

Supporting Information

The construction of indolizine scaffolds from α,ω -alkynoic acids and α,ω -vinylamines via a sequential-relay catalysis in “one pot”

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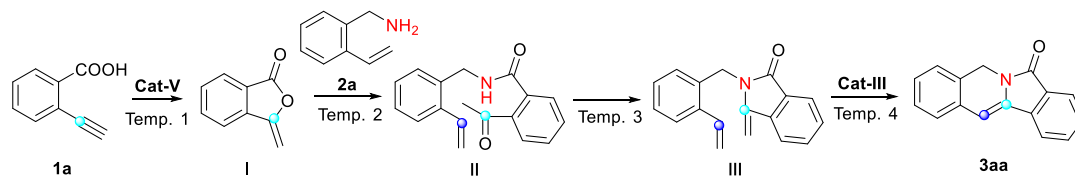
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General Chemistry Information

The chemicals and reagents were purchased from Acros, Alfa Aesar, and National Chemical Reagent Group Co. Ltd., P. R. China, and used without further purification. Anhydrous solvents (THF, MeOH, DMF, DCM, and CH₃CN) used in the reactions were dried and freshly distilled before use. Petroleum ether (PE) used had a boiling range of 60–90 °C. All the reactions were carried out under Ar atmosphere, otherwise stated else. Oxygen and/or moisture sensitive solids and liquids were transferred appropriately. Concentration of solutions in *vacuo* was accomplished using a rotary evaporator fitted with a water aspirator. Residual solvents were removed under high vacuum (0.1 - 0.2 mm Hg). The progress of the reactions was monitored by TLC (silica-coated glass plates) and visualized under UV light, and by using iodine, ceric ammonium molybdate stain or phosphomolybdic acid. ¹H NMR and ¹³C NMR spectra were recorded either on a 400 MHz Varian Instrument at 25 °C or 600 MHz Bruke Instrument at 25 °C, using TMS as an internal standard, respectively. Multiplicity is tabulated as s for singlet, d for doublet, dd for doublet of doublet, t for triplet, and m for multiplet. Coupling constants (J) are reported in Hertz. ¹³C NMR spectra were completely hetero-decoupled and measured at 150 MHz. HRMS spectra were recorded on Finnigan-Mat-95 mass spectrometer, equipped with ESI source. Single crystal X-ray diffraction measurements were performed with a diffractometer working with graphite-monochromated Cu K α radiation.

Additional Optimization of Reaction Conditions

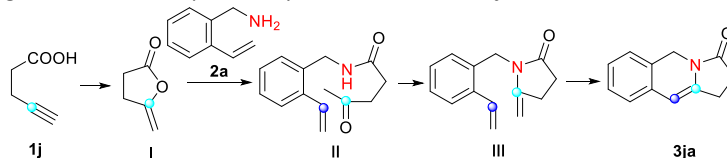
Table S1. The influence of temperature on all four steps of the procedure^a.



Entry	Temp. 1 (°C)	Yield (I) ^b	Temp. 2 (°C)	Yield (II) ^b	Temp. 3 (°C)	Yield (III) ^b	Temp. 4 (°C)	Yield 3aa ^b
1	rt.	N.D. ^c	-	-	-	-	-	-
2	80	90%	-	-	-	-	-	-
3	115	98%	-	-	-	-	-	-
4	115	98%	rt.	40%	-	-	-	-
5	115	98%	80	70%	-	-	-	-
6	115	98%	115	96%	-	-	-	-
7	115	98%	115	96%	rt.	N.D. ^c	-	-
8	115	98%	115	96%	80	20%	-	-
9	115	98%	115	96%	115	95%	-	-
10	115	98%	115	96%	115	95%	rt.	N.D. ^c
11	115	98%	115	96%	115	95%	80	30%
12	115	98%	115	96%	115	95%	115	97%

^a Conditions: substrate **1a** (1.0 mmol), **2a** (1.0 mmol), anhydrous toluene (15 mL), **Cat-V** (5 mol%), **Cat-III** (5 mol%), the temperature is measured by the temperature setting of the oil bath. ^b Determined by crude NMR analysis. ^c Not detected.

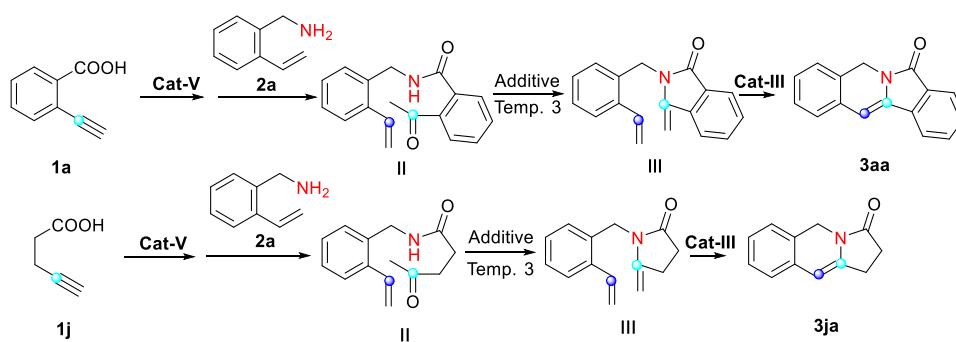
Table S2. Optimizing the solvent for aliphatic alkynoic acid substrate **1j**^a.



Entry	Solvent	Conversion (1j) ^b	Yield (III) ^c
1	tol	53%	45%
2	DCM	95%	26%
3	DCE	96%	36%

^a Conditions: substrate **1j** (1.0 mmol), **2a** (1.0 mmol), anhydrous solvent (15 mL), refluxed overnight. ^b Determined by crude NMR analysis. ^c Isolated yield.

Table S3. Optimizing the additive for aryl and aliphatic substrates^a.



Entry	Substrate	Additive	Temp. 3 (°C)	Yield (III) ^b
1	1a	TFA	80	95%
2	1a	CH ₃ COOH	80	80%
3	1a	Ac ₂ O	80	78%
4	1j	TFA	80/40	N.D. ^c
5	1j	CH ₃ COOH	80/40	N.D. ^c
6	1j	Ac ₂ O	80/40	N.D. ^c

^a Conditions: substrate **1** (1.0 mmol), **2a** (1.0 mmol), anhydrous toluene (15 mL), **Cat-V** (5 mol%), **Cat-III** (5 mol%). ^b Determined by crude NMR analysis. ^c Not detected.

Synthesis

Synthesis of α,ω -alkynoic acid substrates (**1x**)

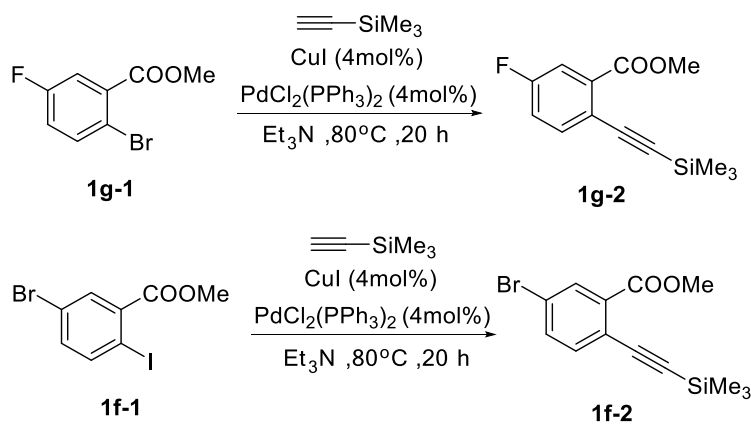
The α,ω -alkynoic acid substrates (**1x**) were synthesized according to the methods reported in the reference below.^[1-3]

Table S4. Synthesis of α,ω -alkynoic acid substrates

Compound	Ar	Yield (%)			
		1x-2	1x-3	1x	Total
1a	C ₆ H ₅	90	99	99	88
1b	4-CH ₃ -C ₆ H ₅	92	99	75	68
1c	3-CH ₃ -C ₆ H ₅	86	98	93	79
1d	4-CH ₃ -C ₆ H ₅	76	98	85	63
1e	4-OCH ₃ -C ₆ H ₅	10	97	99	10
1f	4-Br-C ₆ H ₅	99	96	88	84
1g	4-F-C ₆ H ₅	90	99	47	42
1h	4-F-C ₆ H ₅	90	98	50	44
1i		69	99	95	65

Representative procedure for the synthesis of **1a-2**, **1(f-i)-2**

*Methyl 4-fluoro-2-[(trimethylsilyl)ethynyl]benzoate (**1g-2**)*

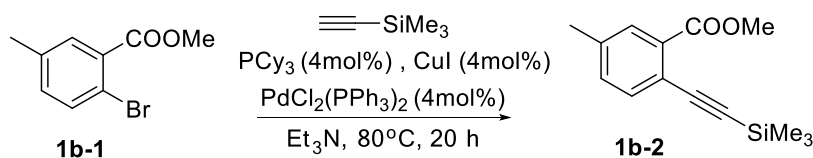


To a flame dried round bottom flask containing **1g-1** (2.33 g, 10.0 mmol, 1.0 eq), was added Et₃N 20 mL, ethynyltrimethylsilane (2.2 mL, 15.0 mmol, 1.5 eq) and PdCl₂(PPh₃)₂ (0.280 g, 0.4 mmol, 0.04 eq). The mixture was stirred at room temperature for 5 min, and was added

CuI (0.080 g, 0.4 mmol, 0.04 eq), and then stirred at 80 °C for 20 h. After completion of the reaction, the mixture was filtered and concentrated in *vacuo*. The residue obtained was purified by silica gel chromatography to afford **1g-2** as transparent liquid (2.25 g, 90%). **TLC**: $R_f = 0.79$ (PE/EA=20/1); **ESI-MS** (m/z) 251.3 $[M+H]^+$.

Representative procedure for the synthesis of 1(b-e)-2

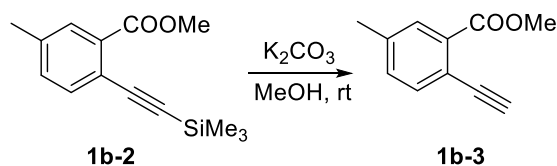
Methyl 4-methyl-2-[(trimethylsilyl)ethynyl]benzoate (**1b-2**)



To a flame dried round bottom flask containing **1b-1** (2.76 g, 10.0 mmol, 1.0 eq) were added Et_3N 20 mL and ethynyltrimethylsilane (2.2 mL, 15.0 mmol, 1.5 eq). Then $\text{PdCl}_2(\text{PPh}_3)_2$ (0.280 g, 0.4 mmol, 0.04 eq) and PCy_3 (0.112 g, 0.4 mmol, 0.04 eq) were subsequently added to the reacting mixture and stirred at room temperature for 5 min, and CuI (0.080 g, 0.4 mmol, 0.04 eq) were added. The mixture was stirred at 80 °C for 20 h, then filtered and concentrated in *vacuo*. The residue obtained was purified by silica gel chromatography to afford **1b-2** as colorless liquid (2.26 g, 92%). **TLC**: $R_f = 0.20$ (PE); **ESI-MS** (m/z) 247.1 $[M+H]^+$.

Representative procedure for the synthesis of 1x-3

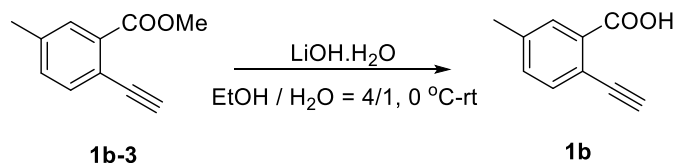
Methyl 2-ethynyl-4-methylbenzoate (**1b-3**)



To a flame dried round bottom flask containing **1b-2** (0.257 g, 1.0 mmol, 1.0 eq) were added methanol 5 mL and K_2CO_3 (0.015 g, 0.1 mmol, 0.1 eq). The mixture was stirred at room temperature for 5 h. After completion of the reaction as indicated by thin layer chromatography, the reacting mixture was concentrated in *vacuo*, diluted with 10 mL H_2O , extracted with DCM (3×20 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and subjected to the next step without further purification after removal of DCM in *vacuo*. **TLC**: $R_f = 0.67$ (PE/EA=5/1); **ESI-MS** (m/z) 175.2 $[M+H]^+$.

Representative procedure for the synthesis of alkynoic acid 1x

2-Ethynyl-4-methylbenzoic acid (**1b**)



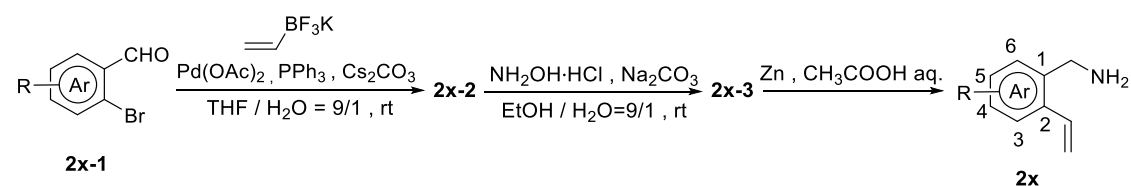
To a flame dried round bottom flask containing **1b-3** (0.174 g, 1.0 mmol, 1.0 eq), was added $\text{EtOH}/\text{H}_2\text{O}$ (4/1, 0.2 M) and stirred ice bath for 10 min. $\text{LiOH}\cdot\text{H}_2\text{O}$ (0.082 g, 2 mmol, 2.0 eq) was then added under ice bath, then warmed to room temperature and reacted for another 4 h till the completion of the reaction as indicated by thin layer chromatography. Then mixture was then concentrated in *vacuo*, diluted with 10 mL H_2O , carefully added 1 M HCl until pH 2-3, then extracted with DCM (3×20 mL). The combined organic layer was washed with brine

(2×20 mL), dried over anhydrous Na₂SO₄, concentrated in *vacuo* and then purified by silica gel chromatography to afford **1b** as light yellow solid (0.155 g, 97%). **TLC**: *R_f* = 0.22 (PE/EA=1/1); **¹H NMR** (400 MHz, CDCl₃) δ 7.91 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 3.42 (s, 1H), 2.42 (s, 3H). **¹³C NMR** (150 MHz, CDCl₃) δ 169.4, 138.5, 134.4, 132.8, 131.2, 130.4, 119.4, 81.9, 81.3, 20.7. **HRMS** (*m/z*): [M+H]⁺ calculated for C₁₀H₉O₂⁺: 161.0596, found: 161.0596.

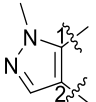
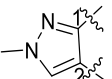
Synthesis of α,ω-vinylamine substrates (2x)

The α,ω-vinylamine substrates (**2a-2s**) were synthesized according to the methods reported in the reference below.^[4-6]

Table S5. Synthesis of α,ω-vinylamine substrates **2a-2s**

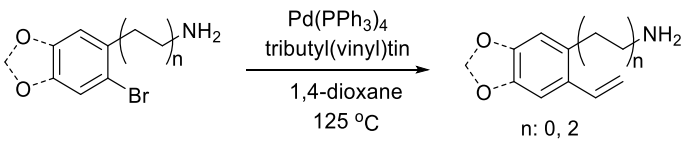
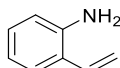
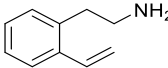
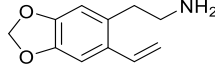


Compound	Ar	Yield(%)			
		2x-2	2x-3	2	Total
2a	C ₆ H ₅	91	98	89	79
2b	4-F-C ₆ H ₄	91	99	58	52
2c	4-F-C ₆ H ₄	75	97	60	44
2d	6-F-C ₆ H ₄	98	99	37	36
2e	3-F-C ₆ H ₄	62	96	71	42
2f	4-CF ₃ -C ₆ H ₄	77	97	90	67
2g	4-Cl-C ₆ H ₄	81	98	42	33
2h	6-Cl-C ₆ H ₄	90	95	15	13
2i	4-Cl-C ₆ H ₄	82	98	33	27
2j	4-CH ₃ -C ₆ H ₄	92	97	54	48
2k	4-OCH ₃ -C ₆ H ₄	44	98	70	30
2l	4-OCH ₃ -C ₆ H ₄	94	99	61	57
2m	4,4-dioxol-C ₆ H ₄	97	98	72	68
2n	4,4-dimethoxy-C ₆ H ₄	98	99	61	60
2o		79	99	89	70
2p		91	97	85	75
2q		92	96	99	87

2r		42	98	80	33
2s		82	97	86	69

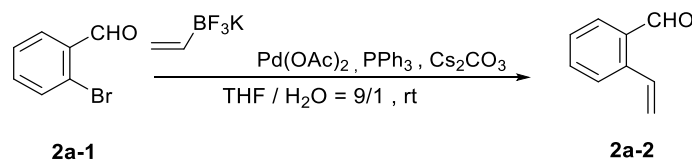
The α,ω -vinylamine substrates (**2t**, **2v**, **2w**) were synthesized according to the methods reported in the reference below.^[7]

Table S6. Synthesis of α,ω -vinylamine **2t**, **2v** and **2w**

		
No.	Compound	Yield(%)
2t		46
2v		88
2w		75

Representative procedure for the synthesis of **2(a-s)-2**

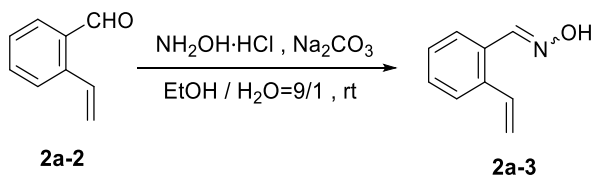
2-Vinylbenzaldehyde (**2a-2**)



To a flame dried round bottom flask containing **2a-1** (3.68 g, 20.0 mmol, 1.0 eq), were added THF/H₂O (9/1, 0.1 M), Pd(OAc)₂ (224 mg, 1.0mmol, 0.05 eq), PPh₃ (524 mg, 2.0 mmol, 0.1 eq), Potassium vinyltrifluoroborate (24.0 mmol, 1.2 eq) and Cs₂CO₃ (18.2 g, 60.0 mmol, 3.0 eq). The reaction mixture were stirred at 70 °C for 6 h. H₂O were then added to quench the reaction after completion of the reaction indicated by thin layer chromatography. The mixture was extracted with EA (3×30 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, concentrated in *vacuo* and then purified by silica gel chromatography to afford **2a-2** as colorless liquid (2.40 g, 91%). **TLC**: *R_f* = 0.28 (PE/EA=10/1); **¹H NMR** ((400 MHz, CDCl₃) δ 10.29 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.49 (m, 3H), 7.47 – 7.39 (m, 1H), 5.70 (d, *J* = 17.4 Hz, 1H), 5.51 (d, *J* = 11.0 Hz, 1H).^[6] **HRMS** (*m/z*): [M+H]⁺ calculated for C₉H₉O⁺: 133.0621, found: 133.0624.

Representative procedure for the synthesis of **2(a-s)-3**

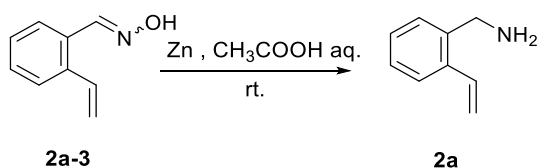
2-Vinylbenzaldehyde oxime (**2a-3**)



To a flame dried round bottom flask containing **2a-2** (15.0 mmol, 1.0 eq), were added EtOH/H₂O (9/1, 0.1M), NH₂OH HCl (1.77 g, 25 mmol, 1.7 eq) and Na₂CO₃ (1.86 g, 17.5 mmol, 0.75 eq). The mixture were stirred at room temperature for 1h, and 5 mL H₂O was added to quench the reaction after completion of the reaction. The mixture was concentrated in *vacuo*, extracted with DCM (3×50 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, concentrated in *vacuo* to afford **2a-3** as white solid (2.15 g, 98%) which was used without further purification in the next step. **TLC**: *R_f* = 0.62 (PE/EA=5/1); **¹H NMR** (400 MHz, CDCl₃) δ 9.06 (s, 1H), 8.48 (s, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.43 – 7.35 (m, 1H), 7.35 – 7.28 (m, 1H), 7.07 (dd, *J* = 17.3 Hz, 11.0 Hz, 1H), 5.65 (d, *J* = 16.0 Hz, 1H), 5.42 (d, *J* = 12.3 Hz, 1H). **¹³C NMR** (150 MHz, CDCl₃) δ 149.0, 137.5, 134.1, 130.0, 129.1, 127.9, 127.1, 127.0, 118.0. **ESI-MS** (*m/z*) 148.2 [M+H]⁺.

Representative procedure for the synthesis of 2(a-s)

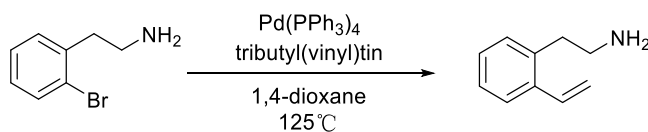
(2-Vinylphenyl)methanamine (2a)



To a flame dried round bottom flask containing **2a-3** (5.21 g, 35.2 mmol, 1.0 eq), was added CH₃COOH 300 mL (8.5 mL/mmol), and stirred at room temperature for 5 min. Zn dust (13.7 g, 211 mmol, 6.0 eq) was added afterwards, and the mixture was stirred at room temperature overnight. The reaction mixture was filtered and concentrated in *vacuo* after completion of reaction indicated by thin layer chromatography. Then 1 M NaOH aq. was added till emulsification and demulsification was observed. The mixture was then extracted with DCM (3×100 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, concentrated in *vacuo* and then purified by silica gel chromatography to afford **2a** as light purple liquid (4.10 g, 89%). **TLC**: *R_f* = 0.62 (PE/EA=5/1); **¹H NMR** (400 MHz, CDCl₃) δ 7.56 – 7.45 (m, 1H), 7.32 – 7.21 (m, 3H), 7.02 (dd, *J* = 17.9 Hz, 10.5 Hz, 1H), 5.68 (d, *J* = 17.4 Hz, 1H), 5.34 (d, *J* = 9.8 Hz, 1H), 3.90 (s, 2H), 1.43 (s, 2H). **¹³C NMR** (150 MHz, CDCl₃) δ 140.3, 136.2, 134.0, 128.1, 128.0, 127.3, 126.0, 116.3, 44.2. **HRMS** (*m/z*): [M+H]⁺ calculated for C₉H₁₂N⁺: 134.0964, found: 134.0963.

Representative procedure for the synthesis of 2(t, v, w)

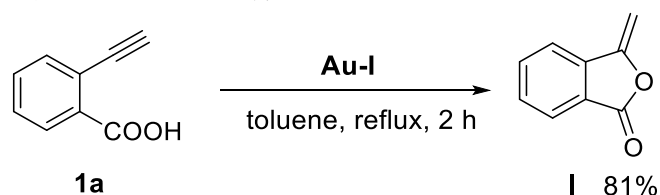
2-(2-Vinylphenyl)ethan-1-amine (2v)



To a flame dried round bottom flask containing 2-(2-bromophenyl)ethan-1-amine (2.00 g, 10.0 mmol, 1.0 eq) were added 1, 4-dioxane (0.1M), Pd(PPh₃)₄ (0.230 g, 0.2 mmol, 0.02 eq), and tributyl(vinyl)stannane (3.80 g, 24 mmol, 1.2 eq). The mixture was stirred at 125 °C for 5 h, cooled to room temperature after completion of the reaction and was added 10% KF aq. (100 mL). The mixture was stirred at room temperature for 2 h, then filtered and extracted with EA (3×50 mL). The combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, concentrated in *vacuo* and then purified by silica gel chromatography to afford **2v** as colorless oil (1.29 g, 88%). **TLC:** *R_f*= 0.24 (DCM/MeOH=10/1); **¹H NMR** (600 MHz, CDCl₃) δ 7.50 (m, 1H), 7.21 (m, 2H), 7.16 (m, 1H), 7.01 (dd, *J* =17.3 Hz, 10.9, 1H), 5.65 (d, *J* =17.3 Hz, 1H), 5.30 (d, *J* =10.9 Hz, 1H), 2.92 (t, *J* =7.1 Hz, 2H), 2.84 (t, *J* =7.1 Hz, 2H).^[64] **¹³C NMR** (150 MHz, CDCl₃) δ 136.5, 136.2, 133.9, 129.4, 127.1, 126.0, 125.3, 115.1, 42.5, 36.8. **HRMS** (*m/z*): [M+H]⁺ calculated for C₁₀H₁₄N⁺: 148.1121, found: 148.1122.

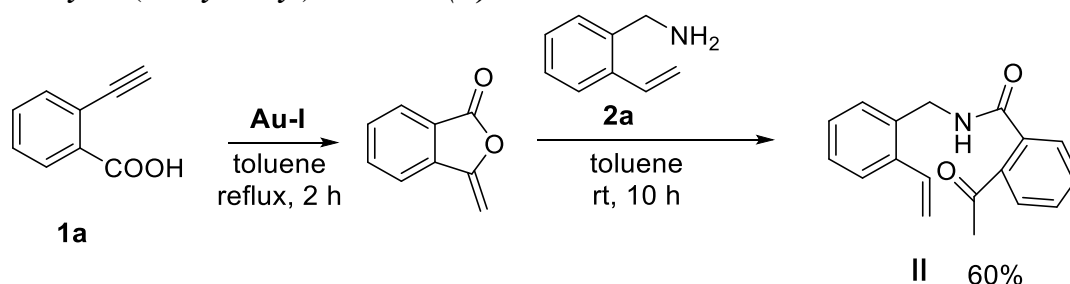
Synthesis and characterization of the representative intermediates (I-III)

3-Methyleneisobenzofuran-1(3H)-one (I)



To a flame dried sealed tube containing **1a** (0.146 g, 1.0 mmol, 1.0 eq) was added **Au-I** catalyst (0.025g, 0.05 mmol, 0.05 eq) and 10 mL anhydrous toluene. The mixture was refluxed in oil bath (115 °C) for 2 h, and concentrated in *vacuo* to remove solvent after total conversion of **1a** as indicated by thin layer chromatography. The residue obtained was purified by silica gel chromatography to afford **I** as transparent oil (0.118 g, 81%). **TLC:** *R_f*= 0.47 (PE/EA=5/1); **¹H NMR** (400 MHz, CDCl₃) δ 7.91 (d, *J* = 7.7, 1H), 7.72 (m, 2H), 7.58 (m, 1H), 5.23 (s, 2H). **¹³C NMR** (150 MHz, CDCl₃) δ 166.2, 151.2, 138.4, 133.8, 129.8, 124.7, 124.5, 120.0, 90.6. **HRMS** (*m/z*): [M+H]⁺ calculated for C₉H₇O₂⁺: 147.0441, found: 147.0438.

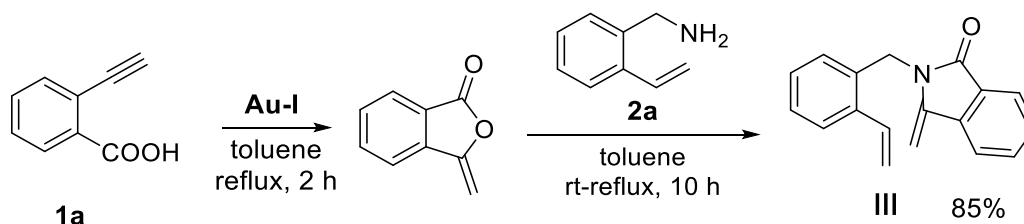
2-Acetyl-N-(2-vinylbenzyl)benzamide (II)



To a flame dried sealed tube containing **1a** (0.146 g, 1.0 mmol, 1.0 eq) was added **Au-I** catalyst (0.025 g, 0.05 mmol, 0.05 eq) and 10 mL anhydrous toluene. The mixture was refluxed in oil bath (115 °C) for 2 h, then cooled to room temperature after total conversion of **1a** as indicated by thin layer chromatography. **2a** (0.133 g, 1.0 mmol, 1.0 eq) was then solved in 5 mL anhydrous toluene, and added to the reaction mixture. The mixture was stirred at room temperature overnight (10 h), and concentrated in *vacuo* after completion of the reaction as indicated by thin layer chromatography. The residue obtained was purified by silica gel

chromatography to afford **II** as light yellow liquid (0.167 g, 60%). **TLC**: $R_f = 0.36$ (PE/EA=5/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.69 (d, $J = 7.9$ Hz, 1H), 7.65 – 7.52 (m, 2H), 7.52 – 7.41 (m, 2H), 7.24 – 7.12 (m, 3H), 7.06 (dd, $J = 17.1, 10.4$ Hz, 1H), 5.62 (d, $J = 17.2$ Hz, 1H), 5.36 (d, $J = 10.7$ Hz, 1H), 4.58 (d, $J = 16.3$ Hz, 1H), 4.44 (d, $J = 16.3$ Hz, 1H), 3.86 (s, 1H), 1.43 (s, 3H). $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 166.9, 147.9, 135.8, 134.0, 133.6, 132.0, 129.2, 128.9, 127.2, 127.2, 126.8, 125.5, 122.8, 121.1, 116.1, 88.6, 38.5, 23.9. **ESI-MS** (m/z) 280.1 $[\text{M}+\text{H}]^+$.

3-Methylene-2-(2-vinylbenzyl)isoindolin-1-one (**III**)

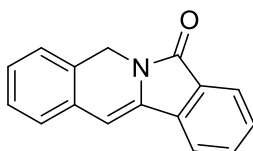


To a flame dried sealed tube containing **1a** (0.146 g, 1.0 mmol, 1.0 eq) was added **Au-I** catalyst (0.025 g, 0.05 mmol, 0.05 eq) and 10 mL anhydrous toluene. The mixture was refluxed in oil bath (115 °C) for 2 h, then cooled to room temperature after total conversion of **1a** as indicated by thin layer chromatography. **2a** (0.133 g, 1.0 mmol, 1.0 eq) was then solved in 5 mL anhydrous toluene, and added to the reaction mixture. The mixture was stirred at room temperature overnight (10 h), and then refluxed for another 10 h after total conversion of **I** as indicated by thin layer chromatography. The mixture was then concentrated in *vacuo* and the residue obtained was purified by silica gel chromatography to afford **III** as light yellow liquid (0.220 g, 85%). **TLC**: $R_f = 0.52$ (PE/EA=5/1); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.90 (d, $J = 7.5$ Hz, 1H), 7.69 (d, $J = 7.5$ Hz, 1H), 7.65 – 7.57 (m, 1H), 7.57 – 7.51 (m, 1H), 7.49 (d, $J = 7.6$ Hz, 1H), 7.26 – 7.21 (m, 1H), 7.21 – 7.14 (m, 1H), 7.09 (dd, $J = 17.3, 10.9$ Hz, 1H), 7.00 (d, $J = 7.7$ Hz, 1H), 5.67 (d, $J = 17.3$ Hz, 1H), 5.39 (d, $J = 11.4$ Hz, 1H), 5.13 (s, 1H), 5.09 (s, 2H), 4.68 (s, 1H). $^{13}\text{C NMR}$ (150 MHz, CDCl_3) δ 166.7, 140.9, 135.7, 135.6, 133.2, 132.7, 131.5, 128.9, 128.5, 127.4, 126.8, 125.9, 125.8, 122.8, 119.3, 116.5, 89.7, 40.2. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{18}\text{H}_{16}\text{NO}^+$: 262.1226, found: 262.1225.

Representative procedure for the synthesis of compound 3

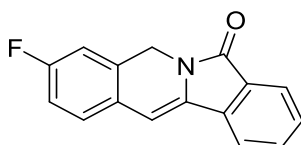
To a flame dried sealed tube containing α,ω -alkynoic acid **1** (1.0 mmol, 1.0 eq) was added **Au-I** catalyst (0.025 g, 0.05 mmol, 0.05 eq) and 10 mL anhydrous toluene. The mixture was refluxed in oil bath (115 °C) for 2 h, then α,ω -vinylamine **2** (1.0 mmol, 1.0 eq) was solved in 5 mL anhydrous toluene, and added to the reaction mixture after total conversion of α,ω -alkynoic acid **1** as indicated by thin layer chromatography. The mixture was refluxed overnight, and **Ru-III** catalyst (0.032g, 0.05 mmol, 0.05 eq) was added to the reaction mixture. The mixture was stirred for 10 h, and concentrated in *vacuo* after completion of the reaction as indicated by thin layer chromatography. The residue obtained was purified by silica gel chromatography to afford the desired indolizine **3**.

Isoindolo[2,1-b]isoquinolin-7(5H)-one (**3aa**)



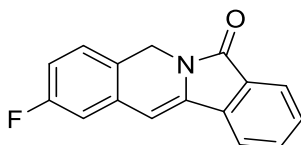
Yellow solid (0.186g, 80%) **TLC**: $R_f = 0.31$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 7.92 (d, $J = 7.6$ Hz, 1H), 7.79 (d, $J = 7.6$ Hz, 1H), 7.66 – 7.58 (m, 1H), 7.58 – 7.51 (m, 1H), 7.32 – 7.22 (m, 4H), 6.50 (s, 1H), 5.14 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 165.6, 134.0, 133.5, 130.8, 129.7, 128.8, 128.7, 127.4, 127.3, 126.7, 126.2, 122.5, 119.6, 102.9, 42.4. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{12}\text{NO}^+$: 234.0913, found: 234.0912.

3-Fluoroisoindolo[2,1-b]isoquinolin-7(5H)-one (3ab)



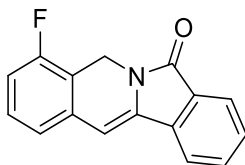
Light yellow solid (0.200 g, 78%) **TLC**: $R_f = 0.29$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 7.91 (d, $J = 7.5$ Hz, 1H), 7.77 (d, $J = 7.7$ Hz, 1H), 7.62 (m, 1H), 7.54 (m, 2H), 7.23 (m, 1H), 6.97 (m, 2H), 6.46 (s, 1H), 5.12 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 165.6, 133.9, 133.5 (d, $J = 14.1$ Hz), 133.0, 131.3, 130.9, 128.8, 128.5 (d, $J = 9.4$ Hz), 128.1 (d, $J = 8.3$ Hz), 126.0, 122.6, 119.5, 114.1 (d, $J = 21.6$ Hz), 113.5 (d, $J = 23.3$ Hz), 101.8, 42.4. **$^{19}\text{F NMR}$** (376 MHz, CDCl_3) δ -112.20. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{FNO}^+$: 252.0819, found: 252.0818.

2-Fluoroisoindolo[2,1-b]isoquinolin-7(5H)-one (3ac)



Light yellow solid (0.160 g, 64%) **TLC**: $R_f = 0.31$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 7.91 (d, $J = 7.7$ Hz, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.68 – 7.60 (m, 1H), 7.60 – 7.52 (m, 1H), 7.22 – 7.16 (m, 1H), 6.99 – 6.90 (m, 2H), 6.41 (s, 1H), 5.08 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 165.5, 161.6 (d, $J = 245.7$ Hz), 134.5, 133.7, 131.8 (d, $J = 8.3$ Hz), 131.0, 129.1, 128.7, 127.4 (d, $J = 8.5$ Hz), 124.1 (d, $J = 3.2$ Hz), 122.6, 119.7, 113.8 (d, $J = 21.9$ Hz), 113.0 (d, $J = 22.6$ Hz), 101.7, 41.9. **$^{19}\text{F NMR}$** (376 MHz, CDCl_3) δ -114.76. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{FNO}^+$: 252.0819, found: 252.0813.

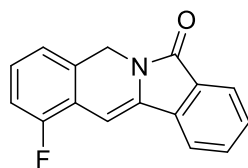
4-Fluoroisoindolo[2,1-b]isoquinolin-7(5H)-one (3ad)



Light yellow solid (0.125 g, 49%) **TLC**: $R_f = 0.33$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 7.92 (d, $J = 8.4$ Hz, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.63 (m, 1H), 7.56 (m, 1H), 7.23 (m, 1H), 7.04 (m, 1H), 6.96 (m, 1H), 6.46 (s, 1H), 5.13 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 165.5, 159.0 (d, $J = 246.6$ Hz), 134.1, 133.7, 131.8 (d, $J = 4.7$ Hz), 130.9, 129.1, 128.6, 128.5 (d, $J = 8.4$ Hz), 122.6, 122.0, 119.7, 115.7 (d, $J = 16.8$ Hz), 114.1 (d, $J = 21.3$ Hz), 101.5 (d, $J =$

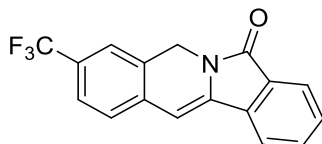
4.0 Hz), 37.5 (d, $J = 6.5$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -118.25. HRMS (m/z): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{16}\text{H}_{10}\text{FNONa}^+$: 274.0639, found: 274.0642.

1-Fluoroisoindolo[2,1-b]isoquinolin-7(5H)-one (3ae)



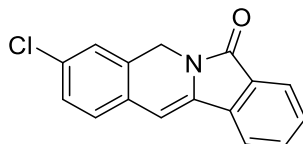
Light yellow solid (0.082 g, 33%) TLC: $R_f = 0.36$ (PE/EA=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, $J = 7.6$ Hz, 1H), 7.82 (d, $J = 8.5$ Hz, 1H), 7.64 (m, 1H), 7.56 (m, 1H), 7.21 (m, 1H), 7.07 – 6.97 (m, 2H), 6.74 (s, 1H), 5.14 (s, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.7, 158.1 (d, $J = 250.4$ Hz), 134.0, 133.9, 131.0, 130.4 (d, $J = 3.6$ Hz), 129.0, 128.6, 128.2 (d, $J = 8.5$ Hz), 122.6, 121.7 (d, $J = 3.2$ Hz), 119.8, 118.4 (d, $J = 16.2$ Hz), 113.9 (d, $J = 21.1$ Hz), 94.7 (d, $J = 6.2$ Hz), 42.0. ^{19}F NMR (376 MHz, CDCl_3) δ -121.53. HRMS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{FNO}^+$: 252.0819, found: 252.0816.

3-(Trifluoromethyl)isoindolo[2,1-b]isoquinolin-7(5H)-one (3af)



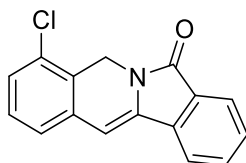
Yellow solid (0.187 g, 62%) TLC: $R_f = 0.30$ (PE/EA=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, $J = 7.5$ Hz, 1H), 7.79 (d, $J = 7.7$ Hz, 1H), 7.65 (m, 1H), 7.58 (m, 1H), 7.51 (d, $J = 8.0$ Hz, 1H), 7.45 (s, 1H), 7.34 (d, $J = 8.1$ Hz, 1H), 6.48 (s, 1H), 5.16 (s, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.5, 135.5, 133.6, 133.4, 131.1, 129.4, 129.0, 128.7, 126.5, 124.3, 124.3, 123.0, 122.9, 122.7, 119.9, 101.0, 42.2. ^{19}F NMR (376 MHz, CDCl_3) δ -62.62. HRMS (m/z): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{17}\text{H}_{11}\text{F}_3\text{NO}^+$: 324.0607, found: 324.0610.

3-Chloroisoindolo[2,1-b]isoquinolin-7(5H)-one (3ag)



Transparent oil (0.160 g, 60%) TLC: $R_f = 0.38$ (PE/EA=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, $J = 6.6$ Hz, 1H), 7.77 (d, $J = 7.4$ Hz, 1H), 7.65 – 7.59 (m, 1H), 7.58 – 7.52 (m, 1H), 7.25 – 7.20 (m, 2H), 7.18 (d, $J = 8.1$ Hz, 1H), 6.44 (s, 1H), 5.10 (s, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.5, 133.8, 132.9, 131.0, 130.3, 129.0, 128.6, 128.4, 128.2, 127.6, 127.5, 126.4, 122.7, 119.7, 101.7, 42.1. HRMS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{ONCl}^+$: 268.0524, found: 268.0519.

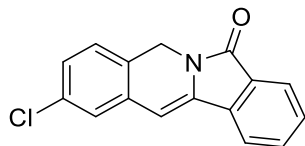
4-Chloroisoindolo[2,1-b]isoquinolin-7(5H)-one (3ah)



Transparent oil (0.142 g, 53%) TLC: $R_f = 0.34$ (PE/EA=5/1); ^1H NMR (400 MHz, CDCl_3) δ

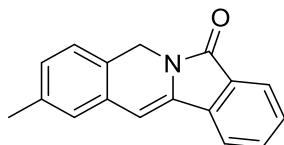
7.94 (d, $J = 7.4$ Hz, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.67 – 7.61 (m, 1H), 7.60 – 7.54 (m, 1H), 7.29 – 7.24 (m, 1H), 7.24 – 7.19 (m, 1H), 7.14 (d, $J = 7.4$ Hz, 1H), 6.43 (s, 1H), 5.14 (s, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.4, 134.0, 133.6, 132.5, 131.9, 131.0, 129.1, 128.8, 128.2, 127.9, 126.7, 124.9, 122.7, 119.8, 101.7, 41.3. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{ONCl}^+$: 268.0524, found: 268.0523.

2-Chloroisoindolo[2,1-b]isoquinolin-7(5H)-one (3ai)



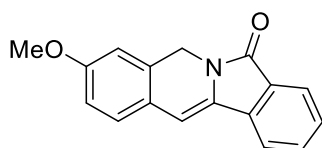
Transparent oil (0.198 g, 74%) **TLC**: $R_f = 0.28$ (PE/EA=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, $J = 7.5$ Hz, 1H), 7.78 (d, $J = 7.1$ Hz, 1H), 7.69 – 7.60 (m, 1H), 7.60 – 7.52 (m, 1H), 7.25 – 7.18 (m, 2H), 7.18 – 7.13 (m, 1H), 6.40 (s, 1H), 5.08 (s, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.6, 134.6, 133.7, 133.0, 131.6, 131.0, 129.2, 128.7, 127.3, 127.0, 126.9, 126.2, 122.7, 119.8, 101.4, 42.0. **HRMS** (m/z): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{OCIN}^+$: 290.0343, found: 290.0337.

2-Methylisoindolo[2,1-b]isoquinolin-7(5H)-one (3aj)



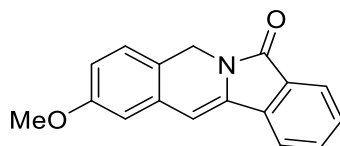
Yellow solid (0.138 g, 56%) **TLC**: $R_f = 0.29$ (PE/EA=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, $J = 7.4$ Hz, 1H), 7.75 (d, $J = 7.6$ Hz, 1H), 7.64 – 7.55 (m, 1H), 7.55 – 7.46 (m, 1H), 7.13 – 7.00 (m, 3H), 6.41 (s, 1H), 5.05 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.6, 136.9, 134.0, 133.4, 130.7, 129.5, 128.7, 128.6, 128.1, 127.4, 126.0, 125.7, 122.5, 119.5, 103.0, 42.2, 20.4. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{13}\text{NO}^+$: 248.1070, found: 248.1071.

3-Methoxyisoindolo[2,1-b]isoquinolin-7(5H)-one (3ak)



Light yellow solid (0.052 g, 20%) **TLC**: $R_f = 0.39$ (PE/EA=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.90 (d, $J = 7.4$ Hz, 1H), 7.75 (d, $J = 7.7$ Hz, 1H), 7.65 – 7.57 (m, 1H), 7.57 – 7.48 (m, 1H), 7.25 – 7.16 (m, 1H), 6.87 – 6.77 (m, 2H), 6.47 (s, 1H), 5.11 (s, 2H), 3.84 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.6, 159.0, 134.1, 131.5, 130.7, 130.5, 128.4, 128.3, 128.0, 122.6, 122.5, 119.3, 112.5, 112.2, 102.9, 54.8, 42.5. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{14}\text{NO}_2^+$: 264.1019, found: 264.1018.

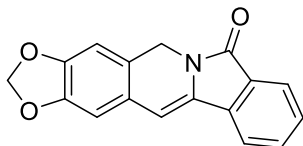
2-Methoxyisoindolo[2,1-b]isoquinolin-7(5H)-one (3al)



Light yellow solid (0.152 g, 58%) **TLC**: $R_f = 0.41$ (PE/EA=5/1); ^1H NMR (400 MHz,

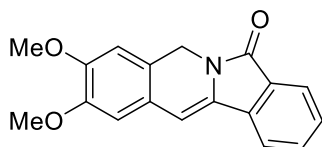
CDCl₃) δ 7.89 (d, $J = 7.6$ Hz, 1H), 7.75 (d, $J = 7.7$ Hz, 1H), 7.64 – 7.56 (m, 1H), 7.56 – 7.49 (m, 1H), 7.13 (d, $J = 8.6$ Hz, 1H), 6.82 – 6.75 (m, 2H), 6.43 (s, 1H), 5.04 (s, 2H), 3.83 (s, 3H). ¹³C NMR (150 MHz, CDCl₃) δ 165.6, 158.5, 133.9, 133.8, 130.8, 128.8, 128.7, 127.0, 122.5, 120.8, 119.6, 112.8, 111.9, 102.9, 54.8, 41.9. HRMS (m/z): [M+H]⁺ calculated for C₁₇H₁₄NO₂⁺: 264.1019, found: 264.1020.

[1,3]Dioxolo[4,4-g]isoindolo[2,1-b]isoquinolin-7(5H)-one (3am)



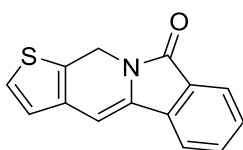
Black solid (0.078 g, 28%) TLC: $R_f = 0.19$ (PE/EA=5/1); ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, $J = 7.6$ Hz, 1H), 7.74 (d, $J = 7.6$ Hz, 1H), 7.68 – 7.56 (m, 1H), 7.56 – 7.47 (m, 1H), 6.73 (d, $J = 2.9$ Hz, 2H), 6.38 (s, 1H), 6.00 (s, 2H), 5.04 (s, 2H). ¹³C NMR (150 MHz, CDCl₃) δ 165.6, 147.1, 146.6, 133.9, 132.0, 130.7, 128.4, 128.4, 123.7, 123.0, 122.5, 119.4, 106.9, 106.7, 103.0, 100.9, 42.6. HRMS (m/z): [M+H]⁺ calculated for C₁₇H₁₂NO₃⁺: 278.0812, found: 278.0814.

2,3-Dimethoxyisoindolo[2,1-b]isoquinolin-7(5H)-one (3an)



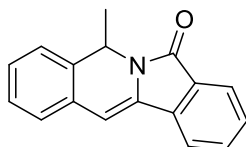
Light yellow solid (0.070 g, 24%) TLC: $R_f = 0.35$ (PE/EA=5/1); ¹H NMR (400 MHz, CDCl₃) δ 7.91 (d, $J = 7.5$ Hz, 1H), 7.75 (d, $J = 7.8$ Hz, 2H), 7.65 – 7.57 (m, 1H), 7.57 – 7.48 (m, 2H), 6.78 (s, 1H), 6.74 (s, 1H), 6.44 (s, 1H), 5.07 (s, 2H), 3.93 (s, 6H). ¹³C NMR (150 MHz, CDCl₃) δ 166.2, 149.1, 148.4, 134.6, 132.6, 131.3, 129.0, 123.1, 123.0, 122.1, 119.9, 110.3, 110.0, 103.5, 65.6, 56.1, 56.1, 42.9. HRMS (m/z): [M+H]⁺ calculated for C₁₈H₁₆NO₃⁺: 294.1125, found: 294.1123.

Thieno[3',2':4,5]pyrido[2,1-a]isoindol-9(11H)-one (3aq)



Grey solid (0.055 g, 23%) TLC: $R_f = 0.20$ (PE/EA=5/1); ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, $J = 7.4$ Hz, 1H), 7.72 (d, $J = 7.5$ Hz, 1H), 7.64 – 7.55 (m, 1H), 7.54 – 7.45 (m, 1H), 7.30 – 7.22 (m, 2H), 6.99 (d, $J = 4.8$ Hz, 1H), 6.51 (s, 1H), 5.22 (s, 2H). ¹³C NMR (150 MHz, CDCl₃) δ 165.9, 134.1, 132.4, 131.3, 130.8, 129.0, 128.4, 128.1, 124.6, 124.2, 122.5, 119.3, 98.1, 41.3. HRMS (m/z): [M+Na]⁺ calculated for C₁₄H₉ONSN⁺: 262.0297, found: 262.0301.

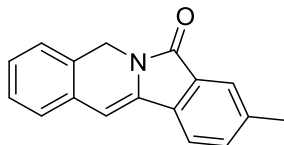
4-Methylisoindolo[2,1-b]isoquinolin-7(5H)-one (3ap)



Light colored oil (0.067 g, 27%) TLC: $R_f = 0.31$ (PE/EA=5/1); ¹H NMR (600 MHz, CDCl₃) δ 7.87 (d, $J = 7.5$ Hz, 1H), 7.74 (d, $J = 7.6$ Hz, 1H), 7.63 – 7.55 (m, 1H), 7.52 – 7.47 (m, 1H),

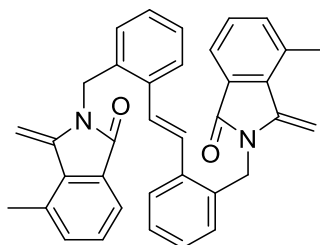
7.25 – 7.19 (m, 4H), 6.48 (s, 1H), 5.63 (q, $J = 6.6$ Hz, 1H), 1.49 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.7, 134.6, 134.2, 132.8, 130.9, 129.1, 128.9, 128.7, 127.5, 127.2, 126.4, 126.0, 122.6, 119.6, 102.9, 49.2, 22.7. HRMS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{14}\text{NO}^+$: 248.1070, found: 248.1070.

9-Methylisoindolo[2,1-b]isoquinolin-7(5H)-one (3ba)



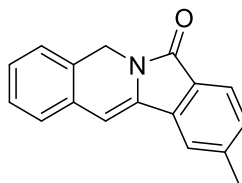
Light yellow solid (0.173 g, 70%) TLC: $R_f = 0.30$ (PE/Ea=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.71 (s, 1H), 7.65 (d, $J = 7.8$ Hz, 1H), 7.42 (d, $J = 7.9$ Hz, 1H), 7.32 – 7.17 (m, 5H), 6.42 (s, 1H), 5.11 (s, 2H), 2.49 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.7, 139.3, 133.6, 131.9, 131.5, 129.9, 128.9, 128.6, 127.3, 127.2, 126.6, 126.1, 122.7, 119.4, 102.2, 42.4, 21.1. HRMS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{14}\text{NO}^+$: 248.1070, found: 248.1073.

(3-2ac')



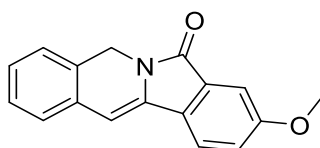
Light yellow solid (0.176 g, 67%) TLC: $R_f = 0.20$ (PE/Ea=5/1); ^1H NMR (600 MHz, CDCl_3) δ 7.78 (d, $J = 7.1$ Hz, 2H), 7.66 (d, $J = 7.8$ Hz, 2H), 7.44 – 7.37 (m, 6H), 7.32 – 7.27 (m, 2H), 7.23 – 7.19 (m, 2H), 7.04 (d, $J = 7.7$ Hz, 2H), 5.18 (s, 6H), 4.84 (d, $J = 2.6$ Hz, 2H), 2.57 (s, 6H). ^{13}C NMR (150 MHz, CDCl_3) δ 167.2, 142.5, 135.6, 134.9, 133.8, 133.6, 133.4, 130.1, 129.2, 128.1, 128.1, 127.6, 126.8, 126.6, 121.4, 94.9, 40.9, 20.6. HRMS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{36}\text{H}_{31}\text{N}_2\text{O}_2^+$: 523.2380, found: 523.2389.

10-Methylisoindolo[2,1-b]isoquinolin-7(5H)-one (3da)



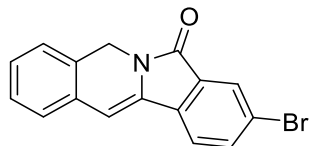
Light yellow solid (0.126 g, 51%) TLC: $R_f = 0.35$ (PE/Ea=5/1); ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, $J = 6.5$ Hz, 1H), 7.57 (s, 1H), 7.33 (d, $J = 8.0$ Hz, 1H), 7.29 – 7.17 (m, 5H), 6.44 (s, 1H), 5.11 (s, 2H), 2.51 (s, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.7, 141.5, 134.4, 133.6, 129.9, 129.8, 128.7, 127.3, 127.3, 126.6, 126.3, 126.2, 122.3, 119.9, 102.5, 42.4, 21.4. HRMS (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{14}\text{NO}^+$: 248.1070, found: 248.1068.

9-Methoxyisoindolo[2,1-b]isoquinolin-7(5H)-one (3ea)



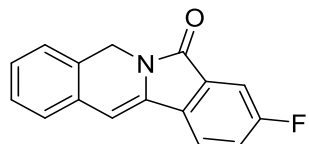
Grey solid (0.213 g, 81%) **TLC**: $R_f = 0.34$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 7.65 (d, $J = 6.7$ Hz, 1H), 7.37 (s, 1H), 7.31 – 7.18 (m, 4H), 7.18 – 7.11 (m, 1H), 6.37 (s, 1H), 5.09 (s, 2H), 3.90 (s, 3H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 165.5, 160.6, 133.3, 130.4, 129.9, 128.3, 127.3, 127.0, 126.7, 126.5, 126.1, 120.9, 119.3, 105.2, 101.8, 55.2, 42.4. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{14}\text{NO}_2^+$: 264.1019, found: 264.1021.

9-Bromoisindolo[2,1-b]isoquinolin-7(5H)-one (3fa)



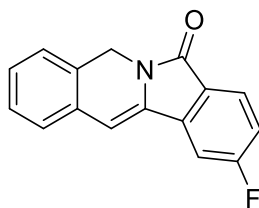
Light yellow solid (0.251 g, 81%) **TLC**: $R_f = 0.39$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 8.04 (s, 1H), 7.72 (d, $J = 8.2$ Hz, 1H), 7.64 (d, $J = 8.1$ Hz, 1H), 7.31 – 7.19 (m, 4H), 6.50 (s, 1H), 5.12 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 164.1, 133.8, 132.6, 132.5, 130.3, 129.4, 128.6, 127.7, 127.4, 126.9, 126.2, 125.8, 122.8, 121.0, 103.8, 42.5. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{BrNO}^+$: 312.0019, found: 312.0019.

9-Fluoroisindolo[2,1-b]isoquinolin-7(5H)-one (3ga)



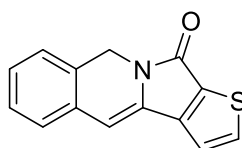
Light yellow solid (0.141 g, 56%) **TLC**: $R_f = 0.36$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 7.8 – 7.7 (m, 1H), 7.6 (d, $J = 8.2$ Hz, 1H), 7.4 – 7.2 (m, 5H), 6.5 (s, 1H), 5.1 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 164.4, 162.9 (d, $J = 250.3$ Hz), 132.5, 130.6 (d, $J = 8.8$ Hz), 129.8, 129.4, 128.3, 127.5, 127.4, 126.7, 126.1, 121.3 (d, $J = 8.8$ Hz), 118.6 (d, $J = 24.5$ Hz), 109.3 (d, $J = 24.0$ Hz), 103.0, 42.5. **$^{19}\text{F NMR}$** (376 MHz, CDCl_3) δ -109.57. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{FNO}^+$: 252.0819, found: 252.0820.

