

Supporting Information

Rhodium(III)-catalyzed oxidative annulation of isoquinolones with allyl alcohols: synthesis of isoindolo[2,1-*b*]isoquinolin-5(7*H*)-ones

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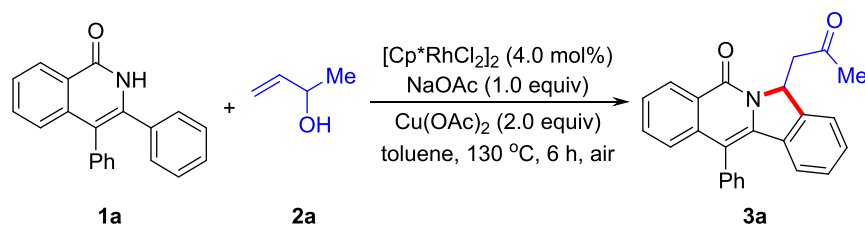
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1. General information

All reactions were carried out without any particular precautions to extrude moisture or oxygen. The NMR spectra were recorded on the Bruker spectrometer in CDCl₃ at room temperature. ¹H NMR (600 MHz) chemical shifts (δ) were referenced to internal standard TMS ($\delta = 0.00$ ppm), and ¹³C{¹H} NMR (151 MHz) chemical shifts were referenced to internal solvent CDCl₃ ($\delta = 77.16$ ppm) and chemical shifts are reported as parts per million (ppm). The high-resolution mass spectrometric data was recorded on Waters Synapt G2 Si tandem mass spectrometer with electron spray ionization (ESI) source. Products were purified by flash column chromatography on silica gel (200-300 mesh) with freshly distilled ethyl acetate (EA) and petroleum ether (PE). But-3-en-2-ol **2a** is a commercial material, isoquinolones **1**,¹ and allyl alcohols **2b-2n**² were prepared according to the reported procedures. Other reagents and solvents were obtained from commercial suppliers and used without further purification unless otherwise noted.

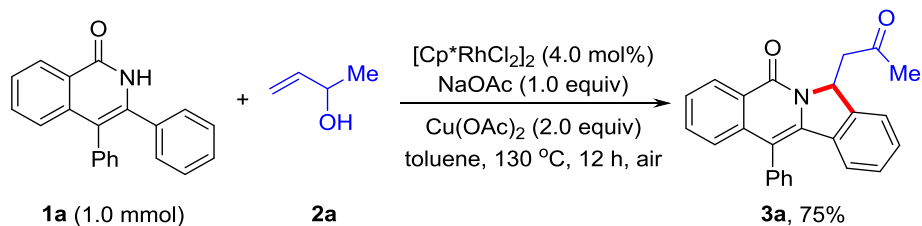
2. General procedure for the synthesis of isoindoloisoquinolones 3



To an oven-dried sealed tube charged with isoquinolone **1a** (59.4 mg, 0.2 mmol), [Cp*RhCl₂]₂ (5 mg, 4 mol%), NaOAc (16.4 mg, 0.2 mmol), and Cu(OAc)₂ (73 mg, 0.4 mmol) were added but-3-en-2-ol **2a** (22 mg, 0.3 mmol) and toluene (1 mL) at room temperature. The reaction mixture was allowed to stir in an oil bath at 130 °C under air for 6 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 4:1) to afford 62.8 mg of **3a** in 86% yield as a yellow solid.

3. Scale-up experiment and one-pot synthesis of isoindoloisoquinolones

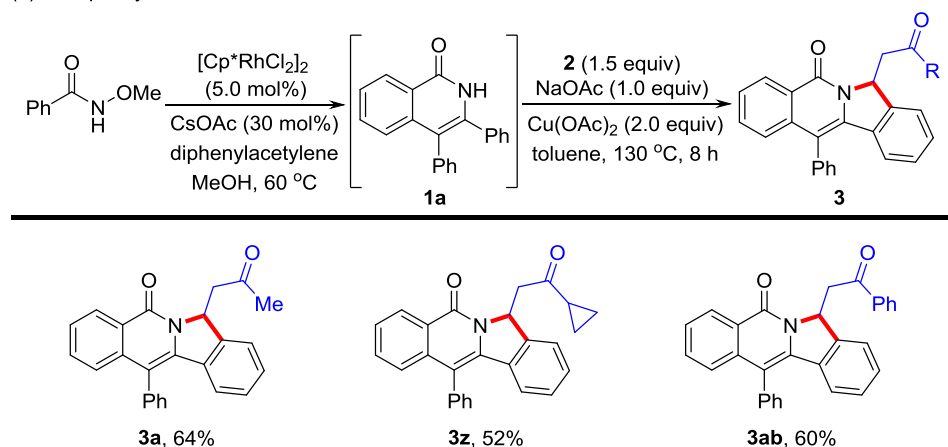
(a) Scale-up synthesis of **3a**



To an oven-dried sealed tube charged with isoquinolone **1a** (297 mg, 1.0 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (25 mg, 4 mol%), NaOAc (82 mg, 1.0 mmol), and $\text{Cu}(\text{OAc})_2$ (364 mg, 2.0 mmol) were added but-3-en-2-ol **2a** (108 mg, 1.5 mmol) and toluene (5 mL) at room temperature. The reaction mixture was allowed to stir in an oil bath at 130 °C under air for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 4:1) to afford 274 mg of **3a** in 75% yield as a yellow solid.

(b) One-pot synthesis of **3** from *N*-methoxybenzamides

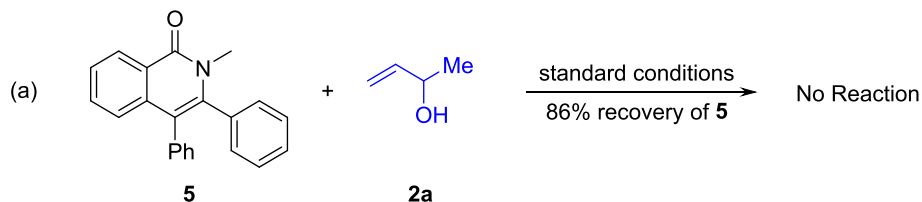
(b) One-pot synthesis



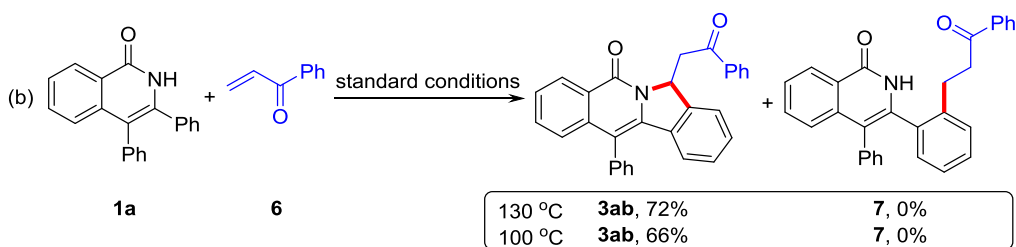
To an oven-dried sealed tube charged with *N*-methoxybenzamide (30.2 mg, 0.2 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (6 mg, 5 mol%), CsOAc (12 mg, 30 mol%), and diphenylacetylene (40 mg, 0.22 mmol) were added methanol (1 mL) at room temperature. The reaction mixture was allowed to stir in an oil bath at 60 °C under air for 14 h. After removal of methanol under reduced pressure, NaOAc (16.4 mg, 0.2 mmol), $\text{Cu}(\text{OAc})_2$ (73 mg, 0.4 mmol), but-3-en-2-ol **2a** (22 mg, 0.3 mmol), and toluene (1 mL) were added. The reaction mixture was allowed to stir in an oil bath at 130 °C under air for 8 h. After completion of the reaction, the reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and

concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 4:1) to afford 46.7 mg of **3a** in 64% yield as a yellow solid.

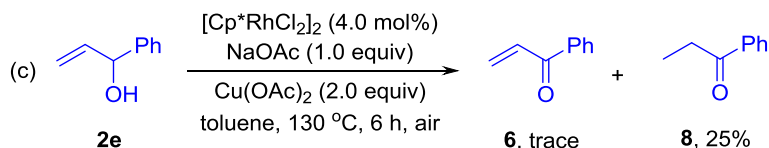
4. Mechanistic studies



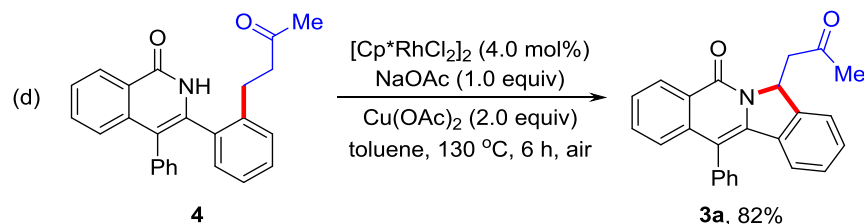
To an oven-dried sealed tube charged with *N*-methyl substituted isoquinolone **5** (63 mg, 0.2 mmol), [Cp**RhCl*₂]₂ (5 mg, 4 mol%), NaOAc (16.4 mg, 0.2 mmol), and Cu(OAc)₂ (73 mg, 0.4 mmol) were added but-3-en-2-ol **2a** (22 mg, 0.3 mmol) and toluene (1 mL) at room temperature. The reaction mixture was allowed to stir in an oil bath at 130 °C under air for 6 h. After isolation and purification, *N*-methyl substituted isoquinolone **5** was recovered in 86%, showing that the relatively acidic NH in **1a** plays a pivotal role in aryl C-H activation.



To an oven-dried sealed tube charged with isoquinolone **1a** (59.4 mg, 0.2 mmol), [Cp**RhCl*₂]₂ (5 mg, 4 mol%), NaOAc (16.4 mg, 0.2 mmol), and Cu(OAc)₂ (73 mg, 0.4 mmol) were added phenyl vinyl ketone **6** (40 mg, 0.3 mmol) and toluene (1 mL) at room temperature. The reaction mixture was allowed to stir in an oil bath at 130 °C under air for 6 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 4:1) to afford 61.5 mg of **3ab** in 72% yield as a yellow solid (56.4 mg of **3ab** in 66% yield at 100 °C).



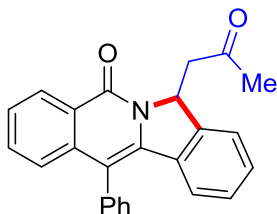
To an oven-dried sealed tube charged with $[\text{Cp}^*\text{RhCl}_2]_2$ (5 mg, 4 mol%), NaOAc (16.4 mg, 0.2 mmol), and Cu(OAc)_2 (73 mg, 0.4 mmol) were added 1-phenylprop-2-en-1-ol **2e** (40 mg, 0.3 mmol) and toluene (1 mL) at room temperature. The reaction mixture was allowed to stir in an oil bath at 130 °C under air for 6 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 20:1) to afford 10 mg of **8** in 25% yield as a colorless oil.



To an oven-dried sealed tube charged with the C-H alkylated product **4** (74 mg, 0.2 mmol), $[\text{Cp}^*\text{RhCl}_2]_2$ (5 mg, 4 mol%), NaOAc (16.4 mg, 0.2 mmol), and Cu(OAc)_2 (73 mg, 0.4 mmol) were added toluene (1 mL) at room temperature. The reaction mixture was allowed to stir in an oil bath at 130 °C under air for 6 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA = 4:1) to afford 60 mg of **3a** in 82% yield as a yellow solid.

5. Characterization data of products

7-(2-Oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3a)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 86% yield;

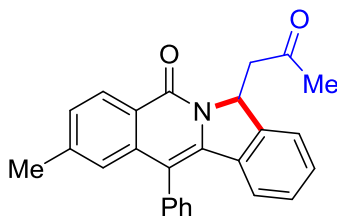
M.p. = 196-197 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.52 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.62-7.55 (m, 4H), 7.53-7.48 (m, 2H), 7.46-7.43 (m, 1H), 7.37-7.34 (m, 1H), 7.32-7.29 (m, 1H), 7.21 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.07 (dd, *J* = 8.2, 7.1 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 6.07 (dd, *J* = 8.3, 3.2 Hz, 1H), 4.02 (dd, *J* = 17.7, 3.2 Hz, 1H), 2.89 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.22 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.9, 161.0, 142.7, 138.9, 138.1, 135.3, 133.4, 132.3, 131.2, 131.1, 129.70, 129.66, 129.6, 128.6, 128.4, 127.4, 126.5, 125.4, 124.8, 124.1, 123.4, 114.7, 59.6, 45.9, 30.6;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₅H₁₉NNaO₂ 388.1308; Found 388.1312.

2-Methyl-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3b)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 77% yield;

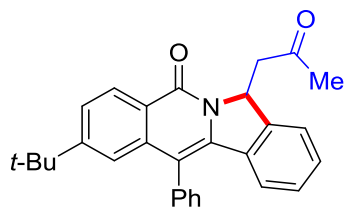
M.p. = 188-189 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.39 (d, *J* = 8.1 Hz, 1H), 7.62-7.56 (m, 3H), 7.51-7.49 (m, 1H), 7.45-7.42 (m, 1H), 7.36-7.34 (m, 1H), 7.31-7.26 (m, 2H), 7.07-7.03 (m, 1H), 6.96 (s, 1H), 6.33 (d, *J* = 8.0 Hz, 1H), 6.04 (dd, *J* = 8.3, 3.2 Hz, 1H), 4.01 (dd, *J* = 17.7, 3.2 Hz, 1H), 2.87 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.36 (s, 3H), 2.21 (s, 3H);

^{13}C NMR (151 MHz, CDCl_3): δ 205.9, 160.8, 142.8, 142.7, 138.9, 138.1, 135.4, 133.4, 131.2, 131.1, 129.6, 129.51, 129.50, 128.5, 128.3, 128.1, 127.3, 125.0, 123.9, 123.3, 122.6, 114.5, 59.4, 45.9, 30.5, 22.0;

HRMS (ESI) m/z: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{26}\text{H}_{21}\text{NNaO}_2$ 402.1465; Found 402.1473.

2-(*Tert*-butyl)-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3c)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a light-yellow solid in 73% yield;

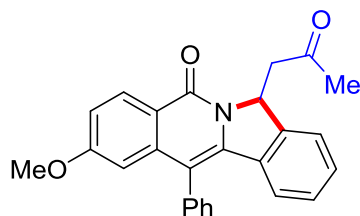
M.p. = 231-232 °C;

^1H NMR (600 MHz, CDCl_3): δ 8.44 (d, J = 8.4 Hz, 1H), 7.62-7.55 (m, 4H), 7.51 (dd, J = 7.7, 1.1 Hz, 1H), 7.46-7.44 (m, 1H), 7.37-7.34 (m, 1H), 7.31-7.28 (m, 1H), 7.17 (d, J = 1.8 Hz, 1H), 7.08-7.06 (m, 1H), 6.38 (d, J = 8.0 Hz, 1H), 6.06 (dd, J = 8.3, 3.2 Hz, 1H), 4.01 (dd, J = 17.6, 3.2 Hz, 1H), 2.87 (dd, J = 17.6, 8.3 Hz, 1H), 2.22 (s, 3H), 1.24 (s, 9H);

^{13}C NMR (151 MHz, CDCl_3): δ 205.9, 155.7, 142.7, 138.8, 138.0, 135.4, 133.5, 131.2, 131.1, 129.6, 129.5, 128.5, 128.3, 127.1, 124.7, 124.0, 123.4, 122.7, 121.4, 115.1, 59.5, 46.0, 35.4, 31.1, 30.6 (overlapped);

HRMS (ESI) m/z: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{29}\text{H}_{27}\text{NNaO}_2$ 444.1934; Found 444.1933.

2-Methoxy-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3d)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/2) as a yellow solid in 83% yield;

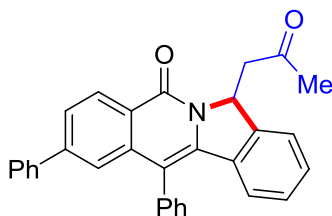
M.p. = 172-173 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.42 (d, *J* = 8.8 Hz, 1H), 7.60-7.54 (m, 3H), 7.51-7.48 (m, 1H), 7.44-7.42 (m, 1H), 7.36-7.33 (m, 1H), 7.30-7.27 (m, 1H), 7.07-7.03 (m, 2H), 6.54 (d, *J* = 2.5 Hz, 1H), 6.36-6.32 (m, 1H), 6.02 (dd, *J* = 8.3, 3.2 Hz, 1H), 4.01 (dd, *J* = 17.6, 3.2 Hz, 1H), 3.71 (s, 3H), 2.86 (dd, *J* = 17.6, 8.3 Hz, 1H), 2.21 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.9, 162.8, 160.6, 142.9, 140.9, 138.6, 135.3, 133.3, 131.1, 131.0, 129.63, 129.61, 129.6, 129.4, 128.6, 128.3, 124.0, 123.4, 118.8, 115.2, 114.3, 107.1, 59.4, 55.4, 46.0, 30.5;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₆H₂₁NNaO₃ 418.1414; Found 418.1401.

7-(2-Oxopropyl)-2,12-diphenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3e)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 65% yield;

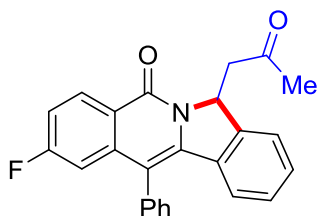
M.p. = 202-203 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.58 (d, *J* = 8.3 Hz, 1H), 7.72 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.63-7.56 (m, 3H), 7.54-7.48 (m, 4H), 7.42-7.39 (m, 4H), 7.36-7.34 (m, 1H), 7.33-7.30 (m, 1H), 7.10-7.06 (m, 1H), 6.38 (d, *J* = 8.0 Hz, 1H), 6.09 (dd, *J* = 8.3, 3.2 Hz, 1H), 4.04 (dd, *J* = 17.7, 3.2 Hz, 1H), 2.91 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.24 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.9, 160.8, 145.1, 142.8, 140.5, 139.3, 138.5, 135.2, 133.4, 131.2, 131.1, 129.73, 129.68, 129.0, 128.7, 128.4, 128.1, 128.0, 127.6, 125.8, 124.1, 123.8, 123.6, 123.4, 114.8, 59.6, 45.9, 30.6 (overlapped);

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₃₁H₂₃NNaO₂ 464.1621; Found 464.1614.

2-Fluoro-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3f)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 74% yield;

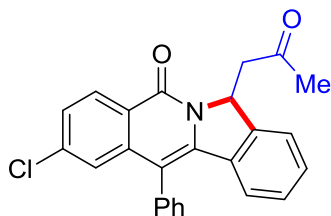
M.p. = 158-159 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.48 (dd, *J* = 8.8, 5.8 Hz, 1H), 7.61-7.55 (m, 3H), 7.50 (d, *J* = 7.7 Hz, 1H), 7.43-7.40 (m, 1H), 7.35-7.28 (m, 2H), 7.16-7.12 (m, 1H), 7.08-7.05 (m, 1H), 6.80 (dd, *J* = 10.4, 2.5 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 6.02 (dd, *J* = 8.3, 3.2 Hz, 1H), 3.98 (dd, *J* = 17.7, 3.2 Hz, 1H), 2.89 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.21 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.7, 165.36 (d, *J* = 251.9 Hz), 160.2, 142.9, 141.35 (d, *J* = 9.9 Hz), 139.4, 134.7, 133.0, 131.1, 130.9, 130.4 (d, *J* = 10.0 Hz), 130.0, 129.8, 129.7, 128.8, 128.4, 124.2, 123.3, 121.4, 114.9 (d, *J* = 23.7 Hz), 113.9 (d, *J* = 3.4 Hz), 110.3 (d, *J* = 23.2 Hz), 59.6, 45.7, 30.5;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₅H₁₈FNNaO₂ 406.1214; Found 406.1214.

2-Chloro-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3g)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 58% yield;

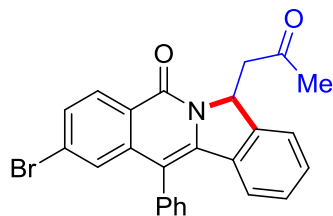
M.p. = 195-196 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.43 (d, *J* = 8.5 Hz, 1H), 7.63-7.59 (m, 3H), 7.53-7.50 (m, 1H), 7.44-7.40 (m, 2H), 7.35-7.30 (m, 2H), 7.15 (d, *J* = 2.0 Hz, 1H), 7.09-7.07 (m, 1H), 6.35 (d, *J* = 8.0 Hz, 1H), 6.04 (dd, *J* = 8.2, 3.2 Hz, 1H), 3.99 (dd, *J* = 17.7, 3.2 Hz, 1H), 2.89 (dd, *J* = 17.7, 8.2 Hz, 1H), 2.22 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.7, 160.4, 142.9, 140.3, 139.5, 139.0, 134.6, 133.1, 131.2, 131.0, 130.1, 129.9, 129.8, 129.2, 128.9, 128.5, 127.0, 124.6, 124.3, 123.4, 123.1, 113.7, 59.7, 45.7, 30.6;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₅H₁₈ClNNaO₂ 422.0918; Found 422.0919.

2-Bromo-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3h)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a white solid in 51% yield;

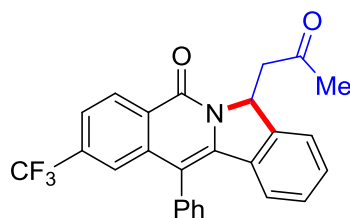
M.p. = 210-211 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.34 (d, *J* = 8.5 Hz, 1H), 7.63-7.58 (m, 3H), 7.56 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.51 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.44-7.41 (m, 1H), 7.35-7.29 (m, 3H), 7.09-7.06 (m, 1H), 6.34 (d, *J* = 8.0 Hz, 1H), 6.03 (dd, *J* = 8.3, 3.1 Hz, 1H), 3.98 (dd, *J* = 17.7, 3.1 Hz, 1H), 2.89 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.22 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.7, 160.5, 142.9, 140.4, 139.5, 134.5, 133.1, 131.2, 131.0, 130.1, 129.9, 129.8, 129.7, 129.2, 128.9, 128.5, 127.8, 127.7, 124.2, 123.44, 123.40, 113.6, 59.7, 45.7, 30.6;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₅H₁₉BrNO₂ 444.0594; Found 444.0593.

7-(2-Oxopropyl)-12-phenyl-2-(trifluoromethyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3i)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a light-yellow solid in 64% yield;

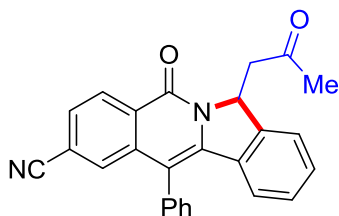
M.p. = 214-215 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.62 (d, *J* = 8.3 Hz, 1H), 7.67 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.65-7.60 (m, 3H), 7.52 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.47-7.43 (m, 2H), 7.37-7.32 (m, 2H), 7.12-7.07 (m, 1H), 6.37 (d, *J* = 8.0 Hz, 1H), 6.07 (dd, *J* = 8.2, 3.2 Hz, 1H), 3.99 (dd, *J* = 17.7, 3.2 Hz, 1H), 2.93 (dd, *J* = 17.7, 8.2 Hz, 1H), 2.23 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.6, 160.2, 142.8, 139.7, 139.0, 134.3, 134.0 (q, *J* = 32.4 Hz), 133.0, 131.2, 131.0, 130.2, 130.0, 129.9, 129.1, 128.6, 128.5, 126.7, 124.4, 123.8 (q, *J* = 273.3 Hz), 123.4, 122.48 (q, *J* = 4.1 Hz), 122.37 (q, *J* = 3.1 Hz), 114.3, 59.8, 45.6, 30.6;

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{19}F_3NO_2$ 434.1362; Found 434.1363.

5-Oxo-7-(2-oxopropyl)-12-phenyl-5,7-dihydroisoindolo[2,1-*b*]isoquinoline-2-carbonitrile (3j)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 66% yield;

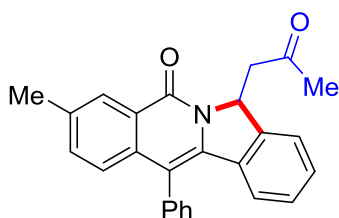
M.p. = 172-173 °C;

¹H NMR (600 MHz, $CDCl_3$): δ 8.57 (d, J = 8.2 Hz, 1H), 7.66-7.61 (m, 4H), 7.54-7.49 (m, 2H), 7.44-7.40 (m, 1H), 7.37-7.31 (m, 2H), 7.13-7.07 (m, 1H), 6.40 (d, J = 8.0 Hz, 1H), 6.04 (dd, J = 8.1, 3.0 Hz, 1H), 3.95 (dd, J = 17.8, 3.1 Hz, 1H), 2.93 (dd, J = 17.8, 8.2 Hz, 1H), 2.22 (s, 3H);

¹³C NMR (151 MHz, $CDCl_3$): δ 205.5, 159.8, 142.8, 140.2, 139.0, 133.8, 132.7, 131.1, 130.9, 130.4, 130.2, 130.1, 130.0, 129.3, 128.6, 128.5, 127.9, 126.8, 124.4, 123.4, 118.5, 115.8, 113.4, 59.9, 45.4, 30.5;

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{19}N_2O_2$ 391.1441; Found 391.1437.

3-Methyl-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3k)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a light-yellow solid in 78% yield;

M.p. = 100-101 °C;

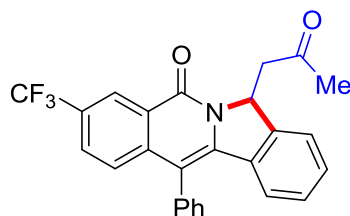
¹H NMR (600 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.60-7.55 (m, 3H), 7.50 (d, J = 7.7 Hz, 1H), 7.43 (d, J = 6.9 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.36-7.32 (m, 1H), 7.30-7.26 (m, 1H), 7.10 (d, J = 8.3 Hz, 1H),

7.08-7.04 (m, 1H), 6.37 (d, $J = 8.0$ Hz, 1H), 6.05 (dd, $J = 8.2, 3.2$ Hz, 1H), 4.00 (dd, $J = 17.6, 3.2$ Hz, 1H), 2.87 (dd, $J = 17.6, 8.2$ Hz, 1H), 2.49 (s, 3H), 2.22 (s, 3H);

^{13}C NMR (151 MHz, CDCl_3): δ 205.9, 160.9, 142.5, 137.1, 136.7, 136.5, 135.4, 133.7, 133.4, 131.1, 131.0, 129.54, 129.49, 129.4, 128.5, 128.3, 126.9, 125.3, 124.7, 123.8, 123.3, 114.7, 59.5, 46.0, 30.5, 21.4;

HRMS (ESI) m/z: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{26}\text{H}_{21}\text{NNaO}_2$ 402.1465; Found 402.1465.

7-(2-Oxopropyl)-12-phenyl-3-(trifluoromethyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3l)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 66% yield;

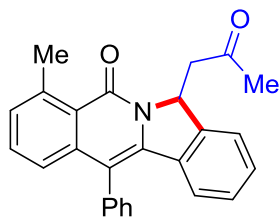
M.p. = 128-129 °C;

^1H NMR (600 MHz, CDCl_3): δ 8.79 (s, 1H), 7.72 (dd, $J = 8.6, 1.8$ Hz, 1H), 7.65-7.57 (m, 3H), 7.53 (d, $J = 7.7$ Hz, 1H), 7.46-7.41 (m, 1H), 7.36-7.30 (m, 3H), 7.12-7.08 (m, 1H), 6.41 (d, $J = 8.0$ Hz, 1H), 6.06 (dd, $J = 8.1, 3.0$ Hz, 1H), 3.98 (dd, $J = 17.7, 3.2$ Hz, 1H), 2.94 (dd, $J = 17.7, 8.1$ Hz, 1H), 2.23 (s, 3H);

^{13}C NMR (125 MHz, CDCl_3): 205.6, 160.3, 142.9, 141.2, 140.4, 134.5, 132.9, 131.1, 131.0, 130.4, 129.9, 129.8, 129.0, 128.6, 128.23 (q, $J = 3.2$ Hz), 128.16 (q, $J = 33.1$ Hz), 126.2, 125.1 (q, $J = 4.0$ Hz), 124.5, 124.4, 124.1 (q, $J = 272.3$ Hz), 123.4, 113.9, 59.8, 45.5, 30.5;

HRMS (ESI) m/z: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{26}\text{H}_{18}\text{F}_3\text{NNaO}_2$ 456.1182; Found 456.1187.

4-Methyl-7-(2-oxopropyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3m)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 70% yield;

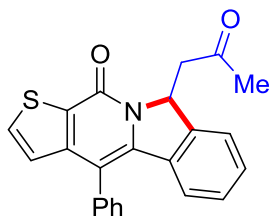
M.p. = 151-152 °C;

¹H NMR (600 MHz, CDCl₃): δ 7.61-7.55 (m, 3H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.43-7.40 (m, 1H), 7.38 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.33-7.31 (m, 1H), 7.30-7.27 (m, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.07-7.02 (m, 2H), 6.29 (d, *J* = 8.0 Hz, 1H), 6.05 (dd, *J* = 8.4, 3.0 Hz, 1H), 3.99 (dd, *J* = 17.6, 3.1 Hz, 1H), 3.02 (s, 3H), 2.83 (dd, *J* = 17.6, 8.5 Hz, 1H), 2.22 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 206.1, 161.8, 142.9, 141.8, 140.6, 137.9, 136.0, 133.4, 131.4, 131.3, 131.2, 129.8, 129.7, 129.66, 129.59, 128.5, 128.3, 124.0, 123.8, 123.4, 123.3, 114.5, 59.7, 46.1, 30.7, 24.2;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₆H₂₁NNaO₂ 402.1465; Found 402.1461.

9-(2-Oxopropyl)-4-phenylthieno[3',2':4,5]pyrido[2,1-*a*]isoindol-11(9*H*)-one (3n)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a light-yellow solid in 54% yield;

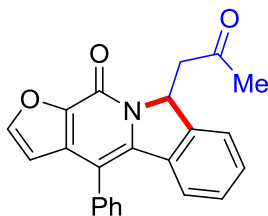
M.p. = 190-191 °C;

¹H NMR (600 MHz, CDCl₃): δ 7.62 (d, *J* = 5.2 Hz, 1H), 7.58-7.51 (m, 4H), 7.50-7.46 (m, 1H), 7.42-7.38 (m, 1H), 7.32-7.29 (m, 1H), 7.11-7.07 (m, 1H), 6.89 (d, *J* = 5.2 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.04 (dd, *J* = 8.2, 3.0 Hz, 1H), 4.07 (dd, *J* = 17.7, 3.1 Hz, 1H), 2.90 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.22 (s, 3H);

¹³C NMR (125 MHz, CDCl₃): δ 205.8, 157.2, 147.9, 142.7, 139.9, 135.5, 133.2, 133.0, 130.6, 130.4, 129.6, 129.5, 129.4, 128.6, 128.4, 128.1, 124.5, 123.54, 123.51, 113.7, 59.6, 45.6, 30.6;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₃H₁₇NNaO₂S 394.0872; Found 394.0871.

