Green synthesis for diverse bioactive benzo-fused spiroindolines through DBU-catalysed post-Ugi double cyclization

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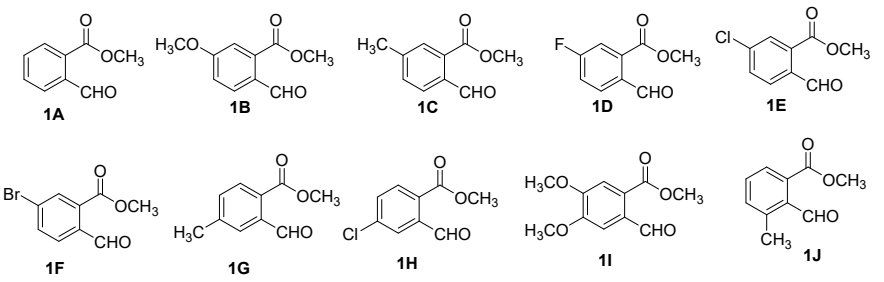
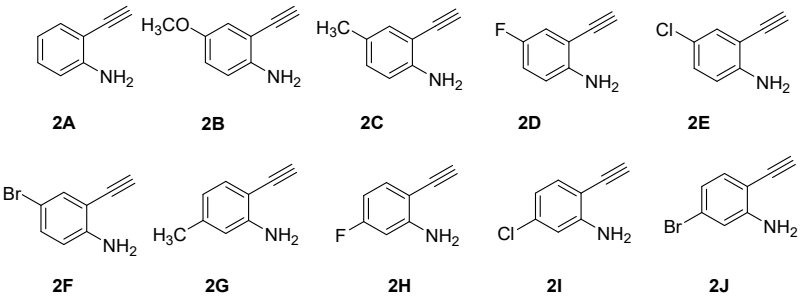
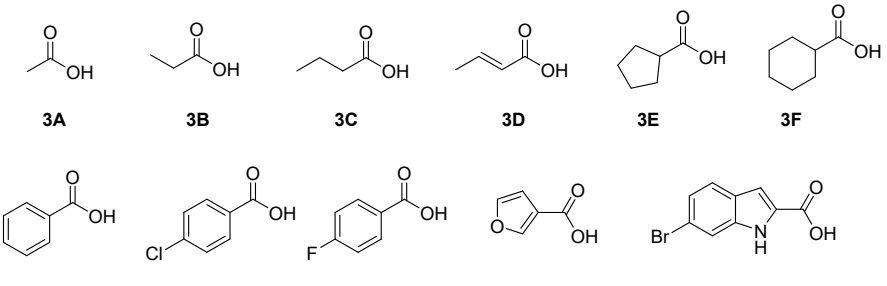
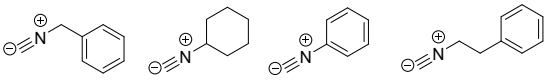
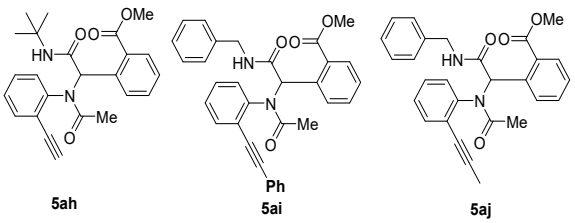
General Methods

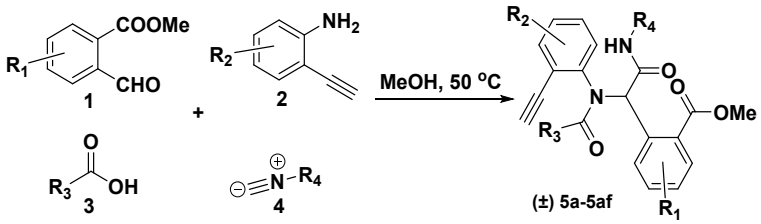
NMR spectra were recorded on a Bruker AVANCE III 600 instrument using $CDCl_3$ as solvent. The ^{1}H and ^{13}C chemical shifts are reported in parts per million relatives to tetramethylsilane as an internal standard. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, brs = broad singlet, coupling constant (s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Microwave reaction was performed on Anton Paar microwave pro. High-resolution mass spectra (HRMS) were performed on Bruker Solarix 7.0 T. Crystals suitable for X-ray crystallographic analysis were obtained by slow evaporation from DCM/PE solution. X-ray crystallography analysis of a single crystal was performed on an Agilent Super Nova-CCD X-ray diffractometer. For chromatography, analytical TLC plates and 70-230 mesh silica gel were used. All the solvents and chemicals were purchased and used as available. Unless otherwise stated, all reagents were purchased from commercial suppliers (Adamas, J&K, Sigma-Aldrich, TCI, Bide Pharmatech) and used without further purification.

General procedure for the synthesis of Ugi product 5a-5al

Table S1: Starting materials for the post-Ugi cyclization

Aldehyde	
Amines	
Acids	
Isonitriles	
Incompatible substrates	

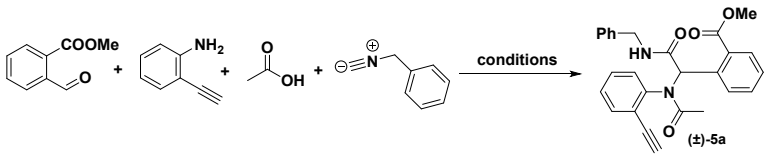
Synthesis of Ugi products 5a-5aj



To a solution of aldehyde 1 (1A-J, 0.61 mmol, 1.0 equiv) in methanol (3 mL) was added

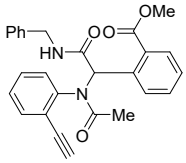
successively amine 2 (2A-J, 0.67 mmol, 1.1 equiv), acid 3 (3A-K, 0.67 mmol, 1.1 equiv.) and isonitrile 4 (4A-D, 0.61 mmol, 1.0 equiv) in a screw-capped vial equipped with a magnetic stir bar. The reaction mixture was stirred at 50 ℃ for 24 h. The reaction mixture was evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/Petroleum ether = 1: 2) to afford the Ugi product 5a-5aj.

Table S2 Optimization of the Ugi reaction



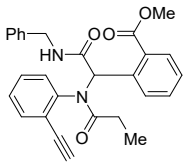
Entry	Solvent	T (℃)	Time (h)	Yield (%)
1	MeOH	50	24	60
2	DCM	50	24	11
3	THF	50	24	Trace
4	EtOH	50	24	34
5	DMF	50	24	Trace
6	MeOH	rt	24	55
7	MeOH	rt	5	70

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)benzoate **(5a)**



Pale yellow solid, 943 mg, 70% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.89 (dd, *J* = 7.8, 1.3 Hz, 0.3H), 7.86 – 7.81 (m, 1.4H), 7.71 (d, *J* = 7.4 Hz, 0.3H), 7.51 – 7.46 (m, 0.3H), 7.42 – 7.36 (m, 1H), 7.38 – 7.26 (m, 5.7H), 7.25 – 7.24 (m, 1.3H), 7.24 – 7.22 (m, 1H), 7.21 – 7.17 (m, 1.4H), 7.00 (t, *J* = 5.8 Hz, 0.3H), 6.78 (t, *J* = 5.5 Hz, 0.7H), 6.71 (s, 0.3H), 4.61 – 4.54 (m, 0.8H), 4.55 – 4.47 (m, 0.2H), 3.94 (s, 2H), 3.89 (s, 1H), 2.94 (s, 0.7H), 2.90 (s, 0.3H), 2.00 (s, 1H), 1.95 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.0, 171.2, 170.3, 169.3, 168.3, 167.9, 161.2, 147.2, 144.2, 142.9, 138.4, 138.3, 136.5, 134.3, 133.7, 133.3, 132.1, 131.9, 131.8, 131.8, 131.1, 131.0, 130.9, 130.4, 130.2, 130.0, 129.8, 128.8, 128.64, 128.61, 128.4, 128.2, 128.1, 127.9, 127.6, 127.4, 127.3, 124.6, 124.1, 123.2, 122.7, 119.2, 82.9, 82.4, 81.1, 80.1, 64.4, 60.0, 52.6, 52.5, 43.9, 43.7, 23.1, 22.8. **HRMS** (ESI) calculated for $C_{27}H_{25}N_2O_4^+$ ([M+H]$^+$): 441.1814, found 441.1810.

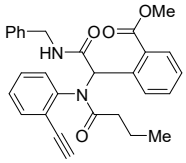
Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)propionamido)-2-oxoethyl)benzoate **(5b)**



Pale yellow solid, 128 mg, 46% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.82 (dd, *J* = 7.8, 1.2 Hz, 0.3H),

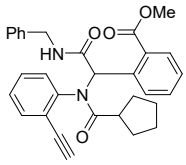
7.77 – 7.73 (m, 1.4H), 7.65 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.44 – 7.39 (m, 0.3H), 7.35 – 7.31 (m, 1H), 7.29 (t, *J* = 0.6 Hz, 0.3H), 7.29 – 7.27 (m, 0.5H), 7.27 – 7.26 (m, 0.7H), 7.26 – 7.25 (m, 0.5H), 7.26 – 7.22 (m, 1H), 7.24 – 7.21 (m, 1H), 7.23 – 7.18 (m, 1H), 7.19 – 7.17 (m, 1.7H), 7.17 – 7.16 (m, 1H), 7.17 – 7.13 (m, 1.7H), 7.14 – 7.10 (m, 1H), 6.92 (t, *J* = 5.4 Hz, 0.3H), 6.72 (t, *J* = 5.4 Hz, 0.7H), 6.63 (s, 0.3H), 4.51 – 4.41 (m, 2H), 3.88 (s, 2H), 3.82 (s, 1H), 2.85 (s, 0.7H), 2.80 (s, 0.3H), 2.11 – 1.99 (m, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 175.2, 174.4, 170.4, 169.4, 168.4, 167.9, 143.9, 142.6, 138.5, 138.3, 136.7, 134.4, 133.7, 133.3, 132.04, 132.02, 131.9, 131.1, 131.0, 130.8, 130.4, 130.4, 130.18, 130.15, 129.8, 128.63, 128.61, 128.3, 128.2, 128.1, 128.0, 128.0, 127.6, 127.4, 127.3, 123.4, 122.9, 82.8, 82.3, 81.2, 80.2, 77.2, 64.6, 60.1, 52.6, 52.5, 43.9, 43.8, 28.3, 9.4. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_4^+$ ($[M+H]^+$): 455.1965, found 455.1966.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)butyramido)-2-oxoethyl)benzoate **(5c)**



Pale yellow solid, 132 mg, 46% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.82 (dd, *J* = 7.8, 1.8 Hz, 0.3H), 7.76 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.71 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 7.63 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.43 – 7.41 (m, 0.3H), 7.34 – 7.31 (m, 1H), 7.30 – 7.26 (m, 1.4H), 7.26 – 7.22 (m, 3H), 7.22 – 7.19 (m, 1H), 7.19 – 7.16 (m, 3H), 7.16 – 7.15 (m, 1H), 7.14 – 7.11 (m, 1H), 6.94 (t, *J* = 5.4 Hz, 0.3H), 6.71 (t, *J* = 6.0 Hz, 0.7H), 6.63 (s, 0.3H), 4.49 (d, *J* = 5.4 Hz, 1.5H), 4.44 (dd, *J* = 9.6, 6.0 Hz, 0.5H), 3.88 (s, 2H), 3.82 (s, 1H), 2.84 (s, 0.7H), 2.78 (s, 0.3H), 2.07 – 1.97 (m, 2H), 1.67 – 1.60 (m, 2H), 0.85 – 0.81 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.5, 173.7, 170.3, 169.4, 168.4, 167.9, 143.8, 142.6, 138.5, 136.7, 134.4, 133.7, 133.4, 132.0, 131.99, 131.1, 130.8, 130.5, 130.4, 130.2, 130.1, 129.8, 128.6, 128.6, 128.3, 128.2, 128.0, 127.6, 127.4, 127.3, 123.4, 123.0, 82.9, 82.4, 81.3, 80.3, 77.2, 64.6, 60.1, 52.6, 52.5, 43.9, 43.8, 36.8, 36.8, 18.5, 13.9, 13.9. **HRMS** (ESI) calculated for $C_{29}H_{29}N_2O_4^+$ ($[M+H]^+$): 469.2122, found 469.2121.

