

Supporting Information for

Rhodium-catalyzed C-H bond activation alkylation and
cyclization of 2-arylquinazolin-4-ones

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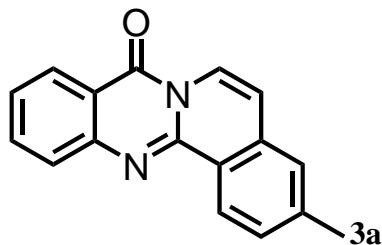
1. General Information

Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60 Å pore size, 32–63 mm, standard grade). Analytical thinlayer chromatography was performed using glass plates precoated with 0.25 mm 230-400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ca. 20 Torr(house vacuum) at 25–35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale.¹H and ¹³C NMR spectra were recorded in CDCl₃ on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz.

2. General experimental procedure for synthesis of 3 and 4

2-arylquinazolin-4-one (0.2 mmol), vinyl trifluoroacetate (0.6 mmol), [Cp^{*}RhCl₂]₂(2.5 mol%), AgSbF₆ (10 mol%), AgTFA (2 equiv) were added to an 18 x 180 test tube, and then 2 ml of solvent was added. The reaction was stirred at 110°C for 18 hours. Upon completion of the reaction as indicated by TLC, the reaction was cooled to room temperature, extracted with ethyl acetate and washed with water. The crude product was isolated by silica gel column chromatography to give the desired product.

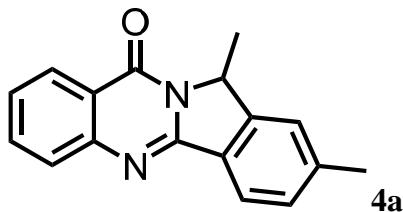
3. Spectroscopic Data



3-Methyliisoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 62%; mp: 178–181°C; ¹H NMR (400 MHz, CDCl₃) δ 8.79 (d, *J* = 8.0 Hz, 1H), 8.49 (d, *J* = 7.6 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.77 – 7.73 (m, 2H), 7.39 (ddd, *J* = 2.0 2.0, 5.6 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.26 (s, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 2.40 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.4, 147.6, 146.2, 142.8, 134.6, 132.9, 129.9, 127.3, 127.2, 127.1, 126.3, 125.4, 125.0, 121.9, 117.6, 113.1, 21.7.

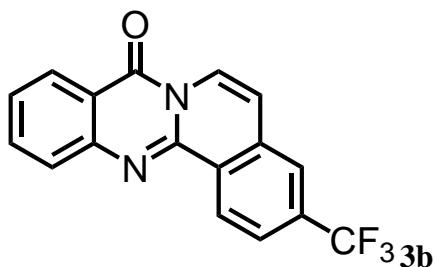
HRMS calcd. for C₁₇H₁₃N₂O (M+H)⁺: 261.1022, found: 261.1032.



2,12-Dimethyl-12H-isoindolo[1,2-b]quinazolin-10-one

Compound was obtained as a yellow solid: yield 13%; mp: 192–196 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.27 (d, J = 7.6 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.25 (s, 1H), 5.41 (q, J = 6.8 Hz, 1H), 2.42 (s, 3H), 1.73 (d, J = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.8, 154.6, 149.4, 146.2, 143.4, 134.1, 130.0, 128.7, 127.1, 126.5, 126.1, 123.2, 123.0, 121.1, 58.4, 22.0, 18.5.

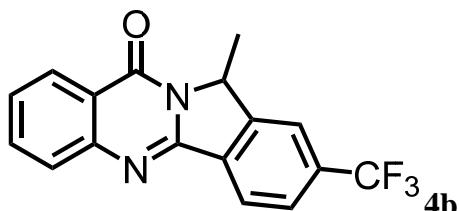
HRMS calcd. for C₁₇H₁₅N₂O (M+H)⁺: 263.1179, found: 263.1197.



3-Trifluoromethyl-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 75%; mp: 200–202 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.12 (d, J = 8.4 Hz, 1H), 8.66 (d, J = 8.0 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H), 7.91 – 7.83 (m, 3H), 7.81 (d, J = 8.4 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.01 (d, J = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 159.1, 147.2, 145.1, 135.1, 133.7 (q, ²J_{C-F} = 32.7 Hz), 132.9, 130.0, 128.2, 127.7, 127.4, 126.5, 124.5 (q, ³J_{C-F} = 3.4 Hz), 123.6 (q, ¹J_{C-F} = 271.2 Hz), 123.5 (q, ³J_{C-F} = 4.0 Hz), 123.4, 118.1, 112.2.

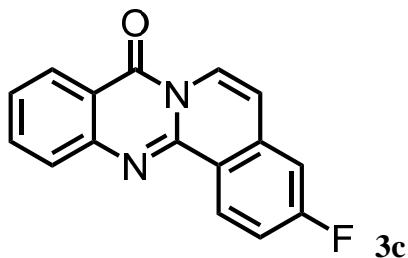
HRMS calcd. for C₁₇H₁₀F₃N₂O (M+H)⁺: 315.0740, found: 315.0750.



12-methyl-2-(trifluoromethyl)-12H-isoindolo[1,2-b]quinazolin-10-one

Compound was obtained as a yellow solid: yield 6%; mp: 165–166 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.38 (d, J = 7.6 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.88 – 7.75 (m, 4H), 7.58 – 7.49 (m, 1H), 5.63 (q, J = 6.8 Hz, 1H), 1.88 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.6, 153.1, 149.1, 146.2, 134.9, 134.5 (q, J_{C-F} = 32.3 Hz), 134.4, 127.6, 127.0, 126.6, 126.2 (q, J_{C-F} = 3.6 Hz), 124.1, 123.6 (q, J_{C-F} = 271.1 Hz), 121.5, 112.0 (q, J_{C-F} = 3.9 Hz), 58.8, 18.4.

HRMS calcd. for C₁₇H₁₂F₃N₂O (M+H)⁺: 317.0896, found: 315.0910.

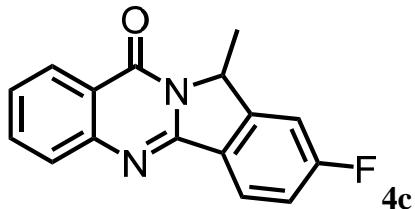


3-Fluoro-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 61%; mp: 226-228°C;

¹H NMR (400 MHz, CDCl₃) δ 9.07 (s, 1H), 8.66 (d, *J* = 6.4 Hz, 1H), 8.44 (d, *J* = 6.4 Hz, 1H), 7.85 (s, 2H), 7.50 (s, 1H), 7.34 (s, 1H), 7.26 (s, 1H), 6.95 (d, *J* = 6.0 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 165.1 (d, ¹J_{CF} = 251.8 Hz), 159.3, 147.5, 145.6, 135.1 (d, ³J_{CF} = 9.7 Hz), 134.9, 130.3 (d, ³J_{CF} = 9.5 Hz), 127.3, 127.4, 125.8, 123.9 (d, ⁴J_{CF} = 2.2 Hz), 123.3, 117.6, 116.8 (d, ²J_{CF} = 22.8 Hz), 112.3 (d, ⁴J_{CF} = 2.6 Hz), 111.7 (d, ²J_{CF} = 22.0 Hz).

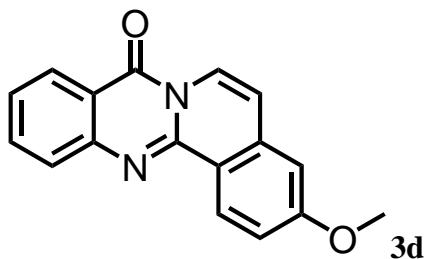
HRMS calcd. for C₁₆H₁₀FN₂O (M+H)⁺: 265.0772, found: 265.0787.



2-Fluoro-12-methyl-12H-isoindolo[1,2-b]quinazolin-10-one

Compound was obtained as a yellow solid: yield 7%; mp: 123-126°C; ¹H NMR (400 MHz, CDCl₃) δ 8.35 (d, *J* = 7.6 Hz, 1H), 8.14 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.80 – 7.78 (m, 2H), 7.48 (ddd, *J* = 8.4, 6.0, 2.4 Hz, 1H), 7.29– 7.23 (m, 2H), 5.53 (q, *J* = 6.8 Hz, 1H), 1.84 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.6 (d, ¹J_{CF} = 252.0 Hz), 160.7, 153.5, 149.3, 148.3 (d, ³J_{CF} = 9.5 Hz), 134.3, 127.5 (d, ⁴J_{CF} = 2.0 Hz), 127.3, 126.6, 126.4, 125.6 (d, ³J_{CF} = 9.6 Hz), 121.0, 117.0 (d, ²J_{CF} = 23.5 Hz), 110.1 (d, ²J_{CF} = 24.1 Hz), 58.4 (d, ⁴J_{CF} = 2.7 Hz), 18.4.

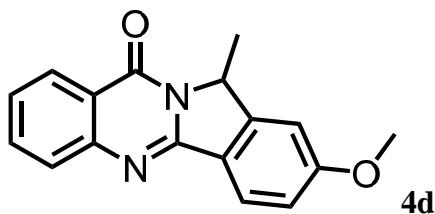
HRMS calcd. for C₁₆H₁₂FN₂O (M+H)⁺: 267.0928, found: 267.0940.



3-methoxy-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 65%; mp: 209-212°C; ¹H NMR (400 MHz, CDCl₃) δ 8.96 (d, *J* = 8.8 Hz, 1H), 8.63 (d, *J* = 7.6 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.80 (m, 2H), 7.46 (ddd, *J* = 8.4, 5.6, 2.8 Hz, 1H), 7.20 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 3.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 159.5, 147.9, 146.2, 134.9, 134.7, 129.2, 127.3, 127.2, 125.2, 122.5, 120.8, 117.4, 117.3, 113.0, 108.0, 55.6.

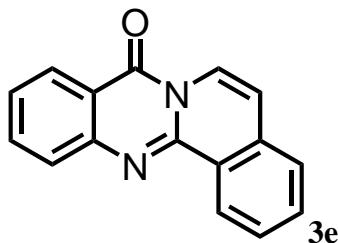
HRMS calcd. for C₁₇H₁₃N₂O₂ (M+H)⁺: 277.0972, found: 277.0987.



2-Methoxy-12-methyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a yellow solid: yield 11%; mp: 176–178°C; ^1H NMR (400 MHz, CDCl_3) δ 8.34 (d, $J = 8.0$ Hz, 1H), 8.12 (d, $J = 8.4$ Hz, 1H), 7.83 – 7.75 (m, 2H), 7.47 (t, $J = 8.0$ Hz, 1H), 7.11 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.01 (s, 1H), 5.50 (q, $J = 6.8$ Hz, 1H), 3.93 (s, 3H), 1.83 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.9, 160.6, 154.6, 148.6, 148.4, 134.4, 126.6, 126.4, 126.1, 125.4, 123.1, 120.6, 116.0, 107.3, 58.6, 55.8, 18.5.

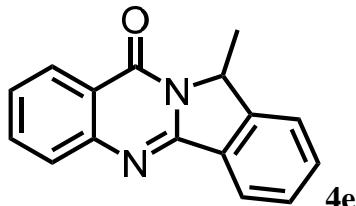
HRMS calcd. for $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_2$ ($\text{M}+\text{H}$) $^+$: 279.1128, found: 279.1137.



Isoquinolino[1,2-*b*]quinazolin-8-one

Compound was obtained as a white solid: yield 60%; mp: 165–167°C; ^1H NMR (400 MHz, CDCl_3) δ 9.06 (d, $J = 8.0$ Hz, 1H), 8.63 (d, $J = 7.6$ Hz, 1H), 8.45 (d, $J = 7.6$ Hz, 1H), 7.89 – 7.84 (m, 2H), 7.73 – 7.69 (m, 1H), 7.66 – 7.61 (m, 2H), 7.50 (ddd, $J = 8.0, 6.8, 1.6$ Hz, 1H), 7.01 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.5, 147.5, 146.1, 134.8, 132.9, 132.1, 128.4, 127.5, 127.4, 127.3, 127.2, 126.4, 125.7, 121.9, 117.8, 113.1.

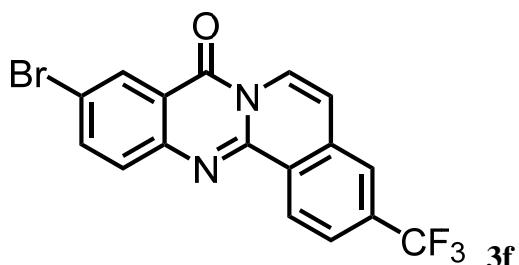
HRMS calcd. for $\text{C}_{16}\text{H}_{11}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 247.0866, found: 247.0876.



12-Methyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

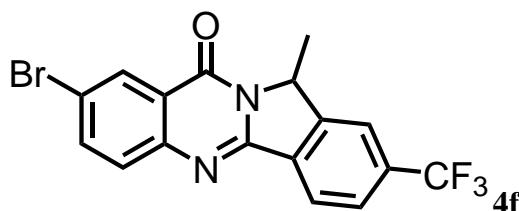
Compound was obtained as a yellow solid: yield 12%; mp: 143–146°C; ^1H NMR (400 MHz, CDCl_3) δ 8.37 (d, $J = 8.0$ Hz, 1H), 8.16 (d, $J = 7.6$ Hz, 1H), 7.86 – 7.73 (m, 2H), 7.64 (t, $J = 7.4$ Hz, 1H), 7.56 (t, $J = 7.8$ Hz, 2H), 7.48 (t, $J = 7.2$ Hz, 1H), 5.56 (q, $J = 6.6$ Hz, 1H), 1.84 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.8, 154.5, 149.3, 145.8, 134.2, 132.4, 131.4, 128.9, 127.3, 126.5, 126.3, 123.5, 122.6, 121.2, 58.6, 18.5.

HRMS calcd. for $\text{C}_{16}\text{H}_{13}\text{N}_2\text{O}$ ($\text{M}+\text{H}$) $^+$: 249.1022, found: 249.1033.



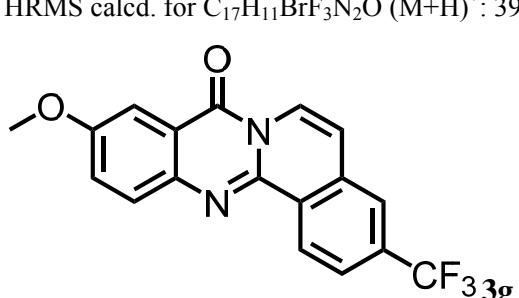
10-Bromo-3-(trifluoromethyl)-isoquinolino[1,2-*b*]quinazolin-8-one

Compound was obtained as a white solid: yield 60%; mp: 202–205 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.09 (d, *J* = 8.4 Hz, 1H), 8.63 (d, *J* = 7.8 Hz, 1H), 8.47 – 8.57 (m, 1H), 7.96 – 7.85 (m, 2H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 158.0, 145.9, 145.3, 138.2, 134.0 (q, *J*_{C-F} = 32.8 Hz), 132.9, 129.8, 129.7, 129.5, 128.2, 124.7 (q, *J*_{C-F} = 3.4 Hz), 123.6 (q, *J*_{C-F} = 3.9 Hz), 123.5 (q, *J*_{C-F} = 271.2 Hz), 123.2, 119.8, 119.2, 112.7. HRMS calcd. for C₁₇H₉BrF₃N₂O (M+H)⁺: 392.9845, found: 392.9845.



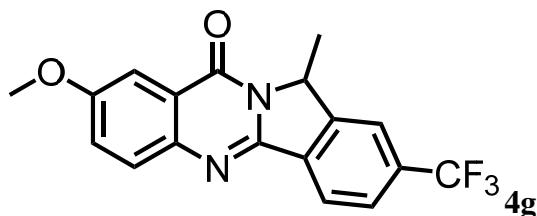
8-Bromo-12-methyl-2-(trifluoromethyl)-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a yellow solid: yield 7%; mp: 178–180 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.48 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.88 – 7.83 (m, 3H), 7.68 (d, *J* = 8.8 Hz, 1H), 5.61 (q, *J* = 6.8 Hz, 1H), 1.87 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.4, 153.4, 147.9, 146.2, 137.6, 134.6, 134.5 (q, ²*J*_{C-F} = 32.6 Hz), 129.3, 129.2, 126.3 (q, ³*J*_{C-F} = 3.7 Hz), 124.2, 123.6 (q, ¹*J*_{C-F} = 271.5 Hz), 122.8, 120.6, 120.0 (q, ³*J*_{C-F} = 3.8 Hz), 59.0, 18.3. HRMS calcd. for C₁₇H₁₁BrF₃N₂O (M+H)⁺: 395.0001, found: 395.0003.