9-(2-Oxopropyl)-4-phenylfuro[3',2':4,5]pyrido[2,1-*a*]isoindol-11(9*H*)-one (3o)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a colorless solid in 58% yield;

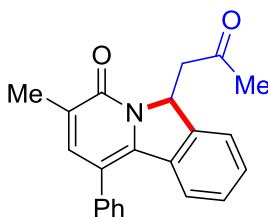
M.p. = 208-209 °C;

¹H NMR (600 MHz, CDCl₃): δ 7.70 (d, *J* = 1.9 Hz, 1H), 7.57-7.46 (m, 5H), 7.43-7.39 (m, 1H), 7.32-7.24 (m, 1H), 7.11-7.06 (m, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.42 (d, *J* = 1.9 Hz, 1H), 6.02 (dd, *J* = 8.2, 3.0 Hz, 1H), 4.03 (dd, *J* = 17.7, 3.1 Hz, 1H), 2.90 (dd, *J* = 17.7, 8.2 Hz, 1H), 2.20 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.7, 151.9, 148.5, 143.0, 141.8, 138.8, 136.0, 134.7, 132.9, 130.3, 130.0, 129.4, 129.32, 129.25, 128.6, 128.3, 123.4, 123.2, 110.9, 107.2, 59.8, 45.5, 30.5;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₃H₁₇NNaO₃ 378.1101; Found 378.1102.

3-Methyl-6-(2-oxopropyl)-1-phenylpyrido[2,1-*a*]isoindol-4(6*H*)-one (3p)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a light-yellow solid in 45% yield;

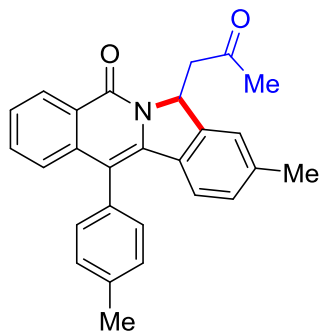
M.p. = 170-171 °C;

¹H NMR (600 MHz, CDCl₃): δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.50-7.34 (m, 5H), 7.33-7.29 (m, 1H), 7.28 (s, 1H), 7.13-7.09 (m, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 5.94 (dd, *J* = 8.1, 2.4 Hz, 1H), 4.06 (dd, *J* = 17.7, 3.0 Hz, 1H), 2.83 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.23 (s, 3H), 2.21 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.7, 161.6, 142.8, 141.2, 141.0, 137.4, 133.1, 129.84, 129.76, 129.6, 129.1, 129.0, 128.3, 128.2, 126.9, 123.5, 123.3, 116.9, 60.3, 45.0, 30.5, 16.5;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₂H₁₉NNaO₂ 352.1308; Found 352.1308.

9-Methyl-7-(2-oxopropyl)-12-(*p*-tolyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3q)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 80% yield;

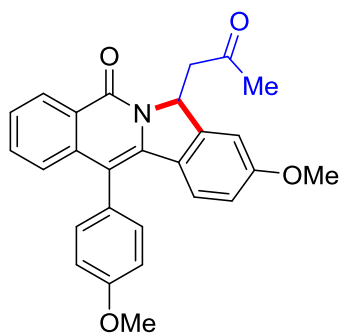
M.p. = 222-223 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.49 (d, *J* = 7.4, 1H), 7.55-7.51 (m, 1H), 7.47-7.43 (m, 1H), 7.40-7.36 (m, 2H), 7.32-7.29 (m, 2H), 7.21 (d, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 1H), 6.34 (d, *J* = 8.1 Hz, 1H), 6.01 (dd, *J* = 8.2, 2.8 Hz, 1H), 4.01 (dd, *J* = 17.7, 3.0 Hz, 1H), 2.85 (dd, *J* = 17.7, 8.3 Hz, 1H), 2.52 (s, 3H), 2.33 (s, 3H), 2.23 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 206.0, 161.0, 142.9, 140.1, 139.1, 138.21, 138.17, 132.2, 132.1, 131.0, 130.9, 130.8, 130.3, 130.2, 129.4, 127.2, 126.1, 125.2, 124.6, 123.82, 123.77, 113.9, 59.4, 46.0, 30.5, 21.7, 21.6;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₇H₂₃NNaO₂ 416.1621; Found 416.1626.

9-Methoxy-12-(4-methoxyphenyl)-7-(2-oxopropyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3r)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/2) as a yellow solid in 77% yield;

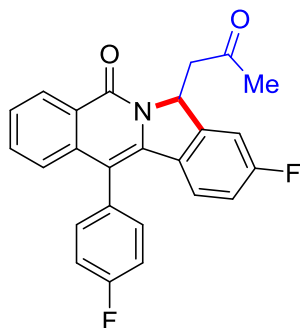
M.p. = 173-174 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.47 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.56-7.52 (m, 1H), 7.46-7.42 (m, 1H), 7.35-7.31 (m, 1H), 7.26-7.23 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.13-7.09 (m, 2H), 7.04 (d, *J* = 2.3 Hz, 1H), 6.65 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.38 (d, *J* = 8.7 Hz, 1H), 6.00 (dd, *J* = 8.4, 3.0 Hz, 1H), 4.03 (dd, *J* = 17.8, 3.1 Hz, 1H), 3.94 (s, 3H), 3.78 (s, 3H), 2.83 (dd, *J* = 17.8, 8.4 Hz, 1H), 2.23 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 206.1, 161.1, 161.0, 159.7, 144.8, 139.4, 138.4, 132.4, 132.3, 132.2, 127.5, 127.3, 126.1, 125.9, 125.3, 125.0, 124.3, 115.3, 115.00, 114.97, 112.6, 108.2, 59.4, 55.7, 55.5, 46.0, 30.6;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₇H₂₃NNaO₄ 448.1519; Found 448.1516.

9-Fluoro-12-(4-fluorophenyl)-7-(2-oxopropyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3s)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 67% yield;

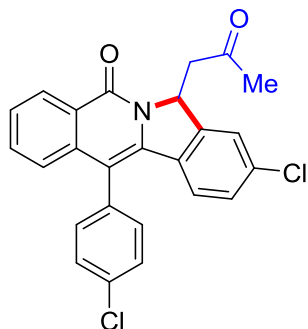
M.p. =185-186 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.47 (d, *J* = 8.0 Hz, 1H), 7.59-7.55 (m, 1H), 7.50-7.49 (m, 1H), 7.43-7.39 (m, 1H), 7.35-7.28 (m, 3H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 1H), 6.83-6.79 (m, 1H), 6.36 (dd, *J* = 8.7, 5.0 Hz, 1H), 6.02-5.97 (m, 1H), 4.05 (dd, *J* = 18.0, 2.4 Hz, 1H), 2.86 (dd, *J* = 18.0, 8.6 Hz, 1H), 2.22 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.7, 163.6 (d, *J* = 251.0 Hz), 163.0 (d, *J* = 248.5 Hz), 160.8, 145.1 (d, *J* = 9.3 Hz), 138.7, 137.6, 132.99 (d, *J* = 7.9 Hz), 132.89 (d, *J* = 8.0 Hz), 132.4, 130.96 (d, *J* = 3.4 Hz), 129.30 (d, *J* = 2.4 Hz), 127.4, 126.6, 125.5 (d, *J* = 8.9 Hz), 125.0, 124.5, 116.9 (d, *J* = 15.4 Hz), 116.8 (d, *J* = 15.3 Hz), 116.06 (d, *J* = 23.0 Hz), 112.9 (d, *J* = 1.6 Hz), 111.15 (d, *J* = 24.5 Hz), 59.3 (d, *J* = 2.5 Hz), 45.5, 30.5;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₅H₁₇F₂NNaO₂ 424.1120; Found 424.1120.

9-Chloro-12-(4-chlorophenyl)-7-(2-oxopropyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3t)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 68% yield;

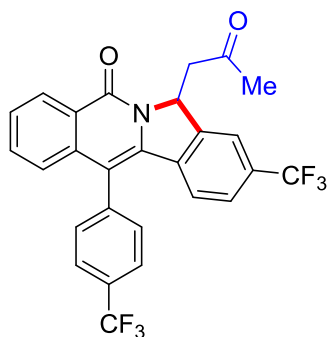
M.p. = 194-195 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.49 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.60-7.56 (m, 3H), 7.54 (s, 1H), 7.52-7.48 (m, 1H), 7.40-7.37 (m, 1H), 7.31-7.28 (m, 1H), 7.15 (d, *J* = 8.1 Hz, 1H), 7.10 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.36 (d, *J* = 8.4 Hz, 1H), 6.01 (dd, *J* = 8.5, 2.9 Hz, 1H), 4.03 (dd, *J* = 18.1, 2.9 Hz, 1H), 2.90 (dd, *J* = 18.1, 8.5 Hz, 1H), 2.23 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.7, 160.8, 144.4, 138.4, 137.4, 136.0, 134.9, 133.5, 132.6, 132.55, 132.52, 131.7, 130.1, 130.0, 129.0, 127.5, 126.9, 125.1, 124.9, 124.8, 124.0, 113.4, 59.3, 45.5, 30.5;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₅H₁₈Cl₂NO₂ 434.0709; Found 434.0712.

7-(2-oxopropyl)-9-(trifluoromethyl)-12-(4-(trifluoromethyl)phenyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3u)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a yellow solid in 63% yield;

M.p. = 205-206 °C;

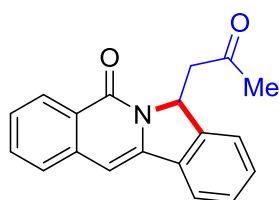
¹H NMR (600 MHz, CDCl₃): δ 8.47 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.94-7.86 (m, 2H), 7.78 (s, 1H), 7.65-7.55 (m, 3H), 7.52-7.47 (m, 1H), 7.38 (d, *J* = 8.3 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.45 (d, *J* = 8.3 Hz,

1H), 6.01 (dd, $J = 8.2, 2.8$ Hz, 1H), 4.01 (dd, $J = 18.1, 3.0$ Hz, 1H), 2.99 (dd, $J = 18.1, 8.2$ Hz, 1H), 2.22 (s, 3H);

$^{13}\text{C NMR}$ (151 MHz, CDCl_3): δ 205.5, 160.6, 143.3, 138.9, 137.9, 136.9, 136.4, 132.7, 131.73, 131.66, 131.7 (q, $J = 31.7$ Hz), 131.3 (q, $J = 33.2$ Hz), 127.5, 127.4, 126.8 (q, $J = 3.0$ Hz), 126.7 (q, $J = 4.5$ Hz), 125.7 (q, $J = 3.5$ Hz), 125.22, 125.11, 124.1 (q, $J = 273.3$ Hz), 123.9, 123.7 (q, $J = 271.8$ Hz), 120.7 (q, $J = 3.7$ Hz), 114.5, 59.5, 45.2, 30.4;

HRMS (ESI) m/z: $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{18}\text{F}_6\text{NO}_2$ 502.1236; Found 502.1238.

7-(2-Oxopropyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3v)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/2) as a brown solid in 61% yield;

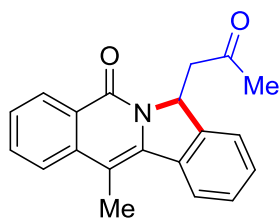
M.p. = 150-151 °C;

$^1\text{H NMR}$ (600 MHz, CDCl_3): δ 8.42 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.74 (dd, $J = 7.3, 1.3$ Hz, 1H), 7.66-7.63 (m, 1H), 7.60 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.55 (dd, $J = 7.5, 1.3$ Hz, 1H), 7.47-7.40 (m, 3H), 6.98 (s, 1H), 5.99 (dd, $J = 8.6, 3.2$ Hz, 1H), 4.01 (dd, $J = 17.8, 3.2$ Hz, 1H), 2.82 (dd, $J = 17.8, 8.6$ Hz, 1H), 2.19 (s, 3H);

$^{13}\text{C NMR}$ (151 MHz, CDCl_3): δ 205.9, 161.3, 142.2, 141.9, 137.9, 133.1, 132.4, 130.3, 128.8, 127.5, 126.5, 126.4, 125.4, 123.9, 120.9, 98.2, 60.1, 45.4, 30.5;

HRMS (ESI) m/z: $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{15}\text{NNaO}_2$ 312.0995; Found 312.0996.

12-Methyl-7-(2-oxopropyl)isoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3w)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/4) as a light-yellow solid in 70% yield;

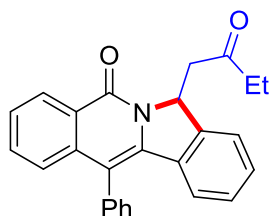
M.p. = 150-151 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.47 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.73-7.69 (m, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.50-7.44 (m, 2H), 7.42-7.38 (m, 1H), 5.97 (dd, *J* = 8.1, 2.6 Hz, 1H), 3.91 (dd, *J* = 17.6, 3.0 Hz, 1H), 2.81 (dd, *J* = 17.6, 8.2 Hz, 1H), 2.68 (s, 3H), 2.18 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 205.9, 160.6, 142.8, 138.6, 137.8, 134.2, 132.3, 129.3, 128.7, 127.6, 126.3, 125.1, 124.4, 123.7, 123.3, 108.2, 59.3, 46.0, 30.5, 12.6;

HRMS (ESI) m/z: [M+Na]⁺ Calcd for C₂₀H₁₇NNaO₂ 326.1151; Found 326.1151.

7-(2-Oxobutyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3y)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 45% yield;

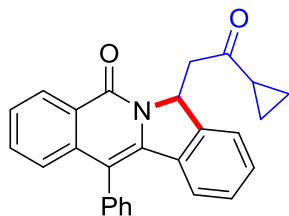
M.p. = 132-133 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.52 (d, *J* = 8.0 Hz, 1H), 7.63-7.54 (m, 4H), 7.52-7.47 (m, 2H), 7.47-7.43 (m, 1H), 7.37-7.34 (m, 1H), 7.32-7.28 (m, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.09-7.05 (m, 1H), 6.38 (d, *J* = 8.0 Hz, 1H), 6.10 (dd, *J* = 8.3, 3.0 Hz, 1H), 4.01 (dd, *J* = 17.5, 3.1 Hz, 1H), 2.86 (dd, *J* = 17.5, 8.4 Hz, 1H), 2.57 (dq, *J* = 17.6, 7.3 Hz, 1H), 2.41 (dq, *J* = 17.6, 7.3 Hz, 1H), 1.10 (t, *J* = 7.3 Hz, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 208.7, 161.0, 142.8, 138.9, 138.1, 135.3, 133.4, 132.2, 131.3, 131.1, 129.7, 129.65, 129.59, 128.6, 128.3, 127.4, 126.5, 125.4, 124.8, 124.0, 123.4, 114.7, 59.7, 44.7, 36.5, 7.9;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₆H₂₂NO₂ 380.1645; Found 380.1645.

7-(2-Cyclopropyl-2-oxoethyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3z)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 68% yield;

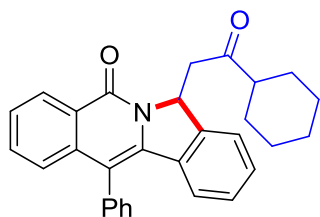
M.p. = 161-162 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.53 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.62-7.54 (m, 4H), 7.51-7.47 (m, 2H), 7.46-7.43 (m, 1H), 7.37-7.33 (m, 1H), 7.31-7.27 (m, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.08-7.04 (m, 1H), 6.38 (d, *J* = 8.0 Hz, 1H), 6.11 (dd, *J* = 8.8, 2.6 Hz, 1H), 4.21 (dd, *J* = 17.1, 2.8 Hz, 1H), 3.03 (dd, *J* = 17.1, 8.9 Hz, 1H), 1.95 (tt, *J* = 7.9, 4.5 Hz, 1H), 1.14-1.10 (m, 1H), 1.07-1.02 (m, 1H), 0.93-0.87 (m, 1H), 0.86-0.81 (m, 1H);

¹³C NMR (151 MHz, CDCl₃): δ 208.0, 161.0, 142.7, 138.8, 138.1, 135.3, 133.3, 132.2, 131.2, 131.1, 129.63, 129.61, 129.57, 128.6, 128.3, 127.4, 126.4, 125.3, 124.9, 124.0, 123.6, 114.6, 59.7, 45.4, 21.2, 11.23, 11.15;

HRMS (ESI) calcd for C₂₇H₂₂NO₂: [M+H]⁺ 392.1645, found: 392.1642.

7-(2-Cyclohexyl-2-oxoethyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3aa)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 65% yield;

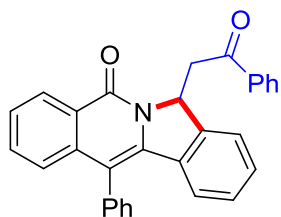
M.p. = 153-154 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.54 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.63-7.55 (m, 4H), 7.51-7.46 (m, 3H), 7.39-7.35 (m, 1H), 7.32-7.28 (m, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.09-7.06 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.12 (dd, *J* = 8.9, 2.7 Hz, 1H), 4.14 (dd, *J* = 17.7, 2.9 Hz, 1H), 2.87 (dd, *J* = 17.7, 8.9 Hz, 1H), 2.40 (ddd, *J* = 11.5, 8.0, 3.4 Hz, 1H), 1.96-1.91 (m, 1H), 1.86-1.74 (m, 3H), 1.69-1.63 (m, 1H), 1.43 (ddd, *J* = 15.5, 12.4, 3.5 Hz, 1H), 1.35 (ddd, *J* = 15.1, 12.3, 3.4 Hz, 1H), 1.30-1.18 (m, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 211.4, 160.8, 143.0, 138.8, 138.1, 135.3, 133.3, 132.1, 131.2, 131.1, 129.6, 129.5, 128.5, 128.2, 127.3, 126.4, 125.3, 124.8, 124.0, 123.4, 114.5, 59.7, 51.2, 43.0, 28.5, 28.3, 25.9, 25.7, 25.6 (overlapped);

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₀H₂₈NO₂ 434.2115; Found 434.2119.

7-(2-Oxo-2-phenylethyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3ab)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 83% yield;

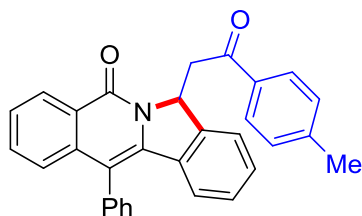
M.p. = 183-184 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.54 (d, *J* = 7.7 Hz, 1H), 8.03 (d, *J* = 7.4 Hz, 2H), 7.62-7.52 (m, 6H), 7.52-7.48 (m, 1H), 7.48-7.43 (m, 3H), 7.37 (d, *J* = 7.1 Hz, 1H), 7.29-7.26 (m, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.09-7.05 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.31 (dd, *J* = 9.0, 2.3 Hz, 1H), 4.70 (dd, *J* = 17.0, 2.7 Hz, 1H), 3.34 (dd, *J* = 17.0, 9.1 Hz, 1H);

¹³C NMR (151 MHz, CDCl₃): δ 197.7, 161.0, 142.6, 138.9, 138.1, 136.8, 135.3, 133.5, 133.4, 132.3, 131.3, 131.1, 129.65, 129.63, 129.61, 128.8, 128.6, 128.40, 128.37, 127.4, 126.5, 125.4, 124.9, 124.0, 123.8, 114.7, 60.1, 41.5;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₀H₂₂NO₂ 428.1645; Found 428.1649.

7-(2-Oxo-2-(*p*-tolyl)ethyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3ac)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 75% yield;

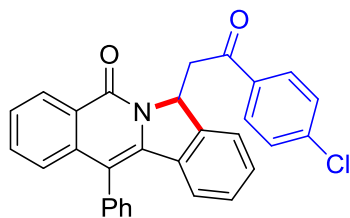
M.p. = 210-211 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.54 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.63-7.56 (m, 4H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.51-7.48 (m, 1H), 7.47-7.45 (m, 1H), 7.38-7.36 (m, 1H), 7.28-7.26 (m, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.07-7.05 (m, 1H), 6.39 (d, *J* = 8.0 Hz, 1H), 6.31 (dd, *J* = 9.1, 2.3 Hz, 1H), 4.68 (dd, *J* = 16.9, 2.8 Hz, 1H), 3.29 (dd, *J* = 16.9, 9.2 Hz, 1H), 2.39 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 197.3, 161.0, 144.3, 142.7, 138.9, 138.2, 135.4, 134.4, 133.4, 132.2, 131.3, 131.1, 129.64, 129.60, 129.4, 128.6, 128.5, 128.4, 127.4, 126.5, 125.4, 124.9, 124.0, 123.9, 114.7, 60.2, 41.4, 21.8 (overlapped);

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₁H₂₄NO₂ 442.1802; Found 442.1804.

7-(2-(4-Chlorophenyl)-2-oxoethyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3ad)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 72% yield;

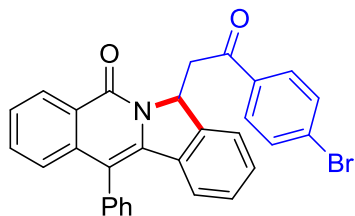
M.p. = 189-190 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.52 (d, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 8.6 Hz, 2H), 7.63-7.56 (m, 4H), 7.52-7.48 (m, 2H), 7.46 (d, *J* = 6.8 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.38-7.35 (m, 1H), 7.28 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.07 (dd, *J* = 7.7, 7.6 Hz, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.26 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.64 (dd, *J* = 16.9, 2.8 Hz, 1H), 3.31 (dd, *J* = 16.9, 8.9 Hz, 1H);

¹³C NMR (151 MHz, CDCl₃): δ 196.5, 161.0, 142.4, 139.9, 138.9, 138.0, 135.3, 135.1, 133.4, 132.3, 131.2, 131.1, 129.8, 129.7, 129.65, 129.61, 129.1, 128.6, 128.5, 127.4, 126.6, 125.4, 124.8, 124.1, 123.7, 114.8, 60.0, 41.5;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₀H₂₁ClNO₂ 462.1255; Found 462.1258.

7-(2-(4-Bromophenyl)-2-oxoethyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3ae)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 70% yield;

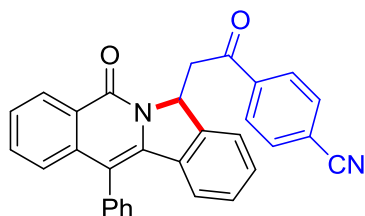
M.p. = 122-123 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.52 (d, *J* = 7.9 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.64-7.54 (m, 6H), 7.52-7.48 (m, 2H), 7.47-7.44 (m, 1H), 7.38-7.35 (m, 1H), 7.30-7.25 (m, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.09-7.05 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.25 (dd, *J* = 8.8, 2.6 Hz, 1H), 4.63 (dd, *J* = 16.9, 2.9 Hz, 1H), 3.31 (dd, *J* = 16.9, 8.9 Hz, 1H);

¹³C NMR (151 MHz, CDCl₃): δ 196.6, 161.0, 142.4, 138.8, 138.0, 135.5, 135.2, 133.4, 132.3, 132.0, 131.2, 131.0, 129.8, 129.623, 129.616, 129.58, 128.65, 128.60, 128.4, 127.3, 126.5, 125.4, 124.8, 124.0, 123.6, 114.7, 59.9, 41.4;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₀H₂₁BrNO₂ 506.0750; Found 506.0754.

4-(2-(5-Oxo-12-phenyl-5,7-dihydroisoindolo[2,1-*b*]isoquinolin-7-yl)acetyl)benzonitrile (3af)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 66% yield;

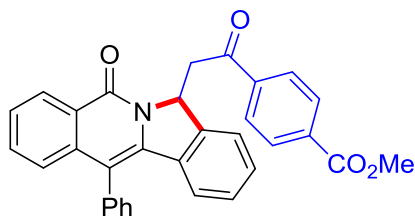
M.p. = 144-145 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.50 (d, *J* = 7.9 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.65-7.56 (m, 4H), 7.53-7.48 (m, 2H), 7.44 (d, *J* = 6.9 Hz, 1H), 7.39-7.34 (m, 1H), 7.32-7.28 (m, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.11-7.07 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.24 (dd, *J* = 8.3, 2.8 Hz, 1H), 4.60 (dd, *J* = 17.0, 3.1 Hz, 1H), 3.41 (dd, *J* = 17.0, 8.4 Hz, 1H);

¹³C NMR (151 MHz, CDCl₃): δ 196.4, 161.1, 142.1, 139.7, 138.8, 137.9, 135.1, 133.5, 132.6, 132.4, 131.14, 131.05, 129.72, 129.70, 129.6, 128.8, 128.7, 128.6, 127.3, 126.7, 125.4, 124.8, 124.1, 123.5, 118.0, 116.6, 115.0, 59.8, 41.9;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₁H₂₁N₂O₂ 453.1598; Found 453.1594.

Methyl 4-(2-(5-oxo-12-phenyl-5,7-dihydroisoindolo[2,1-*b*]isoquinolin-7-yl)acetyl)benzoate (3ag)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 70% yield;

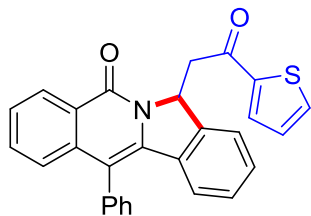
M.p. = 189-190 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.51 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.13-8.08 (m, 2H), 8.08-8.03 (m, 2H), 7.63-7.56 (m, 4H), 7.53 (dd, *J* = 7.7, 0.5 Hz, 1H), 7.51-7.48 (m, 1H), 7.46 (dd, *J* = 6.5, 1.2 Hz, 1H), 7.39-7.34 (m, 1H), 7.30-7.27 (m, 1H), 7.22 (d, *J* = 8.1 Hz, 1H), 7.09-7.06 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.29 (dd, *J* = 8.7, 2.7 Hz, 1H), 4.67 (dd, *J* = 17.2, 2.9 Hz, 1H), 3.93 (s, 3H), 3.40 (dd, *J* = 17.2, 8.8 Hz, 1H);

¹³C NMR (151 MHz, CDCl₃): δ 197.2, 166.2, 161.0, 142.4, 139.9, 138.8, 138.0, 135.2, 134.1, 133.4, 132.3, 131.2, 131.1, 129.9, 129.7, 129.65, 129.60, 128.6, 128.5, 128.2, 127.3, 126.5, 125.4, 124.8, 124.1, 123.6, 114.8, 59.9, 52.6, 41.9;

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₃₂H₂₄NO₄ 486.1700; Found 486.1703.

7-(2-Oxo-2-(thiophen-2-yl)ethyl)-12-phenylisoindolo[2,1-*b*]isoquinolin-5(7*H*)-one (3ah)



Following the general procedure, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether =1/4) as a yellow solid in 68% yield;

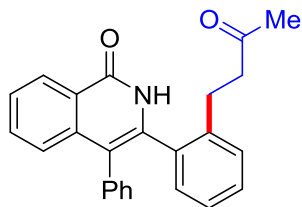
M.p. = 176-177 °C;

¹H NMR (600 MHz, CDCl₃): δ 8.54 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.88 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.63 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.62-7.53 (m, 5H), 7.50-7.45 (m, 2H), 7.38-7.35 (m, 1H), 7.30-7.25 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.10 (dd, *J* = 4.9, 3.9 Hz, 1H), 7.08-7.04 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 6.23 (dd, *J* = 9.0, 2.8 Hz, 1H), 4.64 (dd, *J* = 16.3, 2.9 Hz, 1H), 3.26 (dd, *J* = 16.3, 9.1 Hz, 1H);

¹³C NMR (151 MHz, CDCl₃): δ 190.2, 161.0, 144.0, 142.2, 138.8, 138.0, 135.2, 134.1, 133.3, 132.9, 132.2, 131.2, 131.0, 129.59, 129.56, 128.6, 128.41, 128.38, 127.3, 126.5, 125.3, 124.8, 124.0, 123.7, 114.7, 60.1, 41.8 (overlapped);

HRMS (ESI) m/z: [M+H]⁺ Calcd for C₂₈H₂₀NO₂S 434.1209; Found 434.1211.

