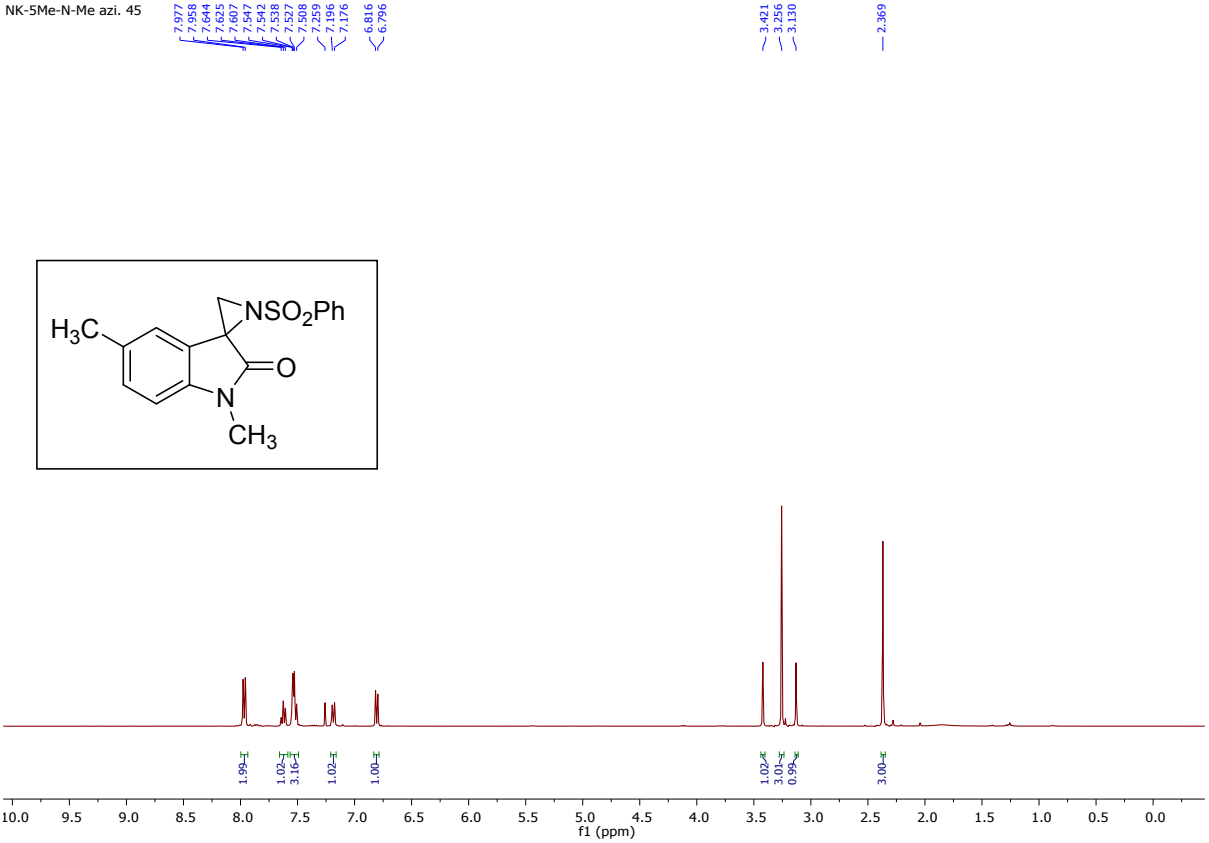
One Pot Synthesis of Enantiopure Spiro[3,4-dihydrobenzo[b][1,4]oxazine-2,3'-oxindole] via Regio- and Stereoselective Tandem Ring Opening/Cyclization of Spiroaziridine Oxindoles with Bromophenols

Saumen Hajra,* Atanu Hazra, and SK Abu Saleh

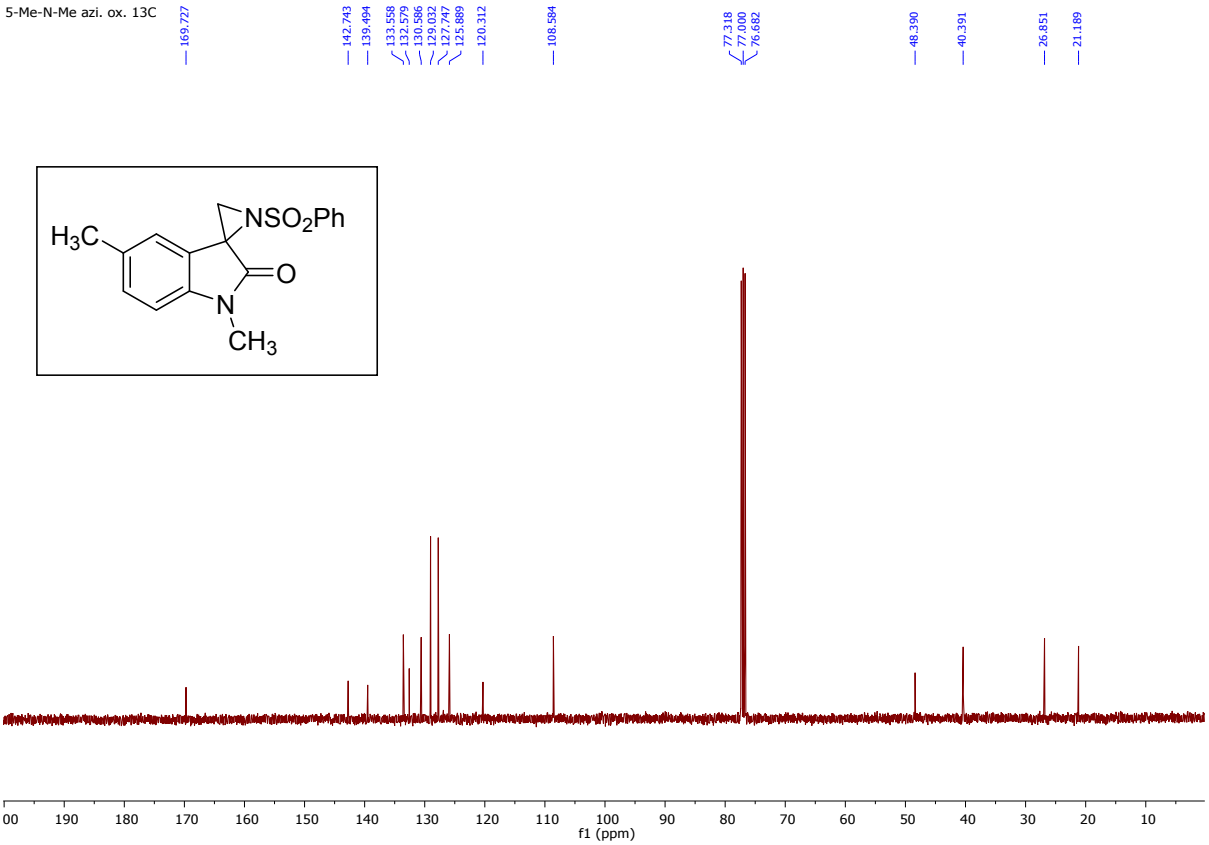
Centre of Biomedical Research, Sanjay Gandhi Post-Graduate Institute of Medical Sciences Campus, Raebareli Road, Lucknow 226014, INDIA

Table of Contents

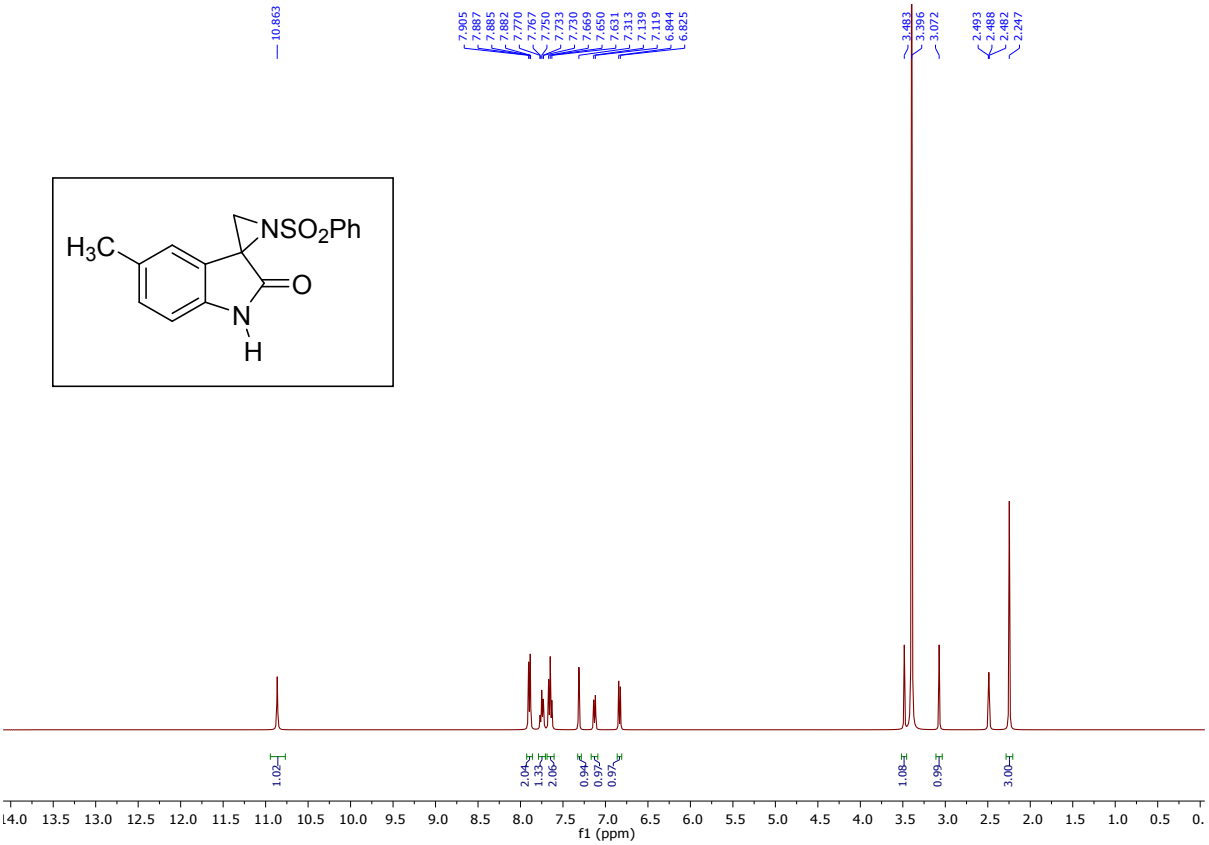
1	**^{1}H, ^{13}C and ^{19}F NMR spectra of compounds**	**S2-S41**
2	**X-ray crystal structure details**	**S42-S43**
3	**HPLC Chromatography of compounds**	**S44-S56**



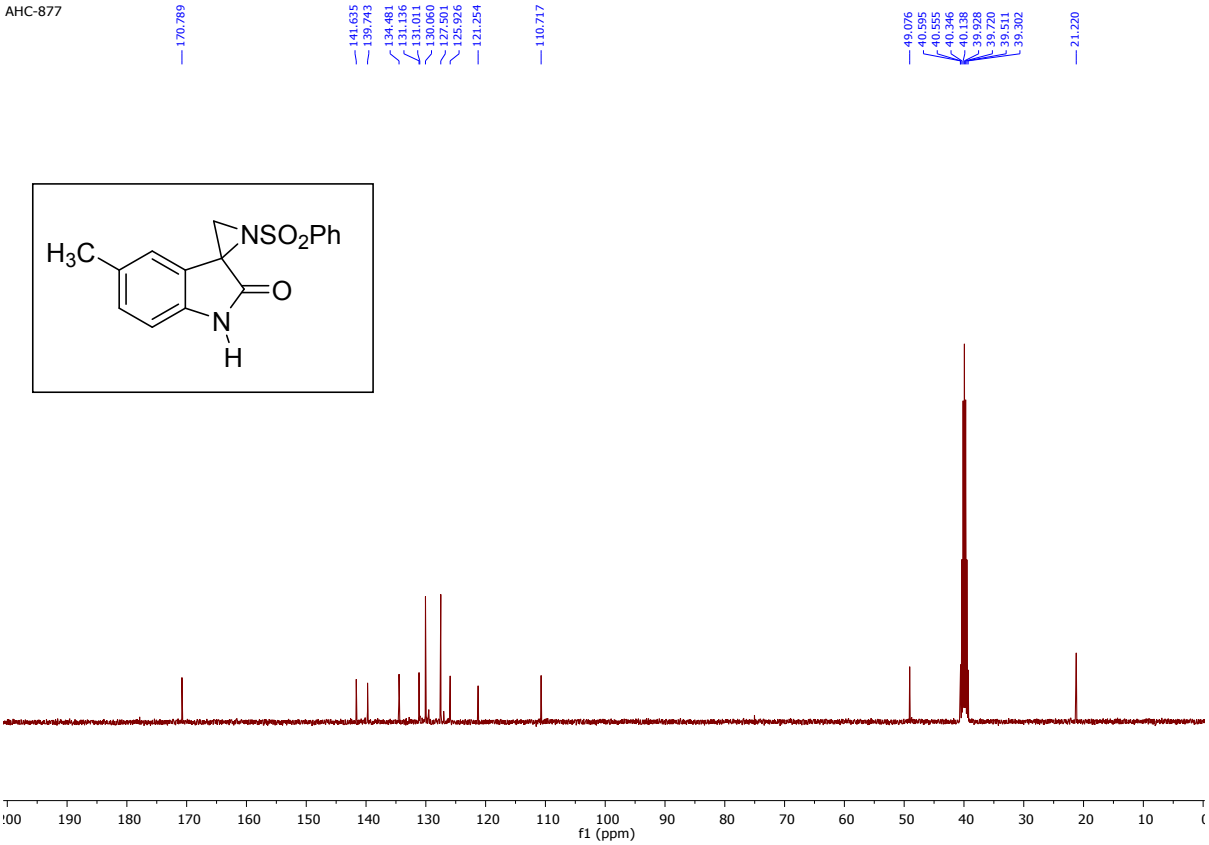
^{1}H NMR of compound (±)-1e (400 MHz, $CDCl_3$)



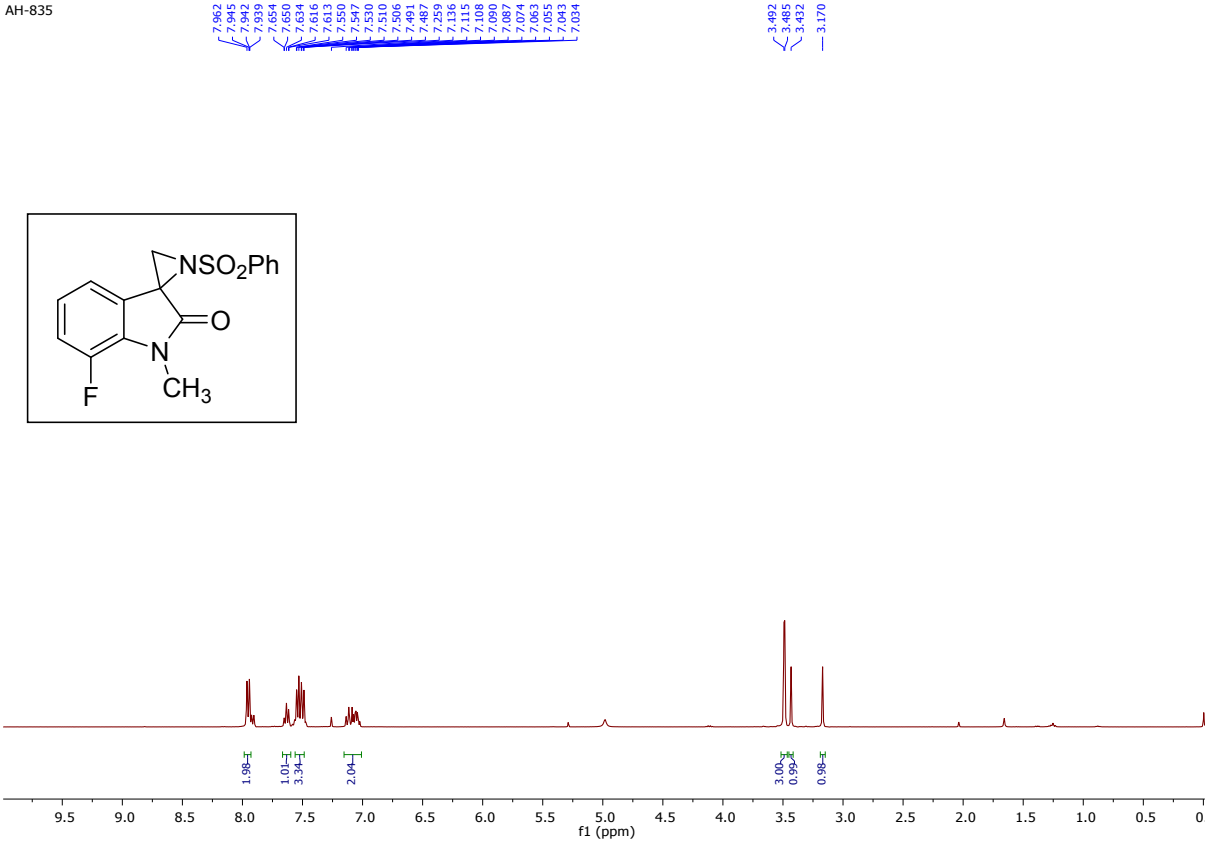
^{13}C NMR of compound (±)-1e (100 MHz, $CDCl_3$)



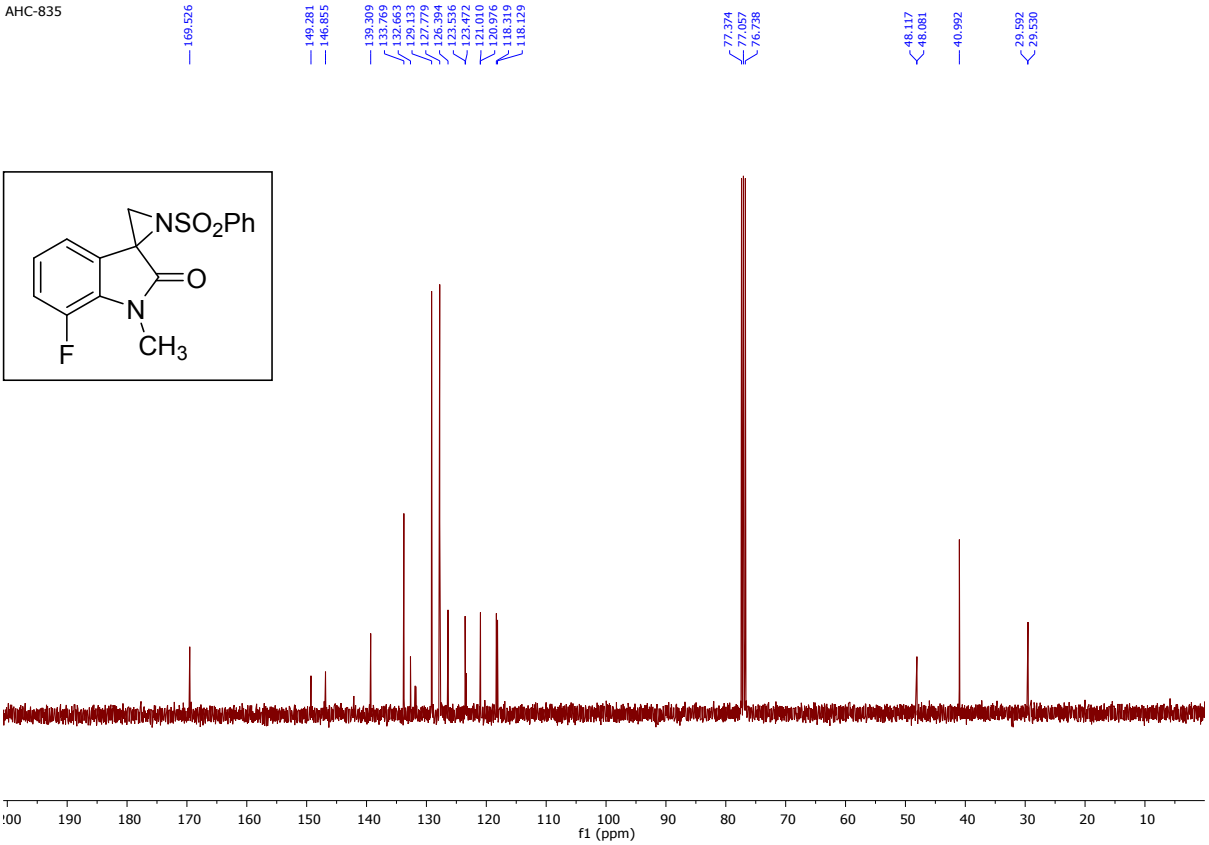
^{1}H NMR of compound (±)-1f (400 MHz, DMSO-d_6)



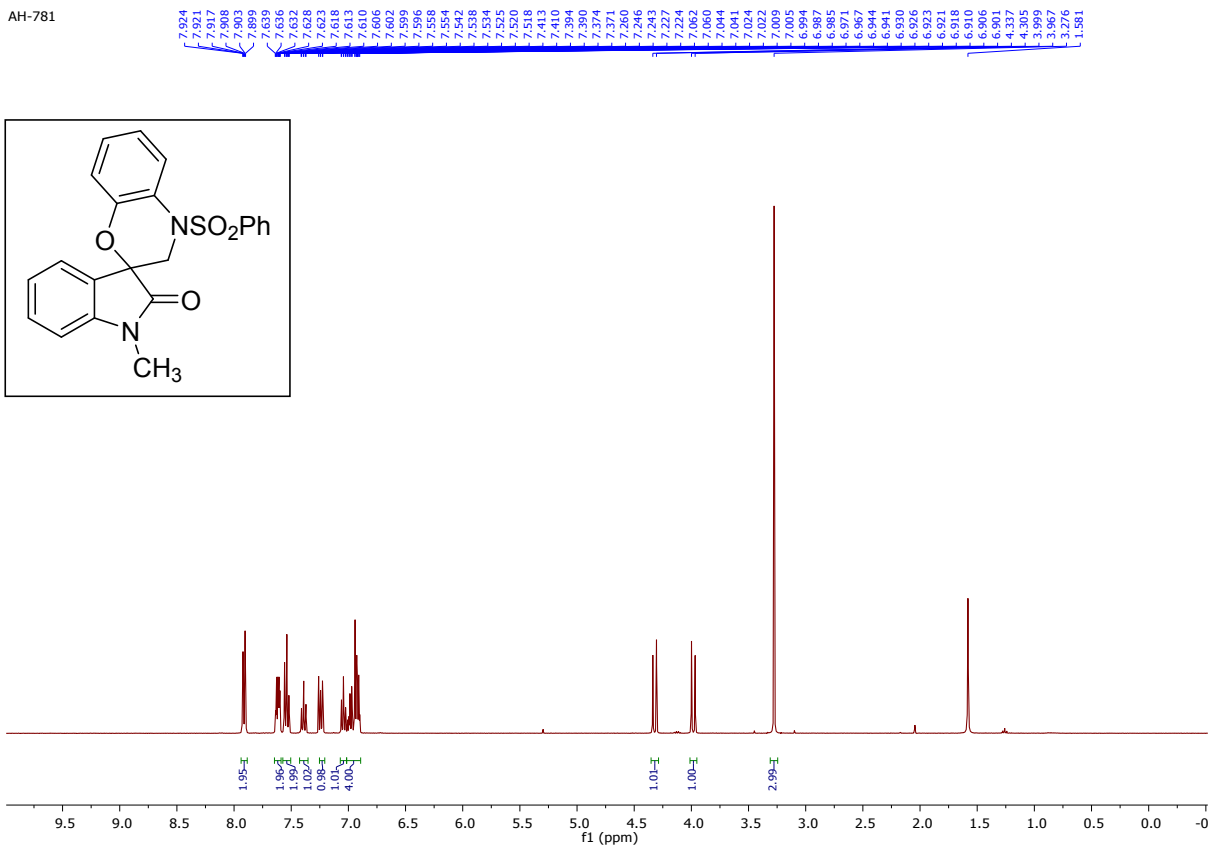
^{13}C NMR of compound (±)-1f (100 MHz, DMSO-d_6)



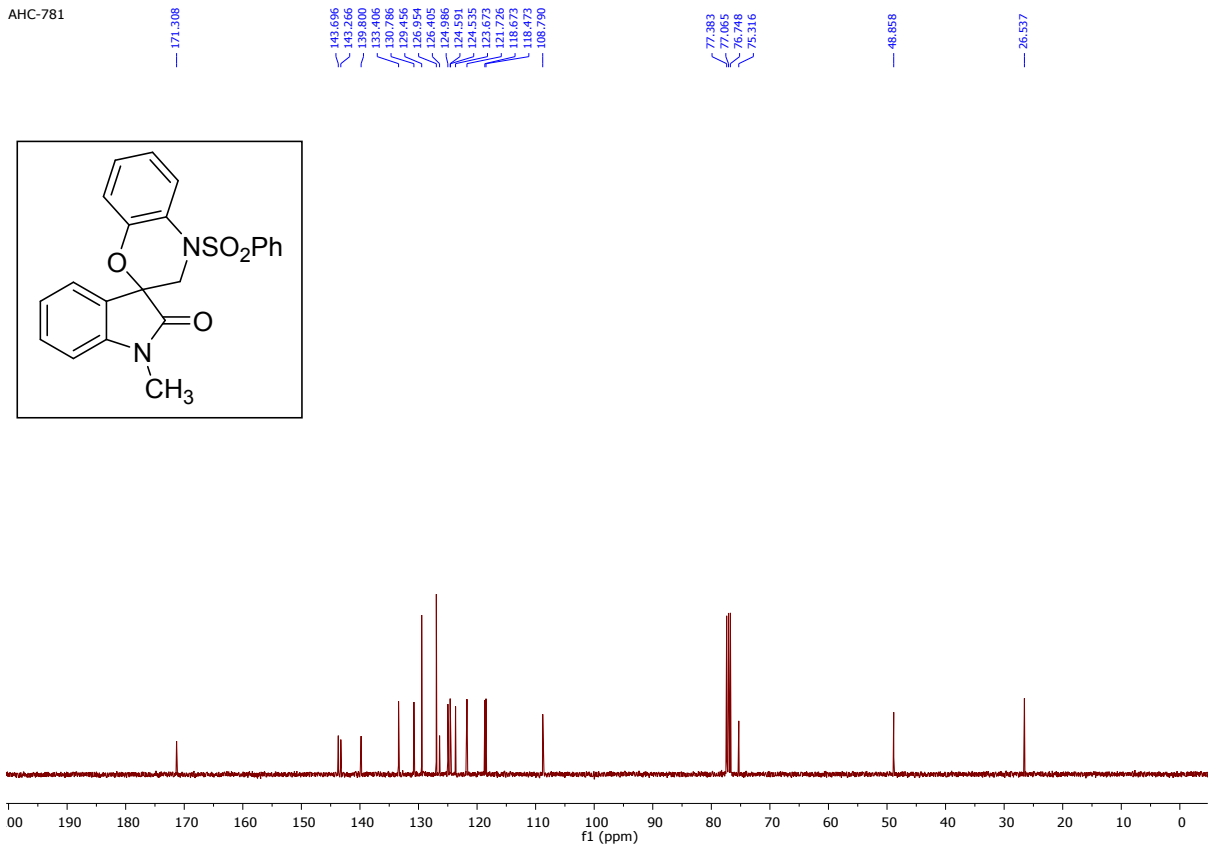
^{1}H NMR of compound (±)-1g (400 MHz, $CDCl_3$)



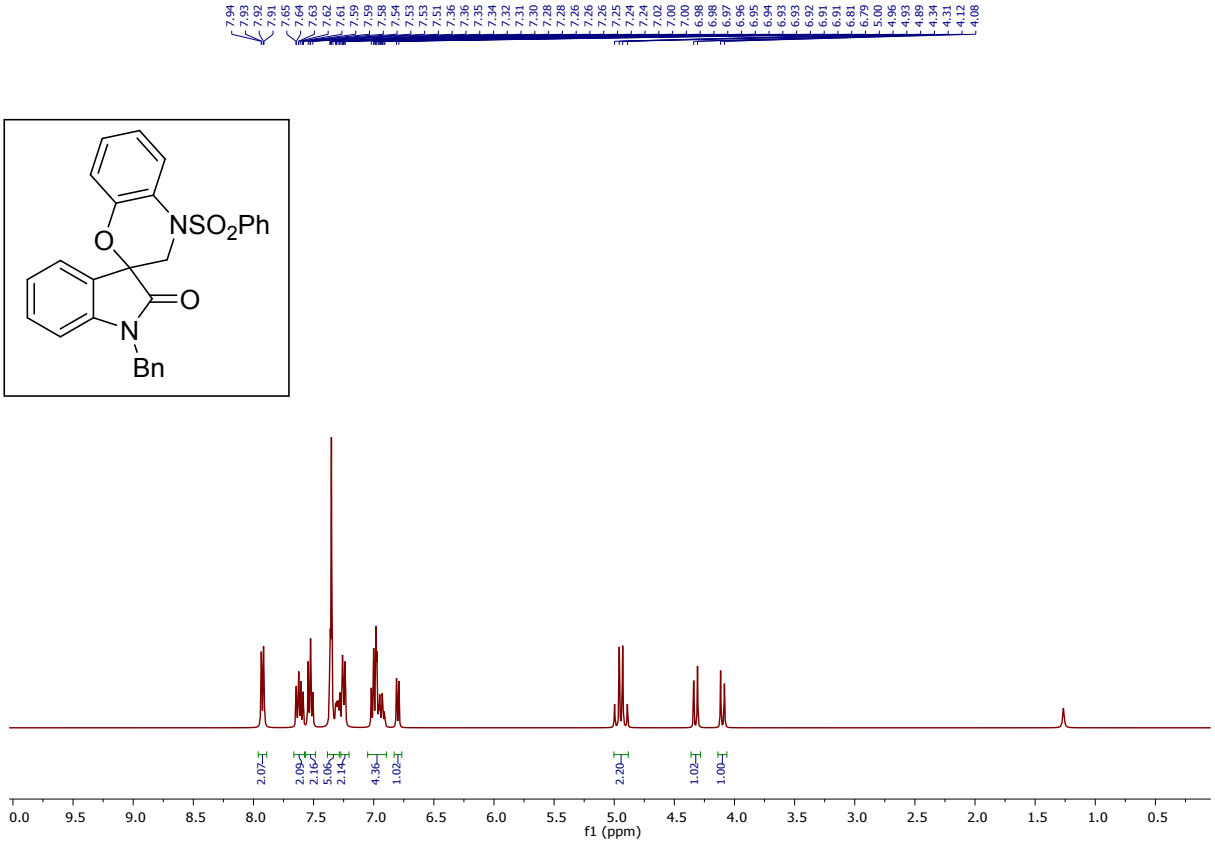
^{13}C NMR of compound (±)-1g (100 MHz, $CDCl_3$)



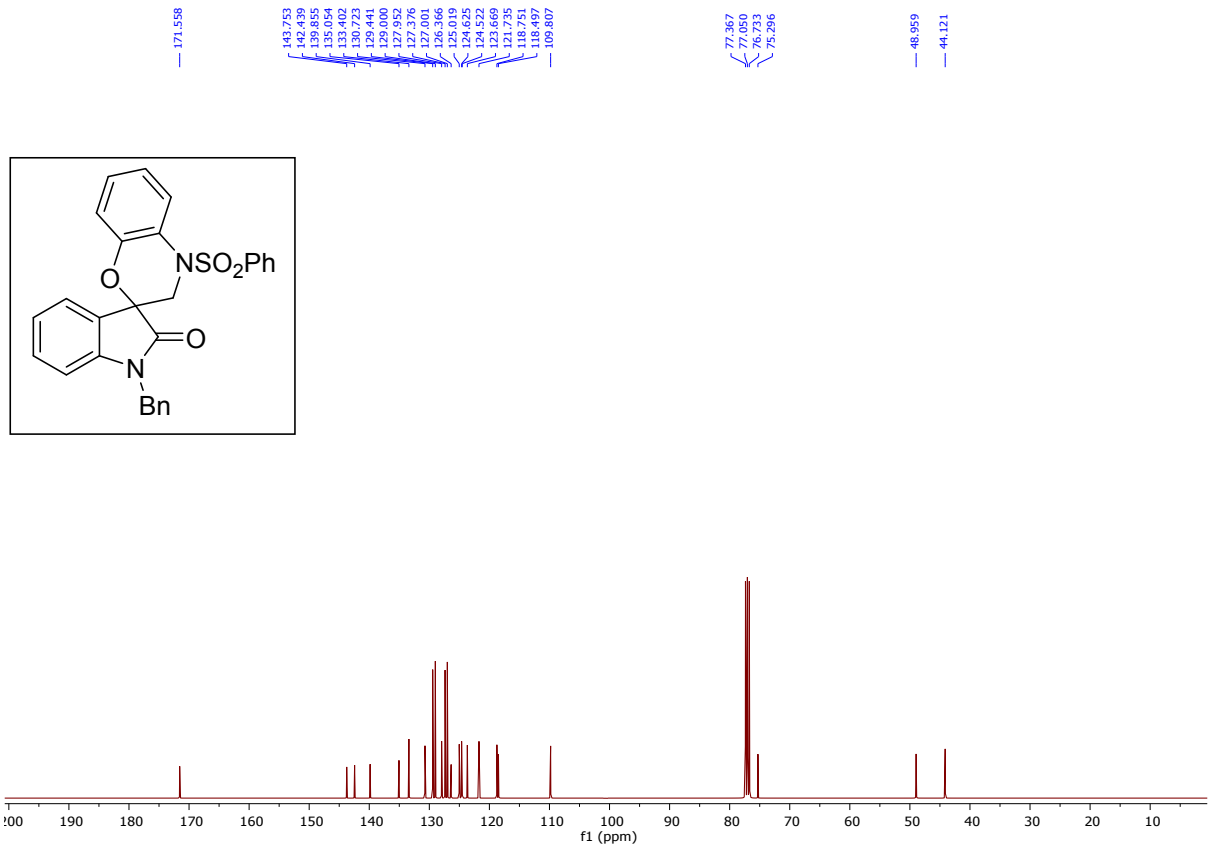
^{1}H NMR of compound (±)-3aa (400 MHz, $CDCl_3$)



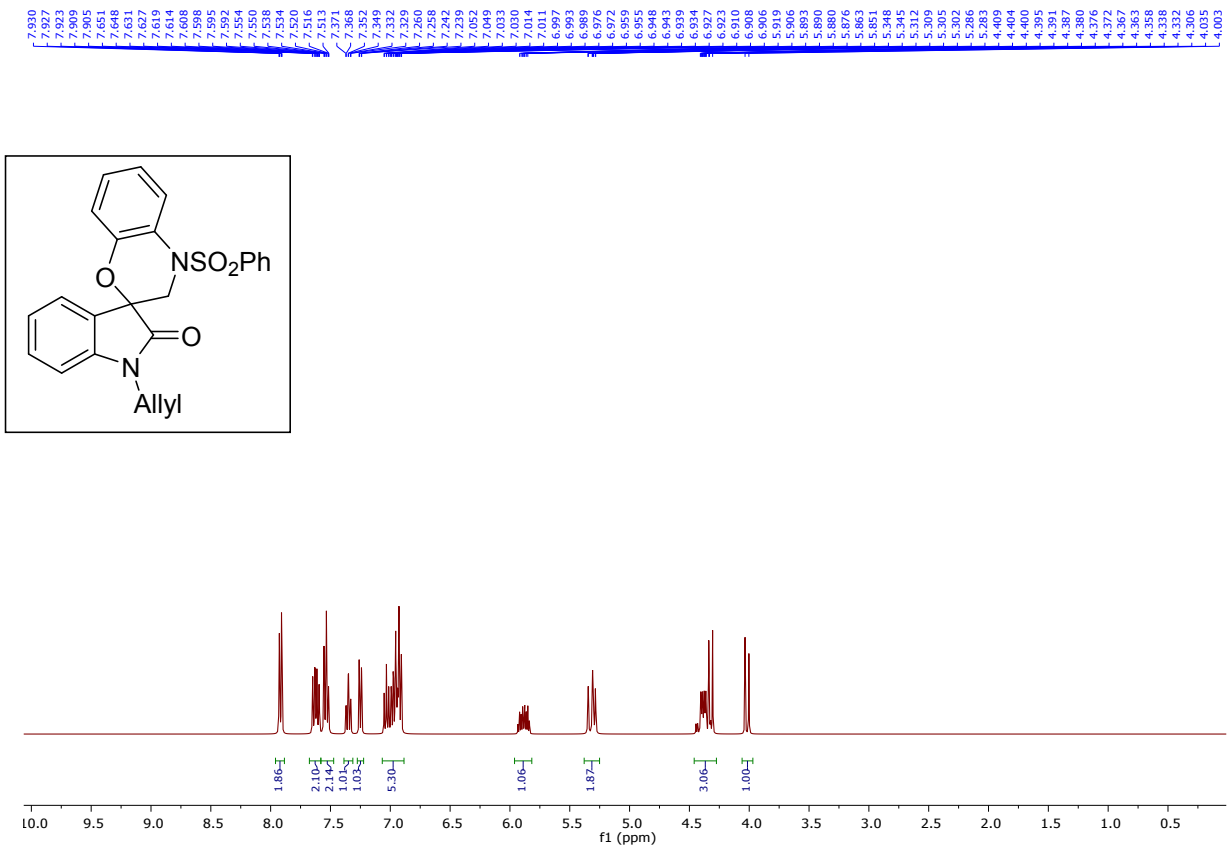
^{13}C NMR of compound (±)-3aa (100 MHz, $CDCl_3$)



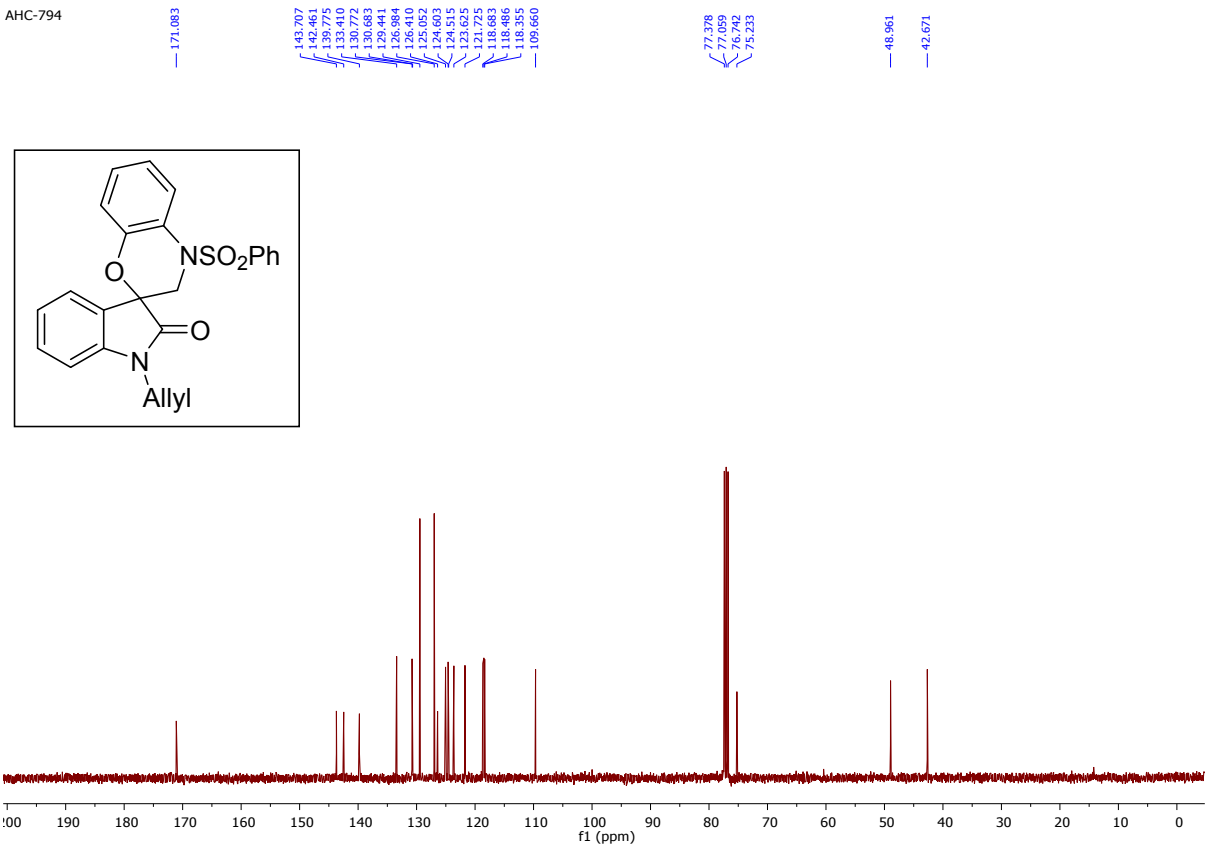
^{1}H NMR of compound (±)-3ba (400 MHz, $CDCl_3$)



