 equiv.). Then 20 mL anhydrous acetonitrile was added to the reaction mixture under the protection of N_2. The system was stirred at room temperature for 12 h. Then, $MeONH_2$ solution (4 M in THF, 1.0 equiv.) was added and then stirred at room temperature for another 6 h (when most of indole was consumed by TLC detection). Upon completion, the resultant was extracted with EtOAc (30 mL), The combined organic phase

was extracted with sodium bicarbonate (2 × 50 mL), saturated salt water (2 × 50 mL). The combined organic phase was dried over $MgSO_4$. The extract was concentrated under reduced pressure and the crude mixture was purified by silica gel column chromatography to obtain products (eluent: Petroleum ether/EtOAc = 3:1 ~ 1:1).

Procedure B



Step 1: Terminal alkynes (6 mmol, 1.2 equiv.) was added to a solution of 2-iodoaniline A (5 mmol, 1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (0.125 mmol, 0.025 equiv.) and CuI (0.25 mmol, 0.05 equiv.). Then 5 mL Et_3N was added to the reaction mixture under the protection of N_2. The mixture was stirred at 50 °C overnight. The reaction was monitored by TLC. After reaction completed, the mixture was diluted with water and organic compound was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and the solvent was evaporated. Purification by flash column chromatography (silica gel, ethyl acetate/ petroleum ether 1:10) yielded products B.

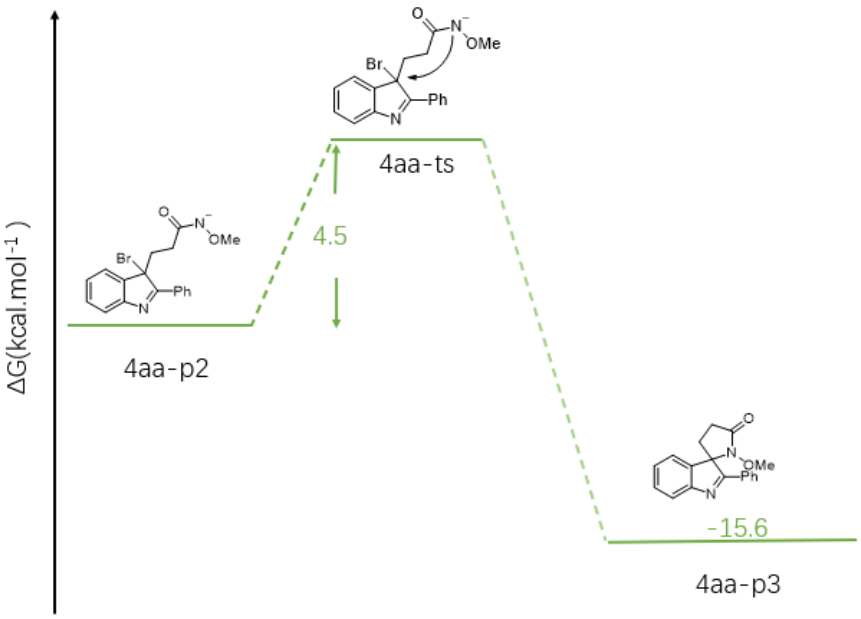
Step 2: A solution of B, $FeCl_3·6H_2O$ (2 mol%) and $PdCl_2$ (1 mol%) was heated in DCE (1mL/0.15mmol) at 80 °C under the protection of N_2 for 4 h. After cooling to room temperature, the reaction mixture was diluted with water. The aqueous layers were extracted with DCM, and the combined organic phases were dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography (silica gel, ethyl acetate/petroleum ether 1:10).

Step 3: A solution of indole (3.0 mmol, 1 equiv.) was dissolved in acetic acid (1.6 M). Acrylic acid (7.2 mmol, 2.4 equiv.) and acetic acid anhydride (6.3 mmol, 2.1 equiv.) were added and the reaction mixture was heated to 95 °C for 24 hours. The reaction was then cooled to room temperature, which was then extracted with ethyl acetate and NaOH (4 N) solution. The aqueous layer was added the HCl (6 N) solution until the pH value was 2 and then extracted with ethyl acetate. The combined organics were dried and concentrated in vacuo. The residue was subjected to column

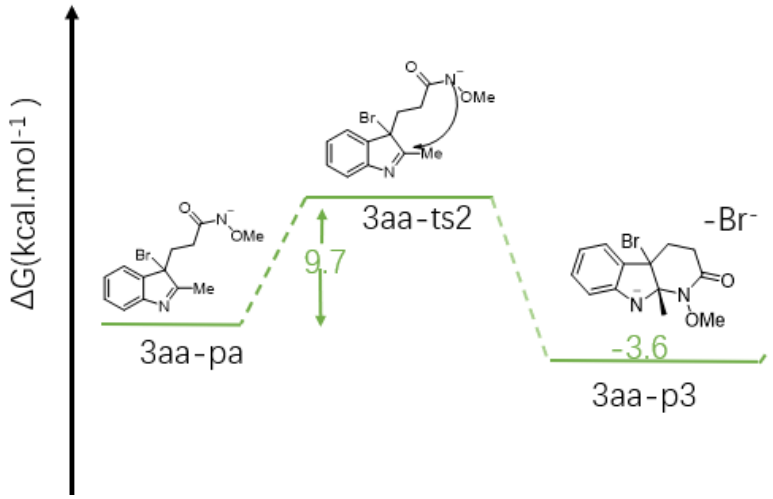
chromatography on silica gel and eluted with petroleum ether/ethyl acetate (4:1 and 2:1, v/v) to afford corresponding product.

Step 4: To a 100 mL round bottle charged with stirring bar was added 1*H*-indole-carboxylic acid (5.0 mmol, 1.0 equiv.) and 1,1'-carbonyldiimidazole (CDI, 5.0 mmol, 1.0 equiv.). Then 20 mL anhydrous acetonitrile was added to the reaction mixture under the protection of N_2 and it was stirred at room temperature for 12 h. Then, $MeONH_2$ solution (4 M in THF, 2.0 equiv.) was added and the reaction was stirred at room temperature for another 6 hours (when most of indole was consumed by TLC detection). Upon completion, the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 1:1) to products.

DFT computed energy surface for the formation of 4aa & 3aa



DFT computed energy surface for the formation of 4aa (R=Ph)



DFT computed energy surface for the formation of 3aa (R=Me)

The molecular geometry optimized using the Density Functional Theory (DFT) method of B3LYP with the basis set of 6-31+g(d,p) . All calculations were performed using GAUSSIAN 2016 package[1]. All the optimized stationary points had been identified as minima (zero imaginary frequencies) and transition states (one imaginary frequency), via the vibrational analysis.

References

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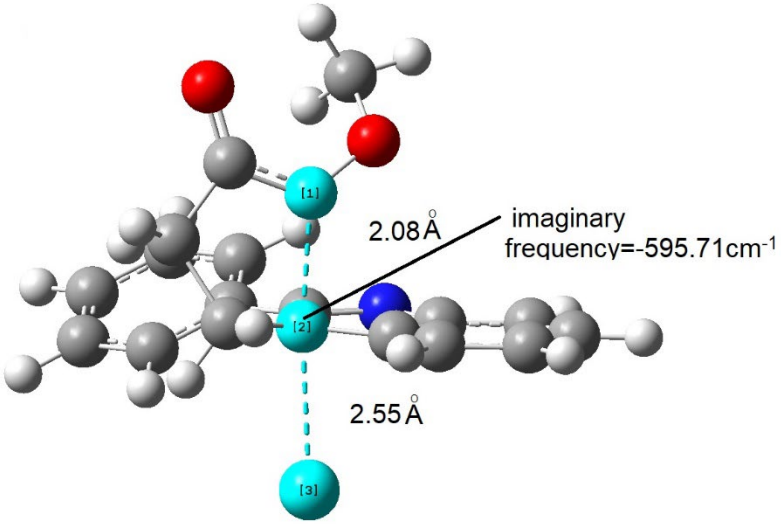
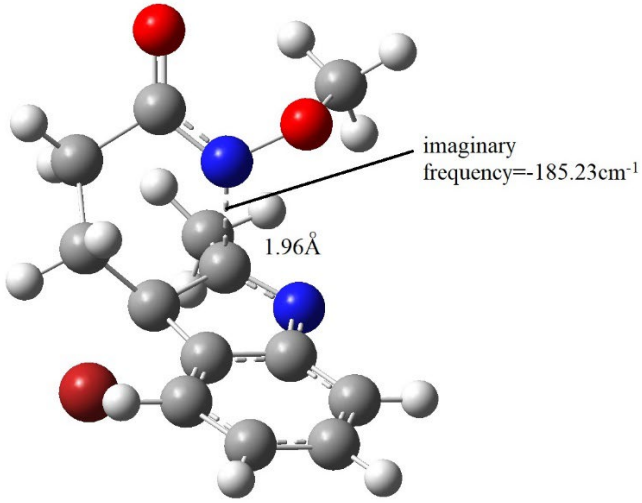
J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, D. J. Fox, *Gaussian*16, Gaussian, Inc., Wallingford, CT, **2016**.

DFT details for mechanistic studies



The bond lengths and only one imaginary frequency for 4aa-ts2



The bond lengths and only one imaginary frequency for 3aa-ts2

1. The free energy for the species in the calculation

Species	Free energy (a.u.)	Species	Free energy (a.u.)
4aa-p2	-3527.0419	**4aa-ts2**	-3527.0348
4aa-p3	-955.247401	**Br^-**	-2571.81937
3aa-p2	-3335.343379	**3aa-ts2**	-3335.327906
3aa-p3	-3335.349092		

2. The coordination for the species.

4aa-p2

C	-3.28544400	-3.24326600	-0.68904800
C	-4.22488100	-2.43747200	-1.34652900
C	-4.02116800	-1.05787900	-1.47900200
C	-2.86115800	-0.51761300	-0.92761300
C	-1.92193000	-1.32049600	-0.26627000
C	-2.11427400	-2.68948600	-0.14911700
N	-2.46030700	0.83197700	-0.96981900
C	-1.31507900	0.93930400	-0.36090300
C	-0.78789700	-0.42259300	0.15600000
C	0.56782400	-0.94957800	-0.34189700
C	1.87888300	-0.26293200	0.03214200
C	3.06343100	-1.17987100	-0.36568200
N	4.00814300	-0.47787000	-0.98553100
O	2.99943000	-2.40235700	-0.05321300
Br	-0.83515100	-0.37793900	2.18439800
O	5.11593500	-1.34131800	-1.38429500
C	5.96874000	-1.58331600	-0.28757200
C	-0.64861200	2.25470300	-0.28474900
C	0.36458000	2.55316900	0.64203000
C	0.95176000	3.81924700	0.66911600

C	0.53883800	4.81081200	-0.22201400
C	-0.47618100	4.52883800	-1.14392000
C	-1.06266900	3.26688100	-1.17529400
H	-3.46037500	-4.31207000	-0.60383400
H	-5.12039800	-2.89057800	-1.76360400
H	-4.73313100	-0.42239000	-1.99679000
H	-1.38643800	-3.31578300	0.35817700
H	0.65801100	-1.98899900	-0.00752700
H	0.47709000	-0.98592600	-1.43811000
H	2.00106600	0.71010500	-0.44729800
H	1.92215900	-0.12821900	1.12106400
H	6.82404800	-2.15490500	-0.67481200
H	6.33718000	-0.63733900	0.14687900
H	5.46648900	-2.17065400	0.49399900
H	0.69512300	1.80156300	1.34478800
H	1.74274700	4.02266600	1.38505800
H	1.00657300	5.79161100	-0.20479300
H	-0.80134900	5.29076000	-1.84745800
H	-1.84485700	3.03796500	-1.89024900

4aa-ts2

C	4.13410500	0.53362000	-0.15612600
C	3.97010200	0.62076400	-1.55953600
C	2.72363400	0.45410800	-2.14994400
C	1.63471500	0.18379000	-1.30912500
C	1.81476300	0.05316200	0.10163500
C	3.05834600	0.27432000	0.69020100
N	0.31777200	0.02754200	-1.68445200
C	-0.39467600	-0.21541000	-0.59692400
C	0.45065700	-0.15228300	0.64120400

C	0.04967700	-0.17554000	2.10836900
C	-1.02219700	0.87723000	2.46070300
C	-0.82924300	2.15145600	1.66723600
N	0.11140400	1.90530600	0.68837700
O	-1.37502900	3.22926400	1.89225500
Br	1.10662800	-2.60585000	0.47504900
O	0.40748700	2.80169200	-0.26830200
C	-0.69601000	3.51650000	-0.89559000
C	-1.83020700	-0.51099200	-0.68197000
C	-2.47227400	-1.33684700	0.25810200
C	-3.83678600	-1.60566600	0.14756700
C	-4.57884700	-1.05932400	-0.90238000
C	-3.94407400	-0.25578700	-1.85689300
C	-2.58217900	0.01347300	-1.75104000
H	5.12226700	0.68291100	0.26838200
H	4.83723800	0.82717100	-2.17934900
H	2.57816800	0.53638900	-3.22184400
H	3.19864000	0.21584100	1.76465600
H	-0.29057100	-1.16922500	2.39612800
H	0.95811100	0.01850100	2.68704000
H	-2.02682900	0.50368000	2.23108400
H	-1.00795200	1.11469100	3.52812700
H	-1.49562200	2.81427800	-1.14141800
H	-1.06211700	4.29599500	-0.22809000
H	-0.25694800	3.93074000	-1.80338100
H	-1.89643100	-1.80716600	1.04624300
H	-4.31688700	-2.25323800	0.87511200
H	-5.64153700	-1.26738600	-0.98485900
H	-4.51312500	0.16129600	-2.68248400
H	-2.07933800	0.62323300	-2.49409700

4aa-p3

C	4.13201100	-0.99689000	-0.24561600
C	3.84014400	-2.31950500	0.10938000
C	2.51585600	-2.74652000	0.27622700
C	1.50223400	-1.81234200	0.07779700
C	1.78904500	-0.48853400	-0.28416800
C	3.09986500	-0.06482300	-0.44843300
N	0.11376200	-2.03739000	0.21474400
C	-0.50694300	-0.92601100	-0.02956800
C	0.45493300	0.21979300	-0.45735500
C	0.18430300	0.71745400	-1.92126000
C	0.45236100	2.23493600	-1.89321700
C	0.29210700	2.63739800	-0.43081000
N	0.32376100	1.46783700	0.28674300
O	0.18880800	3.76030300	0.03865300
O	0.14632500	1.43143800	1.65842400
C	1.31067000	1.90133200	2.37468100
C	-1.97682500	-0.84187000	0.01029300
C	-2.66598600	0.38320200	0.08226700
C	-4.06149000	0.41028200	0.12266100
C	-4.79146400	-0.77933500	0.08954500
C	-4.11652200	-2.00414400	0.02158800
C	-2.72579400	-2.03653700	-0.01649800
H	5.16595400	-0.68718200	-0.36485300
H	4.65302200	-3.02374800	0.26060800
H	2.27753500	-3.76798900	0.55492700
H	3.33599700	0.96116900	-0.71971300
H	0.81001800	0.17657000	-2.63259000

H	-0.86172900	0.52775000	-2.17435800
H	-0.24026200	2.80981600	-2.51205800
H	1.46863600	2.49099400	-2.21324200
H	1.03526100	1.80729500	3.42654400
H	2.17734300	1.27104500	2.15547500
H	1.50803600	2.94748400	2.12900800
H	-2.12069600	1.31672800	0.14073300
H	-4.57524400	1.36473400	0.18864700
H	-5.87695700	-0.75469000	0.11954400
H	-4.67734500	-2.93403100	-0.00315700
H	-2.19432100	-2.98032900	-0.06762600

3aa-p2

C	-3.35558100	2.37834100	-0.96638000
C	-4.24090300	2.18053700	0.10094700
C	-3.97964100	1.21806900	1.08718800
C	-2.81543400	0.46491500	0.96944200
C	-1.93169700	0.65836500	-0.10378200
C	-2.18693000	1.60931700	-1.08061800
N	-2.35331200	-0.53692400	1.86092400
C	-1.21235700	-0.95980400	1.41670200
C	-0.76466400	-0.26264300	0.12122700
C	0.60241200	0.42412500	0.07156800
C	1.87098700	-0.39202500	0.32527900
C	3.10621100	0.48254800	0.00119400
N	3.99659400	0.41654800	0.98792500
O	3.12143400	1.10412900	-1.09839000
Br	-0.86246700	-1.71480200	-1.29523700
O	5.15092700	1.26359500	0.70356600

C	6.02937800	0.61283100	-0.18770600
H	-3.57656600	3.13339600	-1.71566100
H	-5.14000100	2.78737400	0.17000600
H	-4.65334000	1.06497600	1.92493500
H	-1.49961300	1.76120000	-1.90771800
H	0.71401100	0.89496300	-0.91143700
H	0.54678800	1.24475300	0.80302600
H	1.94546400	-0.74678400	1.35553200
H	1.88460200	-1.26122400	-0.34470500
H	6.91366500	1.25845100	-0.28451300
H	6.34392300	-0.36851400	0.20894300
H	5.57257100	0.47520300	-1.17770300
C	-0.43176100	-2.00450300	2.14679700
H	0.36338100	-1.53837500	2.74003500
H	-1.09901600	-2.54481900	2.82246600
H	0.04849400	-2.70211400	1.45558600

3aa-ts2

C	3.06538100	1.98501600	1.31527000
C	2.86522700	2.85022600	0.22516400
C	1.90677500	2.58583100	-0.75595600
C	1.12166000	1.42362200	-0.64462300
C	1.33948600	0.55011500	0.45405900
C	2.29490700	0.81810000	1.42481800
N	0.11621900	1.00752800	-1.48902900
C	-0.48196600	-0.03855100	-0.89318500
C	0.37065200	-0.56740600	0.30653100
C	-0.29898800	-1.10088300	1.58521400
C	-1.78771700	-1.43810000	1.44442400

C	-2.62609500	-0.22578800	1.01368200
N	-1.86533900	0.64311100	0.32113300
O	-3.82704700	-0.12196800	1.33013800
Br	1.46927700	-2.18212100	-0.49801400
O	-2.45847600	1.86389000	-0.02444600
C	-3.35157700	1.77271600	-1.13504900
H	3.81411500	2.21894900	2.06740200
H	3.46609400	3.75486800	0.14976300
H	1.74572900	3.26817900	-1.58583800
H	2.44903700	0.13696900	2.25949100
H	0.25488800	-1.96909800	1.95289700
H	-0.20384000	-0.31504000	2.34235400
H	-1.94725200	-2.26782500	0.74419400
H	-2.18731700	-1.76682200	2.40960300
H	-3.83422700	2.75400500	-1.19593900
H	-2.80279200	1.58457100	-2.06457000
H	-4.11162800	1.00291300	-0.96296000
C	-1.27647200	-0.94985900	-1.80508900
H	-1.99739300	-1.58184300	-1.28446200
H	-1.80570100	-0.32940900	-2.52968400
H	-0.58402000	-1.59626500	-2.35357900

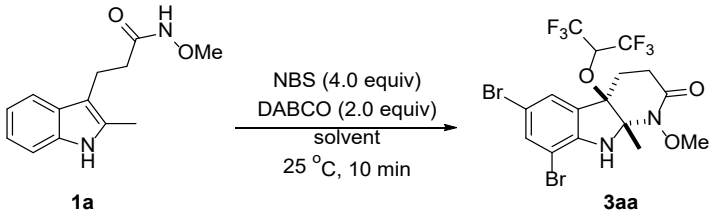
3aa-p3

C	-4.61080600	1.37194500	0.30301000
C	-5.01394100	0.11874700	-0.31255600
C	-4.11447900	-0.81555100	-0.73038300
C	-2.70066200	-0.55360500	-0.54602000
C	-2.29769500	0.73438800	0.06271300

C	-3.29449400	1.67842500	0.48927500
N	-1.71195400	-1.34675800	-0.84163300
C	-0.48573300	-0.56839300	-0.54624400
C	-0.93632200	0.70807200	0.14148600
C	0.05460400	1.50209600	0.89301900
C	0.58270400	0.56981300	2.01067500
C	0.86295700	-0.87615100	1.59620900
N	0.41861700	-1.27913800	0.35876400
O	1.49538300	-1.62663000	2.33627400
Br	3.29549600	1.28306100	-0.56308600
O	0.84092400	-2.51826200	-0.11623500
C	2.26984900	-2.53929500	-0.36475300
H	-5.38477400	2.06895300	0.61261200
H	-6.07833000	-0.06656900	-0.43881800
H	-4.42377400	-1.74889800	-1.19098700
H	-2.99635900	2.61958100	0.94416000
H	0.91590000	1.77022200	0.25900200
H	-0.37631500	2.41351600	1.32162100
H	1.53893200	0.94505400	2.38654500
H	-0.12289400	0.52773300	2.84960100
H	2.40744600	-3.30160000	-1.13743700
H	2.62293400	-1.56290600	-0.71036300
H	2.79747000	-2.81545000	0.55175100
C	0.19623400	-0.26458500	-1.90374400
H	1.11753900	0.30513100	-1.74433200
H	0.42131200	-1.21611800	-2.39046800
H	-0.49181100	0.29919200	-2.54122200

Optimization of the Reaction Conditions (fused-indoline)

Table S1 Screening of solvent using NBS as catalyst[a,b]



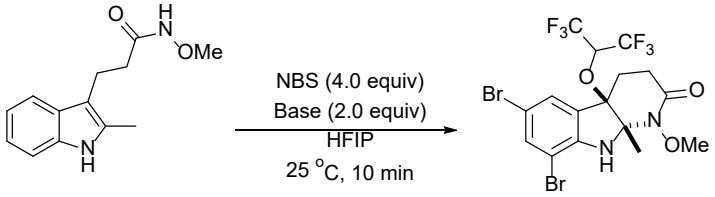
1a **3aa**

Entry	Solvent	Yield (%)
1	HFIP	62
2	DMF	N.R.
3	DMSO	N.R.
4	MeCN	14
5	EA	18
6	DCE	14
7	H_2O	Messy
8	THF	N.R.

[a]Reaction conditions: **1a** (0.1 mmol), DABCO (2.0 equiv), NBS (4.0 equiv), air, room temperature, 10 min.

[b]Yields are based on **1a**, determined by LC-MS.

Table S2 Screening of base using HFIP as solvent[a,b]



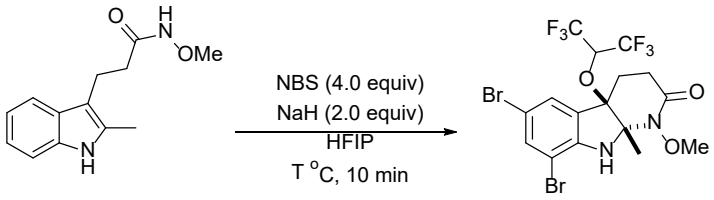
1a **3aa**

Entry	Base	Yield
1	DABCO	62[c]
2	NaH	72[c]
3	K_2CO_3	42

4	Et_3N	10
5	DMAP	42
6	DBU	N.R.
7	t-BuOK	45
8	NaOAc	N.R.
9	NaOH	N.R.

[a]Reaction conditions: **1a** (0.1 mmol), NBS (4.0 equiv), HFIP (1 mL), air, room temperature, 10 min. [b]Yields are based on **1a**, determined by LC-MS. [c]Isolated yield.

Table S3 Screening of temperature[a,b]



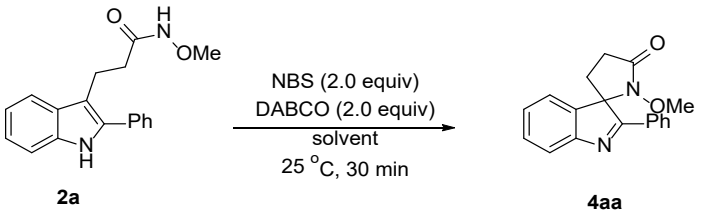
1a **3aa**

Entry	T °C	Yield
1	0	53
2	25	72[c]
3	40	43
4	60	40

[a]Reaction conditions: **1a** (0.1 mmol), NBS (4.0 equiv), HFIP (1 mL), air, 10 min. [b]Yields are based on **1a**, determined by LC-MS. [c]Isolated yield.

Optimization of the Reaction Conditions (Spiro-indolines)

Table S4 Screening of solvent using NBS as catalyst[a,b]



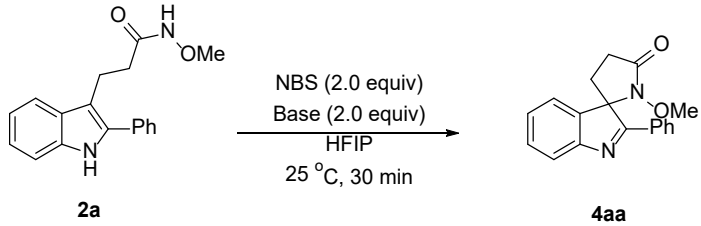
2a **4aa**

Entry	Solvent	Yield (%)
1	HFIP	87[c]
2	DMF	21
3	DMSO	11
4	MeCN	45
5	EA	42
6	DCE	50
7	H_2O	N.R.
8	THF	35

[a]Reaction conditions: **2a** (0.1 mmol), DABCO (2.0 equiv), NBS (2.0 equiv), air, room temperature, 30 min.

[b]Yields are based on **2a**, determined by LC-MS. [c]Isolated yield.

Table S5 Screening of base using HFIP as solvent[a,b]



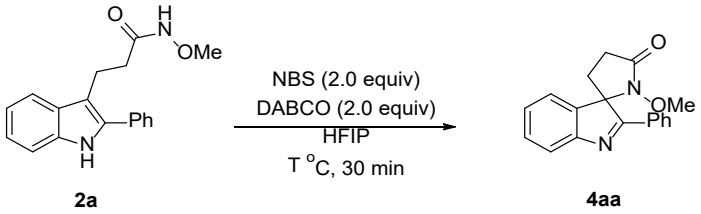
2a **4aa**

Entry	Base	Yield
1	DABCO	87[c]
2	NaH	77[c]
3	K_2CO_3	71
4	Et_3N	45
5	DMAP	42

6	DBU	N.R.
7	t-BuOK	45
8	NaOAc	N.R.
9	NaOH	N.R.

[a]Reaction conditions: **2a** (0.1 mmol), NBS (2.0 equiv), HFIP (1 mL), air, room temperature, 30 min. [b]Yields are based on **2a**, determined by LC-MS. [c]Isolated yield.

Table S6 Screening of temperature[a,b]

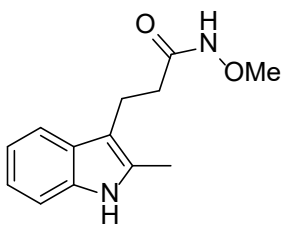


2a **4aa**

Entry	T ºC	Yield
1	0	76
2	25	87[c]
3	40	48
4	60	45

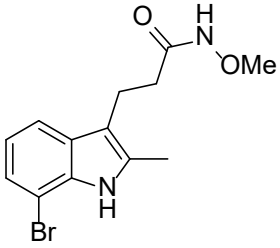
[a]Reaction conditions: **2a** (0.1 mmol), NBS (2.0 equiv), HFIP (1 mL), air, 30 min. [b]Yields are based on **2a**, determined by LC-MS. [c]Isolated yield.

Spectral Characterization Data for the Reaction Substrates

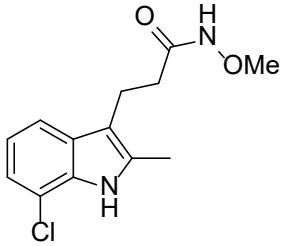


1a. **(Procedure A)** white solid. Analytical data for **1a**: m.p. = 129-130 ºC. **^{1}H NMR (300 MHz, DMSO)** δ 10.93 (s, 1H), 10.66 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.7 Hz, 1H), 6.97 – 6.94 (m, 2H), 3.51 (s, 3H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.32

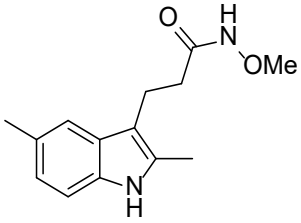
(s, 3H), 2.22 (t, J = 7.6 Hz, 2H).**^{13}C NMR (75 MHz, DMSO)** δ 169.4, 135.7, 132.2, 128.5, 120.4, 118.6, 117.9, 110.8, 109.5, 63.5, 34.3, 20.3, 11.7. **IR (film)**: 3298, 2938, 1635, 1459, 1070, 743, 697, 421 cm^{-1}. **HRMS (ESI)** calcd for $C_{13}H_{17}N_2O_2^+$ $[M+H]^+$: 255.1104, Found: 255.1097.



1b. **(Procedure A)** yellow solid. Analytical data for **1b**: m.p. = 154-155 °C. **^{1}H NMR (300 MHz, DMSO)** δ 10.90 (d, J = 9.7 Hz, 2H), 7.43 (d, J = 7.8 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 6.88 (t, J = 7.7 Hz, 1H), 3.51 (s, 3H), 2.89 (t, J = 7.4 Hz, 2H), 2.37 (s, 3H), 2.21 (t, J = 7.4 Hz, 2H). **^{13}C NMR (75 MHz, DMSO)** δ 169.1, 134.2, 134.0, 130.2, 122.9, 120.0, 117.4, 111.0, 103.8, 63.5, 34.1, 20.3, 11.6. **IR (film)**: 3364, 3175, 2970, 1643, 1077, 574 cm^{-1}. **HRMS (ESI)** calcd for $C_{13}H_{15}BrN_2NaO_2^+$ $[M+Na]^+$: 333.0209, Found: 333.0224.

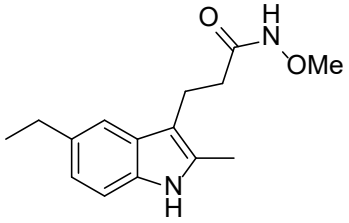


1c. **(Procedure A)** white solid. Analytical data for **1c**: m.p. = 147-148 °C **^{1}H NMR (300 MHz, DMSO)** δ 11.02 (s, 1H), 10.93 (s, 1H), 7.41 (d, J = 7.7 Hz, 1H), 7.06 (d, J = 7.5 Hz, 1H), 6.94 (t, J = 7.7 Hz, 1H), 3.52 (s, 3H), 2.91 (t, J = 7.4 Hz, 2H), 2.37 (s, 3H), 2.22 (t, J = 7.4 Hz, 2H). **^{13}C NMR (75 MHz, DMSO)** δ 169.2, 134.1, 132.4, 130.4, 119.9, 119.6, 117.0, 115.4, 110.9, 63.5, 34.1, 20.2, 11.6. **IR (film)**: 3356, 2968, 1642, 1079, 935, 727, 576 cm^{-1}. **HRMS (ESI)** calcd for $C_{13}H_{15}ClN_2NaO_2^+$ $[M+Na]^+$: 289.0714, Found: 289.0718.

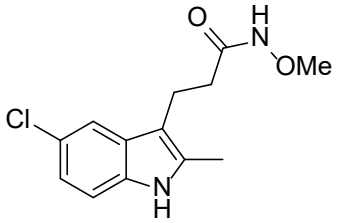


1d. **(Procedure A)** white solid. Analytical data for **1d**: m.p. = 130-131 °C. **^{1}H NMR (300 MHz, DMSO)** δ 10.92 (s, 1H), 10.51 (s, 1H), 7.19 (s, 1H), 7.11 (d, J = 8.1 Hz, 1H), 6.79 – 6.73 (m, 1H), 3.52 (s, 3H), 2.86 (t, J = 7.5 Hz, 2H), 2.35 (s, 3H), 2.29 (s, 3H), 2.20 (t, J = 7.5 Hz, 2H). **^{13}C NMR (75 MHz, DMSO)** δ 169.4, 134.0, 132.2, 128.7, 126.8, 121.9, 117.6, 110.5, 109.0, 63.5, 34.3,

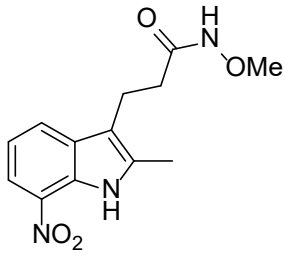
21.8, 20.3, 11.7. **IR (film)**: 3384, 3183, 2929, 1657, 1303, 793, 505 cm^{-1}. **HRMS (ESI)** calcd for $C_{14}H_{18}N_2NaO_2^+$ $[M+Na]^+$: 269.1260, Found: 269.1267.



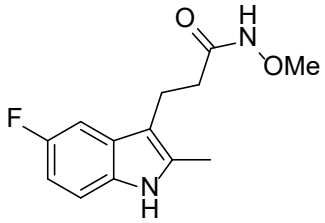
1e. **(Procedure A)** yellow solid. Analytical data for **1e**: m.p. = 141-142 °C. **^{1}H NMR (300 MHz, DMSO)** δ 10.95 (s, 1H), 10.54 (s, 1H), 7.24 (s, 1H), 7.15 (d, *J* = 8.2 Hz, 1H), 6.85 – 6.83 (m, 1H), 3.55 (s, 3H), 2.89 (t, *J* = 7.5 Hz, 2H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.32 (s, 3H), 2.22 (t, *J* = 7.6 Hz, 2H), 1.24 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (75 MHz, DMSO)** δ 169.4, 134.20, 133.7, 132.2, 128.6, 120.7, 116.4, 110.6, 109.2, 63.5, 34.3, 29.1, 20.3, 17.2, 11.7. **IR (film)**: 3380, 2916, 2323, 1654, 803, 516 cm^{-1}. **HRMS (ESI)** calcd for $C_{15}H_{20}N_2NaO_2^+$ $[M+Na]^+$: 283.1417, Found: 283.1414.



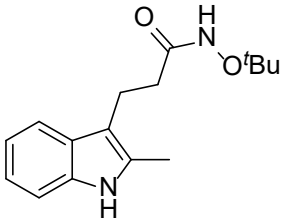
1f. **(Procedure A)** white solid. Analytical data for **1f**: m.p. = 144-145 °C. **^{1}H NMR (300 MHz, DMSO)** δ 10.92 (d, *J* = 4.8 Hz, 2H), 7.46 (d, *J* = 2.1 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 6.97 – 6.93 (m, 1H), 3.51 (s, 3H), 2.88 (t, *J* = 7.4 Hz, 2H), 2.33 (s, 3H), 2.20 (t, *J* = 7.4 Hz, 2H). **^{13}C NMR (75 MHz, DMSO)** δ 169.2, 134.4, 134.1, 129.7, 123.3, 120.1, 117.3, 112.2, 109.6, 63.5, 34.1, 20.1, 11.7. **IR (film)**: 3365, 3187, 2369, 1647, 1507, 785, 601 cm^{-1}. **HRMS (ESI)** calcd for $C_{13}H_{15}ClN_2NaO_2^+$ $[M+Na]^+$: 289.0714, Found: 289.0714.



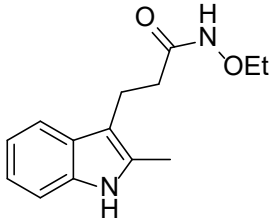
1g. **(Procedure A)** White solid. Analytical data for **1g**: m.p. = 77-78 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.91 (s, 1H), 10.50 (s, 1H), 7.11 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 2.4 Hz, 1H), 6.62 – 6.60 (m, 1H), 3.75 (s, 3H), 3.52 (s, 3H), 2.84 (t, *J* = 7.4 Hz, 2H), 2.29 (s, 2H), 2.18 (t, *J* = 7.5 Hz, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.3, 153.4, 133.0, 130.8, 128.8, 111.3, 109.8, 109.4, 100.5, 63.5, 34.1, 20.2, 11.8. **IR (film)**: 3297, 2950, 1619, 1215, 1026, 798, 623 cm^{-1}. **HRMS (ESI)** calcd for $C_{13}H_{15}N_3NaO_4^+$ $[M+Na]^+$: 300.0955, Found: 300.0950.



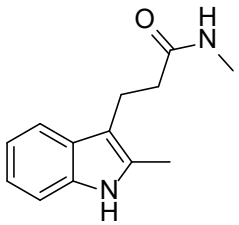
1h. **(Procedure A)** White solid. Analytical data for **1h**: m.p. = 137-138 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.92 (s, 1H), 10.80 (s, 1H), 7.23 – 7.16 (m, 2H), 6.83 – 6.78 (m, 1H), 3.51 (s, 3H), 2.86 (t, *J* = 7.4 Hz, 2H), 2.33 (d, *J* = 4.3 Hz, 3H), 2.20 (t, *J* = 7.4 Hz, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.3, 158.3, 156.0, 134.6, 132.2, 128.9, 128.8, 111.5, 111.4, 110.0, 109.9, 108.1, 107.9, 103.0, 102.7, 63.5, 34.0, 20.2, 11.7. **^{19}F NMR (376 MHz, DMSO)** δ -126.01. **IR (film)**: 3290, 1625, 1487, 1071, 800, 624, 482 cm^{-1}. **HRMS (ESI)** calcd for $C_{13}H_{15}FN_2NaO_2^+$ $[M+Na]^+$: 273.1010, Found: 273.1012.



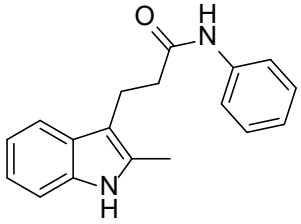
1i. **(Procedure A)** White solid. Analytical data for **1i**: m.p. = 84-85 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.92 (s, 1H), 10.80 (s, 1H), 7.21 – 7.18 (m, 2H), 6.82 – 6.78 (m, 1H), 3.51 (s, 3H), 2.86 (t, *J* = 7.4 Hz, 2H), 2.33 (d, *J* = 4.3 Hz, 3H), 2.20 (t, *J* = 7.4 Hz, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.3, 158.3, 156.0, 134.6, 132.2, 128.9, 128.8, 111.5, 111.4, 110.0, 109.9, 108.1, 107.9, 103.0, 102.7, 63.5, 34.0, 20.2, 11.7. **IR (film)**: 3388, 3206, 2976, 1650, 1461, 1366, 1182, 1066, 739 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{22}N_2NaO_2^+$ $[M+Na]^+$: 297.1573, Found: 297.1584.



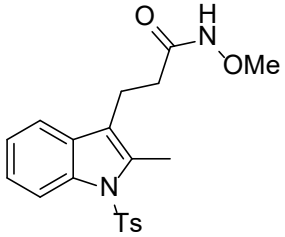
1j. **(Procedure A)** White solid. Analytical data for **1j**: m.p. = 134-135 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.78 (s, 1H), 10.67 (s, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 6.97 – 6.95 (m, 2H), 3.72 (q, *J* = 7.0 Hz, 2H), 2.89 (t, *J* = 7.5 Hz, 2H), 2.32 (s, 3H), 2.22 (t, *J* = 7.5 Hz, 2H), 1.06 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 169.3, 135.7, 132.2, 128.5, 120.3, 118.5, 117.9, 110.8, 109.5, 70.8, 34.2, 20.3, 13.8, 11.7. **IR (film)**: 3305, 3138, 2972, 1630, 1453, 1031, 736, 667 cm^{-1}. **HRMS (ESI)** calcd for $C_{14}H_{18}N_2NaO_2^+$ $[M+Na]^+$: 269.1260, Found: 269.1266.



