

Supplementary Information

For

Cascade Cyclization for the Synthesis of Indolo[2,1- α]isoquinoline Derivatives via Visible-Light-Induced Halogen-Atom-Transfer (XAT) and Hydrogen-Atom-Transfer (HAT)

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1. Experimental Section

a) General information

¹H NMR (400 MHz), ¹³C NMR (101 MHz) and ¹⁹F NMR (376 MHz) spectra are recorded on a Bruker AV-400 spectrometer in CDCl₃ with TMS as internal standard. For ¹H NMR (400 MHz), CDCl₃ (δ = 7.26 ppm) served as internal standard and data are reported as follows: chemical shift (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet), coupling constant (in Hz), and integration. GC-MS analysis was performed on 7890A-5975C/Agilent. HR-MS spectra were recorded on a Waters Xevo G2QTOF/UPLC mass spectrometer using TOF as the mass analyzer type.

SPECTROPHOTOCOLORMETER ANALYSIS REPORT

Color Parameters:

CIE(1931:) x =0.1776 y =0.0296

CIE(1960:) u =0.2367 v =0.0592

CIE (1976:) u' =0.2367 v' =0.0888

Color Temperature : Tc=25000K Dominant

Wave: WL.D=435.20nm Purity: PUR=93.54

Peak Wave: WL.P=392.5nm Delta Wave:

WL.H=18.0nm

Color Tolerance: SDCM=186.7 Ra:Ra=15.0

CRI1=56.1 CRI2=16.3 CRI3=0.0 CRI4=0.0

CRI5=47.6

CRI6=0.0 CRI7=0.0 CRI8=0.0 CRI9=0.0

CRI10=0.0

CRI11=0.0 CRI12=0.0 CRI13=42.0

CRI14=6.3 CRI15=66.7

Photology Parameters:

Lum Flux: Φ(lm)=4.75lm Optical Power:

Φe(mW)=2769.6mW η(lm/W)=0.4lm/W

Electric Parameters:

Forward Voltage: VF = 22.68 V Forward

Current: IF = 498.9 mA Power = 11.32 W

Status:

Wavelength Range: 380nm---780nm

Intergration Time: 1000 ms³

Test Project : LED COB TESTING

Test Equipment : ZP OPTO

SYSTEM

Product Model: HIGH POWER COB

Manufacturer: LEARNEW OPTO

Temperature: 25 Humidity: 40%

Tester: MESSI LAN Time: 2019-02-20

15:01

Test Mechanism: ZP OPTO LAB

The photoreaction instrument for large-scale reaction was purchased from WATTCAS (WP-TEC1020SL, Figure S1), China.



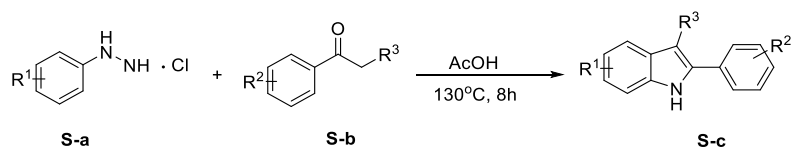
Figure S1. Photoreactor for large-scale reaction

Chemicals were purchased from commercial sources without further purification. Glassware was dried in oven and cooled before use. Solvents were dried and purified according to the procedure from “Purification of Laboratory Chemicals book”. Reactions were monitored by TLC and visualized by UV lamp (254 nm). Yields generally referred to chromatographically isolated yields, unless otherwise noted.

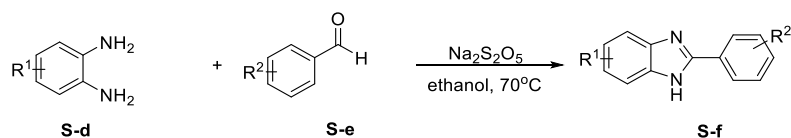
b) Synthesis of starting materials^[1-3]

All the starting materials used in this paper are known compounds. They can be either directly purchased from chemical companies, or easily synthesized through the following procedures.

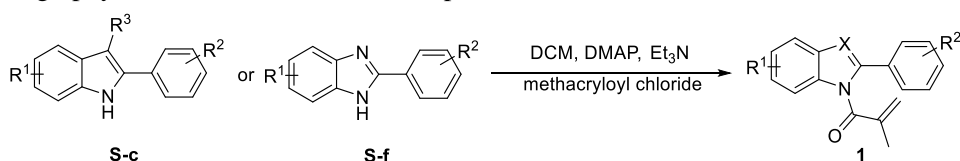
Synthesis of substrate 1:



According to a modified literature procedure¹, a mixture of substituted phenylhydrazine hydrochloride **S-a** (2.0 mmol, 2.0 equiv.) and acetic acid **S-b** was stirred at 50 °C in a 250 mL round-bottomed flask under N₂ atmosphere for 30 minutes, followed by the substituted ketone (1.0 mmol, 1.0 equiv.) was added to a solution was heated to 130 °C for 8 h After completion of the reaction, the reaction mixture was cooled, water was added, and the mixture was allowed to stir in 0 °C to obtain a precipitate. Then, the obtained crude solid indole compounds **S-c** can be directly used in the next synthesis after drying. Sometimes the obtained crude solid should purified by column chromatography to afford indole compound **S-c**.



According to a modified literature procedure², a mixture of substituted o-phenylenediamine **S-d** (1.0 mmol, 1.0 equiv.), Na₂S₂O₅ (1.5 mmol, 1.5 equiv.), and ethanol was stirred at 70 °C in a 250 mL round-bottomed flask under O₂ atmosphere, followed by the substituted benzaldehyde **S-e** (1.0 mmol, 1.0 equiv.) was added to a solution. After completion of the reaction, the reaction mixture was cooled, water was added, and the mixture was allowed to stir in 0 °C to obtain a precipitate. Then, the obtained crude solid benzimidazole compounds **S** can be directly used in the next synthesis after drying. Sometimes the obtained crude solid should purified by column chromatography to afford benzimidazole compounds **S-f**.



According to a modified literature procedure³, to the solution of indole **S-c** / **f** (5 mmol, 1 equiv.) and DMAP:4-dimethylaminopyridine (2.0 mmol, 0.4 equiv.) in DCM was added Et₃N (10 mmol, 2.0 equiv.) at 0 °C. Then, methacryloyl chloride (10 mmol, 2.0 equiv.) was slowly dropped into the solution. The solution was warmed up to room temperature after adding methacryloyl chloride and stirred for 2-3 days. The mixture was diluted with DCM (20 mL) and saturated NH₄Cl solution (20 mL). The organic and aqueous layers were separated. The aqueous layer was extracted with DCM (20 mL x 3 times). The combined organic layer was washed with brine, dried over Na₂SO₄, after evaporation of solvent, the crude product **1** was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent.

c) Optimization studies

As shown in Table S1 to S6, reactions were performed using **1a** (0.1 mmol), 2-iodopropane (0.5 mmol), $i\text{Pr}_2\text{NEt}$ (0.3 mmol), TBHP (0.5 mmol), Na_2CO_3 (0.5 mmol) and Eosin Y (5 mol%) in Acetone (0.1 M) under irradiation of a 10 W, 455nm blue LED strip for 24 h. Isolated yields were indicated.

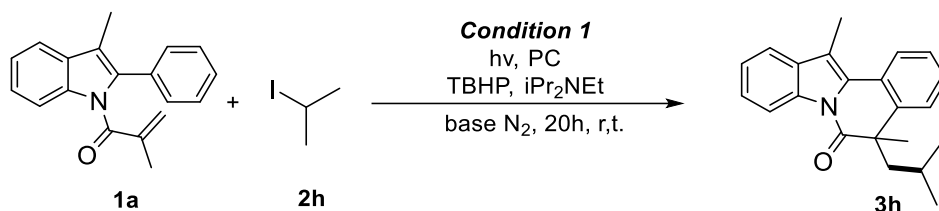


Table S1. Proportion optimization

Entry	1a	2a	TBHP	$i\text{Pr}_2\text{NEt}$	yield
1	1eq	1eq	5eq	3eq	20%
2	1eq	3eq	5eq	3eq	57%
3	1eq	5eq	5eq	3eq	61%
4	1eq	10eq	5eq	3eq	56%
5	1eq	5eq	3eq	3eq	39%
6	1eq	5eq	5eq	2eq	22%
7	1eq	5eq	5eq	2.5eq	28%
9	1eq	5eq	5eq	4eq	19%
10	1eq	5eq	10eq	6eq	60%

Table S2. Light source and reaction atmosphere optimization

Entry	PC	Light source	Atmosphere	Yield
1	Ir[dF(CF ₃)ppy] ₂ (dtbbpy)PF ₆	10W,455nm	N ₂	20%
2	Ru(bpy) ₃ Cl ₂	10W,455nm	N ₂	46%
3	Eosin B	10W,455nm	N ₂	58%
4	Mes-Acr-Me ⁺ ClO ₄ ⁻	10W,455nm	N ₂	32%
5	Eosin Y	10W, 455nm	N₂	61%
6	Eosin Y	5W,455nm	N ₂	45%
7	Eosin Y	1W, 455nm	N ₂	28%
8	Eosin Y	10W,455nm	Air	trace
9	Eosin Y	/	N ₂	0%

Table S3. Base optimization

Entry	PC	Base	Solvent	Yield
1	Eosin Y	Cs ₂ CO ₃	Acetone	trace
2	Eosin Y	Li ₂ CO ₃	Acetone	trace
3	Eosin Y	Na₂CO₃	Acetone	61%
4	Eosin Y	K ₂ CO ₃	Acetone	48%
5	Eosin Y	NaOAc	Acetone	34%
6	Eosin Y	/	Acetone	0%

Table S4. Solvent optimization

Entry	PC	base	Solvent	Yield
1	Eosin Y	Na ₂ CO ₃	MeCN	52%
2	Eosin Y	Na₂CO₃	Acetone	61%
3	Eosin Y	Na ₂ CO ₃	DCM	0%
4	Eosin Y	Na ₂ CO ₃	DMF	0%
5	Eosin Y	Na ₂ CO ₃	DMSO	0%
6	Eosin Y	Na ₂ CO ₃	THF	trace

Table S5. Tertiary amine optimization

Entry	Tertiary amine	base	Solvent	Yield
1	BnNMe ₂	Na ₂ CO ₃	Acetone	0%
2	Et ₃ N	Na ₂ CO ₃	Acetone	51%
3	PhNMe ₂	Na ₂ CO ₃	Acetone	0%
4	PhNEt ₂	Na ₂ CO ₃	Acetone	0%
5	Ph ₂ NMe	Na ₂ CO ₃	Acetone	0%
6	iPr₂NEt	Na₂CO₃	Acetone	61%
7	/	Na ₂ CO ₃	Acetone	0%

Table S6. Peroxide optimization

Entry	Peroxide	base	Solvent	Yield
1	BPO	Na ₂ CO ₃	Acetone	0%
2	DTBP	Na ₂ CO ₃	Acetone	47%
3	TBHP	Na₂CO₃	Acetone	61%
4	TBPB	Na ₂ CO ₃	Acetone	0%
5	/	Na ₂ CO ₃	Acetone	0%

As shown in Table S7, reactions were performed using **1a** (0.1 mmol), 4-MeOC₆H₄N₂BF₄ (0.5 mmol), base (0.5 mmol) Eosin Y (5 mol%) in CH₂Cl₂ (0.1 M) under irradiation of a 10 W, 455nm blue LED strip for 20 h. Isolated yields were indicated.

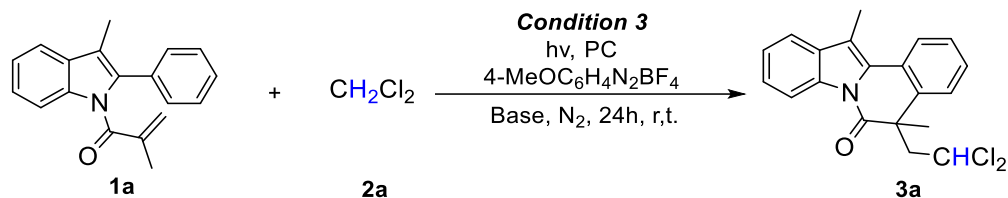
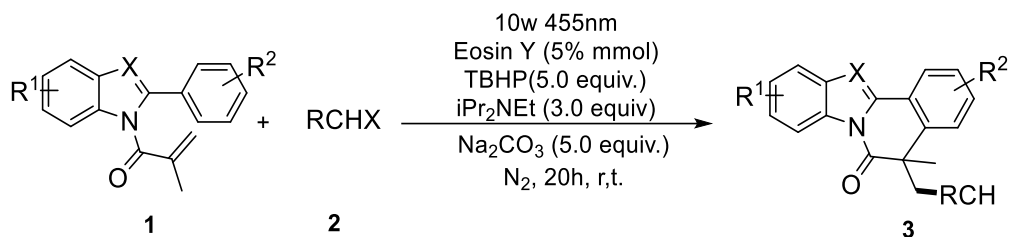


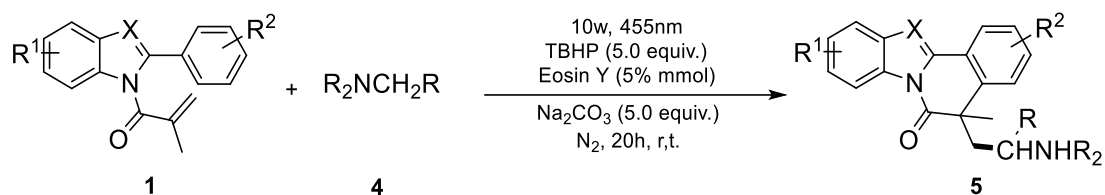
Table S7. Optimization of the HAT Reaction Conditions

Entry	Variation from the optimal reaction conditions	Yield
1	None	73%
2	Ru(bpy) ₃ Cl ₂ instead of Eosin Y	61%
3	Ru(bpz) ₃ Cl ₂ instead of Eosin Y	50%
4	<i>fac</i> -Ir(ppy) ₃ instead of Eosin Y	38%
5	Mes-Acr-Me ⁺ ClO ₄ ⁻ instead of Eosin Y	68%
6	air instead of Ar	trace
7	4-ClC ₆ H ₄ N ₂ BF ₄ instead of 4-MeOC ₆ H ₄ N ₂ BF ₄	63%
8	4-MeC ₆ H ₄ N ₂ BF ₄ instead of 4-MeOC ₆ H ₄ N ₂ BF ₄	68%
9	C ₆ H ₄ N ₂ BF ₄ instead of 4-MeOC ₆ H ₄ N ₂ BF ₄	66%
10	without 4-MeOC ₆ H ₄ N ₂ BF ₄	0%
11	K ₂ CO ₃ instead of Na ₂ CO ₃	68%
12	Li ₂ CO ₃ instead of Na ₂ CO ₃	trace
13	without Na ₂ CO ₃	0%
14	without Eosin Y	46%
15	without light	0%

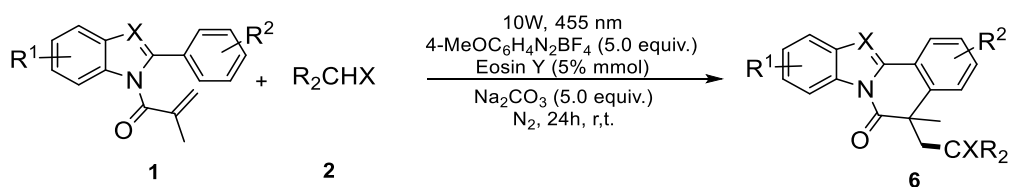
d) General procedure for the synthesis of products



General Procedure 1: To a 20 mL reaction vial (silica tube) were added substrate **1** (0.1 mmol), **2** (0.5 mmol), iPr_2NEt (0.3 mmol), TBHP (0.5 mmol), Acetone (anhydrous, 1.0 mL), Na_2CO_3 (0.5 mmol), Eosin Y (0.005 mmol). The mixture was charged with N_2 three times and then was stirred under a 455 nm (10 W) LED lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature for 20-24h. After the substrate was completed (monitored by TLC), the mixture was filtered and the filtrate concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 50:1) to afford the desired product **3**.



General Procedure 2: To a 20 mL reaction vial (silica tube) were added substrate **1** (0.1 mmol), **4** (0.3 mmol), TBHP (0.5 mmol), Acetone (anhydrous, 1.0 mL), Na_2CO_3 (0.5 mmol), Eosin Y (0.005 mmol). The mixture was charged with N_2 three times and then was stirred under a 455 nm (10 W) LED lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature for 20h. After the substrate was completed (monitored by TLC), the mixture was filtered and the filtrate concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 20:1) to afford the desired product **5**.



General Procedure 3: To a 20 mL reaction vial (silica tube) were added substrate **1** (0.1 mmol), **2** (as solvent, 1.0 ml), 4-MeOC₆H₄N₂BF₄ (0.5 mmol), Na_2CO_3 (0.5 mmol), Eosin Y (0.005 mmol). The mixture was charged with N_2 three times and then was stirred under a 455 nm (10 W) LED

lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature for 24h. After the substrate was completed (monitored by TLC), the mixture was filtered and the filtrate concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 50:1) to afford the desired product **6**.

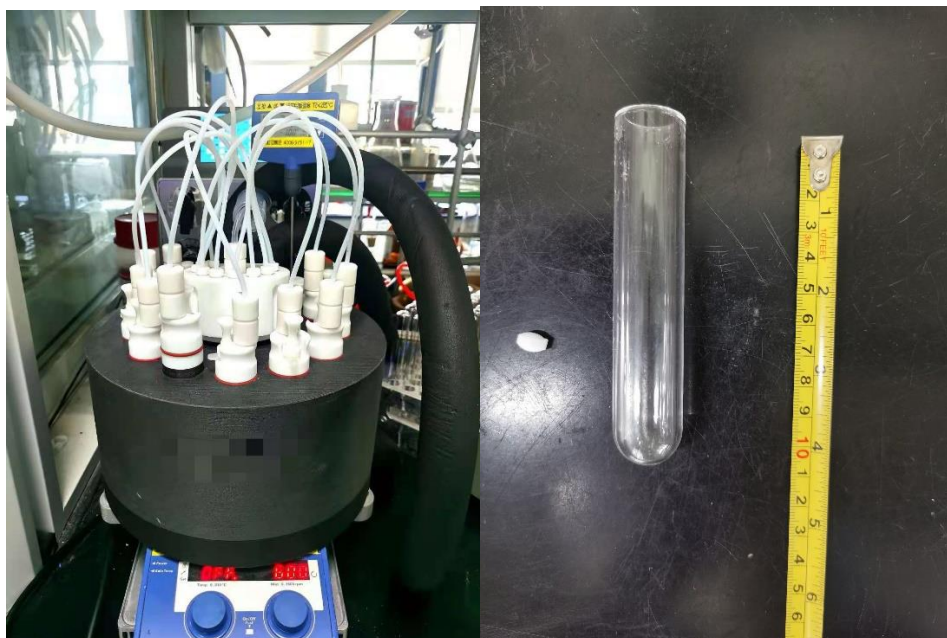
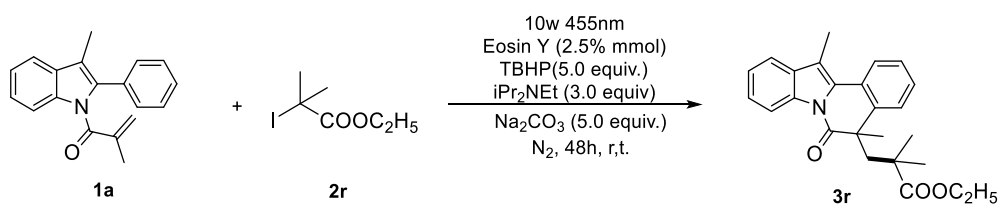


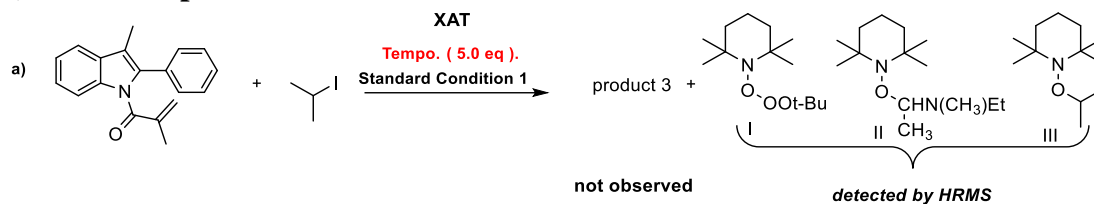
Figure S2. Reaction setup for general photoreaction

e) Procedure for the large-scale experiment

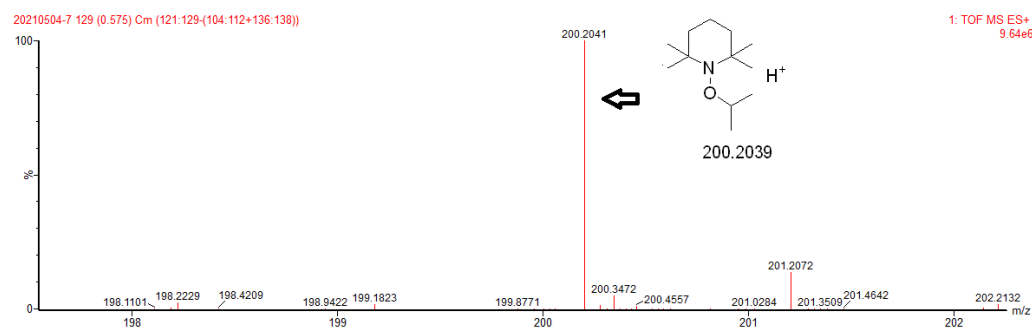
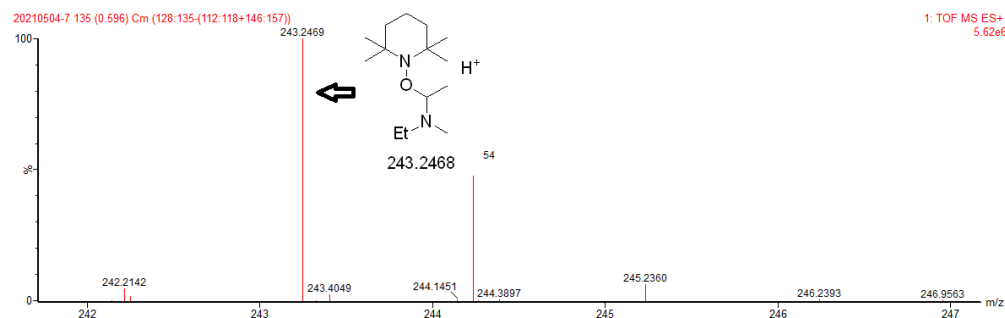
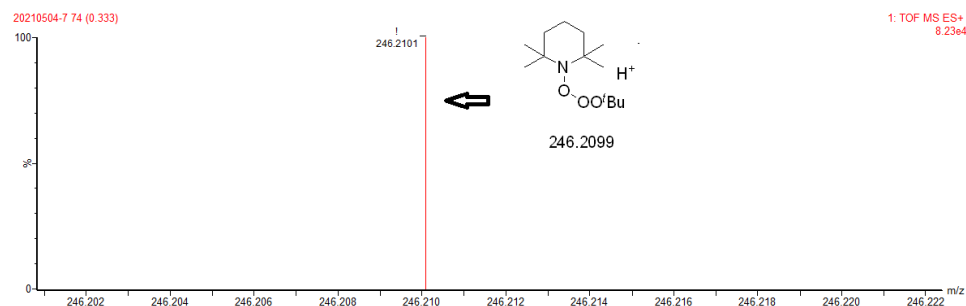


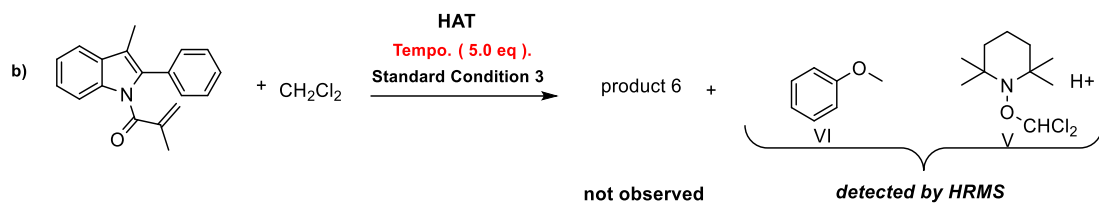
To a 20 mL reaction vial (silica tube) were added substrate **1a** (1.0 mmol), **2r** (5.0 mmol), $i\text{Pr}_2\text{NEt}$ (3.0 mmol), TBHP (5.0 mmol), Acetone (anhydrous, 8.0 mL), Na_2CO_3 (5.0 mmol), Eosin Y (0.025 mmol). The mixture was charged with N_2 three times and then was stirred under a 455 nm (10 W) LED lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature for 48 h. After the substrate was completed (monitored by TLC), the mixture was filtered and the filtrate concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 50:1) to afford the desired product **3r** as a white solid (331 mg, 85% yield).

f) Control experiments

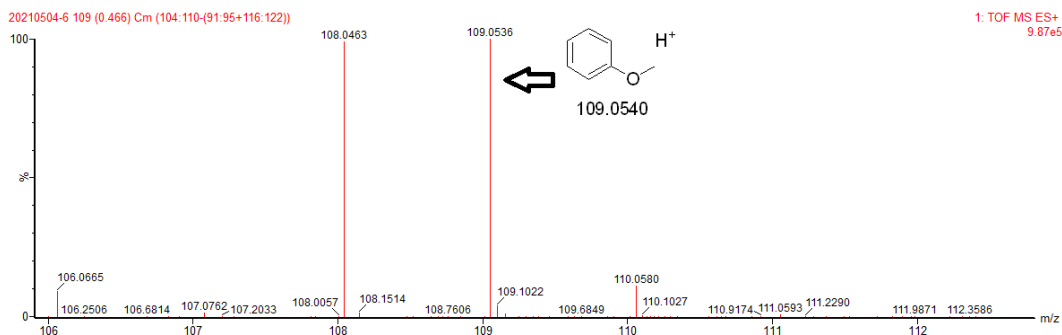


To a 50 mL reaction vial (silica tube) were added substrate **1** (0.1 mmol), **2** (0.5 mmol), $i\text{Pr}_2\text{NEt}$ (0.3 mmol), TBHP (0.5 mmol), Acetone (anhydrous, 1.0 mL), Na_2CO_3 (0.5 mmol), Eosin Y (0.005 mmol), TEMPO (0.5 mmol). The mixture was charged with N_2 three times and then was stirred under a 455 nm (10 W) LED lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature. After reaction for 24h, the mixture was diluted with EtOAc and filtered through an inch of silica gel. Then the filtrate was used for HRMS analysis.





To a 50 mL reaction vial (silica tube) were added substrate **1** (0.1 mmol), CH2Cl2 (as solvent, 1.0 ml), 4-MeOC₆H₄N₂BF₄ (0.5 mmol), Na₂CO₃ (0.5 mmol), Eosin Y (0.005 mmol), TEMPO (0.5 mmol). The mixture was charged with N₂ three times and then was stirred under a 455 nm (10 W) LED lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature. After reaction for 24h, the mixture was diluted with EtOAc and filtered through an inch of silica gel. Then the filtrate was used for HRMS analysis.



g) Kinetic isotope effect (KIE) experiment

XAT System

To a 50 mL reaction vial (silica tube) were added substrate **1** (0.1 mmol), $\text{CHCl}_3:\text{CDCl}_3$ (0.5 ml: 0.5 ml), iPr_2NEt (0.3 mmol), TBHP (0.5 mmol), Na_2CO_3 (0.5 mmol), Eosin Y (0.005 mmol). The mixture was charged with N_2 ten times and then was stirred under a 455 nm (10 W) LED lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature for 20h. After the substrate was consumed (monitored by TLC), the mixture was filtered and the filtrate concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 50/1) to afford the corresponding products **1a** and **1a'**. The products were under ^1H -NMR analysis (Figure S3.).

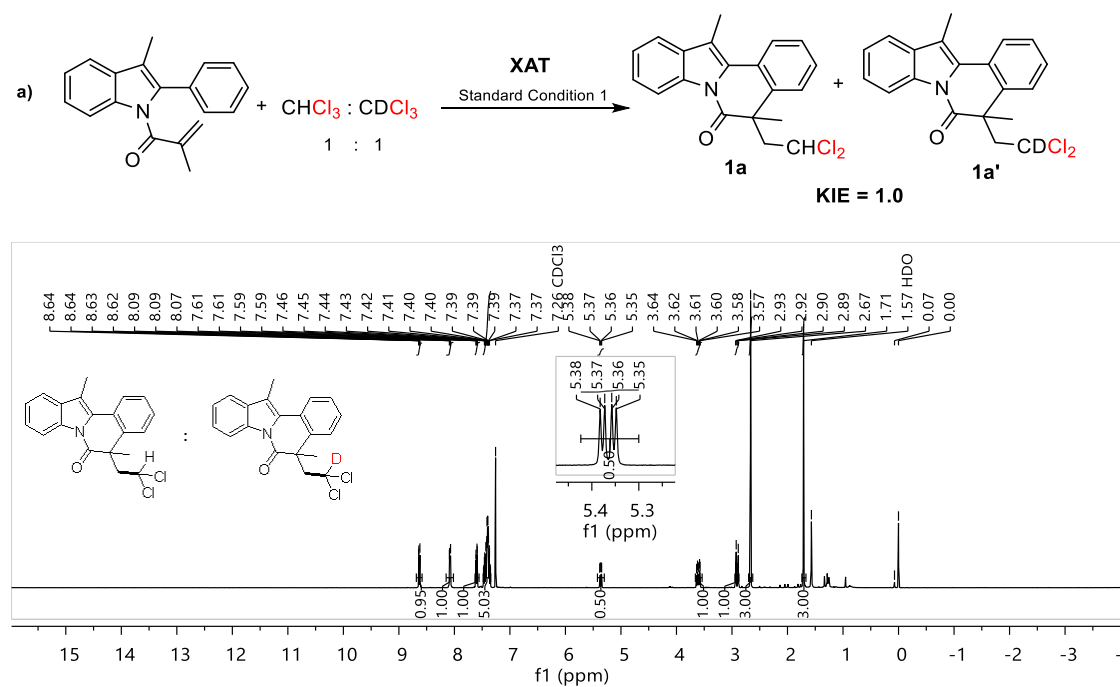


Figure S3. ^1H -NMR Spectra for KIE experiment in XAT system

HAT System

To a 50 mL reaction vial (silica tube) were added substrate **1** (0.1 mmol), CH₂Cl₂:CD₂Cl₂ (as solvent, 0.5 ml: 0.5 ml), 4-MeOC₆H₄N₂BF₄ (0.5 mmol), Na₂CO₃ (0.5 mmol), Eosin Y (0.005 mmol). The mixture was charged with N₂ ten times and then was stirred under a 455 nm (10 W) LED lamp (WATTCAS: WP-TEC-1020SL, as shown in Figure S2) at room temperature for 24h. After the substrate was consumed (monitored by TLC), the mixture was filtered and the filtrate concentrated in vacuo. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 50/1) to afford the corresponding products **1a** and **1a'**. The products were under ¹H-NMR analysis (Figure S4.).

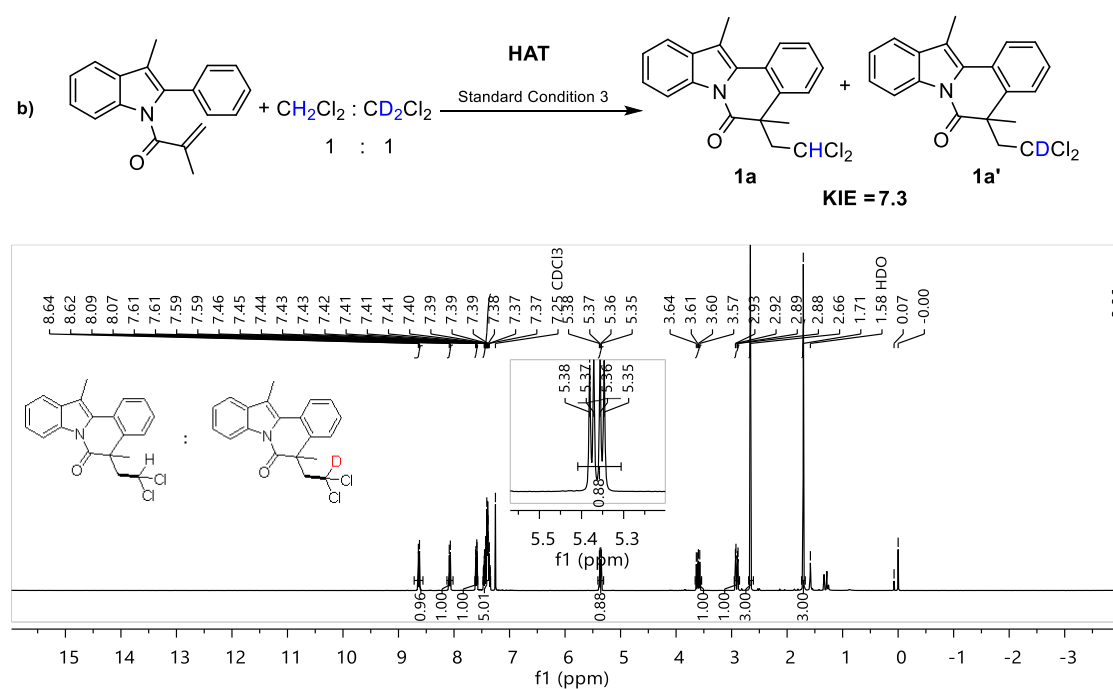


Figure S4. ¹H-NMR Spectra for KIE experiment in HAT system

h) Other plausible reaction mechanisms

On the basis of the reported literatures^[4], $t\text{-BuO}\cdot$ could self-decompose to give $\text{Me}\cdot$ and acetone. $\text{Me}\cdot$ has the ability to abstract halogen to form alkyl radicals. Hence, we suggest another possible reaction mechanism. As shown in Figure S5, in the XAT reaction system, excited Eosin Y promotes the decomposition of TBHP via single-electron-transfer (SET) process to form the $t\text{BuO}\cdot$ radical. Then $t\text{BuO}\cdot$ radicals continue to self-decompose to give acetone and $\text{Me}\cdot$ (**B'**). As an important intermediate, $\text{Me}\cdot$ (**B'**) could abstract halogen from alkyl halides through halogen-atom-transfer (XAT) process, generating the alkyl radical **C**. And the alkyl radical **C** undergoes radical-addition-cyclization cascade to release the final indolo[2,1- α]isoquinoline products **3**.

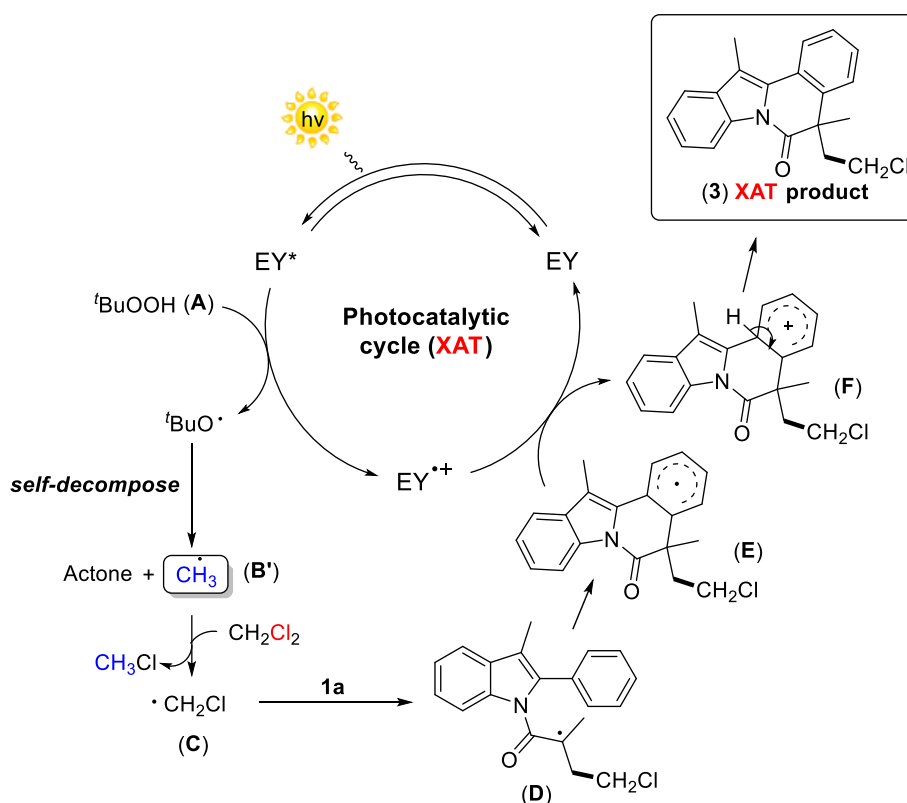
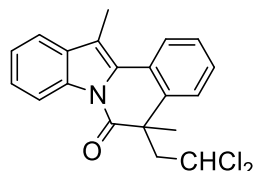


Figure S5. Other plausible reaction mechanisms

i) Reference

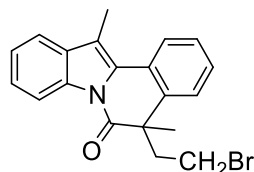
- (1) Fang, X.-X.; Gao, S.; Wu, Z.-J.; Yao, H.-Q.; Lin, A.-J. *Org. Chem. Front.* 2017, 4, 292.
- (2) Kamal, A.; Reddy, M. Kashi.; Shaik, T. B.; Rajender.; Srikanth, Y. V. V.; Reddy, V. Santhosh.; Kumar, G. Bharath.; Kalivendi, S. V. *Eur. J. Med. Chem.* 2012, 50, 9.
- (3) Stuart, D. R.; Villemure, E.; Fagnou, K. J. *Am. Chem. Soc.* 2007, 129, 12072.
- (4) Xiong, H.; Li, Y.; Qian, B.; Wei, R.; Eycken, E. V.; Bao, H. *Org. Lett.* 2019, 21, 776.

2. Characterization Data of Products



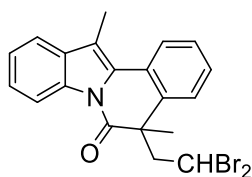
5-(2,2-dichloroethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3a):

White solid, 80% isolated yield, 28.6 mg. mp: 112.9-114.6 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.77 – 8.62 (m, 1H), 8.18 – 8.07 (m, 1H), 7.67 – 7.62 (m, 1H), 7.53 – 7.39 (m, 5H), 5.42 (dd, *J* = 9.8, 3.9 Hz, 1H), 3.65 (dd, *J* = 14.8, 9.9 Hz, 1H), 2.96 (dd, *J* = 14.8, 3.9 Hz, 1H), 2.71 (s, 3H), 1.76 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.4, 135.7, 134.2, 132.3, 129.1, 128.0, 127.7, 126.7, 126.4, 125.9, 125.4, 124.4, 118.4, 116.9, 114.9, 70.0, 53.0, 47.1, 31.3, 11.6. GC-MS(ED): 357.0, 271.1, 260.1, 245.1, 232.1, 217.1, 202.1, 130.1, 120.6, 108.5, 97.0, 88.0, 77.0, 61.0, 51.0. HRMS (ESI, *m/z*): calcd for C₂₀H₁₇Cl₂NO [M+H]⁺ 358.0765, found 358.0763.



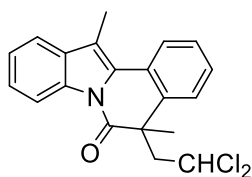
5-(2-bromoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3b):

Light yellow oil, 31% isolated yield, 11.4 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 6.9 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.47 – 7.34 (m, 5H), 3.23 – 2.79 (m, 3H), 2.65 (s, 3H), 2.59 – 2.40 (m, 1H), 1.70 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.5, 136.9, 134.1, 132.4, 129.3, 128.2, 127.5, 126.5, 126.1, 125.9, 125.2, 124.4, 118.4, 116.6, 114.8, 48.8, 44.9, 28.9, 27.4, 11.5. GC-MS(ED): 367.1, 260.1, 245.1, 230.1, 217.1, 202.1, 189.0, 130.1, 120.6, 108.6, 95.6, 87.0, 77.1, 63.1, 51.1. HRMS (ESI, *m/z*): calcd for C₂₀H₁₈BrNO [M+H]⁺ 368.0645, found 368.0643.



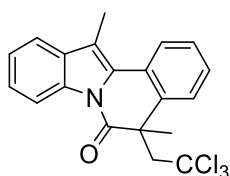
5-(2,2-dibromoethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3c):

Light yellow oil, 48% isolated yield, 21.5 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.64 (d, $J = 7.2$ Hz, 1H), 8.08 (d, $J = 7.8$ Hz, 1H), 7.60 (d, $J = 7.4$ Hz, 1H), 7.49 – 7.34 (m, 5H), 5.28 (dd, $J = 10.4, 3.9$ Hz, 1H), 3.84 (dd, $J = 15.1, 10.4$ Hz, 1H), 3.17 (dd, $J = 15.1, 3.9$ Hz, 1H), 2.66 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.3, 135.3, 134.3, 132.4, 129.2, 128.0, 127.7, 126.9, 126.4, 125.9, 125.5, 124.4, 118.4, 116.9, 114.9, 54.3, 48.5, 40.4, 31.6, 11.6. GC-MS(EI): 447.1, 303.1, 287.1, 275.1, 260.1, 245.1, 232.1, 217.1, 207.1, 189.1, 176.1, 163.0, 151.1, 130.5, 108.6, 88.0, 77.1, 63.1, 51.1. HRMS (ESI, m/z): calcd for $\text{C}_{20}\text{H}_{17}\text{Br}_2\text{NO}$ $[\text{M}+\text{H}]^+$ 445.9750, found 445.9753.



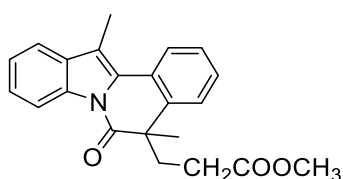
5-(2,2-dichloroethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3d):

White solid, 63% isolated yield, 22.5 mg. mp: 112.9–114.6 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.77 – 8.62 (m, 1H), 8.18 – 8.07 (m, 1H), 7.67 – 7.62 (m, 1H), 7.53 – 7.39 (m, 5H), 5.42 (dd, $J = 9.8, 3.9$ Hz, 1H), 3.65 (dd, $J = 14.8, 9.9$ Hz, 1H), 2.96 (dd, $J = 14.8, 3.9$ Hz, 1H), 2.71 (s, 3H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.4, 135.7, 134.2, 132.3, 129.1, 128.0, 127.7, 126.7, 126.4, 125.9, 125.4, 124.4, 118.4, 116.9, 114.9, 70.0, 53.0, 47.1, 31.3, 11.6. GC-MS(EI): 357.0, 271.1, 260.1, 245.1, 232.1, 217.1, 202.1, 130.1, 120.6, 108.5, 97.0, 88.0, 77.0, 61.0, 51.0. HRMS (ESI, m/z): calcd for $\text{C}_{20}\text{H}_{17}\text{Cl}_2\text{NO}$ $[\text{M}+\text{H}]^+$ 358.0765, found 358.0763.



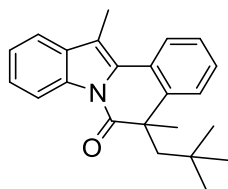
5,12-dimethyl-5-(2,2,2-trichloroethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3e):

White solid, 85% isolated yield, 33.2 mg. mp: 178.4-180.2 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.71 – 8.51 (m, 1H), 8.14 – 7.94 (m, 1H), 7.65 – 7.56 (m, 1H), 7.52 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.45 – 7.31 (m, 4H), 4.09 (d, *J* = 15.2 Hz, 1H), 3.45 (d, *J* = 15.2 Hz, 1H), 2.67 (s, 3H), 1.81 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.8, 134.6, 134.3, 132.5, 129.5, 128.4, 127.7, 127.2, 126.9, 125.8, 125.1, 124.4, 118.4, 116.9, 114.8, 96.1, 63.4, 47.7, 31.6, 11.6. GC-MS(ED): 391.0, 294.1, 279.0, 266.1, 251.0, 230.1, 216.1, 202.1, 189.1, 147.3, 114.1, 102.0, 88.0, 77.0, 61.0, 51.0. HRMS (ESI, *m/z*): calcd for C₂₀H₁₆Cl₃NO [M+H]⁺ 392.0376, found 392.0382.



methyl 3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)propanoate (3f):

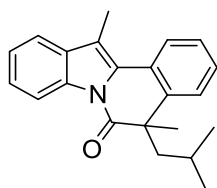
Light yellow oil, 67% isolated yield, 23.2 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, *J* = 7.0 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 7.1 Hz, 1H), 7.51 – 7.32 (m, 5H), 3.50 (s, 3H), 2.66 (s, 4H), 2.34 – 2.25 (m, 1H), 2.09 (m, *J* = 16.6, 11.4, 5.4 Hz, 1H), 1.94 (m, *J* = 16.2, 11.4, 4.9 Hz, 1H), 1.71 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 173.0, 172.2, 137.6, 134.1, 132.4, 132.3, 128.1, 127.3, 126.7, 126.3, 125.8, 125.1, 124.3, 118.4, 116.6, 114.5, 51.5, 47.8, 37.0, 30.0, 28.6, 11.5. GC-MS(ED): 347.2, 332.1, 316.2, 300.1, 290.1, 281.1, 272.1, 260.1, 245.1, 232.1, 217.1, 202.1, 189.1, 176.1, 165.1, 152.1, 136.5, 120.6, 108.6, 95.6, 87.1, 77.1, 68.1, 59.1, 50.1. HRMS (ESI, *m/z*): calcd for C₂₂H₂₁NO₃ [M+H]⁺ 348.1594, found 348.1590.



5,12-dimethyl-5-neopentylindolo[2,1-a]isoquinolin-6(5H)-one (3g):

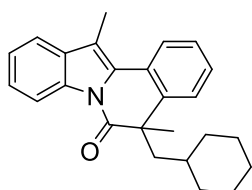
Colorless oil, 68% isolated yield, 22.5 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.73 – 8.64 (m, 1H), 8.08 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.51 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.42 (tdd, *J* = 6.8, 3.1, 1.7 Hz, 3H), 7.38 – 7.34 (m, 1H), 2.72 (s, 3H), 2.63 (d, *J* = 14.2 Hz, 1H), 2.10 (d, *J* =

14.2 Hz, 1H), 1.72 (s, 3H), 0.57 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 139.1, 134.2, 132.4, 129.7, 128.0, 127.2, 126.8, 126.0, 125.5, 124.8, 124.1, 118.2, 117.0, 114.0, 55.7, 46.7, 33.1, 31.9, 30.7, 11.6. GC-MS(EI): 331.2, 260.1, 245.1, 232.2, 217.1, 207.1, 189.1, 177.0, 165.0, 152.1, 139.1, 128.0, 108.6, 95.8, 87.0, 77.0, 65.1, 57.1. HRMS (ESI, m/z): calcd for C₂₃H₂₅NO [M+H]⁺ 332.2009, found 332.2013.



5-isobutyl-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3h):

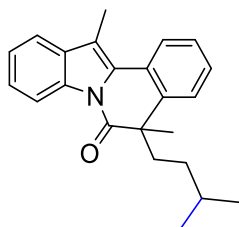
Light yellow oil, 61% isolated yield, 19.3 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.74 – 8.62 (m, 1H), 8.10 – 8.06 (m, 1H), 7.66 – 7.59 (m, 1H), 7.50 – 7.37 (m, 5H), 2.71 (s, 3H), 2.45 (dd, *J* = 14.0, 8.2 Hz, 1H), 2.02 (dd, *J* = 14.0, 5.1 Hz, 1H), 1.70 (s, 3H), 1.40 – 1.32 (m, 1H), 0.67 (d, *J* = 6.7 Hz, 3H), 0.62 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 139.0, 134.2, 132.4, 129.8, 127.6, 127.0, 126.8, 126.3, 125.6, 124.9, 124.1, 118.2, 116.9, 113.9, 50.9, 47.6, 31.1, 25.5, 24.0, 22.4, 11.5. GC-MS(EI): 317.3, 302.1, 286.1, 274.1, 260.1, 245.2, 232.2, 217.2, 202.1, 189.1, 176.1, 152.1, 139.1, 128.1, 120.6, 108.6, 101.1, 89.1, 77.1, 65.1, 57.1. HRMS (ESI, m/z): calcd for C₂₂H₂₃NO [M+H]⁺ 318.1852, found 318.1856.



5-(cyclohexylmethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3i):

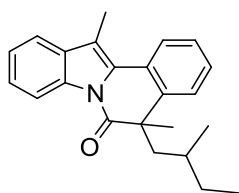
Light yellow oil, 67% isolated yield, 24.0 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.67 (dd, *J* = 7.1, 1.7 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.47 – 7.39 (m, 5H), 2.71 (s, 3H), 2.46 (dd, *J* = 14.1, 7.9 Hz, 1H), 1.99 (dd, *J* = 14.1, 5.0 Hz, 1H), 1.66 (s, 3H), 1.50 (dd, *J* = 9.1, 5.2 Hz, 1H), 1.30 – 0.76 (m, 10H). ¹³C NMR (101 MHz, CDCl₃) δ 173.4, 139.0, 134.2, 132.4, 129.8, 129.6, 127.6, 126.9, 126.8, 125.5, 125.0, 124.0, 118.2, 116.8, 113.8, 49.0, 47.4, 34.8, 34.3, 32.9, 31.3, 26.1, 26.0, 26.0, 11.5. GC-MS(EI): 357.2, 342.2, 327.1, 314.2, 298.1, 281.1, 261.1, 253.1,

245.1, 232.2, 217.1, 207.1, 197.1, 189.1, 176.1, 165.0, 152.0, 139.1, 128.0, 115.1, 106.8, 97.1, 89.0, 77.1, 67.1, 55.1. HRMS (ESI, m/z): calcd for C₂₅H₂₇NO [M+H]⁺358.2165, found 358.2163..



5-isopentyl-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3j):

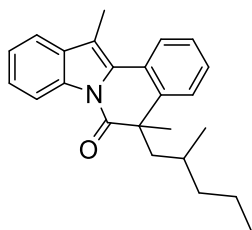
Light yellow oil, 40% isolated yield, 13.2 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.69 – 8.47 (m, 1H), 7.89 (dd, *J* = 8.6, 2.8 Hz, 1H), 7.62 – 7.58 (m, 1H), 7.56 – 7.46 (m, 2H), 7.38 (dddd, *J* = 10.1, 8.7, 7.1, 5.6 Hz, 2H), 2.63 (d, *J* = 2.9 Hz, 3H), 2.44 – 2.37 (m, 1H), 1.92 (ddd, *J* = 14.2, 5.4, 2.9 Hz, 1H), 1.64 (d, *J* = 2.9 Hz, 3H), 1.47 – 1.27 (m, 2H), 1.06 – 0.77 (m, 1H), 0.66 (dd, *J* = 6.8, 2.8 Hz, 3H), 0.57 (dd, *J* = 6.7, 2.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 172.5, 141.1, 134.2, 132.2, 130.1, 130.0, 128.9, 126.3, 125.9, 125.3, 124.3, 121.6, 118.4, 116.9, 114.6, 50.8, 47.6, 31.0, 25.5, 24.0, 22.4, 11.6. GC-MS(EI): 331.2, 260.1, 245.1, 232.2, 217.1, 202.1, 189.1, 176.1, 165.1, 152.1, 142.1, 128.1, 120.5, 108.6, 101.1, 89.0, 77.1, 63.0. HRMS (ESI, m/z): calcd for C₂₃H₂₅NO [M+H]⁺ 332.2009, found 332.2010.



5,12-dimethyl-5-((S)-2-methylbutyl)indolo[2,1-a]isoquinolin-6(5H)-one (3k):

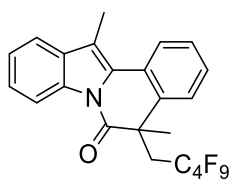
Light yellow oil, 62% isolated yield, 20.6 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.66 (ddd, *J* = 7.7, 3.9, 1.9 Hz, 1H), 8.11 – 8.03 (m, 1H), 7.67 – 7.61 (m, 1H), 7.49 – 7.37 (m, 5H), 2.70 (d, *J* = 1.3 Hz, 3H), 2.49 – 2.44 (m, 1H), 1.87 (dd, *J* = 13.9, 6.4 Hz, 1H), 1.71 (s, 2H), 1.70 (s, 1H), 1.20 – 1.06 (m, 2H), 0.93 (ddd, *J* = 19.8, 7.1, 5.7 Hz, 1H), 0.72 (t, *J* = 7.0 Hz, 1H), 0.64 (t, *J* = 7.3 Hz, 2H), 0.52 (dd, *J* = 9.5, 6.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 173.5, 173.2, 139.3, 138.8, 134.2, 134.1, 132.4, 132.4, 129.9, 129.8, 127.6, 127.6, 127.0, 127.0, 126.8, 126.8, 126.4, 126.3, 125.5, 125.5, 124.9, 124.9, 124.1, 124.0, 118.2, 118.2, 116.8, 116.8, 113.9, 113.9, 49.8, 48.5, 47.8,

47.4, 31.7, 31.6, 31.0, 30.6, 29.9, 29.6, 20.2, 19.0, 11.5, 11.5, 11.1, 10.8. GC-MS(EI): 331.2, 260.1, 245.1, 232.2, 217.1, 202.1, 189.1, 176.1, 165.1, 152.1, 142.1, 128.1, 120.5, 108.6, 101.1, 89.0, 77.1, 63.0. HRMS (ESI, m/z): calcd for C₂₃H₂₅NO [M+H]⁺ 332.2009, found 332.2011.



5,12-dimethyl-5-((S)-2-methylpentyl)indolo[2,1-a]isoquinolin-6(5H)-one (3l):

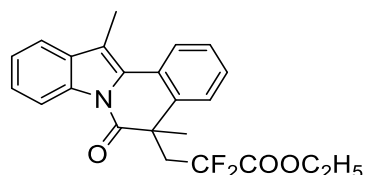
Light yellow oil, 59% isolated yield, 20.4 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.61 (dd, *J* = 8.3, 1.4 Hz, 1H), 8.11 – 7.92 (m, 1H), 7.62 – 7.57 (m, 1H), 7.46 – 7.42 (m, 1H), 7.40 – 7.32 (m, 4H), 2.66 (s, 3H), 2.34 – 2.25 (m, 1H), 1.86 (ddd, *J* = 13.4, 11.3, 4.7 Hz, 1H), 1.67 (s, 3H), 1.34 (q, *J* = 6.7 Hz, 1H), 1.00 (dq, *J* = 7.1, 4.2, 2.4 Hz, 2H), 0.92 – 0.84 (m, 2H), 0.68 (t, *J* = 7.0 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 173.2, 139.0, 134.1, 132.4, 129.9, 127.8, 126.8, 126.6, 126.3, 125.6, 124.9, 124.0, 118.2, 116.6, 113.9, 48.6, 43.0, 38.8, 28.5, 27.4, 22.8, 22.5, 22.4, 11.5. GC-MS(EI): 345.3, 260.1, 245.1, 232.1, 217.1, 207.1, 189.1, 176.1, 165.1, 152.1, 128.1, 119.1, 108.6, 95.9, 77.1, 65.1, 55.1. HRMS (ESI, m/z): calcd for C₂₄H₂₇NO [M+H]⁺ 346.2165, found 346.2169.



