Electronic Supplementary Material (ESI) for Chemical Science.

Supporting information

Shining light on tryptamine-derived isocyanides: access to constrained spirocylic scaffolds

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1. General information

Commercially available reagents were purchased from Sigma-Aldrich, Fischer Scientific, Strem Chemicals, TCI Chemicals, Activate Scientific, or Fluorochem and were used as purchased unless mentioned otherwise. Solvents were purchased from VWR Chemicals or Sigma-Aldrich and used without purification unless stated otherwise. Reagent-grade solvents were used for the optimization. Thin layer chromatography (TLC) was performed using plates from Merck (SiO_2, Kieselgel 60 F254 neutral, on aluminium with fluorescence indicator) and compounds were visualized by UV detection (254 nm), $KMnO_4$, and/or *p*-anisaldehyde stain. Flash column chromatography was performed by employing silica (200-300 mesh) as support and *n*-heptane/ethyl acetate. NMR spectra were recorded on a Brüker Avance 300 using the residual $CDCl_3$ as internal reference (^{1}H: δ 7.26 ppm, 13C: δ 77.16 ppm). Chemical shifts (δ) are given in ppm and coupling constants (*J*) are quoted in hertz (Hz). Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), br (broad singlet), and m (multiplet) or combinations thereof. Ultra-high resolution mass-spectrometer Bruker solariX XR FT-ICR-MS was used for accurate mass measurements. Samples were ionized by electrospray ionization (ESI) in positive ion mode. UV-Vis spectroscopy at various temperatures was performed using a Varian Cary 100 UV/Vis spectrophotometer coupled with a Varian Cary temperature controller. The solid-state lifetime spectra were acquired using a TCSPC setup with a 450 nm laser at a repetition rate of 8.33 MHz. NMR Data were processed with Mestrenova version 12.

Chemicals: Dioxane (99.8%, extra dry), DCE (99.8%, extra dry), and DMSO (99.8%, extra dry) were purchased from Acros Organics and used as purchased. Dry toluene is obtained from SPS system. The photocatalysts $Ru(bpy)_3(PF_6)_2$ and $[Ir\{dFCF_3ppy\}_2(bpy)]PF_6$, *fac*-Ir, Mes-Acr-$Me^+$ were purchased from commercial sources. The organic photocatalysts 4CzIPN, 4DPAIPN and 5CzIPN were prepared in the lab by the procedure outlined in previous publications.[1] Deuterated solvents were used as purchased ($CDCl_3$, DMSO-d_6, DMF-d_7). 2-methyl indole was purchaged from Sigma-Aldrich and TCI.

Photochemical experiments were performed in a 10 mL microwave (MW) vial equipped with teflon septa. The tubes were irradiated with two Kessil blue LED lights (456 nm) of power 40W. To maintain a constant reaction temperature of 30°C, the setup was cooled by a constant airflow (Figure S1).

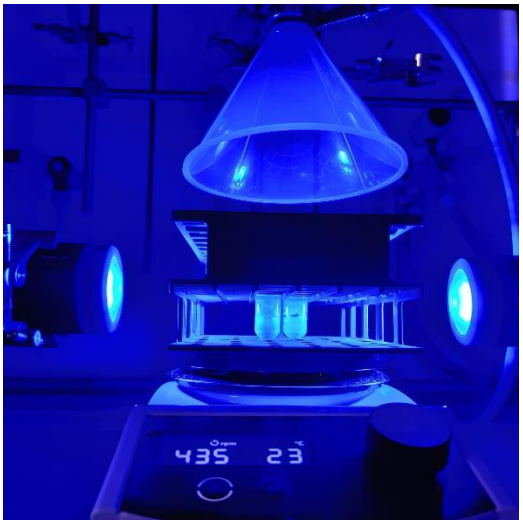
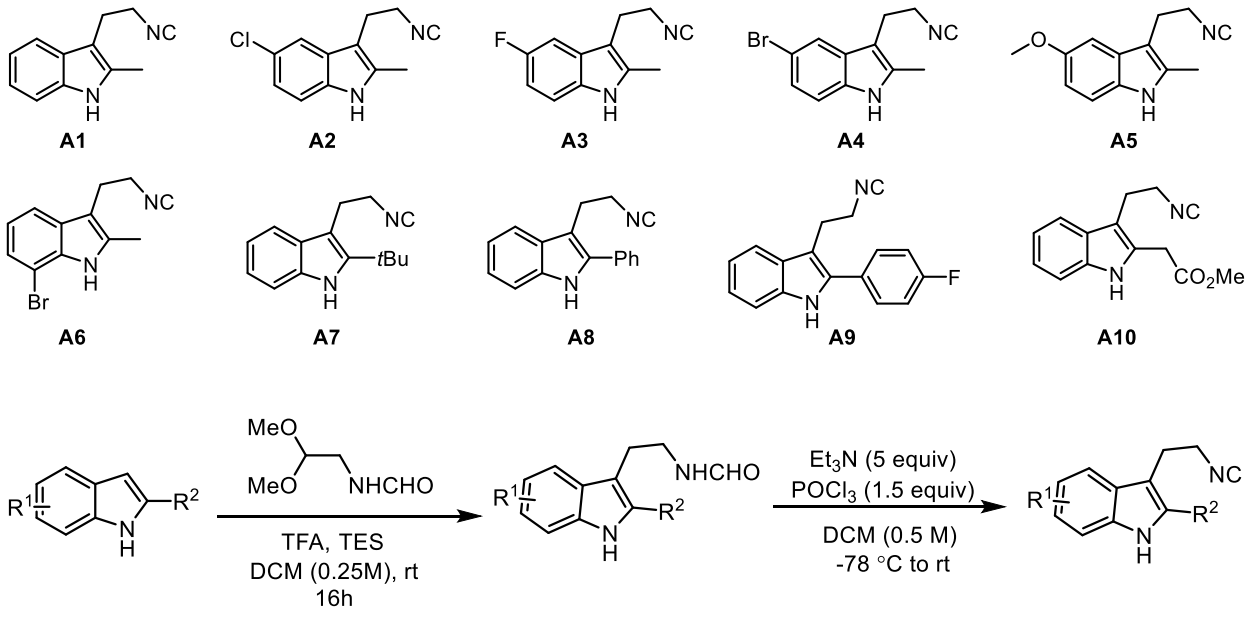


Figure S1: Reaction setup.

2. Synthesis and characterization of starting materials

Isocyanide Synthesis: Isocyanides **A1**-**A10** were synthesized according to previous literature as shown below.[2]



In a round bottom flask, triethylsilane (TES, 3.0 equiv) was dissolved in DCM (0.5 M) followed by TFA (5.0 equiv). A solution of dimethyl acetal (1.1 equiv) and indole (1.0 equiv) in DCM (0.5 M) was added dropwise to the above solution at room temperature. The reaction mixture was

stirred for 16 hours at rt and cooled down to 0 ºC before quenching with a saturated $NaHCO_3$ solution. The organic layer was separated and the aqueous layer was extracted three times with DCM. The organic layers were combined together, washed with brine and dried over Na_2SO_4. The solvent was removed in vacuo and the crude mixture was purified by flash chromatography using EtOAc/Heptane (1:2 to 1:1) to obtain substituted tryptamine formamide.

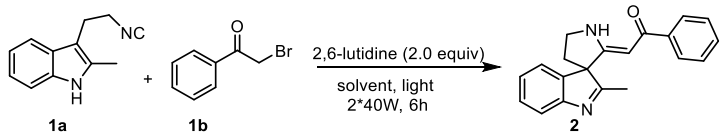
The formamide obtained from the previous step was then dissolved in anhydrous DCM (0.5 M) followed by the addition of triethylamine (5.0 equiv). The reaction mixture was cooled down to -78 ºC and then phosphoryl chloride (1.5 equiv) was added dropwise. After mixing the reaction mixture for 2 h at this temperature, the mixture was brought to 0 ºC and stirred for another 30 min. before quenching with water. The aqueous layer was extracted with DCM and the combined organic layer was washed with brine, dried over sodium sulfate and concentrated in vacuo. The crude reaction mixture was loaded on a short silica column and purified using pure DCM.

3. Optimization studies

3.1 General procedure for optimization

GP1: (without PC): An oven-dried 10 mL MW vial equipped with a magnetic stirring bar was charged with 2-bromo-1-phenylethan-1-one (**1b**) and 3-(2-isocyanoethyl)-2-methyl-1H-indole (**1a**). Afterwards, solvent was added followed by base. The MW vial was then closed with a cap containing teflon septum and degassed with nitrogen for 5 min. The vial was then placed for irradiation with two Kessil blue LEDs as shown in figure S1 (40W, 456 nm) for 6-12h. The progress of the reaction was monitored through TLC and LC/MS. After completion, the solution was diluted with EtOAc and washed with water. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4. The solvent was removed in a vacuum and the reaction yield was calculated through the ^{1}H-NMR integration method using CH_2Br_2 as an internal standard.

Table S1. Optimization results for the synthesis of spiroindolenines without photocatalyst.



Entry	Solvent (0.1M)	LED (nm)	Ratio (1a:1b)	Yield[a] (%)
1	DCE	456	1:1.5	70
2[c]	DCE	390	1:1.5	64
3	$CHCl_3$	456	1:1.5	56
4	**Toluene**	**456**	1:1.5	**82**
5[c]	Toluene	456	1:1.5	76
5	Dioxane	456	1:1.5	66
6	ACN	456	1:1.5	30
7	Acetone	456	1:1.5	22
Effect of ratio				
8	Toluene	456	1:1.25	46
9	Toluene	456	1:1	26
10	Toluene	456	1.25:1	54
11	Toluene	456	1.5:1	70

[a]NMR yield determined by using CH_2Br_2 as an internal standard. [c]Power of LED = 40W.

Table S2. Control experiments for the synthesis of spiroindolenines without photocatalyst.[a]

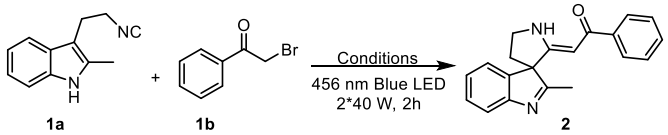
Entry	Deviations from optimized conditions	Yield[b]
1	None	82
2	No light	0
3	No light, 50 ºC	0
4	Air instead of N_2	0
5	10% H_2O	72
6	50% H_2O	64
7	0.05 M instead of 0.1M	70
8	0.16 M instead of 0.1M	67
9	0.2 M instead of 0.1M	66
10	Et_3N instead of 2,6 lutidine	72
11	Morpholine instead of 2,6 lutidine	16
12	No 2,6-lutidine	6

[a]All reactions were performed using **1a** (0.2 mmol, 1 equiv) and **1b** (0.3 mmol, 1.5 equiv).[b]Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

GP2: (with PC): An oven-dried 10 mL MW vial equipped with a magnetic stirring bar was charged with 2-bromo-1-phenylethan-1-one (**1b**), photocatalyst (PC), and 3-(2-isocyanoethyl)-2-methyl-1H-indole (**1b**). Afterwards, solvent was added followed by base. The MW vial was then closed with a cap containing teflon septum and degassed with nitrogen for 5 min. The vial was then placed for irradiation with two Kessil blue LEDs as shown in figure S1 (40W, 456 nm) for 2h. The progress of the reaction was monitored through TLC and LC/MS. After completion, the solution was diluted with EtOAc and washed with water. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4.

The solvent was removed in a vacuum and the reaction yield was calculated through the ^{1}H-NMR integration method using CH_2Br_2 as an internal standard.

Table S3. Optimization results for the synthesis of spiroindolenines using photocatalysts.



Entry	PC (mol %)	Solvent (0.1M)	Base (2.0 equiv)	Ratio (1a:1b)	Yield[a] (%)
Photocatalyst screening (PC)					
1	PC 6 (5)	DCE	2,6-lutidine	1.5:1	67
2	PC 5 (1)	DCE	2,6-lutidine	1.5:1	72
3	PC 7 (5)	DCE	2,6-lutidine	1.5:1	63
4	**PC 1 (5)**	**DCE**	**2,6-lutidine**	**1.5:1**	**65**
5	PC 2 (1)	DCE	2,6-lutidine	1.5:1	69
6	PC 4 (1)	DCE	2,6-lutidine	1.5:1	33
7	PC 3 (5)	DCE	2,6-lutidine	1.5:1	10
8	PC 6 (2)	DCE	2,6-lutidine	1.5:1	58
9	PC 6 (8)	DCE	2,6-lutidine	1.5:1	62
Solvents screening					
10	PC 6 (5)	1,4-Dioxane	2,6-lutidine	1.5:1	51
11	PC 6 (5)	Toluene	2,6-lutidine	1.5:1	52
12	PC 6 (5)	MeOH	2,6-lutidine	1.5:1	20
13	PC 6 (5)	DMSO	2,6-lutidine	1.5:1	40
14	PC 6 (5)	Acetone	2,6-lutidine	1.5:1	35
15	PC 6 (5)	ACN	2,6-lutidine	1.5:1	40
Base screening					
16	PC 6 (5)	DCE	2,4,6-collidine	1.5:1	55
17	PC 6 (5)	DCE	DIPEA	1.5:1	7
18	PC 6 (5)	DCE	Et_3N	1.5:1	26
19	PC 6 (5)	DCE	$NaHCO_3$	1.5:1	8
20	PC 6 (5)	DCE	-	1.5:1	16
Effect of ratio					
21	PC 6 (5)	DCE	2,6-lutidine	1:1	53
22	PC 6 (5)	DCE	2,6-lutidine	1.5:1	68
23	PC 6 (5)	DCE	2,6-lutidine	1.25:1	62

[a]NMR yield determined by using CH_2Br_2 as an internal standard.

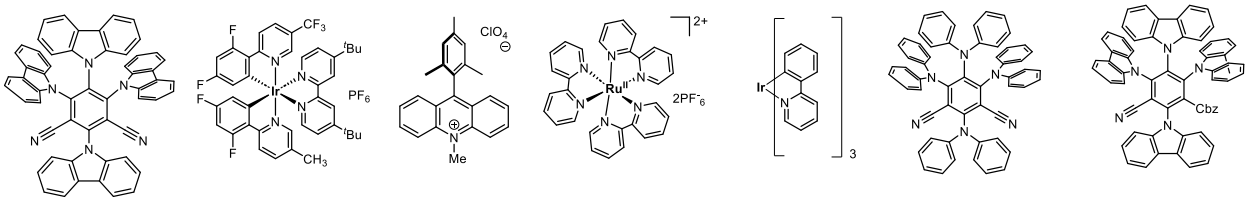
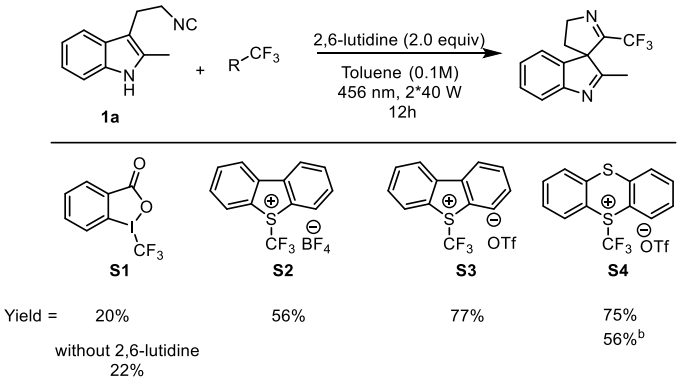


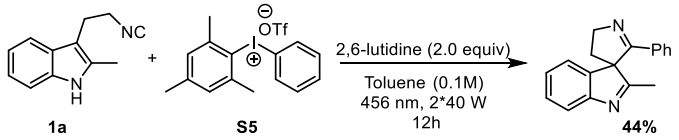
Figure S2: Photocatalysts used in the optimization studies.

Table S4. Synthesis of spiroindolenines without photocatalyst employing trifluromethyl radical sources.



[a]All reactions were performed using **1a** (0.2 mmol, 1 equiv) and a **CF_3 source** (0.3 mmol, 1.5 equiv); yields were determined by ^1H NMR using CH_2Br_2 as an internal standard. [b]Isolated yield.

Table S5. Synthesis of spiroindolenines without photocatalyst employing diaryl iodonium salts.



[a]All reactions were performed using **1a** (0.2 mmol, 1 equiv) and **S5** (0.3 mmol, 1.5 equiv), isolated yield.

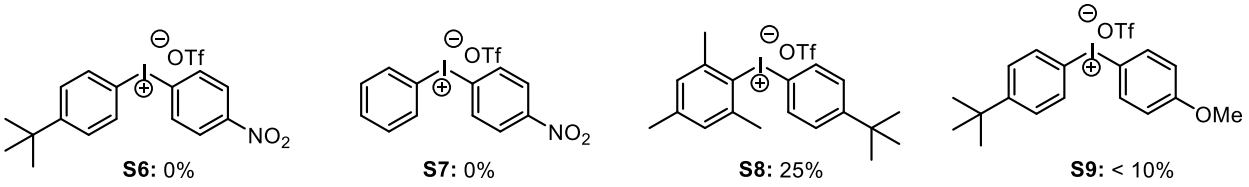
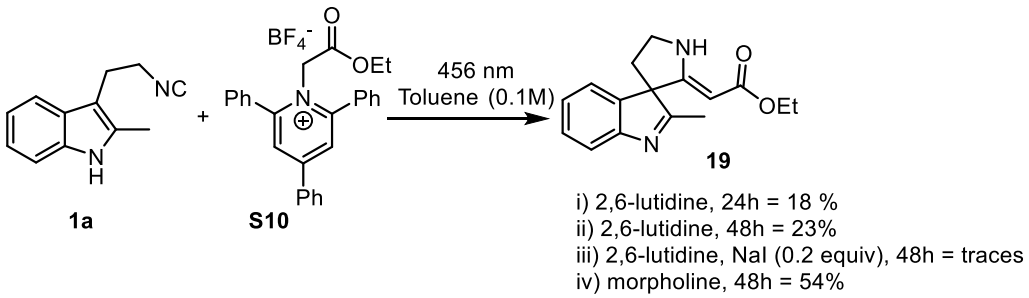


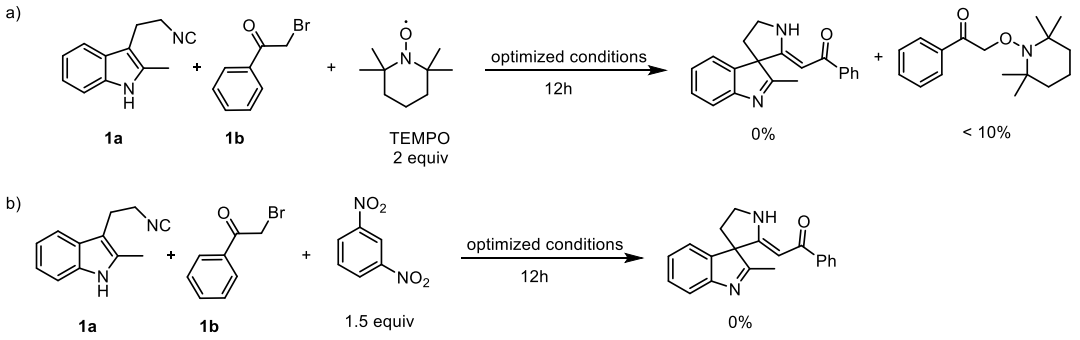
Table S6. Synthesis of spiroindolenines without photocatalyst employing pyridinium salt.



[a]All reactions were performed using **1a** (0.2 mmol, 1 equiv) and **S10** (0.3 mmol, 1.5 equiv), isolated yield.

4. Mechanistic investigations

A. Radical inhibition experiment: Under our optimized reaction conditions, we added 2 equiv of TEMPO. The reaction mixture was analysed by NMR and GC-MS.



Scheme S1: a) radical inhibition experiment with TEMPO b) radical inhibition experiment with 1,3-dinitrobenzene.

We observed 0 % yield of the desired product alongside a <10 % formation of the TEMPO-adduct. This result can be deriving from a minor pathway involving EDA complex between TEMPO and **1b**, as shown by Prof. Melchiorre[3] in his work. Based on our mechanistic hypothesis, we assumed that the quenching of our reaction could be due to the interaction of TEMPO with the excited state of isocyanide **1a**. However, we could not provide experimental evidence through static fluorescence quenching experiments probably due to the low lifetime of the excited state of **1a** in solution. The addition of 1,3-dinitrobenzene also quenched the reaction showing the involvement of SET step.

B. Quantum yield determination: The quantum yield of the reaction was determined according to a reported procedure.[4]

The photon flux of the blue LED system was determined through standard ferrioxalate actinometry. A 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (736 mg) in 10.0 mL of 0.05 M aqueous sulfuric acid. A buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (50 mg) and sodium acetate (11.25 g) in 50 mL of 0.5 M aqueous sulfuric acid.

To a 10 mL MW vial equipped with a stirring bar, 1 mL of the ferrioxalate solution was added. The vial was sealed and placed 4 cm away from the walls of the irradiation system as shown in figure **S1** and irradiated for the indicated time (see Table S7). After irradiation for the indicated

time, 20 µL of the irradiated solutions were added to 2 mL of the phenanthroline solution. The resulting reaction mixture was left equilibrating in the dark for 1 h. Next, the resultant reaction solutions were further diluted by taking 50 µL and adding 3 mL of distilled water. The final solution was analyzed via UV-Vis spectroscopy.

The absorbance of the resulting solution in a cuvette (l = 10 mm) at 510 nm was measured by a UV-Vis spectrometer. The procedure was repeated at different reaction times and the absorbance of a non-irradiated sample was measured as well.

Table S7: Photon flux calculation.

Time (s)	A (510 nm)	ΔA_{510nm}	mol Fe^{2+}
0	0.0045		
5	0.0114	0.0069	1.8959 x 10^{-9}
10	0.0197	0.0152	4.1765 x 10^{-9}
15	0.0246	0.0201	5.5229 x 10^{-9}
20	0.0278	0.0233	6.4022 x 10^{-9}

To calculate the amount of Fe^{2+}, the following equation was used:

$$mol\ Fe^{2+} = \frac{V \text{ x } \Delta A}{l \text{ x } \varepsilon}$$

Where V is the total volume (0.00305 L), ΔA is the difference in the absorbance at 510 nm between the irradiated and non-irradiated sample, l is the path length (1.00 cm), and ε is the molar absorptivity at 510 nm (11,100 L/mol x cm).

The photon flux was calculated as follows:

$$photon\ flux = \frac{mol\ Fe^{2+}}{\Phi \text{ x } t \text{ x } f}$$

From which

$$mol\ Fe^{2+} = (F \times \Phi \times f) \times t$$

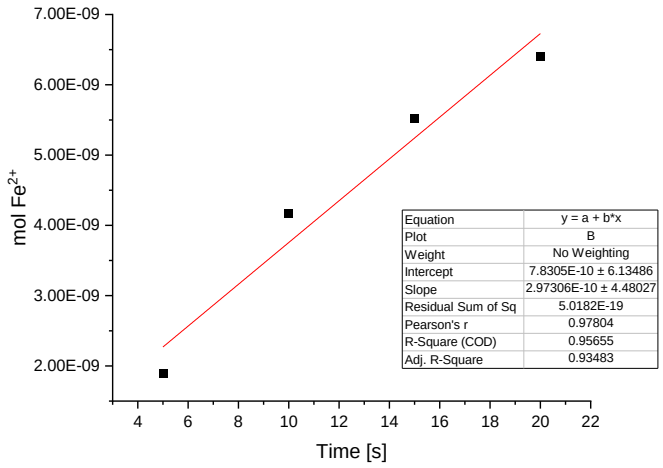


Figure S3: Plot of the moles of Fe^{2+} vs time to calculate the photon flux.

From the graph,

Slope = $(F \times \Phi \times f)$ = 2.9730 x 10^{-10}

So, F (photon flux) = 3.5183 x 10^{-10} Einstein/s.

where Φ is the quantum yield for the ferrioxalate actinometer (approximated as 0.845, which was reported for a 0.15 M solution at λ = 457.9 nm) and f is the fraction of light absorbed (close to 1).

Quantum yield determination: An oven-dried 10 mL MW vial equipped with a magnetic stirring bar was charged with 2-bromo-1-phenylethan-1-one (1.5 equiv, 0.15 mmol) and 3-(2-isocyanoethyl)-2-methyl-1H-indole (1 equiv, 0.1 mmol). Afterwards, dry toluene (0.1 M) was added followed by 2,6-lutidine (2 equiv, 0.2 mmol). The MW vial was then closed with a cap containing teflon septum and degassed with nitrogen for 5 min. The vial was then placed for irradiation with two Kessil blue LEDs as shown in figure S1 (40W, 456 nm) for 2 h. After this reaction yield was calculated through the ^{1}H-NMR integration method using CH_2Br_2 as an internal standard. The calculated yield was 24%.

The quantum yield was calculated through the formula:

$$\Phi = \frac{mol\ product}{flux \text{ x } t \text{ x } f}$$

Where flux is the photon flux determined by ferrioxalate actinometry (3.5183 x 10^{-10} Einstein/s), t is the time (7200 s), and f is the fraction of light absorbed by reaction mixture in toluene at 456 nm (0.3824, average of three measurements). The fraction of light absorbed at 456 nm was calculated:

f = 1.0000 – $10^{-0.3824}$ = 1.0000 –$10^{-2.77}$ = 0.4715

The calculated quantum yield for the reaction therefore is: 20

C. **Optical absorption Spectra:** UV-vis spectra were recorded using a Shimadzu UV-Vis Spectrophotometer UV-3600 system or Varian Cary 100 UV/Vis spectrophotometer coupled with a Varian Cary temperature controller. Measurement details: cuvettes path length (10 mm or 1 mm); baseline: respective solvents; scan rate: medium; slit width: 2 nm.

Purification of chemicals:

2-methyl indole (TCI source): The solution of 2-methyl indole in DCM was passed through activated charcoal and then further purified by column chromatography with methyl tert-butyl ether and heptane. The purified sample was further recrystallized using a $CHCl_3$ and heptane solution.

3-methyl indole (Sigma-Aldrich): Purified by vacuum sublimation

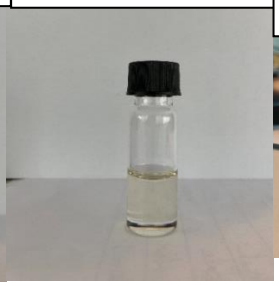
1b: Solution of **1b** in DCM was passed through activated charcoal and then further purified by recrystallization using a $CHCl_3$ and heptane solution.

1a: A freshly prepared **1a** solution in DCM was passed through activated charcoal and dried and stored under nitrogen at -78 ºC.

a) Fresh Isocyanide **1a**

b) Isocyanide **1a** after 24h at RT

c) after filtration of sample b RT



d) freshly prepared but after passing through activated charcoal after 24 h.

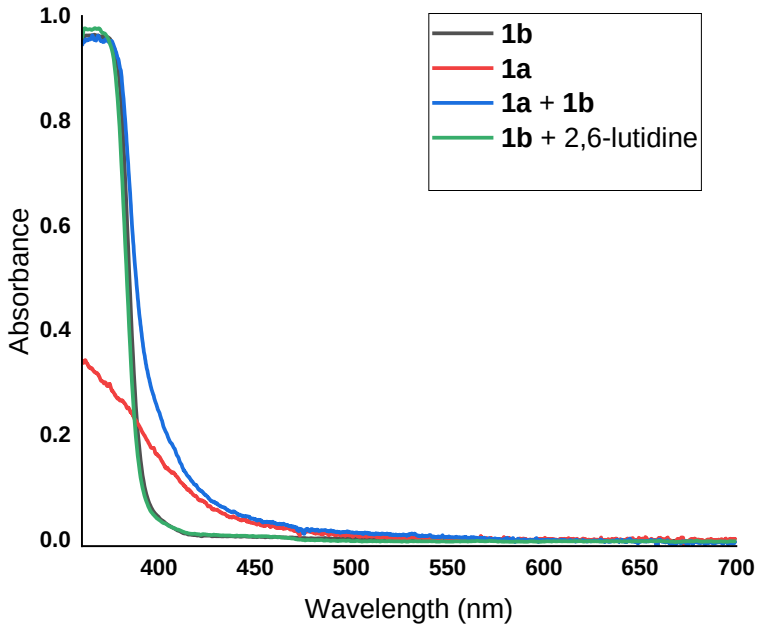


Figure S4: Absorption spectra of individual components and reaction mixture, recorded in toluene: [**1b**] = 0.15 M; [**1a**] = 0.1 M; [**2,6-lutidine**] = 0.2 M; [**1a**+**1b**] = solution of 0.15 mmol of **1b** and 0.1 mmol of **1a** in toluene (0.1 M); [**1b**+**2,6-lutidine**] = solution of 0.1 mmol of **1b** and 0.13 mmol of 2,6-lutidine in toluene (0.1M). Note: Aborption values are normalized. Cuvette: 10 mm

Implication: Bromide **1b**, **2,6-lutidine**, and the mixture of **2,6-lutidine** and bromide **1a** did not show any absorption peak in the visible region. The mixture of **1a** and **1b** exhibits slightly higher absorption as compared to isocyanide **1a** alone. Based on this data we concluded that the main absorbing species under our optimized conditions is **1a**.

