

Bicyclization reaction with two molecular allenyl ketones and isocyanides: a synthesis of lactone-containing azaspirocycle derivative

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1 General Information

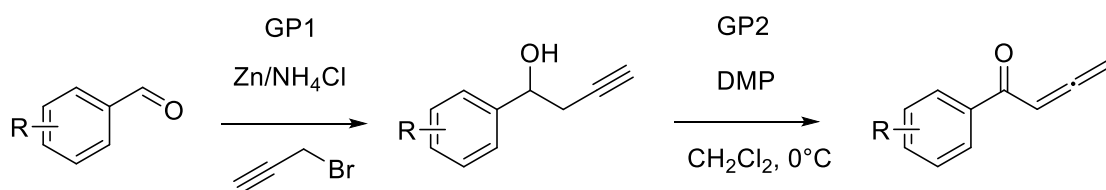
The NMR spectra were recorded on Bruker AC-500 spectrometer (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR) with CDCl_3 as the solvent and TMS as internal reference. ^1H NMR spectral data were reported as follows: chemical shift (δ , ppm), multiplicity, integration, and coupling constant (Hz). ^{13}C 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.

2 General Procedure

2.1 General procedure for the synthesis of product

Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with allenyl ketone **1** (0.5 mmol), isocyanide **2** (1.0 mmol), in toluene (5.0 mL) at room temperature. Then capped it with a septum and stirred at 100 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 8:1) to give the desired product **3** or **4**.

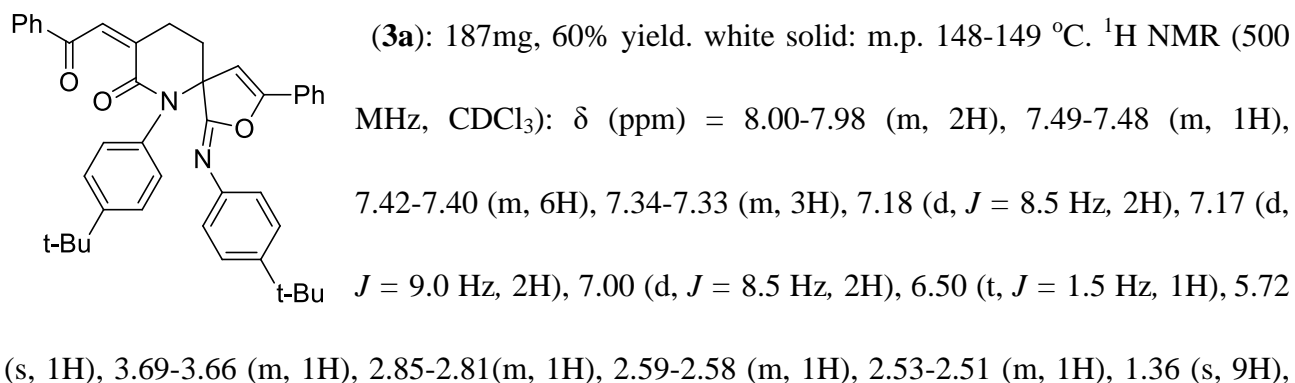
2.2 Representative procedure for the preparation of substituted Allenyl ketone .



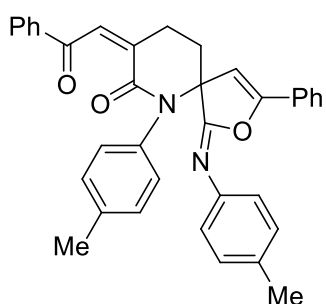
General Procedure 1: To a stirred suspension of the corresponding aldehyde (1 equiv.), propargyl bromide (2.0 equiv.; 80% in toluene) and zinc dust (5.0 equiv.) in THF at 0 °C was added to a saturated aqueous NH₄Cl solution dropwise. The mixture was allowed to warm up to room temperature and was stirred until full conversion was detected by TLC. The mixture was filtered over celite and the filter cake rinsed with CH₂Cl₂. The combined filtrates were washed with a saturated aqueous NH₄Cl solution and distilled water. After drying over MgSO₄, filtration and evaporation of the solvent in vacuo gave the crude product which was purified by flash column chromatography.

General Procedure 2. The Dess-Martin periodinane reagent (1.5 equiv.) as a solid was added to a solution of the corresponding homopropargyl alcohol dissolved in CH₂Cl₂ at 0°C. The solution was warmed up to room temperature and the reaction monitored by TLC (usually a fast reaction with reaction times < 1 h). Upon full conversion the solvent was partially removed under reduced pressure at low temperature and the crude material directly purified by flash column chromatography.

3 Characterization Data

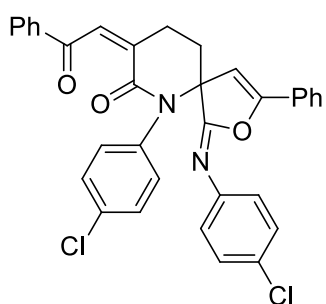


1.14 (s, 9H) . ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.7, 163.3, 158.2, 153.8, 150.6, 148.4, 141.9, 136.4, 136.3, 135.9, 134.3, 132.9, 130.2, 129.0, 128.7, 128.5, 128.1, 125.9, 125.8, 125.5, 123.3, 103.7, 71.1, 34.6, 34.5, 34.4, 31.6, 31.3, 25.3. HRMS (ESI): calcd for $\text{C}_{42}\text{H}_{43}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 623.3268, Found: 623.3274 .



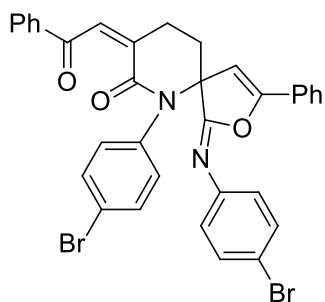
(3b): 153 mg, 57% yield. white solid: m.p. 118-119 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 8.02-8.00 (m, 2H), 7.44-7.34 (m, 8H), 7.23 (d, $J = 8.0$ Hz, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 6.97 (s, 4H), 6.51 (s, 1H), 5.78 (s, 1H), 3.69-3.64 (m, 1H), 2.86-2.83 (m, 1H), 2.62-2.61 (m, 1H),

2.54-2.52 (m, 1H), 2.40 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.5, 163.1, 158.0, 153.5, 141.9, 137.6, 136.2, 136.1, 135.6, 134.8, 134.1, 132.6, 129.9, 129.4, 129.3, 128.9, 128.8, 128.5, 128.2, 127.8, 125.2, 123.3, 103.3, 70.8, 34.1, 25.2, 21.0, 20.9. HRMS (ESI): calcd for $\text{C}_{36}\text{H}_{31}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 539.2329, Found: 539.2339.



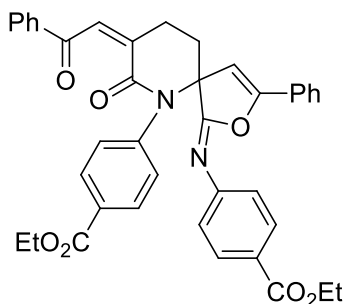
(3c): 147mg, 51% yield. white solid: m.p. 112-113 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.98-7.97 (m, 2H), 7.52-7.49 (m, 1H), 7.43-7.35 (m, 9H), 7.14 (t, $J = 8.5$ Hz, 4H), 7.01 (d, $J = 8.5$ Hz, 2H), 6.56 (s, 1H), 5.79 (s, 1H), 3.62-3.57 (m, 1H), 2.88-2.84 (m, 1H), 2.63-2.61 (m, 1H), 2.53-2.51 (m, 1H) . ^{13}C NMR (125 MHz, CDCl_3): δ

(ppm) = 195.4, 163.3, 159.1, 154.1, 143.1, 137.4, 136.7, 136.3, 134.1, 133.7, 133.1, 131.0, 130.8, 130.6, 129.3, 129.1, 128.9, 128.6, 127.4, 125.4, 124.7, 103.1, 71.3, 34.3, 25.5. HRMS (ESI): calcd for $\text{C}_{34}\text{H}_{25}\text{Cl}_2\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 579.1237, Found: 579.1237 .



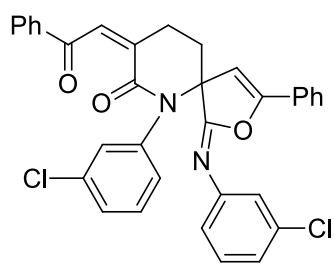
(3d): 130mg, 39% yield. white solid: m.p. 129-130 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.98-7.97 (m, 2H), 7.52-7.49 (m, 3H), 7.43-7.30 (m, 9H), 7.06 (d, J = 8.5 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 6.56 (s, 1H), 5.79 (s, 1H), 3.62-3.56 (m, 1H), 2.89-2.84 (m, 1H),

2.65-2.59 (m, 1H), 2.54-2.48 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.4, 163.2, 159.1, 154.1, 143.6, 137.9, 136.7, 136.3, 133.7, 133.1, 132.2, 132.1, 131.3, 130.7, 128.8, 128.6, 127.4, 125.4, 125.0, 122.4, 118.7, 103.1, 71.2, 34.3, 25.4. HRMS (ESI): calcd for $\text{C}_{34}\text{H}_{25}\text{Br}_2\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 667.0226, Found: 667.0225.

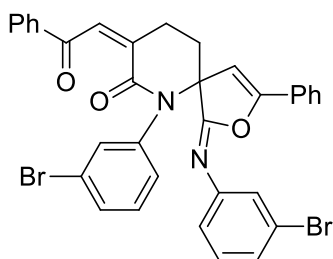


(3e): 193mg, 59% yield. white solid: m.p. 103-104 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 8.07 (d, J = 8.5 Hz, 2H), 7.97-7.96 (m, 2H), 7.88 (m, J = 8.5 Hz, 2H), 7.49-7.48 (m, 1H), 7.42-7.39 (m, 2H), 7.34-7.33 (m, 5H), 7.19-7.17 (m, 2H), 7.15-7.13 (m, 2H), 6.58 (s, 1H),

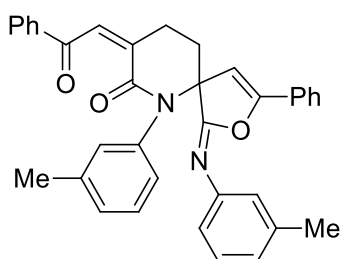
5.81 (s, 1H), 4.39 (q, J = 7.0 Hz, 2H), 4.26 (q, J = 7.0 Hz, 2H), 3.66-3.63 (m, 1H), 2.90-2.86 (m, 1H), 2.64-2.63 (m, 1H), 2.59-2.56 (m, 1H), 1.41(t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.4, 166.4, 165.9, 163.1, 159.8, 154.1, 149.1, 143.1, 136.9, 136.3, 133.6, 133.1, 130.7, 130.6, 130.4, 130.3, 129.6, 128.9, 128.8, 128.6, 127.3, 127.2, 125.4, 122.5, 103.2, 71.1, 61.2, 61.1, 34.4, 25.3, 14.5, 14.3. HRMS (ESI): calcd for $\text{C}_{40}\text{H}_{35}\text{N}_2\text{O}_7$ $[\text{M}+\text{H}]^+$ 655.2439, Found: 655.2432.



(3f): 153mg, 53% yield. white solid: m.p. 103-104 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.99-7.97 (m, 2H), 7.51-7.49 (m, 1H), 7.43-7.32 (m, 8H), 7.19-7.12 (m, 5H), 7.06-7.04 (m, 1H), 6.99-6.97 (m, 1H), 6.57 (s, 1H), 5.78 (s, 1H), 3.62-3.59 (m, 1H), 2.88-2.87 (m, 1H), 2.63-2.59 (m, 1H), 2.55-2.50 (m, 1H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 195.5, 163.2, 159.6, 154.2, 145.9, 139.9, 136.9, 136.2, 134.6, 134.4, 133.6, 133.2, 130.7, 130.3, 130.1, 129.9, 128.9, 128.8, 128.7, 128.6, 127.8, 127.4, 125.5, 125.4, 123.2, 121.2, 103.2, 71.2, 34.2, 25.4. HRMS (ESI): calcd for C₃₄H₂₅Cl₂N₂O₃ [M+H]⁺ 579.1237, Found: 579.1245.

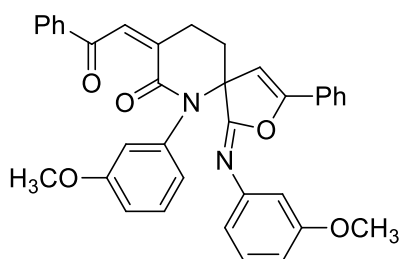


(3g): 110mg, 33% yield. white solid: m.p. 78-79 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.99-7.97 (m, 2H), 7.53-7.50 (m, 1H), 7.44-7.41 (m, 2H), 7.38-7.24 (m, 10H), 7.09-7.02 (m, 3H), 6.57 (s, 1H), 5.78 (s, 1H), 3.64-3.58 (m, 1H), 2.89-2.83 (m, 1H), 2.64-2.59 (m, 1H), 2.55-2.49 (m, 1H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 195.4, 163.1, 159.7, 154.2, 146.1, 139.9, 136.9, 136.2, 133.6, 133.2, 131.6, 130.7, 130.4, 130.2, 128.9, 128.8, 128.6, 128.3, 127.4, 126.1, 125.5, 122.6, 122.3, 121.6, 103.1, 71.2, 34.2, 25.4. HRMS (ESI): calcd for C₃₄H₂₅Br₂N₂O₃ [M+H]⁺ 667.0226, Found: 667.0223



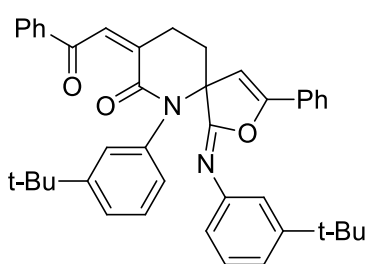
(3h): 140mg, 52% yield. white solid: m.p. 104-105 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 8.01-7.99 (m, 2H), 7.51-7.48 (m, 1H), 7.43-7.32 (m, 8H), 7.06-7.05 (m, 1H), 7.02-6.95 (m, 6H), 6.52 (s, 1H), 5.76 (s, 1H), 3.70-3.63 (m, 1H), 2.89-2.83 (m, 1H), 2.66-2.61 (m, 1H), 2.55-2.49 (m, 1H), 2.40 (s, 3H), 2.17 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 195.6, 163.2,

158.6, 153.8, 144.9, 138.7, 138.6, 136.4, 135.9, 134.2, 132.8, 130.4, 130.2, 128.9, 128.7, 128.6, 128.5, 127.8, 126.3, 125.9, 125.4, 123.8, 119.8, 103.5, 70.9, 34.2, 25.4, 21.6, 21.3. HRMS (ESI): calcd for C₃₆H₃₁N₂O₃ [M+H]⁺ 539.2329, Found: 539.2327.



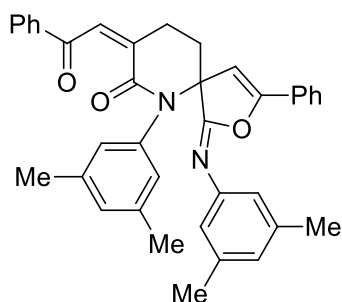
(3i): 131 mg, 46% yield. white solid: m.p. 107-108 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 8.01-7.98 (m, 2H), 7.49-7.47 (m, 1H), 7.41-7.39 (m, 4H), 7.34-7.32 (m, 4H), 7.10-7.08 (m, 1H), 6.82-6.79 (m, 1H), 6.77-6.75 (m, 2H), 6.69-6.67(m, 3H),

6.53-6.52 (m, 1H), 5.78 (s, 1H), 3.82 (s, 3H), 3.64-3.62 (m, 1H), 3.55 (s, 3H), 2.88-2.86 (m, 1H), 2.63-2.61 (m, 1H), 2.54-2.52 (m, 1H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 195.4, 162.9, 159.9, 159.7, 158.7, 153.7, 145.8, 139.7, 136.2, 136.0, 133.9, 132.8, 130.1, 129.5, 129.4, 128.8, 128.6, 128.3, 127.6, 125.2, 121.5, 115.3, 114.6, 114.3, 111.1, 108.5, 103.3, 70.9, 55.2, 55.0, 34.1, 25.2. HRMS (ESI): calcd for C₃₆H₃₁N₂O₅ [M+H]⁺ 571.2227, Found: 571.2227.



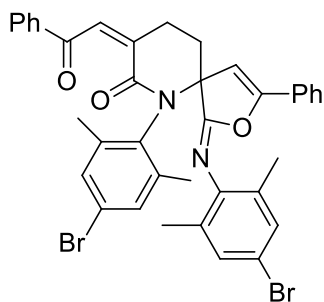
(3j): 156mg, 50% yield. white solid: m.p. 104-105 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 8.02-8.00 (m, 2H), 7.49-7.38 (m, 6H), 7.32-7.29 (m, 4H), 7.23-7.21 (m, 2H), 7.12-7.01 (m, 3H), 6.93-6.92(m, 1H), 6.53 (s, 1H), 5.80 (s, 1H), 3.67-3.63 (m, 1H),

2.91-2.87 (m, 1H), 2.69-2.67 (m, 1H), 2.55-2.50 (m, 1H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 195.7, 162.9, 158.4, 153.8, 151.9, 151.7, 144.4, 138.5, 136.4, 135.8, 134.5, 132.9, 130.2, 128.9, 128.7, 128.5, 128.4, 127.9, 127.0, 125.8, 125.2, 125.0, 122.3, 120.9, 120.5, 103.4, 71.2, 34.8, 34.5, 34.2, 31.5, 31.2, 25.7. HRMS (ESI): calcd for C₄₂H₄₃N₂O₃ [M+H]⁺ 623.3268, Found: 623.3273 .



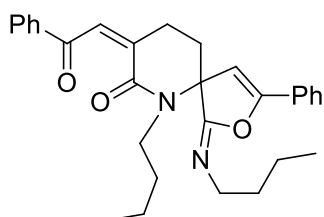
(3k): 139 mg, 49% yield. white solid: m.p. 101-102 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.99-7.98 (m, 2H), 7.50-7.47 (m, 1H), 7.42-7.32 (m, 7H), 6.83 (s, 1H), 6.77-6.74 (m, 5H), 6.51 (s, 1H), 5.75 (s, 1H), 3.65-3.61 (m, 1H), 2.87-2.85 (m, 1H), 2.62-2.61 (m, 1H), 2.53-2.49 (m, 1H), 2.35 (s, 6H), 2.12 (s, 6H). ¹³C NMR (125 MHz,

CDCl₃): δ (ppm) = 195.5, 162.9, 158.4, 153.6, 144.9, 138.3, 138.1, 136.3, 135.7, 134.1, 132.7, 130.0, 129.8, 128.9, 128.5, 128.3, 127.9, 127.2, 126.5, 125.2, 120.2, 103.4, 70.7, 33.9, 25.4, 21.3, 21.0. HRMS (ESI): calcd for C₃₈H₃₅N₂O₃ [M+H]⁺ 567.2642, Found: 567.2647.



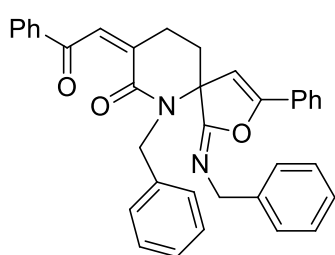
(3l): 134mg, 37% yield. white solid: m.p. 145-146 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.97 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.52-7.49 (m, 1H), 7.39-7.35 (m, 7H), 7.17 (s, 2H), 7.08 (d, *J* = 2.0 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.64 (t, *J* = 2.0 Hz, 1H), 5.83 (s, 1H), 3.57-3.53 (m, 1H),

3.10-3.07 (m, 1H), 2.81-2.78 (m, 1H), 2.57-2.55 (m, 1H), 2.18 (s, 3H), 2.12 (s, 3H), 1.89 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 195.1, 162.9, 157.1, 153.7, 142.3, 140.9, 138.3, 137.6, 137.0, 136.4, 133.6, 133.1, 131.6, 130.7, 130.6, 128.9, 128.8, 128.7, 128.5, 127.4, 125.4, 122.1, 116.9, 102.7, 70.4, 36.8, 24.9, 19.9, 19.8, 18.1. HRMS (ESI): calcd for C₃₈H₃₃Br₂N₂O₃[M+H]⁺ 723.0852, Found: 723.0853 .



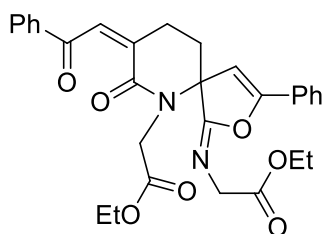
(3m): 106mg, 45% yield. yellow oil. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 8.00-7.99 (m, 2H), 7.65-7.63 (m, 2H), 7.53-7.49 (m, 1H), 7.45-7.42 (m, 5H), 6.32 (s, 1H), 5.68 (s, 1H), 3.54 (t, *J* = 7.0 Hz, 2H),

3.37-3.32 (m, 1H), 3.18-3.12 (m, 1H), 3.01-2.95 (m, 1H), 2.63-2.58 (m, 1H), 2.31-2.19 (m, 2H), 1.67-1.61 (m, 2H), 1.46-1.33 (m, 4H), 1.06-1.02 (m, 2H), 0.97 (t, $J = 7.0$ Hz, 3H), 0.70 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 196.0, 162.9, 158.5, 153.8, 136.7, 134.9, 134.2, 132.8, 130.3, 128.9, 128.5, 128.4, 125.4, 103.2, 68.6, 47.7, 45.5, 34.4, 32.7, 30.6, 25.1, 20.7, 20.4, 14.0, 13.8 . HRMS (ESI):calcd for $\text{C}_{30}\text{H}_{35}\text{N}_2\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 471.2642, Found: 471.2658 .



(3n): 137mg, 51% yield. white solid: m.p. 70-71 °C. ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 8.05-8.03 (m, 2H), 7.56-7.53 (m, 1H), 7.51-7.49 (m, 2H), 7.45-7.42 (m, 5H), 7.37-7.36 (m, 4H), 7.29-7.27 (m, 1H), 7.11-7.06 (m, 3H), 6.96-6.94 (m, 2H), 6.44-6.43 (m, 1H), 5.39 (s,

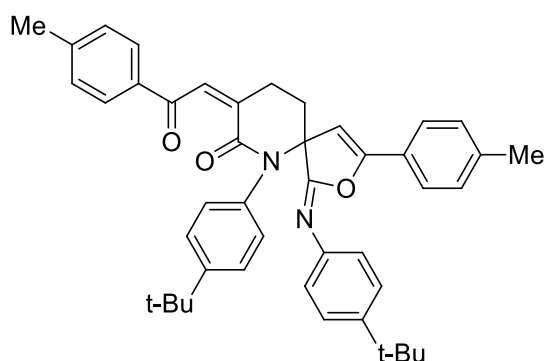
1H), 4.77 (d, $J = 15.0$ Hz, 1H), 4.68 (d, $J = 15.0$ Hz, 1H), 4.43 (d, $J = 15.0$ Hz, 1H), 4.22 (d, $J = 15.0$ Hz, 1H), 3.67-3.60 (m, 1H), 2.65-2.60 (m, 1H), 2.34-2.22 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.9, 163.6, 159.5, 153.4, 139.8, 138.3, 136.8, 135.1, 134.7, 132.8, 130.3, 128.8, 128.7, 128.5, 128.4, 128.3, 128.1, 128.0, 127.5, 126.9, 126.8, 125.4, 103.9, 68.3, 51.4, 47.8, 34.0, 24.5 . HRMS (ESI): calcd for $\text{C}_{36}\text{H}_{31}\text{N}_2\text{O}_3$ [$\text{M}+\text{H}$] $^+$ 539.2329, Found: 539.2325



(3o): 114mg, 43% yield. yellow oil . ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.98-7.97 (m, 2H), 7.57-7.55 (m, 2H), 7.52-7.50 (m, 1H), 7.45-7.41 (m, 5H), 6.40 (s, 1H), 5.85 (s, 1H), 4.44 (d, $J = 17.0$ Hz, 1H), 4.36 (s, 2H), 4.22 (q, $J = 7.0$ Hz, 2H), 3.99 (q, $J = 7.0$ Hz, 2H), 3.46-3.39 (m, 1H),

3.36 (d, $J = 17.5$ Hz, 1H), 2.72-2.67 (m, 1H), 2.42-2.35 (m, 2H), 1.29 (t, $J = 7.5$ Hz, 3H), 1.07 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 195.6, 169.5, 169.0, 163.1, 162.6, 153.9,

136.4, 135.5, 133.6, 132.9, 130.6, 128.9, 128.8, 128.6, 127.8, 125.4, 103.5, 69.3, 61.2, 61.1, 49.9, 46.0, 33.8, 25.0, 14.3, 14.1. HRMS (ESI): calcd for $C_{30}H_{31}N_2O_7$ $[M+H]^+$ 531.2126, Found: 531.2129.



(**4a**): 221mg, 68% yield. white solid: m.p. 116-117 °C.

1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.88 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 7.28 (t, J = 8.5 Hz, 2H), 7.19-7.14 (m, 8H), 7.00 (d, J = 8.5 Hz, 2H), 6.49-6.48 (m, 1H), 5.66 (s, 1H), 3.66-3.63 (m, 1H),

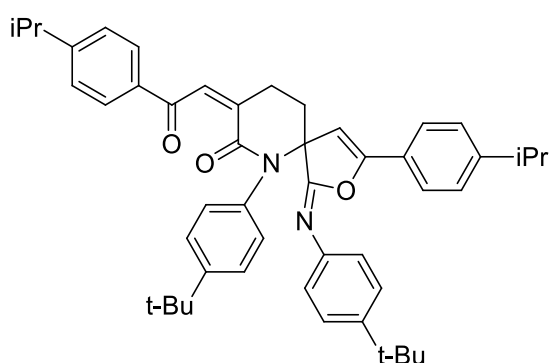
2.84-2.79 (m, 1H), 2.59-2.57 (m, 1H), 2.52-2.49 (m, 1H), 2.37 (s, 3H), 2.34 (s, 3H), 1.36 (s, 9H),

1.15 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 195.2, 163.1, 158.2, 153.7, 150.3, 148.1,

143.4, 141.9, 140.3, 136.3, 135.9, 133.9, 133.8, 129.2, 129.1, 128.9, 128.6, 125.7, 125.6, 125.3,

125.2, 123.2, 102.7, 70.9, 34.5, 34.4, 34.3, 31.4, 31.1, 25.3, 21.7, 21.4. HRMS (ESI): calcd

for $C_{44}H_{47}N_2O_3$ $[M+H]^+$ 651.3581, Found: 651.3588.



