Organocatalyzed [4+2] cycloaddition of α,β-unsaturated ketones and isatylidene malononitrile: Accessing to spiro[3-arylcyclohexa- none]oxindole derivatives

Baliram R. Patil, [ab] Chandrakant B. Nichinde, [ab] Suryakant S. Chaudhari, [ab] Gamidi Rama Krishna, [c] and Anil K. Kinage *[ab]

[a.] *Chemical Engineering and Process Development Division, Council of Scientific and Industrial Research-National Chemical Laboratory (CSIR-NCL), Pune 411008, India.*
[b.] *Academy of Scientific and Innovative Research (AcSIR), Ghaziabad-201002, India.*
[c.] *Organic Chemistry Division, Council of Scientific and Industrial Research-National Chemical Laboratory (CSIR-NCL), Pune 411008, India.*

Supporting Information

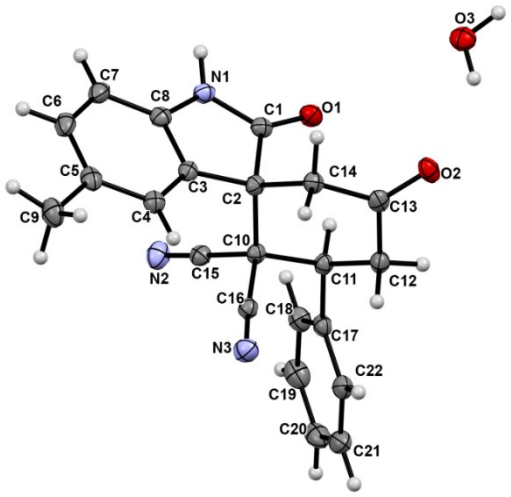
Contents.

1. GENERAL INFORMATION: ^{1}H NMR spectra, ^{13}C NMR spectra and ^{19}F NMR spectra was acquired in appropriate deuterated solvents at room temperature on Bruker: Ultrashield AV 400 MHz, Ultrashield AV 500 MHz spectrometer. Chemical shifts (δ) are reported for ^{1}H NMR in ppm from TMS as internal standard solvent signals as secondary standards. ^{13}C NMR from the residual solvent peak. ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity designated as *s* (singlet), *d* (doublet), *t* (triplet), *dd* (doublet of doublet), *q* (quartet), *m* (multiplet), etc., coupling constant (Hz). Data for ^{13}C NMR spectra are reported in terms of chemical shift (δ ppm). HRMS data was recorded on a Thermo scientific Q-Exactive, Accela 1250 pump. Single crystal x-ray diffraction measurements were carried out on Bruker D8 venture dual micro focus source diffractometer.

Materials: unless otherwise noted, materials obtained from commercial suppliers were used without further purification. All solvents were used anhydrous grade from commercial suppliers.

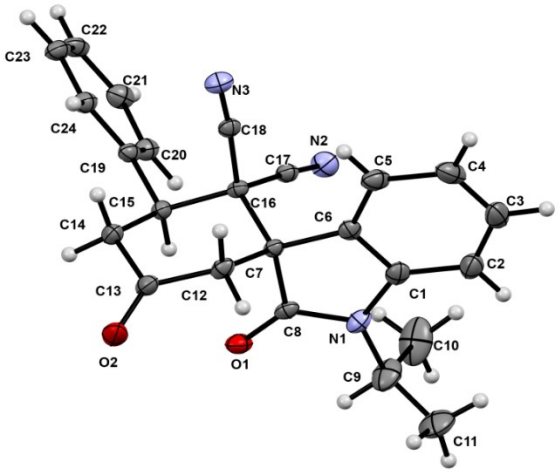
2. SINGLE CRYSTAL X-RAY DIFFRACTION STUDIES

Crystals grown from methanol solvent through the slow evaporation method, the single crystals are harvested after 2-3 days. The diffraction measurements were performed to determine the crystal structure of compounds 3Ac and 3Bd at 100 K using APEX3 (Bruker, 2016; Bruker D8 VENTURE Kappa Duo PHOTON II CPAD) diffractometer having graphite-monochromatized (MoKα = 0.71073 Å). The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of unit cell parameters and an orientation matrix were calculated from 36 frames, and the cell refinement was performed by SAINT-Plus (Bruker, 2016). An optimized strategy used for data collection consisted of different sets of φ and ω scans with **SC-XRD Experiments:** The single crystals which are suitable for SC-XRD measurements were 0.5^{o} steps φ/ω. The data were collected with a time frame of 10 sec for both the components by setting the sample to detector distance fixed at 40 cm. All the data points were corrected for Lorentzian, polarization, and absorption effects using SAINT-Plus and SADABS programs (Bruker, 2016). SHELXS-97 (Sheldrick, 2008) was used for structure solution, and full-matrix least-squares refinement on F^2.[1, 2] The molecular graphics of ORTEP diagrams were performed by Mercury software. The crystal symmetry of the components was cross-checked by running the cif files through PLATON (Spek, 2020) software and notified that no additional symmetry was observed. The Encifer software was used to correct the cif files.



3Ac: CCDC: 2302588

Figure 1. ORTEP diagram of compound **3Ac**, the asymmetric unit contains a single molecule. Herein, the ellipsoids are drawn with a 50% probability.



3Bd: CCDC: 2302589

Figure 2. ORTEP diagram of compound **3Bd**, the asymmetric unit contains a single molecule. Herein, the ellipsoids are drawn with a 50% probability.

Table 1. Crystallographic information details of compounds 3Ac and 3Bd.

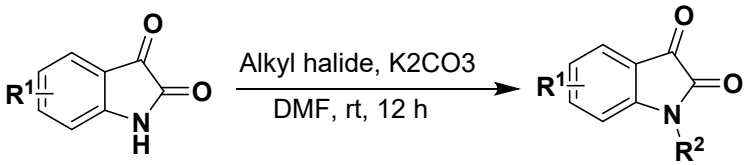
Crystal data	Compound 3Ac	Compound 3Bd
Chemical formula	$2(C_{22}H_{17}N_3O_2)\cdot H_2O$	$C_{24}H_{21}N_3O_2$
Formula weight (M_r)	728.79	383.44
Crystal system	Tetragonal	Monoclinic
Space group	$I4_1/a$	$P2_1/c$
Temperature T (K)	100	100
a (Å)	15.7011 (14)	9.9591 (4)
b (Å)	15.7011 (14)	17.0919 (6)
c (Å)	29.337 (3)	11.8583 (5)
α (°)	90	90
β (°)	90	105.357 (1)
γ (°)	90	90
Z	8	4
Volume (Å^3)	7232.2 (15)	1946.45 (13)
Source of radiation	MoKα	MoKα
D_{calc} (Mg m^{-3})	1.339	1.308
Crystal size (mm)	0.26×0.11×0.09	0.29×0.13×0.08
μ (mm^{-1})	0.09	0.09
Data collection		
Diffractometer	Bruker D8 VENTURE Kappa Duo PHOTON II CPAD	Bruker D8 VENTURE Kappa Duo PHOTON II CPAD
Absorption correction	Multi-scan (SADABS; Bruker, 2016)	Multi-scan (SADABS; Bruker, 2016)

T_{min}, T_{max}	0.4605, 0.7455	0.5563, 0.7456
No. of measured, independent and observed [I > 2σ(I)] reflections	39894, 3952, 3375	14764, 4189, 3736
Theta range (°)	2.301-26.999	3.370-26.999
R_{int}	0.081	0.049
Refinement		
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$	0.037, 0.097	0.051, 0.127
GOF on F^2	1.02	1.03
No. of independent reflections	3952	4189
No. of parameters	259	264
F_000	3056	808
No. of restraints	0	0
H-atom treatment	Constr	Constr
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $A^{\circ -3}$)	0.25, −0.19	0.62, −0.34
CCDC number	2302588	2302589

Table 2. Hydrogen-bond geometry (A˚, °) of compounds **3Ac** and **3Bd** are given as below.

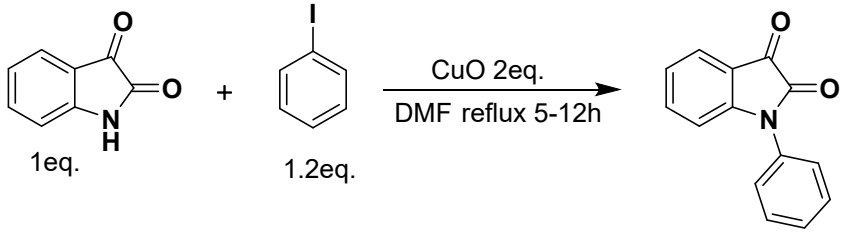
Name of the compound	*D*–H···*A*	*D*–H	H···*A*	*D*···*A*	*D*–H···*A*
Compound 3Ac	N1–H1•••O3	0.920	2.010	2.9160(3)	169
	O3–H3•••O2	0.890	2.060	2.7716(3)	136
	C11–H11•••O1	1.000	2.290	3.0093(3)	128
	C14–H14A•••O1	0.990	2.430	3.2831(3)	144
	C14–H14B•••O2	0.990	2.470	3.0846(3)	120
Compound 3Bd	C9–H9•••O1	0.980	2.380	2.8431(1)	108
	C9–H9•••O2	0.980	2.570	3.4314(1)	147
	C15–H15•••O1	0.980	2.330	2.9870(1)	124

3.(a). General Procedure for the preparation of N- alkyl substituted isatine[3] : N-Substituted isatin derivatives were synthesized from commercially available isatins and alkyl or aryl halides in the presence of potassium carbonate as base in DMF solution. Alkyl halides (12 mmol, 1.2 equiv) was added to a stirred solution of isatin (10 mmol, 1.0 equiv) and K_2CO_3 (12 mmol, 1.2 equiv) in DMF and stirred for 12 h at room temperature. Reactions were monitored by TLC until completion. The reaction mixture was quenched with water (20 mL) and extracted with dichloromethane (3 x 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum. The crude residue was then purified by column chromatography on silica gel with ethyl acetate-pet ether (10/90 to 20/80) to provide N-protected isatin derivatives.

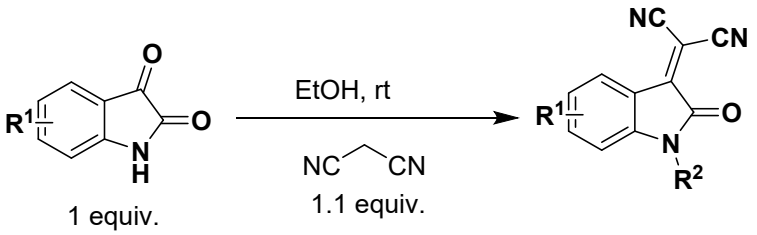


(b). General Procedure for the preparation of N-Aryl substituted isatin[4] :

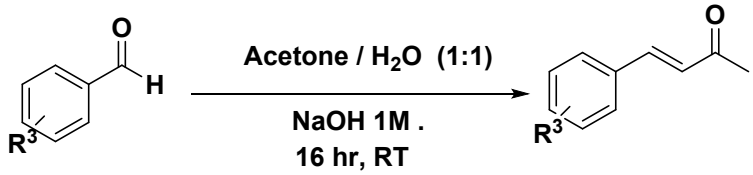
N-Arylation of isatin were synthesized from commercially available isatin and aryl halide (1.2eq.) in the presence of CuO (2eq.) in DMF solvent at reflux condition for 5-12 h. After reaction cooled to room temperature and filter to remove CuO. The filtrate was poured in cold water and ethyl acetate was added. The organic and aqueous layers were separated. The organic layer dried over anhydrous Na2SO4, filtered and concentrated in vacuum and resulting crude product, which was purified by
column chromatography to afford pure product.



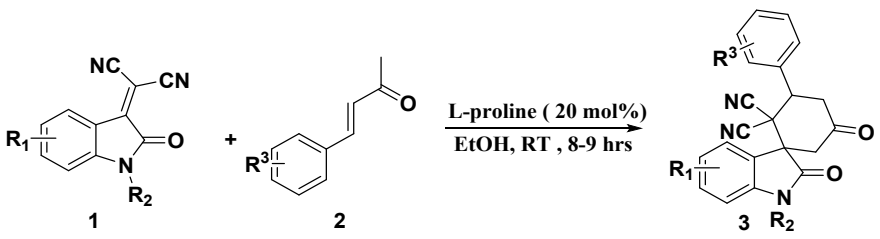
4. General procedure for the synthesis of isatylidine malononitrile[5] : A mixture of isatin (0.5 mmol, 1 equiv.) and malononitrile (0.55 mmol, 1.1 equiv.) in EtOH (1 mL) was stirred at room temperature until isatin was totally converted to product (monitored by TLC). After completion of reaction solvent was removed under low pressure. Obtained residue was washed with cold methanol to get pure product.



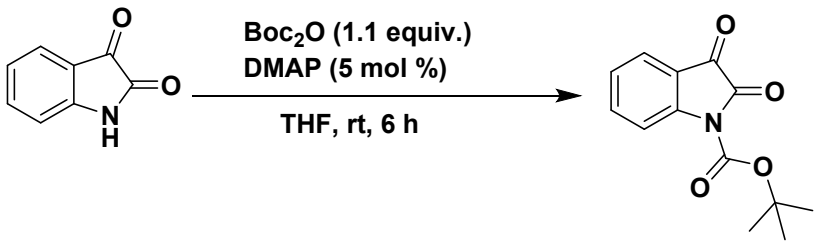
5. General Procedure for the preparation of α, β-unsaturated ketones[6] : To a stirred solution of aldehyde (7.5 mmol) in acetone/water (1/1, 10 mL), sodium hydroxide (1 M, 2.5 mL) was added and the reaction vessel was sealed with a stopper and stirred for 16 h. After quenching with HCl (1 M) to pH 1 and extracting three times with DCM (15 mL), the combined organic layers was washed with water (15 mL) and brine (15 mL) before being dried over Na_2SO_4 and reduced under vacuum. The crude material was then purified by column chromatography (Petrolium ether/EtOAc) to yield the enone as a yellow oil, which are solidify on cooling.



6. General Procedure for the Synthesis of Products 3 : unless otherwise specified, all reactions were carried out in oven dried reaction tube with magnetic stirring. Isatylidine malonitrile **1** (0.5 mmol), α, β-unsaturated ketone **2** (0.75 mmol), catalyst L-proline (20 mol%), and ethanol solvent added in reaction tube. The reaction mixture was stirred for 8-9 hours at room temperature. Reaction was monitored by analytical thin layer chromatography (TLC). TLC was performed on 0.25 mm precoated silica gel plates (60 f 254). After elution, the plate was visualized under uv 254 nm and stained with basic $KMnO_4$ solution. After the completion of the reaction brine solution was added to the reaction mixture and extracted with DCM (5 ml × 3). The organic layer was collected and dried over anhydrous Na_2SO_4. After evaporation under vacuum the crude product obtained was purified by silica gel column chromatography to afford product **3** (Petroleum ether/Ethyl acetate 75:25).



7. General procedure for the preparation of *tert*-Butyl 2,3-dioxoindoline-1-carboxylate[7]: Isatin (2.95 g, 20 mmol) was added to a solution of DMAP (122 mg, 1 mmol) in anhydrous THF (100mL) at room temperature. Di-*tert* butyl dicarbonate (4.80 g, 22 mmol) was slowly added and the solution stirred for 6 h. Upon completion, brine (50 mL) was added and the organic layer extracted with EtOAc (2 x 50 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated *in vacuo* and recrystallized from CH_2Cl_2:hexane (1:1) to give *tert*-butyl 2,3-dioxoindoline-1-carboxylate as a yellow solid (3.54 g, 14.2 mmol, 72%).



References

1.G. M. Sheldrick, Crystal structure refinement with SHELXL, *Acta Cryst*. 2015**. C71**, 3–8.

2.G. M. Sheldrick, SHELXT - Integrated space-group and crystal-structure determination, *Acta Cryst*. 2015. **A71**, 3–8.

3. P. Zhao, Y. Li, G. Gao, S. Wang, Y. Yan, X. Zhan, Z. Liu, Z. Mao, S. Chen and L. Wang, *Eur. J. Med. Chem.*, 2014, **86**, 165 —174; (b) Y.O. Teng, H.Y. Zhao, J. Wang, H. Liu, M.L. Gao, Y. Zhou, K.L. Han, Z.C. Fan, Y.M. Zhang, H. Sun, P. Yu, *Eur. J. Med. Chem.,* 2016, **112**, 145–156.

4.G. M. Coppola, *J. Heterocycl. Chem.*1987, **24**, 1249-1251.

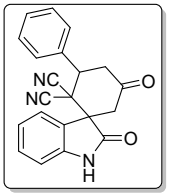
5. C. B. Nichinde, B. R. Patil, S. S. Chaudhari, B. P. Mali, R. G. Gonnade and A. K. Kinage., *RSC Advances,* 2023*,* **13,** 13206 - 13212.

6. W. J. Kerr, R. J. Mudd, L. C. Paterson and J. A. Brown, *Chem. – Eur. J.*, 2014, **20**, 14604 — 14607

7. M. D. Greenhalgh , S. M. Smith , D. M. Walden , J. E. Taylor , Z. Brice , E. R. T. Robinson , C. Fallan , D. B. Cordes , A. M. Z. Slawin , H. C. Richardson , M. A. Grove , P. H. Y. Cheong and A. D. Smith , *Angew. Chem. Int. Ed.*, 2018, **57** , 3200 —3206

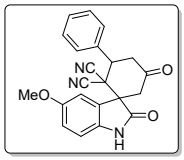
Characterization data of products

2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Aa):



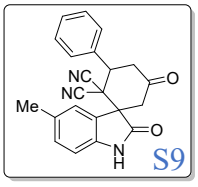
The titled compound was prepared by following the procedure A, obtained as a Solid, 156 mg, 92% yield, **mp** = 272−274°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR:** (400 MHz, *Acetone*) δ 10.23 (s, 1H), 7.63 (d, *J*=7.63 Hz, 1H), 7.46 (d, *J*=7.32 Hz, 2H), 7.28 - 7.40 (m, 4H), 7.09 (t, *J*=7.63 Hz, 1H), 7.00 (d, *J*=7.93 Hz, 1H), 4.69 (dd, *J*=13.73, 4.27 Hz, 1H), 3.27 - 3.41 (m, 2H), 2.65 (dd, *J*=15.56, 2.14 Hz, 1H), 2.51 (d, *J*=15.56 Hz, 1H); **^{13}C NMR** (101 MHz, *Acetone*) δ 201.5, 175.8, 142.9, 136.5, 131.9, 130.3, 130.1, 129.9, 127.3, 125.5, 124.1, 113.4, 113.3, 111.9, 54.2, 48.0, 43.9, 43.5, 42.5; **HRMS (ESI)** calcd for: $C_{21}H_{15}O_2N_3Na$, [M + Na]$^+$ 364.1062, found: 364.1056.

5'-methoxy-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ab):



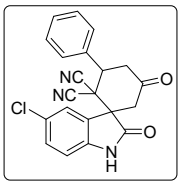
The titled compound was prepared by following the procedure A, obtained as a Solid, 156 mg, 84% yield, **mp** = 174−176°C; column chromatography on silica gel (petroleum ether/EtOAc 76:24); **^{1}H NMR:** (500 MHz, *CHLOROFORM-d*) δ 8.50 (s, 1H), 7.32 - 7.49 (m, 5H), 7.22 - 7.32 (m, 1H), 6.86 (s, 2H), 4.74 (dd, *J*=13.45, 3.69 Hz, 1H), 3.74 (s, 3H), 3.06 - 3.25 (m, 2H), 2.77 - 2.88 (m, 1H), 2.60 (d, J=14.35, 1H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 201.3, 174.7, 156.7, 134.4, 133.4, 129.7, 129.2, 128.9, 126.7, 116.0, 112.0, 111.8, 111.6, 111.5, 55.9, 53.8, 47.0, 43.2, 43.1, 42.0; **HRMS (ESI)** calcd for: $C_{22}H_{18}O_3N_3$, [M + H]$^+$ 372.1348, found: 372.1343.

5'-methyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ac):



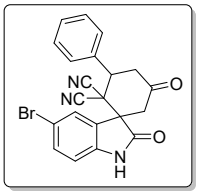
The titled compound was prepared by following the procedure A, obtained as a Solid, 151 mg, 85% yield, **mp** = 250−252°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 8.13 (s, 1H), 7.40 - 7.58 (m, 6H), 7.17 - 7.28 (m, 1H), 6.92 (d, *J*=8.00 Hz, 1H), 4.82 (dd, *J*=13.51, 4.13 Hz, 1H), 3.18 - 3.33 (m, 2H), 2.92 (dd, *J*=15.70, 2.19 Hz, 1H), 2.65 (d, *J*=15.70, 1H), 2.40 (s, 3H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 201.5, 174.9, 137.9, 134.8, 134.3, 132.0, 130.0, 129.5, 129.2, 126.0, 125.6, 112.4, 112.0, 111.1, 53.8, 47.4, 43.6, 43.4, 42.3, 21.6; **HRMS (ESI)** calcd for: $C_{22}H_{17}O_2N_3Na$, [M + Na]$^+$ 378.1218, found: 378.1213.

5'-chloro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ad):



The titled compound was prepared by following the procedure A, obtained as a Solid, 161 mg, 86% yield, **mp** = 260−262°C; column chromatography on silica gel (petroleum ether/EtOAc 76:24); **^{1}H NMR** (500 MHz, *Acetone d^6*) δ 10.41 (s, 1H), 7.74 (s, 1H), 7.52 - 7.57 (m, 2H), 7.40 - 7.49 (m, 4H), 7.11 (d, *J*=8.26 Hz, 1H), 4.81 (dd, *J*=14.4, 3.4 Hz, 1H), 3.33 - 3.46 (m, 2H), 2.82 (d, *J*=15.45 Hz, 1H), 2.64 (d, *J*= 15.45 Hz, 1H). **^{13}C NMR** (125 MHz, *Acetone*) δ 199.7, 173.8, 140.0, 134.4, 130.5, 129.0, 128.5, 128.5, 127.8, 127.2, 124.4, 111.9, 111.6, 111.4, 52.9, 46.3, 42.4, 42.1, 41.2; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3ClNa$, [M + Na]$^+$ 398.0672, found: 398.0667.

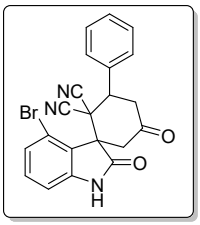
5'-bromo-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ae):



The titled compound was prepared by following the procedure A, obtained as a Solid, 188 mg, 90% yield, **mp** = 254−256°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *Acetone*) δ 10.47 (s, 1H), 7.91 (d, *J*=2.00 Hz, 1H), 7.54 - 7.65 (m, 3H), 7.40 - 7.54 (m, 3H), 7.12 (d, *J*=8.38 Hz, 1H), 4.79 (dd, *J*=13.76, 4.13 Hz, 1H), 3.42 - 3.56 (m, 2H), 2.79 (dd, *J*=15.63, 4.13 Hz, 1H), 2.72 (d, *J*=15.63 Hz, 1H); **^{13}C NMR** (101 MHz, *Acetone*) δ 201.3, 175.5, 142.5, 136.5, 135.0, 130.6, 130.2, 130.1, 129.6, 128.9, 116.0, 114.0,

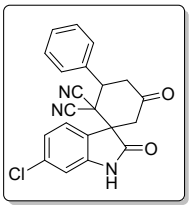
113.4, 113.3, 54.5, 48.0, 44.1, 43.4, 42.6; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3BrNa$, $[M + Na]^+$ 442.0167, found: 442.0162.

4'-bromo-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Af):



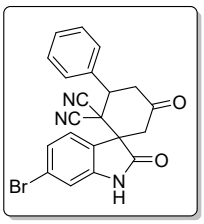
The titled compound was prepared by following the procedure A, obtained as a Solid, 192.74 mg, 92% yield, **mp** = 250−252°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *Acetone*) δ 10.56 (br. s., 1H), 7.56 (d, *J*=8.25 Hz, 1H), 7.39 - 7.50 (m, 2H), 7.31 - 7.38 (m, 3H), 7.28 (dd, *J*=8.19, 1.81 Hz, 1H), 7.19 (d, *J*=1.75 Hz, 1H), 4.64 (dd, *J*=13.63, 4.13 Hz, 1H), 3.27 - 3.40 (m, 2H), 2.64 - 2.68 (m, 1H), 2.56 (dd, *J*=16.01, 2.00 Hz, 1H); **^{13}C NMR** (125 MHz, *Acetone*) δ 201.5, 175.7, 144.6, 136.4, 130.6, 130.2, 130.1, 127.4, 127.0, 126.6, 125.30, 115.2, 113.4, 113.3, 54.3, 48.0, 44.0, 43.3, 42.60; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3BrNa$, $[M + Na]^+$ 442.0167, found: 442.0162

6'-chloro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ag)



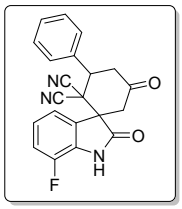
The titled compound was prepared by following the procedure A, obtained as a Solid, 189 mg, 89% yield, **mp** = 258−260°C, column chromatography on silica gel (petroleum ether/EtOAc 76:24); **^{1}H NMR** (400 MHz, *Acetone- d_6*) δ 10.65 (br. s., 4 H), 7.75 (d, *J*=8.25 Hz, 7 H), 7.54 - 7.64 (m, 15 H), 7.42 - 7.54 (m, 22 H), 7.26 (dd, *J*=8.25, 2.00 Hz, 7 H), 7.17 (d, *J*=1.88 Hz, 7 H), 4.77 (dd, *J*=13.76, 4.13 Hz, 7 H), 3.36 - 3.54 (m, 15 H), 2.63 - 2.85 (m, 16 H) **^{13}C NMR** (101 MHz, *Acetone- d_6*) δ 201.1, 136.9, 136.1, 130.2, 129.8, 129.7, 126.8, 125.8, 123.7, 113.1, 113.0, 112.0, 53.9, 47.7, 43.7, 43.1, 42.2 **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3ClNa$, $[M + Na]^+$ 398.0672, found: 398.0667.

6'-bromo-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ah)



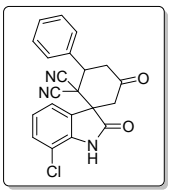
The titled compound was prepared by following the procedure A, obtained as a Solid, 180 mg, 86% yield, **mp** = 252−254°C; column chromatography on silica gel (petroleum ether/EtOAc 76:25); **^{1}H NMR** (400 MHz, *Acetone*) d 10.65 (br. s., 4 H), 7.69 (d, *J*=8.25 Hz, 8 H), 7.55 - 7.63 (m, 15 H), 7.44 - 7.55 (m, 22 H), 7.42 (dd, *J*=8.19, 1.81 Hz, 8 H), 7.32 (d, *J*=1.75 Hz, 7 H), 4.77 (dd, *J*=13.70, 4.06 Hz, 7 H), 3.37 - 3.54 (m, 15 H), 2.79 (ddd, *J*=15.70, 4.13, 1.94 Hz, 7 H), 2.69 (dd, *J*=15.95, 1.94 Hz, 7 H); **^{13}C NMR** (101 MHz, *Acetone*) d 201.3, 175.6, 144.5, 136.2, 130.4, 130.0, 129.9, 127.2, 126.9, 125.1, 115.1, 113.1, 54.1, 47.8, 43.9, 43.2, 42.4

7'-fluoro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ai):



The titled compound was prepared by following the procedure A, obtained as a Solid, 158 mg, 88% yield, **mp** = 268−270°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *Acetone*) δ 10.90 (s, 1H), 7.56 - 7.70 (m, 3H), 7.39 - 7.54 (m, 3H), 7.20 - 7.36 (m, 2H), 4.79 (dd, *J*=13.70, 4.06 Hz, 1H), 3.38 - 3.55 (m, 2H), 2.77 - 2.82 (m, 1H), 2.74 (dd, *J*=15.95, 1.94 Hz, 1H); **^{13}C NMR** (125 MHz, *Acetone*) δ 201.1, 175.4, 136.3, 130.4, 130.0, 129.9, 125.2, 125.1, 121.6, 121.6, 119.0, 118.8, 113.3, 113.1, 54.7, 48.0, 43.4, 43.3, 42.5; **^{19}F NMR** (376 MHz, *Acetone*) d -132.64 **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3FNa$, $[M + Na]^+$ 382.0968, found: 382.0962.

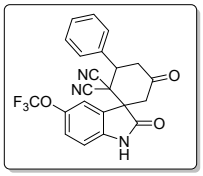
7'-chloro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Aj):



The titled compound was prepared by following the procedure A, obtained as a Solid, 163 mg, 87% yield, **mp** = 276−278°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *Acetone*) δ 10.62 (s, 1H), 7.68 (d, *J*=7.63 Hz, 1H), 7.52

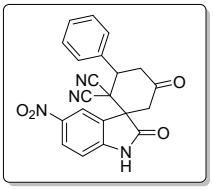
(d, *J*=6.25 Hz, 2H), 7.43 (dd, *J*=7.63, 2.25 Hz, 4H), 7.19 (t, *J*=8.00 Hz, 1H), 4.76 (dd, *J*=13.70, 3.94 Hz, 1H), 3.31 - 3.44 (m, 2H), 2.77 (dd, *J*=16.26, 2.63 Hz, 1H), 2.65 (d, *J*=16.26 Hz, 1H); **^{13}C NMR** (101 MHz, *Acetone*) δ 199.1, 173.4, 138.7, 134.1, 130.0, 128.5, 128.0, 128.0, 126.7, 123.4, 122.1, 114.9, 111.1, 111.0, 53.2, 45.9, 42.0 (s), 41.7, 40.7; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3ClNa$, $[M + Na]^+$ 398.0672, found: 398.0667.

2',5-dioxo-3-phenyl-5'-(trifluoromethoxy)spiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ak):



The titled compound was prepared by following the procedure A, obtained as a Solid, 198 mg, 93% yield, **mp** = 230−232°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); **^{1}H NMR** (500 MHz, *Acetone*) δ 10.60 (s, 1H), 7.70 - 7.81 (m, 1H), 7.55 - 7.64 (m, 2H), 7.39 - 7.55 (m, 4H), 7.25 (d, *J*=8.63 Hz, 1H), 4.79 (dd, *J*=13.76, 4.00 Hz, 1H), 3.41 - 3.59 (m, 2H), 2.79 - 2.85 (m, 1H), 2.74 (dd, *J*=16.01, 1.75 Hz, 1H); **^{13}C NMR** (125 MHz, *Acetone*) δ 200.9, 175.5, 145.1, 142.0, 136.0, 130.3, 129.8, 129.7, 128.5, 125.1, 122.6, 119.5, 113.0, 112.9, 112.8, 54.3, 47.7, 43.71, 42.9, 42.3; **^{19}F NMR** (376 MHz, *Acetone*) δ -59.15 **HRMS (ESI)** calcd for: $C_{22}H_{15}O_3N_3F_3$, $[M + H]^+$ 426.1066, found: 426.10

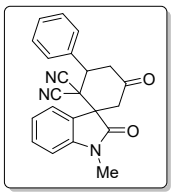
5'-nitro-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Al):



The titled compound was prepared by following the procedure A, obtained as a Solid, 181 mg, 94% yield, **mp** = 258−260°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); two diastereomers are not separable by column chromatography given NMR for mixture of two diastereomer. **^{1}H NMR** (500 MHz, *Acetone*) δ 10.96 (br. s., 1 H), 8.53 (d, *J*=2.25 Hz, 1H), 8.28 (ddd, *J*=8.66, 6.53, 2.19 Hz, 2H), 8.17 (d, *J*=2.13 Hz, 1H), 7.42 - 7.52 (m, 3H), 7.29 - 7.42 (m, 5H), 7.25 (dd, *J*=8.38, 7.25 Hz, 2H), 4.63 (dd, *J*=13.76, 4.00 Hz, 1H), 4.35 (dd, *J*=14.07, 3.94 Hz, 1H), 3.47 - 3.63 (m, 2H), 3.34 - 3.45 (m, 2H), 2.95 (dd, *J*=3.94, 1.94 Hz, 1H), 2.91 (dd, *J*=3.88, 1.88 Hz, 1H), 2.67 - 2.74 (m, 1H), 2.59 - 2.67 (m, 1H); **^{13}C NMR** (125 MHz, *Acetone*) δ 202.8, 201.00, 176.0, 174.0, 149.5, 149.1, 144.5, 144.4, 136.0, 135.5, 130.5, 130.5, 130.2, 130.00, 129.9, 129.6, 128.8, 128.7, 127.9, 127.4, 122.8, 121.6, 113.1, 112.9, 112.9,

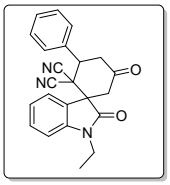
112.2, 112.1, 111.6, 55.0, 54.3, 47.6, 47.20, 46.7, 44.00, 43.0, 42.8, 42.8, 42.4 **HRMS (ESI)** calcd for: $C_{21}H_{15}O_4N_4$, [M + H]$^+$ 387.1093, found: 387.1088.

1'-methyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ba):



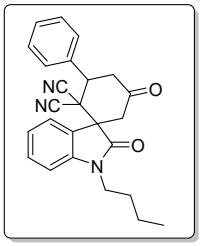
The titled compound was prepared by following the procedure A, obtained as a Solid, 163 mg, 92% yield, **mp** = 230−232°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 7.77 (d, *J*=7.13 Hz, 1H), 7.37 - 7.55 (m, 6H), 7.19 - 7.28 (m, 1H), 6.99 (d, *J*=7.88 Hz, 1H), 4.86 (dd, *J*=13.57, 4.19 Hz, 1H), 3.31 (s, 3H), 3.19 - 3.28 (m, 2H), 2.92 (dd, *J*=15.70, 2.19 Hz, 1H), 2.57 (dd, *J*=15.88, 1.88 Hz, 1H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 201.0, 173.1, 143.2, 134.6, 131.3, 129.7, 129.2, 128.9, 125.2, 124.4, 124.2, 112.3, 111.7, 109.5, 53.2, 47.2, 43.1, 43.1, 42.0, 26.9; **HRMS (ESI)** calcd for: $C_{22}H_{17}O_2N_3Na$, [M + Na]$^+$ 378.1218, found: 378.1213.

1'-ethyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bb):



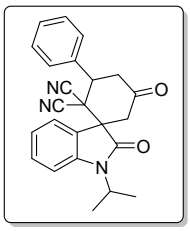
The titled compound was prepared by following the procedure A, obtained as a Solid, 170 mg, 92% yield, **mp** = 210−212°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 7.77 (d, *J*=7.50 Hz, 1H), 7.34 - 7.58 (m, 6H), 7.16 - 7.30 (m, 1H), 7.00 (d, *J*=7.88 Hz, 1H), 4.87 (dd, *J*=13.51, 4.13 Hz, 1H), 3.98 (dq, *J*=14.27, 7.25 Hz, 1H), 3.58 - 3.79 (m, 1H), 3.16 - 3.34 (m, 2H), 2.86 - 2.98 (m, 1H), 2.56 (dd, *J*=15.88, 1.75 Hz, 1H), 1.34 (t, *J*=7.25 Hz, 3H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 201.0, 172.7, 142.3, 134.6, 131.2, 129.6, 129.1, 128.9, 125.4, 124.6, 123.9, 112.2, 111.6, 109.6, 52.8, 47.1, 43.1, 43.0, 41.9, 35.5, 12.3**;** **HRMS (ESI)** calcd for: $C_{23}H_{19}O_2N_3Na$, [M + Na]$^+$ 392.1375, found: 392.1369.

1'-butyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bc):



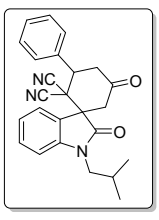
The titled compound was prepared by following the procedure A, obtained as a Solid, 173 mg, 87% yield, **mp** = 170−172°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 7.77 (d, *J*=7.63 Hz, 1H), 7.34 - 7.57 (m, 6H), 7.11 - 7.31 (m, 1H), 6.99 (d, *J*=8.00 Hz, 1H), 4.87 (dd, *J*=13.51, 4.13 Hz, 1H), 3.90 (dt, *J*=14.26, 7.38 Hz, 1H), 3.64 (dt, *J*=14.20, 7.29 Hz, 1H), 3.17 - 3.31 (m, 2H), 2.92 (dd, *J*=15.70, 2.31 Hz, 1H), 2.54 (dd, *J*=15.88, 1.75 Hz, 1H), 1.73 (quin, *J*=7.50 Hz, 2H), 1.37 - 1.52 (m, 2H), 0.99 (t, *J*=7.38 Hz, 3H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 201.0, 173.0, 142.8, 134.6, 131.2, 129.6, 129.1, 128.9, 125.3, 124.5, 123.9, 112.3, 111.7, 109.7, 52.9, 47.1, 43.2, 43.1, 41.9, 40.5, 29.2, 20.2, 13.6; **HRMS (ESI)** calcd for: $C_{25}H_{24}O_2N_3$ [M + H]$^+$ 398.1869, found: 398.1863.

1'-isopropyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bd):



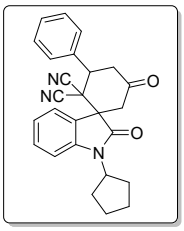
The titled compound was prepared by following the procedure A, obtained as a Solid, 170 mg, 89% yield, **mp** = 198−200°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 7.76 (d, *J*=7.38 Hz, 1H), 7.36 - 7.56 (m, 6H), 7.09 - 7.24 (m, 2H), 4.85 (dd, *J*=13.57, 4.06 Hz, 1H), 4.63 (spt, *J*=6.98 Hz, 1H), 3.08 - 3.35 (m, 2H), 2.80 - 2.98 (m, 1H), 2.56 (dd, *J*=15.82, 1.69 Hz, 1H), 1.54 (d, *J*=7.00 Hz, 6H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 201.2, 172.8, 142.0, 134.6, 131.0, 129.6, 129.0, 128.9, 125.4, 124.6, 123.5, 112.2, 111.7, 110.9, 52.6, 47.3, 45.1, 43.0, 42.9, 41.9, 19.2, 19.0; **HRMS (ESI)** calcd for: $C_{24}H_{21}O_2N_3Na$, [M + Na]$^+$ 406.1531, found: 406.1526.

1'-isobutyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Be):



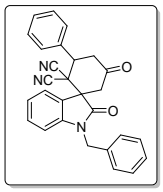
The titled compound was prepared by following the procedure A, obtained as a Solid, 171 mg, 86% yield, **mp** = 180−182°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 7.78 (d, *J*=7.63 Hz, 1H), 7.35 - 7.57 (m, 6H), 7.21 (t, *J*=7.69 Hz, 1H), 6.99 (d, *J*=7.88 Hz, 1H), 4.88 (dd, *J*=13.45, 3.94 Hz, 1H), 3.72 (dd, *J*=13.95, 7.32 Hz, 1H), 3.45 (dd, *J*=13.88, 7.25 Hz, 1H), 3.18 - 3.33 (m, 2H), 2.91 (dd, *J*=15.76, 3.88 Hz, 1H), 2.52 (d, *J*=15.76Hz, 1H), 2.17 - 2.22 (m, 1H), 1.03 (dd, *J*=15.13, 6.63 Hz, 6H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 201.2, 173.6, 143.4, 134.8, 131.4, 129.9, 129.4, 129.1, 125.5, 124.6, 124.1, 112.5, 112.1, 110.2, 53.1, 48.6, 47.2, 43.8, 43.4, 42.1, 27.6, 20.7, 20.6; **HRMS (ESI)** calcd for: $C_{25}H_{23}O_2N_3Na$ [M + Na]$^+$ 420.1688, found: 420.1682.

1'-cyclopentyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bf):



The titled compound was prepared by following the procedure A, obtained as a Solid, 174 mg, 85% yield, **mp** = 182−184°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 7.76 (d, *J*=7.38 Hz, 1H), 7.36 - 7.55 (m, 6H), 7.17 - 7.27 (m, 1H), 7.07 (d, *J*=8.00 Hz, 1H), 4.85 (dd, *J*=13.63, 4.13 Hz, 1H), 4.75 (quin, *J*=8.63 Hz, 1H), 3.13 - 3.31 (m, 2H), 2.84 - 2.96 (m, 1H), 2.57 (dd, *J*=15.88, 1.75 Hz, 1H), 2.08 - 2.20 (m, 2H), 1.91 - 2.06 (m, 4H), 1.67 - 1.81 (m, 2H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 201.2, 173.0, 142.0, 134.6, 130.9, 129.6, 129.1, 128.9, 125.4, 124.6, 123.6, 112.2, 111.6, 110.9, 53.4, 52.9, 47.3, 43.0, 42.9, 41.9, 27.9, 27.6, 25.2; **HRMS (ESI)** calcd for: $C_{26}H_{24}O_2N_3$ [M + H]$^+$ 410.1869, found: 410.1863.

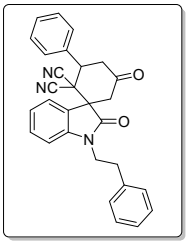
1'-benzyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bg):



The titled compound was prepared by following the procedure A, obtained as a Solid, 181 mg, 84% yield, **mp** = 162−164°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 7.79 (d, *J*=7.63 Hz, 1H), 7.50 - 7.59 (m, 2 H), 7.39 - 7.50 (m, 3H), 7.27 - 7.39 (m, 6H), 7.11 - 7.24 (m, 1H), 6.83 (d, *J*=7.88 Hz,

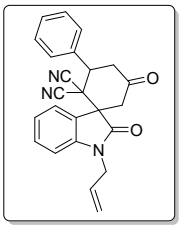
1H), 5.10 (d, *J*=15.63 Hz, 1H), 4.83 - 4.97 (m, 2H), 3.26 (m, 2H), 2.95 (dt, *J*=15.67, 1.92 Hz, 5 H), 2.60 (d, *J*=15.67 Hz, 1H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 200.6, 173.0, 142.0, 134.2, 133.9, 130.8, 129.4, 128.8, 128.7, 128.6, 127.8, 126.9, 124.9, 124.0, 123.9, 111.9, 111.6, 110.3, 52.8, 46.7, 44.3, 43.3, 42.9, 41.7; **HRMS (ESI)** calcd for: $C_{28}H_{22}O_2N_3$, $[M + H]^+$ 432.1712, found: 432.1707.

2',5-dioxo-1'-phenethyl-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bh):



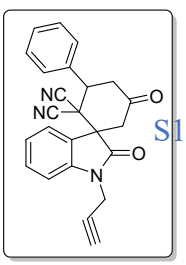
The titled compound was prepared by following the procedure A, obtained as a Solid, 200 mg, 90% yield, **mp** = 178−180°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 7.76 (d, *J*=7.13 Hz, 1H), 7.38 - 7.56 (m, 6H), 7.16 - 7.36 (m, 6H), 6.91 (d, *J*=7.88 Hz, 1H), 4.84 (dd, *J*=13.57, 4.19 Hz, 1H), 4.08 (ddd, *J*=14.20, 8.50, 6.07 Hz, 1H), 3.87 - 4.00 (m, 1H), 3.12 - 3.31 (m, 2H), 2.97 - 3.12 (m, 2H), 2.89 (ddd, *J*=15.73, 4.16, 1.88 Hz, 1H), 2.42 (dd, *J*=15.88, 1.88 Hz, 1H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 200.8, 173.0, 142.4, 137.4, 134.5, 131.1, 129.6, 129.1, 128.9, 128.8, 128.7, 127.0, 125.2, 124.5, 124.0, 112.2, 111.7, 109.7, 52.8, 47.0, 43.1, 43.0 , 42.1, 41.9, 33.4; **HRMS (ESI)** calcd for: $C_{29}H_{23}O_2N_3Na$, $[M + Na]^+$ 468.1688, found: 468.1682.

1'-allyl-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bi):



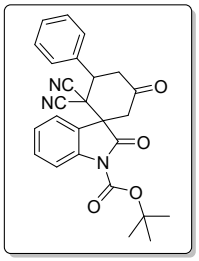
The titled compound was prepared by following the procedure A, obtained as a Solid, 171 mg, 90% yield, **mp** = 188−190°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 7.73 - 7.84 (m, 1H), 7.38 - 7.57 (m, 6H), 7.17 - 7.29 (m, 1H), 6.98 (d, *J*=7.88 Hz, 1H), 5.75 - 5.96 (m, 1H), 5.25 - 5.42 (m, 2H), 4.86 (dd, *J*=13.51, 4.13 Hz, 1H), 4.58 (ddt, *J*=16.26, 5.03, 1.67, 1.67 Hz, 1H), 4.25 (ddt, *J*=16.26, 5.69, 1.41, 1.41 Hz, 1H), 3.17 - 3.34 (m, 2H), 2.92 (ddd, *J*=15.76, 4.19, 1.94 Hz, 1H), 2.57 (dd, *J*=15.88, 1.88 Hz, 1H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 200.9, 172.9, 142.5, 134.5, 131.2, 130.1, 129.7, 129.2, 128.9, 125.2, 124.4, 124.1, 118.8, 112.2, 111.8, 110.5, 53.0, 47.1, 43.3, 43.2, 43.1, 42.0; **HRMS (ESI)** calcd for: $C_{24}H_{20}O_2N_3$, $[M + H]^+$ 382.1556, found: 382.1551.

2',5-dioxo-3-phenyl-1'-(prop-2-yn-1-yl)spiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bj):



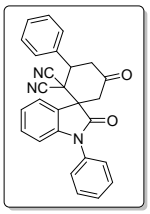
The titled compound was prepared by following the procedure A, obtained as a Solid, 155 mg, 82% yield, **mp** = 212−214°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 7.79 (d, *J*=7.63 Hz, 1H), 7.41 - 7.55 (m, 5H), 7.19 - 7.30 (m, 3H), 4.81 (dd, *J*=13.57, 3.94 Hz, 1H), 4.58 (s, 2H), 3.18 - 3.36 (m, 2H), 2.85 - 3.01 (m, 1H), 2.60 (d, *J*=14.35 Hz, 1H), 2.32 (s, 1H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 200.4, 172.0, 141.0, 134.0, 131.0, 129.4, 128.9, 128.6, 124.7, 124.2, 124.1, 111.8, 111.0, 110.3 , 75.0, 73.3, 52.7, 46.8, 42.9, 42.7, 41.6, 29.6; **HRMS (ESI)** calcd for: $C_{24}H_{17}O_2N_3Na$, $[M + Na]^+$ 402.1218, found: 402.1213.

tert-butyl 2,2-dicyano-2',5-dioxo-3-phenylspiro[cyclohexane-1,3'-indoline]-1'-carboxylate (3Bl):



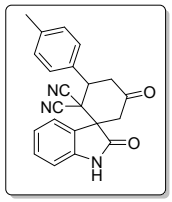
The titled compound was prepared by following the procedure A, obtained as a Solid, 182.01 mg, 79% yield, **mp** = 260-262°C; column chromatography on silica gel (petroleum ether/EtOAc 85:15); **^{1}H NMR** (400 MHz, *Acetone-d_6*) δ 8.00 (d, *J*=8.25 Hz, 4 H), 7.80 - 7.94 (m, 4 H), 7.54 - 7.67 (m, 13 H), 7.33 - 7.54 (m, 17 H), 4.59 (dd, *J*=13.63, 4.13 Hz, 4 H), 3.41 - 3.60 (m, 9 H), 2.82 - 2.90 (m, 9 H), 1.64 (s, 39 H) **^{13}C NMR** (101 MHz, *Acetone-d_6*) δ 201.2, 173.2, 149.0, 141.0, 136.0, 132.2, 130.5, 130.1, 129.9, 126.3, 125.5, 125.4, 116.5, 113.1, 112.8, 86.1, 55.0, 48.7, 44.6, 43.3, 42.3, 28.2 **HRMS (ESI)** calcd for: $C_{26}H_{23}N_3O_4Na$ [M + Na]$^+$ 464.1586, found: 464.1580.

2',5-dioxo-1',3-diphenylspiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Bl):



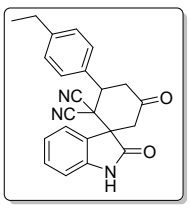
The titled compound was prepared by following the procedure A, obtained as a Solid, 173 mg, 83% yield, **mp** = 204−206°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 7.78 - 7.87 (m, 1H), 7.54 - 7.60 (m, 2H), 7.48 - 7.54 (m, 3H), 7.37 - 7.48 (m, 6H), 7.21 - 7.31 (m, 1H), 6.88 (d, *J*=8.00 Hz, 1 H), 4.83 (dd, *J*=13.51, 4.13 Hz, 1H), 3.22 - 3.37 (m, 2H), 2.92 (dd, *J*=15.70, 2.19 Hz, 1H), 2.77 (dd, *J*=16.01, 1.88 Hz, 1H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 200.7, 172.7, 143.6, 134.5, 132.9, 131.3, 129.9, 129.7, 129.2, 129.1, 128.9, 126.7, 124.8, 124.6, 124.5, 112.1, 111.8, 110.7, 53.3, 47.5, 43.1, 42.9, 41.9; **HRMS (ESI)** calcd for: $C_{27}H_{20}O_2N_3$ [M + H]$^+$ 418.1556, found: 418.1550.

2',5-dioxo-3-(p-tolyl)spiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ca):



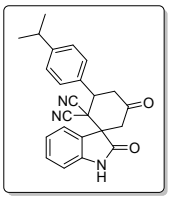
The titled compound was prepared by following the procedure A, obtained as a Solid, 156 mg, 88% yield, **mp** = 248−250°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 8.81 (br. s., 1H), 7.73 (d, *J*=7.75 Hz, 1H), 7.34 - 7.47 (m, 3H), 7.13 - 7.31 (m, 3H), 7.02 (d, *J*=7.75 Hz, 1H), 4.77 (dd, *J*=13.45, 3.56 Hz, 1H), 3.12 - 3.34 (m, 2H), 2.78 - 2.95 (m, 1H), 2.64 (d, *J*=13.65 Hz, 1H), 2.37 (s, 3H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 201.5, 174.8, 139.7, 131.5, 131.2, 129.8, 128.7, 125.7, 124.6, 123.9, 112.2, 111.8, 111.2, 53.5, 53.4, 47.2, 43.2, 42.8, 42.0, 21.1; **HRMS (ESI)** calcd for: $C_{22}H_{17}O_2N_3Na$, [M + Na]$^+$ 378.1218, found: 378.1213.

3-(4-ethylphenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cb):



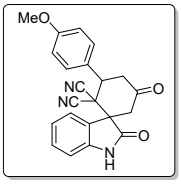
The titled compound was prepared by following the procedure A, obtained as a Solid, 158 mg, 86% yield, **mp** = 224−226°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 8.53 (s, 1H), 7.75 (d, *J*=7.63 Hz, 1H), 7.34 - 7.52 (m, 3H), 7.17 - 7.34 (m, 3H), 7.03 (d, *J*=7.75 Hz, 1H), 4.76 (dd, *J*=13.51, 4.00 Hz, 1H), 3.13 - 3.34 (m, 2H), 2.82 - 2.99 (m, 1H), 2.61 - 2.73 (m, 3H), 1.26 (t, *J*=7.63 Hz, 3H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 201.6, 174.8, 145.9, 140.3, 131.6, 131.2, 128.8, 128.6, 125.7, 124.7, 124.0, 112.2, 111.7, 111.2, 53.5, 47.2, 43.2, 42.9, 42.1, 28.5, 15.2; **HRMS (ESI)** calcd for: $C_{23}H_{19}O_2N_3Na$, $[M + Na]^+$ 392.1375, found: 392.1369.

3-(4-isopropylphenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cc):



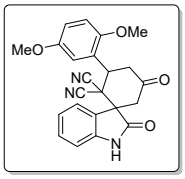
The titled compound was prepared by following the procedure A, obtained as a Solid, 165 mg, 86% yield, **mp** = 214−216°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 8.58 (s, 1H), 7.75 (d, *J*=7.50 Hz, 1H), 7.36 - 7.50 (m, 3H), 7.25 - 7.36 (m, 2H), 7.15 - 7.25 (m, 1H), 7.03 (d, *J*=7.75 Hz, 1H), 4.76 (dd, *J*=13.51, 4.13 Hz, 1H), 3.15 - 3.31 (m, 2H), 2.91 - 3.00 (m, 1H), 2.88 (dd, *J*=4.13, 1.88 Hz, 1H), 2.54 - 2.74 (m, 1H), 1.26 (d, *J*=7.00 Hz, 6H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 201.6, 174.8, 150.5, 140.3, 131.7, 131.2, 128.8, 127.2, 125.7, 124.7, 124.0, 112.2, 111.7, 111.2, 53.6, 47.2, 43.2, 42.9, 42.1, 33.8, 23.8, 23.7; **HRMS (ESI)** calcd for: $C_{24}H_{21}O_2N_3Na$, $[M + Na]^+$ 406.1531, found: 406.1526.

3-(4-methoxyphenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cd):



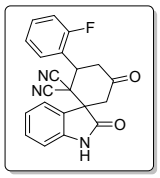
The titled compound was prepared by following the procedure A, obtained as a Solid, 158 mg, 85% yield, **mp** = 230−232°C; column chromatography on silica gel (petroleum ether/EtOAc 72:28); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 9.53 (s, 1H), 7.64 (d, *J*=7.38 Hz, 1H), 7.22 - 7.44 (m, 3H), 7.03 - 7.20 (m, 1H), 6.98 (d, *J*=7.63 Hz, 1H), 6.77 - 6.92 (m, 2H), 4.70 (d, J=15.67 Hz 1H), 3.74 (s, 3H), 2.99 - 3.24 (m, 2H), 2.76 (d, *J*=13.63 Hz, 1H), 2.79 (d, *J*= 1H), 2.52 (d, *J*=13.63 Hz 1H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 201.18, 160.3, 130.9, 129.9, 126.5, 124.4, 123.5, 114.3, 112.2, 111.8, 111.0, 55.1, 53.2, 47.3, 43.0, 42.3, 42.0; **HRMS (ESI)** calcd for: $C_{22}H_{17}O_3N_3Na$, $[M + Na]^+$ 394.1168, found: 394.1162.

3-(2,5-dimethoxyphenyl)-2',5-dioxospiro[cyclohexane-1,3'-in doline]-2,2-dicarbonitrile (3Ce):



The titled compound was prepared by following the procedure A, obtained as a Solid, 166 mg, 83% yield**, mp** = 240−242°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); two diastereomers are not separable by column chromatography given NMR for mixture of two diastereomer. **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 10.96 (s, 2H), 7.62 (d, *J*=7.25 Hz, 2H), 7.17 - 7.40 (m, 3H), 6.92 - 7.17 (m, 5H), 6.68 - 6.89 (m, 4H), 5.55 (dd, *J*=13.88, 4.00 Hz, 1H), 5.01 (dd, *J*=14.51, 3.50 Hz, 1H), 3.80 - 3.52 (m, 12H), 3.26 - 3.40 (m, 2H), 3.11 - 3.20 (m, 2H), 2.71 (d, *J*=15.13 Hz, 1H), 2.61 (dd, *J*=15.70, 2.56 Hz, 1H), 2.36 - 2.51 (m, 2H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 202.5, 201.3, 174.7, 173.0, 153.6, 153.5, 151.4, 150.9, 142.5, 142.0, 131.0, 130.8, 126.0, 125.7, 125.4, 124.4, 124.2, 123.6, 123.0, 122.3, 114.9, 114.6, 114.4, 114.1, 112.8, 112.2, 112.0, 111.9, 111.6, 111.4, 111.0, 55.9, 55.6, 54.0, 53.0, 46.3, 45.5, 43.2, 43.1, 42.2, 41.9, 36.1, 33.7; **HRMS (ESI)** calcd for: $C_{23}H_{20}O_4N_3$, $[M + H]^+$ 402.1454, found: 402.1448.

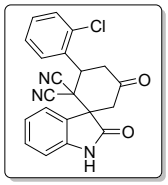
3-(2-fluorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cf):



The titled compound was prepared by following the procedure A, obtained as a Solid, 154 mg, 86% yield, **mp** = 262−264°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *Acetone*) δ 10.31 (s, 1H), 7.68 - 7.90 (m, 2H), 7.47 - 7.57 (m, 1H), 7.41 - 7.47 (m, 1H), 7.33 - 7.41 (m, 1H), 7.18 - 7.29 (m, 2H), 7.13 (d, *J*=7.75 Hz, 1H), 5.44 (dd, *J*=13.88, 4.13 Hz, 1H), 3.36 - 3.56 (m, 2H), 2.76 (dd, *J*=15.63, 2.13 Hz, 1H), 2.66 (dd, *J*=16.07, 1.81 Hz, 1H); **^{13}C NMR** (101 MHz, *Acetone*) δ 201.0, 175.6, 162.9, 160.4, 142.9, 132.3, 132.2, 132.0, 130.1, 130.0, 127.2, 126, 125.9, 125.5, 124.1, 124.0, 123.8, 116.9, 116.7, 113.4, 113.0,

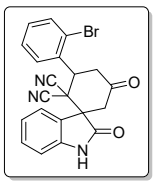
111.9, 54.0, 47.3, 43.6, 42.1, 35.3, 35.2; **^{19}F NMR** (376 MHz, *Acetone-d_6*) δ -115.64; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3FNa$, [M + Na]$^+$ 382.0968, found: 382.0962

3-(2-chlorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cg):



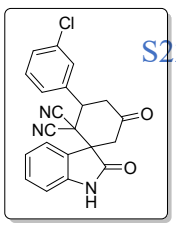
The titled compound was prepared by following the procedure A, obtained as a Solid, 165 mg, 88% yield, **mp** = 272−274°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 10.98 (br. s., 1H), 7.81 (d, *J*=7.88 Hz, 1 H), 7.71 (d, *J*=7.63 Hz, 1H), 7.42 - 7.54 (m, 2H), 7.34 - 7.42 (m, 2H), 7.16 (t, *J*=7.63 Hz, 1 H), 7.06 (d, *J*=7.75 Hz, 1H), 5.84 (dd, *J*=13.70, 3.94 Hz, 1H), 3.15 - 3.36 (m, 2H), 2.76 (dd, *J*=15.13, 2.13 Hz, 1H), 2.62 (d, *J*=15.13 Hz, 1H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 199.8, 173.9, 141.3, 134.4, 132.2, 130.3, 129.8, 129.7, 128.0, 127.0, 125.0, 123.6, 122.4, 111.7, 110.6, 52.3, 45.2, 42.4, 41.6, 36.3; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3ClNa$, [M + Na]$^+$ 398.0672, found: 398.0667.