10-Methoxy-3-(trifluoromethyl)-isoquinolino[1,2-*b*]quinazolin-8-one

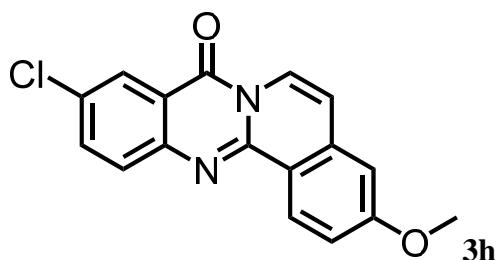
Compound was obtained as a white solid: yield 62%; mp: 177–178 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.07 (d, *J* = 8.4 Hz, 1H), 8.65 (d, *J* = 8.0 Hz, 1H), 7.89 – 7.77 (m, 3H), 7.74 (d, *J* = 2.8 Hz, 1H), 7.46 (dd, *J* = 9.0, 3.2 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 3.96 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 158.8, 158.3, 143.1, 142.0, 133.3 (q, *J*_{C-F} = 32.6 Hz), 132.4, 130.2, 129.4, 127.8, 126.1, 124.5 (q, *J*_{C-F} = 3.4 Hz), 123.7 (q, *J*_{C-F} = 271.0 Hz), 123.5 (q, *J*_{C-F} = 4.0 Hz), 123.4, 118.7, 112.3, 105.9, 55.9. HRMS calcd. for C₁₈H₁₂F₃N₂O₂ (M+H)⁺: 345.0845, found: 345.0852.



8-Methoxy-12-methyl-2-(trifluoromethyl)-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a white solid: yield 10%; mp: 214-216°C; ¹H NMR (400 MHz, CDCl₃) δ 8.23 (d, *J* = 8.0 Hz, 1H), 7.85 – 7.79 (m, 2H), 7.79 – 7.73 (m, 2H), 7.40 (dd, *J* = 8.8, 3.0 Hz, 1H), 5.62 (q, *J* = 6.6 Hz, 1H), 3.95 (s, 3H), 1.88 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.4, 158.7, 151.2, 145.7, 143.5, 135.0, 133.9 (q, *J*_{C-F} = 32.6 Hz), 129.1, 126.2 (q, *J*_{C-F} = 3.7 Hz), 124.5, 123.7, 123.6 (q, *J*_{C-F} = 271.9 Hz), 119.9 (q, *J*_{C-F} = 3.8 Hz), 106.3, 58.7, 55.9, 18.4.

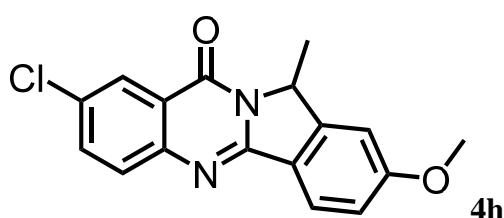
HRMS calcd. for C₁₈H₁₄F₃N₂O₂(M+H)⁺: 347.1002, found: 347.1008.



10-Chloro-3-methoxy-isoquinolino[1,2-*b*]quinazolin-8-one

Compound was obtained as a white solid: yield 57%; mp: 246-249°C; ¹H NMR (400 MHz, CDCl₃) δ 8.94 (d, *J* = 8.8 Hz, 1H), 8.61 (d, *J* = 8.0 Hz, 1H), 8.37 (d, *J* = 2.0 Hz, 1H), 7.81– 7.69 (m, 2H), 7.22 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.04– 6.95 (m, 2H), 3.98 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.0, 158.6, 146.5, 146.4, 135.2, 135.0, 130.7, 129.3, 129.0, 126.4, 122.4, 120.7, 118.1, 117.7, 113.5, 108.1, 55.7.

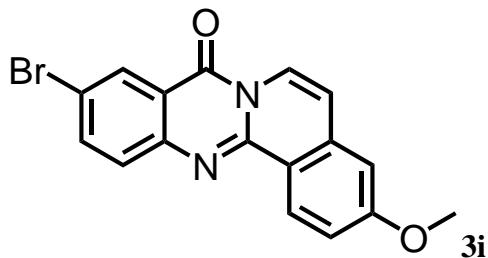
HRMS calcd. for C₁₇H₁₂ClN₂O₂(M+H)⁺: 311.0582, found: 311.0586.



8-Chloro-2-methoxy-12-methyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a yellow solid: yield 14%; mp: 189-190°C; ¹H NMR (400 MHz, CDCl₃) δ 8.27 (d, *J* = 1.6 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.74 – 7.61 (m, 2H), 7.07 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.98 (s, 1H), 5.46 (q, *J* = 6.6 Hz, 1H), 3.93 (s, 3H), 1.81 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.7, 159.7, 154.6, 148.1, 148.0, 134.4, 131.5, 128.5, 125.9, 124.9, 123.3, 121.8, 116.0, 107.2, 58.5, 55.8, 18.4.

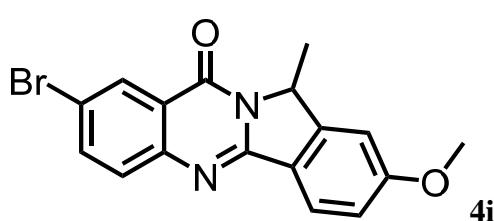
HRMS calcd. for C₁₇H₁₄ClN₂O₂(M+H)⁺: 313.0738, found: 313.0743.



10-Bromo-3-methoxy-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 52%; mp: 175-176°C; ^1H NMR (400 MHz, CDCl_3) δ 9.06 (d, $J = 8.4$ Hz, 1H), 8.65 (d, $J = 7.6$ Hz, 1H), 7.88 – 7.64 (m, 4H), 7.46 (dd, $J = 8.8, 3.2$ Hz, 1H), 6.99 (d, $J = 7.6$ Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.8, 158.2, 143.1, 142.0, 133.1, 132.3, 130.2, 129.4, 127.7, 126.1, 124.5, 123.5, 123.3, 118.7, 112.3, 105.8, 55.9.

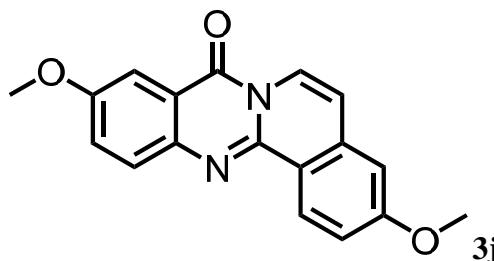
HRMS calcd. for $\text{C}_{17}\text{H}_{12}\text{BrN}_2\text{O}_2(\text{M}+\text{H})^+$: 355.0077, found: 355.0086.



8-Bromo-2-methoxy-12-methyl-12H-isoindolo[1,2-b]quinazolin-10-one

Compound was obtained as a yellow solid: 10%; mp: 177-178°C; ^1H NMR (400 MHz, CDCl_3) δ 8.42 (d, $J = 2.0$ Hz, 1H), 8.00 (d, $J = 8.4$ Hz, 1H), 7.79 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.60 (d, $J = 8.4$ Hz, 1H), 7.07 (dd, $J = 8.8, 1.6$ Hz, 1H), 6.98 (s, 1H), 5.45 (q, $J = 6.6$ Hz, 1H), 3.93 (d, $J = 8.0$ Hz, 3H), 1.80 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.7, 159.5, 154.7, 148.4, 148.1, 137.1, 129.0, 128.7, 124.9, 123.3, 122.2, 119.1, 116.0, 107.2, 58.5, 55.8, 18.4.

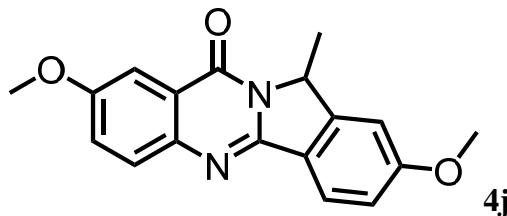
HRMS calcd. for $\text{C}_{17}\text{H}_{14}\text{BrN}_2\text{O}_2(\text{M}+\text{H})^+$: 357.0233, found: 357.0243.



3,10-Dimethoxy-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 56%; mp: 237-240°C; ^1H NMR (400 MHz, CDCl_3) δ 8.94 (d, $J = 9.2$ Hz, 1H), 8.64 (d, $J = 8.0$ Hz, 1H), 7.79 (d, $J = 9.2$ Hz, 1H), 7.76 (d, $J = 3.2$ Hz, 1H), 7.46 (dd, $J = 9.2, 3.2$ Hz, 1H), 7.21 (dd, $J = 8.8, 2.4$ Hz, 1H), 7.00 (d, $J = 2.4$ Hz, 1H), 6.96 (d, $J = 7.6$ Hz, 1H), 3.96 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.5, 159.3, 157.4, 144.5, 142.9, 134.4, 128.9, 128.8, 126.0, 122.5, 121.1, 117.8, 117.3, 113.2, 108.1, 105.7, 55.8, 55.6.

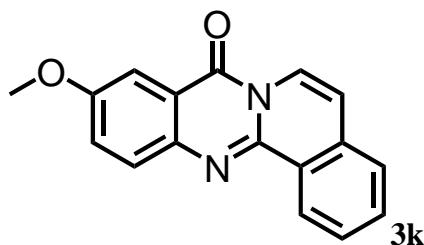
HRMS calcd. for $\text{C}_{18}\text{H}_{15}\text{N}_2\text{O}_3(\text{M}+\text{H})^+$: 307.1077, found: 307.1083.



2,8-Dimethoxy-12-methyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a yellow solid: yield 24%; mp: 183-187°C; ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 8.4 Hz, 1H), 7.70-7.67 (m, 2H), 7.33 (dd, *J* = 8.8, 3.2 Hz, 1H), 7.05 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.97 (s, 1H), 5.46 (q, *J* = 6.4 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 1.82 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.2, 160.6, 157.8, 152.5, 147.6, 143.9, 128.4, 124.4, 124.2, 123.8, 121.5, 115.7, 107.2, 106.0, 58.3, 55.7, 55.6, 18.5.

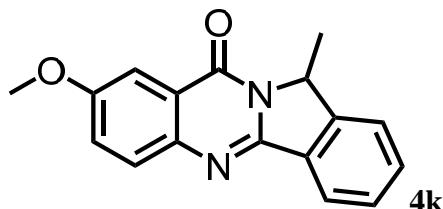
HRMS calcd. for C₁₈H₁₇N₂O₃ (M+H)⁺: 309.1234, found: 309.1244.



10-Methoxy-isoquinolino[1,2-*b*]quinazolin-8-one

Compound was obtained as a yellow solid: yield 46%; mp: 225-226°C; ¹H NMR (400 MHz, CDCl₃) δ 9.01 (d, *J* = 8.0 Hz, 1H), 8.63 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 9.0 Hz, 1H), 7.77 (d, *J* = 2.8 Hz, 1H), 7.72 – 7.57 (m, 3H), 7.46 (dd, *J* = 9.0, 2.8 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 3.96 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 157.8, 144.3, 142.5, 132.4, 131.7, 129.2, 128.4, 127.7, 126.9, 126.4, 126.0, 121.9, 118.4, 113.2, 105.7, 55.9.

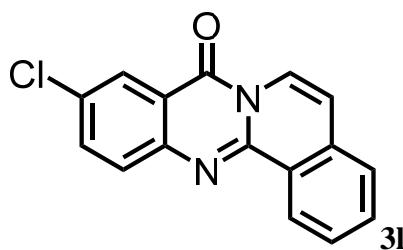
HRMS calcd. for C₁₇H₁₃N₂O₂ (M+H)⁺: 277.0972, found: 277.0981.



8-Methoxy-12-methyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a yellow solid: yield 10%; mp: 139-143°C; ¹H NMR (400 MHz, CDCl₃) δ 8.14 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.73 (d, *J* = 2.8 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 2H), 7.38 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.56 (q, *J* = 6.8 Hz, 1H), 3.94 (s, 3H), 1.84 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.5, 158.2, 152.7, 145.4, 143.2, 132.2, 131.1, 129.0, 128.5, 124.4, 123.3, 122.5, 121.9, 106.1, 58.7, 55.8, 18.4.

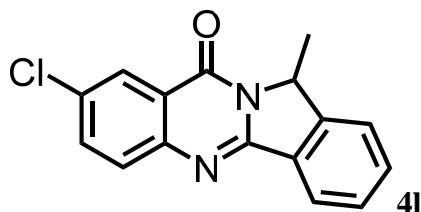
HRMS calcd. for C₁₇H₁₅N₂O₂ (M+H)⁺: 279.1128, found: 279.1138.



10-Chloro-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 56%; mp: 247-250°C; ¹H NMR (400 MHz, CDCl₃) δ 9.05 (d, *J* = 8.0 Hz, 1H), 8.62 (d, *J* = 7.8 Hz, 1H), 8.41 (d, *J* = 2.2 Hz, 1H), 7.83 - 7.61 (m, 5H), 7.06 (d, *J* = 7.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 158.6, 146.1, 135.3, 132.9, 132.4, 131.4, 130.9, 129.2, 128.8, 128.7, 127.3, 126.6, 126.4, 121.8, 118.6, 113.7.

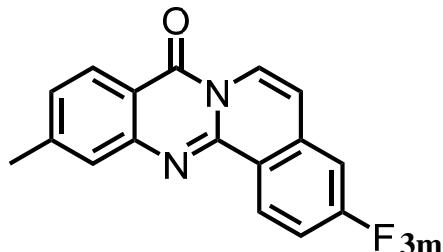
HRMS calcd. for C₁₆H₁₀ClN₂O (M+H)⁺: 281.0476, found: 281.0488.



8-Chloro-12-methyl-12*H*-isoindolo[1,2-b]quinazolin-10-one

Compound was obtained as a yellow solid: yield 11%; mp: 160-162°C; ¹H NMR (400 MHz, CDCl₃) δ 8.29 (d, *J* = 1.2 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.82 – 7.61 (m, 3H), 7.56 (t, *J* = 7.8 Hz, 2H), 5.23 (q, *J* = 6.6 Hz, 1H), 1.83 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.7, 154.7, 147.8, 145.7, 134.5, 132.6, 132.0, 131.0, 129.0, 128.8, 125.9, 123.4, 122.7, 122.2, 58.8, 18.3.

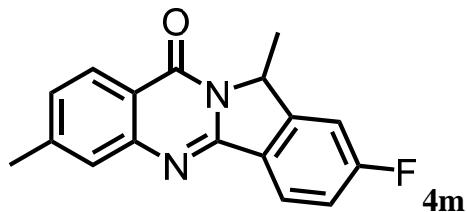
HRMS calcd. for C₁₆H₁₂ClN₂O (M+H)⁺: 283.0633, found: 283.0652.



3-Fluoro-11-methyl-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 58%; mp: 220-222°C; ¹H NMR (400 MHz, CDCl₃) δ 8.96 (dd, *J* = 8.8, 5.6 Hz, 1H), 8.57 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.2 Hz, 1H), 7.56 (s, 1H), 7.35 - 7.23 (m, 2H), 7.19 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 2.52 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.0 (d, ¹J_{C-F} = 251.5 Hz), 159.1, 147.6, 146.1, 145.6, 135.1 (d, ³J_{C-F} = 10.1 Hz), 130.2 (d, ³J_{C-F} = 9.5 Hz), 127.6, 127.1, 127.0, 123.9, 123.3, 116.6 (d, ²J_{C-F} = 23.1 Hz), 115.3, 111.9, 111.6 (d, ²J_{C-F} = 22 Hz), 22.1.

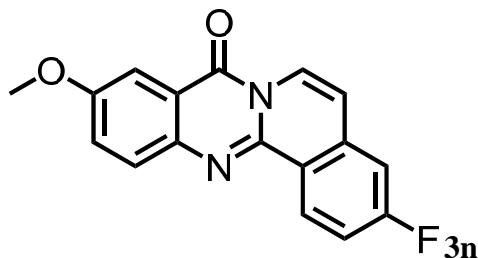
HRMS calcd. for C₁₇H₁₂FN₂O (M+H)⁺: 279.0928, found: 279.0939.



2-Fluoro-7,12-dimethyl-12H-isoindolo[1,2-b]quinazolin-10-one

Compound was obtained as a yellow solid: yield 9%; mp: 143–146 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.23 (d, J = 8.0 Hz, 1H), 8.13 (dd, J = 8.4, 5.2 Hz, 1H), 7.58 (s, 1H), 7.35 – 7.19 (m, 3H), 5.52 (q, J = 6.6 Hz, 1H), 2.52 (s, 3H), 1.83 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.6 (d, ¹J_{C-F} = 251.7 Hz), 160.7, 153.6, 149.4, 148.3 (d, ³J_{C-F} = 9.4 Hz), 145.3, 128.0, 127.6 (d, ⁴J_{C-F} = 2.6 Hz), 127.1, 126.4, 125.5 (d, ³J_{C-F} = 9.6 Hz), 118.6, 116.9 (d, ²J_{C-F} = 23.6 Hz), 110.1 (d, ²J_{C-F} = 24.1 Hz), 58.3 (d, ⁴J_{C-F} = 2.7 Hz), 21.9, 18.5.