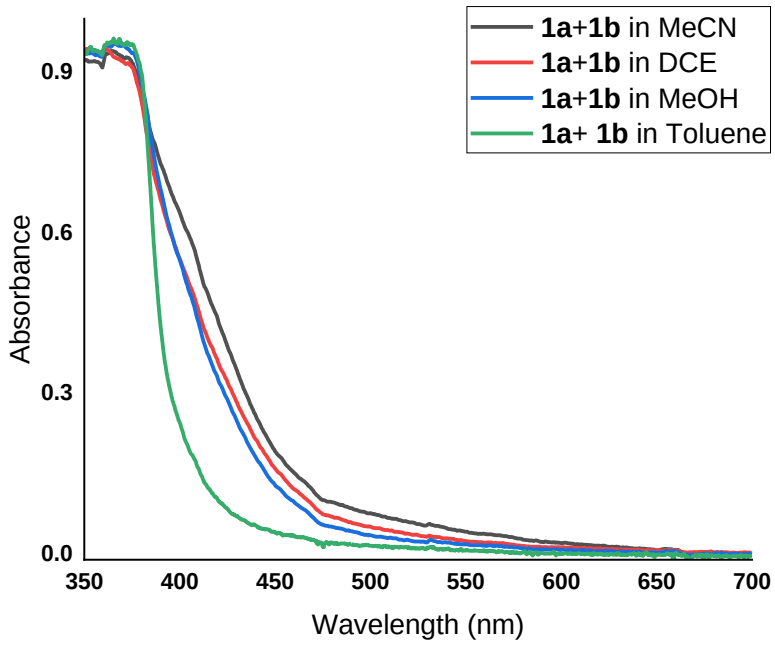


Figure S5: Absorption spectra of the mixture **1a** and **1b** in different solvents after stirring for 30 minutes: [**1a**+**1b**] = solution of 0.15 mmol of **1b** and 0.1 mmol of **1a** in an appropriate solvent. Note: Aborption values are normalized. Cuvette: 10 mm

Implication: The mixture of **1a** and **1b** exhibits higher absorption in polar solvents, which are more effective at stabilizing the EDA intermediates compared to non-polar solvents. This observation suggests that intermolecular EDA could be the primary pathway in polar environments. However, we obtained lower yields in these solvents except DCE (Table S3) which indicates that under our reaction conditions, the aggregation-based charge transfer pathway prevails over the intermolecular EDA-complex pathway.

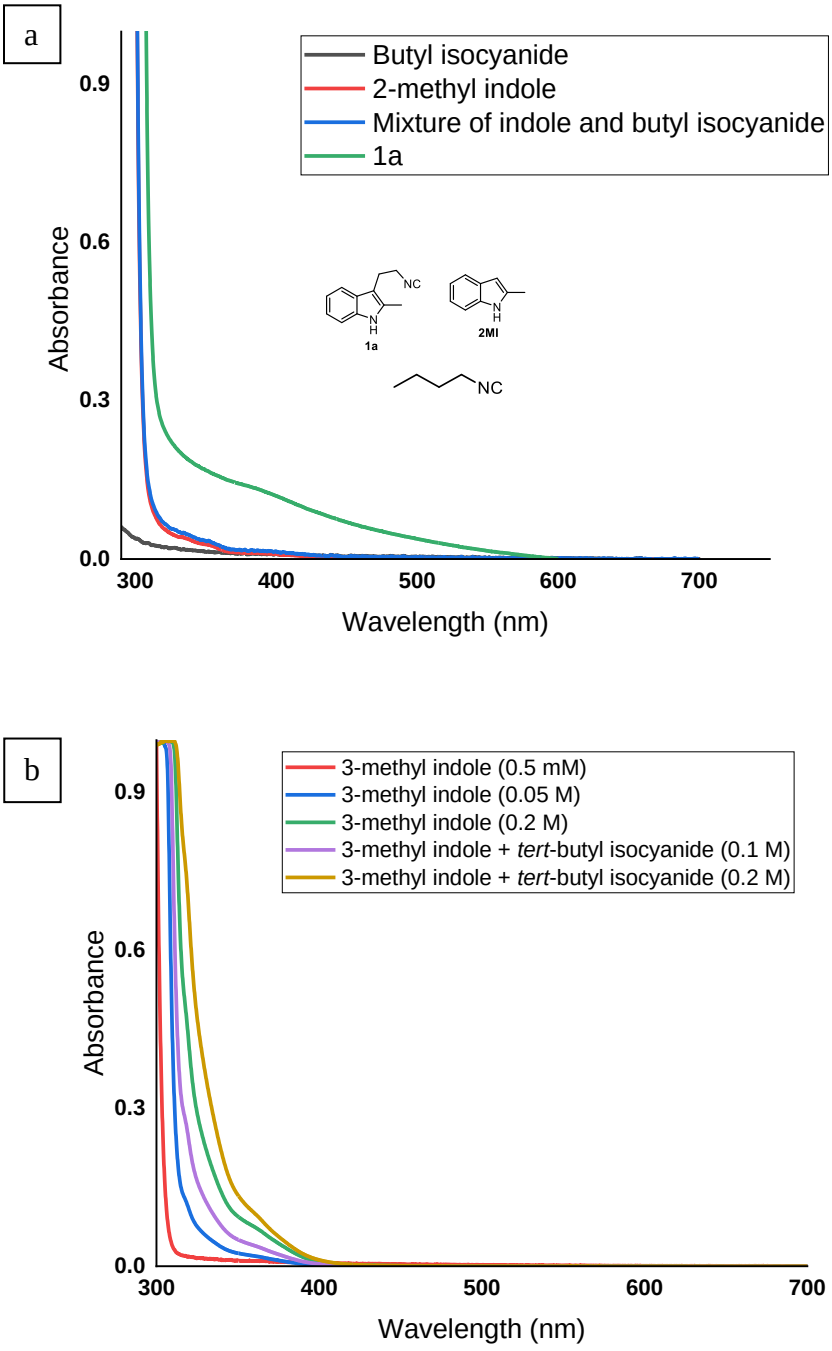


Figure S6: (a) Absorption spectra of 2-methyl indole (0.1M), butyl isocyanide (0.1M) and a mixture of butyl isocyanide and 2-methyl indole (1:1) in toluene. Cuvette: 1 mm; (b) Absorption spectra of 3-methyl indole and a mixture of tert-butyl isocyanide isocyanide and 3-methyl indole (1:1) in toluene. Cuvette: 10 mm

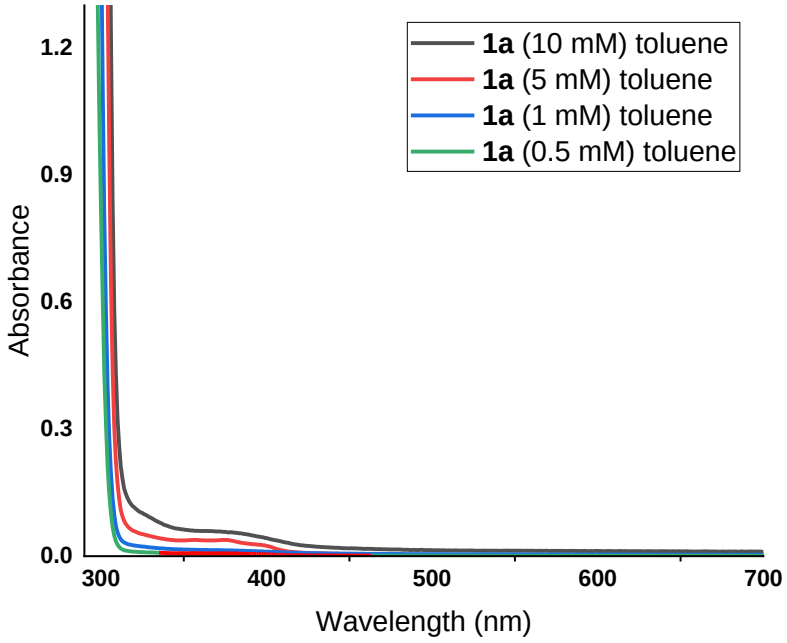


Figure S7: Absorption spectra of **1a** at different concentrations in toluene and acetonitrile using Cary-60 spectrophotometer. Cuvette: 10 mm

5. Computational analysis

The choice of a suitable TD-DFT functional was explored using various functional with the triple-zeta basis set and a detailed analysis is presented in Table S8. The three functionals (CAM-B3LYP, M06-2X and WB97X-D) yield a similar value for S_1 state, however M06-2X overestimates the T_1 energy. The other two functionals B3LYP and PBE which are not suitable for charge-transfer interactions predicts the S_1 absorption towards a slightly longer wavelength. We chose WB97X-D functional for our further analysis as it was designed to treat both long-range and short-range charge-transfer interactions effectively and demonstrated satisfactory accuracy for both covalent and non-covalent interactions.[5]

We have explored a model-dimer system with an interdimer separation of ~3.50 Å, as shown in Figure S9(i). There is a bathochromic shift in the absorption as compared to the monomer, which should be more prominent in the case of higher-order oligomers. Moreover, the HOMO and

LUMO are located on different fragments, thus indicating a possibility of inter-fragment charge transfer.

A similar trend is observed in a model-trimer system with a more profound red shift as the TD-DFT results suggest absorption at ~263 nm in its first excited singlet state (Table S9).

Table S8: Excited states of **1a** calculated using various TD-DFT functionals with cc-pVTZ basis set.

State	B3LYP	CAM-B3LYP	PBE	M06-2X	WB97X-D
$E(S_1)$ [nm]	265	247	287	245	245
$E(T_1)$ [nm]	383	396	381	342	373

Table S9: Excited states of **1a** and model systems calculated at Wb97XD/cc-pVTZ level of theory.

State	Monomer	Model-dimer	Model-trimer
$E(S_1)$ [nm]	245	256	263
f_{osc}	0.0602	0.0135	0.001

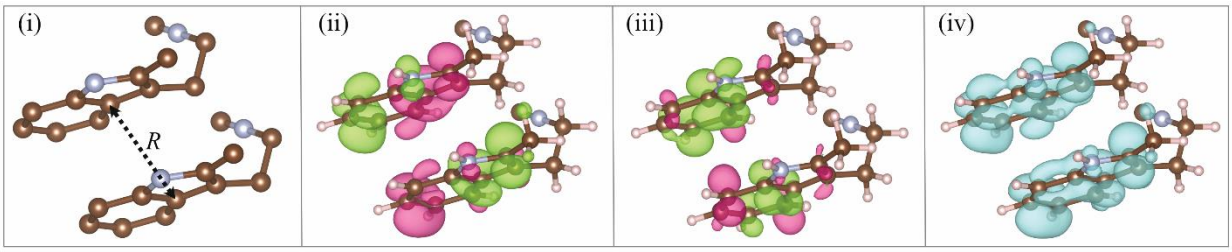


Figure S8: (i) A slip-stacked model dimer system with interdimer separation (*R*) of ~3.50 Å; (ii) the transition density; (iii) difference density and (iv) overlap of hole-electron for the first excited singlet (S_1) state.

6. Fluorescence lifetime measurement of **1a**

Fluorescence lifetime measurements in solution were recorded using Horiba, Deltapro instrument.
Specifications: Excitation using 450nm laser diode
Long pass filter used: LP 500 nm
Polarizer + magic angle: before sample 180º and after sample 55º
Calibration: Cumarin 6 in MeOH (3 μM)
Data analysis: EzTime software (from Horiba, Deltaflex)
Results obtained:

A) 4 mM solution of **1a** in acetonitrile

1-5 exponentials: A+ B1*exp(-i/T1)+ B2*exp(-i/T2)+ B3*exp(-i/T3)							
		Value		3σ		Rel. Amplitude %	Norm. pre-exponential
T1	=	1.4066	±	0.31576	ns	4.64	0.00
T2	=	8.66268	±	0.455612	ns	20.52	0.00
T3	=	0.0189413	±	0.00475091	ns	74.85	1.00
A	=	1.61237	±	0.298906			
Average LifeTime	=	0.025271	±	0.554354	ns		
Chi sq.	1.099091						

B) 20 mM solution of **1a** in acetonitrile

1-5 exponentials: A+ B1*exp(-i/T1)+ B2*exp(-i/T2)+ B3*exp(-i/T3)							
		Value		3σ		Relative Amplitude/%	Normalised pre-exponential
T1	=	1.01042	±	0.13748	ns	9.04	0.00
T2	=	6.50825	±	0.171191	ns	41.83	0.00
T3	=	0.0269861	±	0.00710246	ns	49.12	0.99
A	=	3.30519	±	0.432718			
Average LifeTime	=	0.054474	±	0.219676	ns		
Chi sq.	1.19104						

C) 40 mM solution of **1a** in acetonitrile

1-5 exponentials: A+ B1*exp(-i/T1)+ B2*exp(-i/T2)+ B3*exp(-i/T3)							
		Value		3σ		Relative Amplitude/%	Normalised pre-exponential
T1	=	1.34151	±	0.157499	ns	16.71	0.02
T2	=	6.47338	±	0.122658	ns	49.10	0.01
T3	=	0.0513488	±	0.00875105	ns	34.19	0.91
A	=	3.49741	±	0.284003			
Average LifeTime	=	0.14578	±	0.199818	ns		
Chi sq.	1.269965						

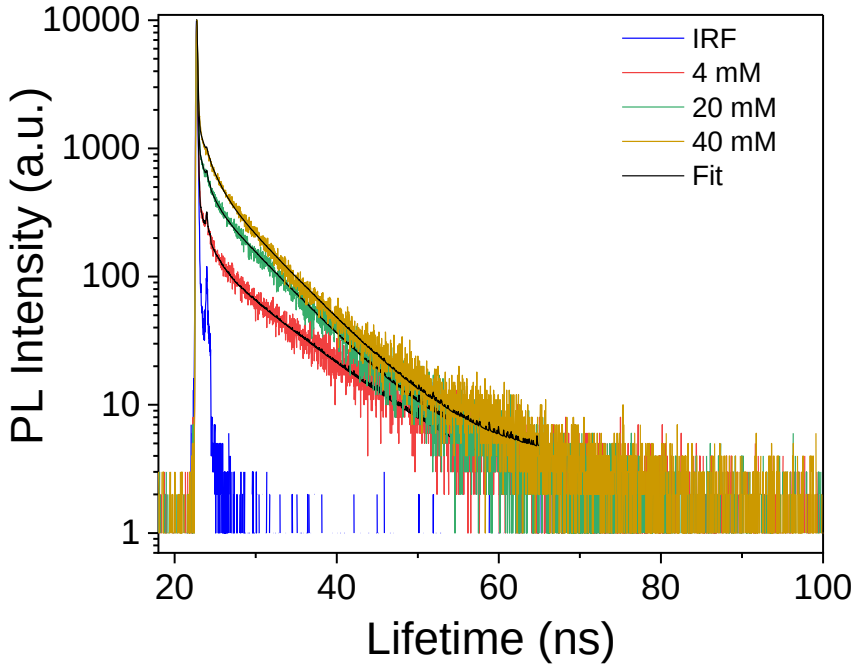


Figure S9: Time-resolved fluorescence of **1a** in MeCN at different concentrations.

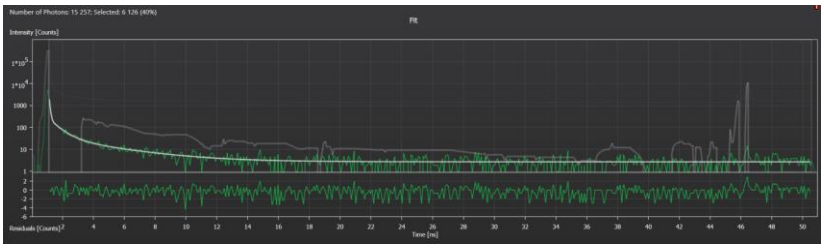
Fluorescence lifetime measurements in solid: The lifetime spectra were acquired using TCSPC instrument with a 450 nm laser at a repetition rate of 8.33 MHz.

Emission scan: 490-600 nm

Fixed/Offset: 465 nm

Scan polariser: none

Sample (Film)	T1	T2	T3
	0.055 ± 0.102 ns	0.0623 ± 0.373 ns	3.322 ± 1.138 ns
Amplitude	1.682 ± 1.666 KCnts	0.206 ± 0.077 KCnts	0.035 ± 0.015 KCnts
Mean LifeTime	1.393 ± 0.364 ns		
Chi sq.	1.167		



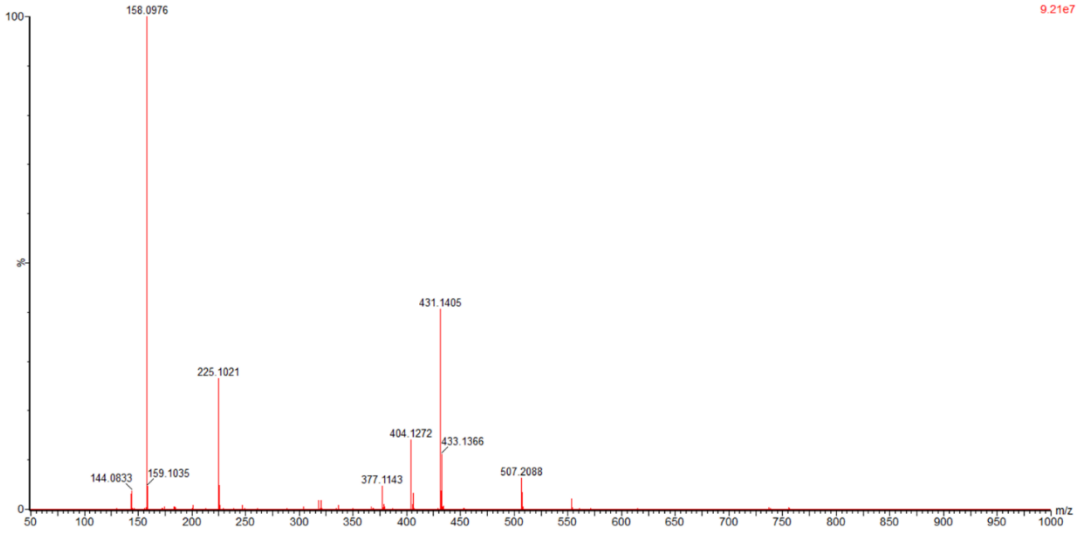
Implication: Our findings suggest that T3 is associated with the lifetime of the monomer, as its amplitude increases with decreasing concentration. T1 and T2 may be related to distinct aggregation states, which are more prevalent at higher concentrations. However, aggregation-based emission is a complex phenomenon[6,7] which needs further detailed investigation. Considering these results, we believe that the association of phenylacyl bromide is important for the efficient bimolecular electron transfer, since the aliphatic counterpart of bromides provided lower yields.

7. On-line analysis using mass spectrometric analysis

Experimental procedure: **1b** (0.025 mmol, 1 equiv), **1a** (0.031 mmol, 1.25 equiv), 2,6-lutidine (0.05 mM, 2 equiv) and 4DPAIPN (0.0012 mmol, 0.25 equiv) were mixed in MeCN (5mL) and degassed with nitrogen for 5 mins. The solution was injected into the flow reactor by a 5mL SGE gas-tight syringe with a flow rate of 0.66 mL/hour at room temperature. The reactor included a PFA tube (ID 0.01inch, 0.11 mL) and a Philips Hue Lightstrip (peak wavelength 464 nm, 2 meters) and was cooled down by compressed air flow. After the reaction, the solution was first diluted with MeCN (0.66 mL/hour) and the mixture was further diluted with a mixture (MeCN/H_2O, 8:2, 11.88 ml/hour). The resulting flow was split by ASI 600-P010-06 flow splitter and directly analyzed by MS with 9.46 μl/min.

Data evaluations: Data were acquired three times after two residence times using Synapt G2S High Definition Mass Spectrometry (HDMS) (Waters, Milford, MA, USA). Samples were ionized by electrospray ionization (ESI) in positive ion mode. Spectrum was analysed by MassLynx v4.2. We observed the higher molecular mass present in the spectrum, which can be assigned to the aggregates of isocyanides (Figure S11). This result was consistent with our optical results where isocyanides showed an aggregation-based absorption in visible light.

(a)



(b)

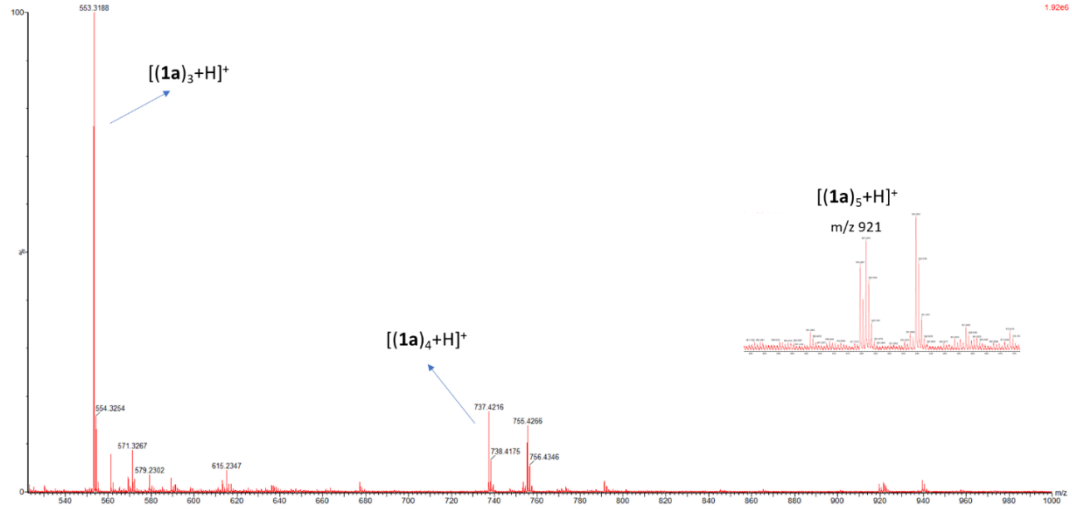


Figure S10: (a) Blank experiment: general MS spectrum of on-line analysis on **1a** without photocatalyst. No irradiation.

(b) Zoom-in spectrum. Aggregation was observed as m/z 553, m/z 737 and m/z 921

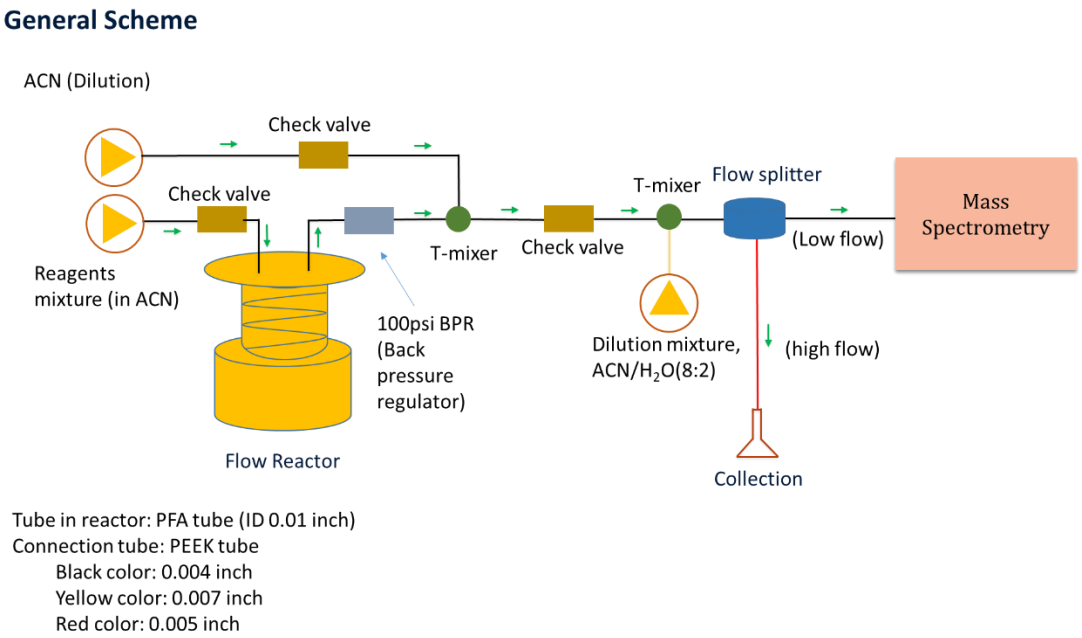
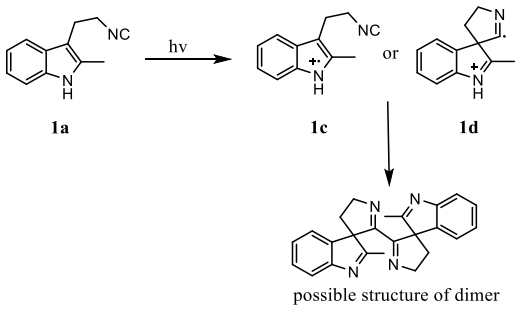


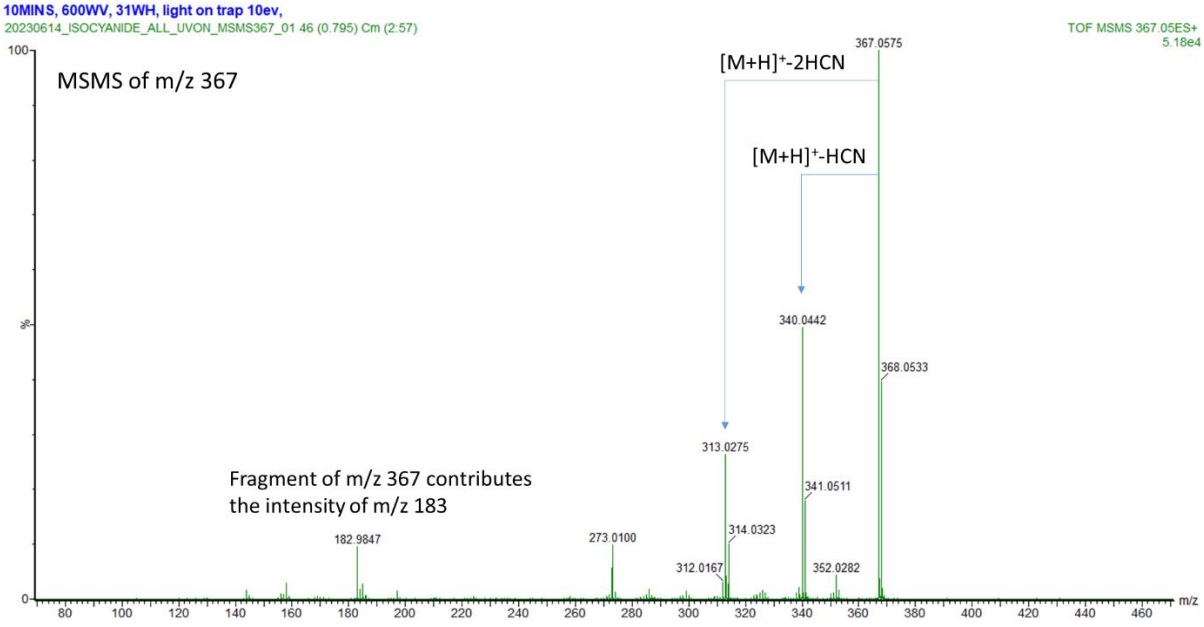
Figure S11: Schematic diagram of the flow setup

Details of reactor and tubing:
Tube used in the reactor: PFA tube (ID 0.01 inch)
Connection tube: PEEK tube
Black color: 0.004 inch
Yellow color: 0.007 inch
Red color: 0.005 inch

On-line MS measurement of 1a in the presence of light and PC (4DPAIPN):




3.80e7
157.9986
143.9822
183.9898
200.9906
367.0575
m/z


10MINS, 600WV, 31WH, light on trap 10ev,
20230614_ISOCYANIDE_ALL_UVON_MSMS367_01 46 (0.795) Cm (2:57)
TOF MSMS 367.05ES+
5.18e4
MSMS of m/z 367
[M+H]+-2HCN
[M+H]+-HCN
Fragment of m/z 367 contributes
the intensity of m/z 183
367.0575
340.0442
368.0533
313.0275
341.0511
314.0323
182.9847
273.0100
312.0167
352.0282
m/z

