

Phosphine-mediated sequential annulations of allenyl ketone and isocyanide: a bicyclization strategy to access furan-fused eight-membered ring and spirocycle

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Supporting Information

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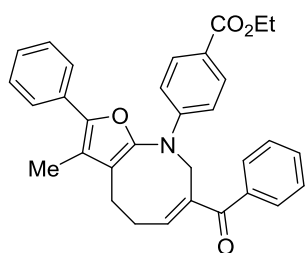
1 General Information

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. Purification of products was accomplished by column chromatography packed with silica gel. Unless otherwise stated, all reagents were commercially purchased and used without further purification. Enantiomeric excesses were determined by chiral HPLC using a Shimadzu instrument.

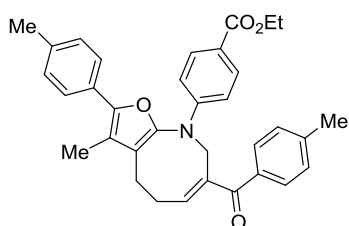
2 General Procedure

Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with isocyanide **1** (0.5 mmol), allenyl ketone **2** (0.5mmol) and triphenylphosphine (1.0 equiv.) in THF (5.0 mL) at room temperature. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 130 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford product **3-4**.

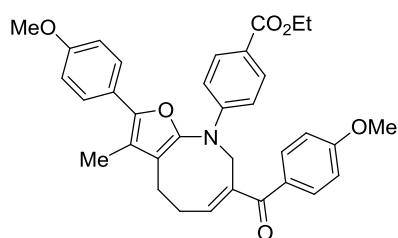
3 Characterization Data



(3a): 90.4 mg, 75% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.96 (d, J = 8.8 Hz, 2H), 7.64-7.61 (m, 4H), 7.54-7.50 (m, 1H), 7.41 (td, J = 7.7, 3.8 Hz, 4H), 7.27 (t, J = 7.4 Hz, 1H), 6.78 (d, J = 8.9 Hz, 2H), 6.66 (t, J = 8.4 Hz, 1H), 4.79 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 2.64-2.55 (m, 4H), 2.23 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.0, 166.5, 151.7, 145.4, 145.2, 144.7, 138.1, 137.9, 131.9, 131.3, 131.2, 129.3, 128.4, 128.1, 126.9, 125.6, 120.8, 118.2, 117.1, 112.7, 60.3, 49.2, 23.3, 22.8, 14.3, 9.9. HRMS (ESI): calcd. for $\text{C}_{32}\text{H}_{30}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 492.2169, Found: 492.2158. R_f Value: 0.40 (PE/EA – 5:1).

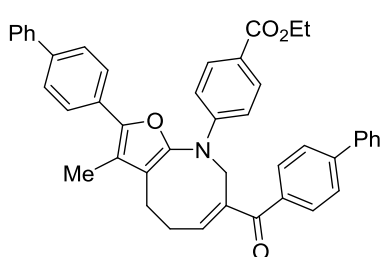


(3b): 83.0 mg, 65% yield, white solid: m.p. 194-195 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.95 (d, J = 8.9 Hz, 2H), 7.53 (t, J = 8.5 Hz, 4H), 7.22 (d, J = 8.0 Hz, 4H), 6.77 (d, J = 8.9 Hz, 2H), 6.63 (t, J = 8.5 Hz, 1H), 4.77 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 2.63-2.53 (m, 4H), 2.40 (s, 3H), 2.37 (s, 3H), 2.21 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 197.8, 196.5, 151.9, 145.6, 144.4, 144.2, 142.7, 138.2, 136.7, 135.1, 131.2, 129.6, 129.1, 128.8, 128.6, 125.6, 120.7, 118.2, 116.4, 112.7, 60.3, 49.4, 23.2, 22.9, 21.5, 21.1, 14.3, 9.9. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 520.2482, Found: 520.2473. R_f Value: 0.42 (PE/EA – 5:1).



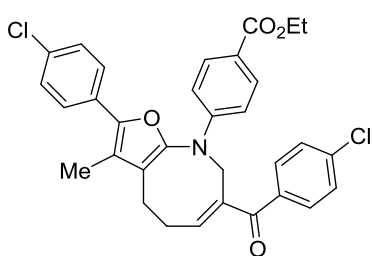
(3c): 63.0 mg, 40% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.95-7.92 (m, 2H), 7.66-7.63 (m, 2H), 7.56-7.53 (m, 2H), 6.95-6.88 (m, 4H), 6.77-6.74 (m, 2H), 6.55 (t, J = 8.5 Hz, 1H),

4.73 (s, 2H), 4.32 (q, $J = 7.1$ Hz, 2H), 3.84 (s, 3H), 3.82 (s, 3H), 2.62-2.51 (m, 4H), 2.19 (s, 3H), 1.36 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 196.9, 166.6, 162.9, 158.6, 151.9, 145.5, 144.2, 142.6, 138.2, 131.9, 131.2, 130.2, 127.1, 124.2, 120.7, 118.2, 115.6, 113.9, 113.4, 112.7, 60.3, 55.4, 55.2, 49.7, 23.2, 23.0, 14.4, 9.9. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{NO}_6$ $[\text{M}+\text{H}]^+$ 552.2381, Found: 552.2380. R_f Value: 0.50 (PE/EA – 2:1).



(3d): 93.3 mg, 57% yield, white solid: m.p. 95-96 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.98 (d, $J = 8.4$ Hz, 2H), 7.74-7.71 (m, 4H), 7.67-7.61 (m, 8H), 7.47 (q, $J = 7.2$ Hz, 4H), 7.42-7.35 (m, 2H), 6.81 (d, $J = 8.5$ Hz, 2H), 6.72 (t, $J = 8.2$ Hz, 1H), 4.82 (s, 2H),

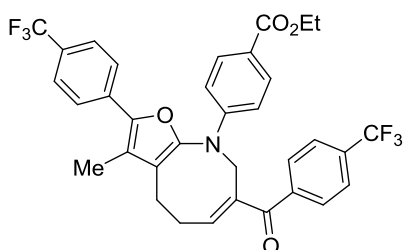
4.35 (q, $J = 7.1$ Hz, 2H), 2.68-2.61 (m, 4H), 2.29 (s, 3H), 1.38 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 197.7, 166.5, 151.8, 145.2, 144.9, 144.8, 144.7, 140.5, 139.8, 139.5, 138.3, 136.5, 131.3, 130.3, 130.1, 128.9, 128.7, 128.1, 127.3, 127.1, 126.9, 126.8, 125.9, 120.1, 118.4, 117.4, 112.7, 60.3, 49.4, 23.4, 22.9, 14.4, 10.1. HRMS (ESI): calcd. for $\text{C}_{44}\text{H}_{38}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 644.2795, Found: 644.2792. R_f Value: 0.38 (PE/EA – 5:1).



(3e): 44.2 mg, 32% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.95-7.92 (m, 2H), 7.56-7.52 (m, 4H), 7.40-7.35 (m, 4H), 6.74-6.71 (m, 2H), 6.62 (t, $J = 8.3$ Hz, 1H), 4.74 (s, 2H), 4.33 (q, $J = 7.1$ Hz, 2H), 2.63-2.54 (m, 4H), 2.20 (s, 3H), 1.36 (t, $J = 7.1$ Hz, 3H).

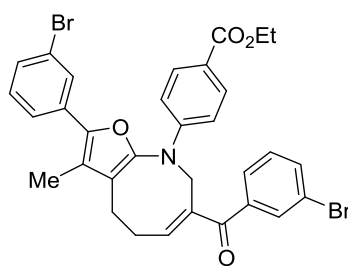
^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 196.8, 166.5, 151.6, 145.3, 144.9, 144.5, 138.4, 138.1, 136.1, 132.7, 131.3, 130.8, 129.7, 128.7, 128.5, 126.8, 121.1, 118.4, 117.7, 112.7, 60.4, 49.2, 23.4,

22.8, 14.4, 10.0. HRMS (ESI): calcd. for $C_{32}H_{28}Cl_2NO_4$ $[M+H]^+$ 560.1390, Found: 560.1384. R_f Value: 0.46 (PE/EA – 5:1).



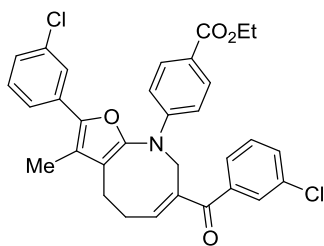
(3f): 71.9 mg, 50% yield, white solid: m.p. 78-79 °C. 1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.96 (d, J = 8.8 Hz, 2H), 7.69 (m, 8H), 6.76 (d, J = 8.8 Hz, 2H), 6.69 (t, J = 8.0 Hz, 1H), 4.81 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 2.65-2.62 (m, 4H), 2.27 (s, 3H),

1.37 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 196.8, 166.4, 151.4, 147.0, 145.6, 144.1, 141.2, 138.2, 134.5, 133.3 (q, J = 32.6 Hz), 131.4, 129.5, 128.5 (q, J = 32.3 Hz), 125.5 (q, J = 3.8 Hz), 125.4, 125.2 (q, J = 3.6 Hz), 124.1 (q, J = 270.2 Hz), 123.6 (q, J = 271.1 Hz), 121.3, 119.3, 118.6, 112.8, 60.4, 48.9, 23.5, 22.6, 14.3, 10.1. HRMS (ESI): calcd. for $C_{34}H_{28}F_6NO_4$ $[M+H]^+$ 628.1917, Found: 628.1925. R_f Value: 0.48 (PE/EA – 5:1).



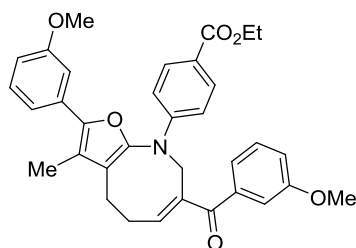
(3g): 90.4 mg, 63% yield, yellow oil. 1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.96-7.93 (m, 2H), 7.75 (t, J = 1.7 Hz, 1H), 7.66 (t, J = 1.7 Hz, 1H), 7.64-7.62 (m, 1H), 7.54-7.50 (m, 2H), 7.39-7.37 (m, 1H), 7.30-7.24 (m, 2H), 6.75-6.72 (m, 2H), 6.64 (t, J = 8.3 Hz, 1H), 4.74 (s,

2H), 4.33 (q, J = 7.1 Hz, 2H), 2.64-2.57 (m, 4H), 2.23 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 196.2, 166.4, 151.4, 146.2, 144.9, 144.0, 139.7, 137.9, 134.7, 133.1, 132.2, 131.3, 129.9, 129.7, 128.3, 127.8, 123.9, 122.6, 122.3, 121.1, 118.4, 118.3, 112.7, 60.3, 48.8, 23.5, 22.5, 14.3, 10.0. HRMS (ESI): calcd. for $C_{32}H_{28}Br_2NO_4$ $[M+H]^+$ 648.0380, Found: 648.0380. R_f Value: 0.47 (PE/EA – 5:1).



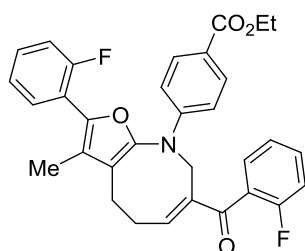
(3h): 79.2 mg, 55% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.96-7.93 (m, 2H), 7.59 (t, J = 1.8 Hz, 1H), 7.51 (t, J = 1.7 Hz, 1H), 7.49-7.45 (m, 3H), 7.35-7.29 (m, 2H), 7.22-7.20 (m, 1H), 6.76-6.73 (m, 2H), 6.64 (t, J = 8.3 Hz, 1H), 4.74 (s, 2H), 4.32 (q, J = 7.1

Hz, 2H), 2.64-2.56 (m, 4H), 2.22 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 196.4, 166.4, 151.4, 146.2, 144.9, 144.1, 139.5, 137.9, 134.4, 134.3, 132.8, 131.8, 131.3, 129.7, 129.5, 129.3, 127.3, 126.8, 125.3, 123.5, 121.1, 118.5, 118.3, 112.7, 60.3, 48.8, 23.5, 22.5, 14.3, 10.0. HRMS (ESI): calcd. for $\text{C}_{32}\text{H}_{28}\text{Cl}_2\text{NO}_4$ $[\text{M}+\text{H}]^+$ 560.1390, Found: 560.1379. R_f Value: 0.35 (PE/EA – 5:1).



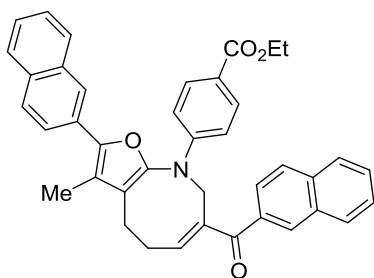
(3i): 85.6 mg, 60% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.95 (d, J = 9.0 Hz, 2H), 7.31 (td, J = 7.9, 2.9 Hz, 2H), 7.21 (d, J = 7.9 Hz, 1H), 7.16-7.14 (m, 3H), 7.06-7.04 (m, 1H), 6.82 (dd, J = 8.0, 2.2 Hz, 1H), 6.76 (d, J = 9.0 Hz, 2H), 6.67 (t, J = 8.4 Hz, 1H),

4.77 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 3.80 (s, 3H), 2.63-2.54 (m, 4H), 2.22 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 197.7, 166.4, 159.6, 159.3, 151.7, 145.3, 145.2, 144.6, 139.2, 138.0, 132.5, 131.2, 129.5, 129.1, 121.9, 120.8, 118.3, 118.1, 118.0, 117.4, 114.0, 112.7, 111.0, 60.3, 55.3, 55.2, 49.1, 23.3, 22.7, 14.3, 10.0. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{NO}_6$ $[\text{M}+\text{H}]^+$ 552.2381, Found: 552.2394. R_f Value: 0.21 (PE/EA – 5:1).

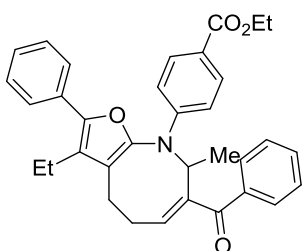


(3j): 70.2 mg, 53% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.96-7.93 (m, 2H), 7.50 (td, J = 7.5, 1.8 Hz, 1H), 7.47-7.43 (m,

1H), 7.37 (td, $J = 7.5, 1.8$ Hz, 1H), 7.33-7.29 (m, 1H), 7.21-7.17 (m, 2H), 7.16-7.08 (m, 2H), 6.76-6.72 (m, 3H), 4.79 (s, 2H), 4.33 (q, $J = 7.1$ Hz, 2H), 2.61-2.52 (m, 4H), 2.03 (d, $J = 2.9$ Hz, 3H), 1.36 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.1, 166.5, 160.4, 159.9, 158.4, 158.0, 147.8, 145.9, 140.7, 139.3, 132.5, 132.4, 131.3, 130.2, 130.1, 130.0, 129.5, 129.4, 127.2, 127.1, 124.2, 124.1, 124.0, 120.9, 119.9, 119.2, 119.0, 117.8, 116.1, 116.0, 112.7, 60.3, 48.6, 23.3, 22.7, 9.6, 9.5. HRMS (ESI): calcd. for $\text{C}_{32}\text{H}_{28}\text{F}_2\text{NO}_4$ $[\text{M}+\text{H}]^+$ 528.1981, Found: 528.1988. R_f Value: 0.34 (PE/EA – 5:1).

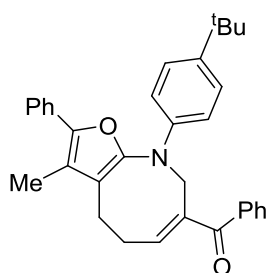


(3k): 55.3 mg, 33% yield, white solid: m.p. 92-93 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 8.08 (d, $J = 4.8$ Hz, 2H), 8.01-7.98 (m, 2H), 7.88-7.85 (m, 5H), 7.84-7.80 (m, 2H), 7.75 (dd, $J = 8.5, 1.6$ Hz, 1H), 7.59-7.55 (m, 1H), 7.52-7.45 (m, 3H), 6.86-6.83 (m, 2H), 6.73 (t, $J = 8.5$, 1H), 4.87 (s, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 2.70-2.60 (m, 4H), 2.36 (s, 3H), 1.38 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.1, 166.5, 151.8, 145.7, 145.0, 144.9, 138.4, 135.1, 135.0, 133.3, 132.2, 132.1, 131.3, 130.8, 129.2, 128.8, 128.2, 128.1, 127.7, 127.6, 126.7, 126.3, 125.9, 125.4, 124.3, 123.8, 120.9, 118.6, 117.7, 112.8, 60.4, 49.3, 23.5, 22.8, 14.4, 10.2. HRMS (ESI): calcd. for $\text{C}_{40}\text{H}_{34}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 592.2482, Found: 592.2471. R_f Value: 0.28 (PE/EA – 5:1).



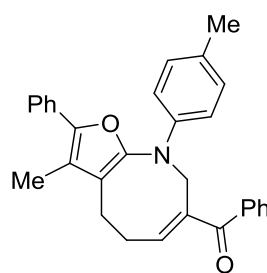
(3l): 63.4 mg, 46% yield, white solid: m.p. 66-67 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.95 (d, $J = 8.9$ Hz, 2H), 7.74-7.73 (m, 2H), 7.67-7.65 (m, 2H), 7.57-7.54 (m, 1H), 7.47-7.42 (m, 4H), 7.30 (t, $J = 7.4$ Hz, 1H),

6.82 (d, $J = 9.0$ Hz, 2H), 6.45-6.41 (m, 1H), 5.52 (q, $J = 6.8$, 1H), 4.33 (q, $J = 7.1$ Hz, 2H), 2.84-2.79 (m, 1H), 2.75-2.67 (m, 2H), 2.58-2.52 (m, 1H), 2.43-2.36 (m, 1H), 2.33-2.27 (m, 1H), 1.36 (t, $J = 7.1$ Hz, 3H), 1.32 (t, $J = 7.5$ Hz, 3H), 1.26 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 199.1, 166.6, 151.9, 145.3, 144.2, 143.4, 140.2, 138.1, 132.4, 131.4, 131.3, 129.6, 128.6, 128.3, 127.1, 125.6, 123.6, 120.9, 119.3, 112.5, 60.3, 54.4, 23.7, 22.3, 19.9, 17.9, 14.5, 14.4. HRMS (ESI): calcd. for $\text{C}_{34}\text{H}_{34}\text{NO}_4$ $[\text{M}+\text{H}]^+$ 520.2482, Found: 520.2475. R_f Value: 0.46 (PE/EA – 5:1).



(3m): 72.9 mg, 65% yield, white solid: m.p. 83-84 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.70 (d, $J = 8.2$ Hz, 2H), 7.66 (dd, $J = 7.0$, 1.2 Hz, 2H), 7.57-7.54 (m, 1H), 7.45 (t, $J = 7.8$ Hz, 4H), 7.35-7.29 (m, 3H), 6.81 (dd, $J = 8.7$, 1.7 Hz, 2H), 6.71-6.68 (m, 1H), 4.80 (s, 2H), 2.70 (s, 4H), 1.37 (s, 9H).

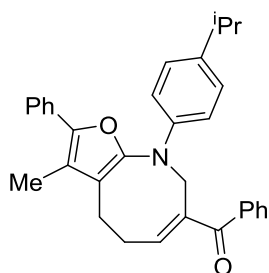
^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.4, 146.0, 145.4, 145.2, 144.7, 141.5, 139.0, 138.1, 131.7, 131.6, 129.3, 128.4, 128.0, 126.5, 125.9, 125.5, 117.7, 117.0, 113.2, 48.9, 33.8, 31.4, 23.9, 22.7, 10.0. HRMS (ESI): calcd. for $\text{C}_{33}\text{H}_{34}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 476.2584, Found: 476.2580. R_f Value: 0.50 (PE/EA – 6:1).



(3n): 62.9 mg, 58% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.66-7.61 (m, 4H), 7.54-7.51 (m, 1H), 7.42 (td, $J = 7.8$, 3.1 Hz, 4H), 7.28-7.25 (m, 1H), 7.09-7.07 (m, 2H), 6.73-6.72 (m, 2H), 6.66-6.65 (m, 1H), 4.75 (s, 2H), 2.65 (d, $J = 4.0$ Hz, 4H), 2.30 (s, 3H), 2.25 (s, 3H). ^{13}C NMR

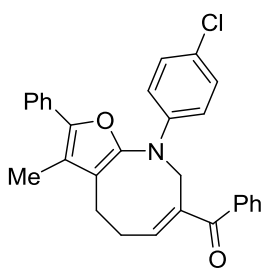
(125 MHz, CDCl_3): δ (ppm) = 198.5, 146.2, 145.6, 145.2, 144.7, 139.0, 138.2, 131.8, 131.6, 129.7,

129.4, 128.4, 128.1, 128.0, 126.6, 125.5, 117.6, 117.1, 113.6, 49.1, 23.8, 22.8, 20.3, 10.0. HRMS (ESI): calcd. for C₃₀H₂₈NO₂ [M+H]⁺ 434.2115, Found: 434.2102. R_f Value: 0.50 (PE/EA – 5:1).



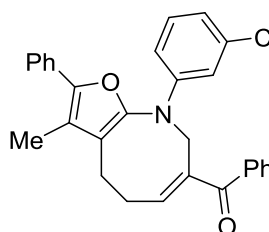
(3o): 54.6 mg, 43% yield, white solid: m.p. 59-60 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.63 (dd, *J* = 20.5, 7.4 Hz, 4H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 4H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 6.66-6.64 (m, 1H), 4.74 (s, 2H), 2.91-2.83 (m, 1H),

2.65 (s, 4H), 2.25 (s, 3H), 1.25 (d, *J* = 6.9, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.4, 146.1, 145.8, 145.2, 144.7, 139.3, 139.0, 138.2, 131.7, 131.6, 129.4, 128.4, 128.0, 127.0, 126.6, 125.5, 117.7, 117.0, 113.6, 49.0, 33.0, 24.1, 23.9, 22.8, 10.0. HRMS (ESI): calcd. for C₃₂H₃₂NO₂ [M+H]⁺ 462.2428, Found: 462.2422. R_f Value: 0.48 (PE/EA – 10:1).



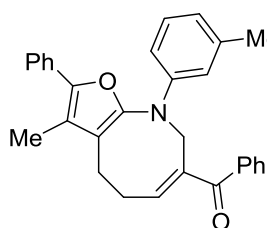
(3p): 75.3 mg, 66% yield, white solid: m.p. 73-74 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.64-7.60 (m, 4H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41 (td, *J* = 7.7, 3.0 Hz, 4H), 7.27 (t, *J* = 7.5 Hz, 1H), 7.21-7.18 (m, 2H), 6.72-6.70 (m, 2H), 6.66 (t, *J* = 8.0 Hz, 1H), 4.71 (s, 2H), 2.65-2.58 (m, 4H), 2.23 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.3, 146.6, 145.4, 145.3, 145.1, 138.5, 138.0, 131.9, 131.4, 129.4, 129.1, 128.5, 128.2, 126.8, 125.6, 123.9, 118.0, 117.1, 114.8, 49.3, 23.7, 22.8, 10.0. HRMS (ESI): calcd. for C₂₉H₂₅ClNO₂ [M+H]⁺ 454.1568, Found: 454.1565. R_f Value: 0.46 (PE/EA – 5:1).



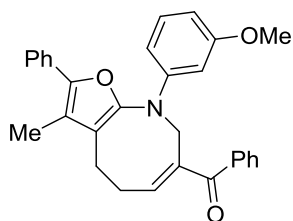
(3q): 68.3 mg, 53% yield, white solid: m.p. 61-62 °C. ¹H NMR (500 MHz,

CDCl₃): δ (ppm) = 7.65-7.61 (m, 4H), 7.54-7.51 (m, 1H), 7.44-7.40 (m, 4H), 7.30-7.26 (m, 1H), 7.16 (t, J = 8.1 Hz, 1H), 6.83 (dd, J = 7.8, 1.2 Hz, 1H), 6.78 (t, J = 2.1 Hz, 1H), 6.68-6.65 (m, 2H), 4.72 (s, 2H), 2.65-2.59 (m, 4H), 2.24 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.2, 149.2, 145.3, 145.2, 144.9, 138.4, 138.0, 135.1, 131.9, 131.4, 130.2, 129.4, 128.5, 128.1, 126.8, 125.6, 119.0, 118.2, 117.1, 113.6, 111.7, 49.3, 23.5, 22.8, 10.0. HRMS (ESI): calcd. for C₂₉H₂₅ClNO₂ [M+H]⁺ 454.1568, Found: 454.1575. R_f Value: 0.43 (PE/EA – 5:1).



(3r): 68.9 mg, 60% yield, white solid: m.p. 56-57°C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.65 (dd, J = 18.5, 7.8 Hz, 4H), 7.53 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.6 Hz, 4H), 7.28 (t, J = 7.4, 1H), 7.17 (t, J = 7.7 Hz, 1H), 6.70

(t, J = 7.3 Hz, 1H), 6.64 (t, J = 12.3 Hz, 3H), 4.76 (s, 2H), 2.65 (d, J = 3.4 Hz, 4H), 2.33 (s, 3H), 2.26 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.5, 148.0, 146.0, 145.1, 144.9, 139.0, 138.9, 138.2, 131.8, 131.6, 129.4, 129.0, 128.4, 128.1, 126.6, 125.5, 119.9, 117.8, 117.1, 114.2, 110.8, 49.1, 23.6, 22.9, 21.8, 10.1. HRMS (ESI): calcd. for C₃₀H₂₈NO₂ [M+H]⁺ 434.2115, Found: 434.2121. R_f Value: 0.45 (PE/EA – 5:1).

