

Ytterbium and Silver Co-Catalyzed Synthesis of Pyrrole-Fused Bicyclic Skeletons From Enynones and Isocyanides

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Supporting Information

Table of Contents

1	General Information	S2
2	General Procedure	S2
3	Characterization Data	S3
	Spectroscopic Data of All Compounds	S3
4	¹H NMR and ¹³C NMR Spectra of All Compounds	S12

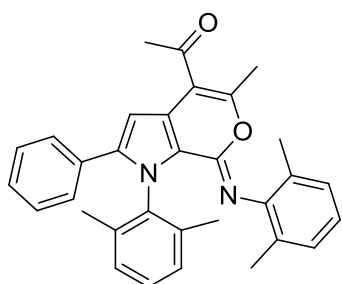
1 General Information

The NMR spectra were recorded on Bruker AC – 500 spectrometer (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR) with CDCl_3 as the solvent and TMS as internal reference. ^1H NMR spectral data were reported as follows: chemical shift (δ , ppm), multiplicity, integration, and coupling constant (Hz). ^{13}C NMR spectral data were reported in terms of the chemical shift. The following abbreviations were used to indicate multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. Low-resolution mass spectra were obtained on a Shimadzu LCMS-2010EV spectrometer in ESI mode and reported as m/z. High-resolution mass spectra (HRMS) were recorded on a Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS instrument. Melting points were obtained on a X-4 digital melting point apparatus without correction. Chemical yields referred to pure isolated product. Purification of products was accomplished by column chromatography packed with silica gel. Unless otherwise stated, anhydrous toluene was used upon purification with sodium metal.

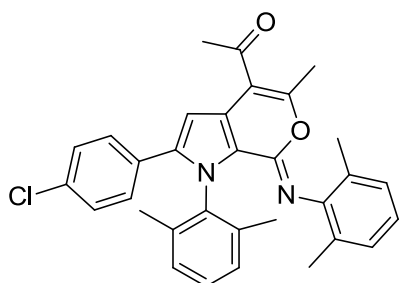
2 General Procedure

Under nitrogen atmosphere, $\text{Yb}(\text{OTf})_3$ (0.2 equiv), Ag_2CO_3 (0.6 equiv) were added to a solution of enynone **1** (0.5 mmol) and isocyanide **2** (1.0 mmol) in 3 mL toluene. The stirred mixture was heated at 70 $^\circ\text{C}$ for 12 hours and the progress was monitored using TLC detection. After completion of present reaction, the reaction mixture was concentrated under vacuum. The residue was purified by column chromatography on alumina [neutral alumina: 200-300; eluant: petroleum ether/ethyl acetate = 40:1] to afford the desired product **3-5**.

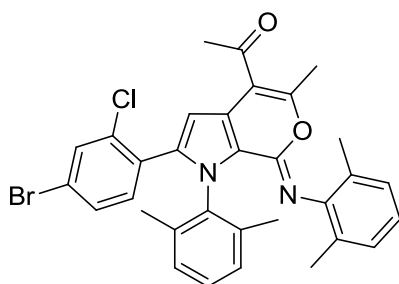
3 Characterization Data



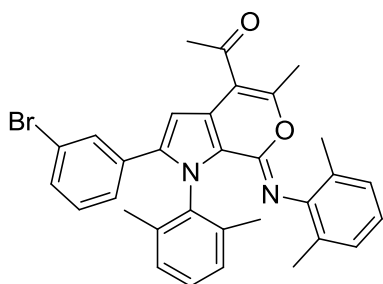
(3a): 178 mg, 75% yield, reddish brown solid: m.p. 135-137 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.23 (s, 5H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.5 Hz, 2H), 6.94 (d, *J* = 7.5 Hz, 2H), 6.81 (t, *J* = 7.5 Hz, 2H), 2.65 (s, 3H), 2.26 (s, 3H), 2.05 (s, 6H), 1.91 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 144.8, 141.3, 140.0, 137.4, 136.5, 131.4, 128.5, 128.3, 128.2, 128.0, 127.8, 127.3, 124.0, 122.0, 118.4, 114.6, 104.9, 31.7, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₂H₃₀N₂O₂ [M+H]⁺ 475.2380, Found: 475.2380.



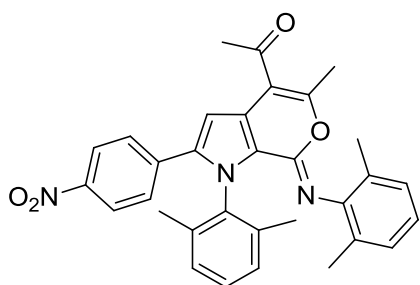
(3b): 196 mg, 77% yield, yellow solid: m.p. 185-186 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.21-7.18 (m, 2H), 7.15-7.12 (m, 3H), 7.02 (d, *J* = 7.5 Hz, 2H), 6.94 (d, *J* = 7.5 Hz, 2H), 6.81 (t, *J* = 6.8 Hz, 2H), 2.64 (s, 3H), 2.26 (s, 3H), 2.03 (s, 6H), 1.90 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.2, 157.1, 144.6, 140.0, 139.9, 137.2, 136.4, 134.0, 129.9, 129.0, 128.7, 128.6, 128.1, 127.9, 127.3, 124.1, 122.0, 118.7, 114.5, 105.1, 31.8, 19.4, 18.3, 18.1. HRMS (ESI): calcd. for C₃₂H₂₉ClN₂O₂ [M+H]⁺ 509.1990, Found: 509.1995.



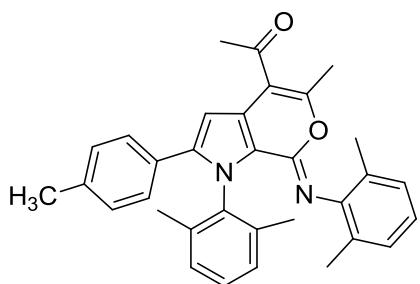
(3c): 190 mg, 65% yield, yellow solid: m.p. 208-210 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.60 (d, *J* = 2.0 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.94 (dd, *J* = 9.9, 7.7 Hz, 4H), 6.86 (s, 1H), 6.80 (t, *J* = 7.4 Hz, 2H), 2.62 (s, 3H), 2.25 (s, 3H), 2.07 (s, 6H), 1.89 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.2, 157.1, 144.6, 139.9, 136.5, 136.4, 135.9, 134.8, 132.9, 132.1, 129.4, 128.8, 128.5, 128.1, 127.7, 127.3, 123.3, 122.5, 122.1, 118.3, 114.5, 108.3, 31.7, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₂H₂₈BrClN₂O₂ [M+H]⁺ 587.1101, Found: 587.1095.



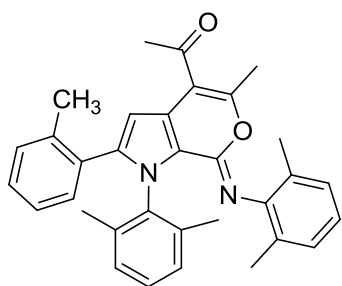
(3d): 171 mg, 62% yield, yellow solid: m.p. 209-210 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.43 (d, *J* = 7.5 Hz, 1H), 7.36-7.34 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.06-7.02 (m, 4H), 6.94 (d, *J* = 7.5 Hz, 2H), 6.85 (s, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 2.65 (s, 3H), 2.26 (s, 3H), 2.04 (s, 6H), 1.90 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.2, 157.2, 144.6, 139.9, 139.4, 137.1, 136.4, 133.3, 130.9, 130.8, 129.8, 128.7, 128.1, 127.9, 127.3, 126.0, 124.0, 122.4, 122.1, 118.9, 114.5, 105.4, 31.8, 19.4, 18.3, 18.0. HRMS (ESI): calcd. for C₃₂H₂₉BrN₂O₂ [M+H]⁺ 553.1485, Found: 553.1488.



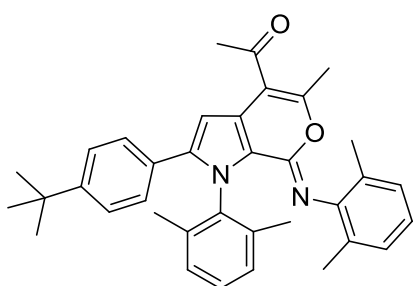
(3e): 207 mg, 80% yield, yellow solid: m.p. 240-241 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 8.06 (d, *J* = 8.9 Hz, 2H), 7.33 (d, *J* = 8.9 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 3H), 6.93 (d, *J* = 7.5 Hz, 2H), 6.81 (t, *J* = 7.5 Hz, 1H), 2.64 (s, 3H), 2.27 (s, 3H), 2.02 (s, 6H), 1.88 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 197.9, 157.5, 146.8, 144.3, 139.6, 138.3, 137.6, 136.9, 136.3, 129.1, 128.1, 128.0, 127.9, 127.3, 124.3, 123.7, 122.3, 119.9, 114.3, 106.8, 31.8, 19.5, 18.2, 17.9. HRMS (ESI): calcd. for C₃₂H₂₉N₃O₄ [M+H]⁺ 520.2231, Found: 520.2231.



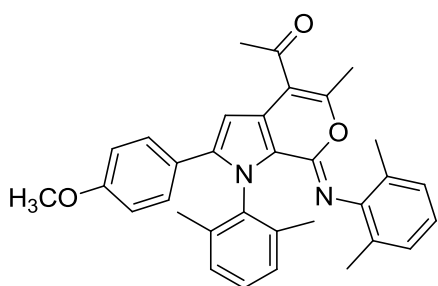
(3f): 149 mg, 61% yield, yellow solid: m.p. 197-199 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.15-7.12 (m, 3H), 7.03 (q, *J* = 6.9 Hz, 4H), 6.96 (d, *J* = 7.5 Hz, 2H), 6.82 (q, *J* = 6.5 Hz, 2H), 2.66 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H), 2.07 (s, 6H), 1.93 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 156.9, 144.9, 141.5, 140.1, 137.9, 137.5, 136.5, 129.1, 128.6, 128.5, 128.2, 127.8, 127.7, 127.3, 124.0, 121.9, 118.2, 114.6, 104.5, 31.8, 21.2, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₃H₃₂N₂O₂ [M+H]⁺ 489.2537, Found: 489.2545.



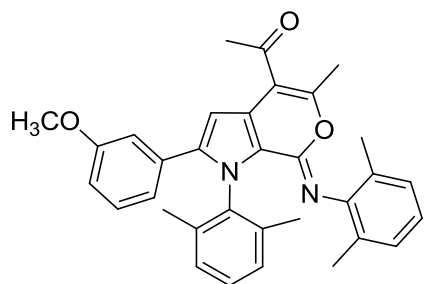
(3g): 210 mg, 86% yield, yellow solid: m.p. 176-177 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.24 (d, *J* = 7.7 Hz, 1H), 7.16-7.12 (m, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.94 (t, *J* = 6.8 Hz, 5H), 6.89 (t, *J* = 3.9 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 6.65 (s, 1H), 2.63 (s, 3H), 2.47 (s, 3H), 2.26 (s, 3H), 2.06 (s, 6H), 1.92 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 156.9, 144.8, 140.1, 139.7, 137.0, 136.9, 136.4, 130.7, 130.7, 130.3, 129.8, 128.2, 128.1, 127.5, 127.3, 125.1, 123.3, 121.9, 117.7, 114.6, 106.9, 31.7, 21.0, 19.2, 18.3, 18.2. HRMS (ESI): calcd. for C₃₃H₃₂N₂O₂ [M+H]⁺ 489.2537, Found: 489.2549.



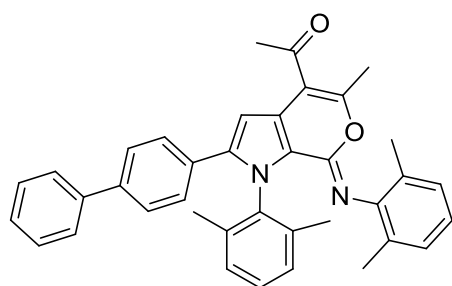
(3h): 170 mg, 64% yield, yellow solid: m.p. 199-201 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.25-7.23 (m, 2H), 7.17-7.12 (m, 3H), 7.02 (d, *J* = 7.5 Hz, 2H), 6.94 (d, *J* = 7.5 Hz, 2H), 6.80 (q, *J* = 5.0 Hz, 2H), 2.64 (s, 3H), 2.24 (s, 3H), 2.05 (s, 6H), 1.90 (s, 6H), 1.28 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 156.9, 150.9, 144.9, 141.2, 140.0, 137.6, 136.6, 128.5, 128.4, 128.2, 127.8, 127.2, 125.3, 124.0, 121.0, 118.2, 114.6, 104.6, 34.6, 31.7, 31.2, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₆H₃₈N₂O₂ [M+H]⁺ 531.3006, Found: 531.3015.



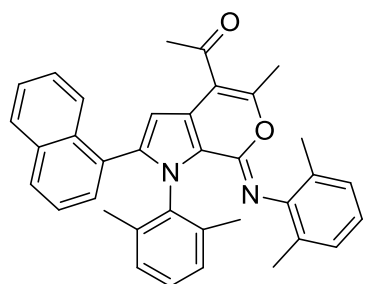
(3i): 133 mg, 53% yield, yellow solid: m.p. 167-168 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.15-7.10 (m, 3H), 7.00 (d, *J* = 7.6 Hz, 2H), 6.93 (d, *J* = 7.6 Hz, 2H), 6.80 (t, *J* = 5.0 Hz, 1H), 6.76-6.73 (m, 3H), 3.76 (s, 3H), 2.64 (s, 3H), 2.24 (s, 3H), 2.04 (s, 6H), 1.90 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.5, 159.3, 156.9, 144.9, 141.2, 140.1, 137.5, 136.5, 129.1, 128.4, 128.2, 127.7, 127.2, 124.0, 123.9, 121.8, 117.9, 114.6, 113.8, 104.1, 55.2, 31.7, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₃H₃₂N₂O₃ [M+H]⁺ 505.2486, Found: 505.2473.



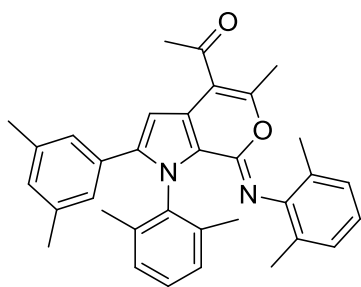
(3j): 121 mg, 48% yield, yellow solid: m.p. 139-141 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.18-7.11 (m, 2H), 7.02 (d, *J* = 7.5 Hz, 2H), 6.95-6.91 (m, 3H), 6.84-6.78 (m, 3H), 6.68 (t, *J* = 1.3 Hz, 1H), 3.59 (s, 3H), 2.65 (s, 3H), 2.26 (s, 3H), 2.06 (s, 6H), 1.91 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 159.3, 156.9, 144.8, 140.9, 140.0, 137.6, 136.5, 132.6, 129.4, 128.6, 128.2, 127.8, 127.3, 124.0, 122.0, 120.4, 118.5, 114.6, 114.3, 112.4, 104.9, 55.1, 31.8, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₃H₃₂N₂O₃ [M+H]⁺ 505.2486, Found: 505.2471.



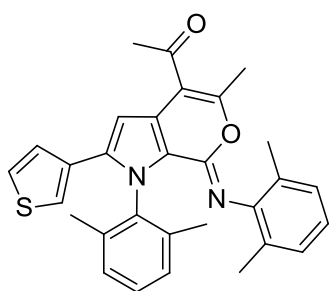
(3k): 184 mg, 67% yield, yellow solid: m.p. 128-129 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.55 (d, *J* = 7.2 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 6.8 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 7.4 Hz, 2H), 6.87 (s, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 2.66 (s, 3H), 2.56 (s, 3H), 2.07 (s, 6H), 1.91 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 157.0, 144.8, 140.8, 140.4, 140.2, 140.0, 137.5, 136.5, 130.3, 128.8, 128.6, 128.3, 128.2, 128.0, 127.8, 127.5, 127.3, 127.0, 126.9, 124.1, 121.9, 118.5, 114.6, 104.9, 31.8, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₈H₃₄N₂O₂ [M+H]⁺ 551.2693, Found: 551.2698.



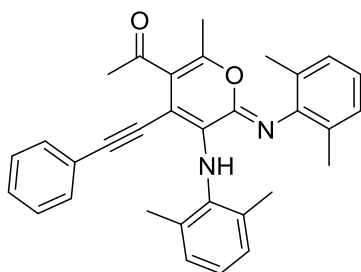
(3l): 141 mg, 54% yield, yellow solid: m.p. 176-177 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 8.31-8.29 (m, 1H), 7.86-7.84 (m, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.55-7.49 (m, 2H), 7.25 (dd, *J* = 8.1, 7.3 Hz, 1H), 7.13 (dd, *J* = 7.2, 1.1 Hz, 1H), 6.99-6.94 (m, 3H), 6.88 (d, *J* = 7.4 Hz, 2H), 6.84 (s, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 2.64 (s, 3H), 2.29 (s, 3H), 2.05 (s, 6H), 1.93 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.5, 157.0, 144.8, 140.1, 138.8, 137.0, 136.5, 133.8, 132.3, 128.8, 128.5, 128.3, 128.2, 128.1, 127.8, 127.6, 127.3, 126.5, 125.9, 125.7, 124.6, 123.5, 122.0, 118.2, 114.6, 107.9, 31.7, 19.3, 18.4, 18.3. HRMS (ESI): calcd. for C₃₆H₃₂N₂O₂ [M+H]⁺ 525.2537, Found: 525.2536.



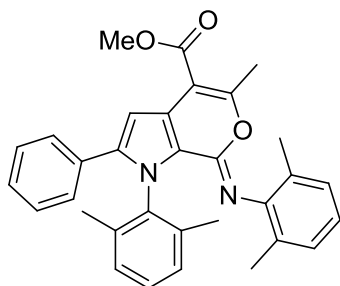
(3m): 191 mg, 76% yield, yellow solid: m.p. 191-192 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.11 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 7.5 Hz, 2H), 6.87 (s, 1H), 6.81 (q, *J* = 5.5 Hz, 4H), 2.66 (s, 3H), 2.25 (s, 3H), 2.19 (s, 6H), 2.05 (s, 6H), 1.91 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.5, 156.9, 144.9, 141.6, 140.1, 137.7, 137.6, 136.5, 131.2, 129.6, 128.4, 128.2, 127.8, 127.6, 127.3, 125.6, 123.9, 121.9, 118.2, 114.6, 104.7, 31.8, 21.3, 19.3, 18.3, 18.1. HRMS (ESI): calcd. for C₃₄H₃₄N₂O₂ [M+H]⁺ 503.2693, Found: 503.2691.



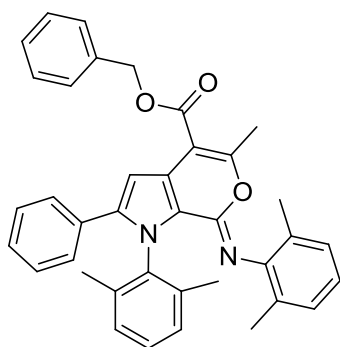
(3n): 127 mg, 53% yield, yellow oil. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.22–7.19 (m, 2H), 7.11–7.08 (m, 3H), 6.93 (d, *J* = 7.5 Hz, 2H), 6.87 (s, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 6.58 (dd, *J* = 3.0, 1.5 Hz, 1H), 2.65 (s, 3H), 2.25 (s, 3H), 2.03 (s, 6H), 1.91 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 157.1, 144.8, 140.0, 137.8, 136.7, 136.2, 131.7, 128.9, 128.3, 128.1, 127.3, 127.1, 125.4, 124.0, 122.0, 121.0, 117.9, 114.6, 104.1, 31.8, 19.4, 18.3, 17.9. HRMS (ESI): calcd. for C₃₀H₂₉N₂O₂S [M+H]⁺ 481.1950, Found: 481.1958.



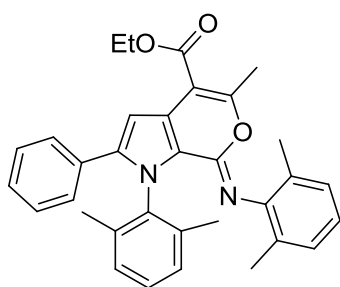
(3a'): 185 mg, 78% yield, yellow solid: m.p. 178-180 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.41 (s, 1H), 7.23-7.18 (m, 3H), 7.16-7.10 (m, 5H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.86-6.84 (m, 2H), 2.53 (s, 3H), 2.38 (s, 6H), 2.20 (s, 6H), 2.01 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 201.3, 146.0, 144.3, 143.9, 137.0, 136.4, 132.4, 131.4, 128.4, 128.1, 128.0, 127.8, 127.7, 126.7, 123.3, 122.7, 119.9, 100.7, 92.6, 83.5, 31.6, 18.9, 18.4, 17.2. HRMS (ESI): calcd. for C₃₂H₃₁N₂O₂ [M+H]⁺ 475.2380, Found: 475.2381.



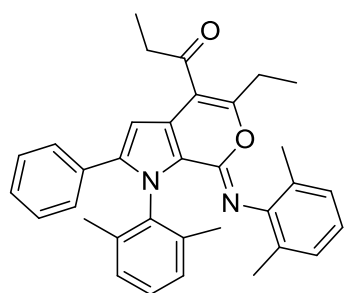
(**4a**): 157 mg, 64% yield, yellow solid: m.p. 131-133 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.27-7.23 (m, 5H), 7.13 (t, $J = 7.5$ Hz, 1H), 7.05 (d, $J = 1.1$ Hz, 1H), 7.02 (d, $J = 7.6$ Hz, 2H), 6.96 (d, $J = 7.5$ Hz, 2H), 6.82 (t, $J = 7.5$ Hz, 1H), 3.98 (s, 3H), 2.41 (s, 3H), 2.07 (s, 6H), 1.93 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 166.6, 160.7, 144.8, 141.2, 140.0, 137.5, 136.6, 131.6, 128.5, 128.3, 128.2, 127.9, 127.8, 127.7, 124.3, 122.0, 118.1, 106.1, 105.1, 51.7, 19.5, 18.3, 18.1. HRMS (ESI): calcd. for $\text{C}_{32}\text{H}_{30}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 491.2329, Found: 491.2337.