5,12-dimethyl-5-((5,5,5,5,5,5,5,5-nonafluoro-5H12-penta-2,4-diyne-1-yl)indolo[2,1-a]isoquinolin-6(5H)-one (3m):

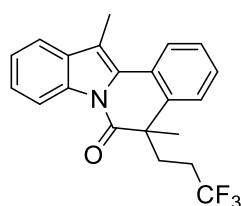
Light yellow oil, 88% isolated yield, 43.5 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.62 (dd, *J* = 7.0, 1.6 Hz, 1H), 8.07 (d, *J* = 7.9 Hz, 1H), 7.60 (dd, *J* = 7.0, 1.7 Hz, 1H), 7.47 – 7.34 (m, 5H), 3.54 (dd, *J* = 33.7, 15.4 Hz, 1H), 2.82 (ddd, *J* = 27.9, 15.5, 8.6 Hz, 1H), 2.66 (s, 3H), 1.74 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.7, 135.7, 134.3, 132.5, 129.2, 127.6, 127.5, 126.96 (d, *J* = 2.3 Hz), 125.9, 125.8, 125.2, 124.4, 118.4, 116.9, 115.0, 44.33 (d, *J* = 2.4 Hz), 39.91 (t, *J* = 19.3 Hz), 31.9, 11.6. ¹⁹F NMR (376 MHz, CDCl₃) δ -81.07 (t, *J* = 10.0 Hz), -107.39 – -108.40 (m), -112.63 (m, *J* =

273.8, 25.8, 12.0 Hz), -124.69 (t, $J = 11.7$ Hz), -125.56 – -126.17 (m). GC-MS(EI): 493.1, 474.1, 458.0, 281.1, 260.1, 245.1, 232.1, 217.1, 207.0, 189.1, 130.1, 108.6, 95.7, 78.1, 69.0, 51.0. HRMS (ESI, m/z): calcd for $C_{23}H_{16}F_9NO$ $[M+H]^+$ 494.1161, found 494.1157..



ethyl 3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)-2,2-difluoropropanoate (3n):

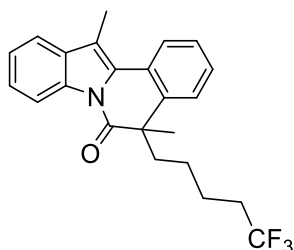
Light yellow oil, 86% isolated yield, 34.2 mg. 1H NMR (400 MHz, $CDCl_3$) δ 8.67 – 8.54 (m, 1H), 8.10 – 8.01 (m, 1H), 7.65 – 7.56 (m, 1H), 7.46 – 7.31 (m, 5H), 3.91 (qq, $J = 7.1, 3.6$ Hz, 2H), 3.40 (q, $J = 14.7$ Hz, 1H), 2.96 (ddd, $J = 19.7, 15.1, 12.5$ Hz, 1H), 2.66 (s, 3H), 1.72 (s, 3H), 1.13 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 135.7, 134.3, 132.4, 129.3, 127.5, 127.3, 127.2, 126.2, 125.8, 125.1, 124.3, 118.4, 116.8, 114.8, 62.9, 44.6, 44.3, 44.1, 31.4, 13.6, 11.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.55 (t, $J = 13.4$ Hz), -103.35 (dd, $J = 20.7, 13.3$ Hz), -103.95 – -104.26 (m). GC-MS(EI): 397.2, 362.2, 352.1, 341.0, 326.9, 316.0, 308.0, 289.0, 281.1, 269.0, 260.0, 245.1, 232.1, 217.1, 207.0, 191.0, 177.0, 163.0, 147.0, 133.0, 118.9, 108.6, 96.0, 88.0, 73.1, 61.1, 51.0. HRMS (ESI, m/z): calcd for $C_{23}H_{21}F_2NO_3$ $[M+H]^+$ 398.1562, found 398.1568.



5,12-dimethyl-5-(3,3,3-trifluoropropyl)indolo[2,1-a]isoquinolin-6(5H)-one (3o):

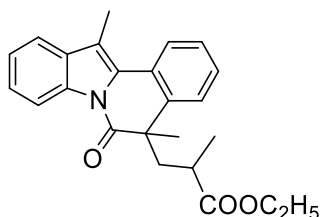
Light yellow oil. 84% isolated yield, 30 mg. 1H NMR (400 MHz, $CDCl_3$) δ 8.62 – 8.55 (m, 1H), 8.03 (dd, $J = 8.0, 1.9$ Hz, 1H), 7.60 (dd, $J = 7.6, 1.4$ Hz, 1H), 7.47 – 7.35 (m, 5H), 2.72 – 2.63 (m, 4H), 2.18 (m, $J = 13.2, 3.8$ Hz, 1H), 1.94 – 1.83 (m, 1H), 1.69 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 136.9, 134.0, 132.4, 129.3, 128.4, 127.6, 126.7, 125.94 (d, $J = 2.0$ Hz), 125.3, 124.4, 118.5, 116.6, 114.9, 47.5, 33.22 (d, $J = 3.2$ Hz), 30.4, 30.1, 29.8, 29.5, 11.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.39 (t, $J = 10.9$ Hz). GC-MS(EI): 357.3, 342.2, 322.2, 307.1, 299.1, 287.1,

272.1, 260.1, 245.2, 232.2, 217.2, 202.1, 189.1, 178.6, 163.1, 151.1, 139.1, 130.2, 120.7, 108.6, 95.6, 87.1, 77.1, 69.1, 59.1, 51.1. HRMS (ESI, m/z): calcd for C₂₁H₁₈F₃NO [M+H]⁺ 358.1413, found 358.1415.



5,12-dimethyl-5-(5,5,5-trifluoropentyl)indolo[2,1-a]isoquinolin-6(5H)-one (3p):

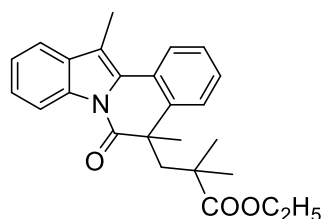
Light yellow oil. 80% isolated yield, 30.8 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.65 (d, *J* = 8.1 Hz, 1H), 8.09 – 8.05 (m, 1H), 7.67 – 7.62 (m, 1H), 7.49 – 7.40 (m, 5H), 2.70 (s, 3H), 2.42 (m, *J* = 12.7, 4.7 Hz, 1H), 2.00 – 1.85 (m, 3H), 1.73 (s, 3H), 1.46 (m, *J* = 11.5, 9.2, 6.1 Hz, 2H), 1.12 – 0.97 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 172.8, 138.4, 134.0, 132.4, 129.7, 128.0, 127.1, 126.6, 126.2, 125.7, 125.0, 124.2, 118.3, 116.7, 114.2, 48.4, 42.2, 33.8-33.2 (q, *J* = 29.1, 28.6 Hz), 33.4, 32.9, 28.8, 24.3, 21.9-21.8 (q, *J* = 2.9 Hz), 11.5. ¹⁹F NMR (376 MHz, CDCl₃) δ -66.63 (t, *J* = 11.0 Hz). GC-MS(ED): 385.3, 370.2, 260.1, 245.2, 232.2, 217.2, 202.1, 189.1, 176.1, 128.1, 120.6, 108.6, 101.1, 85.1, 77.1, 61.1, 51.1. HRMS (ESI, m/z): calcd for C₂₃H₂₂F₃NO [M+H]⁺ 386.1726, found 386.1731.



ethyl (2R)-3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)-2-methylpropanoate (3q):

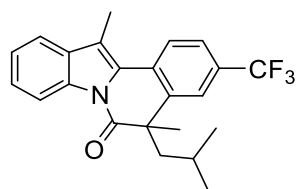
White solid. 88% isolated yield, 33.1 mg. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.72 – 8.59 (m, 1H), 8.12 – 8.01 (m, 1H), 7.63 (td, *J* = 8.6, 8.0, 1.5 Hz, 1H), 7.50 – 7.36 (m, 5H), 3.76 (m, *J* = 22.5, 10.7, 7.1 Hz, 1H), 3.49 (m, *J* = 34.1, 10.8, 7.1 Hz, 1H), 2.70 (d, *J* = 1.7 Hz, 3H), 2.64 – 2.50 (m, 1H), 2.32 – 2.20 (m, 1H), 1.71 (s, 3H), 1.05 – 0.82 (m, 6H). ¹³C NMR (101 MHz, CDCl₃) δ

175.9, 175.6, 172.6, 171.9, 138.2, 137.1, 134.1, 132.4, 132.2, 129.7, 129.6, 127.8, 127.6, 127.3, 127.1, 126.6, 126.4, 126.2, 125.6, 125.1, 124.7, 124.2, 124.0, 118.3, 118.2, 116.7, 116.5, 114.2, 114.0, 60.2, 60.1, 47.7, 47.6, 45.6, 45.0, 36.9, 36.2, 30.3, 29.3, 18.9, 18.6, 13.7, 13.4, 11.5, 11.4. GC-MS(EI): 375.2, 355.1, 330.2, 281.1, 260.1, 245.1, 232.1, 217.1, 207.1, 191.1, 165.0, 147.0, 133.0, 120.6, 108.5, 96.0, 73.1, 59.1, 50.1. HRMS (ESI, m/z): calcd for C₂₄H₂₅NO₃ [M+H]⁺ 376.1907, found 376.1901.



ethyl 3-(5,12-dimethyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinolin-5-yl)-2,2-dimethylpropanoate (3r):

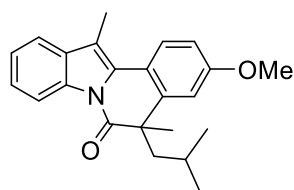
White solid. 89% isolated yield, 34.6 mg. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.68 – 8.56 (m, 1H), 8.03 (d, *J* = 7.9 Hz, 1H), 7.63 – 7.56 (m, 1H), 7.45 – 7.26 (m, 5H), 3.72 – 3.40 (m, 2H), 2.80 – 2.62 (m, 5H), 1.66 (s, 3H), 1.06 – 0.97 (m, 6H), 0.78 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 176.9, 173.0, 137.0, 134.2, 132.5, 129.6, 128.0, 127.0, 127.0, 126.3, 125.6, 124.8, 124.2, 118.3, 116.9, 114.3, 60.2, 50.9, 46.7, 41.6, 33.0, 28.9, 23.2, 13.7, 11.6. GC-MS(EI): 389.2, 344.2, 328.1, 315.2, 300.1, 281.1, 260.1, 245.1, 232.2, 217.1, 202.1, 189.1, 176.1, 165.1, 152.1, 128.1, 119.0, 108.6, 95.8, 77.1, 65.1. HRMS (ESI, m/z): calcd for C₂₅H₂₇NO₃ [M+H]⁺ 390.2064, found 390.2066..



5-isobutyl-5,12-dimethyl-3-(trifluoromethyl)indolo[2,1-a]isoquinolin-6(5H)-one (3s):

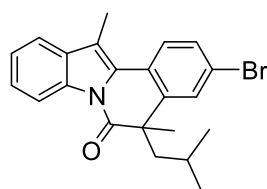
Colorless oil. 48% isolated yield, 18.5 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.3 Hz, 1H), 7.75 – 7.59 (m, 3H), 7.51 – 7.39 (m, 2H), 2.74 (s, 3H), 2.49 (dd, *J* = 14.2, 8.1 Hz, 1H), 2.02 (dd, *J* = 14.1, 5.2 Hz, 1H), 1.72 (s, 3H), 1.37 (dd, *J* = 13.3, 6.9 Hz, 1H), 0.67 (d,

$J = 6.6$ Hz, 3H), 0.62 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 172.5, 139.6, 134.3, 132.0, 129.7, 129.5, 129.4, 129.1, 128.5, 126.4, 125.1, 124.4, 123.9, 123.6, 118.7, 116.9, 116.2, 50.7, 47.8, 31.0, 25.6, 23.9, 22.4, 11.7. ^{19}F NMR (376 MHz, CDCl_3) δ -62.59. GC-MS(EI): 385.3, 366.2, 342.2, 328.2, 313.1, 300.1, 285.1, 272.1, 258.1, 241.2, 228.2, 216.1, 202.1, 189.1, 176.1, 164.2, 155.1, 139.6, 128.1, 115.1, 102.1, 89.1, 77.1, 69.1, 57.1. HRMS (ESI, m/z): calcd for $\text{C}_{23}\text{H}_{22}\text{F}_3\text{NO}$ $[\text{M}+\text{H}]^+$ 386.1726, found 386.1722.



(R)-5-isobutyl-3-methoxy-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3t):

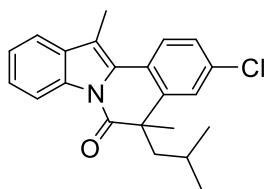
Colorless oil. 67% isolated yield, 23.3 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.67 – 8.54 (m, 1H), 7.97 (d, $J = 8.7$ Hz, 1H), 7.57 – 7.51 (m, 1H), 7.38 – 7.30 (m, 2H), 6.99 – 6.89 (m, 2H), 3.88 (s, 3H), 2.61 (s, 3H), 2.40 (dd, $J = 13.9, 8.1$ Hz, 1H), 1.93 (dd, $J = 13.9, 5.1$ Hz, 1H), 1.64 (s, 3H), 1.42 – 1.34 (m, 1H), 0.65 (d, $J = 6.7$ Hz, 3H), 0.58 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 173.2, 159.1, 141.0, 134.0, 132.6, 129.9, 126.4, 125.0, 124.0, 119.6, 117.9, 116.7, 112.5, 111.9, 55.4, 51.0, 47.8, 31.1, 25.5, 24.0, 22.4, 11.3. GC-MS(EI): 347.1, 332.1, 316.1, 175.1, 162.1, 153.1, 138.1, 127.1, 115.2, 103.1, 88.1, 77.1, 68.1, 55.1. HRMS (ESI, m/z): calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 348.1958, found 348.1958.



3-bromo-5-isobutyl-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3u):

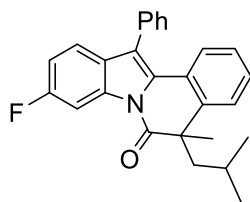
Colorless oil. 58% isolated yield, 23.0 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.61 (d, $J = 8.1$ Hz, 1H), 7.89 (d, $J = 8.6$ Hz, 1H), 7.60 (d, $J = 7.6$ Hz, 1H), 7.57 – 7.43 (m, 2H), 7.43 – 7.33 (m, 2H), 2.63 (s, 3H), 2.40 (dd, $J = 14.1, 8.3$ Hz, 1H), 1.92 (dd, $J = 14.1, 5.2$ Hz, 1H), 1.64 (s, 3H), 1.37 (dd, $J = 13.4, 6.7$ Hz, 1H), 0.66 (d, $J = 6.7$ Hz, 3H), 0.57 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3)

δ 172.5, 141.1, 134.2, 132.2, 130.1, 130.0, 128.9, 126.3, 125.9, 125.3, 124.3, 121.6, 118.4, 116.8, 114.6, 50.7, 47.6, 31.0, 25.5, 24.0, 22.4, 11.6. GC-MS(ED): 397.1, 395.1, 316.1, 315.1, 177.1, 165.1, 153.1, 138.1. 128.1, 115.2, 103.1, 88.1, 77.1, 55.1. HRMS (ESI, m/z): calcd for $C_{22}H_{22}BrNO$ $[M+H]^+$ 396.0958, found 396.0958.



3-chloro-5-isobutyl-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (3v):

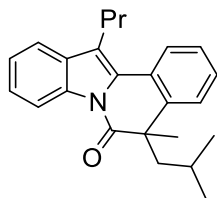
Colorless oil. 52% isolated yield, 18.3 mg. 1H NMR (400 MHz, $CDCl_3$) δ 8.65 – 8.57 (m, 1H), 7.96 (d, $J = 8.6$ Hz, 1H), 7.62 – 7.57 (m, 1H), 7.38 (m, $J = 8.5, 6.2, 1.9$ Hz, 4H), 2.64 (s, 3H), 2.43 – 2.38 (m, 1H), 1.92 (dd, $J = 14.1, 5.2$ Hz, 1H), 1.64 (s, 3H), 1.36 (m, $J = 13.6, 6.9, 5.4, 2.4$ Hz, 1H), 0.66 (d, $J = 6.6$ Hz, 3H), 0.57 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 140.9, 134.2, 133.4, 132.2, 130.8, 128.9, 127.2, 127.1, 126.1, 125.9, 124.9, 124.3, 118.3, 116.8, 114.4, 50.8, 47.7, 31.0, 25.5, 24.0, 22.4, 11.5. GC-MS(ED): 351.2, 294.1, 279.1, 266.1, 251.1, 241.2, 230.2, 216.1, 202.1, 189.1, 176.1, 163.1, 152.1, 139.1, 128.1, 114.1, 102.1, 88.1, 77.1, 67.0, 57.1. HRMS (ESI, m/z): calcd for $C_{22}H_{22}ClNO$ $[M+H]^+$ 352.1463, found 352.1461..



9-fluoro-5-isobutyl-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (3w):

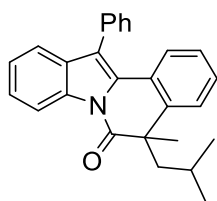
Colorless oil. 50% isolated yield, 20.0 mg. 1H NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, $J = 9.0, 4.7$ Hz, 1H), 7.66 – 7.45 (m, 5H), 7.43 (d, $J = 8.1$ Hz, 1H), 7.38 (d, $J = 8.1$ Hz, 1H), 7.30 (d, $J = 7.7$ Hz, 1H), 7.13 – 7.08 (m, 1H), 7.01 (t, $J = 7.7$ Hz, 1H), 6.93 (dd, $J = 8.8, 2.5$ Hz, 1H), 2.42 (dd, $J = 14.0, 8.1$ Hz, 1H), 2.01 (dd, $J = 14.0, 5.2$ Hz, 1H), 1.70 (s, 3H), 1.43 – 1.36 (m, 1H), 0.66 (d, $J = 6.7$ Hz, 3H), 0.63 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 160.49 (d, $J = 241.2$ Hz), 139.4, 133.8, 133.7, 131.2, 130.5, 130.2, 130.0, 129.4, 128.8, 128.46 (d, $J = 26.6$ Hz), 126.9, 126.5, 125.4, 124.9, 119.57 (d, $J = 4.3$ Hz), 117.99 (d, $J = 8.7$ Hz), 113.32 (d, $J = 24.7$ Hz), 105.08

(d, $J = 24.5$ Hz), 51.0, 47.8, 31.0, 25.7, 24.0, 22.6. ^{19}F NMR (376 MHz, CDCl_3) δ -117.87. GC-MS(EI): 397.0, 378.0, 202.0, 198.0, 176.0, 165.0, 152.0, 138.0, 127.0, 115.0, 95.0, 86.0, 77.0, 65.0, 55.1. HRMS (ESI, m/z): calcd for $\text{C}_{27}\text{H}_{24}\text{FNO}$ $[\text{M}+\text{H}]^+$ 398.1915, found 398.1918.



5-isobutyl-5-methyl-12-propylindolo[2,1-a]isoquinolin-6(5H)-one (3x):

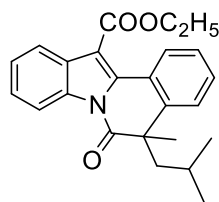
Colorless oil. 64% isolated yield, 22 mg. ^1H NMR (600 MHz, CDCl_3) δ 8.64 (d, $J = 7.7$ Hz, 1H), 7.96 (d, $J = 7.7$ Hz, 1H), 7.60 (d, $J = 8.1$ Hz, 1H), 7.42 (dd, $J = 7.4, 1.8$ Hz, 1H), 7.40 – 7.33 (m, 4H), 3.09 (dd, $J = 9.3, 6.6$ Hz, 2H), 2.38 (dd, $J = 14.0, 8.1$ Hz, 1H), 1.96 (dd, $J = 14.0, 5.1$ Hz, 1H), 1.83 (dt, $J = 9.1, 7.1$ Hz, 2H), 1.65 (s, 3H), 1.34 (dtd, $J = 13.0, 6.5, 1.4$ Hz, 1H), 1.13 (t, $J = 7.4$ Hz, 3H), 0.62 (d, $J = 6.6$ Hz, 3H), 0.56 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 172.5, 141.1, 134.2, 132.2, 130.1, 130.0, 128.9, 126.3, 125.9, 125.3, 124.3, 121.6, 118.4, 116.9, 114.6, 50.8, 47.6, 31.0, 29.7, 25.5, 24.0, 23.8, 22.4, 11.6. GC-MS(EI): 345.3, 316.2, 288.1, 260.1, 246.1, 230.2, 217.1, 207.1, 191.0, 177.0, 165.1, 139.1, 115.1, 96.0, 77.1, 57.1. HRMS (ESI, m/z): calcd for $\text{C}_{24}\text{H}_{27}\text{NO}$ $[\text{M}+\text{H}]^+$ 346.2165, found 346.2164.



5-isobutyl-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (3y):

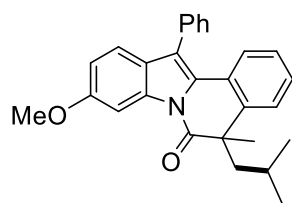
Colorless oil. 60% isolated yield, 22.7 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.72 (d, $J = 8.2$ Hz, 1H), 7.63 – 7.50 (m, 5H), 7.49 – 7.40 (m, 3H), 7.38 – 7.31 (m, 3H), 7.05 (ddd, $J = 8.3, 7.2, 1.3$ Hz, 1H), 2.47 (dd, $J = 14.0, 8.1$ Hz, 1H), 2.04 (dd, $J = 13.9, 5.2$ Hz, 1H), 1.74 (s, 3H), 1.47 – 1.39 (m, 1H), 0.71 (d, $J = 6.7$ Hz, 3H), 0.68 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 173.9, 139.2, 134.3, 132.4, 130.3, 130.2, 129.7, 129.3, 128.3, 128.1, 126.8, 126.5, 125.8, 125.3, 125.2, 124.5, 120.0, 119.4, 116.9, 50.9, 47.8, 31.0, 25.7, 24.0, 22.6. GC-MS(EI): 379.3, 322.2, 304.1, 294.1, 280.1, 265.1, 252.1, 239.1, 230.2, 217.2, 202.1, 189.1, 176.1, 165.1, 153.7, 145.6, 132.6, 115.1,

102.1, 91.1, 77.1, 65.1, 57.1. HRMS (ESI, m/z): calcd for C₂₇H₂₅NO [M+H]⁺ 380.2009, found 380.2007.



ethyl 5-isobutyl-5-methyl-6-oxo-5,6-dihydroindolo[2,1-a]isoquinoline-12-carboxylate (3z):

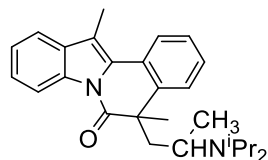
Colorless oil. 40% isolated yield, 15 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.63 (dd, *J* = 7.5, 1.9 Hz, 1H), 8.47 (d, *J* = 7.7 Hz, 1H), 8.03 – 7.88 (m, 1H), 7.45 – 7.34 (m, 5H), 4.56 (q, *J* = 7.2 Hz, 2H), 2.33 (dd, *J* = 14.1, 8.0 Hz, 1H), 1.99 (dd, *J* = 14.1, 5.2 Hz, 1H), 1.68 (s, 3H), 1.51 (t, *J* = 7.2 Hz, 3H), 1.40 (ddd, *J* = 8.1, 5.9, 1.5 Hz, 1H), 0.65 (d, *J* = 6.7 Hz, 3H), 0.58 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 174.1, 165.9, 140.1, 134.1, 130.0, 129.0, 127.7, 126.8, 126.4, 126.1, 125.1, 123.6, 120.9, 116.6, 61.3, 51.1, 48.1, 29.8, 25.4, 23.9, 22.7, 14.4. GC-MS(EI): 375.2, 355.0, 346.1, 331.1, 319.2, 290.1, 281.1, 272.1, 246.1, 229.1, 217.1, 207.1, 191.0, 177.0, 163.0, 147.0, 133.0, 118.9, 96.1, 73.1, 57.0. HRMS (ESI, m/z): calcd for C₂₄H₂₅NO₃ [M+H]⁺ 376.1907, found 376.1900.



5-isobutyl-9-methoxy-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (3aa):

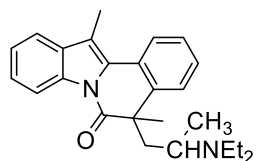
Light yellow oil. 62% isolated yield, 25.4 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.57 (dd, *J* = 9.0, 3.2 Hz, 1H), 7.59 – 7.53 (m, 2H), 7.50 (m, *J* = 7.3, 3.2, 2.5 Hz, 3H), 7.40 – 7.35 (m, 2H), 7.28 – 7.20 (m, 2H), 7.01 – 6.98 (m, 2H), 6.72 (t, *J* = 2.6 Hz, 1H), 3.78 (s, 3H), 2.42 (m, *J* = 13.8, 8.1, 2.5 Hz, 1H), 1.99 (m, *J* = 14.0, 5.1, 2.1 Hz, 1H), 1.69 (d, *J* = 2.1 Hz, 3H), 1.39 (h, *J* = 5.8, 4.5 Hz, 1H), 0.66 (dd, *J* = 6.6, 2.3 Hz, 3H), 0.63 (dd, *J* = 6.7, 2.5 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 173.3, 157.2, 139.2, 134.2, 133.4, 130.3, 130.2, 130.1, 130.0, 129.3, 128.8, 128.6, 128.1, 128.0, 126.7, 126.3, 125.1, 119.7, 117.6, 113.9, 102.1, 55.6, 50.9, 47.5, 30.9, 25.6, 23.9, 22.5. GC-MS(EI): 409.4, 352.3, 337.2, 324.2, 309.2, 293.1, 280.1, 265.1, 252.2, 204.1, 176.1, 139.2, 126.1,

113.1, 101.1, 91.1, 77.1, 65.1, 57.1. HRMS (ESI, m/z): calcd for C₂₈H₂₇NO₂ [M+H]⁺ 410.2115, found 410.2111.



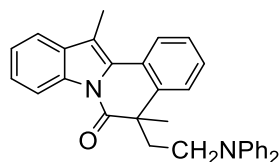
5-(2-(diisopropylamino)propyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (5a):

Colorless oil. 75% isolated yield, 30.1 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.65 (d, *J* = 7.6 Hz, 1H), 8.01 (dt, *J* = 6.0, 2.9 Hz, 1H), 7.63 – 7.54 (m, 1H), 7.48 – 7.29 (m, 5H), 2.93 (d, *J* = 13.9 Hz, 2H), 2.77 (s, 1H), 2.65 (d, *J* = 2.6 Hz, 3H), 1.94 (d, *J* = 14.7 Hz, 1H), 1.63 (s, 3H), 1.26 (d, *J* = 2.6 Hz, 2H), 0.84 (dd, *J* = 25.8, 6.6 Hz, 9H), 0.49 (d, *J* = 6.2 Hz, 5H). ¹³C NMR (101 MHz, CDCl₃) δ 172.4, 139.2, 134.2, 132.3, 130.1, 127.5, 127.0, 126.7, 126.6, 125.3, 125.0, 123.7, 118.1, 117.0, 113.5, 47.1, 47.0, 46.6, 44.6, 33.1, 23.1, 22.2, 11.5. GC-MS(ED): 402.4, 387.3, 302.1, 287.1, 272.1, 260.1, 245.1, 232.1, 217.2, 202.1, 193.1, 172.7, 165.1, 142.2, 128.2, 108.6, 98.2, 86.2, 70.1, 58.1, 50.1. HRMS (ESI, m/z): calcd for C₂₇H₃₄N₂O [M+H]⁺ 403.2744, found 403.2743.



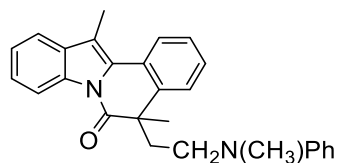
5-(2-(diethylamino)propyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (5b):

Light yellow oil. 66% isolated yield, 24.7 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.64 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.03 (dd, *J* = 7.6, 2.4 Hz, 1H), 7.62 – 7.55 (m, 1H), 7.45 – 7.29 (m, 5H), 2.92 (dd, *J* = 14.5, 11.6 Hz, 1H), 2.65 (s, 3H), 2.46 (d, *J* = 26.6 Hz, 1H), 2.27 – 2.07 (m, 2H), 1.90 – 1.74 (m, 4H), 1.58 (s, 3H), 0.77 (d, *J* = 6.6 Hz, 3H), 0.33 (t, *J* = 7.1 Hz, 5H). ¹³C NMR (101 MHz, CDCl₃) δ 172.6, 134.3, 132.2, 130.2, 127.4, 127.2, 126.8, 126.5, 125.0, 124.9, 123.4, 118.0, 117.2, 52.1, 46.3, 45.9, 41.8, 32.0, 29.7, 13.2, 12.2, 11.6. GC-MS(ED): 374.2, 359.3, 341.1, 331.0, 314.9, 302.1, 281.1, 269.1, 260.1, 245.1, 230.1, 217.1, 207.0, 191.0, 176.9, 162.9, 147.0, 133.0, 125.0, 114.1, 100.1, 84.0, 72.1, 56.1. HRMS (ESI, m/z): calcd for C₂₅H₃₀N₂O [M+H]⁺ 375.2431, found 375.2434..



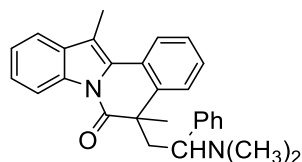
5-(2-(diphenylamino)ethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (5c):

Light yellow oil. 88% isolated yield, 40.1 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.69 (t, $J = 6.7$ Hz, 1H), 8.07 (t, $J = 6.7$ Hz, 1H), 7.64 (t, $J = 6.5$ Hz, 1H), 7.51 – 7.39 (m, 5H), 7.19 (td, $J = 8.0, 4.1$ Hz, 4H), 6.92 (q, $J = 6.8$ Hz, 2H), 6.85 (t, $J = 6.6$ Hz, 4H), 3.52 (m, $J = 14.5, 11.5, 5.5$ Hz, 1H), 3.38 (m, $J = 18.5, 11.1, 3.8$ Hz, 1H), 2.84 (tt, $J = 11.7, 5.3$ Hz, 1H), 2.69 (d, $J = 5.6$ Hz, 3H), 2.35 – 2.26 (m, 1H), 1.72 (d, $J = 5.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 147.4, 137.8, 134.1, 132.4, 129.6, 129.1, 127.9, 127.3, 126.6, 126.2, 125.8, 125.1, 124.2, 121.1, 120.5, 118.4, 116.6, 114.5, 47.9, 47.0, 39.0, 28.8, 11.4. GC-MS(EI): 456.1, 429.1, 415.0, 405.0, 355.0, 341.0, 331.0, 316.1, 281.1, 267.1, 253.1, 234.8, 221.0, 207.0, 191.0, 177.0, 162.9, 147.1, 133.0, 119.0, 96.1, 87.0, 73.1, 57.0. HRMS (ESI, m/z): calcd for $\text{C}_{32}\text{H}_{28}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 457.2274, found 457.2279.



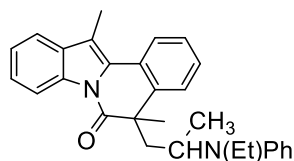
5,12-dimethyl-5-(2-(methyl(phenyl)amino)ethyl)indolo[2,1-a]isoquinolin-6(5H)-one (5d):

Light yellow oil. 84% isolated yield, 33.1 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.64 (d, $J = 7.9$ Hz, 1H), 8.05 – 7.99 (m, 1H), 7.59 – 7.55 (m, 1H), 7.53 – 7.49 (m, 1H), 7.45 – 7.33 (m, 4H), 7.05 (t, $J = 8.0$ Hz, 2H), 6.59 (t, $J = 7.2$ Hz, 1H), 6.34 (d, $J = 8.2$ Hz, 2H), 3.03 – 2.90 (m, 2H), 2.71 (s, 4H), 2.61 (s, 3H), 2.14 (m, $J = 13.4, 10.1, 4.4$ Hz, 1H), 1.69 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 172.4, 148.6, 138.0, 134.1, 132.4, 129.6, 128.9, 127.9, 127.2, 126.7, 126.2, 125.6, 125.1, 124.1, 118.3, 116.7, 116.1, 114.4, 112.0, 48.2, 46.8, 38.4, 38.0, 29.4, 11.5. GC-MS(EI): 394.2, 377.2, 355.0, 341.0, 331.1, 315.1, 281.0, 261.1, 246.1, 230.1, 217.1, 207.1, 191.0, 176.9, 165.1, 156.1, 147.0, 134.1, 120.1, 104.1, 91.1, 77.1, 65.0, 51.1. HRMS (ESI, m/z): calcd for $\text{C}_{27}\text{H}_{26}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 395.2118, found 395.2123..



5-(2-(benzyl(methyl)amino)ethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (5e):

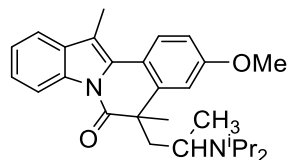
Light yellow oil. 92% isolated yield, 37.5 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.70 – 8.60 (m, 1H), 8.07 – 8.02 (m, 1H), 7.65 (dd, $J = 7.3, 1.9$ Hz, 1H), 7.48 – 7.42 (m, 2H), 7.42 – 7.36 (m, 3H), 7.11 (t, $J = 7.3$ Hz, 1H), 7.05 (t, $J = 7.4$ Hz, 2H), 6.92 (d, $J = 7.4$ Hz, 2H), 3.23 (q, $J = 13.0$ Hz, 2H), 2.86 (m, $J = 11.7, 8.7, 3.2$ Hz, 1H), 2.71 – 2.67 (m, 3H), 2.19 – 2.08 (m, 3H), 1.96 (s, 3H), 1.72 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 172.7, 138.4, 134.3, 132.4, 129.8, 128.8, 127.8, 127.8, 126.9, 126.6, 126.6, 126.5, 125.5, 124.9, 123.9, 118.2, 116.8, 113.8, 62.3, 53.8, 47.0, 41.5, 39.4, 30.0, 11.5. GC-MS(EI): 408.1, 393.1, 331.1, 316.1, 281.1, 260.1, 245.1, 230.1, 217.1, 207.0, 191.0, 176.9, 162.9, 147.1, 133.0, 119.0, 96.1, 87.0, 77.1, 58.1. HRMS (ESI, m/z): calcd for $\text{C}_{28}\text{H}_{28}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 409.2274, found 409.2270.



5-(2-(ethyl(phenyl)amino)propyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (5f):

Light yellow oil. 79% isolated yield, 33.3 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.63 (dd, $J = 11.2, 8.0$ Hz, 1H), 7.72 (d, $J = 7.8$ Hz, 1H), 7.51 (d, $J = 7.3$ Hz, 1H), 7.42 (d, $J = 7.9$ Hz, 1H), 7.39 – 7.28 (m, 5H), 6.89 – 6.76 (m, 1H), 6.53 (dd, $J = 8.5, 6.9$ Hz, 1H), 6.35 (dt, $J = 38.8, 7.3$ Hz, 1H), 6.19 (d, $J = 8.2$ Hz, 1H), 5.66 (d, $J = 8.2$ Hz, 1H), 3.77 – 3.52 (m, 1H), 3.07 – 2.91 (m, 2H), 2.67 – 2.61 (m, 1H), 2.51 (s, 1H), 2.27 (s, 1H), 1.66 (d, $J = 3.8$ Hz, 3H), 1.00 (d, $J = 6.8$ Hz, 2H), 0.92 (dd, $J = 8.8, 6.8$ Hz, 3H), 0.75 (t, $J = 7.0$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 173.1, 172.1, 146.8, 146.7, 138.2, 138.2, 134.2, 134.0, 132.5, 132.4, 129.4, 129.3, 128.6, 127.8, 127.5, 127.3, 127.0, 126.8, 126.7, 126.6, 126.3, 126.1, 125.4, 125.1, 124.9, 124.1, 123.5, 118.2, 118.1, 116.7, 116.6, 115.8, 115.5, 114.3, 113.9, 112.5, 50.2, 49.8, 48.3, 46.8, 46.2, 37.3, 36.5, 31.2, 31.0, 29.7, 18.4, 18.3, 13.7, 12.5, 11.5, 11.4. GC-MS(EI): 422.2, 405.1, 388.9, 355.1, 341.0, 331.0, 315.0, 301.1, 281.1, 261.1, 245.1, 230.1, 217.1, 207.1, 191.0, 177.0, 162.1, 148.1, 133.0, 120.1, 104.1,

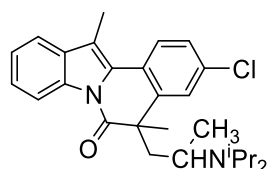
91.0, 81.9, 73.0, 61.0, 51.1. HRMS (ESI, m/z): calcd for C₂₉H₃₀N₂O [M+H]⁺ 423.2433, found 423.2438.



5-(2-(diisopropylamino)propyl)-3-fluoro-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one

(5g):

Colorless oil. 79% isolated yield, 34.2 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.68 – 8.55 (m, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.35 – 7.29 (m, 2H), 6.99 – 6.85 (m, 2H), 3.90 (s, 3H), 3.10 – 2.88 (m, 3H), 2.84 – 2.75 (m, 1H), 2.60 (s, 3H), 1.89 (dd, *J* = 14.4, 4.5 Hz, 1H), 1.57 (s, 3H), 1.27 (d, *J* = 11.8 Hz, 1H), 0.84 (dd, *J* = 20.1, 6.5 Hz, 9H), 0.53 (d, *J* = 6.7 Hz, 5H). ¹³C NMR (101 MHz, CDCl₃) δ 172.2, 159.0, 141.3, 134.0, 132.5, 130.2, 126.5, 124.8, 123.7, 120.3, 117.7, 116.9, 112.3, 112.3, 111.5, 55.4, 47.4, 47.0, 46.9, 44.6, 33.0, 23.1, 22.3, 11.3. GC-MS(ED): 432.3, 417.3, 401.2, 332.2, 290.1, 275.1, 262.1, 247.1, 232.1, 217.1, 204.1, 191.1, 176.1, 142.1, 126.2, 112.1, 95.1, 86.1, 70.1, 56.1. HRMS(ESI, m/z): calcd for C₂₈H₃₃F₃N₂O [M+H]⁺ 433.2850, found 433.2845.

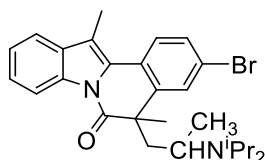


3-chloro-5-(2-(diisopropylamino)propyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one

(5h):

Colorless oil. 72% isolated yield, 31.4 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.63 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.96 (dd, *J* = 20.5, 8.9 Hz, 1H), 7.59 (m, *J* = 7.1, 5.2, 1.8 Hz, 1H), 7.46 – 7.31 (m, 4H), 3.07 (p, *J* = 6.6 Hz, 1H), 2.99 – 2.86 (m, 2H), 2.83 – 2.69 (m, 1H), 2.63 (d, *J* = 12.0 Hz, 3H), 1.88 (dd, *J* = 14.6, 4.5 Hz, 1H), 1.77 – 1.67 (m, 1H), 1.59 (d, *J* = 19.5 Hz, 3H), 1.36 – 1.23 (m, 1H), 0.92 – 0.80 (m, 9H), 0.56 (dd, *J* = 42.4, 6.6 Hz, 5H). ¹³C NMR (101 MHz, CDCl₃) δ 172.7, 171.6, 141.2, 140.3, 134.2, 134.2, 133.5, 133.2, 132.2, 132.1, 129.2, 128.8, 127.5, 127.2, 127.1, 126.8, 126.2, 126.2, 125.8, 125.6, 125.6, 124.8, 124.2, 123.9, 118.3, 118.2, 117.0, 116.9, 114.4, 114.0, 48.5,

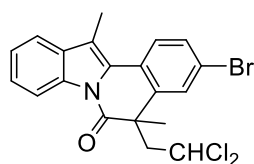
47.2, 47.1, 47.0, 46.7, 46.3, 44.7, 44.6, 32.9, 32.6, 23.6, 23.2, 22.3, 22.2, 19.2, 11.5, -0.0. GC-MS(ED): 436.3, 421.2, 336.1, 321.1, 306.1, 294.1, 279.1, 266.1, 251.1, 241.1, 230.2, 219.0, 210.7, 202.1, 189.2, 176.1, 163.1, 152.1, 142.2, 128.2, 114.2, 98.1, 86.1, 70.1, 58.1. HRMS (ESI, m/z): calcd for C₂₇H₃₃ClN₂O [M+H]⁺ 437.2354, found 437.2355.



3-bromo-5-(2-(diisopropylamino)propyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one

(5i):

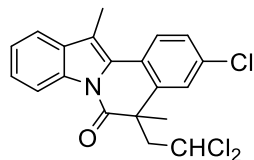
Colorless oil. 77% isolated yield, 37.0 mg. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 8.6 Hz, 1H), 7.63 (dd, *J* = 7.2, 1.7 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.36 (m, 2H), 2.95 (q, *J* = 6.1 Hz, 2H), 2.80 – 2.71 (m, 1H), 2.65 (s, 3H), 2.23 – 1.95 (m, 1H), 1.91 (dd, *J* = 14.6, 4.5 Hz, 1H), 1.60 (s, 3H), 1.29 (d, *J* = 2.5 Hz, 1H), 0.92 (d, *J* = 6.6 Hz, 4H), 0.86 (d, *J* = 6.6 Hz, 5H), 0.54 (d, *J* = 6.6 Hz, 5H). ¹³C NMR (101 MHz, CDCl₃) δ 171.6, 141.4, 134.2, 132.1, 130.0, 129.7, 129.2, 126.4, 126.0, 125.7, 124.0, 121.4, 118.2, 117.0, 114.1, 47.3, 47.0, 46.7, 44.6, 32.9, 23.2, 22.2, 11.5. GC-MS(ED): 482.2, 480.2, 467.2, 465.2, 439.2, 413.1, 402.3, 382.1, 380.1, 365.1, 340.0, 338.0, 325.0, 310.1, 297.0, 286.1, 271.1, 259.1, 242.1, 230.1, 216.1, 202.1, 189.1, 176.1, 142.2, 128.2, 98.1, 86.1, 70.1, 58.1. HRMS(ESI, m/z): calcd for C₂₇H₃₃BrN₂O [M+H]⁺ 481.1849, found 481.1845.



3-bromo-5-(2,2-dichloroethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (6a):

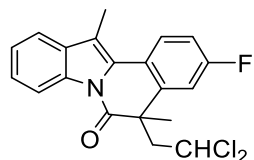
Colorless oil. 59% isolated yield, 25.7 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.67 – 8.54 (m, 1H), 7.93 (d, *J* = 8.6 Hz, 1H), 7.62 – 7.54 (m, 2H), 7.52 (d, *J* = 2.0 Hz, 1H), 7.46 – 7.34 (m, 2H), 5.41 (dd, *J* = 9.4, 4.3 Hz, 1H), 3.58 (dd, *J* = 14.9, 9.5 Hz, 1H), 2.87 (dd, *J* = 14.9, 4.4 Hz, 1H), 2.63 (s, 3H), 1.70 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.6, 137.9, 134.3, 132.2, 131.0, 129.4, 128.3, 126.8, 126.2, 125.7, 124.6, 121.8, 118.5, 116.9, 115.5, 69.6, 52.9, 47.1, 31.2, 11.6. GC-MS(ED):

437.0, 435.0, 340.0, 338.0, 325.0, 323.0, 312.0, 310.0, 297.0, 295.0, 259.1, 241.1, 230.1, 228.1, 216.1, 202.1, 189.1, 170.0, 147.5, 127.1, 114.2, 102.0, 88.0, 77.0, 61.0, 51.1. HRMS (ESI, m/z): calcd for C₂₀H₁₆BrCl₂NO [M+H]⁺435.9871, found 435.9862.



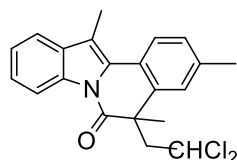
3-chloro-5-(2,2-dichloroethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (6b):

Colorless oil. 52% isolated yield, 20.4 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.61 (m, *J* = 8.2, 0.9 Hz, 1H), 8.00 (d, *J* = 8.6 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.44 – 7.35 (m, 4H), 5.41 (dd, *J* = 9.5, 4.4 Hz, 1H), 3.58 (dd, *J* = 14.9, 9.5 Hz, 1H), 2.87 (dd, *J* = 14.9, 4.4 Hz, 1H), 2.64 (s, 3H), 1.70 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.6, 137.7, 134.2, 133.7, 132.2, 128.3, 128.1, 126.6, 126.5, 126.2, 125.3, 124.6, 118.5, 116.9, 115.4, 69.6, 52.9, 47.1, 31.2, 11.6. GC-MS(EI): 391.0, 294.1, 279.0, 266.1, 251.0, 230.1, 216.1, 202.1, 189.1, 147.3, 114.1, 102.0, 88.0, 77.0, 61.0, 51.0. HRMS (ESI, m/z): calcd for C₂₀H₁₆Cl₃NO [M+H]⁺ 392.0376, found 392.0370.



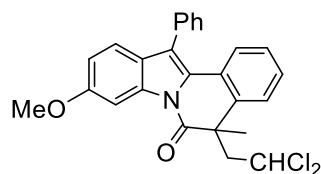
5-(2,2-dichloroethyl)-3-fluoro-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (6c):

Colorless oil. 37% isolated yield, 13.9 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.64 – 8.57 (m, 1H), 8.06 (dd, *J* = 8.9, 5.6 Hz, 1H), 7.59 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.39 (m, *J* = 7.3, 1.4 Hz, 2H), 7.18 (m, *J* = 8.7, 7.8, 2.6 Hz, 1H), 7.10 (dd, *J* = 9.7, 2.6 Hz, 1H), 5.41 (dd, *J* = 9.4, 4.3 Hz, 1H), 3.58 (dd, *J* = 14.9, 9.4 Hz, 1H), 2.85 (dd, *J* = 14.9, 4.3 Hz, 1H), 2.63 (s, 3H), 1.71 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.6, 138.4, 134.1, 132.3, 127.5, 127.4, 126.0, 124.5, 118.4, 116.9, 115.6, 115.3, 114.4, 113.4, 113.2, 69.6, 53.1, 47.3, 31.2, 11.5. ¹⁹F NMR (376 MHz, CDCl₃) δ -111.65. GC-MS(EI): 375.1, 373.1, 360.1, 356.1, 343.1, 298.1, 265.1, 203.1, 145.1, 133.1, 115.1, 97.1, 77.1, 61.1, 51.1. HRMS (ESI, m/z): calcd for C₂₀H₁₆Cl₂FNO [M+H]⁺ 376.0671, found 376.0676.



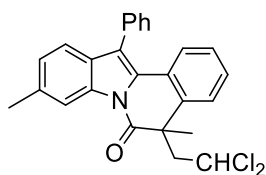
5-(2,2-dichloroethyl)-3,5,12-trimethylindolo[2,1-a]isoquinolin-6(5H)-one (6d):

Colorless oil. 75% isolated yield, 27.8 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.66 – 8.57 (m, 1H), 7.96 (d, $J = 8.2$ Hz, 1H), 7.60 – 7.55 (m, 1H), 7.41 – 7.33 (m, 2H), 7.25 (d, $J = 8.5$ Hz, 1H), 7.17 (s, 1H), 5.38 (dd, $J = 9.8, 3.9$ Hz, 1H), 3.59 (dd, $J = 14.8, 9.9$ Hz, 1H), 2.89 (dd, $J = 14.8, 3.9$ Hz, 1H), 2.63 (s, 3H), 2.45 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.5, 138.0, 135.7, 134.2, 132.5, 129.4, 128.7, 126.7, 125.6, 125.4, 124.3, 124.0, 118.2, 116.8, 113.9, 70.1, 53.1, 47.0, 31.3, 21.5, 11.5. GC-MS(ED): 371.1, 285.1, 274.1, 259.1, 246.1, 231.1, 216.1, 202.1, 189.0, 152.0, 137.1, 127.1, 120.6, 115.4, 102.0, 89.0, 77.0, 61.0, 51.0. HRMS (ESI, m/z): calcd for $\text{C}_{21}\text{H}_{19}\text{Cl}_2\text{NO}$ $[\text{M}+\text{H}]^+$ 372.0922, found 372.0928.



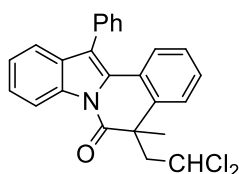
5-(2,2-dichloroethyl)-9-methoxy-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (6e):

Colorless oil. 89% isolated yield, 40 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.56 (d, $J = 8.9$ Hz, 1H), 7.59 – 7.47 (m, 5H), 7.42 (d, $J = 8.1$ Hz, 1H), 7.31 (qd, $J = 7.9, 1.5$ Hz, 2H), 7.03 (ddd, $J = 18.4, 8.6, 2.2$ Hz, 2H), 6.70 (d, $J = 2.5$ Hz, 1H), 5.38 (dd, $J = 9.9, 3.9$ Hz, 1H), 3.78 (s, 3H), 3.61 (dd, $J = 14.8, 9.9$ Hz, 1H), 2.92 (dd, $J = 14.8, 3.9$ Hz, 1H), 1.75 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.3, 157.4, 135.9, 133.9, 133.4, 130.1, 129.7, 129.3, 128.8, 128.5, 128.2, 127.2, 126.1, 125.6, 125.5, 120.6, 117.7, 114.2, 102.2, 70.0, 55.7, 53.1, 47.0, 31.1. GC-MS(EI): 449.1, 352.2, 324.1, 310.1, 291.1, 280.1, 267.1, 252.1, 239.1, 226.1, 217.1, 204.1, 189.1, 175.6, 162.1, 151.1, 145.6, 139.2, 126.1, 113.0, 100.1, 87.0, 77.1, 61.0, 51.0. HRMS (ESI, m/z): calcd for $\text{C}_{26}\text{H}_{21}\text{Cl}_2\text{NO}_2$ $[\text{M}+\text{H}]^+$ 450.1028, found 450.1035.



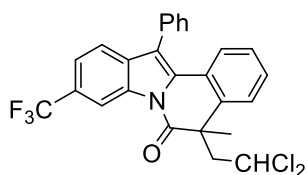
5-(2,2-dichloroethyl)-5,9-dimethyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (6f):

White solid, 88% isolated yield, 38.3 mg. mp: 132.4-135.0 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.53 (d, *J* = 8.4 Hz, 1H), 7.59 – 7.41 (m, 6H), 7.35 – 7.27 (m, 2H), 7.25 – 7.20 (m, 2H), 7.08 – 7.00 (m, 2H), 5.38 (dd, *J* = 9.8, 3.9 Hz, 1H), 3.61 (dd, *J* = 14.8, 9.8 Hz, 1H), 2.91 (dd, *J* = 14.8, 4.0 Hz, 1H), 2.39 (s, 3H), 1.75 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.54, 135.89, 134.53, 134.14, 132.56, 132.46, 130.19, 129.29, 129.13, 128.44, 128.13, 127.35, 127.24, 126.12, 125.71, 125.66, 120.65, 119.36, 116.55, 69.99, 53.24, 47.10, 31.08, 21.42. GC-MS(EI): 434.9, 433.0, 336.0, 320.9, 308.0, 291.0, 278.0, 265.0, 251.9, 240.0, 230.0, 216.8, 202.0, 188.9, 178.0, 167.6, 145.5, 132.4, 115.0, 96.9, 77.0, 60.9, 50.9. HRMS (ESI, *m/z*): calcd for C₂₆H₂₁Cl₂NO [M+H]⁺ 434.1078, found 434.1082.



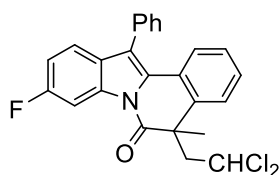
5-(2,2-dichloroethyl)-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (6g):

Colorless oil. 87% isolated yield, 36.5 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J* = 8.3 Hz, 1H), 7.57 – 7.45 (m, 6H), 7.41 (m, *J* = 8.4, 5.1, 3.4 Hz, 1H), 7.35 – 7.26 (m, 4H), 7.05 (m, *J* = 8.3, 6.7, 1.9 Hz, 1H), 5.39 (dd, *J* = 9.9, 3.9 Hz, 1H), 3.63 (dd, *J* = 14.8, 9.9 Hz, 1H), 2.92 (dd, *J* = 14.8, 3.9 Hz, 1H), 1.75 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.8, 135.8, 134.2, 133.9, 132.3, 130.1, 129.3, 129.0, 128.6, 128.2, 127.3, 126.1, 126.0, 125.7, 125.5, 124.7, 120.8, 119.5, 116.8, 70.0, 53.0, 47.1, 31.2. GC-MS(EI): 419.1, 417.1, 325.1, 280.1, 240.1, 226.1, 145.1, 133.1, 115.1, 97.1, 77.1, 61.1, 51.1. HRMS (ESI, *m/z*): calcd for C₂₅H₁₉Cl₂NO [M+H]⁺ 420.0922, found 420.0918.



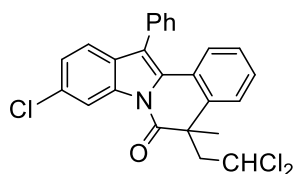
5-(2,2-dichloroethyl)-5-methyl-12-phenyl-9-(trifluoromethyl)indolo[2,1-a]isoquinolin-6(5H)-one (6h):

Colorless oil. 39% isolated yield, 19 mg. ¹H NMR (400 MHz, CDCl₃) δ 8.78 (d, *J* = 8.6 Hz, 1H), 7.70 – 7.45 (m, 8H), 7.36 (d, *J* = 4.1 Hz, 2H), 7.10 (dq, *J* = 8.3, 4.3 Hz, 1H), 5.37 (dd, *J* = 10.1, 3.7 Hz, 1H), 3.63 (dd, *J* = 14.8, 10.1 Hz, 1H), 2.95 (dd, *J* = 14.8, 3.7 Hz, 1H), 1.78 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 172.1, 135.8, 135.7, 133.0, 132.2, 130.7, 130.1, 129.6, 129.2, 128.6, 127.5, 127.2, 126.9, 126.2, 126.0, 125.0, 122.7, 120.4, 117.1, 116.8, 69.9, 53.2, 47.3, 31.2. ¹⁹F NMR (376 MHz, CDCl₃) δ -61.24. GC-MS(ED): 487.1, 390.1, 362.1, 348.1, 291.1, 217.1, 194.6, 170.2, 160.6, 145.6, 132.6, 99.0, 77.1, 61.0, 51.0. HRMS (ESI, *m/z*): calcd for C₂₆H₁₈Cl₂F₃NO [M+H]⁺ 488.0796, found 488.0792.



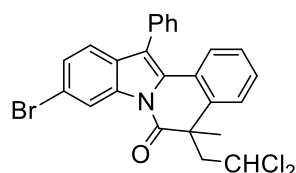
5-(2,2-dichloroethyl)-9-fluoro-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (6i):

White solid, 48% isolated yield, 21 mg. mp: 150.7-155.4 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.62 (dd, *J* = 9.0, 4.7 Hz, 1H), 7.60 – 7.44 (m, 6H), 7.37 – 7.30 (m, 2H), 7.16 – 7.04 (m, 2H), 6.92 (dd, *J* = 8.8, 2.6 Hz, 1H), 5.37 (dd, *J* = 10.0, 3.8 Hz, 1H), 3.61 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.93 (dd, *J* = 14.9, 3.8 Hz, 1H), 1.76 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.6, 161.7, 159.3, 136.0, 133.6, 133.4, 130.5, 130.0, 129.4, 128.9, 128.4, 127.4, 126.1, 125.8, 125.2, 120.3, 118.0, 113.6, 105.2, 69.9, 53.1, 47.1, 31.2. ¹⁹F NMR (376 MHz, CDCl₃) δ -117.34. GC-MS(ED): 437.1, 340.1, 312.1, 298.1, 235.1, 217.1, 207.1, 183.0, 169.6, 154.6, 145.6, 134.1, 125.1, 115.1, 106.9, 99.0, 87.0, 77.0, 61.0, 51.1. HRMS (ESI, *m/z*): calcd for C₂₅H₁₈Cl₂FNO [M+H]⁺ 438.0828, found 438.0833.



