

Supplementary Information

For

Visible-light-driven cascade radical cyclization toward the synthesis of α -carbonyl alkyl-substituted benzimidazo[2,1-*a*]isoquinolin-6(5*H*)-ones

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1. General information

All starting materials were purchased from commercial sources without further purification. Glassware was dried in oven and cooled before use. All reactions were monitored by TLC and visualized by UV lamp (254nm). The solvents were distilled from the appropriate drying reagents. Yields generally referred to chromatographically isolated yields, unless otherwise noted.

¹H NMR (600 MHz) and ¹³C NMR (151 MHz) spectra were obtained on Bruker AV-600 instrument in CDCl₃ or DMSO-d₆. For ¹H NMR (600MHz), CDCl₃ (δ = 7.26 ppm) and DMSO-d₆ (δ = 2.5 ppm) served as internal standard and data is reported as follows: chemical shift (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet), coupling constant (in Hz), and integration. HRMS (ESI) spectra were recorded on a Bruker Esquire LC mass spectrometer using electrospray ionization. Flash column chromatography was performed using 200-300 mesh silica gel.

2. Typical Procedures for Preparation of Substrates 1

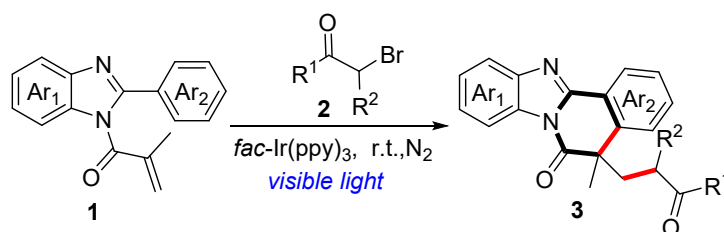
Substrates **1** were synthesized according to literature procedures, and the NMR spectroscopies were consisted with those data. [S1]

Reference:

[S1] (a) Pan, C.; Yuan, C.; Yu, J.-T. *Org. Biomol. Chem.*, **2021**, *19*, 619-626. (b) Liu, L.; Yang, D.Y.; He, Y.-H.; Guan, Z. *J. Org. Chem.*, **2020**, *85*, 11892-11901. (c) Yuan, Y.; Zheng, Y.; Xu, B.; Liao, J.; Bu, F.; Wang, S.; Hu, J.-G.; Lei, A. *ACS Catal.* **2020**, *10*, 6676.

3. General Procedures

(1) General Procedures for Cascade Radical Cyclization



To a 10 mL bottom flask were added substrate **1** (0.1 mmol), **2** (0.2 mmol), DMF (anhydrous, 1.0 mL), *fac*-Ir(ppy)₃ (0.005 mmol) and 2,6-lutidine (0.2 mmol). The mixture was charged with Ar three times under -78 °C and then was stirred under a blue LEDs (5 W) at room temperature. After the substrate was consumed (monitored by TLC), the reaction mixture was quenched with brine (3 mL) and was extracted with EtOAc (5 mL × 4). The organic layer was combined, dried (Na₂SO₄), filtered, and concentrated in *vacuo*. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc) to afford the desired product **3**.

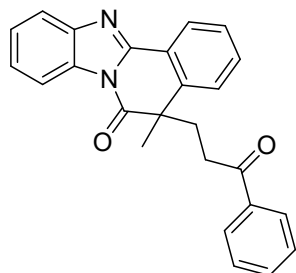
(2) General Procedures for Cell Cytotoxicity of Compounds 3

The cell viability experiment was conducted using a Cell Counting Kit-8 (CCK8, Beyotime). U87 cells or MDA-MB-231 cells were seeded in 96-well plates with ~5000 cells in each well and incubated overnight. Solutions of 100 μM compound **3** were made up in medium, and a serial three-fold dilution of the solution was performed to obtain a range of concentrations from 0.4115 to 100 μM. The media of cells were removed and the solutions were added for 72 h incubation at 37 °C.

At the end of the incubation, 10 μ L of CCK8 solution were added to each well and incubated from 1 to 4 h. The absorbance (450 nm) was recorded using a microplate reader. Cell viability was determined according to the manufacturer's description. IC₅₀ values at 72 h were calculated using Graph Pad based on the viability curve data.

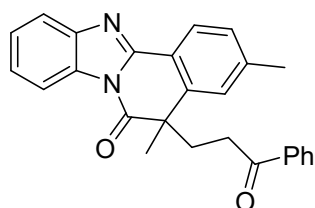
4. Characterization of new substrates

3aa



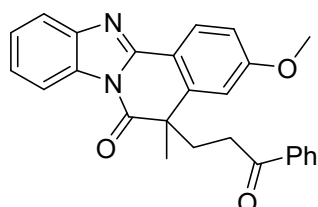
Yellow oil. ¹H NMR (600 MHz, CDCl₃) δ _H 8.51 (dd, J = 7.8, 0.8 Hz, 1H), 8.37 (d, J = 8.6 Hz, 1H), 7.84 (d, J = 7.2 Hz, 1H), 7.70 (d, J = 7.3 Hz, 2H), 7.61-7.56 (m, 1H), 7.54-7.49 (m, 2H), 7.48-7.43 (m, 3H), 7.32 (t, J = 7.8 Hz, 2H), 2.88-2.77 (m, 2H), 2.61-2.53 (m, 1H), 2.48-2.43 (m, 1H), 1.79 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ _C 198.4, 172.8, 149.7, 144.0, 140.9, 136.2, 133.2, 132.3, 131.3, 128.5, 128.1, 127.9, 126.2, 126.1, 126.0, 125.7, 122.9, 119.8, 115.7, 48.8, 35.8, 34.1, 29.7. HRMS m/z (ESI) calcd for C₂₅H₂₀N₂NaO₂⁺ [M+Na]⁺: 403.1417, found: 403.1426.

3ba



Light yellow oil. ¹H NMR (600 MHz, CDCl₃) δ _H 8.38 (dd, J = 17.7, 7.9 Hz, 2H), 7.82 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 7.4 Hz, 2H), 7.47-7.41 (m, 3H), 7.34-7.31 (m, 4H), 2.86-2.76 (m, 2H), 2.57-2.51 (m, 1H), 2.49-2.43 (m, 4H), 1.78 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ _C 198.5, 173.0, 149.9, 144.0, 143.0, 141.0, 136.3, 133.2, 131.3, 129.2, 128.5, 127.9, 126.5, 126.1, 126.0, 125.5, 120.3, 119.7, 115.7, 48.7, 35.9, 34.2, 29.7, 22.0. HRMS m/z (ESI) calcd for C₂₆H₂₂N₂NaO₂⁺ [M+Na]⁺: 417.1573, found: 417.1580.

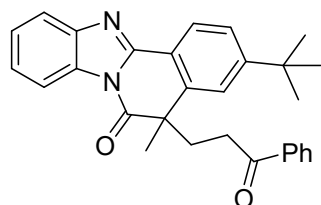
3ca



Light yellow solid, mp = 167.6-170.8 °C;. ¹H NMR (600 MHz, CDCl₃) δ _H 8.45 (d, J = 8.7 Hz, 1H), 8.34 (d, J = 7.9 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 8.0 Hz, 2H), 7.48-7.39 (m, 3H), 7.33 (t, J = 7.6 Hz, 2H), 7.04 (dd, J = 8.8, 2.3 Hz, 1H), 6.99 (d, J = 2.4 Hz, 1H), 3.90 (s, 3H), 2.87-2.77

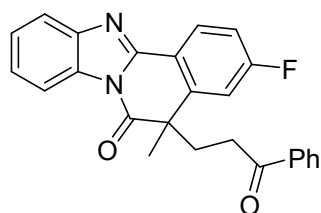
(m, 2H), 2.55-2.46 (m, 2H), 1.78 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ_{C} 197.4, 171.8, 161.9, 148.8, 143.1, 142.0, 135.3, 132.1, 130.2, 127.5, 127.1, 126.9, 124.9, 124.2, 118.4, 114.6, 113.1, 110.4, 54.6, 47.9, 34.9, 33.1, 28.8. HRMS m/z (ESI) calcd for $\text{C}_{26}\text{H}_{22}\text{N}_2\text{NaO}_3^+$ $[\text{M}+\text{Na}]^+$: 433.1523, found: 433.1528.

3da



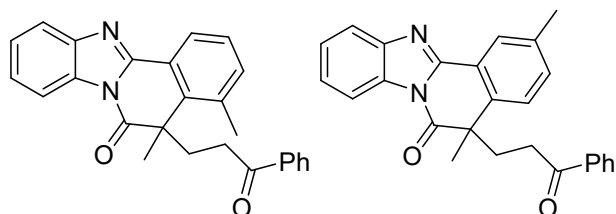
Light yellow oil. ^1H NMR (600 MHz, CDCl_3) δ_{H} 8.40 (dd, $J = 37.7, 7.8$ Hz, 2H), 7.84 (d, $J = 8.8$ Hz, 1H), 7.69 (d, $J = 7.6$ Hz, 2H), 7.54-7.51 (m, 2H), 7.48-7.41 (m, 3H), 7.32 (t, $J = 7.6$ Hz, 2H), 2.86-2.74 (m, 2H), 2.63-2.56 (m, 1H), 2.53-2.43 (m, 1H), 1.80 (s, 3H), 1.37 (s, 9H). ^{13}C NMR (151 MHz, CDCl_3) δ_{C} 197.4, 172.0, 155.1, 148.8, 142.8, 139.6, 135.2, 132.1, 130.2, 127.5, 126.9, 125.0, 124.9, 124.6, 124.5, 121.6, 119.1, 118.6, 114.7, 48.0, 35.0, 34.3, 33.1, 30.1, 28.5. HRMS m/z (ESI) calcd for $\text{C}_{29}\text{H}_{28}\text{N}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 459.2043, found: 459.2051.

3ea



Light yellow oil. ^1H NMR (600 MHz, CDCl_3) δ_{H} 8.59-8.53 (m, 1H), 8.36 (d, $J = 7.6$ Hz, 1H), 7.85 (d, $J = 7.4$ Hz, 1H), 7.71 (d, $J = 7.6$ Hz, 2H), 7.49-7.44 (m, 3H), 7.34 (t, $J = 7.7$ Hz, 2H), 7.24-7.21 (m, 2H), 2.88-2.78 (m, 2H), 2.53-2.47 (m, 2H), 1.79 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ_{C} 197.0, 171.1, 164.3 (d, $J = 255.2$ Hz), 147.8, 142.9 (d, $J = 7.6$ Hz), 135.2, 132.2, 130.0, 127.9, 127.5, 126.9, 125.2, 124.9, 118.6, 115.2 (d, $J = 22.7$ Hz), 114.7, 112.2 (d, $J = 22.7$ Hz), 48.0, 34.9, 33.0, 28.5. HRMS m/z (ESI) calcd for $\text{C}_{25}\text{H}_{20}\text{FN}_2\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 399.1503, found: 399.1508.

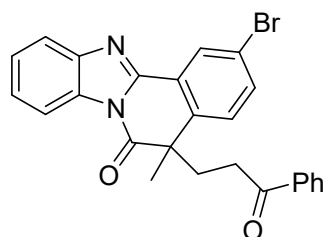
3fa + 3fa'



Light yellow oil. ^1H NMR (600 MHz, CDCl_3) δ_{H} 8.37 (d, $J = 6.7$ Hz, 1H), 8.33 (s, 0.79H), 7.84 (d, $J = 8.6$ Hz, 1H), 7.69 (d, $J = 8.3$ Hz, 2H), 7.47-7.38 (m, 5H), 7.32 (t, $J = 7.7$ Hz, 2H), 3.00-2.88 (m, 0.42H), 2.86-2.74 (m, 1.72H), 2.66 (s, 0.54H), 2.55-2.41 (m, 4.5H), 1.91 (s, 0.55H), 1.77 (s, 2.55 H). ^{13}C NMR (151 MHz, CDCl_3) δ_{C} 197.5, 197.4, 172.6, 172.0, 149.1, 148.8, 143.9, 142.8, 137.1, 137.0, 136.1, 135.5, 135.5, 135.2, 132.4, 132.1, 132.0, 130.2, 127.5, 127.4, 126.9, 126.8, 125.3, 125.2, 125.0, 124.9, 124.6, 124.5, 124.2, 121.5, 118.7, 118.6, 114.8, 114.7, 49.2, 47.5, 34.8,

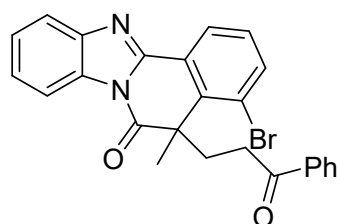
33.4, 33.1, 31.8, 28.7, 25.3, 22.1, 19.9. **HRMS** m/z (ESI) calcd for $C_{26}H_{22}N_2NaO_2^+$ $[M+Na]^+$: 417.1573, found: 417.1572.

3ga



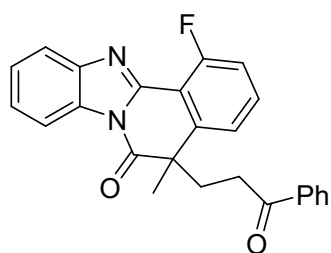
Colorless oil. **1H NMR** (600 MHz, $CDCl_3$) δ_H 8.65 (s, 1H), 8.36 (d, $J = 7.7$ Hz, 1H), 7.84 (d, $J = 7.2$ Hz, 1H), 7.68 (t, $J = 9.7$ Hz, 3H), 7.48 (q, $J = 7.2$ Hz, 3H), 7.40 (d, $J = 8.4$ Hz, 1H), 7.33 (t, $J = 7.6$ Hz, 2H), 2.88-2.76 (m, 2H), 2.56-2.42 (m, 2H), 1.77 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ_C 197.1, 171.2, 147.2, 142.8, 138.6, 135.2, 134.1, 132.2, 130.3, 127.8, 127.5, 126.9, 126.8, 125.2, 125.1, 123.8, 121.2, 119.0, 114.8, 47.7, 34.6, 33.0, 28.6. **HRMS** m/z (ESI) calcd for $C_{25}H_{20}BrN_2O_2^+$ $[M+H]^+$: 459.0703, found: 459.0710.

3ga'

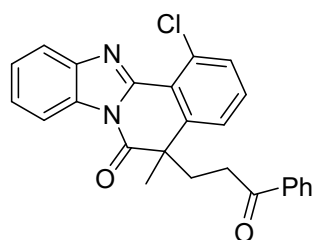


Colorless oil. **1H NMR** (600 MHz, $CDCl_3$) δ_H 8.65 (dd, $J = 7.8, 1.4$ Hz, 1H), 8.40 (dd, $J = 6.8, 1.7$ Hz, 1H), 7.85 (td, $J = 7.9, 1.5$ Hz, 2H), 7.66 (dd, $J = 8.3, 1.4$ Hz, 2H), 7.51-7.44 (m, 3H), 7.34 (dt, $J = 24.8, 8.0$ Hz, 3H), 3.65-3.56 (m, 1H), 2.90-2.82 (m, 1H), 2.72-2.62 (m, 1H), 2.58-2.50 (m, 1H), 2.07 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ_C 197.3, 171.6, 147.4, 138.6, 136.8, 135.2, 132.1, 130.1, 127.5, 127.4, 126.9, 125.6, 125.5, 125.1, 121.0, 118.7, 115.0, 49.7, 33.6, 30.9, 24.3. **HRMS** m/z (ESI) calcd for $C_{25}H_{19}BrN_2NaO_2^+$ $[M+Na]^+$: 481.0522, found: 481.0531.

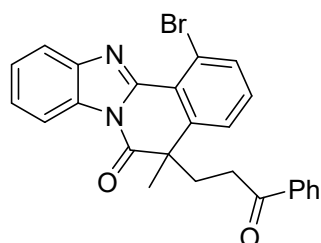
3ha



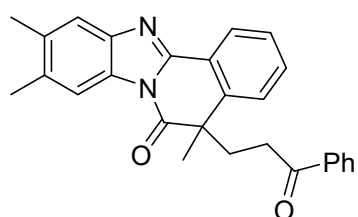
Colorless oil. **1H NMR** (600 MHz, $CDCl_3$) δ_H 8.39-8.38 (m, 1H), 7.95-7.93 (m, 1H), 7.71 (d, $J = 8.0$ Hz, 2H), 7.57-7.53 (m, 1H), 7.50-7.45 (m, 3H), 7.36 (d, $J = 8.0$ Hz, 1H), 7.33 (t, $J = 7.6$ Hz, 2H), 7.27-7.23 (m, 1H), 2.88-2.79 (m, 2H), 2.58-2.46 (m, 2H), 1.80 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ_C 198.2, 172.1, 160.5 (d, $J = 262.7$ Hz), 147.7 (d, $J = 9.1$ Hz), 144.2 (d, $J = 3.0$ Hz), 143.4, 136.2, 133.2, 132.8 (d, $J = 9.1$ Hz), 130.3, 128.5, 127.9, 126.3, 126.1, 122.0 (d, $J = 3.0$ Hz), 120.6, 115.9 (d, $J = 21.1$ Hz), 115.6, 113.3 (d, $J = 10.6$ Hz), 48.8, 36.0, 34.1, 29.9. **HRMS** m/z (ESI) calcd for $C_{25}H_{19}FN_2NaO_2^+$ $[M+Na]^+$: 421.1323, found: 421.1324.

3ia

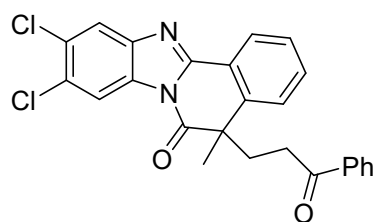
Colorless oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.42-8.37 (m, 1H), 7.99-7.93 (m, 1H), 7.71 (d, $J = 7.6$ Hz, 2H), 7.58 (d, $J = 7.7$ Hz, 1H), 7.52-7.43 (m, 5H), 7.33 (t, $J = 7.7$ Hz, 2H), 2.88-2.79 (m, 2H), 2.58-2.45 (m, 2H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 198.2, 172.0, 146.9, 143.8, 143.7, 136.2, 133.8, 133.3, 131.6, 131.5, 130.4, 128.5, 127.9, 126.5, 126.1, 124.9, 121.1, 120.8, 115.7, 49.0, 36.0, 34.1, 29.9. **HRMS** m/z (ESI) calcd for $\text{C}_{25}\text{H}_{19}\text{ClN}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 437.1027, found: 437.1031.

3ja

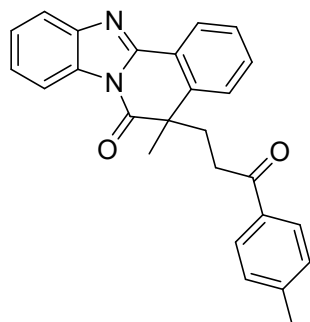
Colorless oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.42-8.36 (m, 1H), 7.97-7.92 (m, 1H), 7.82 (d, $J = 7.9$ Hz, 1H), 7.71 (d, $J = 8.1$ Hz, 2H), 7.54 (d, $J = 8.0$ Hz, 1H), 7.49-7.45 (m, 3H), 7.38-7.31 (m, 3H), 2.88-2.78 (m, 2H), 2.58-2.44 (m, 2H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 197.2, 170.8, 146.1, 142.9, 142.6, 135.2, 134.5, 132.2, 130.5, 129.6, 127.5, 126.9, 125.4, 125.0, 124.5, 121.4, 120.6, 119.8, 114.6, 48.1, 35.0, 33.0, 28.9. **HRMS** m/z (ESI) calcd for $\text{C}_{25}\text{H}_{19}\text{BrN}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 481.0522, found: 481.0527.

3ka

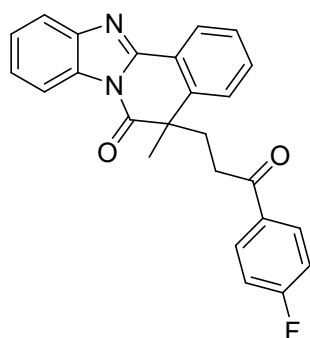
White solid, mp = 163.8-170.2 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.49 (d, $J = 8.0$ Hz, 1H), 8.16 (s, 1H), 7.69 (d, $J = 8.0$ Hz, 2H), 7.61 (s, 1H), 7.59-7.54 (m, 1H), 7.53-7.44 (m, 3H), 7.32 (t, $J = 7.6$ Hz, 2H), 2.90-2.72 (m, 2H), 2.58-2.51 (m, 1H), 2.48-2.41 (m, 7H), 1.78 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 198.4, 172.7, 148.8, 140.7, 136.3, 135.2, 135.1, 133.1, 132.0, 129.5, 128.5, 128.0, 127.9, 126.1, 126.0, 119.9, 116.0, 48.7, 35.9, 34.1, 29.6, 20.5, 20.4. **HRMS** m/z (ESI) calcd for $\text{C}_{27}\text{H}_{24}\text{N}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 431.1730, found: 431.1736.

3la

Yellow solid, mp = 176.2-180.1 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.50-8.44 (m, 2H), 7.89 (d, J = 3.3 Hz, 1H), 7.69 (d, J = 7.8 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.56-7.46 (m, 3H), 7.34 (t, J = 7.6 Hz, 2H), 2.87-2.75 (m, 2H), 2.59-2.45 (m, 2H), 1.80 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 197.1, 171.5, 150.1, 142.3, 140.1, 135.2, 132.2, 131.8, 129.2, 129.1, 128.5, 127.5, 127.2, 126.8, 125.4, 125.2, 121.3, 119.9, 116.1, 47.8, 34.9, 33.0, 28.4. **HRMS** m/z (ESI) calcd for $\text{C}_{25}\text{H}_{18}\text{Cl}_2\text{N}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 471.0638, found: 471.0645.

3ab

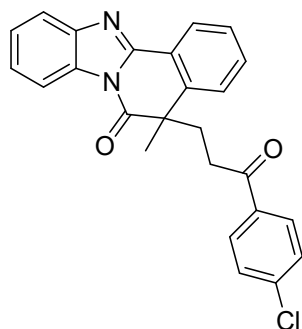
Colorless oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.43 (d, J = 7.8 Hz, 1H), 8.29 (d, J = 7.2 Hz, 1H), 7.76 (d, J = 7.1 Hz, 1H), 7.51-7.49 (m, 3H), 7.46-7.34 (m, 4H), 7.03 (d, J = 7.8 Hz, 2H), 2.77-2.66 (m, 2H), 2.50-2.45 (m, 1H), 2.37-2.31 (m, 1H), 2.24 (s, 3H), 1.71 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 197.0, 171.8, 148.7, 143.1, 142.9, 140.0, 132.8, 131.2, 130.3, 128.1, 127.1, 127.0, 125.1, 125.0, 124.9, 124.7, 122.0, 118.8, 114.7, 47.8, 34.9, 33.0, 28.6, 20.5. **HRMS** m/z (ESI) calcd for $\text{C}_{26}\text{H}_{22}\text{N}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 417.1573, found: 417.1583.

3ac

Yellow oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.54 (d, J = 7.5 Hz, 1H), 8.37 (d, J = 7.3 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.74-7.71 (m, 2H), 7.60 (t, J = 7.6 Hz, 1H), 7.54-7.44 (m, 4H), 6.99 (t, J = 8.6 Hz, 2H), 2.88-2.82 (m, 1H), 2.79-2.73 (m, 1H), 2.58-2.53 (m, 1H), 2.46-2.41 (m, 1H), 1.80 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 195.7, 171.8, 164.7 (d, J = 255.2 Hz), 148.6, 142.9 (d, J = 15.9 Hz), 139.9, 131.7 (d, J = 2.9 Hz), 131.3, 130.2, 129.6 (d, J = 9.4 Hz), 127.1, 125.2, 125.1, 125.0,

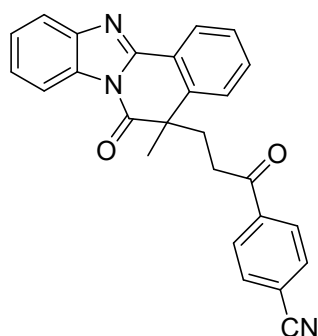
124.8, 121.8 (d, $J = 9.4$ Hz), 118.8, 114.7 (d, $J = 9.6$ Hz), 114.5, 47.8, 34.7, 33.0, 28.7. **HRMS** m/z (ESI) calcd for $C_{25}H_{20}FN_2O_2^+$ $[M+H]^+$: 399.1503, found: 399.1513.