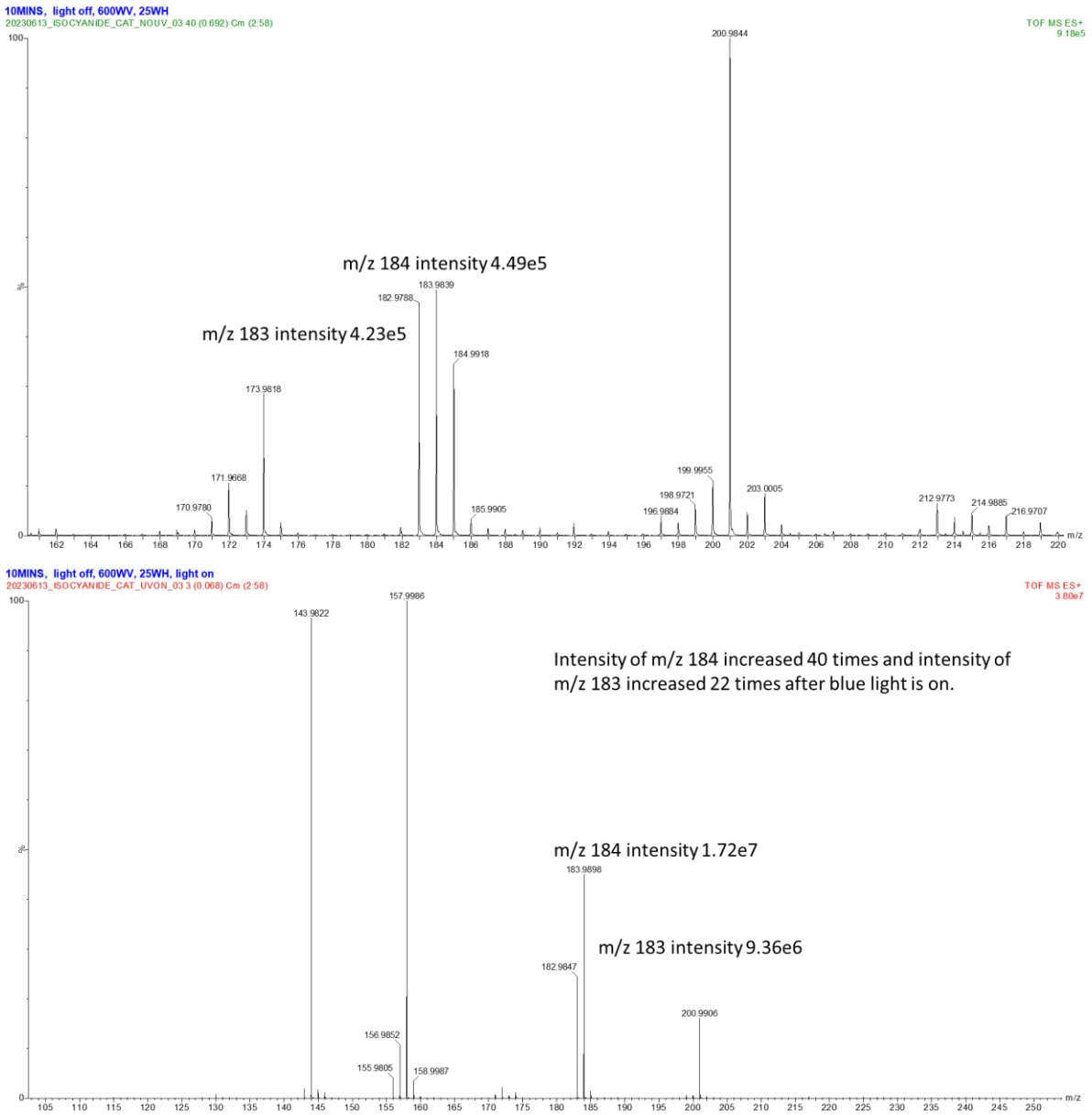
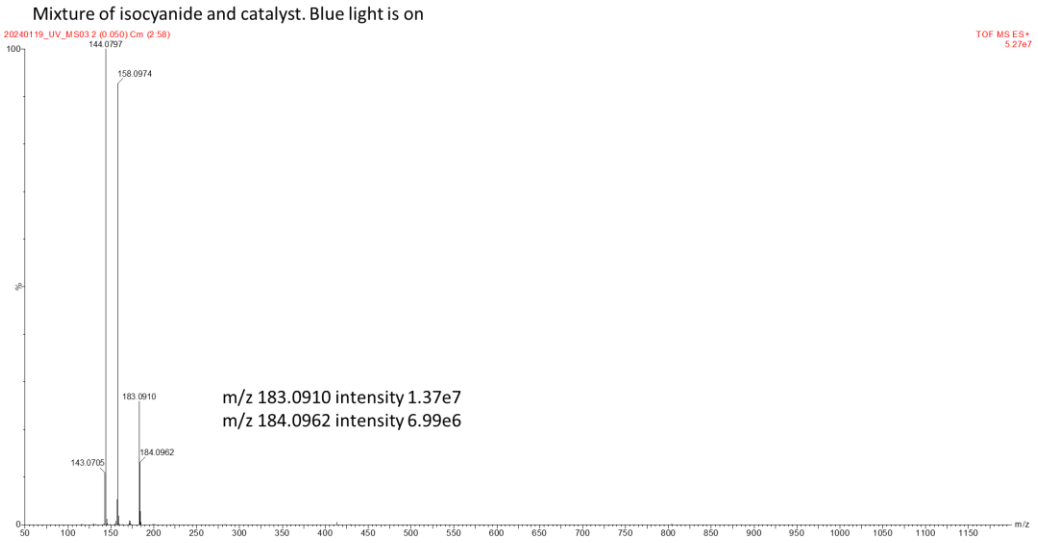


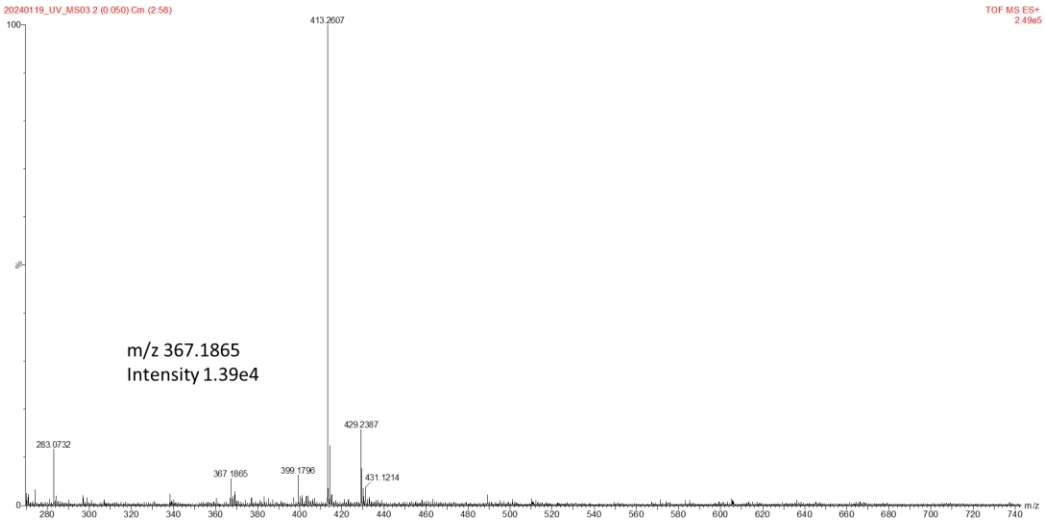
Figure S12: MS spectrum of on-line analysis on **1a** with 4DPAIPN after irradiation under blue LED. Intermediate m/z 184 was detected and the intensity of dimer m/z 367 raised significantly.

Note: To improve the mass accuracy, we further tuned the instrument and reperformed the analysis to validate our observations.



Theoretical mass of radical cation **1a** = 184.0995

Observed mass: 184.0962

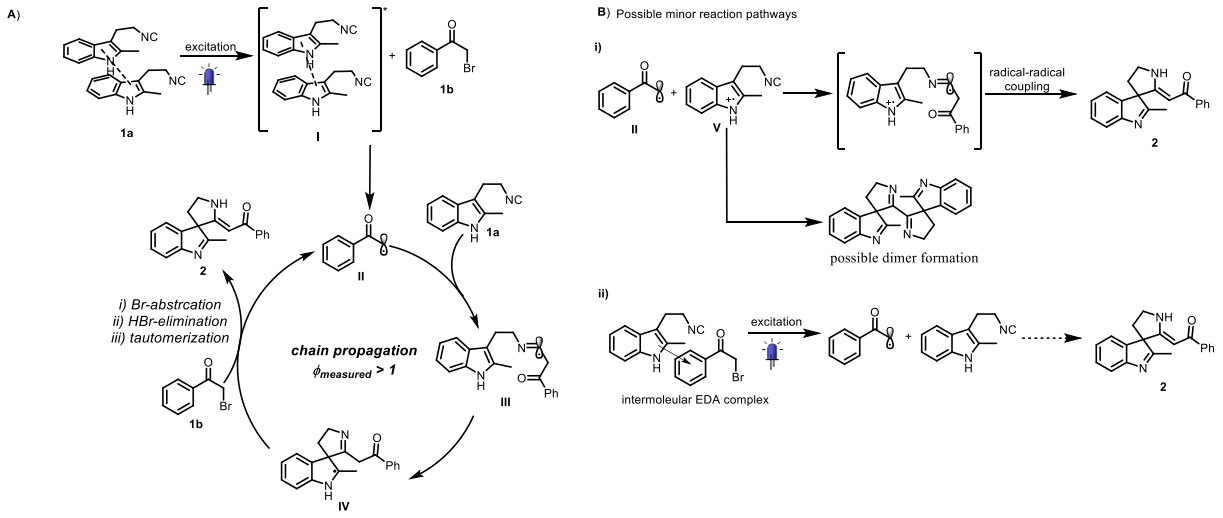


Theoretical mass of dimer = 367.1917

Observed mass: 367.1865

Figure S13: Reproducibility of the online HRMS results for better mass accuracy.

8. Mechanistic discussion



Scheme S2: Proposed mechanism and side pathway.

Discussion: After the SET from intermediate **I**, the radical cation of **1a** can undergo further reaction with radical **II** to generate the final product or can form a dimer. Since the reaction involves a radical chain mechanism, the amount of radical cation of **1a** will be minimal in the reaction mixture (Scheme S2 A and B).

Based on the UV-Vis measurement, we cannot exclude the involvement of EDA-complex formation between isocyanide **1a** (donor) and **1b** (acceptor), especially in the case of diaryl iodonium, trifluoromethyl thianthrenium triflate and pyridinium salts or in polar solvents. Moreover, there is also a possibility of intermolecular charge transfer between the isocyanide group and the indole ring of **1a** at higher concentrations or with other combinations of indole and isocyanides. Our current experimental evidence suggests that, within the tested conditions, such processes do not significantly contribute to the photophysical properties observed of **1a**.

9. General procedure for the synthesis of spiro-compounds

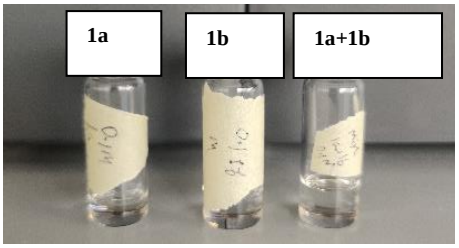
GP1: In an oven-dried 10 mL MW vial equipped with a magnetic stirring bar, tryptamine-derived isocyanide (0.2 mmol, 1 equiv) and bromide (1.5 equiv) were added. Then dry toluene (0.1 M) was added followed by 2,6-lutidine (2 equiv). The MW vial was then closed with a cap containing teflon septum and degassed with nitrogen for 5 min. The vial was then placed for irradiation with two Kessil blue LEDs as shown in figure S1 (40W, 456 nm) for 6-12 h. The progress of the reaction was monitored through TLC and LC/MS. After completion, the solution was diluted with EtOAc

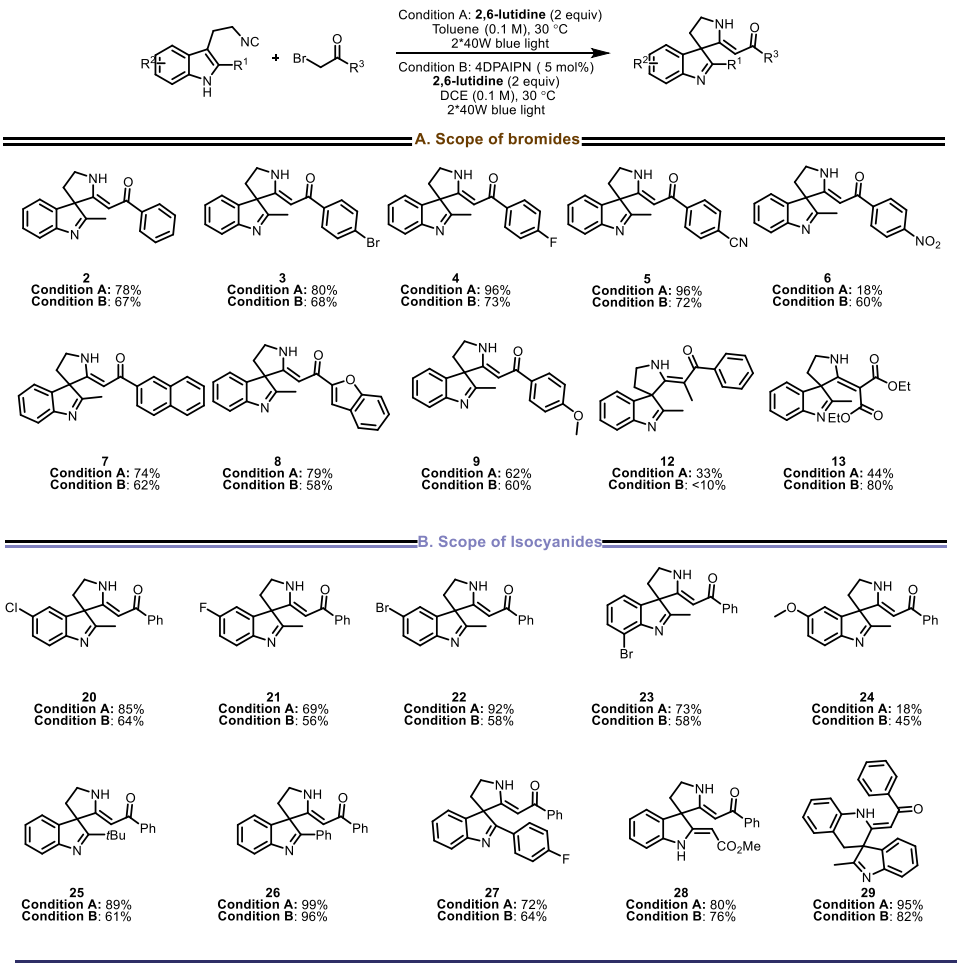
and washed with water. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4. The solvent was removed under vacuum and the product was isolated through an auto column using an ecoflex silica column (30-70 % EtOAc/heptane).

GP2: In an oven-dried 10 mL MW vial equipped with a magnetic stirring bar, tryptamine-derived isocyanide (1.5 equiv), bromide (0.2 mmol, 1 equiv) and 4DPAIPN (5 mol%) were added. Then dry DCE (0.1 M) was added followed by 2,6-lutidine (2 equiv). The MW vial was then closed with a cap containing teflon septum and degassed with nitrogen for 5 min. The vial was then placed for irradiation with two Kessil blue LEDs as shown in figure S1 (40W, 456 nm) for 2 h. The progress of the reaction was monitored through TLC and LC/MS. After completion, the solution was diluted with EtOAc and washed with water. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4. The solvent was removed under vacuum and the product was isolated through an auto column using an ecoflex silica column (30-70 % EtOAc/heptane).

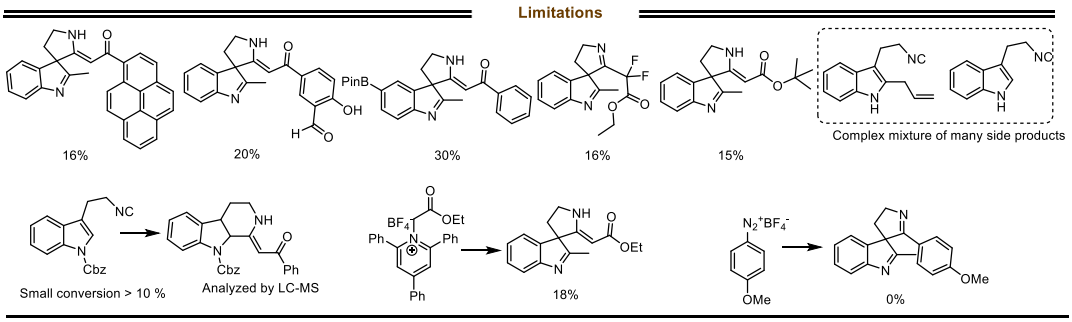
GP3: In an oven-dried 10 mL MW vial equipped with a magnetic stirring bar, tryptamine-derived isocyanide (0.2 mmol, 1 equiv) and **S4**/**S5** (1.5 equiv) were added. Then dry toluene (0.1 M) was added followed by 2,6-lutidine (2 equiv). The MW vial was then closed with a cap containing teflon septum and degassed with nitrogen for 5 min. The vial was then placed for irradiation with two Kessil blue LEDs as shown in figure S1 (40W, 456 nm) for 12 h. The progress of the reaction was monitored through TLC and LC/MS. After completion, the solution was diluted with EtOAc and washed with water. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na_2SO_4. The solvent was removed under vacuum and the product was isolated through an auto column using an ecoflex silica column (20-50 % EtOAc/heptane).

Note: For reproducibility, it is recommended to check the purity of the isocyanides. If isocyanides and bromides are pure, no appreciable colour changes were observed as shown below in the picture. However, a commercial solution of bromide without purification can give a colour to a mixture. In the same way, if isocyanides are not stored properly, that can also lead to a change in colour upon mixing with bromides.





Scheme S3: Scope without photocatalyst (Condition A) and with photocatalyst (Condition B).

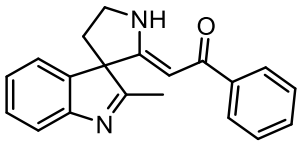


Scheme S4: Substrates which did not work or provide lower yields.

We obtained a lower yield with α-substituted bromides under our optimized conditions possibly due to steric hindrance. This trend was also similar with our optimized conditions using 4DPAIPN as a photocatalyst.

10. Product Characterization

2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **2** was prepared according to the general procedure (GP1 and GP2) and isolated as a yellow solid.

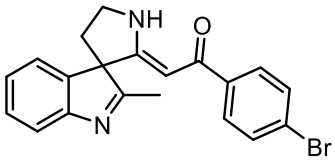
Column Chromatography: Silica, gradient 20- 50 % EtOAc/Heptane

^{1}H NMR (300 MHiz, $CDCl_3$) δ 10.54 (s, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.45 – 7.36 (m, 3H), 7.30 – 7.19 (m, 3H), 5.02 (s, 1H), 4.12 – 3.93 (m, 2H), 2.54 – 2.34 (m, 2H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 188.14, 181.45, 167.29, 155.32, 141.77, 138.34, 131.41, 129.14, 128.81, 126.47, 125.68, 122.25, 120.48, 84.98, 68.72, 46.84, 31.19, 16.50.

HRMS (ESI^+): $[M+H]^+$cal'd for: 303.14918, found: 303.14887

1-(4-bromophenyl)-2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)ethan-1-one



Compound **3** was prepared according to the general procedure (GP1 and GP2) and isolated as a red solid.

Column Chromatography: Silica, gradient 20- 50 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.53 (s, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.45 – 7.35 (m, 3H), 7.29 – 7.18 (m, 2H), 5.02 (s, 1H), 4.10-3.94 (m, 2H), 2.50 – 2.35 (m, 2H), 2.31 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 188.14, 181.45, 167.29, 155.32, 141.77, 138.34, 131.41, 129.14, 128.81, 126.47, 125.68, 122.25, 120.48, 84.98, 68.72, 46.83, 31.19, 16.49, 16.50.

HRMS (ESI^+): $[M+H]^+$cal'd for: 381.05974, found: 381.05936

1-(4-fluorophenyl)-2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)ethan-1-one

Compound **4** was prepared according to the general procedure (GP1 and GP2) and isolated as an orange solid.

Column Chromatography: Silica, gradient 40-60 % EtOAc/Heptane

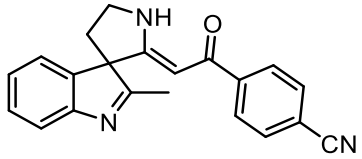
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.47 (s, 1H), 7.72 – 7.63 (m, 2H), 7.60 (dt, *J* = 7.7, 0.8 Hz, 1H), 7.39 (td, *J* = 7.5, 1.5 Hz, 1H), 7.30-7.25 (m, 1H), 7.20 (m, 1H), 7.00 – 6.90 (m, 2H), 5.01 (s, 1H), 4.00 (qdd, *J* = 11.0, 7.8, 6.0 Hz, 2H), 2.49 – 2.33 (m, 2H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 188.02, 181.52, 166.94, 164.57 (d, *J* = 250.9 Hz), 155.31, 141.85, 135.78 (d, *J* = 2.8 Hz), 129.43 (d, *J* = 8.8 Hz), 129.06, 126.40, 122.22, 120.42, 115.09 (d, *J* = 21.6 Hz), 84.88, 68.69, 46.73, 31.17, 16.43.

^{19}F NMR (282 MHz, $CDCl_3$) δ -109.32.

HRMS (ESI^+): $[M+H]^+$cal'd for: 321.13975, found: 321.14006

4-(2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)acetyl)benzonitrile



Compound **5** was prepared according to the general procedure (GP1 and GP2) and isolated as a white solid.

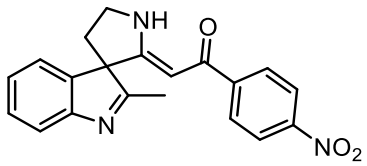
Column Chromatography: Silica, gradient 40-60 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.64 (s, 1H), 7.75 – 7.67 (m, 2H), 7.61 – 7.53 (m, 3H), 7.38 (td, *J* = 7.5, 1.6 Hz, 1H), 7.23 (m, 2H), 5.01 (s, 1H), 4.04 (qdd, *J* = 11.3, 7.8, 6.1 Hz, 2H), 2.53 – 2.34 (m, 2H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.93, 181.06, 168.23, 155.31, 143.20, 141.51, 132.07, 129.21, 127.62, 126.48, 122.18, 120.51, 118.55, 114.04, 85.18, 68.78, 47.00, 31.00, 16.42.

HRMS (ESI^+): $[M+H]^+$cal'd for: 328.14443, found: 328.14427

2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-(4-nitrophenyl)ethan-1-one



Compound **6** was prepared according to the general procedure (GP1 and GP2) and isolated as a pale yellow solid.

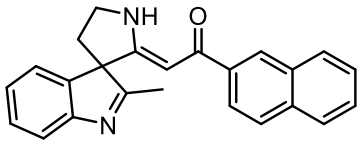
Column Chromatography: Silica, gradient 20- 50 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.69 (s, 1H), 8.19 – 8.07 (m, 2H), 7.84 – 7.73 (m, 2H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.40 (td, *J* = 7.5, 1.6 Hz, 1H), 7.30 – 7.29 (m, 1H), 7.25 – 7.20 (m, 1H), 5.05 (s, 1H), 4.17 – 3.97 (m, 2H), 2.56 – 2.35 (m, 2H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.64, 181.05, 168.46, 155.34, 149.07, 144.90, 141.48, 129.30, 128.08, 126.55, 123.48, 122.22, 120.58, 85.47, 68.82, 47.09, 31.03, 16.48.

HRMS (ESI^+): $[M+H]^+$cal'd for: 348.13425, found: 348.13437

2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-(naphthalen-2-yl)ethan-1-one



Compound **7** was prepared according to the general procedure (GP1 and GP2) and isolated as a brown solid.

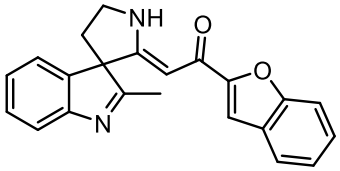
Column Chromatography: Silica, gradient 20- 50 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.60 (s, 1H), 8.16 (s, 1H), 7.86-7.75 (m, 4H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.50-7.38 (m, 3H), 7.32-7.29 (m, 1H), 7.25-7.20 (m, 1H) 5.25 (s, 1H), 4.11 – 3.95 (m, 2H), 2.54-2.38 (m, 2H), 2.35 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 188.94, 181.28, 166.38, 154.89, 141.54, 134.28, 128.82, 128.63, 127.50, 127.22, 127.14, 126.91, 126.01, 125.88, 123.69, 121.86, 120.01, 85.13, 68.30, 46.32, 30.86,16.09.

HRMS (ESI^+): $[M+H]^+$cal'd for: 353.16483, found: 353.16464

1-(benzofuran-2-yl)-2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)ethan-1-one



Compound **8** was prepared according to the general procedure (GP1 and GP2) and isolated as a brown solid.

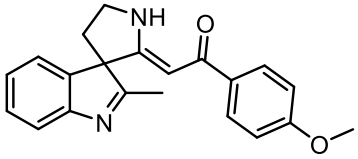
Column Chromatography: Silica, gradient 20- 50 % EtOAc/Heptane

1H NMR (300 MHz, Chloroform-*d*) δ 10.49 (s, 1H), 7.63 (d, J = 7.7 Hz, 1H), 7.56 (dt, J = 7.6, 1.1 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.34 – 7.27 (m, 2H), 7.26 – 7.16 (m, 3H), 5.22 (s, 1H), 4.15-3.96 (m, 2H), 2.55 – 2.35 (m, 2H), 2.33 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 181.21, 179.45, 167.36, 155.26, 155.08, 154.57, 141.66, 129.08, 127.81, 126.45, 126.41, 123.22, 122.34, 122.16, 120.43, 112.03, 108.69, 85.74, 68.62, 46.91, 31.14, 16.41.

HRMS (ESI^+): $[M+H]^+$cal'd for: 343.14409, found: 343.14381

1-(4-methoxyphenyl)-2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)ethan-1-one



Compound **9** was prepared according to the general procedure (GP1 and GP2) and isolated as a brown oil.

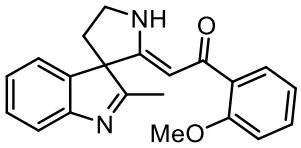
Column Chromatography: Silica, gradient 10-40 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.41 (s, 1H), 7.69 – 7.62 (m, 2H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.38 (td, *J* = 7.5, 1.5 Hz, 1H), 7.32 – 7.14 (m, 2H), 6.85 – 6.75 (m, 2H), 5.05 (s, 1H), 4.13-3.92 (m, 2H), 3.78 (s, 3H), 2.53 – 2.35 (m, 2H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, CDCl3) δ 188.56, 181.74, 166.03, 161.93, 155.23, 141.97, 132.22, 129.00, 128.88, 126.27, 122.20, 120.27, 113.32, 84.81, 68.56, 55.30, 46.52, 31.20, 16.39.

HRMS (ESI^{+}): [M+H]$^{+}$cal'd for: 333.15974, found: 333.15975

1-(2-methoxyphenyl)-2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)ethan-1-one



Compound **10** was prepared according to the general procedure (GP1) and isolated as a brown oil.

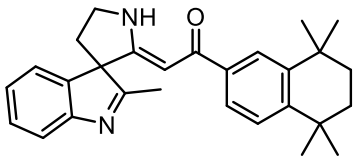
Column Chromatography: Silica, gradient 10-40 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.26 (s, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.47 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.38 – 7.27 (m, 3H), 7.25-7.18 (m, 1H), 6.92 – 6.77 (m, 2H), 5.04 (s, 1H), 4.01 (qdd, *J* = 10.9, 7.8, 6.1 Hz, 2H), 3.66 (s, 3H), 2.51 – 2.36 (m, 2H), 2.34 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 190.18, 181.66, 165.51, 157.19, 155.21, 142.02, 131.22, 130.43, 129.71, 128.76, 126.11, 122.21, 120.33, 120.15, 111.43, 90.54, 68.42, 55.42, 46.60, 31.03, 16.33.

HRMS (ESI^{+}): [M+H]$^{+}$cal'd for: 333.15978, found: 333.15970

2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)ethan-1-one



Compound **11** was prepared according to the general procedure (GP1) and isolated as a brown oil.

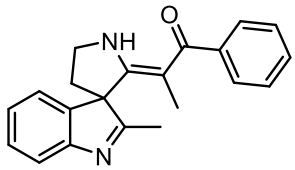
Column Chromatography: Silica, gradient 10-40 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.46 (s, 1H), 7.74 (d, *J* = 1.9 Hz, 1H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.42 – 7.26 (m, 3H), 7.24 – 7.16 (m, 2H), 5.05 (s, 1H), 4.01 (qdd, *J* = 10.9, 7.8, 6.1 Hz, 2H), 2.50 – 2.36 (m, 2H), 2.32 (s, 3H), 1.64 (s, 4H), 1.25 (s, 6H), 1.23 (s, 3H), 1.21 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.75, 181.61, 166.26, 155.21, 148.29, 144.92, 141.93, 136.85, 128.87, 126.24, 125.42, 124.24, 122.17, 120.26, 85.42, 77.49, 77.06, 76.64, 68.55, 46.55, 35.02, 34.88, 34.42, 34.33, 31.76, 31.72, 31.68, 31.19, 16.37.

HRMS (ESI^+): $[M+H]^+$cal'd for: 413.2587, found: 413.2587

2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylpropan-1-one



Compound **12** was prepared according to the general procedure (GP1 and GP2) and isolated as a yellow oil.

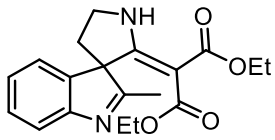
Column Chromatography: Silica, gradient 10-40 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 11.38 (s, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.30-7.27 (m, 4H), 7.25-7.22 (m, 1H), 4.06 – 3.85 (m, 2H), 2.50-2.43 (m, 1H), 2.39 (s, 3H), 2.29 – 2.18 (m, 1H), 0.98 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 195.45, 181.36, 165.29, 154.76, 142.19, 141.63, 128.90, 128.76, 127.81, 127.00, 126.22, 121.83, 120.57, 96.13, 68.81, 45.85, 33.43, 16.75, 12.72.

HRMS (ESI^+): $[M+H]^+$cal'd for: 317.16483, found: 317.16476

diethyl 2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)malonate



Compound **13** was prepared according to the general procedure (GP1 and GP2) and isolated as a brown viscous liquid.

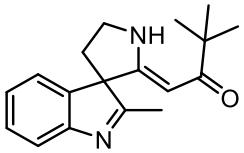
Column Chromatography: Silica, gradient 10-30% EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.32 (td, *J* = 7.5, 1.5 Hz, 1H), 7.27 – 7.11 (m, 2H), 4.22 – 4.06 (m, 2H), 3.91 – 3.77 (m, 2H), 3.44 (p, *J* = 7.1 Hz, 2H), 2.39 – 2.15 (m, 5H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (75 MHz, Acetone) δ 181.97, 168.94, 165.83, 165.64, 156.69, 142.87, 128.96, 126.12, 122.72, 120.56, 90.20, 69.32, 59.87, 45.88, 35.97, 16.92, 14.71, 13.90.

HRMS (ESI^+): $[M+H]^+$cal'd for: 343.16522, found: 343.16551

3,3-dimethyl-1-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)butan-2-one



Compound **14** was prepared according to the general procedure (GP1) and isolated as a brown solid.

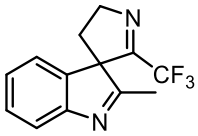
Column Chromatography: Silica, gradient 20-50% EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.07 (s, 1H), 7.55 (d, J = 7.7 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.27 – 7.17 (m, 2H), 4.57 (s, 1H), 3.99-3.83 (m, 2H), 2.44 – 2.29 (m, 2H), 2.27 (s, 3H), 0.98 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 205.72, 181.81, 165.55, 155.09, 142.02, 128.75, 126.14, 122.09, 120.18, 84.14, 68.37, 46.25, 41.64, 31.33, 27.61, 16.29.