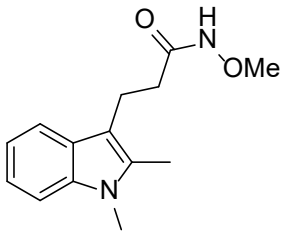
1k. **(Procedure A)** White solid. Analytical data for **1k**: m.p. = 134-135 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.71 (s, 1H), 7.18 (s, 1H), 7.45 (d, *J* = 7.1 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.92 (t, *J* = 7.6 Hz, 1H), 3.10 – 2.96 (m, 2H), 2.46 – 2.40 (m, 2H) 2.66 (s, 3H), 2.31 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 171.8, 136.8, 132.1, 129.1, 123.4, 119.8, 118.6, 112.0, 108.7, 36.7, 26.2, 22.5, 12.1. **IR (film)**: 3310, 3130, 1651, 1453, 1038, 740, 661 cm^{-1}. **HRMS (ESI)** calcd for $C_{13}H_{16}N_2NaO^+$ $[M+Na]^+$: 239.1155, Found: 239.1150.



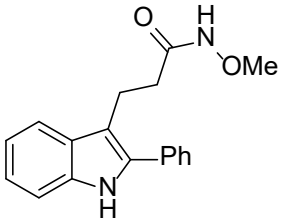
1l. **(Procedure A)** White solid. Analytical data for **1l**: m.p. = 134-135 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.69 (s, 1H), 9.86 (s, 1H), 7.61 (d, *J* = 7.1 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.33 – 7.23 (m, 3H), 7.05 – 6.92 (m, 3H), 3.06 – 2.93 (m, 2H), 2.66 – 2.55 (m, 2H), 2.36 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 171.5, 139.8, 135.7, 132.1, 129.1, 128.6, 123.4, 120.4, 119.6, 118.5, 118.0, 110.8, 109.7, 38.3, 20.4, 11.7. **IR (film)**: 3310, 3130, 1651, 1453, 1038, 740, 661 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{18}N_2NaO^+$ $[M+Na]^+$: 301.1311, Found: 301.1311.



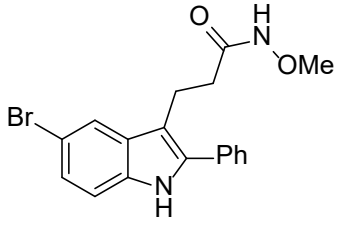
1n. **(Procedure A)** Yellow liquid. Analytical data for **1n**: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.18 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.28 – 7.22 (m, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 3.50 (s, 3H), 2.95 (m, 2H), 2.52 (s, 3H), 2.32 (s, 3H), 2.31 – 2.16 (m, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 168.5, 145.5, 135.9, 135.7, 133.4, 130.6, 130.2, 126.6, 124.4, 123.8, 119.5, 119.2, 114.4, 63.4, 32.8, 21.4, 12.9. **HRMS (ESI)** calcd for $C_{20}H_{22}N_2NaO_4S^+$ $[M+Na]^+$: 409.1192, Found: 409.1192.



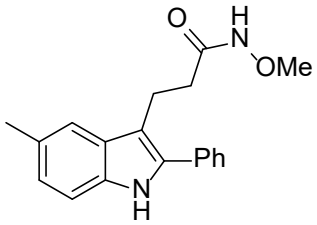
1o. **(Procedure A)** White solid. Analytical data for **1o**: m.p. = 147-148 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.90 (s, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.04 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 6.96 (td, *J* = 7.4, 6.9, 1.1 Hz, 1H), 3.60 (s, 3H), 3.51 (s, 3H), 2.94 – 2.86 (m, 2H), 2.31 (s, 3H), 2.18 (t, *J* = 7.5 Hz, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.2, 136.7, 133.7, 127.5, 120.5, 118.7, 118.0, 109.5, 109.3, 63.5, 34.4, 29.7, 20.5, 10.3. **IR (film)**: 3144, 2936, 1641, 1471, 1331, 1076, 739, 559 cm^{-1}. **HRMS (ESI)** calcd for $C_{14}H_{18}N_2NaO_2^+$ $[M+Na]^+$: 269.1260, Found: 269.1259.



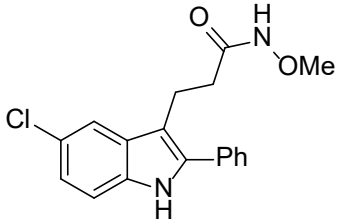
2a. **(Procedure B)** White solid. Analytical data for **2a**: m.p. = 107-108 °C. **^{1}H NMR (300 MHz, DMSO)** δ 11.20 (s, 1H), 11.08 (s, 1H), 7.68 (d, *J* = 7.1 Hz, 2H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 2H), 7.17 – 7.09 (m, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 3.57 (s, 3H), 3.21 – 3.04 (m, 2H), 2.46 – 2.29 (m, 2H). **^{13}C NMR (75 MHz, DMSO)** δ 169.2, 136.5, 134.6, 133.3, 129.2, 128.9, 128.3, 127.8, 122.1, 119.2, 111.7, 111.1, 63.6, 34.4, 21.1. IR (film): 3296, 2925, 2325, 1624, 736 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{18}N_2NaO_2^+$ $[M+Na]^+$: 317.1260, Found: 317.1247.



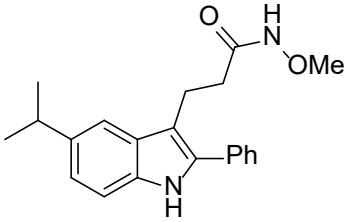
2b. **(Procedure B)** White solid. Analytical data for **2b**: m.p. = 140-141 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.43 (s, 1H), 11.06 (s, 1H), 7.78 (s, 1H), 7.65 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.24 – 7.20 (m, 1H), 3.55 (s, 3H), 3.11 – 3.00 (m, 2H), 2.40 – 2.22 (m, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.1, 136.2, 135.1, 132.7, 130.7, 129.3, 128.4, 128.3, 124.5, 121.5, 113.6, 111.8, 110.9, 63.6, 34.3, 20.8. **IR (film)**: 3361, 3215, 1636, 1456, 699 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{17}BrN_2NaO_2^+$ $[M+Na]^+$: 395.0366, Found: 395.0362.



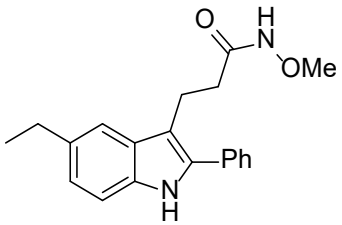
2c. **(Procedure B)** White solid. Analytical data for **2c**: m.p. = 125-126 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.07 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 6.9 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.42 – 7.35 (m, 2H), 7.27 (d, *J* = 8.1 Hz, 1H), 6.97 – 6.94 (m, 1H), 3.58 (s, 3H), 3.14 – 3.03 (m, 2H), 2.42 (s, 3H), 2.40 – 2.28 (m, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.2, 134.9, 134.7, 133.4, 129.2, 129.1, 128.2, 127.7, 127.6, 123.7, 118.7, 111.4, 110.6, 63.6, 34.3, 21.8, 21.1. **IR (film)**: 3367, 3217, 1641, 1312, 699, 609 cm^{-1}. **HRMS (ESI)** calcd for $C_{19}H_{20}N_2NaO_2^+$ $[M+Na]^+$: 331.1417, Found: 331.1404.



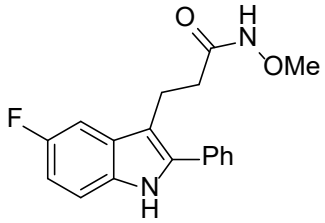
2d. **(Procedure B)** White solid. Analytical data for **2d**: m.p. = 150-151 °C. **^{1}H NMR (300 MHz, DMSO)** δ 11.42 (s, 1H), 11.06 (s, 1H), 7.66 (d, *J* = 6.7 Hz, 3H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.39 (m, 2H), 7.13 – 7.10 (m, 1H), 3.55 (s, 3H), 3.07 (t, *J* = 7.8 Hz, 2H), 2.33 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR (75 MHz, DMSO)** δ 169.1, 136.4, 134.9, 132.8, 130.0, 129.3, 128.4, 128.2, 123.9, 121.9, 118.5, 113.1, 111.0, 63.6, 34.3, 20.8. **IR (film)**: 3358, 3209, 1636, 1072, 767, 699 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{18}ClN_2O_2^+$ $[M+H]^+$: 329.1052, Found: 329.1068.



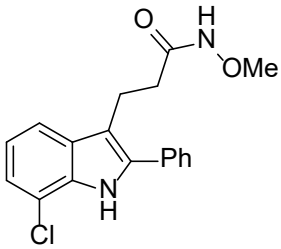
2e. **(Procedure B)** Yellow solid. Analytical data for **2e**: m.p. = 97-98 °C. **^{1}H NMR (300 MHz, DMSO)** δ 11.08 (d, *J* = 9.7 Hz, 2H), 7.66 (d, *J* = 7.0 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.41 (d, *J* = 15.3 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.05 – 7.03 (m, 1H), 3.59 (s, 3H), 3.14 – 3.08 (m, 2H), 2.98 (q, *J* = 6.9 Hz, 1H), 2.37 (t, *J* = 8.0 Hz, 2H), 1.30 (s, 3H), 1.28 (s, 3H) **^{13}C NMR (75 MHz, DMSO)** δ 169.2, 139.3, 135.2, 134.7, 133.5, 129.2, 128.9, 128.2, 127.7, 121.0, 116.0, 111.5, 111.0, 63.6, 34.4, 34.3, 25.1, 21.0, 14.4. **IR (film)**: 3196, 2955, 1645, 1448, 1076, 765, 648 cm^{-1}. **HRMS (ESI)** calcd for $C_{21}H_{24}N_2NaO_2^+$ $[M+Na]^+$: 359.1730, Found: 359.1726.



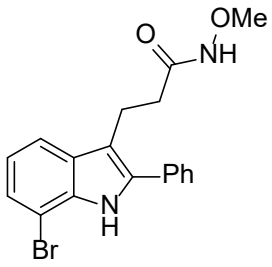
2f. **(Procedure B)** Light yellow solid. Analytical data for **2f**: m.p. = 118-119 °C. **^{1}H NMR (300 MHz, DMSO)** δ 11.07 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 6.9 Hz, 2H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.35 (m, 2H), 7.30 (d, *J* = 8.3 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 3.58 (s, 3H), 3.11 (t, *J* = 8.0 Hz, 2H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.37 (t, *J* = 8.0 Hz, 2H), 1.25 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (75 MHz, DMSO)** δ 169.3, 135.1, 134.7, 134.5, 133.5, 129.2, 129.1, 128.2, 127.7, 122.6, 117.6, 111.5, 110.8, 63.6, 34.4, 29.1, 21.1, 17.2. **IR (film)**: 3190, 1640, 1447, 1076, 764, 567 cm^{-1}. **HRMS (ESI)** calcd for $C_{20}H_{23}N_2O_2^+$ $[M+H]^+$: 323.1754, Found: 323.1753.



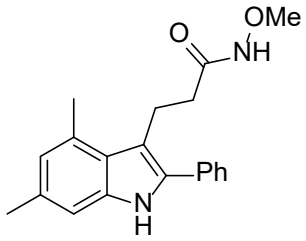
2g. **(Procedure B)** White solid. Analytical data for **2g**: m.p. = 113-114 °C. **^{1}H NMR (300 MHz, DMSO)** δ 11.31 (s, 1H), 11.06 (s, 1H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.41 – 7.38 (m, 3H), 6.98 – 6.95 (m, 1H), 3.56 (s, 3H), 3.08 (t, *J* = 7.8 Hz, 2H), 2.35 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR (75 MHz, DMSO)** δ 169.1, 158.9, 155.8, 136.7, 133.1, 133.0, 129.3, 129.2, 129.1, 128.4, 128.1, 112.6, 112.5, 111.4, 111.3, 110.3, 109.9, 104.1, 103.8, 63.6, 34.2, 21.0. **^{19}F NMR (376 MHz, DMSO)** δ -124.88. **IR (film)**: 3282, 2935, 1622, 1174, 767, 698, 563 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{18}FN_2O_2^+$ $[M+H]^+$: 313.1347, Found: 313.1346.



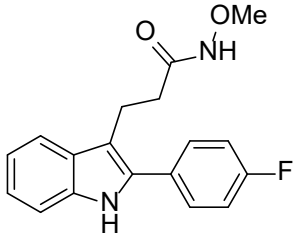
2h. **(Procedure B)** Yellow solid. Analytical data for **2h**: m.p. = 143-144 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.41 (s, 1H), 11.05 (s, 1H), 7.68 (d, *J* = 7.1 Hz, 2H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.19 (d, *J* = 7.3 Hz, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 3.55 (s, 3H), 3.11 – 3.01 (m, 2H), 2.43 – 2.24 (m, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.0, 136.7, 133.4, 132.5, 130.7, 129.3, 129.0, 128.3, 121.6, 120.3, 118.2, 116.2, 112.4, 63.6, 34.2, 20.9. **IR (film)**: 3284, 1629, 1071, 766, 734, 629 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{18}ClN_2O_2^+$ $[M+H]^+$: 329.1052, Found: 329.1049.



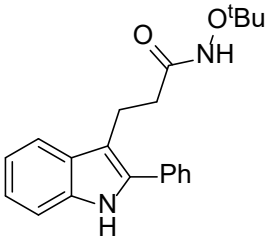
2i. **(Procedure B)** White solid. Analytical data for **2i**: m.p. = 121-122 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.22 (s, 1H), 11.00 (s, 1H), 7.63 (d, *J* = 6.9 Hz, 2H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.44 – 7.39 (m, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 3.51 (s, 3H), 3.03 – 2.98 (m, 2H), 2.31 – 2.27 (m, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.0, 136.7, 134.9, 132.4, 130.4, 129.4, 128.9, 124.7, 120.7, 118.7, 113.6, 112.5, 104.4, 63.6, 34.2, 20.9. **IR (film)**: 3285, 3200, 1650, 1630, 1067, 765, 743 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{17}BrN_2NaO_2^+$ $[M+Na]^+$: 395.0366, Found: 395.0362.



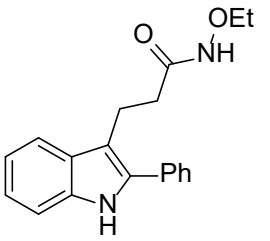
2j. **(Procedure B)** White solid. Analytical data for **2j**: m.p.= 67-68 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.04 (s, 1H), 10.95 (s, 1H), 7.55 (d, *J* = 6.8 Hz, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 6.95 (s, 1H), 6.56 (s, 1H), 3.55 (s, 3H), 3.13 – 3.03 (m, 2H), 2.60 (s, 3H), 2.31 (s, 3H), 2.29 – 2.22 (m, 2H). **^{13}C NMR (100MHz, DMSO)** δ 168.8, 137.4, 134.2, 133.6, 130.9, 129.7, 129.1, 128.6, 127.6, 124.9, 123.1, 111.8, 109.5, 63.7, 36.5, 21.7, 20.3, 14.6. **IR (film)**: 2933, 1646, 1443, 1072, 762, 697 cm^{-1}. **HRMS (ESI)** calcd for $C_{20}H_{22}N_2NaO_2^+$ $[M+Na]^+$: 345.1573, Found: 345.1571.



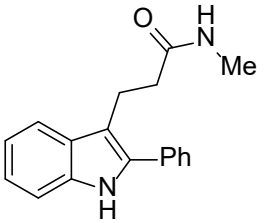
2k. **(Procedure B)** White solid. Analytical data for **2k**: m.p. = 111-112 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.17 (s, 1H), 10.99 (s, 1H), 7.66 – 7.63 (m, 2H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.36 – 7.30 (m, 3H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 3.51 (s, 3H), 3.03 – 3.00 (m, 2H), 2.38 – 2.22 (m, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.1, 163.2, 160.8, 136.4, 133.7, 130.4, 130.32, 129.8, 129.8, 128.8, 122.1, 119.2, 116.2, 116.0, 111.6, 111.0, 63.6, 34.2, 20.9. **^{19}F NMR (376 MHz, DMSO)** δ -114.53. **IR (film)**: 3197, 1639, 1501, 1457, 1215, 841, 746, 563 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{18}FN_2O_2^+$ $[M+H]^+$: 313.1347, Found: 313.1336.



2l. **(Procedure B)** White solid. Analytical data for **2l**: m.p. = 69-70 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.34 (s, 1H), 7.74 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 7.3 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.32 (q, *J* = 7.7 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 3.23 (t, *J* = 7.7 Hz, 2H), 2.45 (t, *J* = 7.7 Hz, 2H), 1.11 (d, *J* = 28.4 Hz, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.6, 136.0, 132.9, 129.0, 128.0, 127.8, 122.3, 120.9, 119.7, 119.0, 116.0, 112.4, 111.1, 81.9, 34.2, 31.6, 27.0, 26.1. **IR (film)**: 2973, 1647, 1452, 1366, 1188, 741, 697 cm^{-1}. **HRMS (ESI)** calcd for $C_{21}H_{24}N_2NaO_2^+$ $[M+Na]^+$: 359.1730, Found: 359.1739.

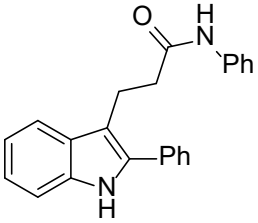


2m. **(Procedure B)** White solid. Analytical data for **2m**: m.p. = 169-170 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.17 (s, 1H), 10.91 (s, 1H), 7.66 – 7.60 (m, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.34 (m, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 3.75 (q, *J* = 7.0 Hz, 2H), 3.13 – 3.02 (m, 2H), 2.44 – 2.24 (m, 2H), 1.08 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 169.2, 136.5, 134.6, 133.3, 129.2, 128.8, 128.28, 127.8, 122.0, 119.1, 111.6, 111.1, 70.9, 34.3, 21.0, 13.9.**IR (film)**: 3195, 2932, 1631, 1450, 1308, 1967, 734, 570 cm^{-1}. **HRMS (ESI)** calcd for $C_{19}H_{20}N_2NaO_2^+$ $[M+Na]^+$: 331.1417, Found: 331.1418.

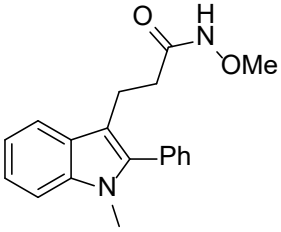


2n. **(Procedure A)** White solid. Analytical data for **2n**: m.p. = 144-145 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.22 (s, 1H), 7.90 (s, 1H), 7.71 (d, *J* = 7.7 Hz, 2H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 8.8 Hz, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 3.16 (t, *J* = 7.9 Hz, 2H), 2.53 (t, *J* = 8.2 Hz, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 172.8, 136.6, 134.5, 133.5, 129.2, 129.0, 128.3, 127.8, 122.1, 119.3, 119.2, 111.7, 111.6, 37.4, 26.0, 21.5. **IR (film)**: 3255, 3057, 2929, 1705,

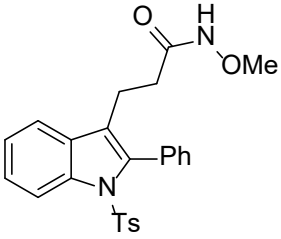
1615, 1450, 738, 433 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{18}N_2NaO^+$ $[M+Na]^+$: 301.1311, Found: 301.1320.



2o. **(Procedure A)** White solid. Analytical data for **2o**: m.p. = 151-152 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.23 (s, 1H), 10.00 (s, 1H), 7.76 – 7.69 (m, 3H), 7.67 (d, *J* = 7.4 Hz, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.45 – 7.37 (m, 2H), 7.35 – 7.28 (m, 2H), 7.15 (t, *J* = 7.0 Hz, 1H), 7.05 (q, *J* = 7.0 Hz, 2H), 3.32 – 3.20 (m, 2H), 2.84 – 2.71 (m, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 171.4, 139.8, 136.6, 134.7, 133.5, 129.3, 129.2, 129.0, 128.4, 127.8, 123.5, 122.1, 119.7, 119.4, 119.2, 111.7, 111.4, 38.3, 21.2. **IR (film)**: 3417, 3251, 1649, 1599, 1548, 1441, 1345, 738, 686 cm^{-1}. **HRMS (ESI)** calcd for $C_{23}H_{20}N_2NaO^+$ $[M+Na]^+$: 363.1468, Found: 363.1472.

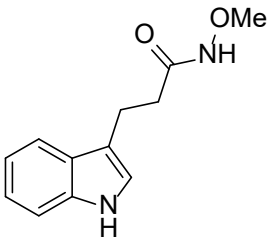


2p. **(Procedure A)** White solid. Analytical data for **2p**: m.p. = 130-131 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (d, *J* = 7.9 Hz, 1H), 7.52 – 7.41 (m, 3H), 7.38 – 7.33 (m, 3H), 7.27 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 3.57 (s, 6H), 3.12 – 3.01 (m, 2H), 2.40 – 2.35 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 138.3, 137.2, 131.6, 130.6, 128.6, 128.5, 128.3, 127.2, 121.9, 119.5, 118.8, 109.5, 64.4, 34.5, 30.8, 20.6. **IR (film)**: 3130, 2928, 1647, 1467, 1357, 979, 746, 702, 592 cm^{-1}. **HRMS (ESI)** calcd for $C_{19}H_{20}N_2NaO_2^+$ $[M+Na]^+$: 331.1417, Found: 331.1424.

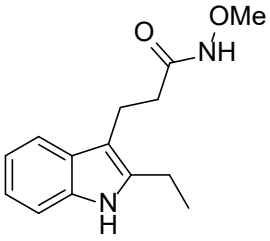


2q. **(Procedure A)** White solid. Analytical data for **2q**: m.p. = 161-162 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.3 Hz, 1H), 7.99 (s, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.45 – 7.34 (m, 4H), 7.32 – 7.28 (m, 4H), 7.07 (d, *J* = 8.2 Hz, 2H), 3.50 (s, 3H), 2.87 – 2.77 (m, 2H), 2.30 (s, 3H), 2.15 - 2.10 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 144.6, 137.2, 137.1, 135.3, 131.2, 131.0, 130.1, 129.34, 128.83, 127., 126.8, 125.1, 124.0, 121.9, 119.2, 116.0, 64.3, 33.0, 21.6, 20.0. **IR (film)**: 3342, 1703, 1442,

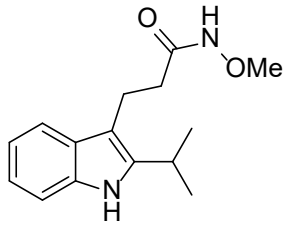
1357, 1172, 753, 664, 542 cm^{-1}. **HRMS (ESI)** calcd for $C_{25}H_{25}N_2O_4S^+$ $[M+H]^+$: 449.1530, Found: 449.1531.



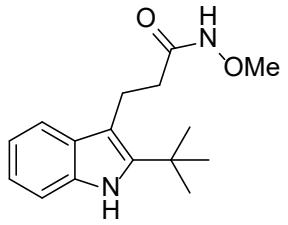
5. **(Procedure A)** White solid. Analytical data for **5**: m.p. = 129-130 °C. **^{1}H NMR (400 MHz, DMSO)** δ 10.94 (s, 1H), 10.73 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.03 (dd, *J* = 15.1, 8.1 Hz, 2H), 6.93 (t, *J* = 7.5 Hz, 1H), 3.50 (s, 3H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.27 (t, *J* = 7.6 Hz, 2H). **^{13}C NMR (100 MHz, DMSO)** δ 169.3, 136.7, 127.4, 122.7, 121.4, 118.8, 118.7, 113.9, 111.8, 63.6, 33.8, 21.1. **IR (film)**: 3403, 3110, 2928, 2888, 1651, 1088, 1056, 1002, 740, 492 cm^{-1}. **HRMS (ESI)** calcd for $C_{15}H_{20}N_2NaO_2^+$ $[M+Na]^+$: 283.1417, Found: 283.1424.



6. **(Procedure B)** White solid. Analytical data for **6**: m.p. = 84-54 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.42 (s, 1H), 8.09 (s, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.12 (dt, *J* = 19.9, 6.8 Hz, 2H), 3.57 (s, 3H), 3.08 (t, *J* = 7.4 Hz, 2H), 2.75 (d, *J* = 7.6 Hz, 2H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.26 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.9, 137.8, 135.4, 128.1, 121.1, 119.2, 117.9, 110.6, 108.8, 64.1, 34.3, 20.1, 19.2, 14.3. **IR (film)**: 3387, 2975, 1709, 1654, 1461, 749 cm^{-1}. **HRMS (ESI)** calcd for $C_{14}H_{18}N_2NaO_2^+$ $[M+Na]^+$: 269.1260, Found: 269.1257.

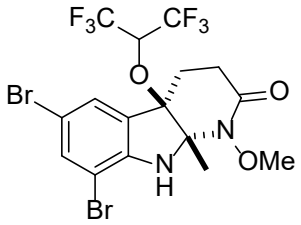


7. **(Procedure B)** White solid. Analytical data for **7**: m.p. = 65-66 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.23 (s, 1H), 8.03 (s, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.18 – 7.14 (m, 1H), 7.12 – 7.09 (m, 1H), 3.61 (s, 3H), 3.34 – 3.27 (m, 1H), 3.11 (t, *J* = 7.4 Hz, 2H), 2.43 (d, *J* = 7.6 Hz, 2H), 1.32 (d, *J* = 7.1 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.90, 141.61, 135.28, 128.01, 121.14, 119.26, 117.98, 110.66, 107.93, 64.29, 34.41, 25.34, 22.81, 20.00. **IR (film)**: 3321, 2957, 1645, 459, 1073, 742 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{23}N_2O_2^+$ $[M+H]^+$: 297.1573, Found: 297.1576.

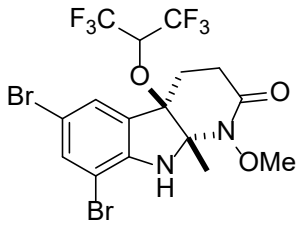


8. **(Procedure B)** White solid. Analytical data for **8**: m.p. = 65-66 °C. **^{1}H NMR (400 MHz, DMSO)** δ 11.03 (s, 1H), 10.40 (s, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 1H), 7.04 – 6.97 (m, 1H), 6.94 – 6.91 (m, 1H), 3.58 (s, 3H), 3.12 – 2.98 (m, 2H), 2.34 – 2.06 (m, 2H), 1.43 (s, 9H) **^{13}C NMR (100 MHz, DMSO)** δ 174.0, 147.4, 139.7, 134.0, 125.4, 123.3, 122.6, 115.9, 112.9, 68.4, 39.9, 38.2, 35.8, 26.2. **IR (film)**: 3321, 2957, 1645, 459, 1073, 742 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{23}N_2O_2^+$ [M+H]$^+$: 297.1573, Found: 297.1576.

Spectral Characterization Data for the product Substrates

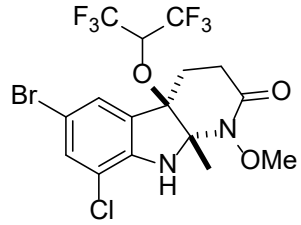


3aa. Yellow solid (41.5 mg, 72% yield). Analytical data for **3aa**: m.p. = 164-165 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.92 (s, 1H), 7.64 (s, 1H), 7.49 (s, 1H), 5.54 – 5.48 (m, 1H), 3.65 (s, 3H), 2.62 (s, 1H), 2.40 (d, *J* = 12.8 Hz, 1H), 2.10 (s, 2H), 1.66 (s, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 164.9, 148.2, 137.4, 127.1, 123.9, 122.6, 122.1, 119.8, 119.3, 111.3, 105.9, 89.7, 88.0, 70.8, 70.5, 70.1, 69.8, 69.5, 64.4, 28.7, 24.2, 18.0. **^{19}F NMR (376 MHz, DMSO)** δ -72.81 (q, *J* = 9.6 Hz), -73.37 (q, *J* = 9.6 Hz). **IR (film)**: 3421, 2951, 1664, 1286, 1184, 876, 684 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{14}Br_2F_6N_2NaO_3^+$ [M+Na]$^+$: 576.9168, Found: 576.9149.

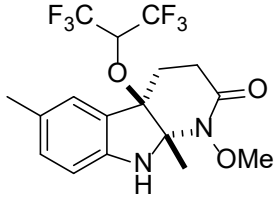


3ab. white solid (43.8 mg, 72% yield). Analytical data for **3ab**: m.p. = 164-165 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.92 (d, *J* = 1.8 Hz, 1H), 7.65 (d, *J* = 1.8 Hz, 1H), 7.49 (s, 1H), 5.54 – 5.47 (m, 1H), 3.65 (s, 3H), 2.69 – 2.57 (m, 1H), 2.47 – 2.33 (m, 1H), 2.15 – 2.04 (m, 2H), 1.66 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.2, 148.0, 136.2, 127.8, 127.5, 123.4, 123.0, 120.5, 120.2, 109.1, 103.3, 89.1, 87.2, 69.5, 69.2, 68.9, 68.6, 68.2, 64.0, 28.5, 21.8, 17.3. **^{19}F NMR (376 MHz, DMSO)** δ -72.81 (q, *J* = 9.9 Hz), -72.94 (q, *J* = 9.8 Hz). **IR (film)**: 3421, 2951, 1664, 1286, 1184, 876, 684

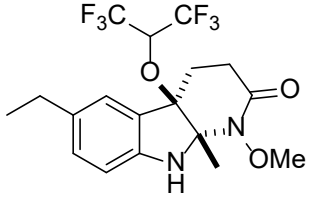
cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{14}Br_2F_6N_2NaO_3^+$ $[M+Na]^+$: 576.9168, Found: 576.9149.



3ac. Yellow solid (25.5 mg, 50% yield). Analytical data for **3ac**: m.p. = 165-166 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.89 (d, *J* = 1.9 Hz, 1H), 7.68 (s, 1H), 7.55 (d, *J* = 1.8 Hz, 1H), 5.55 – 5.49 (m, 1H), 3.65 (s, 3H), 2.70 – 2.58 (m, 1H), 2.48 – 2.35 (m, 1H), 2.20 – 2.02 (m, 2H), 1.67 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.3, 146.5, 133.6, 127.7, 127.4, 123.4, 123.0, 115.2, 108.8, 89.3, 87.1, 69.2, 68.9, 68.6, 64.0, 28.5, 21.8, 17.4. **^{19}F NMR (376 MHz, DMSO)** δ -72.71 (q, *J* = 9.8 Hz), -72.90 (q, *J* = 9.8 Hz). **IR (film)**: 1663, 1287, 1184, 876, 685, 470 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{14}BrClF_6N_2NaO_3^+$ $[M+Na]^+$: 532.9673, Found: 532.9650.

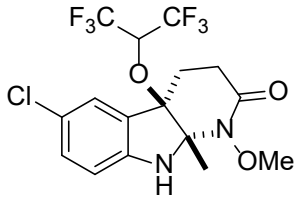


3ad. Yellow solid (24.3 mg, 59% yield). Analytical data for **3ad**: m.p. = 144-145 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.41 (s, 1H), 7.03 (d, *J* = 8.2 Hz, 1H), 6.92 (s, 1H), 6.60 (d, *J* = 7.9 Hz, 1H), 5.16 (s, 1H), 3.66 (s, 3H), 2.59 – 2.55 (m, 1H), 2.43 – 2.32 (m, 1H), 2.24 (s, 3H), 2.07 (s, 2H), 1.63 (s, 3H).**^{13}C NMR (100 MHz, DMSO)** δ 164.6, 148.6, 132.6, 127.0, 126.2, 123.0, 110.4, 89.9, 87.4, 69.6, 69.3, 69.0, 68.7, 68.4, 63.8, 29.1, 22.5, 20.9, 18.2. **^{19}F NMR (376 MHz, DMSO)** δ -72.29 (q, *J* = 9.8 Hz), -72.77 (q, *J* = 9.9 Hz). **IR (film)**: 3648, 2356, 1651, 1280, 1186, 1098, 884, 685 cm^{-1}. **HRMS (ESI)** calcd for $C_{17}H_{18}F_6N_2NaO_3^+$ $[M+Na]^+$: 435.1114, Found: 435.1106.

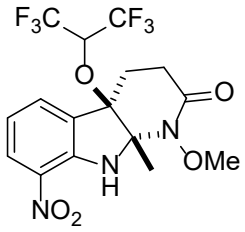


3ae. Yellow solid (29.8 mg, 63% yield). Analytical data for **3ae**: m.p. = 146-147 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.38 (s, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.86 (s, 1H), 6.54 (d, *J* = 8.0 Hz, 1H), 5.15 – 5.09 (m, 1H), 3.60 (s, 3H), 2.57 – 2.55 (m, 1H), 2.49 – 2.44 (m, 2H), 2.38 – 2.28 (m, 1H), 2.10

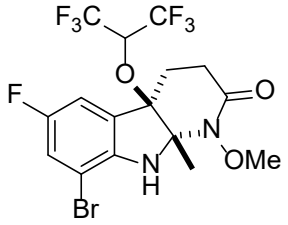
– 1.90 (m, 2H), 1.56 (s, 3H), 1.09 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.6, 148.6, 134.0, 131.4, 125.0, 123.2, 110.3, 89.8, 87.4, 69.6, 69.3, 69.0, 68.7, 68.4, 63.8, 29.1, 28.2, 22.4, 18.2, 16.7. **^{19}F NMR (376 MHz, DMSO)** δ -72.27 (q, *J* = 9.9 Hz), -72.96 (q, *J* = 9.9 Hz). **IR (film)**: 3648, 2356, 1651, 1280, 1186, 1098, 884, 685 cm^{-1}. **HRMS (ESI)** calcd for $C_{17}H_{18}F_6N_2NaO_3^+$ $[M+Na]^+$: 435.1114, Found: 435.1106.



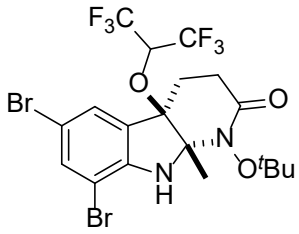
3af. Yellow solid (28.7 mg, 68% yield). Analytical data for **3af**: m.p. = 187-188 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.77 (s, 1H), 7.50 – 7.07 (m, 2H), 6.68 (d, *J* = 8.4 Hz, 1H), 5.58 – 5.32 (m, 1H), 3.68 (s, 3H), 2.64 – 2.57 (m, 1H), 2.43 – 2.39 (m, 1H), 2.14 – 1.98 (m, 2H), 1.64 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.6, 149.4, 131.8, 125.70, 125.5, 121.7, 111.6, 89.8, 86.8, 69.6, 69.2, 68.9, 68.6, 68.3, 63.8, 28.8, 22.0, 18.0. **^{19}F NMR (376 MHz, DMSO)** δ -72.37 (q, *J* = 9.9 Hz), -72.90 (q, *J* = 10.0 Hz). **IR (film)**: 3434, 1656, 1281, 1189, 1097, 822, 492 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{15}ClF_6N_2NaO_3^+$ $[M+Na]^+$: 445.0568, Found: 445.0577.



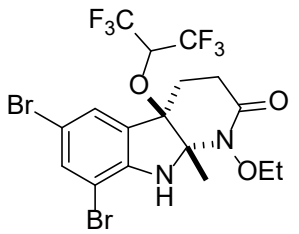
3ag. Brown solid (25.7 mg, 58% yield). Analytical data for **3ag**: m.p. = 114-115 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.29 (d, *J* = 2.6 Hz, 1H), 6.82 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.68 – 6.58 (m, 2H), 5.33 – 5.27 (m, 1H), 3.71 (s, 3H), 3.65 (s, 3H), 2.59 – 2.57 (m, 1H), 2.42 – 2.32 (m, 1H), 2.14 – 1.98 (m, 2H), 1.61 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.6, 152.9, 144.6, 124.3, 118.0, 111.8, 111.3, 90.2, 87.5, 69.3, 69.0, 68.7, 63.8, 56.2, 29.0, 22.3, 18.3. **^{19}F NMR (376 MHz, DMSO)** δ -72.22 (q, *J* = 9.8 Hz), -72.70 (q, *J* = 9.8 Hz). **IR (film)**: 3150, 3070, 1690, 1184, 820, 639, 426 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{15}F_6N_3NaO_5^+$ $[M+Na]^+$: 466.0808, Found: 466.0805.



3ah. White solid (23.2 mg, 43% yield). Analytical data for **3ah**: m.p. = 158-159 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.67 (dd, *J* = 8.1, 2.5 Hz, 1H), 7.43 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.09 (s, 1H), 5.50 – 5.44 (m, 1H), 3.66 (s, 3H), 2.68 – 2.54 (m, 1H), 2.47 – 2.34 (m, 1H), 2.20 – 2.04 (m, 2H), 1.67 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.3, 156.6, 154.3, 145.4, 126.4, 126.3, 123.4, 123.0, 121.3, 121.0, 120.6, 120.2, 113.1, 112.9, 102.1, 102.2, 89.6, 87.4, 87.40, 69.6, 69.2, 68.9, 68.6, 68.3, 64.0, 28.5, 22.0, 17.5. **^{19}F NMR (376 MHz, DMSO)** δ -72.34 (q, *J* = 9.8 Hz), -73.02 (q, *J* = 9.8 Hz), -124.21. **IR (film)**: 2944, 2321, 1654, 1457, 1214, 1098, 894, 687 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{14}ClBrF_6N_2NaO_3^+$ $[M+Na]^+$: 516.9968, Found: 516.9962.

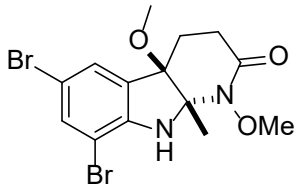


3ai. Yellow liquid (27.3 mg, 48% yield). Analytical data for **3ai**: m.p. = 166-167 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 1.7 Hz, 1H), 7.19 – 7.15 (m, 1H), 5.12 (s, 1H), 4.00 – 3.95 (m, 1H), 2.55 – 2.46 (m, 1H), 2.37 – 2.26 (m, 3H), 1.65 (s, 3H), 1.19 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 171.5, 148.0, 137.2, 126.9, 110.8, 105.2, 89.6, 89.0, 84.2, 29.0, 28.0, 26.0, 22.7, 18.8, 14.1. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -72.75 (q, *J* = 9.5 Hz), -73.31 (q, *J* = 9.6 Hz). **IR (film)**: 3312, 2979, 1727, 1464, 1366, 1228, 1191, 1044, 685 cm^{-1}. **HRMS (ESI)** calcd for $C_{19}H_{21}Br_2F_6N_2O_3^+$ $[M+H]^+$: 598.9797, Found: 598.9796.