3ad



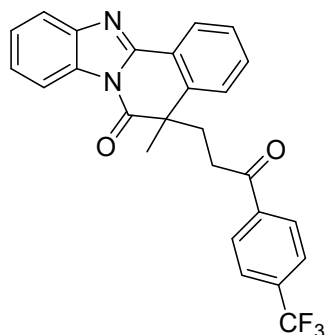
Colorless oil. **1H NMR** (600 MHz, $CDCl_3$) δ_H 8.54 (d, $J = 7.5$ Hz, 1H), 8.36 (d, $J = 7.6$ Hz, 1H), 7.85 (d, $J = 7.3$ Hz, 1H), 7.64-7.58 (m, 3H), 7.54-7.50 (m, 2H), 7.49-7.43 (m, 2H), 7.29 (d, $J = 8.3$ Hz, 2H), 2.90-2.80 (m, 1H), 2.78-2.70 (m, 1H), 2.60-2.52 (m, 1H), 2.46-2.40 (m, 1H), 1.79 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ_C 196.1, 171.7, 148.6, 142.8, 139.8, 138.6, 133.5, 131.3, 130.2, 128.4, 128.3, 127.9, 127.8, 127.1, 125.2, 125.1, 125.0, 124.8, 121.9, 118.8, 114.7, 47.7, 34.7, 33.1, 28.7. **HRMS** m/z (ESI) calcd for $C_{25}H_{19}ClN_2NaO_2^+$ $[M+Na]^+$: 437.1027, found: 437.1035.

3ae



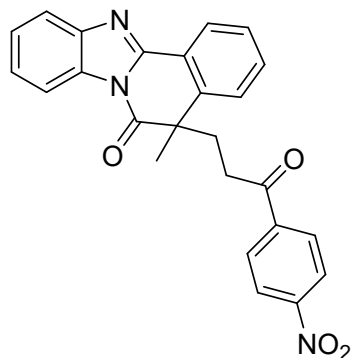
Yellow oil. **1H NMR** (600 MHz, $CDCl_3$) δ_H 8.50 (d, $J = 7.5$ Hz, 1H), 8.34 (d, $J = 7.4$ Hz, 1H), 7.85-7.81 (m, 1H), 7.80-7.75 (m, 2H), 7.65-7.57 (m, 3H), 7.54-7.49 (m, 2H), 7.49-7.42 (m, 2H), 2.90-2.83 (m, 1H), 2.82-2.75 (m, 1H), 2.60-2.52 (m, 1H), 2.50-2.44 (m, 1H), 1.79 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ_C 196.0, 171.7, 148.5, 143.1, 139.6, 138.1, 131.4, 131.3, 130.2, 127.3, 127.2, 125.2, 125.1, 125.0, 124.8, 122.0, 118.9, 116.8, 115.4, 114.7, 47.7, 34.4, 33.5, 28.8. **HRMS** m/z (ESI) calcd for $C_{26}H_{20}N_3O_2^+$ $[M+H]^+$: 406.1550 found: 406.1553.

3af



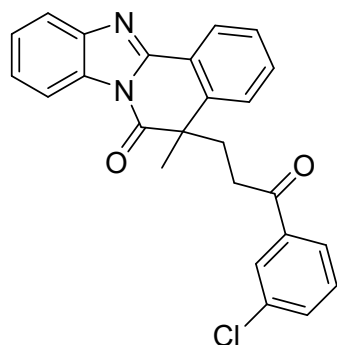
Light yellow oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.58 (d, $J = 8.5$ Hz, 1H), 8.38-8.34 (m, 1H), 8.17 (d, $J = 8.1$ Hz, 2H), 7.90-7.83 (m, 3H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.56-7.52 (m, 2H), 7.51-7.44 (m, 2H), 2.92-2.79 (m, 2H), 2.62-2.50 (m, 2H), 1.81 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 196.4, 171.7, 148.5, 139.7, 137.8, 133.4 (q, $J = 32.6$), 131.4, 130.2, 127.3, 127.2, 125.2, 125.0 (d, $J = 19.6$ Hz), 124.8, 124.5 (q, $J = 3.8$ Hz), 122.4 (q, $J = 273.0$ Hz), 121.8, 118.8, 114.7, 47.7, 34.5, 33.5, 28.7. **HRMS** m/z (ESI) calcd for $\text{C}_{26}\text{H}_{20}\text{F}_3\text{N}_2\text{O}_2^+$ $[\text{M}+\text{H}]^+$: 449.1471, found: 449.1479.

3ag

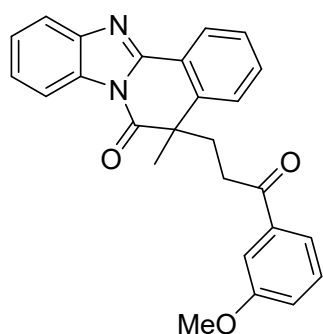


Colorless oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.58 (d, $J = 1.5$ Hz, 1H), 8.35 (d, $J = 7.6$ Hz, 1H), 8.17 (d, $J = 8.2$ Hz, 2H), 7.86 (t, $J = 9.9$ Hz, 3H), 7.62 (t, $J = 7.5$ Hz, 1H), 7.55-7.45 (m, 4H), 2.91-2.80 (m, 2H), 2.61-2.51 (m, 2H), 1.81 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 195.8, 171.6, 149.3, 148.4, 139.7, 139.5, 131.6, 130.0, 127.9, 127.4, 125.6, 125.4, 125.0, 124.9, 123.1, 122.7, 118.7, 114.7, 47.7, 34.4, 33.8, 28.8. **HRMS** m/z (ESI) calcd for $\text{C}_{25}\text{H}_{20}\text{N}_3\text{O}_4^+$ $[\text{M}+\text{H}]^+$: 426.1448, found: 426.1453.

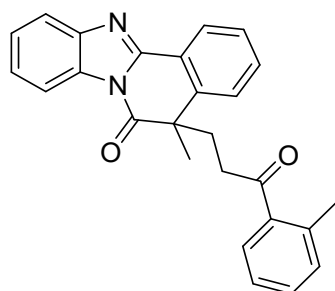
3ah



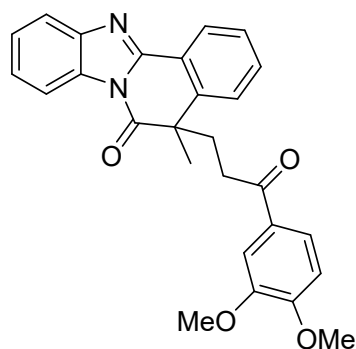
Colorless oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.52 (d, $J = 7.8$ Hz, 1H), 8.38-8.34 (m, 1H), 7.86-7.82 (m, 1H), 7.67 (t, $J = 1.8$ Hz, 1H), 7.62-7.57 (m, 1H), 7.56-7.49 (m, 3H), 7.48-7.41 (m, 3H), 7.26 (t, $J = 1.5$ Hz, 1H), 2.90-2.82 (m, 1H), 2.80-2.71 (m, 1H), 2.59-2.52 (m, 1H), 2.49-2.40 (m, 1H), 1.78 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 196.1, 171.7, 148.5, 142.8, 139.8, 136.7, 133.9, 132.1, 131.3, 130.2, 128.8, 127.2, 126.9, 125.3, 125.1, 125.0, 124.9, 124.8, 121.8, 118.8, 114.7, 47.7, 34.5, 33.3, 28.8. **HRMS** m/z (ESI) calcd for $\text{C}_{25}\text{H}_{19}\text{ClN}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 437.1027, found: 437.1037.

3ai

White solid, mp = 170.2-175.8 °C; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.53 (d, $J = 7.7$ Hz, 1H), 8.36 (dd, $J = 7.3, 1.8$ Hz, 1H), 7.85 (d, $J = 7.2$ Hz, 1H), 7.59 (t, $J = 7.8$ Hz, 1H), 7.54-7.51 (m, 2H), 7.48-7.42 (m, 2H), 7.26-7.19 (m, 3H), 7.00 (dt, $J = 7.0, 2.3$ Hz, 1H), 3.76 (s, 3H), 2.88-2.82 (m, 1H), 2.80-2.74 (m, 1H), 2.58-2.52 (m, 1H), 2.49-2.42 (m, 1H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 197.2, 171.7, 158.7, 148.6, 139.9, 136.6, 131.3, 130.2, 128.5, 127.1, 125.3, 125.1, 125.0, 124.8, 121.7, 119.6, 118.7, 118.6, 114.7, 111.1, 54.4, 47.8, 34.9, 33.3, 28.7. **HRMS** m/z (ESI) calcd for $\text{C}_{26}\text{H}_{22}\text{N}_2\text{NaO}_3^+$ $[\text{M}+\text{Na}]^+$: 433.1523, found: 433.1516.

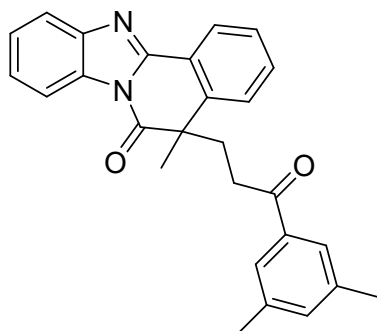
3aj

Yellow oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.53 (d, $J = 7.7$ Hz, 1H), 8.37 (d, $J = 1.5$ Hz, 1H), 7.85 (d, $J = 1.5$ Hz, 1H), 7.60 (t, $J = 7.5$ Hz, 1H), 7.56-7.49 (m, 2H), 7.48-7.42 (m, 2H), 7.30-7.25 (m, 2H), 7.14 (d, $J = 7.5$ Hz, 1H), 7.09 (t, $J = 7.6$ Hz, 1H), 2.85-2.78 (m, 1H), 2.74-2.66 (m, 1H), 2.57-2.51 (m, 1H), 2.44-2.38 (m, 1H), 2.37 (s, 3H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 201.1, 171.8, 148.6, 142.7, 140.0, 137.1, 136.0, 131.3, 130.9, 130.4, 130.2, 127.4, 127.1, 125.2, 125.1, 124.8, 124.6, 121.8, 118.7, 114.7, 47.7, 35.8, 35.0, 28.6, 20.3. **HRMS** m/z (ESI) calcd for $\text{C}_{26}\text{H}_{22}\text{N}_2\text{NaO}_2^+$ $[\text{M}+\text{Na}]^+$: 417.1573, found: 417.1578.

3ak

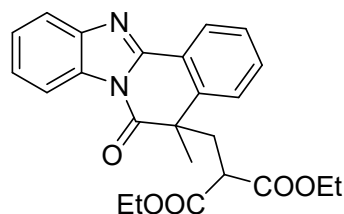
Yellow solid, mp = 174.2-179.5 °C; ¹H NMR (600 MHz, CDCl₃) δ_H 8.57 (t, *J* = 8.6 Hz, 1H), 8.37 (d, *J* = 7.7 Hz, 1H), 7.87-7.85 (m, 1H), 7.60 (d, *J* = 6.1 Hz, 1H), 7.55-7.51 (m, 2H), 7.49-7.44 (m, 2H), 7.30 (d, *J* = 1.9 Hz, 1H), 7.23 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 2.88-2.83 (m, 1H), 2.77-2.72 (m, 1H), 2.56-2.51 (m, 1H), 2.43-2.38 (m, 1H), 1.79 (s, 3H), 1.79 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ_C 197.0, 172.8, 153.3, 149.7, 148.9, 143.9, 141.0, 132.3, 131.3, 129.5, 128.1, 126.2, 126.1, 126.0, 125.7, 122.9, 122.7, 119.8, 115.7, 109.9, 109.8, 68.0, 56.0, 55.9, 48.9, 36.4, 33.7, 28.7, 25.6. HRMS *m/z* (ESI) calcd for C₂₇H₂₅N₂O₄⁺ [M+H]⁺: 441.1809, found: 441.1817.

3al

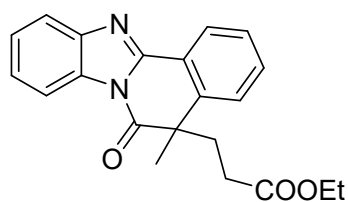


Colorless oil. ¹H NMR (600 MHz, CDCl₃) δ_H 8.52 (d, *J* = 7.4 Hz, 1H), 8.36 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 7.1 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.56-7.48 (m, 2H), 7.48-7.41 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.95 (s, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 2.84-2.76 (m, 1H), 2.73-2.65 (m, 1H), 2.56-2.49 (m, 1H), 2.43-2.37 (m, 1H), 2.37 (s, 3H), 2.26 (s, 3H), 1.78 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ_C 200.3, 171.8, 148.6, 141.1, 140.0, 137.7, 133.0, 131.8, 131.2, 130.2, 128.0, 127.0, 125.2, 125.1, 125.0, 124.9, 124.7, 118.8, 114.7, 47.8, 35.5, 35.2, 28.6, 20.5, 20.3. HRMS *m/z* (ESI) calcd for C₂₇H₂₄N₂NaO₂⁺ [M+Na]⁺: 431.1730, found: 431.1739.

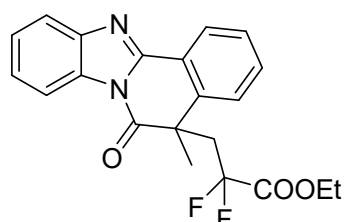
3am



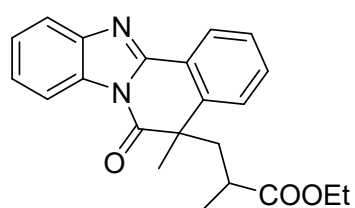
Light yellow oil. ¹H NMR (600 MHz, CDCl₃) δ_H 8.49 (d, *J* = 8.5 Hz, 1H), 8.33 (d, *J* = 7.4 Hz, 1H), 7.82 (d, *J* = 7.4 Hz, 1H), 7.57 (td, *J* = 7.6, 1.5 Hz, 1H), 7.51-7.46 (m, 2H), 7.46-7.39 (m, 2H), 3.98-3.91 (m, 1H), 3.88-3.81 (m, 1H), 3.77-3.65 (m, 2H), 3.11-3.02 (m, 2H), 2.81-2.73 (m, 1H), 1.76 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ_C 172.0, 168.5, 168.4, 149.5, 143.9, 139.9, 131.9, 131.3, 128.2, 126.5, 126.1, 126.0, 125.7, 123.0, 119.8, 115.7, 61.7, 61.6, 48.7, 47.8, 39.3, 30.3, 13.7, 13.6. HRMS *m/z* (ESI) calcd for C₂₄H₂₄N₂NaO₅⁺ [M+Na]⁺: 443.1577, found: 443.1587.

3an

Light yellow oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.49 (d, $J = 7.6$ Hz, 1H), 8.36 (d, $J = 7.1$ Hz, 1H), 7.83 (dd, $J = 7.0, 1.5$ Hz, 1H), 7.60 (t, $J = 8.2$ Hz, 1H), 7.53-7.48 (m, 2H), 7.47-7.41 (m, 2H), 3.94 (q, $J = 7.1$ Hz, 2H), 2.80-2.71 (m, 1H), 2.46-2.36 (m, 1H), 2.10-1.99 (m, 1H), 1.92-1.84 (m, 1H), 1.77 (s, 3H), 1.10 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 172.6, 172.1, 149.6, 144.0, 140.6, 132.1, 131.3, 128.1, 126.2, 126.1, 126.0, 125.7, 123.0, 119.9, 115.7, 60.6, 48.7, 36.9, 30.2, 29.1, 14.0. **HRMS** m/z (ESI) calcd for $\text{C}_{21}\text{H}_{21}\text{N}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$: 349.1547, found: 349.1542.

3ao

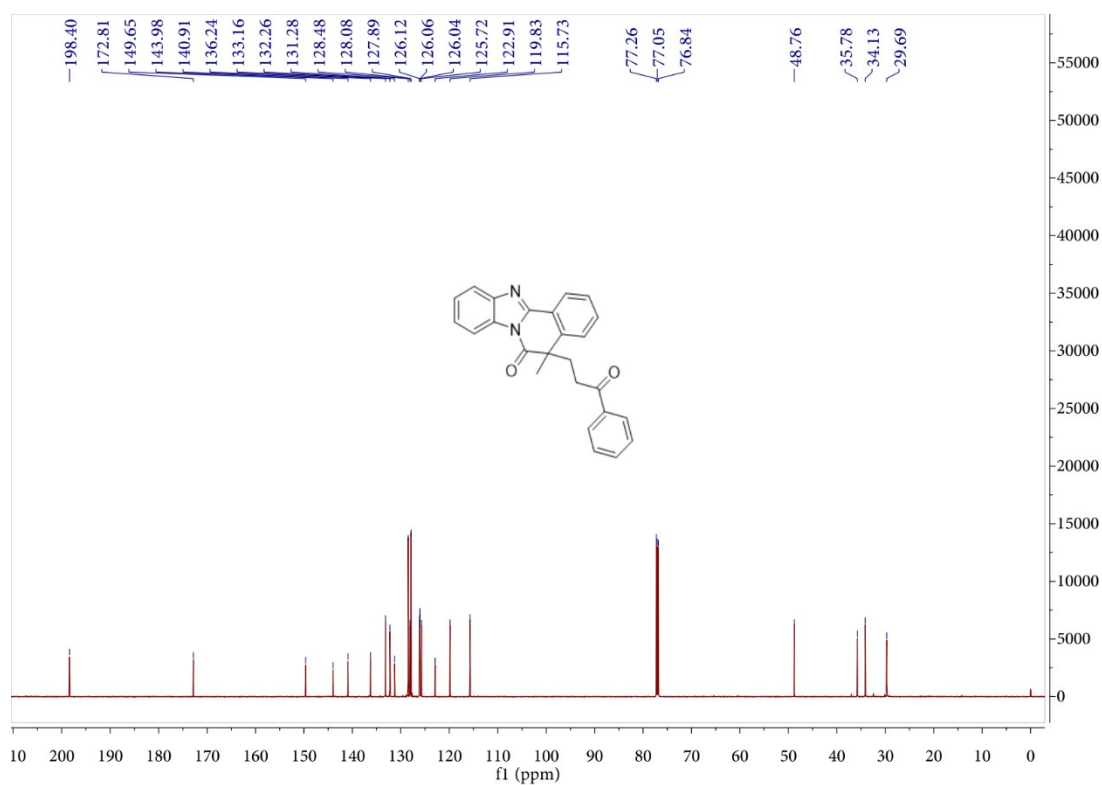
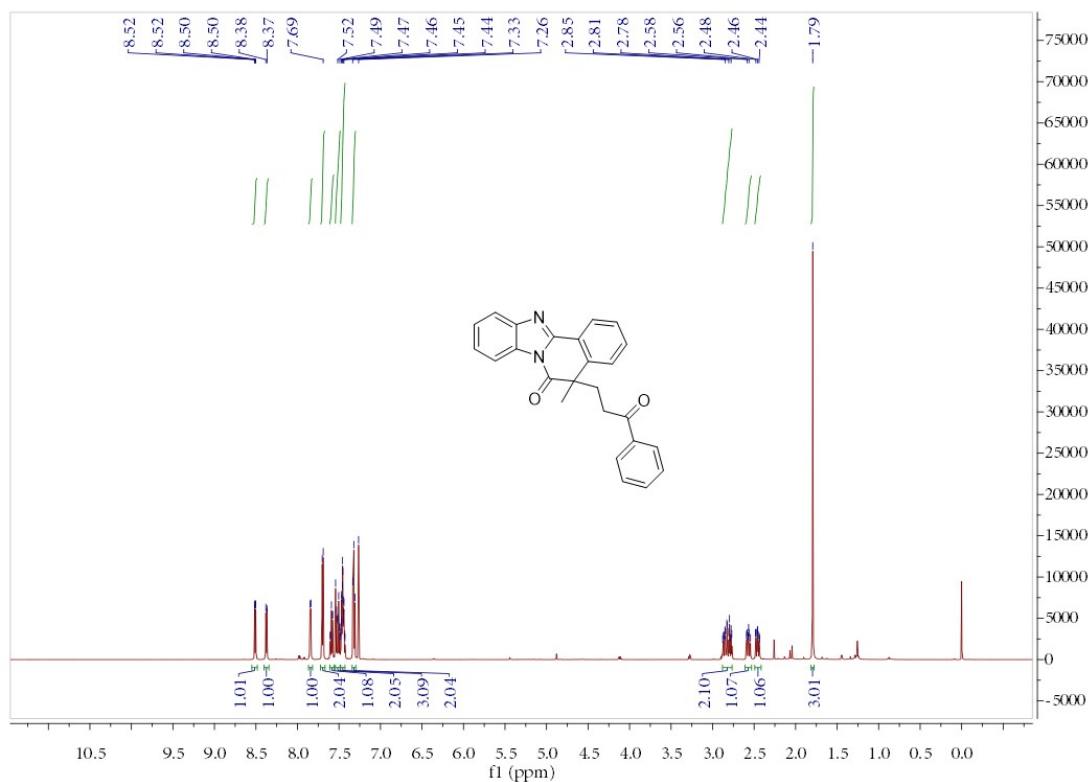
Yellow oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.51 (dd, $J = 7.8, 1.2$ Hz, 1H), 8.36 (dd, $J = 7.0, 1.8$ Hz, 1H), 7.84 (dd, $J = 6.9, 1.6$ Hz, 1H), 7.56 (td, $J = 7.6, 1.4$ Hz, 1H), 7.52-7.50 (m, 1H), 7.48-7.42 (m, 3H), 3.94-3.75 (m, 2H), 3.45-3.38 (m, 1H), 3.09-3.01 (m, 1H), 1.76 (s, 3H), 1.13 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 171.4, 163.5 (t, $J = 31.7$ Hz), 149.3, 144.0, 138.7, 131.5, 131.3, 128.3, 126.9, 126.2, 126.0, 125.7, 122.7, 119.9, 115.7, 114.3 (t, $J = 250.7$ Hz), 63.1, 45.2 (d, $J = 5.3$ Hz), 44.4 (d, $J = 22.7$ Hz), 31.3, 13.6. **HRMS** m/z (ESI) calcd for $\text{C}_{21}\text{H}_{19}\text{F}_2\text{N}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$: 385.1358, found: 385.1352.