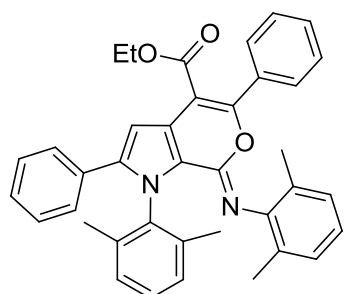
(**4b**): 127 mg, 45% yield, yellow solid: m.p. 111-113 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.51 (d, $J = 7.0$ Hz, 2H), 7.43-7.40 (m, 2H), 7.39-7.35 (m, 1H), 7.20-7.15 (m, 5H), 7.11 (t, $J = 7.6$ Hz, 1H), 7.00 (t, $J = 7.4$ Hz, 3H), 6.93 (d, $J = 7.5$ Hz, 2H), 6.80 (t, $J = 7.5$ Hz, 1H), 5.41 (s, 2H), 2.38 (s, 3H), 2.02 (s, 6H), 1.88 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 165.9, 160.8, 144.8, 141.0, 139.9, 137.5, 136.5, 135.9, 131.6, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.7, 127.6, 127.2, 124.3, 121.9, 118.1, 106.2, 105.0, 66.7, 19.5, 18.2, 18.0. HRMS (ESI): calcd. for $\text{C}_{38}\text{H}_{34}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 567.2642, Found: 567.2656.



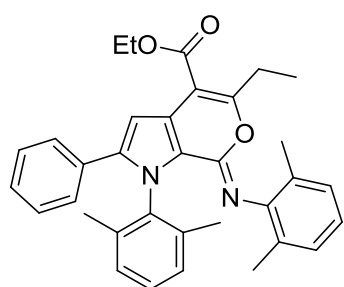
(**4c**): 181 mg, 72% yield, yellow solid: m.p. 155-156 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.28-7.24 (m, 5H), 7.14 (t, $J = 7.6$ Hz, 1H), 7.09 (s, 1H), 7.03 (d, $J = 7.5$ Hz, 2H), 6.97 (d, $J = 7.5$ Hz, 2H), 6.84 (t, $J = 7.5$ Hz, 1H), 4.47 (q, $J = 7.2$ Hz, 2H), 2.42 (s, 3H), 2.08 (s, 6H), 1.94 (s, 6H), 1.50 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 166.2, 160.4, 144.7, 141.1, 140.1, 137.5, 136.6, 131.7, 128.5, 128.3, 128.2, 127.9, 127.8, 127.3, 124.5, 122.0, 118.2, 106.2, 105.3, 60.8, 19.5, 18.3, 18.1, 14.5. HRMS (ESI): calcd. for $\text{C}_{33}\text{H}_{32}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 505.2486, Found: 505.2479.



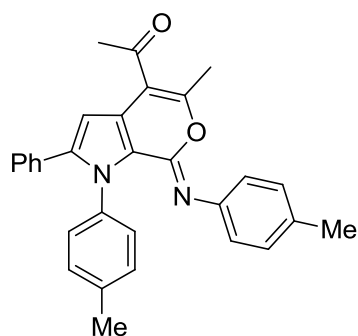
(**4d**): 168 mg, 67% yield, yellow solid: m.p. 123-125 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.23 (s, 5H), 7.12 (t, $J = 7.6$ Hz, 1H), 7.01 (d, $J = 7.5$ Hz, 2H), 6.95 (d, $J = 7.2$ Hz, 2H), 6.81 (t, $J = 7.6$ Hz, 1H), 6.68 (s, 1H), 2.96 (q, $J = 7.3$ Hz, 2H), 2.51 (q, $J = 7.5$ Hz, 2H), 2.07 (s, 6H), 1.93 (s, 6H), 1.29 (t, $J = 7.3$ Hz, 3H), 1.02 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 202.7, 158.9, 145.2, 141.3, 140.5, 137.4, 136.5, 131.4, 128.5, 128.3, 128.0, 127.9, 127.8, 127.7, 127.2, 124.0, 121.8, 118.4, 113.9, 104.4, 36.9, 25.3, 18.2, 18.1, 12.0, 8.7. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 503.2693, Found: 503.2696.



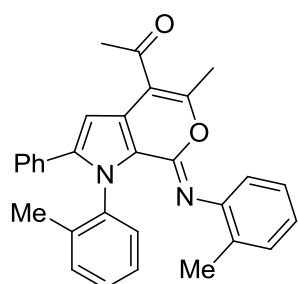
(**4e**): 141 mg, 50% yield, yellow solid: m.p. 149-151 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.36-7.31 (m, 1H), 7.29 (d, $J = 4.4$ Hz, 4H), 7.27-7.23 (m, 5H), 7.14 (t, $J = 7.5$ Hz, 1H), 7.03 (d, $J = 7.5$ Hz, 2H), 6.98 (s, 1H), 6.92 (d, $J = 7.5$ Hz, 2H), 6.77 (t, $J = 7.5$ Hz, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 2.09 (s, 6H), 1.94 (s, 6H), 1.15 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 166.6, 155.7, 144.9, 141.6, 140.1, 137.4, 136.5, 133.3, 131.5, 129.6, 128.6, 128.3, 128.0, 127.9, 127.8, 127.7, 127.3, 124.8, 121.9, 118.7, 106.5, 105.2, 61.1, 18.3, 18.1, 13.8. HRMS (ESI): calcd. for $\text{C}_{38}\text{H}_{34}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 567.2642, Found: 567.2630.



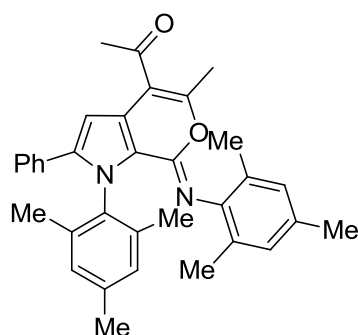
(**4f**): 135 mg, 52% yield, yellow solid: m.p. 96-97 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.25-7.21 (m, 5H), 7.12 (t, $J = 7.5$ Hz, 1H), 7.04 (s, 1H), 7.00 (d, $J = 7.5$ Hz, 2H), 6.94 (d, $J = 7.5$ Hz, 2H), 6.80 (t, $J = 7.5$ Hz, 1H), 4.44 (q, $J = 7.1$ Hz, 2H), 2.74 (t, $J = 7.5$ Hz, 2H), 2.06 (s, 6H), 1.91 (s, 6H), 1.47 (t, $J = 7.1$ Hz, 3H), 0.85 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 166.1, 163.5, 145.2, 141.1, 140.3, 137.5, 136.5, 131.7, 128.5, 128.3, 127.9, 127.8, 127.7, 127.2, 124.5, 121.8, 118.1, 106.1, 105.2, 60.8, 33.9, 20.8, 18.2, 18.1, 14.5, 13.7. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 519.2642, Found: 519.2647.



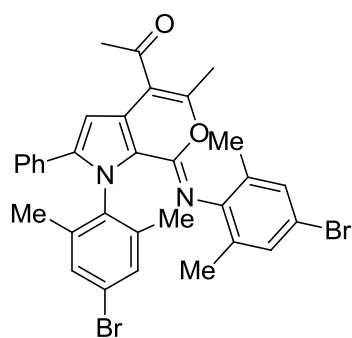
(5a): 125 mg, 56% yield, white solid: m.p. 177-178 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.23-7.18 (m, 5H), 7.12 (q, $J = 9.4$ Hz, 4H), 7.02 (d, $J = 7.8$ Hz, 2H), 6.91 (d, $J = 8.0$ Hz, 2H), 6.64 (s, 1H), 2.62 (s, 3H), 2.41 (s, 3H), 2.37 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.3, 156.6, 142.8, 142.6, 140.6, 137.6, 135.7, 132.7, 131.7, 129.0, 128.9, 128.5, 128.1, 127.7, 124.0, 123.5, 120.0, 114.7, 105.1, 31.7, 21.3, 21.0, 19.0. HRMS (ESI): calcd. for $\text{C}_{30}\text{H}_{26}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 447.2067, Found: 447.2067.



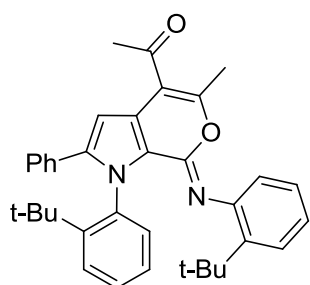
(5b): 145 mg, 65% yield, yellow solid: m.p. 158-160 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.23-7.11 (m, 10H), 7.10-7.05 (m, 2H), 6.89 (t, $J = 7.1$ Hz, 1H), 6.74 (s, 1H), 2.64 (s, 3H), 2.36 (s, 3H), 2.06 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.3, 156.8, 144.5, 142.3, 140.6, 138.1, 136.8, 131.9, 131.5, 130.2, 129.2, 128.5, 128.2, 127.9, 126.1, 125.5, 124.0, 122.8, 121.3, 119.9, 114.7, 105.0, 31.8, 19.0, 18.0, 17.9. HRMS (ESI): calcd. for $\text{C}_{30}\text{H}_{26}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 447.2067, Found: 447.2068.



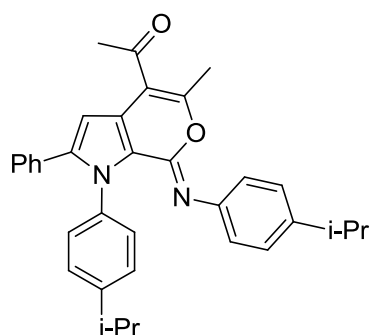
(5c): 118 mg, 47% yield, red oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.23 (s, 5H), 6.78 (d, $J = 5.6$ Hz, 5H), 2.64 (s, 3H), 2.26 (s, 3H), 2.23 (s, 6H), 1.98 (s, 6H), 1.87 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.5, 156.9, 142.2, 141.3, 139.9, 137.9, 135.9, 134.8, 131.6, 131.1, 128.5, 128.3, 128.1, 128.0, 127.8, 123.7, 118.6, 114.5, 104.7, 31.7, 21.1, 20.7, 19.3, 18.2, 18.0. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 503.2693, Found: 503.2699.



(5d): 200 mg, 70% yield, yellow solid: m.p. 150-152 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.26-7.24 (m, 3H), 7.20-7.18 (m, 2H), 7.16 (s, 2H), 7.08 (s, 2H), 6.79 (s, 1H), 2.63 (s, 3H), 2.25 (s, 3H), 1.99 (s, 6H), 1.86 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.2, 156.9, 143.7, 141.8, 140.6, 138.6, 136.5, 130.9, 130.6, 130.4, 130.0, 128.5, 128.3, 127.8, 124.6, 122.2, 118.1, 114.7, 105.2, 31.7, 19.2, 18.1, 17.9. HRMS (ESI): calcd. for $\text{C}_{32}\text{H}_{29}\text{Br}_2\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 631.0596, Found: 631.0590.



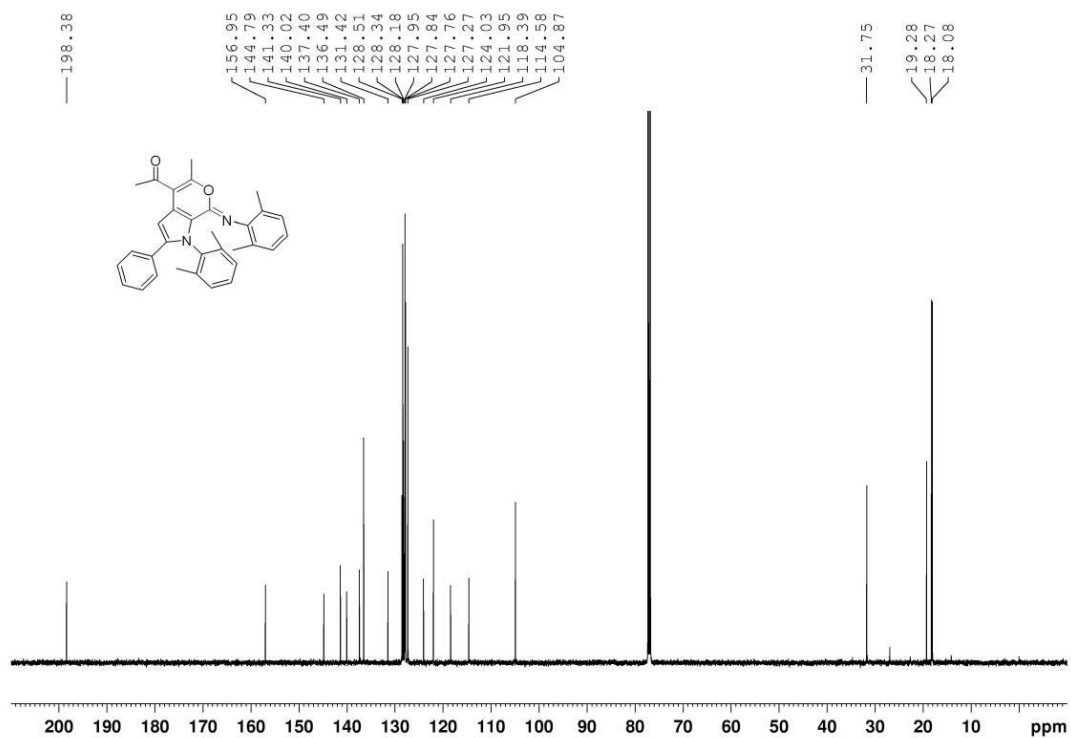
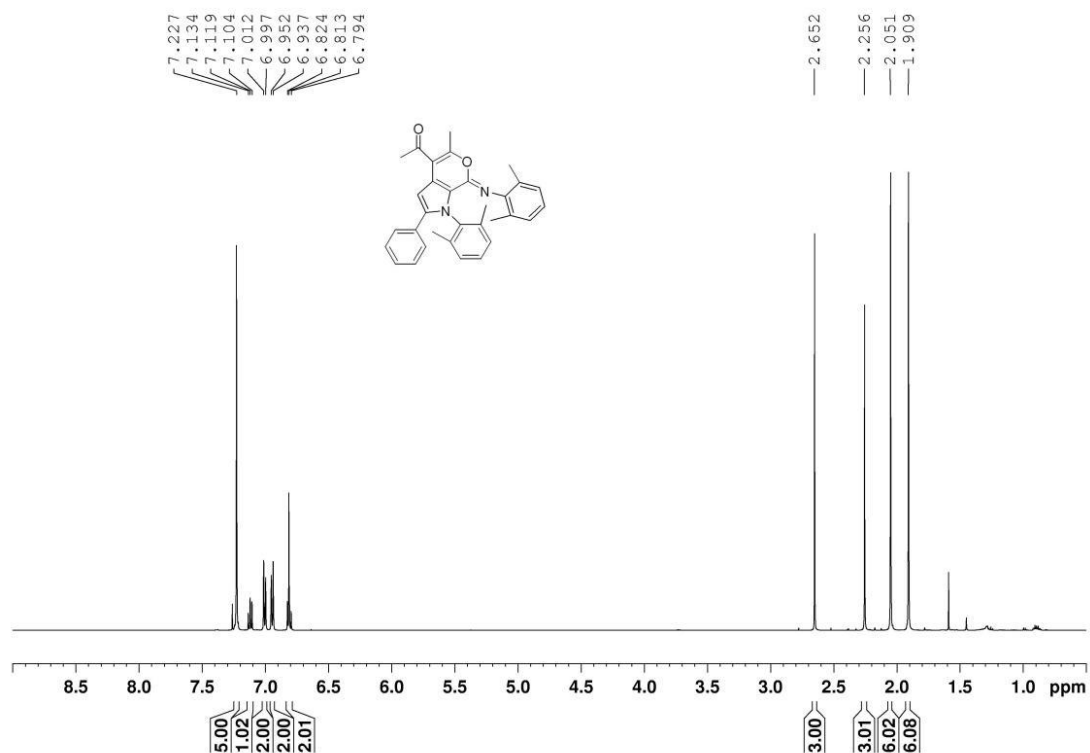
(5e): 135 mg, 51% yield, reddish brown solid: m.p. 83-85 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.41 (dd, J = 8.1, 1.0 Hz, 1H), 7.27-7.24 (m, 2H), 7.22-7.13 (m, 7H), 7.07-7.04 (m, 1H), 6.93-6.90 (m, 1H), 6.74-6.73 (m, 2H), 2.63 (s, 3H), 2.25 (s, 3H), 1.02 (s, 9H), 1.01 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.4, 157.3, 146.6, 145.7, 143.3, 141.5, 141.4, 135.6, 132.2, 131.9, 129.9, 128.7, 128.6, 128.2, 127.7, 126.1, 125.9, 125.8, 124.3, 122.9, 122.4, 121.3, 114.4, 104.9, 36.3, 34.8, 31.7, 31.4, 29.7, 18.9. HRMS (ESI): calcd. for $\text{C}_{36}\text{H}_{38}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 531.3006, Found: 531.3004.



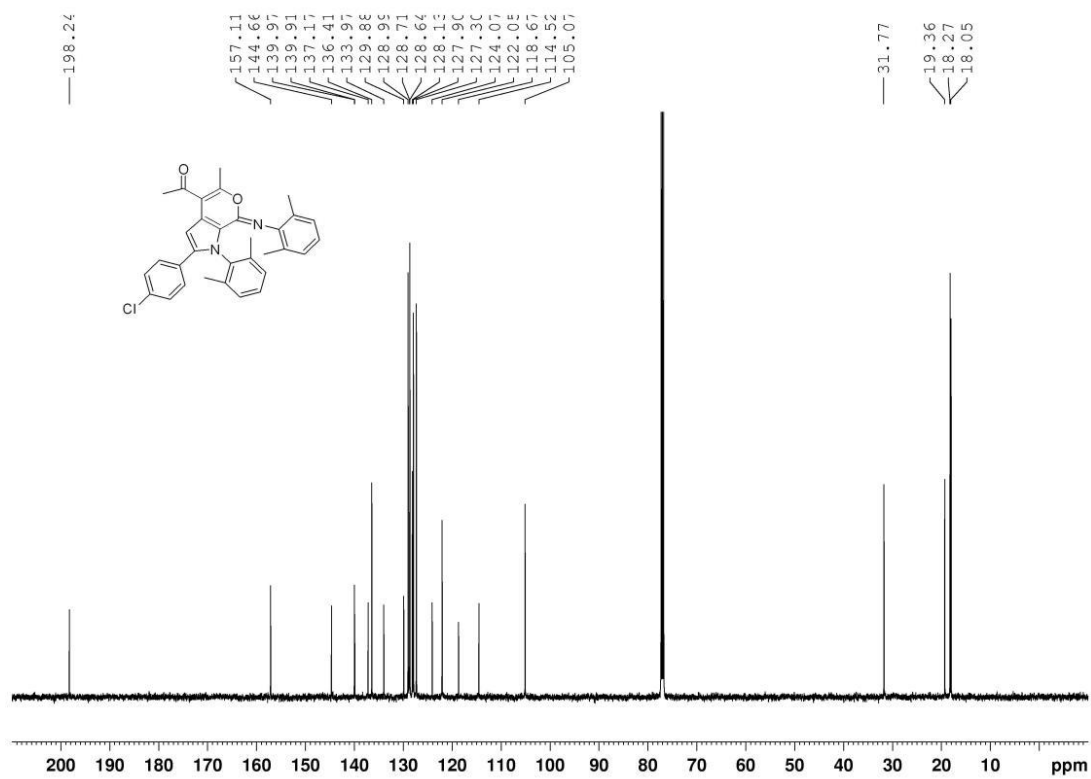
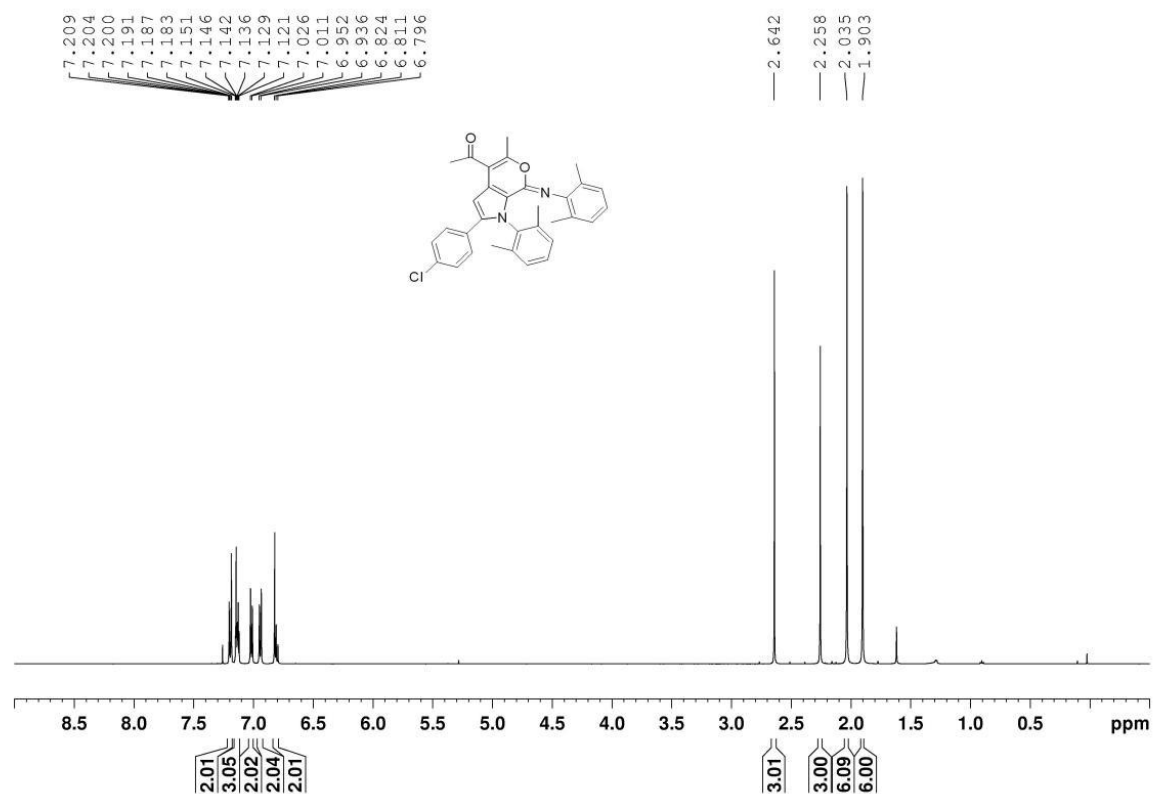
(5f): 110 mg, 44% yield, yellow solid: m.p. 145-146 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.23-7.20 (m, 5H), 7.18 (s, 4H), 7.06 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 8.5 Hz, 2H), 6.64 (s, 1H), 2.97-2.91 (m, 1H), 2.86-2.81 (m, 1H), 2.63 (s, 3H), 2.44 (s, 3H), 1.27 (d, J = 7.0 Hz, 6H), 1.21 (d, J = 6.9 Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.3, 156.6, 146.6, 143.9, 142.7, 142.5, 140.3, 136.1, 131.6, 129.1, 128.9, 128.1, 127.6, 126.2, 125.8, 124.0, 123.8, 120.2, 114.7, 104.9, 33.8, 33.6, 31.7, 24.1, 24.0, 19.0. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 503.2693, Found: 503.2696.