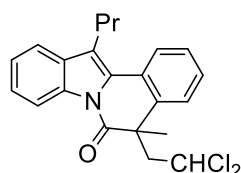
9-chloro-5-(2,2-dichloroethyl)-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (6j):

White solid, 57% isolated yield, 25.8 mg. mp: 186.7-188.4 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.59 (d, *J* = 8.7 Hz, 1H), 7.56 (m, *J* = 13.8, 6.9 Hz, 3H), 7.50 – 7.43 (m, 3H), 7.38 – 7.30 (m, 3H), 7.24 (d, *J* = 13.0 Hz, 1H), 7.07 (m, *J* = 8.4, 4.5 Hz, 1H), 5.36 (dd, *J* = 10.0, 3.7 Hz, 1H), 3.61 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.93 (dd, *J* = 14.8, 3.8 Hz, 1H), 1.76 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.8, 135.9, 133.7, 133.2, 132.5, 130.5, 130.3, 130.1, 129.4, 129.0, 128.5, 127.4, 126.1, 126.1, 125.9, 125.2, 119.9, 119.1, 117.9, 69.9, 53.2, 47.1, 31.1. GC-MS(EI): 452.9, 401.2, 383.8, 366.7, 356.0, 336.4, 320.9, 304.5, 291.0, 277.8, 214.9, 200.1, 186.9, 162.9, 150.9, 138.9, 127.7, 115.1, 96.9, 82.9, 77.0, 61.0, 50.9. HRMS (ESI, *m/z*): calcd for C₂₅H₁₈Cl₃NO [M+H]⁺ 454.0532, found 454.0526.



9-bromo-5-(2,2-dichloroethyl)-5-methyl-12-phenylindolo[2,1-a]isoquinolin-6(5H)-one (6k):

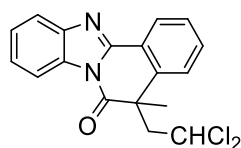
White solid, 76% isolated yield, 37.8 mg. mp: 189.1-192.2 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.54 (d, *J* = 8.7 Hz, 1H), 7.60 – 7.43 (m, 7H), 7.39 – 7.30 (m, 3H), 7.07 (m, *J* = 7.7, 5.8, 3.0 Hz, 1H), 5.36 (dd, *J* = 9.9, 3.8 Hz, 1H), 3.60 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.92 (dd, *J* = 14.8, 3.8 Hz, 1H), 1.76 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 171.8, 136.0, 134.1, 133.3, 132.9, 130.2, 130.1, 129.5, 129.0, 128.8, 128.5, 127.4, 126.2, 125.9, 125.2, 122.2, 119.8, 118.3, 118.3, 69.9, 53.3, 47.2, 31.1. GC-MS(EI): 497.0, 401.1, 322.1, 304.1, 291.1, 278.1, 265.1, 250.1, 239.1, 226.1, 216.1, 200.4, 189.1, 173.1, 160.1, 145.6, 132.5, 118.6, 99.0, 87.0, 77.0, 61.0, 51.0. HRMS (ESI, *m/z*): calcd for C₂₅H₁₈BrCl₂NO [M+H]⁺ 498.0027, found 498.0022



5-(2,2-dichloroethyl)-5-methyl-12-propylindolo[2,1-a]isoquinolin-6(5H)-one (6l):

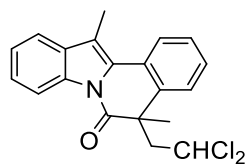
White solid, 72% isolated yield, 27.7 mg. mp: 124.7-129.5 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.71 – 8.55 (m, 1H), 8.01 (dd, *J* = 7.4, 1.4 Hz, 1H), 7.60 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.47 – 7.33 (m, 5H),

5.36 (dd, $J = 9.8, 3.9$ Hz, 1H), 3.59 (dd, $J = 14.8, 9.8$ Hz, 1H), 3.13 – 3.04 (m, 2H), 2.90 (dd, $J = 14.8, 3.9$ Hz, 1H), 1.87 – 1.77 (m, 2H), 1.71 (s, 3H), 1.13 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.5, 135.7, 134.4, 132.2, 128.7, 128.1, 127.8, 126.5, 126.4, 125.9, 125.1, 124.4, 120.3, 118.5, 117.0, 70.0, 53.2, 47.0, 31.2, 27.3, 22.2, 14.4. ^{19}F NMR (376 MHz, CDCl_3) δ -117.34. GC-MS(ED): 385.1, 356.1, 288.1, 260.1, 246.1, 230.1, 217.1, 202.1, 189.1, 176.1, 143.6, 127.1, 115.1, 102.1, 77.1, 62.0, 51.1. HRMS (ESI, m/z): calcd for $\text{C}_{22}\text{H}_{21}\text{Cl}_2\text{NO}$ $[\text{M}+\text{H}]^+$ 386.1078, found 386.1073.



5-(2,2-dichloroethyl)-5-methylbenzo[4,5]imidazo[2D,1-a]isoquinolin-6(5H)-one (6m):

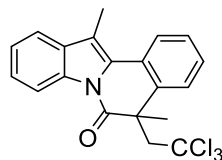
Colorless oil, 70% isolated yield, 24 mg. ^1H NMR (400 MHz, CDCl_3) δ 8.54 (dd, $J = 7.9, 1.4$ Hz, 1H), 8.41 – 8.35 (m, 1H), 7.86 – 7.80 (m, 1H), 7.63 (m, $J = 7.6, 1.5$ Hz, 1H), 7.55 (m, $J = 7.6, 1.2$ Hz, 1H), 7.48 – 7.42 (m, 3H), 5.30 (dd, $J = 10.3, 3.6$ Hz, 1H), 3.63 (dd, $J = 14.9, 10.4$ Hz, 1H), 3.00 (dd, $J = 14.9, 3.7$ Hz, 1H), 1.75 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.7, 149.1, 143.9, 138.5, 132.0, 131.4, 128.5, 126.6, 126.0, 125.9, 125.8, 123.2, 119.9, 115.8, 69.5, 52.7, 47.8, 31.3. GC-MS(ED): 344.1, 247.1, 219.2, 190.1, 165.1, 140.1, 128.1, 115.1, 102.1, 90.1, 77.1, 61.0, 51.1. HRMS(ESI, m/z): calcd for $\text{C}_{18}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$ 345.0561, found 345.0570.



5-(2,2-dichloroethyl)-5,12-dimethylindolo[2,1-a]isoquinolin-6(5H)-one (6n):

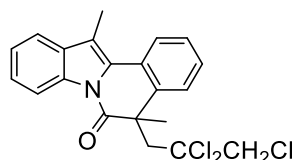
White solid, 73% isolated yield, 26 mg. mp: 112.9-114.6 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.77 – 8.62 (m, 1H), 8.18 – 8.07 (m, 1H), 7.67 – 7.62 (m, 1H), 7.53 – 7.39 (m, 5H), 5.42 (dd, $J = 9.8, 3.9$ Hz, 1H), 3.65 (dd, $J = 14.8, 9.9$ Hz, 1H), 2.96 (dd, $J = 14.8, 3.9$ Hz, 1H), 2.71 (s, 3H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 171.4, 135.7, 134.2, 132.3, 129.1, 128.0, 127.7, 126.7, 126.4, 125.9, 125.4, 124.4, 118.4, 116.9, 114.9, 70.0, 53.0, 47.1, 31.3, 11.6. GC-MS(ED): 357.0, 271.1,

260.1, 245.1, 232.1, 217.1, 202.1, 130.1, 120.6, 108.5, 97.0, 88.0, 77.0, 61.0, 51.0. HRMS (ESI, m/z): calcd for $C_{20}H_{17}Cl_2NO$ $[M+H]^+$ 358.0765, found 358.0763.



5,12-dimethyl-5-(2,2,2-trichloroethyl)indolo[2,1-a]isoquinolin-6(5H)-one (6o):

White solid, 69% isolated yield, 27.0 mg. mp: 178.4-180.2 °C. 1H NMR (400 MHz, $CDCl_3$) δ 8.71 – 8.51 (m, 1H), 8.14 – 7.94 (m, 1H), 7.65 – 7.56 (m, 1H), 7.52 (dd, $J = 7.9, 1.4$ Hz, 1H), 7.45 – 7.31 (m, 4H), 4.09 (d, $J = 15.2$ Hz, 1H), 3.45 (d, $J = 15.2$ Hz, 1H), 2.67 (s, 3H), 1.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 134.6, 134.3, 132.5, 129.5, 128.4, 127.7, 127.2, 126.9, 125.8, 125.1, 124.4, 118.4, 116.9, 114.8, 96.1, 63.4, 47.7, 31.6, 11.6. GC-MS(EI): 391.0, 294.1, 279.0, 266.1, 251.0, 230.1, 216.1, 202.1, 189.1, 147.3, 114.1, 102.0, 88.0, 77.0, 61.0, 51.0. HRMS (ESI, m/z): calcd for $C_{20}H_{16}Cl_3NO$ $[M+H]^+$ 392.0376, found 392.0382.

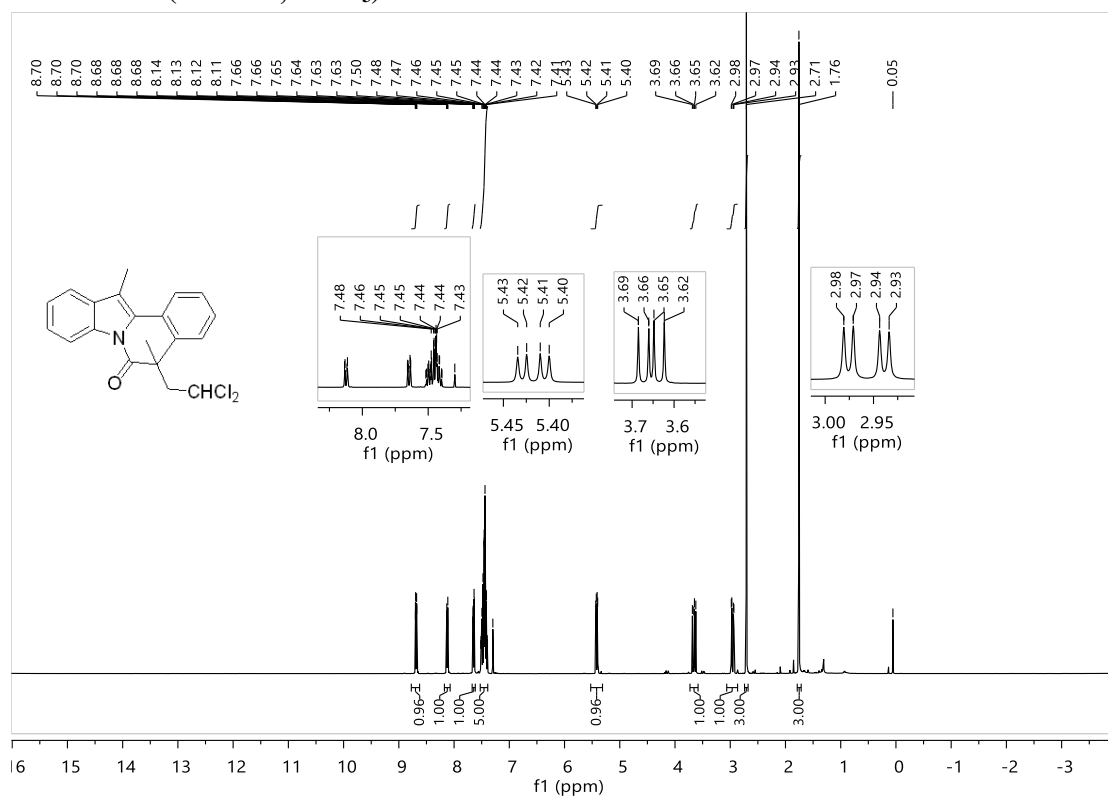


5,12-dimethyl-5-(2,2,3-trichloropropyl)indolo[2,1-a]isoquinolin-6(5H)-one (6p):

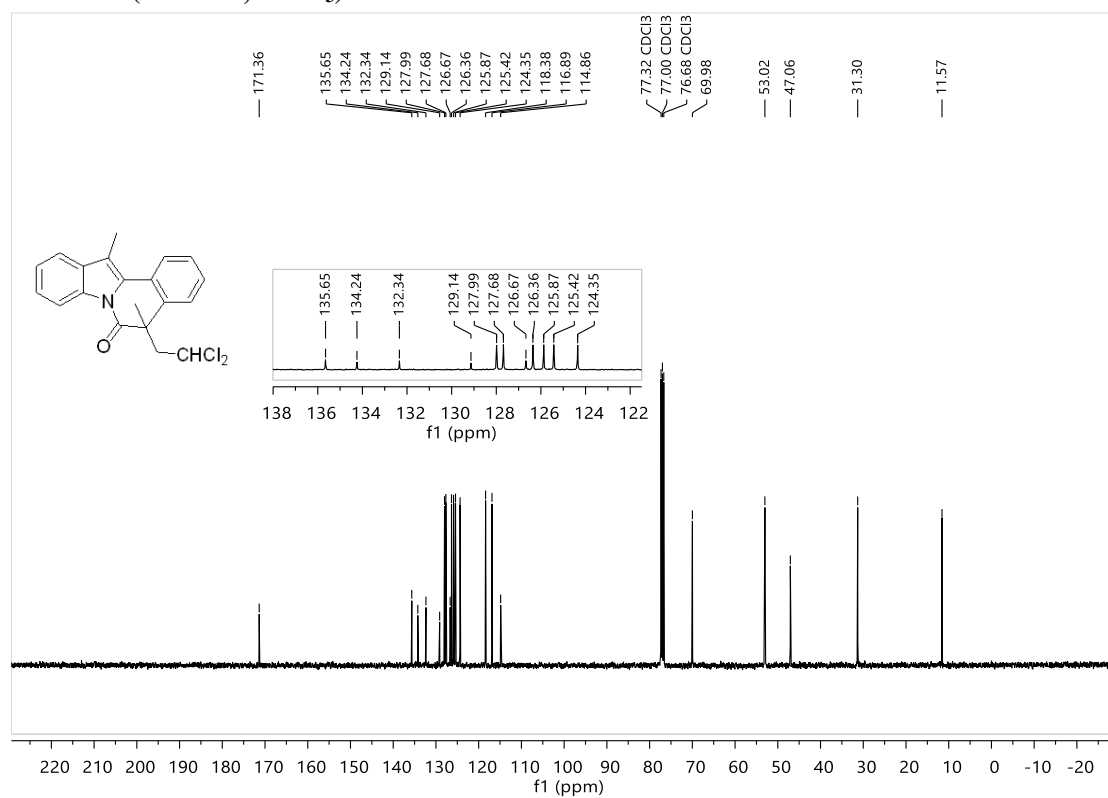
Colorless oil. 63% isolated yield, 25.6 mg. 1H NMR (400 MHz, $CDCl_3$) δ 8.75 – 8.51 (m, 1H), 8.07 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.62 – 7.54 (m, 2H), 7.45 (td, $J = 7.6, 1.5$ Hz, 1H), 7.38 (td, $J = 7.3, 1.5$ Hz, 3H), 3.91 – 3.50 (m, 2H), 3.35 – 2.98 (m, 2H), 2.67 (s, 3H), 1.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 135.2, 134.3, 132.4, 129.3, 128.0, 127.8, 127.3, 126.5, 125.9, 125.1, 124.4, 118.4, 117.0, 114.8, 87.8, 55.0, 52.2, 47.4, 32.2, 11.6. GC-MS(EI): 404.9, 260.0, 245.0, 230.1, 217.0, 202.0, 188.9, 176.0, 139.0, 128.0, 109.0, 95.9, 84.9, 75.0, 63.0, 51.0. HRMS(ESI, m/z): calcd for $C_{21}H_{18}Cl_3NO$ $[M+H]^+$ 406.0532, found 406.0527.

3. ^1H NMR and ^{13}C NMR Spectra for Products

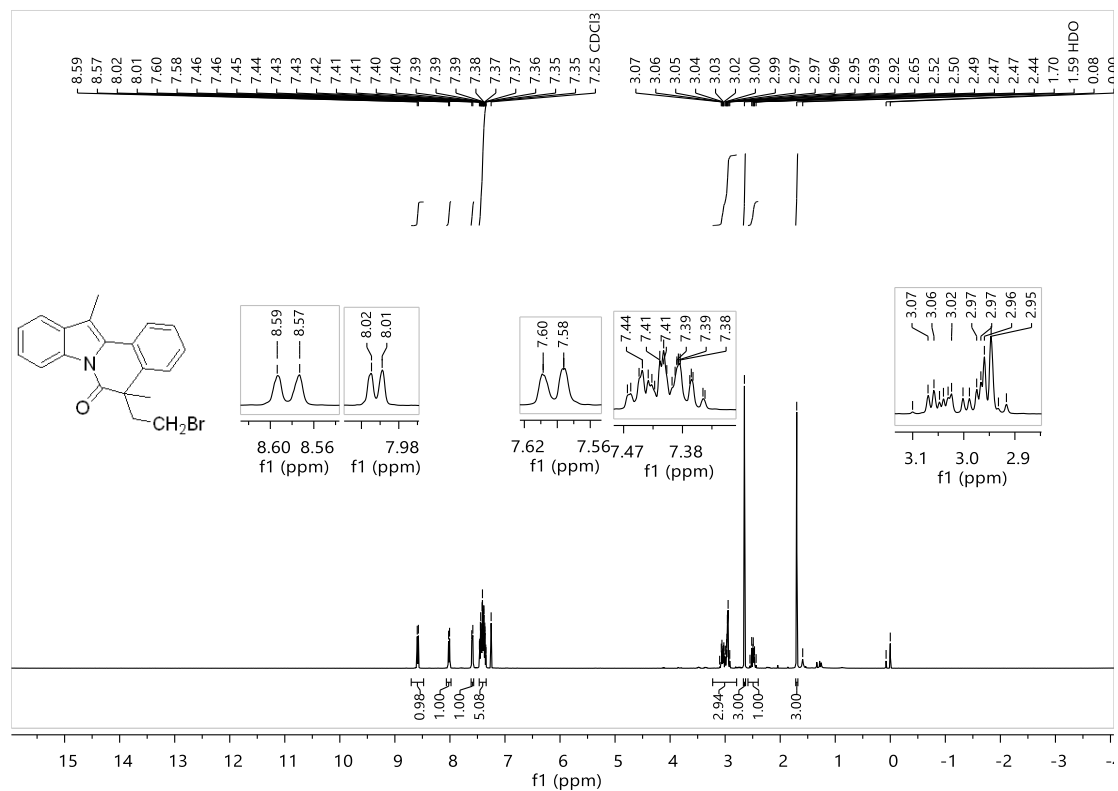
3a: ^1H NMR (400MHz, CDCl_3)



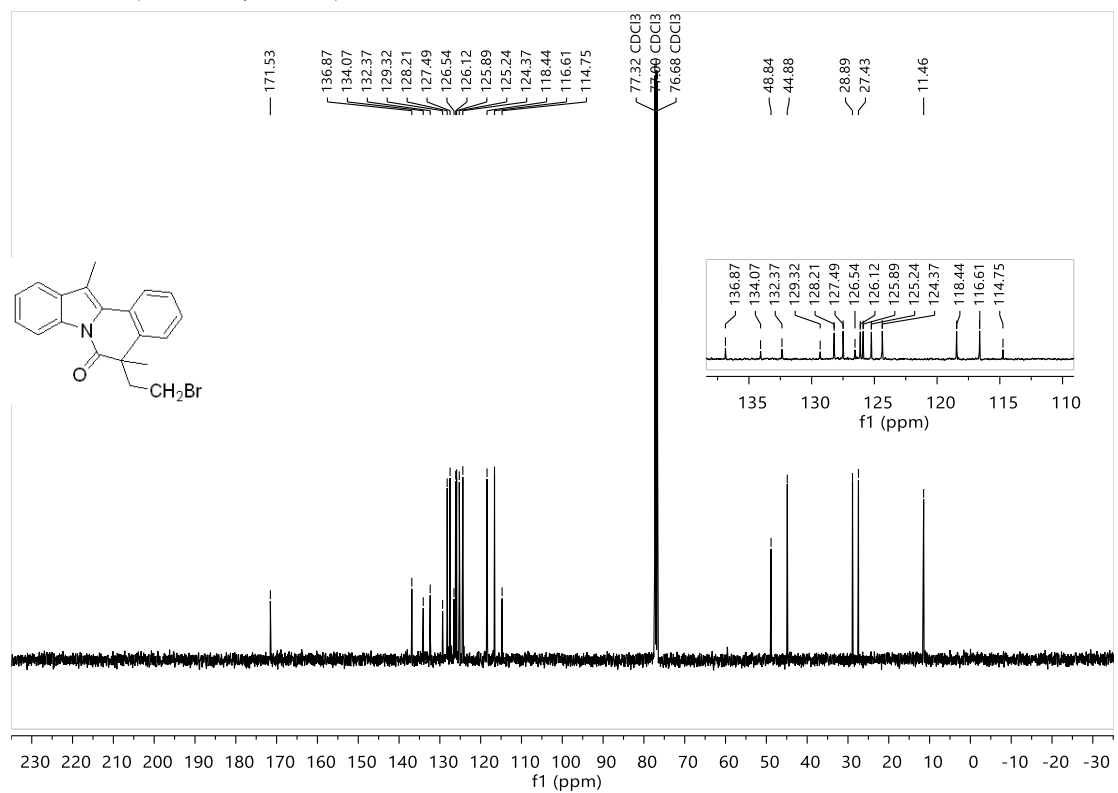
^{13}C NMR (101MHz, CDCl_3)



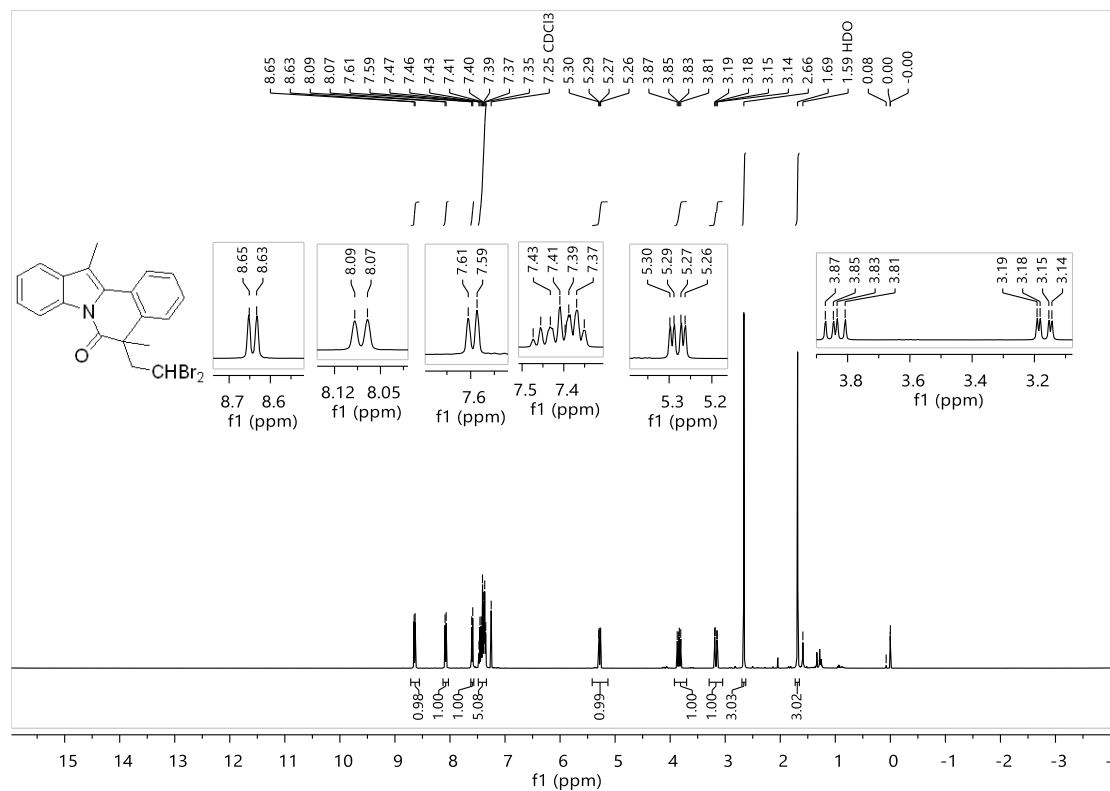
3b: ¹H NMR (400MHz, CDCl₃)



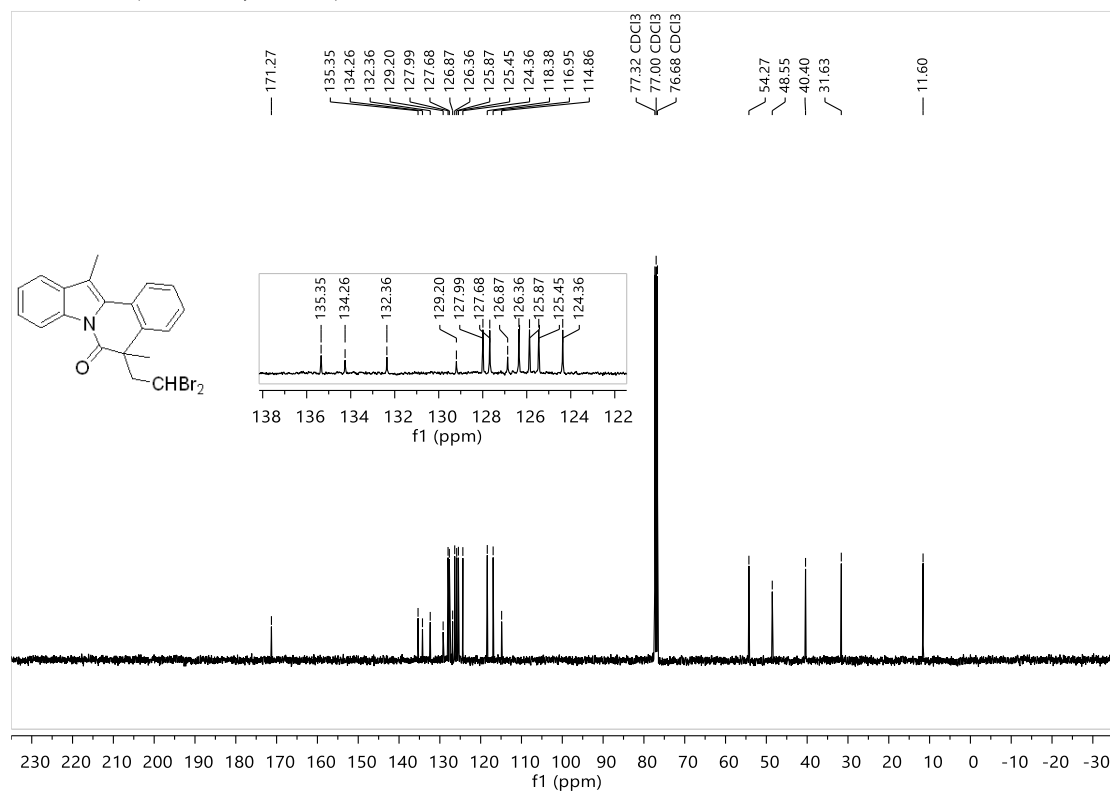
¹³C NMR (101MHz, CDCl₃)



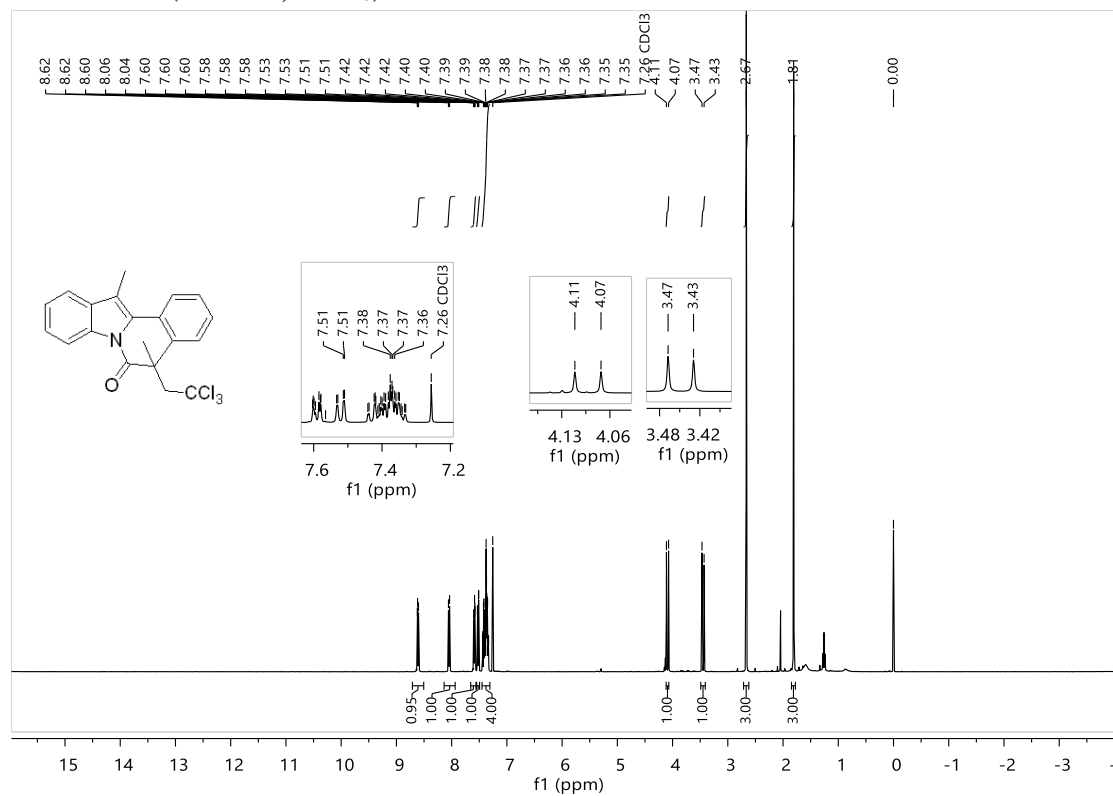
3c: ^1H NMR (400MHz, CDCl_3)



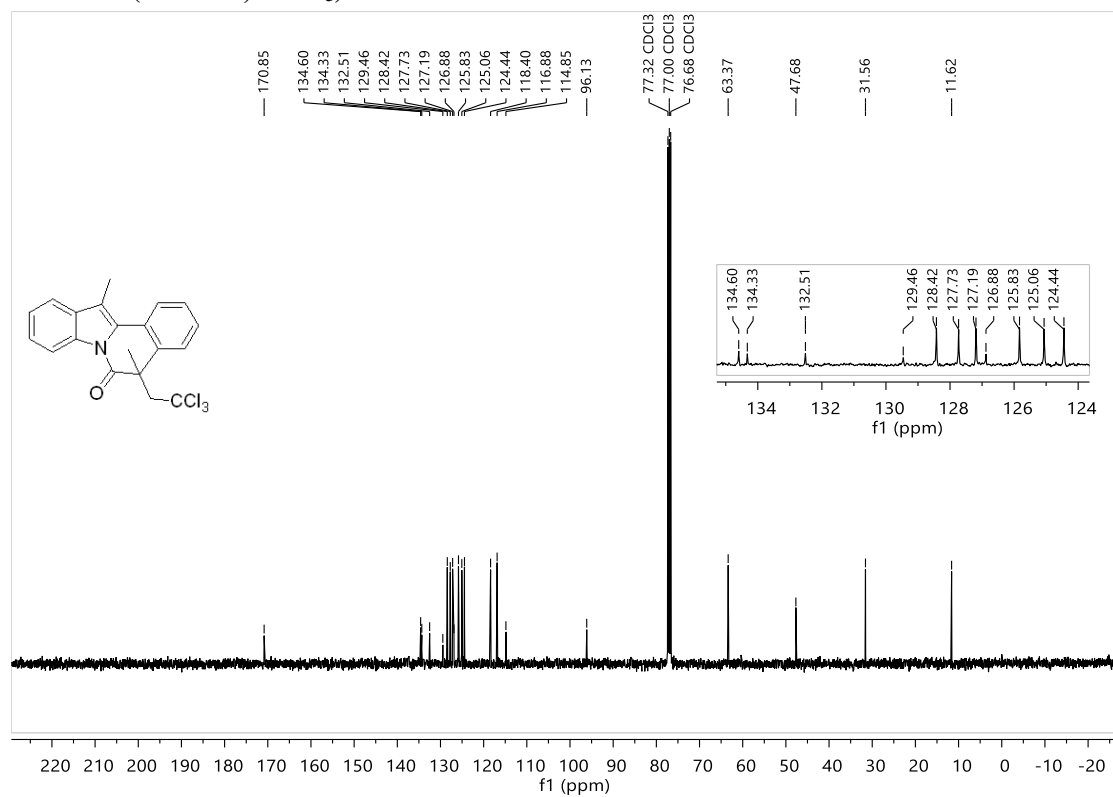
^{13}C NMR (101MHz, CDCl_3)



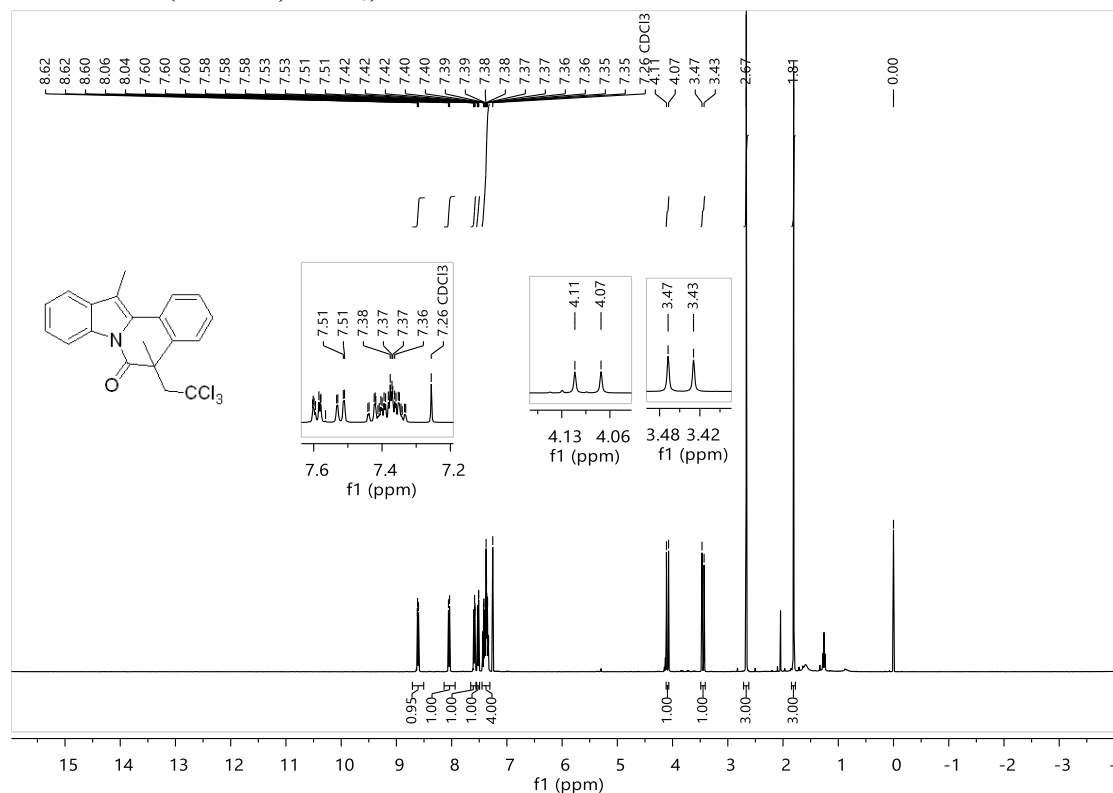
3d: ^1H NMR (400MHz, CDCl_3)



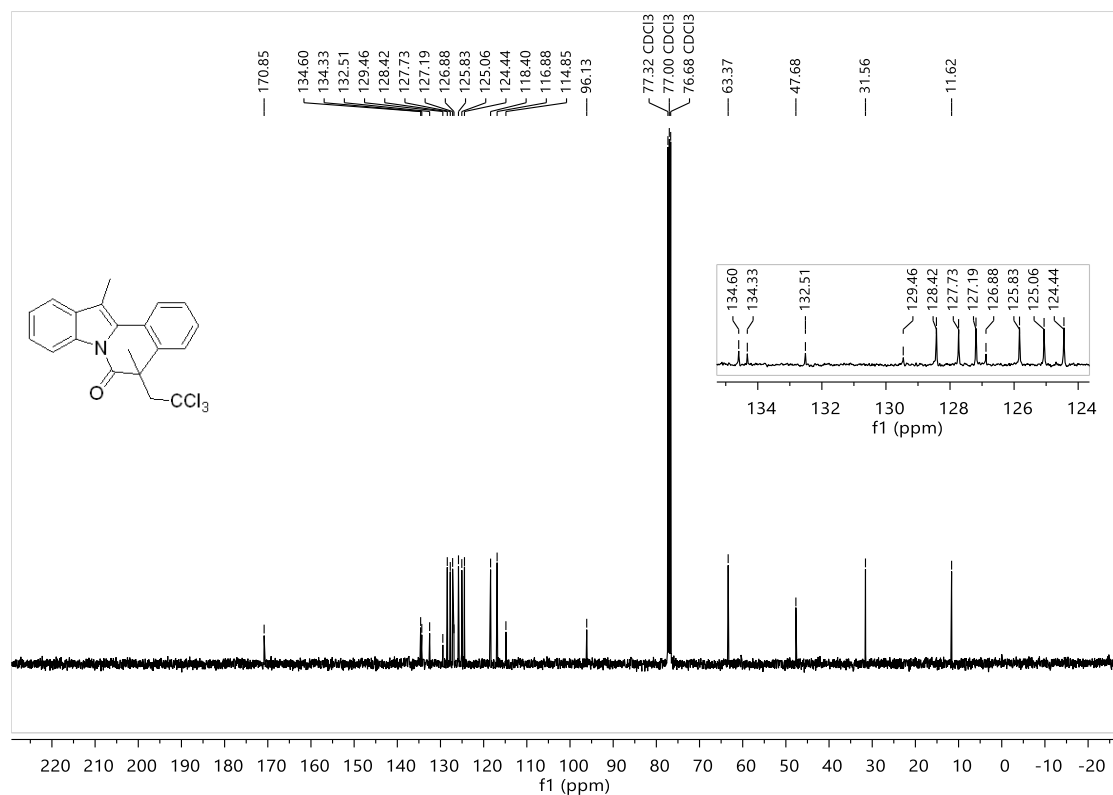
^{13}C NMR (101MHz, CDCl_3)



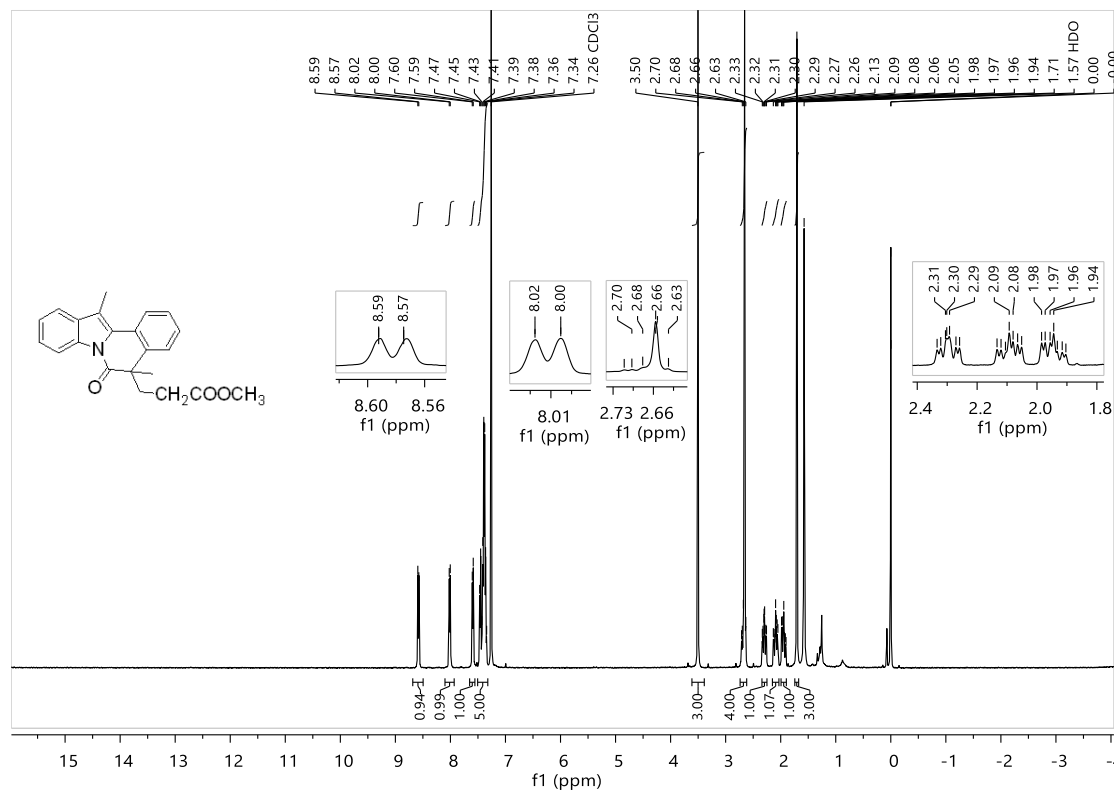
3e: ^1H NMR (400MHz, CDCl_3)



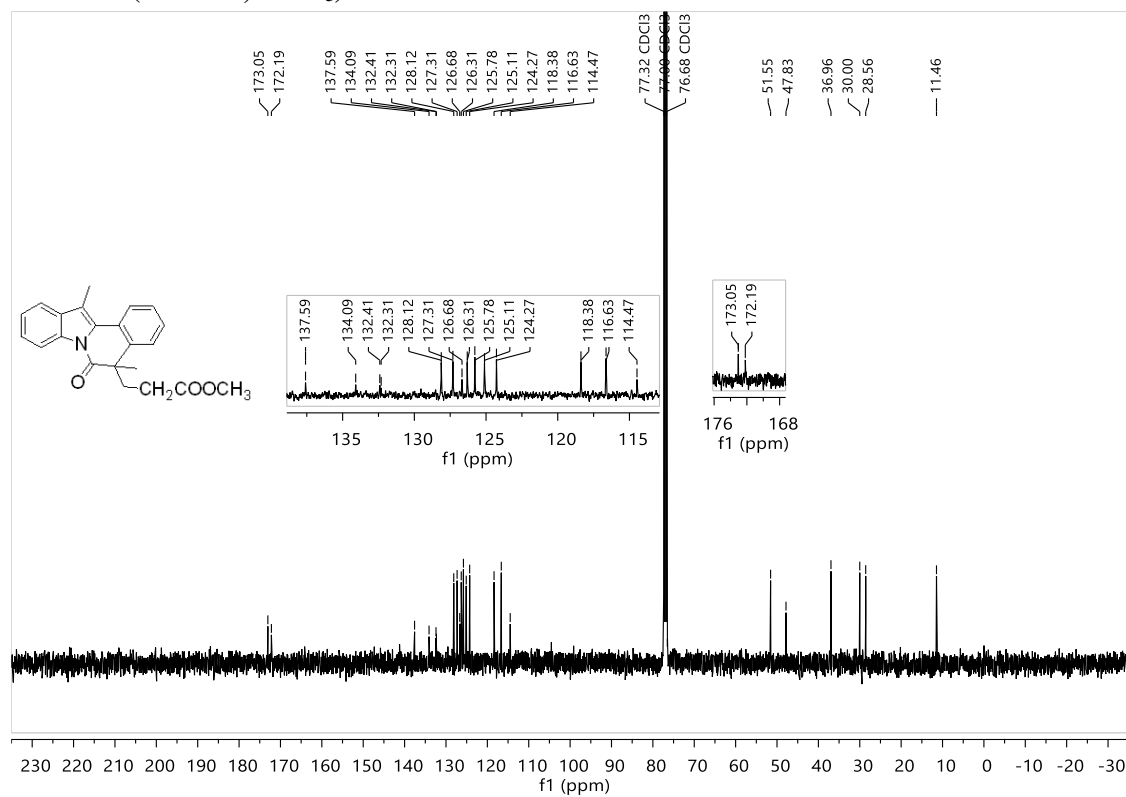
^{13}C NMR (101MHz, CDCl_3)



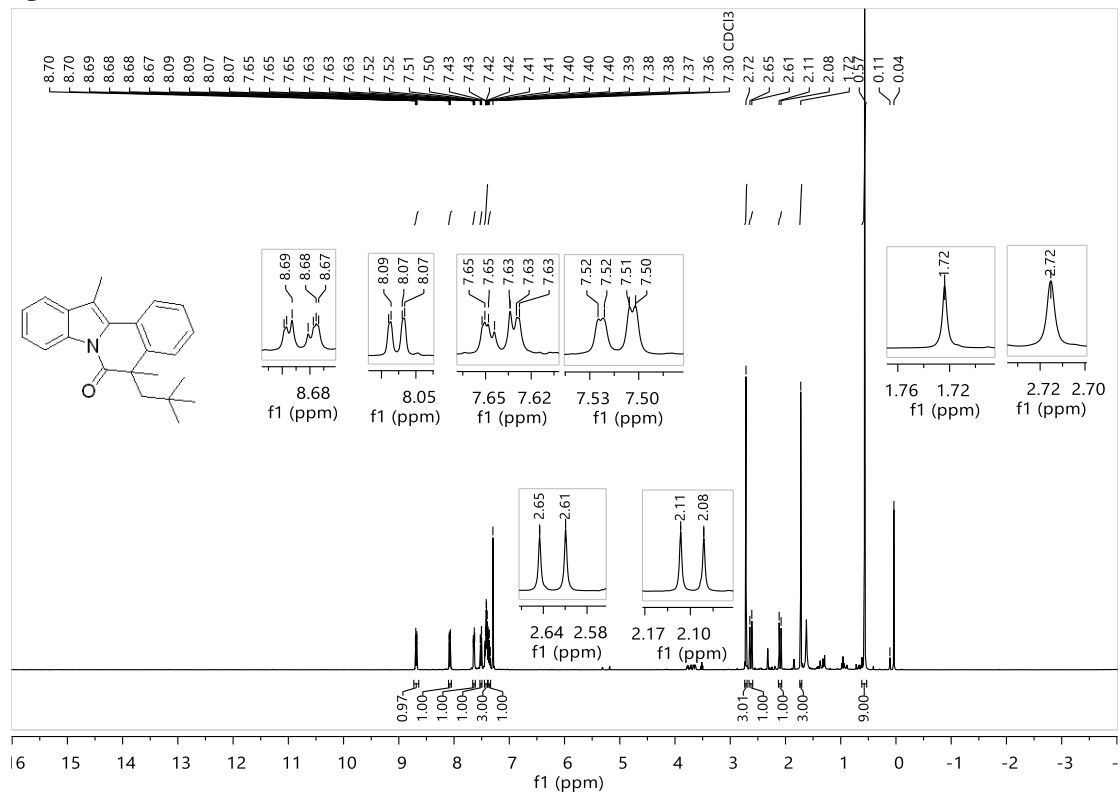
3f: ¹H NMR (400MHz, CDCl₃)



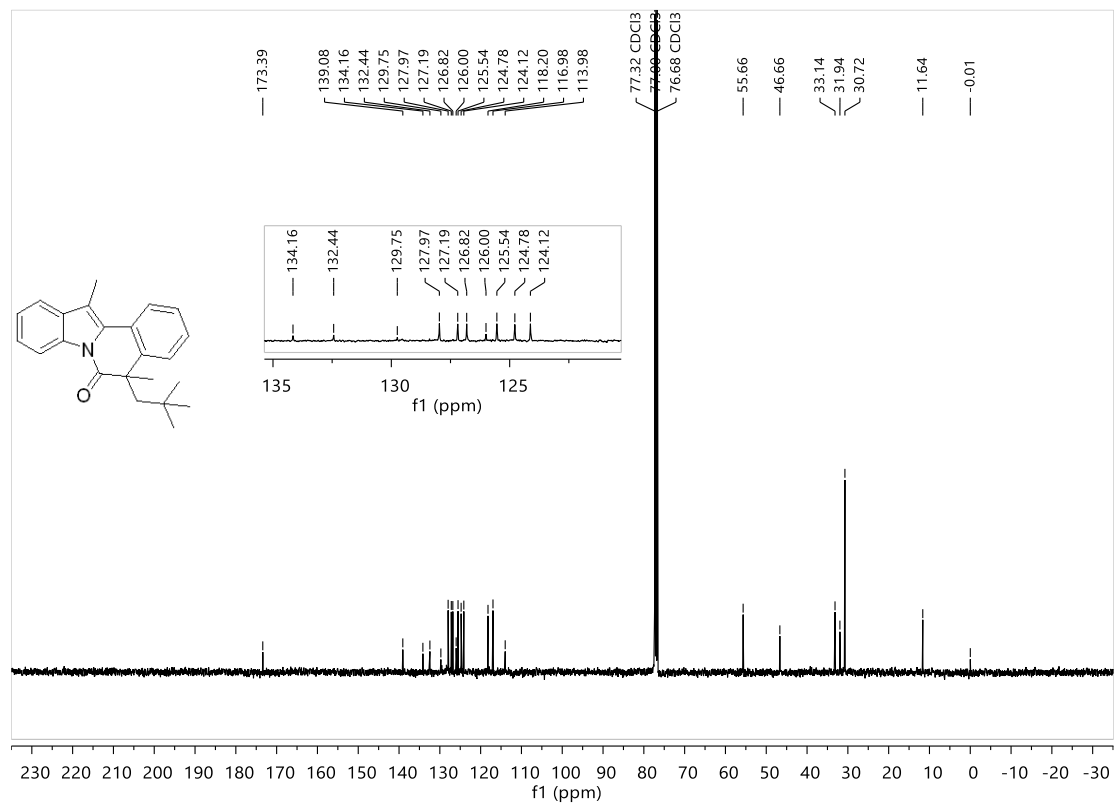
¹³C NMR (101MHz, CDCl₃)



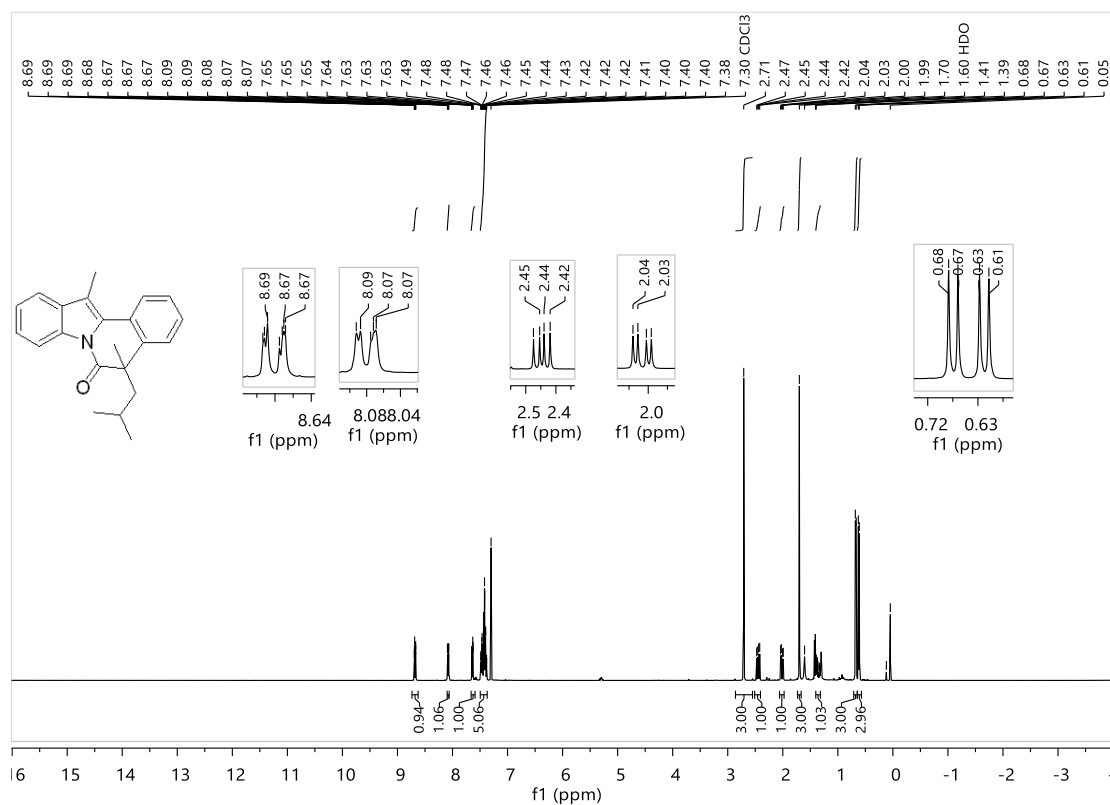
3g: ¹H NMR (400MHz, CDCl₃)



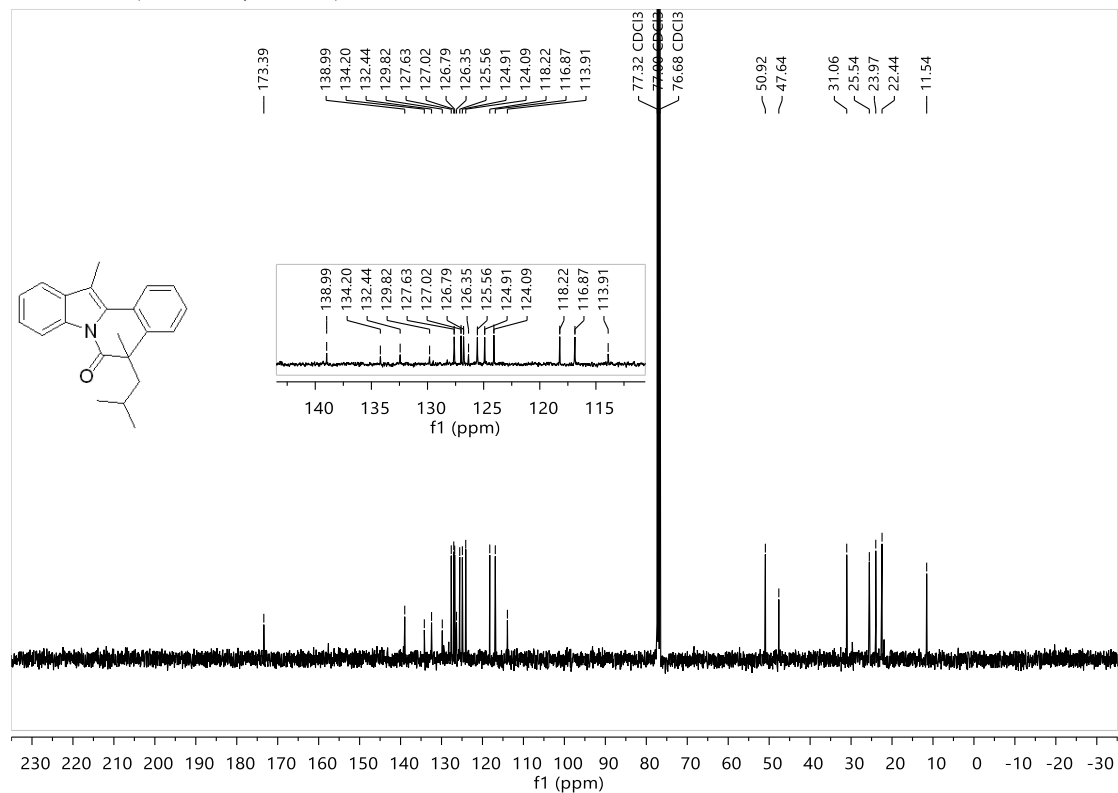
¹³C NMR (101MHz, CDCl₃)