(**4b**): 230mg, 65% yield. white solid: m.p. 152-153 °C. 1H

NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.93 (d, J = 8.5 Hz,

2H), 7.41 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H),

7.26 (d, J = 8.5 Hz, 2H), 7.21-7.17 (m, 6H), 7.01 (d, J =

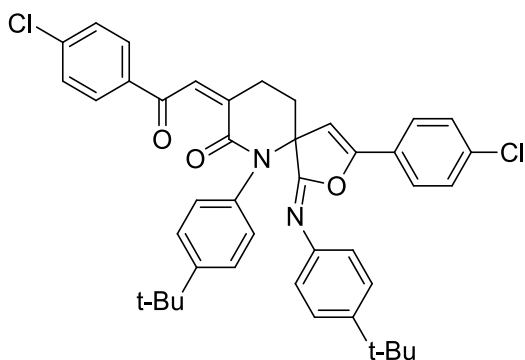
8.5 Hz, 1H), 6.49 (s, 1H), 5.69 (s, 1H), 3.70-3.64 (m,

1H), 2.96-2.79 (m, 3H), 2.61-2.57 (m, 1H), 2.52-2.47 (m, 1H), 1.37 (s, 9H), 1.24 (t, J = 7.5 Hz,

12H), 1.16 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 195.4, 163.3, 158.4, 154.3, 153.9,

151.4, 150.5, 148.2, 142.1, 136.5, 136.2, 134.3, 134.0, 129.3, 128.7, 126.8, 126.6, 125.9, 125.8,

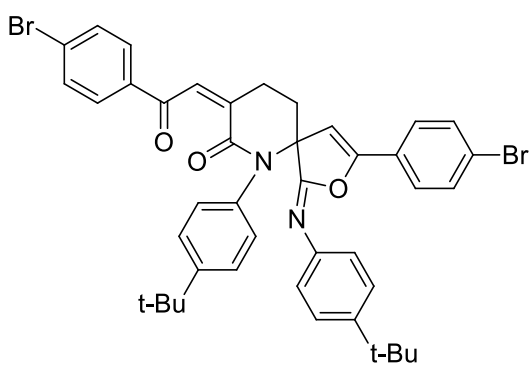
125.6, 123.3, 103.0, 71.1, 34.6, 34.5, 34.4, 34.2, 31.6, 31.3, 25.4, 23.9, 23.8. HRMS (ESI): calcd for $C_{48}H_{55}N_2O_3$ $[M+H]^+$ 707.4207, Found: 707.4202.



(**4c**): 166mg, 48% yield. white solid: m.p. 120-121 °C.

1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.92 (d, J = 9.0 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 7.33-7.29 (m, 4H), 7.19-7.17 (m, 4H), 6.97 (d, J = 9.0 Hz, 2H), 6.46-6.45 (m, 1H), 5.69 (s, 1H), 3.73-3.66

(m, 1H), 2.85-2.79 (m, 1H), 2.61-2.56 (m, 1H), 2.53-2.48 (m, 1H), 1.37 (s, 9H), 1.15 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 194.4, 163.2, 157.8, 152.8, 150.8, 148.6, 141.8, 139.2, 136.2, 135.4, 134.9, 134.6, 130.3, 129.0, 128.8, 128.5, 126.8, 126.5, 126.0, 125.9, 123.2, 104.1, 71.0, 34.7, 34.6, 34.1, 31.5, 31.3, 25.1. HRMS (ESI): calcd for $C_{42}H_{41}Cl_2N_2O_3$ $[M+H]^+$ 691.2489, Found: 691.2493.

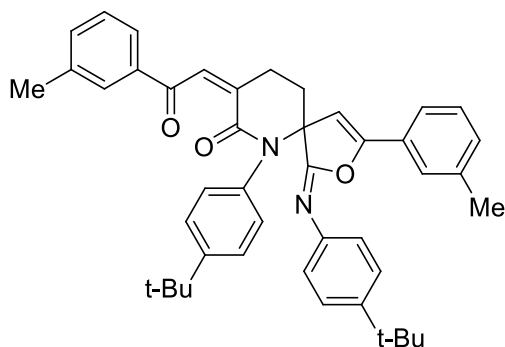


(**4d**): 215mg, 55% yield. white solid: m.p. 124-125 °C.

1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.85 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.5 Hz, 2H), 7.47-7.42 (m, 4H), 7.25-7.23 (m, 2H), 7.19-7.16 (m, 4H), 6.97 (d, J = 8.5 Hz, 2H), 6.45 (s, 1H), 5.71 (s, 1H), 3.72-3.66 (m, 1H),

2.85-2.79 (m, 1H), 2.60-2.55 (m, 1H), 2.53-2.47 (m, 1H), 1.37 (s, 9H), 1.15 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 194.6, 163.2, 157.8, 152.9, 150.8, 148.6, 141.7, 136.2, 135.4, 135.3, 134.6,

131.9, 131.8, 130.5, 128.5, 127.9, 126.9, 126.8, 126.1, 125.9, 124.5, 123.2, 104.2, 71.0, 34.7, 34.6, 34.1, 31.5, 31.3, 25.1. HRMS (ESI): calcd for C₄₂H₄₁Br₂N₂O₃ [M+H]⁺ 781.1458, Found: 781.1457.



(**4e**): 182mg, 56% yield. white solid: m.p. 123-124 °C. ¹H

NMR (500 MHz, CDCl₃): δ (ppm) = 7.84-7.80 (m, 2H),

7.43 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 4.5 Hz, 2H),

7.22-7.18 (m, 8H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.51 (s, 1H),

5.73 (s, 1H), 3.70-3.65 (m, 1H), 2.85-2.81 (m, 1H),

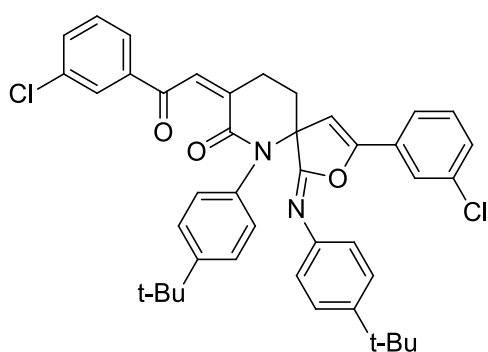
2.62-2.58 (m, 1H), 2.54-2.48 (m, 1H), 2.38 (s, 3H), 2.34 (s, 3H), 1.38 (s, 9H), 1.17 (s, 9H). ¹³C

NMR (125 MHz, CDCl₃): δ (ppm) = 195.8, 163.3, 158.2, 153.9, 150.5, 148.3, 141.9, 138.4, 138.2,

136.4, 136.3, 136.1, 134.2, 133.8, 130.9, 129.3, 128.7, 128.5, 128.3, 128.0, 126.4, 125.9, 125.8,

123.3, 122.7, 103.6, 71.4, 34.6, 34.5, 34.4, 31.5, 31.3, 25.3, 21.5, 21.4. HRMS (ESI): calcd

for C₄₄H₄₇N₂O₃ [M+H]⁺ 651.3581, Found: 651.3578.



(**4f**): 197mg, 57% yield. white solid: m.p. 115-116 °C. ¹H NMR

(500 MHz, CDCl₃): δ (ppm) = 7.96-7.95 (m, 1H), 7.88-7.86

(m, 1H), 7.47-7.42 (m, 3H), 7.36-7.31 (m, 3H), 7.27-7.26 (m,

2H), 7.21-7.19 (m, 4H), 6.99-6.98 (m, 2H), 6.47-6.46 (m,

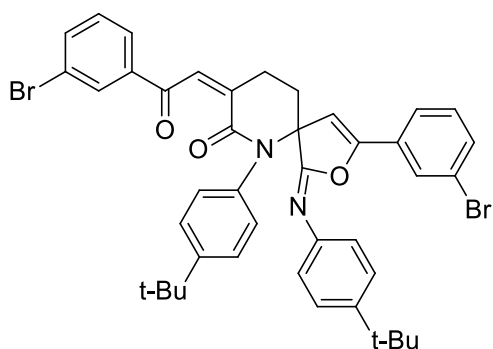
1H), 5.75 (s, 1H,), 3.74-3.67 (m, 1H), 2.86-2.81 (m, 1H),

2.61-2.60 (m, 1H), 2.49-2.48 (m, 1H), 1.37 (s, 9H), 1.16 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ

(ppm) = 194.2, 163.2, 157.5, 152.6, 150.9, 148.6, 141.6, 138.0, 136.2, 135.2, 134.9, 134.8, 134.7,

132.8, 130.3, 130.0, 129.9, 129.8, 129.7, 128.9, 128.5, 127.0, 126.1, 125.9, 125.5, 123.6, 123.4,

104.9, 70.9, 34.7, 34.6, 34.1, 31.5, 31.3, 25.1. HRMS (ESI): calcd for C₄₂H₄₁Cl₂N₂O₃ [M+H]⁺ 691.2489, Found: 691.2499.



(**4g**): 176mg, 45% yield. white solid: m.p. 126-127 °C. ¹H

NMR (500 MHz, CDCl₃): δ (ppm) = 8.10-8.09 (m, 1H),

7.92-7.90 (m, 1H), 7.62-7.59 (m, 1H), 7.51-7.50 (m, 1H),

7.48-7.46 (m, 1H), 7.43-7.41 (m, 2H), 7.32-7.27 (m,

2H), 7.22-7.19 (m, 5H), 6.99-6.98 (m, 2H), 6.46-6.45 (m,

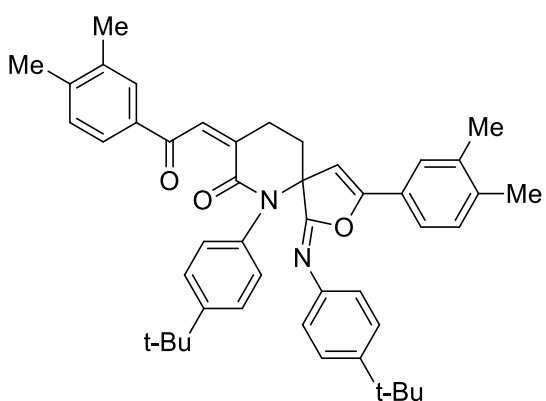
1H), 5.74 (s, 1H), 3.73-3.67 (m, 1H), 2.85-2.80 (m, 1H), 2.61-2.59 (m, 1H), 2.53-2.48 (m, 1H), 1.36

(s, 9H), 1.16 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 194.1, 163.2, 157.4, 152.5, 150.9,

148.6, 141.6, 138.2, 136.2, 135.7, 135.2, 134.9, 133.2, 131.8, 130.3, 130.2, 130.0, 128.5, 128.4,

127.5, 126.1, 125.9, 124.1, 123.4, 122.8, 104.9, 70.9, 34.7, 34.6, 34.2, 31.5, 31.3, 25.1. HRMS

(ESI): calcd for C₄₂H₄₁Br₂N₂O₃ [M+H]⁺ 781.1458, Found: 781.1450.



(**4h**): 176mg, 52% yield. white solid: m.p. 122-123 °C.

¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.77 (d, *J* = 1.5

Hz, 1H), 7.73-7.71 (m, 1H), 7.41-7.40 (m, 2H),

7.19-7.08 (m, 8H), 7.01-6.99 (m, 2H), 6.49 (s, 1H),

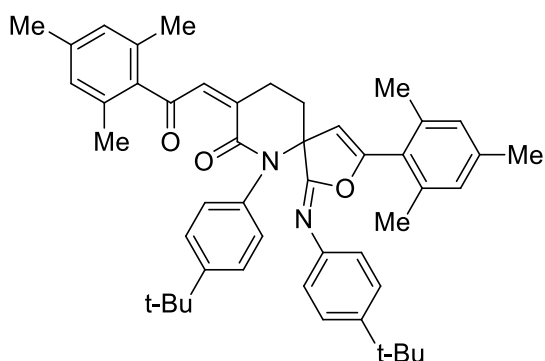
5.67 (s, 1H), 3.65-3.62 (m, 1H), 2.84-2.79 (m, 1H),

2.61-2.57 (m, 1H), 2.51-2.48 (m, 1H), 2.27-2.24 (m,

12H), 1.36 (s, 9H), 1.15 (s, 9H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 195.7, 163.3, 158.5, 154.0,

150.4, 148.2, 142.4, 142.1, 139.2, 136.9, 136.8, 136.5, 136.2, 134.3, 133.9, 129.9, 129.8, 129.7,

128.8, 126.9, 126.5, 125.9, 125.8, 125.7, 123.4, 123.1, 102.8, 71.1, 34.6, 34.5, 31.6, 31.3, 25.5, 20.2, 19.9, 19.8. HRMS (ESI): calcd for $C_{46}H_{51}N_2O_3$ $[M+H]^+$ 679.3894, Found: 679.3891 .

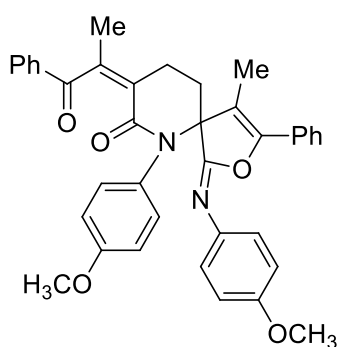


(4i): 187mg, 53% yield. white solid: m.p. 124-125 °C.

1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.35-7.33 (m, 2H), 7.29 (d, J = 10.0 Hz, 2H), 7.19-7.18 (m, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.83 (s, 2H), 6.78(s, 2H), 6.42 (d, J = 2.0 Hz, 1H), 5.24(s, 1H), 3.91-3.83 (m, 1H),

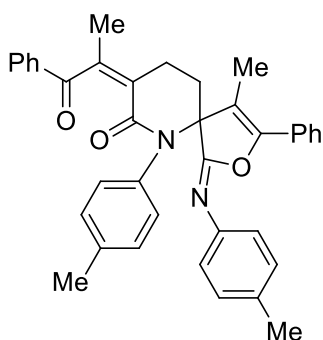
2.59-2.53 (m, 3H), 2.42 (s, 6H), 2.28 (s, 3H), 2.23 (s, 3H), 1.82 (s, 6H), 1.32 (s, 9H), 1.28 (s, 9H) .

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 199.1, 163.4, 159.4, 152.7, 150.7, 148.2, 142.0, 139.7, 139.3, 137.7, 137.2, 137.2, 136.8, 136.6, 136.2, 129.4, 129.2, 128.5, 128.3, 126.3, 125.7, 125.6, 123.5, 122.7, 110.3, 70.7, 35.5, 34.6, 34.5, 31.5, 31.4, 26.8, 21.2, 21.1, 19.7. HRMS (ESI): calcd for $C_{48}H_{55}Br_2N_2O_3$ $[M+H]^+$ 707.4207, Found: 707.4217.



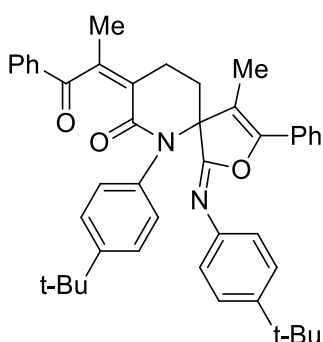
(4j): 188mg, 63% yield. white solid: m.p. 119-120 °C. 1H NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.98 (d, J = 5.5 Hz, 2H), 7.43-7.37 (m, 10H), 6.98 (s, 4H), 6.67 (d, J = 8.5 Hz, 2H), 3.86 (s, 3H), 3.64 (s, 4H), 2.85 (s, 1H), 2.57 (s, 1H), 2.37 (s, 1H), 2.06-1.86 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 199.4, 165.1, 158.5, 157.3, 147.9, 146.1, 137.9,

135.2, 132.4, 132.2, 129.3, 129.1, 128.8, 128.5, 128.4, 127.0, 125.6, 114.1, 113.9, 112.0, 72.0, 55.5, 55.2, 30.9, 20.4, 17.9, 9.9. HRMS (ESI): calcd for $C_{38}H_{35}N_2O_5$ $[M+H]^+$ 599.2540, Found: 599.2548.



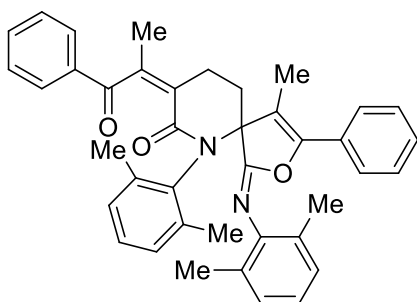
(4k): 187mg, 66% yield. white solid: m.p. 118-119 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.97 (d, *J* = 5.0 Hz, 2H), 7.45-7.30 (m, 12H), 6.95 (s, 4H), 3.69-6.63 (m, 1H), 2.86-2.83 (m, 1H), 2.59 (s, 1H), 2.41-2.36 (m, 4H), 2.18 (s, 3H), 2.06-1.85 (m, 6H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 199.4, 164.9, 159.1, 147.8, 146.2, 142.4, 137.3,

136.8, 135.2, 134.8, 132.4, 129.5, 129.4, 129.2, 129.1, 128.8, 128.5, 128.4, 127.8, 127.0, 126.3, 123.7, 112.2, 71.8, 30.9, 21.1, 21.0, 20.4, 17.9, 9.9 . HRMS (ESI): calcd for C₃₈H₃₅N₂O₃ [M+H]⁺ 567.2642, Found: 567.2640



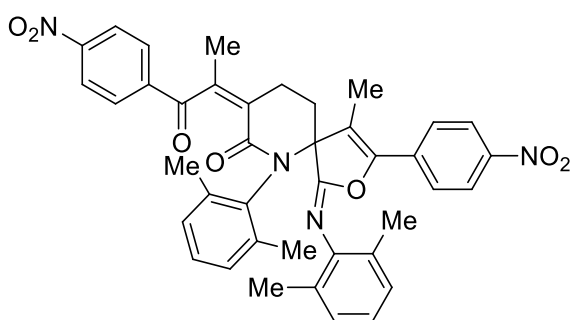
(4l): 185mg, 57% yield. white solid: m.p. 123-124 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.99 (d, *J* = 7.5 Hz, 2H), 7.47-7.28 (m, 12H), 7.18 (d, *J* = 8.5 Hz, 2H), 7.01 (s, 2H,), 3.71-3.65 (m, 1H), 2.85 (d, *J* = 12.5 Hz, 1H), 2.61 (s, 1H), 2.38 (s, 1H), 2.06 (s, 3H), 1.81 (s, 3H), 1.39 (s, 9H), 1.19 (s, 9H). ¹³C NMR (125 MHz, DMSO): δ (ppm) = 197.7, 159.3,

149.8, 147.1, 142.1, 132.3, 129.4, 128.6, 128.5, 128.4, 127.8, 126.7, 125.6, 125.1, 122.7, 112.4, 56.0, 54.9, 34.1, 31.2, 31.0, 30.9, 19.8, 17.5, 9.3. HRMS (ESI): calcd for C₄₄H₄₇N₂O₃ [M+H]⁺ 651.3581, Found: 651.3585.



(4m): 146mg, 49% yield. white solid: m.p. 150-151 °C . ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 8.00 (d, *J* = 6.0 Hz, 2H), 7.52-7.33 (m, 8H), 7.14-6.93 (m, 6H), 3.67 (s, 1H), 3.03 (d, *J* = 16.0 Hz, 1H), 2.87-2.81 (m, 1H), 2.66 (s, 1H), 2.25-2.09 (m,

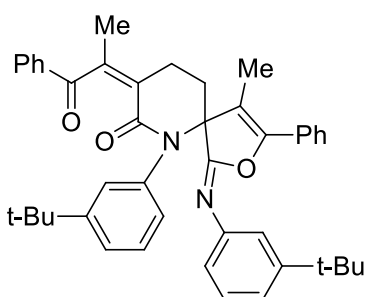
15H), 1.75 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 198.9, 163.9, 148.4, 147.8, 143.7, 138.9, 136.6, 132.3, 129.5, 128.7, 128.6, 128.5, 128.4, 127.9, 127.7, 127.4, 125.3, 123.7, 112.3, 70.4, 34.2, 21.3, 19.8, 18.6, 18.0, 10.4. HRMS (ESI): calcd for $\text{C}_{40}\text{H}_{39}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]^+$ 595.2955, Found: 595.2943.



(**4n**): 219mg, 64% yield. white solid: m.p. 133-134 °C.

^1H NMR (500 MHz, CDCl_3): δ (ppm) = 8.22-8.17 (m, 4H), 8.07 (d, J = 10.0 Hz, 2H), 7.44 (d, J = 10.0 Hz, 2H), 7.12 (d, J = 10.0 Hz, 2H), 7.03-7.00 (m, 3H), 6.91 (d, J = 5.0 Hz, 1H), 3.69 (s, 1H), 3.04 (d, J = 20.0

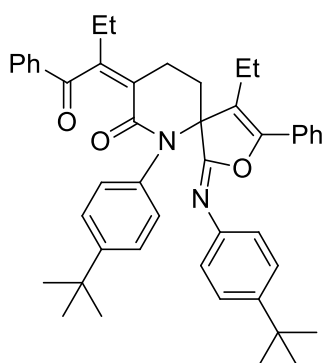
Hz, 1H), 2.89-2.83 (m, 1H), 2.63-2.59 (m, 1H), 2.16-2.09 (m, 15H), 1.69 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (ppm) = 196.4, 164.2, 157.0, 149.8, 147.8, 147.0, 146.6, 143.2, 140.3, 138.5, 137.4, 136.3, 134.5, 129.2, 128.9, 128.8, 128.3, 128.2, 128.1, 126.4, 124.2, 123.8, 123.7, 116.0, 70.4, 33.7, 20.9, 19.8, 19.6, 18.7, 17.7, 10.6. HRMS (ESI): calcd for $\text{C}_{40}\text{H}_{37}\text{N}_4\text{O}_7$ $[\text{M}+\text{H}]^+$ 685.2657, Found: 685.2655



(**4o**): 176mg, 54% yield. yellow oil . ^1H NMR (500 MHz, CDCl_3): δ (ppm) = 7.99 (d, J = 7.0 Hz, 2H), 7.40-7.29 (m, 11H), 7.18 (d, J = 7.0 Hz, 1H), 7.13-7.05 (m, 3H), 6.95 (s, 1H), 3.74-3.68 (m, 1H), 2.87 (d, J = 12.5 Hz, 1H), 2.61 (s, 1H), 2.42 (s, 1H), 2.07 (s, 3H),

1.85 (s, 3H), 1.39 (s, 9H), 1.04 (s, 9H). ^{13}C NMR (125 MHz, DMSO): δ (ppm) = 198.2, 159.9, 151.9, 151.4, 147.1, 145.0, 132.8, 129.8, 129.1, 128.9, 128.4, 126.8, 126.5, 124.6, 122.4, 120.8,

120.4, 113.0, 56.5, 55.4, 34.9, 34.6, 31.6, 31.3, 20.4, 17.9, 9.9 . HRMS (ESI): calcd for C₄₄H₄₇N₂O₃ [M+H]⁺ 651.3581, Found: 651.3590.

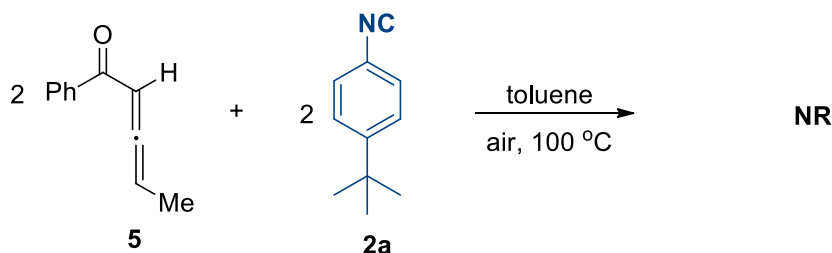


(4p): 159mg, 47% yield. white solid: m.p. 119-120 °C. ¹H NMR (500 MHz, CDCl₃): δ (ppm) = 7.99 (d, *J* = 10.0 Hz, 2H), 7.47-7.31 (m, 10H), 7.24-7.14 (m, 4H), 6.98-6.97 (m, 2H), 3.81-3.74 (m, 1H), 2.85-2.82 (m, 1H), 2.58-2.18 (m, 6H), 1.38 (s, 9H), 1.16-1.10 (m, 12H), 0.91 (s, 3H) . ¹³C NMR (125 MHz, CDCl₃): δ (ppm) = 198.8, 165.1, 159.3, 151.1,

150.2, 148.6, 148.2, 142.4, 136.9, 136.1, 132.3, 129.5, 129.3, 128.9, 128.5, 128.4, 128.1, 127.4, 127.2, 126.5, 126.4, 126.1, 125.9, 125.7, 123.6, 118.3, 72.4, 34.6, 34.5, 31.6, 31.3, 31.2, 24.8, 19.8, 17.3, 13.5, 11.7. HRMS (ESI): calcd for C₄₆H₅₁N₂O₃ [M+H]⁺ 679.3894, Found: 679.3890.

4 Control Experiment and Mechanistic Study

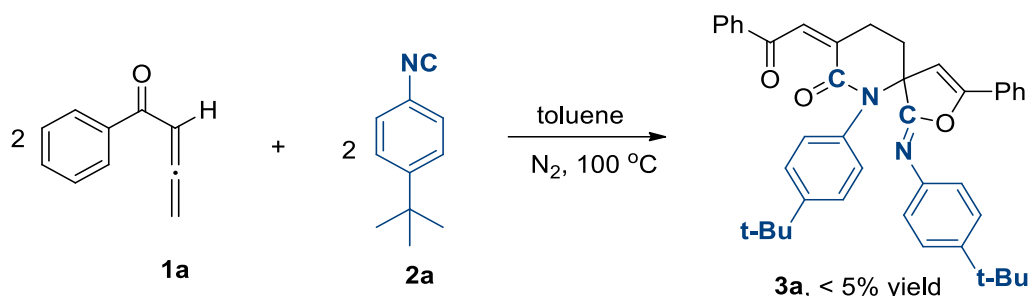
1) Experiment with γ -substituted allenyl ketone



Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with γ -substituted allenyl ketone **5** (0.5 mmol), isocyanide **2a** (1.0 mmol), in toluene (5.0 mL) at room temperature. Then capped it with a septum and stirred at 100 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by

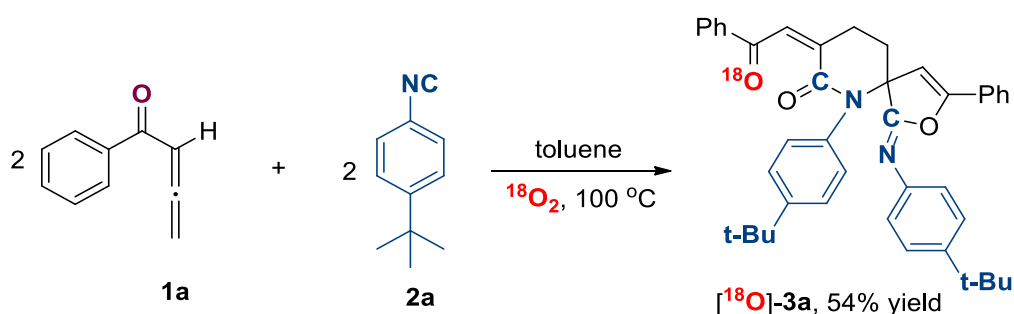
TLC. And the reaction mixture was concentrated under vacuum. No formation of desired product was observed.

2) Experiment under nitrogen atmosphere



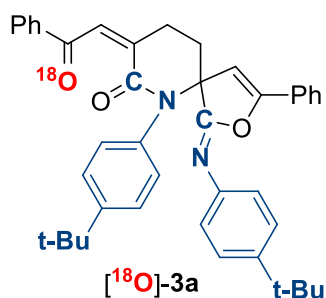
Under nitrogen atmosphere, a screw cap vial was charged with allenyl ketone **1a** (0.5 mmol), isocyanide **2a** (1.0 mmol) in toluene (5.0 mL) at room temperature. Then the vial was purged with nitrogen atmosphere and this mixture was stirred at $100\text{ }^\circ\text{C}$ for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 8:1) to give product **3a**.