3-(2-bromophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ch):



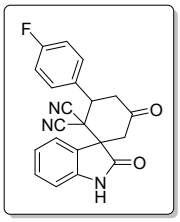
The titled compound was prepared by following the procedure A, obtained as a Solid, 186 mg, 89% yield, **mp** = 270−272°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); **^{1}H NMR** (500 MHz, *Acetone*) δ 10.38 (br. s., 1H), 7.92 (d, *J*=7.63 Hz, 1H), 7.77 (t, *J*=8.09 Hz, 2H), 7.59 (t, *J*=7.63 Hz, 1H), 7.45 (t, *J*=7.78 Hz, 1H), 7.40 (t, *J*=7.78 Hz, 1H), 7.23 (t, *J*=7.78 Hz, 1H), 7.13 (d, *J*=7.93 Hz, 1H), 5.79 (dd, *J*=13.58, 3.81 Hz, 1H), 3.35 - 3.51 (m, 2H), 2.72 - 2.81 (m, 1H), 2.69 (d, *J*=14.13 Hz, 1H); **^{13}C NMR (**125 MHz, *Acetone*) δ 200.8, 175.3, 142.9, 135.9, 134.6, 131.9, 131.8, 130.2, 129.3, 127.0, 126.6, 125.4, 123.9, 113.4, 112.5, 111.7, 53.8, 46.8, 43.5, 42.9, 40.6; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3BrNa$, [M + Na]$^+$ 442.0167, found: 442.0162.

3-(3-chlorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ci):



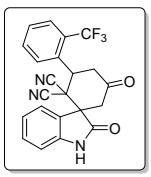
The titled compound was prepared by following the procedure A, obtained as a Solid, 165 mg, 88% yield**,** **mp** = 270−272°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); **^{1}H NMR** (400 MHz, *Acetone*) δ 10.58 (br. s., 1H), 7.62 (d, *J*=7.63 Hz, 1H), 7.51 (s, 1H), 7.37 - 7.46 (m, 3H), 7.32 (td, *J*=7.75, 1.00 Hz, 1H), 7.05 - 7.12 (m, 1H), 6.99 (d, *J*=7.88 Hz, 1H), 4.72 (dd, *J*=13.63, 4.13 Hz, 1H), 3.26 - 3.44 (m, 2H), 2.70 (dd, *J*=15.70, 2.19 Hz, 1H), 2.51 (dd, *J*=16.01, 2.00 Hz, 1H); **^{13}C NMR** (101 MHz, *Acetone*) δ 201.1, 175.7, 143.0, 138.8, 135.1, 132.0, 131.6, 130.4, 130.1, 128.8, 127.2, 125.5, 124.0, 113.3, 113.1, 111.2, 54.2, 47.7, 43.5, 42.2, 40.3; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_2N_3ClNa$, $[M + Na]^+$ 398.0672, found: 398.066

3-(4-fluorophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cj):



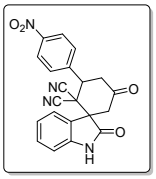
The titled compound was prepared by following the procedure A, obtained as a Solid, 162 mg, 90% yield, **mp**= 264−266°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 10.50 (br. s., 1H), 7.69 (d, *J*=7.63 Hz, 1 H), 7.49 (dd, *J*=7.88, 5.38 Hz, 2H), 7.28 - 7.43 (m, 1H), 7.07 - 7.25 (m, 3H), 7.03 (d, *J*=7.75 Hz, 1H), 4.88 (dd, *J*=13.51, 3.88 Hz, 1H), 3.20 (dd, *J*=15.38, 10.51 Hz, 2H), 2.78 - 2.96 (m, 1H), 2.60 (d, *J*=14.13 Hz, 1H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 200.4, 174.4, 164.0, 161.5, 141.0, 130.6, 130.3, 130.2, 125.2, 123.9, 123.0, 115.8, 115.6, 111.7, 111.3, 110.9, 52.8, 46.6, 42.7, 41.8, 41.6; **^{19}F NMR** (376 MHz, *CHLOROFORM-d*) δ -111.45; **HRMS (ESI)** calcd for: : $C_{21}H_{14}O_2N_3FNa$, $[M + Na]^+$ 382.0968, found: 382.0962.

2',5-dioxo-3-(2-(trifluoromethyl)phenyl)spiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Ck):



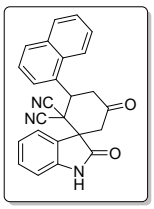
The titled compound was prepared by following the procedure A, obtained as a Solid, 190 mg, 93% yield, **mp** = 262−264°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); **^{1}H NMR** (400 MHz, *Acetone*) δ 10.22 (br. s., 1H), 8.16 (d, *J*=8.00 Hz, 1H), 7.72 - 7.80 (m, 2H), 7.68 (d, *J*=7.63 Hz, 1H), 7.53 - 7.60 (m, 1H), 7.33 (td, *J*=7.75, 1.00 Hz, 1 H), 7.07 - 7.15 (m, 1H), 7.00 (d, *J*=7.88 Hz, 1H), 5.41 (dd, *J*=13.38, 4.00 Hz, 1H), 3.28 - 3.39 (m, 2H), 2.66 (dd, *J*=4.00, 1.88 Hz, 1H), 2.59 (dd, *J*=16.32, 1.81 Hz, 1H); **^{13}C NMR** (101 MHz, *Acetone*) δ 200.4, 175.2, 142.8, 135.6, 134.0, 131.9, 130.5, 129.9, 127.6, 127.6, 126.9, 125.4, 123.8, 114.1, 112.4, 111.7, 53.8, 46.8, 44.1, 43.5, 37.1, 37.1; **^{19}F NMR** (376 MHz, *Acetone-d_6*) δ -57.57; **HRMS (ESI)** calcd for: $C_{22}H_{14}O_2N_3F_3Na$, [M + Na]$^+$ 432.0936, found: 432.0930.

3-(4-nitrophenyl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cl):



The titled compound was prepared by following the procedure A, obtained as a Solid, 181 mg, 94% yield, **mp** = 256−258°C; column chromatography on silica gel (petroleum ether/EtOAc 70:30); **^{1}H NMR** (500 MHz, *Acetone*) δ 10.29 (s, 1H), 8.24 (d, *J*=8.00 Hz, 2H), 7.78 (d, *J*=7.88 Hz, 2H), 7.63 (d, *J*=7.50 Hz, 1H), 7.33 (t, *J*=7.63 Hz, 1H), 7.10 (t, *J*=7.57 Hz, 1H), 7.01 (d, *J*=7.75 Hz, 1H), 4.76 - 5.02 (m, H), 3.23 - 3.53 (m, H), 2.53 - 2.57 (m, 1H), 2.01 (d, *J*=14.31 Hz, 1H); **^{13}C NMR** (125 MHz, *Acetone*) δ 200.8, 175.6, 149.6, 143.3, 142.9, 132.1, 131.7, 127.0, 125.5, 124.8, 124.2, 113.1, 112.9, 112.0, 54.2, 47.4, 43.6, 43.5, 42.0; **HRMS (ESI)** calcd for: $C_{21}H_{14}O_4N_4Na$, [M + Na]$^+$ 409.0913, found: 409.0908.

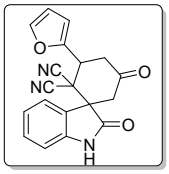
3-(naphthalen-1-yl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cm):



The titled compound was prepared by following the procedure A, obtained as a Solid, 176 mg, 90% yield, **mp** = 246−248°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 10.87 (s, 1H), 8.08 (d, *J*=8.00 Hz, 1H), 7.74 - 7.93 (m, 3H), 7.66 (d, *J*=7.63 Hz, 1H), 7.37 - 7.57 (m, 3H), 7.28 (t, *J*=7.88 Hz, 1H), 7.07 (t, *J*=7.63 Hz, 1H), 6.95 (d, *J*=7.75 Hz, 1H), 6.12 (dd *J*=13.83, 4.13 Hz, 1H), 3.31 (t, *J*=14.51 Hz, 1H), 3.19 (dd, *J*=14.51, 4.13 Hz, 1H), 2.77 (d, *J*=13.65 Hz, 1H), 2.60 (d, *J*=13.65 Hz, 1H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 200.8, 174.8, 141.3, 133.5, 131.2, 130.9, 130.5, 129.5,

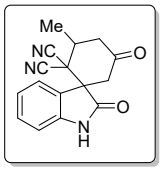
128.6, 126.3, 125.7, 125.3, 125.1, 124.8, 123.8, 122.8, 122.2, 112.1, 111.2, 110.8, 52.9, 46.1, 43.0, 42.8, 34.4; **HRMS (ESI)** calcd for: $C_{25}H_{17}O_2N_3Na$, $[M + Na]^+$ 414.1218, found: 414.1213.

3-(furan-2-yl)-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Cn):



The titled compound was prepared by following the procedure A, obtained as a Solid, 132 mg, 80% yield, **mp** = 250−252°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (500 MHz, *CHLOROFORM-d*) δ 9.70 (s, 1H), 7.63 - 7.81 (m, 1H), 7.47 - 7.57 (m, 1H), 7.41 (t, *J*=7.32 Hz, 1H), 7.15 - 7.24 (m, 1H), 7.04 - 7.11 (m, 1H), 6.49 - 6.60 (m, 1H), 6.38 - 6.48 (m, 1H), 4.98 (dd, *J*=13.26, 4.50 Hz, 1H), 3.11 - 3.30 (m, 2H), 2.92 (dd, *J*=15.70, 2.19 Hz, 1H), 2.60 (dd, *J*=15.35, 1.88 Hz, 1H); **^{13}C NMR** (125 MHz, *CHLOROFORM-d*) δ 200.4, 174.6, 148.7, 143.9, 141.3, 131.3, 125.7, 124.5, 123.8, 112.1, 111.8, 111.4, 110.9, 110.3, 53.0, 45.4, 43.2, 40.8, 38.2; **HRMS (ESI)** calcd for: $C_{19}H_{13}O_3N_3Na$, $[M + Na]^+$ 354.0855, found: 354.0849.

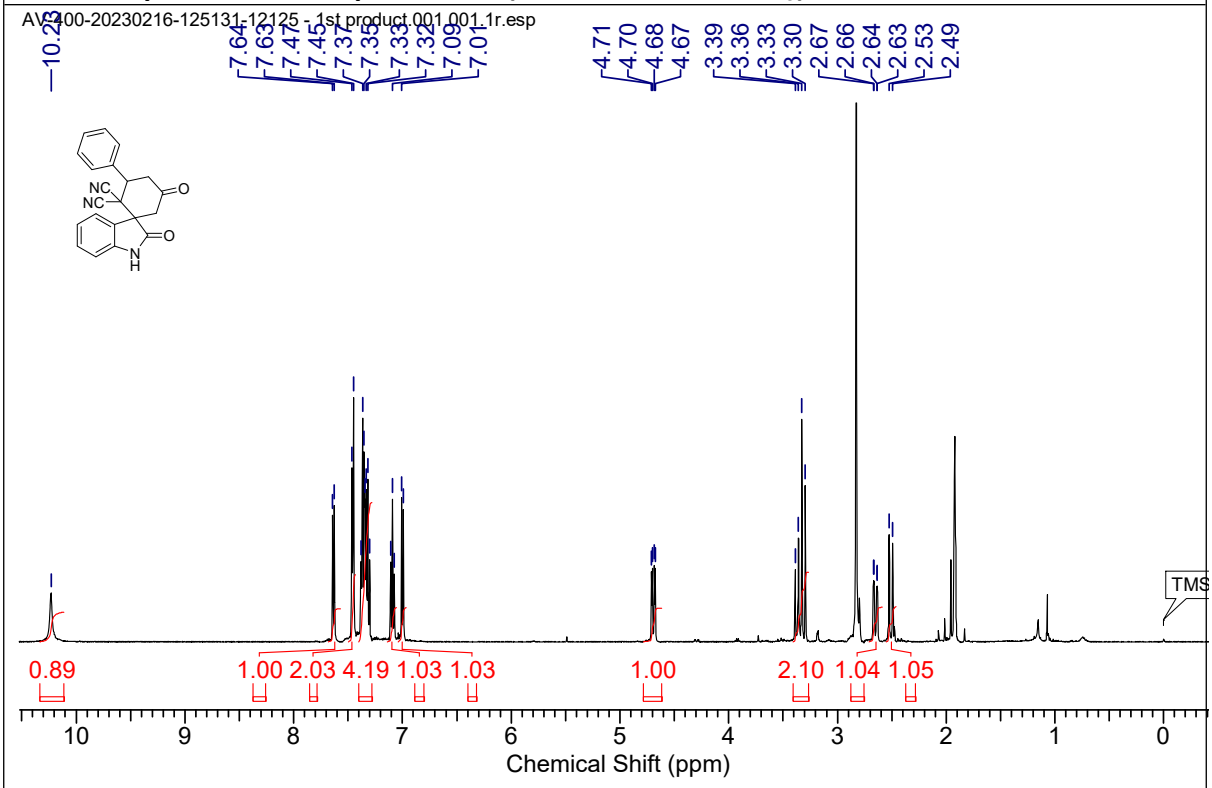
3-methyl-2',5-dioxospiro[cyclohexane-1,3'-indoline]-2,2-dicarbonitrile (3Co) :



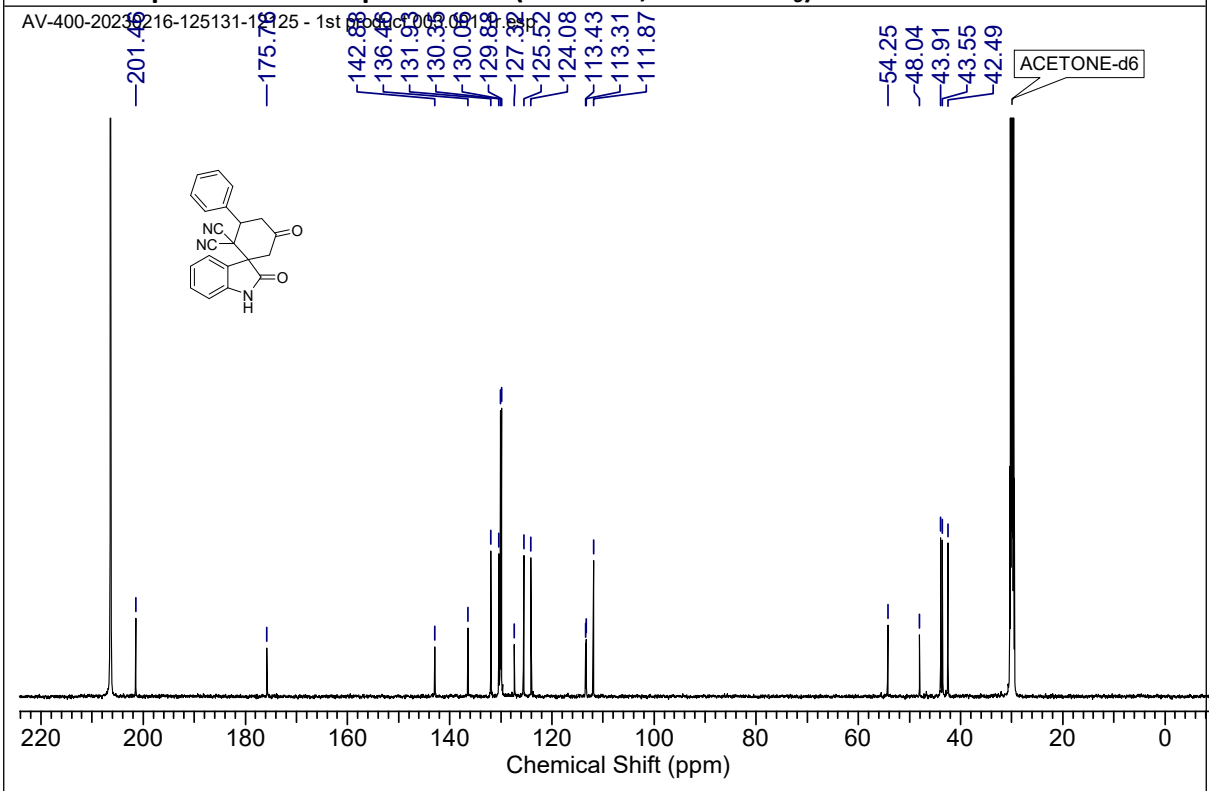
The titled compound was prepared by following the procedure A, obtained as a Solid, 108.92 mg, 78% yield, **mp** = 270−272°C; column chromatography on silica gel (petroleum ether/EtOAc 75:25); **^{1}H NMR** (400 MHz, *CHLOROFORM-d*) δ 9.74 (br. s., 7 H), 7.67 (d, *J*=7.63 Hz, 7 H), 7.37 (td, *J*=7.79, 1.06 Hz, 8 H), 7.26 (s, 3 H), 7.10 - 7.20 (m, 8 H), 6.99 (d, *J*=7.88 Hz, 8 H), 3.61 - 3.74 (m, 7 H), 2.99 (s, 4 H), 3.03 (s, 4 H), 2.71 (ddd, *J*=16.01, 4.44, 1.94 Hz, 8 H), 2.43 - 2.53 (m, 14 H), 1.41 (d, *J*=6.75 Hz, 23 H); **^{13}C NMR** (101 MHz, *CHLOROFORM-d*) δ 201.2, 174.5, 141.2, 131.0, 125.8, 124.2, 123.5, 112.3, 111.8, 111.2, 52.9, 46.2, 43.9, 43.0, 33.8, 18.2**;** **HRMS (ESI)** calcd for: $C_{16}H_{13}O_2N_3Na$, $[M + Na]^+$ 302.0905, found: 302.090.

NMR Spectra of Compounds

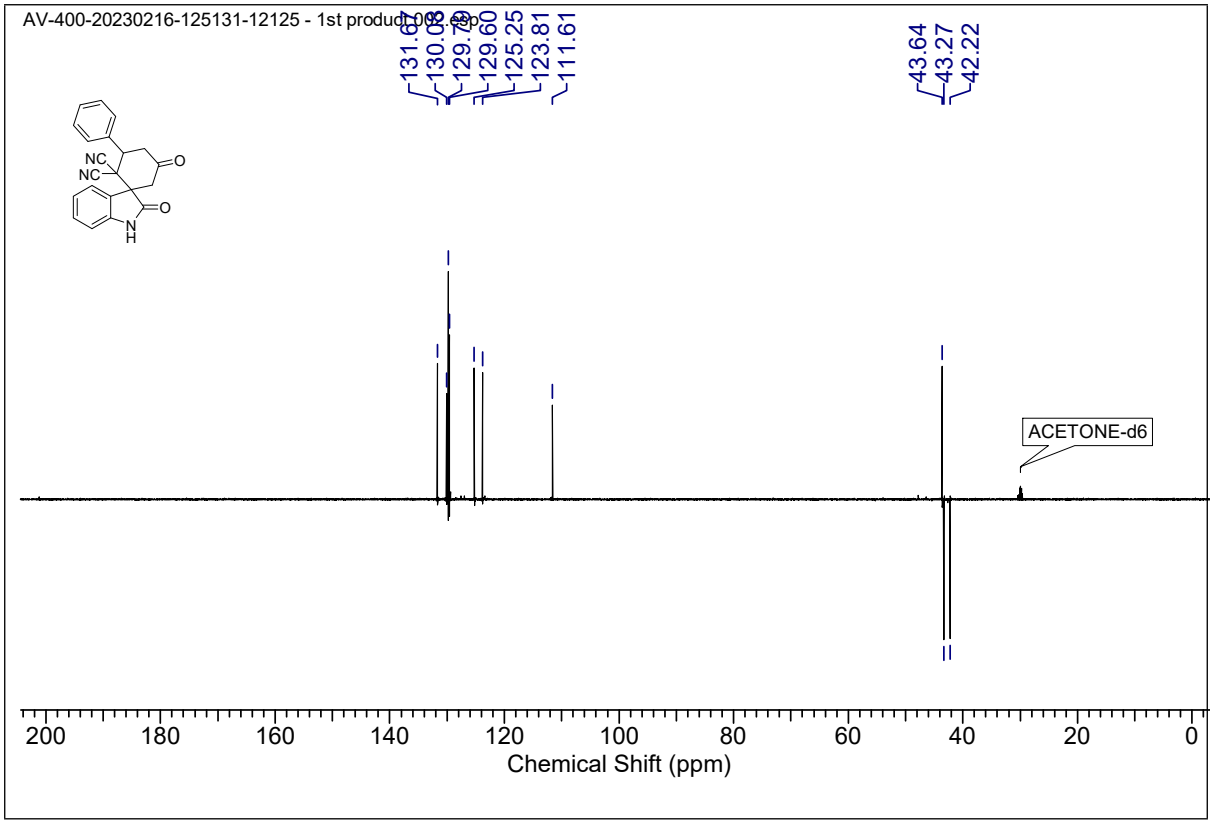
^{1}H NMR spectrum of compound 3Aa (400 MHz, Acetone-d_6)



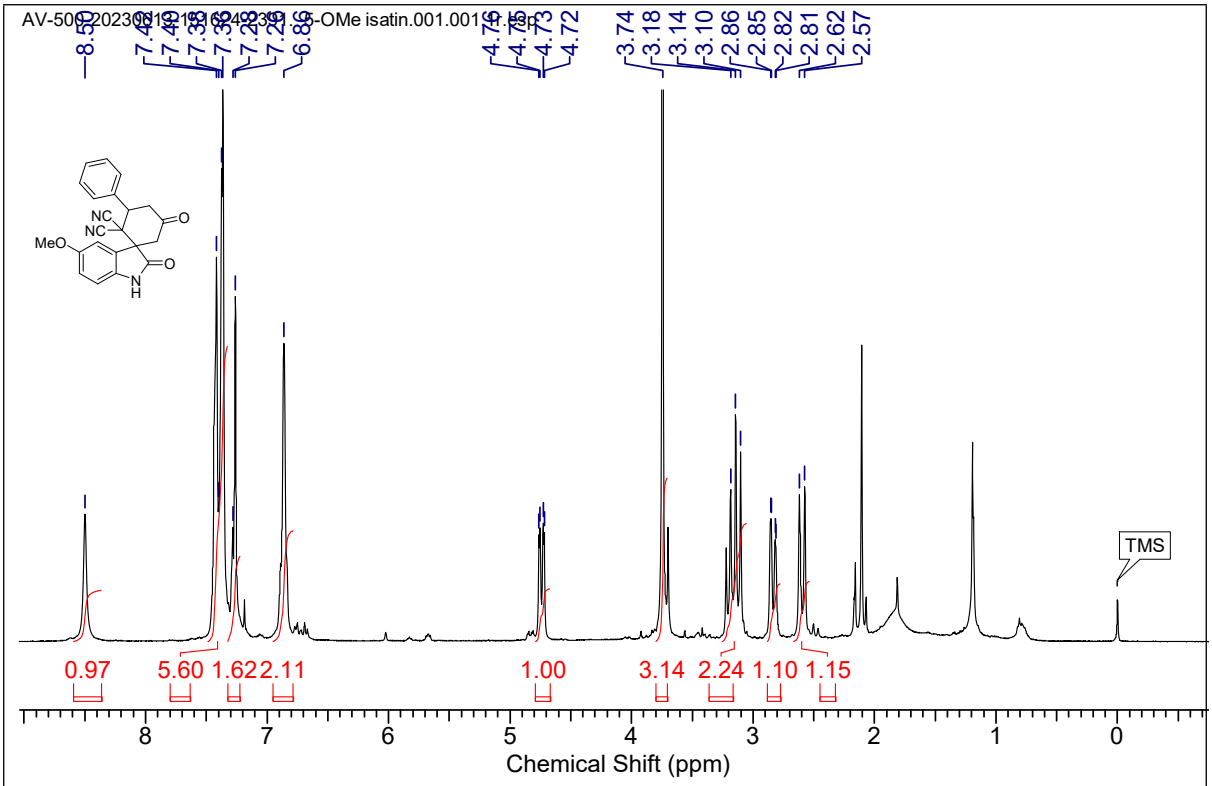
^{13}C NMR spectrum of compound 3Aa (101 MHz, Acetone-d_6)



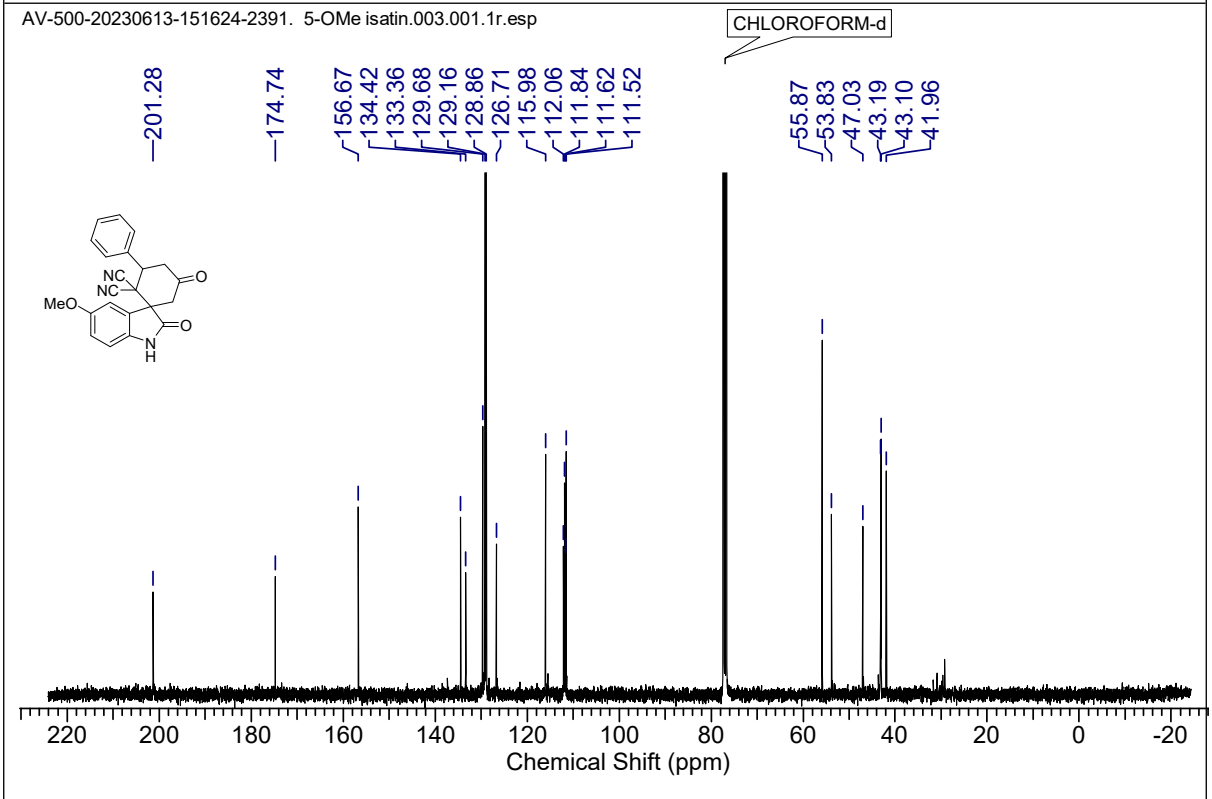
135 DEPT NMR spectrum of compound 3Aa



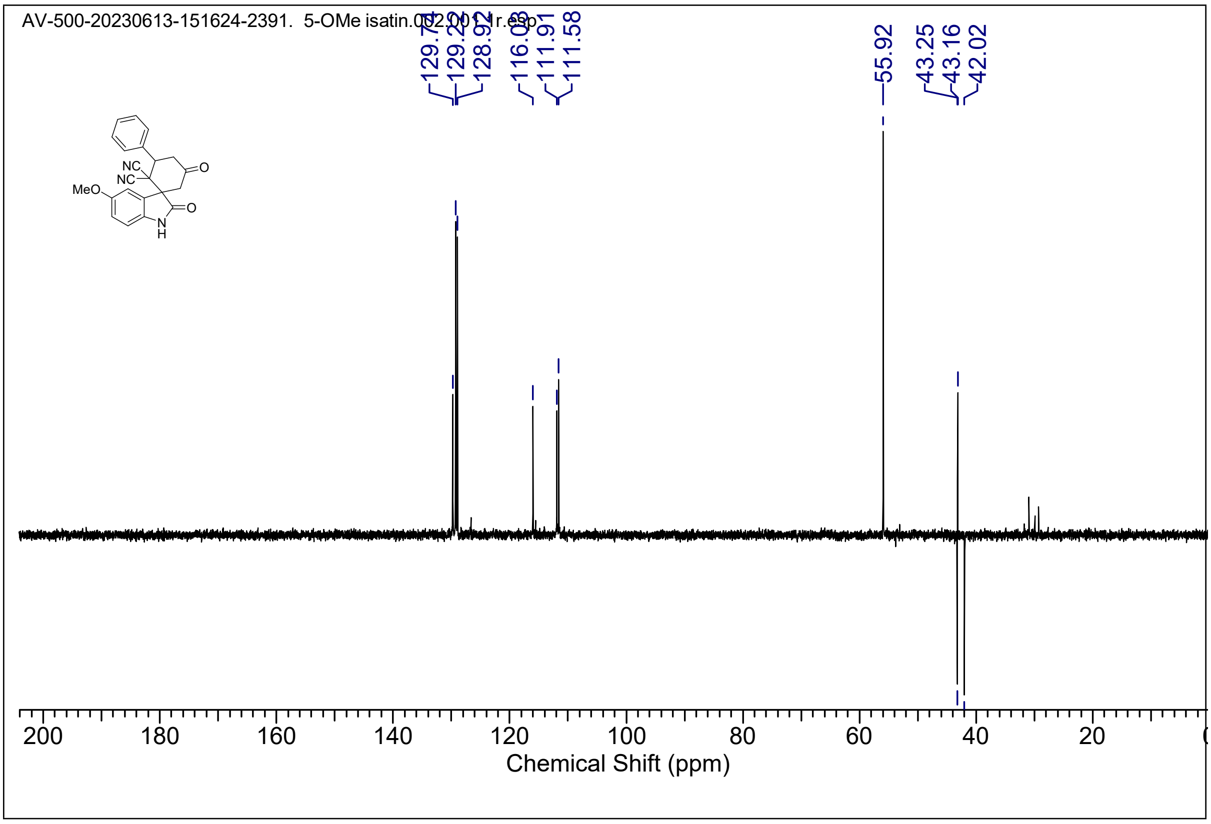
^{1}H NMR spectrum of compound 3Ab (500 MHz, $CDCl_3$)



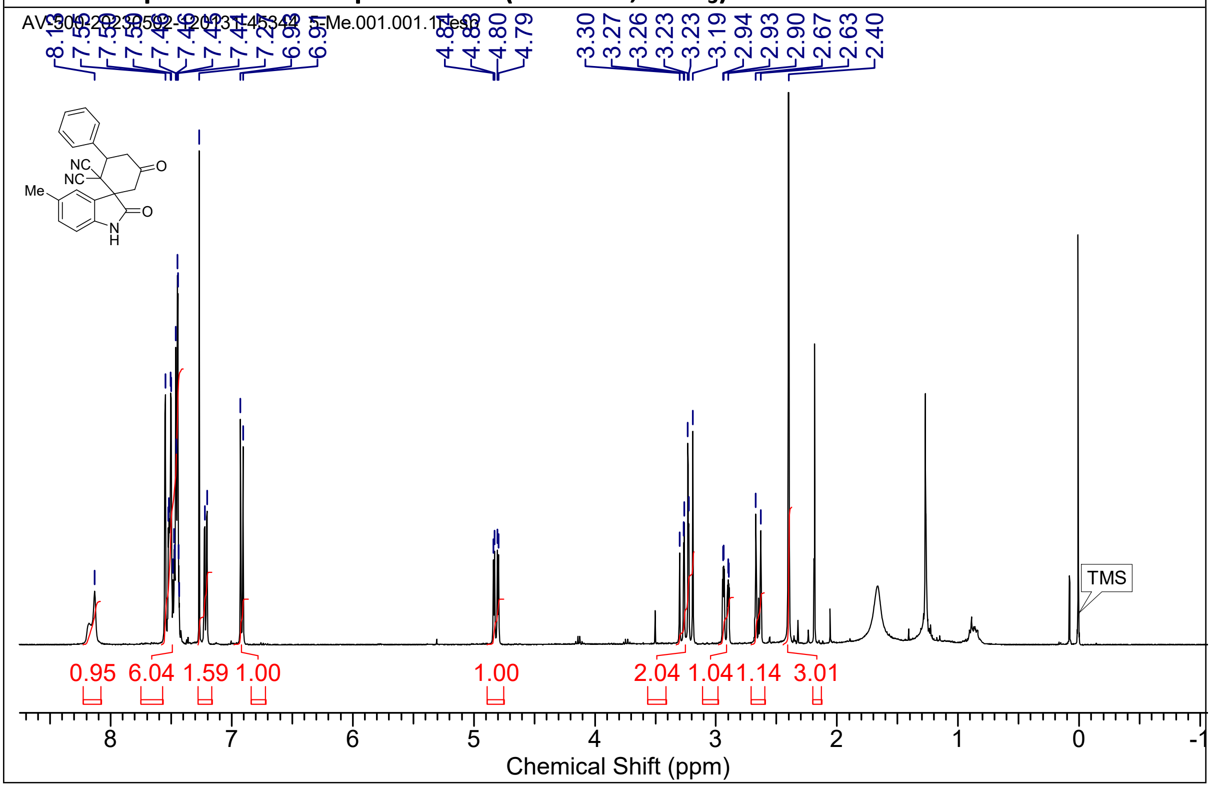
^{13}C NMR spectrum of compound 3Ab (125 MHz, $CDCl_3$)



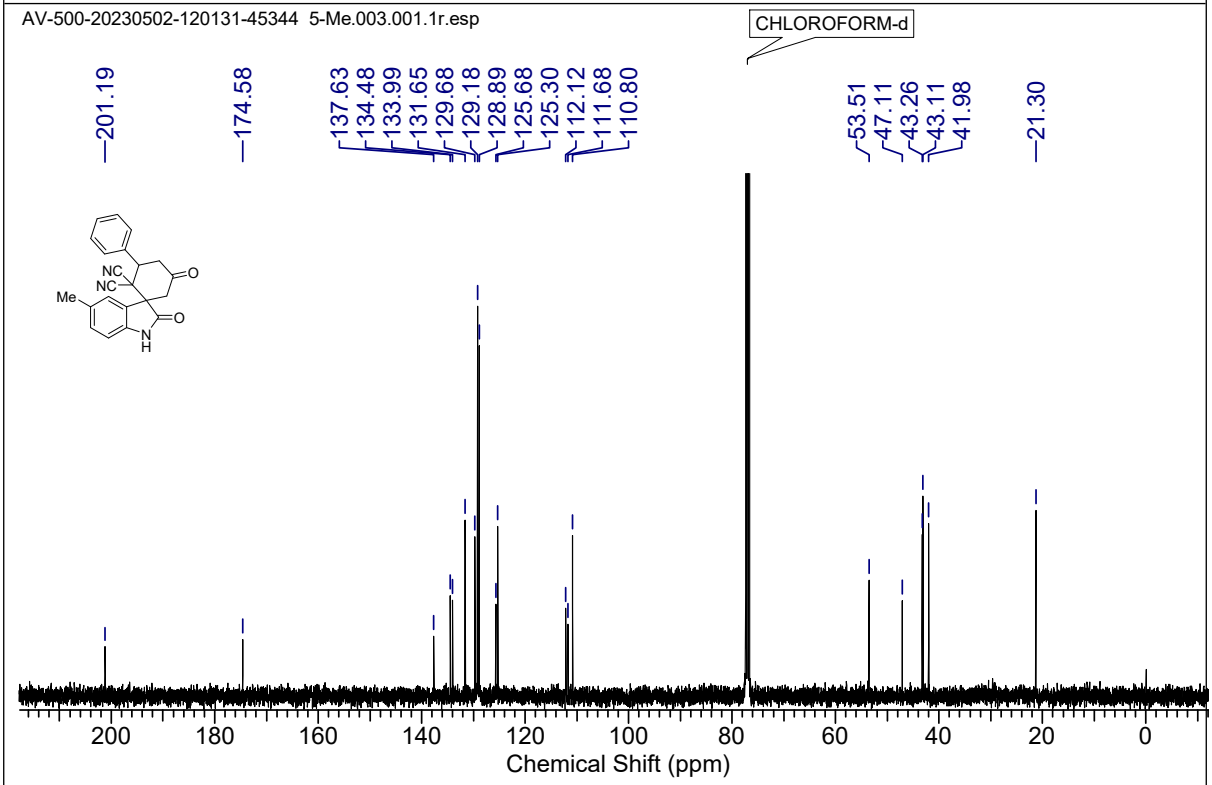
135 DEPT NMR spectrum of compound 3Ab



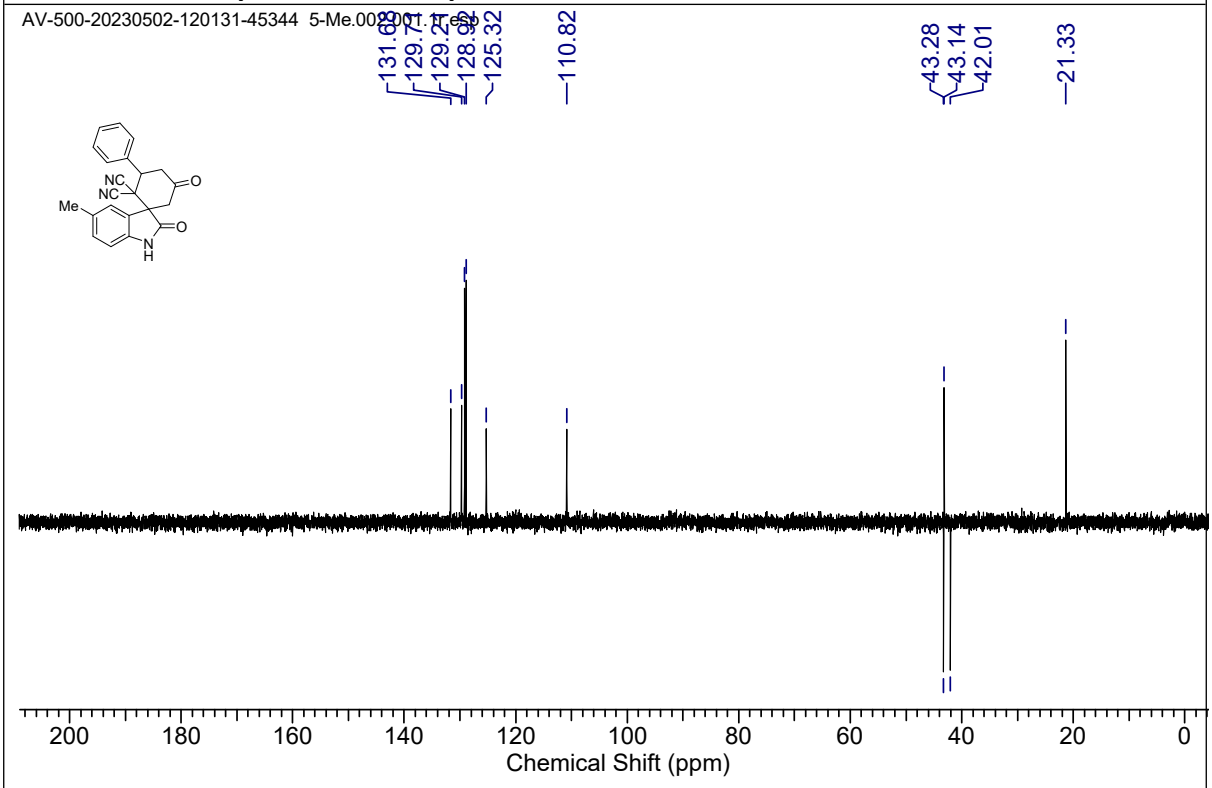
^{1}H NMR spectrum of compound 3Ac (500 MHz, $CDCl_3$)



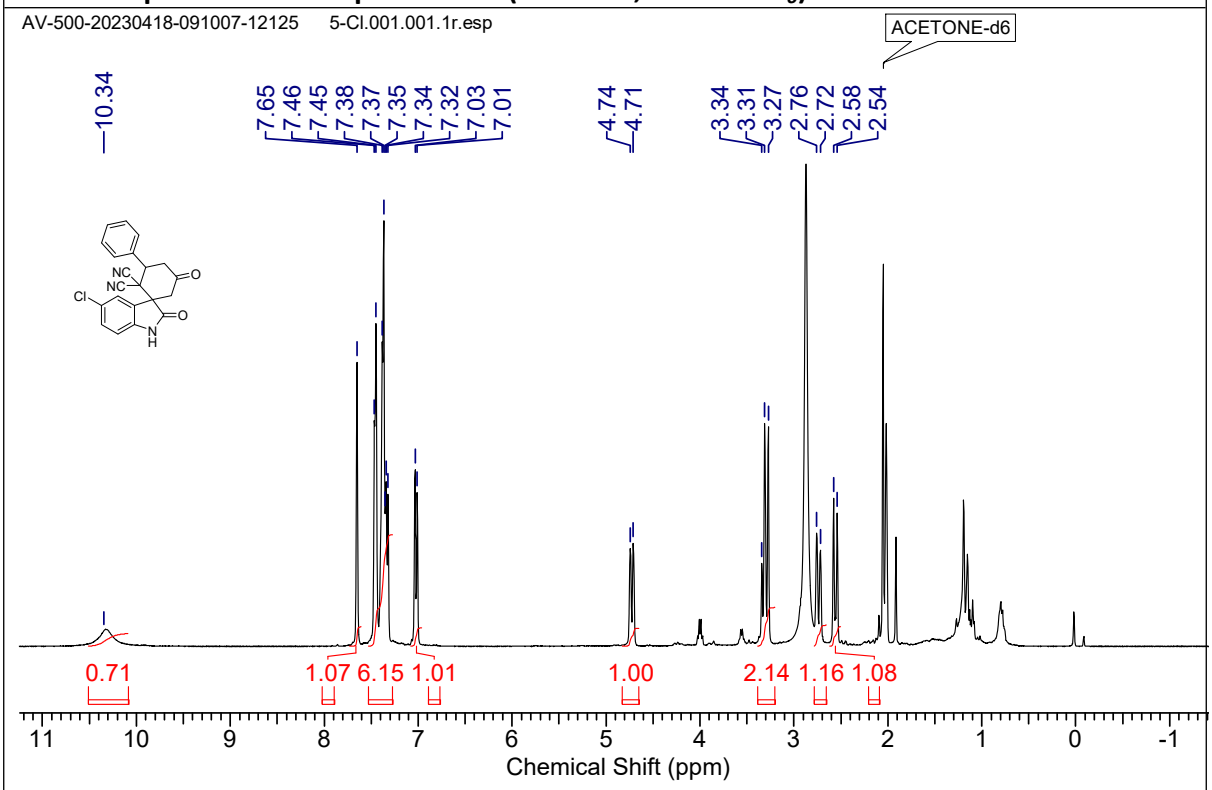
^{13}C NMR spectrum of compound 3Ac (125 MHz, $CDCl_3$)



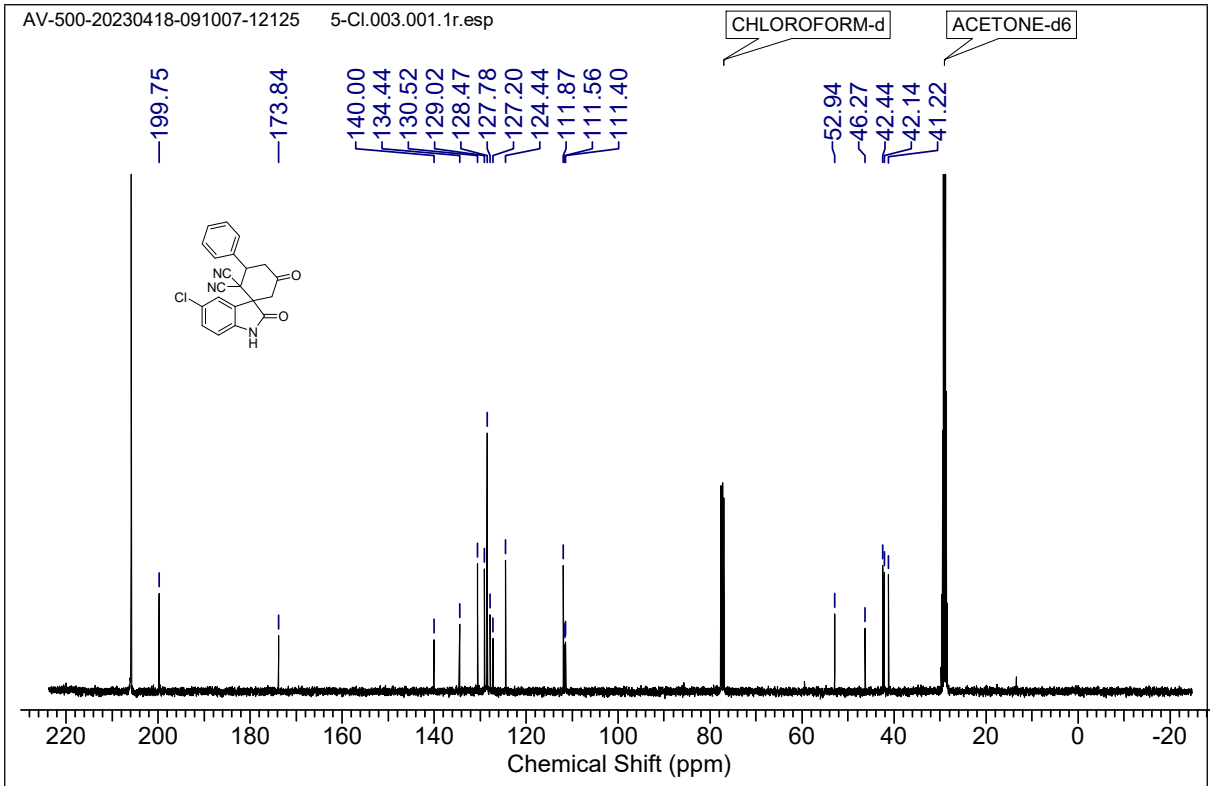
135 DEPT NMR spectrum of compound 3Ac



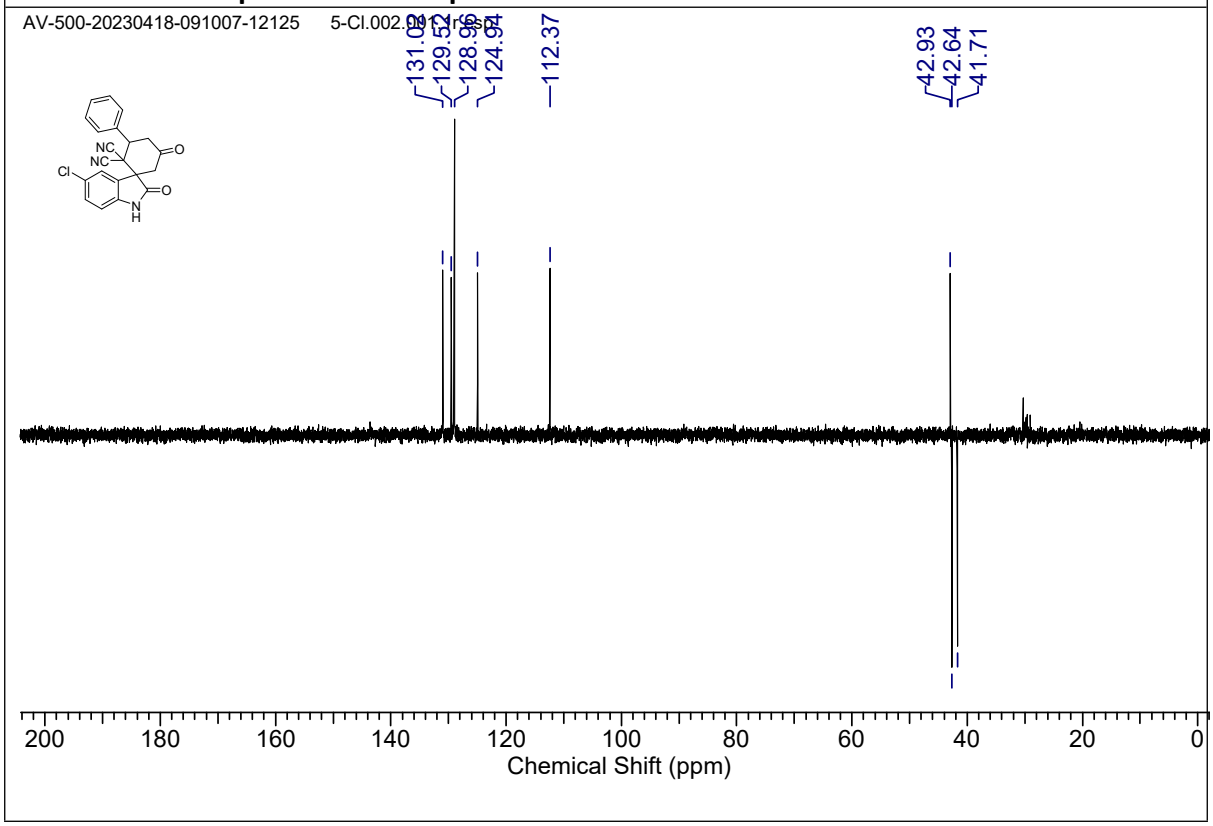
^{1}H NMR spectrum of compound 3Ad (500 MHz, Acetone-d_6)



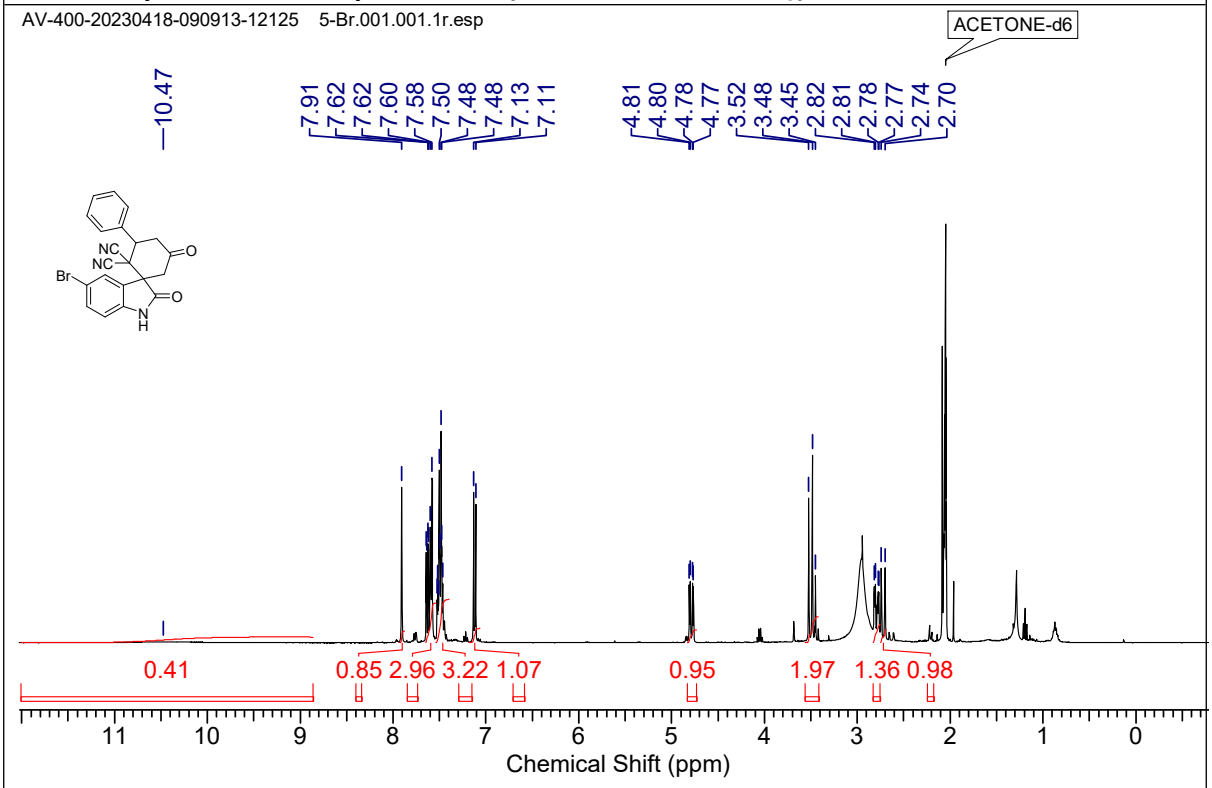
^{13}C NMR spectrum of compound 3Ad (125 MHz, Acetone-d_6)



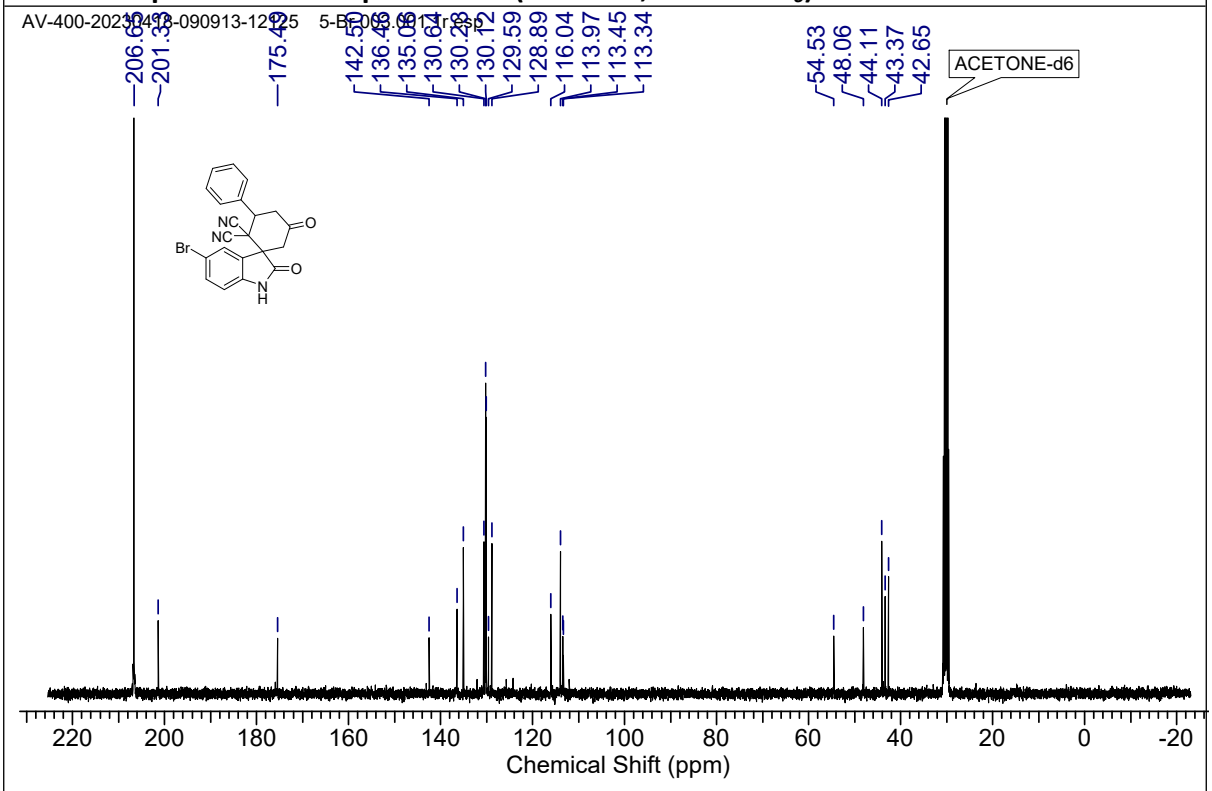
135 DEPT NMR spectrum of compound 3Ad



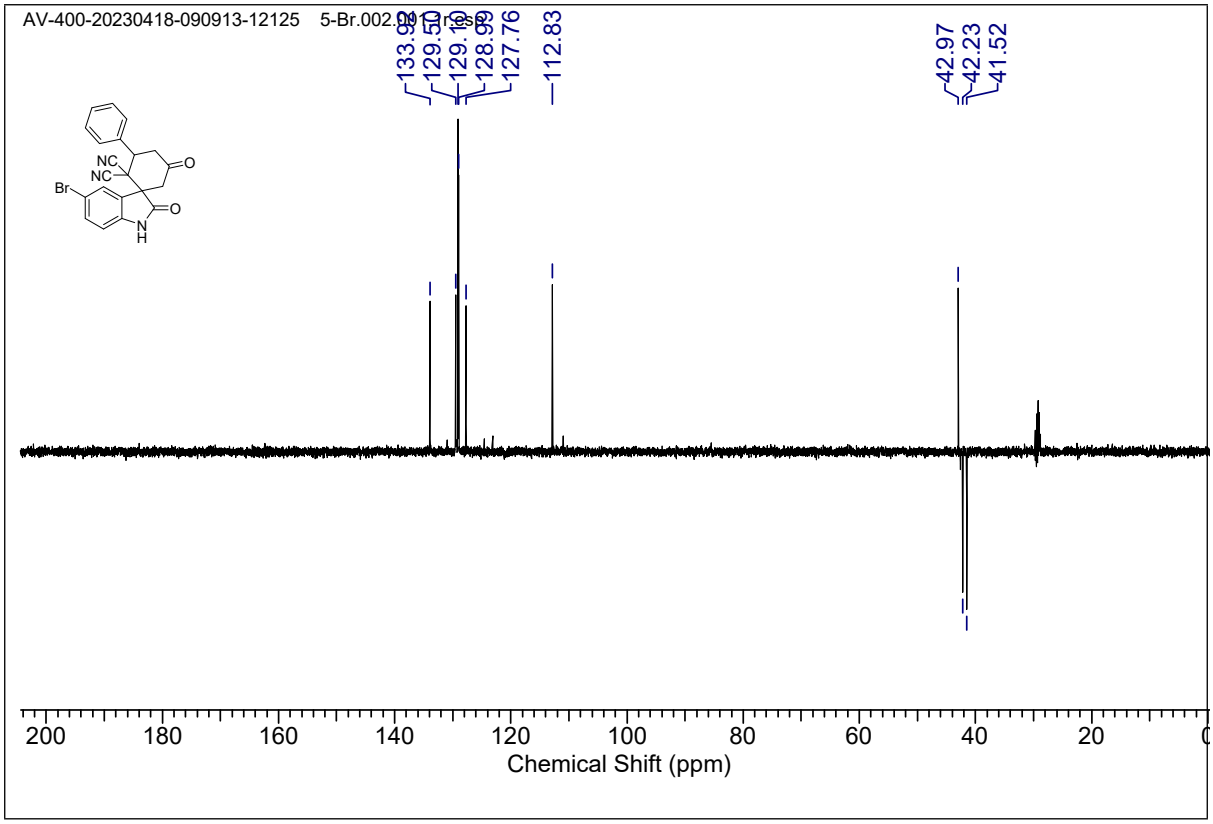
^{1}H NMR spectrum of compound 3Ae (400 MHz, Acetone-d_6)