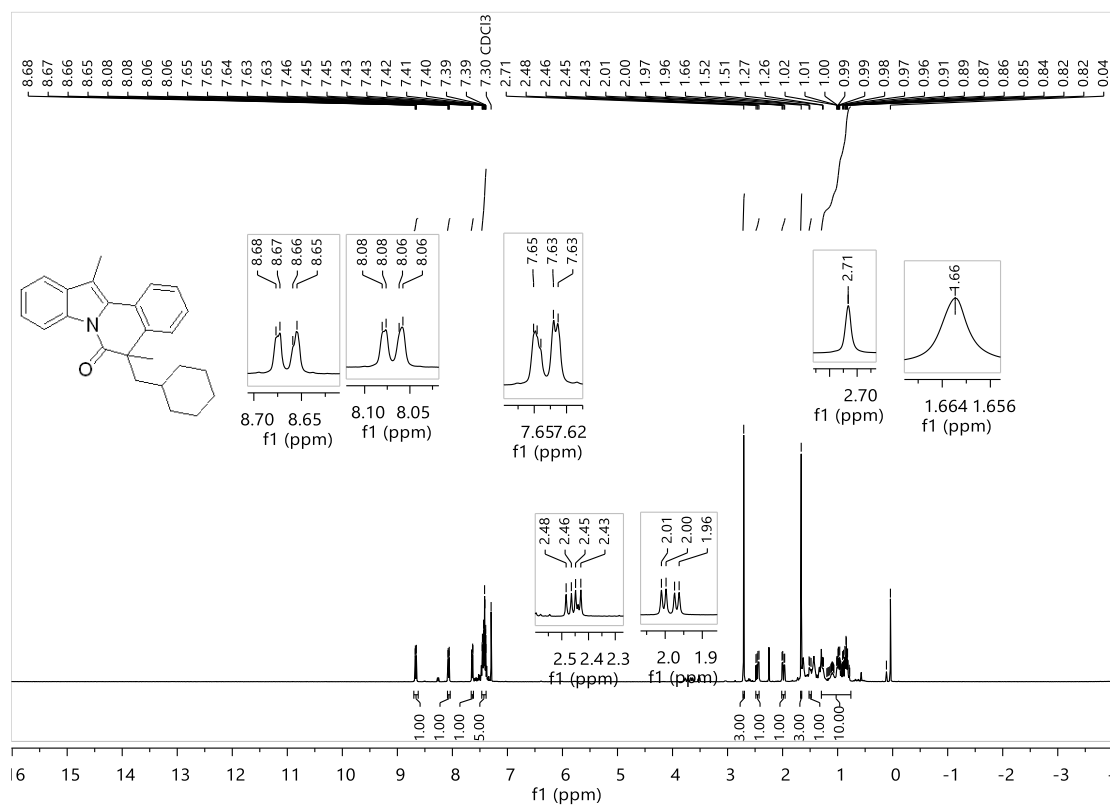
3h: ¹H NMR (400MHz, CDCl₃)



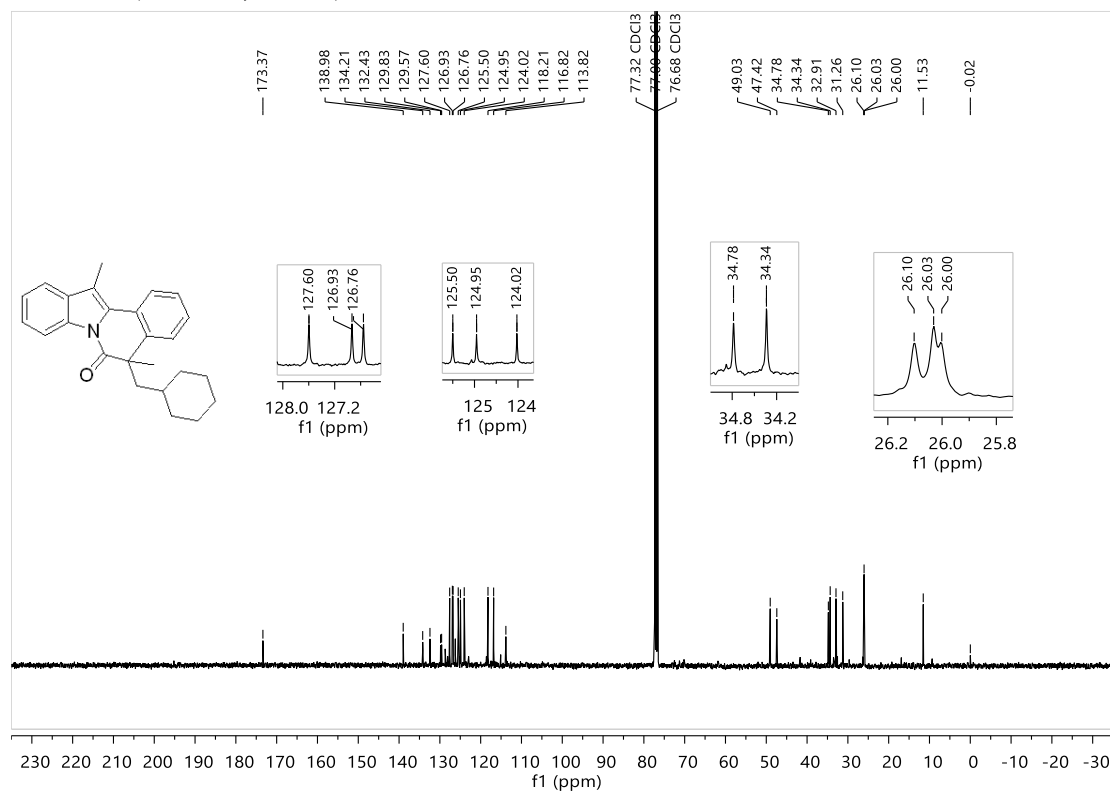
¹³C NMR (101MHz, CDCl₃)



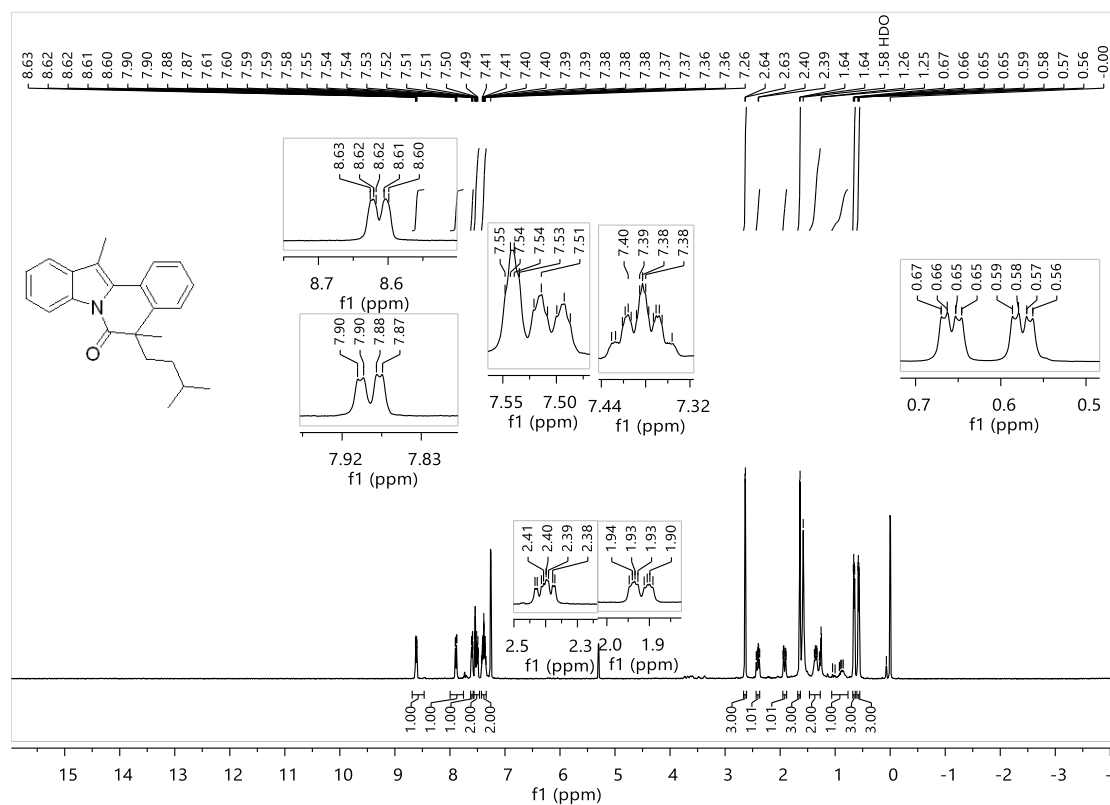
3i: ¹H NMR (400MHz, CDCl₃)



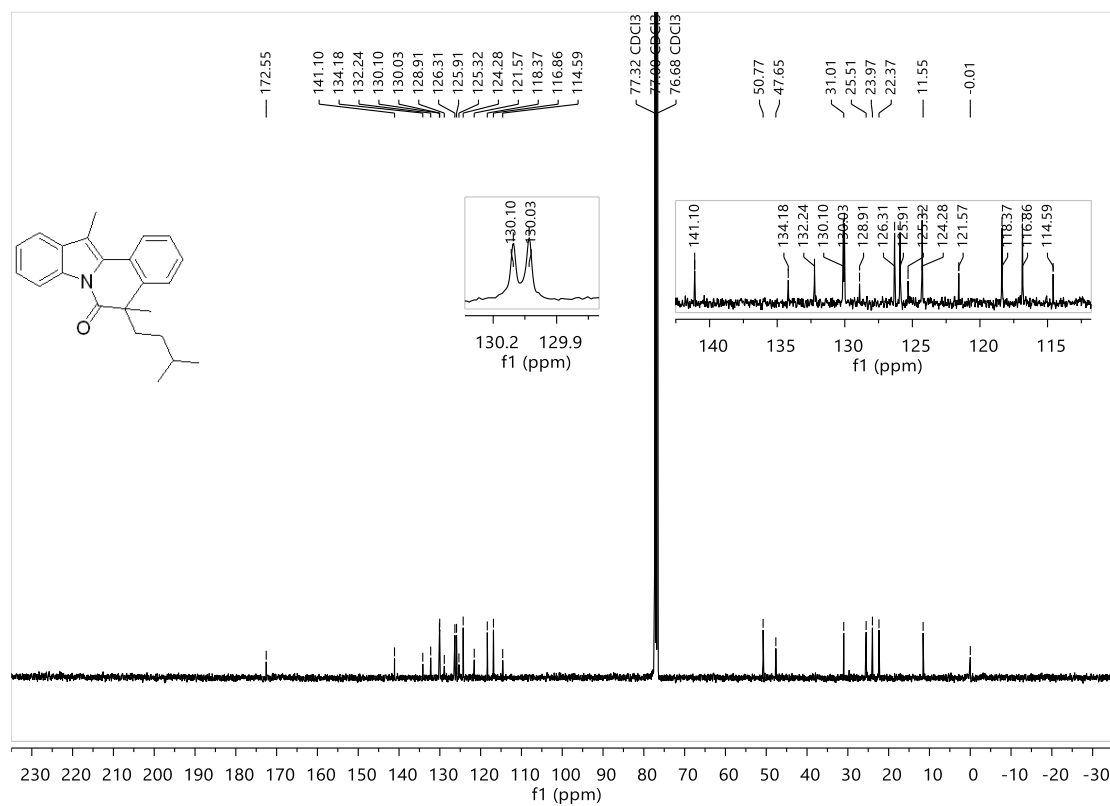
¹³C NMR (101MHz, CDCl₃)



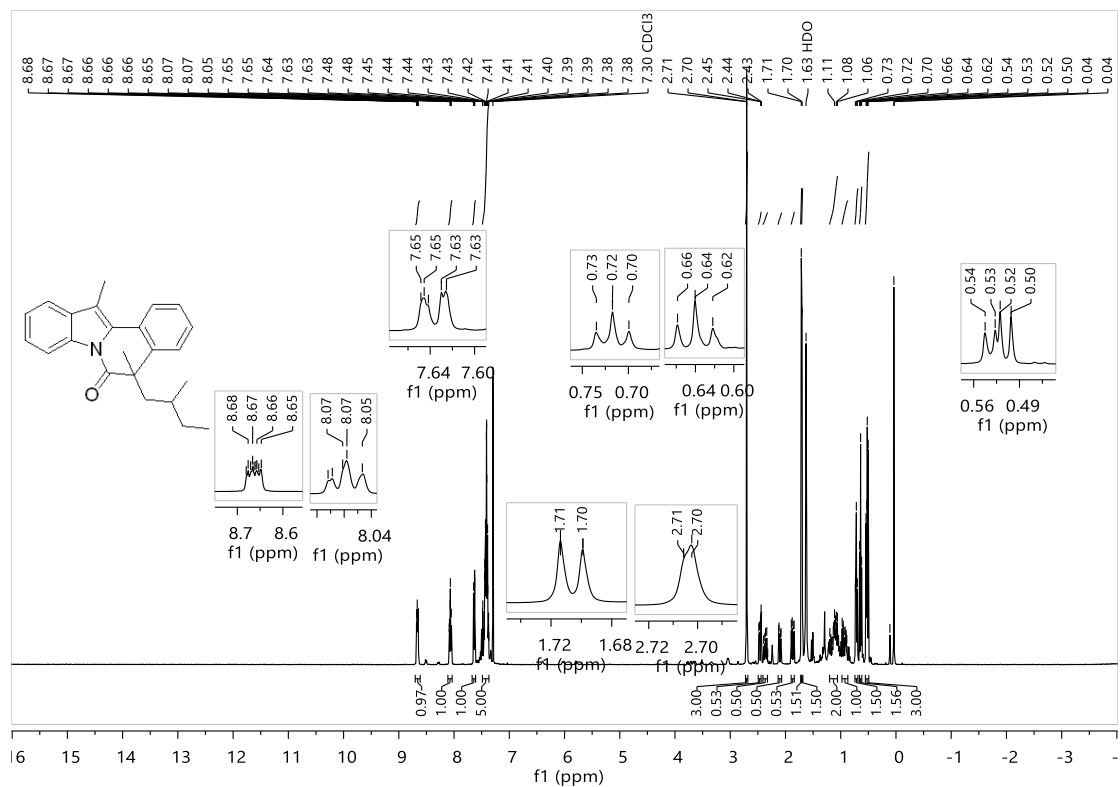
3j: ¹H NMR (400MHz, CDCl₃)



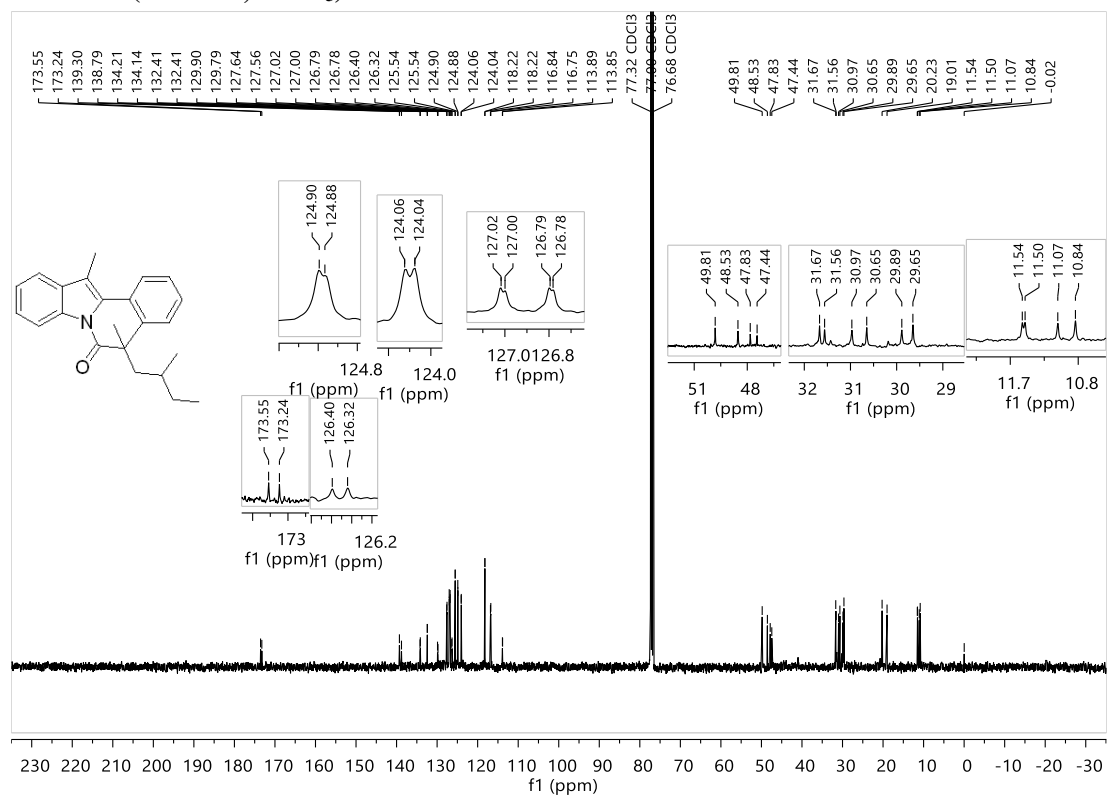
¹³C NMR (101MHz, CDCl₃)



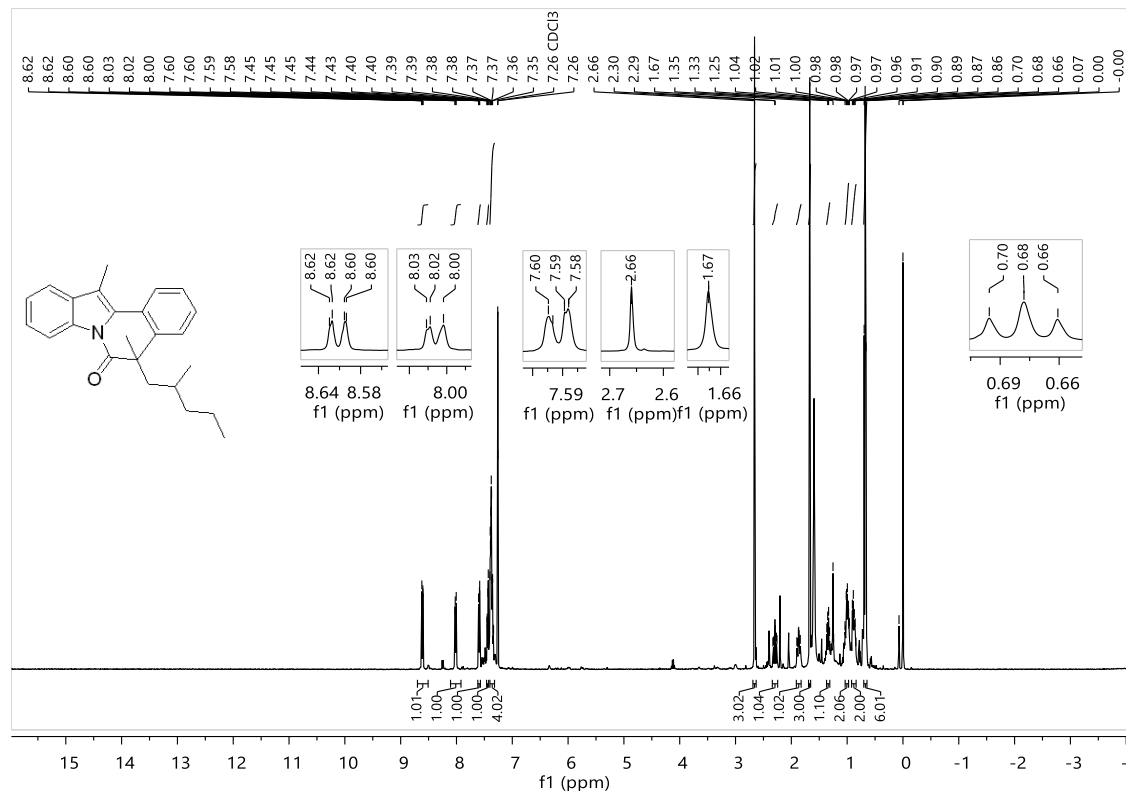
3k: ¹H NMR (400MHz, CDCl₃)



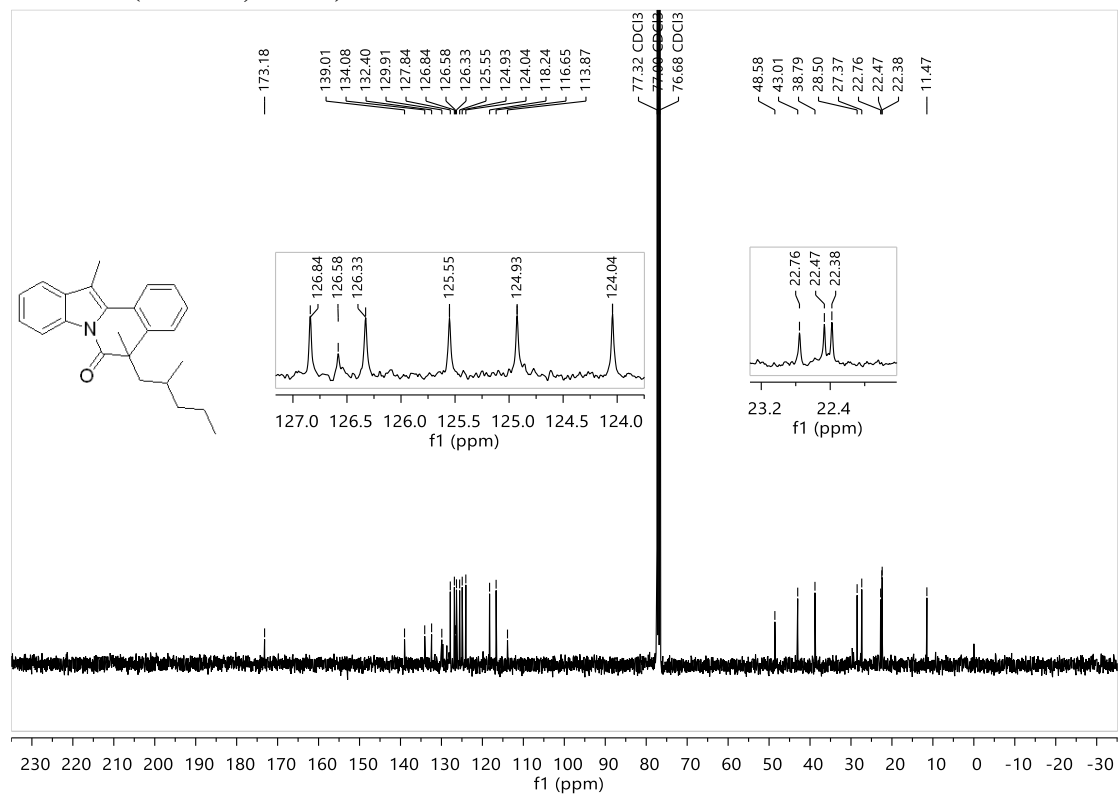
¹³C NMR (101MHz, CDCl₃)



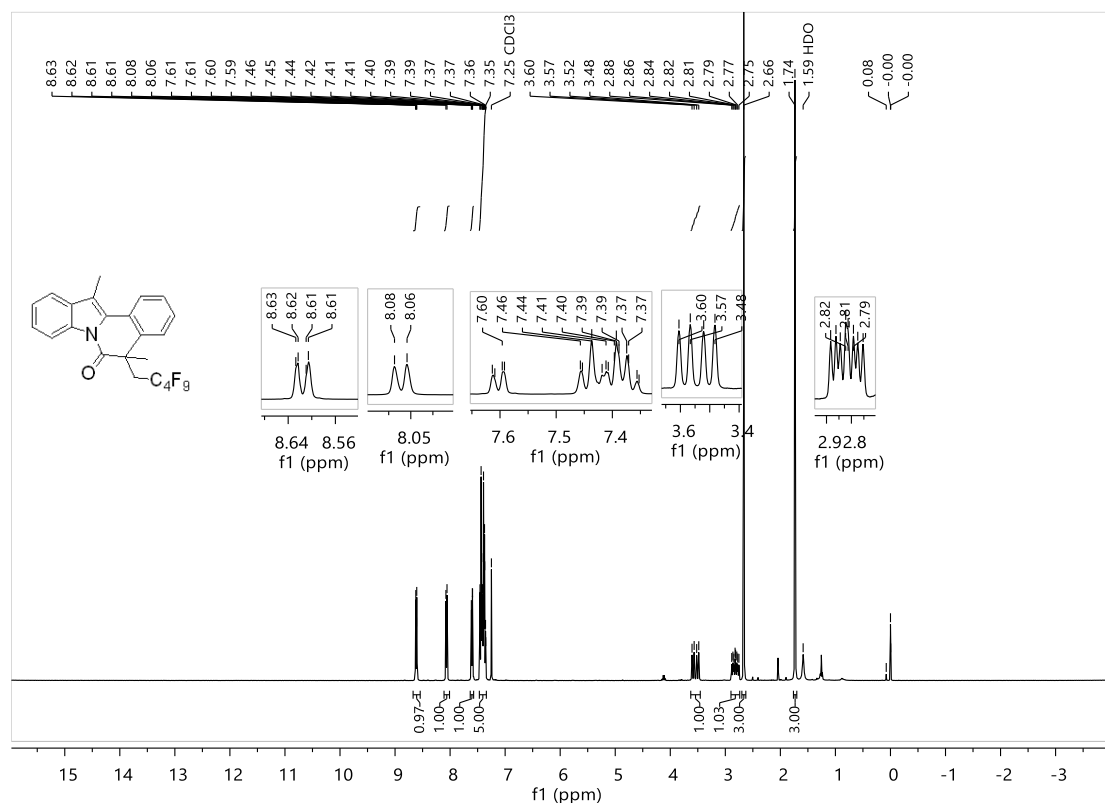
3l: ¹H NMR (400MHz, CDCl₃)



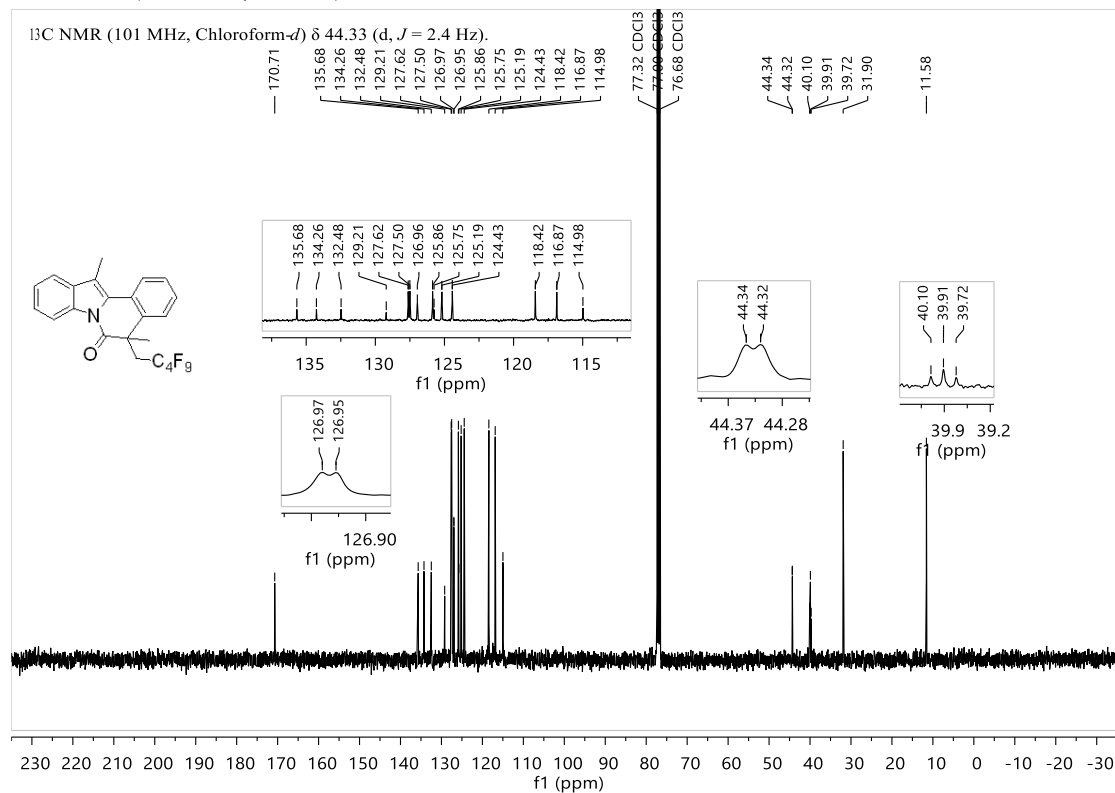
3l: ¹³C NMR (101MHz, CDCl₃)



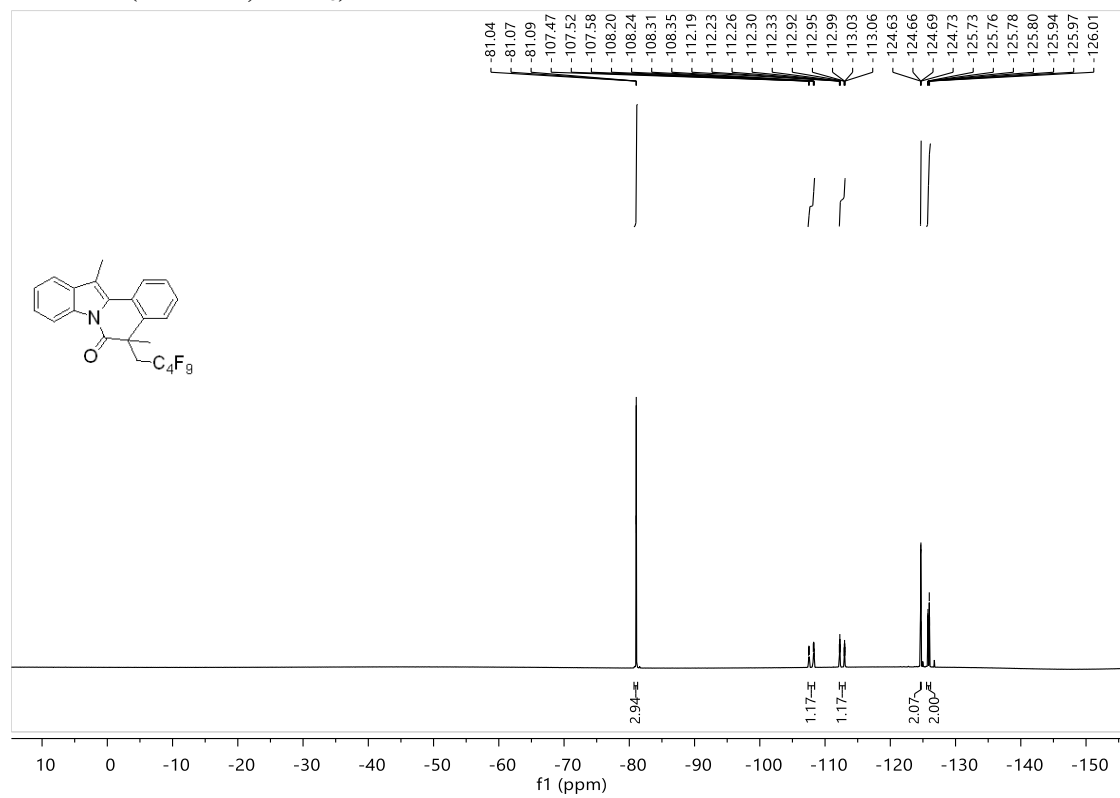
3m: ¹H NMR (400MHz, CDCl₃)



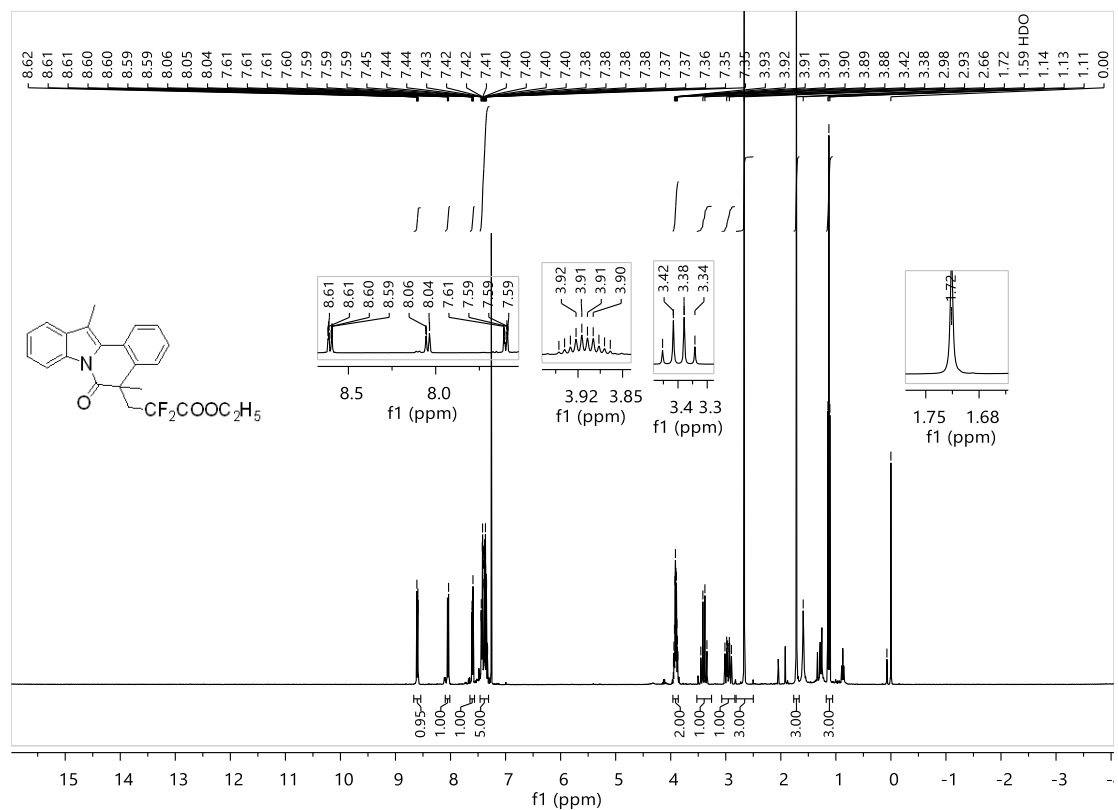
¹³C NMR (101MHz, CDCl₃)



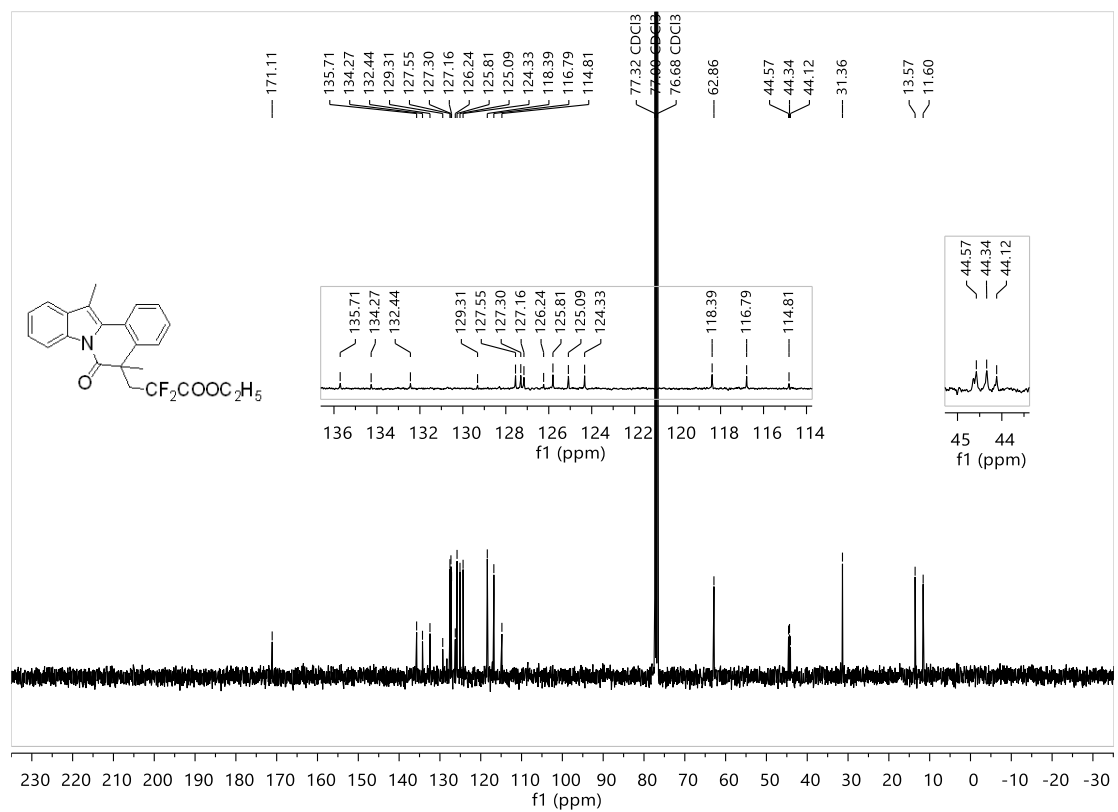
¹⁹F NMR (376 MHz, CDCl₃)



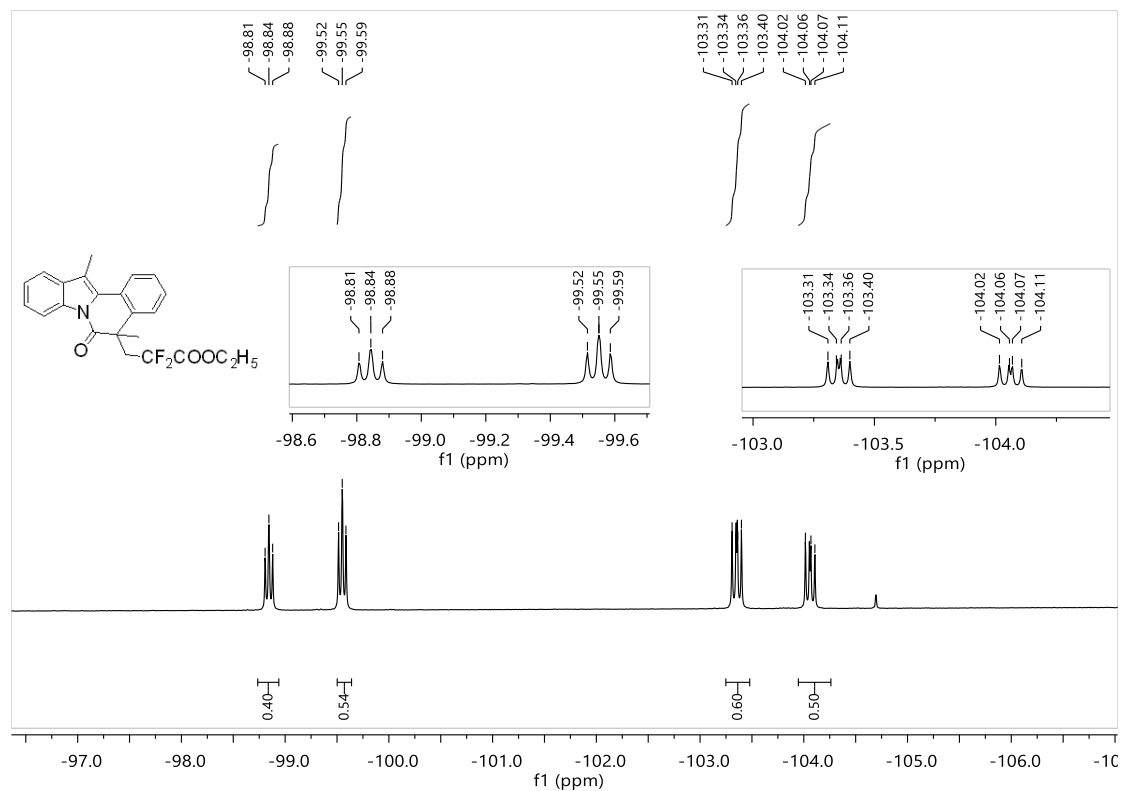
3n: ¹H NMR (400MHz, CDCl₃)



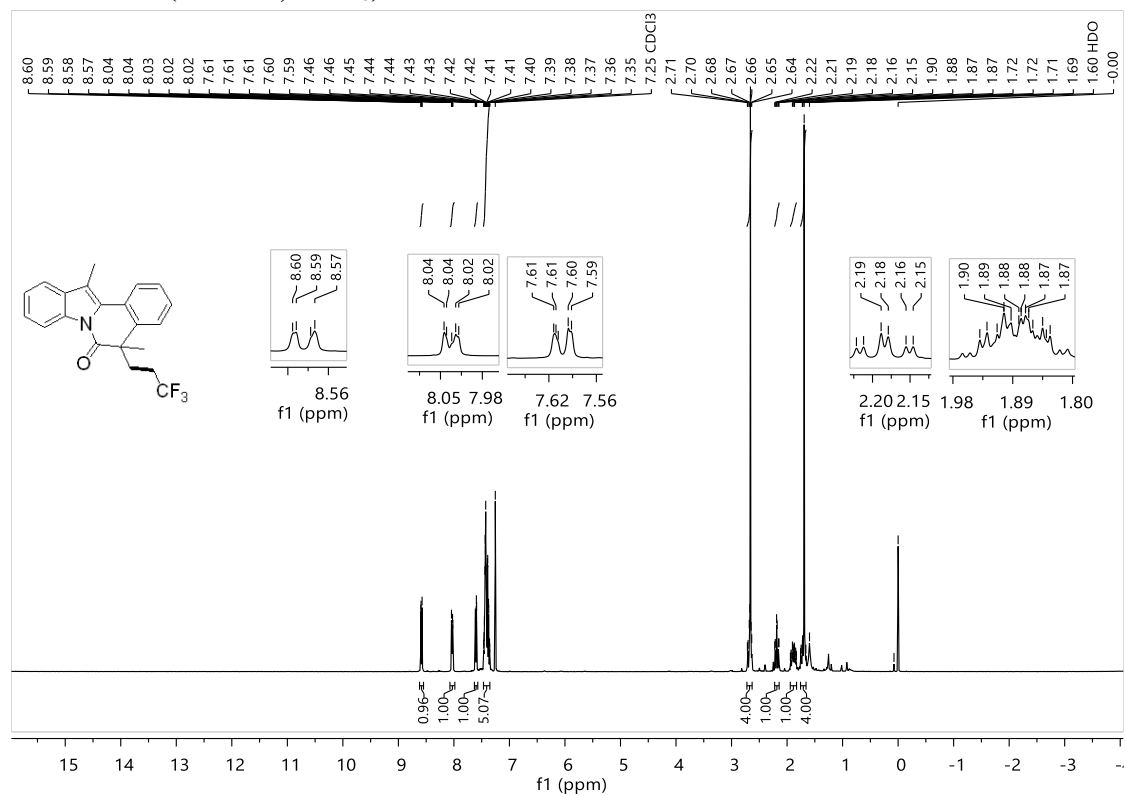
¹³C NMR (101MHz, CDCl₃)



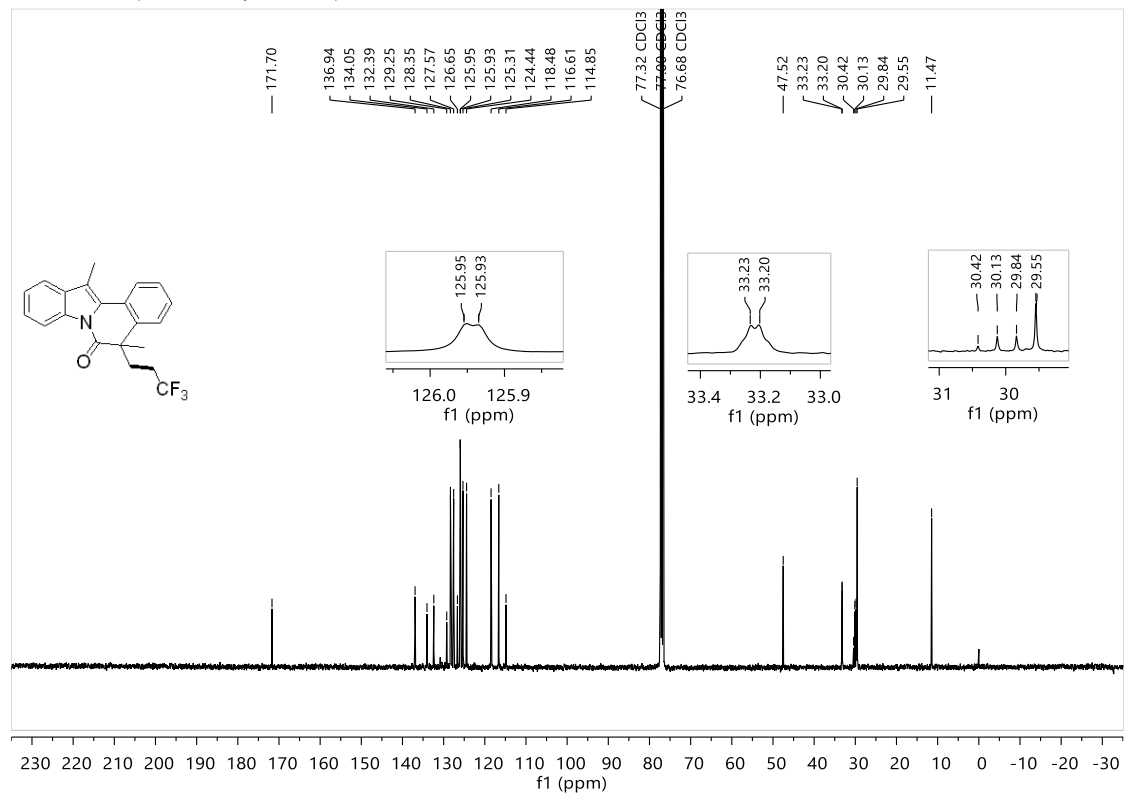
¹⁹F NMR (376MHz, CDCl₃)



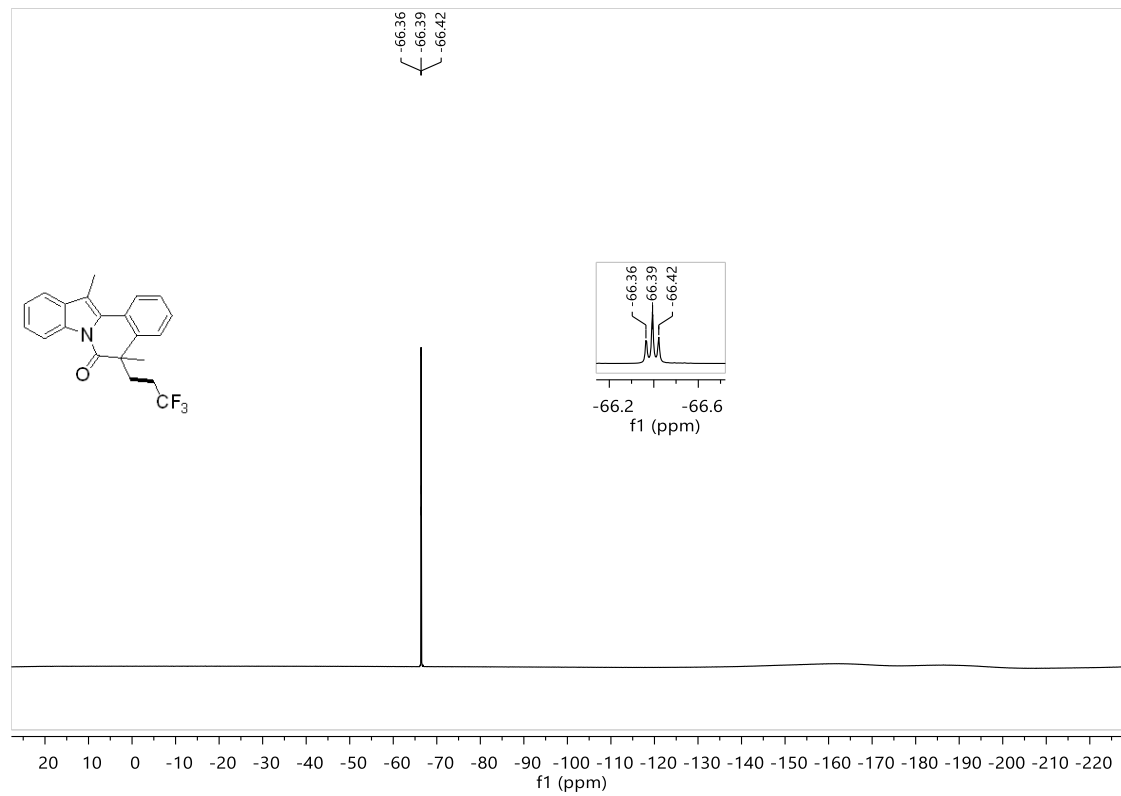
3o: ¹H NMR (400MHz, CDCl₃)



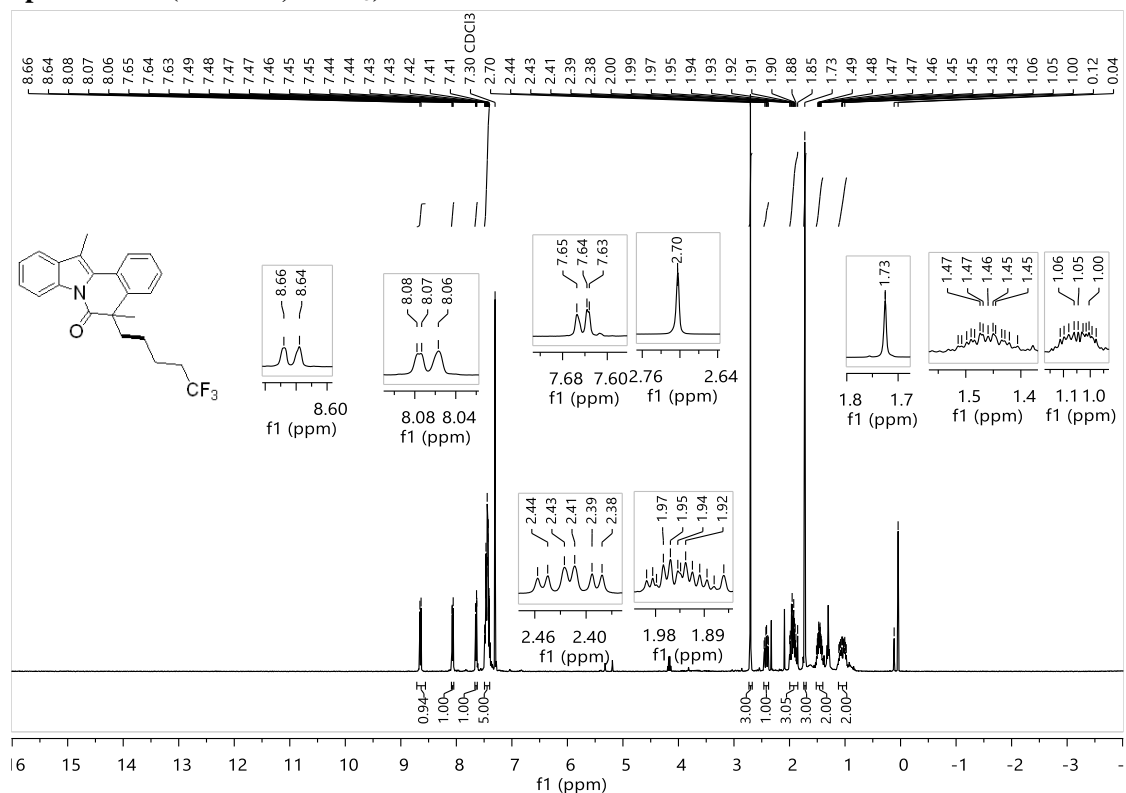
¹³C NMR (101MHz, CDCl₃)



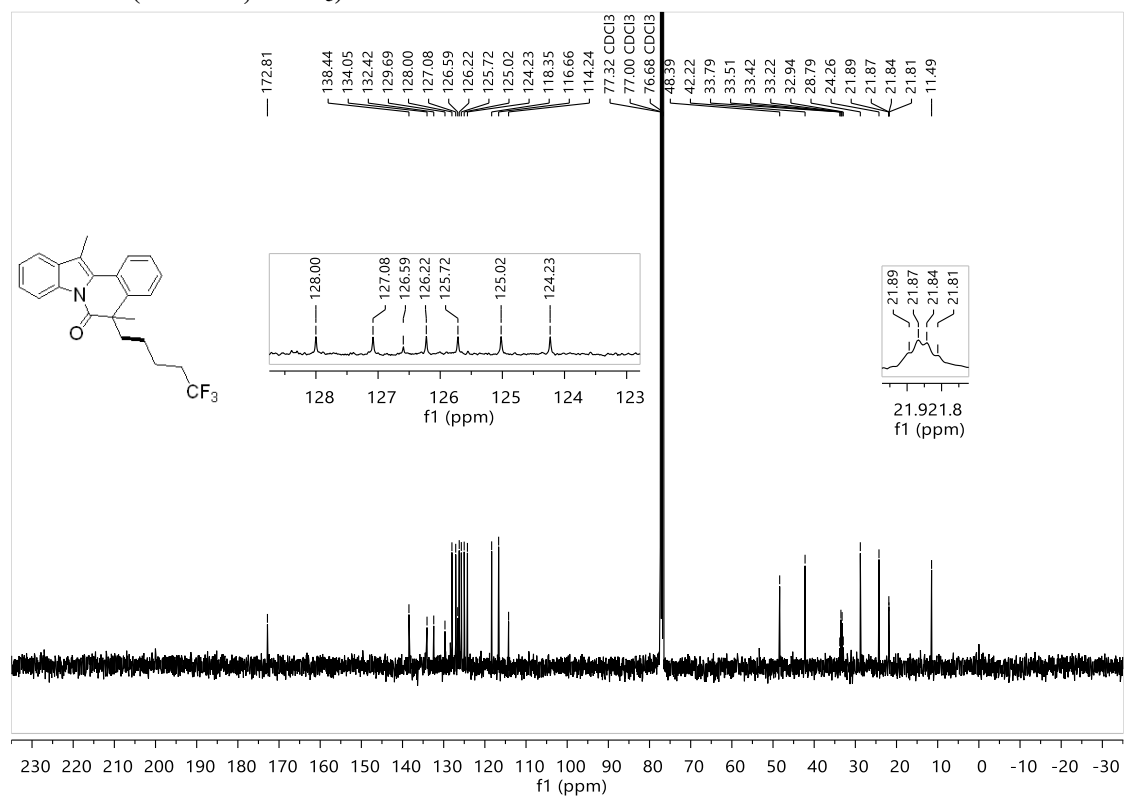
¹⁹F NMR (376MHz, CDCl₃)