3ap

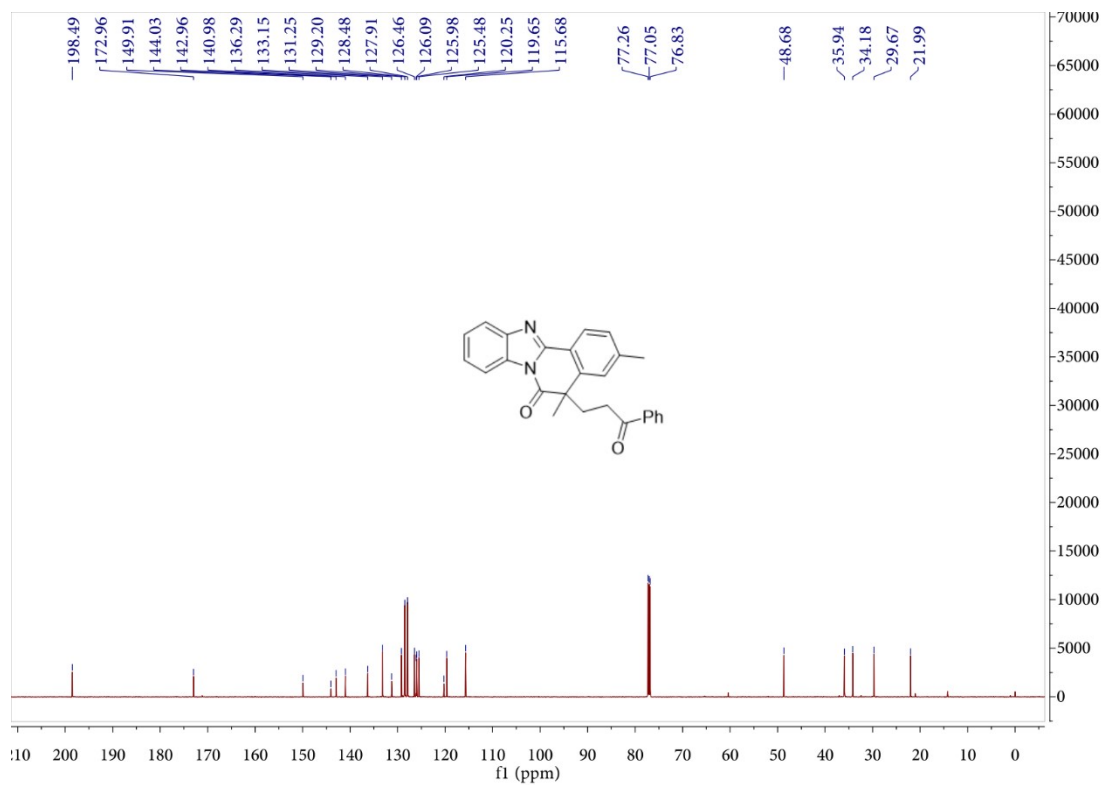
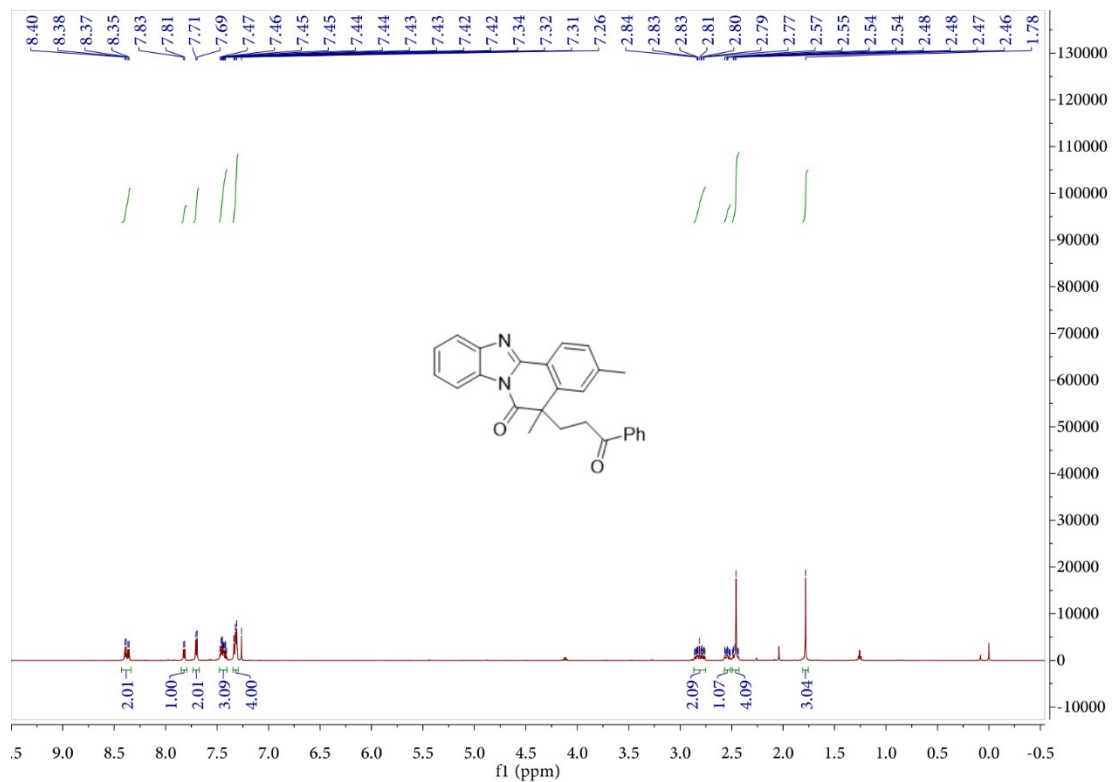
Yellow oil. $^1\text{H NMR}$ (600 MHz, CDCl_3) δ_{H} 8.62-8.46 (m, 1H), 8.36 (dd, $J = 19.5, 7.4$ Hz, 1H), 7.84 (p, $J = 3.6$ Hz, 1H), 7.63-7.38 (m, 5H), 3.80-3.60 (m, 1H), 3.45-3.28 (m, 1H), 3.02-2.90 (m, 0.50 H), 2.67-2.58 (m, 0.59 H), 2.56-2.48 (m, 0.60H), 2.20-2.04 (m, 1.65H), 1.71 (s, 3H), 1.00 (d, $J = 7.0$ Hz, 1.66H), 0.98 (d, $J = 7.1$ Hz, 1.31H), 0.92 (t, $J = 7.1$ Hz, 1.64H), 0.74 (t, $J = 7.2$ Hz, 1.36 H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ_{C} 175.4, 175.2, 172.9, 172.3, 149.7, 149.6, 141.2, 140.2, 132.1, 132.8, 131.2, 128.0, 127.9, 127.1, 126.4, 126.1, 126.0, 125.9, 125.8, 125.7, 125.6, 122.7, 119.7, 119.6, 115.8, 115.7, 60.5, 60.4, 48.8, 48.5, 45.3, 45.0, 40.0, 36.3, 30.7, 30.5, 18.8, 18.7, 13.7, 13.4. **HRMS** m/z (ESI) calcd for $\text{C}_{22}\text{H}_{23}\text{N}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$: 363.1703, found: 363.1714.

5. ¹H NMR and ¹³C NMR spectra for new substrates

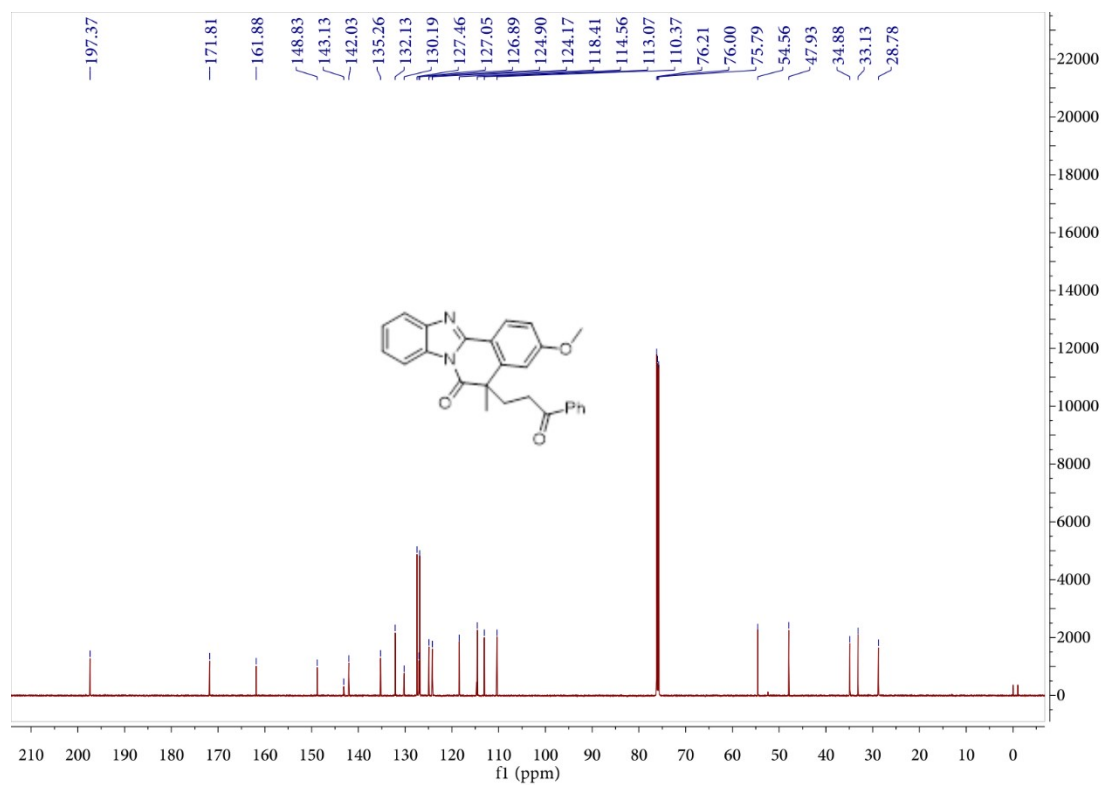
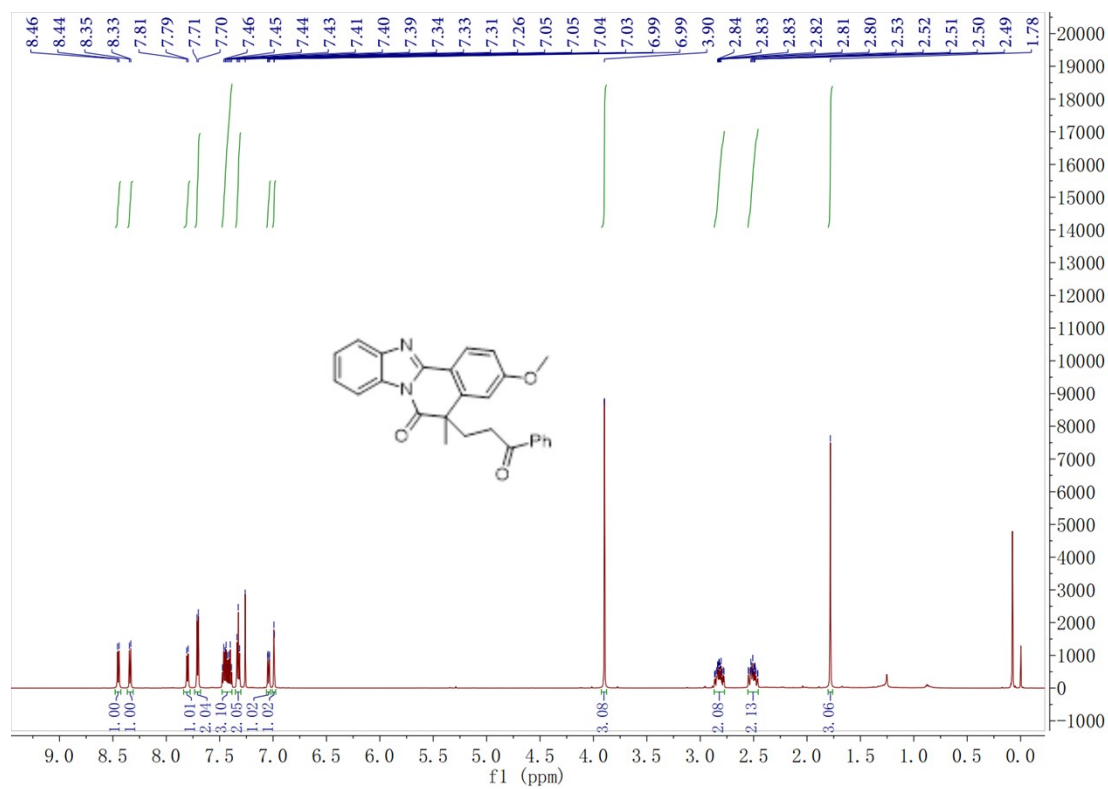
3aa



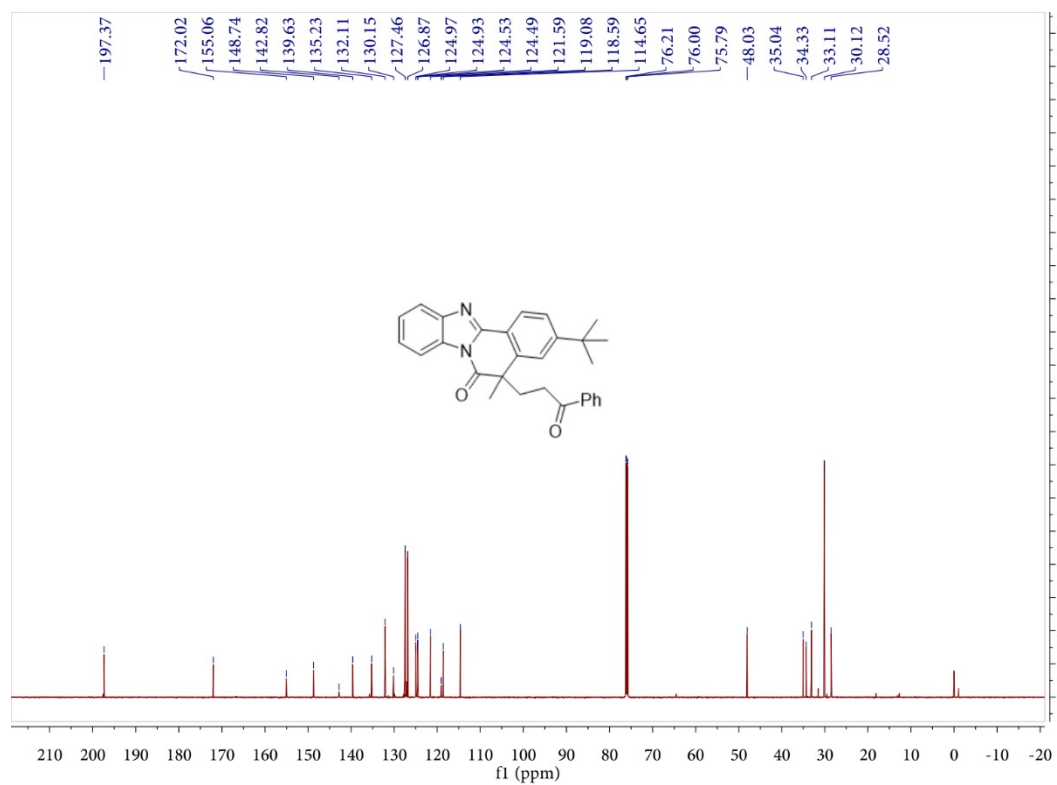
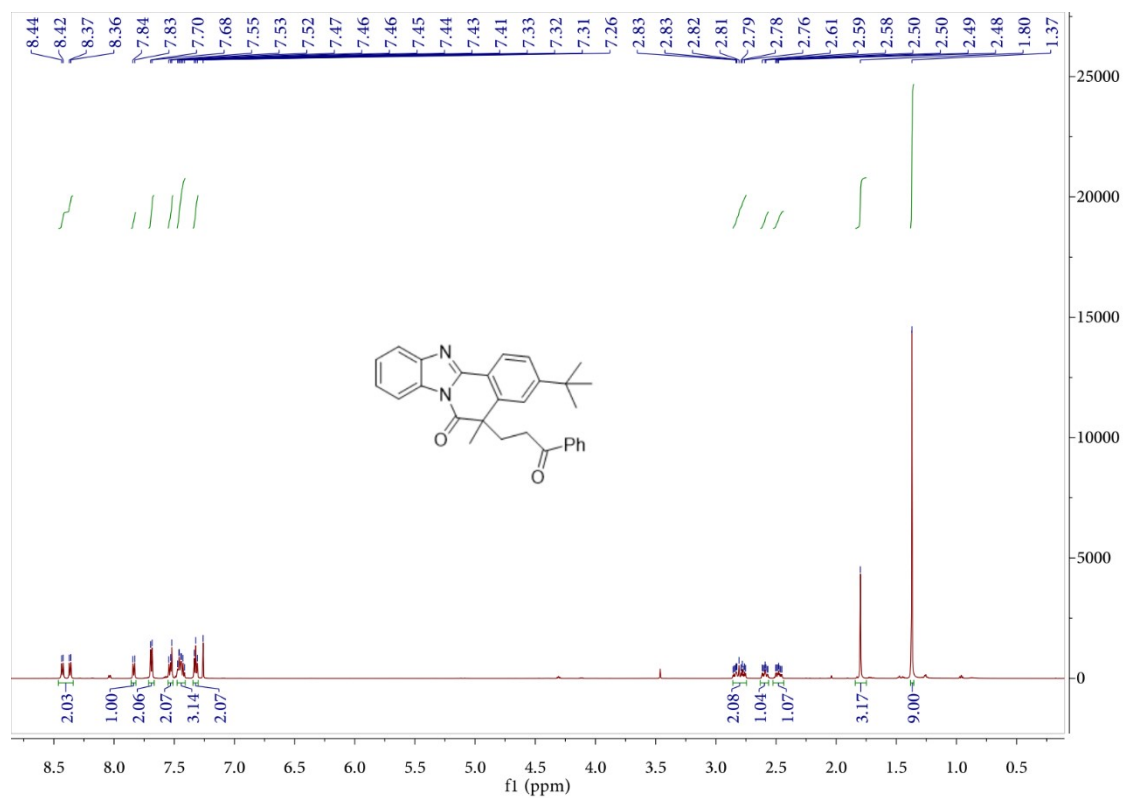
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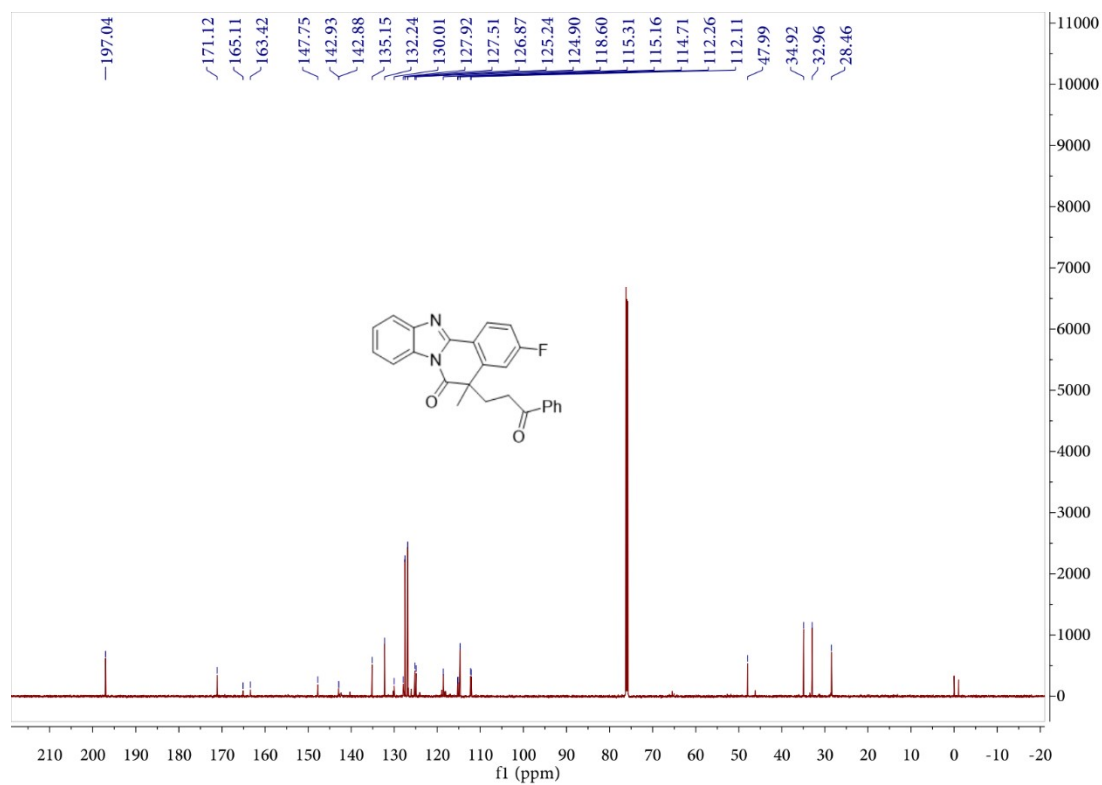
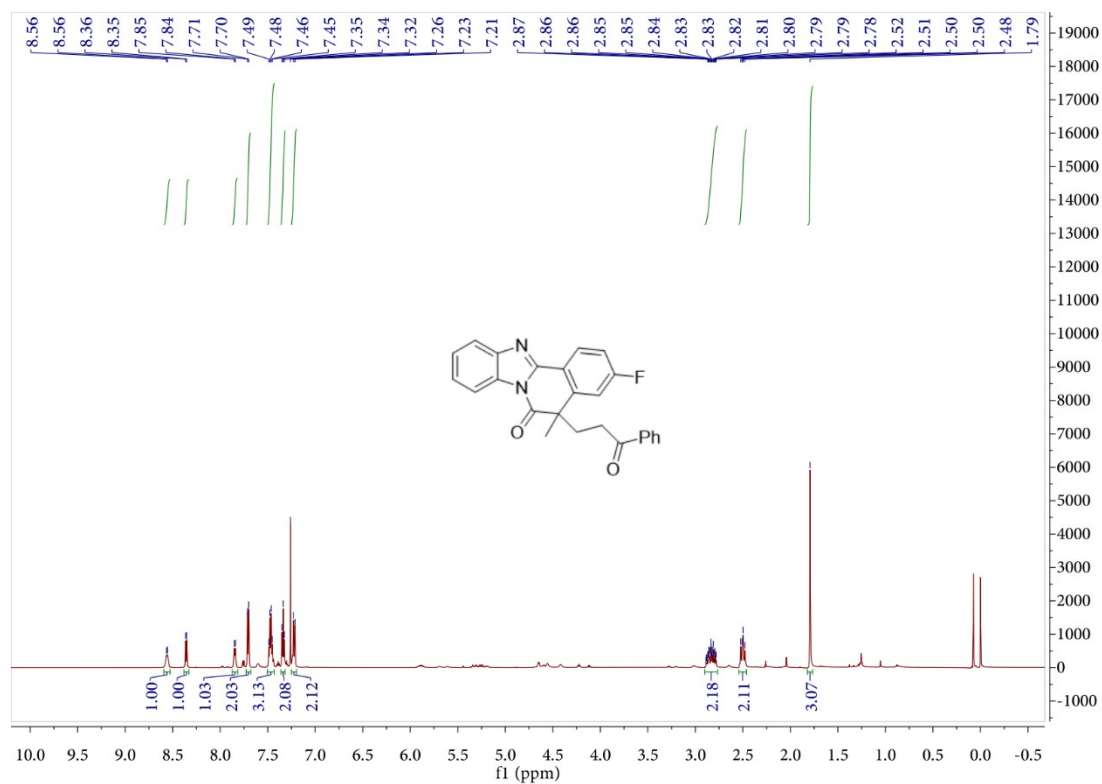
3ca