HRMS (ESI^+): $[M+H]^+$cal'd for: 283.18047, found: 283.18048

2-methyl-2'-(trifluoromethyl)-4',5'-dihydrospiro[indole-3,3'-pyrrole]



Compound **15** was prepared according to the general procedure (GP3) and isolated as a yellow liquid.

Column Chromatography: Silica, gradient 20-40% EtOAc/Heptane

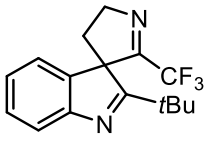
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.39 (dt, *J* = 7.8, 4.3 Hz, 1H), 7.23 (d, *J* = 5.4 Hz, 2H), 4.58 – 4.35 (m, 2H), 2.56 (m, 1H), 2.42 (m, 1H), 2.29 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 178.57, 164.51 (q is not visible), 155.33, 139.16, 129.45, 126.37, 122.19, 120.66, 119.13 (q, *J* = 276.07 Hz), 72.37, 61.10, 34.64, 16.45.

^{19}F NMR (282 MHz, $CDCl_3$) δ -67.12.

HRMS (ESI^+): $[M+H]^+$cal'd for: 253.09470, found: 253.09485

2-(tert-butyl)-2'-(trifluoromethyl)-4',5'-dihydrospiro[indole-3,3'-pyrrole]



Compound **16** was prepared according to the general procedure (GP3) and isolated as a yellow liquid.

Column Chromatography: Silica, gradient 20-40% EtOAc/Heptane

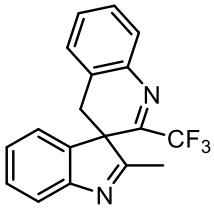
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.59 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.38 (td, *J* = 7.6, 1.3 Hz, 1H), 7.22 (td, *J* = 7.5, 1.1 Hz, 1H), 7.14 – 7.08 (m, 1H), 4.57 (tq, *J* = 7.5, 2.5 Hz, 2H), 2.96 (dt, *J* = 14.0, 7.8 Hz, 1H), 2.36 (dt, *J* = 14.2, 7.1 Hz, 1H), 1.39 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 188.16, 166.15 (q, *J* = 33.96 Hz), 154.08, 140.35, 129.37, 126.49, 121.40, 120.69, 119.19 (q, *J* = 276.64 Hz), 72.13, 61.57, 37.94, 33.44, 30.11.

^{19}F NMR (282 MHz, $CDCl_3$) δ -65.61.

HRMS (ESI^+): $[M+H]^+$cal'd for: 295.14164, found: 295.14179

2-methyl-2'-(trifluoromethyl)-4'H-spiro[indole-3,3'-quinoline]



Compound **17** was prepared according to the general procedure (GP3) and isolated as a yellow liquid.

Column Chromatography: Silica, gradient 20-40% EtOAc/Heptane

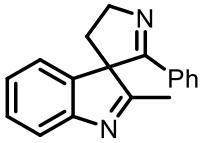
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.66 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.59 (dt, *J* = 7.8, 0.8 Hz, 1H), 7.48 – 7.32 (m, 3H), 7.18 – 7.09 (m, 2H), 7.03 (m, 1H), 3.22 – 3.01 (m, 2H), 2.22 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 179.25, 154.93, 154.18 (q, *J* = 33.27 Hz), 140.86, 138.97, 130.55, 129.59, 129.12, 128.89, 128.27, 126.21, 125.37, 122.77, 120.82, 119.86 (q, *J* = 276.71 Hz), 58.90, 34.31, 17.64.

^{19}F NMR (282 MHz, $CDCl_3$) δ -68.72.

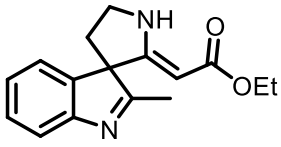
HRMS (ESI^+): $[M+H]^+$cal'd for: 315.11035, found: 315.11041

2-methyl-2'-phenyl-4',5'-dihydrospiro[indole-3,3'-pyrrole][8]



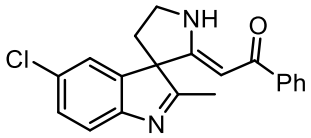
Compound **18** was prepared according to the general procedure (GP3).

Ethyl-2-(2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)acetate[9]



Compound **19** was prepared according to the general procedure (GP3).

2-(5-chloro-2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **20** was prepared according to the general procedure (GP1 and GP2) and isolated as a red solid.

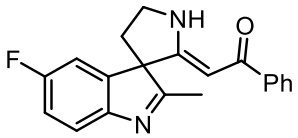
Column Chromatography: Silica, gradient 40-70 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.48 (s, 1H), 7.73 – 7.65 (m, 2H), 7.51 (d, *J* = 8.3 Hz, 1H), 7.42 – 7.26 (m, 5H), 5.09 (s, 1H), 4.14 – 3.93 (m, 2H), 2.51 – 2.34 (m, 2H), 2.31 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.78, 182.21, 165.74, 153.89, 143.65, 139.48, 132.13, 131.22, 129.27, 128.33, 127.24, 122.88, 121.33, 85.51, 68.93, 46.72, 31.20, 16.51.

HRMS (ESI^+): $[M+H]^+$cal'd for: 337.11020, found: 337.11038

2-(5-fluoro-2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **21** was prepared according to the general procedure (GP1 and GP2) and isolated as an organe solid.

Column Chromatography: Silica, gradient 20-50 % EtOAc/Heptane

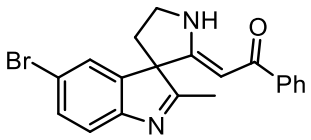
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.47 (s, 1H), 7.71 – 7.64 (m, 2H), 7.52 (dd, *J* = 8.4, 4.6 Hz, 1H), 7.41 – 7.28 (m, 3H), 7.11 – 6.96 (m, 2H), 5.09 (s, 1H), 4.00 (m, 2H), 2.50 – 2.32 (m, 2H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.24, 181.08 (d, *J* = 3.5 Hz), 165.51, δ 161.16 (d, *J* = 245.7 Hz), 150.93 (d, *J* = 2.3 Hz), 143.22 (d, *J* = 8.8 Hz), 139.04, 130.72, 127.85, 126.74, 120.71 (d, *J* = 8.8 Hz), 115.25 (d, *J* = 23.5 Hz), 109.76 (d, *J* = 25.1 Hz), 84.98, 68.60 (d, *J* = 2.2 Hz), 46.23, 30.77, 16.01.

^{19}F NMR (282 MHz, $CDCl_3$) δ -115.42.

HRMS (ESI^+): $[M+H]^+$cal'd for: 321.13975, found: 321.13997

2-(5-bromo-2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **22** was prepared according to the general procedure (GP1 and GP2) and isolated as a red solid.

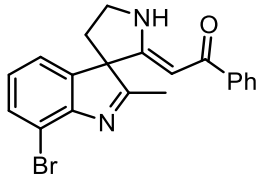
Column Chromatography: Silica, gradient 10-40 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.47 (s, 1H), 7.73 – 7.66 (m, 2H), 7.51 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.42 – 7.29 (m, 4H) 5.09 (s, 1H), 4.08-3.93 (m, 2H), 2.50 – 2.34 (m, 2H), 2.30 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.60, 182.11, 165.55, 154.20, 143.90, 139.35, 132.16, 132.06, 131.09, 128.20, 127.10, 125.58, 121.67, 119.81, 85.35, 68.82, 46.60, 31.03, 16.37.

HRMS (ESI^+): $[M+H]^+$cal'd for: 381.05974, found: 381.05987

2-(7-bromo-2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **23** was prepared according to the general procedure (GP1 and GP2) and isolated as a brown solid.

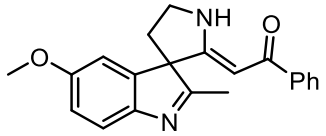
Column Chromatography: Silica, gradient 20-50 % EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.47 (s, 1H), 7.69 (m, 2H), 7.54 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.44 – 7.28 (m, 3H), 7.21 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.09 (t, *J* = 7.7 Hz, 1H), 5.12 (s, 1H), 4.12 – 3.94 (m, 2H), 2.51 – 2.31 (m, 5H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.63, 183.19, 165.57, 153.54, 143.49, 139.30, 132.38, 131.10, 128.19, 127.72, 127.11, 121.18, 114.01, 85.48, 70.16, 46.57, 31.32, 16.63.

HRMS (ESI^+): $[M+H]^+$cal'd for: 381.05974, found: 381.05995

2-(5-methoxy-2-methylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **24** was prepared according to the general procedure (GP1 and GP2) and isolated as a brown viscous liquid.

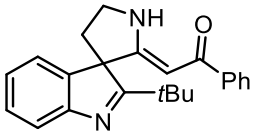
Column Chromatography: Silica, gradient 30-60% EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.49 (s, 1H), 7.72 – 7.65 (m, 2H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.41 – 7.27 (m, 3H), 6.89 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.83 (d, *J* = 2.5 Hz, 1H), 5.11 (s, 1H), 4.09 – 3.89 (m, 2H), 3.79 (s, 3H), 2.51 – 2.32 (m, 2H), 2.28 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.54, 179.28, 166.87, 158.62, 148.80, 143.35, 139.51, 130.94, 128.14, 127.09, 120.60, 113.58, 108.77, 85.39, 68.72, 55.74, 46.62, 31.36, 16.26.

HRMS (ESI^+): $[M+H]^+$cal'd for: 333.15974, found: 333.16004

2-(2-(tert-butyl)spiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **25** was prepared according to the general procedure (GP1 and GP2) and isolated as a white solid.

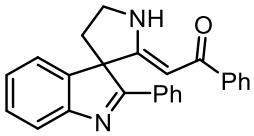
Column Chromatography: Silica, gradient 20-50% EtOAc/Heptane

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.64 (s, 1H), 7.72 – 7.64 (m, 2H), 7.60 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.40 – 7.27 (m, 4H), 7.22 – 7.13 (m, 2H), 5.19 (s, 1H), 4.22 – 3.95 (m, 2H), 2.94 (ddd, *J* = 13.7, 9.4, 7.5 Hz, 1H), 2.32 (ddd, *J* = 13.6, 8.3, 4.0 Hz, 1H), 1.44 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 190.11, 188.69, 167.44, 153.64, 144.06, 139.62, 130.82, 128.65, 128.16, 126.99, 126.51, 120.93, 120.37, 85.23, 68.73, 47.00, 38.10, 30.29, 29.65.

HRMS (ESI^+): $[M+H]^+$cal'd for: 345.19612, found: 345.19616

1-phenyl-2-(2-phenylspiro[indole-3,3'-pyrrolidin]-2'-ylidene)ethan-1-one



Compound **26** was prepared according to the general procedure (GP1 and GP2) and isolated as a yellow solid.

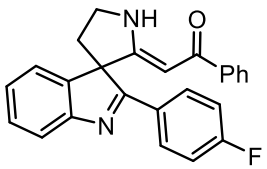
Column Chromatography: Silica, gradient 20-50 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.67 (s, 1H), 7.99 – 7.94 (m, 2H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.48 – 7.38 (m, 4H), 7.34 – 7.28 (m, 2H), 7.27 – 7.20 (m, 3H), 5.29 (s, 1H), 4.21 – 4.00 (m, 2H), 2.77 – 2.60 (m, 1H), 2.27 – 2.17 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.46, 177.88, 167.80, 153.98, 143.92, 139.42, 131.67, 131.24, 130.92, 129.04, 128.89, 128.59, 128.09, 127.12, 126.84, 121.38, 85.76, 67.32, 46.84, 32.58.

HRMS (ESI^+): $[M+H]^+$cal'd for: 365.16483, found: 365.16523

2-(2-(4-fluorophenyl)spiro[indole-3,3'-pyrrolidin]-2'-ylidene)-1-phenylethan-1-one



Compound **27** was prepared according to the general procedure (GP1 and GP2) and isolated a yellow solid.

Column Chromatography: Silica, gradient 20-50 % EtOAc/Heptane

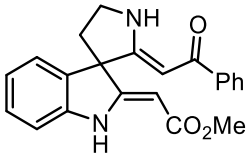
^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.64 (s, 1H), 8.03 – 7.93 (m, 2H), 7.74 (d, *J* = 7.7 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.45-7.39 (m, 1H), 7.37 – 7.20 (m, 5H), 7.17 – 7.07 (m, 2H), 5.28 (s, 1H), 4.21 – 4.00 (m, 2H), 2.67 (dt, *J* = 13.3, 9.1 Hz, 1H), 2.25 (ddd, *J* = 13.2, 7.3, 2.8 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.55, 176.69 (d, *J* = 1.1 Hz), 167.53, 164.55 (d, *J* = 253.1 Hz), 153.84, 143.80, 139.33, 131.00, 130.78(d, *J* = 8.6Hz), 129.10, 128.11, 127.93 (d, *J* = 3.3 Hz), 127.11, 126.85, 121.35, 116.24, 115.95, 85.78, 67.21, 46.80, 32.67.

^{19}F NMR (282 MHz, $CDCl_3$) δ -107.83.

HRMS (ESI^+): $[M+H]^+$cal'd for: 383.15540, found: 383.15553

methyl(Z)-2-((Z)-2'-(2-oxo-2-phenylethylidene)spiro[indoline-3,3'-pyrrolidin]-2-ylidene)acetate



Compound **28** was prepared according to the general procedure (GP1 and GP2) and isolated light yellow soild.

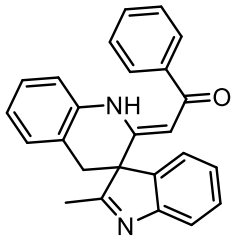
Column Chromatography: Silica, gradient 20-50% EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.45 (s, 1H), 9.74 (s, 1H), 7.75-7.68 (m, 2H), 7.41 – 7.28 (m, 3H), 7.25-7.20 (m, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 6.98 – 6.88 (m, 2H), 5.34 (s, 1H), 4.92 (s, 1H), 3.94 (t, *J* = 6.8 Hz, 2H), 3.71 (s, 3H), 2.53 – 2.34 (h, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 189.91, 170.51, 169.18, 166.66, 143.80, 139.86, 132.37, 130.99, 129.42, 128.24, 127.27, 123.50, 122.16, 109.58, 87.15, 82.77, 61.96, 54.21, 51.00, 46.08, 38.61.

HRMS (ESI^+): $[M+H]^+$cal'd for: 361.15465, found: 361.15492

2-(2-methyl-1',4'-dihydro-2'H-spiro[indole-3,3'-quinolin]-2'-ylidene)-1-phenylethan-1-one



Compound **29** was prepared according to the general procedure (GP1 and GP2) and isolated as a yellow solid.

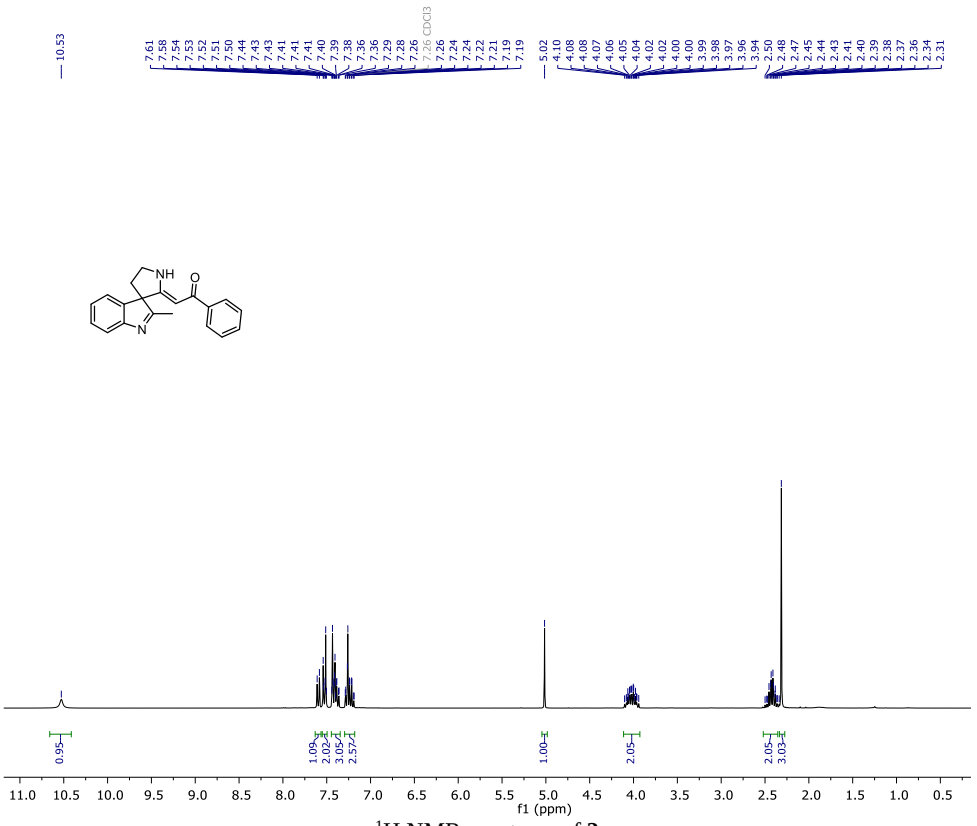
Column Chromatography: Silica, gradient 20-50 % EtOAc/Heptane

^{1}H NMR (300 MHz, $CDCl_3$) δ 13.40 (s, 1H), 7.73 – 7.67 (m, 2H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.46 – 7.29 (m, 5H), 7.13 – 6.99 (m, 4H), 6.90 (d, *J* = 6.9 Hz, 1H), 5.38 (s, 1H), 3.25 (d, *J* = 15.7 Hz, 1H), 2.84 (d, *J* = 15.6 Hz, 1H), 2.36 (s, 3H).

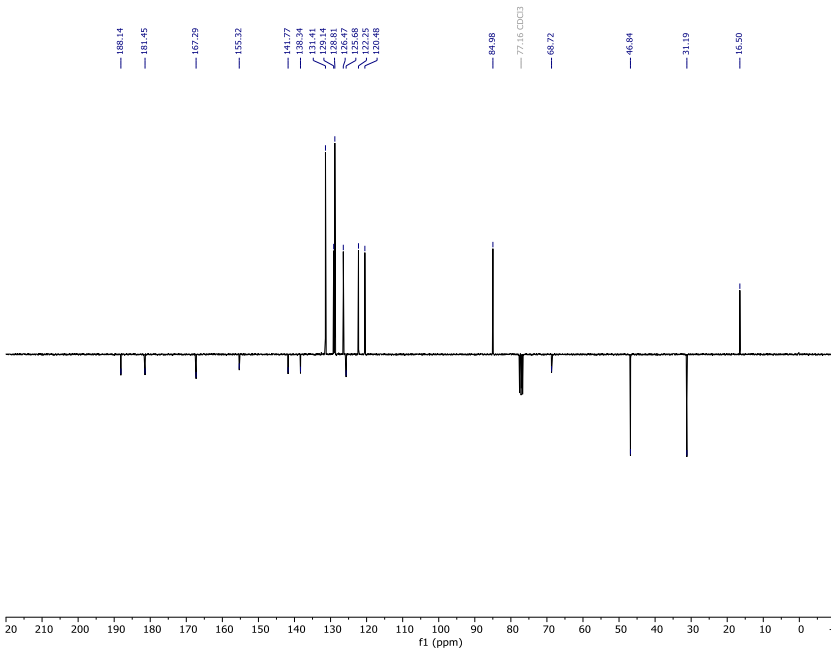
^{13}C NMR (75 MHz, $CDCl_3$) δ 190.66, 181.63, 156.28, 154.30, 141.55, 139.25, 136.47, 131.66, 129.09, 129.04, 128.75, 128.45, 127.24, 126.26, 123.63, 122.64, 121.51, 120.77, 116.50, 89.98, 60.42, 32.91, 17.35.