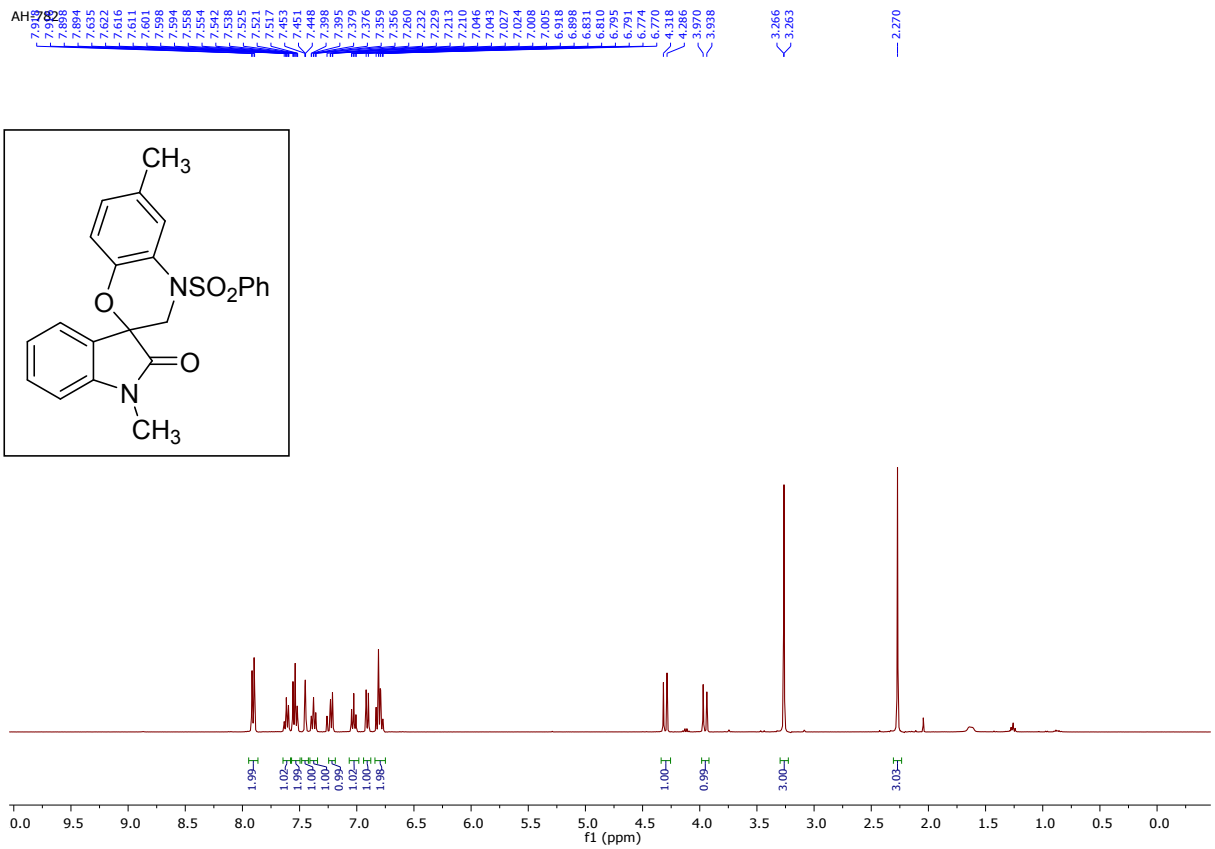
^{13}C NMR of compound (±)-3ba (100 MHz, $CDCl_3$)



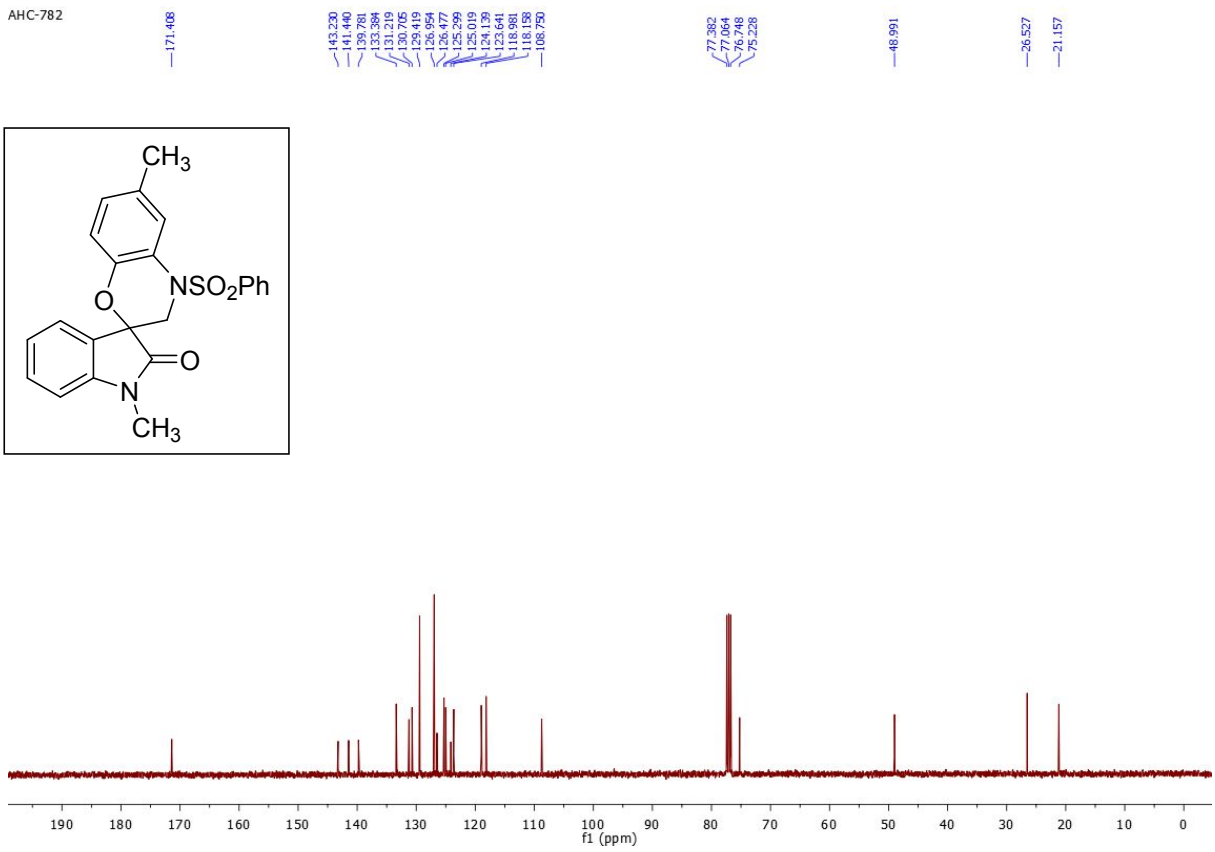
^{1}H NMR of compound (±)-3ca (400 MHz, $CDCl_3$)



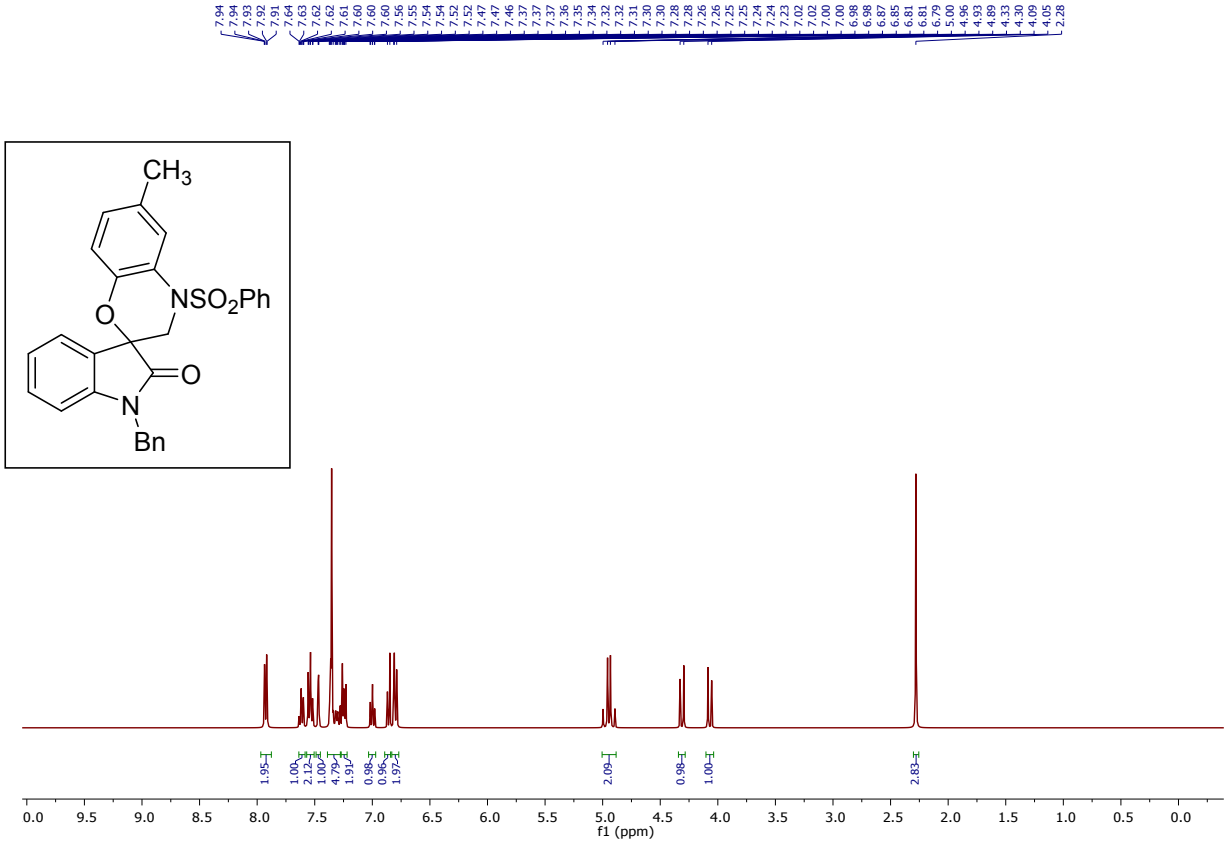
^{13}C NMR of compound (±)-3ca (100 MHz, $CDCl_3$)



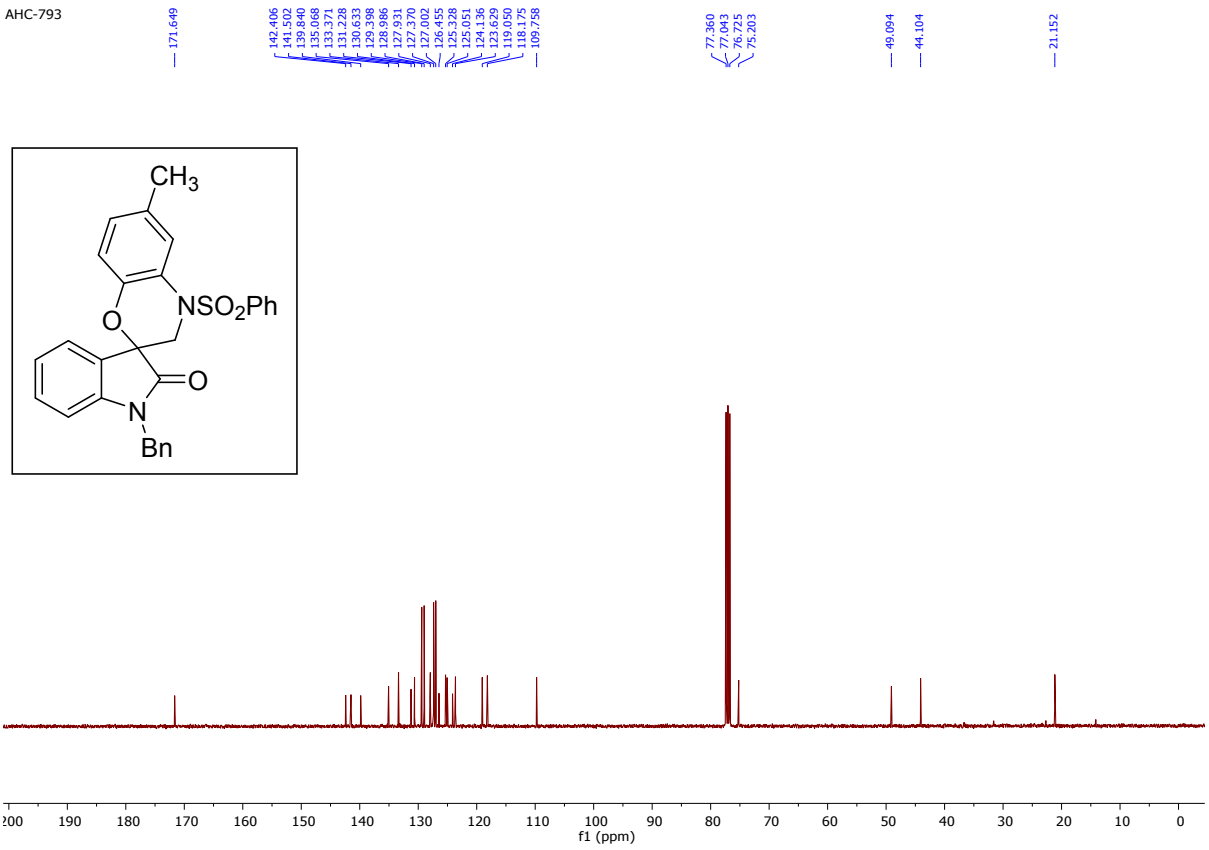
^{1}H NMR of compound (±)-3ab (400 MHz, $CDCl_3$)



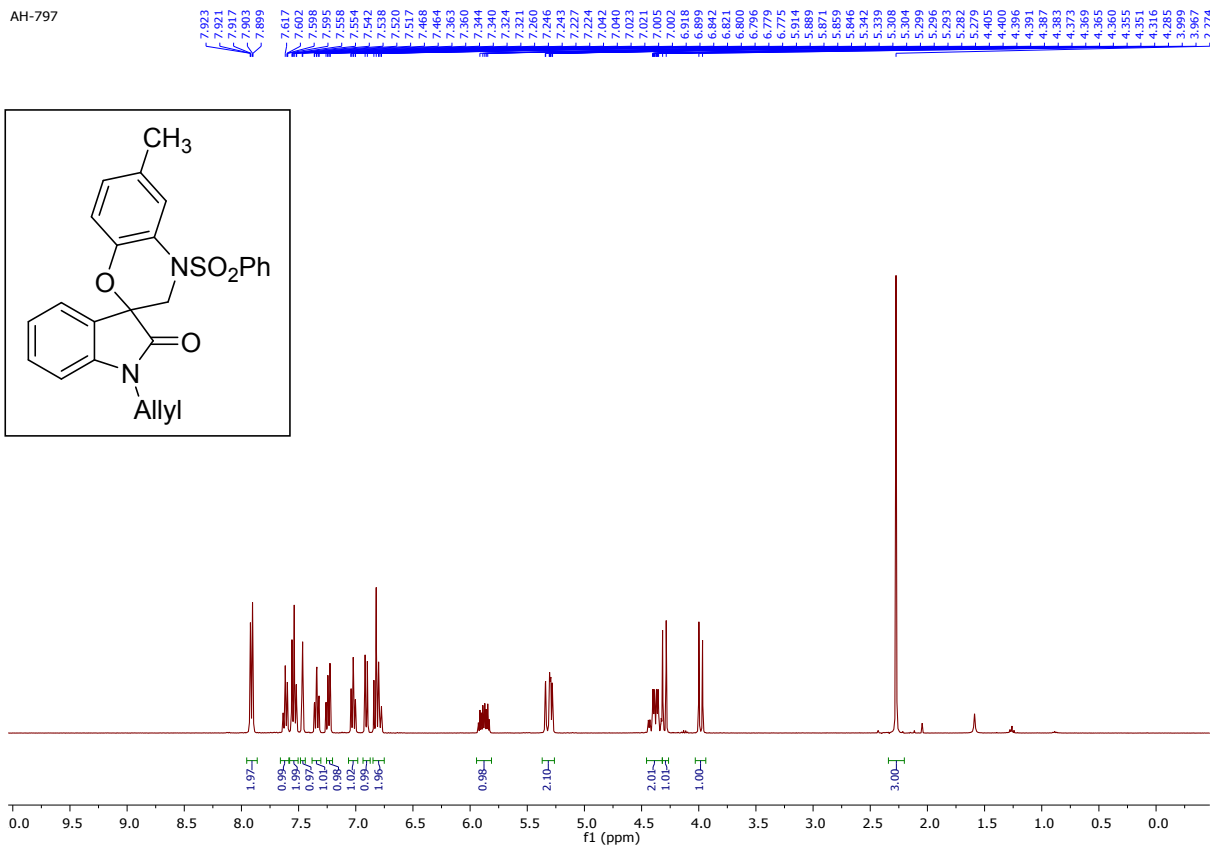
^{13}C NMR of compound (±)-3ab (100 MHz, $CDCl_3$)



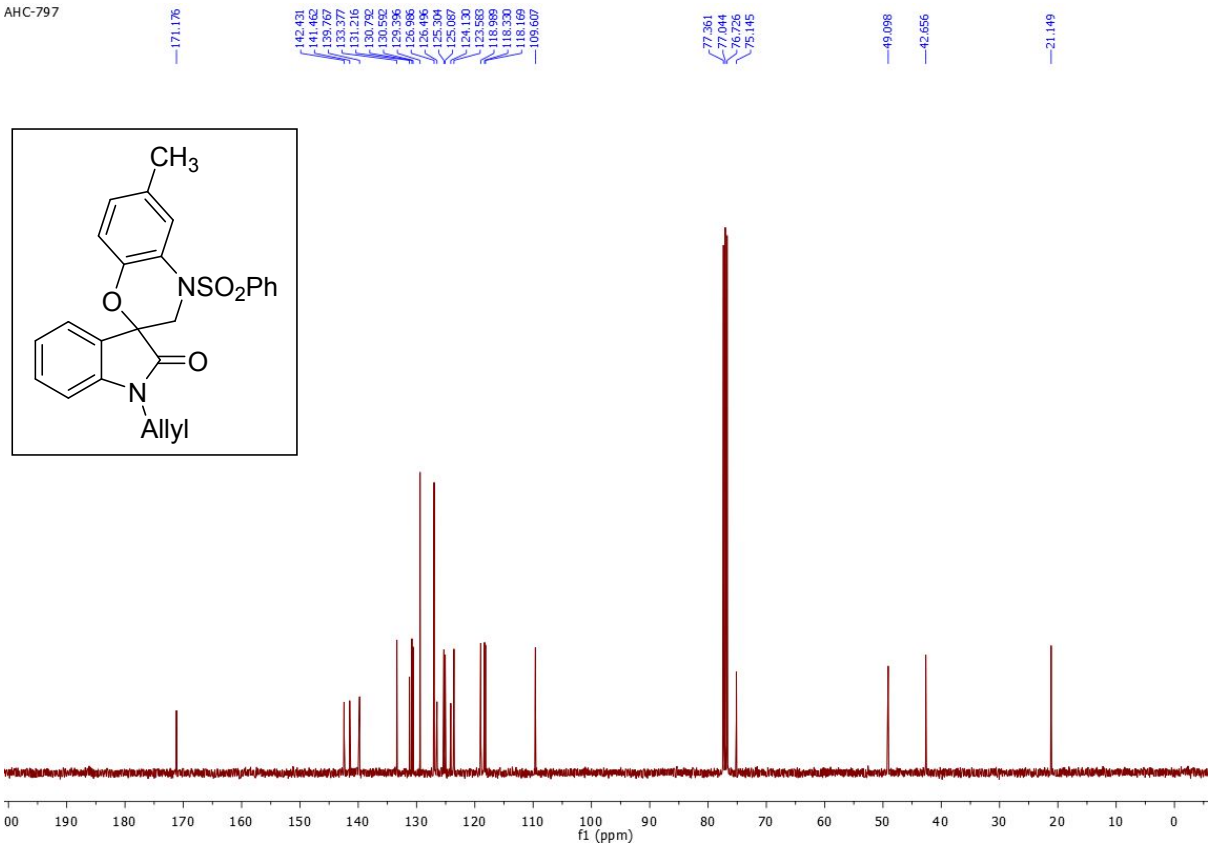
^{1}H NMR of compound (±)-3bb (400 MHz, $CDCl_3$)



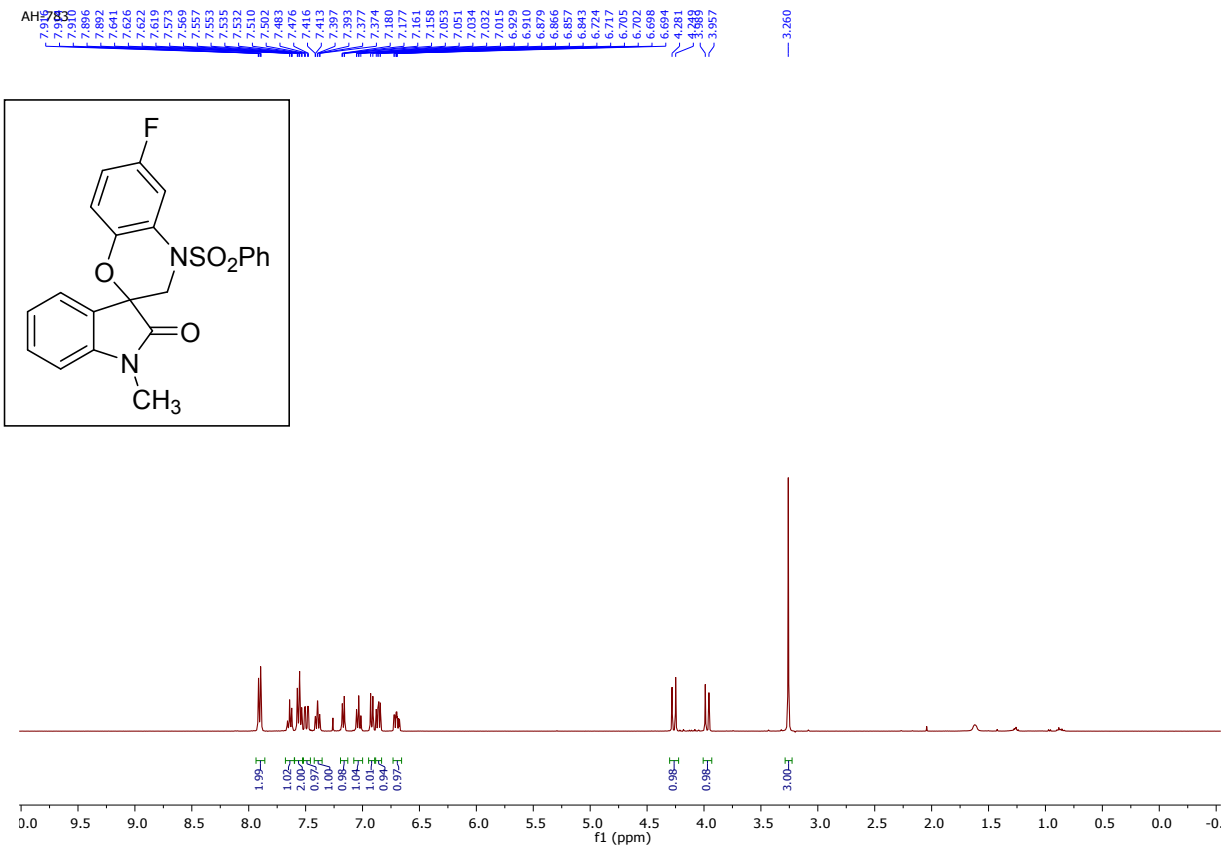
^{13}C NMR of compound (±)-3bb (100 MHz, $CDCl_3$)



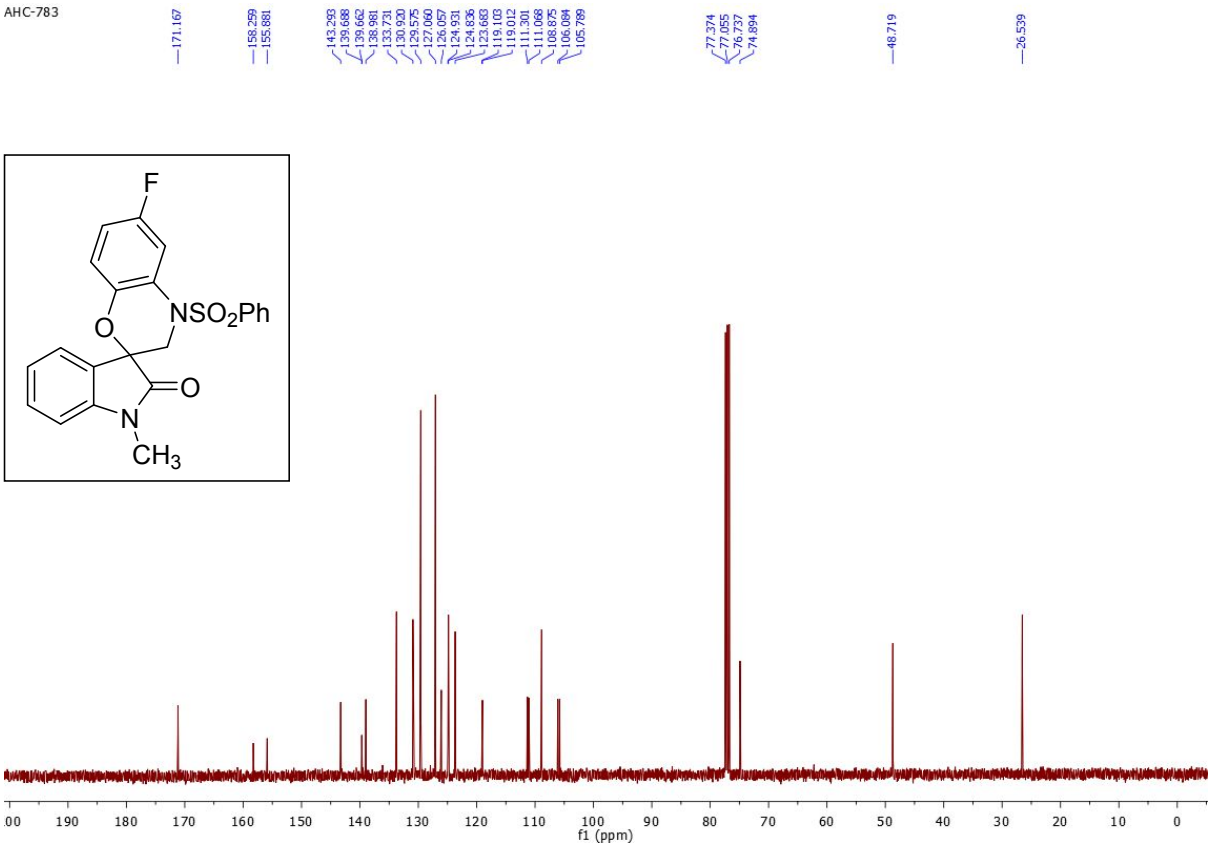
^{1}H NMR of compound (±)-3cb (400 MHz, $CDCl_3$)



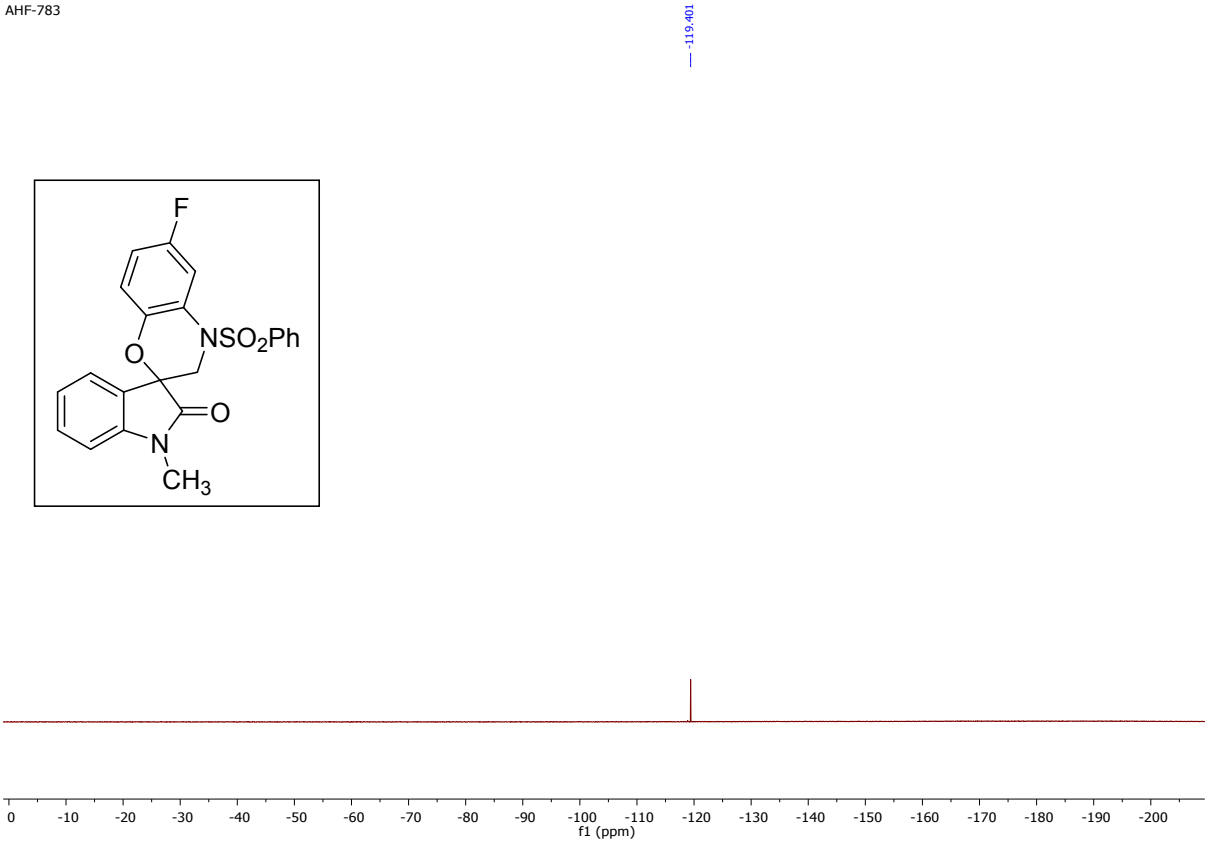
^{13}C NMR of compound (±)-3cb (100 MHz, $CDCl_3$)



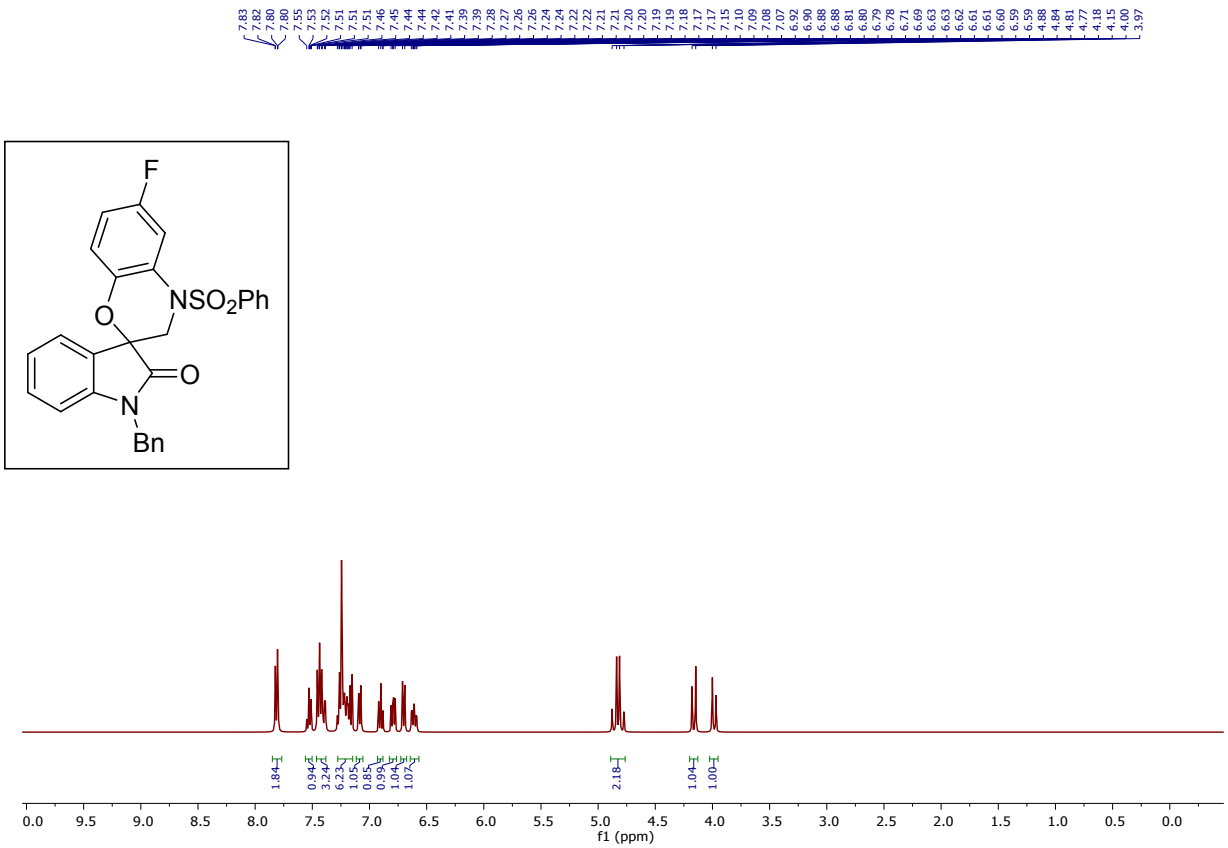
^{1}H NMR of compound (±)-3ac (400 MHz, $CDCl_3$)



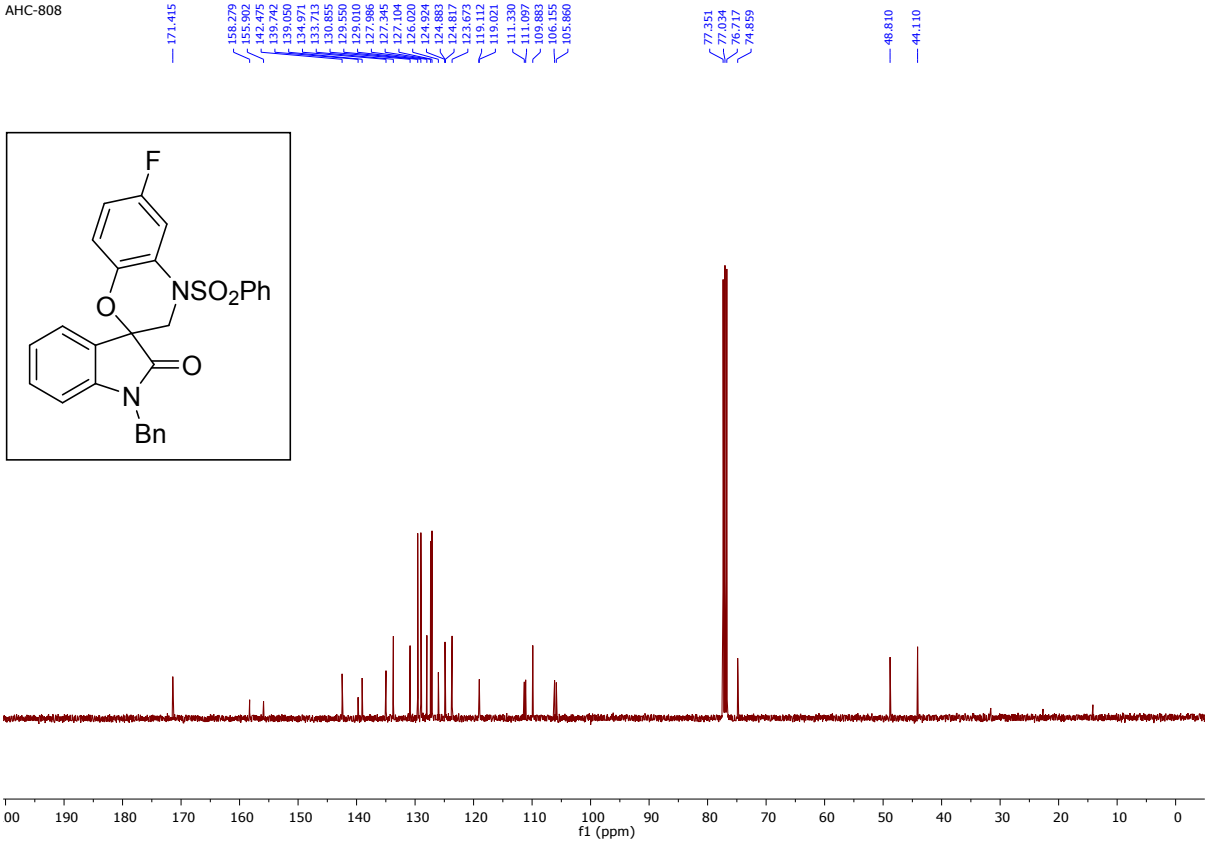
^{13}C NMR of compound (±)-3ac (100 MHz, $CDCl_3$)



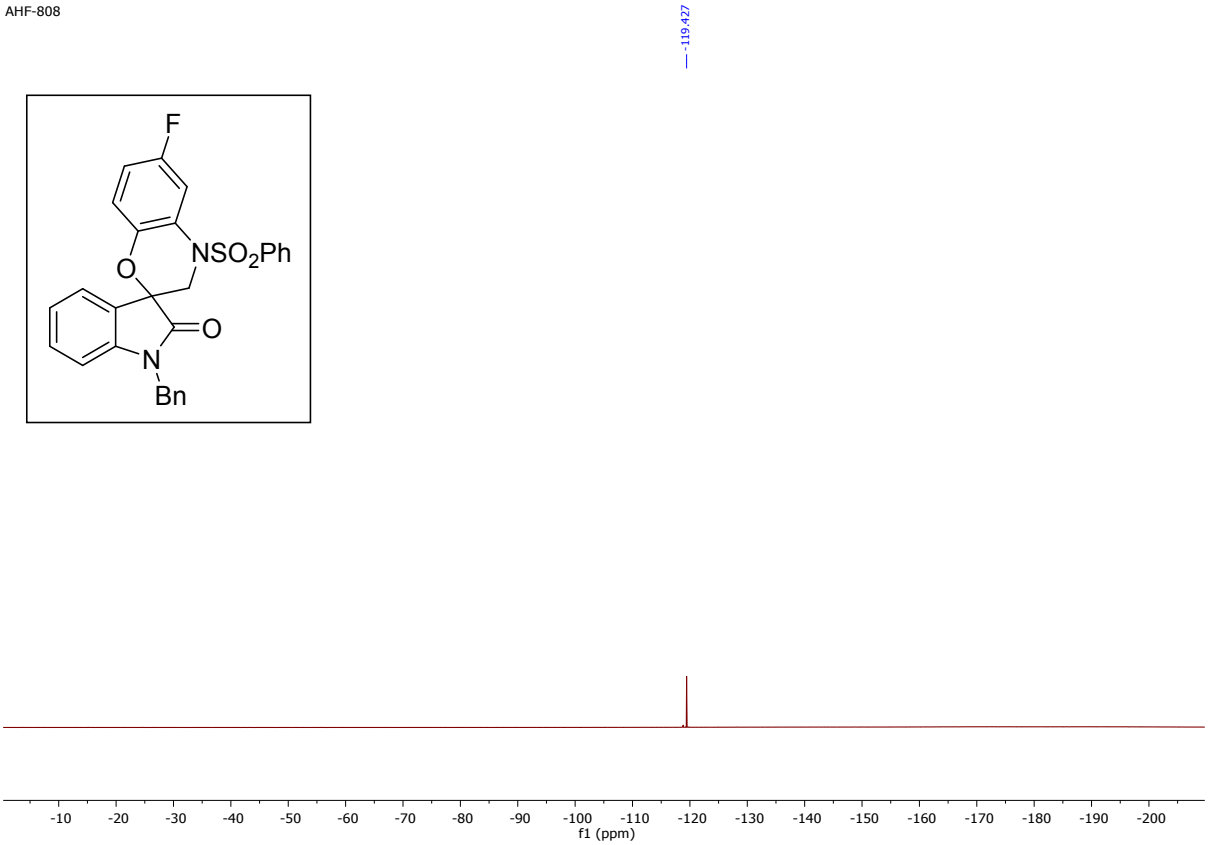
^{19}F NMR of compound (±)-3ac (376 MHz, $CDCl_3$)