5 ^1H NMR and ^{13}C NMR Spectra of All Compounds

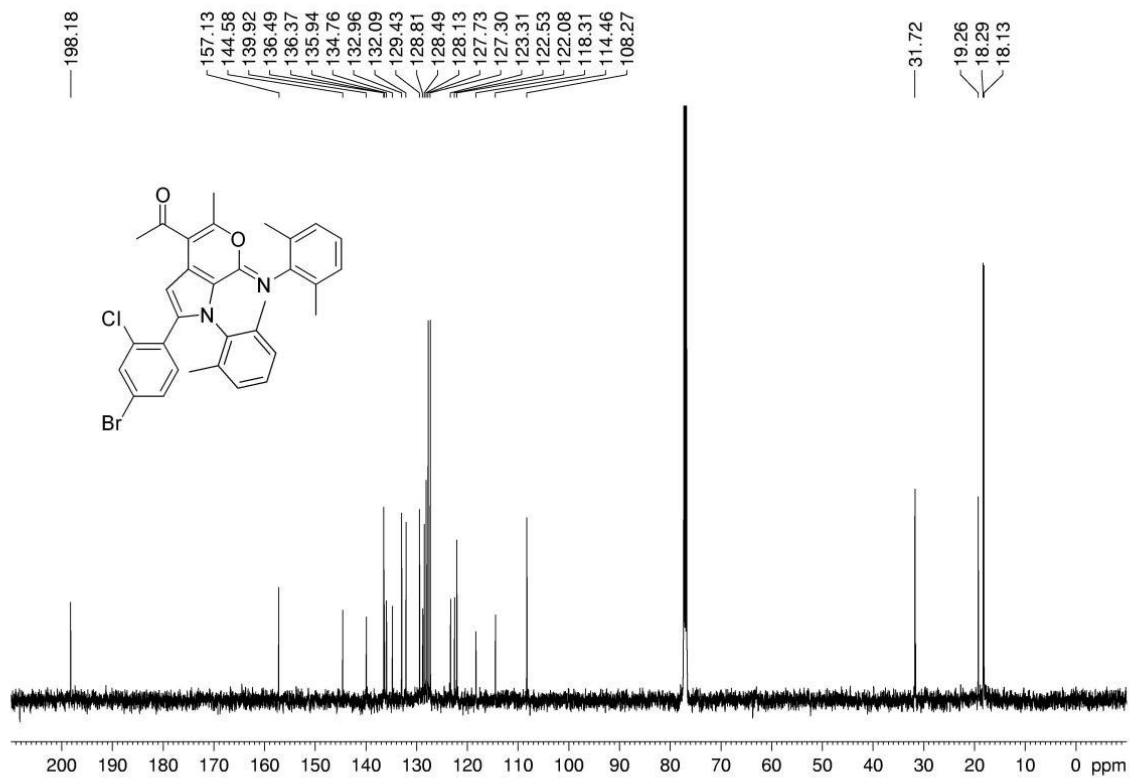
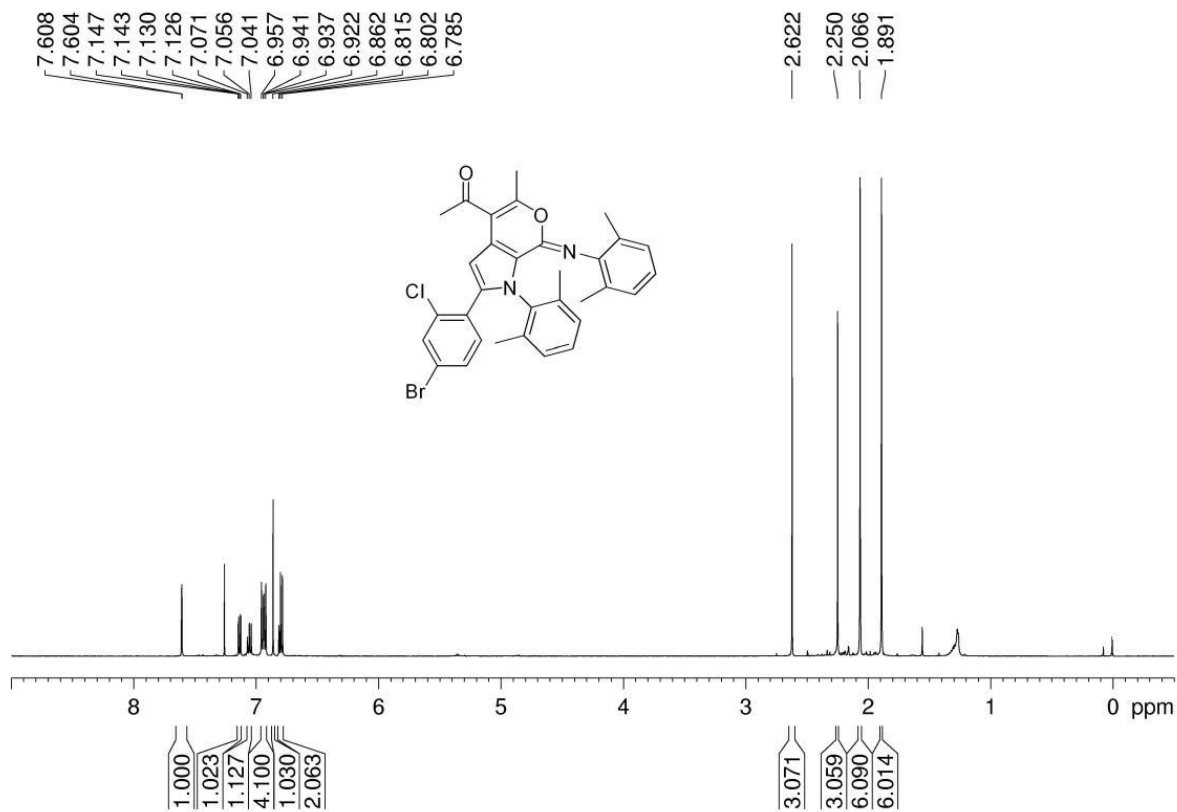
Compound 3a



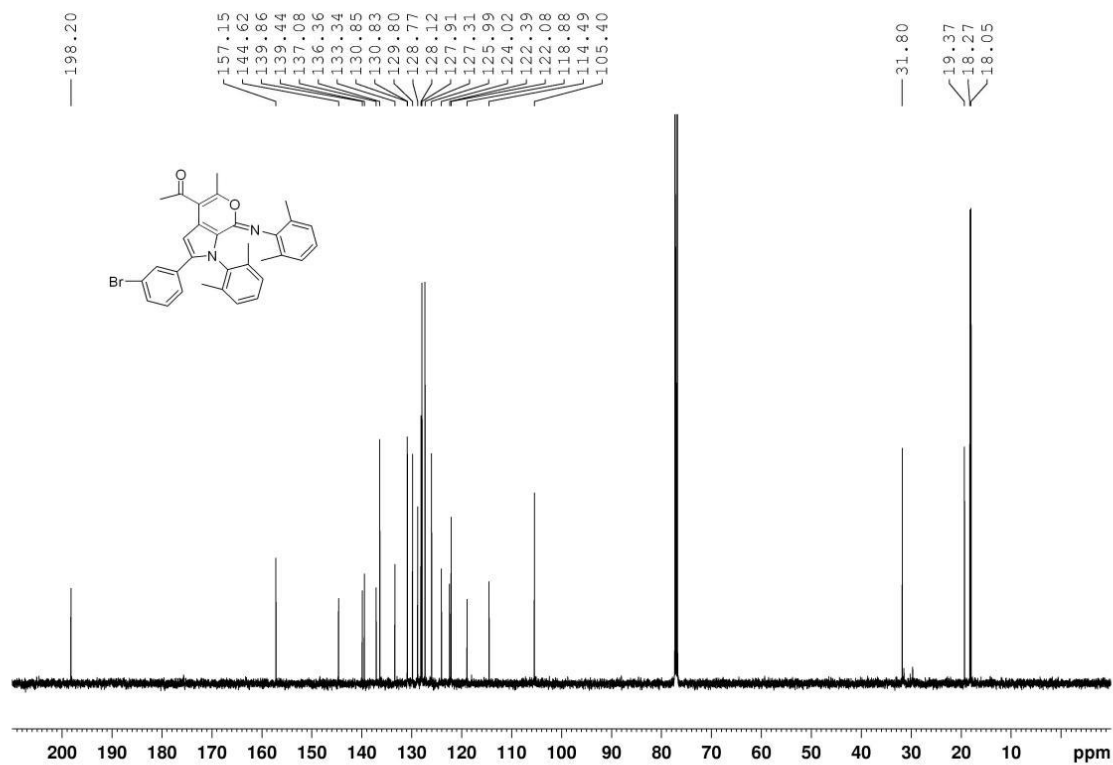
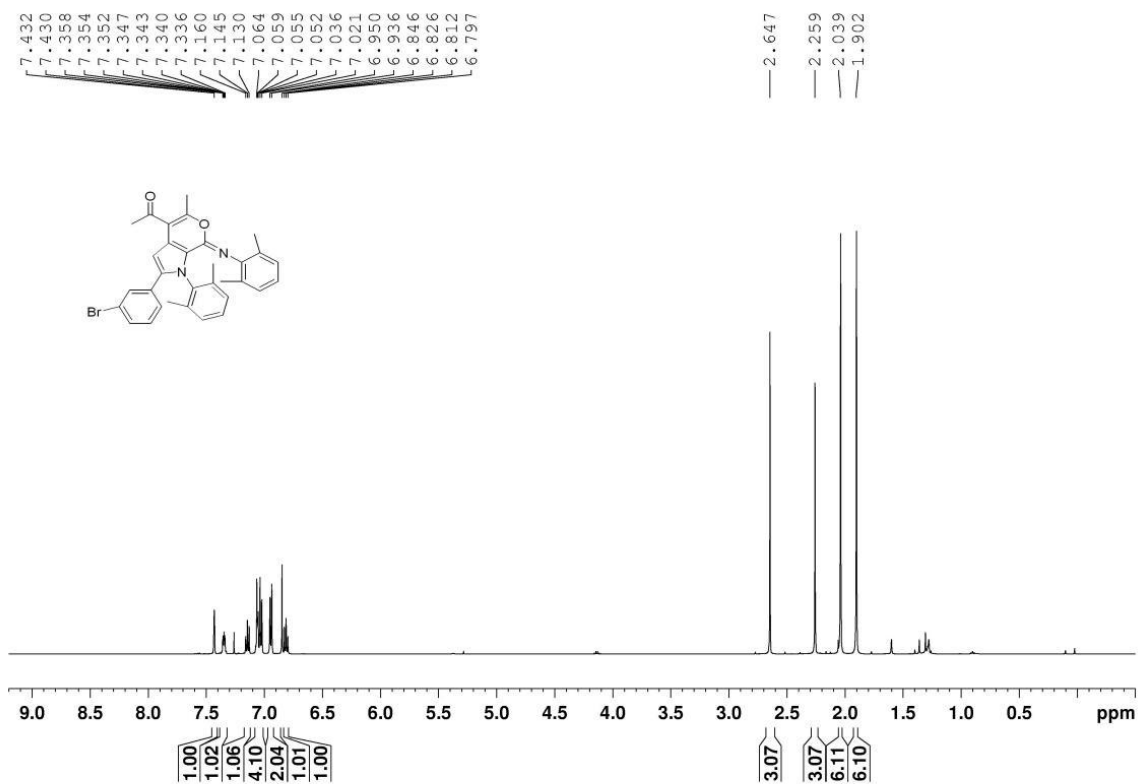
Compound 3b



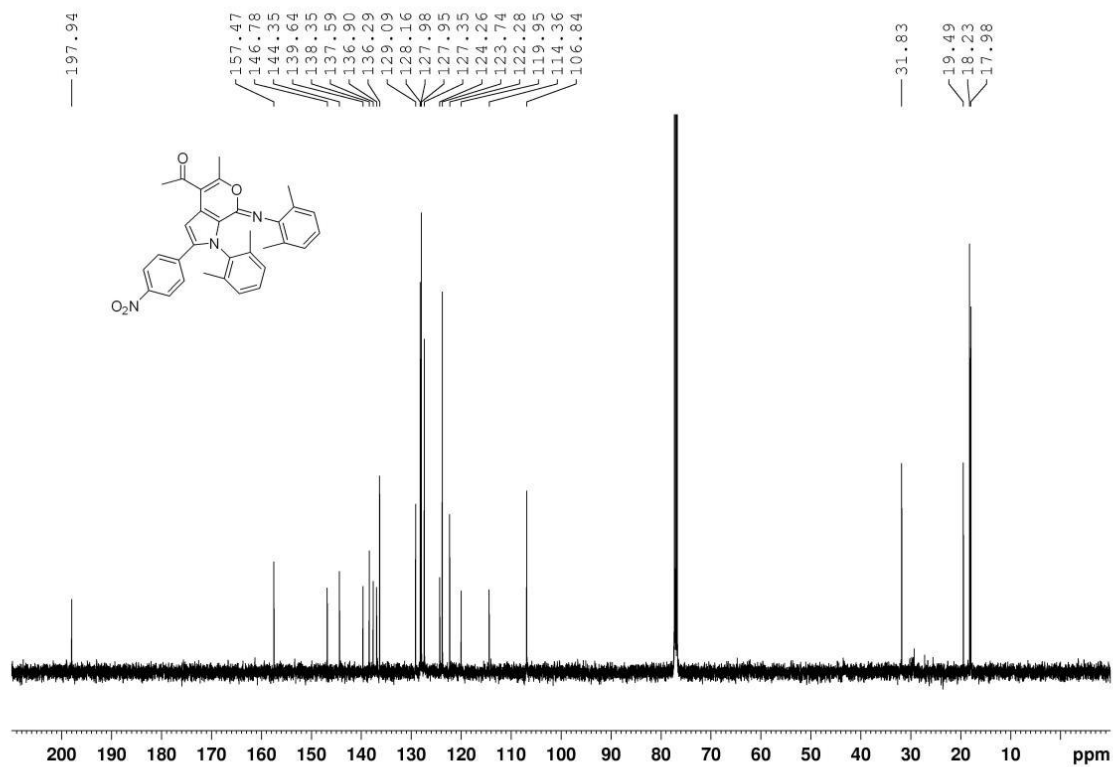
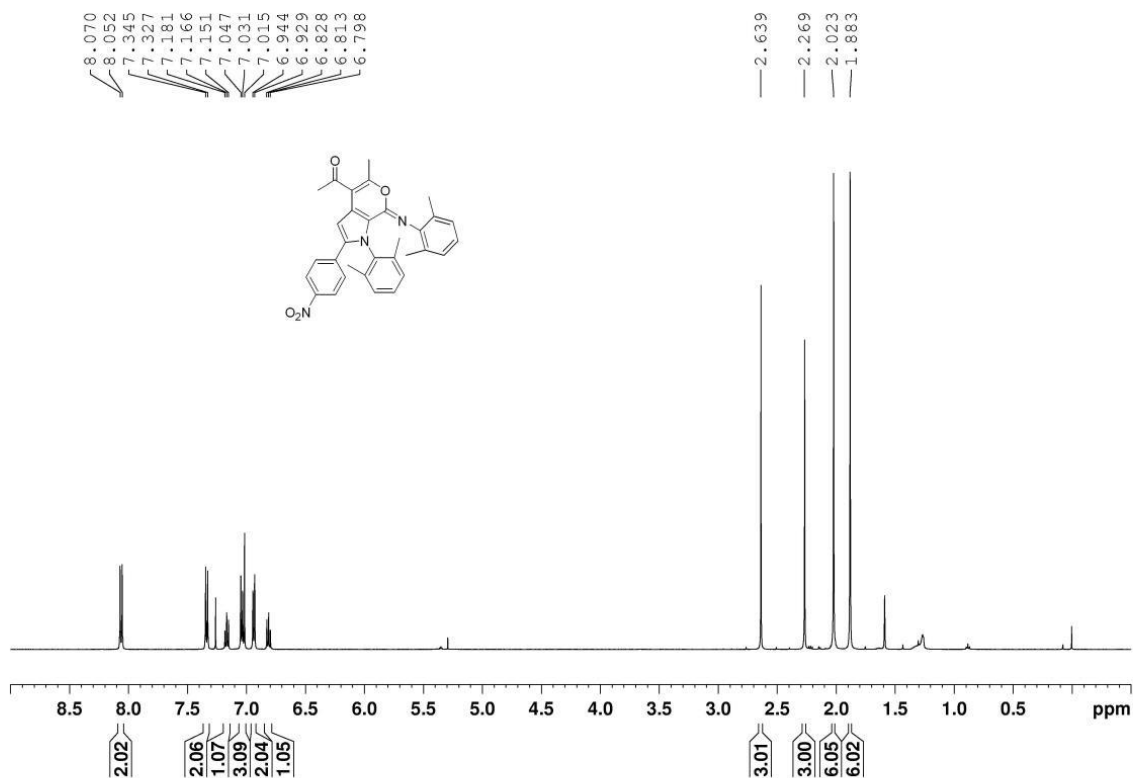
Compound 3c



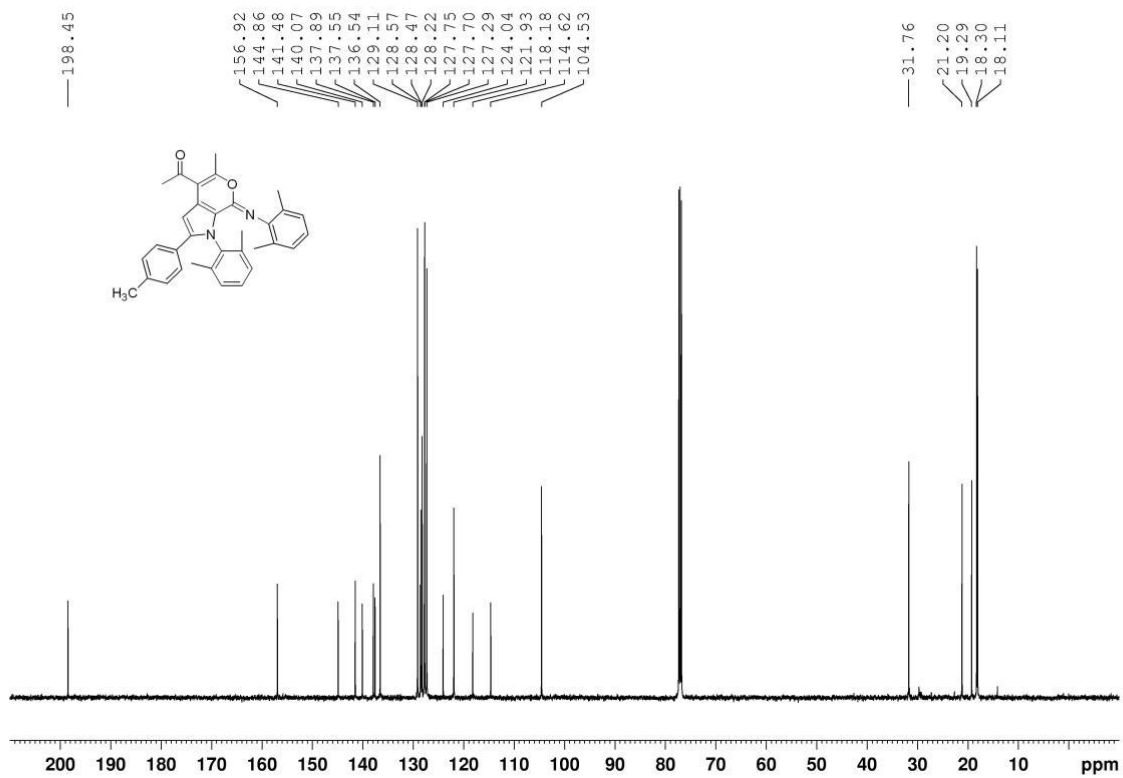
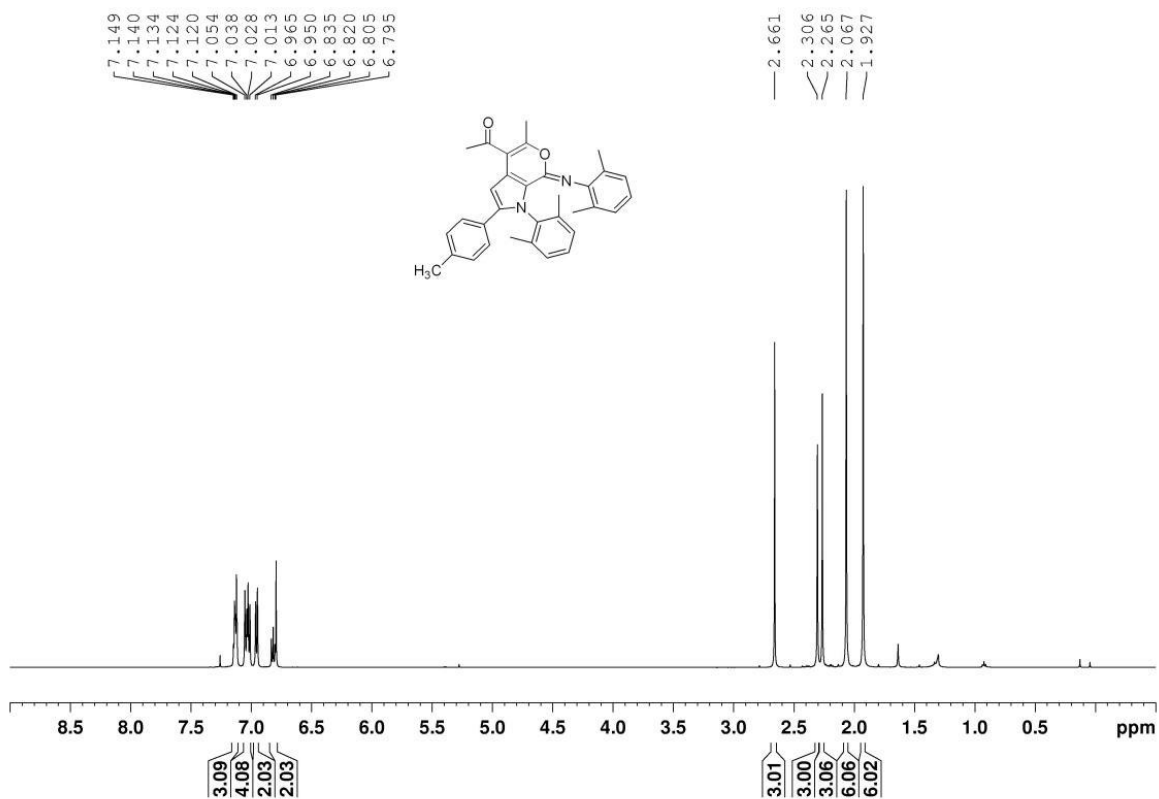
Compound 3d