HRMS (ESI^+): $[M+H]^+$cal'd for: 365.16483, found: 365.16510

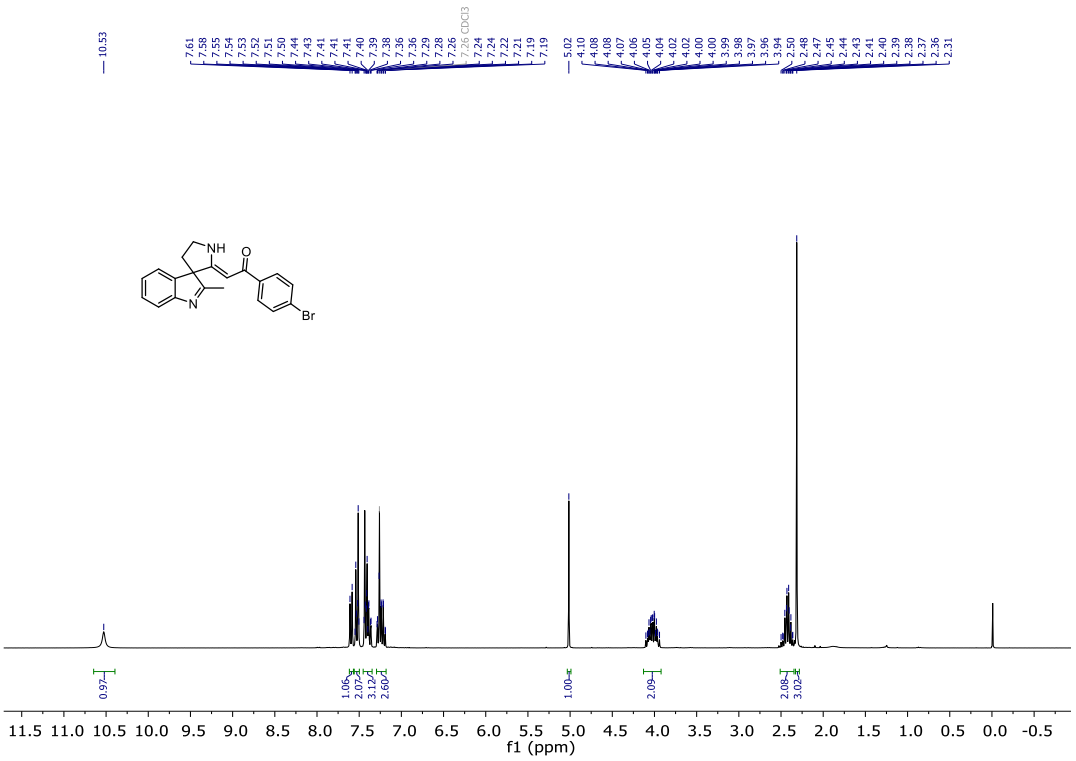
11. NMR Spectrum



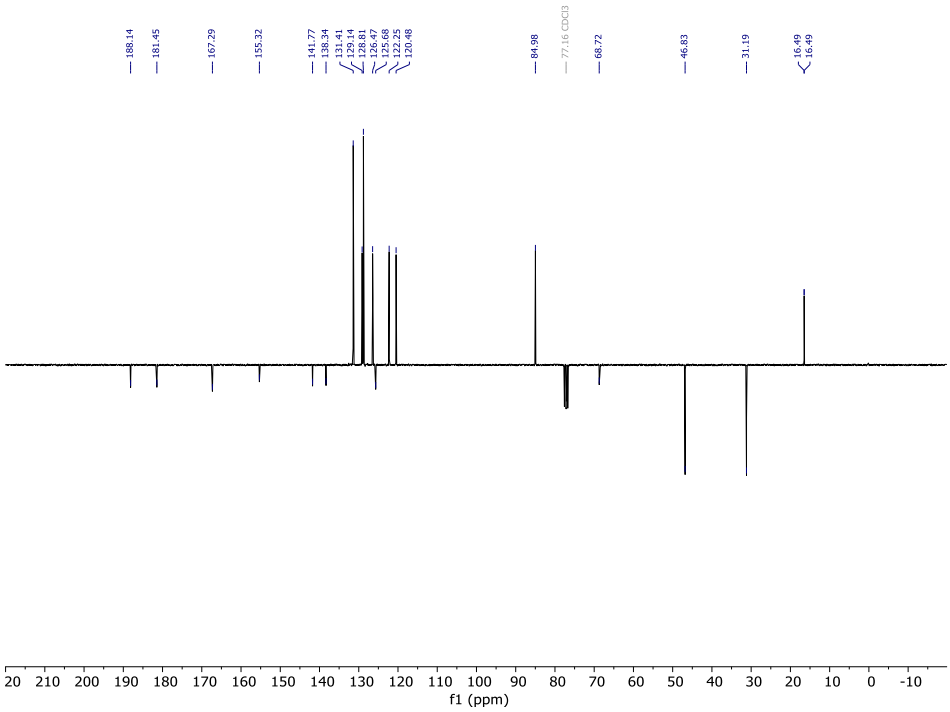
^{1}H NMR spectrum of **2**



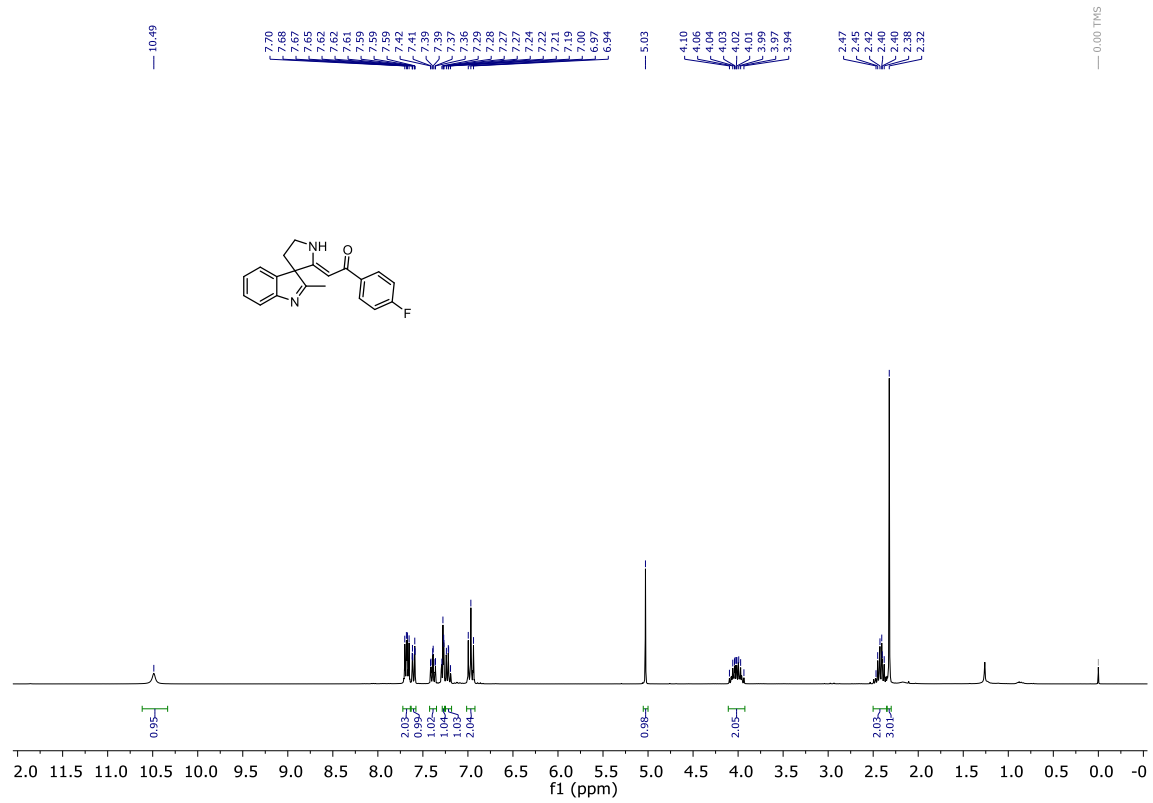
^{13}C APT NMR spectrum of **2**



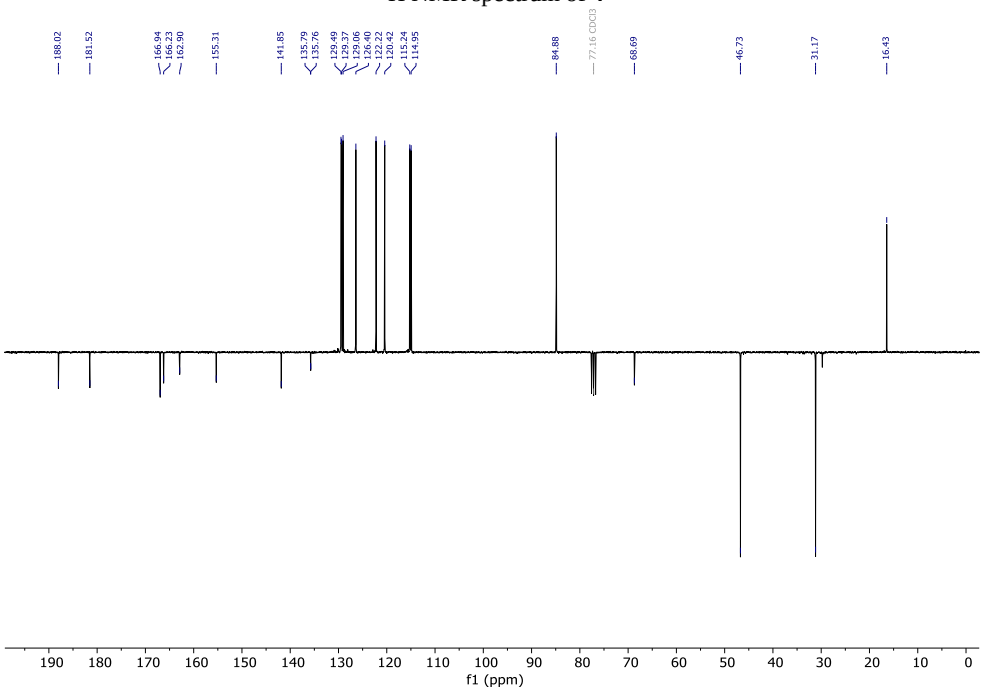
^{1}H NMR spectrum of **3**



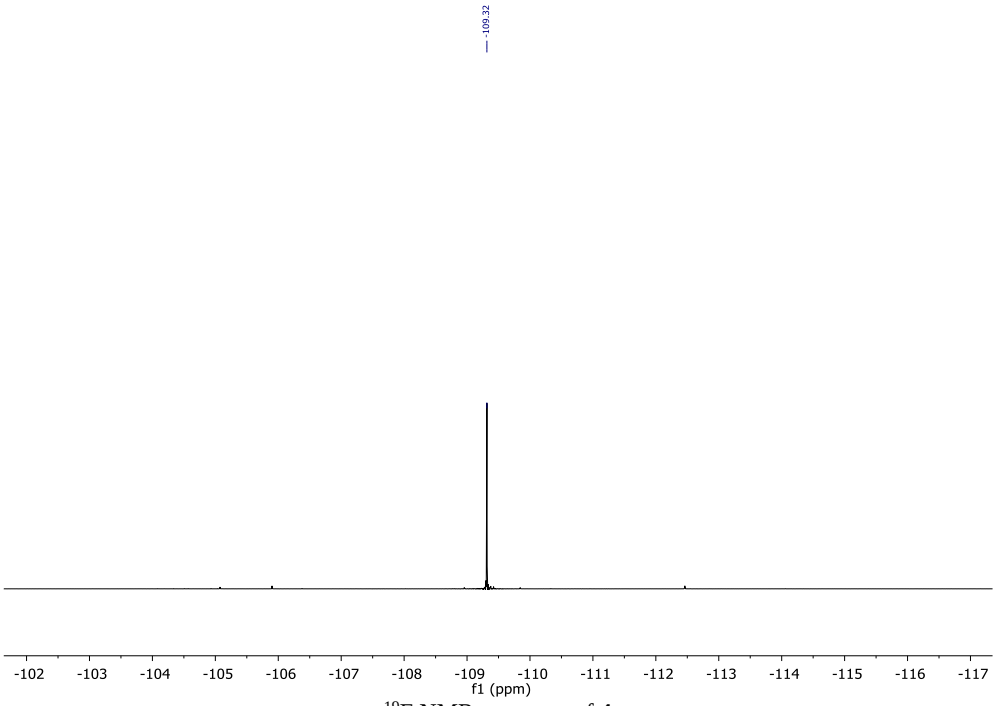
^{13}C APT NMR spectrum of **3**



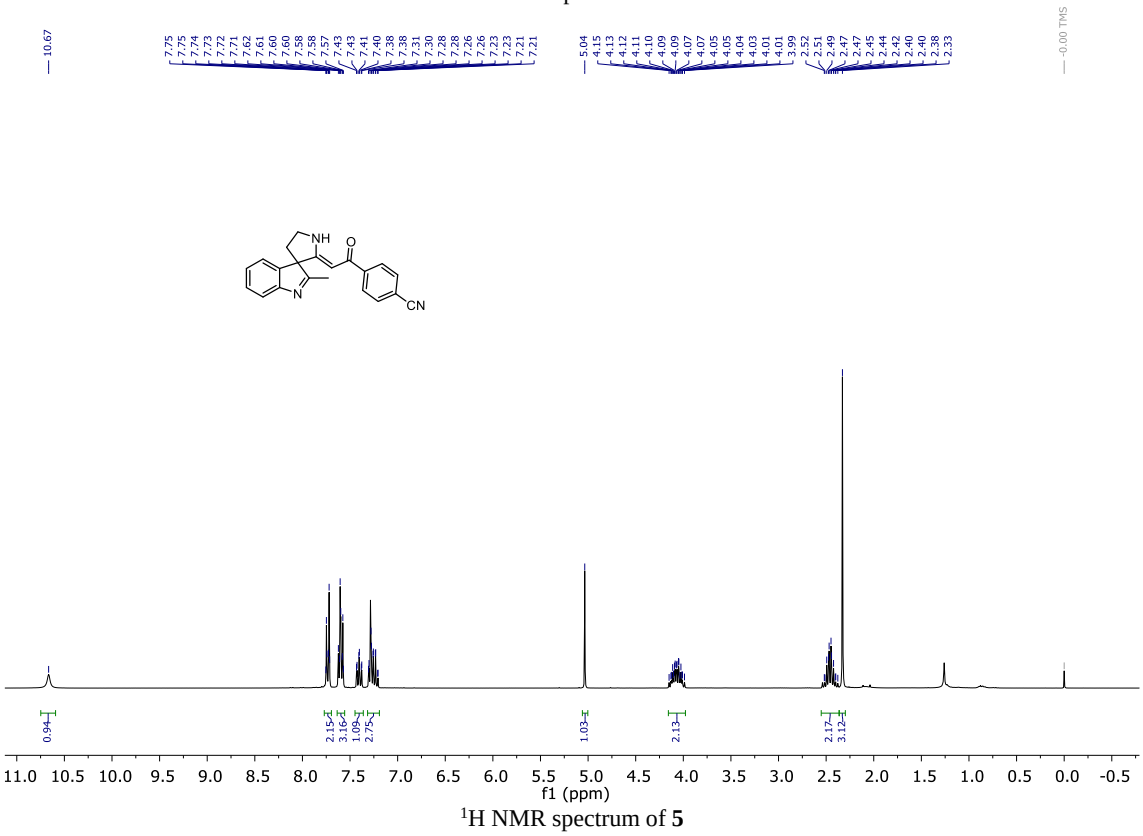
^{1}H NMR spectrum of **4**



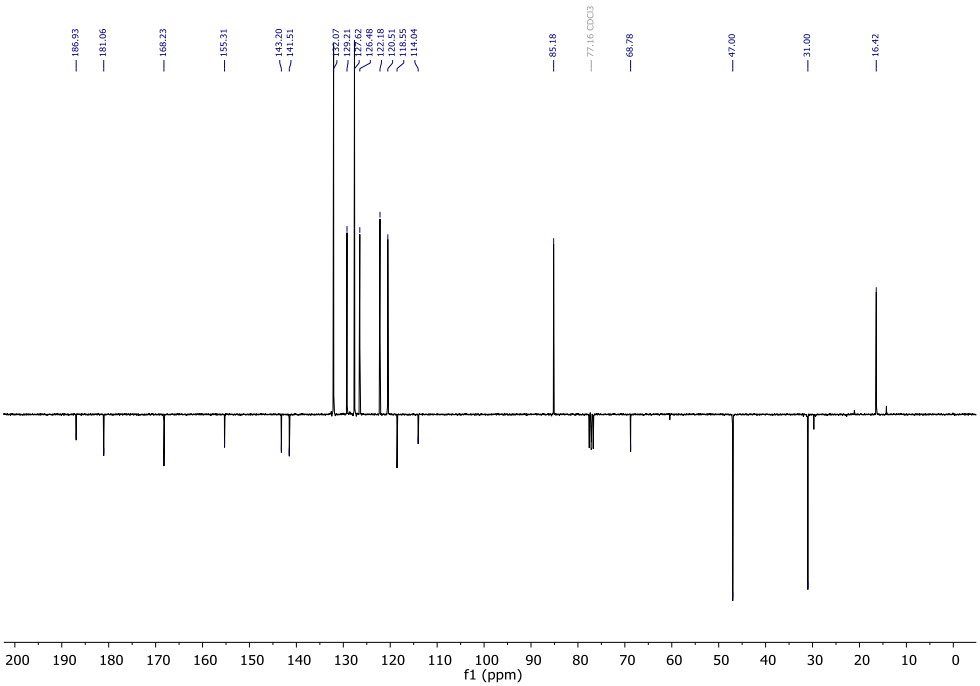
^{13}C APT NMR spectrum of **4**



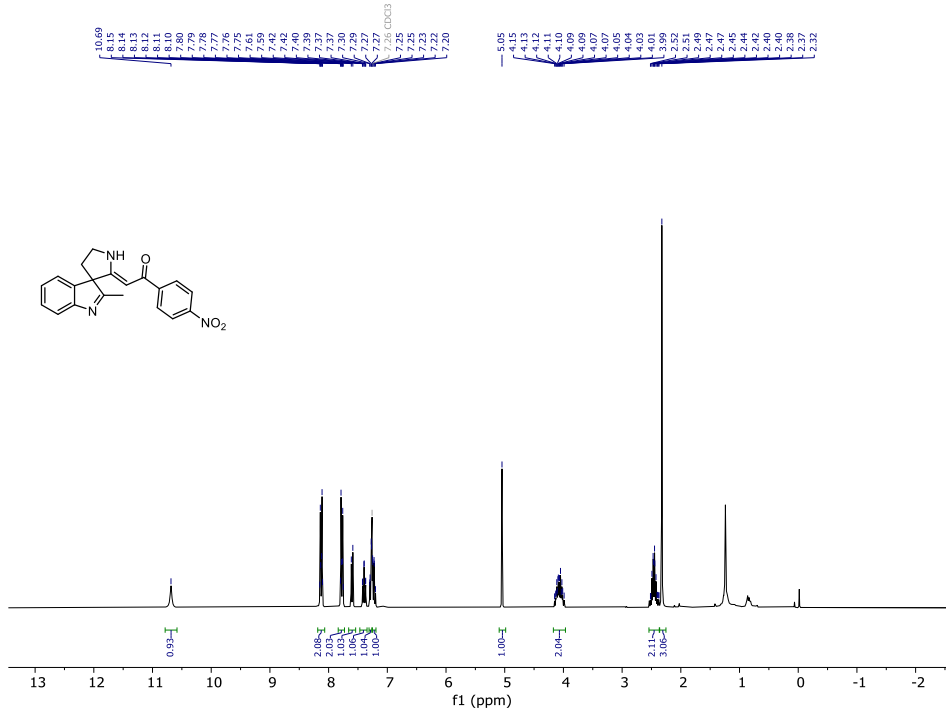
^{19}F NMR spectrum of **4**



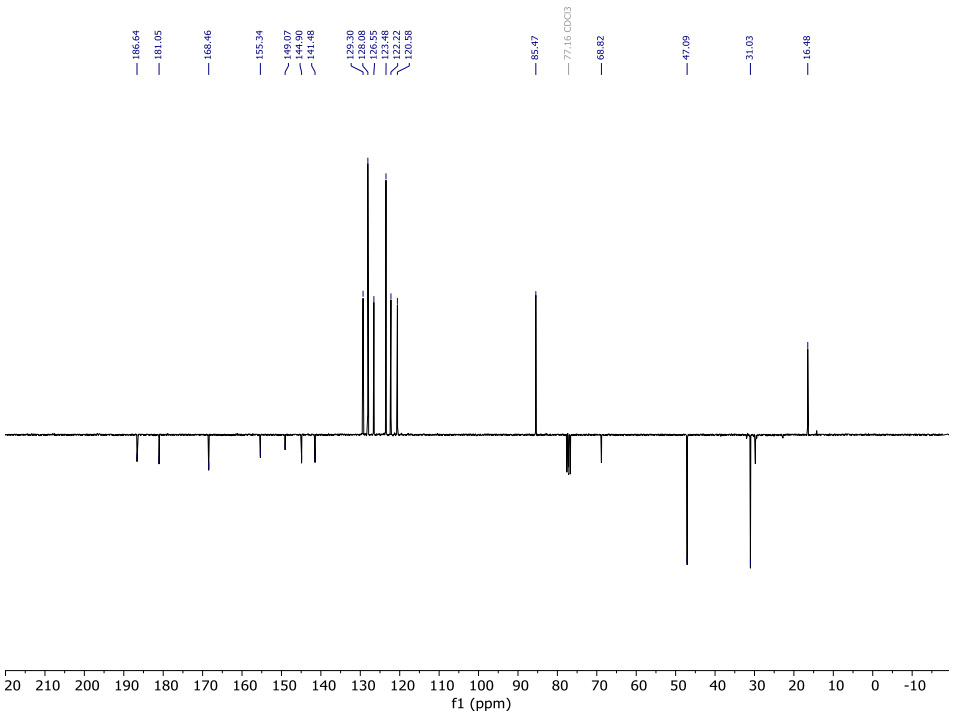
^{1}H NMR spectrum of **5**



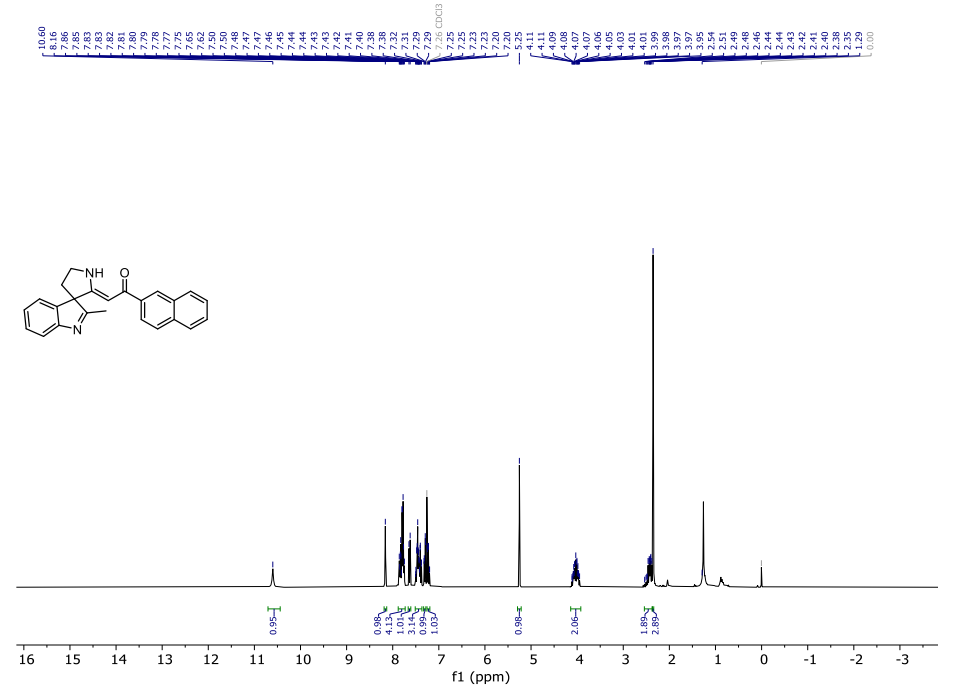
^{13}C APT NMR spectrum of **5**



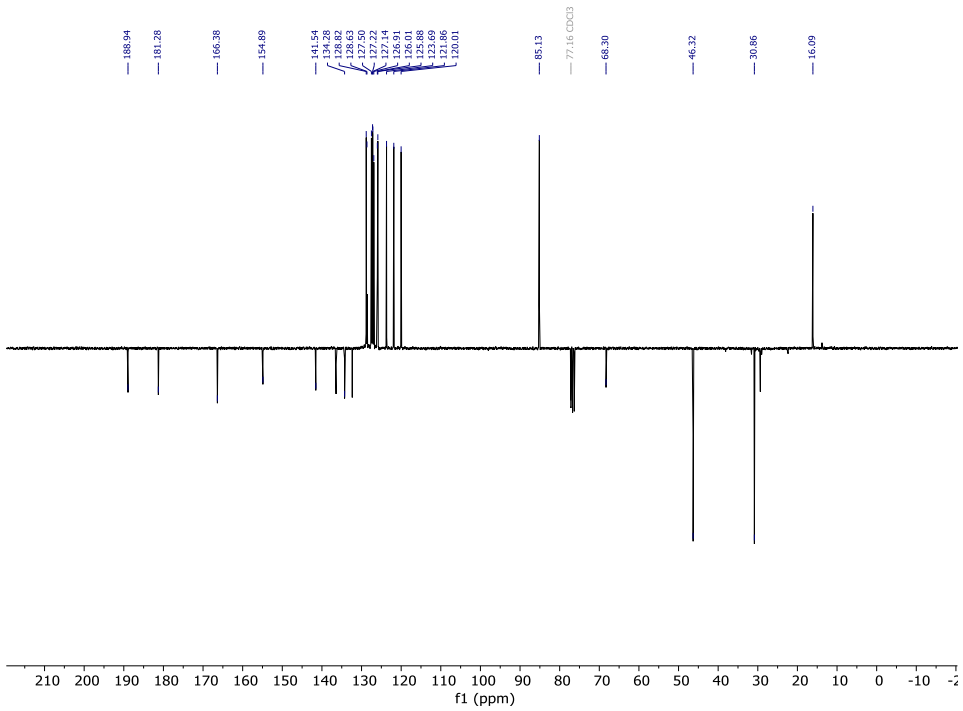
^{1}H NMR spectrum of **6**



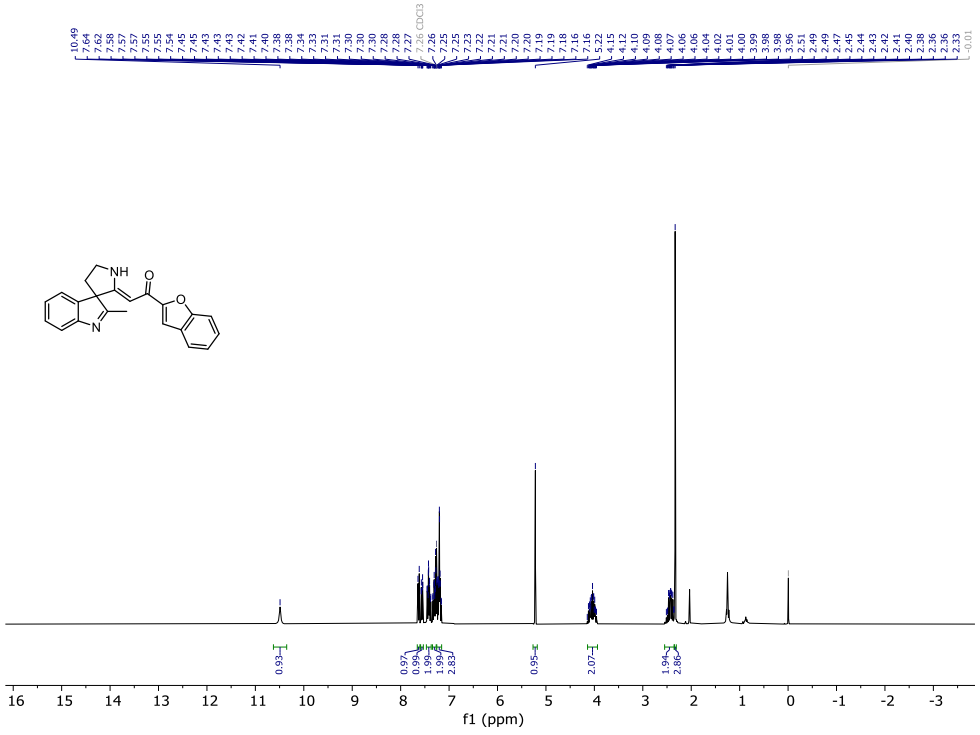
^{13}C APT NMR spectrum of **6**



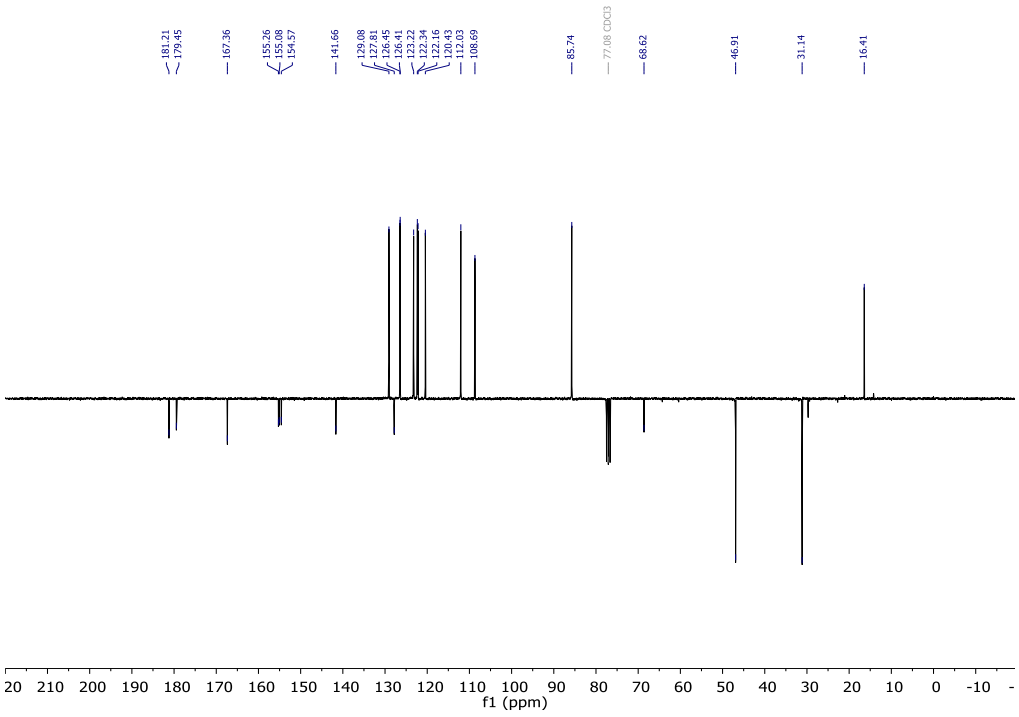
^{1}H NMR spectrum of **7**



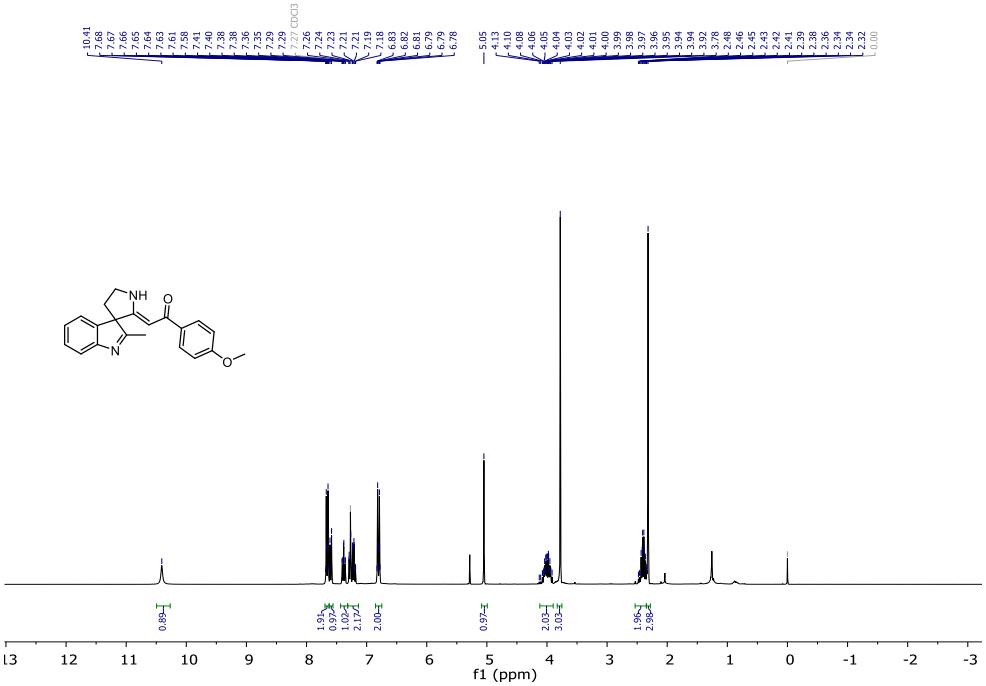
^{13}C APT NMR spectrum of **7**



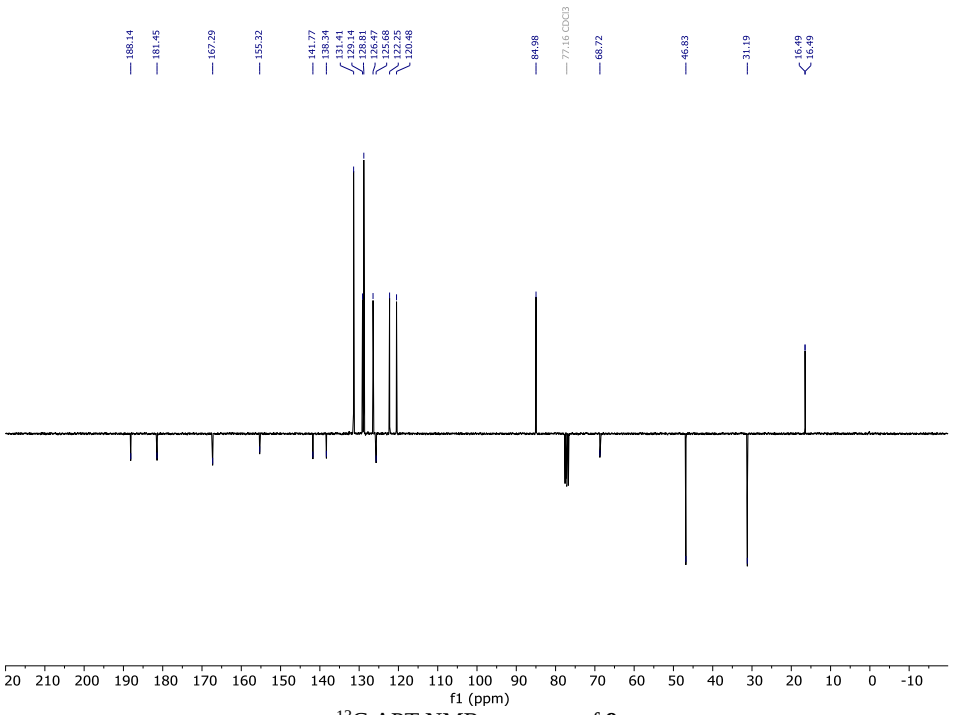
^{1}H NMR spectrum of **8**



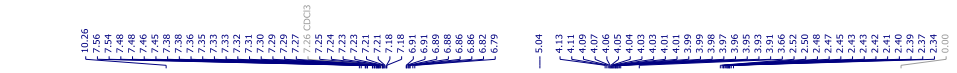
^{13}C APT NMR spectrum of **8**

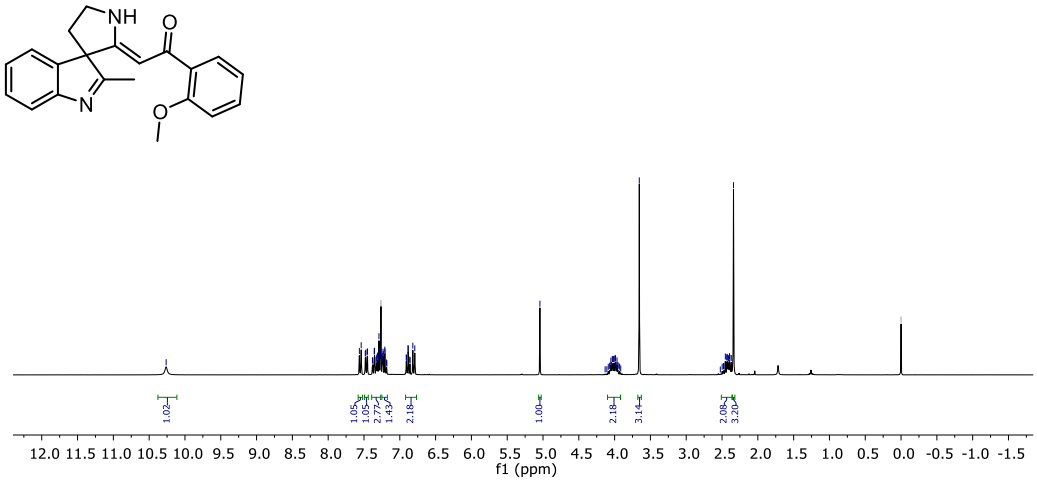


^{1}H NMR spectrum of **9**

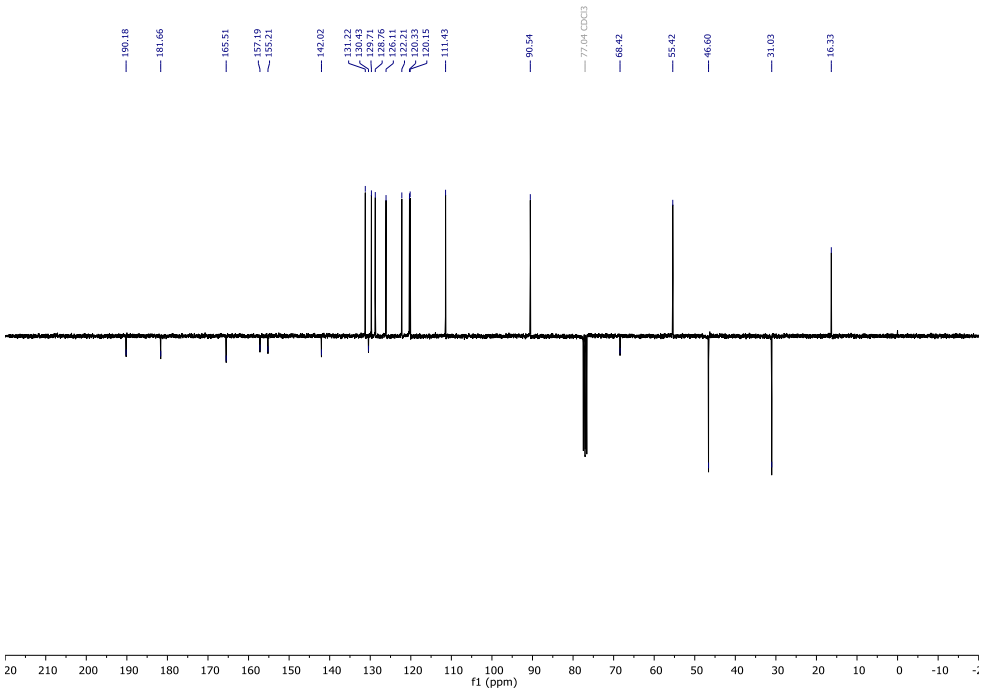


^{13}C APT NMR spectrum of **9**