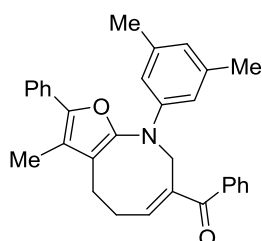


(3s): 79.6 mg, 70% yield, yellow oil. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.68-7.64 (m, 4H), 7.55-7.51 (m, 1H), 7.43 (td, J = 7.8, 2.9 Hz, 4H), 7.28 (t, J = 7.4 Hz, 1H), 7.19 (t, J = 8.2 Hz, 1H), 6.67 (t, J = 4.0 Hz, 1H),

6.46-6.43 (m, 2H), 6.40 (t, J = 2.3 Hz, 1H), 4.78 (s, 2H), 3.79 (s, 3H), 2.65 (d, J = 4.1 Hz, 4H), 2.25 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.3, 160.0, 149.3, 145.6, 145.1, 144.9, 138.7, 138.0, 131.7, 131.5, 129.9, 129.3, 128.3, 128.0, 126.6, 125.5, 117.9, 117.0, 106.4, 103.7, 100.2,

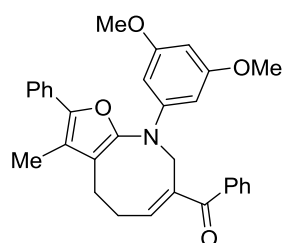
55.0, 49.2, 23.4, 22.8, 9.9. HRMS (ESI): calcd. for $C_{30}H_{28}NO_3$ $[M+H]^+$ 450.2064, Found: 450.2059.

R_f Value: 0.46 (PE/EA – 5:1).



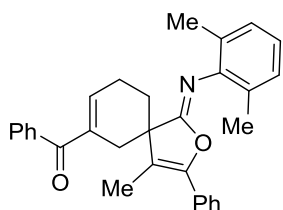
(3t): 77.2 mg, 67% yield, white solid: m.p. 70-71 °C. 1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.67 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.1 Hz, 2H), 7.54-7.51 (m, 1H), 7.42 (t, J = 7.7 Hz, 4H), 7.28 (t, J = 7.4 Hz, 1H), 6.67-6.66 (m, 1H), 6.54 (s, 1H), 6.44 (s, 2H), 4.74 (s, 2H), 2.66-2.65 (m, 4H),

2.29 (s, 6H), 2.27 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 198.5, 148.0, 146.0, 145.1, 144.8, 139.0, 138.8, 138.2, 131.7, 131.6, 129.4, 128.4, 128.1, 126.6, 125.6, 121.0, 117.8, 117.1, 111.5, 49.2, 23.7, 22.9, 21.6, 10.1. HRMS (ESI): calcd. for $C_{31}H_{30}NO_2$ $[M+H]^+$ 448.2271, Found: 448.2261. R_f Value: 0.49 (PE/EA – 7:1).



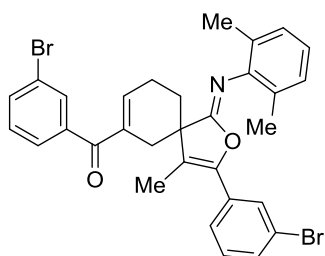
(3u): 78.2 mg, 68% yield, yellow oil. 1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.64-7.59 (m, 4H), 7.53 (m, 1H), 7.40 (td, J = 7.8, 3.2 Hz, 4H), 7.27-7.24 (m, 1H), 6.66-6.63 (m, 1H), 6.03-6.02 (m, 1H), 5.97 (q, J = 1.0 Hz, 2H), 4.72 (s, 2H), 3.74 (s, 6H), 2.63-2.62 (m, 4H), 2.21 (s, 3H). ^{13}C NMR (125

MHz, $CDCl_3$): δ (ppm) = 198.4, 161.6, 150.1, 145.6, 145.2, 145.0, 138.8, 138.1, 131.8, 131.6, 129.4, 128.4, 128.1, 126.7, 125.6, 118.0, 117.1, 92.9, 90.8, 55.2, 49.4, 23.5, 22.9, 10.0. HRMS (ESI): calcd. for $C_{31}H_{30}NO_4$ $[M+H]^+$ 480.2169, Found: 480.2169. R_f Value: 0.30 (PE/EA – 5:1).

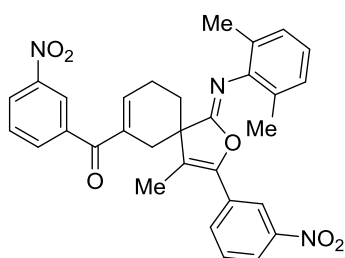


(4a): 65.8 mg, 54% yield, white solid: m.p. 62-63 °C. 1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.77-7.75 (m, 2H), 7.55-7.52 (m, 1H), 7.47-7.44 (m, 4H),

7.39-7.36 (m, 2H), 7.34-7.31 (m, 1H), 7.06 (d, $J = 7.5$ Hz, 2H), 6.93 (t, $J = 7.5$ Hz, 1H), 6.81-6.79 (m, 1H), 3.26-3.18 (m, 1H), 2.91 (s, 2H), 2.59-2.52 (m, 1H), 2.18 (s, 6H), 2.10-2.07 (m, 2H), 2.03 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 197.6, 163.4, 145.7, 145.0, 143.4, 138.4, 135.1, 131.5, 129.7, 129.2, 128.4, 128.2, 128.0, 127.5, 127.4, 127.0, 122.5, 116.2, 48.1, 30.9, 28.5, 22.9, 18.1, 9.2. HRMS (ESI): calcd. for $\text{C}_{31}\text{H}_{30}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 448.2271, Found: 448.2269. R_f Value: 0.50 (PE/EA – 6:1).

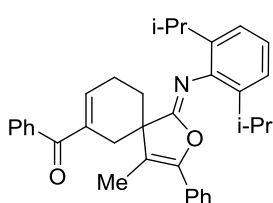


(4b): 73.3 mg, 50% yield, yellow oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.84 (t, $J = 1.7$ Hz, 1H), 7.65-7.61 (m, 2H), 7.56 (t, $J = 1.7$ Hz, 1H), 7.44-7.43 (m, 1H), 7.34 (d, $J = 7.9$ Hz, 1H), 7.30 (t, $J = 7.8$ Hz, 1H), 7.21 (t, $J = 7.9$ Hz, 1H), 7.03 (d, $J = 7.6$ Hz, 2H), 6.91 (t, $J = 15.0$, 1H), 6.78-6.77 (m, 1H), 3.23-3.15 (m, 1H), 2.89-2.79 (m, 2H), 2.58-2.53 (m, 1H), 2.12 (s, 6H), 2.07-2.04 (m, 2H), 1.99 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.7, 162.7, 144.6, 144.5, 144.2, 140.3, 134.8, 134.4, 131.9, 131.6, 131.5, 129.8, 129.6, 127.8, 127.6, 127.3, 125.7, 122.7, 122.4, 122.3, 117.5, 48.1, 30.7, 28.4, 23.0, 18.1, 9.2. HRMS (ESI): calcd. for $\text{C}_{31}\text{H}_{28}\text{Br}_2\text{NO}_2$ $[\text{M}+\text{H}]^+$ 604.0481, Found: 604.0476. R_f Value: 0.48 (PE/EA – 5:1).



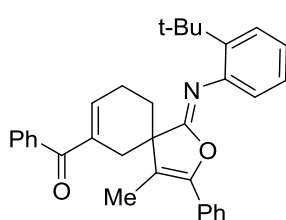
(4c): 87.5 mg, 62% yield, white solid: m.p. 80-81 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 8.53 (s, 1H), 8.36 (d, $J = 7.1$ Hz, 1H), 8.29 (s, 1H), 8.15 (d, $J = 7.5$ Hz, 1H), 8.01 (d, $J = 6.6$ Hz, 1H), 7.70 (d, $J = 7.2$ Hz, 1H), 7.63 (t, $J = 7.3$ Hz, 1H), 7.53 (t, $J = 7.6$ Hz, 1H), 7.03 (d, $J = 7.3$ Hz, 2H), 6.91 (t, $J = 7.2$ Hz, 1H), 6.80 (s, 1H), 3.23 (d, $J = 18.8$ Hz, 1H), 2.96 (d, $J = 17.7$ Hz,

1H), 2.84 (d, $J = 17.8$ Hz, 1H), 2.61 (d, $J = 19.8$ Hz, 1H), 2.12-2.07 (m, 11H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 194.7, 162.1, 148.1, 148.0, 145.2, 144.3, 143.9, 139.8, 134.8, 134.6, 132.7, 131.2, 129.6, 129.4, 127.6, 127.2, 125.9, 123.9, 123.1, 123.0, 121.8, 118.9, 48.2, 30.5, 28.2, 23.1, 18.1, 9.3. HRMS (ESI): calcd. for $\text{C}_{31}\text{H}_{28}\text{N}_3\text{O}_6$ $[\text{M}+\text{H}]^+$ 538.1973, Found: 538.1976. R_f Value: 0.50 (PE/EA – 2:1).



(4d): 66.9 mg, 51% yield, colorless oil. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.74-7.72 (m, 2H), 7.54-7.51 (m, 1H), 7.46-7.43 (m, 4H), 7.37-7.29 (m, 3H), 7.15 (s, 2H), 7.11-7.08 (m, 1H), 6.83-6.81 (m, 1H), 3.26-3.18 (m,

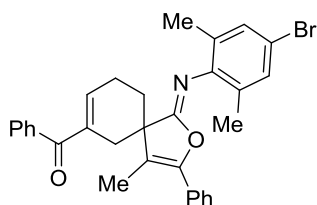
1H), 3.03-2.95 (m, 2H), 2.91 (d, $J = 0.9$ Hz, 2H), 2.59-2.53 (m, 1H), 2.11-2.08 (m, 2H), 2.02 (s, 3H), 1.27-1.15 (m, 12H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.8, 163.6, 144.6, 144.0, 143.8, 140.0, 134.8, 134.4, 134.3, 131.6, 131.2, 130.2, 129.7, 129.6, 129.5, 129.1, 128.8, 127.4, 127.0, 125.2, 117.7, 115.3, 48.3, 30.7, 28.4, 23.0, 17.9, 9.3. HRMS (ESI): calcd. for $\text{C}_{35}\text{H}_{38}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 504.2897, Found: 504.2899. R_f Value: 0.49 (PE/EA – 6:1).



(4e): 47.2 mg, 32% yield, white solid: m.p. 172-173 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.73-7.71 (m, 2H), 7.54-7.49 (m, 3H), 7.46-7.43 (m, 2H), 7.39-7.36 (m, 3H), 7.34-7.31 (m, 1H), 7.19-7.16 (m, 1H), 7.07-7.04 (m, 1H), 6.96 (dd, $J = 7.8, 1.3$ Hz, 1H), 6.85 (d, $J = 1.5$ Hz, 1H),

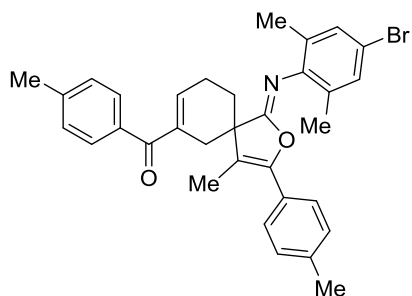
3.18-3.11 (m, 1H), 2.96 (d, $J = 18.1$ Hz, 1H), 2.83 (dd, $J = 18.1, 1.6$ Hz, 1H), 2.54-2.49 (m, 1H), 2.07-2.05 (m, 2H), 2.03 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 197.3, 162.7, 145.7, 145.6, 144.1, 140.1, 138.5, 135.4, 131.3, 129.8, 129.1, 128.4, 128.3, 128.0, 127.0, 126.1,

126.0, 123.3, 123.0, 116.1, 48.5, 35.0, 29.8, 29.7, 22.8, 9.3. HRMS (ESI): calcd. for C₃₃H₃₄NO₂ [M+H]⁺ 476.2584, Found: 476.2589. R_f Value: 0.50 (PE/EA – 6:1).



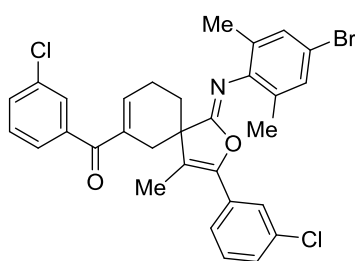
(4f): 78.1 mg, 57% yield, white solid: m.p. 178-179 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.73-7.72 (m, 2H), 7.54-7.51 (m, 1H), 7.44 (t, *J* = 7.5 Hz, 4H), 7.38-7.35 (m, 2H), 7.33-7.30 (m, 1H), 7.17 (s, 2H), 6.78

(d, *J* = 1.4 Hz, 1H), 3.18-3.10 (m, 1H), 2.87 (s, 2H), 2.57-2.52 (m, 1H), 2.11 (s, 6H), 2.08-2.04 (m, 2H), 2.01 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 197.5, 145.6, 144.1, 143.3, 138.3, 135.0, 131.5, 130.1, 129.7, 129.5, 129.2, 128.6, 128.3, 128.1, 126.9, 116.4, 115.1, 48.3, 30.9, 28.5, 22.9, 17.9, 9.2. HRMS (ESI): calcd. for C₃₁H₂₉BrNO₂ [M+H]⁺ 526.1376, Found: 526.1378. R_f Value: 0.50 (PE/EA – 8:1).



(4g): 92.9 mg, 61% yield, colorless oil. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.65 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.18-7.15 (m, 4H), 6.73 (d, *J* = 1.2 Hz, 1H), 3.15-3.08 (m, 1H), 2.88-2.80 (m, 2H), 2.55-2.50 (m, 1H),

2.41 (s, 3H), 2.35 (s, 3H), 2.09 (s, 6H), 2.06-2.02 (m, 2H), 1.98 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 197.3, 164.5, 145.7, 144.3, 142.3, 142.2, 138.6, 135.6, 135.1, 130.1, 129.8, 129.5, 129.0, 128.8, 126.9, 126.7, 115.6, 115.1, 48.3, 31.1, 28.7, 22.9, 21.5, 21.3, 17.9, 9.2. HRMS (ESI): calcd. for C₃₃H₃₃BrNO₂ [M+H]⁺ 554.1689, Found: 554.1679. R_f Value: 0.50 (PE/EA – 8:1).



(4h): 91.3 mg, 65% yield, colorless oil. ^1H NMR (500 MHz, CDCl_3):

δ (ppm) = 7.66 (t, J = 1.7 Hz, 1H), 7.55 (dt, J = 7.8, 1.3 Hz, 1H), 7.49

(dq, J = 8.0, 1.1 Hz, 1H), 7.39-7.38 (m, 1H), 7.36 (t, J = 7.8 Hz, 1H),

7.30-7.27 (m, 3H), 7.15 (s, 2H), 6.77 (d, J = 1.6 Hz, 1H), 3.17-3.09

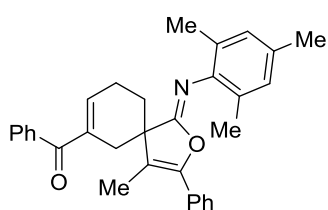
(m, 1H), 2.87-2.77 (m, 2H), 2.57-2.53 (m, 1H), 2.07 (s, 6H), 2.05-2.01 (m, 2H), 1.98 (s, 3H). ^{13}C

NMR (125 MHz, CDCl_3): δ (ppm) = 197.5, 163.1, 145.6, 143.8, 142.6, 138.4, 135.0, 131.4, 129.7,

129.2, 128.4, 128.2, 128.0, 127.0, 123.1, 122.4, 116.2, 48.1, 30.7, 28.4, 28.3, 23.1, 9.2. HRMS

(ESI): calcd. for $\text{C}_{31}\text{H}_{27}\text{BrCl}_2\text{NO}_2$ $[\text{M}+\text{H}]^+$ 594.0597, Found: 594.0591. R_f Value: 0.47 (PE/EA –

5:1).



(4i): 56.7 mg, 45% yield, white solid m.p. 64-65°C. ^1H NMR (500 MHz,

CDCl_3): δ (ppm) = 7.75 (d, J = 7.8 Hz, 2H), 7.53 (t, J = 7.3 Hz, 1H),

7.46-7.43 (m, 4H), 7.36 (t, J = 7.4 Hz, 2H), 7.33-7.30 (m, 1H), 6.87 (s,

2H), 6.78 (s, 1H), 3.21-3.17 (m, 1H), 2.89 (s, 2H), 2.53 (dd, J = 19.7, 4.4 Hz, 1H), 2.29 (s, 3H),

2.13 (s, 6H), 2.06-2.05 (m, 2H), 2.01 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 197.6, 145.7,

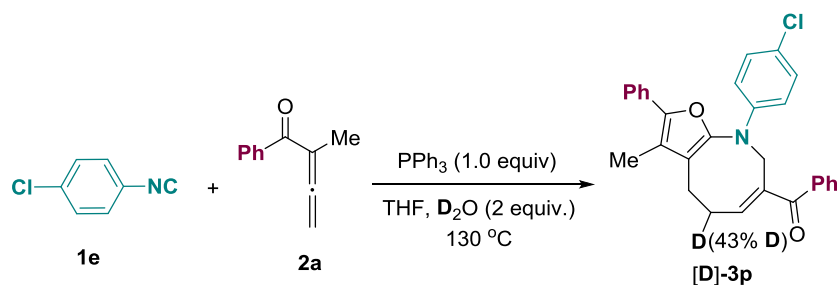
143.4, 142.3, 138.4, 135.1, 131.6, 131.5, 129.8, 129.3, 128.4, 128.2, 128.1, 128.0, 127.2, 127.1,

116.2, 48.1, 31.0, 28.6, 23.0, 20.7, 18.0, 9.2. HRMS (ESI): calcd. for $\text{C}_{32}\text{H}_{32}\text{NO}_2$ $[\text{M}+\text{H}]^+$ 462.2428,

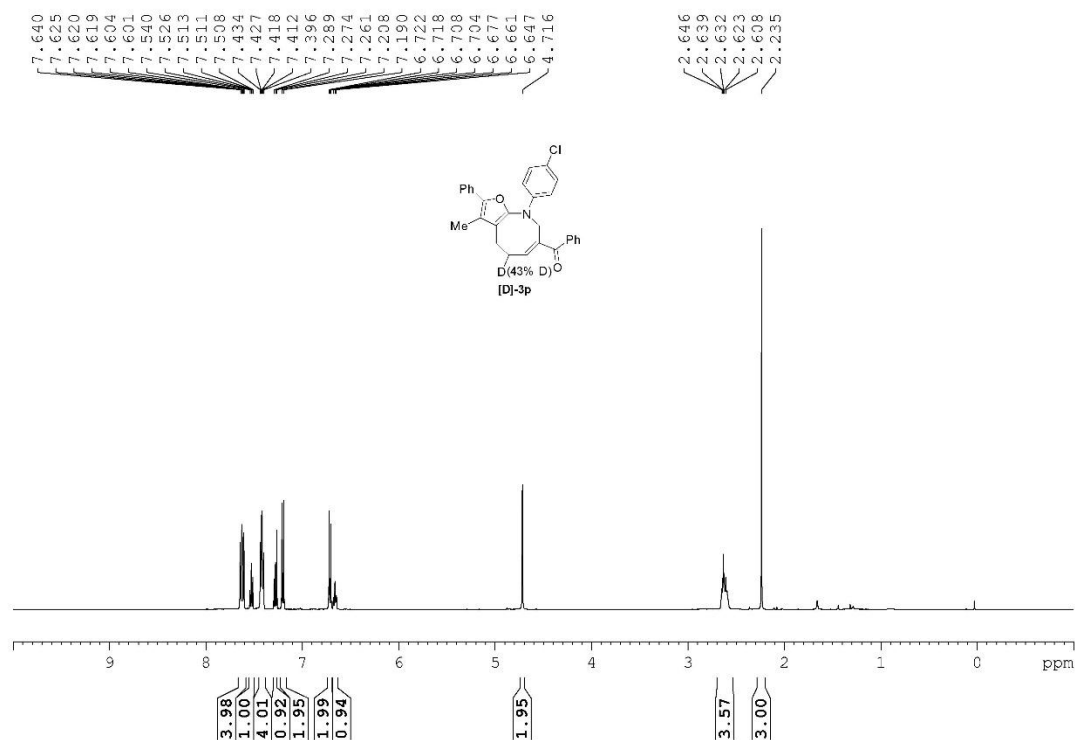
Found: 462.2414. R_f Value: 0.50 (PE/EA – 8:1).

4 Preliminary Mechanistic Study and Control Experiment

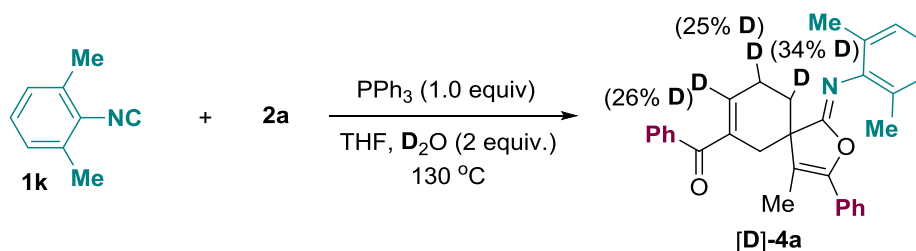
a) Reaction for Furan-fused eight-membered ring formation with D₂O under the optimal conditions



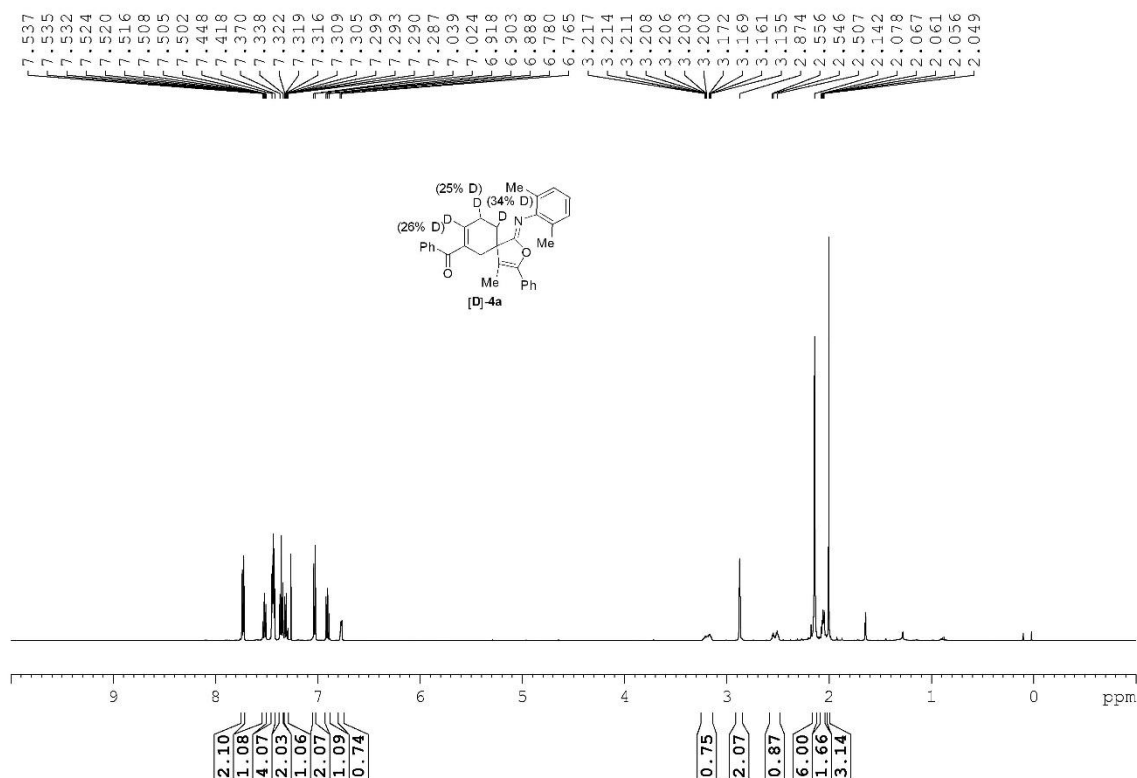
Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with isocyanide **1e** (0.5 mmol), allenyl ketone **2a** (0.5mmol) and triphenylphosphine (1.0 equiv.) in THF (5.0 mL) at room temperature. To this mixture D_2O (2 equiv.) was added. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at $130\text{ }^\circ\text{C}$ for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford product **[D]-3p**.