10-Fluoroisindolo[2,1-b]isoquinolin-7(5H)-one (3ha)



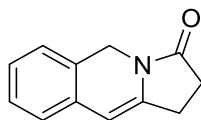
Light yellow solid (0.208 g, 83%) **TLC**: $R_f = 0.31$ (PE/EA=5/1); **$^1\text{H NMR}$** (400 MHz, CDCl_3) δ 8.0 – 7.8 (m, 1H), 7.4 (d, $J = 7.9$ Hz, 1H), 7.3 – 7.2 (m, 5H), 6.5 (s, 1H), 5.1 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 165.3, 164.1 (d, $J = 145.1$ Hz), 136.1 (d, $J = 10.5$ Hz), 132.6 (d, $J = 3.9$ Hz), 129.3, 128.7, 127.8, 127.4, 126.9, 126.2, 124.7, 124.6 (d, $J = 10.0$ Hz), 116.5 (d, $J = 23.8$ Hz), 106.6 (d, $J = 24.7$ Hz), 103.8, 42.4. **$^{19}\text{F NMR}$** (376 MHz, CDCl_3) δ -107.24. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{16}\text{H}_{11}\text{FNO}^+$: 252.0819, found: 252.0821.

Thieno[3',2':3,4]pyrrolo[1,2-b]isoquinolin-11(9H)-one (3ia)



Light purple solid (0.170 g, 71%) **TLC**: $R_f = 0.43$ (PE/Ea=5/1); **$^1\text{H NMR}$** (600 MHz, CDCl_3) δ 7.7 (d, $J = 4.8$ Hz, 1H), 7.3 – 7.2 (m, 5H), 6.4 (s, 1H), 5.1 (s, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 160.8, 144.4, 133.8, 132.7, 130.4, 129.0, 128.6, 127.3, 126.9, 126.7, 125.8, 117.8, 104.4, 42.3. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{14}\text{H}_{10}\text{NOS}^+$: 240.0478, found: 240.0477.

1,4-Dihydropyrrolo[1,2-b]isoquinolin-3(2H)-one (3ja)



To a flame dried sealed tube containing **1j** (0.100 g, 1.0 mmol, 1.0 eq) was added **Au-I** catalyst (0.025 g, 0.05 mmol, 0.05 eq) and 10 mL anhydrous DCE. The mixture was stirred at 80 °C for 2 h, then **2a** (0.133 g, 1.0 mmol, 1.0 eq) was solved in 5 mL anhydrous DCE, and added to the reaction mixture after total conversion of **1j** as indicated by thin layer chromatography. The mixture was stirred under 80 °C for 3 h, and evaporated to remove solvent after total conversion of enol lactone **I** indicated by thin layer chromatography. Then **Ru-III** catalyst (0.032 g, 0.05 mmol, 0.05 eq) and 10 mL anhydrous toluene was added to the reaction mixture. The mixture was refluxed for 10 h, and concentrated in *vacuo* after completion of the reaction as indicated by thin layer chromatography. The residue obtained was purified by silica gel chromatography to afford the desired **3ja** as transparent oil (0.133g, 72%).

Transparent oil (0.133 g, 72%) **TLC**: $R_f = 0.31$ (PE/Ea=5/1); **$^1\text{H NMR}$** (600 MHz, CDCl_3) δ 7.14 (m, 1H), 7.07 (m, 1H), 7.02 (d, $J = 7.3$ Hz, 1H), 6.92 (d, $J = 7.5$ Hz, 1H), 5.48 (s, 1H), 4.89 (s, 2H), 2.81 – 2.78 (m, 2H), 2.59 – 2.53 (m, 2H). **$^{13}\text{C NMR}$** (150 MHz, CDCl_3) δ 175.1, 140.6, 131.6, 127.8, 126.2, 126.1, 124.7, 119.7, 99.6, 43.6, 28.8, 23.0. **HRMS** (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{12}\text{H}_{12}\text{NO}^+$: 186.0913, found: 186.0912.

Reference

- [1] E. Marchal, P. Uriac, B. Legouin, L. Toupet and P. van de Weghe, *Tetrahedron*, 2007, **63**, 9979-9990.
- [2] J. Alzeer, J. Chollet, I. Heinze-Krauss, C. Hubschwerlen, H. Matile and R. G. Ridley, *J. Med. Chem.*, 2000, **43**, 560-568.
- [3] A. S. K. Hashmi, C. Lothschütz, R. Döpp, M. Ackermann, J. D. B. Becker, M. Rudolph, C. Scholz and F. Rominger, *Adv. Synth. Catal.*, 2012, **354**, 133-147.
- [4] M. L. Bannasar, T. Roca, M. Monerris and D. García-Díaz, *J. Org. Chem.*, 2006, **71**, 7028-7034.
- [5] B. Aneja, M. Irfan, C. Kapil, M. A. Jairajpuri, R. Maguire, K. Kavanagh, M. M. A. Rizvi, N. Manzoor, A. Azamb and M. Abid, *Org. Biomol. Chem.*, 2016, **14**, 10599-10619.
- [6] L. Jarrige, A. Carboni, G. Dagousset, G. Levitre, E. Magnier and G. Masson, *Org. Lett.*, 2016, **18**, 2906-2909.
- [7] J. Zhang, X. Li, X. Li, H. Shi, F. Sunb and Y. Du, *ChemCommun*, 2021, **57**, 460-463.

Single Crystal X-ray Data for Compound 3af

CCDC 2073382

DOI: 10.5517/ccdc.csd.cc27lj9p

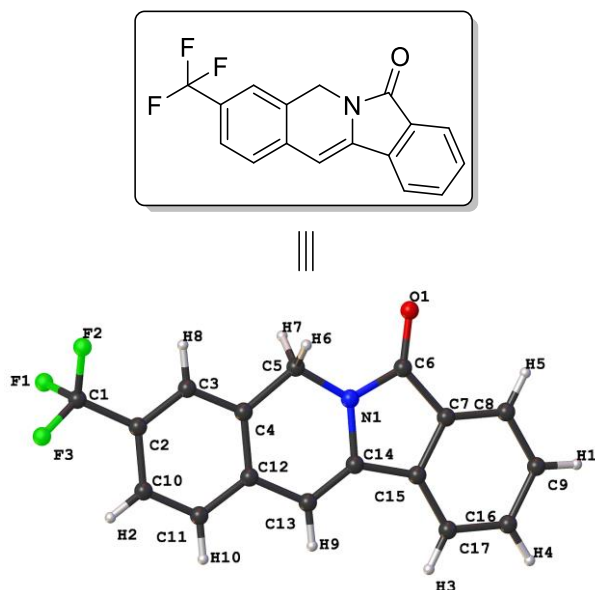


Table 1 Crystal data and structure refinement for 3-1af.

Identification code	3-1af
Empirical formula	C ₁₇ H ₁₀ NOF ₃
Formula weight	301.26
Temperature/K	298(2)
Crystal system	triclinic
Space group	P-1
a/Å	7.2327(11)
b/Å	7.6558(11)
c/Å	13.5621(18)
α /°	100.334(4)
β /°	95.405(4)
γ /°	109.676(4)
Volume/Å ³	685.89(17)
Z	2
ρ_{calc} /cm ³	1.459
μ /mm ⁻¹	0.119
F(000)	308.0
Crystal size/mm ³	0.21 × 0.18 × 0.07
Radiation	MoK α (λ = 0.71073)
2 θ range for data collection/°	5.8 to 50.044
Index ranges	-8 ≤ h ≤ 8, -9 ≤ k ≤ 9, -15 ≤ l ≤ 16
Reflections collected	18581

Independent reflections 2418 [$R_{\text{int}} = 0.2218$, $R_{\text{sigma}} = 0.0945$]
 Data/restraints/parameters 2418/0/199
 Goodness-of-fit on F^2 0.959
 Final R indexes [$I \geq 2\sigma(I)$] $R_1 = 0.0614$, $wR_2 = 0.1446$
 Final R indexes [all data] $R_1 = 0.1572$, $wR_2 = 0.1908$
 Largest diff. peak/hole / $e \text{ \AA}^{-3}$ 0.20/-0.19

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3-1af. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{H} tensor.

Atom	x	y	z	$U(\text{eq})$
F1	2157(7)	4390(5)	177(2)	173.7(17)
F2	575(6)	2046(6)	739(2)	175.1(17)
F3	3207(7)	2150(6)	199(2)	181.2(19)
O1	1286(4)	7919(4)	6075(2)	101.0(10)
N1	3730(4)	7468(4)	5218(2)	66.9(9)
C1	2403(11)	3198(9)	734(4)	120.1(19)
C2	3531(8)	4215(6)	1767(3)	88.4(13)
C3	2574(6)	4729(6)	2524(3)	80.5(12)
C4	3586(6)	5770(5)	3484(3)	68.9(10)
C5	2450(5)	6307(5)	4279(3)	76.8(11)
C6	3048(6)	8185(5)	6044(3)	75.1(11)
C7	4817(6)	9245(5)	6824(3)	71.3(10)
C8	4967(7)	10227(6)	7803(3)	91.5(13)
C9	6834(8)	11110(7)	8378(3)	100.4(15)
C10	5567(8)	4716(6)	1951(3)	94.5(14)
C11	6611(6)	5752(6)	2901(3)	82.8(12)
C12	5661(5)	6307(5)	3673(2)	64.7(10)
C13	6752(5)	7434(5)	4668(3)	64.0(10)
C14	5812(5)	7975(5)	5390(3)	61.2(9)
C15	6469(5)	9108(5)	6429(3)	65.2(10)
C16	8487(7)	10992(6)	7993(3)	96.9(14)
C17	8346(6)	9991(5)	7011(3)	78.5(12)

Table 3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3-1af. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^2U_{11}+2hka*b*U_{12}+\dots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F1	268(5)	126(3)	80.6(18)	4.9(18)	-63(2)	46(3)
F2	171(4)	161(3)	102(2)	-10(2)	-50(2)	-16(3)

Table 3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3-1af. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hkab^*U_{12}+\dots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F3	240(5)	171(3)	94(2)	-48(2)	-24(2)	78(3)
O1	64(2)	107(2)	125(2)	14.3(19)	22.1(17)	26.6(16)
N1	51.5(18)	71(2)	67.9(19)	8.2(16)	-0.6(16)	15.4(15)
C1	155(5)	103(4)	70(3)	6(3)	-30(3)	26(4)
C2	110(4)	72(3)	64(3)	3(2)	-13(3)	23(3)
C3	75(3)	74(3)	72(3)	15(2)	-15(2)	10(2)
C4	65(3)	62(2)	65(2)	15.8(19)	-5(2)	7.9(18)
C5	56(2)	81(3)	77(3)	13(2)	-8(2)	12(2)
C6	67(3)	70(3)	87(3)	16(2)	16(2)	23(2)
C7	75(3)	64(2)	71(3)	13(2)	9(2)	23(2)
C8	104(4)	86(3)	83(3)	9(2)	17(3)	36(3)
C9	129(4)	85(3)	76(3)	-5(2)	7(3)	39(3)
C10	118(4)	95(3)	62(3)	4(2)	9(3)	35(3)
C11	81(3)	92(3)	71(3)	12(2)	8(2)	30(2)
C12	68(3)	61(2)	58(2)	14.1(18)	-0.8(19)	17.0(18)
C13	53(2)	68(2)	66(2)	13.4(19)	3.5(19)	19.5(18)
C14	53(2)	62(2)	60(2)	11.4(18)	-2.6(18)	13.7(17)
C15	66(2)	61(2)	61(2)	7.4(18)	-3(2)	19.9(19)
C16	102(4)	86(3)	76(3)	-12(2)	-20(3)	25(3)
C17	69(3)	77(3)	74(3)	0(2)	-8(2)	20(2)

Table 4 Bond Lengths for 3-1af.

Atom Atom	Length/ \AA	Atom Atom	Length/ \AA
F1 C1	1.329(6)	C6 C7	1.467(5)
F2 C1	1.321(7)	C7 C8	1.379(5)
F3 C1	1.301(7)	C7 C15	1.382(5)
O1 C6	1.227(4)	C8 C9	1.373(6)
N1 C5	1.445(5)	C9 C16	1.372(6)
N1 C6	1.365(5)	C10 C11	1.380(5)
N1 C14	1.407(4)	C11 C12	1.387(5)
C1 C2	1.483(6)	C12 C13	1.453(5)
C2 C3	1.364(6)	C13 C14	1.327(4)
C2 C10	1.376(6)	C14 C15	1.457(5)
C3 C4	1.386(5)	C15 C17	1.383(5)
C4 C5	1.497(5)	C16 C17	1.388(5)
C4 C12	1.401(5)		

Table 5 Bond Angles for 3-1af.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C6	N1	C5	123.6(3)	C8	C7	C6	129.8(4)
C6	N1	C14	112.4(3)	C8	C7	C15	121.8(4)
C14	N1	C5	123.9(3)	C15	C7	C6	108.4(3)
F1	C1	C2	112.0(4)	C9	C8	C7	117.7(4)
F2	C1	F1	104.4(5)	C16	C9	C8	121.0(4)
F2	C1	C2	113.2(5)	C2	C10	C11	119.2(4)
F3	C1	F1	105.9(5)	C10	C11	C12	121.7(4)
F3	C1	F2	105.4(5)	C4	C12	C13	119.1(3)
F3	C1	C2	115.0(5)	C11	C12	C4	118.8(3)
C3	C2	C1	120.4(5)	C11	C12	C13	122.1(3)
C3	C2	C10	119.8(4)	C14	C13	C12	120.9(3)
C10	C2	C1	119.8(5)	N1	C14	C15	105.1(3)
C2	C3	C4	122.2(4)	C13	C14	N1	121.2(3)
C3	C4	C5	119.6(3)	C13	C14	C15	133.8(3)
C3	C4	C12	118.4(3)	C7	C15	C14	108.4(3)
C12	C4	C5	122.0(3)	C7	C15	C17	120.3(3)
N1	C5	C4	112.7(3)	C17	C15	C14	131.3(4)
O1	C6	N1	124.1(4)	C9	C16	C17	121.7(4)
O1	C6	C7	130.2(4)	C15	C17	C16	117.5(4)
N1	C6	C7	105.8(3)				

Table 6 Torsion Angles for 3-1af.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
F1	C1	C2	C3	84.5(7)	C5	C4	C12	C13	-0.5(5)
F1	C1	C2	C10	-92.7(7)	C6	N1	C5	C4	177.9(3)
F2	C1	C2	C3	-33.2(7)	C6	N1	C14	C13	-179.0(3)
F2	C1	C2	C10	149.6(5)	C6	N1	C14	C15	0.4(4)
F3	C1	C2	C3	-154.5(5)	C6	C7	C8	C9	-179.8(4)
F3	C1	C2	C10	28.4(8)	C6	C7	C15	C14	0.4(4)
O1	C6	C7	C8	0.1(7)	C6	C7	C15	C17	179.9(4)
O1	C6	C7	C15	179.1(4)	C7	C8	C9	C16	-1.0(7)
N1	C6	C7	C8	-179.2(4)	C7	C15	C17	C16	0.3(6)
N1	C6	C7	C15	-0.2(4)	C8	C7	C15	C14	179.5(4)
N1	C14	C15	C7	-0.5(4)	C8	C7	C15	C17	-1.0(6)
N1	C14	C15	C17	-179.9(4)	C8	C9	C16	C17	0.4(7)

C1 C2 C3 C4	-176.4(4)	C9 C16 C17 C15	0.0(7)
C1 C2 C10 C11	176.5(4)	C10 C2 C3 C4	0.7(6)
C2 C3 C4 C5	179.4(4)	C10 C11 C12 C4	1.1(6)
C2 C3 C4 C12	0.1(6)	C10 C11 C12 C13	-178.6(4)
C2 C10 C11 C12	-0.3(7)	C11 C12 C13 C14	178.8(4)
C3 C2 C10 C11	-0.6(7)	C12 C4 C5 N1	2.1(5)
C3 C4 C5 N1	-177.1(3)	C12 C13 C14 N1	0.4(5)
C3 C4 C12 C11	-1.0(5)	C12 C13 C14 C15	-178.7(4)
C3 C4 C12 C13	178.7(3)	C13 C14 C15 C7	178.7(4)
C4 C12 C13 C14	-0.8(5)	C13 C14 C15 C17	-0.7(7)
C5 N1 C6 O1	0.0(6)	C14 N1 C5 C4	-2.7(5)
C5 N1 C6 C7	179.4(3)	C14 N1 C6 O1	-179.5(4)
C5 N1 C14 C13	1.5(5)	C14 N1 C6 C7	-0.1(4)
C5 N1 C14 C15	-179.1(3)	C14 C15 C17 C16	179.7(4)
C5 C4 C12 C11	179.8(4)	C15 C7 C8 C9	1.3(6)

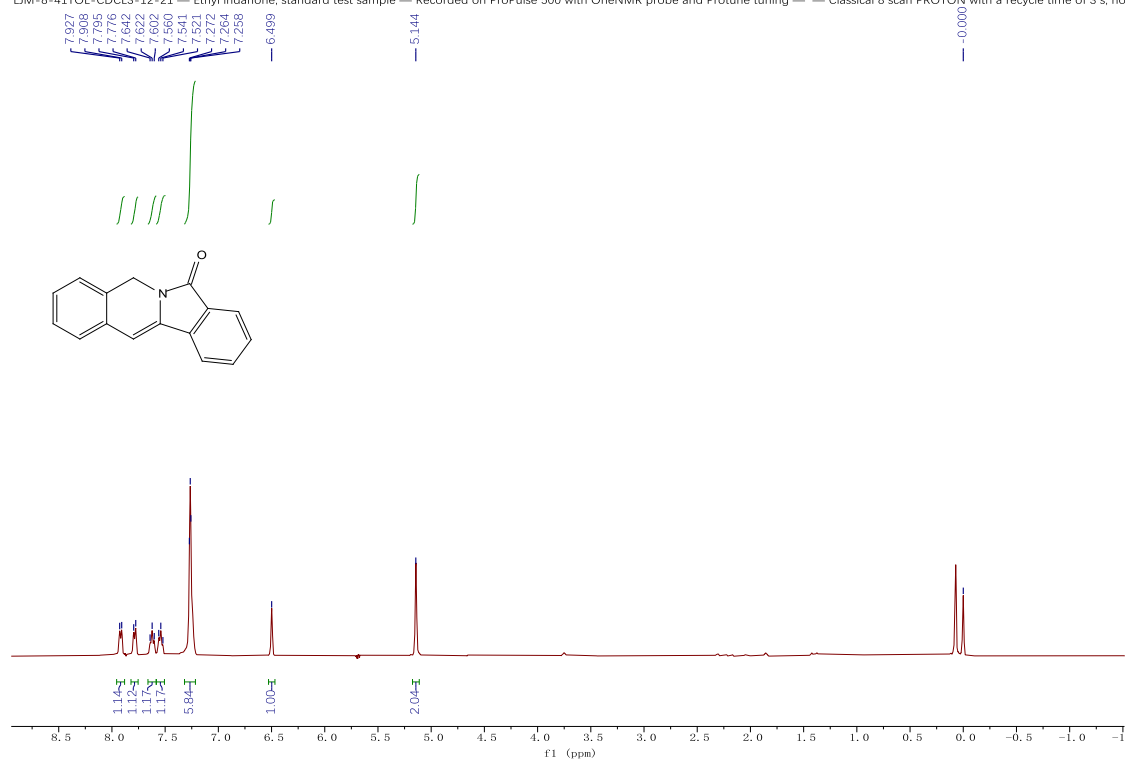
Table 7 Hydrogen Atom Coordinates ($\text{\AA} \times 10^4$) and Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3-1af.

Atom	x	y	z	U(eq)
H8	1196.06	4368.1	2392.02	97
H7	1680.19	6998.26	4020.36	92
H6	1524.48	5157.52	4413.7	92
H5	3843.13	10289.79	8065.65	110
H1	6981	11799.04	9037.26	121
H2	6230.75	4361.55	1441.77	113
H10	7986.31	6086.34	3025.32	99
H9	8128.48	7781.29	4801.44	77
H4	9732.57	11597.75	8400.22	116
H3	9471.96	9916.05	6754.9	94

^1H and ^{13}C NMR Spectra of Compounds

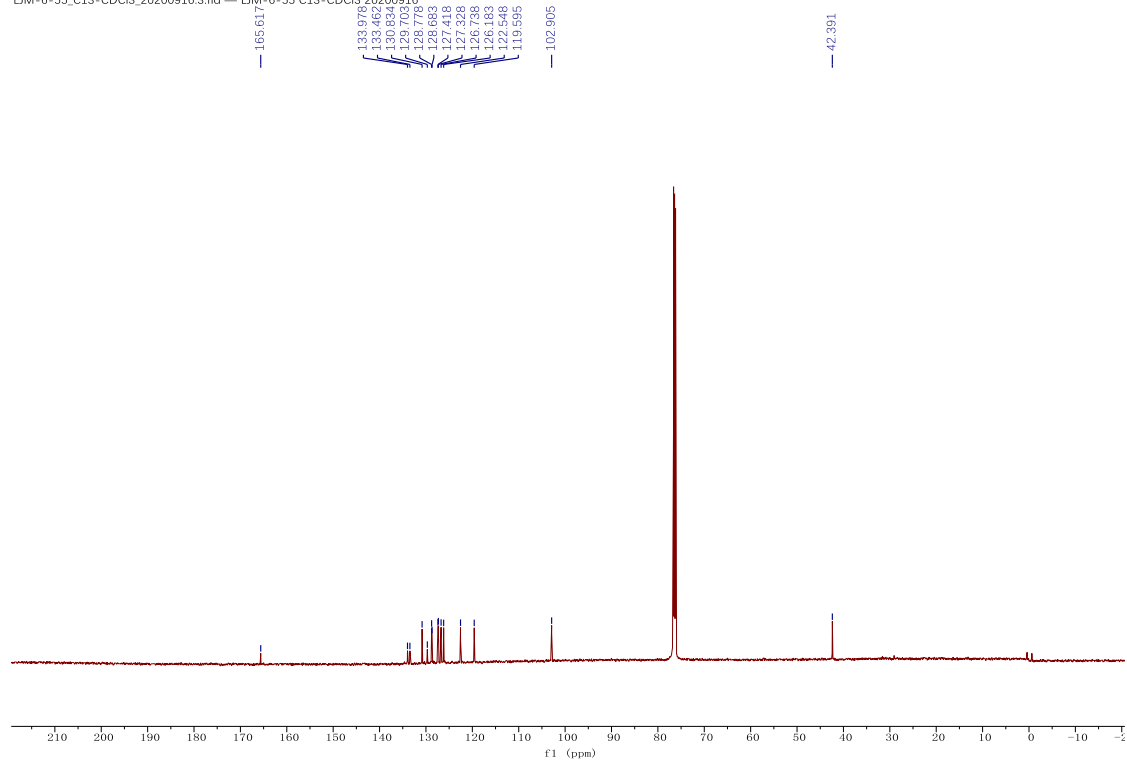
^1H NMR spectrum of compound 3aa (400 MHz, CDCl_3):

LJM-8-41TOL- CDCl_3 -12-21 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, no



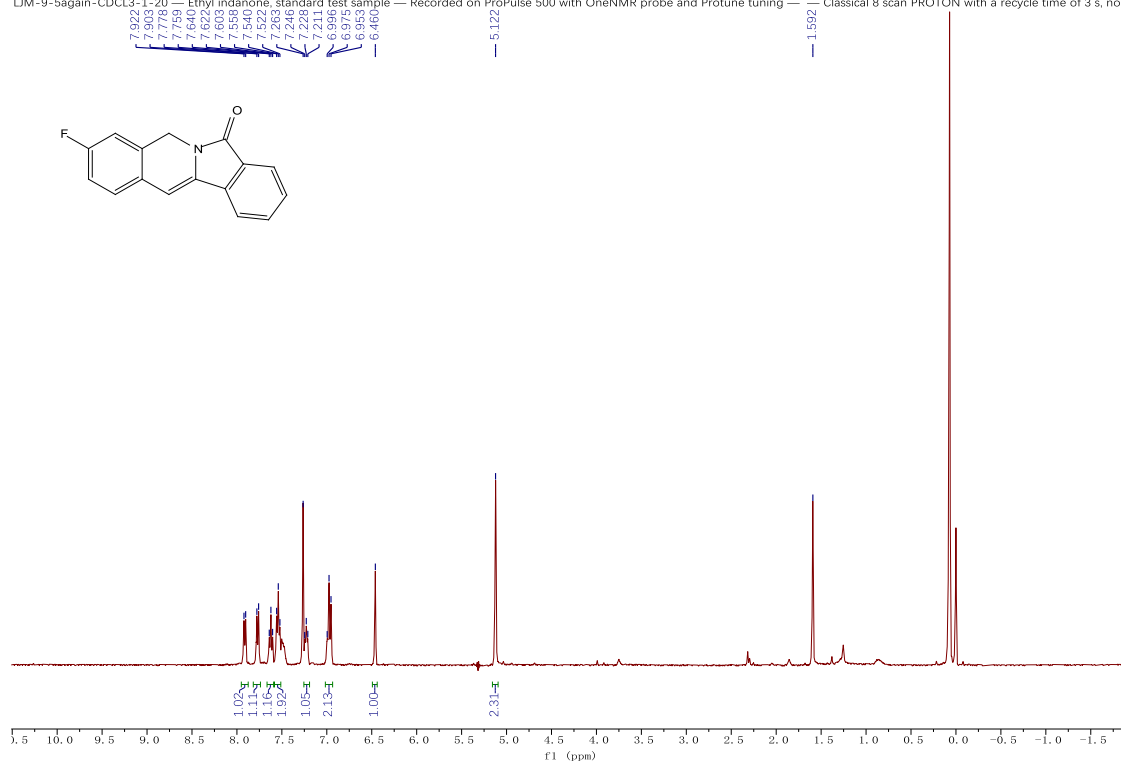
^{13}C NMR spectrum of compound 3aa (150 MHz, CDCl_3):

LJM-6-55_C13- CDCl_3 _20200916.3.fid — LJM-6-55 C13- CDCl_3 20200916



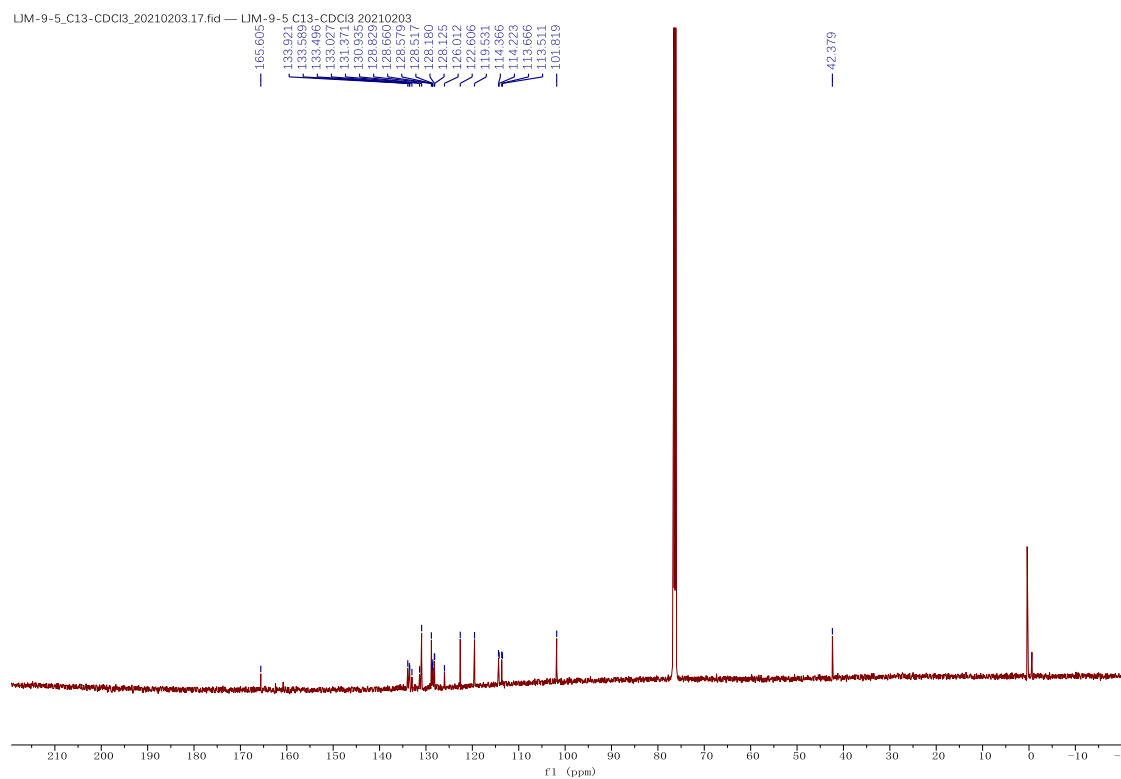
¹H NMR spectrum of compound 3ab (400 MHz, CDCl₃):

LJM-9-5again-CDCl3-1-20 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, nor



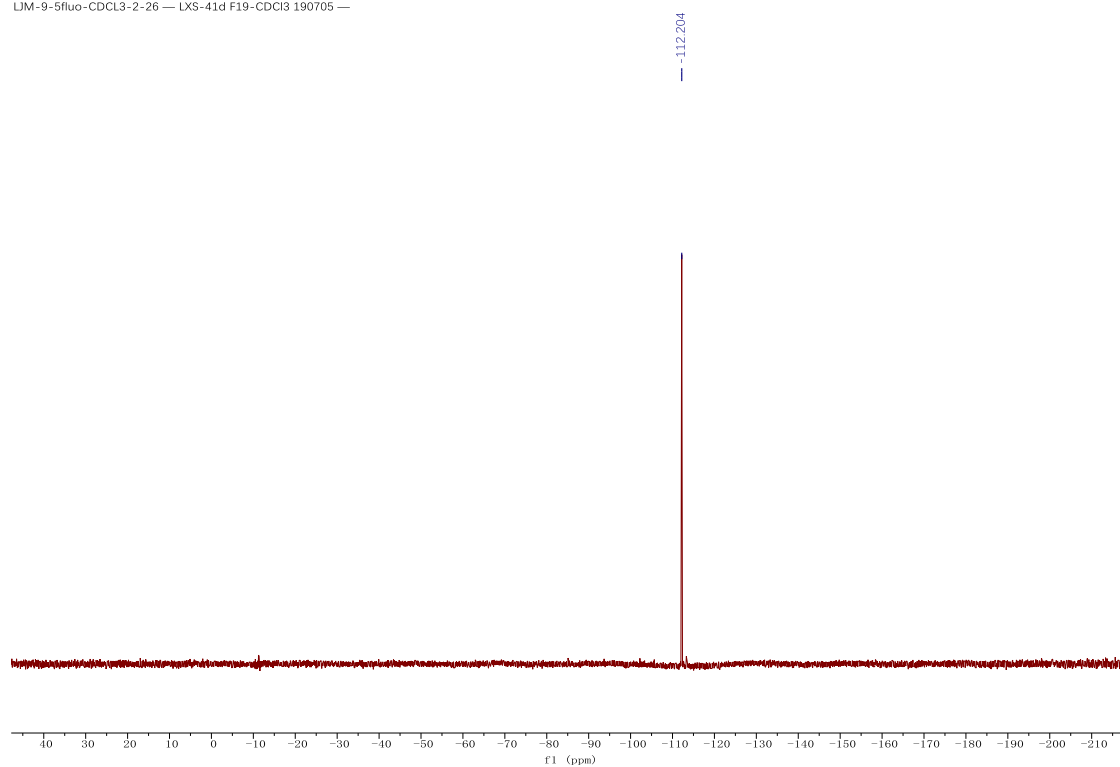
¹³C NMR spectrum of compound 3ab (150 MHz, CDCl₃):

LJM-9-5_C13-CDCl3_20210203.17.fid — LJM-9-5_C13-CDCl3_20210203



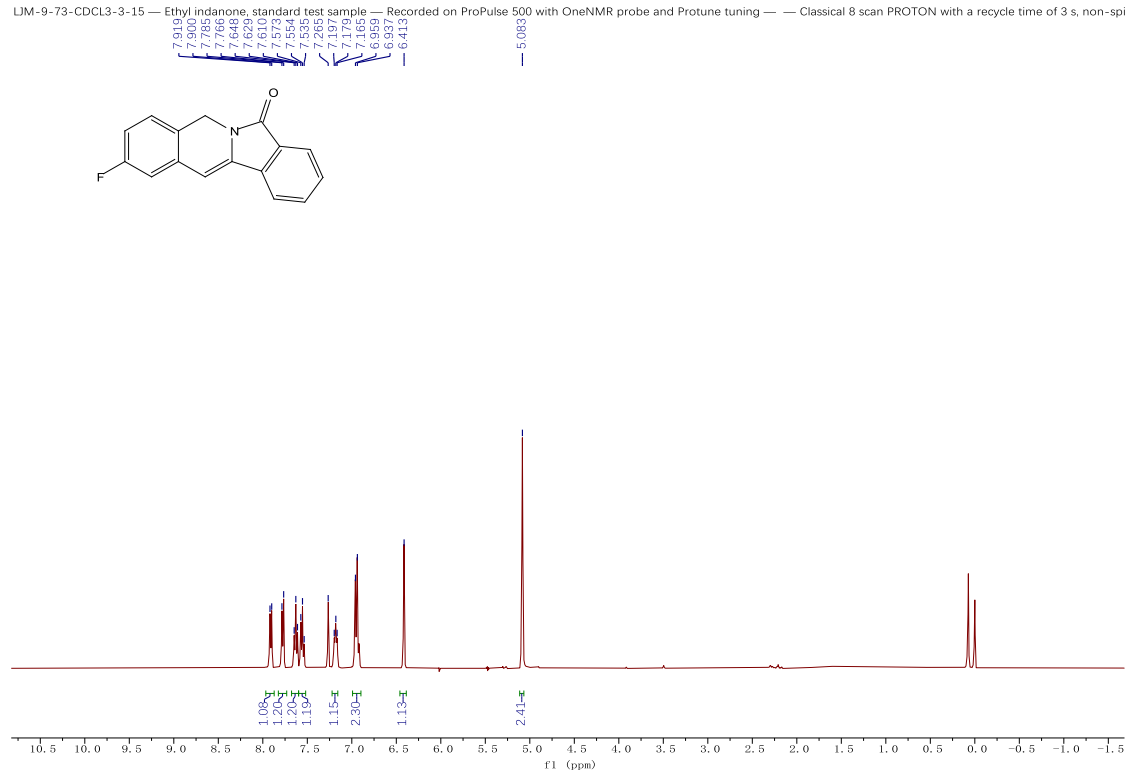
^{19}F NMR spectrum of compound 3ab (376 MHz, CDCl_3):

LJM-9-5fluo-CDCL3-2-26 — LXS-41d F19-CDCl3 190705 —

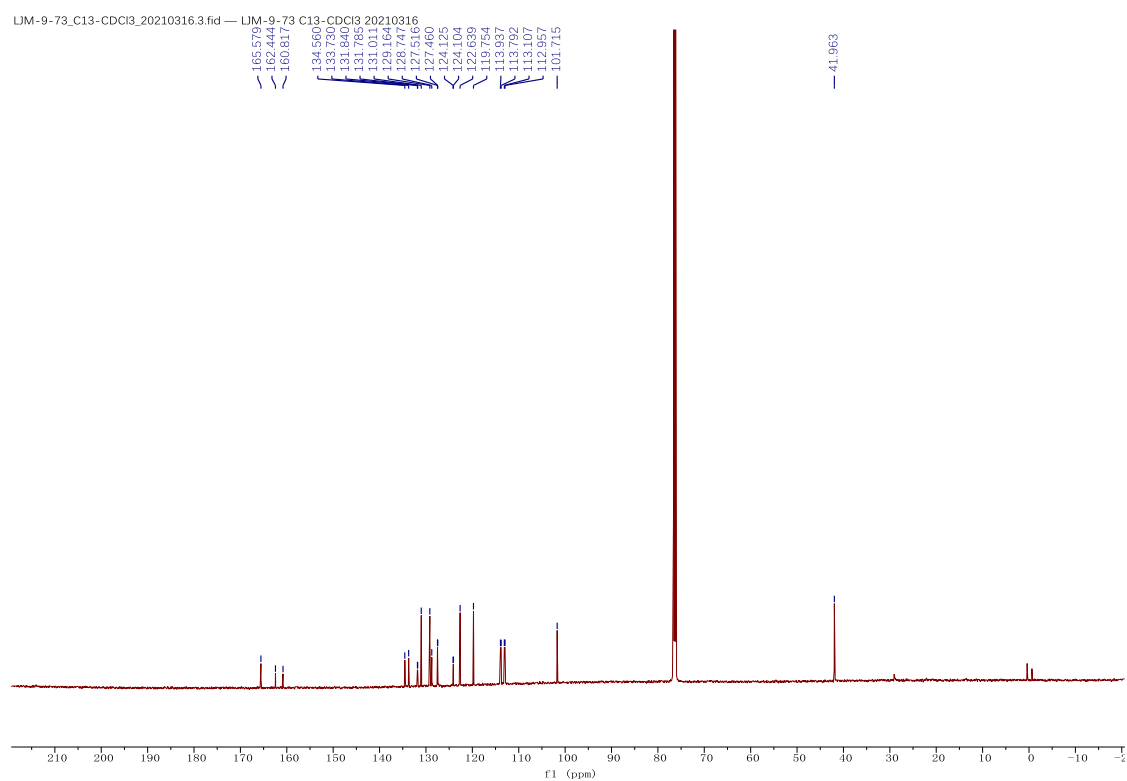


^1H NMR spectrum of compound 3ac (400 MHz, CDCl_3):

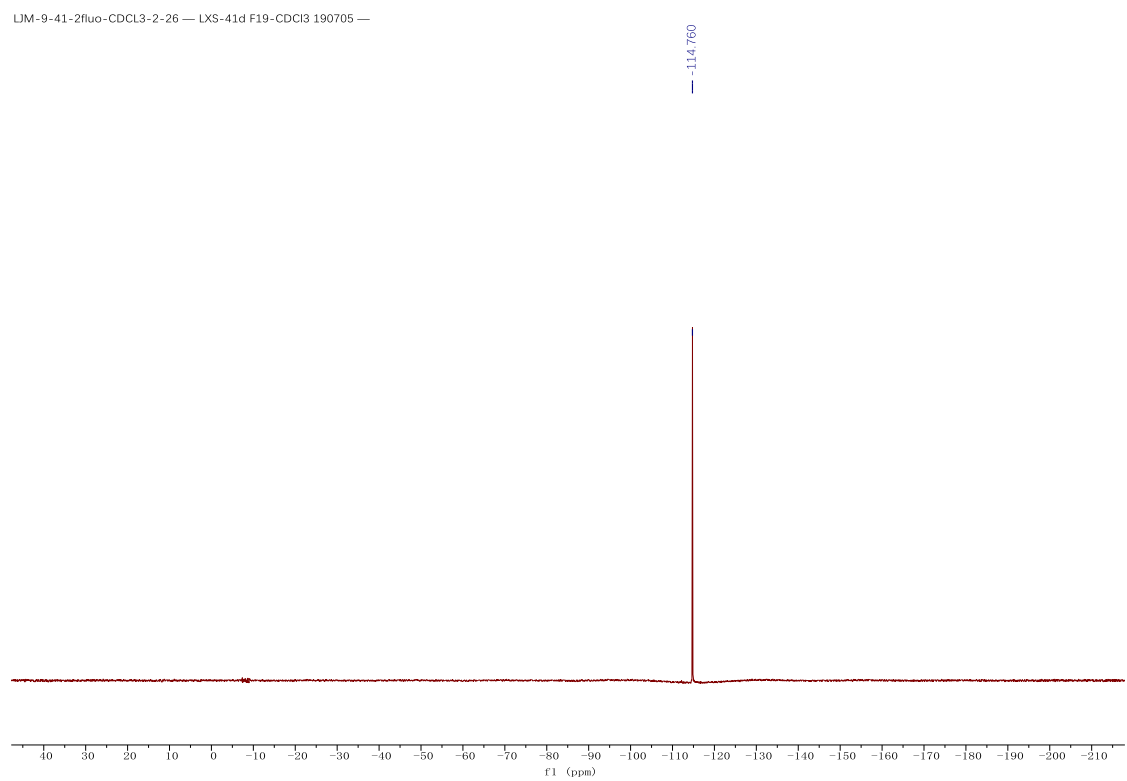
LJM-9-73-CDCL3-3-15 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



¹³C NMR spectrum of compound 3ac (150 MHz, CDCl₃):

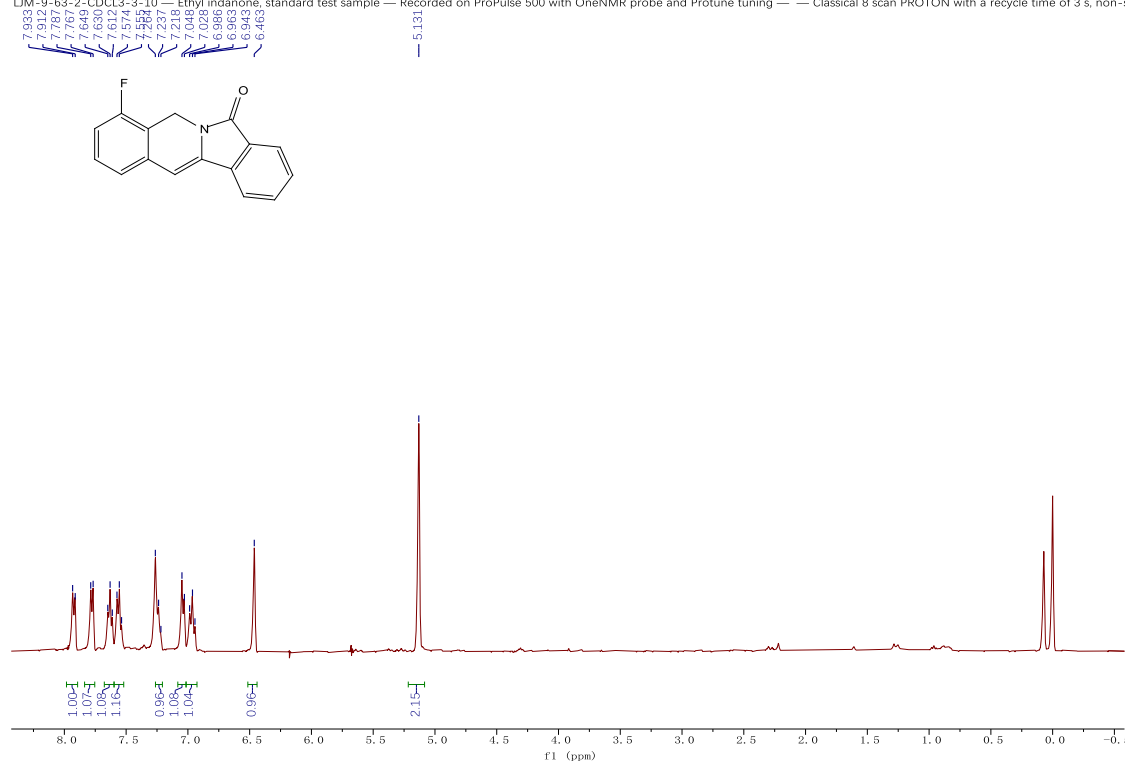


¹⁹F NMR spectrum of compound 3ac (376 MHz, CDCl₃):



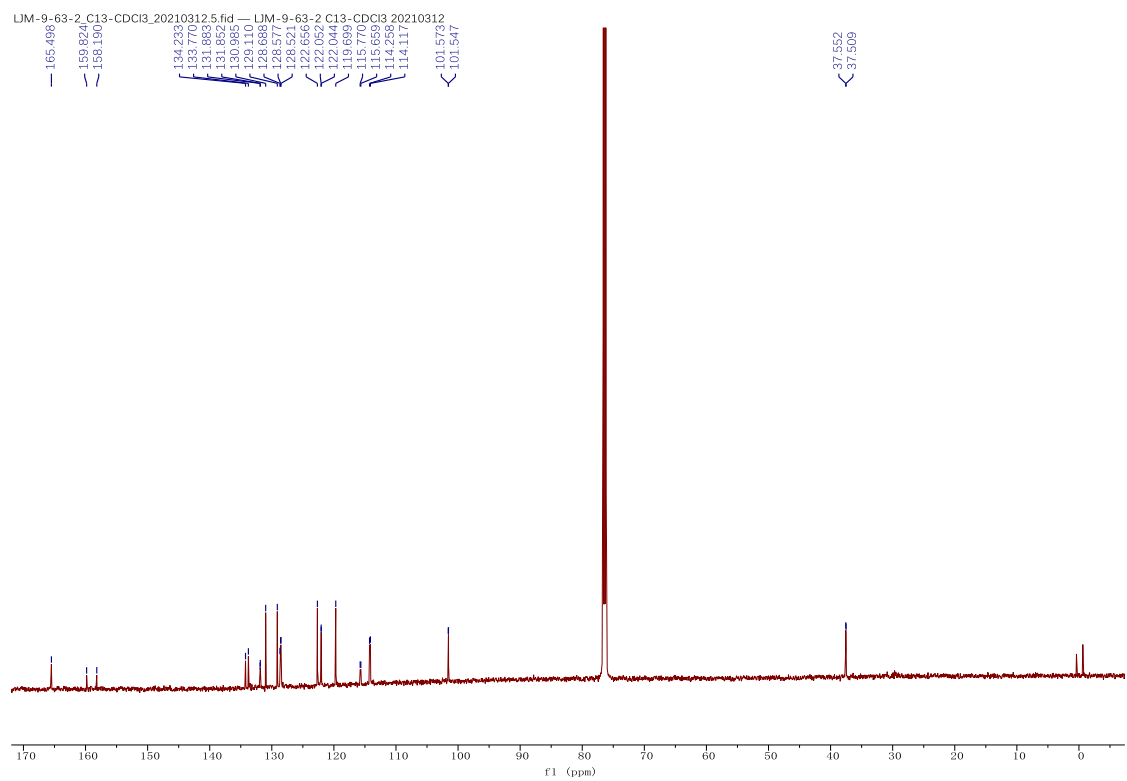
¹H NMR spectrum of compound 3ad (400 MHz, CDCl₃):

LJM-9-63-2-CDCl3-3-10 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-



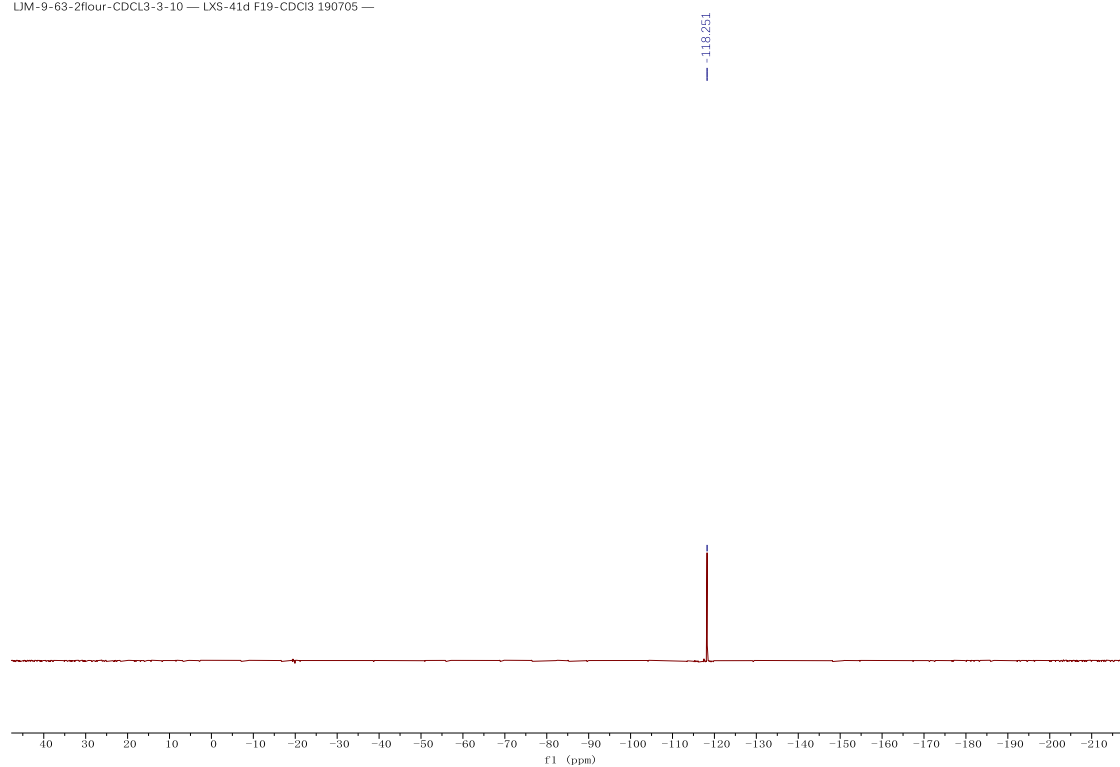
¹³C NMR spectrum of compound 3ad (150 MHz, CDCl₃):

LJM-9-63-2-C13-CDCl3_20210312.5.fid — LJM-9-63-2-C13-CDCl3_20210312



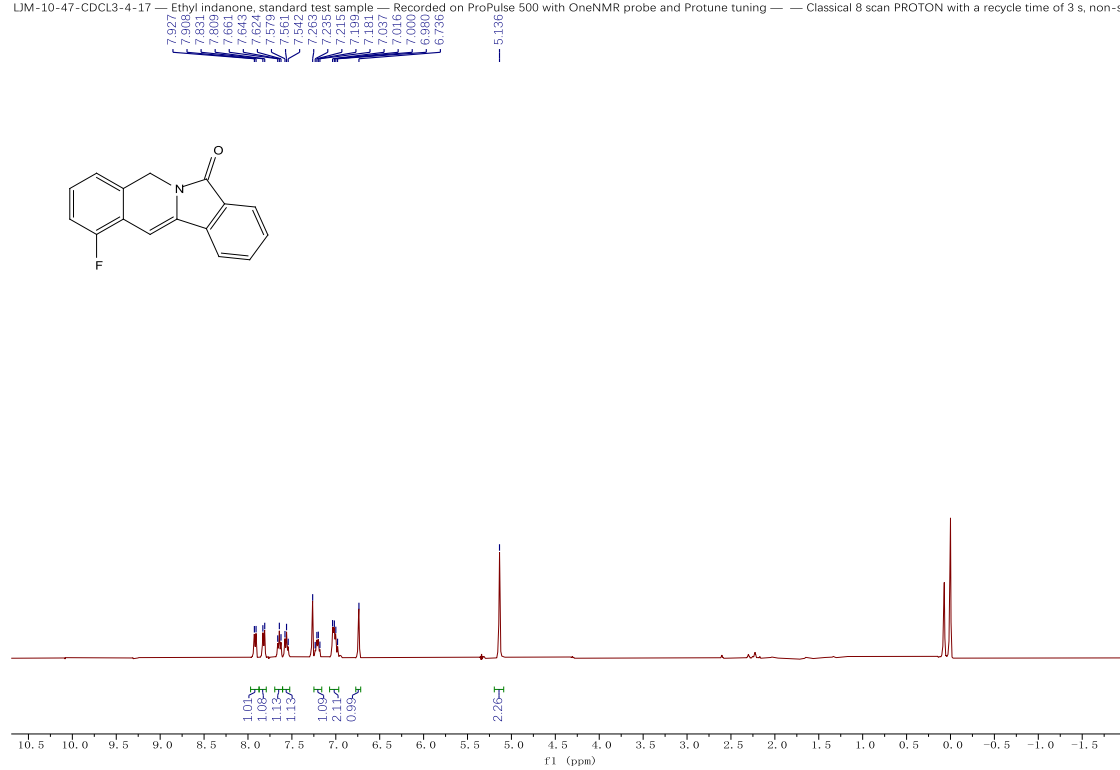
¹⁹F NMR spectrum of compound 3ad (376 MHz, CDCl₃):

LJM-9-63-2four-CDCl3-3-10 — LXS-41d F19-CDCl3 190705 —

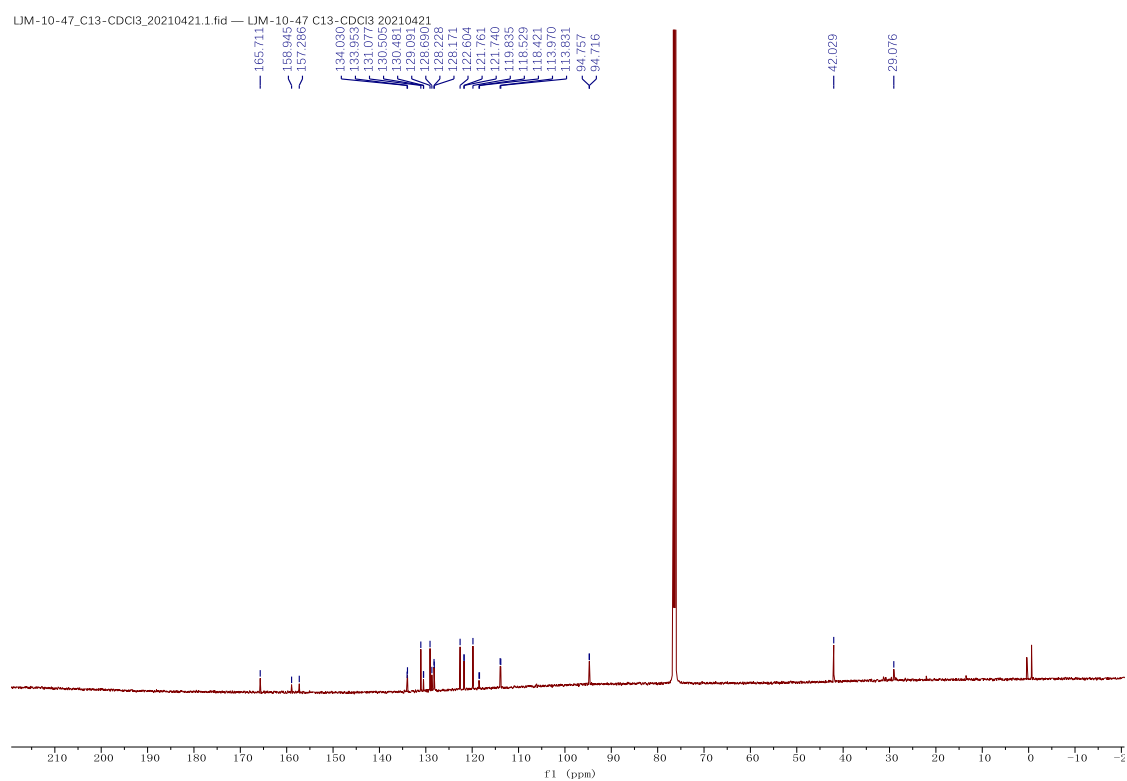


¹H NMR spectrum of compound 3ae (400 MHz, CDCl₃):