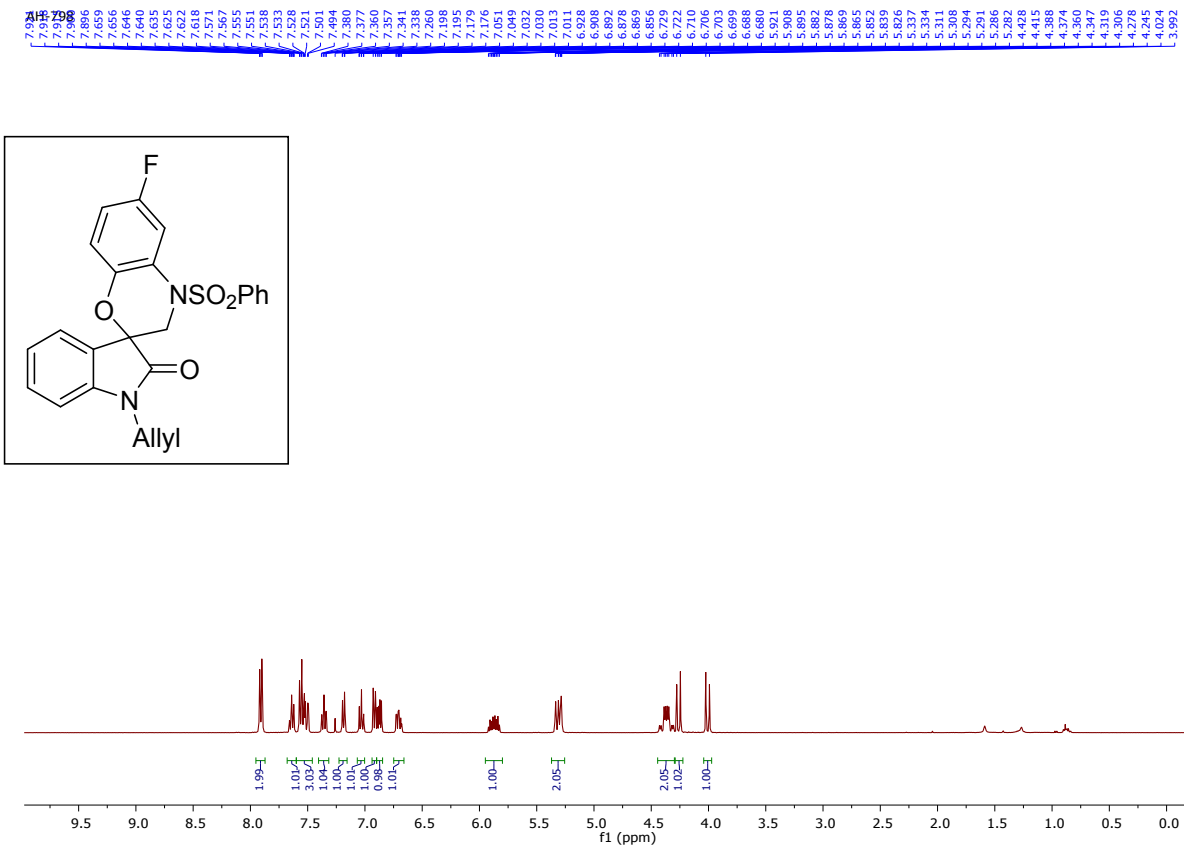
^{1}H NMR of compound (±)-3bc (400 MHz, $CDCl_3$)



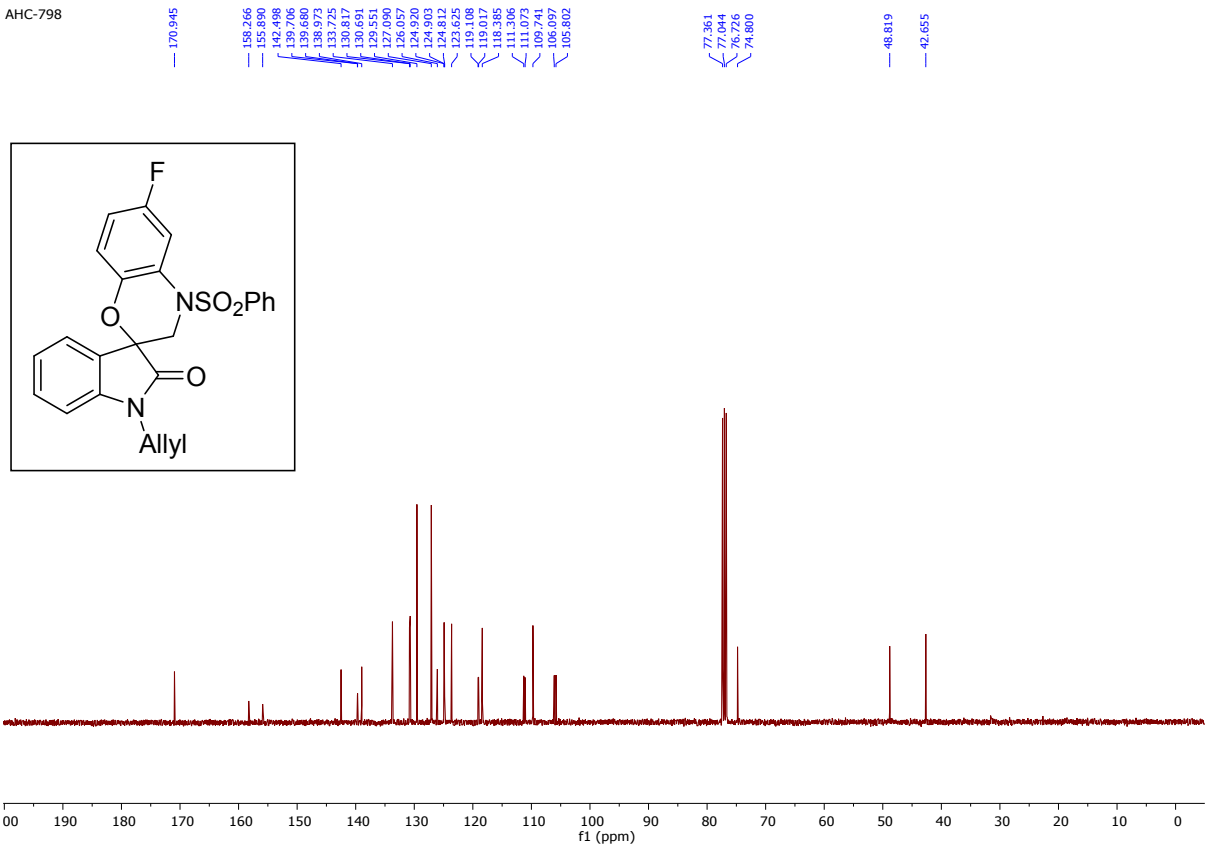
^{13}C NMR of compound (±)-3bc (100 MHz, $CDCl_3$)



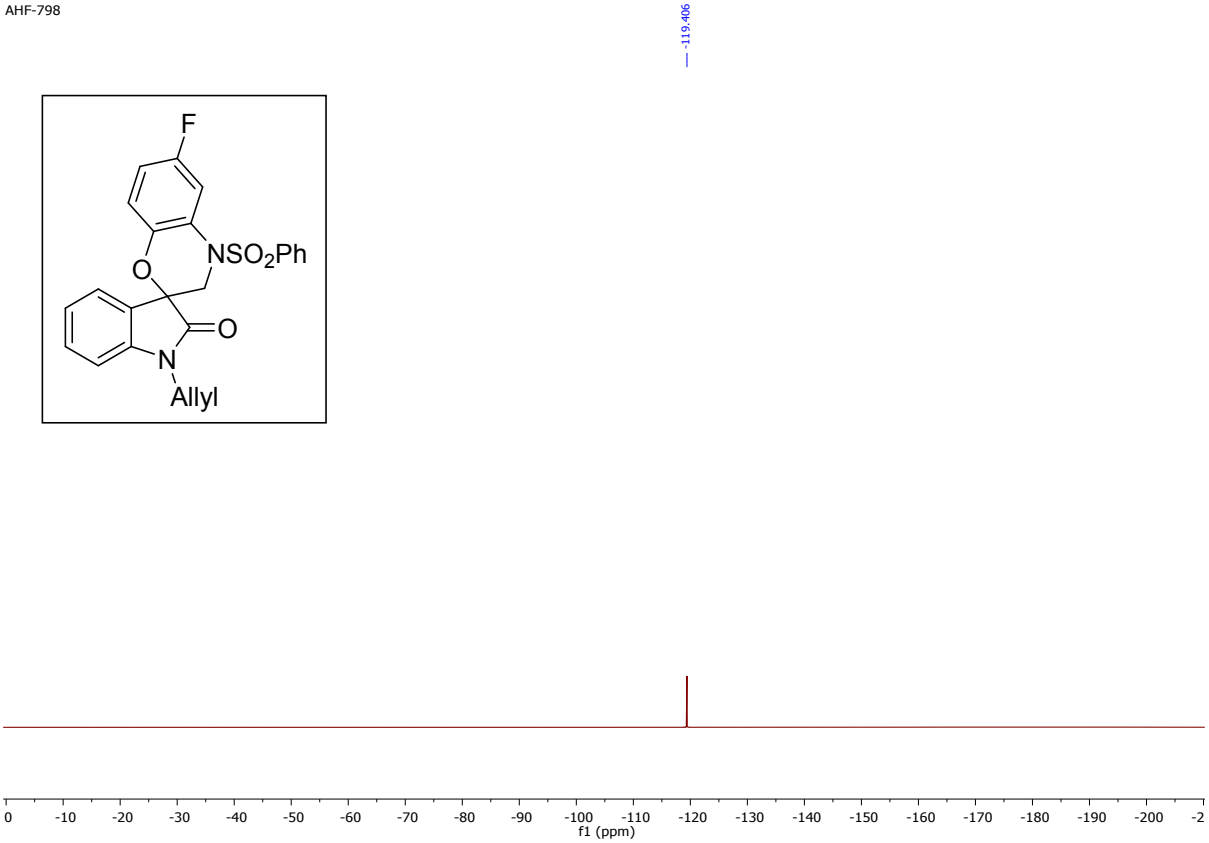
^{19}F NMR of compound (±)-3bc (376 MHz, $CDCl_3$)



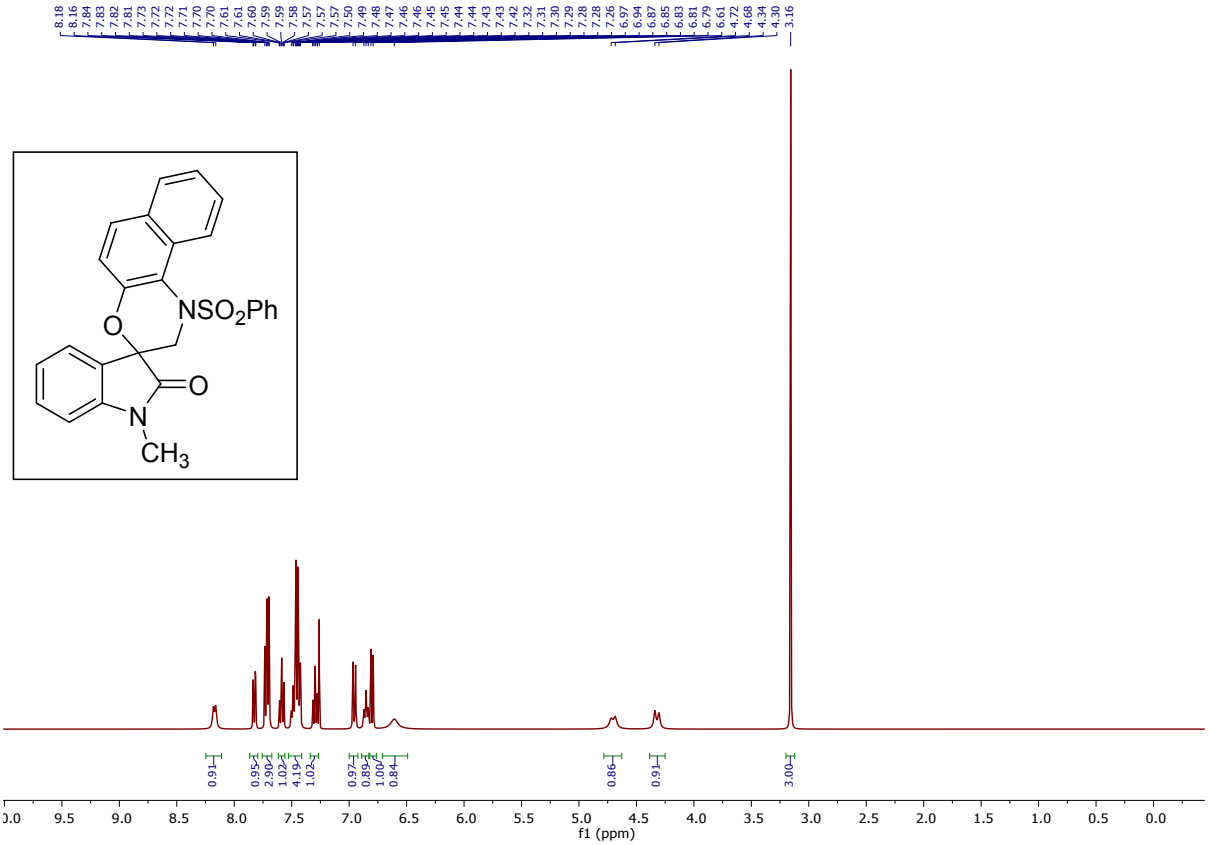
^{1}H NMR of compound (±)-3cc (400 MHz, $CDCl_3$)



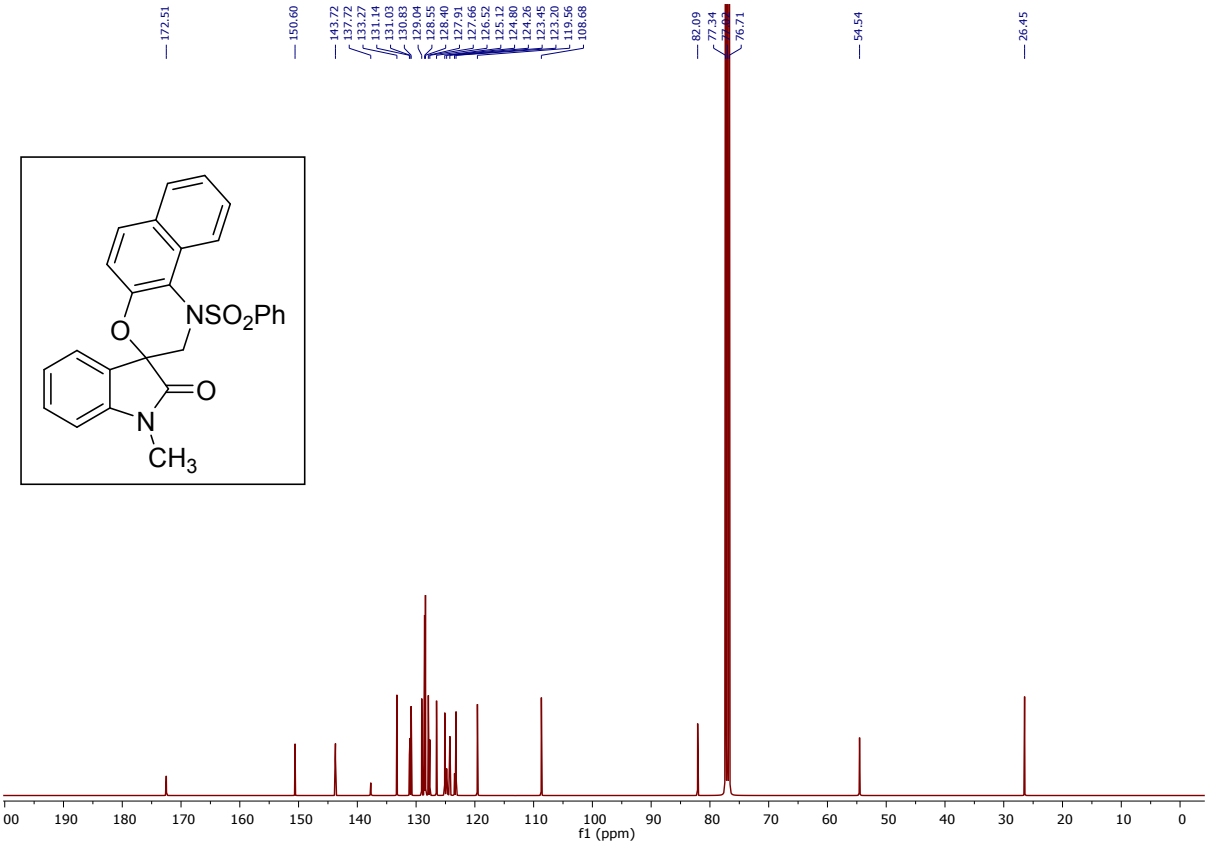
^{13}C NMR of compound (±)-3cc (100 MHz, $CDCl_3$)



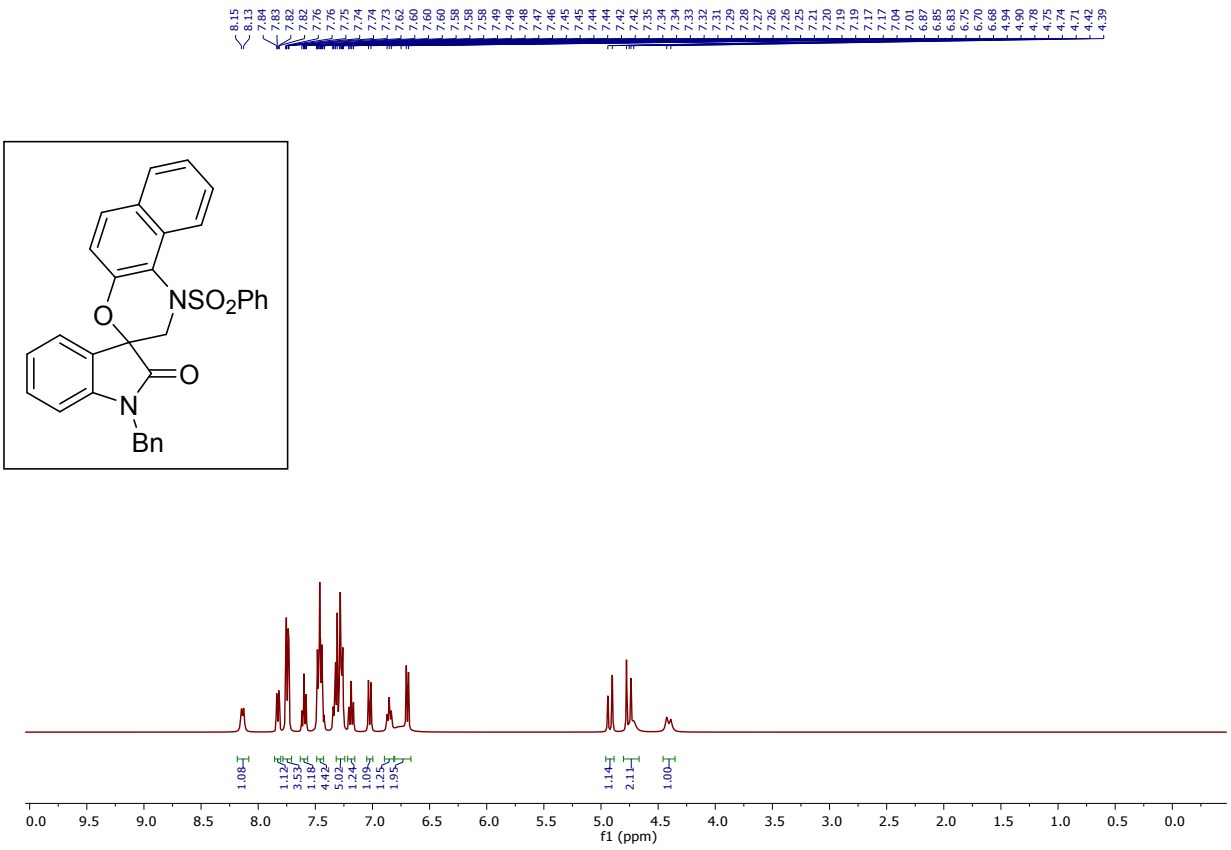
^{19}F NMR of compound (±)-3cc (376 MHz, $CDCl_3$)



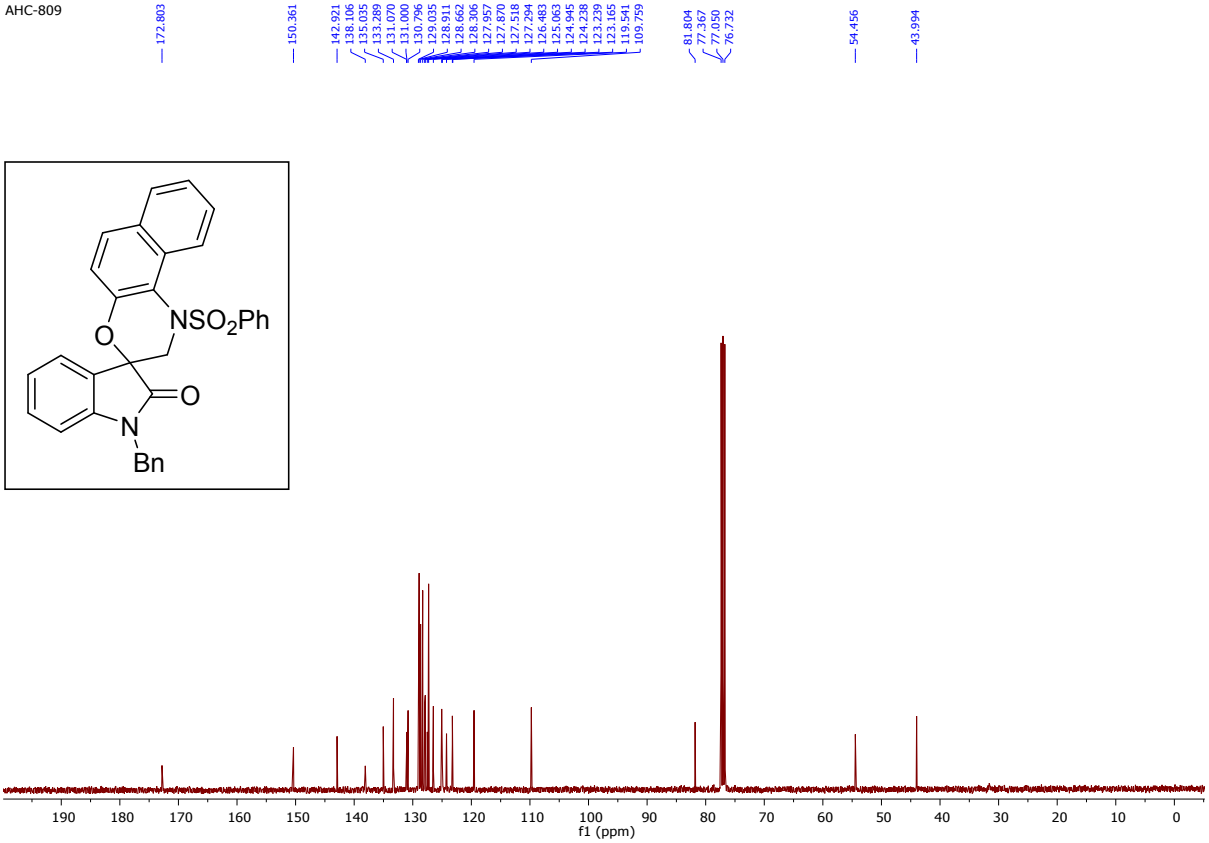
^{1}H NMR of compound (±)-3ad (400 MHz, $CDCl_3$)



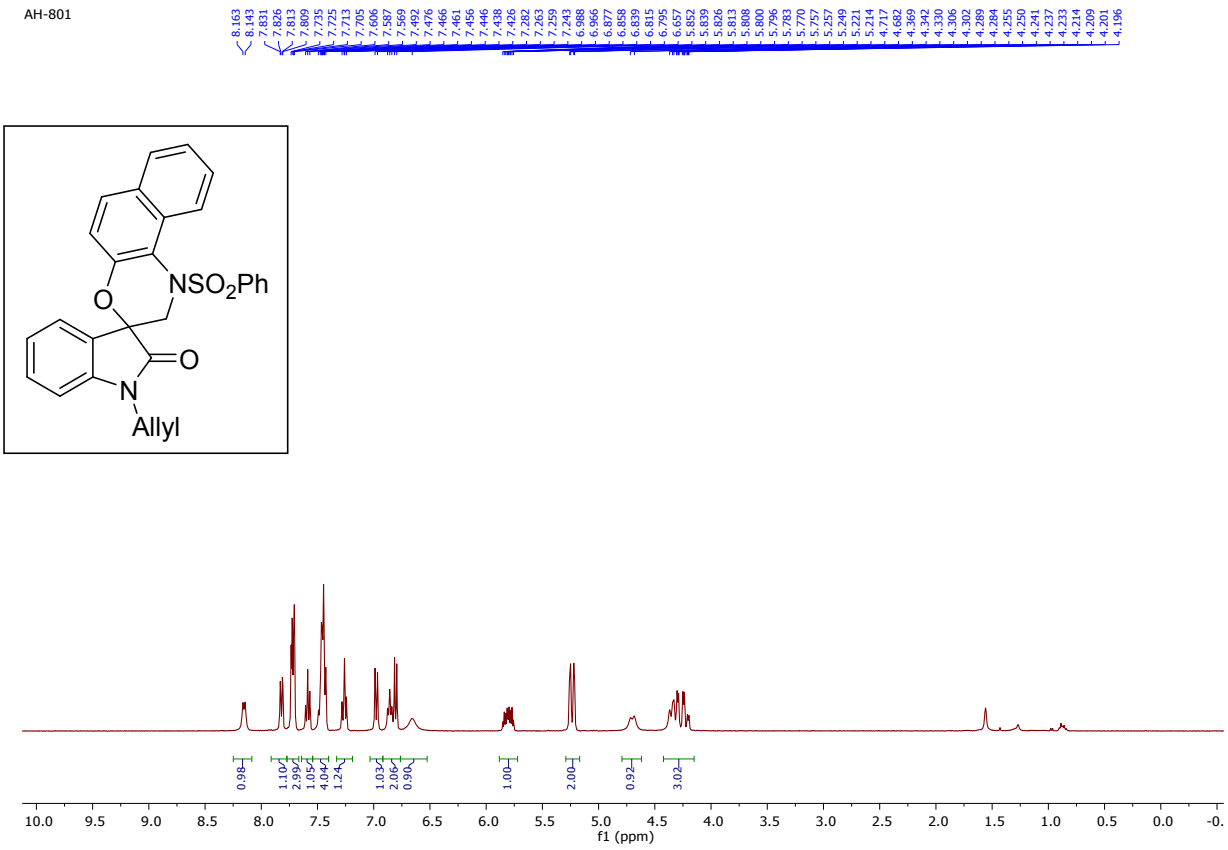
^{13}C NMR of compound (±)-3ad (100 MHz, $CDCl_3$)



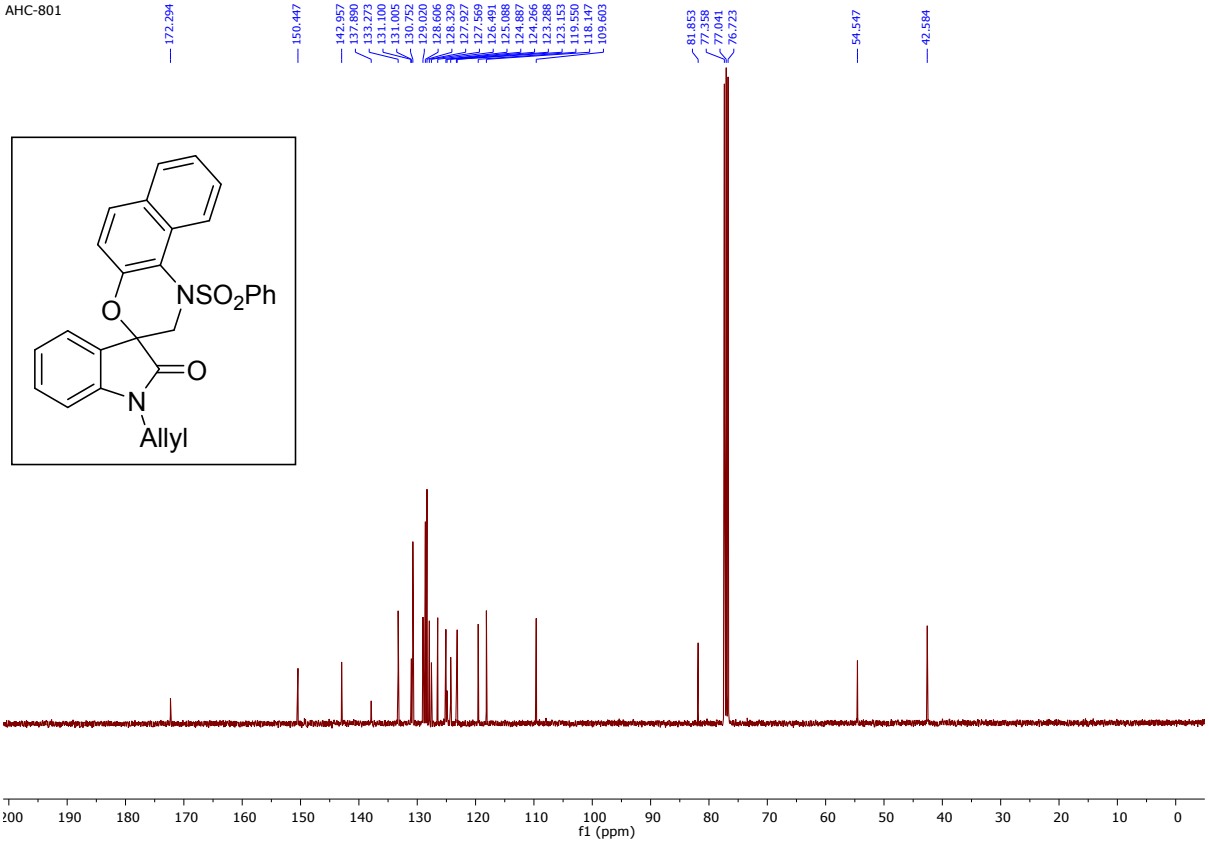
^{1}H NMR of compound (±)-3bd (400 MHz, $CDCl_3$)



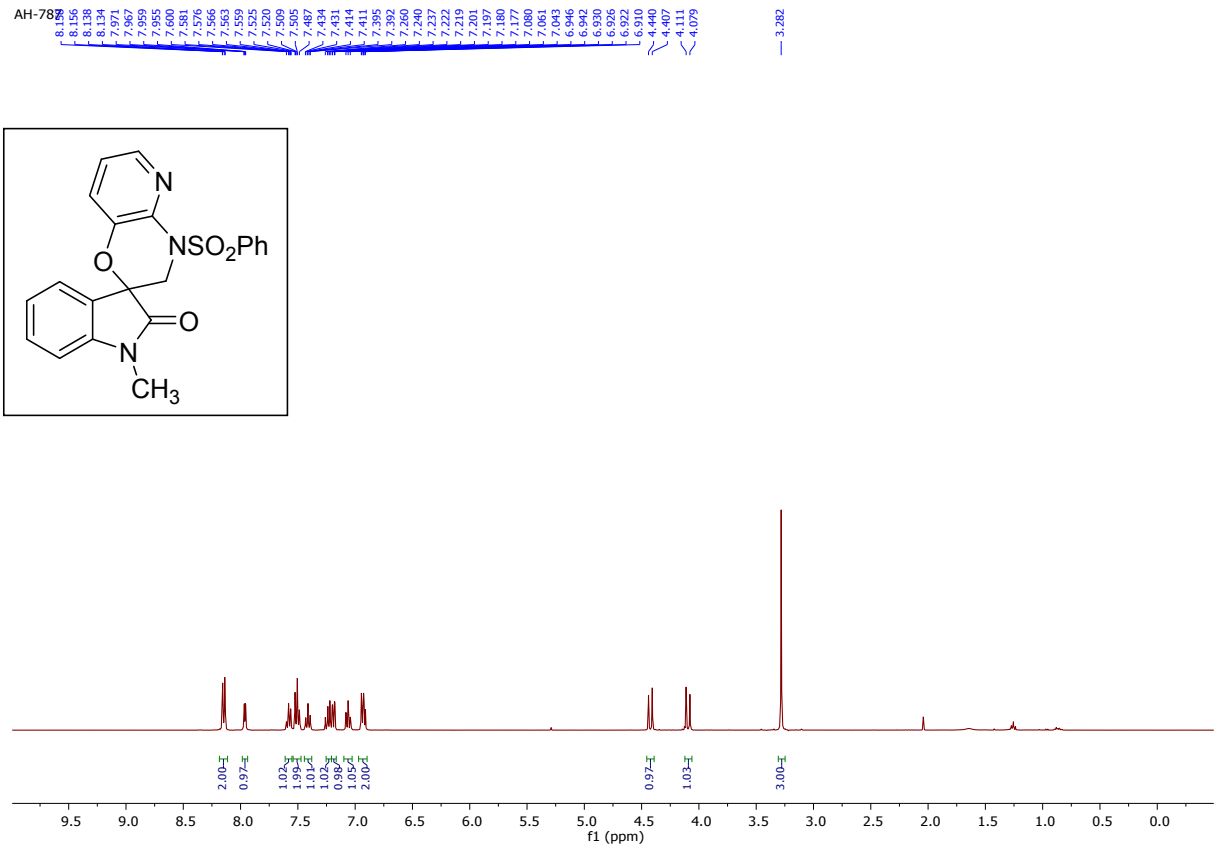
^{13}C NMR of compound (±)-3bd (100 MHz, $CDCl_3$)



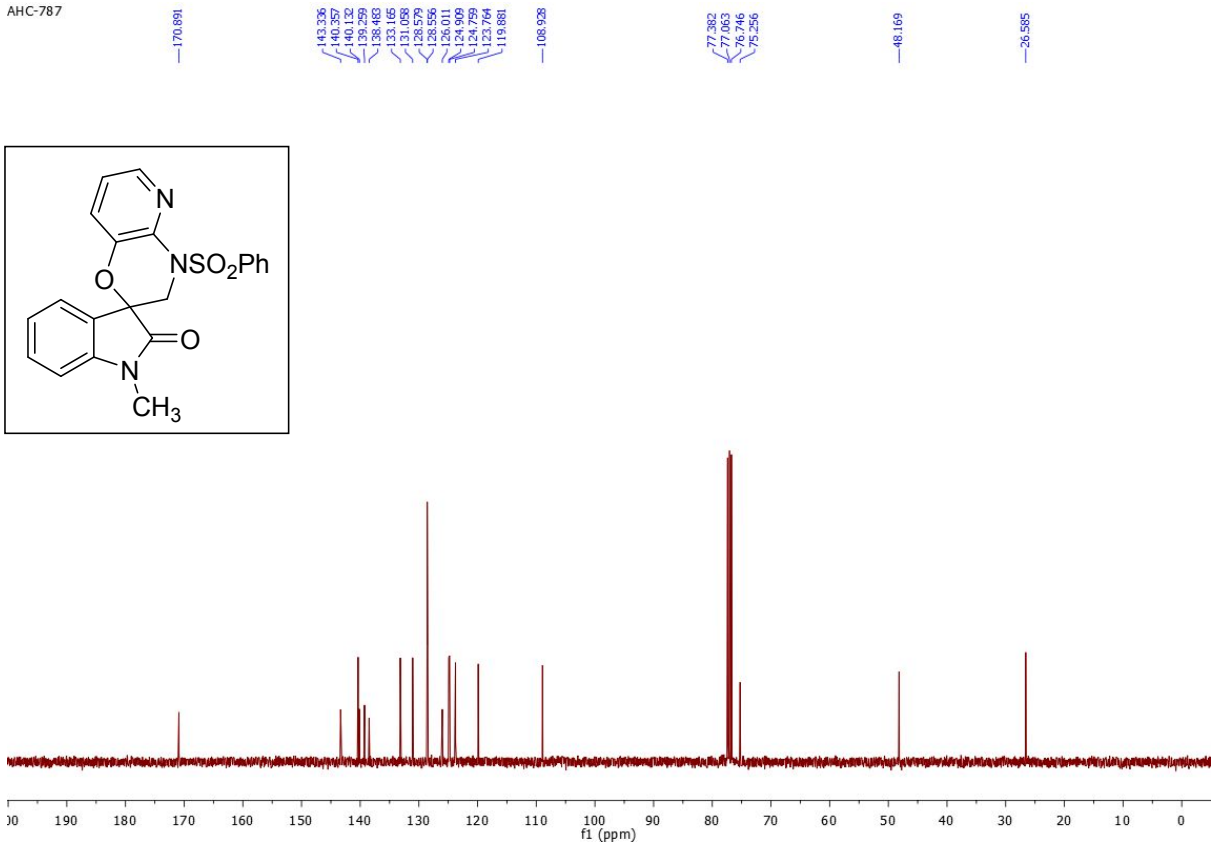
^{1}H NMR of compound (±)-3cd (400 MHz, $CDCl_3$)