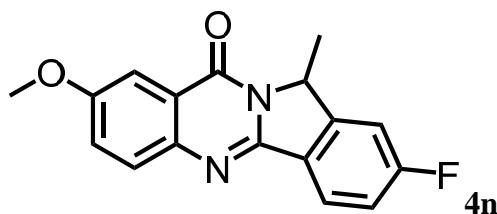
HRMS calcd. for C₁₇H₁₄FN₂O (M+H)⁺: 281.1085, found: 281.1094.



3-Fluoro-10-methoxy-isoquinolino[1,2-b]quinazolin-8-one

Compound was obtained as a white solid: yield 58%; mp: 252–255 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.05 (dd, J = 8.8, 5.6 Hz, 1H), 8.67 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 9.2 Hz, 1H), 7.78 (d, J = 2.8 Hz, 1H), 7.48 (dd, J = 8.8, 2.8 Hz, 1H), 7.34 (dt, J = 8.8, 2.0 Hz, 1H), 7.28 (d, J = 2.0 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 3.97 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 164.8 (d, ¹J_{C-F} = 251.3 Hz), 159.1, 157.9, 143.8, 143.4, 142.5, 134.6, 129.9 (d, ³J_{C-F} = 9.6 Hz), 129.2, 126.2, 123.3, 118.2, 116.8 (d, ²J_{C-F} = 22.8 Hz), 112.4 (d, ⁴J_{C-F} = 2.6 Hz), 111.7 (d, ²J_{C-F} = 22.2 Hz), 105.8, 55.9.

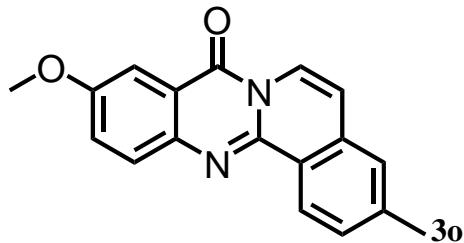
HRMS calcd. for C₁₇H₁₂FN₂O₂ (M+H)⁺: 295.0877, found: 295.0888.



2-Fluoro-8-methoxy-12-methyl-12H-isoindolo[1,2-b]quinazolin-10-one

Compound was obtained as a yellow solid: yield 7%; mp: 191–193 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (dd, J = 8.4, 5.2 Hz, 1H), 7.73 (s, 1H), 7.71 (d, J = 7.2 Hz, 1H), 7.37 (dd, J = 8.8, 3.2 Hz, 1H), 7.25–7.21 (m, 2H), 5.53 (q, J = 6.6 Hz, 1H), 3.94 (s, 3H), 1.83 (d, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.4 (d, ¹J_{C-F} = 251.4 Hz), 160.5, 158.3, 151.7, 147.8 (d, ³J_{C-F} = 9.4 Hz), 143.7, 128.8, 127.6 (d, ⁴J_{C-F} = 2.0 Hz), 125.2 (d, ³J_{C-F} = 9.6 Hz), 124.4, 121.8, 116.9 (d, ²J_{C-F} = 23.6 Hz), 110.0 (d, ²J_{C-F} = 24.1 Hz), 106.2, 58.4 (d, ⁴J_{C-F} = 2.7 Hz), 55.8, 18.4.

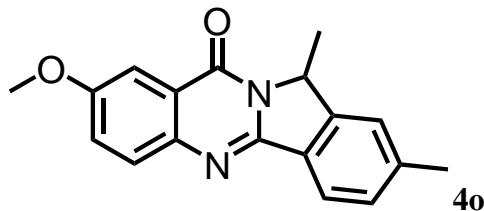
HRMS calcd. for C₁₇H₁₄FN₂O₂ (M+H)⁺: 297.1034, found: 297.1049.



10-Methoxy-3-methyl-isoquinolino[1,2-*b*]quinazolin-8-one

Compound was obtained as a white solid: yield 50%; mp: 193–195 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.86 (d, *J* = 8.4 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 9.2 Hz, 1H), 7.75 (d, *J* = 2.4 Hz, 1H), 7.50 – 7.40 (m, 2H), 7.37 (s, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 3.96 (s, 3H), 2.51 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 157.5, 144.4, 142.6, 142.3, 132.4, 129.9, 129.0, 128.8, 126.7, 126.3, 125.9, 121.9, 118.1, 113.2, 105.6, 55.8, 21.7.

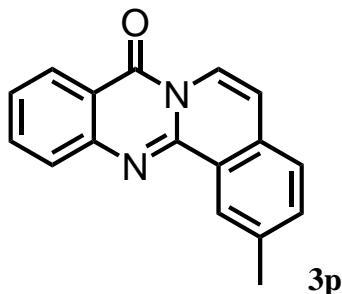
HRMS calcd. for C₁₈H₁₅N₂O₂ (M+H)⁺: 291.1128, found: 291.1139.



8-Methoxy-2,12-dimethyl-12*H*-isoindolo[1,2-*b*]quinazolin-10(12*H*)-one

Compound was obtained as a yellow solid: yield 15%; mp: 192–195 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 7.6 Hz, 1H), 7.74 (s, 1H), 7.72 (d, *J* = 6.4 Hz, 1H), 7.38 – 7.33 (m, 3H), 5.50 (q, *J* = 6.6 Hz, 1H), 3.94 (s, 3H), 2.51 (s, 3H), 1.82 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.7, 158.0, 152.8, 145.8, 143.9, 142.9, 130.0, 128.8, 128.7, 124.3, 123.0, 122.9, 121.9, 106.1, 58.4, 55.8, 22.0, 18.5.

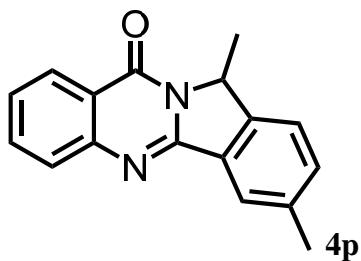
HRMS calcd. for C₁₈H₁₇N₂O₂ (M+H)⁺: 293.1285, found: 293.1296.



2-Methyl-isoquinolino[1,2-*b*]quinazolin-8-one

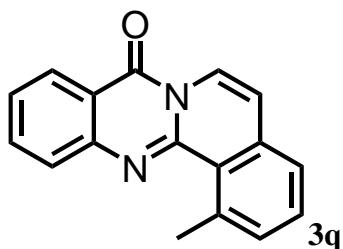
Compound was obtained as a white solid: yield 55%; mp: 173–175 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.66 (s, 1H), 8.44 (d, *J* = 7.8 Hz, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 3.6 Hz, 2H), 7.46 – 7.39 (m, 1H), 7.37 – 7.34 (m, 2H), 6.85 (d, *J* = 7.8 Hz, 1H), 2.47 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 147.3, 145.8, 138.5, 134.4, 133.3, 130.3, 127.3, 127.1, 127.0, 126.7, 126.1, 125.4, 120.8, 117.5, 112.8, 21.6.

HRMS calcd. for C₁₇H₁₃N₂O (M+H)⁺: 261.1022, found: 261.1035.



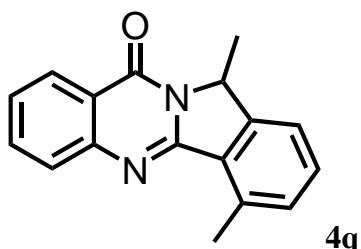
3,12-Dimethyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a white solid: yield 18%; mp: 142–146 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (d, *J* = 8.0 Hz, 1H), 7.96 (s, 1H), 7.79 – 7.74 (m, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.43 (s, 2H), 5.50 (q, *J* = 6.6 Hz, 1H), 2.49 (s, 3H), 1.81 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.8, 154.7, 149.3, 143.2, 139.1, 134.1, 133.5, 131.4, 127.2, 126.5, 126.2, 123.6, 122.3, 121.2, 58.5, 21.3, 18.6. HRMS calcd. for C₁₇H₁₅N₂O (M+H)⁺: 263.1179, found: 263.1199.



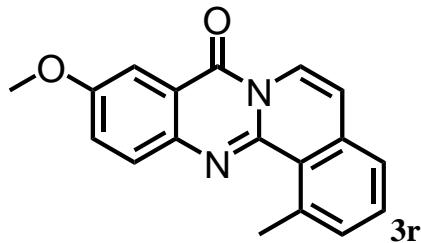
1-Methyl-isoquinolino[1,2-*b*]quinazolin-8-one

Compound was obtained as a white solid: yield 40%; mp: 179–183 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.56 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.40 (d, *J* = 8.0 Hz, 1H), 7.86 – 7.75 (m, 2H), 7.52 – 7.43 (m, 2H), 7.40 – 7.38 (m, 2H), 6.90 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.18 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.5, 146.8, 141.6, 134.5, 134.4, 132.6, 131.0, 130.9, 128.8, 127.7, 126.9, 125.8, 125.0, 121.5, 117.2, 113.9, 27.0. HRMS calcd. for C₁₇H₁₃N₂O (M+H)⁺: 261.1022, found: 261.1035.



4,12-Dimethyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

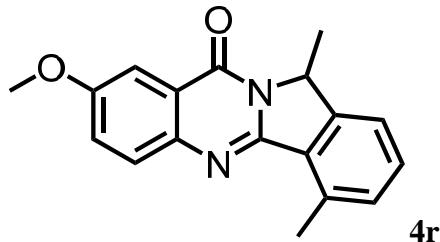
Compound was obtained as a yellow solid: yield 20%; mp: 105–107 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.81 (d, *J* = 7.6 Hz, 1H), 7.77 – 7.73 (m, 1H), 7.50 – 7.43 (m, 2H), 7.33 (dd, *J* = 16.4, 7.6 Hz, 2H), 5.49 (q, *J* = 6.6 Hz, 1H), 2.95 (s, 3H), 1.80 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 161.0, 155.5, 149.6, 146.4, 138.3, 133.9, 131.7, 130.9, 128.8, 127.8, 126.3, 126.2, 120.8, 119.8, 57.9, 19.0, 18.8. HRMS calcd. for C₁₇H₁₅N₂O (M+H)⁺: 263.1179, found: 263.1188.



10-Methoxy-1-methyl-isoquinolino[1,2-*b*]quinazolin-8-one

Compound was obtained as a yellow solid: yield 45%; mp: 195–196 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.58 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.72 (d, *J* = 2.8 Hz, 1H), 7.49 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.45 – 7.34 (m, 3H), 6.91 (d, *J* = 7.8 Hz, 1H), 3.95 (s, 3H), 3.18 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.2, 157.8, 145.0, 141.8, 141.2, 134.0, 132.6, 130.6, 129.4, 125.9, 125.7, 124.9, 121.5, 117.8, 114.1, 105.3, 55.8, 27.0.

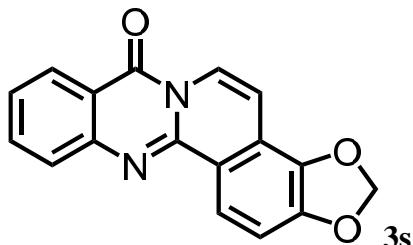
HRMS calcd. for C₁₈H₁₅N₂O₂ (M+H)⁺: 291.1128, found: 291.1134.



8-Methoxy-4,12-dimethyl-12*H*-isoindolo[1,2-*b*]quinazolin-10-one

Compound was obtained as a yellow solid: yield 15%; mp: 176–180 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.77 – 7.67 (m, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.36–7.31 (m, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 5.47 (q, *J* = 6.5 Hz, 1H), 3.93 (s, 3H), 2.91 (s, 3H), 1.79 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 160.7, 158.0, 153.5, 145.8, 144.1, 137.8, 131.2, 130.7, 129.3, 128.9, 124.1, 121.4, 119.7, 105.7, 57.8, 55.7, 18.9, 18.7.

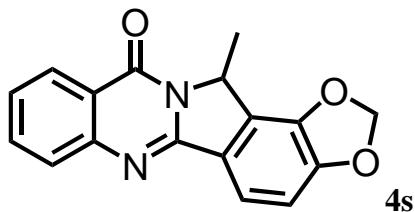
HRMS calcd. for C₁₈H₁₇N₂O₂ (M+H)⁺: 293.1285, found: 293.1292.



[1,3]dioxolo[4',5':5,6]isoquinolino[1,2-*b*]quinazolin-7-one

Compound was obtained as a white solid: yield 50%; mp: 227–229 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.65 (d, *J* = 8.6 Hz, 1H), 8.58 (d, *J* = 8.0 Hz, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 7.86–7.81 (m, 2H), 7.49 – 7.45 (m, 1H), 7.13 (d, *J* = 8.6 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 1H), 6.20 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 159.5, 150.0, 147.6, 145.9, 142.2, 134.9, 130.9, 128.9, 127.3, 125.5, 122.5, 122.3, 117.7, 116.8, 109.7, 106.0, 102.7.

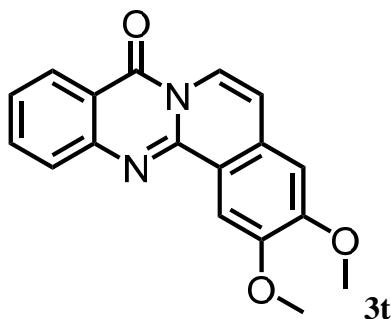
HRMS calcd. for C₁₇H₁₁N₂O₃ (M+H)⁺: 291.0764, found: 291.0778.



13-methyl-[1,3]dioxolo[4',5':4,5]-13H-isoindolo[1,2-b]quinazolin-11-one

Compound was obtained as a yellow solid: yield 18%; mp: 182–186 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.33 (d, $J = 7.8$ Hz, 1H), 7.85 – 7.73 (m, 2H), 7.70 (d, $J = 8.0$ Hz, 1H), 7.54 – 7.38 (m, 1H), 7.01 (d, $J = 8.0$ Hz, 1H), 6.27 – 6.03 (m, 2H), 5.58 (q, $J = 6.4$ Hz, 1H), 1.85 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 160.7, 153.9, 151.4, 149.3, 142.1, 134.1, 127.1, 126.5, 126.2, 126.0, 125.6, 120.9, 117.9, 109.7, 102.5, 56.4, 16.9.

HRMS calcd. for $\text{C}_{17}\text{H}_{13}\text{N}_2\text{O}_3 (\text{M}+\text{H})^+$: 293.0921, found: 293.0931.