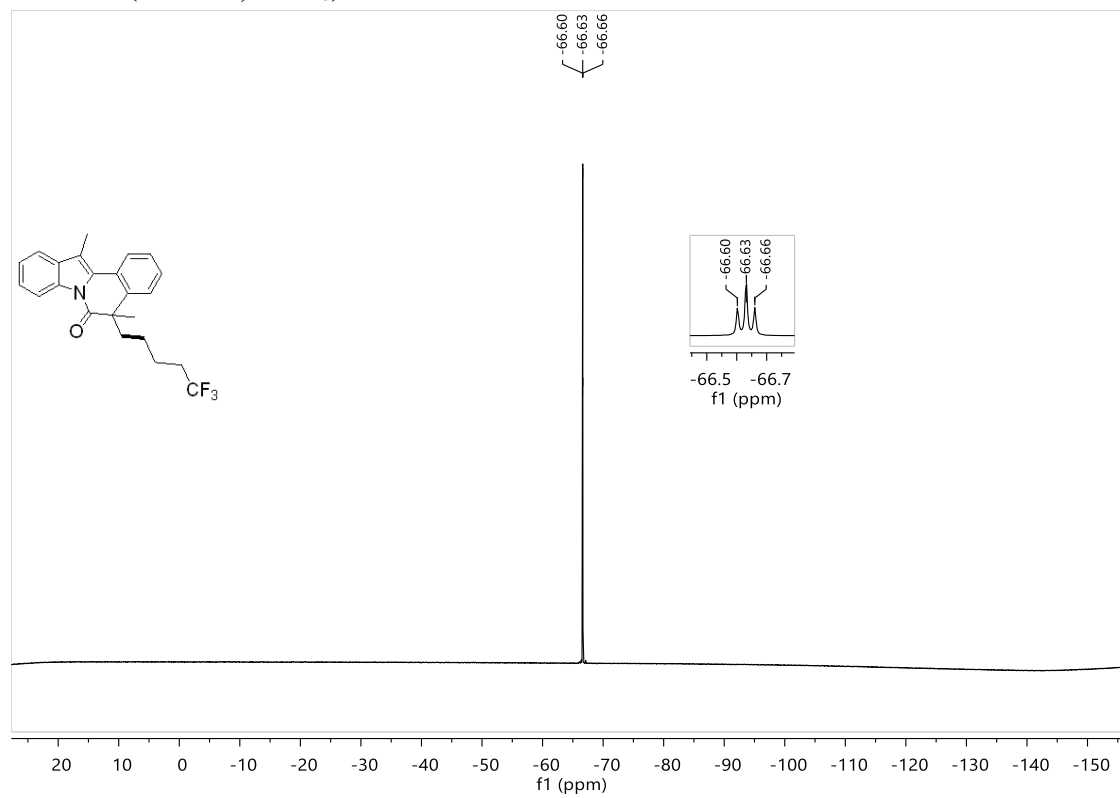
3p: ¹H NMR (400MHz, CDCl₃)



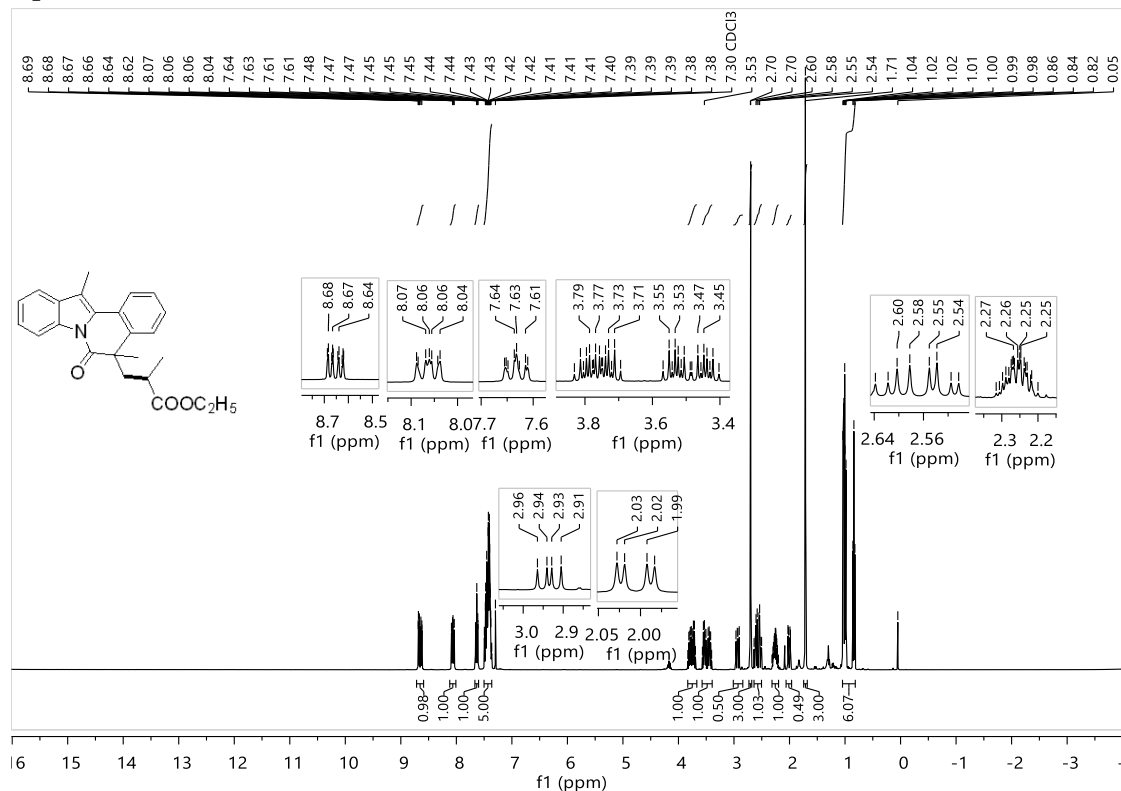
¹³C NMR (101MHz, CDCl₃)



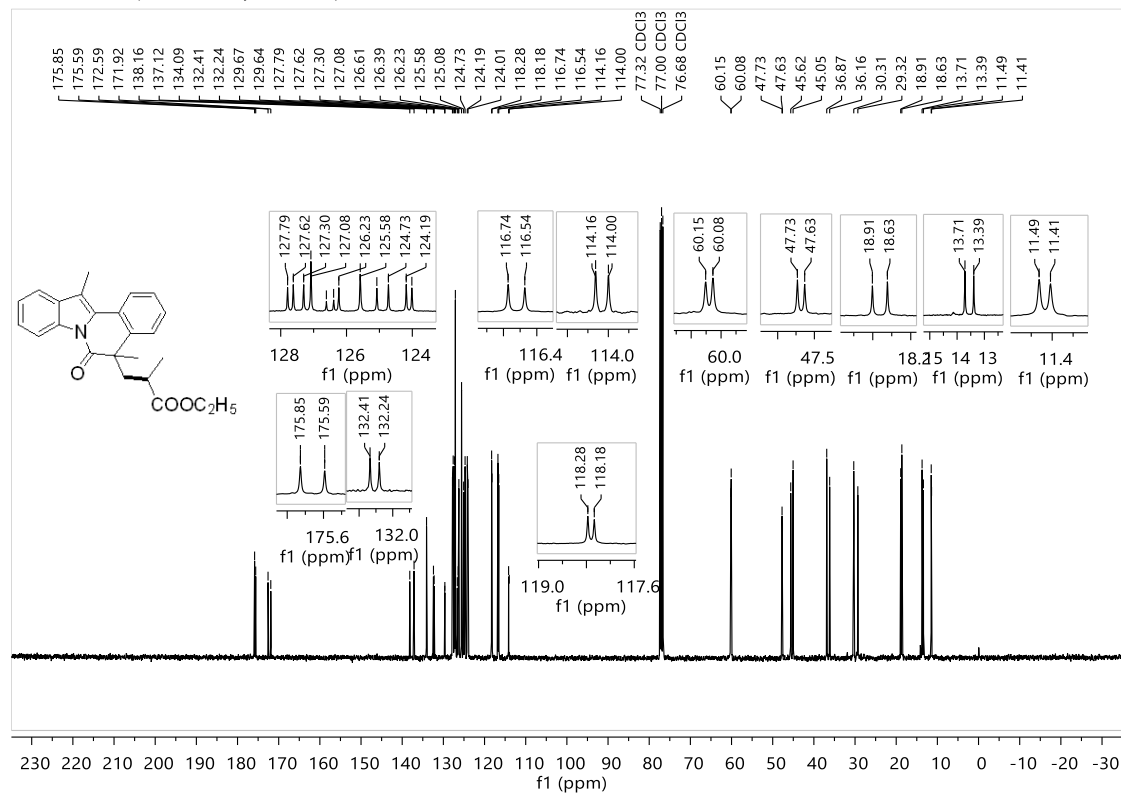
¹⁹F NMR (376MHz, CDCl₃)



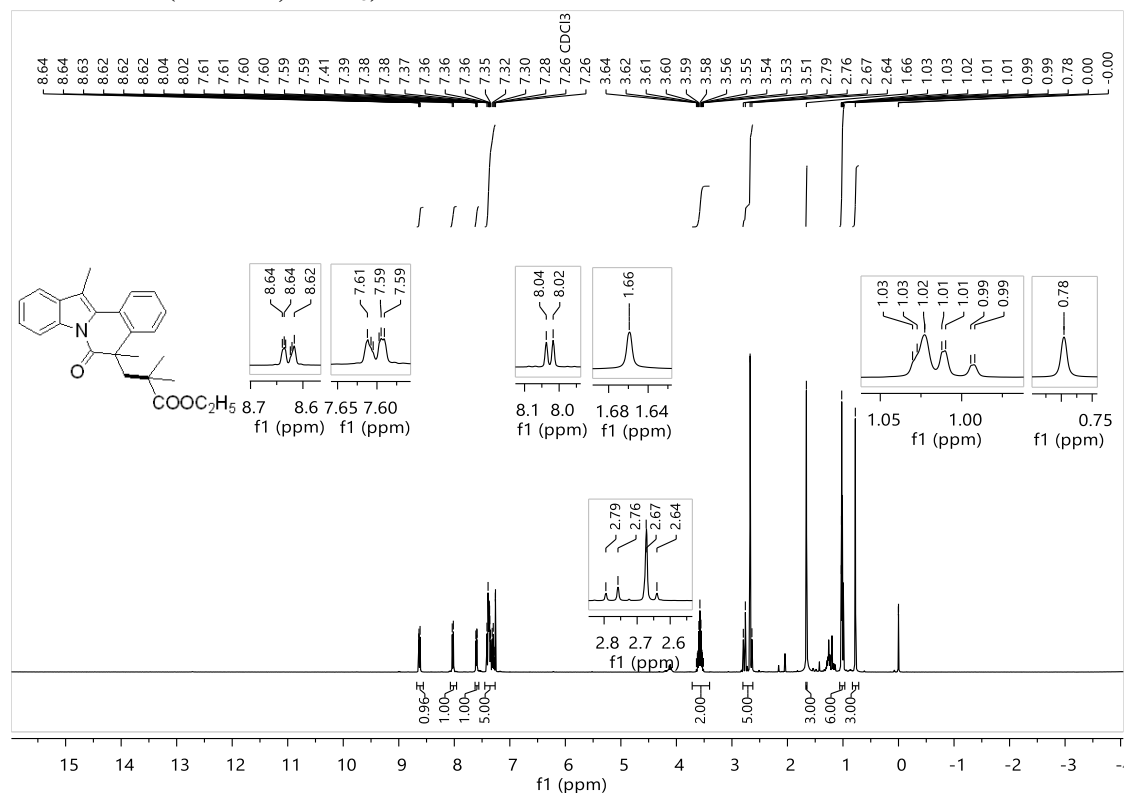
3q: ¹H NMR (400MHz, CDCl₃)



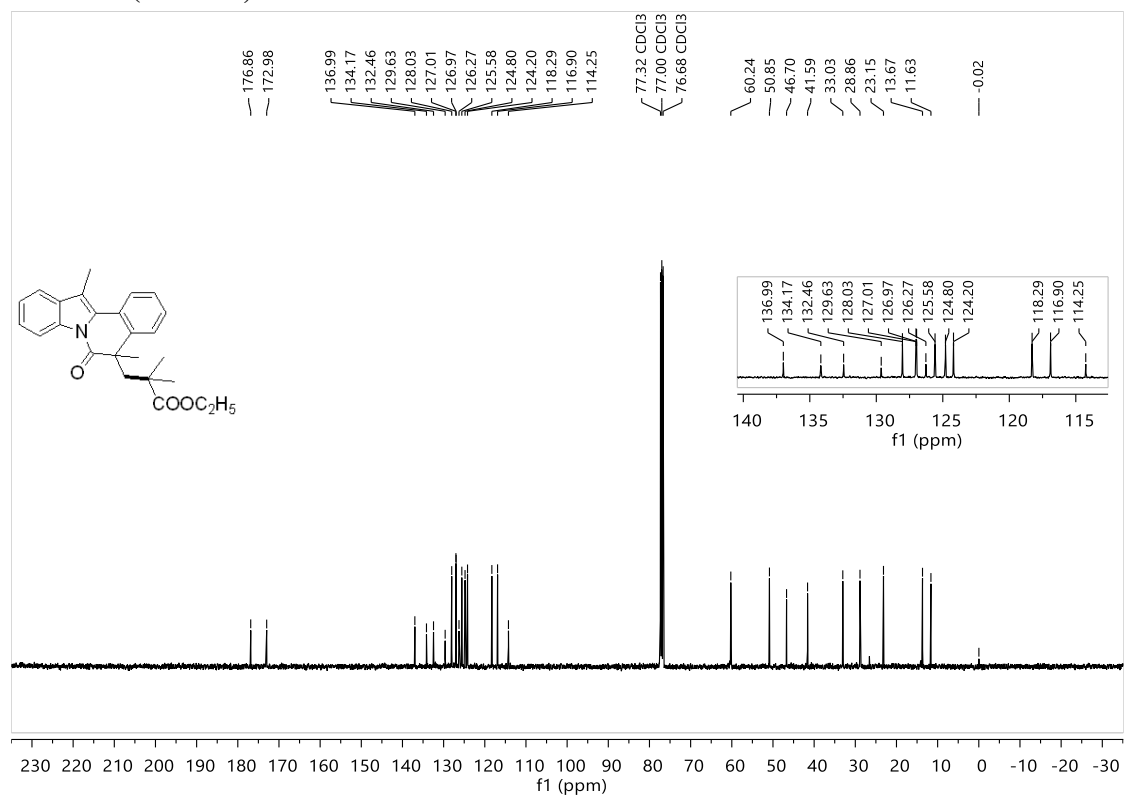
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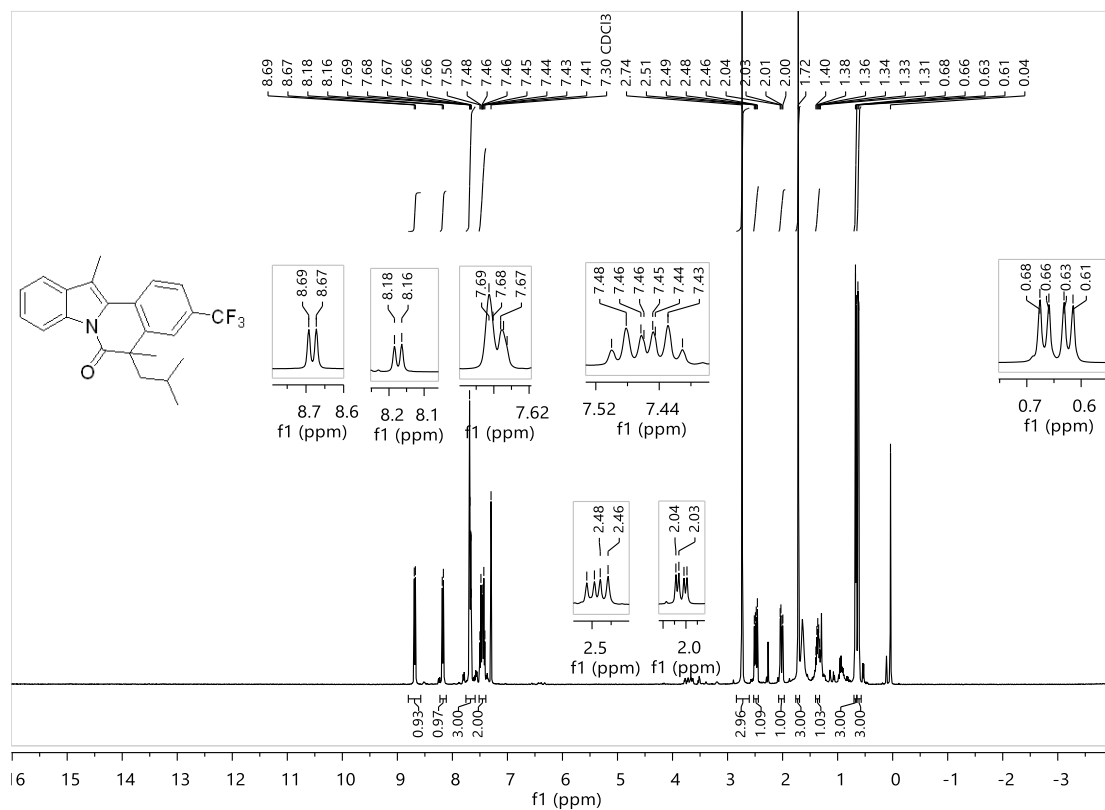
3r: ^1H NMR (400MHz, CDCl_3)



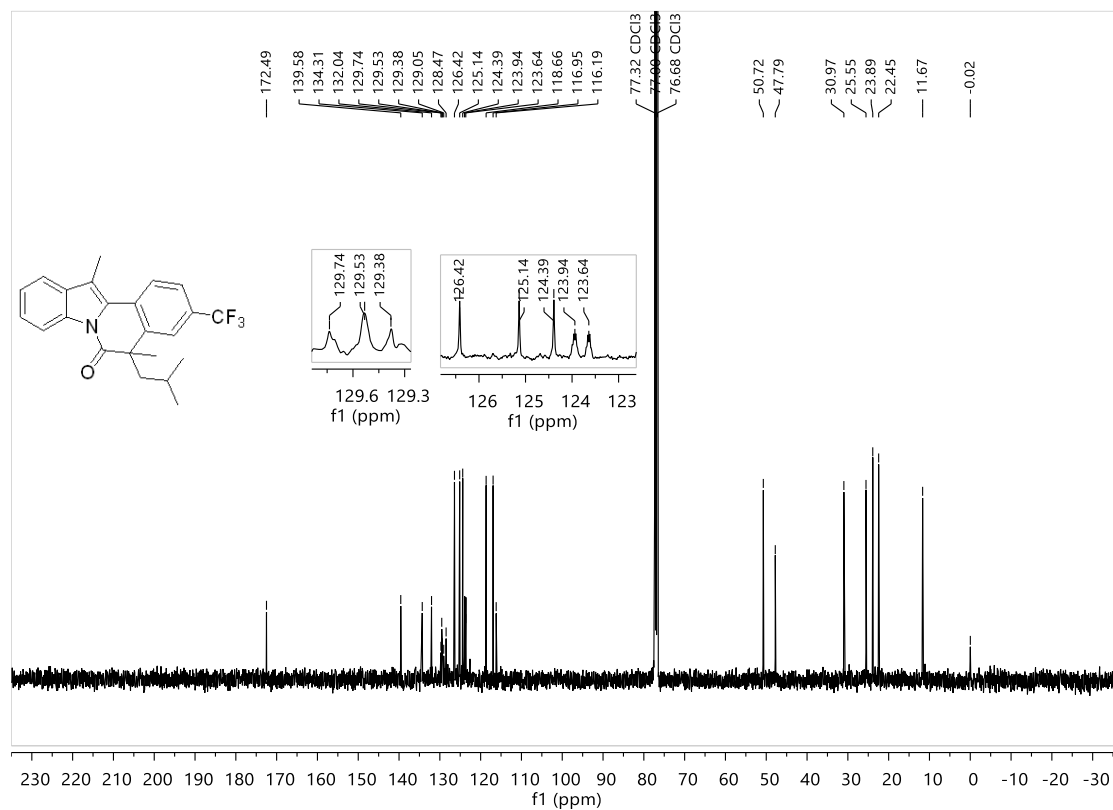
^{13}C NMR (101MHz, CDCl_3)



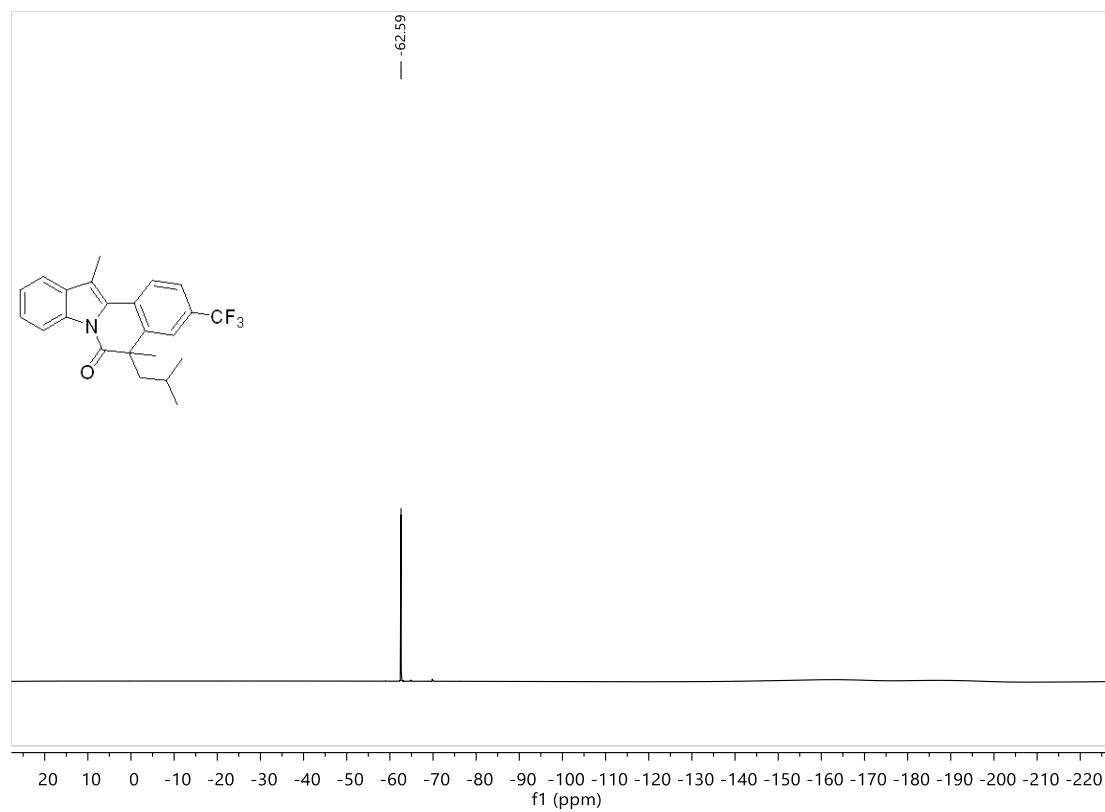
3s: ¹H NMR (400MHz, CDCl₃)



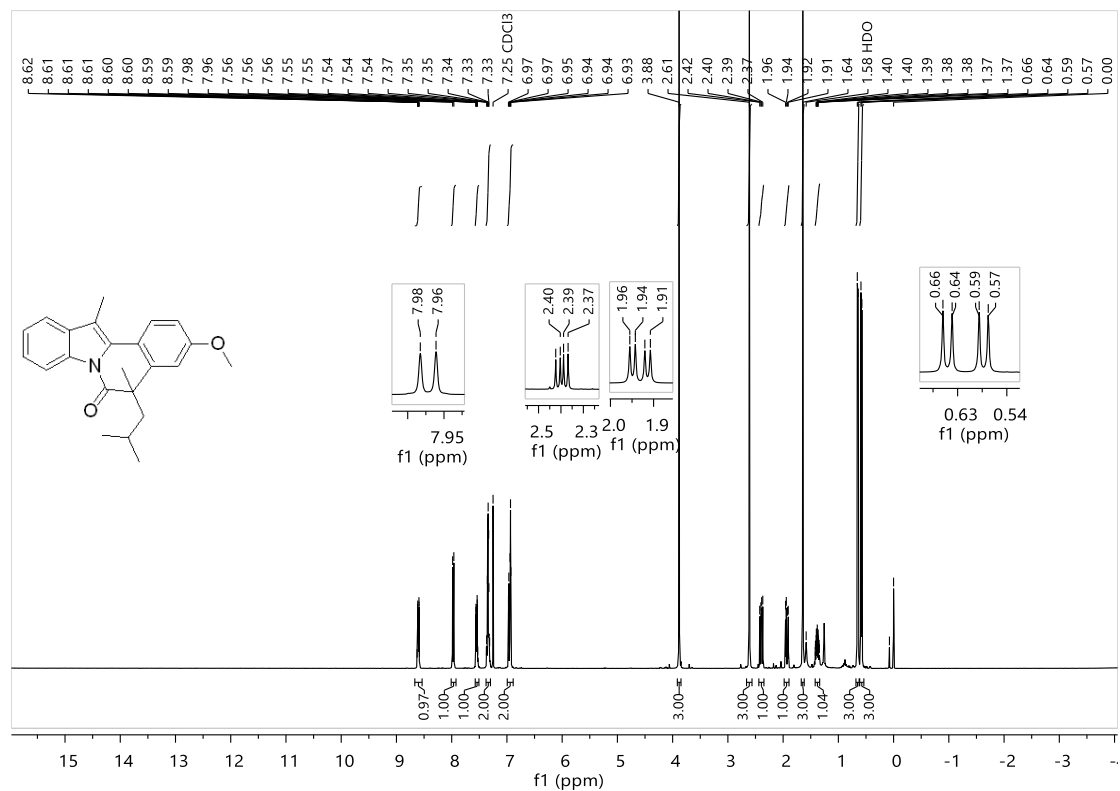
¹³C NMR (101MHz, CDCl₃)



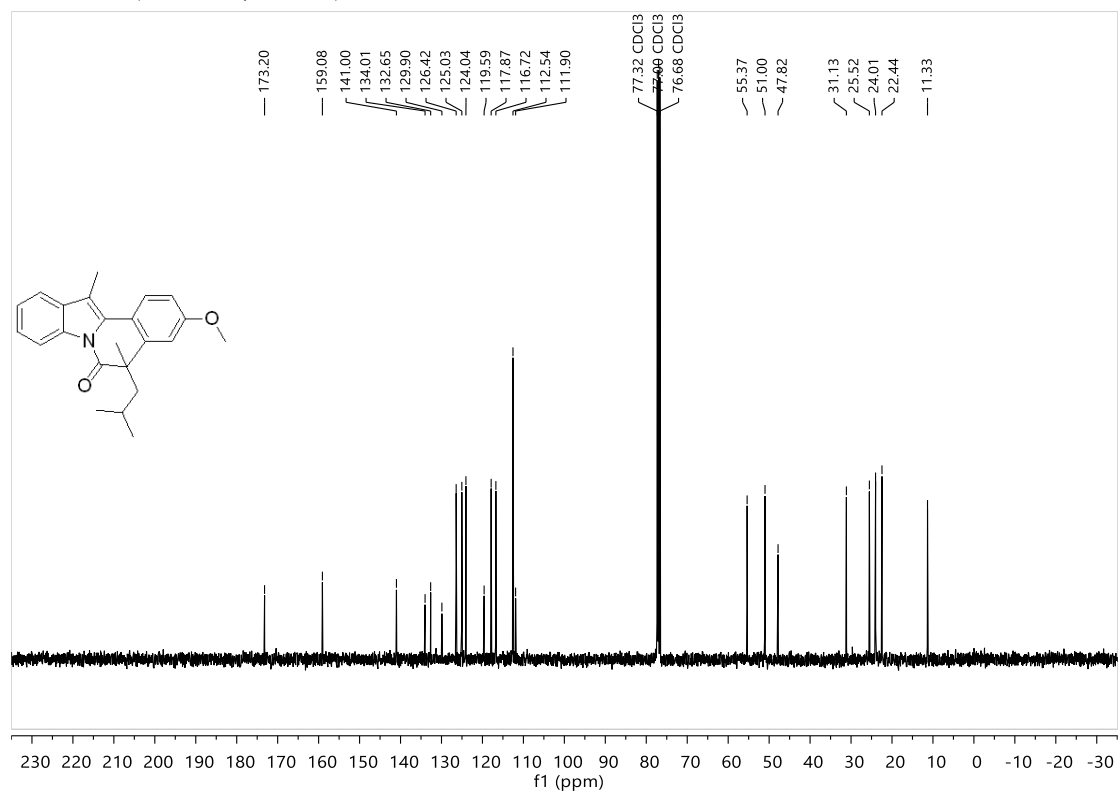
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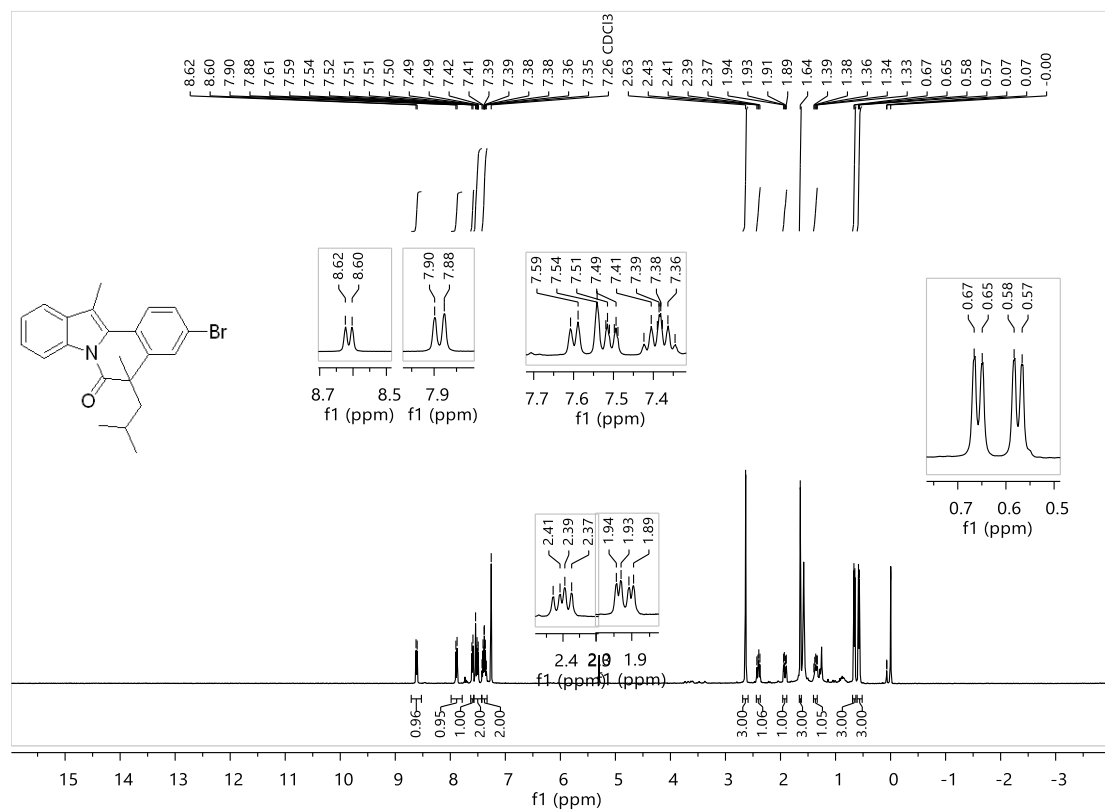
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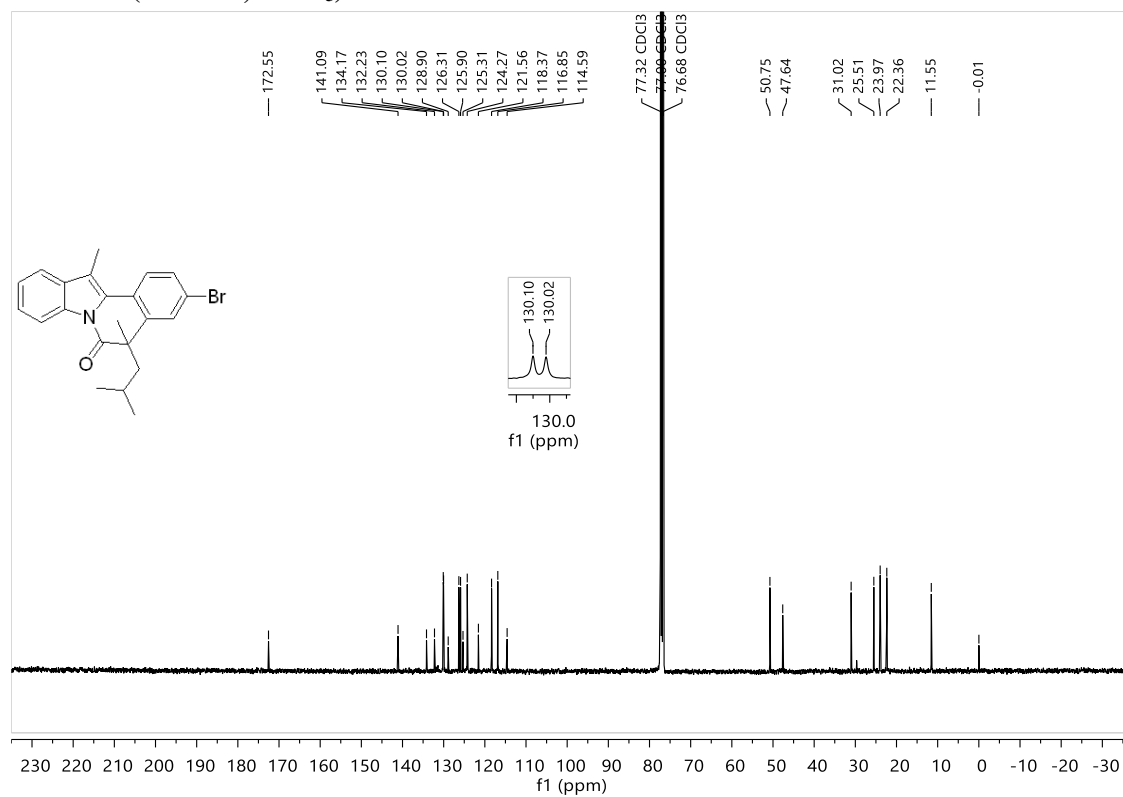
¹³C NMR (101MHz, CDCl₃)



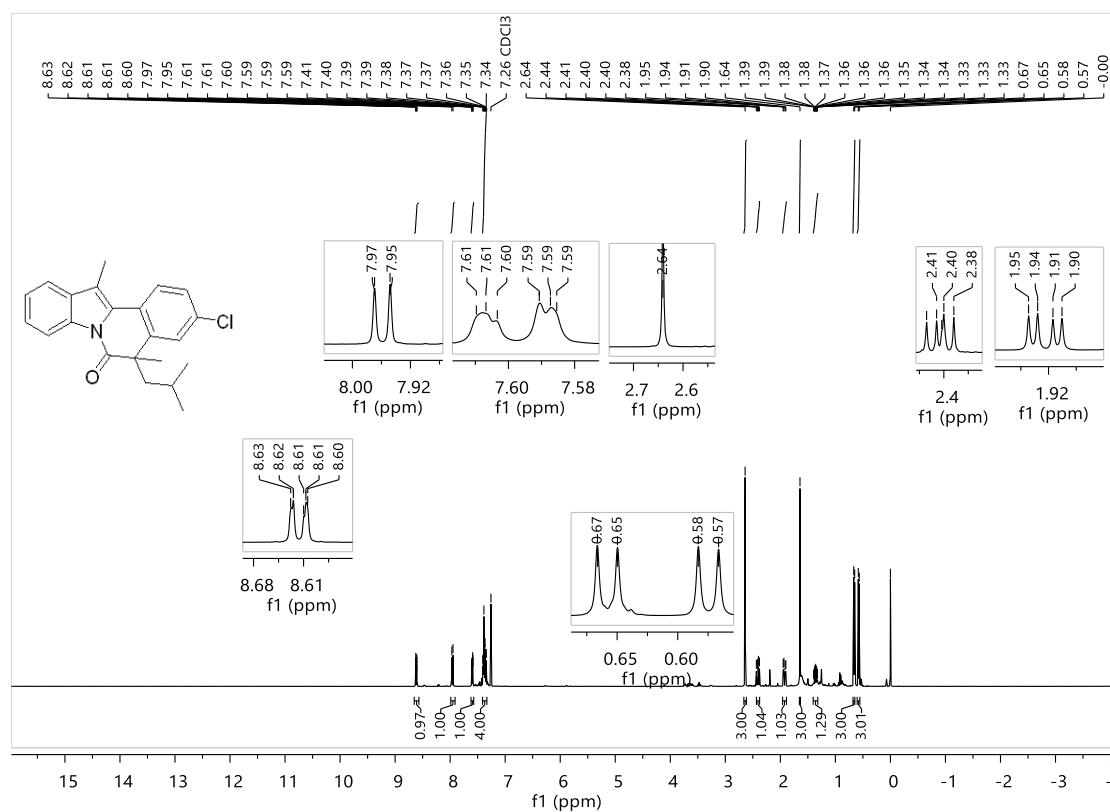
3u: ^1H NMR (400MHz, CDCl_3)



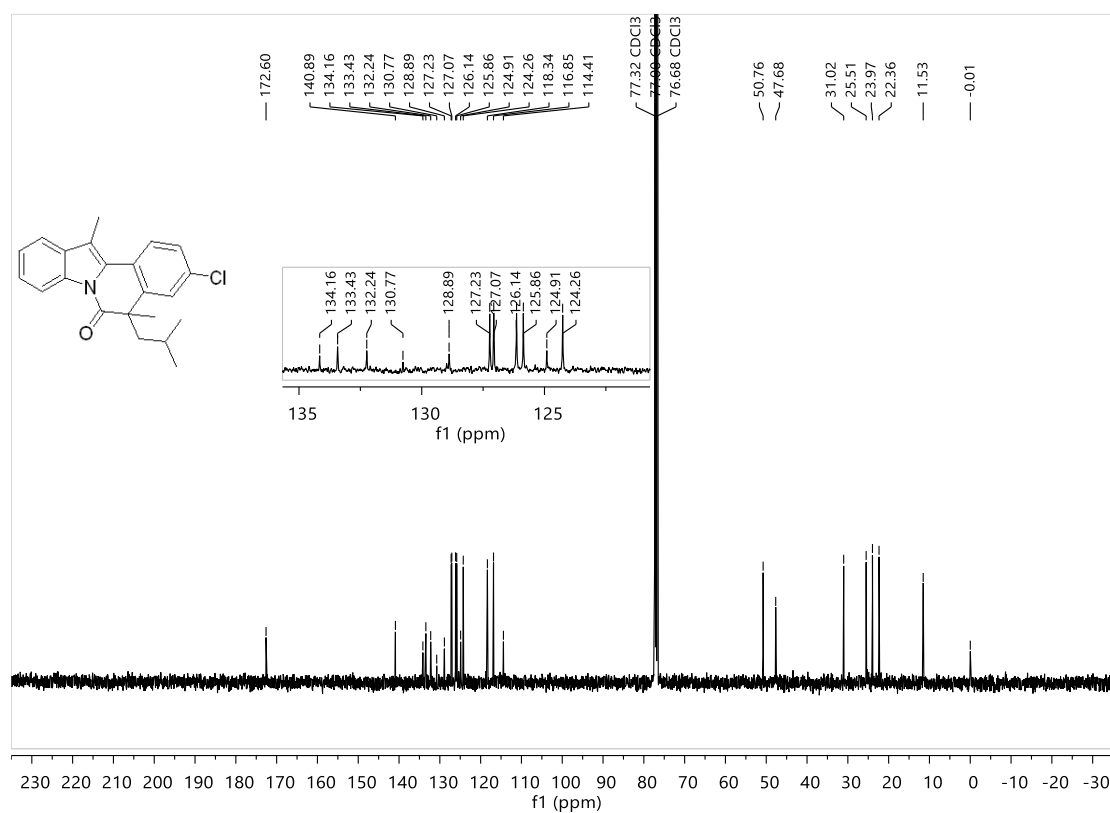
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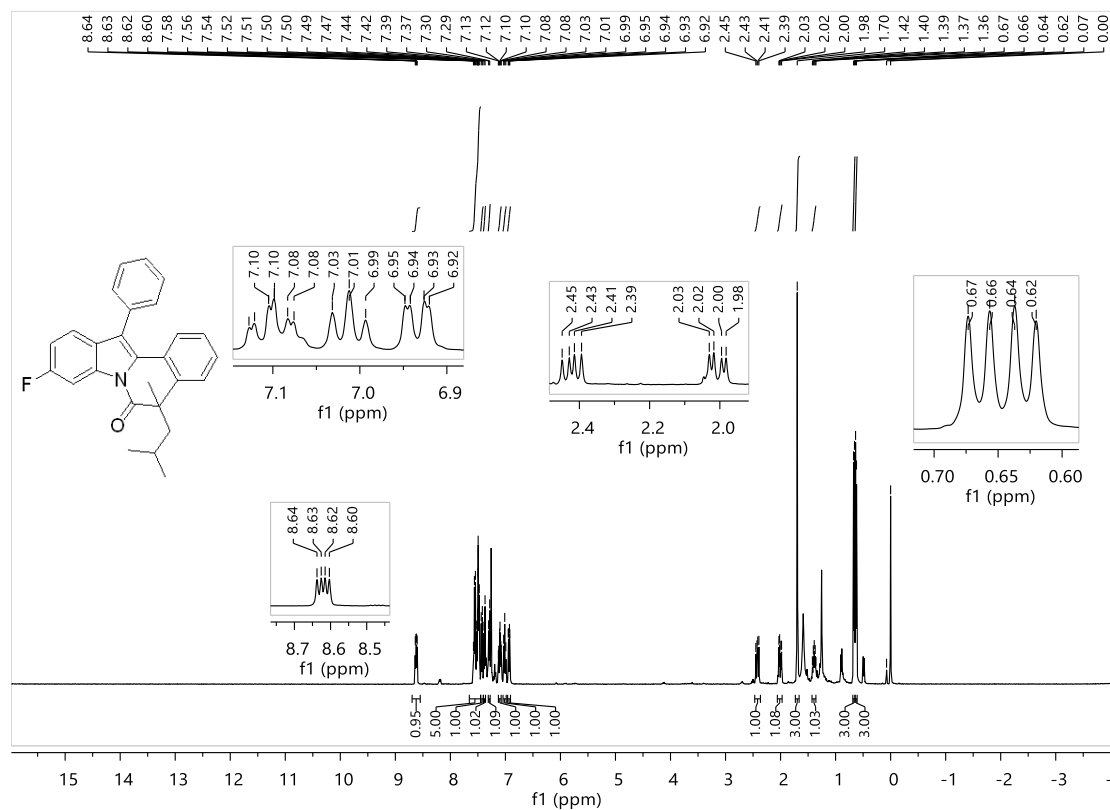
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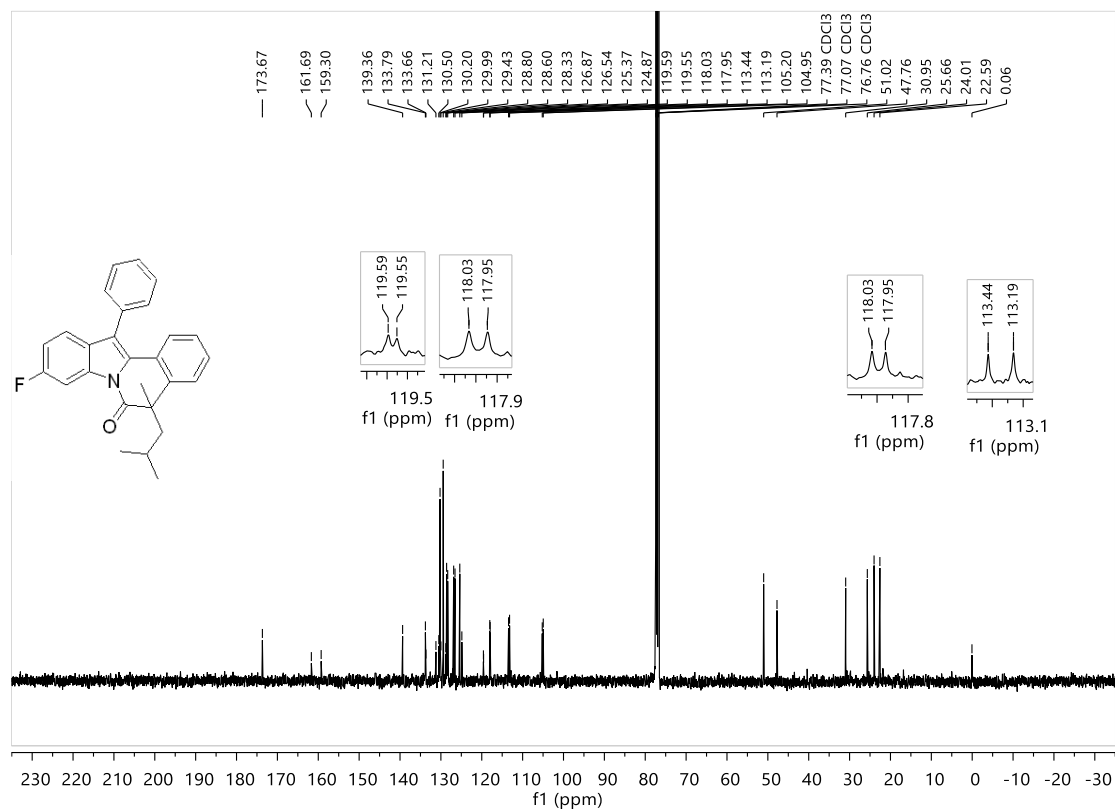
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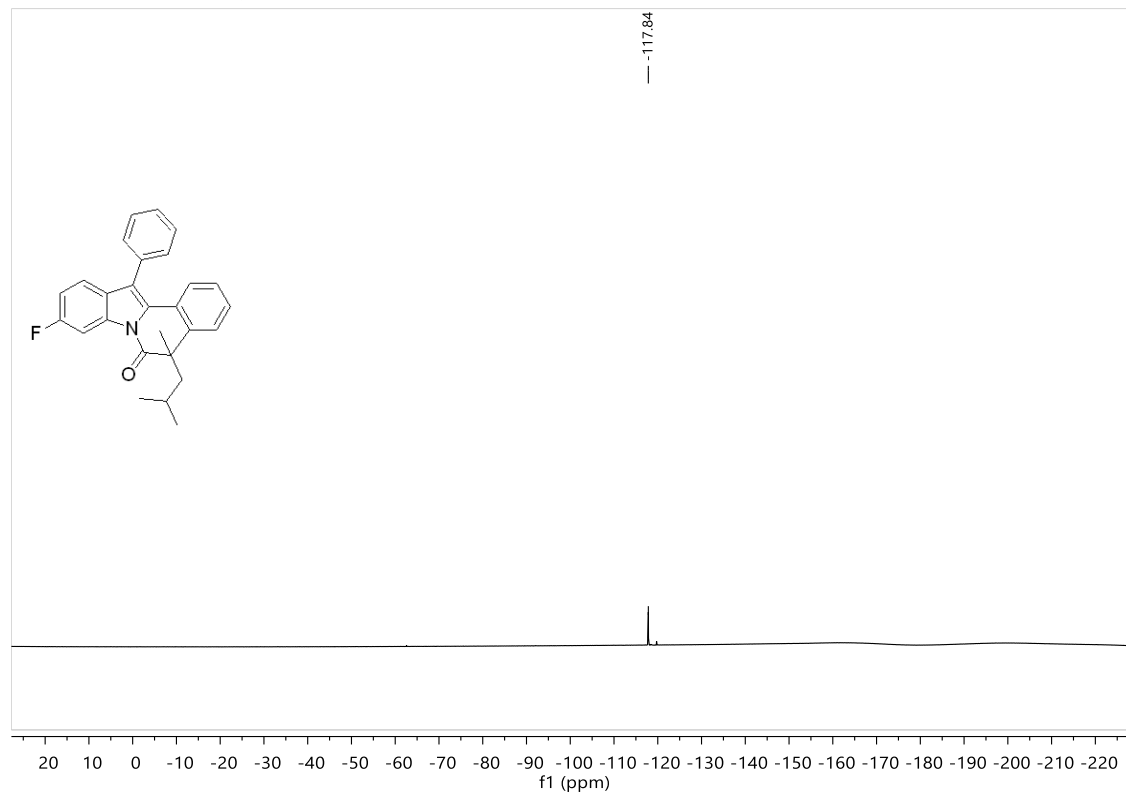
3w: ^1H NMR (400MHz, CDCl_3)



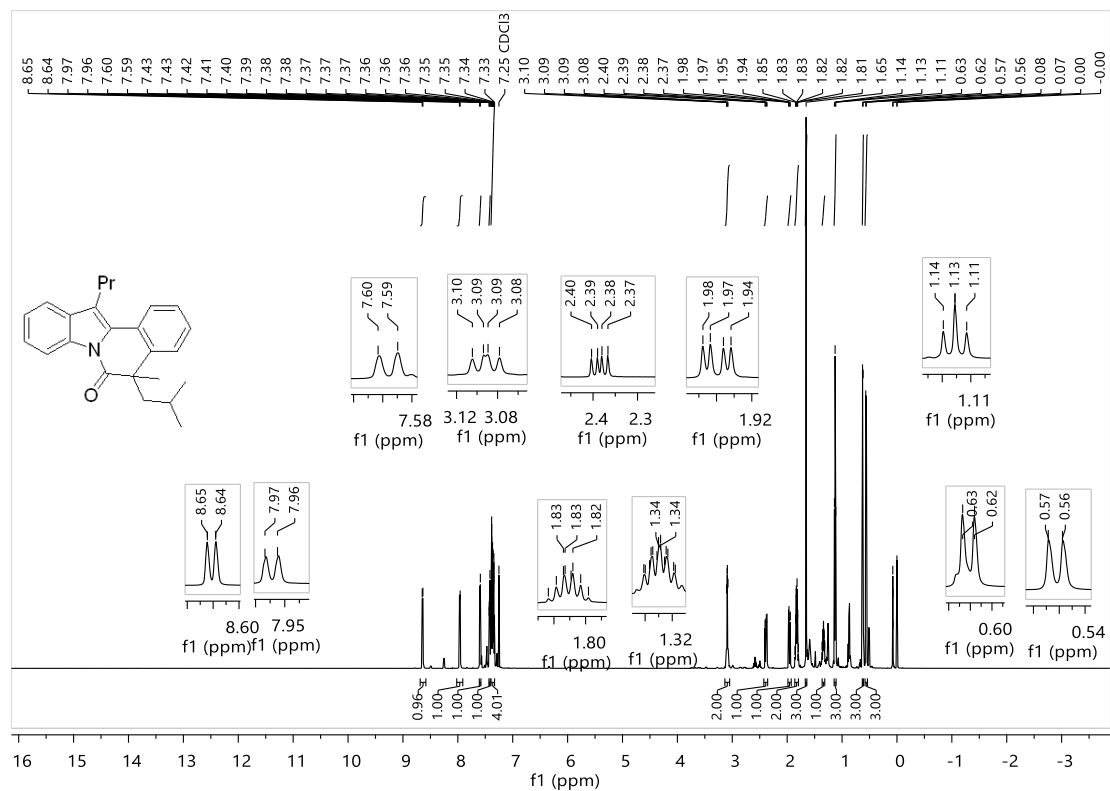
^{13}C NMR (101MHz, CDCl_3)



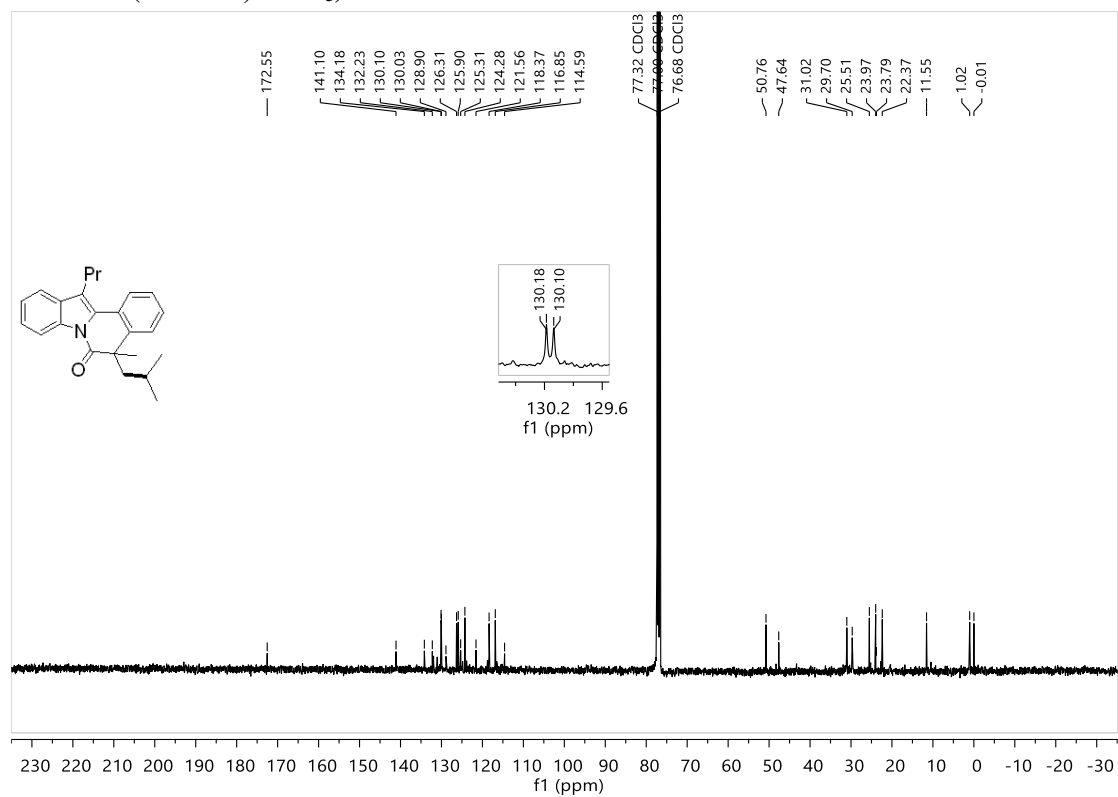
¹⁹F NMR (376MHz, CDCl₃)