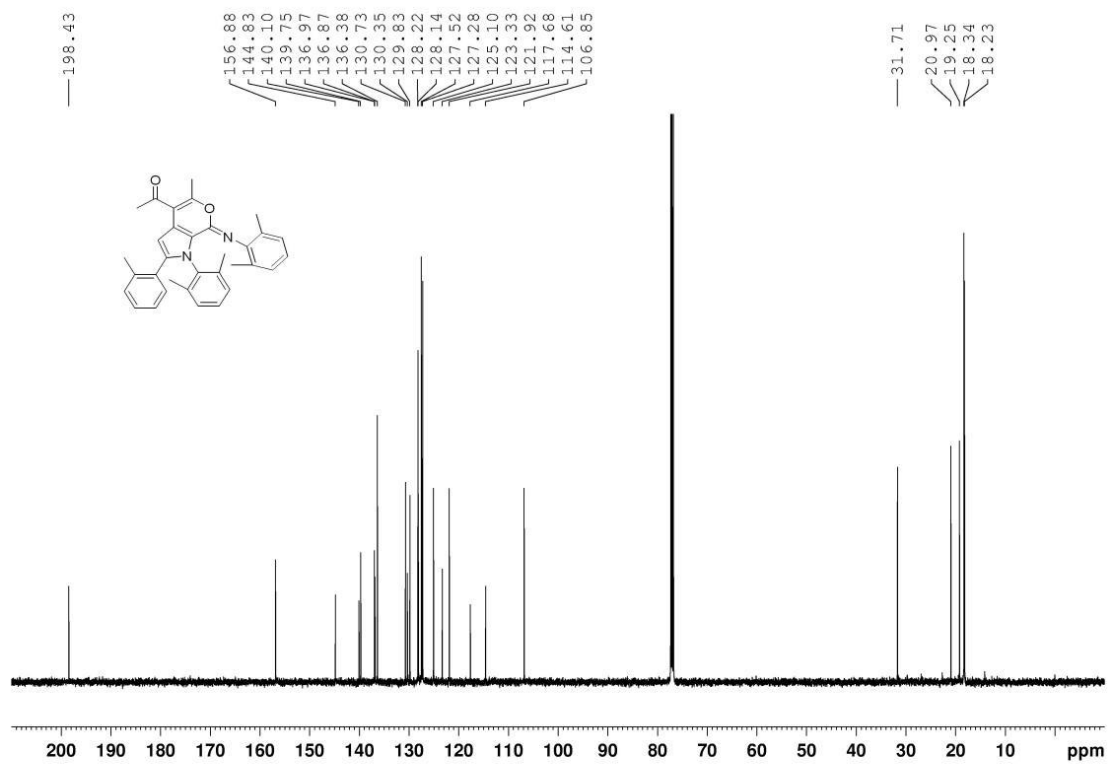
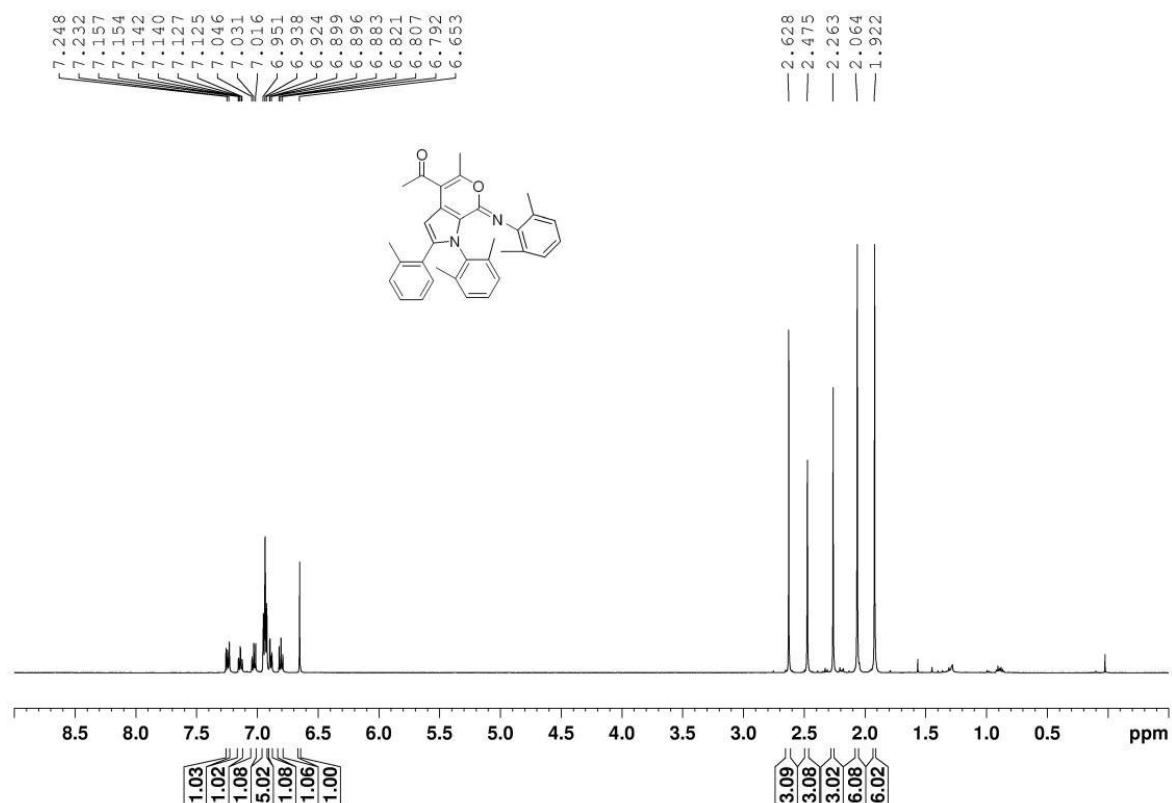
Compound 3e



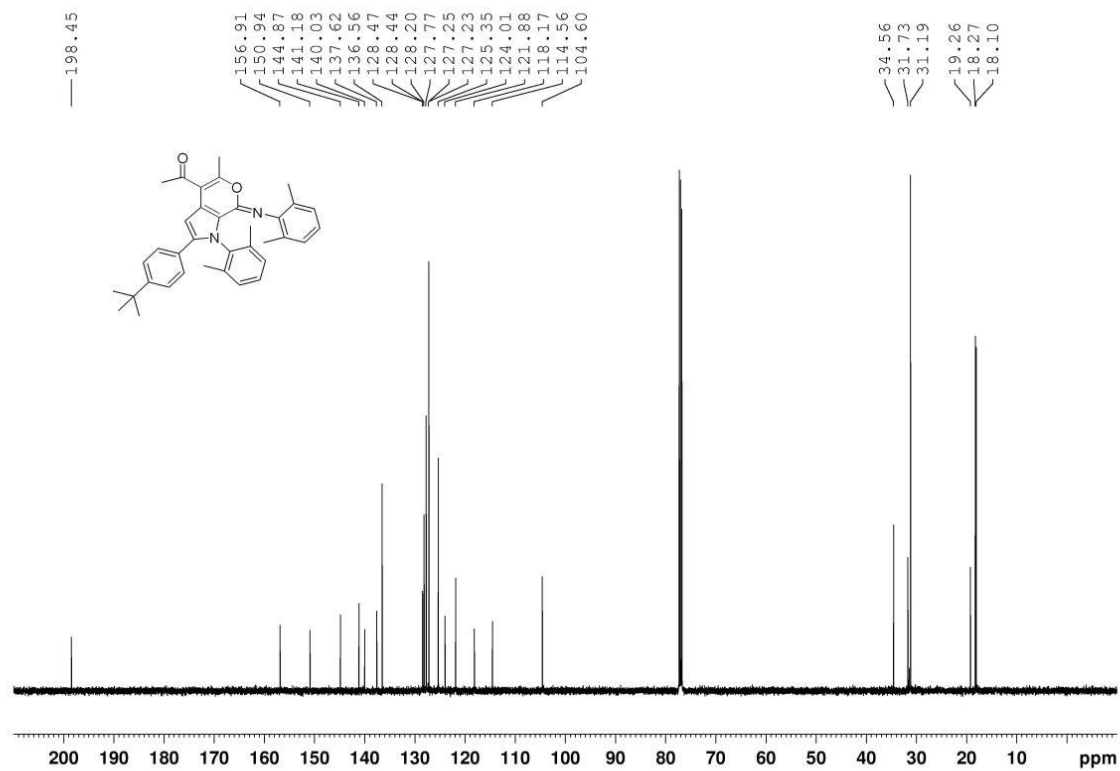
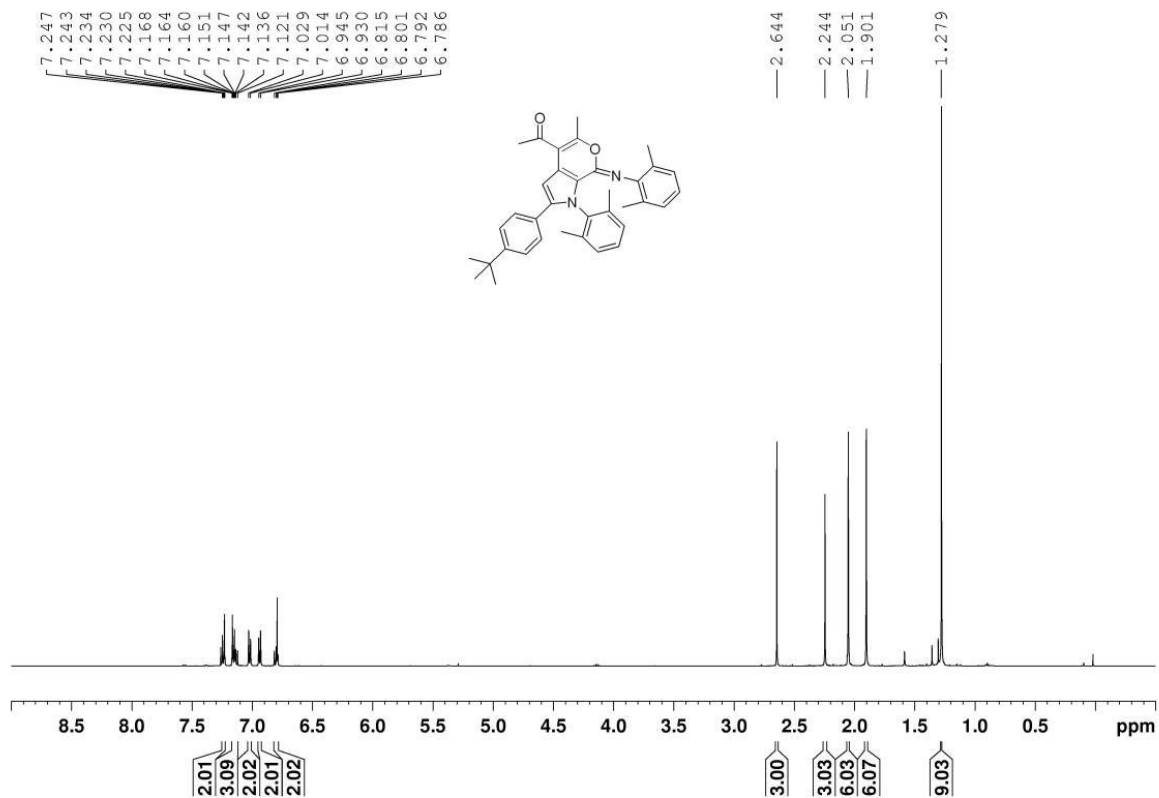
Compound 3f



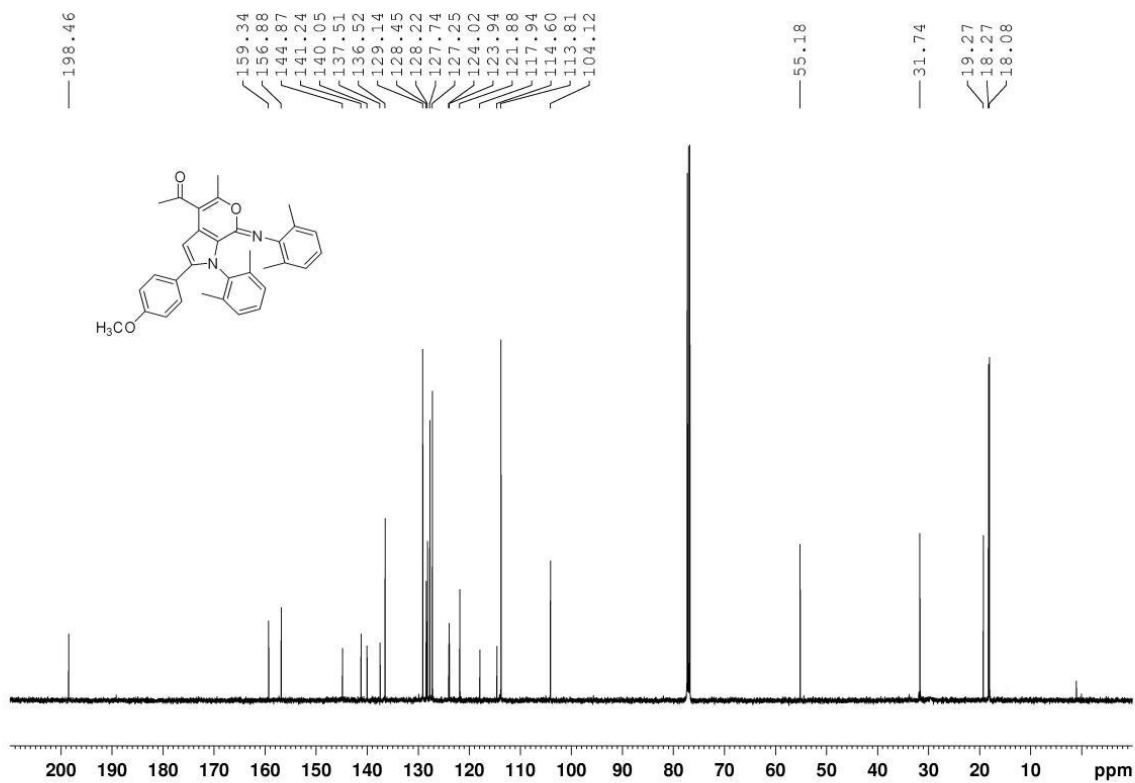
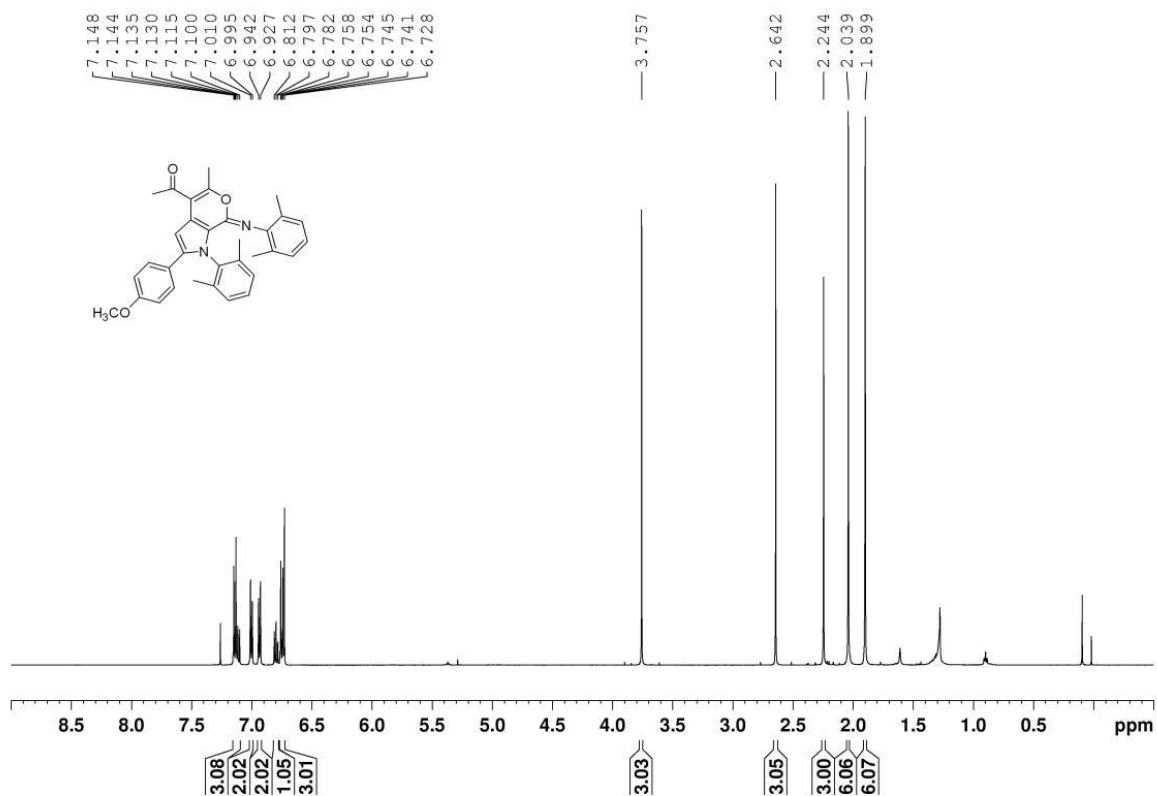
Compound 3g



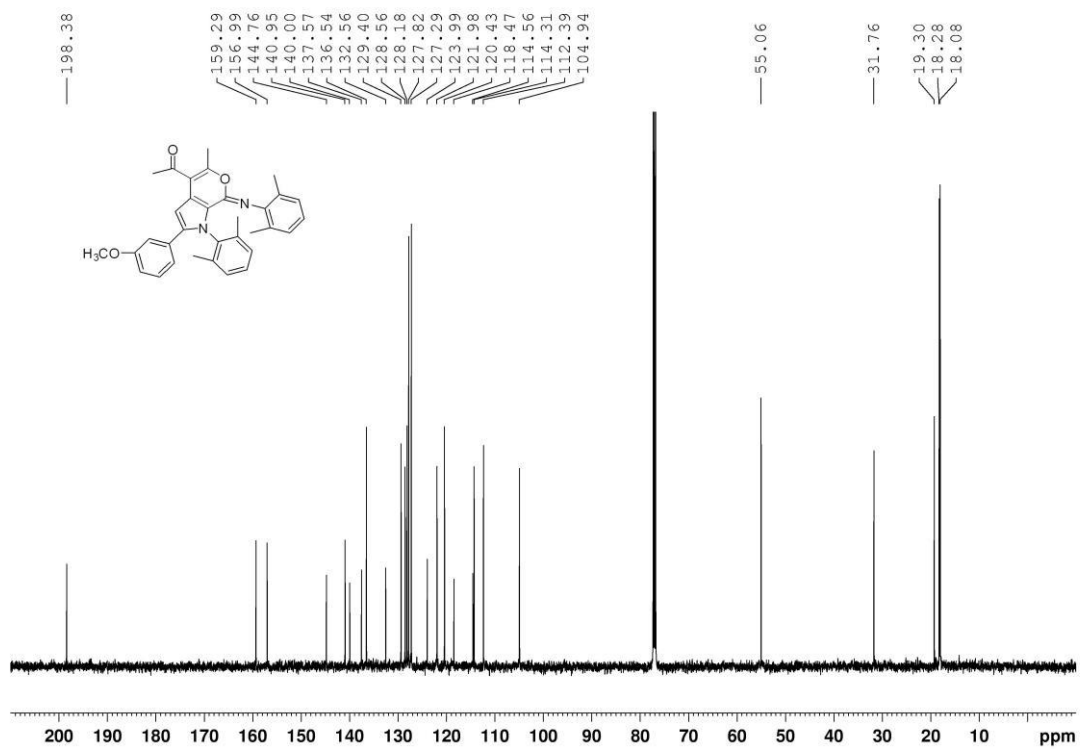
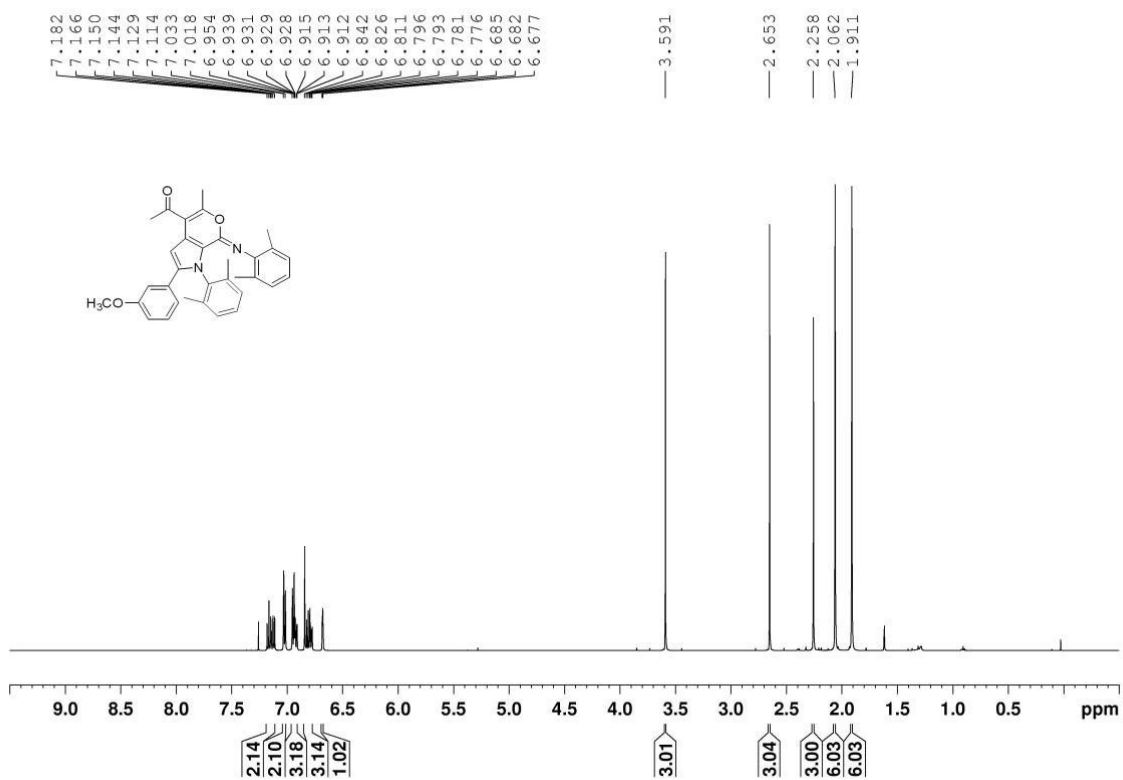
Compound 3h