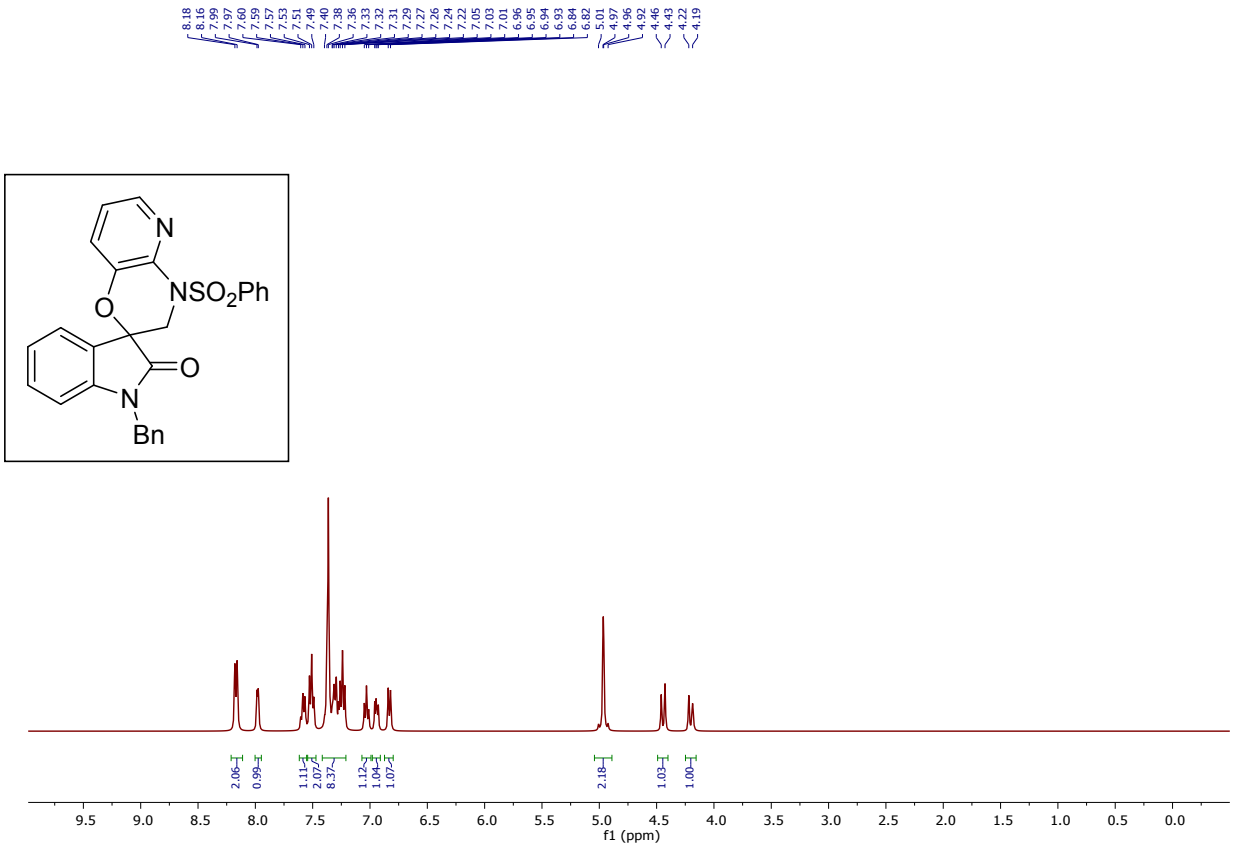
^{13}C NMR of compound (±)-3cd (100 MHz, $CDCl_3$)



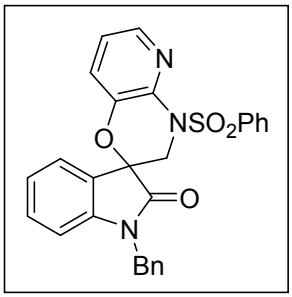
^{1}H NMR of compound (±)-3ae (400 MHz, $CDCl_3$)

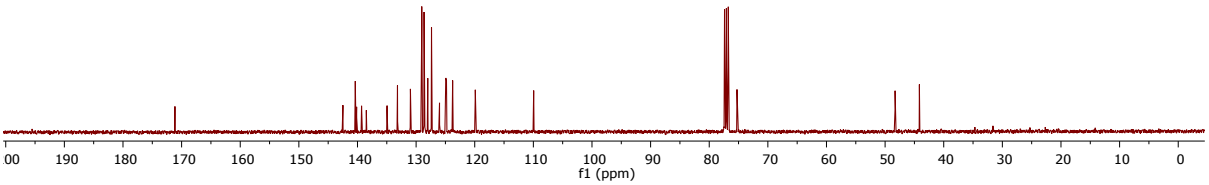


^{13}C NMR of compound (±)-3ae (100 MHz, $CDCl_3$)

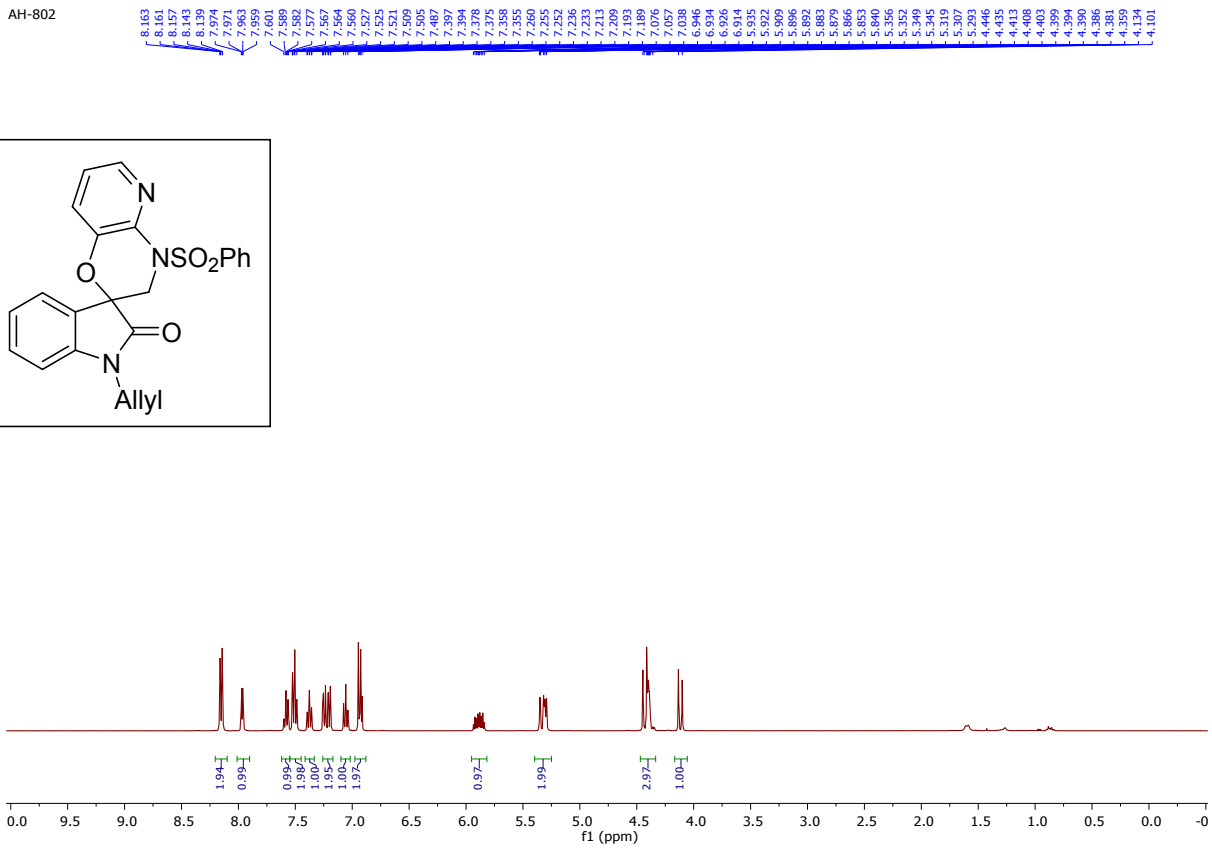


^{1}H NMR of compound (±)-3be (400 MHz, $CDCl_3$)

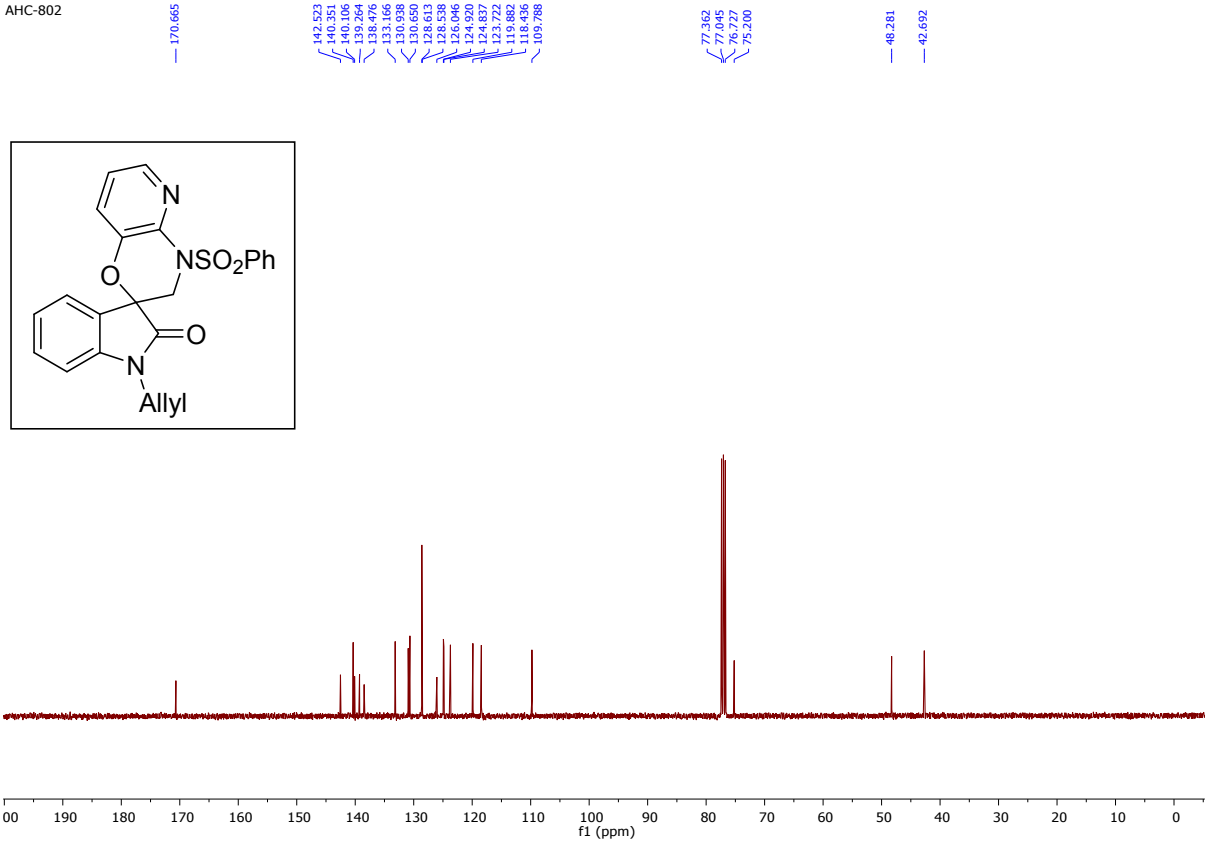




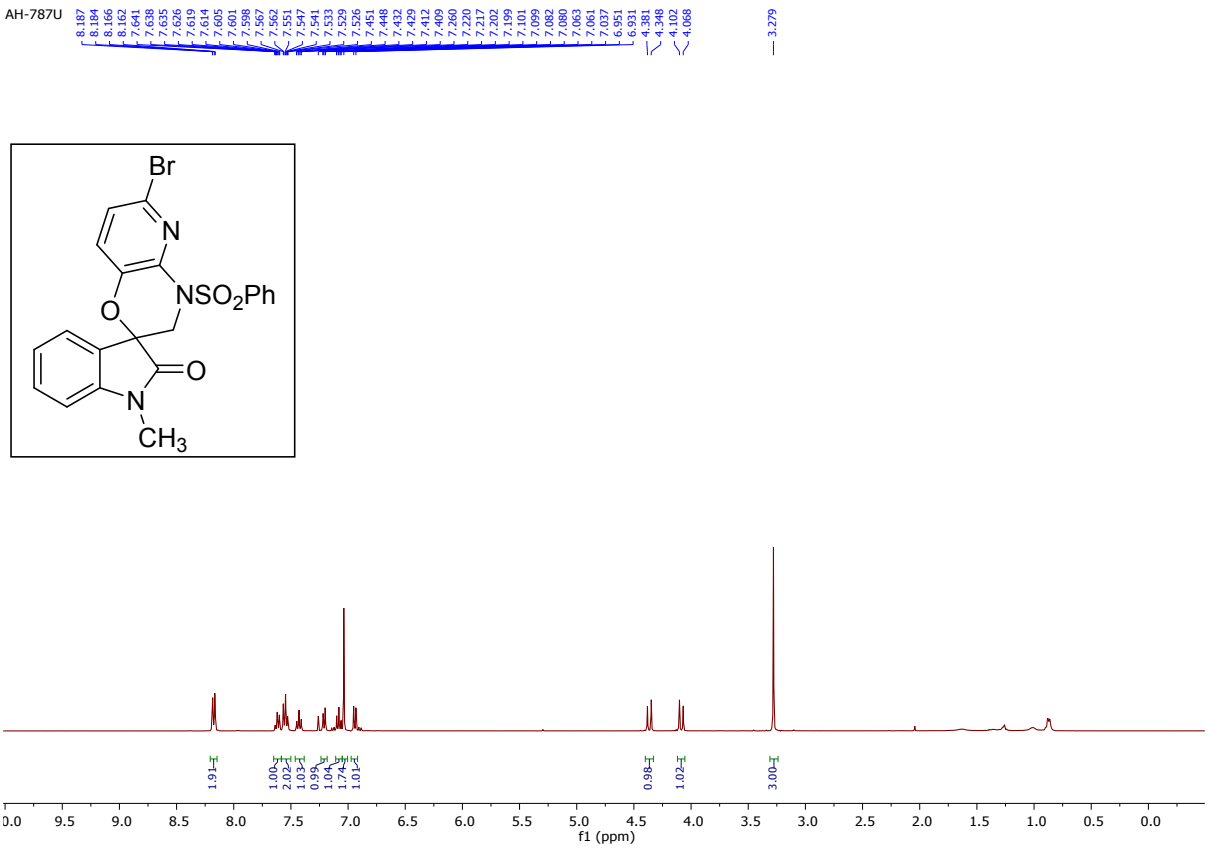
^{13}C NMR of compound (±)-3be (100 MHz, $CDCl_3$)



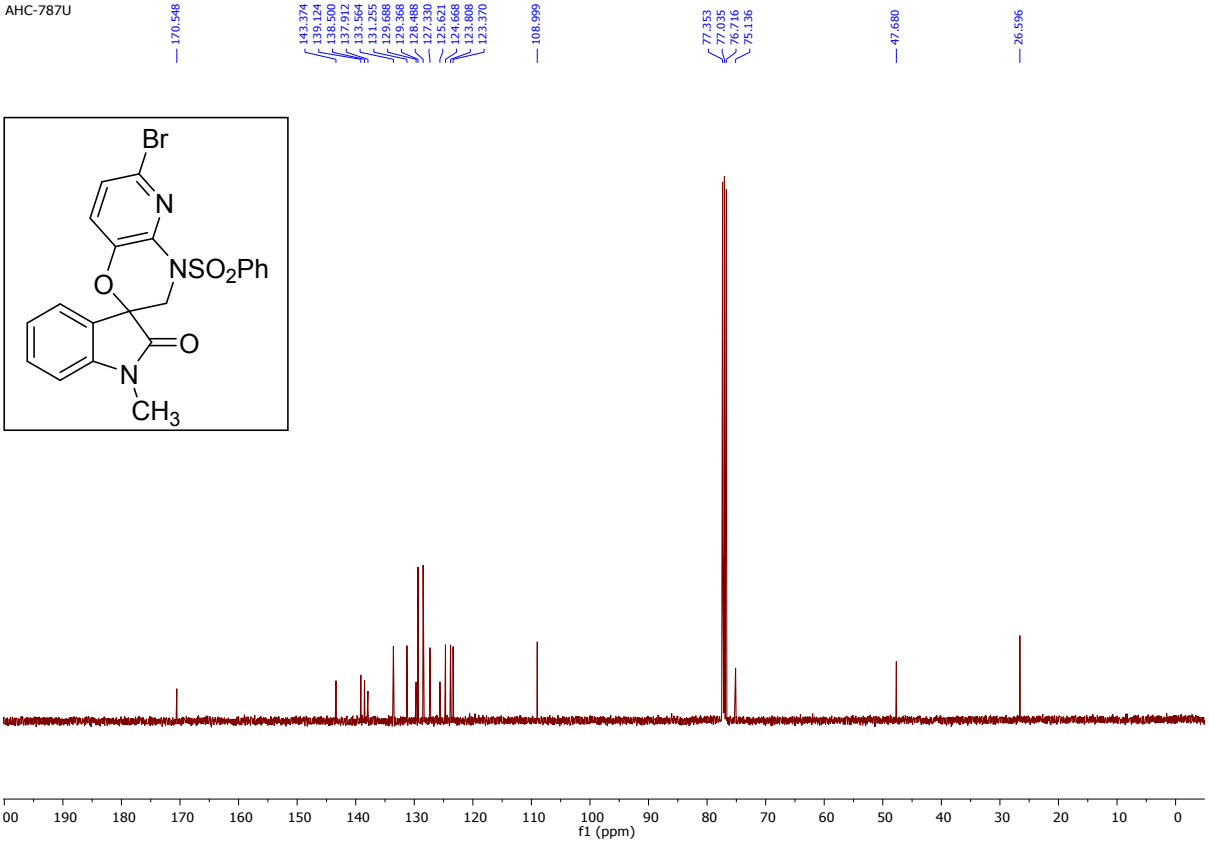
^{1}H NMR of compound (±)-3ce (400 MHz, $CDCl_3$)



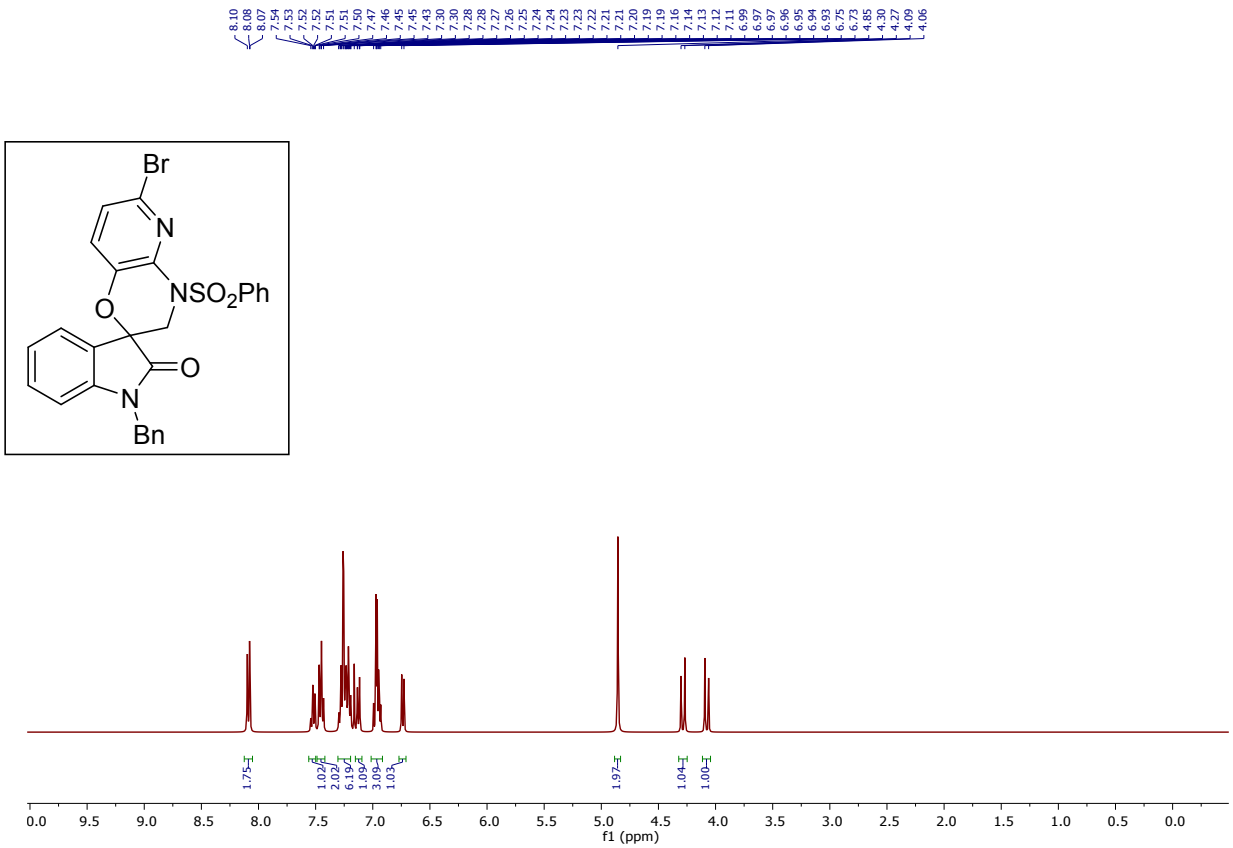
^{13}C NMR of compound (±)-3ce (100 MHz, $CDCl_3$)



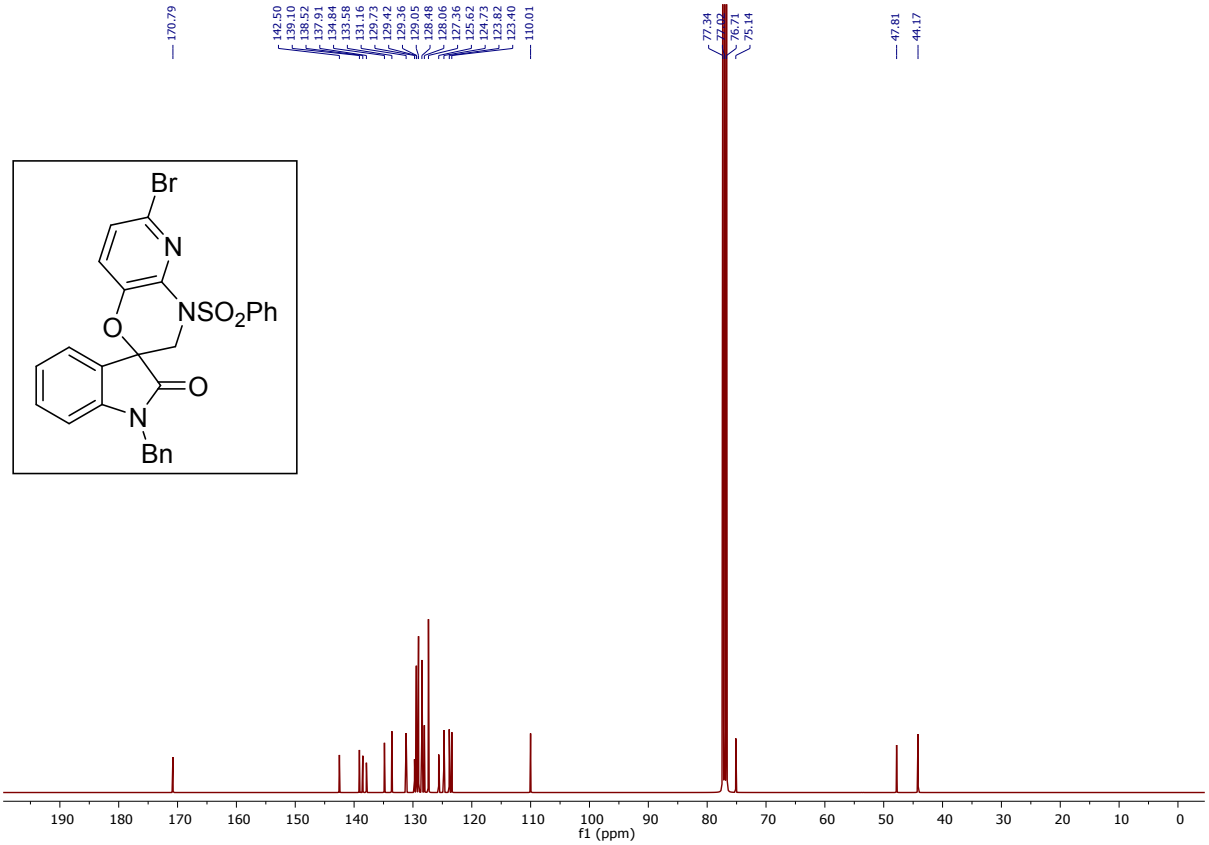
^{1}H NMR of compound (±)-3af (400 MHz, $CDCl_3$)



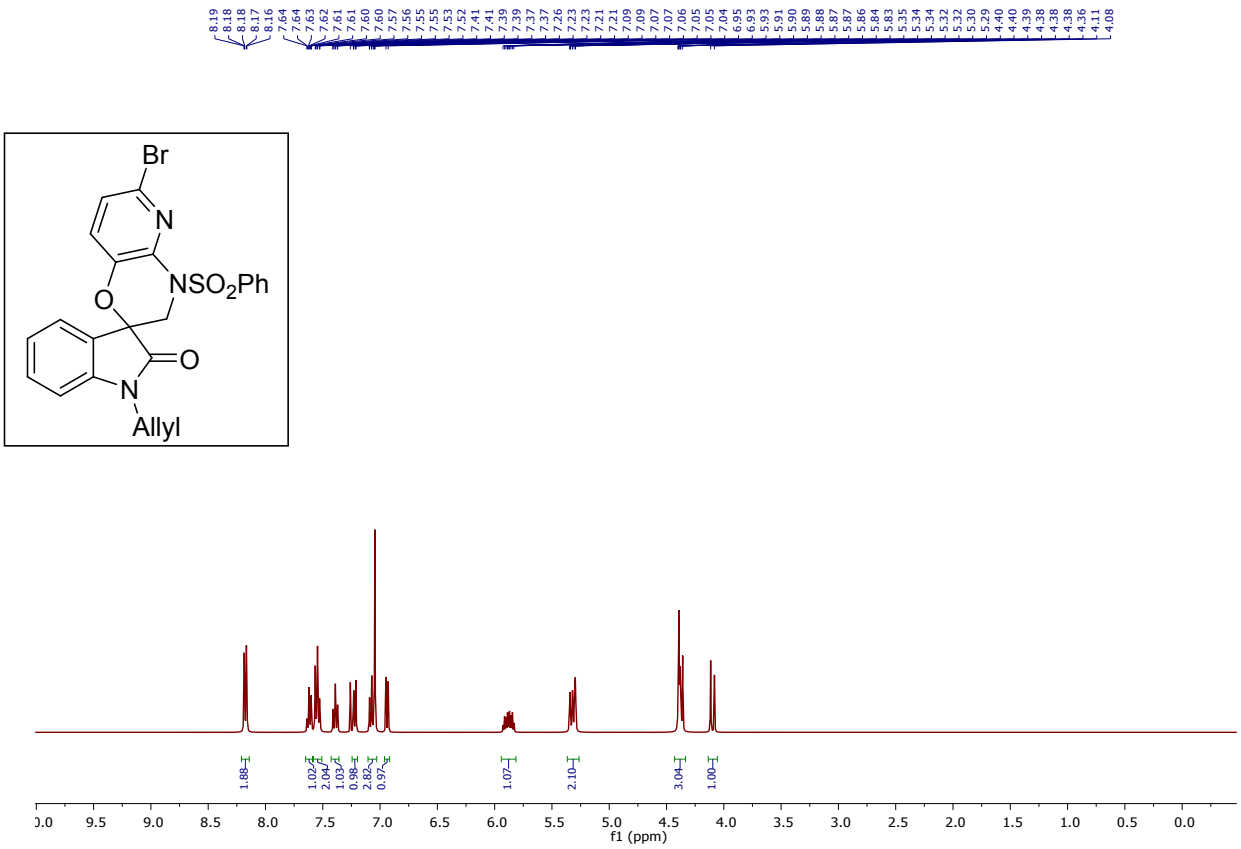
^{13}C NMR of compound (±)-3af (100 MHz, $CDCl_3$)



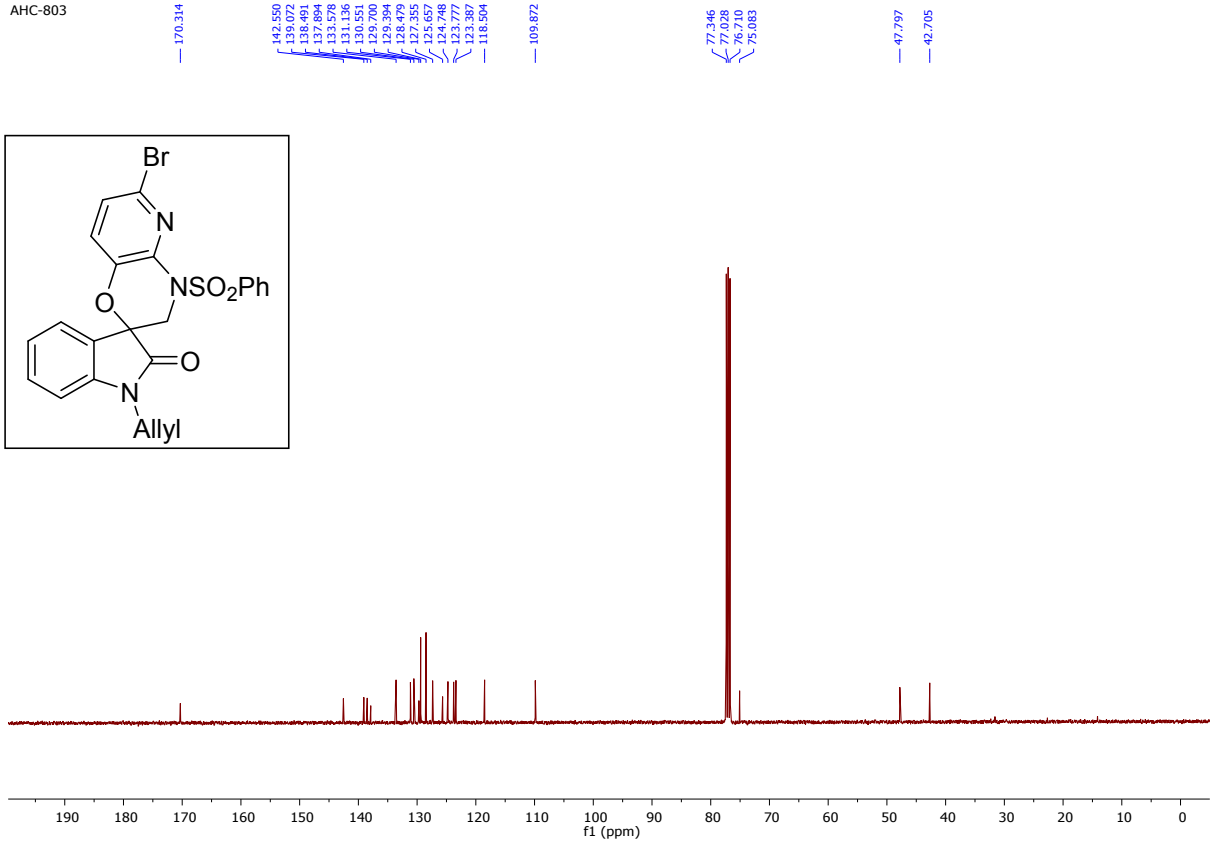
^{1}H NMR of compound (±)-3bf (400 MHz, $CDCl_3$)



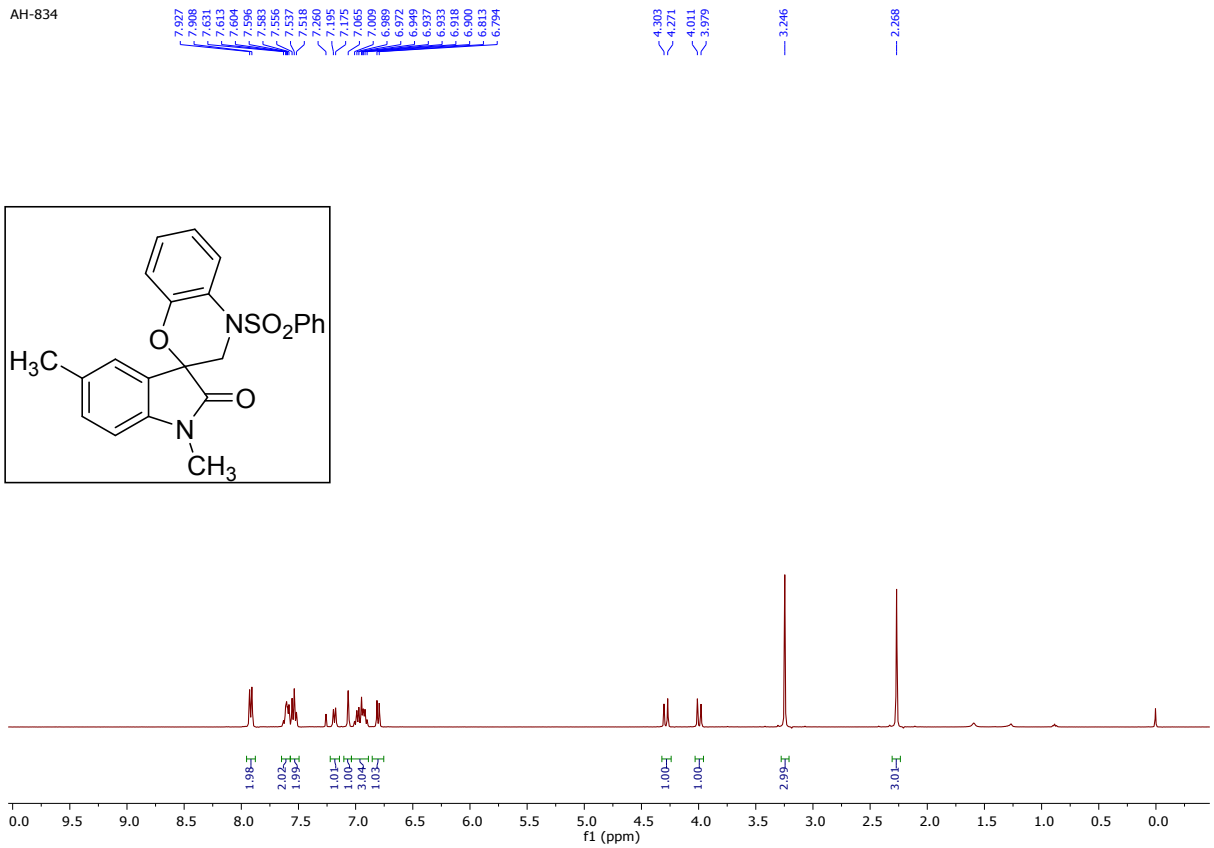
^{13}C NMR of compound (±)-3bf (100 MHz, $CDCl_3$)



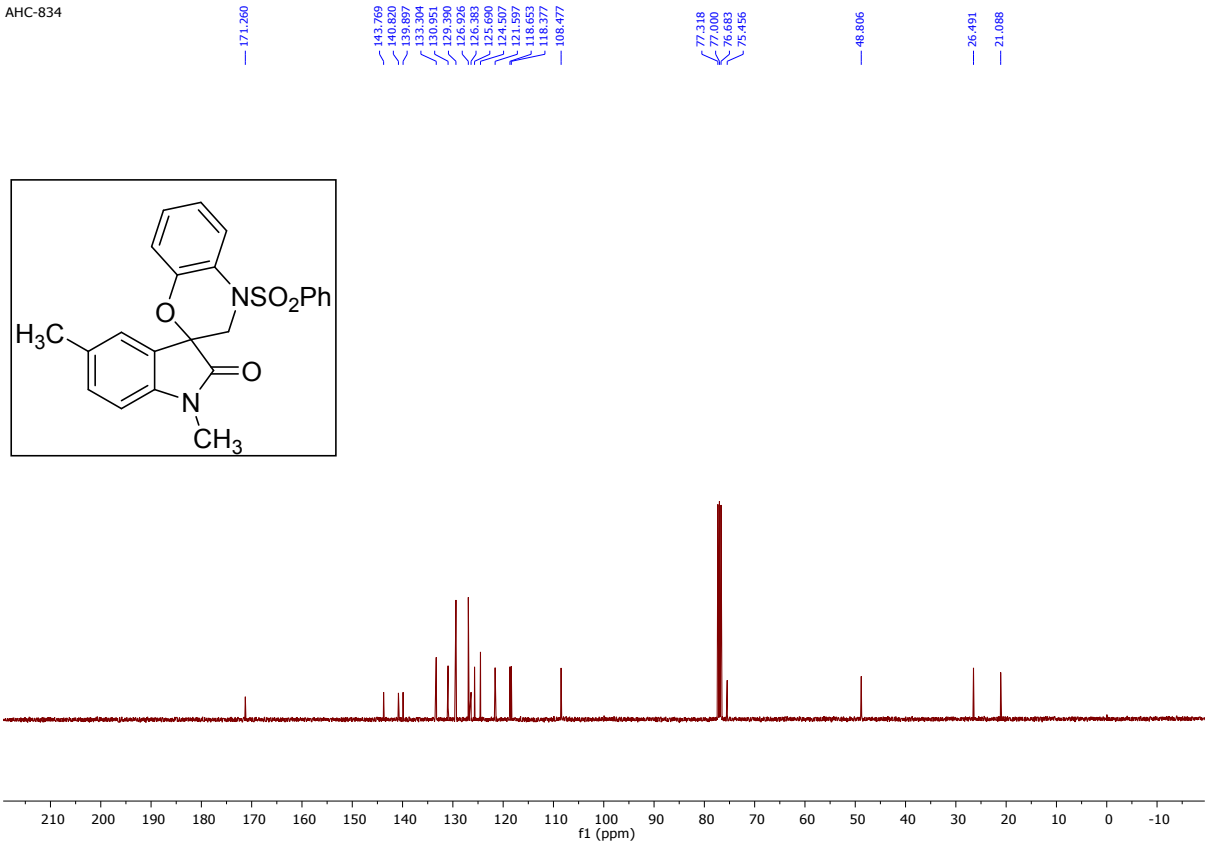
^{1}H NMR of compound (±)-3cf (400 MHz, $CDCl_3$)



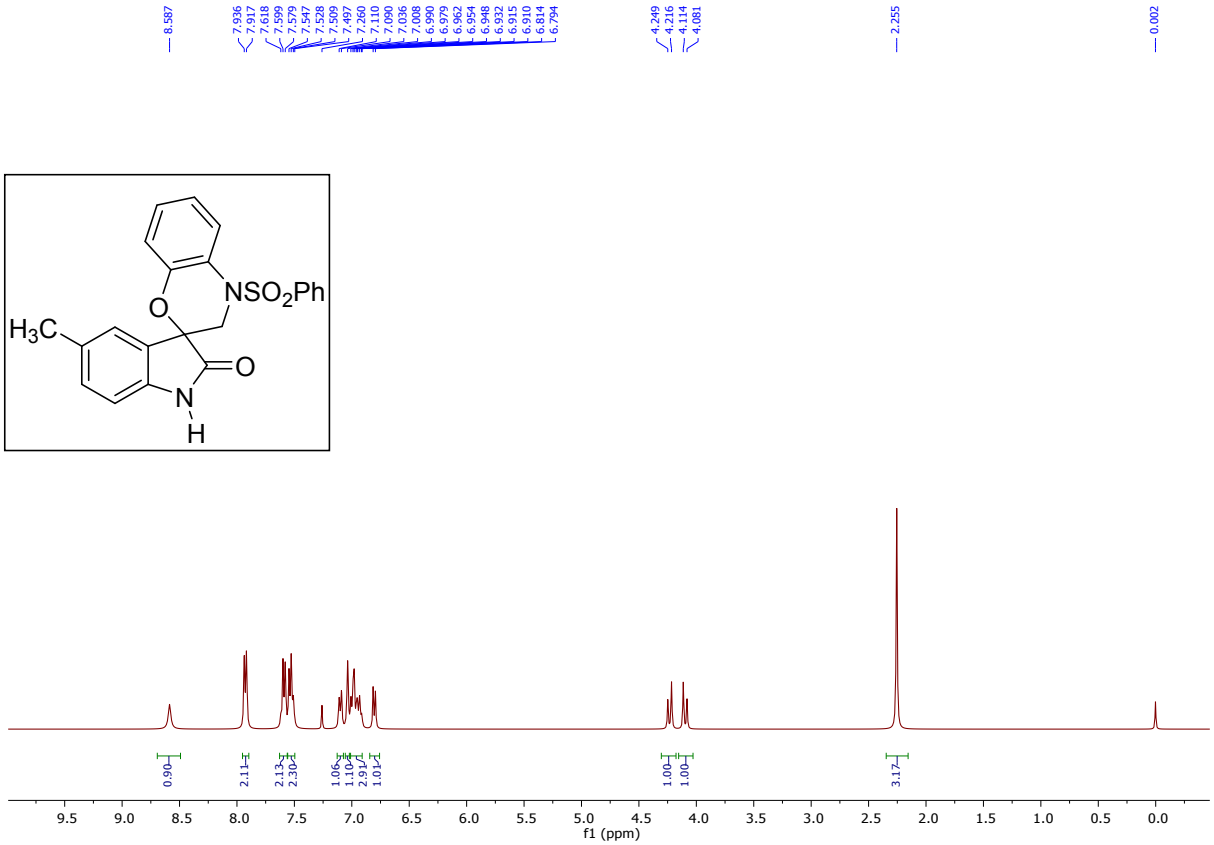
^{13}C NMR of compound (±)-3cf (100 MHz, $CDCl_3$)