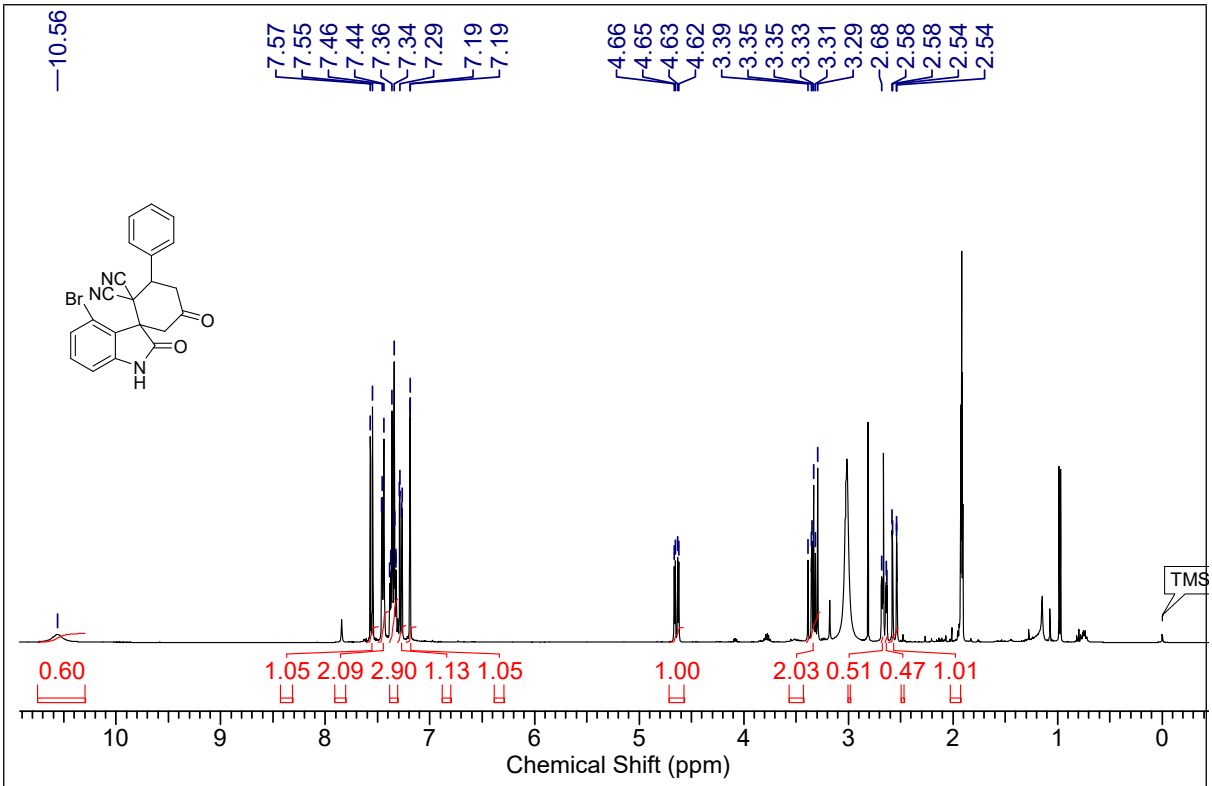
^{13}C NMR spectrum of compound 3Ae (101 MHz, Acetone-d_6)



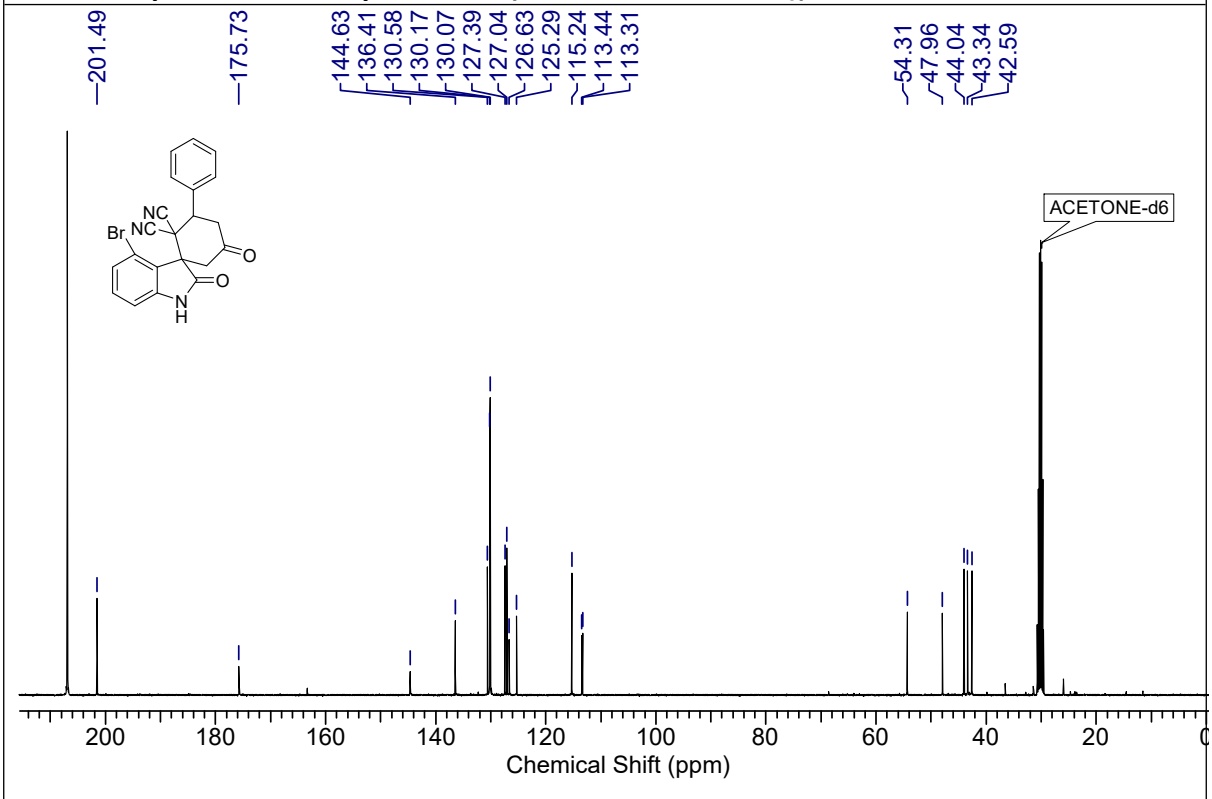
135 DEPT NMR spectrum of compound 3Ae



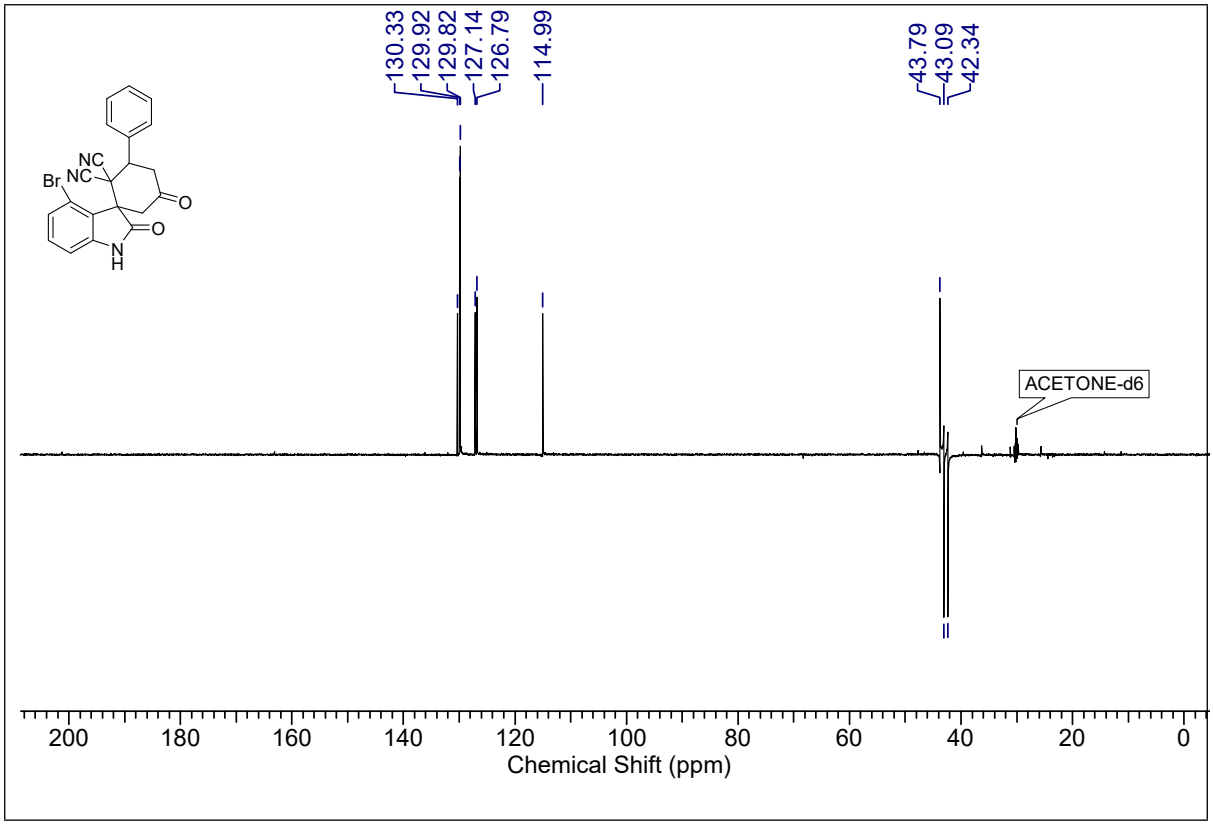
^{1}H NMR spectrum of compound 3Af (500 MHz, Acetone-d_6)



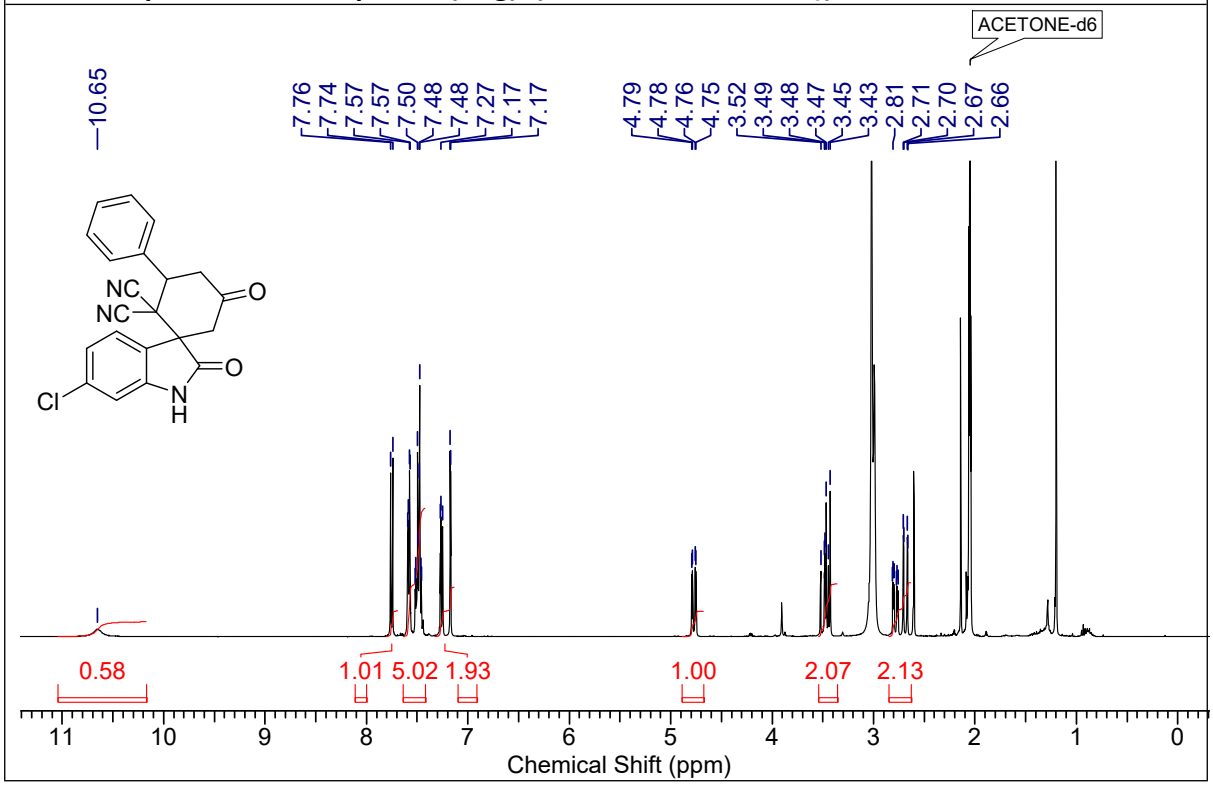
^{13}C NMR spectrum of compound 3Af (125 MHz, Acetone-d_6)



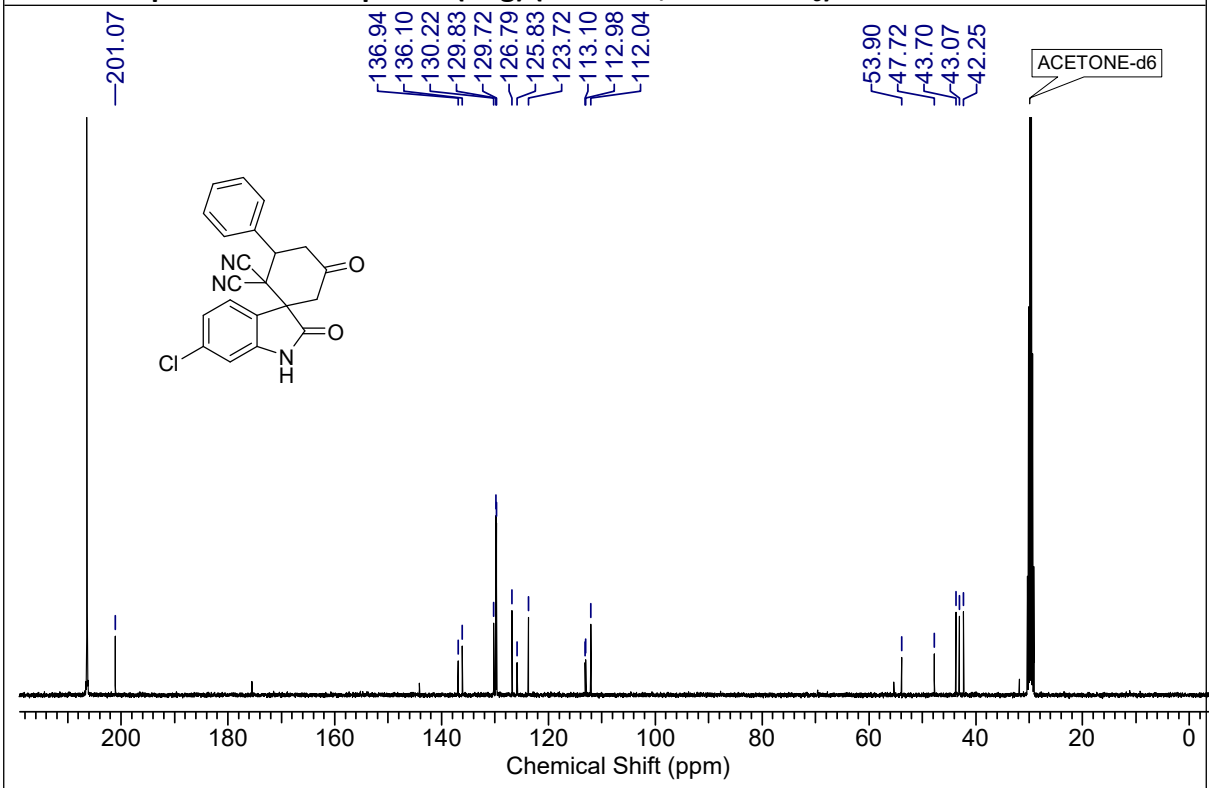
135 DEPT NMR spectrum of compound 3Af



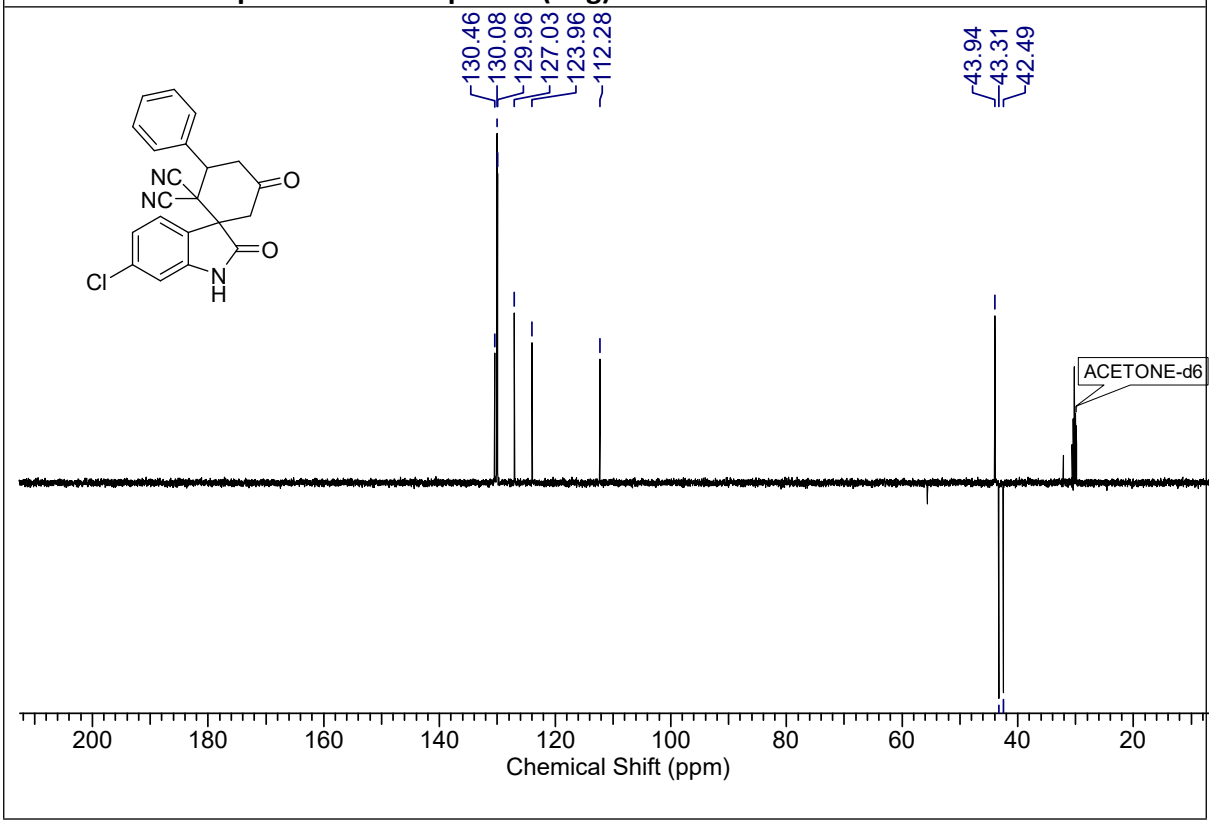
^{1}H NMR spectrum of compound (3Ag) (400 MHz, Acetone-d_6)



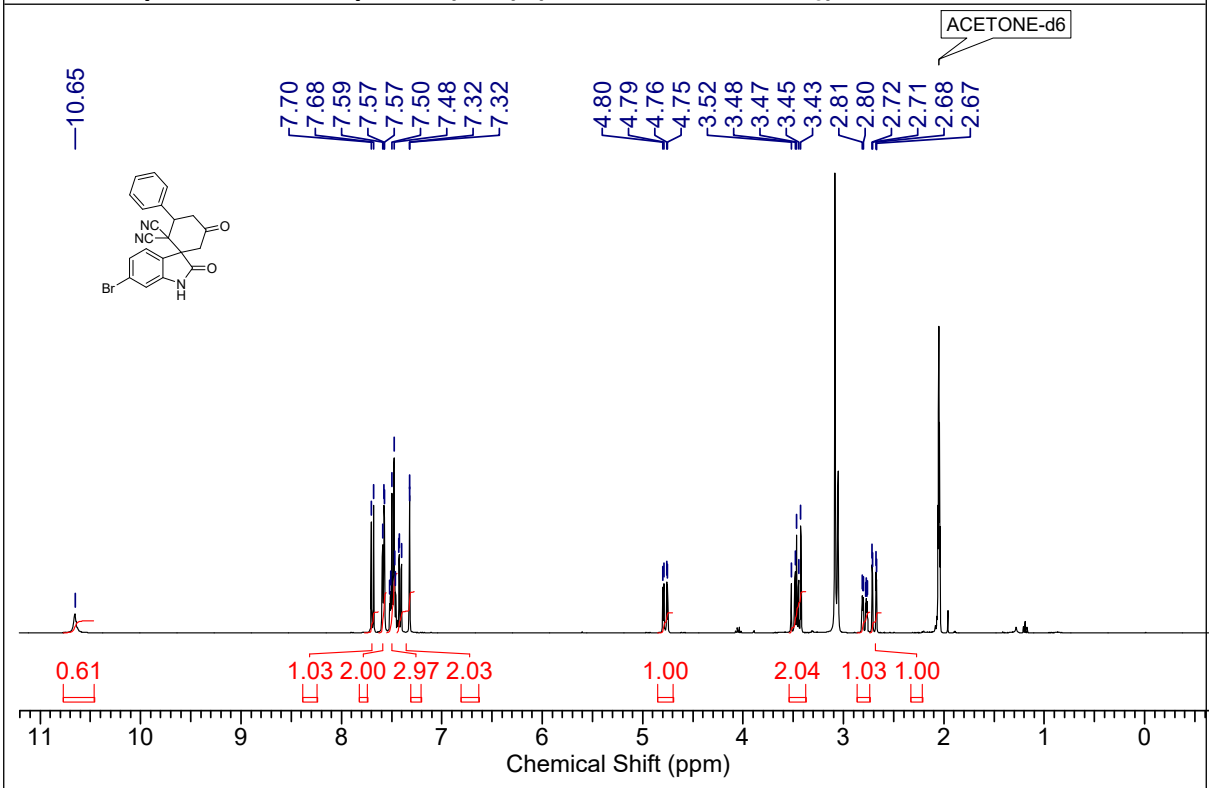
^{13}C NMR spectrum of compound (3Ag) (101 MHz, Acetone-d_6)



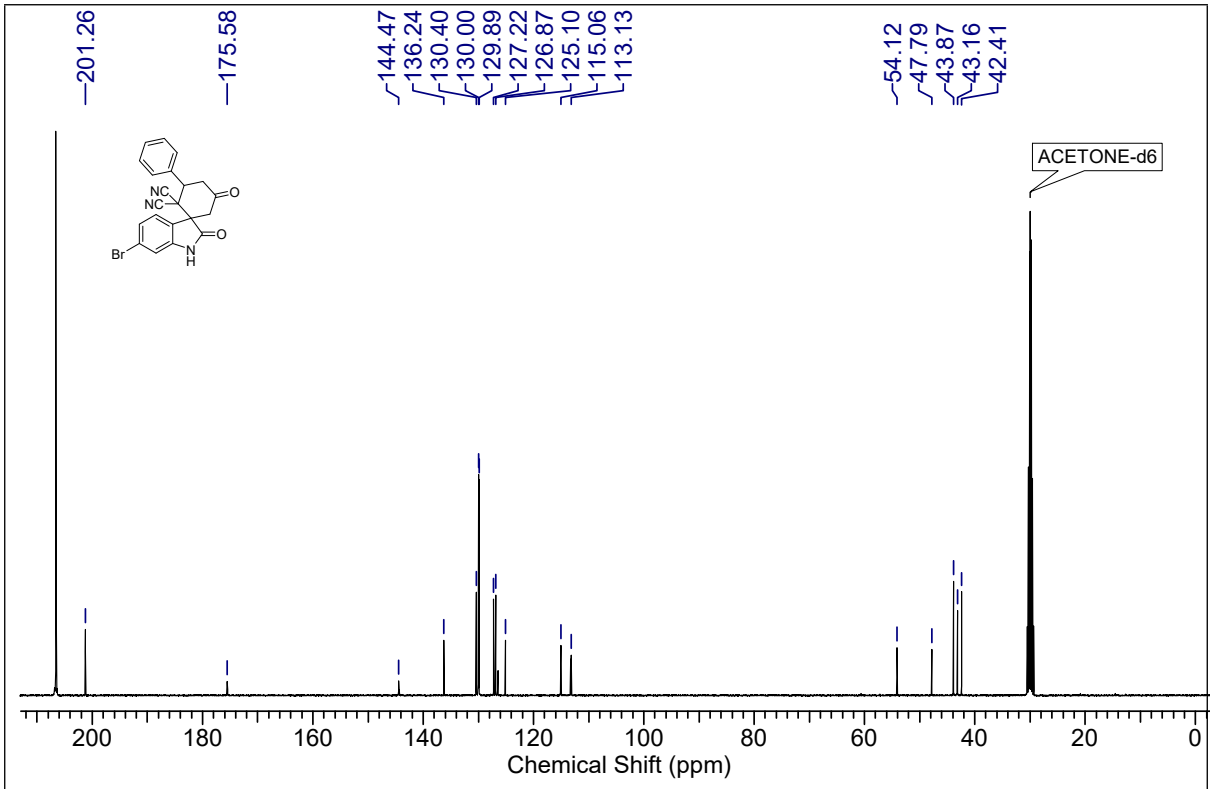
135 DEPT NMR spectrum of compound (3Ag)



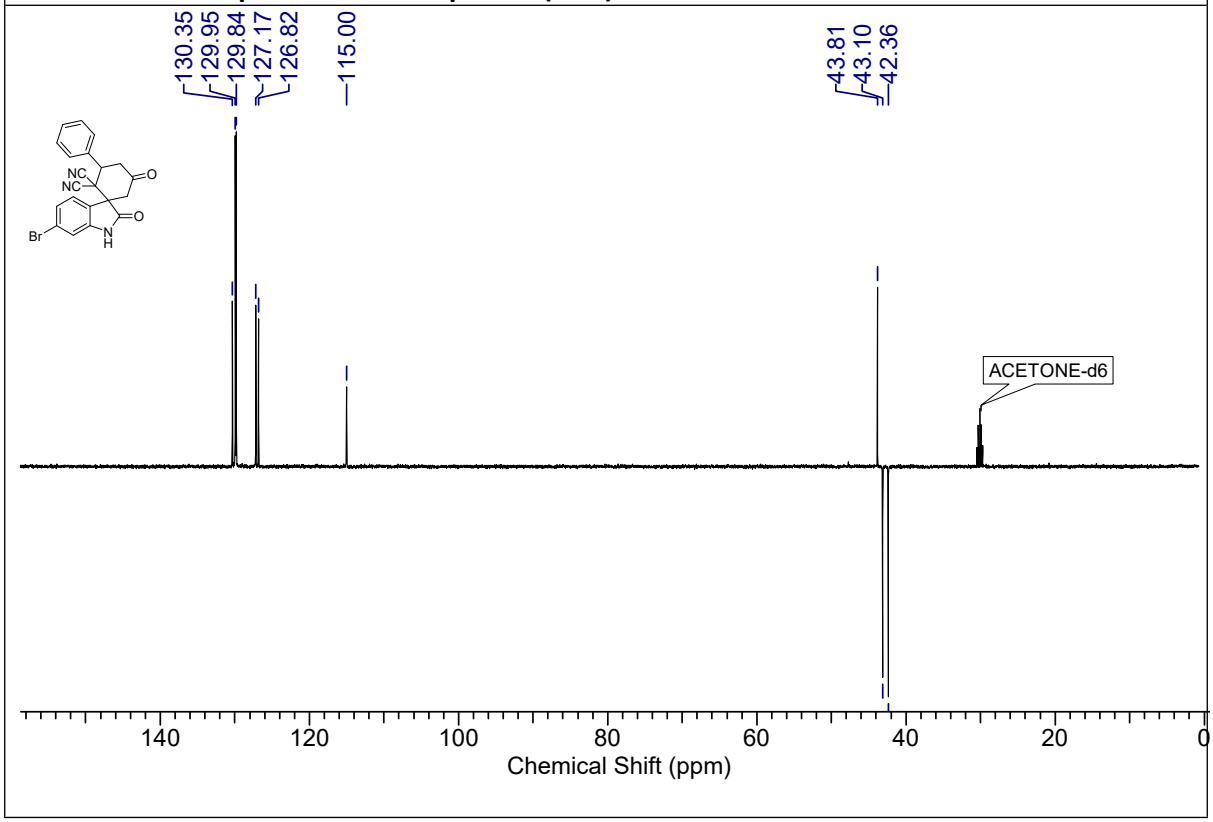
^{1}H NMR spectrum of compound (3Ah) (400 MHz, Acetone-d_6)



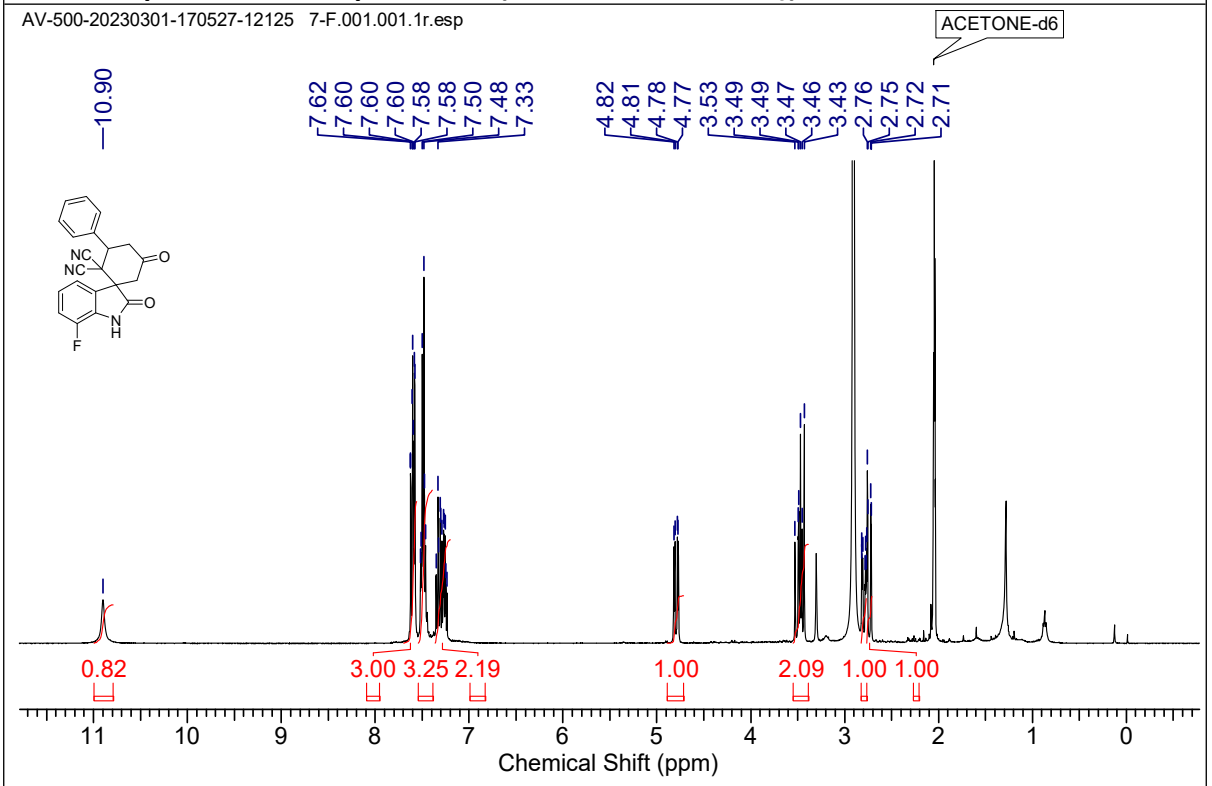
^{13}C NMR spectrum of compound (3Ah) (101 MHz, Acetone-d_6)



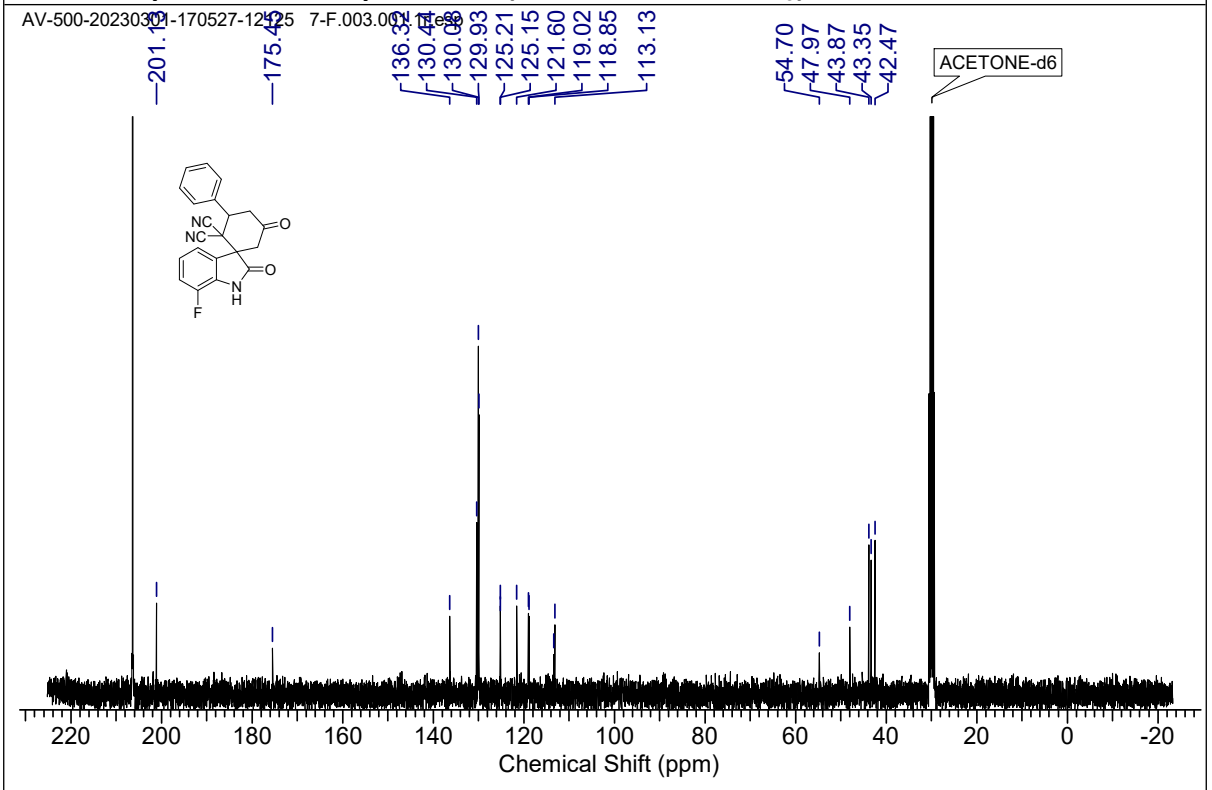
135 DEPT NMR spectrum of compound (3Ah)



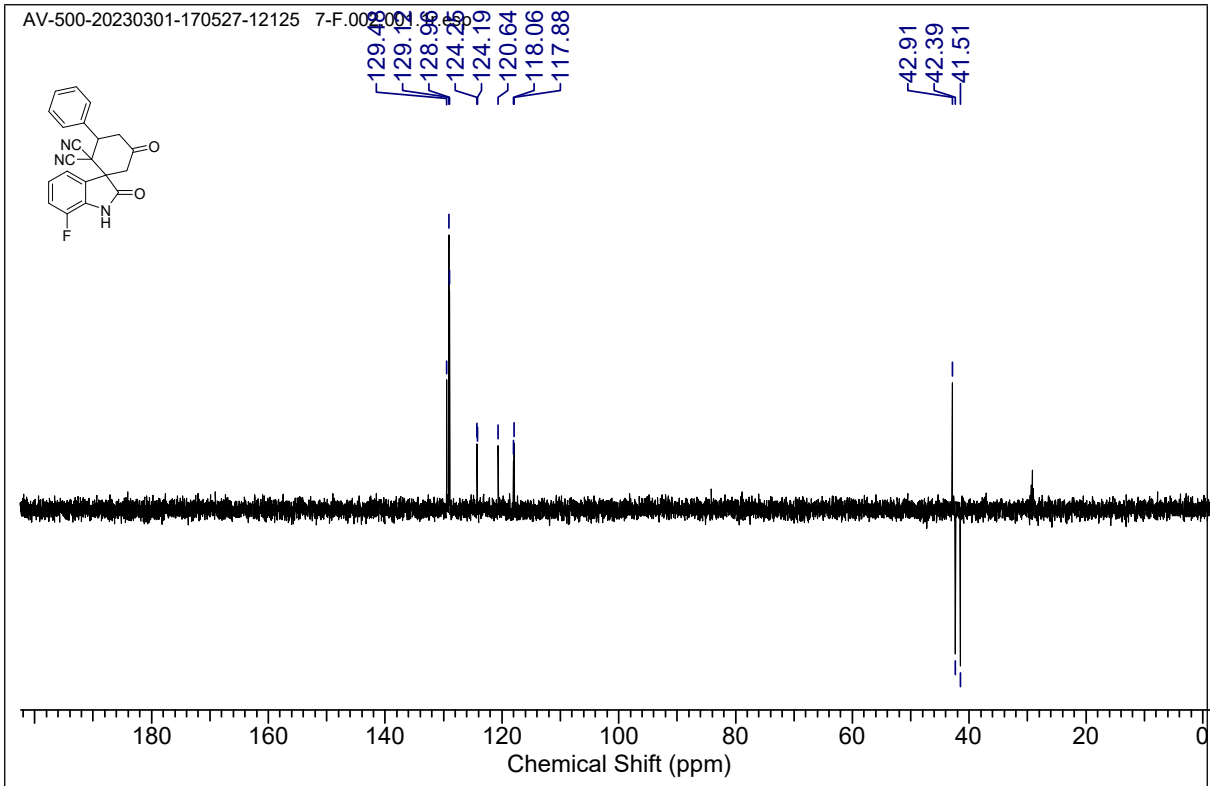
^{1}H NMR spectrum of compound 3Ai (500 MHz, Acetone-d_6)



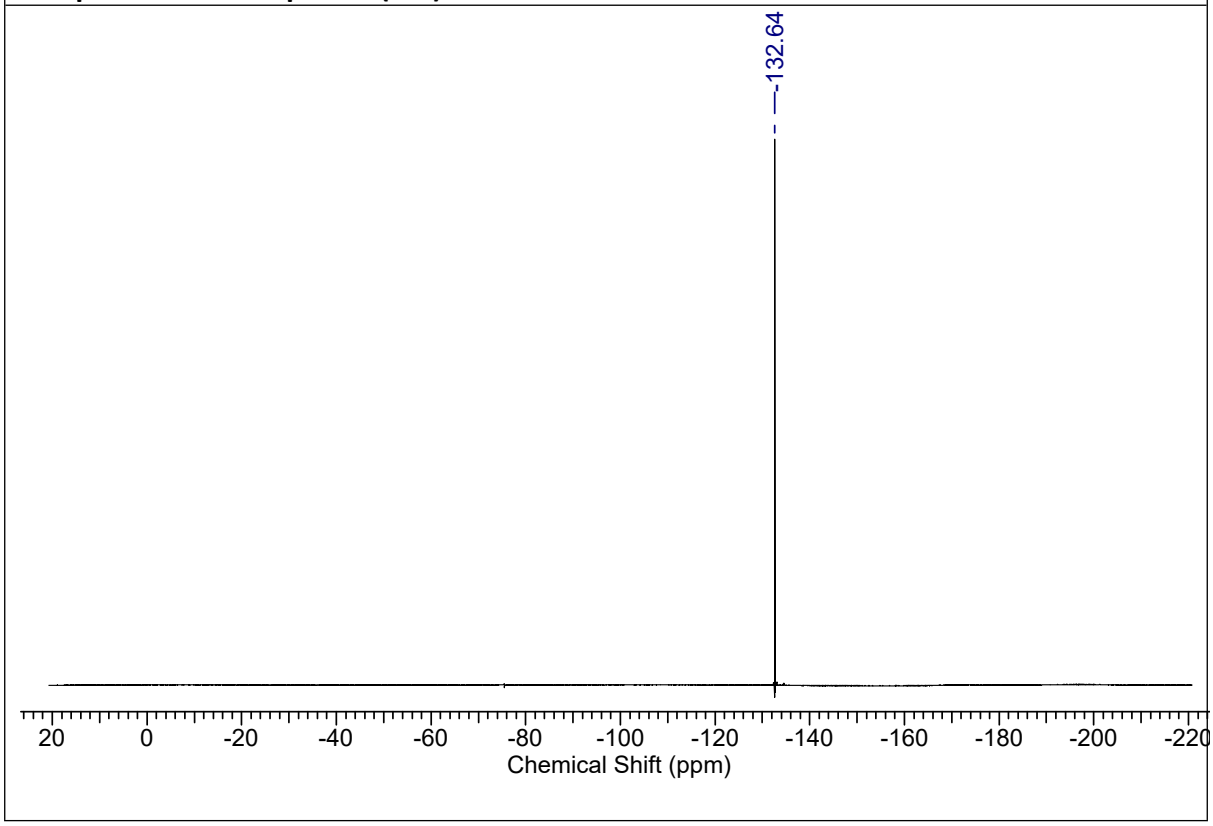
^{13}C NMR spectrum of compound 3Ai (125 MHz, Acetone-d_6)



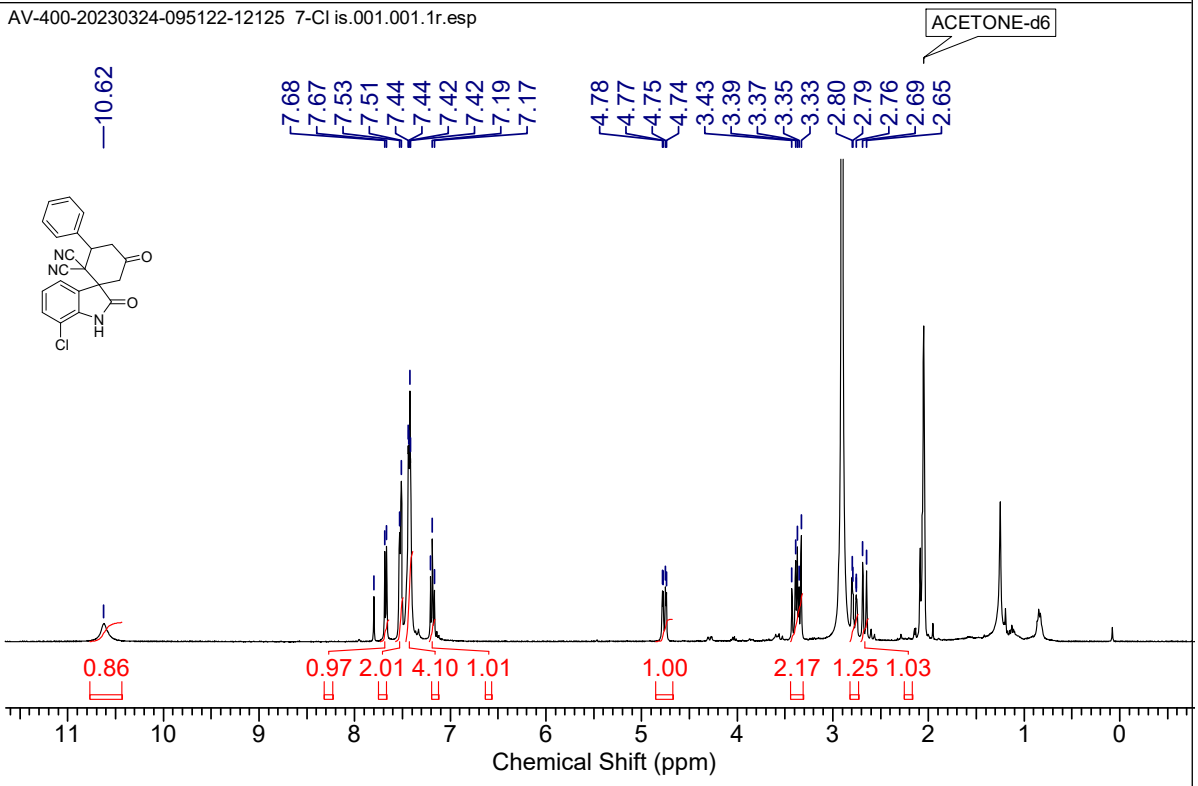
135 DEPT NMR spectrum of compound 3Ai



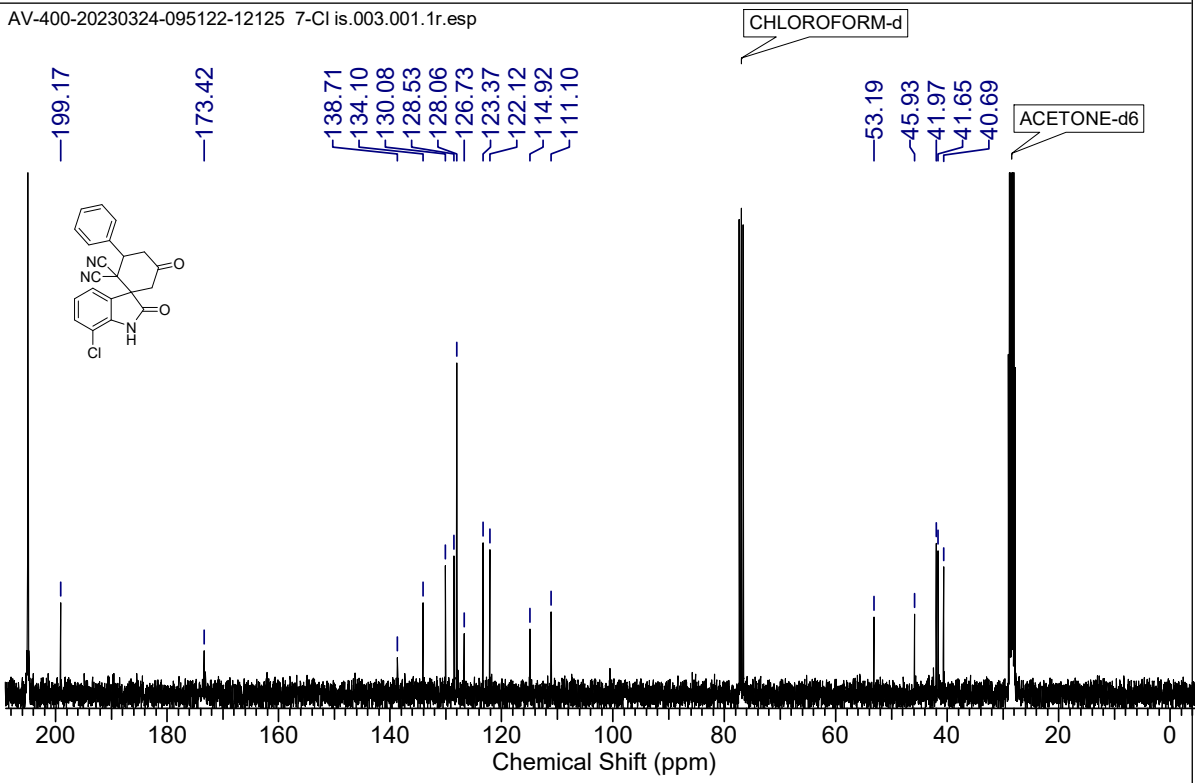
^{19}F spectrum of compound (3Ai)



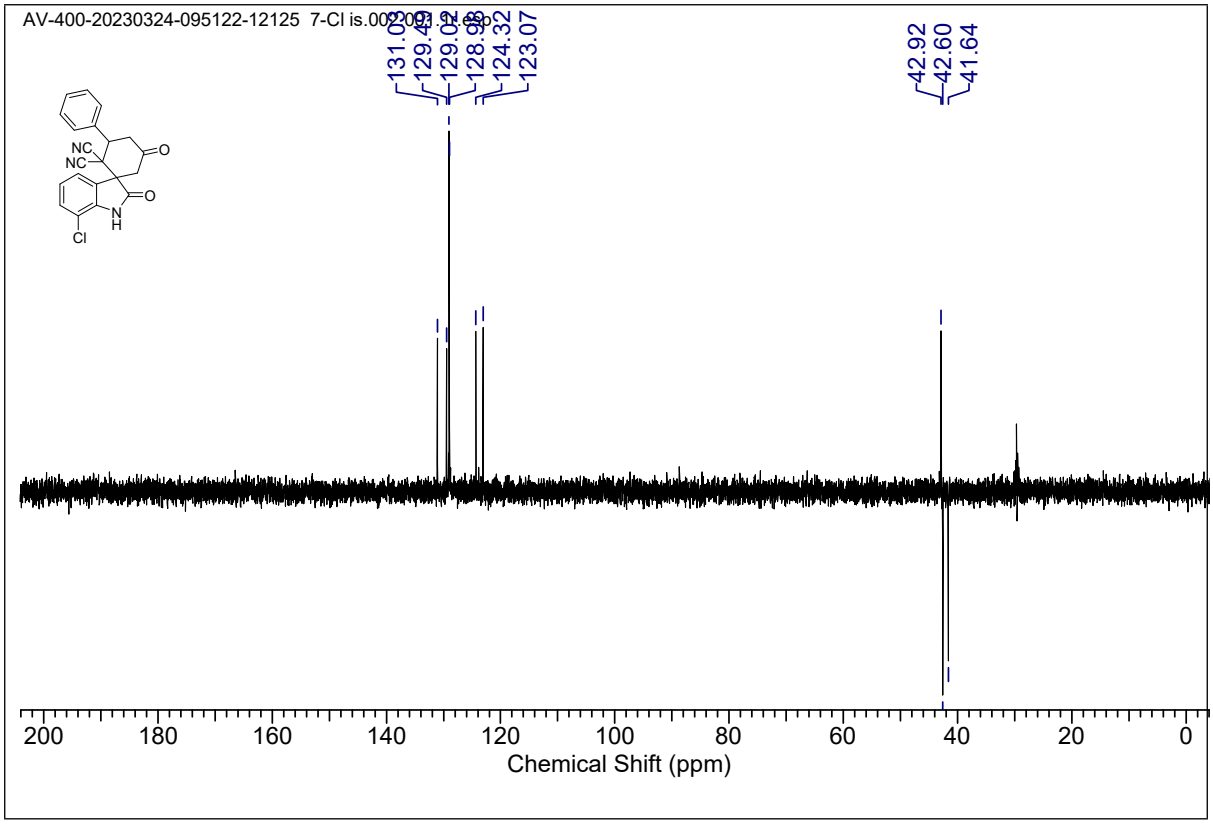
^{1}H NMR spectrum of compound 3Aj (400 MHz, Acetone-d_6)



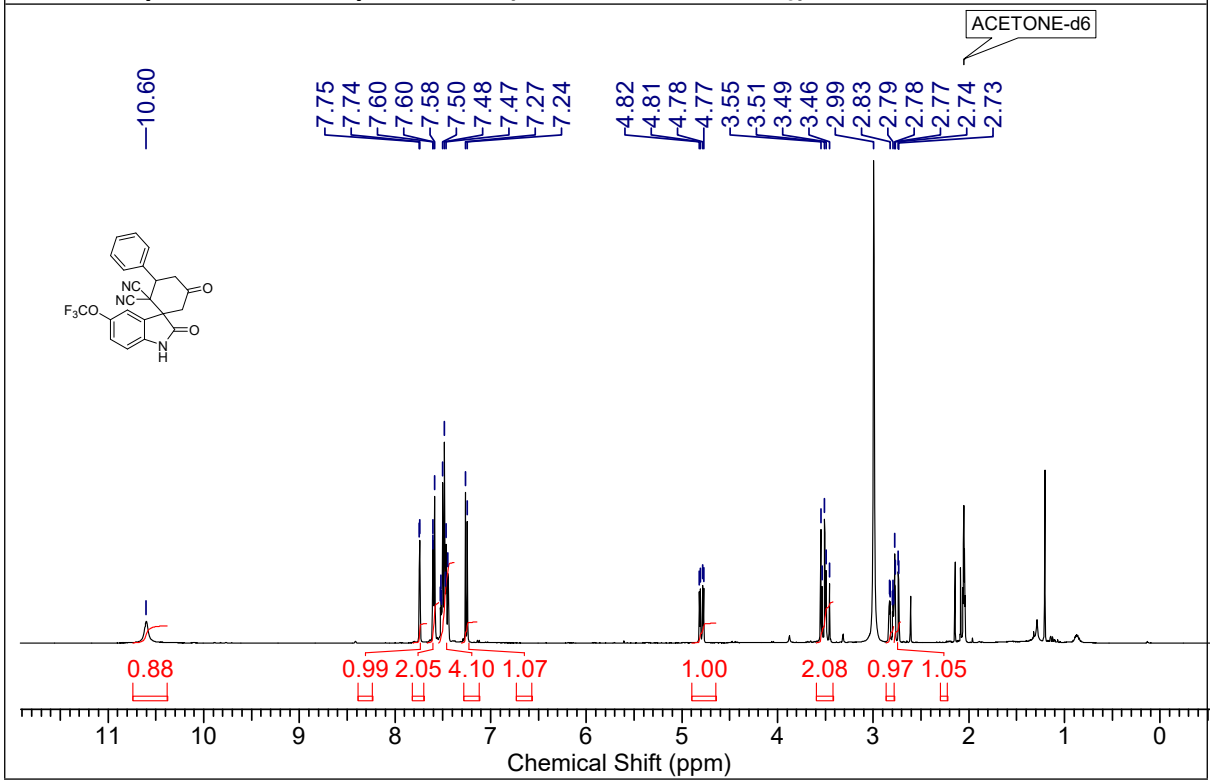
^{13}C NMR spectrum of compound 3Aj (101 MHz, Acetone-d_6)