3-(2-(3-Oxobutyl)phenyl)-4-phenylisoquinolin-1(2H)-one (4)



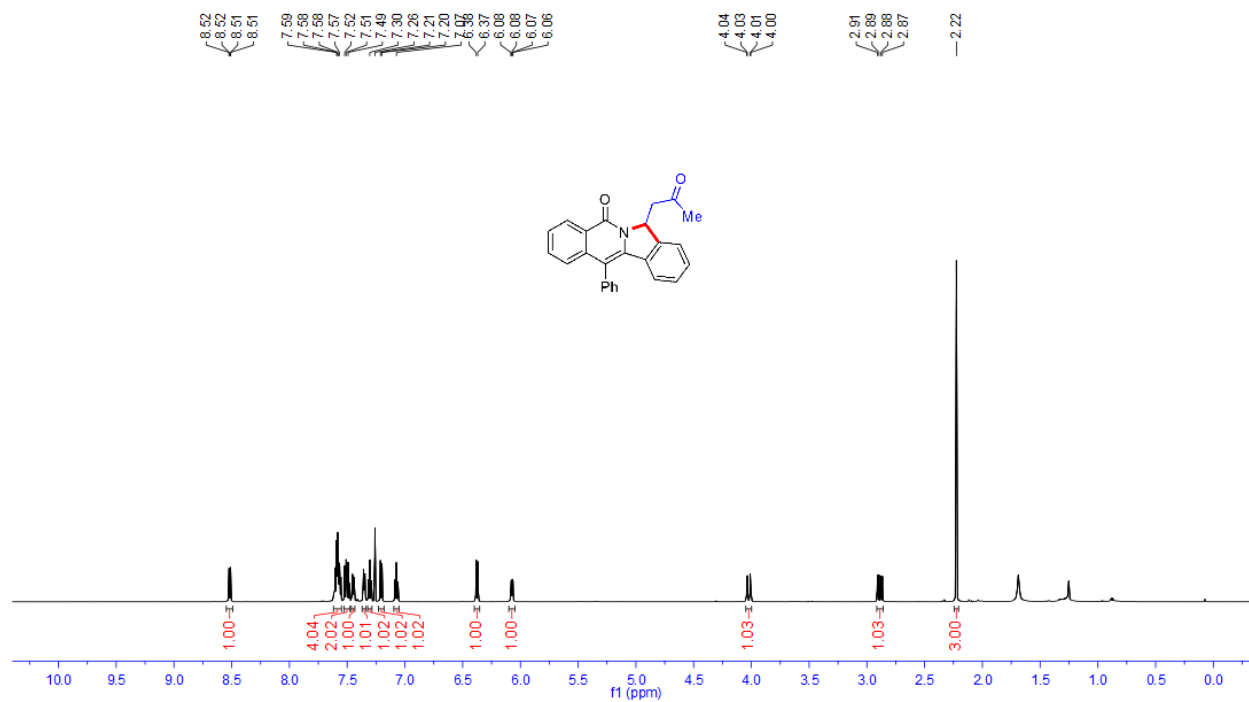
Following the general procedure using [Ru(*p*-cymene)Cl₂]₂ as a catalyst, the title compound was isolated by flash chromatography (eluent: ethyl acetate/petrol ether = 1/2) as a white solid in 83% yield;

M.p. = 207-208 °C;

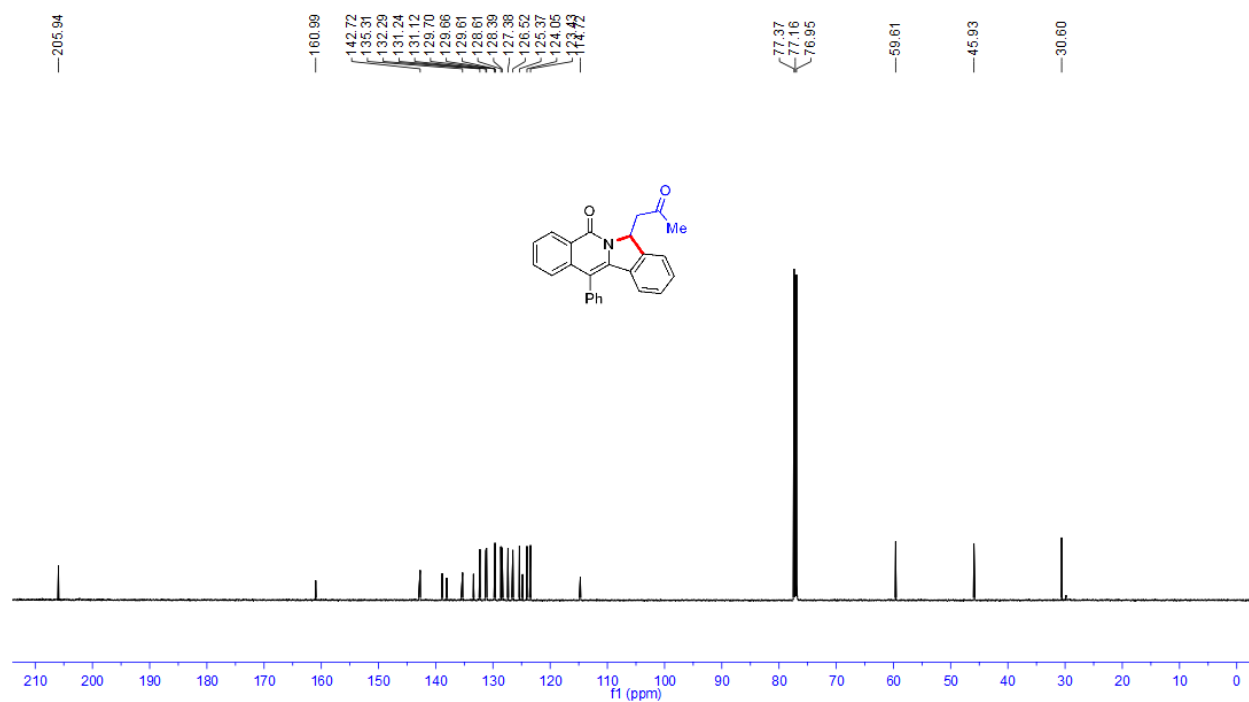
¹H NMR (600 MHz, CDCl₃): δ 10.22 (s, 1H), 8.41 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.59-7.56 (m, 1H), 7.50-7.46 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.26-7.18 (m, 4H), 7.18-7.13 (m, 2H), 7.12-7.06 (m, 3H), 2.88-2.76 (m, 2H), 2.69-2.62 (m, 1H), 2.57-2.49 (m, 1H), 2.02 (s, 3H);

¹³C NMR (151 MHz, CDCl₃): δ 208.0, 162.7, 139.4, 138.5, 137.3, 135.6, 134.2, 132.7, 131.8, 131.2, 131.0, 129.3, 128.2, 127.6, 127.2, 126.7, 126.0, 125.6, 125.4, 118.2, 43.9, 30.0, 26.2;

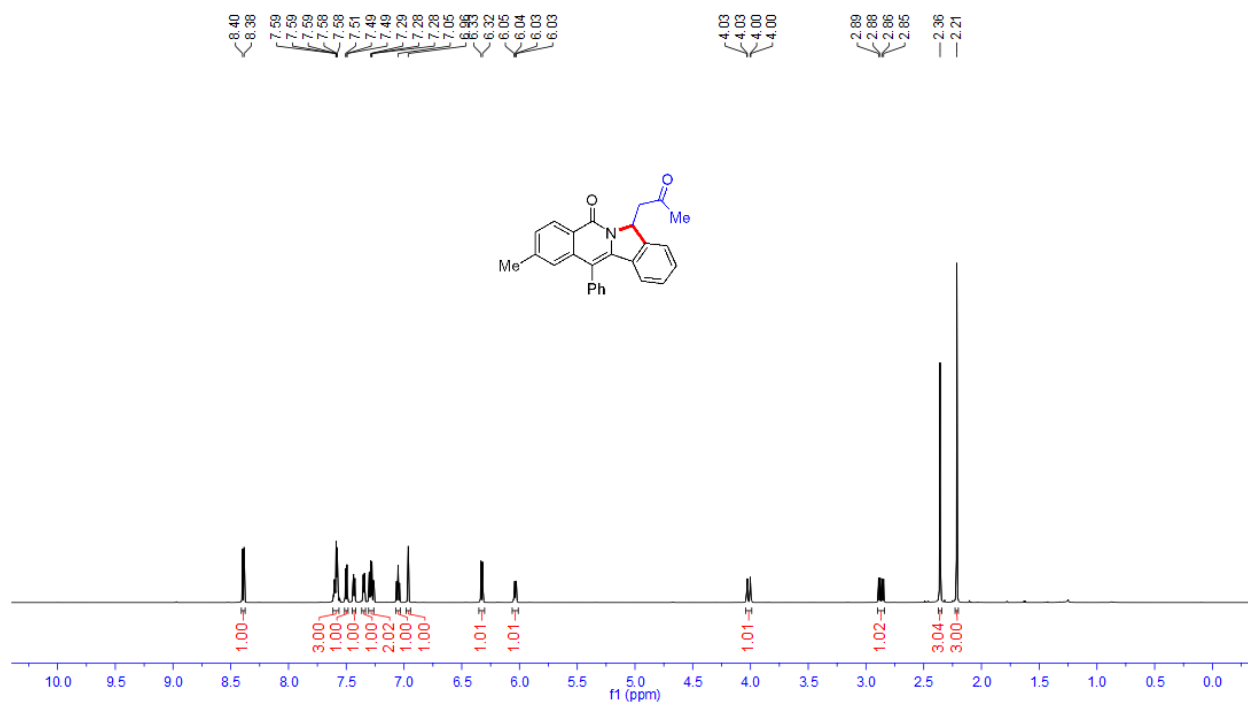
6. Copies of NMR spectra



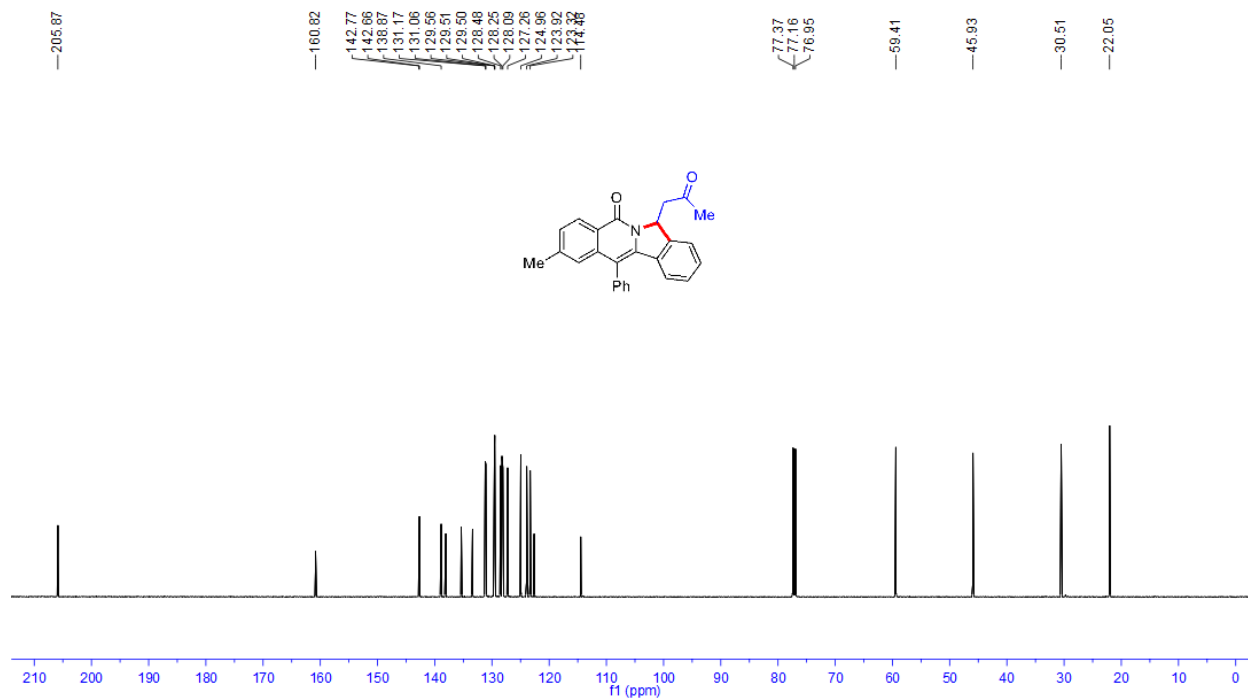
¹H NMR spectrum of **3a** (CDCl₃, 600 MHz)



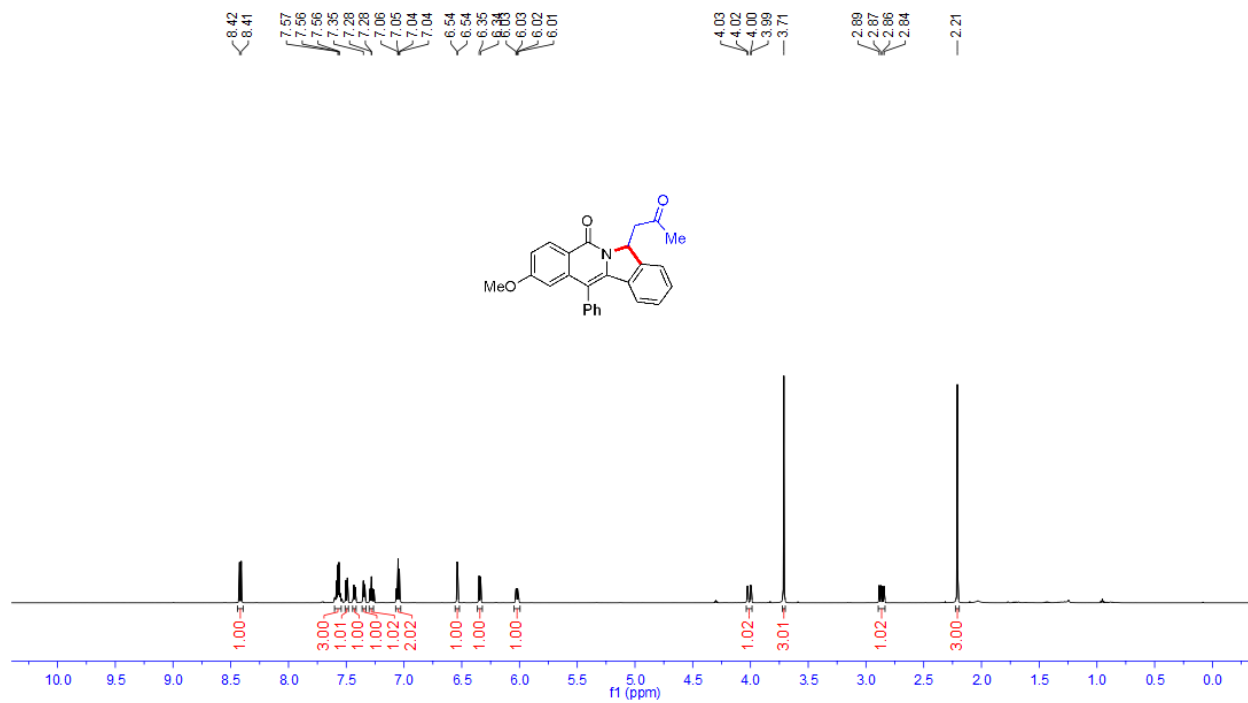
¹³C NMR spectrum of **3a** (CDCl₃, 151 MHz)



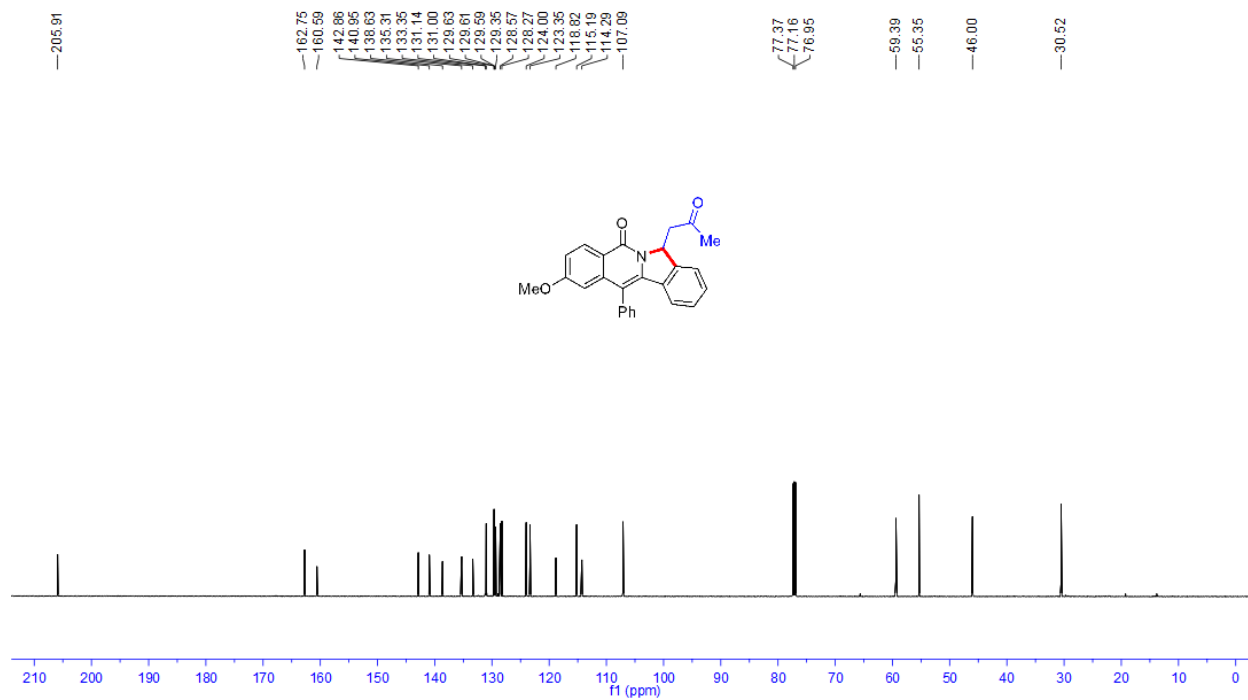
^1H NMR spectrum of **3b** (CDCl_3 , 600 MHz)



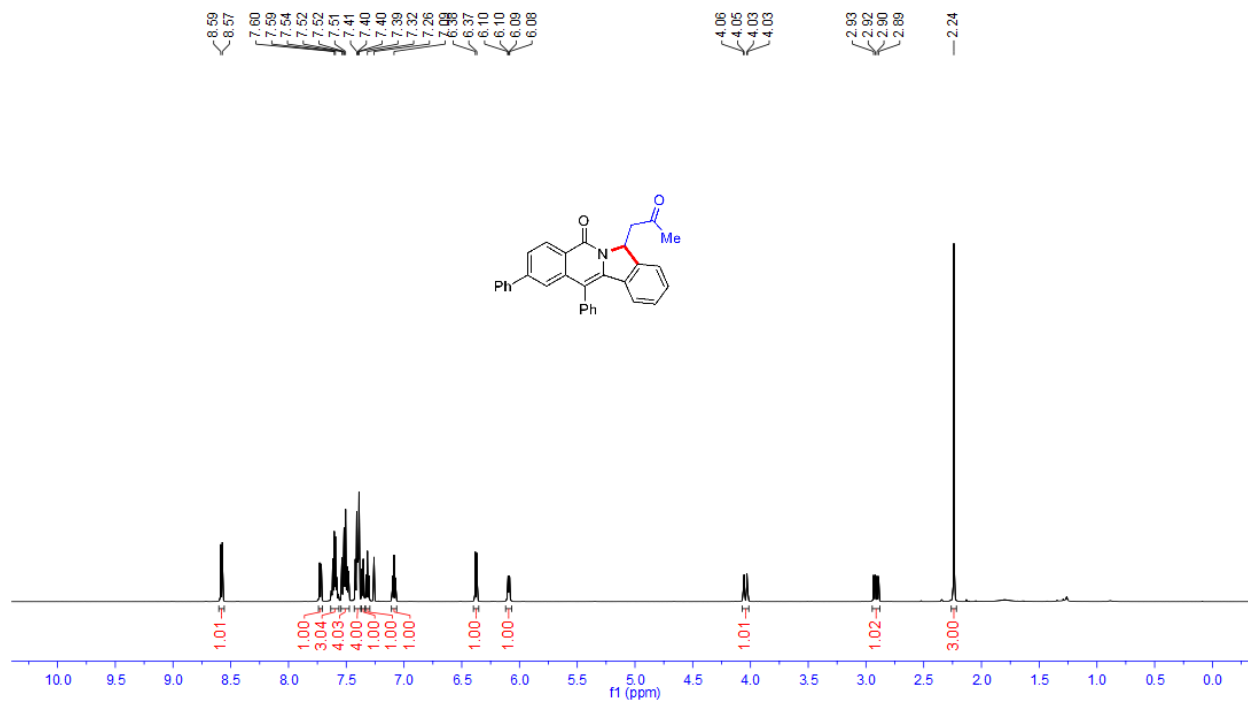
^{13}C NMR spectrum of **3b** (CDCl_3 , 151 MHz)



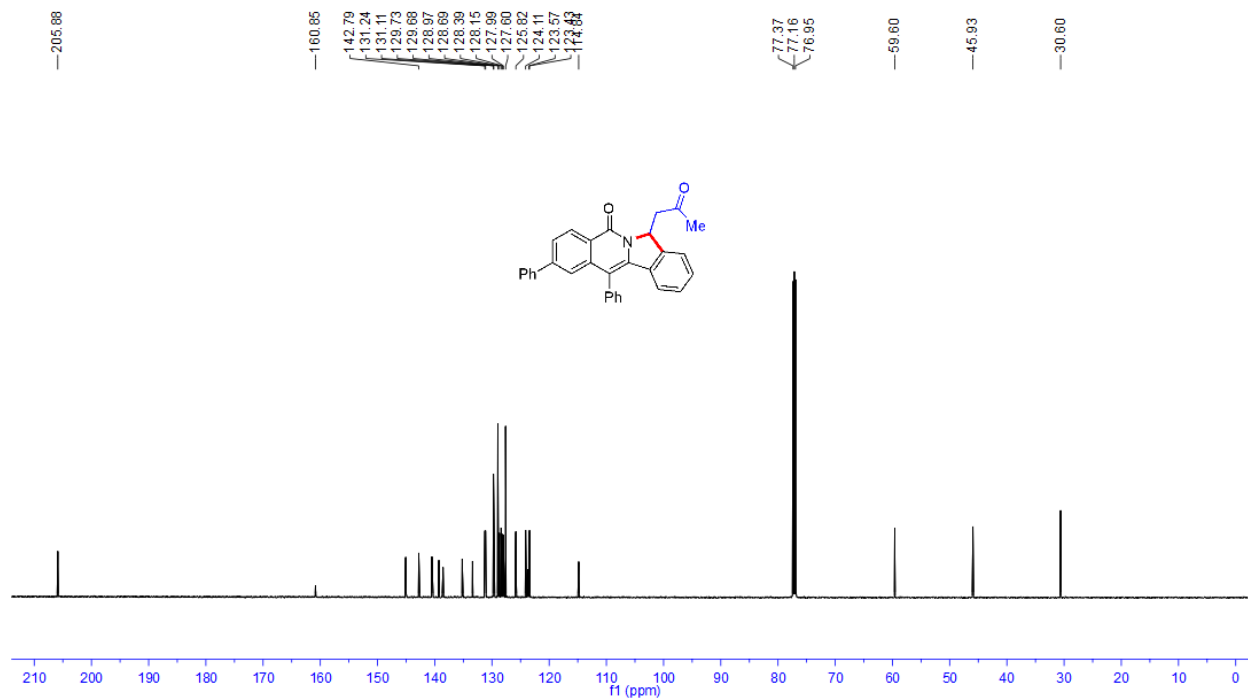
¹H NMR spectrum of **3d** (CDCl₃, 600 MHz)



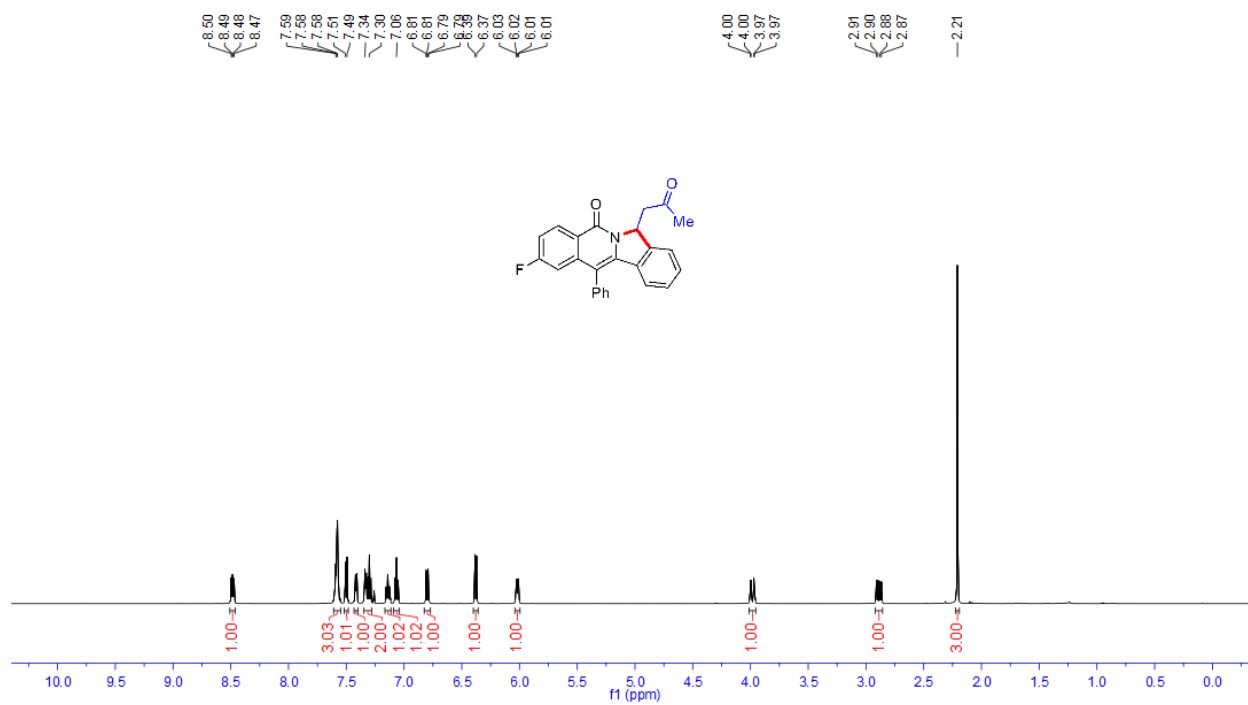
¹³C NMR spectrum of **3d** (CDCl₃, 151 MHz)



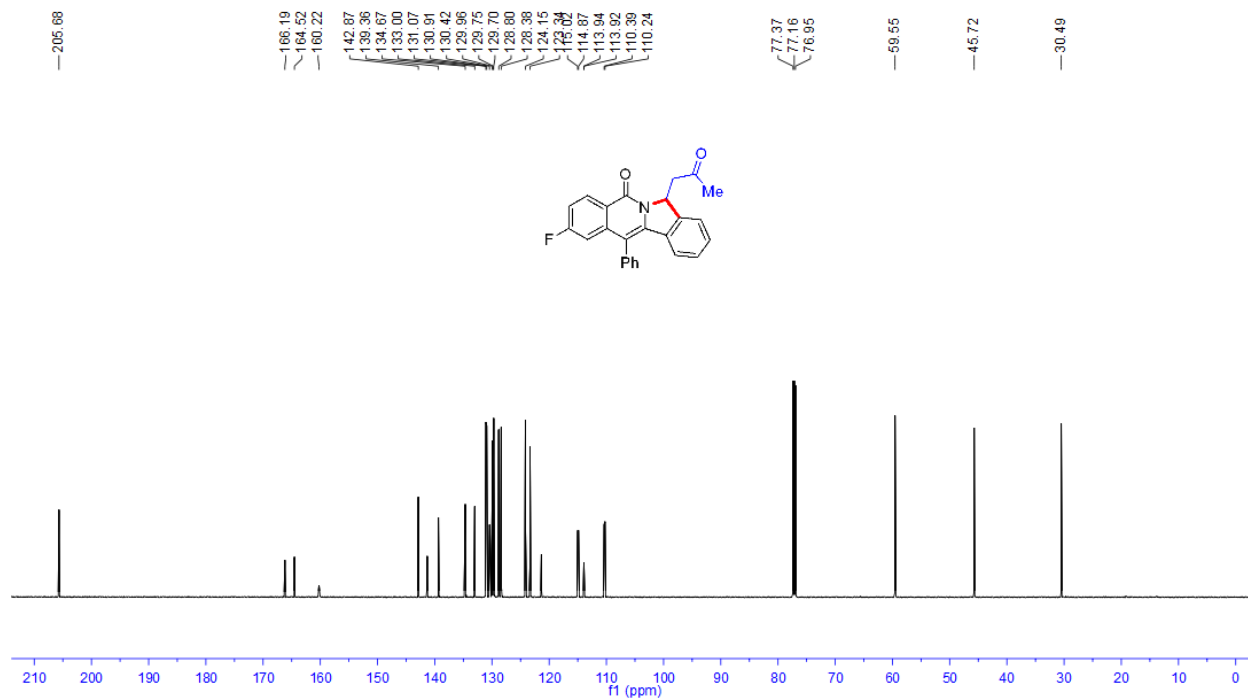
¹H NMR spectrum of **3e** (CDCl₃, 600 MHz)



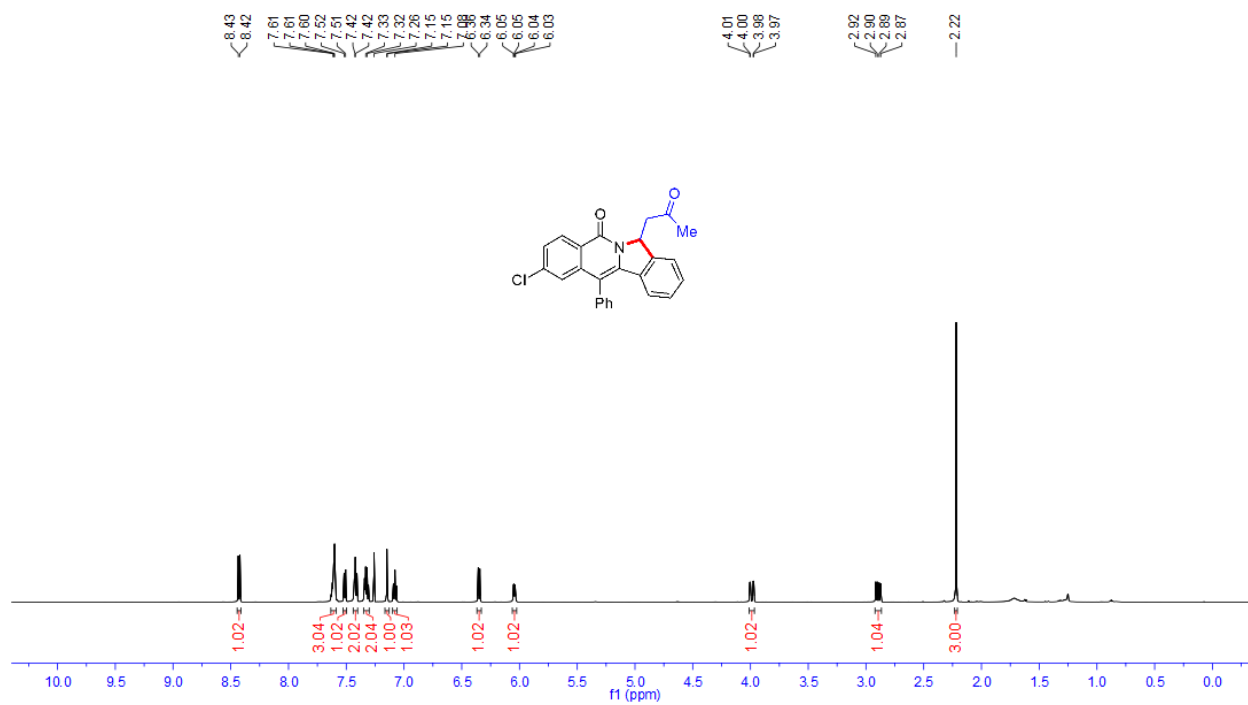
¹³C NMR spectrum of **3e** (CDCl₃, 151 MHz)