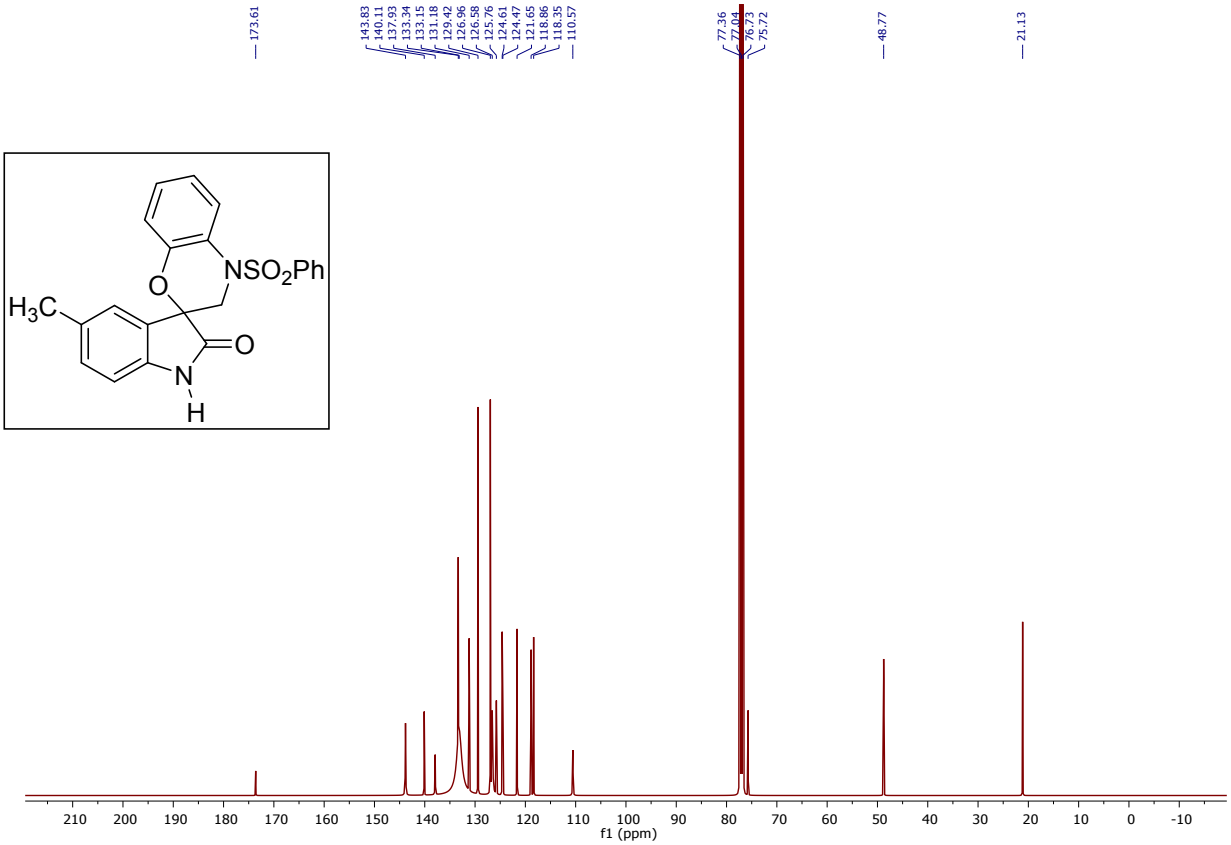
^{1}H NMR of compound (±)-3ea (400 MHz, $CDCl_3$)



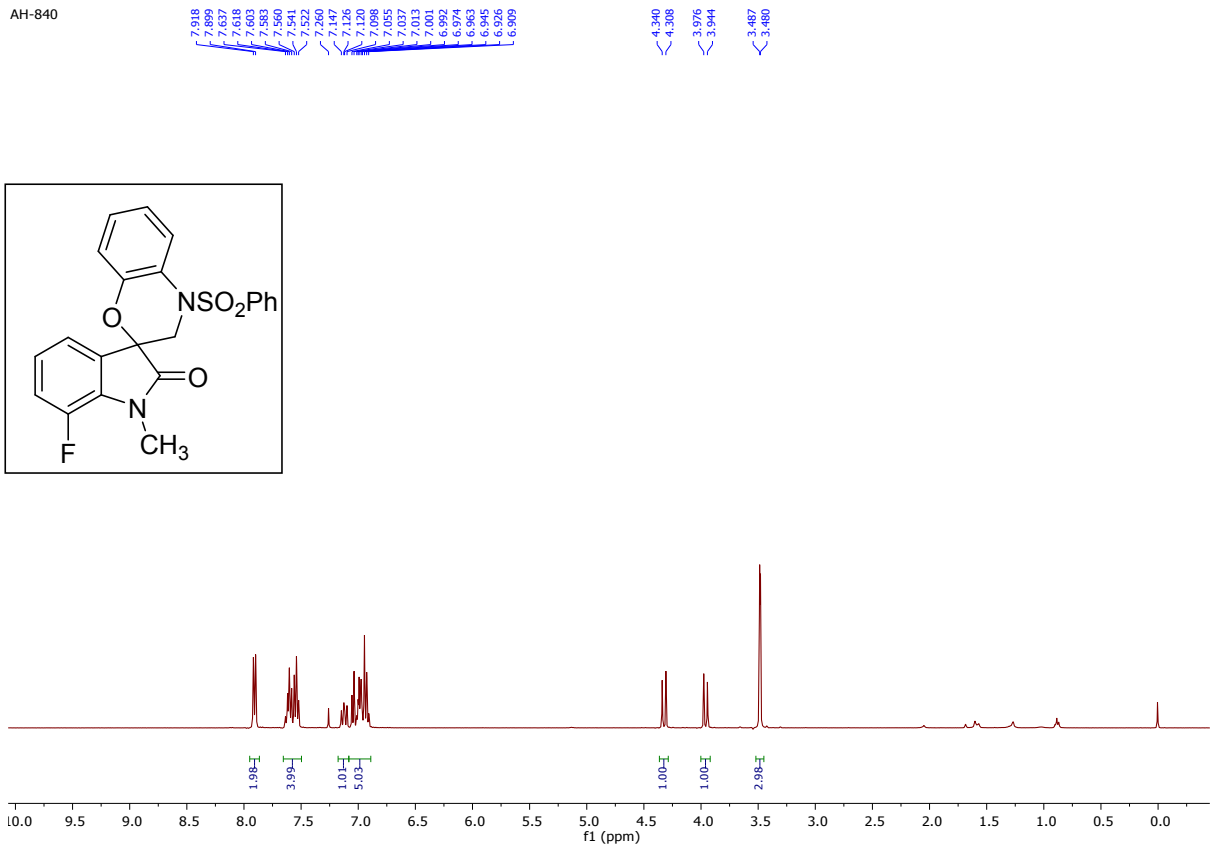
^{13}C NMR of compound (±)-3ea (100 MHz, $CDCl_3$)



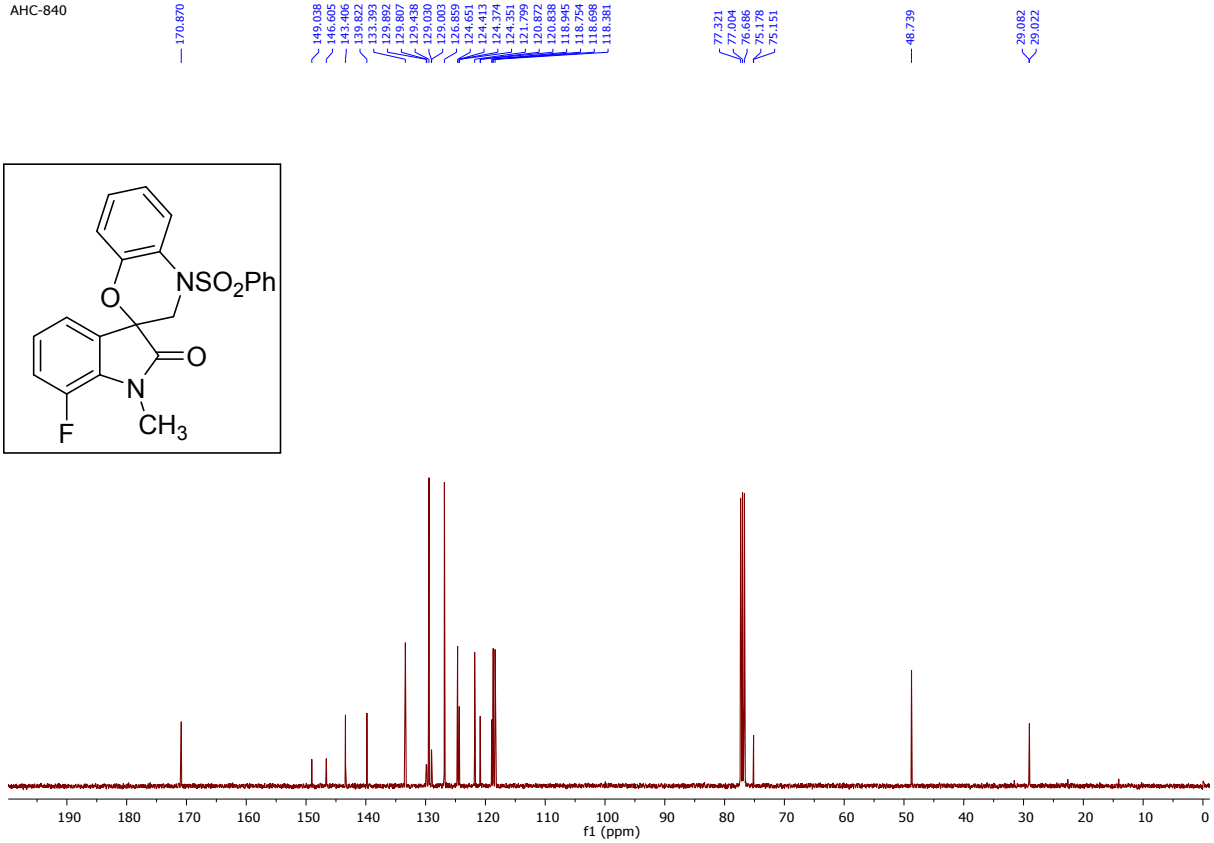
^{1}H NMR of compound (±)-3fa (400 MHz, $CDCl_3$)



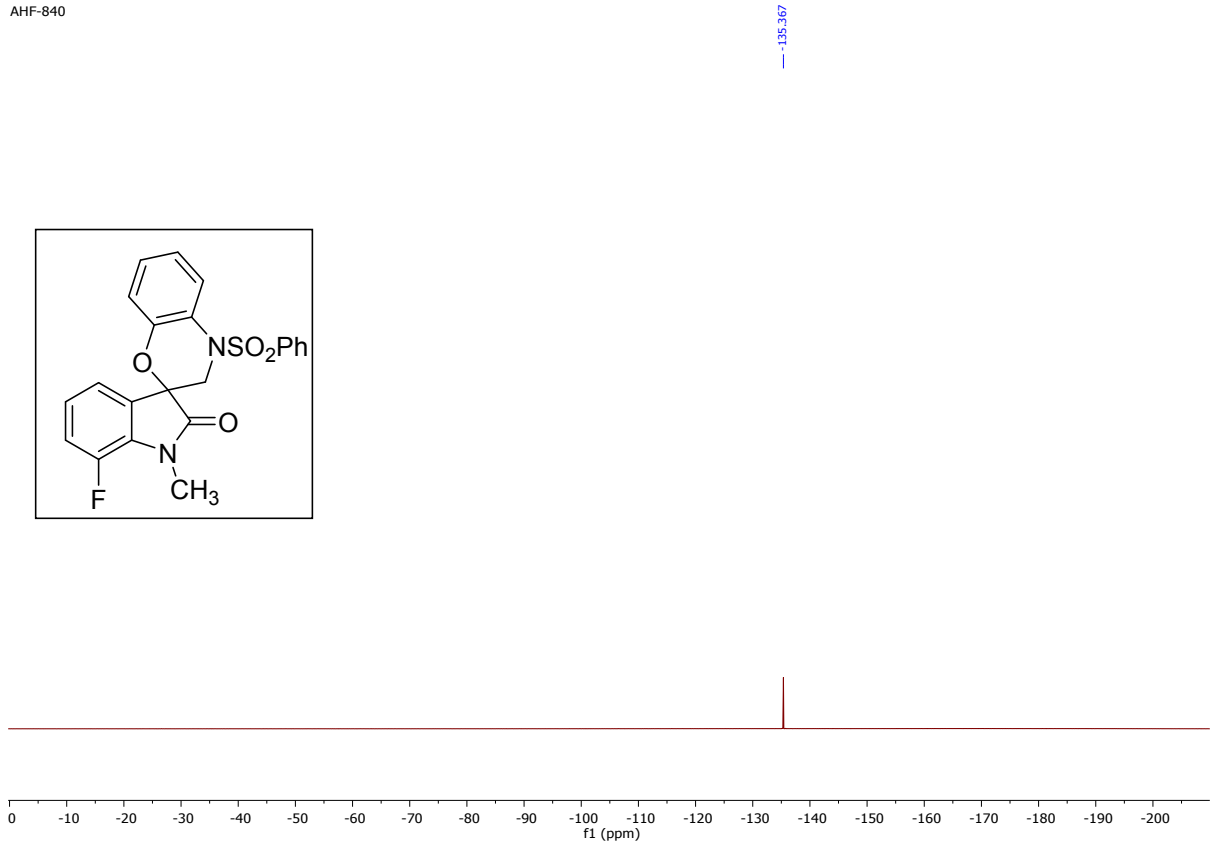
^{13}C NMR of compound (±)-3fa (100 MHz, $CDCl_3$)



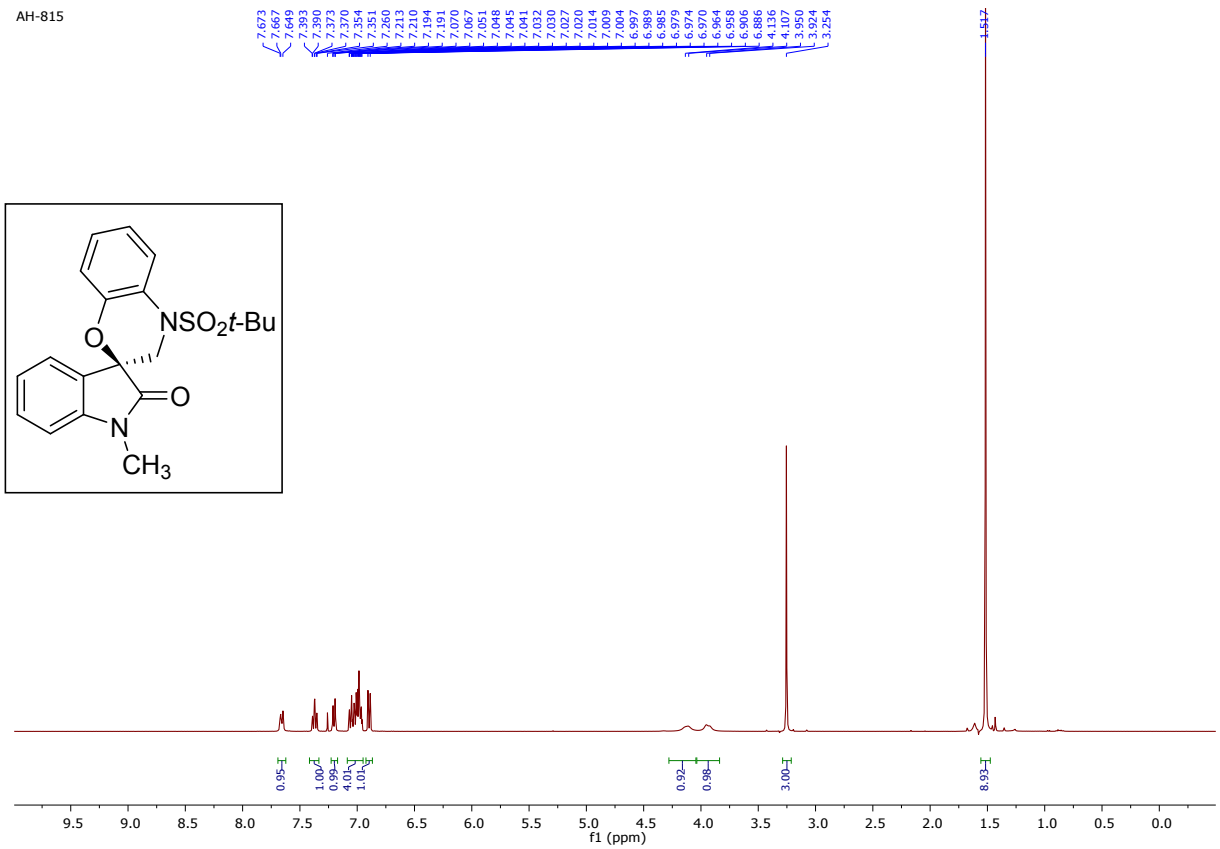
^{1}H NMR of compound (±)-3ga (400 MHz, $CDCl_3$)



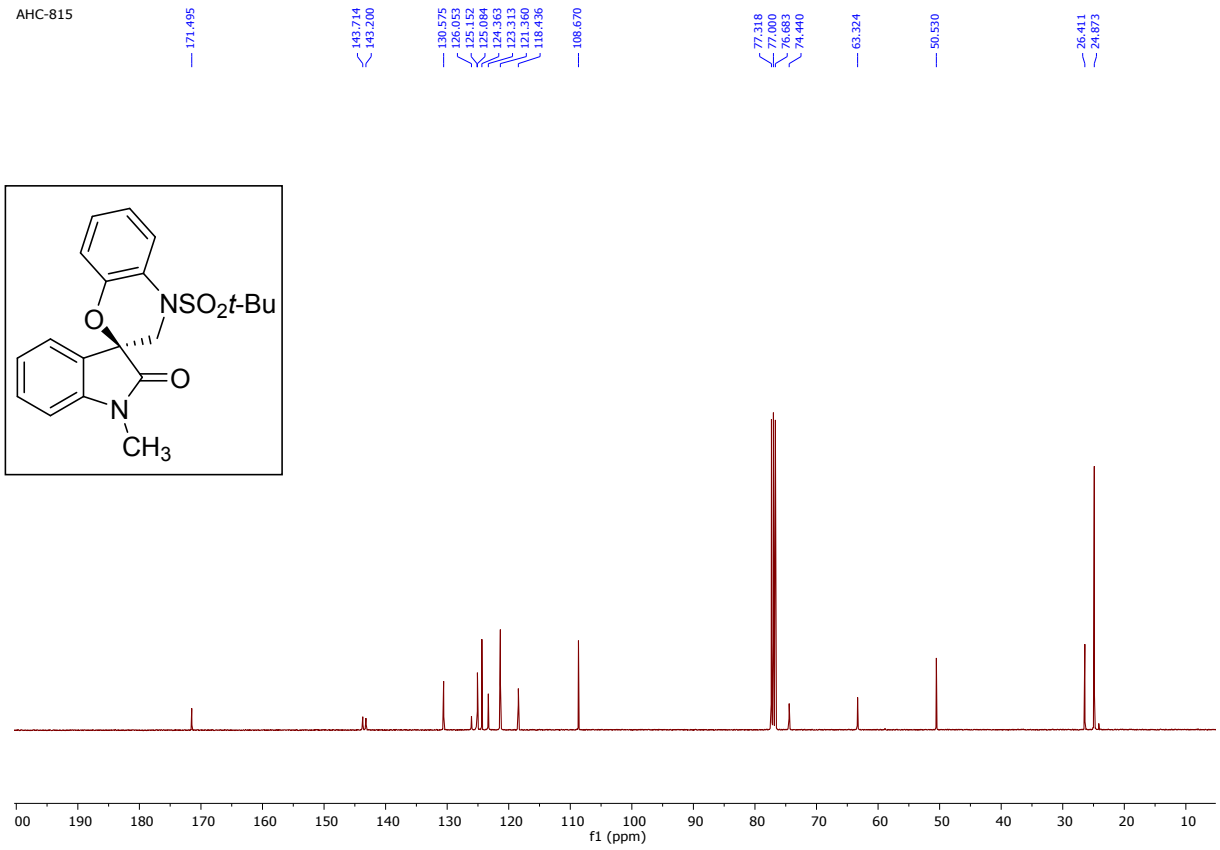
^{13}C NMR of compound (±)-3ga (100 MHz, $CDCl_3$)



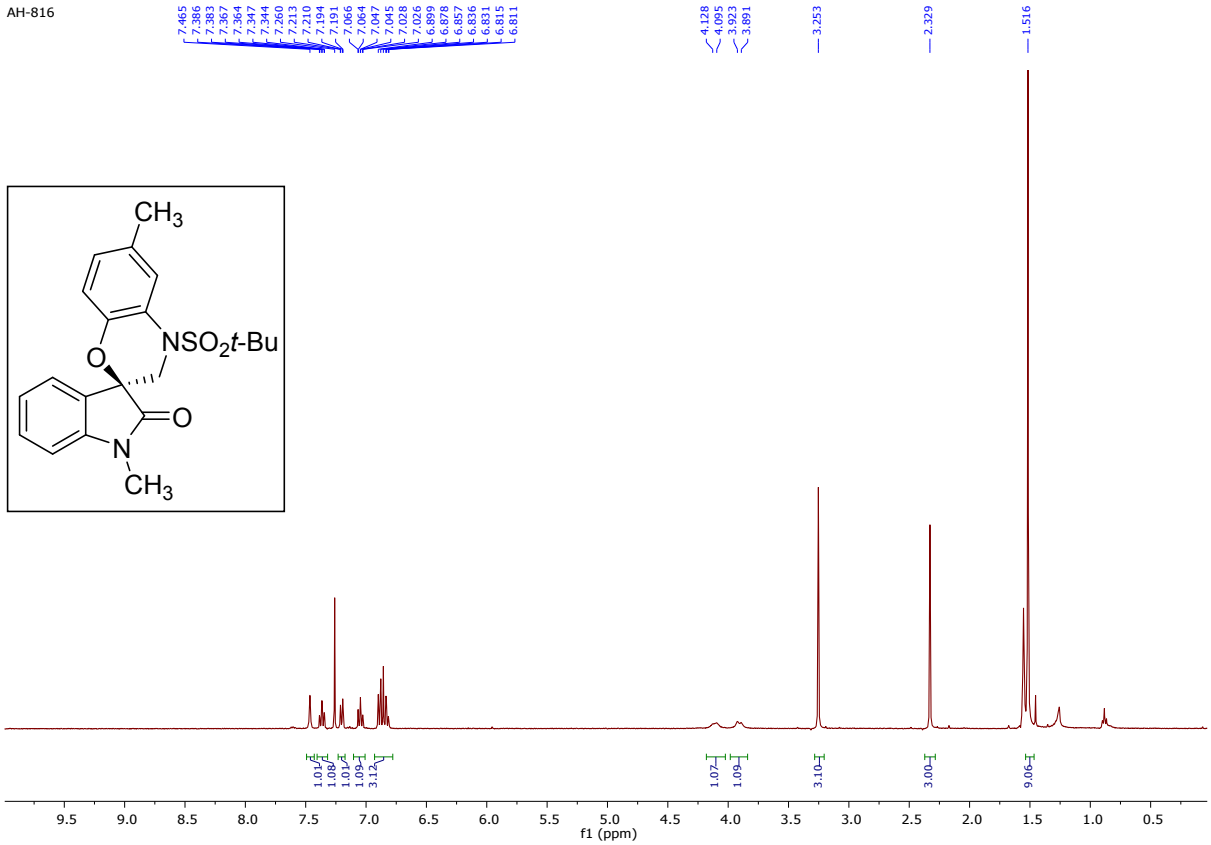
^{19}F NMR of compound (±)-3ga (376 MHz, $CDCl_3$)



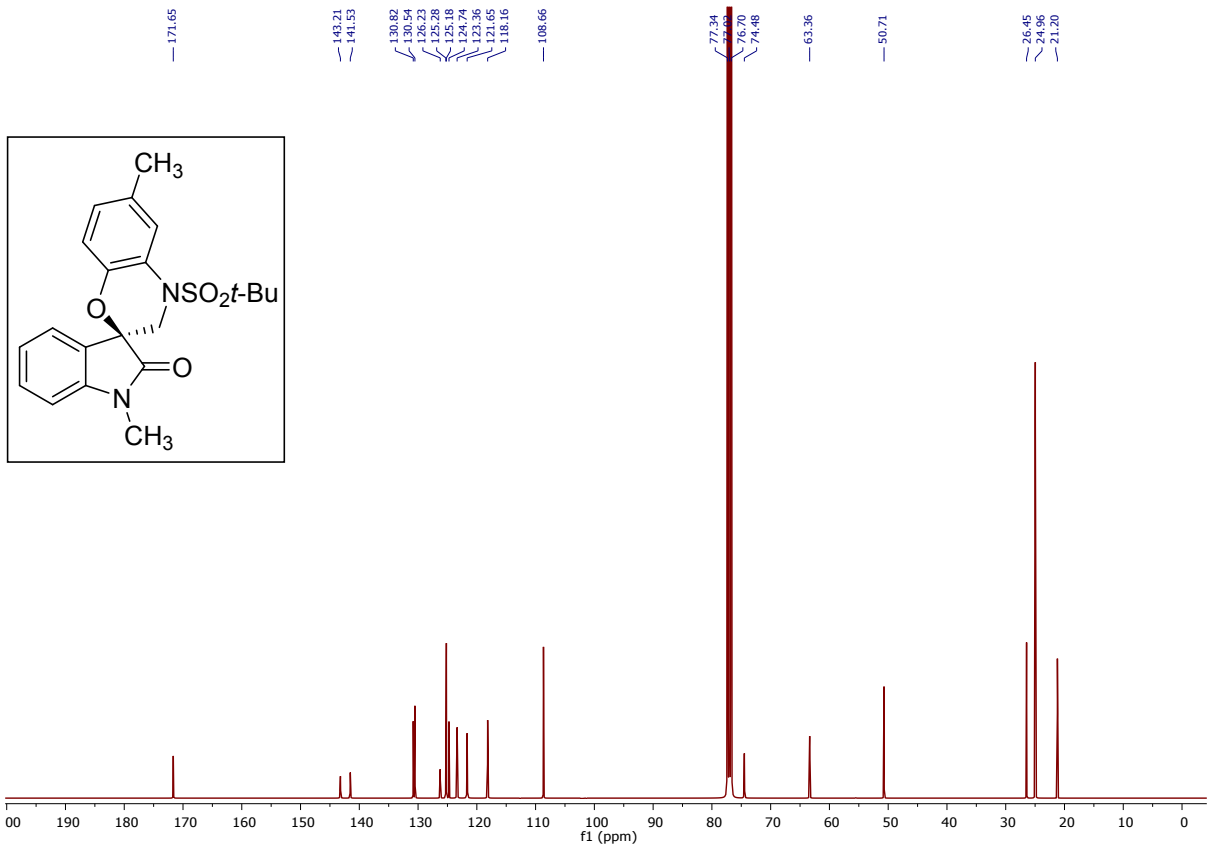
^{1}H NMR of compound 3ha (400 MHz, $CDCl_3$)



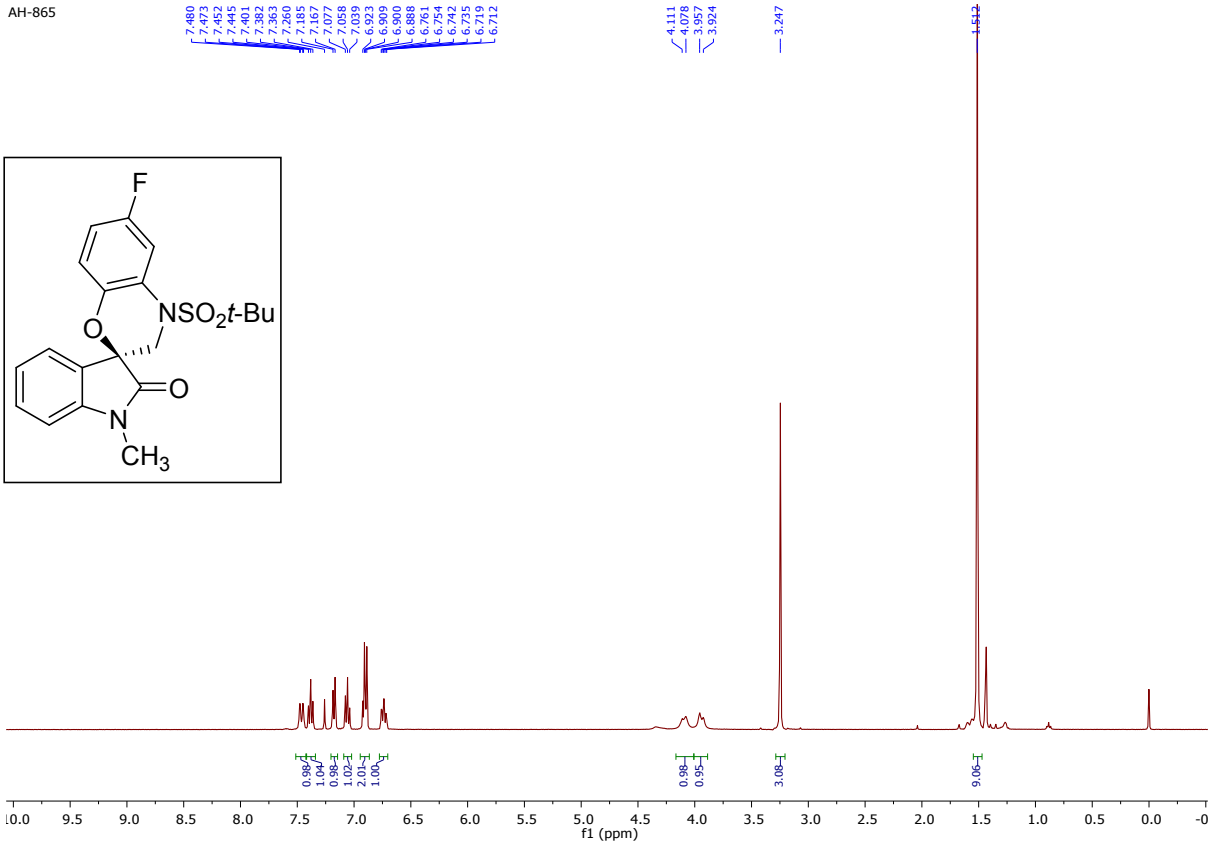
^{13}C NMR of compound 3ha (100 MHz, $CDCl_3$)



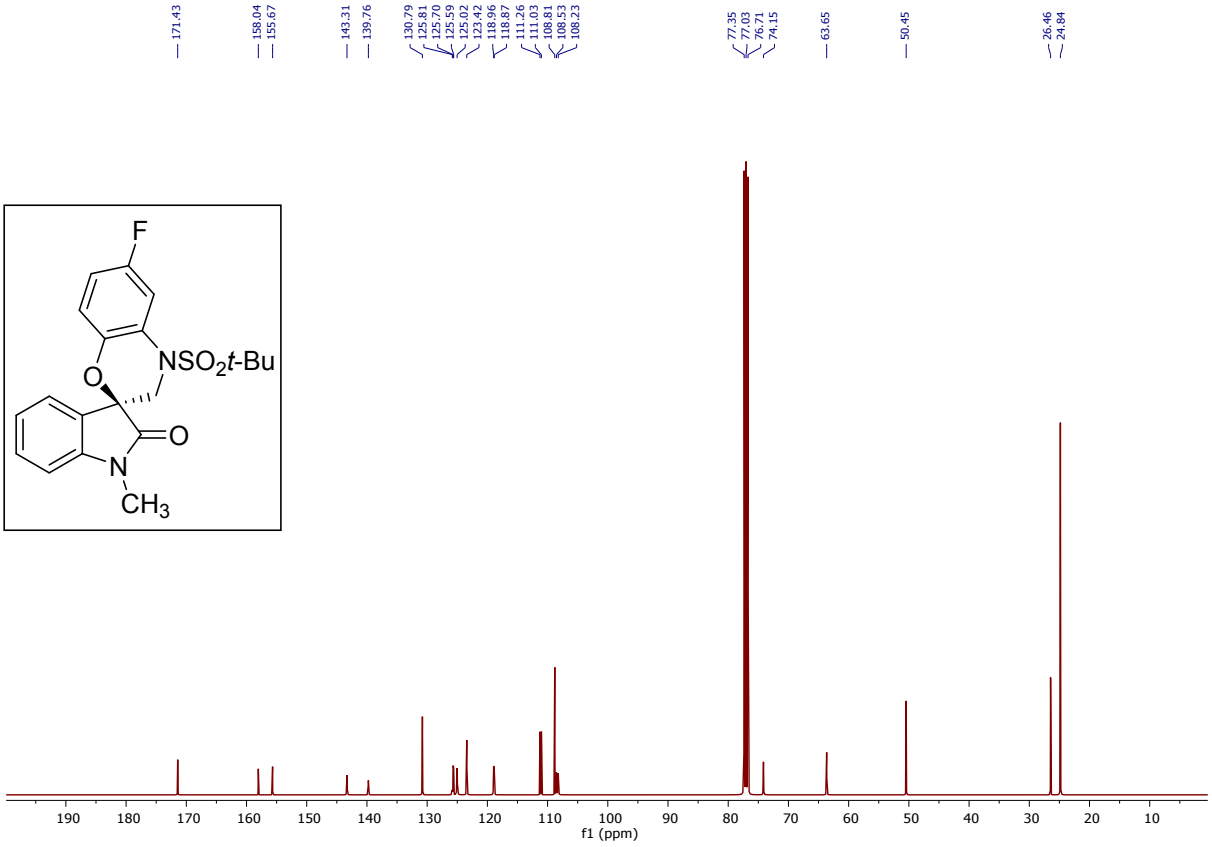
^{1}H NMR of compound 3hb (400 MHz, $CDCl_3$)



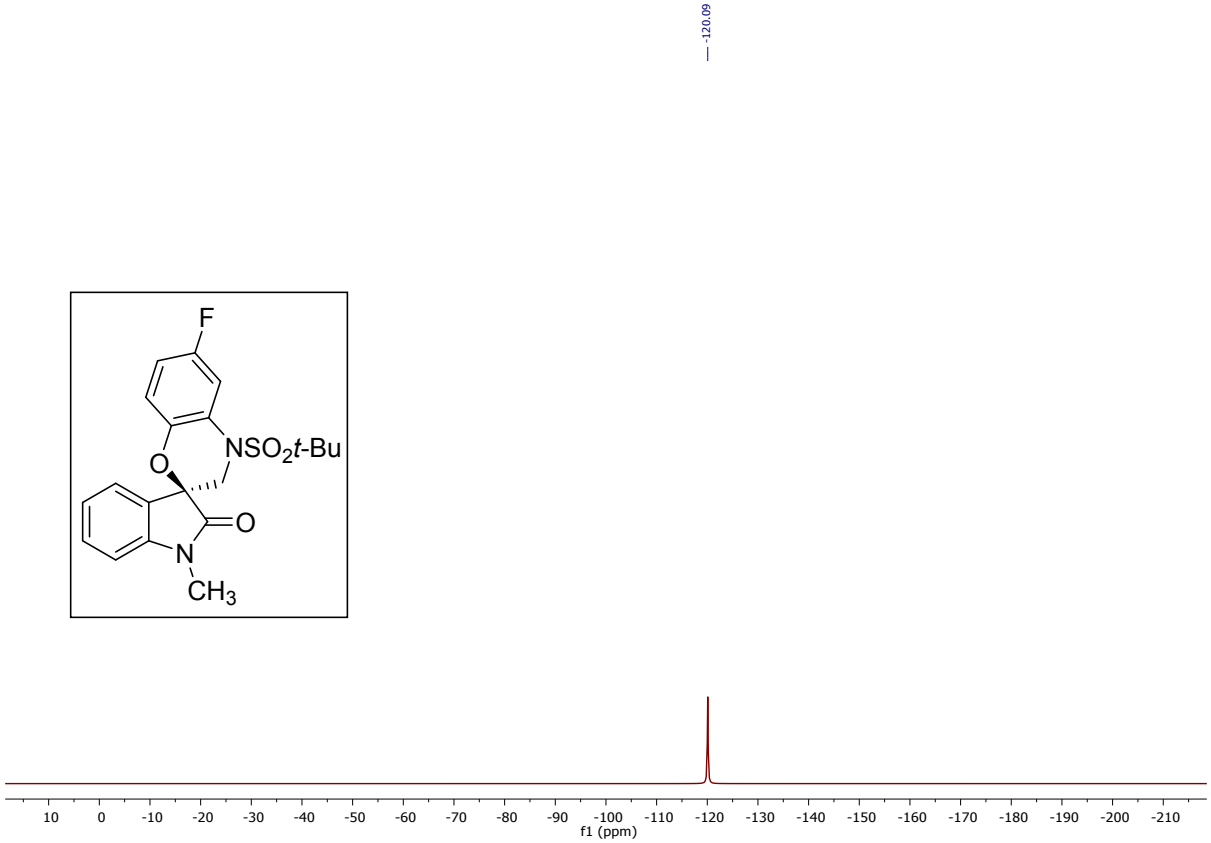
^{13}C NMR of compound 3hb (100 MHz, $CDCl_3$)



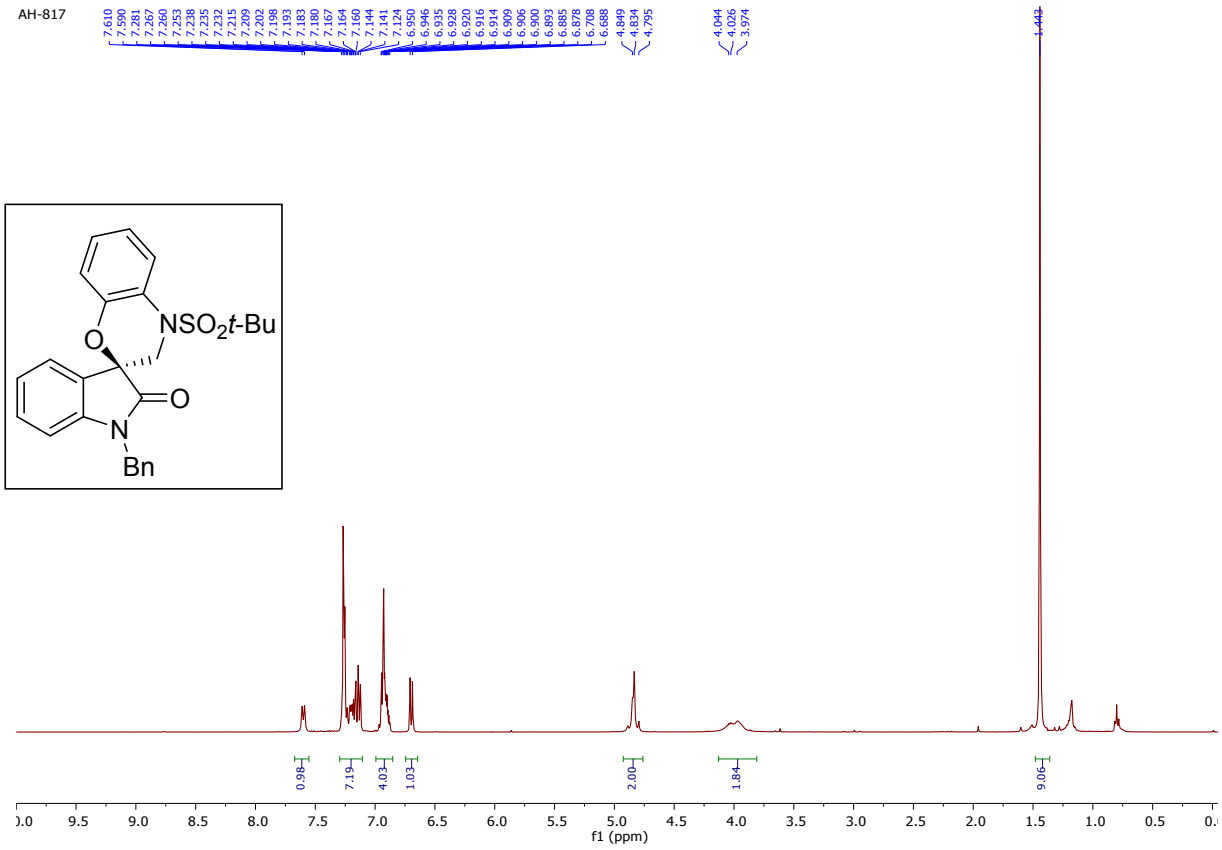
^{1}H NMR of compound 3hc (400 MHz, $CDCl_3$)