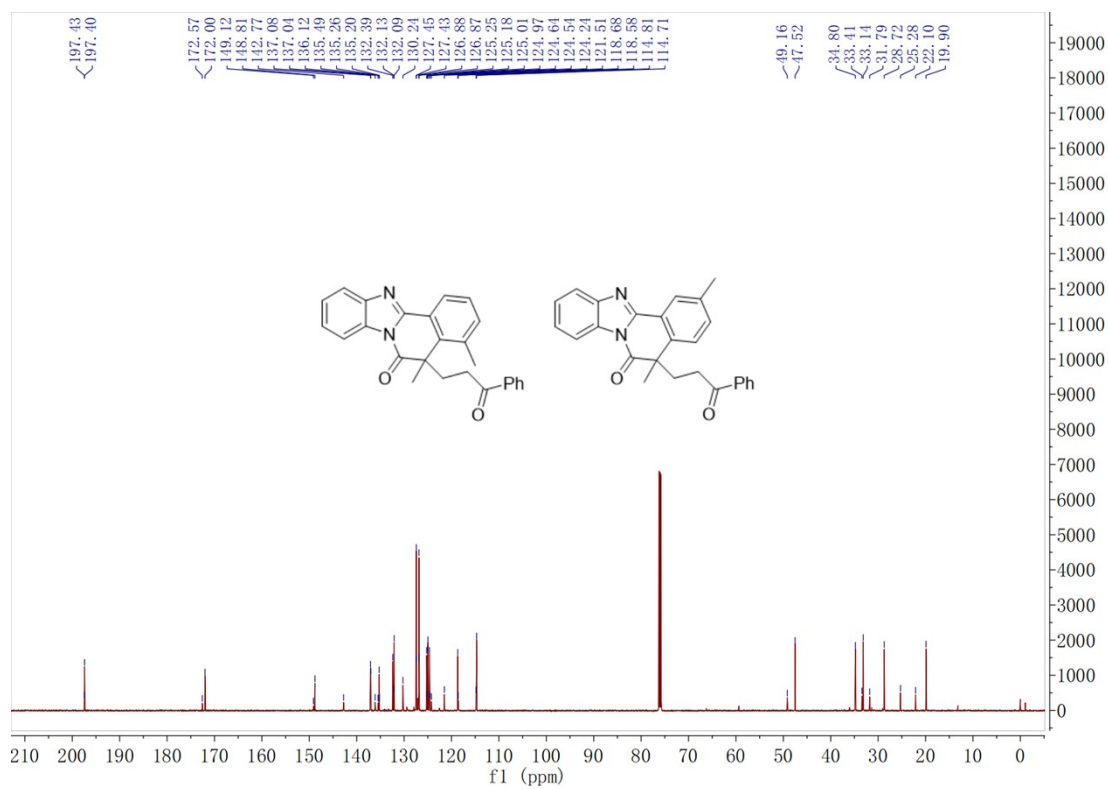
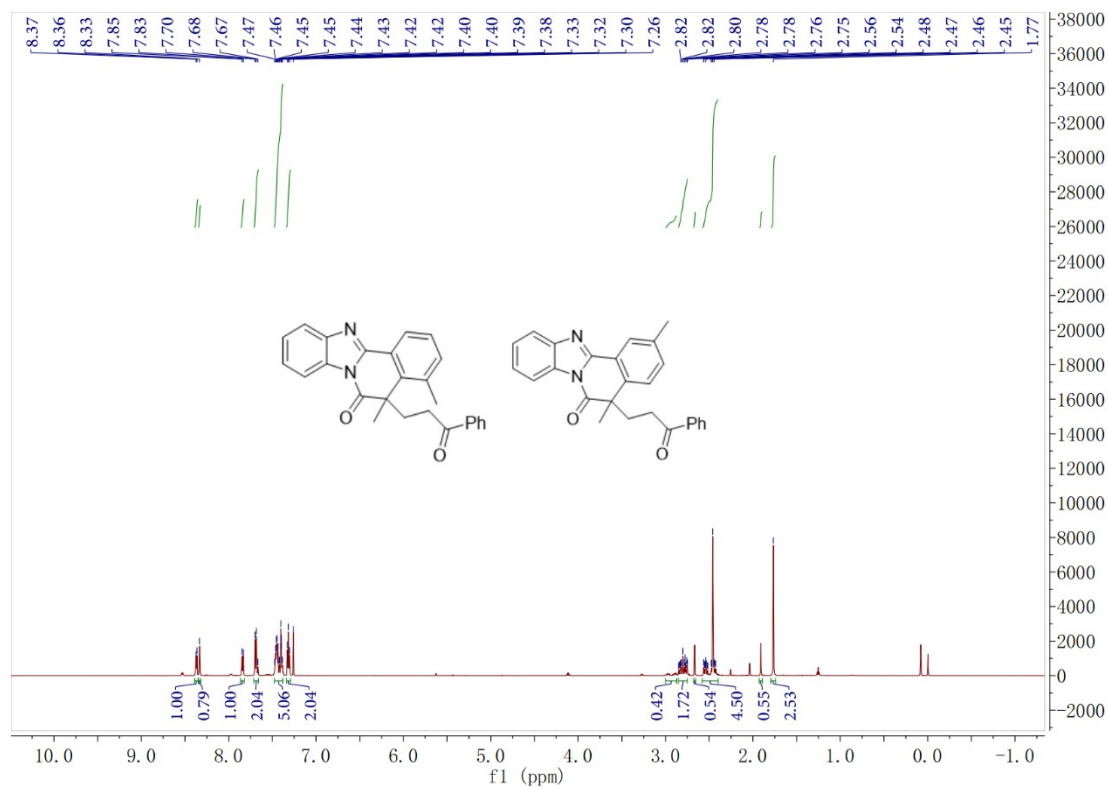
3da



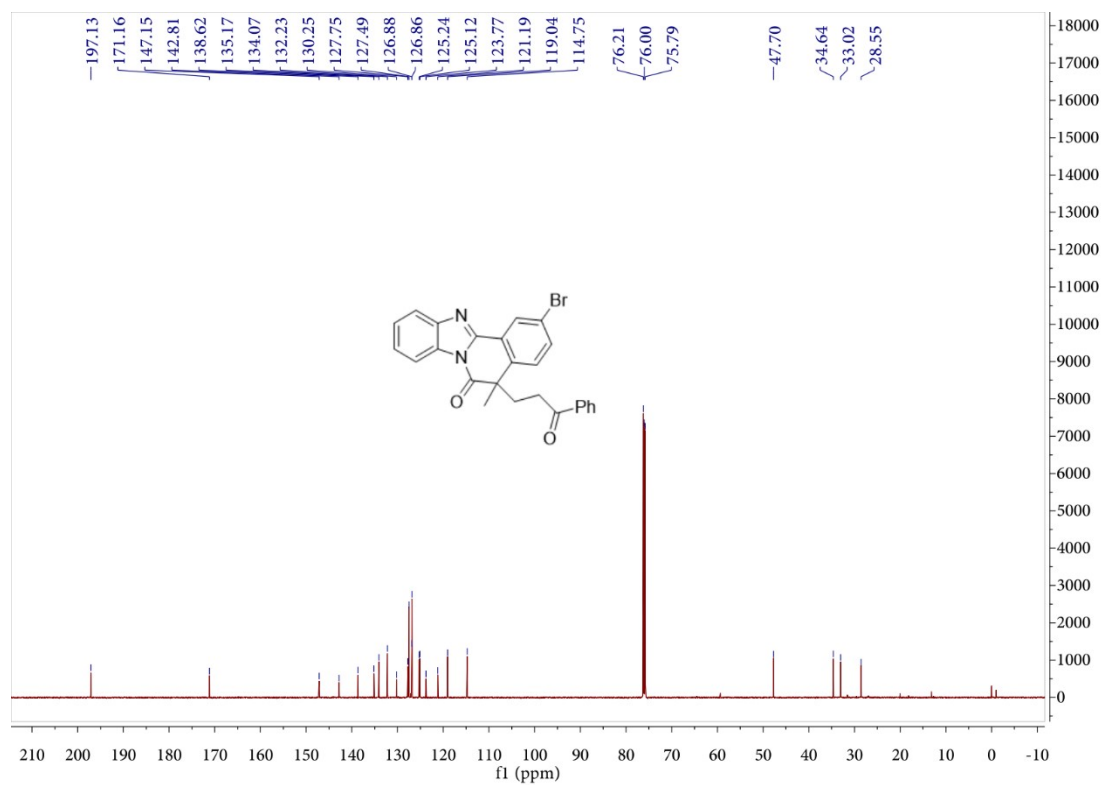
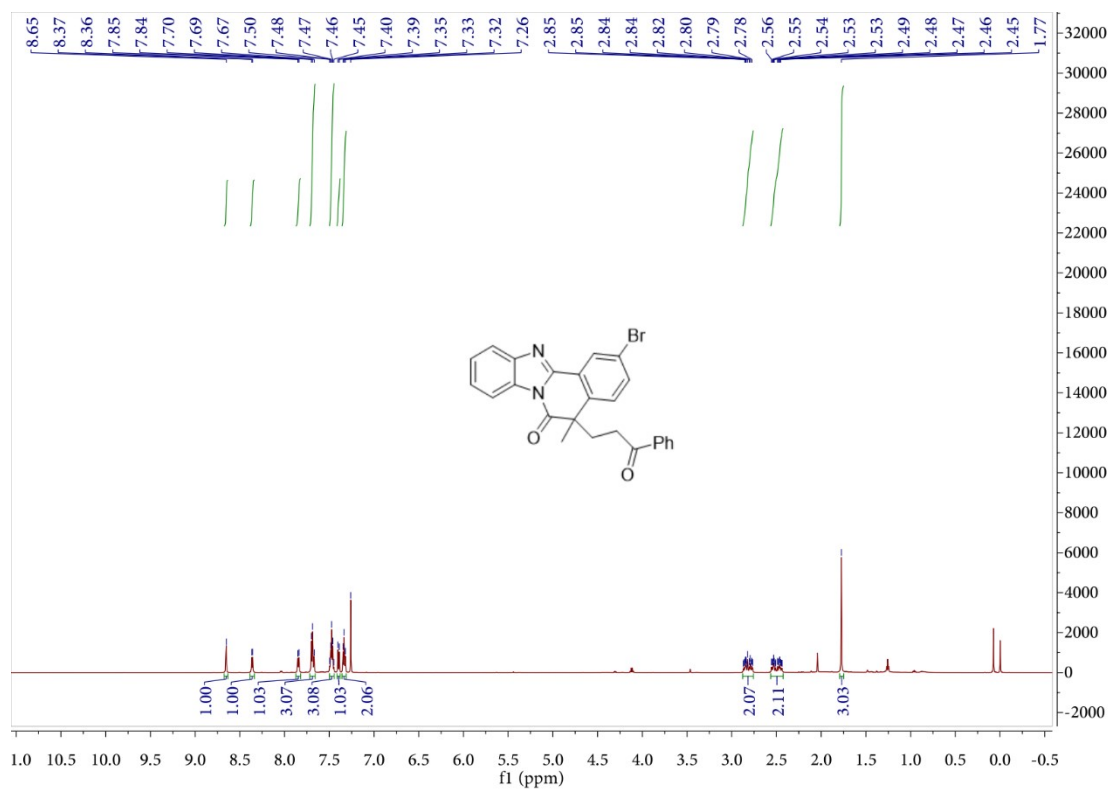
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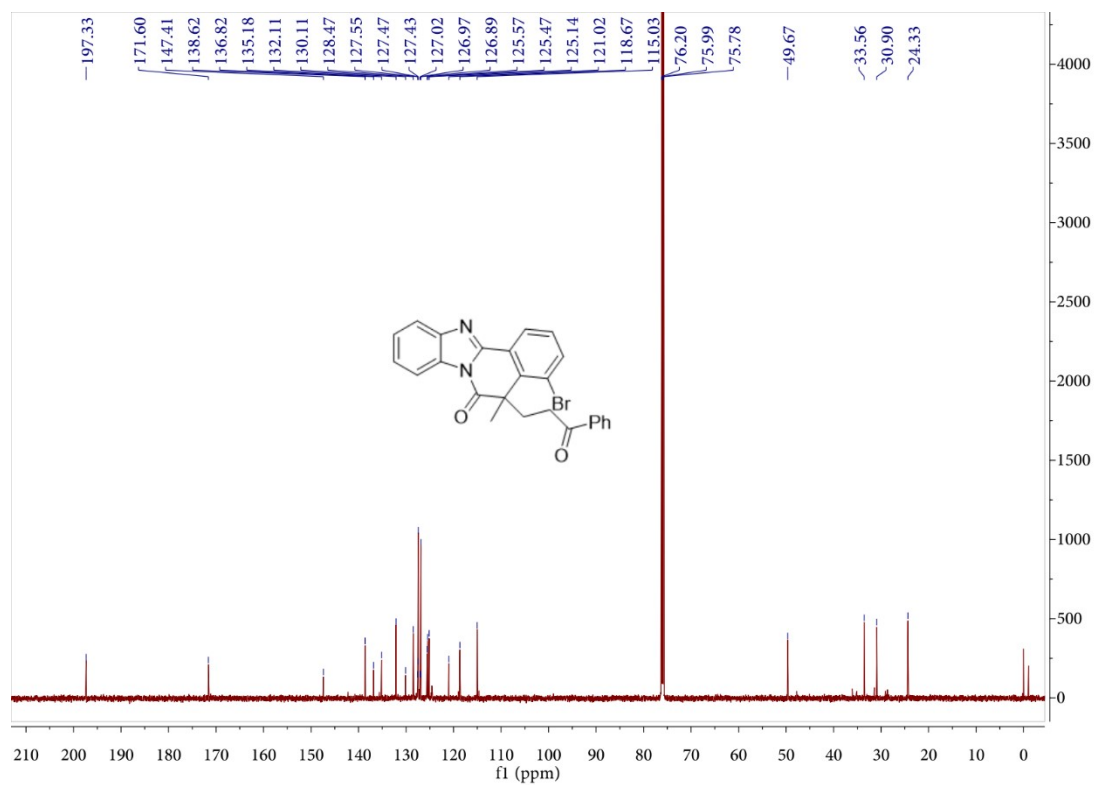
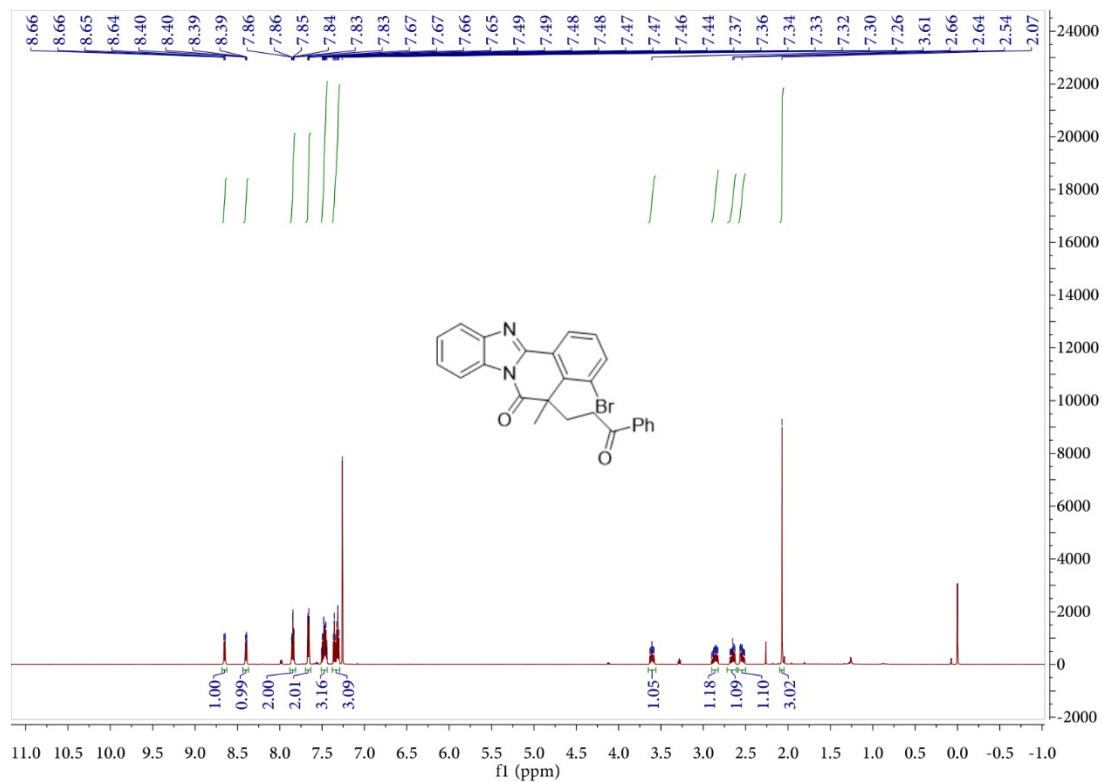
3fa