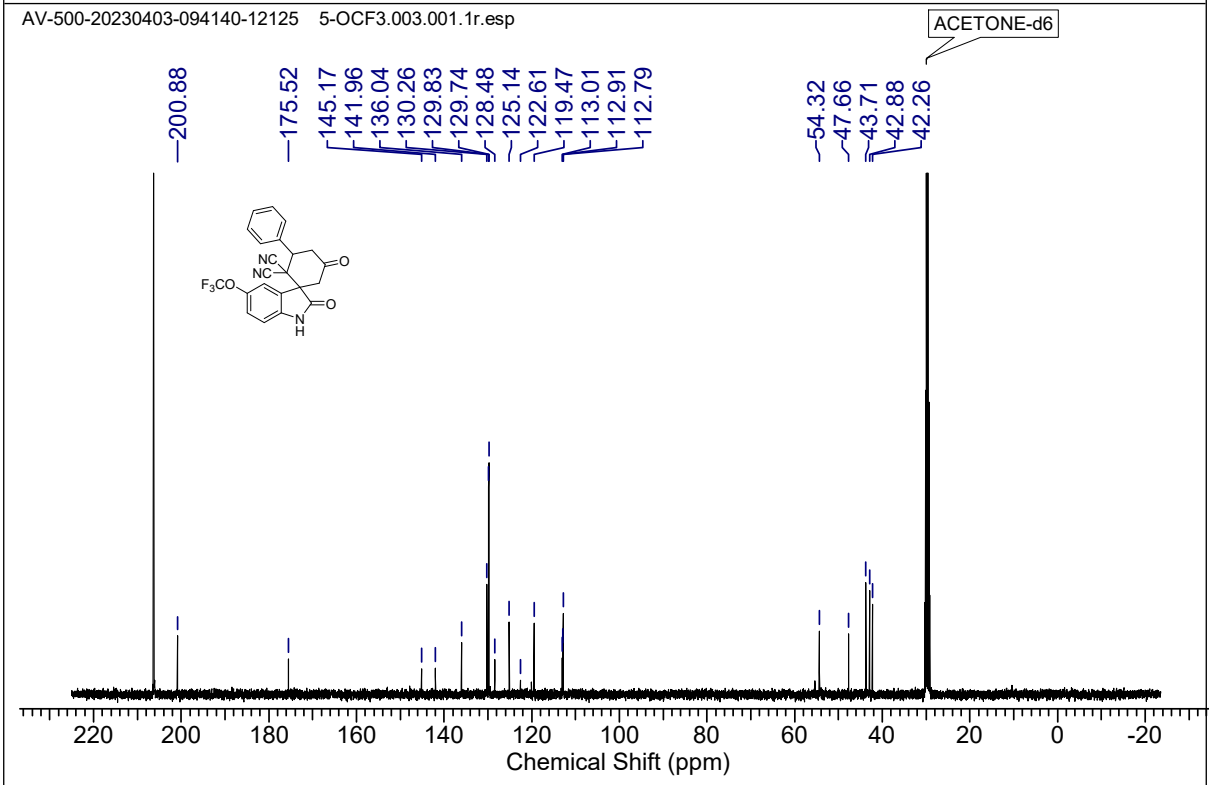
135 DEPT NMR spectrum of compound 3Aj



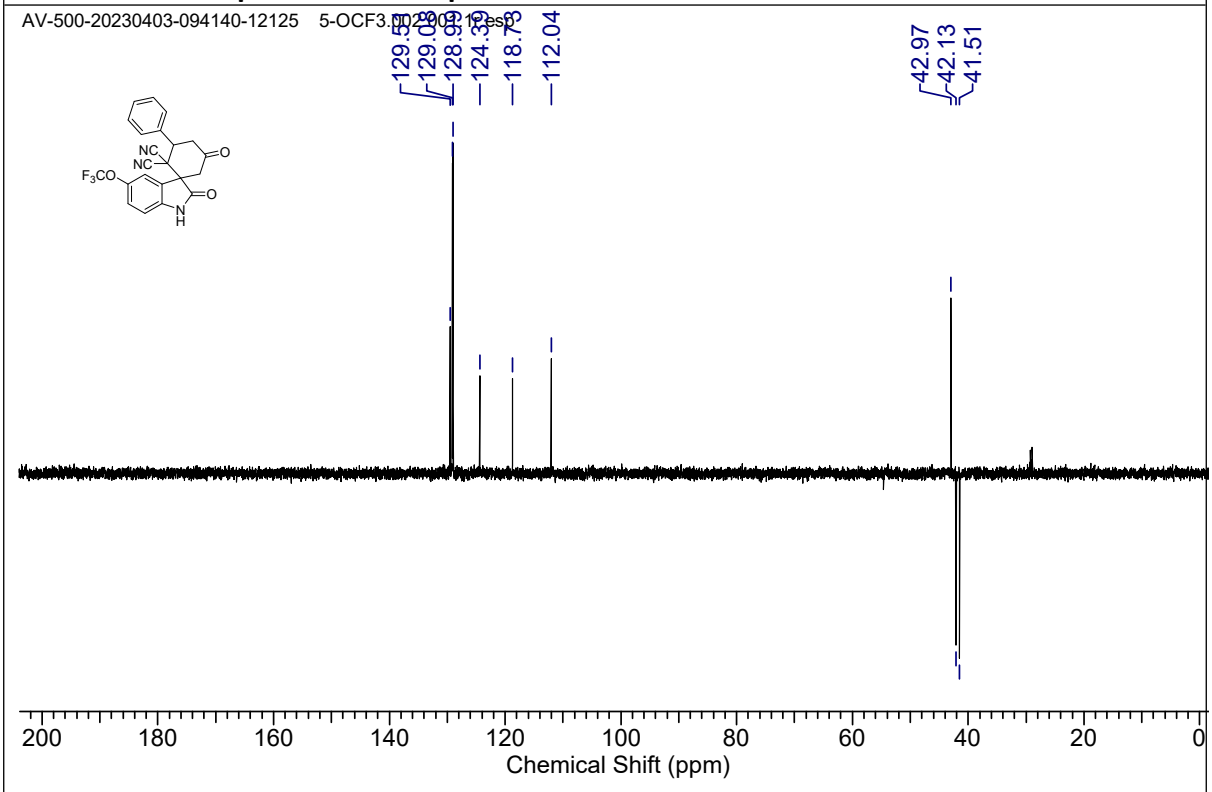
^{1}H NMR spectrum of compound 3Ak (500 MHz, Acetone-d_6)



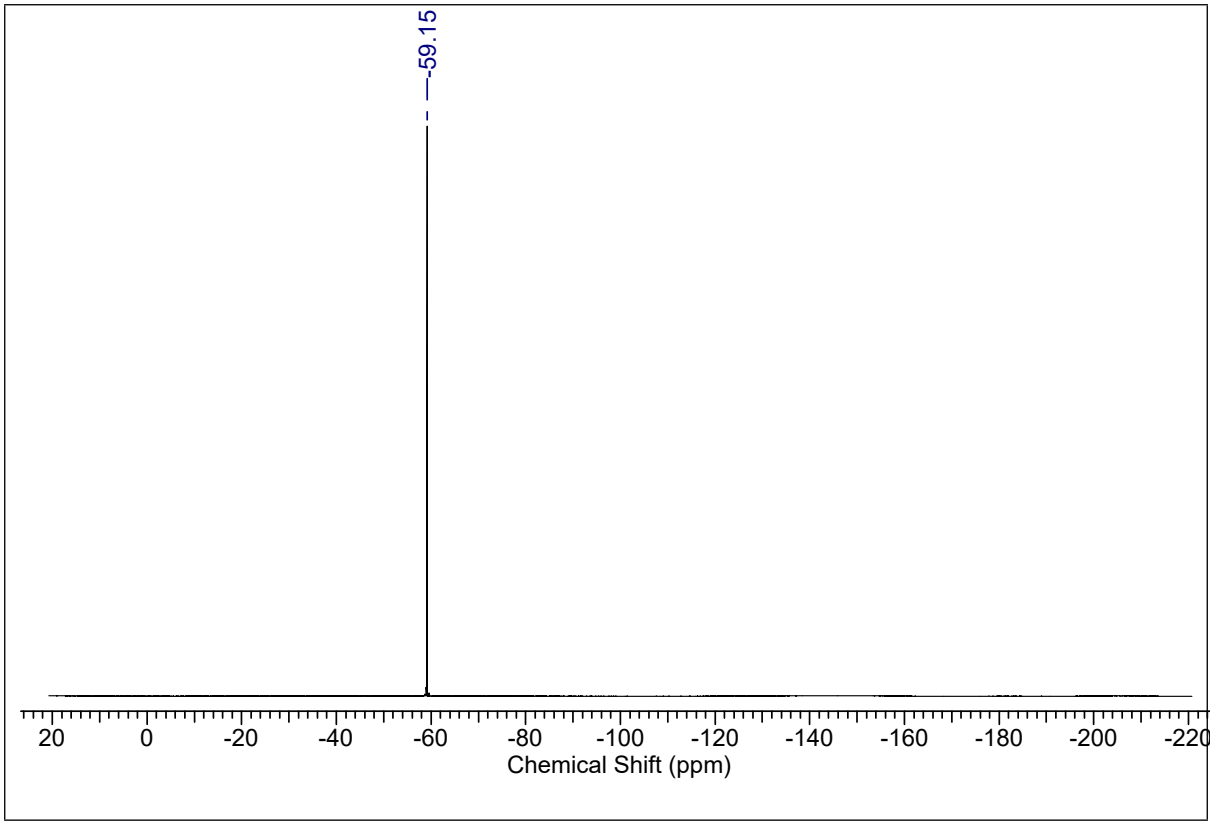
^{13}C NMR spectrum of compound 3Ak (125 MHz, Acetone d^6)



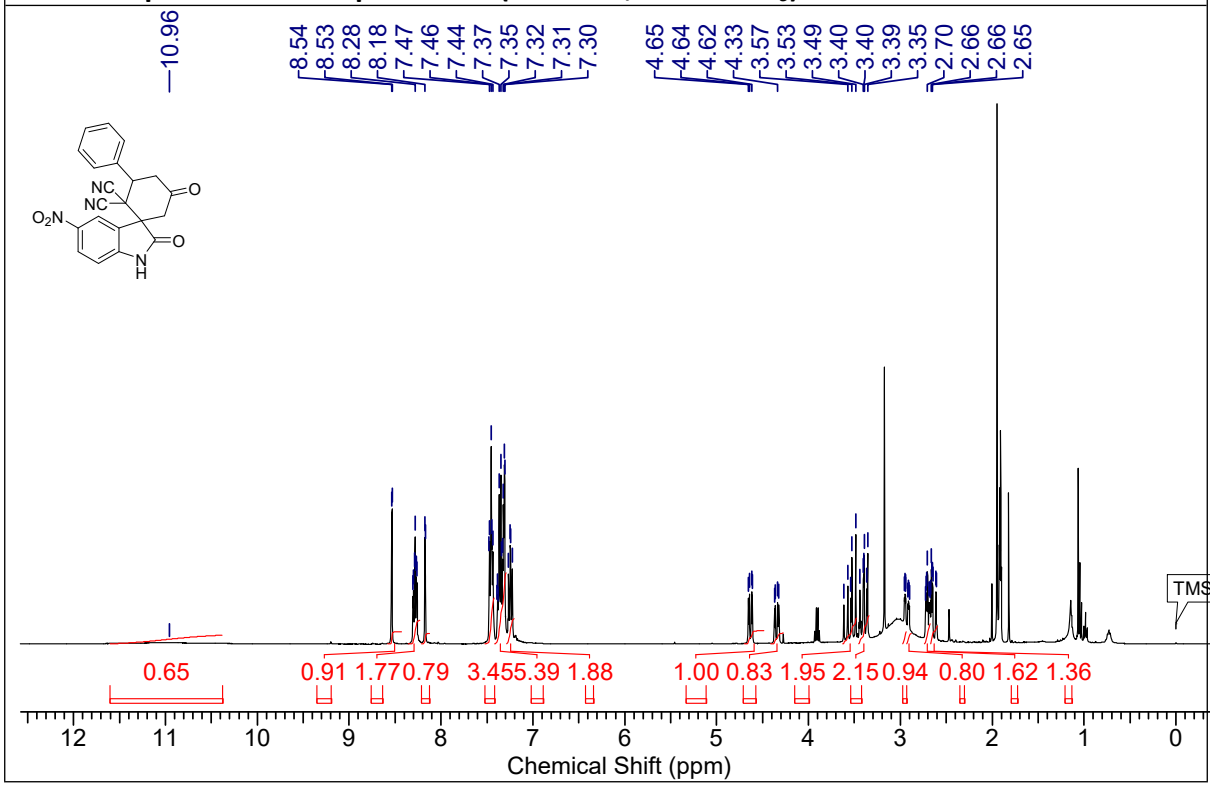
135 DEPT NMR spectrum of compound 3Ak



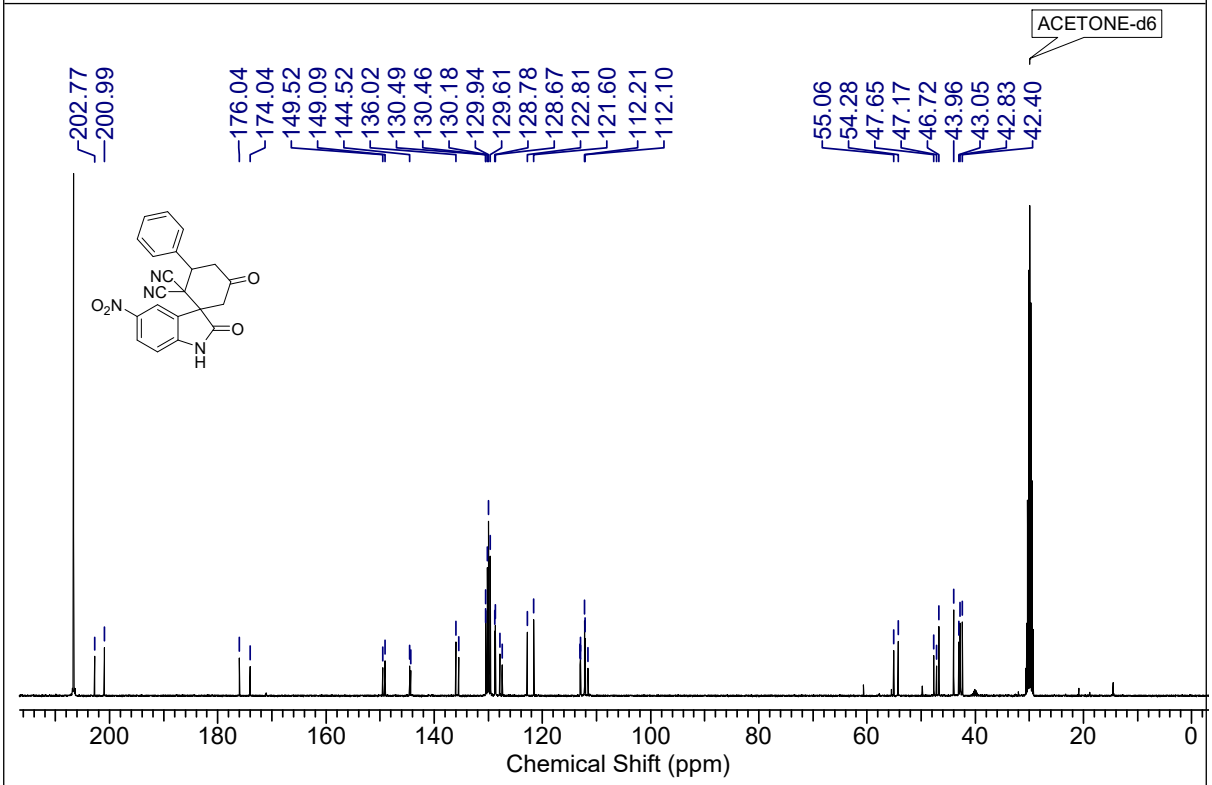
^{19}F spectrum of compound (3Ak)



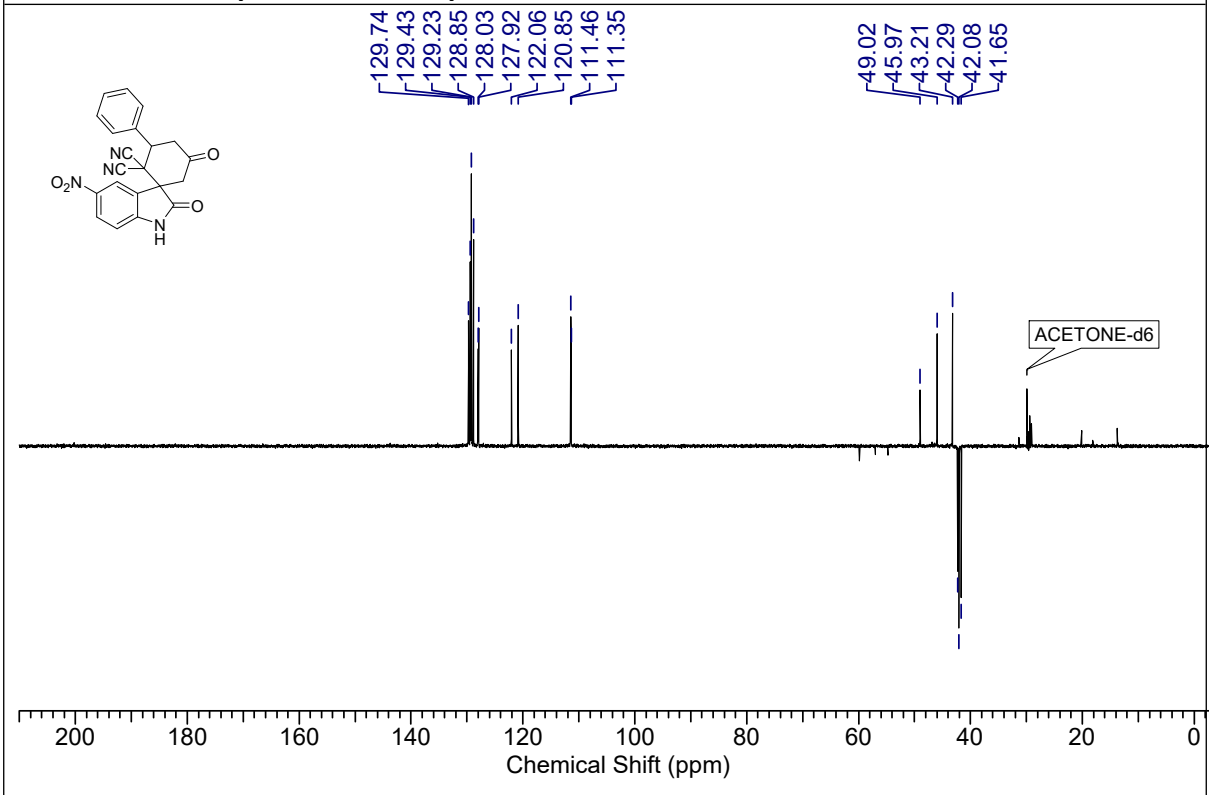
^{1}H NMR spectrum of compound 3Al (500 MHz, Acetone-d_6)



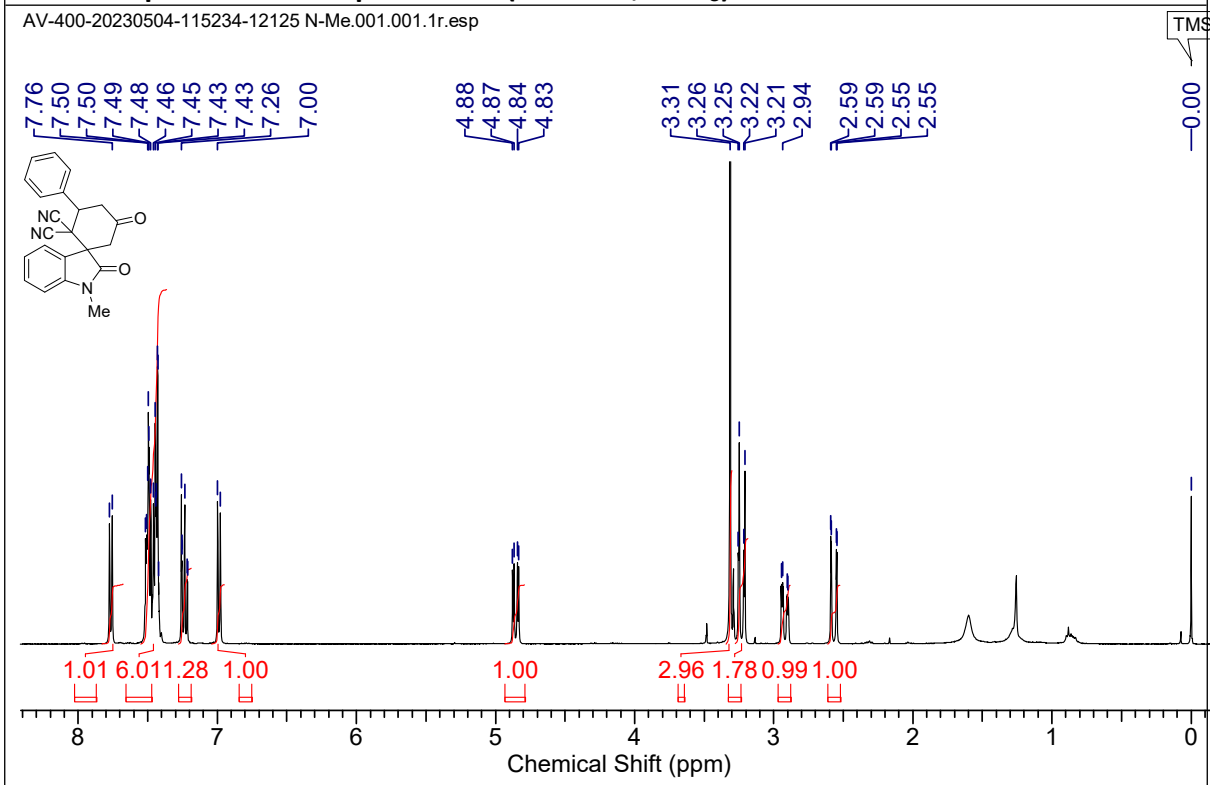
^{13}C NMR spectrum of compound 3Al (125 MHz, Acetone-d_6)



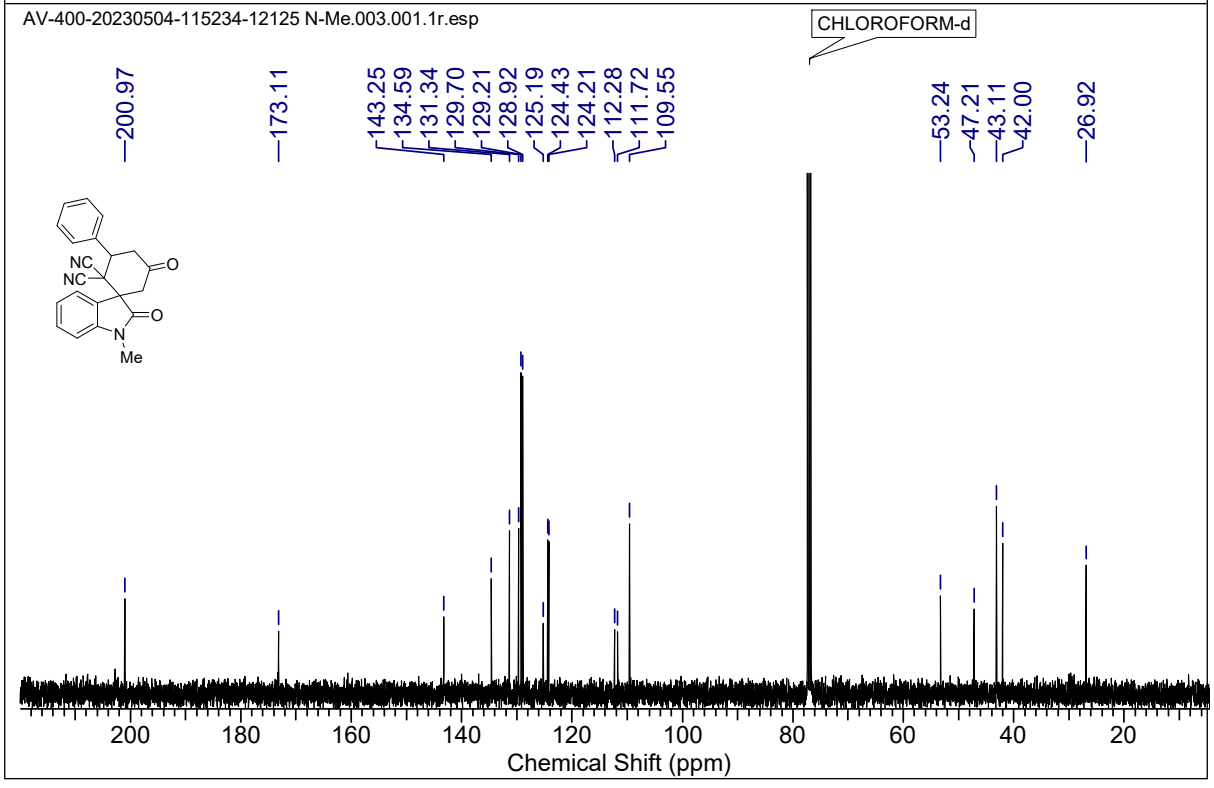
135 DEPT NMR spectrum of compound 3Al



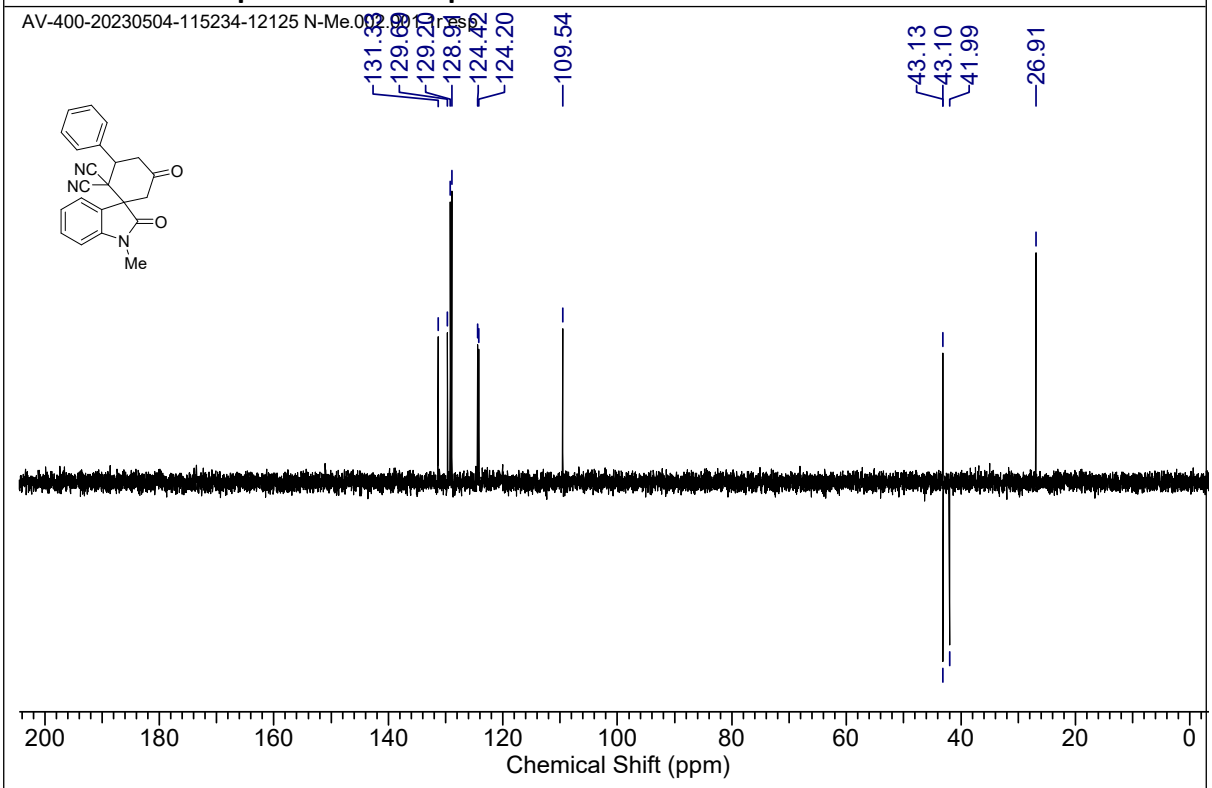
^{1}H NMR spectrum of compound 3Ba (400 MHz, $CDCl_3$)



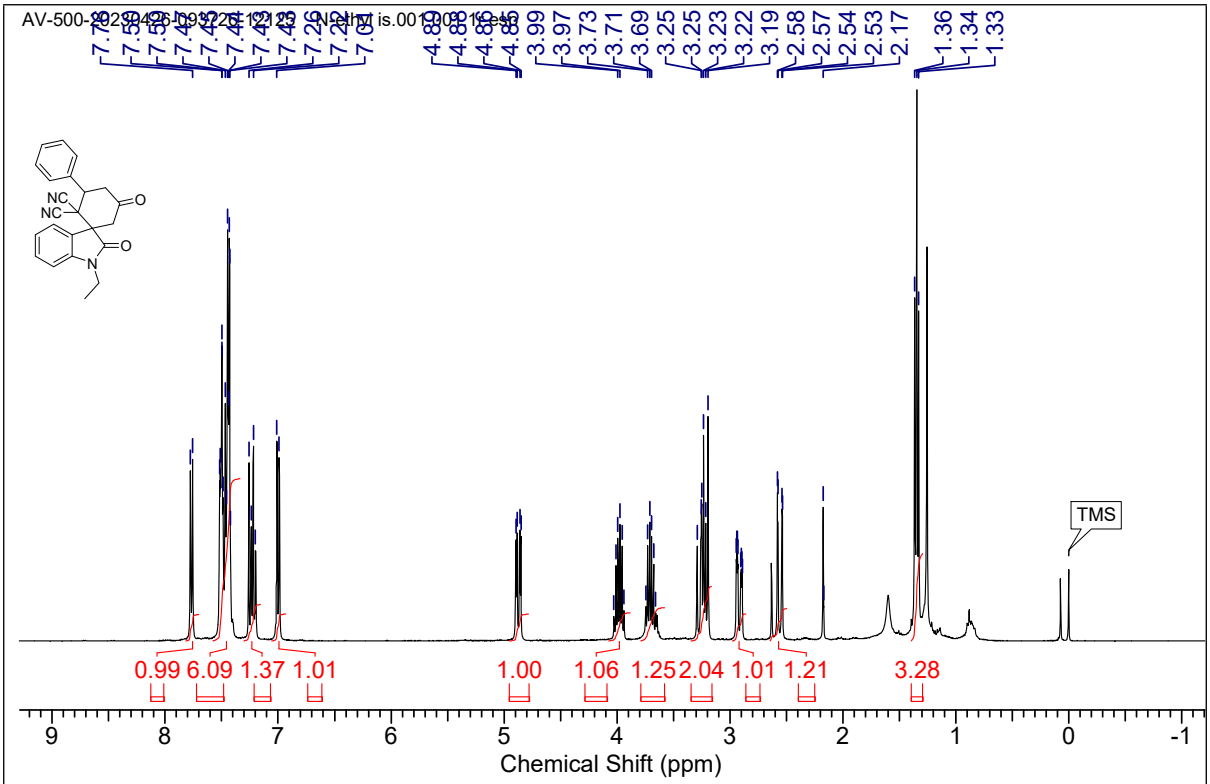
^{13}C NMR spectrum of compound 3Ba (101 MHz, $CDCl_3$)



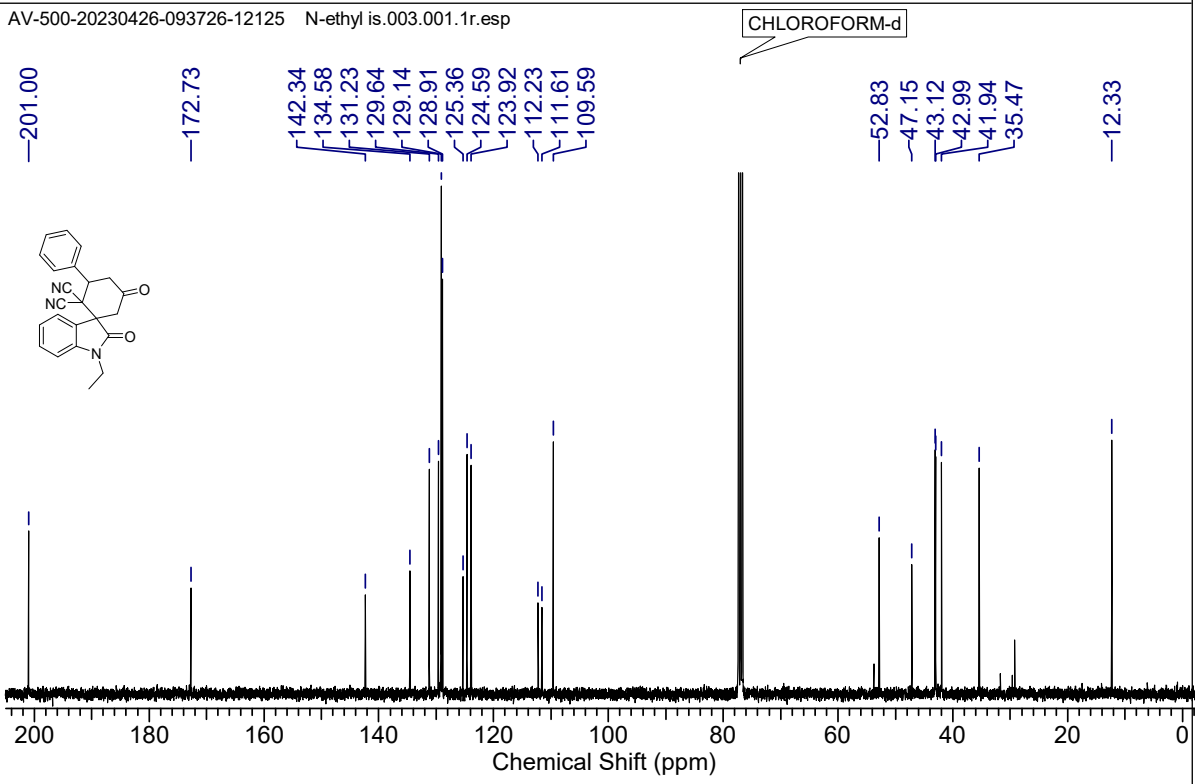
135 DEPT NMR spectrum of compound 3Ba



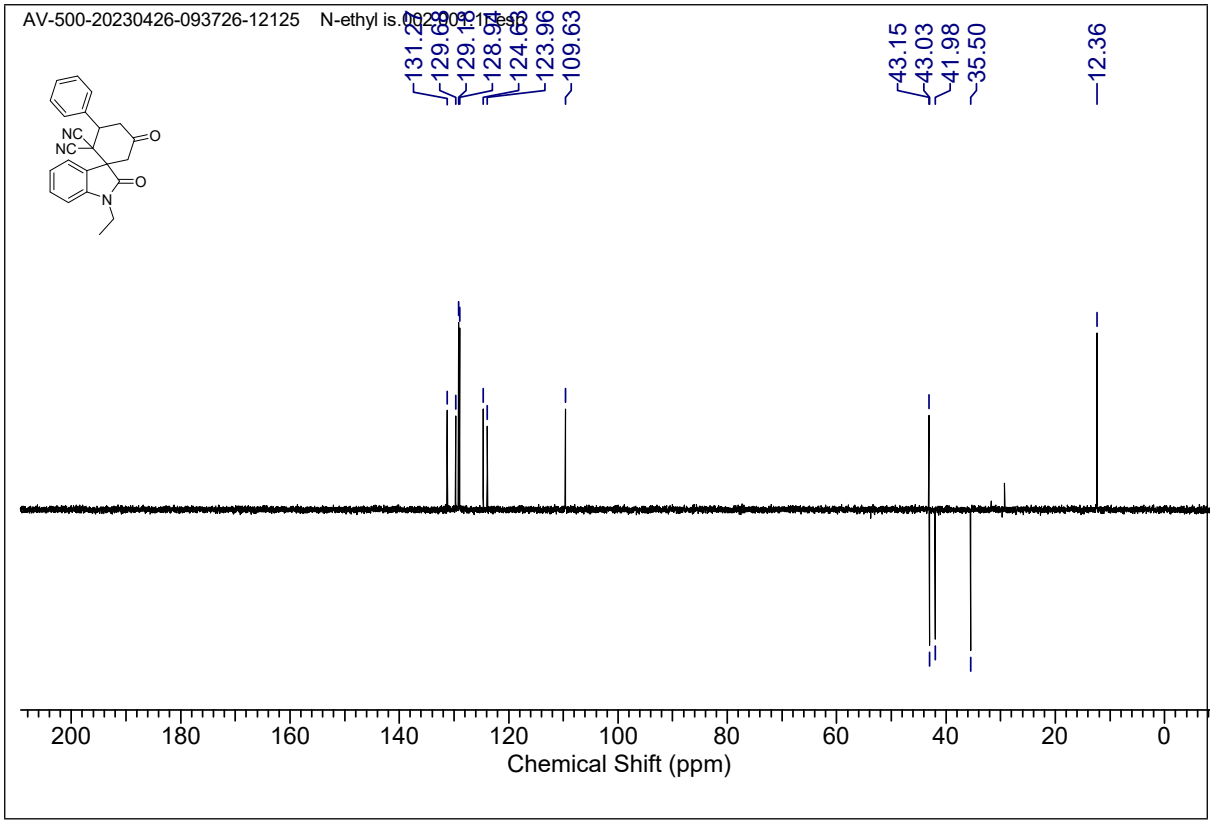
^{1}H NMR spectrum of compound 3Bb (500 MHz, $CDCl_3$)



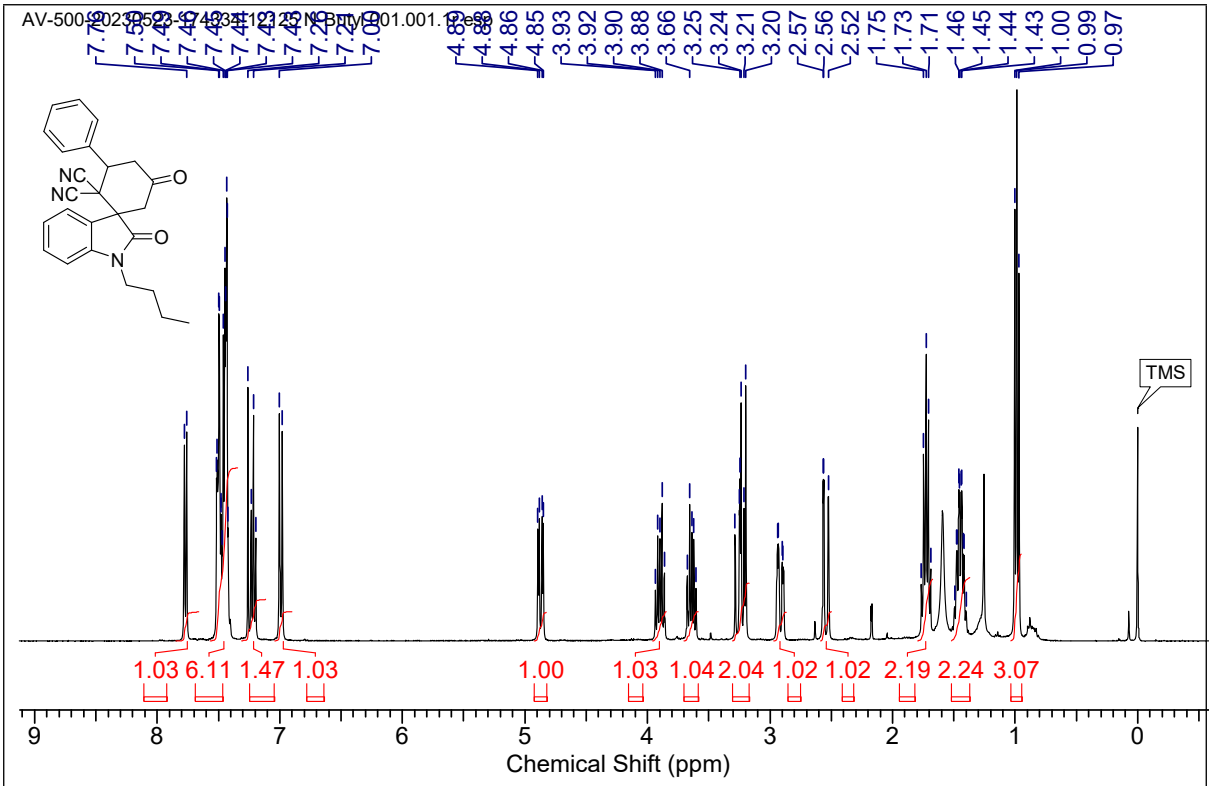
^{13}C NMR spectrum of compound 3Bb (125 MHz, $CDCl_3$)



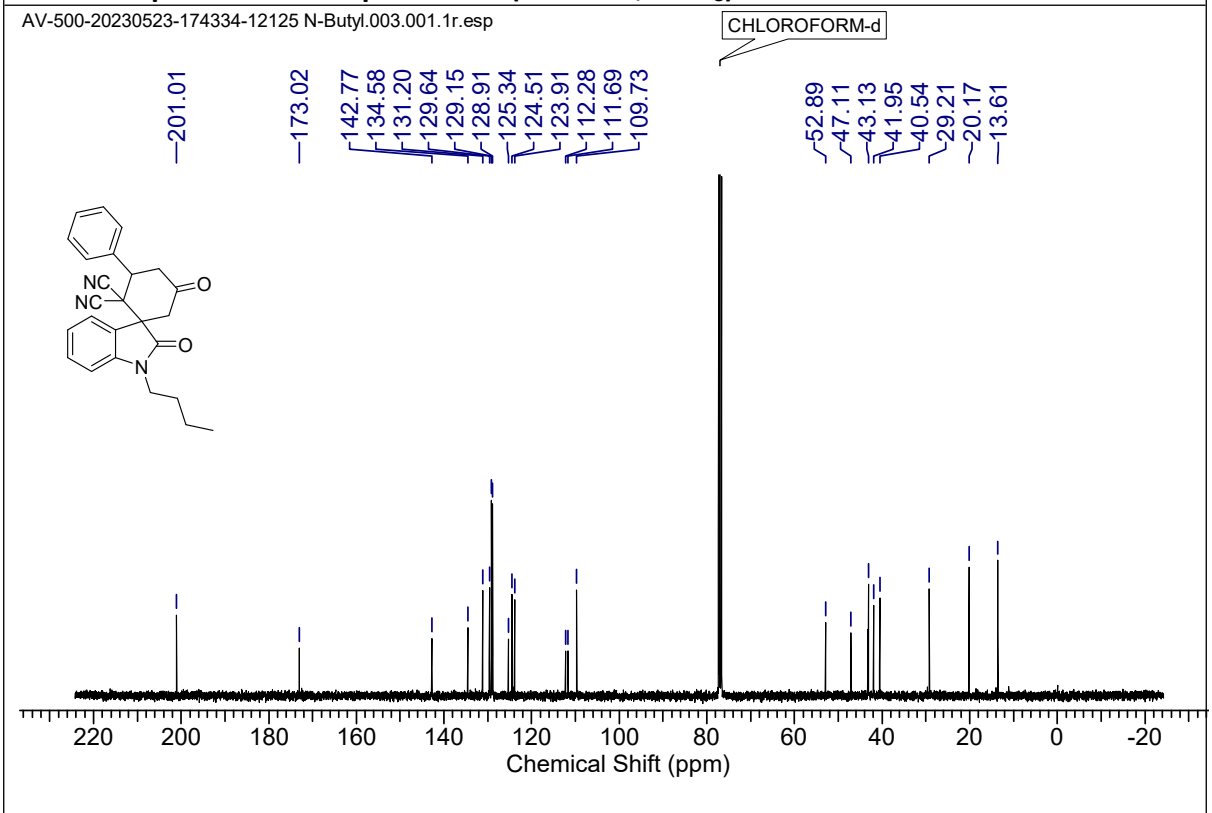
135 DEPT NMR spectrum of compound 3Bb



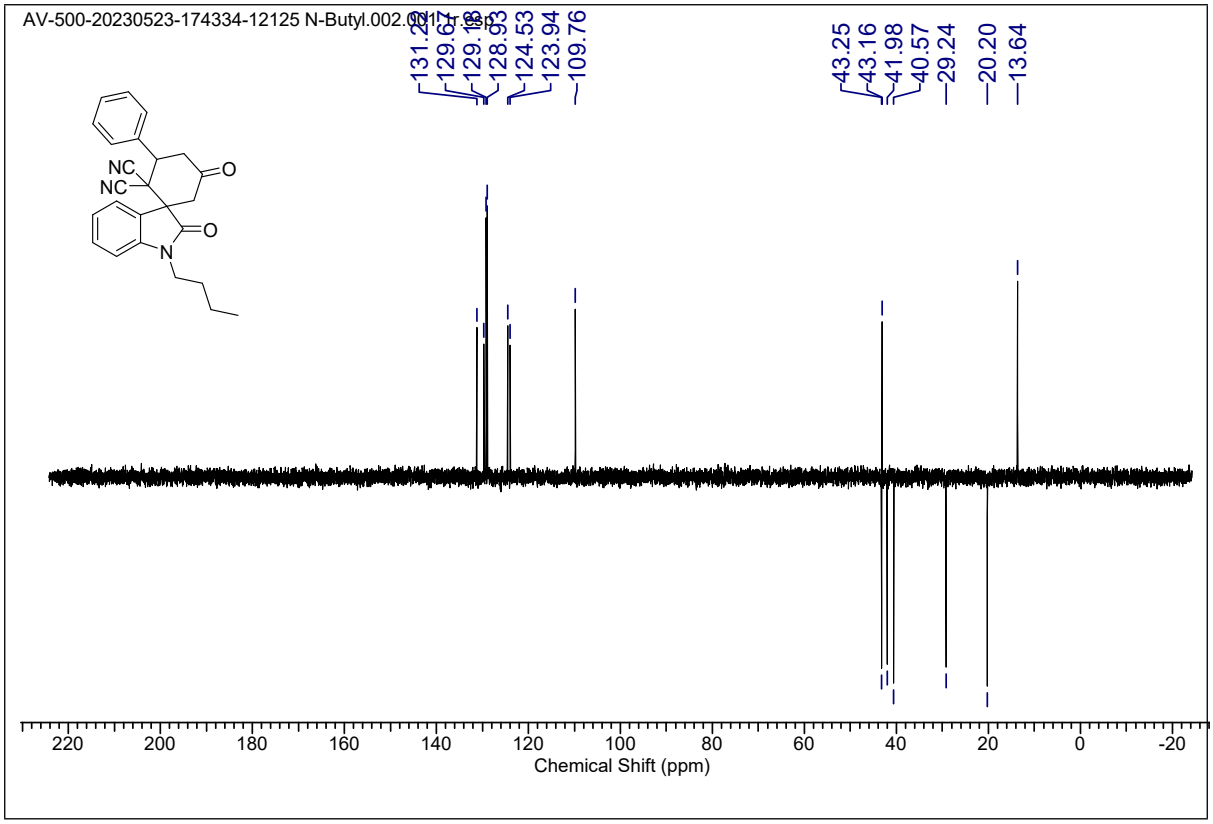
^{1}H NMR spectrum of compound 3Bc (500 MHz, $CDCl_3$)

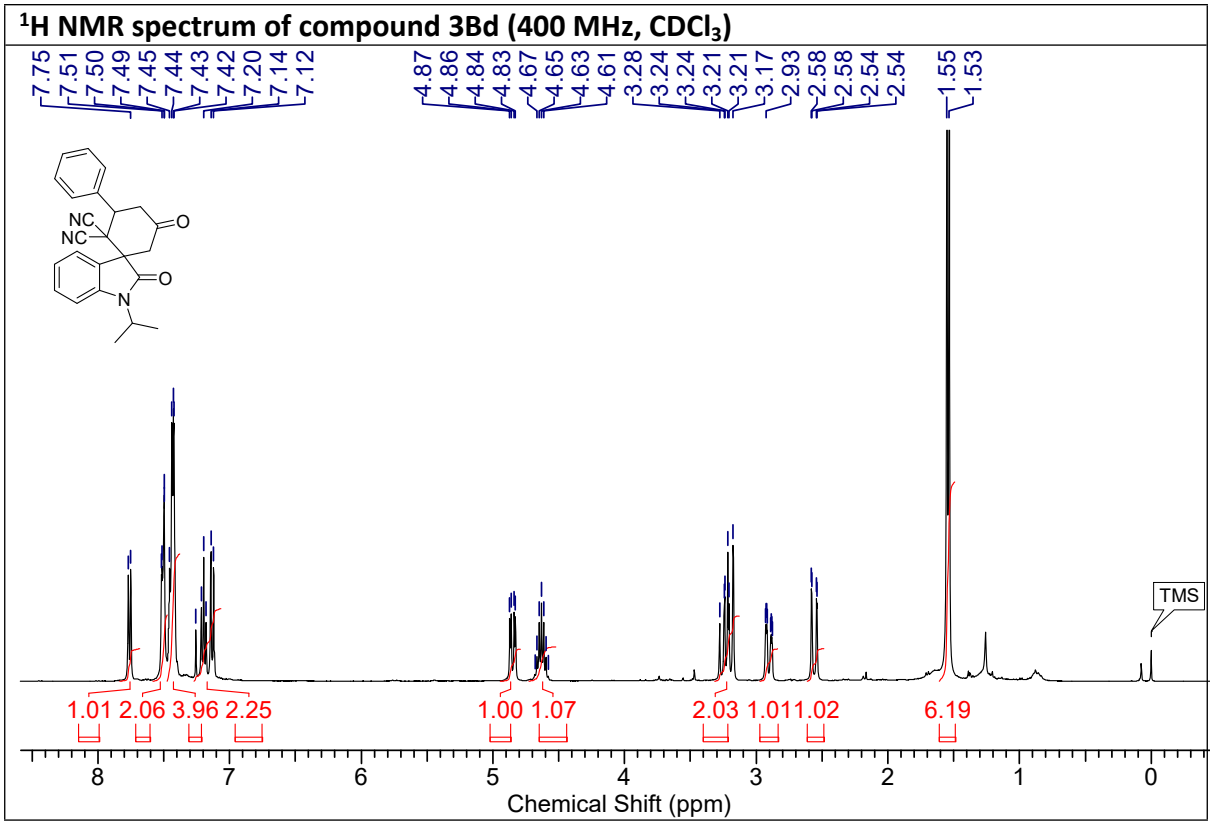


^{13}C NMR spectrum of compound 3Bc (125 MHz, $CDCl_3$)

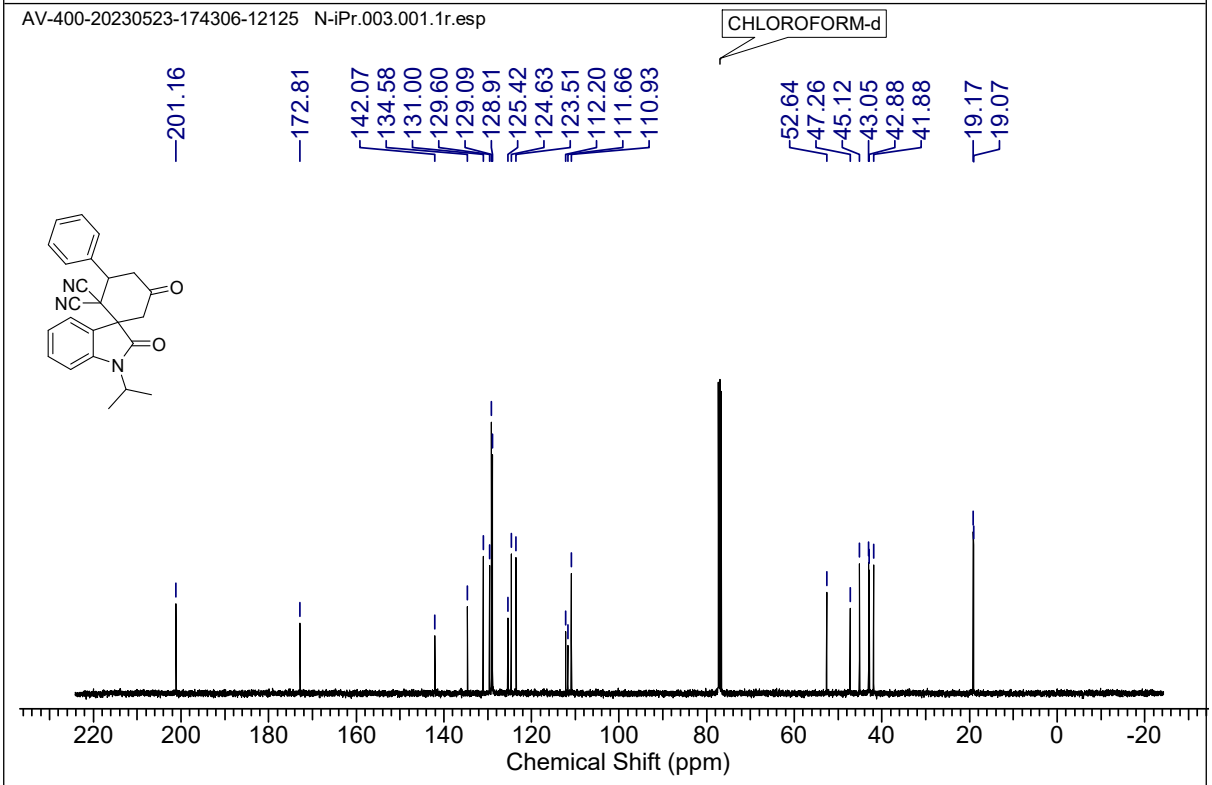


135 DEPT NMR spectrum of compound 3Bc

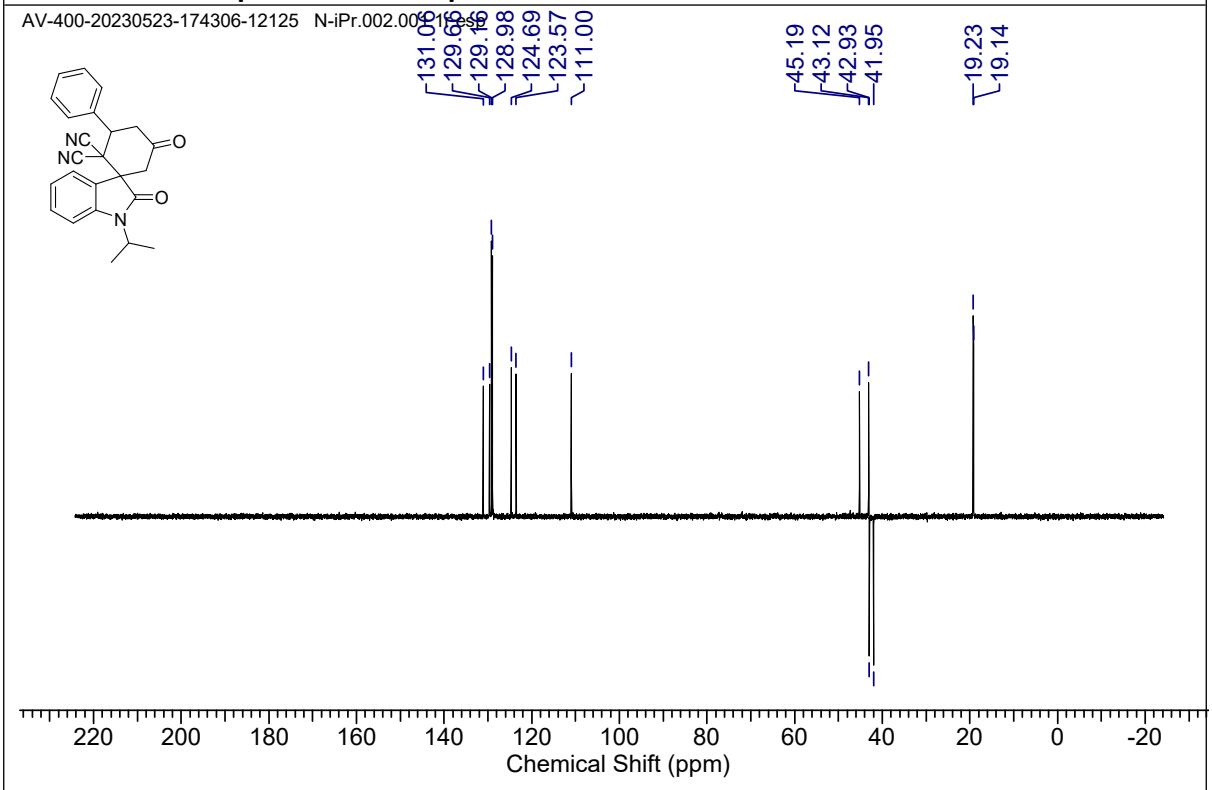

AV-500-20230523-174334-12125 N-Butyl.002.001
131.22
129.67
129.18
128.93
124.53
123.94
109.76
43.25
43.16
41.98
40.57
29.24
20.20
13.64
NC
NC
O
O
N
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)


¹H NMR spectrum of compound 3Bd (400 MHz, CDCl3)
7.75
7.51
7.50
7.49
7.45
7.44
7.43
7.42
7.20
7.14
7.12
4.87
4.86
4.84
4.83
4.67
4.65
4.63
4.61
3.28
3.24
3.24
3.21
3.21
3.17
2.93
2.58
2.58
2.54
2.54
1.55
1.53
NC
NC
O
O
N
TMS
1.01
2.06
3.96
2.25
1.00
1.07
2.03
1.01
1.02
6.19
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