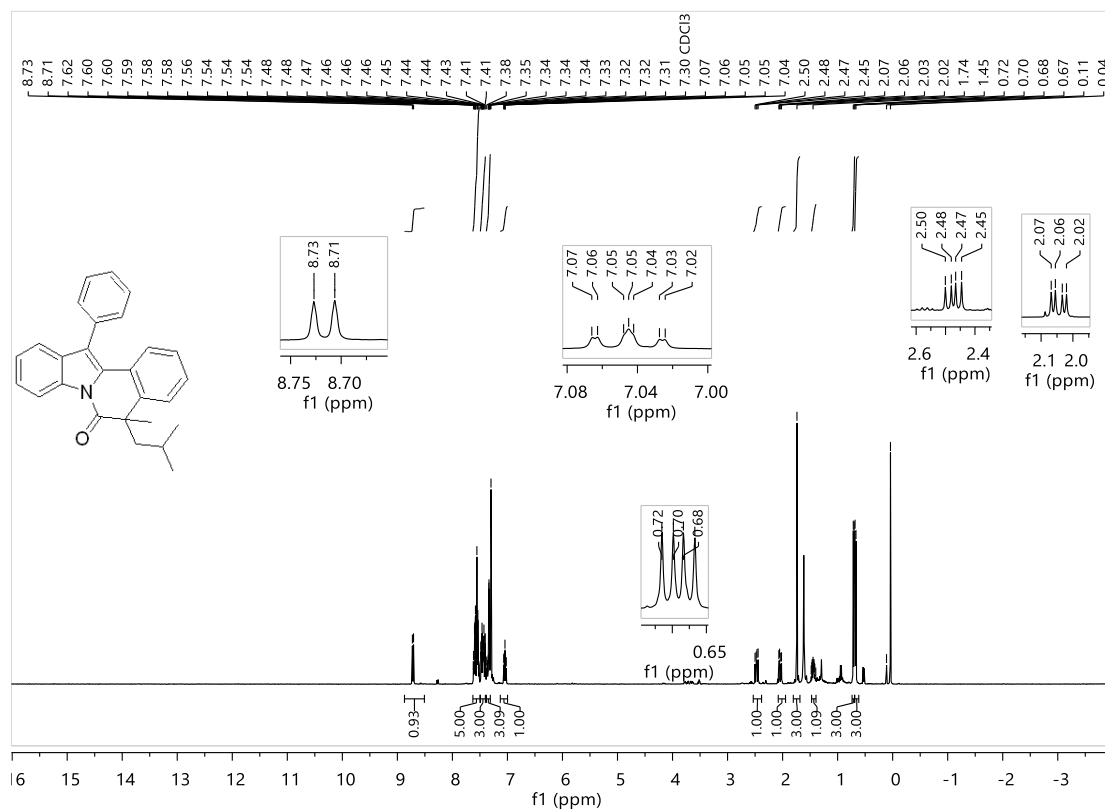
3x: ¹H NMR (400MHz, CDCl₃)



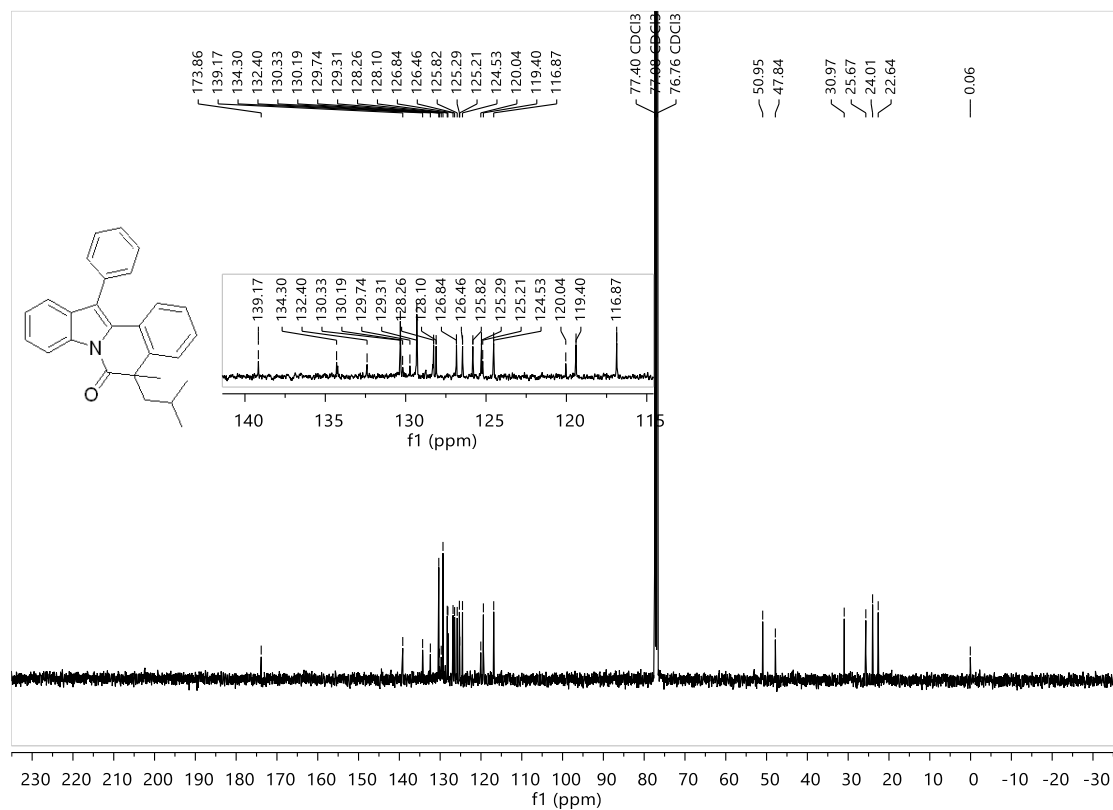
¹³C NMR (101MHz, CDCl₃)



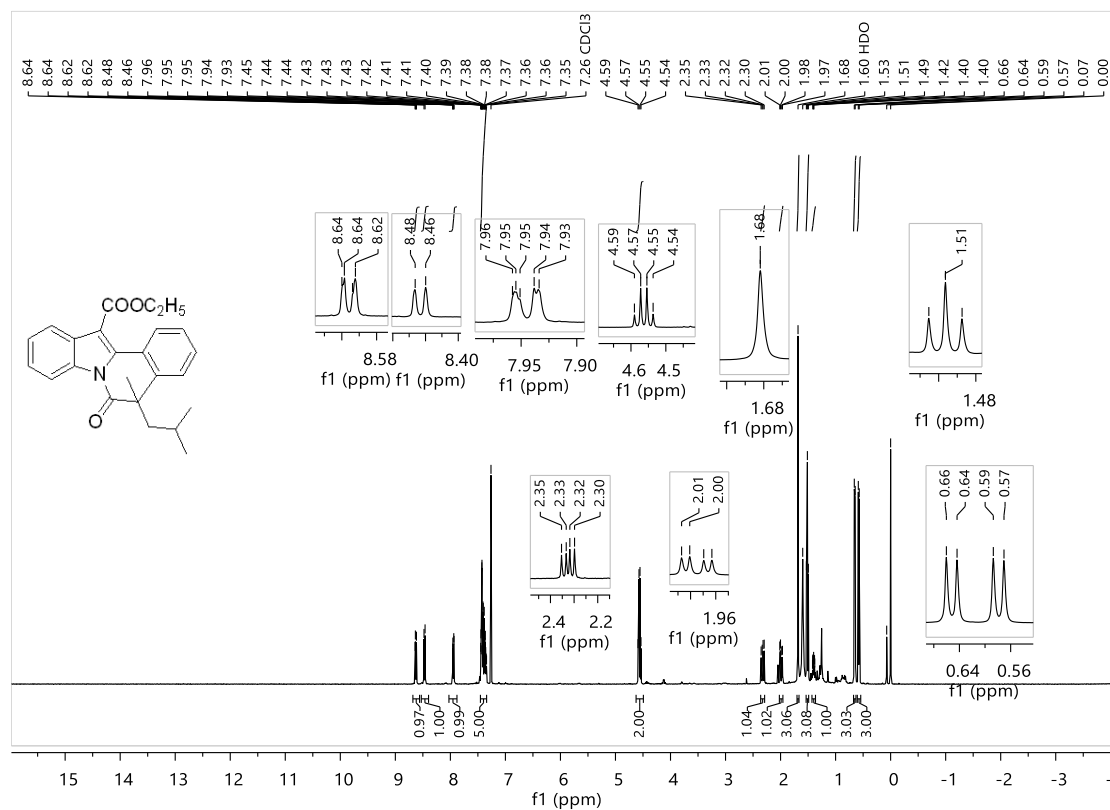
3y: ¹H NMR (400MHz, CDCl₃)



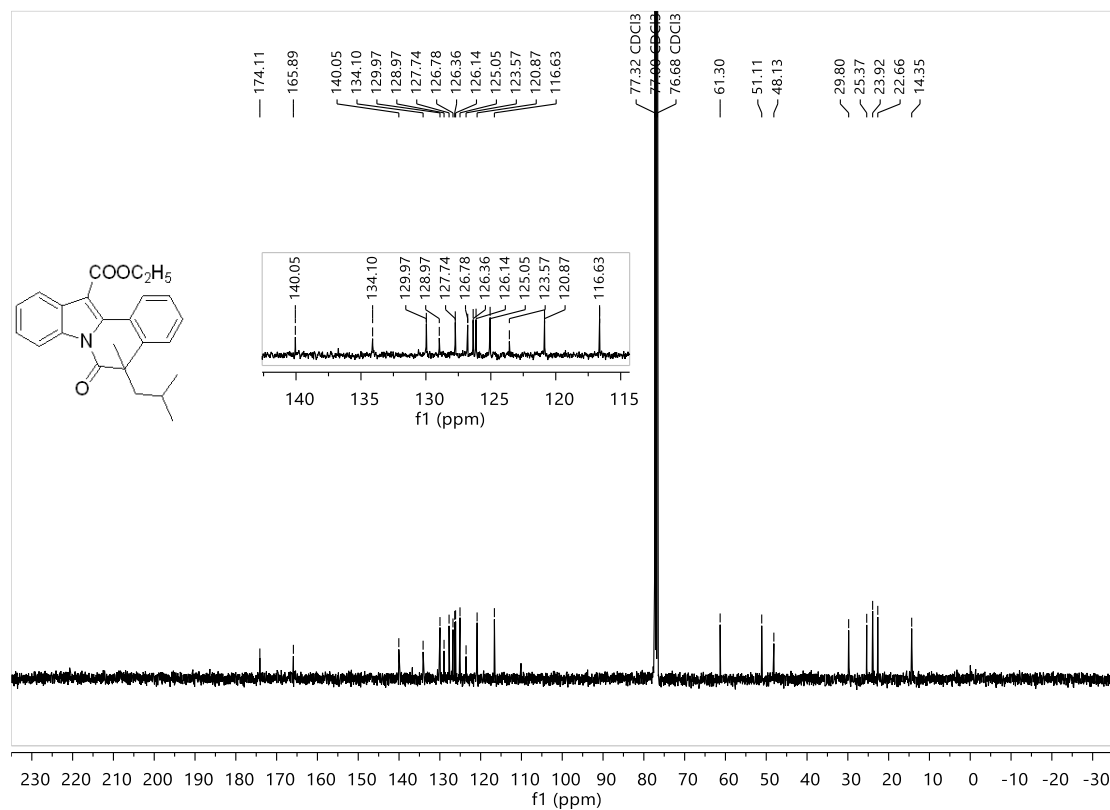
¹³C NMR (101MHz, CDCl₃)



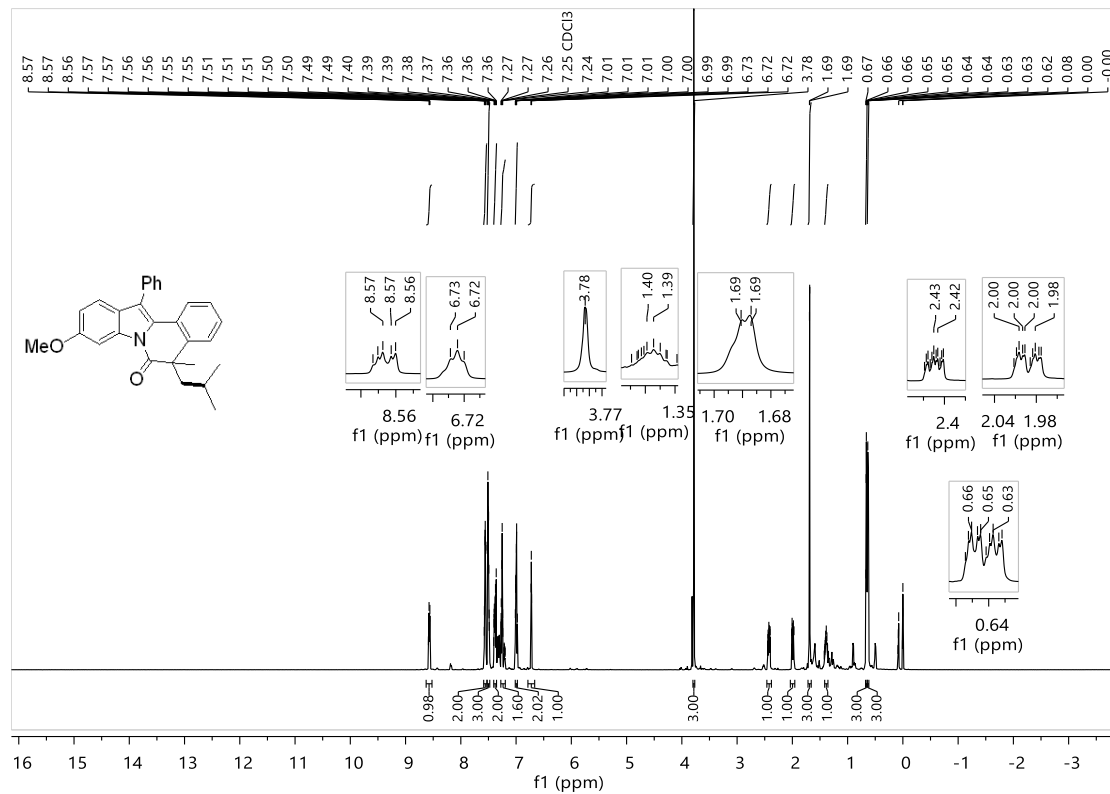
3z: ¹H NMR (400MHz, CDCl₃)



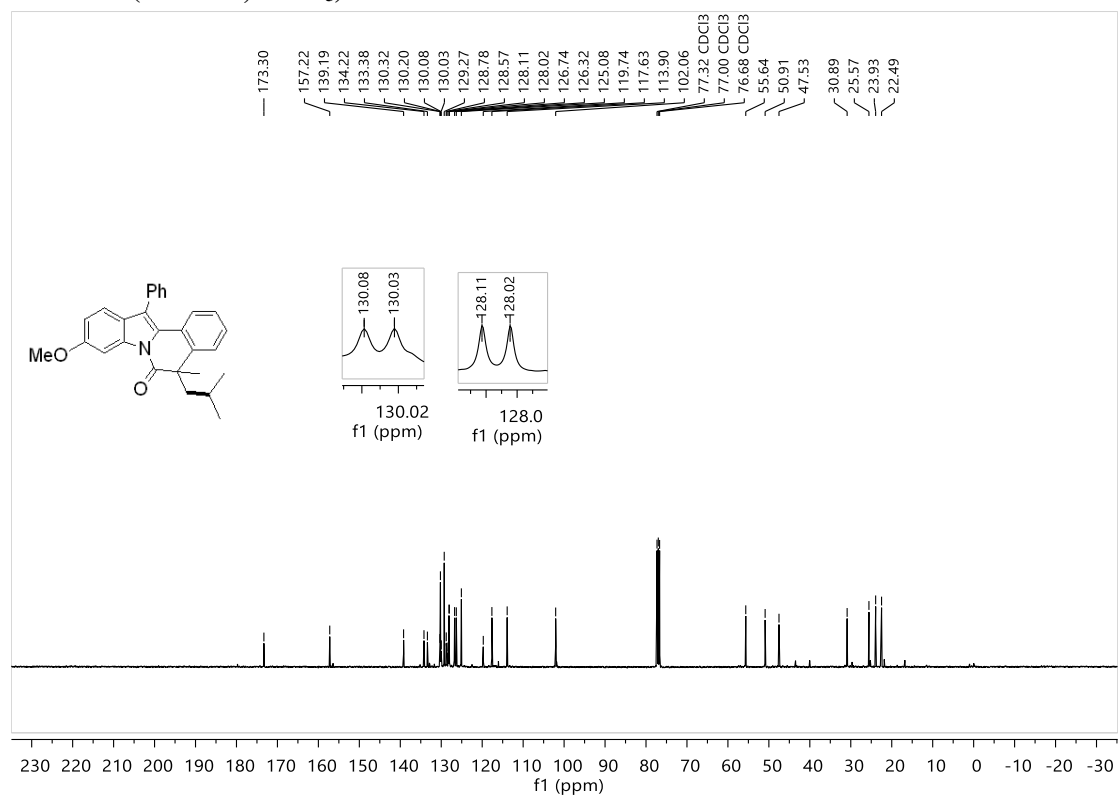
¹³C NMR (101MHz, CDCl₃)



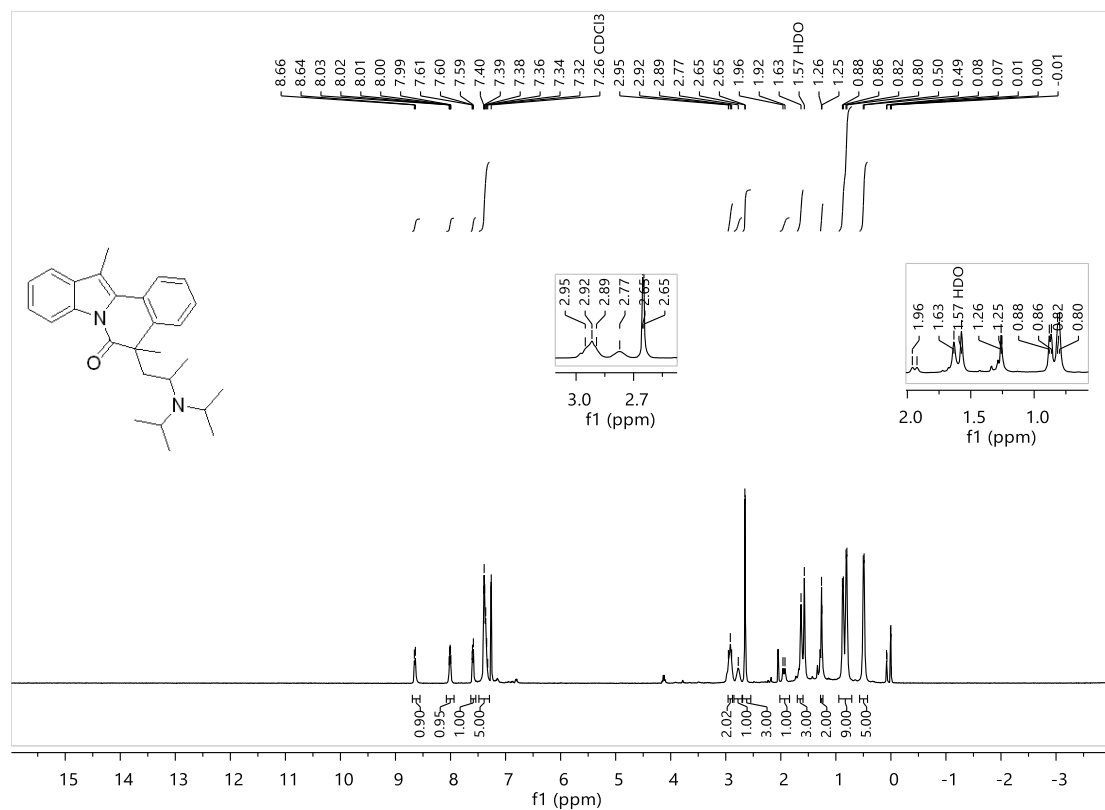
3aa: ^1H NMR (400MHz, CDCl_3)



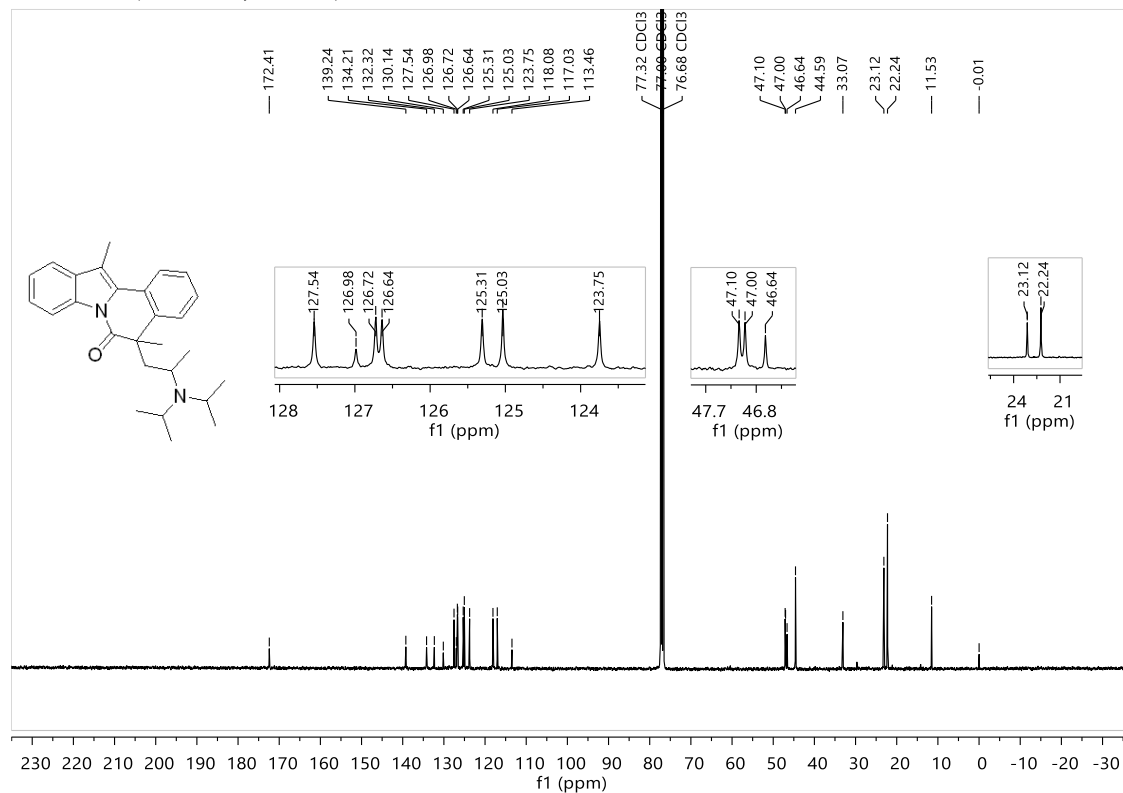
^{13}C NMR (101MHz, CDCl_3)



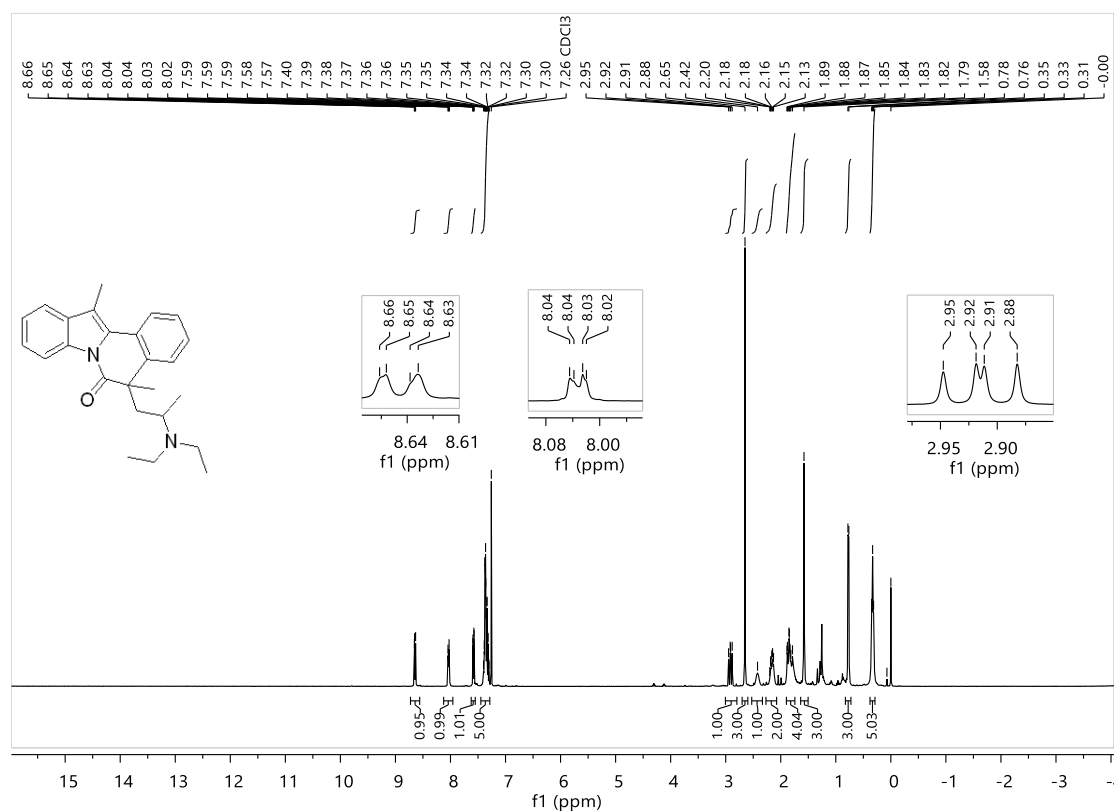
5a: ¹H NMR (400MHz, CDCl₃)



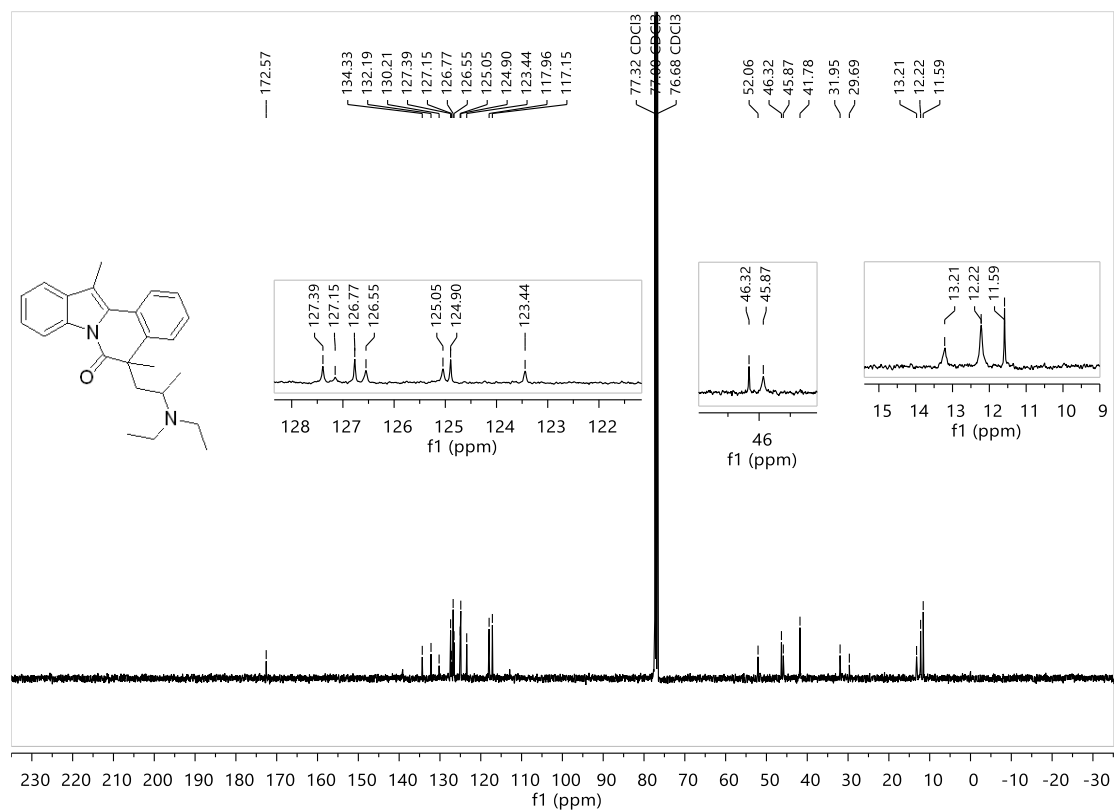
¹³C NMR (101MHz, CDCl₃)



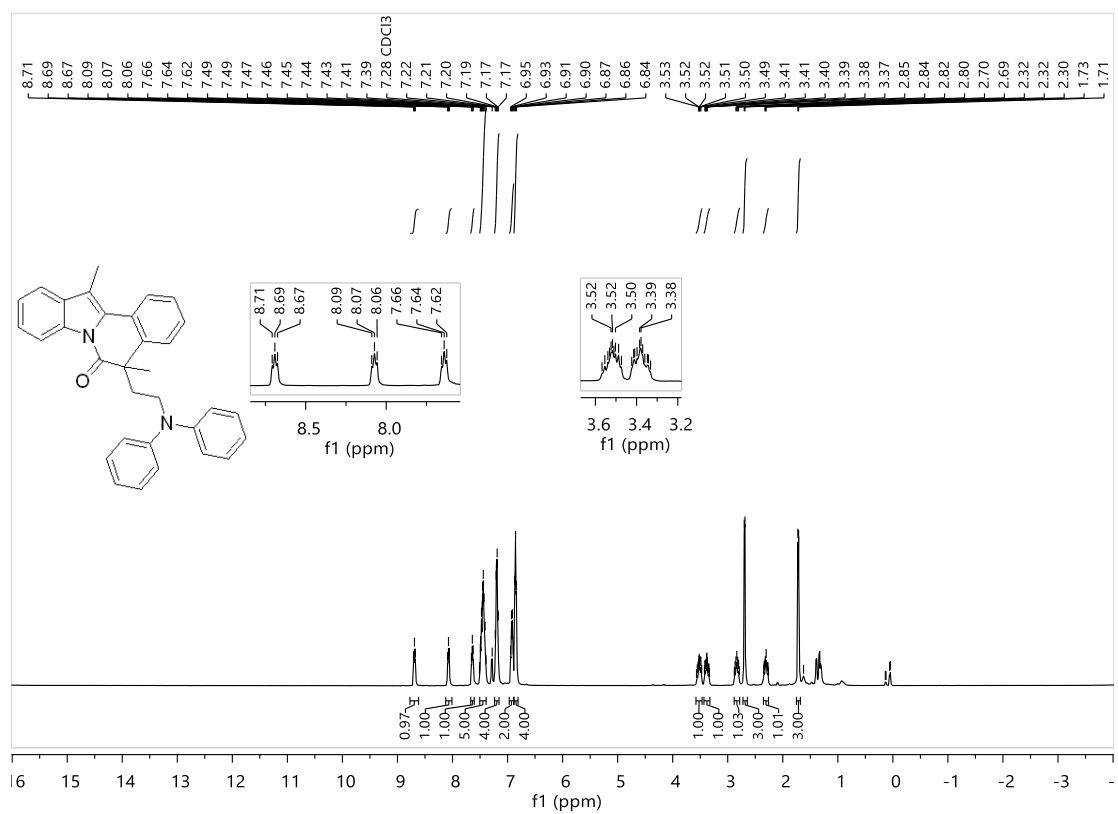
5b: ^1H NMR (400MHz, CDCl_3)



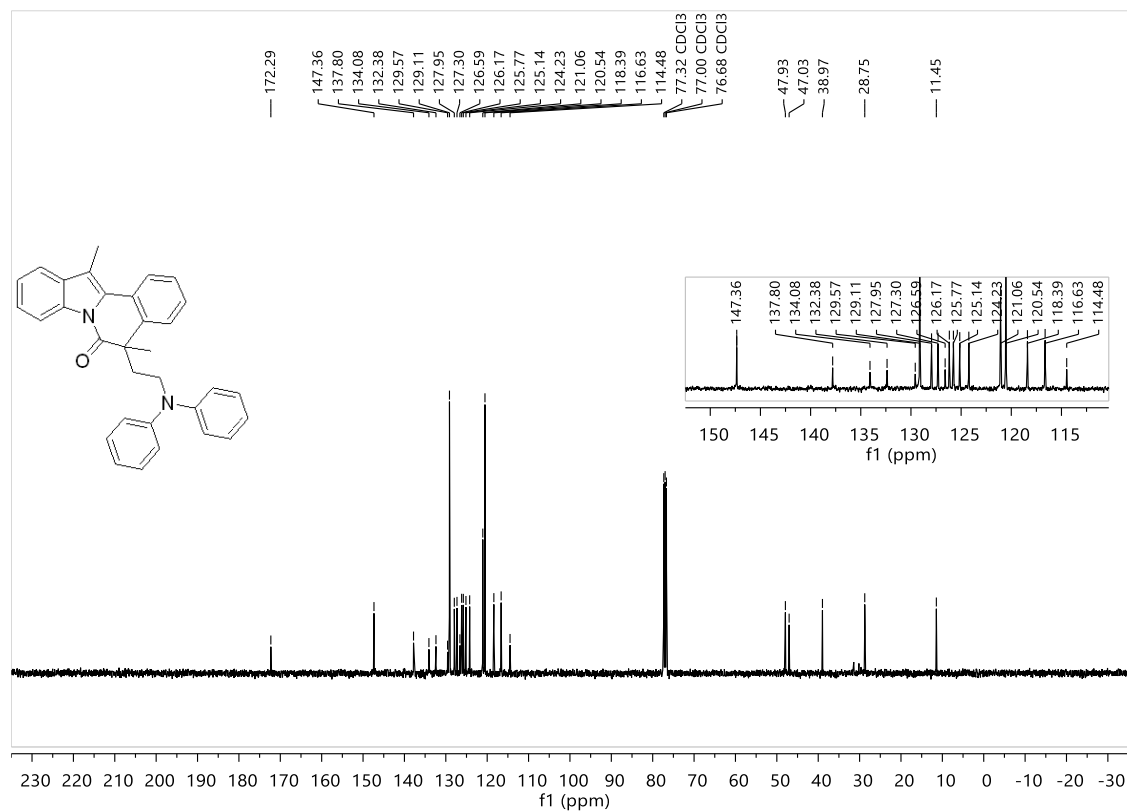
^{13}C NMR (101MHz, CDCl_3)



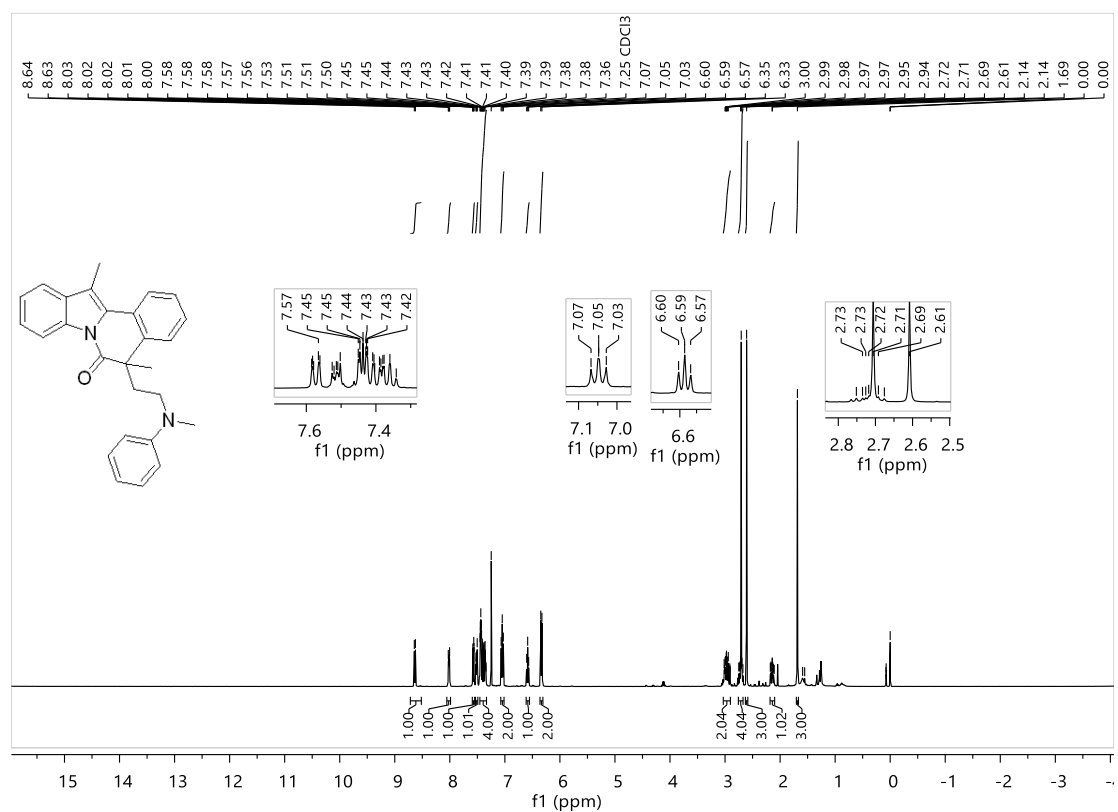
5c: ^1H NMR (400MHz, CDCl_3)



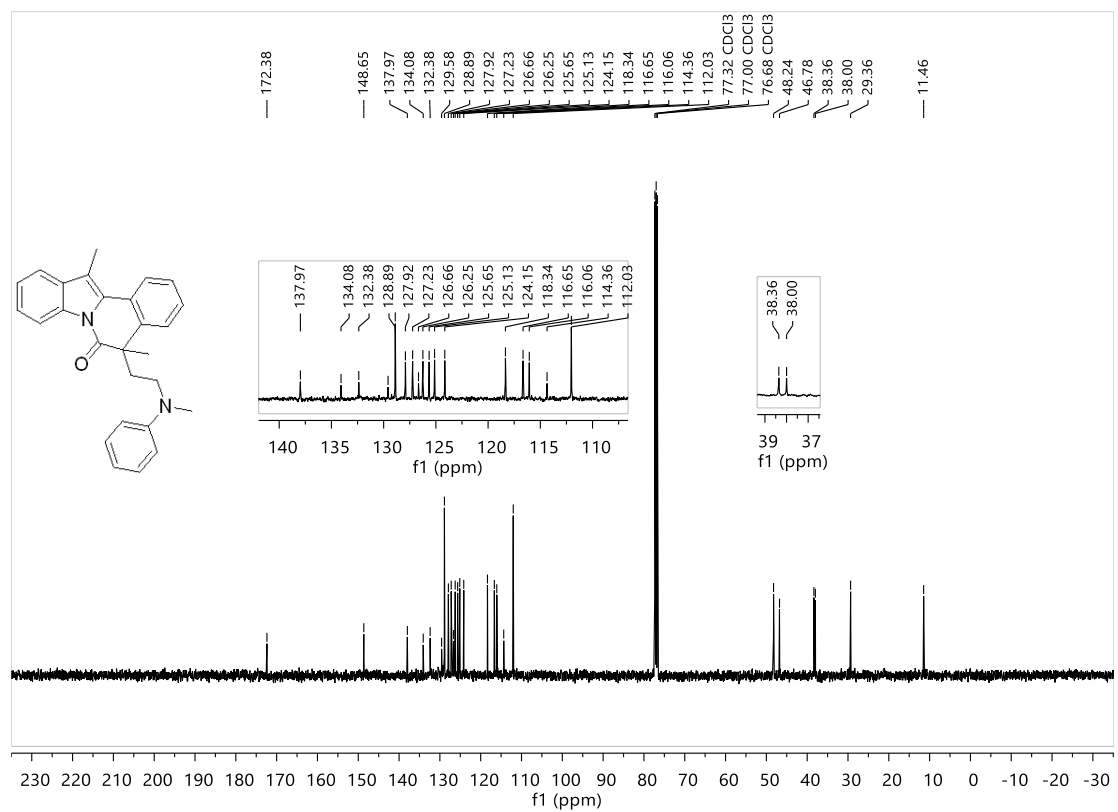
^{13}C NMR (101MHz, CDCl_3)



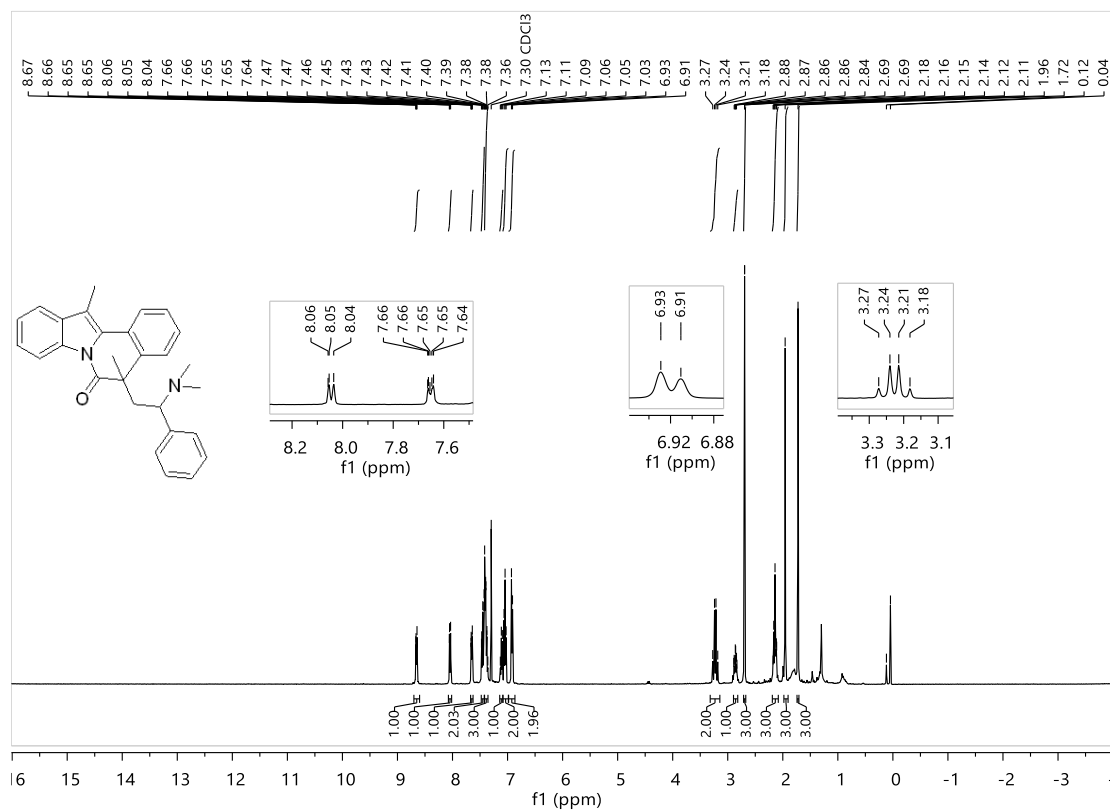
5d: ¹H NMR (400MHz, CDCl₃)



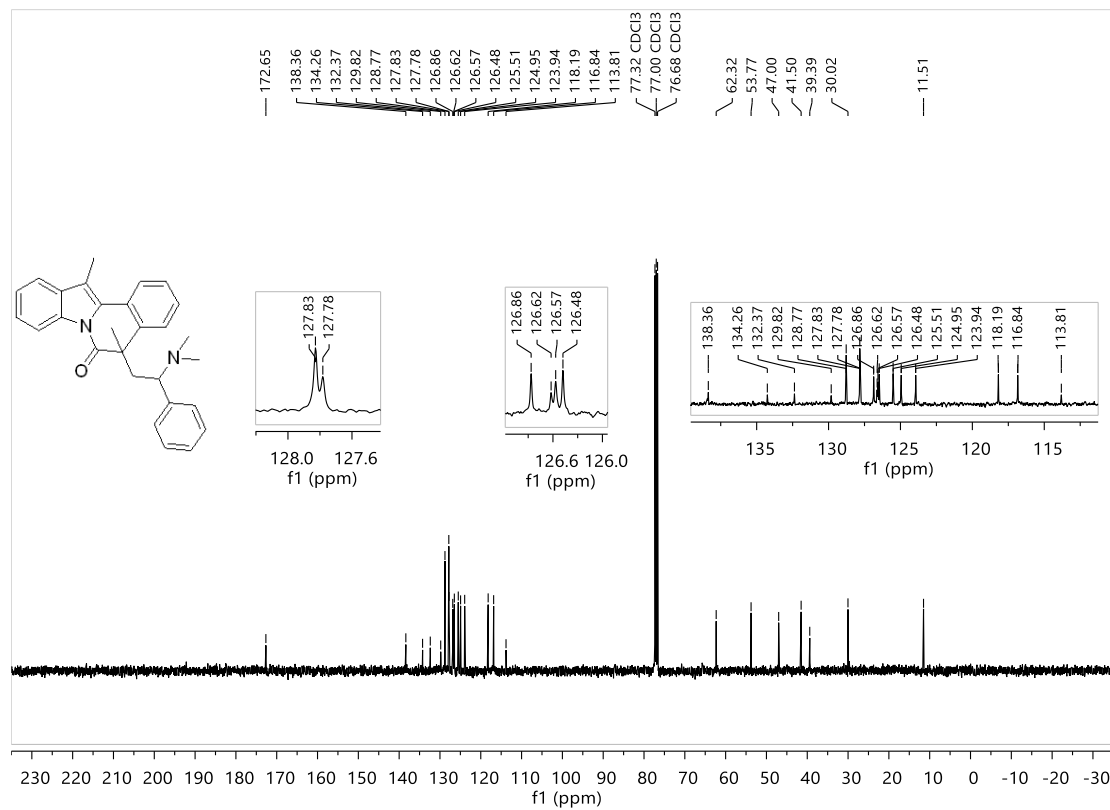
¹³C NMR (101MHz, CDCl₃)



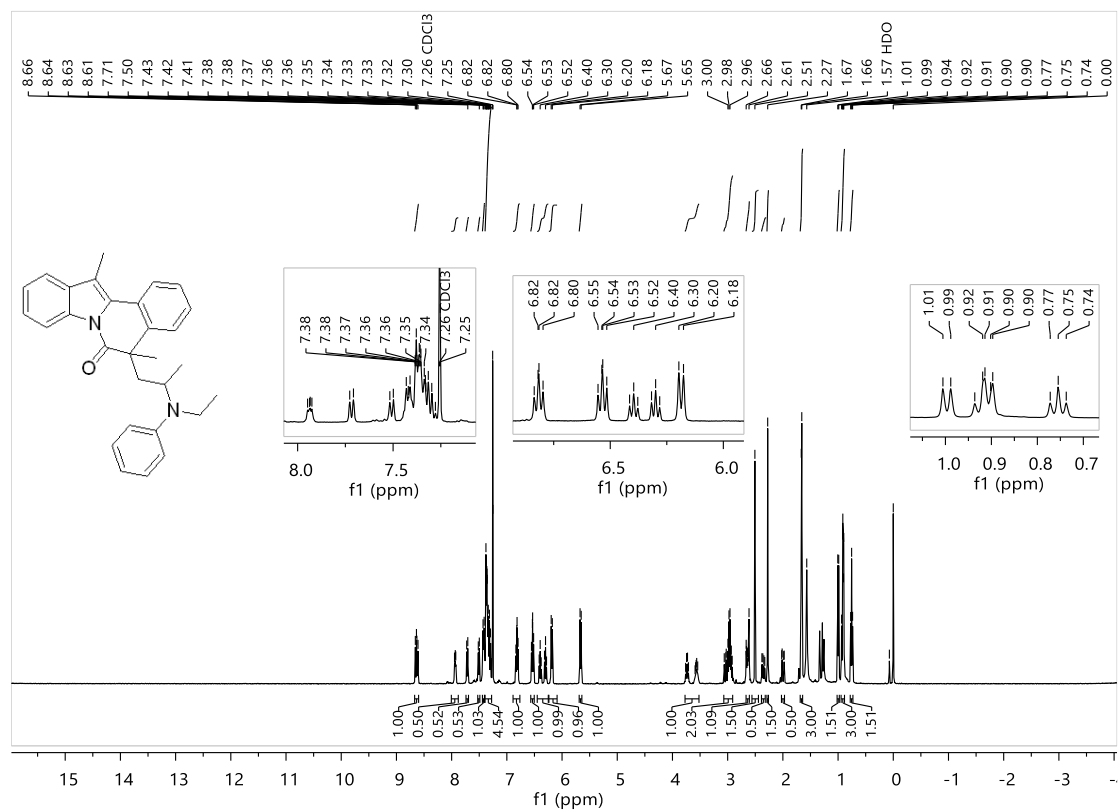
5e: ^1H NMR (400MHz, CDCl_3)



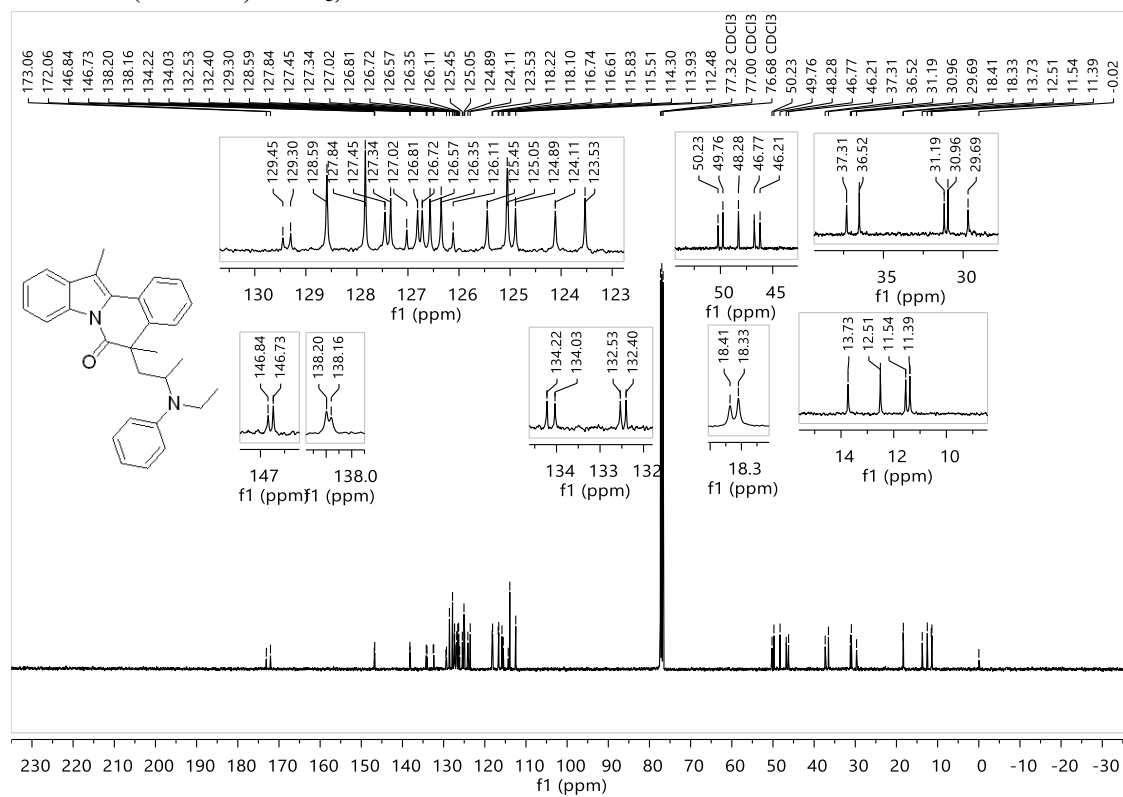
^{13}C NMR (101MHz, CDCl_3)



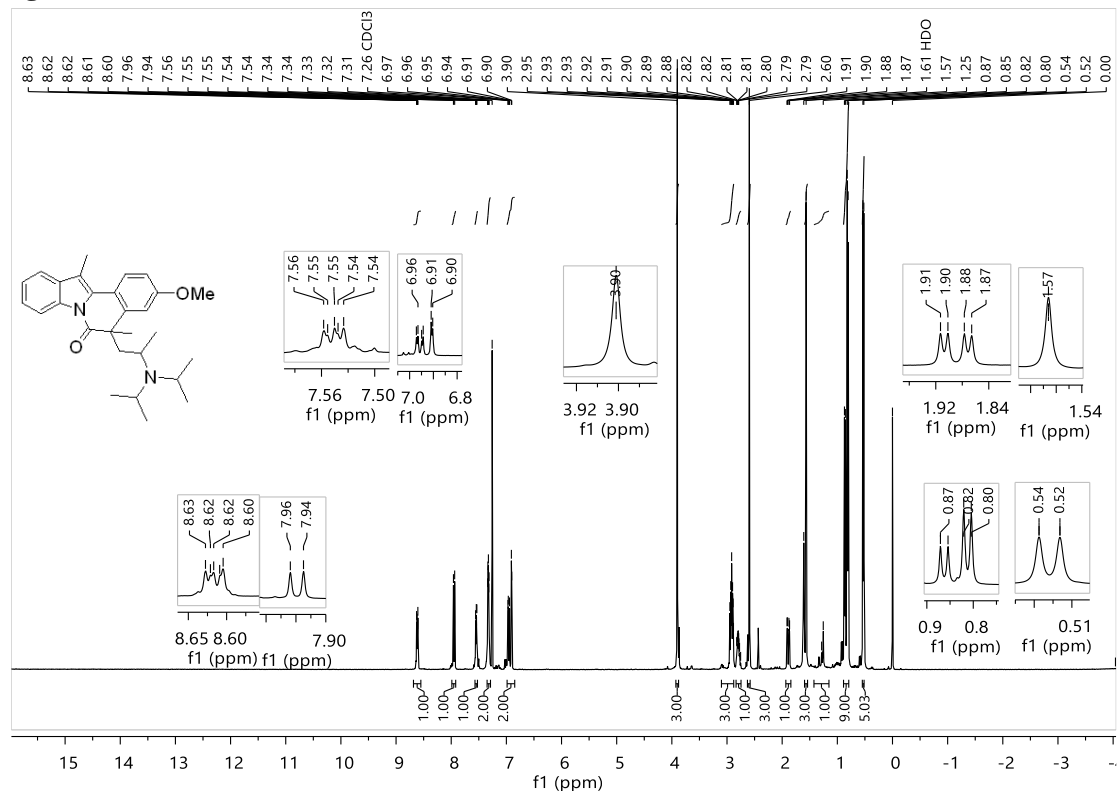
5f: ¹H NMR (400MHz, CDCl₃)