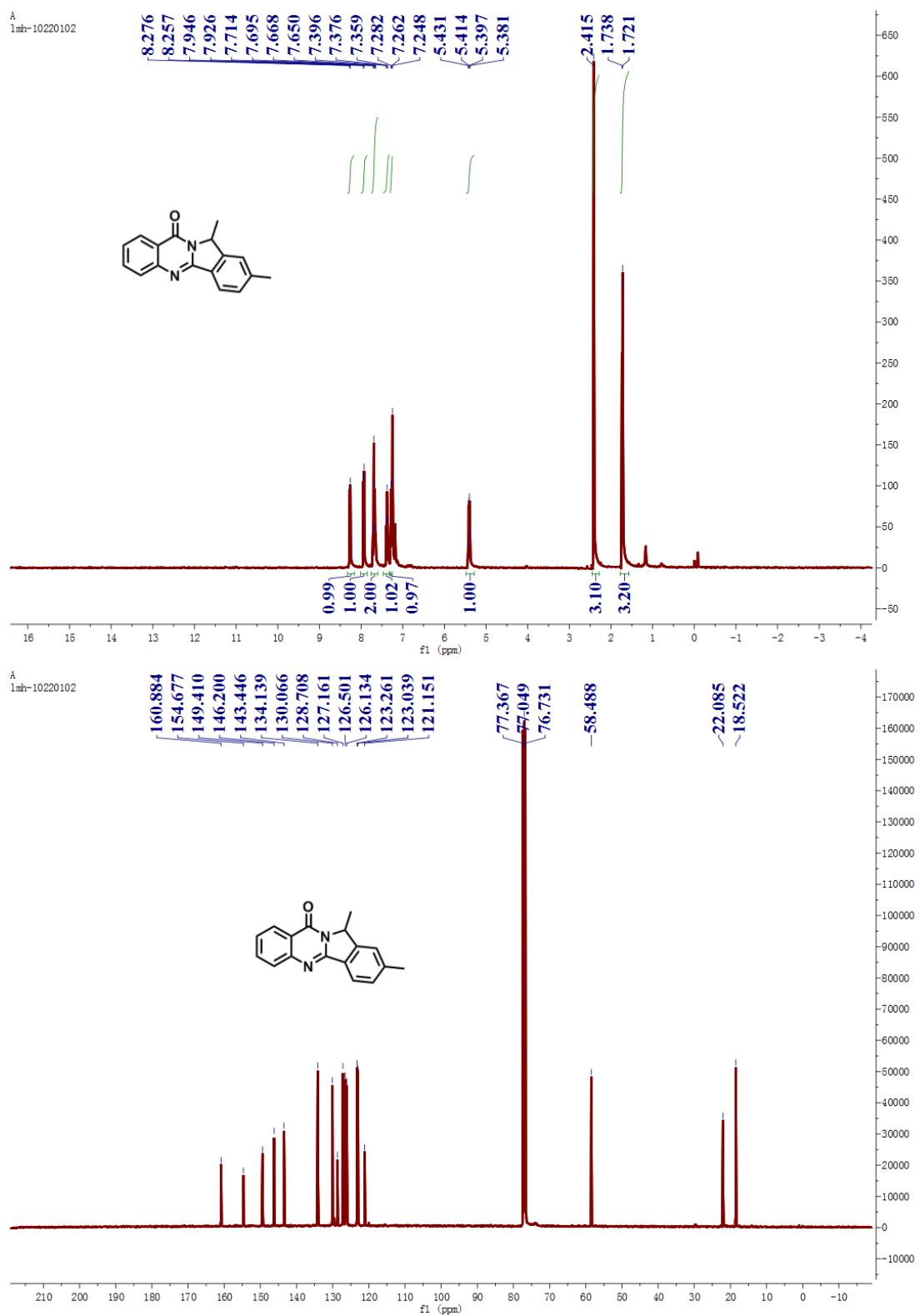


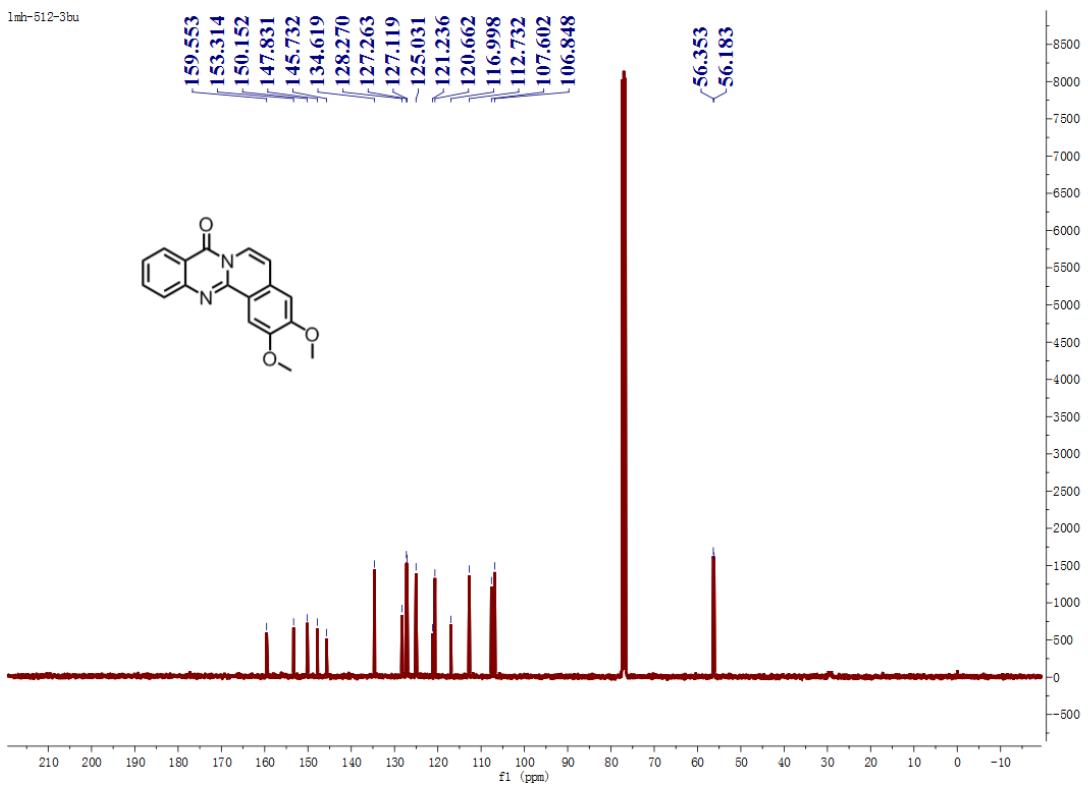
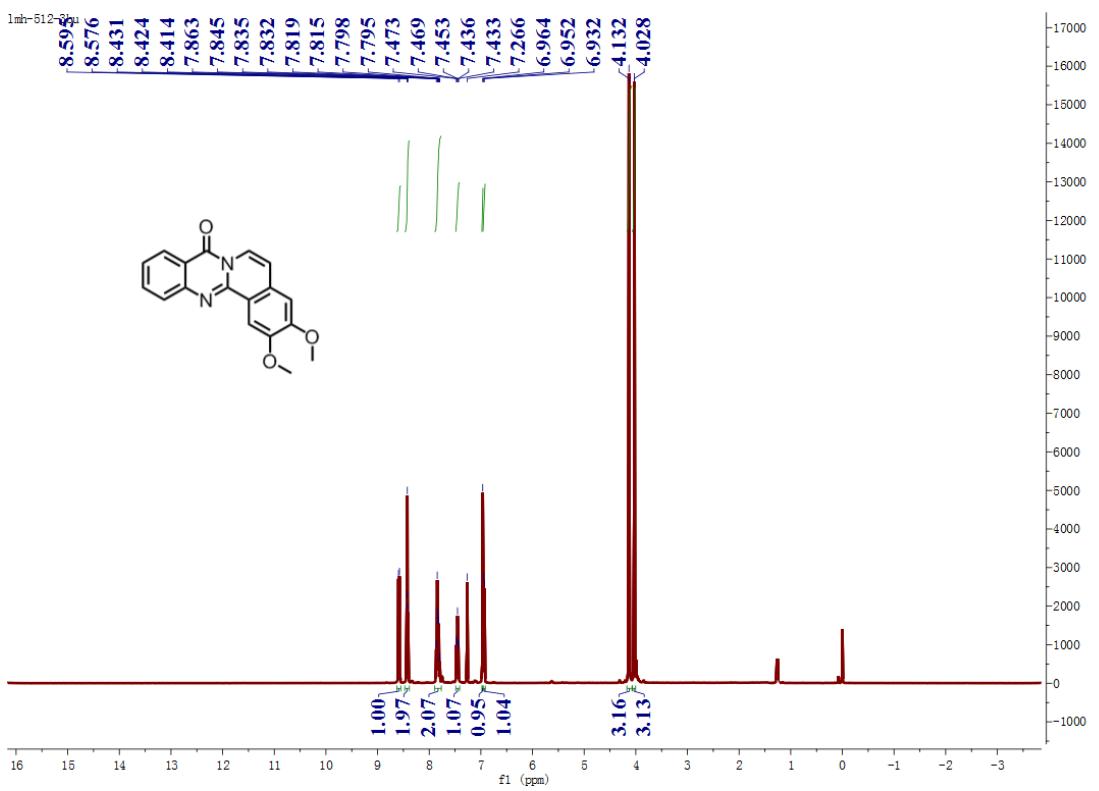
2,3-Dimethoxy-isoquinolino[1,2-b]quinazolin-8-one

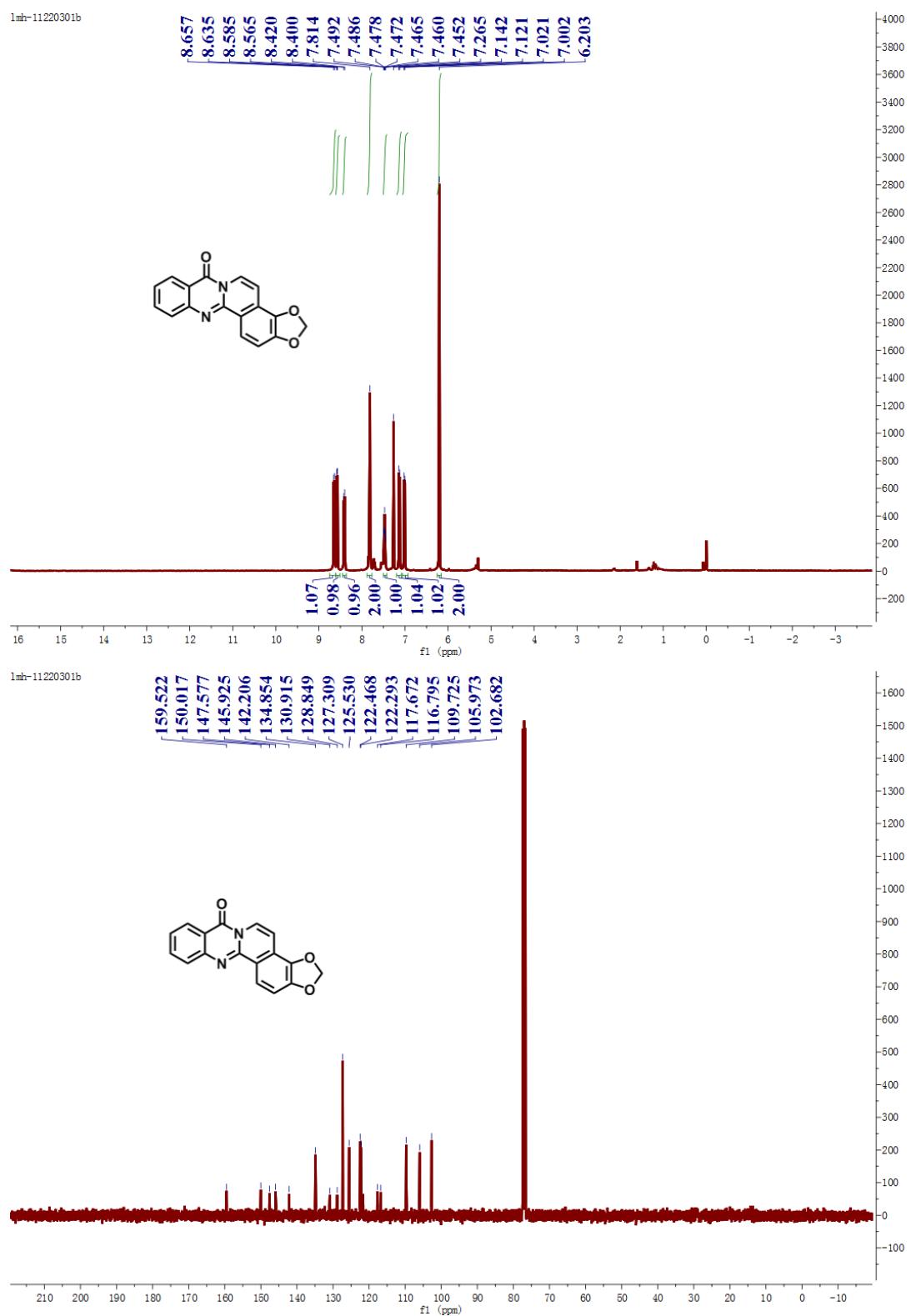
Compound was obtained as a white solid: yield 58%; mp: 230–232 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.59 (d, $J = 7.6$ Hz, 1H), 8.43–8.41 (m, 2H), 7.89 – 7.77 (m, 2H), 7.49 – 7.41 (m, 1H), 6.96 (s, 1H), 6.94 (d, $J = 7.8$ Hz, 1H), 4.13 (s, 3H), 4.03 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 159.6, 153.3, 150.2, 147.8, 145.7, 134.6, 128.3, 127.3, 127.1, 125.0, 121.2, 120.7, 117.0, 112.7, 107.6, 106.9, 56.4, 56.2.

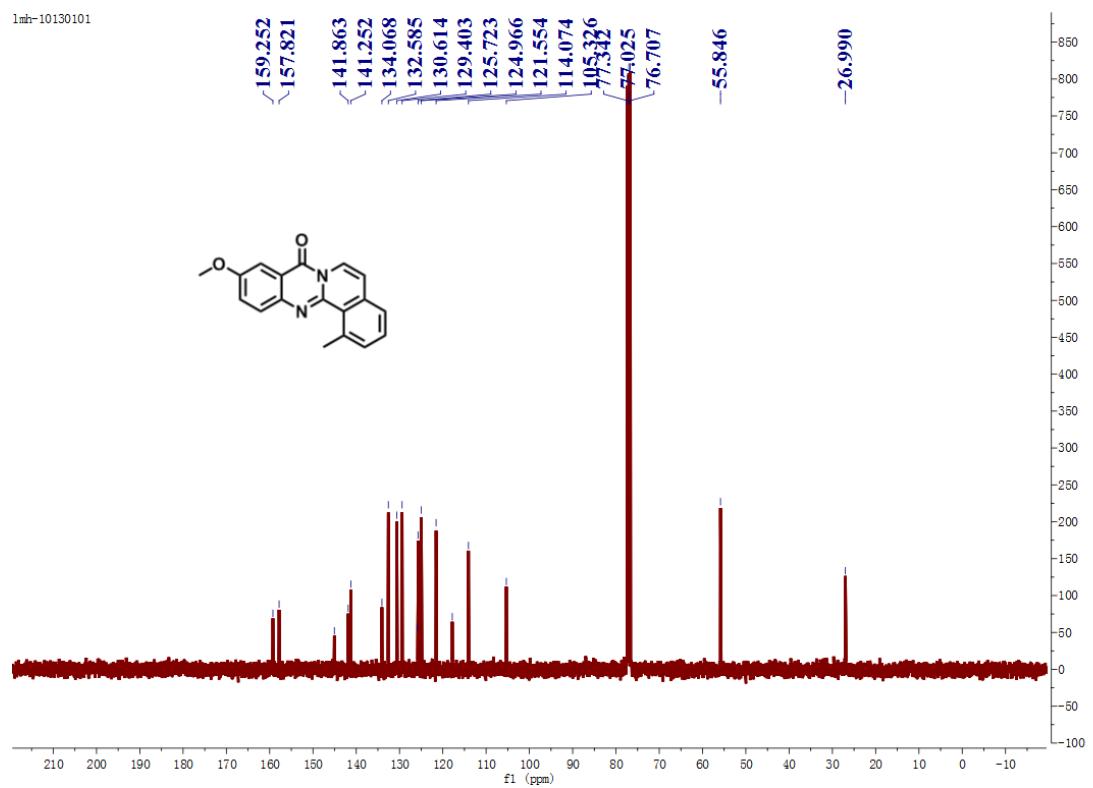
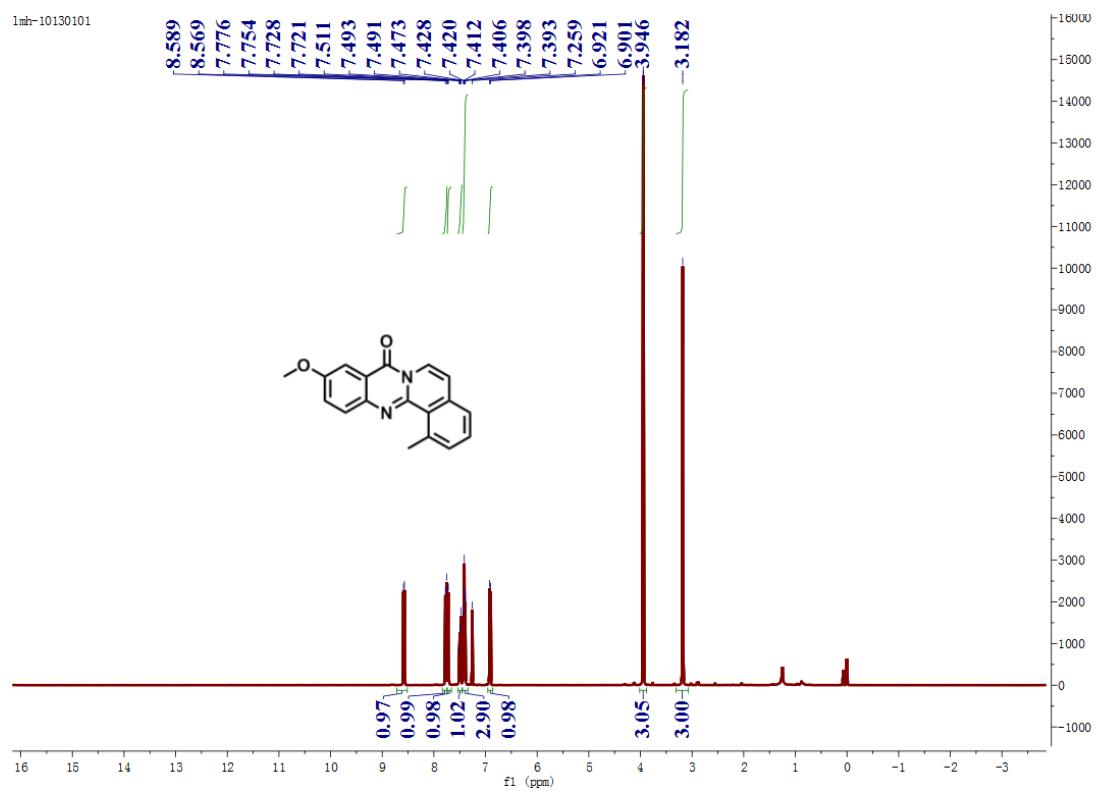
HRMS calcd. for $\text{C}_{18}\text{H}_{15}\text{N}_2\text{O}_3 (\text{M}+\text{H})^+$: 307.1077, found: 307.1086.