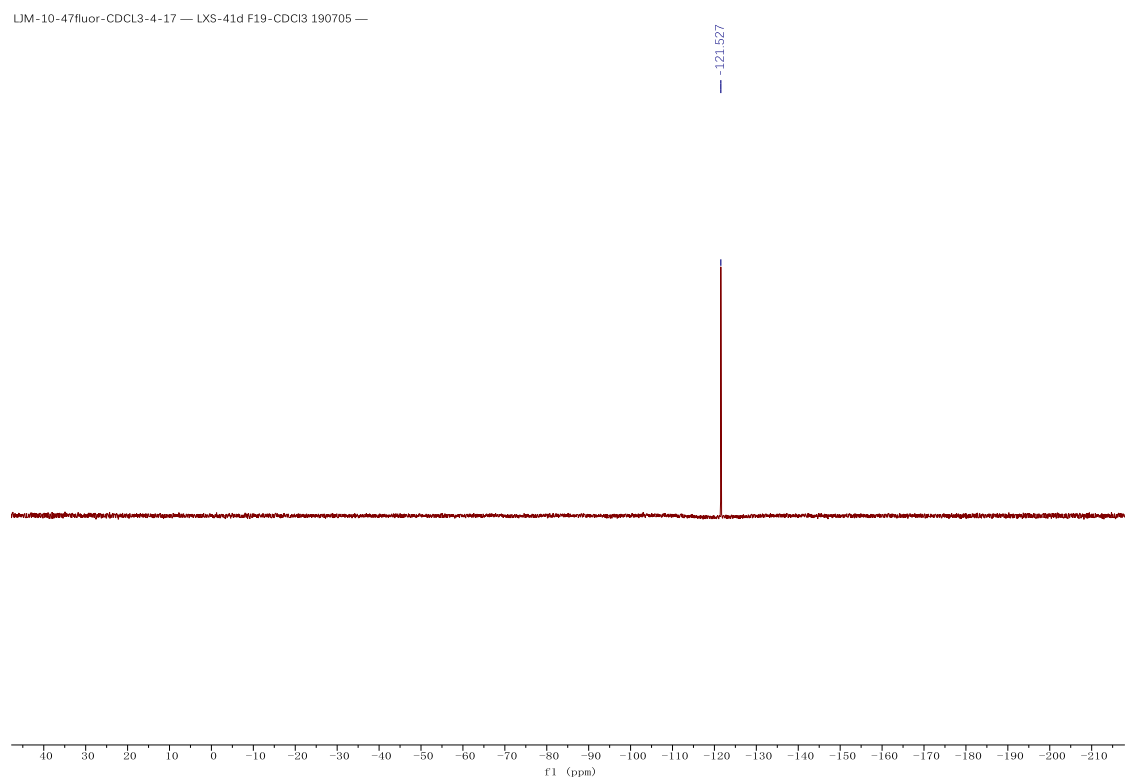
LJM-10-47-CDCl3-4-17 — Ethyl indanone, standard test sample Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



¹³C NMR spectrum of compound 3ae (150 MHz, CDCl₃):

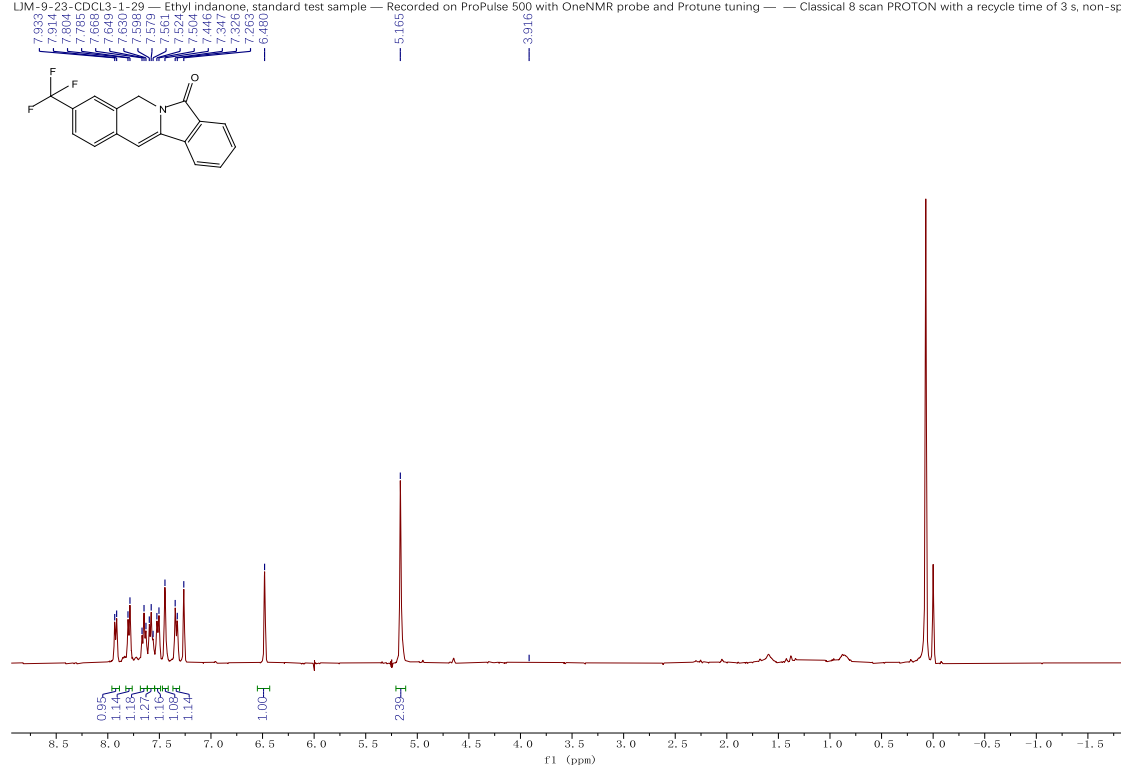


¹⁹F NMR spectrum of compound 3ae (376 MHz, CDCl₃):



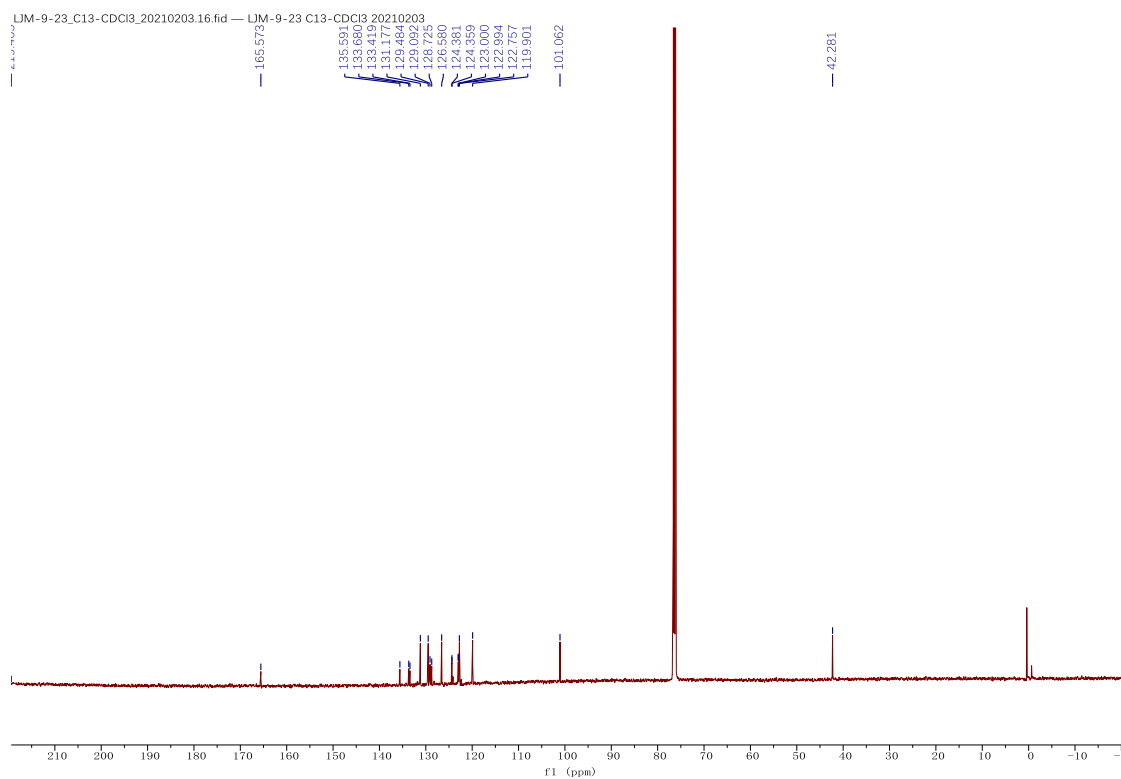
¹H NMR spectrum of compound 3af (400 MHz, CDCl₃):

LJM-9-23-CDCl3-1-29 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



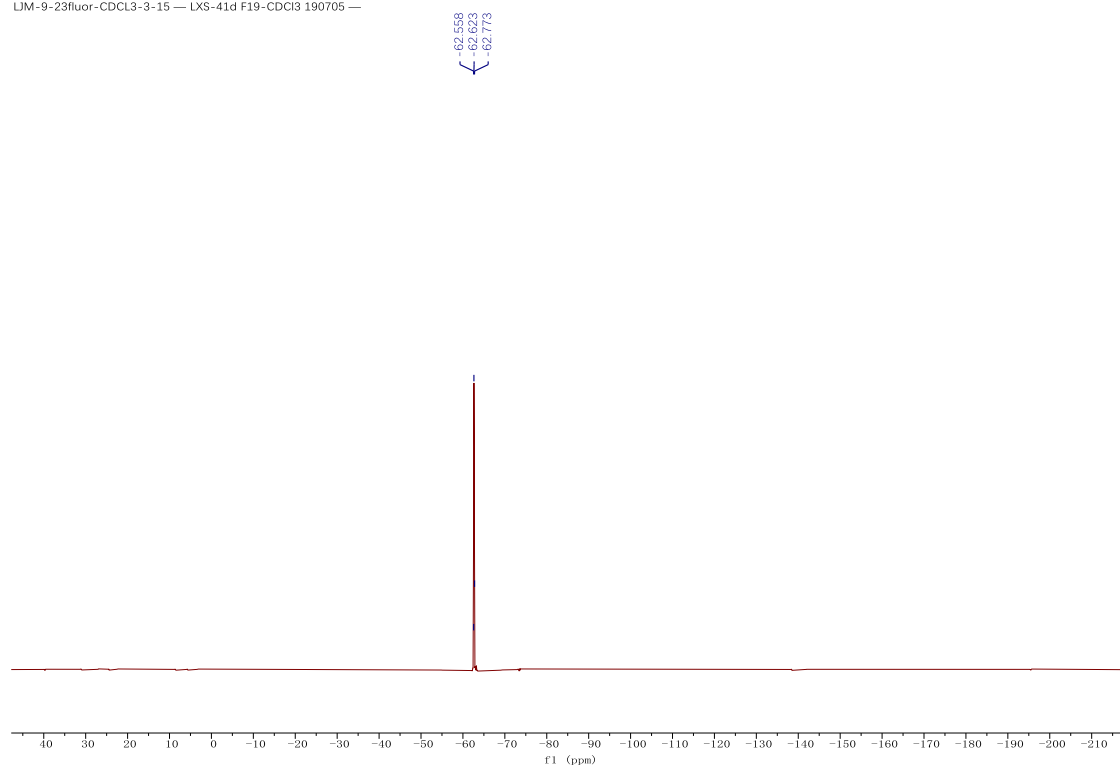
¹³C NMR spectrum of compound 3af (150 MHz, CDCl₃):

LJM-9-23_C13-CDCl3_20210203.16.fid — LJM-9-23 C13-CDCl3 20210203



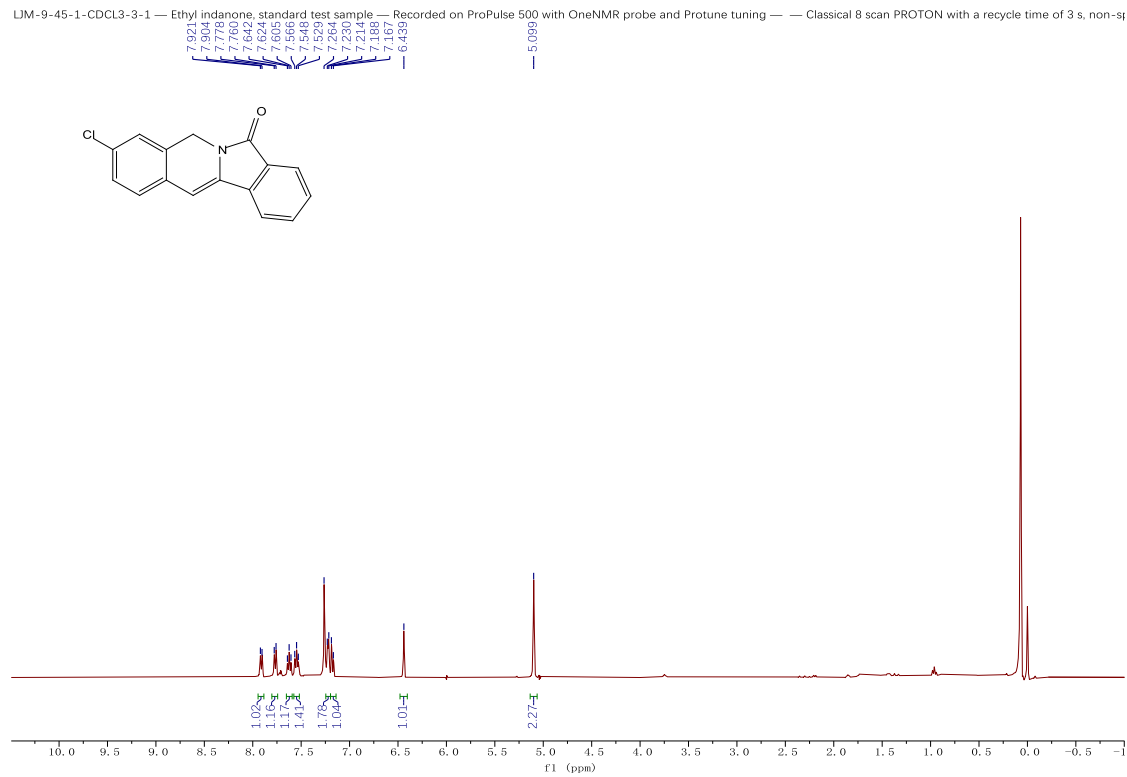
¹⁹F NMR spectrum of compound 3af (376 MHz, CDCl₃):

LJM-9-23fluor-CDCl3-3-15 — LXS-41d F19-CDCl3 190705 —

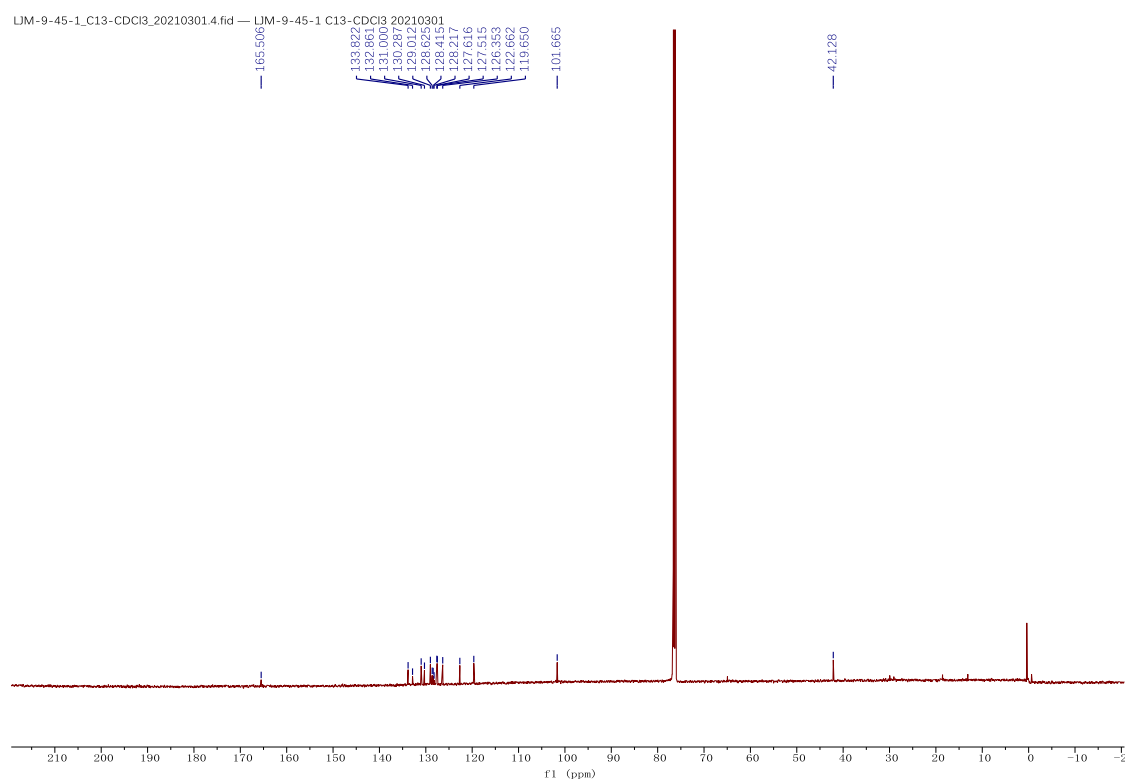


¹H NMR spectrum of compound 3ag (400 MHz, CDCl₃):

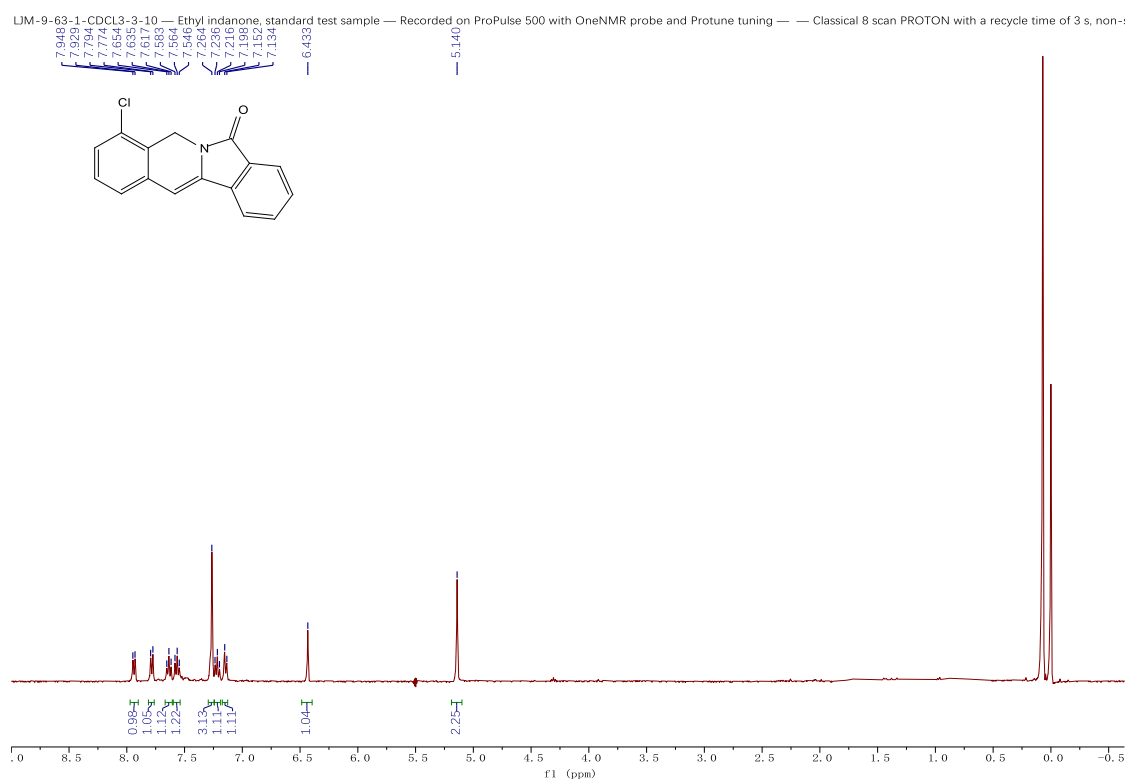
LJM-9-45-1-CDCl3-3-1 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



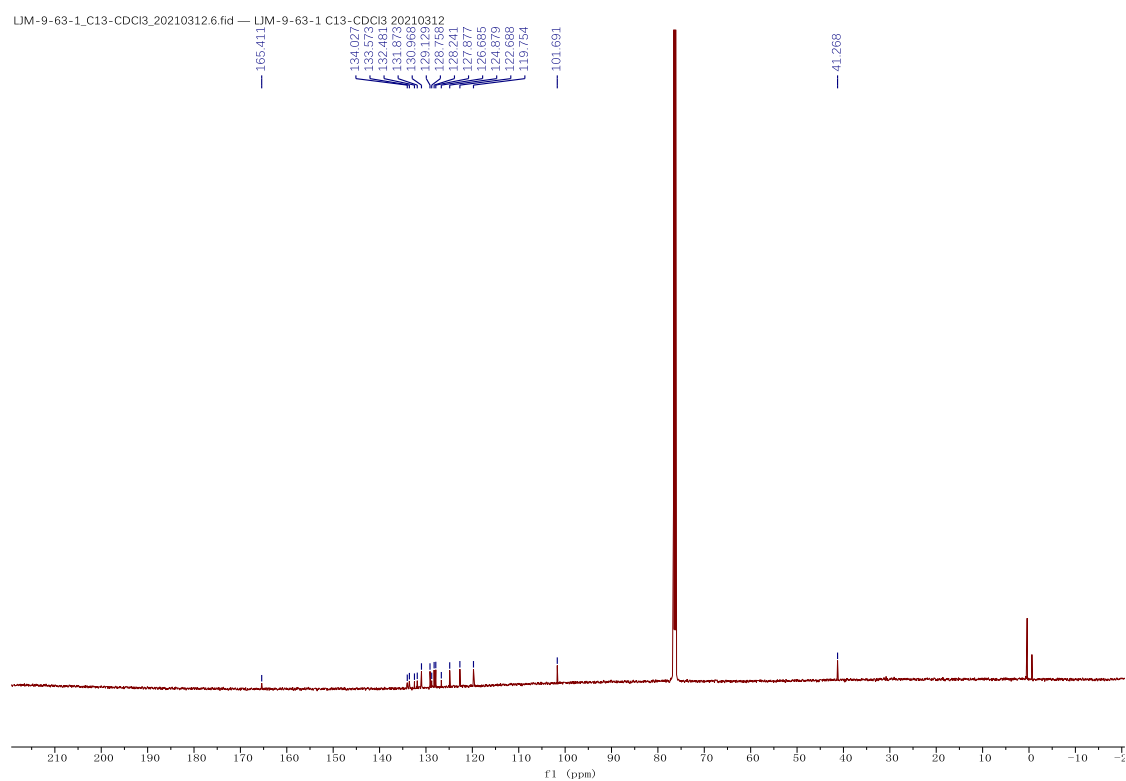
¹³C NMR spectrum of compound 3ag (150 MHz, CDCl₃):



¹H NMR spectrum of compound 3ah (400 MHz, CDCl₃):

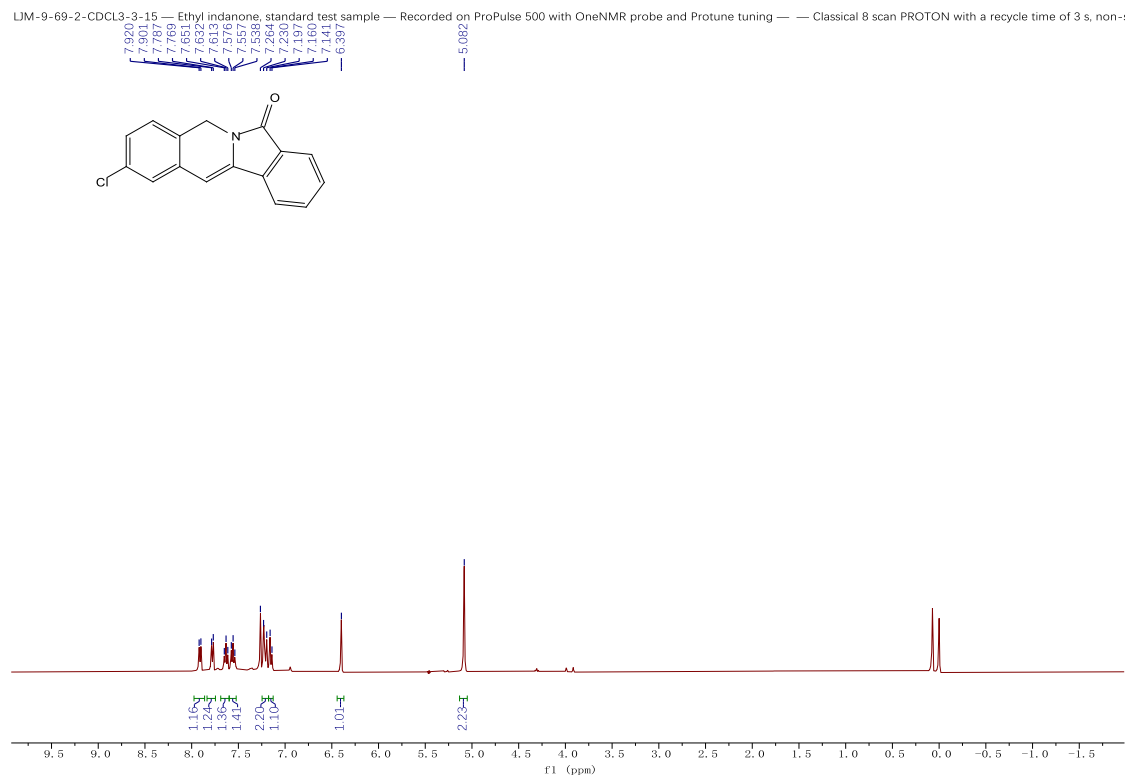


¹³C NMR spectrum of compound 3ah (150 MHz, CDCl₃):

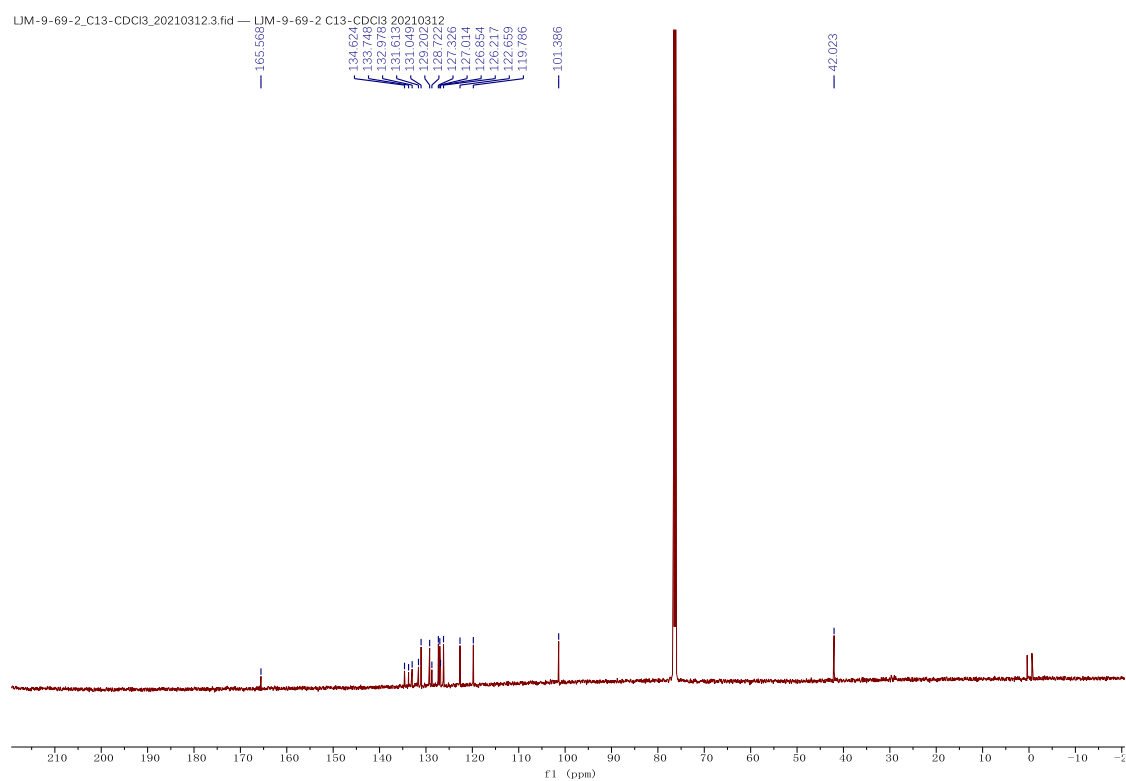


¹H NMR spectrum of compound 3ai (400 MHz, CDCl₃):

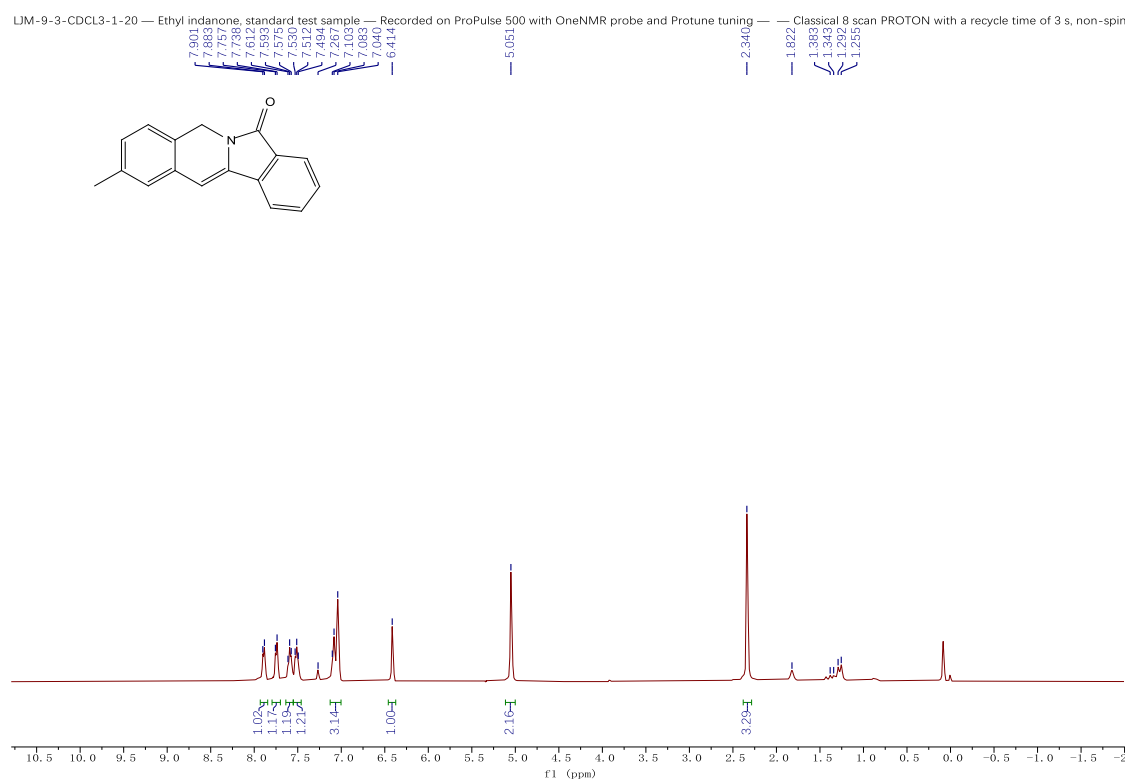
LJM-9-69-2-CDCl3-3-15 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-



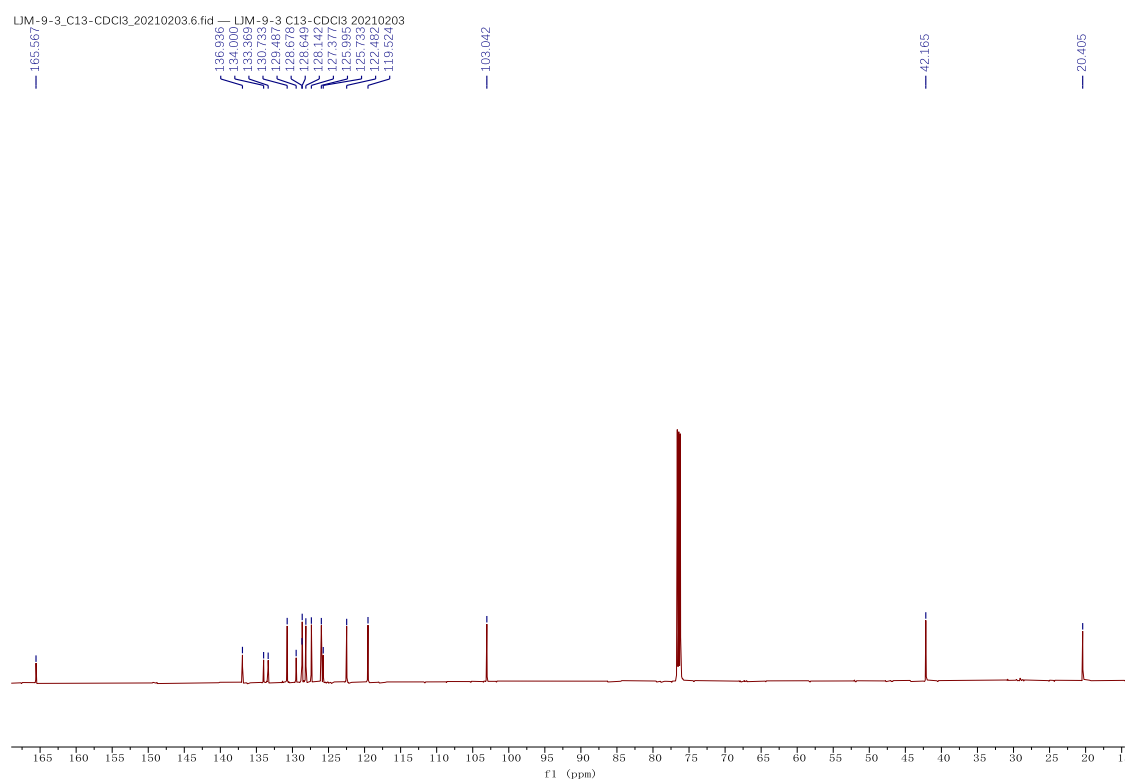
¹³C NMR spectrum of compound 3ai (150 MHz, CDCl₃):



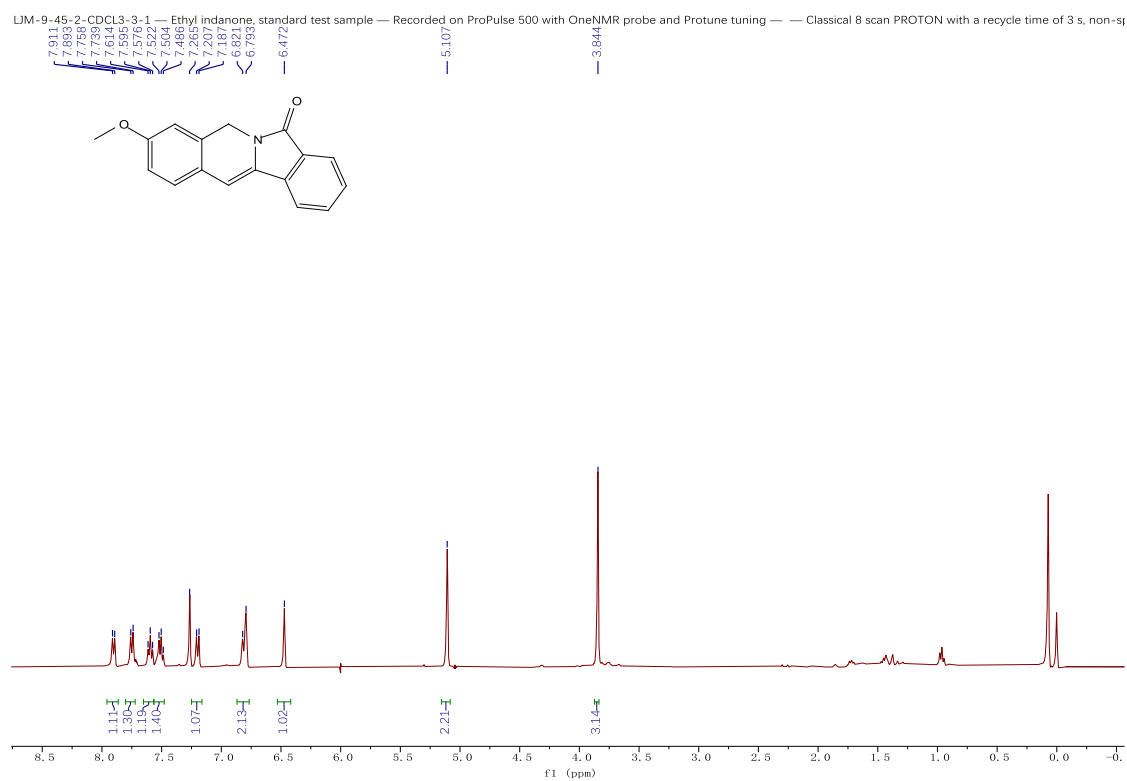
¹H NMR spectrum of compound 3ai (400 MHz, CDCl₃):



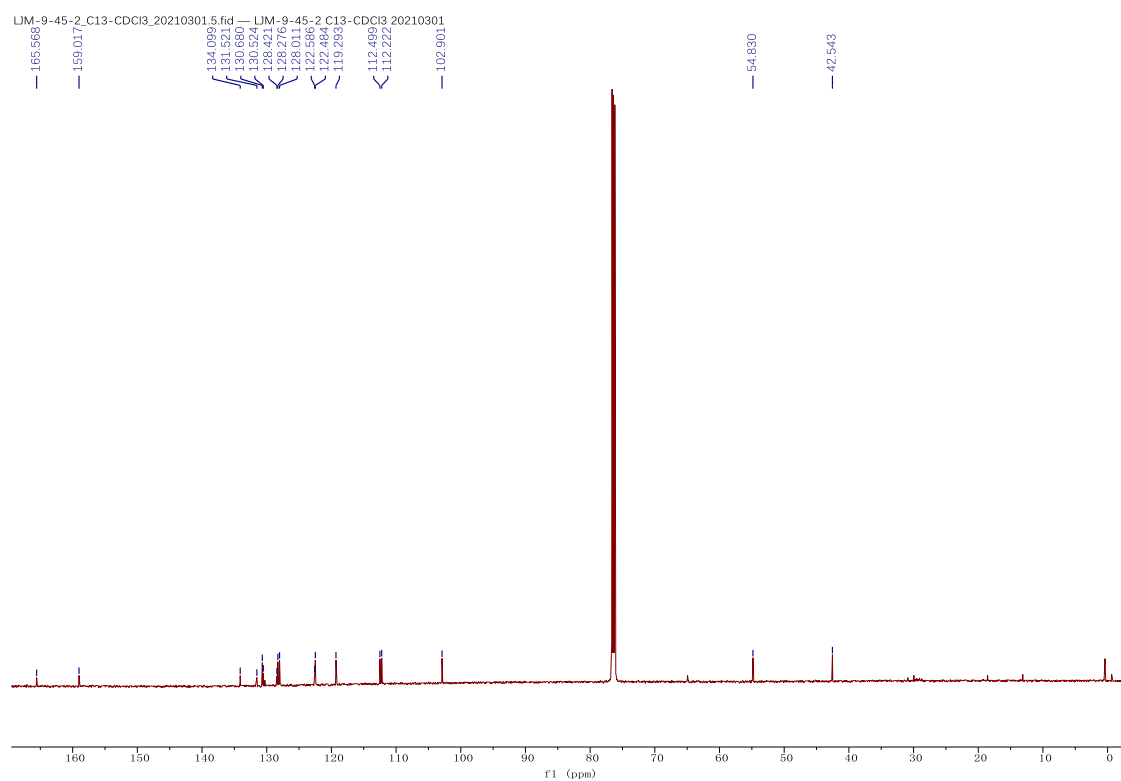
¹³C NMR spectrum of compound 3aj (150 MHz, CDCl₃):



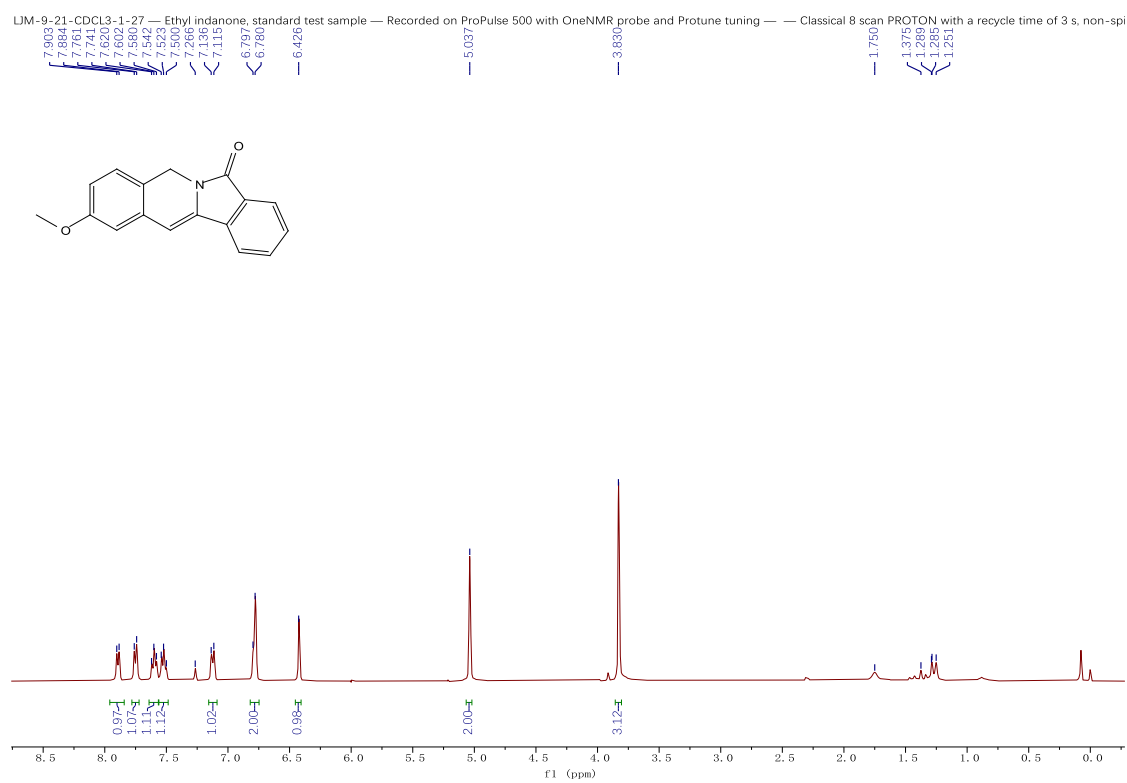
¹H NMR spectrum of compound 3ak (400 MHz, CDCl₃):



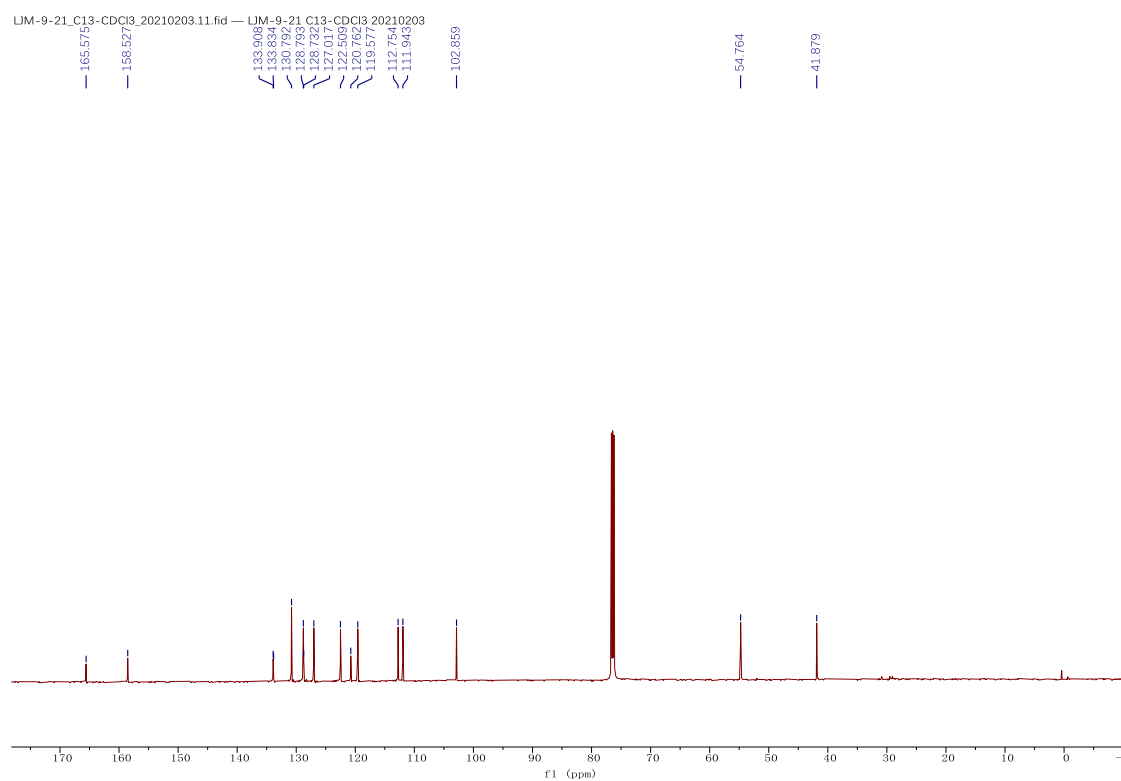
¹³C NMR spectrum of compound 3ak (150 MHz, CDCl₃):



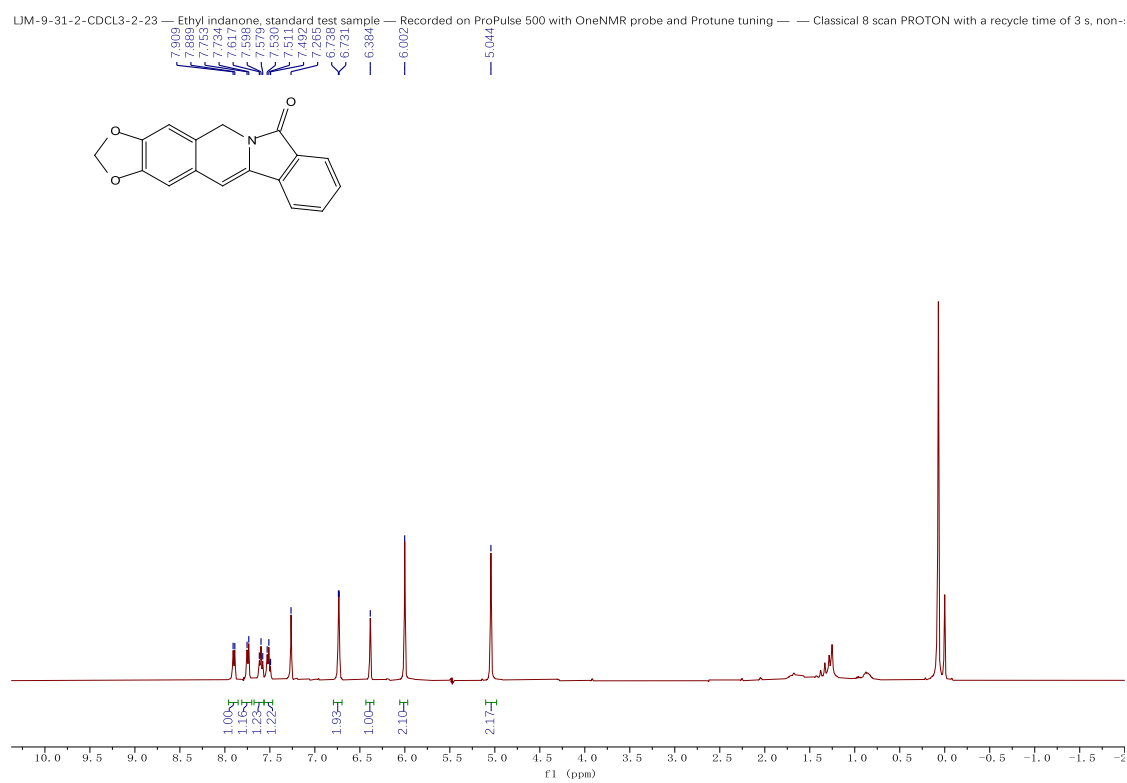
¹H NMR spectrum of compound 3al (400 MHz, CDCl₃):



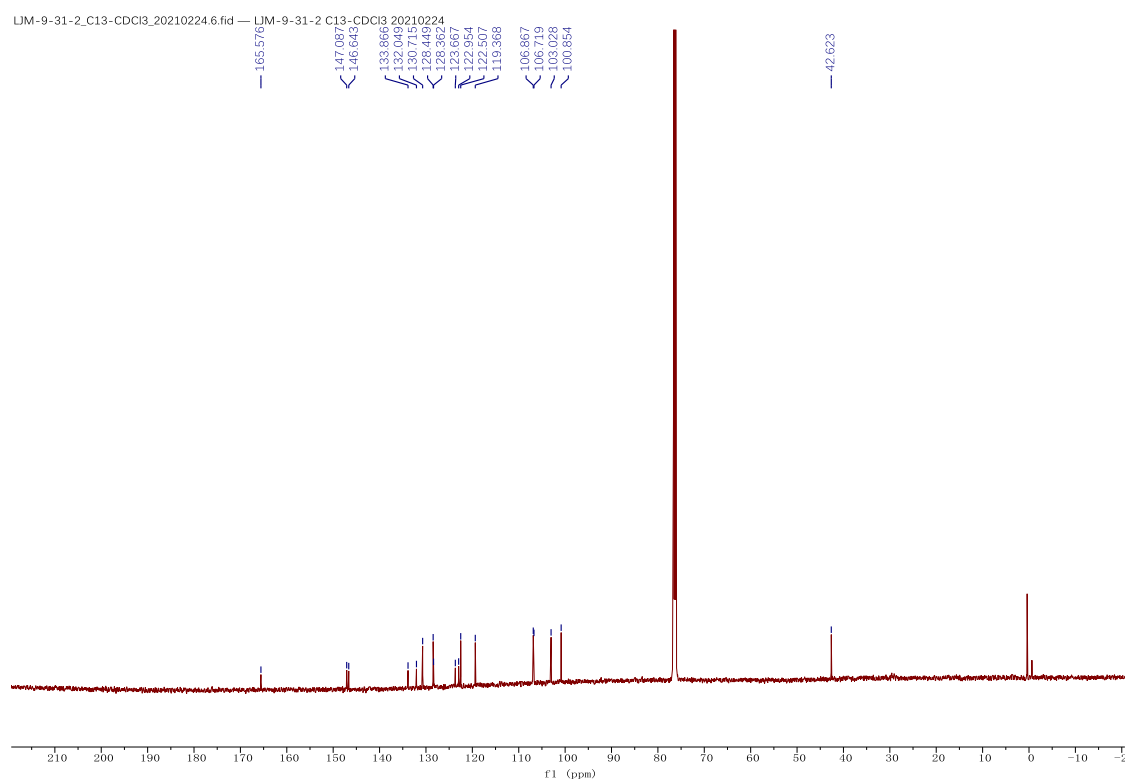
¹³C NMR spectrum of compound 3aI (150 MHz, CDCl₃):



¹H NMR spectrum of compound 3aM (400 MHz, CDCl₃):

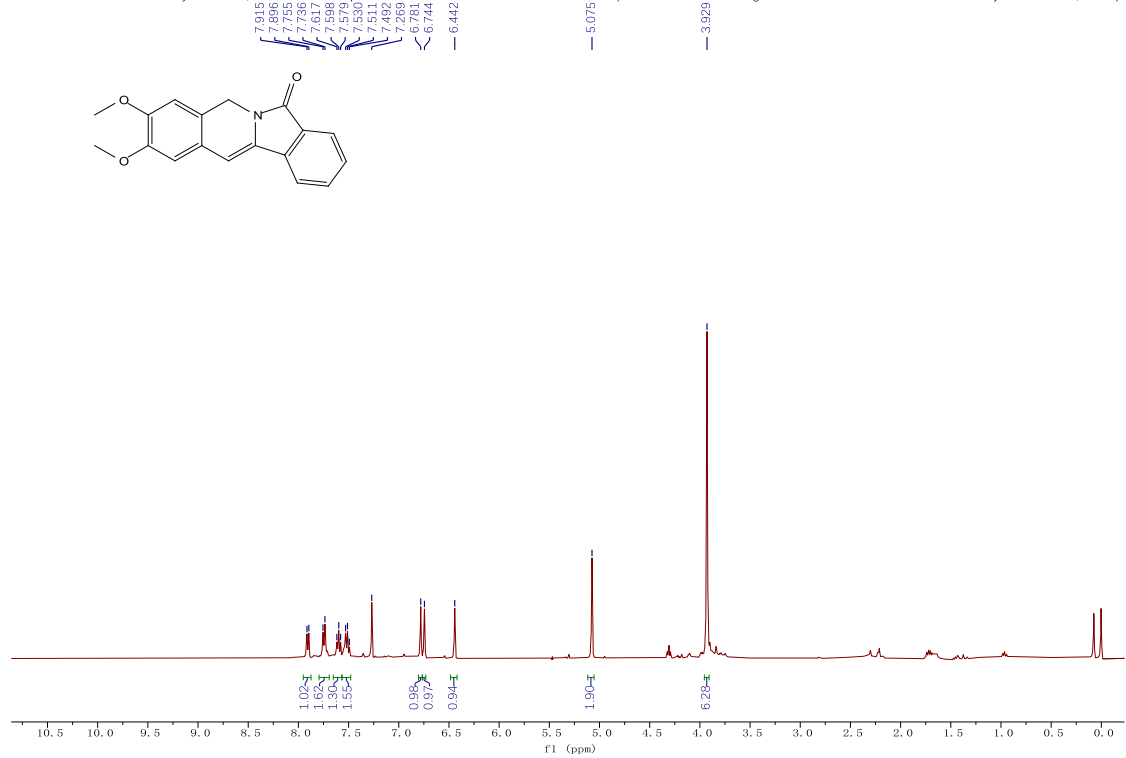


¹³C NMR spectrum of compound 3am (150 MHz, CDCl₃):