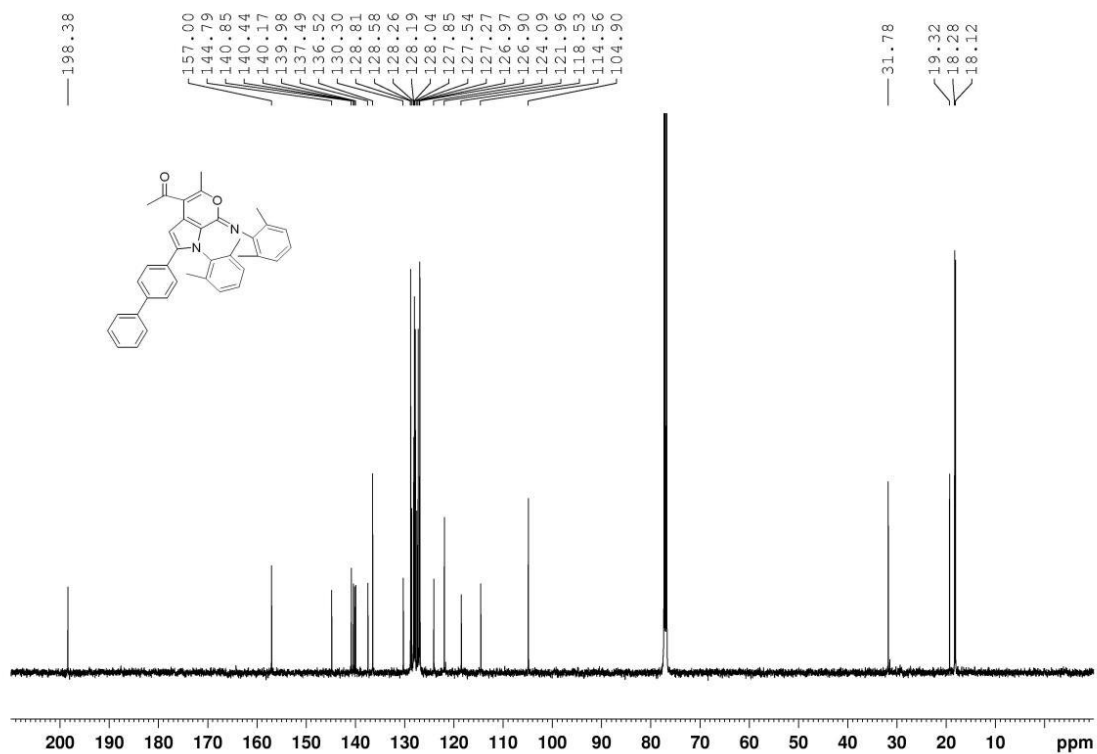
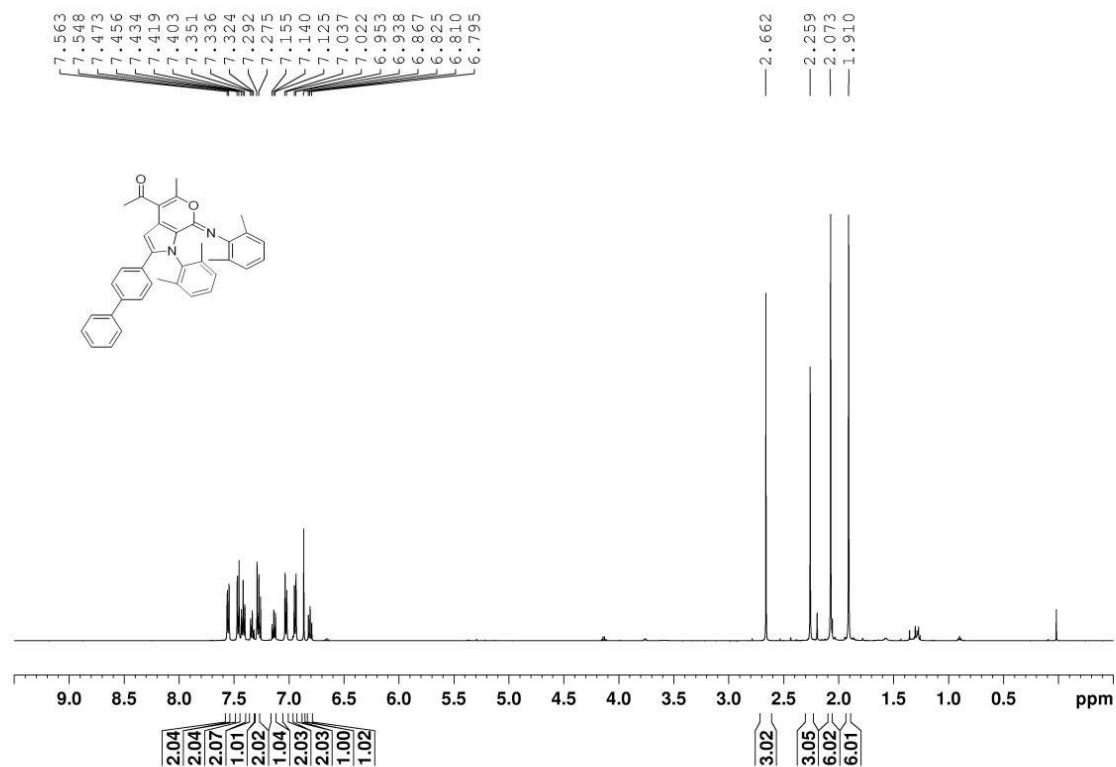
Compound 3i



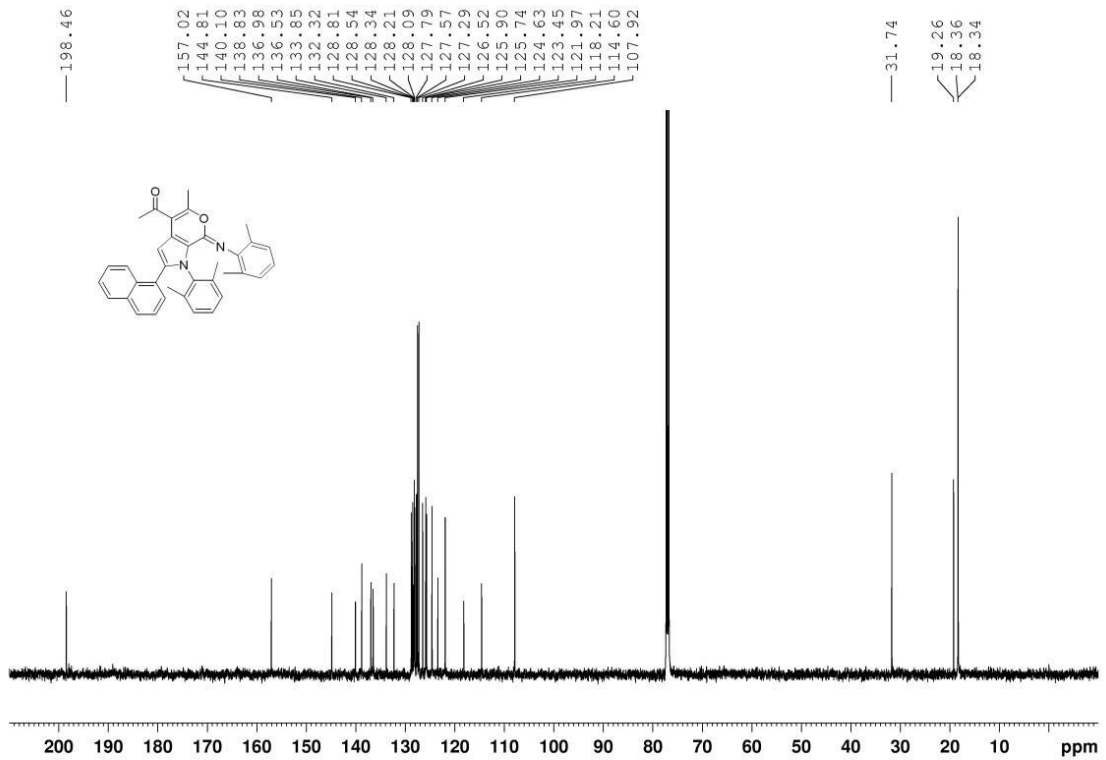
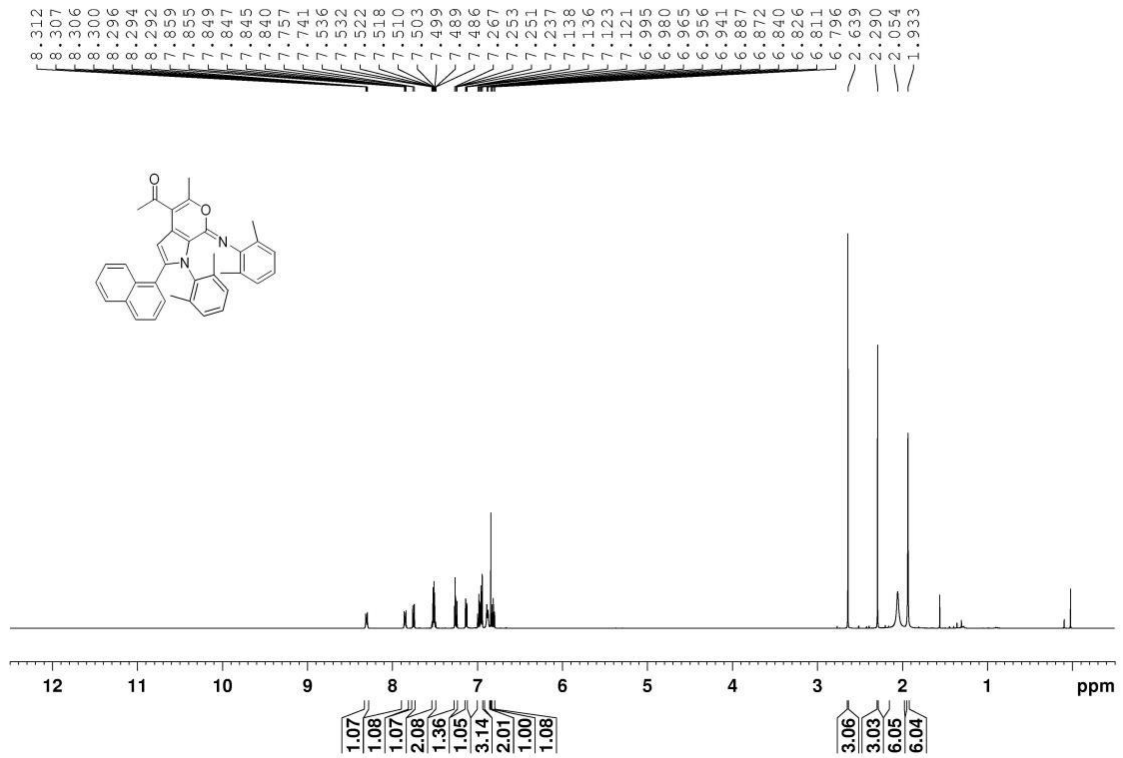
Compound 3j



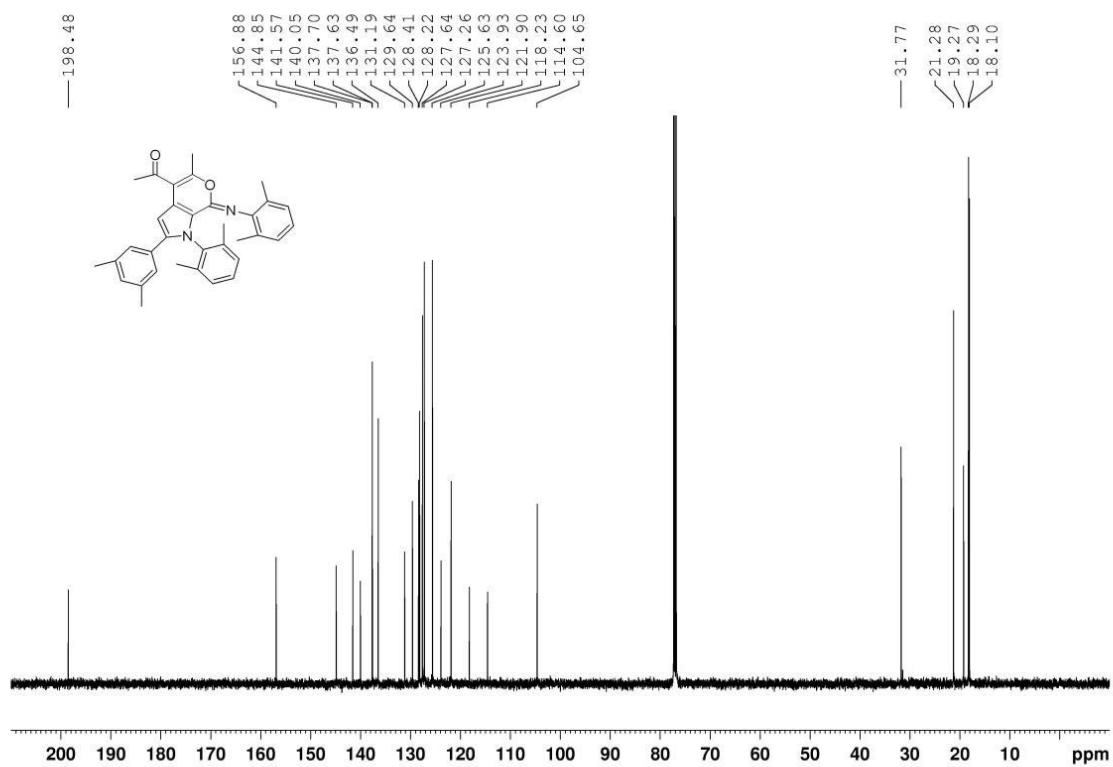
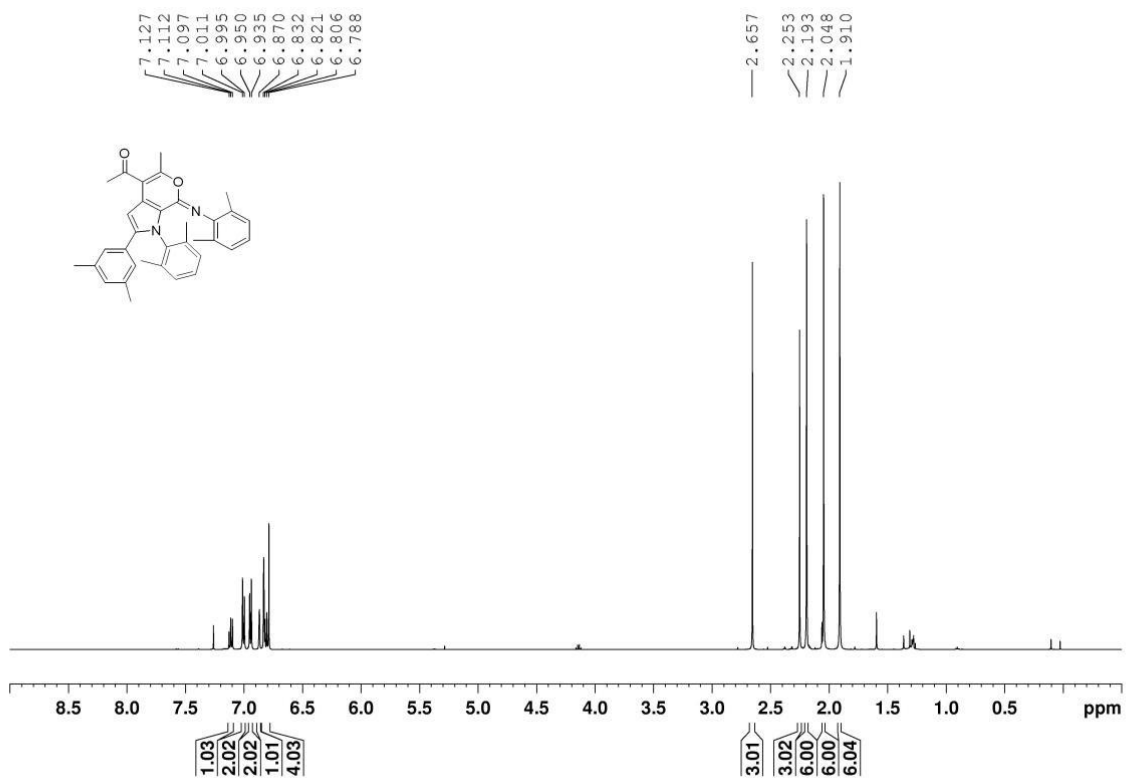
Compound 3k



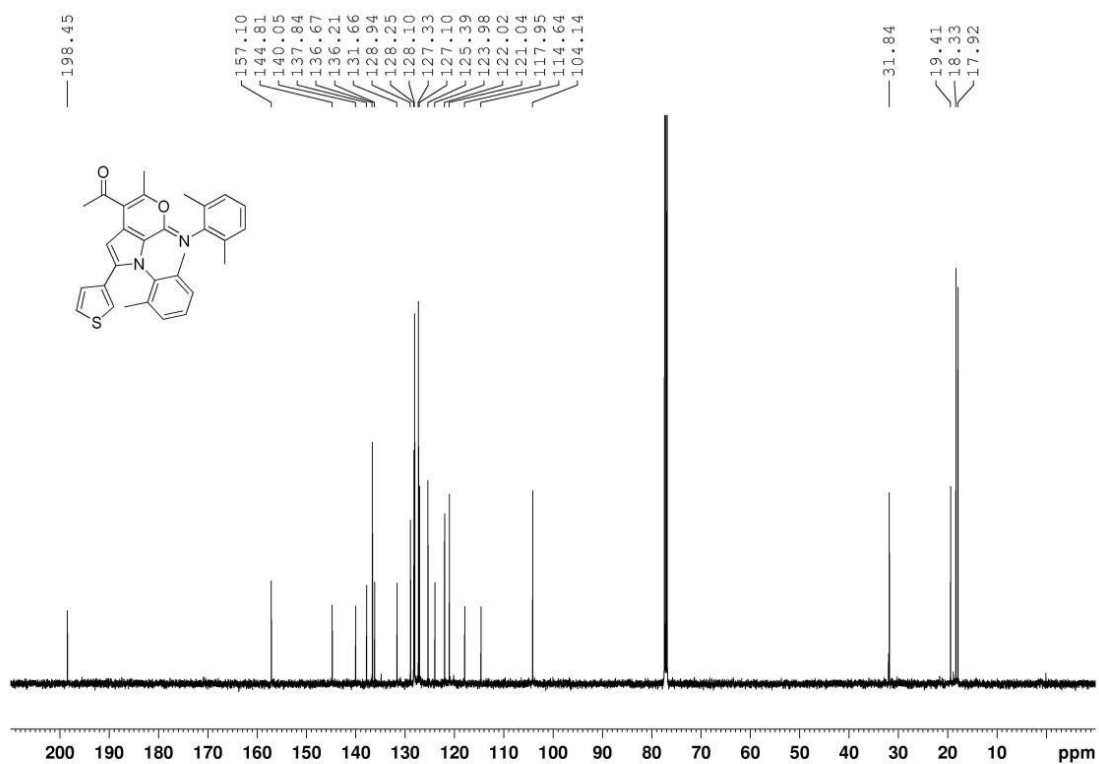
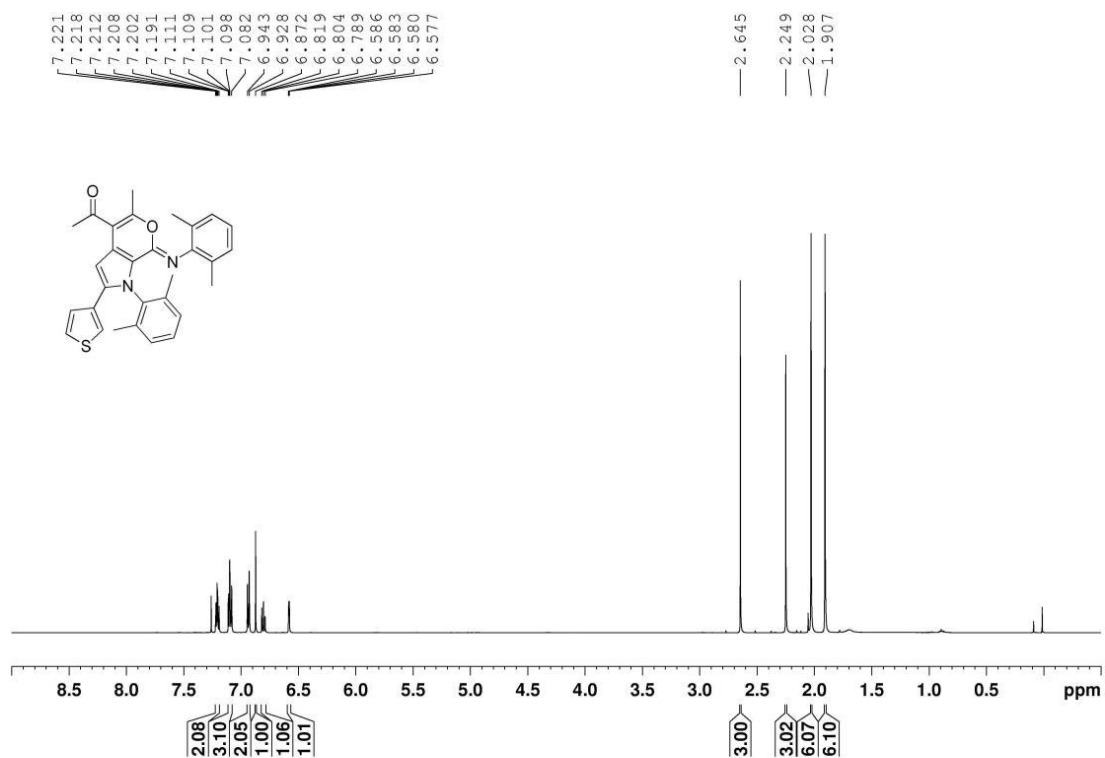
Compound **31**