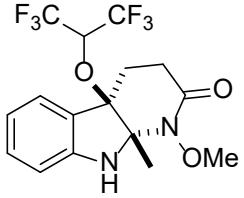


3aj. Yellow solid (32.2 mg, 54% yield). Analytical data for **3aj**: m.p. = 148-149 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 (d, *J* = 1.7 Hz, 1H), 7.27 (d, *J* = 1.8 Hz, 1H), 5.34 (s, 1H), 4.05 – 3.98 (m, 3H), 2.56 – 2.49 (m, 1H), 2.45 – 2.38 (m, 1H), 2.35 – 2.25 (m, 2H), 1.79 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.0, 148.3, 137.4, 127.0, 124.0, 111.3, 106.0, 89.6, 88.1, 72.4, 70.5, 70.2, 28.6, 24.3,

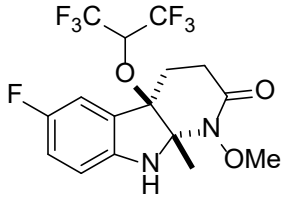
18.1, 13.6. **^{19}F NMR (376 MHz, $CDCl_3$)** δ -72.54 (q, *J* = 9.5 Hz), -72.79 (q, *J* = 9.6 Hz), -73.33 (q, *J* = 9.6 Hz), -73.55 (q, *J* = 9.5 Hz). **IR (film)**: 3214, 2981, 2901, 1723, 1672, 1606, 1466, 1362, 1189, 684 cm^{-1}. **HRMS (ESI)** calcd for $C_{17}H_{17}Br_2F_6N_2O_3^+$ $[M+H]^+$: 570.9484, Found: 570.9481.



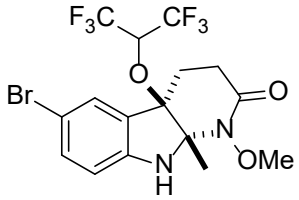
3am. Yellow solid (28.6 mg, 68% yield). Analytical data for **3am**: m.p. = 109-110 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.52 (d, *J* = 1.8 Hz, 1H), 7.24 (d, *J* = 1.8 Hz, 1H), 5.40 (s, 1H), 3.84 (s, 3H), 3.08 (s, 3H), 2.51 – 2.45 (m, 1H), 2.39 – 2.33 (m, 1H), 2.30 – 2.21 (m, 1H), 2.13 – 2.04 (m, 1H), 1.72 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.8, 146.9, 135.2, 127.4, 126.4, 111.1, 105.0, 88.3, 84.0, 64.0, 51.6, 28.6, 23.8, 18.1. **IR (film)**: 3385, 2927, 1656, 1450, 1126, 1058, 711, 637 cm^{-1}. **HRMS (ESI)** calcd for $C_{14}H_{16}Br_2N_2NaO_3^+$ $[M+Na]^+$: 442.9399, Found: 442.9430.



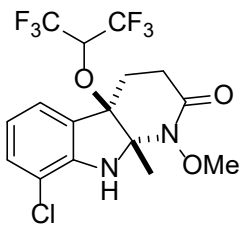
3ba. White solid (27.1 mg, 68% yield). Analytical data for **3ba**: m.p. = 123-124 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.58 (d, *J* = 7.4 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.15 (s, 1H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 5.23 – 5.17 (m, 1H), 3.67 (s, 3H), 2.64 – 2.59 (m, 1H), 2.42 – 2.37 (m, 1H), 2.16 – 2.08 (m, 1H), 2.06 – 1.96 (m, 1H), 1.64 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.6, 150.7, 132.2, 125.8, 123.0, 118.1, 110.5, 89.5, 87.3, 69.2, 68.9, 68.6, 63.8, 29.0, 22.3, 18.1. **^{19}F NMR (376 MHz, DMSO)** δ -72.27 (q, *J* = 9.8 Hz), -72.70 (q, *J* = 9.8 Hz). **IR (film)**: 1651, 1279, 1215, 1188, 1098, 890, 764, 685, 502 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{16}F_6N_2NaO_3^+$ $[M+Na]^+$: 421.0957, Found: 421.0942.



3bb. White solid (30.8 mg, 74% yield). Analytical data for **3bb**: m.p. = 150-151 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.61 (d, *J* = 7.4 Hz, 1H), 7.37 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 7.7 Hz, 1H), 5.37 – 5.31 (m, 1H), 3.66 (s, 3H), 2.66 – 2.62 (m, 1H), 2.46 – 2.33 (m, 1H), 2.18 – 2.10 (m, 1H), 2.09 – 1.98 (m, 1H), 1.68 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.3, 147.0, 131.8, 125.7, 124.5, 119.4, 114.5, 89.3, 87.4, 69.2, 68.9, 68.6, 64.0, 28.7, 22.1, 17.5. **^{19}F NMR (377 MHz, DMSO)** δ -72.38 (q, *J* = 9.7 Hz), -72.95 (q, *J* = 9.8 Hz), -126.45. **IR (film)**: 1651, 1282, 1189, 1097, 889, 684, 500 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{15}F_7N_2NaO_3^+$ $[M+Na]^+$: 439.0863, Found: 439.0856.

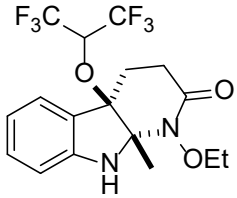


3bc. Yellow solid (19.5 mg, 41% yield). Analytical data for **3bc**: m.p. = 157-158 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.86 (d, *J* = 2.1 Hz, 1H), 7.36 (s, 1H), 7.34 (d, *J* = 2.0 Hz, 1H), 6.62 (d, *J* = 8.3 Hz, 1H), 5.49 – 5.42 (m, 1H), 3.66 (s, 3H), 2.64 – 2.58 (m, 1H), 2.43 – 2.38 (m, 1H), 2.13 – 2.02 (m, 2H), 1.62 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.6, 149.8, 134.6, 128.4, 126.0, 125.8, 112.2, 110.5, 108.9, 89.6, 86.8, 69.6, 69.2, 68.9, 63.9, 28.8, 21.9, 18.0. **^{19}F NMR (376 MHz, DMSO)** δ -72.27 (q, *J* = 9.9 Hz), -72.79 (q, *J* = 9.6 Hz). **IR (film)**: 3364, 3217, 1636, 1457, 1363, 1281, 1187, 685 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{15}BrF_6N_2NaO_3^+$ $[M+Na]^+$: 499.0062, Found: 499.0069.

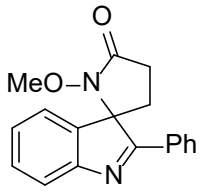


3bd. White solid (18.6 mg, 43% yield). Analytical data for **3bd**: m.p. = 157-158 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.58 (dd, *J* = 8.5, 2.7 Hz, 1H), 7.17 – 6.93 (m, 2H), 6.66 (dd, *J* = 8.6, 4.3 Hz, 1H), 5.43 – 5.37 (m, 1H), 3.67 (s, 3H), 2.68 – 2.55 (m, 1H), 2.49 – 2.33 (m, 1H), 2.21 – 2.00 (m, 2H), 1.63 (s, 3H). **^{13}C NMR (100 MHz, DMSO)** δ 164.6, 157.1, 154.8, 147.06, 124.7, 124.7, 123.4, 123.0, 120.7, 120.2, 118.6, 118.3,

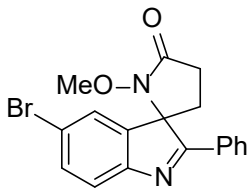
113.2, 113.0, 111.1, 111.0, 90.2, 86.9, 86.9, 69.6, 69.3, 69.0, 68.6, 68.3, 63.8, 28.8, 22.1, 18.1. **^{19}F NMR (376 MHz, DMSO)** δ -72.27 (q, *J* = 9.9 Hz), -72.96 (q, *J* = 9.9 Hz). **IR (film)**: 3419, 2943, 1672, 1278, 1193, 1096, 683, 528 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{15}ClF_6N_2NaO_3^+$ $[M+Na]^+$: 445.0568, Found: 445.0553.



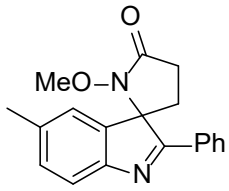
3be. White solid (17.8 mg, 43% yield). Analytical data for **3be**: m.p. = 138 - 139 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.29 (td, *J* = 7.7, 1.3 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.90 (td, *J* = 7.5, 0.9 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.14 (s, 1H), 4.21 – 4.13 (m, 1H), 4.01 – 3.87 (m, 2H), 2.52 – 2.46 (m, 1H), 2.46 – 2.41 (m, 1H), 2.36 – 2.28 (m, 1H), 2.27 – 2.18 (m, 1H), 1.75 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.7, 150.6, 132.9, 125.6, 120.3, 119.9, 112.2, 90.0, 88.1, 72.2, 70.3, 69.9, 69.6, 29.1, 24.5, 18.5, 13.5. **^{19}F NMR (377 MHz, $CDCl_3$)** δ -72.86 (q, *J* = 9.5 Hz), -73.25 (q, *J* = 9.5 Hz). **IR (film)**: 3396, 2948, 1664, 1279, 1178, 763, 686, 494 cm^{-1}. **HRMS (ESI)** calcd for $C_{17}H_{18}F_6N_2NaO_3^+$ $[M+Na]^+$: 435.1114, Found: 435.1127.



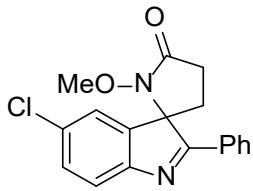
4aa. white solid (25.1 mg, 86% yield). Analytical data for **4aa**: m.p. = 115-116 °C. **^{1}H NMR (400 MHz, DMSO)** δ 8.05 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.64 (t, *J* = 6.7 Hz, 2H), 7.61 – 7.54 (m, 3H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 3.43 (s, 3H), 2.95 – 2.86 (m, 1H), 2.67 – 2.59 (m, 1H), 2.56 – 2.46 (m, 3H), 2.31 – 2.16 (m, 1H).**^{13}C NMR (100 MHz, DMSO)** δ 176.7, 171.7, 152.7, 140.1, 132.0, 131.0, 130.5, 129.5, 128.2, 127.3, 122.8, 121.6, 75.6, 63.9, 26.1, 25.9. **IR (film)**: 2319, 11715, 1540, 1457, 1052, 773, 472 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{16}N_2NaO_2^+$ $[M+Na]^+$: 315.1104, Found: 315.1104.



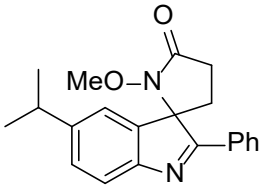
4ab. white solid (23.1mg, 79% yield). Analytical data for **4ab**: m.p. = 132-133 °C. **^{1}H NMR (400 MHz, DMSO)** δ 8.06 (d, *J* = 7.3 Hz, 2H), 7.91 (s, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.61 – 7.50 (m, 4H), 3.45 (s, 3H), 3.01 – 2.95 (m, 1H), 2.66 – 2.61 (m, 1H), 2.56 – 2.45 (m, 1H), 2.32 – 2.24 (m, 1H). **^{13}C NMR (100 MHz, DMSO)** δ 177.2, 171.7, 151.9, 142.6, 133.4, 132.2, 131.5, 129.6, 128.3, 126.0, 123.3, 120.2, 75.8, 64.0, 25.9, 25.7. **IR (film)**: 2363, 1717, 1698, 1540, 1457, 695, 419 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{15}BrN_2NaO_2^+$ $[M+Na]^+$: 393.0209, Found: 393.0195.



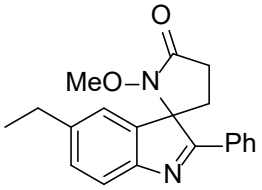
4ac. Yellow solid (19.9 mg, 65% yield). Analytical data for **4ac**: m.p. = 106-107 °C. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.04 (dd, *J* = 7.6, 2.1 Hz, 2H), 7.63 – 7.42 (m, 4H), 7.28 – 7.20 (m, 2H), 3.62 (s, 3H), 2.86 – 2.78 (m, 1H), 2.66 – 2.59 (m, 1H), 2.56 – 2.48 (m, 1H), 2.44 (s, 3H), 2.30 – 2.23 (m, 1H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 175.6, 171.9, 150.7, 139.3, 137.1, 132.0, 131.3, 130.8, 129.0, 127.9, 122.3, 121.4, 75.6, 64.2, 26.3, 26.2, 21.5. **IR (film)**: 2502, 1974, 1710, 1052, 774, 695, 587 cm^{-1}. **HRMS (ESI)** calcd for $C_{19}H_{18}N_2NaO_2^+$ $[M+Na]^+$: 329.1260, Found: 329.1264.



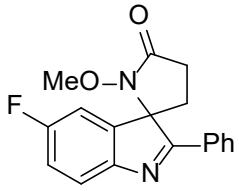
4ad. white solid (18.0 mg, 55% yield). Analytical data for **4ad**: m.p. = 131-132 °C. **^{1}H NMR (400 MHz, DMSO)** δ 8.11 – 7.98 (m, 2H), 7.79 (d, *J* = 2.1 Hz, 1H), 7.66 – 7.50 (m, 5H), 3.44 (s, 3H), 2.83 – 2.75 (m, 1H), 2.65 – 2.57 (m, 1H), 2.56 – 2.45 (m, 1H), 2.30 – 2.23 (m, 1H). **^{13}C NMR (100 MHz, DMSO)** δ 177.3, 171.7, 151.5, 142.3, 132.3, 131.9, 131.5, 130.5, 129.6, 128.3, 123.3, 122.9, 75.8, 64.0, 25.9, 25.7. **IR (film)**: 1727, 1444, 1259, 1059, 827, 696, 562 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{15}ClN_2NaO_2^+$ $[M+Na]^+$: 349.0714, Found: 349.0712.



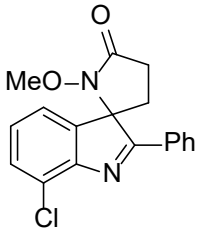
4ae. white solid (25.1 mg, 75% yield). Analytical data for **4ae**: m.p. = 107-108 °C. **^{1}H NMR (300 MHz, DMSO)** δ 8.07 – 7.93 (m, 2H), 7.61 – 7.46 (m, 5H), 7.31 (d, *J* = 8.0 Hz, 1H), 3.42 (s, 3H), 3.02 – 2.86 (m, 2H), 2.67 – 2.53 (m, 1H), 2.53 – 2.39 (m, 1H), 2.30 – 2.17 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR (75 MHz, DMSO)** δ 176.1, 171.5, 151.0, 148.2, 140.3, 132.1, 131.7, 129.5, 128.1, 128.0, 121.3, 121.0, 75.5, 63.8, 34.0, 26.1, 26.0, 24.6, 24.4. **IR (film)**: 2924, 1718, 1507, 1320, 1051, 699, 660 cm^{-1}. **HRMS (ESI)** calcd for $C_{21}H_{22}N_2NaO_2^+$ $[M+Na]^+$: 357.1573, Found: 357.1575.



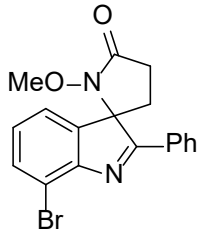
4af. white solid (16.7mg, 56% yield). Analytical data for **4af**: m.p. = 94-95°C. **^{1}H NMR (300 MHz, DMSO)** δ 8.13 – 7.92 (m, 2H), 7.63 – 7.41 (m, 5H), 7.29 (d, *J* = 7.9 Hz, 1H), 3.42 (s, 3H), 2.98 – 2.86 (m, 1H), 2.75 – 2.56 (m, 3H), 2.55 – 2.42 (m, 1H), 2.29 – 2.16 (m, 1H), 1.21 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (75 MHz, DMSO)** δ 175.8, 171.6, 150.8, 143.5, 140.4, 132.0, 131.8, 129.7, 129.5, 128.1, 122.3, 121.3, 75.5, 63.8, 28.6, 26.1, 26.0, 16.3. **IR (film)**: 2170, 1782, 1166, 1029, 843, 686, 422 cm^{-1}. **HRMS (ESI)** calcd for $C_{20}H_{21}N_2O_2^+$ $[M+H]^+$: 321.1598, Found: 321.1601.



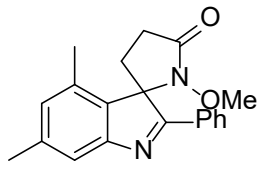
4ag. white solid (23.9 mg, 77% yield). Analytical data for **4ag**: m.p. = 118-119 °C. **^{1}H NMR (300 MHz, DMSO)** δ 8.09 – 7.92 (m, 2H), 7.70 – 7.51 (m, 5H), 7.32 – 7.26 (m, 1H), 3.45 (s, 3H), 3.02 – 2.90 (m, 1H), 2.69 – 2.54 (m, 1H), 2.52 – 2.44 (m, 1H), 2.31 – 2.22 (m, 1H). **^{13}C NMR (75 MHz, DMSO)** δ 177.0, 171.5, 163.4, 160.1, 149.0, 142.4, 142.3, 132.0, 131.7, 129.5, 128.1, 122.8, 122.7, 117.2, 116.8, 111.2, 110.9, 75.9, 75.8, 64.0, 26.0, 25.8. **IR (film)**: 2942, 1710, 1466, 1204, 1051, 778, 667 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{15}FN_2NaO_2^+$ $[M+Na]^+$: 333.1010, Found: 333.1017.



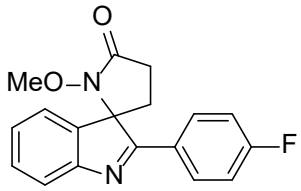
4ah. white solid (20.0 mg, 61% yield). Analytical data for **4ah**: m.p. = 82-83 °C. **^{1}H NMR (400 MHz, DMSO)** δ 8.08 (d, J = 6.9 Hz, 2H), 7.91 (d, J = 1.7 Hz, 1H), 7.83 (d, J = 1.7 Hz, 1H), 7.70 – 7.50 (m, 4H), 3.45 (s, 3H), 3.05 – 2.96 (m, 1H), 2.70 – 2.63 (m, 1H), 2.57 – 2.47 (m, 2H), 2.36 – 2.29 (m, 1H).**^{13}C NMR (100 MHz, DMSO)** δ 178.3, 171.7, 148.6, 144.1, 133.0, 132.8, 131.1, 129.7, 128.5, 126.7, 125.0, 120.6, 77.0, 64.1, 25.8, 25.7. **IR (film)**: 2936, 1684, 1483, 1169, 1008, 814, 692 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{15}ClN_2NaO_2^+$ $[M+Na]^+$: 349.0714, Found: 349.0713.



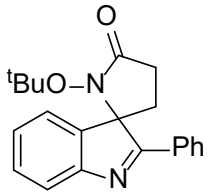
4ai. White solid (25.7 mg, 83% yield). Analytical data for **4ai**: m.p. = 127-128 °C. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.02 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.44 (dd, *J* = 13.1, 7.0 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 17.3 Hz, 2H), 3.59 (s, 3H), 2.81 – 2.75 (m, 1H), 2.66 – 2.58 (m, 1H), 2.55 – 2.48 (m, 1H), 2.31 – 2.22 (m, 1H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 175.7, 171.6, 165.9, 152.7, 139.0, 130.4, 130.3, 130.2, 128.2, 128.2, 126.9, 121.8, 121.6, 116.4, 116.1, 75.7, 64.3, 26.3, 26.2. **IR (film)**: 2976, 1736, 1529, 1458, 1365, 761, 695 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{15}BrN_2NaO_2^+$ $[M+Na]^+$: 371.0390, Found: 371.0413.



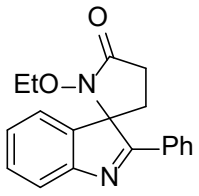
4aj. White solid (24.7 mg, 77% yield). Analytical data for **4aj**: m.p. = 137-138 °C. **^{1}H NMR (400 MHz, CDCl$_3$)** δ 7.93 – 7.90 (m, 2H), 7.47 – 7.44 (m, 3H), 7.29 (d, *J* = 2.2 Hz, 1H), 6.86 (d, *J* = 3.7 Hz, 1H), 3.55 (d, *J* = 4.5 Hz, 3H), 2.78 – 2.55 (m, 2H), 2.39 (d, *J* = 4.6 Hz, 2H), 2.37 (d, *J* = 4.1 Hz, 3H), 2.34 (d, *J* = 3.6 Hz, 3H). **^{13}C NMR (100 MHz, CDCl$_3$)** δ 177.4, 171.1, 153.6, 140.4, 133.3, 132.8, 131.9, 131.2, 129.9, 129.1, 127.7, 120.4, 75.1, 63.5, 26.4, 22.9, 21.5, 17.2. **IR (film)**: 2942, 1707, 1535, 1460, 1055, 863, 701, 634 cm^{-1}. **HRMS (ESI)** calcd for $C_{20}H_{20}N_2NaO_2^+$ $[M+Na]^+$: 343.1417, Found: 343.1420



4ak. White solid (25.7 mg, 83% yield). Analytical data for **4ak**: m.p. = 145-146 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.02 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.44 (dd, *J* = 13.1, 7.0 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 17.3 Hz, 2H), 3.59 (s, 3H), 2.85 – 2.76 (m, 1H), 2.63 – 2.55 (m, 1H), 2.49 – 2.41 (m, 1H), 2.30 – 2.23 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 175.7, 171.6, 165.9, 152.7, 139.0, 130.4, 130.3, 130.2, 128.2, 128.2, 126.9, 121.8, 121.6, 116.4, 116.1, 75.7, 64.3, 26.3, 26.2. **^{19}F NMR (376 MHz, DMSO)** δ -108.08. **IR (film)**: 2976, 1736, 1529, 1458, 1365, 761, 695 cm^{-1}. **HRMS (ESI)** calcd for $C_{18}H_{15}FN_2NaO_2^+$ $[M+Na]^+$: 333.1010, Found: 333.1017.

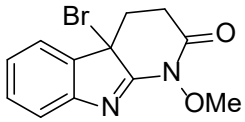


4al. white solid (24.6 mg, 84% yield). Analytical data for **4al**: m.p. = 125-126 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.00 – 7.87 (m, 2H), 7.62 (dd, *J* = 7.5, 3.8 Hz, 1H), 7.52 – 7.36 (m, 5H), 7.31 – 7.28 (m, 1H), 2.83 – 2.68 (m, 1H), 2.53 – 2.38 (m, 2H), 2.35 – 2.25 (m, 1H), 0.95 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 178.2, 176.2, 153.1, 140.1, 132.4, 131.1, 123.0, 128.9, 128.4, 126.6, 122.5, 121.5, 83.5, 77.2, 27.6, 26.7, 26.3. **IR (film)**: 2976, 1736, 1529, 1458, 1365, 761, 695 cm^{-1}. **HRMS (ESI)** calcd for $C_{21}H_{22}N_2NaO_2^+$ $[M+Na]^+$: 357.1573, Found: 357.1573.

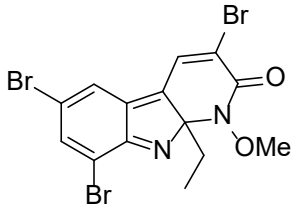


4am. White solid (27.2 mg, 89% yield). Analytical data for **4am**: m.p. = 130-131 °C. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.97 (dd, *J* = 7.7, 1.9 Hz, 2H), 7.63 (dd, *J* = 7.2, 1.4 Hz, 1H), 7.50 – 7.36 (m, 5H), 7.27 – 7.23 (m, 1H), 3.92 – 3.82 (m, 1H), 3.69 – 3.65 (m, 1H), 2.75 – 2.71 (m, 1H), 2.57 – 2.49 (m, 1H), 2.47 – 2.39 (m, 1H), 2.26 – 2.19 (m, 1H), 0.94 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 177.0, 171.9, 152.9, 139.3, 132.0, 131.4, 130.2, 129.0, 127.9, 126.8, 121.7, 121.7, 76.0, 72.5, 26.3, 26.1, 13.6. **IR (film)**: 2923,

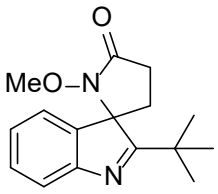
1710, 1455, 1259, 1057, 762, 698 cm^{-1}. **HRMS (ESI)** calcd for $C_{19}H_{18}N_2NaO_2^+$ $[M+Na]^+$: 329.1260, Found: 329.1255.



5a. White solid (24.4 mg, 83% yield). Analytical data for **5a**: m.p. = 109-110 °C. **^{1}H NMR (400 MHz, DMF)** δ 7.68 (d, *J* = 7.4 Hz, 1H), 7.52 – 7.40 (m, 2H), 7.30 – 7.26 (m, 1H), 3.99 (s, 3H), 3.15 – 3.07 (m, 1H), 3.01 – 2.94 (m, 1H), 2.84 – 2.78 (m, 1H), 2.32 – 2.24 (m, 1H). **^{13}C NMR (100 MHz, DMF)** δ 163.7, 132.2, 126.7, 124.3, 121.3, 64.1, 36.6, 36.4, 33.0, 31.5, 31.3, 31.1, 30.8, 30.6, 30.4, 30.2. **IR (film)**: 2956, 1713, 1520, 1260, 1198, 762, 698 cm^{-1}. **HRMS (ESI)** calcd for $C_{12}H_{11}BrN_2NaO_2^+$ $[M+Na]^+$: 316.9896, Found: 316.9890.



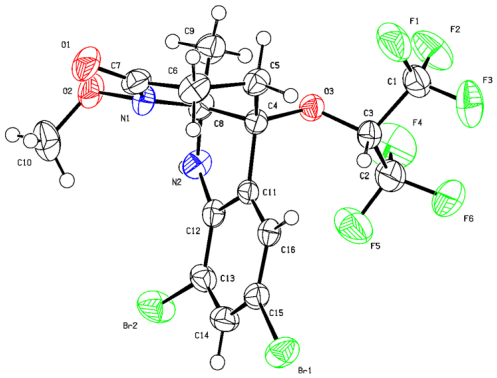
6a. Yellow solid (34.4 mg, 72% yield). Analytical data for **6a**: m.p. = 86-87 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.90 (s, 1H), 7.84 (s, 1H), 6.75 (s, 1H), 3.99 (s, 3H), 2.34 – 2.27 (m, 1H), 2.08 – 2.01 (m, 1H), 0.52 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.5, 160.4, 150.9, 142.9, 137.5, 135.4, 125.9, 125.3, 118.0, 114.7, 65.8, 64.7, 38.7, 8.2. **IR (film)**: 2936, 1684, 1483, 1169, 1008, 814, 692 cm^{-1}. **HRMS (ESI)** calcd for $C_{14}H_{12}Br_3N_2O_2$ $[M+H]^+$: 478.8423, Found: 478.8408.



8a. Light Yellow solid (23.2 mg, 85% yield). Analytical data for **8a**: m.p. = 125-126 °C. **^{1}H NMR (400 MHz, DMSO)** δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.31 (m, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 3.95 (s, 3H), 3.01 – 2.91 (m, 1H), 2.76 – 2.69 (m, 1H), 2.63 – 2.60 (m, 1H), 1.70 – 1.62 (m, 1H), 0.90 (s, 9H). **^{13}C NMR (100 MHz, DMSO)** δ 171.5, 168.5, 154.6, 141.9, 128.5, 123.8, 123.6, 119.1, 63.7, 60.4, 37.4, 31.6, 26.9, 21.2. **IR (film)**: 2944, 1699,

1566, 1272, 1176, 773, 595 cm^{-1}. **HRMS (ESI)** calcd for $C_{16}H_{20}N_2NaO_2^+$ $[M+Na]^+$: 295.1417, Found: 295.1416.

X-Ray crystal structure of 3aa (CCDC 2213700)




```
Bond precision:   C-C = 0.0099 A          Wavelength=0.71073

Cell:             a=8.5935(8)     b=10.4364(9)       c=10.8779(9)
                  alpha=90        beta=94.610(3)     gamma=90
Temperature:      296 K

                  Calculated                  Reported
Volume            972.43(15)                  972.43(15)
Space group       P n                         P 1 n 1
Hall group        P -2yac                     P -2yac
Moiety formula    C16 H14 Br2 F6 N2 O3        C16 H14 Br2 F6 N2 O3
Sum formula       C16 H14 Br2 F6 N2 O3        C16 H14 Br2 F6 N2 O3
Mr                556.09                      556.11
Dx,g cm-3         1.899                       1.899
Z                 2                           2
Mu (mm-1)         4.245                       4.245
F000              544.0                       544.0
F000'             543.24
h,k,lmax          11,13,14                    11,13,14
Nref              4479[ 2246]                 4345
Tmin,Tmax         0.375,0.712                 0.335,0.746
Tmin'             0.333

Correction method= # Reported T Limits: Tmin=0.335 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 1.93/0.97        Theta(max)= 27.510

R(reflections)= 0.0427( 3460)                  wR2(reflections)=
                                               0.1087( 4345)
S = 1.037                  Npar= 264
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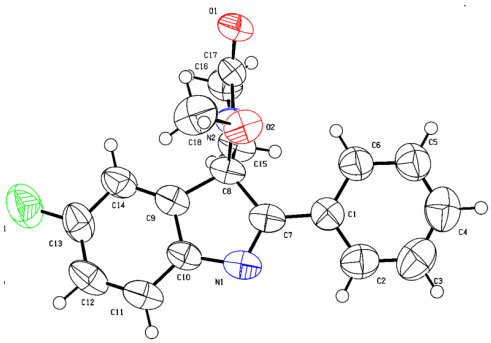
X-Ray crystal structure of 4aa (CCDC 2213712)




```
Bond precision:   C-C = 0.0041 A          Wavelength=0.71073

Cell:             a=11.1831(13)     b=11.7646(14)       c=12.1011(15)
                  alpha=90          beta=103.533(3)     gamma=90
Temperature:      296 K

                  Calculated                  Reported
Volume            1547.9(3)                   1547.9(3)
Space group       P 21/c                      P 1 21/c 1
Hall group        -P 2ybc                     -P 2ybc
Moiety formula    C18 H15 F N2 O2             C18 H15 F N2 O2
Sum formula       C18 H15 F N2 O2             C18 H15 F N2 O2
Mr                310.32                      310.32
Dx,g cm-3         1.332                       1.332
Z                 4                           4
Mu (mm-1)         0.096                       0.096
F000              648.0                       648.0
F000'             648.33
h,k,lmax          13,14,15                    13,14,15
Nref              3173                        3165
Tmin,Tmax         0.983,0.995                 0.551,0.745
Tmin'             0.944

Correction method= # Reported T Limits: Tmin=0.551 Tmax=0.745
AbsCorr = MULTI-SCAN