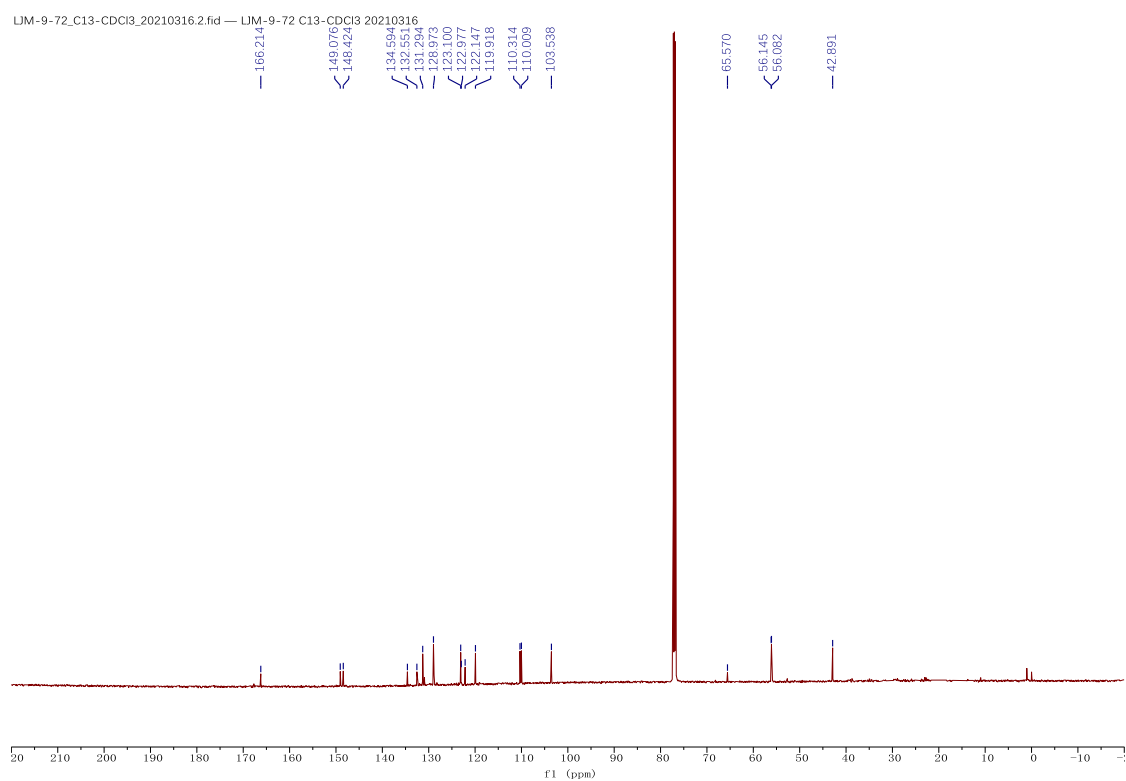


¹H NMR spectrum of compound 3an (400 MHz, CDCl₃):

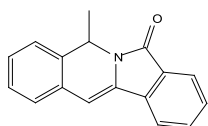
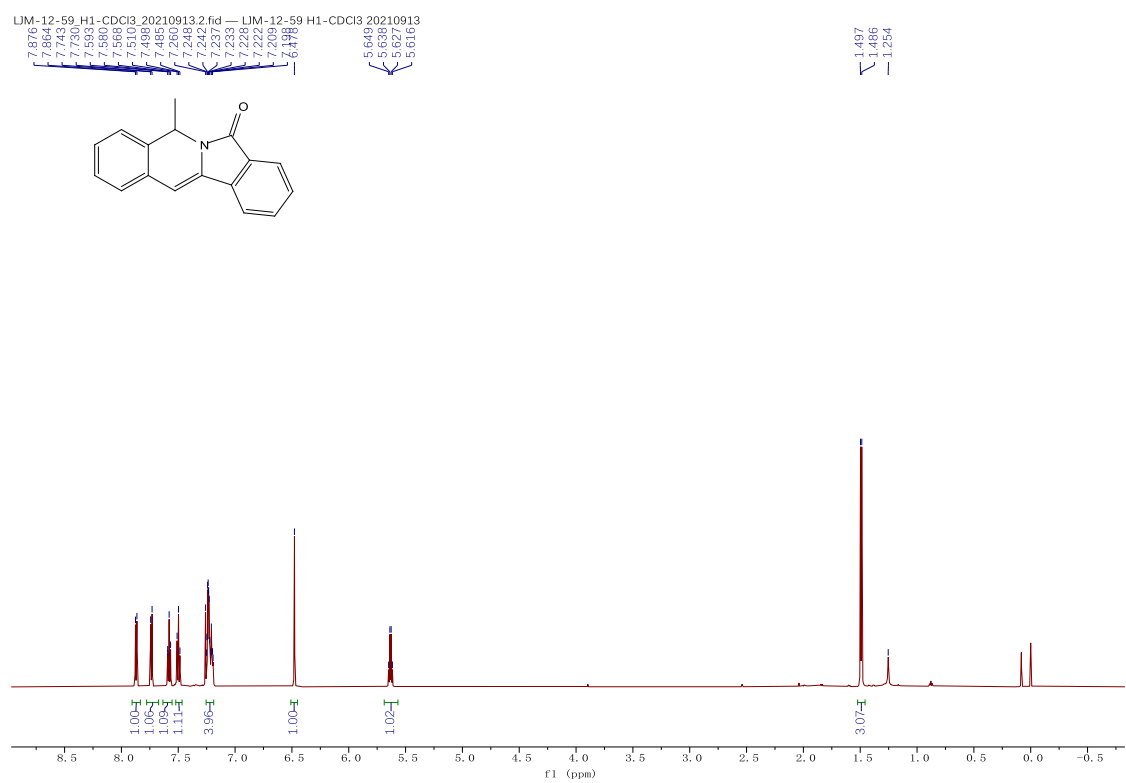
LJM-9-72-CDCl3-3-15 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



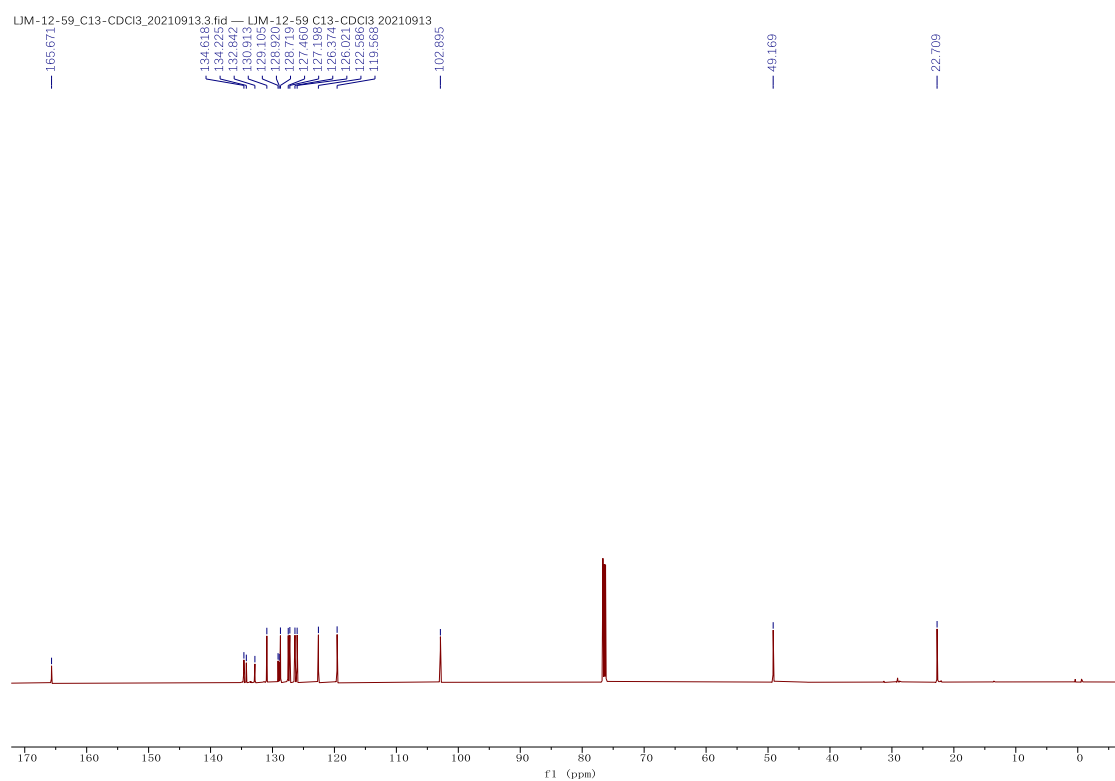
¹³C NMR spectrum of compound 3an (150 MHz, CDCl₃):



¹H NMR spectrum of compound 3ap (400 MHz, CDCl₃):

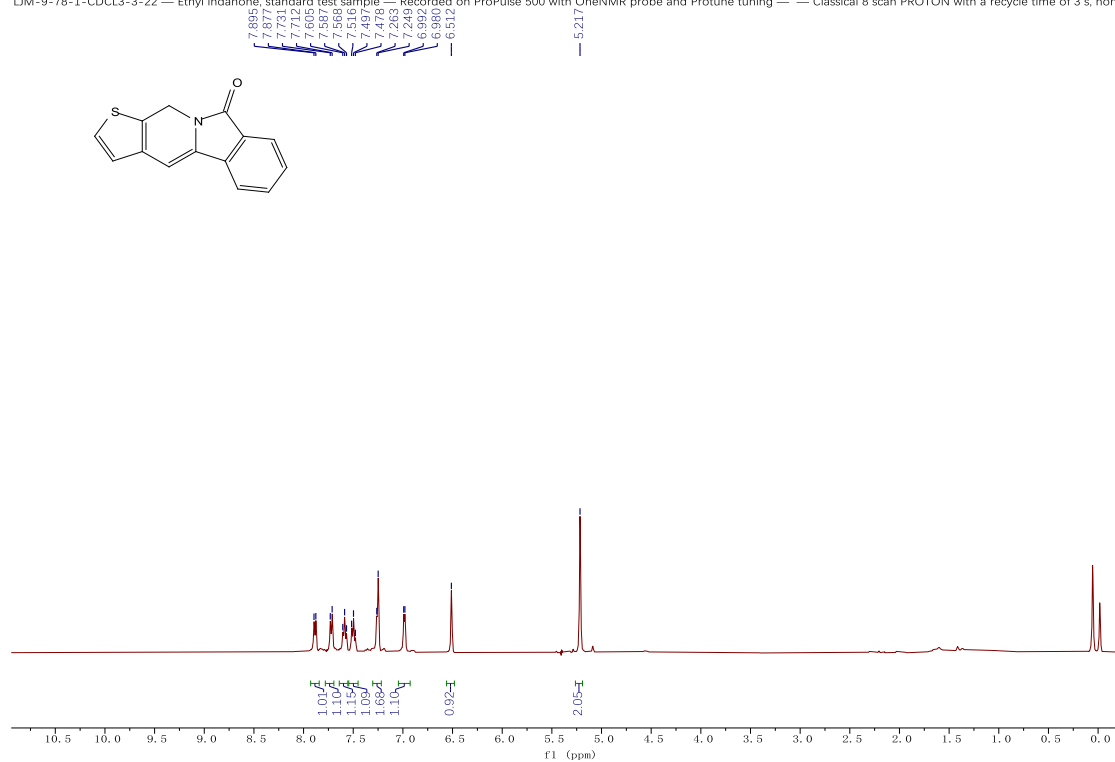


¹³C NMR spectrum of compound 3aq (150 MHz, CDCl₃):

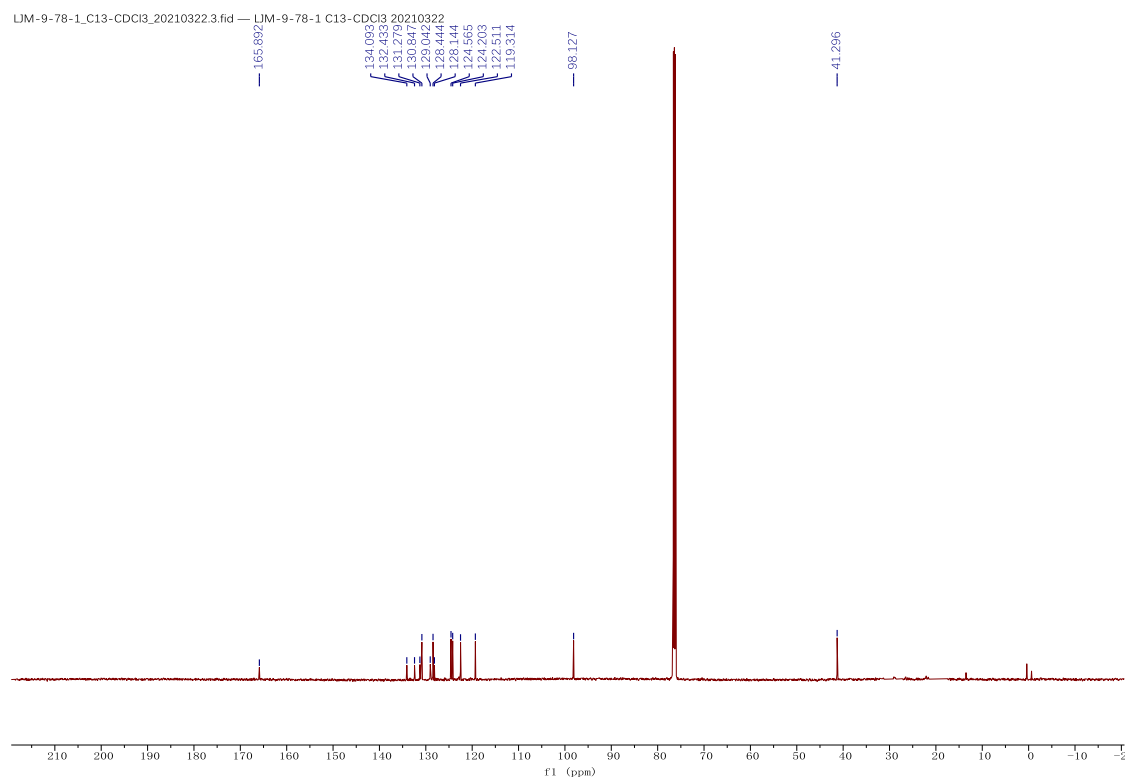


¹H NMR spectrum of compound 3aq (400 MHz, CDCl₃):

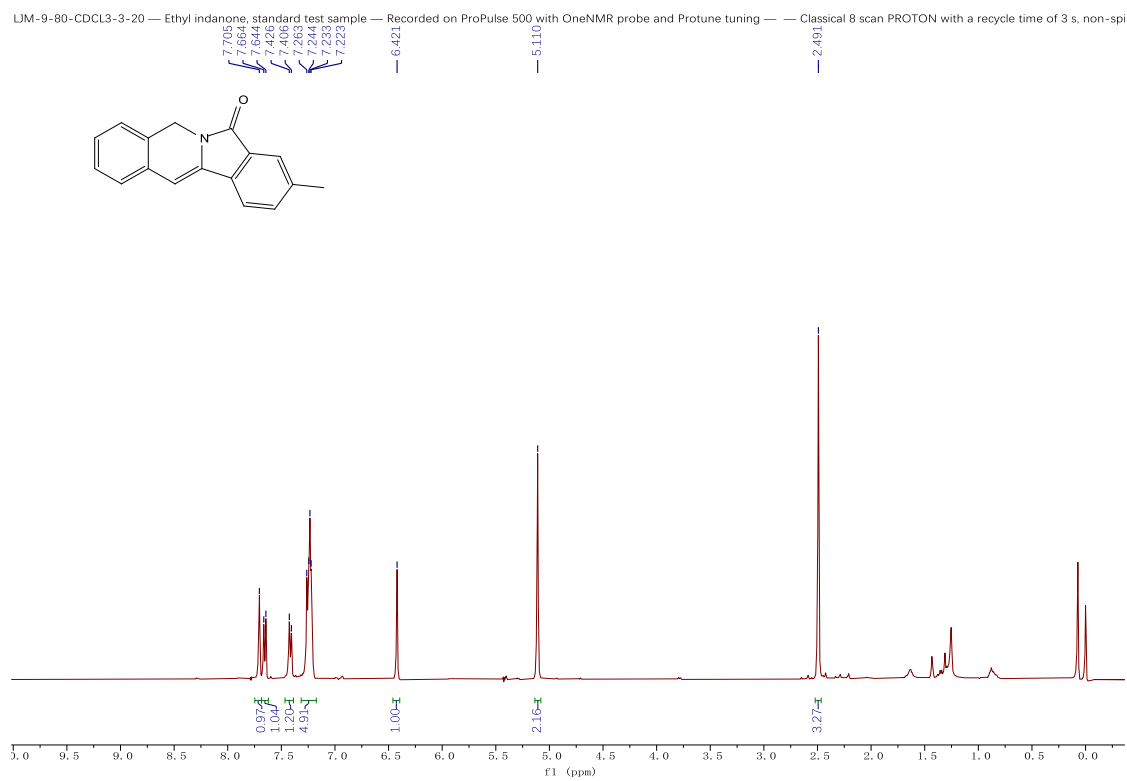
LJM-9-78-1-CDCl3-3-22 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-



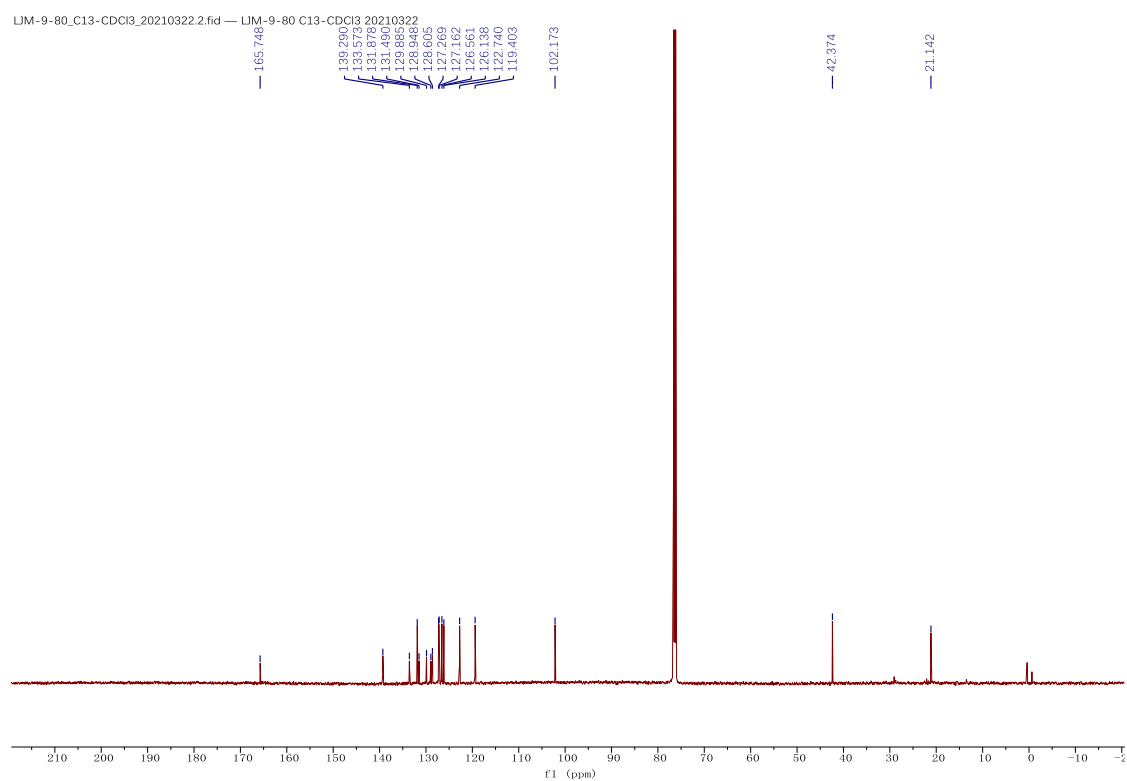
¹³C NMR spectrum of compound 3aq (150 MHz, CDCl₃):



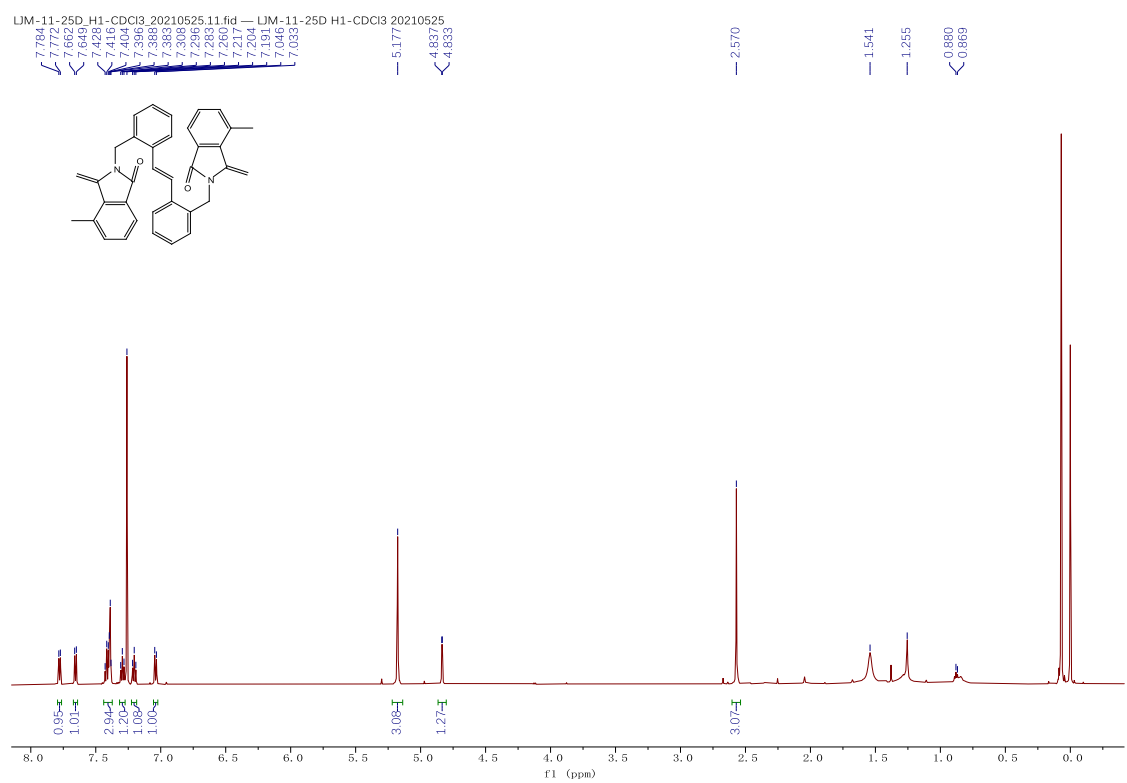
¹H NMR spectrum of compound 3ba (400 MHz, CDCl₃):



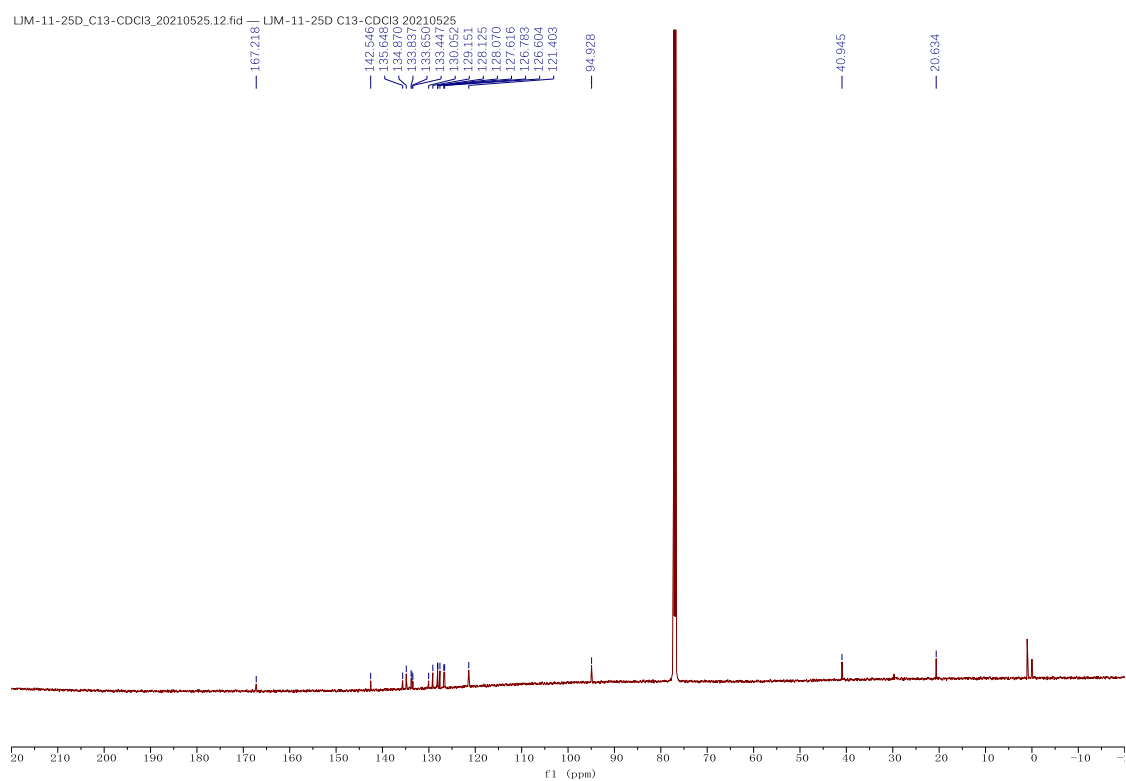
¹³C NMR spectrum of compound 3ba (150 MHz, CDCl₃):



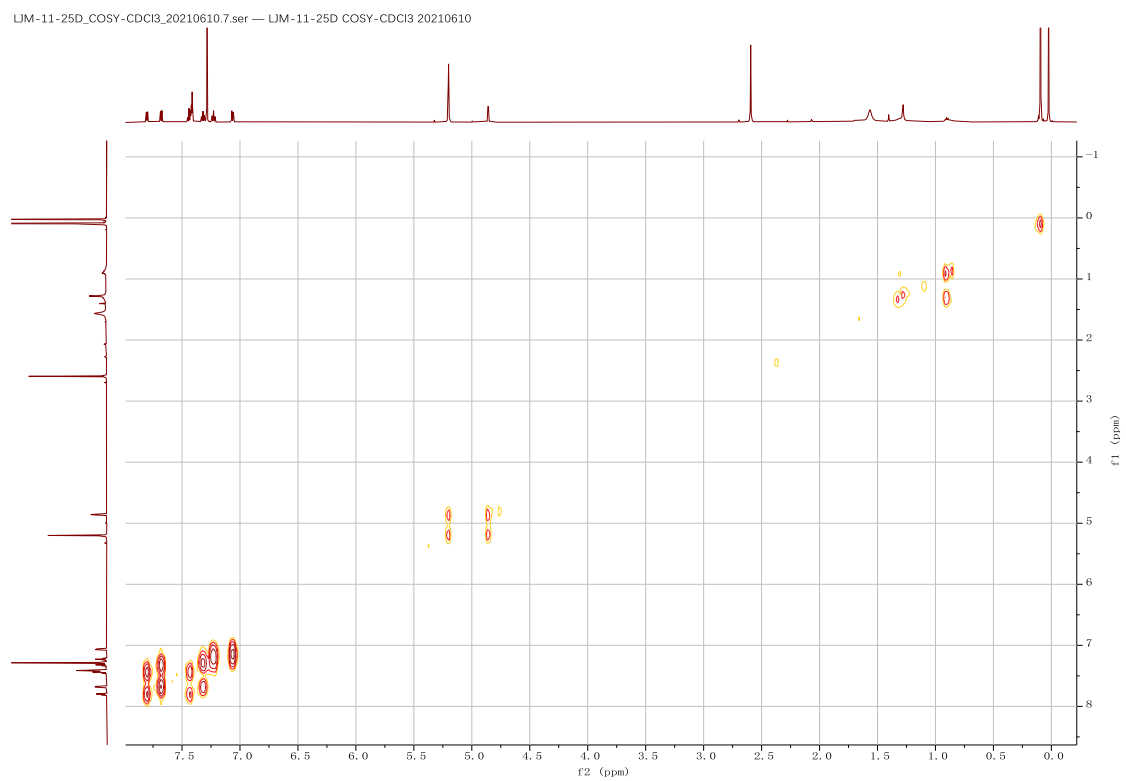
¹H NMR spectrum of compound 3ca' (400 MHz, CDCl₃):



¹³C NMR spectrum of compound 3ca' (150 MHz, CDCl₃):

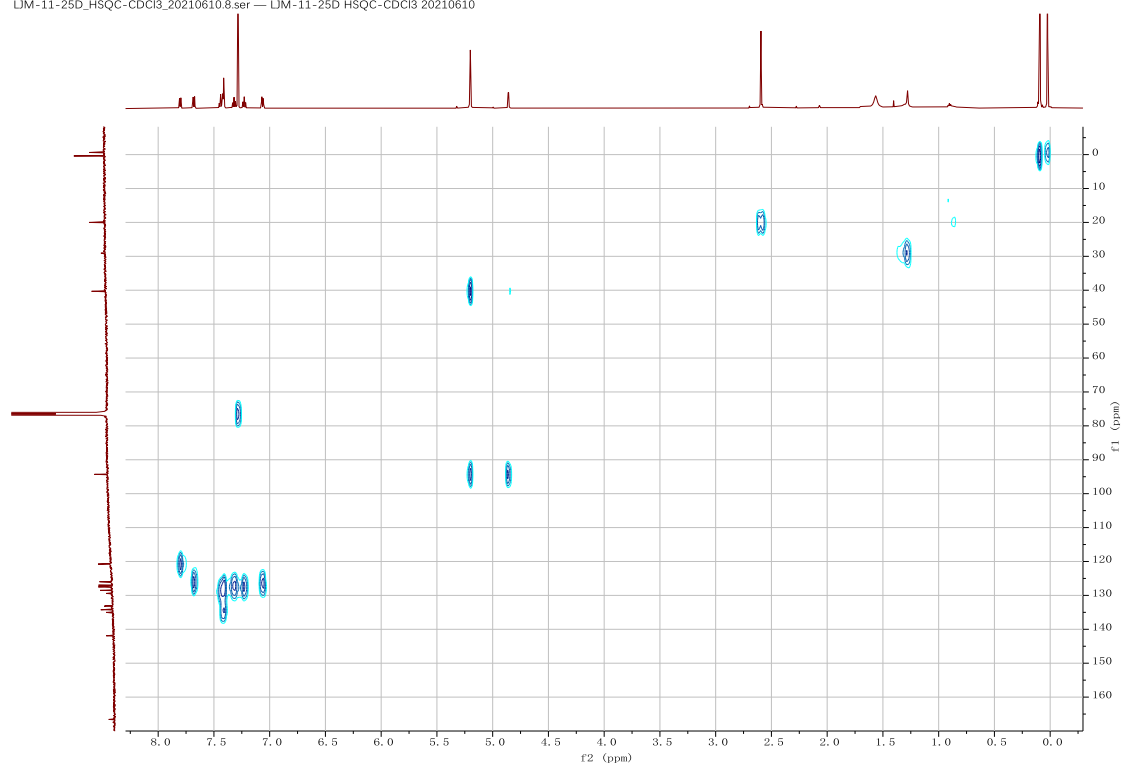


¹H-¹H COSY NMR spectrum of compound 3ca' (600 MHz, CDCl₃):



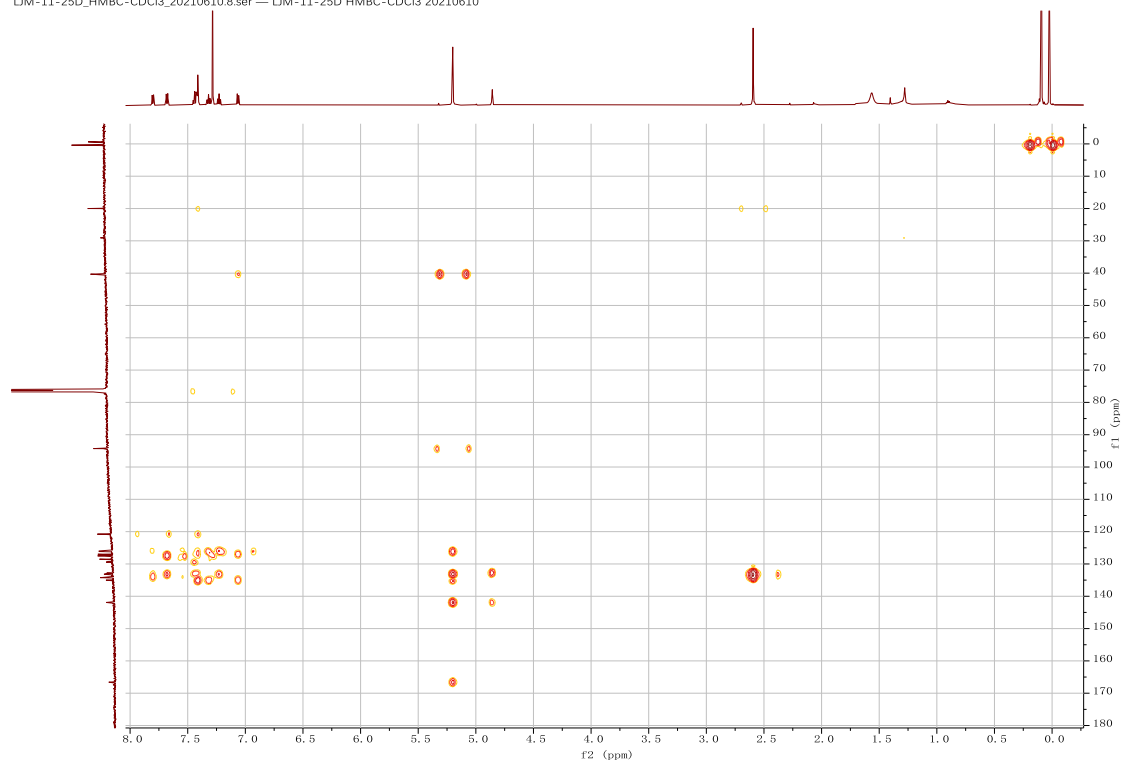
HSQC NMR spectrum of compound 3ca' (600 MHz, CDCl₃):

LJM-11-25D_HSQC-CDCl3_20210610.8.ser — LJM-11-25D HSQC-CDCl3 20210610



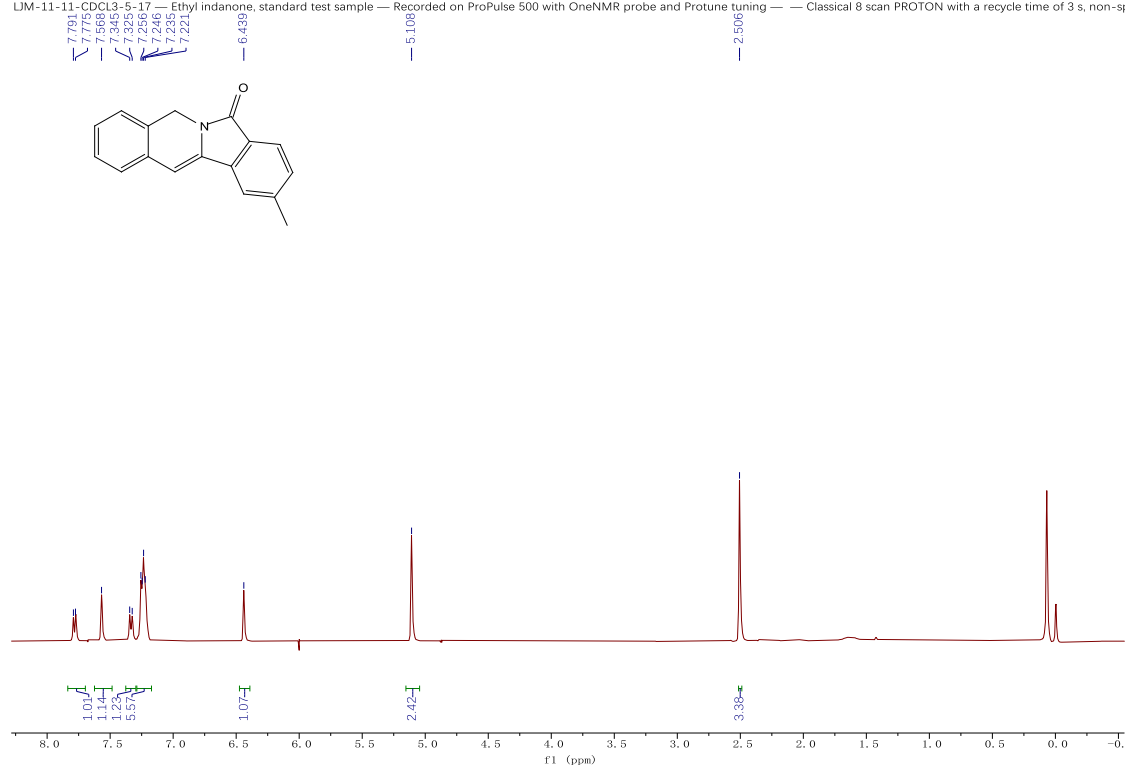
HMBC NMR spectrum of compound 3ca' (600 MHz, CDCl₃):

LJM-11-25D_HMBC-CDCl3_20210610.8.ser — LJM-11-25D HMBC-CDCl3 20210610



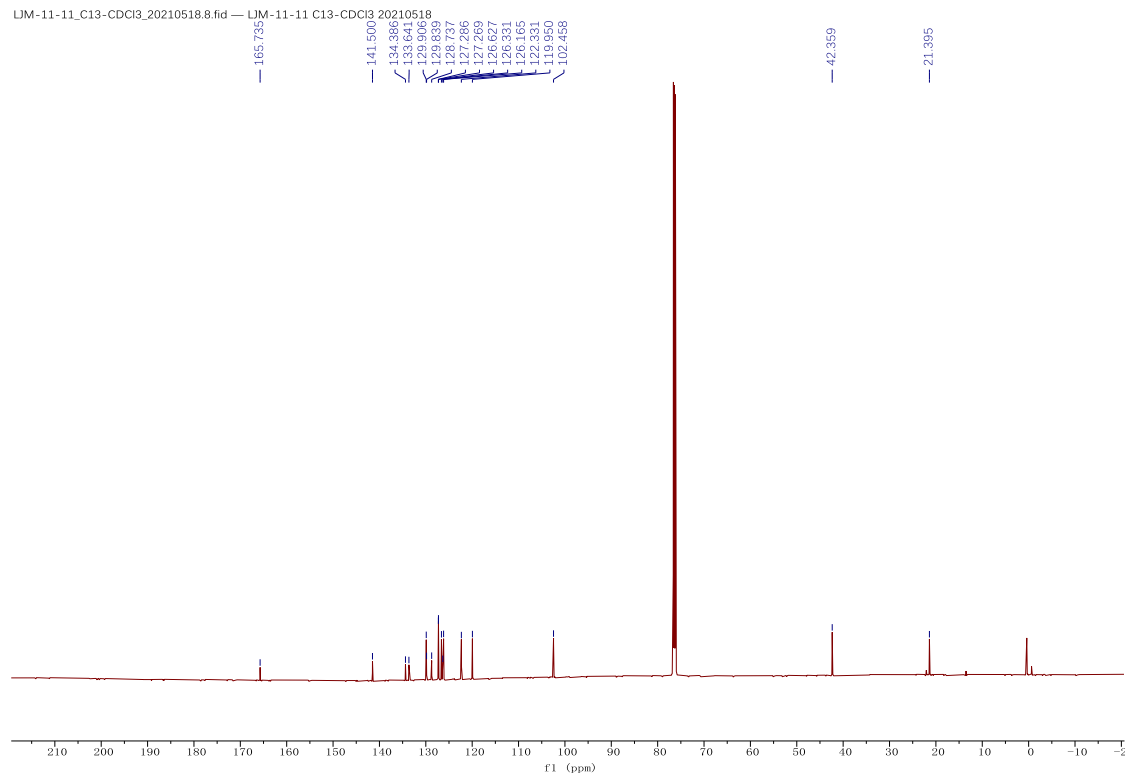
¹H NMR spectrum of compound 3da (400 MHz, CDCl₃):

LJM-11-11-CDCl3-5-17 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



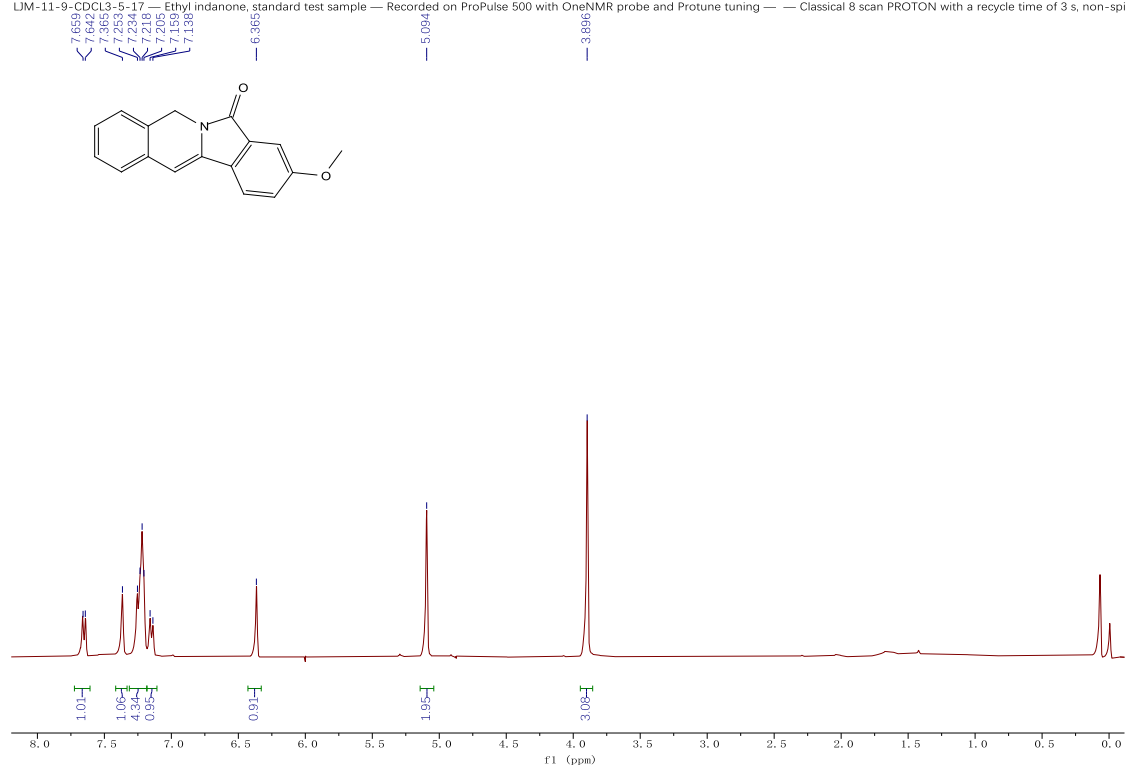
¹³C NMR spectrum of compound 3da (150 MHz, CDCl₃):

LJM-11-11-C13-CDCl3_20210518.8.fid — LJM-11-11 C13-CDCl3 20210518



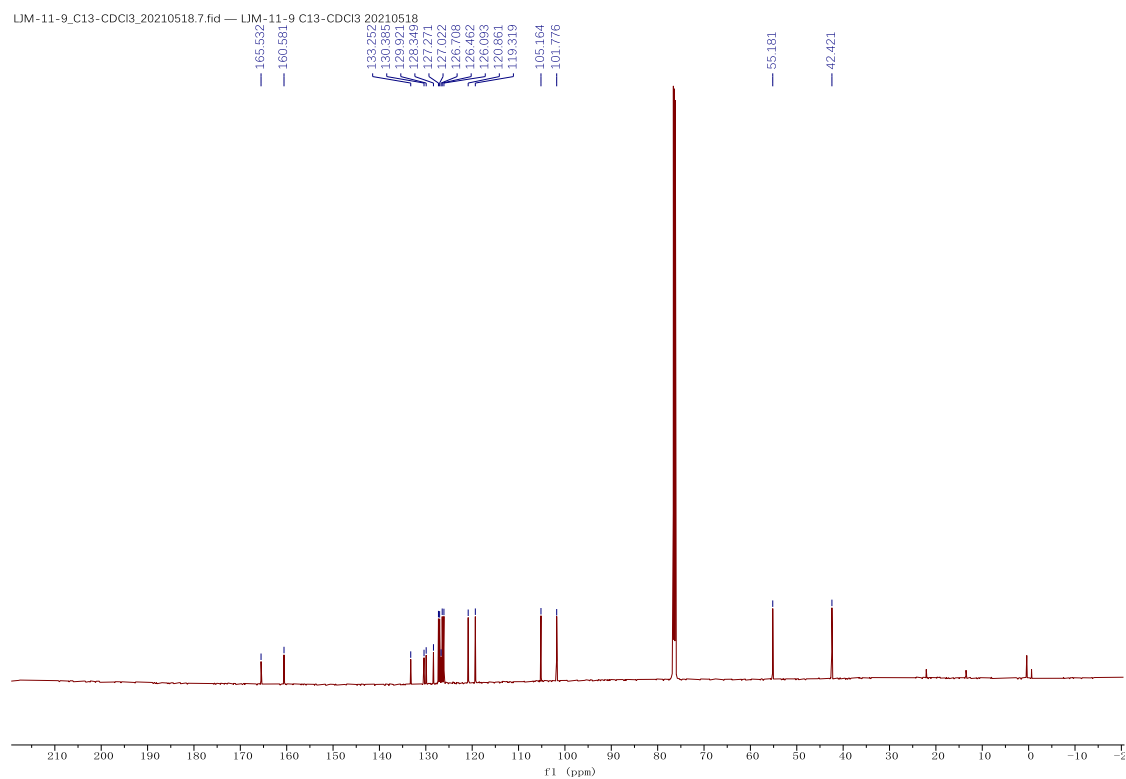
¹H NMR spectrum of compound 3ea (400 MHz, CDCl₃):

LJM-11-9-CDCl3-5-17 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



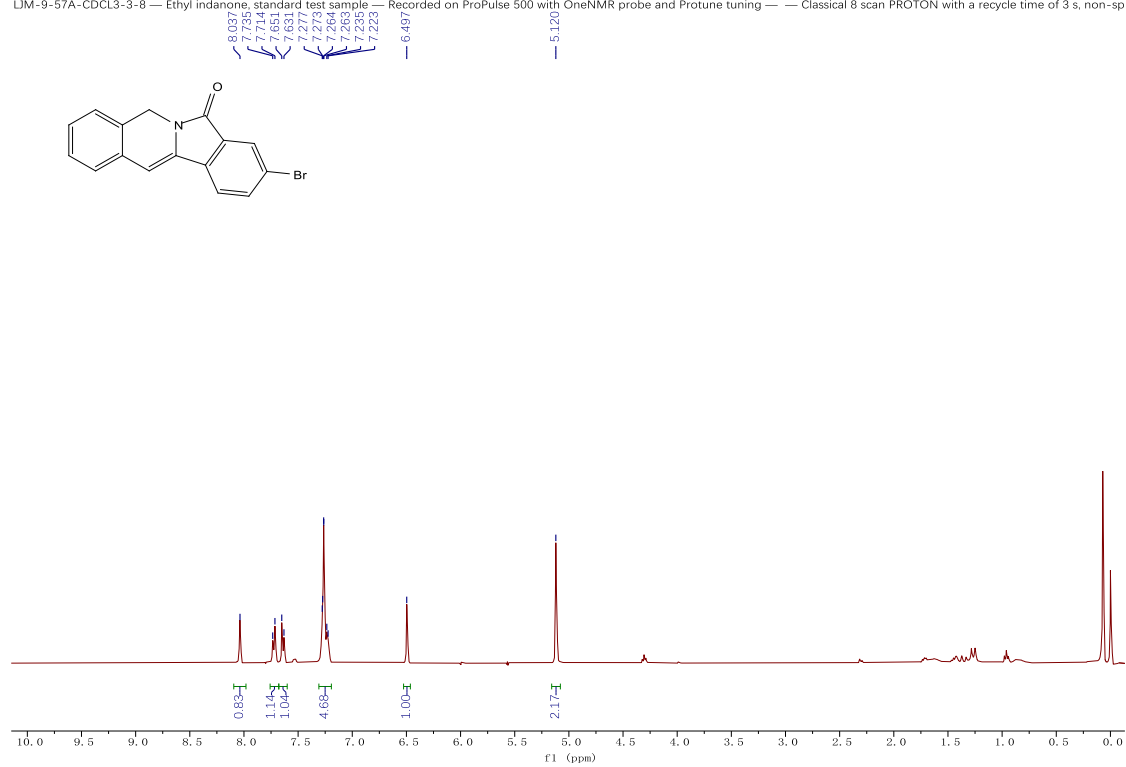
¹³C NMR spectrum of compound 3ea (150 MHz, CDCl₃):

LJM-11-9-C13-CDCl3_20210518.7.fid — LJM-11-9 C13-CDCl3 20210518



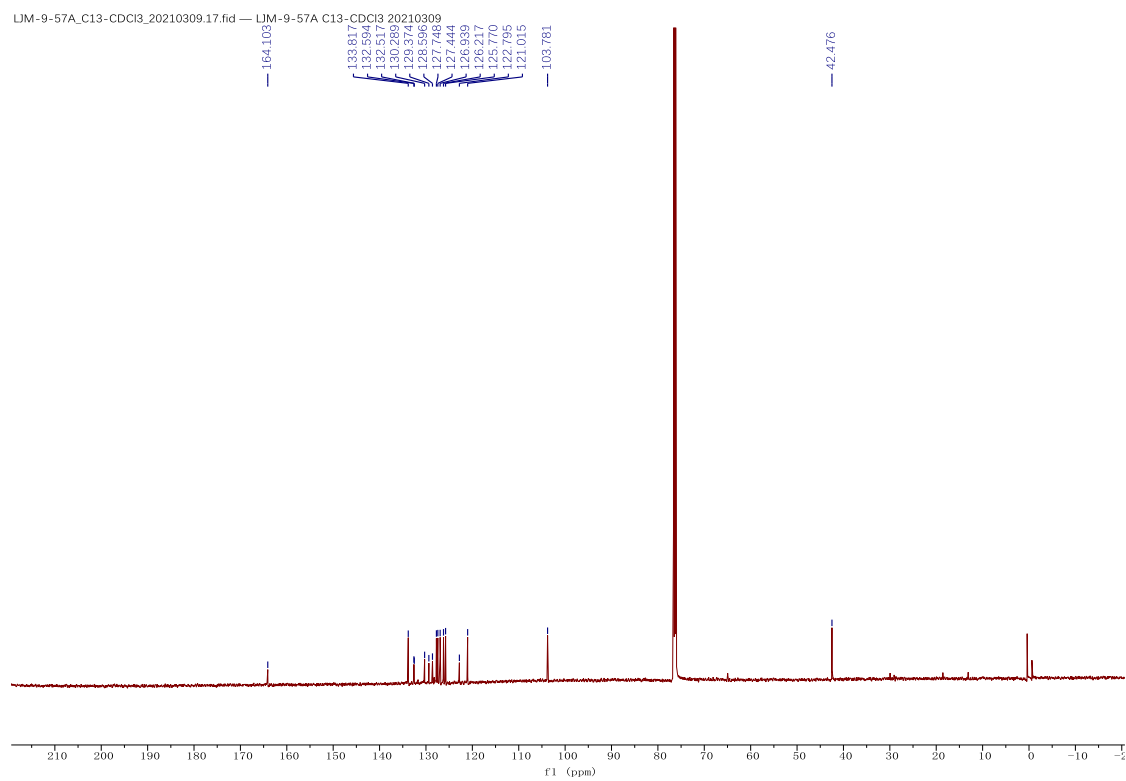
¹H NMR spectrum of compound 3fa (400 MHz, CDCl₃):

LJM-9-57A-CDCl₃-3-8 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sp



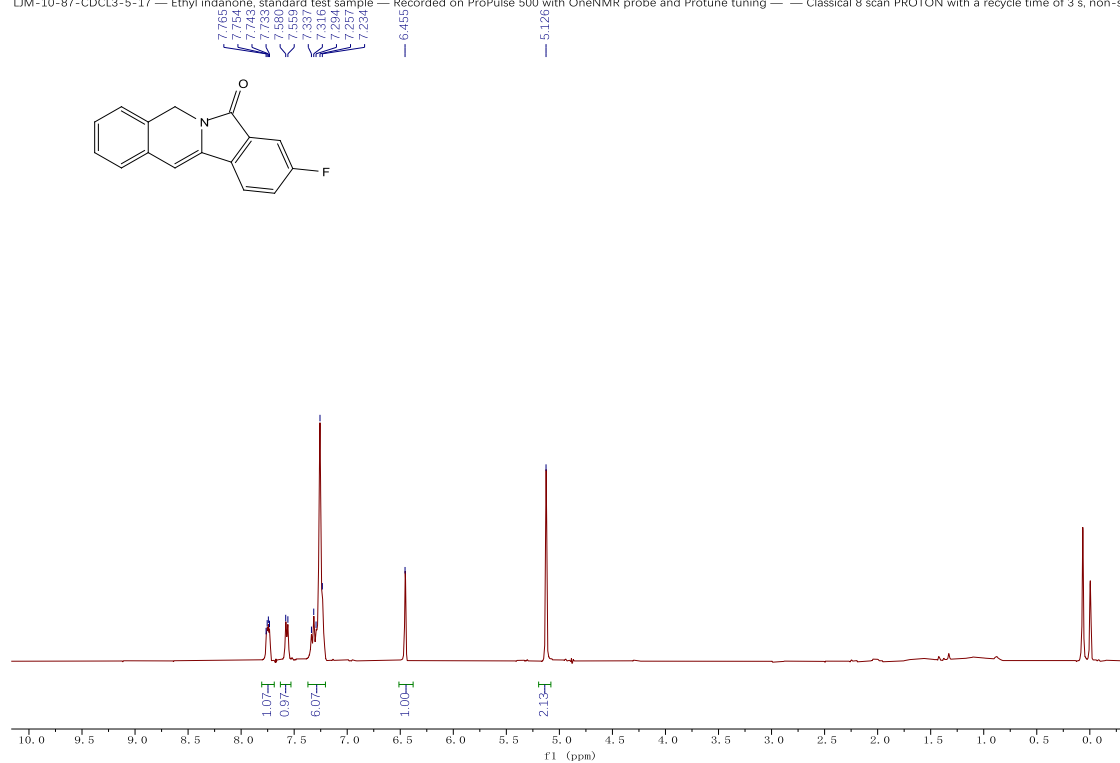
¹³C NMR spectrum of compound 3fa (150 MHz, CDCl₃):