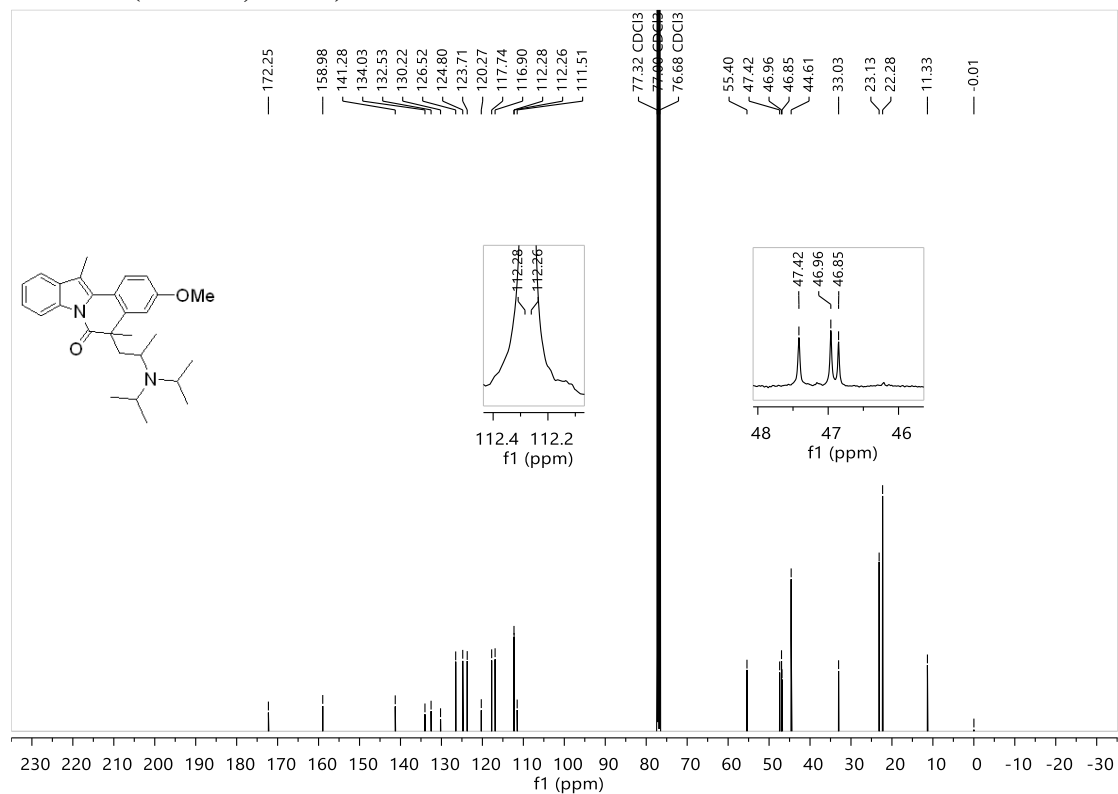
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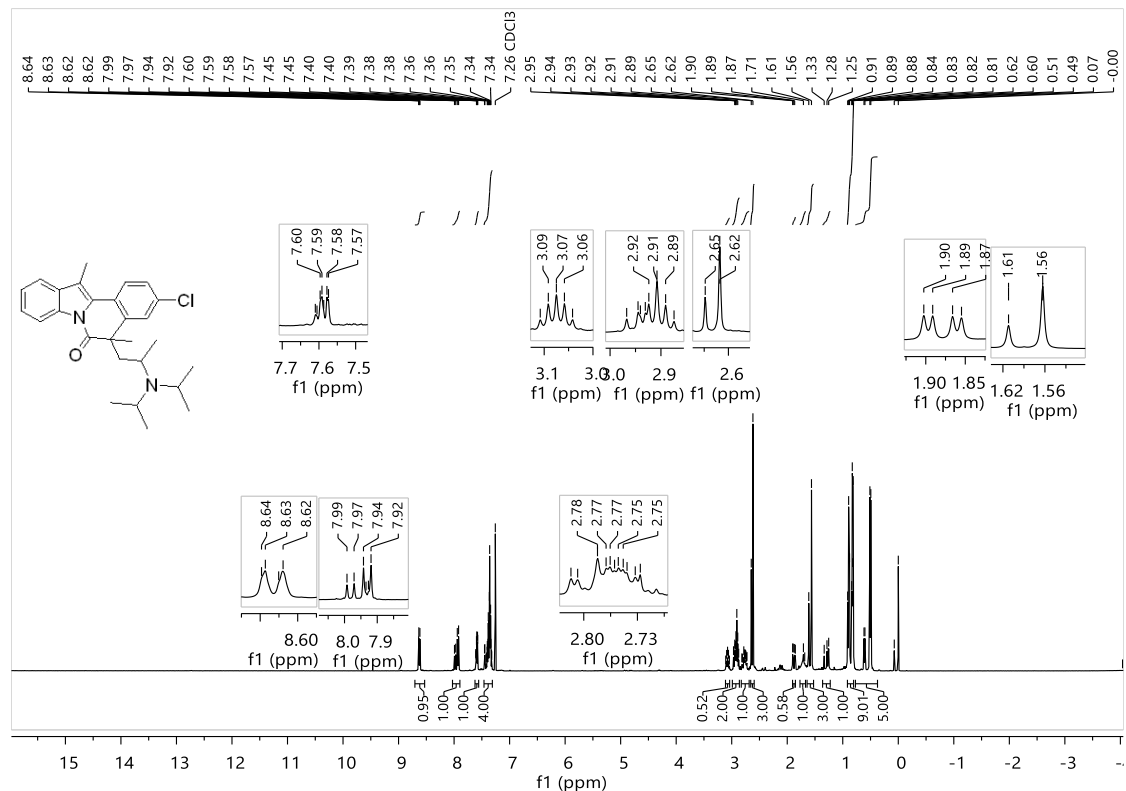
5g: ¹H NMR (400MHz, CDCl₃)



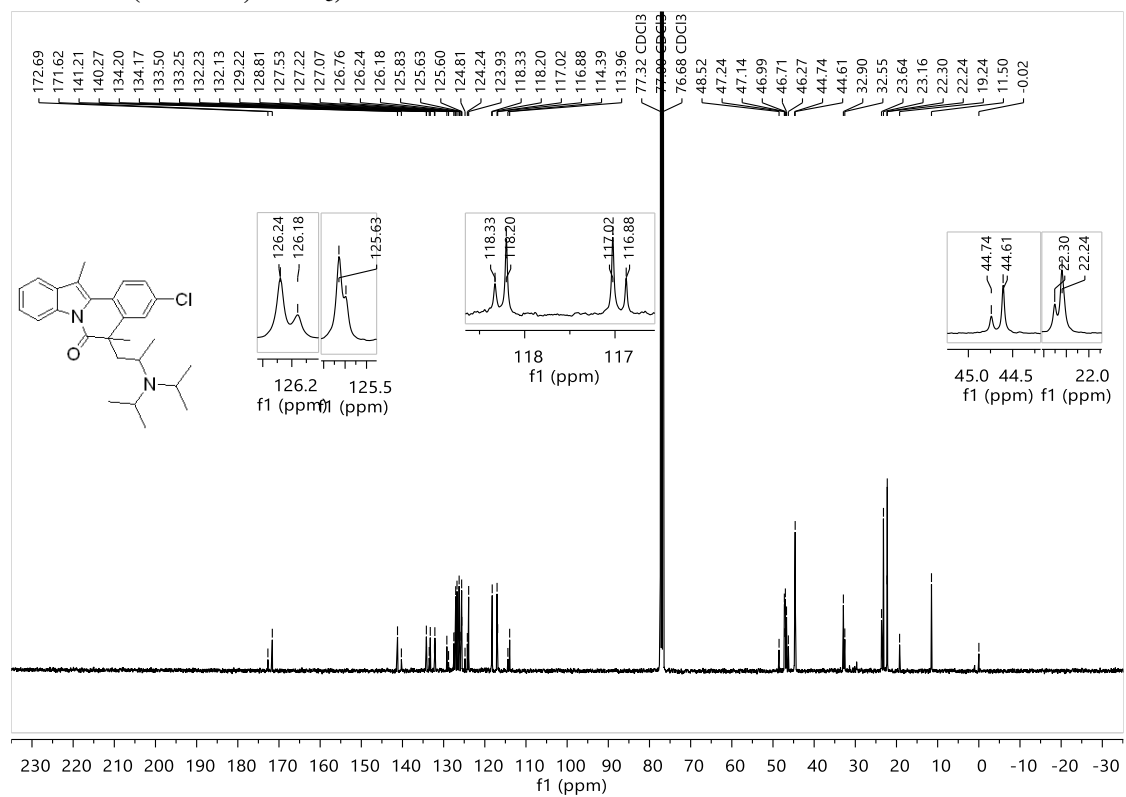
¹³C NMR (101MHz, CDCl₃)



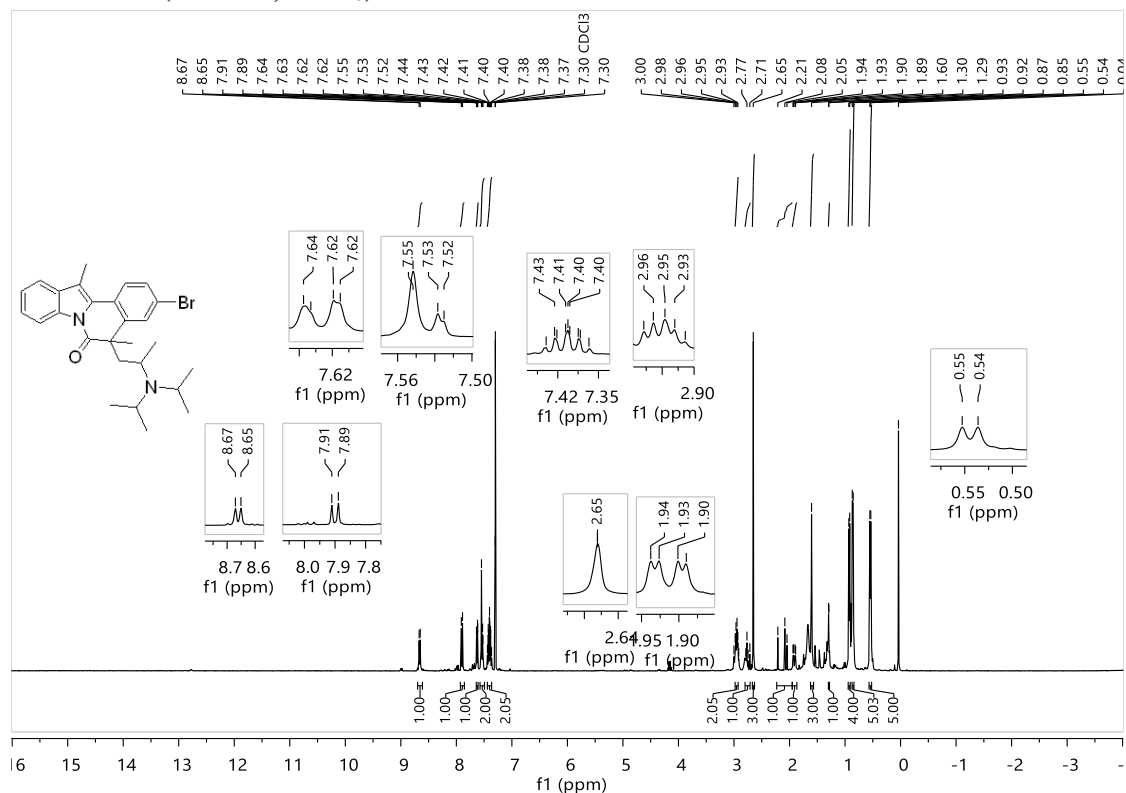
5h: ¹H NMR (400MHz, CDCl₃)



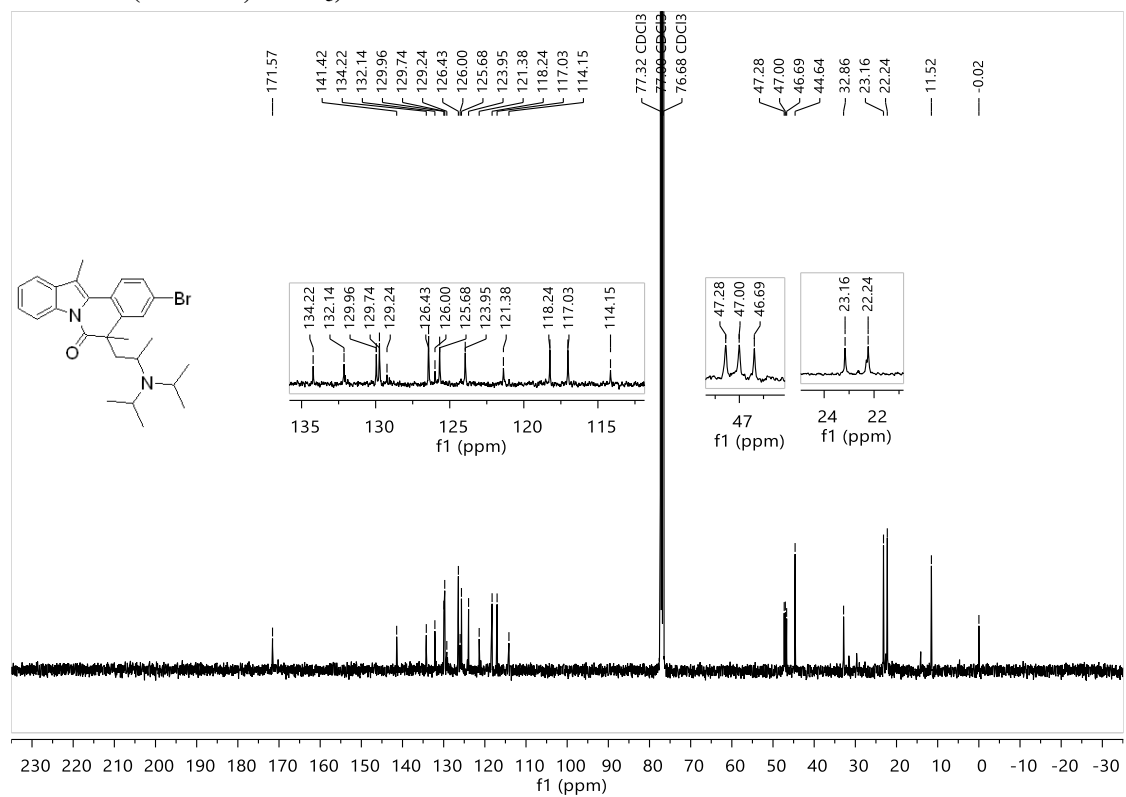
¹³C NMR (101MHz, CDCl₃)



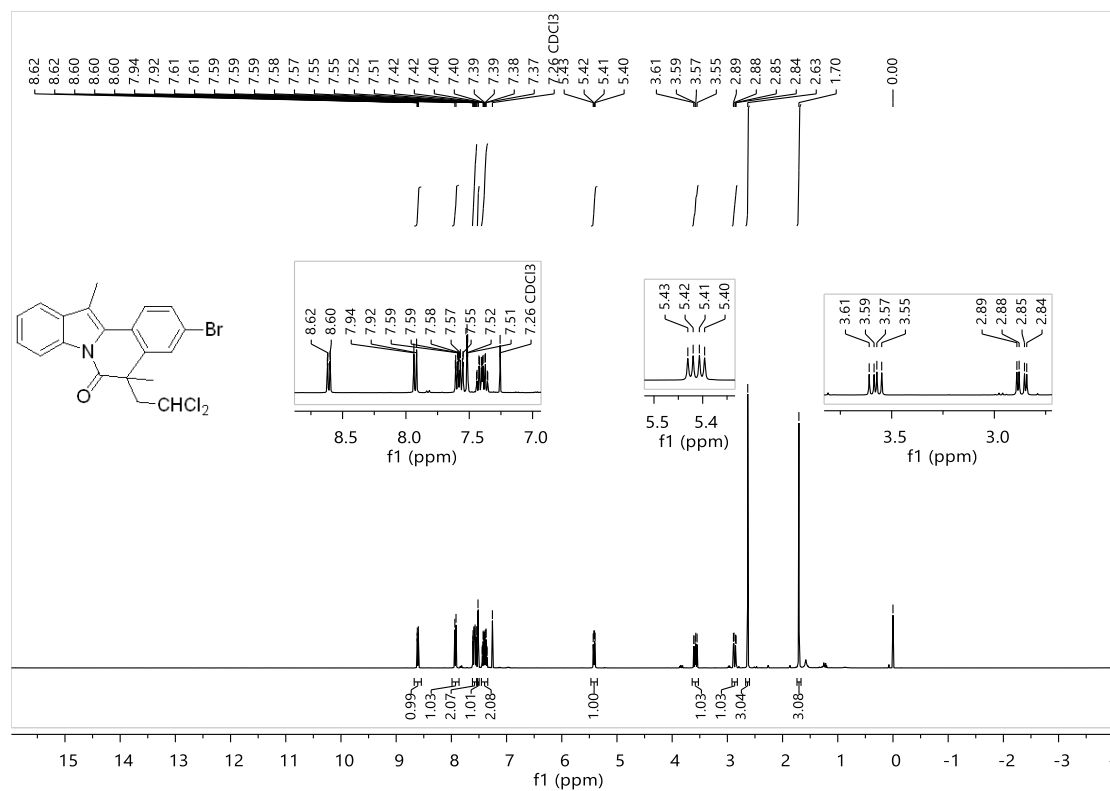
5i: ¹H NMR (400MHz, CDCl₃)



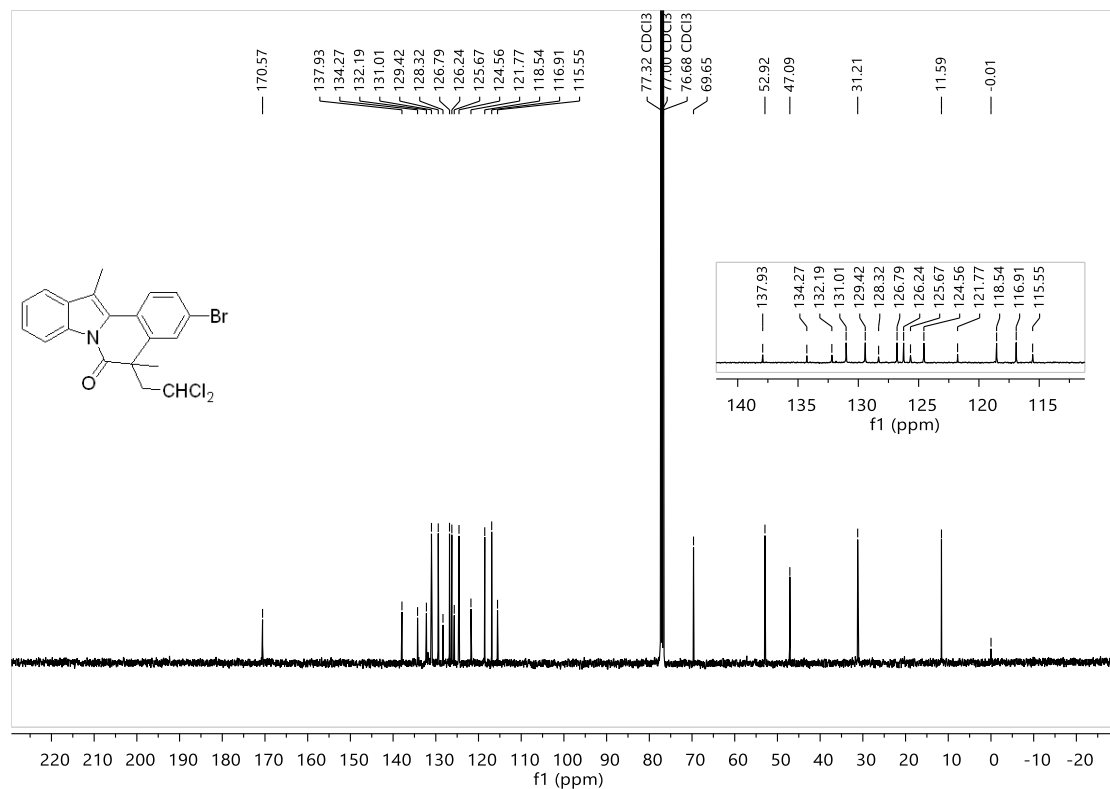
¹³C NMR (101MHz, CDCl₃)



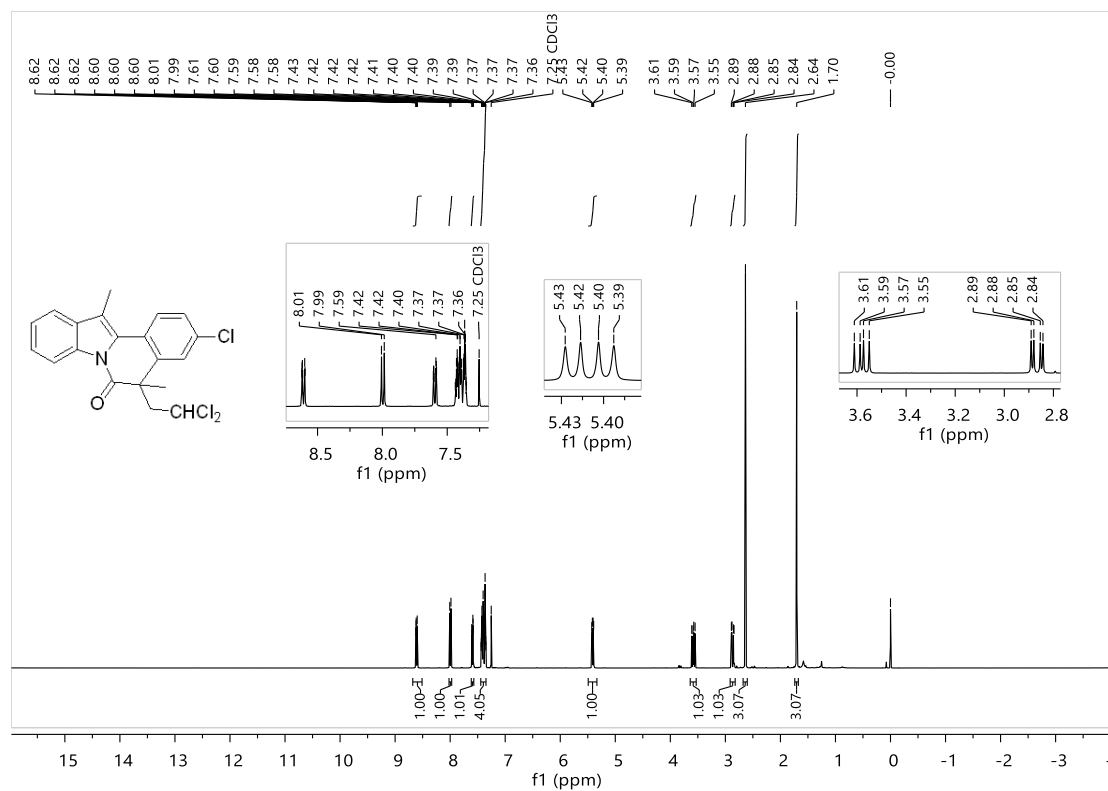
6a: ¹H NMR (400MHz, CDCl₃)



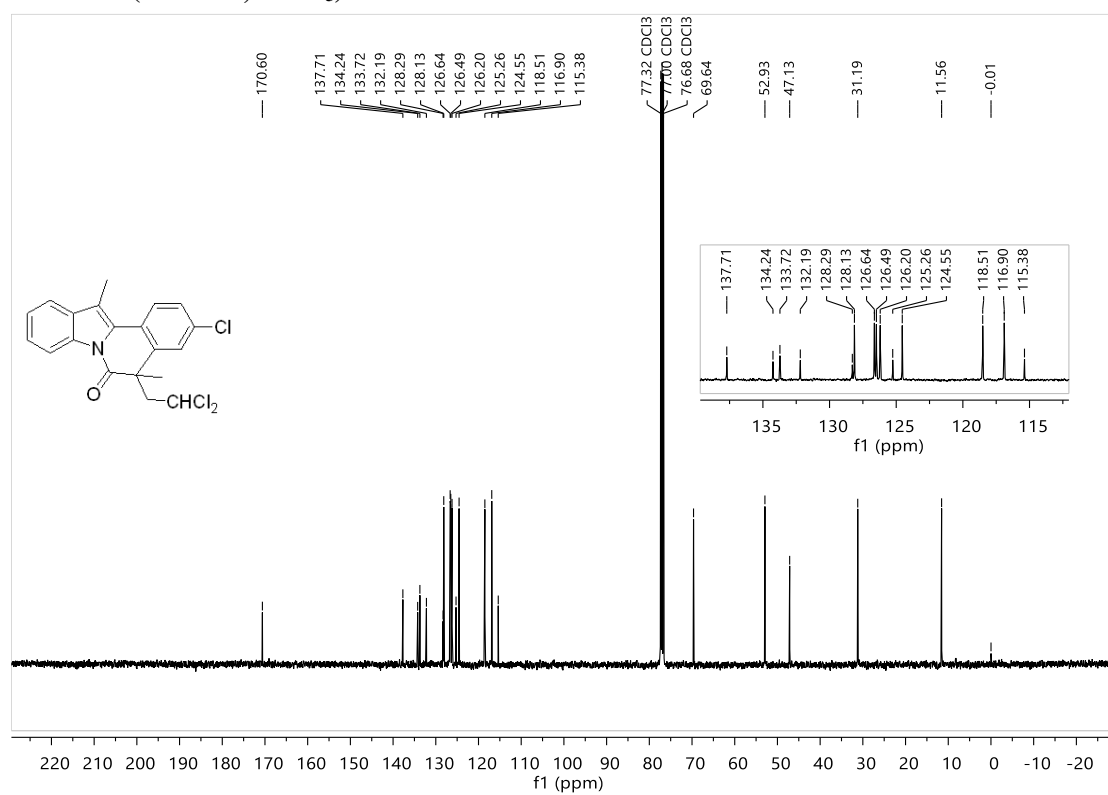
¹³C NMR (101MHz, CDCl₃)



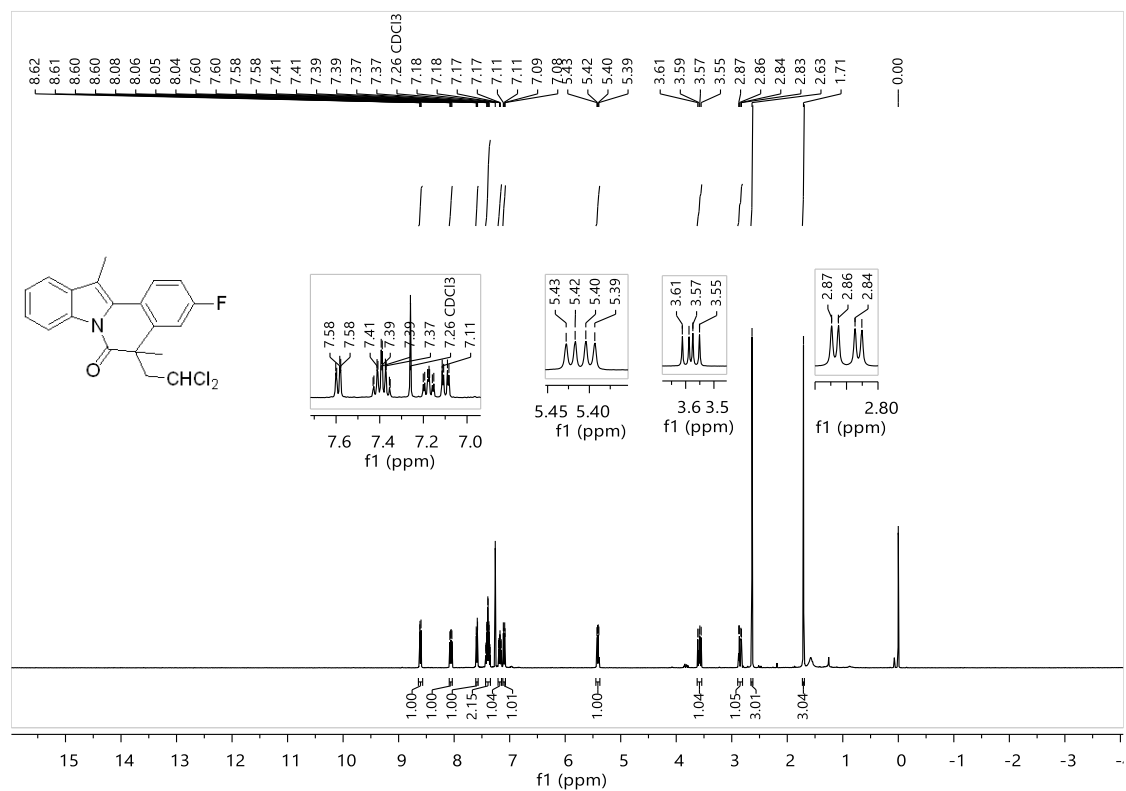
6b: ¹H NMR (400MHz, CDCl₃)



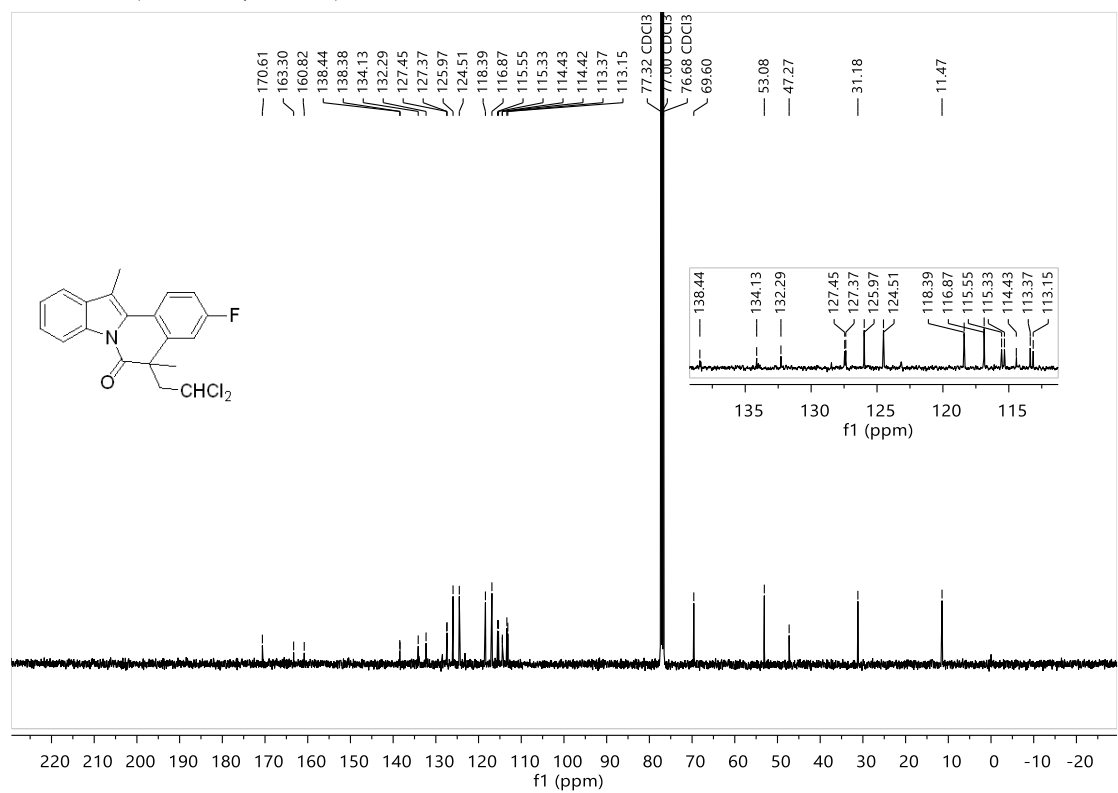
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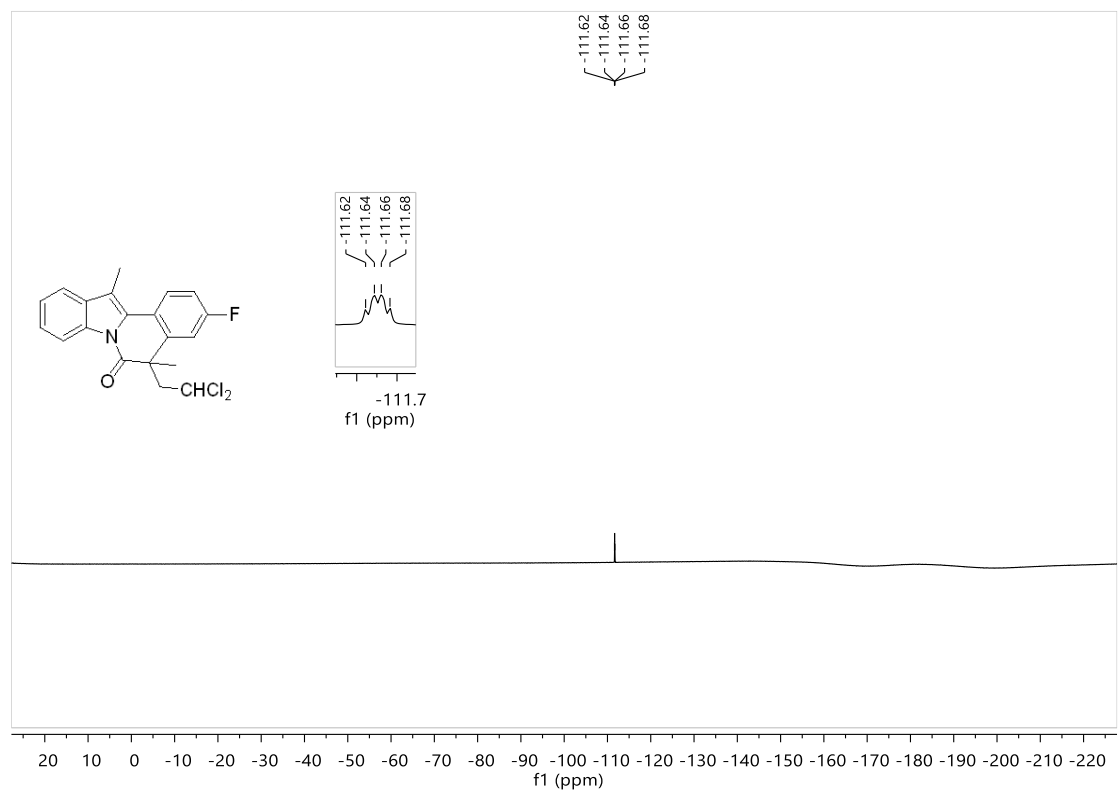
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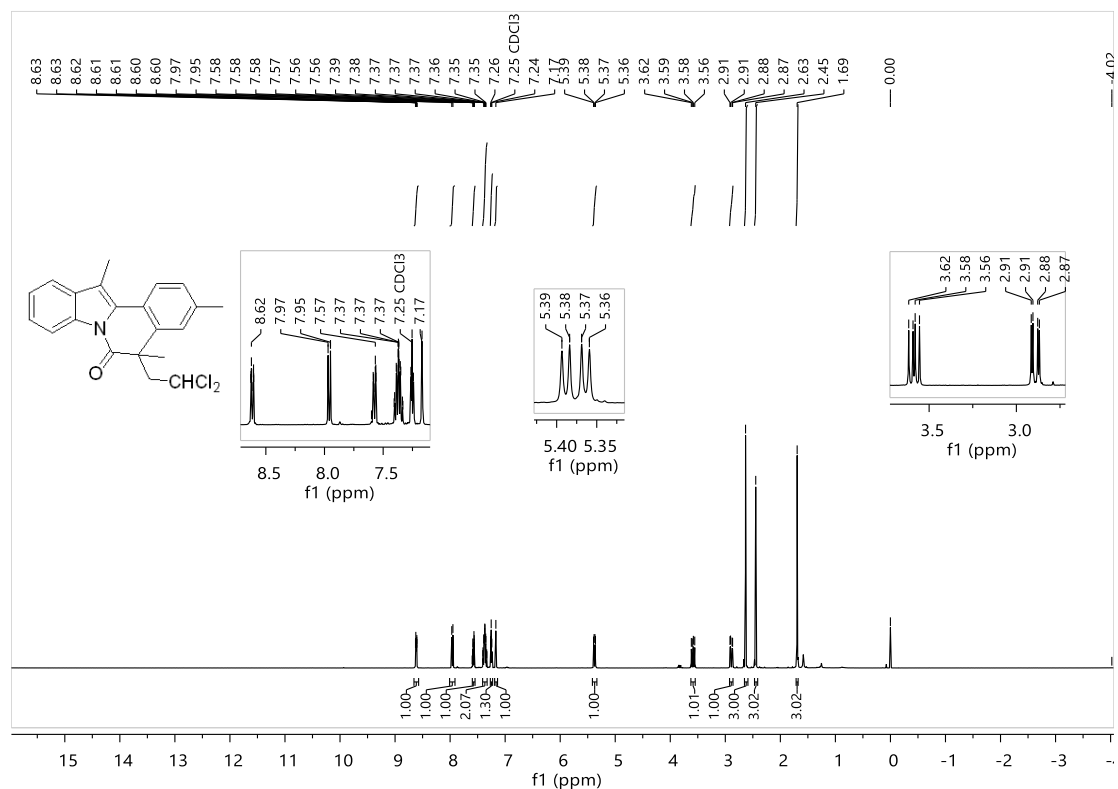
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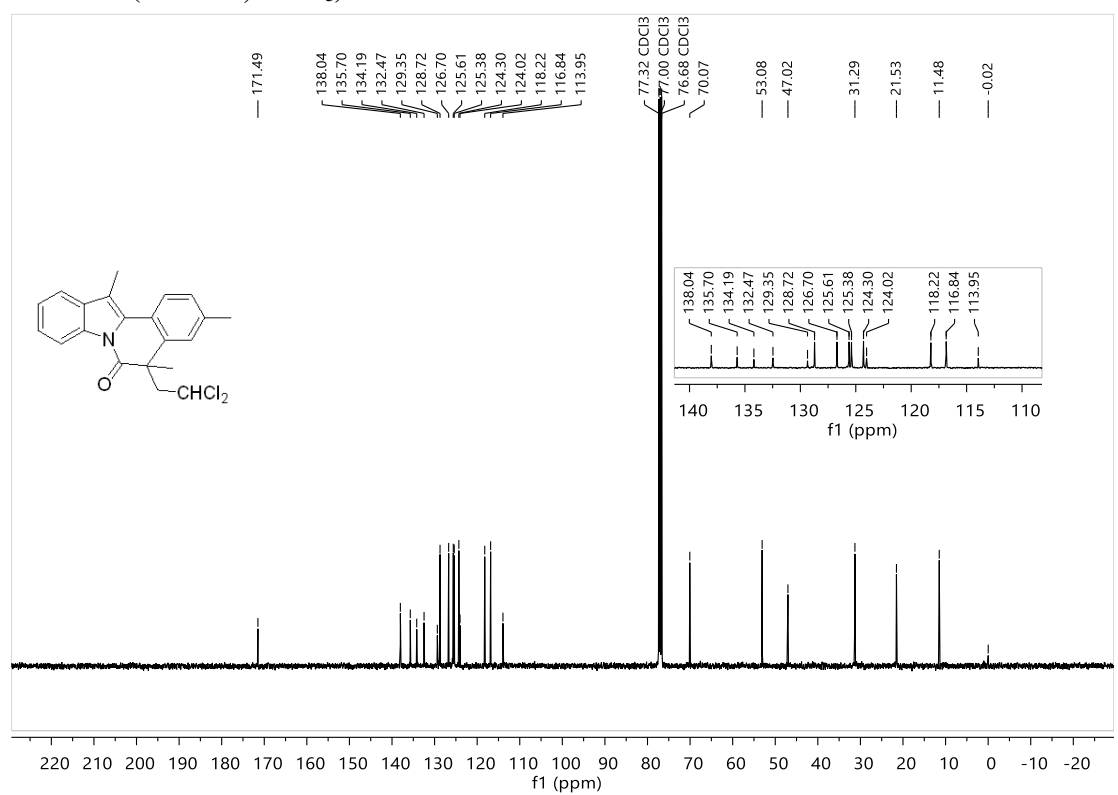
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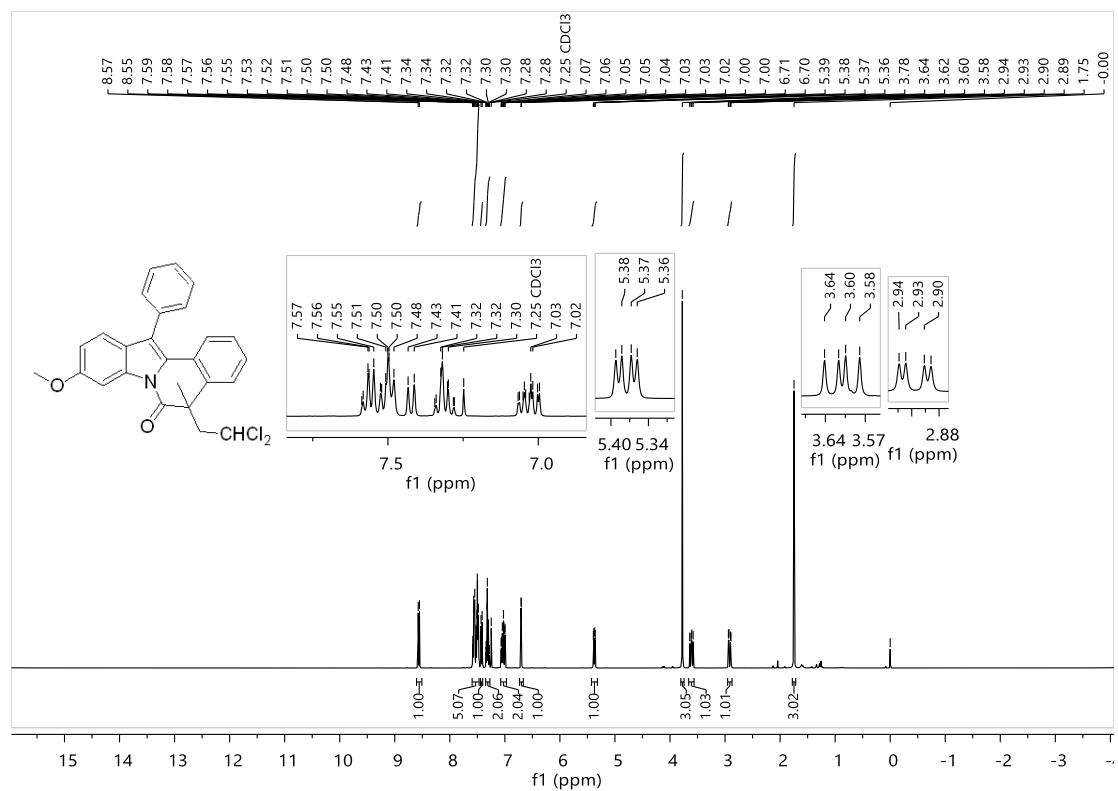
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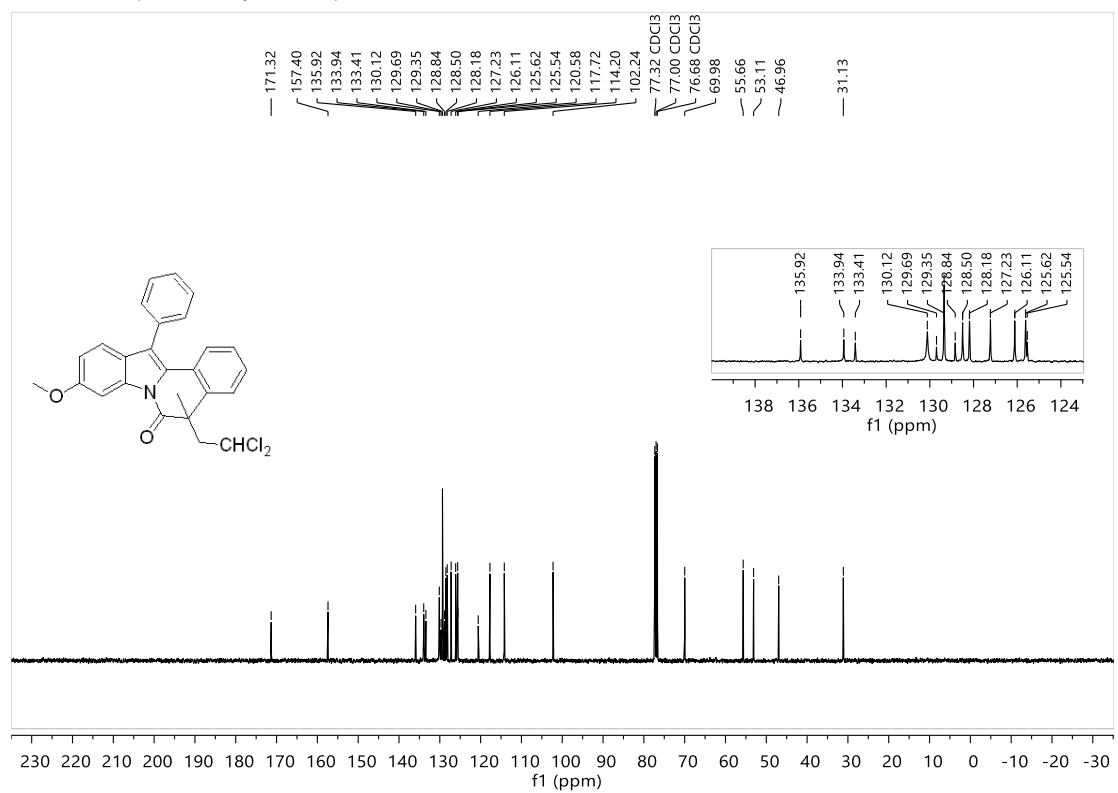
¹³C NMR (101MHz, CDCl₃)



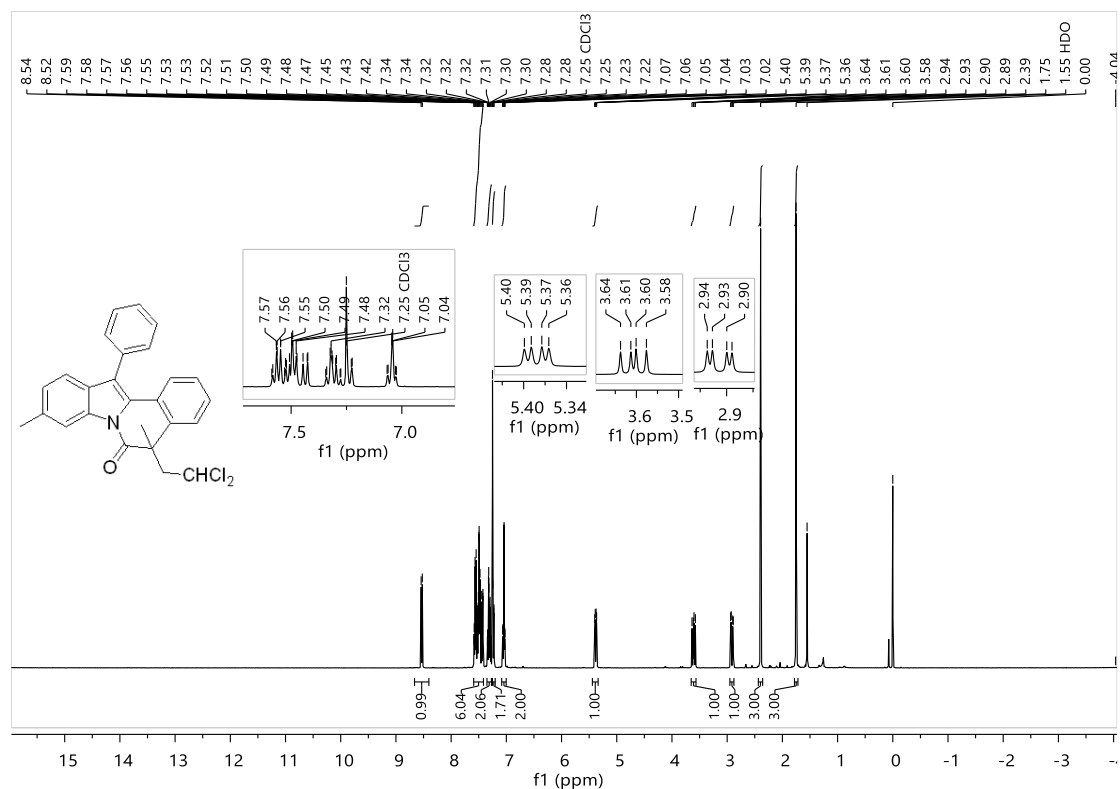
6e: ^1H NMR (400MHz, CDCl_3)



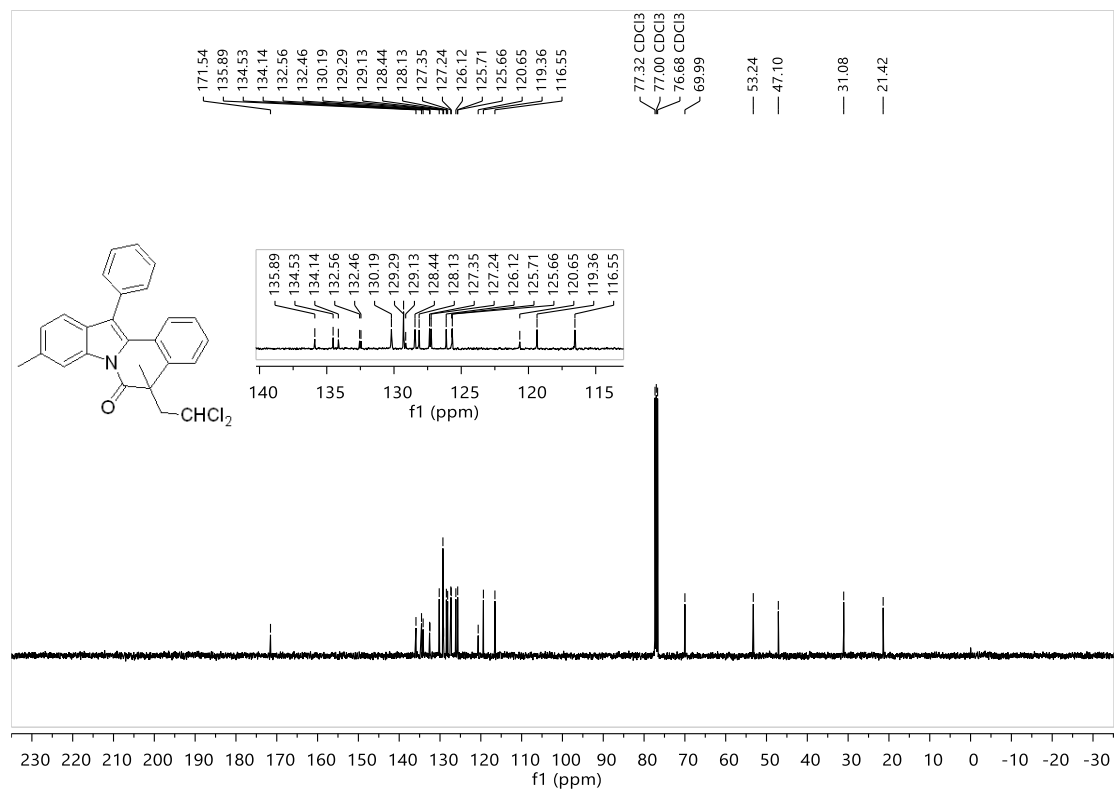
^{13}C NMR (101MHz, CDCl_3)



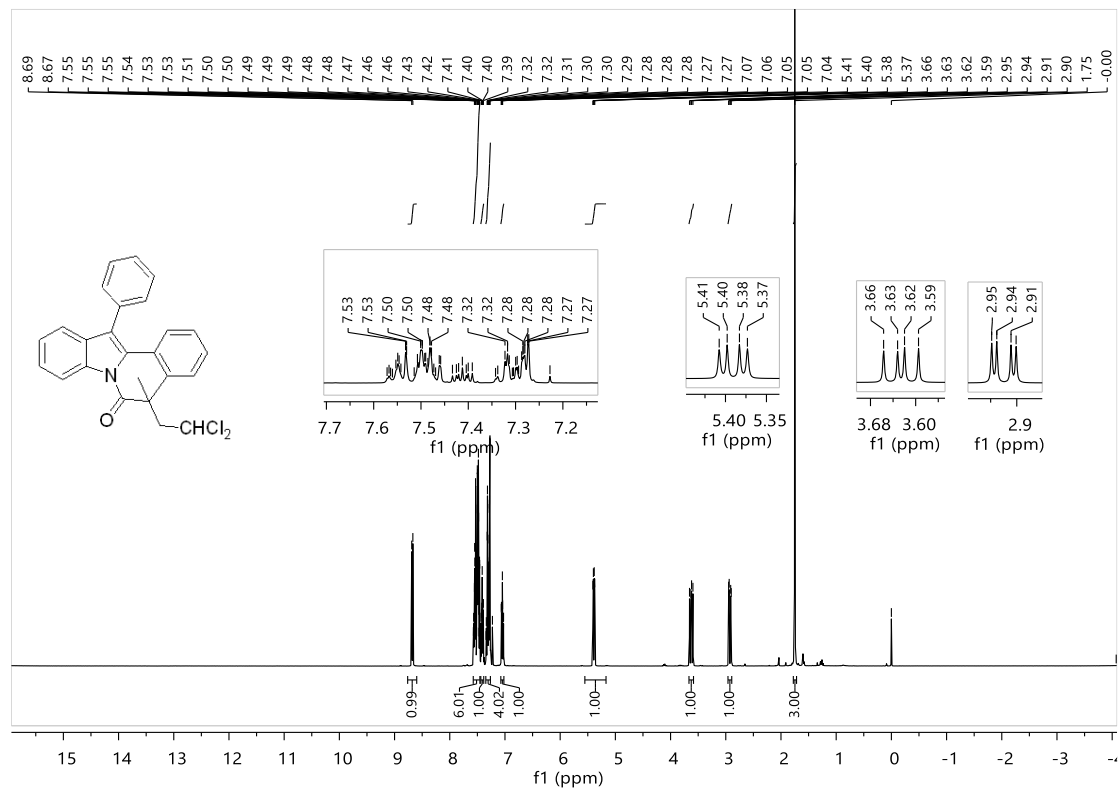
6f: ¹H NMR (400MHz, CDCl₃)



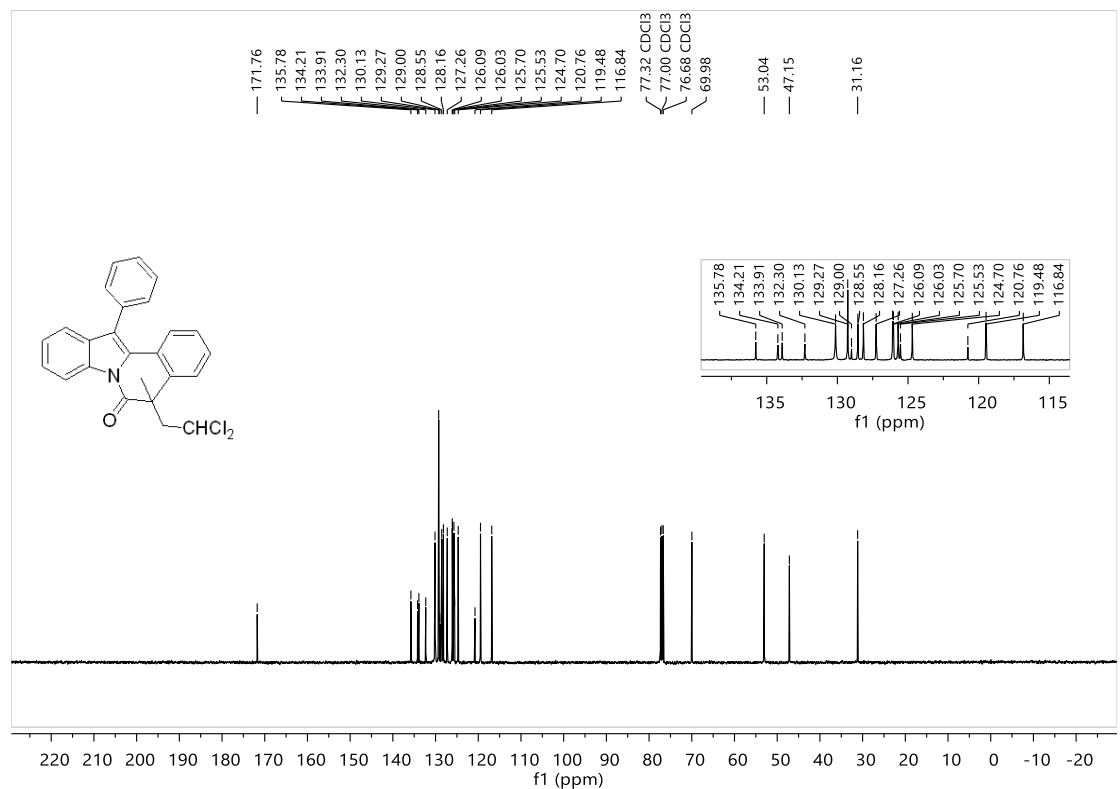
¹³C NMR (101MHz, CDCl₃)