Data completeness= 0.997            Theta(max)= 26.403

R(reflections)= 0.0583( 1428)                   wR2(reflections)=
                                                0.1541( 3165)
S = 1.010                  Npar= 209
```

References

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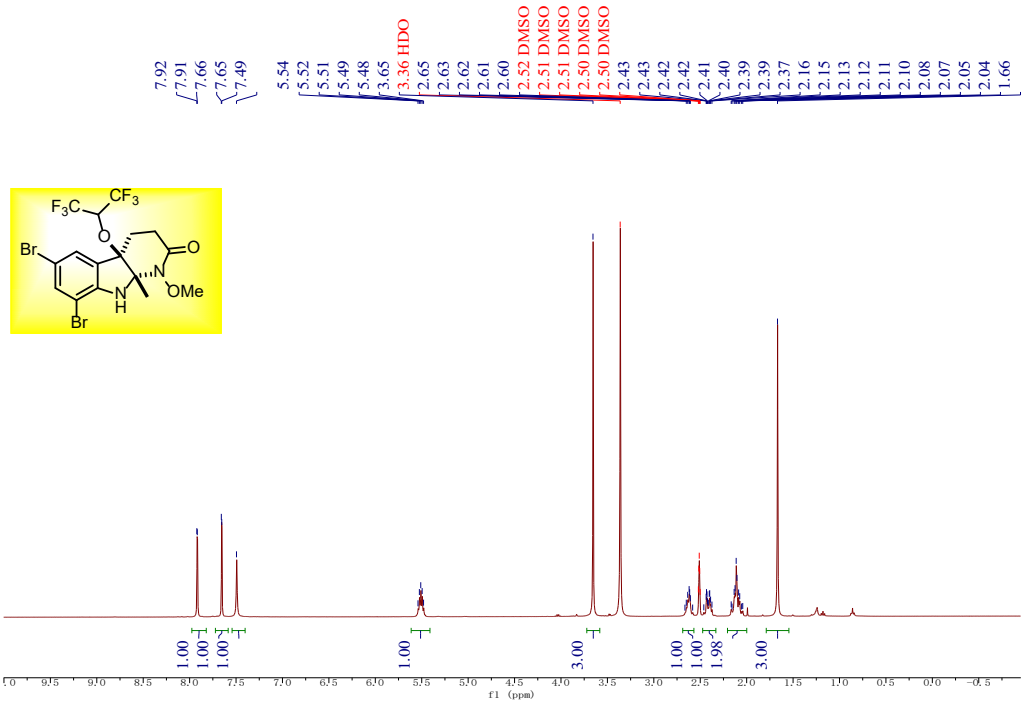
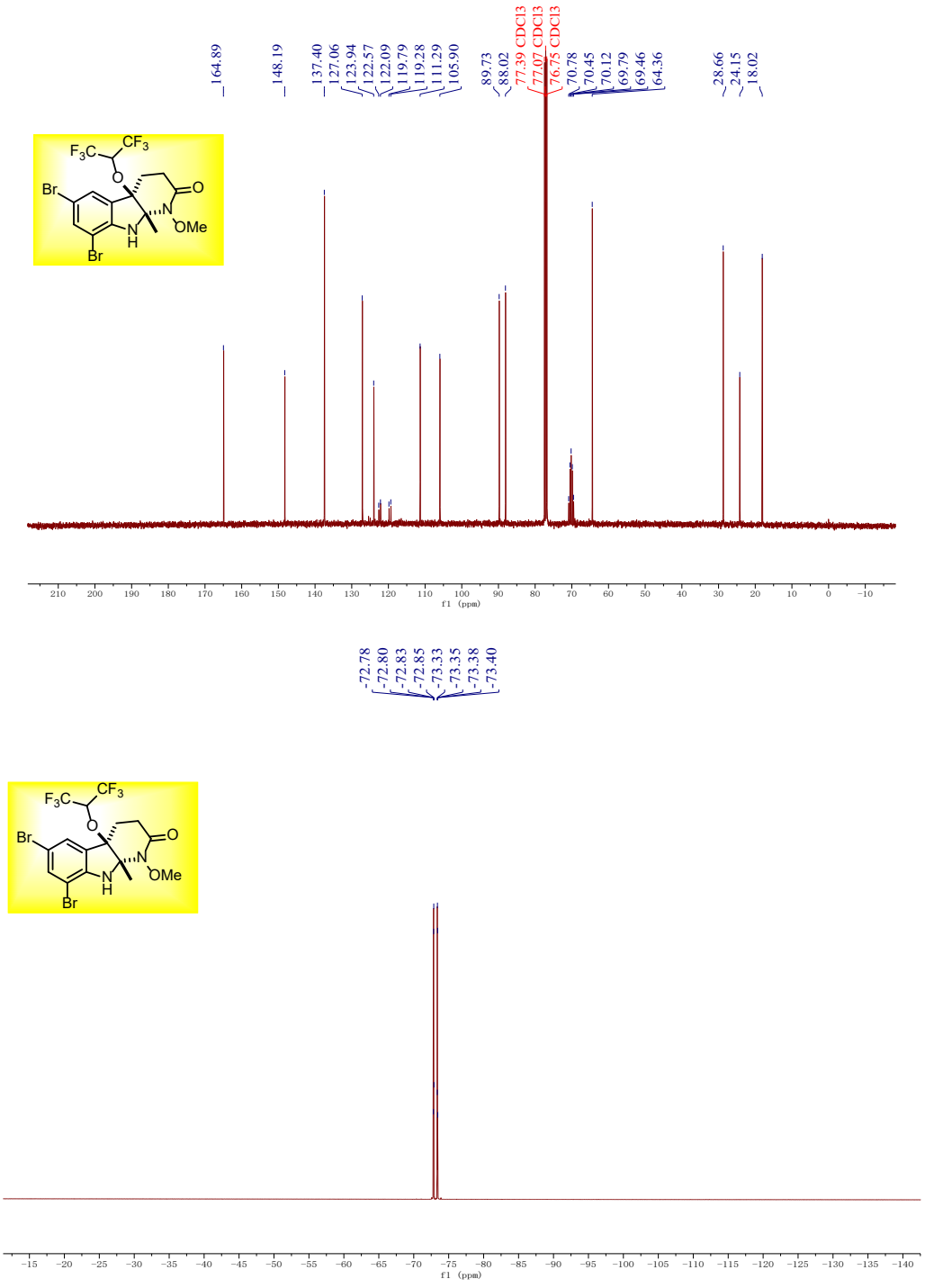
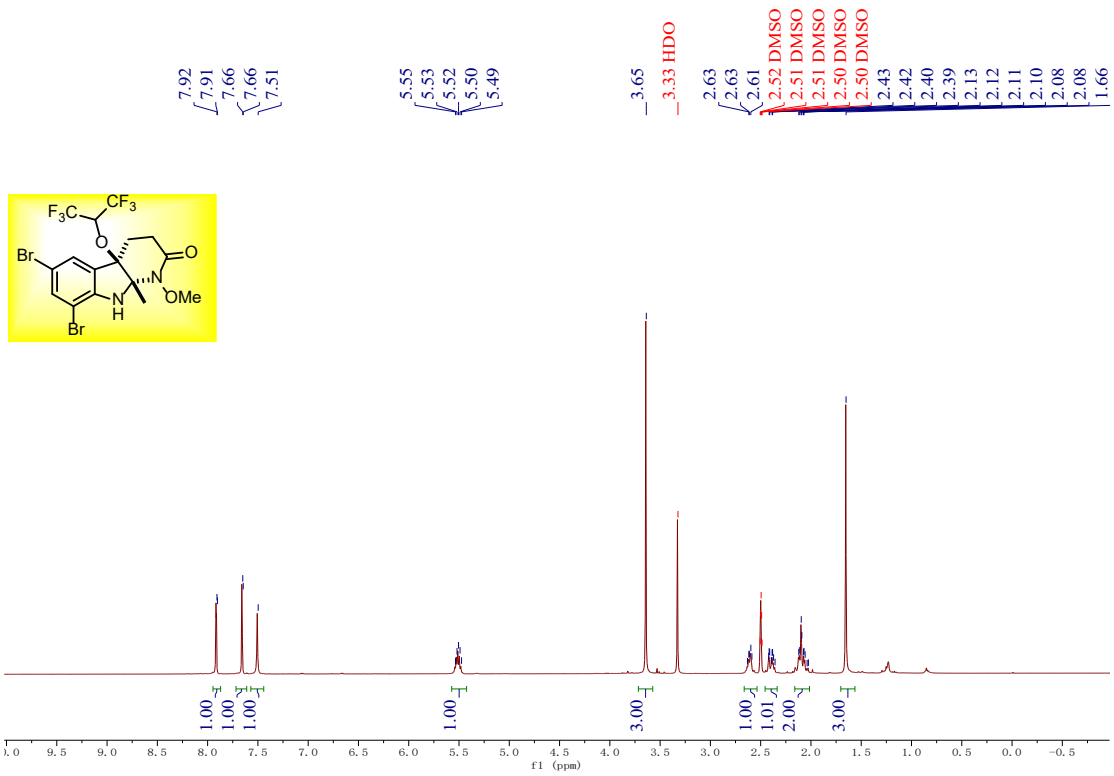
NMR Spectra of products

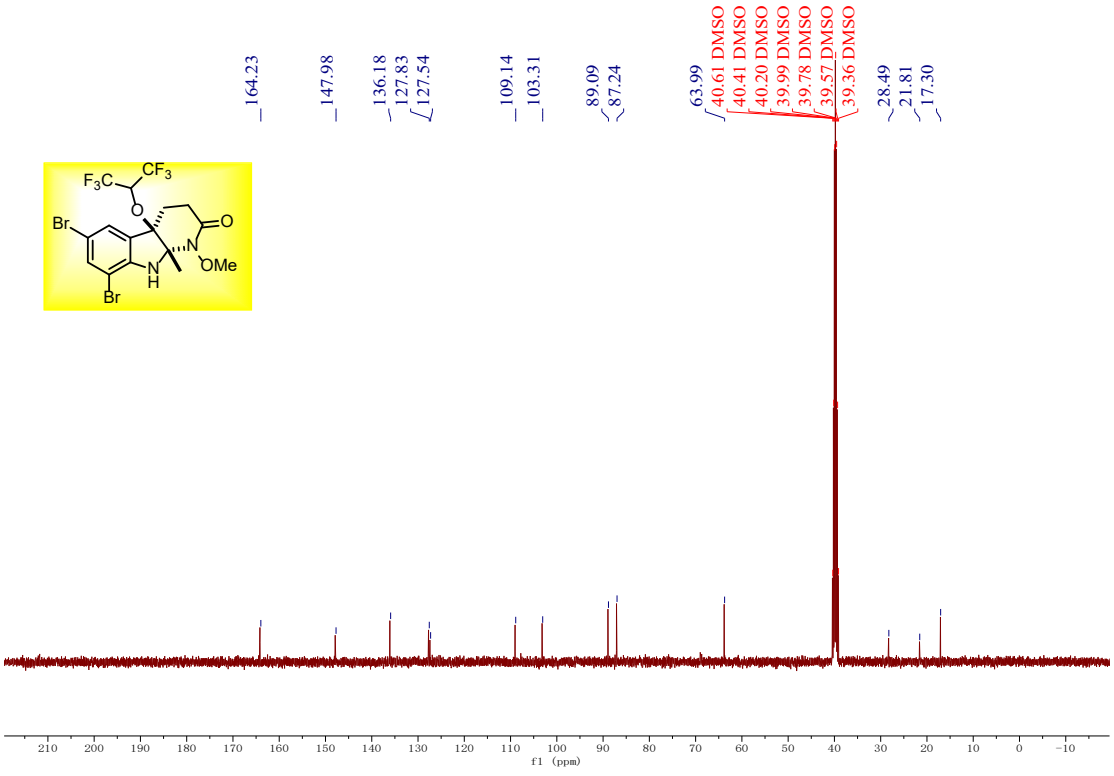
^{1}H NMR， ^{13}C NMR and ^{19}F NMR spectra of 3aa

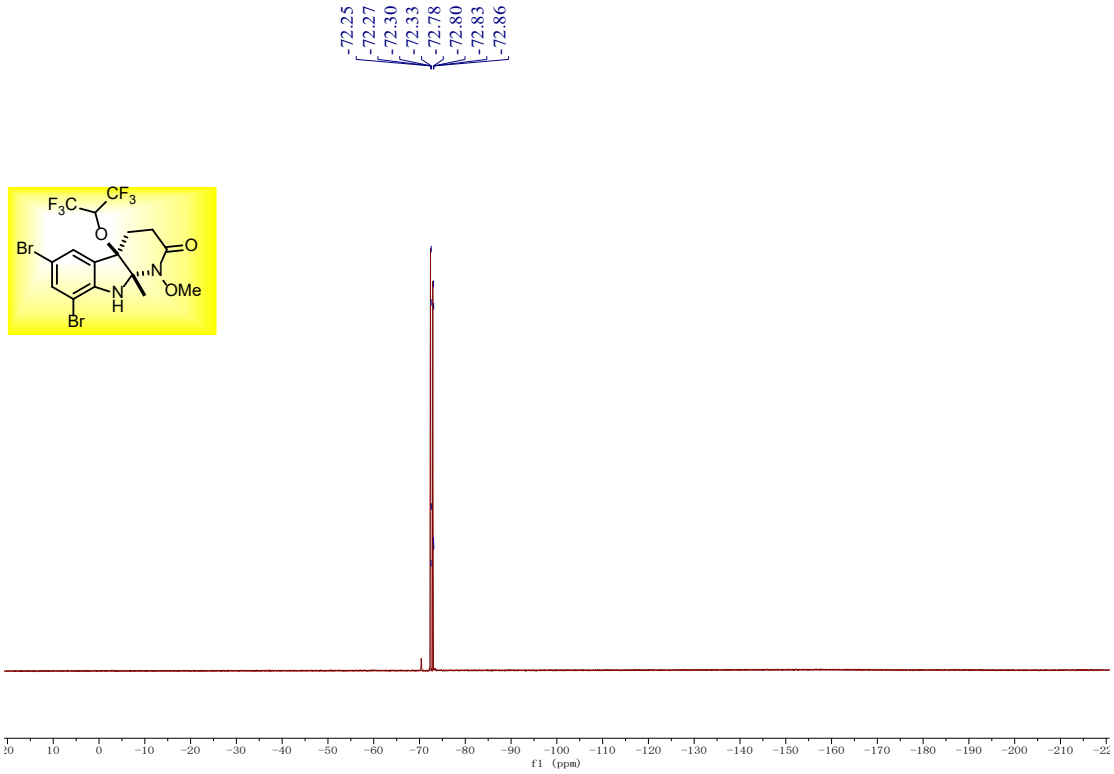




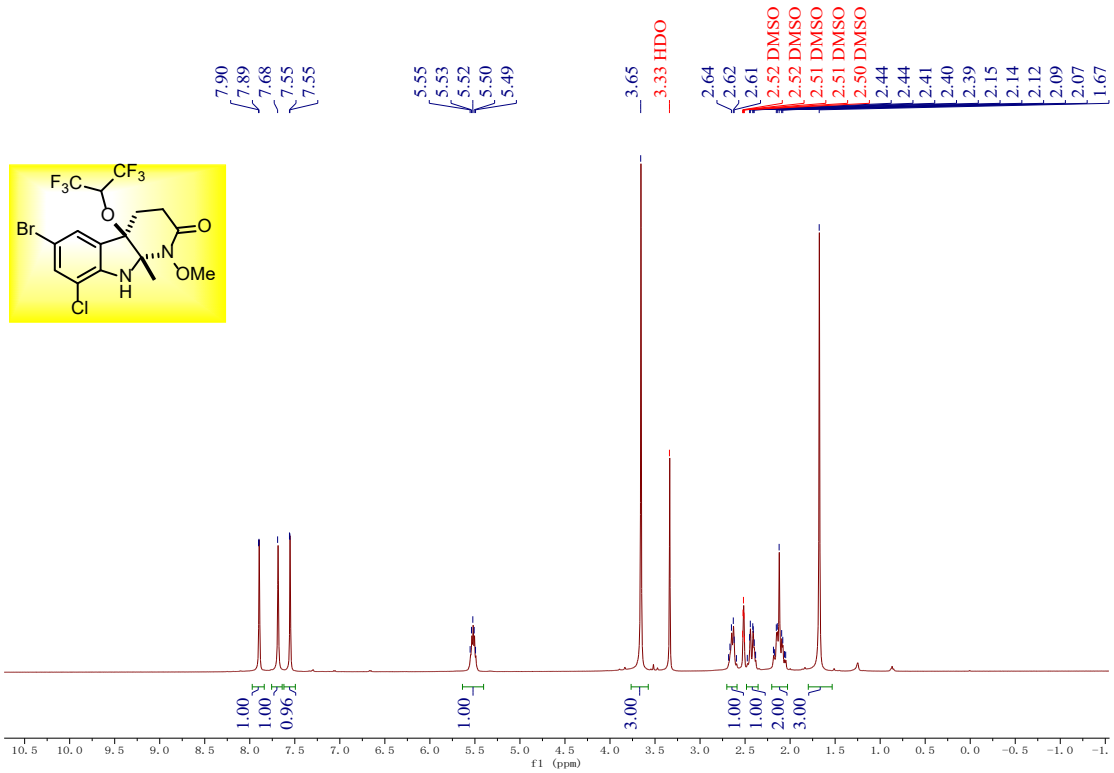
^{1}H NMR， ^{13}C NMR and ^{19}F NMR spectra of 3ab

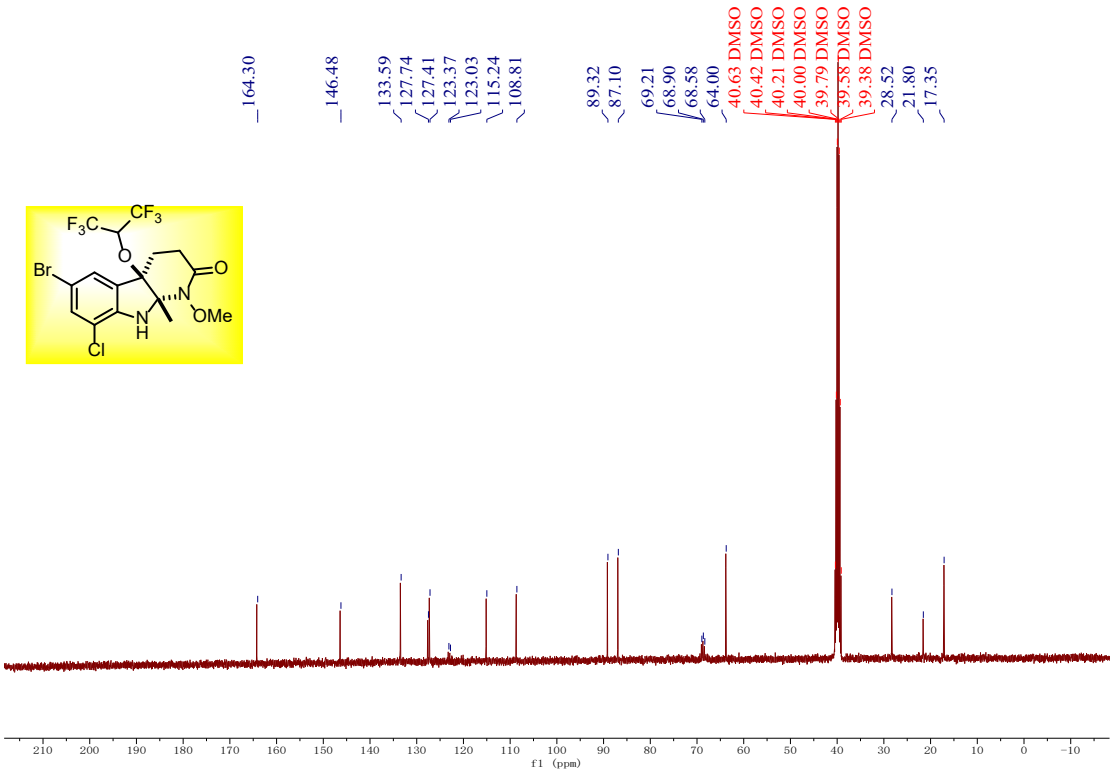

7.92
7.91
7.66
7.66
7.51
5.55
5.53
5.52
5.50
5.49
3.65
3.33 HDO
2.63
2.63
2.61
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.43
2.42
2.40
2.39
2.13
2.12
2.11
2.10
2.08
2.08
1.66
F3C
CF3
O
Br
O
N
OMe
H
Br
1.00
1.00
1.00
1.00
3.00
1.00
1.01
2.00
3.00
f1 (ppm)

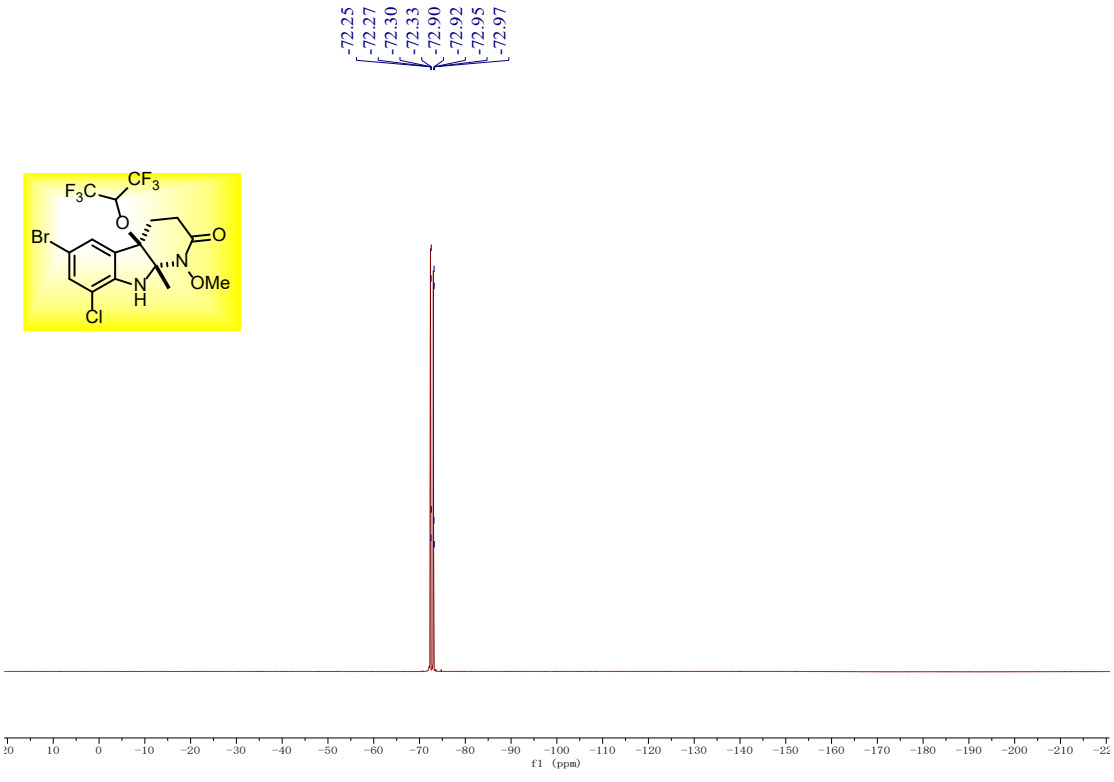

164.23
147.98
136.18
127.83
127.54
109.14
103.31
89.09
87.24
63.99
40.61 DMSO
40.41 DMSO
40.20 DMSO
39.99 DMSO
39.78 DMSO
39.57 DMSO
39.36 DMSO
28.49
21.81
17.30
F3C
CF3
O
Br
O
N
OMe
H
Br
f1 (ppm)



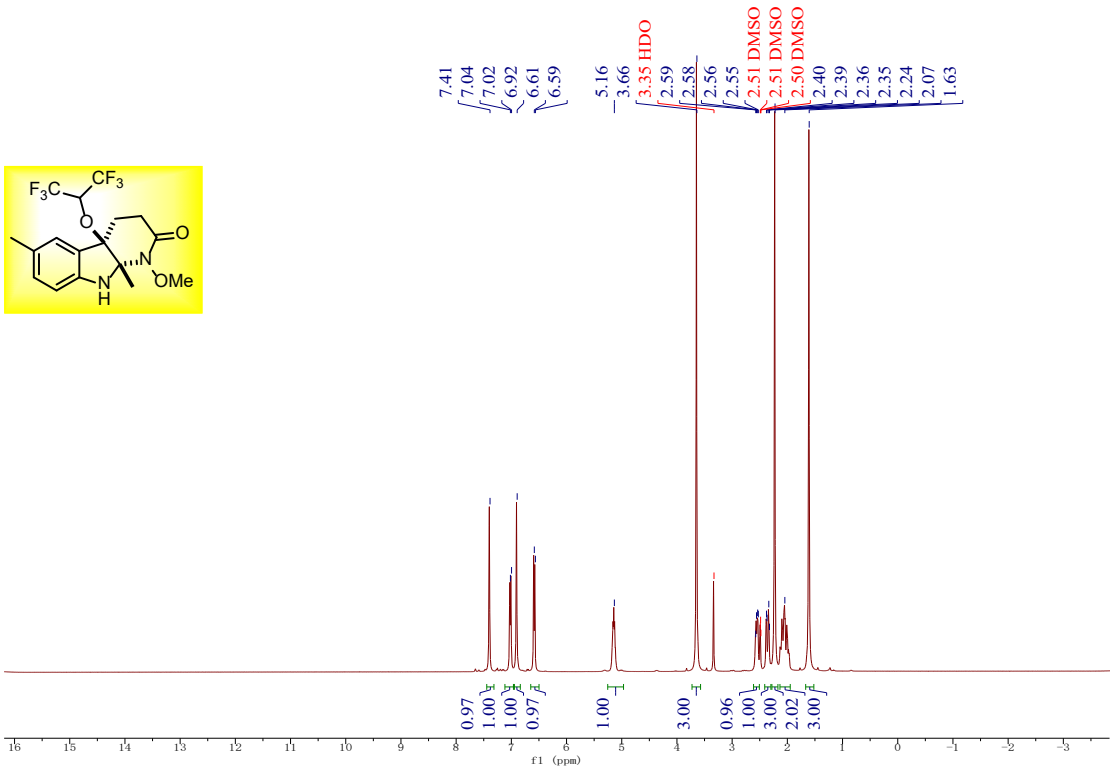
^{1}H NMR， ^{13}C NMR and ^{19}F NMR spectra of 3ac







^{1}H NMR， ^{13}C NMR and ^{19}F NMR spectra of 3ad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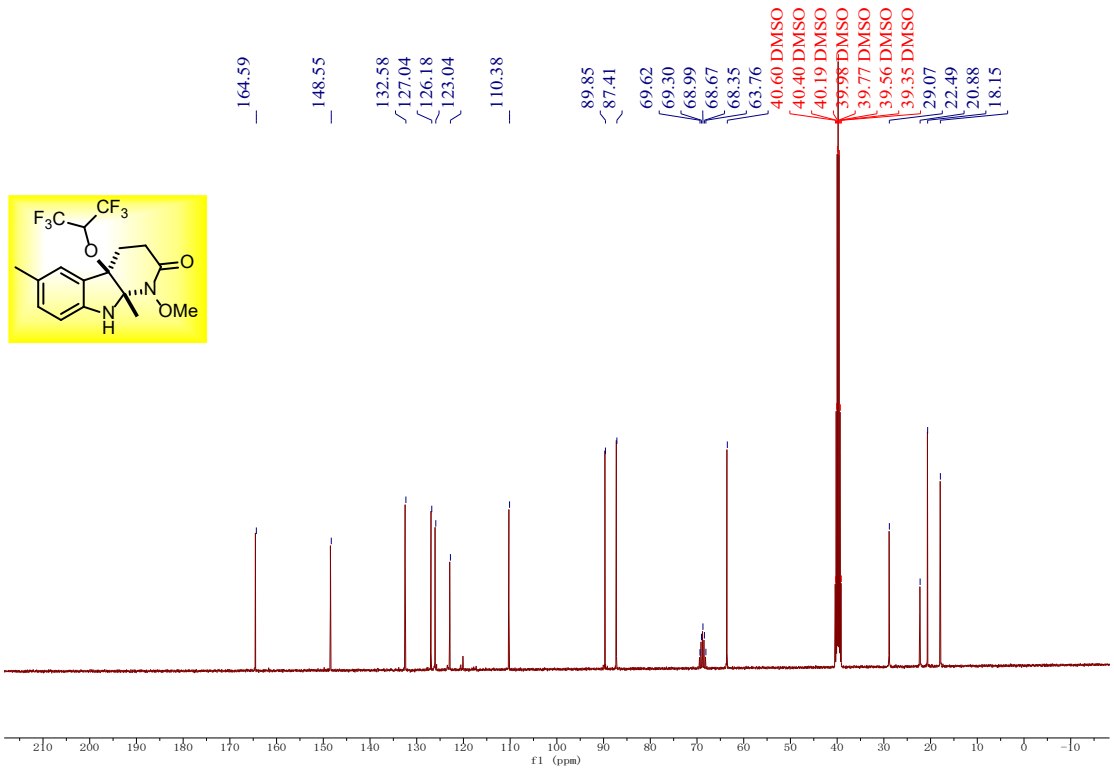
7.04
7.02
6.92
6.61
6.59
5.16
3.66
3.35 HDO
2.59
2.58
2.56
2.55
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.40
2.39
2.36
2.35
2.24
2.07
1.63
0.97
1.00
1.00
0.97
1.00
3.00
0.96
1.00
3.00
2.02
3.00
f1 (ppm)


164.59
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89.85
87.41
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68.99
68.67
68.35
63.76
40.60 DMSO
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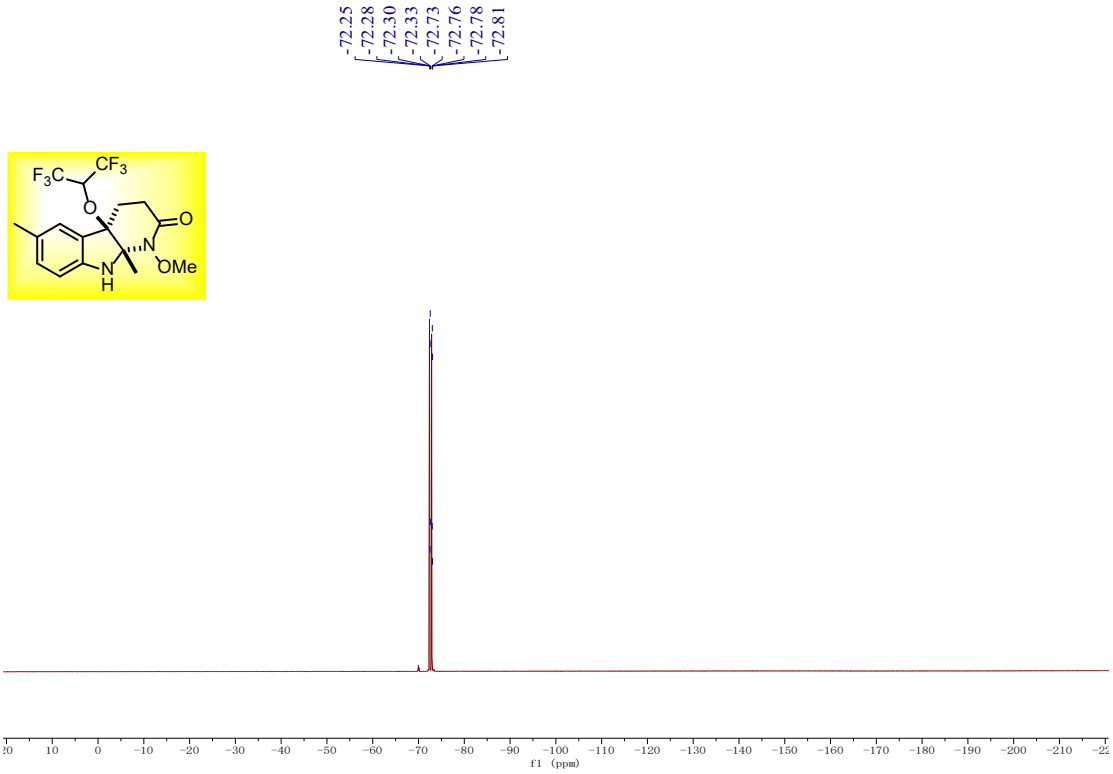
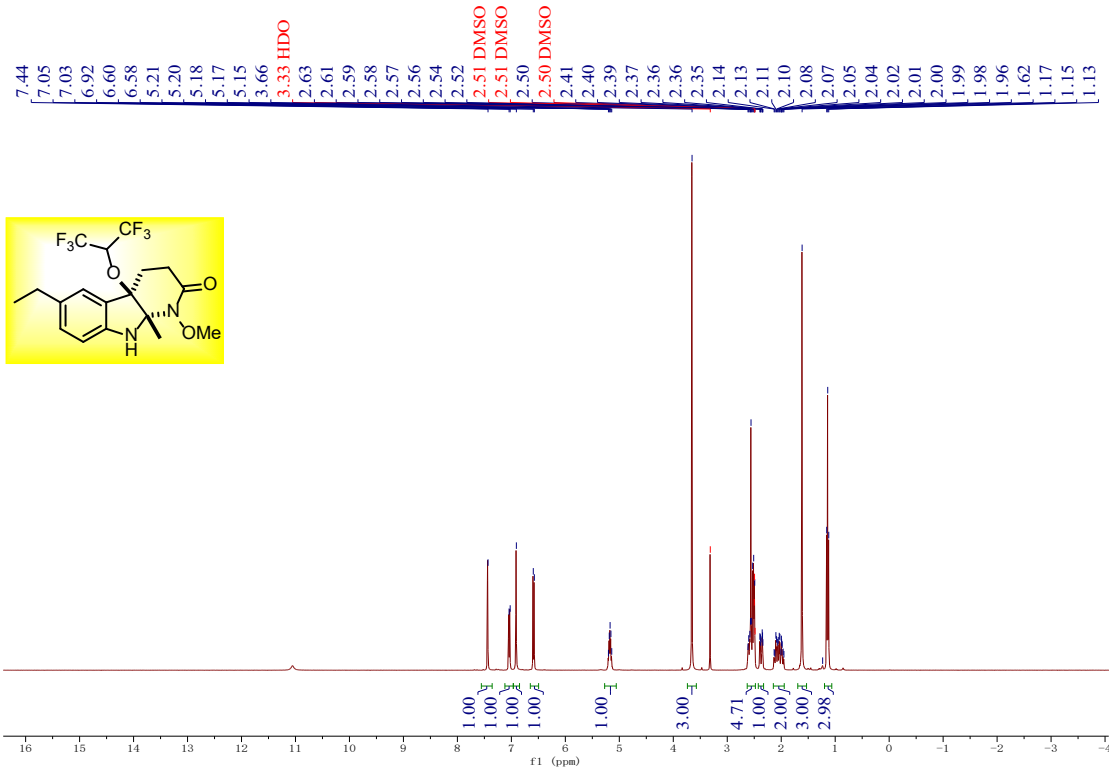