3) Isotope experiment with $^{18}\text{O}_2$ atmosphere



A screw cap vial was charged with allenyl ketone **1a** (0.5 mmol), isocyanide **2a** (1.0 mmol) in toluene (5.0 mL) at room temperature. Then the vial was purged with $^{18}\text{O}_2$ atmosphere and this mixture was stirred at $100\text{ }^\circ\text{C}$ for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The

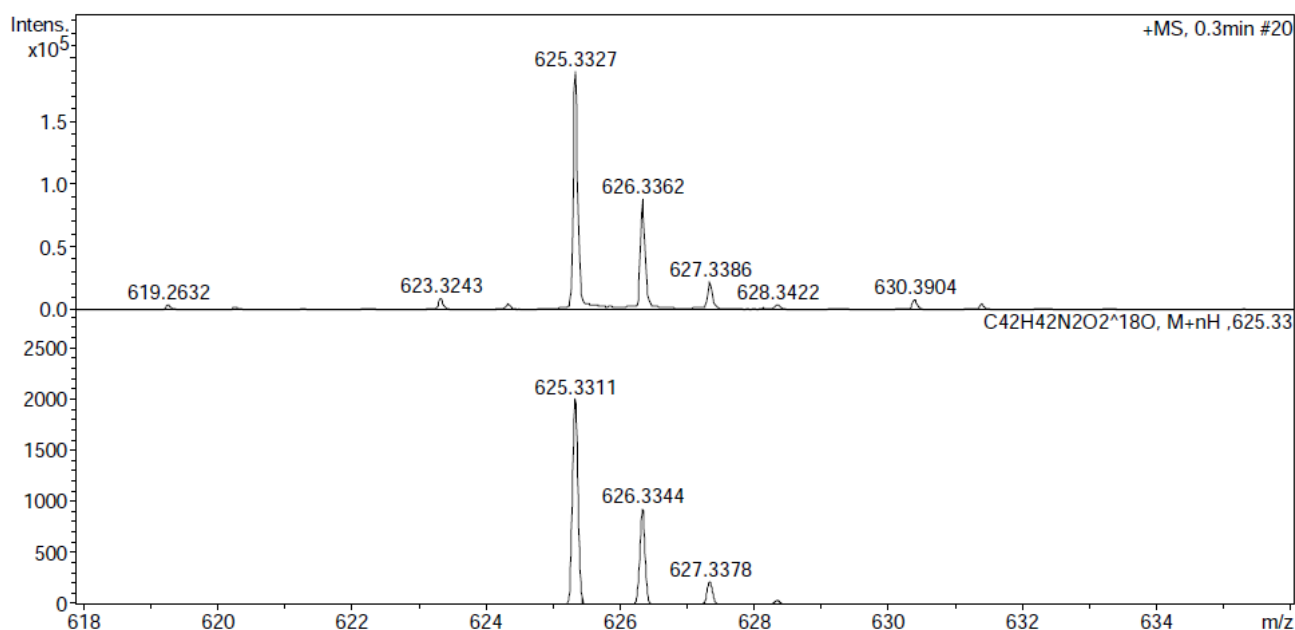
residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 8:1) to give product [^{18}O]-**3a**.



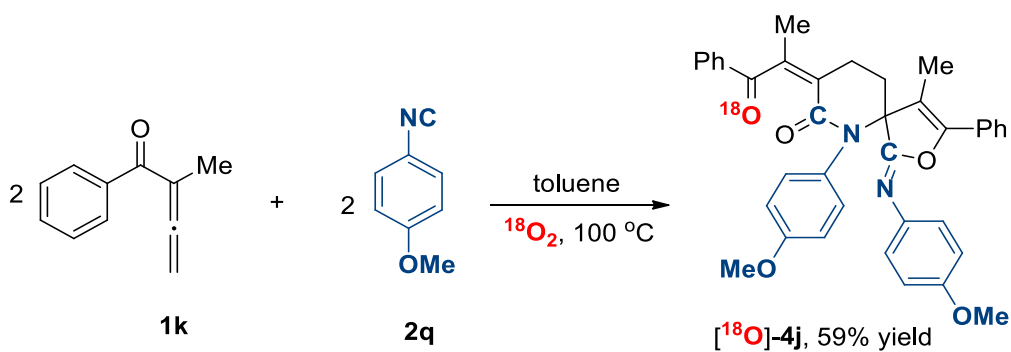
Chemical Formula: $\text{C}_{42}\text{H}_{43}\text{N}_2\text{O}_2^{18}\text{O}$

Calcd: 625.3311

Found: 625.3327

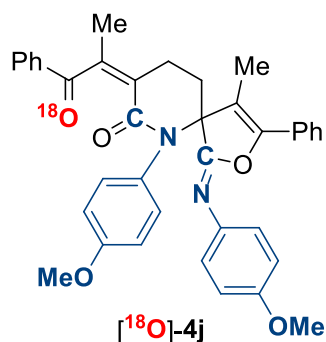


4) Isotope experiment with $^{18}\text{O}_2$ atmosphere

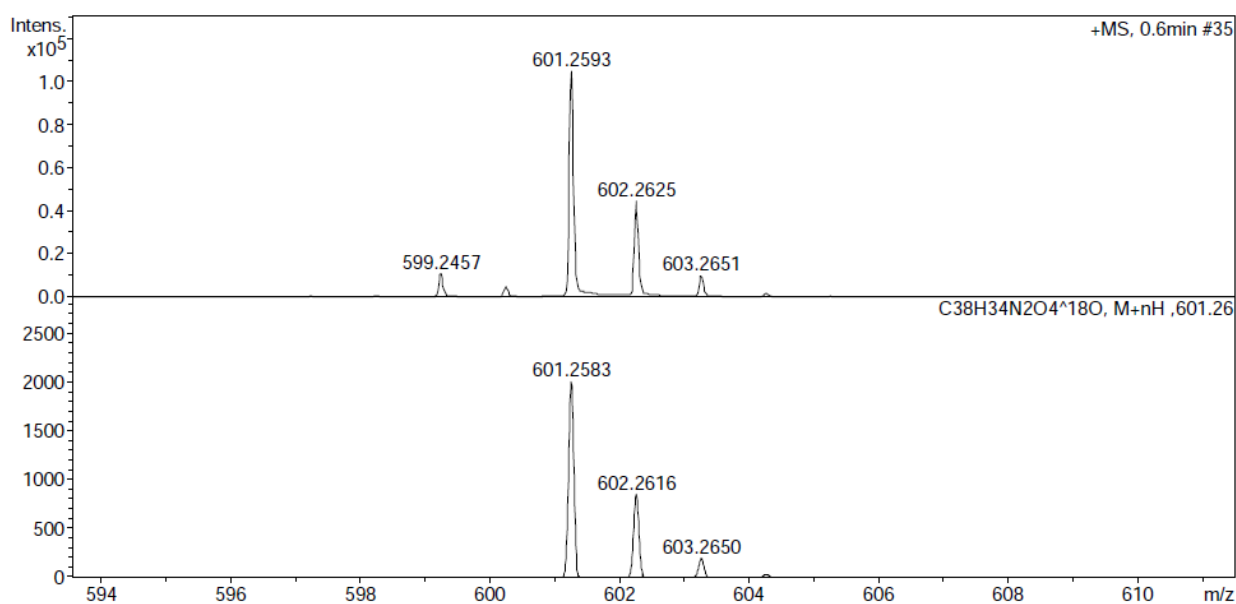


A screw cap vial was charged with allenyl ketone **1k** (0.5 mmol), isocyanide **2q** (1.0 mmol) in toluene (5.0 mL) at room temperature. Then the vial was purged with $^{18}\text{O}_2$ atmosphere and this

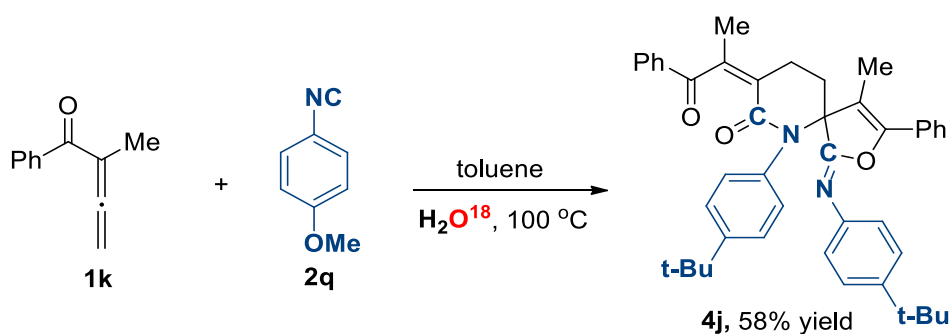
mixture was stirred at 100 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 8:1) to give product [¹⁸O]-4j.



Chemical Formula: C₃₈H₃₅N₂O₄¹⁸O
 Calcd: 601.2583
 Found: 601.2593

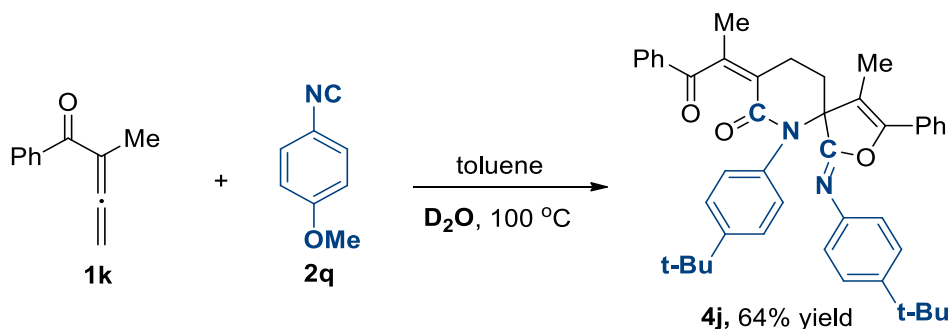


5) Isotope experiment with H₂O¹⁸ atmosphere



Under air atmosphere, a screw cap vial was charged with allenyl ketone **1k** (0.5 mmol), isocyanide **2q** (1.0 mmol), H₂O¹⁸ (6 equiv.) in toluene (5.0 mL) at room temperature. Then capped it with a septum and stirred at 100 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 8:1) to give product **4j**.

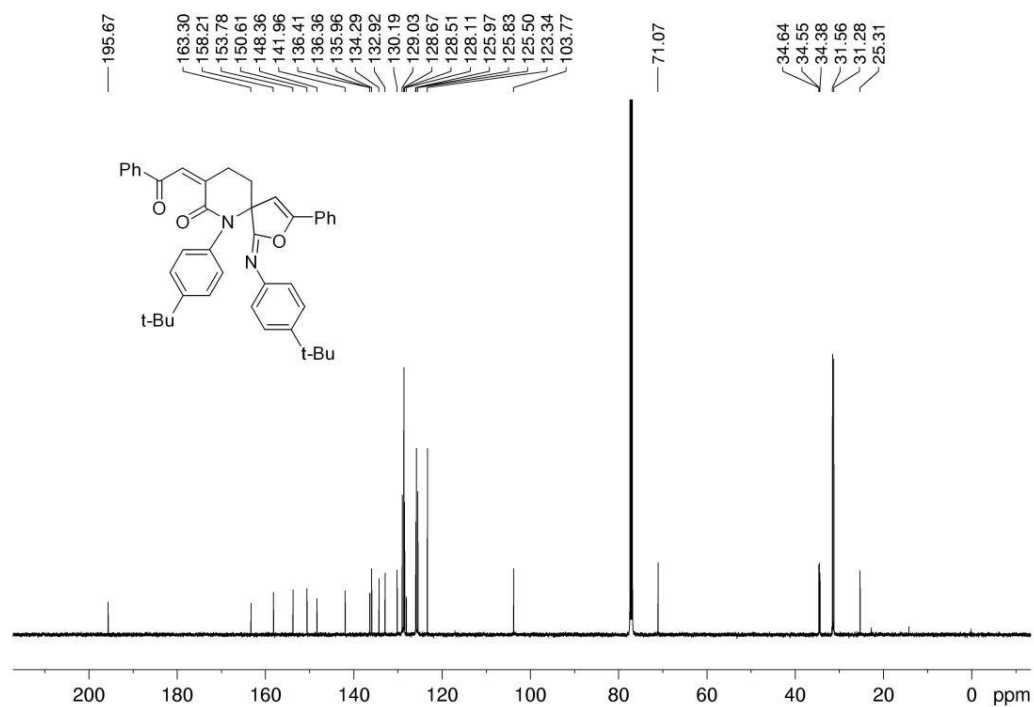
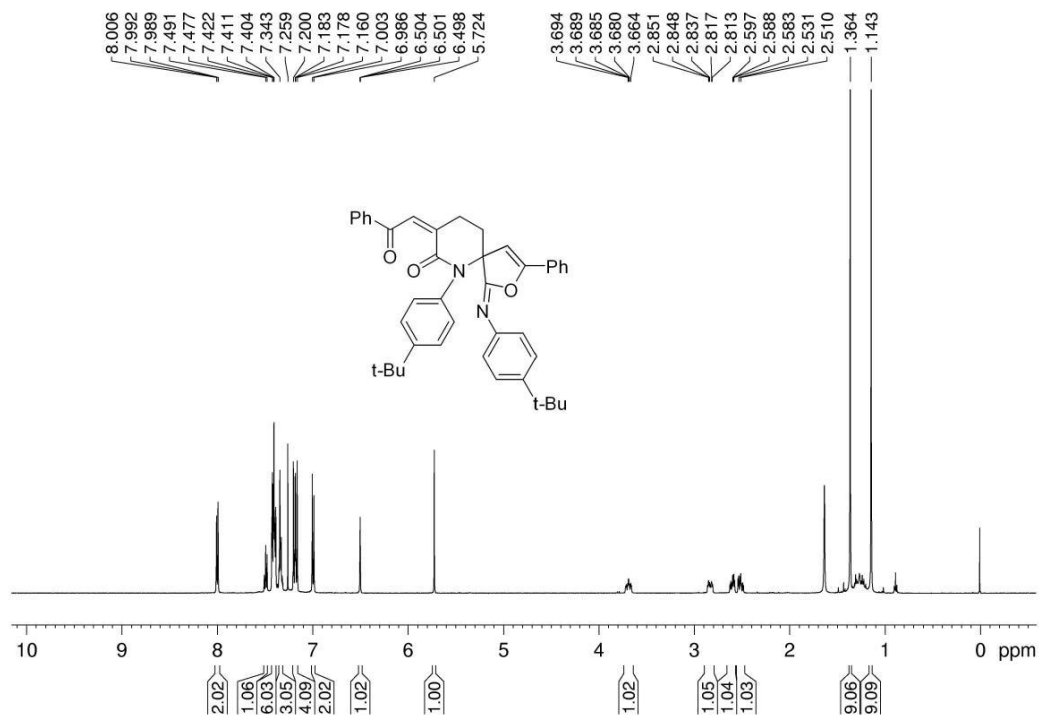
6) Isotope experiment with D₂O atmosphere



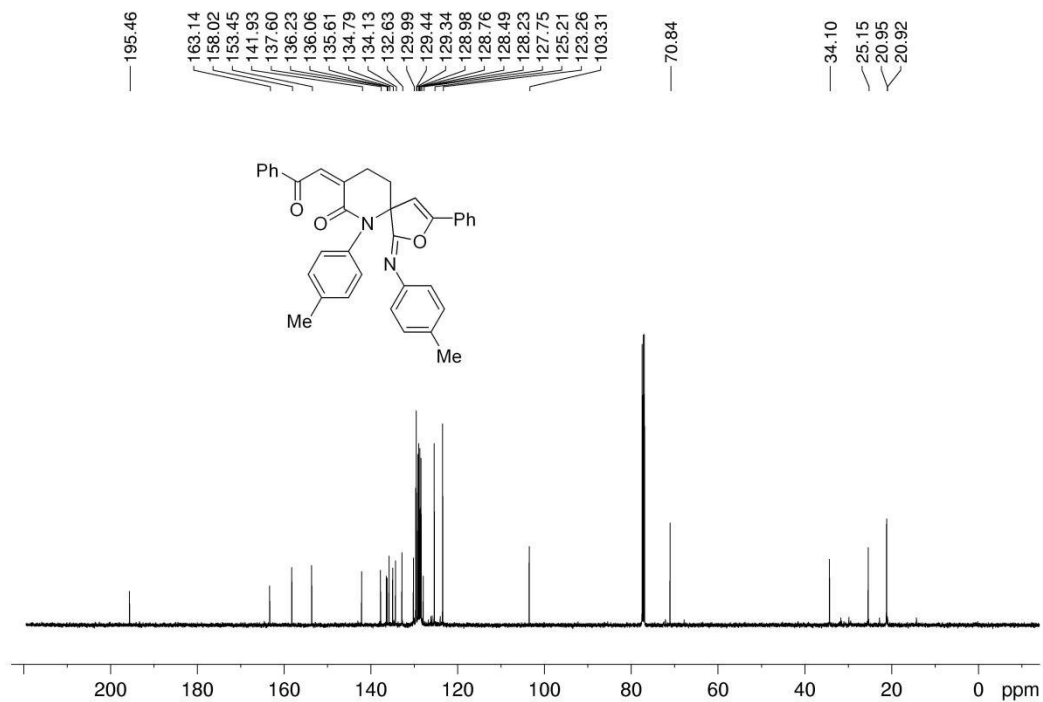
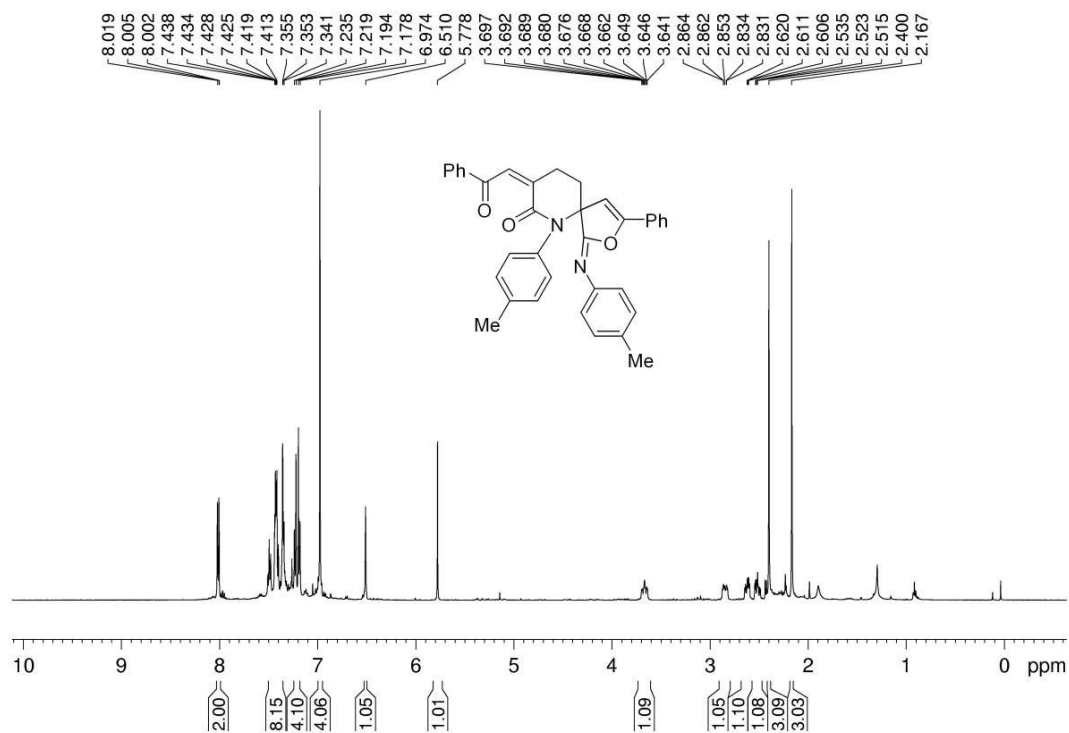
Under air atmosphere, a screw cap vial was charged with allenyl ketone **1k** (0.5 mmol), isocyanide **2q** (1.0 mmol), D₂O (6 equiv.) in toluene (5.0 mL) at room temperature. Then capped it with a septum and stirred at 100 °C for 12 h. After the reaction was completed, it was cooled to room temperature and monitored by TLC. And the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (eluant: petroleum ether/ethyl acetate = 8:1) to give product **4j**.

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

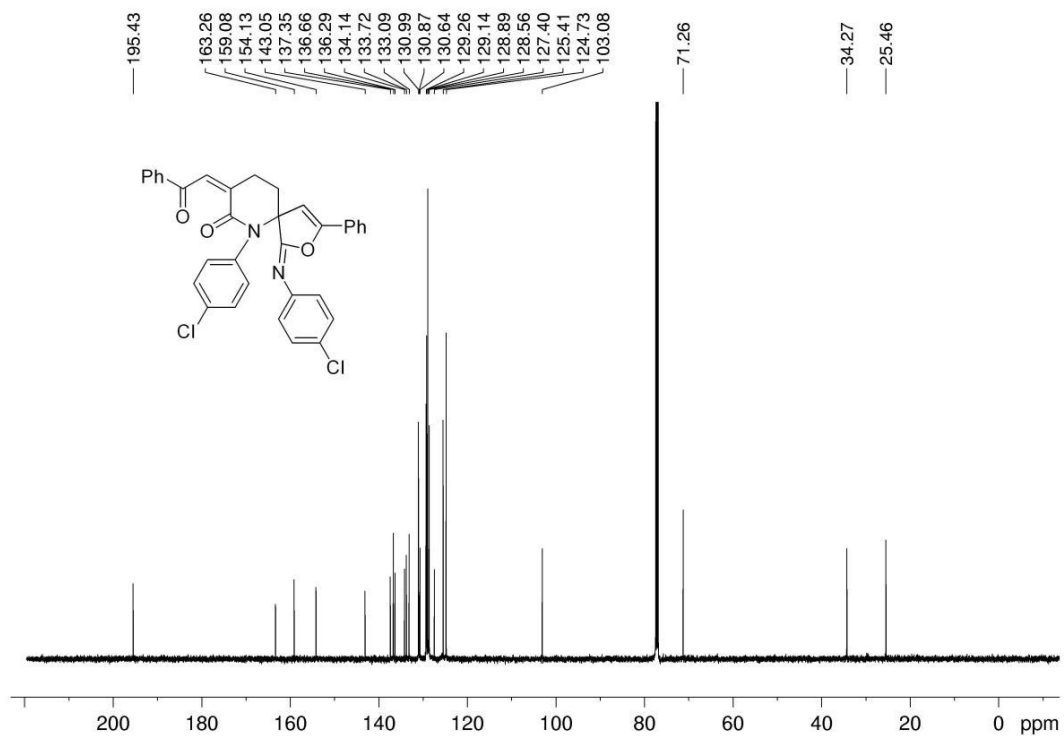
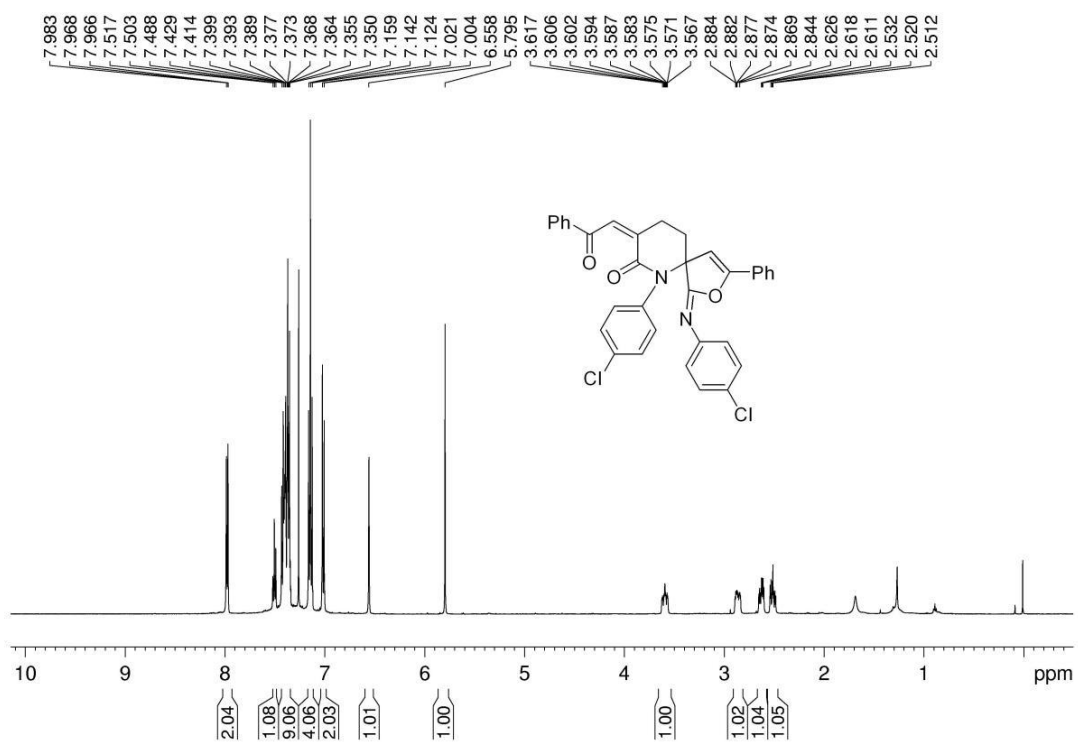
Compound 3a