LJM-9-57A_C13-CDCl3_20210309.17.tif — LJM-9-57A C13-CDCl3 20210309



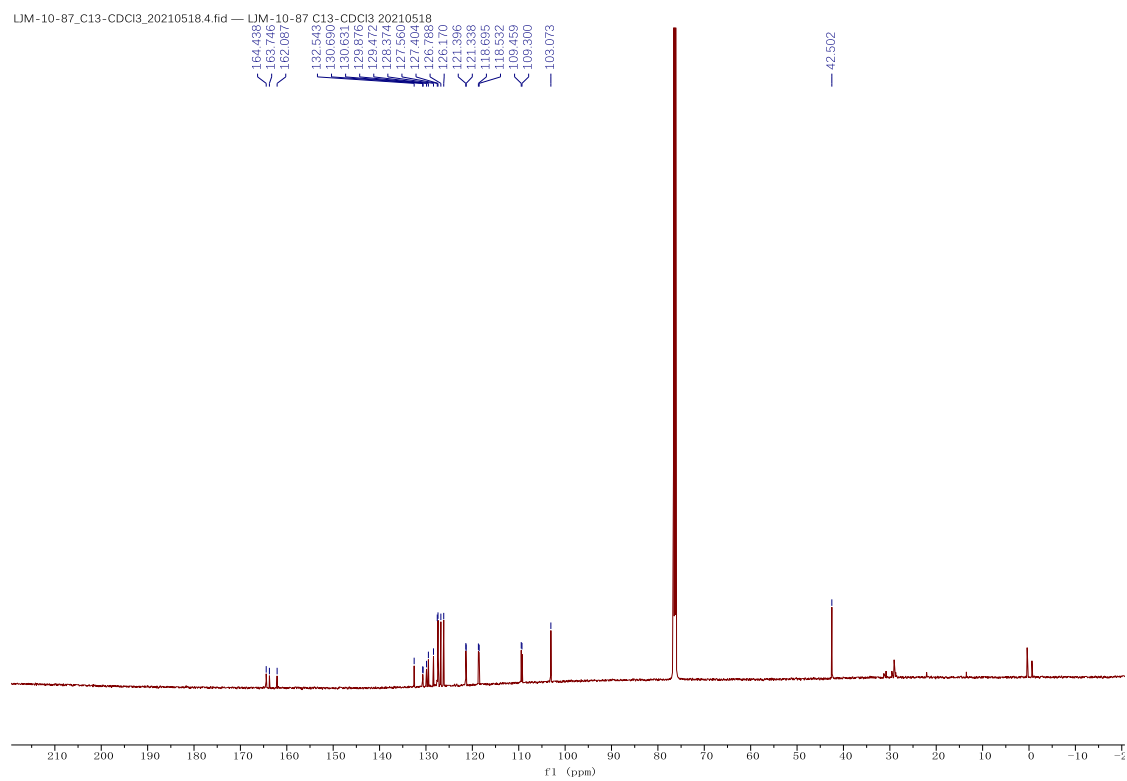
¹H NMR spectrum of compound 3ga (400 MHz, CDCl₃):

LJM-10-87-CDCl3-5-17 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



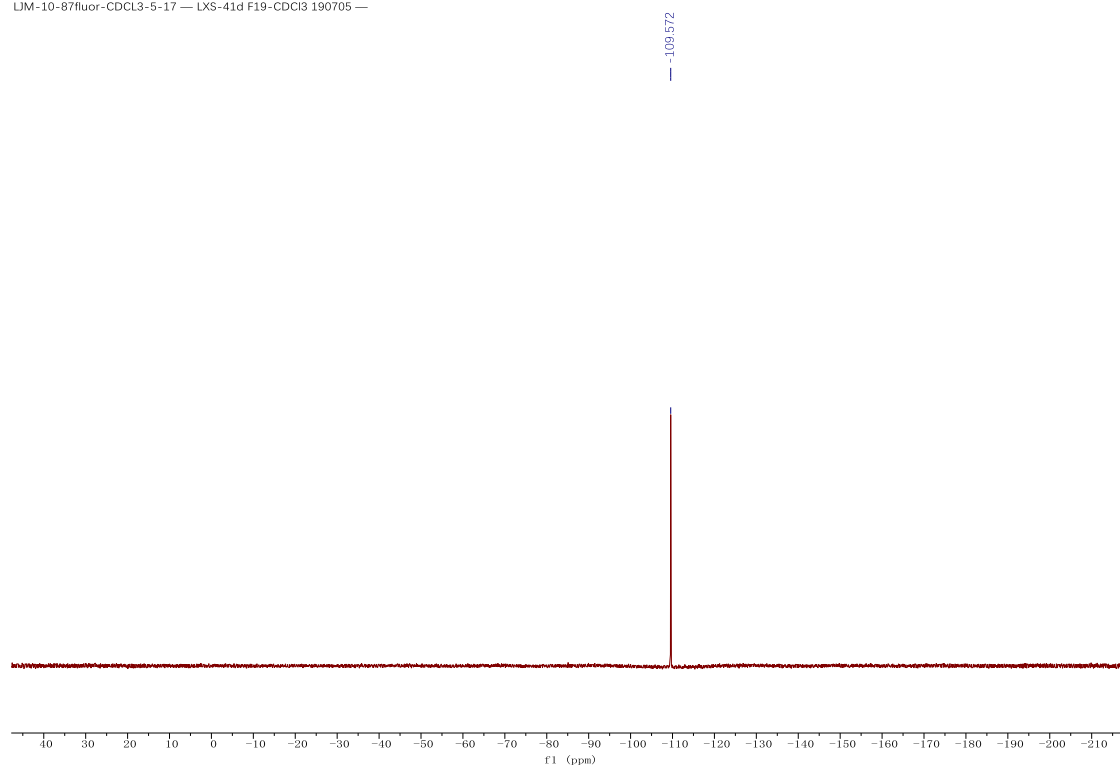
¹³C NMR spectrum of compound 3ga (150 MHz, CDCl₃):

LJM-10-87_C13-CDCl3_20210518.4.fid — LJM-10-87 C13-CDCl3 20210518



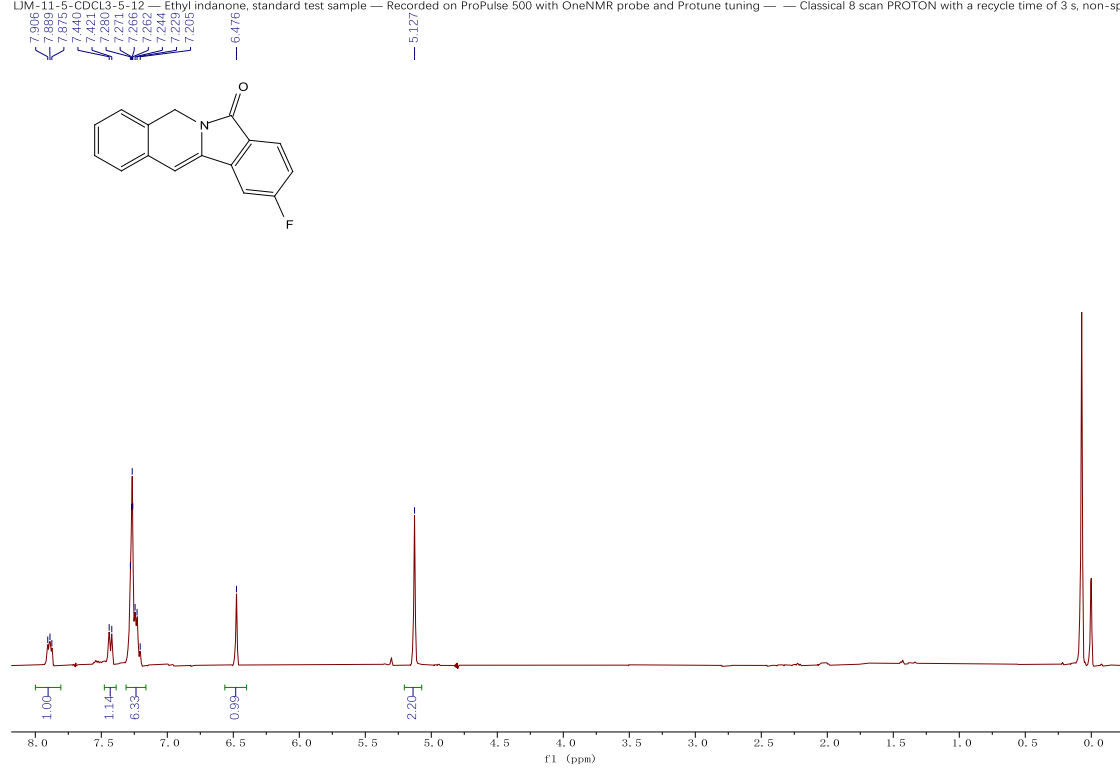
¹⁹F NMR spectrum of compound 3ga (376 MHz, CDCl₃):

LJM-10-87fluor-CDCl3-5-17 — LXS-41d F19-CDCl3 190705 —

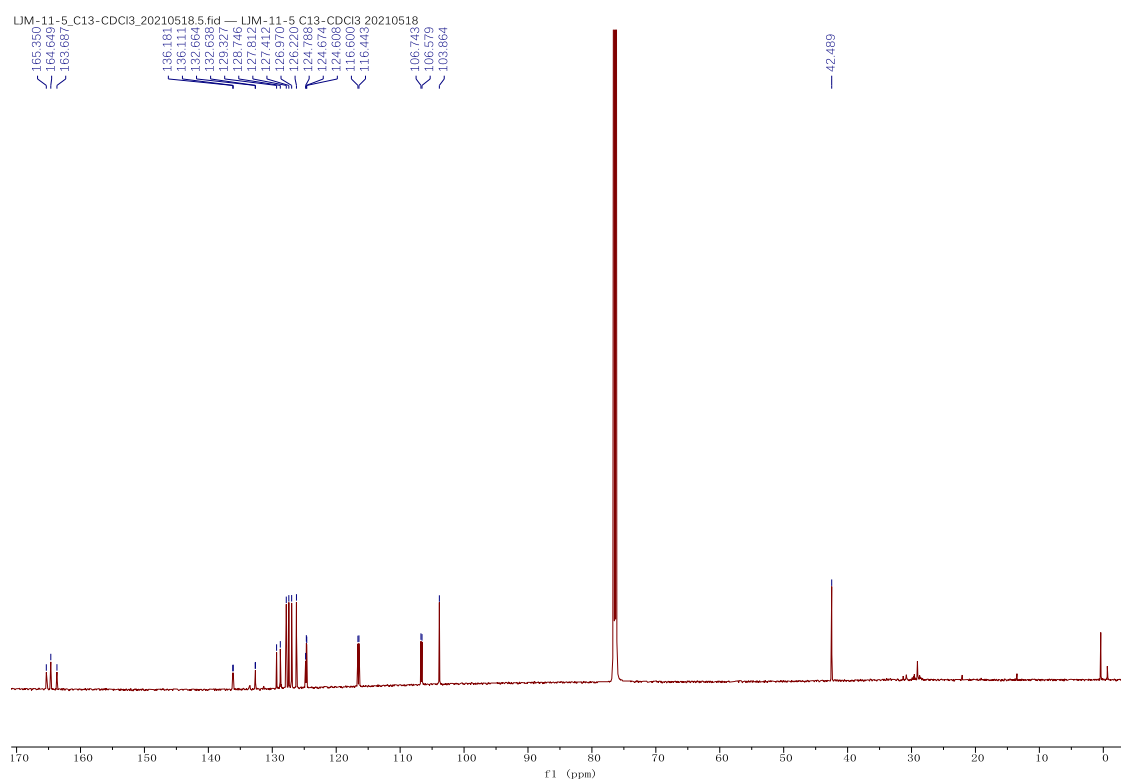


¹H NMR spectrum of compound 3ha (400 MHz, CDCl₃):

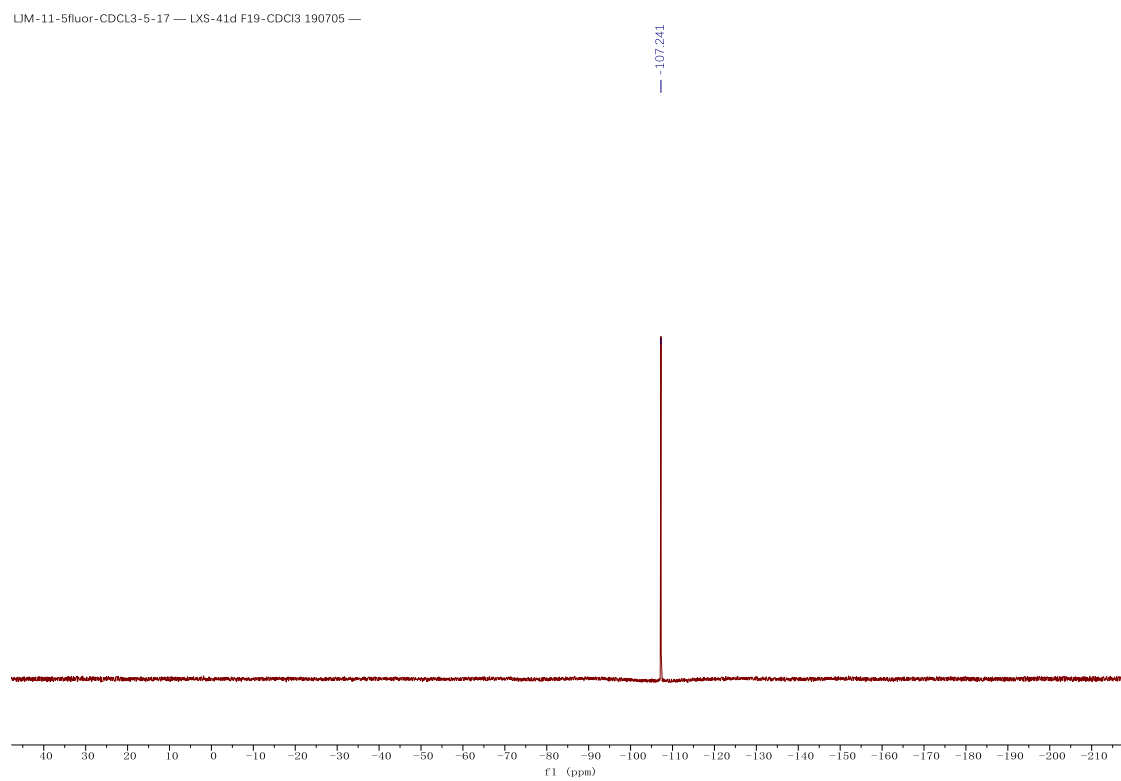
LJM-11-5-CDCl3-5-12 Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



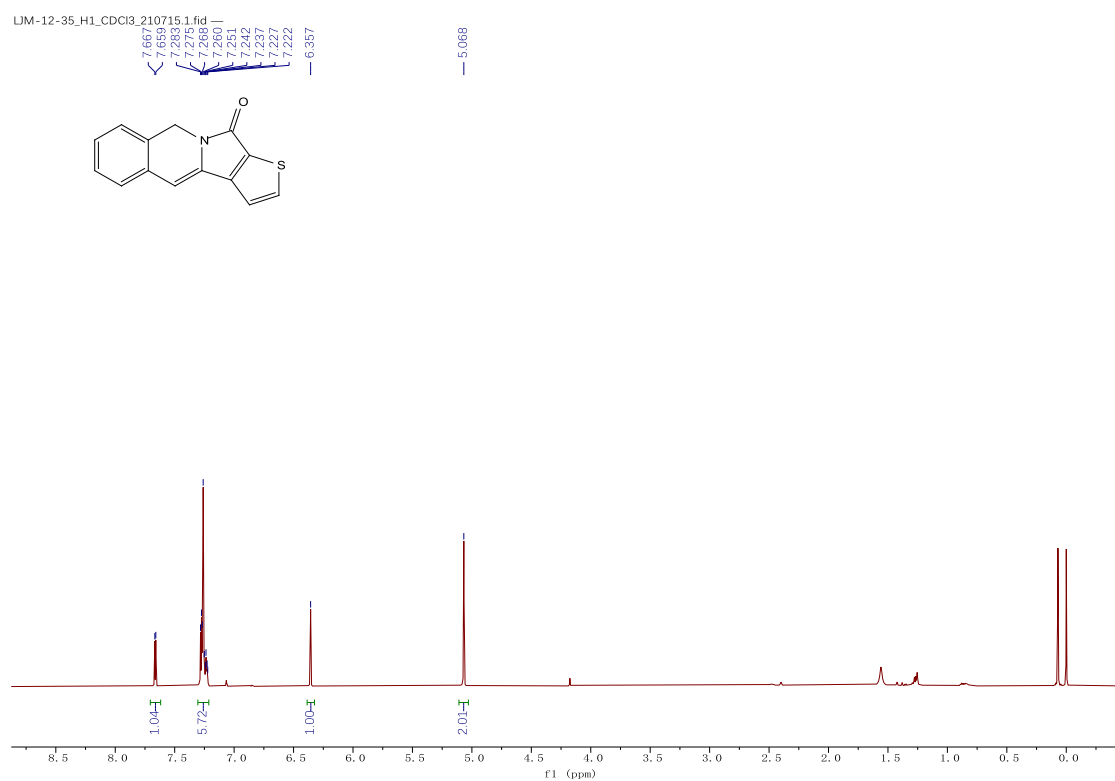
¹³C NMR spectrum of compound 3ha (150 MHz, CDCl₃):



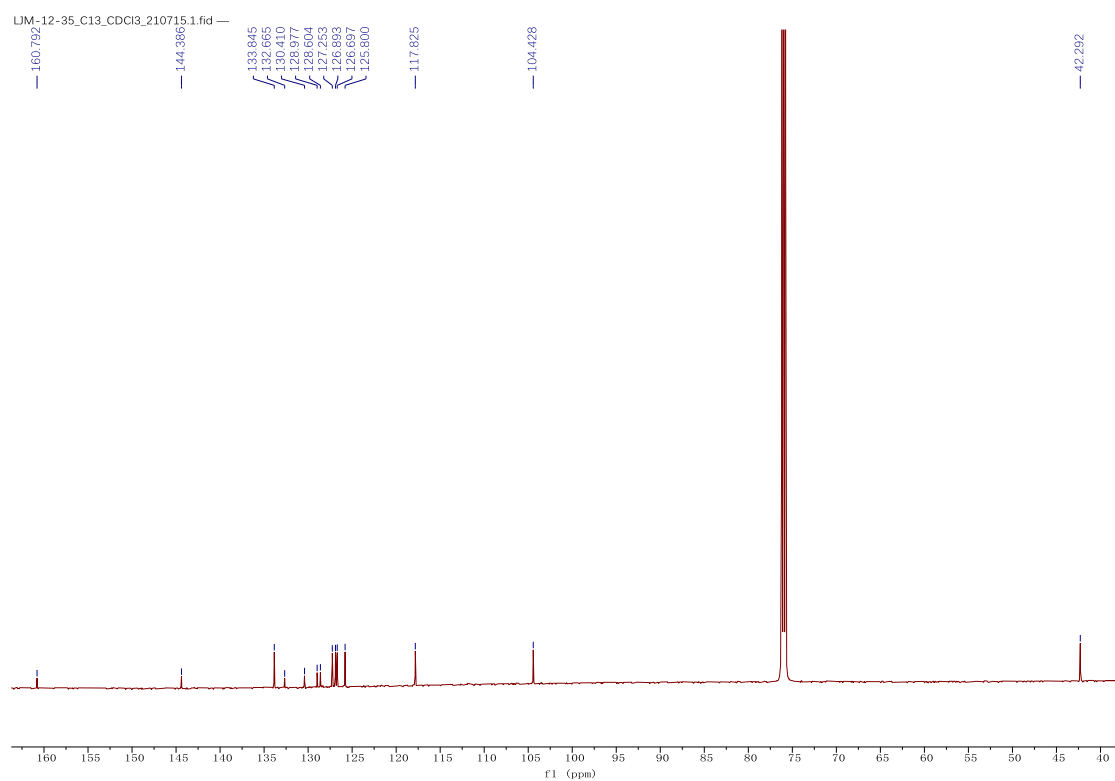
¹⁹F NMR spectrum of compound 3ha (376 MHz, CDCl₃):



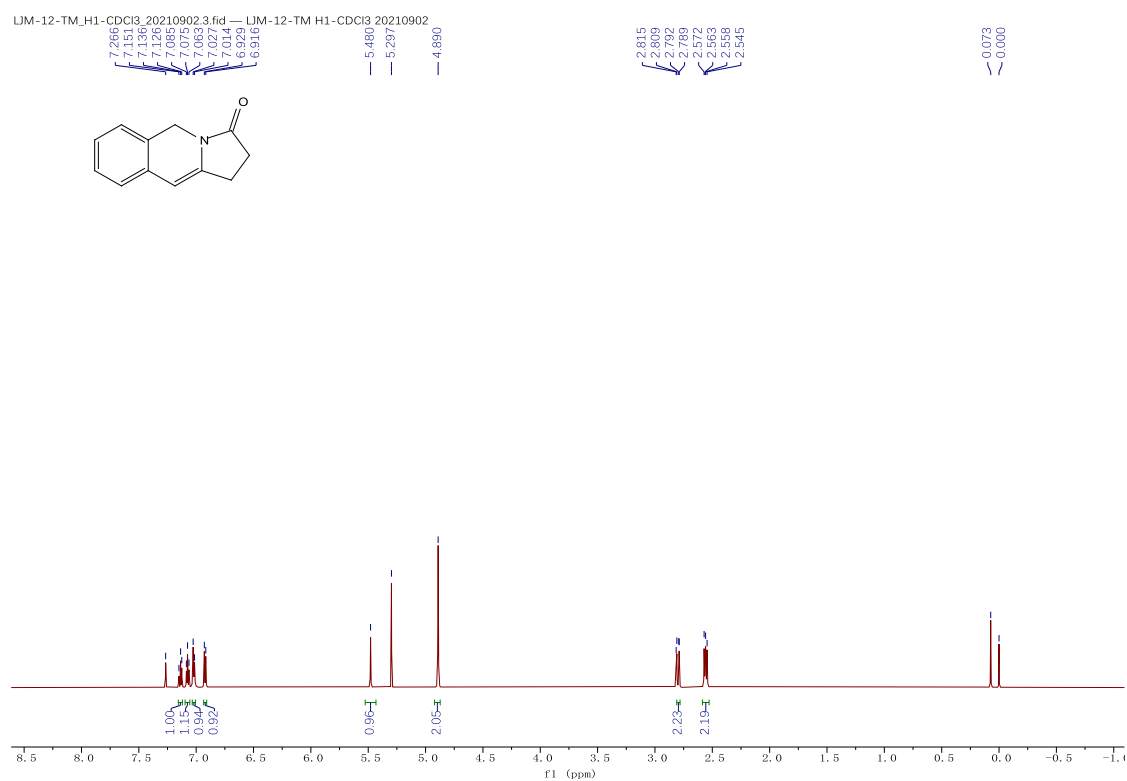
¹H NMR spectrum of compound 3ia (400 MHz, CDCl₃):



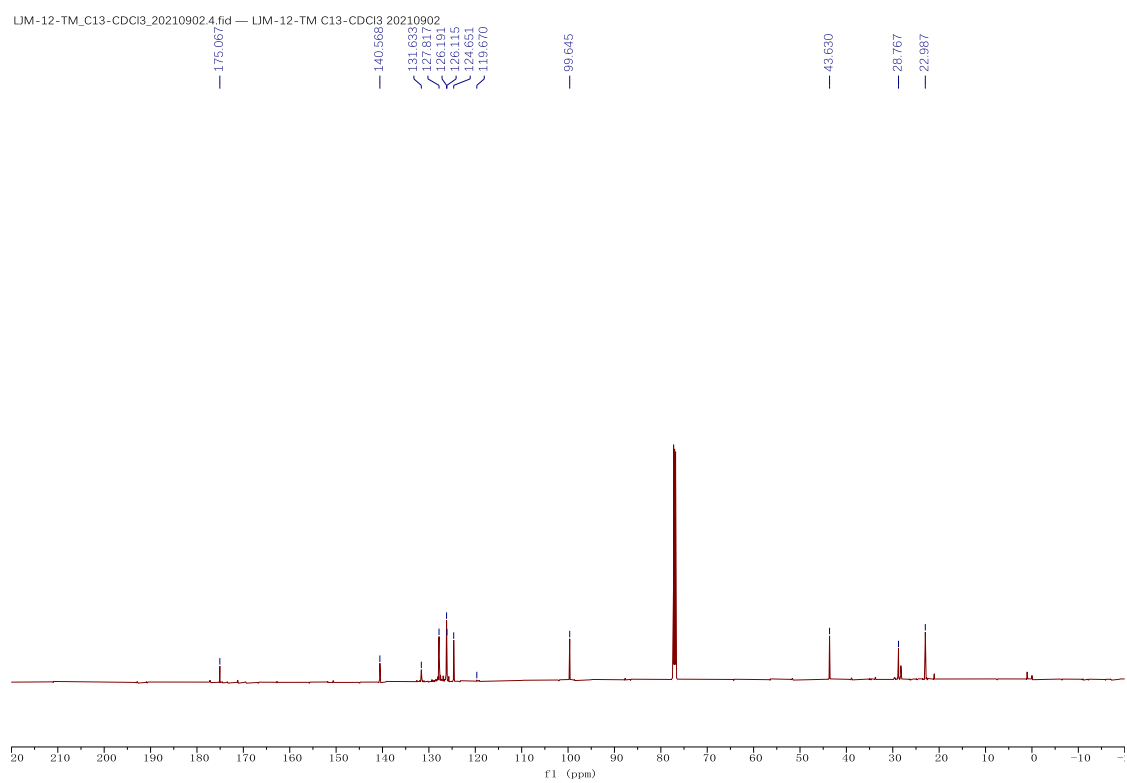
¹³C NMR spectrum of compound 3ia (150 MHz, CDCl₃):



¹H NMR spectrum of compound 3ja (400 MHz, CDCl₃):

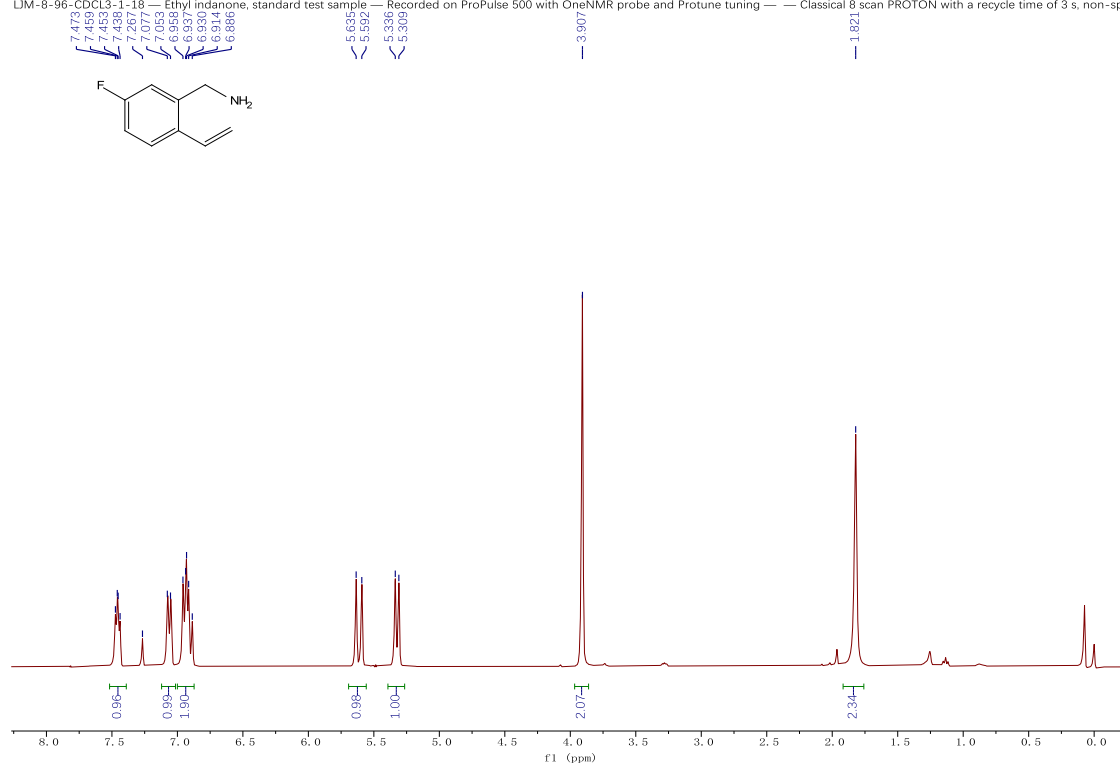


¹³C NMR spectrum of compound 3ja (150 MHz, CDCl₃):



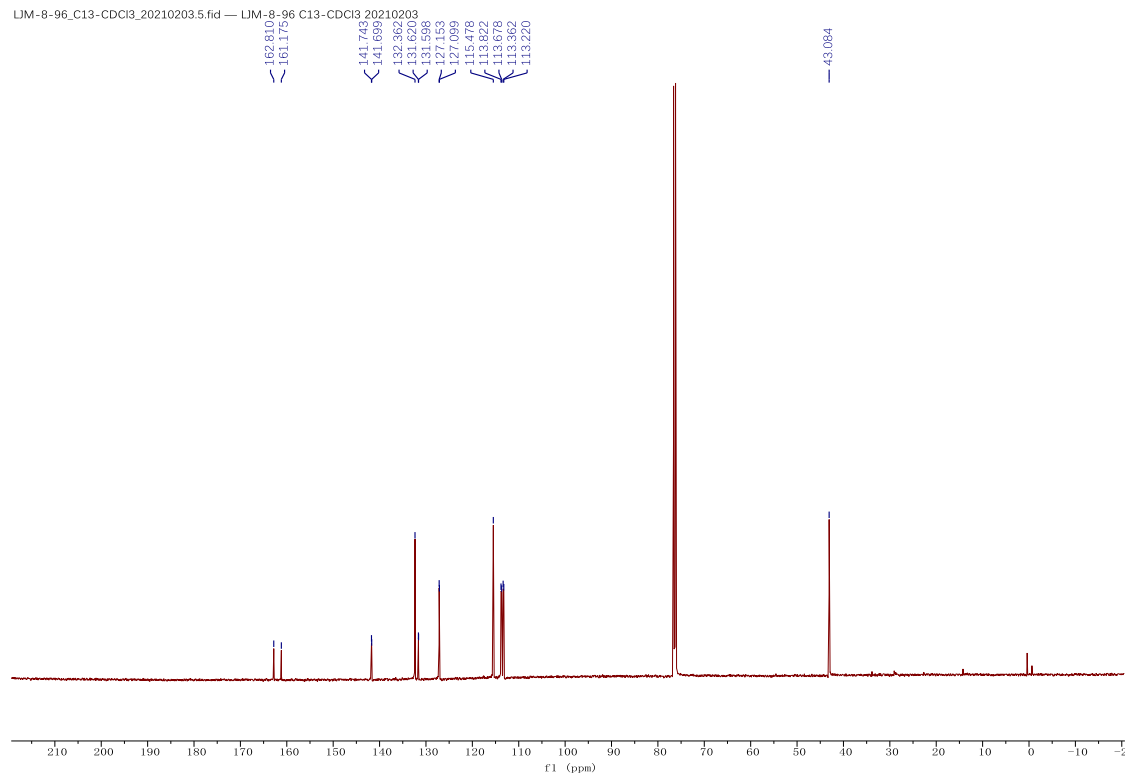
¹H NMR spectrum of compound 2b (400 MHz, CDCl₃):

LJM-8-96-CDCl3-1-18 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



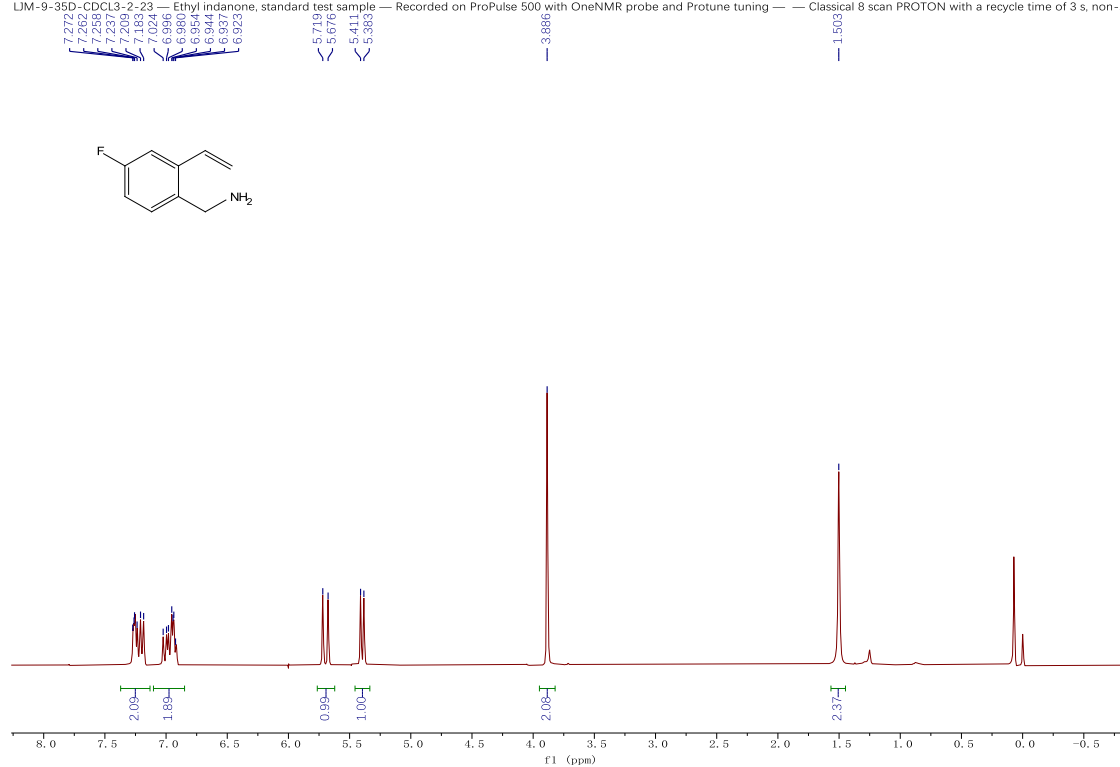
¹³C NMR spectrum of compound 2b (150 MHz, CDCl₃):

LJM-8-96_C13-CDCl3_20210203.5.fid — LJM-8-96 C13-CDCl3 20210203



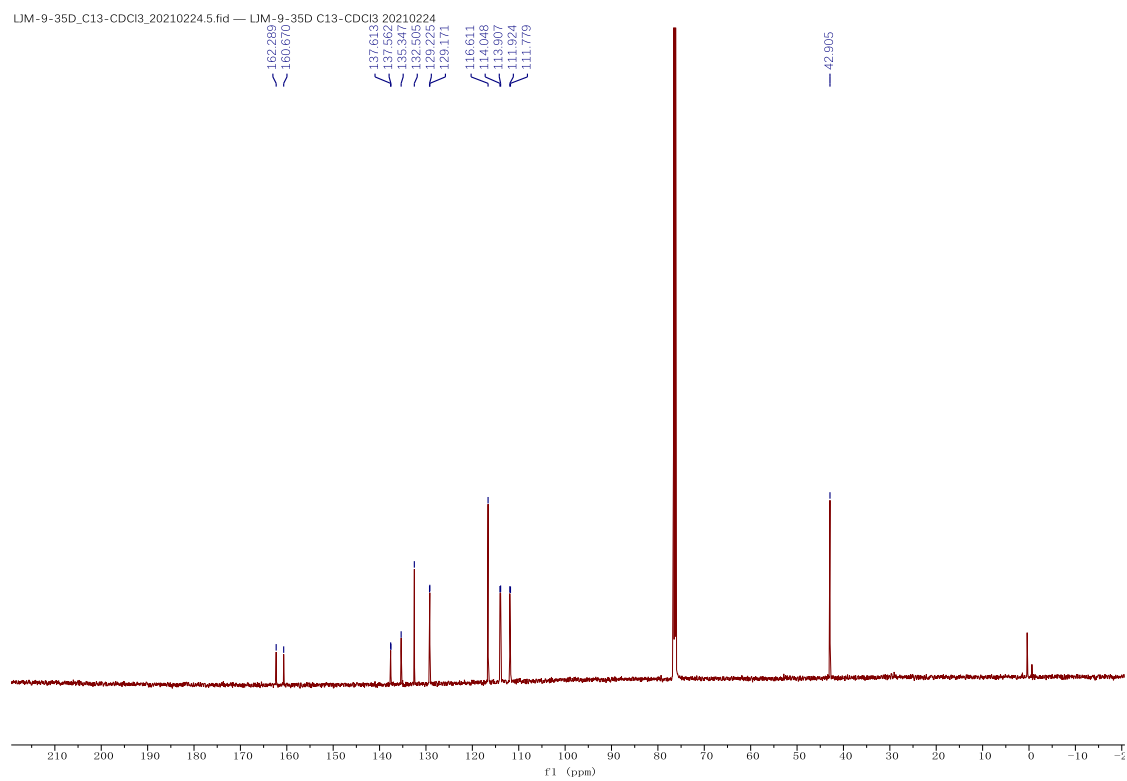
¹H NMR spectrum of compound 2c (400 MHz, CDCl₃):

LJM-9-35D-CDCl3-2-23 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-s



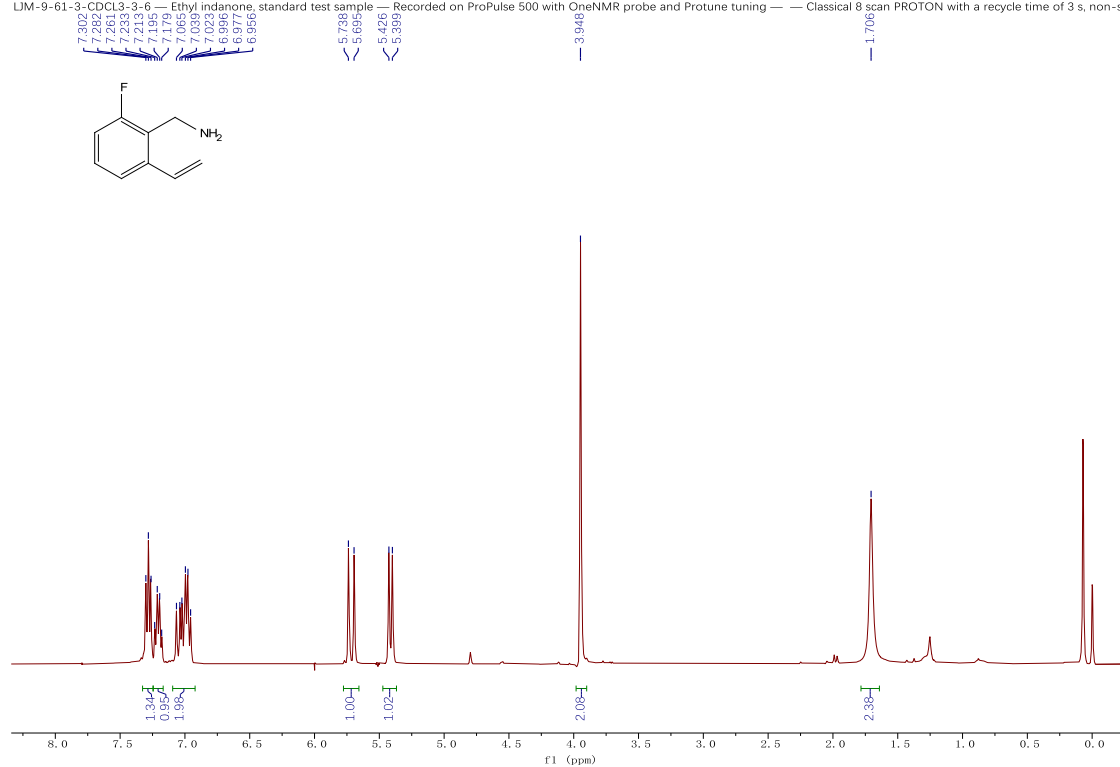
¹³C NMR spectrum of compound 2c (150 MHz, CDCl₃):

LJM-9-35D_C13-CDCl3_20210224.5.fid — LJM-9-35D C13-CDCl3 20210224



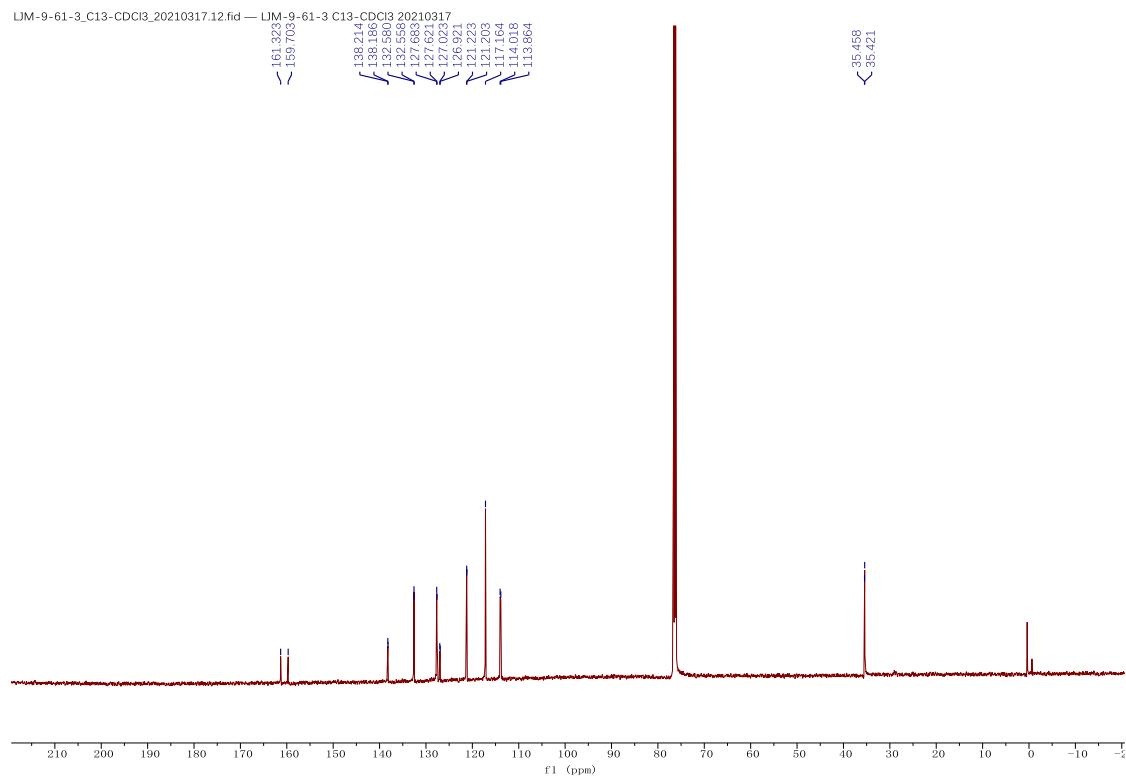
¹H NMR spectrum of compound 2d (400 MHz, CDCl₃):

LJM-9-61-3-CDCl3-3-6 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



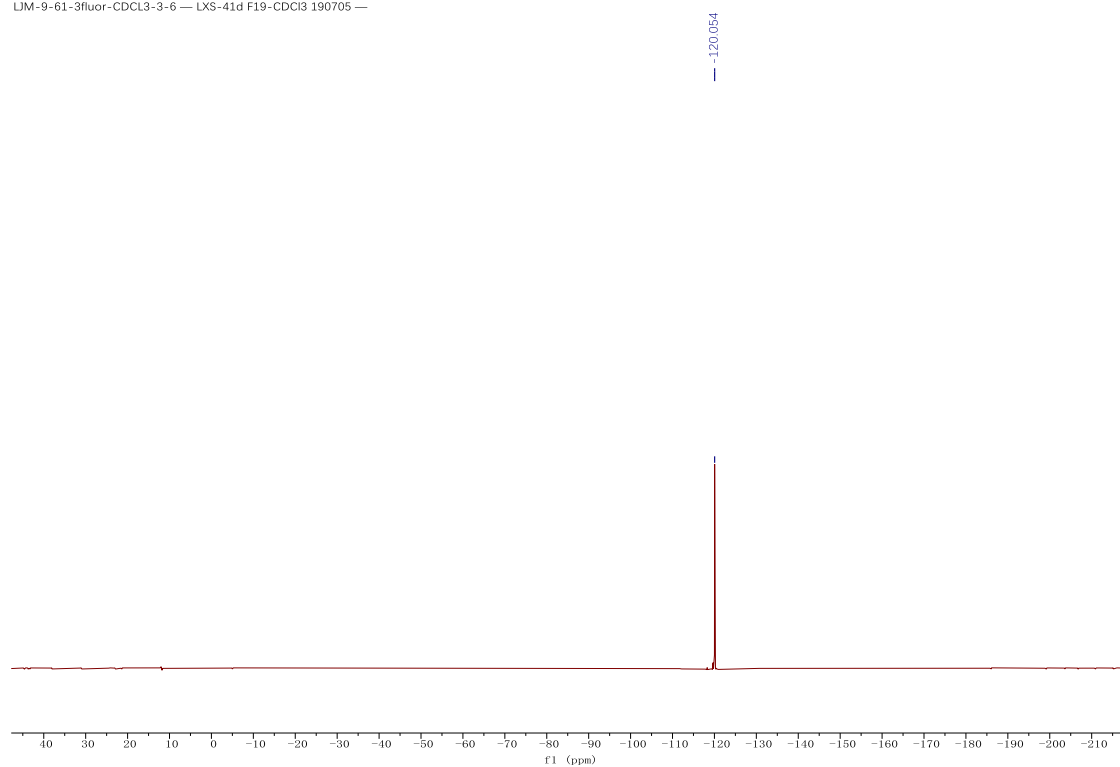
¹³C NMR spectrum of compound 2d (150 MHz, CDCl₃):

LJM-9-61-3_C13-CDCl3_20210317.12.fid — LJM-9-61-3-CDCl3_20210317



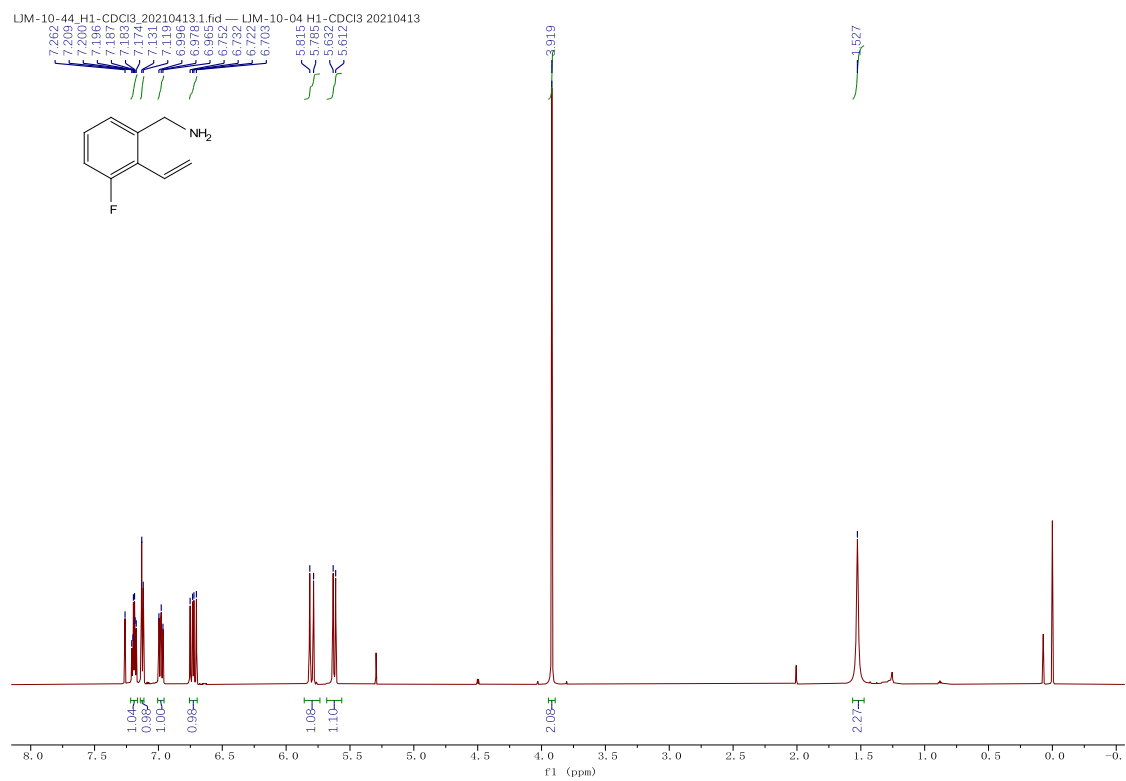
¹⁹F NMR spectrum of compound 2d (376 MHz, CDCl₃):

LJM-9-61-3fluor-CDCl3-3-6 — LXS-41d F19-CDCl3 190705 —

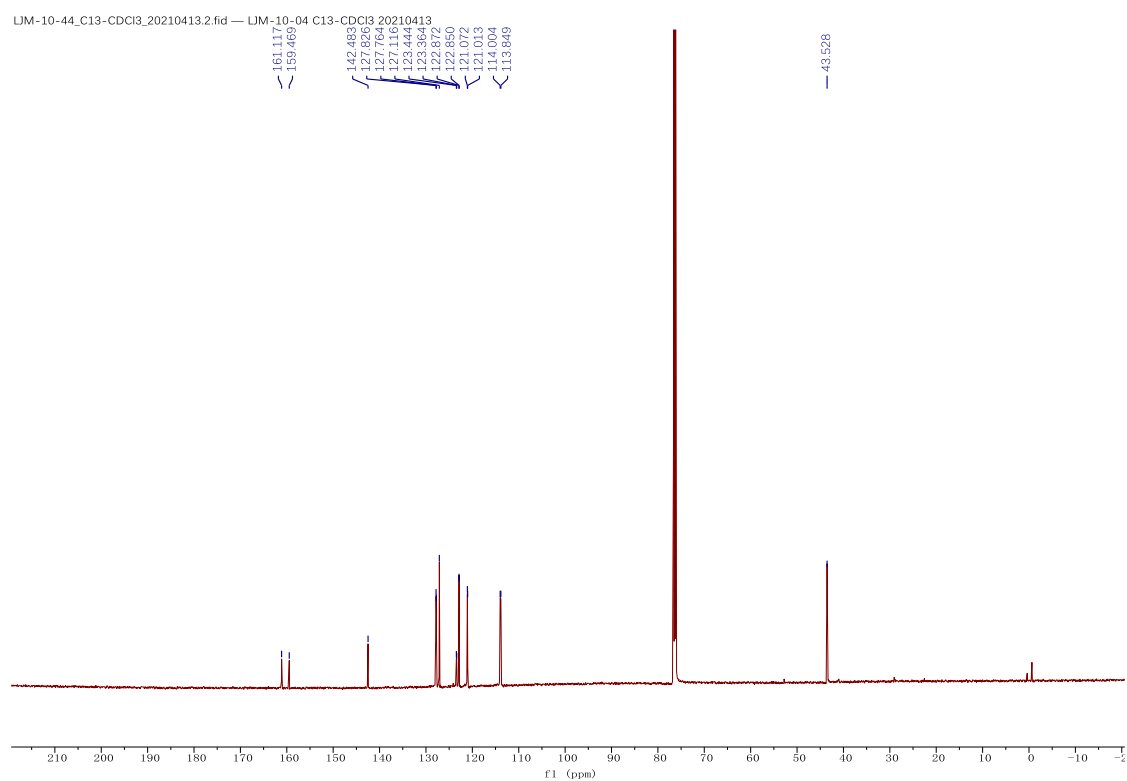


¹H NMR spectrum of compound 2e (400 MHz, CDCl₃):

LJM-10-44-H1-CDCl3 20210413 1.fid — LJM-10-04-H1-CDCl3 20210413

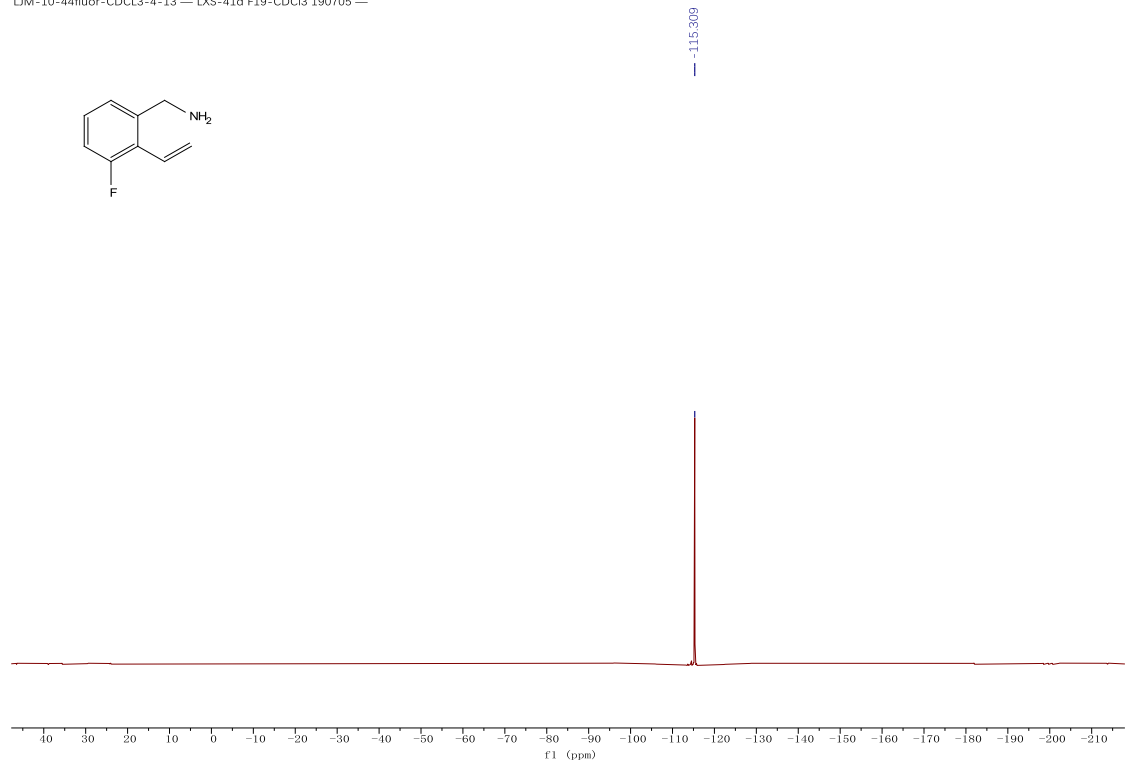


¹³C NMR spectrum of compound 2e (150 MHz, CDCl₃):