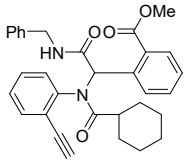
Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)cyclopentanecarboxamido)-2-oxoethyl)benzoate **(5d)**



Pale yellow solid, 117 mg, 39% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.82 (dd, *J* = 7.8, 1.5 Hz, 0.3H), 7.78 – 7.74 (m, 0.7H), 7.67 – 7.63 (m, 1H), 7.54 (dd, *J* = 8.6, 0.7 Hz, 0.1H), 7.42 – 7.39 (m, 0.3H), 7.36 (t, *J* = 2.2 Hz, 0.1H), 7.34 – 7.30 (m, 0.9H), 7.29 – 7.26 (m, 1.3H), 7.26 – 7.23 (m, 2H), 7.23 – 7.21 (m, 1.5H), 7.21 – 7.16 (m, 3.5H), 7.16 – 7.11 (m, 1.3H), 7.09 (s, 0.7H), 6.93 (t, *J* = 5.7 Hz, 0.3H), 6.75 (t, *J* = 5.8 Hz, 0.7H), 6.64 (s, 0.3H), 4.53 – 4.47 (m, 0.3H), 4.47 – 4.40 (m, 0.7H), 3.86 (s, 2H), 3.82 (s, 1H), 2.83 (s, 0.7H), 2.80 (s, 0.3H), 2.57 – 2.52 (m, 0.3H), 2.48 – 2.40 (m, 0.7H), 2.06 – 1.96 (m, 0.6H), 1.95

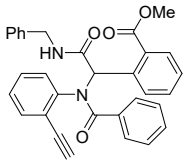
– 1.87 (m, 1H), 1.86 – 1.78 (m, 1.3H), 1.76 – 1.64 (m, 3H), 1.63 – 1.55 (m, 1.6H), 1.54 – 1.47 (m, 0.5H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 178.3, 177.4, 170.1, 169.4, 168.3, 167.9, 143.8, 142.8, 138.5, 138.3, 136.7, 134.7, 133.5, 133.3, 132.0, 131.97, 131.7, 131.0, 130.97, 130.7, 130.4, 130.2, 129.9, 129.6, 128.6, 128.6, 128.2, 128.1, 128.1, 127.9, 127.7, 127.4, 127.2, 124.6, 124.1, 123.4, 123.0, 83.0, 82.6, 81.3, 80.5, 64.7, 60.5, 52.51, 52.48, 43.9, 43.8, 43.1, 43.1, 31.5, 31.5, 30.7, 30.6, 30.3, 26.4, 26.4, 26.3, 26.3. **HRMS** (ESI) calculated for $C_{31}H_{31}N_2O_4^+$ ([M+H]$^+$): 495.2278, found 495.2276.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)cyclohexanecarboxamido)-2-oxoethyl) benzoate **(5e)**



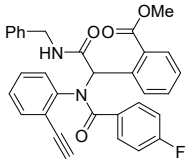
Pale yellow solid, 131 mg, 42% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.82 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.77 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.66 – 7.60 (m, 1H), 7.45 – 7.40 (m, 0.3H), 7.35 – 7.29 (m, 0.6H), 7.32 – 7.26 (m, 1.7H), 7.27 – 7.21 (m, 3H), 7.21 (d, *J* = 2.4 Hz, 0.8H), 7.22 – 7.13 (m, 4.6H), 7.06 (s, 0.7H), 6.91 (t, *J* = 6.0 Hz, 0.3H), 6.71 (t, *J* = 5.4 Hz, 0.7H), 6.62 (s, 0.3H), 4.54 – 4.43 (m, 1.5H), 4.42 (d, *J* = 6.0 Hz, 0.5H), 3.86 (s, 2H), 3.81 (s, 1H), 2.80 (s, 0.7H), 2.78 (s, 0.3H), 2.12 – 2.04 (m, 0.3H), 2.03 – 1.96 (m, 0.7H), 1.85 – 1.79 (m, 0.3H), 1.78 – 1.73 (m, 0.7H), 1.68 – 1.57 (m, 3H), 1.56 – 1.44 (m, 2H), 1.44 – 1.34 (m, 0.5H), 1.25 (s, 0.3H), 1.23 – 1.12 (m, 1H), 1.07 – 0.93 (m, 1.2H), 0.92 – 0.82 (m, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 177.6, 176.9, 170.0, 169.3, 168.3, 167.9, 143.7, 142.7, 138.5, 138.3, 136.7, 134.7, 133.6, 133.4, 132.0, 131.9, 131.7, 131.4, 131.1, 131.0, 130.9, 130.4, 130.4, 130.2, 130.0, 129.7, 128.6, 128.6, 128.2, 128.14, 128.10, 127.9, 127.8, 127.4, 127.3, 123.2, 122.9, 82.9, 82.6, 81.2, 80.5, 64.5, 60.4, 52.5, 43.9, 42.8, 29.9, 29.6, 29.2, 29.1, 25.81, 25.76, 25.5, 25.4. **HRMS** (ESI) calculated for $C_{32}H_{33}N_2O_4^+$ ([M+H]$^+$): 509.2435, found 509.2434.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)benzamido)-2-oxoethyl)benzoate **(5f)**



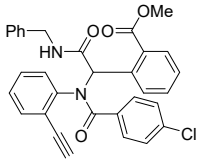
Pale yellow solid, 147 mg, 48% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.98 – 7.90 (m, 0.7H), 7.95 – 7.82 (m, 0.7H), 7.49 – 7.44 (m, 1H), 7.41 (d, *J* = 7.2 Hz, 0.7H), 7.39 – 7.33 (m, 2.6H), 7.30 – 7.26 (m, 2.5H), 7.26 – 7.25 (m, 1.5H), 7.24 – 7.20 (m, 3H), 7.20 – 7.16 (m, 1H), 7.14 – 7.09 (m, 4H), 7.04 – 6.97 (m, 1H), 6.93 – 6.89 (m, 0.3H), 6.81 (s, 0.7H), 6.71 (s, 0.3H), 4.61 – 4.38 (m, 2H), 3.90 (s, 2H), 3.81 (s, 1H), 2.94 (s, 0.7H), 2.86 (s, 0.3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.5, 169.8, 168.4, 143.4, 138.5, 136.3, 134.5, 133.6, 133.1, 132.3, 132.1, 131.6, 131.1, 130.9, 130.7, 130.4, 130.2, 129.6, 129.4, 128.8, 128.6, 128.3, 128.2, 128.1, 127.8, 127.6, 127.3, 123.1, 83.1, 80.8, 65.5, 61.6, 52.6, 43.9. **HRMS** (ESI) calculated for $C_{32}H_{27}N_2O_4^+$ ([M+H]$^+$): 503.1971, found 503.1966.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)-4-fluorobenzamido)-2-oxoethyl)benzoate **(5g)**



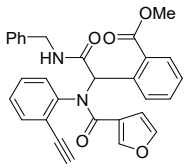
Pale yellow solid, 114 mg, 36% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.10 – 8.04 (m, 0.1H), 7.98 – 7.89 (m, 0.7H), 7.78 (d, *J* = 7.8 Hz, 0.7H), 7.52 (d, *J* = 6.6 Hz, 0.7H), 7.48 – 7.40 (m, 1H), 7.39 – 7.35 (m, 1.7H), 7.32 – 7.26 (m, 3.5H), 7.26 – 7.25 (m, 1H), 7.24 – 7.21 (m, 2.6H), 7.20 – 7.18 (m, 0.8H), 7.17 – 7.12 (m, 1.3H), 7.12 – 7.09 (m, 0.7H), 7.07 – 7.00 (m, 1H), 6.90 – 6.87 (m, 0.3H), 6.83 – 6.78 (m, 2H), 6.74 (s, 0.6H), 6.63 (s, 0.3H), 4.60 – 4.48 (m, 1.5H), 4.46 – 4.41 (m, 0.5H), 3.90 (s, 2H), 3.80 (s, 1H), 2.95 (s, 0.7H), 2.87 (s, 0.3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.5, 169.9, 168.4, 143.2, 138.4, 134.2, 133.7, 133.2, 132.3, 132.1, 131.6, 131.1, 130.8, 130.5, 130.4, 130.3, 129.7, 129.5, 128.7, 128.3, 128.0, 127.9, 127.7, 127.4, 123.1, 114.8, 114.6, 83.1, 80.7, 65.6, 61.5, 52.7, 43.9. **HRMS** (ESI) calculated for $C_{32}H_{26}FN_2O_4^+$ ($[M+H]^+$): 521.1877, found 521.1883

Methyl 2-(2-(benzylamino)-1-(4-chloro-*N*-(2-ethynylphenyl)benzamido)-2-oxoethyl)benzoate **(5h)**



Pale yellow solid, 221 mg, 68% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.00 – 7.90 (m, 0.7H), 7.80 – 7.76 (m, 0.7H), 7.57 – 7.52 (m, 0.7H), 7.49 – 7.43 (m, 0.3H), 7.44 – 7.39 (m, 0.1H), 7.39 – 7.33 (m, 1H), 7.31 (d, *J* = 8.4 Hz, 1.8H), 7.30– 7.26 (m, 2.7H), 7.27– 7.23 (m, 1.5H), 7.22 (d, *J* = 7.2 Hz, 2H), 7.22– 7.11 (m, 2.5H), 7.12 – 7.07 (m, 2.7H), 7.07 – 6.99 (m, 1H), 6.88 (s, 0.3H), 6.73 (t, *J* = 6.0 Hz, 0.7H), 6.64 (t, *J* = 6.0 Hz, 0.3H), 4.59 – 4.48 (m, 1.5H), 4.44 (t, *J* = 6.6 Hz, 0.5H), 3.91 (s, 2H), 3.80 (s, 1H), 2.95 (s, 0.7H), 2.87 (s, 0.3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.8, 170.4, 169.8, 168.7, 168.3, 167.8, 144.4, 142.9, 138.4, 138.2, 136.7, 136.0, 135.6, 134.8, 134.5, 134.1, 133.7, 133.2, 132.4, 132.3, 132.1, 131.6, 131.5, 131.1, 130.9, 130.8, 130.3, 130.2, 130.1, 129.7, 129.55, 129.5s, 128.8, 128.6, 128.4, 128.3, 128.0, 127.89, 127.85, 127.7, 127.65, 127.4, 123.2, 83.2, 81.2, 80.6, 65.6, 61.3, 52.7, 52.5, 43.9, 43.8, 31.5, 30.3. **HRMS** (ESI) calculated for $C_{32}H_{26}ClN_2O_4^+$ ($[M+H]^+$): 537.1581, found 537.1586

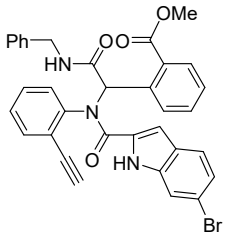
Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)furan-3-carboxamido)-2-oxoethyl)benzoate **(5i)**



Pale yellow solid, 197 mg, 66% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.88 (d, *J* = 7.8 Hz, 0.3H), 7.82 – 7.77 (m, 1H), 7.74 (d, *J* = 7.8 Hz, 0.7H), 7.41 – 7.35 (m, 1H), 7.35 – 7.30 (m, 1.3H), 7.29 – 7.27 (m, 1.5H), 7.26 – 7.25 (m, 1H), 7.24 (d, *J* = 7.2 Hz, 3H), 7.24 – 7.16 (m, 3.3H), 7.18 – 7.13 (m, 1.5H), 6.91

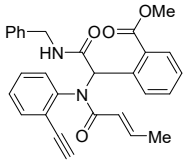
– 6.83 (m, 0.7H), 6.81 – 6.75(m, 1H), 6.72 (s, 0.7H), 6.25 (s, 0.7H), 6.23 (s, 0.3H), 4.55 – 4.50 (m, 1H), 4.52 – 4.36 (m, 1H), 3.88 (s, 2H), 3.82 (s, 1H), 2.81 (s, 0.7H), 2.76 (s, 0.3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.0, 168.4, 163.9, 145.7, 145.4, 142.5, 142.1, 138.5, 134.1, 133.8, 133.4, 132.6, 132.2, 131.9, 131.0, 130.8, 130.6, 130.2, 130.0, 129.8, 128.9, 128.6, 128.3, 128.2, 128.1, 127.6, 127.4, 127.3, 123.9, 122.0, 111.3, 111.2, 83.1, 82.8, 80.0, 65.3, 61.2, 52.6, 43.9, 43.8. **HRMS** (ESI) calculated for $C_{30}H_{25}N_2O_5^+$ ([M+H]$^+$): 493.1763, found 493.1765.

Methyl 2-(2-(benzylamino)-1-(6-bromo-*N*-(2-ethynylphenyl)-1H-indole-2-carboxamido)-2-oxoethyl)benzoate **(5j)**



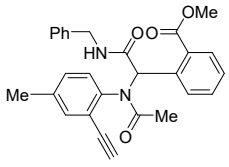
Light yellow oil, 161 mg, 36% yield (mixture of rotamers ≈ 3: 1). Purification by silica gel flash column chromatography (PE:EA=5:1→3:1→2:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 9.94 (s, 1H), 8.03 – 7.74 (m, 2.3H), 7.59 (s, 1H), 7.48 (s, 1H), 7.46 – 7.39 (m, 2H), 7.35 – 7.26 (m, 4H), 7.25 – 7.12 (m, 7H), 7.09 – 7.02 (m, 2H), 6.98 (d, *J* = 7.49 Hz, 0.3H), 6.80 (t, *J* = 5.87 Hz, 0.8H), 5.24 (s, 0.3H), 5.09 (d, *J* = 2.20 Hz, 0.7H), 4.63 – 4.27 (m, 3H), 3.88 (s, 2H), 3.80 (s, 1H), 2.83 (s, 0.7H), 2.80 (s, 0.3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.9, 162.4, 142.2, 138.4, 136.4, 133.8, 133.6, 132.6, 132.2, 132.0, 131.0, 130.8, 130.4, 130.0, 129.1, 128.6, 128.4, 128.1, 127.6, 127.3, 126.7, 124.1, 123.8, 123.6, 118.5, 114.7, 106.8, 82.8, 65.6, 61.6, 52.6, 43.9. **HRMS** (ESI) calculated for $C_{34}H_{27}BrN_3O_4^+$ ([M+H]$^+$): 620.1185, found 620.1193.

Methyl (*E*)-2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)but-2-enamido)-2-oxoethyl)benzoate **(5k)**



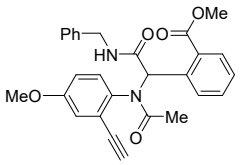
Pale yellow solid, 95 mg, 28% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 5: 1→3: 1→1: 1). **^{1}H NMR (600 MHz, $CDCl_3$)**δ 7.83 (dd, *J* = 40.78, 7.77 Hz, 1H), 7.68 (dd, *J* = 18.25, 7.91 Hz, 1H), 7.49 – 7.41 (m, 0.5H), 7.39 – 7.28 (m, 4H), 7.25 – 7.15 (m, 6H), 7.10 – 6.94 (m, 1.7H), 6.83 (t, *J* = 5.73 Hz, 0.7H), 6.76 (s, 0.3H), 5.61 (m, 1H), 4.68 – 4.34 (m, 2H), 3.88 (s, 2H), 3.83 (s, 1H), 2.83 (s,0.7H), 2.81 (s, 0.3H), 1.73 (s, 2H), 1.72 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.0, 168.3, 166.6, 143.1, 142.8, 142.2, 138.5, 134.5, 133.6, 133.3, 132.04, 132.01, 131.9, 131.7, 131.0, 130.9, 130.6, 130.4, 130.1, 130.0, 129.7, 128.6, 128.5, 128.3, 128.1, 128.1, 128.09, 128.04, 127.6, 127.3, 127.2, 83.0, 82.6, 80.2, 64.5, 60.6, 52.5, 43.8, 43.7, 18.2. **HRMS** (ESI) calculated for $C_{29}H_{27}N_2O_4^+$ ([M+H]$^+$): 467.1971, found 467.1974.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynyl-4-methylphenyl)acetamido)-2-oxoethyl)benzoate **(5l)**