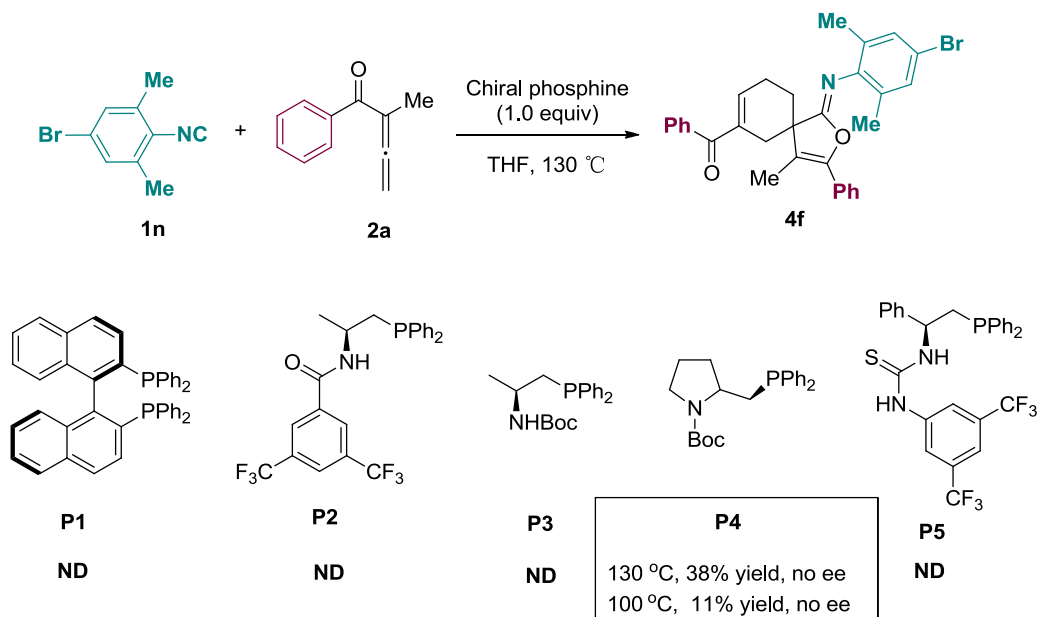
b) Reaction for spirocycle formation with D₂O under the optimal conditions



Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with isocyanide **1k** (0.5 mmol), allenyl ketone **2a** (0.5mmol) and triphenylphosphine (1.0 equiv.) in THF (5.0 mL) at room temperature. To this mixture D₂O (2 equiv.) was added. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 130 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford product [D]-4a.



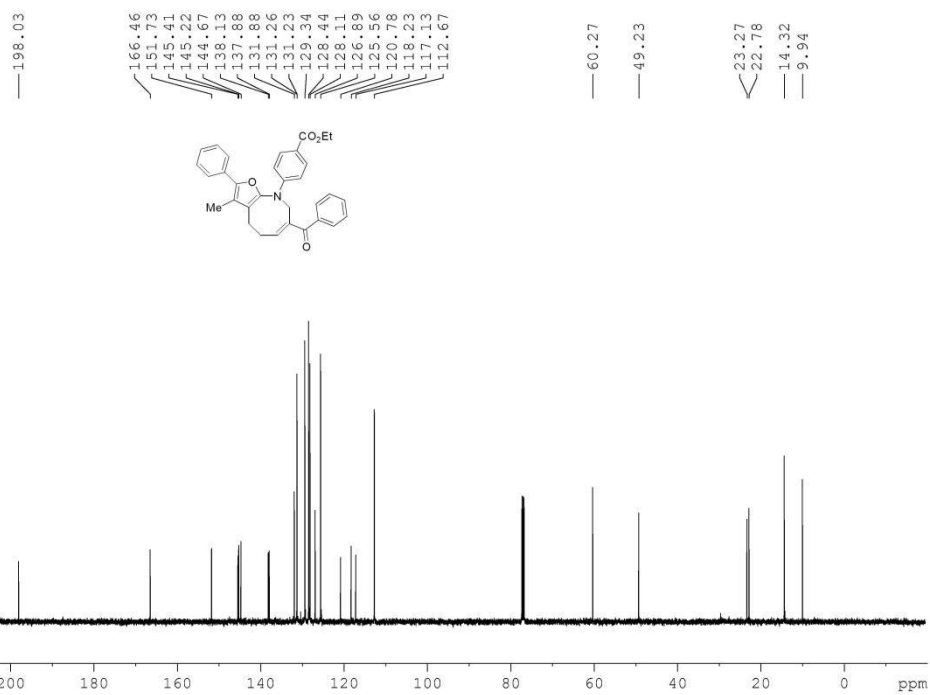
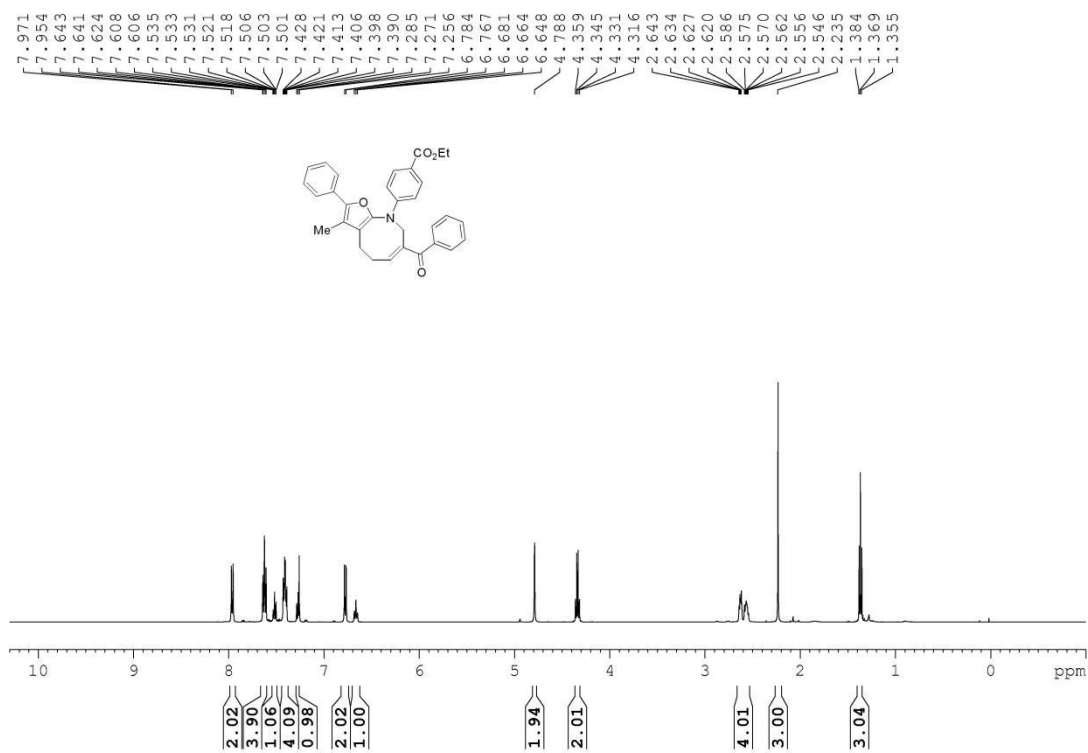
c) Reaction with chiral phosphine for spirocycle formation



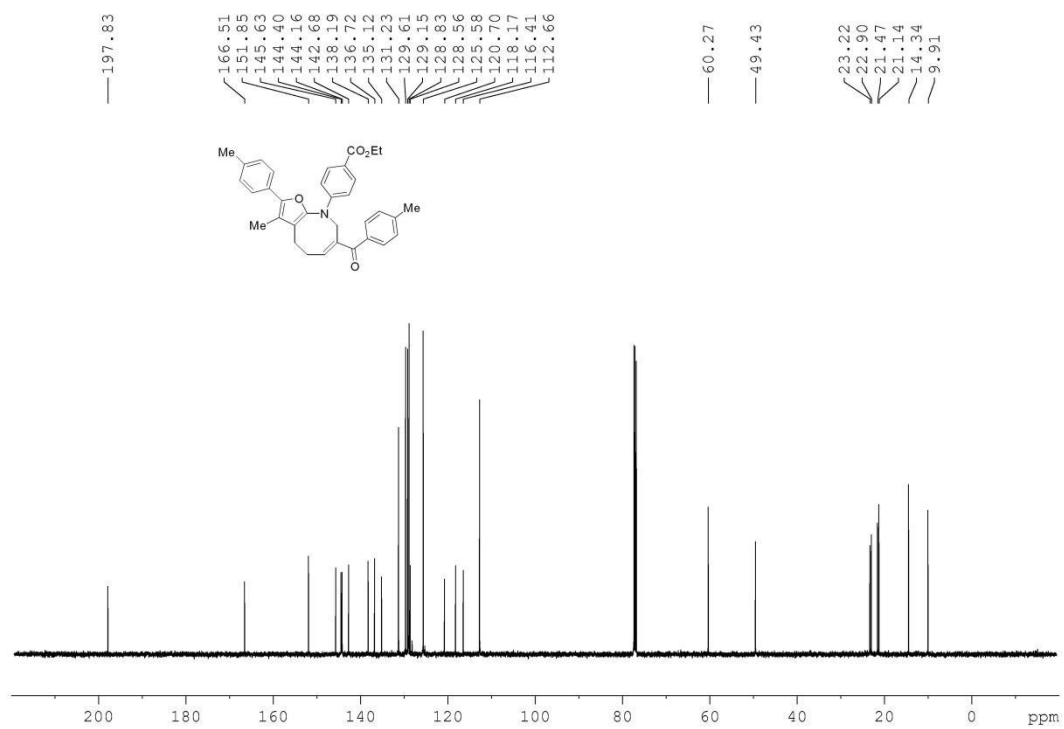
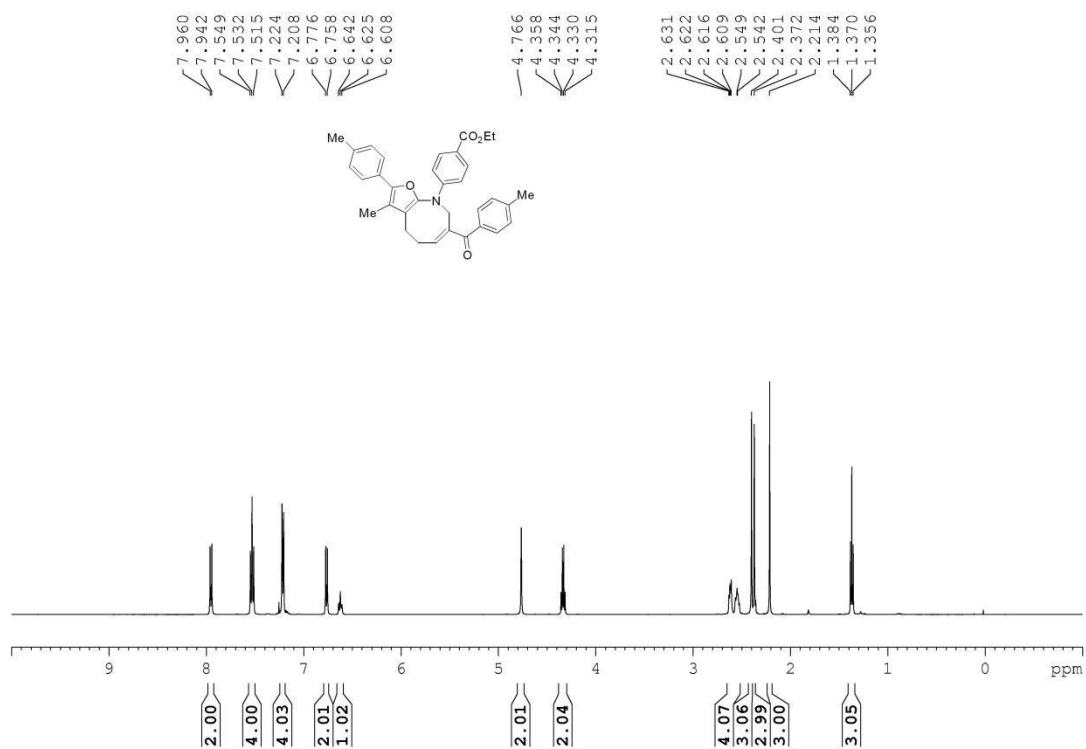
Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with isocyanide **1n** (0.5 mmol), allenyl ketone **2a** (0.5mmol) and chiral phosphine (1.0 equiv.) in THF (5.0 mL) at room temperature. The rubber septum was then replaced by a Teflon-coated screw cap, and the reaction vessel placed in an oil bath at 130 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. The solvent was then removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford product.

5 ¹H NMR and ¹³C NMR Spectra of All Compounds

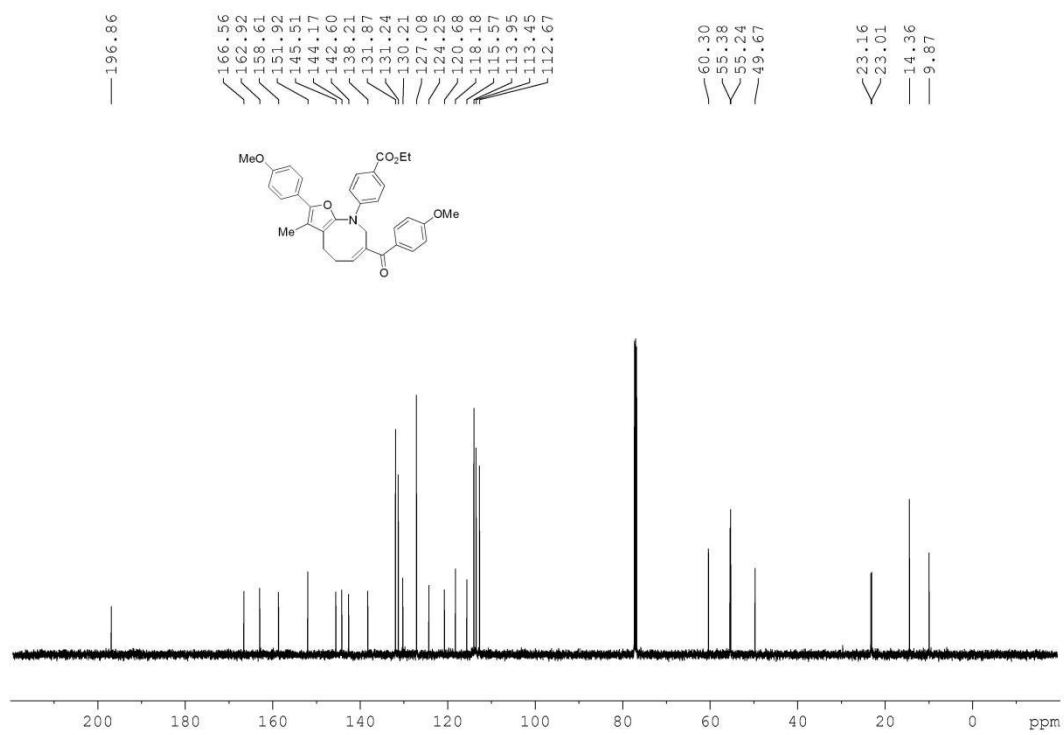
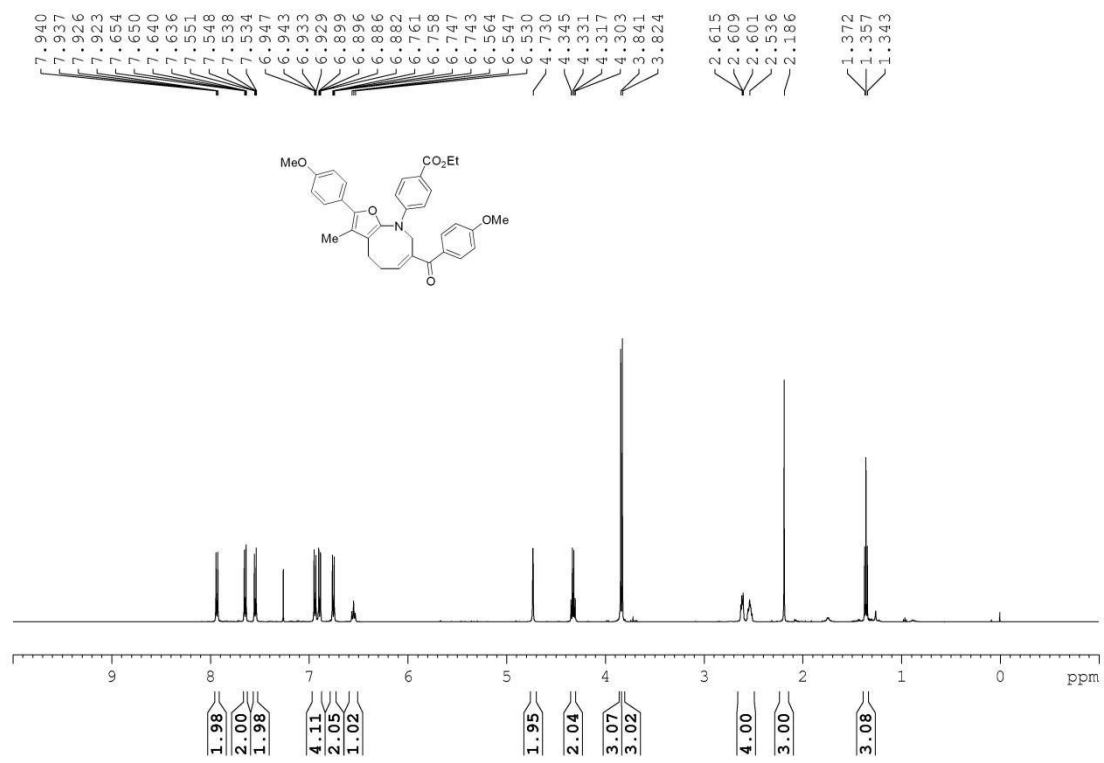
Compound 3a



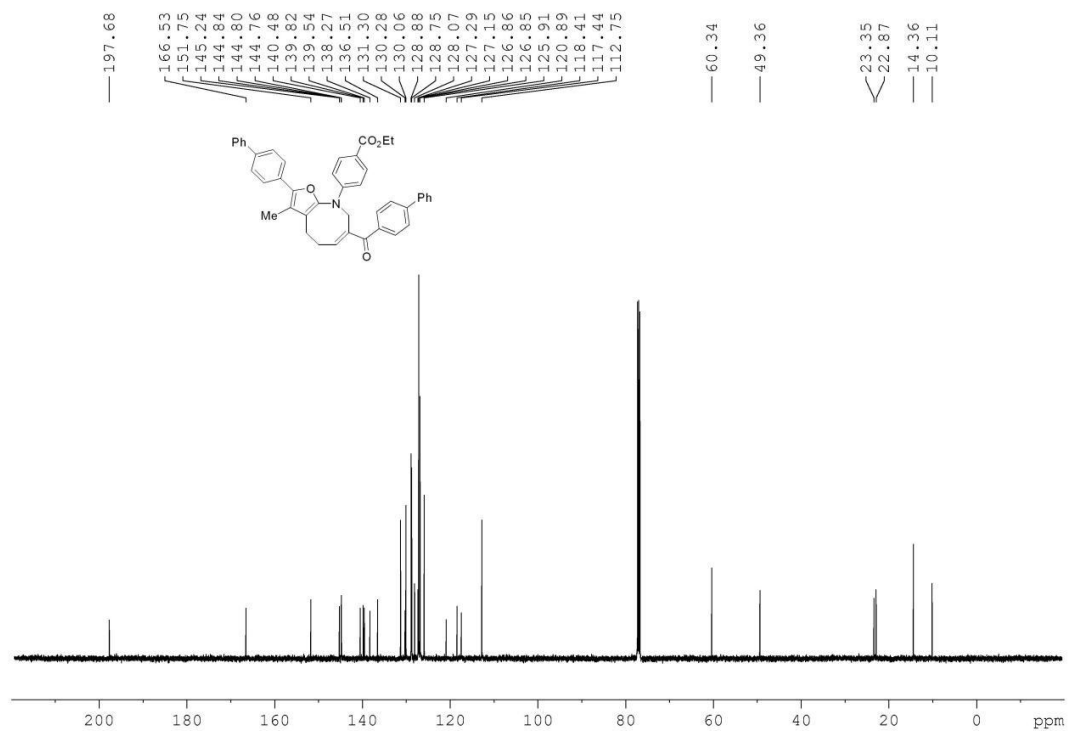
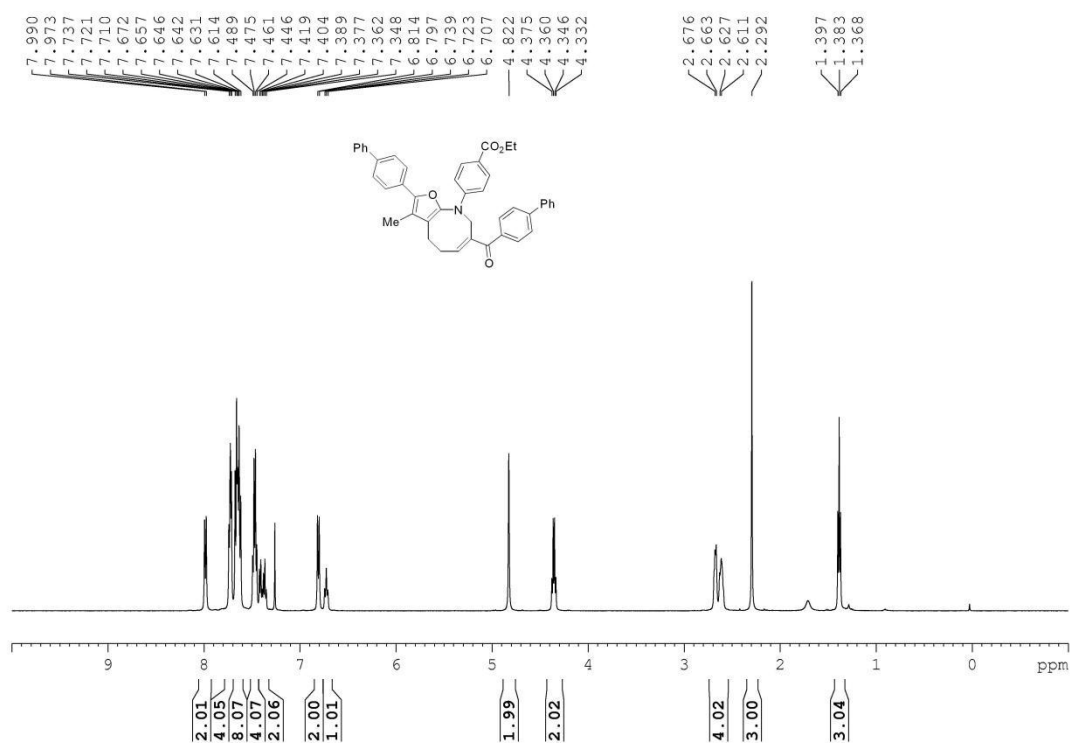
Compound 3b



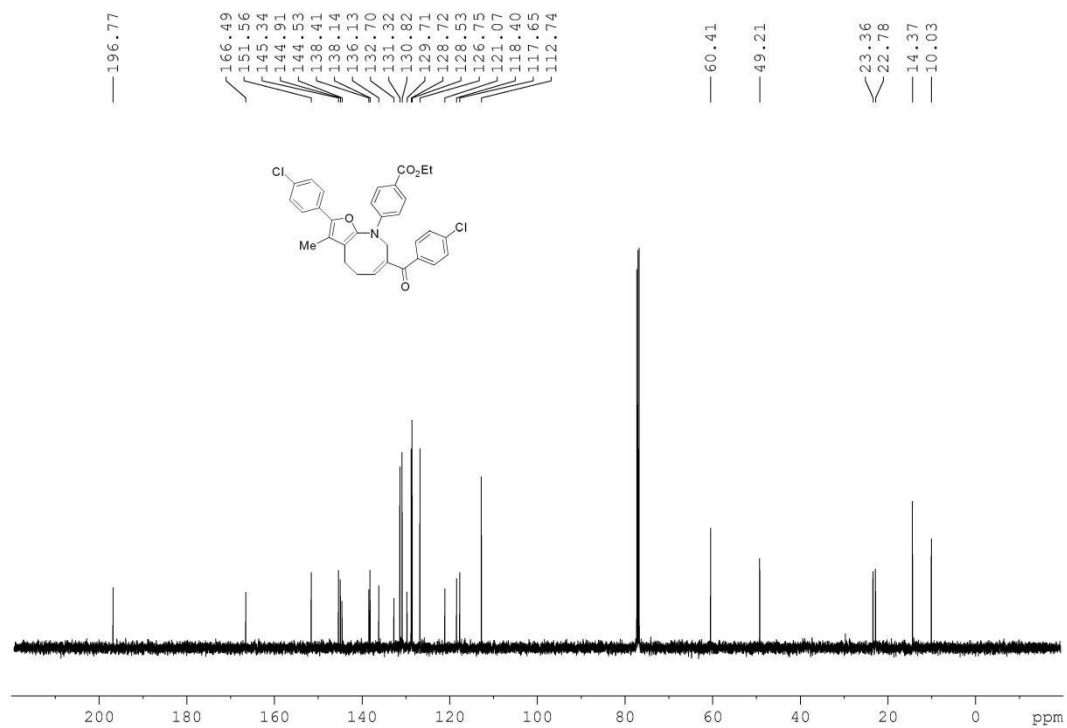
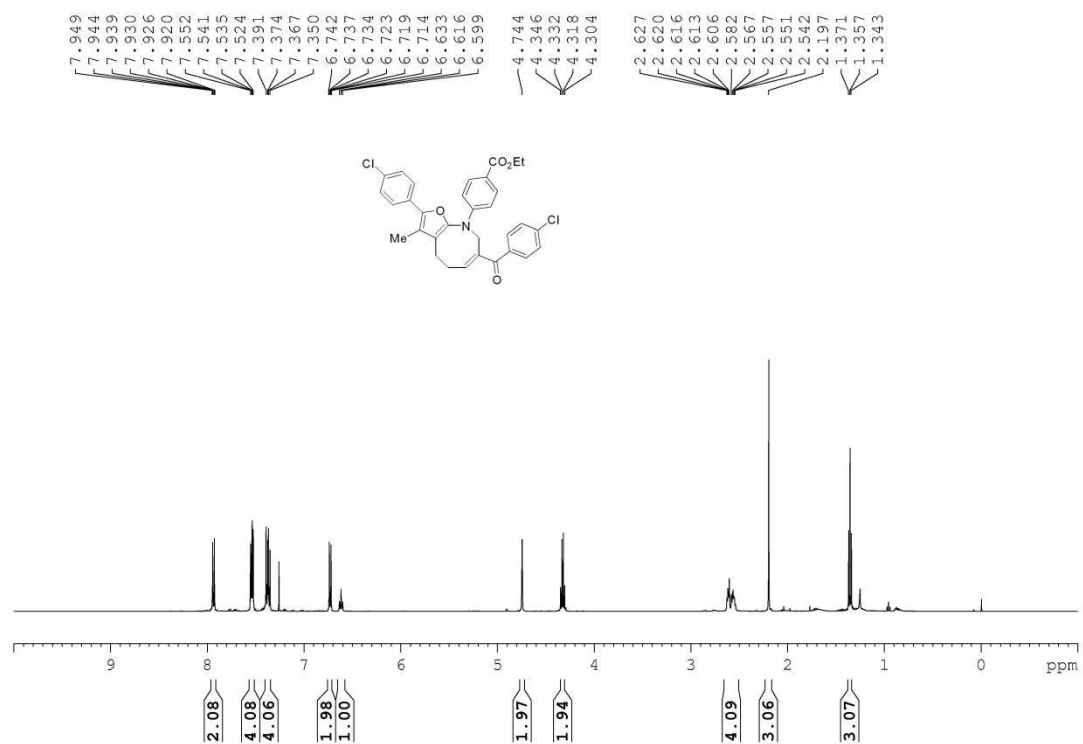
Compound 3c