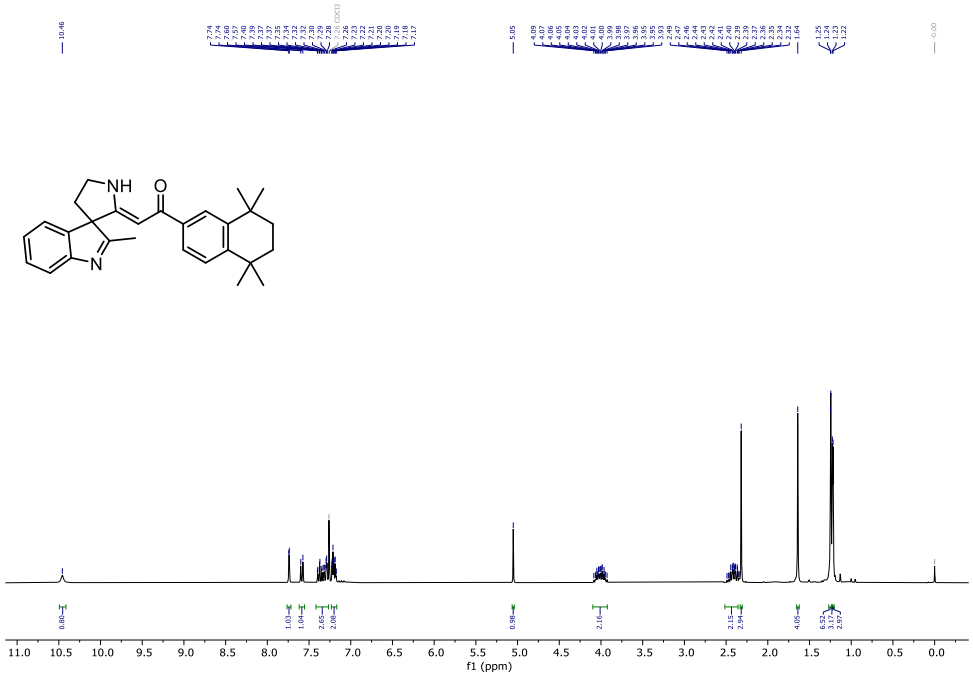




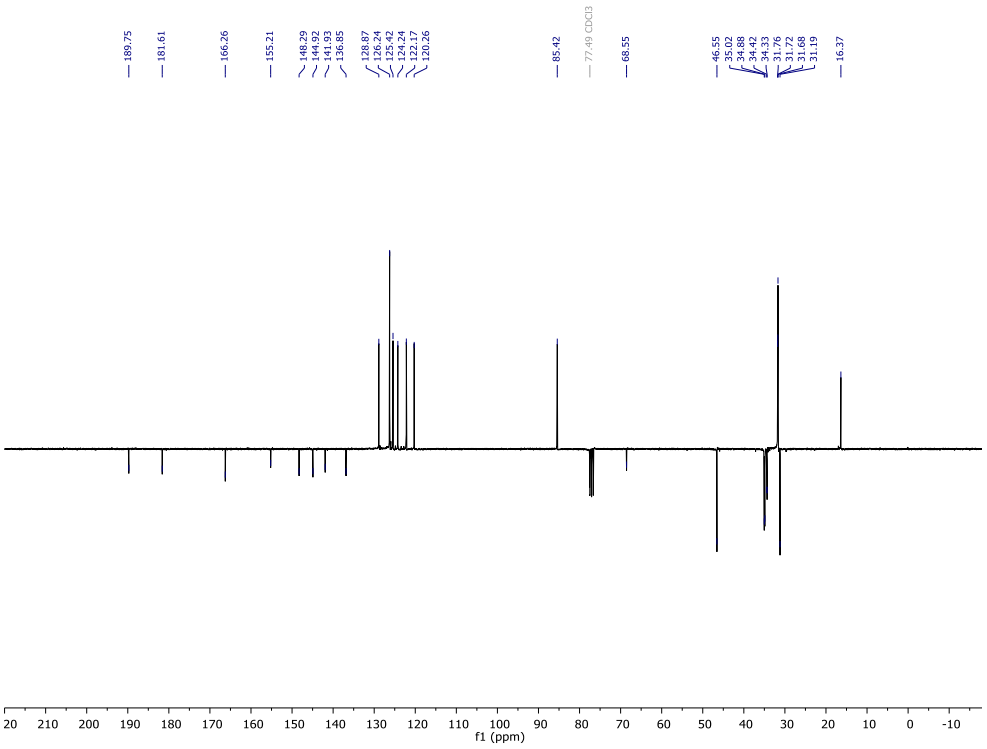
^{1}H NMR spectrum of **10**



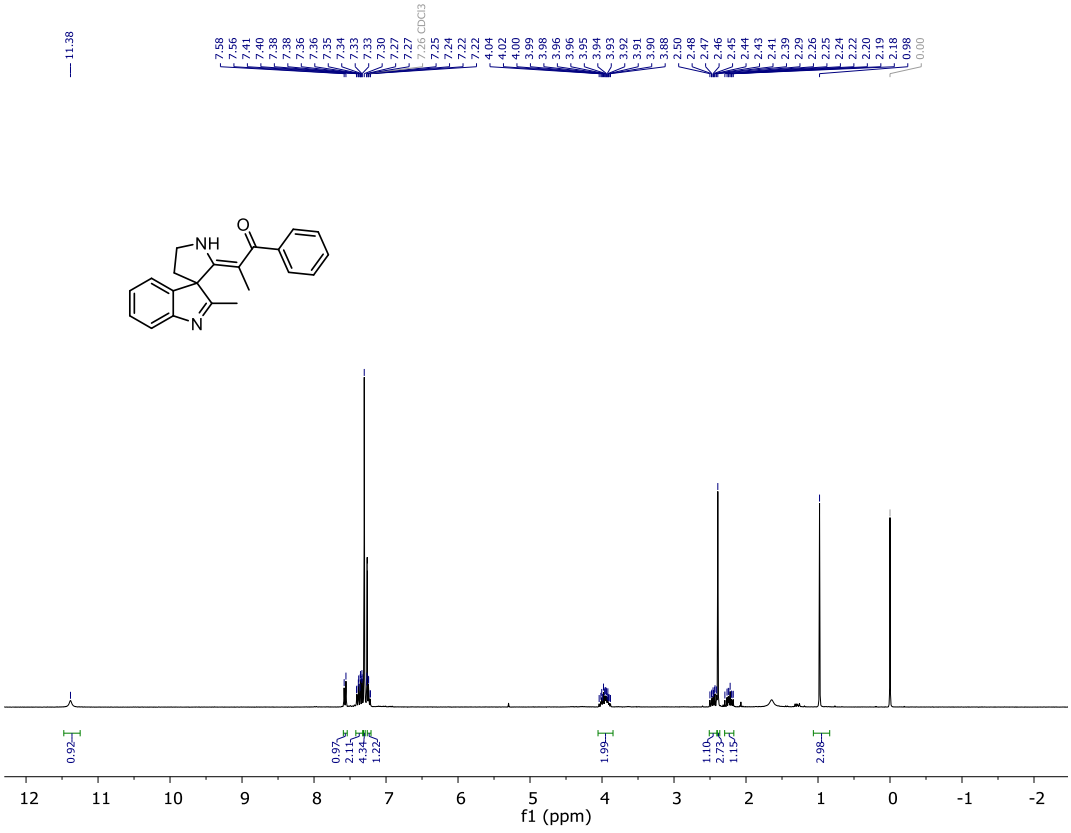
^{13}C APT NMR spectrum of **10**



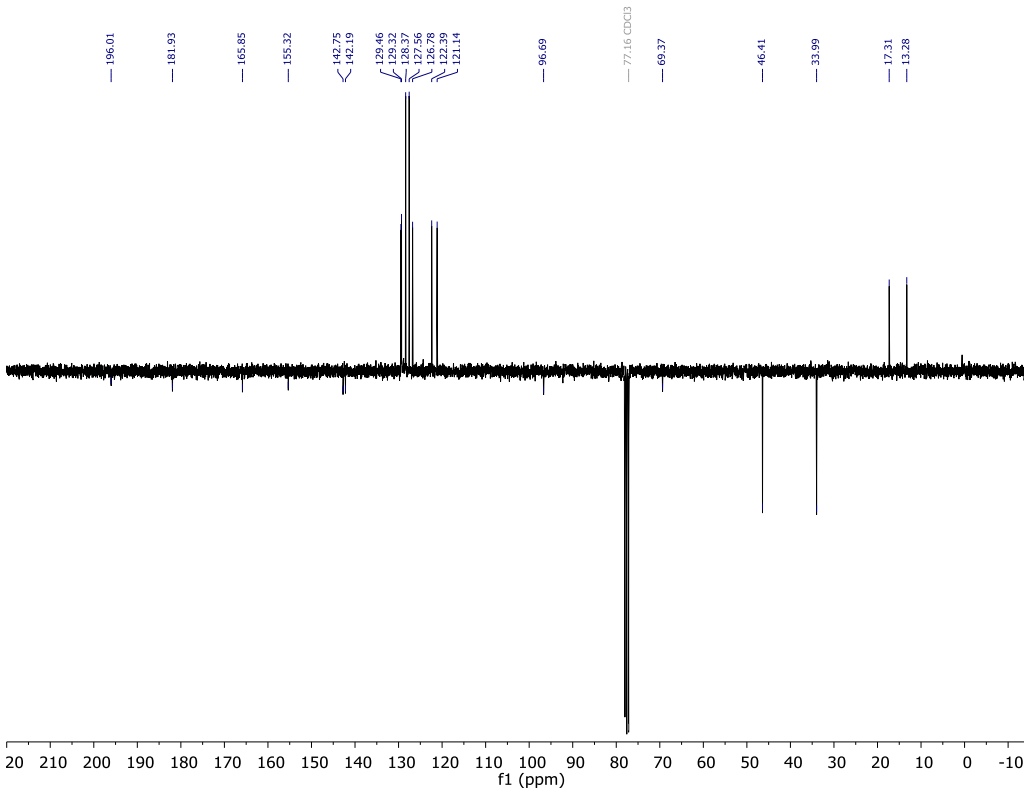
^{1}H NMR spectrum of **11**



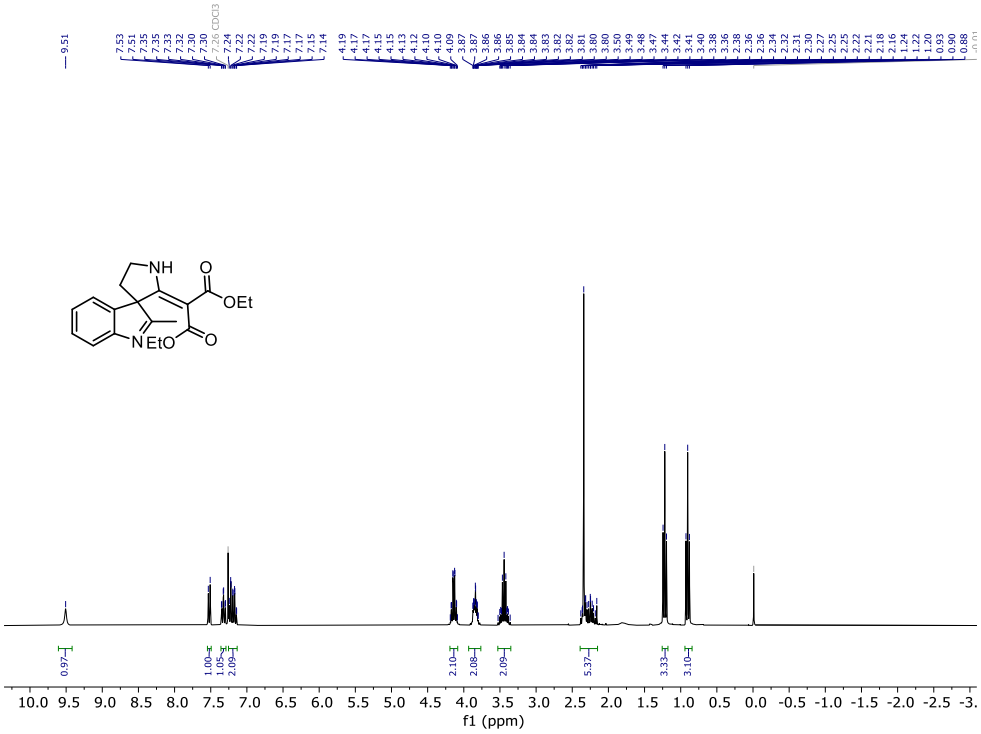
^{13}C APT NMR spectrum of **11**



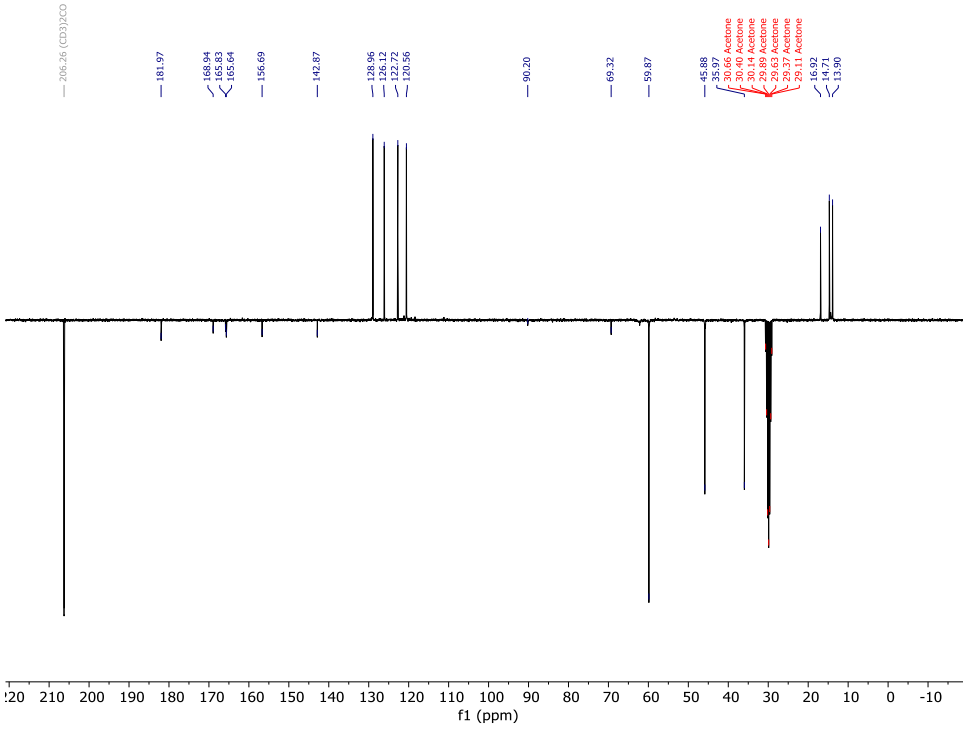
^{1}H NMR spectrum of **12**



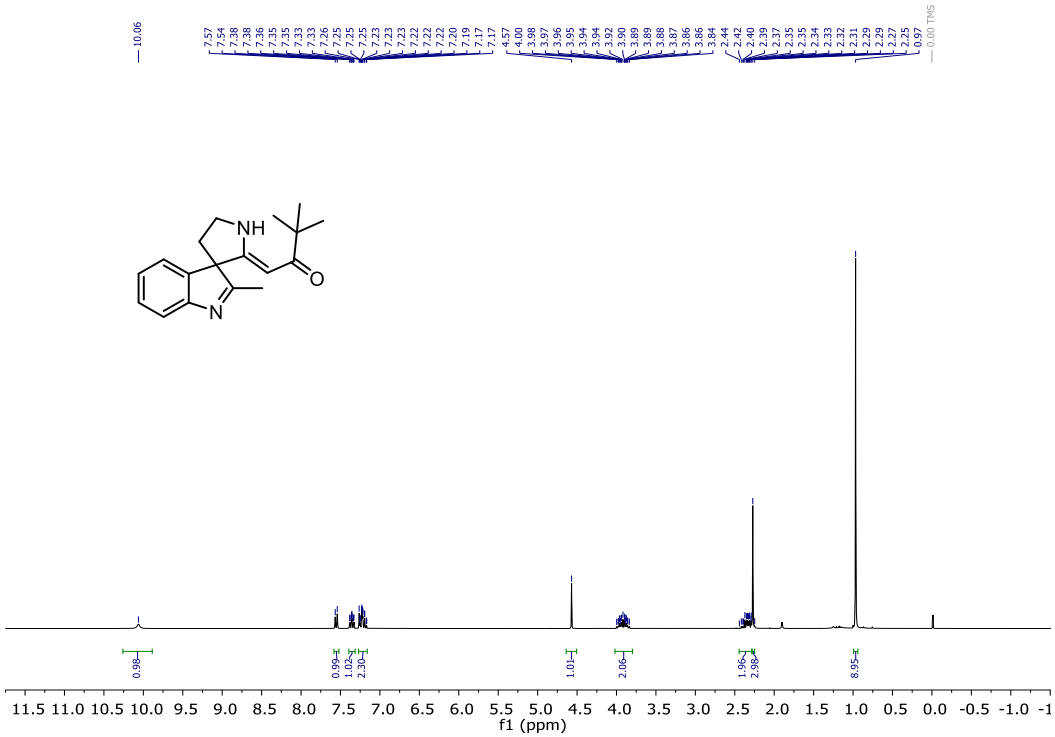
^{13}C APT NMR spectrum of **12**



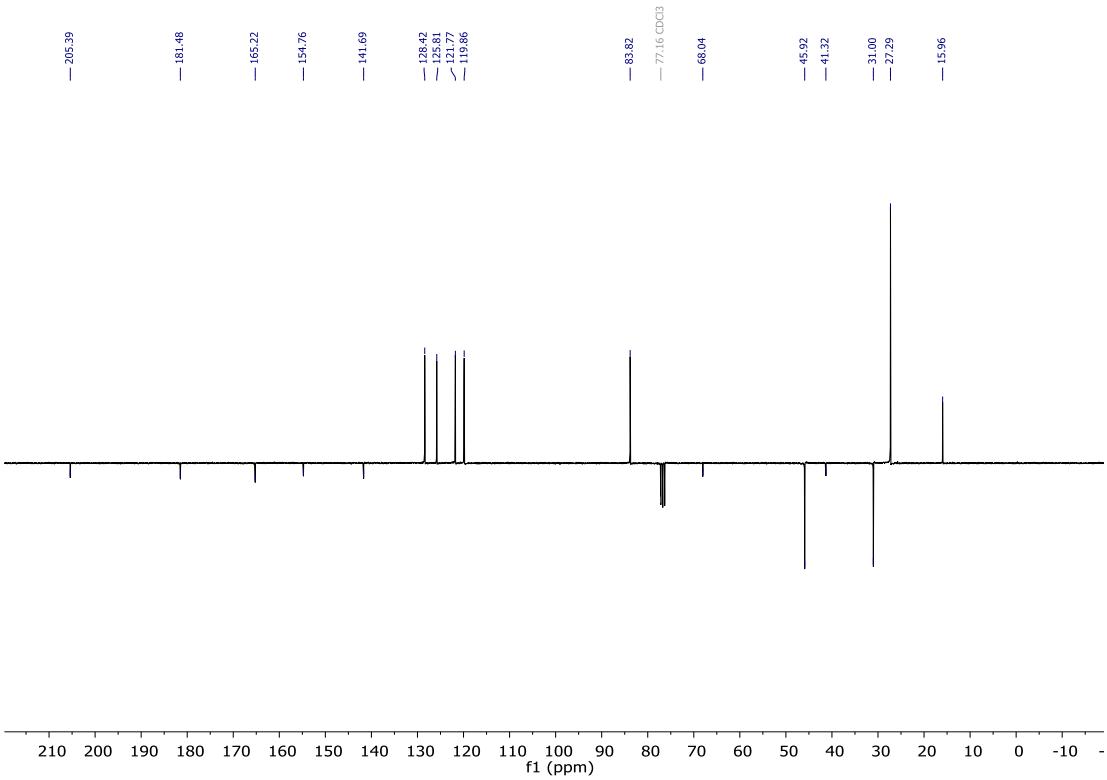
^{1}H NMR spectrum of **13**



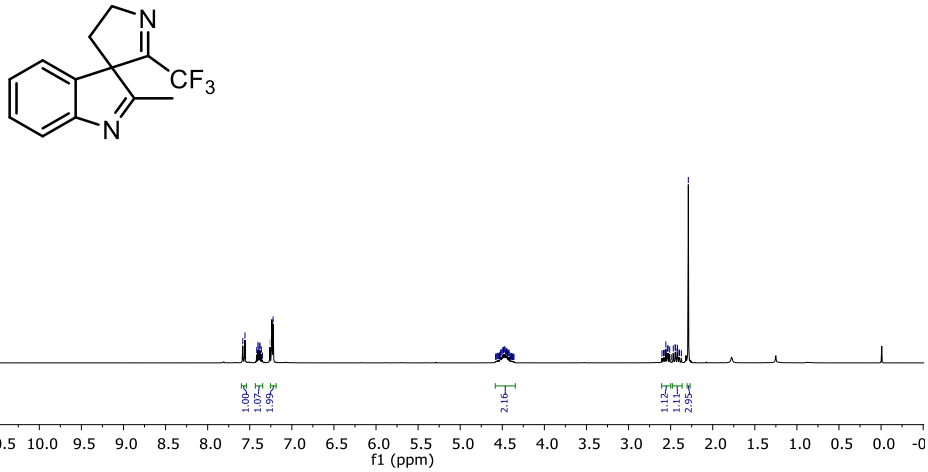
^{13}C APT NMR spectrum of **13**



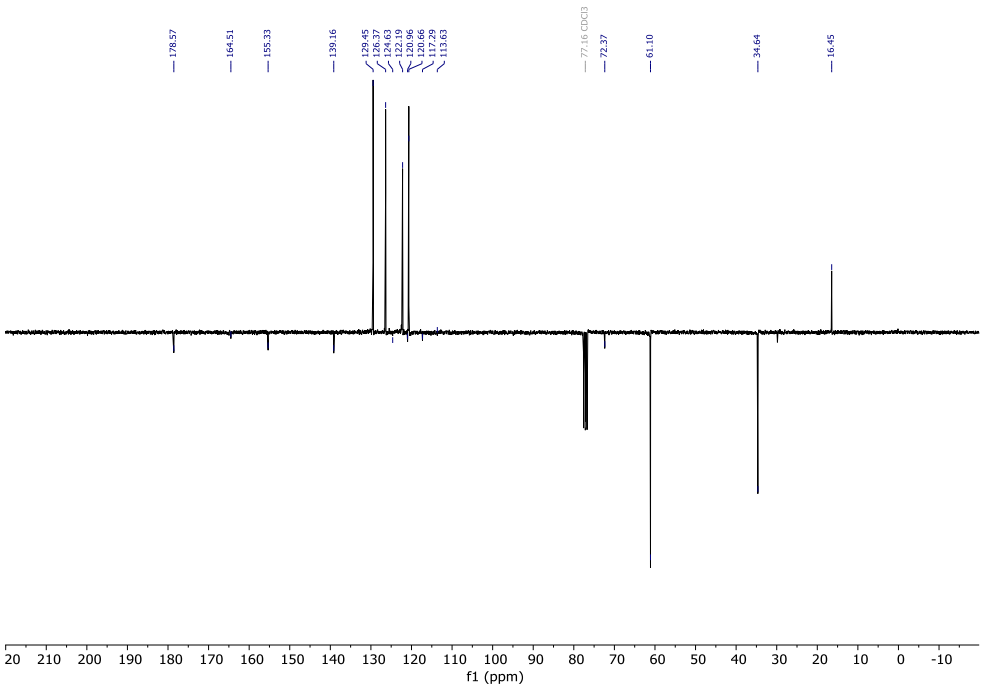
^{1}H NMR spectrum of **14**



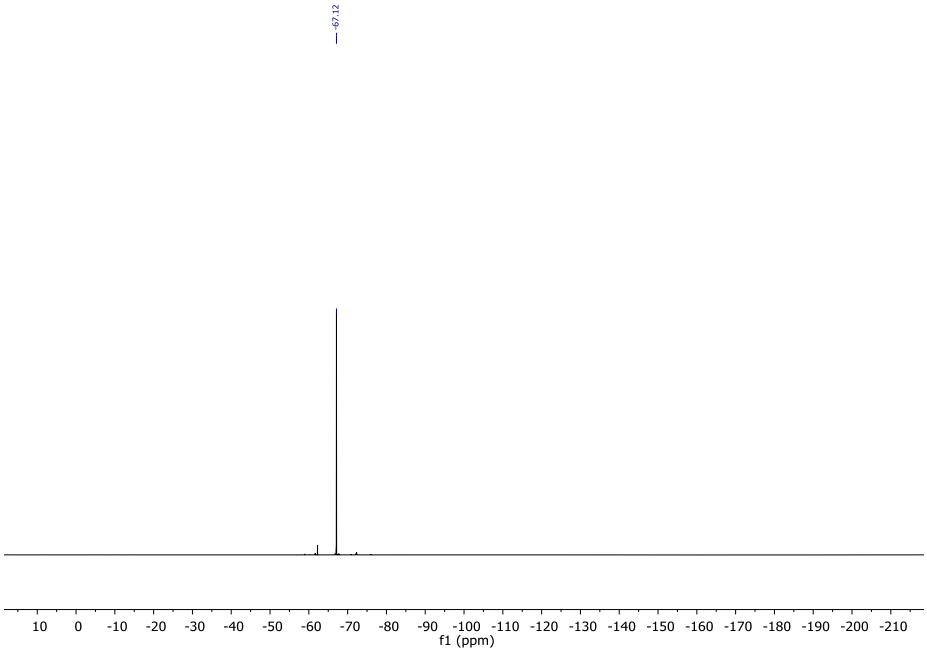
^{13}C APT NMR spectrum of **14**



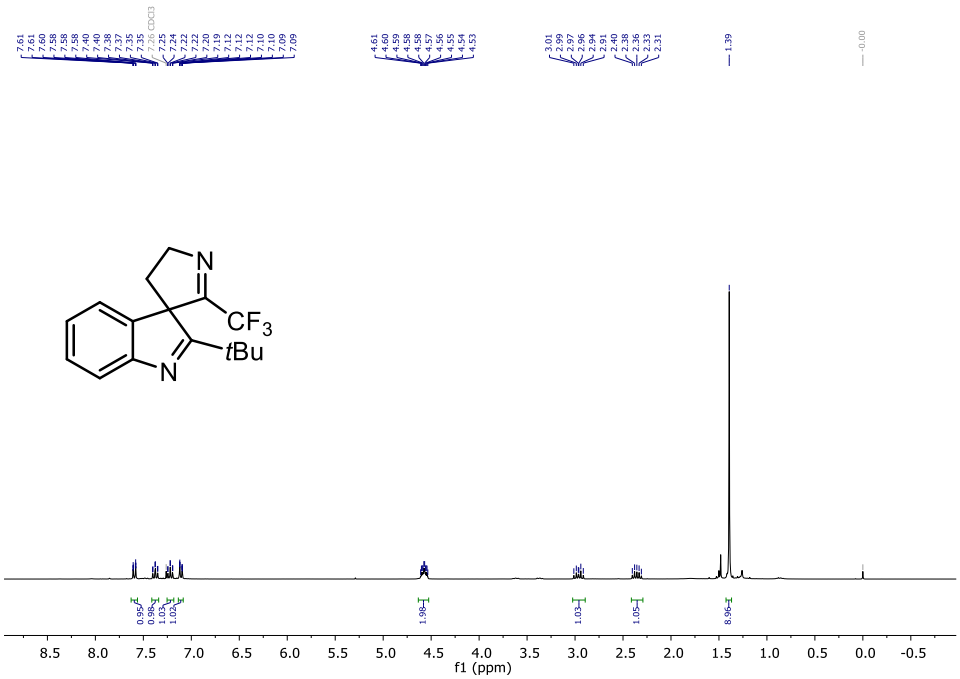
^{1}H NMR spectrum of **15**



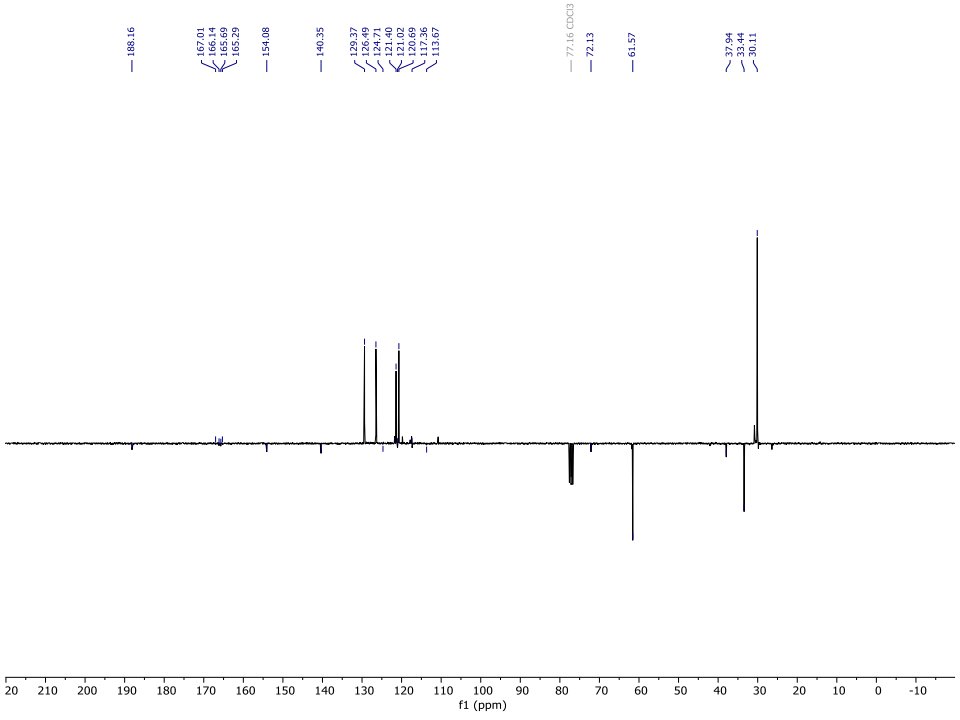
^{13}C APT NMR spectrum of **15**



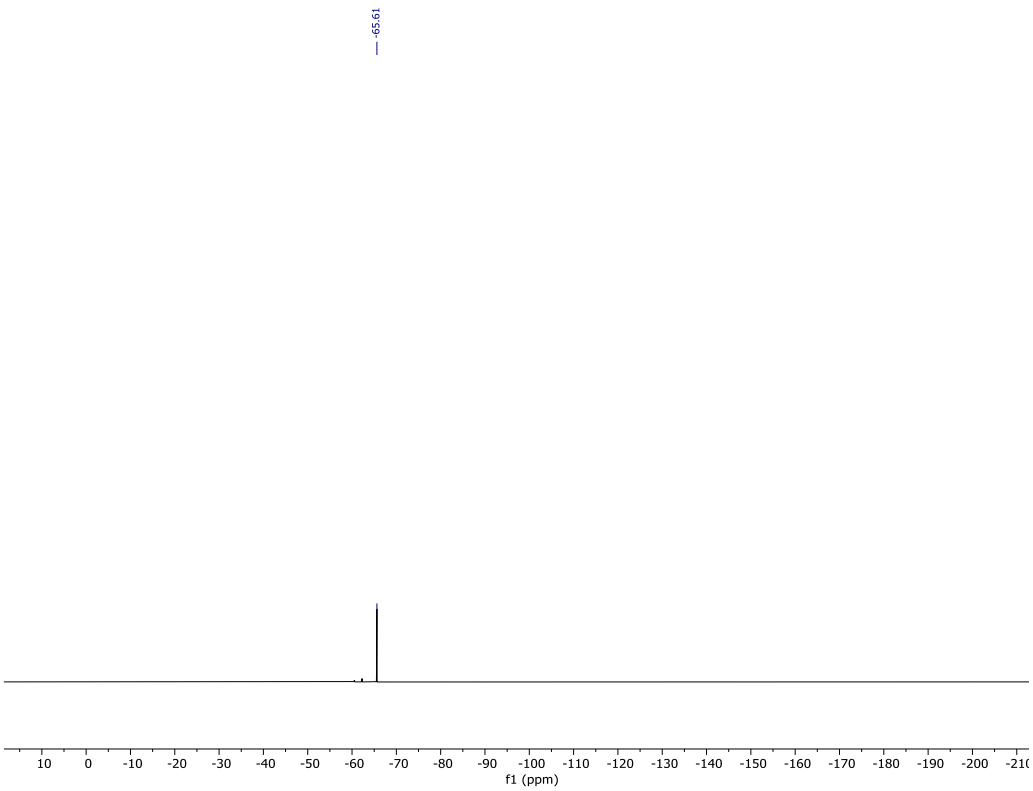
^{19}F NMR spectrum of **15**



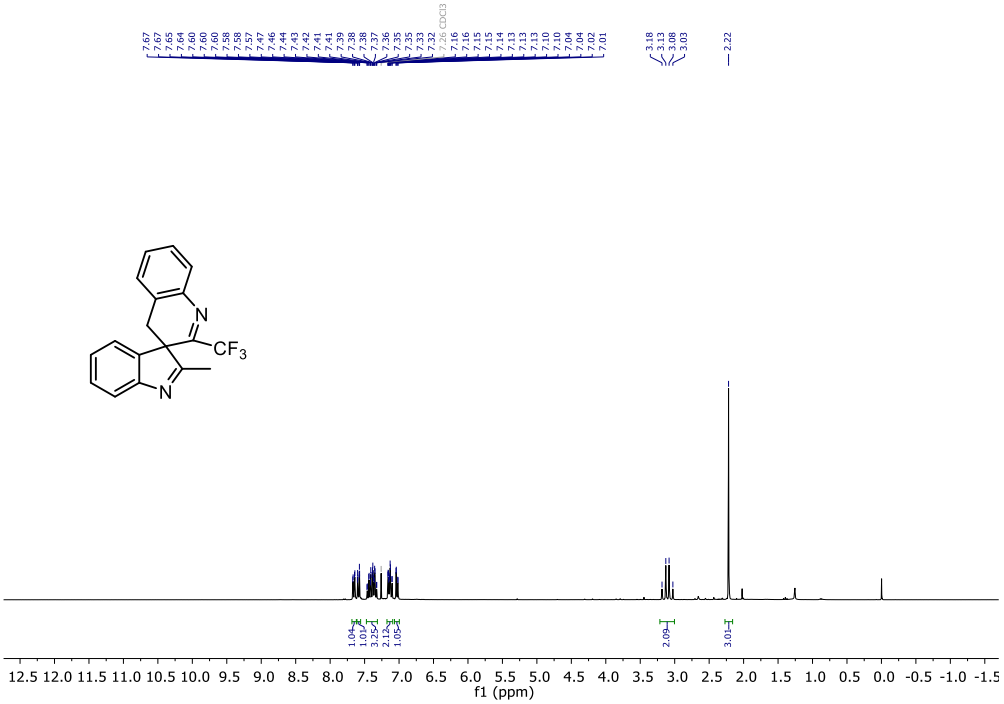
^{1}H NMR spectrum of **16**



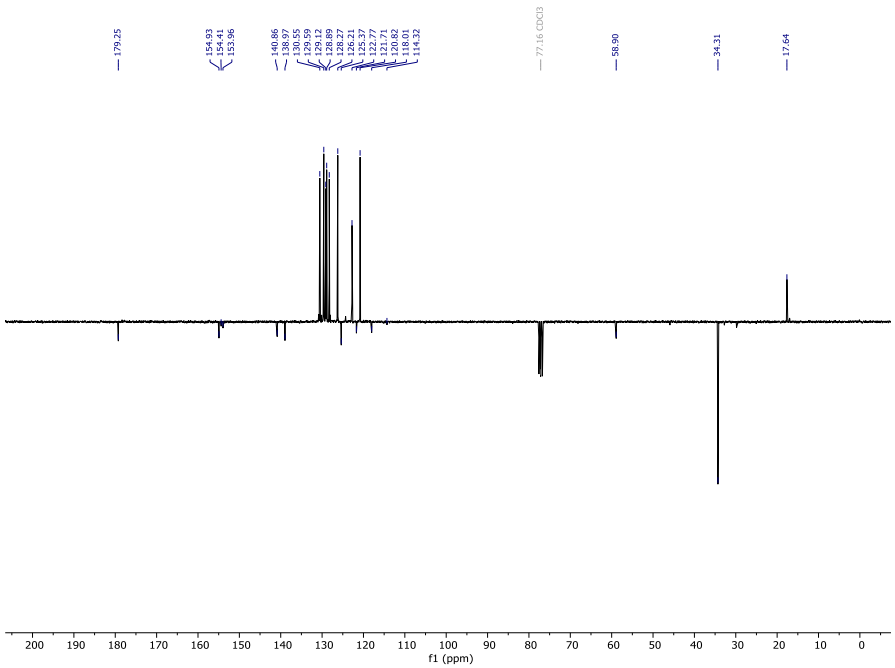
^{13}C APT NMR spectrum of **16**



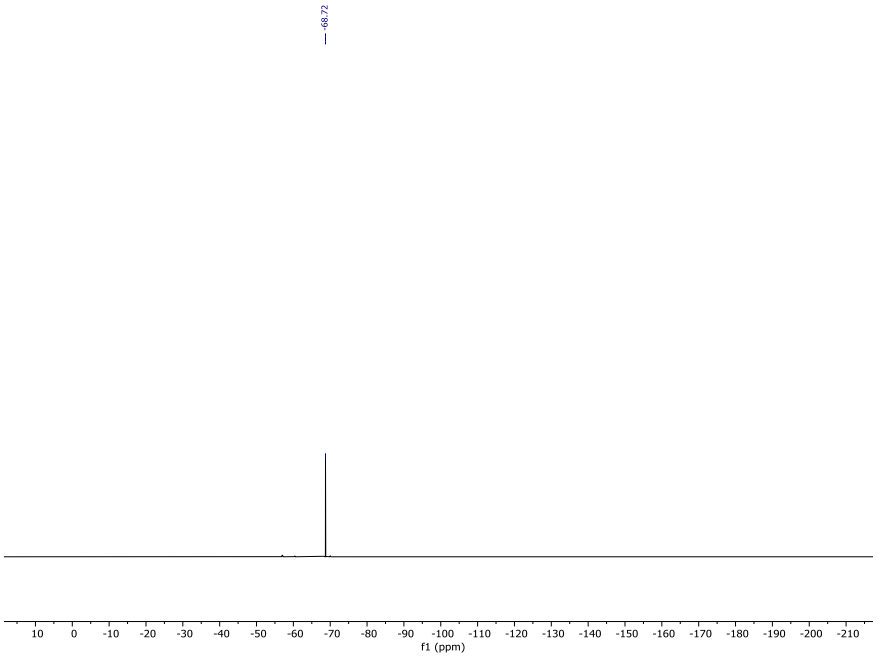
^{19}F NMR spectrum of **16**



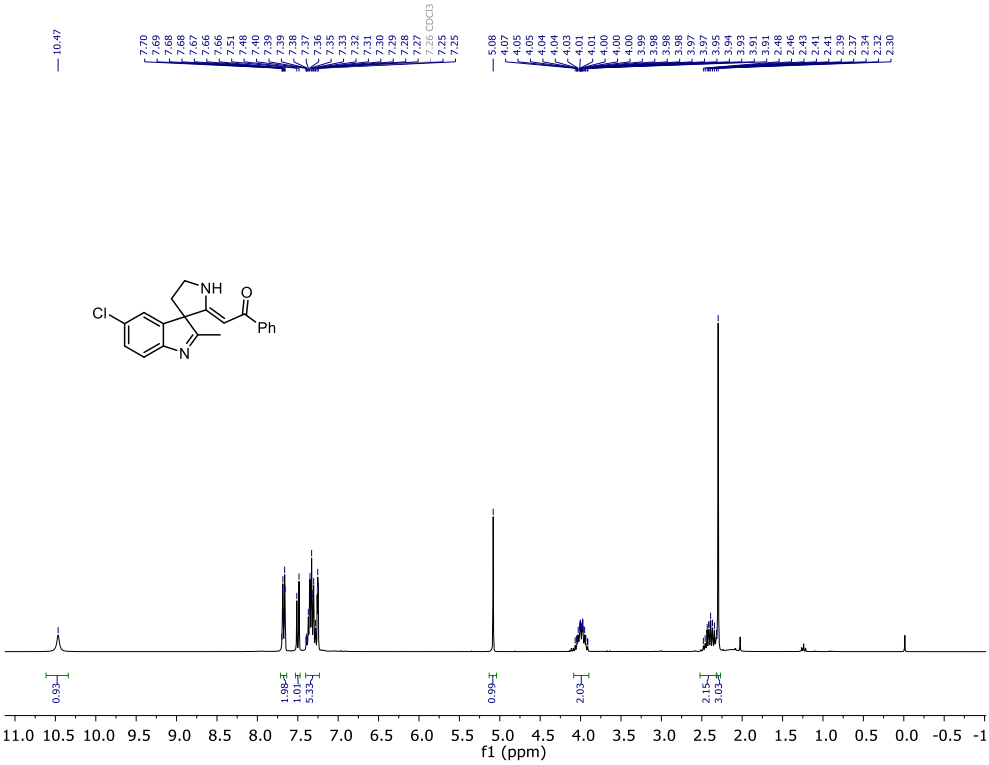
^{1}H NMR spectrum of **17**



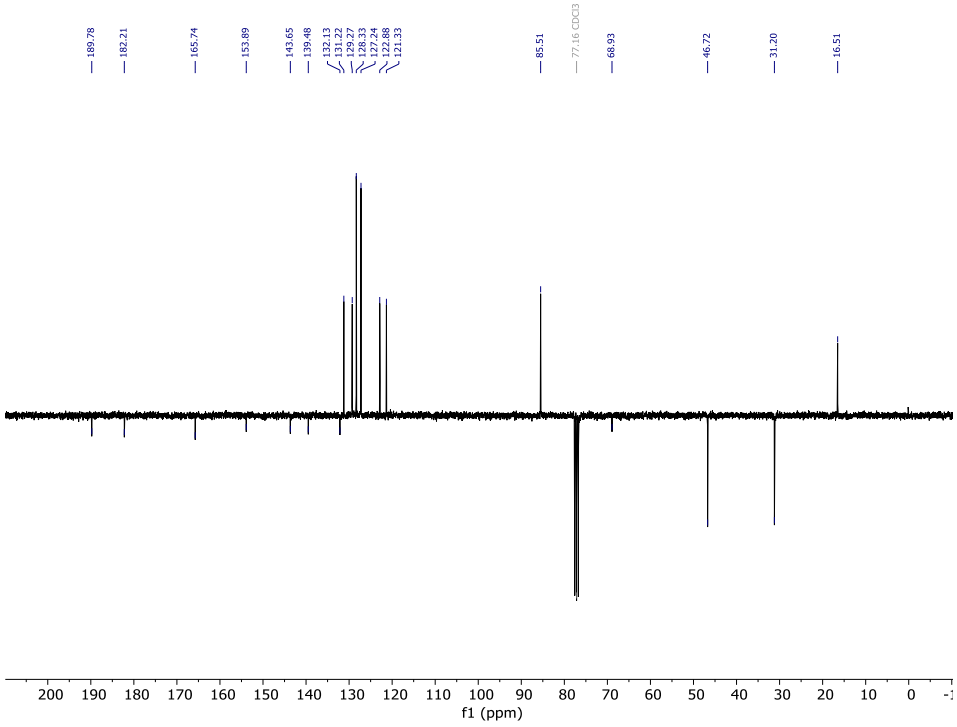
^{13}C APT NMR spectrum of **17**



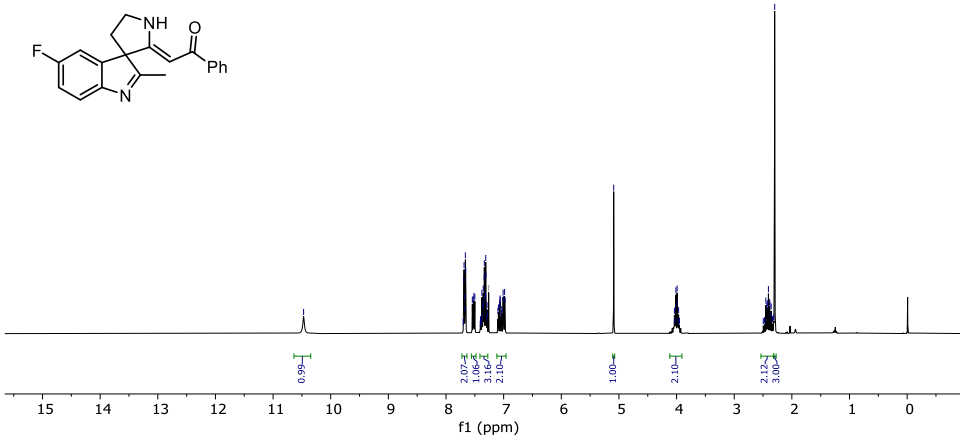