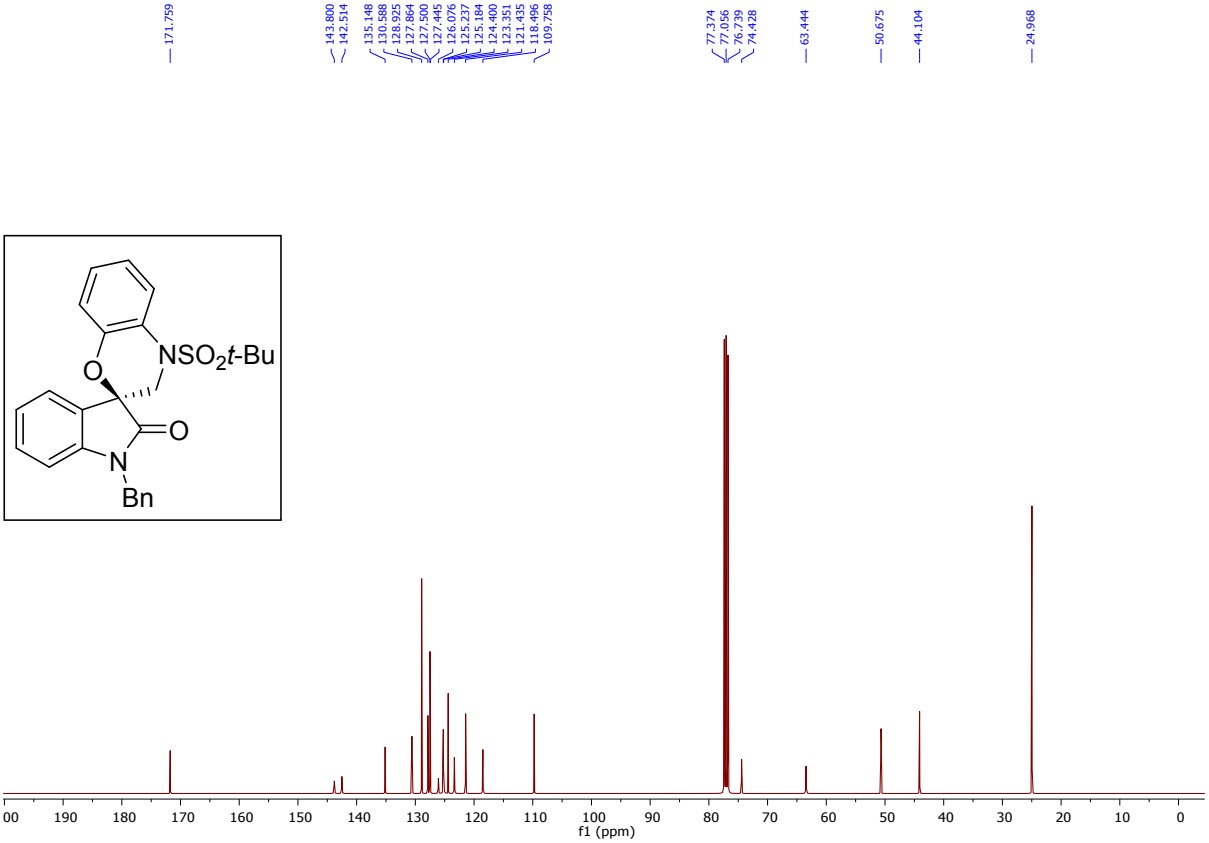
^{13}C NMR of compound 3hc (100 MHz, $CDCl_3$)



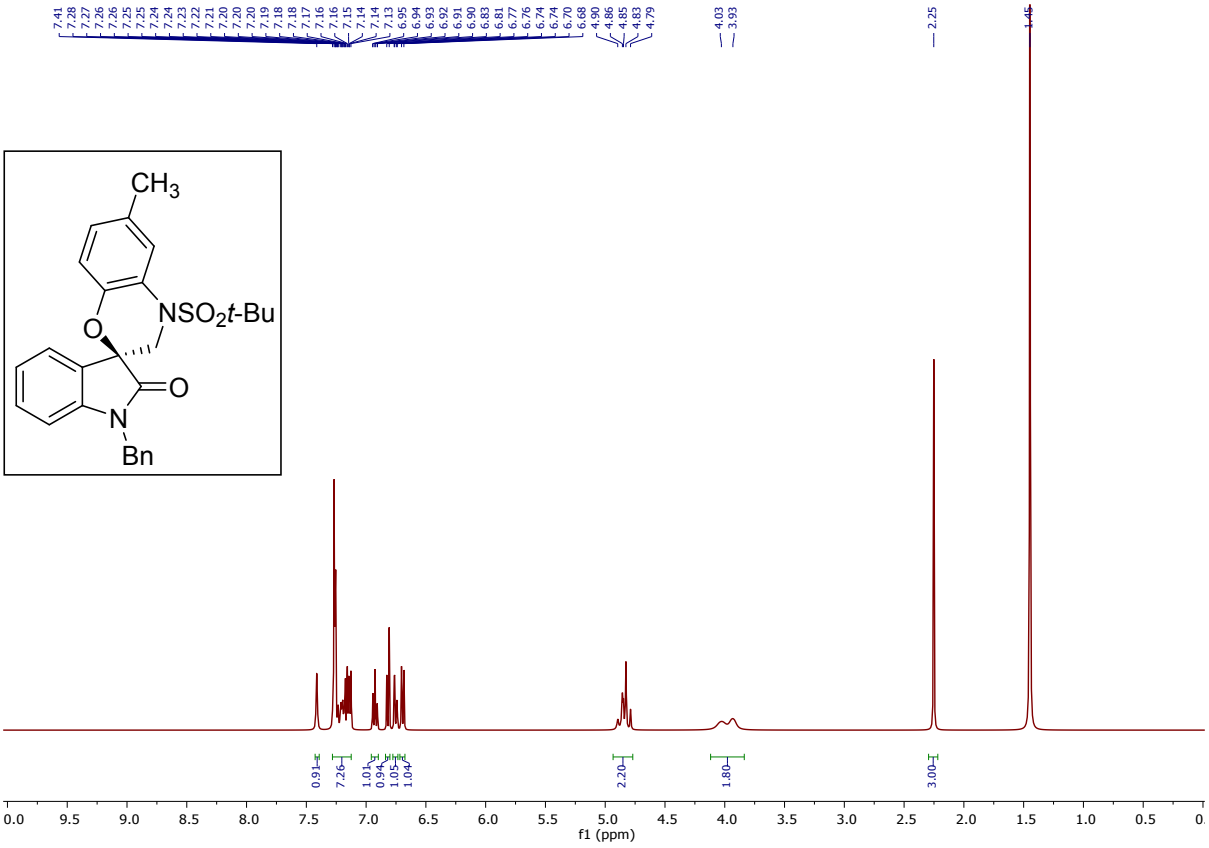
^{19}F NMR of compound 3hc (376 MHz, $CDCl_3$)



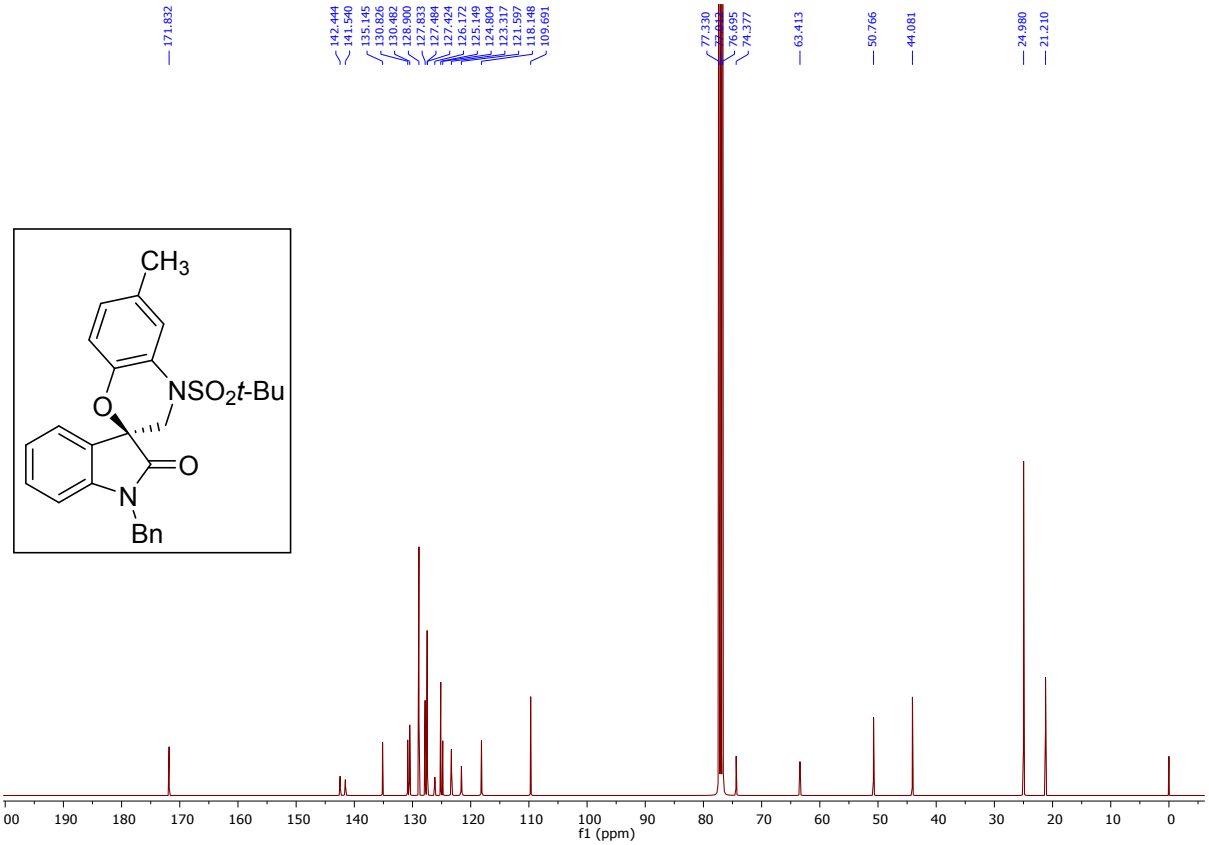
^{1}H NMR of compound 3ia (400 MHz, $CDCl_3$)



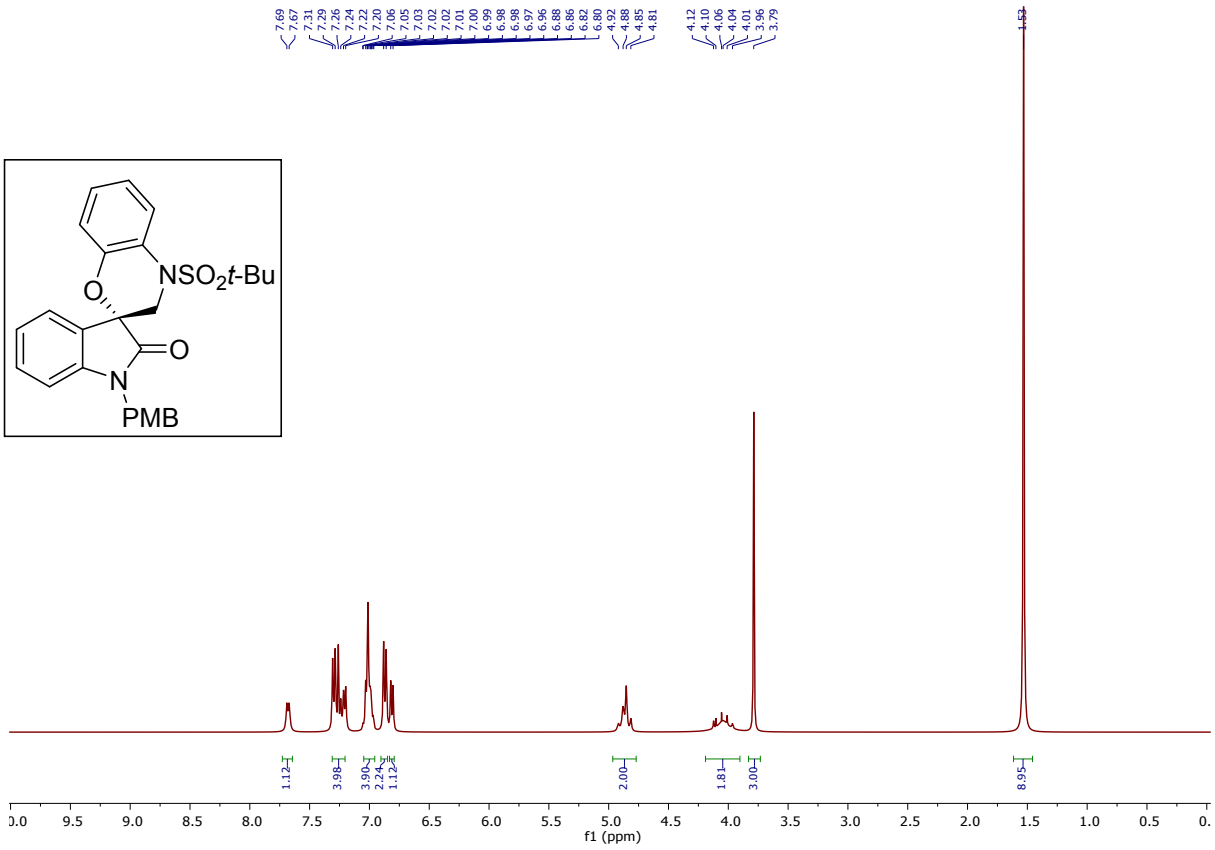
^{13}C NMR of compound 3ia (100 MHz, $CDCl_3$)



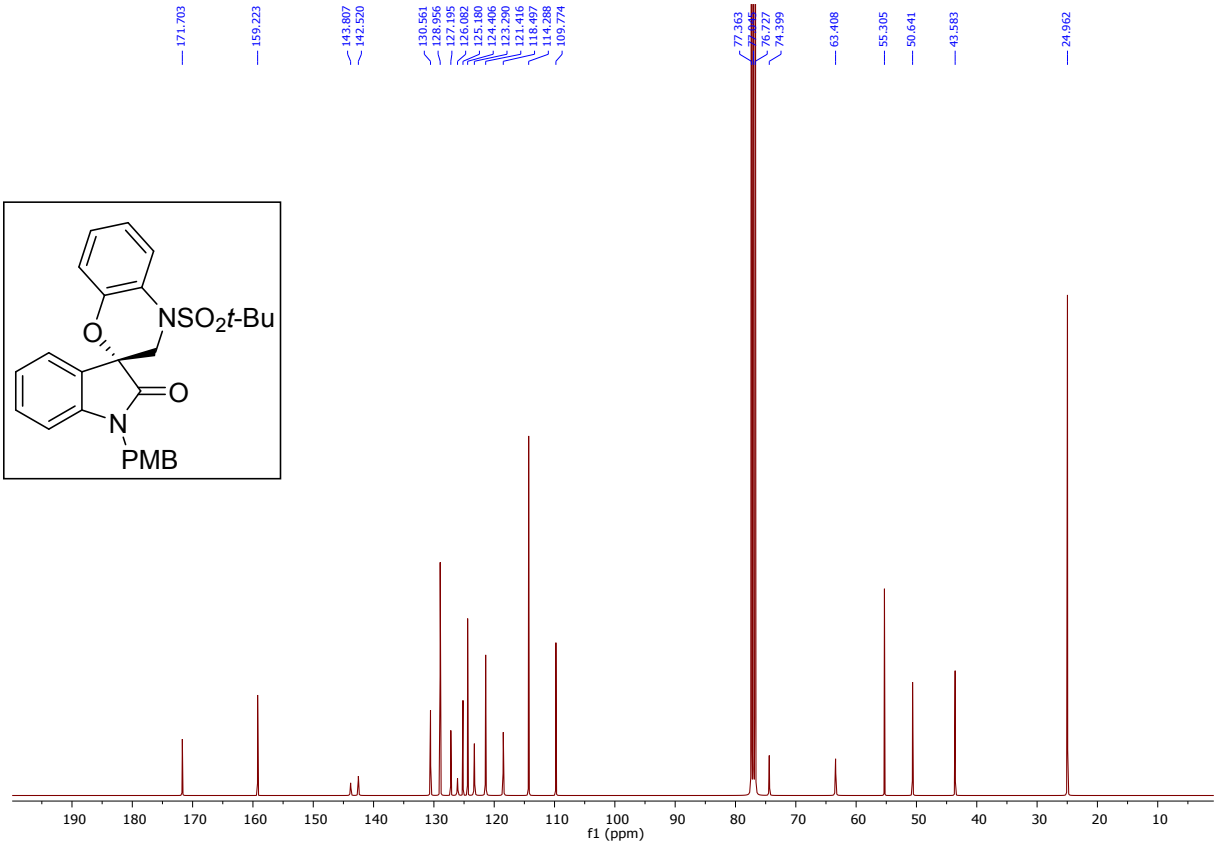
^{1}H NMR of compound 3ib (400 MHz, $CDCl_3$)



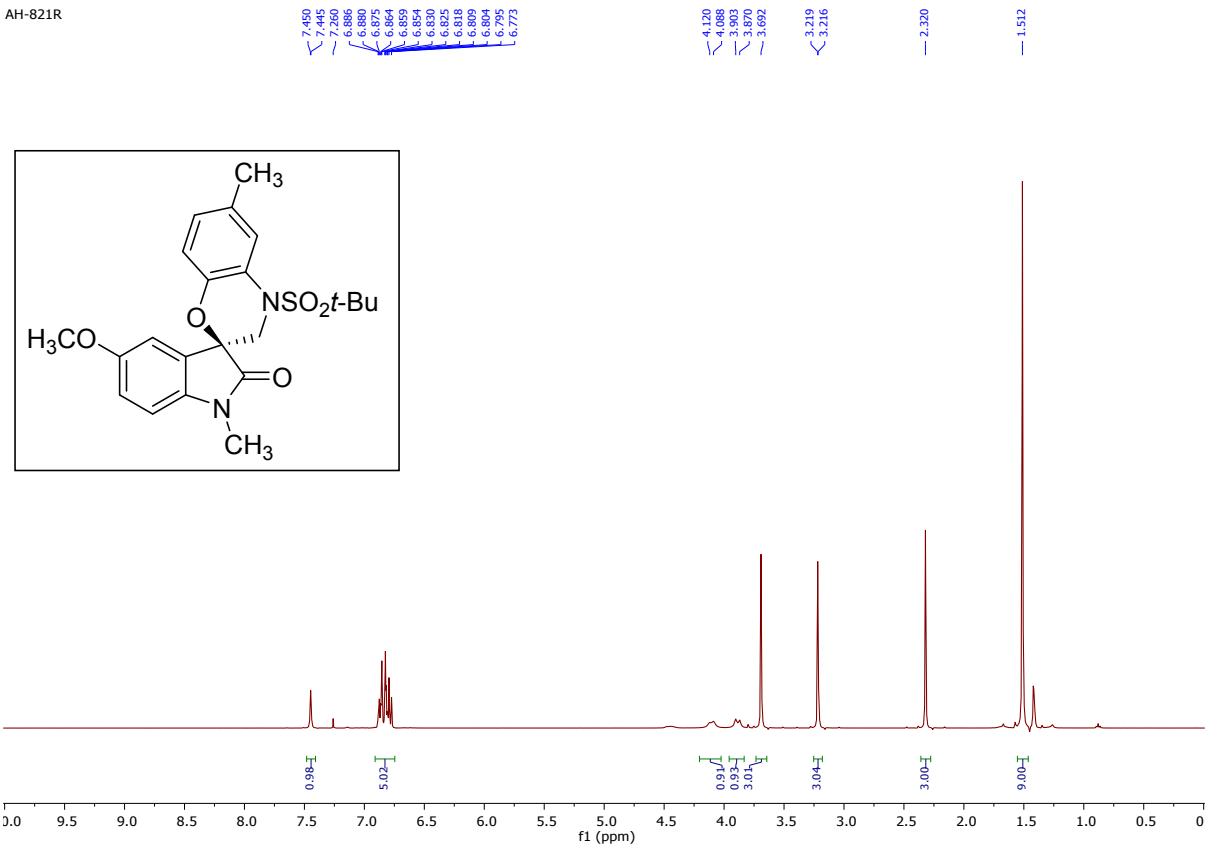
^{13}C NMR of compound 3ib (100 MHz, $CDCl_3$)



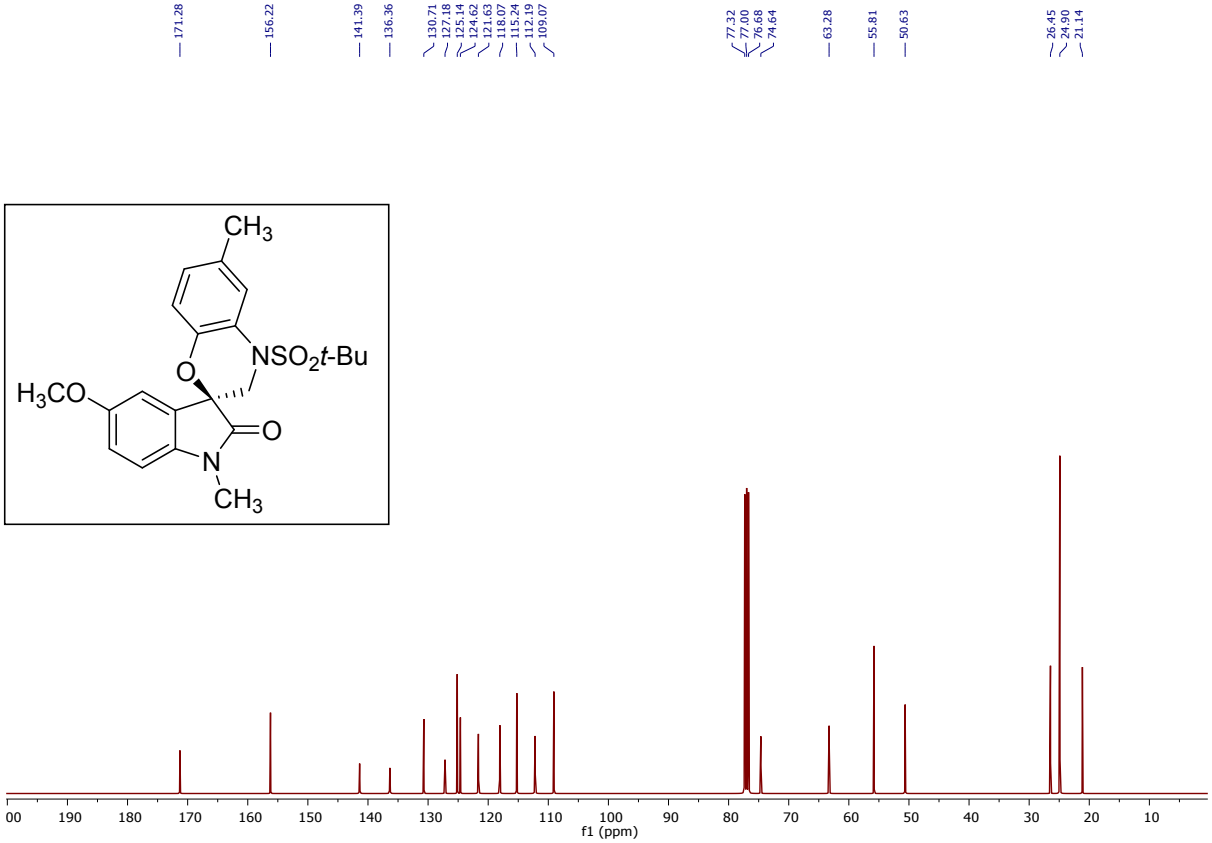
^{1}H NMR of compound *ent*-3ja (400 MHz, $CDCl_3$)



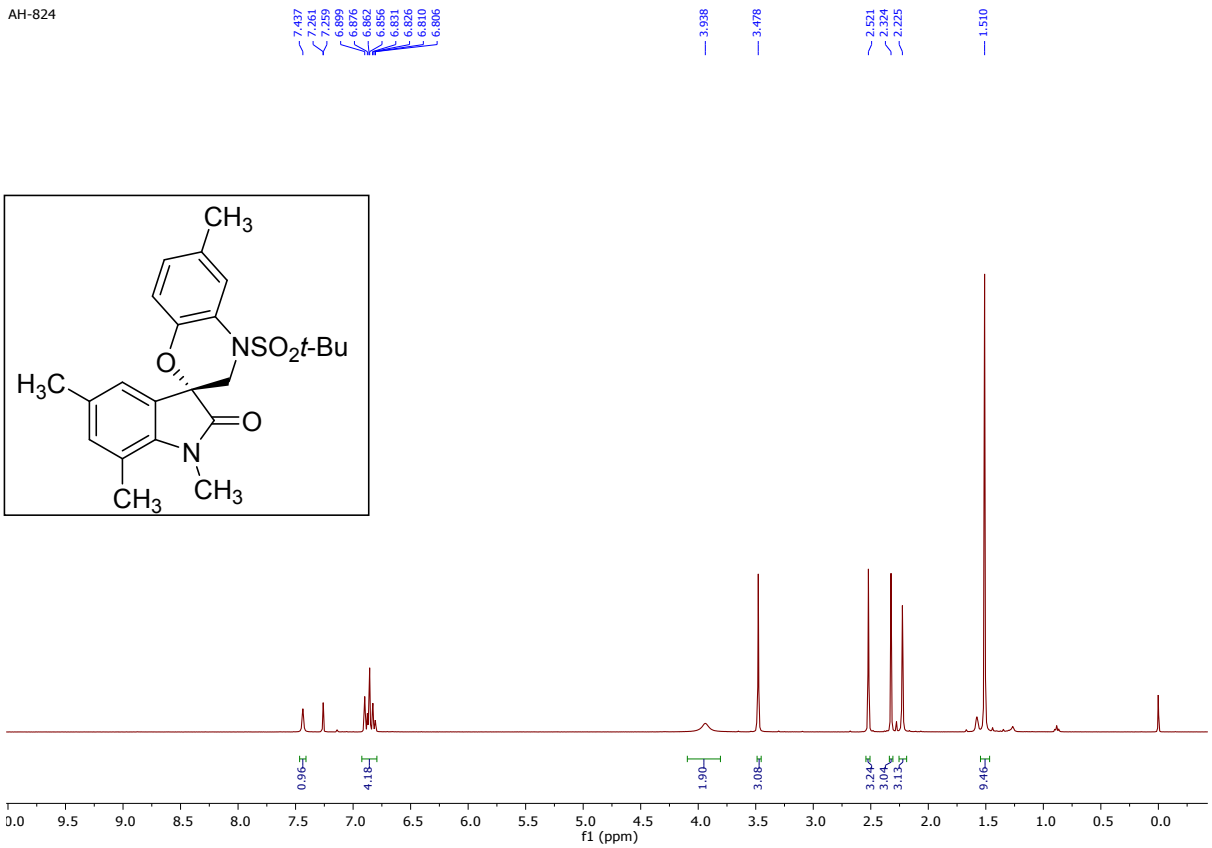
^{13}C NMR of compound *ent*-3ja (100 MHz, $CDCl_3$)



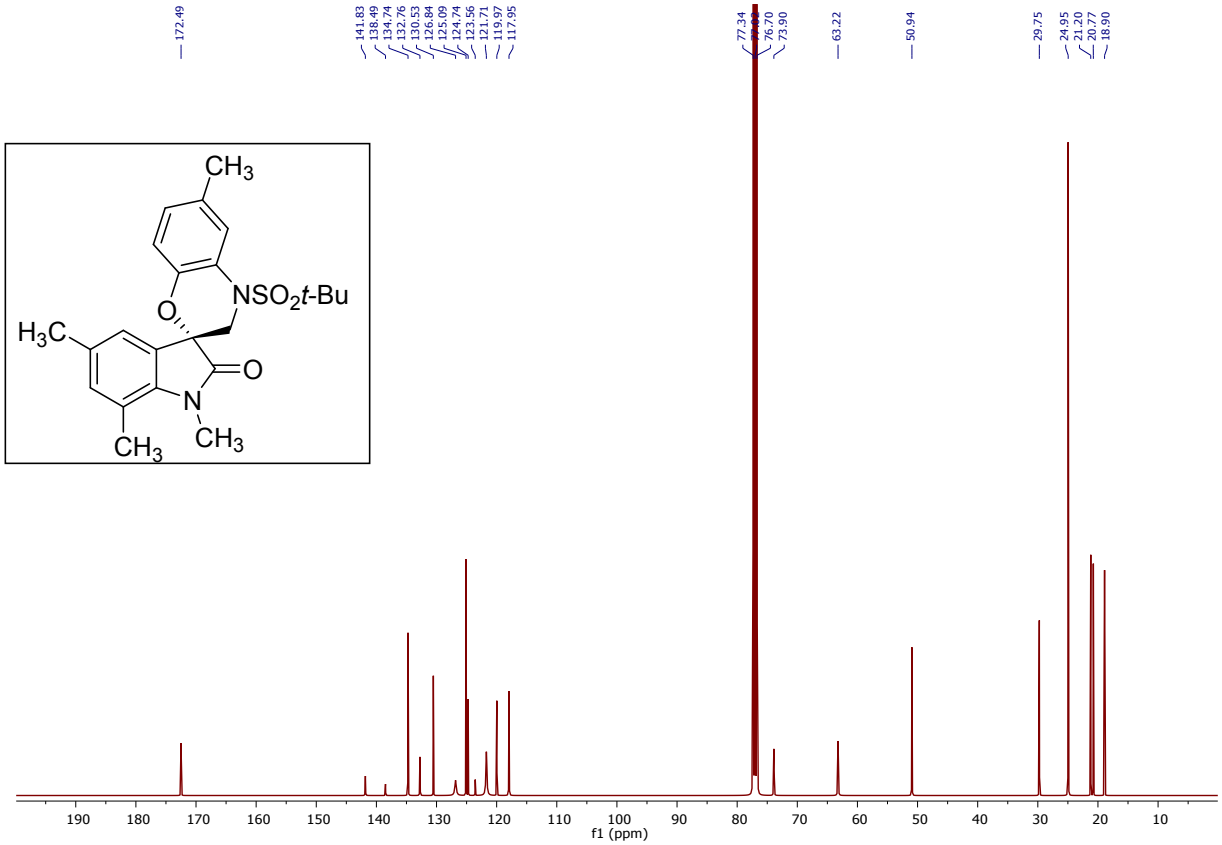
^{1}H NMR of compound 3kb (400 MHz, $CDCl_3$)



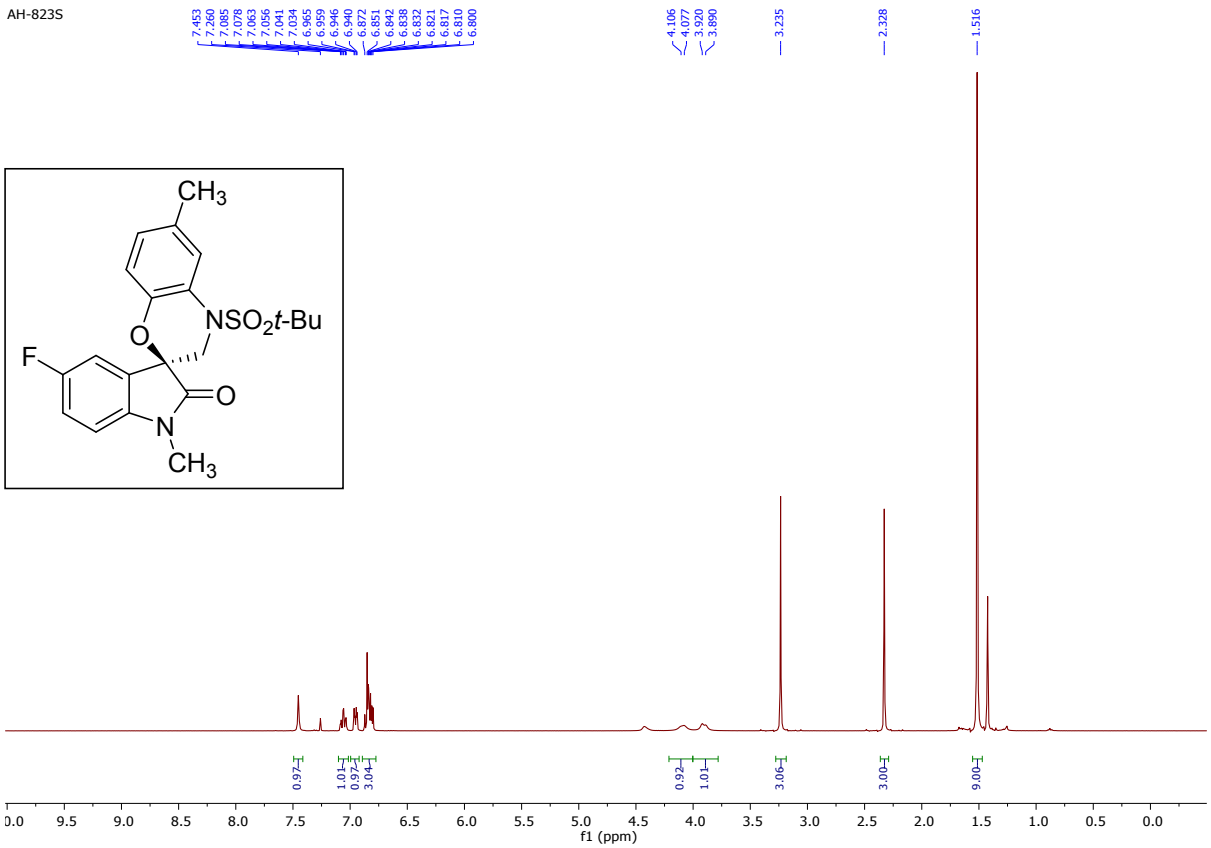
^{13}C NMR of compound 3kb (100 MHz, $CDCl_3$)



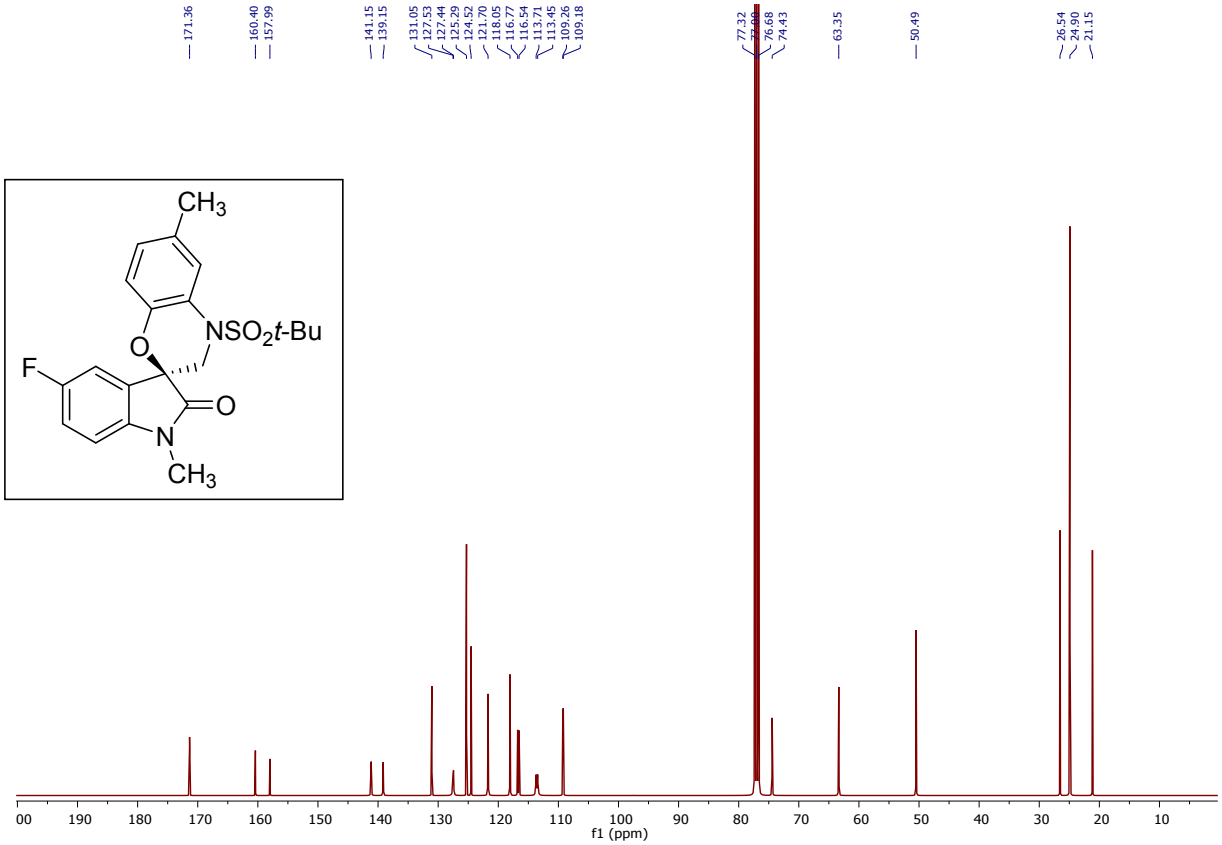
^{1}H NMR of compound *ent*-3lb (400 MHz, $CDCl_3$)



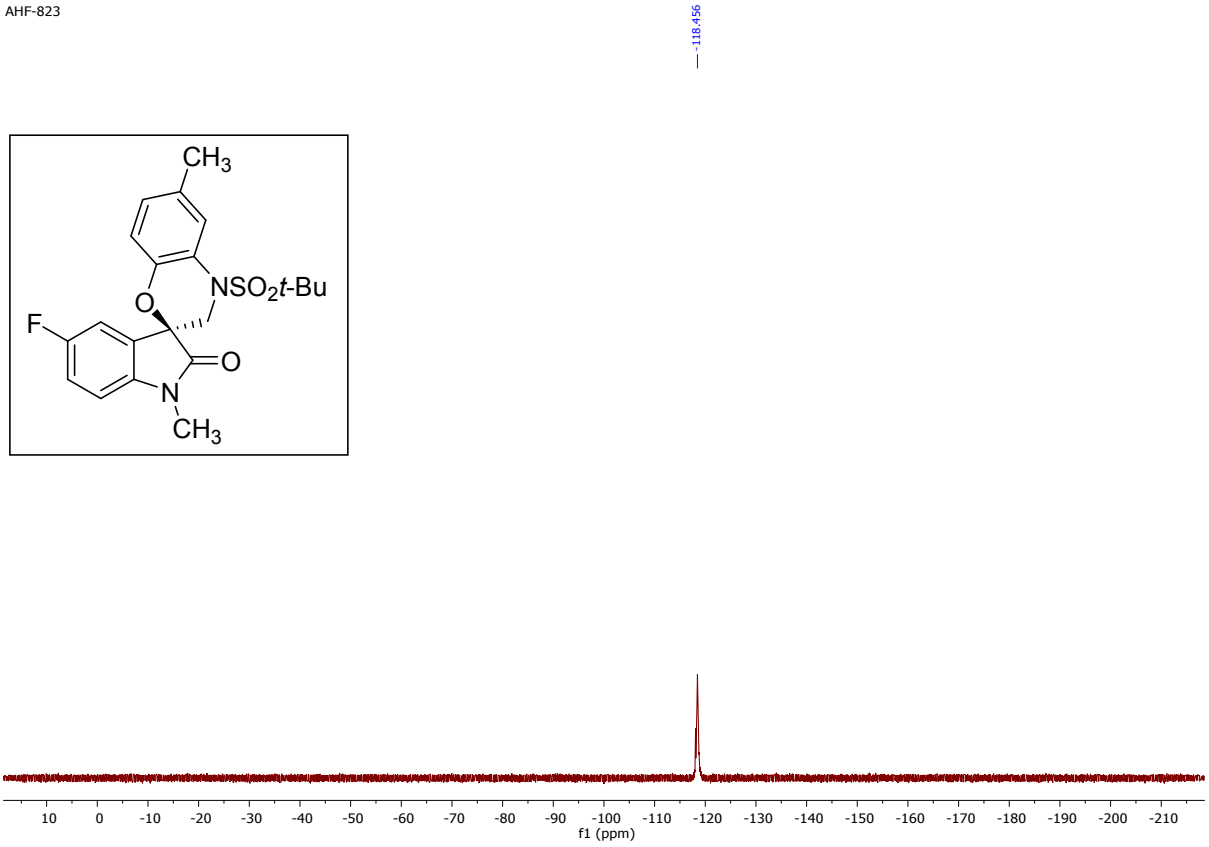
^{13}C NMR of compound *ent*-3lb (100 MHz, $CDCl_3$)