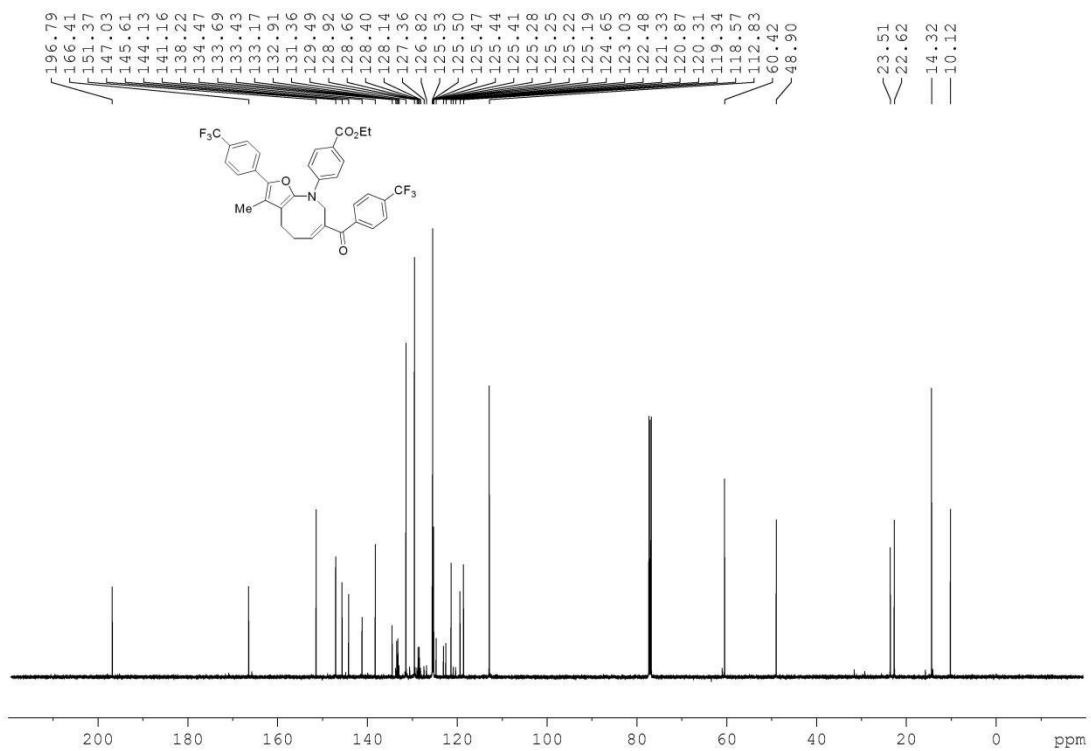
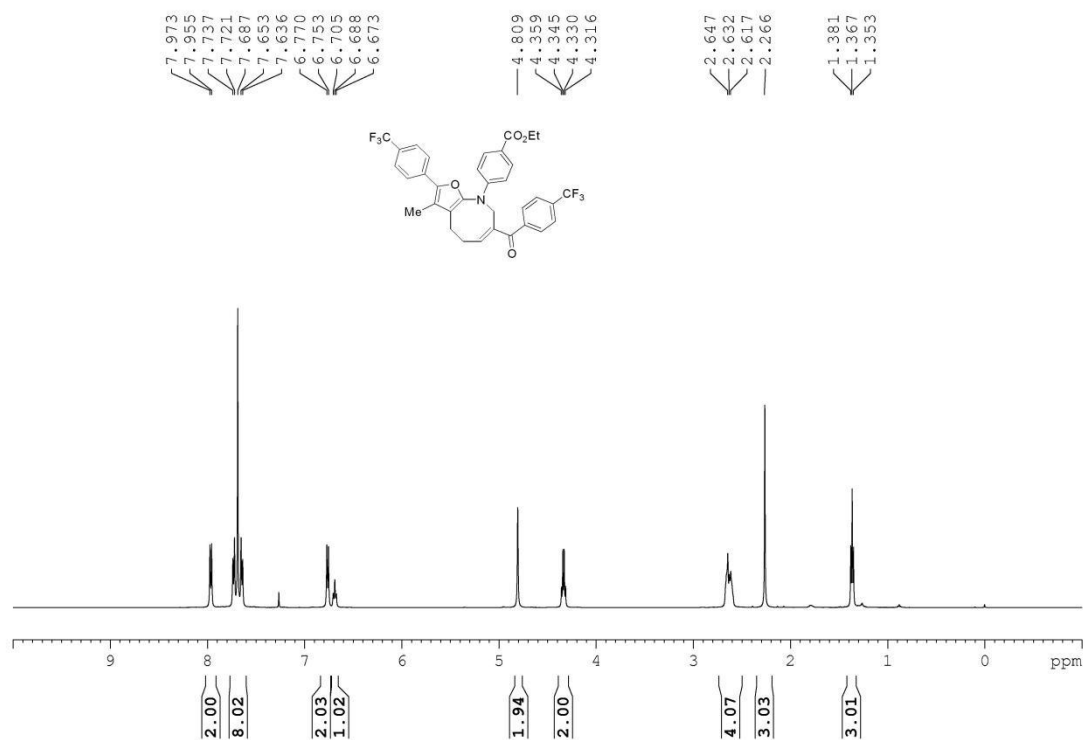
Compound 3d



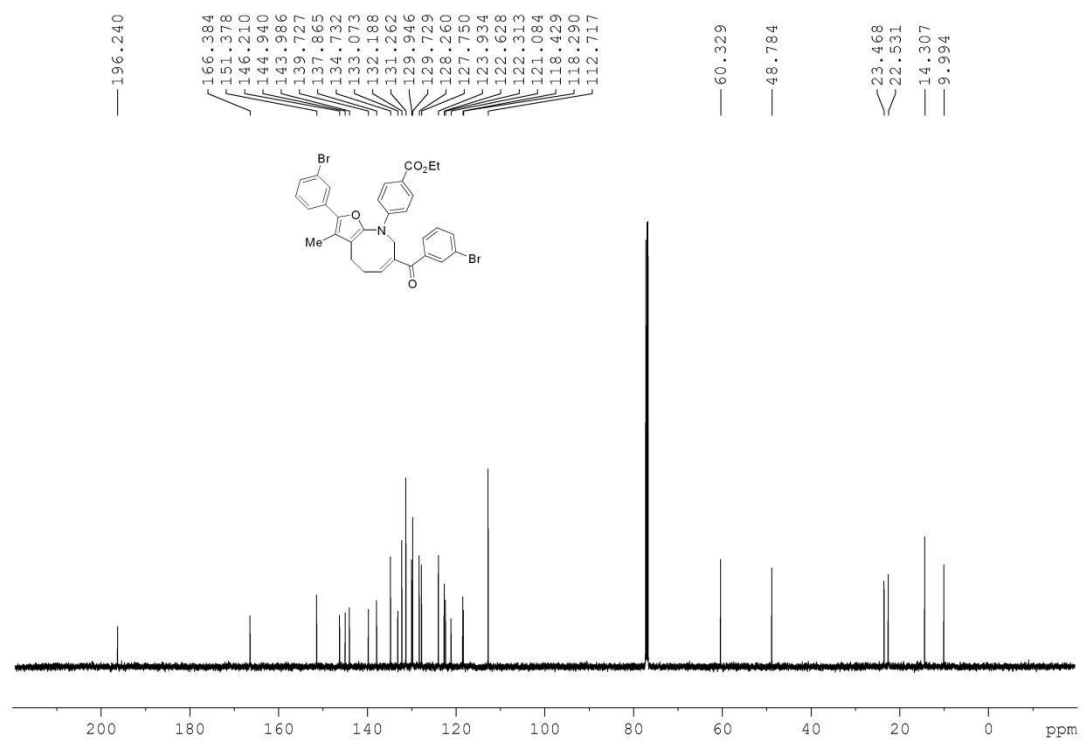
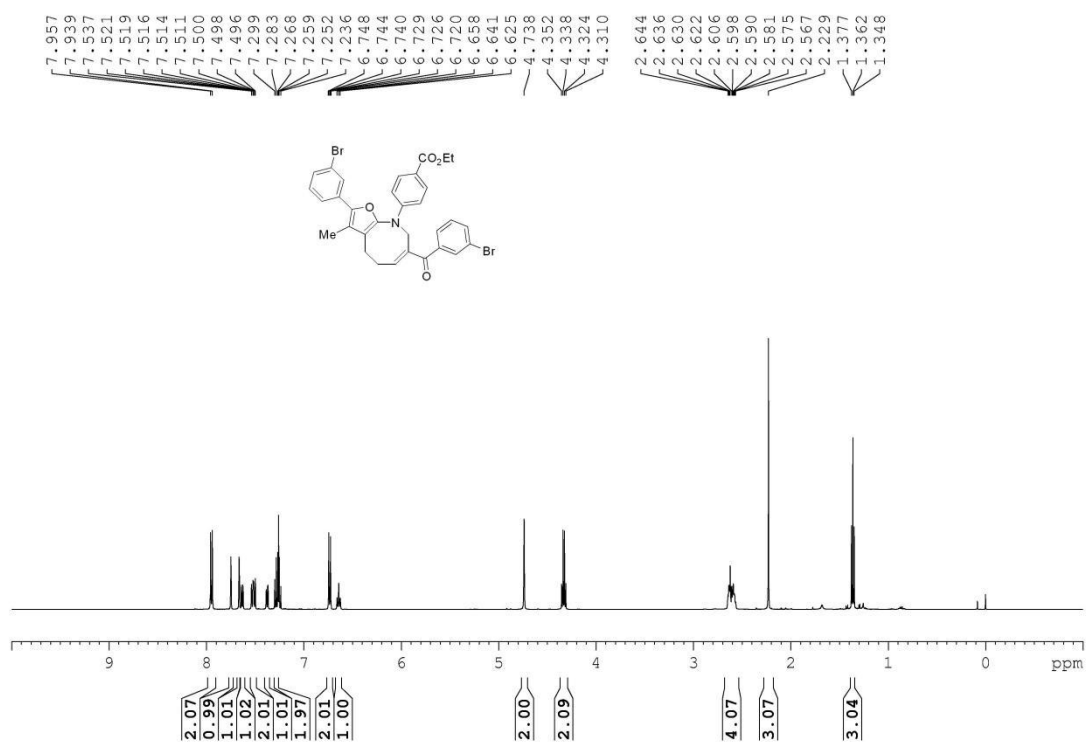
Compound 3e



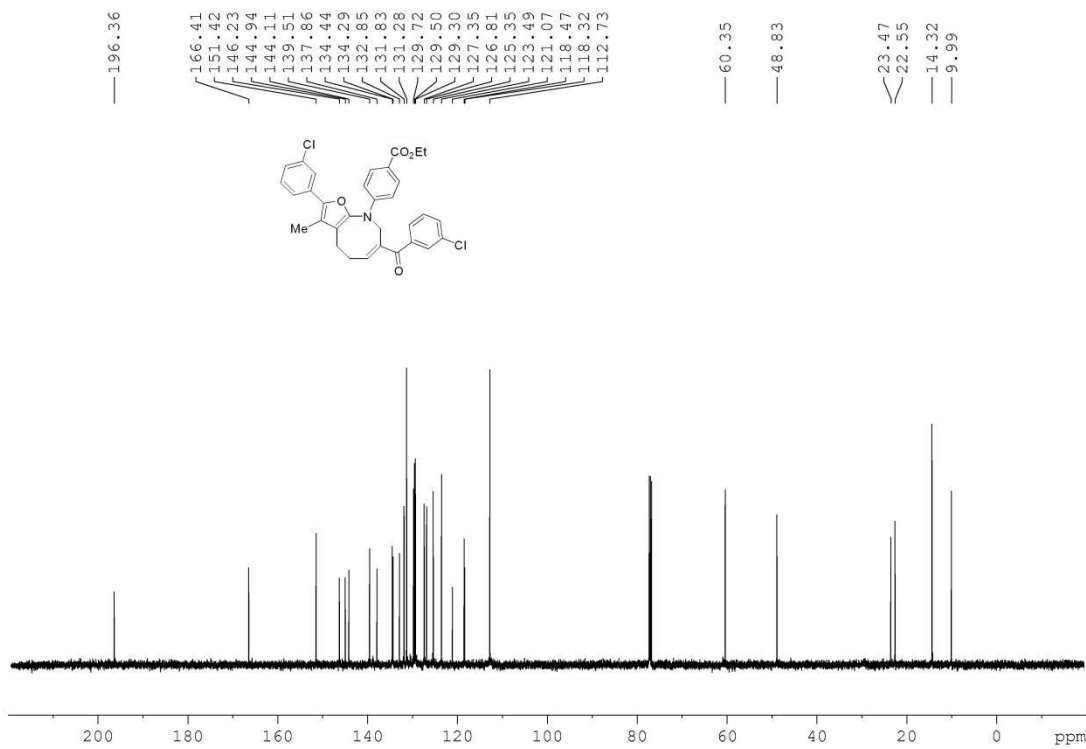
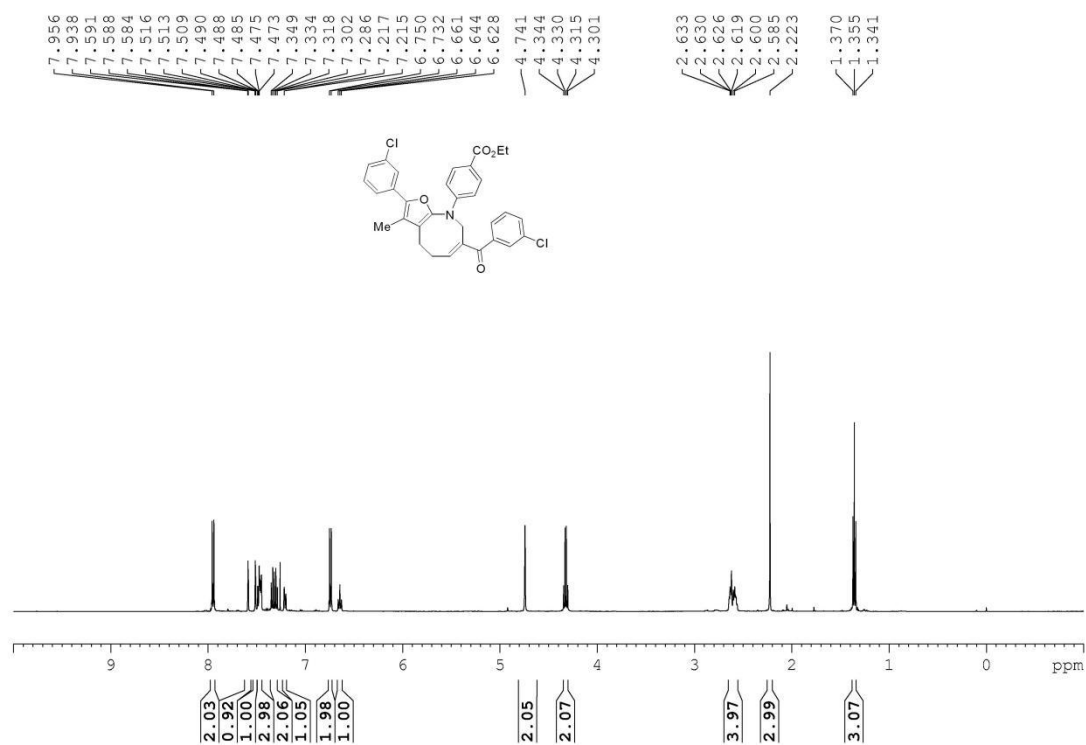
Compound 3f



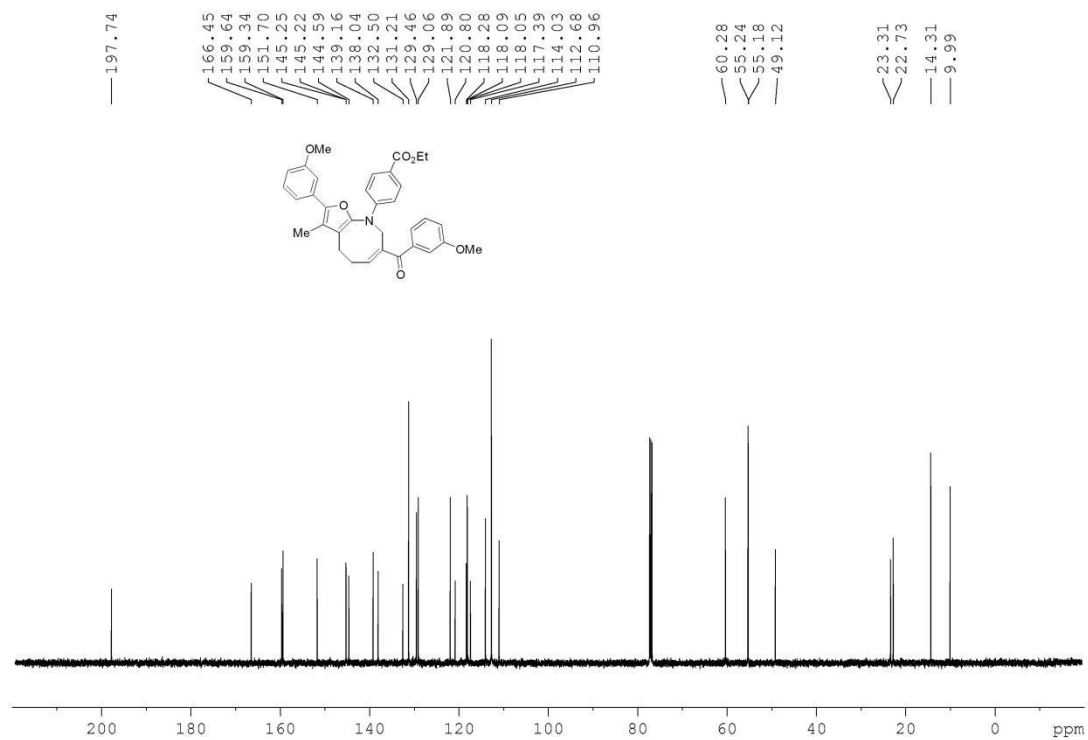
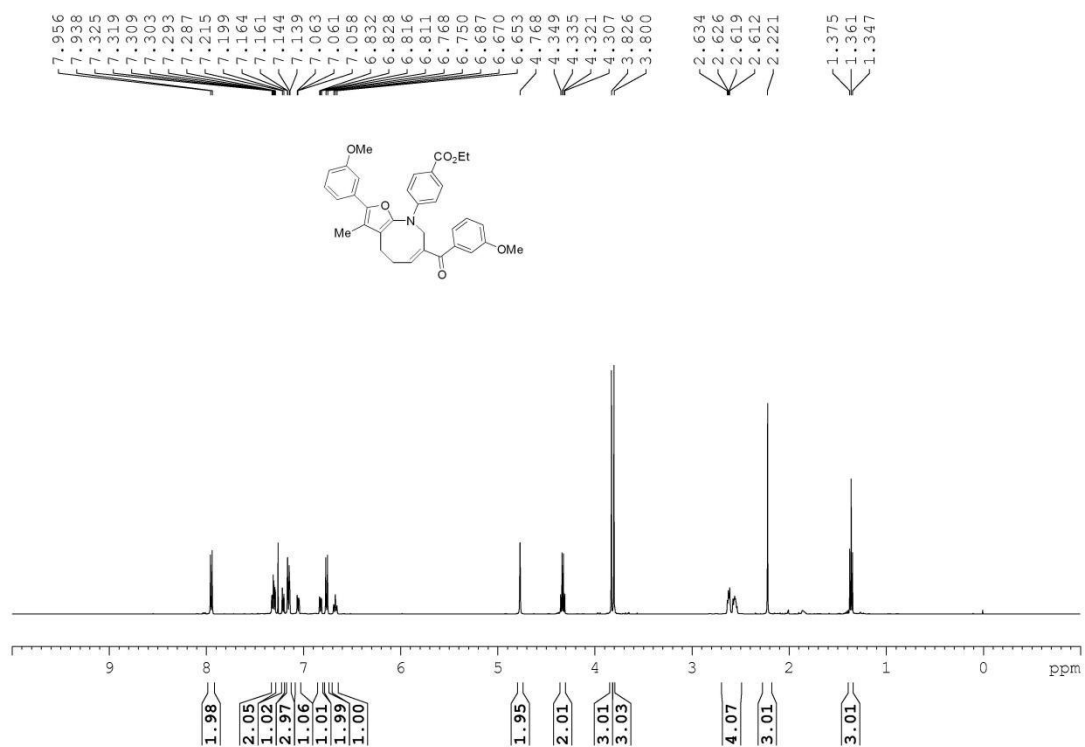
Compound 3g



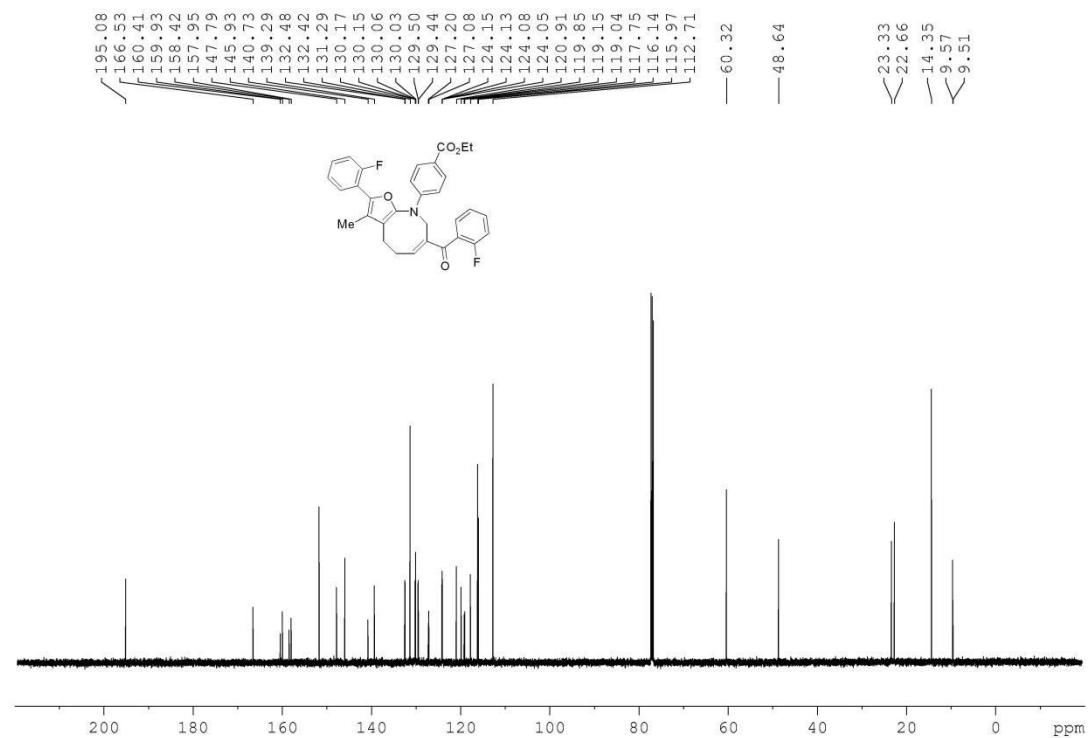
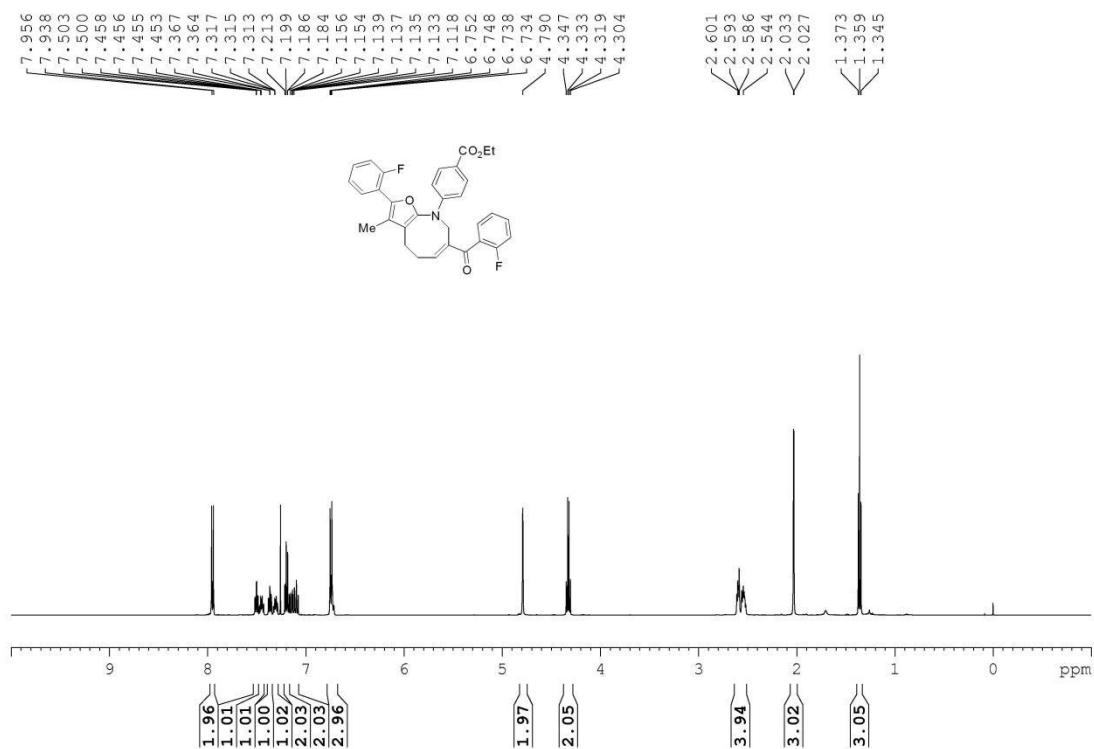
Compound 3h