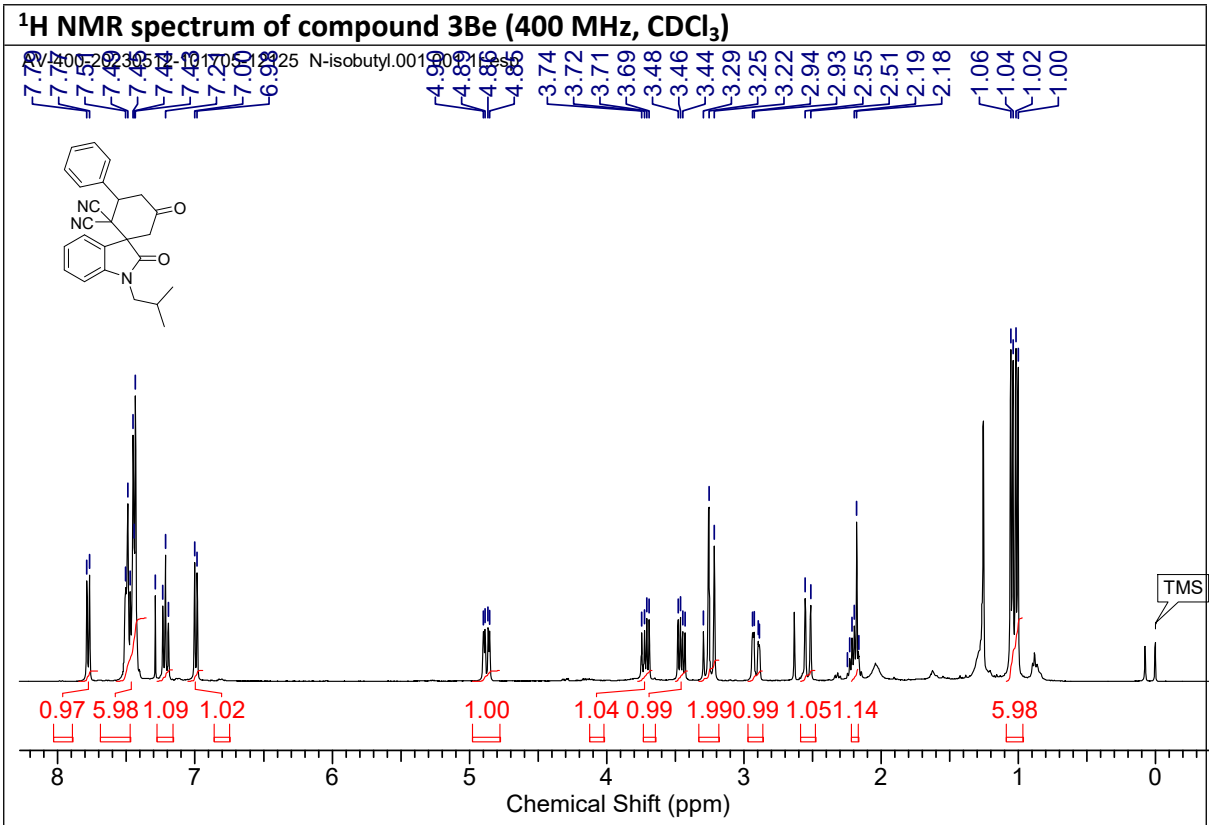
^{13}C NMR spectrum of compound 3Bd (101 MHz, $CDCl_3$)



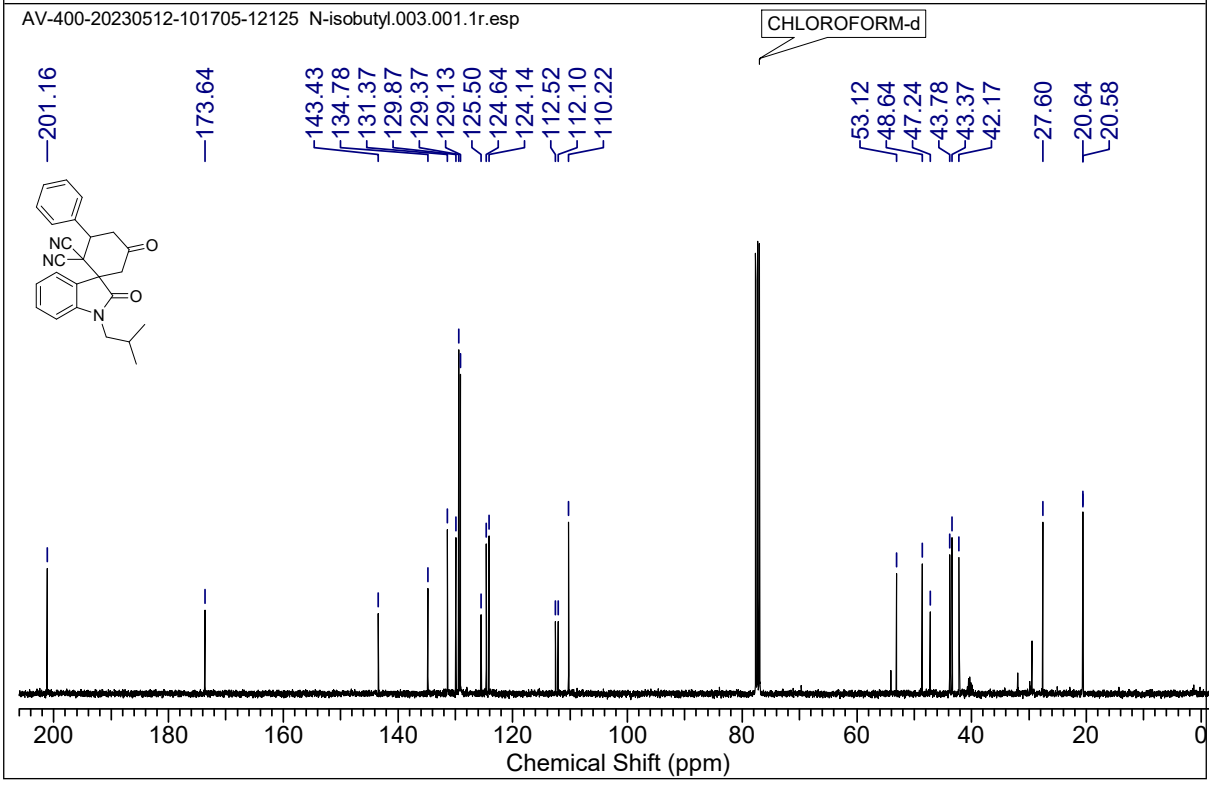
135 DEPT NMR spectrum of compound 3Bd



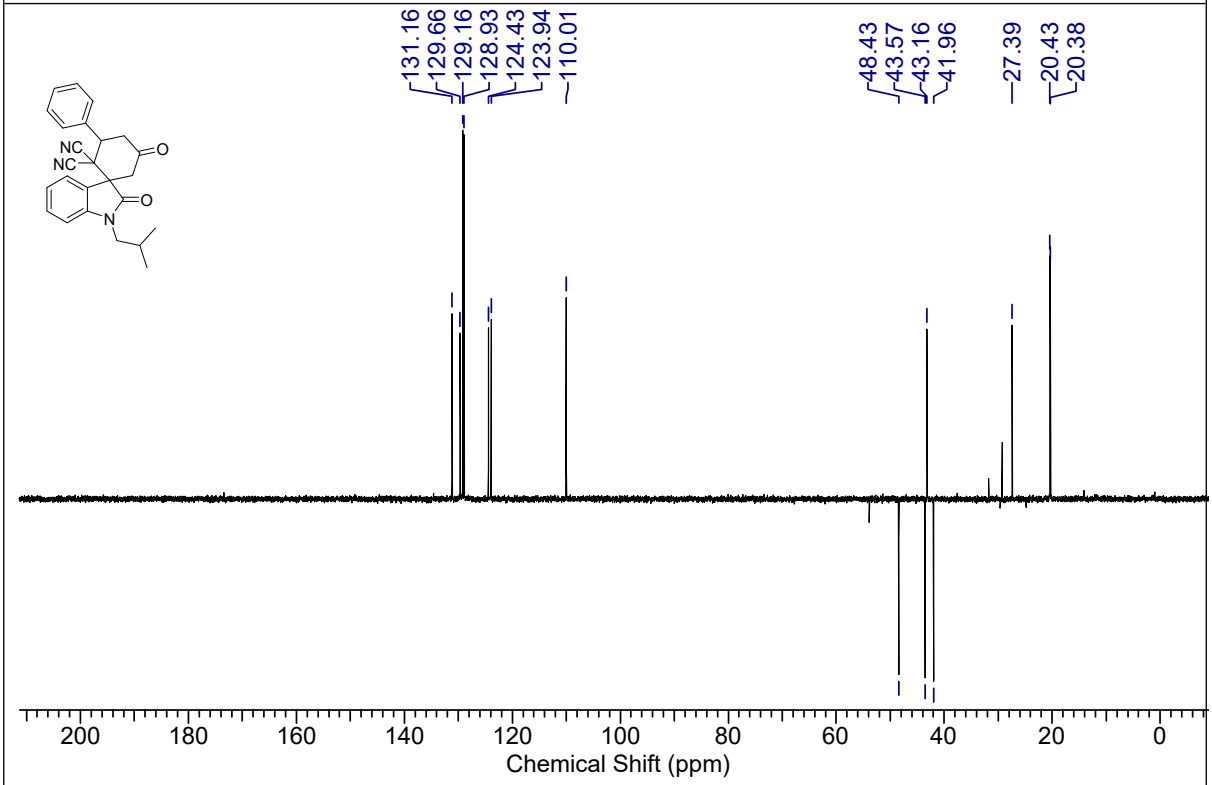
^{1}H NMR spectrum of compound 3Be (400 MHz, $CDCl_3$)



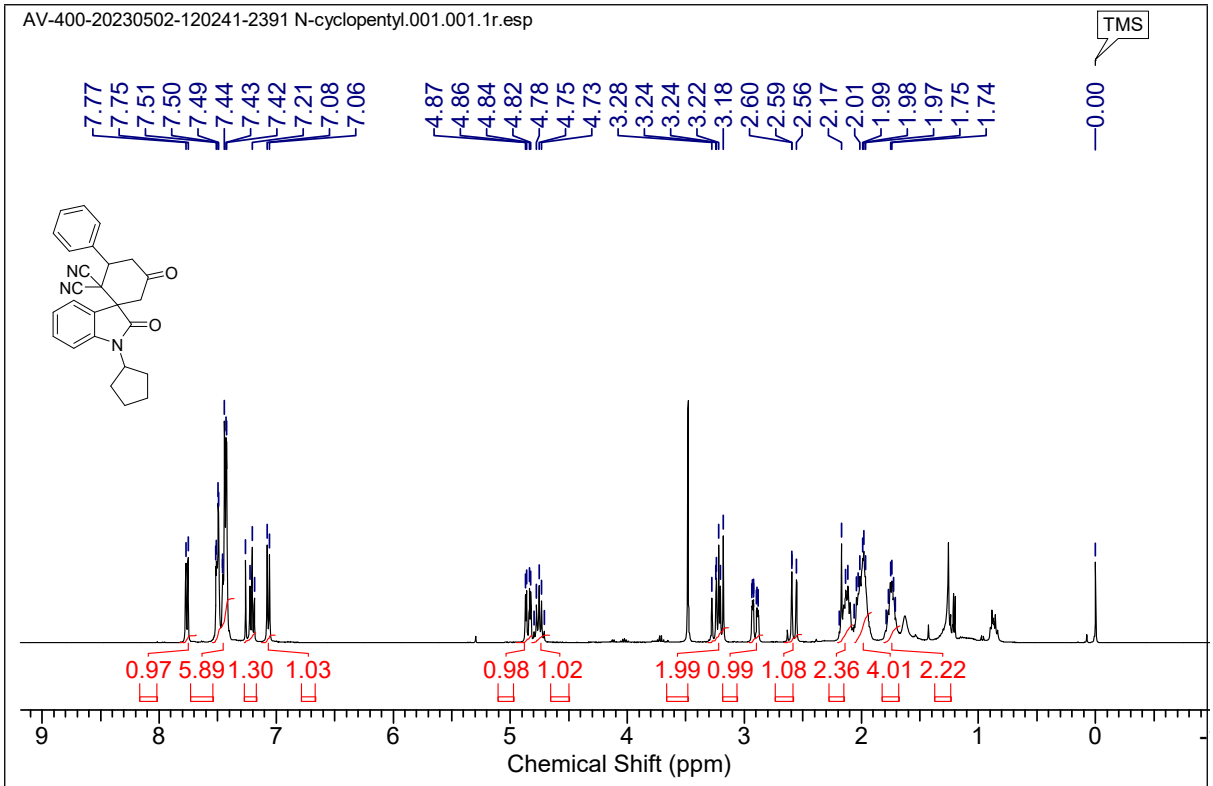
^{13}C NMR spectrum of compound 3Be (101 MHz, $CDCl_3$)



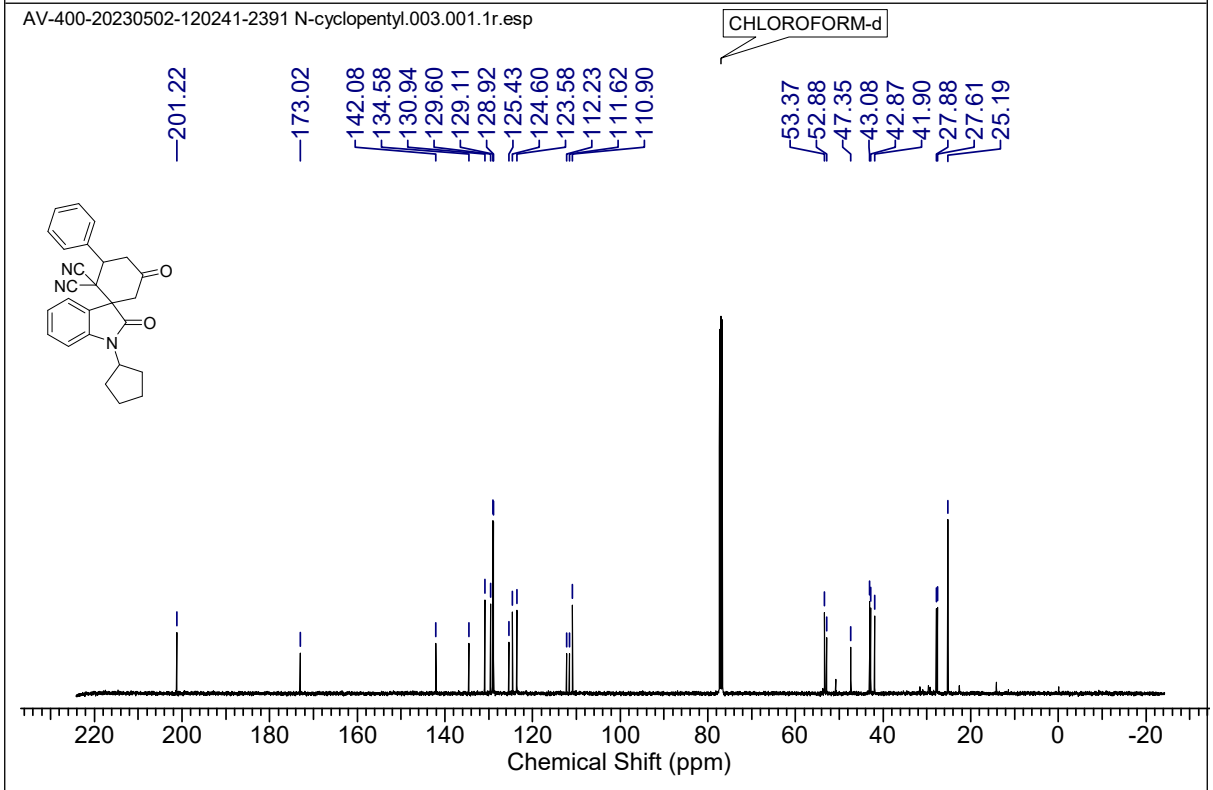
135 DEPT NMR spectrum of compound 3Be



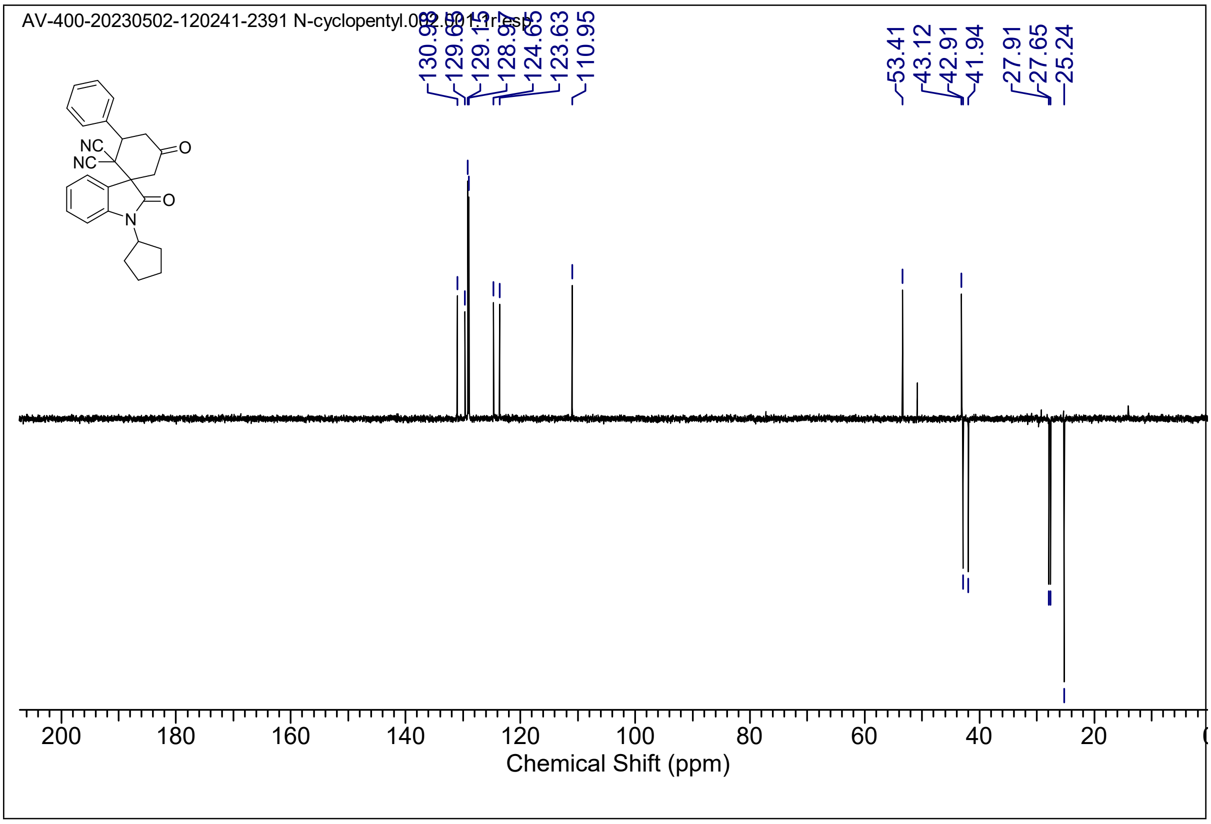
^{1}H NMR spectrum of compound 3Bf (400 MHz, $CDCl_3$)



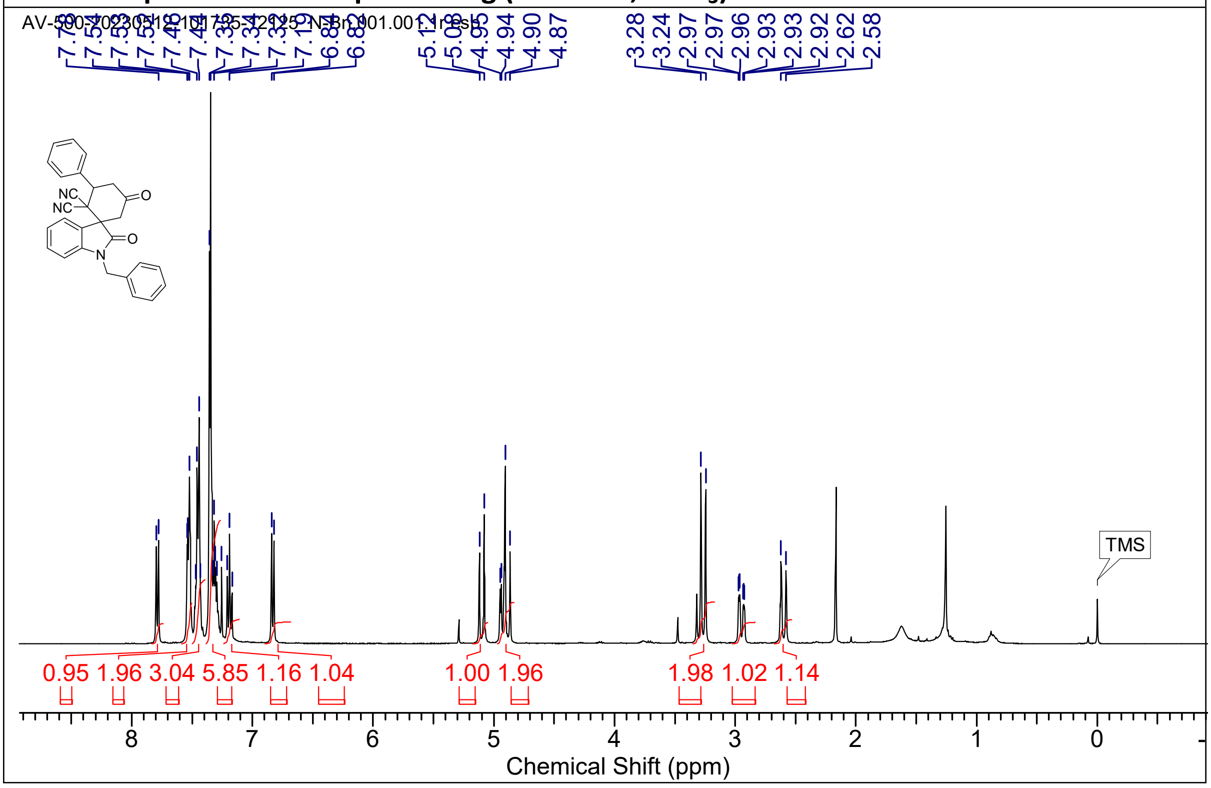
^{13}C NMR spectrum of compound 3Bf (101 MHz, $CDCl_3$)



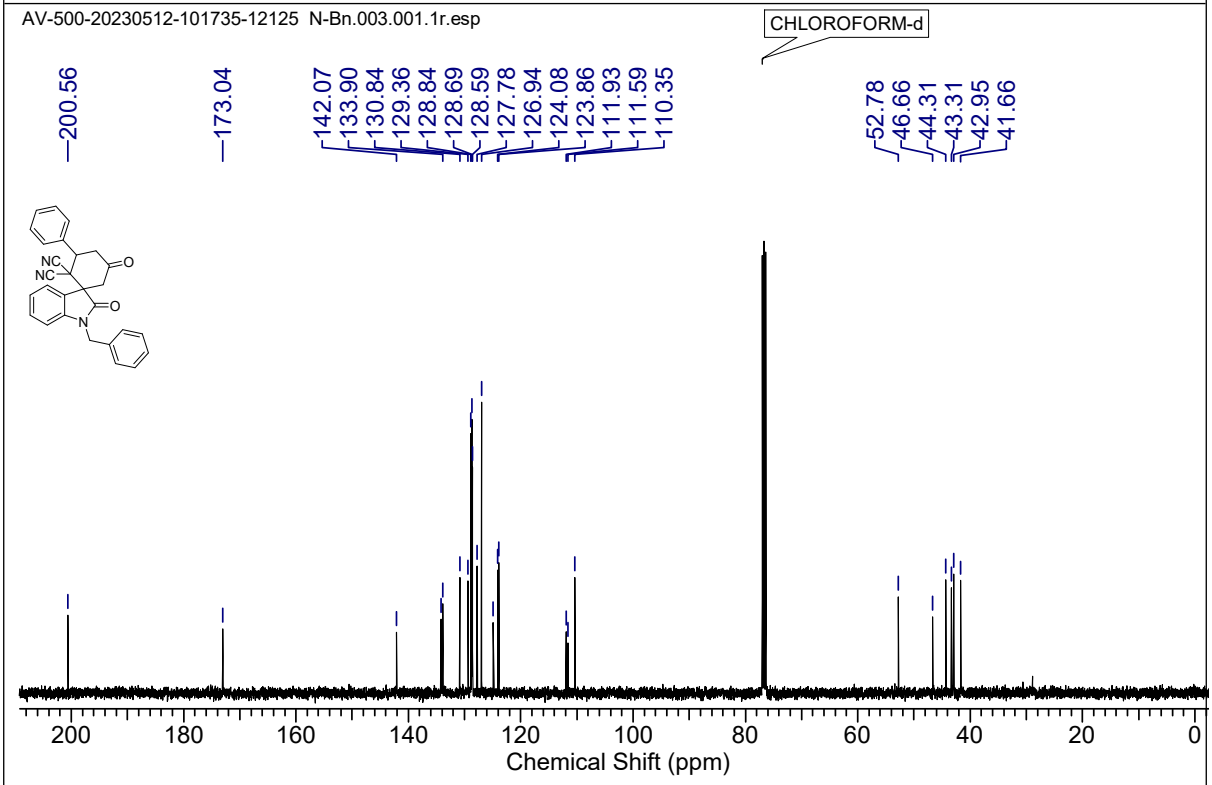
135 DEPT NMR spectrum of compound 3Bf



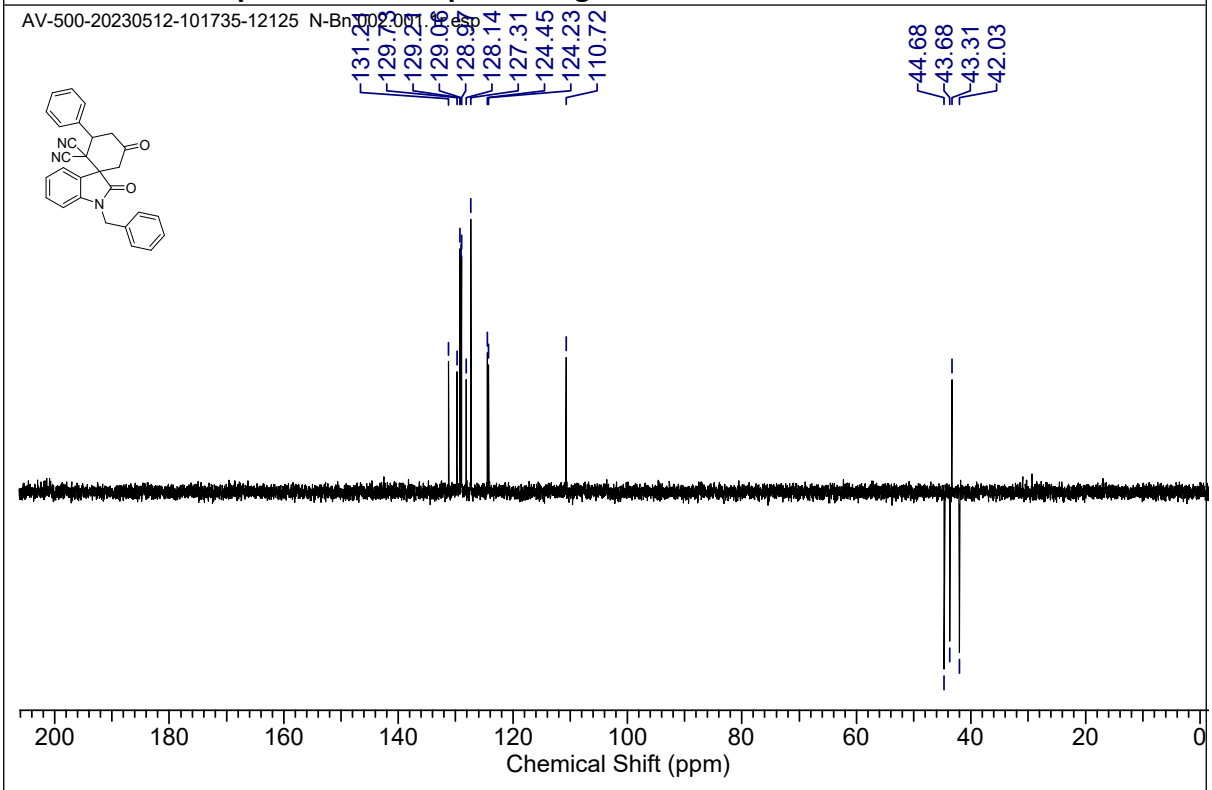
[1]H NMR spectrum of compound 3Bg (500 MHz, $CDCl_3$)



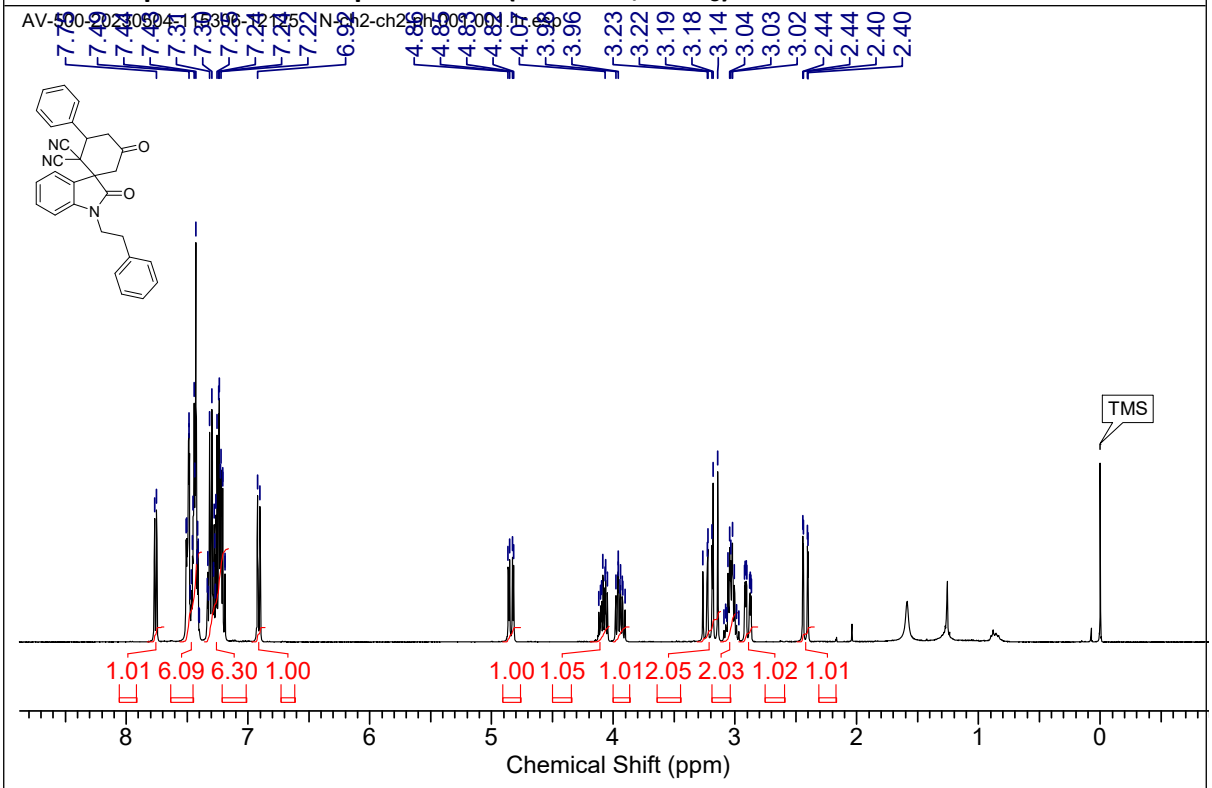
^{13}C NMR spectrum of compound 3Bg (125 MHz, $CDCl_3$)



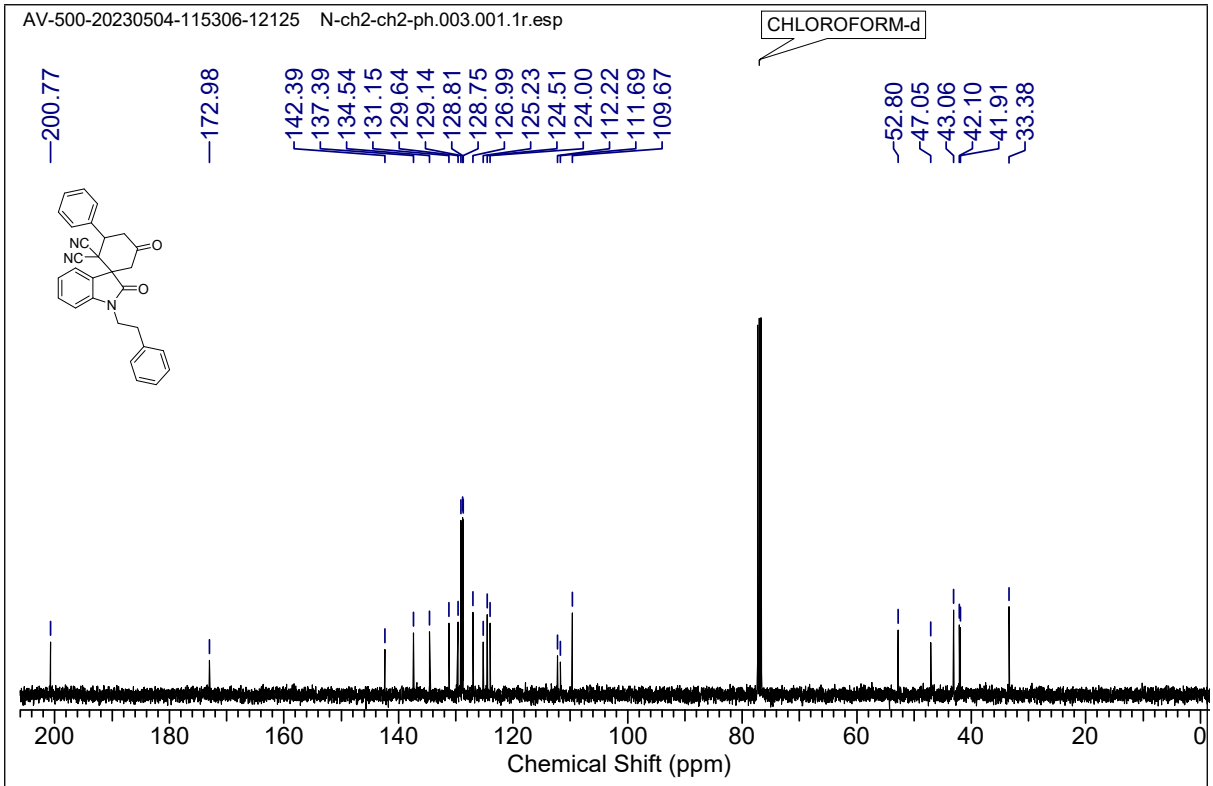
135 DEPT NMR spectrum of compound 3Bg



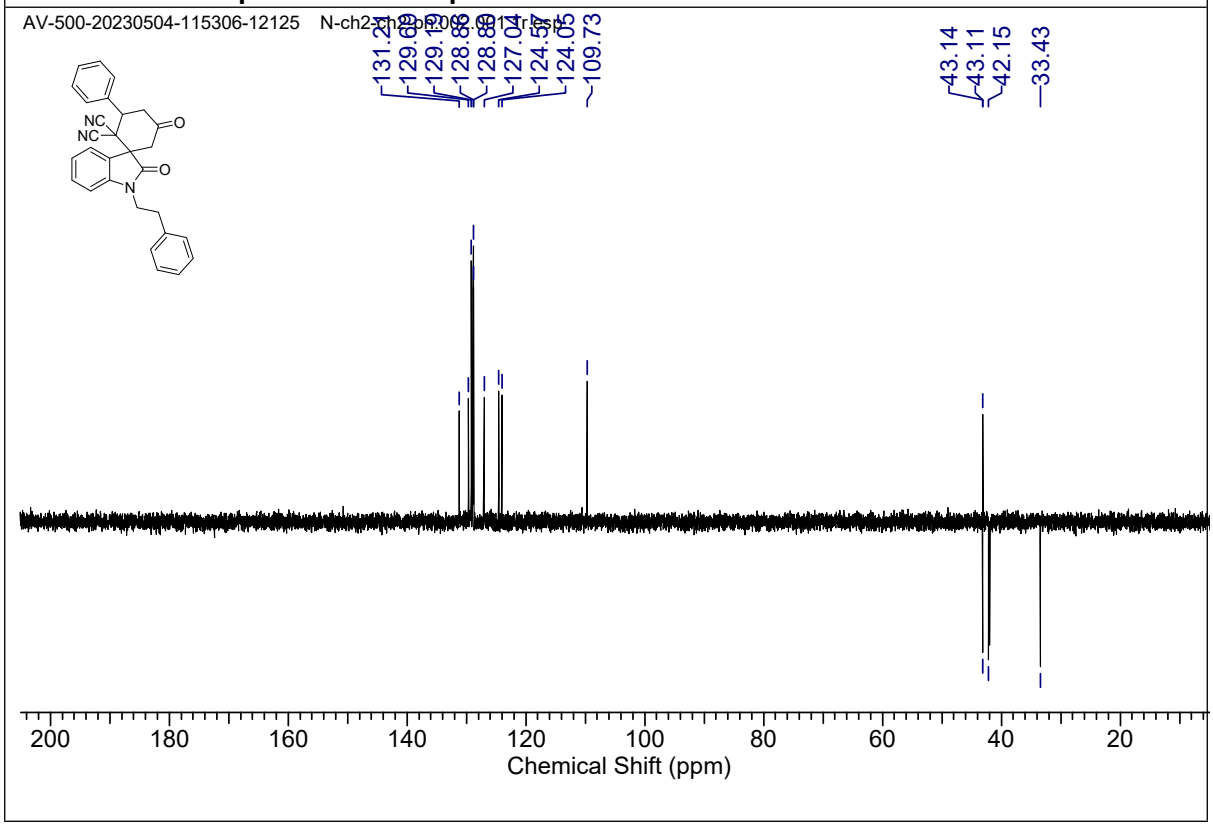
^{1}H NMR spectrum of compound 3Bh (500 MHz, $CDCl_3$)



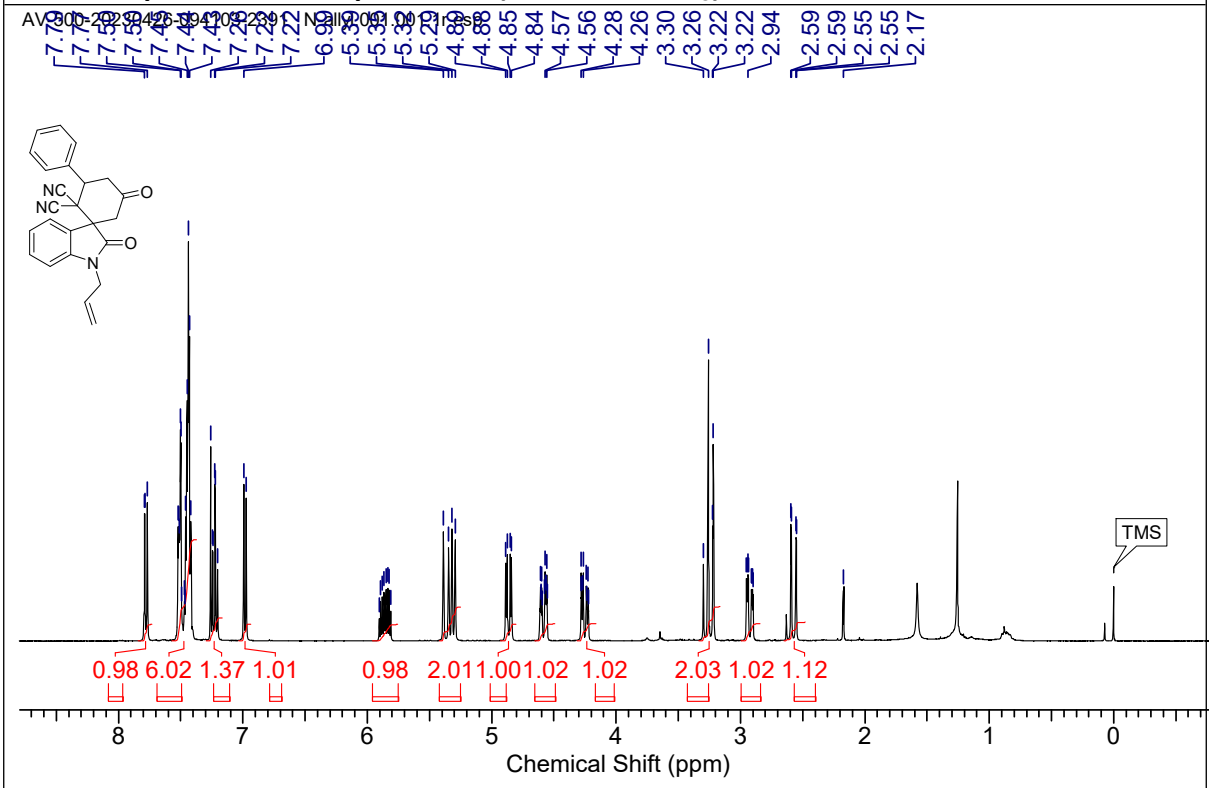
^{13}C NMR spectrum of compound 3Bh (125 MHz, $CDCl_3$)



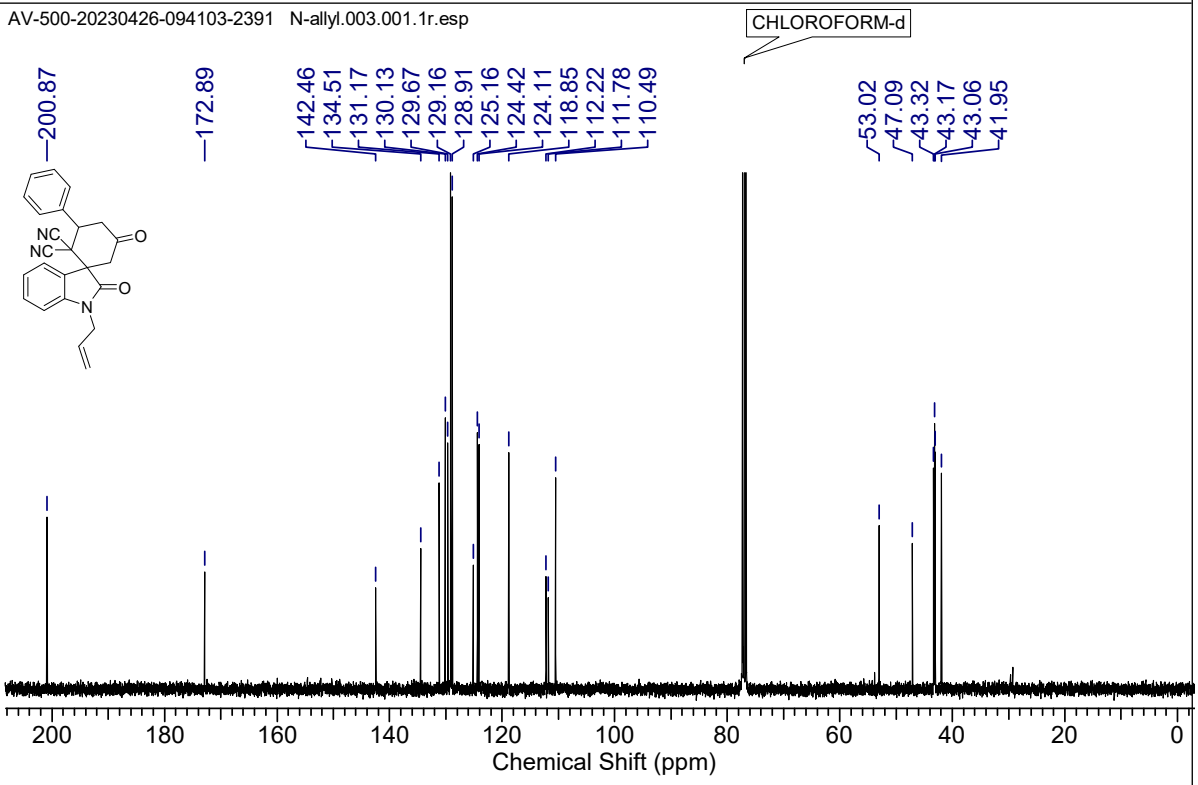
135 DEPT NMR spectrum of compound 3Bh



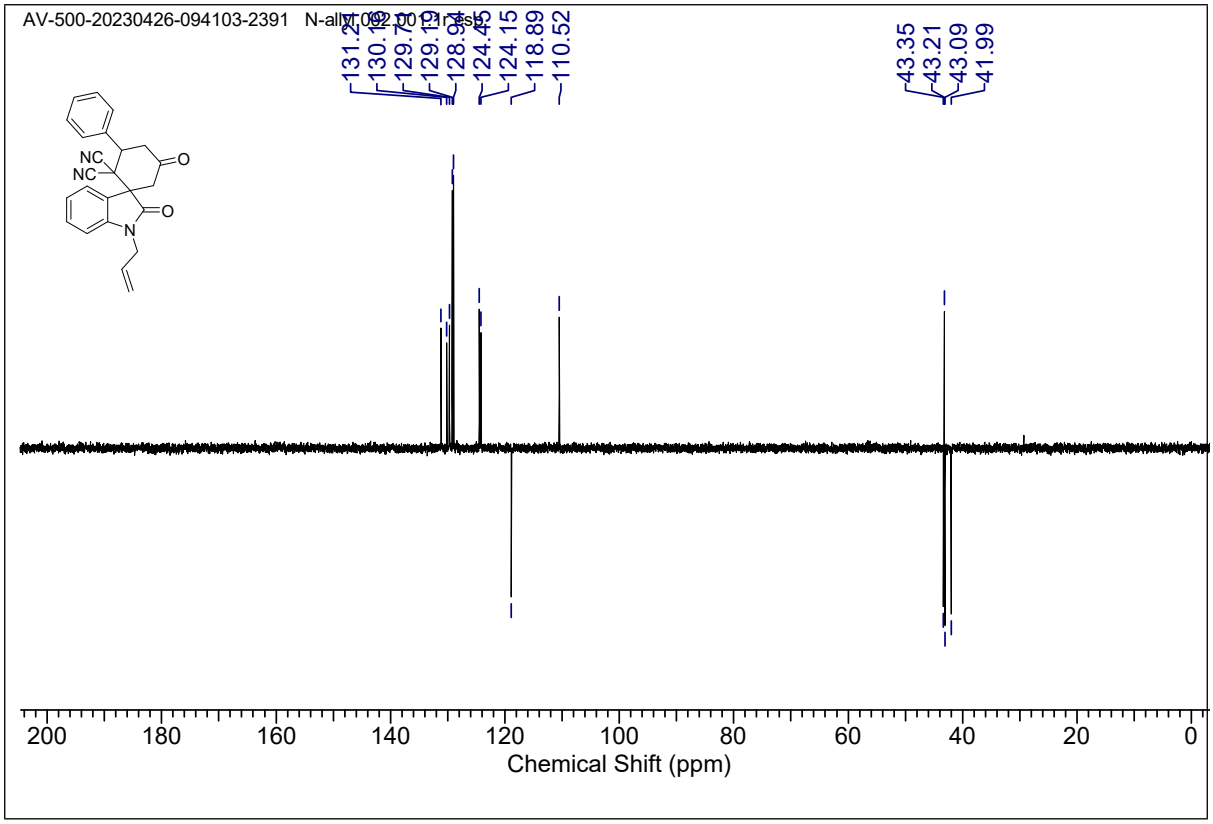
^{1}H NMR spectrum of compound 3Bi (500 MHz, $CDCl_3$)



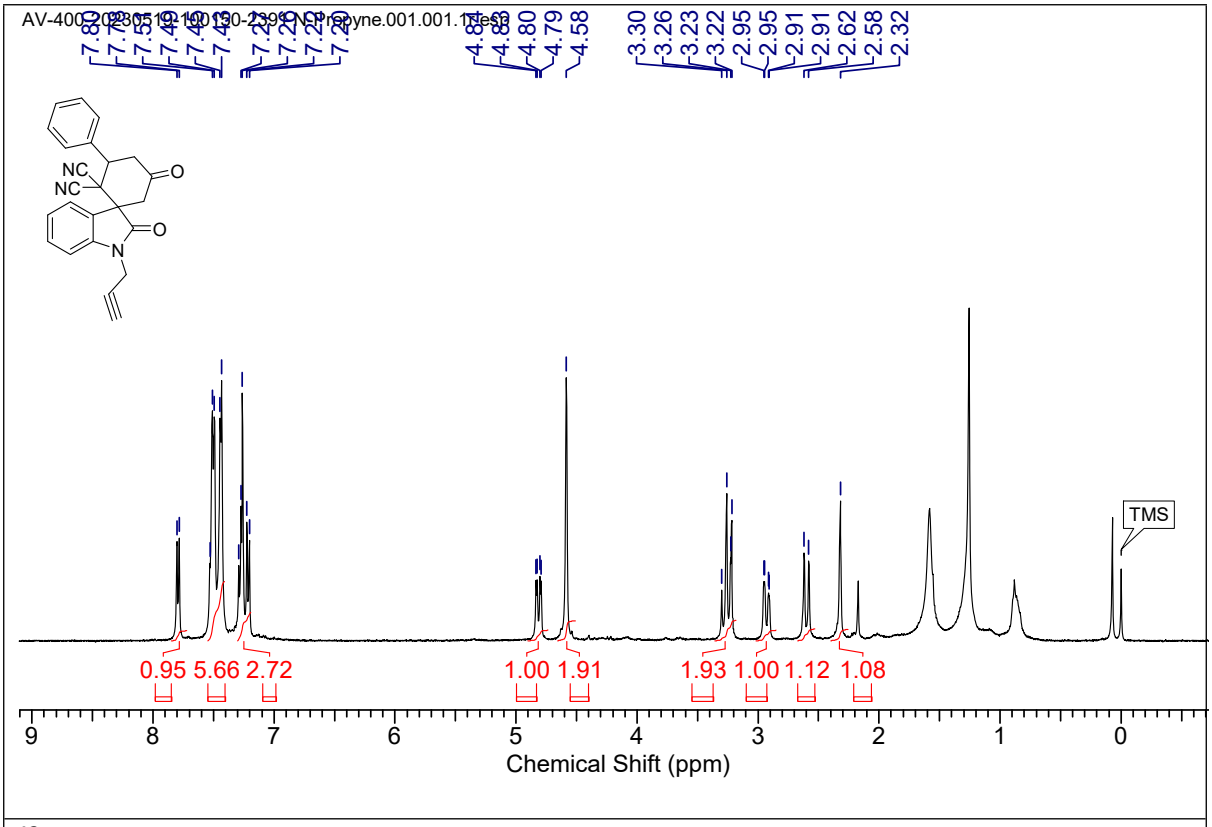
^{13}C NMR spectrum of compound 3Bi (125 MHz, $CDCl_3$)



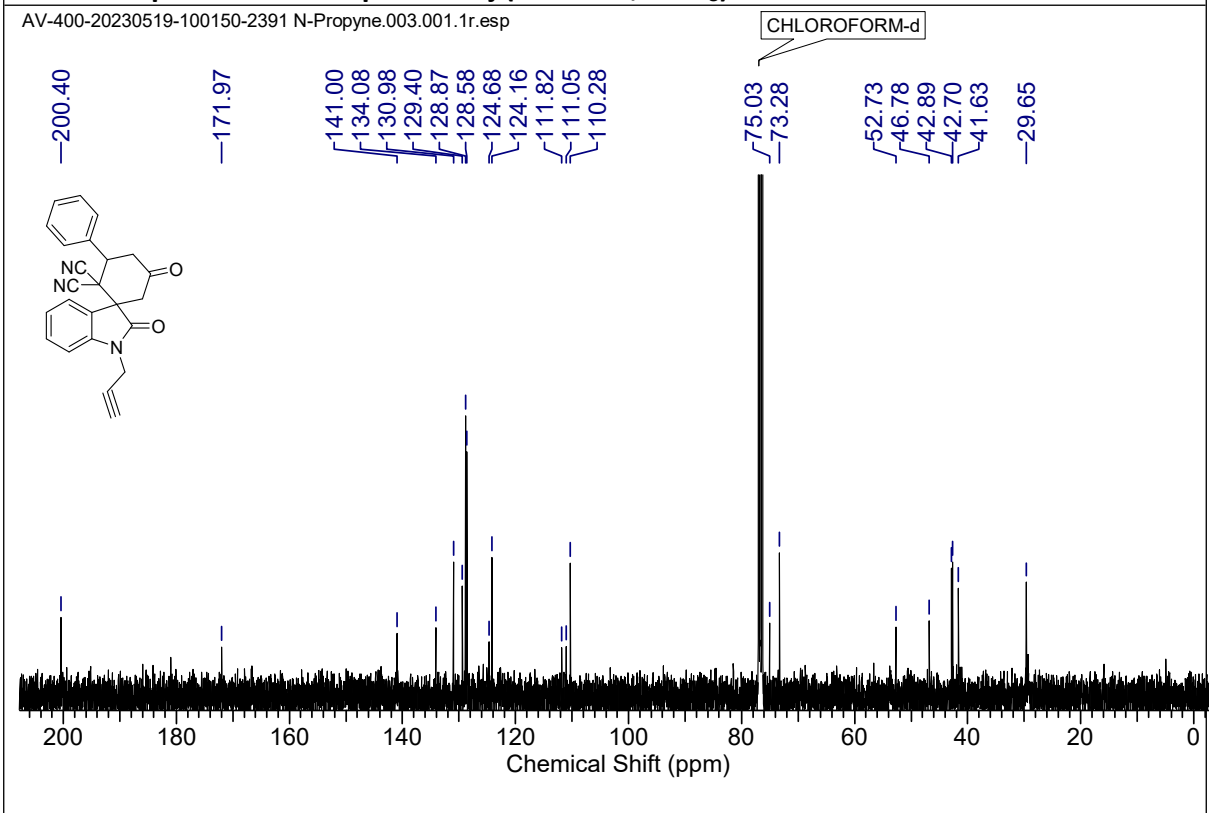
135 DEPT NMR spectrum of compound 3Bi



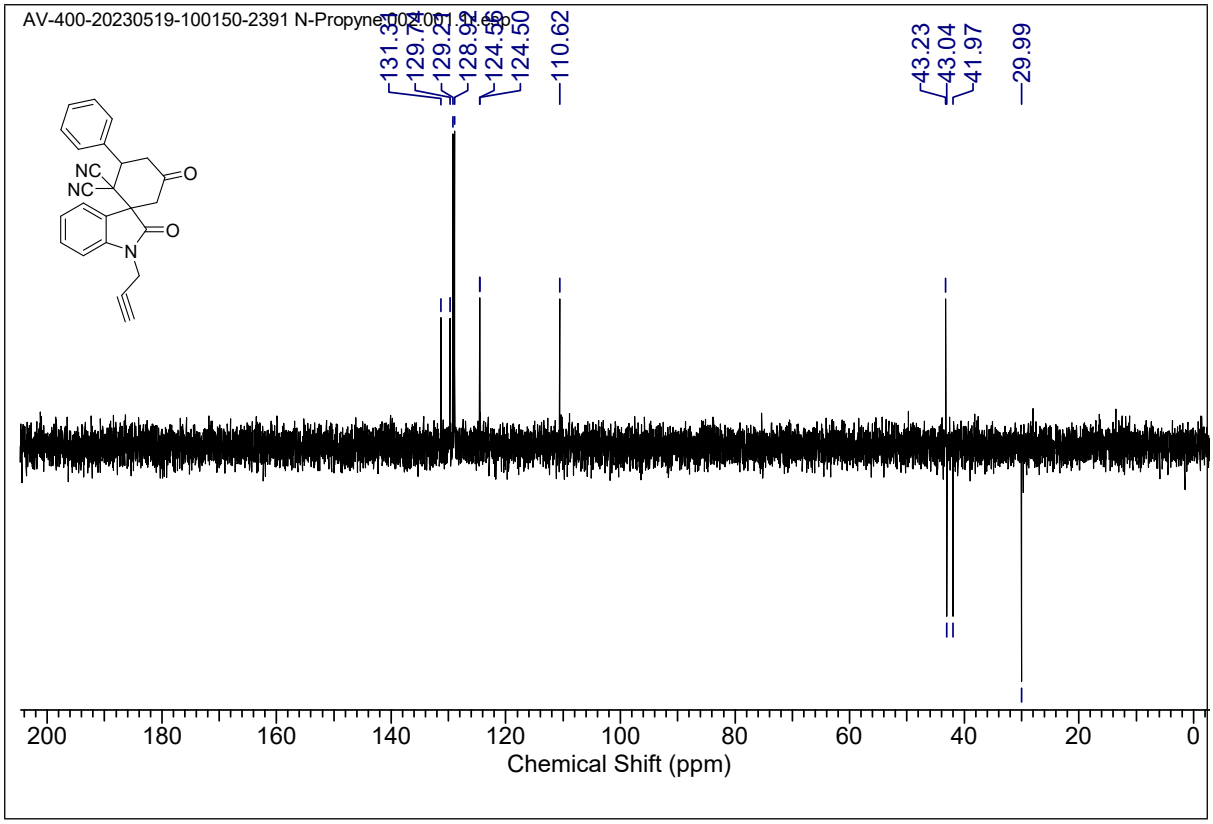
^{1}H NMR spectrum of compound 3Bj (400 MHz, $CDCl_3$)