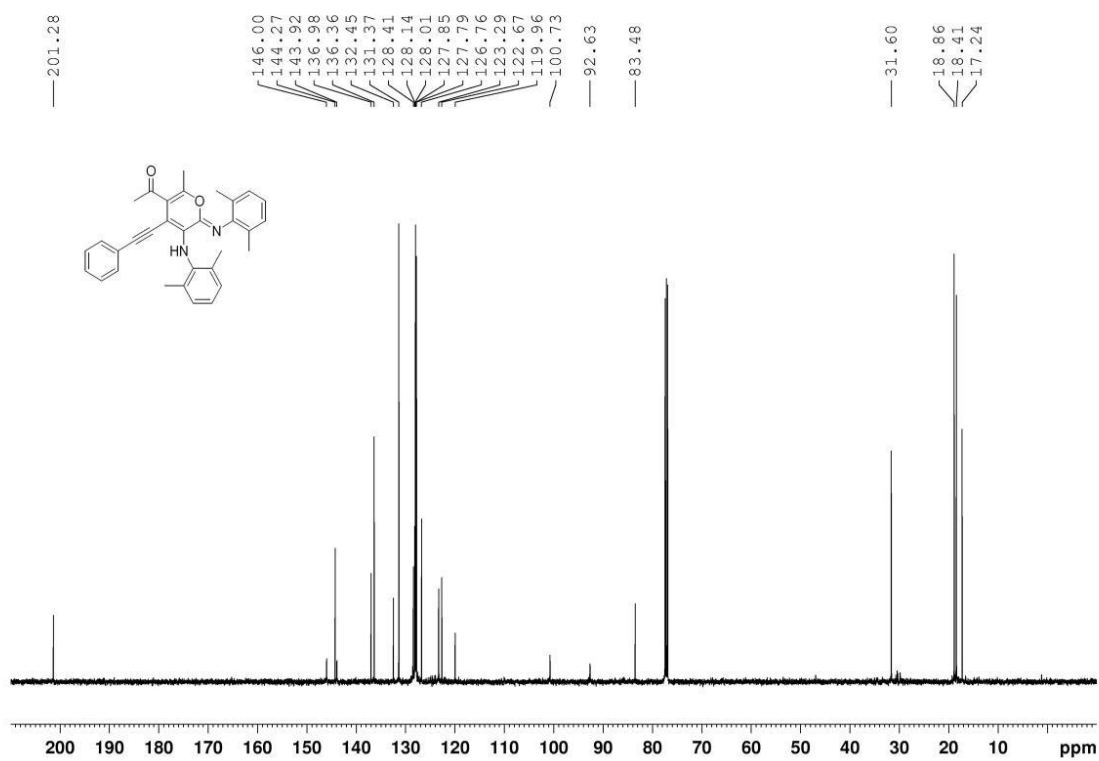
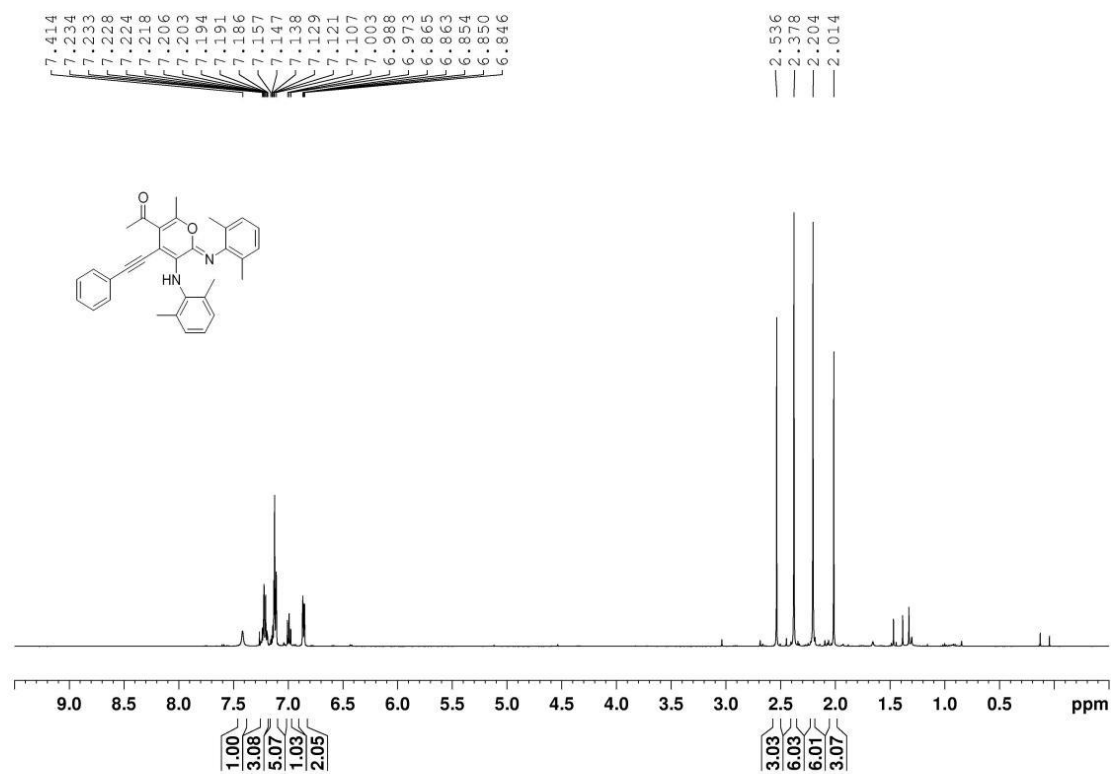
Compound 3m



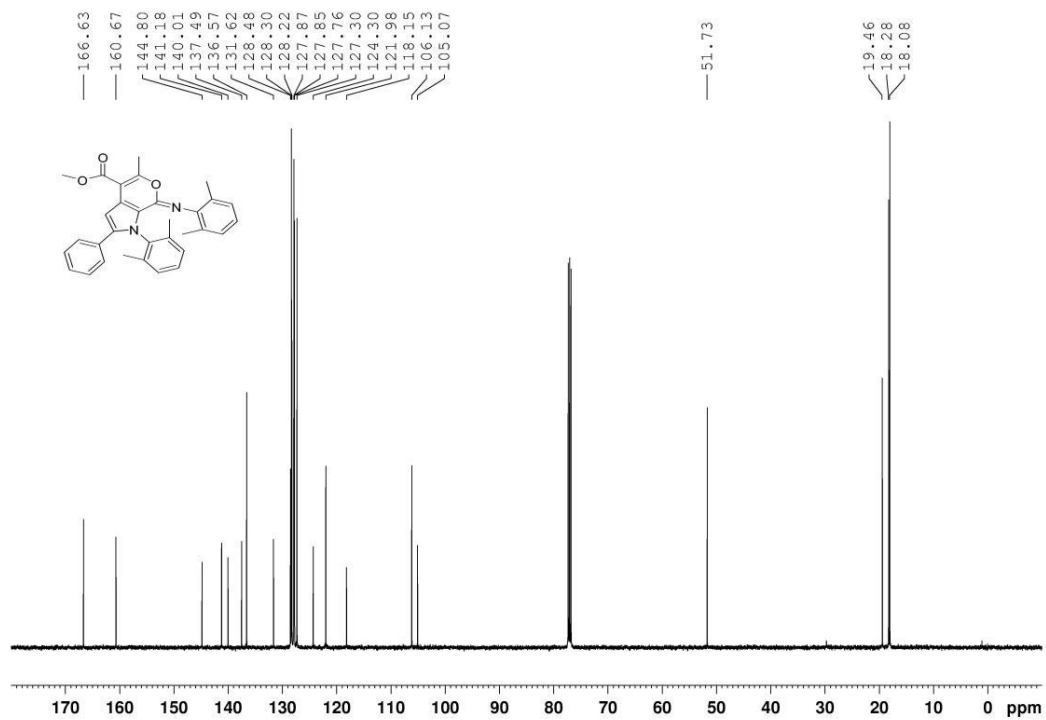
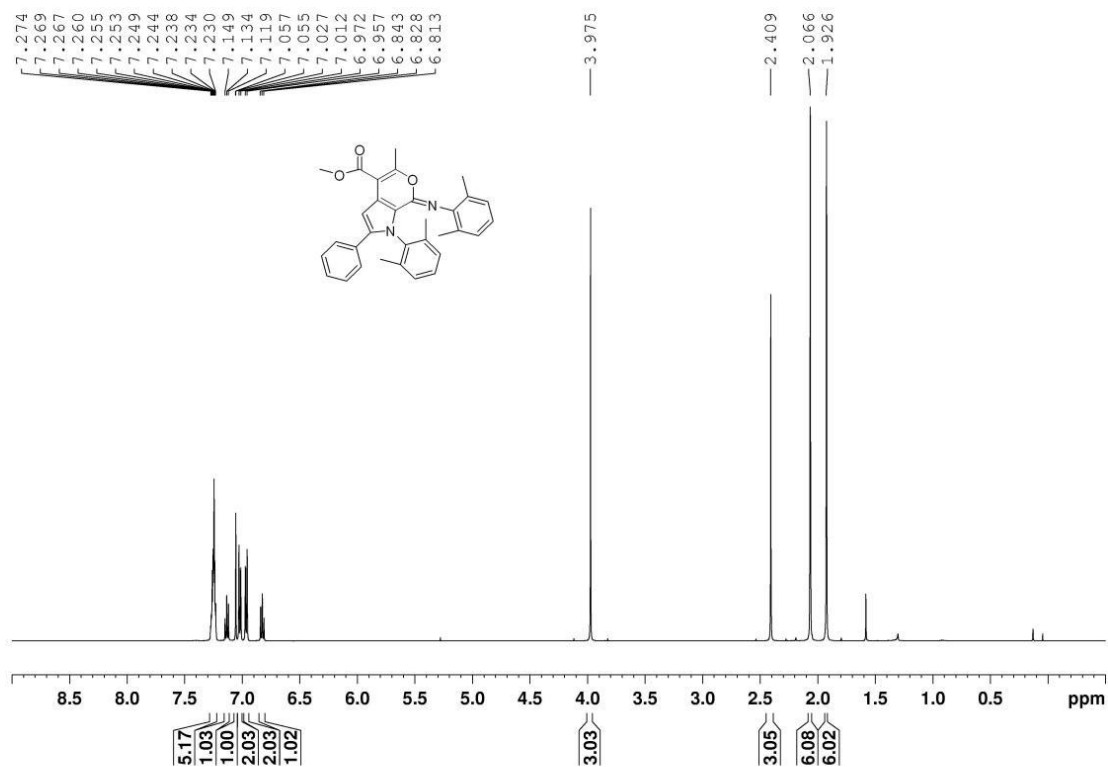
Compound 3n



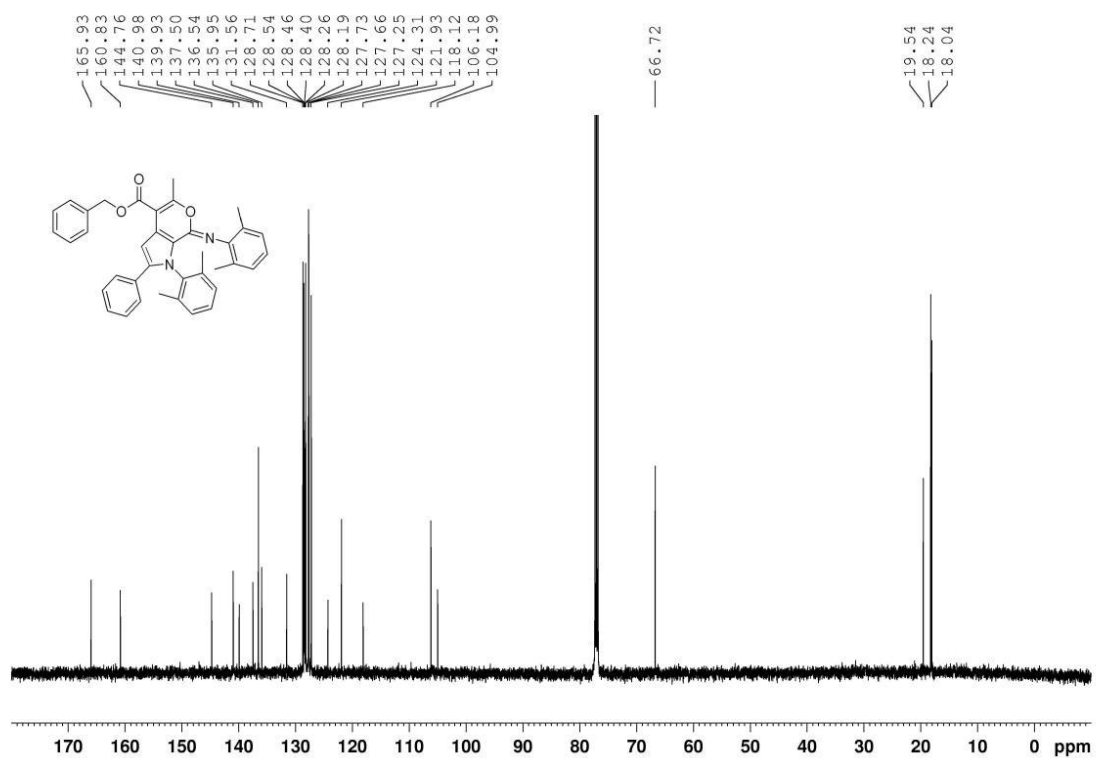
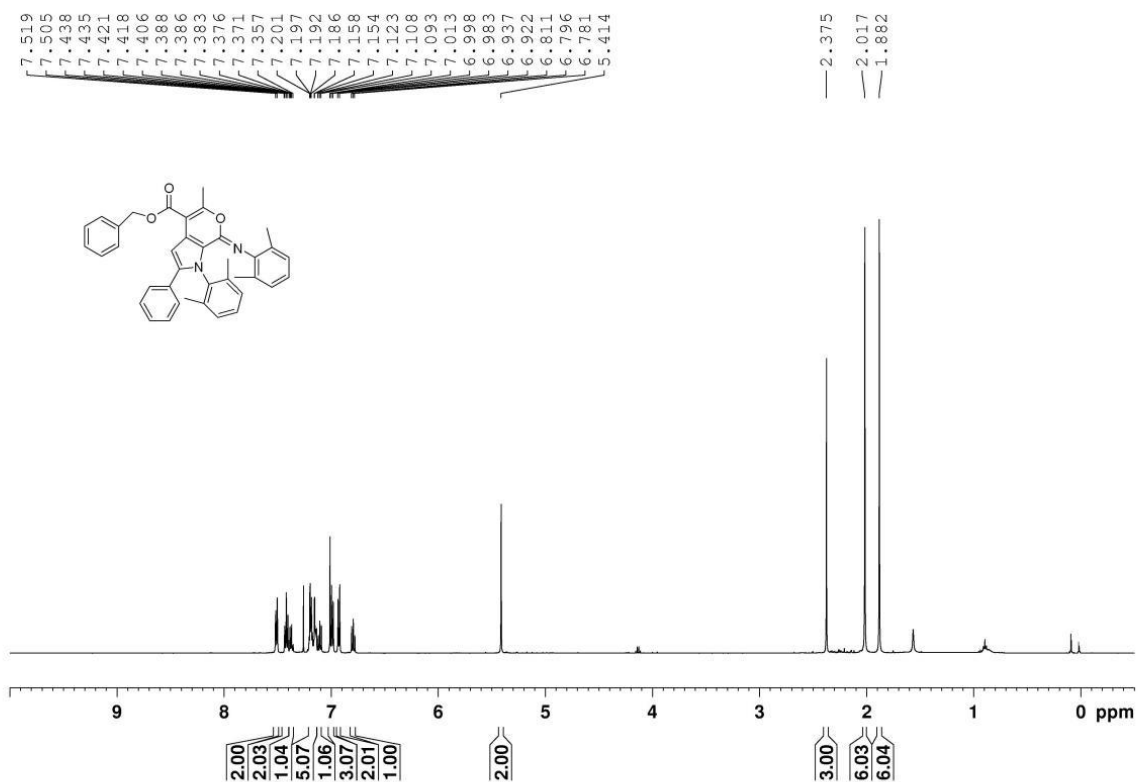
Compound 3a'



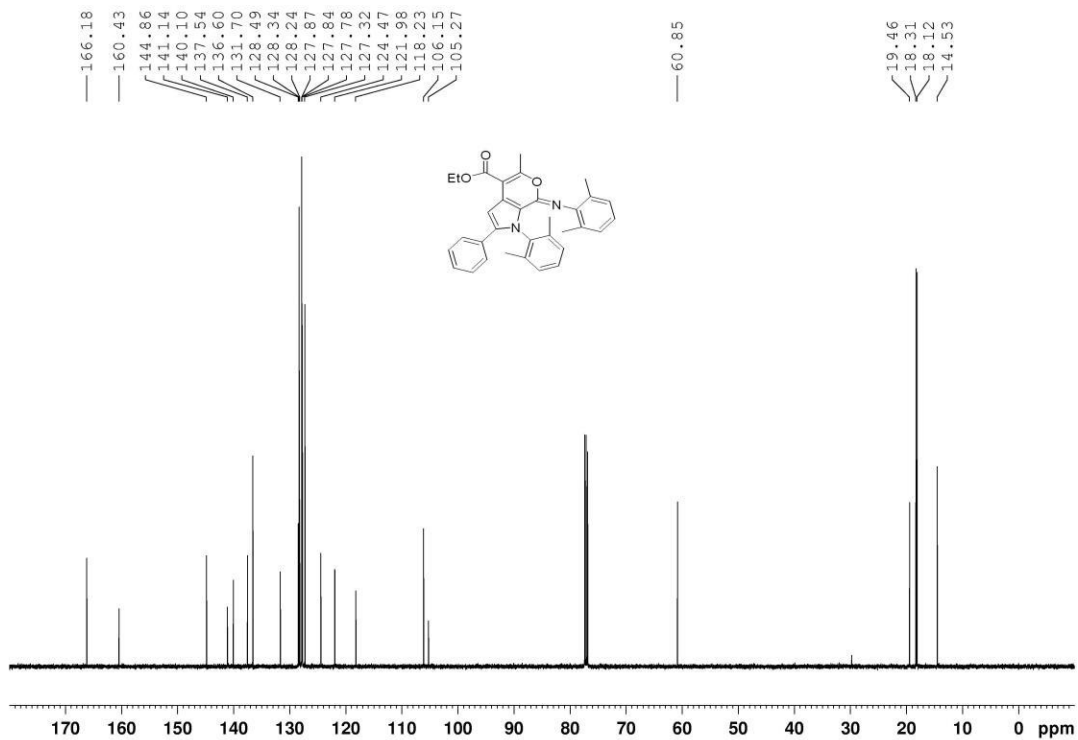
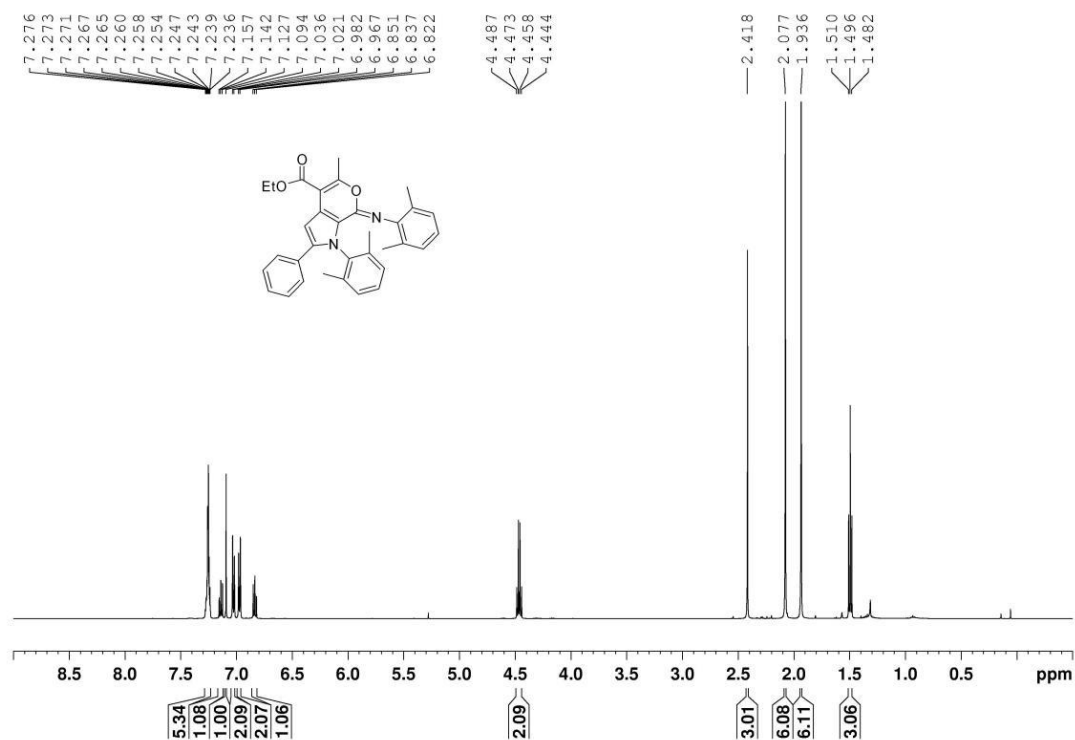
Compound 4a