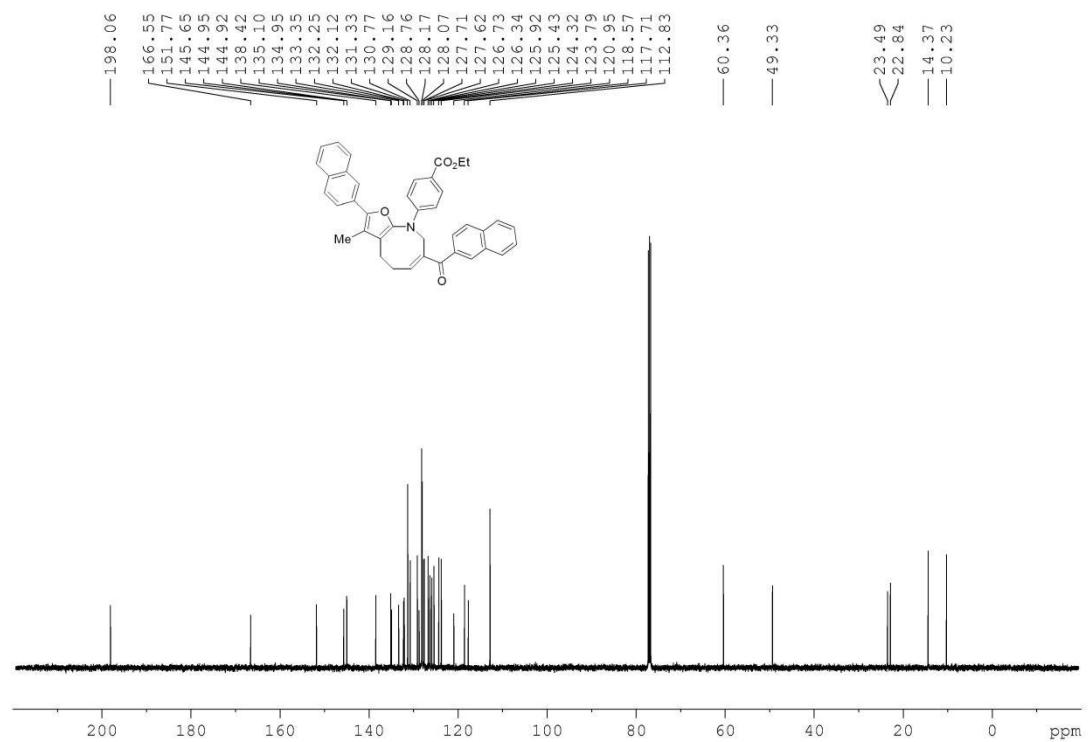
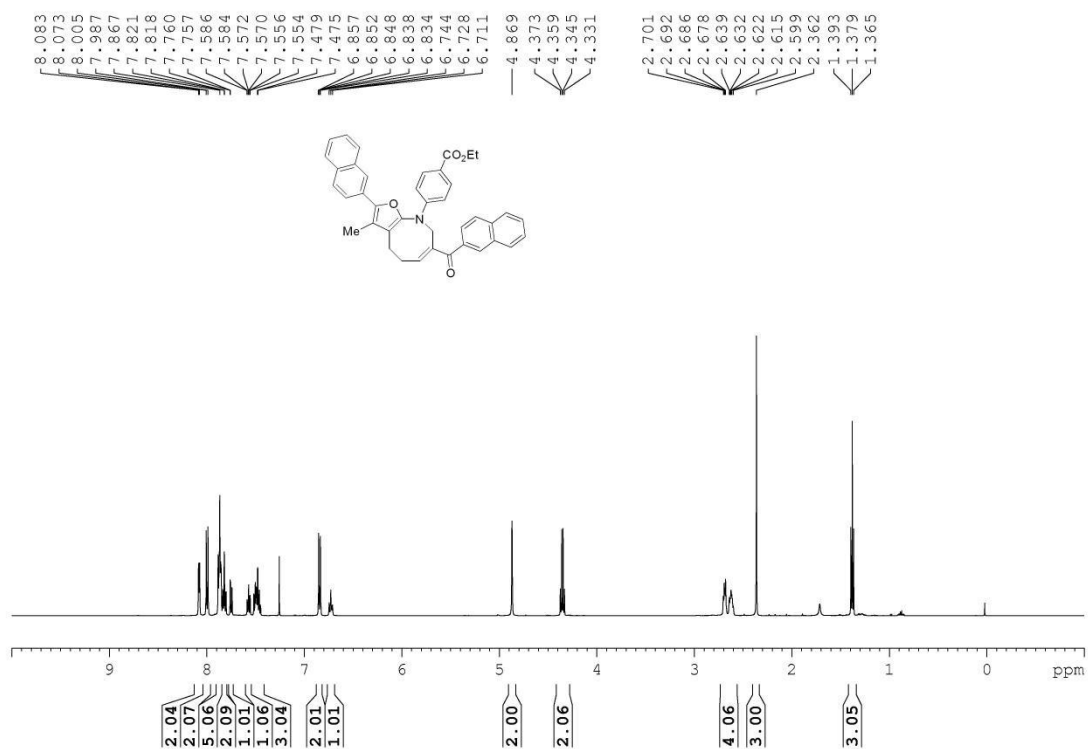
Compound 3i



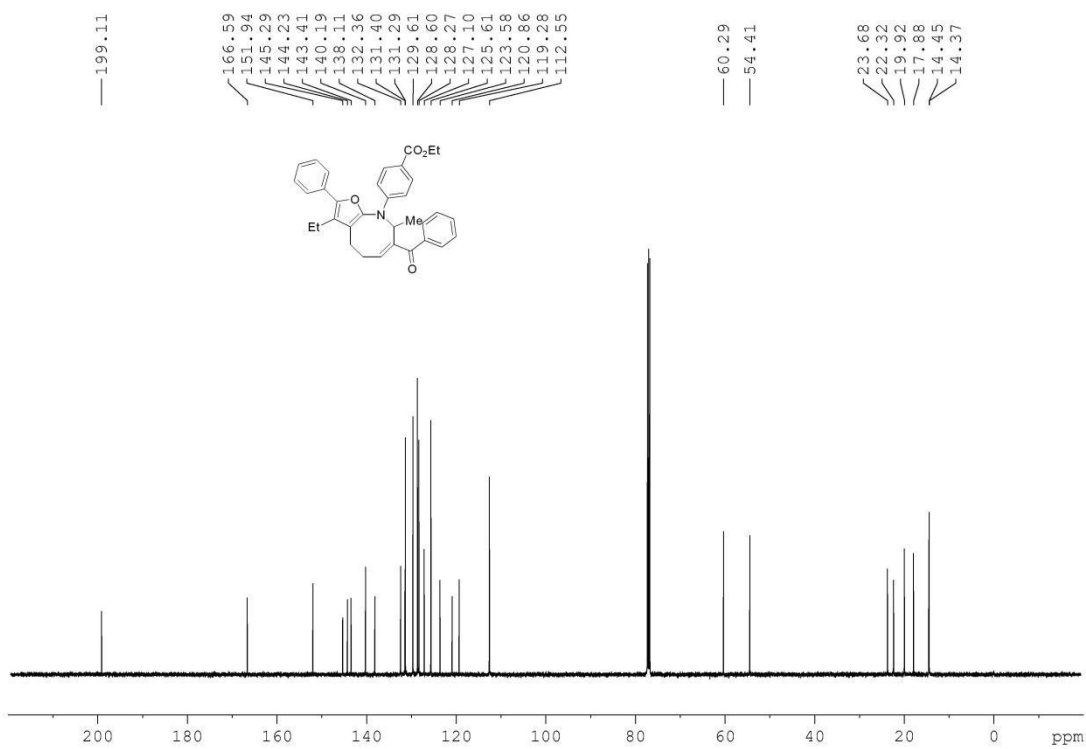
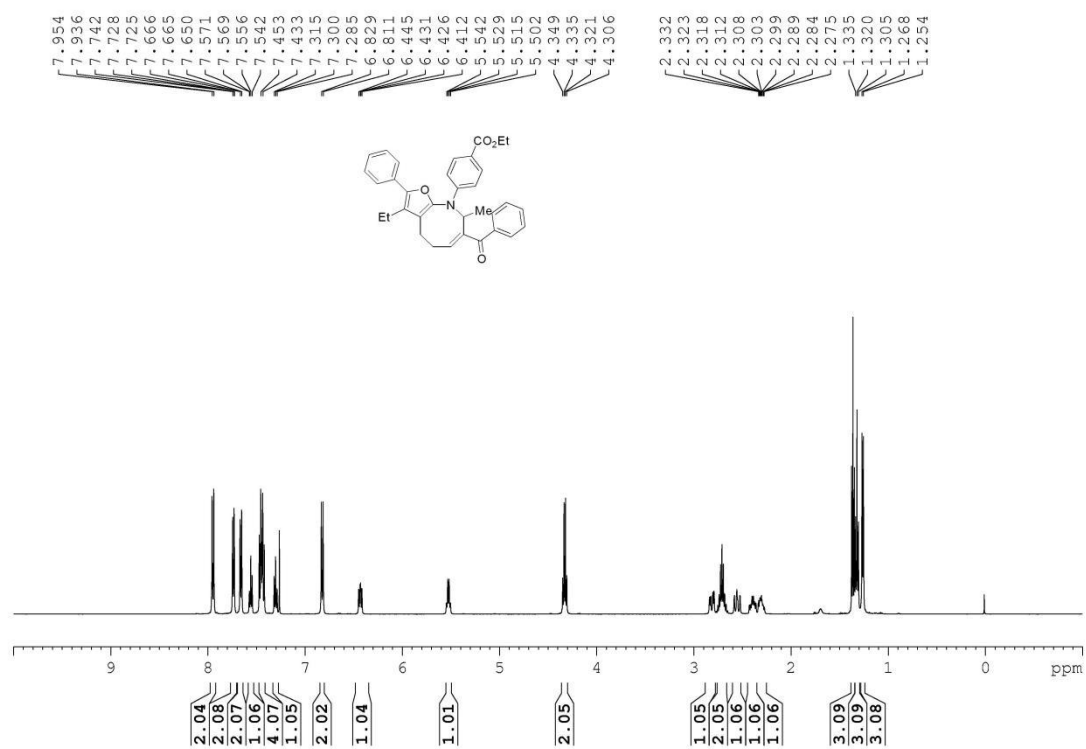
Compound 3j



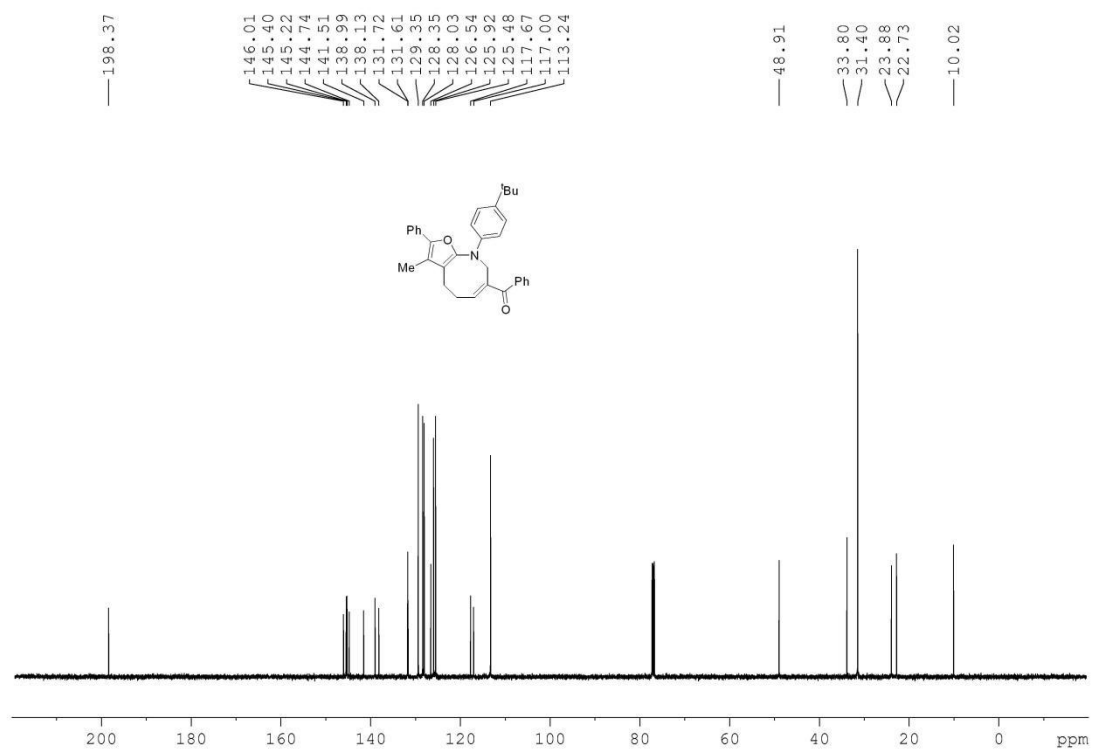
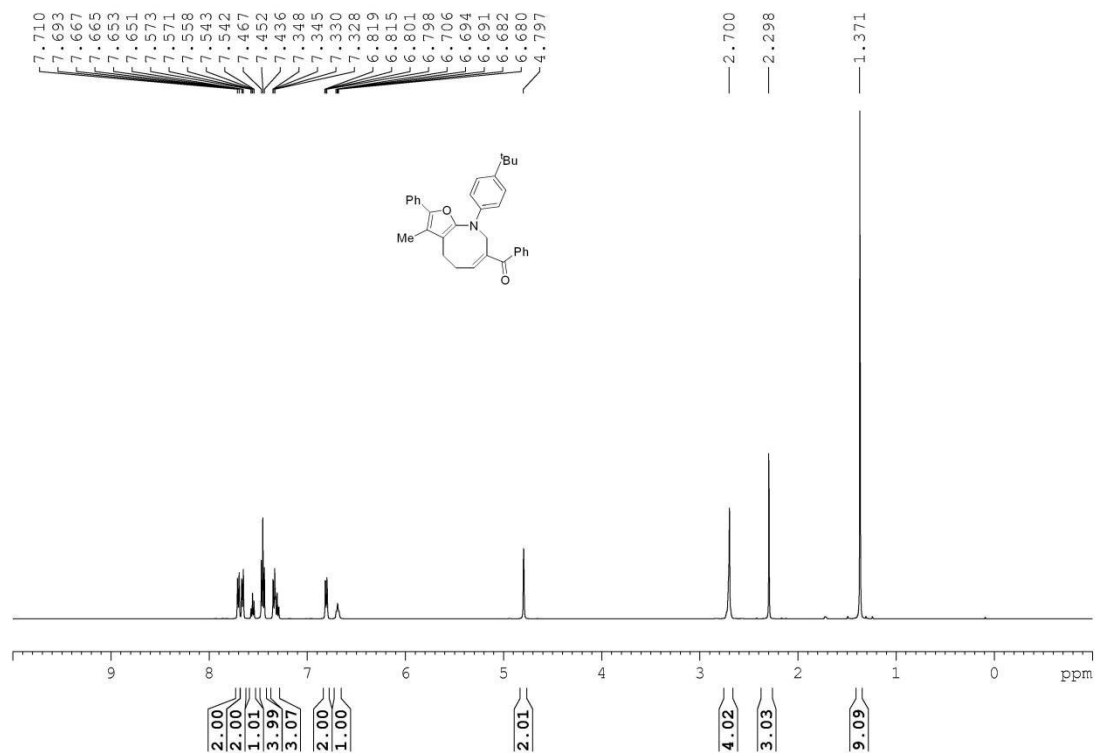
Compound 3k



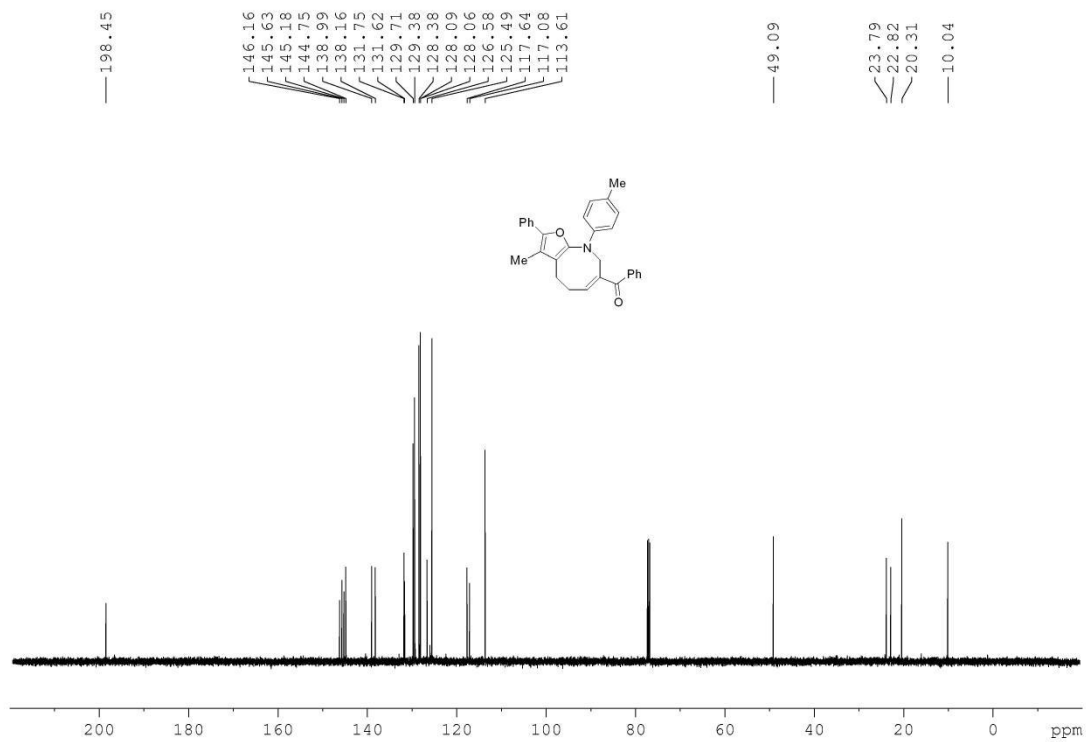
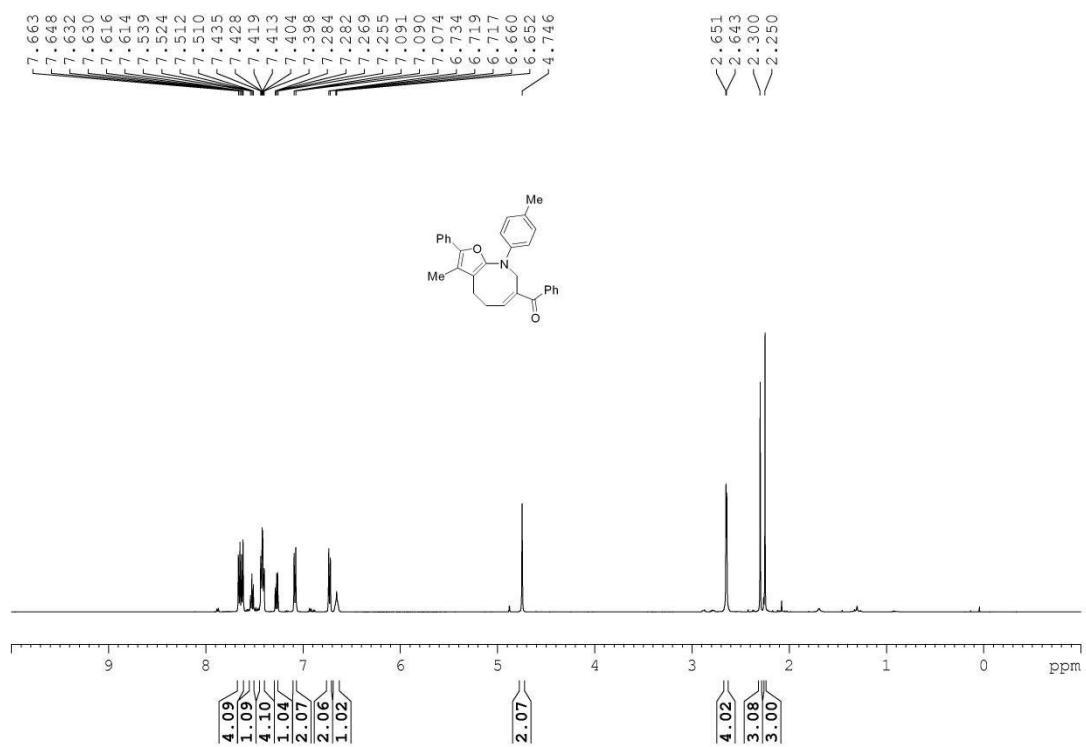
Compound 31