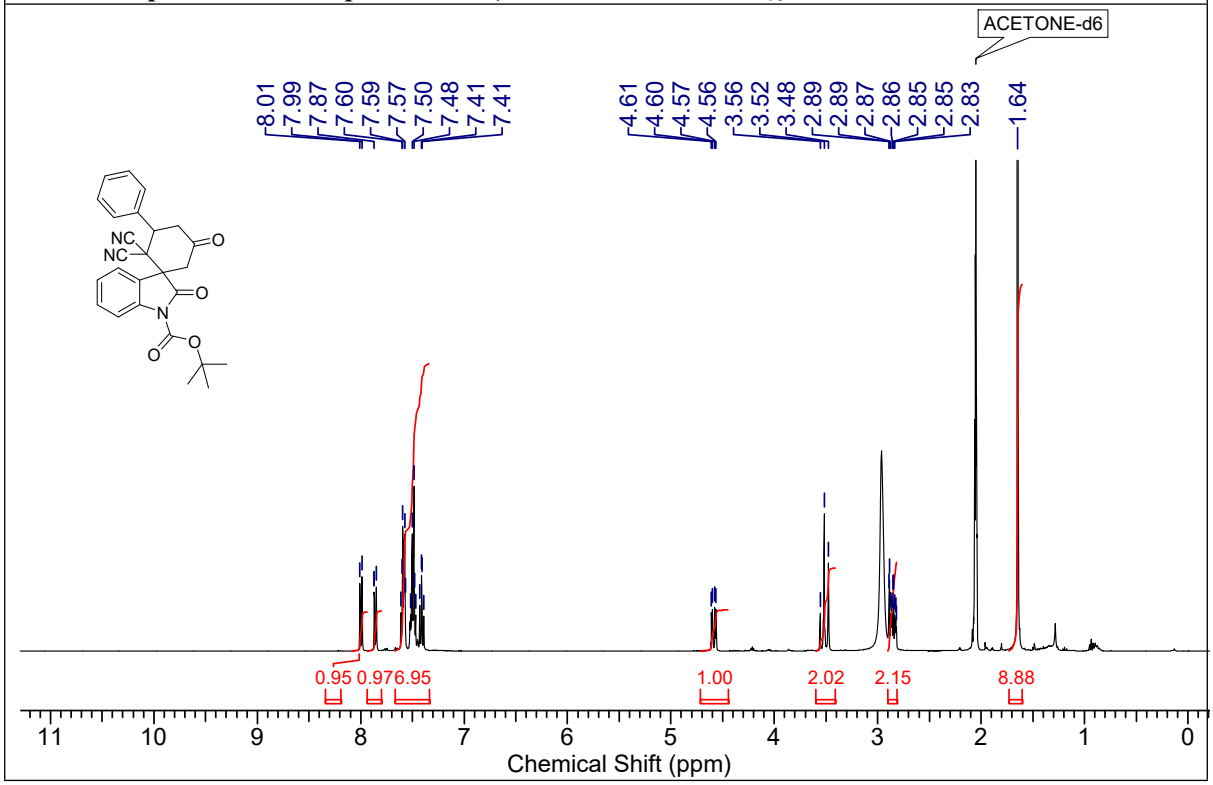
^{13}C NMR spectrum of compound 3Bj (101 MHz, $CDCl_3$)



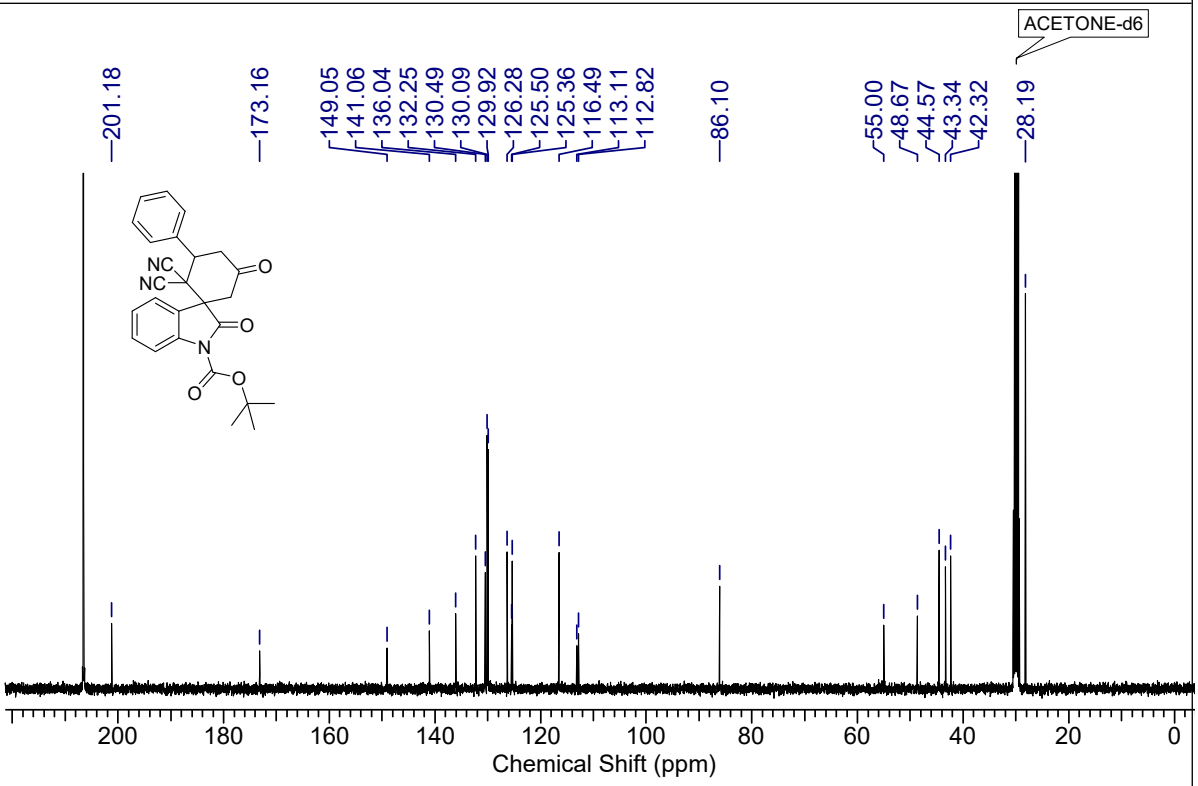
135 DEPT NMR spectrum of compound 3Bj



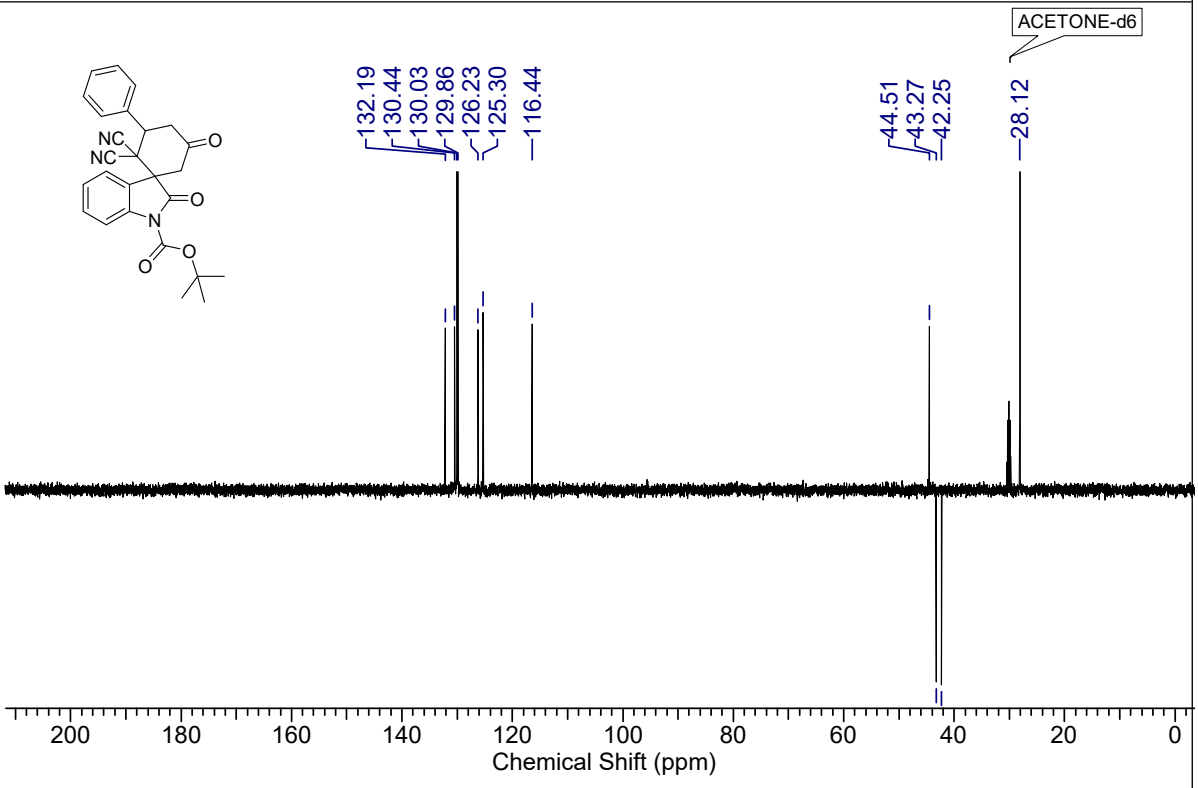
^{1}H NMR spectrum of compound 3Bk (400 MHz, Acetone-d_6)



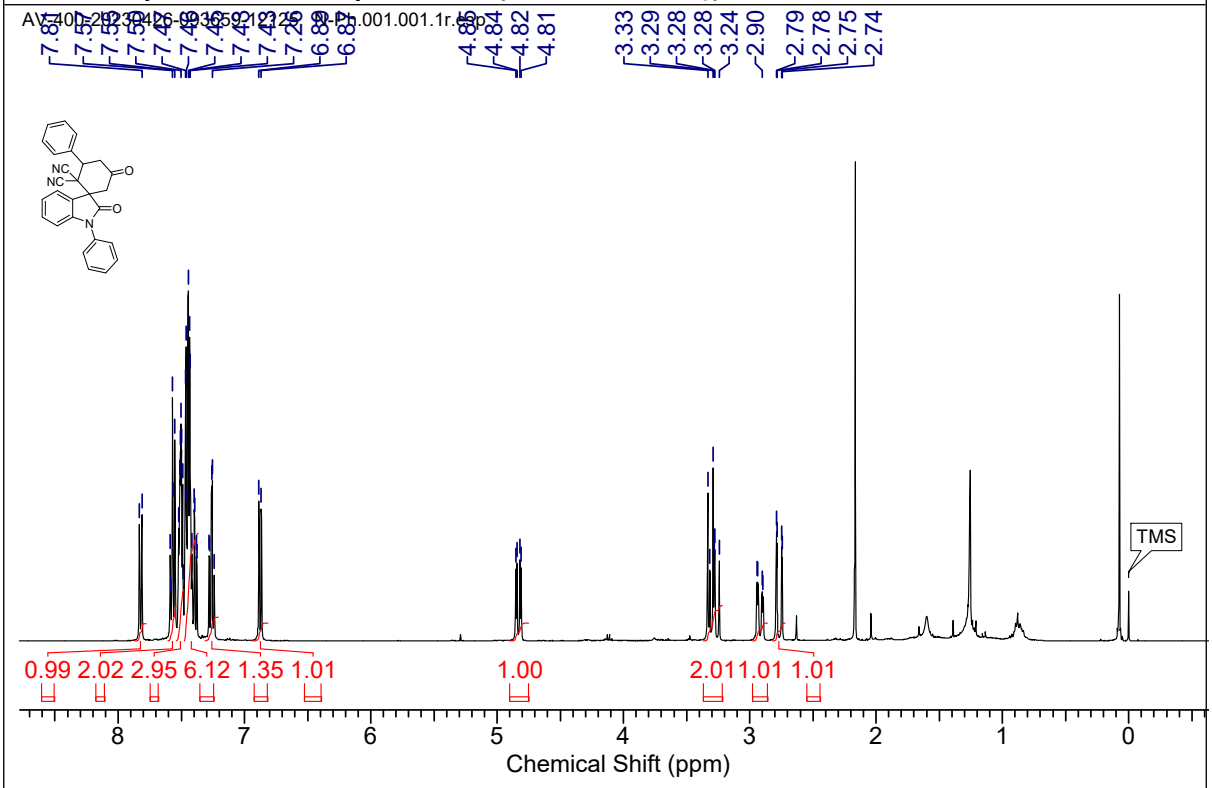
^{13}C NMR spectrum of compound 3Bk (101 MHz, Acetone-d_6)



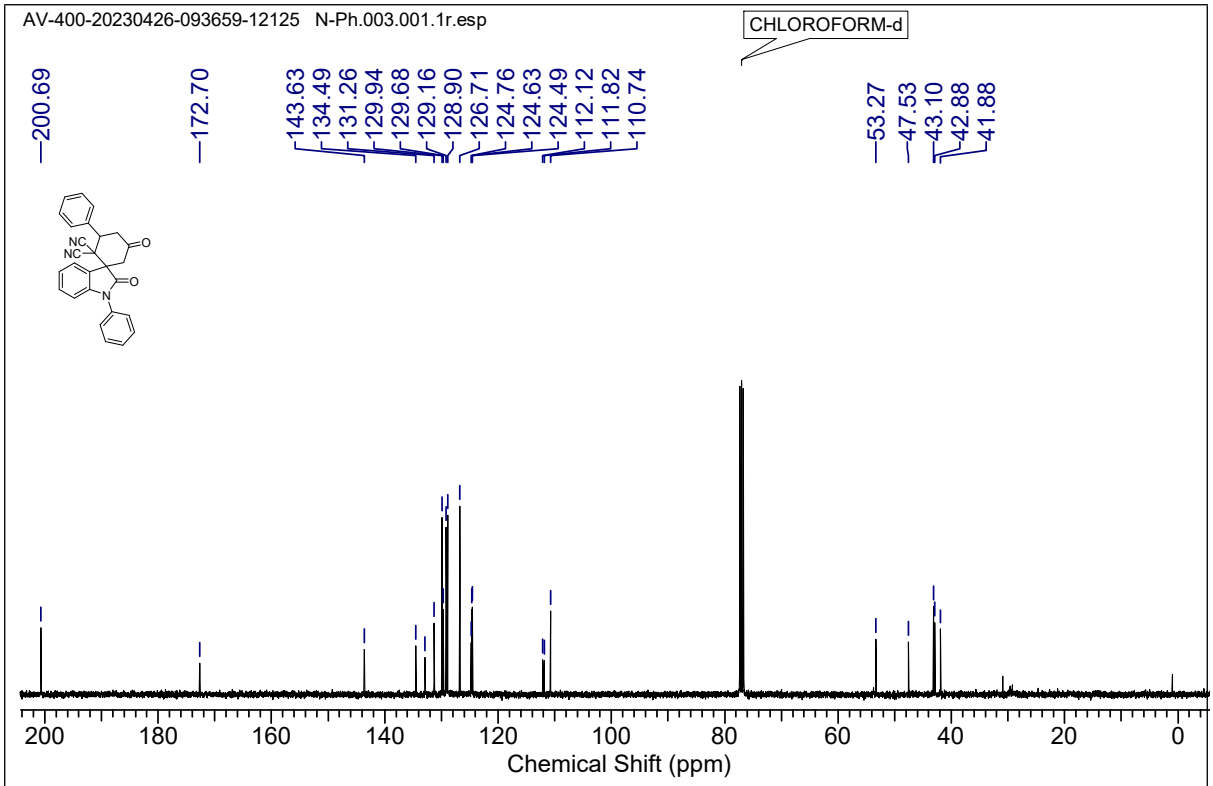
135 DEPT NMR spectrum of compound 3Bk



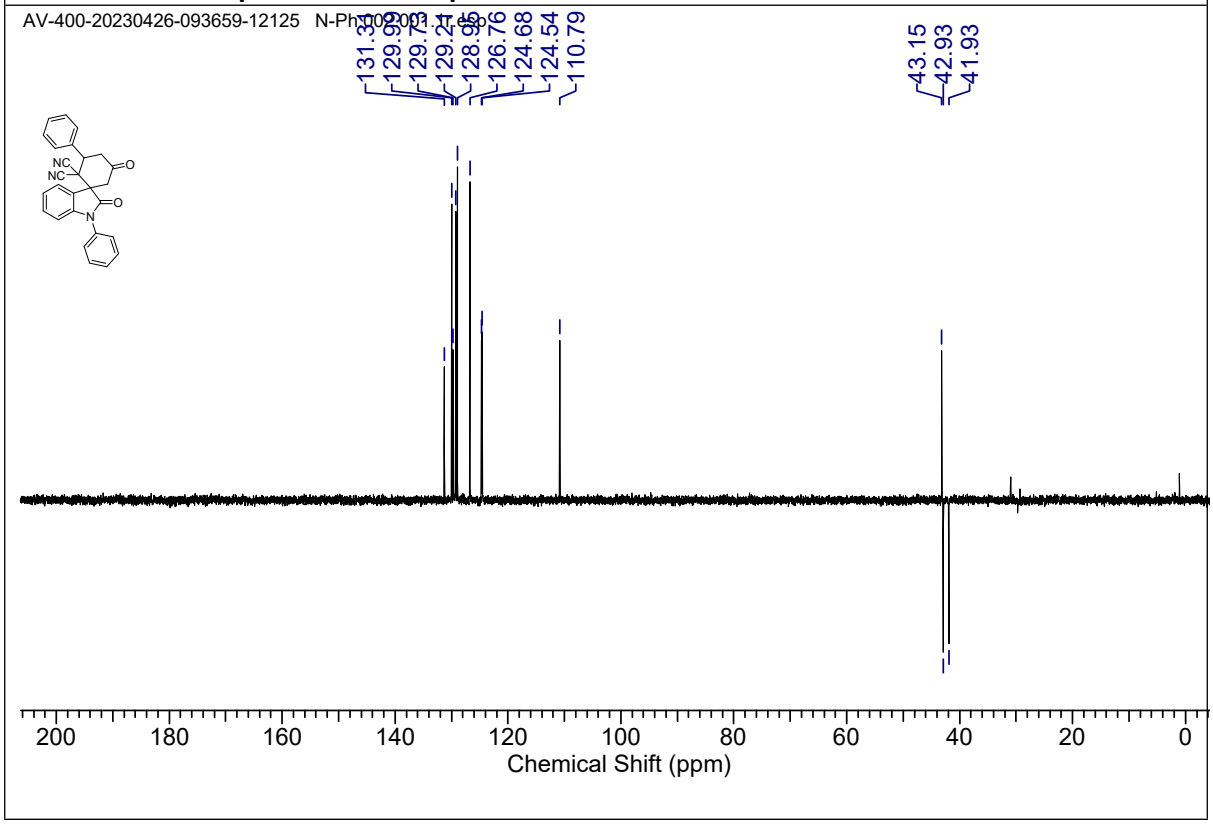
^{1}H NMR spectrum of compound 3Bl (400 MHz, $CDCl_3$)



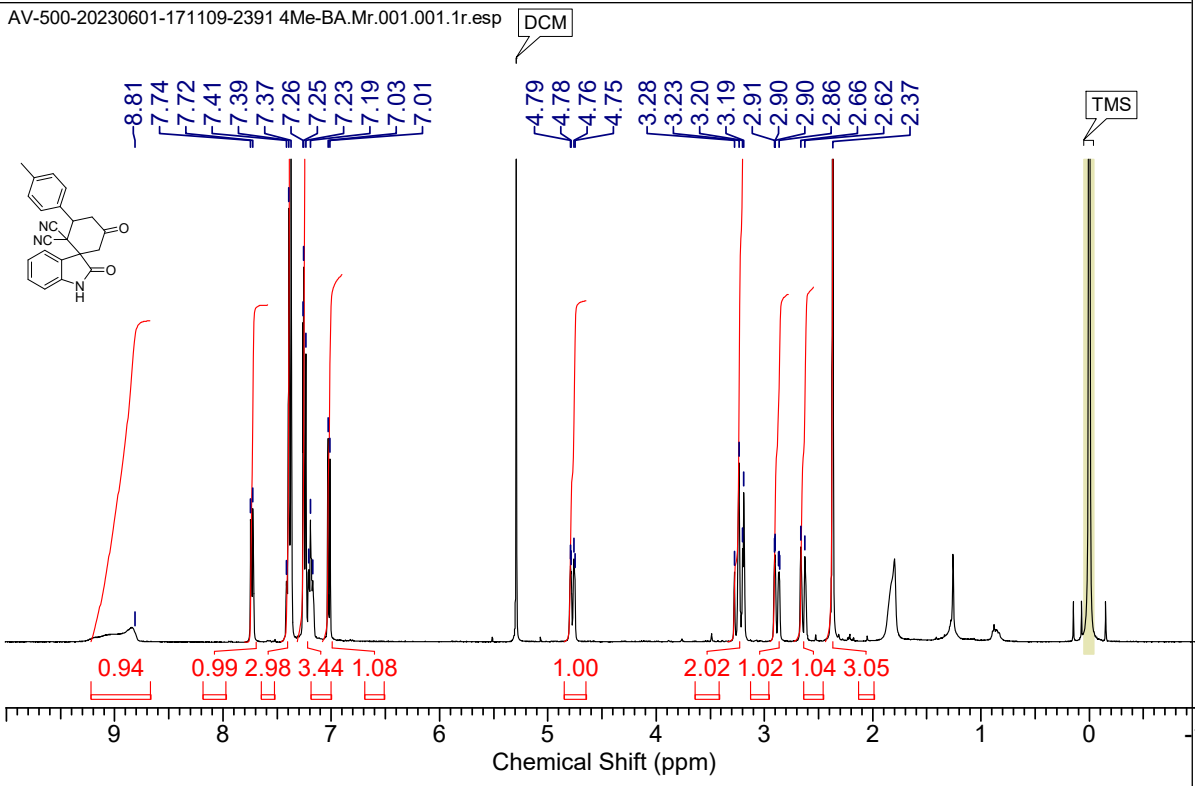
^{13}C NMR spectrum of compound 3Bl (101 MHz, $CDCl_3$)



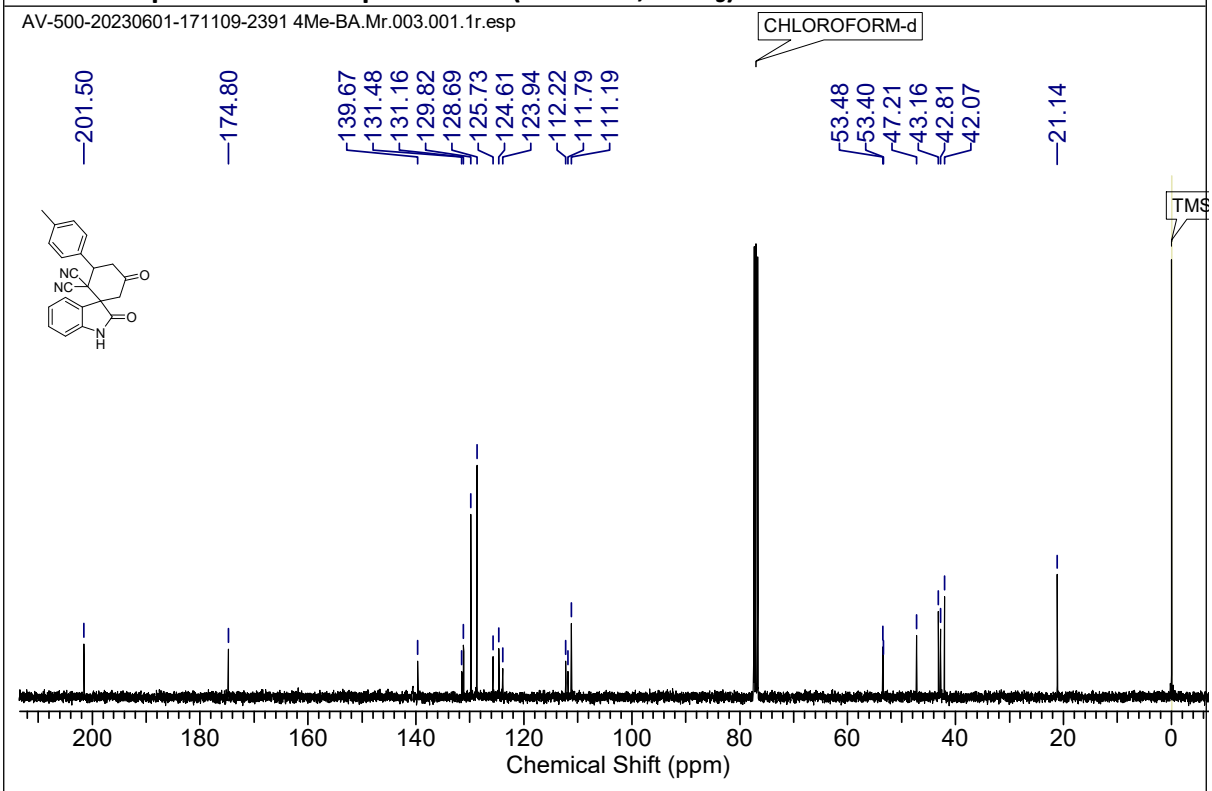
135 DEPT NMR spectrum of compound 3Bl



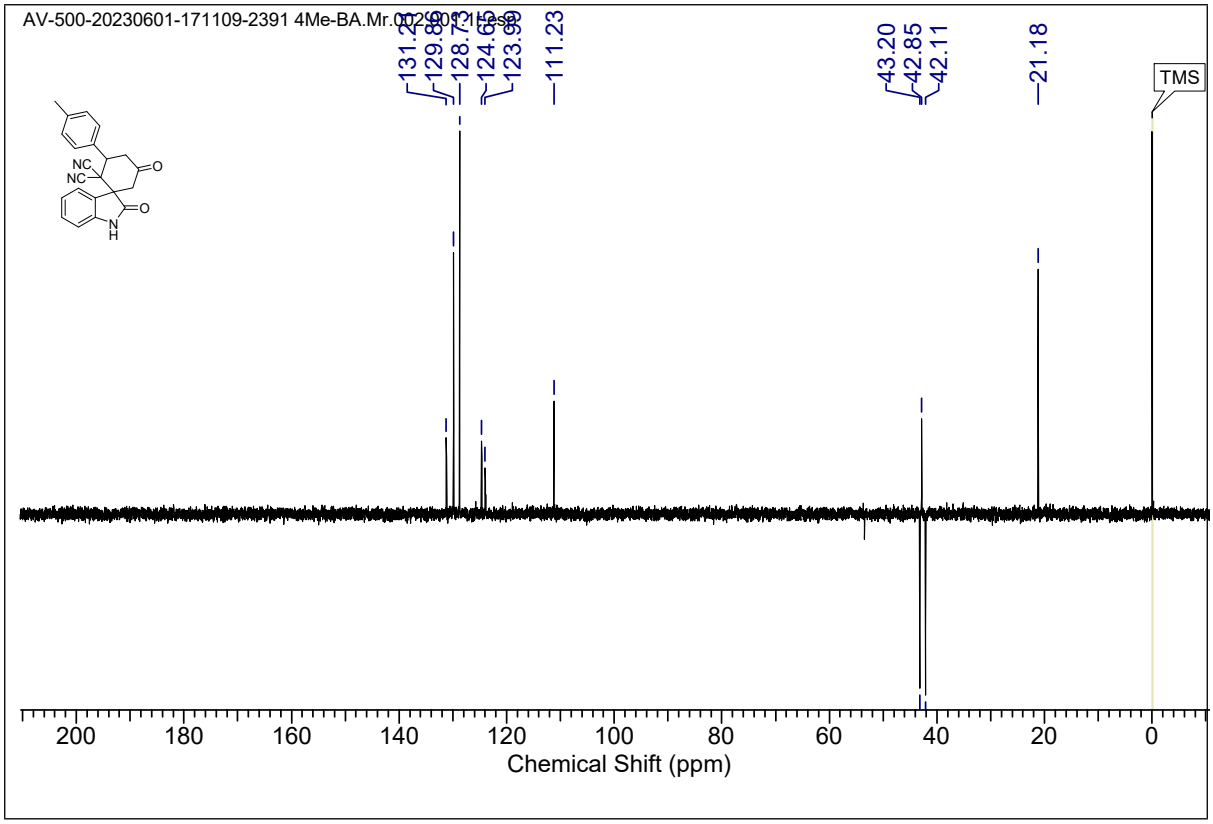
^{1}H NMR spectrum of compound 3Ca (500 MHz, $CDCl_3$)

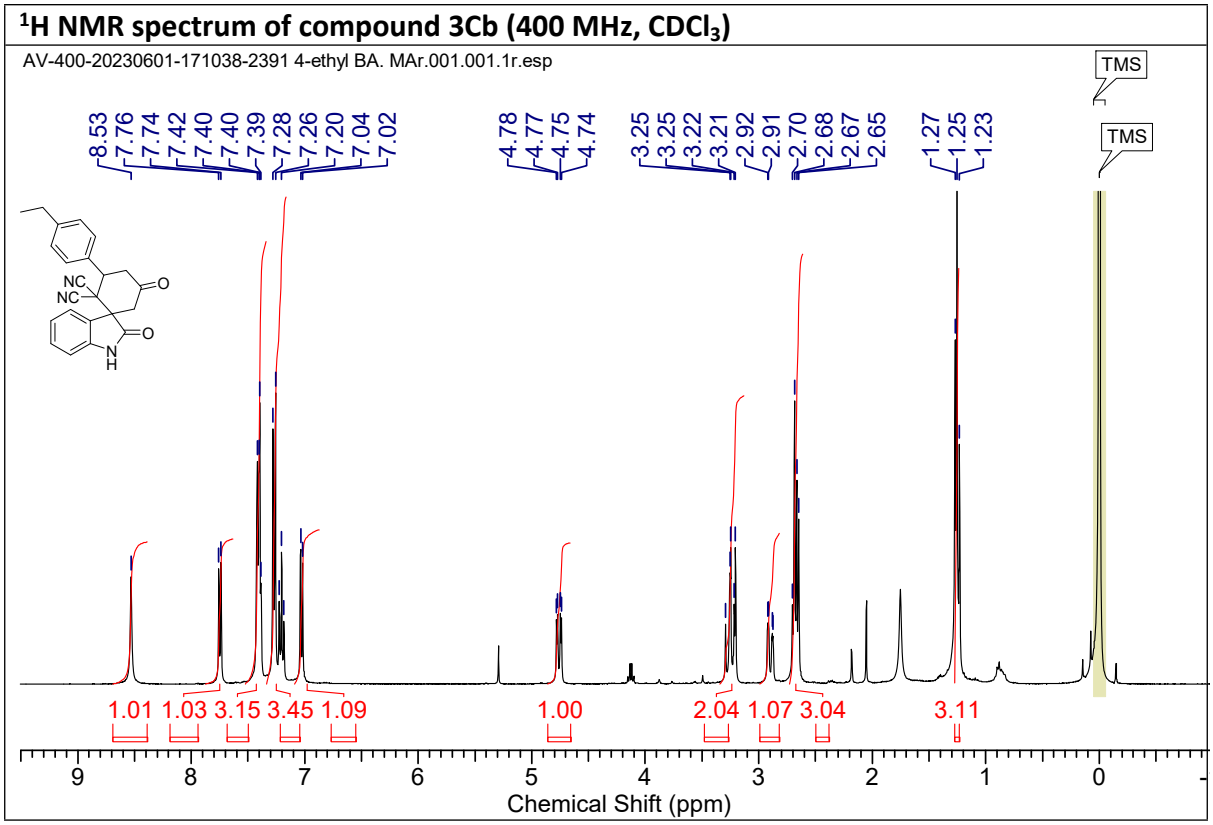


^{13}C NMR spectrum of compound 3Ca (125 MHz, $CDCl_3$)

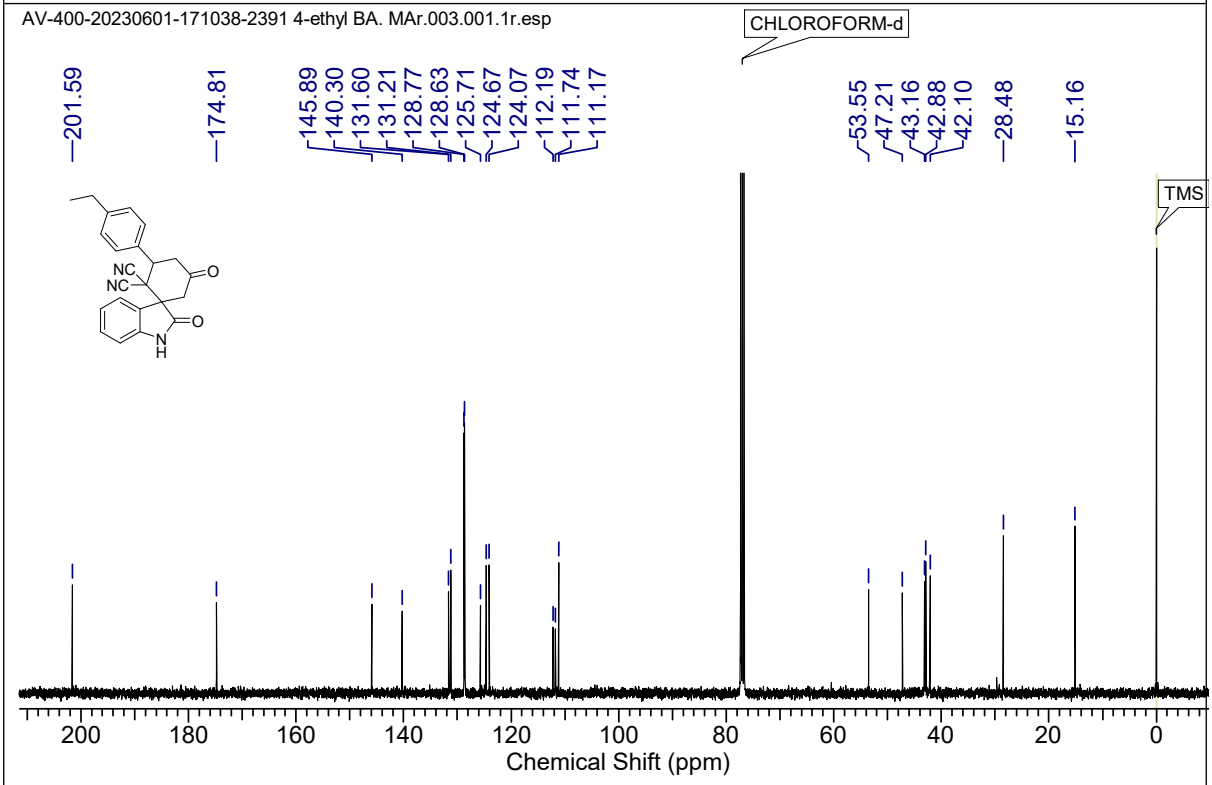


135 DEPT NMR spectrum of compound 3Ca

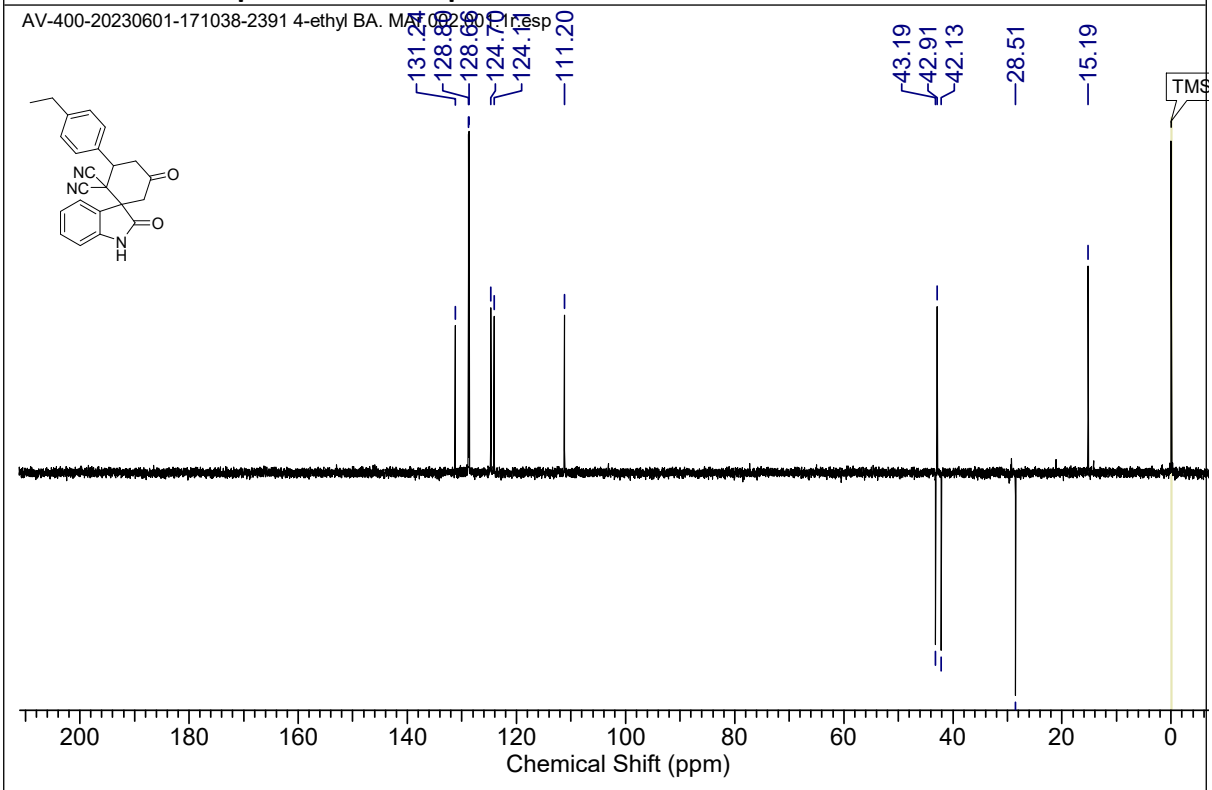

AV-500-20230601-171109-2391 4Me-BA.Mr.002.001.1.esp
131.22
129.88
128.73
124.65
123.99
111.23
43.20
42.85
42.11
21.18
TMS
NC
NC
O
O
N
H
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


¹H NMR spectrum of compound 3Cb (400 MHz, CDCl3)
AV-400-20230601-171038-2391 4-ethyl BA. MAr.001.001.1r.esp
TMS
TMS
8.53
7.76
7.74
7.42
7.40
7.40
7.39
7.28
7.26
7.20
7.04
7.02
4.78
4.77
4.75
4.74
3.25
3.25
3.22
3.21
2.92
2.91
2.70
2.68
2.67
2.65
1.27
1.25
1.23
NC
NC
O
O
N
H
1.01
1.03
3.15
3.45
1.09
1.00
2.04
1.07
3.04
3.11
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

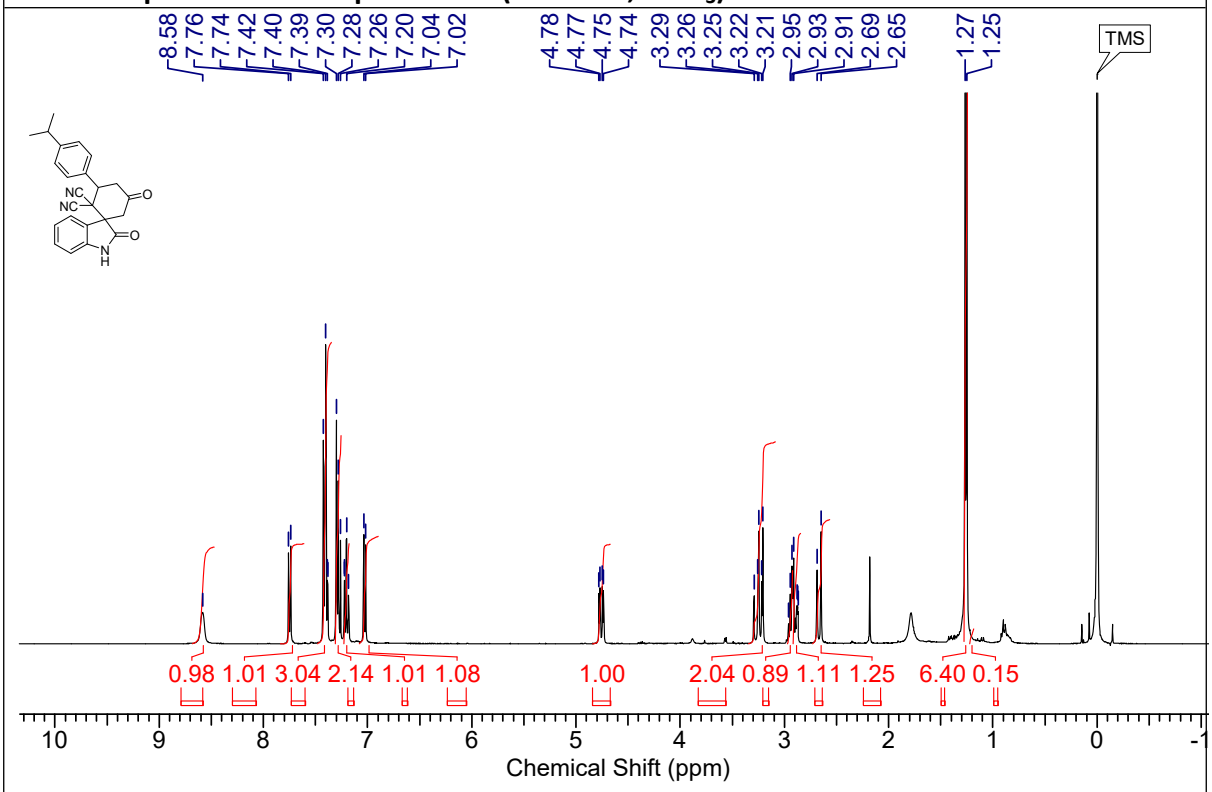
^{13}C NMR spectrum of compound 3Cb (101 MHz, $CDCl_3$)



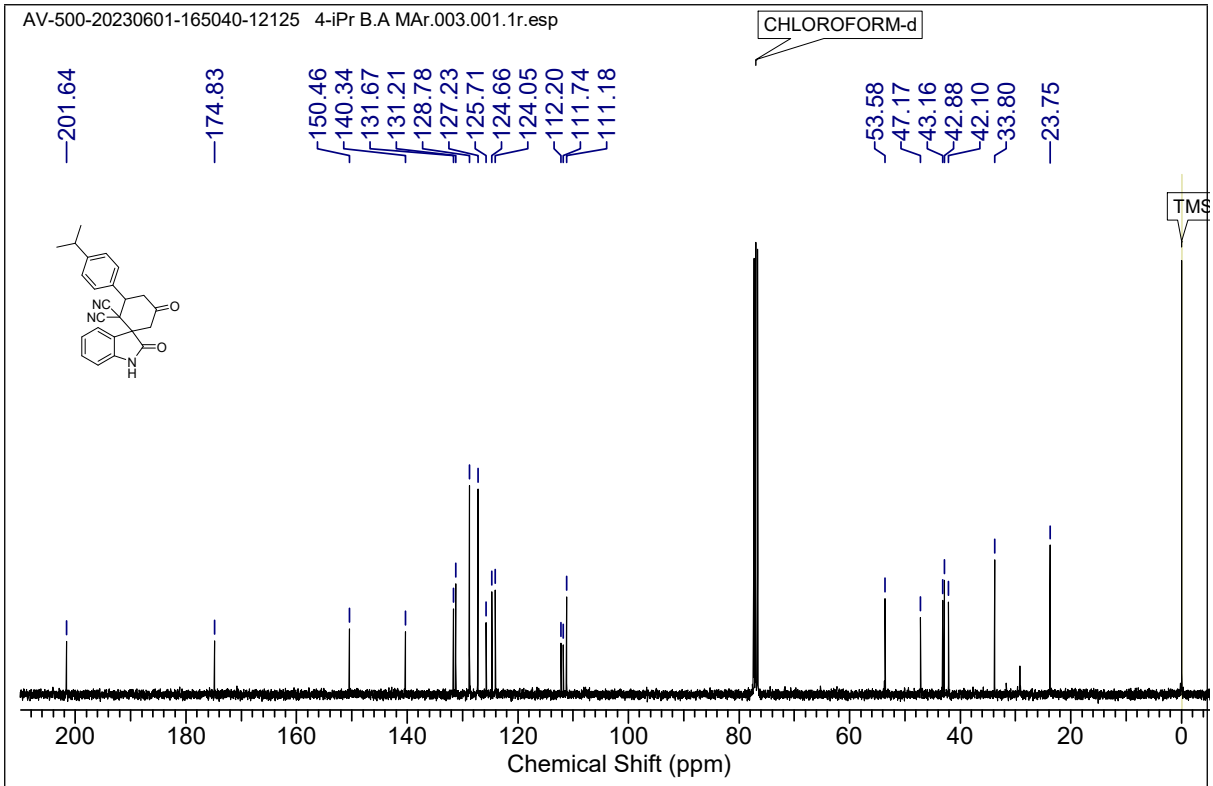
135 DEPT NMR spectrum of compound 3Cb



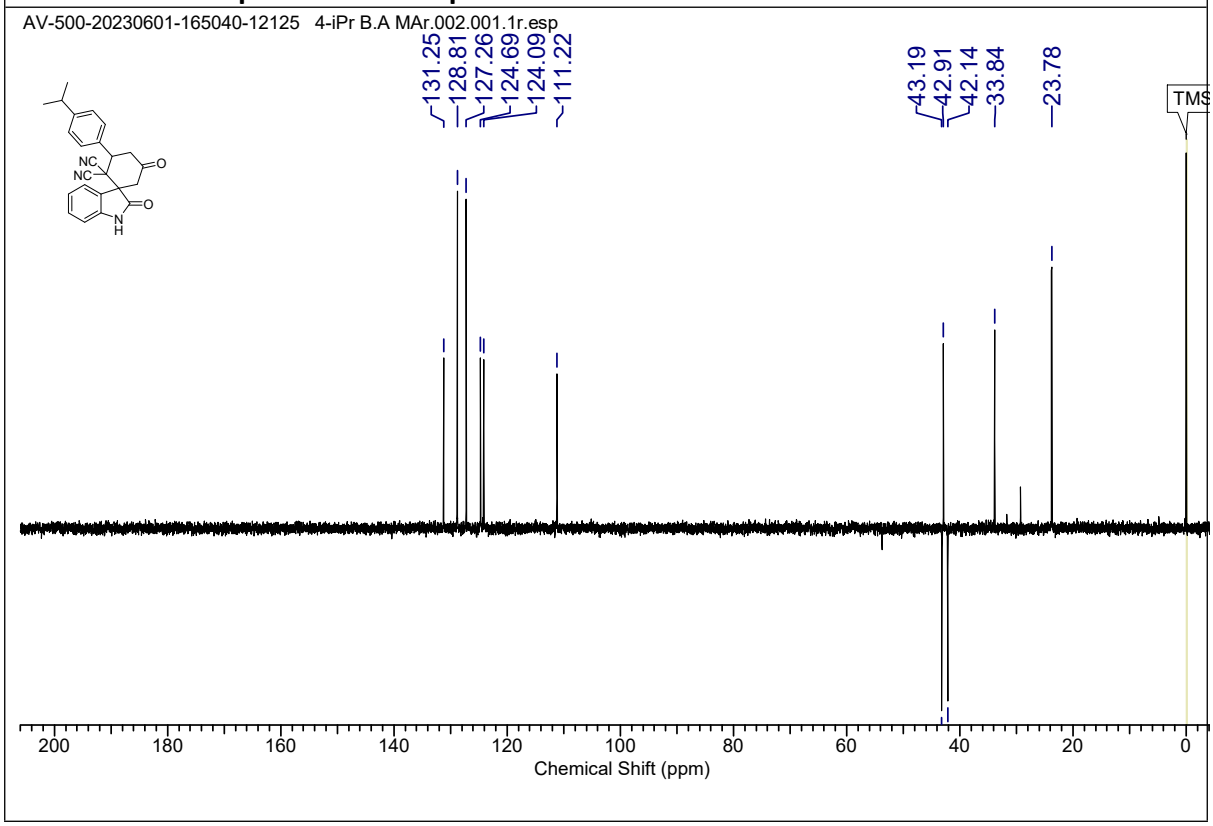
^{1}H NMR spectrum of compound 3Cc (500 MHz, $CDCl_3$)



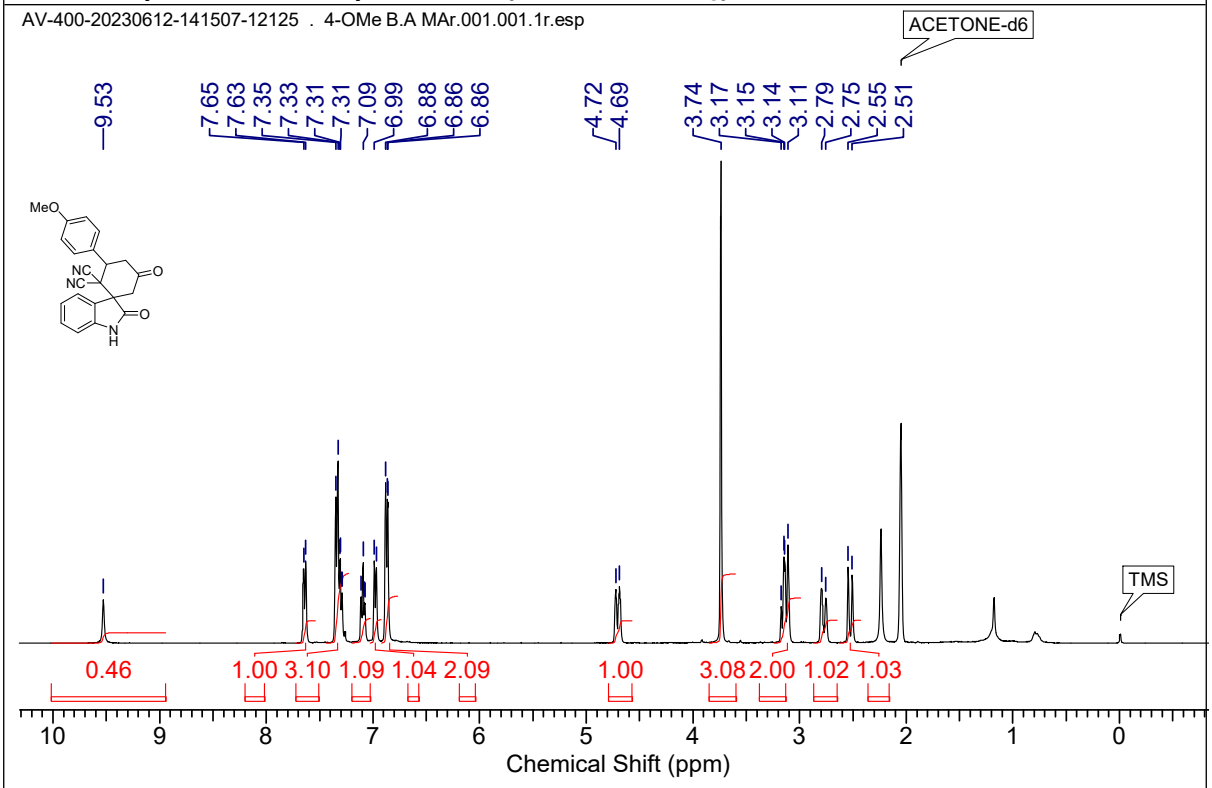
^{13}C NMR spectrum of compound 3Cc (125 MHz, $CDCl_3$)



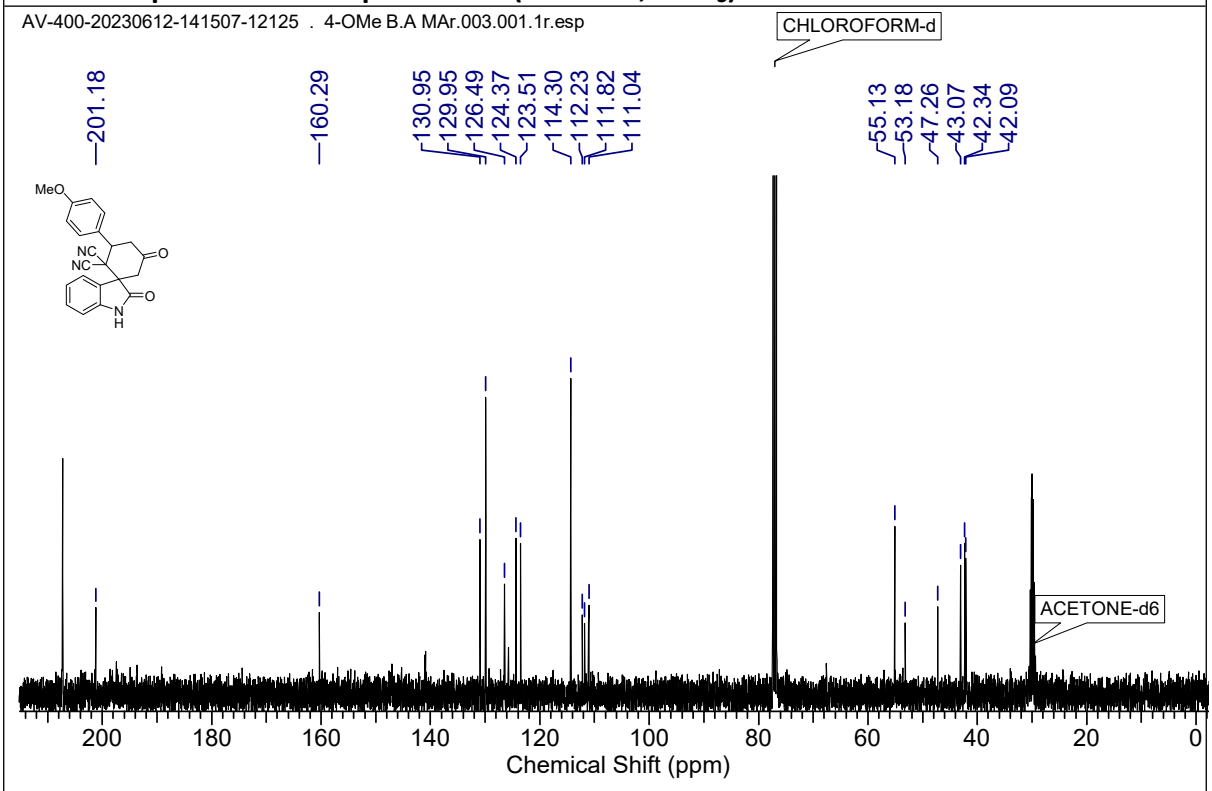
135 DEPT NMR spectrum of compound 3Cc



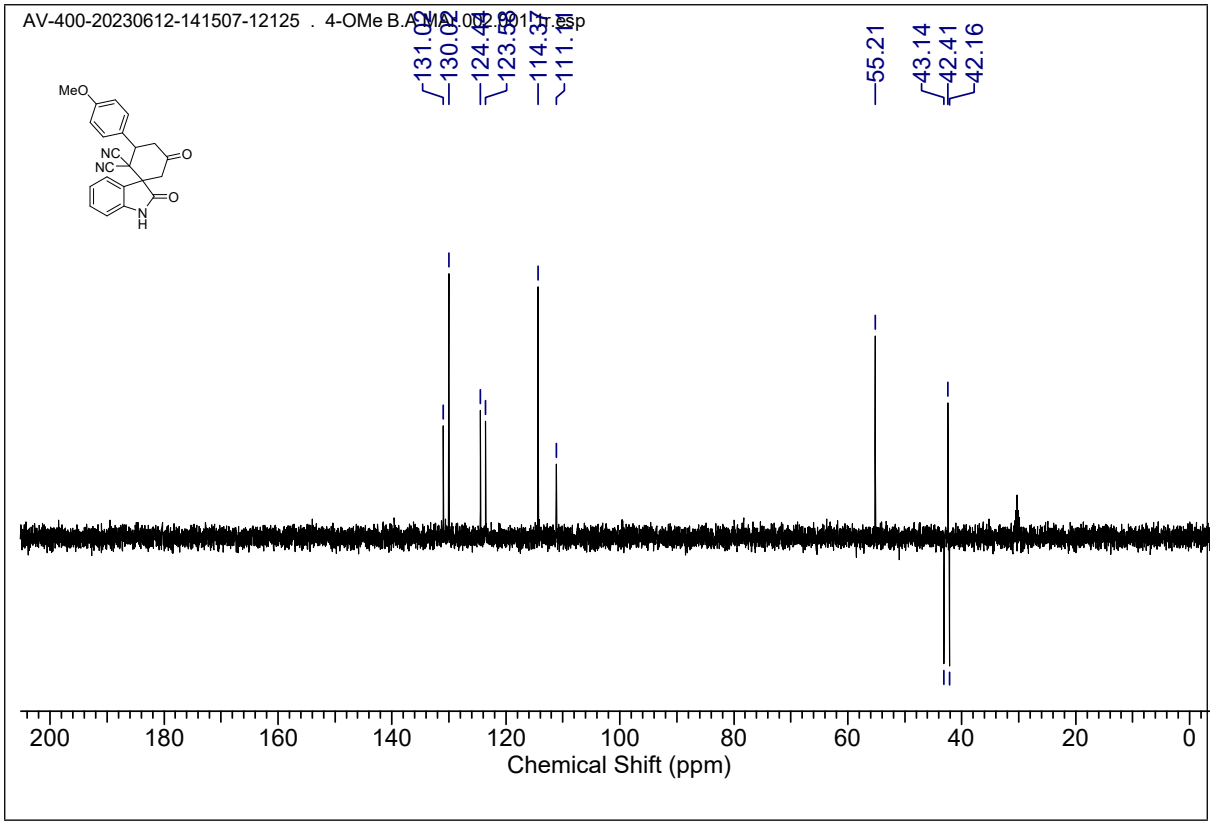
^{1}H NMR spectrum of compound 3Cd (400 MHz, $CDCl_3$)