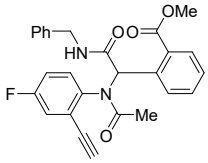
Pale yellow solid, 140 mg, 51% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.25 (s, 0.1H), 7.83 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.77 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.63 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.59 (d, *J* = 7.8 Hz, 0.7H), 7.36 – 7.32 (m, 0.7H), 7.31 – 7.27 (m, 1.8H), 7.26 – 7.23 (m, 1.8H), 7.23 – 7.21 (m, 0.7H), 7.21 – 7.20 (m, 1H), 7.20 – 7.19 (m, 0.7H), 7.18 – 7.15 (m, 1H), 7.15 – 7.09 (m, 1.9H), 7.05 (s, 0.7H), 6.98 (dd, *J* = 8.4, 2.4 Hz, 0.3H), 6.93 (t, *J* = 6.0 Hz, 0.3H), 6.69 (t, *J* = 6.0 Hz, 0.7H), 6.63 (s, 0.3H), 4.54 – 4.49 (m, 0.7H), 4.48 – 4.45 (m, 0.7H), 4.44 – 4.40 (m, 0.6H), 3.88 (s, 2H), 3.83 (s, 1H), 2.81 (s, 0.7H), 2.79 (s, 0.3H), 2.25 (s, 3H), 1.93 (s, 1H), 1.87 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.2, 171.5, 170.3, 169.4, 168.4, 167.9, 141.6, 140.4, 138.4, 138.3, 138.2, 136.7, 134.5, 134.1, 133.8, 132.1, 131.9, 131.8, 131.3, 131.09, 131.07, 130.7, 130.4, 130.2, 129.7, 128.9, 128.6, 128.2, 128.19, 128.13, 127.9, 127.8, 127.7, 127.4, 127.3, 122.7, 122.3, 82.4, 81.9, 80.3, 64.4, 60.1, 52.6, 52.5, 43.9, 43.8, 42.3, 23.1, 20.9. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_4^+$ ([M+H]$^+$): 455.1971, found 455.1976.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynyl-4-methoxyphenyl)acetamido)-2-oxoethyl) benzoate **(5m)**



Yellow solid, 187 mg, 41% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.83 (dd, *J* = 7.75, 1.53 Hz, 0.3 H), 7.77 (dd, *J* = 7.80, 1.42 Hz, 0.7H), 7.67 (d, *J* = 8.80 Hz, 0.7H), 7.61 (dd, *J* = 7.89, 1.30 Hz, 0.3H), 7.34 (td, *J* = 7.61, 1.50 Hz, 0.4H), 7.31 – 7.27 (m, 1.4H), 7.26 – 7.17 (m, 5H), 7.16 – 7.08 (m, 2H), 7.05 – 7.01 (m, 0.2H), 6.97 (d, *J* = 5.80 Hz, 0.4H), 6.89 (d, *J* = 3.00 Hz, 0.3H), 6.85 (dd, *J* = 8.83, 2.98 Hz, 0.7H), 6.71 (d, *J* = 2.99 Hz, 0.7H), 6.69 (dd, *J* = 8.91, 3.02 Hz, 0.3H), 6.64 (t, *J* = 5.82 Hz, 0.7H), 6.61 (s, 0.3H), 4.54 – 4.39 (m, 2H), 3.88 (s, 2H), 3.84 (s, 1H), δ 3.73 (s, 1H), 3.73 (s, 2H), 2.83 (s, 0.7H), 2.78 (s, 0.3H), 1.93 (s, 1H), 1.87 (s, 2H).**^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.8, 170.5, 168.4, 158.9, 138.4, 135.8, 134.4, 132.8, 132.1, 132.0, 132.0, 131.2, 130.9, 130.4, 130.2, 128.6, 128.21, 128.17, 128.1, 127.6, 127.4, 127.3, 124.1, 117.8, 117.5, 116.4, 115.9, 82.6, 82.0, 80.0, 64.2, 59.8, 55.6, 52.61, 52.57, 43.9, 43.7. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_5^+$ ([M+H]$^+$): 471.1914, found 471.1915.

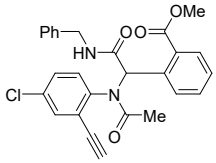
Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynyl-4-fluorophenyl)acetamido)-2 oxoethyl) -benzoate **(5n)**



White solid, 169 mg, 37% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 3: 1→2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.85 (dd, *J* = 8.8, 5.3 Hz, 0.7H), 7.81 (dd, *J* = 7.8, 1.5 Hz, 0.3H), 7.74 (dd, *J* = 7.8, 1.4 Hz, 0.7H), 7.63 (dd, *J* = 7.9, 1.3 Hz, 0.3H), 7.37 – 6.97 (m, 10H), 6.86 (m, 1H), 6.79 (t, *J* = 5.8 Hz, 0.2H), δ 6.56 (s, 0.3H), 6.51 (t, *J* = 5.9 Hz, 0.7H), 4.51 – 4.32 (m, 2H), 3.86 (d, *J* = 0.8 Hz, 2.2H), 3.80 (s, 0.8H), 2.90 (s, 0.7H), 2.84 (s, 0.3H), 1.89 (s, 0.8H), 1.83 (s, 2.2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.2, 170.5, 168.2, 162.3, 160.6, 138.9, 138.3, 136.5, 133.9, 133.9, 132.2, 132.1, 131.9, 131.0, 130.5, 130.4, 128.7, 128.4, 128.3, 128.1, 127.5, 127.4, 127.3,

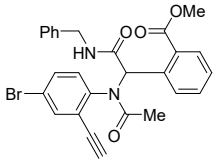
125.3, 120.2, 119.8, 119.6, 117.7, 117.2, 117.0, 83.8, 83.2, 78.9, 64.3, 59.4, 43.9, 43.7, 23.1. **HRMS** (ESI) calculated for $C_{27}H_{24}FN_2O_4^+$ ([M+H]$^+$): 459.1715, found 459.1713.

Methyl 2-(2-(benzylamino)-1-(*N*-(4-chloro-2-ethynylphenyl)acetamido)-2-oxoethyl)benzoate **(5o)**



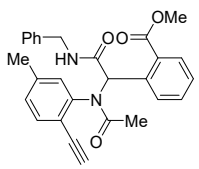
Pale yellow solid, 104 mg, 43% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.87 (d, *J* = 9.0 Hz, 1H), 7.80 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.69 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.43 – 7.36 (m, 0.6H), 7.35 – 7.27 (m, 2.7H), 7.28 – 7.27 (m, 0.6H), 7.25 – 7.23 (m, 1.2H), 7.23 – 7.20 (m, 0.7H), 7.20 – 7.16 (m, 3H), 7.15 (d, *J* = 1.2 Hz, 0.2H), 7.08 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 6.82 (t, *J* = 6.0 Hz, 0.3H), 6.62 (t, *J* = 7.2 Hz, 1H), 4.52 – 4.43 (m, 1.8H), 4.41 – 4.36 (m, 0.2H), 3.90 (s, 2.2H), 3.84 (s, 0.8H), 2.98 (s, 0.7H), 2.94 (s, 0.3H), 1.95 (s, 0.8H), 1.88 (s, 2.2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.7, 170.9, 170.4, 168.9, 168.1, 167.8, 142.8, 141.2, 138.2, 138.1, 136.3, 134.0, 133.8, 133.7, 133.3, 133.2, 132.8, 132.2, 131.83, 131.79, 131.2, 131.0, 130.7, 130.7, 130.47, 130.45, 130.42, 129.9, 128.6, 128.4, 128.3, 128.0, 127.4, 127.4, 127.2, 124.9, 124.2, 84.0, 83.4, 79.6, 78.6, 64.3, 59.4, 52.6, 52.5, 43.8, 43.6, 23.1, 23.0. **HRMS** (ESI) calculated for $C_{27}H_{24}ClN_2O_4^+$ ([M+H]$^+$): 475.1425, found 475.1424.

Methyl 2-(2-(benzylamino)-1-(*N*-(4-bromo-2-ethynylphenyl)acetamido)-2-oxoethyl)benzoate **(5p)**



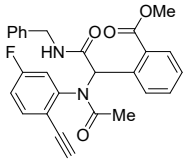
Pale yellow solid, 172 mg, 54% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.81 (dd, *J* = 8.4, 1.8 Hz, 0.3H), 7.76 – 7.72 (m, 1.4H), 7.65 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.51 (d, *J* = 2.4 Hz, 0.3H), 7.42 (dd, *J* = 8.4, 2.4 Hz, 0.7H), 7.35 (td, *J* = 7.2, 1.2 Hz, 0.3H), 7.32 – 7.30 (m, 1H), 7.29 – 7.27 (m, 0.5H), 7.27 – 7.24 (m, 0.7H), 7.24 – 7.19 (m, 3.5H), 7.18 – 7.15 (m, 1H), 7.14 – 7.10 (m, 2H), 7.03 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 6.71 (t, *J* = 6.0 Hz, 0.3H), 6.55 (s, 0.3H), 6.51 (t, *J* = 5.4 Hz, 0.7H), 4.48 – 4.43 (m, 0.8H), 4.43 – 4.38 (m, 0.9H), 4.36 – 4.32 (m, 0.3H), 3.85 (s, 2H), 3.79 (s, 1H), 2.91 (s, 0.7H), 2.87 (s, 0.3H), 1.89 (s, 1H), 1.83 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.7, 170.9, 170.4, 169.0, 168.2, 167.9, 143.5, 141.8, 138.2, 138.1, 136.4, 136.2, 135.8, 133.9, 133.6, 133.4, 133.0, 132.2, 132.0, 131.9, 131.5, 131.1, 130.9, 130.8, 130.52, 130.48, 128.6, 128.4, 128.0, 127.5, 127.4, 127.3, 125.3, 124.6, 121.9, 121.7, 84.1, 83.5, 79.6, 78.6, 64.4, 59.4, 52.62, 52.58, 43.9, 43.7, 23.1, 23.1. **HRMS** (ESI) calculated for $C_{27}H_{24}BrN_2O_4^+$ ([M+H]$^+$): 519.0919, found 519.0925.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynyl-5-methylphenyl)acetamido)-2-oxoethyl)benzoate **(5q)**



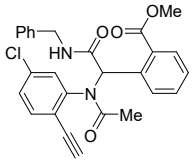
Yellow solid, 148 mg, 32% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA =5: 1→3: 1→2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.84 (dd, *J* = 7.79, 1.52 Hz, 0.3H), 7.76 (dd, *J* = 7.83, 1.47 Hz, 0.6H), 7.72 – 7.64 (m, 0.3H), 7.56 – 7.46 (m, 0.6H), 7.39 – 7.09 (m, 9.7H), 7.07 (s, 0.3H), 6.98 (ddd, *J* = 7.92, 1.80, 0.89 Hz, 1H), 6.81 (s, 0.3H), 6.78 – 6.68 (m, 0.7H), 6.62 (s, 0.3H), δ 4.58 – 4.37 (m, 2H)., 3.88 (s, 2H), 3.83 (s, 1H), 2.81 (s, 0.7H), 2.80 (s, 0.3H), 2.33 (s, 2H), 2.19 (s, 1H), 1.95 (s, 1H), 1.88 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.3, 170.3, 168.4, 142.8, 140.5, 138.4, 134.3, 133.4, 133.1, 132.12, 132.06, 131.9, 131.2, 130.8, 130.5, 130.3, 130.2, 129.2, 129.0, 128.6, 128.3, 128.09, 128.07, 127.6, 127.4, 127.3, 120.1, 82.1, 81.6, 80.3, 64.7, 60.0, 43.9, 43.8, 29.8, 23.1, 21.5. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_4^+$ ([M+H]$^+$): 455.1965, found 455.1962.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynyl-5-fluorophenyl)acetamido)-2-oxoethyl)benzoate **(5r)**



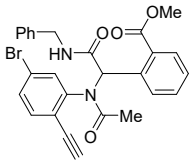
White solid, 48 mg, 14% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 10: 1→5: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.86 (dd, *J* = 7.78, 1.54 Hz, 0.3H), 7.80 (dd, *J* = 7.80, 1.48 Hz, 0.7H), 7.68 (m, 1H), 7.46 – 7.33 (m, 0.7H), 7.33 – 7.28 (m, 2.5H), 7.25 – 7.14 (m, 5H), 7.14 – 7.07 (m, 1H), 6.94 – 6.86 (m, 1H), 6.81 (t, *J* = 5.55 Hz, 0.3H), 6.59 (s, 0.3H), 6.51 (t, *J* = 5.80 Hz, 0.8H), 4.61 – 4.32 (m, 2H), 3.89 (s, 2H), 3.84 (s, 1H), 2.87 (s, 0.7H), 2.82 (s, 0.3H), 1.96 (s, 1H), 1.90 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.8, 170.3, 168.1, 161.7, 138.2, 136.3, 134.6, 134.5, 133.9, 132.2, 131.9, 131.7, 131.1, 130.8, 130.5, 128.68, 128.67, 128.5, 128.4, 128.1, 127.6, 127.5, 127.4, 119.8, 119.8, 119.7, 119.5, 117.5, 116.0, 115.9, 115.8, 82.7, 82.1, 79.1, 64.5, 59.6, 43.9, 43.8, 23.1, 23.0. **HRMS** (ESI) calculated for $C_{27}H_{24}FN_2O_4^+$ ([M+H]$^+$): 459.1720, found 459.1726.

Methyl 2-(2-(benzylamino)-1-(*N*-(5-chloro-2-ethynylphenyl)acetamido)-2-oxoethyl)benzoate **(5s)**



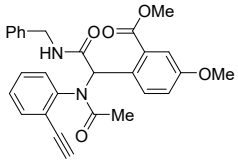
White solid, 64 mg, 18% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography(PE: EA = 5: 1→3: 1→2: 1).**^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.95 (d, *J* = 2.01 Hz, 0.6 H), 7.87 (dd, *J* = 7.88, 0.3 Hz, 0H), 7.78 (dd, *J* = 7.79, 1.50 Hz, 0.7H), 7.71 – 7.58 (m, 0.3H), 7.41 – 7.06 (m, 11H), 6.78 (t, *J* = 5.42 Hz, 0.2H), 6.59 (s, 0.3H), 6.54 (t, *J* = 5.86 Hz, 0.7H), 4.58 – 4.36 (m, 2H), 3.90 (s, 2H), 3.84 (s, 1H), 2.95 (s, 0.7H), 2.88 (s, 0.3H), 1.96 (s, 1H), 1.90 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.8, 170.3, 143.9, 135.4, 134.4, 134.0, 133.9, 132.4, 132.1, 132.0, 131.1, 130.5, 128.8, 128.7, 128.6, 128.5, 128.4, 128.1, 127.6, 127.5, 127.4, 122.2, 83.8, 83.2, 64.4, 59.6, 44.0, 43.9, 23.1. **HRMS** (ESI) calculated for $C_{27}H_{24}ClN_2O_4^+$ ([M+H]$^+$): 475.1419, found 475.1418.