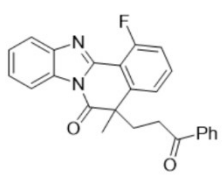
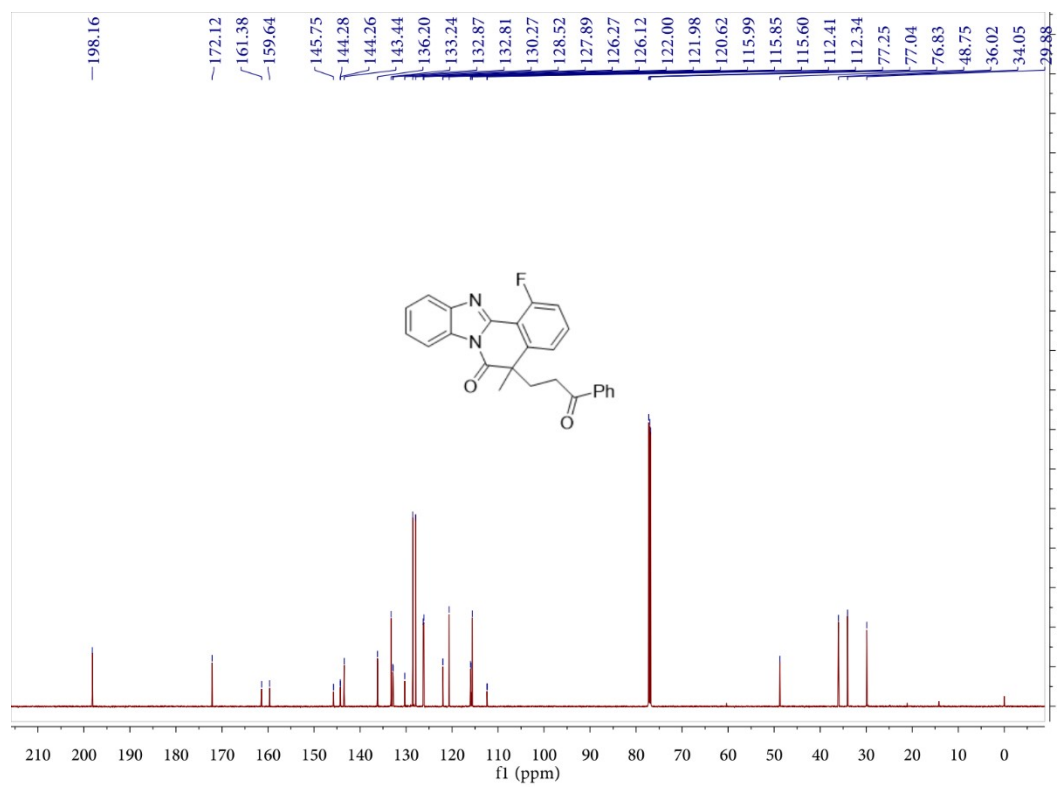
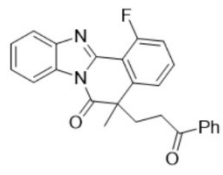
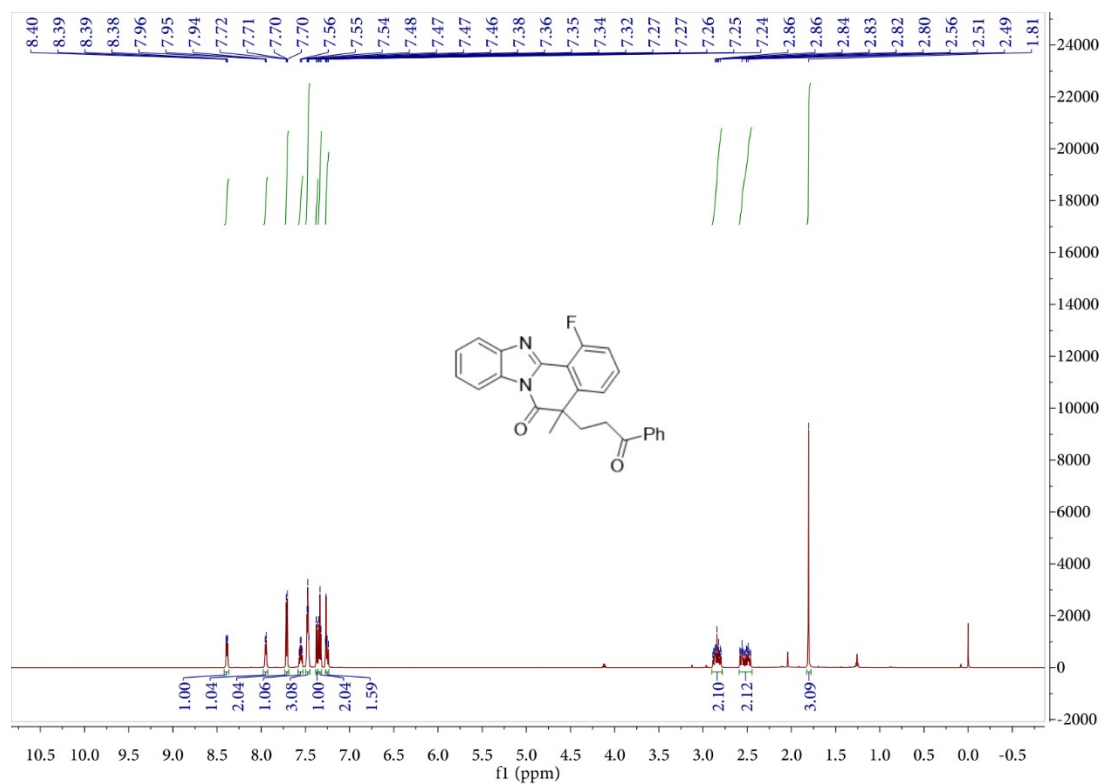
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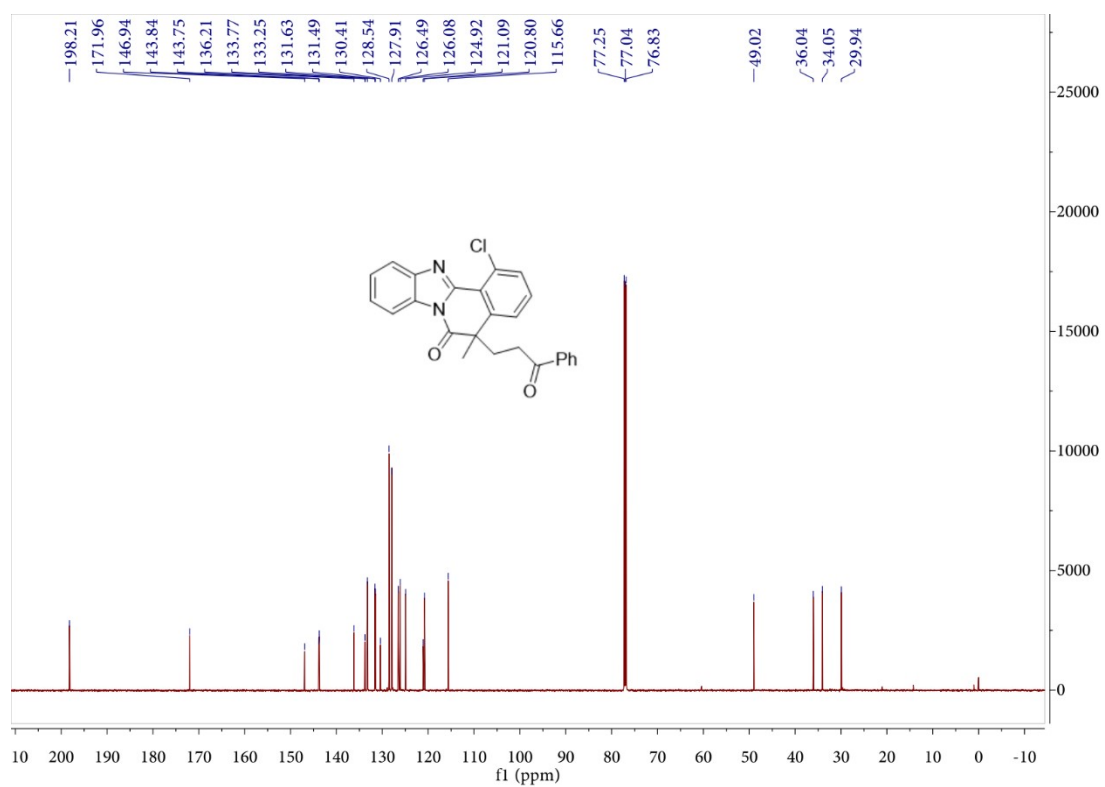
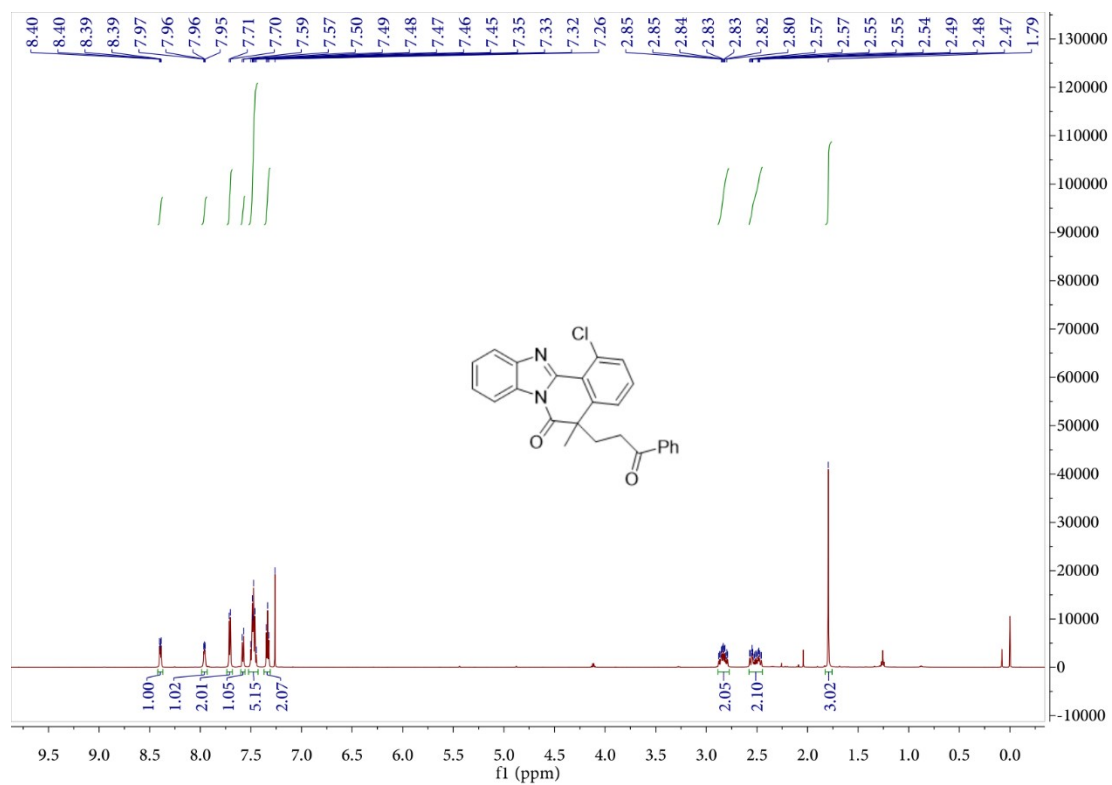
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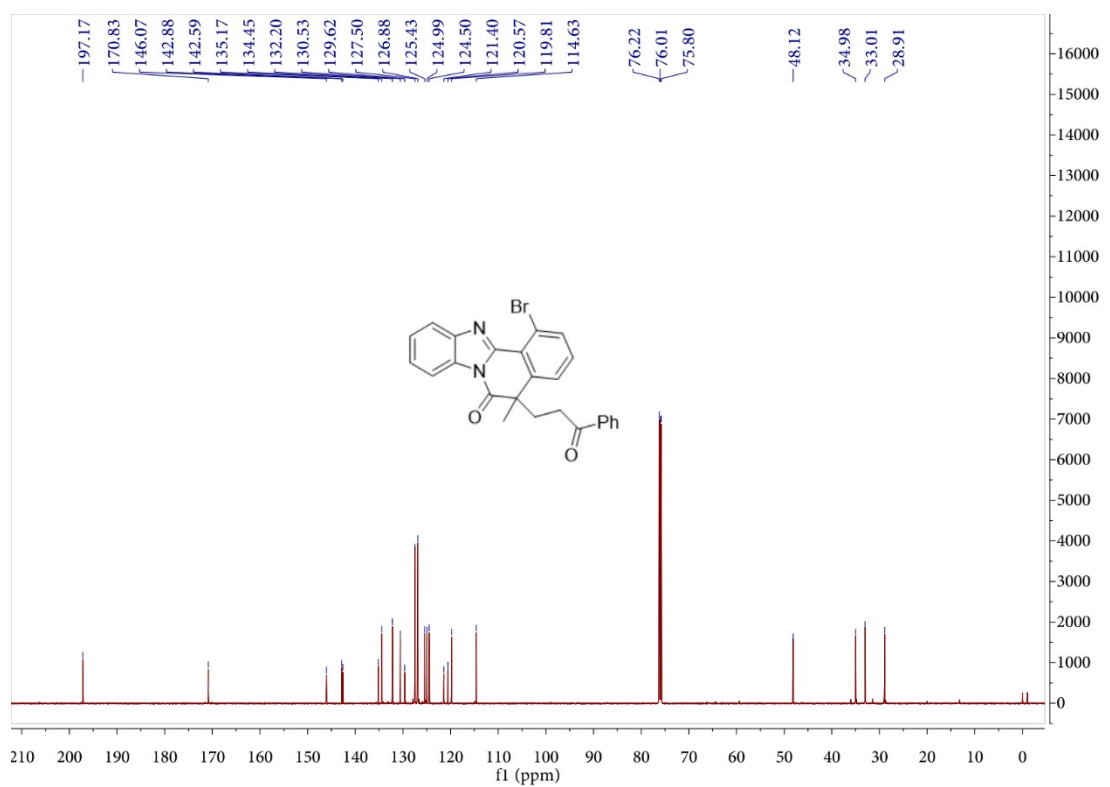
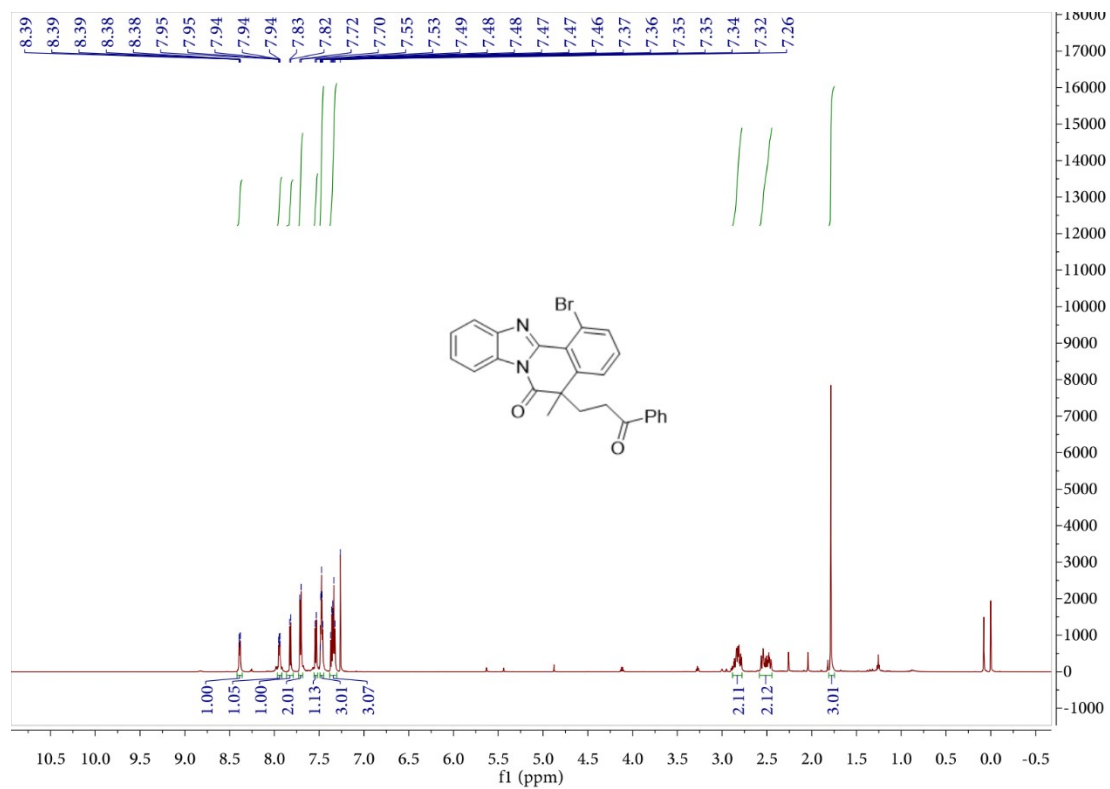
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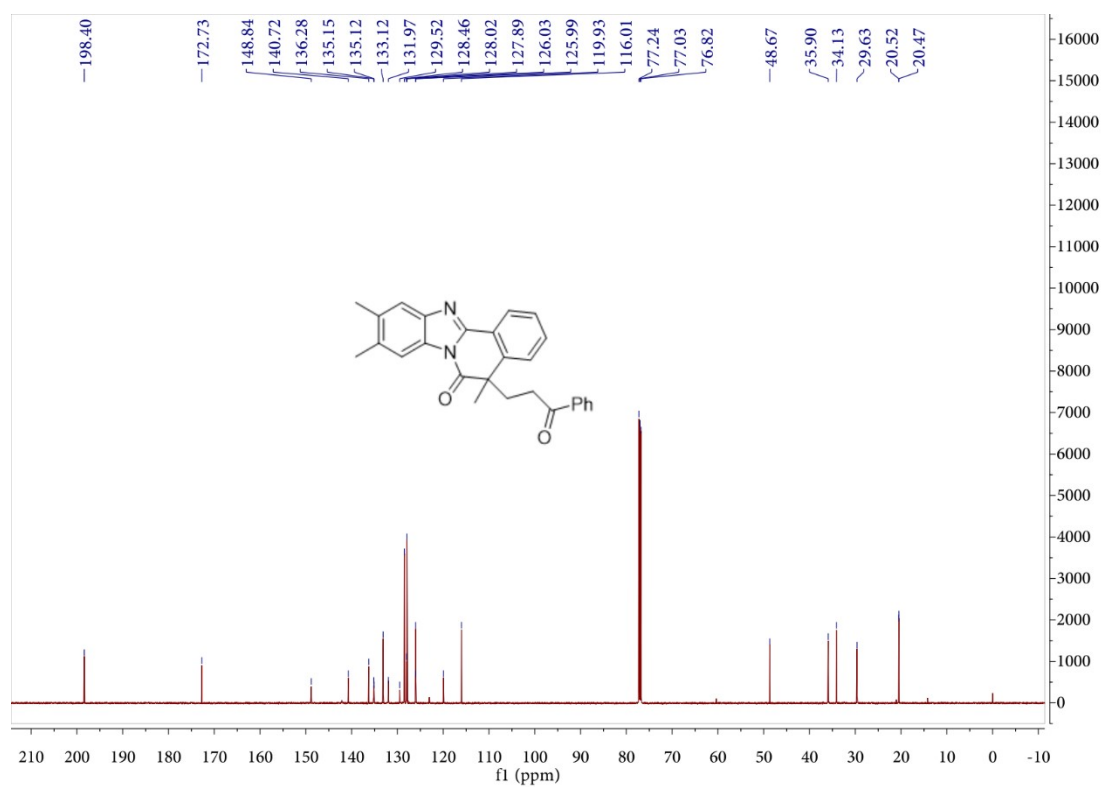
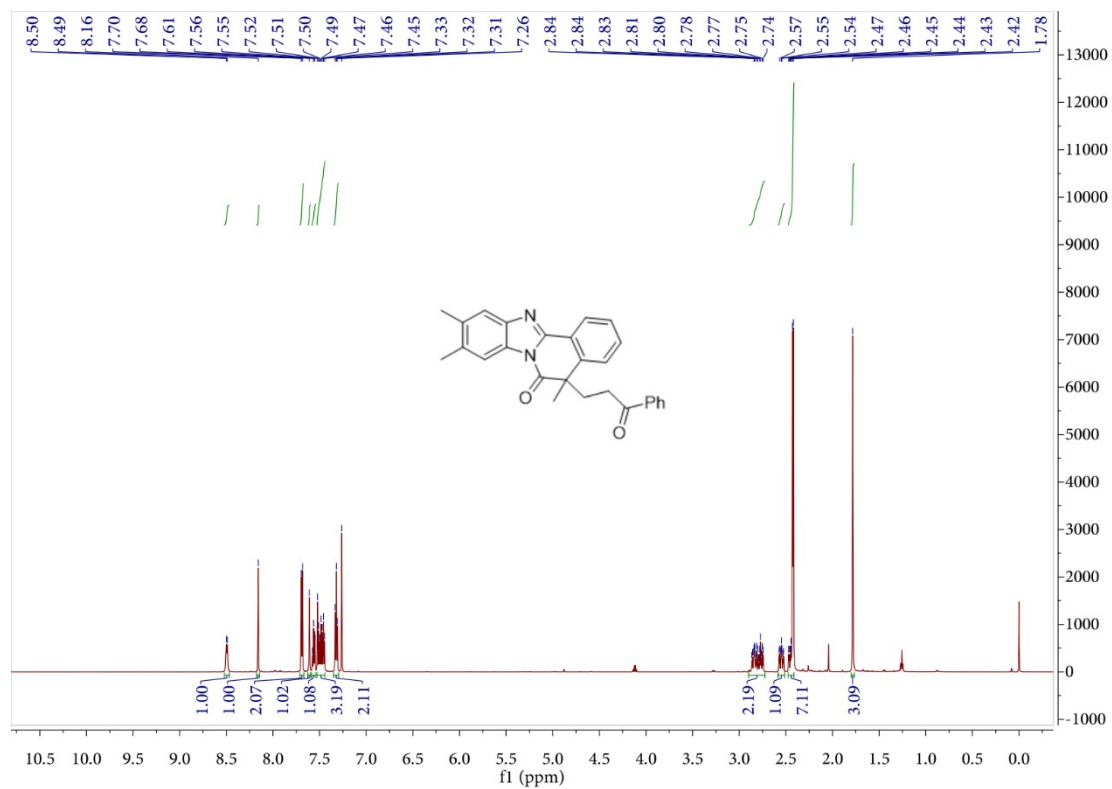
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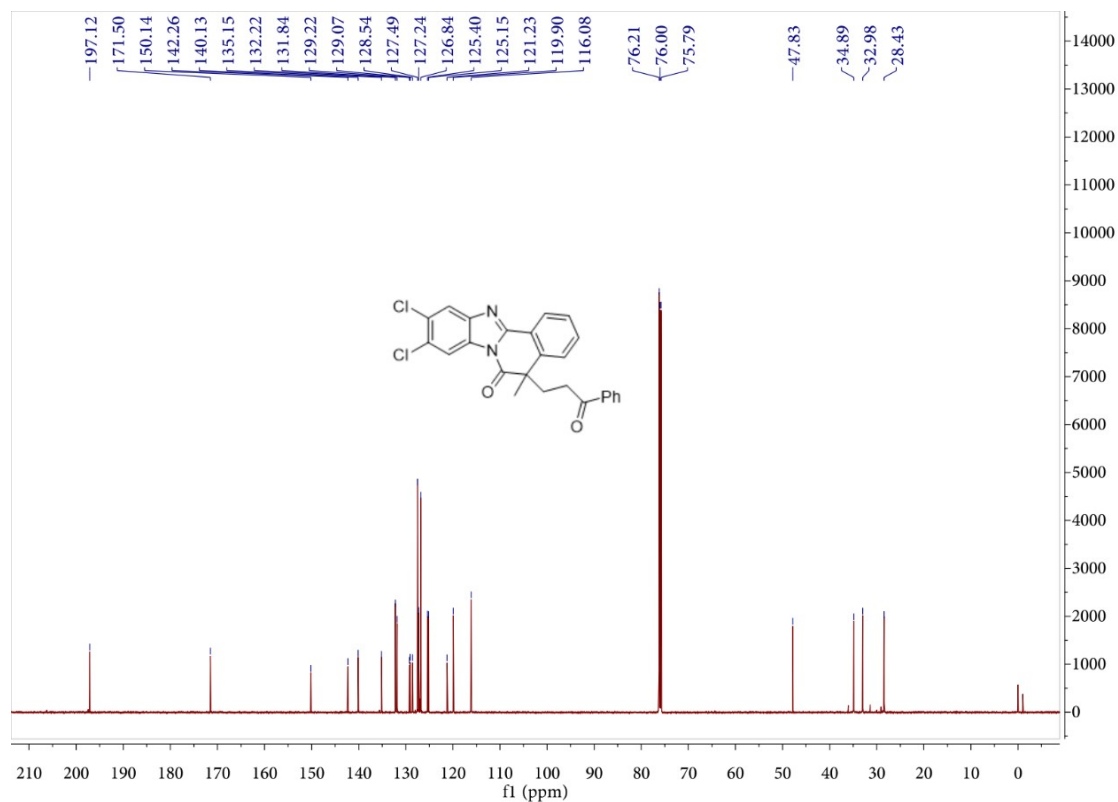