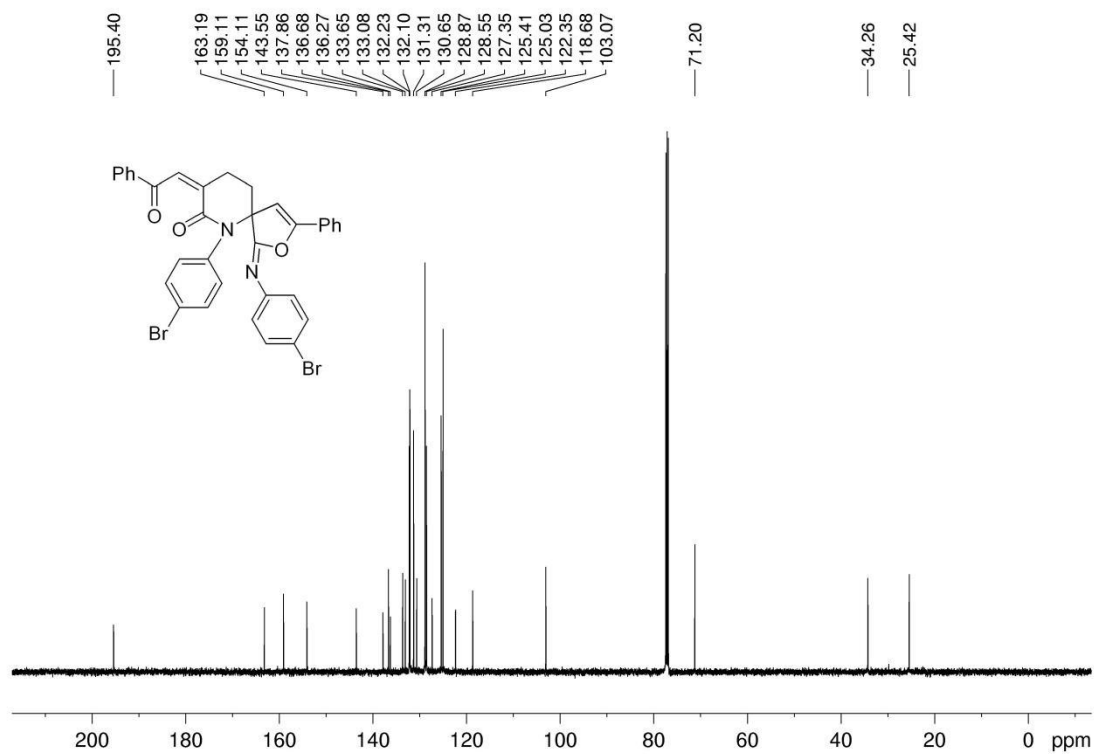
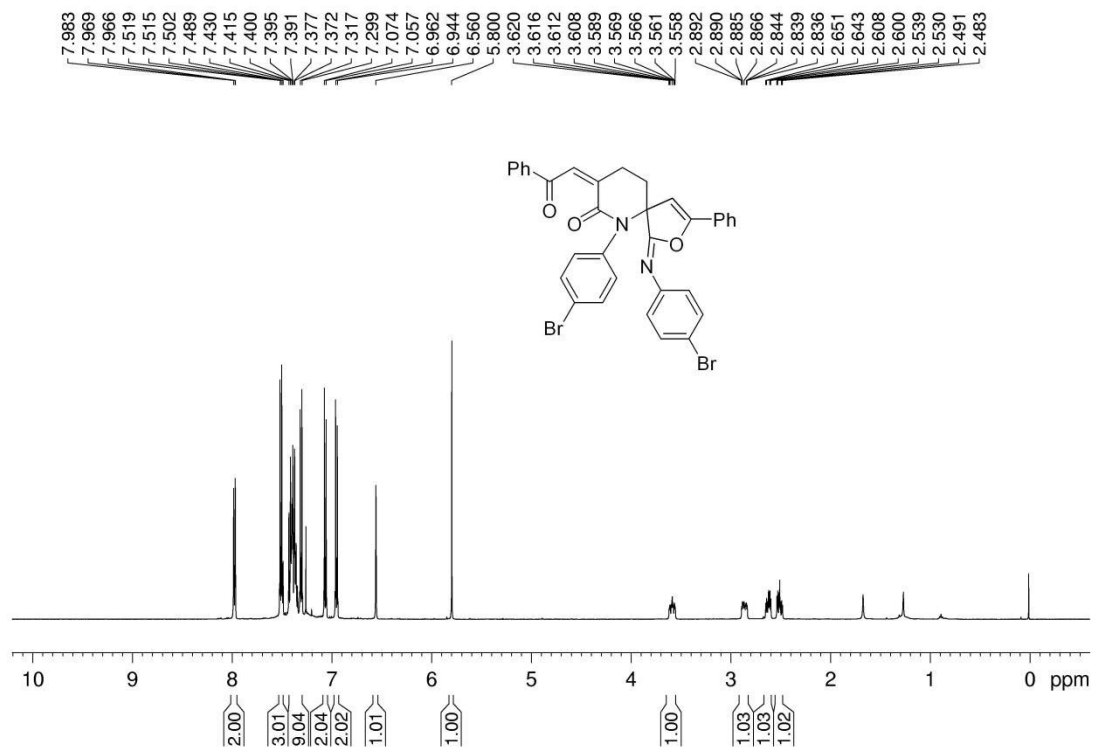
Compound 3b



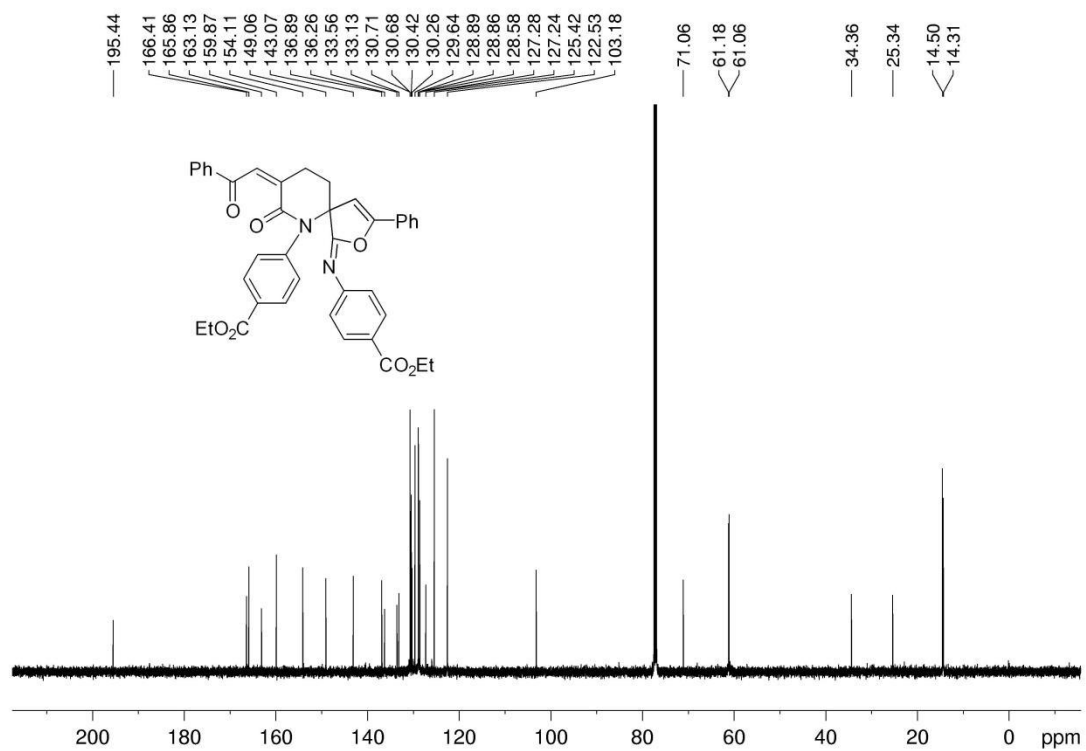
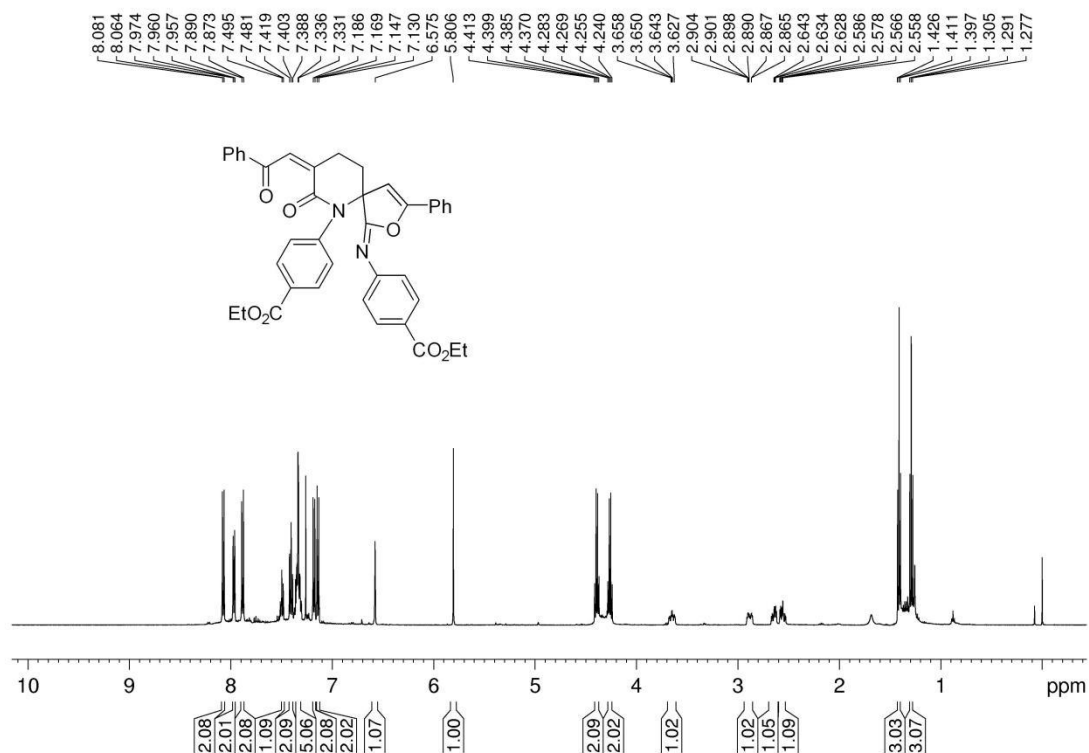
Compound 3c



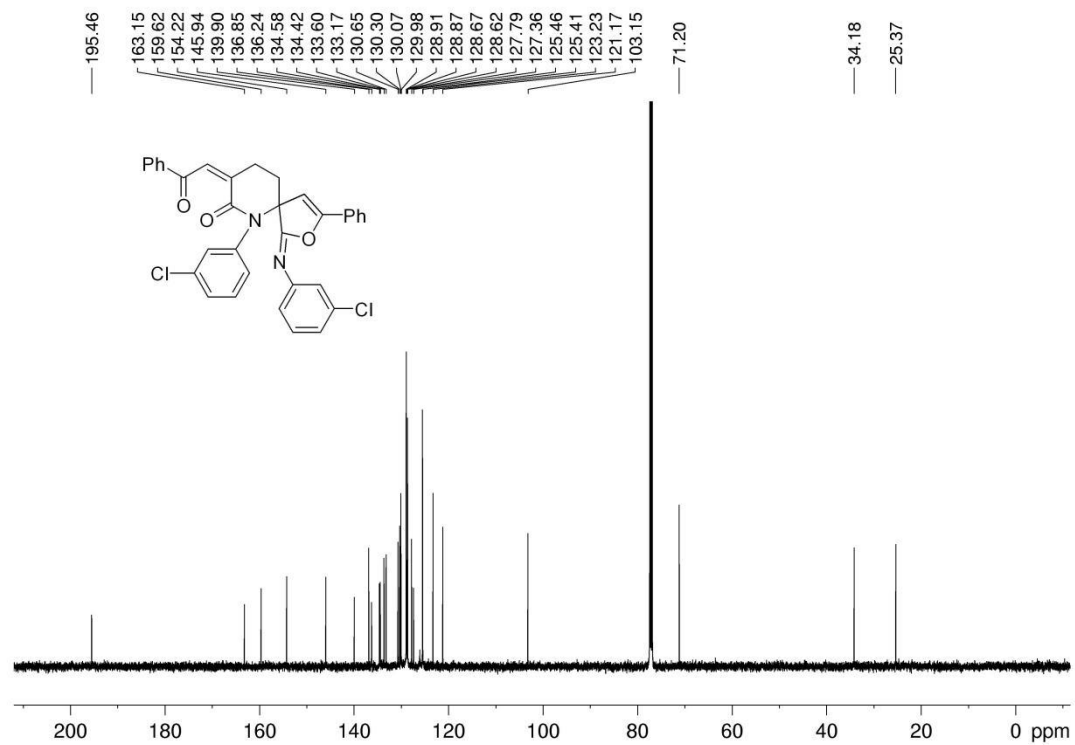
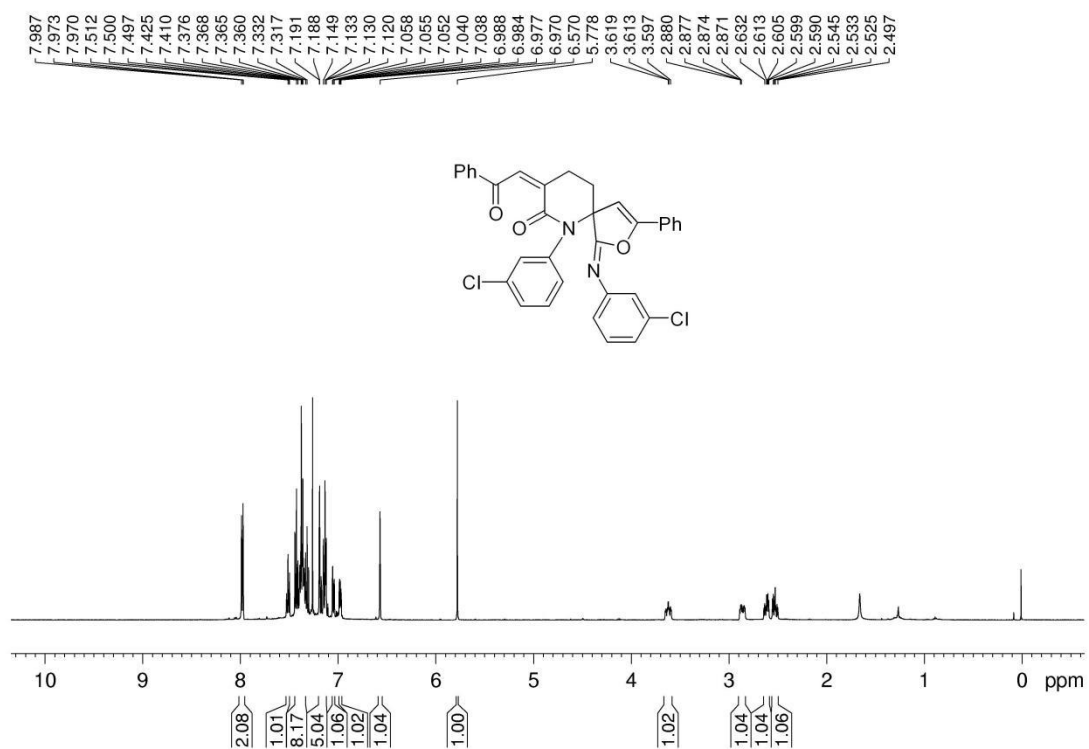
Compound 3d



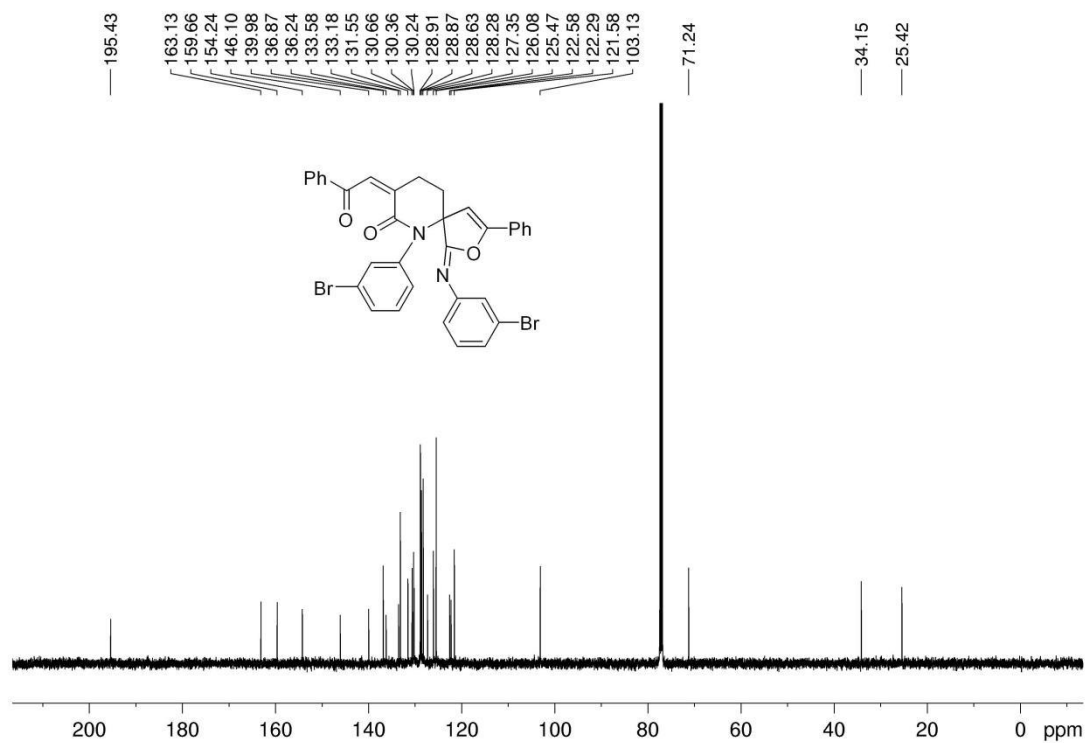
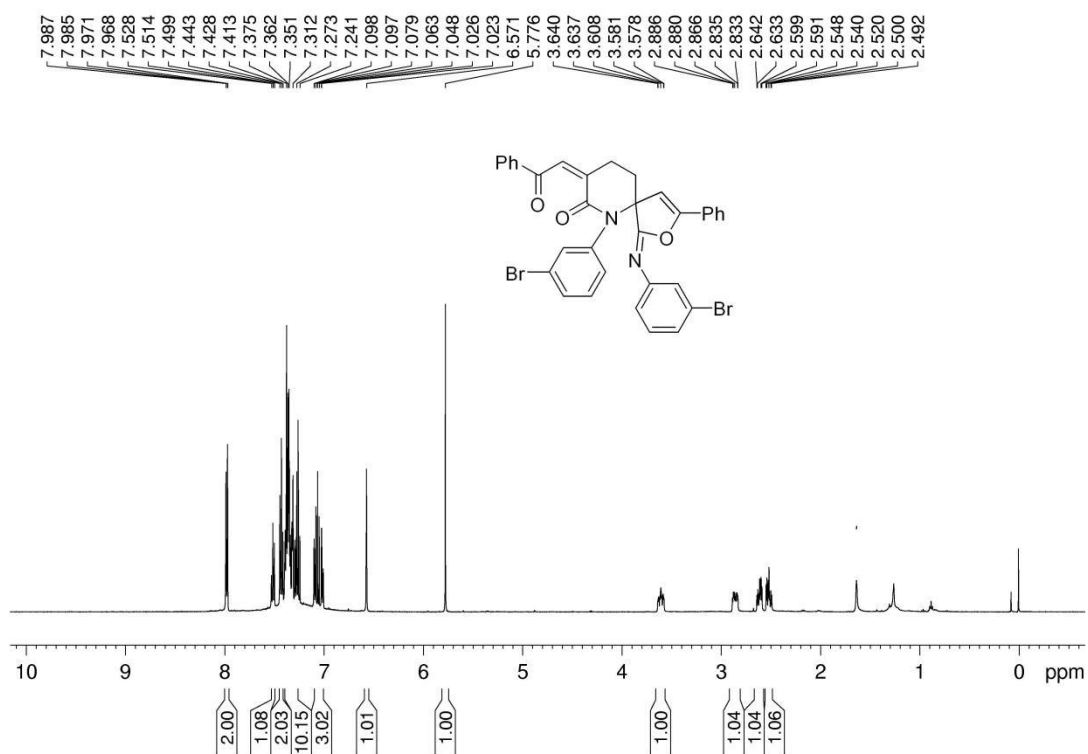
Compound 3e



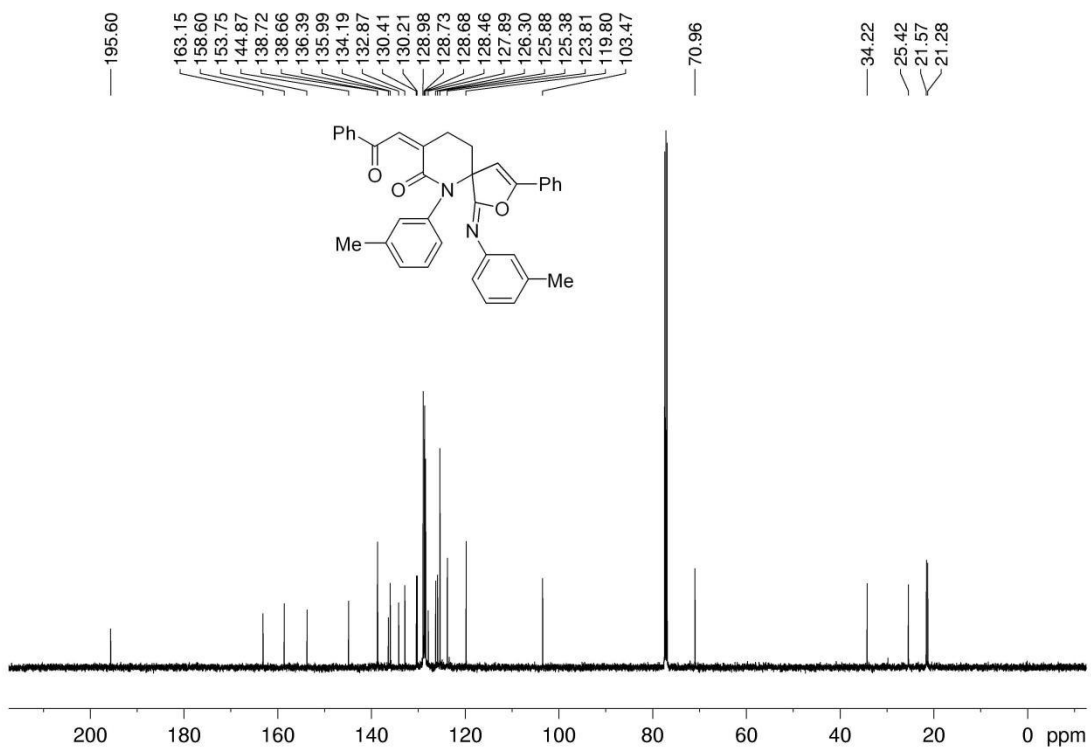
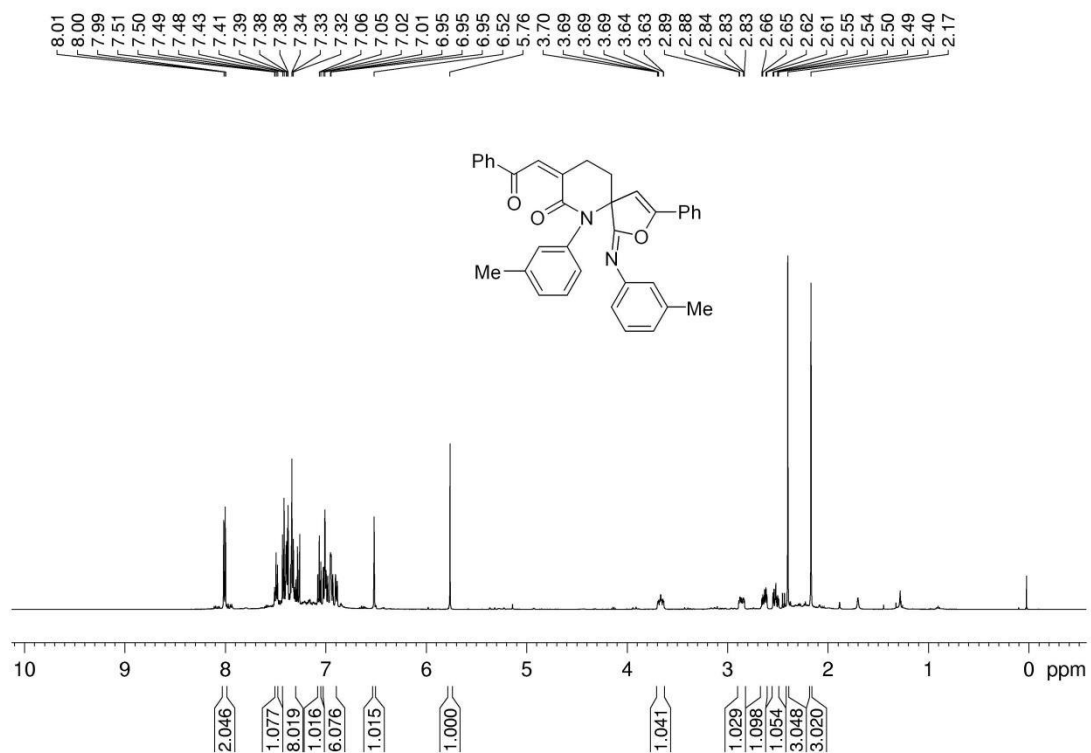
Compound 3f



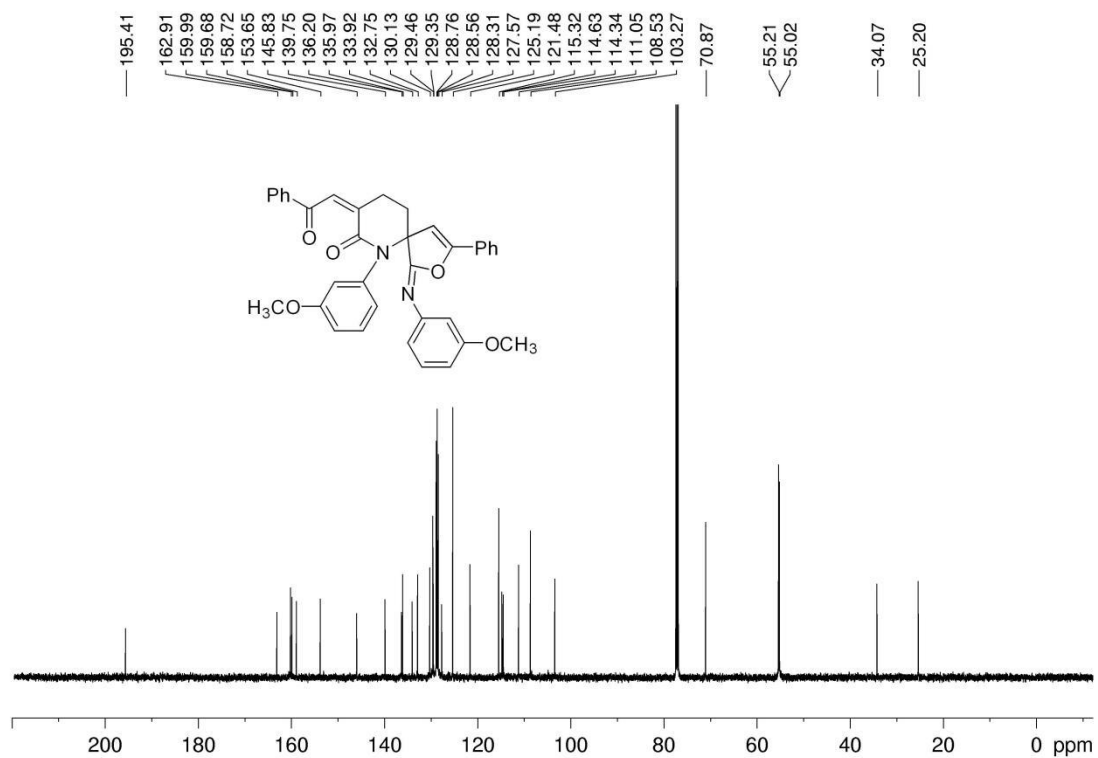
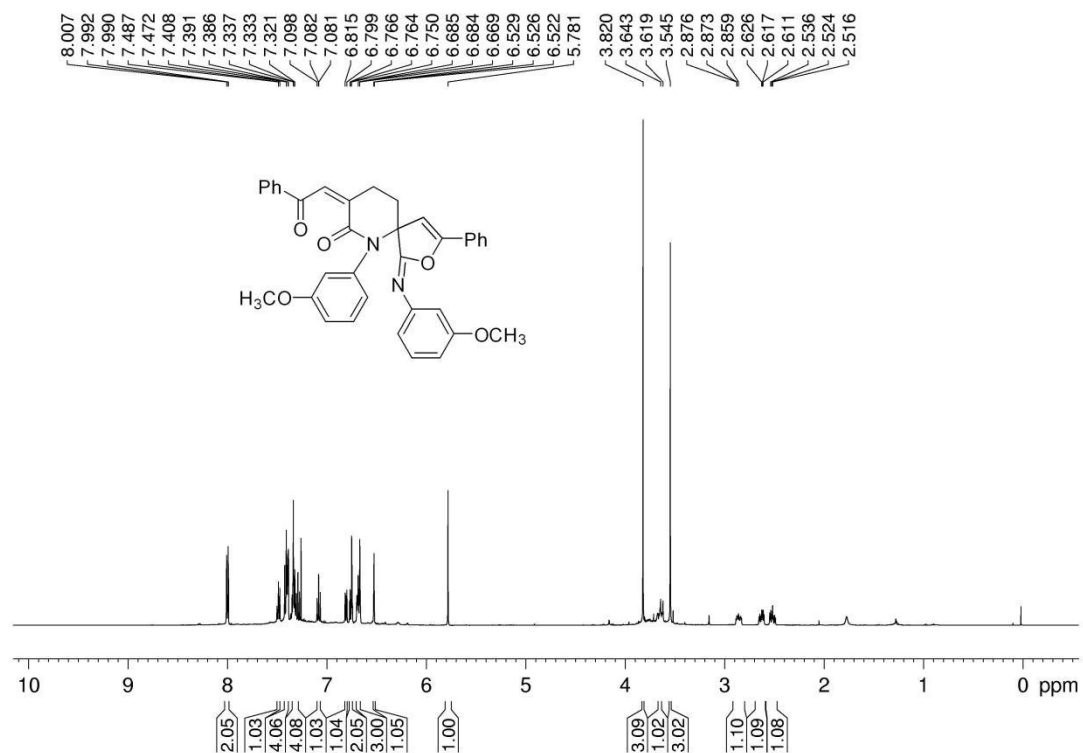
Compound 3g