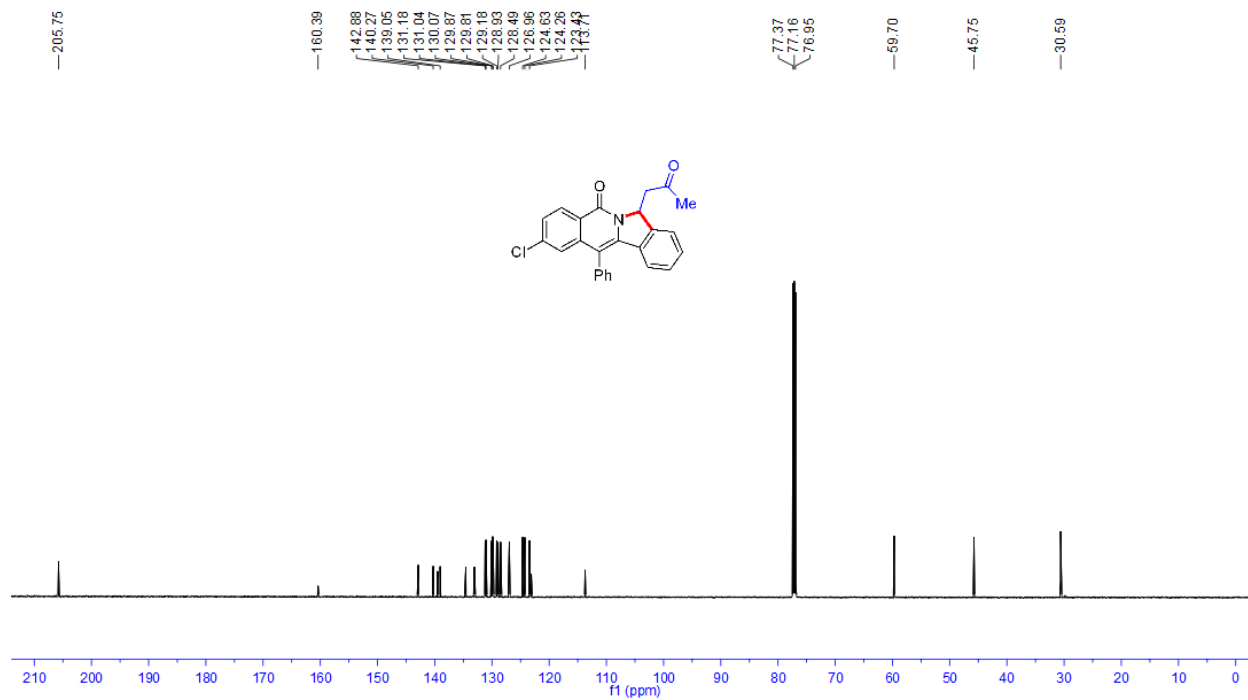
^1H NMR spectrum of **3f** (CDCl_3 , 600 MHz)



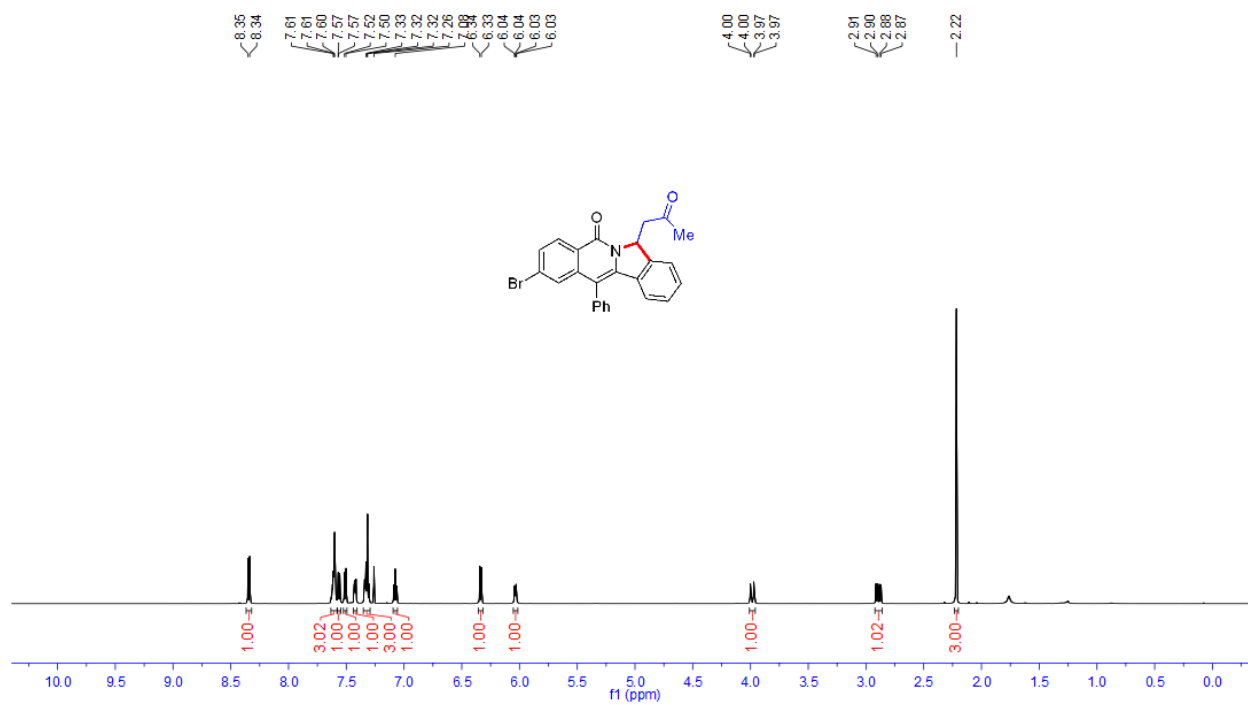
^{13}C NMR spectrum of **3f** (CDCl_3 , 151 MHz)



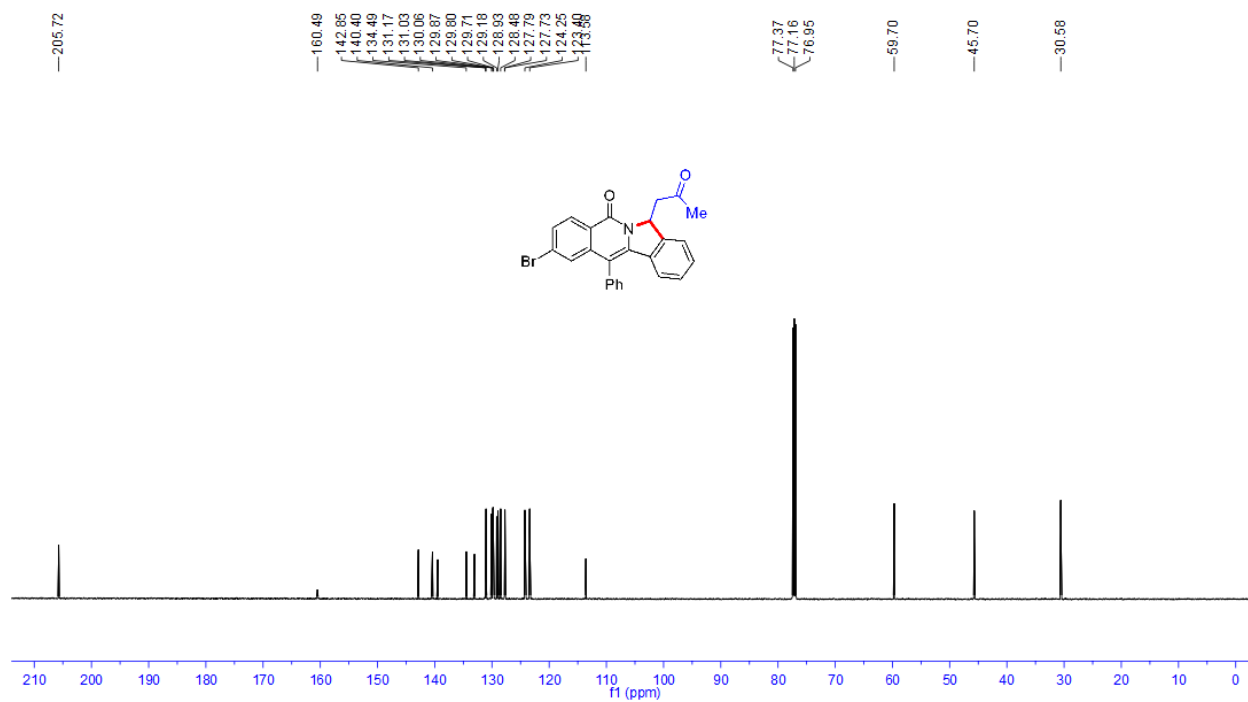
¹H NMR spectrum of **3g** (CDCl₃, 600 MHz)



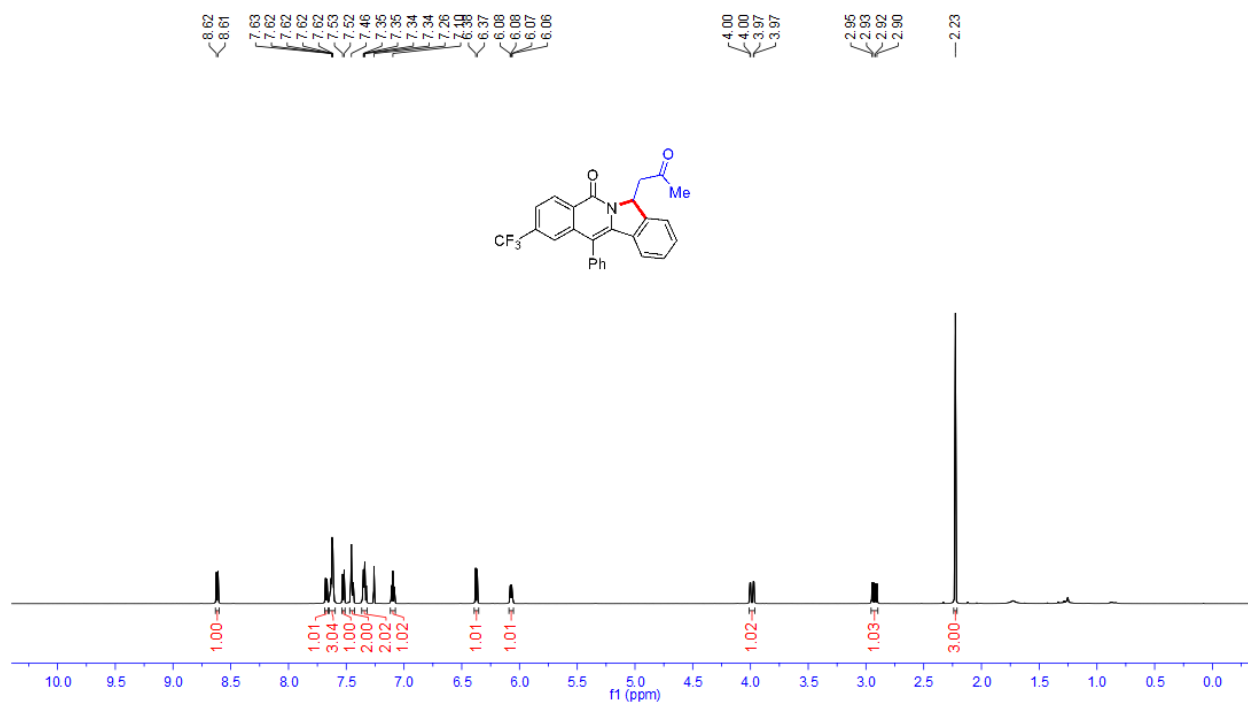
¹³C NMR spectrum of **3g** (CDCl₃, 151 MHz)



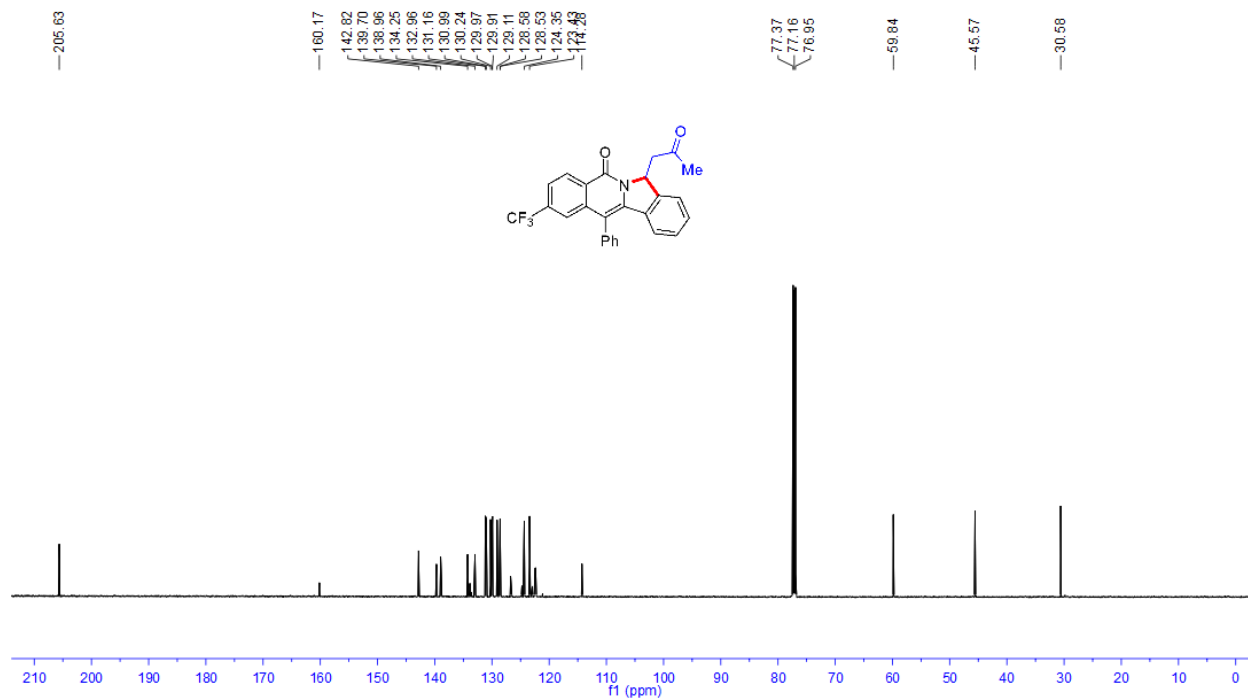
¹H NMR spectrum of **3h** (CDCl₃, 600 MHz)



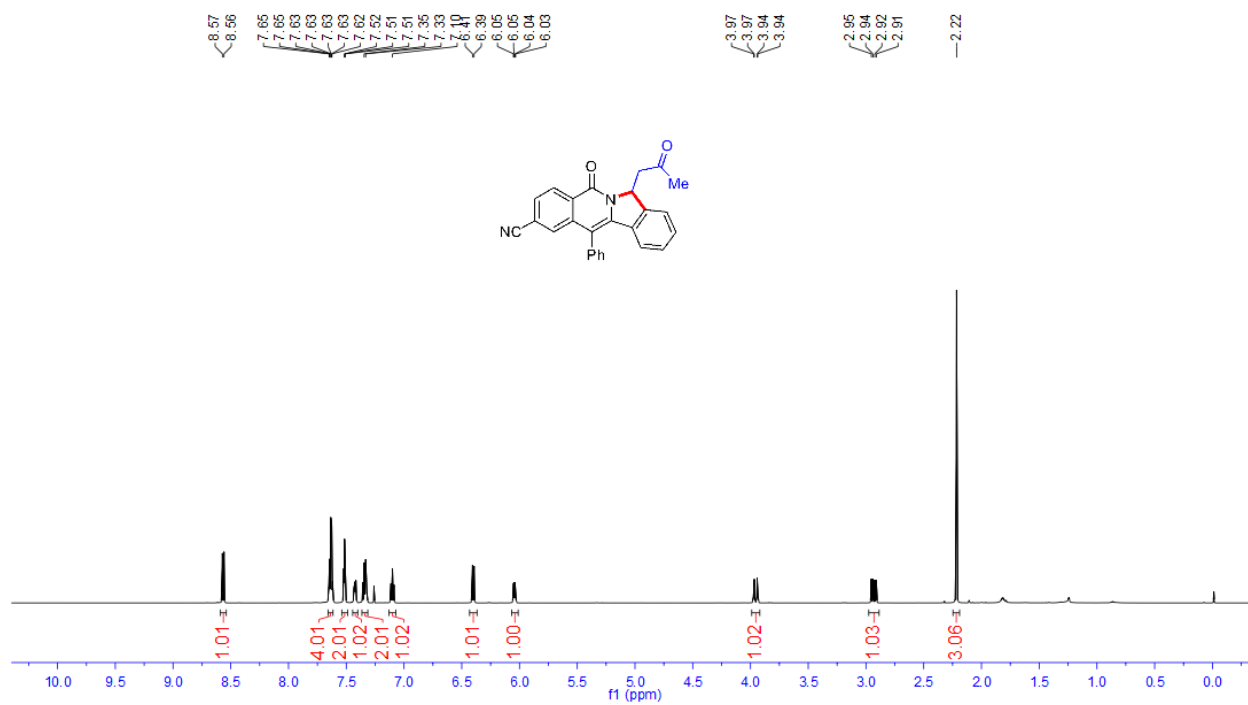
¹³C NMR spectrum of **3h** (CDCl₃, 151 MHz)



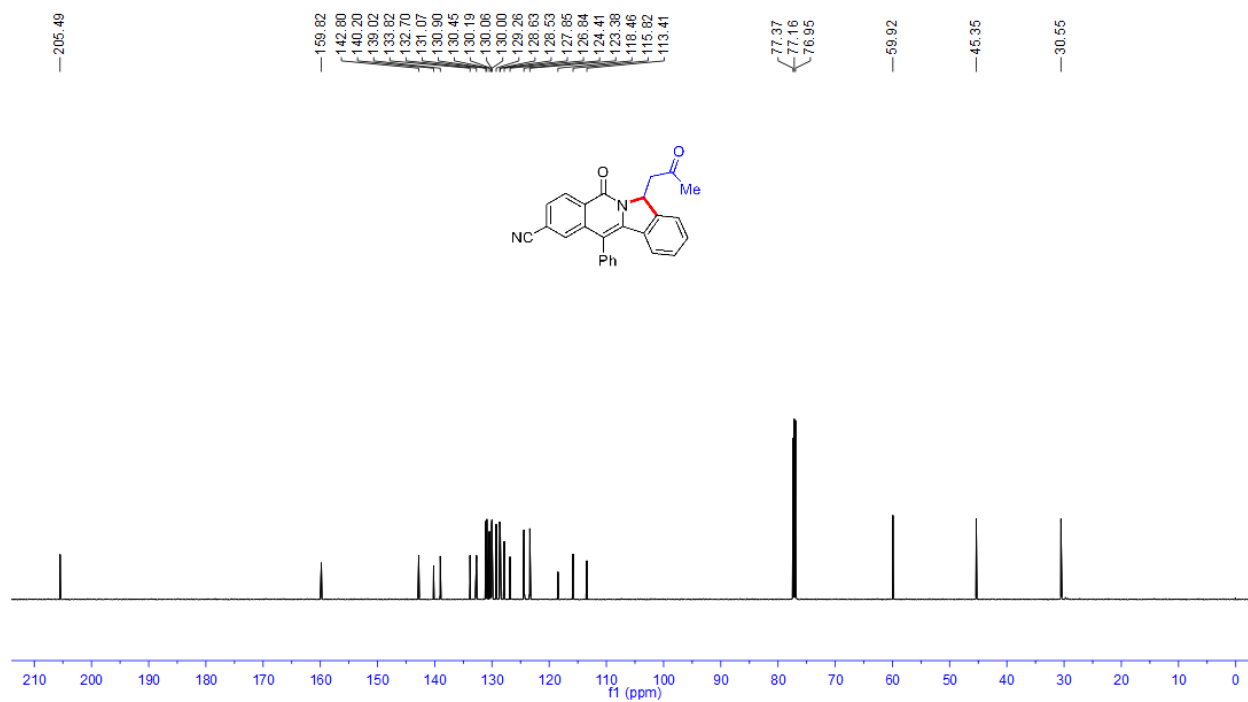
^1H NMR spectrum of **3i** (CDCl_3 , 600 MHz)



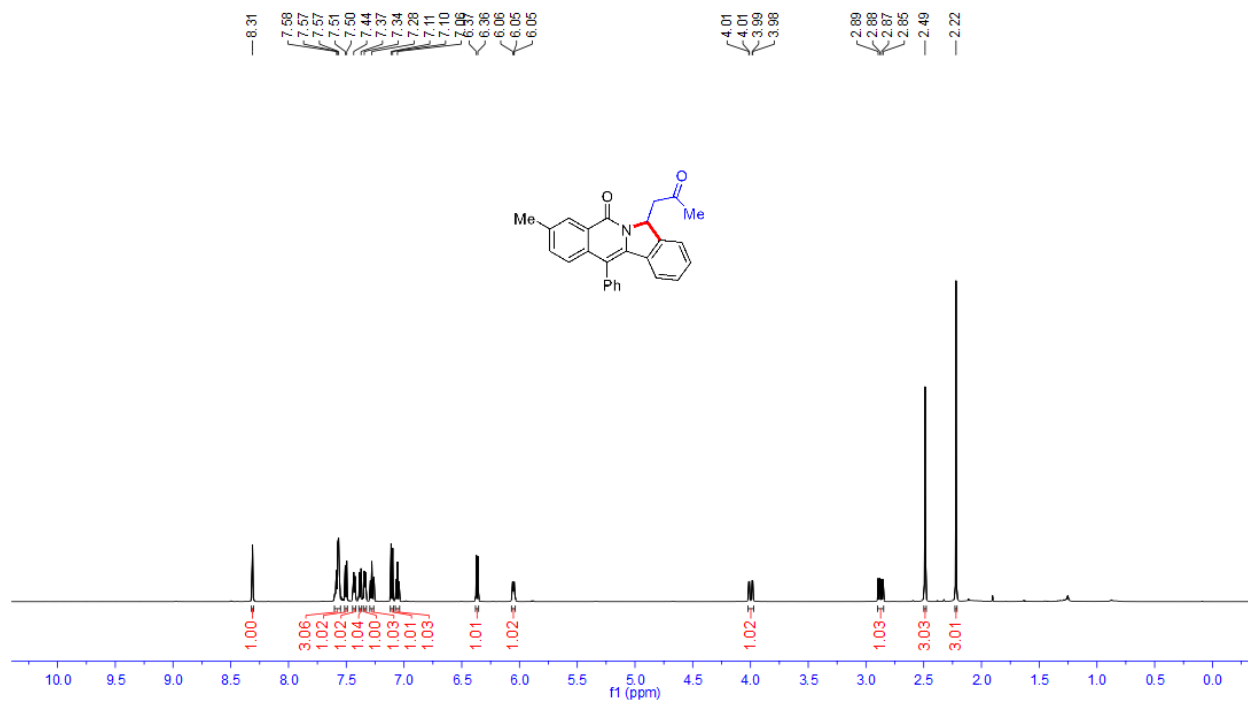
^{13}C NMR spectrum of **3i** (CDCl_3 , 151 MHz)



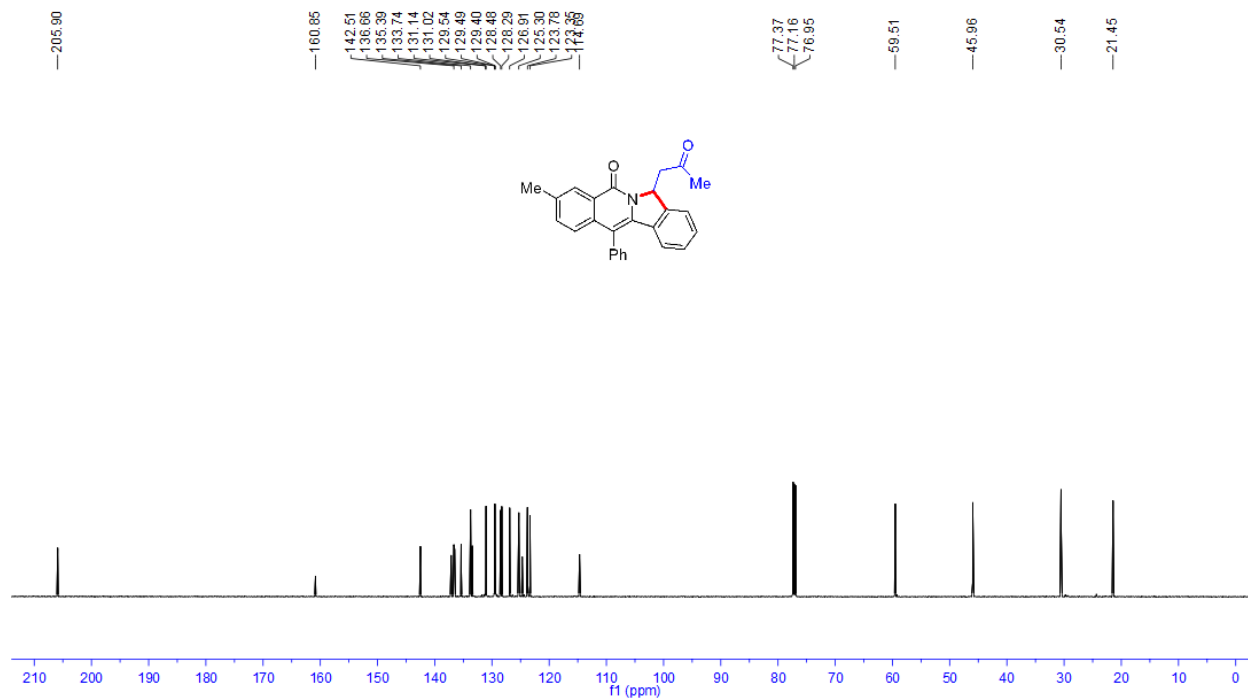
¹H NMR spectrum of **3j** (CDCl₃, 600 MHz)



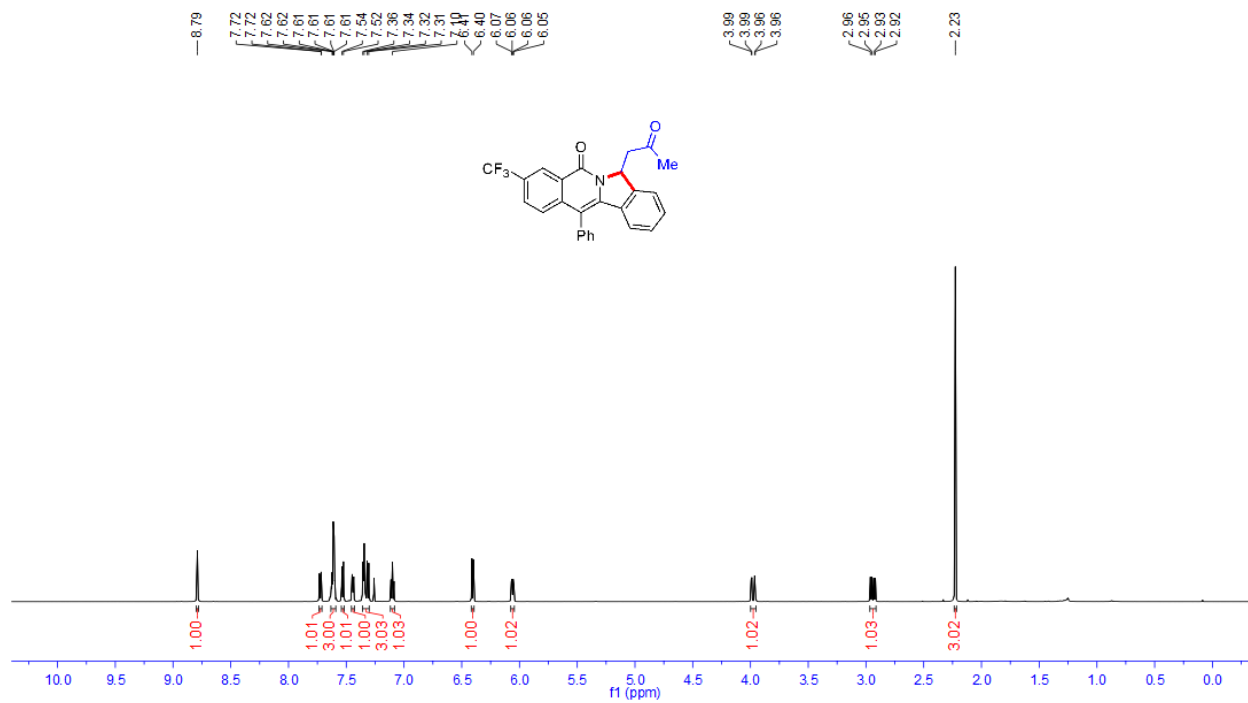
¹³C NMR spectrum of **3j** (CDCl₃, 151 MHz)



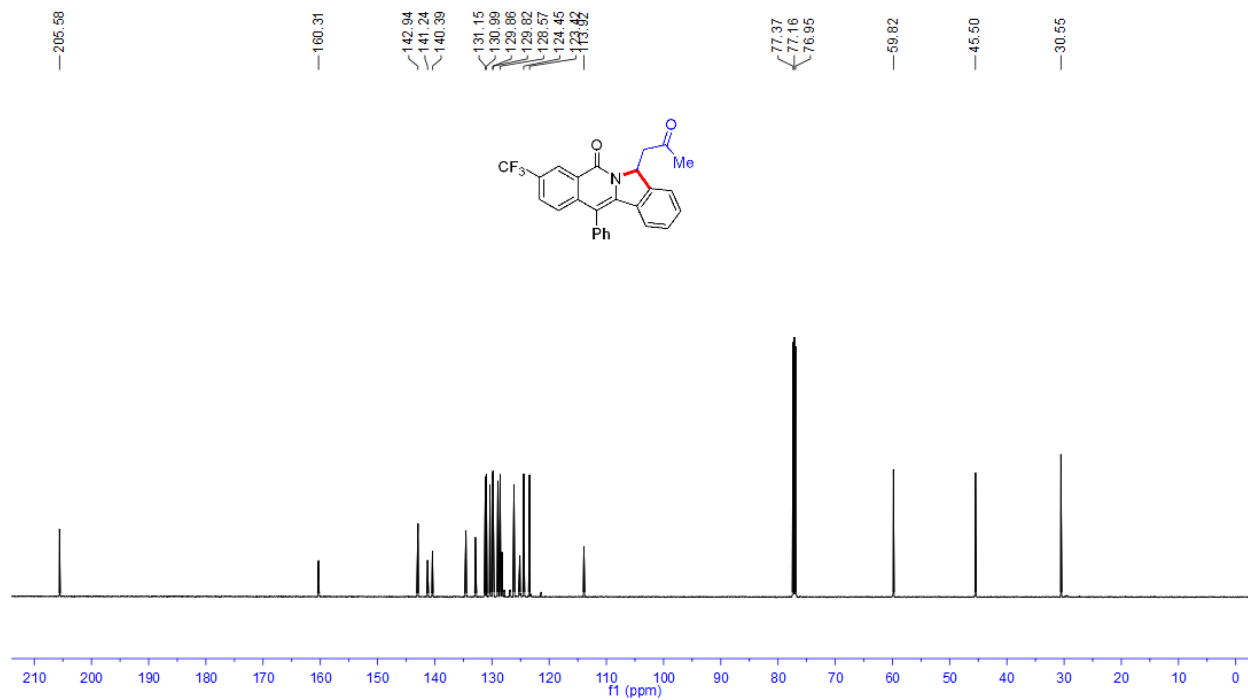
¹H NMR spectrum of **3k** (CDCl₃, 600 MHz)