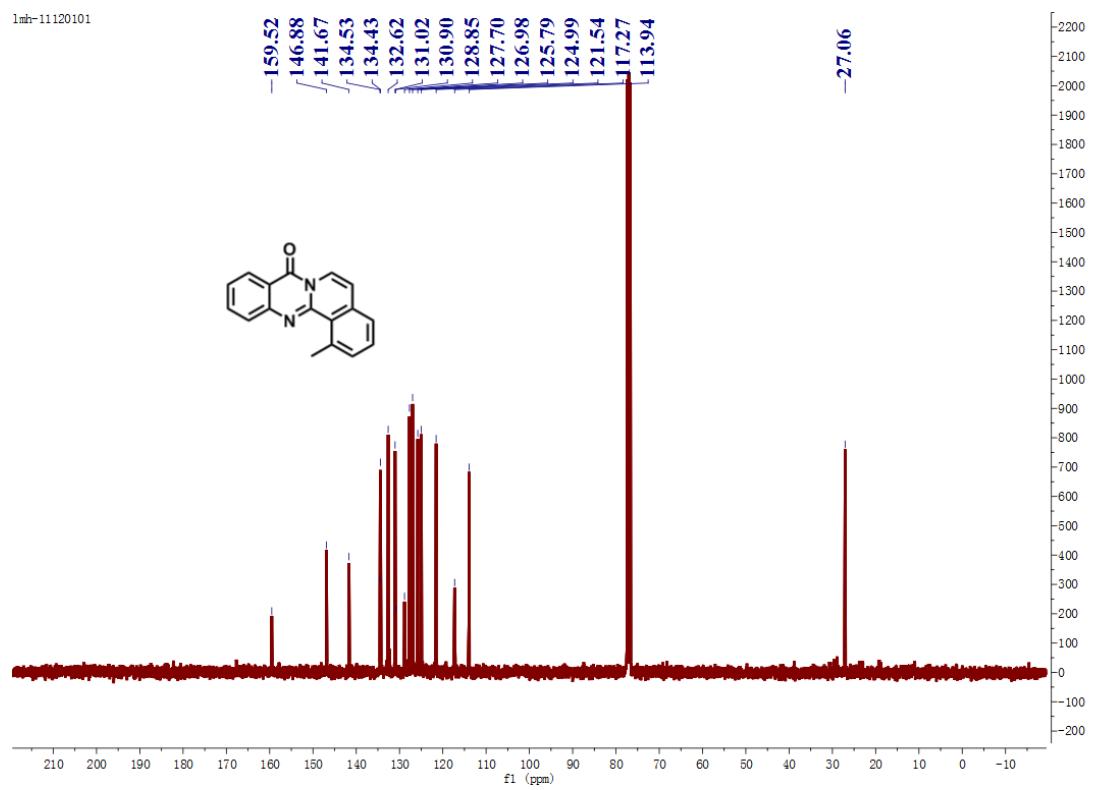
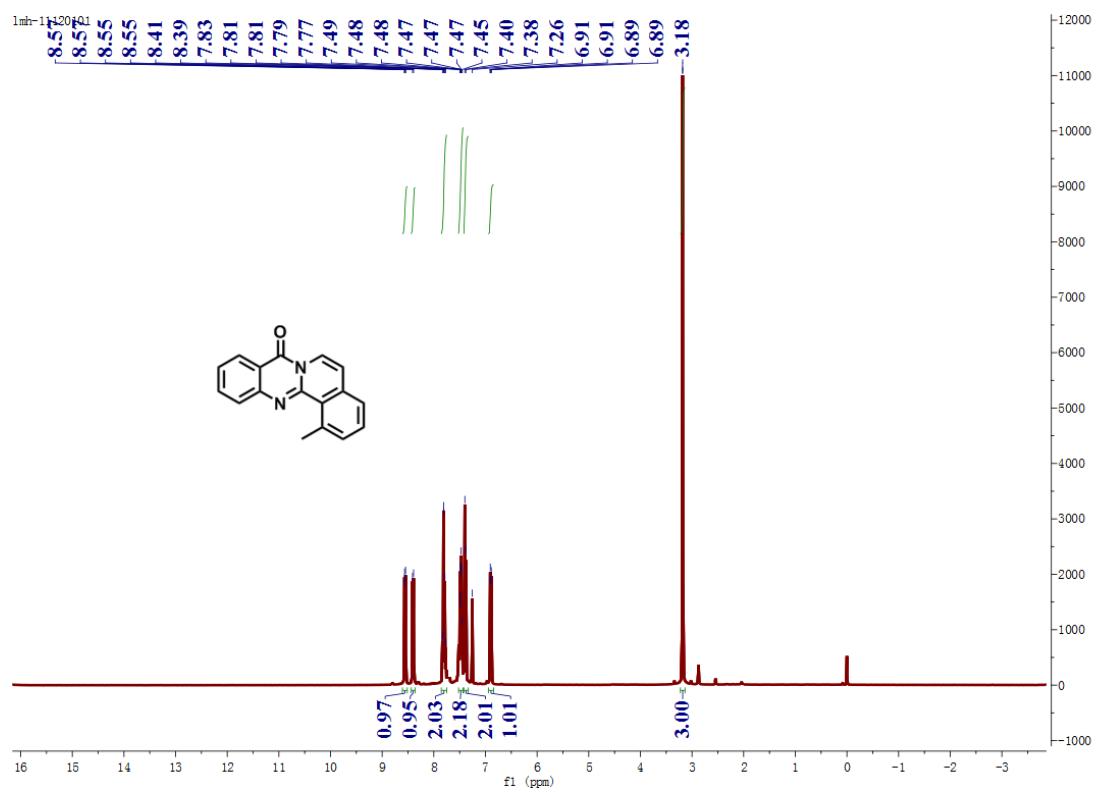
4. NMR Spectra of Products

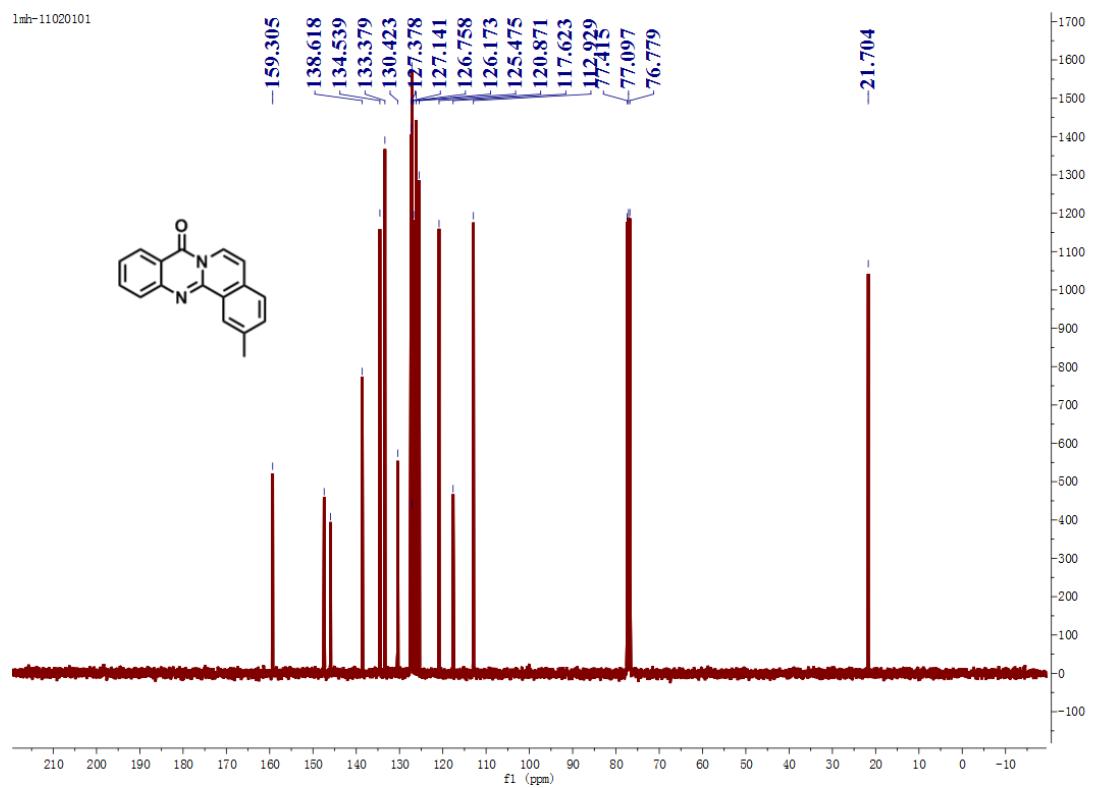
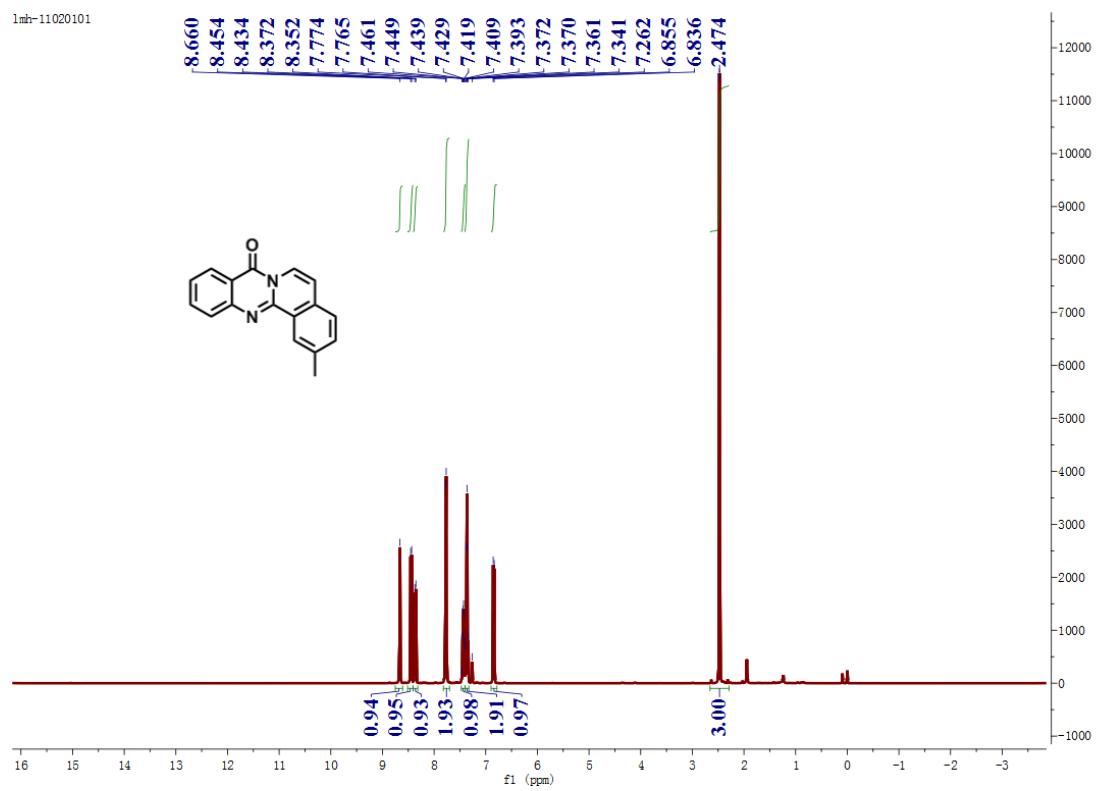


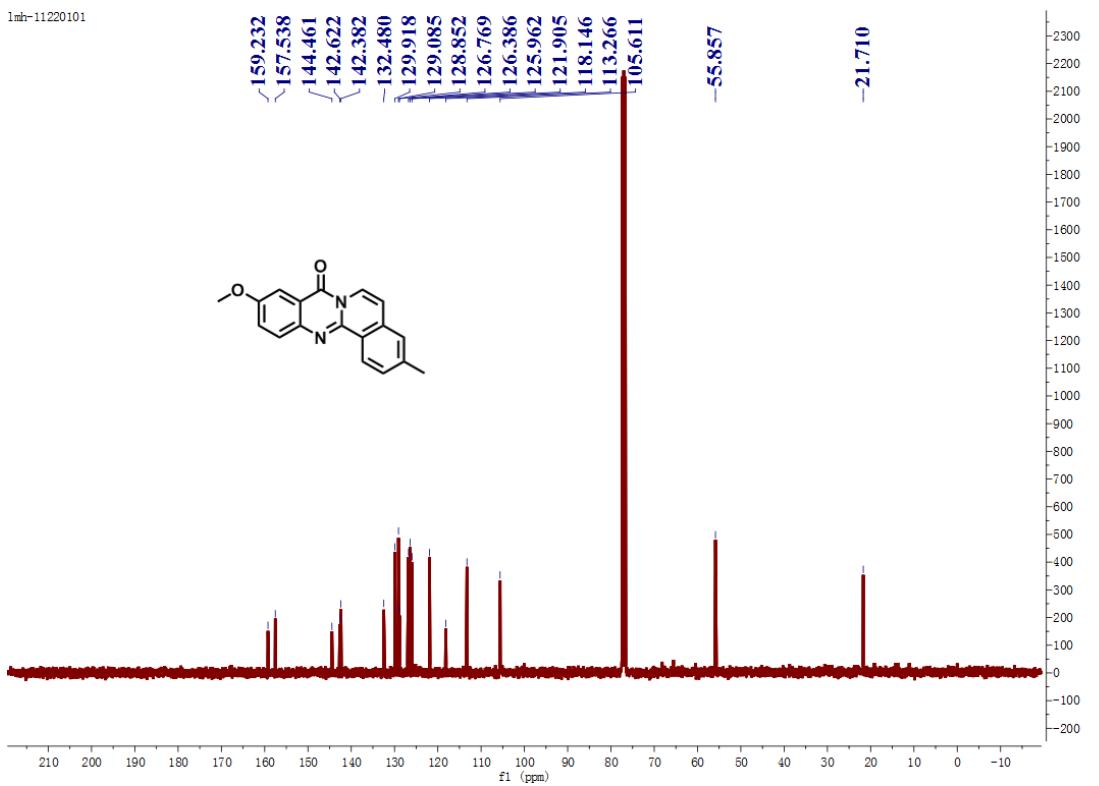
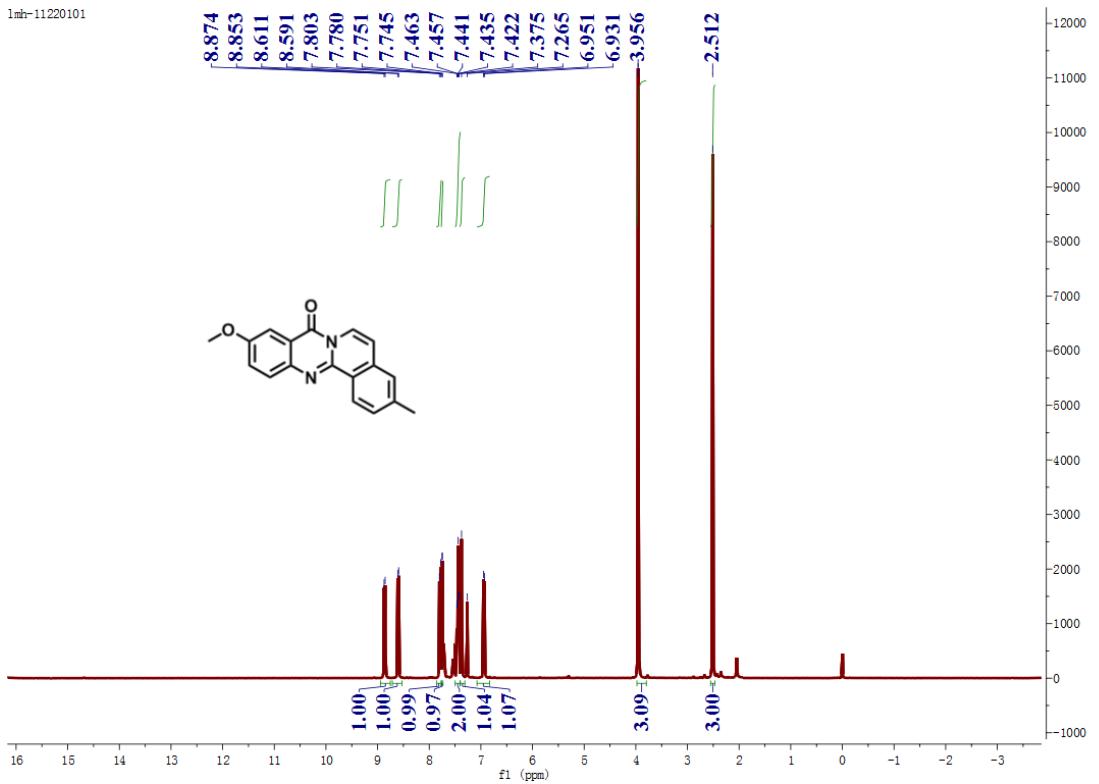