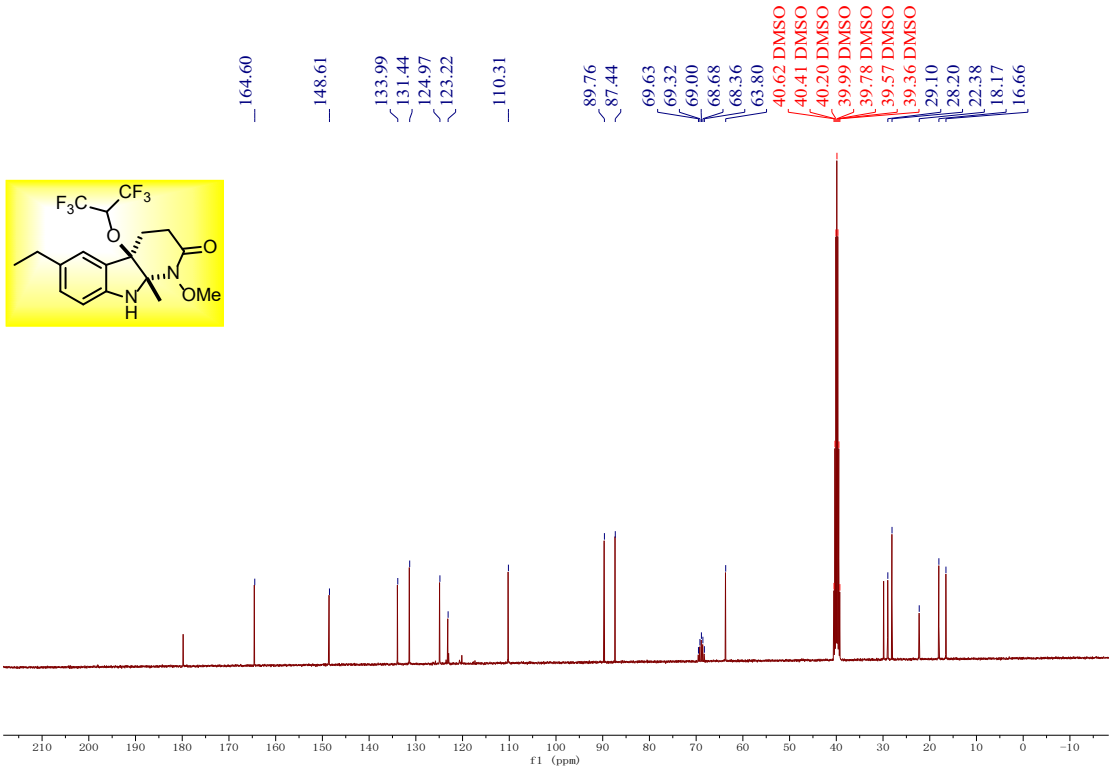
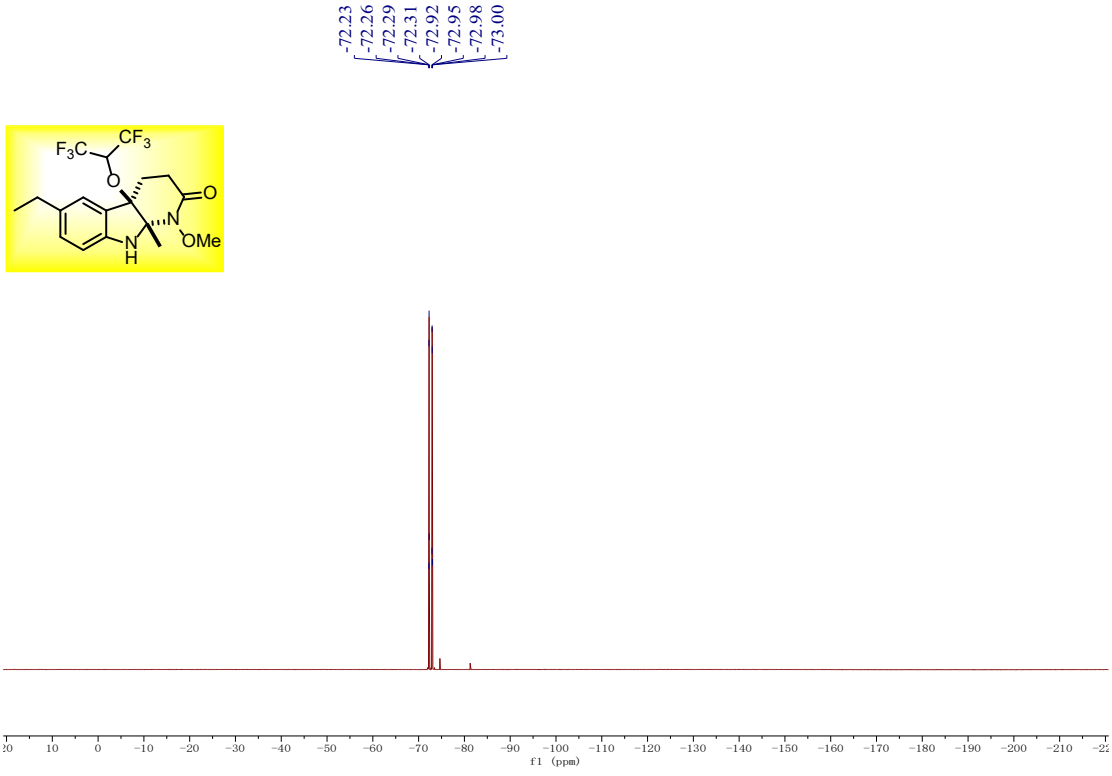
29.07
22.49
20.88
18.15
f1 (ppm)



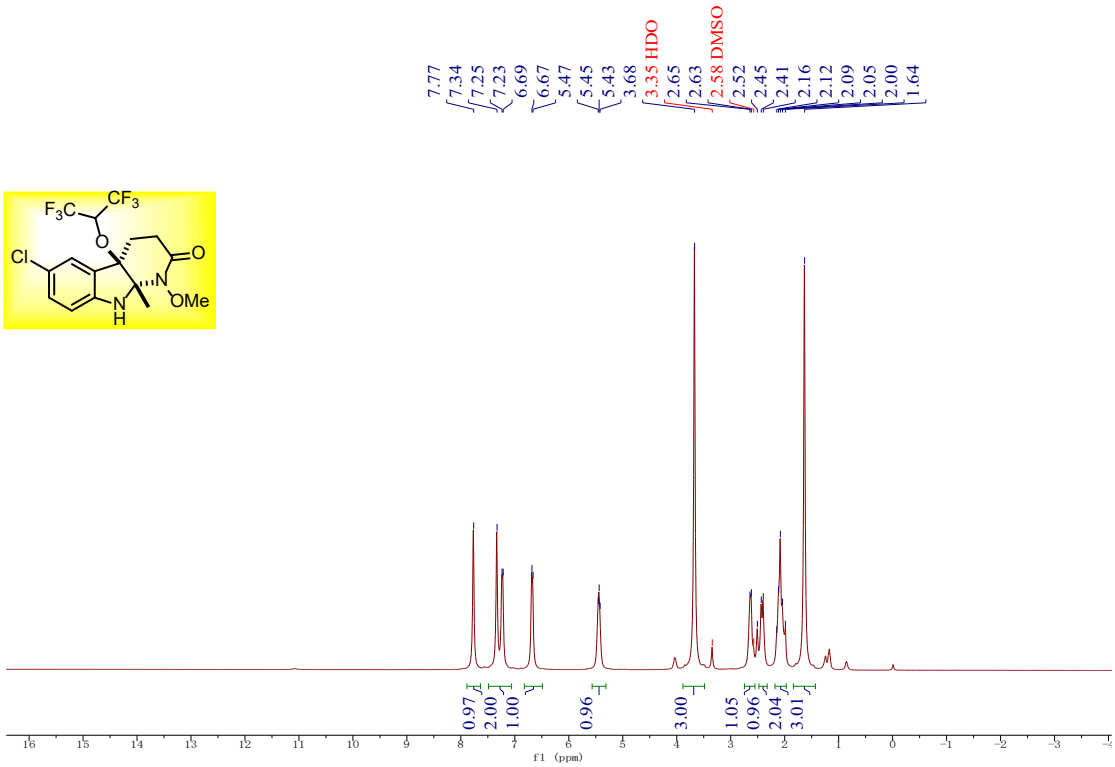
^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 3ae

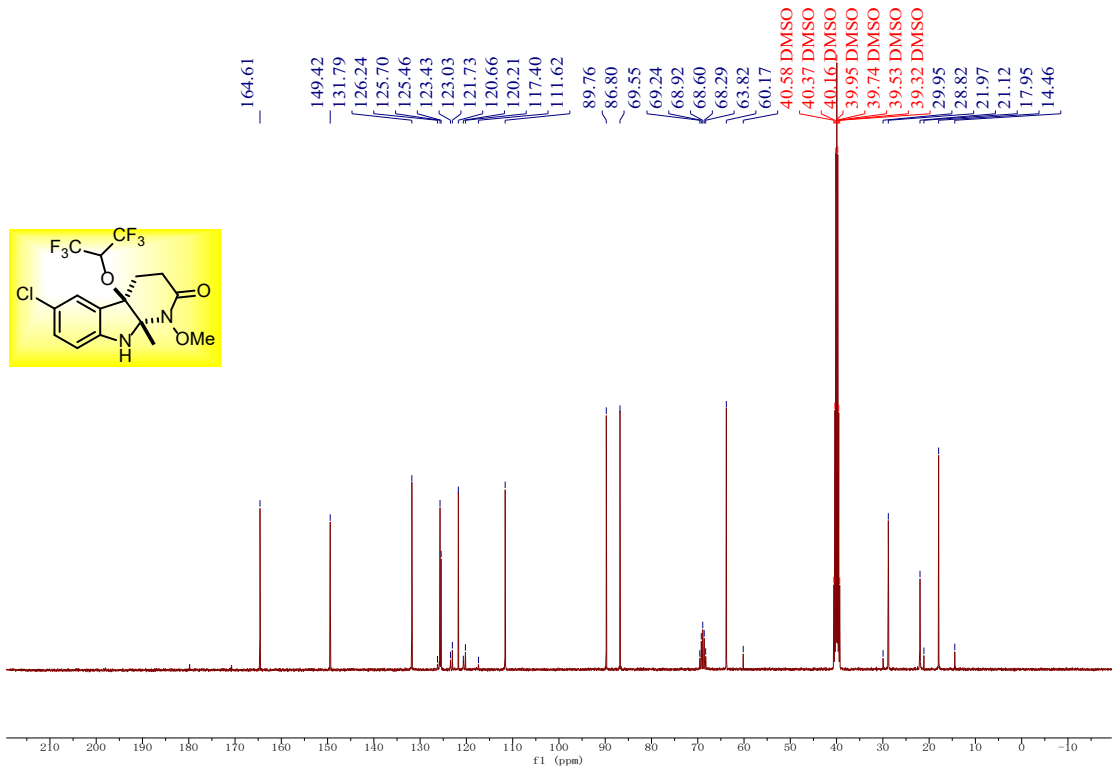






^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 3af


7.77
7.34
7.25
7.23
6.69
6.67
5.47
5.45
5.43
3.68
3.35 HDO
2.65
2.63
2.58 DMSO
2.52
2.45
2.41
2.16
2.12
2.09
2.05
2.00
1.64
0.97
2.00
1.00
0.96
3.00
1.05
0.96
2.04
3.01
f1 (ppm)


164.61
149.42
131.79
126.24
125.70
125.46
123.43
123.03
121.73
120.66
120.21
117.40
111.62
89.76
86.80
69.55
69.24
68.92
68.60
68.29
63.82
60.17
40.58 DMSO
40.37 DMSO
40.16 DMSO
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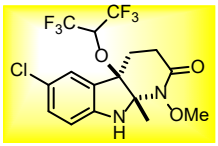
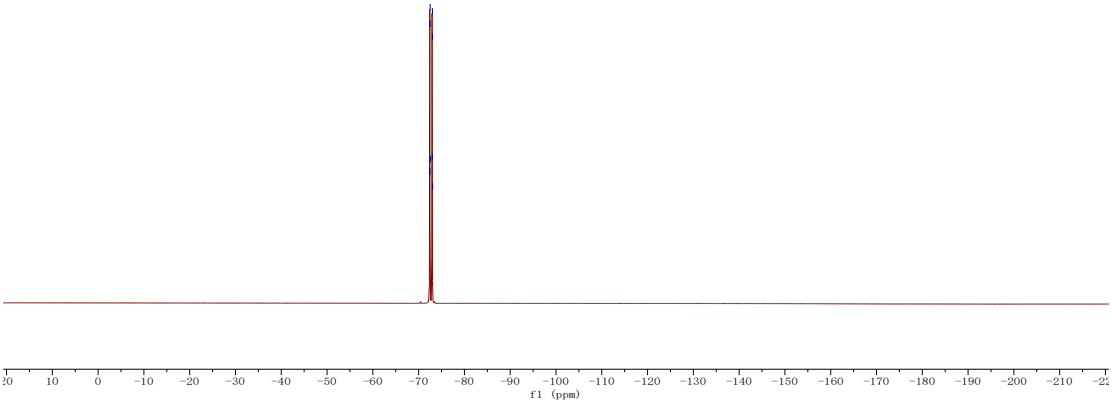
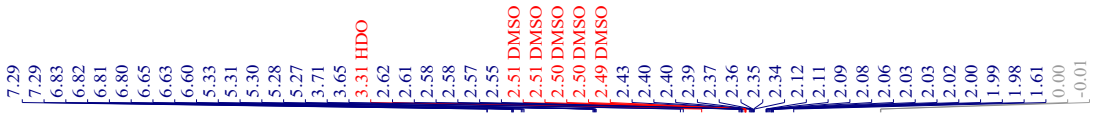
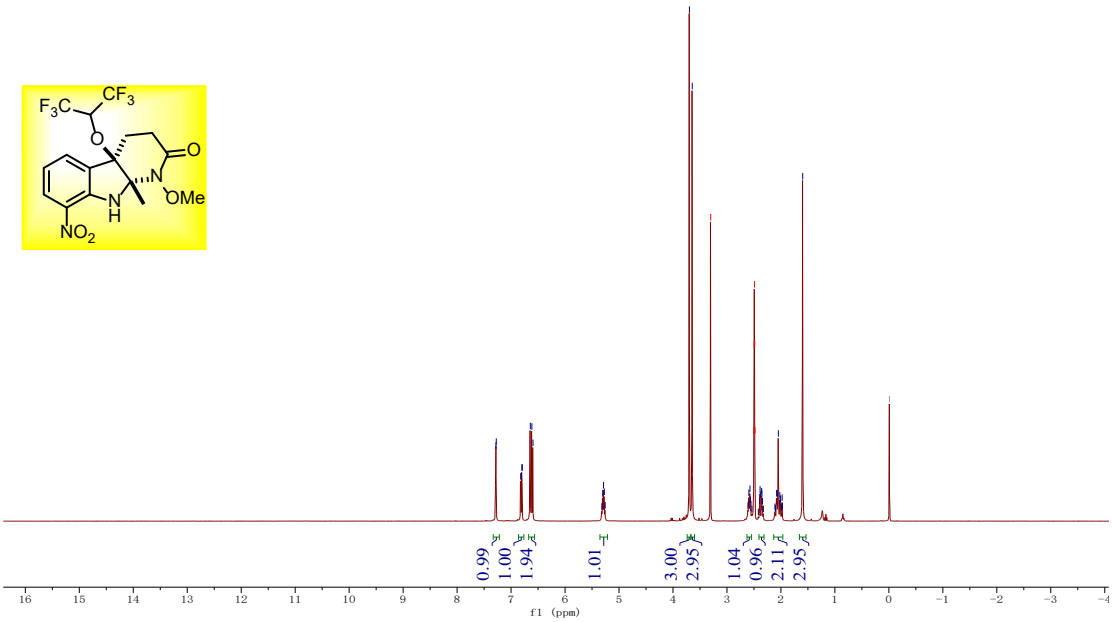
17.95
14.46
f1 (ppm)

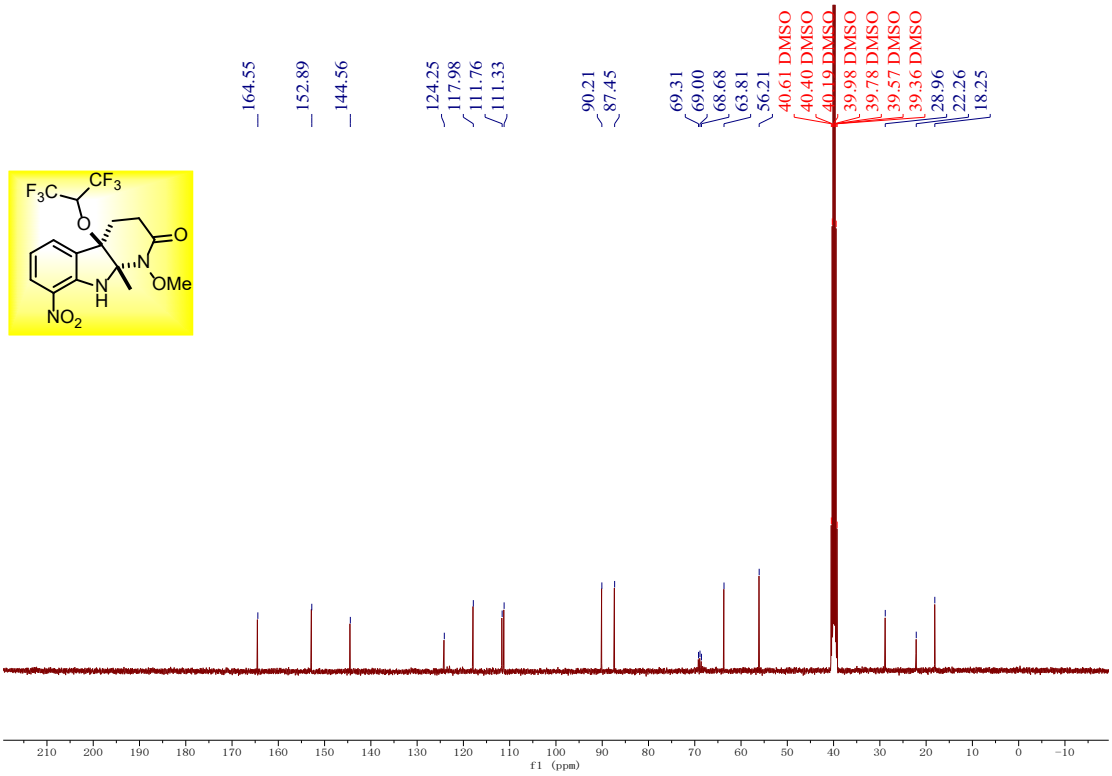


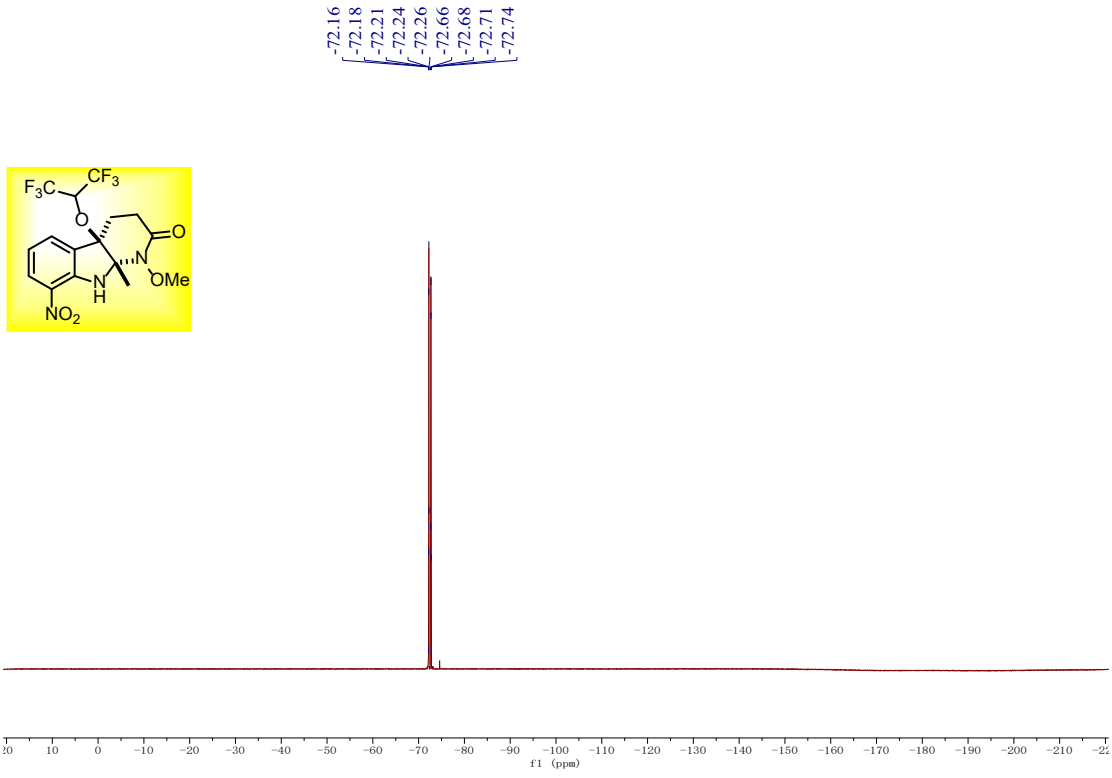


^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 3ag

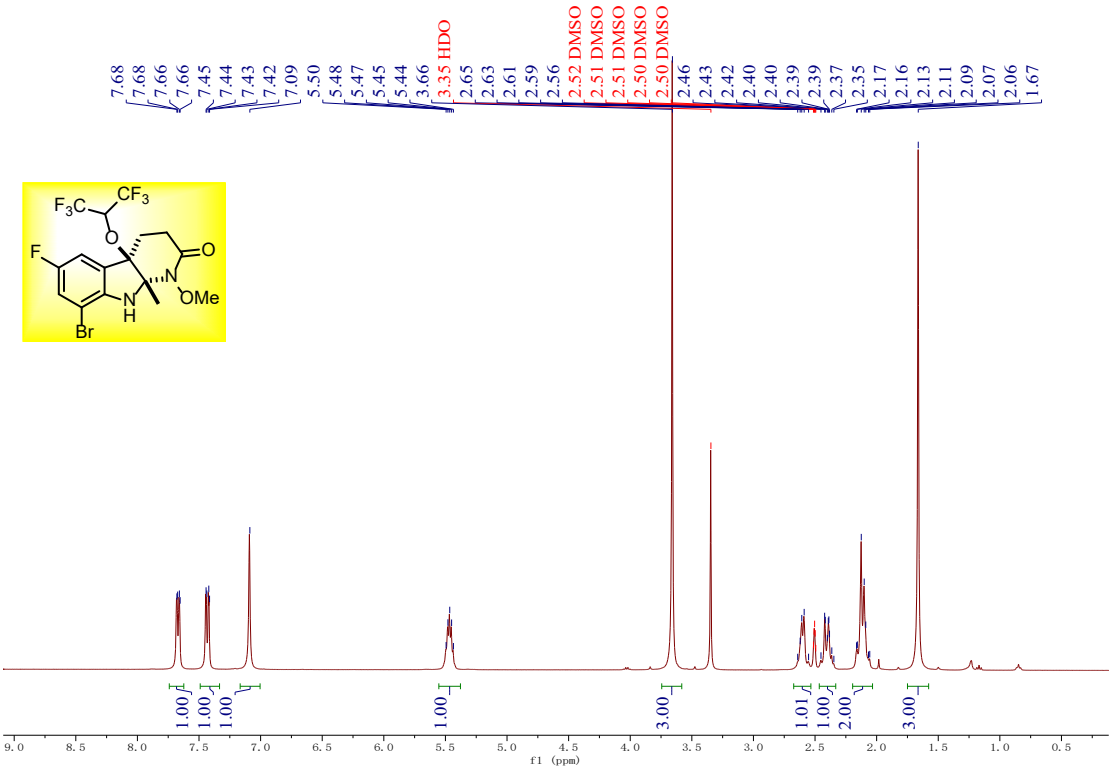


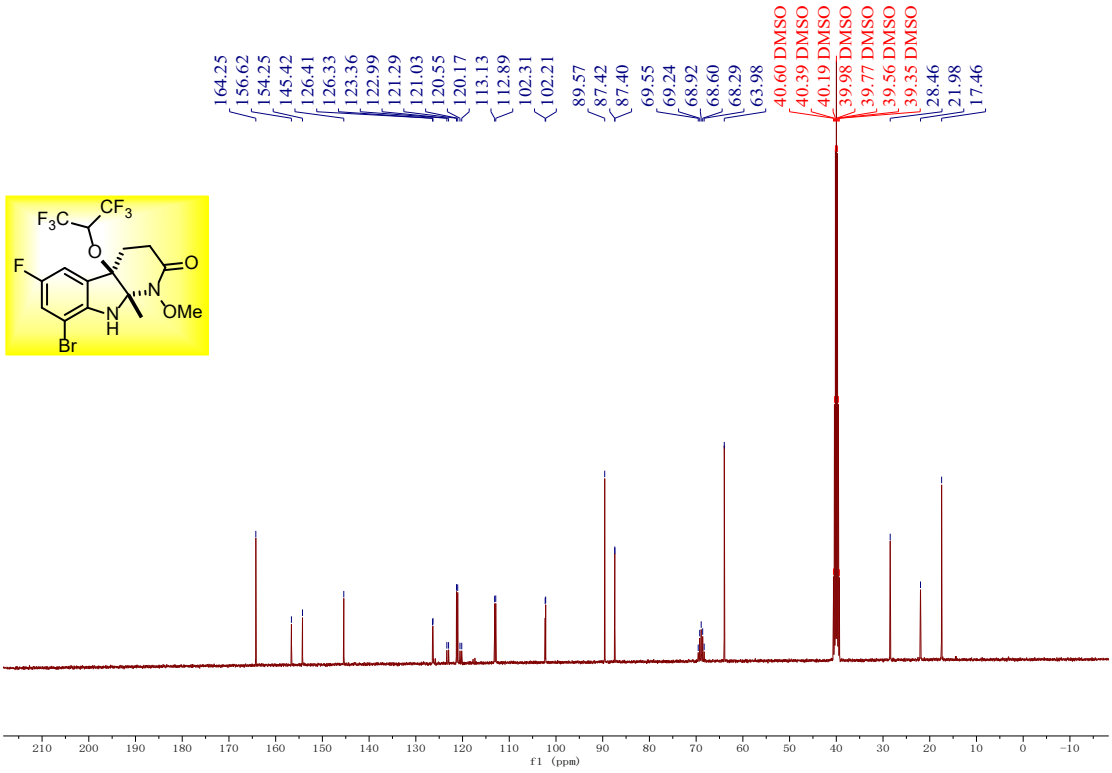


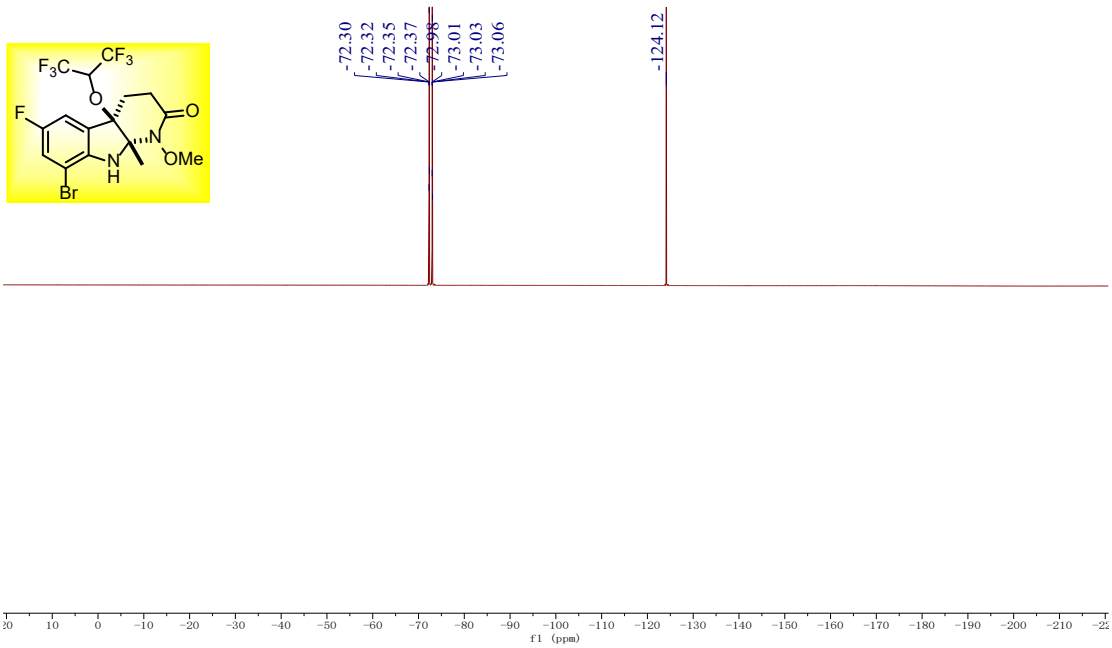




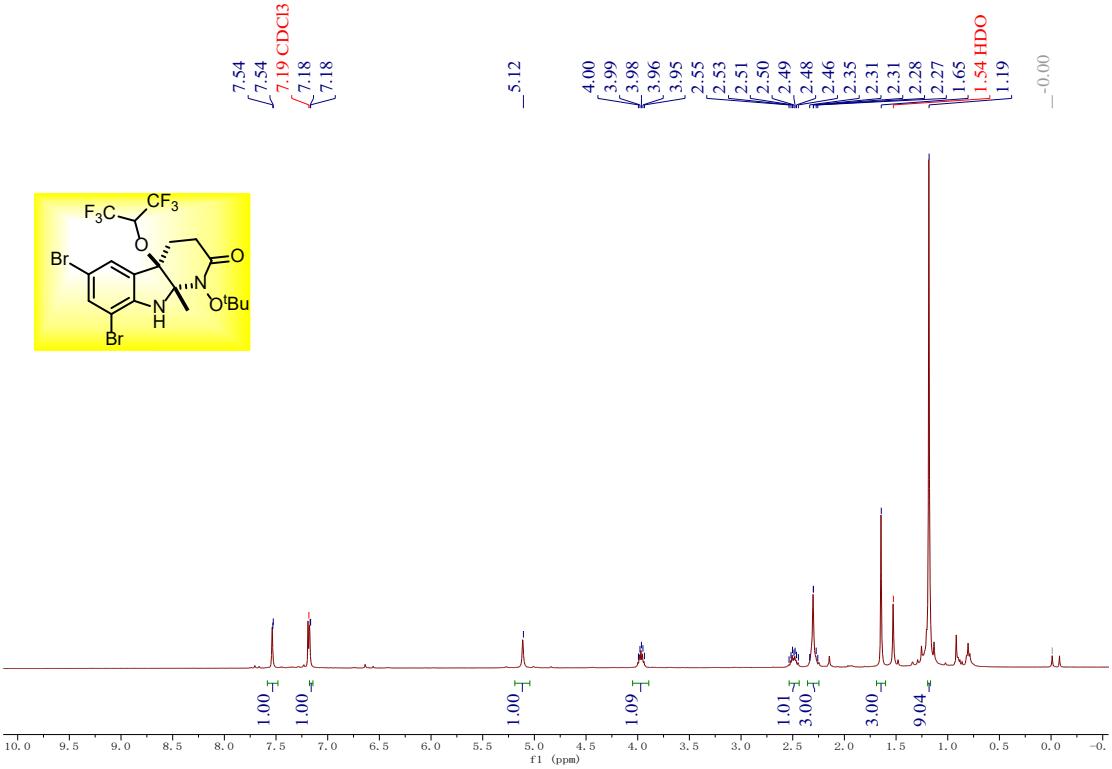
^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 3ah

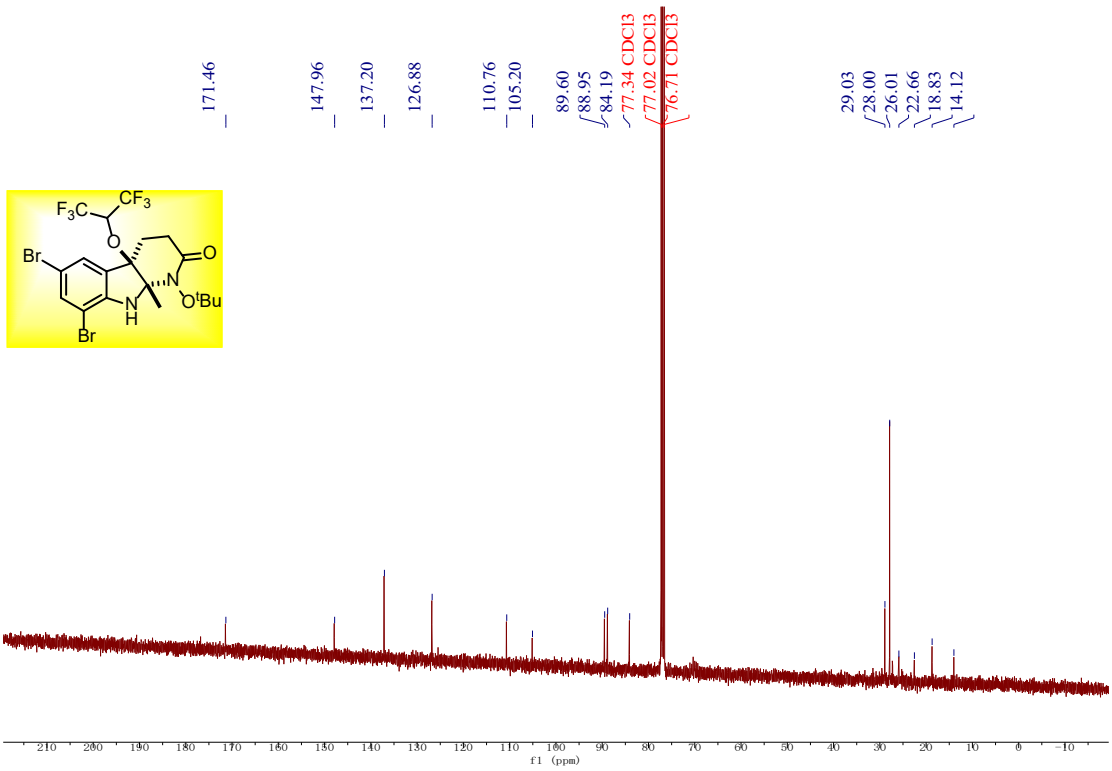

7.68
7.68
7.66
7.66
7.45
7.44
7.43
7.42
7.09
5.50
5.48
5.47
5.45
5.44
3.66
3.35 HDO
2.65
2.63
2.61
2.59
2.56
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.46
2.43
2.42
2.40
2.40
2.39
2.39
2.37
2.35
2.17
2.16
2.13
2.11
2.09
2.07
2.06
1.67
F3C
CF3
O
F
O
N
OMe
H
Br
1.00
1.00
1.00
1.00
3.00
1.01
1.00
2.00
3.00
f1 (ppm)

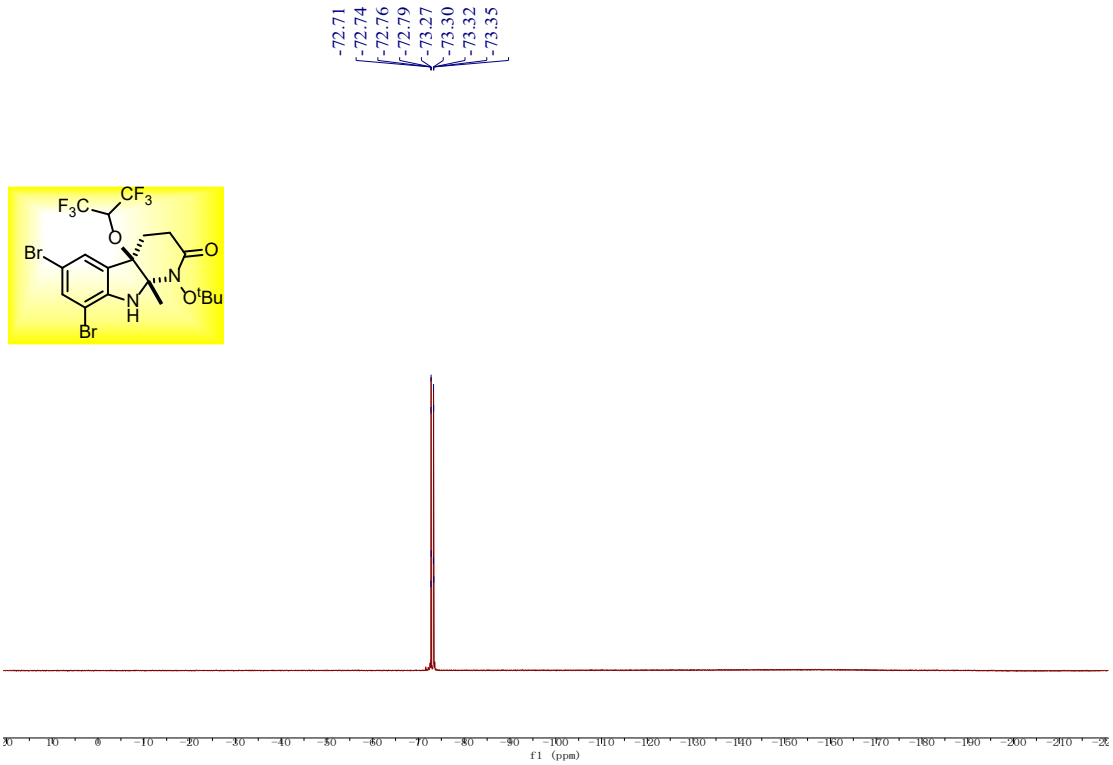

164.25
156.62
154.25
145.42
126.41
126.33
123.36
122.99
121.29
121.03
120.55
120.17
113.13
112.89
102.31
102.21
89.57
87.42
87.40
69.55
69.24
68.92
68.60
68.29
63.98
40.60 DMSO
40.39 DMSO
40.19 DMSO
39.98 DMSO
39.77 DMSO
39.56 DMSO