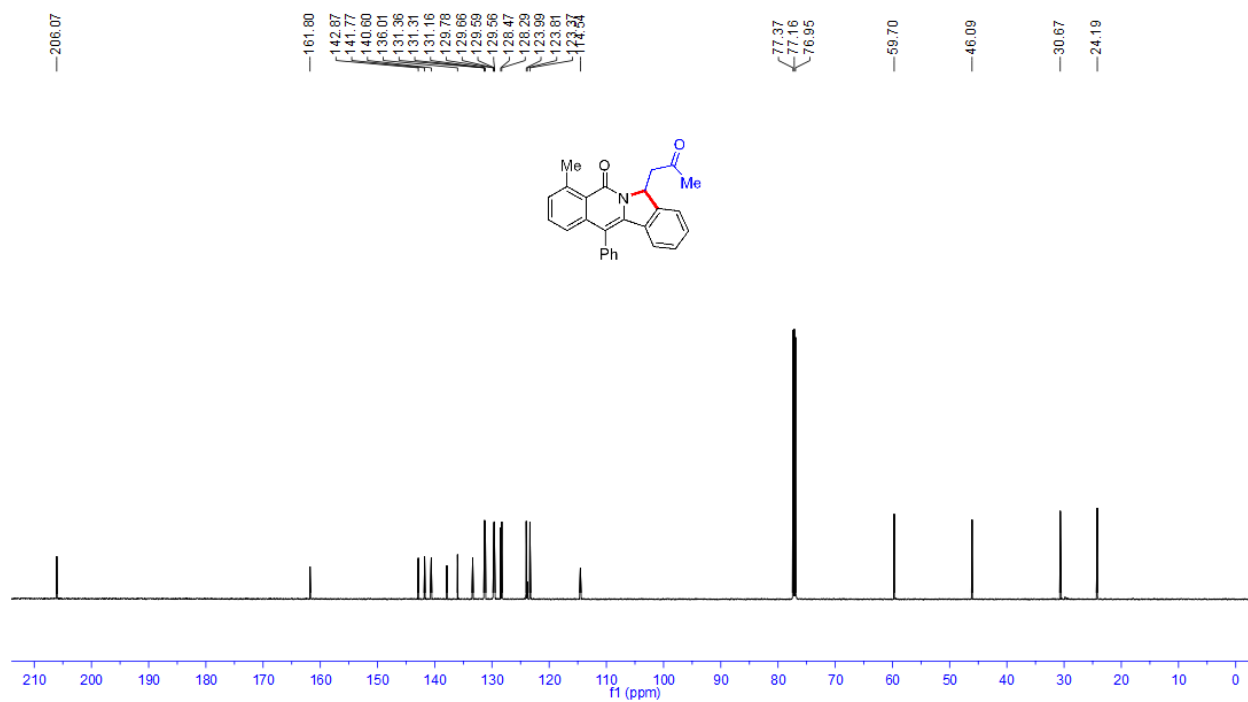
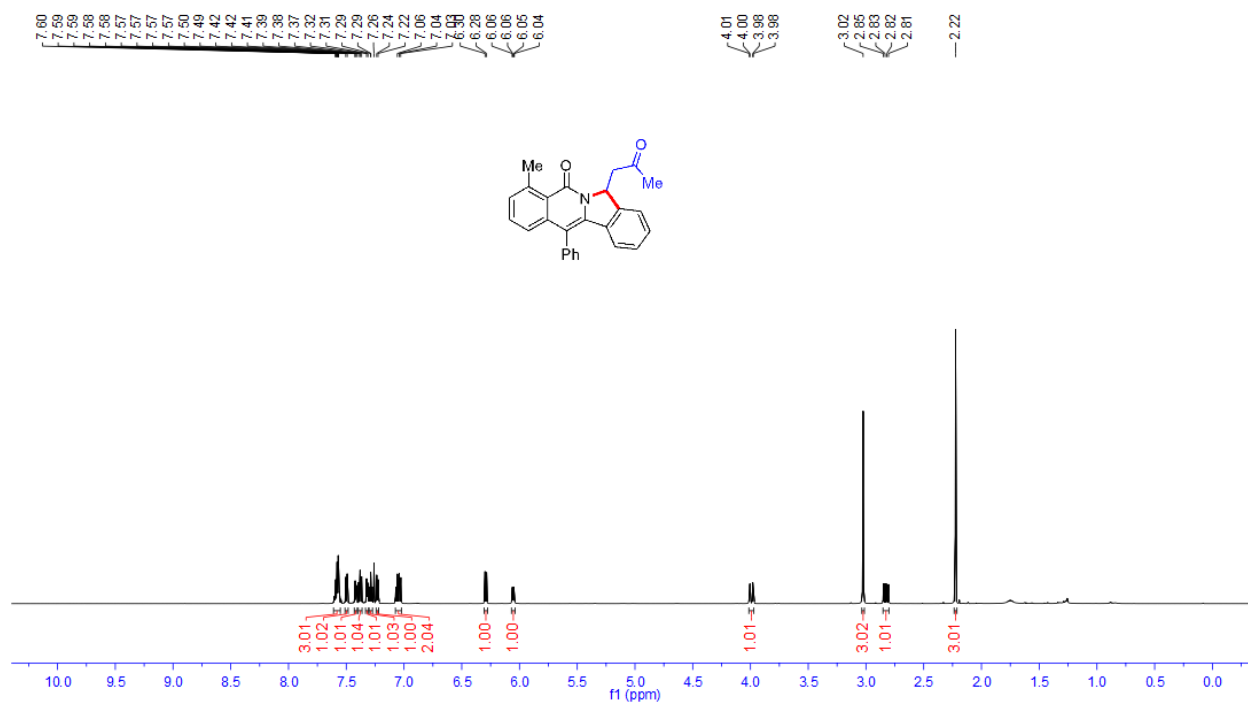
¹³C NMR spectrum of **3k** (CDCl₃, 151 MHz)

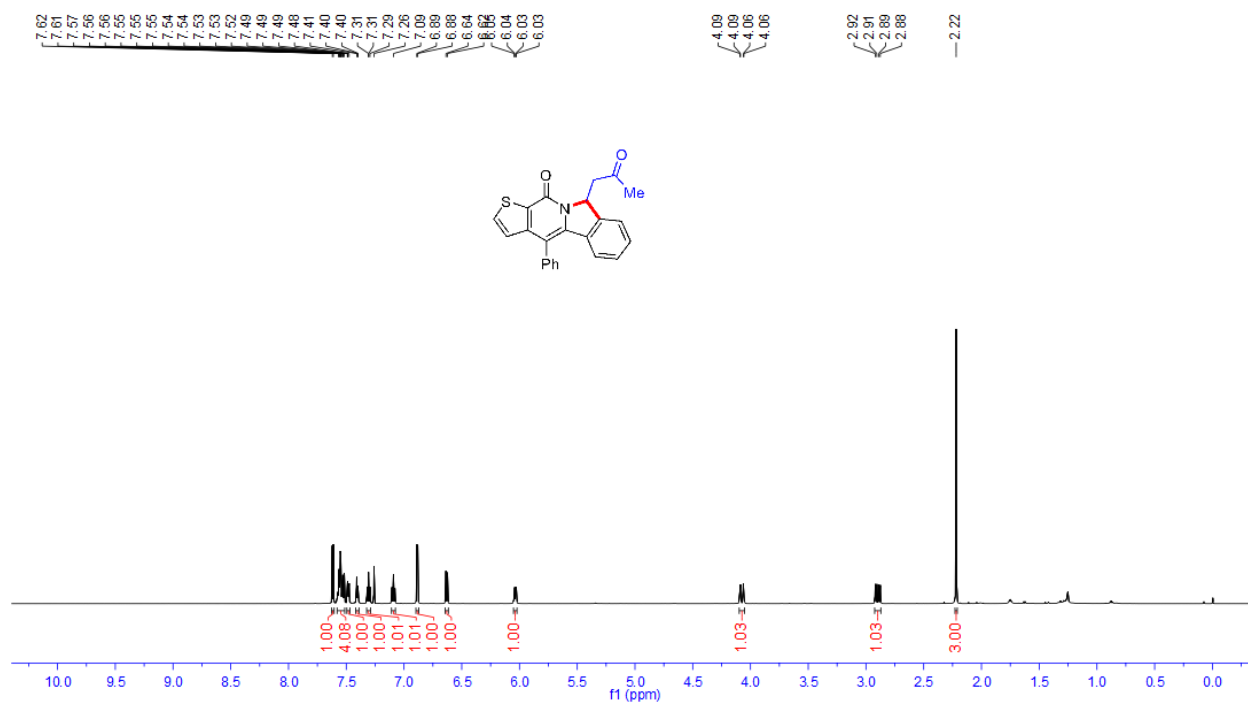


^1H NMR spectrum of **31** (CDCl_3 , 600 MHz)

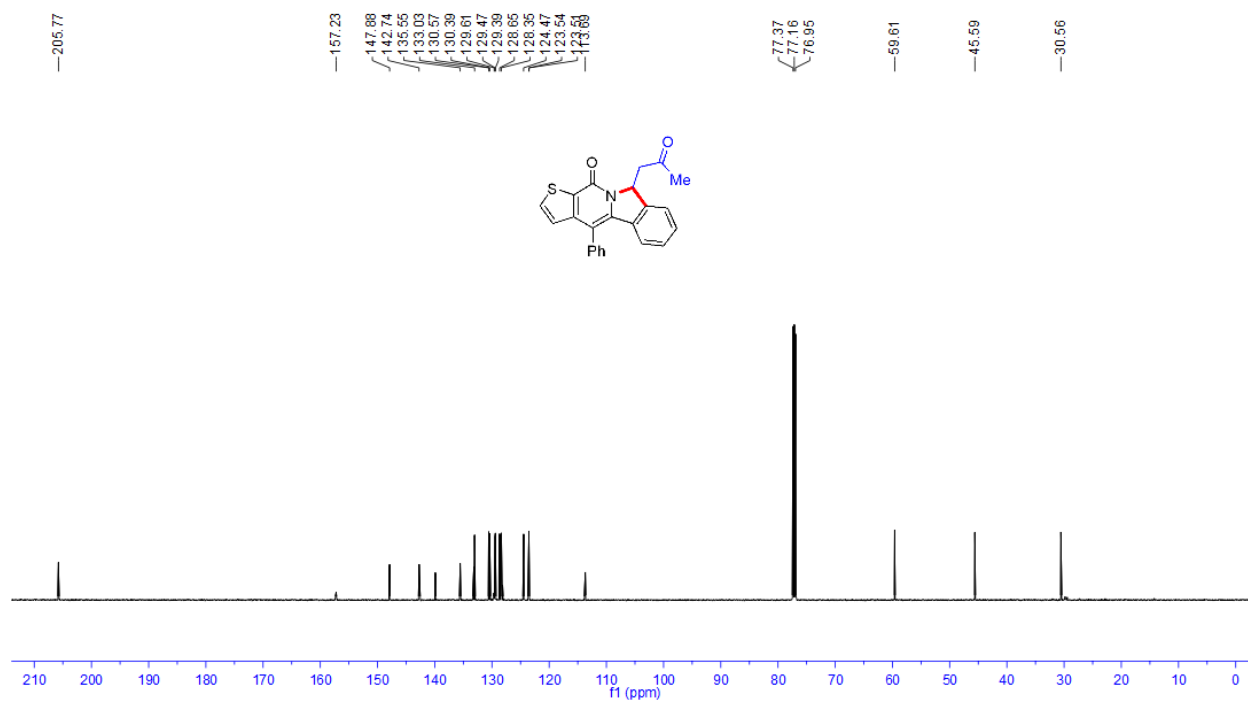


^{13}C NMR spectrum of **31** (CDCl_3 , 151 MHz)

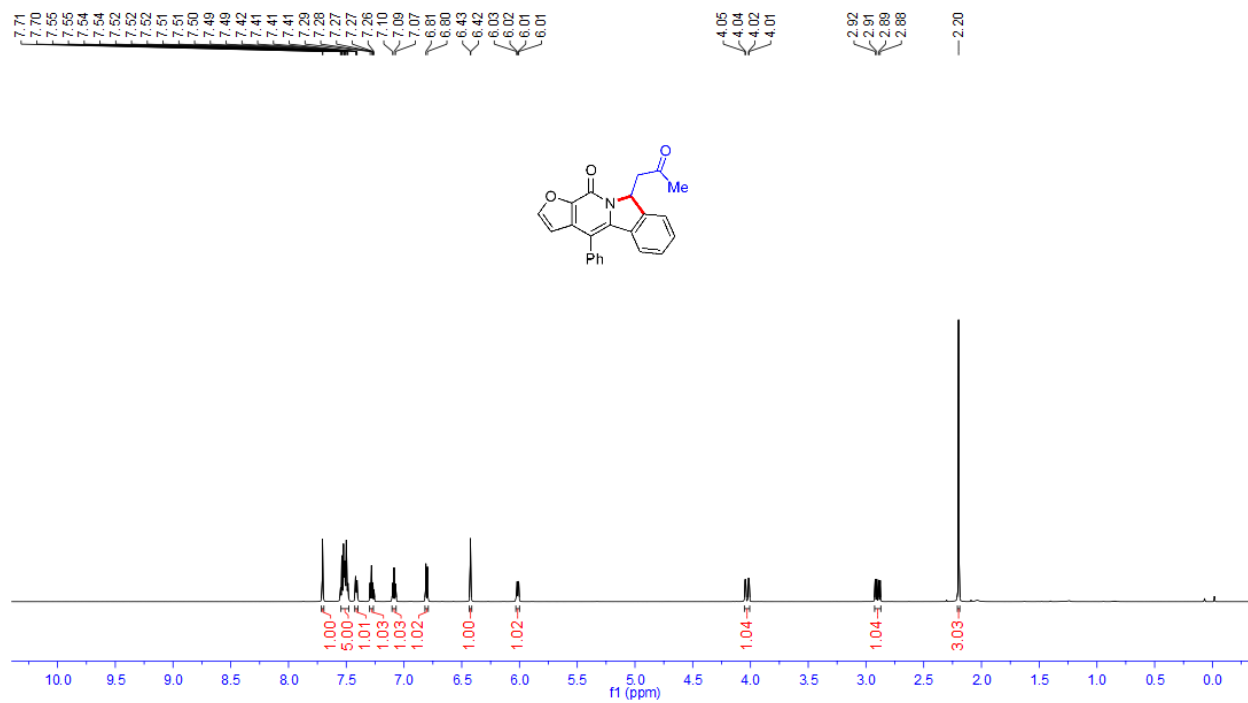




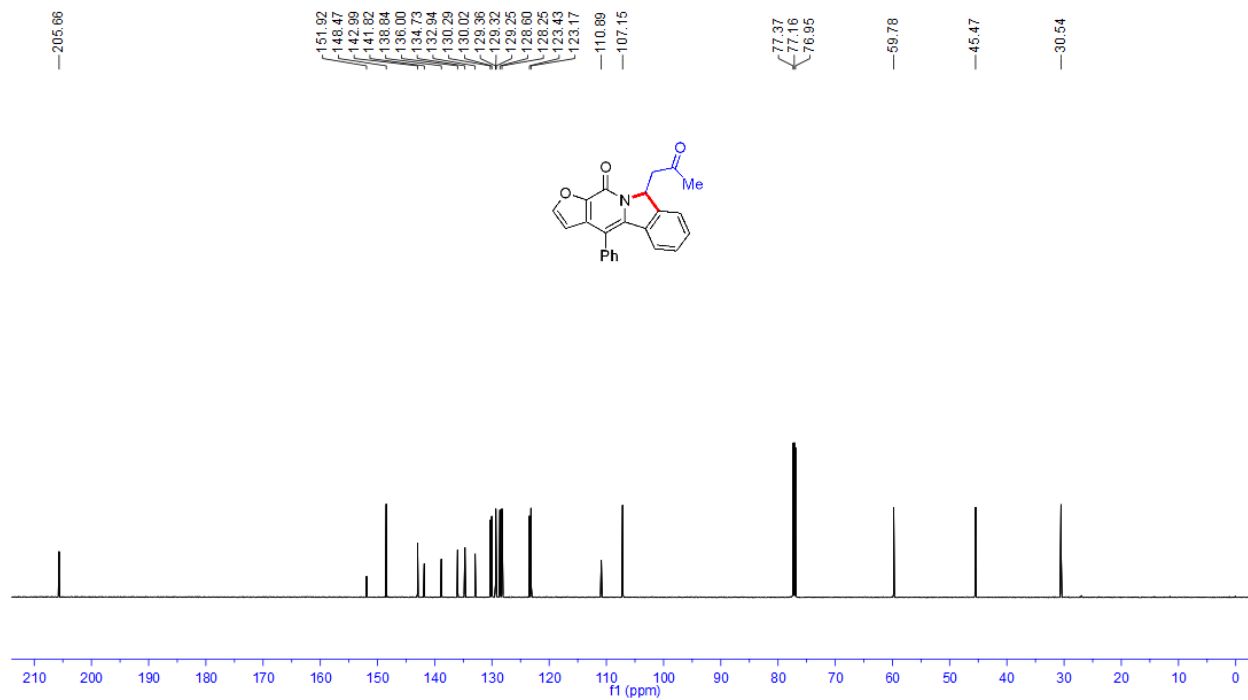
¹H NMR spectrum of **3n** (CDCl₃, 600 MHz)



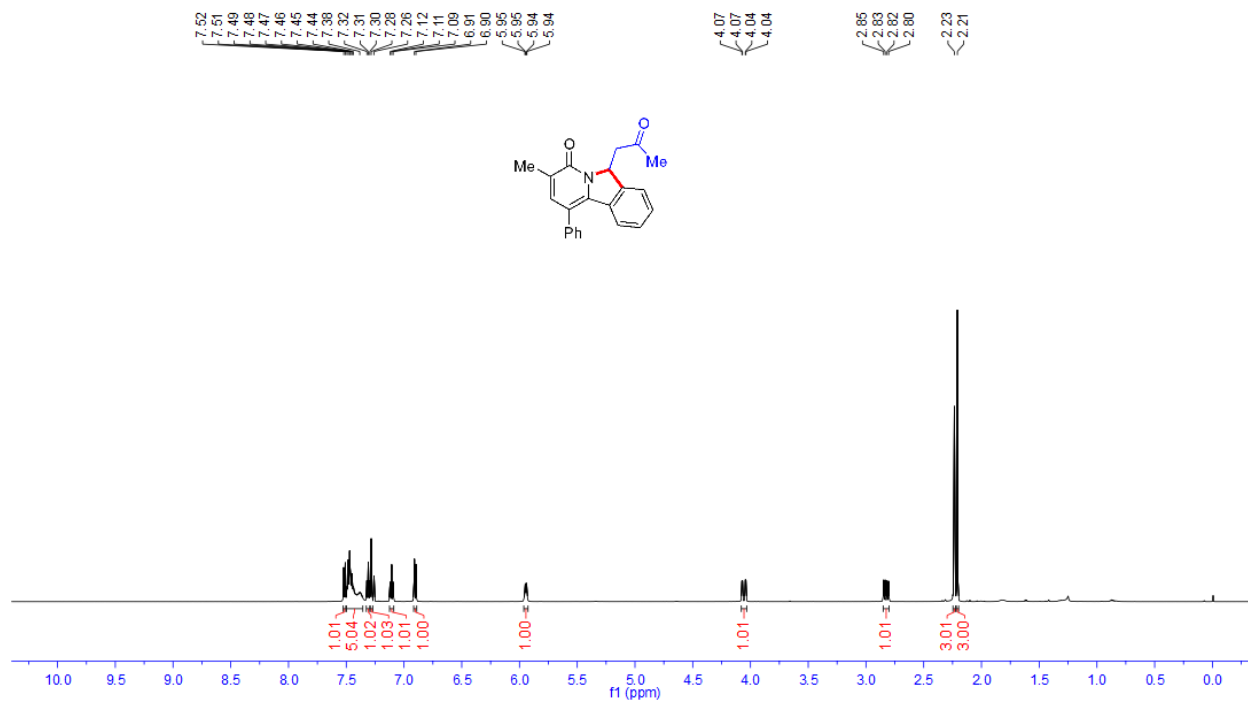
¹³C NMR spectrum of **3n** (CDCl₃, 151 MHz)



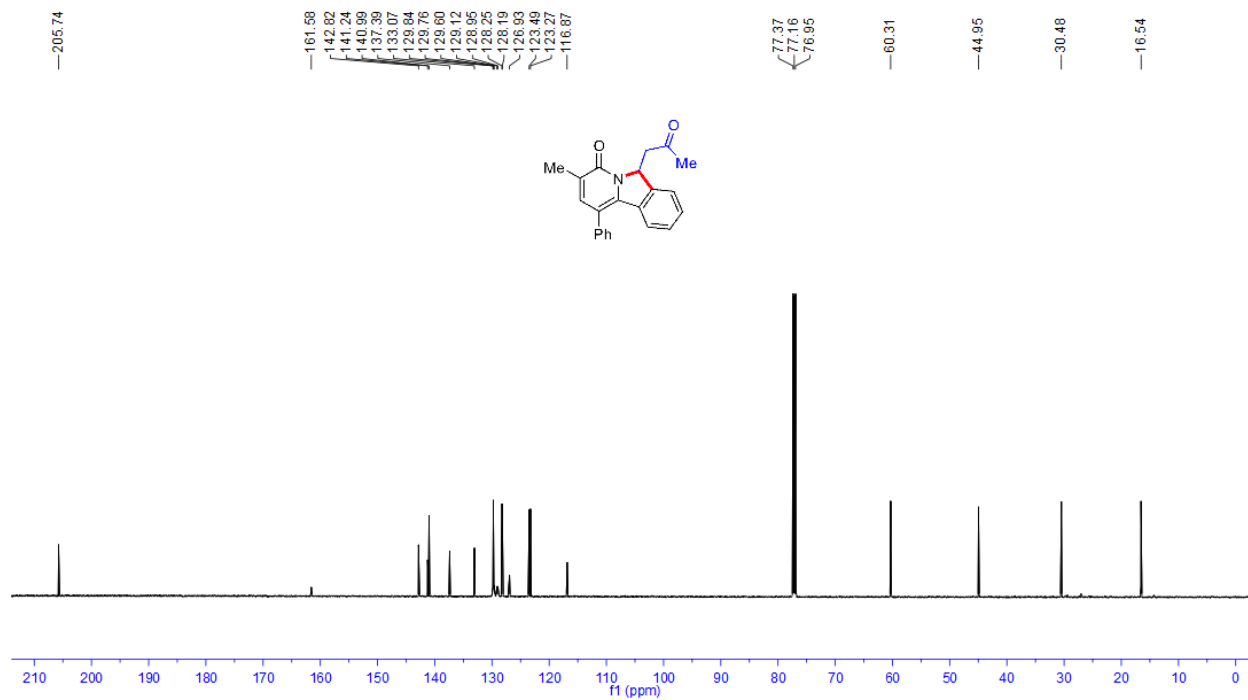
¹H NMR spectrum of **3o** (CDCl₃, 600 MHz)



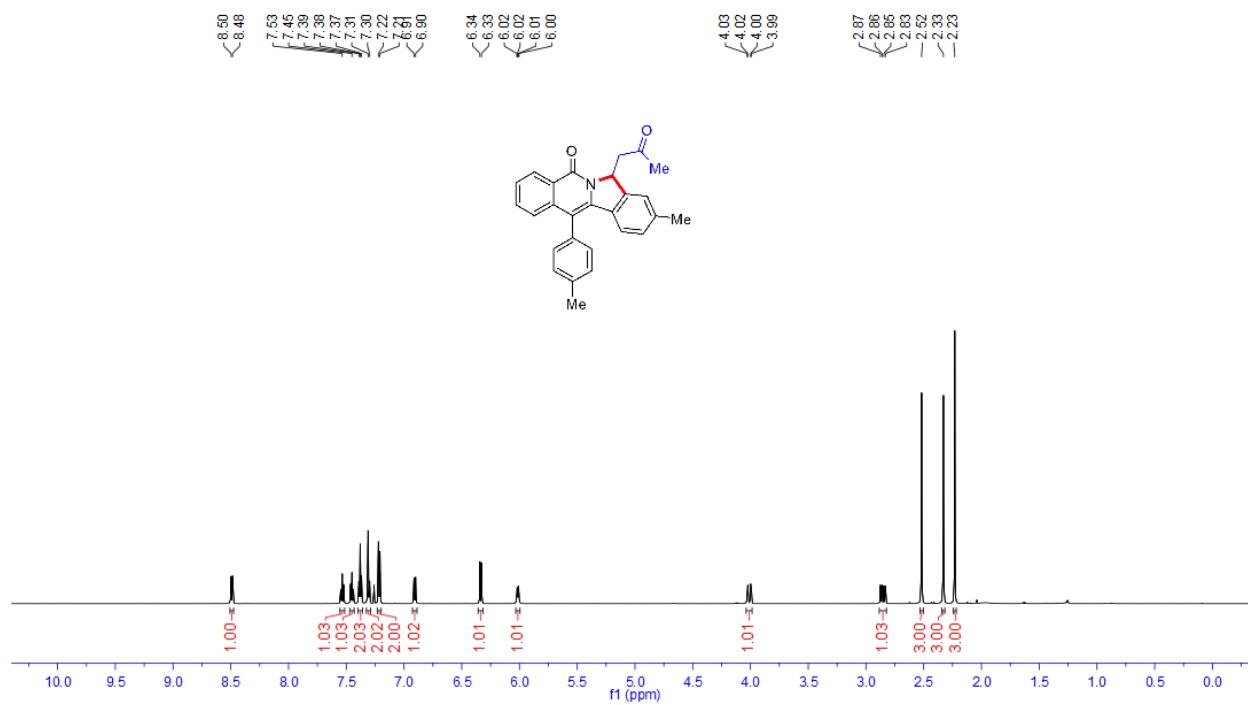
¹³C NMR spectrum of **3o** (CDCl₃, 151 MHz)



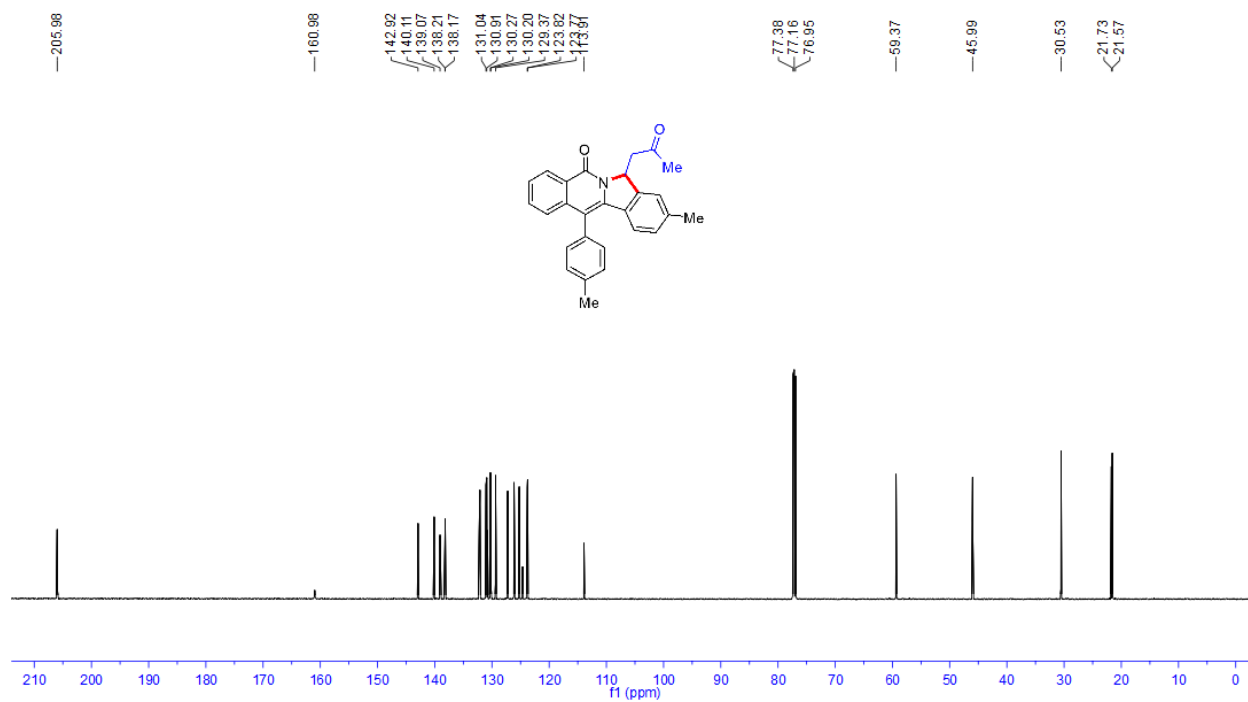
¹H NMR spectrum of **3p** (CDCl₃, 600 MHz)



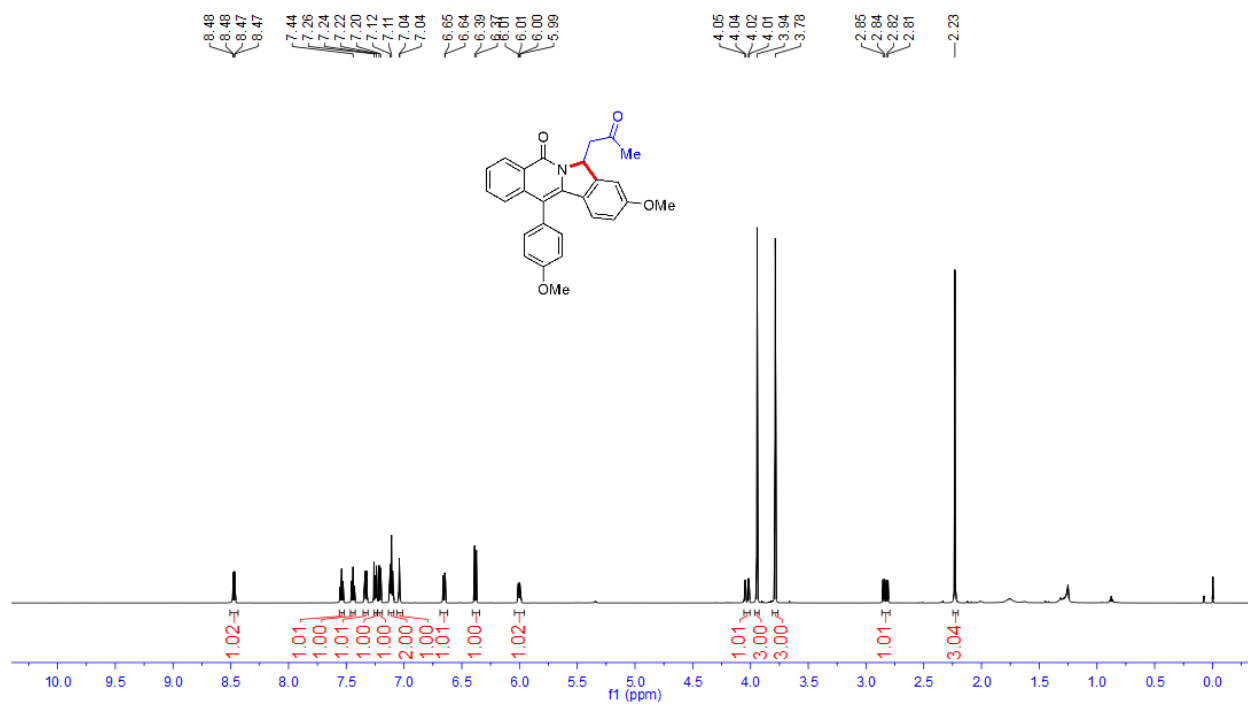
¹³C NMR spectrum of **3p** (CDCl₃, 151 MHz)