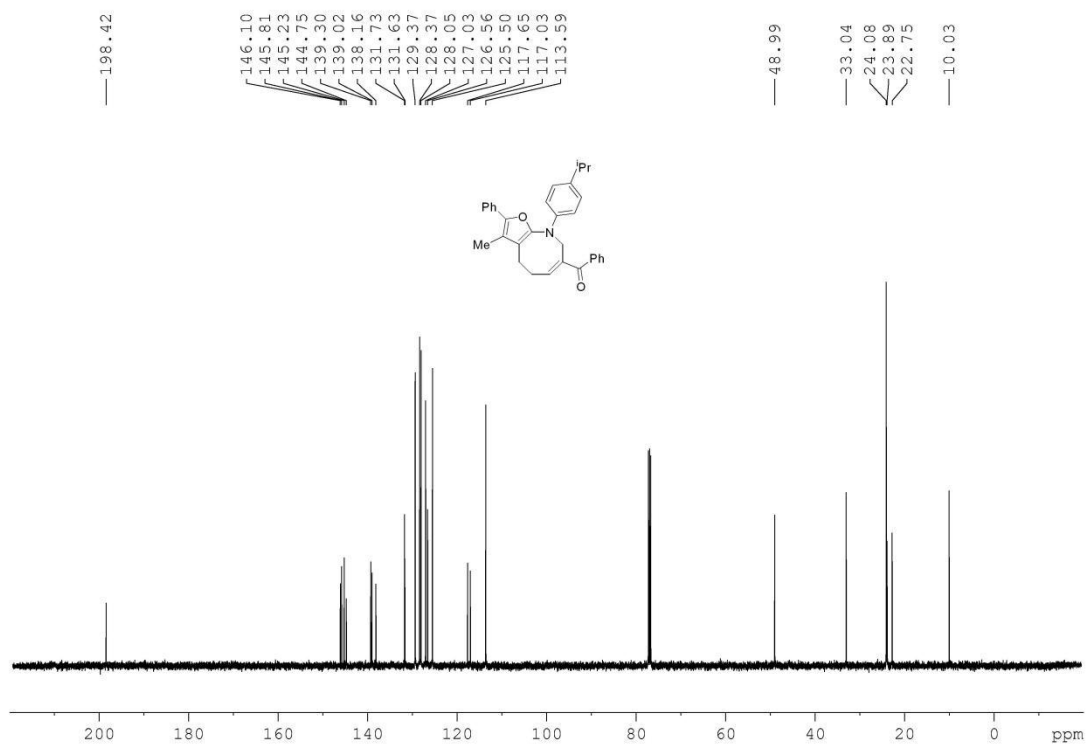
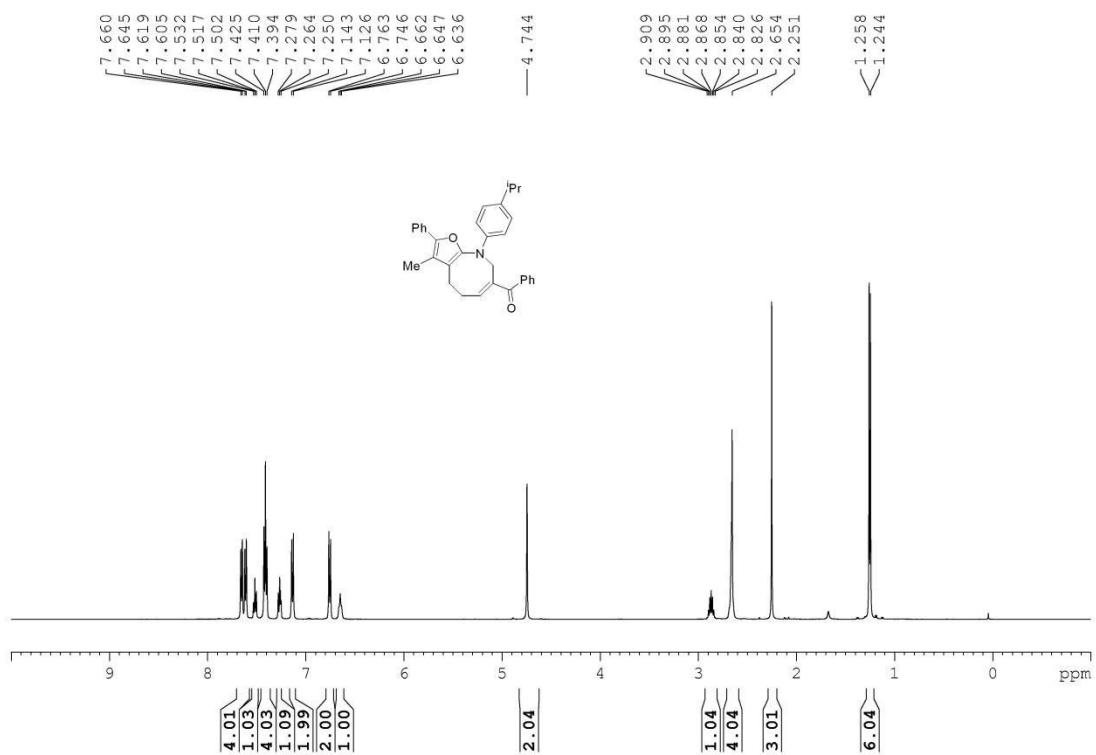
Compound 3m



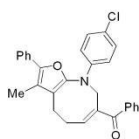
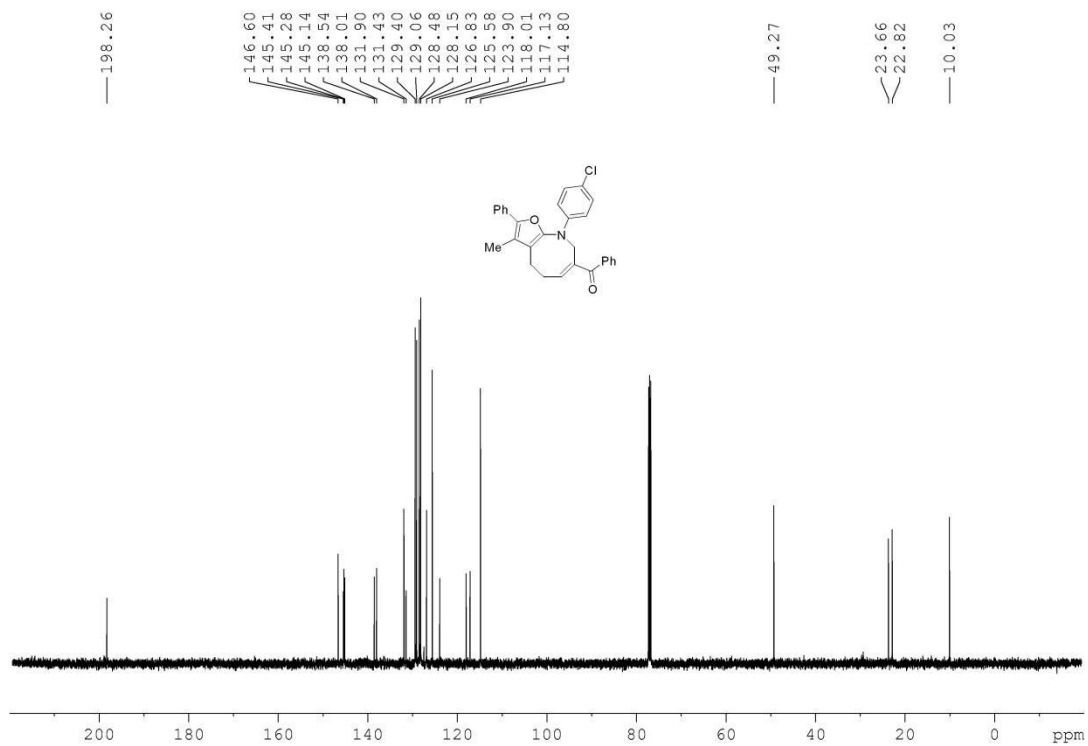
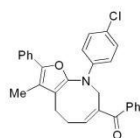
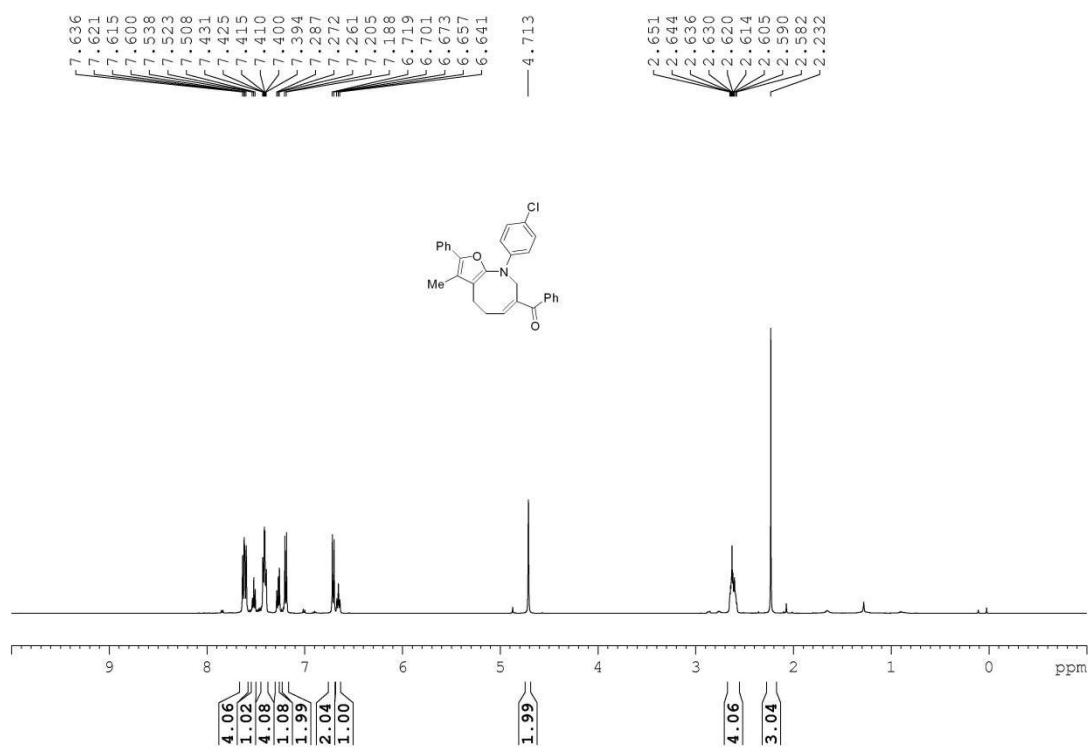
Compound 3n



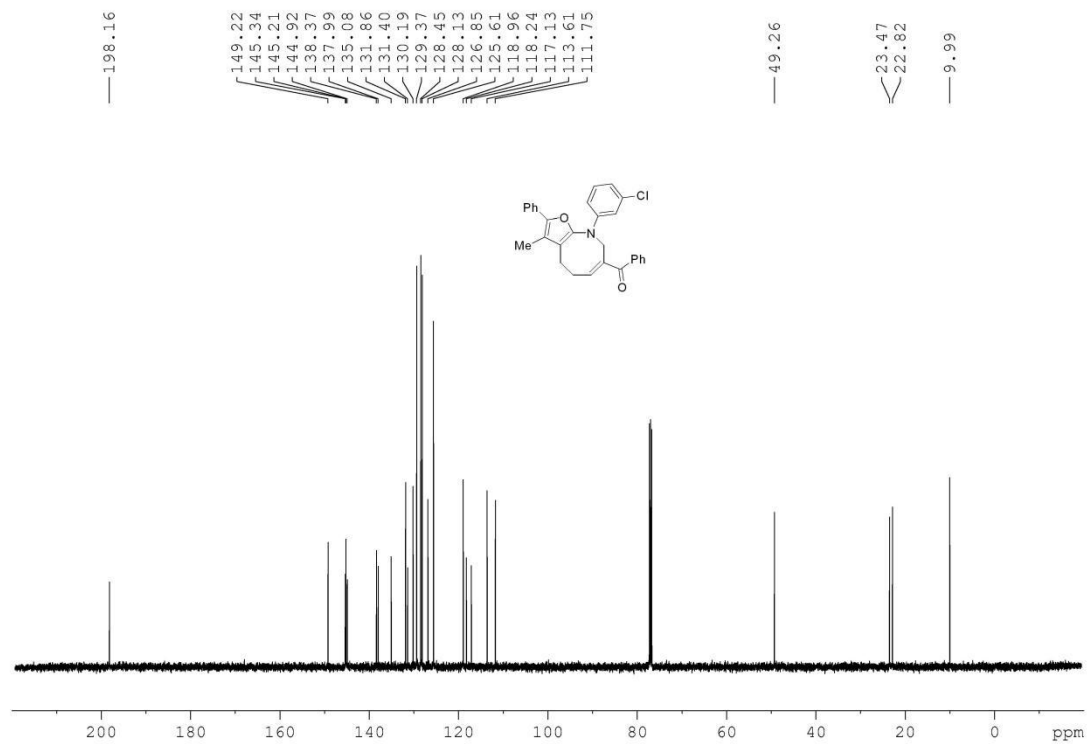
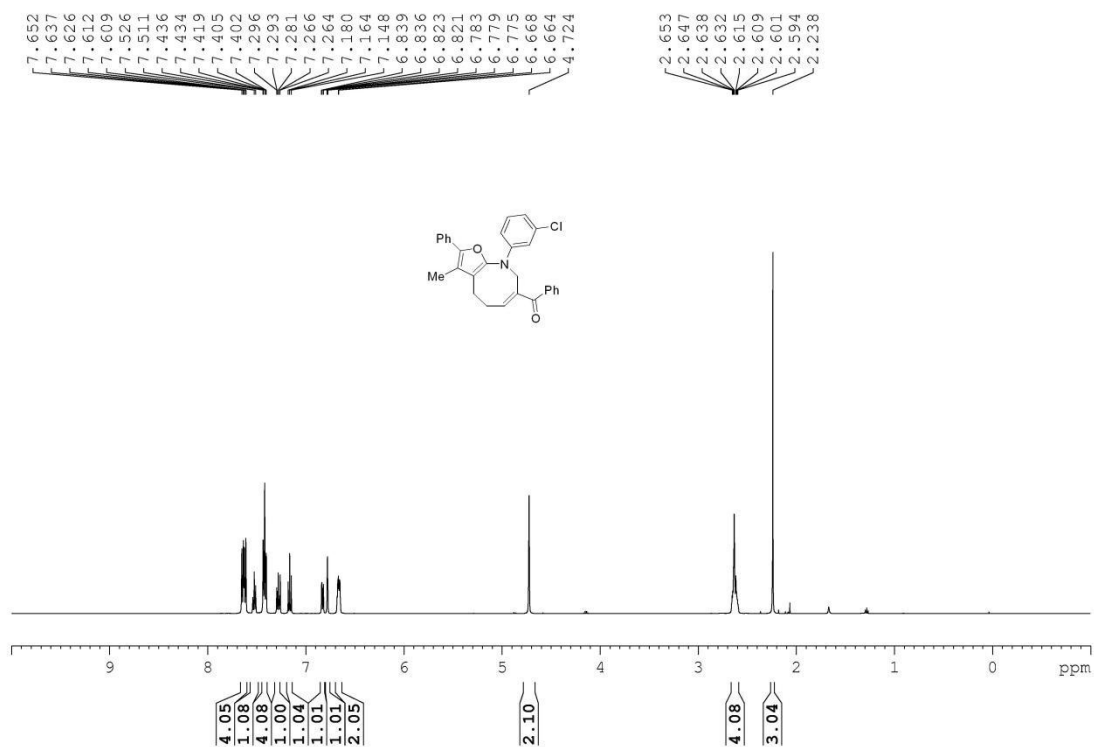
Compound 3o



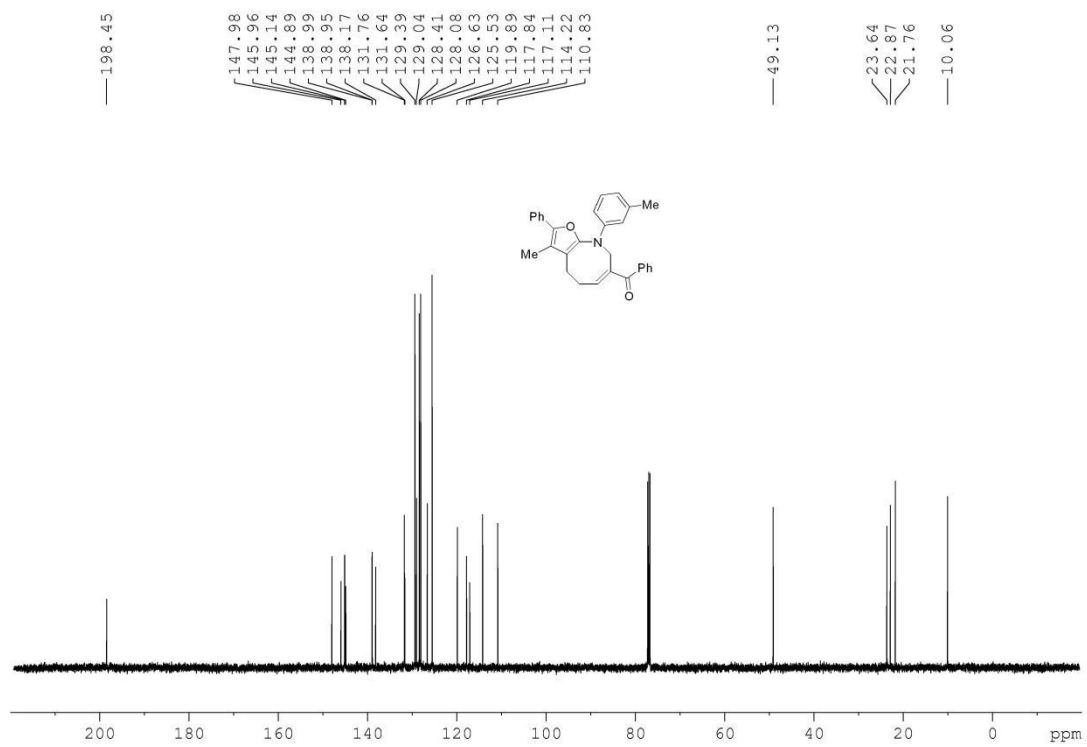
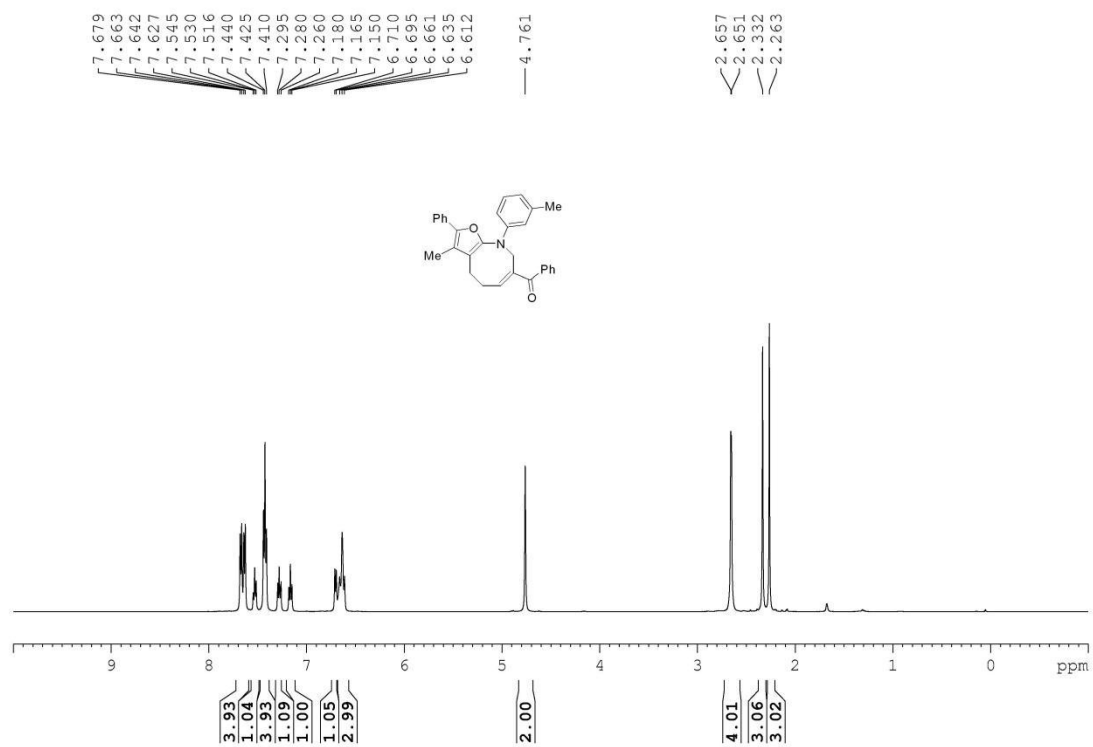
Compound 3p



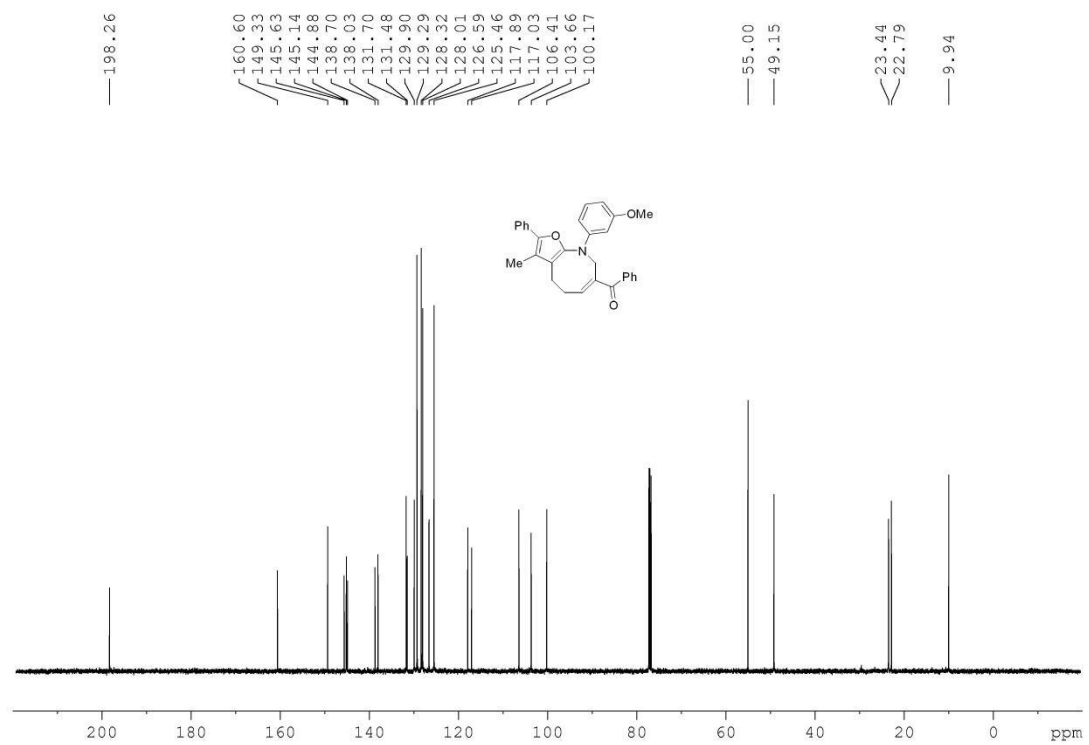
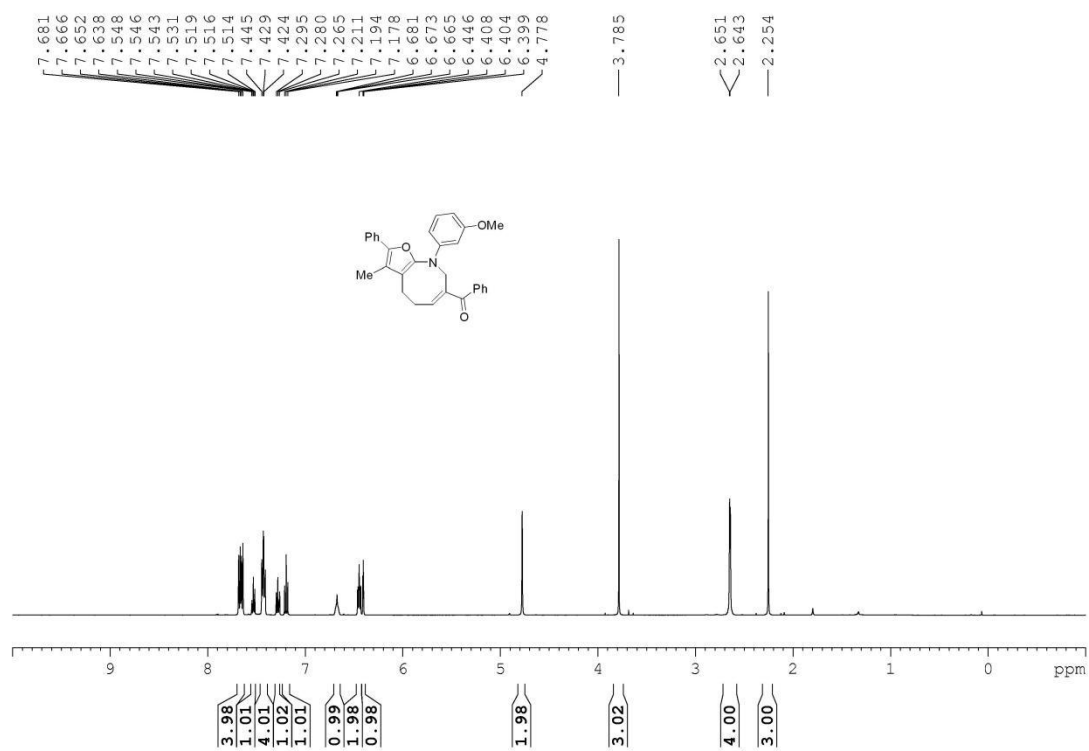
Compound 3q