39.35 DMSO
28.46
21.98
17.46
F3C
CF3
O
F
O
N
OMe
H
Br
f1 (ppm)



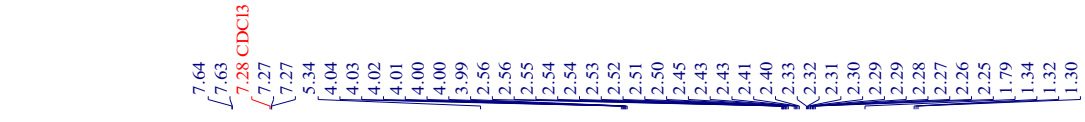
^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 3ai







^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra of 3aj


7.64
7.63
7.28 CDCl3
7.27
7.27
5.34
4.04
4.03
4.02
4.01
4.00
4.00
3.99
2.56
2.56
2.55
2.54
2.54
2.53
2.52
2.51
2.50
2.45
2.43
2.43
2.41
2.40
2.33
2.32
2.31
2.30
2.29
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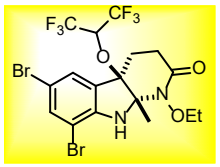
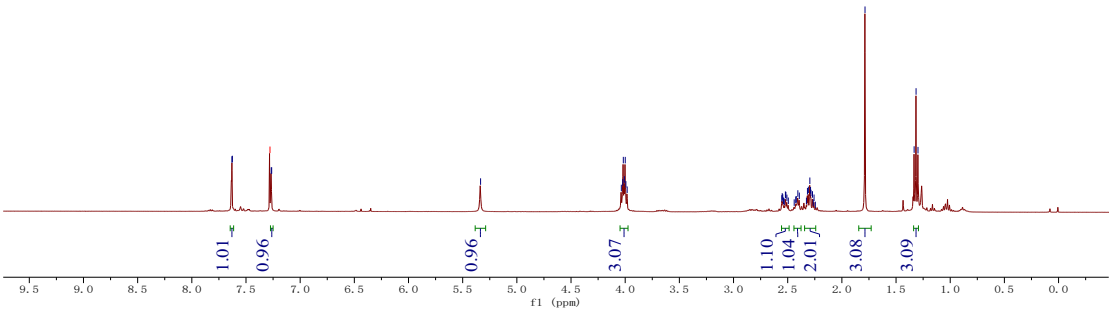
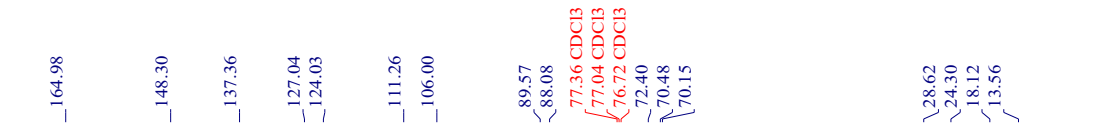
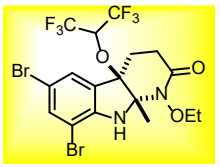
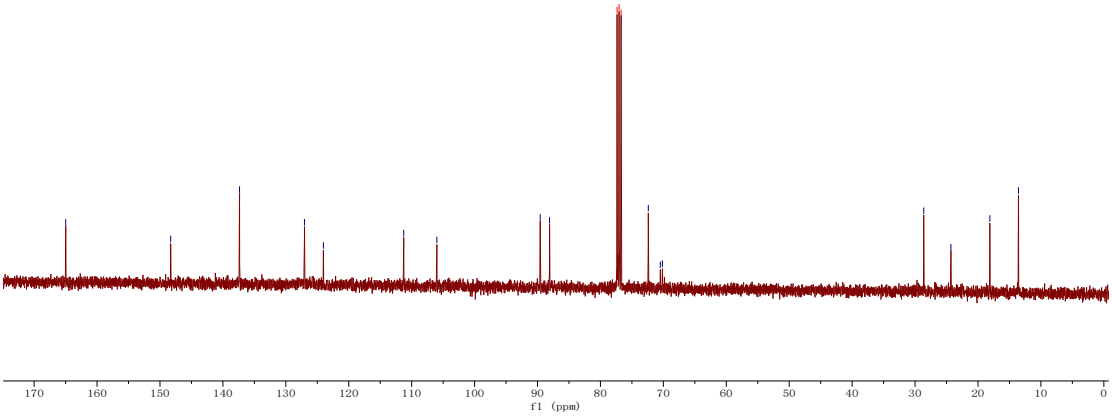
2.26
2.25
1.79
1.34
1.32
1.30

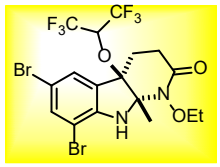

F3C
CF3
O
Br
O
N
OEt
H
Br

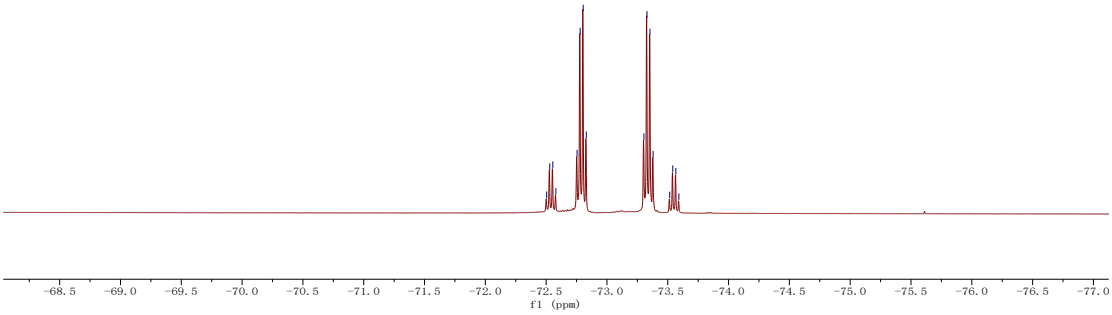

1.01
0.96
0.96
3.07
1.10
1.04
2.01
3.08
3.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


164.98
148.30
137.36
127.04
124.03
111.26
106.00
89.57
88.08
77.36 CDCl3
77.04 CDCl3
76.72 CDCl3
72.40
70.48
70.15
28.62
24.30
18.12
13.56

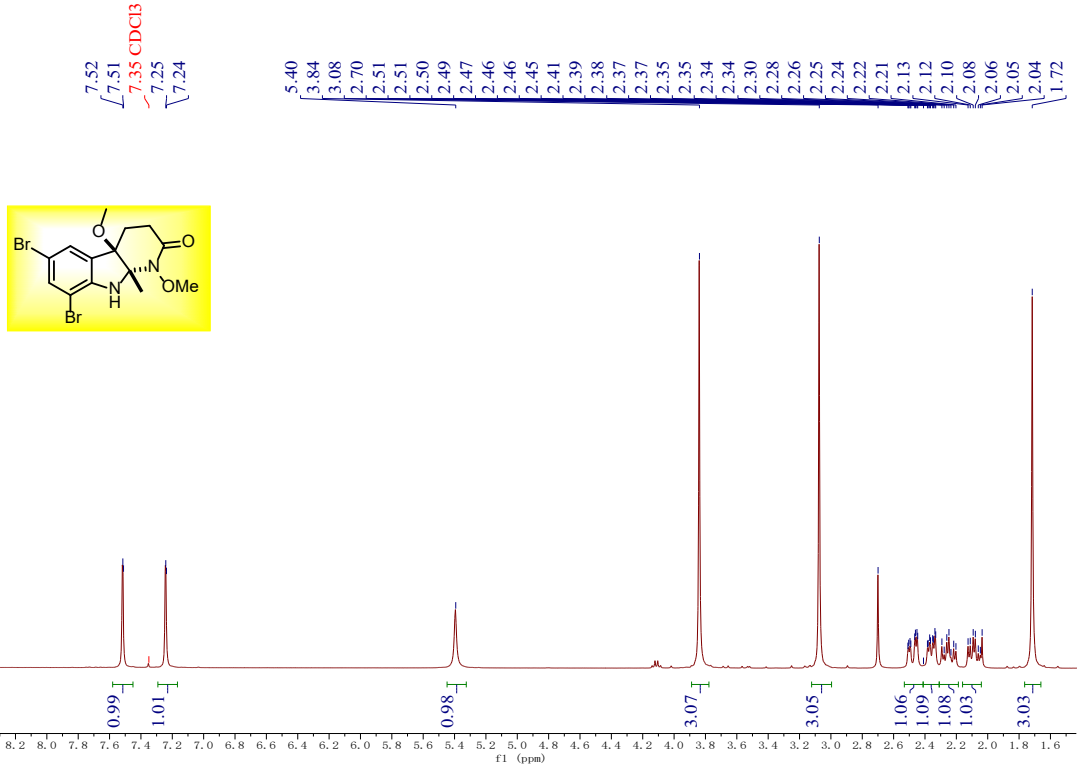

F3C
CF3
O
Br
O
N
OEt
H
Br

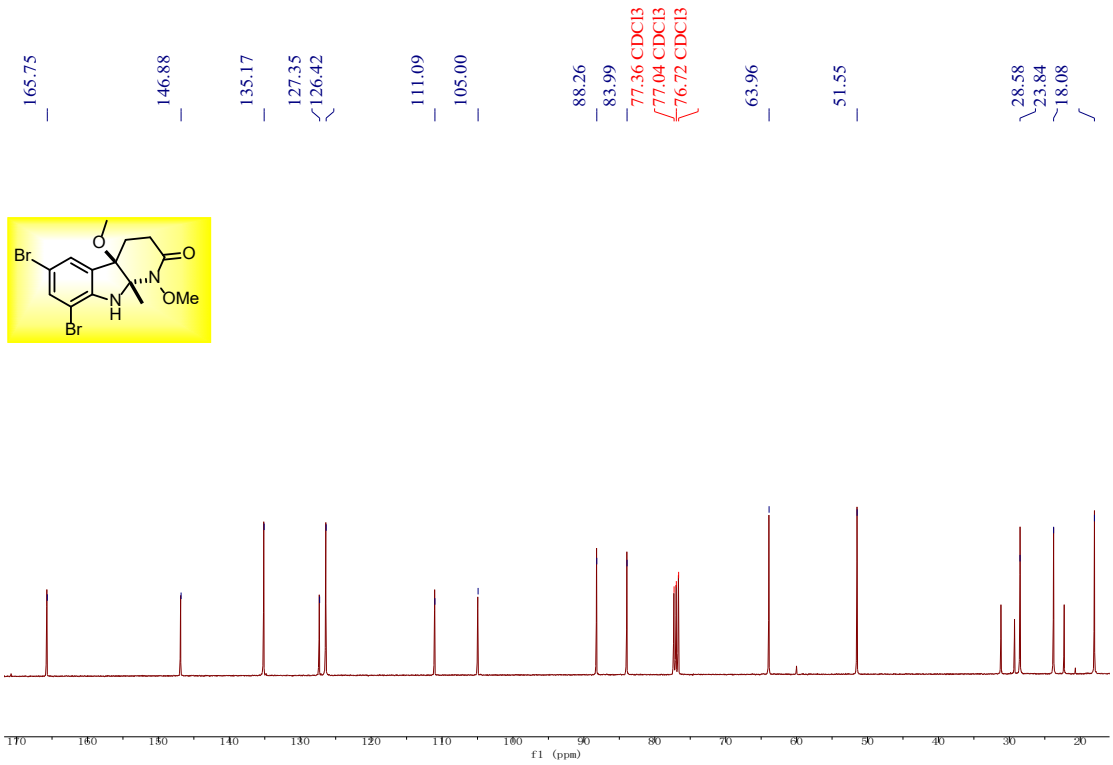

170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



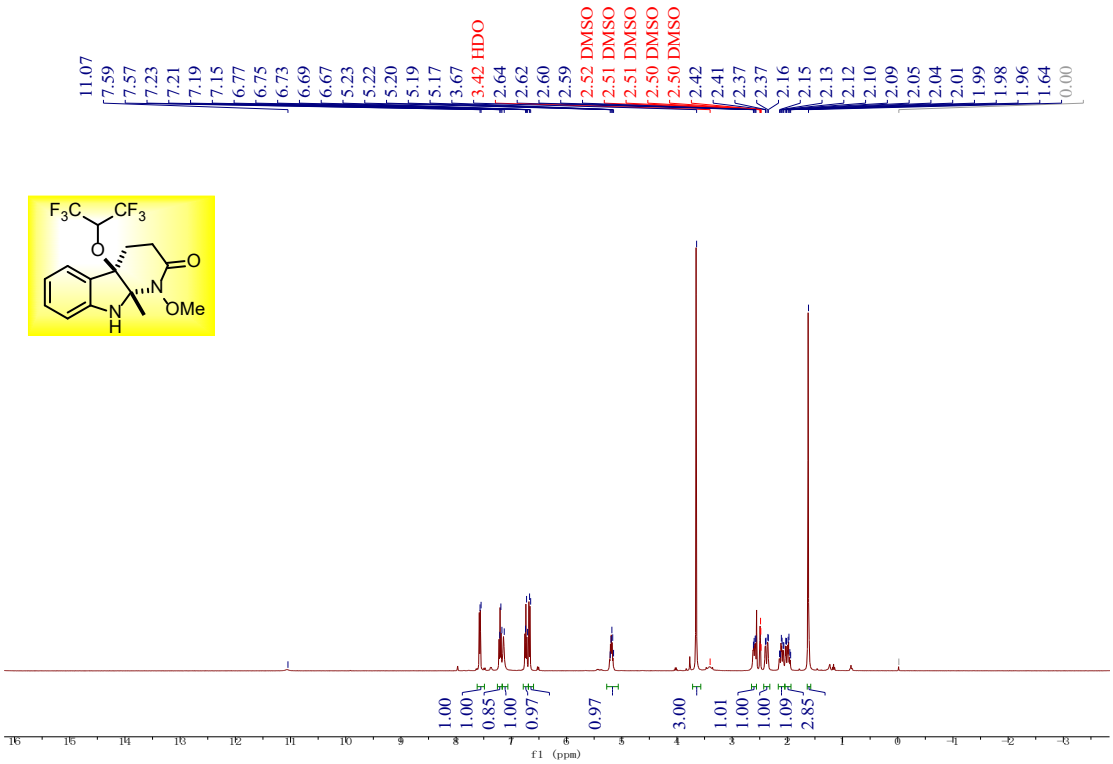


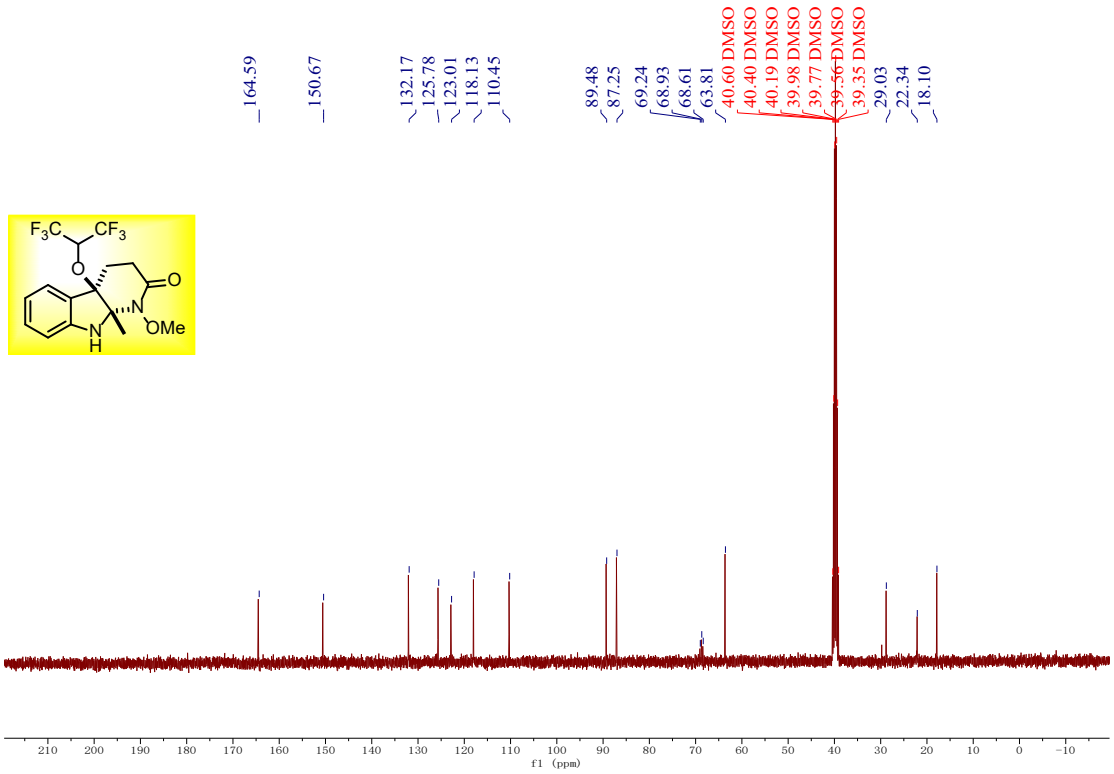
^{1}H NMR ^{13}C NMR spectra of 3am

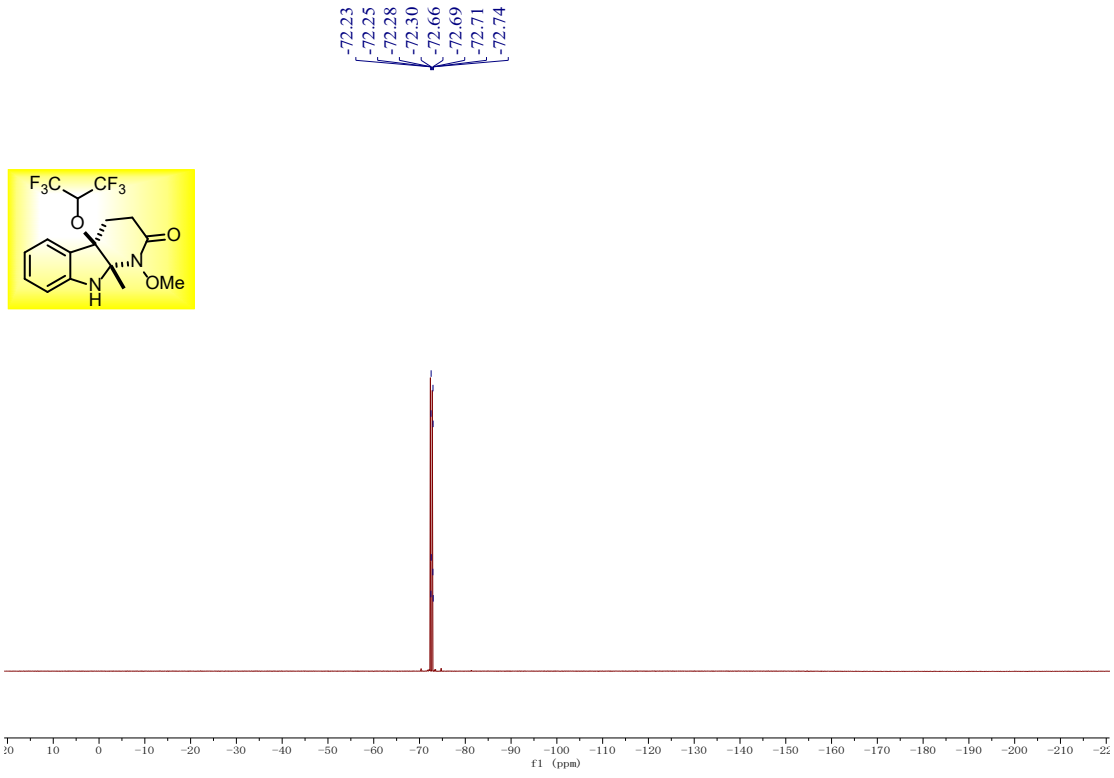




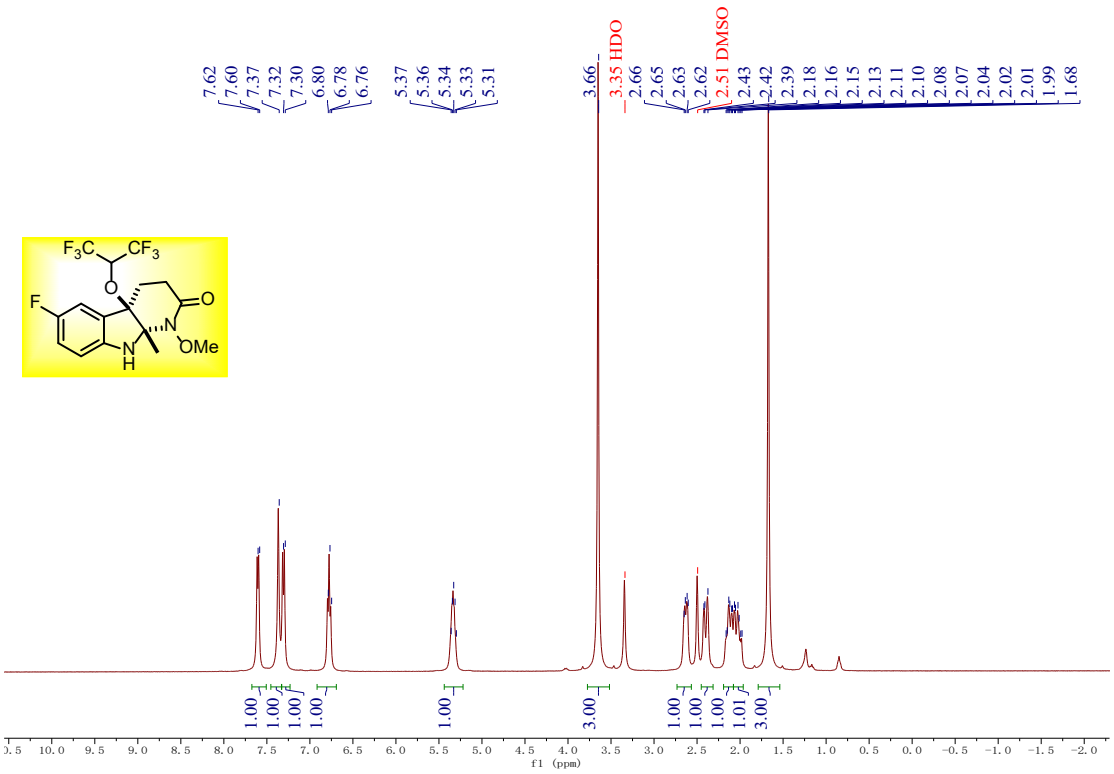
^{1}H NMR ^{13}C NMR and ^{19}F NMR spectra of 3ba

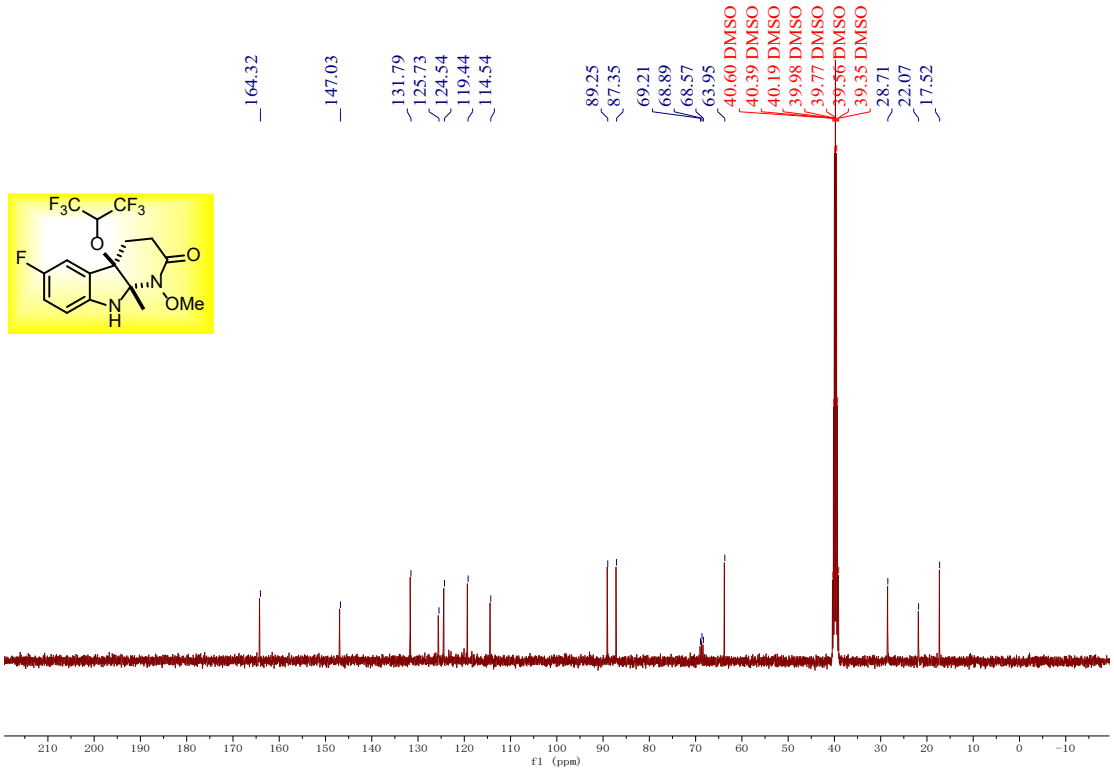


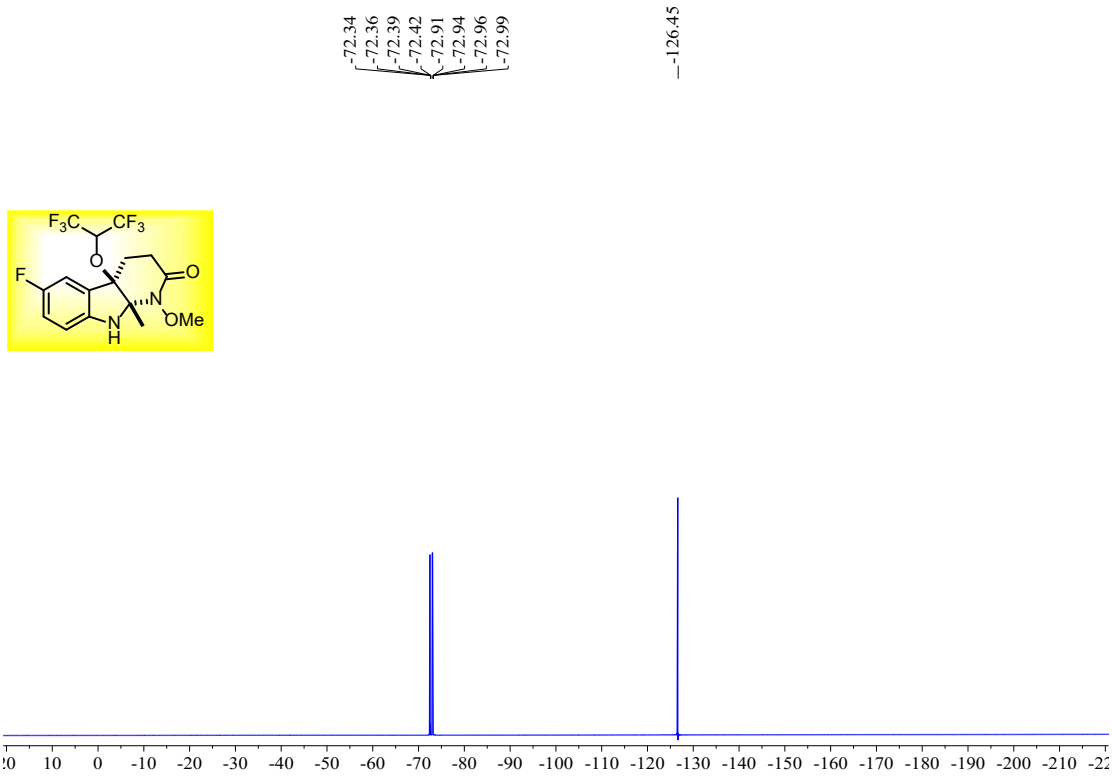




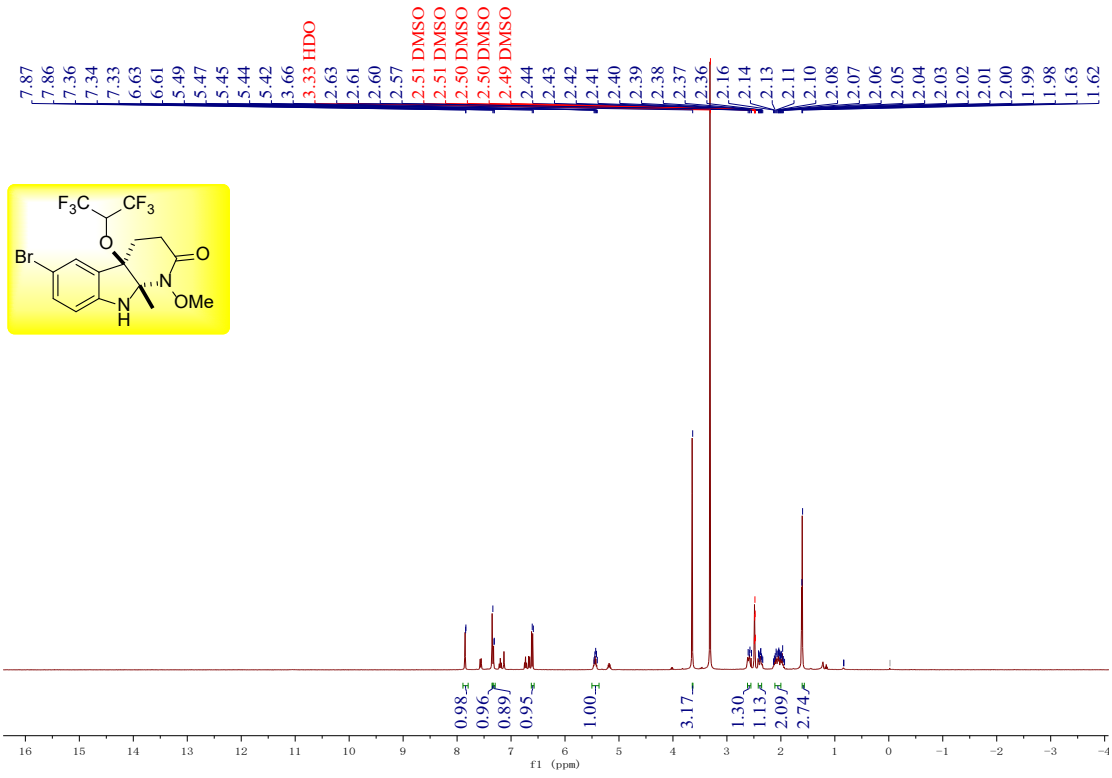
^{1}H NMR ^{13}C NMR and ^{19}F NMR spectra of 3bb

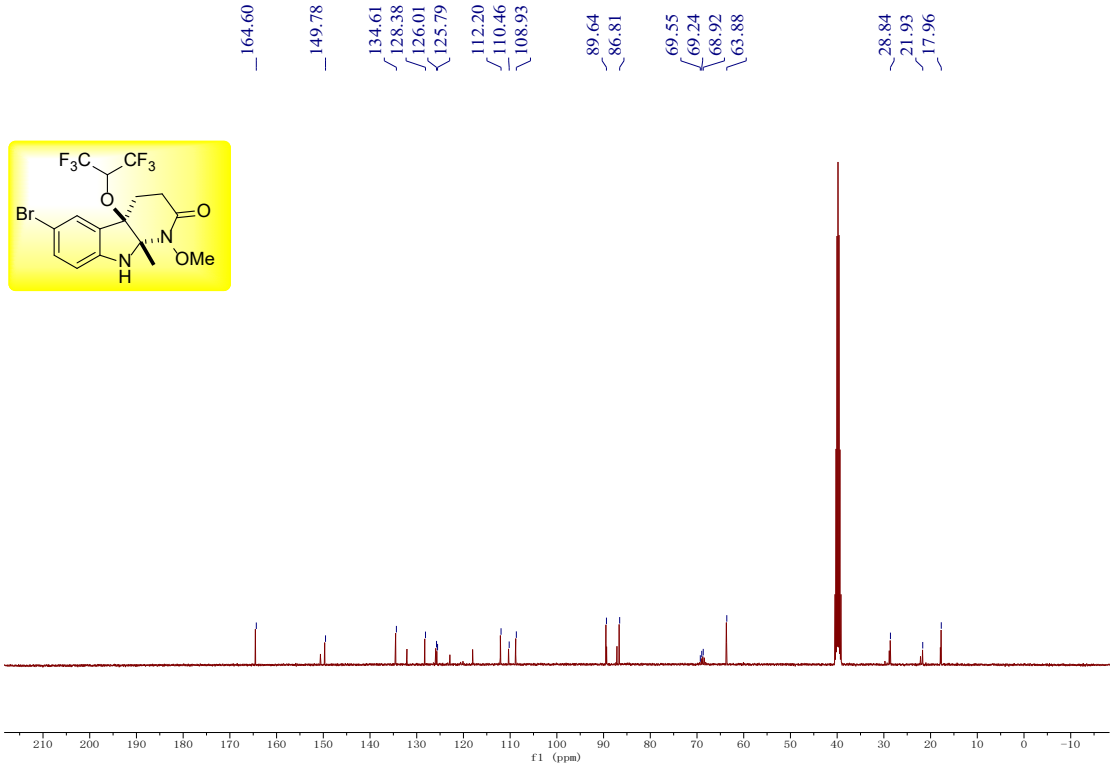

7.62
7.60
7.37
7.32
7.30
6.80
6.78
6.76
5.37
5.36
5.34
5.33
5.31
3.66
3.35 HDO
2.66
2.65
2.63
2.62
2.51 DMSO
2.43
2.42
2.39
2.18
2.16
2.15
2.13
2.11
2.10
2.08
2.07
2.04
2.02
2.01
1.99
1.68
F3C
CF3
O
F
O
N
OMe
N
H
1.00
1.00
1.00
1.00
1.00
3.00
1.00
1.00
1.00
1.01