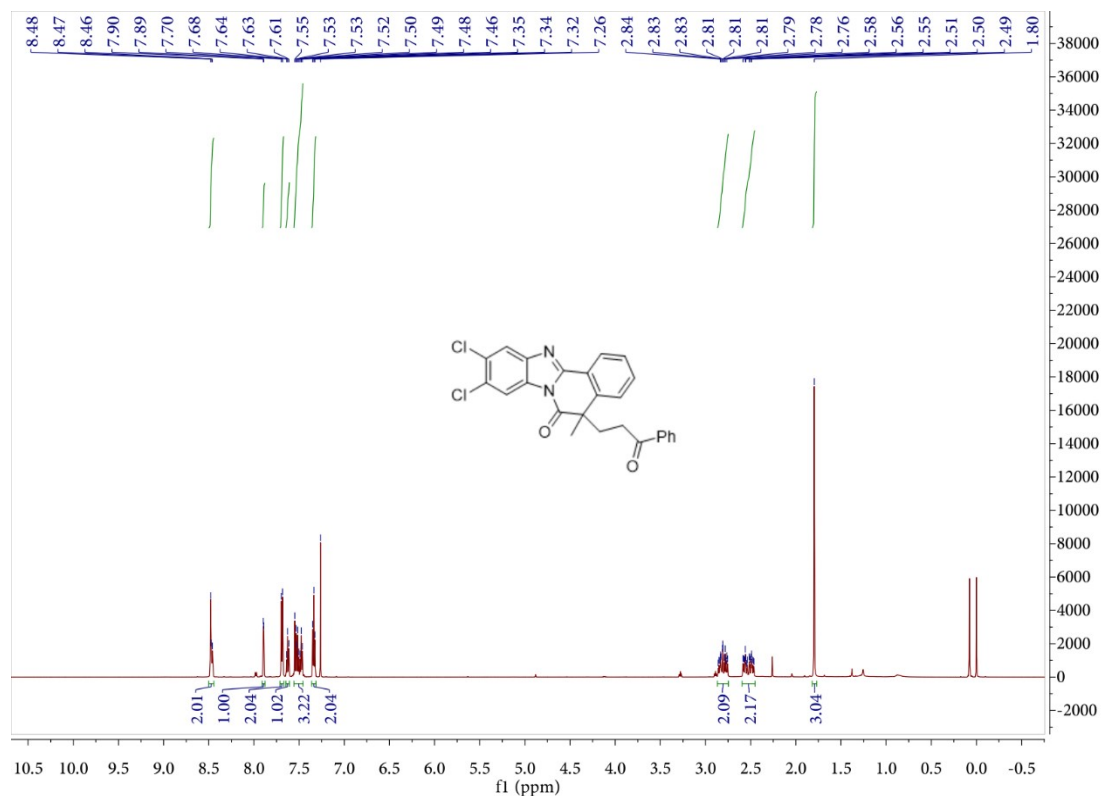
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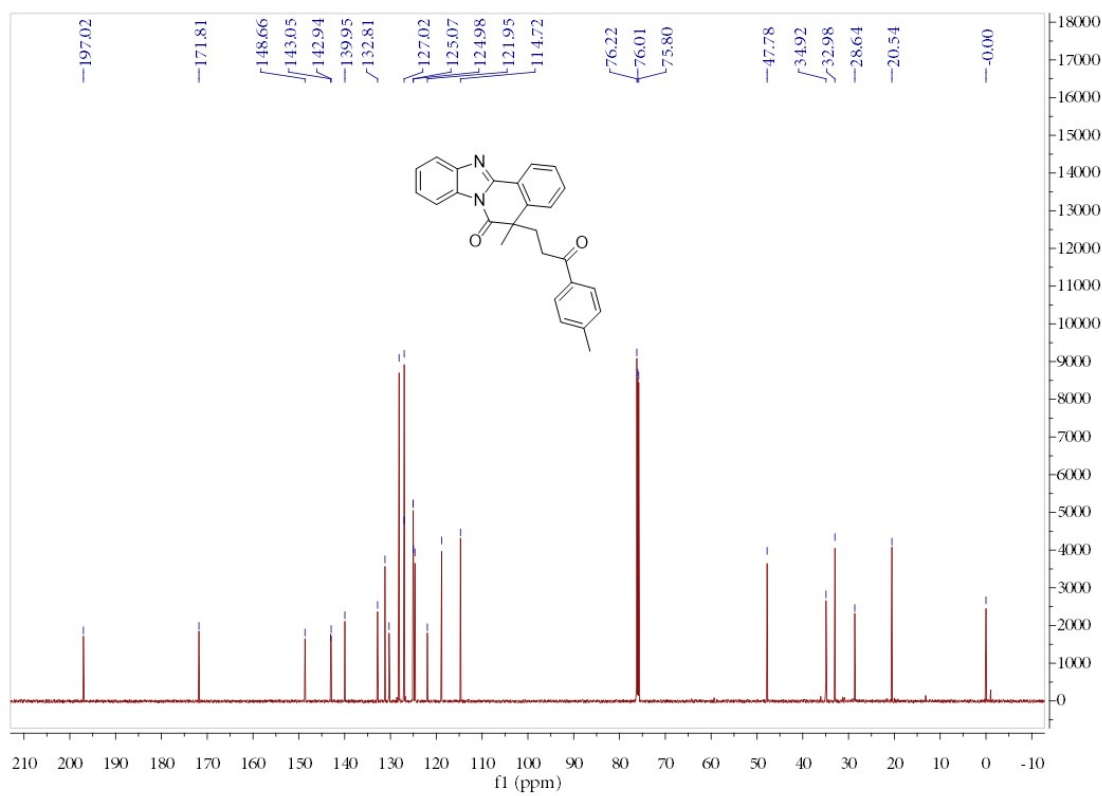
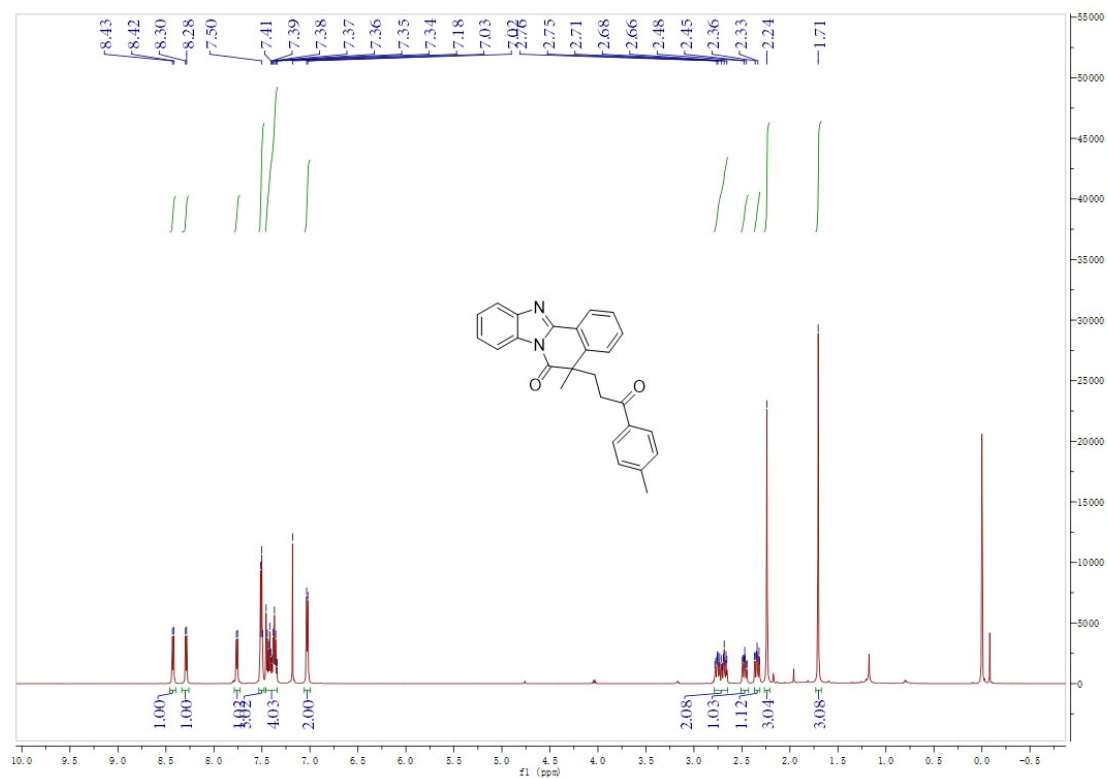
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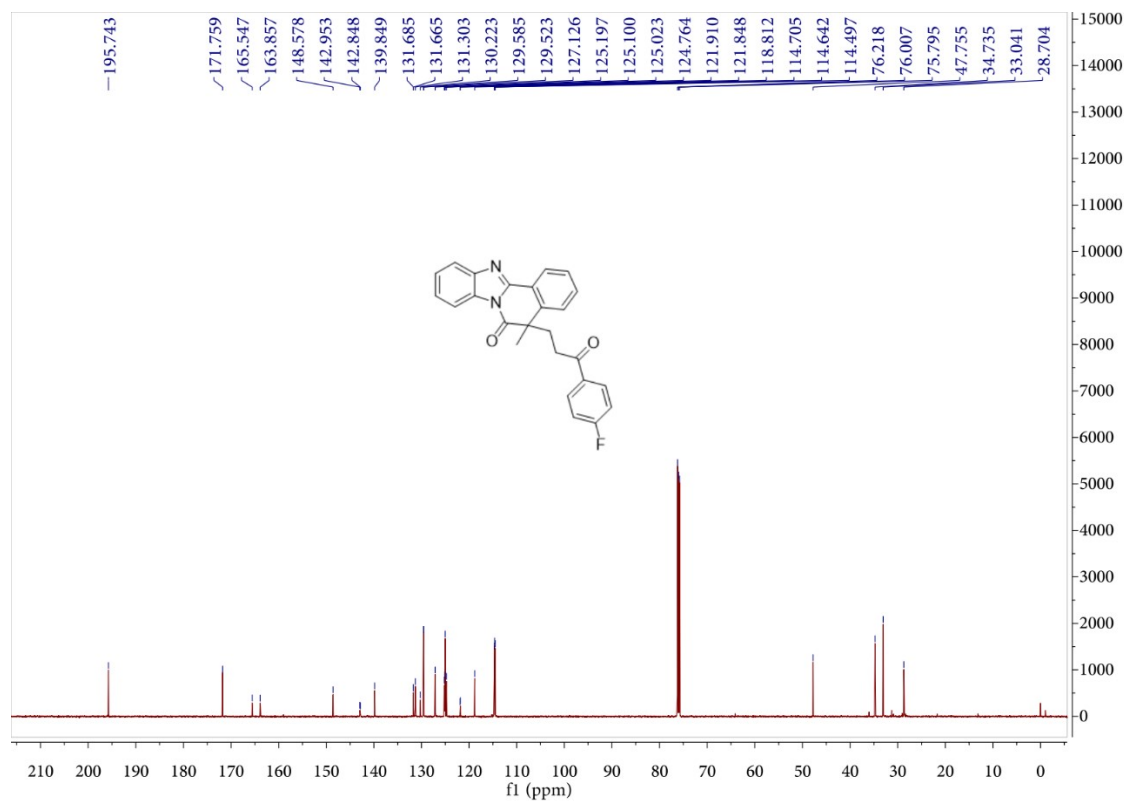
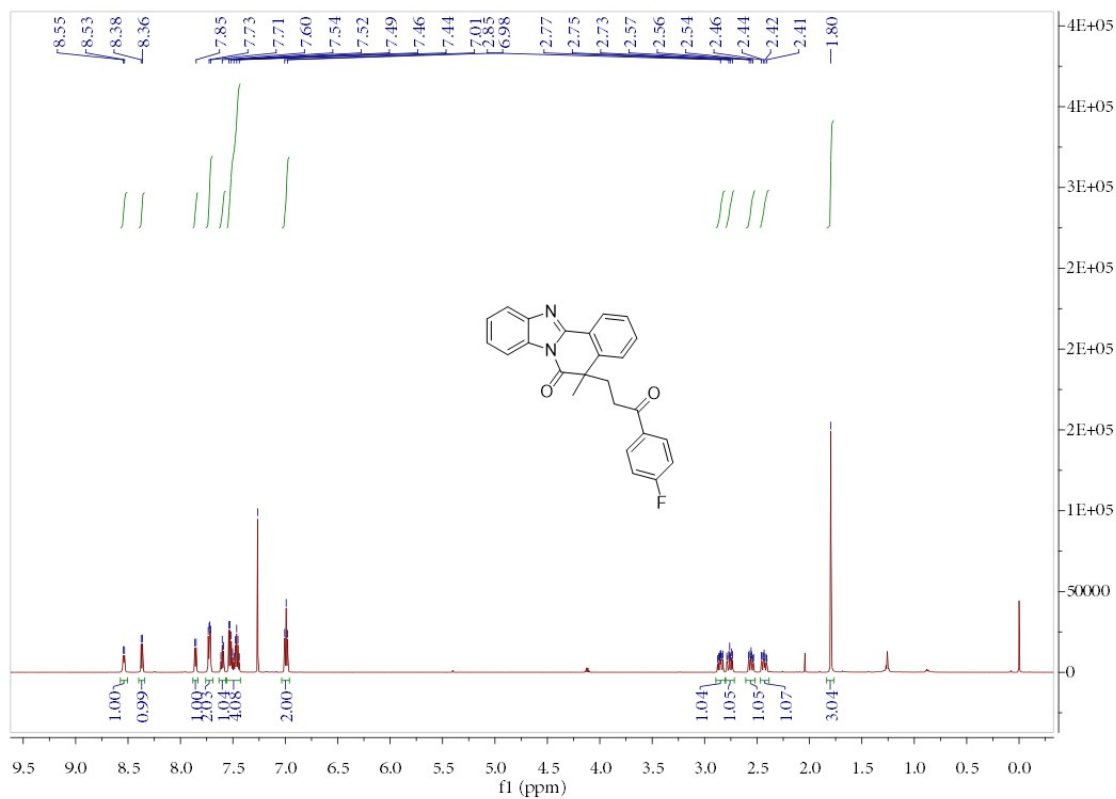
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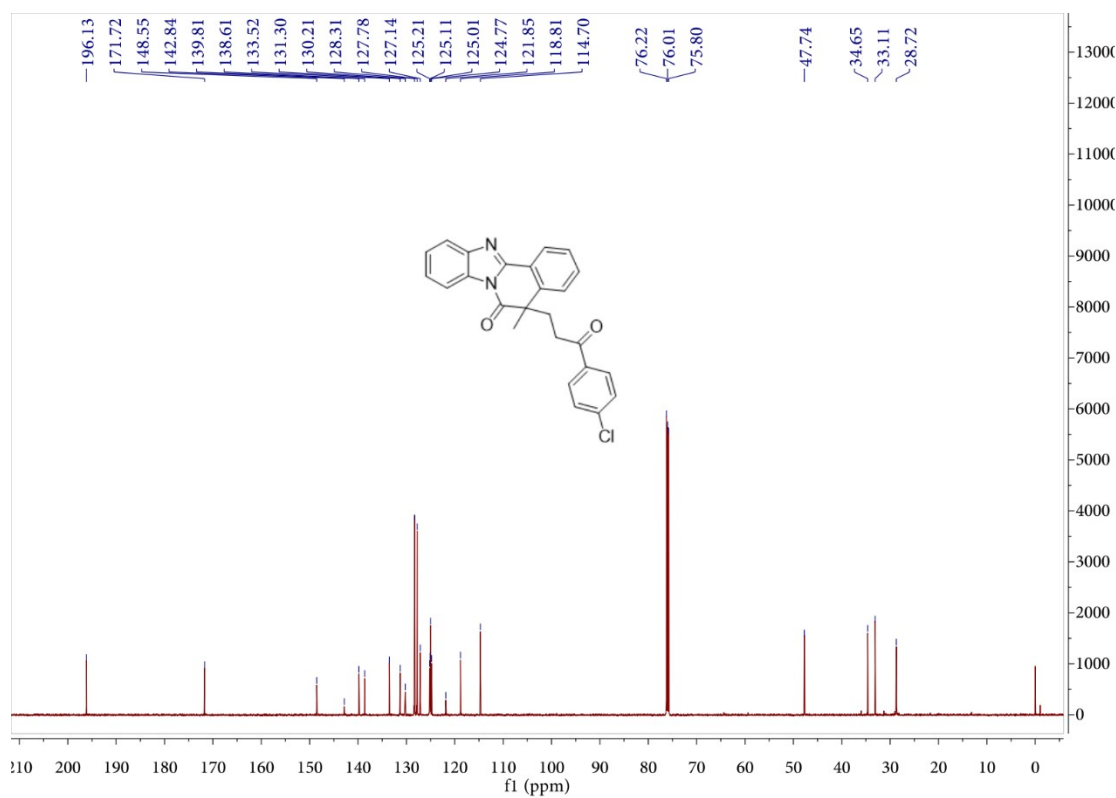
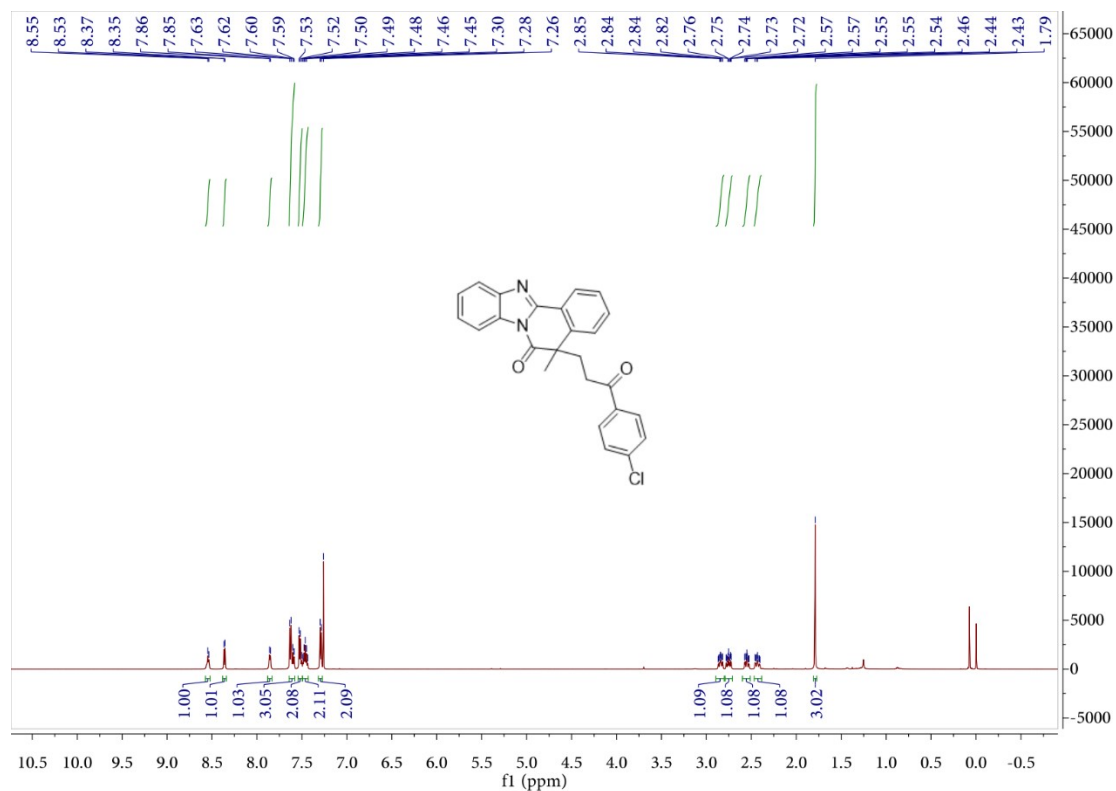
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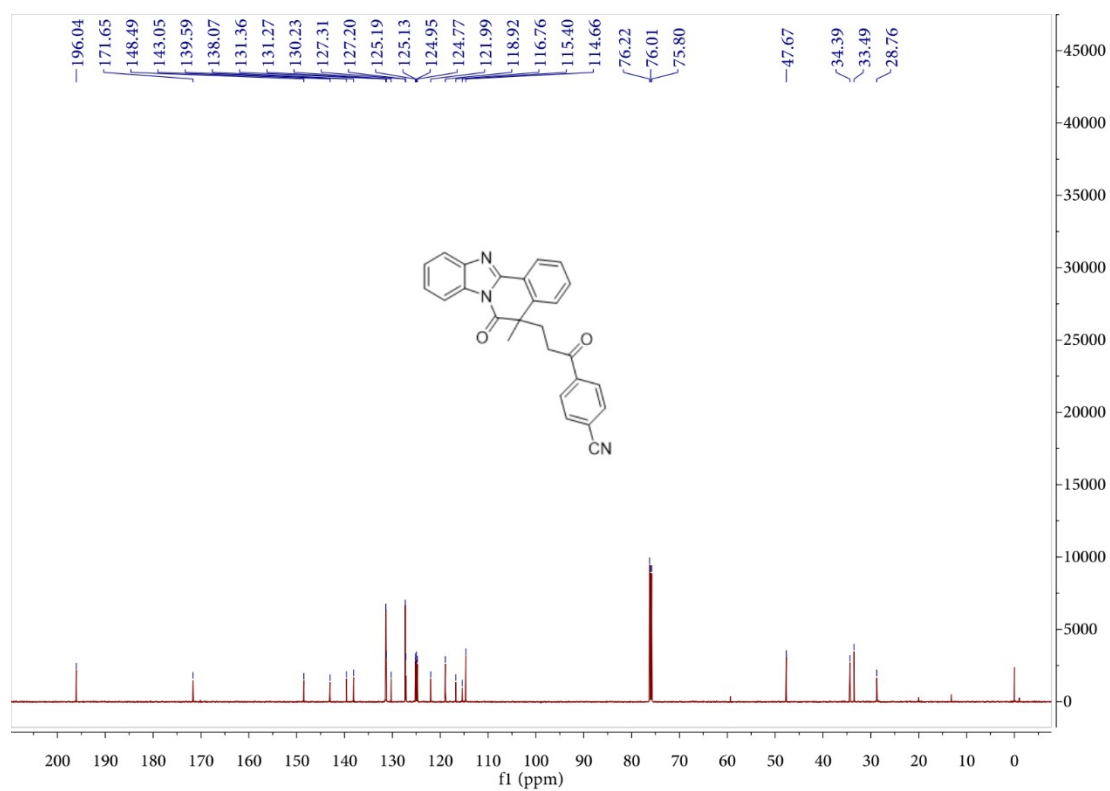
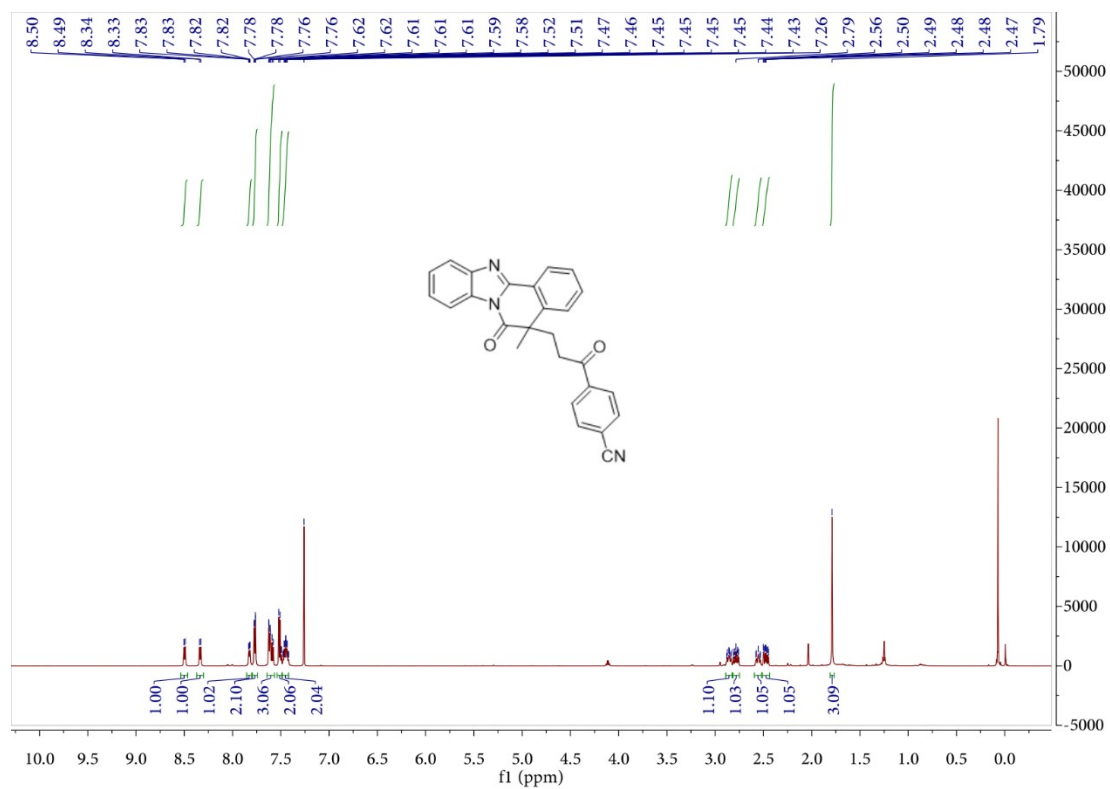