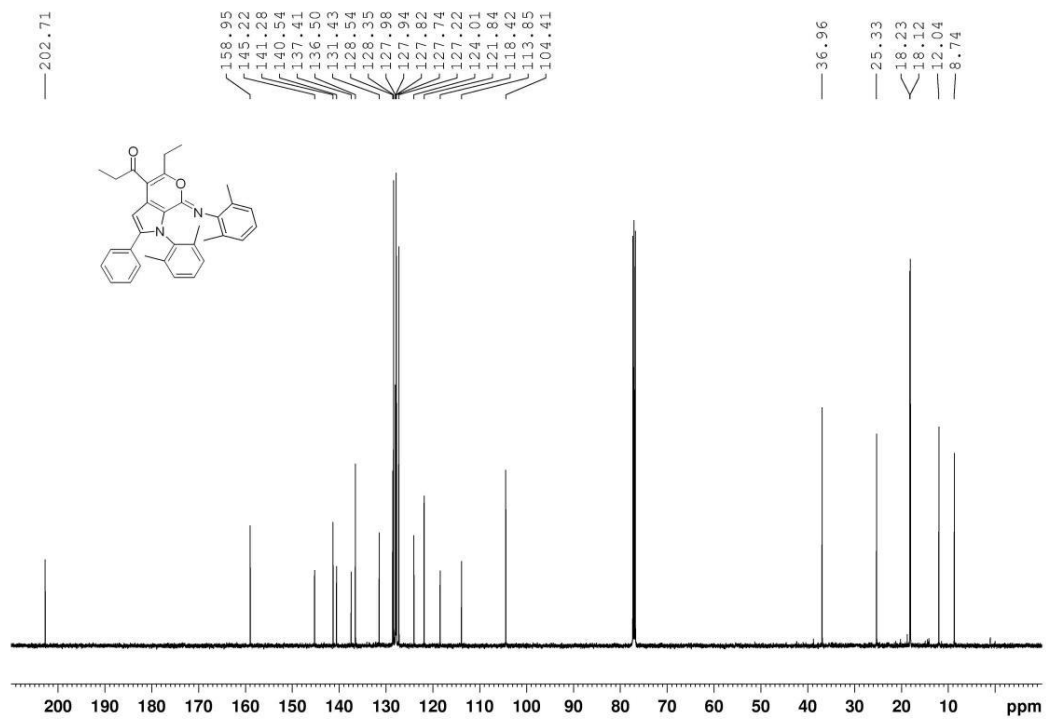
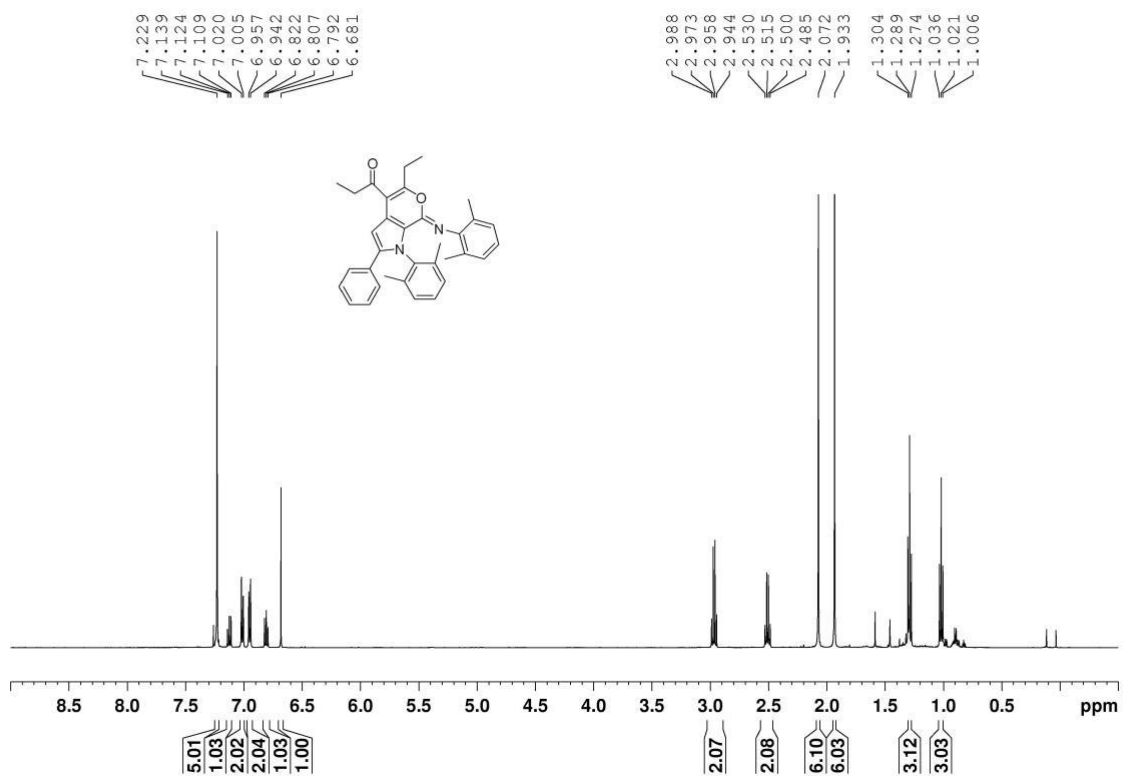
Compound 4b



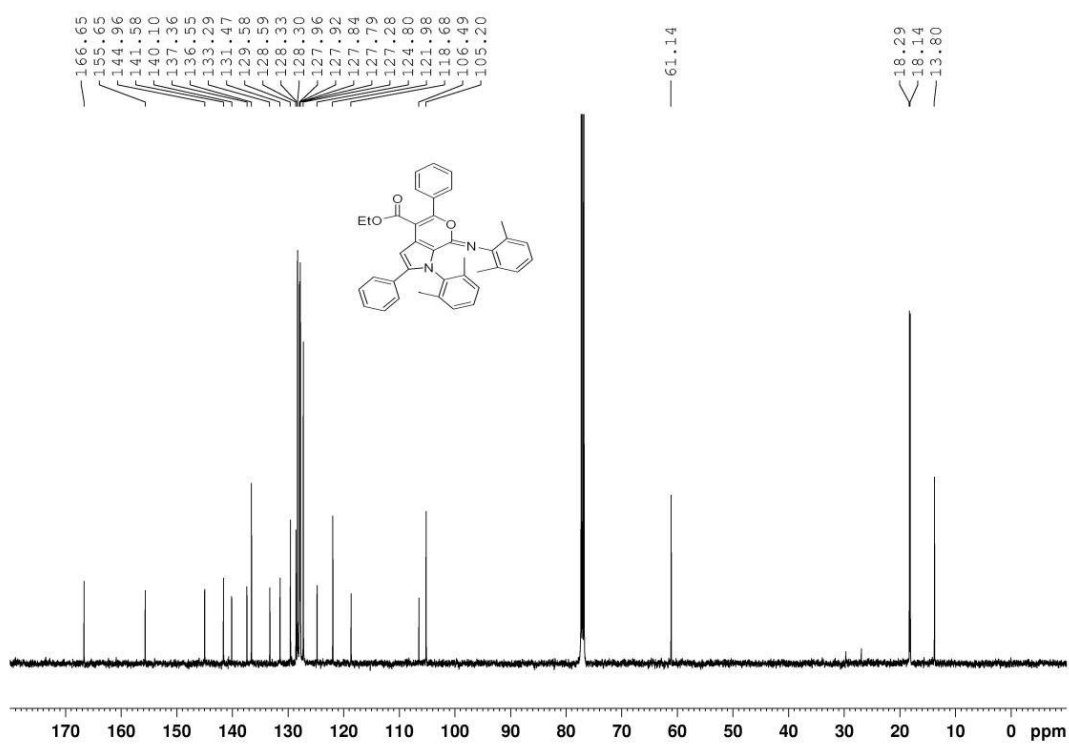
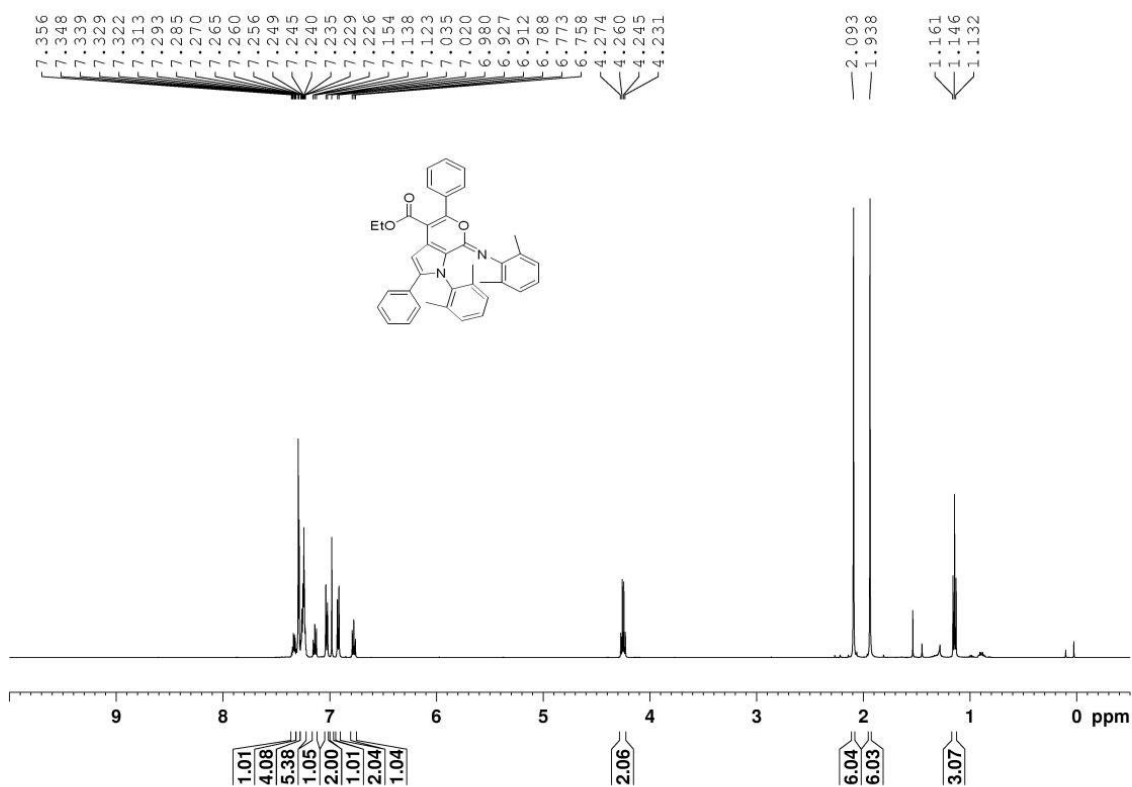
Compound 4c



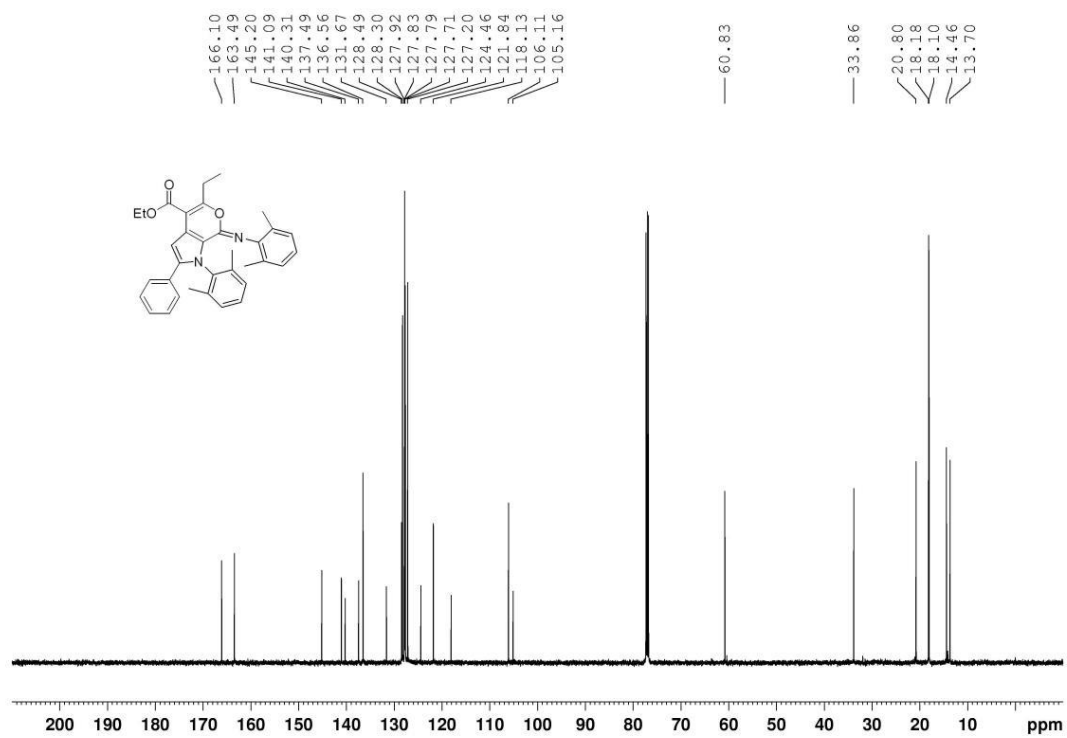
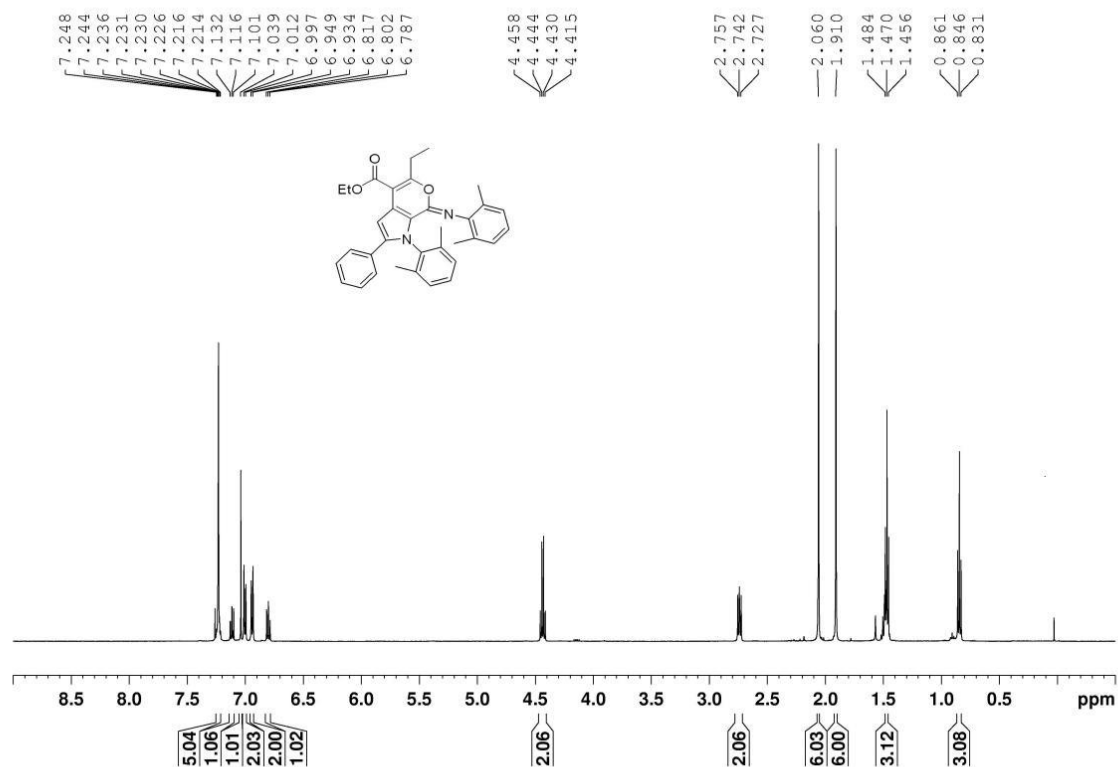
Compound 4d



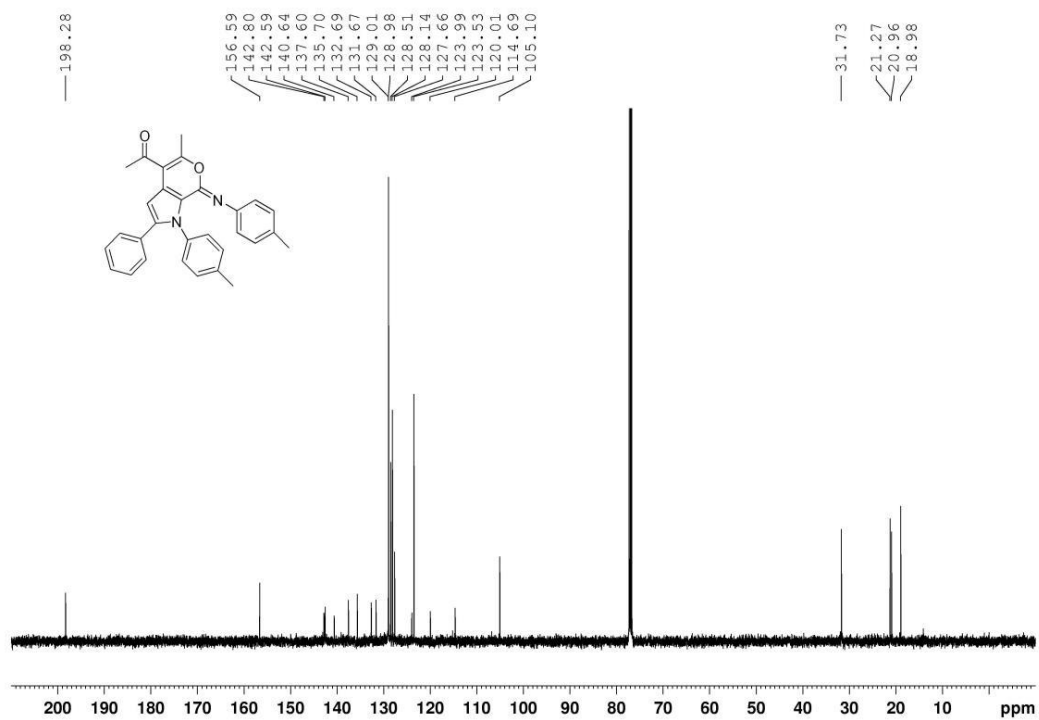
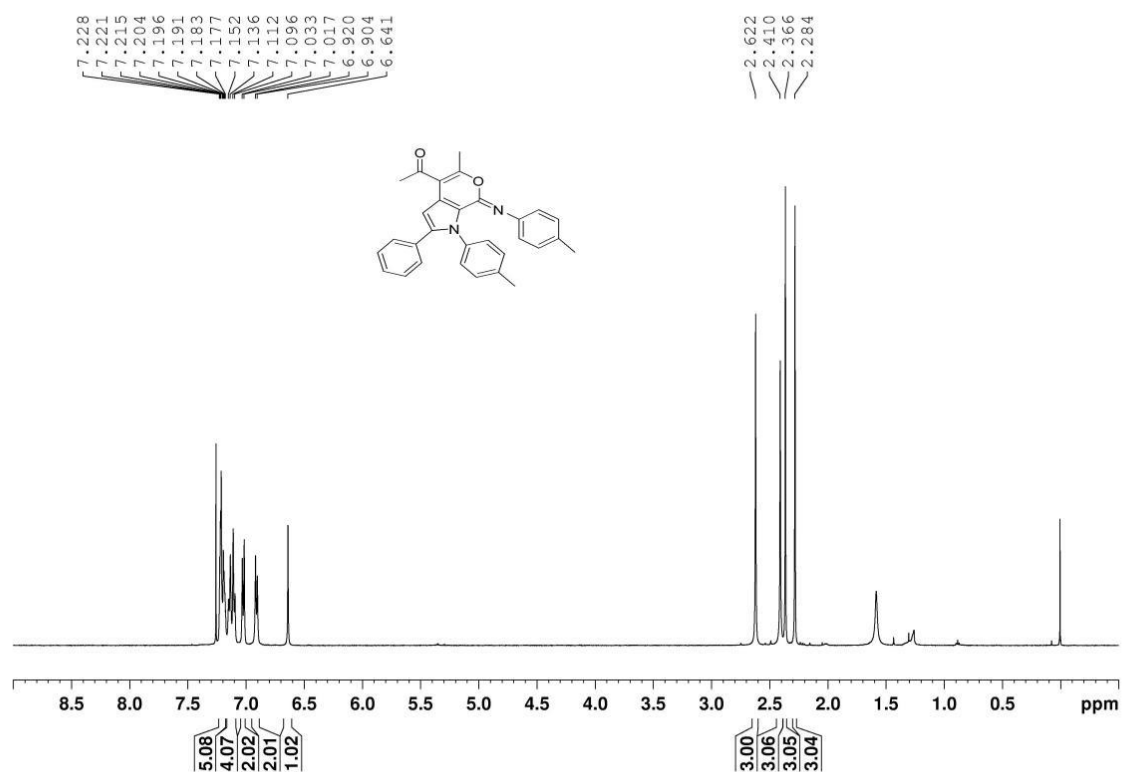
Compound 4e