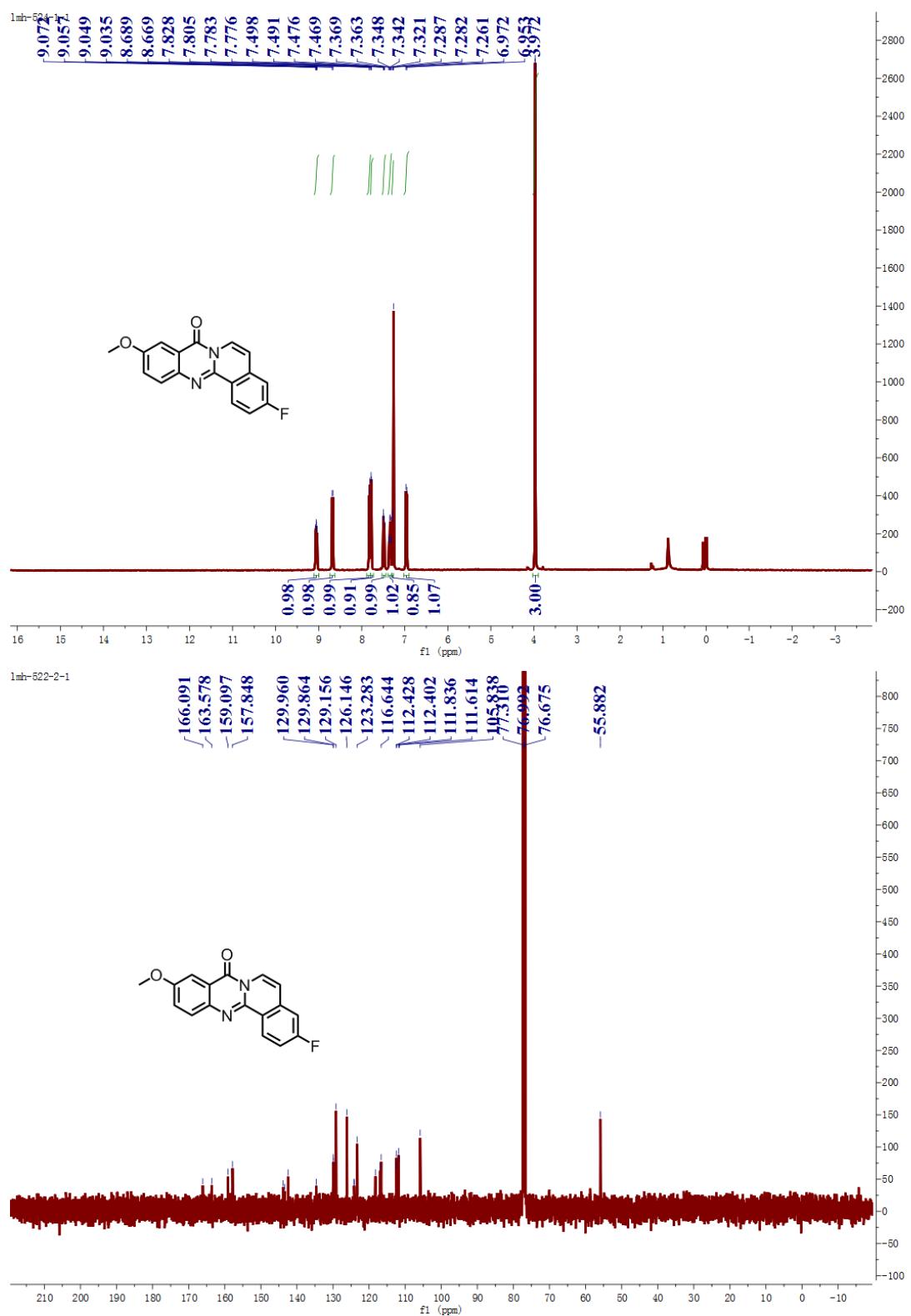


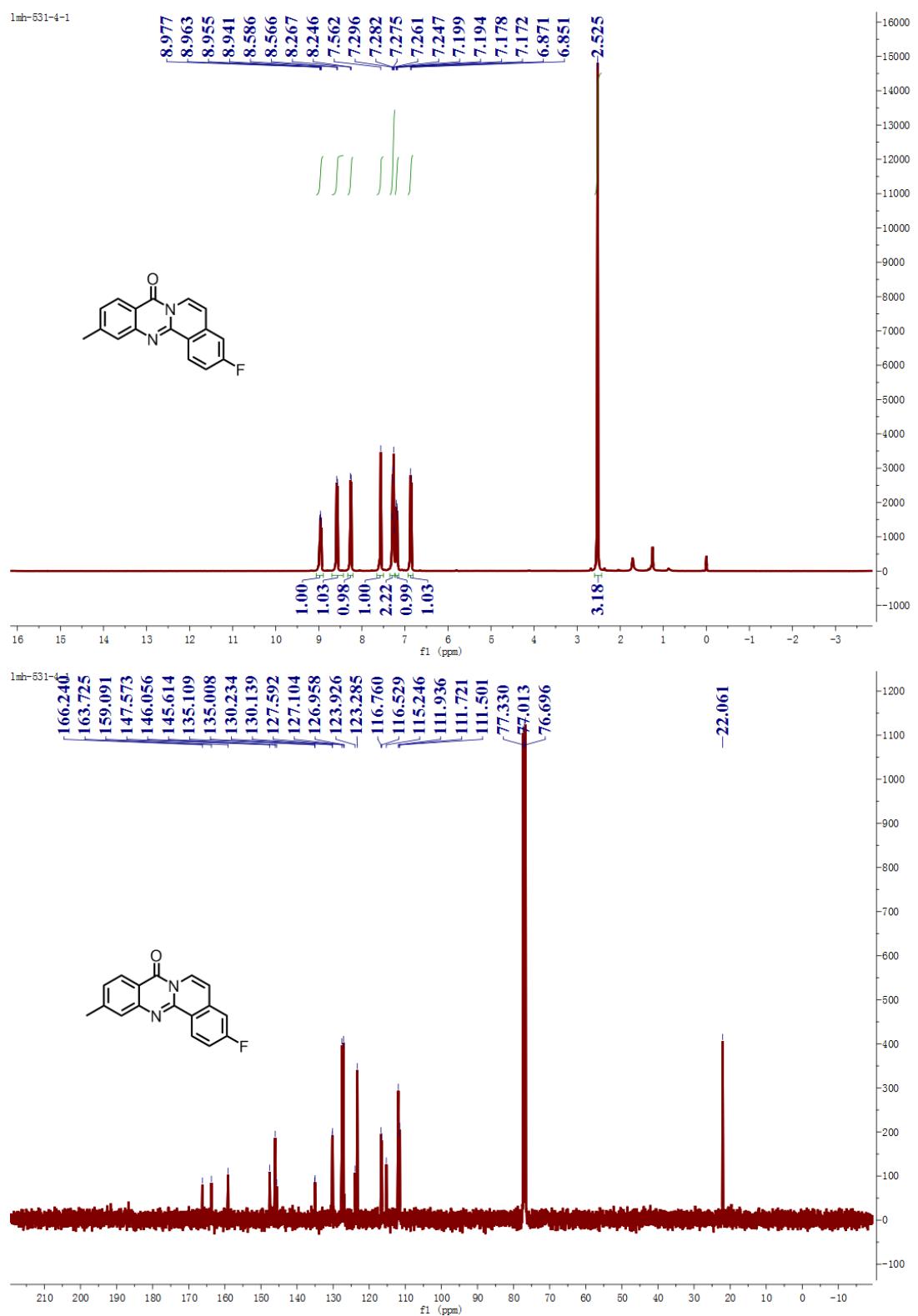


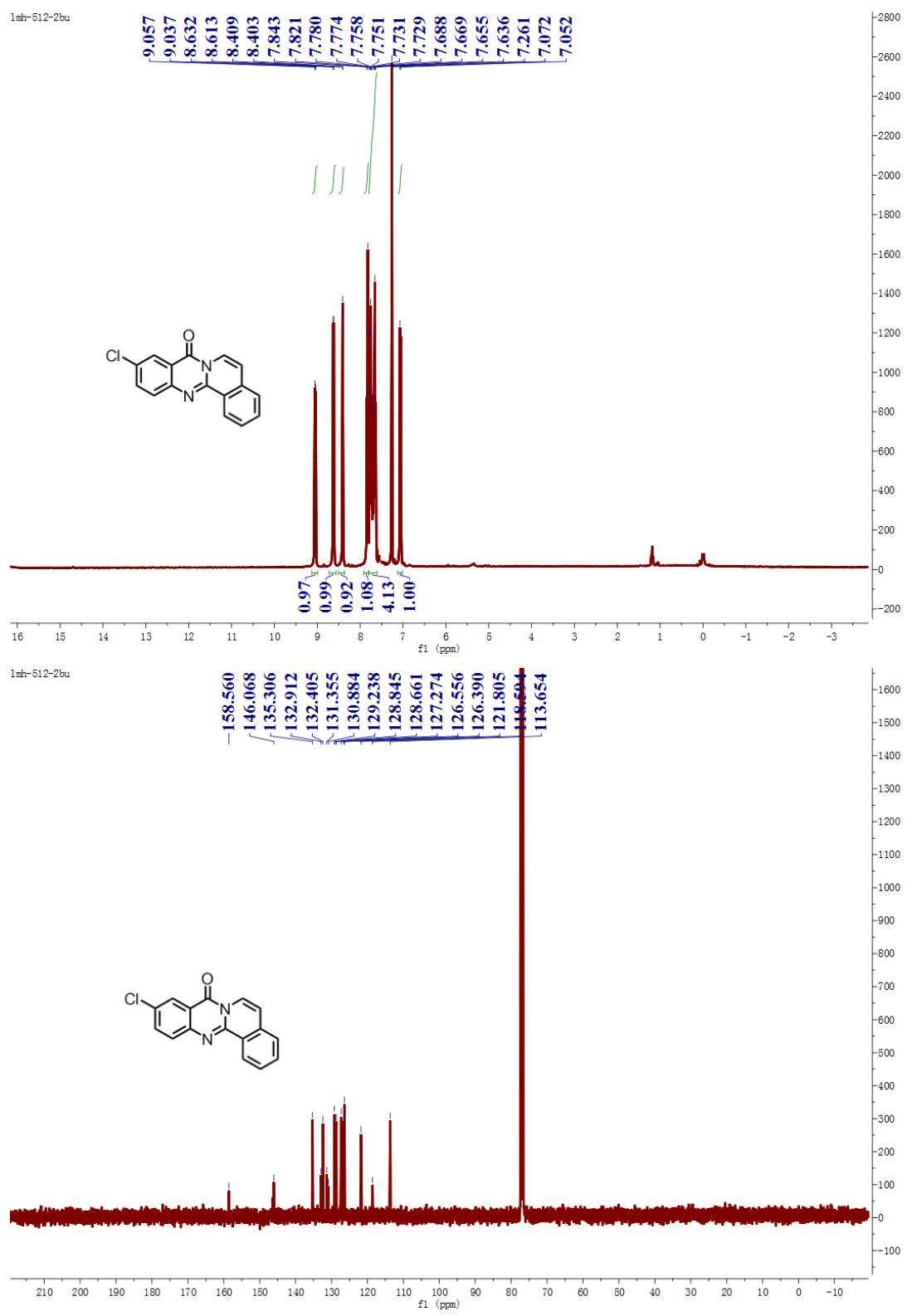


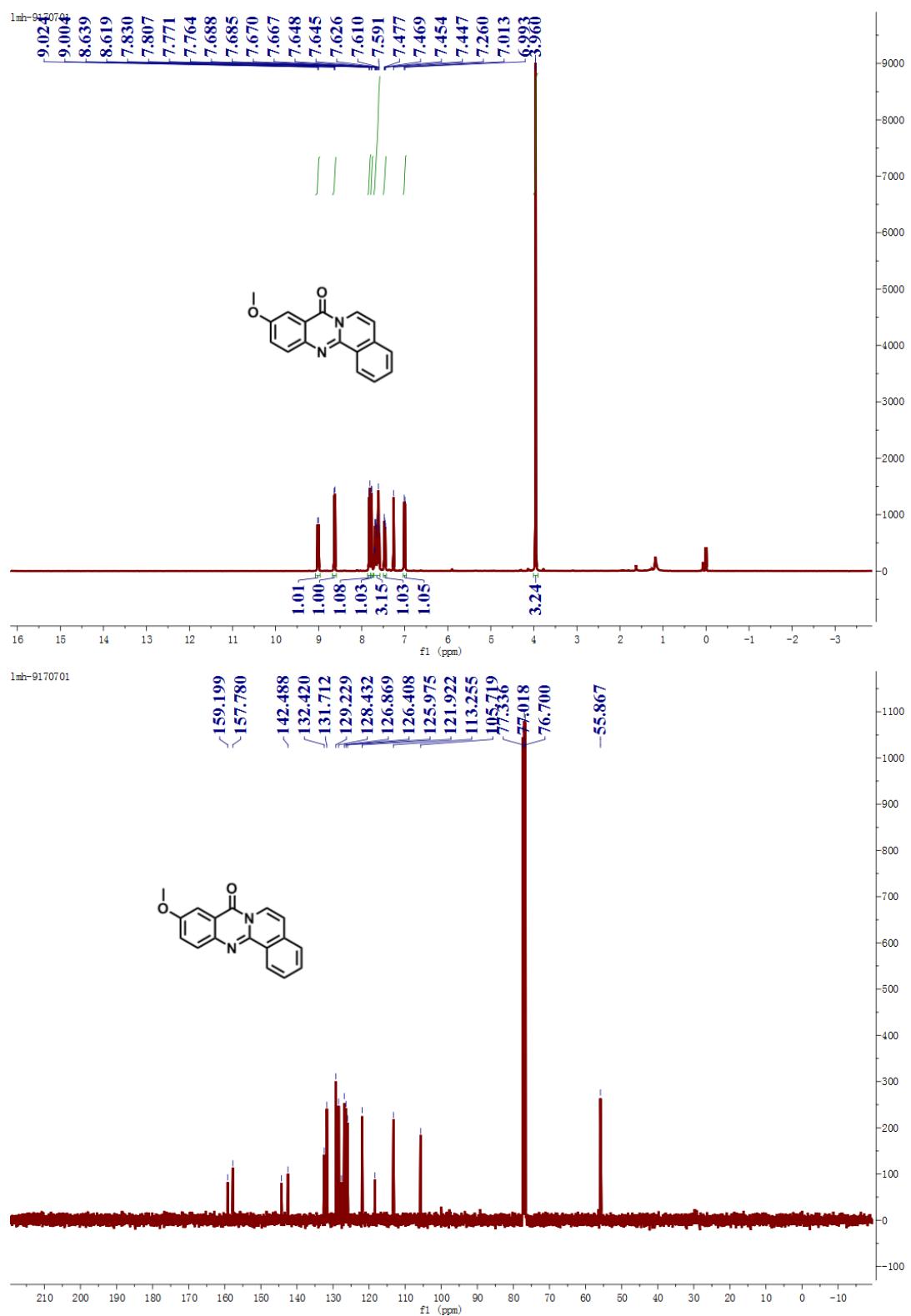