^{19}F NMR spectrum of **17**



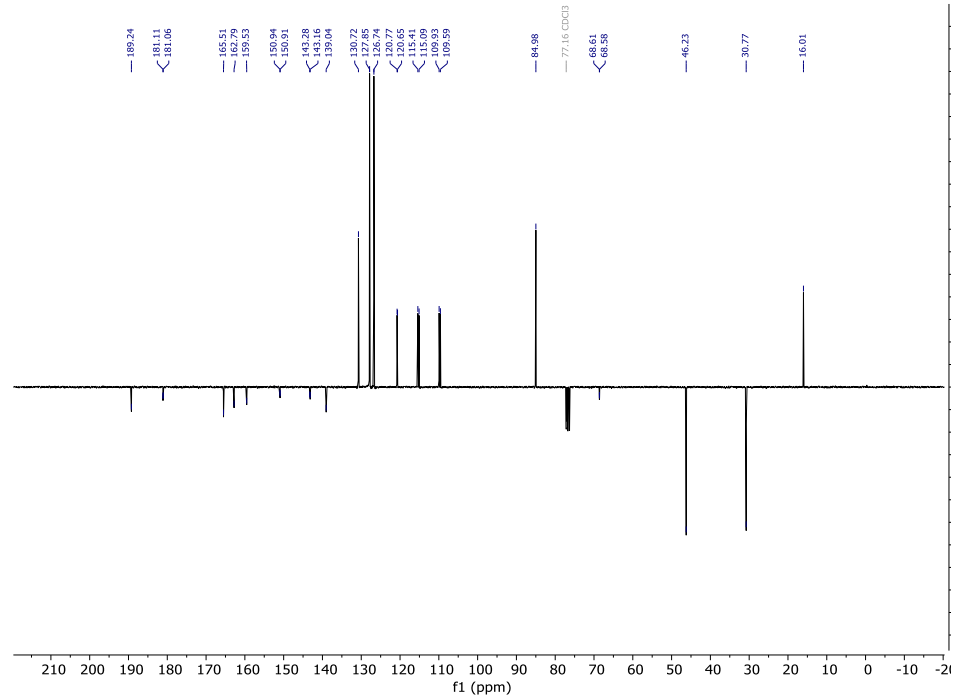
^{1}H NMR spectrum of **19**



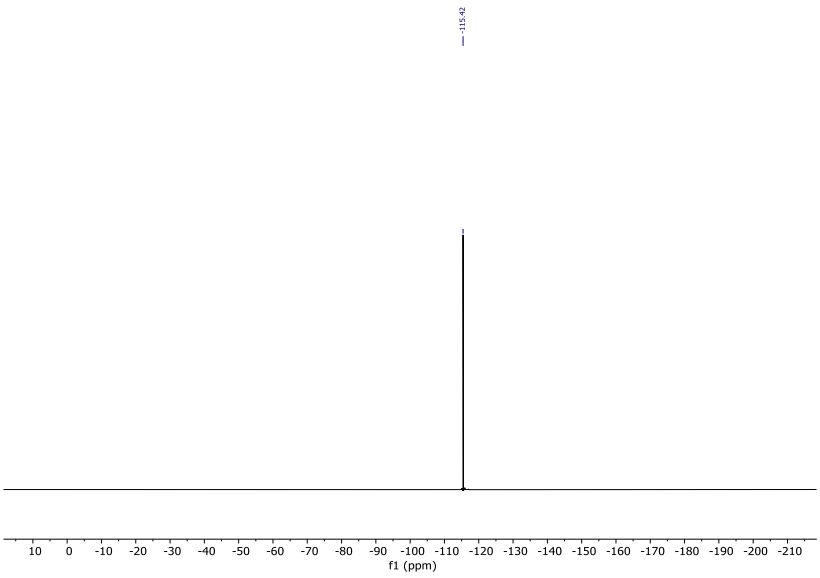
^{13}C APT NMR spectrum of **19**



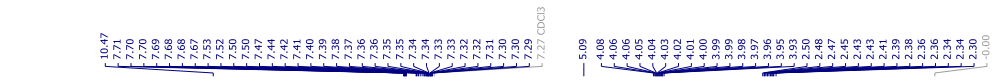
^{1}H NMR spectrum of **20**

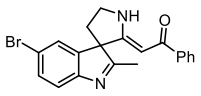


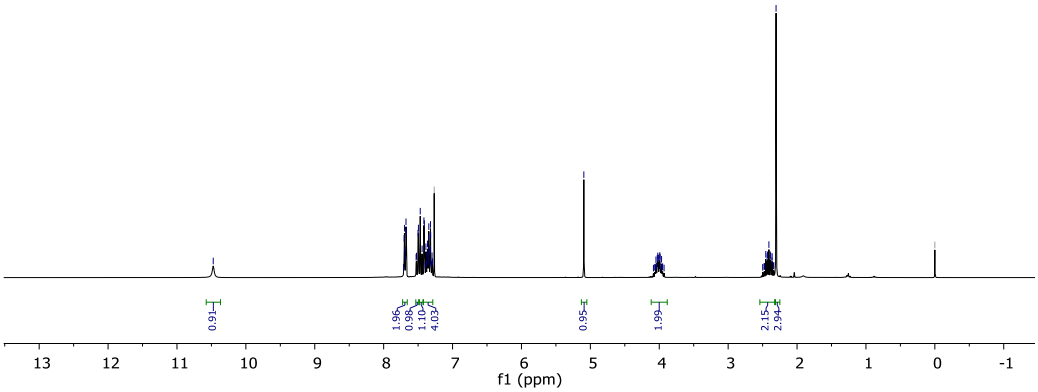
^{13}C APT NMR spectrum of **20**



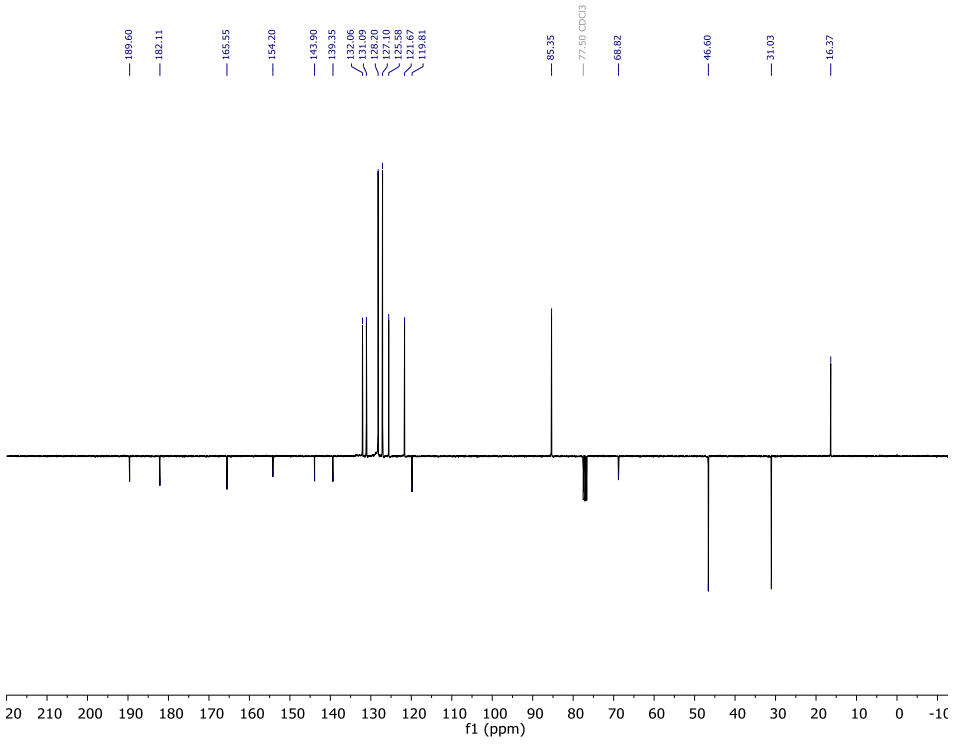
^{19}F NMR spectrum of **20**



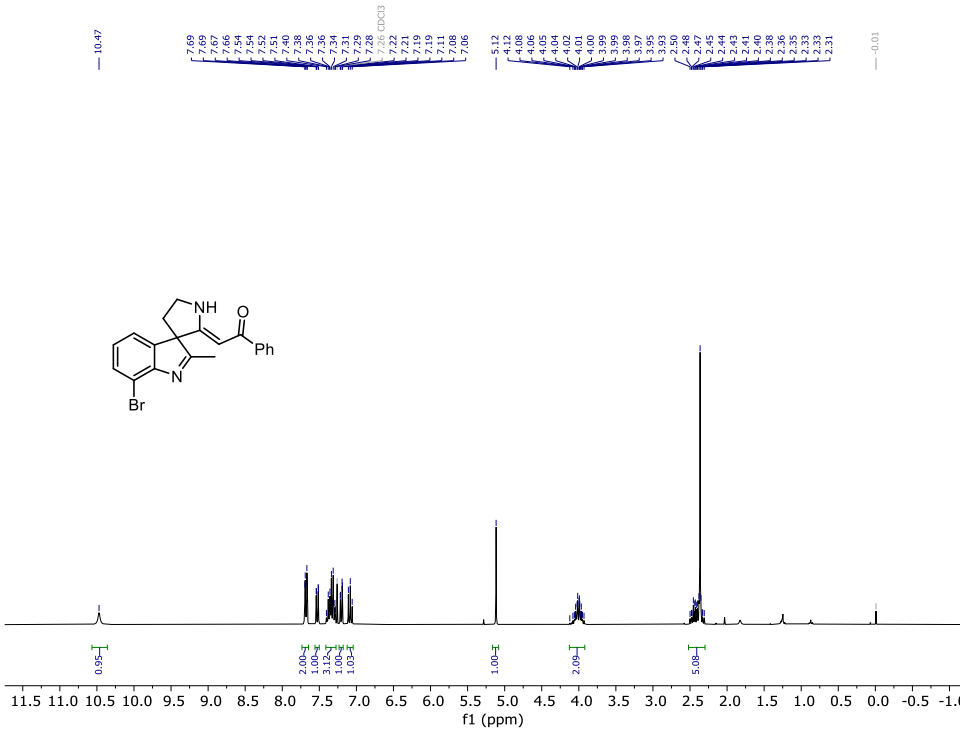




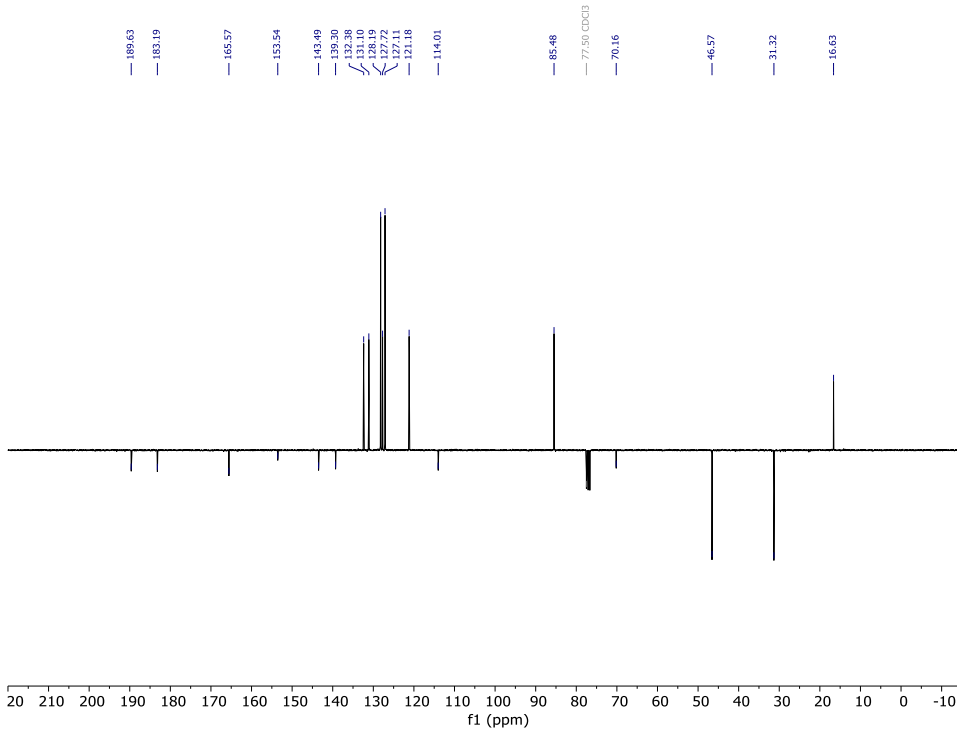
^{1}H NMR spectrum of **21**



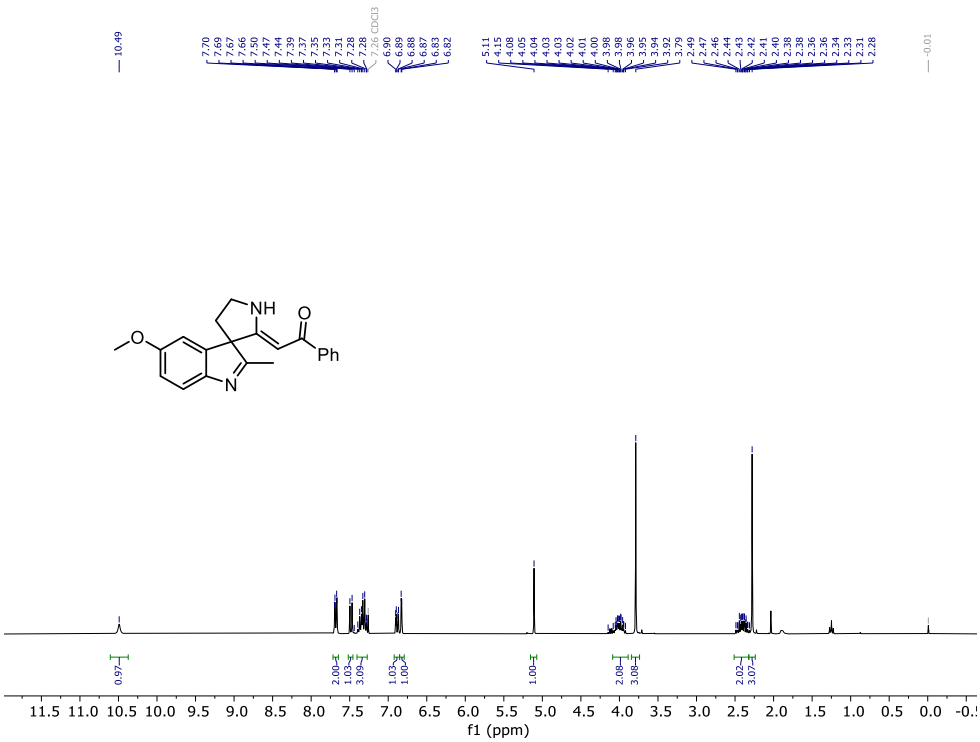
^{13}C APT NMR spectrum of **21**



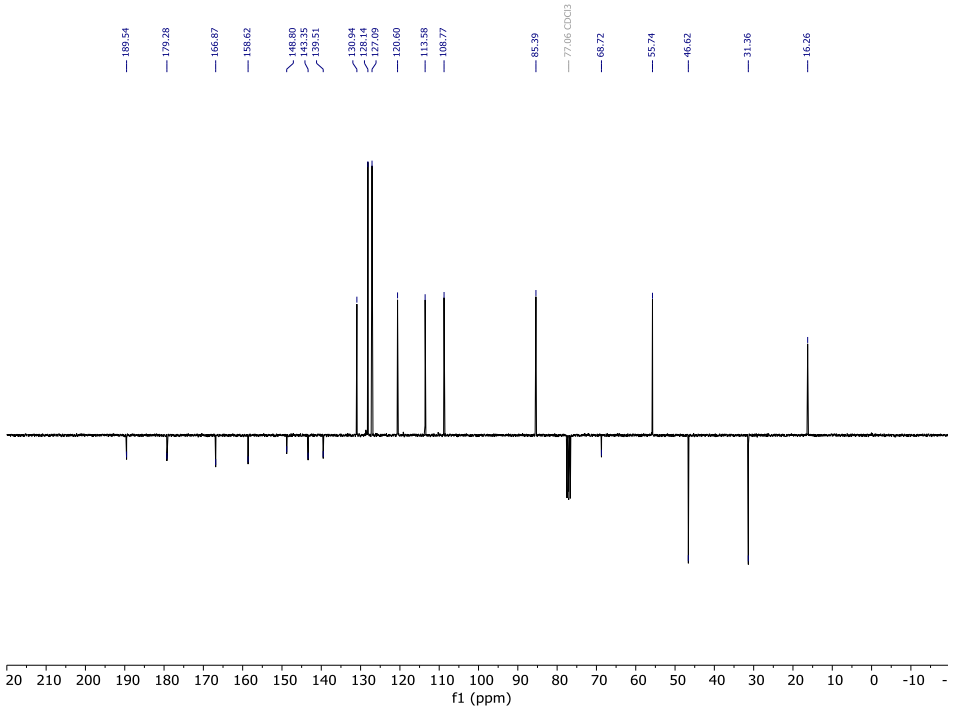
^{1}H NMR spectrum of **22**



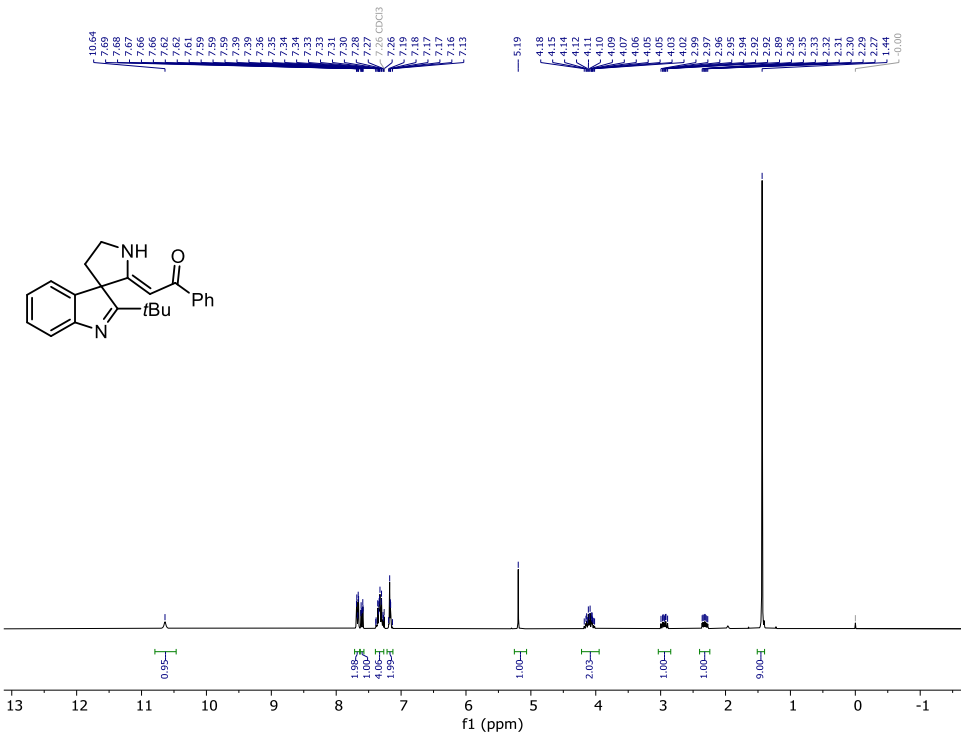
^{13}C APT NMR spectrum of **22**



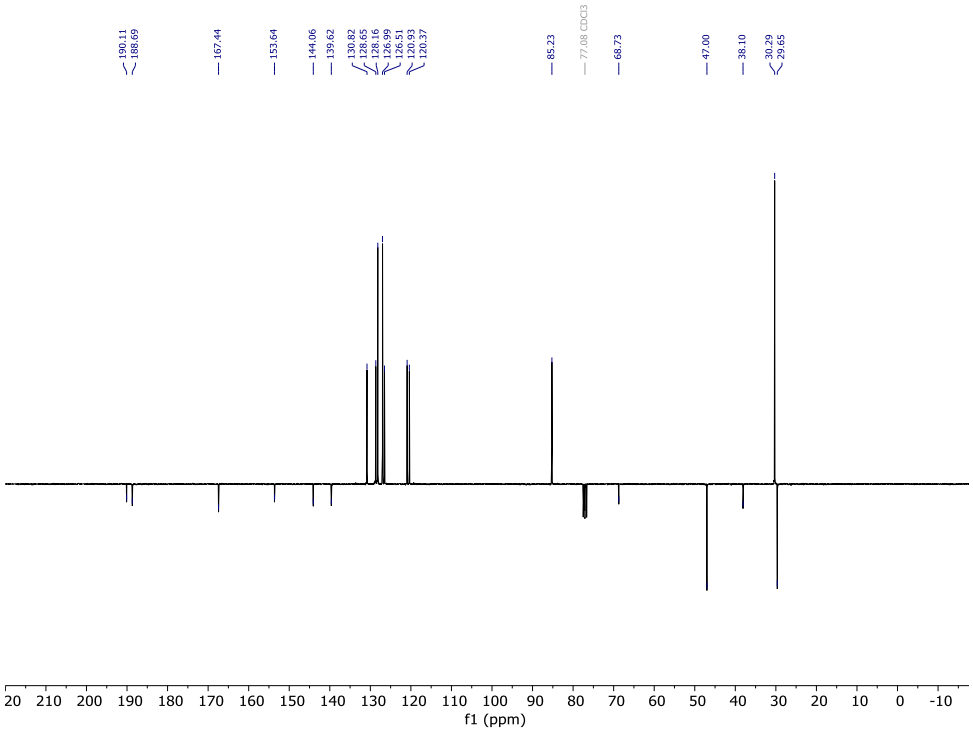
^{1}H NMR spectrum of **23**



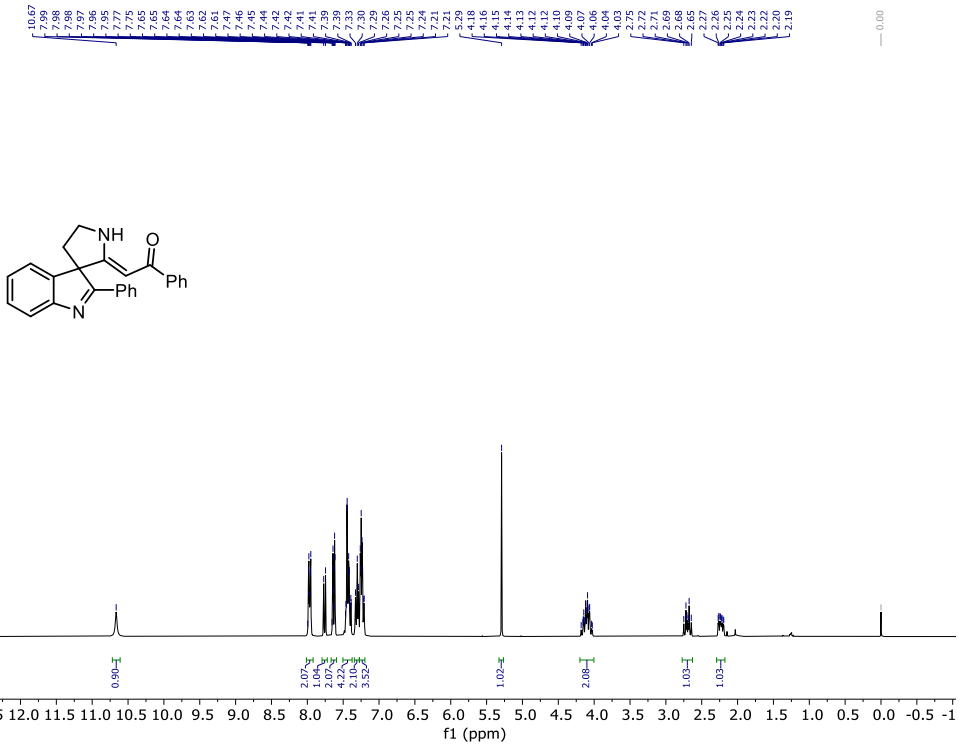
^{13}C APT NMR spectrum of **23**



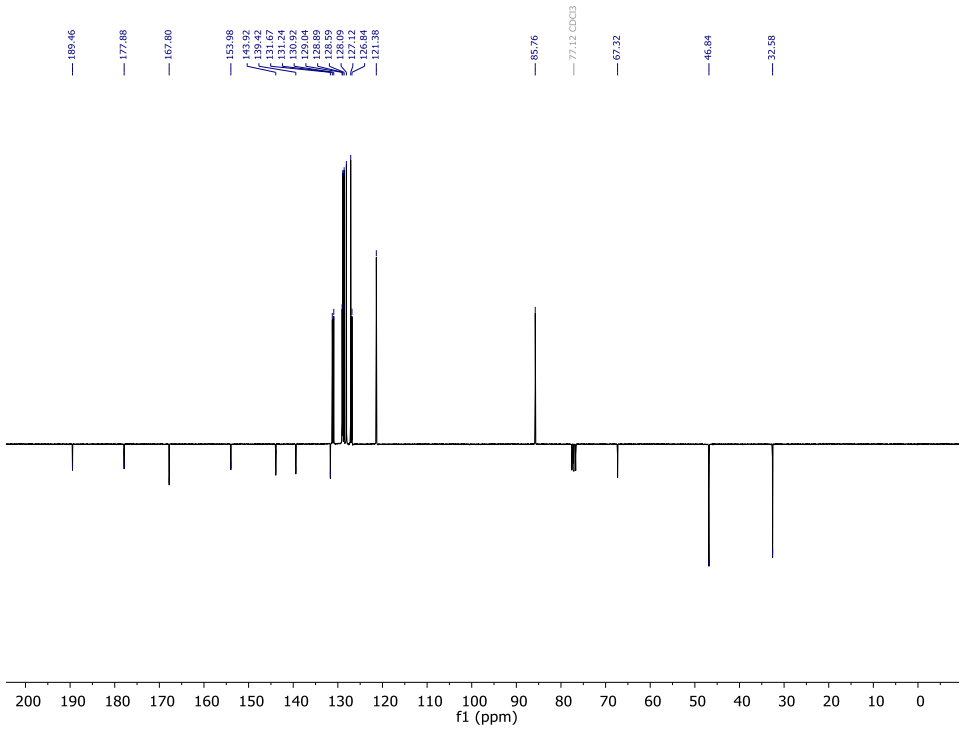
^{1}H NMR spectrum of **24**



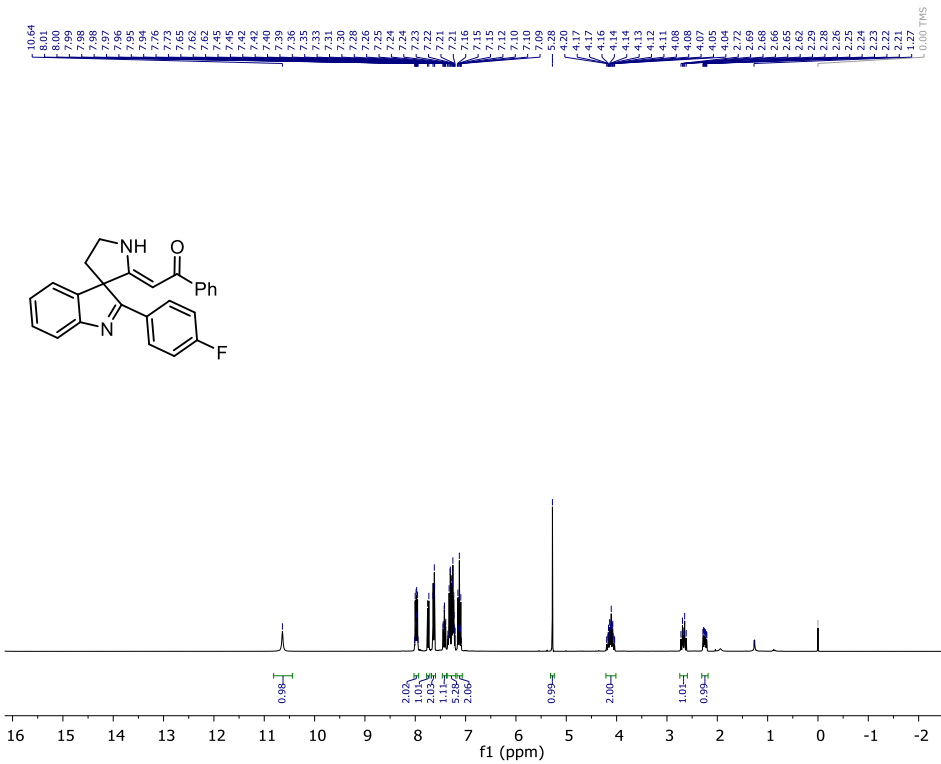
^{13}C APT NMR spectrum of **24**



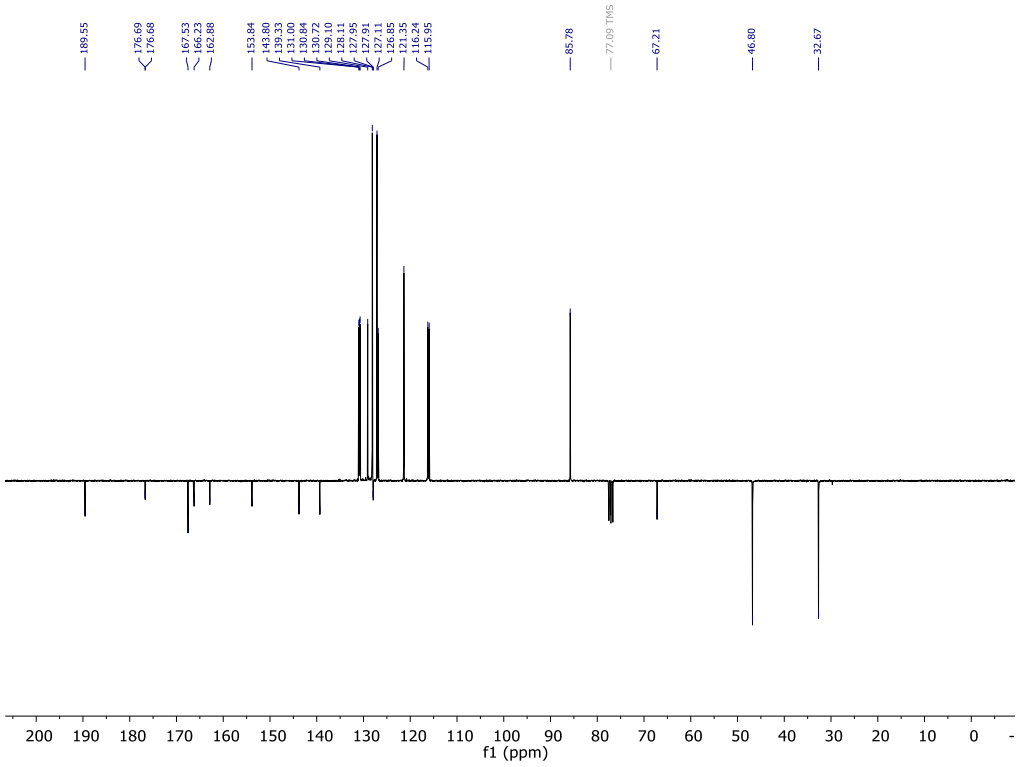
^{1}H NMR spectrum of **25**



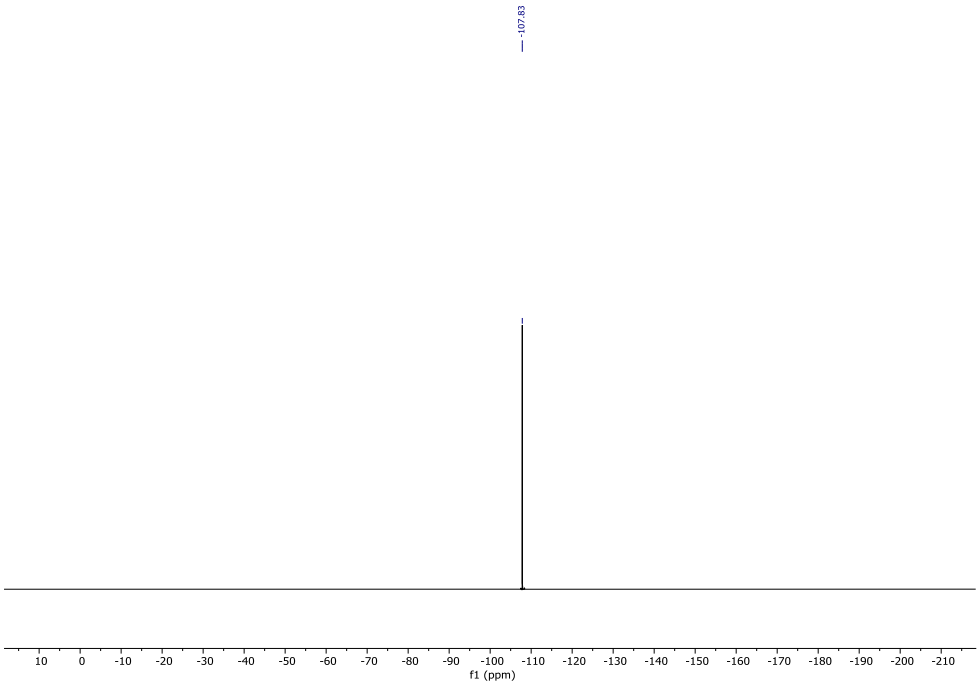
^{13}C APT NMR spectrum of **25**



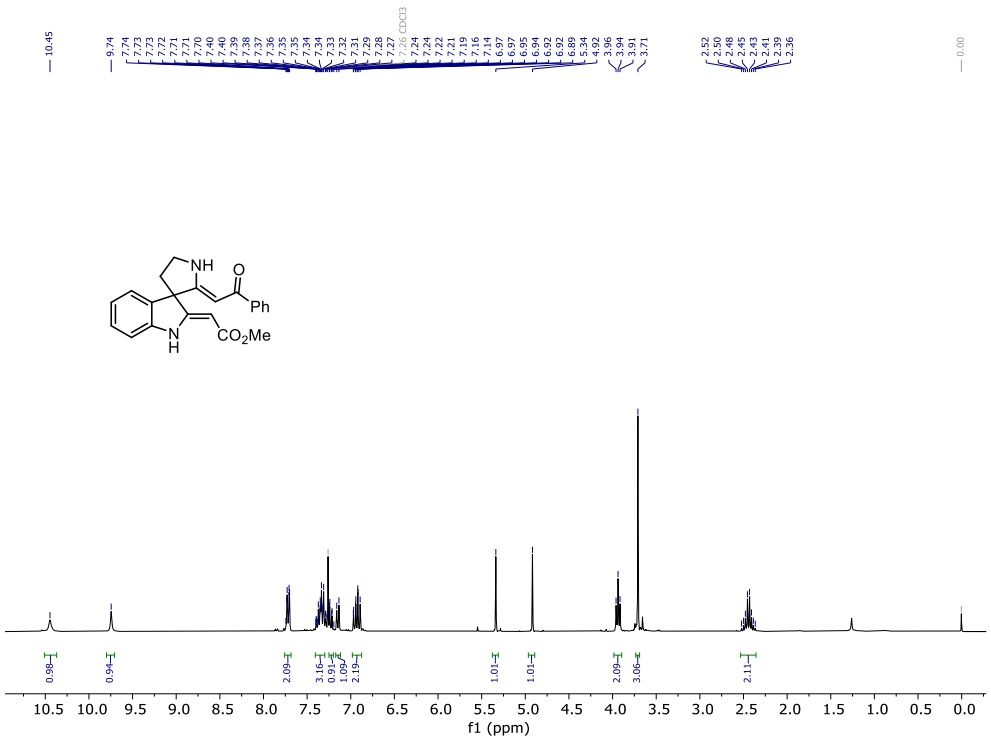
^{1}H NMR spectrum of **26**



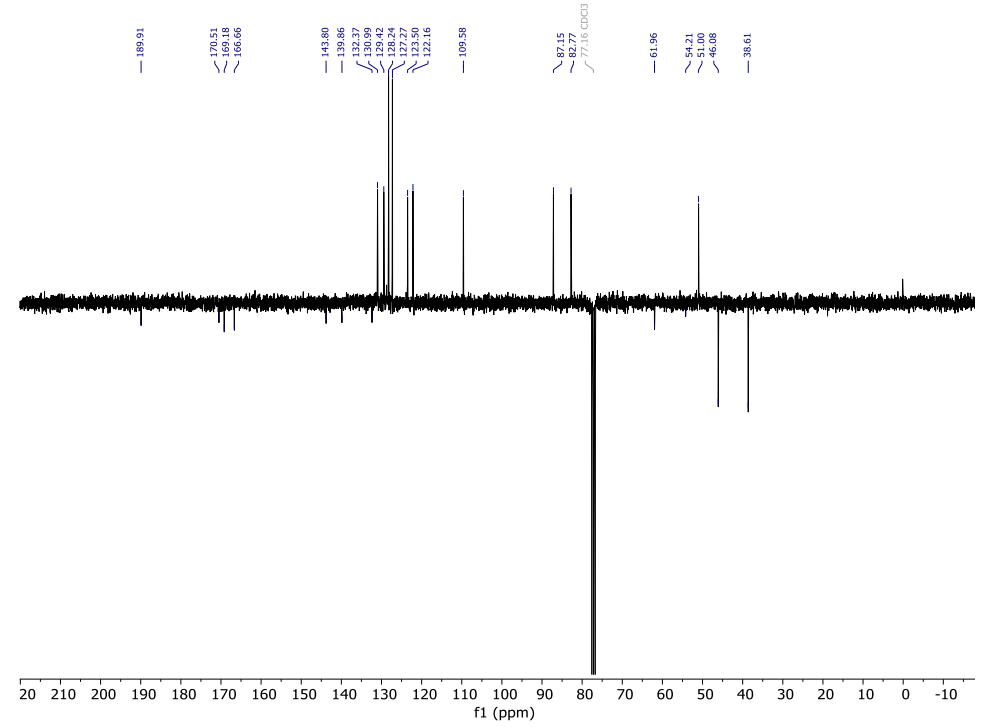
^{13}C APT NMR spectrum of **26**