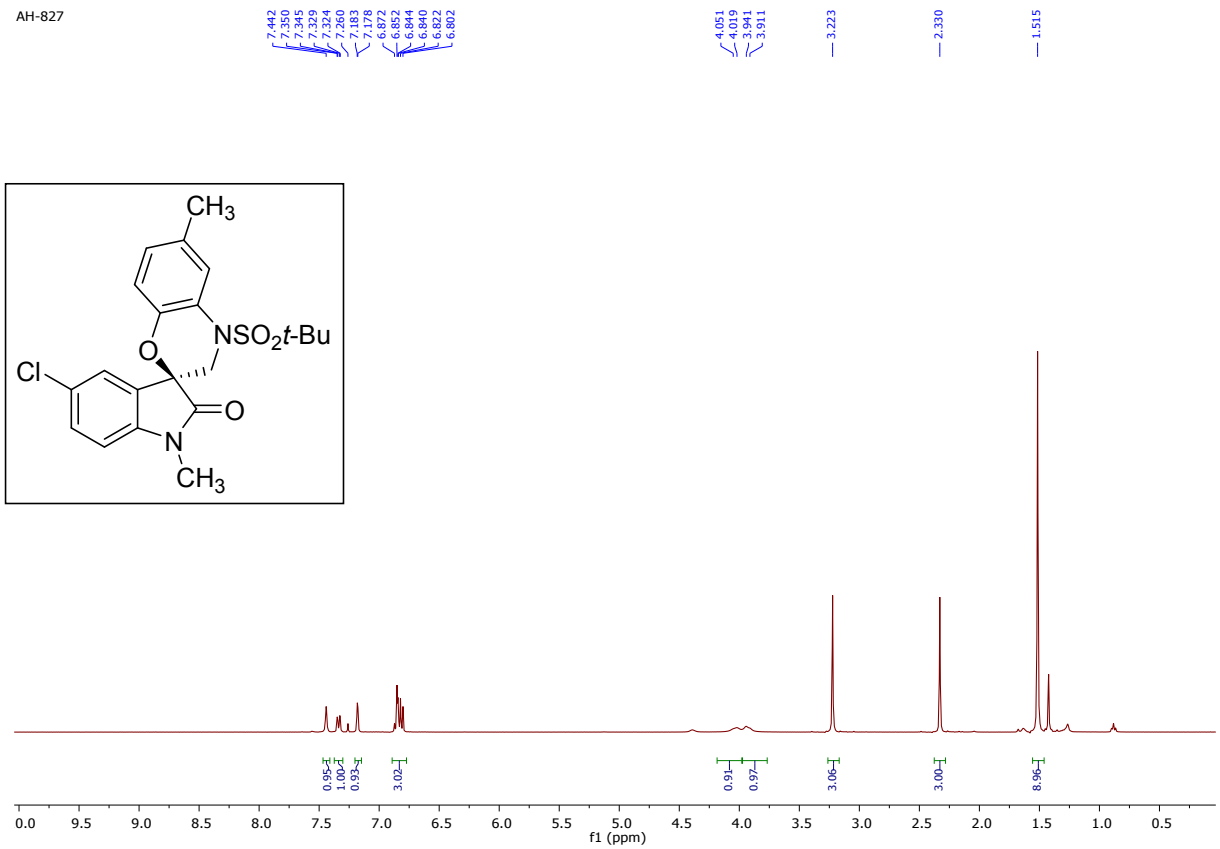
^{1}H NMR of compound 3mb (400 MHz, $CDCl_3$)



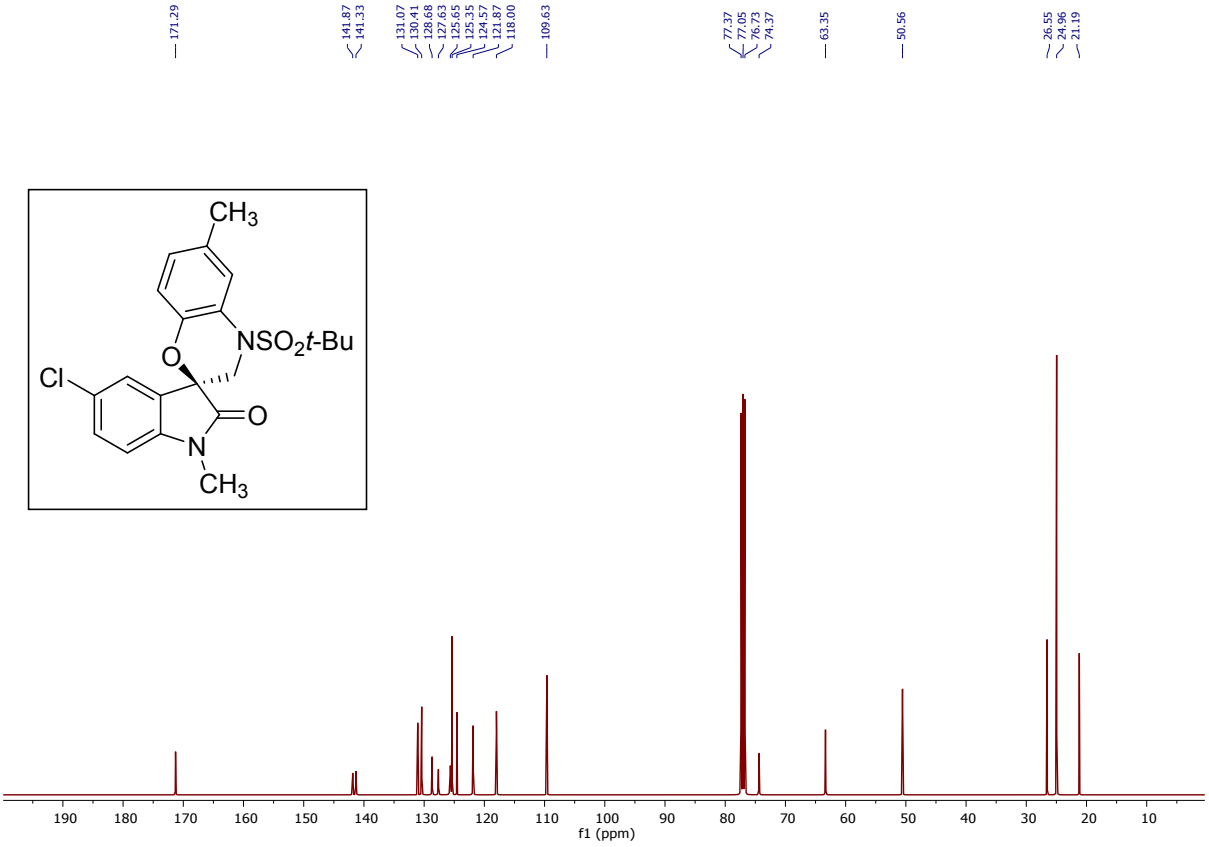
^{13}C NMR of compound 3mb (100 MHz, $CDCl_3$)



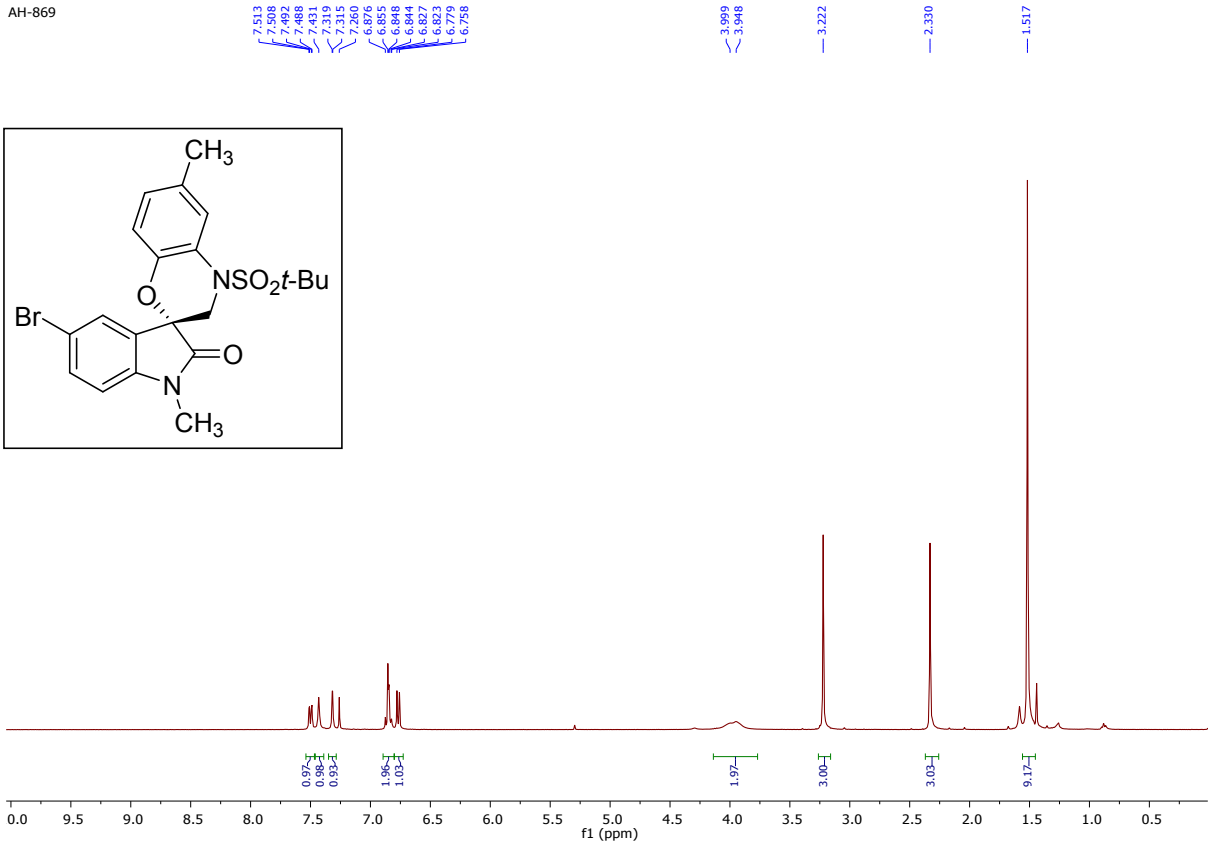
^{19}F NMR of compound 3mb (376 MHz, $CDCl_3$)



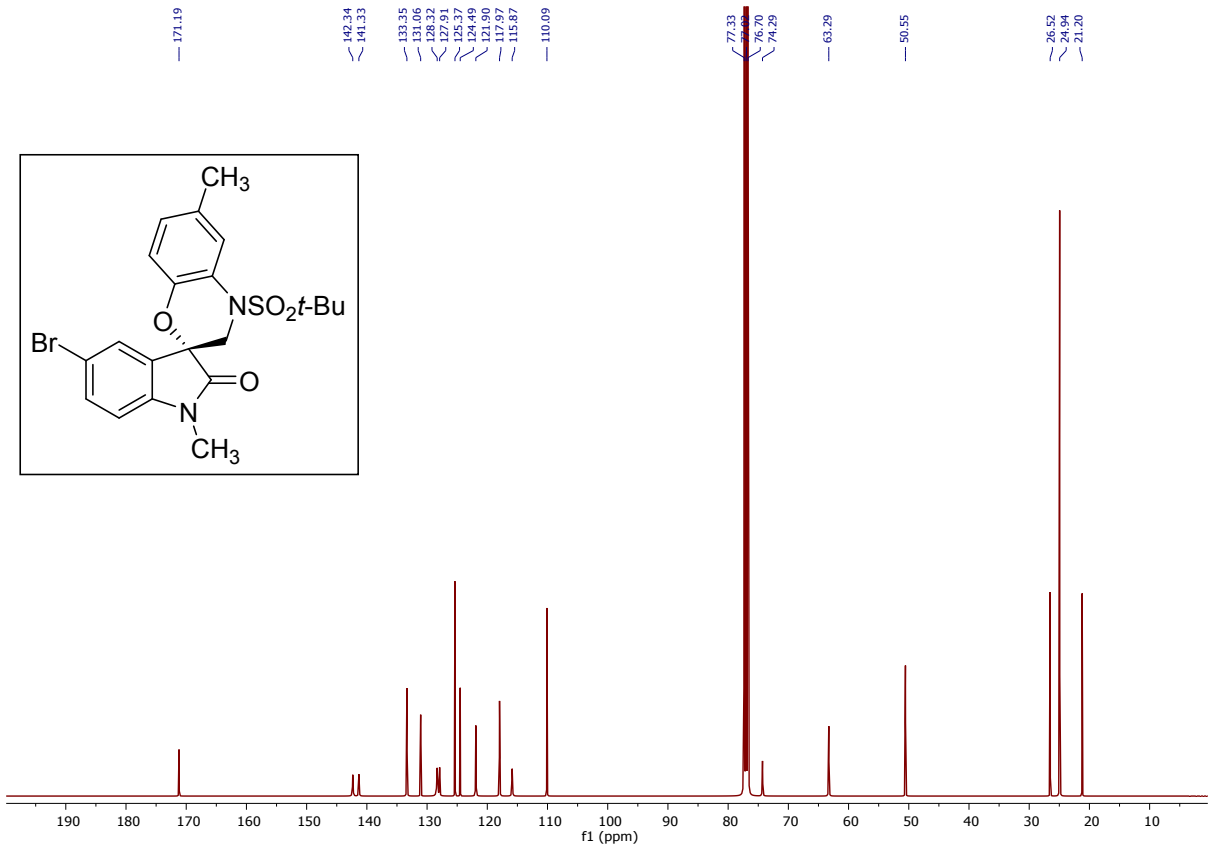
^{1}H NMR of compound 3nb (400 MHz, $CDCl_3$)



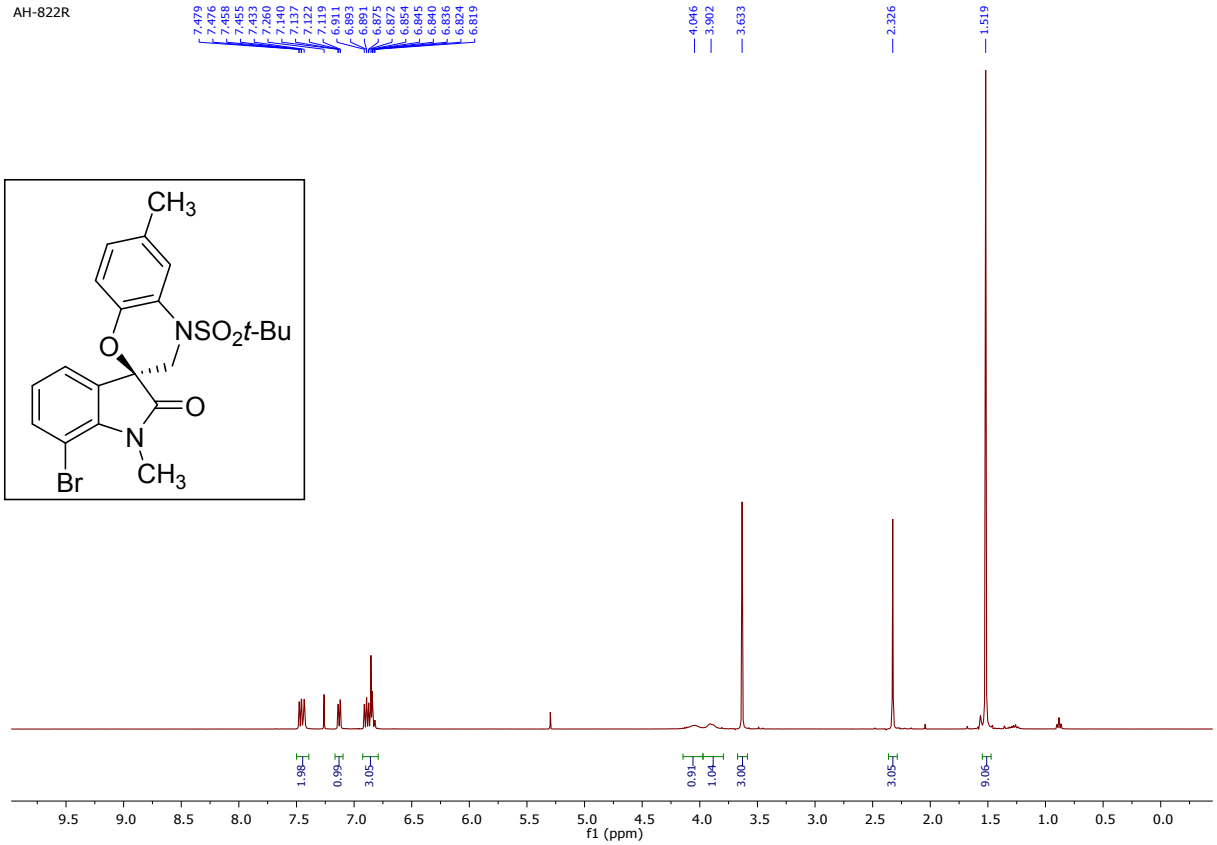
^{13}C NMR of compound 3nb (100 MHz, $CDCl_3$)



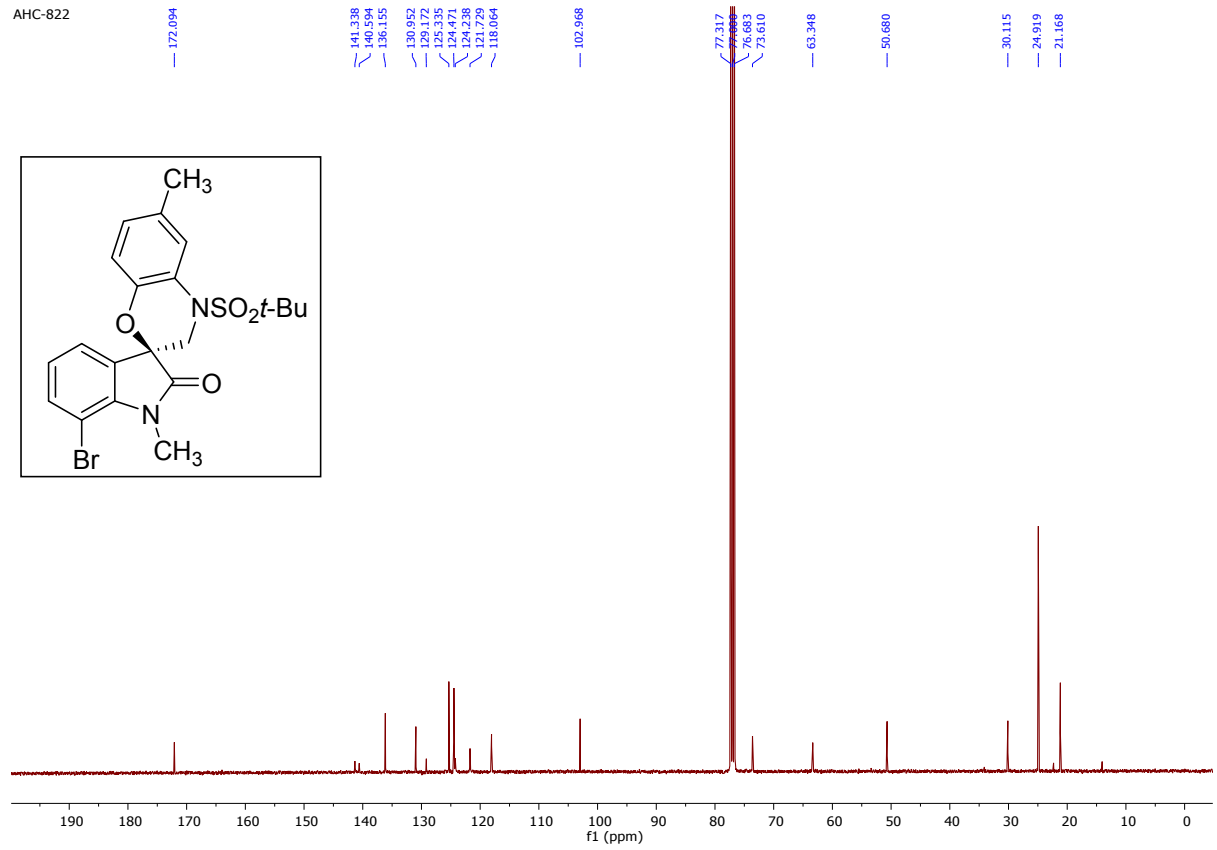
^{1}H NMR of compound *ent*-3ob (400 MHz, $CDCl_3$)



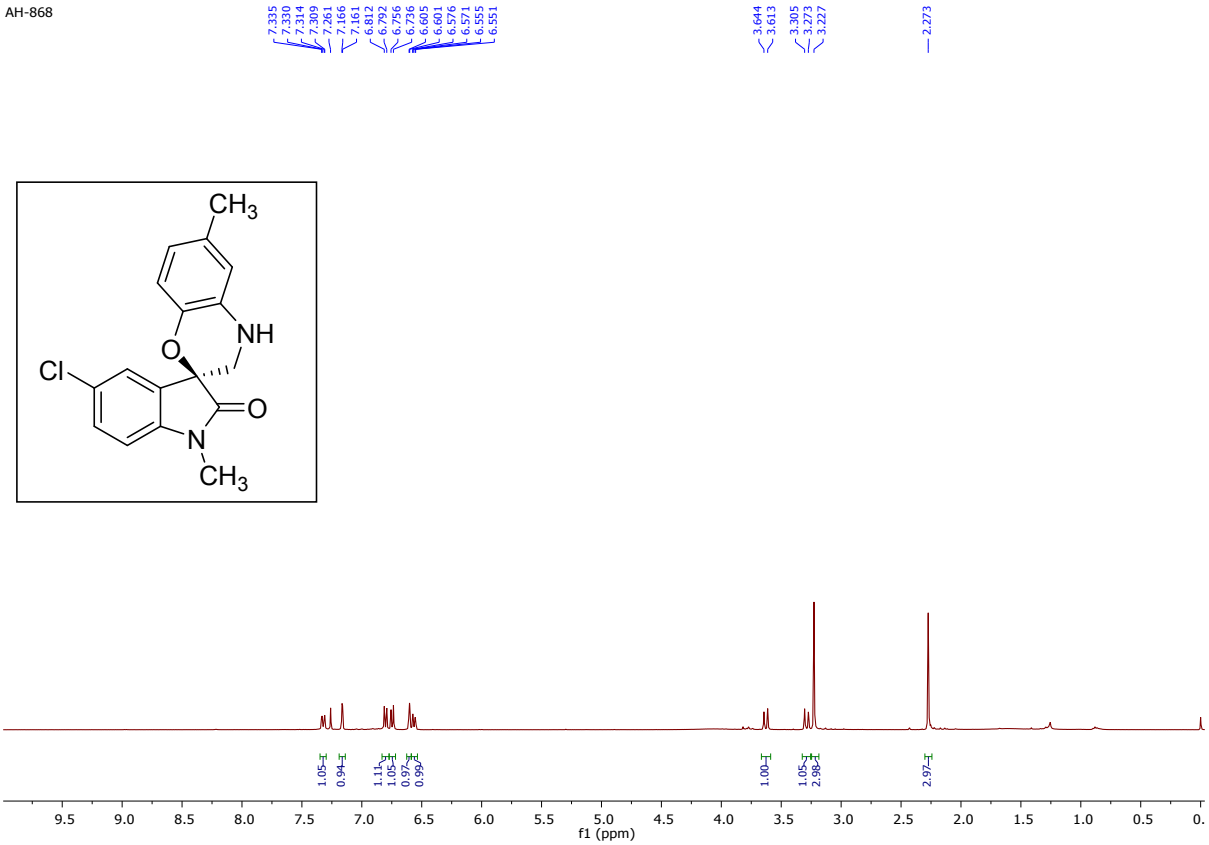
^{13}C NMR of compound *ent*-3ob (100 MHz, $CDCl_3$)



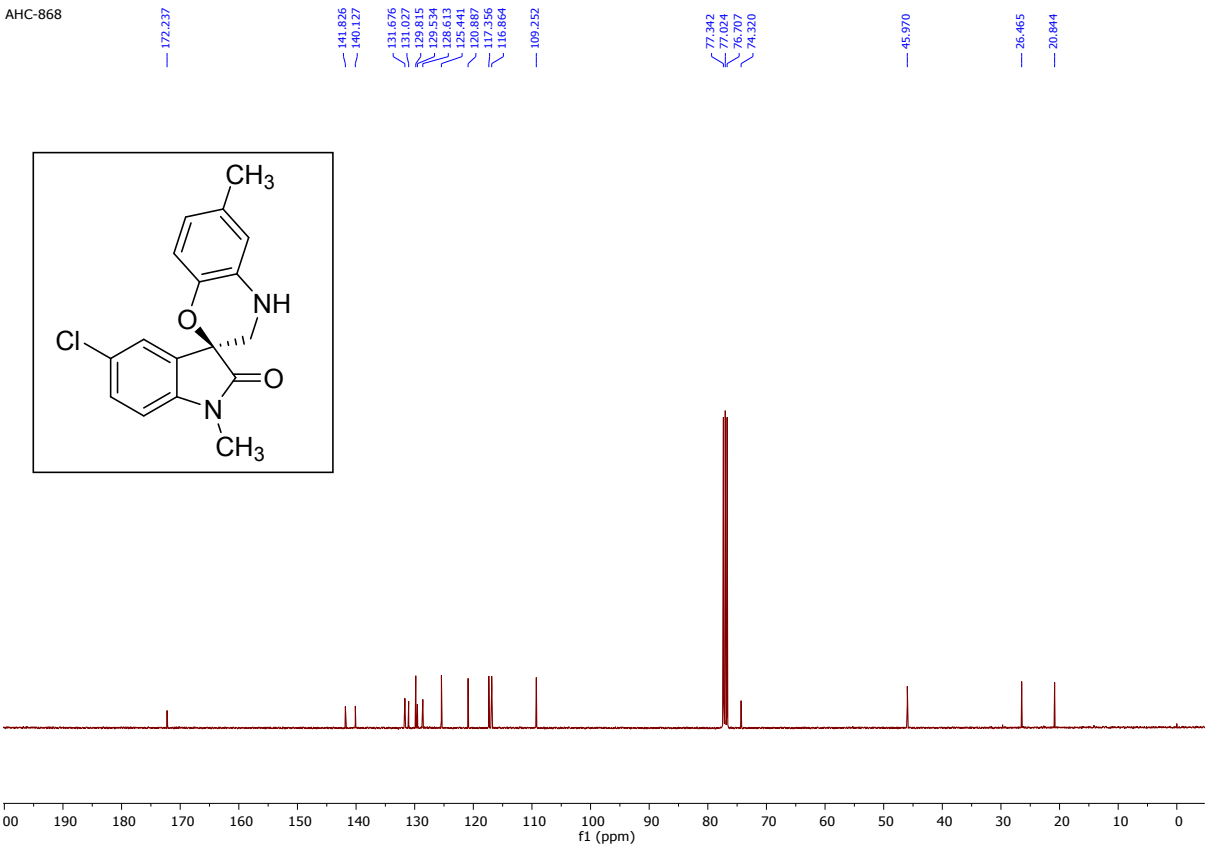
^{1}H NMR of compound 3pb (400 MHz, $CDCl_3$)



^{13}C NMR of compound 3pb (100 MHz, $CDCl_3$)



^{1}H NMR of compound 4nb (400 MHz, $CDCl_3$)



^{13}C NMR of compound 4nb (100 MHz, $CDCl_3$)

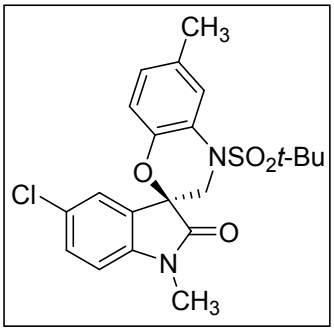
X-ray crystal structure details:

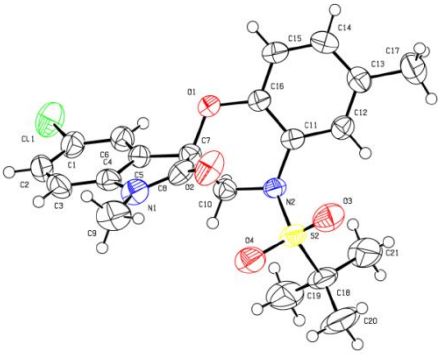
Datablock for the compound 3nb:

The details of crystal data collection and refinement of **3nb** are summarized in Table S1. CCDC 1923276 contains the supplementary crystallographic data for this paper. The compound **3nb** was recrystallized from ethyl acetate at rt. This data can be obtained free of charge from The Cambridge Crystallography Data Center via www.ccdc.cam.ac.uk/data_request/cif.

Datablock: I

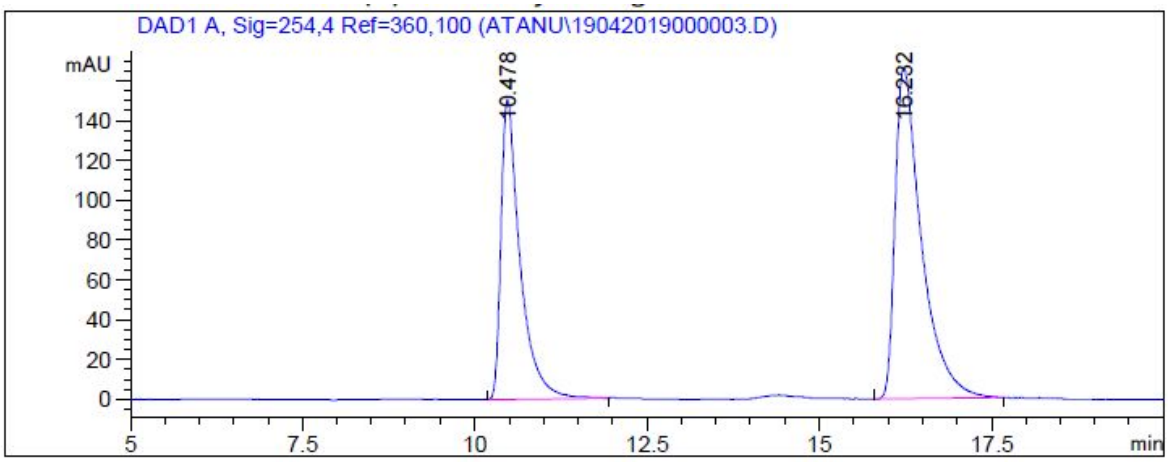
```
Bond precision:  C-C = 0.0027 A          Wavelength=0.71073

Cell:            a=9.0240(9)     b=13.3762(13)        c=18.311(2)
                 alpha=90        beta=103.731(3)      gamma=90
Temperature:     273 K

                Calculated                Reported
Volume          2147.1(4)                 2147.2(4)
Space group     P 21/c                    P 21/c
Hall group      -P 2ybc                   -P 2ybc
Moiety formula  C21 H23 Cl2 N3 O3         C21 H23 Cl2 N3 O3
Sum formula     C21 H23 Cl2 N3 O3         C21 H23 Cl2 N3 O3
Mr              436.32                    436.32
Dx,g cm-3       1.350                     1.350
Z               4                         4
Mu (mm-1)       0.329                     0.329
F000            912.0                     912.0
F000'           913.53
h,k,lmax        12,19,26                  12,19,26
Nref            6616                      6509
Tmin,Tmax
Tmin'

Correction method= Not given

Data completeness= 0.984          Theta(max)= 30.619

R(reflections)= 0.0617( 5727)     wR2(reflections)= 0.2470( 6509)

S = 2.082                 Npar= 267
```



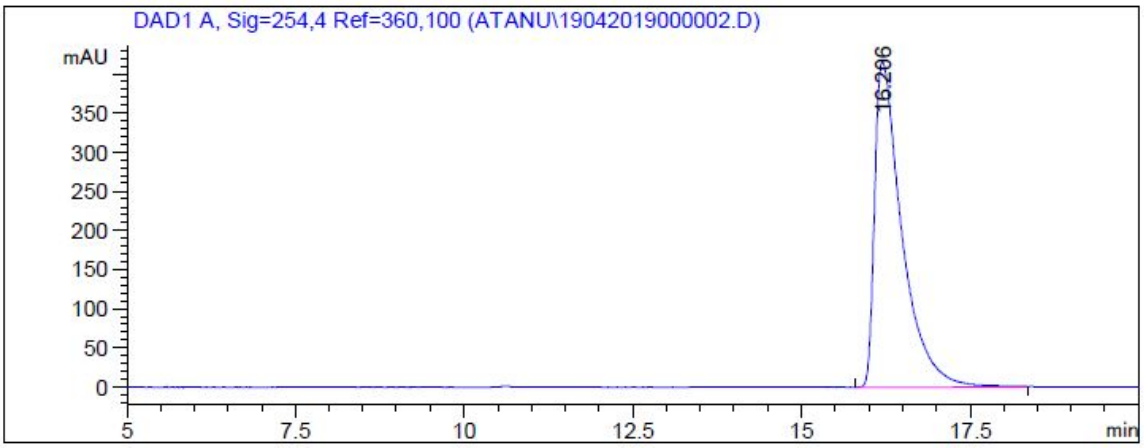


ORTEP diagram of **3nb** showing thermal ellipsoid at the 50% probability level

HPLC data:

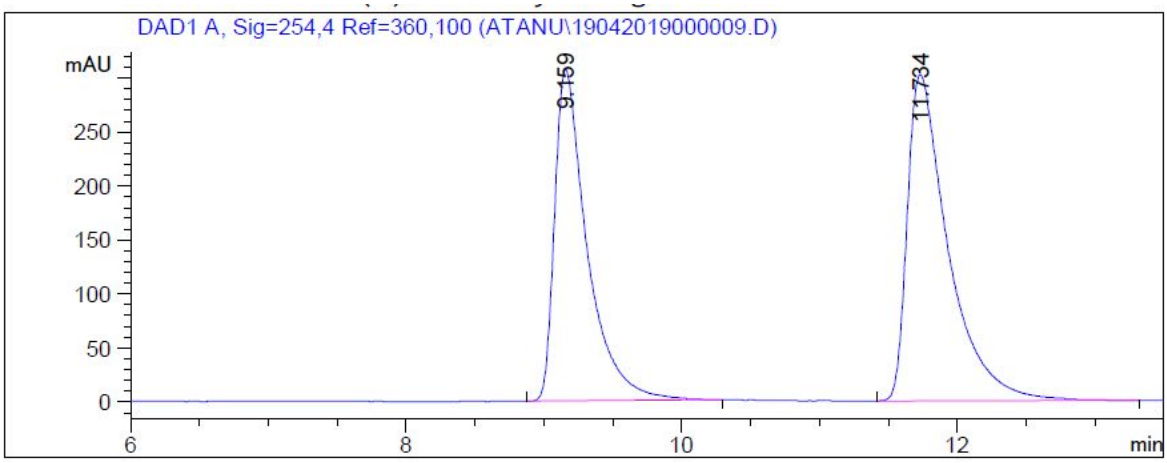


HPLC Chromatogram of Compound (±)-**3ha** (Manual mixing)

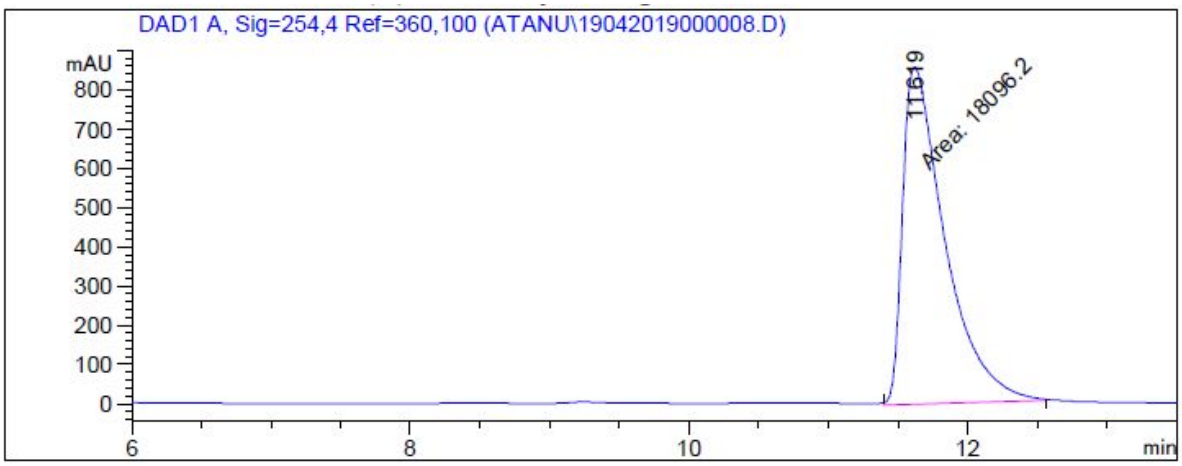



```
=====================================================================
                          Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.206 BB    0.4102 1.16998e4   415.87167 100.0000
```

HPLC Chromatogram of Compound **3ha**

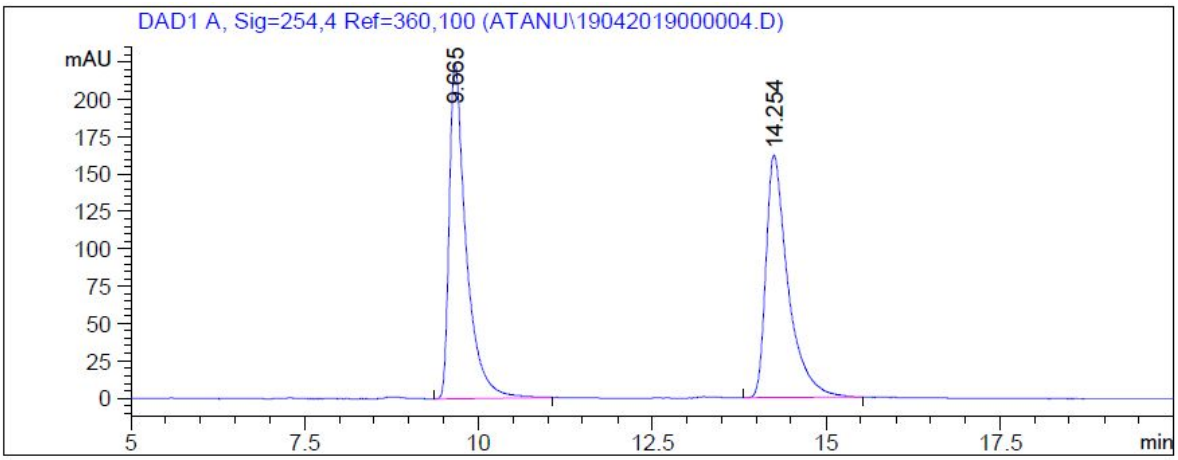


HPLC Chromatogram of Compound (±)-**3hb** (Manual mixing)