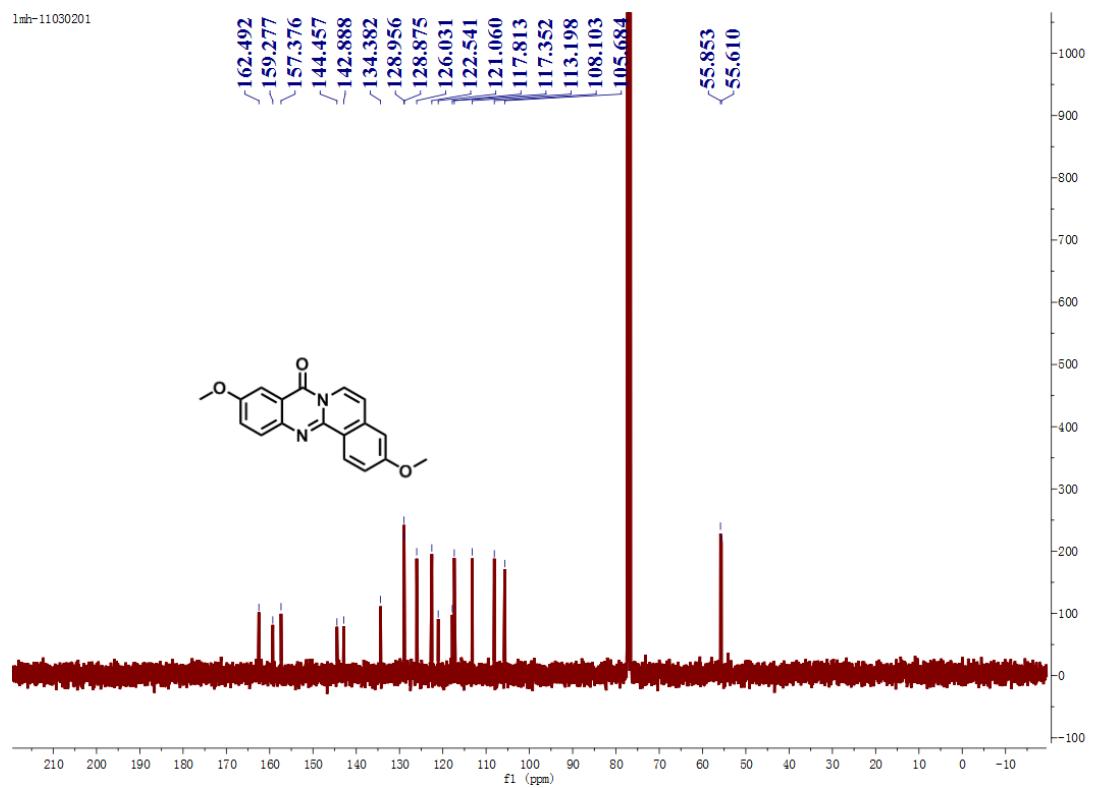
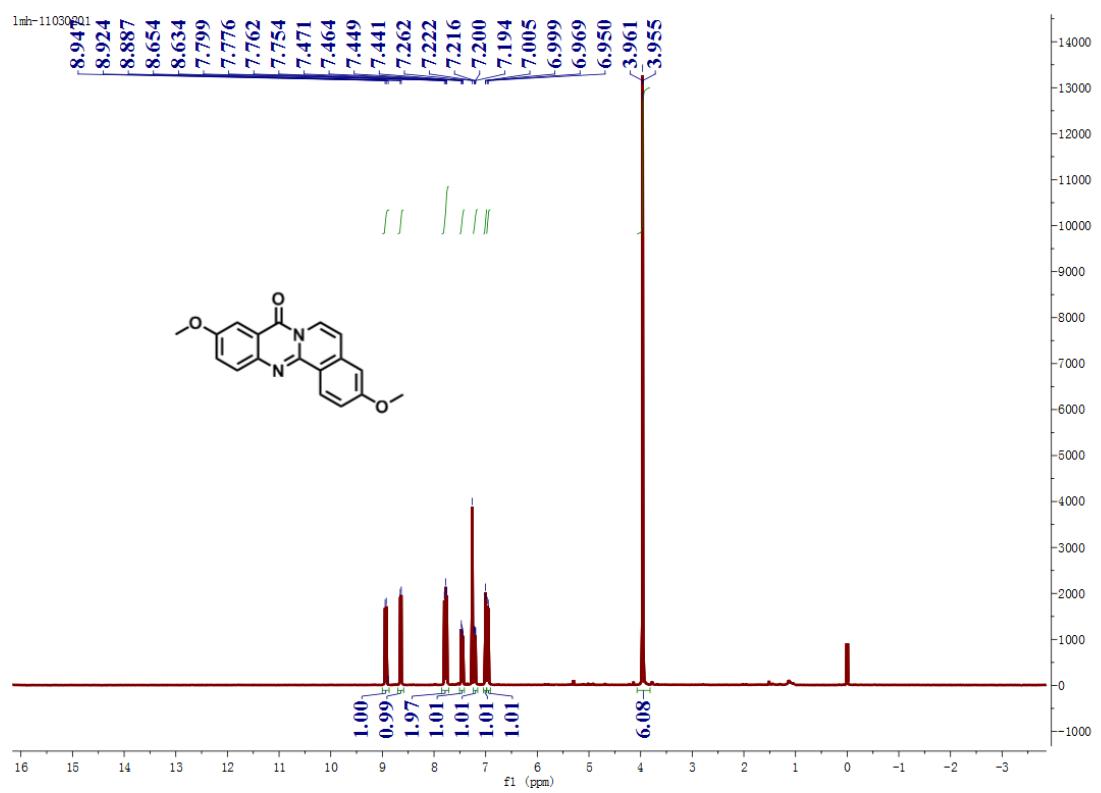


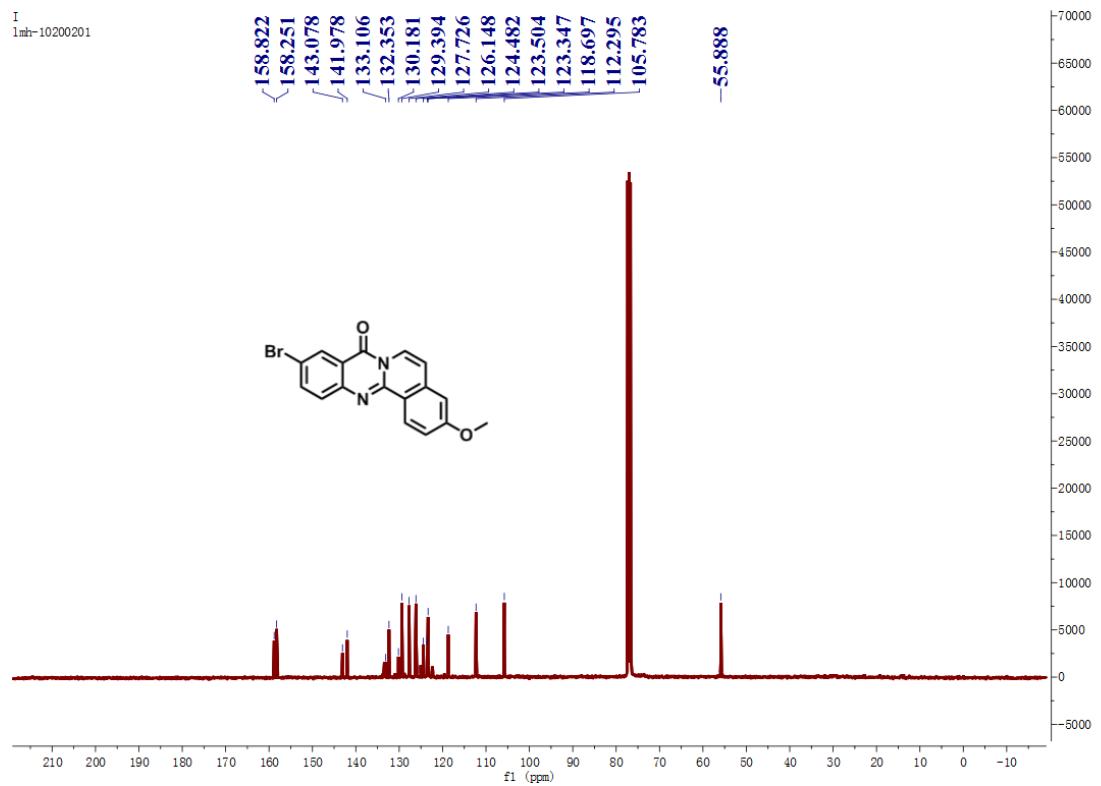
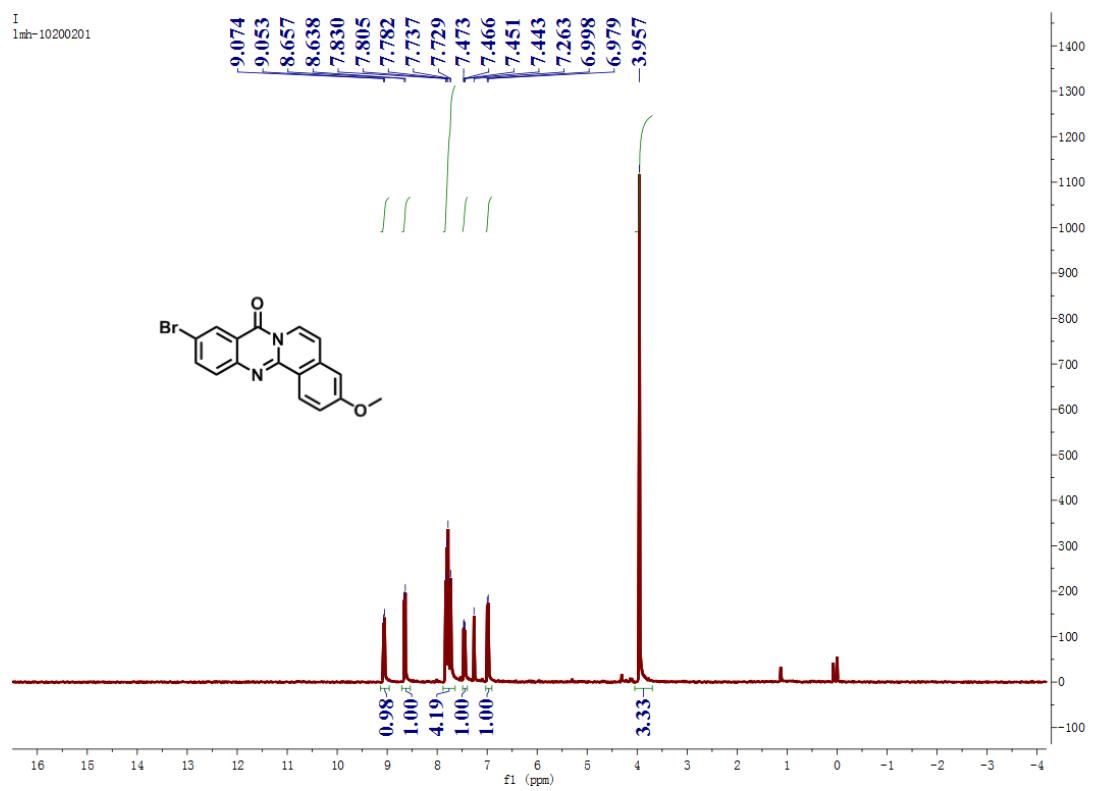