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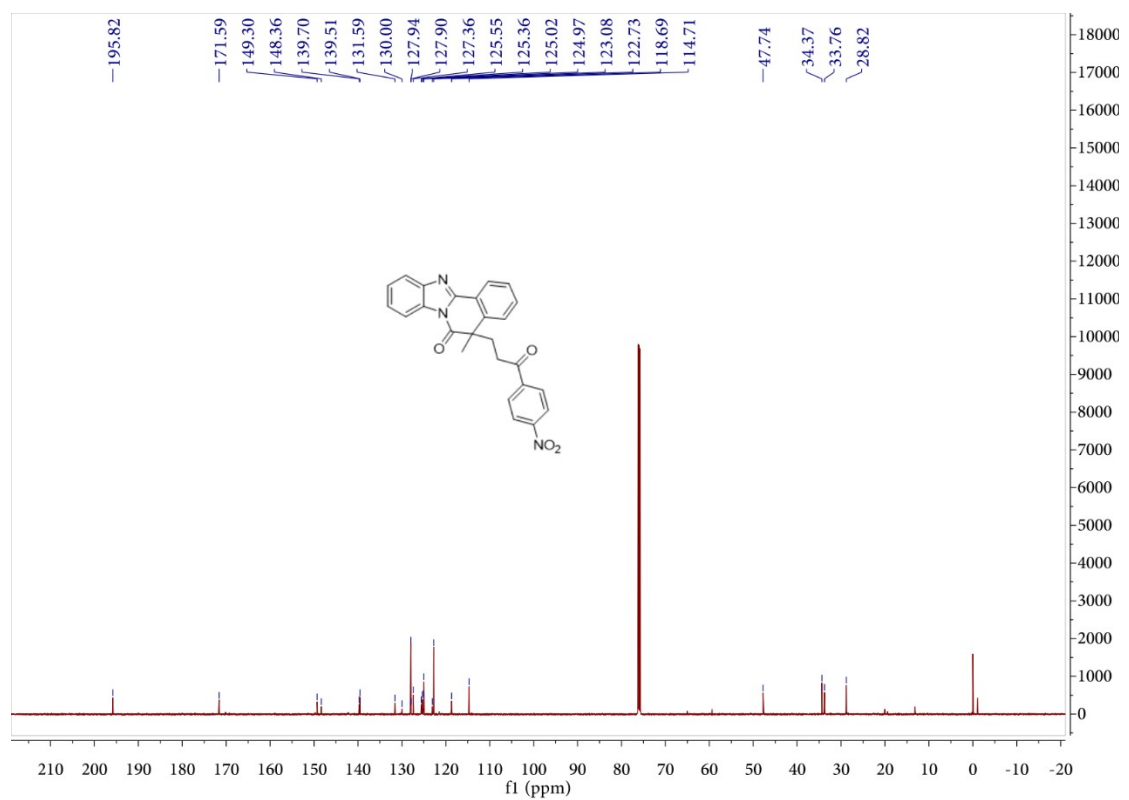
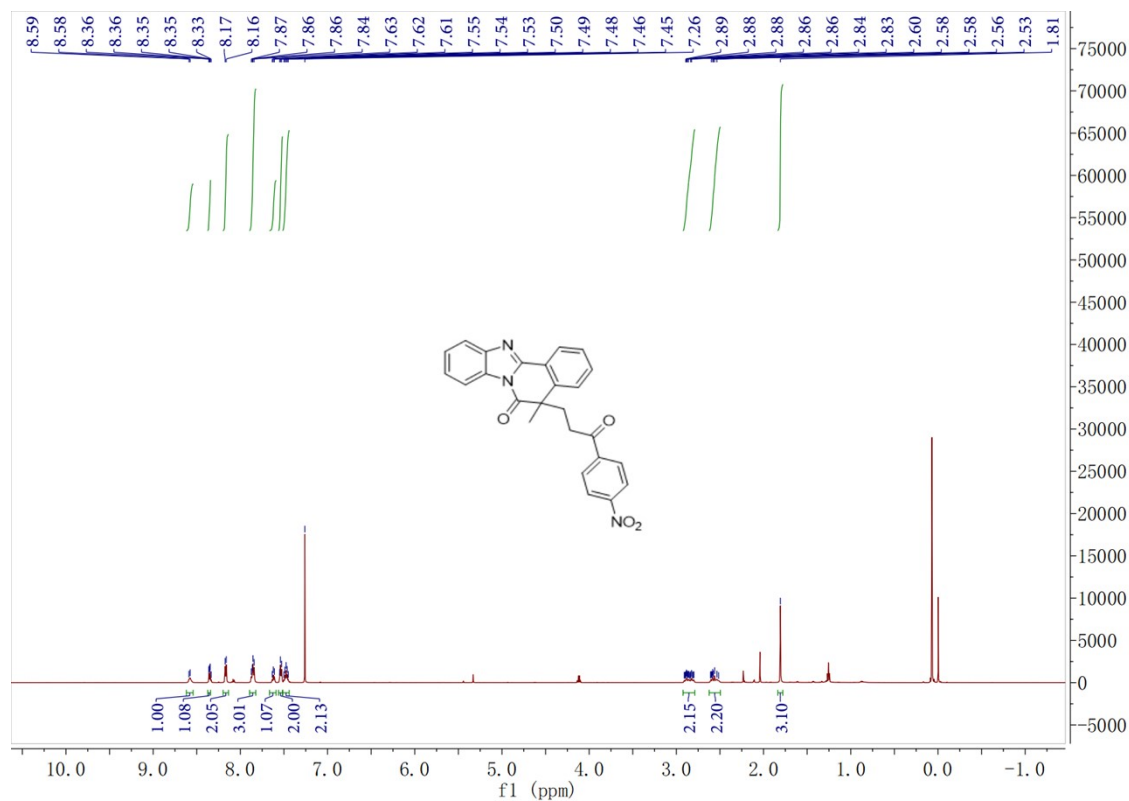
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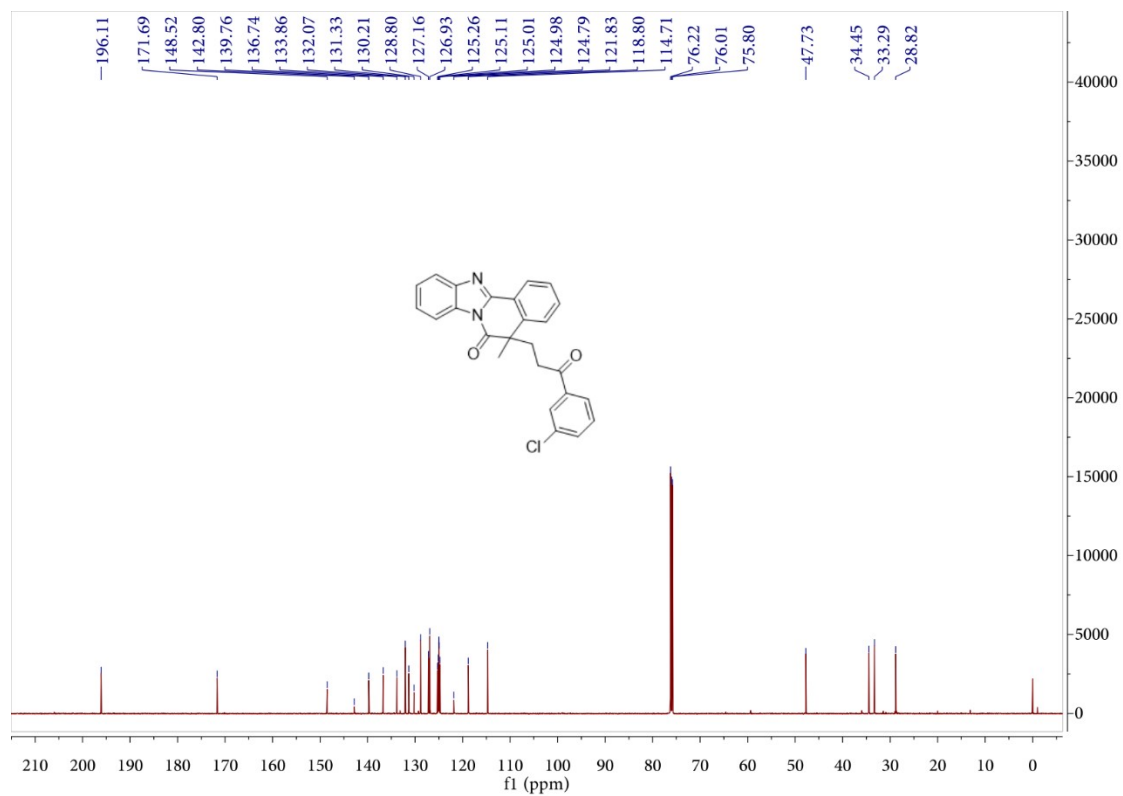
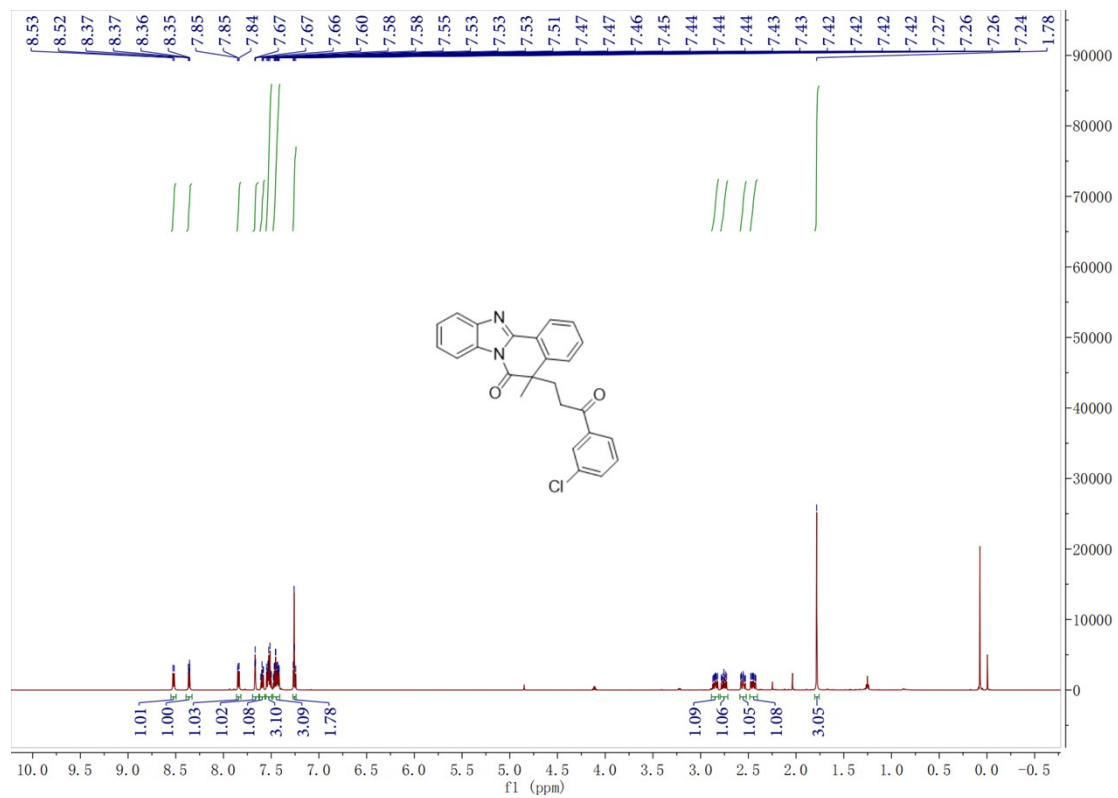
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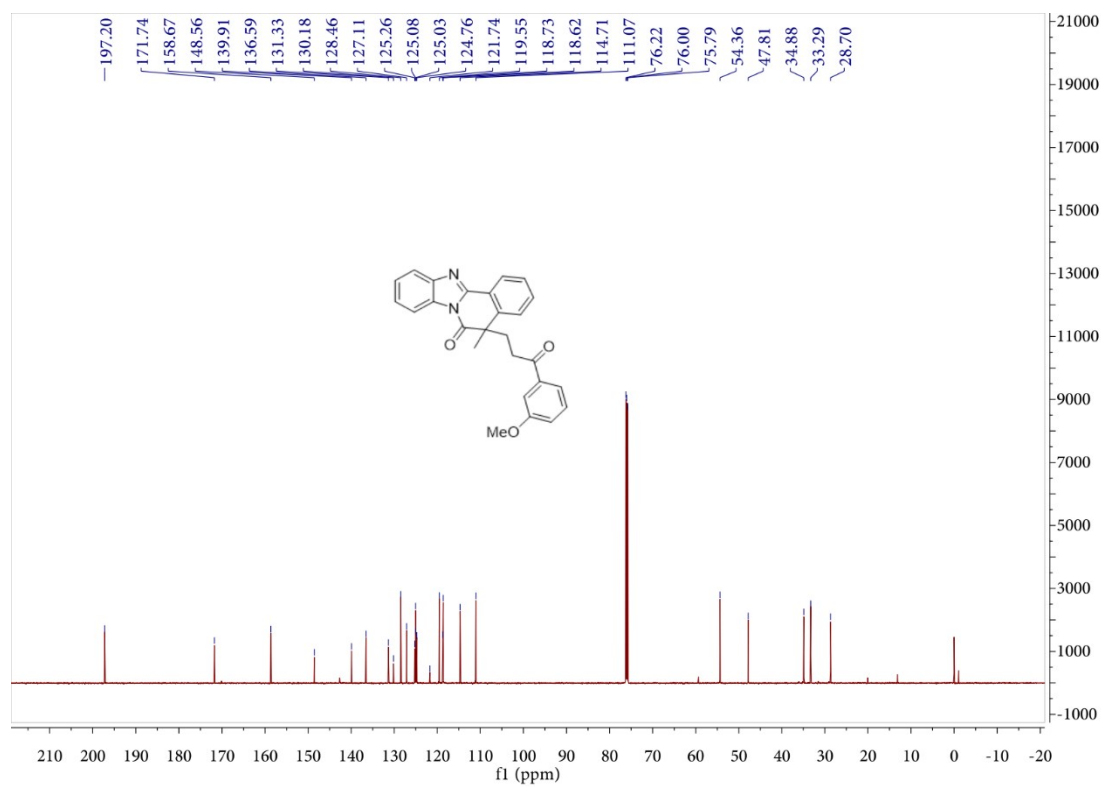
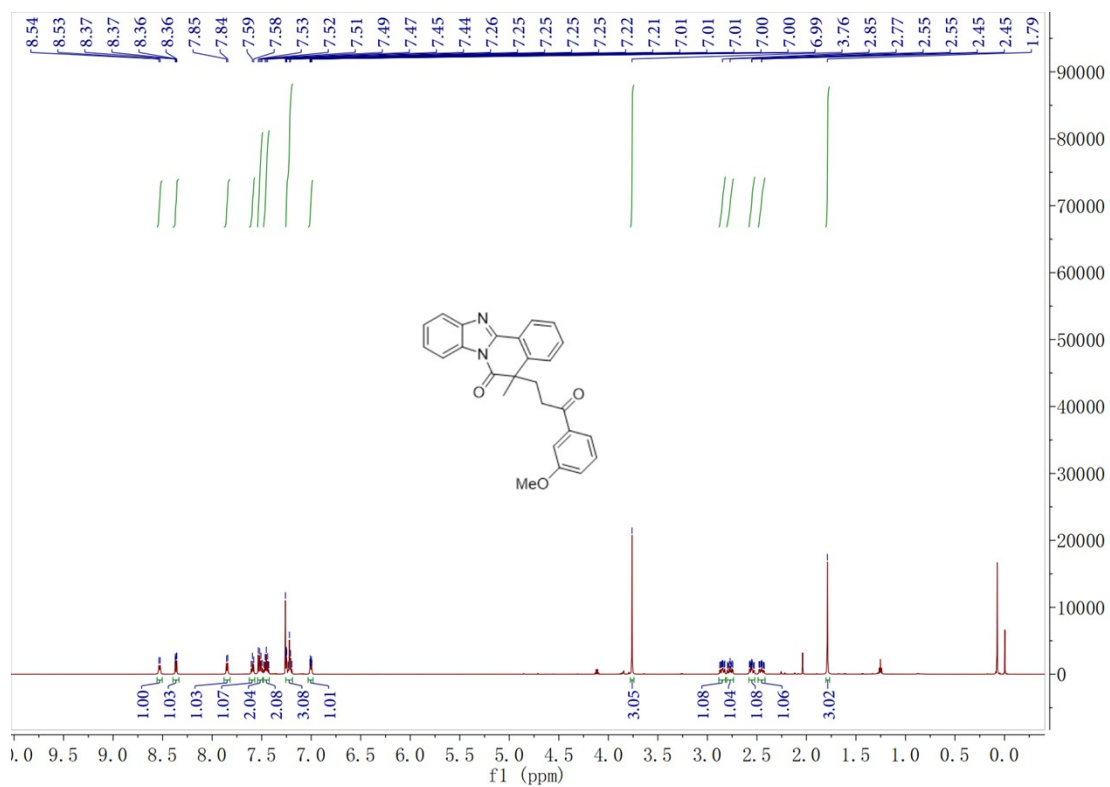
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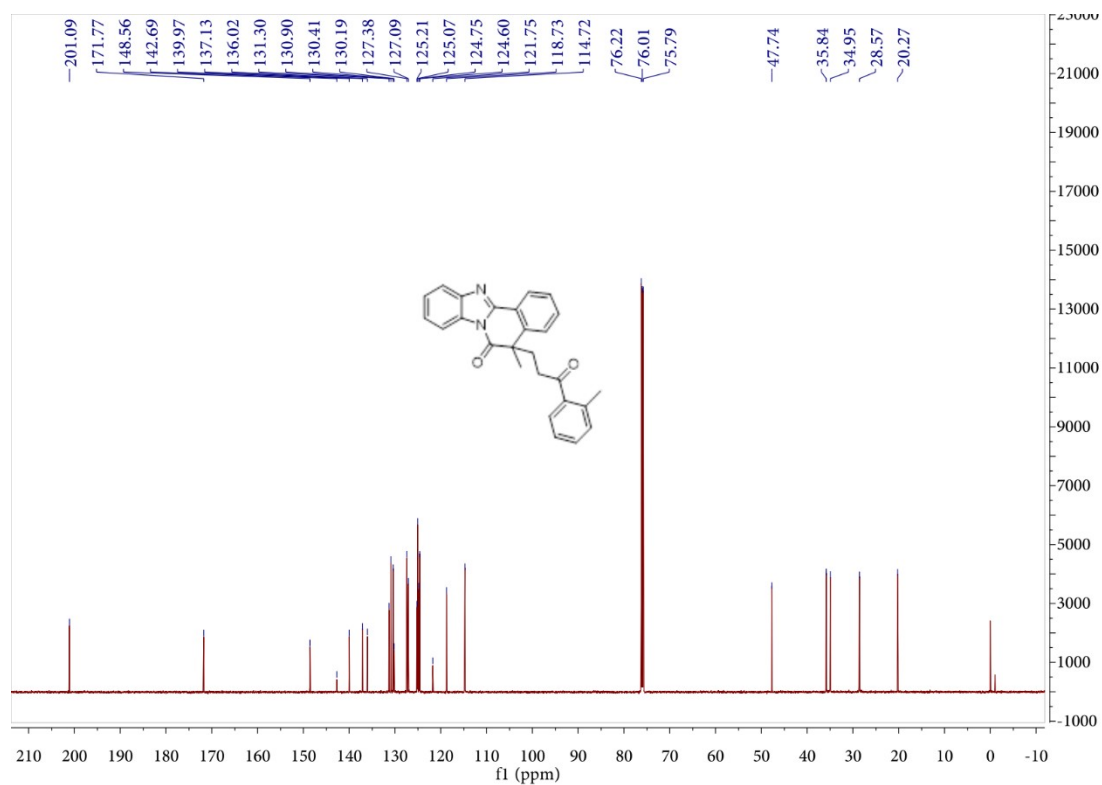
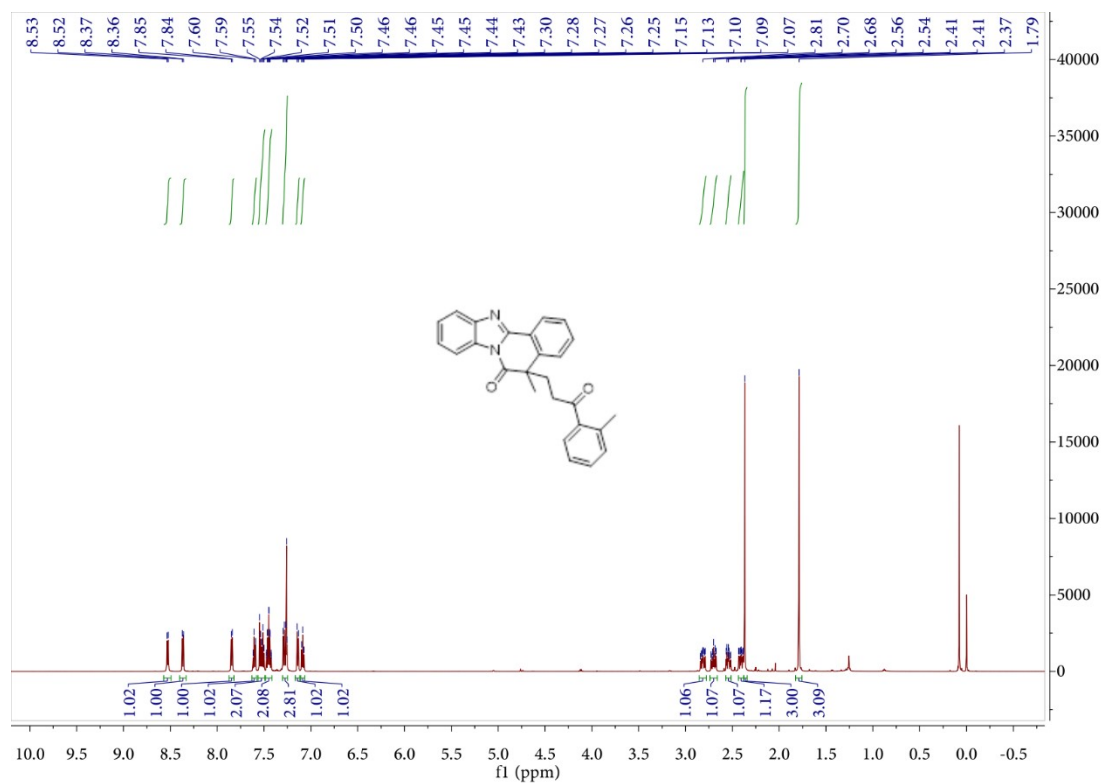
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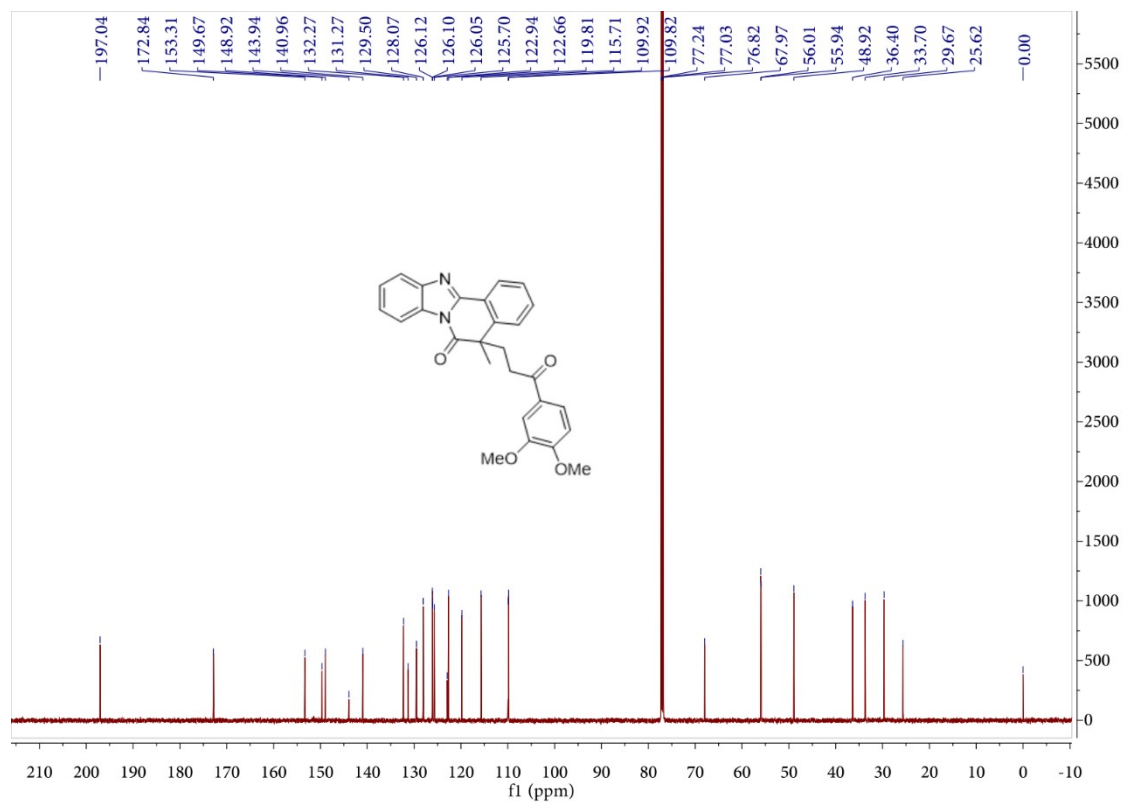