Methyl 2-(2-(benzylamino)-1-(*N*-(5-bromo-2-ethynylphenyl)acetamido)-2-oxoethyl)benzoate **(5t)**



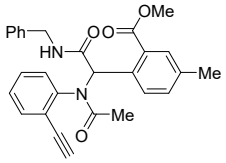
White solid, 75 mg, 20% yield(mixture of rotamers≈2:1). Purification by silica gel flash column chromatography(PE:EA=5:1→3:1→2:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.10 (d, *J* = 2.04 Hz, 0.7H), 7.87 (dd, *J* = 7.78, 1.55 Hz, 0.3H), 7.78 (dd, *J* = 7.81, 1.51 Hz, 0.7H), 7.67 (dd, *J* = 8.08, 1.27 Hz, 0.3H), 7.46 (d, *J* = 1.98 Hz, 0.3H), 7.38 (td, *J* = 7.62, 1.58 Hz, 0.3H), 7.31 (dq, *J* = 8.67, 2.20 Hz, 3H), 7.26 – 7.16 (m, 5H), 7.13 (dd, *J* = 7.96, 1.42 Hz, 0.7H), 7.07 (d, *J* = 8.29 Hz, 0.7H), 6.78 (s, 0.3H), 6.59 (s, 0.3H), 6.53 (s, 0.7H), 4.74 – 4.26 (m, 2H), 3.89 (s, 2H), 3.85 (s, 1H), 2.97 (s, 0.7H), 2.89 (s, 0.3H), 1.95 (s, 1H), 1.90 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.7, 170.2, 168.1, 143.7, 138.1, 135.1, 134.4, 134.0, 133.7, 133.2, 132.1, 131.9, 131.8, 131.6, 131.4, 131.0, 130.9, 130.4, 130.4, 128.6, 128.6, 128.4, 128.3, 128.0, 127.4, 127.3, 123.1, 122.4, 83.8, 83.3, 64.2, 59.5, 52.5, 43.7, 23.1. **HRMS** (ESI) calculated for $C_{27}H_{24}BrN_2O_4^+$ ([M+H]$^+$): 519.0919, found 519.0924.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-5-methoxybenzoate **(5u)**



Pale yellow solid, 158 mg, 55% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.79 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 7.52 (d, *J* = 8.4 Hz 0.3H), 7.45 – 7.40 (m, 0.3H), 7.34 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.32 – 7.31 (m, 0.7H), 7.31 – 7.30 (m, 0.3H), 7.30 – 7.29 (m, 0.8H), 7.28 – 7.26 (m, 1H), 7.25 – 7.23 (m, 1.7H), 7.22 – 7.21 (m, 0.3H), 7.21 – 7.20 (m, 1.3H), 7.19 – 7.18 (m, 1.3H), 7.18 – 7.16 (m, 1.7H), 7.02 (s, 0.3H), 7.00 (s, 0.3H), 6.96 (t, *J* = 5.4 Hz, 0.3H), 6.84 (dd, *J* = 9.0, 3.0 Hz, 0.3H), 6.63 (dd, *J* = 9.0, 3.0 Hz, 0.7H), 6.59 (t, *J* = 5.4 Hz, 0.7H), 6.54 (s, 0.3H), 4.51 (dd, *J* = 15.0, 6.0 Hz, 0.7H), 4.45 (dd, *J* = 9.0, 6.0 Hz, 1.3H), 3.88 (s, 2H), 3.82 (s, 1H), 3.77 (s, 1H), 3.74 (s, 2H), 2.89 (s, 0.7H), 2.79 (s, 0.3H), 1.93 (s, 1H), 1.87 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.9, 171.1, 170.7, 169.6, 168.1, 167.7, 159.2, 159.0, 144.2, 142.9, 138.5, 138.4, 133.7, 133.35, 133.26, 132.7, 132.4, 131.9, 130.2, 130.1, 129.7, 128.8, 128.6, 128.3, 128.3, 128.1, 128.0, 127.9, 127.7, 127.6, 127.4, 127.3, 127.0, 126.2, 123.5, 122.8, 118.0, 116.9, 115.13, 115.06, 82.8, 82.2, 81.1, 80.1, 63.9, 59.3, 55.53, 55.46, 52.54, 52.53, 43.9, 43.7, 23.1, 23.0. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_5^+$ ([M+H]$^+$): 471.1920, found 471.1933.

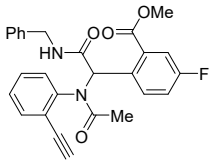
Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-5-methylbenzoate **(5v)**



Pale yellow solid, 190 mg, 59% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.78 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 7.65 – 7.63 (m, 0.3H), 7.58 – 7.56 (m, 0.7H), 7.53 (d, *J* = 7.8 Hz, 0.3H), 7.44 – 7.41 (m, 0.3H), 7.36 – 7.30 (m, 1H), 7.30 – 7.26 (m, 1.7H), 7.26 – 7.23 (m, 2H), 7.22 – 7.21 (m, 0.3H), 7.21 – 7.16 (m, 3H), 7.15 – 7.13 (m, 1H), 7.01 (d, *J* = 7.8 Hz, 0.7H), 6.94 – 6.91 (m, 0.7H), 6.87 (t, *J* = 6.0 Hz, 0.3H), 6.60 (t, *J* = 5.4 Hz, 0.7H), 6.56 (s, 0.3H), 4.52 (dd, *J* = 15.0, 5.4 Hz, 0.7H), 4.44 (dd, *J* = 14.4, 5.4 Hz, 1.3H), 3.87 (s, 2H), 3.81 (s, 1H), 2.88 (s, 0.7H), 2.82 (s, 0.3H), 2.30 (s, 1H), 2.26 (s, 2H), 1.94 (s, 1H), 1.87 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.9, 171.1, 170.6, 169.4, 168.5, 168.0, 144.5, 143.1, 138.5, 138.4,

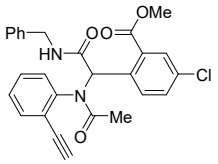
138.2, 138.1, 133.7, 133.5, 133.3, 132.8, 131.92, 131.90, 131.87, 131.6, 131.3, 131.1, 130.9, 130.8, 130.2, 130.1, 129.8, 128.6, 128.3, 128.1, 128.0, 127.6, 127.4, 127.3, 123.4, 122.8, 82.8, 82.3, 81.2, 80.2, 64.4, 59.7, 52.5, 52.4, 43.9, 43.8, 23.1, 23.1, 21.0. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_4^+$ ([M+H]$^+$): 455.1971, found 455.1962.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-5-fluorobenzoate **(5w)**



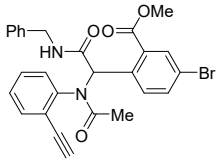
Pale yellow solid, 280 mg, 56% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.77 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 7.73 (dd, *J* = 8.4, 5.4 Hz, 0.3H), 7.62 – 7.59 (m, 0.3H), 7.55 (dd, *J* = 9.0, 3.0 Hz, 0.7H), 7.53 – 7.50 (m, 0.3H), 7.43 – 7.33 (m, 4.4H), 7.32 – 7.27 (m, 3.4H), 7.25 – 7.23 (m, 0.6H), 7.13 – 7.09 (m, 0.3H), 7.01 (t, *J* = 6.0 Hz, 0.3H), 6.93 – 6.88 (m, 0.7H), 6.80 (t, *J* = 6.0 Hz, 0.7H), 6.70 (s, 0.3H), 4.60 – 4.48 (m, 2H), 3.95 (s, 2H), 3.90 (s, 1H), 2.94 (s, 0.7H), 2.93 (s, 0.3H), 2.00 (s, 1H), 1.95 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.0, 171.2, 170.1, 169.0, 166.99, 166.98, 166.6, 162.6, 162.5, 161.3, 161.0, 160.8, 143.9, 142.6, 138.2, 138.1, 133.93, 133.9, 133.88, 133.7, 133.6, 133.5, 133.3, 132.8, 132.8, 132.5, 132.5, 131.5, 130.4, 130.3, 130.3, 130.0, 129.9, 128.7, 128.6, 128.5, 128.3, 128.1, 127.8, 127.6, 127.6, 127.4, 127.3, 123.2, 122.7, 119.1, 119.0, 118.1, 117.9, 117.3, 117.2, 117.14, 117.08, 83.0, 82.5, 80.9, 80.0, 63.5, 59.1, 52.8, 43.9, 43.8, 23.0. **HRMS** (ESI) calculated for $C_{27}H_{24}FN_2O_4^+$ ([M+H]$^+$): 459.1720, found 459.1727.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-5-chlorobenzoate **(5x)**



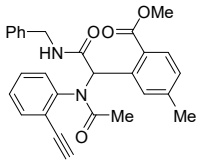
White solid, 69 mg, 42% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 5: 1→3: 1→2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.83 (d, *J* = 2.33 Hz, 0.3H), 7.77 (d, *J* = 2.29 Hz, 0.7H), 7.69 – 7.62 (m, 1H), 7.46 – 7.43 (m, 0.3H), 7.36 – 7.27 (m, 4H), 7.25 – 7.20 (m, 4H), 7.18 – 7.09 (m, 2H), 6.82 (s, 0.3H), 6.72 (t, *J* = 5.77 Hz, 0.7H), 6.61 (s, 0.3H), 4.59 – 4.34 (m, 2H), 3.88 (s, 2H), 3.83 (s, 1H), 2.87 (s, 0.3H), 2.84 (s, 0.7H), 1.93 (s, 1H), 1.88 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.3, 169.8, 142.8, 138.3, 134.3, 133.8, 133.7, 133.3, 133.2, 133.0, 132.6, 132.0, 131.5, 131.0, 130.4, 130.4, 130.2, 130.1, 130.0, 128.7, 128.6, 128.4, 128.1, 127.8, 127.5, 127.4, 123.1, 83.0, 82.6, 80.1, 63.8, 59.5, 44.0, 43.9, 23.1, 22.8. **HRMS** (ESI) calculated for $C_{27}H_{24}ClN_2O_4^+$ ([M+H]$^+$): 475.1425, found 475.1434.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-5-bromobenzoate **(5y)**



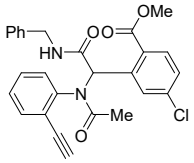
White solid, 96 mg, 41% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 4: 1→3: 1→2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.91 (d, *J* = 2.20 Hz, 0.3H), 7.85 (d, *J* = 2.19 Hz, 0.7H), 7.58 (dd, *J* = 7.97, 1.25 Hz, 0.7H), 7.51 (d, *J* = 8.48 Hz, 0.3H), 7.46 (dd, *J* = 8.61, 0.72 Hz, 0.1H), 7.43 – 7.35 (m, 0.6H), 7.27 (td, *J* = 7.68, 1.61 Hz, 1H), 7.25 – 7.20 (m, 4H), 7.19 – 7.13 (m, 4H), 7.07 – 7.00 (m, 1.5H), 6.75 (t, *J* = 5.82 Hz, 0.3H), 6.67 (t, *J* = 5.76 Hz, 0.7H), 6.52 (s, 0.3H), 4.49 – 4.29 (m, 2H), 3.81 (s, 2H), 3.76 (s, 1H), 2.81 (s, 0.3H), 2.77 (s, 0.7H), 1.86 (s, 1H), 1.81 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)**δ 171.3, 169.7, 167.0, 138.2, 135.0, 133.9, 133.8, 133.7, 133.6, 133.42, 133.37, 133.3, 133.1, 132.8, 131.4, 130.4, 130.1, 130.0, 128.71, 128.70, 128.66, 128.4, 128.1, 127.8, 127.5, 127.4, 123.1, 122.3, 83.0, 82.7, 80.1, 63.9, 59.6, 52.9, 52.8, 44.0, 43.9, 23.1, 22.5. **HRMS** (ESI) calculated for $C_{27}H_{24}BrN_2O_4^+$ ([M+H]$^+$): 519.0914, found 519.0917.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-4-methylbenzoate **(5z)**



Pale white solid, 154 mg, 65% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.82 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 7.75 (d, *J* = 7.8 Hz, 0.3H), 7.66 (d, *J* = 7.8 Hz, 0.7H), 7.49 – 7.45 (m, 0.3H), 7.43 (dd, *J* = 7.2, 1.8 Hz, 0.3H), 7.36 – 7.33 (m, 1H), 7.34 – 7.29 (m, 0.8H), 7.29 – 7.28 (m, 0.3H), 7.28 – 7.27 (m, 0.7H), 7.26 – 7.25 (m, 0.4H), 7.25 – 7.24 (m, 0.7H), 7.23 – 7.22 (m, 1H), 7.22 – 7.21 (m, 0.8H), 7.21 – 7.20 (m, 1H), 7.20 – 7.19 (m, 1H), 7.18 – 7.15 (m, 1H), 7.07 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 7.02 – 6.97 (m, 0.7H), 6.89 (s, 0.7H), 6.84 (t, *J* = 6.0 Hz, 0.3H), 6.67 (t, *J* = 5.4 Hz, 0.7H), 6.63 (s, 0.3H), 4.53 (d, *J* = 5.4 Hz, 0.3H), 4.51 (d, *J* = 5.4 Hz, 0.7H), 4.46 (dd, *J* = 15, 6.0 Hz, 0.7H), 4.38 (dd, *J* =6.0, 5.4 Hz, 0.3H), 3.86 (s, 2H), 3.80 (s, 1H), 2.89 (s, 0.3H), 2.88 (s, 0.7H), 2.24 (s, 1H), 2.05 (s, 2H), 1.95 (s, 1H), 1.88 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.0, 171.1, 170.6, 169.4, 168.3, 167.8, 144.6, 143.0, 142.7, 141.5, 138.5, 136.6, 134.2, 133.7, 133.3, 133.0, 132.1, 131.9, 130.7, 130.4, 130.3, 130.0, 129.5, 129.2, 128.9, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 127.6, 127.4, 127.3, 123.5, 122.8, 82.6, 82.2, 80.1, 64.8, 59.7, 52.4, 52.3, 43.9, 43.7, 23.2, 21.6, 21.2. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_4^+$ ([M+H]$^+$): 455.1971, found 455.1968.