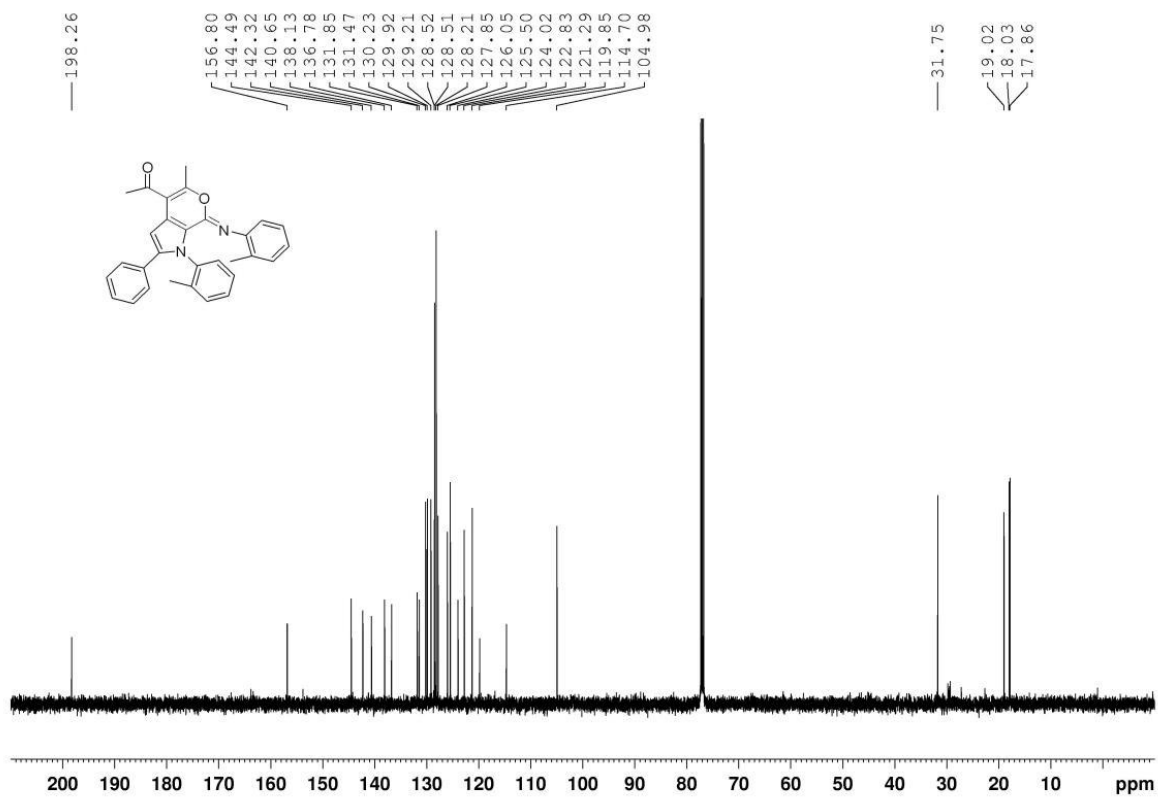
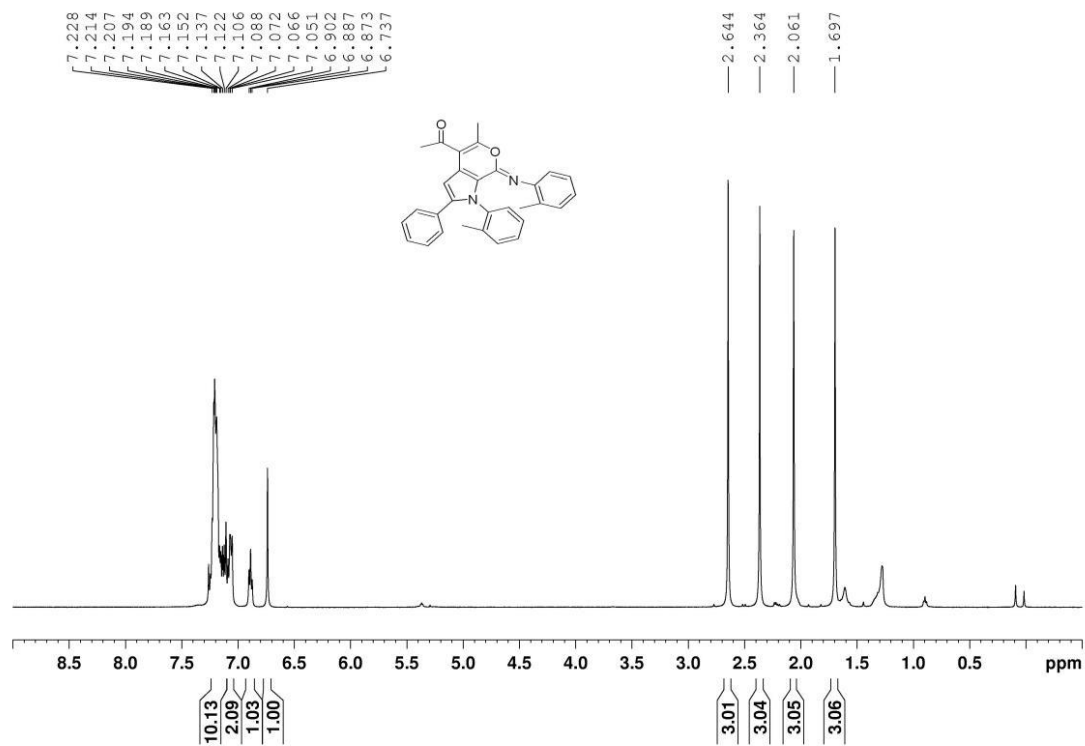
Compound 4f



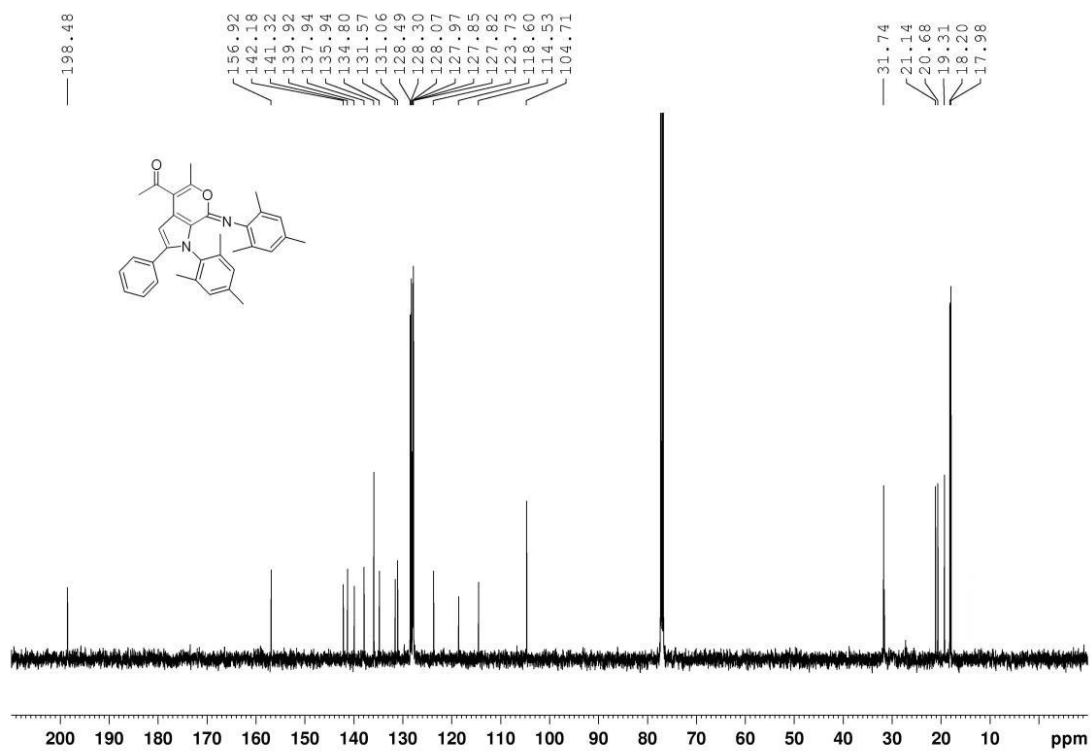
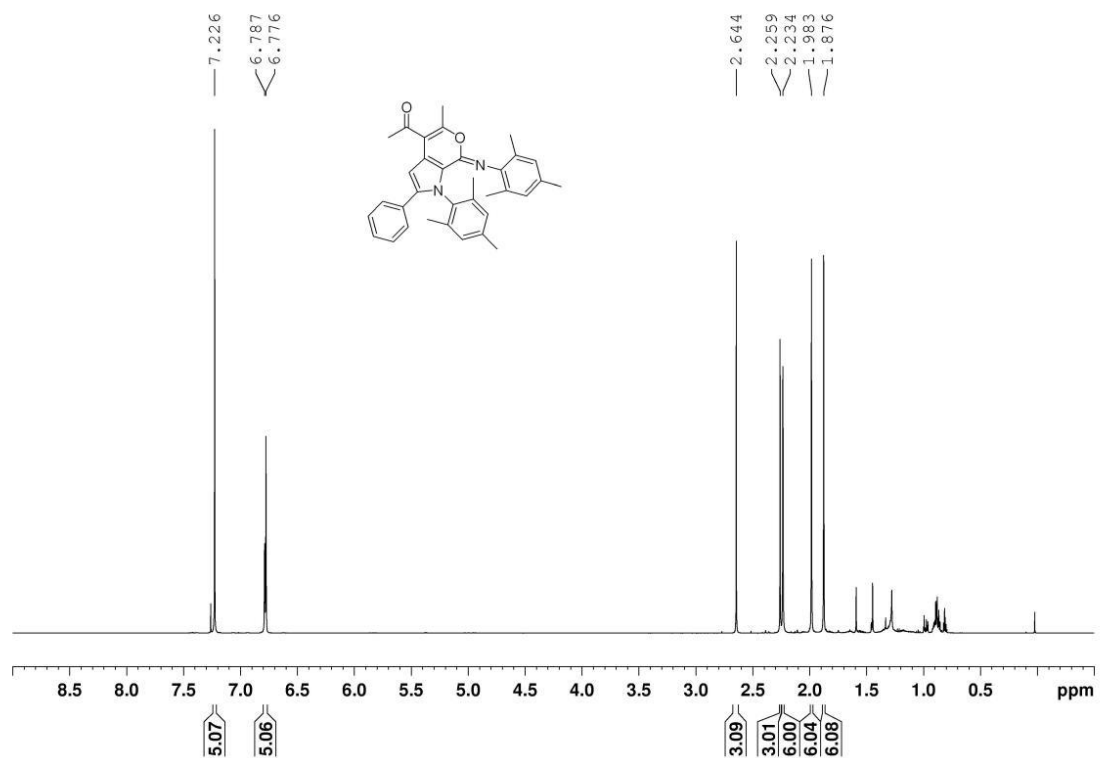
Compound 5a



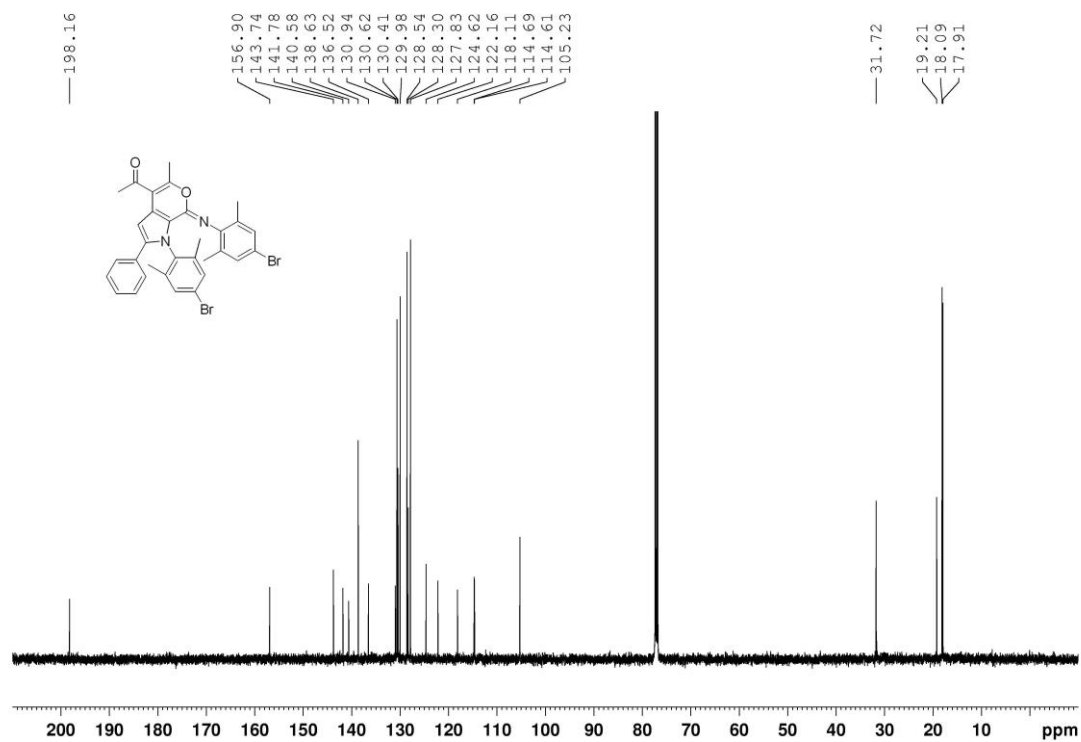
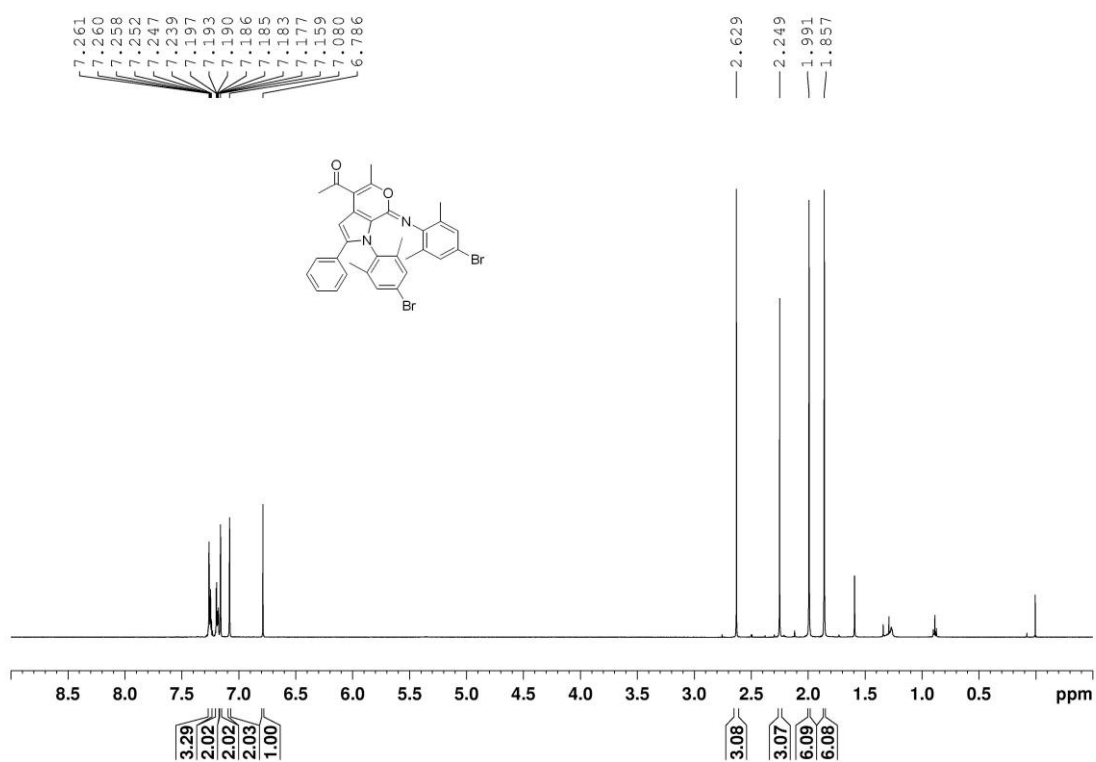
Compound 5b



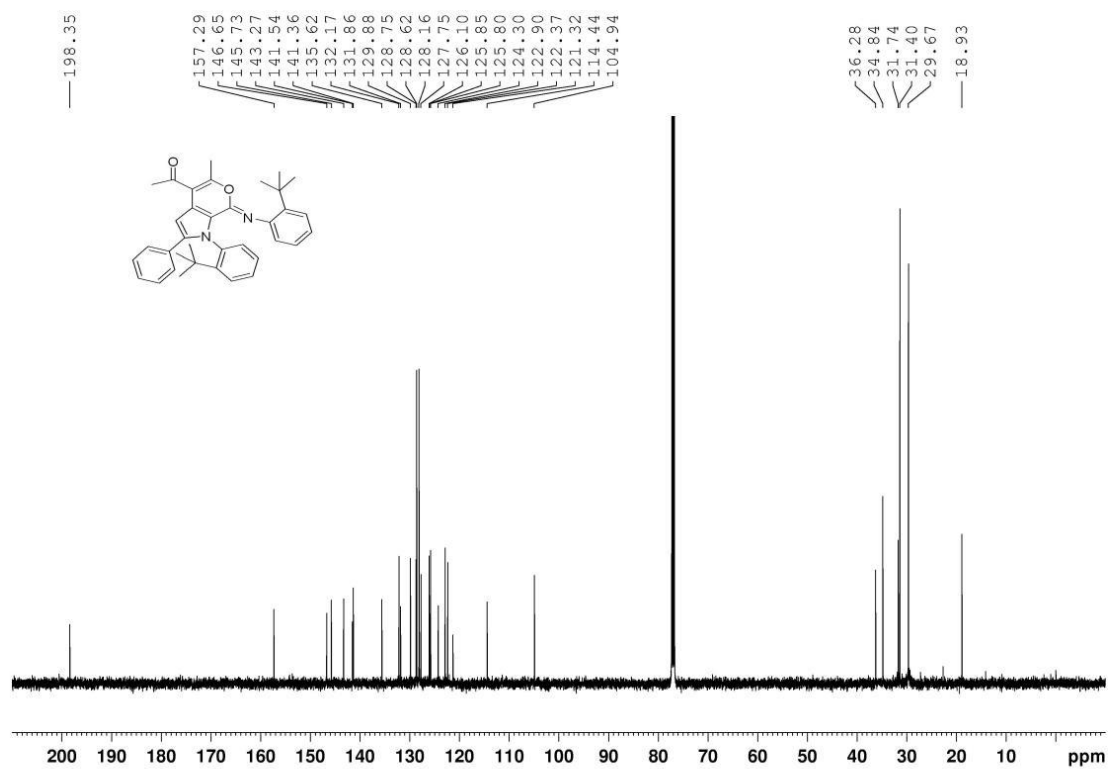
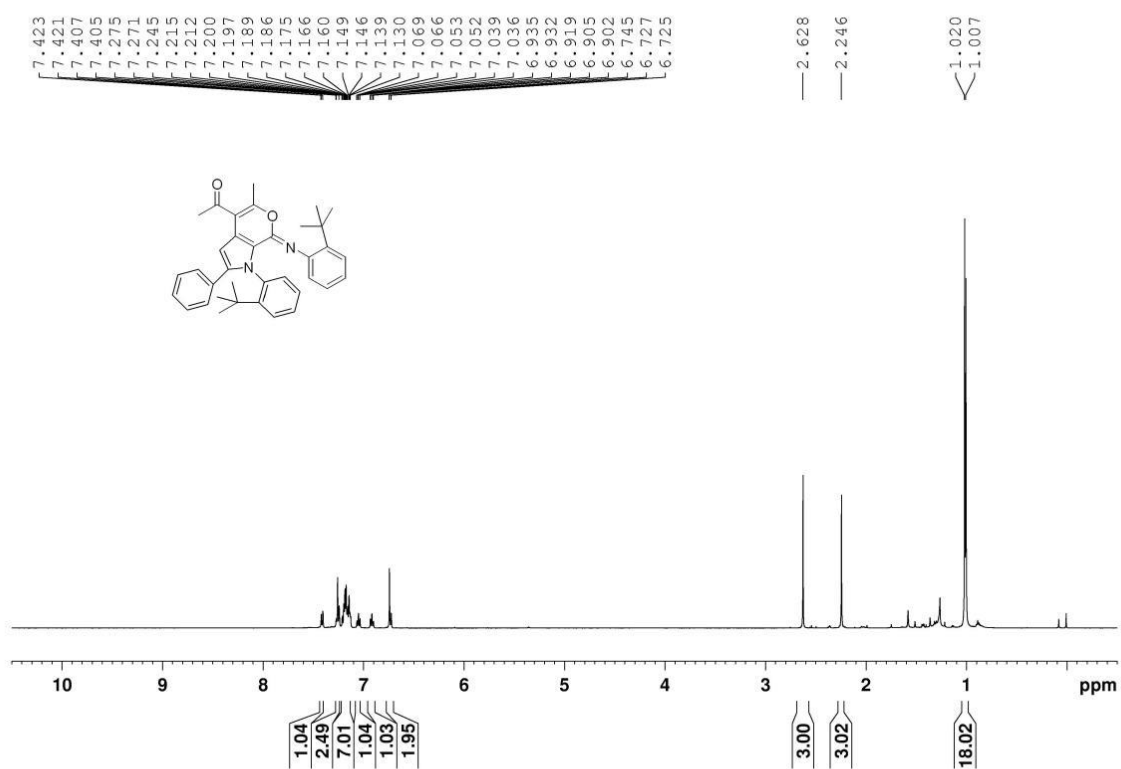
Compound **5c**



Compound 5d



Compound 5e



Compound 5f