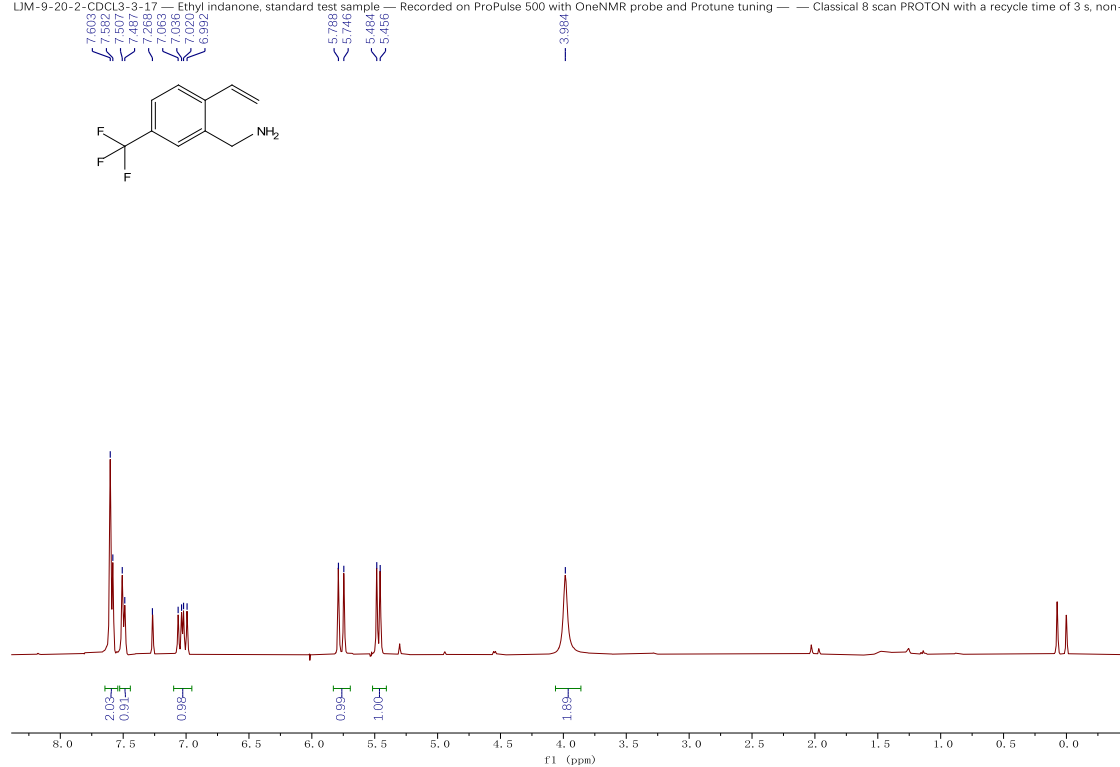
¹⁹F NMR spectrum of compound 2e (376 MHz, CDCl₃):

LJM-10-44fluor-CDCl3-4-13 — LXS-41d F19-CDCl3 190705 —



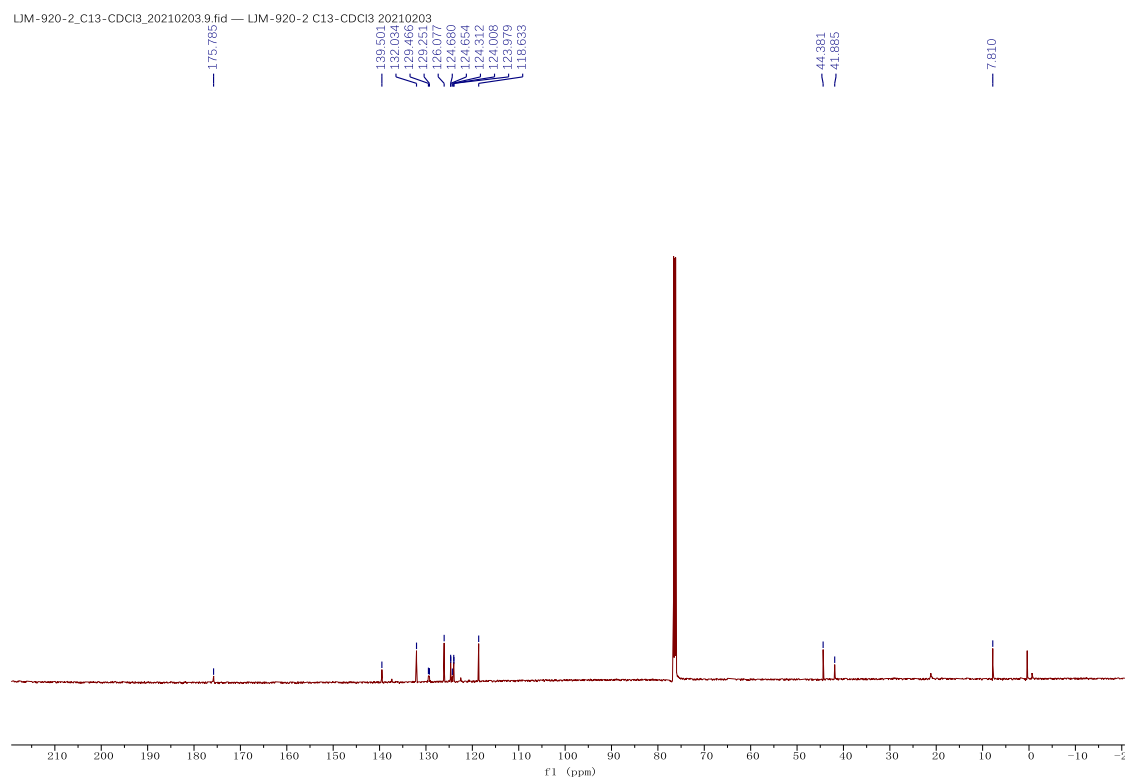
¹H NMR spectrum of compound 2f (400 MHz, CDCl₃):

LJM-9-20-2-CDCl3-3-17 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non--



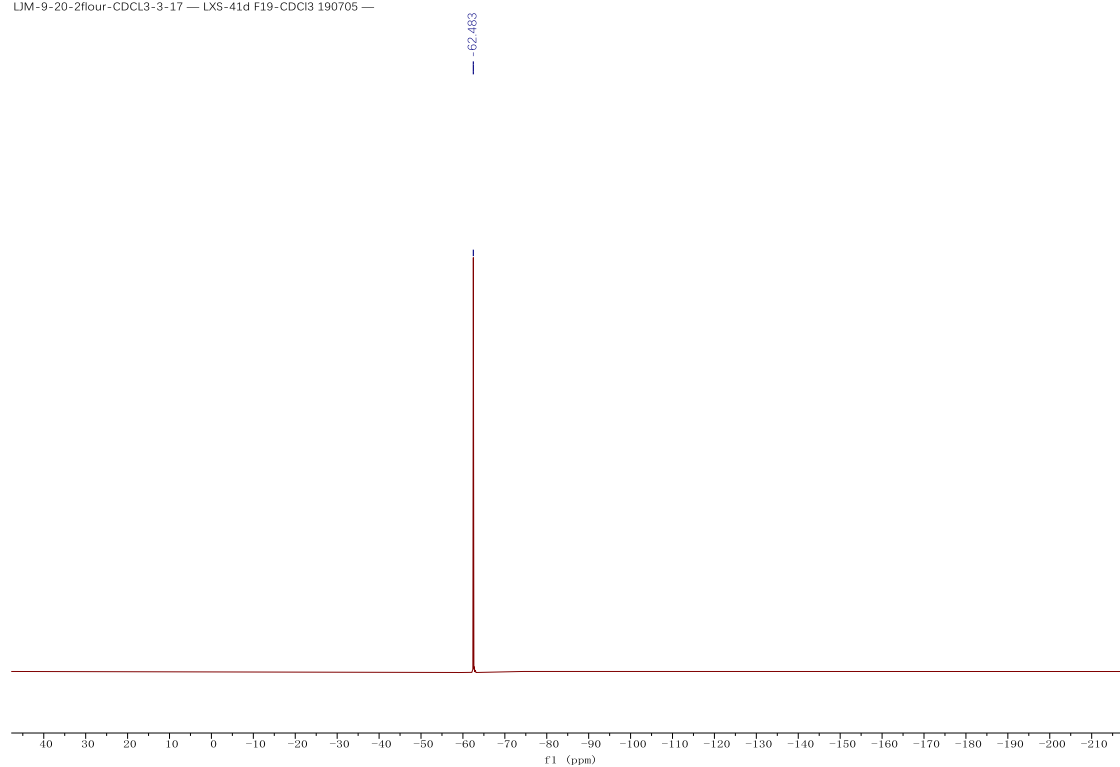
¹³C NMR spectrum of compound 2f (150 MHz, CDCl₃):

LJM-920-2_C13-CDCl3_20210203.9.fid — LJM-920-2_C13-CDCl3_20210203



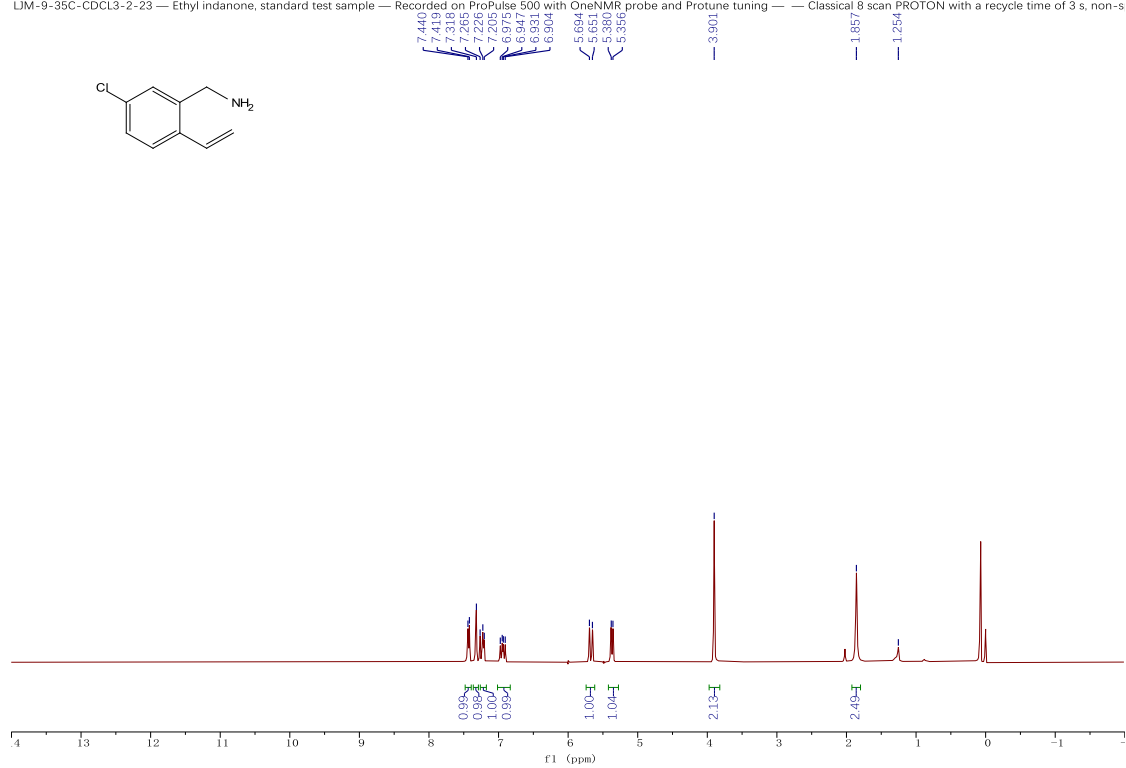
¹⁹F NMR spectrum of compound 2f (376 MHz, CDCl₃):

LJM-9-20-2four-CDCl3-3-17 — LXS-41d F19-CDCl3 190705 —



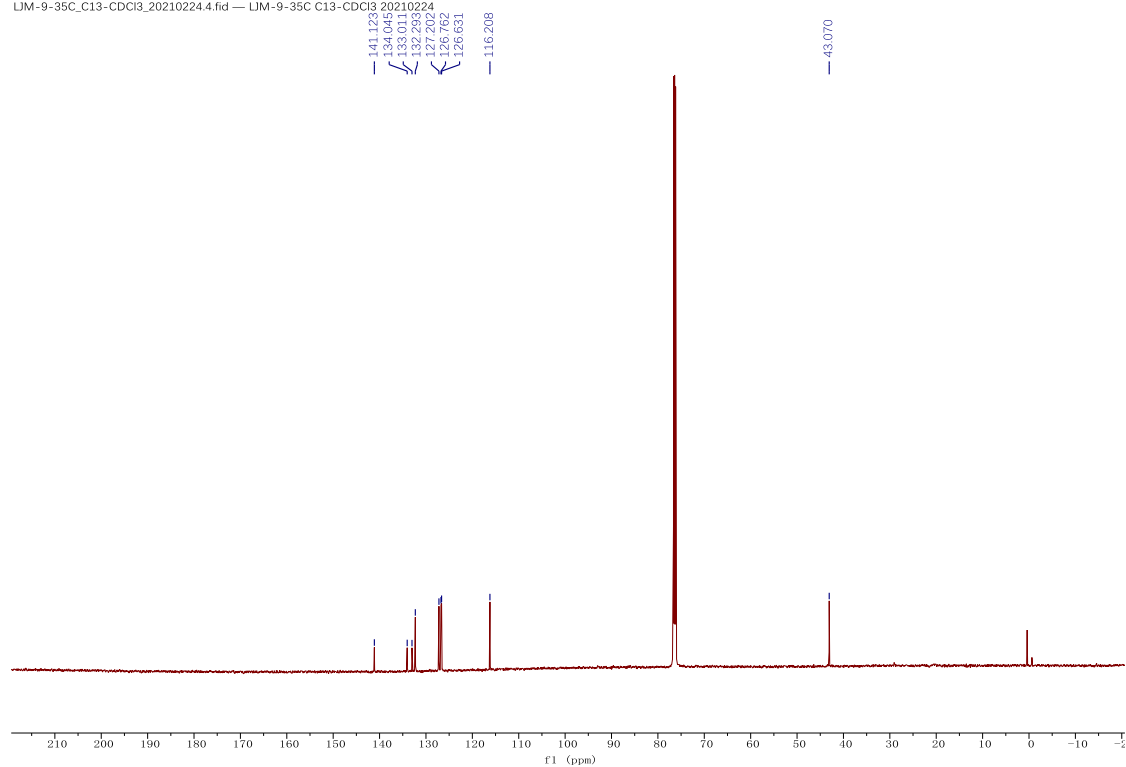
¹H NMR spectrum of compound 2g (400 MHz, CDCl₃):

LJM-9-35C-CDCl3-2-23 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-s



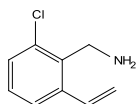
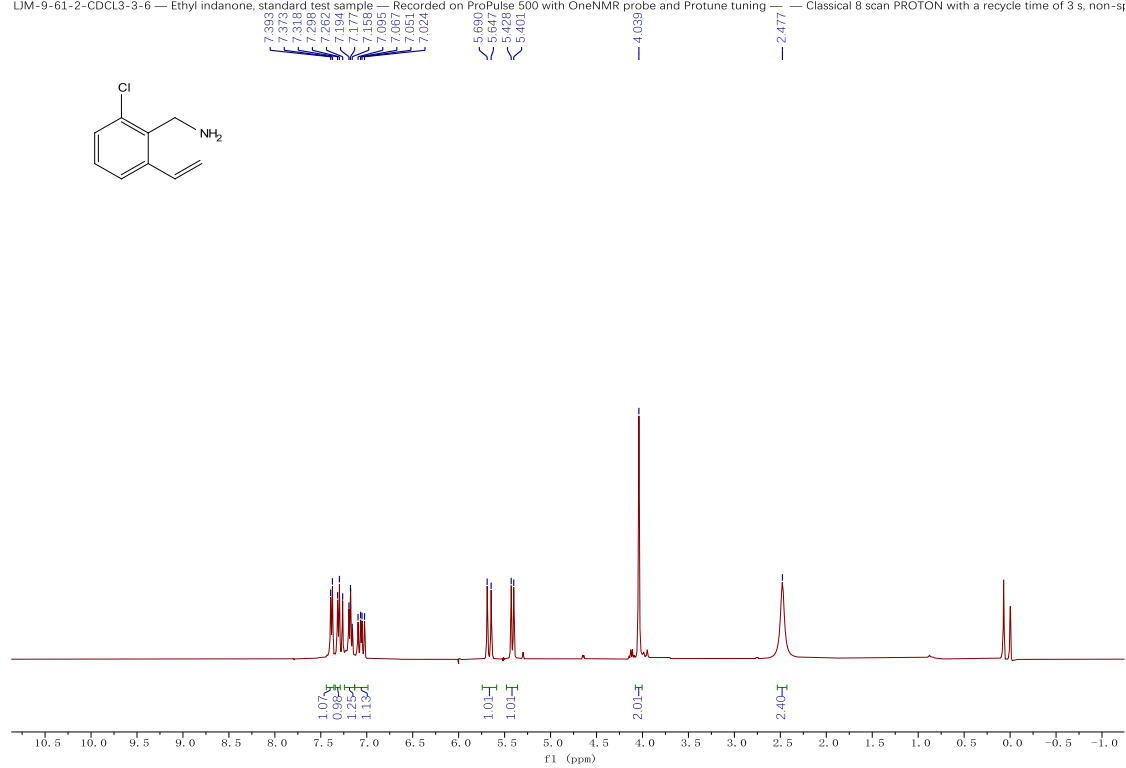
¹³C NMR spectrum of compound 2g (150 MHz, CDCl₃):

LJM-9-35C_C13-CDCl3_20210224.4.fid — LJM-9-35C C13-CDCl3 20210224



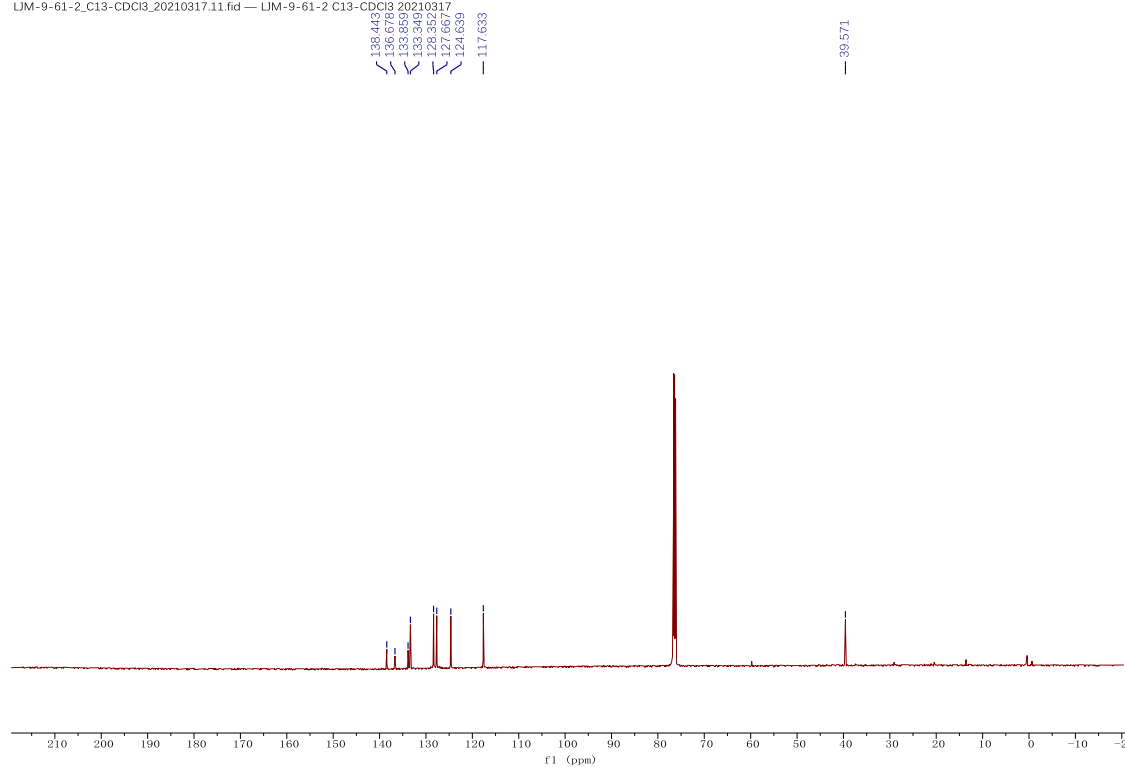
¹H NMR spectrum of compound 2h (400 MHz, CDCl₃):

LJM-9-61-2-CDCl3-3-6 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



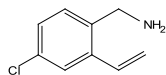
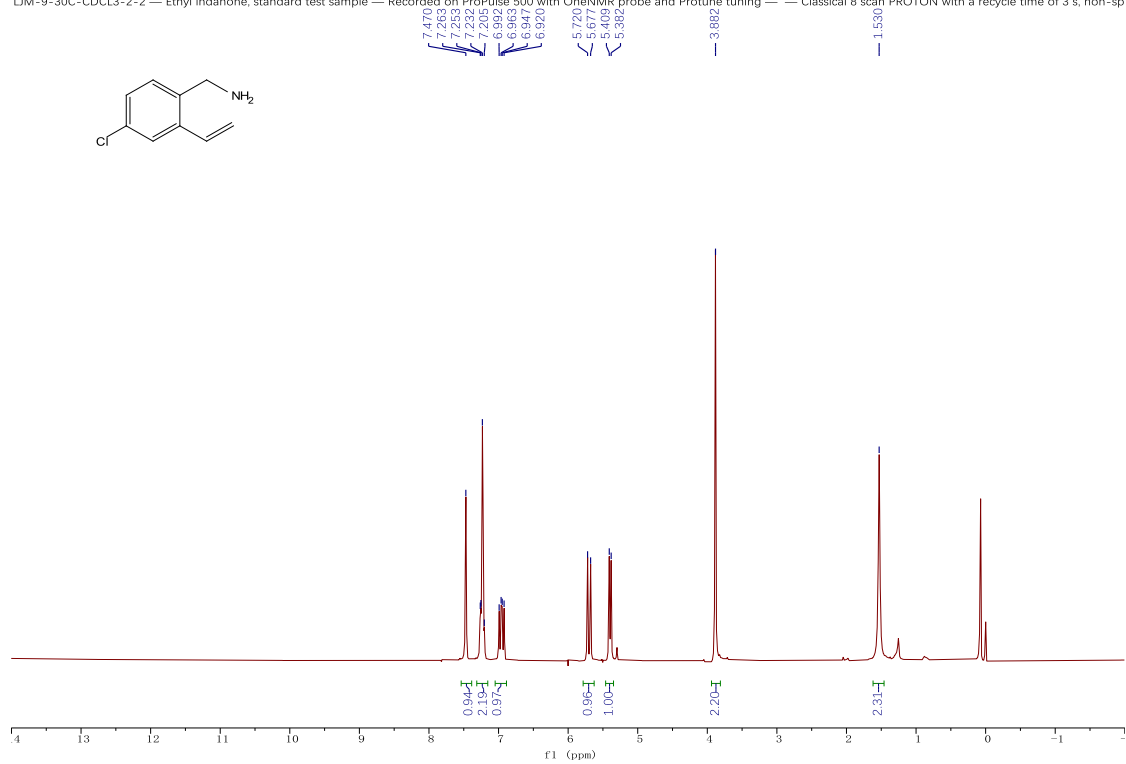
¹³C NMR spectrum of compound 2h (150 MHz, CDCl₃):

LJM-9-61-2_C13-CDCl3_20210317.111.fid — LJM-9-61-2 C13-CDCl3 20210317



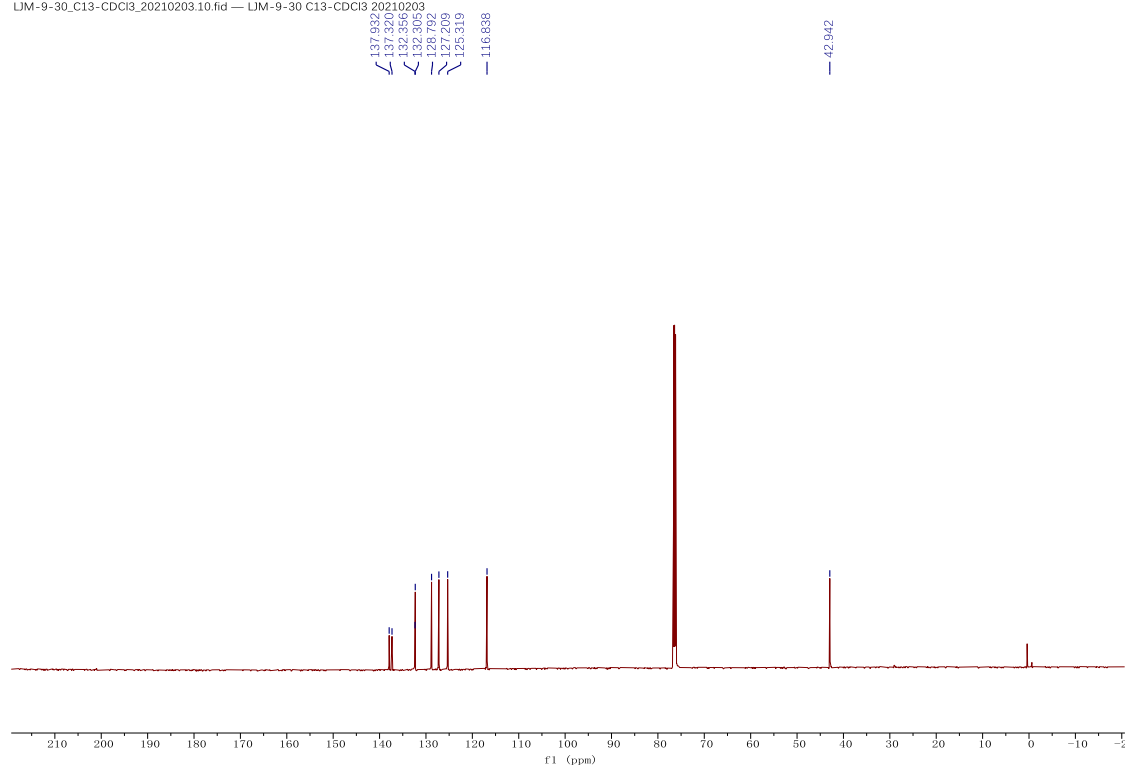
¹H NMR spectrum of compound 2i (400 MHz, CDCl₃):

LJM-9-30C-CDCl3-2-2 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sp



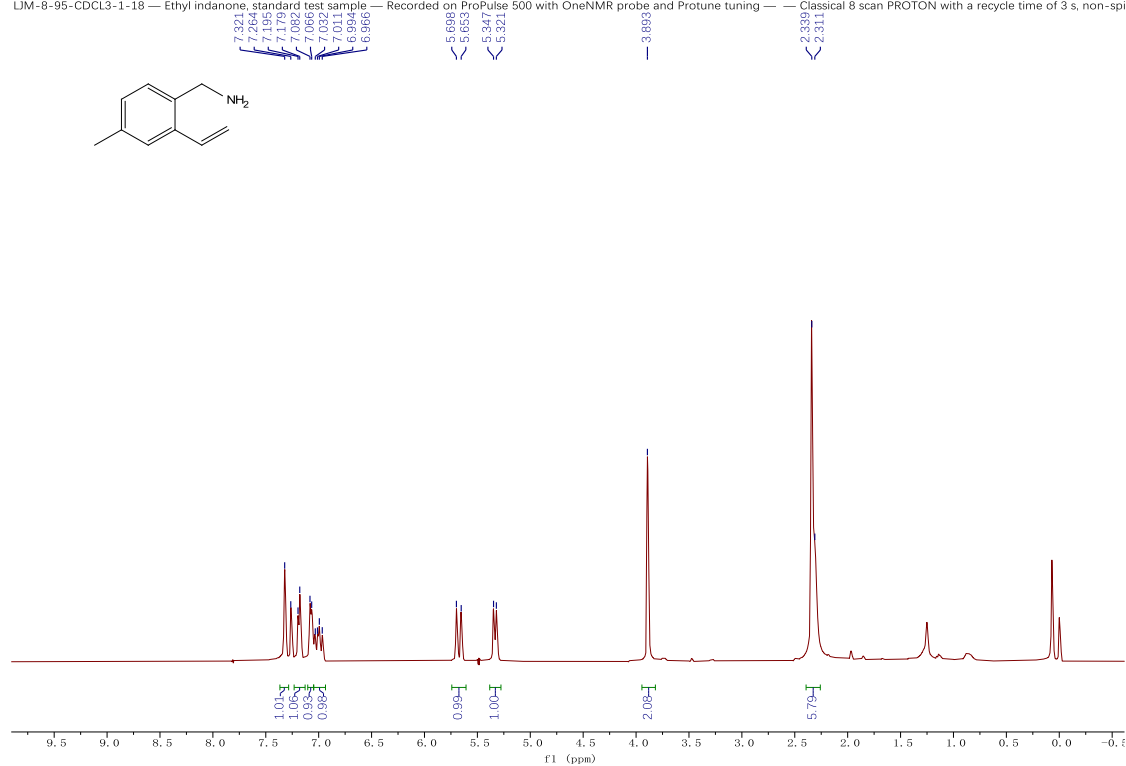
¹³C NMR spectrum of compound 2i (150 MHz, CDCl₃):

LJM-9-30_C13-CDCl3_20210203.10.fid — LJM-9-30 C13-CDCl3 20210203



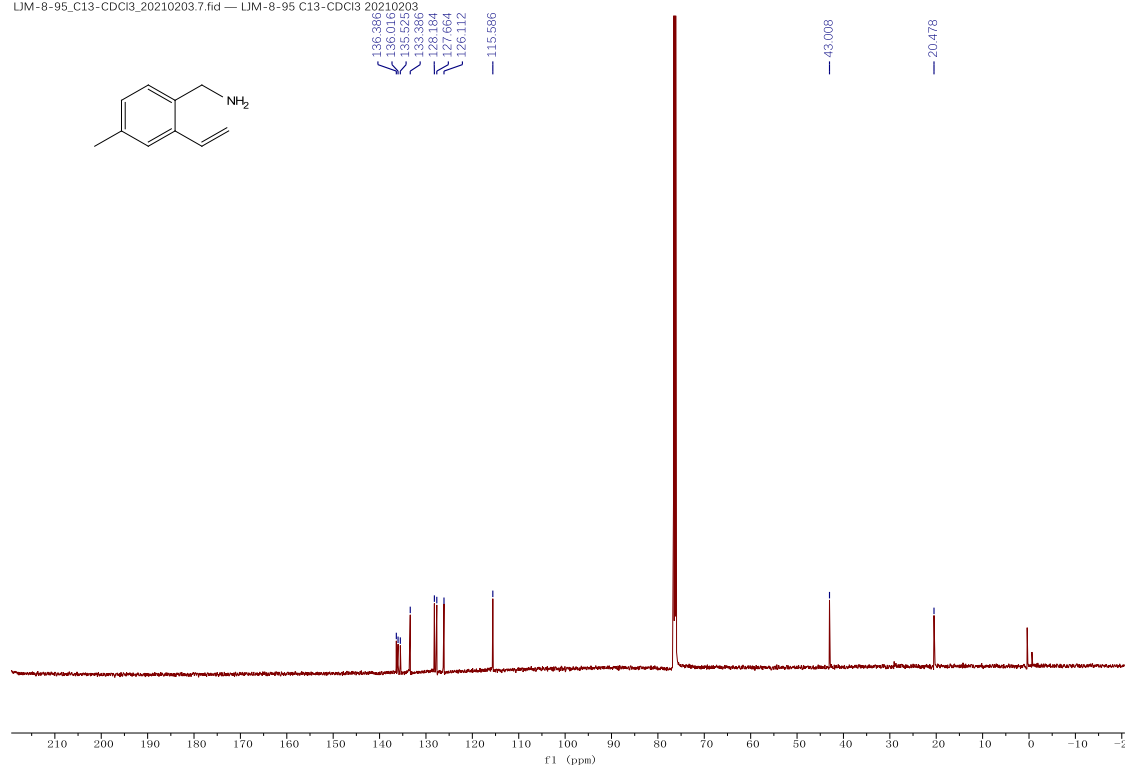
¹H NMR spectrum of compound 2j (400 MHz, CDCl₃):

LJM-8-95-CDCl3-1-18 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



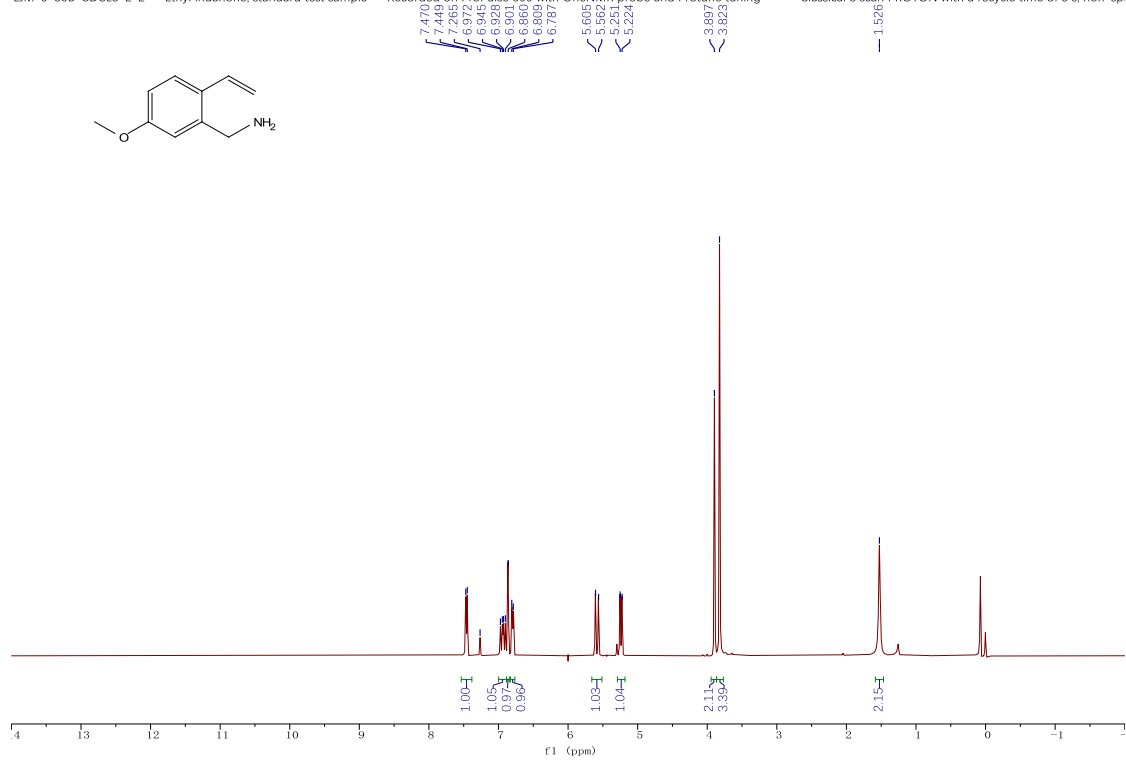
¹³C NMR spectrum of compound 2j (150 MHz, CDCl₃):

LJM-8-95_C13-CDCl3_20210203.7.fid — LJM-8-95 C13-CDCl3 20210203

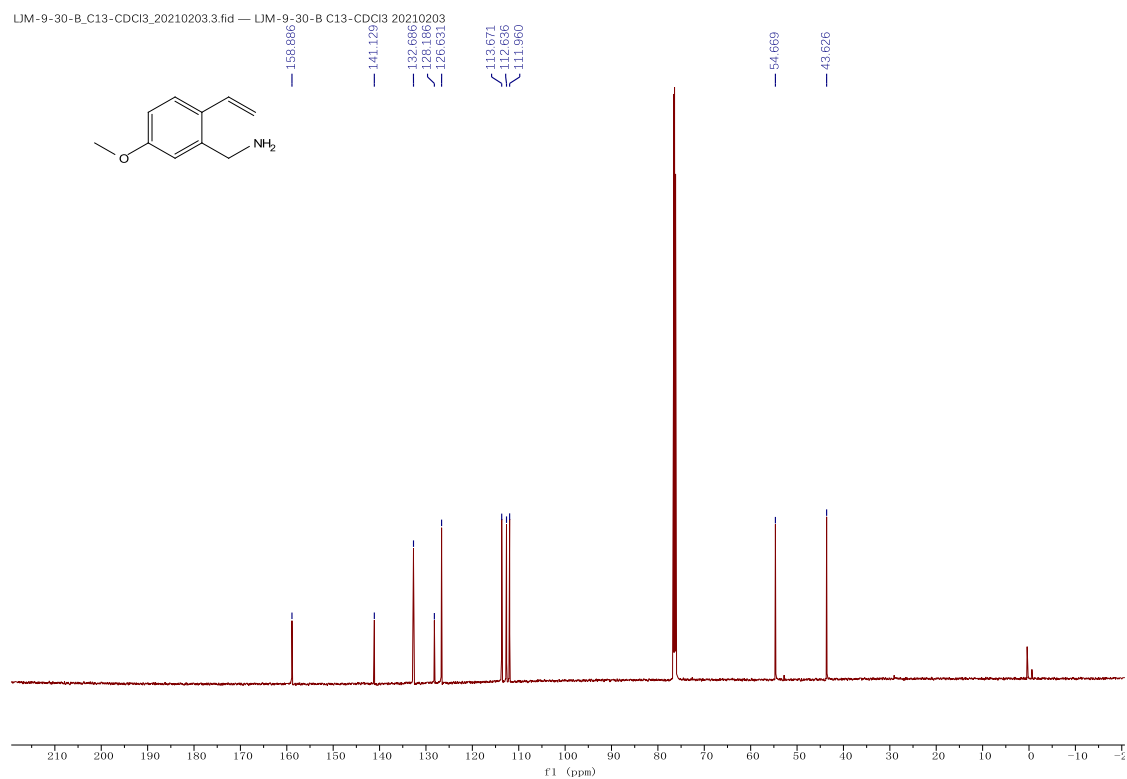


¹H NMR spectrum of compound 2k (400 MHz, CDCl₃):

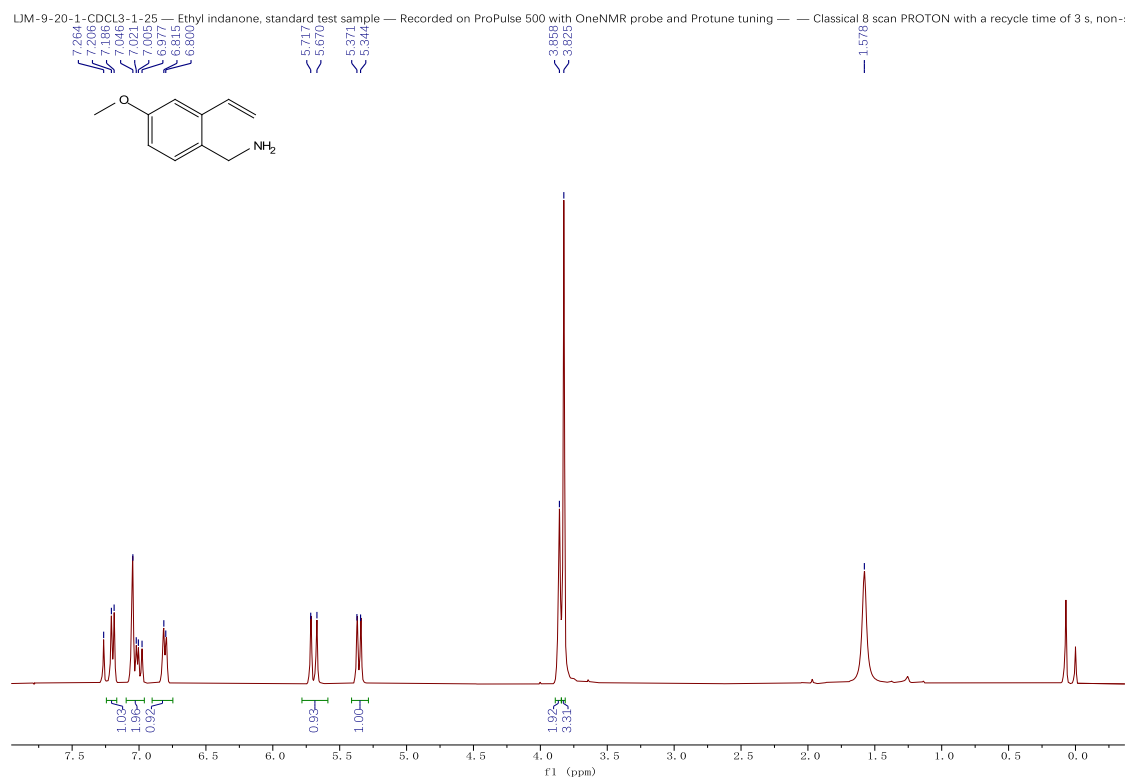
LJM-9-30B-CDCl3-2-2 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



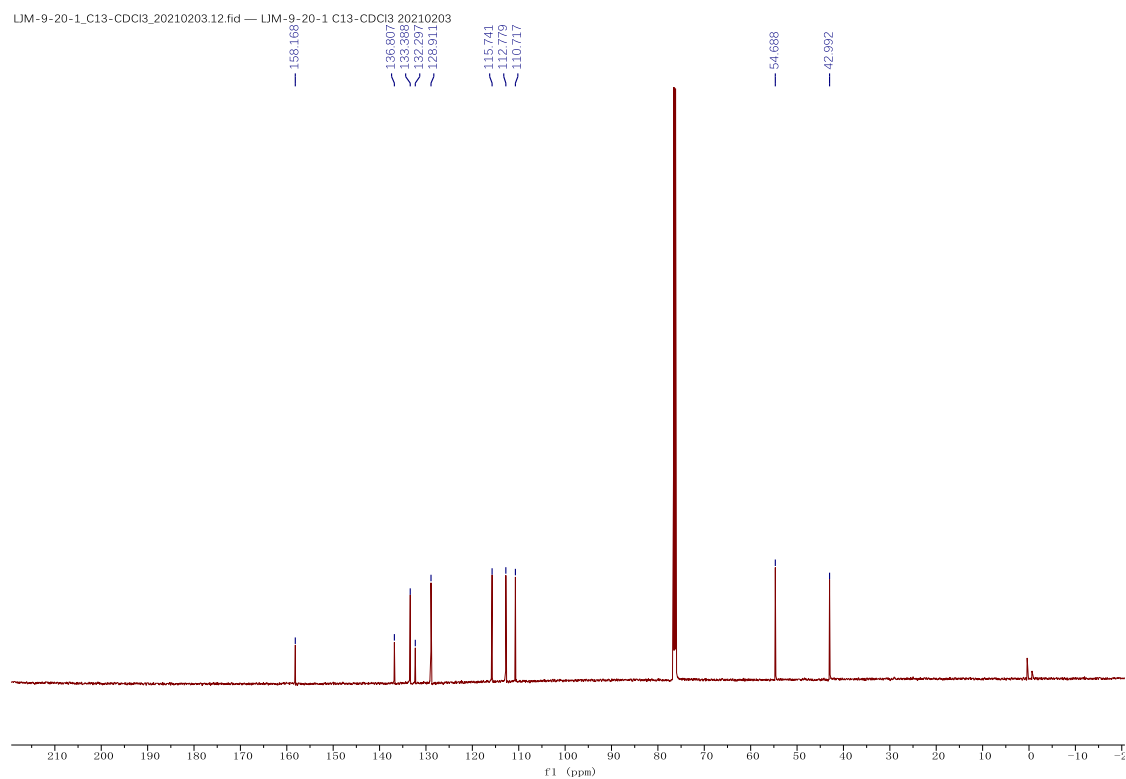
¹³C NMR spectrum of compound 2k (150 MHz, CDCl₃):



¹H NMR spectrum of compound 2l (400 MHz, CDCl₃):

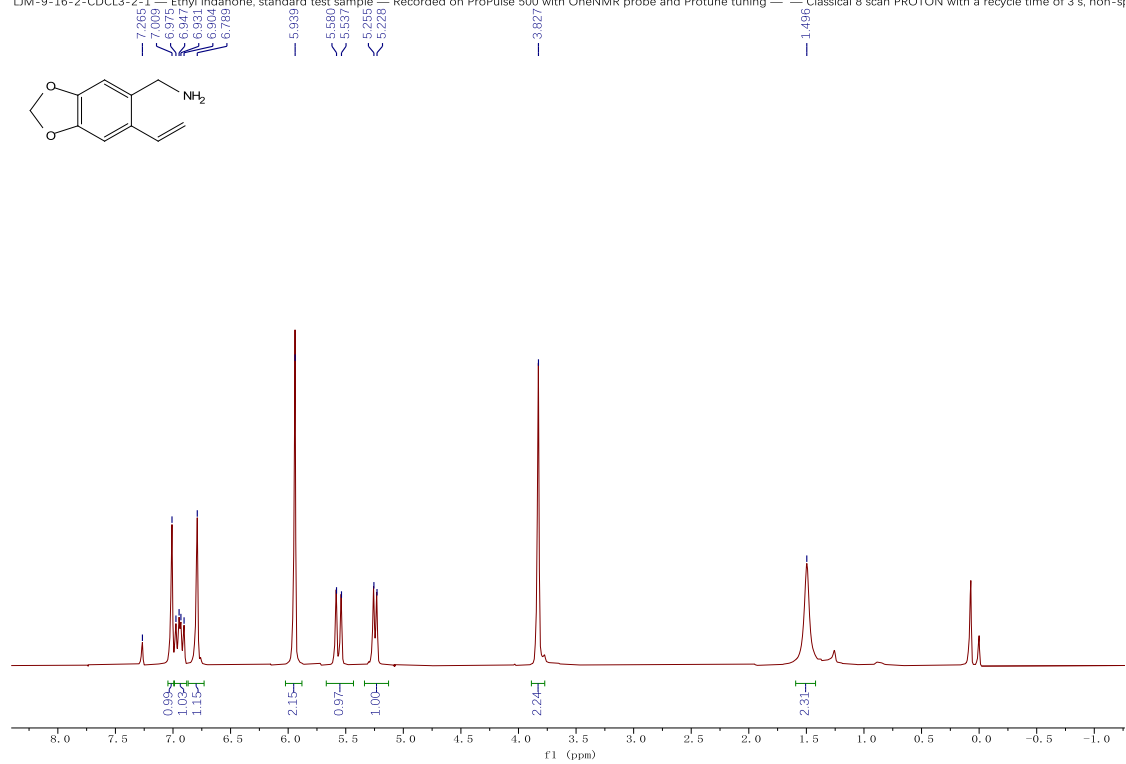


¹³C NMR spectrum of compound 2l (150 MHz, CDCl₃):



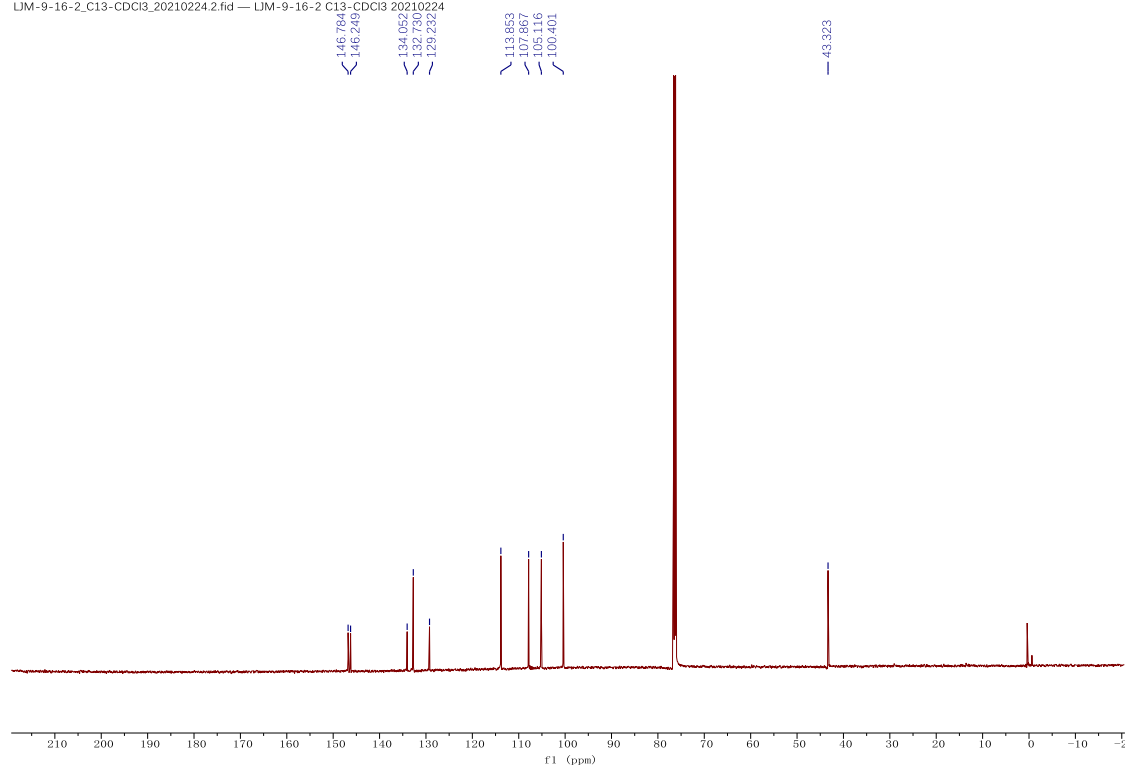
¹H NMR spectrum of compound 2m (400 MHz, CDCl₃):

LJM-9-16-2-CDCl3-2-1 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



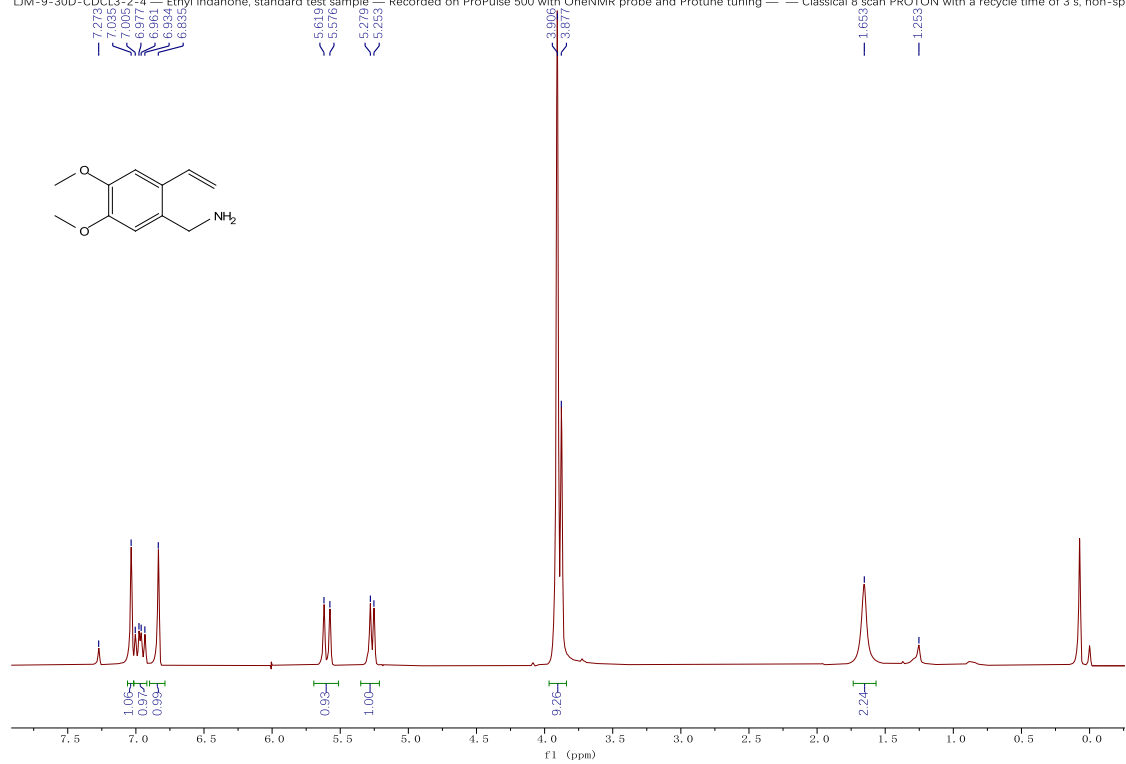
¹³C NMR spectrum of compound 2m (150 MHz, CDCl₃):

LJM-9-16-2_C13-CDCl3_20210224.2.fid — LJM-9-16-2_C13-CDCl3_20210224



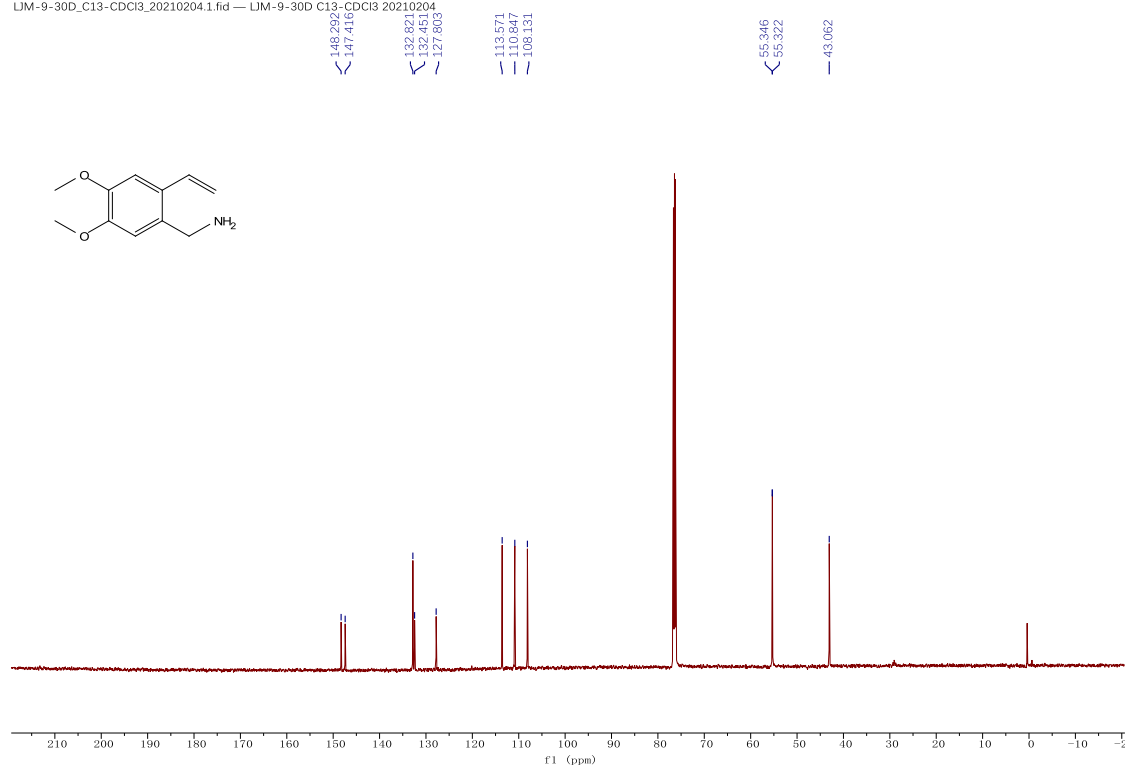
¹H NMR spectrum of compound 2n (400 MHz, CDCl₃):