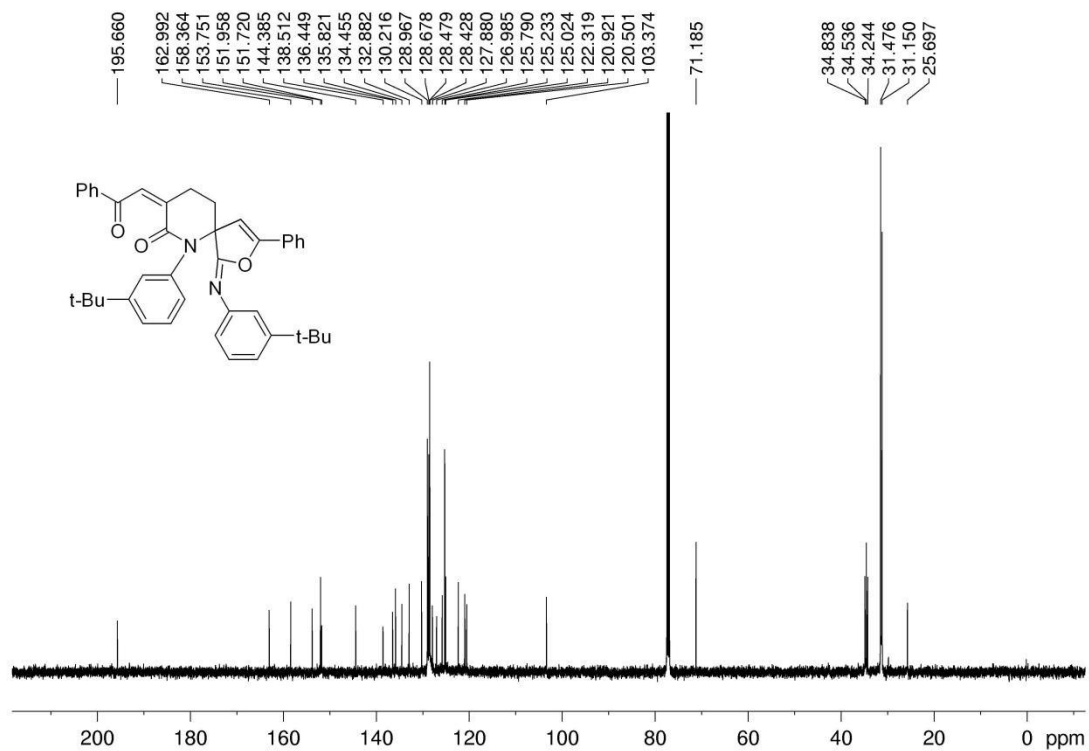
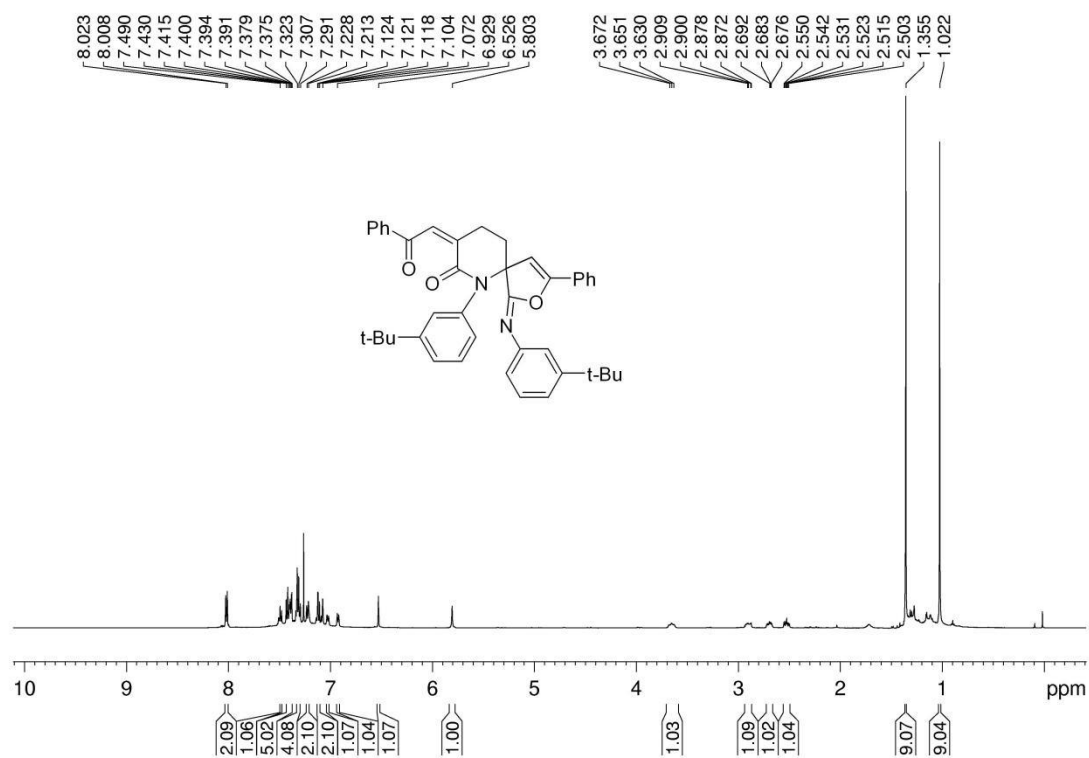
Compound 3h



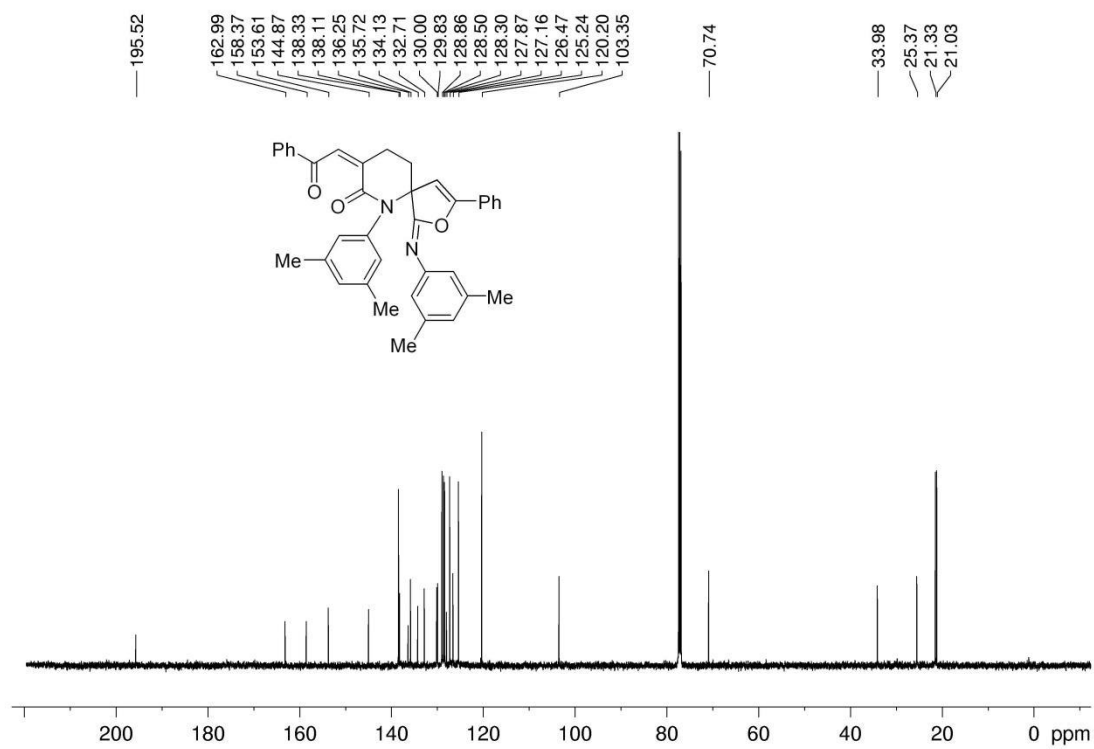
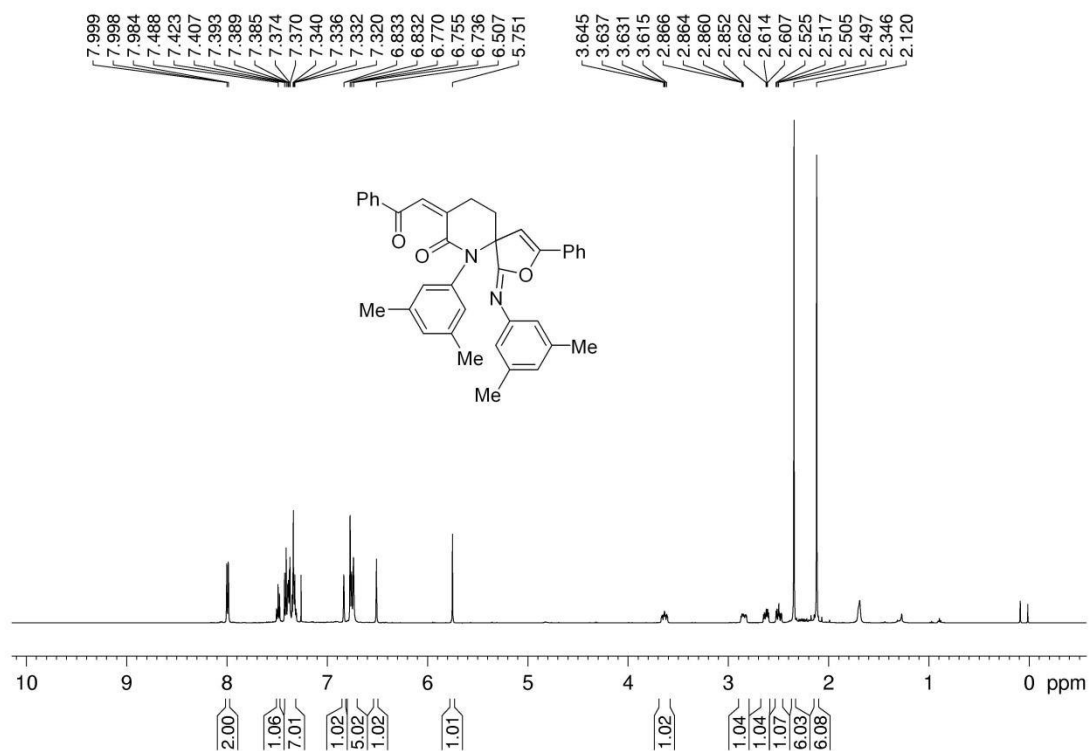
Compound **3i**



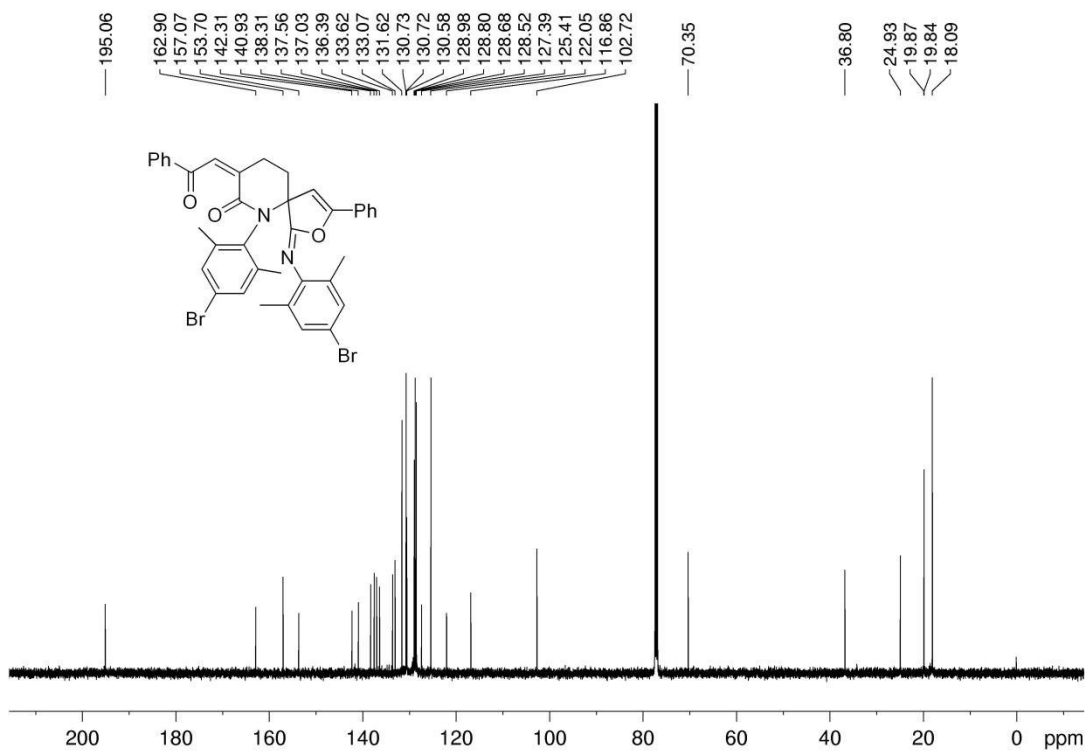
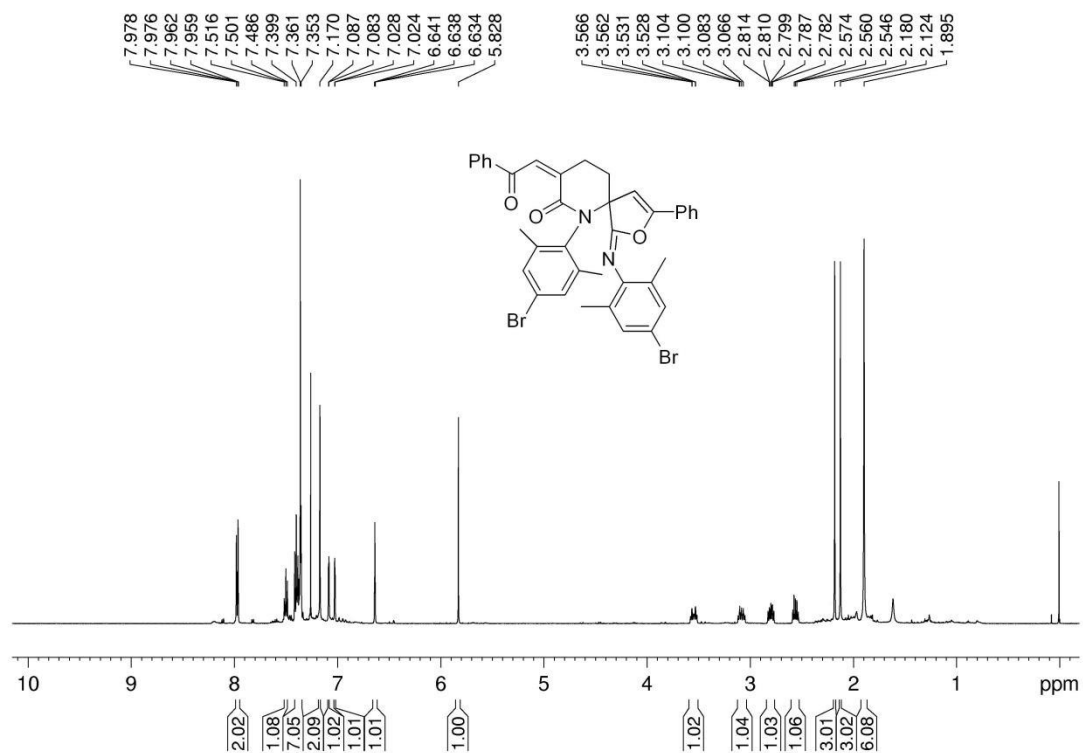
Compound **3j**



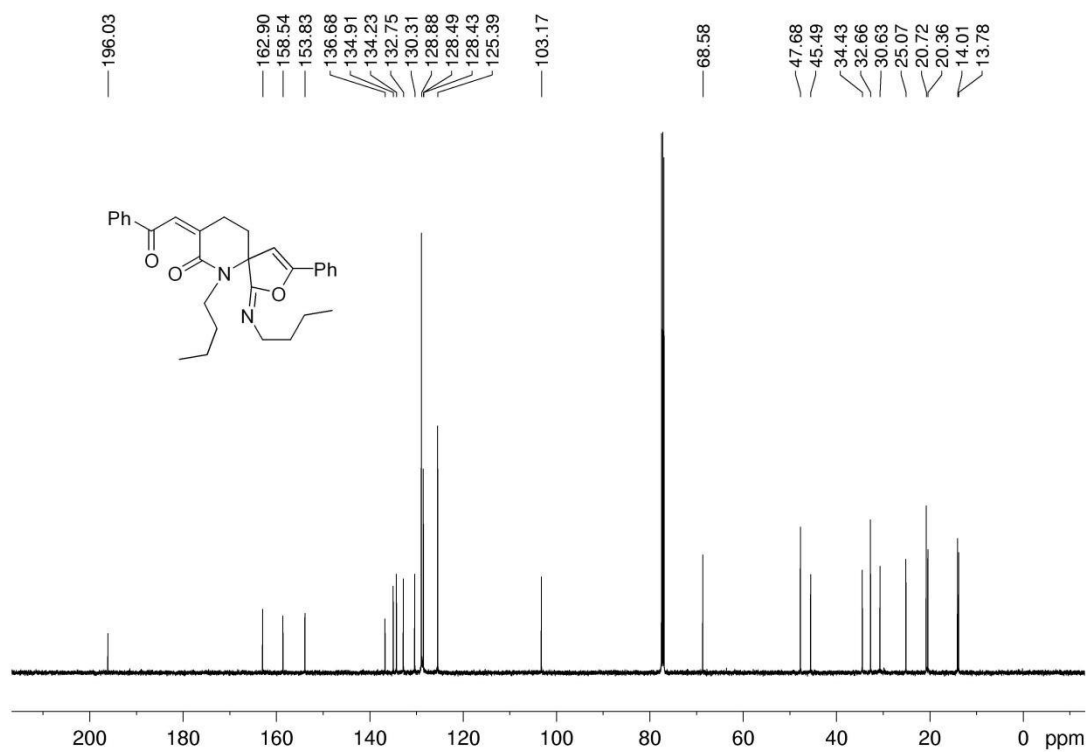
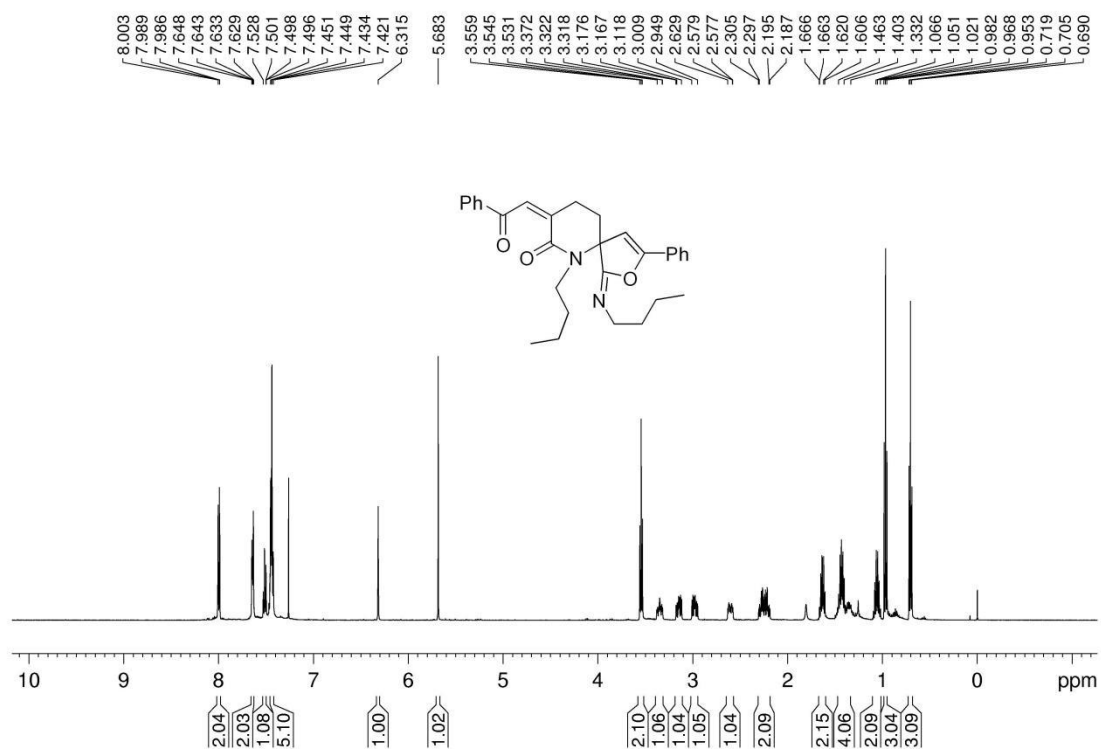
Compound 3k



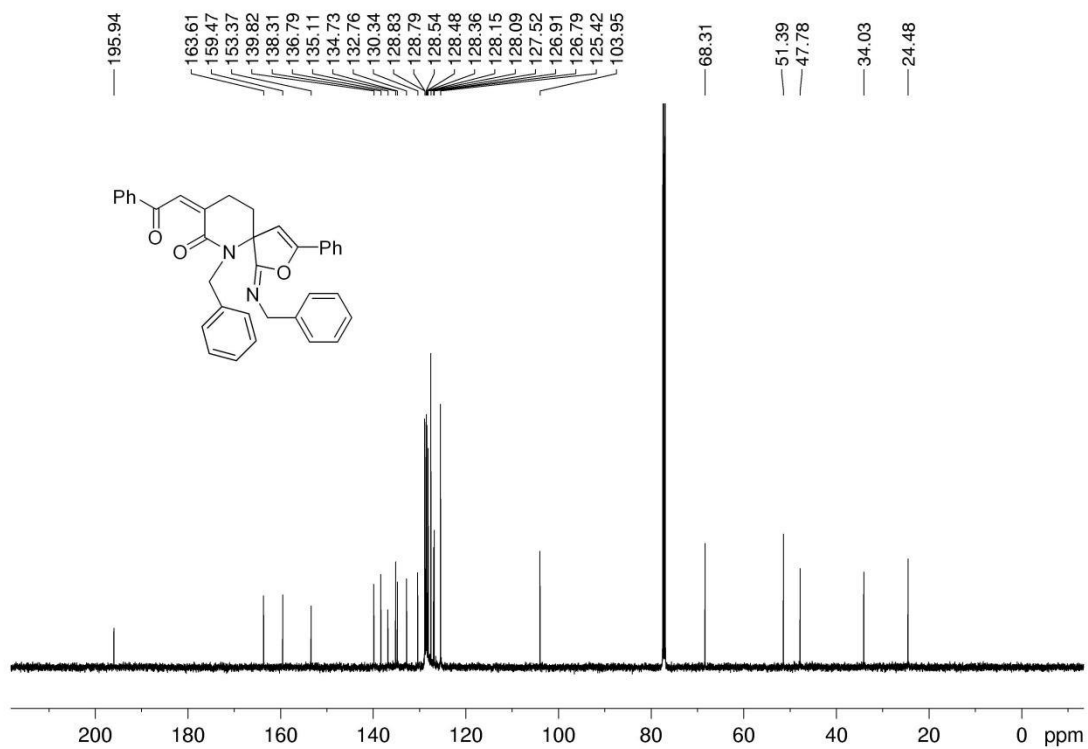
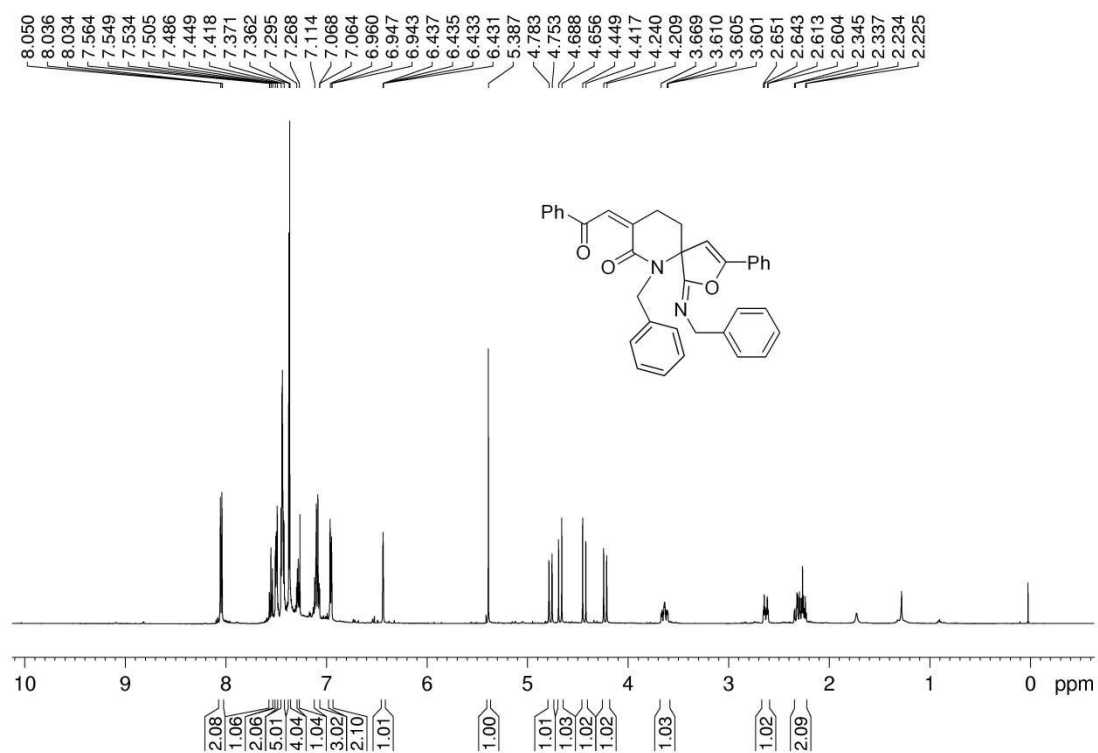
Compound 31