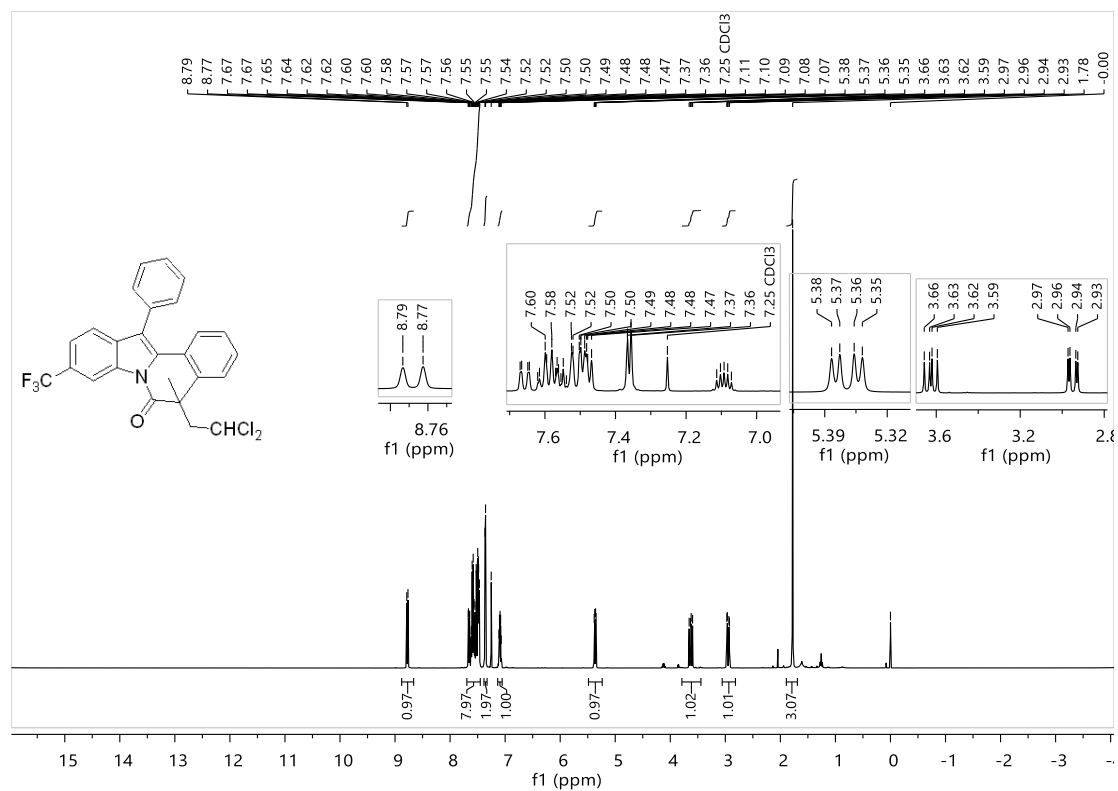
6g: ¹H NMR (400MHz, CDCl₃)



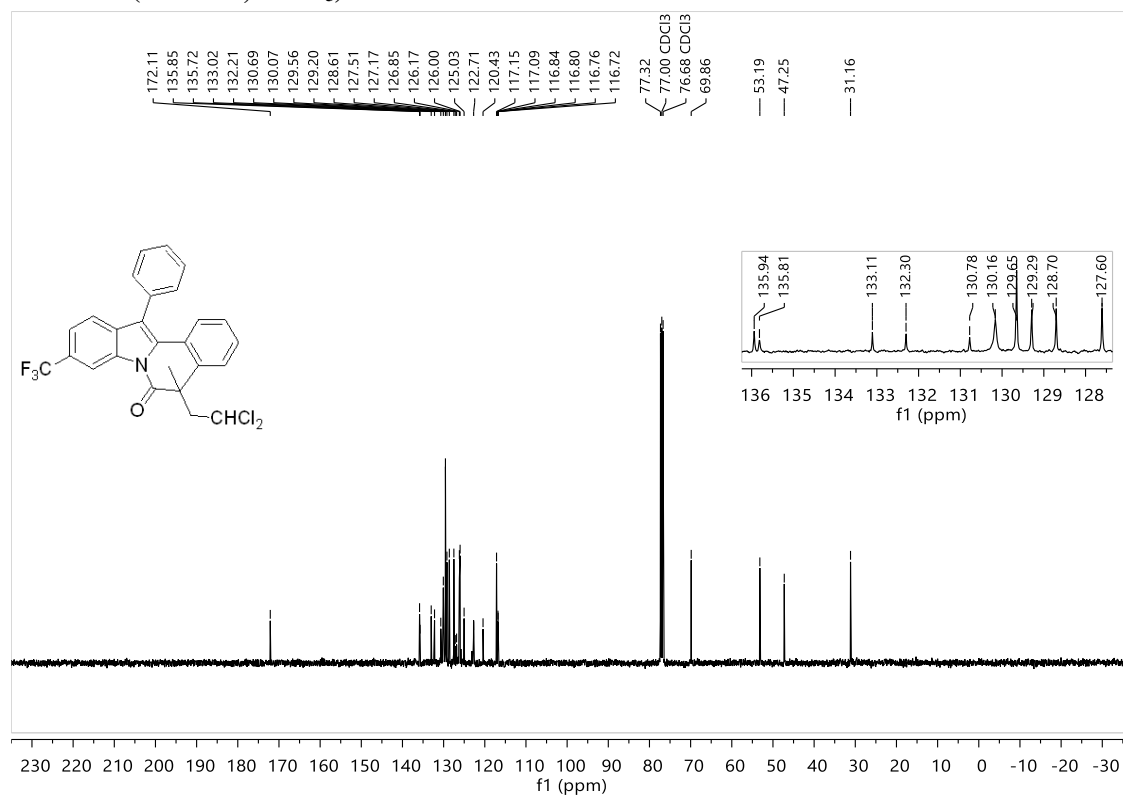
¹³C NMR (101MHz, CDCl₃)



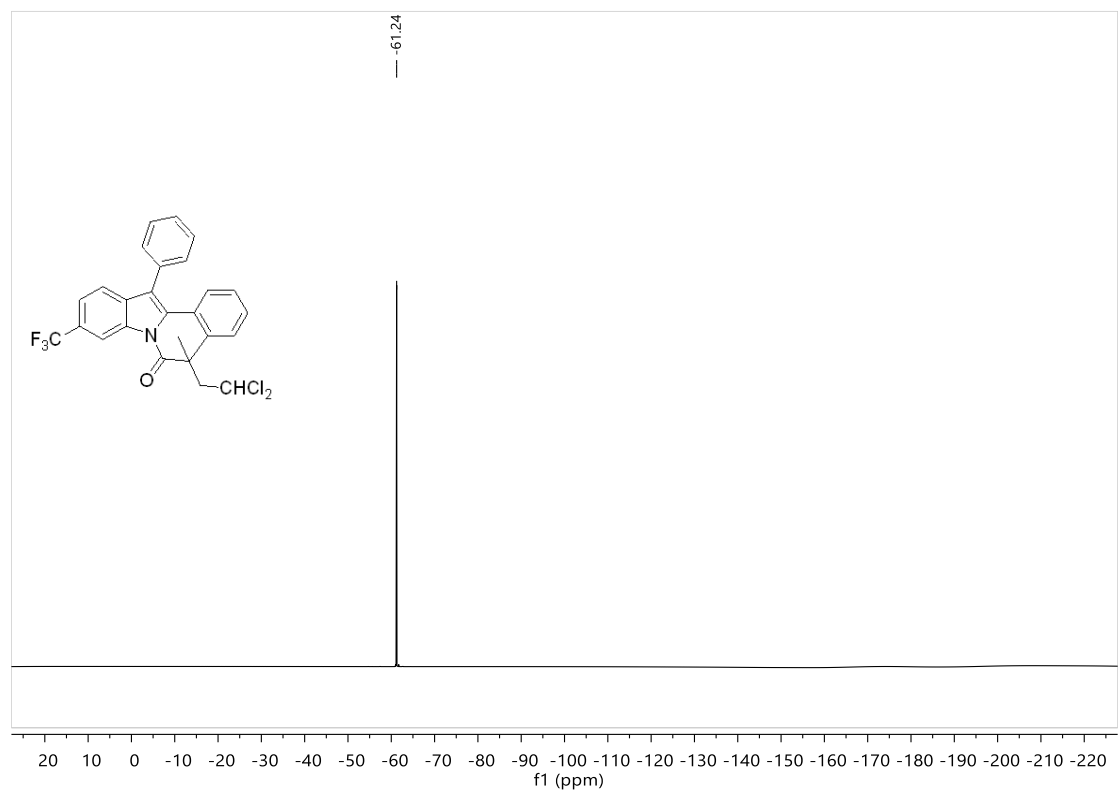
6h: ¹H NMR (400MHz, CDCl₃)



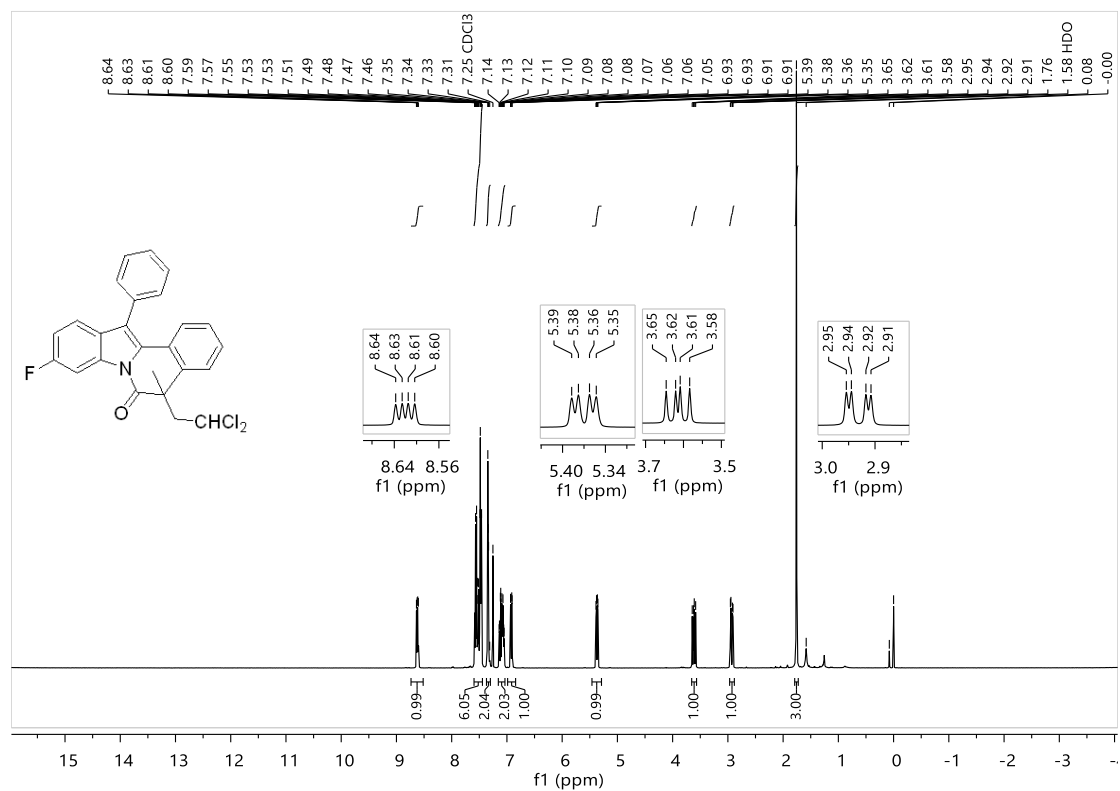
¹³C NMR (101MHz, CDCl₃)



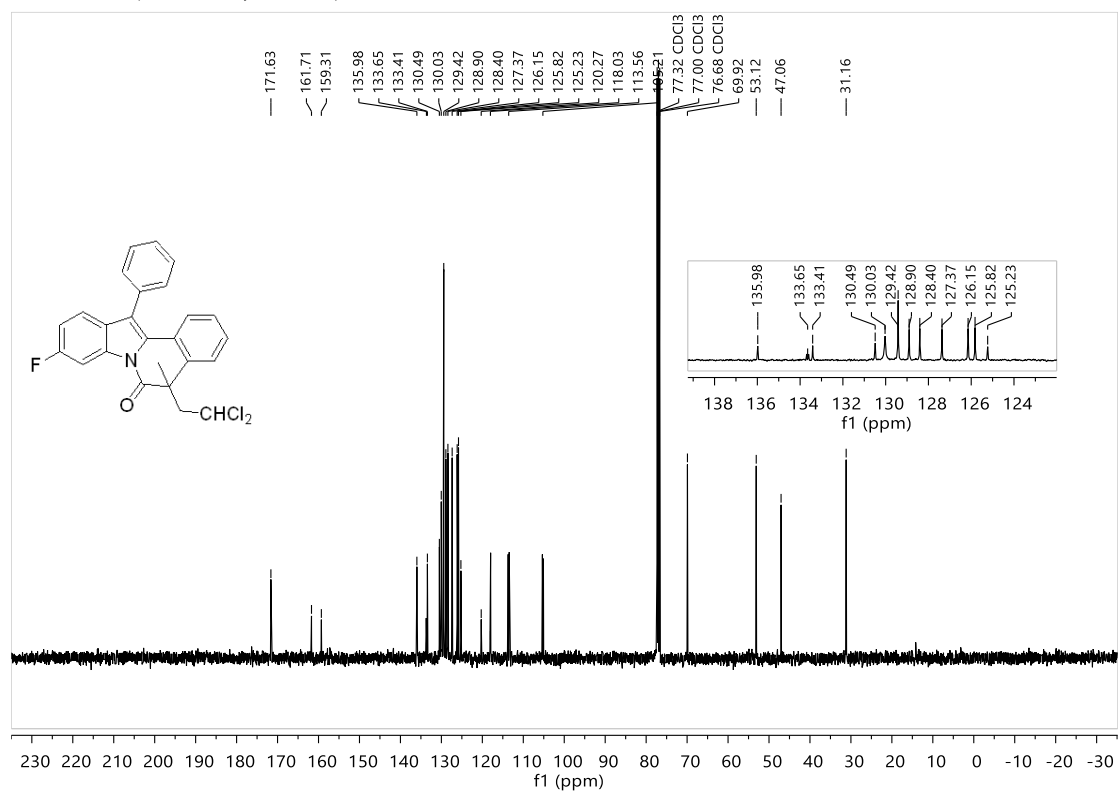
¹⁹F NMR (376MHz, CDCl₃)



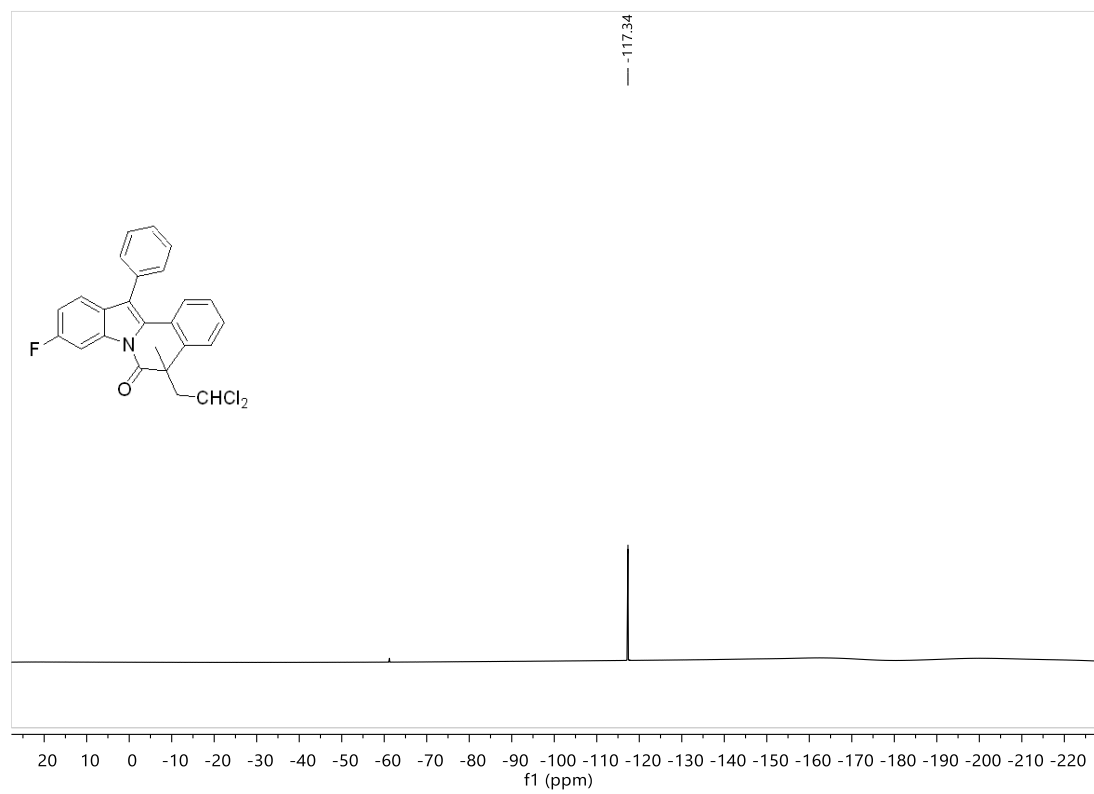
6i: ¹H NMR (400MHz, CDCl₃)



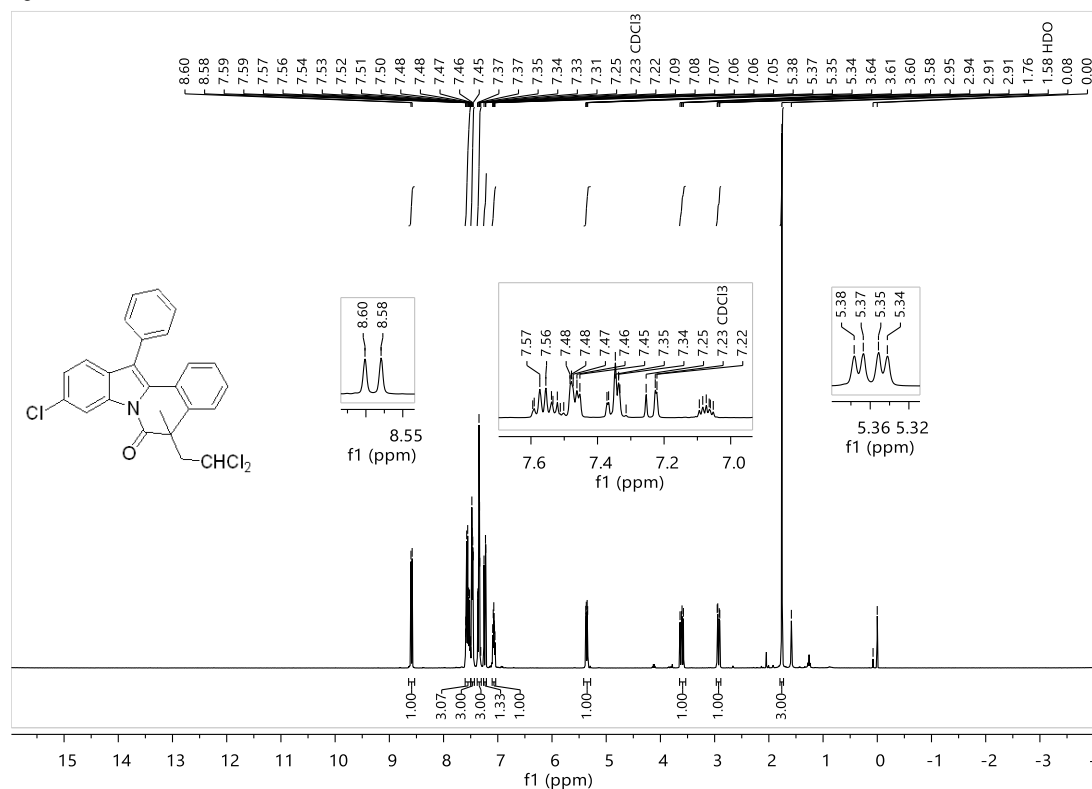
¹³C NMR (101MHz, CDCl₃)



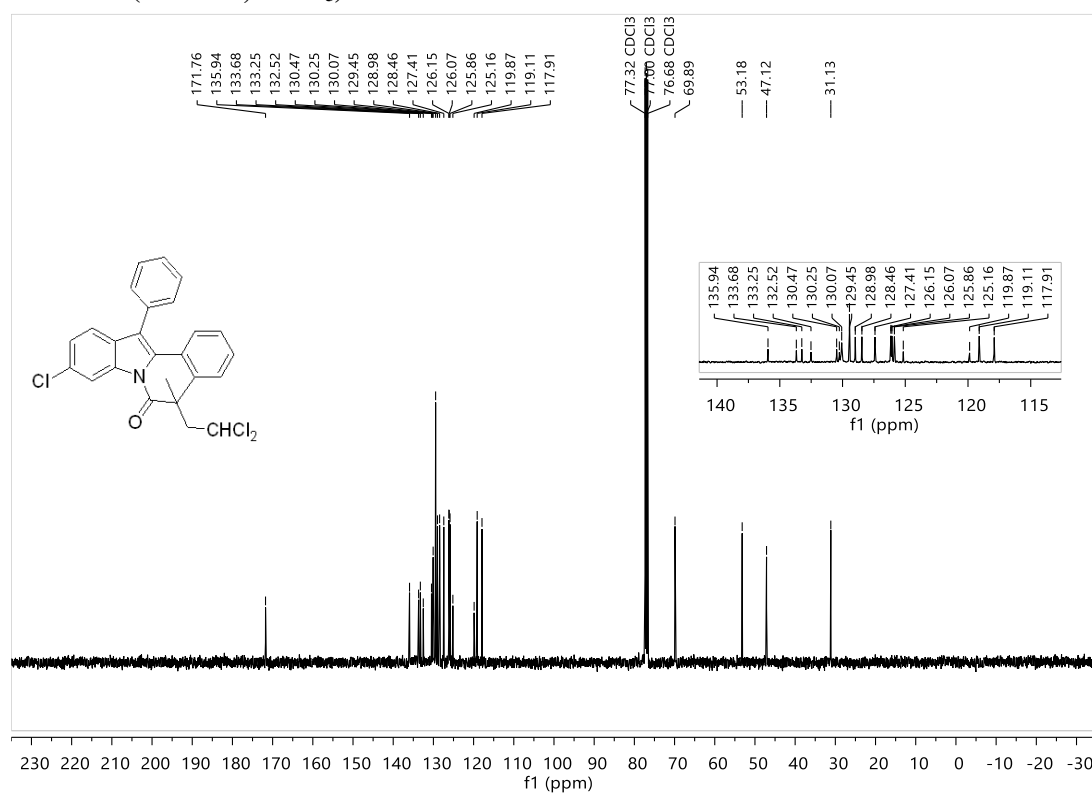
¹⁹F NMR (376MHz, CDCl₃)



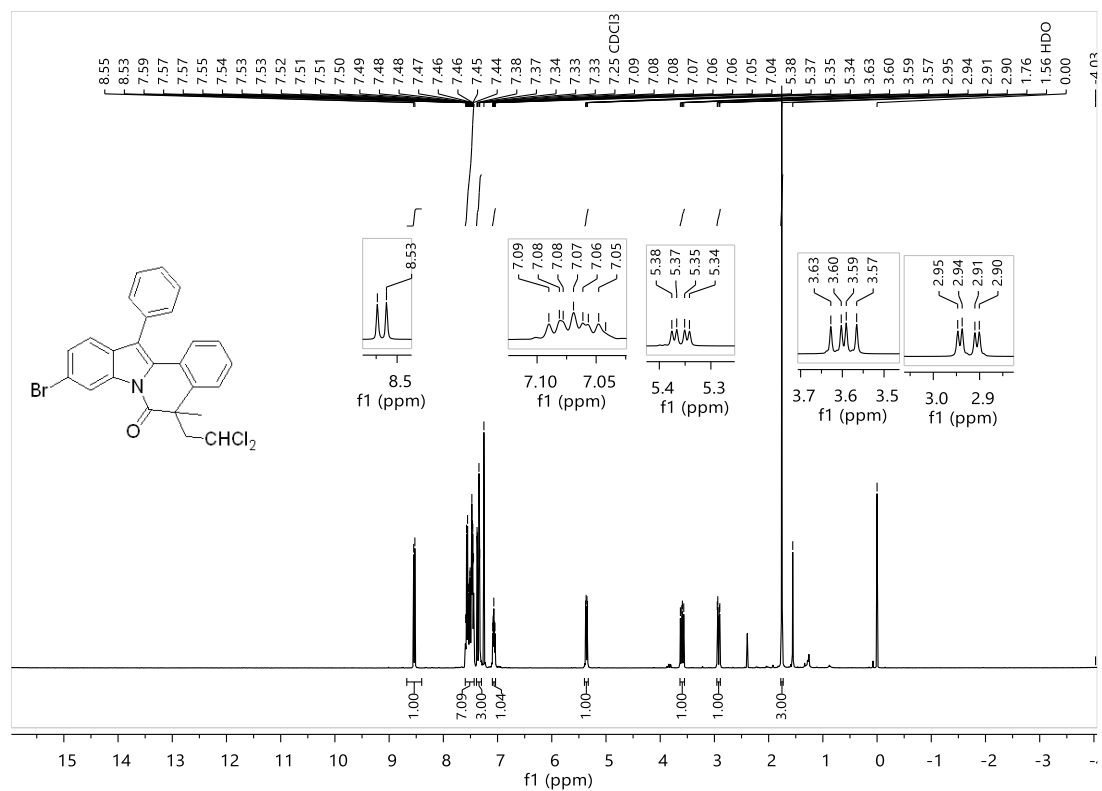
6j: ¹H NMR (400MHz, CDCl₃)



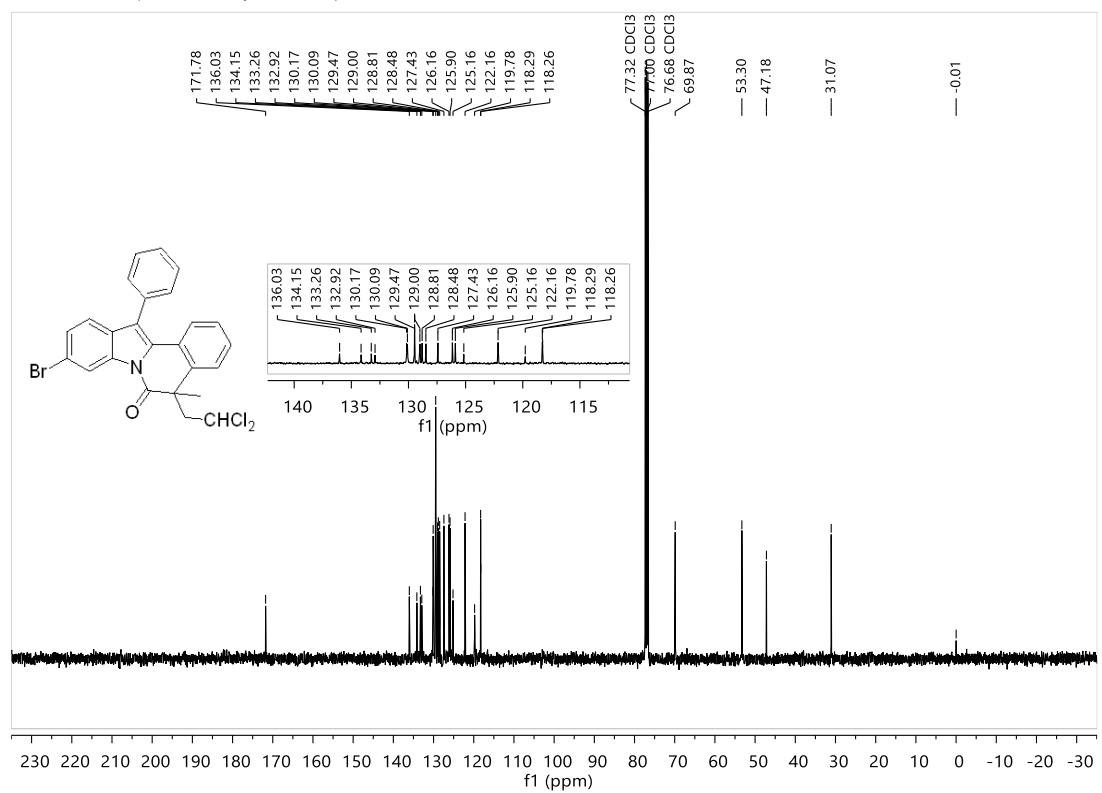
¹³C NMR (101MHz, CDCl₃)



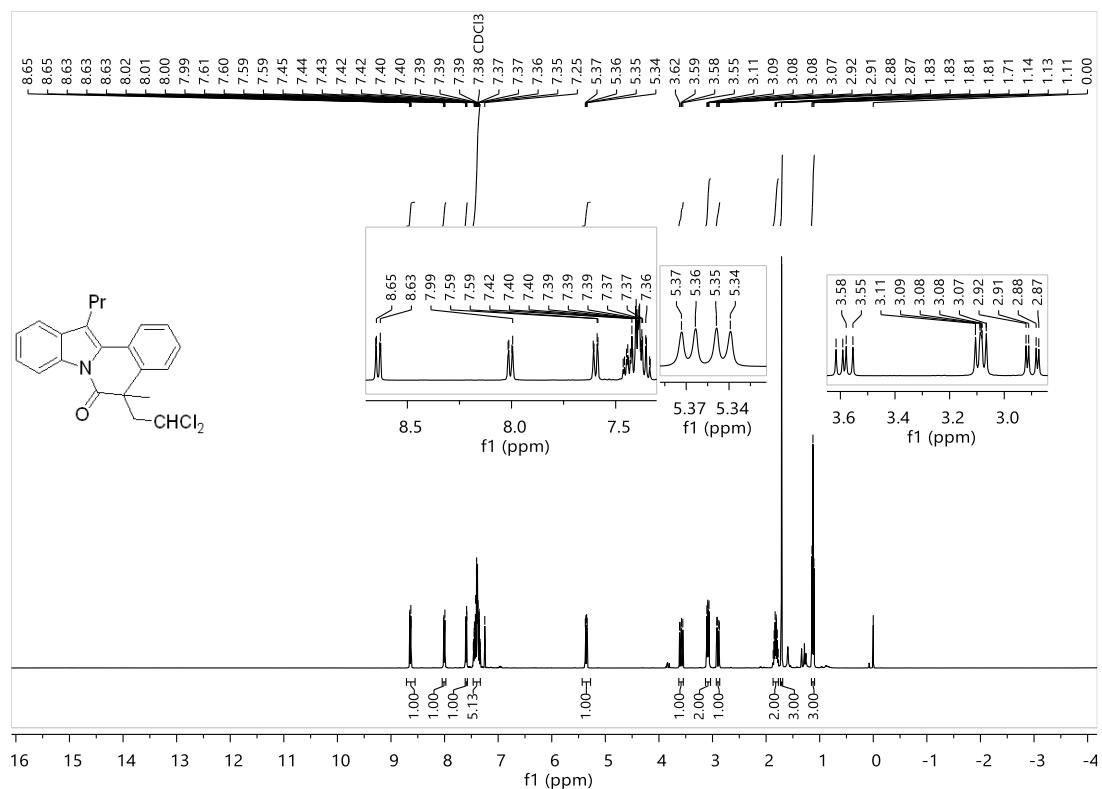
6k: ¹H NMR (400MHz, CDCl₃)



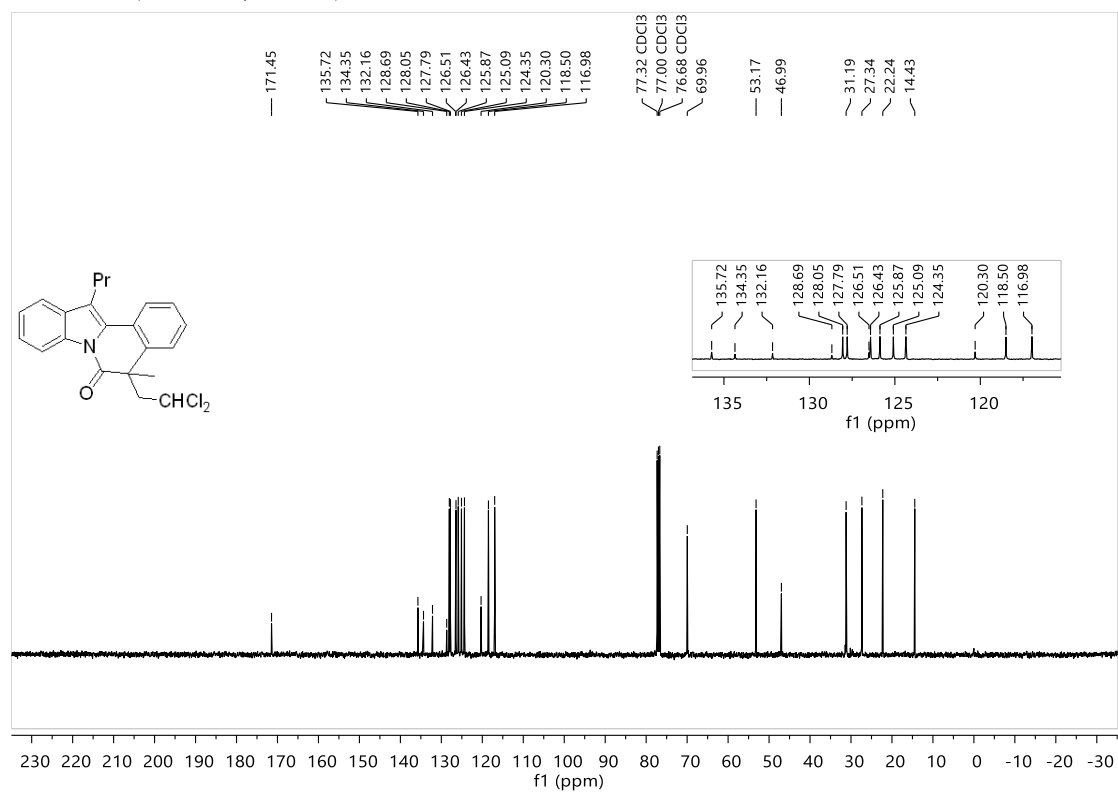
¹³C NMR (101MHz, CDCl₃)



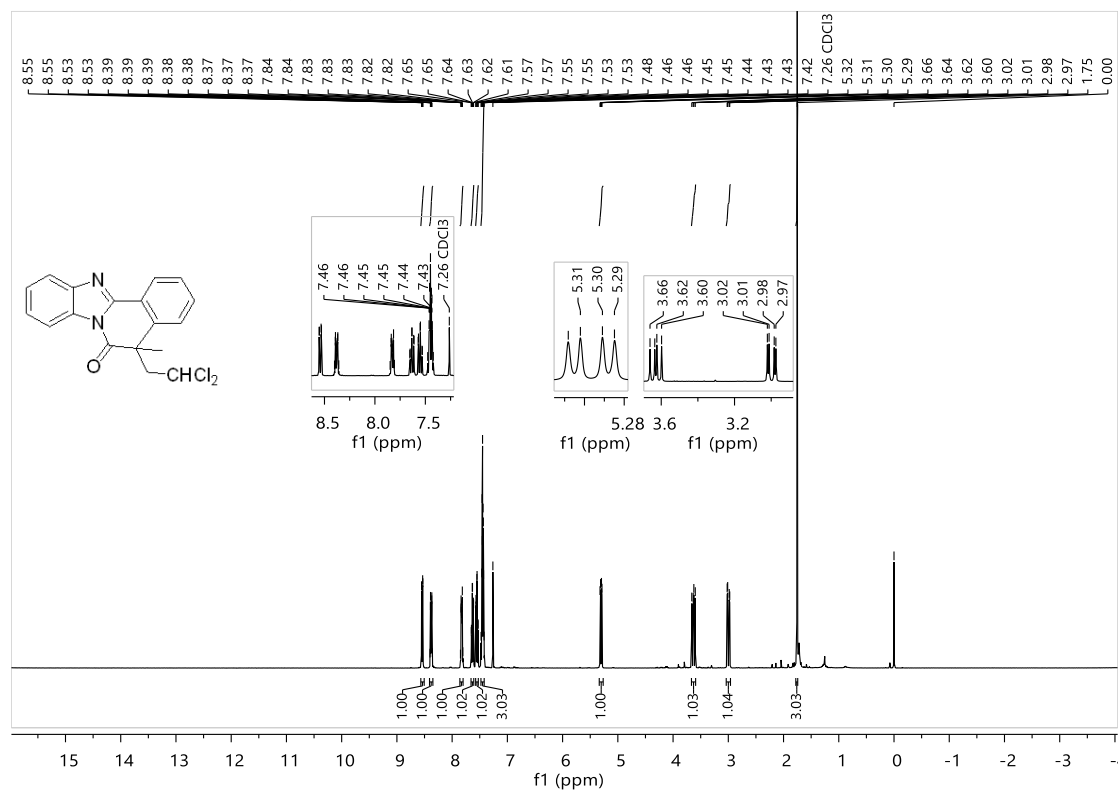
6l: ^1H NMR (400MHz, CDCl_3)



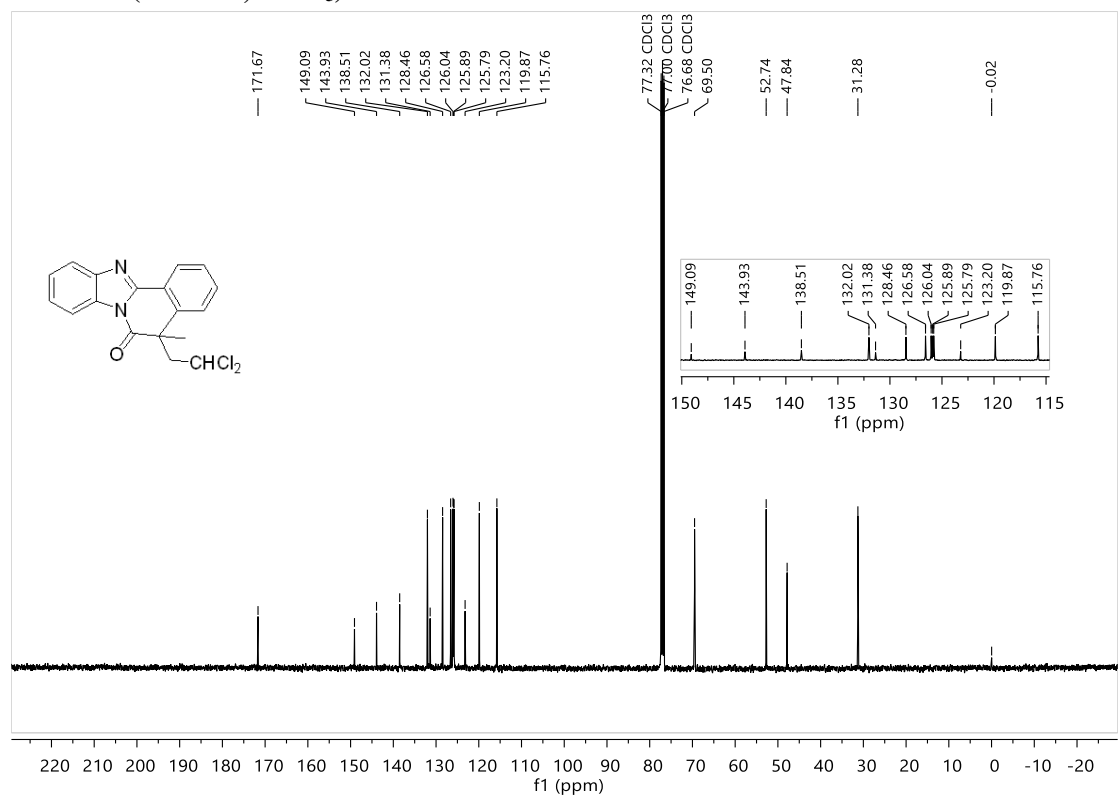
^{13}C NMR (101MHz, CDCl_3)



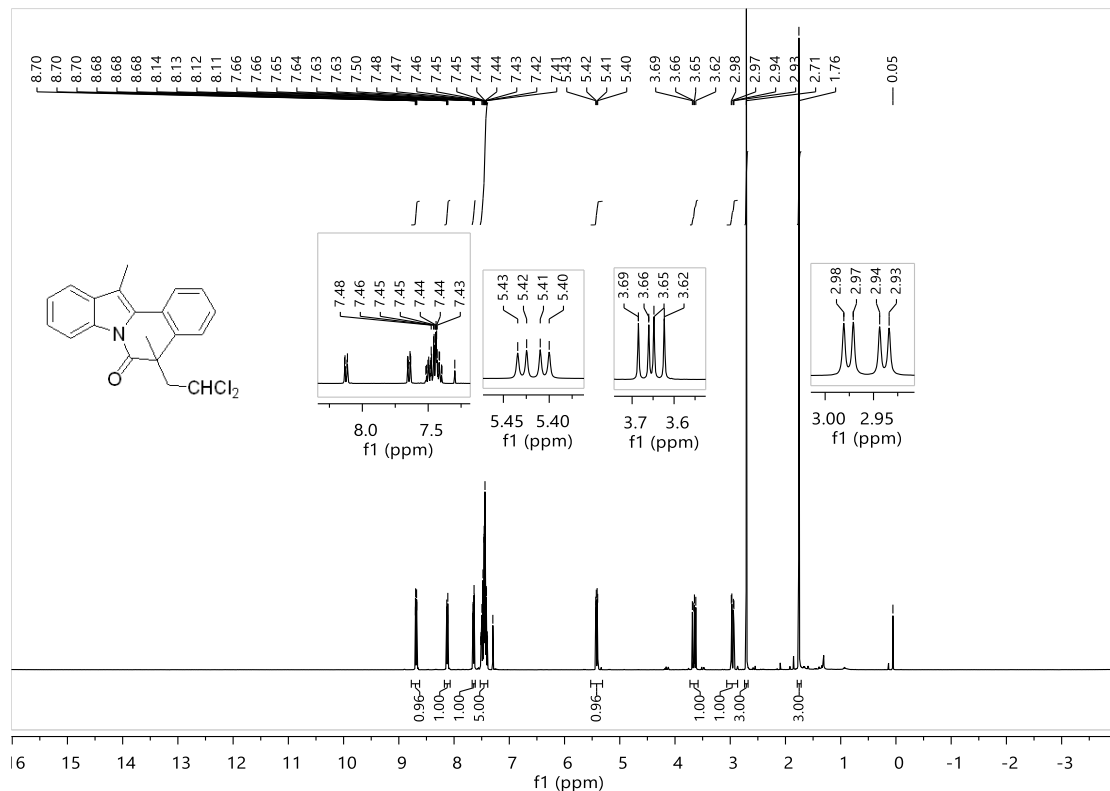
6m: ¹H NMR (400MHz, CDCl₃)



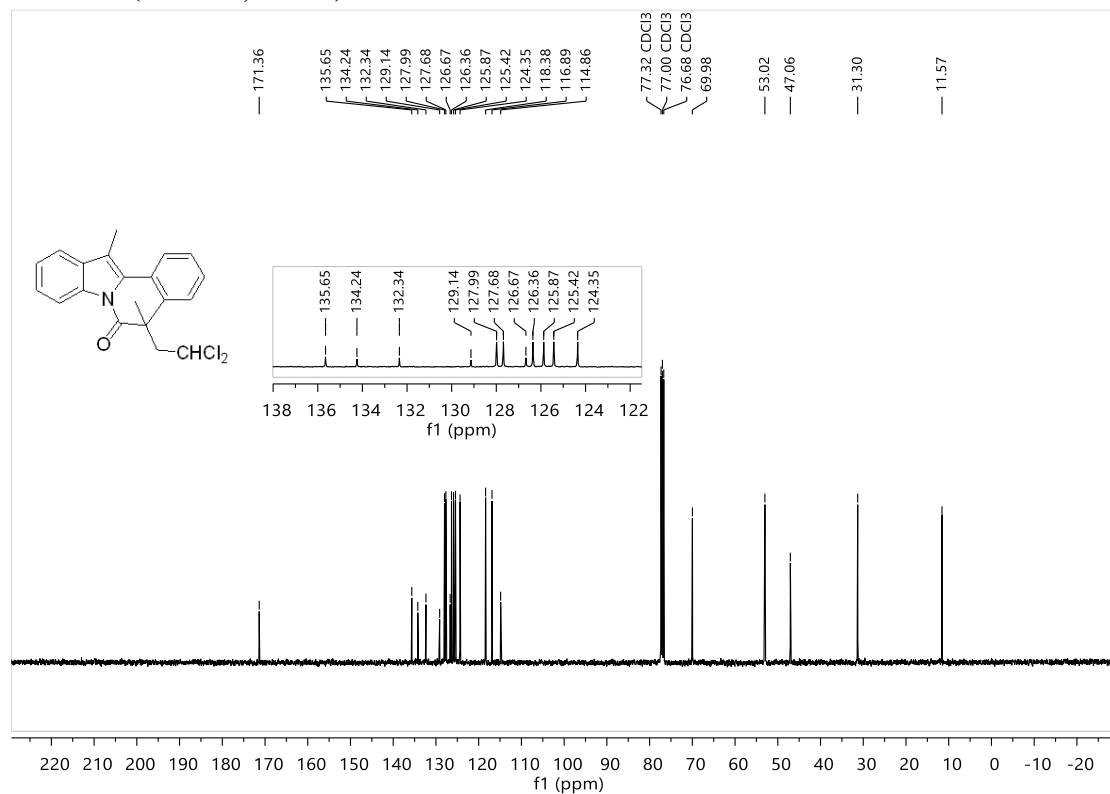
6m: ¹³C NMR (101MHz, CDCl₃)



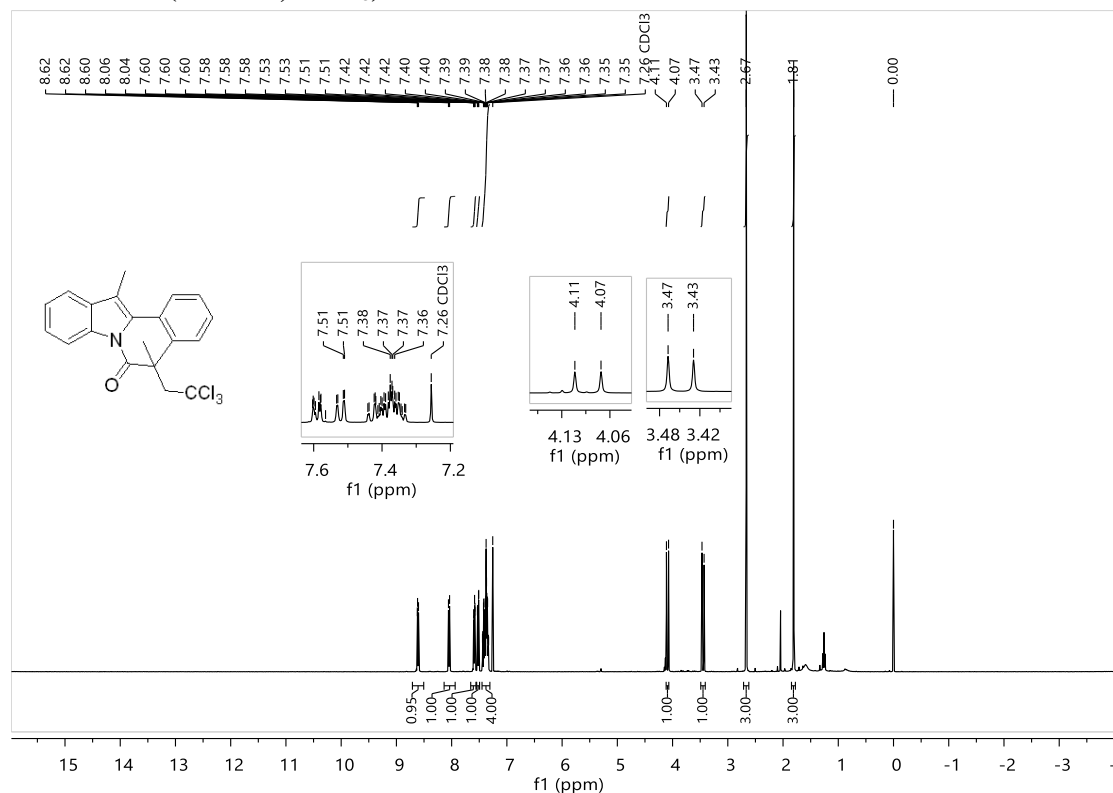
6n: ¹H NMR (400MHz, CDCl₃)



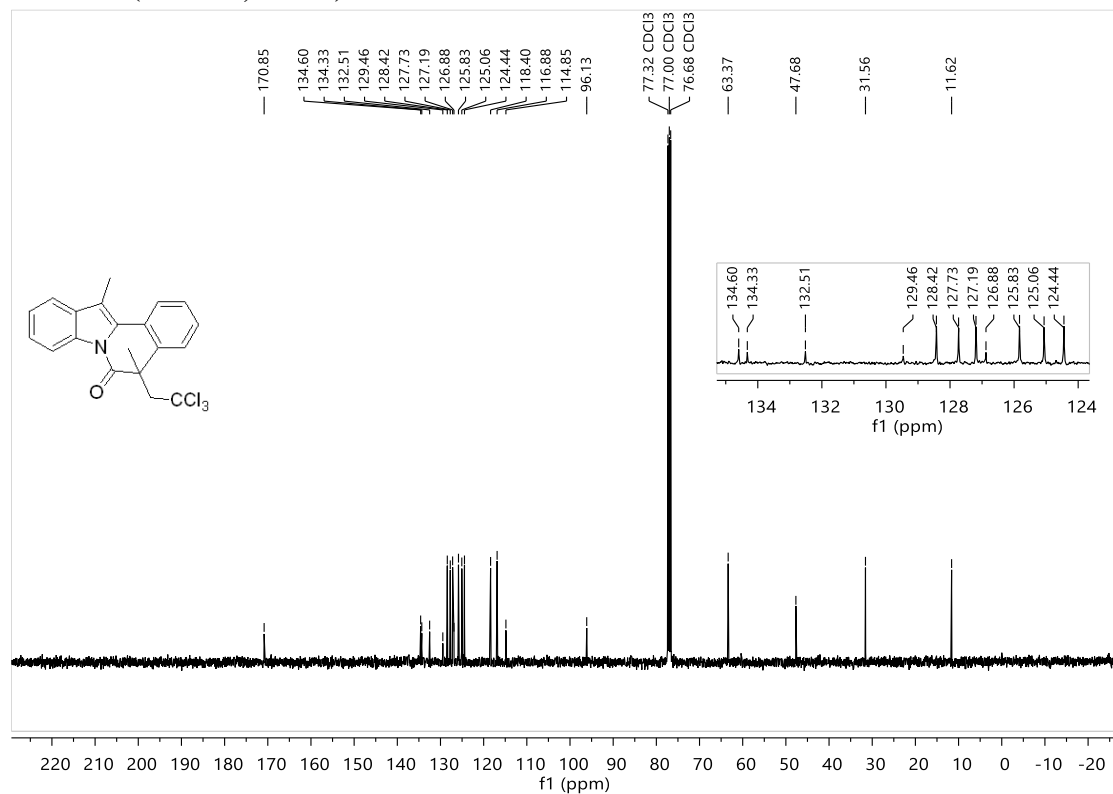
¹³C NMR (101MHz, CDCl₃)



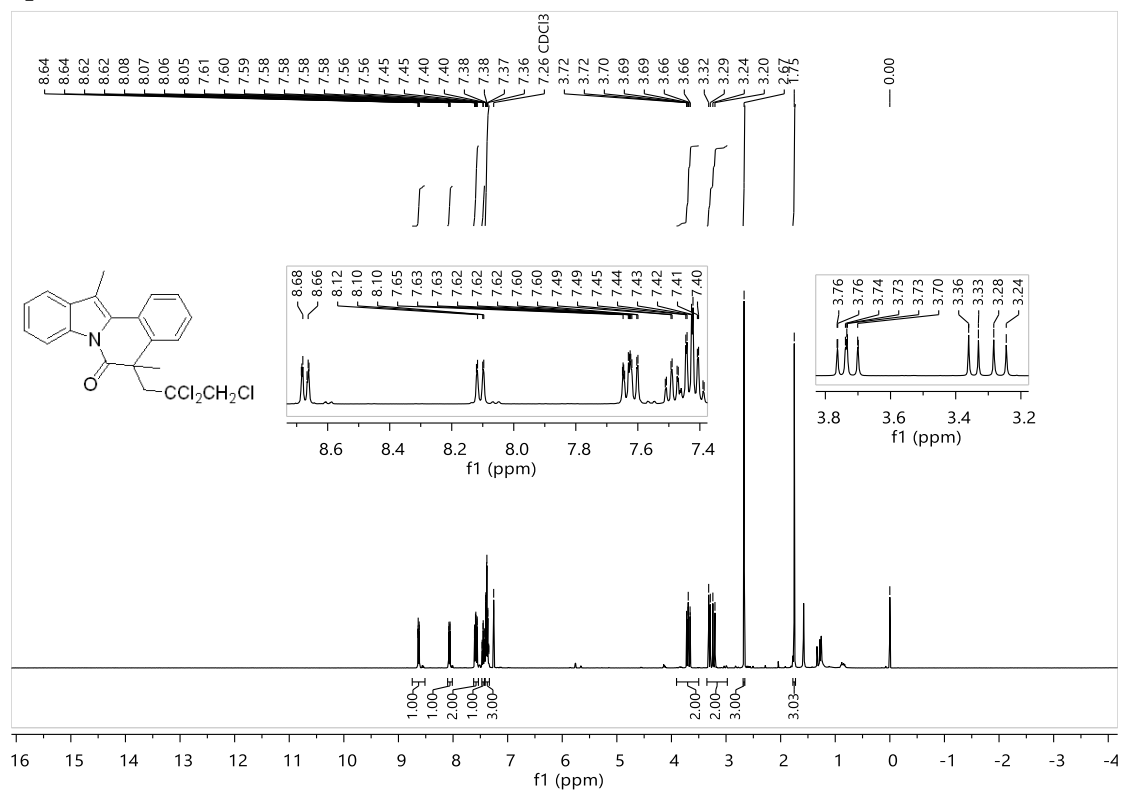
6o: ^1H NMR (400MHz, CDCl_3)



^{13}C NMR (101MHz, CDCl_3)



6p: ¹H NMR (400MHz, CDCl₃)



¹³C NMR (101MHz, CDCl₃)