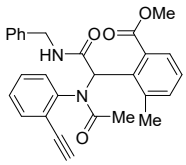
Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-4-chlorobenzoate **(5aa)**



Pale yellow solid, 93 mg, 37% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.86 – 7.82 (m, 0.6H), 7.77 – 7.73 (m, 0.6H), 7.70 (dd, *J* = 7.8, 1.2 Hz, 0.6H), 7.50 – 7.46 (m, 0.6H), 7.46 – 7.37 (m, 0.8H), 7.35 – 7.27 (m, 4.8H), 7.25 – 7.24 (m, 1.8H), 7.24 – 7.20 (m, 1.4H), 7.17 (s, 0.6H), 6.80 (t, *J* = 5.4 Hz, 0.6H), 6.63 – 6.58 (m, 0.6H), 4.57 – 4.44 (m, 1.7H), 4.35 (dd, *J* = 15.0, 5.4 Hz, 0.3H), 3.89 (s, 2H), 3.81 (s, 1H), 3.05 (s, 0.3H), 2.87 (s, 0.7H), 1.99 (s, 1H), 1.92 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.1, 171.2, 169.5, 168.5, 167.4, 166.8, 161.2, 147.2, 144.6, 142.6, 138.9, 138.7, 138.2, 138.1, 137.5, 136.5, 133.8, 133.6, 132.05, 132.97, 131.6, 131.4, 131.2, 130.6, 130.1, 130.0, 129.7, 128.8, 128.70, 128.67, 128.6,

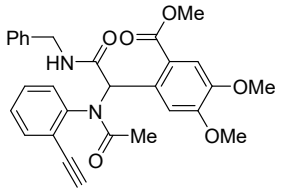
128.4, 128.35, 128.28, 128.0, 127.9, 127.7, 127.42, 127.41, 124.6, 124.1, 123.0, 122.6, 119.2, 82.9, 82.6, 81.0, 80.1, 65.2, 59.7, 52.7, 52.6, 43.9, 43.9, 23.1, 22.8. **HRMS** (ESI) calculated for $C_{27}H_{24}ClN_2O_4^+$ ([M+H]$^+$): 475.1425, found 475.1434.

Methyl 2-(2-(benzylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)-3-methylbenzoate **(5ab)**



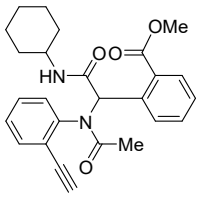
Yellow solid, 191 mg, 53% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.18 (d, *J* = 7.2 Hz, 0.2H), 7.83 (t, *J* = 5.4 Hz, 0.8H), 7.76 (s, 0.2H), 7.62 (dd, *J* = 7.8, 1.8 Hz, 0.8H), 7.51 – 7.45 (m, 1H), 7.43 – 7.39 (m, 1.5H), 7.38 – 7.35 (m, 1.7H), 7.31 – 7.26 (m, 2H), 7.26 – 7.22 (m, 1.4H), 7.17 – 7.14 (m, 1.6H), 7.09 (d, *J* = 7.8 Hz, 0.2H), 6.91 (s, 0.8H), 6.87 (td, *J* = 7.8, 1.2 Hz, 0.8H), 6.23 (d, *J* = 8.4 Hz, 0.8H), 5.90 (s, 0.2H), 4.65 – 4.56 (m, 1H), 4.44 – 4.38 (m, 1H), 3.83 (s, 0.6H), 3.78 (s, 2.4H), 2.74 (s, 0.2H), 2.52 (s, 0.8H), 2.01 (s, 2.3H), 1.96 (s, 2.7H), 1.83 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.1, 171.5, 170.5, 169.7, 169.2, 168.6, 142.0, 141.7, 140.7, 138.3, 138.1, 134.6, 134.5, 134.4, 133.9, 133.8, 133.6, 133.0, 131.3, 130.3, 129.5, 129.2, 128.8, 128.7, 128.7, 128.7, 128.6, 128.5, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.5, 124.4, 123.5, 83.7, 82.3, 81.5, 79.0, 61.6, 57.5, 52.6, 52.4, 44.1, 44.1, 22.8, 22.7, 20.5. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_4^+$ ([M+H]$^+$): 455.1971, found 455.1977.

Methyl 2-(2-(benzylamino)-1-(N-(2-ethynylphenyl)acetamido)-2-oxoethyl)-4,5- dimethoxybenzoate **(5ac)**



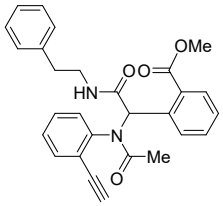
Pale yellow solid, 107 mg, 64% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ δ 7.89 (dd, *J* = 8.4, 1.2 Hz, 0.7H), 7.45 – 7.40 (m, 1H), 7.38 – 7.34 (m, 0.7H), 7.32 – 7.28 (m, 1.8H), 7.27 – 7.26 (m, 0.3H), 7.26 – 7.24 (m, 1.8H), 7.24 – 7.14 (m, 3.3H), 7.16 – 7.11 (m, 0.4H), 7.03 – 6.96 (m, 0.3H), 6.71 (s, 0.3H), 6.58 (t, *J* = 6.0 Hz, 0.7H), 6.49 (s, 0.7H), 4.59 – 4.48 (m, 1H), 4.48 – 4.39 (m, 1H), 3.88 (s, 2H), 3.85 (s, 3H), 3.83 (s, 1H), 3.68 (s, 1H), 3.46 (s, 2H), 2.89 (s, 0.7H), 2.85 (s, 0.3H), 1.93 (s, 1H), 1.87 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.1, 171.2, 170.9, 169.5, 167.8, 167.3, 151.5, 150.6, 148.2, 148.1, 142.9, 138.5, 138.4, 133.7, 133.6, 132.1, 130.4, 130.3, 130.2, 129.6, 128.7, 128.4, 128.2, 128.1, 128.0, 127.5, 127.5, 127.3, 124.4, 123.9, 123.3, 122.9, 114.6, 114.0, 112.7, 112.7, 82.7, 82.2, 79.9, 63.5, 58.8, 55.9, 55.8, 52.49, 52.45, 43.8, 43.7, 23.3, 23.2. **HRMS** (ESI) calculated for $C_{29}H_{29}N_2O_6^+$ ([M+H]$^+$): 501.2026, found 501.2024.

Methyl 2-(2-(cyclohexylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)benzoate **(5ad)**



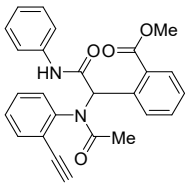
Pale yellow solid, 181 mg, 34% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.97 – 7.92 (m, 1H), 7.87 – 7.82 (m, 1H), 7.57 – 7.54 (m, 0.3H), 7.51 – 7.47 (m, 0.6H), 7.44 – 7.34 (m, 1.6H), 7.32 – 7.27 (m, 1.7H), 7.25 – 7.19 (m, 1H), 7.17 – 7.13 (m, 1.5H), 6.60 (s, 0.3H), 6.27 – 6.19 (m, 1H), 4.00 (s, 2H), 3.92 (s, 1H), 3.89 – 3.82 (m, 0.7H), 3.81 – 3.71 (m, 0.3H), 3.33 (s, 0.3H), 3.09 (s, 0.7H), 2.03 (s, 1H), 1.94 (s, 2H), 1.86 – 1.57 (m, 5H), 1.32 – 1.02 (m, 5H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.8, 171.1, 169.5, 168.3, 167.9, 167.8, 160.5, 144.6, 142.7, 137.0, 134.4, 133.6, 133.2, 132.0, 131.95, 131.89, 130.7, 130.6, 130.4, 130.35, 130.1, 129.7, 129.7, 128.2, 128.0, 128.0, 127.9, 124.5, 124.0, 123.4, 122.8, 82.8, 82.1, 81.1, 80.0, 64.8, 59.5, 52.5, 52.4, 48.7, 48.7, 33.1, 32.9, 32.8, 32.7, 32.6, 25.6, 25.5, 24.9, 24.8, 24.7, 23.1. **HRMS** (ESI) calculated for $C_{26}H_{29}N_2O_4^+$ ([M+H]$^+$): 433.2127, found 433.2135.

Methyl 2-(1-(*N*-(2-ethynylphenyl)acetamido)-2-oxo-2-(phenethylamino)ethyl)benzoate **(5ae)**



Pale yellow solid, 103 mg, 37% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.13 (s, 0.1H), 7.83 – 7.79 (m, 0.3H), 7.78 – 7.72 (m, 1.3H), 7.59 – 7.51 (m, 0.4H), 7.45 – 7.40 (m, 0.3H), 7.37 – 7.33 (m, 0.2H), 7.35 – 7.29 (m, 1H), 7.31 – 7.25 (m, 0.4H), 7.27 – 7.18 (m, 3H), 7.20 – 7.15 (m, 2.3H), 7.17 – 7.13 (m, 1H), 7.13 – 7.10 (m, 0.7H), 7.12 – 7.06 (m, 0.7H), 7.07 – 7.02 (m, 2H), 6.67 – 6.61 (m, 0.3H), 6.55 (s, 0.3H), 6.37 – 6.31 (m, 0.7H), 3.87 (s, 2H), 3.83 (s, 1H), 3.71 – 3.63 (m, 0.2H), 3.61 – 3.46 (m, 1.8H), 3.35 – 3.27 (m, 0.3H), 2.85 (s, 0.7H), 2.81 (s, 0.3H), 2.79 – 2.74 (m, 1.7H), 1.93 (s, 1H), 1.86 (s, 2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.9, 171.2, 170.3, 169.3, 168.3, 161.3, 142.9, 139.6, 139.3, 136.7, 134.3, 133.7, 133.3, 132.1, 132.0, 131.93, 131.86, 131.1, 130.8, 130.4, 130.23, 130.21, 130.0, 129.8, 129.2, 129.0, 128.89, 128.86, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 126.8, 126.4, 126.3, 124.6, 123.4, 82.7, 82.3, 81.0, 80.0, 64.5, 59.7, 52.6, 52.5, 41.2, 41.2, 35.8, 35.6, 23.2, 22.8. **HRMS** (ESI) calculated for $C_{28}H_{27}N_2O_4^+$ ([M+H]$^+$): 455.1965, found 455.1969.

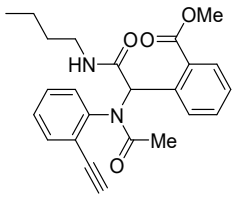
Methyl 2-(1-(*N*-(2-ethynylphenyl)acetamido)-2-oxo-2-(phenylamino)ethyl)benzoate **(5af)**



Yellow solid, 105 mg, 27% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.61 (s, 0.3H), 8.45 (s, 0.7H), 7.89 – 7.86 (m, 0.3H), 7.84 – 7.81 (m, 0.7H), 7.77 – 7.73 (m, 0.6H), 7.72 – 7.69 (m, 0.2H), 7.55 – 7.48

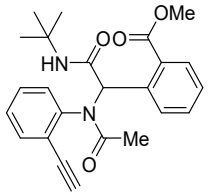
(m, 2H), 7.46 – 7.44 (m, 0.4H), 7.40 – 7.35 (m, 1H), 7.34 – 7.30 (m, 0.5H), 7.29 – 7.26 (m, 1H), 7.25 – 7.24 (m, 0.7H), 7.24 – 7.22 (m, 0.3H), 7.22 – 7.20 (m, 1.4H), 7.20 – 7.17 (m, 0.9H), 7.17 – 7.16 (m, 0.7H), 7.15 – 7.14 (m, 0.4H), 7.14 – 7.12 (m, 0.6H), 7.11 – 7.09 (m, 0.3H), 7.09 – 7.06 (m, 0.8H), 7.06 – 7.02 (m, 0.8H), 6.99 (s, 0.2H), 6.86 (s, 0.2H), 3.96 (s, 2.3H), 3.89 (s, 0.7H), 3.16 (s, 0.3H), 3.05 (s, 0.7H), 1.97 (s, 0.7H), 1.89 (s, 2.3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.4, 171.5, 168.8, 168.7, 168.5, 168.2, 168.0, 167.3, 147.8, 147.7, 147.2, 143.5, 142.7, 140.6, 139.4, 138.6, 138.6, 138.3, 138.1, 135.6, 134.3, 133.8, 133.5, 133.3, 132.14, 132.13, 132.0, 131.8, 131.71, 131.69, 131.6, 131.1, 130.9, 130.5, 130.4, 130.3, 130.2, 130.0, 129.91, 129.87, 129.0, 129.0, 128.92, 128.89, 128.53, 128.47, 128.35, 128.31, 128.2, 124.6, 124.3, 124.2, 124.1, 124.0, 123.4, 123.1, 120.3, 120.0, 119.8, 119.2, 114.2, 83.0, 82.4, 80.7, 80.0, 63.3, 61.7, 60.3, 52.9, 52.8, 52.7, 23.2, 23.1. **HRMS** (ESI) calculated for $C_{26}H_{23}N_2O_4^+$ ($[M+H]^+$): 427.1658, found 427.1653.

Methyl 2-(2-(butylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)benzoat**e (5ag)**



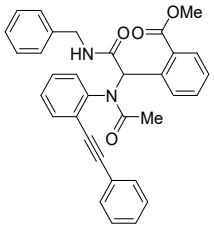
White solid, 93 mg, 18% (mixture of rotamers≈2:1). Purification by silica gel flash column chromatography(PE:EA=5:1→2:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.85 (ddd, *J* = 16.32, 7.92, 1.38 Hz, 1H), 7.76 – 7.70 (m, 1H), 7.49 – 7.44 (m, 0.3H), 7.39 – 7.27 (m, 1.7H), 7.25 – 7.21 (m, 0.4H), 7.20 – 7.17 (m, 2H), 7.17 – 7.13 (m, 1H), 7.07 – 7.02 (m, 1.4H), 6.53 (s, 0.3H), 6.38 (t, *J* = 5.90 Hz, 0.3H), 6.23 (t, *J* = 5.90 Hz, 0.7H), 3.91 (s, 2H), 3.83 (s, 1H), 3.30 – 3.22 (m, 1.3H), 3.22 (s, 0.3H), 3.21 – 3.15 (m,0.7H), 2.98 (s, 0.7H), 1.92 (s, 1H), 1.84 (s, 2H), 1.47 – 1.36 (m, 2H), 1.29 – 1.20 (m, 2H), 0.84 (dt, J = 9.79, 7.36 Hz, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.1, 170.4, 142.7, 134.2, 133.7, 133.2, 132.1, 132.0, 131.0, 130.7, 130.3, 130.1, 130.0, 129.7, 128.3, 128.0, 123.5, 82.6, 82.1, 80.0, 64.5, 59.3, 52.6, 39.6, 39.5, 31.6, 31.5, 23.1, 20.1, 20.0, 13.8. **HRMS (ESI)** calculated for $C_{26}H_{23}N_2O_4^+$ ($[M+H]^+$): 452.1902, found 452.1907.