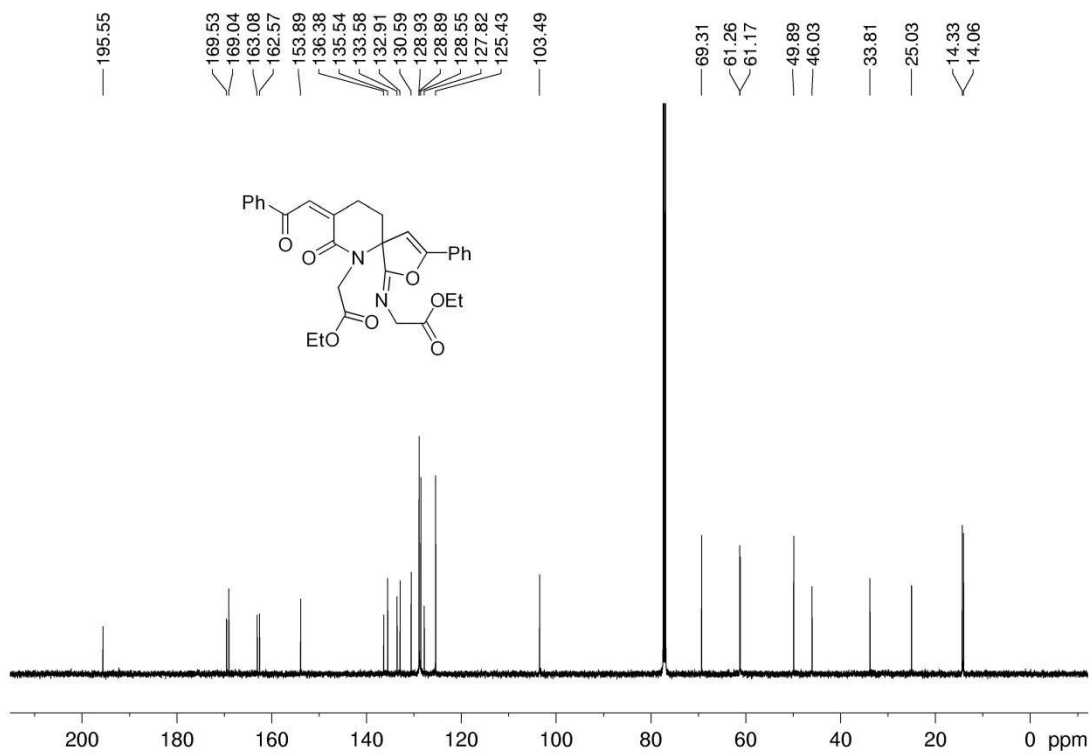
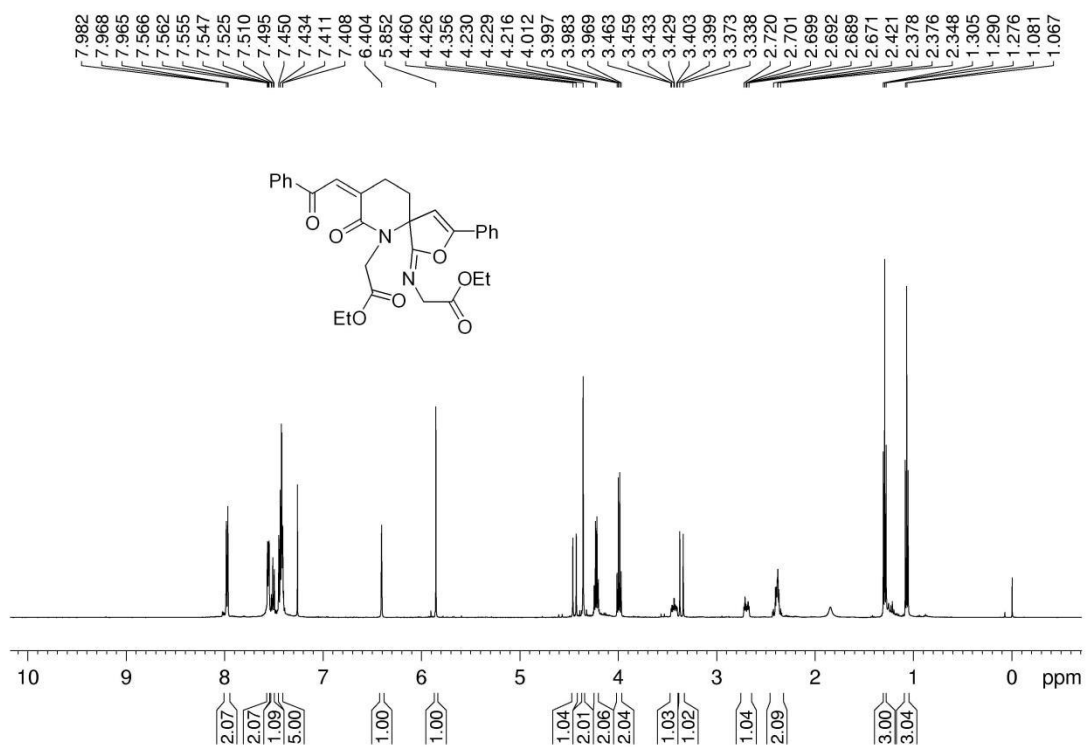
Compound 3m



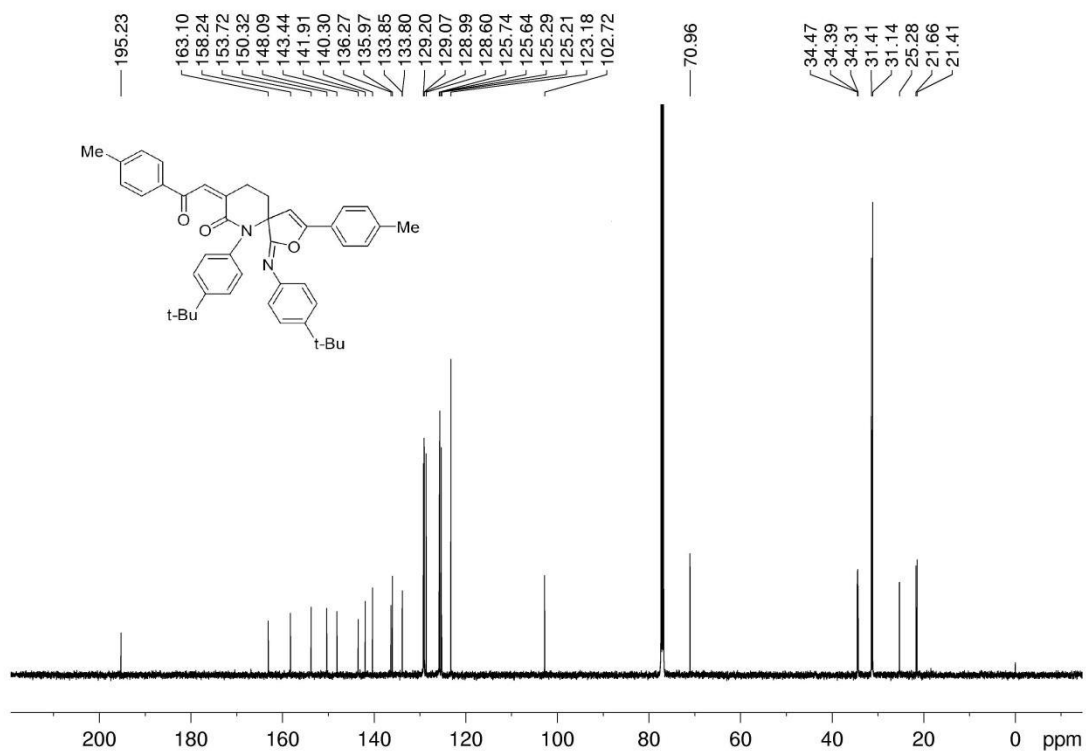
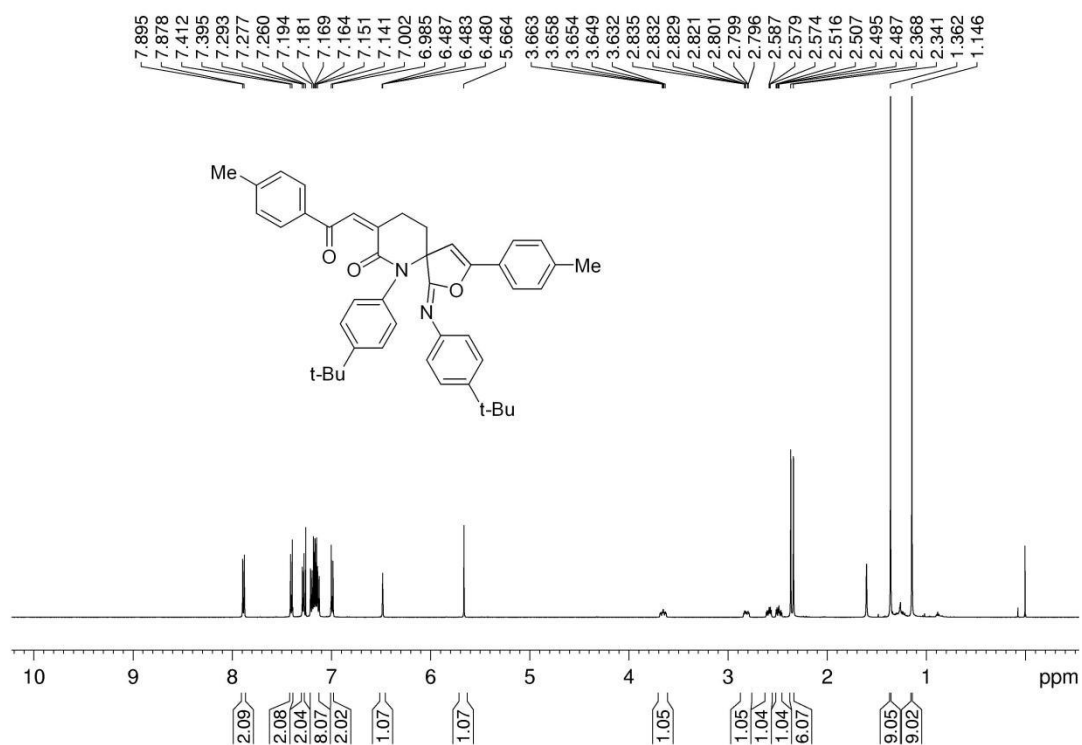
Compound 3n



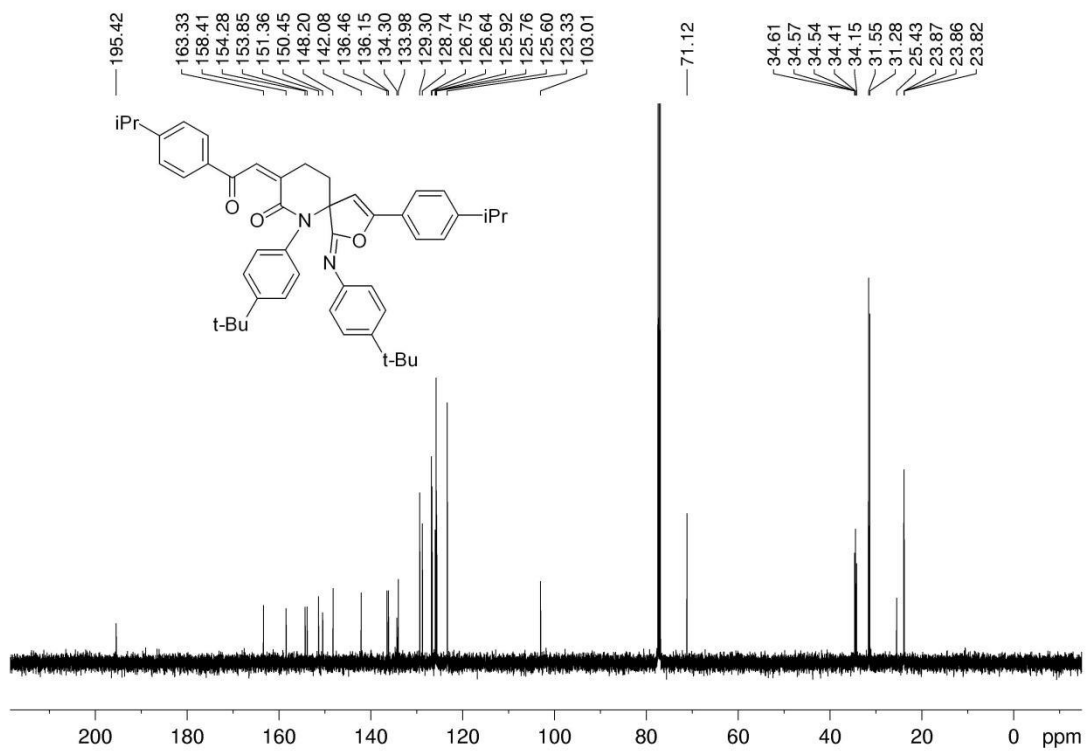
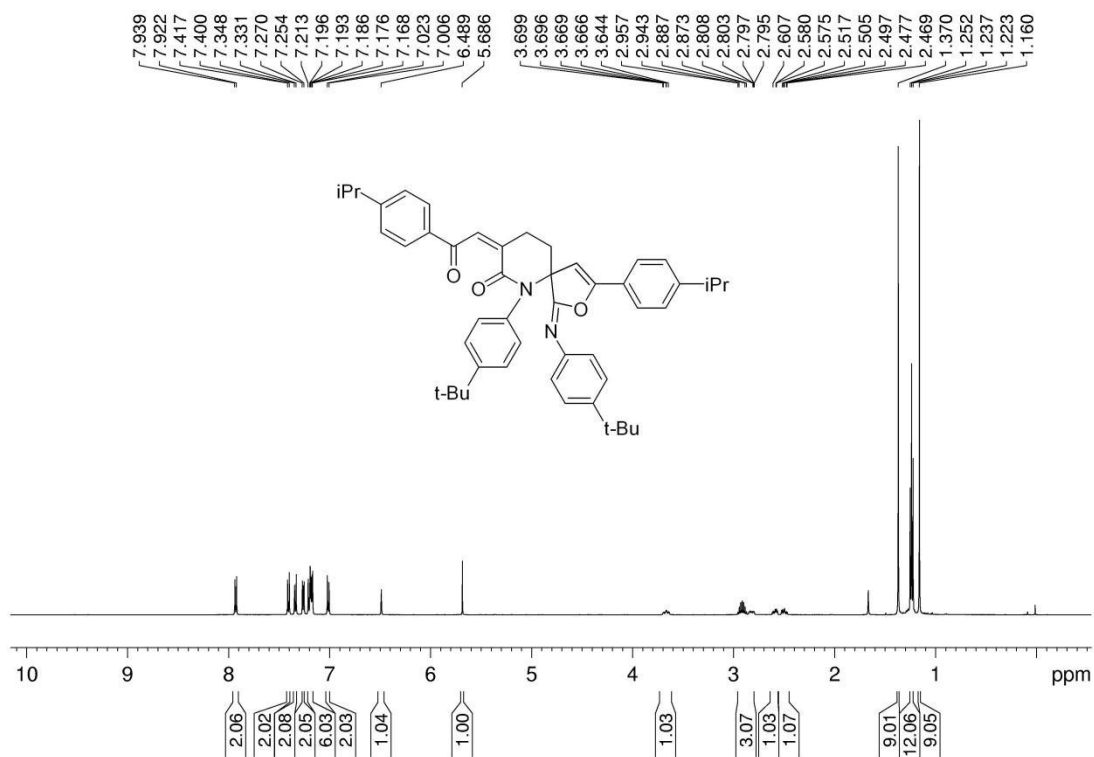
Compound 3o



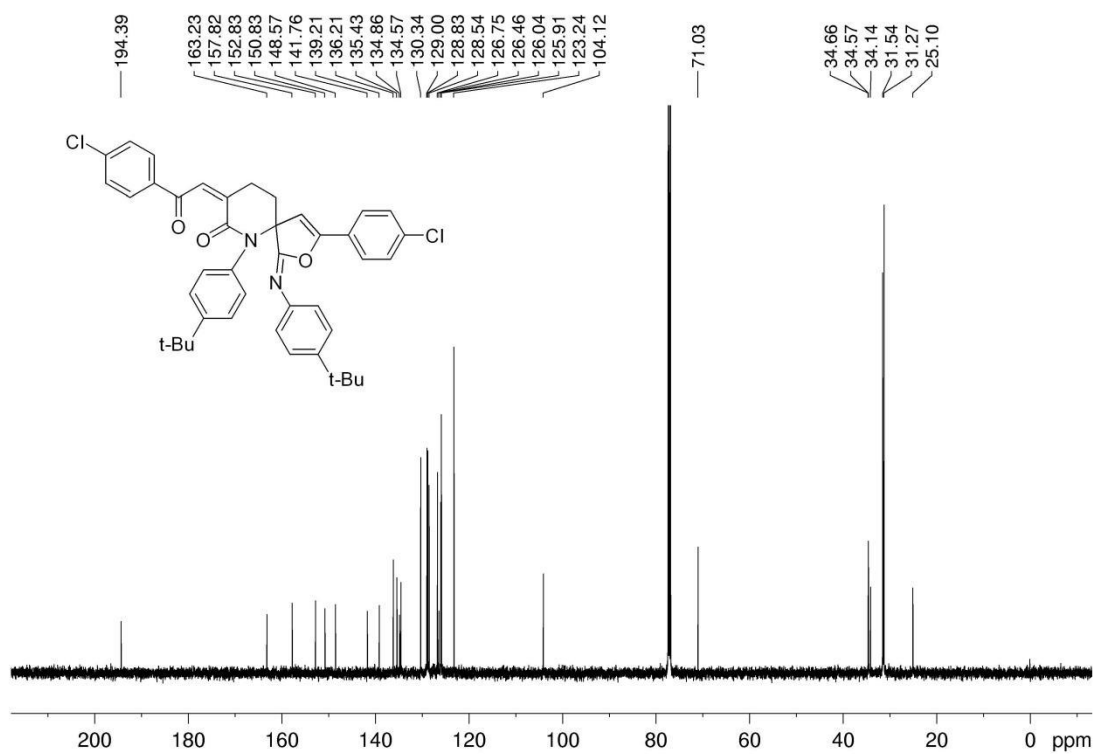
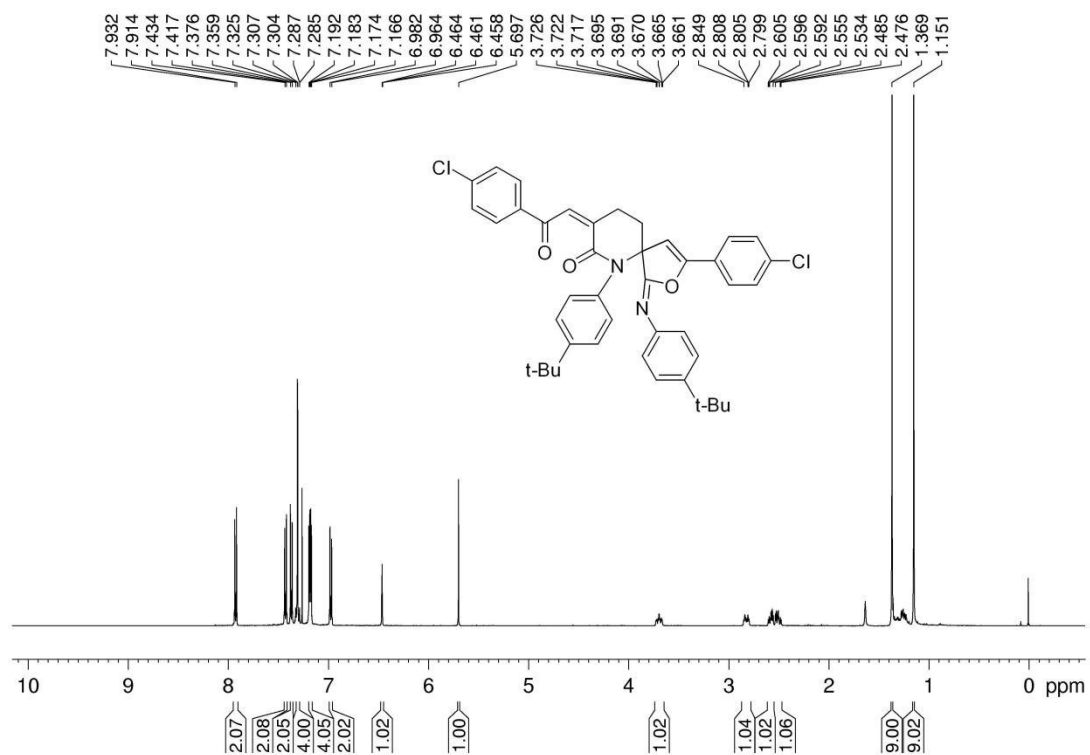
Compound 4a



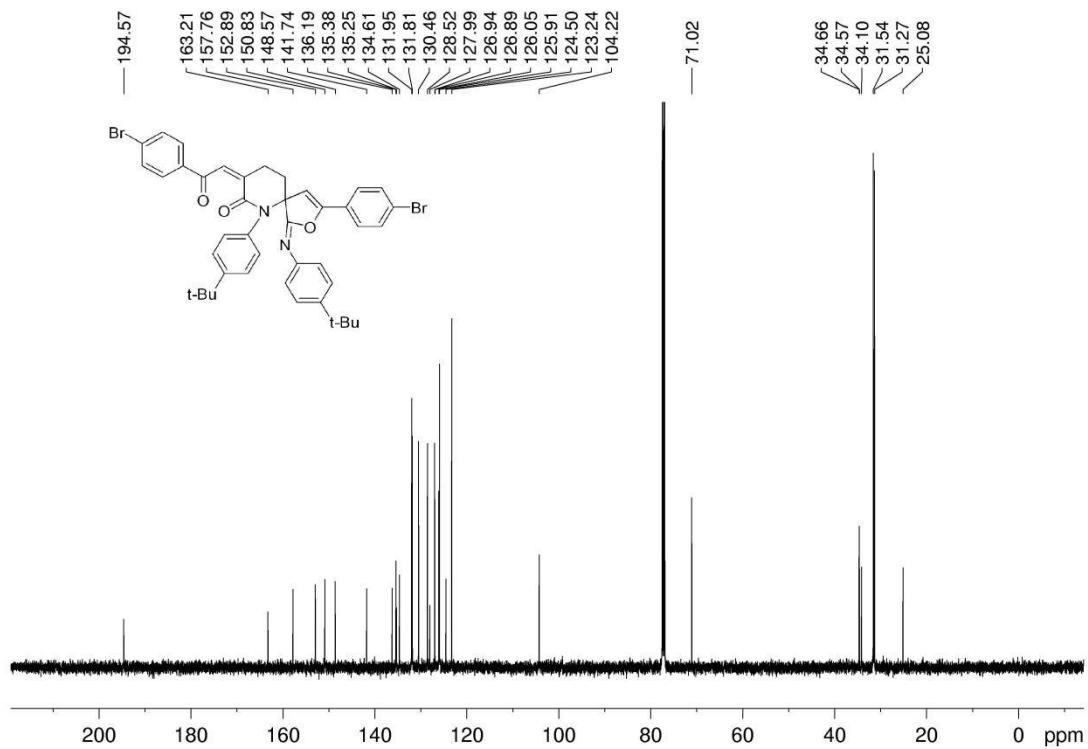
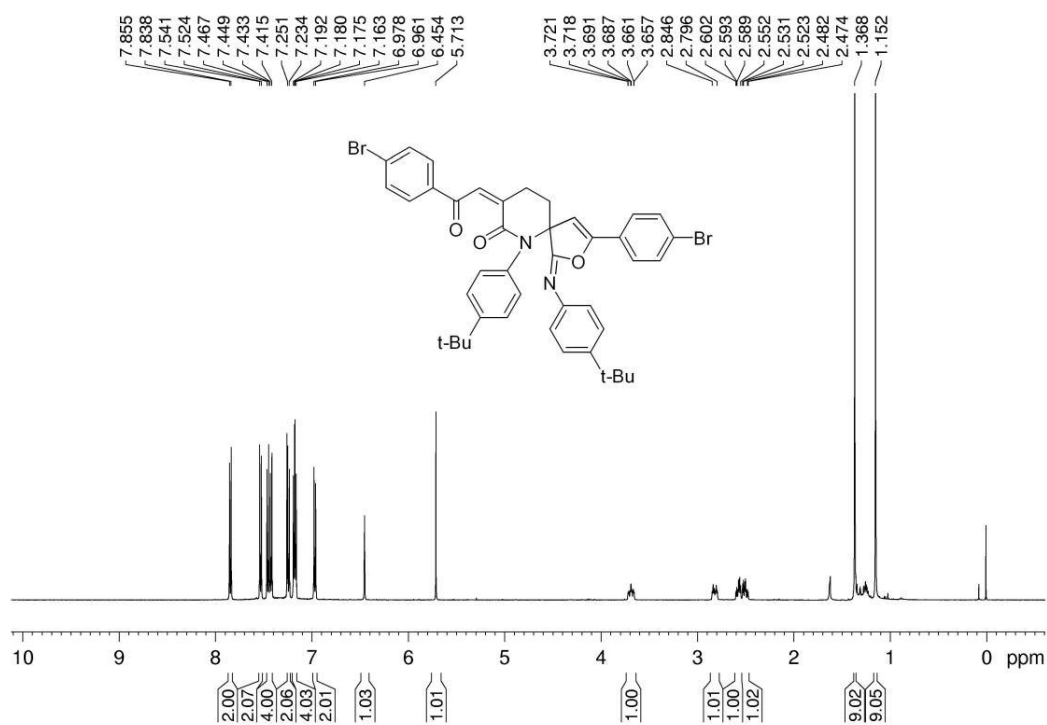
Compound 4b