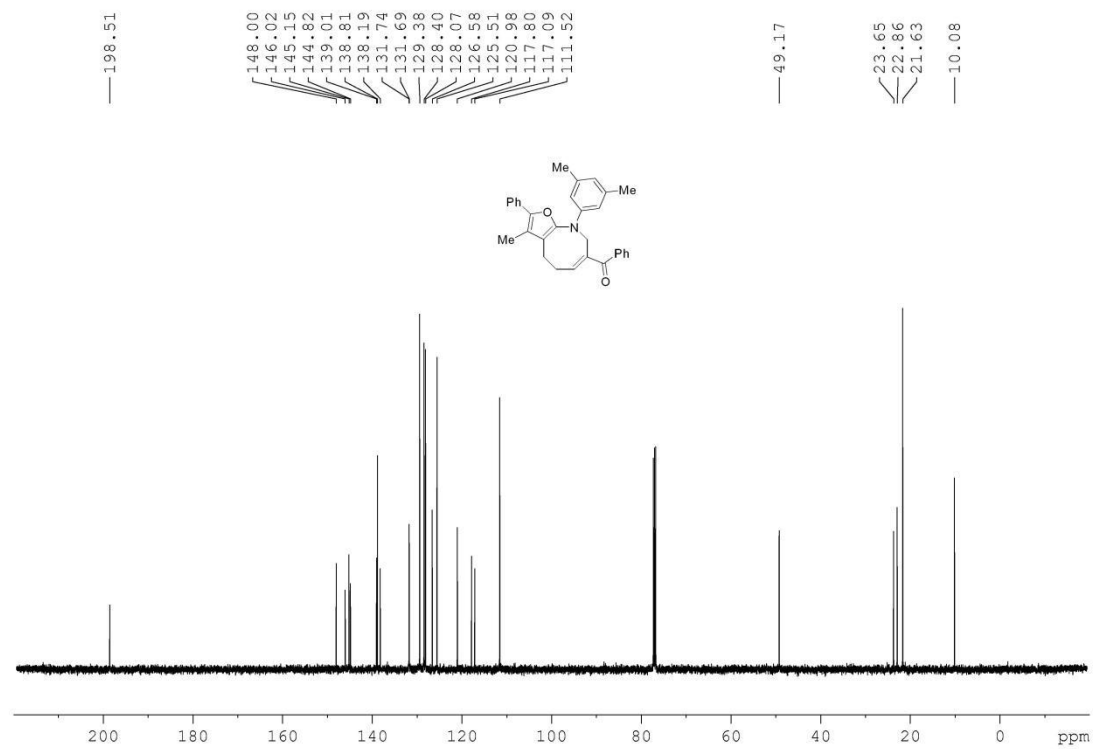
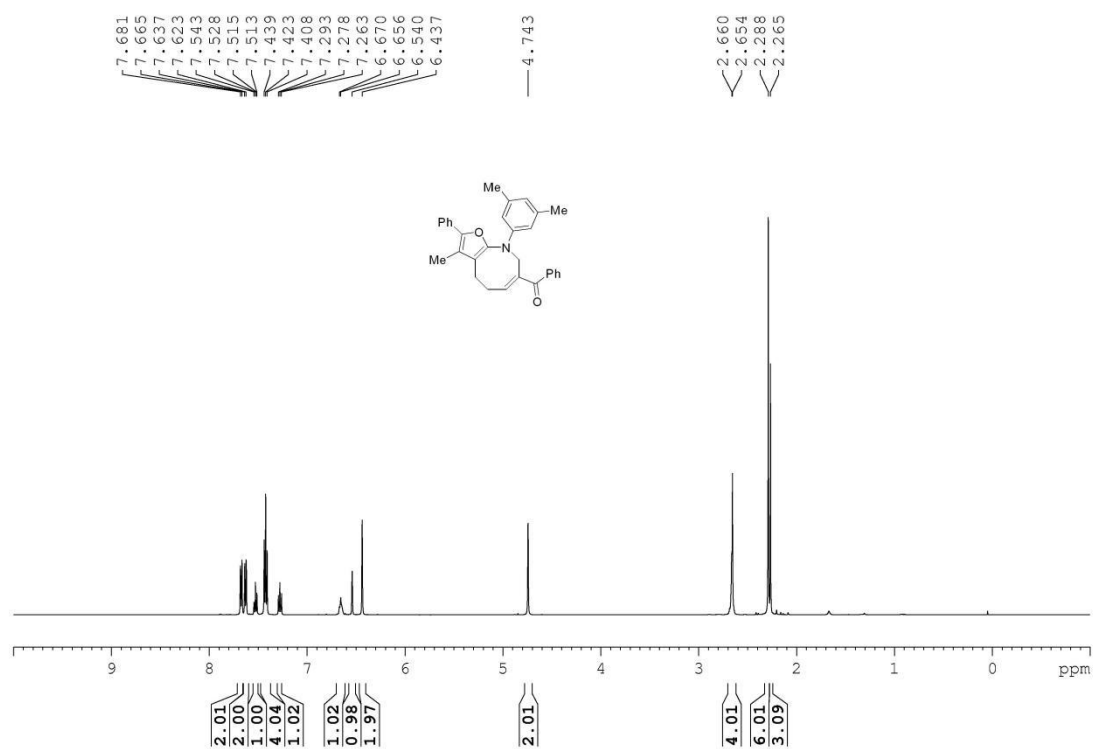
Compound 3r



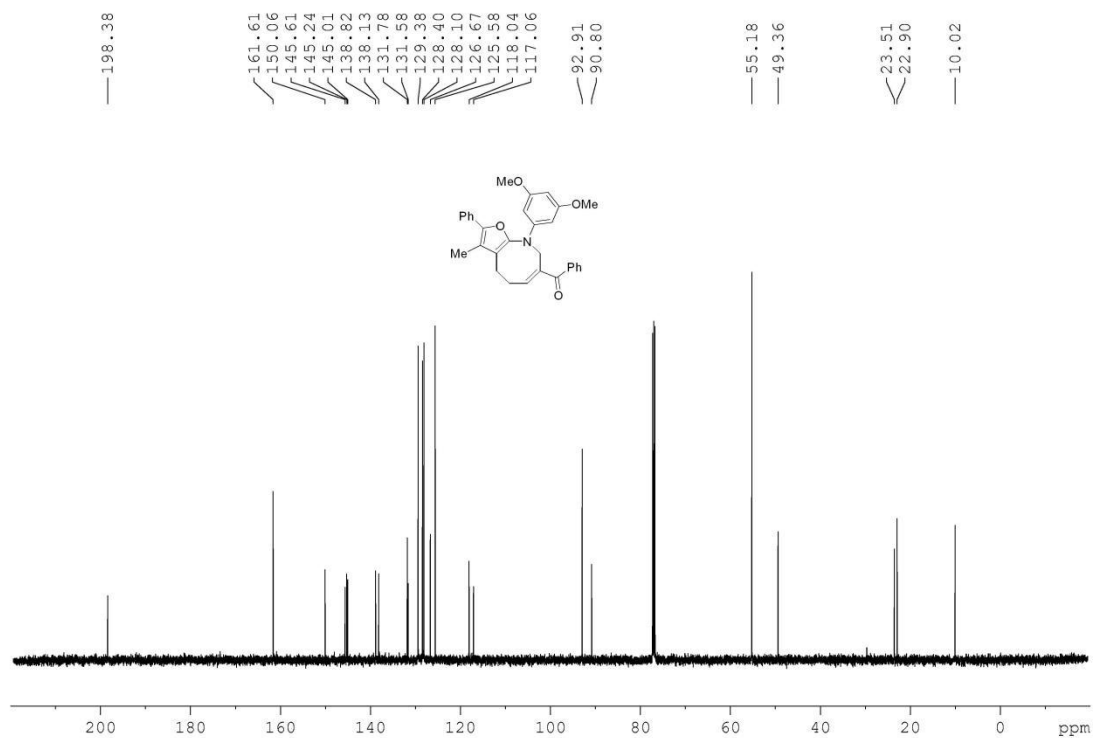
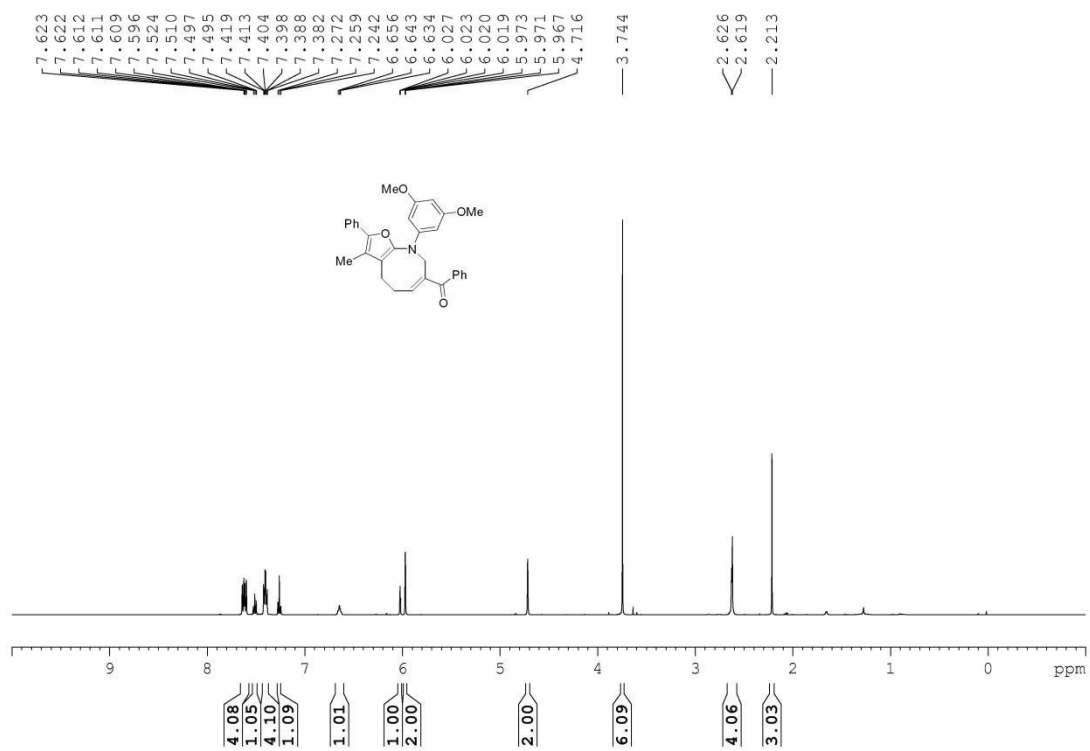
Compound 3s



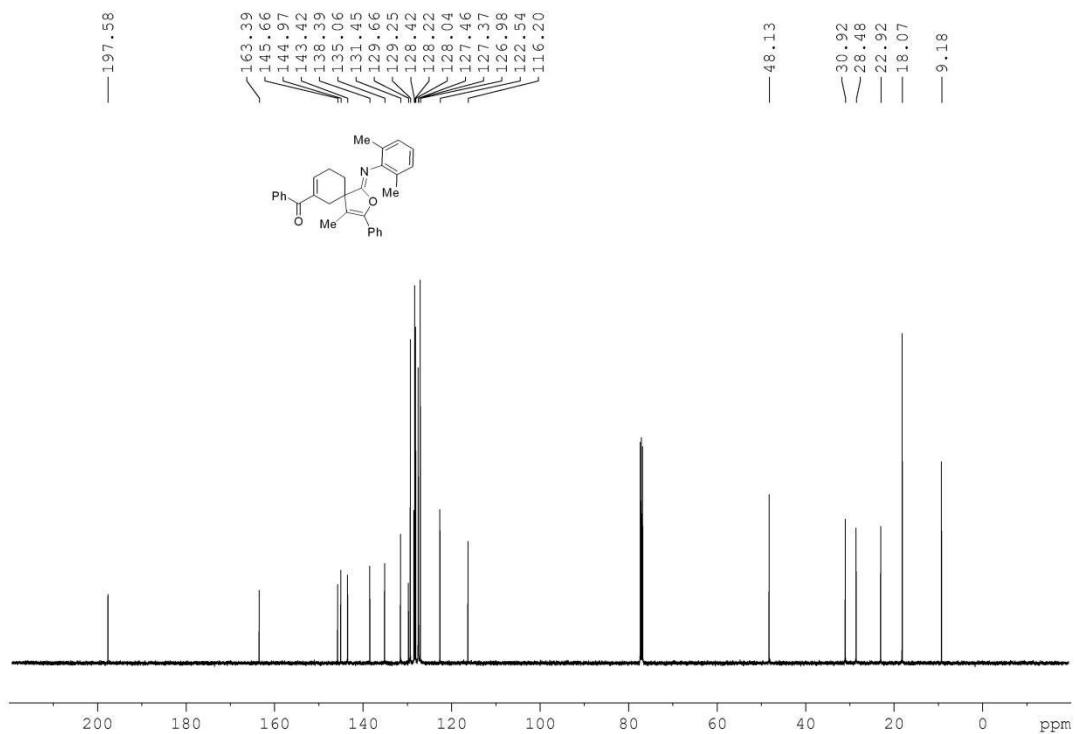
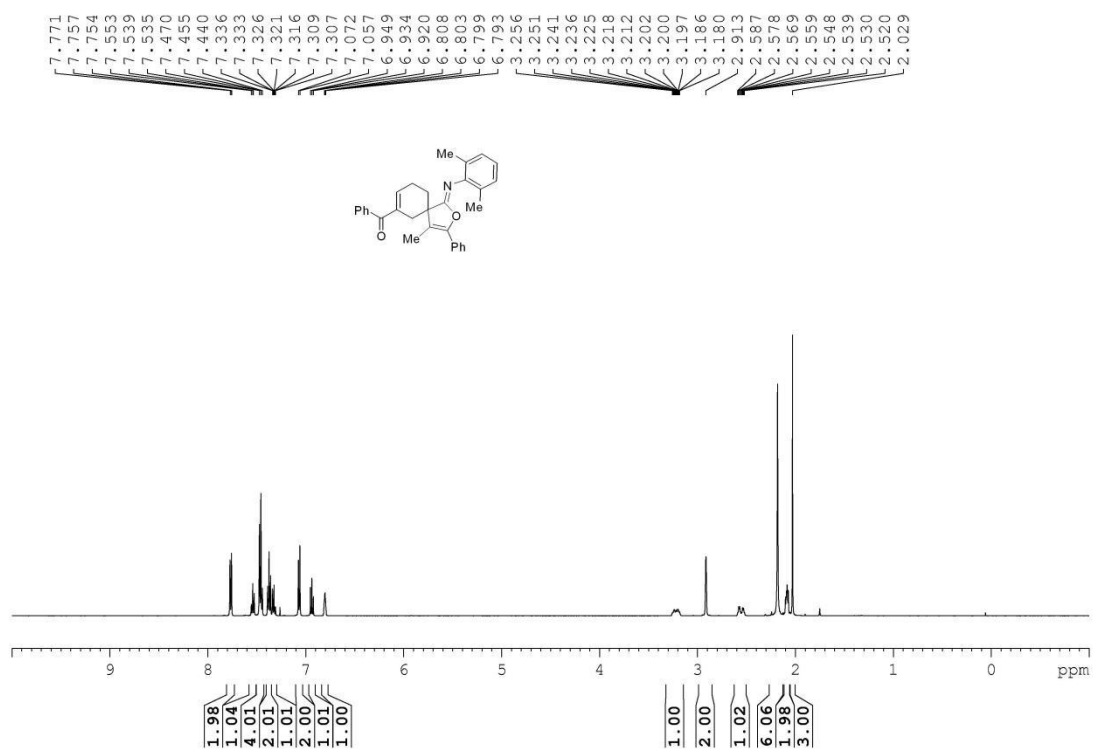
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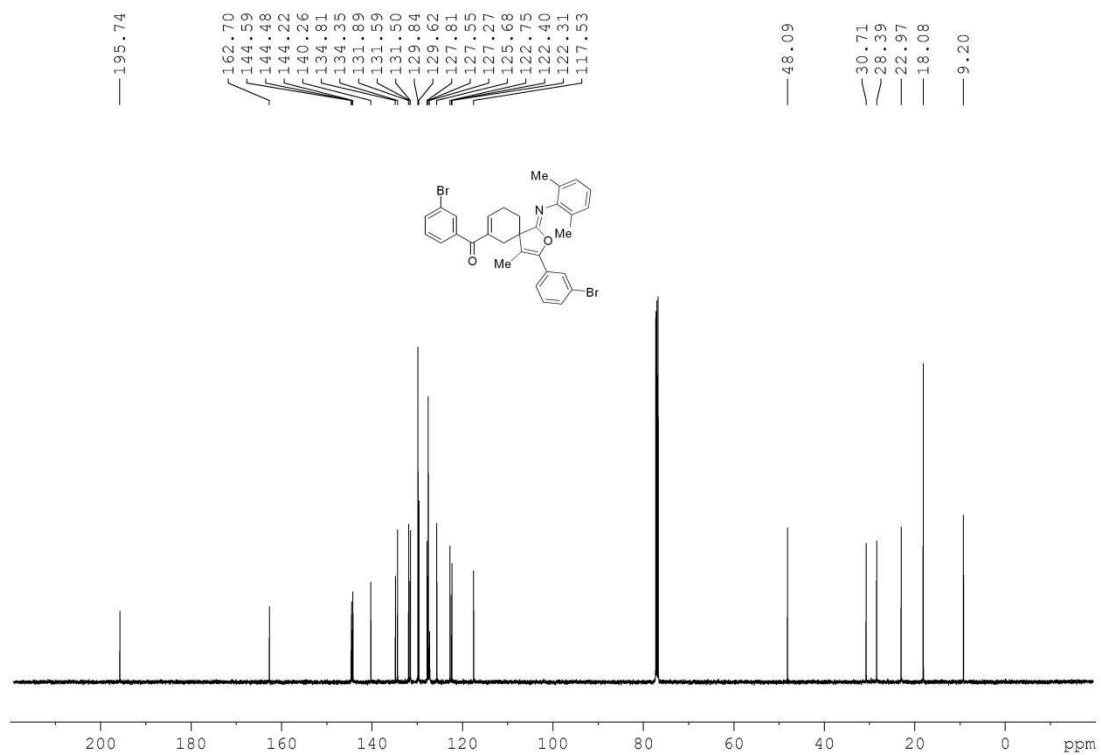
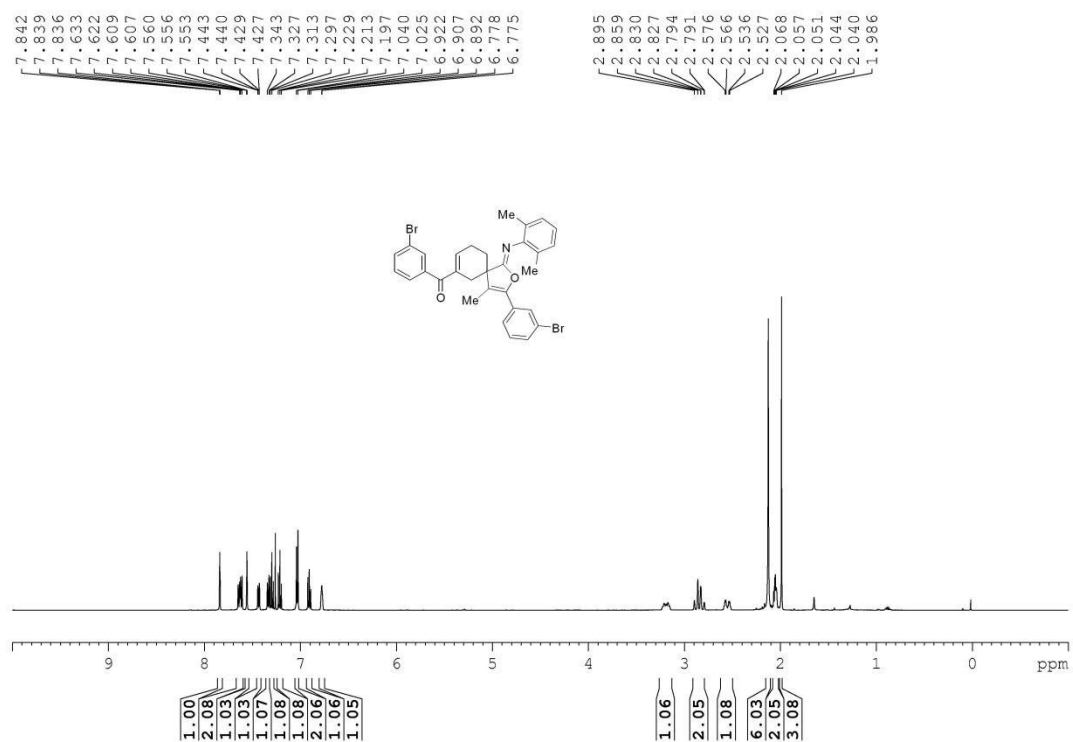
Compound 3u



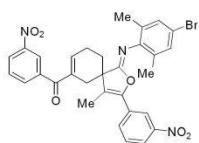
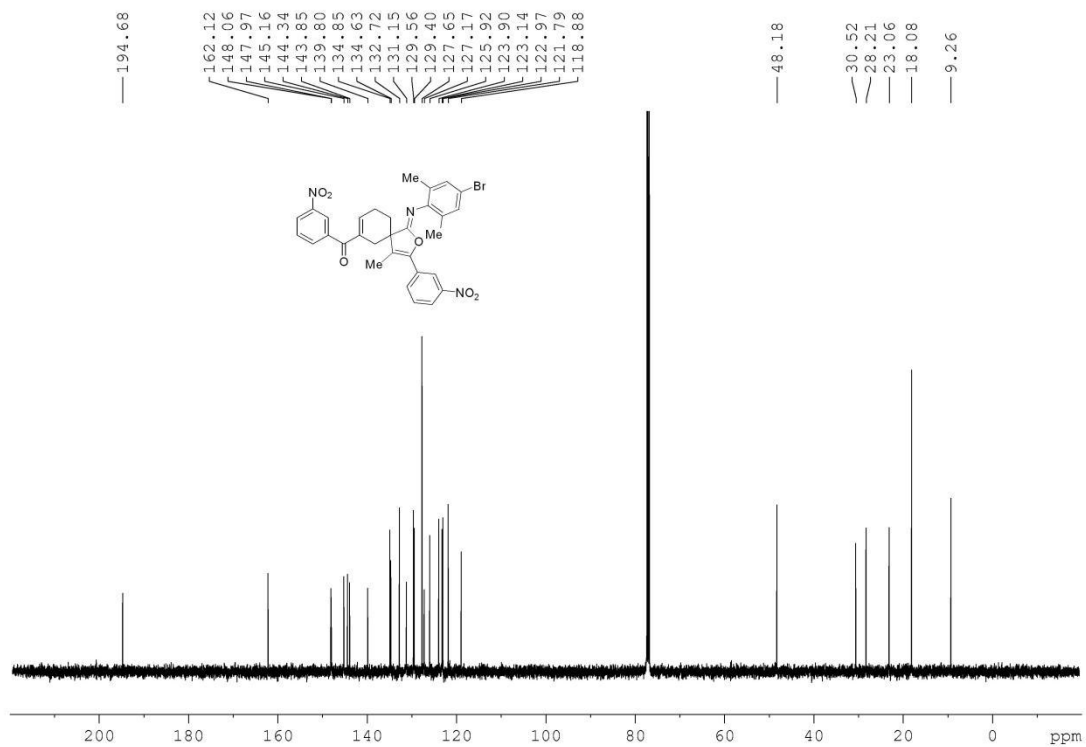
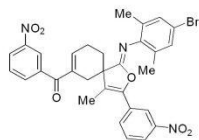
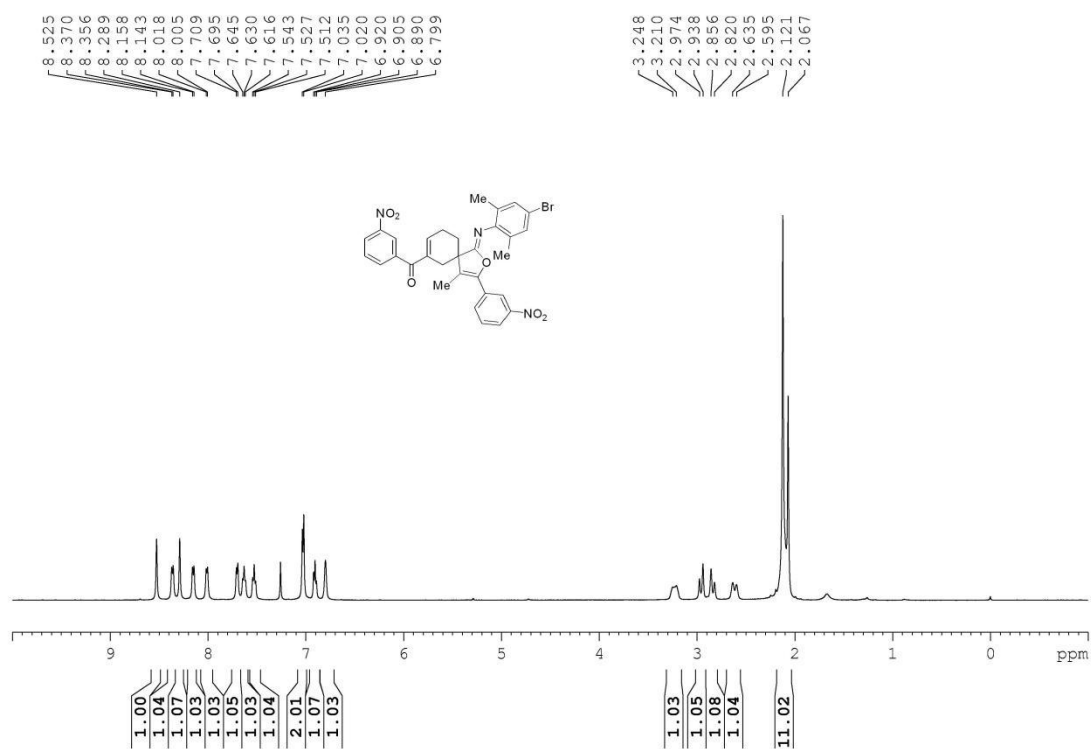
Compound 4a