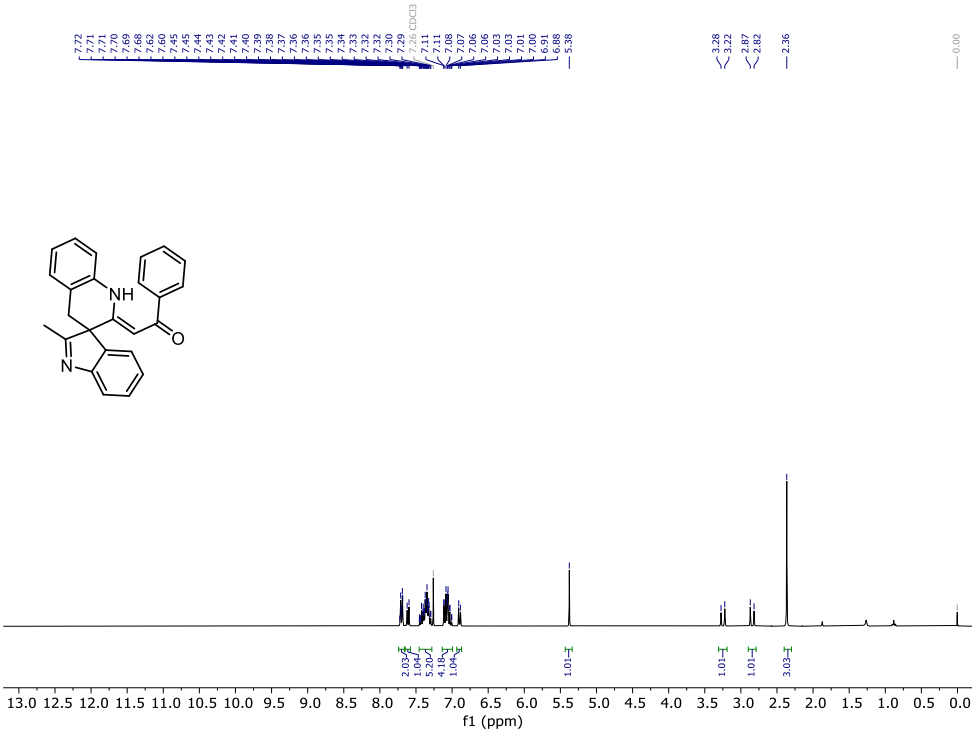
^{19}F NMR spectrum of **26**



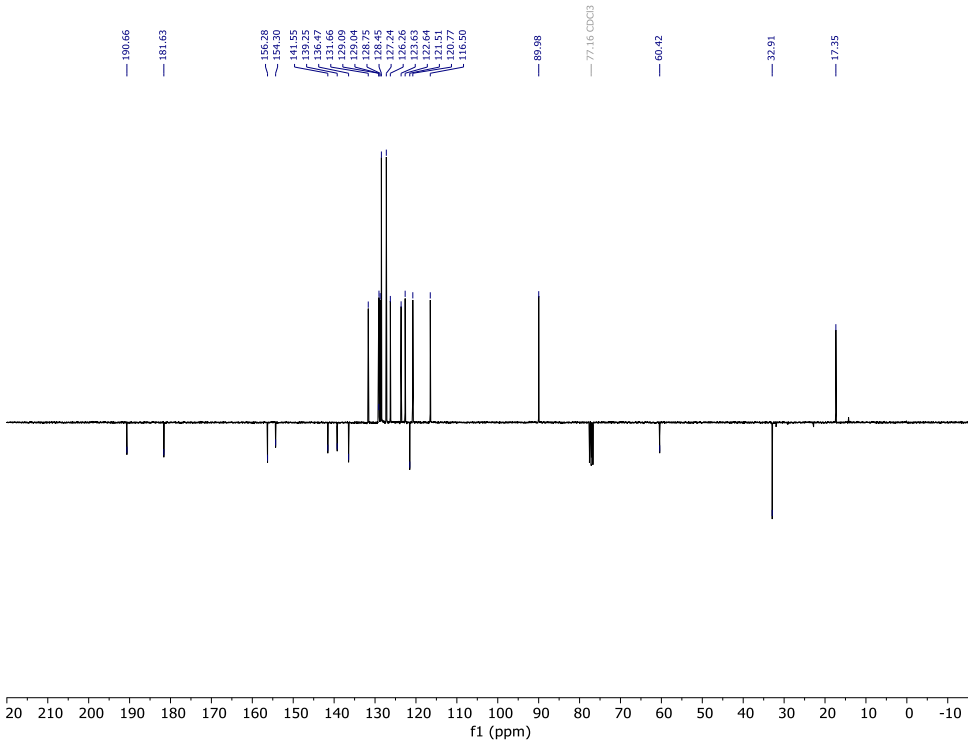
^{1}H NMR spectrum of **27**



^{13}C APT NMR spectrum of **27**



^{1}H NMR spectrum of **28**



^{13}C APT NMR spectrum of **28**

Ground state optimized geometry of **1a** at B3LYP/cc-pVTZ level (*in Å, gas phase*):

```
C  1.07708200 -1.40257600 -0.65927500
C  2.41107900 -1.68590800 -0.42484700
C  0.59063400 -0.12704900 -0.35276900
C  3.27474300 -0.71994400  0.11617500
C  1.47836600  0.82963400  0.19415700
C  2.82049100  0.54966200  0.43442000
H  2.79596900 -2.67077800 -0.65183500
H  4.31158800 -0.97294600  0.29191500
H  0.41680500 -2.16282600 -1.05284600
C -0.69578600  0.50695400 -0.47079600
H  3.48442100  1.29362000  0.85511300
N  0.75207900  1.98080800  0.40132900
C -0.55632300  1.78976600 -0.00103500
C -1.94512600 -0.11812000 -1.00488200
C -2.82550100 -0.79708400  0.05943600
H -1.69505100 -0.85777000 -1.76754500
H -2.56974700  0.63193300 -1.49493100
N -2.19213100 -1.92603500  0.65226200
H -3.76285500 -1.13484700 -0.38663300
H -3.06562600 -0.08813400  0.85282800
C -1.66703200 -2.85732100  1.11673600
H  1.11701500  2.83832800  0.77334200
C -1.54845000  2.89450000  0.11857300
H -2.48937300  2.62399500 -0.35610600
H -1.76177200  3.13210500  1.16430100
H -1.18607800  3.80883200 -0.35810200
```

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