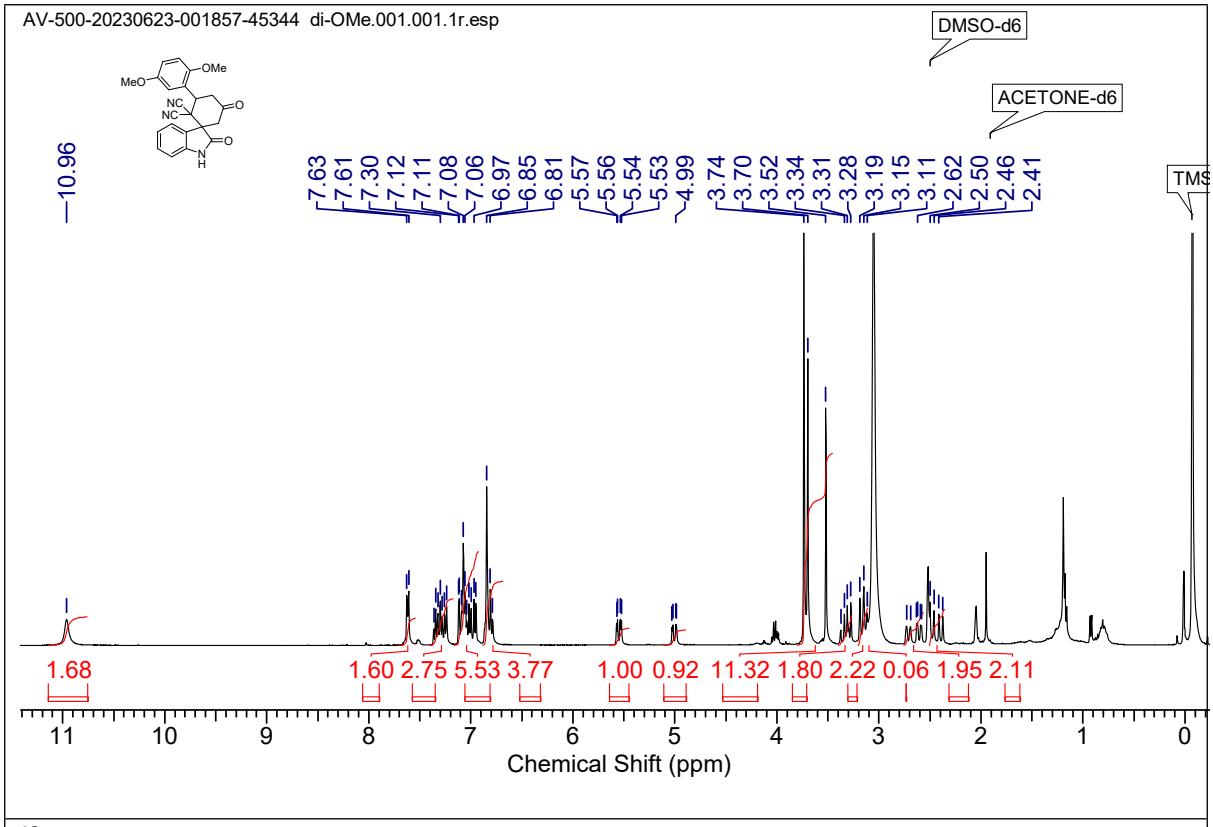
^{13}C NMR spectrum of compound 3Cd (101 MHz, $CDCl_3$)



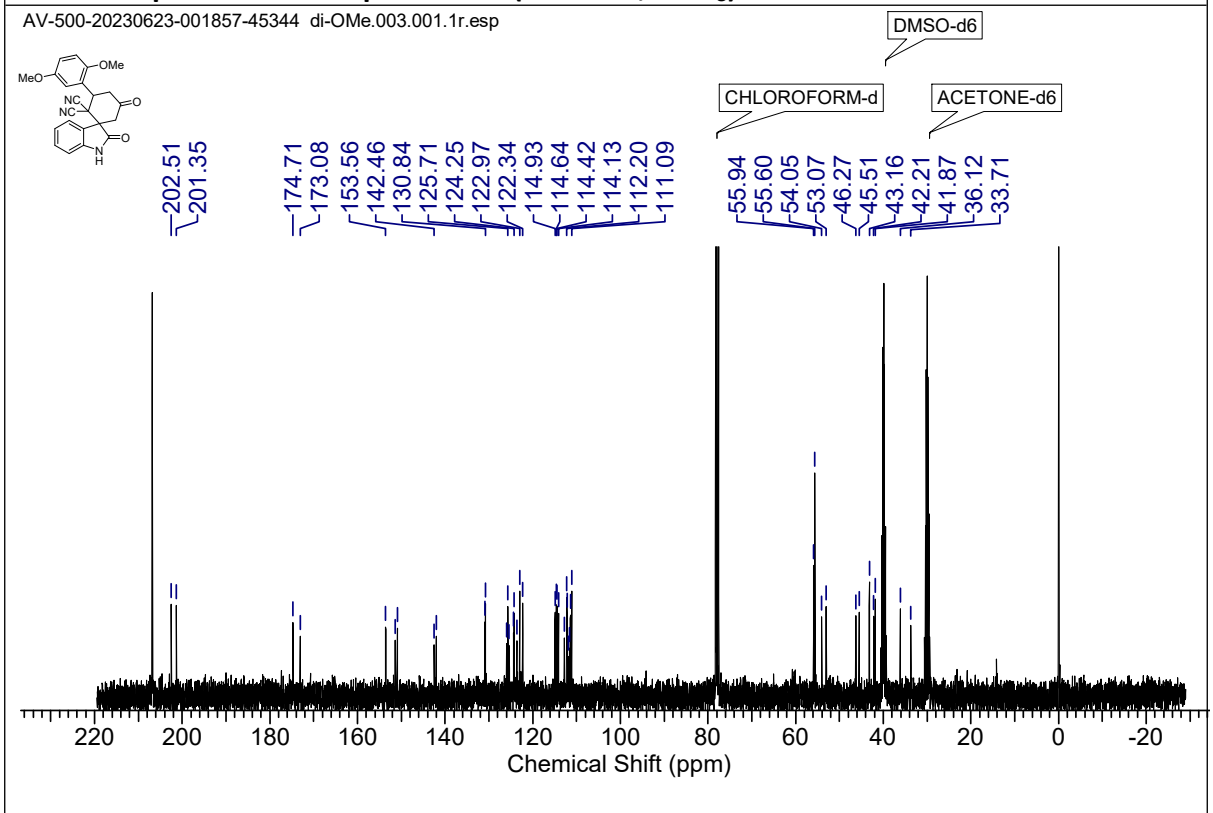
135 DEPT NMR spectrum of compound 3Cd



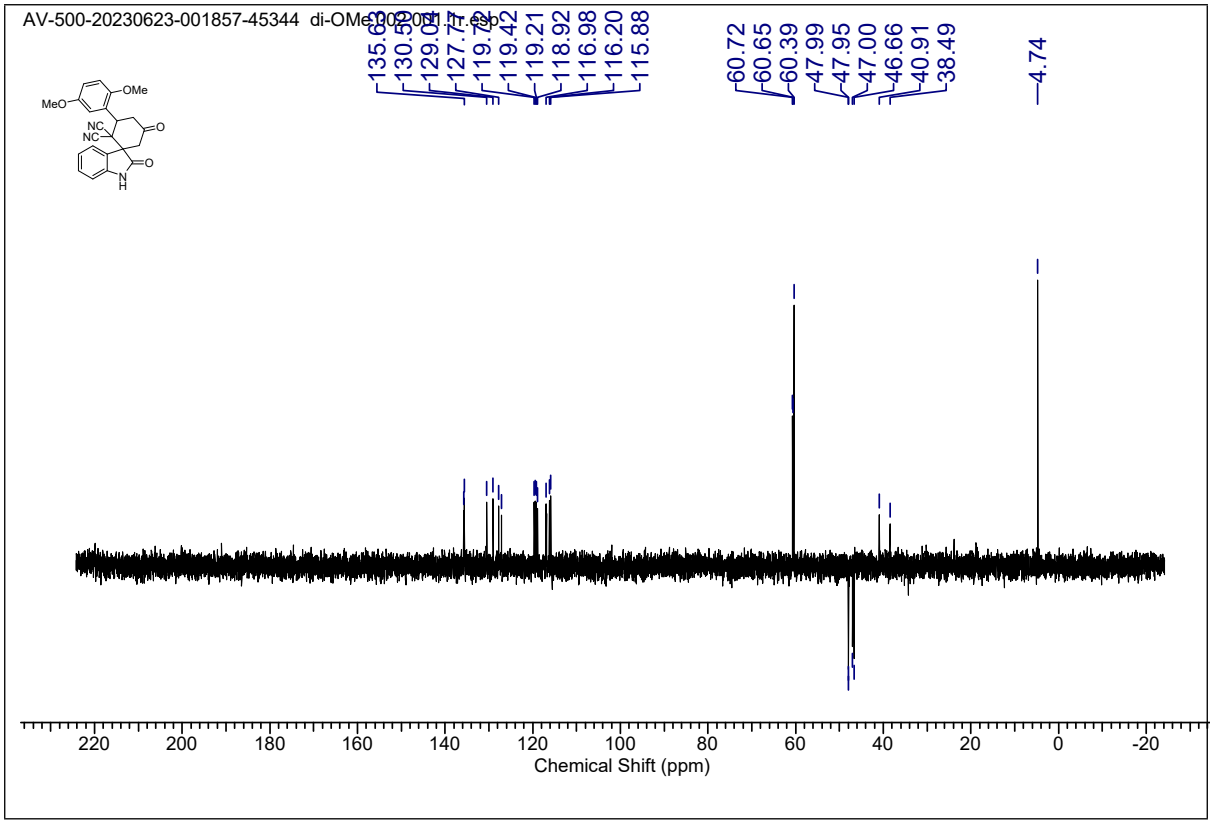
^{1}H NMR spectrum of compound 3Ce (500 MHz, $CDCl_3$)



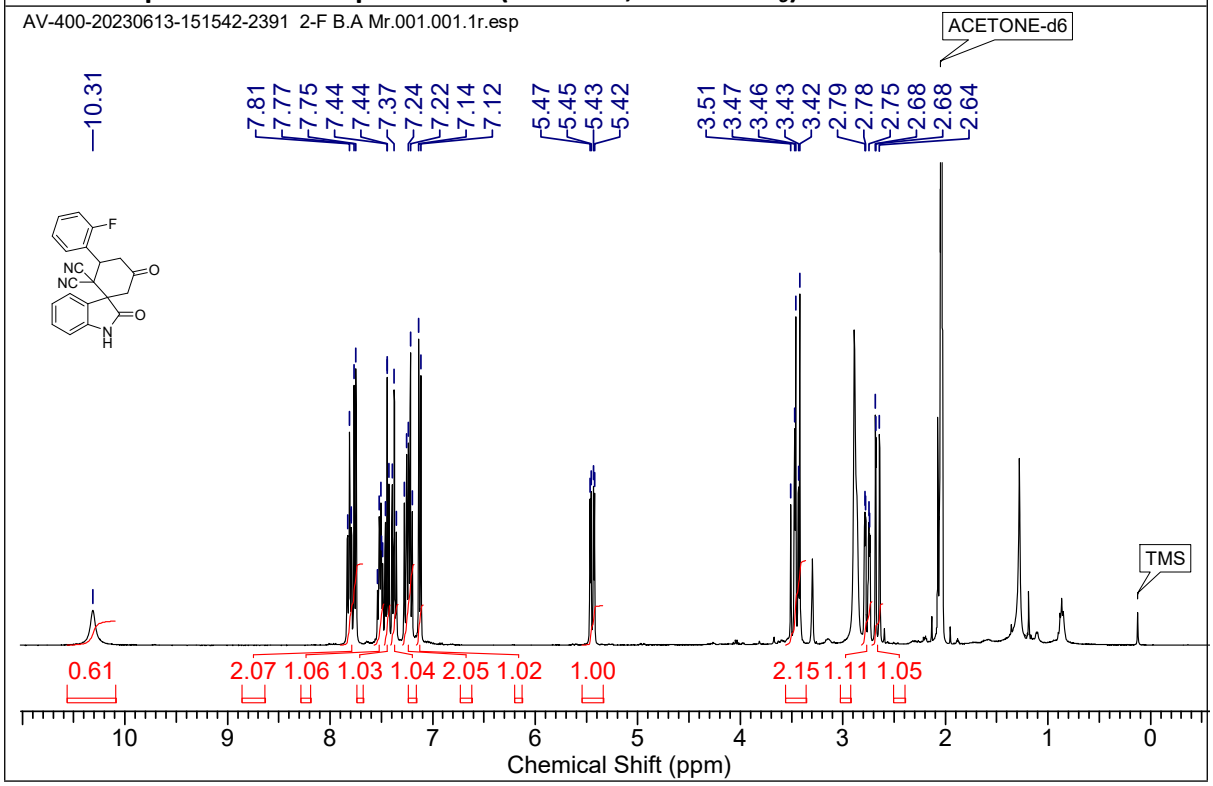
^{13}C NMR spectrum of compound 3Ce (125 MHz, $CDCl_3$)



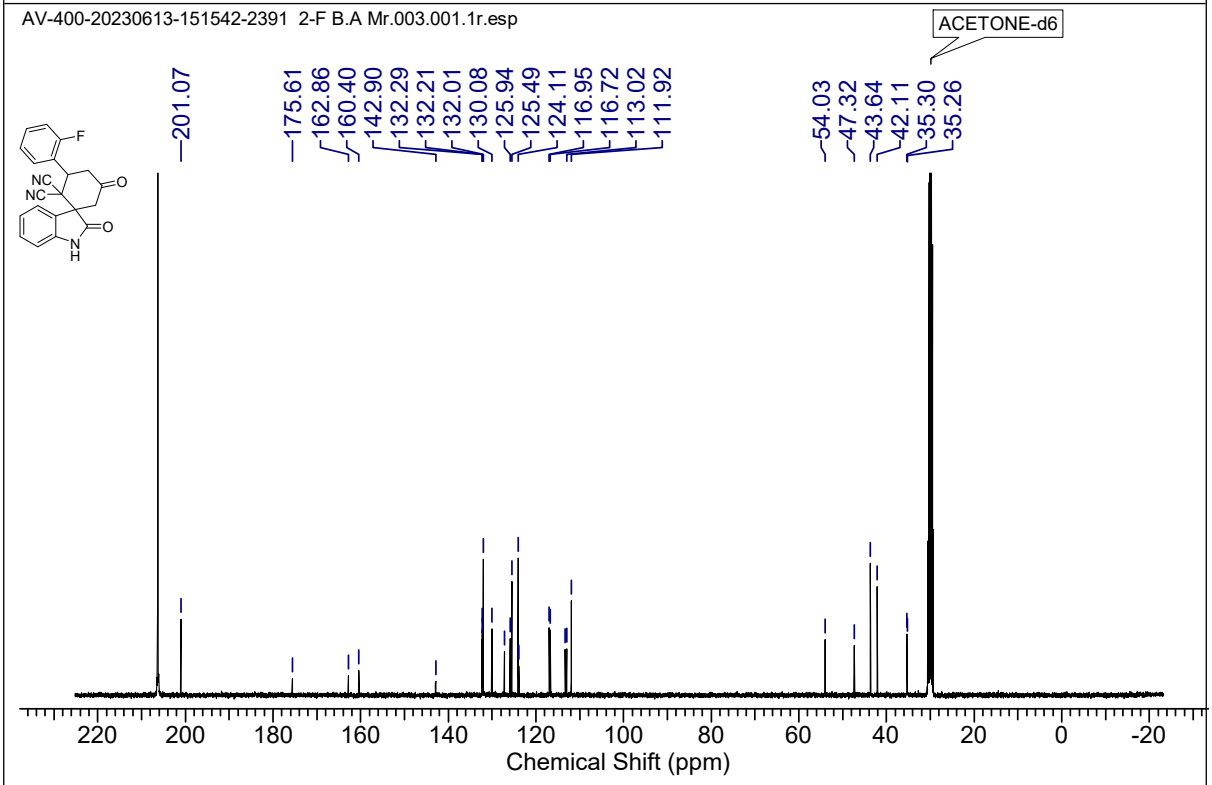
135 DEPT NMR spectrum of compound 3Ce



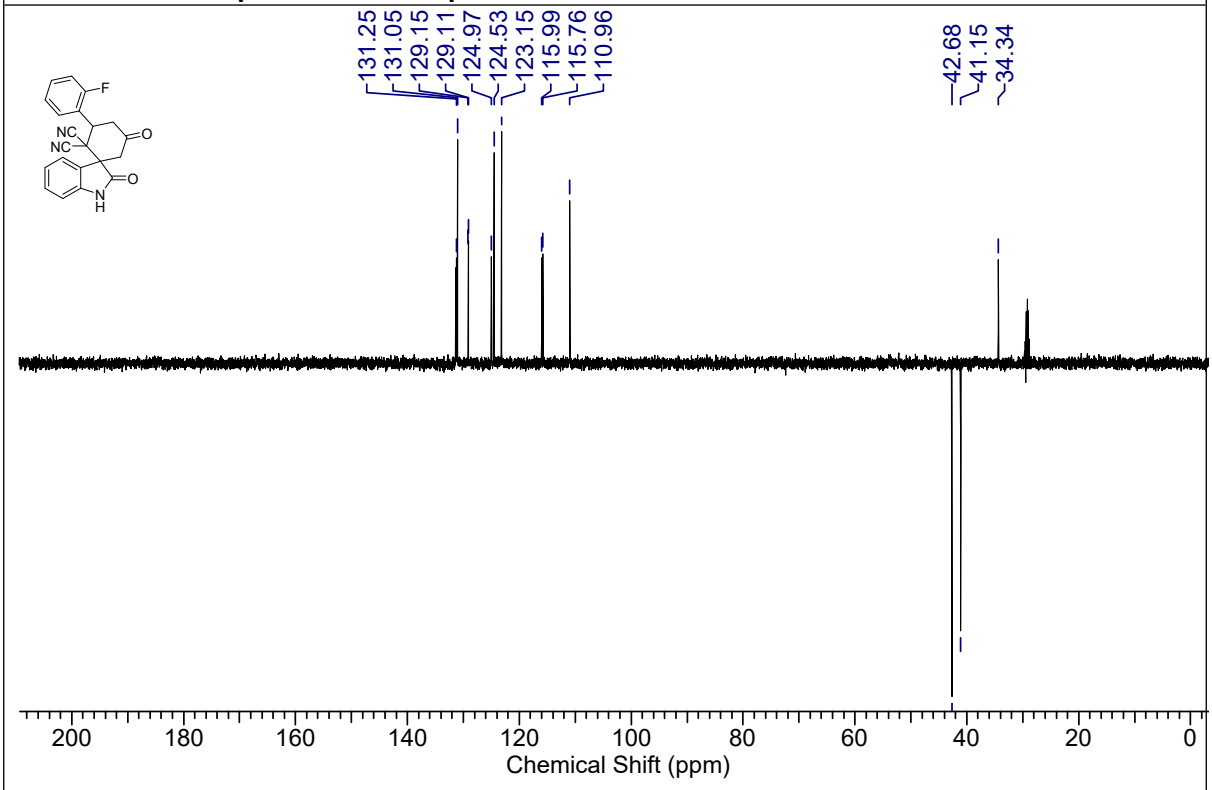
^{1}H NMR spectrum of compound 3Cf (400 MHz, Acetone-d_6)



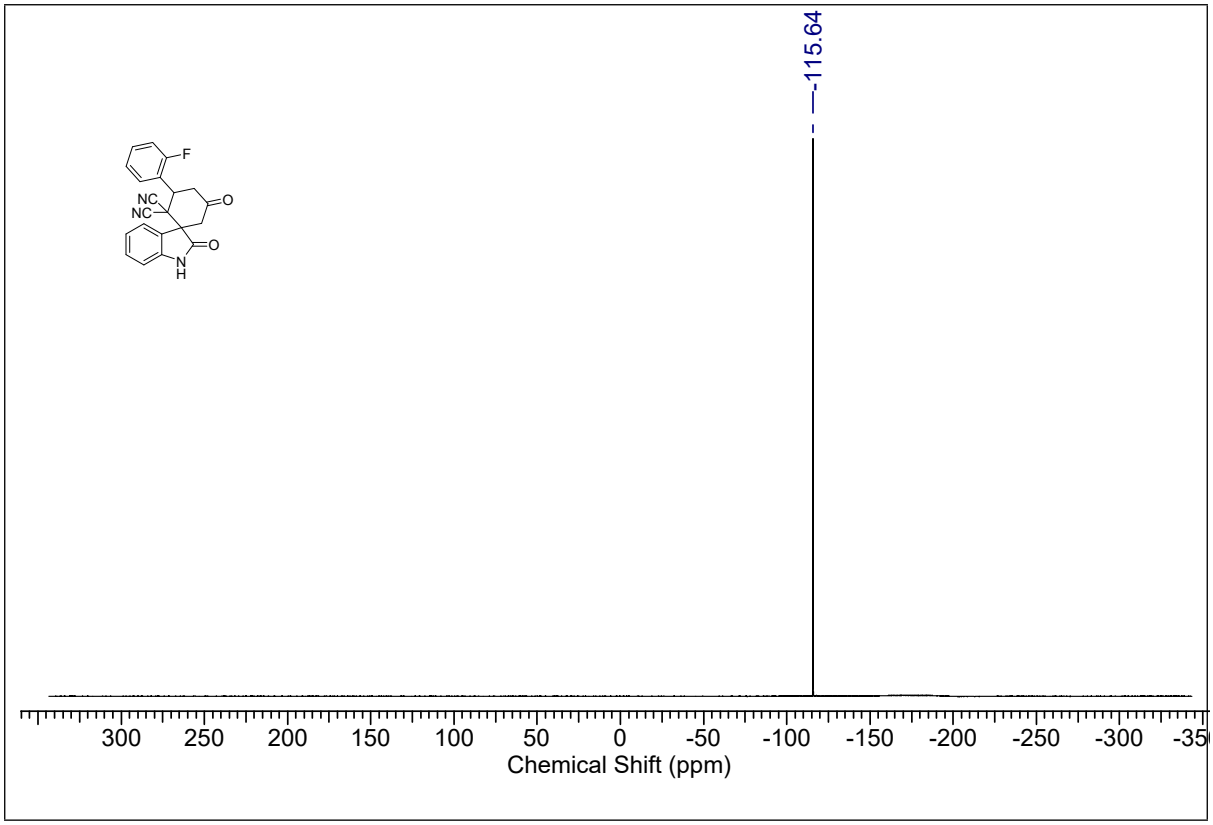
^{13}C NMR spectrum of compound 3Cf (101 MHz, Acetone-d_6)



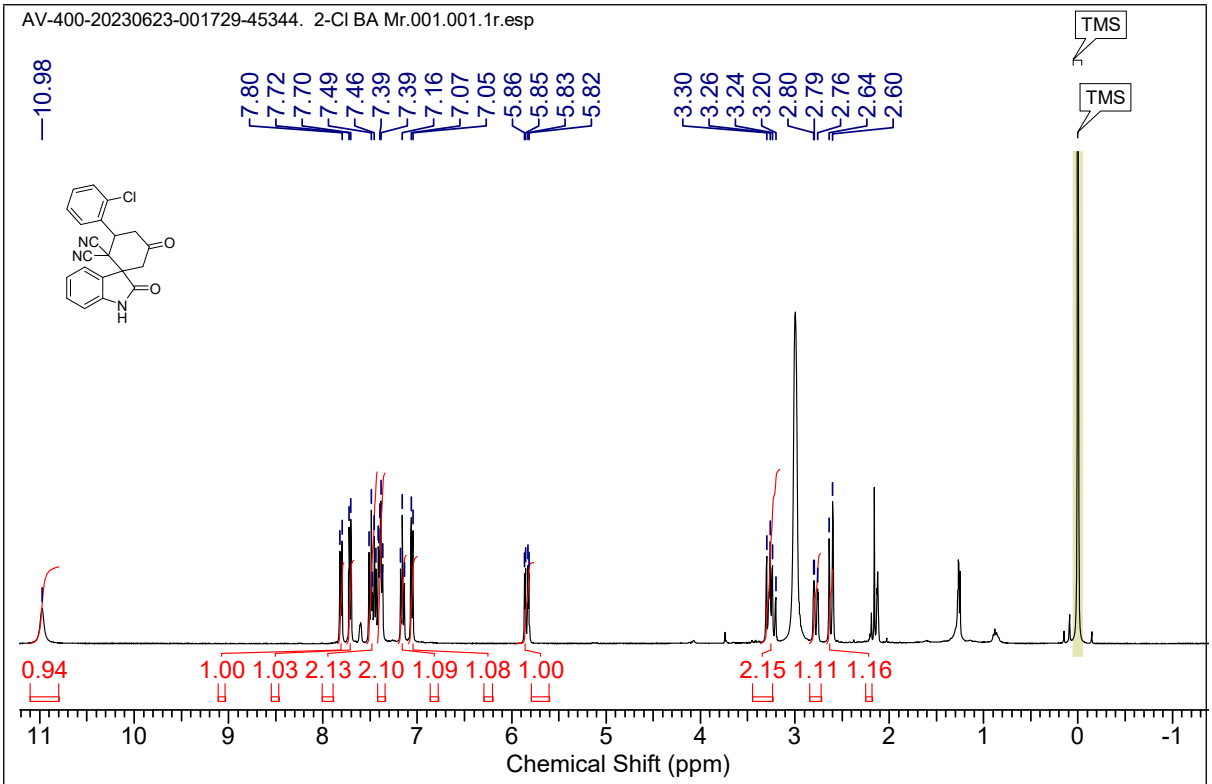
135 DEPT NMR spectrum of compound 3Cf



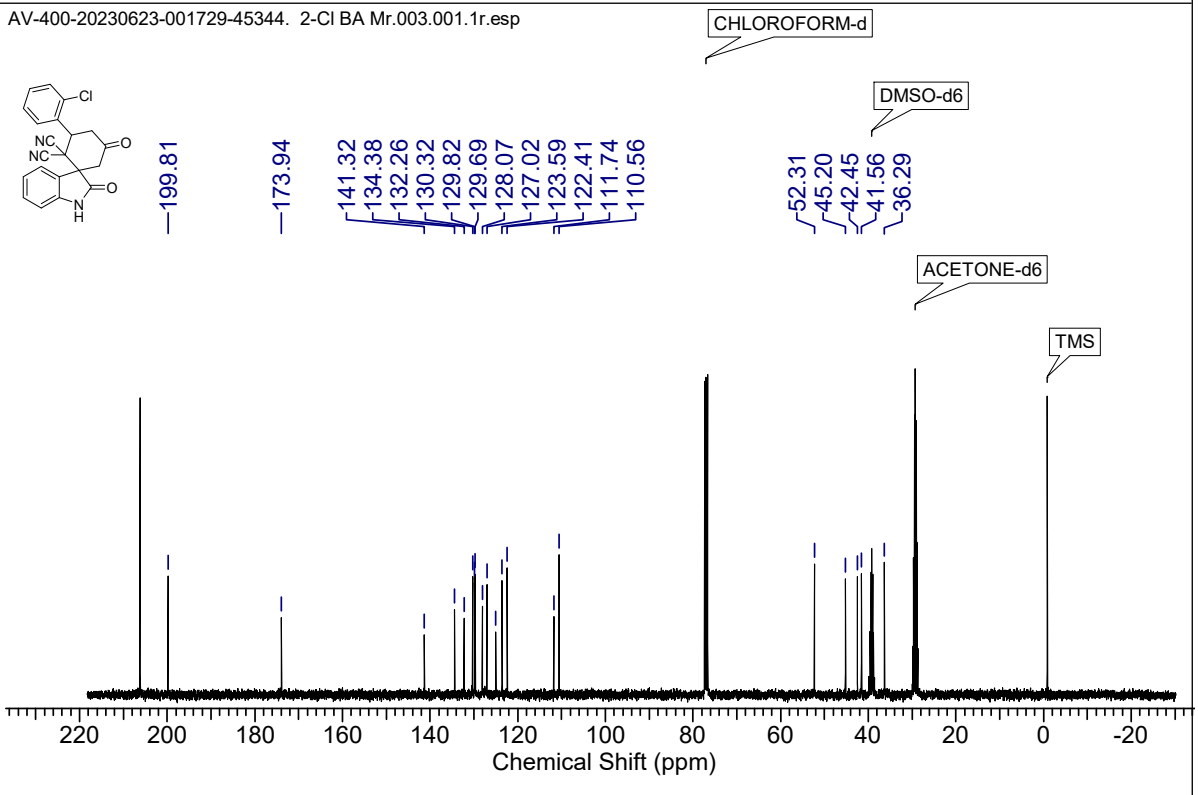
^{19}F spectrum of compound (3Cf)



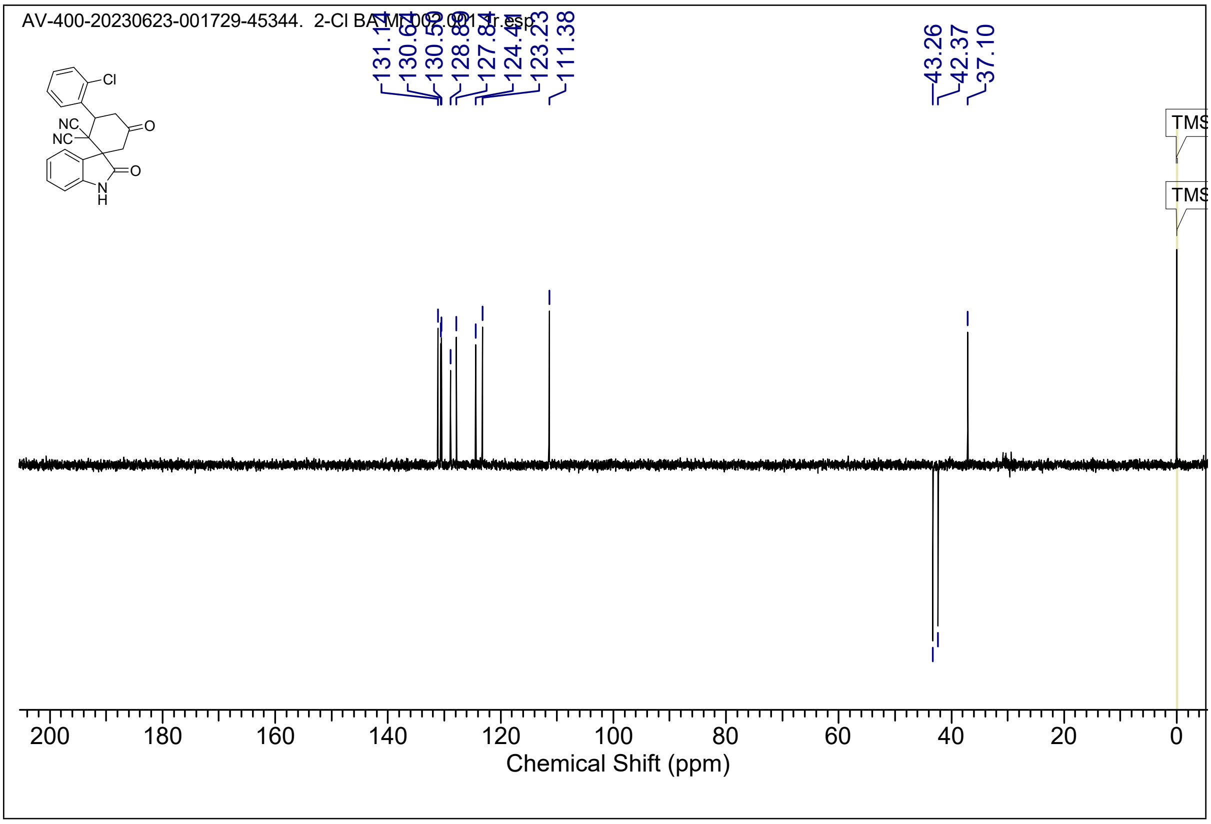
^{1}H NMR spectrum of compound 3Cg (400 MHz, $CDCl_3$)



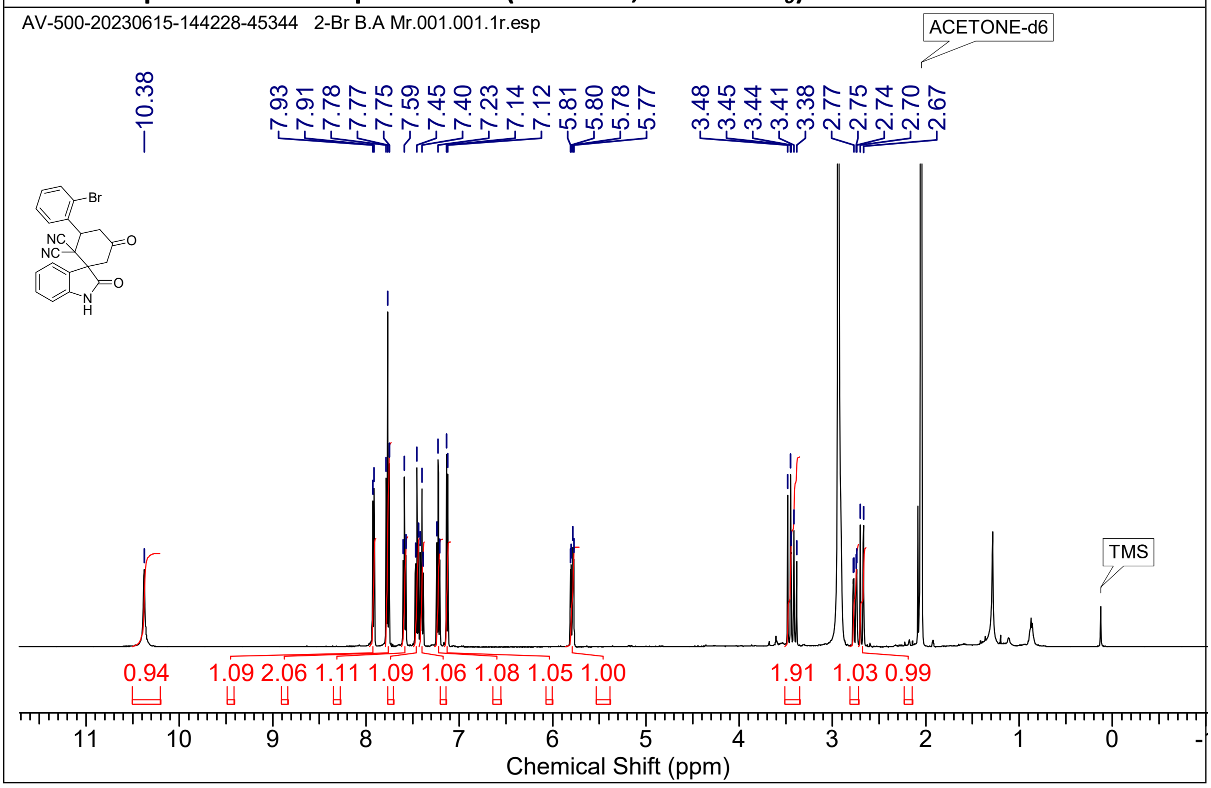
^{13}C NMR spectrum of compound 3Cg (101 MHz, $CDCl_3$)



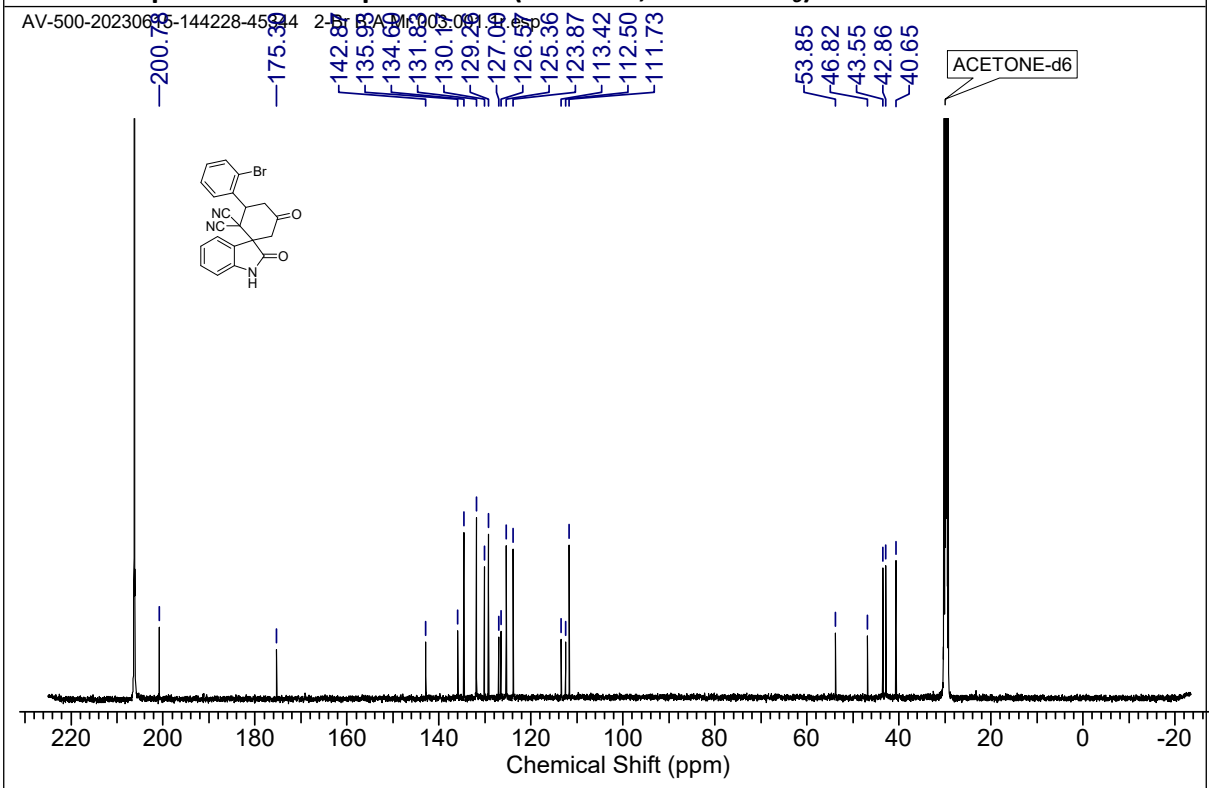
135 DEPT NMR spectrum of compound 3Cg



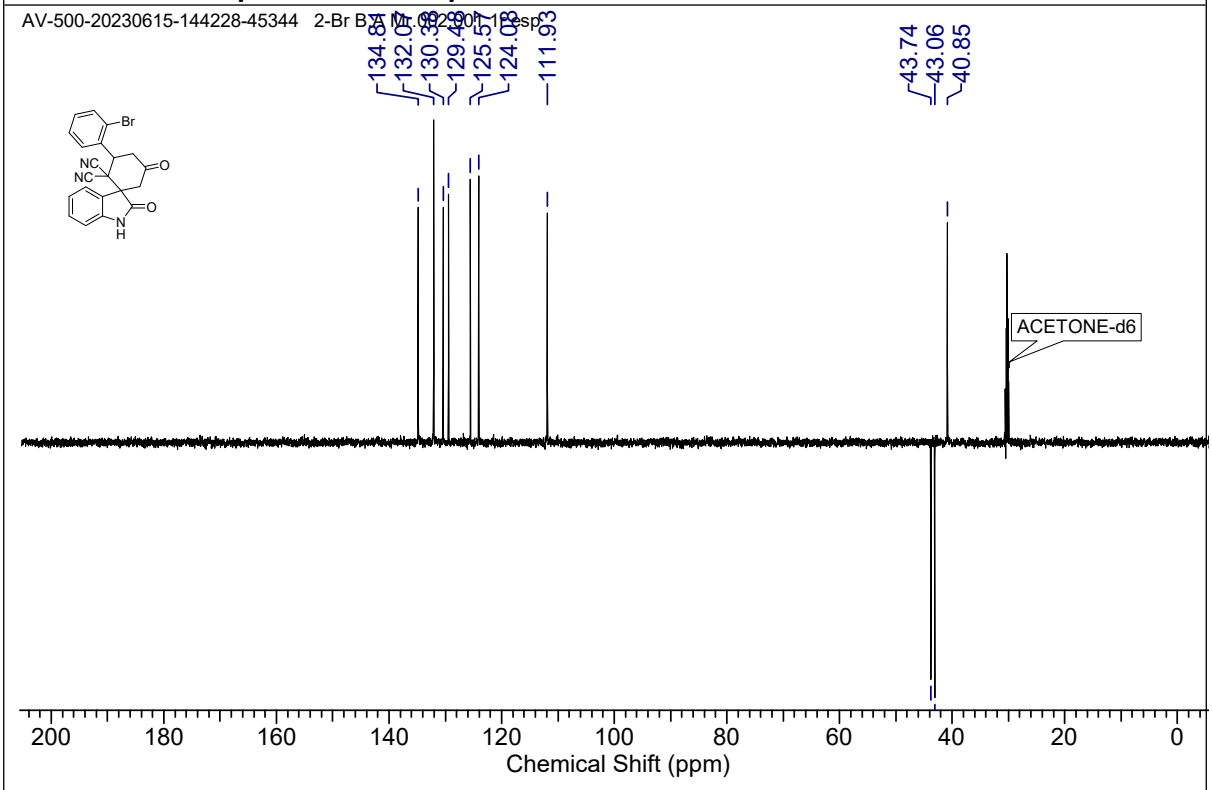
¹H NMR spectrum of compound 3Ch (500 MHz, Acetone-d_6)



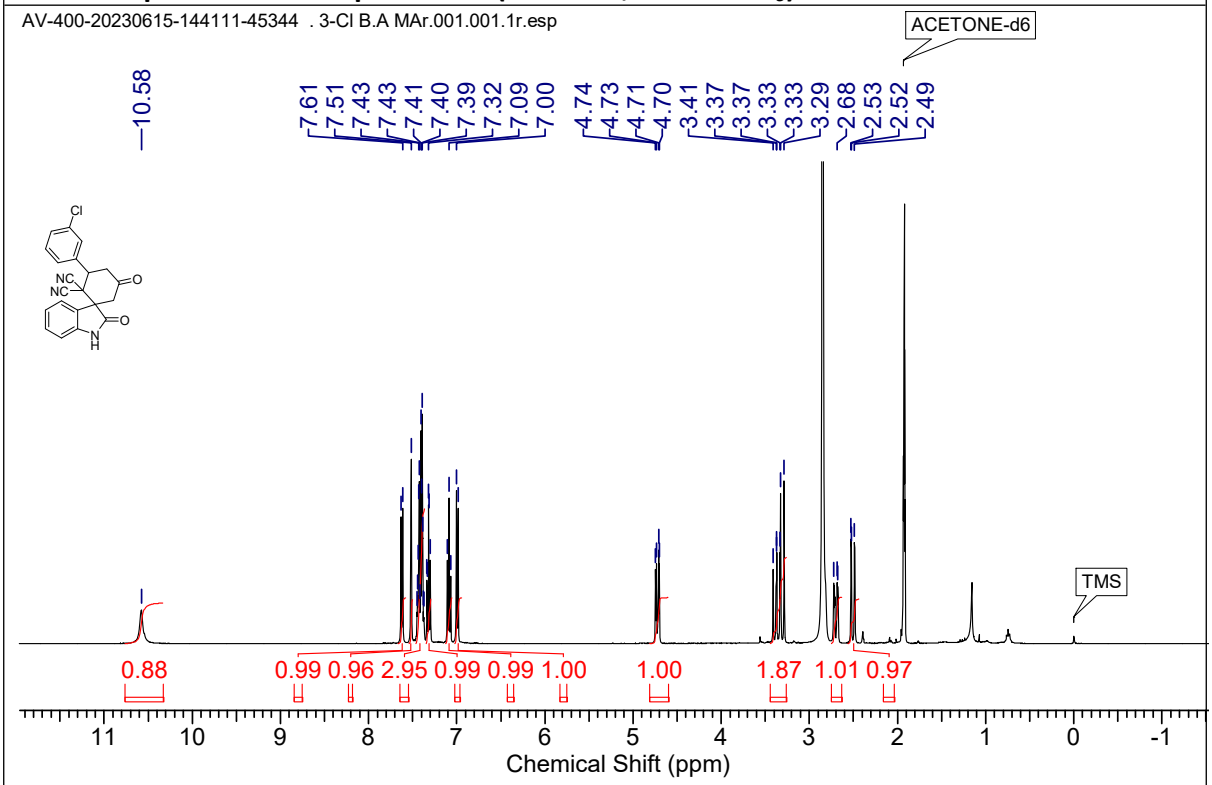
^{13}C NMR spectrum of compound 3Ch (125 MHz, Acetone-d_6)



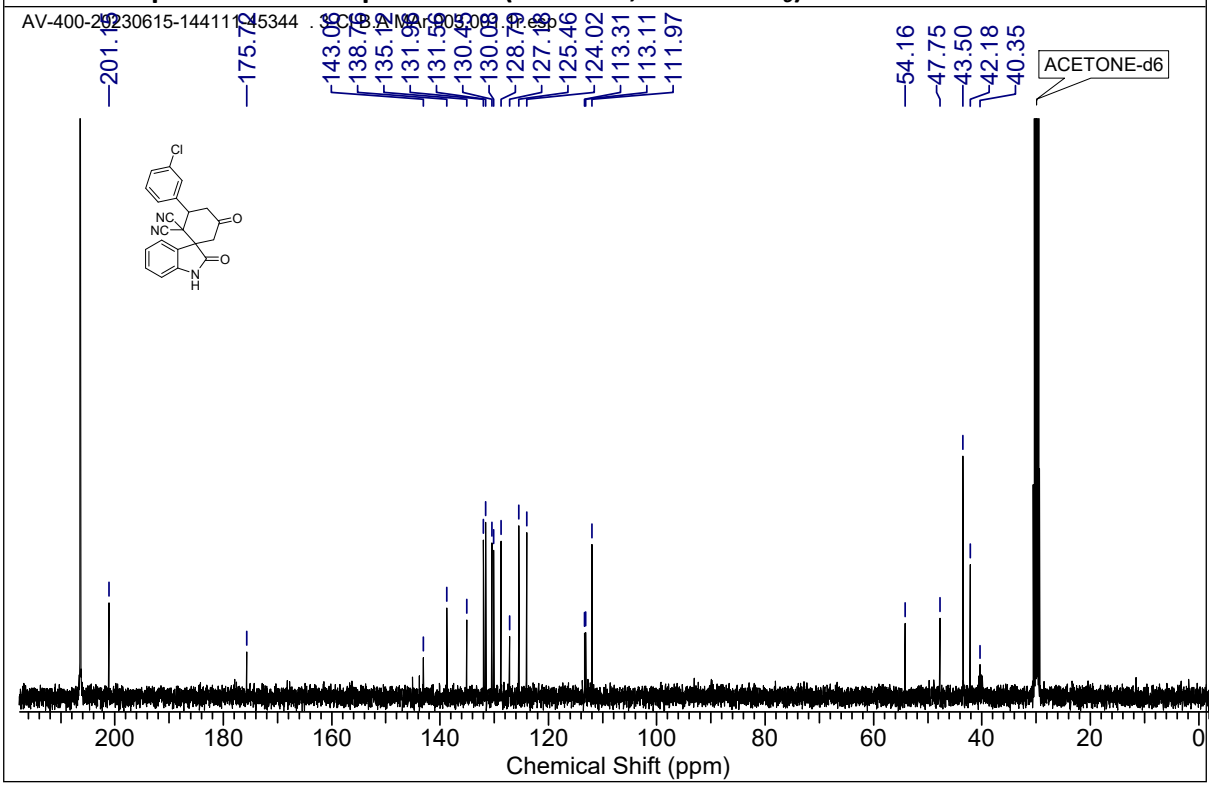
135 DEPT NMR spectrum of compound 3Ch



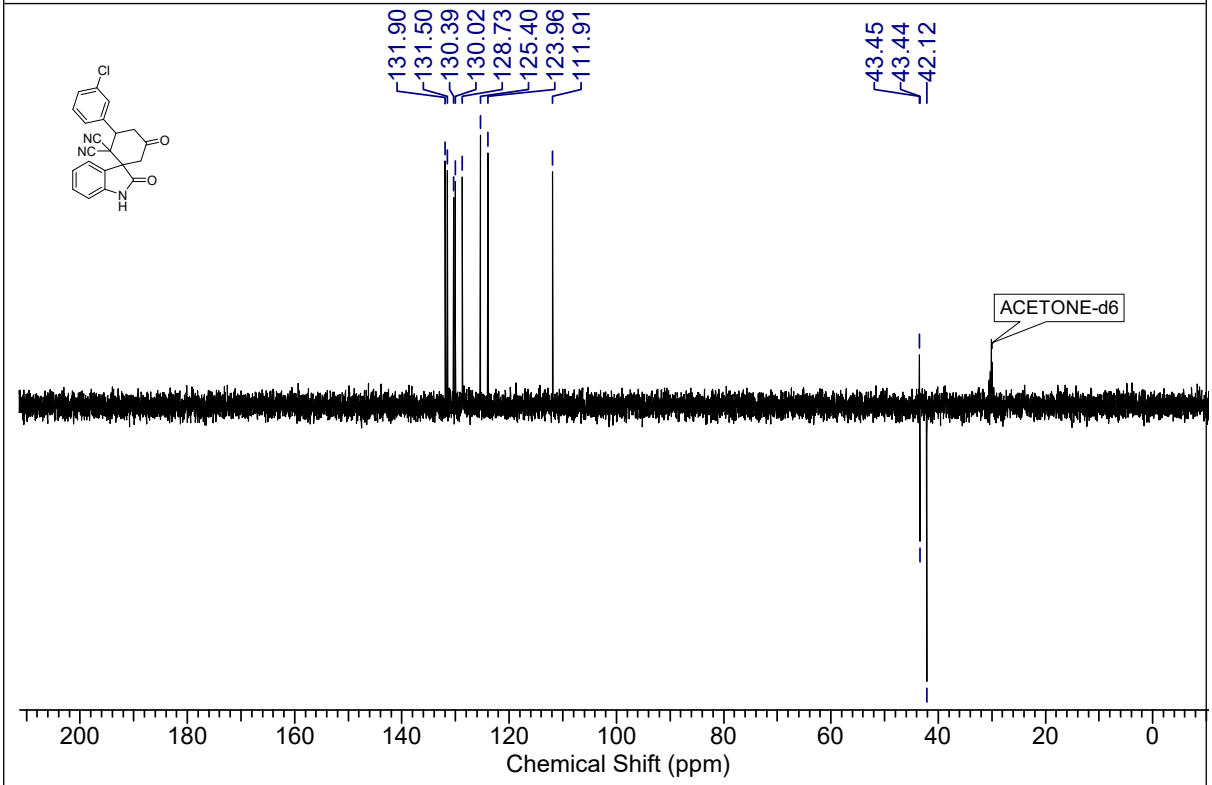
^{1}H NMR spectrum of compound 3Ci (400 MHz, Acetone-d_6)



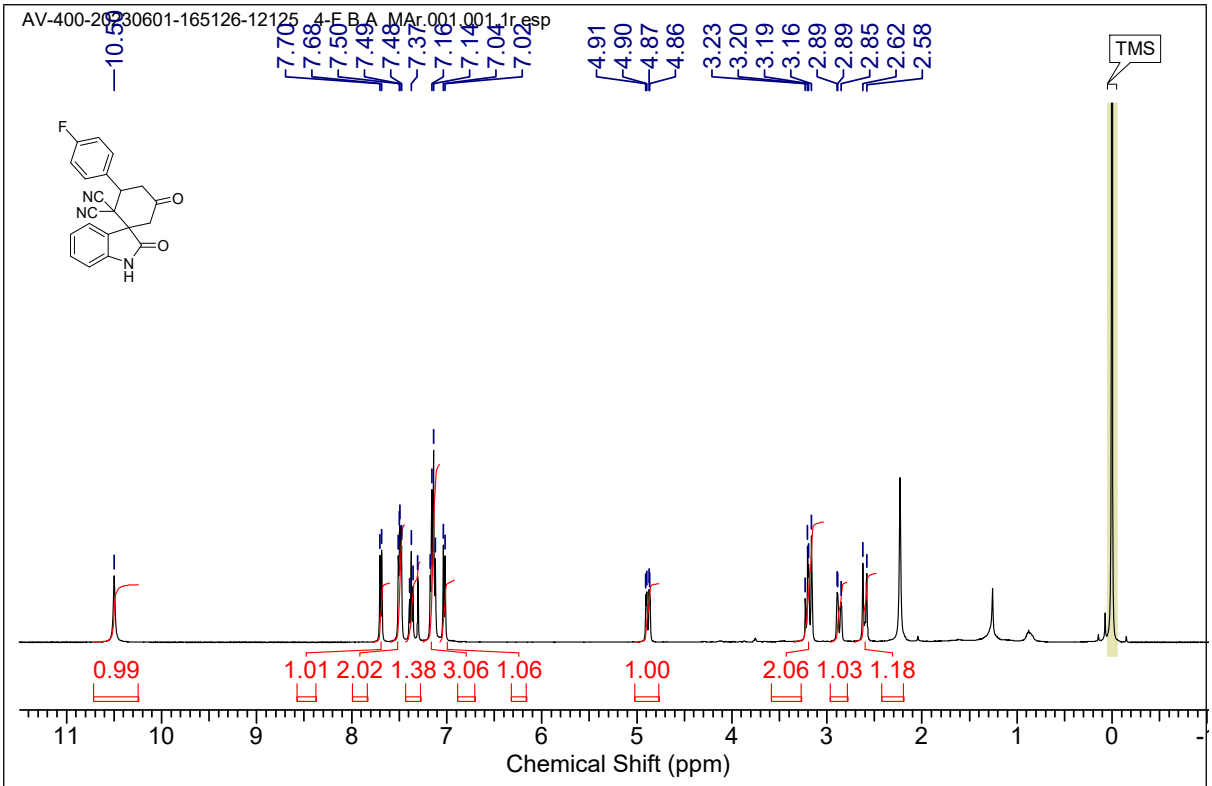
^{13}C NMR spectrum of compound 3Ci (101 MHz, Acetone-d_6)



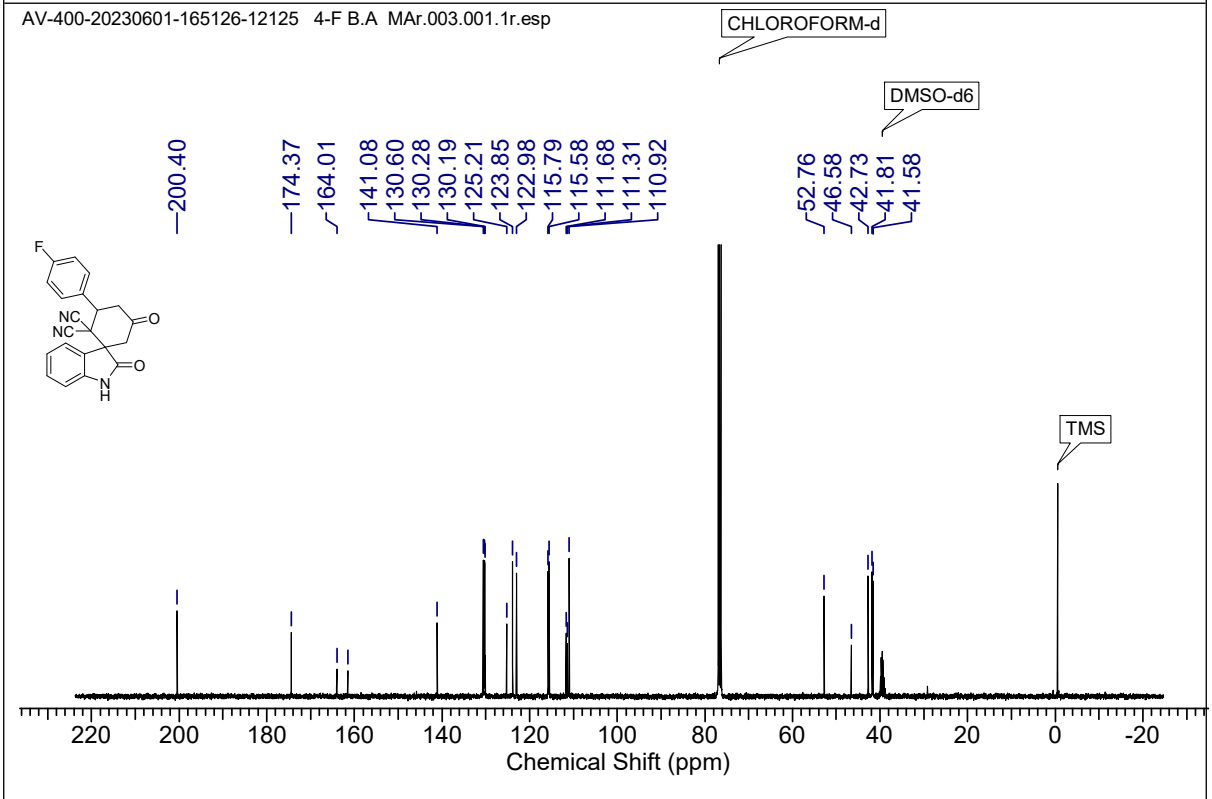
135 DEPT NMR spectrum of compound 3Ci



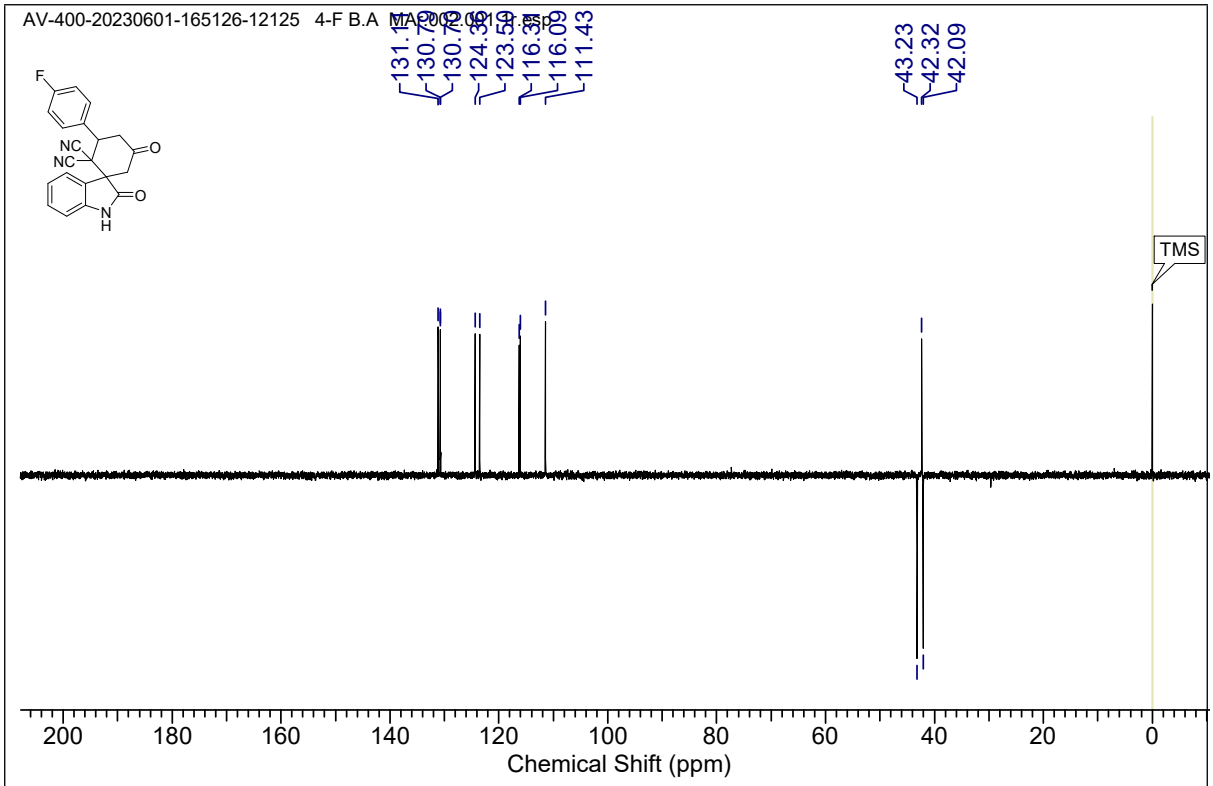
^{1}H NMR spectrum of compound 3Cj (400 MHz, $CDCl_3$)