Methyl 2-(2-(*tert*-butylamino)-1-(*N*-(2-ethynylphenyl)acetamido)-2-oxoethyl)benzoate **(5ah)**



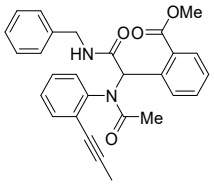
pale yellow solid, 113 mg, 46% (mixture of rotamers≈2:1). Purification by silica gel flash column chromatography(PE:EA=5:1→2:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.87 (ddd, *J* = 17.41, 7.88, 1.34 Hz, 1H), 7.76 – 7.71 (m, 1H), 7.51 – 7.44 (m, 1H), 7.36 – 7.28 (m, 1.4H), δ 7.24 (td, *J* = 7.58, 1.29 Hz, 0.3H), 7.21 – 7.12 (m, 2.2H), 7.10 – 7.04 (m, 2H), 6.11 (s, 0.3H), 6.11 (s, 0.7H), 5.91 (s, 0.3H), 3.92 (s, 2H), 3.83 (s, 1H), 3.25 (s, 0.3H), 2.99 (s, 0.7H)., 1.99 (s, 1H), 1.86 (s, 2H), 1.31 (s, 6H), 1.16 (s, 3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.0, 169.6, 168.4, 142.8, 134.5, 133.6, 133.2, 132.2, 132.1, 132.0, 131.9, 130.7, 130.5, 130.4, 130.1, 129.7, 129.4, 128.2, 128.0, 127.9, 127.7, 123.5, 123.0, 82.8, 82.1, 65.7, 59.8, 52.6, 51.5, 28.8, 28.3, 23.3, 23.2. **HRMS (ESI)** calculated for $C_{24}H_{27}N_2O_4^+$ ($[M+H]^+$): 407.1965, found 407.1968.

Methyl 2-(2-(benzylamino)-2-oxo-1-(*N*-(2-(phenylethynyl)phenyl)acetamido)ethyl)benzoate (**5ai**)



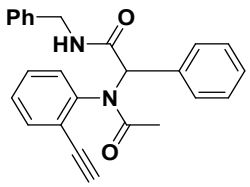
Yellow solid, 283 mg, 67% (mixture of rotamers≈3:1). Purification by silica gel flash column chromatography(PE:EA=5:1→2:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.91 – 7.83 (m, 1.2H), 7.70 (dd, *J* = 7.80, 1.45 Hz, 0.7H), 7.51 (dt, *J* = 7.94, 1.59 Hz, 0.5H), 7.48 – 7.43 (m, 2H), 7.39 – 7.34 (m, 3.3H), 7.33 (d, *J* = 1.69 Hz, 1H), 7.30 (td, *J* = 7.66, 1.80 Hz, 0.4H), 7.28 – 7.21 (m, 4H), 7.21 – 7.15 (m, 4H), 7.15 – 7.07 (m, 1.4H), 6.88 (t, *J* = 5.96 Hz, 0.7H), 6.67 (s, 0.2H), 6.60 (t, *J* = 6.00 Hz, 0.2H), δ 4.56 – 4.29 (m, 2H), 3.79 (s, 0.8H), 3.28 (s, 2.2H), 2.07 (s, 0.8H), 1.97 (s, 2.2H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 170.8, 168.0, 142.3, 138.5, 134.3, 132.9, 132.3, 132.2, 132.2, 132.2, 132.0, 131.8, 131.5, 130.9, 130.6, 130.5, 130.0, 129.8, 129.0, 129.0, 128.8, 128.5, 128.5, 128.5, 128.3, 128.1, 127.9, 127.6, 127.2, 127.1, 124.6, 122.5, 94.8, 85.7, 65.3, 59.6, 52.1, 43.7, 43.5, 23.2. **HRMS (ESI)** calculated for $C_{33}H_{29}N_2O_4^+$ ($[M+H]^+$): 517.2122, found 517.2128.

Methyl 2-(2-(benzylamino)-2-oxo-1-(*N*-(2-(prop-1-yn-1-yl)phenyl)acetamido)ethyl)benzoate **(5aj)**



White solid, 120 mg, 70% (mixture of rotamers≈2:1). Purification by silica gel flash column chromatography(PE:EA=5:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.85 (dd, *J* = 7.80, 1.47 Hz, 0.3H), 7.81 – 7.76 (m, 0.7H), 7.72 (dd, *J* = 7.95, 1.30 Hz, 0.3H), 7.66 (dt, *J* = 7.78, 0.92 Hz, 0.7H), 7.37 (td, *J* = 7.67, 1.53 Hz, 0.3H), 7.33 (ddd, *J* = 14.04, 5.78, 3.67 Hz, 0.6H), 7.28 (ddd, *J* = 14.32, 7.40, 1.28 Hz, 1.4H), 7.26 – 7.23 (m, 2H), 7.22 (dt, *J* = 2.35, 1.22 Hz, 0.5H), 7.22 – 7.18 (m, 2.2H), 7.17 – 7.11 (m, 4H), 6.79 (t, *J* = 5.75 Hz, 1H), 6.59 (s, 0.3H), 4.56 – 4.42 (m, 2H), 3.89 (s, 2H), 3.79 (s, 1H), 1.95 (s, 1H), 1.88 (s, 2H), 1.81 (s, 2H), 1.79 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.5, 170.3, 168.3, 142.0, 138.6, 134.6, 133.2, 132.9, 131.9, 131.8, 131.7, 131.5, 131.1, 130.9, 130.5, 130.0, 129.6, 129.1, 128.6, 128.5, 128.3, 128.1, 128.0, 127.6, 127.4, 127.3, 127.2, 125.1, 91.5, 76.2, 65.1, 59.9, 52.6, 43.7, 43.7, 23.2, 23.2, 4.4. **HRMS (ESI)** calculated for $C_{28}H_{27}N_2O_4^+$ ($[M+H]^+$): 455.1965, found 455.1969.

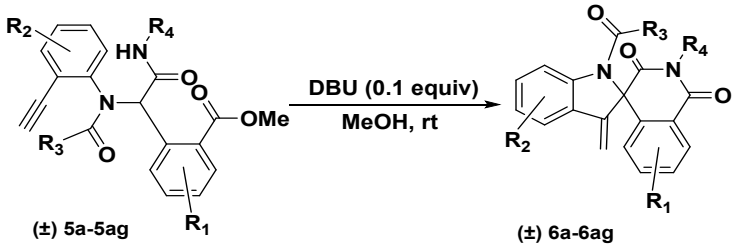
N-benzyl-2-(*N*-(2-ethynylphenyl)acetamido)-2-phenylacetamide **(5ak)**



White solid, 157 mg, 60% (mixture of rotamers≈2:1). Purification by silica gel flash column chromatography(PE:EA=5:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.82 (dd, *J* = 8.0, 1.2 Hz, 0.8H),

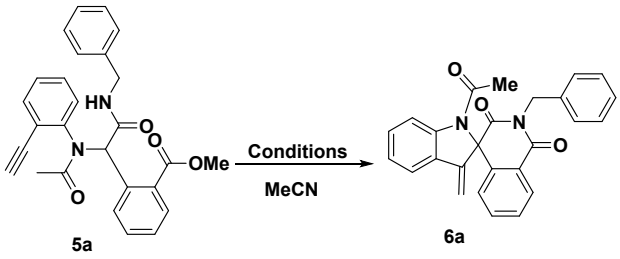
7.47 – 7.43 (m, 0.2H), 7.39 – 7.35 (m, 0.5H), 7.33 – 7.31 (m, 0.6H), 7.30 – 7.27 (m, 2.4H), 7.25 – 7.21 (m, 3.9H), 7.20 – 7.17 (m, 2H), 7.15 – 7.11 (m, 1.7H), 7.10 – 7.06 (m, 1.6H), 7.01 – 6.93 (m, 0.5H), 6.24 – 6.16 (m, 0.8H), 6.09 (s, 0.8H), 5.55 (s, 0.2H), 4.58 – 4.52 (m, 1H), 4.51 – 4.43 (m, 1H), 3.10 (s, 0.8H), 2.70 (s, 0.2H), 1.92 (s, 0.6H), 1.91 (s, 2.4H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.9, 171.3, 170.3, 169.3, 142.3, 138.2, 138.2, 135.1, 133.8, 133.1, 133.1, 131.4, 131.0, 130.3, 130.1, 130.1, 129.7, 128.9, 128.8, 128.8, 128.7, 128.7, 128.6, 128.5, 128.5, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.5, 127.5, 126.2, 123.6, 122.9, 82.8, 82.2, 80.8, 80.6, 68.8, 65.3, 44.0, 43.9, 23.1, 23.0. **HRMS (ESI)** calculated for $C_{25}H_{23}N_2O_4^+$ ([M+H]$^+$): 383.1754, found 383.1757.

General procedure for the synthesis of spiroindolines 6a-6ag.



To a solution of Ugi adduct **5** (0.17 mmol, 1.0 equiv) in methanol (1.7 mL) was added DBU (0.017 mmol, 0.1 equiv). The reaction mixture was stirred at room temperature for 10 minutes that Ugi adduct **5** was fully consumed. After completion, the mixture was evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/Petroleum ether = 1: 2) to afford the desired product **6**.

Table S3: Preliminary screening of catalysts and bases

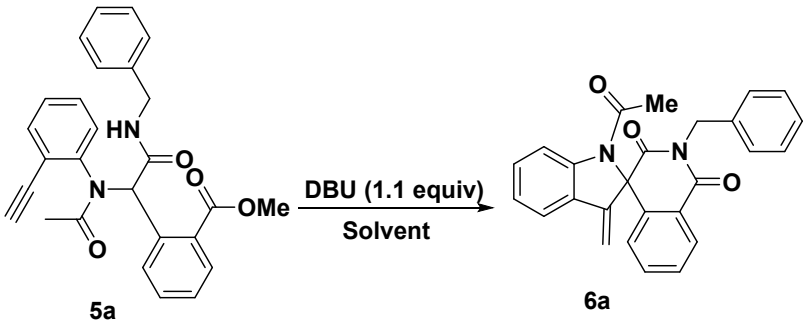


Entry	Catalyst	Base[a] (equiv)	T (℃)	Time	Yield (%)
1	$InCl_3$(20 mol%)	K_2CO_3	80	12 h	95
2	$In(OTf)_3$(20 mol%)	K_2CO_3	80	12 h	81
3	/	DBU	rt	10 min	89
4	/	TEA (5.0)	rt	5 h	Trace
5	/	DIPEA (5.0)	rt	5 h	Trace
6	/	K_2CO_3	rt	1 h	87
7	/	KOH	rt	30 min	56
8	/	NaOH	rt	10 min	39
9	/	DMAP	rt	2 h	0

10	/	DABCO	rt	2 h	0
11	/	PPh_3	rt	13 h	Trace
12	/	DPPE	rt	2 h	Trace
13	/	DPPB	rt	2 h	Trace
14	/	NaOEt	rt	10 min	82
15	/	Cs_2CO_3	rt	30 min	88
16	/	TBD (0.1)	rt	40 min	98
17	/	DBN (0.1)	rt	20 min	95

[a] Base: 1.1 equiv.

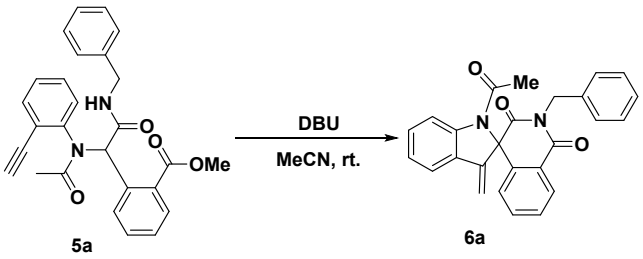
Table S4: Preliminary screening of the solvents



5a 6a

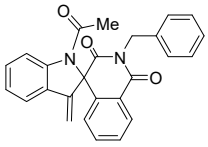
Entry	Solvent	Time	Yield (%)
1	MeOH	10 min	98
2	EtOH	10 min	91
3	IPA	10 min	77
4	THF	10 min	98
5	EA	10 min	88
6	Toluene	10 min	98

Table S5: Preliminary screening of the equivalent of base



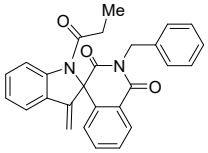
Entry	DBU (equiv)	Time	Yield (%)
1	0.1	10 min	87
2	0.2	10 min	81
3	0.5	10 min	84
4	0.02	3 h	17
5	0.05	3 h	61
6	1.1	10 min	89

1-acetyl-2'-benzyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6a)**



Pale yellow solid, 65 mg, 98% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 5: 1→4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.55 (d, *J* = 8.3 Hz, 0.2H), 8.34 (d, *J* = 7.6 Hz, 0.2H), 8.30 – 8.25 (m, 0.8H), 7.61 (t, *J* = 7.1 Hz, 0.2H), 7.54 (t, *J* = 7.2 Hz, 0.2H), 7.52 – 7.46 (m, 1.6H), 7.48 – 7.41 (m, 1.3H), 7.44 – 7.39 (m, 3.7H), 7.31 – 7.26 (m, 2H), 7.25 – 7.19 (m, 1H), 7.18 – 7.12 (m, 1H), 7.09 (d, *J* = 7.7 Hz, 0.8H), 5.40 (d, *J* = 2.1 Hz, 0.8H), 5.37 (d, *J* = 2.4 Hz, 0.2H), 5.28 (s, 0.4H), 5.26 (s, 0.6H), 5.21 (d, *J* = 7.4 Hz, 0.7H), 5.18 (d, *J* = 7.0 Hz, 0.3H), 4.54 (d, *J* = 2.0 Hz, 0.8H), 4.50 (d, *J* = 2.3 Hz, 0.2H), 2.54 (s, 2H), 1.61 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.4, 169.2, 168.8, 167.3, 164.1, 163.5, 147.0, 146.3, 145.4, 143.9, 141.3, 140.5, 136.8, 136.2, 135.6, 134.6, 131.5, 131.1, 130.1, 129.5, 129.4, 128.7, 128.6, 128.5, 128.4, 128.1, 127.7, 127.5, 125.0, 124.3, 123.9, 123.1, 122.8, 121.4, 113.5, 105.1, 104.3, 73.0, 44.7, 44.2, 25.6, 24.7. **HRMS** (ESI) calculated for $C_{26}H_{21}N_2O_3^+$ ($[M+H]^+$): 409.1547, found 409.1545.