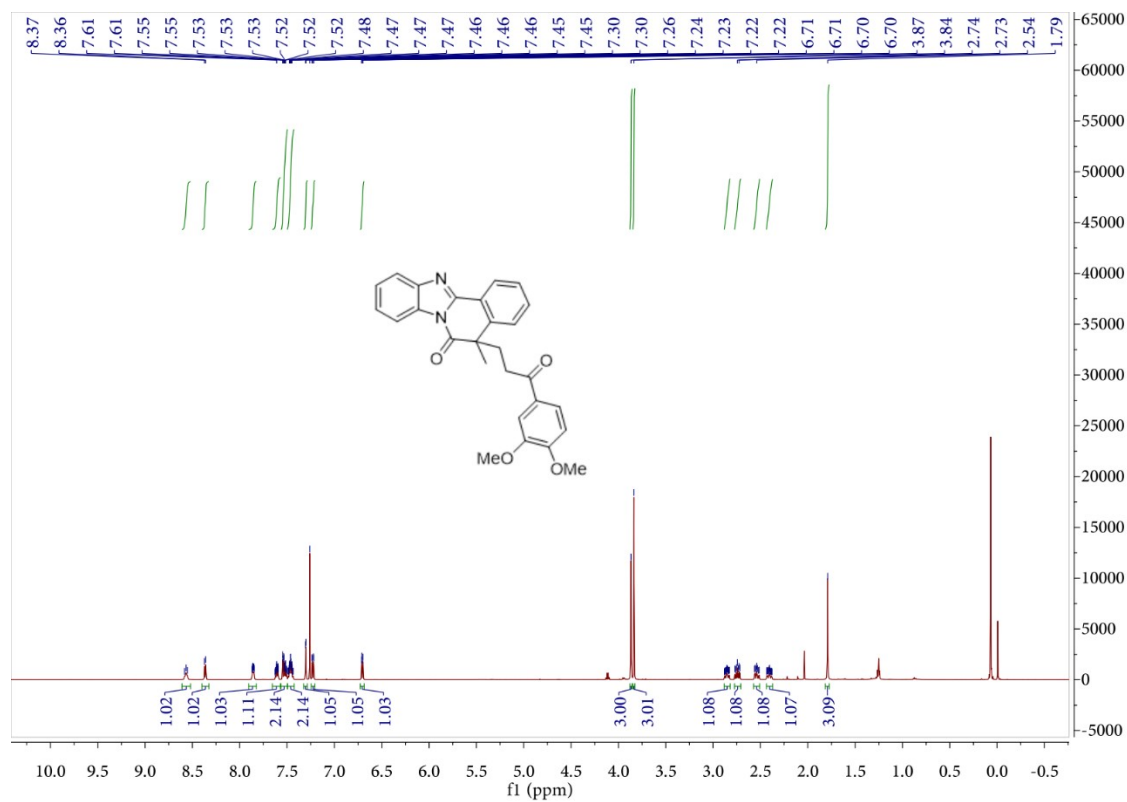
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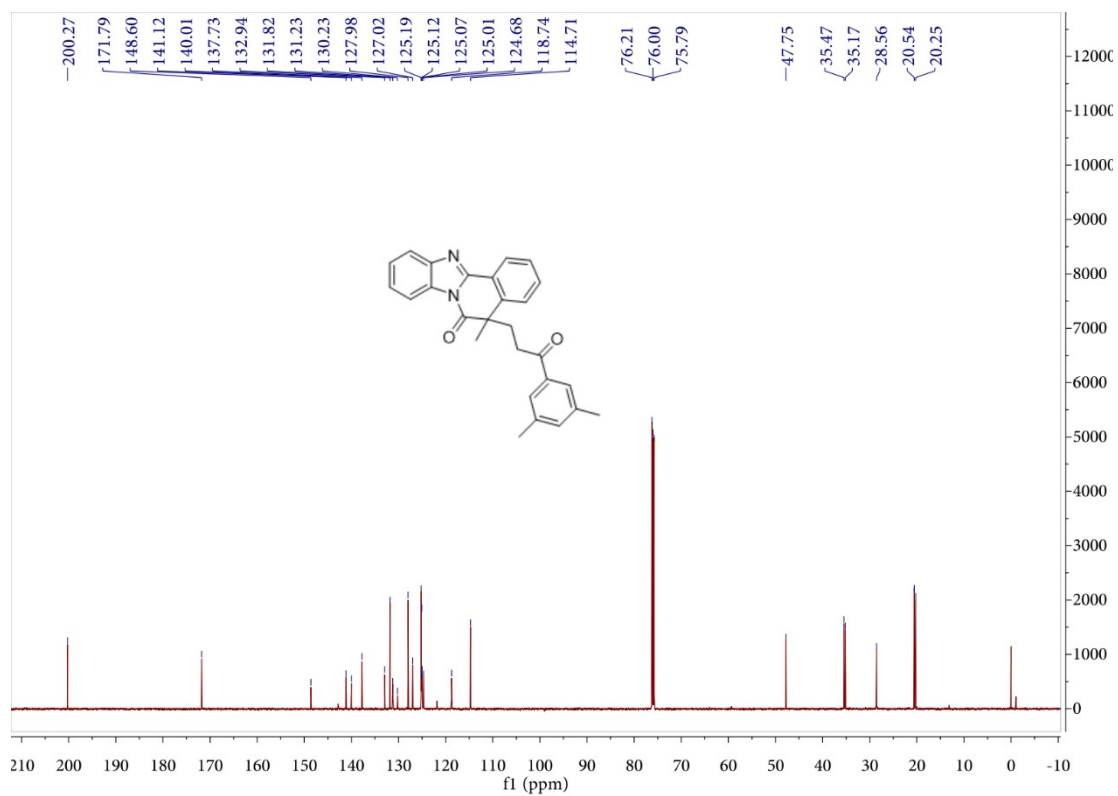
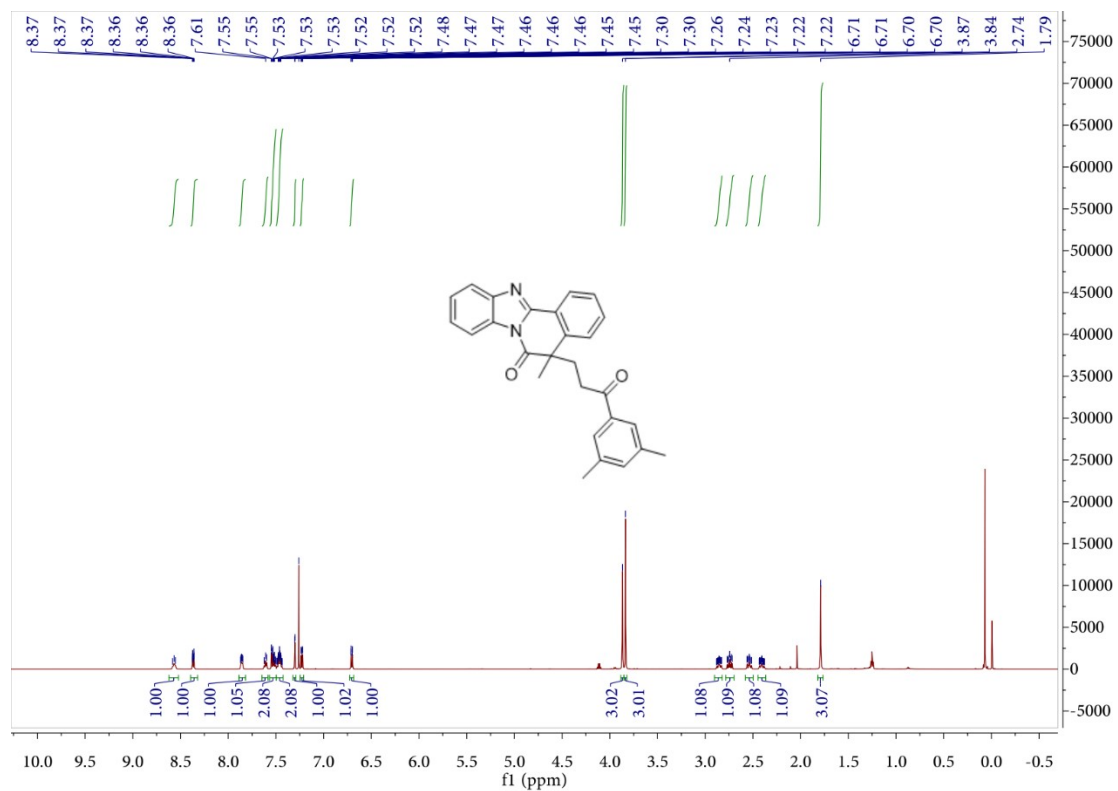
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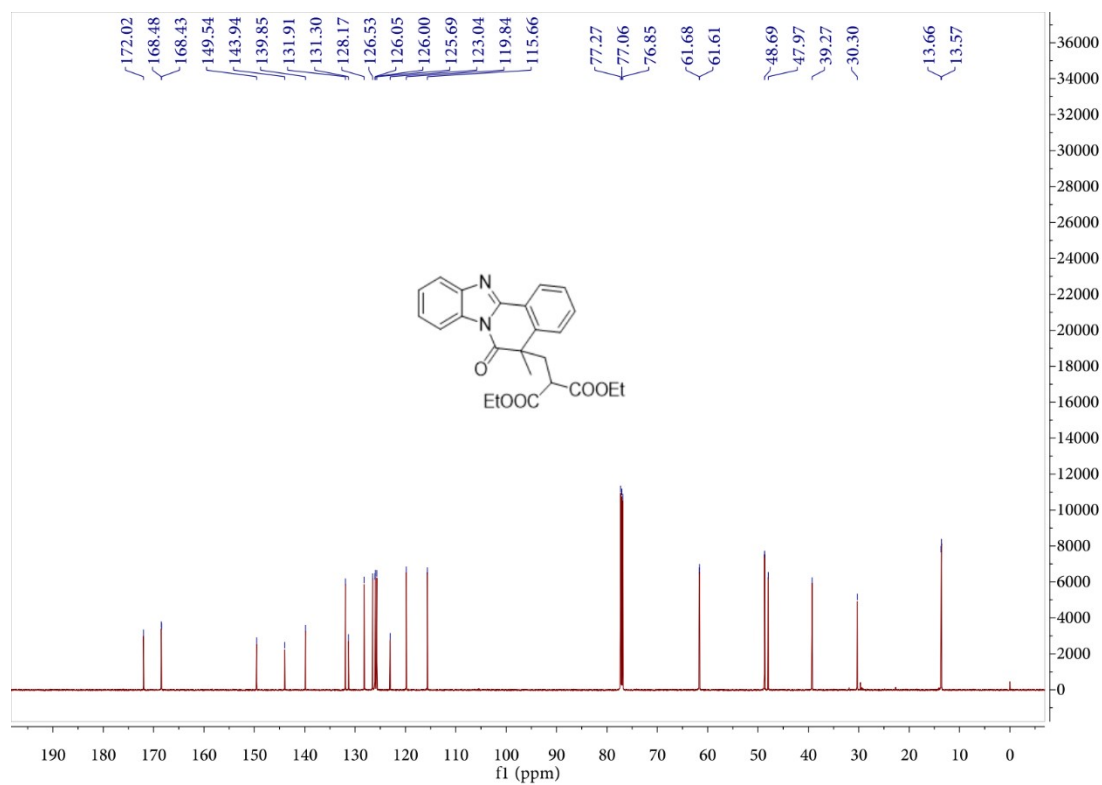
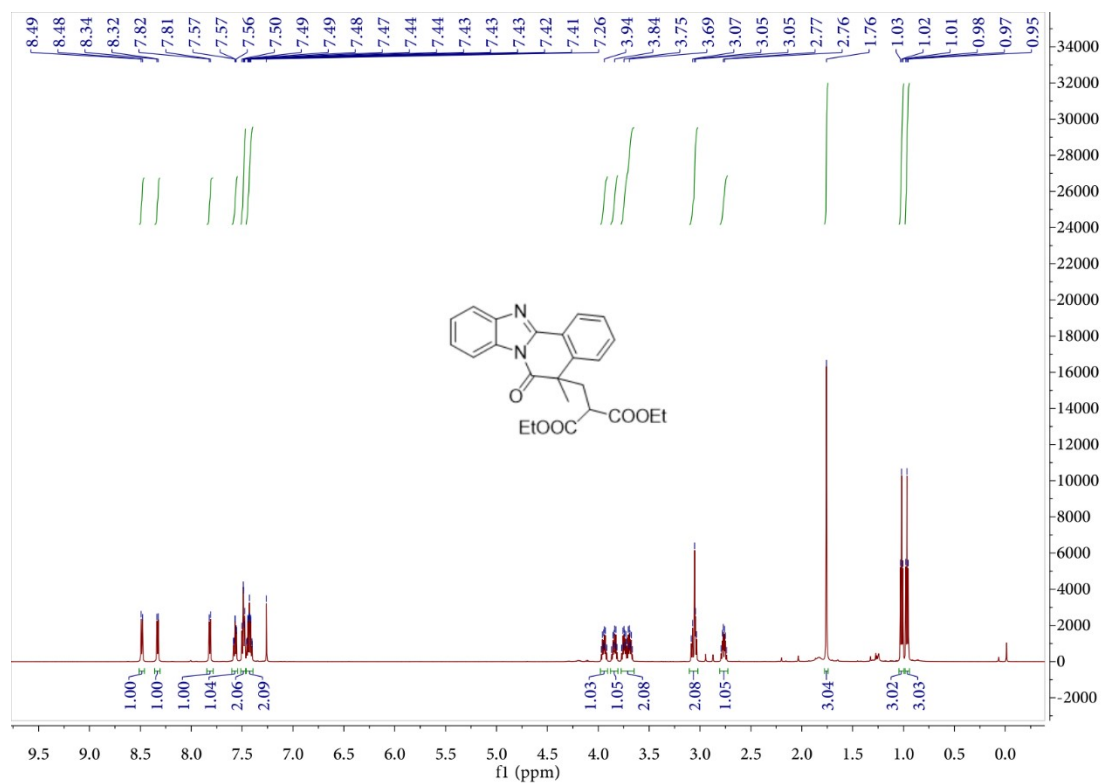
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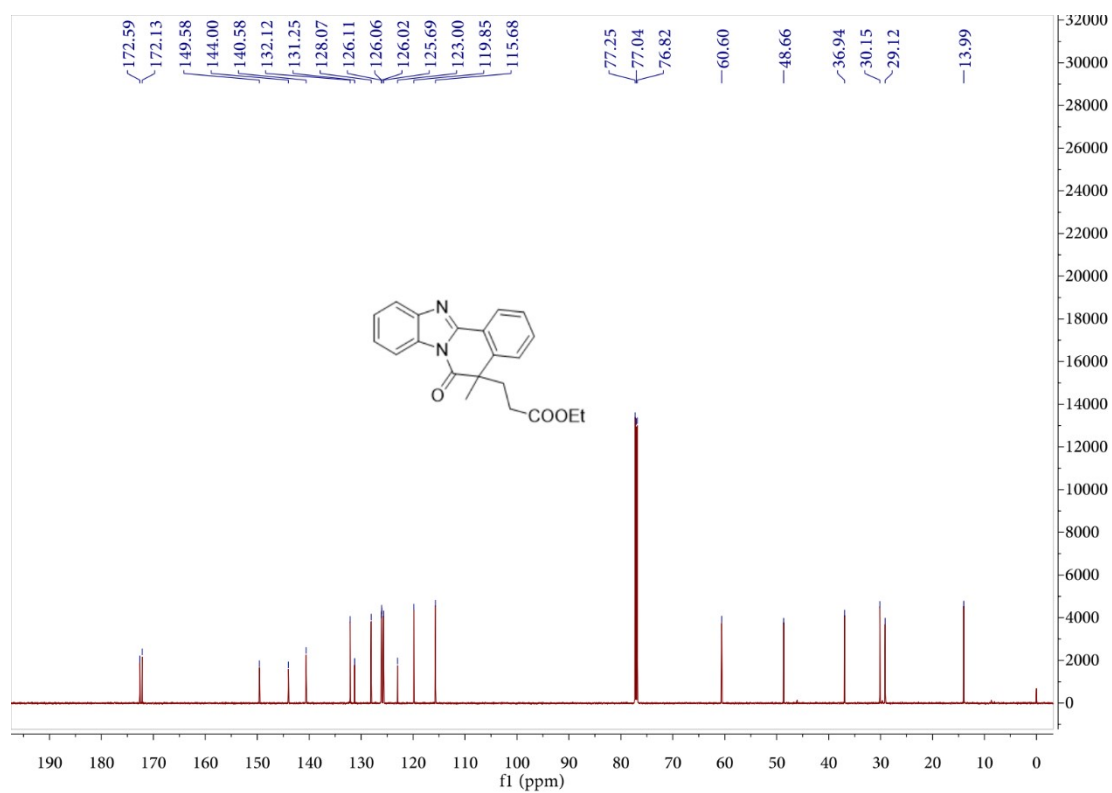
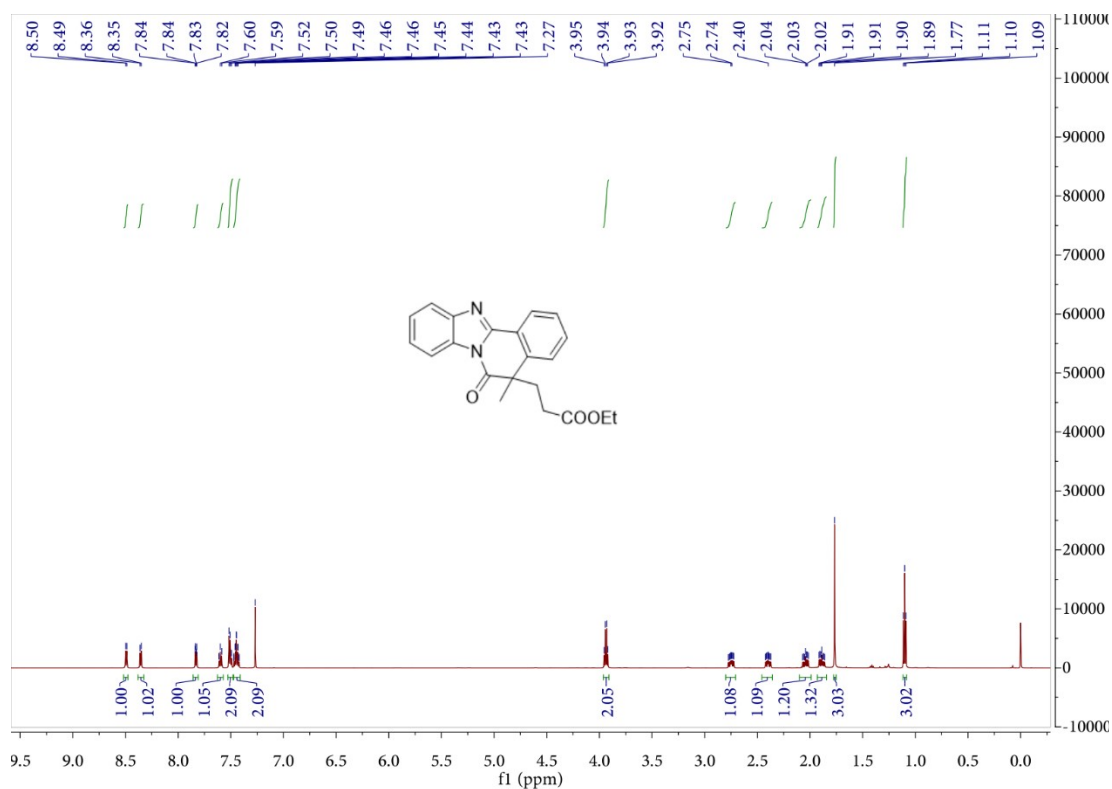
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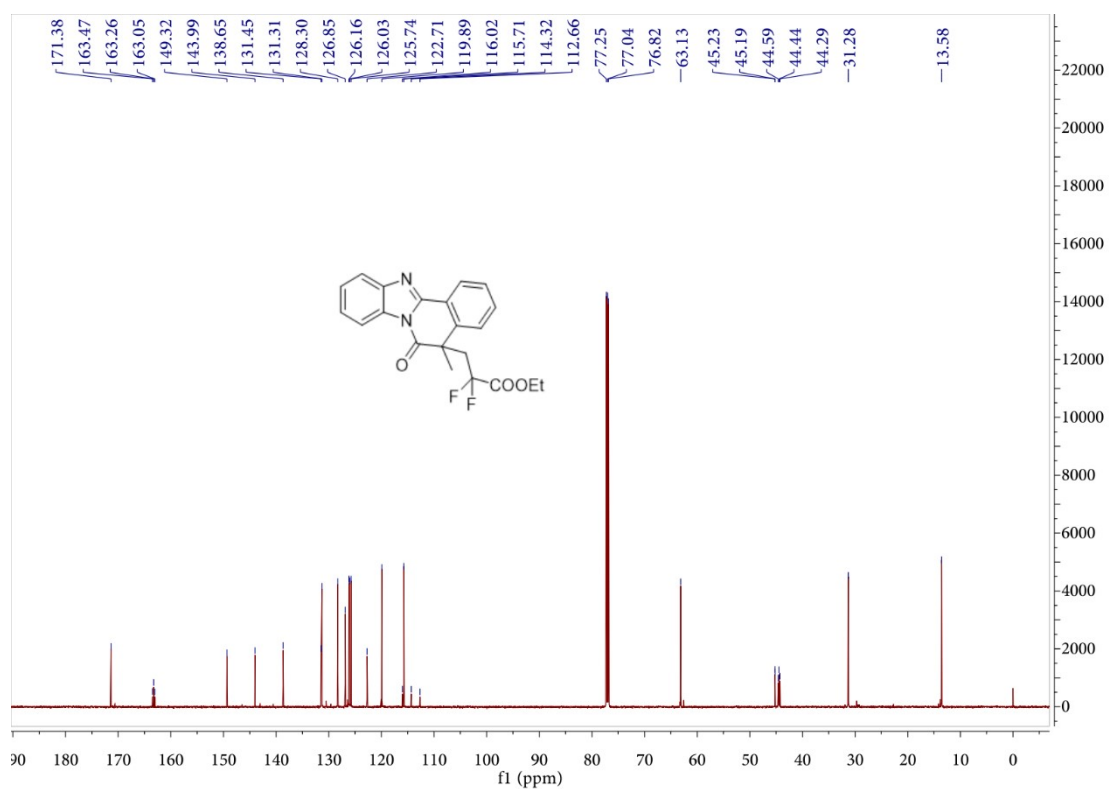
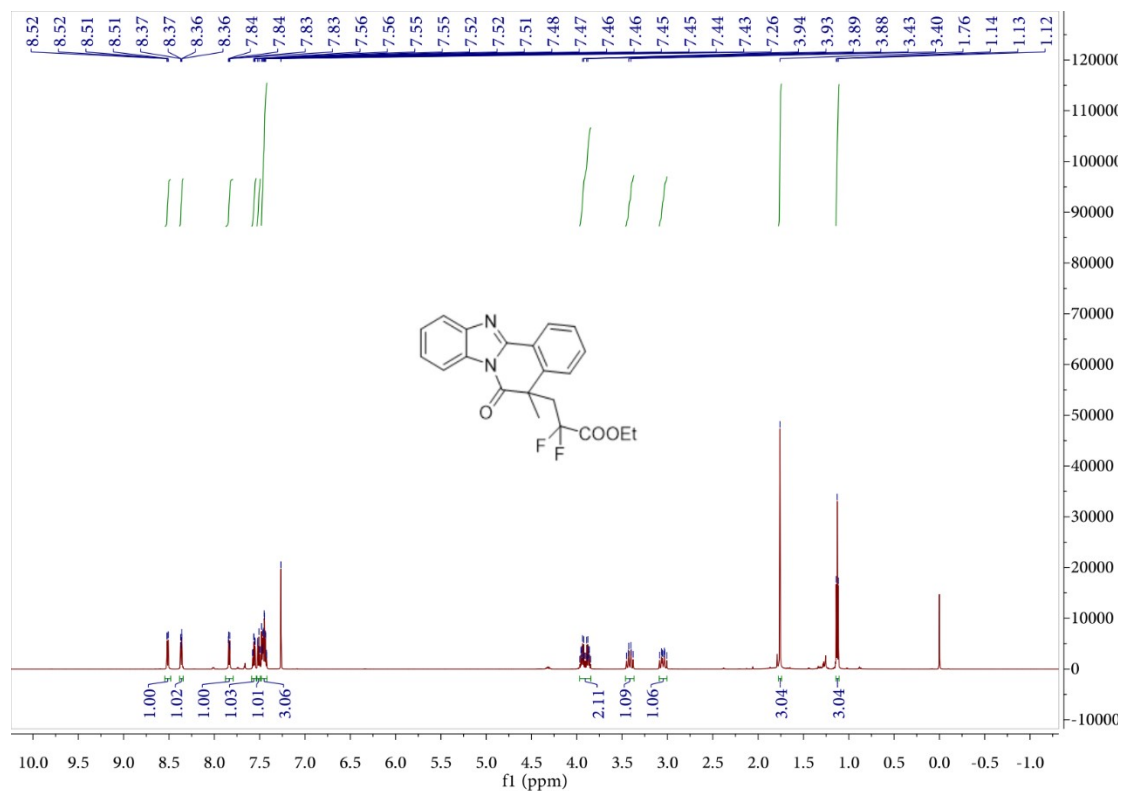
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3an



3ao



3ap