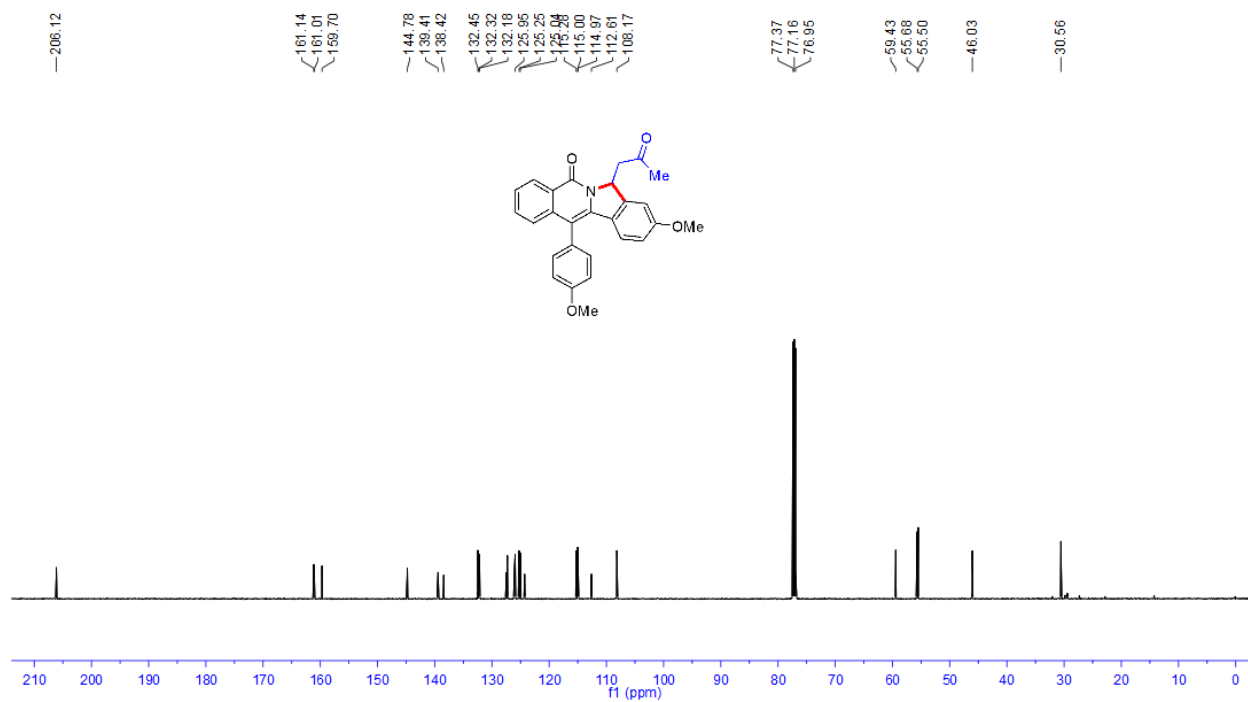
¹H NMR spectrum of **3q** (CDCl₃, 600 MHz)



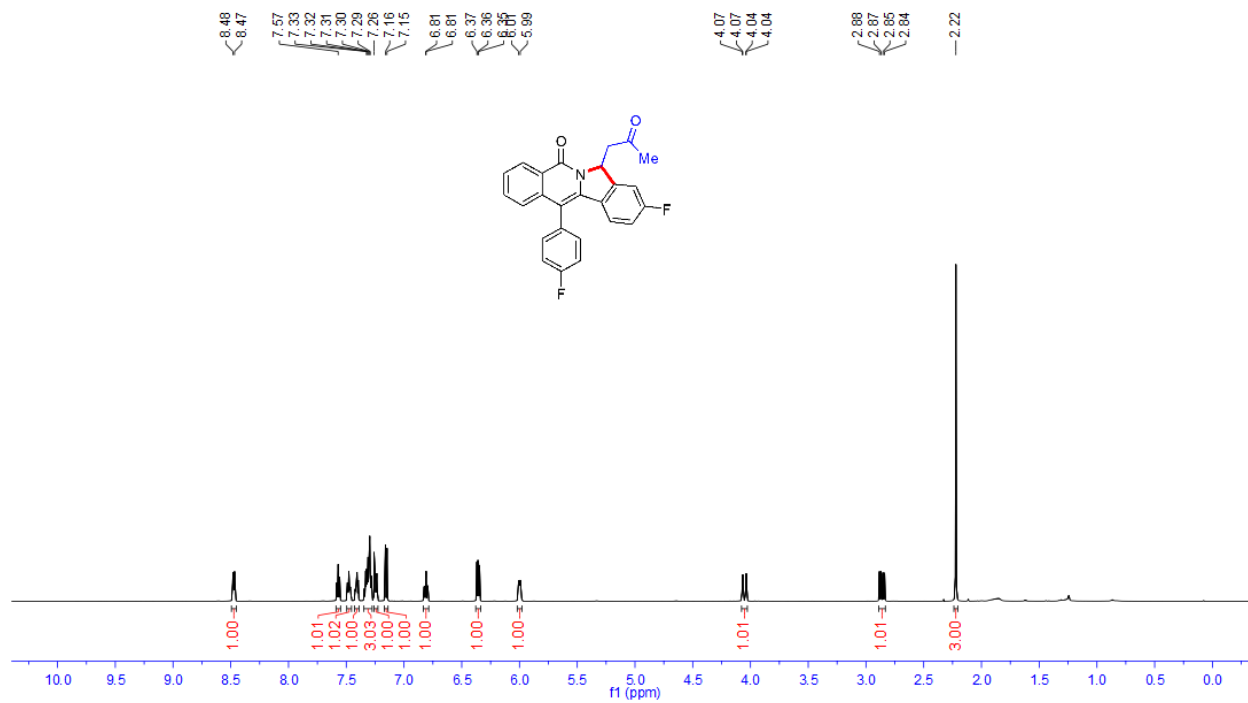
¹³C NMR spectrum of **3q** (CDCl₃, 151 MHz)



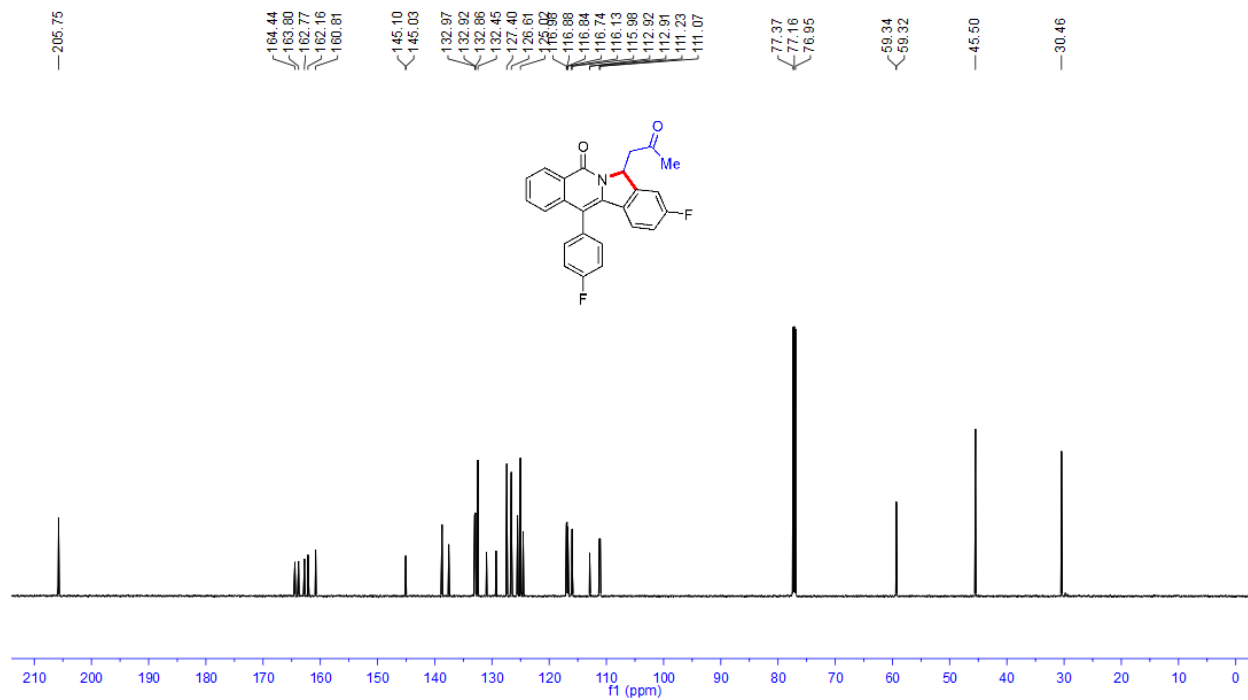
¹H NMR spectrum of **3r** (CDCl₃, 600 MHz)



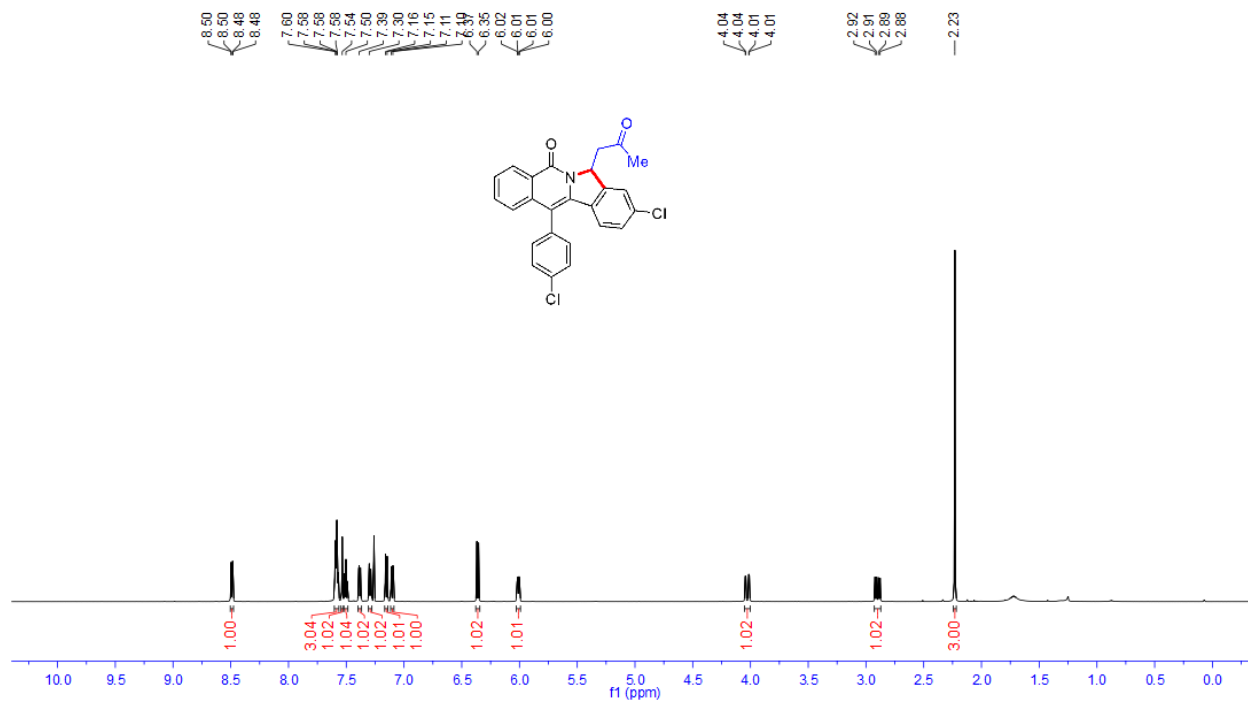
¹³C NMR spectrum of **3r** (CDCl₃, 151 MHz)



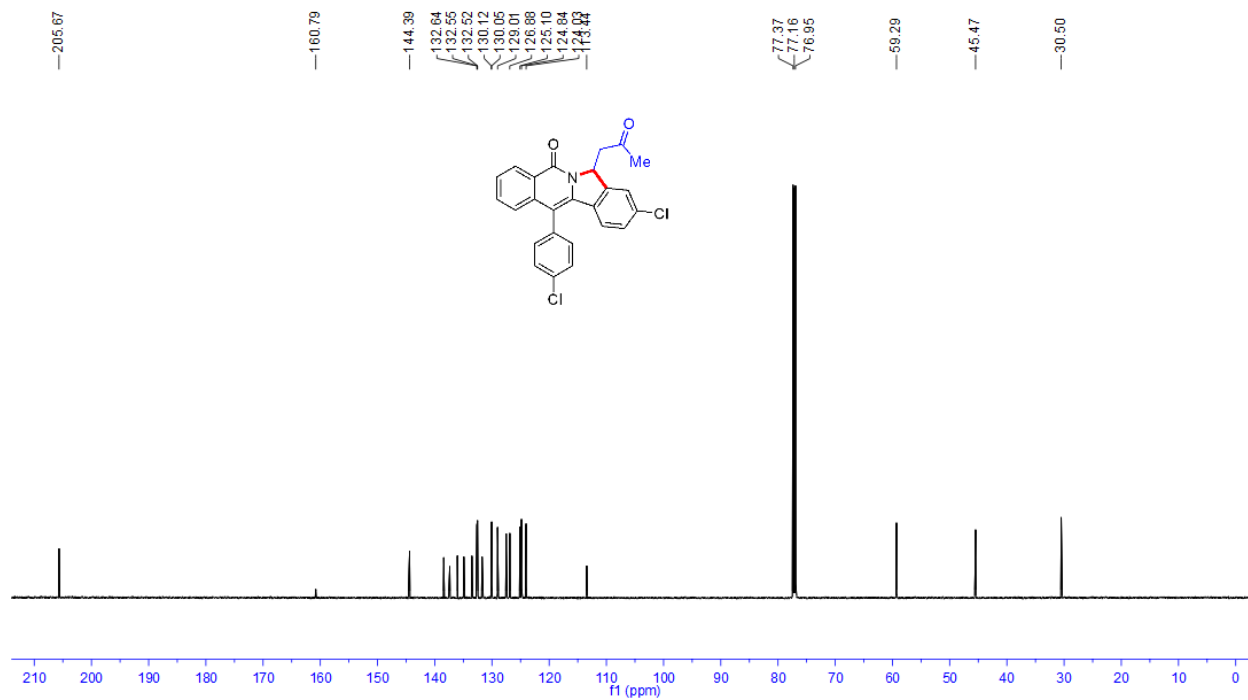
¹H NMR spectrum of **3s** (CDCl₃, 600 MHz)



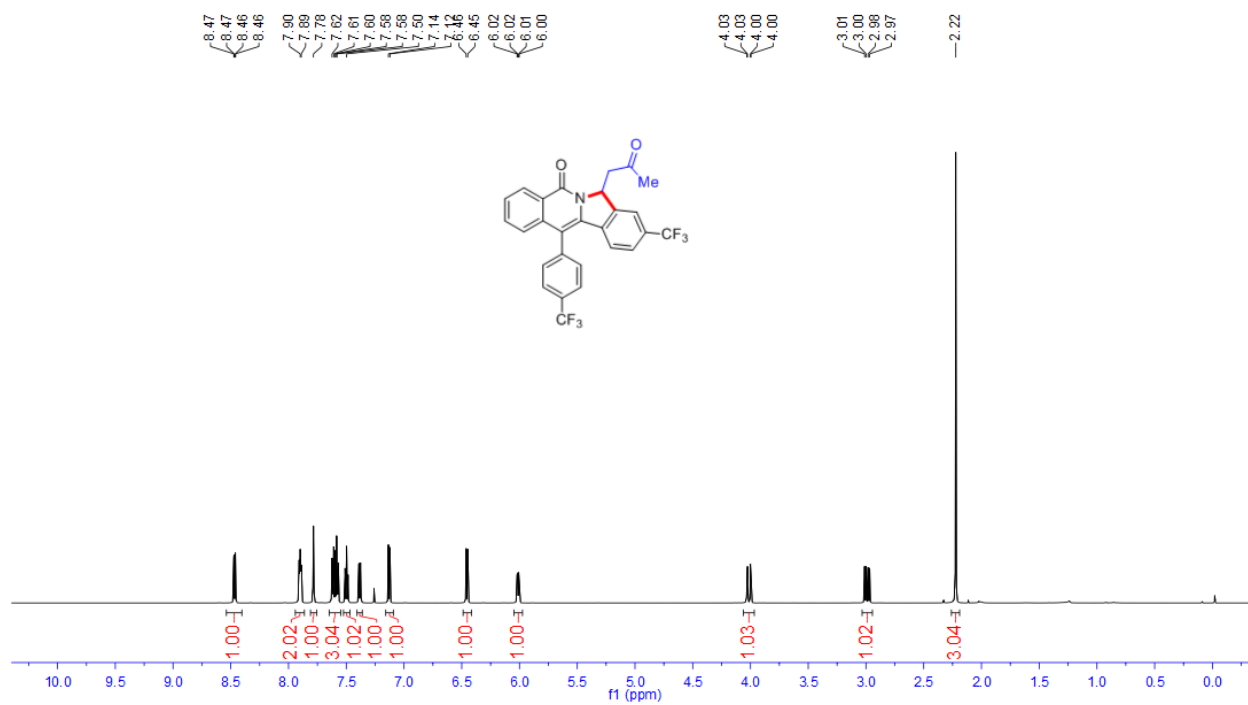
¹³C NMR spectrum of **3s** (CDCl₃, 151 MHz)



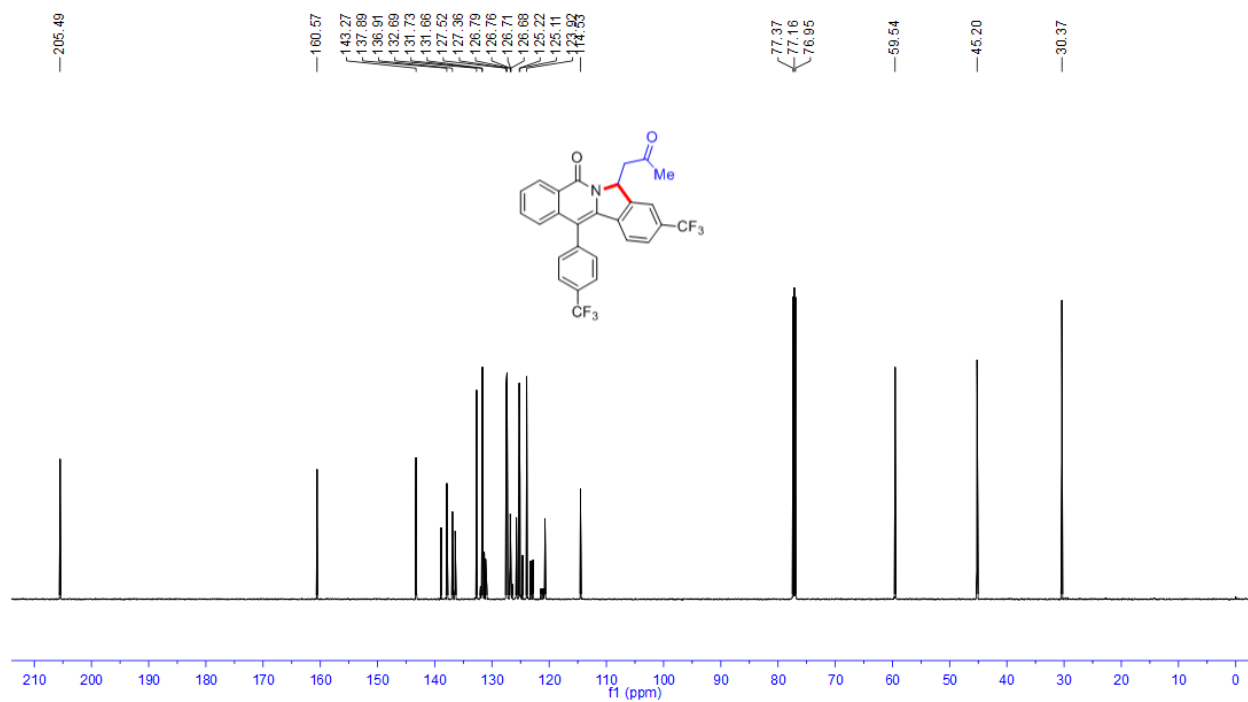
¹H NMR spectrum of **3t** (CDCl₃, 600 MHz)



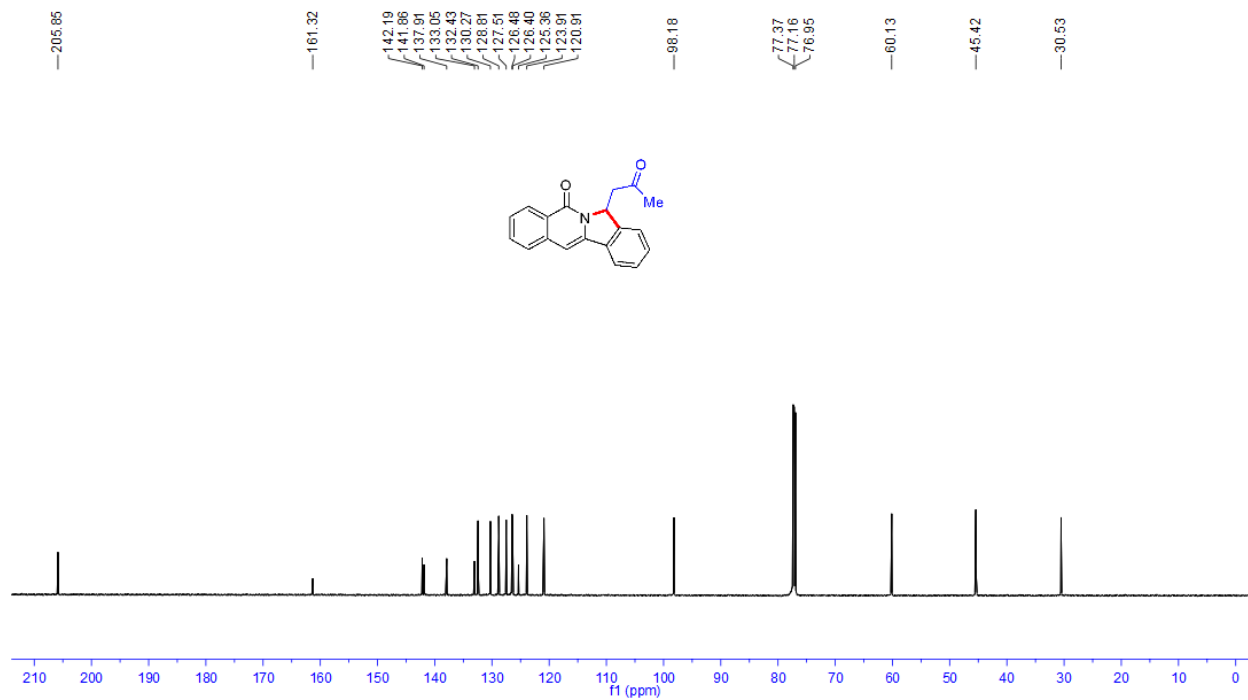
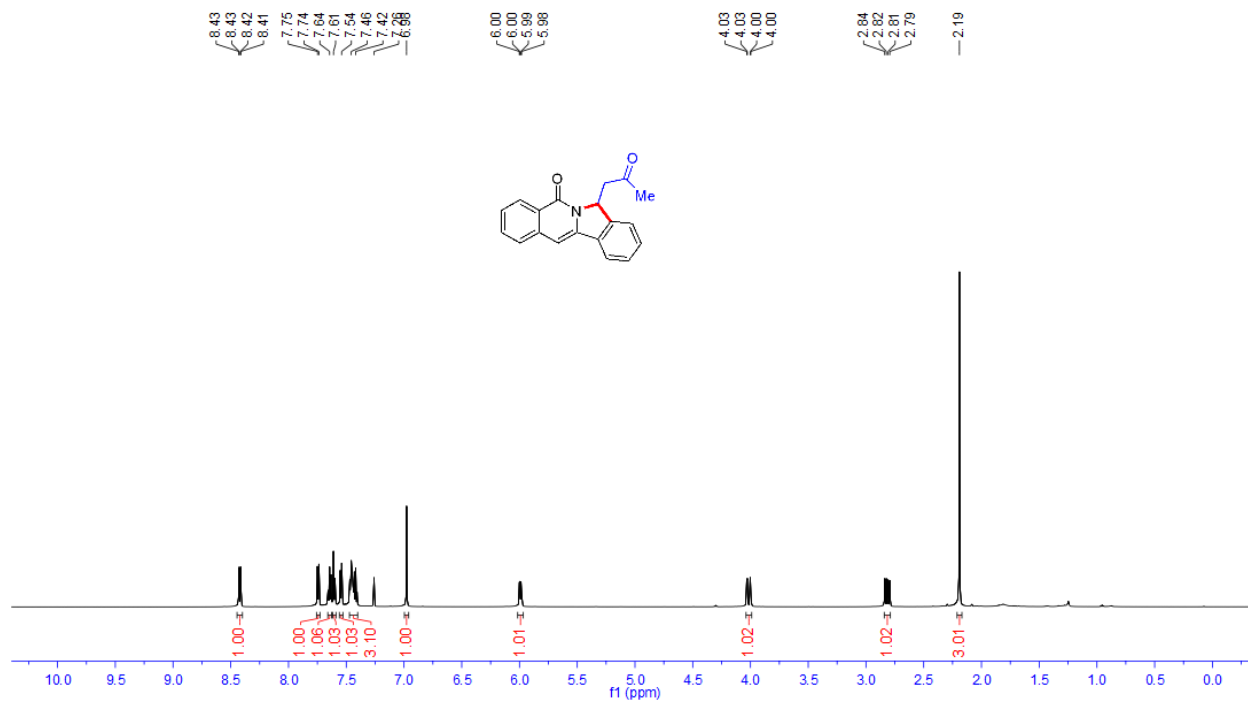
¹³C NMR spectrum of **3t** (CDCl₃, 151 MHz)

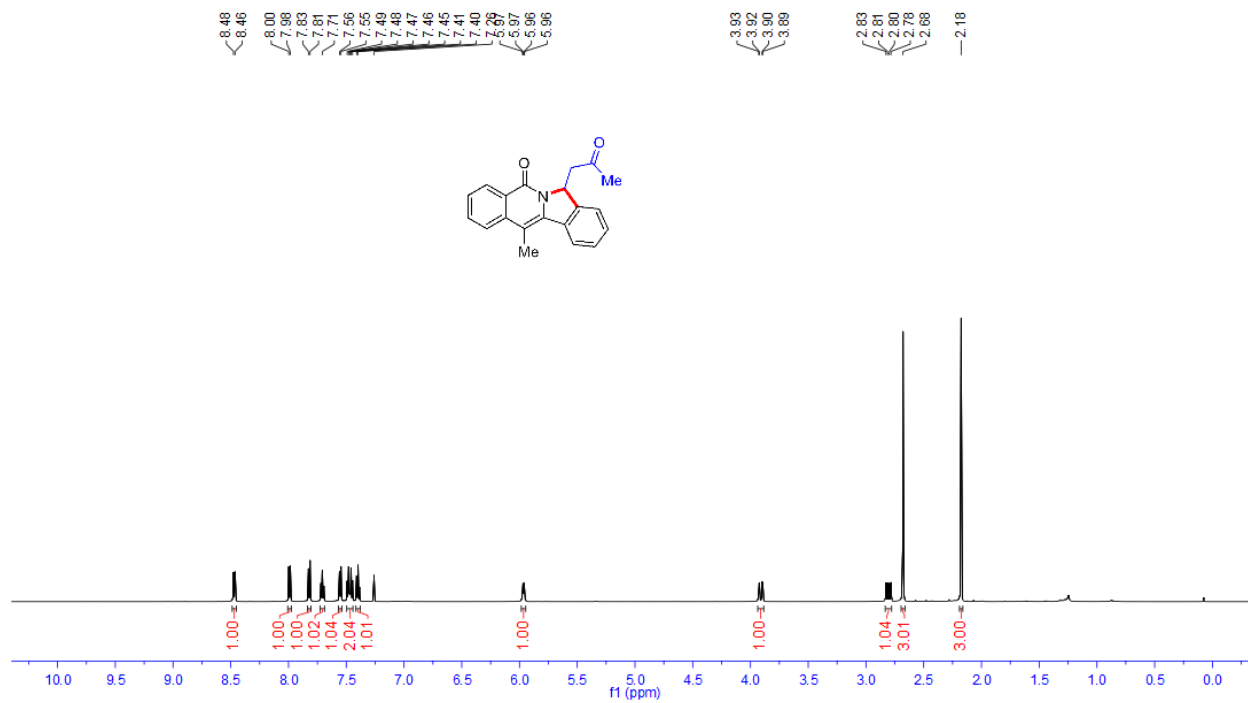


^1H NMR spectrum of **3u** (CDCl_3 , 600 MHz)