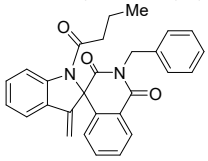
2'-benzyl-3-methylene-1-propionyl-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6b)**



White solid, 66 mg, 89% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.58 (d, *J* = 8.4 Hz, 0.2H), 8.35

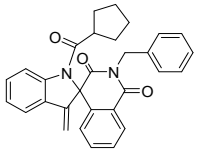
(dd, *J* = 7.8, 1.8 Hz, 0.2H), 8.28 (dd, *J* = 7.8, 1.2 Hz, 0.8H), 7.62 – 7.52 (m, 0.6H), 7.50 – 7.46 (m, 1.7H), 7.46 – 7.39 (m, 4.8H), 7.30 – 7.26 (m, 2H), 7.24 – 7.18 (m, 1H), 7.16 – 7.12 (m, 1H), 7.08 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 5.40 – 5.37 (m, 1H), 5.32 – 5.25 (m, 1H), 5.24 – 5.16 (m, 1H), 4.54 – 4.48 (m, 1H), 2.93 – 2.84 (m, 1H), 2.83 – 2.63 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 2.4H), 0.82 (t, *J* = 7.2 Hz, 0.6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.5, 171.0, 169.5, 169.3, 164.0, 163.5, 147.1, 146.4, 145.4, 143.7, 141.5, 140.6, 136.9, 136.2, 135.5, 134.6, 131.5, 131.0, 130.1, 129.5, 129.4, 129.3, 128.6, 128.5, 128.4, 128.0, 127.7, 127.5, 124.9, 124.8, 124.3, 124.1, 123.8, 123.5, 123.0, 122.7, 121.4, 117.9, 113.8, 105.0, 104.2, 73.0, 44.7, 44.1, 31.6, 30.7, 8.9, 8.4. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ([M+H]$^+$): 423.1703, found 423.1700.

2'-benzyl-1-butyryl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6c)**



Pale yellow solid, 63 mg, 85% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.58 (d, *J* = 8.4 Hz, 0.2H), 8.36 (dd, *J* = 7.8, 1.2 Hz, 0.2H), 8.27 (dd, *J* = 7.8, 1.2 Hz, 0.8H), 7.61 – 7.57 (m, 0.2H), 7.56 – 7.52 (m, 0.4H), 7.50 – 7.40 (m, 6.6H), 7.29 – 7.26 (m, 2H), 7.24 – 7.19 (m, 1H), 7.16 – 7.12 (m, 1H), 7.08 (d, *J* = 1.2 Hz, 0.3H), 7.07 (d, *J* = 1.2 Hz, 0.3H), 5.39 (d, *J* = 1.8 Hz, 1H), 5.34 – 5.24 (m, 1H), 5.23 – 5.14 (m, 1H), 4.53 (d, *J* = 2.4 Hz, 1H), 2.88 – 2.66 (m, 2H), 1.77 – 1.68 (m, 2H), 0.97 (t, *J* = 7.8 Hz, 2.5H), 0.46 (t, *J* = 7.2 Hz, 0.5H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 171.6, 170.3, 169.5, 169.3, 164.0, 163.6, 147.2, 147.1, 146.4, 145.4, 143.7, 141.6, 140.8, 136.9, 135.5, 134.5, 131.5, 131.0, 130.0, 129.5, 129.4, 129.3, 128.6, 128.5, 128.3, 128.0, 127.7, 127.4, 124.9, 124.8, 124.6, 124.4, 124.1, 123.8, 123.4, 123.0, 122.7, 121.4, 119.2, 118.0, 113.9, 105.0, 104.2, 73.1, 44.7, 44.2, 39.1, 38.4, 18.1, 17.6, 13.8, 13.4. **HRMS** (ESI) calculated for $C_{28}H_{25}N_2O_3^+$ ([M+H]$^+$): 437.1860, found 437.1857.

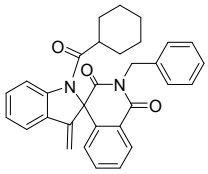
2'-benzyl-1-(cyclopentanecarbonyl)-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6d)**



Pale yellow solid, 57 mg, 76% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.59 (d, *J* = 8.4 Hz, 0.3H), 8.36 (dd, *J* = 7.8, 1.8 Hz, 0.3H), 8.27 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.61 – 7.58 (m, 0.3H), 7.56 – 7.52 (m, 0.4H), 7.50 – 7.45 (m, 2.7H), 7.44 – 7.39 (m, 3.4H), 7.30 – 7.27 (m, 1.7H), 7.26 – 7.24 (m, 0.3H), 7.24 – 7.18 (m, 1H), 7.17 – 7.11 (m, 1.2H), 7.07 (dd, *J* = 7.8, 1.2 Hz, 0.7H), 5.42 – 5.34 (m, 1.3H), 5.26 (d, *J* = 13.8 Hz,0.7H), 5.21 (d, *J* = 13.8 Hz, 0.7H), 5.09 (d, *J* = 13.8 Hz, 0.3H), 4.58 (d, *J* = 2.4 Hz, 0.3H), 4.50 (d, *J* = 1.8 Hz, 0.7H), 3.51 – 3.44 (m, 0.7H), 2.08 – 1.90 (m, 1.3H), 1.89 – 1.83 (m, 0.7H), 1.81 – 1.76 (m, 0.3H), 1.72 – 1.62 (m, 3.3H), 1.45 – 1.36 (m, 0.7H), 1.10 – 1.00 (m, 0.7H), 0.65 – 0.56 (m, 0.3H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 176.7, 173.4, 169.5, 169.2, 164.1, 163.7, 147.2, 146.9, 146.3, 145.3, 143.6, 141.8, 141.0, 136.9, 136.5, 135.3, 134.5, 131.4, 131.0, 130.1, 129.5, 129.4, 129.2, 128.7, 128.6, 128.5, 128.3, 128.0, 127.9, 127.4, 125.0, 124.9, 124.6, 124.6, 124.1, 124.0, 123.8, 123.4, 122.8, 122.7, 121.3,

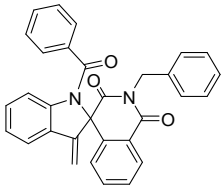
119.2, 119.2, 118.1, 114.0, 104.8, 104.1, 73.3, 73.3, 46.2, 44.9, 44.2, 44.1, 29.9, 29.0, 26.3, 26.3, 25.9, 25.7. **HRMS** (ESI) calculated for $C_{30}H_{27}N_2O_3^+$ ([M+H]$^+$): 463.2016, found 463.2017.

2'-benzyl-1-(cyclohexanecarbonyl)-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6e)**



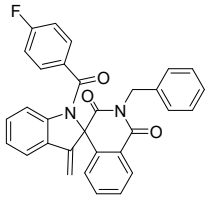
Pale yellow solid, 73 mg, 97% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 5: 1→4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.58 (d, *J* = 7.8 Hz, 0.3H), 8.37 (dd, *J* = 8.4, 1.8 Hz, 0.3H), 8.26 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.61 – 7.58 (m, 0.3H), 7.56 – 7.51 (m, 1H), 7.49 – 7.44 (m, 1.6H), 7.44 – 7.38 (m, 3.3H), 7.34 – 7.26 (m, 2.8H), 7.23 – 7.19 (m, 1H), 7.16 – 7.12 (m, 1H), 7.06 – 7.03 (m, 0.7H), 5.40 (d, *J* = 2.4 Hz, 0.3H), 5.36 (d, *J* = 1.8 Hz, 0.7H), 5.32 (d, *J* = 13.8 Hz, 0.3H), 5.26 (d, *J* = 14.4 Hz, 0.7H), 5.21 (d, *J* = 14.4 Hz, 0.7H), 5.11 (d, *J* = 13.8 Hz, 0.3H), 4.55 (d, *J* = 2.4 Hz, 0.3H), 4.50 (d, *J* = 2.4 Hz, 0.7H), 3.01 – 2.93 (m, 0.7H), 2.02 – 1.92 (m, 1.5H), 1.90 – 1.79 (m, 1.5H), 1.77 – 1.70 (m, 0.7H), 1.54 – 1.35 (m, 4.6H), 1.33 – 1.29 (m, 1H), 1.25 – 1.20 (m, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 175.5, 173.4, 169.5, 169.3, 164.1, 163.6, 147.2, 147.1, 146.3, 145.2, 143.5, 141.7, 140.9, 136.9, 136.3, 135.2, 134.5, 131.4, 131.2, 129.9, 129.5, 129.3, 128.68, 128.65, 128.5, 128.3, 128.1, 127.9, 127.4, 125.1, 124.9, 124.8, 124.6, 124.10, 124.06, 123.8, 123.4, 122.74, 122.68, 121.3, 119.2, 118.2, 113.7, 104.8, 104.1, 73.2, 73.1, 46.1, 45.0, 44.1, 43.4, 28.8, 28.8, 28.0, 25.9, 25.6, 25.5, 25.4. **HRMS** (ESI) calculated for $C_{31}H_{29}N_2O_3^+$ ([M+H]$^+$): 477.2173, found 477.2178.

1-benzoyl-2'-benzyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6f)**



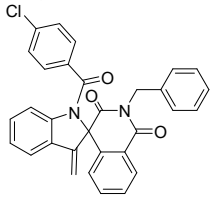
Pale white solid, 63 mg, 77% yield. Purification by silica gel flash column chromatography (PE/EA = 5: 1→4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.32 (d, *J* = 8.4 Hz, 1H), 7.66 – 7.54 (m, 4H), 7.53 – 7.41 (m, 6H), 7.37 – 7.28 (m, 3H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.08 – 6.99 (m, 2H), 6.24 – 6.14 (m, 1H), 5.44 (d, *J* = 2.4 Hz, 1H), 5.34 – 5.21 (m, 2H), 4.59 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.2, 167.4, 164.0, 145.9, 144.5, 140.7, 136.8, 135.2, 134.7, 131.6, 130.3, 129.5, 129.1, 128.7, 128.5, 128.5, 127.7, 127.5, 124.4, 124.2, 123.3, 122.3, 114.4, 105.2, 73.3, 44.2. **HRMS** (ESI) calculated for $C_{31}H_{23}N_2O_3^+$ ([M+H]$^+$): 471.1709, found 471.1712.

2'-benzyl-1-(4-fluorobenzoyl)-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6g)**



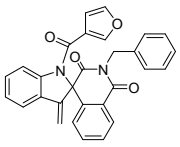
White solid, 62 mg, 85% yield. Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.31 (d, *J* = 6.6 Hz, 1H), 7.66 (s, 2H), 7.57 (td, *J* = 7.8, 1.2 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.46 – 7.41 (m, 3H), 7.34 – 7.27 m, 3H), 7.26 – 7.22 (m, 1H), 7.21 – 7.13 (m, 2H), 7.11 – 7.03 (m, 2H), 6.26 (d, *J* = 9.0 Hz, 1H), 5.45 (d, *J* =1.8 Hz, 1H), 5.32 – 5.22 (m, 2H), 4.59 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.2, 166.5, 165.5, 163.9, 147.2, 145.8, 144.4, 140.6, 136.8, 134.8, 131.3, 130.3, 129.5, 128.7, 128.6, 128.5, 127.5, 124.6, 124.4, 124.1, 123.3, 122.4, 119.2, 116.3, 114.3, 105.4, 73.5, 44.2. **HRMS** (ESI) calculated for $C_{31}H_{22}FN_2O_3^+$ ([M+H]$^+$): 489.1614, found 489.1615.

2'-benzyl-1-(4-chlorobenzoyl)-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6h)**



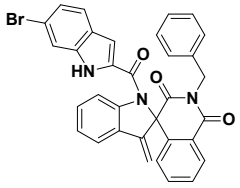
White solid, 61 mg, 81% yield. Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.31 (d, *J* = 7.8 Hz, 1H), 7.63 – 7.54 (m, 3H), 7.48 (t, *J* = 7.2 Hz, 3H), 7.44 (t, *J* = 7.2 Hz, 3H), 7.33 – 7.27 (m, 3H), 7.25 – 7.20 (m, 1H), 7.13 – 7.00 (m, 2H), 6.27 (d, *J* = 8.4 Hz, 1H), 5.44 (d, *J* = 2.4 Hz, 1H), 5.35 – 5.19 (m, 2H), 4.59 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.2, 166.4, 163.9, 145.7, 144.2, 140.5, 137.9, 136.7, 134.8, 133.6, 130.4, 129.6, 129.4, 128.8, 128.6, 128.5, 127.5, 124.5, 124.3, 123.3, 122.4, 114.4, 105.5, 73.5, 44.2. **HRMS** (ESI) calculated for $C_{31}H_{22}ClN_2O_3^+$ ([M+H]$^+$): 505.1319, found 505.1327.

2'-benzyl-1-(furan-3-carbonyl)-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6i)**



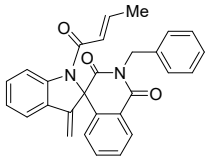
Pale brown solid, 72 mg, 96% yield. Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.24 (d, *J* = 7.8 Hz, 1H), 8.04 – 7.64 (m, 1H), 7.52 (td, *J* = 7.8, 1.8 Hz, 1.3H), 7.46 – 7.36 (m, 4.7H), 7.29 – 7.25 (m, 1H), 7.26 – 7.17 (m, 4H), 7.12 – 7.03 (m, 1H), 7.03 – 6.89 (m, 1H), 6.75 – 6.39 (m, 1H), 5.40 (d, *J* = 2.4 Hz, 1H), 5.25 (s, 0.4H), 5.23 – 5.17 (m, 1.6H), 4.51 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.3, 163.8, 145.7, 143.5, 140.5, 136.6, 134.8, 130.5, 129.5, 128.7, 128.6, 128.5, 127.6, 124.5, 123.5, 122.4, 121.7, 114.3, 109.8, 105.3, 73.5, 44.2. **HRMS** (ESI) calculated for $C_{29}H_{21}N_2O_4^+$ ([M+H]$^+$): 461.1501, found 461.1504.