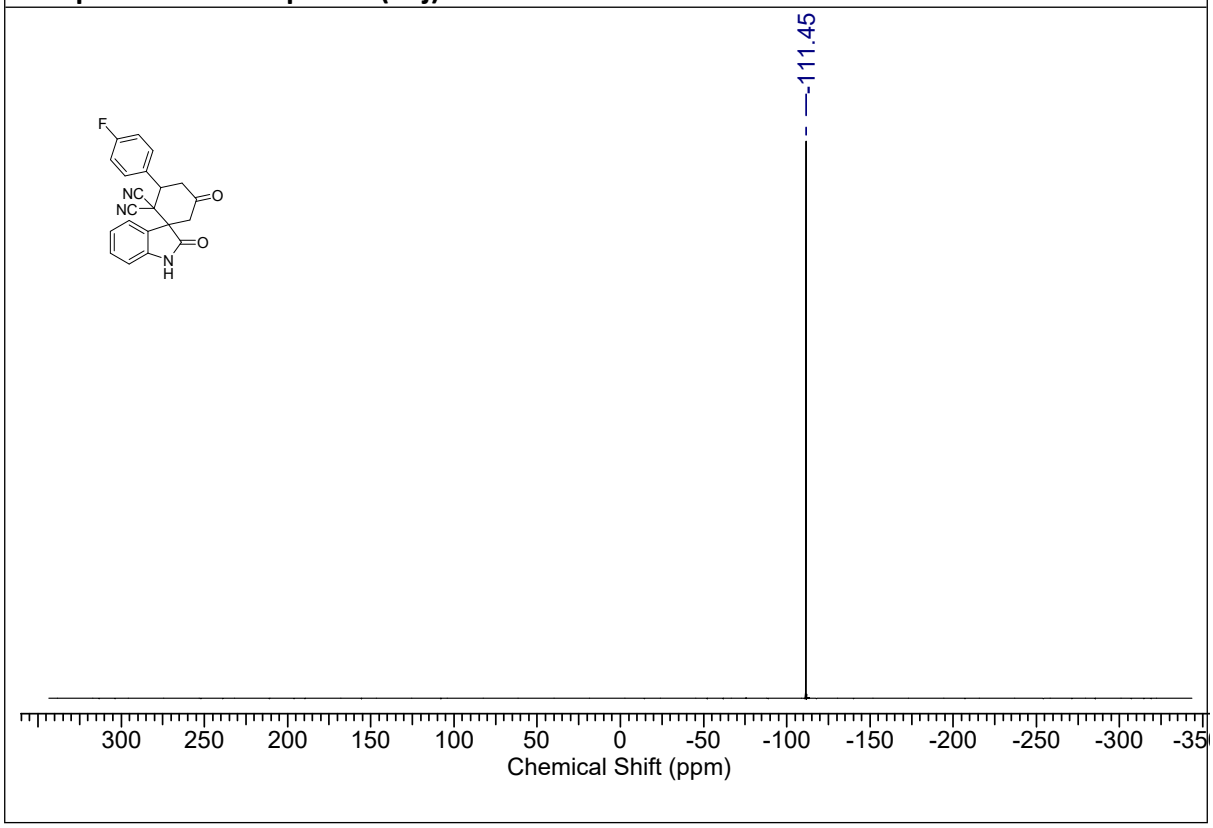
^{13}C NMR spectrum of compound 3Cj (101 MHz, $CDCl_3$)



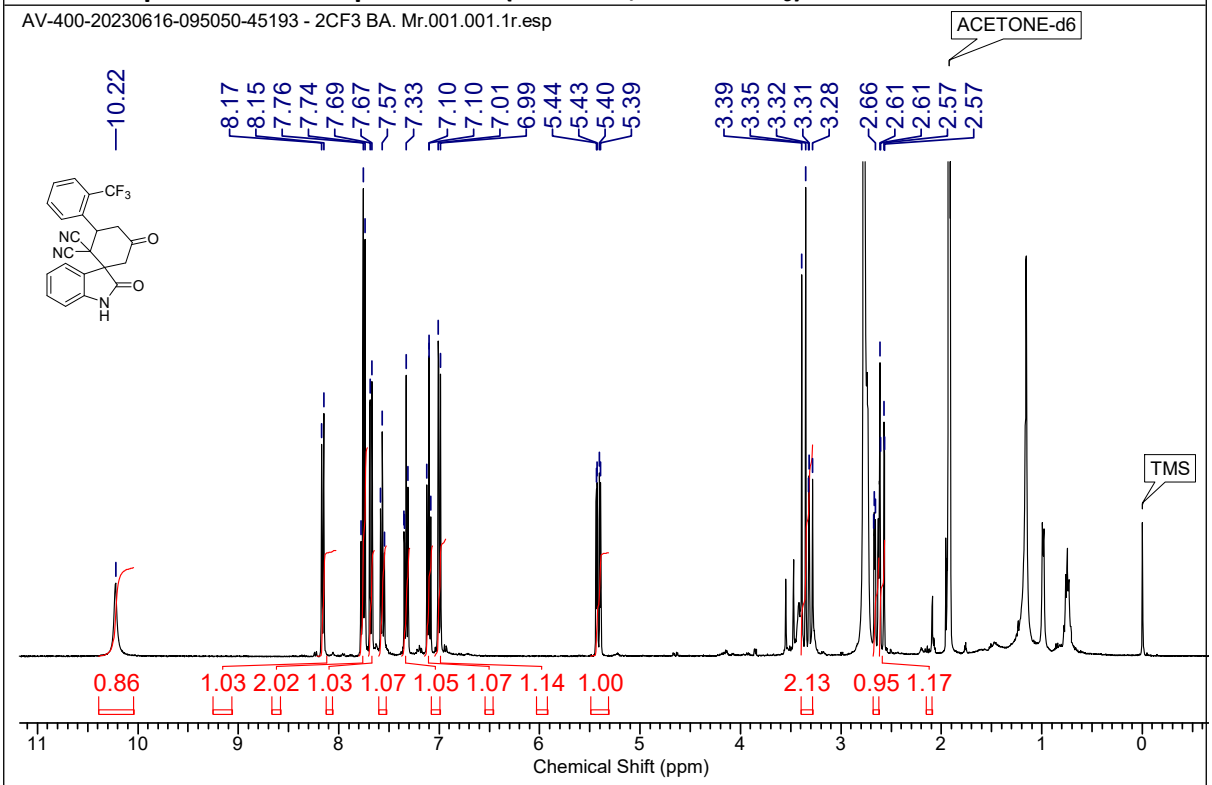
135 DEPT NMR spectrum of compound 3Cj



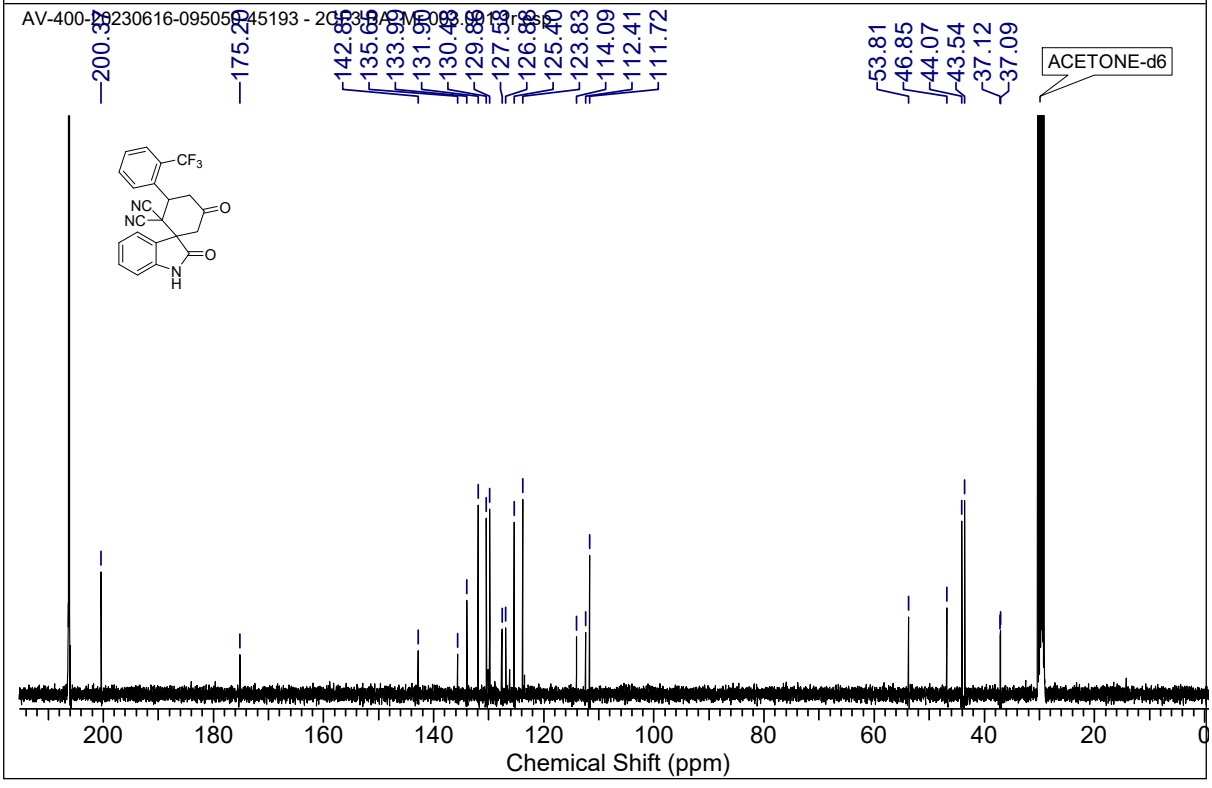
^{19}F spectrum of compound (3Cj)



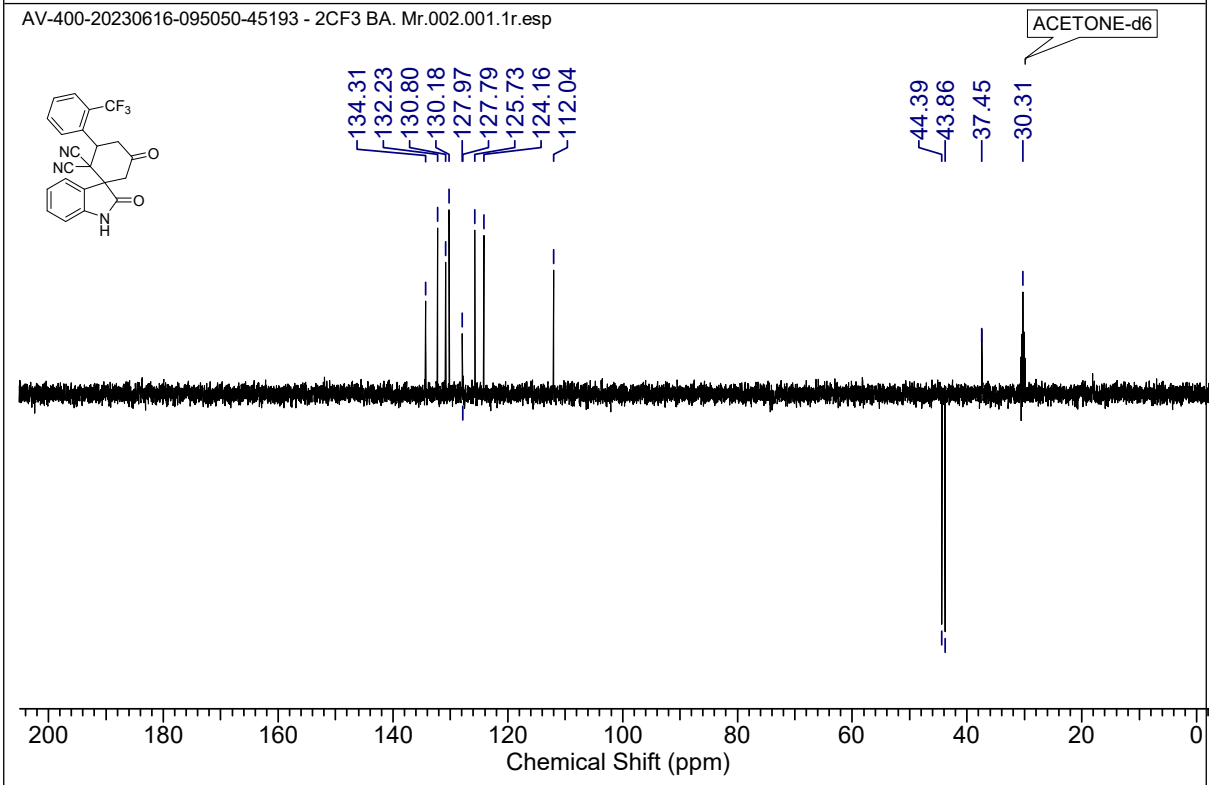
^{1}H NMR spectrum of compound 3Ck (400 MHz, Acetone-d_6)



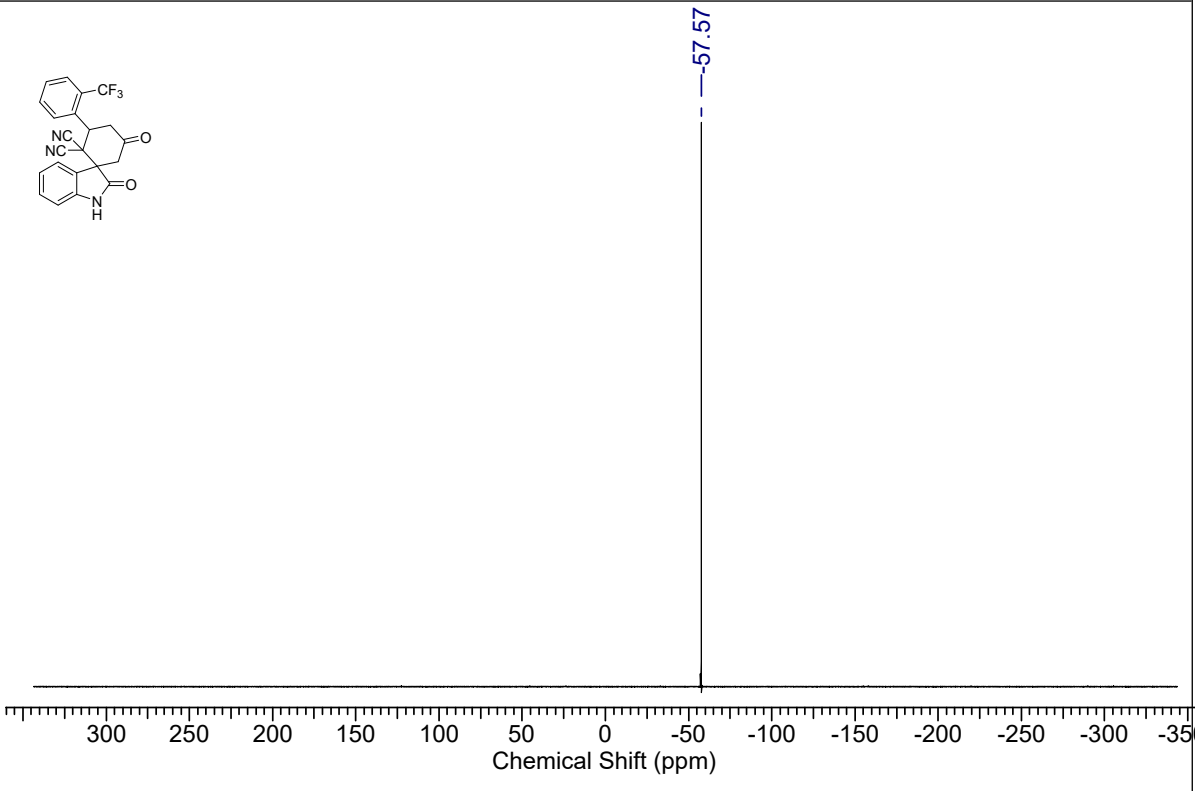
^{13}C NMR spectrum of compound 3Ck (101 MHz, Acetone-d_6)



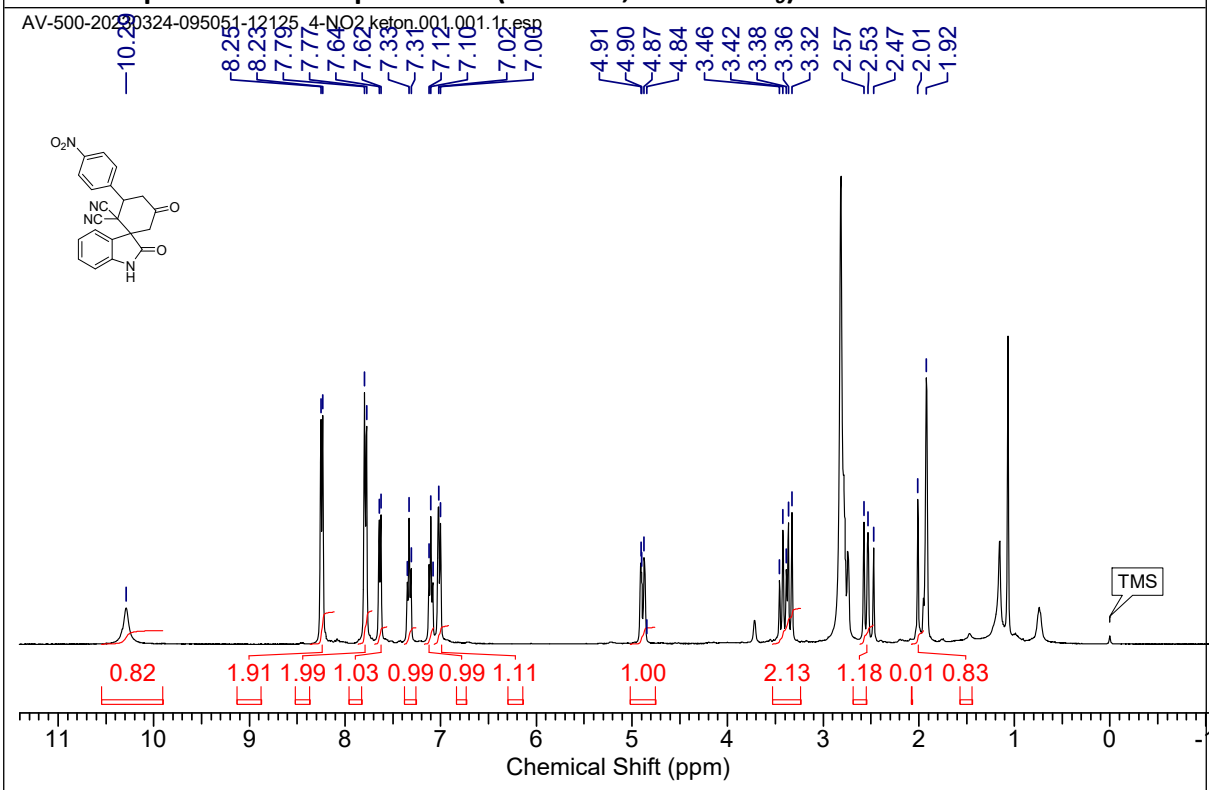
135 DEPT NMR spectrum of compound 3Ck



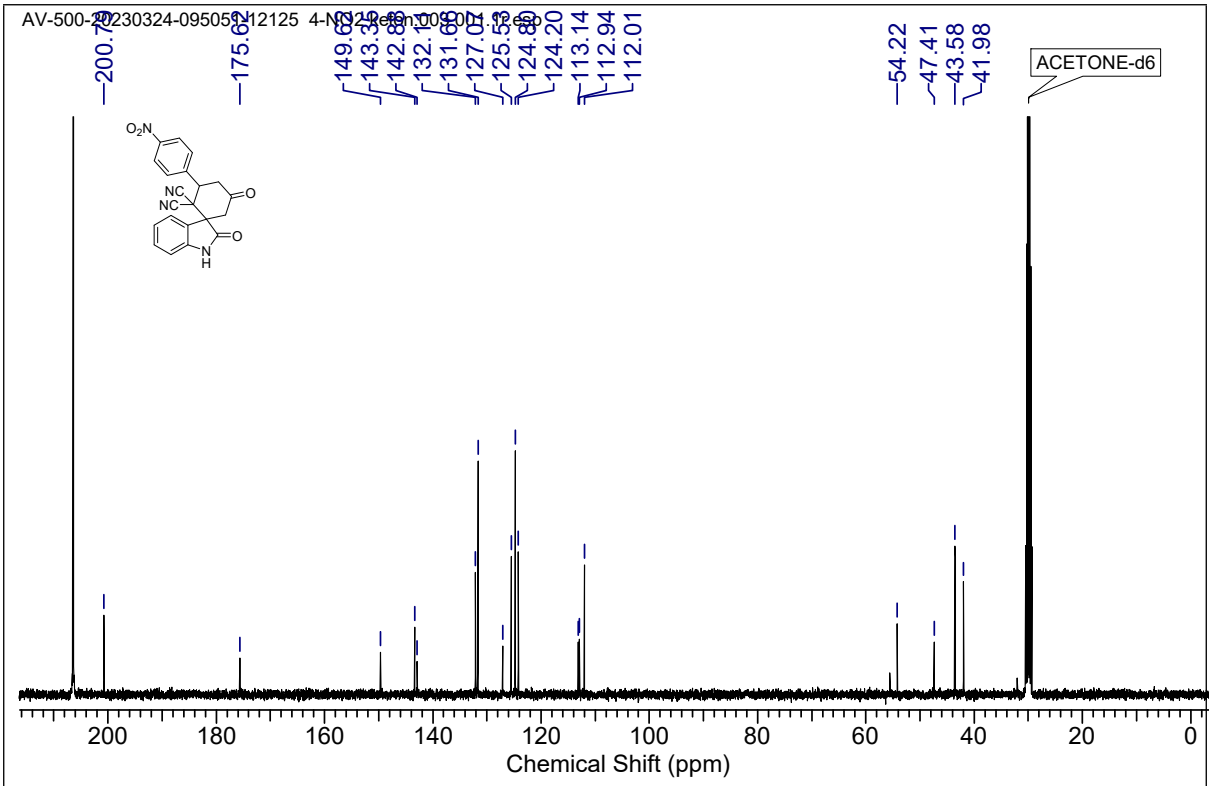
^{19}F spectrum of compound (3Ck)



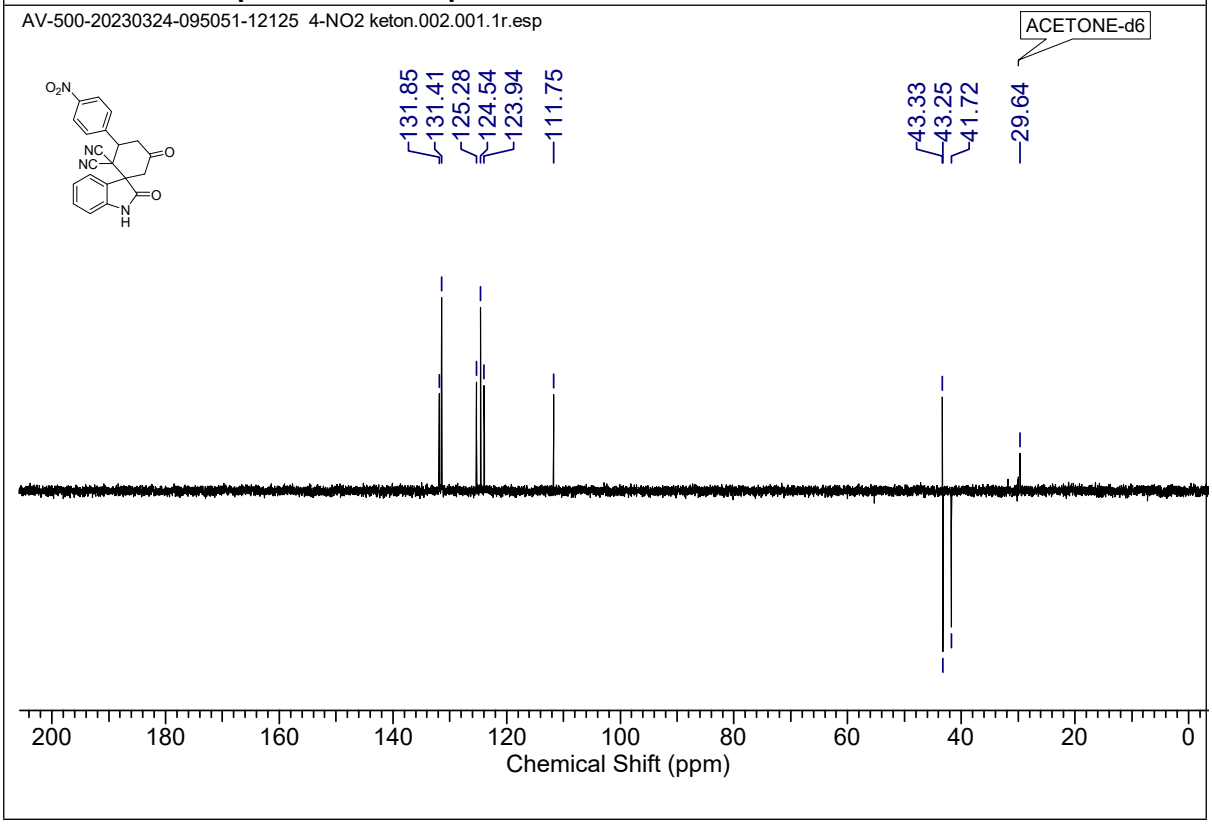
^{1}H NMR spectrum of compound 3Cl (500 MHz, Acetone-d_6)



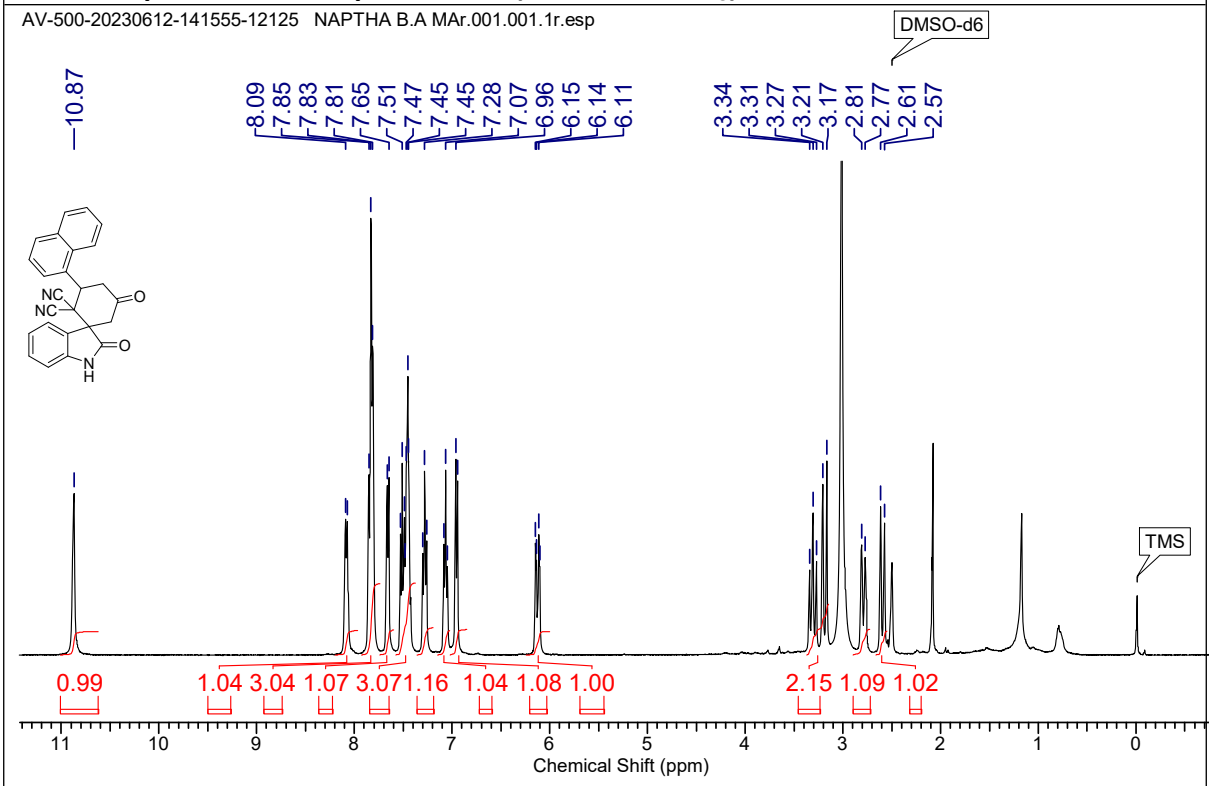
^{13}C NMR spectrum of compound 3Cl (125 MHz, Acetone-d_6)



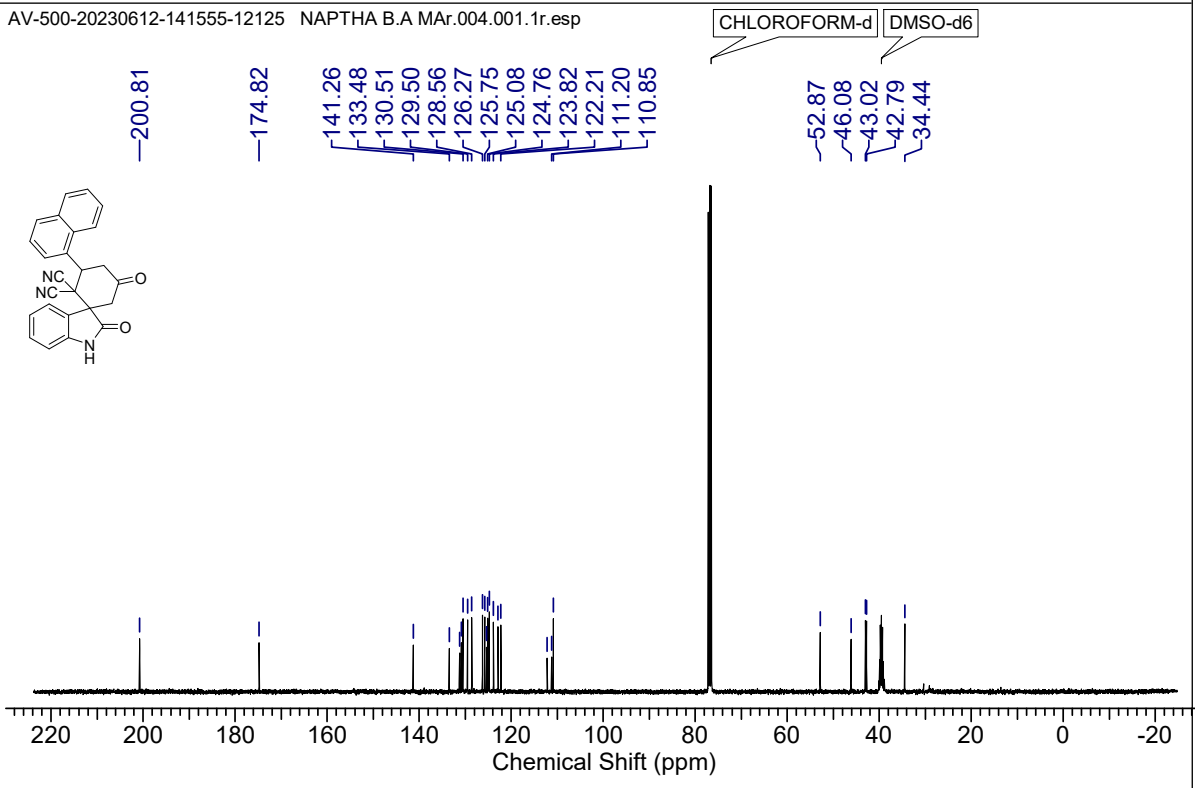
135 DEPT NMR spectrum of compound 3Cl



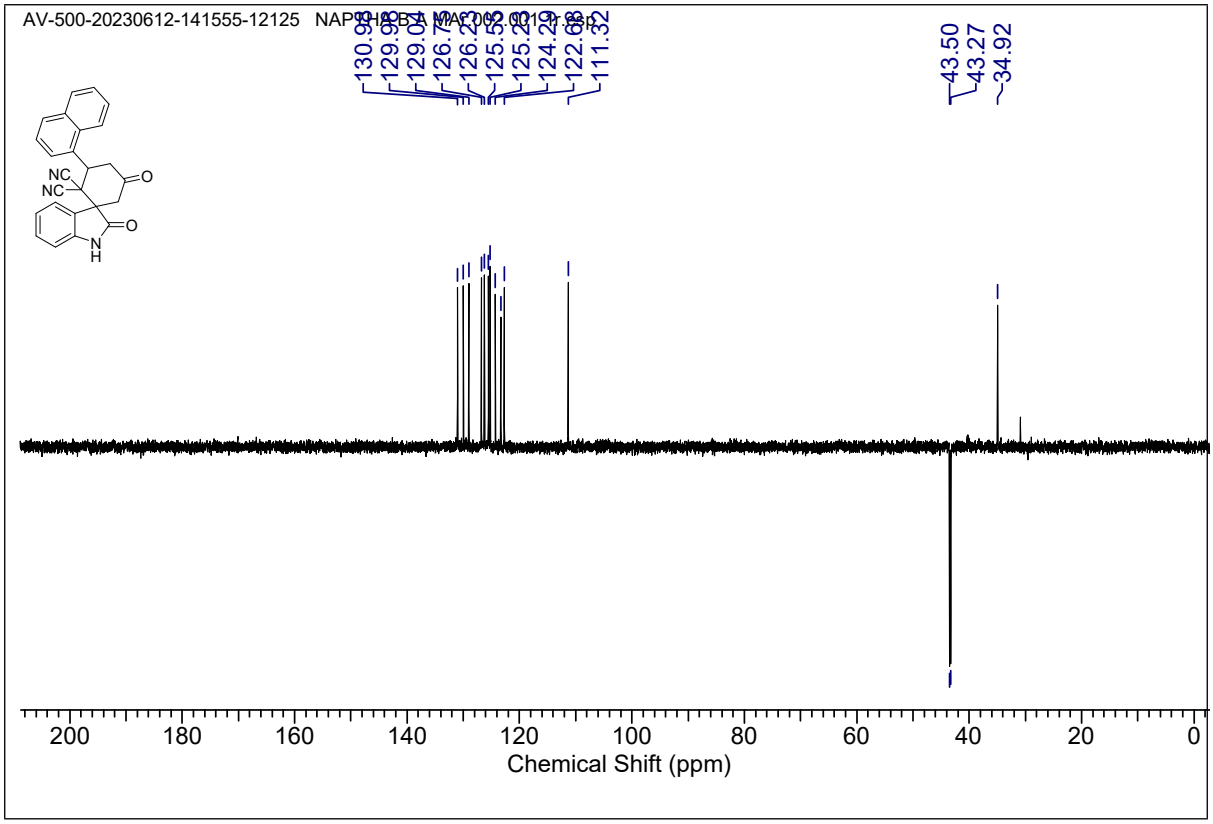
^{1}H NMR spectrum of compound 3Cm (500 MHz, $CDCl_3$)



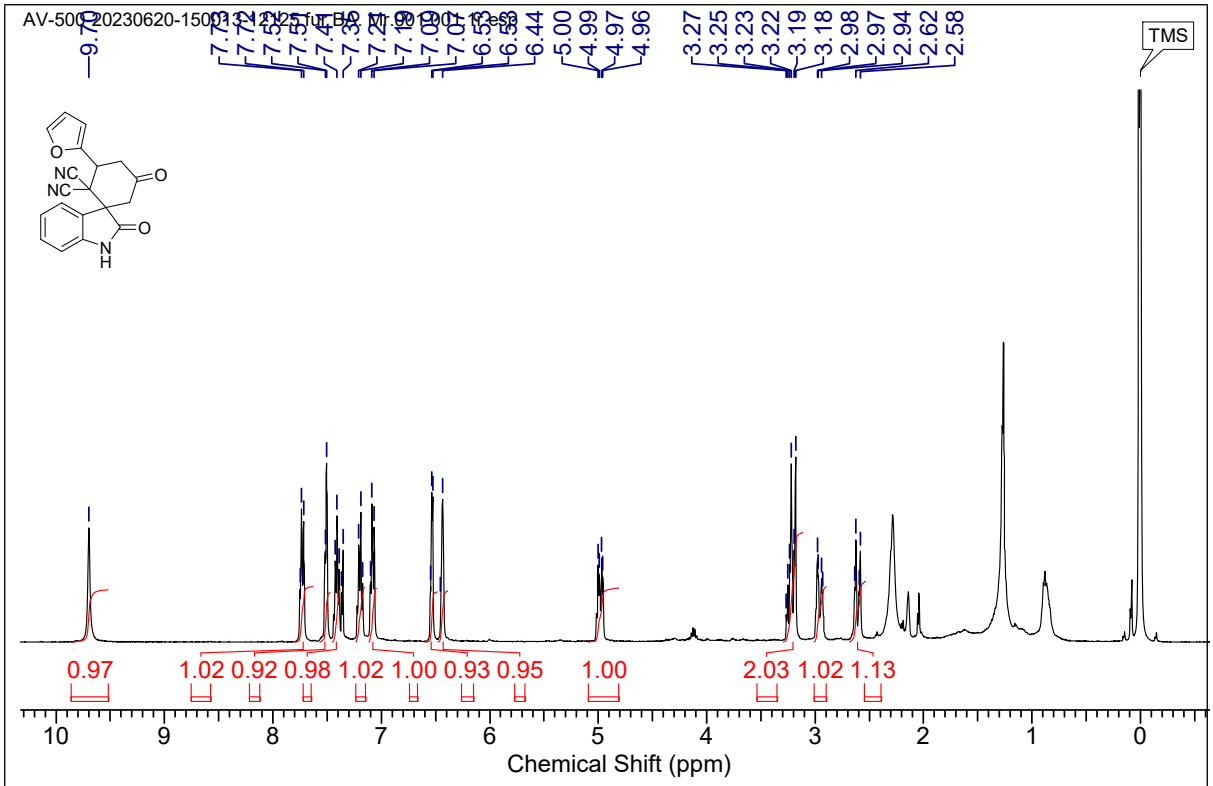
^{13}C NMR spectrum of compound 3Cm (125 MHz, $CDCl_3$)



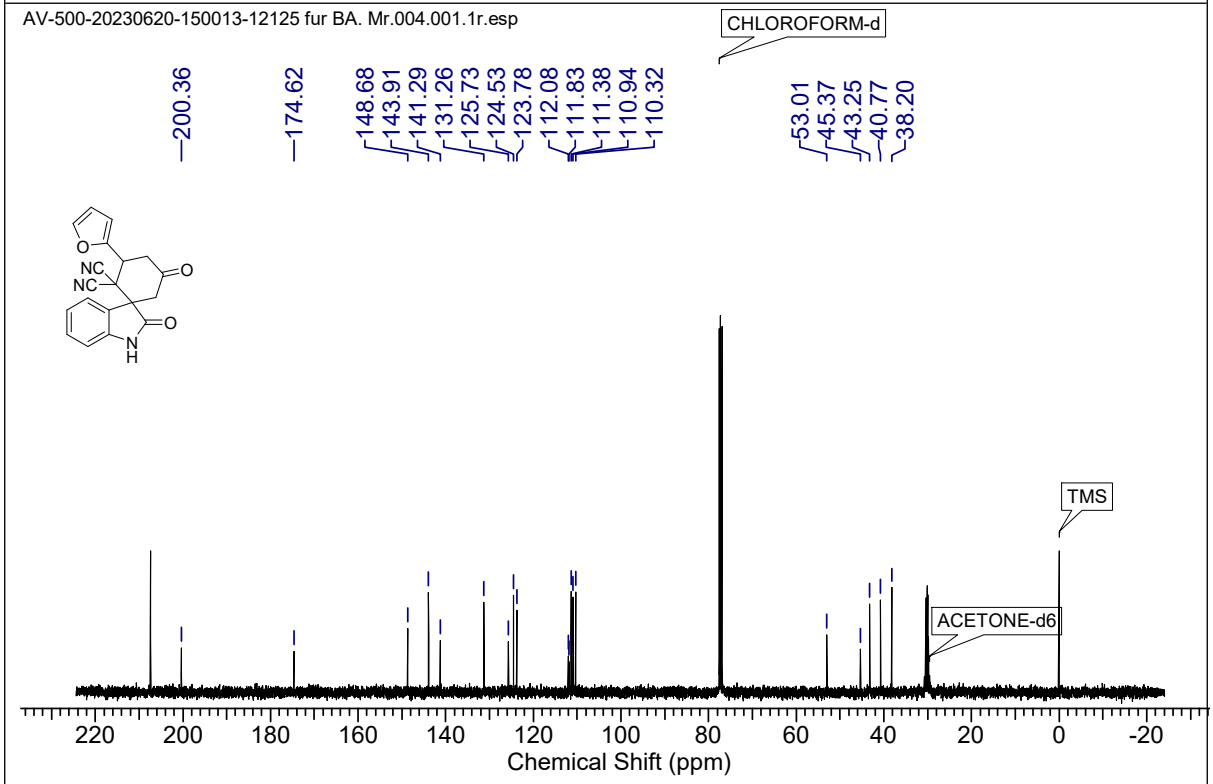
135 DEPT NMR spectrum of compound 3Cm



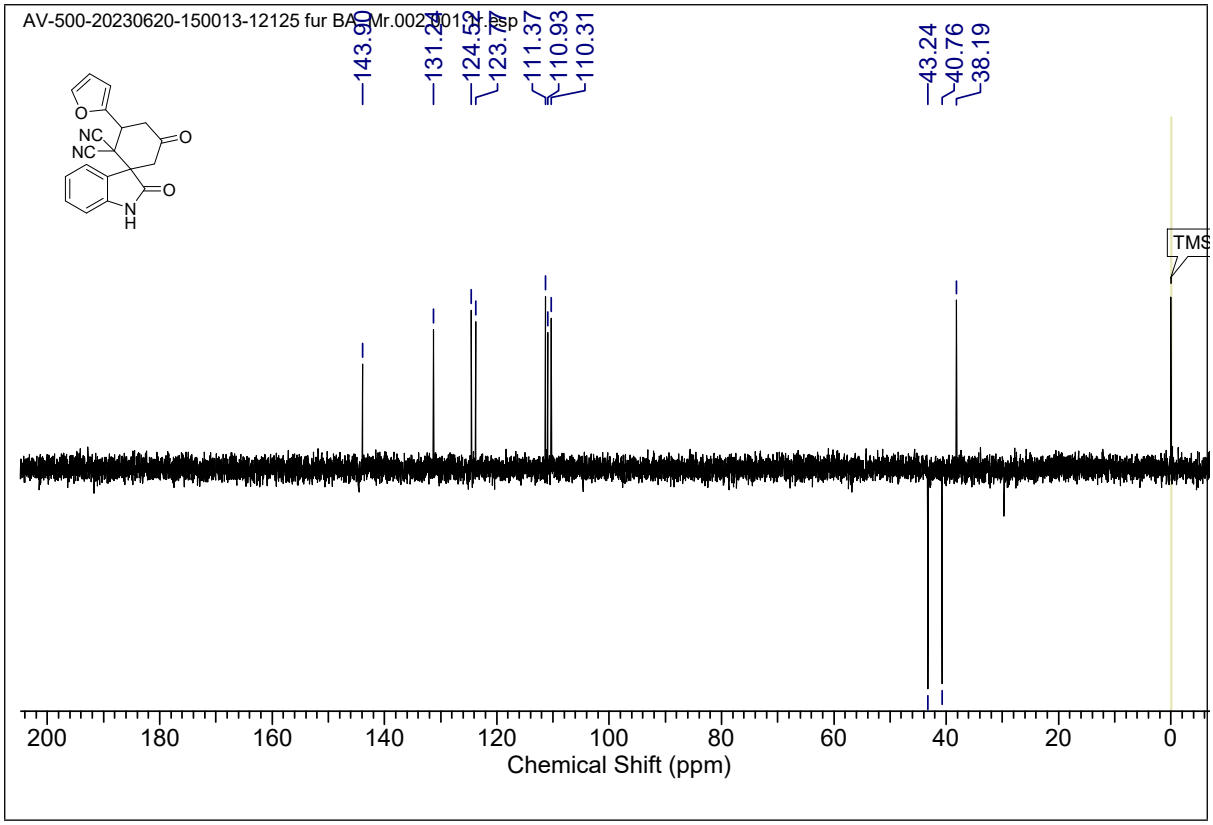
^{1}H NMR spectrum of compound 3Cn (500 MHz, $CDCl_3$)

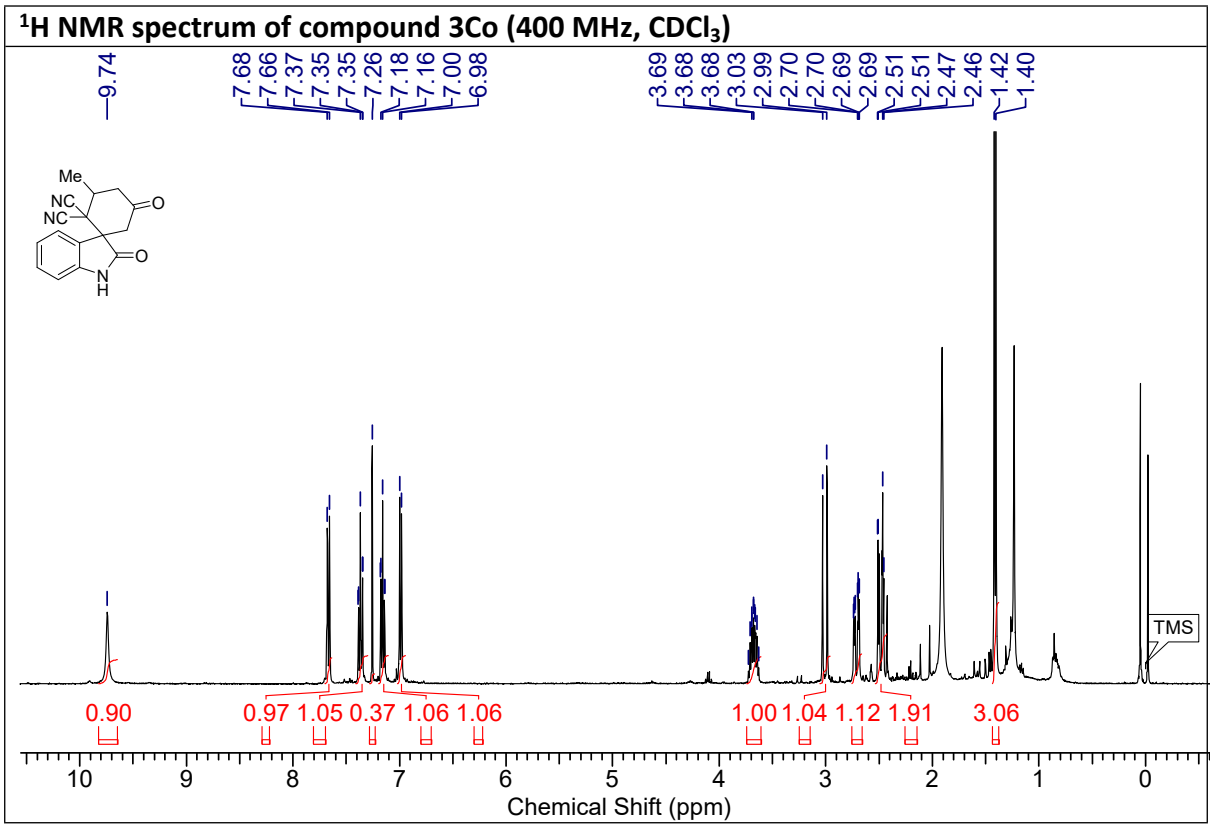


^{13}C NMR spectrum of compound 3Cn (125 MHz, $CDCl_3$)

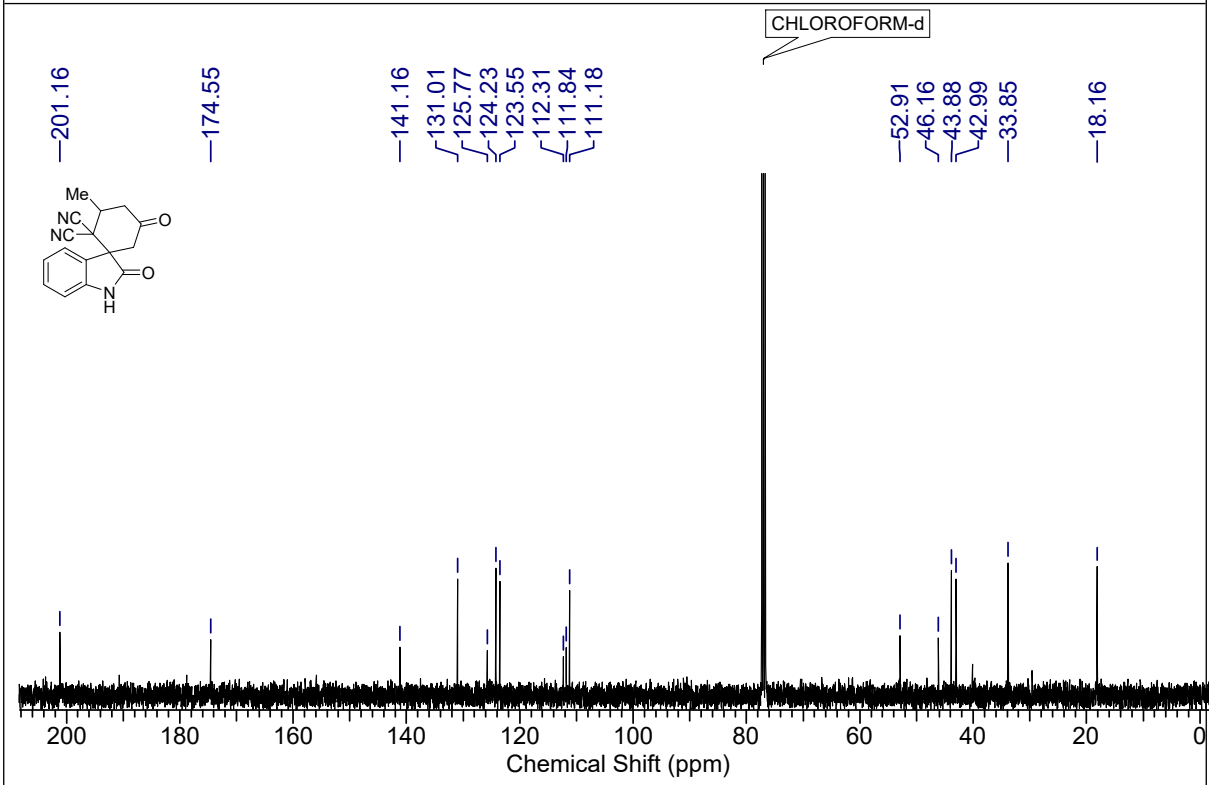


135 DEPT NMR spectrum of compound 3Cn

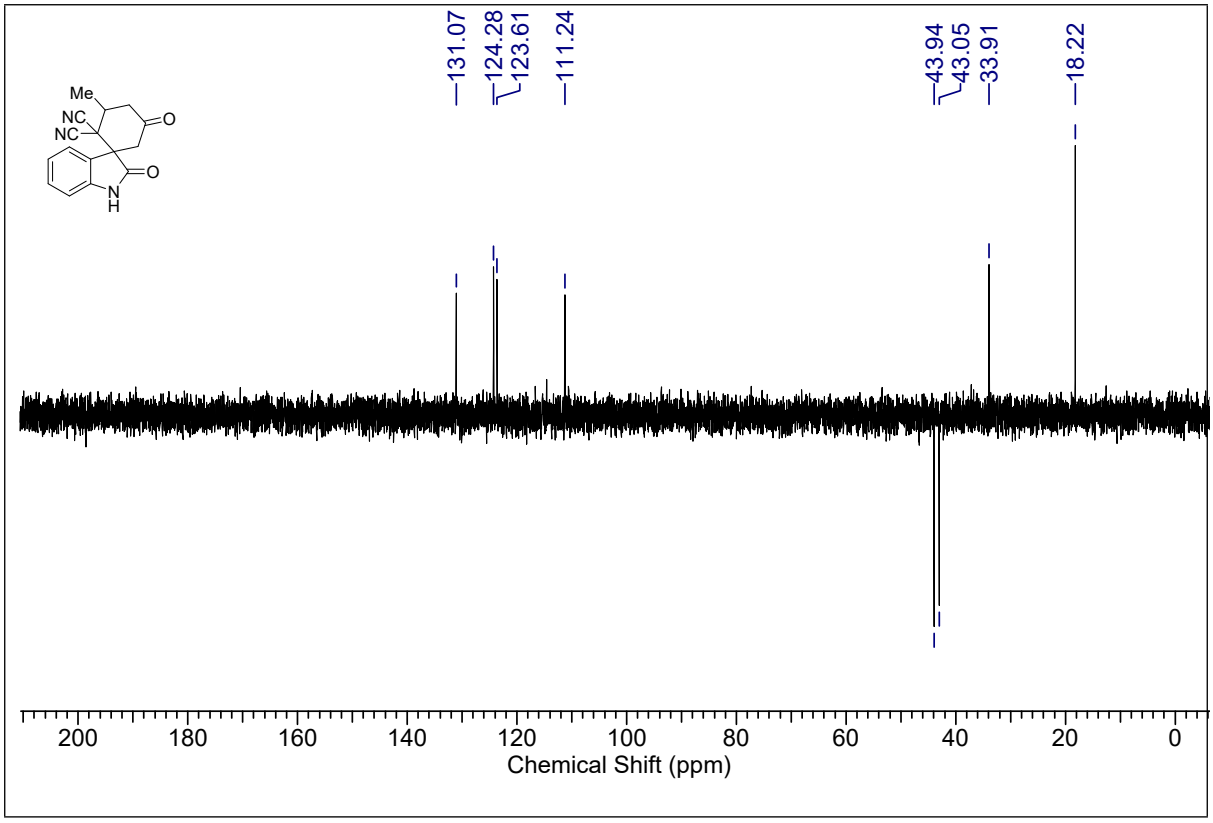

143.90
131.24
124.52
123.77
111.37
110.93
110.31
43.24
40.76
38.19
TMS
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


¹H NMR spectrum of compound 3Co (400 MHz, CDCl3)
9.74
7.68
7.66
7.37
7.35
7.35
7.26
7.18
7.16
7.00
6.98
3.69
3.68
3.68
3.03
2.99
2.70
2.70
2.69
2.69
2.51
2.51
2.47
2.46
1.42
1.40
TMS
0.90
0.97
1.05
0.37
1.06
1.06
1.00
1.04
1.12
1.91
3.06
10
9
8
7
6
5
4
3
2
1
0
Chemical Shift (ppm)

^{13}C NMR spectrum of compound 3Co (101 MHz, $CDCl_3$)



135 DEPT NMR spectrum of compound 3Co


131.07
124.28
123.61
111.24
43.94
43.05
33.91
18.22
Me
NC
NC
O
O
N
H
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)