LJM-9-30D-CDCl3-2-4 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sp



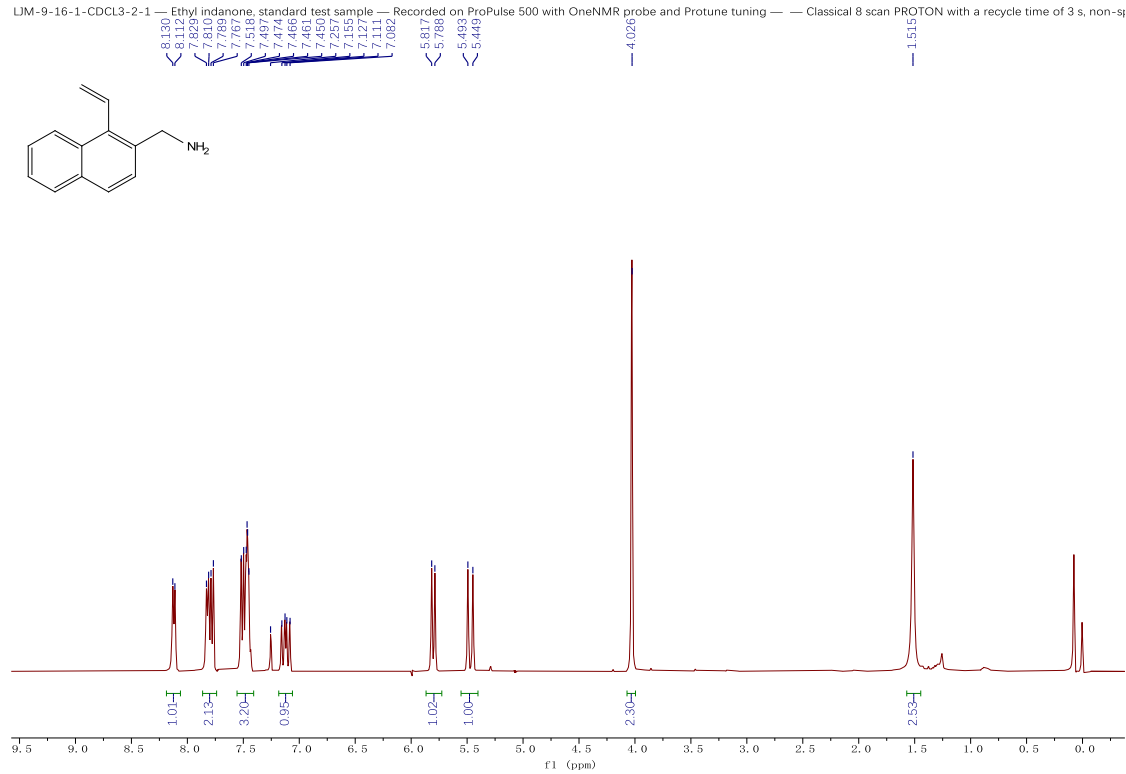
¹³C NMR spectrum of compound 2n (150 MHz, CDCl₃):

LJM-9-30D_C13-CDCl3_20210204.1.fid — LJM-9-30D C13-CDCl3 20210204

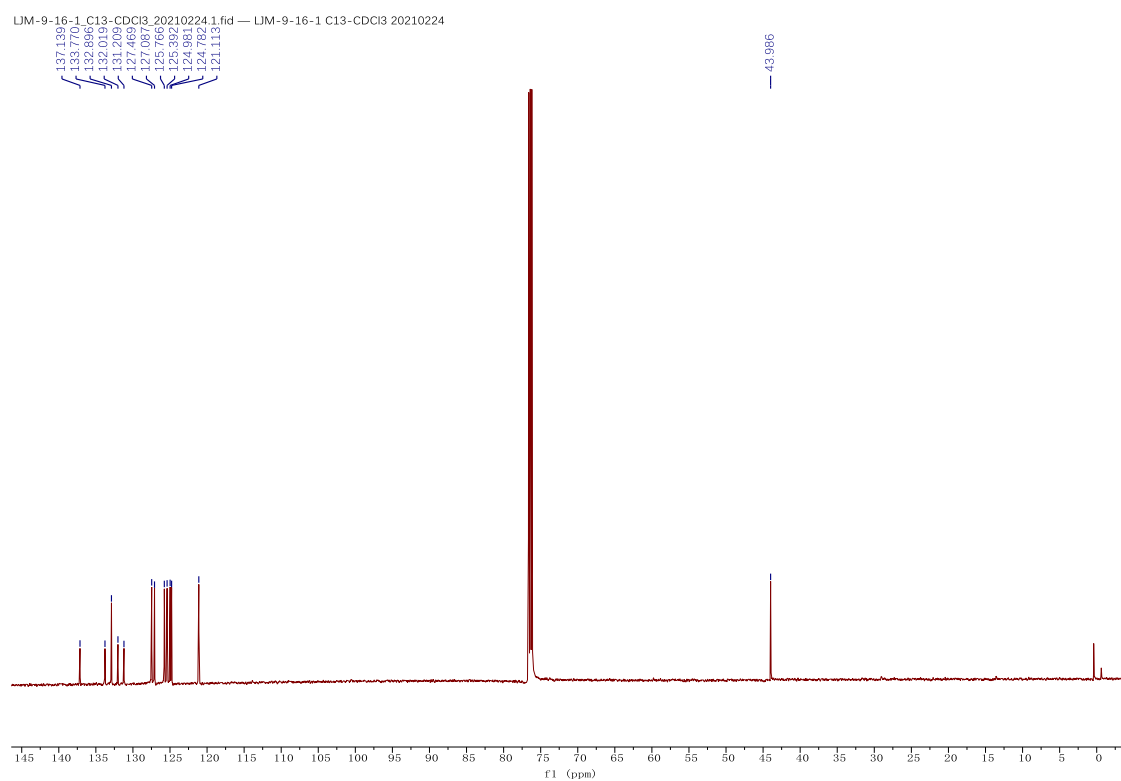


¹H NMR spectrum of compound 2o (400 MHz, CDCl₃):

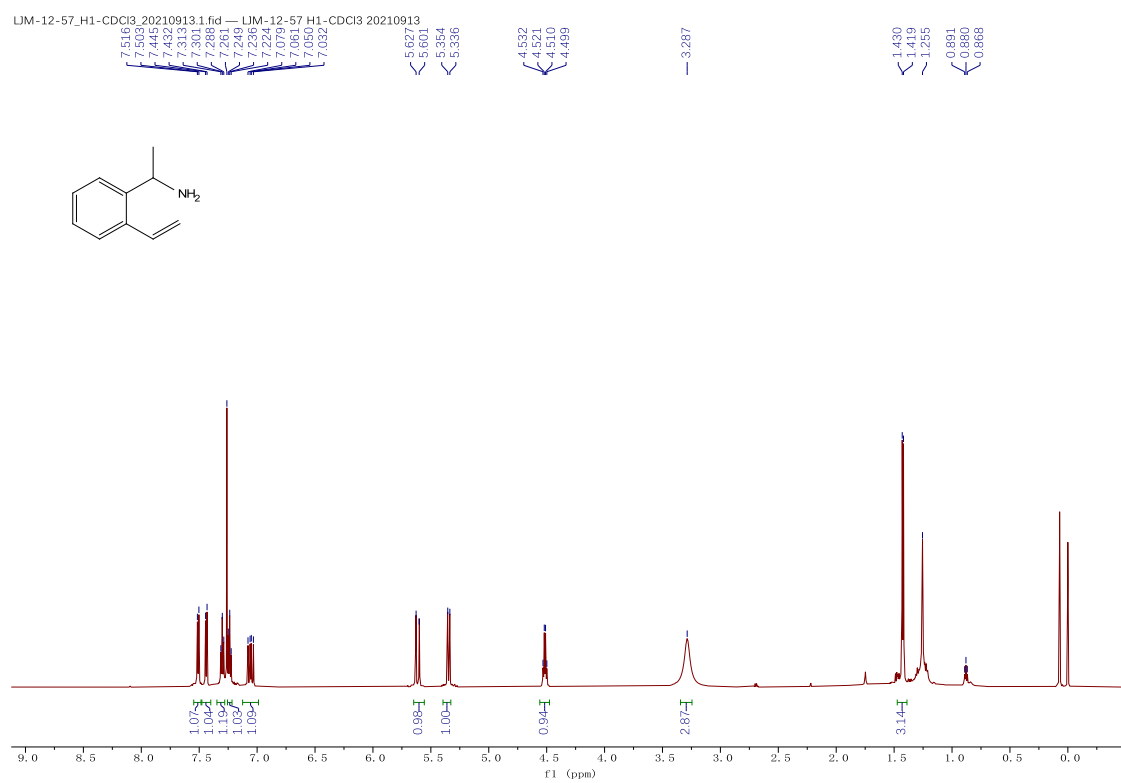
LJM-9-16-1-CDCl3-2-1 — Ethyl indanone standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq



¹³C NMR spectrum of compound 2o (150 MHz, CDCl₃):



¹H NMR spectrum of compound 2p (400 MHz, CDCl₃):



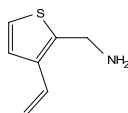
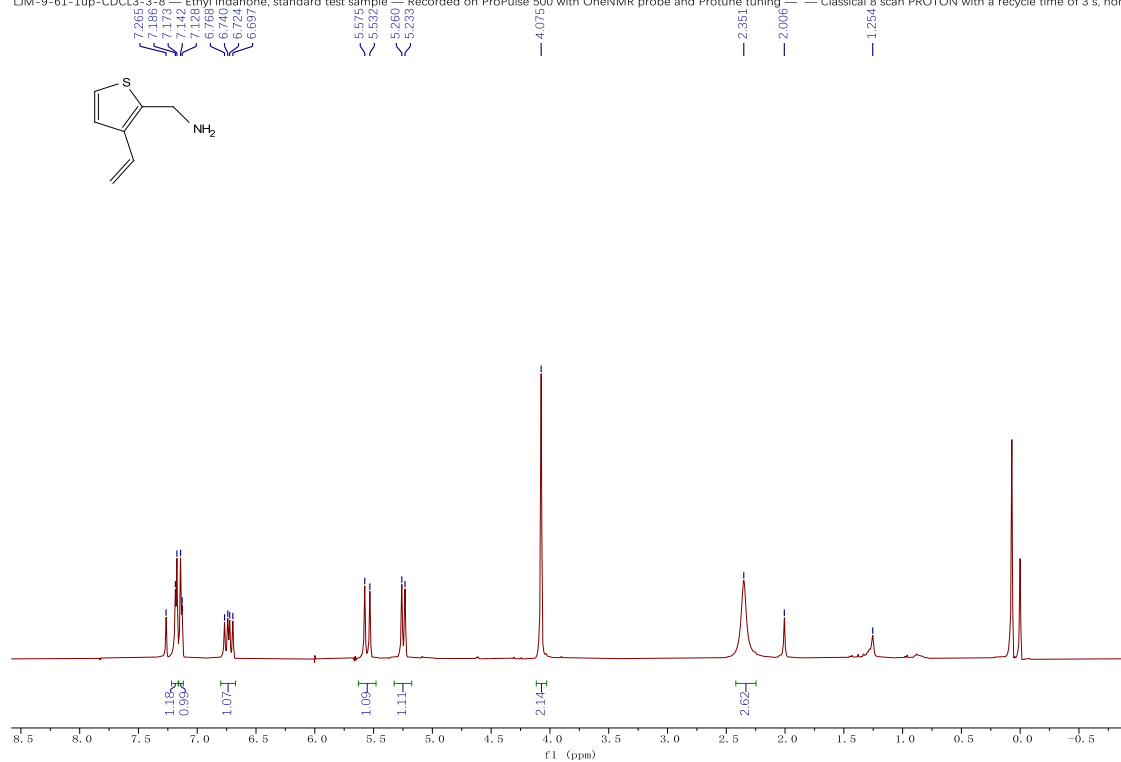
¹³C NMR spectrum of compound 2p (150 MHz, CDCl₃):

LJM-12-57_C13-CDCl3_20210913.2.fid — LJM-12-57 C13-CDCl3 20210913



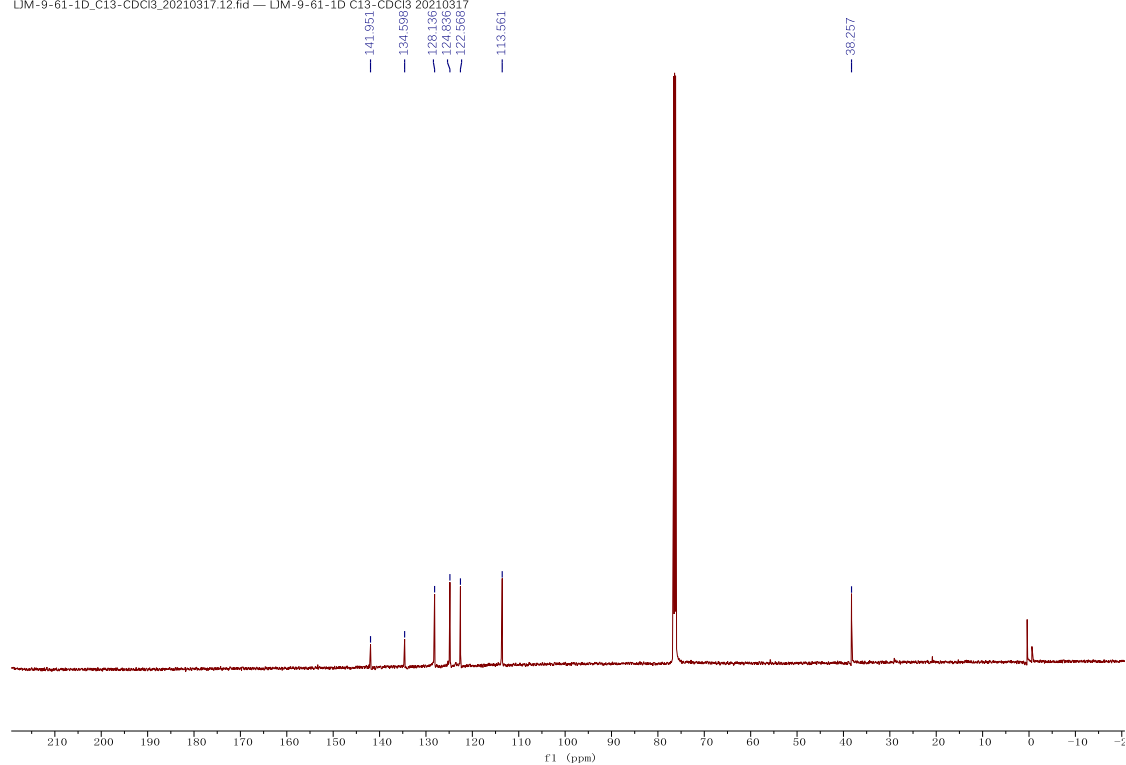
¹H NMR spectrum of compound 2q (400 MHz, CDCl₃):

LJM-9-61-1up-CDCl3-3-8 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non



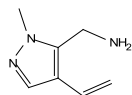
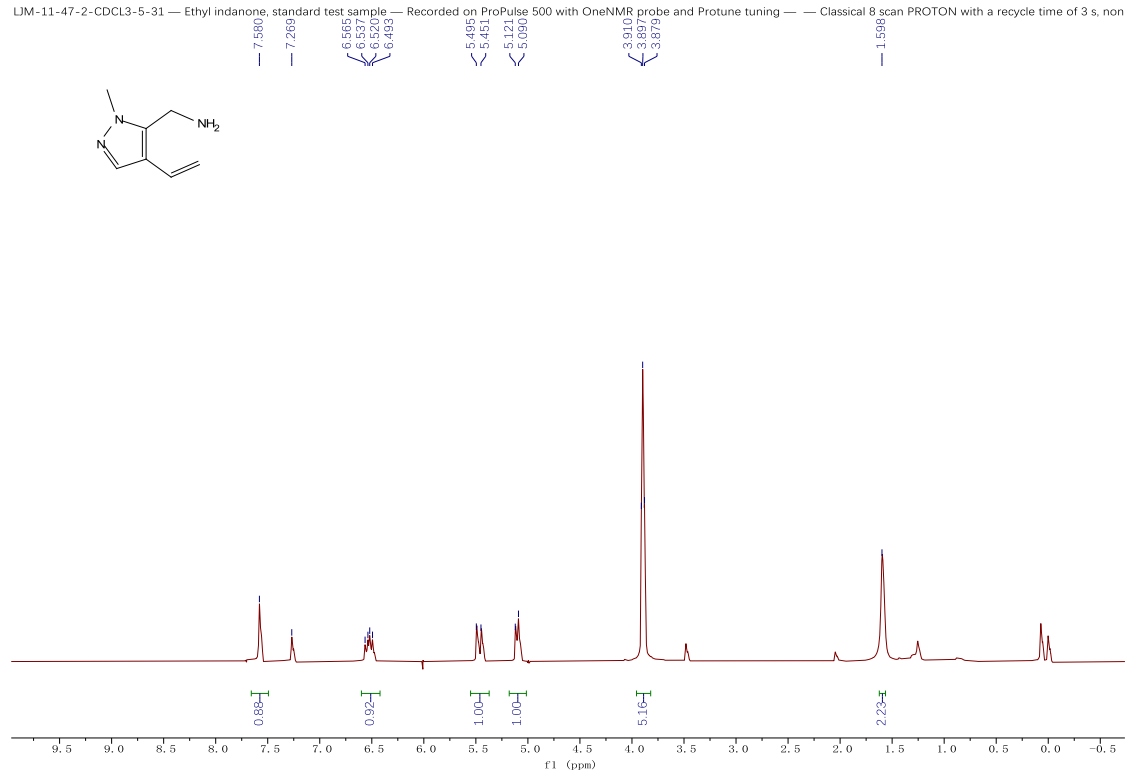
¹³C NMR spectrum of compound 2q (150 MHz, CDCl₃):

LJM-9-61-1D_C13-CDCl3_20210317.12.fid — LJM-9-61-1D C13-CDCl3 20210317



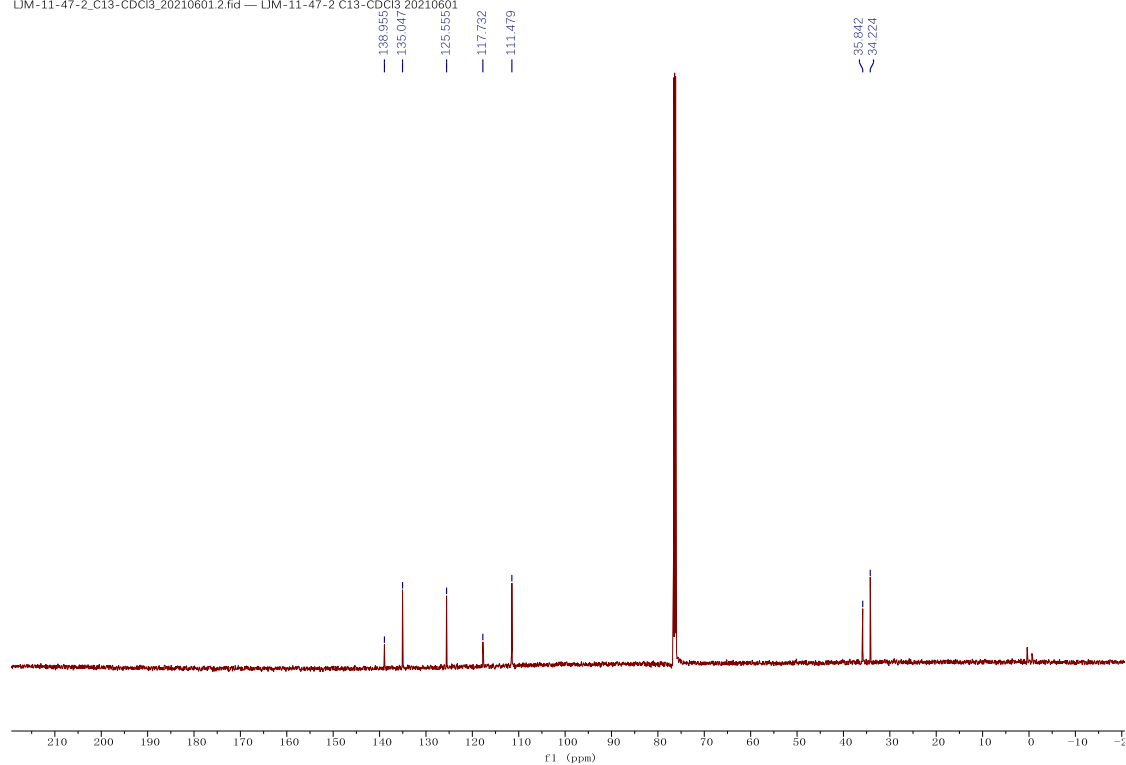
¹H NMR spectrum of compound 2r (400 MHz, CDCl₃):

LJM-11-47-2-CDCl3-5-31 — Ethyl indanone, standard test sample — Recorded on ProNMR 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non



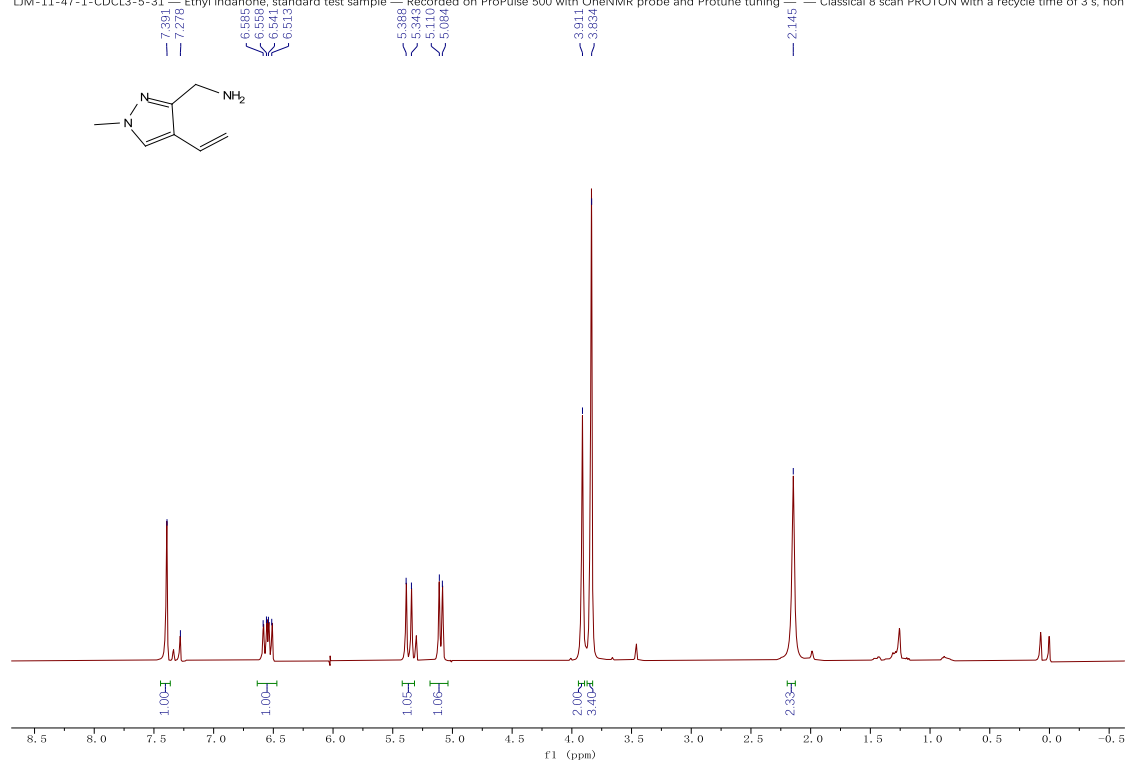
¹³C NMR spectrum of compound 2r (150 MHz, CDCl₃):

LJM-11-47-2_C13-CDCl3_20210601.2.fid — LJM-11-47-2 C13-CDCl3 20210601



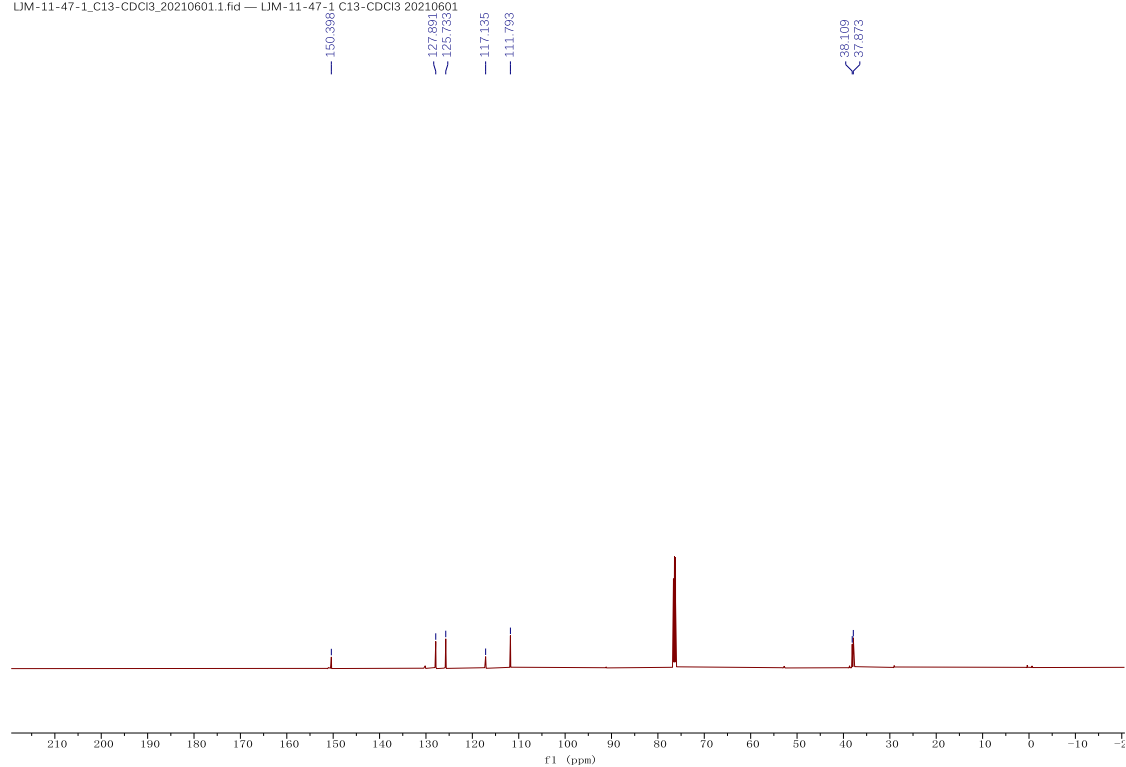
¹H NMR spectrum of compound 2s (400 MHz, CDCl₃):

LJM-11-47-1-CDCl3-5-31 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non



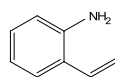
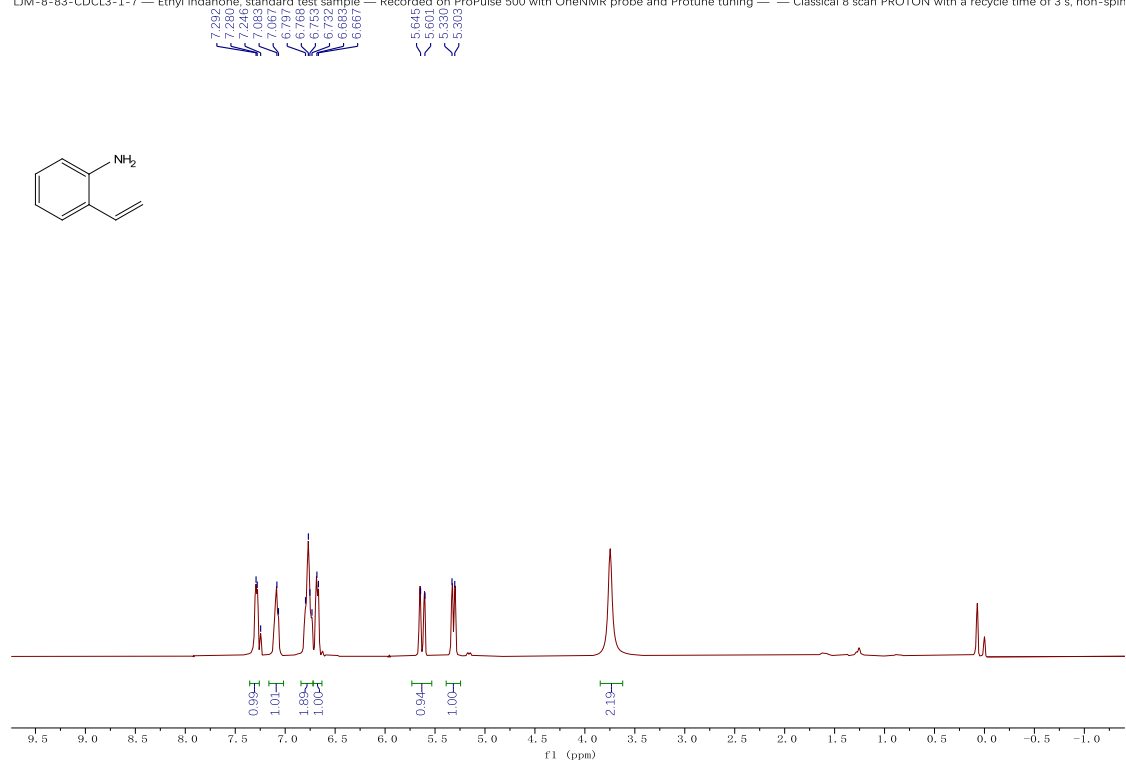
¹³C NMR spectrum of compound 2s (150 MHz, CDCl₃):

LJM-11-47-1_C13-CDCl3_20210601.fid — LJM-11-47-1 C13-CDCl3 20210601



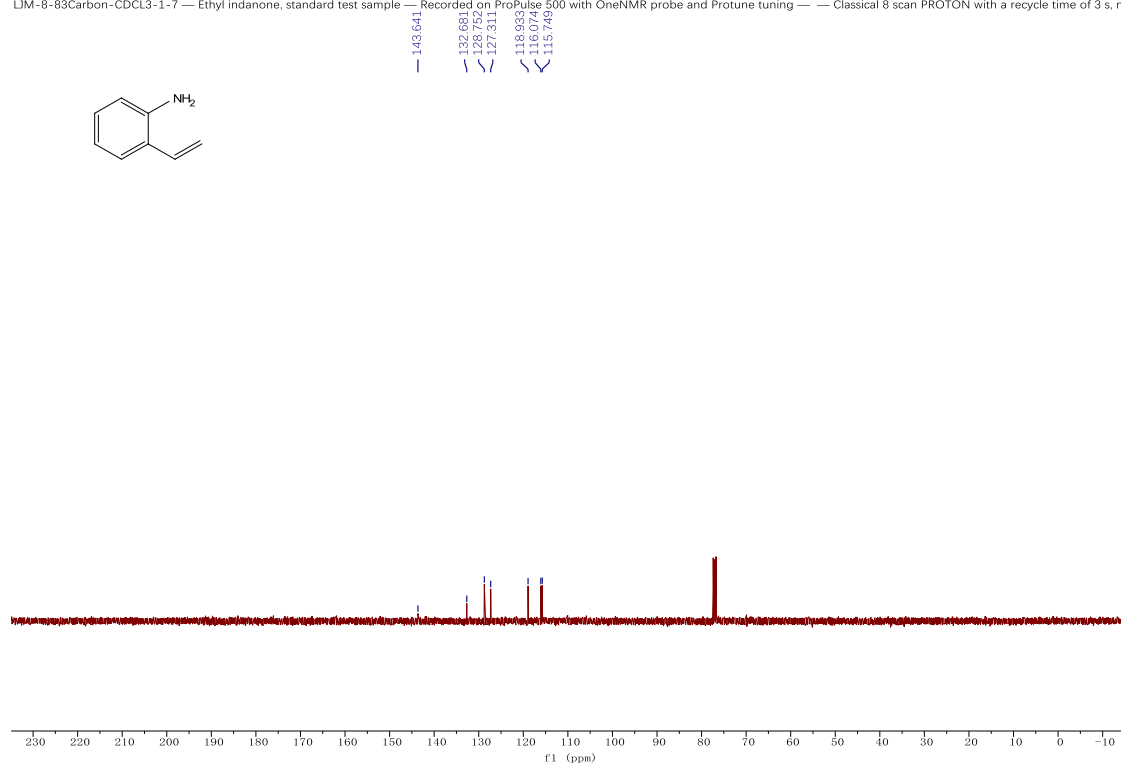
¹H NMR spectrum of compound 2t (400 MHz, CDCl₃):

LJM-8-83-CDCL3-1-7 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spin



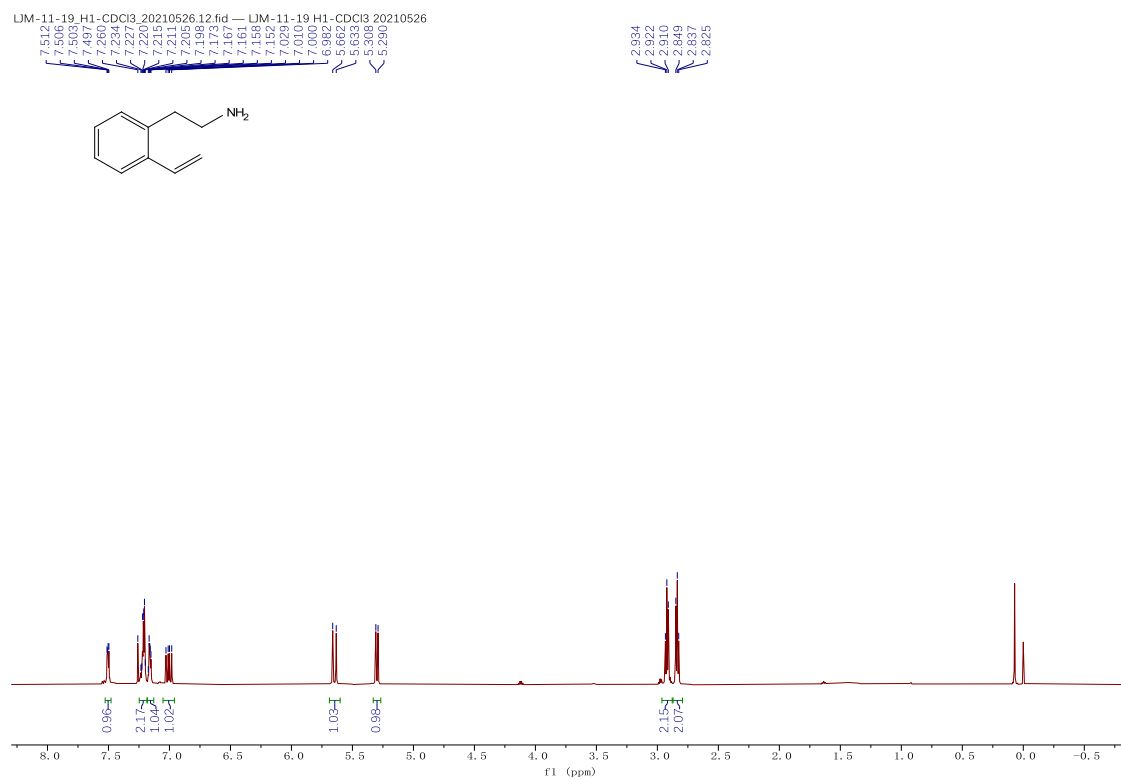
¹³C NMR spectrum of compound 2t (150 MHz, CDCl₃):

LJM-8-83Carbon-CDCl3-1-7 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, n



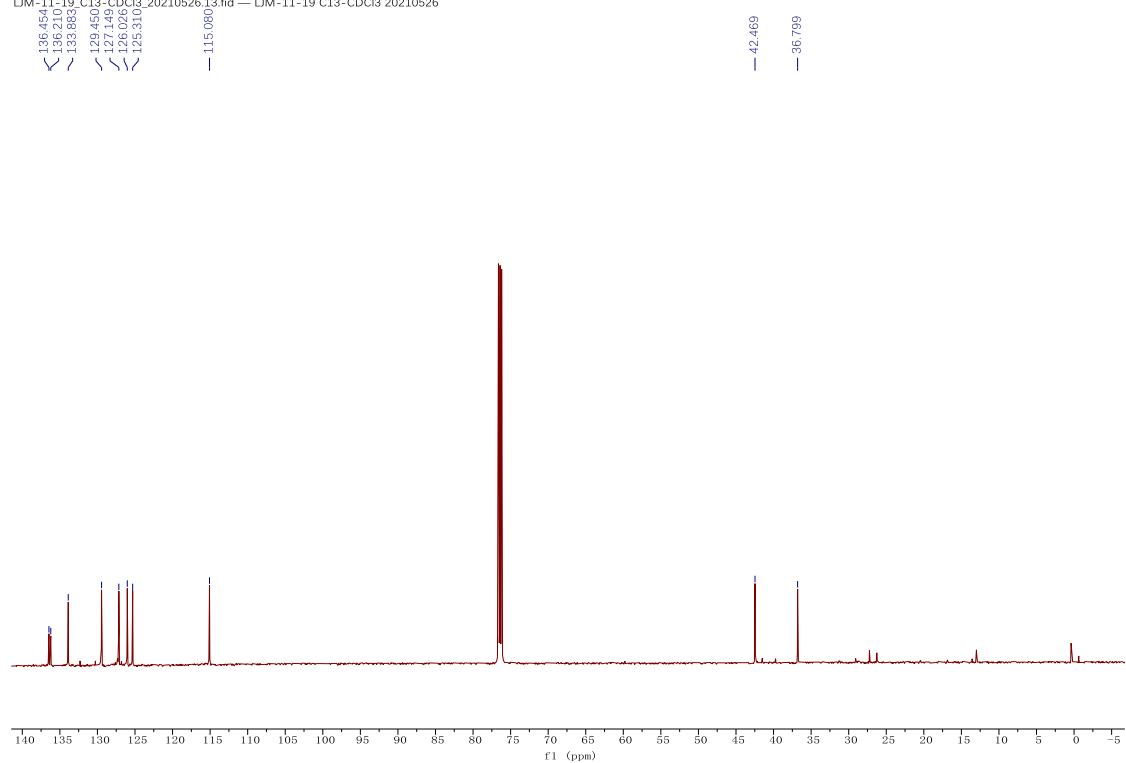
¹H NMR spectrum of compound 2v (400 MHz, CDCl₃):

LJM-11-19_H1-CDCl3_20210526.12.fid LJM-11-19_H1-CDCl3_20210526



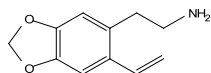
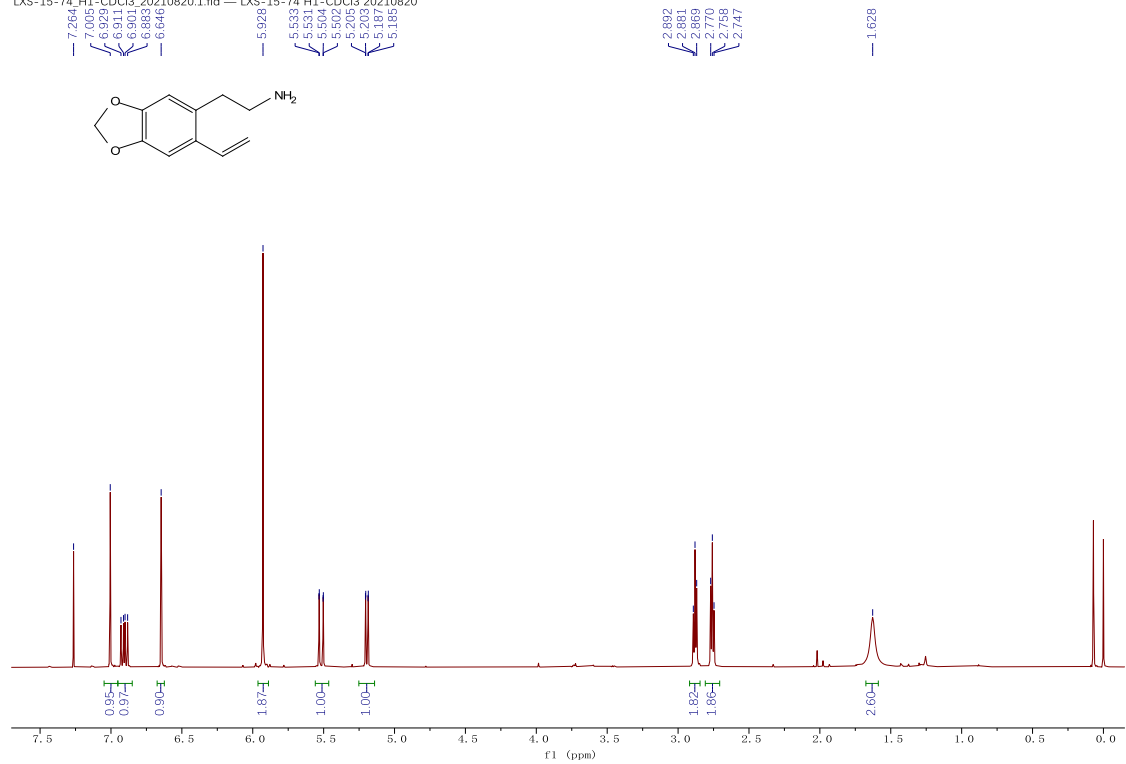
¹³C NMR spectrum of compound 2v (150 MHz, CDCl₃):

LJM-11-19_C13-CDCl3_20210526.13.fid — LJM-11-19 C13-CDCl3 20210526



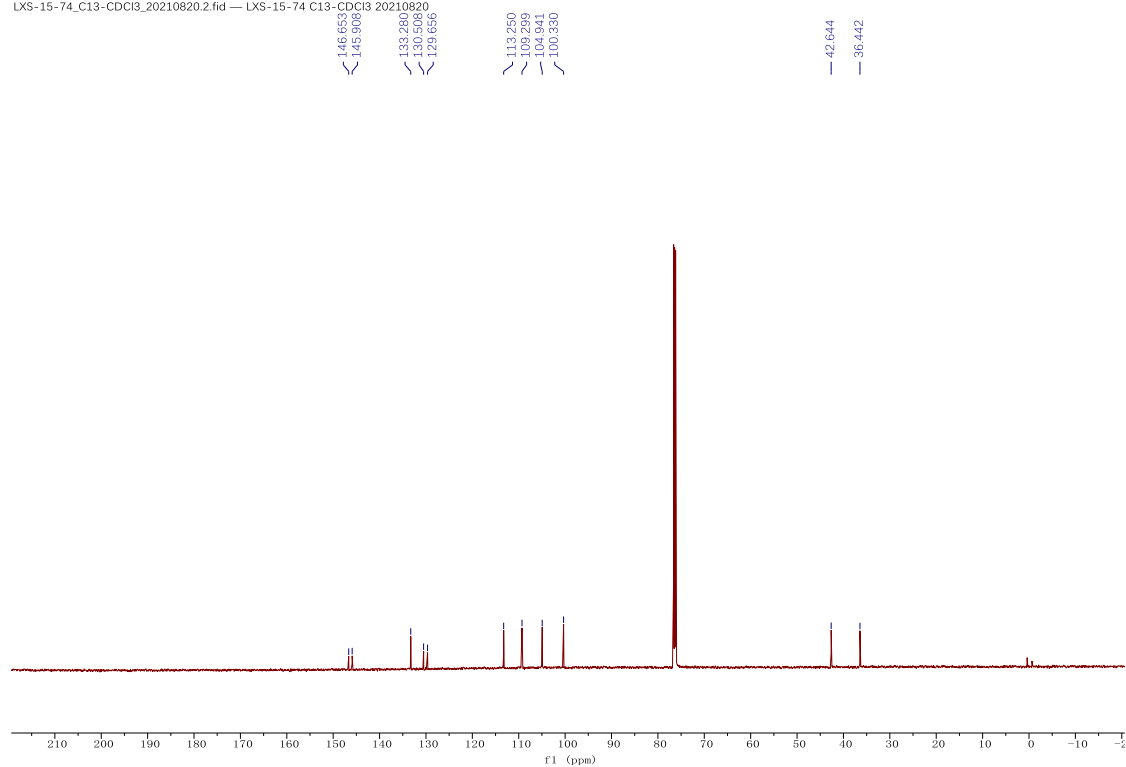
¹H NMR spectrum of compound 2w (400 MHz, CDCl₃):

LXS-15-74_H1-CDCl3_20210820.1.fid — LXS-15-74 H1-CDCl3 20210820



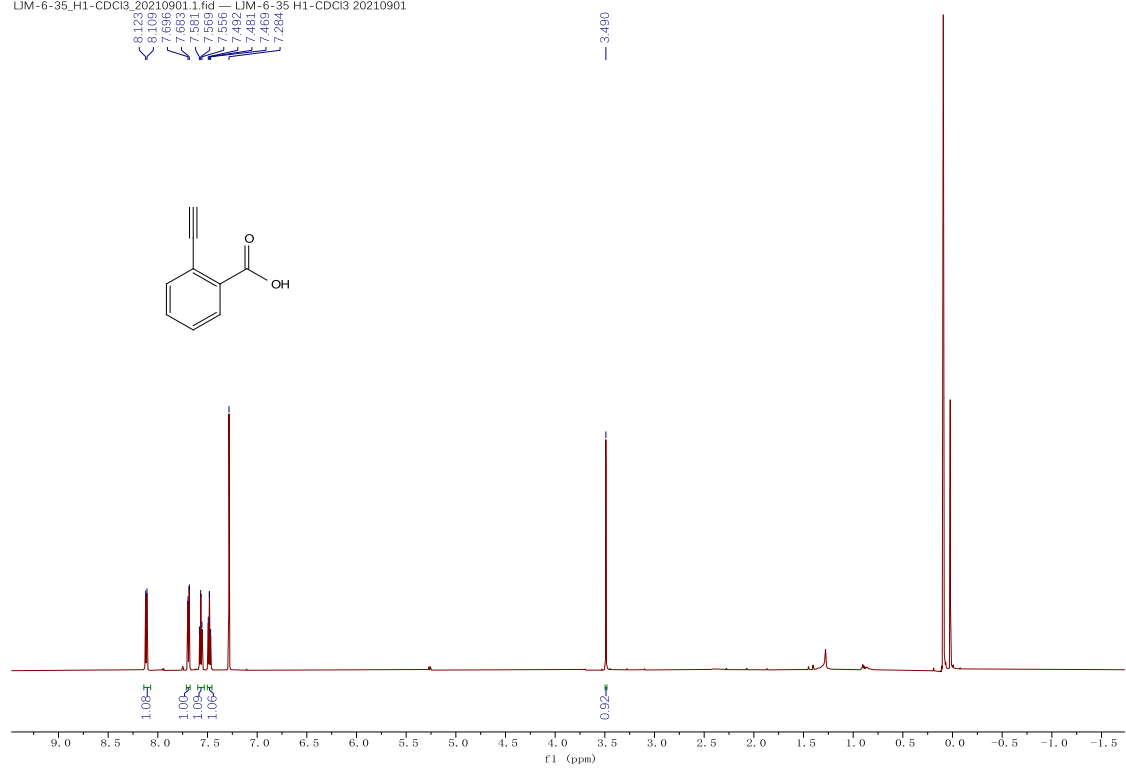
¹³C NMR spectrum of compound 2w (150 MHz, CDCl₃):

LXS-15-74_C13-CDCl3_20210820.2.fid — LXS-15-74 C13-CDCl3 20210820

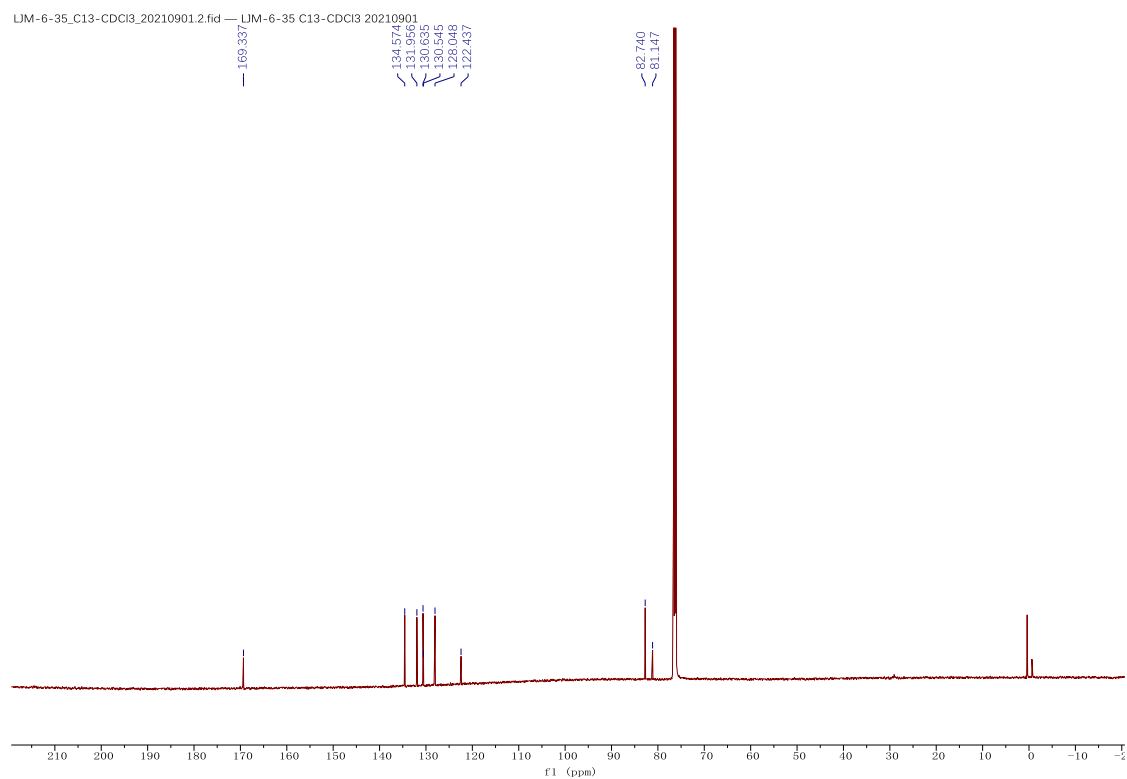


¹H NMR spectrum of compound 1a (400 MHz, CDCl₃):

LJM-6-35_H1-CDCl3_20210901.1.fid — LJM-6-35 H1-CDCl3 20210901

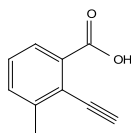
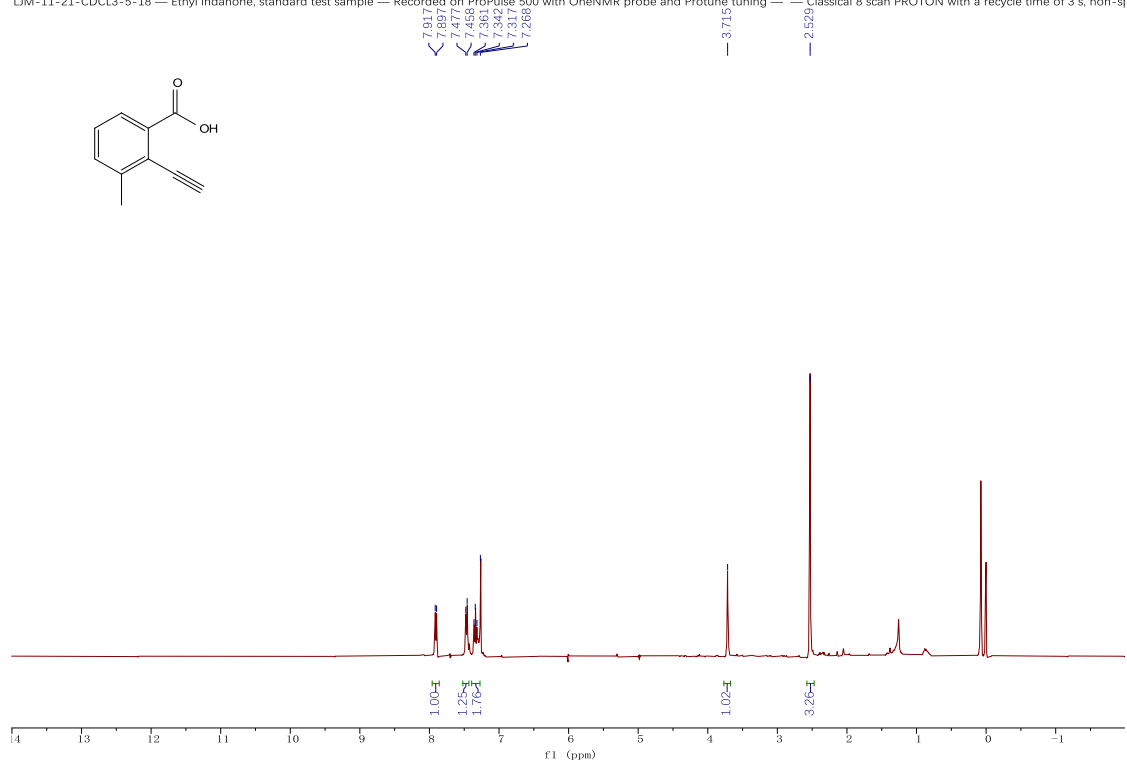


¹³C NMR spectrum of compound 1a (150 MHz, CDCl₃):

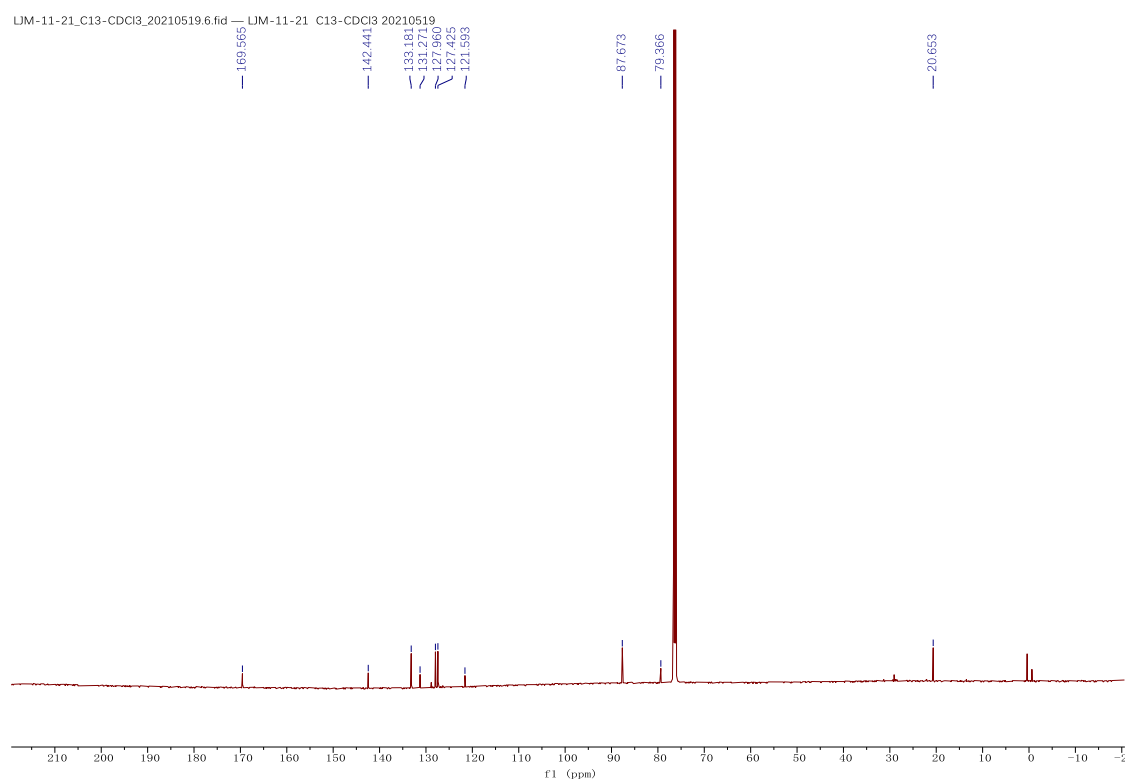


¹H NMR spectrum of compound 1c (400 MHz, CDCl₃):