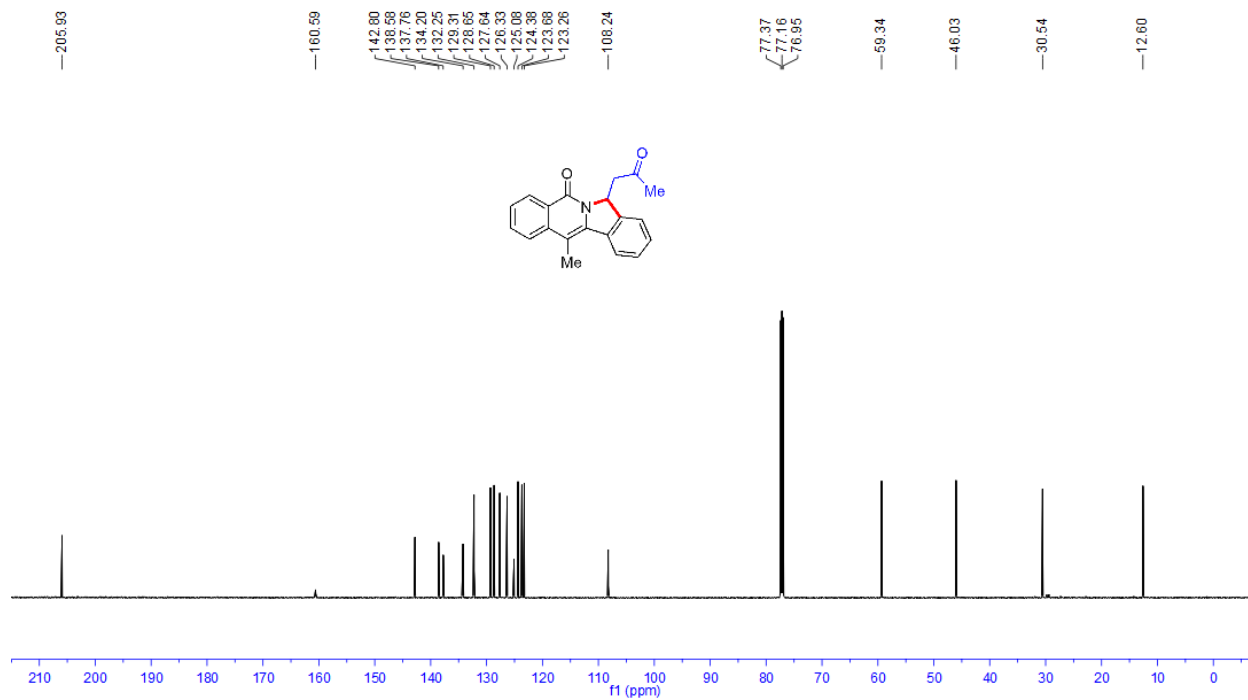


^{13}C NMR spectrum of **3u** (CDCl_3 , 151 MHz)

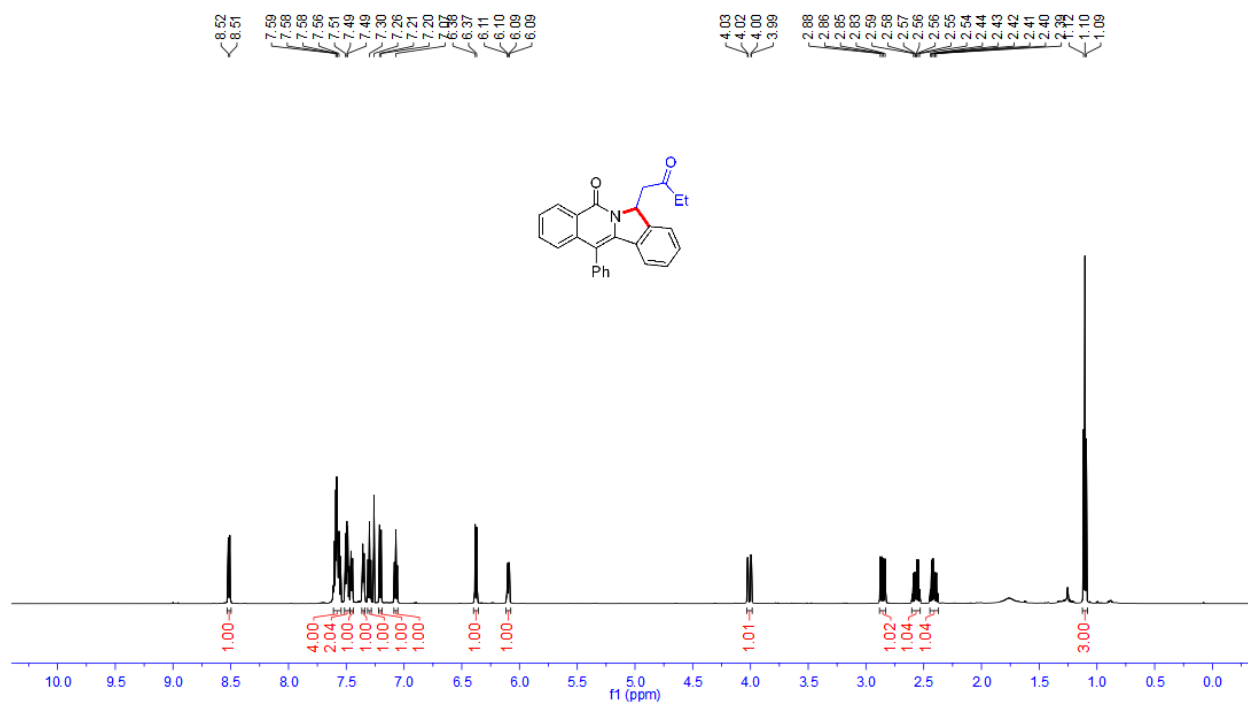




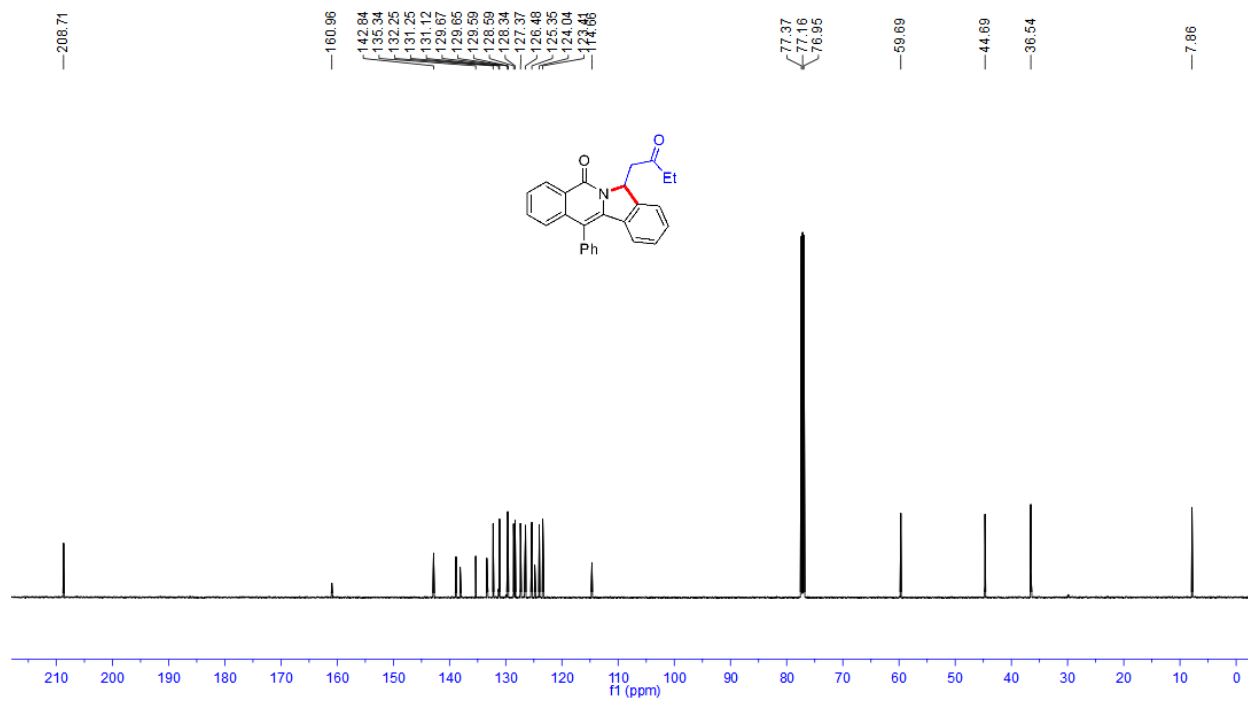
¹H NMR spectrum of **3w** (CDCl₃, 600 MHz)



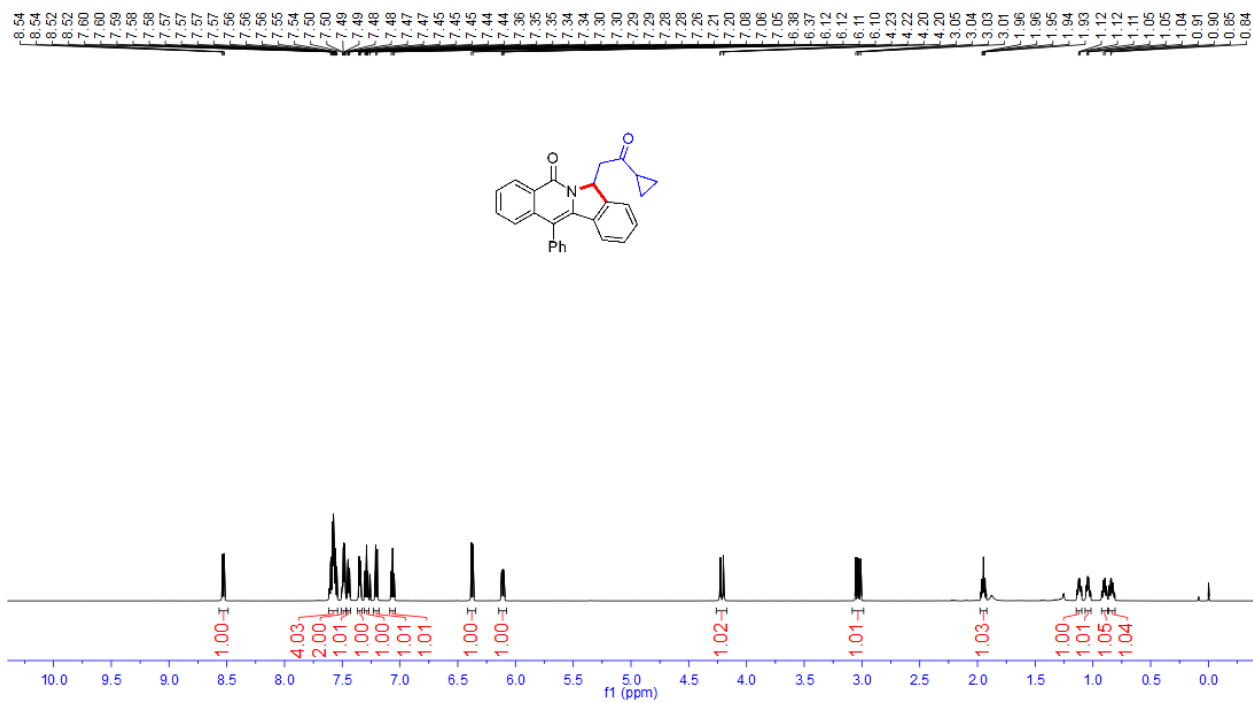
¹³C NMR spectrum of **3w** (CDCl₃, 151 MHz)



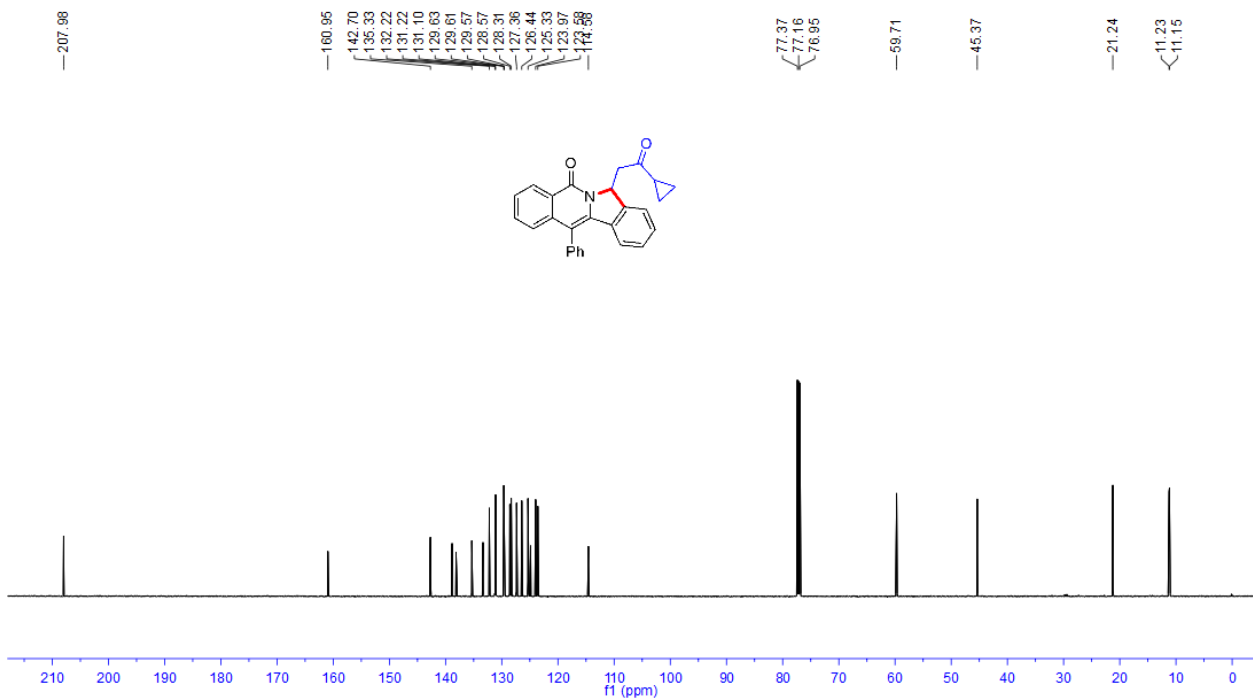
¹H NMR spectrum of **3y** (CDCl₃, 600 MHz)



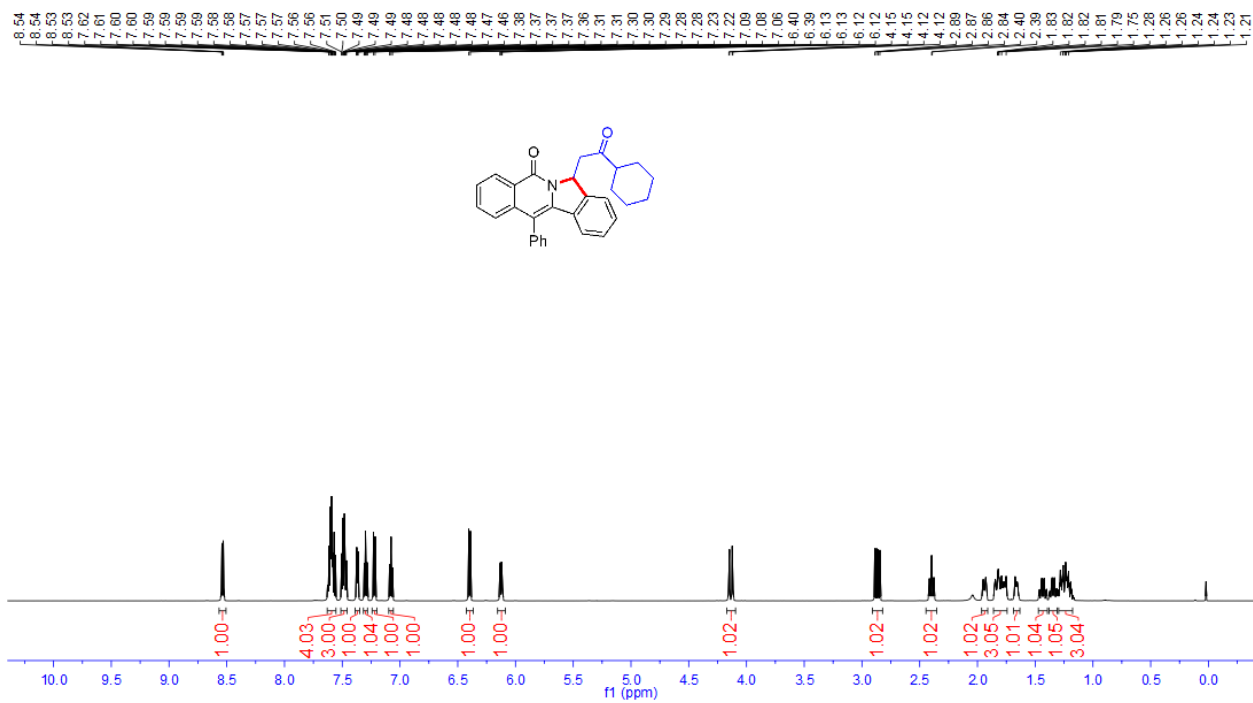
¹³C NMR spectrum of **3y** (CDCl₃, 151 MHz)



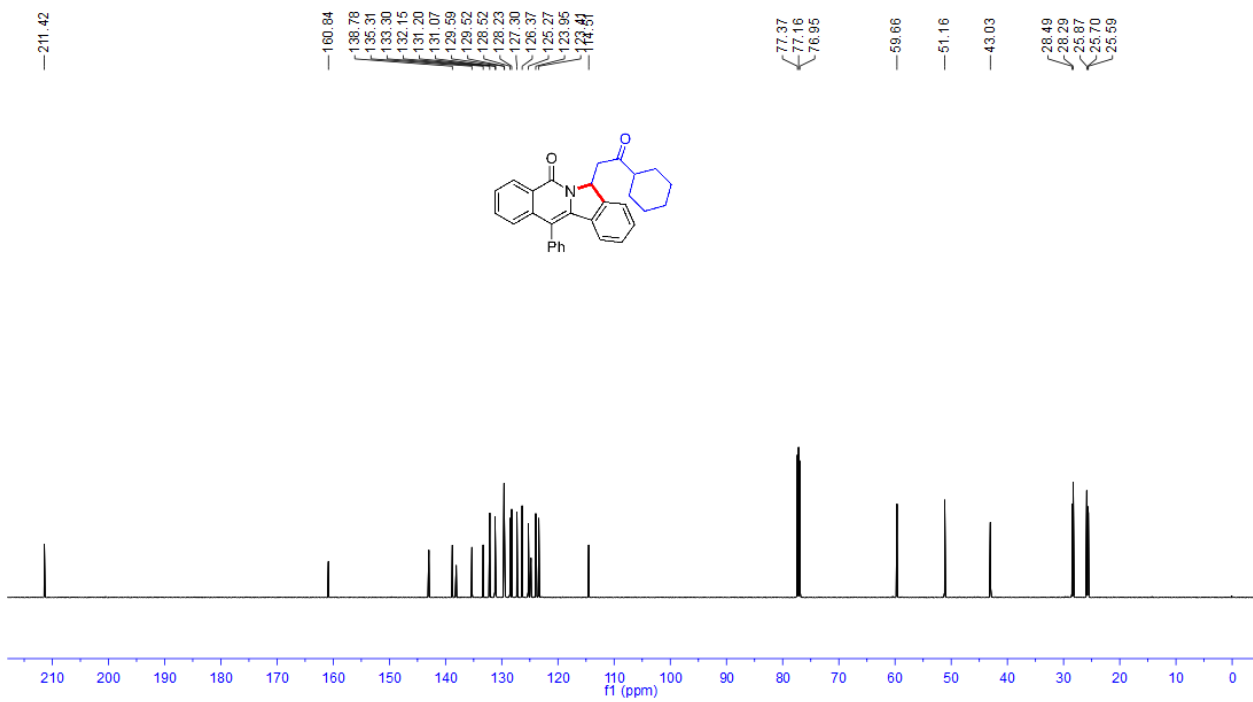
¹H NMR spectrum of **3z** (CDCl₃, 600 MHz)



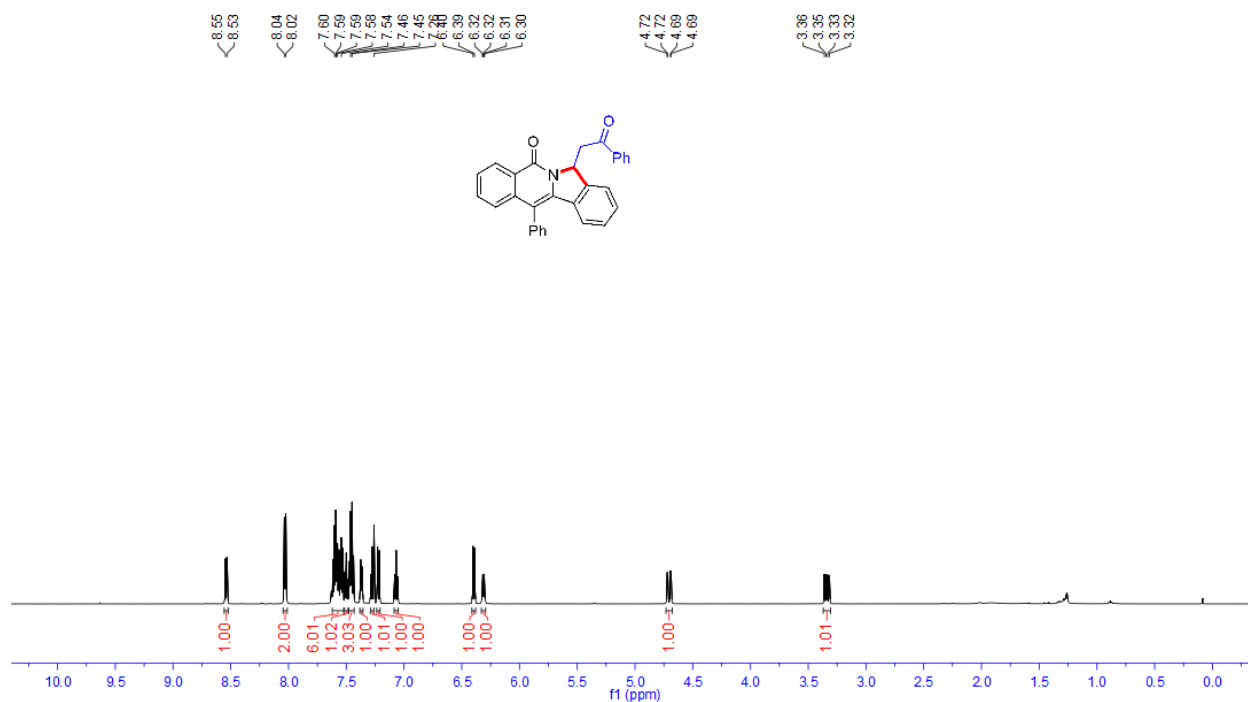
¹³C NMR spectrum of **3z** (CDCl₃, 151 MHz)



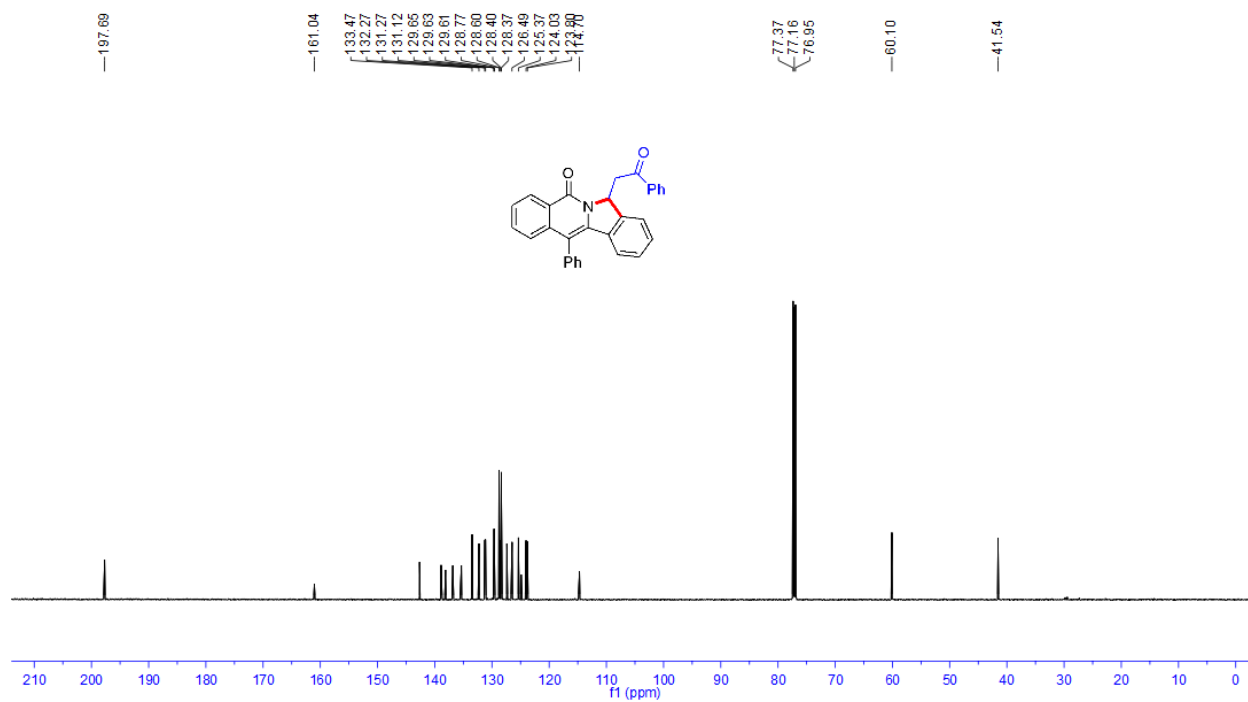
¹H NMR spectrum of **3aa** (CDCl₃, 600 MHz)



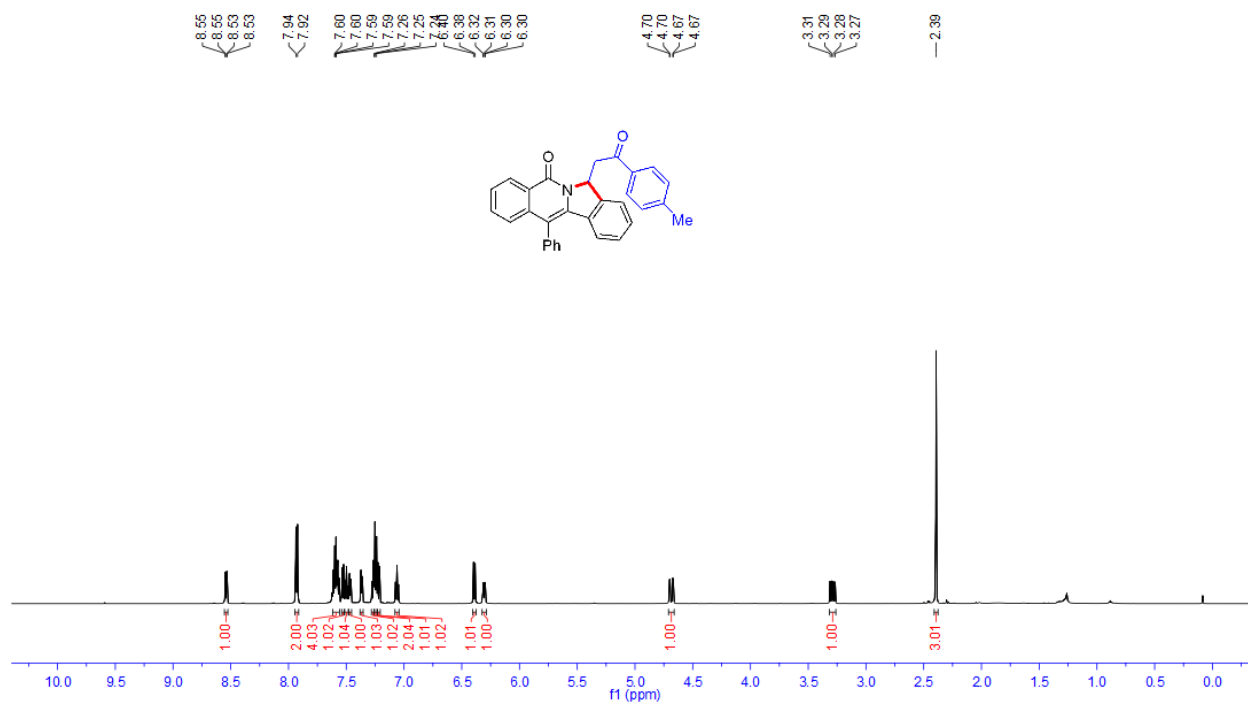
¹³C NMR spectrum of **3aa** (CDCl₃, 151 MHz)



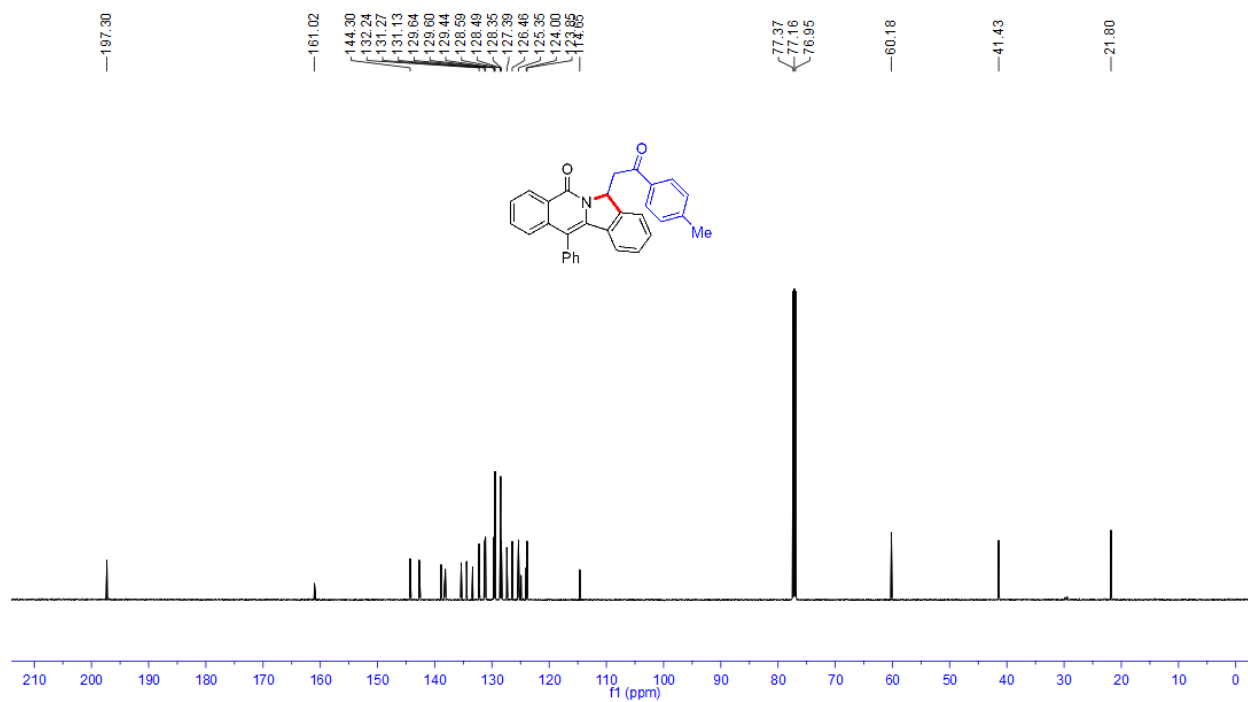
^1H NMR spectrum of **3ab** (CDCl_3 , 600 MHz)