3.00
f1 (ppm)

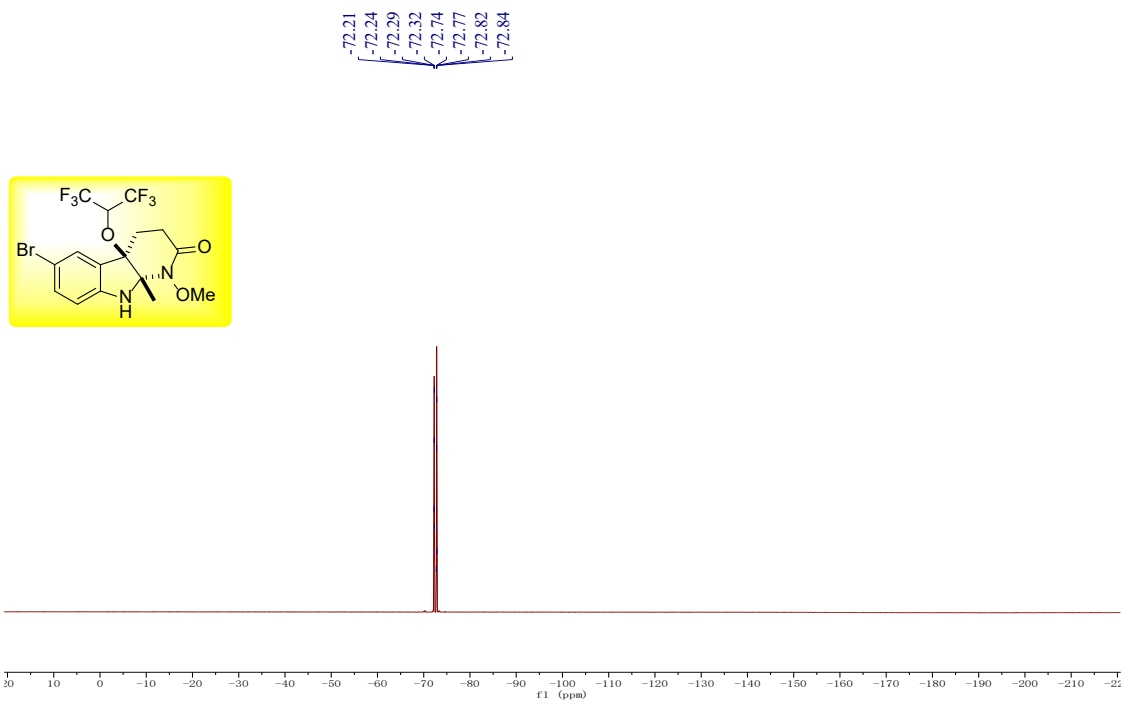

164.32
147.03
131.79
125.73
124.54
119.44
114.54
89.25
87.35
69.21
68.89
68.57
63.95
40.60 DMSO
40.39 DMSO
40.19 DMSO
39.98 DMSO
39.77 DMSO
39.56 DMSO
39.35 DMSO
28.71
22.07
17.52
F3C
CF3
O
F
O
N
OMe
N
H
f1 (ppm)



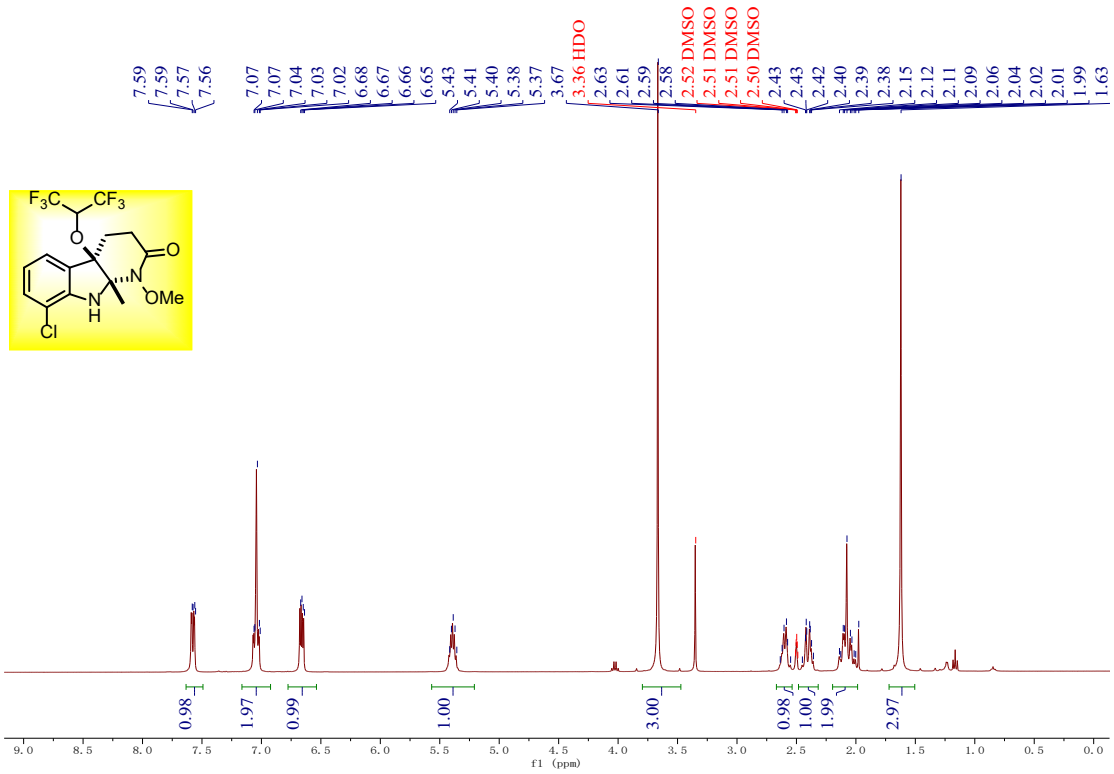
^{1}H NMR ^{13}C NMR and ^{19}F NMR spectra of 3bc

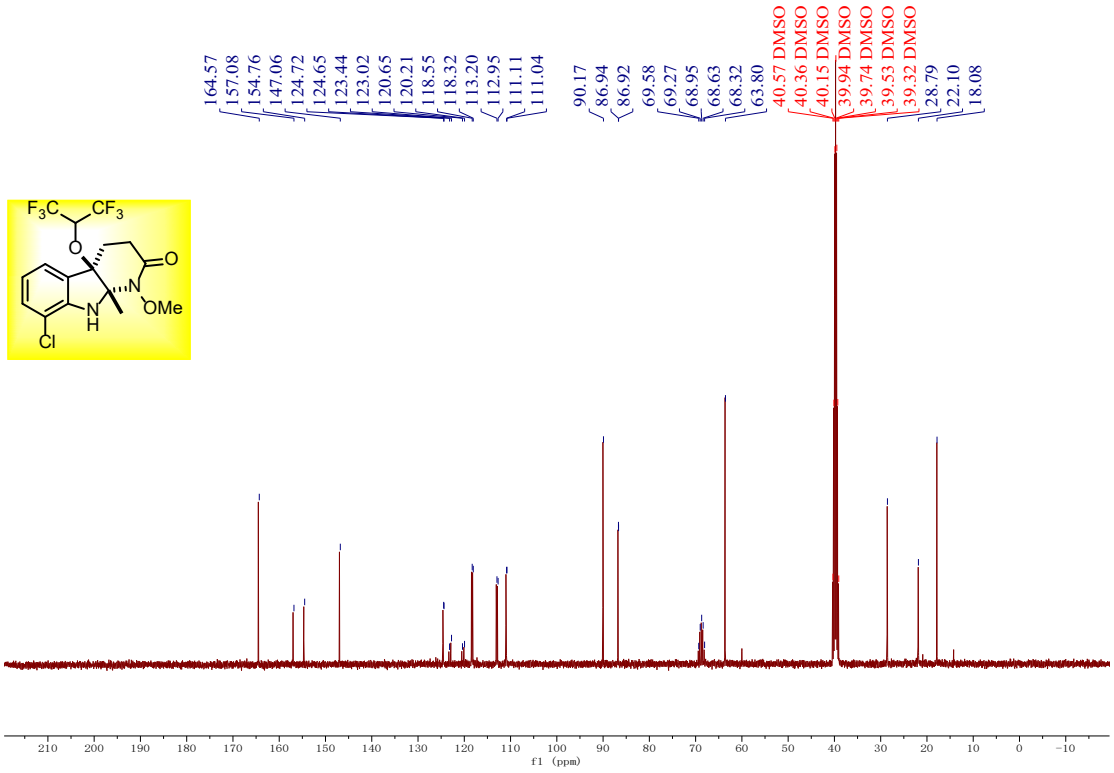


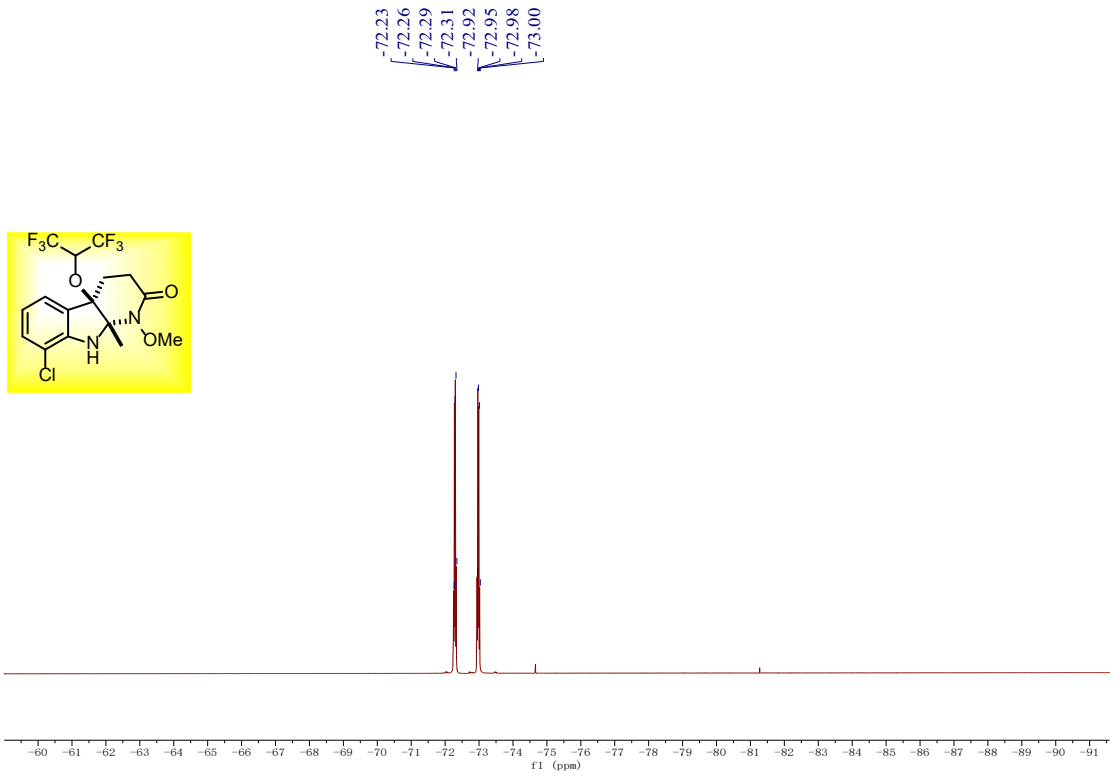




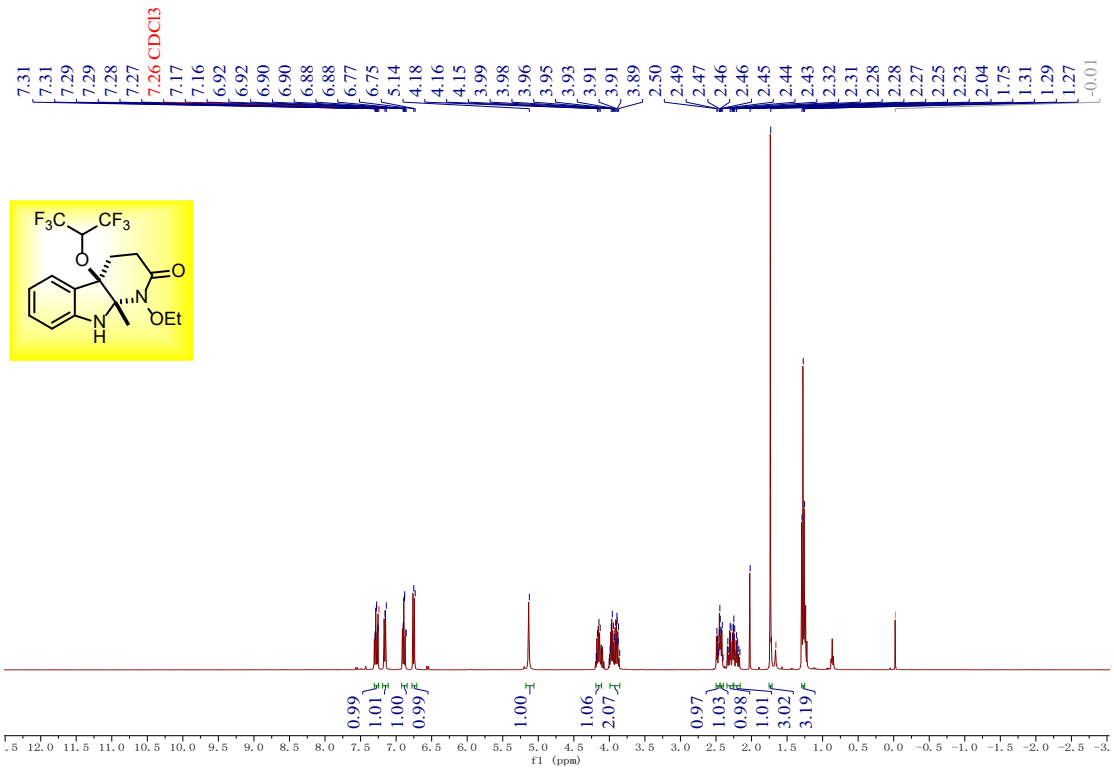
^{1}H NMR ^{13}C NMR and ^{19}F NMR spectra of 3bd

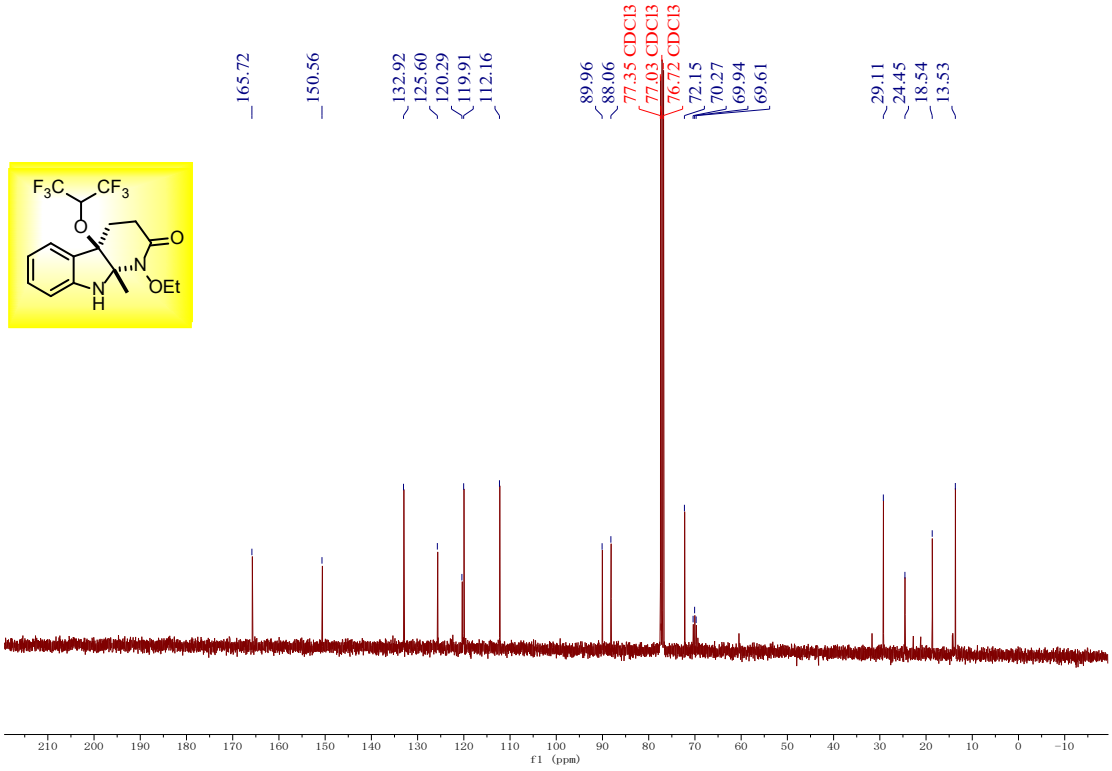

7.59
7.59
7.57
7.56
7.07
7.07
7.04
7.03
7.02
6.68
6.67
6.66
6.65
5.43
5.41
5.40
5.38
5.37
3.67
3.36 HDO
2.63
2.61
2.59
2.58
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.43
2.43
2.42
2.40
2.39
2.38
2.15
2.12
2.11
2.09
2.06
2.04
2.02
2.01
1.99
1.63
F3C
CF3
O
O
N
OMe
N
H
Cl
0.98
1.97
0.99
1.00
3.00
0.98
1.00
1.99
2.97
f1 (ppm)

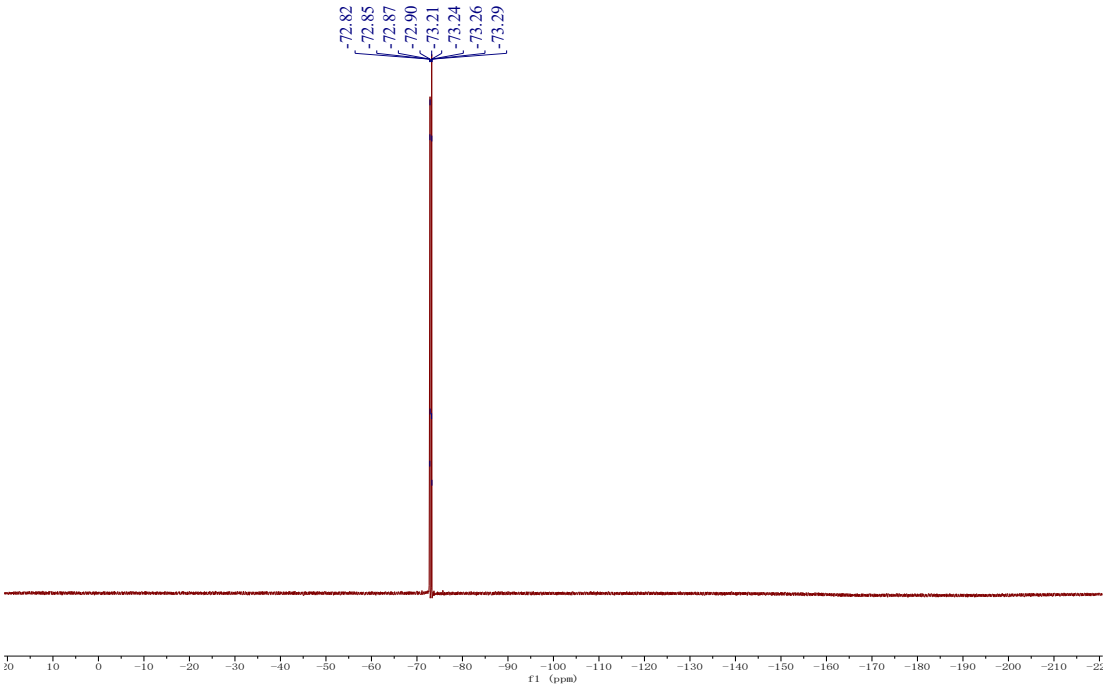

164.57
157.08
154.76
147.06
124.72
124.65
123.44
123.02
120.65
120.21
118.55
118.32
113.20
112.95
111.11
111.04
90.17
86.94
86.92
69.58
69.27
68.95
68.63
68.32
63.80
40.57 DMSO
40.36 DMSO
40.15 DMSO
39.94 DMSO
39.74 DMSO
39.53 DMSO
39.32 DMSO
28.79
22.10
18.08
F3C
CF3
O
O
N
OMe
N
H
Cl
f1 (ppm)



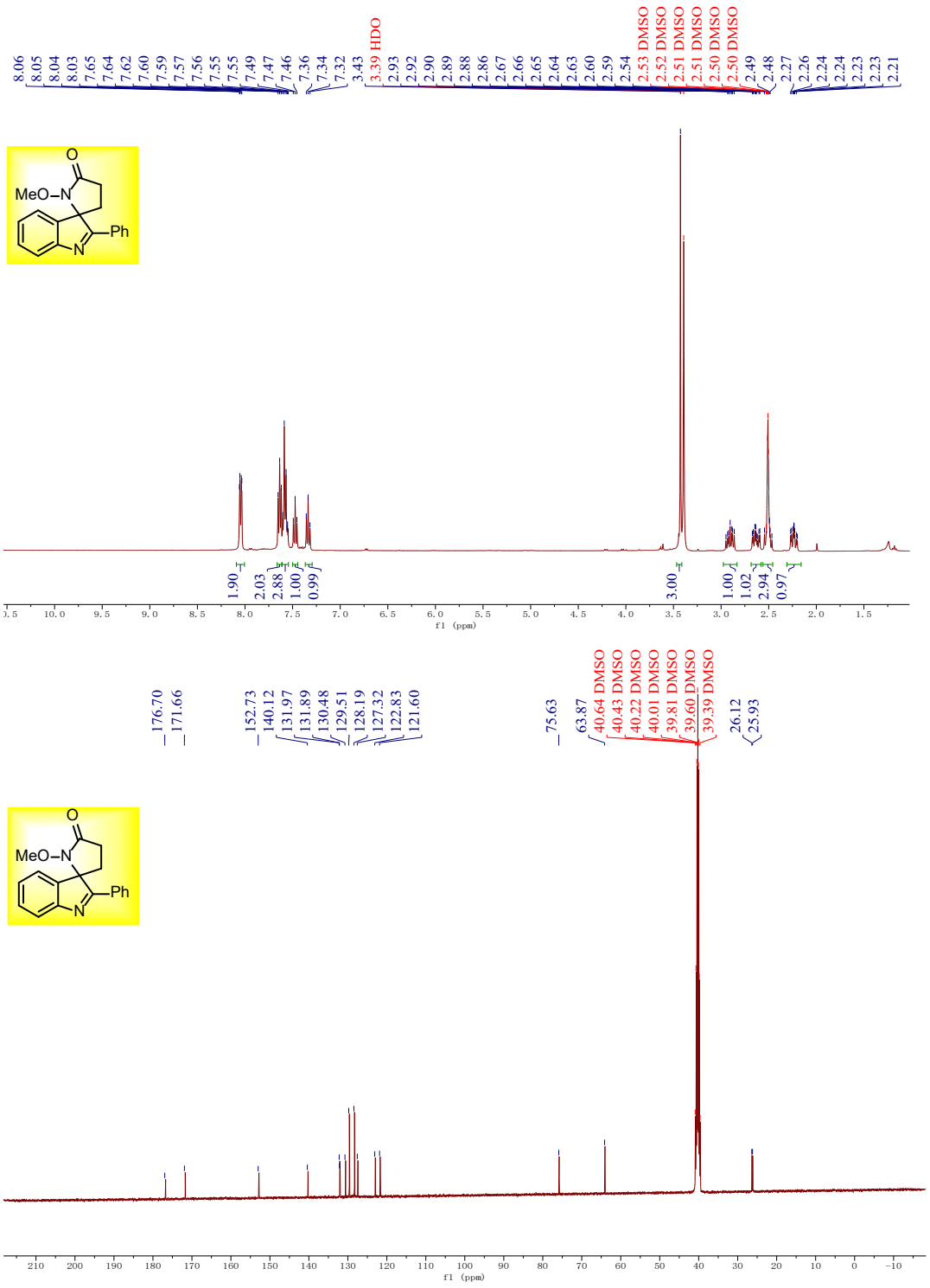
^{1}H NMR ^{13}C NMR and ^{19}F NMR spectra of 3be



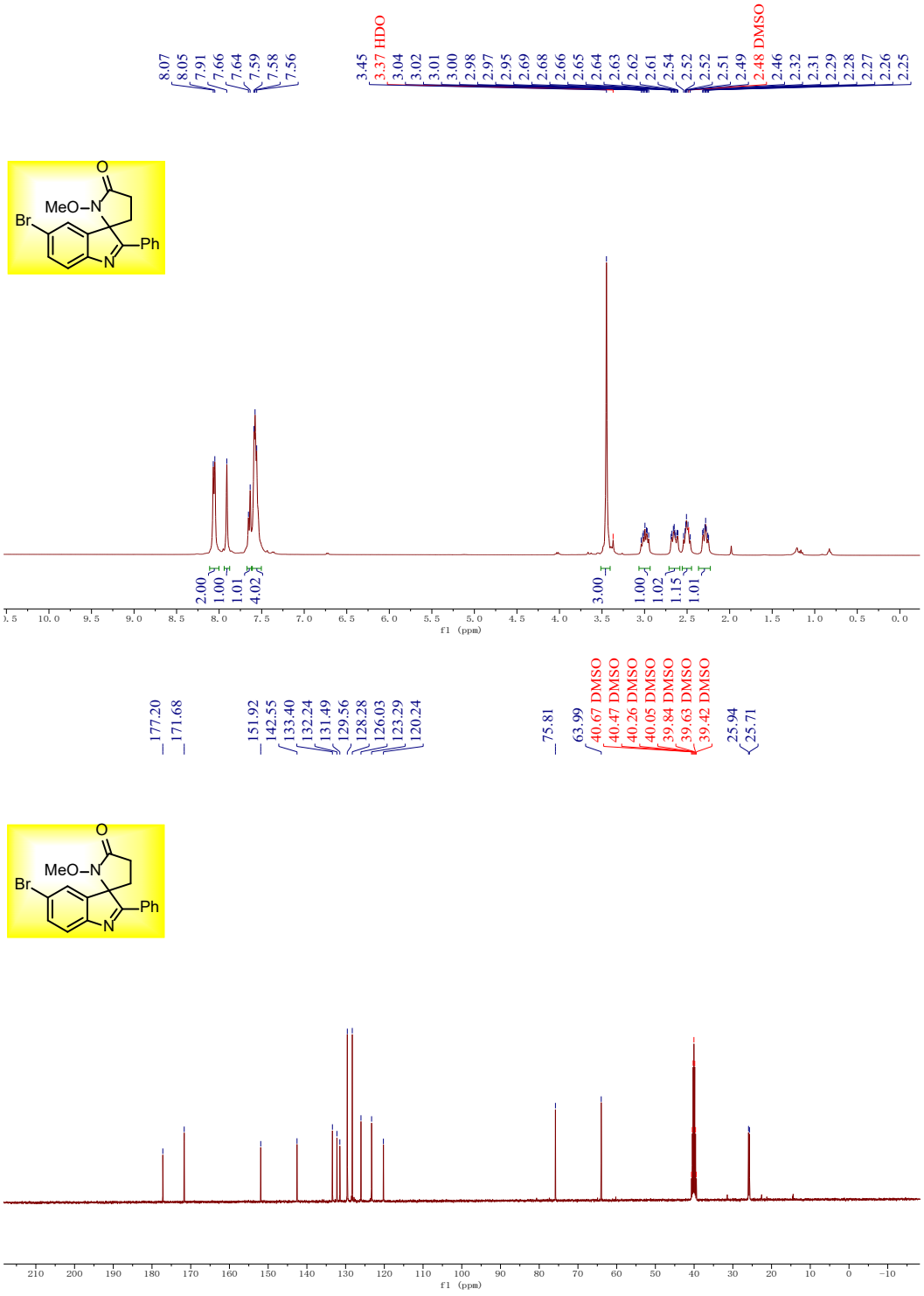




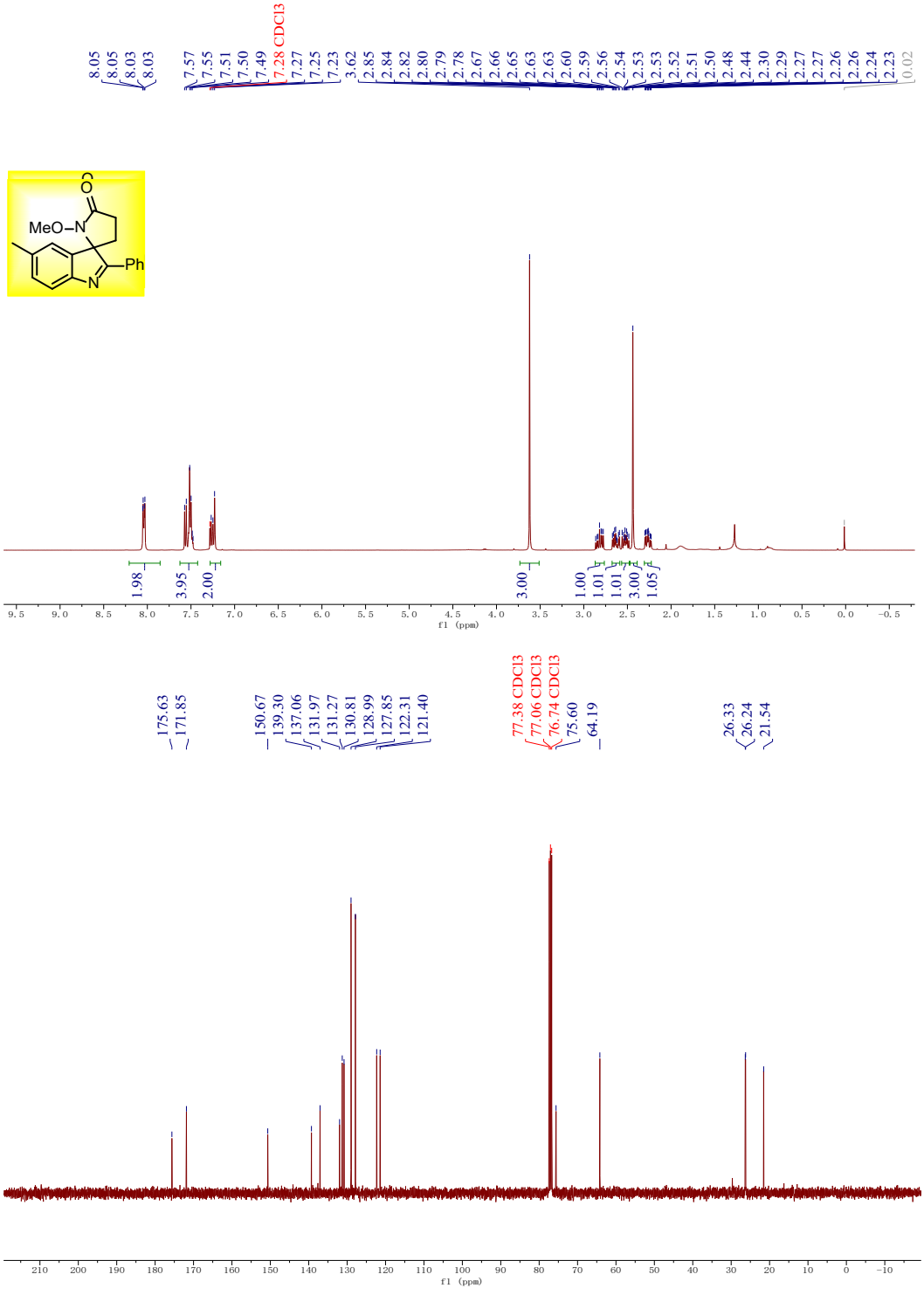
^{1}H NMR and ^{13}C NMR spectra of 4aa



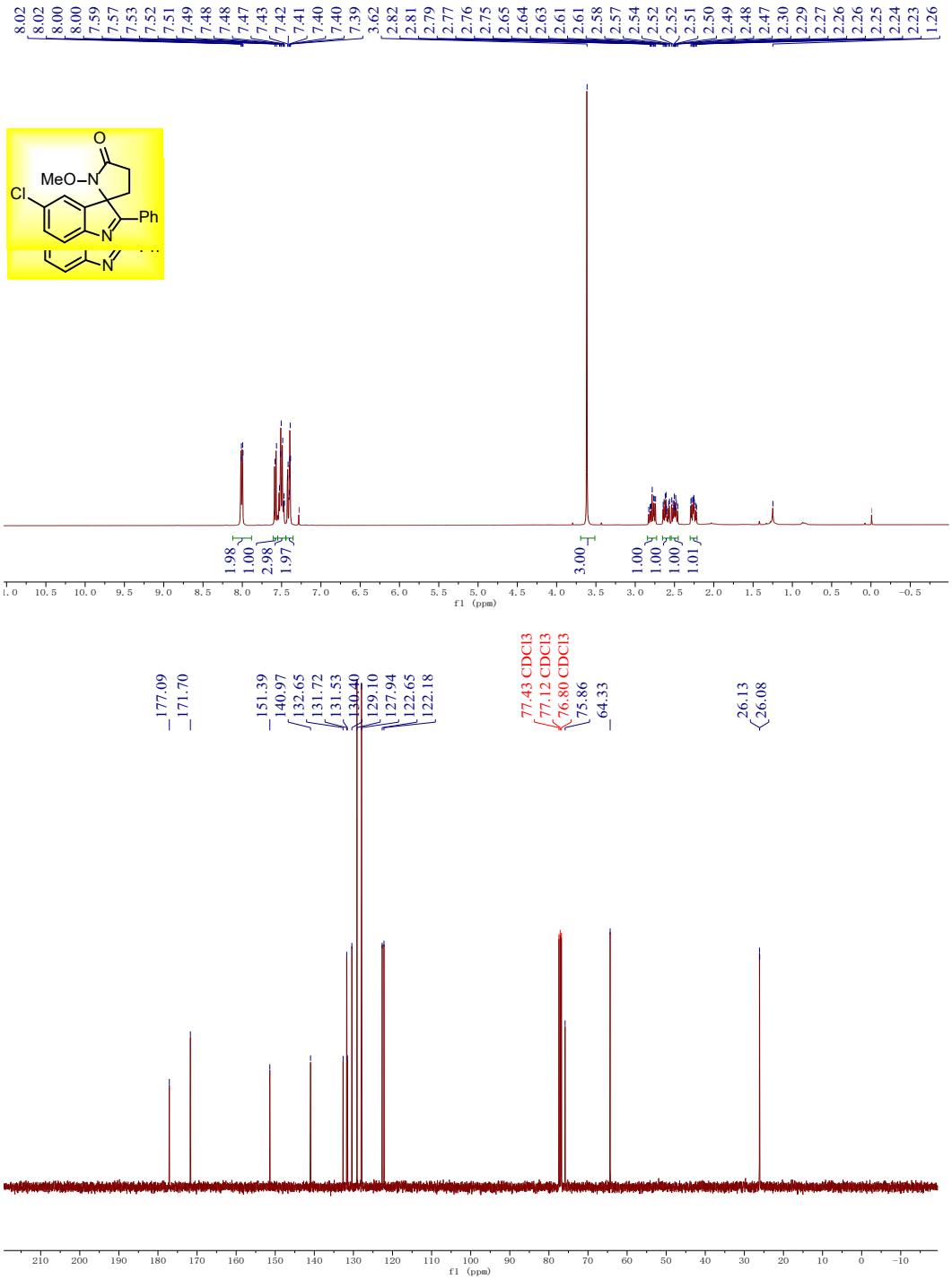
^{1}H NMR and ^{13}C NMR spectra of 4ab



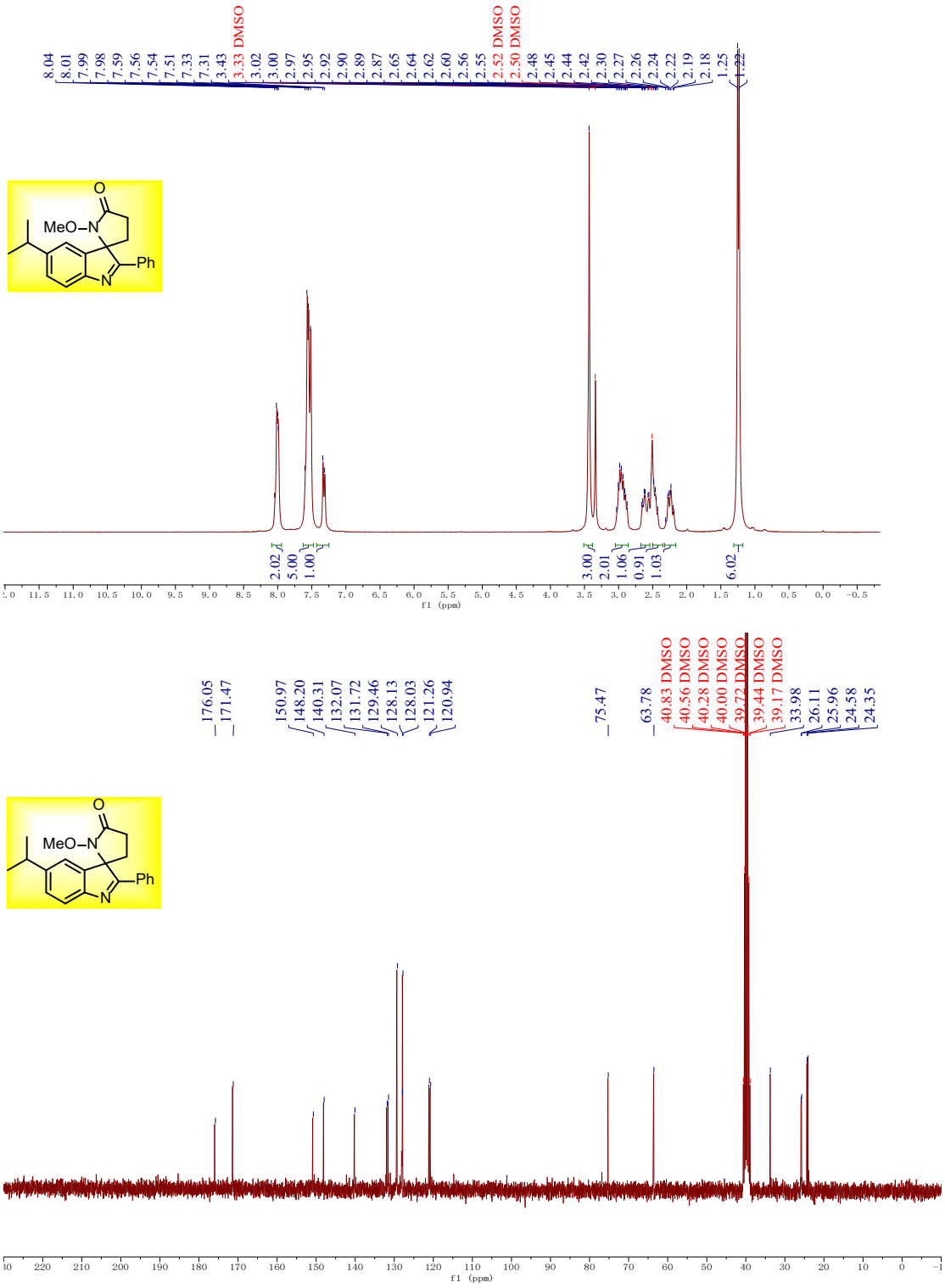
^{1}H NMR and ^{13}C NMR spectra of 4ac



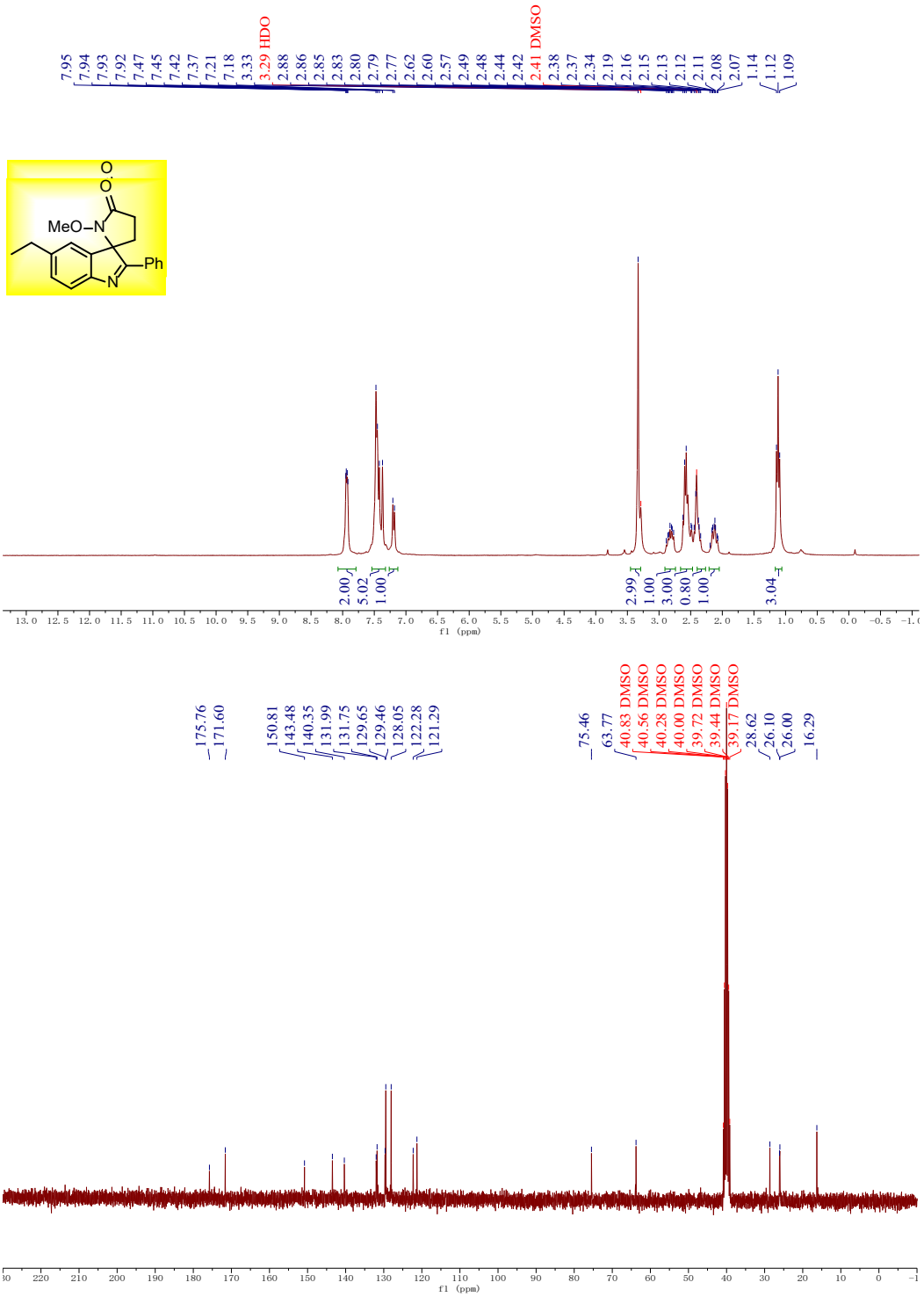
^{1}H NMR and ^{13}C NMR spectra of 4ad



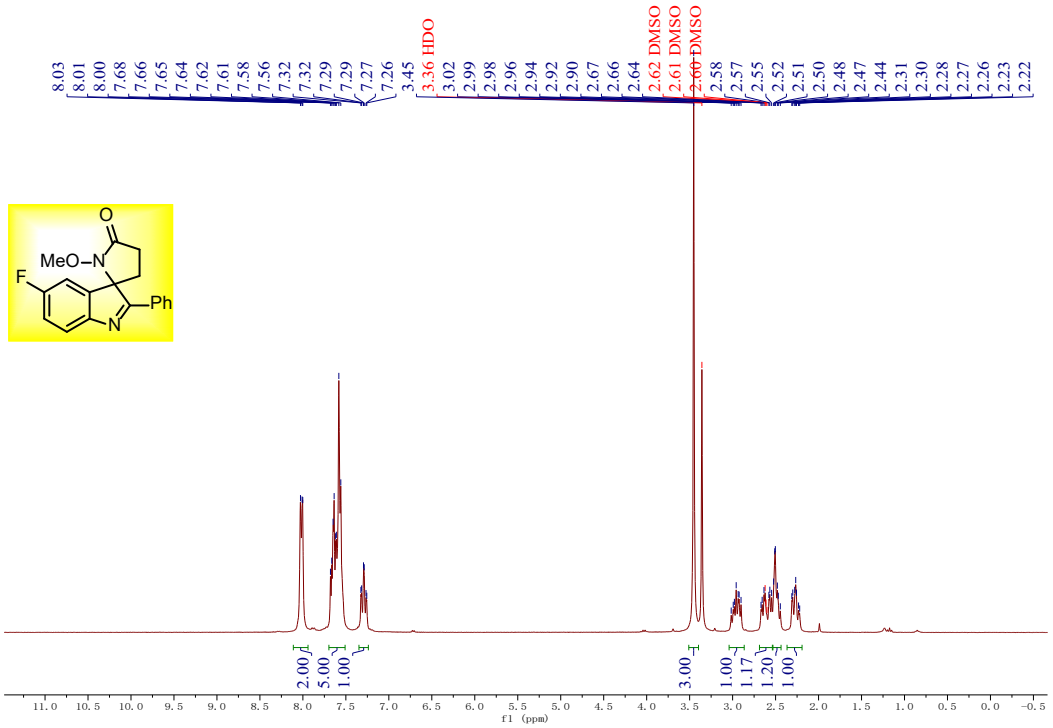
^{1}H NMR and ^{13}C NMR spectra of 4ae

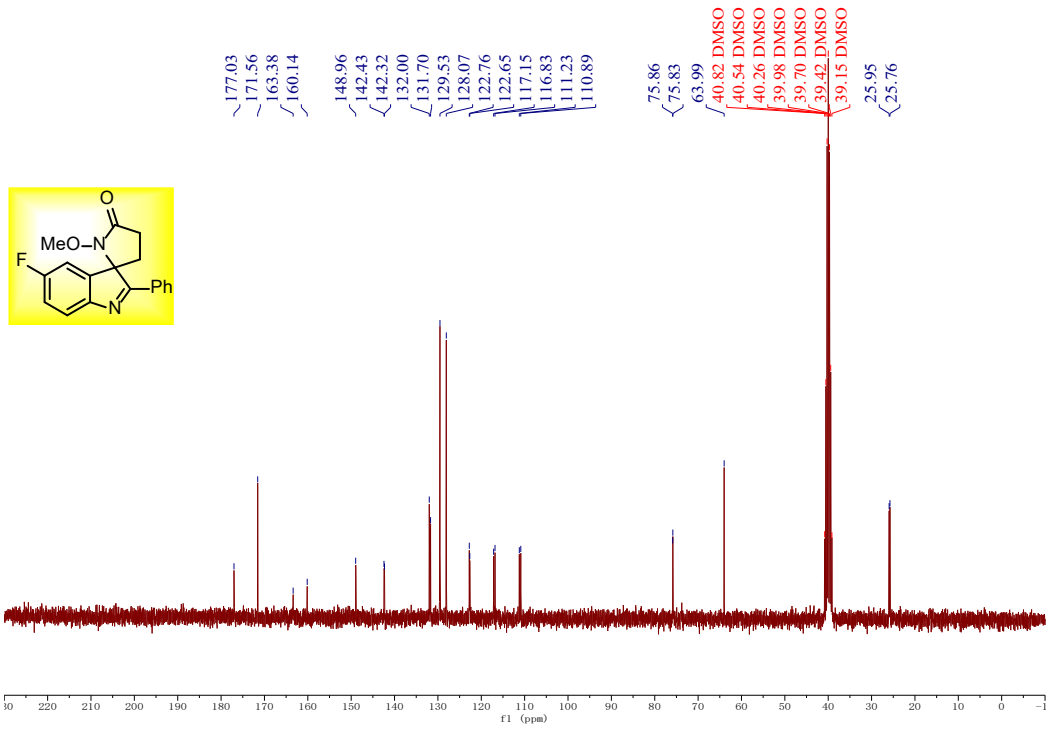


^{1}H NMR and ^{13}C NMR spectra of 4af

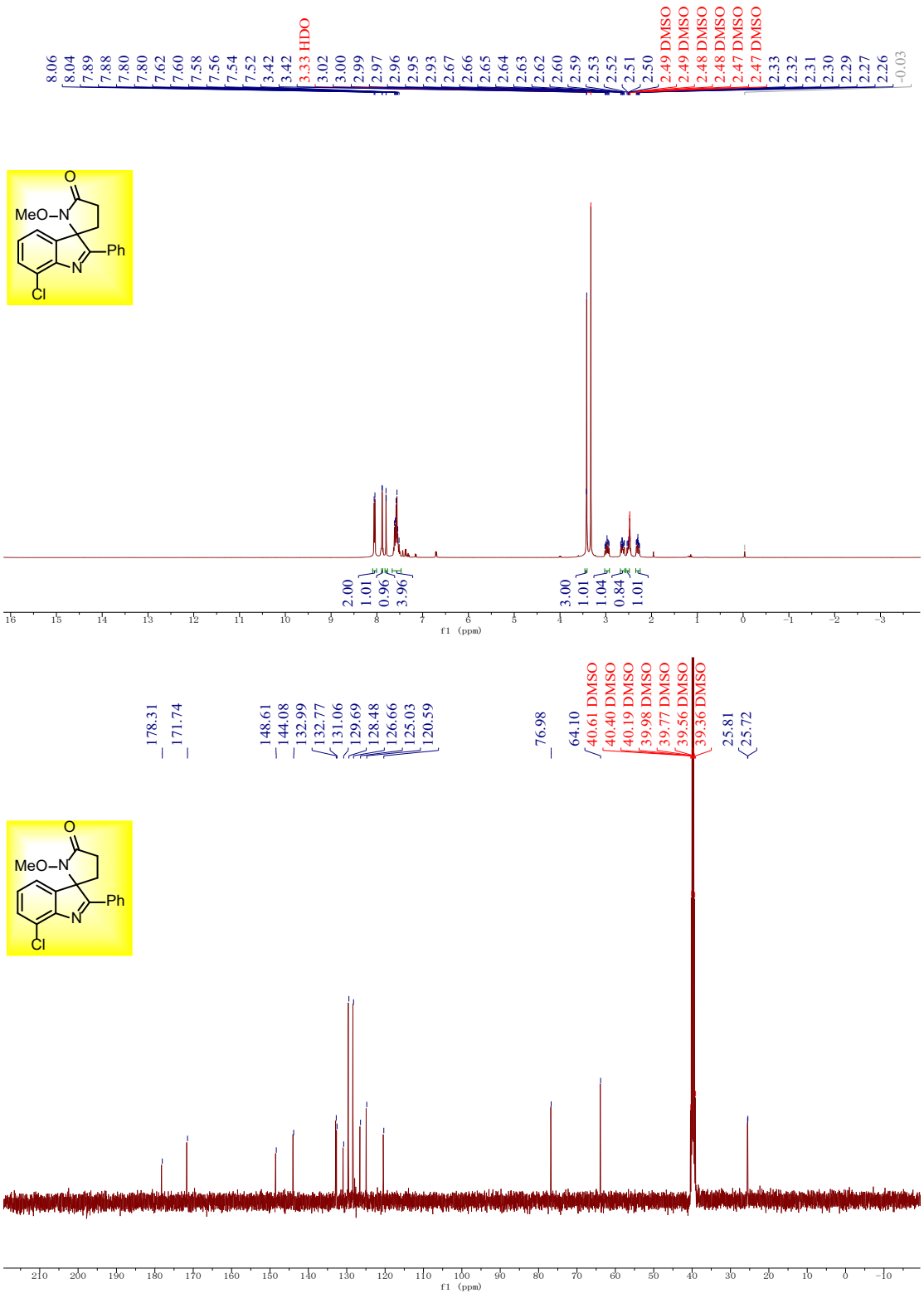