LJM-11-21-CDCl3-5-18 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq

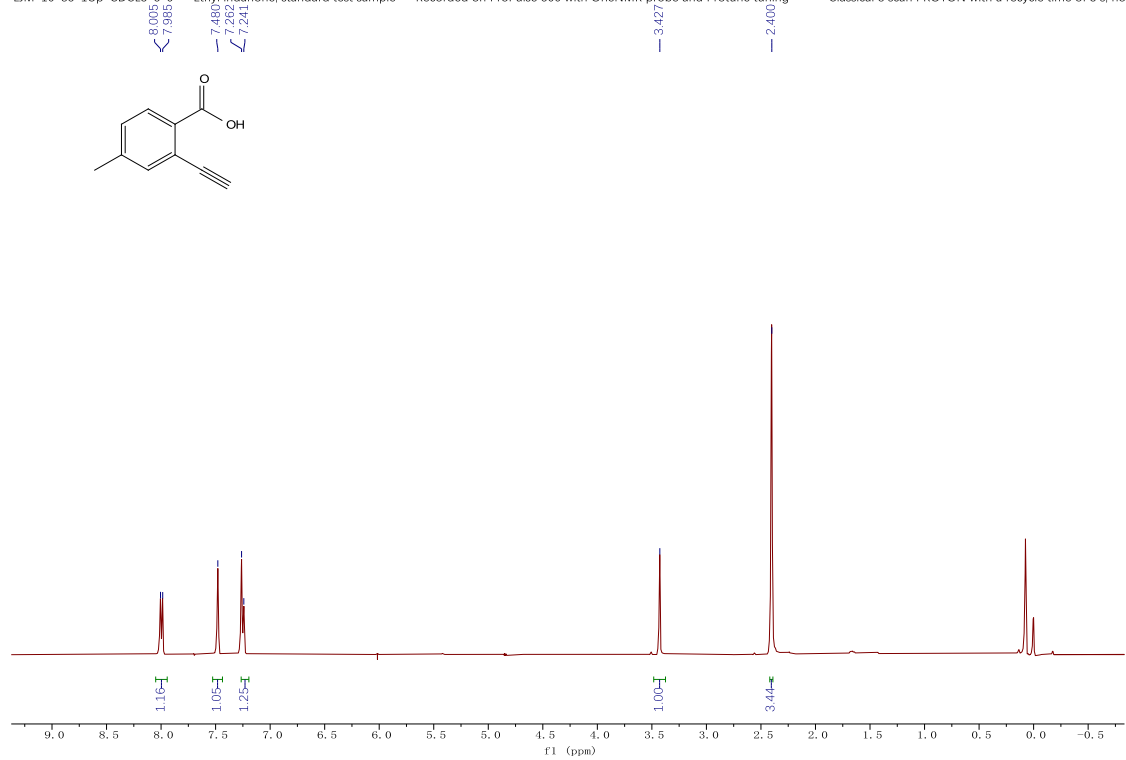


¹³C NMR spectrum of compound 1c (150 MHz, CDCl₃):

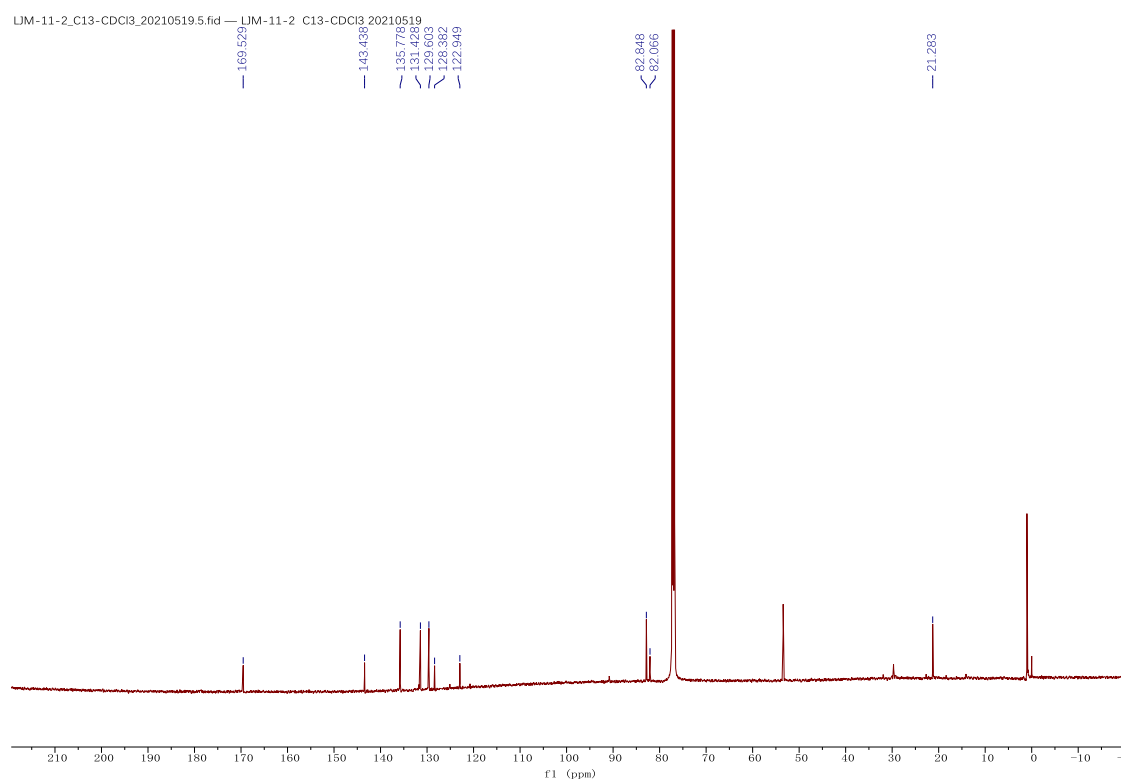


¹H NMR spectrum of compound 1d (400 MHz, CDCl₃):

LJM-10-85-1Up-CDCl3-5-9 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, no

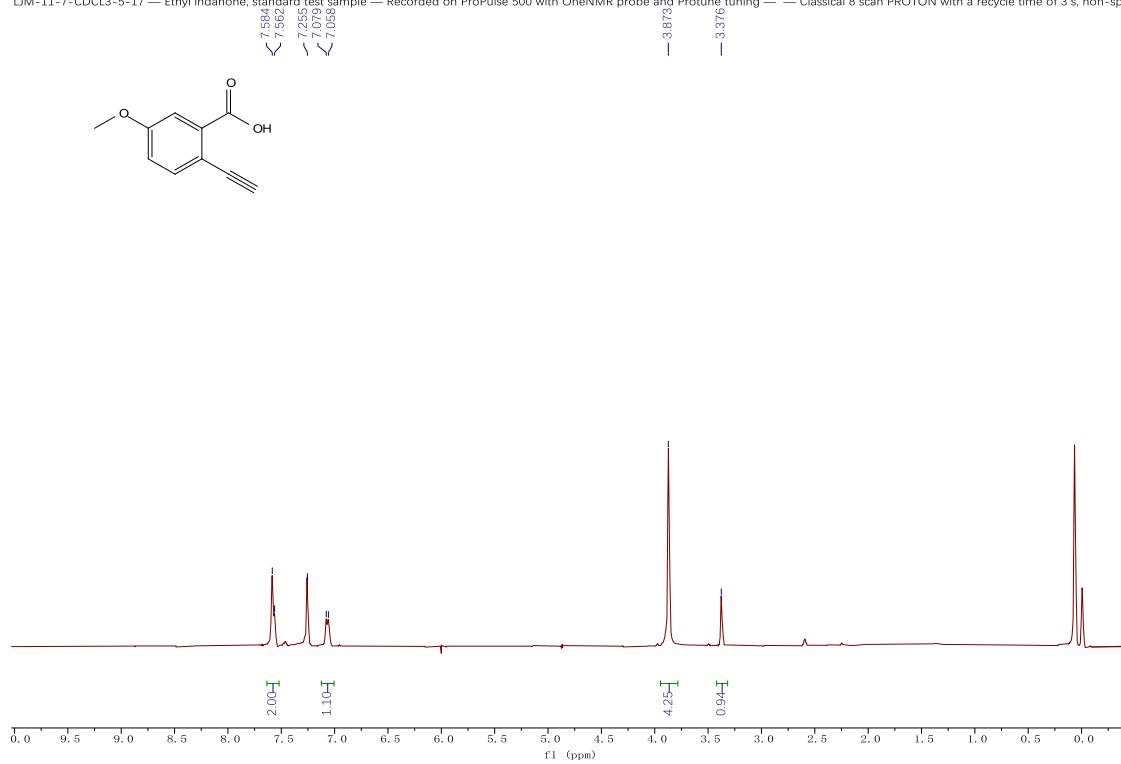


¹³C NMR spectrum of compound 1d (150 MHz, CDCl₃):

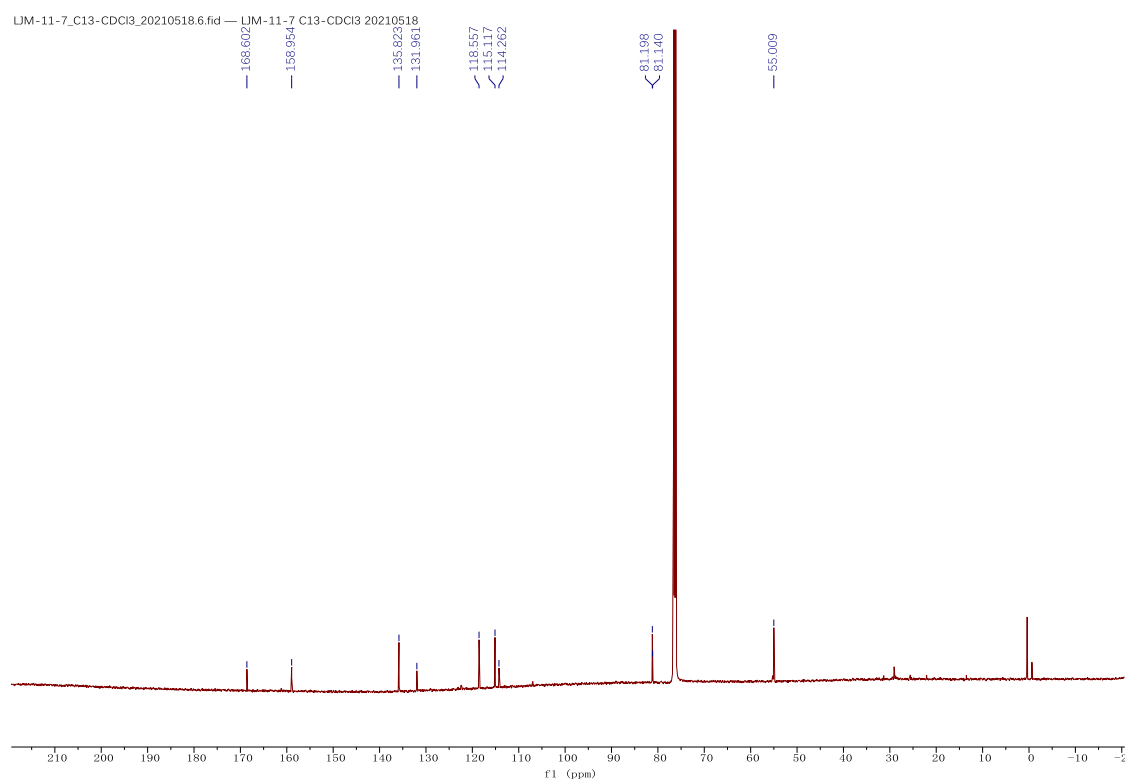


¹H NMR spectrum of compound 1e (400 MHz, CDCl₃):

LJM-11-7-CDCl3-5-17 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi

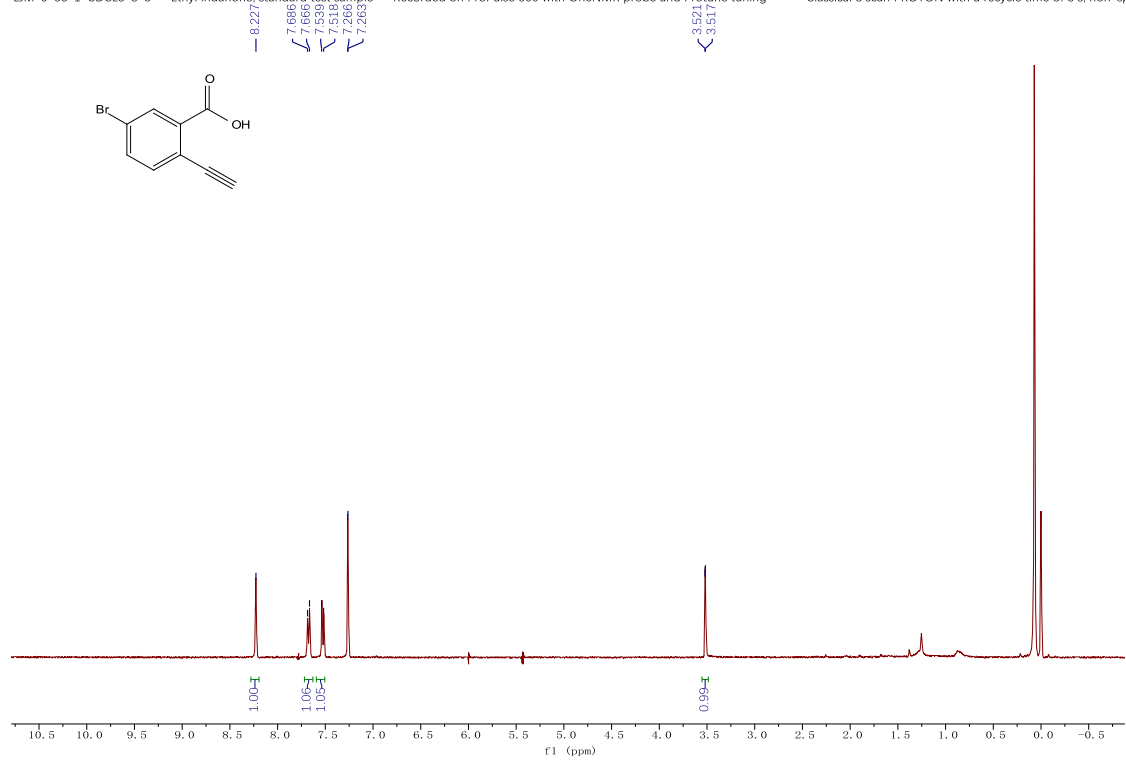


¹³C NMR spectrum of compound 1e (150 MHz, CDCl₃):

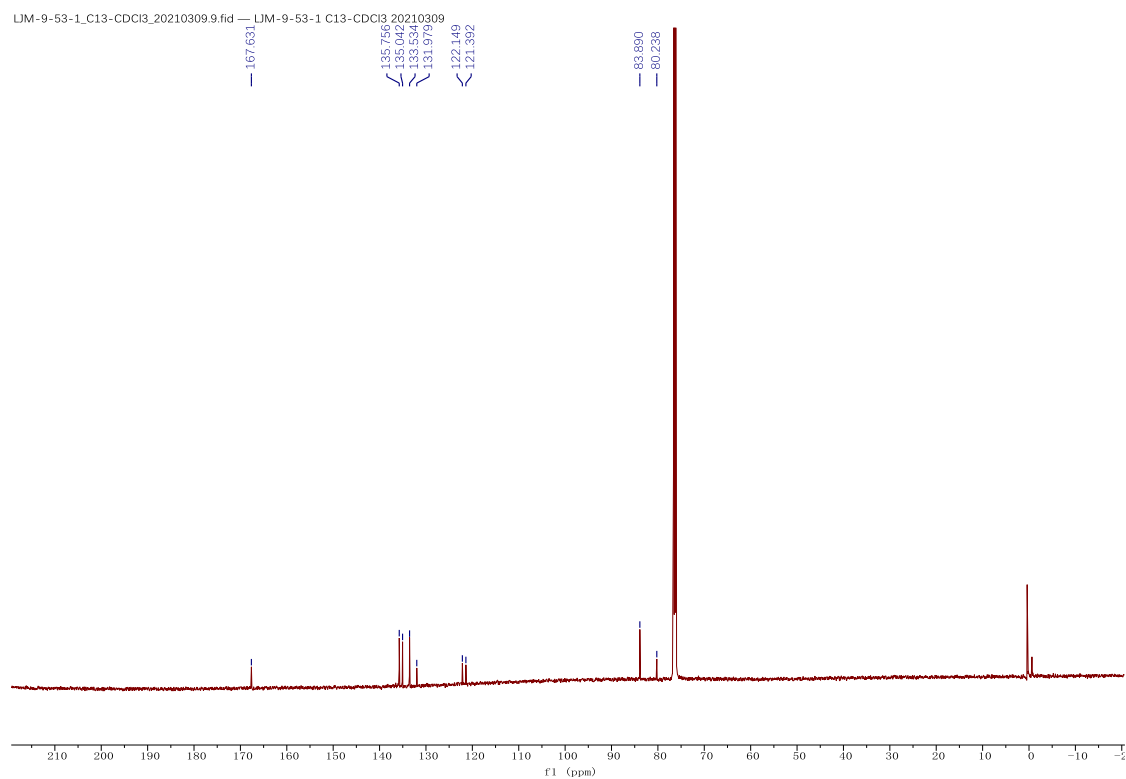


¹H NMR spectrum of compound 1f (400 MHz, CDCl₃):

LJM-9-53-1-CDCL3-3-3 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq

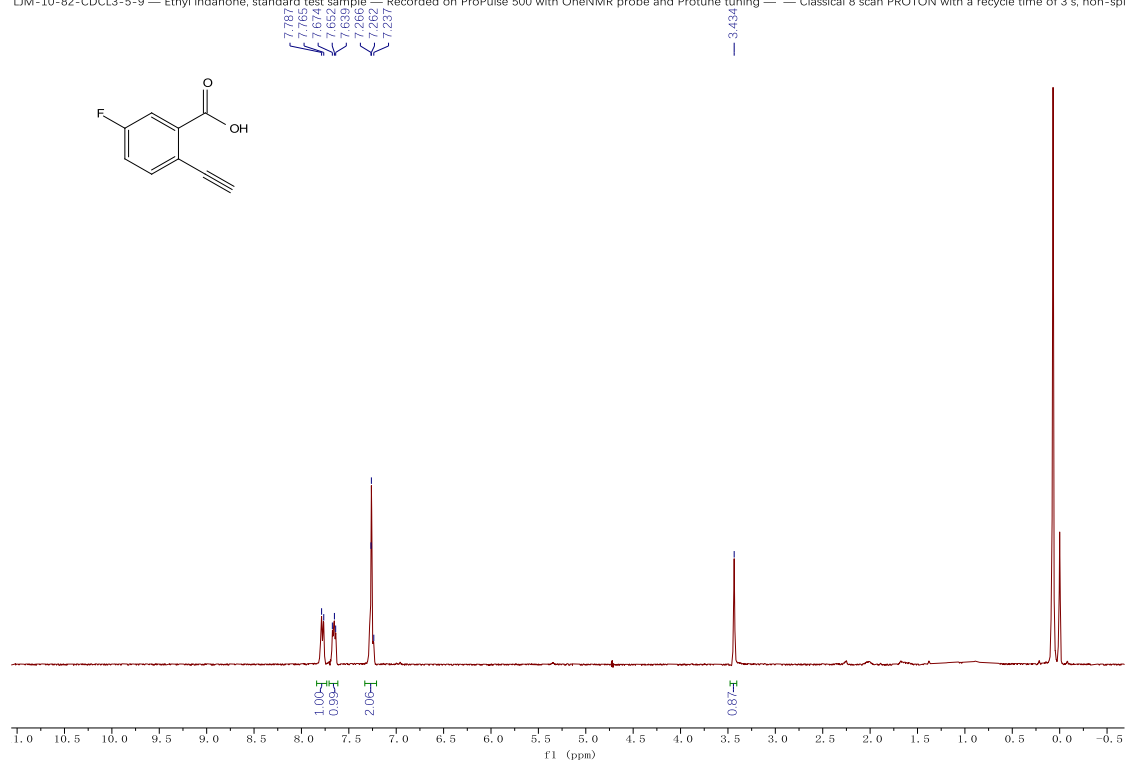


¹³C NMR spectrum of compound 1f (150 MHz, CDCl₃):

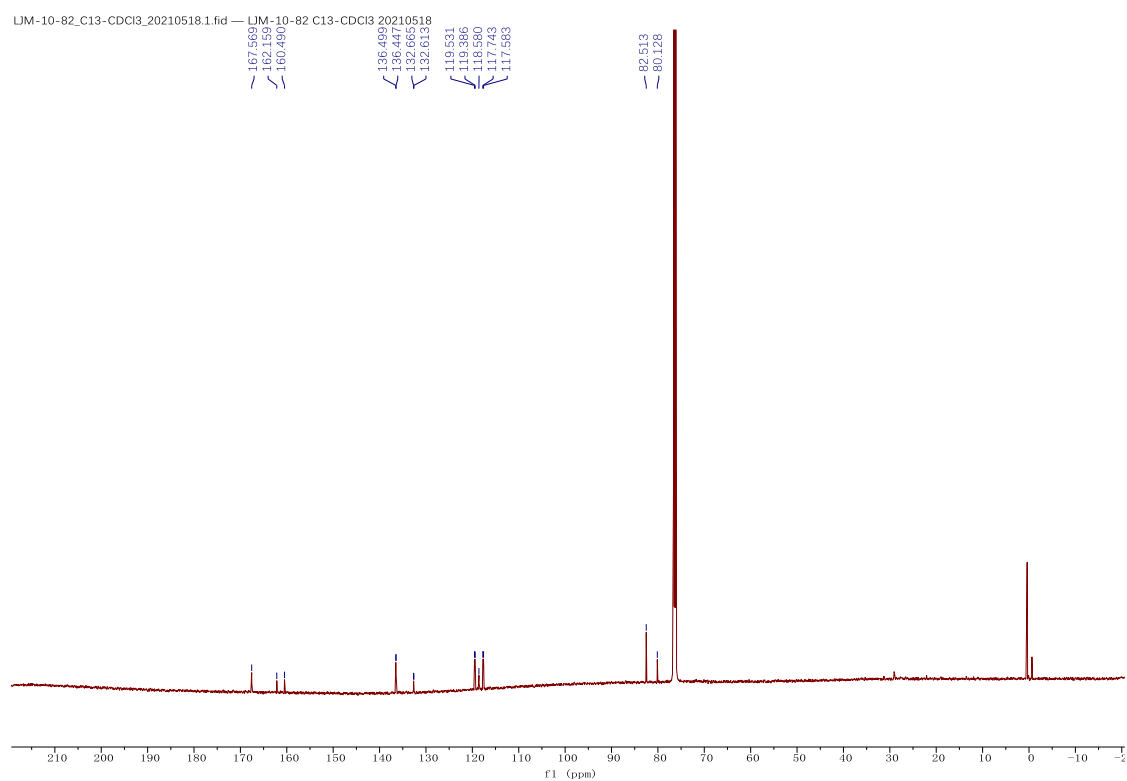


¹H NMR spectrum of compound 1g (400 MHz, CDCl₃):

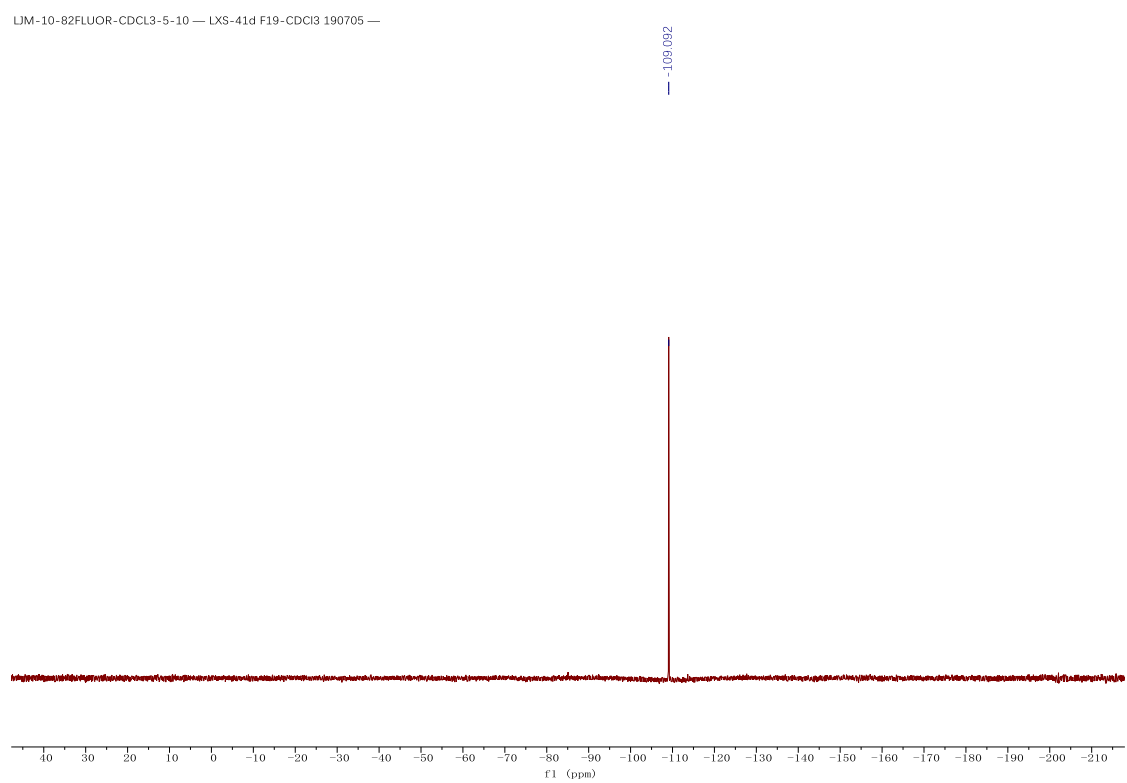
LJM-10-82-CDCl3-5-9 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



¹³C NMR spectrum of compound 1g (150 MHz, CDCl₃):

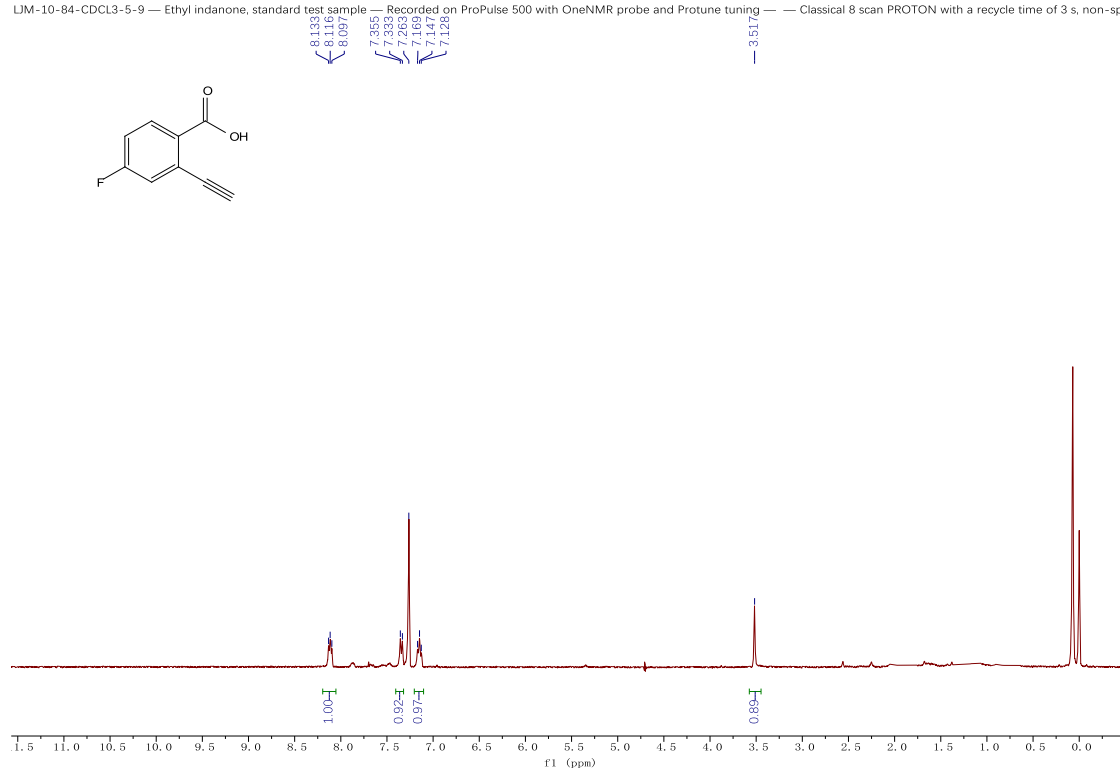


¹⁹F NMR spectrum of compound 1g (376 MHz, CDCl₃):



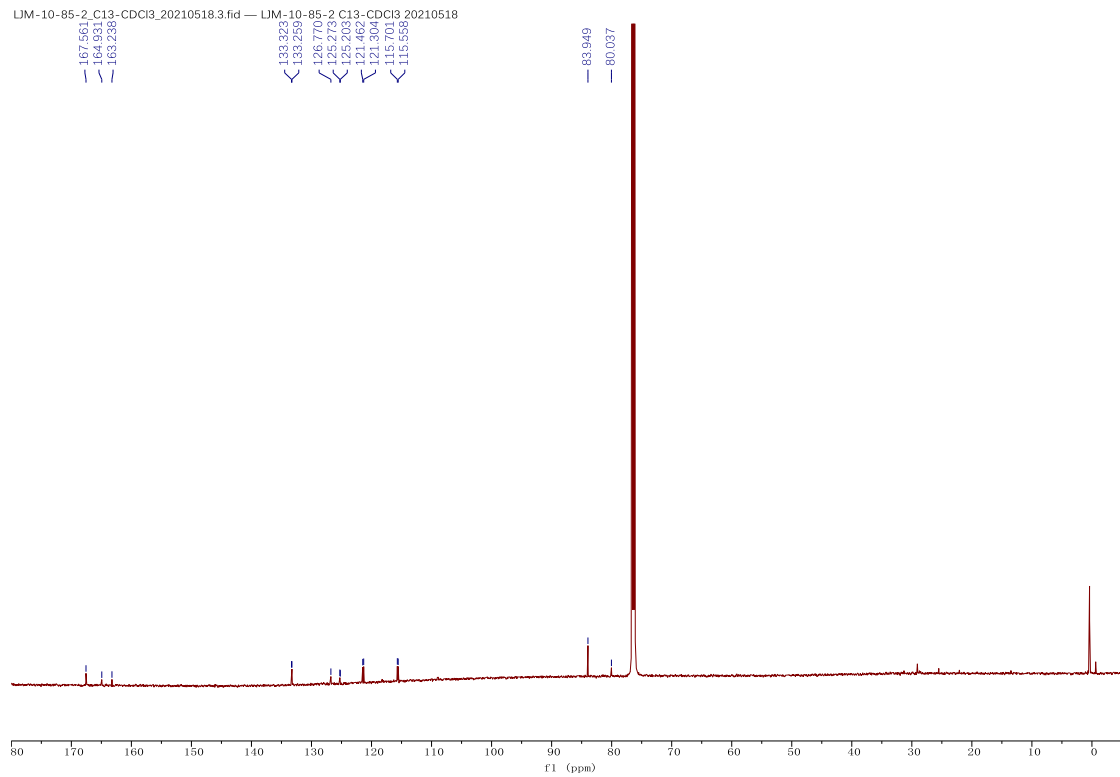
¹H NMR spectrum of compound 1h (400 MHz, CDCl₃):

LJM-10-84-CDCl3-5-9 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-spi



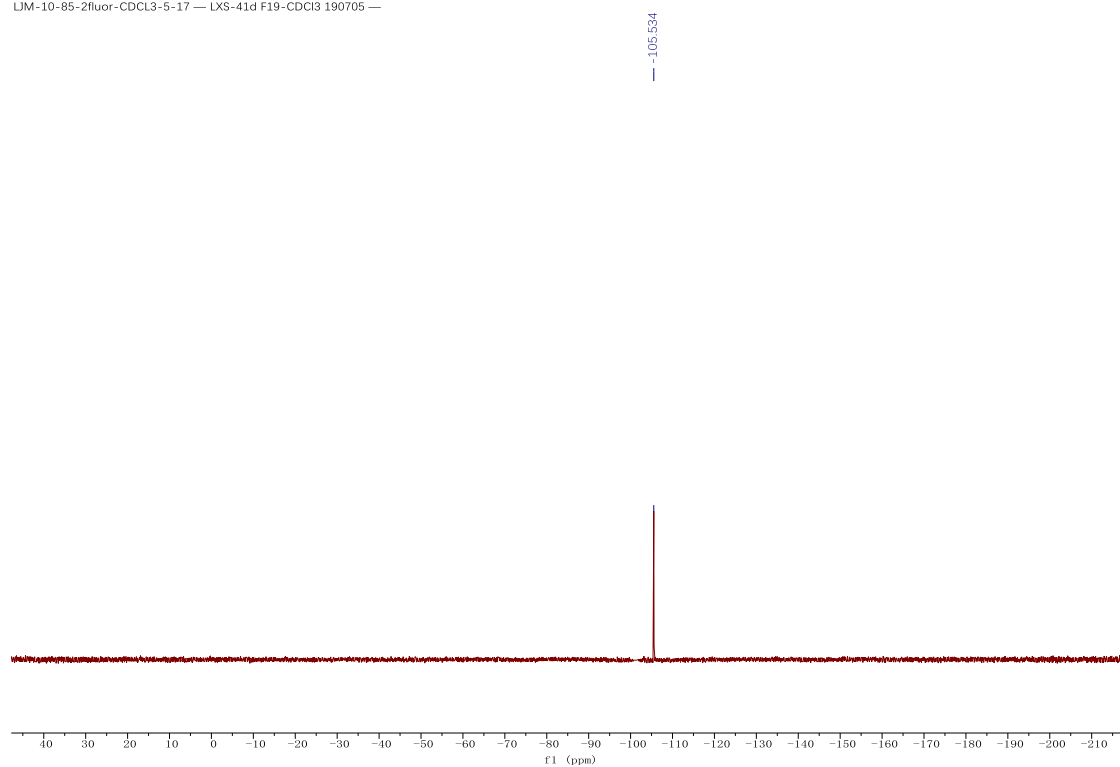
¹³C NMR spectrum of compound 1h (150 MHz, CDCl₃):

LJM-10-85-2_C13-CDCl3_20210518.3.fid — LJM-10-85-2_C13-CDCl3_20210518



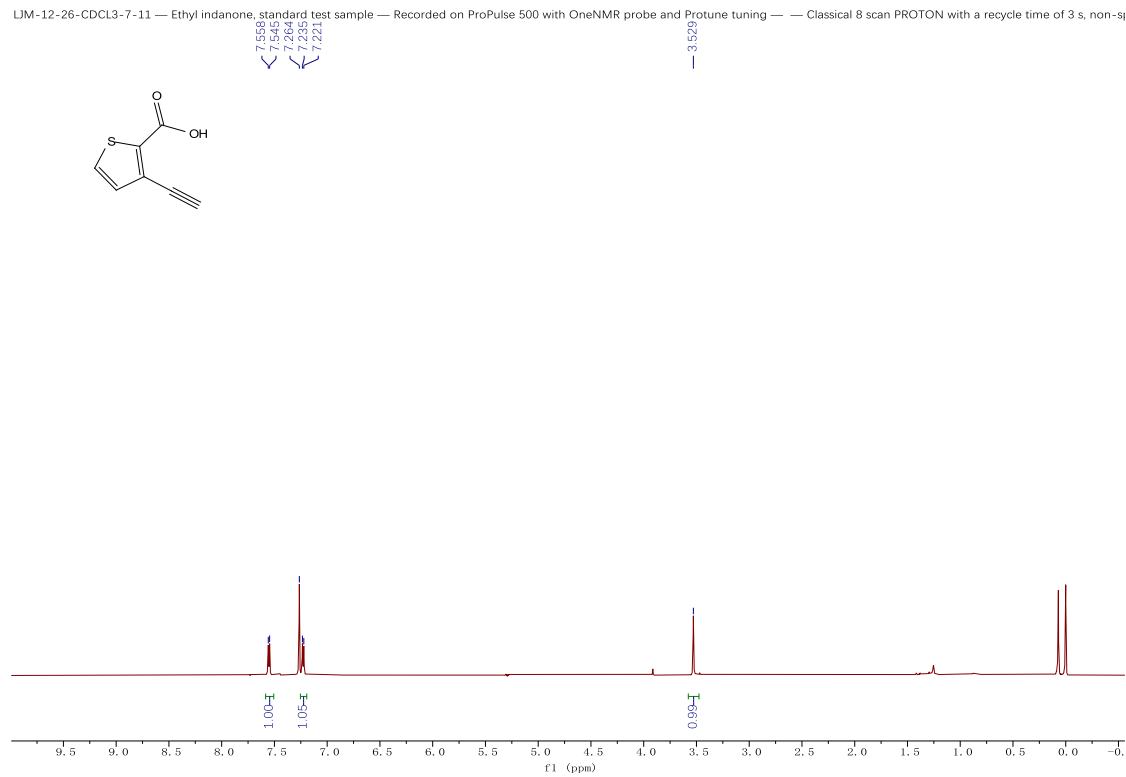
¹⁹F NMR spectrum of compound 1h (376 MHz, CDCl₃):

LJM-10-85-2fluor-CDCl₃-5-17 — LXS-41d F19-CDCl₃ 190705 —

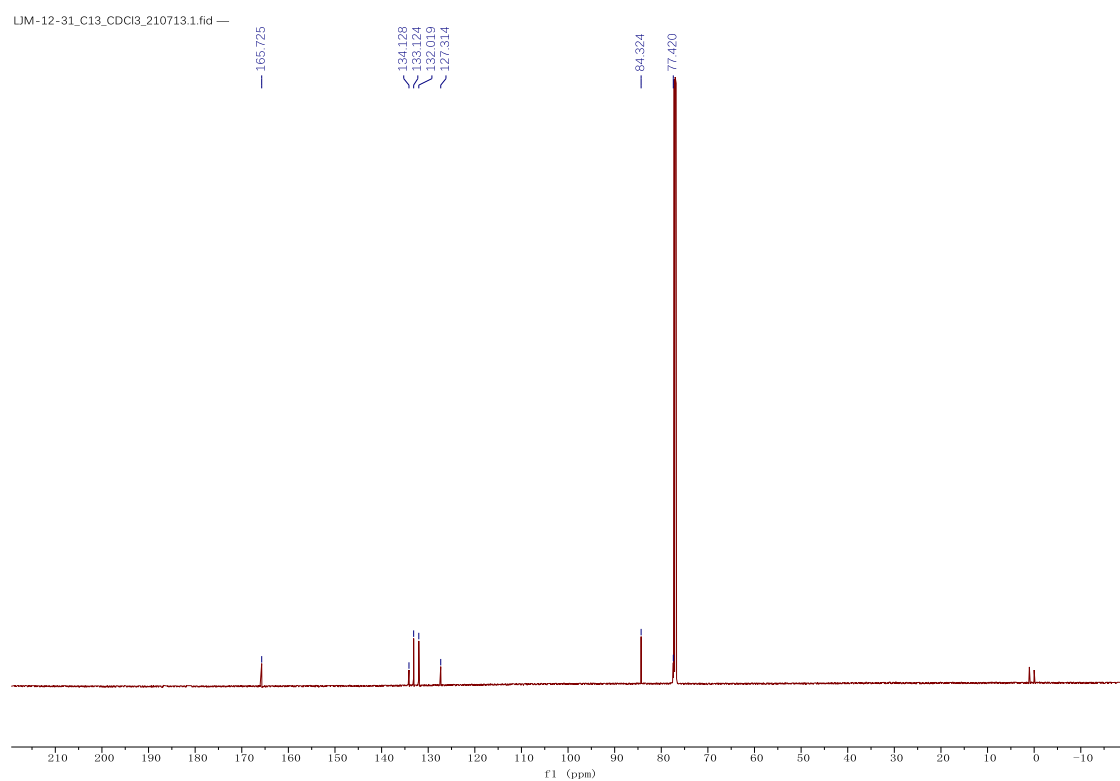


¹H NMR spectrum of compound 1i (400 MHz, CDCl₃):

LJM-12-26-CDCl₃-7-11 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-sq

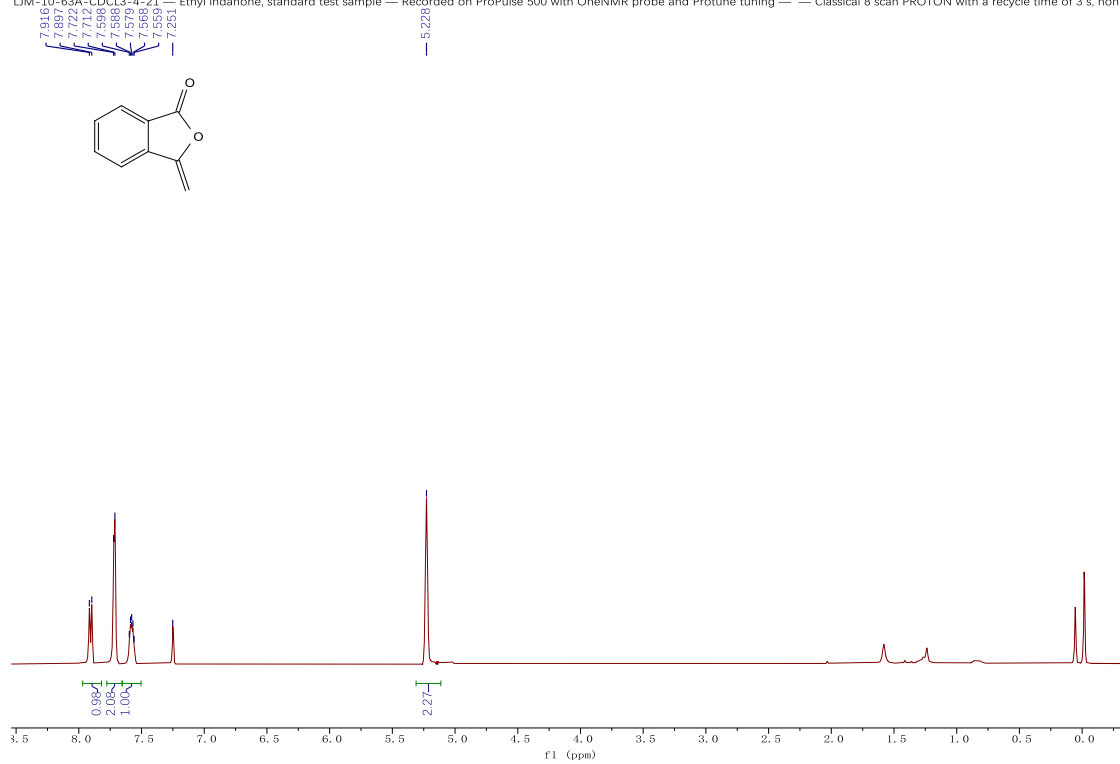


¹³C NMR spectrum of compound 1i (150 MHz, CDCl₃):

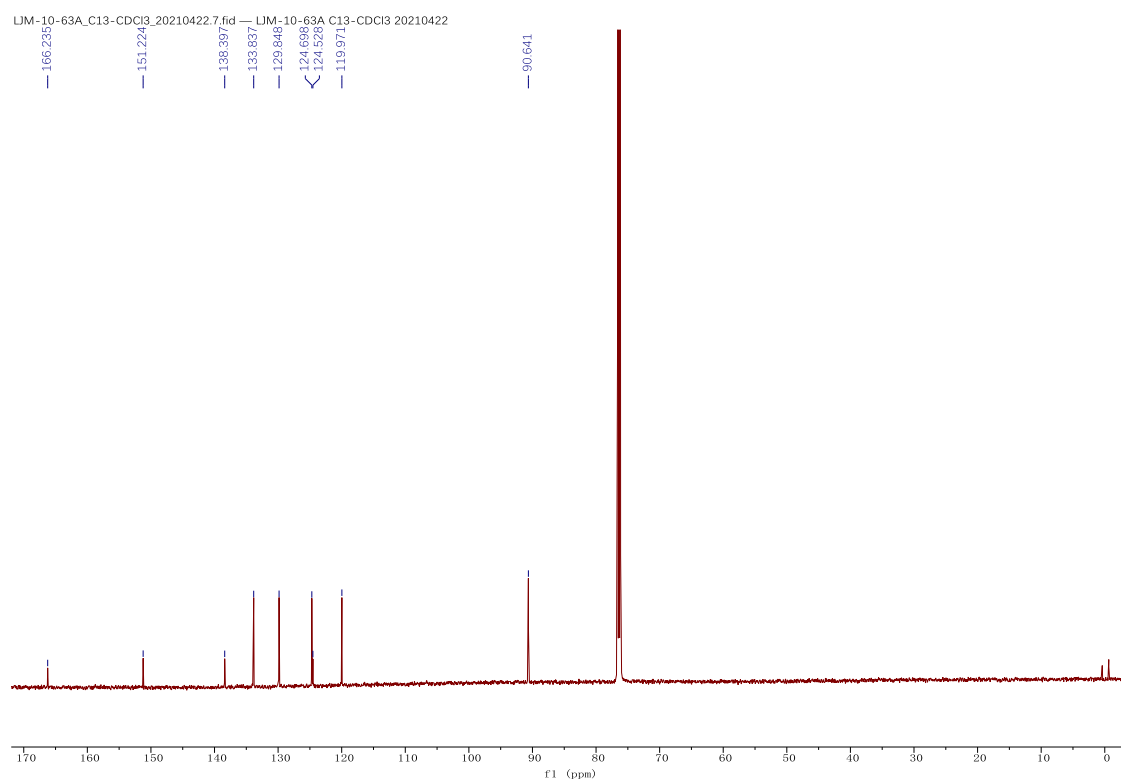


¹H NMR spectrum of compound I (400 MHz, CDCl₃):

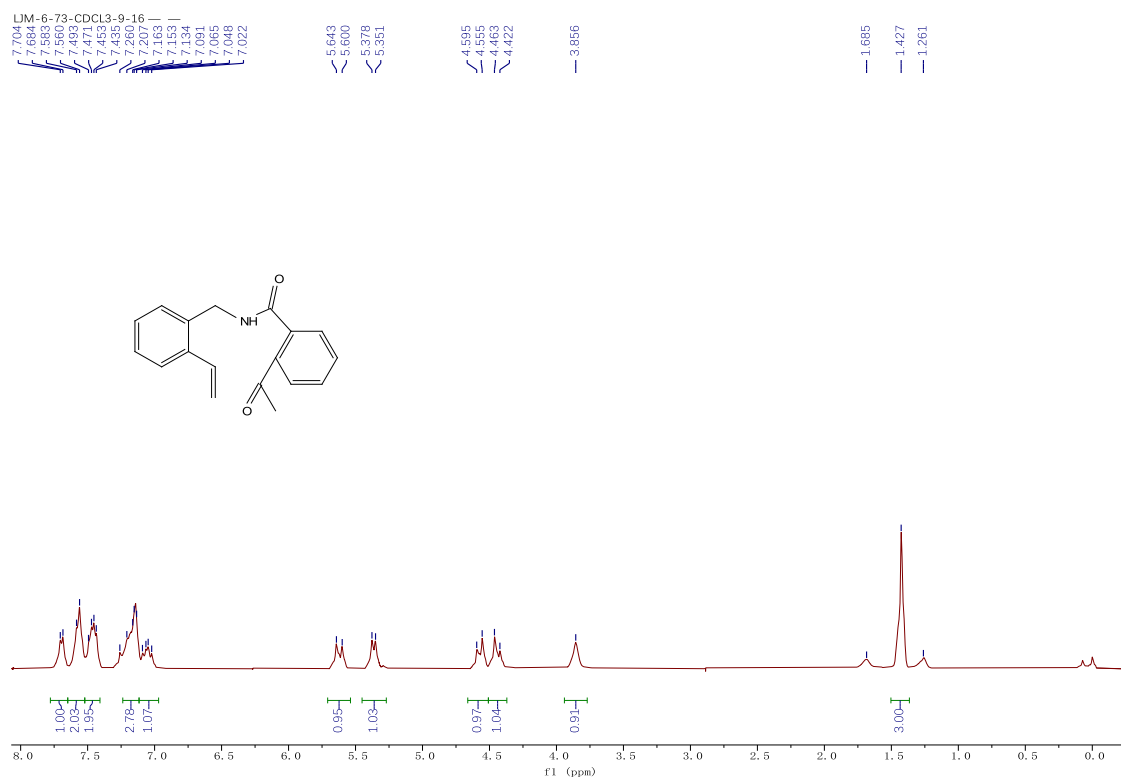
LJM-10-63A-CDCl3-4-21 — Ethyl indanone, standard test sample — Recorded on ProPulse 500 with OneNMR probe and Protune tuning — Classical 8 scan PROTON with a recycle time of 3 s, non-



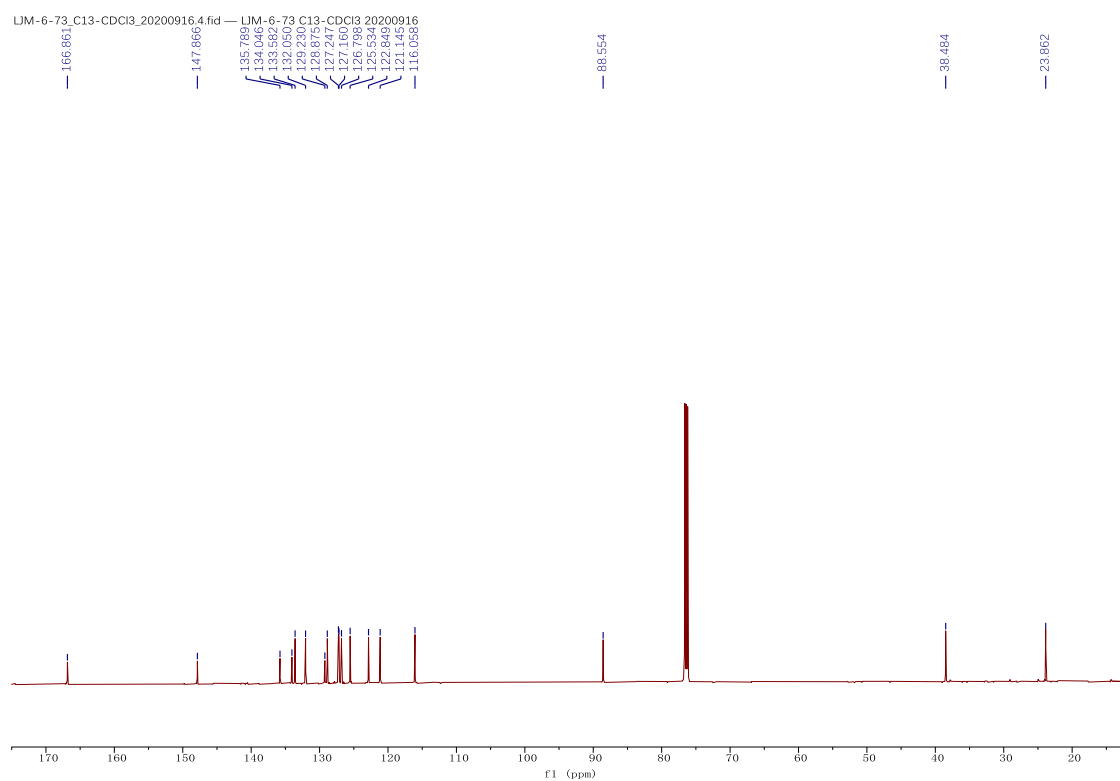
¹³C NMR spectrum of compound I (150 MHz, CDCl₃):



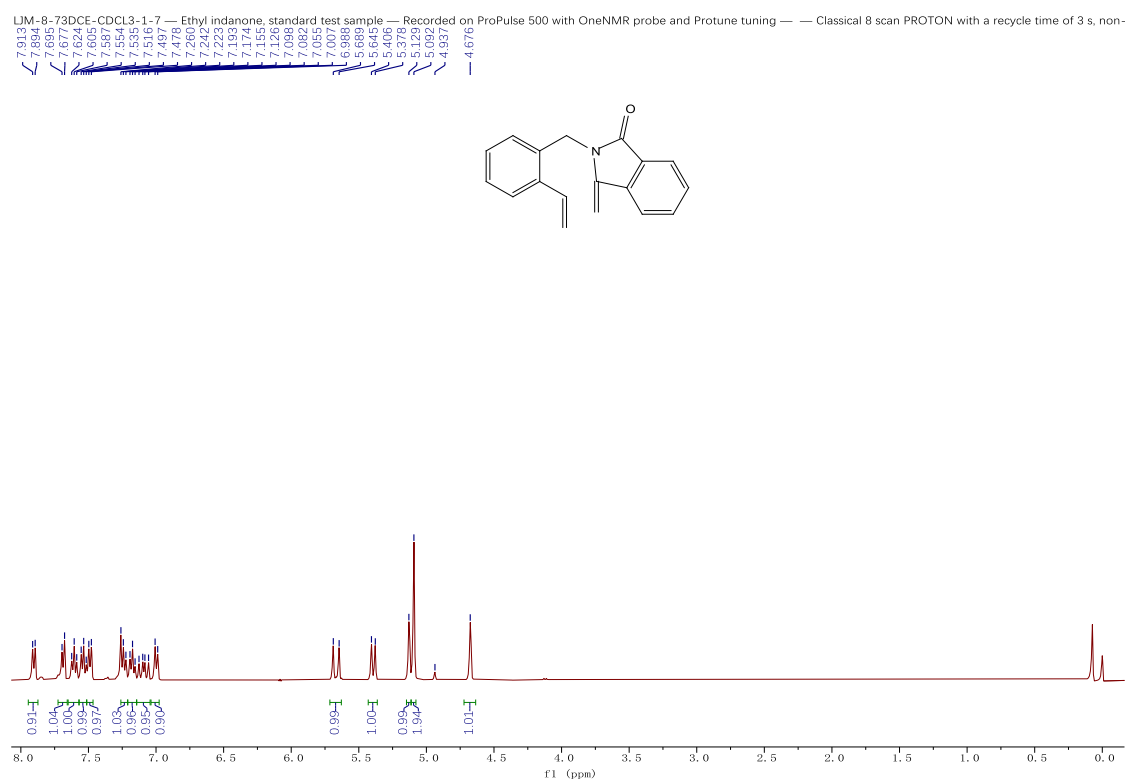
¹H NMR spectrum of compound II (400 MHz, CDCl₃):



¹³C NMR spectrum of compound II (150 MHz, CDCl₃):



¹H NMR spectrum of compound III (400 MHz, CDCl₃):



¹³C NMR spectrum of compound III (150 MHz, CDCl₃):

LJM-6-47_C13-CDCl3_20200916.2.fid — LJM-6-47_C13-CDCl3_20200916