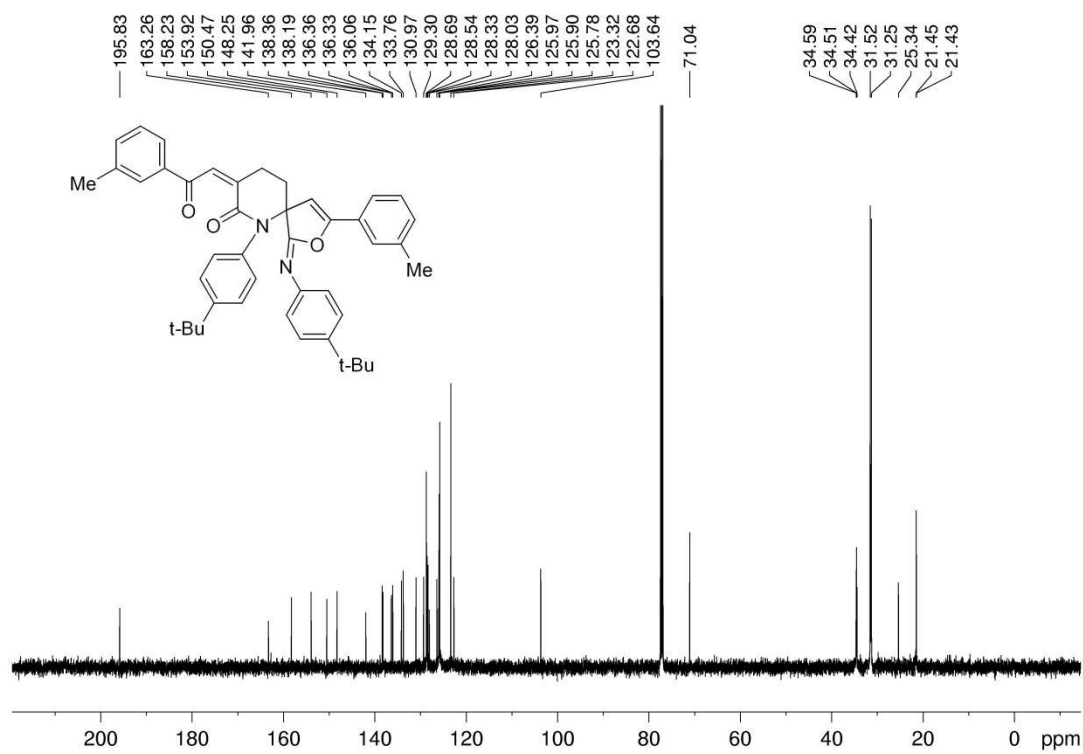
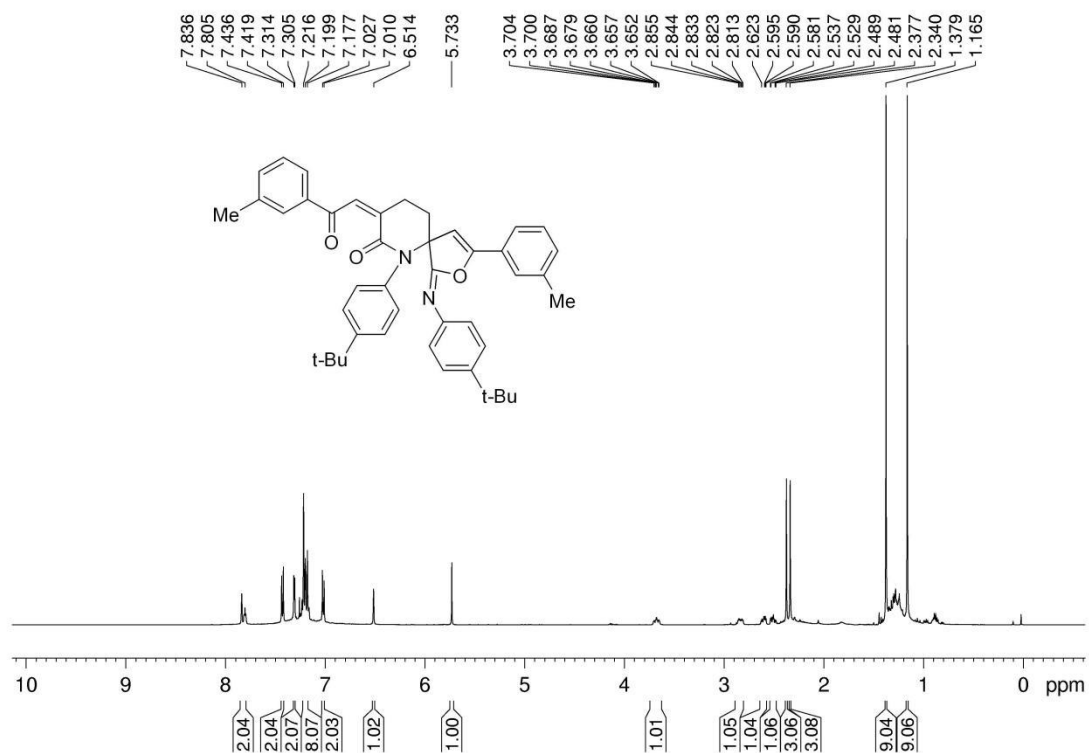
Compound 4c



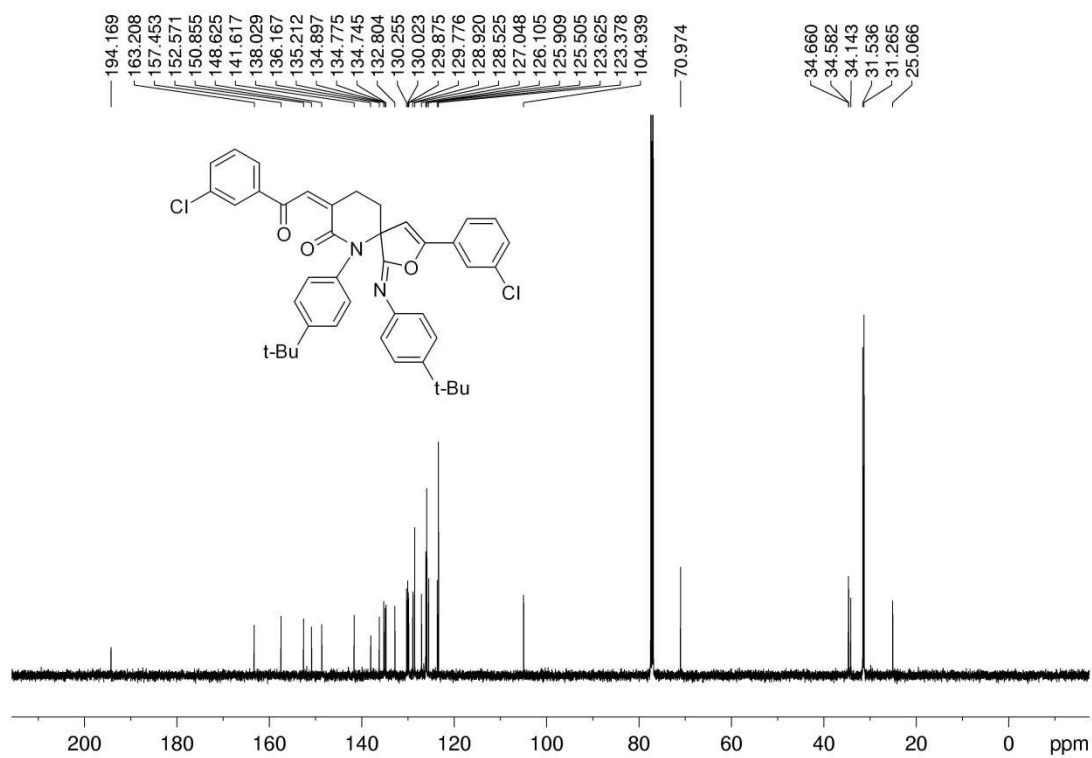
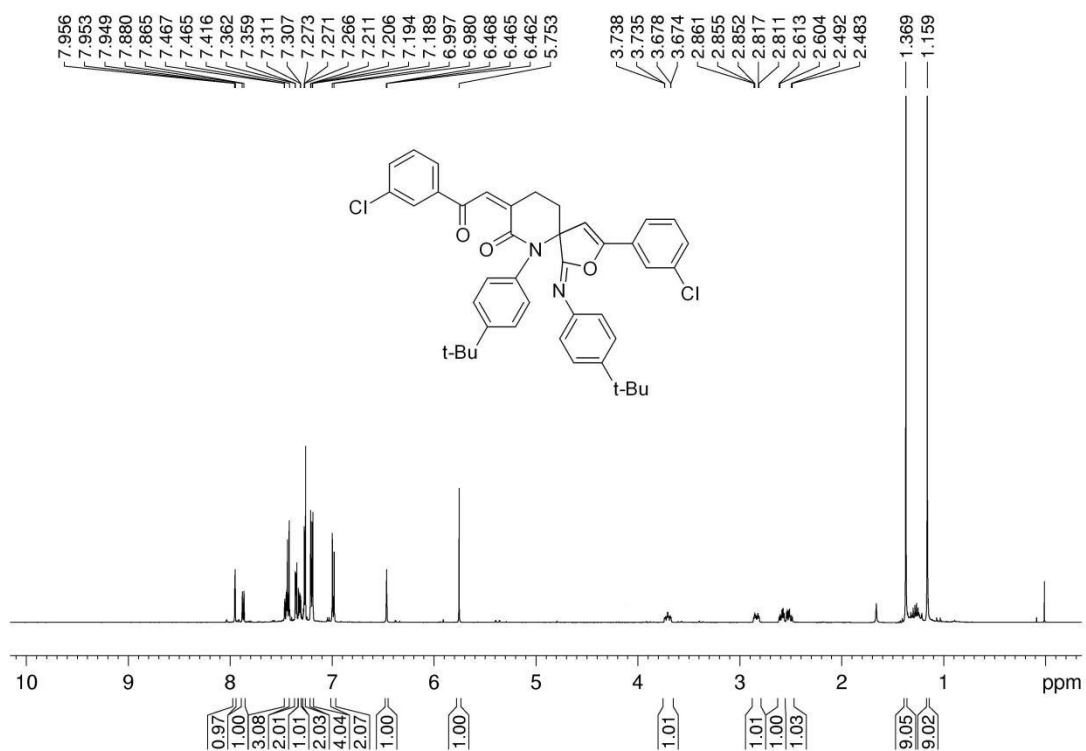
Compound 4d



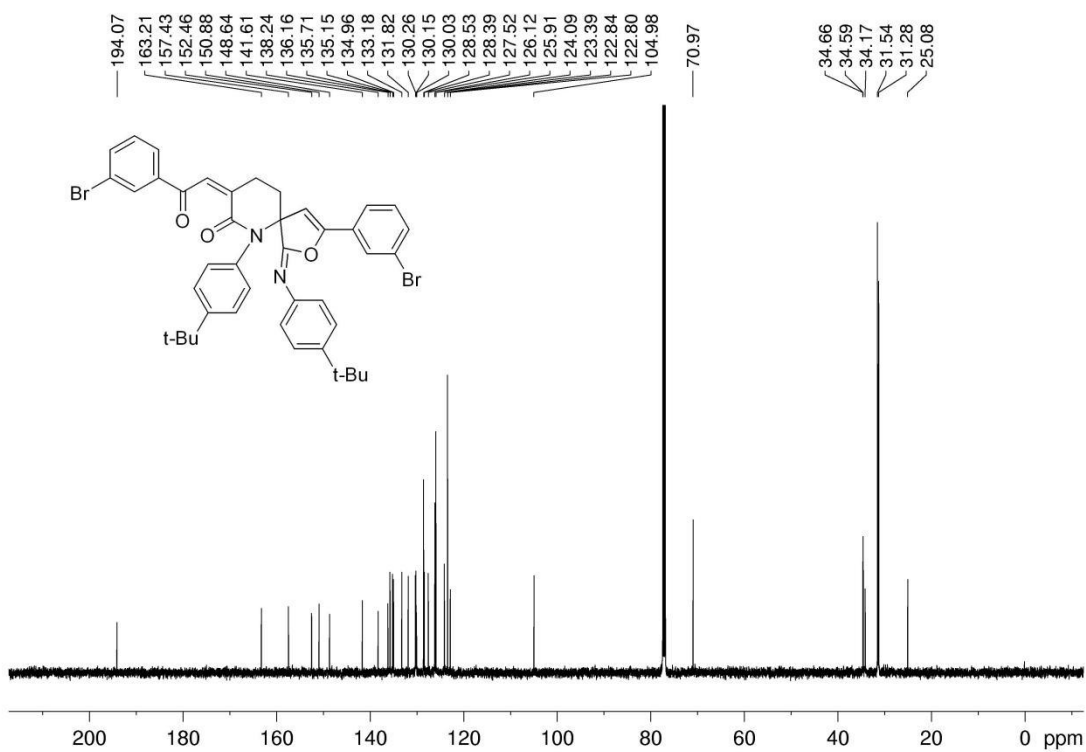
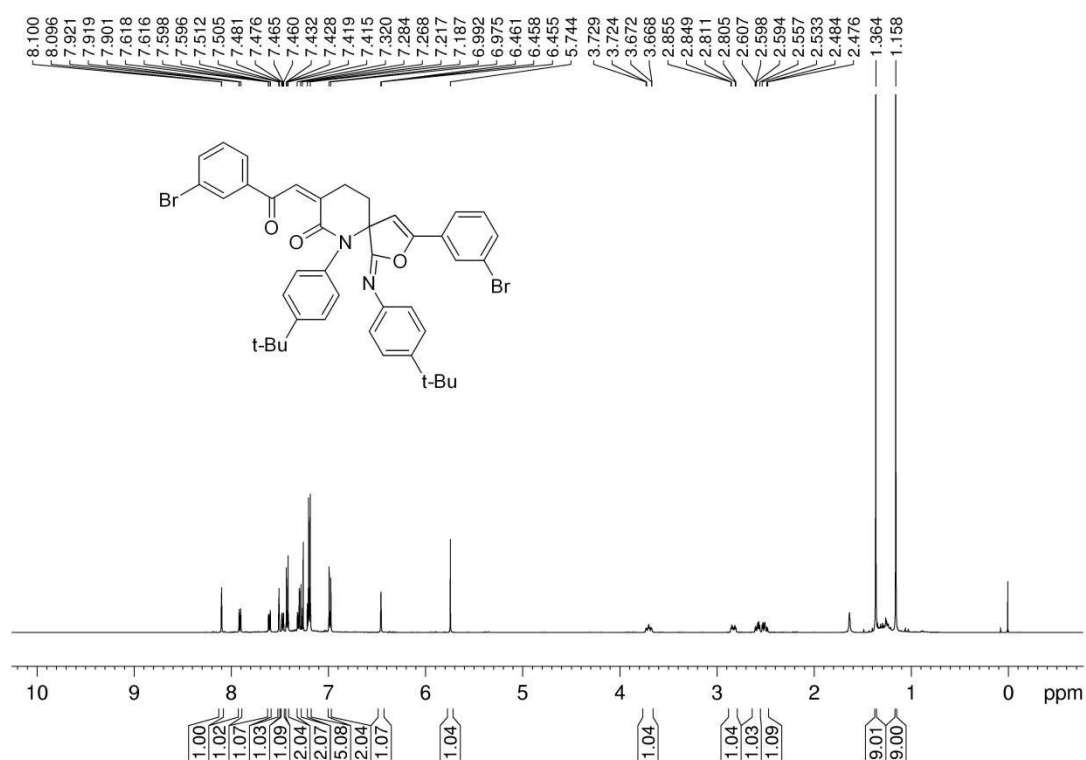
Compound 4e



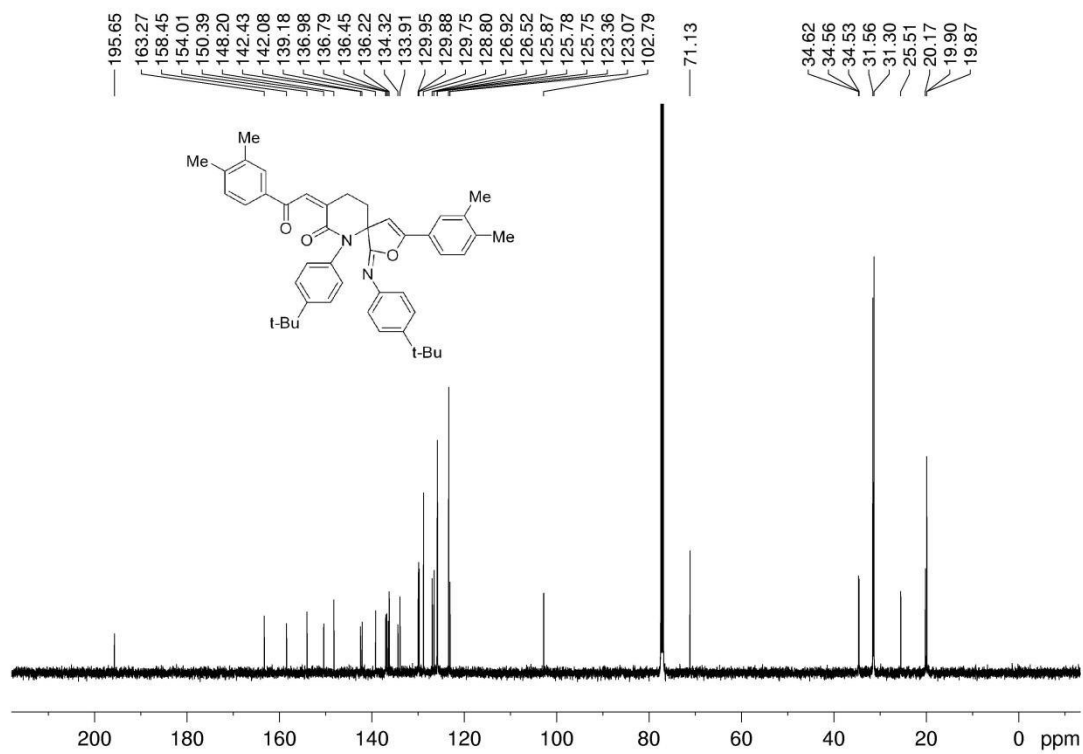
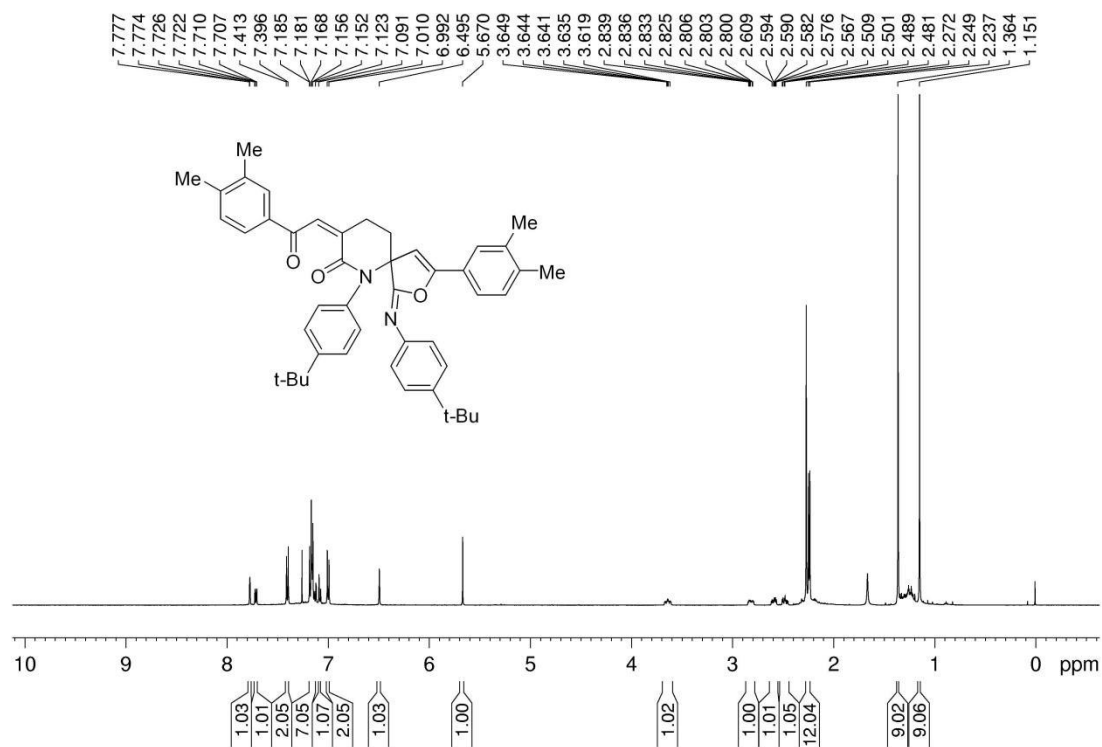
Compound 4f



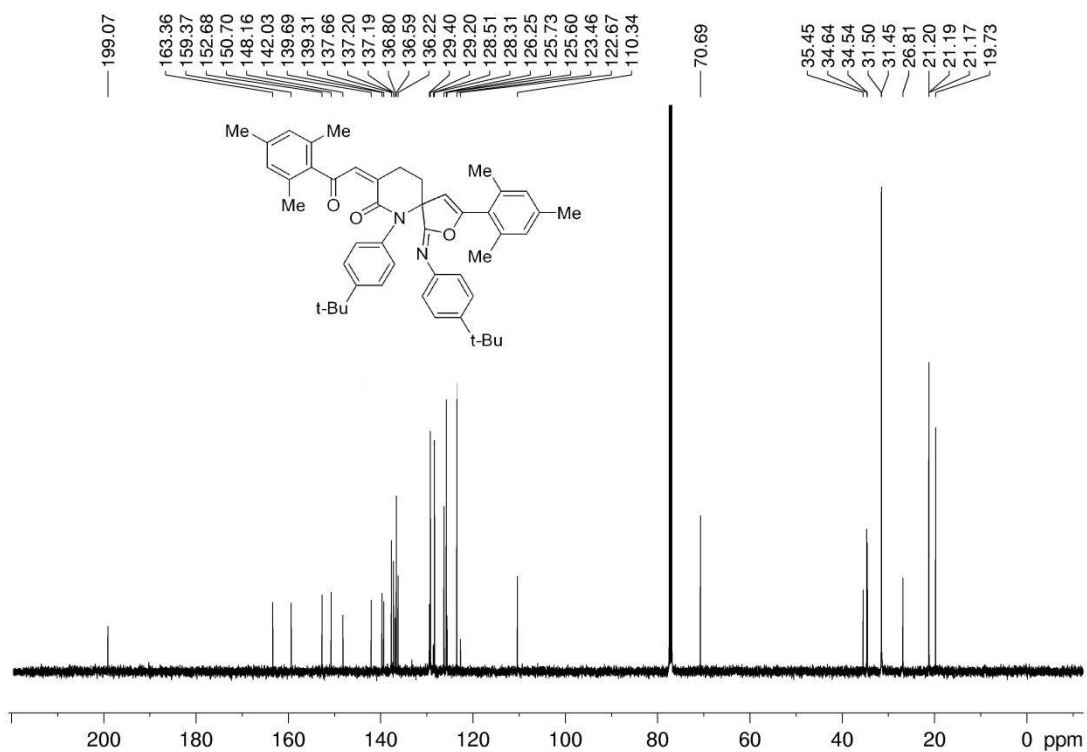
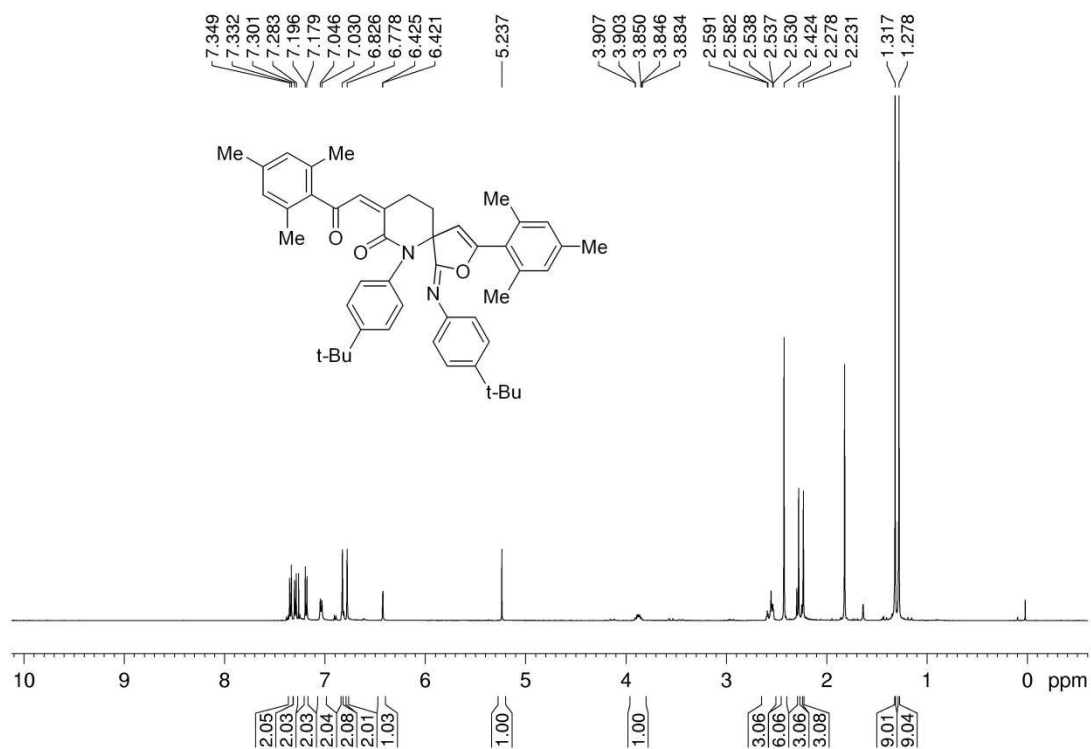
Compound 4g



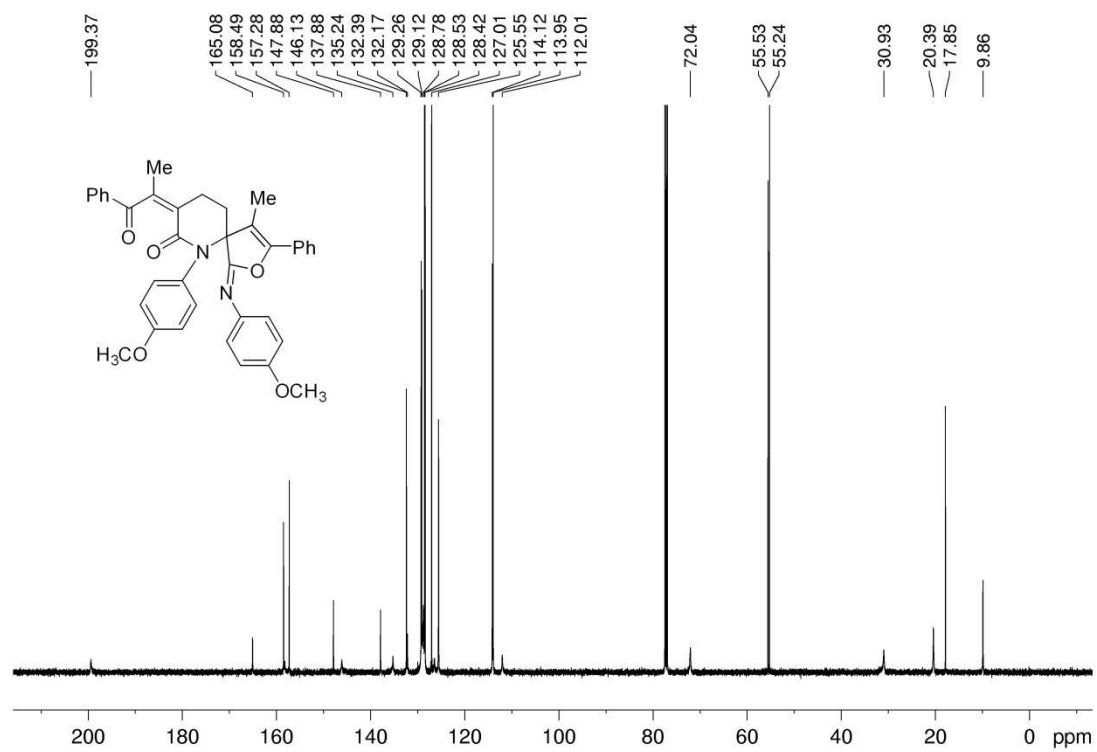
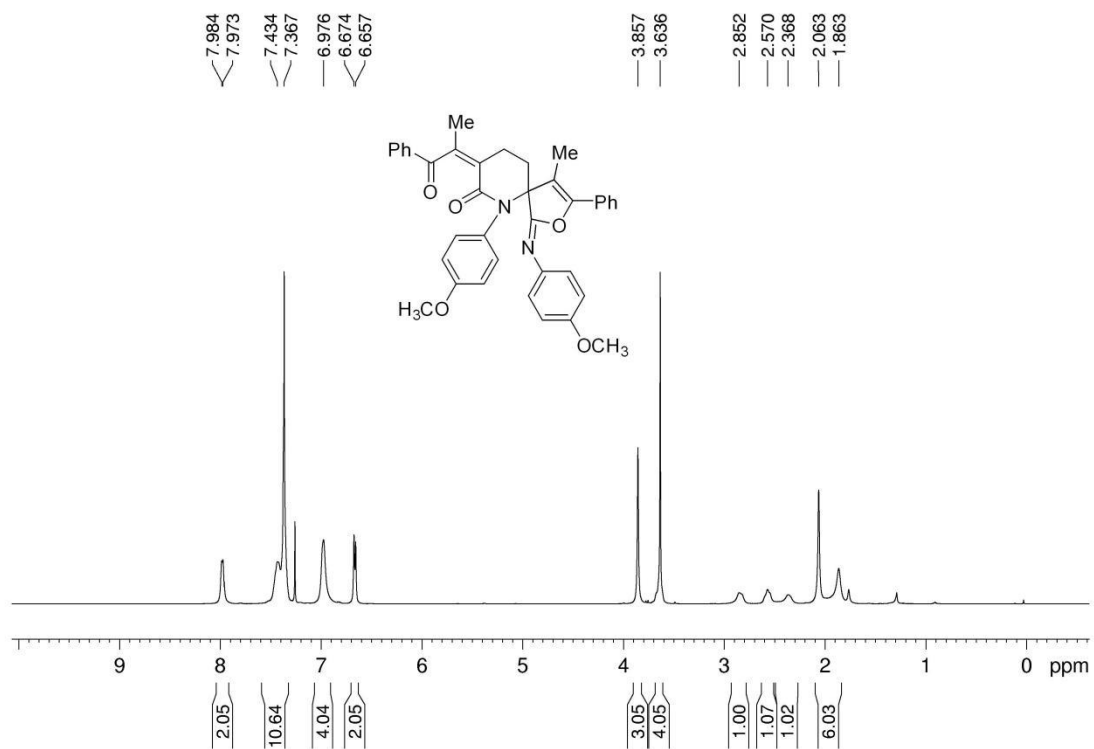
Compound 4h