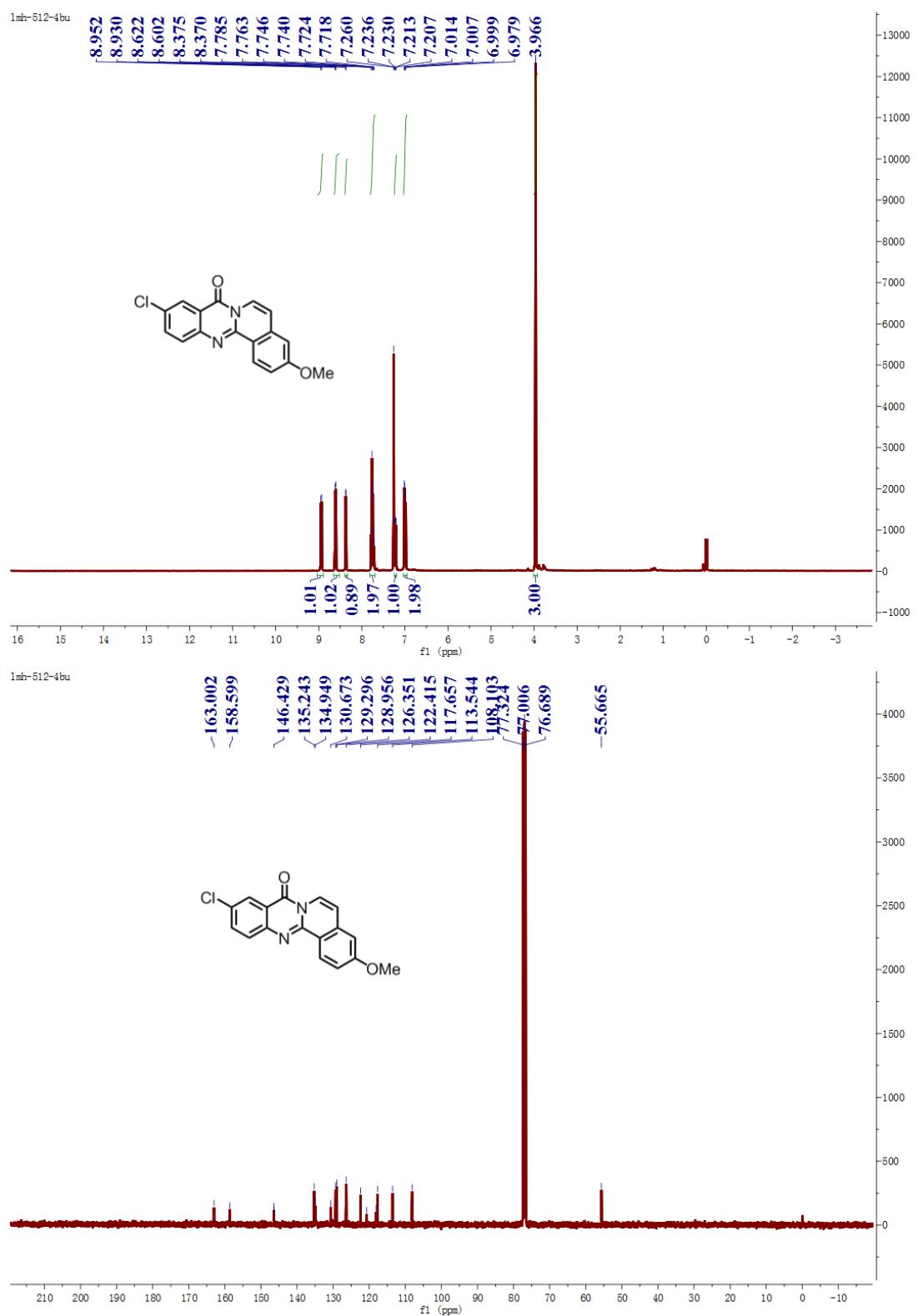


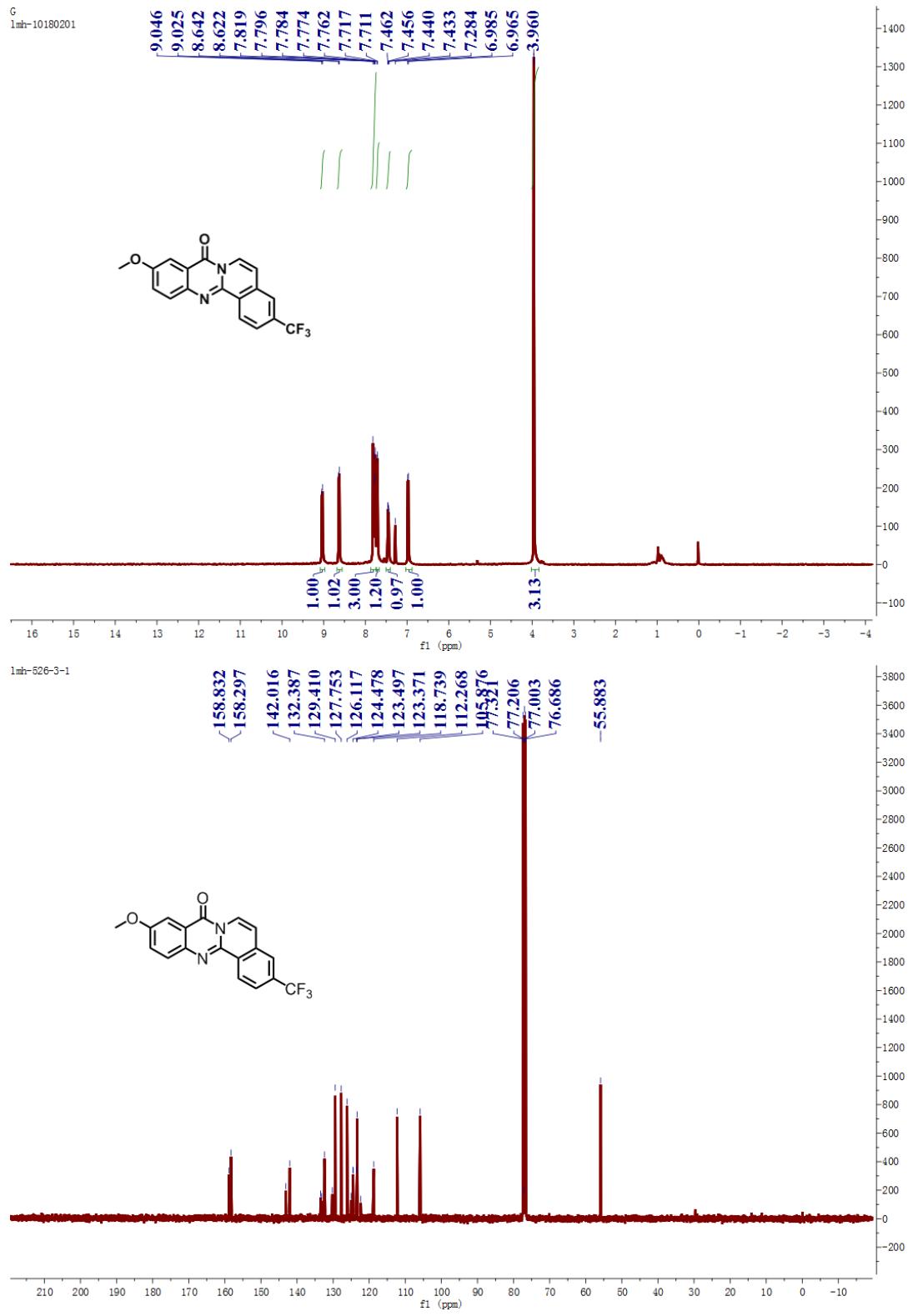


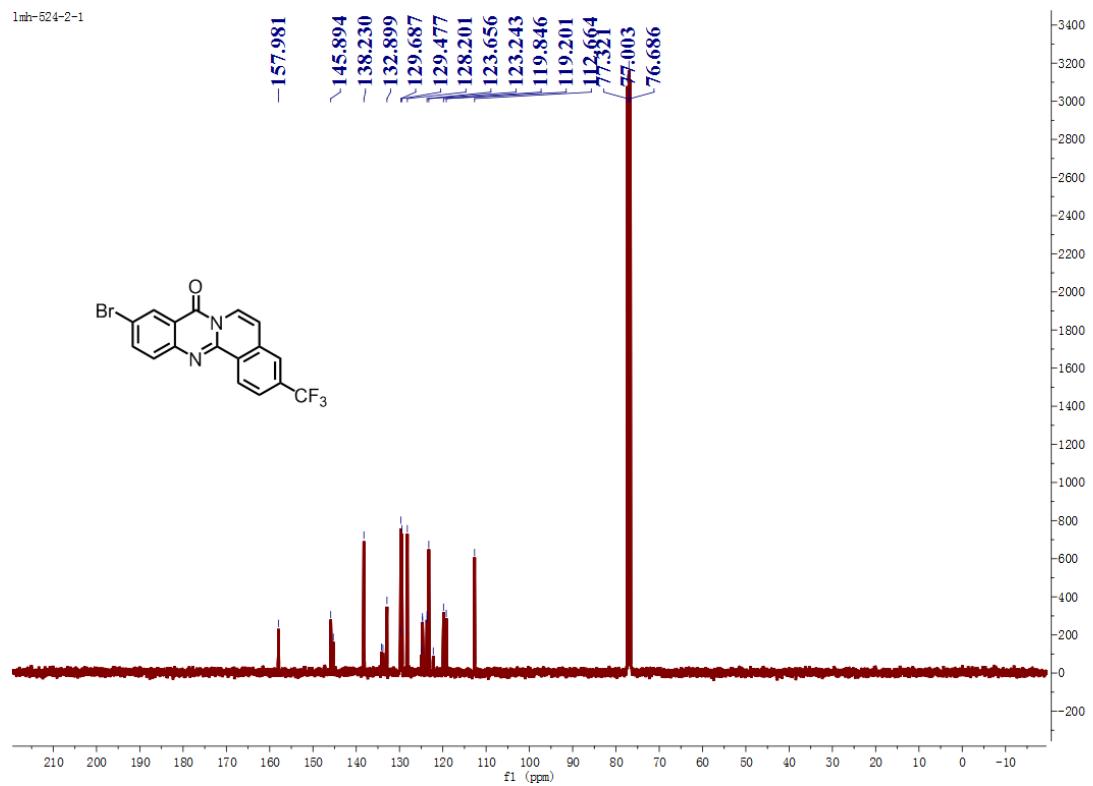
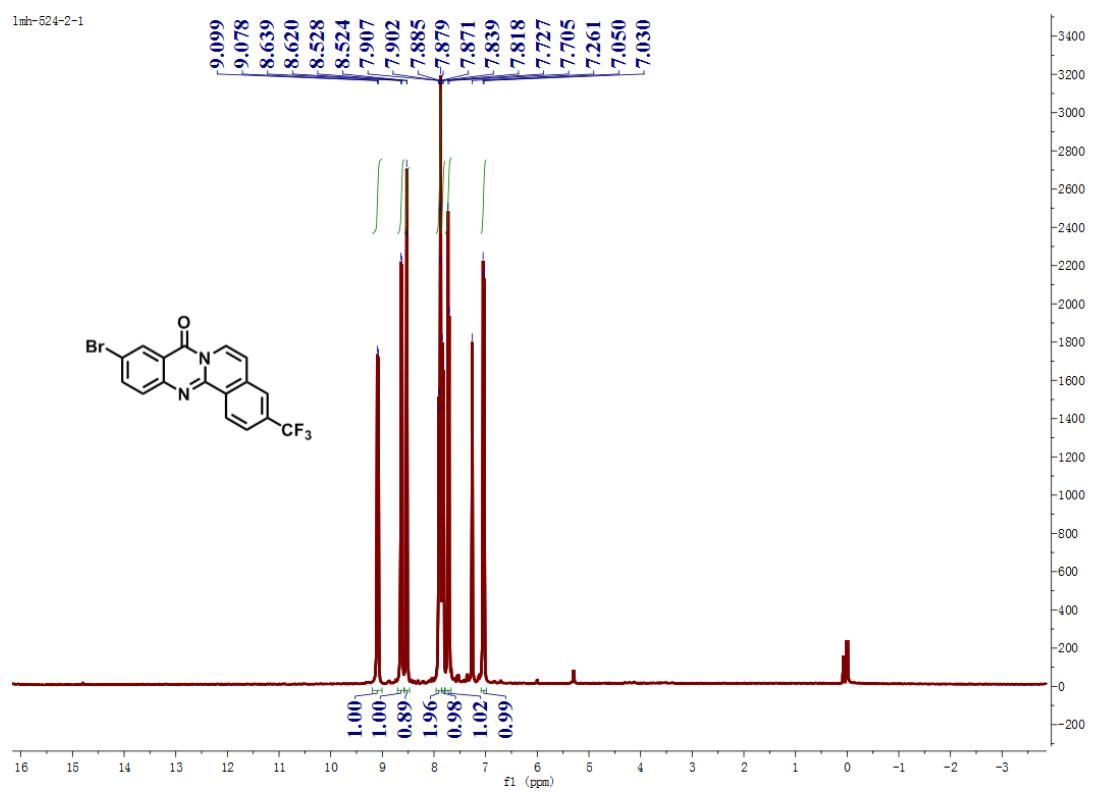


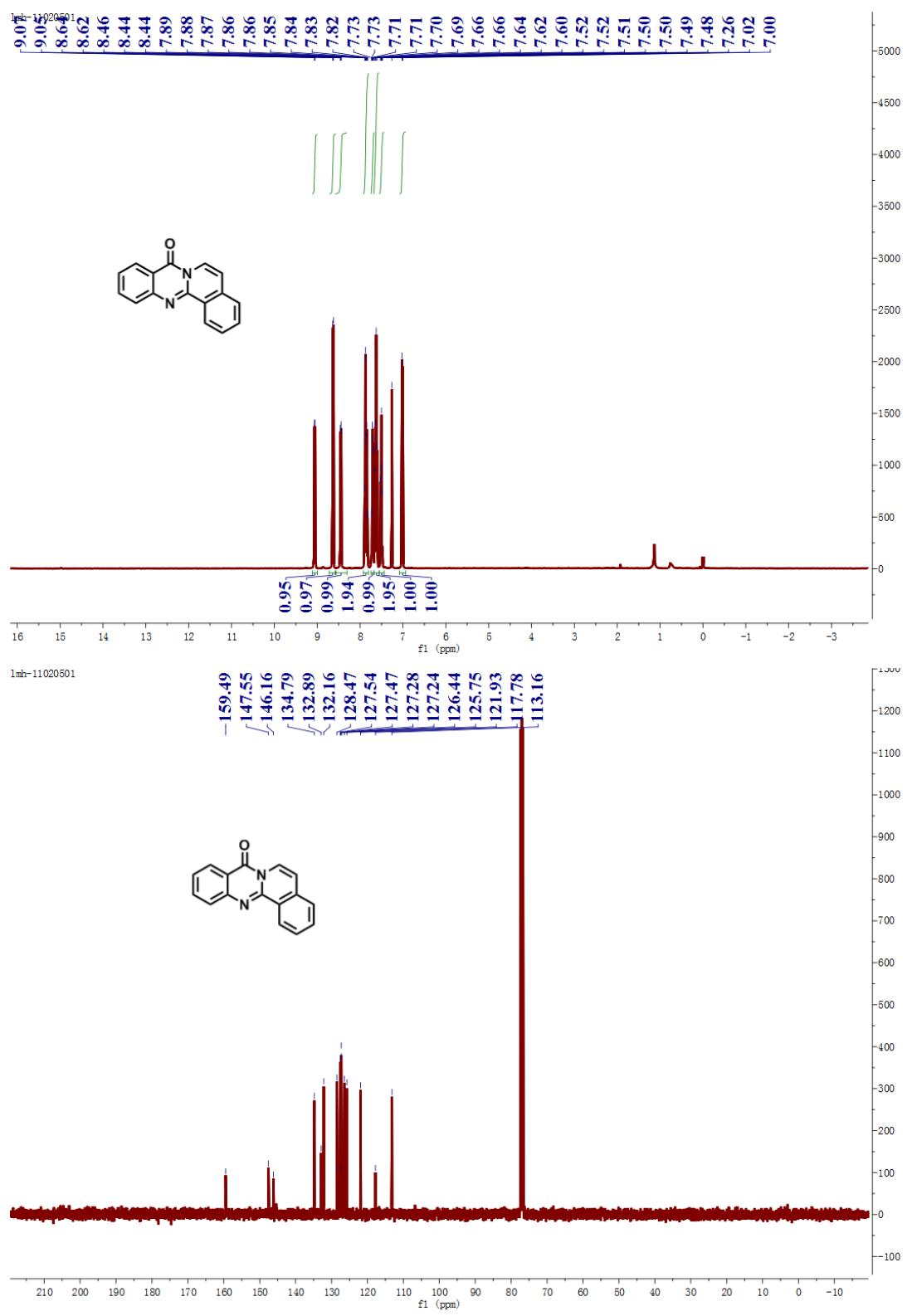


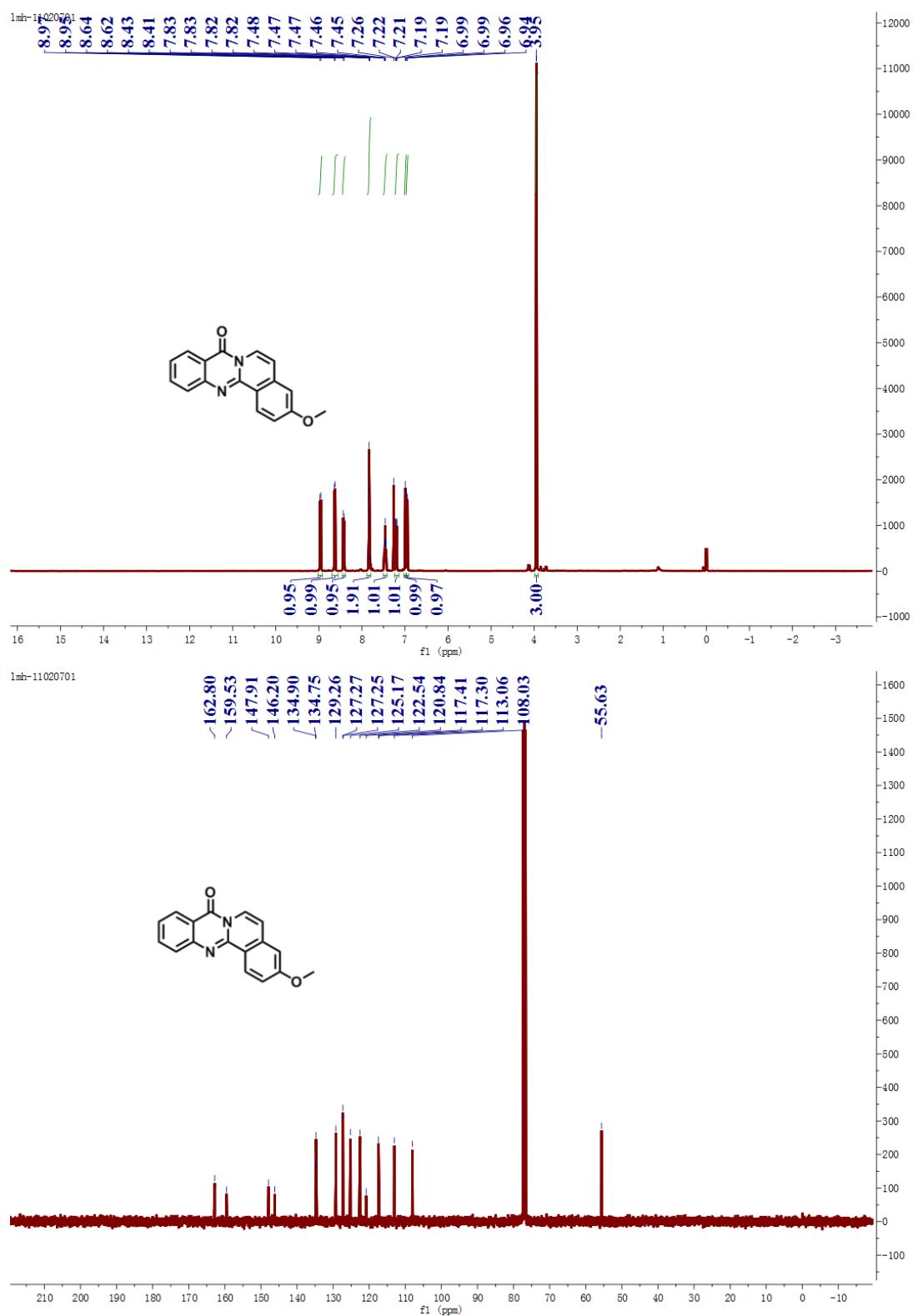




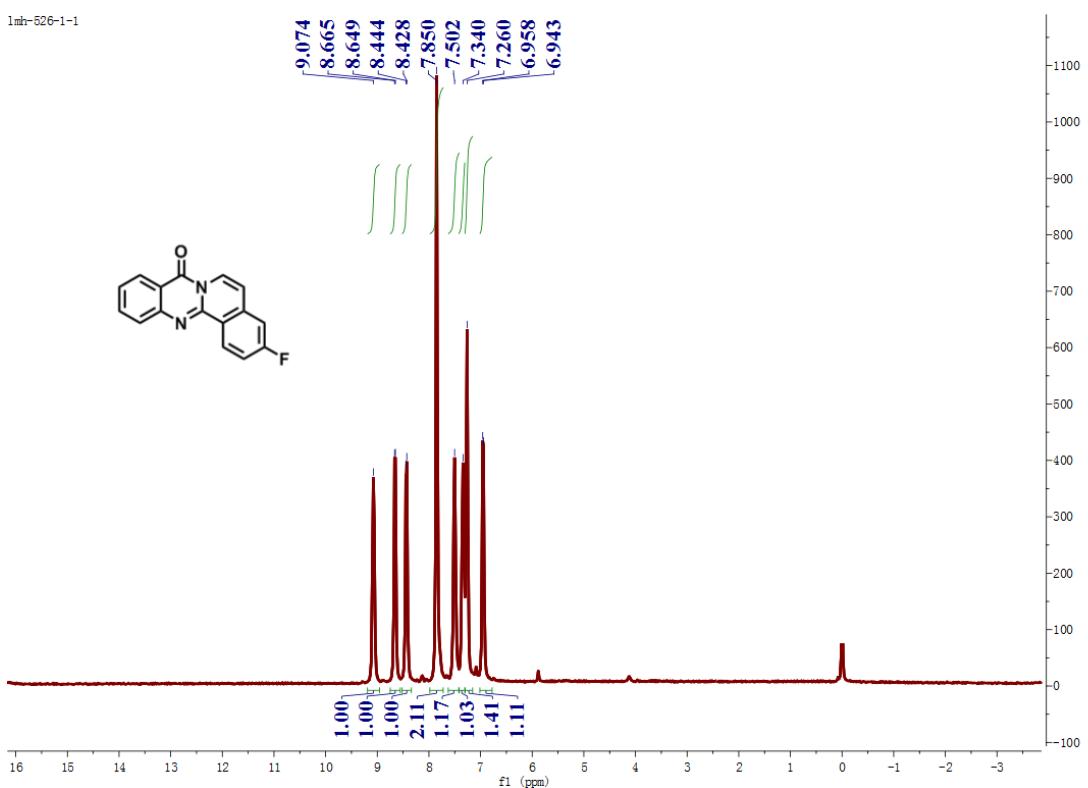








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1mh-526-1-1b