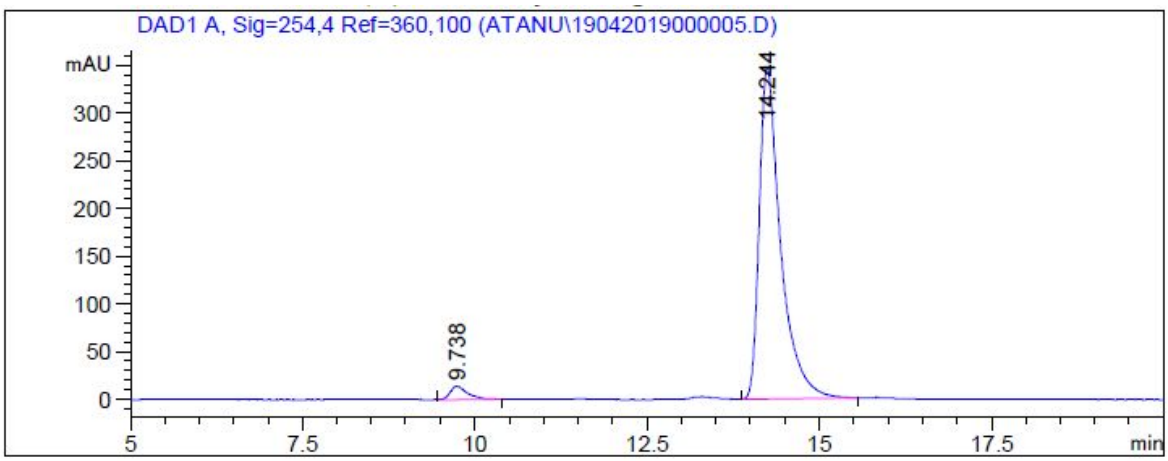



```
==================================================================
                          Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.619 MM    0.3513 1.80962e4   858.57098 100.0000
```

HPLC Chromatogram of Compound **3hb**

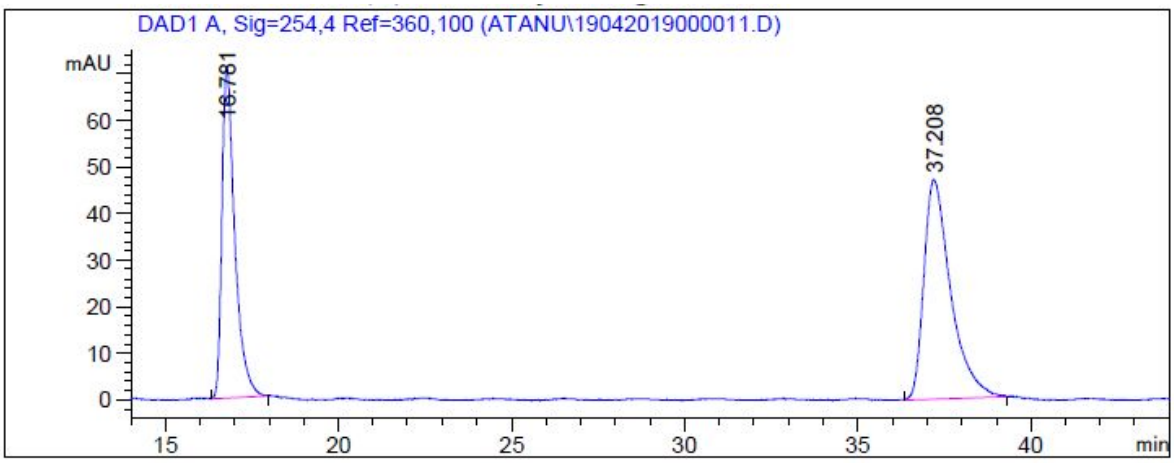


HPLC Chromatogram of Compound (±)-**3hc** (Manual mixing)

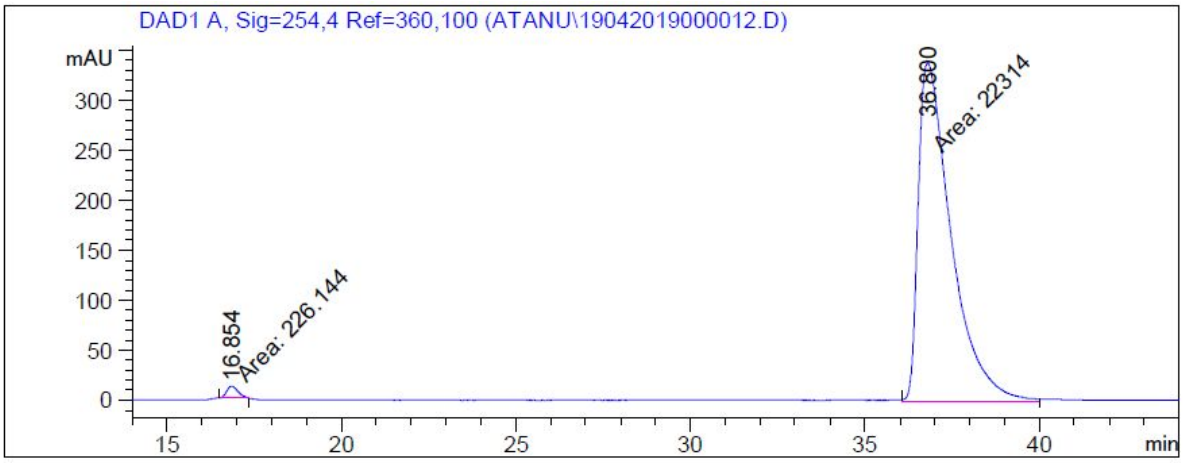



```
==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.738 BB    0.2427  240.11084   13.82232   3.1050
   2  14.244 BB    0.3177 7493.00684  347.34729  96.8950
```

HPLC Chromatogram of Compound **3hc**

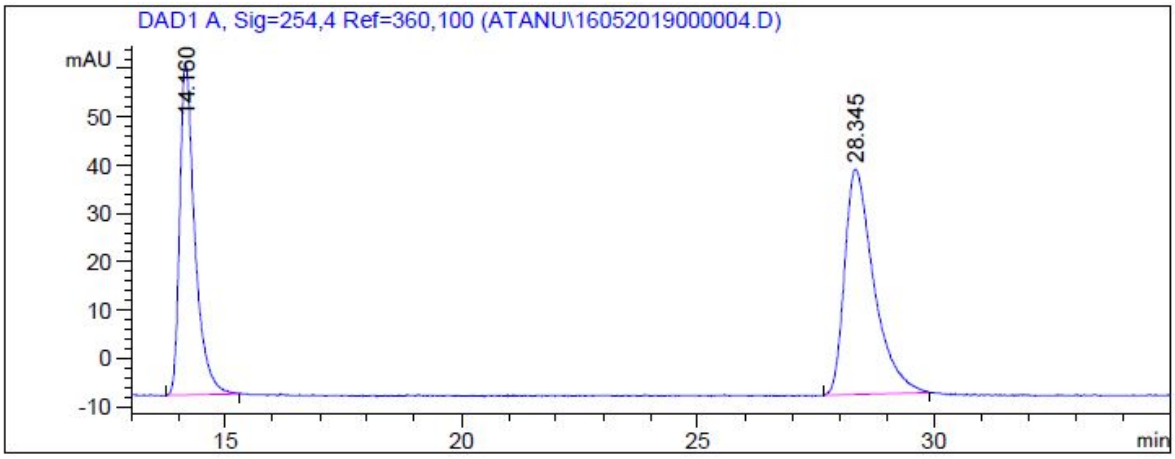


HPLC Chromatogram of Compound (±)-**3ia** (Manual mixing)

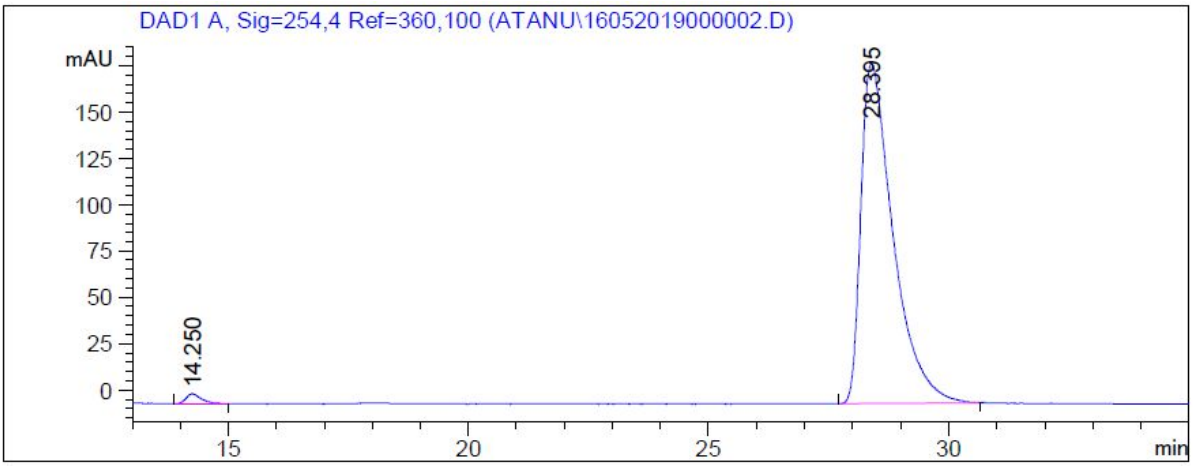



```
==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  16.854 MM    0.3393  226.14400   11.10804   1.0033
   2  36.800 MM    1.0982 2.23140e4   338.63248  98.9967
```

HPLC Chromatogram of Compound **3ia**

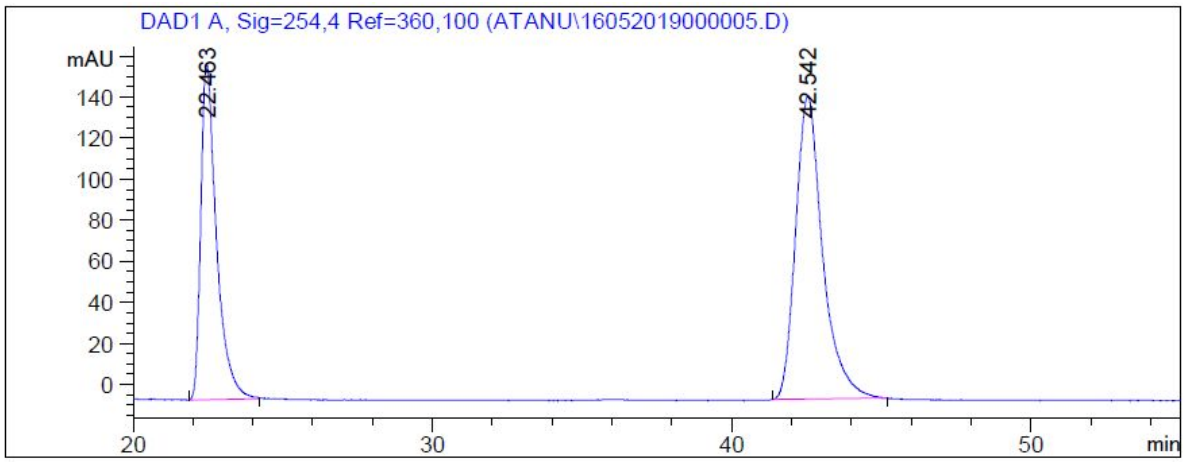


HPLC Chromatogram of Compound (±)-**3ib** (Manual mixing)

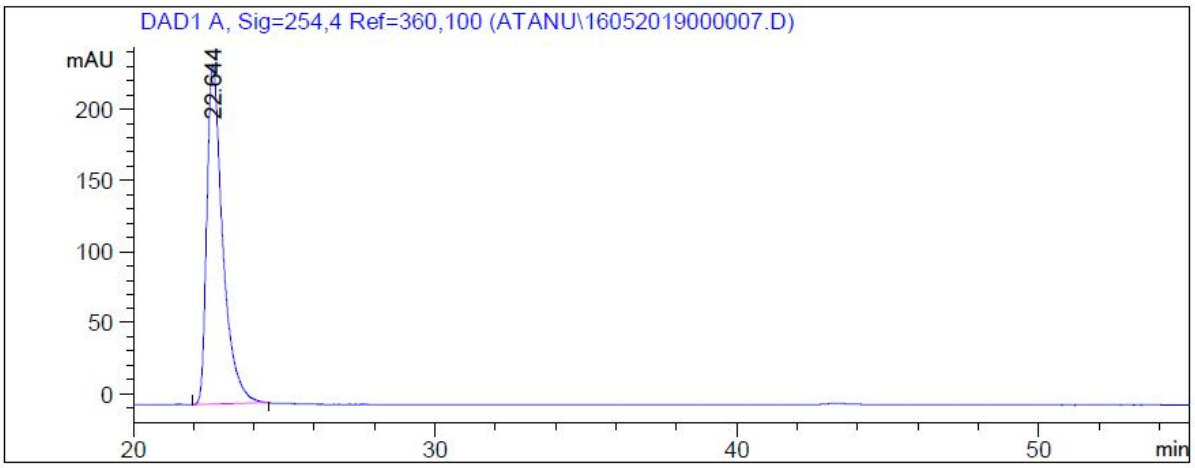



```
=========================================================================
                              Area Percent Report
=========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.250 BB    0.2961  122.86530    5.34711   1.4146
   2  28.395 BB    0.6484 8562.34473  183.48940  98.5854
```

HPLC Chromatogram of Compound **3ib**

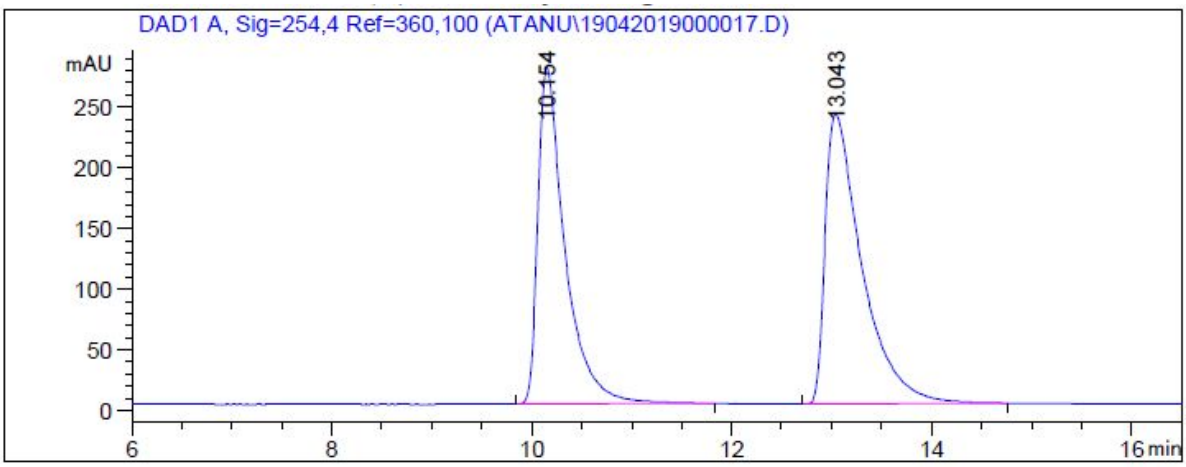


HPLC Chromatogram of Compound (±)-**3ja** (Manual mixing)

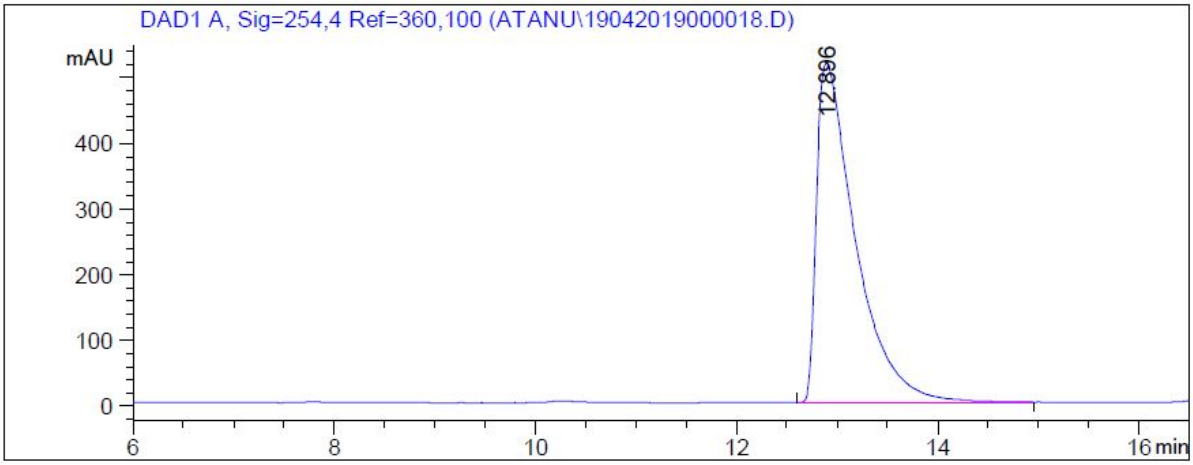



```
=====================================================================
                          Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.644 BB    0.5361 8713.28125  238.58257 100.0000
```

HPLC Chromatogram of Compound ***ent*-3ja**

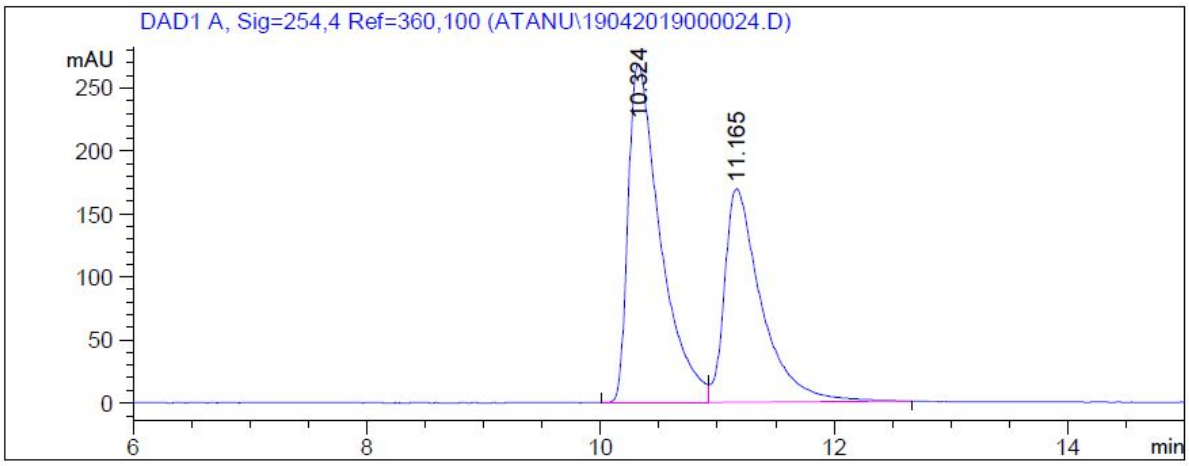


HPLC Chromatogram of Compound (±)-**3kb** (Manual mixing)

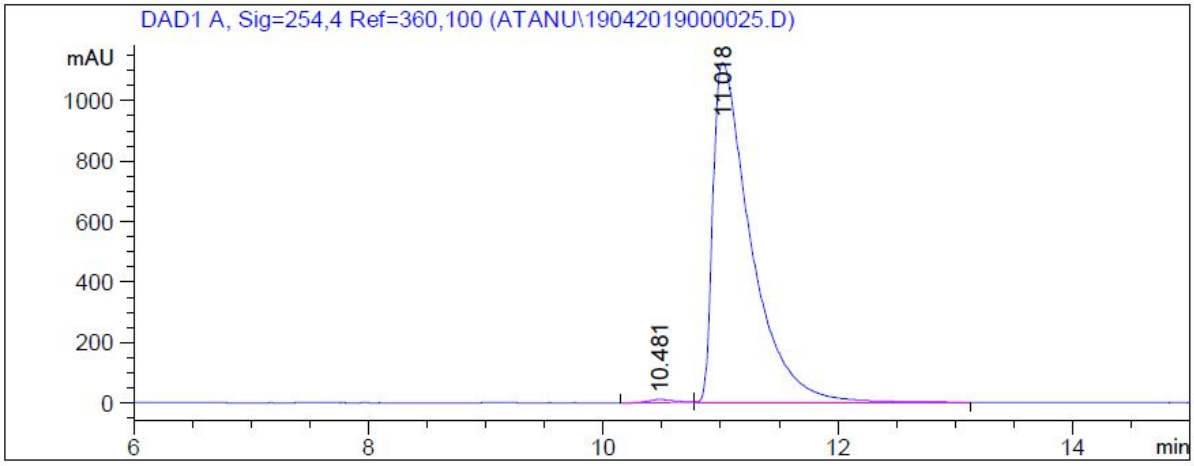



```
=====================================================================
                          Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  12.896 BB    0.3957 1.39146e4   517.56140 100.0000
```

HPLC Chromatogram of Compound **3kb**

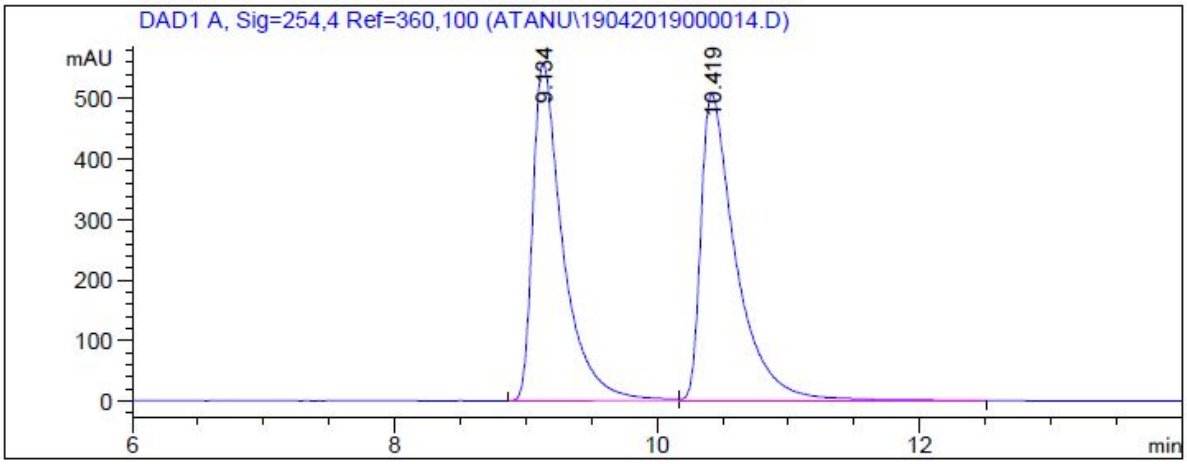


HPLC Chromatogram of Compound (±)-**3lb** (Manual mixing)

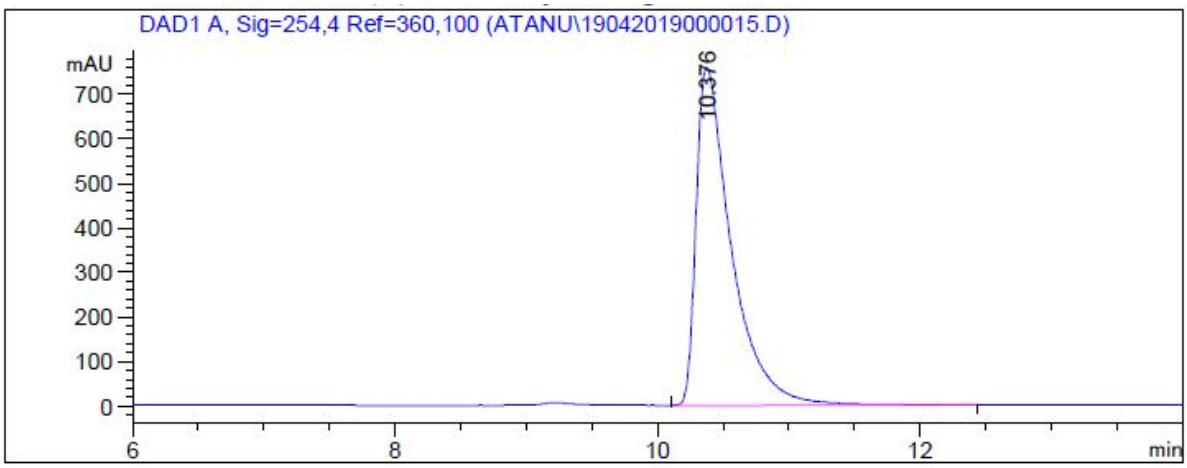



```
=====================================================================
                          Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.481 BV    0.2676  185.90544   10.25213   0.7311
   2  11.018 VB    0.3260 2.52425e4  1124.03882  99.2689
```

HPLC Chromatogram of Compound ***ent*-3lb**

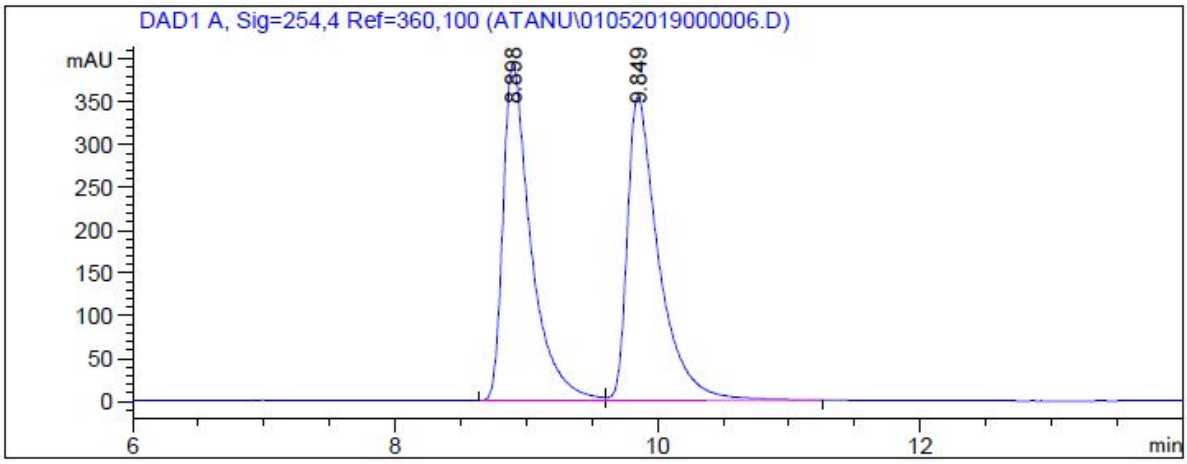


HPLC Chromatogram of Compound (±)-**3mb** (Manual mixing)

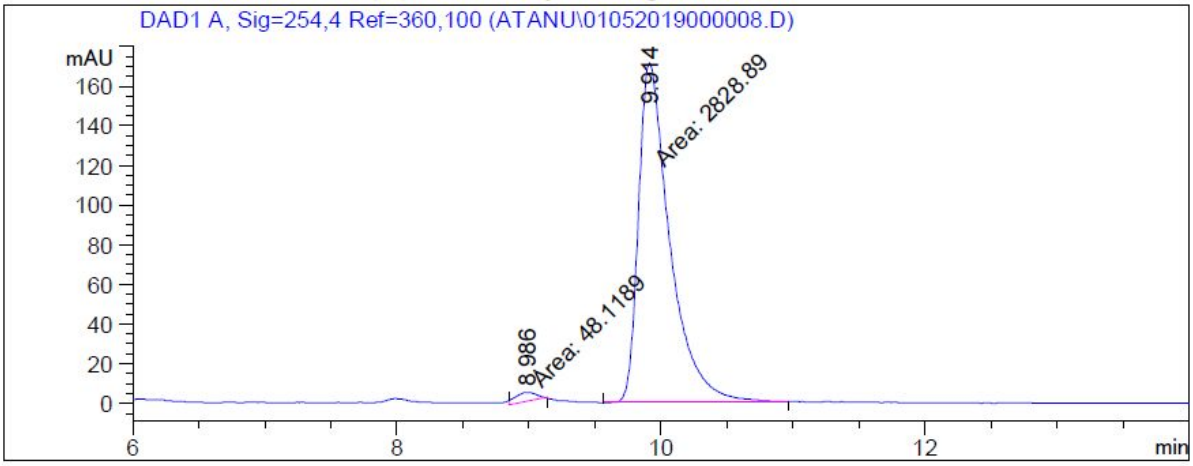



```
==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.376 BB    0.2736 1.41386e4   758.05182 100.0000
```

HPLC Chromatogram of Compound **3mb**

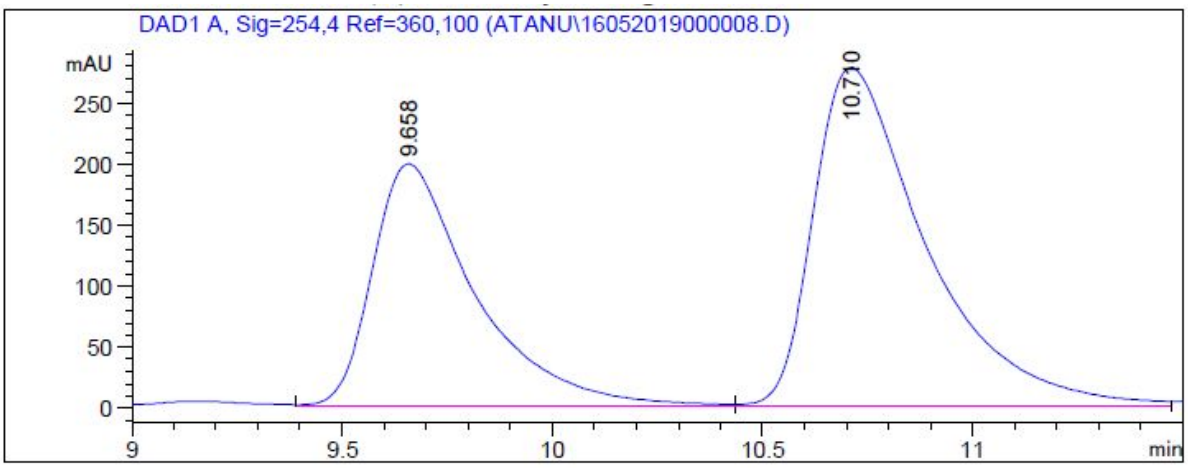


HPLC Chromatogram of Compound (±)-**3nb** (Manual mixing)

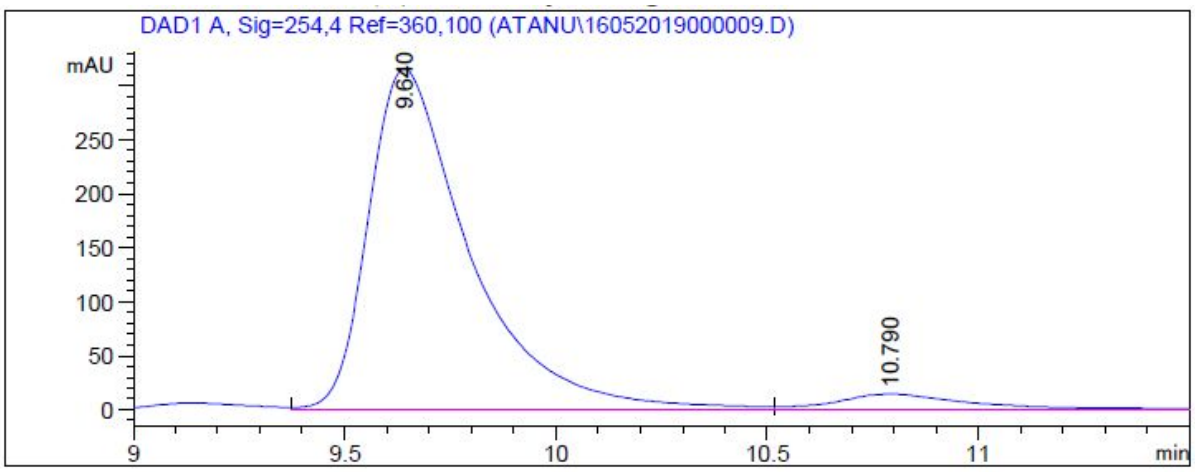



```
=====================================================================
                          Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.986 MM    0.1826   48.11894    4.39291   1.6725
   2   9.914 MM    0.2754 2828.89038  171.17294  98.3275
```

HPLC Chromatogram of Compound **3nb**

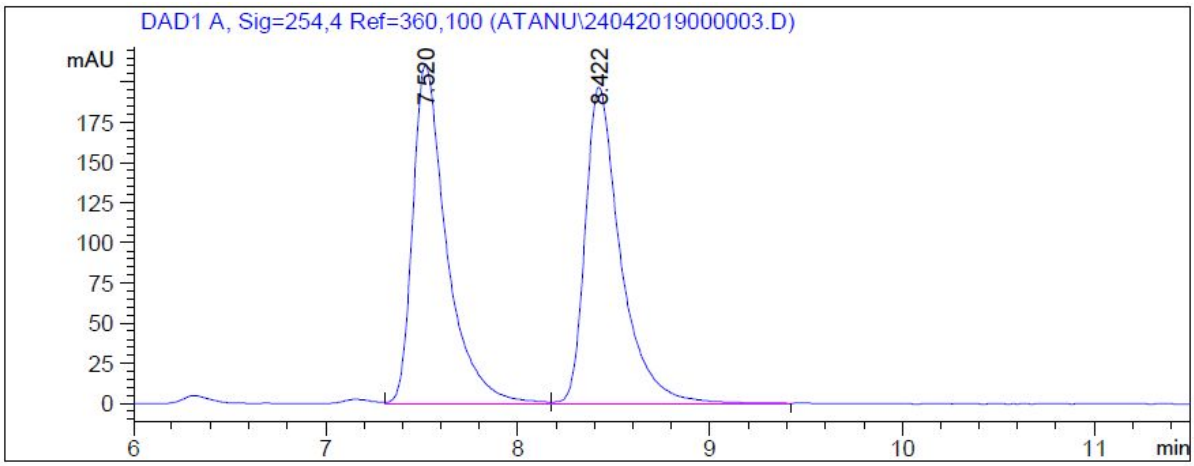


HPLC Chromatogram of Compound (±)-**3ob** (Manual mixing)

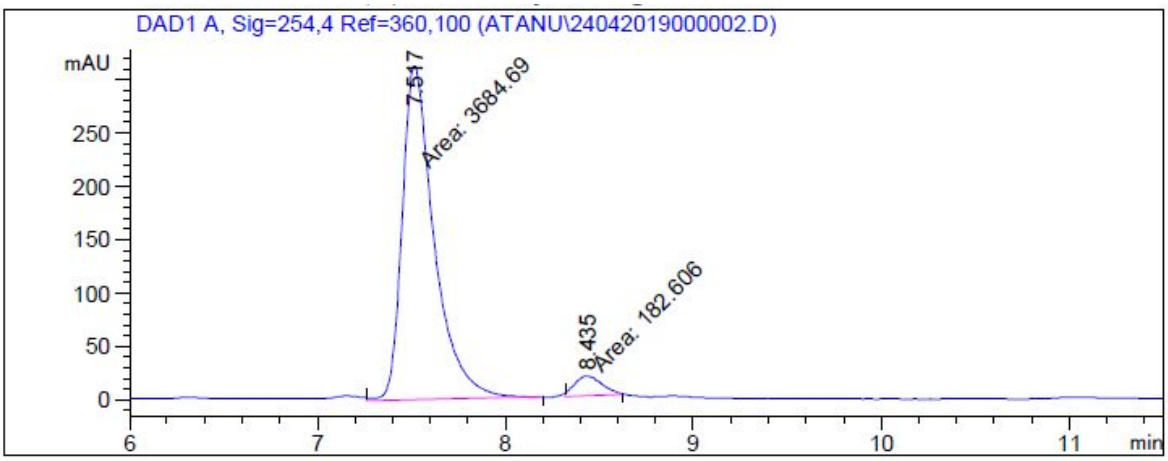



```
==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.640 VV    0.2433 5216.47607  314.91037  94.8913
   2  10.790 VB    0.2869  280.84232   13.71277   5.1087
```

HPLC Chromatogram of Compound ***ent*-3ob**

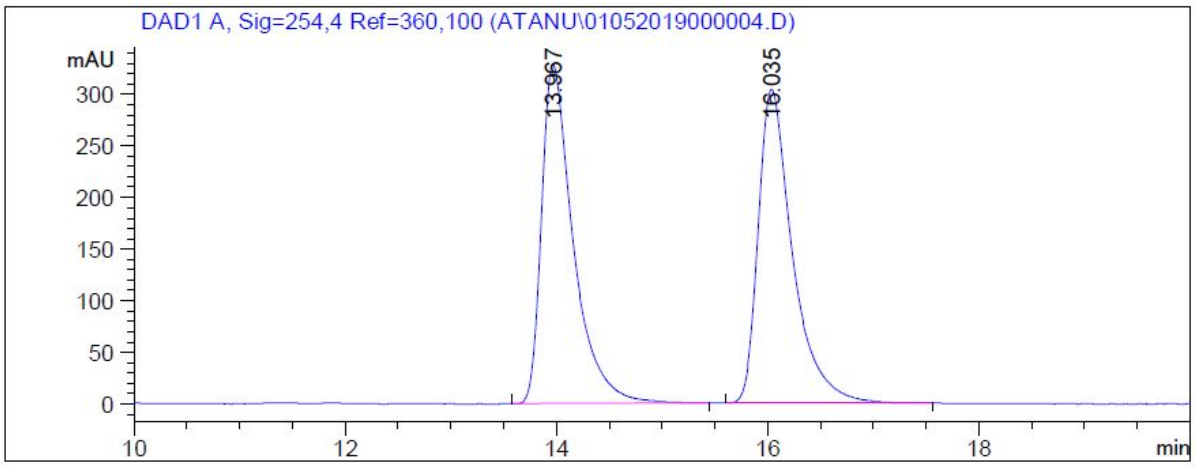


HPLC Chromatogram of Compound (±)-**3pb** (Manual mixing)

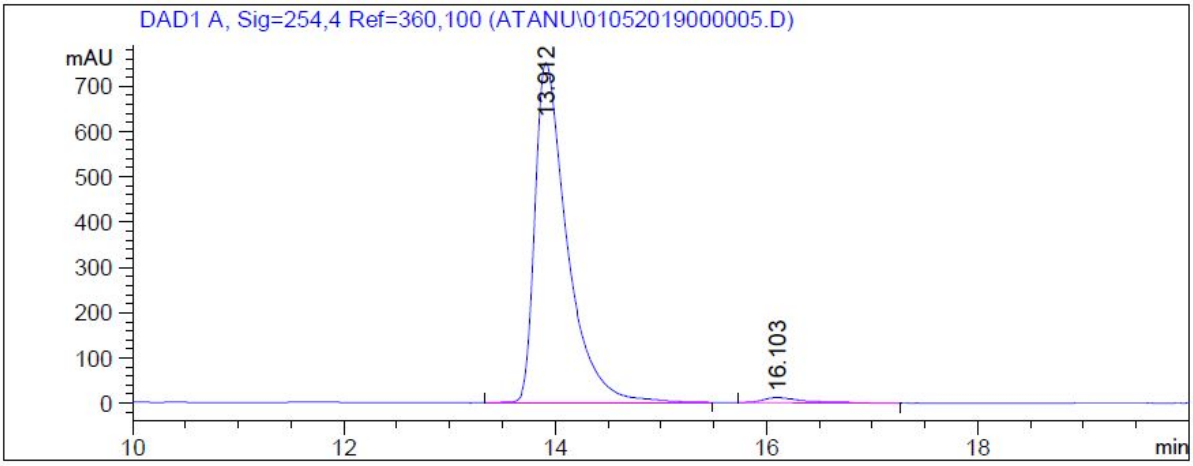



```
=====================================================================
                          Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.517 MM    0.1963 3684.68799  312.80176  95.2782
   2   8.435 MM    0.1669  182.60617   18.23665   4.7218
```

HPLC Chromatogram of Compound **3pb**



HPLC Chromatogram of Compound (±)-**4nb** (Manual mixing)




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  13.912 BB    0.3109 1.57557e4   750.54199  98.2530
   2  16.103 BB    0.3755  280.14944   10.62851   1.7470
```

HPLC Chromatogram of Compound **4nb**