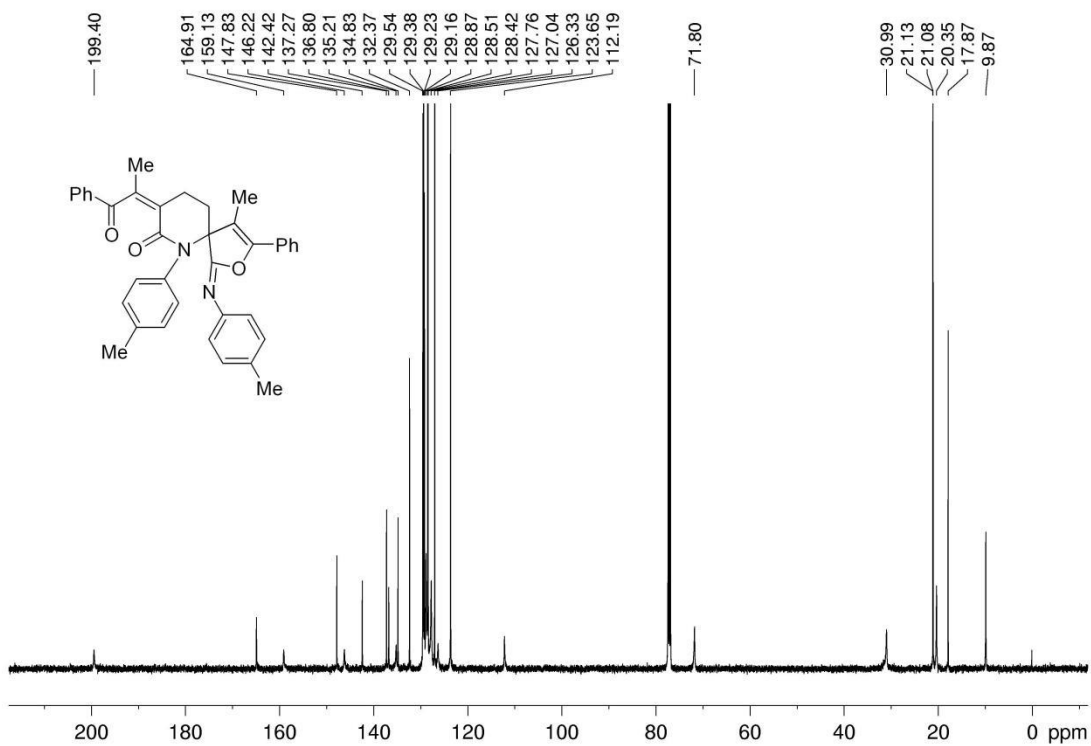
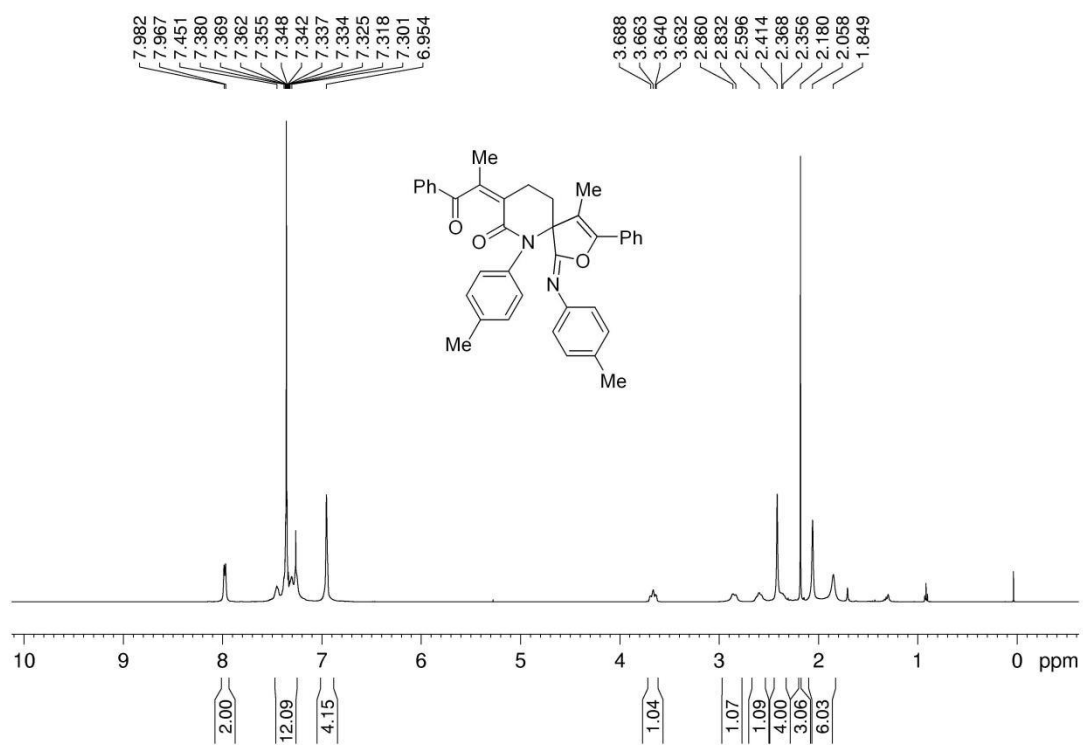
Compound 4i



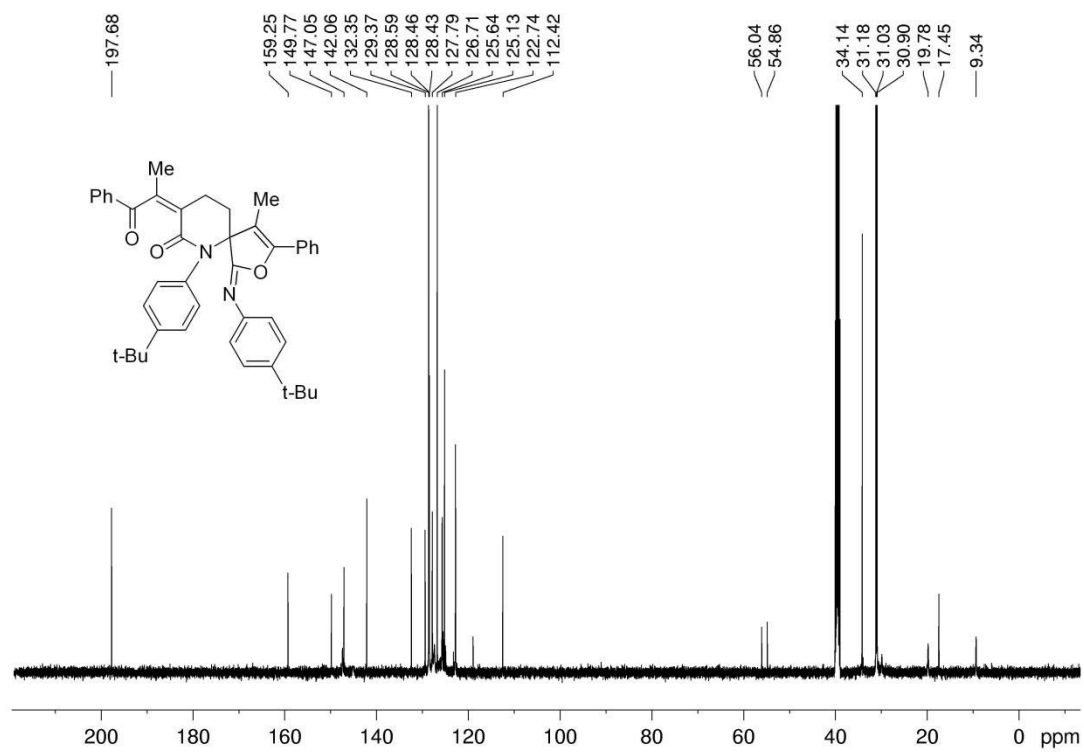
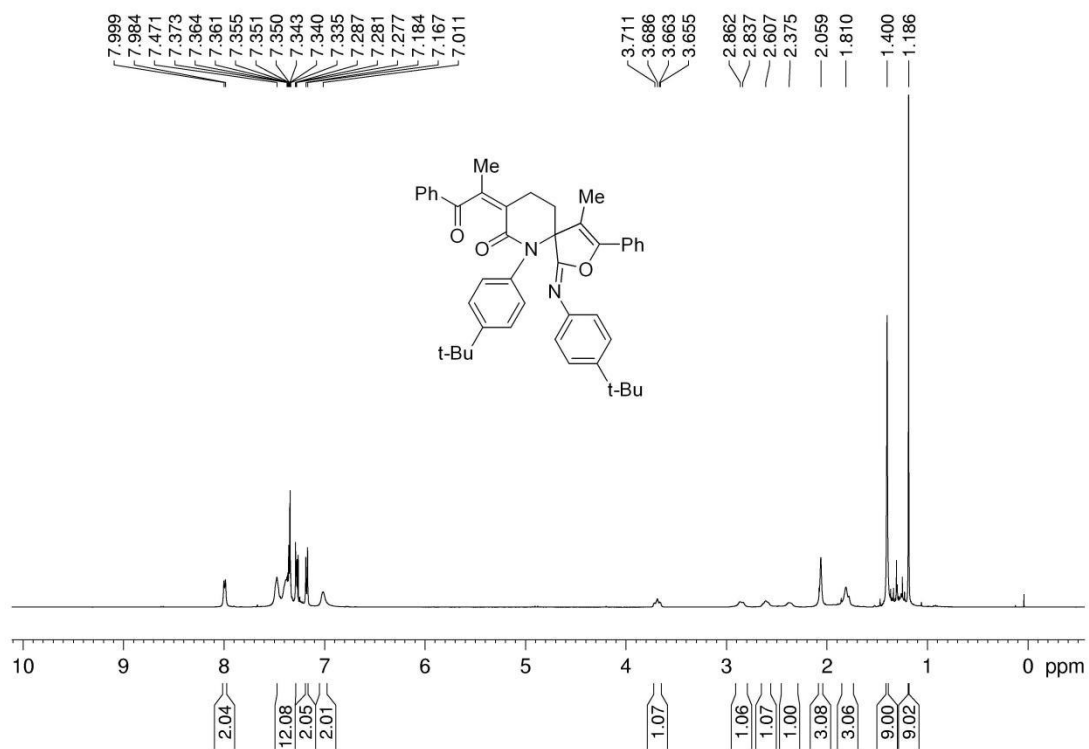
Compound 4j



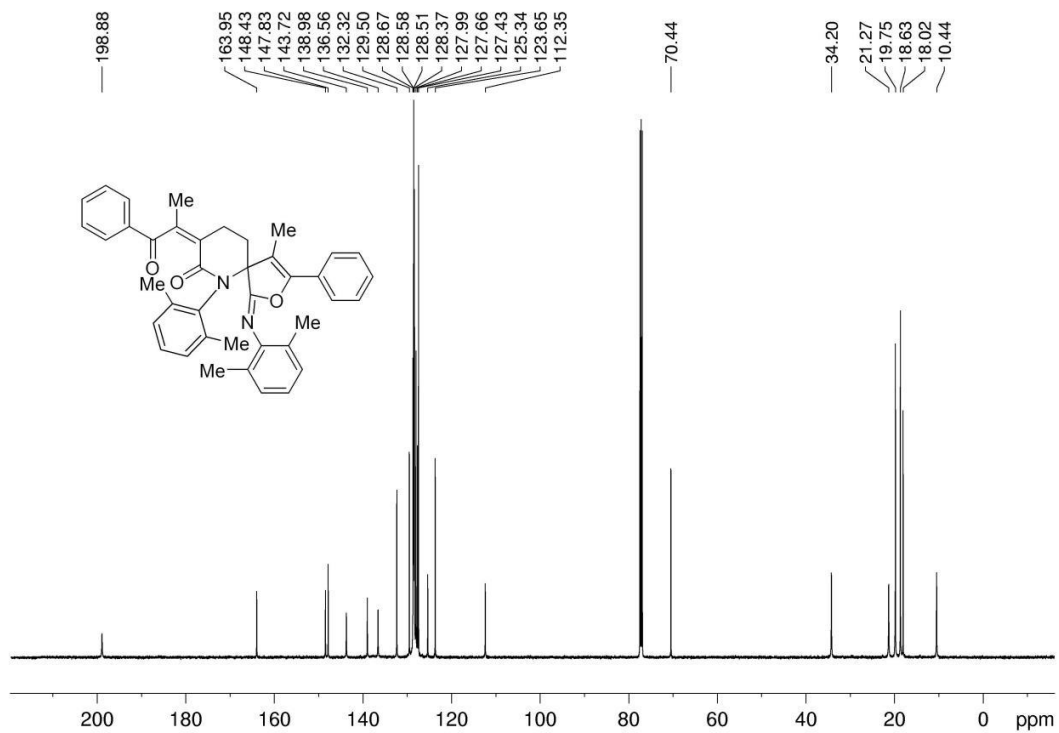
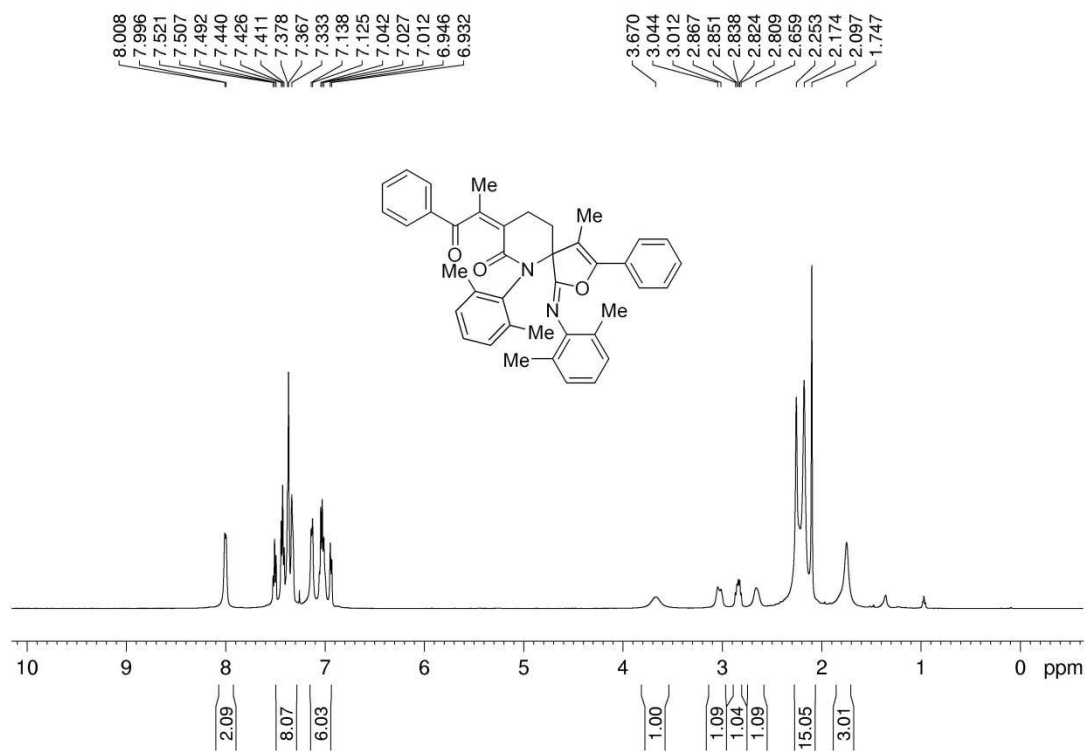
Compound **4k**



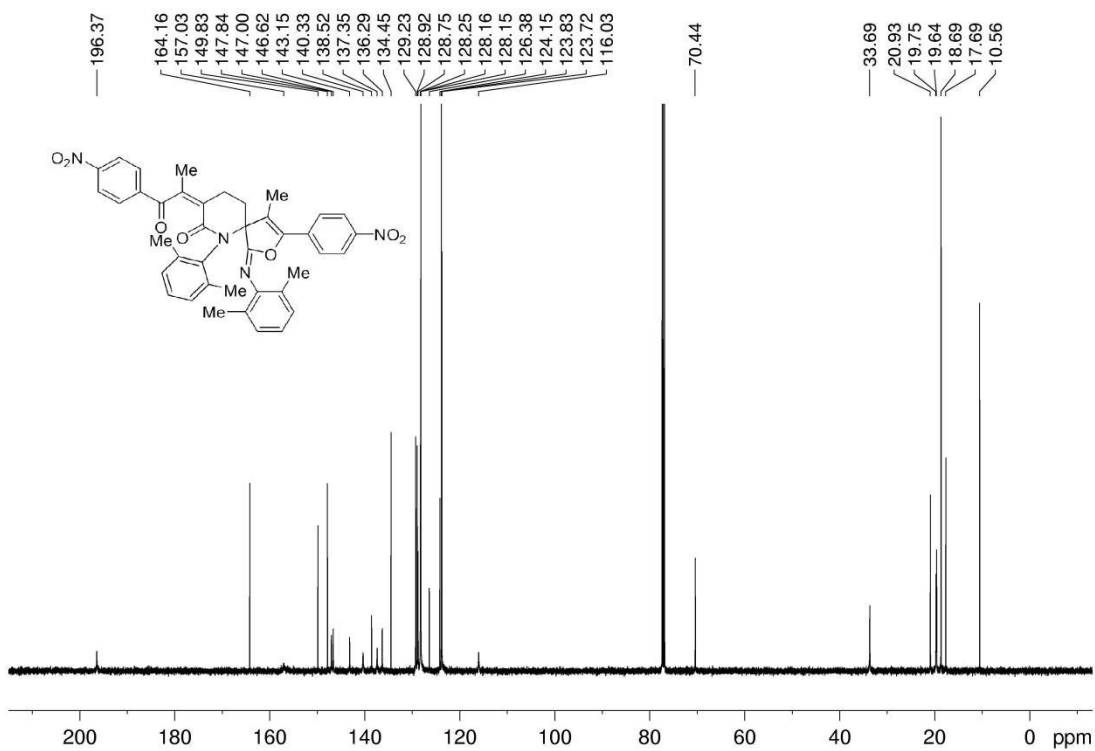
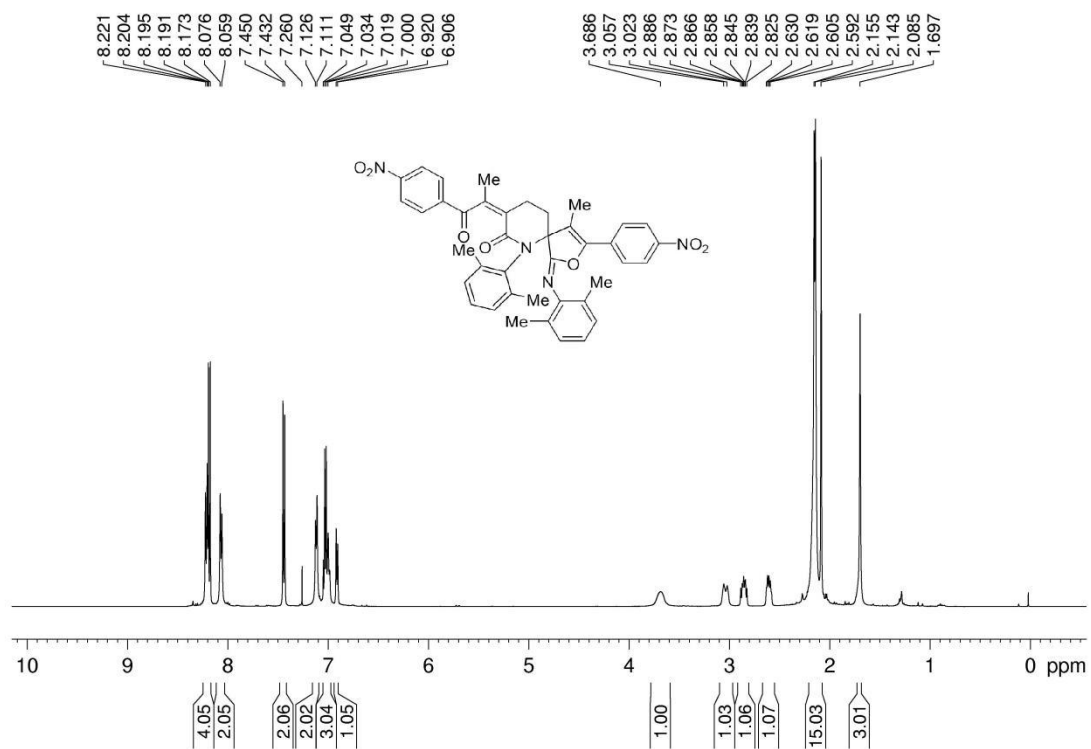
Compound 41



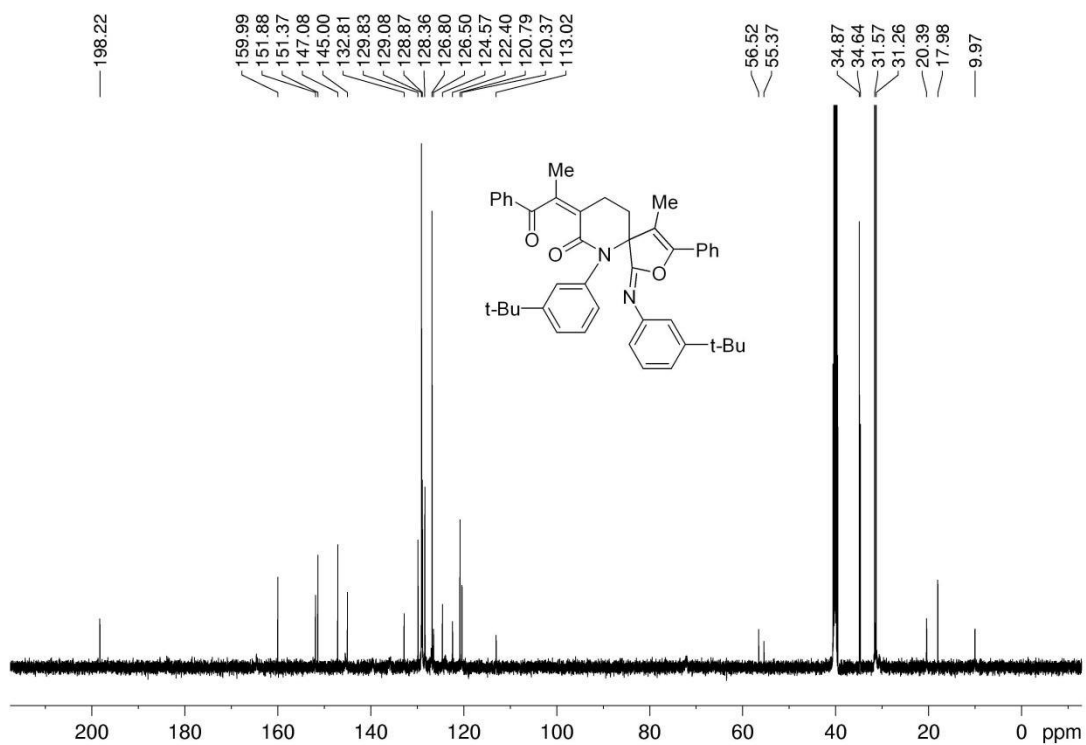
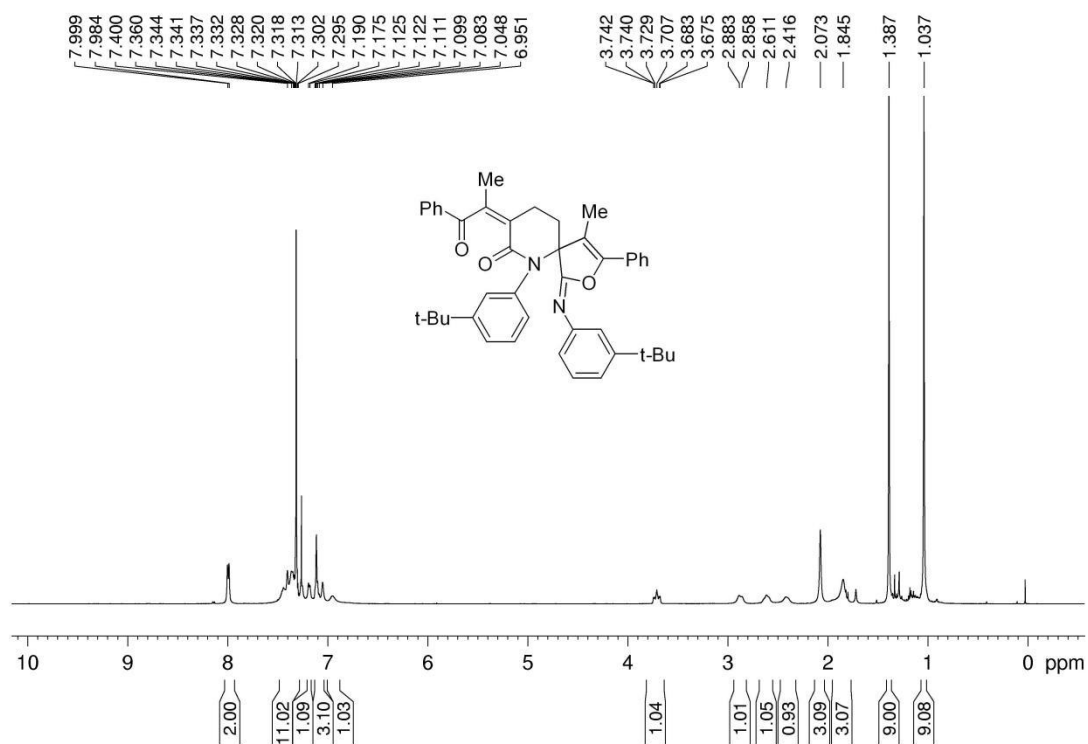
Compound 4m



Compound 4n



Compound 4o



Compound 4p