^{1}H NMR and ^{13}C NMR ^{19}F NMR spectra of 4ag

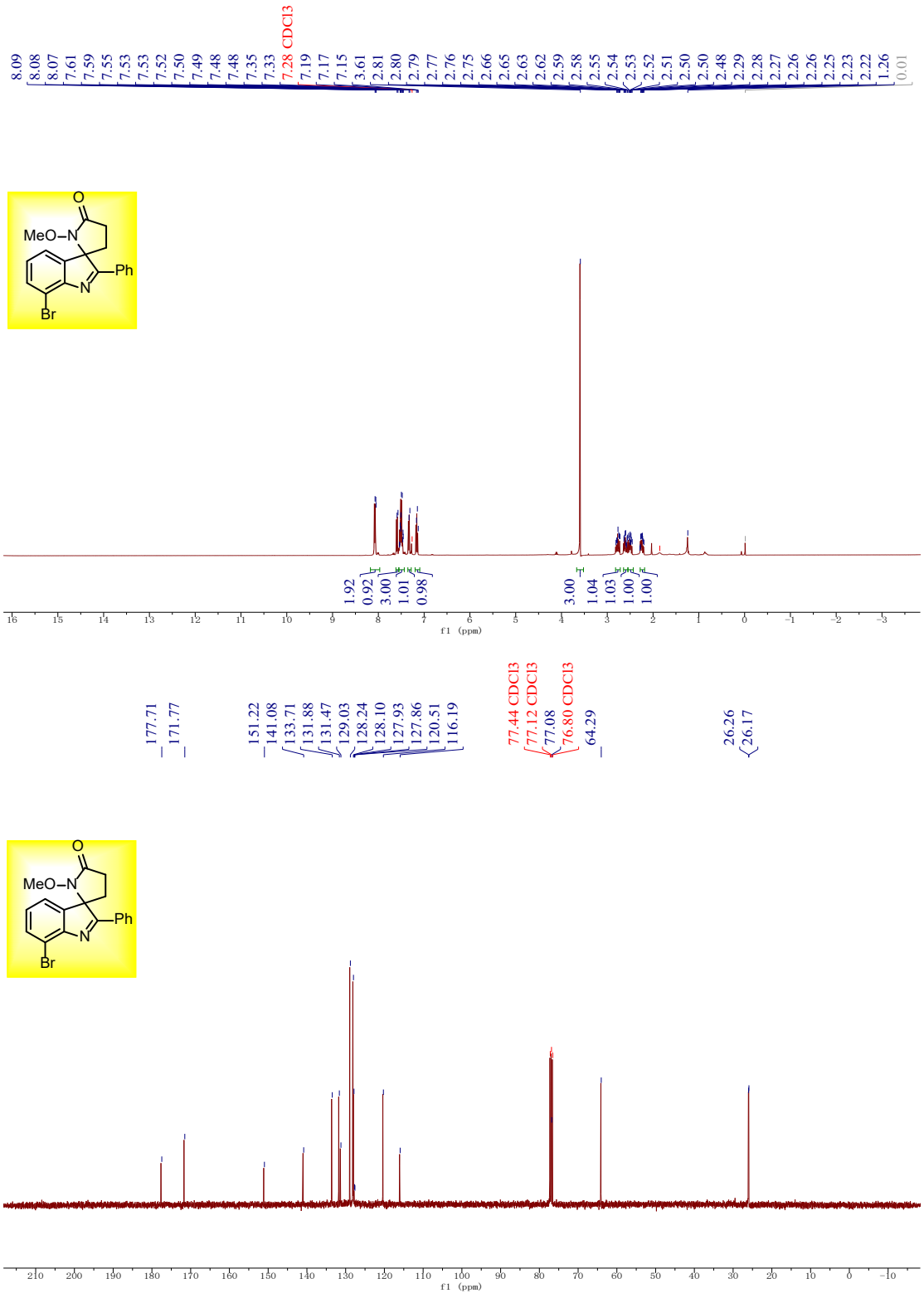




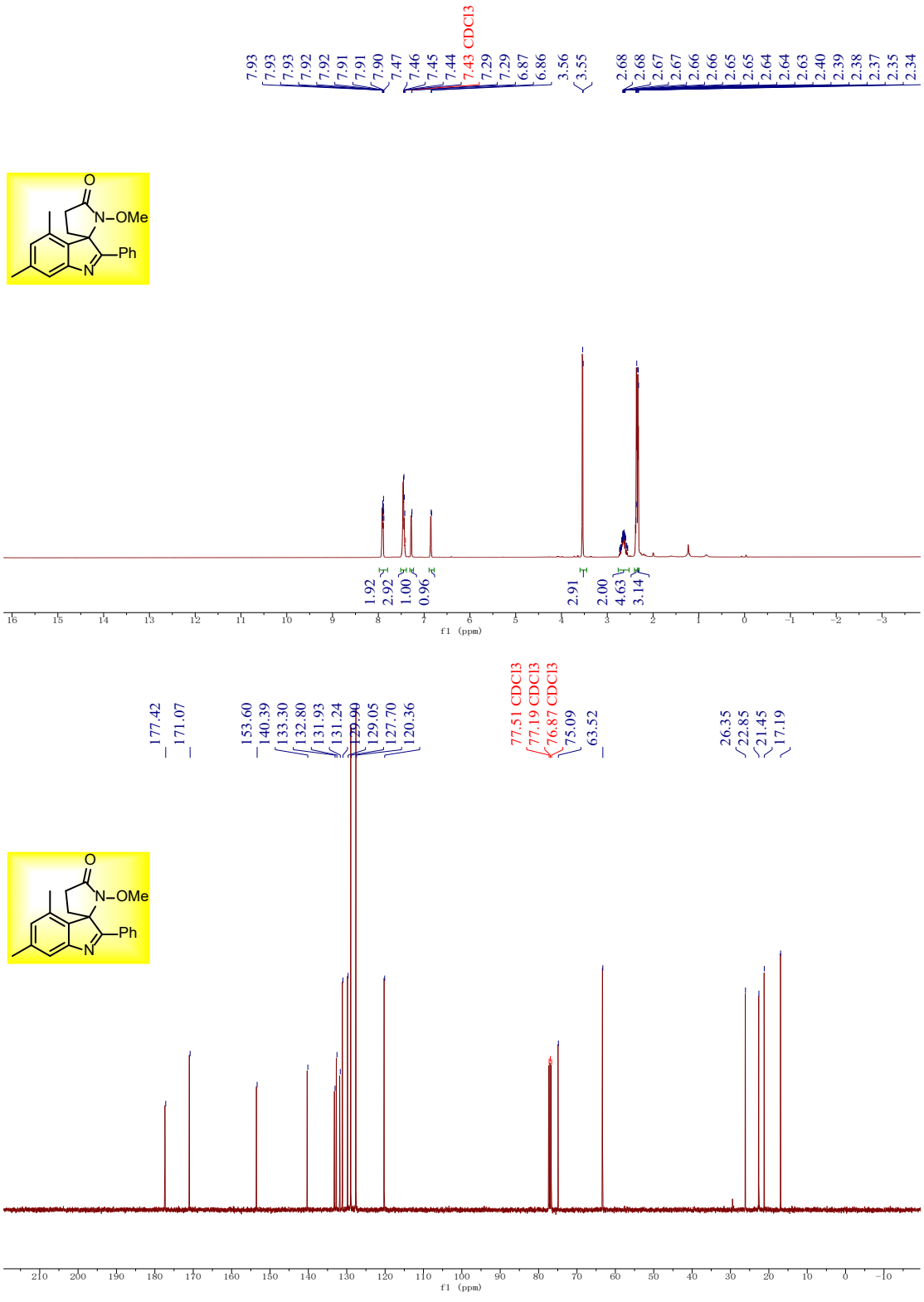
^{1}H NMR and ^{13}C NMR spectra of 4ah



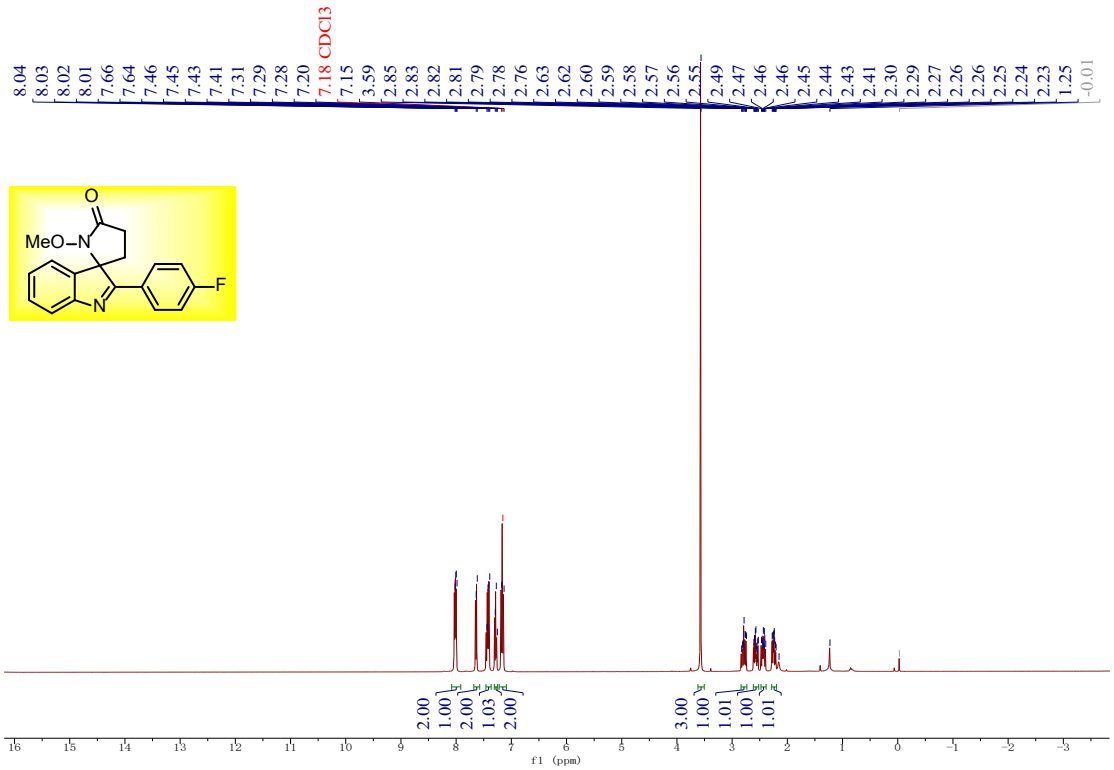
^{1}H NMR and ^{13}C NMR spectra of 4ai

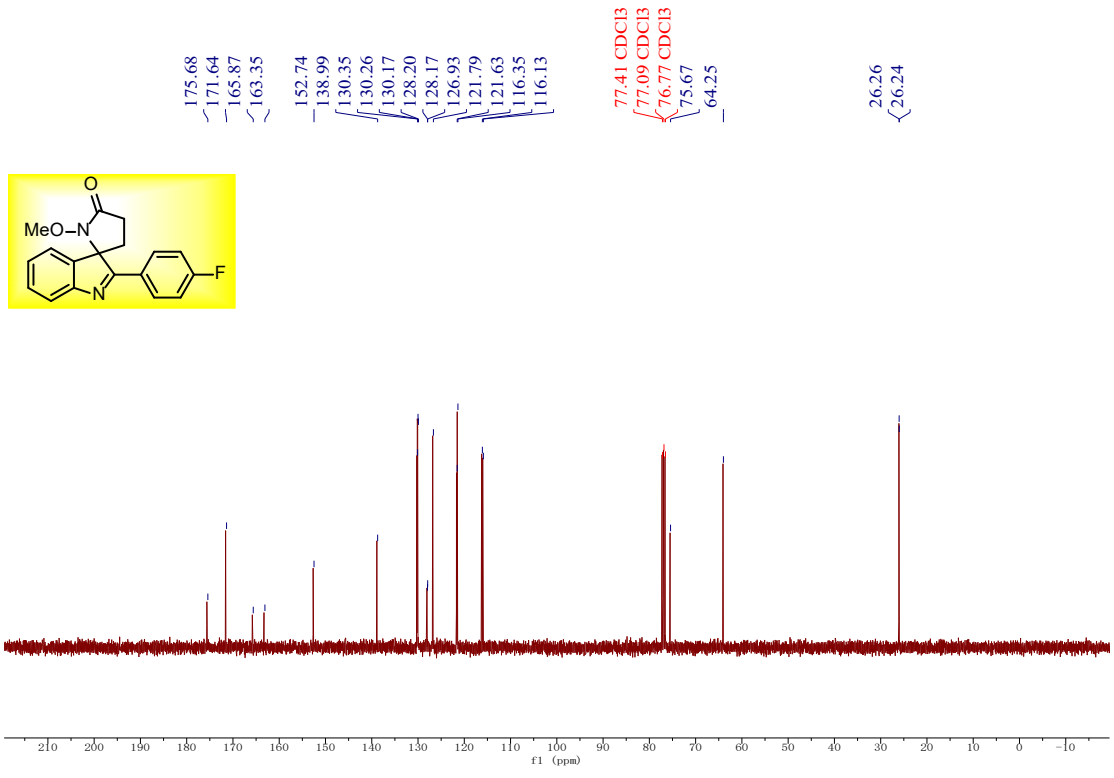


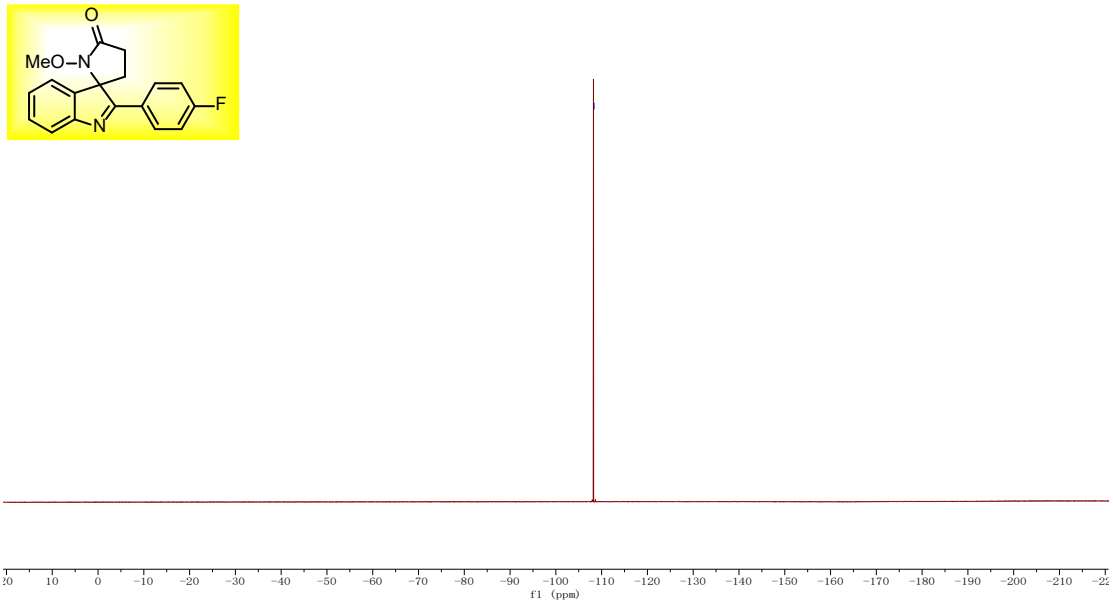
^{1}H NMR and ^{13}C NMR and of 4aj



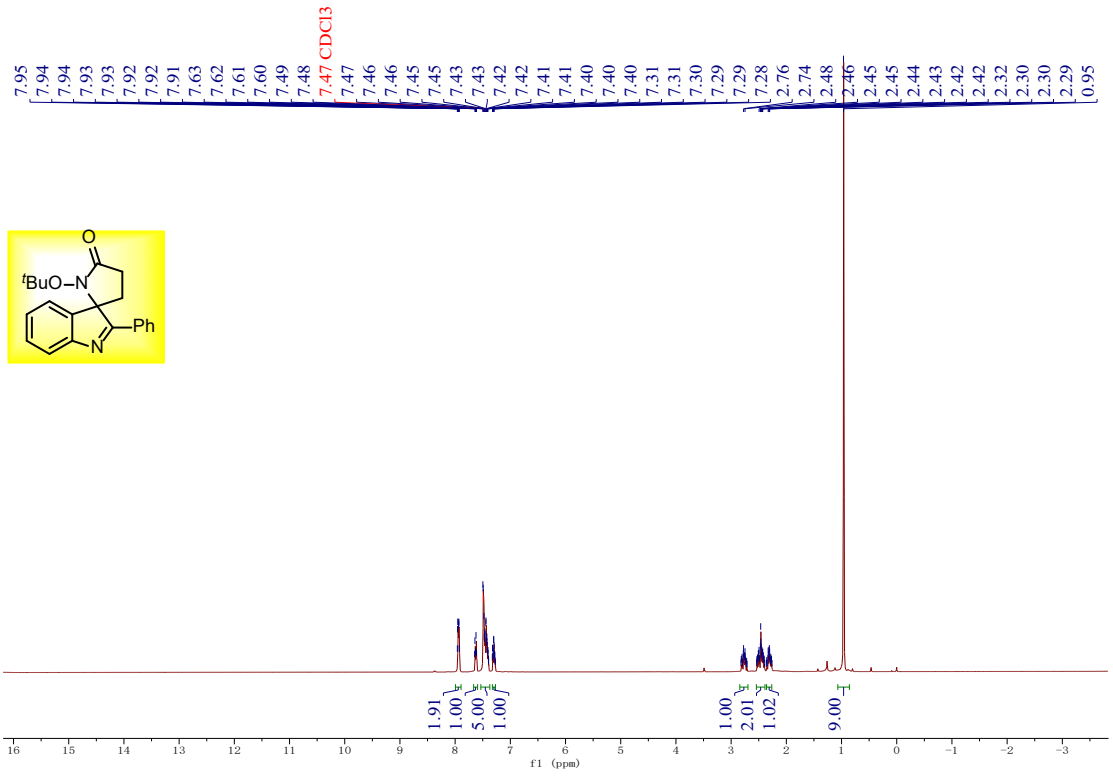
^{1}H NMR ^{13}C NMR and ^{19}F NMR spectra of 4ak

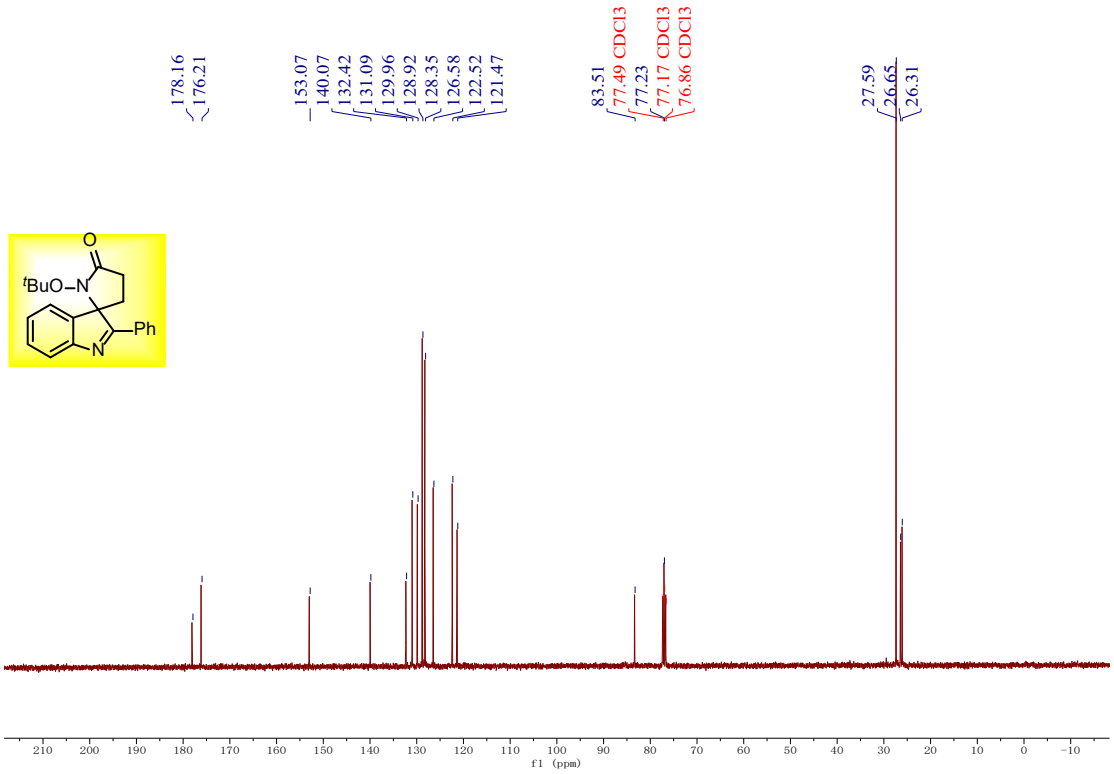

8.04
8.03
8.02
8.01
7.66
7.64
7.46
7.45
7.43
7.41
7.31
7.29
7.28
7.20
7.18 CDCl3
7.15
3.59
2.85
2.83
2.82
2.81
2.79
2.78
2.76
2.63
2.62
2.60
2.59
2.58
2.57
2.56
2.55
2.49
2.47
2.46
2.46
2.45
2.44
2.43
2.41
2.30
2.29
2.27
2.26
2.26
2.25
2.24
2.23
1.25
-0.01
MeO–N
O
N
F
2.00
1.00
2.00
1.03
2.00
3.00
1.00
1.01
1.00
1.01
f1 (ppm)


175.68
171.64
165.87
163.35
152.74
138.99
130.35
130.26
130.17
128.20
128.17
126.93
121.79
121.63
116.35
116.13
77.41 CDCl3
77.09 CDCl3
76.77 CDCl3
75.67
64.25
26.26
26.24
MeO–N
O
N
F
f1 (ppm)

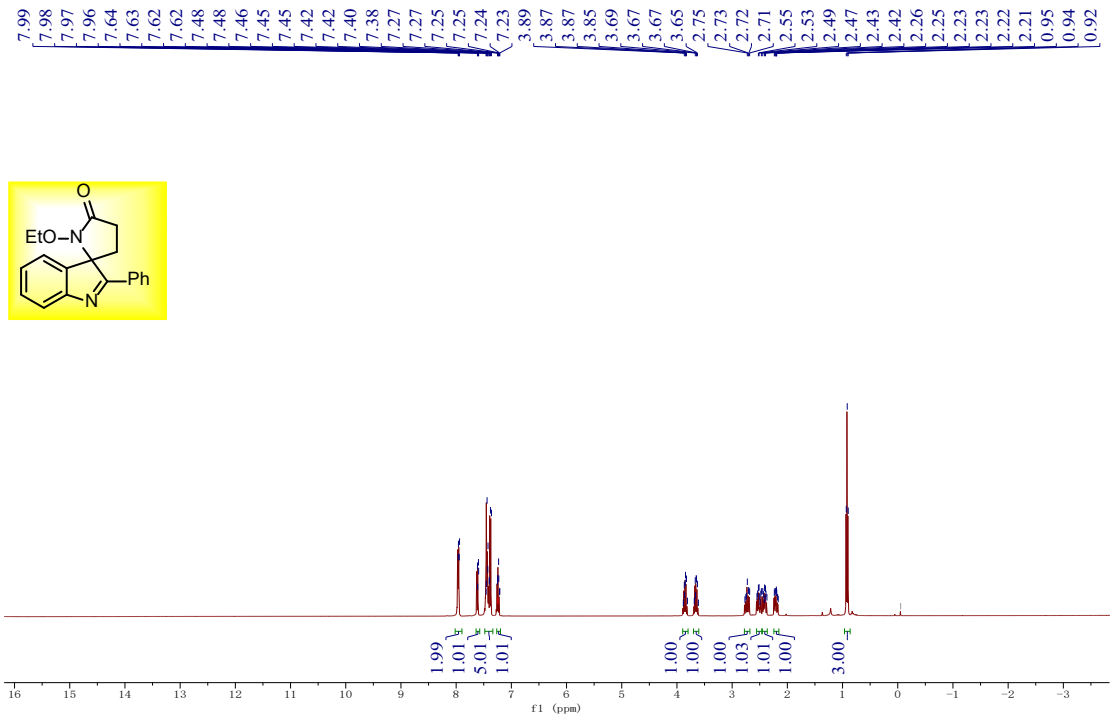


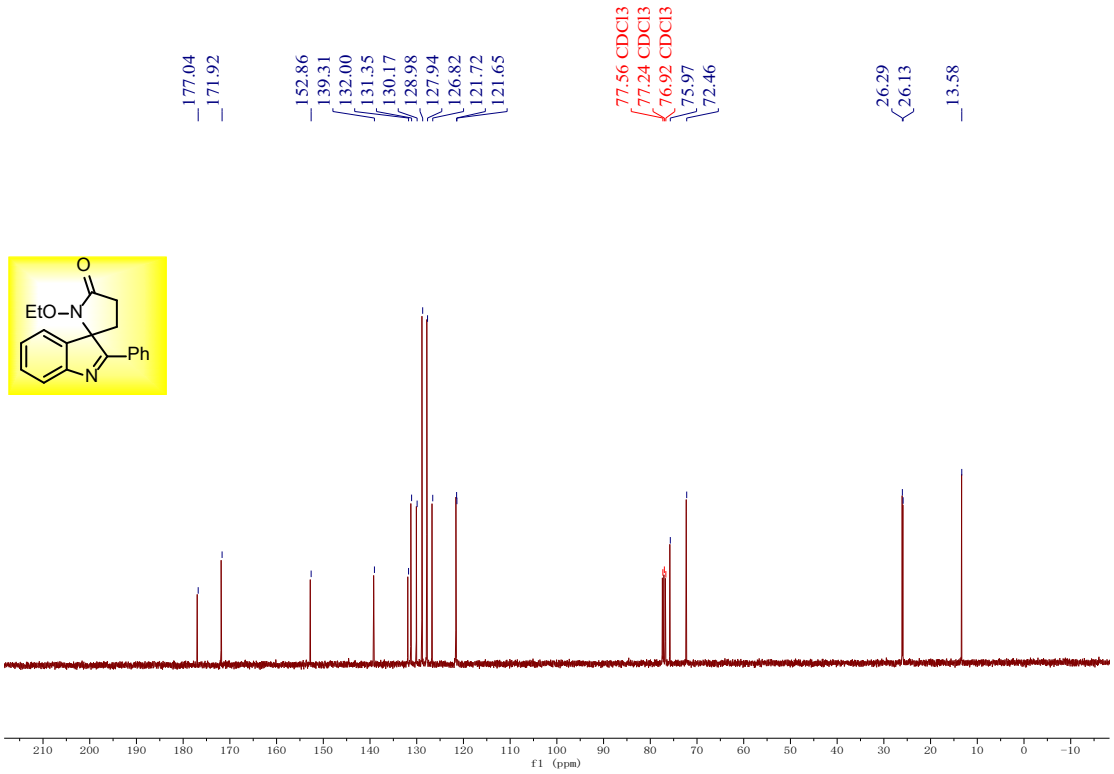
^{1}H NMR and ^{13}C NMR spectra of 4al



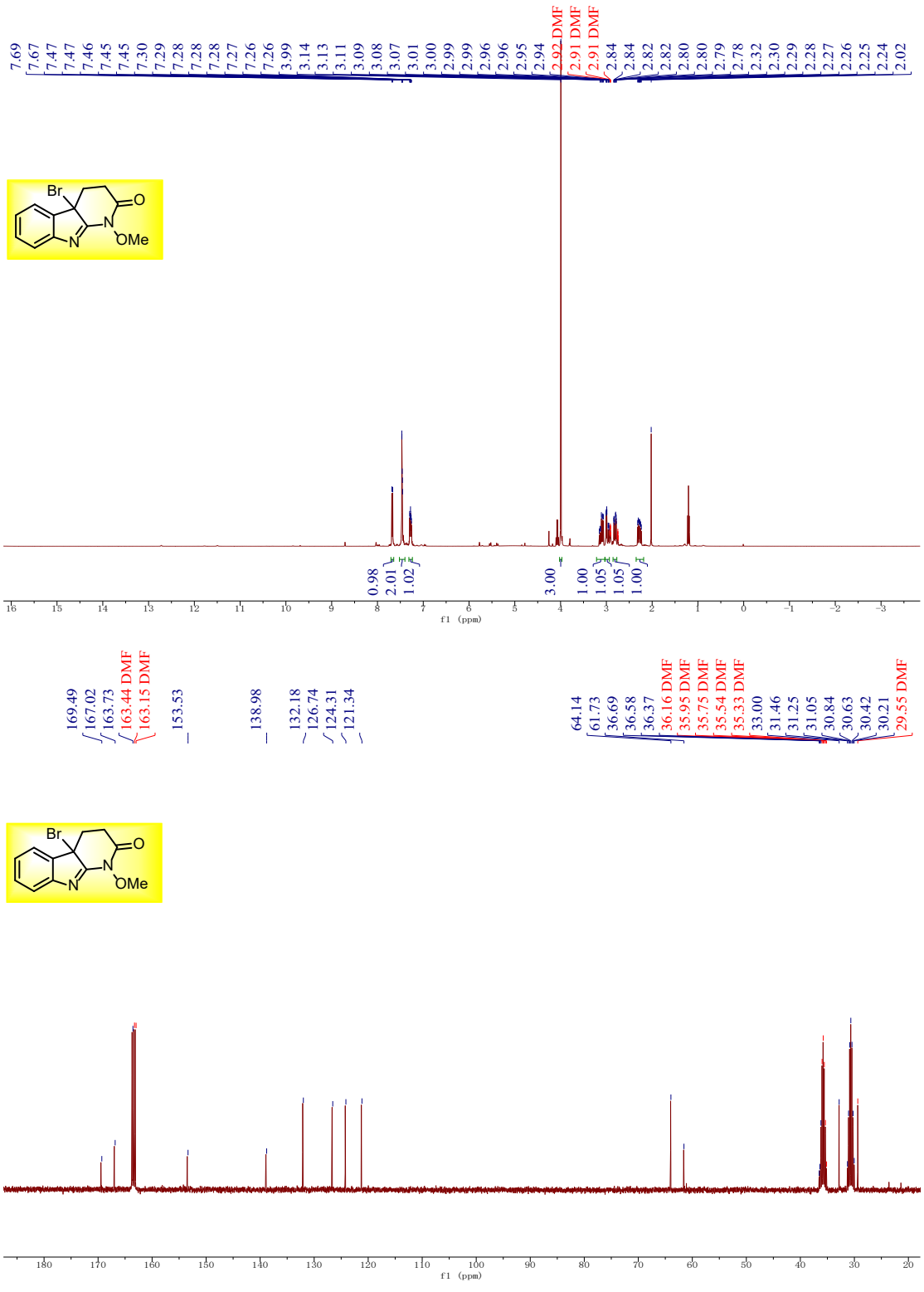


^{1}H NMR and ^{13}C NMR spectra of 4am

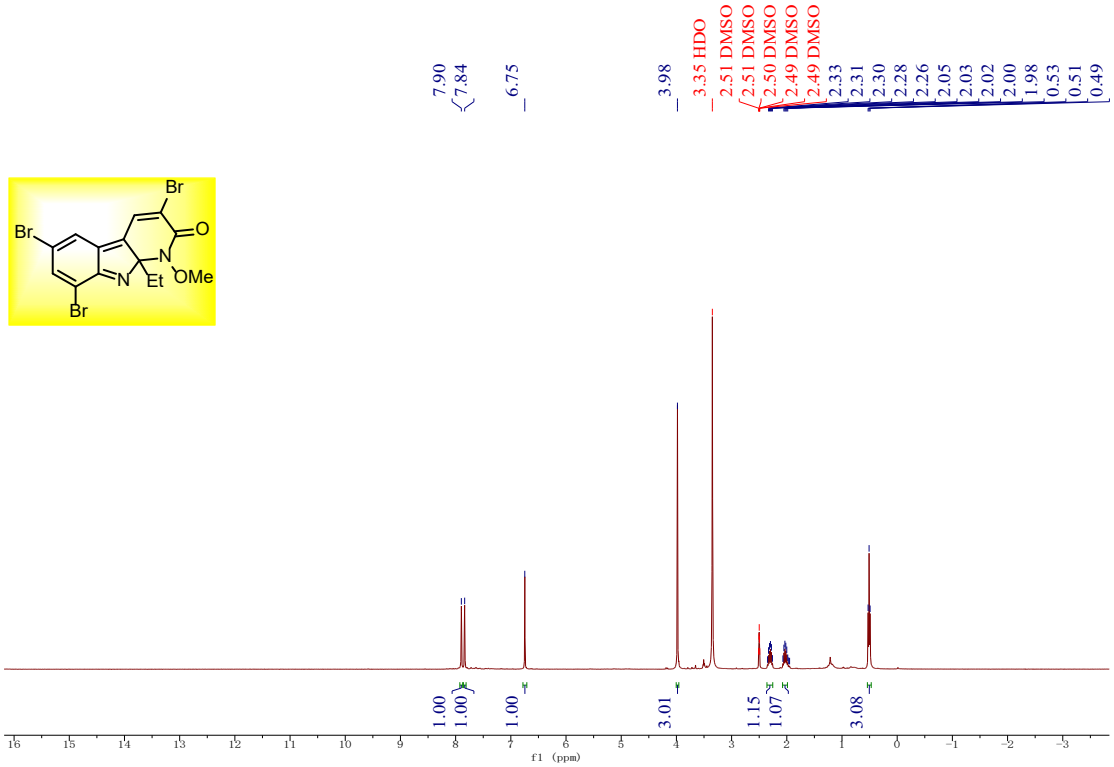


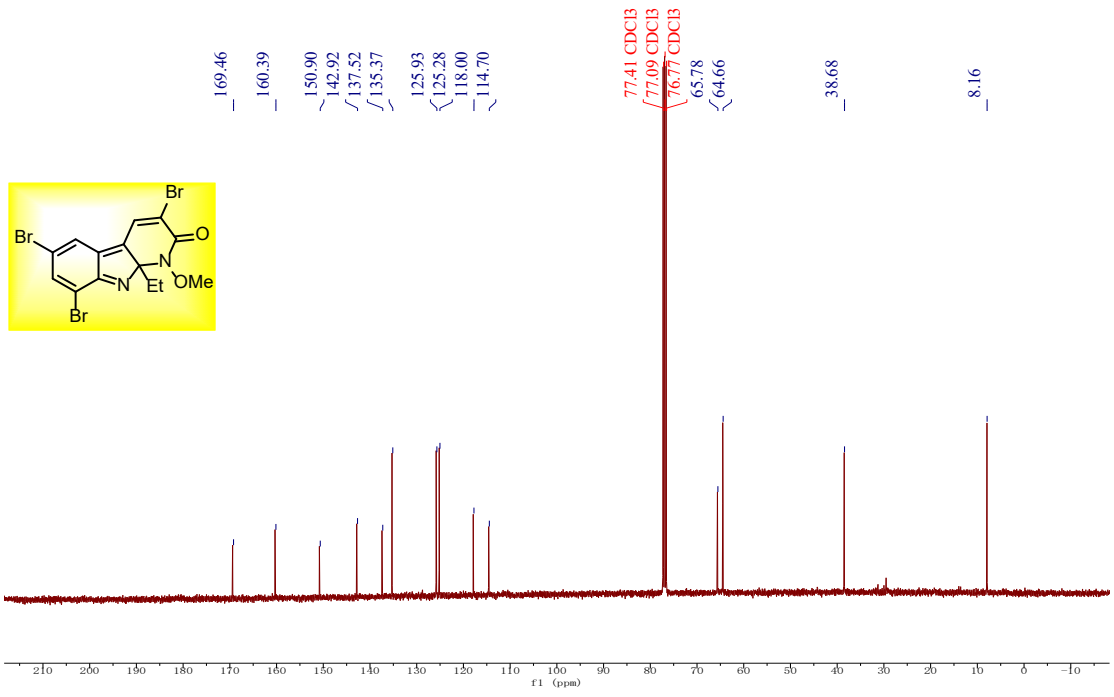


^{1}H NMR and ^{13}C NMR spectra of 5a

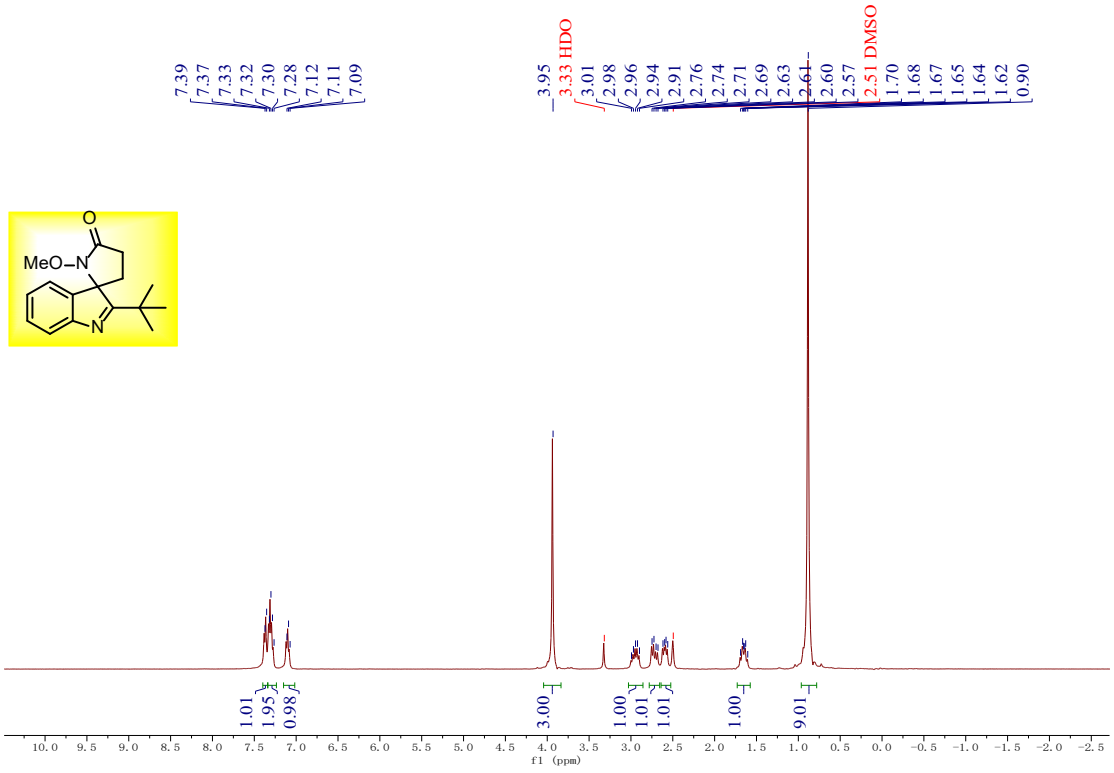


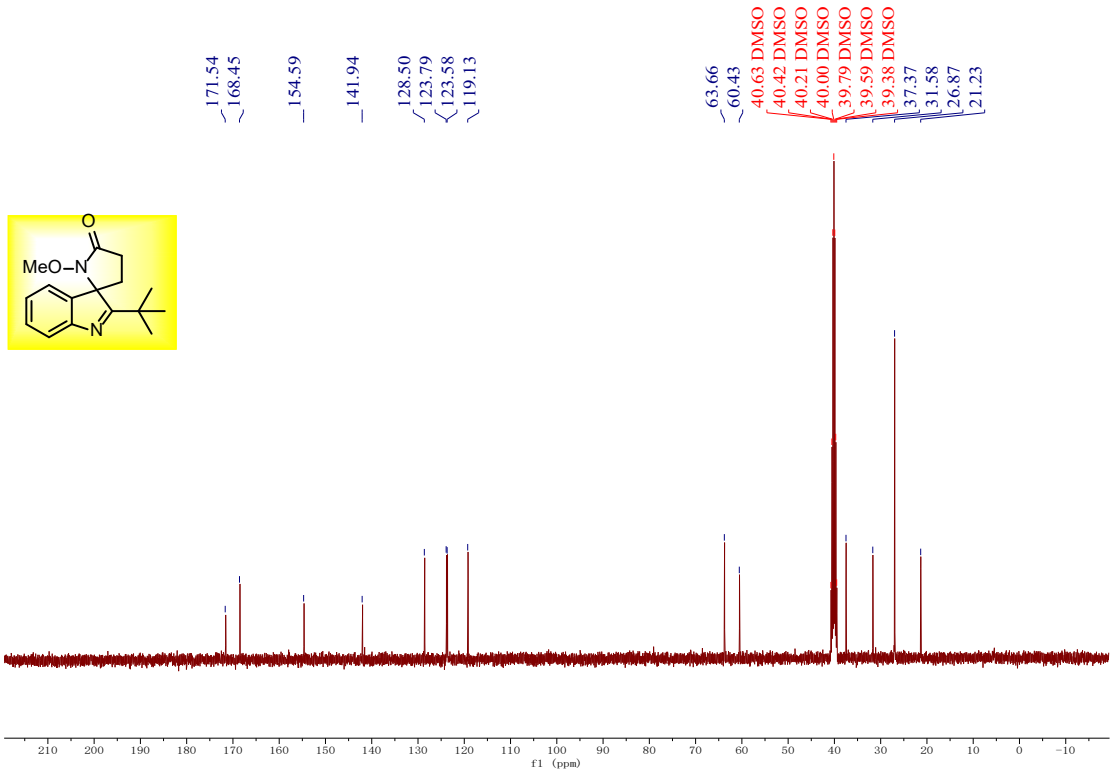
^{1}H NMR and ^{13}C NMR spectra of 6a





^{1}H NMR and ^{13}C NMR spectra of 8a


7.39
7.37
7.33
7.32
7.30
7.28
7.12
7.11
7.09
3.95
3.33 HDO
3.01
2.98
2.96
2.94
2.91
2.76
2.74
2.71
2.69
2.63
2.61
2.60
2.57
2.51 DMSO
1.70
1.68
1.67
1.65
1.64
1.62
0.90
MeO–N
O
N
1.01
1.95
0.98
3.00
1.00
1.01
1.01
1.00
9.01
f1 (ppm)


171.54
168.45
154.59
141.94
128.50
123.79
123.58
119.13
63.66
60.43
40.63 DMSO
40.42 DMSO
40.21 DMSO
40.00 DMSO
39.79 DMSO
39.59 DMSO
39.38 DMSO
37.37
31.58
26.87
21.23
MeO–N
O
N
f1 (ppm)