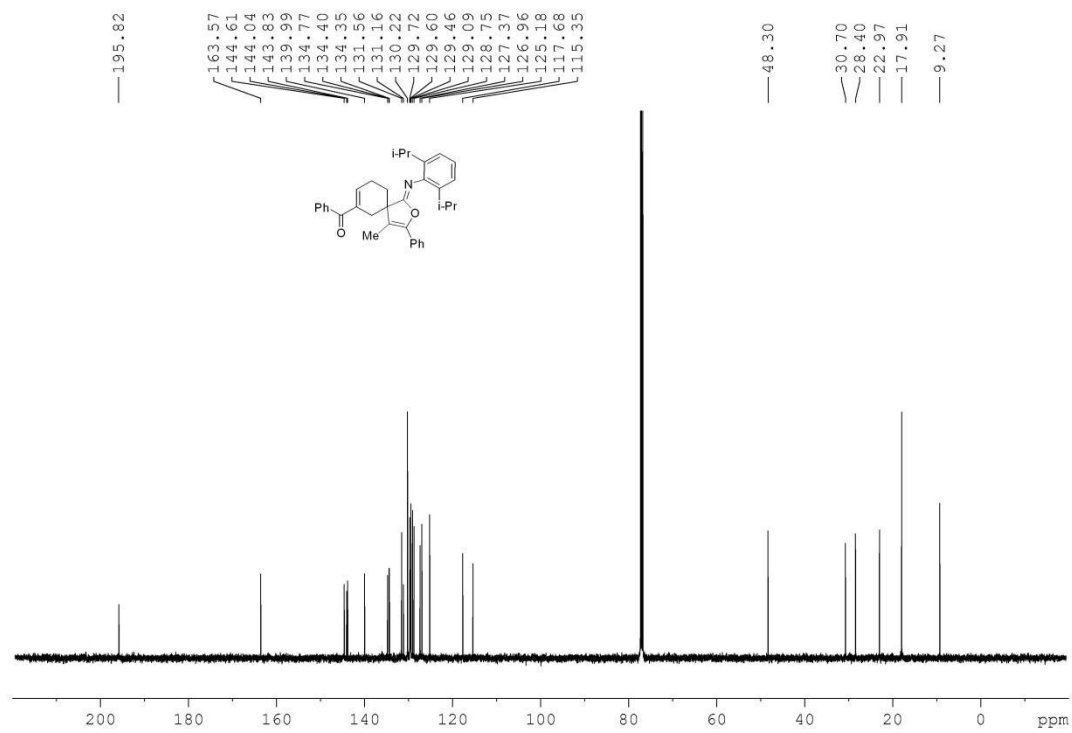
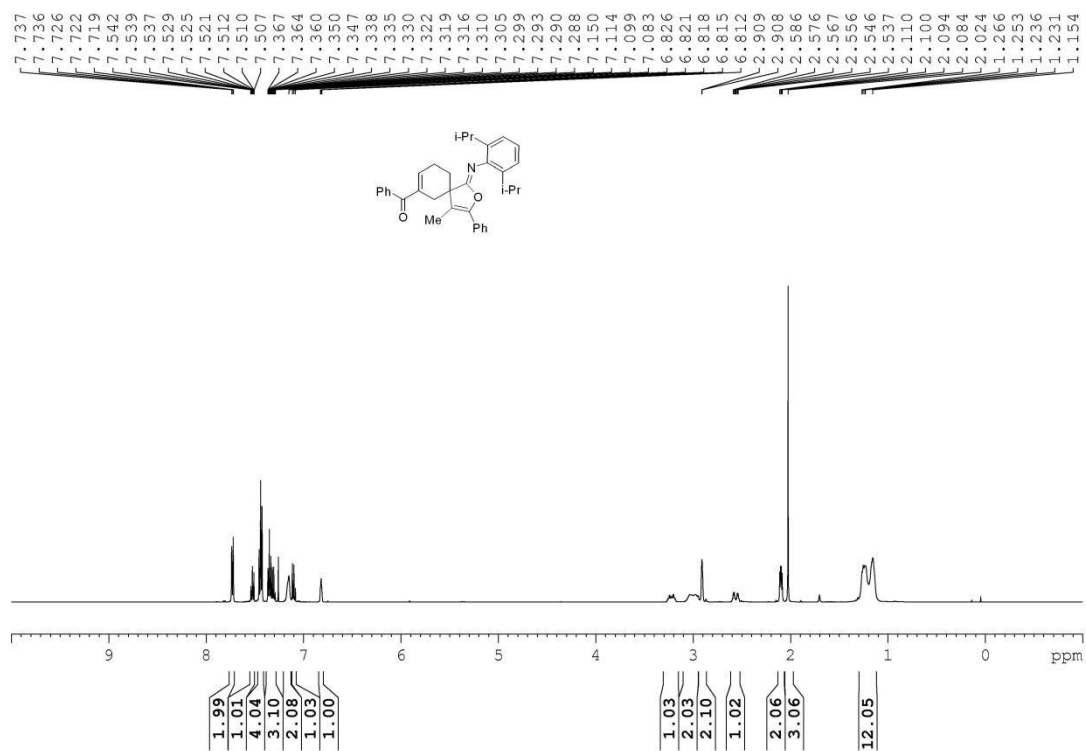
Compound 4b



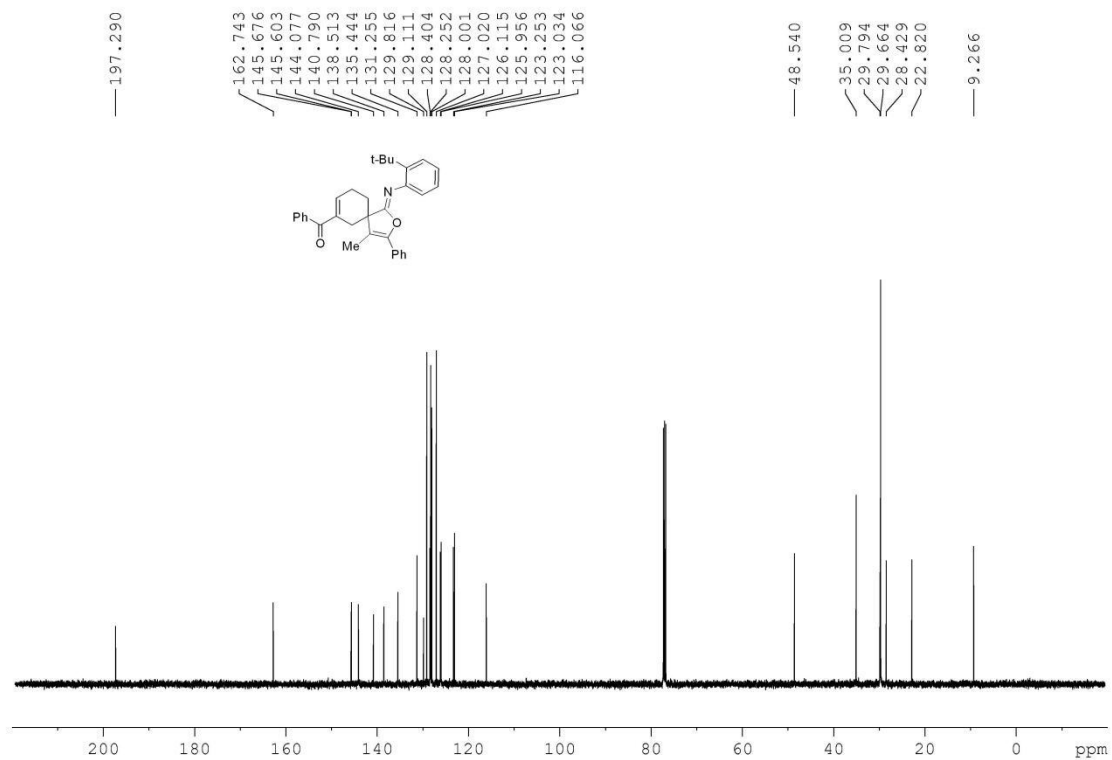
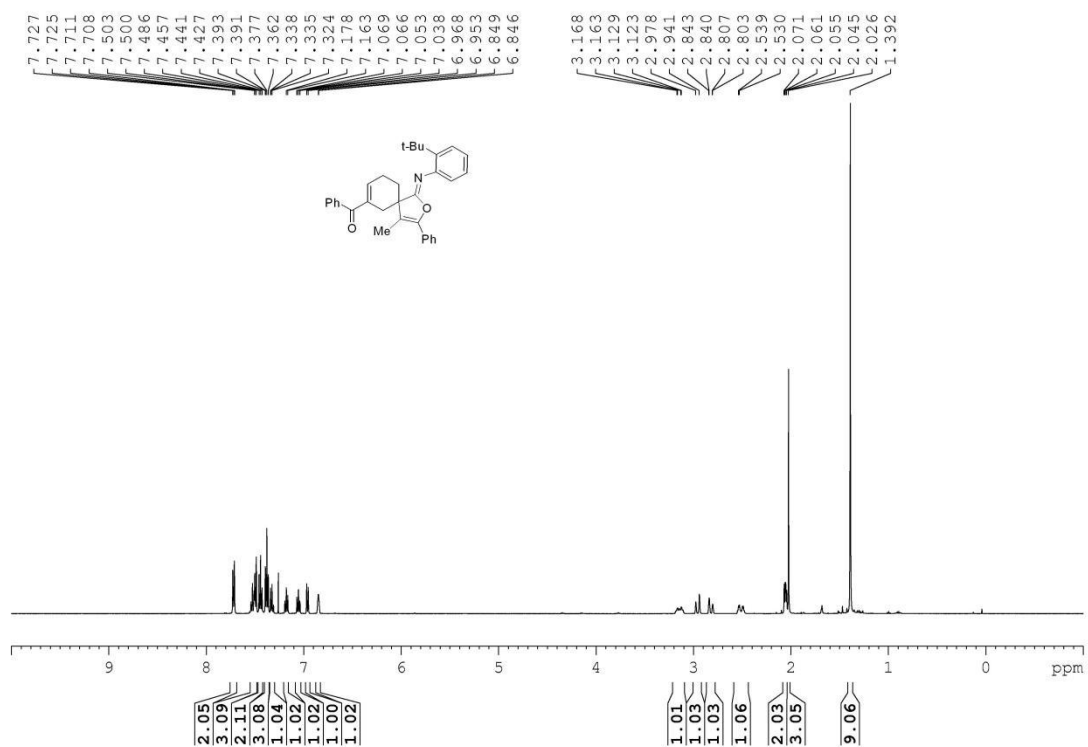
Compound 4c



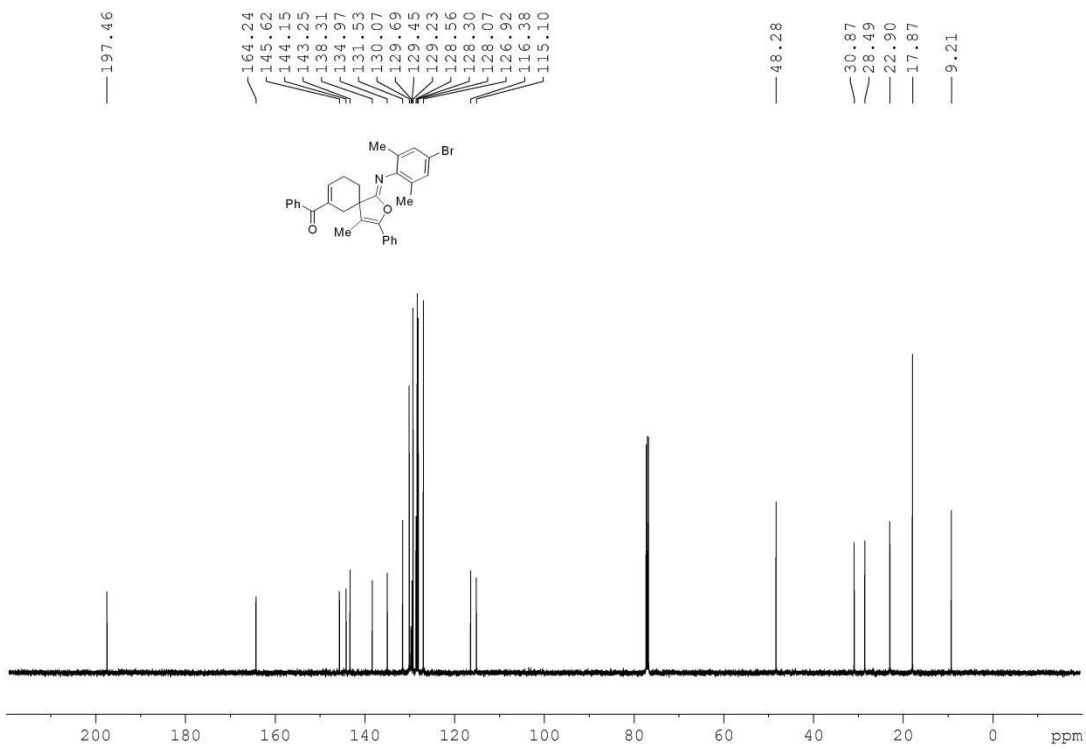
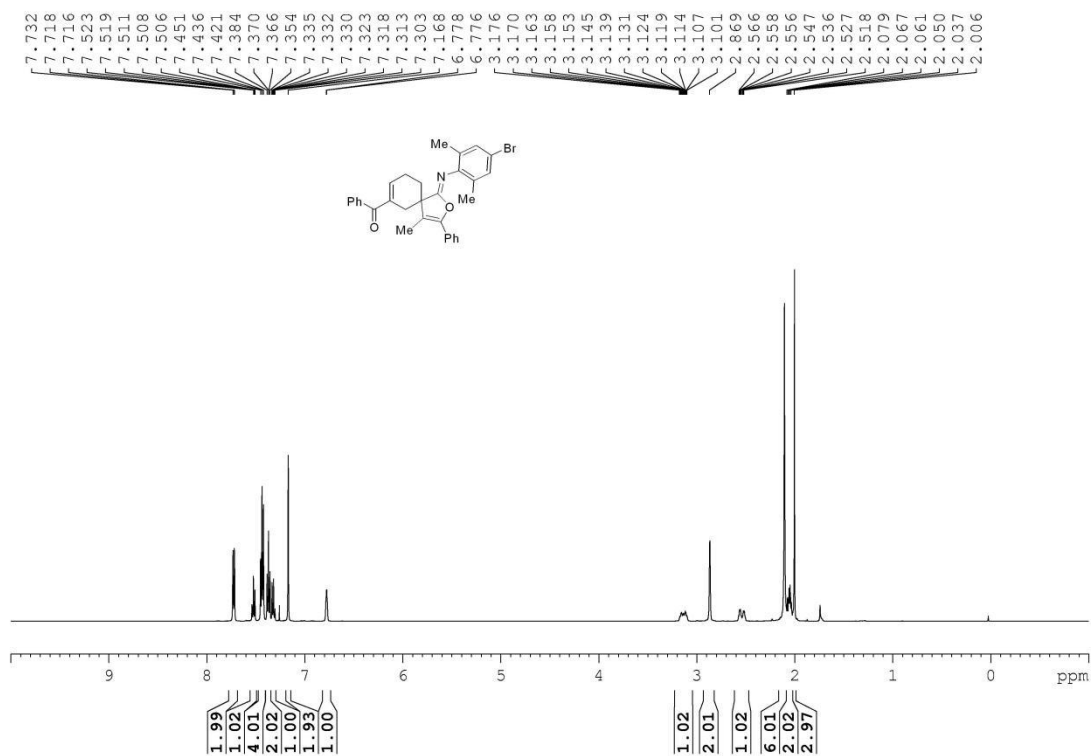
Compound 4d



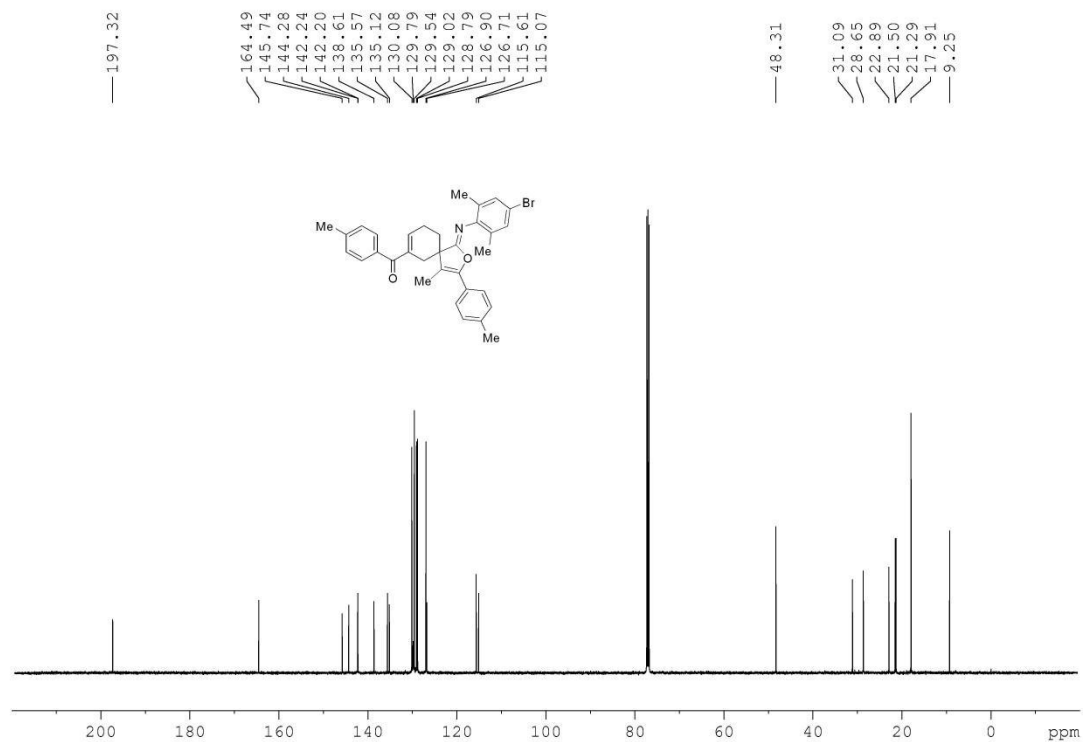
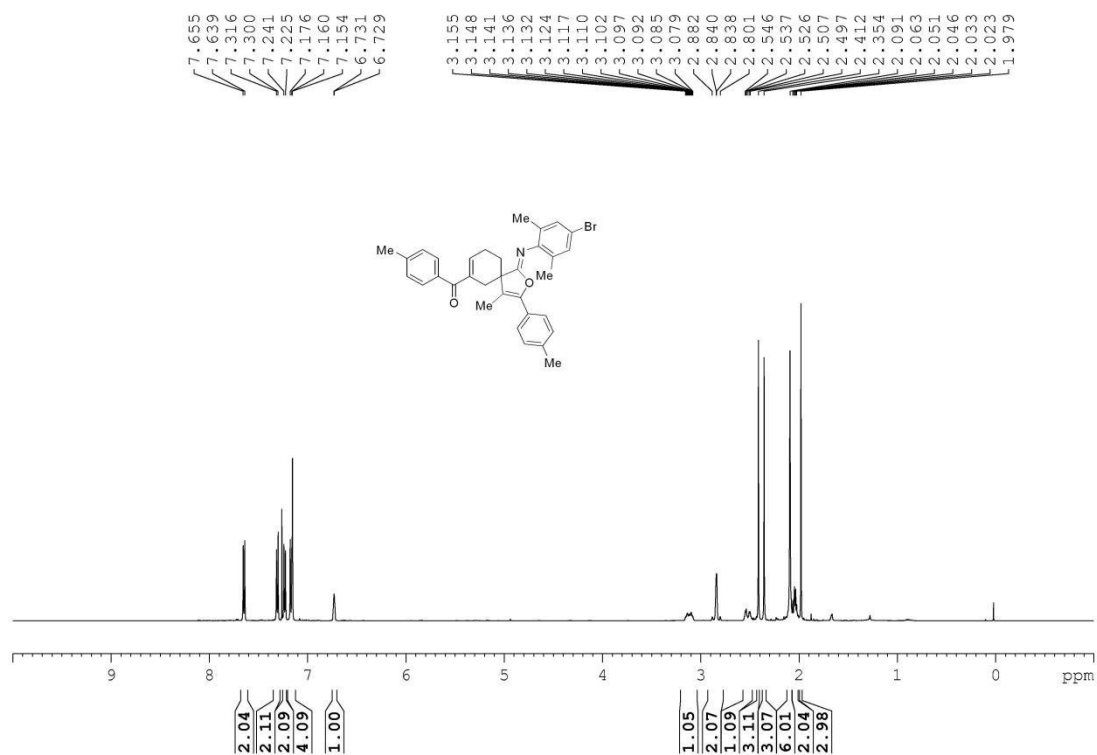
Compound 4e



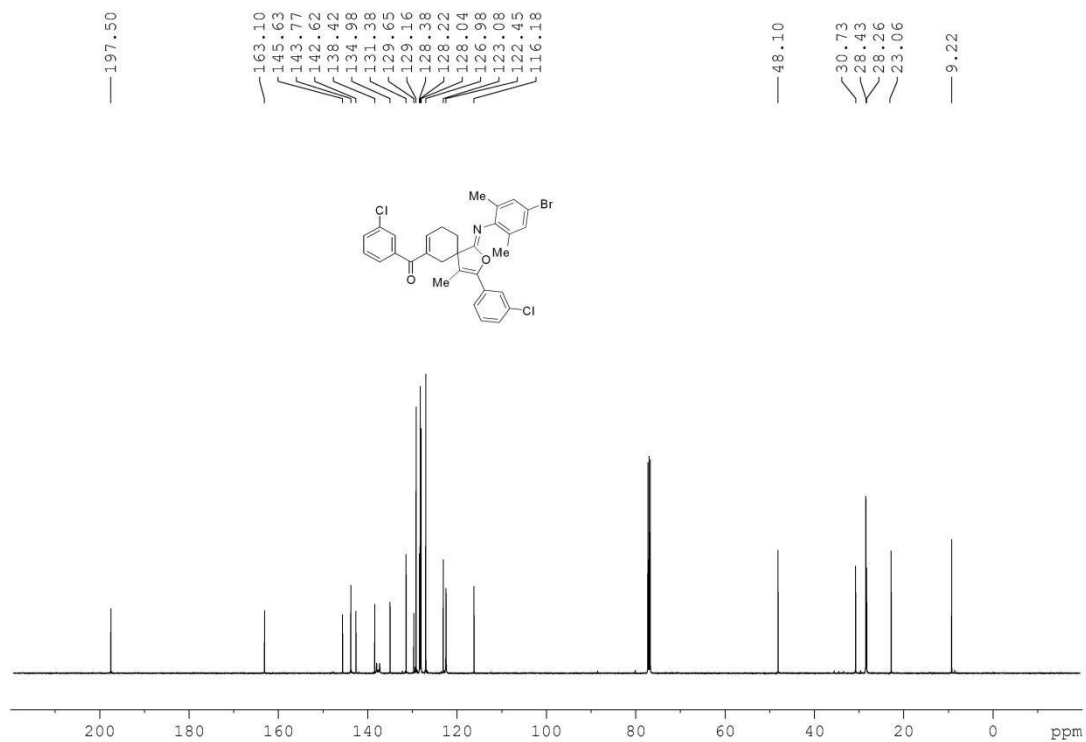
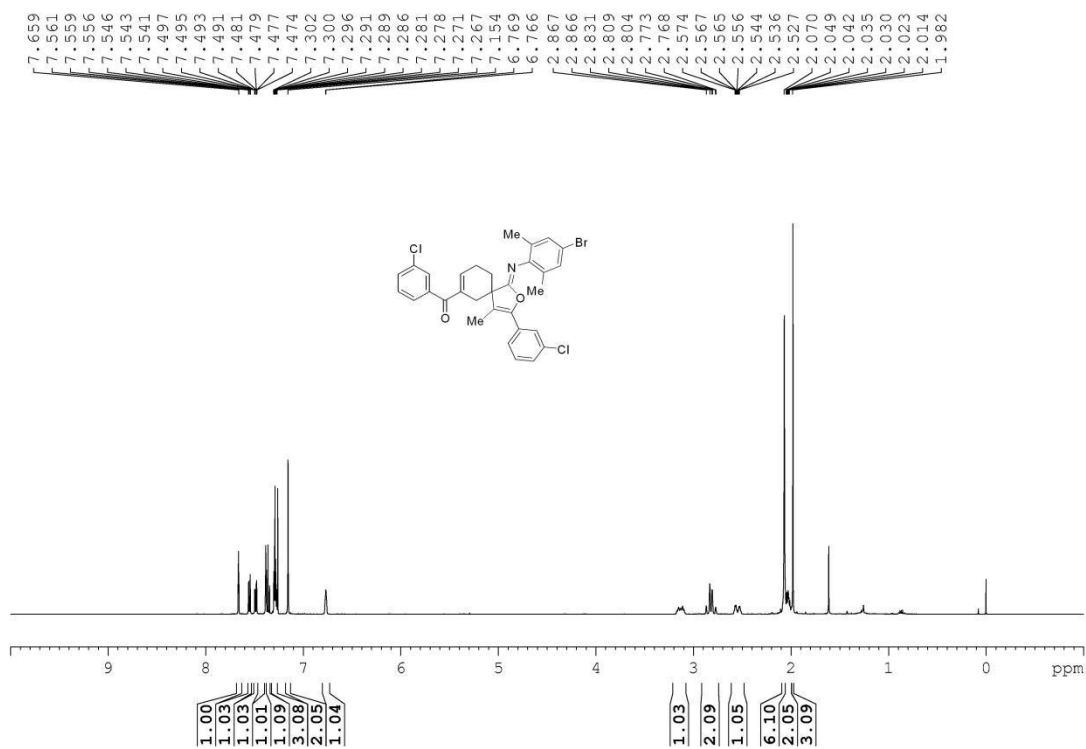
Compound 4f



Compound 4g



Compound 4h



Compound 4i