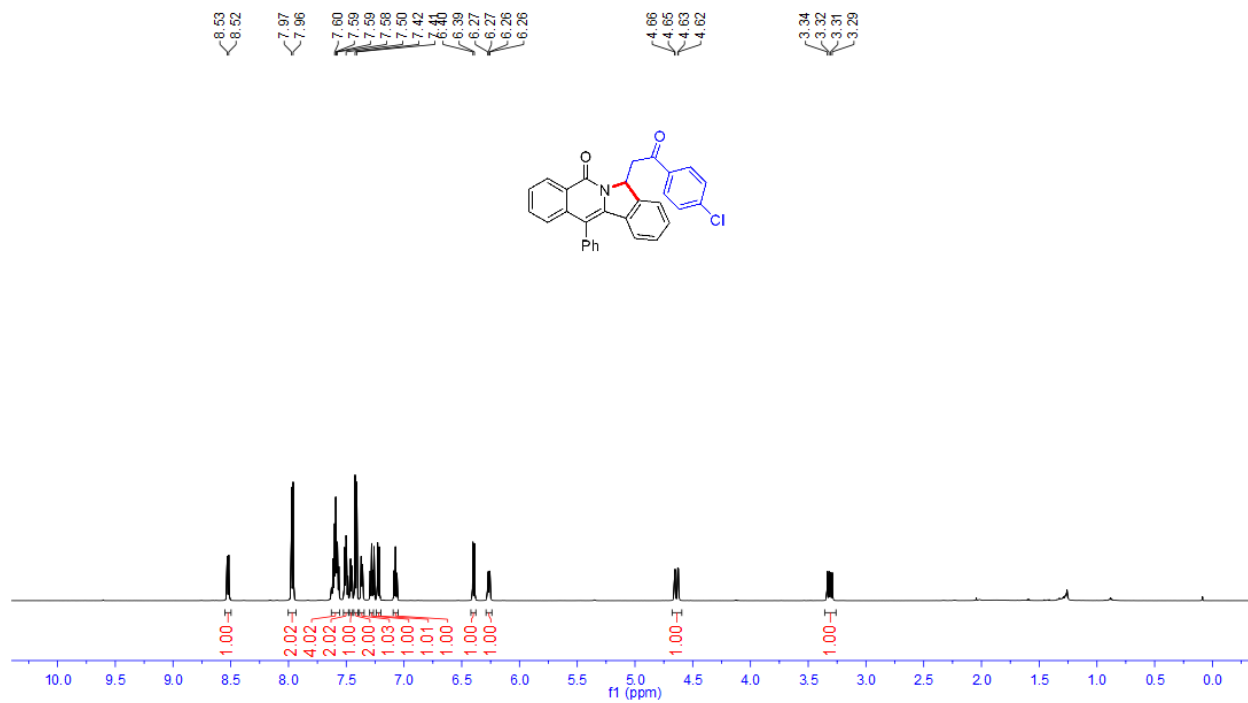
^{13}C NMR spectrum of **3ab** (CDCl_3 , 151 MHz)



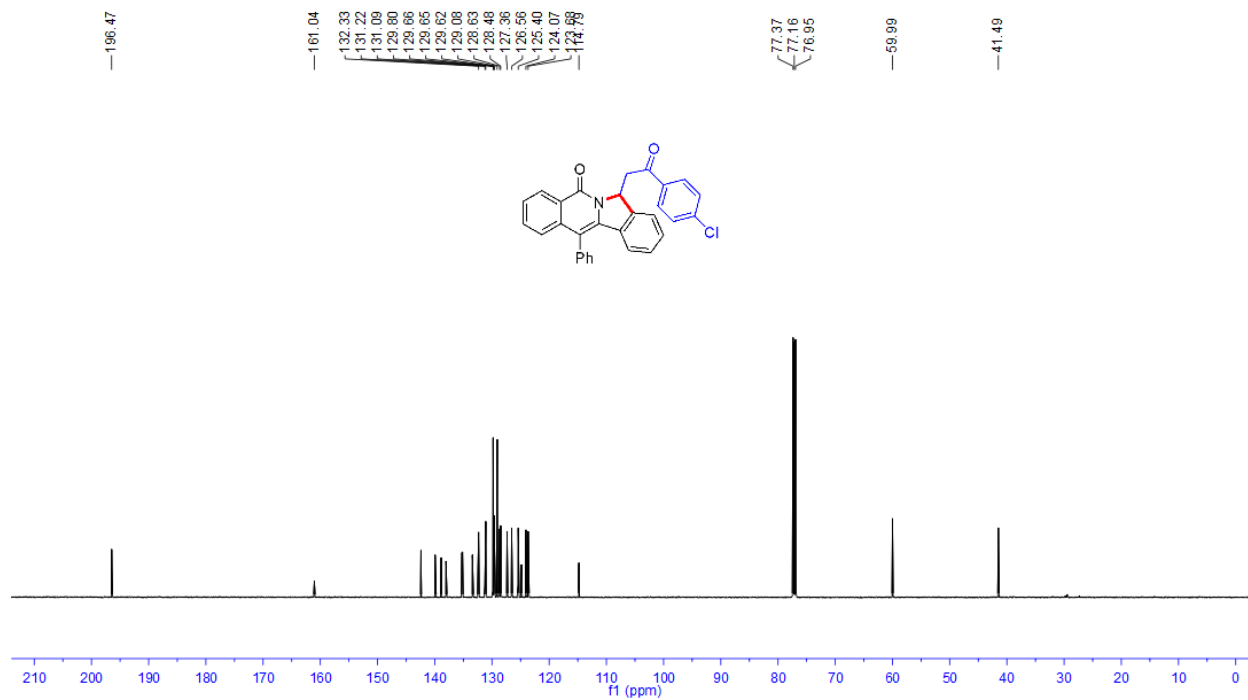
¹H NMR spectrum of **3ac** (CDCl₃, 600 MHz)



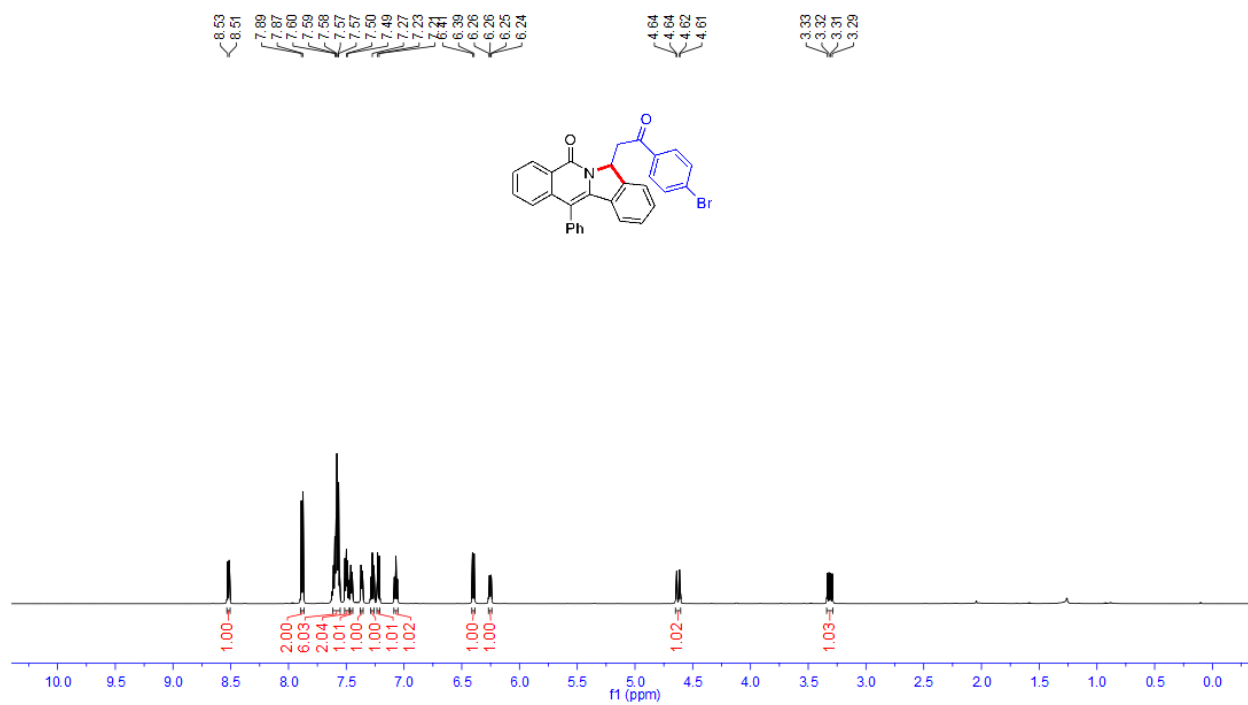
¹³C NMR spectrum of **3ac** (CDCl₃, 151 MHz)



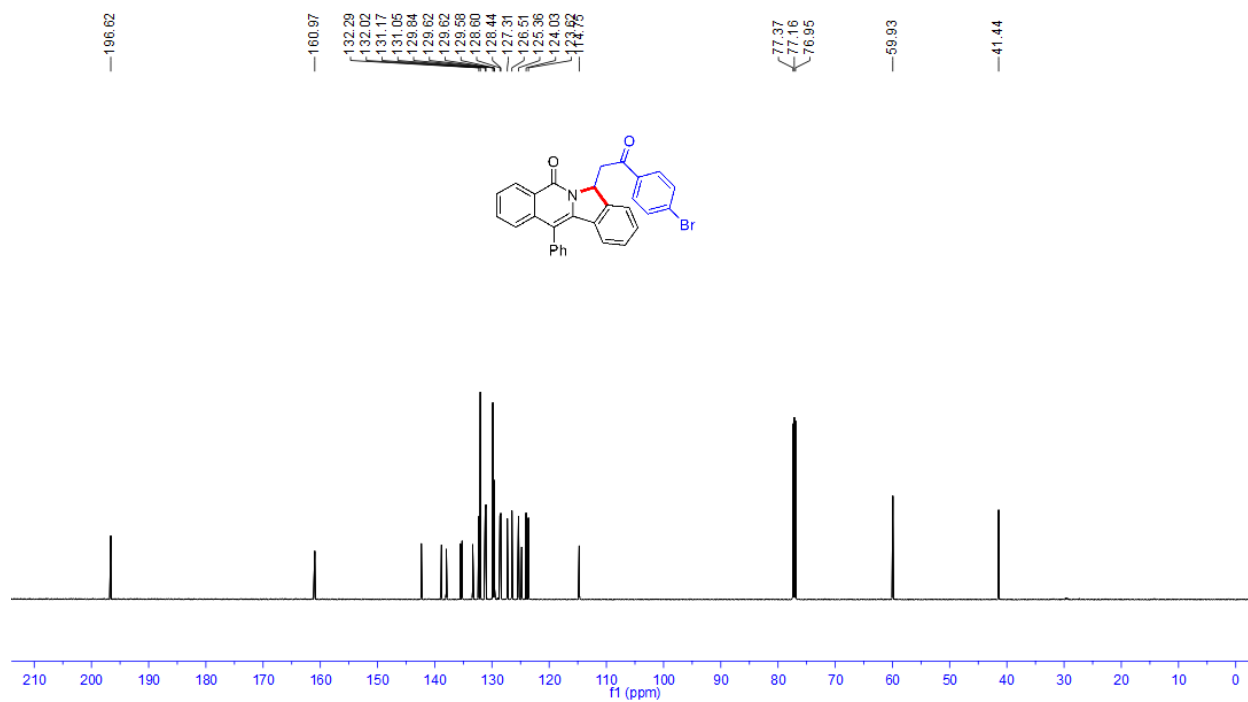
¹H NMR spectrum of **3ad** (CDCl₃, 600 MHz)



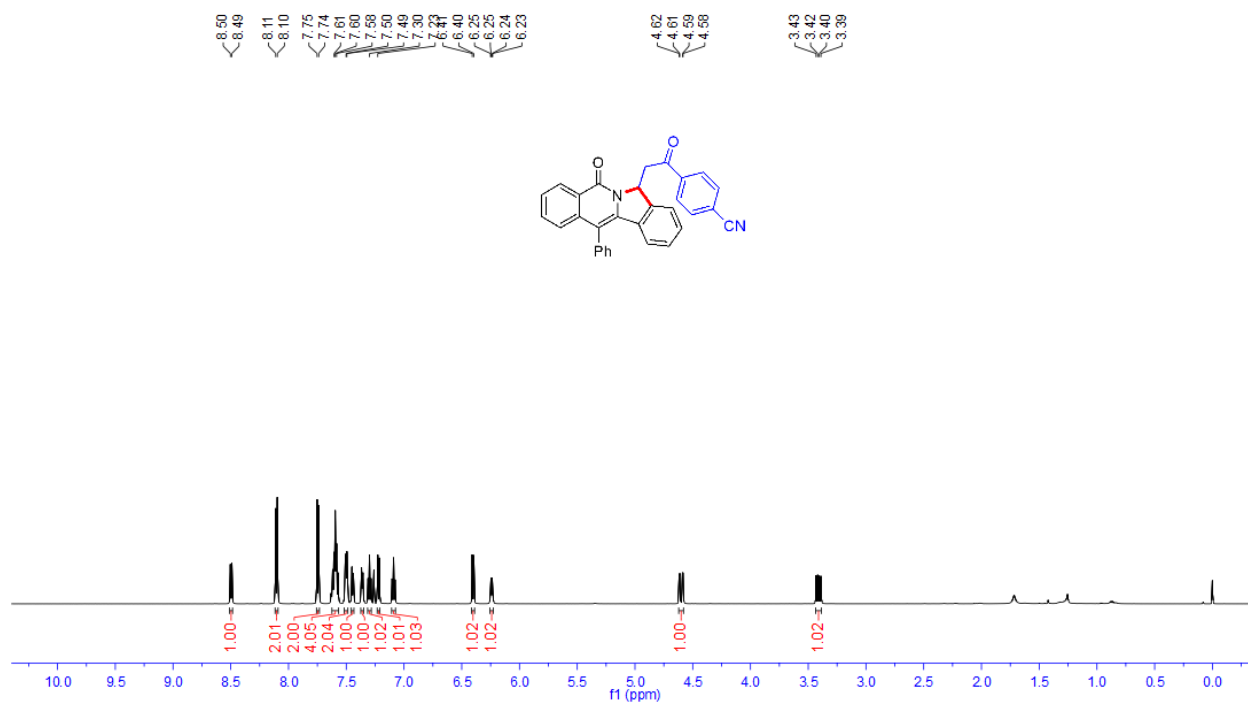
¹³C NMR spectrum of **3ad** (CDCl₃, 151 MHz)



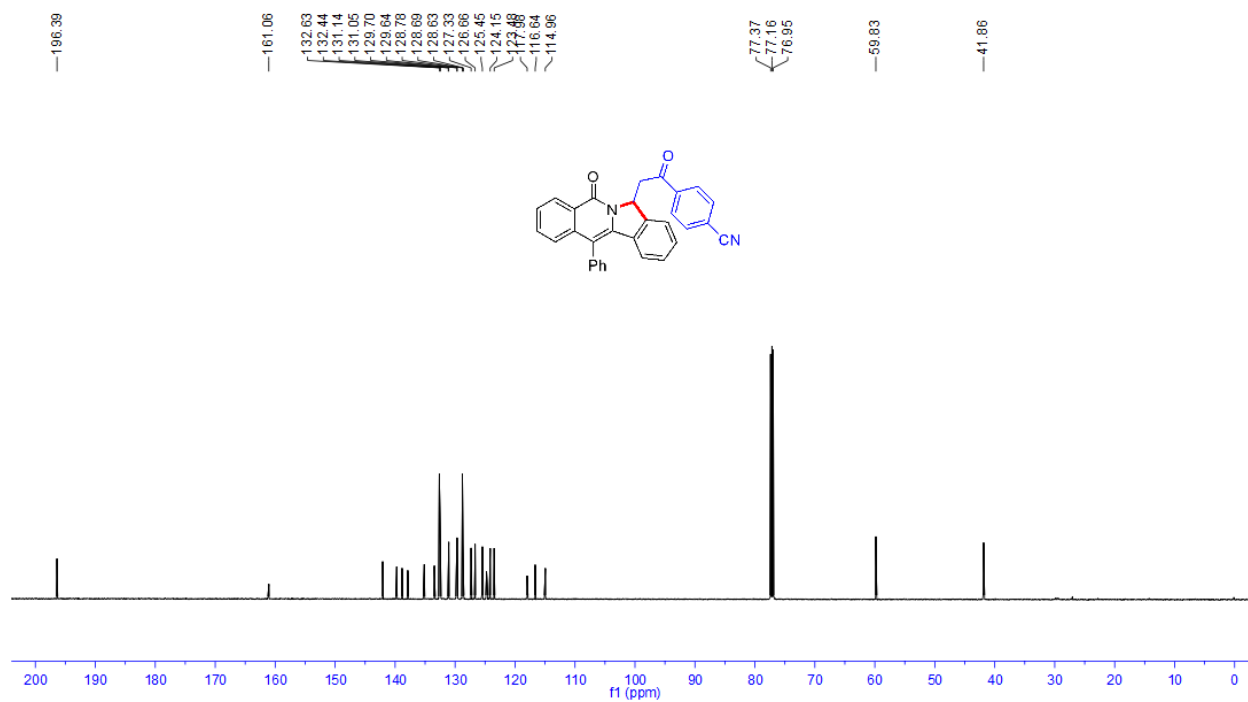
¹H NMR spectrum of **3ae** (CDCl₃, 600 MHz)



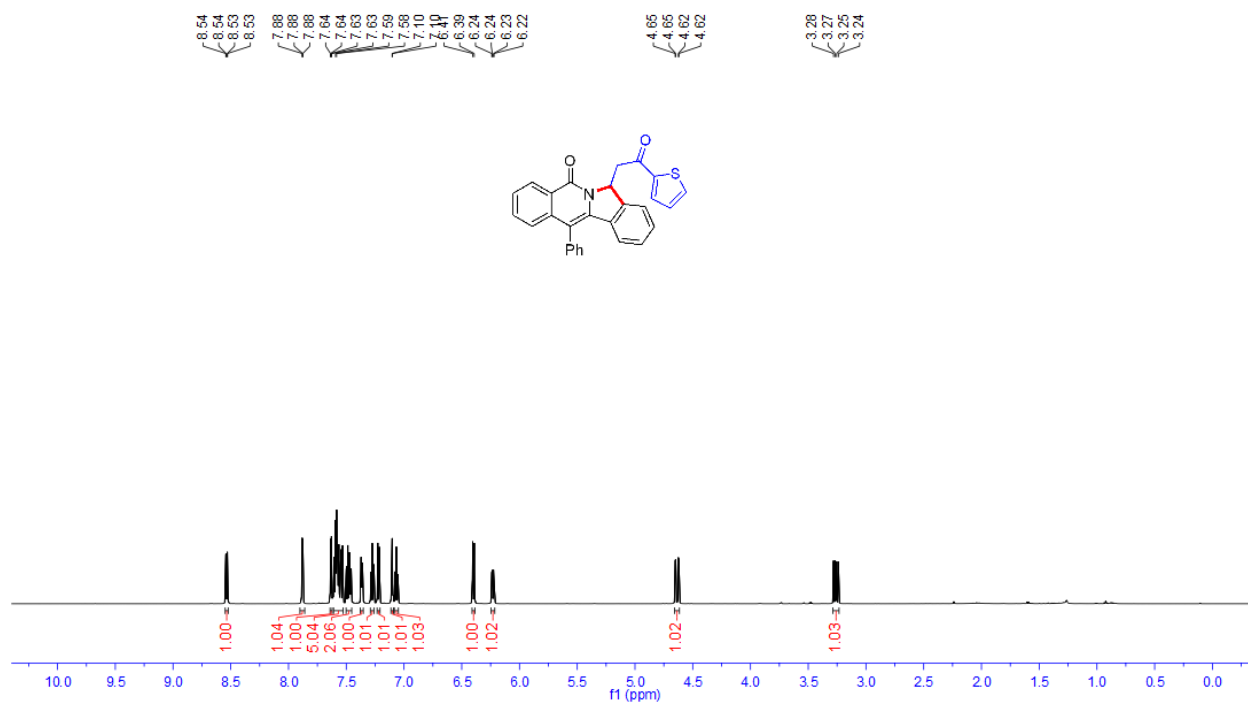
¹³C NMR spectrum of **3ae** (CDCl₃, 151 MHz)



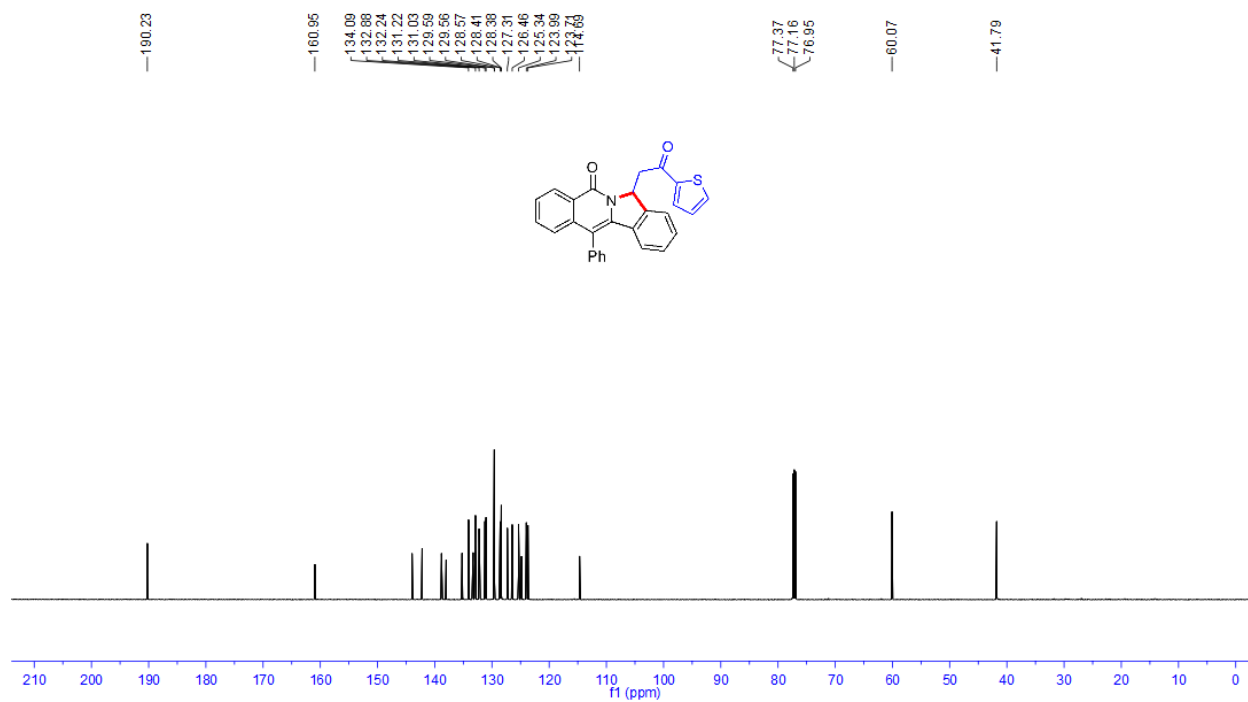
¹H NMR spectrum of **3af** (CDCl₃, 600 MHz)



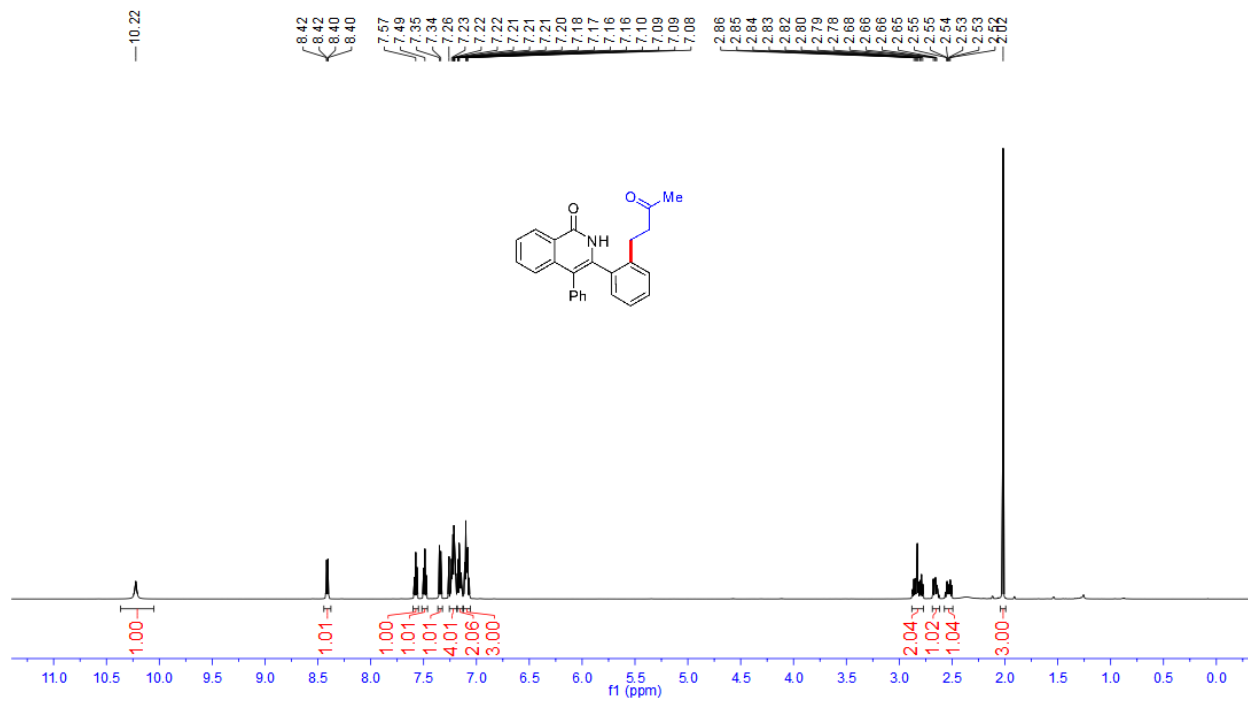
¹³C NMR spectrum of **3af** (CDCl₃, 151 MHz)



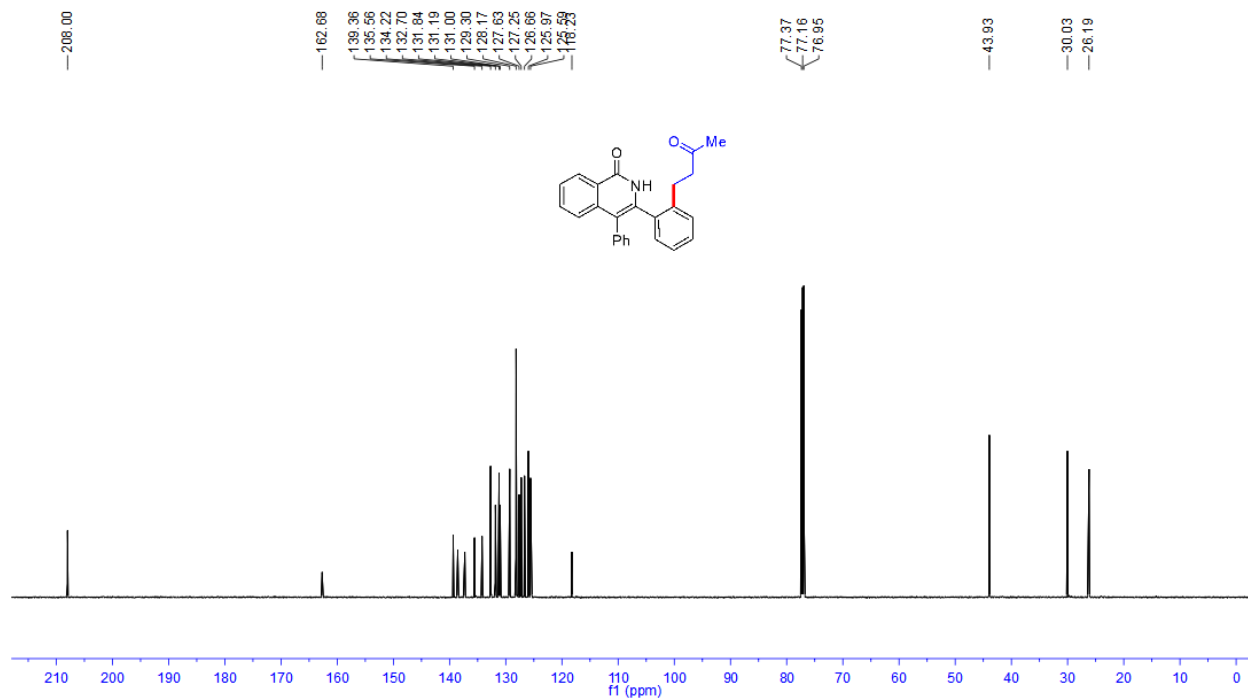
¹H NMR spectrum of **3ah** (CDCl₃, 600 MHz)



¹³C NMR spectrum of **3ah** (CDCl₃, 151 MHz)

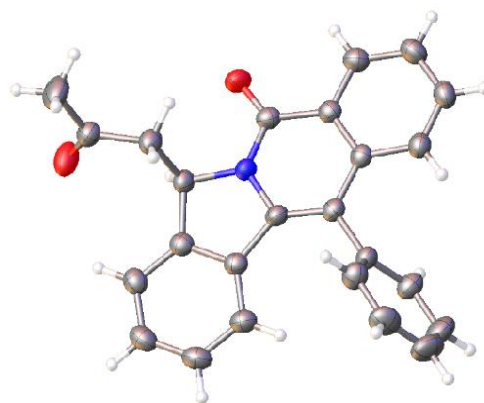
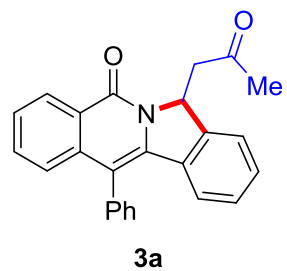


^1H NMR spectrum of **4** (CDCl_3 , 600 MHz)



^{13}C NMR spectrum of **4** (CDCl_3 , 151 MHz)

7. The X-ray crystal structure for compound 3a



CCDC 2104610

8. References

1. (a) N. Guimond, C. Gouliaras and K. Fagnou, *J. Am. Chem. Soc.*, 2010, **132**, 6908-6909; (b) N. Guimond, S. I. Gorelsky and K. Fagnou, *J. Am. Chem. Soc.*, 2011, **133**, 6449-6457; (c) B. Li, H. Feng, S. Xu and B. Wang, *Chem.-Eur. J.*, 2011, **17**, 12573-12577; (d) Y. Shi, X. Zhu, H. Mao, H. Hu, C. Zhu and Y. Cheng, *Chem.-Eur. J.*, 2013, **19**, 11553-11557.
2. M. Lafrance, M. Roggen and E. M. Carreira, *Angew. Chem., Int. Ed.*, 2012, **51**, 3470-3473.