2'-benzyl-1-(6-bromo-1*H*-indole-2-carbonyl)-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6j)**



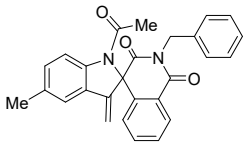
Pale yellow solid, 73 mg, 91% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 4: 1→2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 9.32 (s, 1H), 8.29 (dd, *J* = 7.92, 1.47 Hz, 1H), 7.54 (dd, *J* = 7.63, 1.46 Hz, 1H), 7.52 – 7.34 (m, 7H), 7.29 – 7.16 (m, 6H), 7.12 (s, 1H), 5.49 (d, *J* = 2.18 Hz, 1H), 5.21 (s, 2H), 4.60 (d, *J* = 2.20 Hz, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.3, 163.8, 144.8, 137.5, 136.6, 134.9, 130.5, 130.3, 129.5, 129.1, 128.5, 127.6, 127.4, 125.6, 124.8, 124.7, 123.7, 123.6, 122.4, 119.3, 115.0, 105.5, 44.4. **HRMS** (ESI) calculated for $C_{33}H_{23}BrN_3O_3^+$ ([M+H]$^+$): 588.0923, found 588.0930.

2'-benzyl-1-(but-2-enoyl)-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6k)**



Pale yellow solid, 50 mg, 96% yield (mixture of rotamers≈2:1). Purification by silica gel flash column chromatography(PE:EA=4:1→2:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.60 (d, *J* = 8.15 Hz, 0.3H), 8.31 (dd, *J* = 40.89, 7.65 Hz, 7H), 7.62 – 7.34 (m, 7H), 7.31 – 7.25 (m, 2H), 7.25 – 7.10 (m, 3H), 6.94 (dq, *J* = 13.97, 6.80 Hz, 0.7H), 6.82 (s, 0.3H), 6.65 (d, *J* = 15.19 Hz, 0.7H), 5.40 (d, *J* = 10.34 Hz, 1H), 5.24 (q, *J* = 12.86, 11.95 Hz, 2H), 4.54 (d, *J* = 18.19 Hz, 1H), 1.99 (d, *J* = 6.92 Hz, 2H), 1.29 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.3, 164.0, 145.1, 144.7, 144.1, 141.0, 136.9, 134.6, 130.9, 129.4, 128.6, 128.5, 128.0, 127.7, 127.5, 125.0, 124.2, 124.0, 123.4, 122.7, 121.4, 118.2, 114.2, 105.2, 104.2, 44.7, 44.1, 18.7, 18.2. **HRMS** (ESI) calculated for $C_{28}H_{23}N_2O_3^+$ ([M+H]$^+$): 435.1709, found 435.1720.

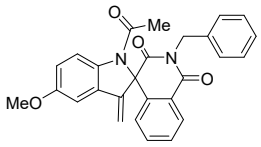
1-acetyl-2'-benzyl-5-methyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6l)**



Pale yellow solid, 67 mg, 90% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.41 (d, *J* = 8.4 Hz, 0.2H), 8.32 (dd, *J* = 7.8, 1.8 Hz, 0.2H), 8.25 (dd, *J* = 7.8, 1.8 Hz, 0.8H), 7.57 (td, *J* = 7.2, 1.2 Hz, 0.2H), 7.53 – 7.49 (m, 0.2H), 7.46 (td, *J* = 7.2, 1.2 Hz, 0.8H), 7.44 – 7.41 (m, 0.7H), 7.41 – 7.38 (m, 2.1H), 7.29 – 7.26 (m, 2.3H), 7.26 – 7.23 (m, 1.4H), 7.22 – 7.16 (m, 2.3H), 7.07 (dd, *J* = 7.8, 1.2 Hz, 0.8H), 5.34 (d, *J* = 1.8 Hz, 0.8H), 5.32 (d, *J* = 2.4 Hz, 0.2H), 5.29 – 5.22 (m, 1H), 5.21 – 5.14 (m, 1H), 4.49 (d, *J* = 1.8 Hz, 0.8H), 4.45 (d, *J* = 3.0 Hz, 0.2H), 2.49 (s, 2.2H), 2.34 (s, 2.2H), 2.33 (s, 0.8H), 1.58 (s, 0.8H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.4, 169.2, 168.5, 167.1, 164.0, 163.4, 146.9, 145.4, 144.2, 141.7, 141.3, 140.5, 136.8, 136.1, 135.6, 134.8, 134.6, 134.0, 132.2, 131.8, 129.9, 129.4, 129.3, 129.3, 128.6, 128.50, 128.47, 128.3, 128.0, 127.6, 127.4, 124.7, 124.2, 123.7, 123.5, 123.1, 123.0, 121.6, 117.6, 113.2, 104.7, 104.0, 73.6,

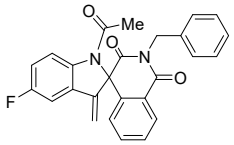
73.0, 44.6, 44.1, 25.4, 24.6, 21.1, 20.9. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ([M+H]$^+$): 423.1709, found 423.1718.

1-acetyl-2'-benzyl-5-methoxy-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6m)**



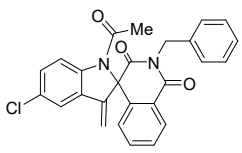
Pale yellow solid, 65 mg, 87% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography(PE:EA=5:1→3:1). **^{1}H NMR (600 MHz, CDCl$_3$)** δ 8.48 (d, *J* = 9.00 Hz, 0.2H), 8.34 (dd, *J* = 7.96, 1.43 Hz, 0.2H), 8.26 (dd, *J* = 7.88, 1.45 Hz, 0.7H), 7.61 (td, *J* = 7.57, 1.45 Hz, 0.3 H), 7.56 – 7.39 (m, 3.7H), 7.35 – 7.27 (m, 2.7H), 7.24 – 7.20 (m, 1H), 7.09 (dd, *J* = 7.85, 1.21 Hz, 0.7 H), 7.02 – 6.93 (m, 1.7H), 6.87 (d, *J* = 2.65 Hz, 0.2H), 5.35 (dd, *J* = 13.75, 2.43 Hz, 1H), 5.31 – 5.24 (m, 1H), 5.22 – 5.17 (m, 1H), 4.52 (dd, *J* = 25.21, 2.42 Hz, 1H), δ 3.82 (s, 2H), 3.81 (s, 1H)., 2.50 (s, 2H), 1.58 (s, 1H). **^{13}C NMR (151 MHz, CDCl$_3$)** δ 169.4, 169.2, 168.2, 166.7, 164.0, 163.5, 157.3, 156.8, 147.0, 145.5, 141.3, 140.5, 140.4, 137.9, 136.8, 136.2, 135.6, 134.6, 130.0, 129.5, 129.4, 129.4, 128.8, 128.65, 128.59, 128.4, 128.1, 127.5, 125.9, 124.3, 123.8, 123.6, 123.1, 118.8, 117.7, 117.6, 114.3, 106.9, 105.6, 105.2, 104.5, 73.7, 73.2, 55.9, 55.9, 44.7, 44.1, 25.3, 24.5. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_4^+$ ([M+H]$^+$): 439.1652, found 439.1651.

1-acetyl-2'-benzyl-5-fluoro-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6n)**



Pale yellow solid, 67 mg, 92% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography(PE: EA =5: 1→2: 1). **^{1}H NMR (600 MHz, CDCl$_3$)** δ 8.51 (dd, *J* = 9.10, 4.70 Hz, 0.3H), 8.33 (dd, *J* = 7.94, 1.43 Hz, 0.3H), 8.25 (dd, *J* = 7.86, 1.43 Hz, 0.7H), 7.61 (td, *J* = 7.62, 1.42 Hz, 0.4H), 7.54 (td, *J* = 7.66, 1.26 Hz, 0.5H), 7.51 – 7.46 (m, 0.8H), 7.45 – 7.40 (m, 1.5H), 7.38 (d, *J* = 7.42 Hz, 1.4H), 7.32 (dd, *J* = 8.94, 3.94 Hz, 0.9H), 7.28 (d, *J* = 6.60 Hz, 1H), 7.25 – 7.23 (m, 1H), 7.20 (tt, *J* = 7.85, 1.33 Hz, 1H), 7.14 – 7.05 (m, 2.5H), 7.02 (dd, *J* = 7.90, 2.64 Hz, 0.3H), 5.34 (dd, *J* = 15.61, 2.54 Hz, 1H), 5.25 (dd, *J* = 13.92, 11.20 Hz, 1H), 5.17 (dd, *J* = 13.91, 2.88 Hz, 1H), 4.54 (dd, *J* = 26.54, 2.53 Hz, 1H), 2.49 (s, 2H), 1.57 (s, 1H). **^{13}C NMR (151 MHz, CDCl$_3$)** δ 169.2, 166.9, 163.9, 144.7, 142.4, 141.0, 140.1, 136.7, 136.1, 135.7, 134.7, 130.1, 129.6, 129.5, 129.5, 129.4, 128.7, 128.6, 128.6, 128.1, 127.5, 124.3, 123.8, 123.1, 119.1, 119.0, 118.2, 117.8, 117.7, 114.4, 114.3, 109.6, 109.4, 107.8, 106.6, 105.8, 44.7, 44.2, 25.4, 24.5. **HRMS** (ESI) calculated for $C_{26}H_{20}FN_2O_3^+$ ([M+H]$^+$): 427.1452, found 427.1452.

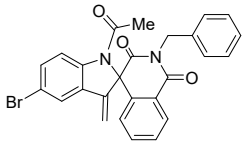
1-acetyl-2'-benzyl-5-chloro-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6o)**



White solid, 61 mg, 82% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column

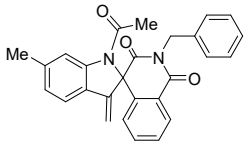
chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.42 (d, *J* = 9.0 Hz, 0.3H), 8.28 (dd, *J* = 7.8, 1.2 Hz, 0.3H), 8.20 (dd, *J* = 7.8, 1.8 Hz, 0.7H), 7.57 – 7.53 (m, 0.3H), 7.51 – 7.46 (m, 0.4H), 7.45 – 7.41 (m, 0.8H), 7.40 – 7.34 (m, 2H), 7.34 – 7.31 (m, 1.3H), 7.31 – 7.26 (m, 1.4H), 7.26 – 7.22 (m, 1.2H), 7.21 – 7.18 (m, 1.6H), 7.17 – 7.11 (m, 1H), 7.04 – 6.96 (m, 0.7H), 5.35 – 5.29 (m, 1H), 5.23 – 5.17 (m, 1H), 5.14 – 5.08 (m, 1H), 4.53 – 4.44 (m, 1H), 2.43 (s, 2H), 1.52 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.1, 168.9, 168.7, 167.1, 163.8, 163.2, 145.8, 144.7, 144.3, 142.4, 140.8, 140.0, 136.6, 136.0, 135.7, 134.7, 131.2, 130.7, 130.2, 130.1, 129.8, 129.6, 129.5, 129.4, 129.3, 128.7, 128.6, 128.5, 128.5, 128.1, 127.5, 126.5, 124.2, 123.7, 123.5, 123.1, 122.6, 121.2, 118.8, 114.4, 106.6, 105.8, 73.7, 73.3, 44.7, 44.2, 25.5, 24.5. **HRMS** (ESI) calculated for $C_{26}H_{20}ClN_2O_3^+$ ($[M+H]^+$): 443.1162, found 443.1166.

1-acetyl-2'-benzyl-5-bromo-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6p)**



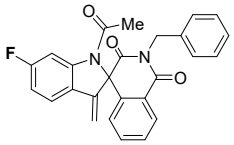
Pale yellow solid, 76 mg, 98% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 5:1→4:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.42 (d, *J* = 8.7 Hz, 0.3H), 8.33 (dd, *J* = 7.9, 1.4 Hz, 0.3H), 8.31 – 8.22 (m, 0.7H), 7.64 – 7.56 (m, 0.8H), 7.55 (d, *J* = 2.1 Hz, 0.8H), 7.55 – 7.50 (m, 0.4H), 7.51 – 7.45 (m, 2H), 7.45 – 7.38 (m, 1.7H), 7.39 – 7.35 (m, 1.3H), 7.30 – 7.25 (m, 1H), 7.24 (d, *J* = 5.8 Hz, 1H), 7.23 – 7.15 (m, 1H), 7.07 – 7.02 (m, 0.7H), 5.41 – 5.33 (m, 1H), 5.27 – 5.21 (m, 1H), 5.16 (dd, *J* = 13.9, 4.7 Hz, 1H), 4.53 (dd, *J* = 27.8, 2.6 Hz, 1H), 2.48 (s, 2H), 1.57 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.1, 168.8, 168.7, 167.1, 165.8, 163.8, 163.2, 145.6, 145.2, 144.1, 142.8, 140.8, 139.9, 136.6, 136.0, 135.7, 134.75, 134.69, 134.0, 133.7, 133.6, 133.2, 130.8, 130.2, 130.1, 129.6, 129.6, 129.5, 129.4, 129.2, 128.64, 128.57, 128.49, 128.45, 128.2, 128.1, 127.7, 127.6, 127.53, 127.51, 127.4, 126.8, 125.6, 125.1, 124.3, 124.2, 124.1, 123.7, 123.5, 123.13, 123.06, 119.2, 117.6, 117.1, 117.0, 115.1, 114.8, 106.6, 105.9, 73.6, 73.2, 44.7, 44.1, 25.5, 24.6. **HRMS** (ESI) calculated for $C_{26}H_{20}BrN_2O_3^+$ ($[M+H]^+$): 487.0657, found 487.0658.

1-acetyl-2'-benzyl-6-methyl-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6q)**



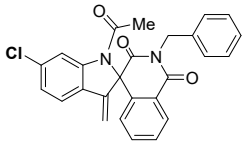
Brown solid, 72 mg, 99% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography(PE:EA = 4: 1→2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.40 (s, 0.2H), 8.34 (d, *J* = 7.87 Hz, 0.2H), 8.27 (dd, *J* = 7.90, 1.50 Hz, 0.7H), 7.62 – 7.38 (m, 4H), 7.36 (d, *J* = 7.78 Hz, 0.8H), 7.31 – 7.27 (m, 2.2H), 7.25 – 7.19 (m, 2H), 7.08 (dd, *J* = 7.80, 1.24 Hz, 0.7H), 6.97 (d, *J* = 7.80 Hz, 1H), 6.85 (dd, *J* = 11.71, 8.04 Hz, 0.6H), 5.33 – 5.24 (m, 2H), 5.23 – 5.16 (m, 1H), 4.44 (dd, *J* = 28.55, 2.28 Hz, 1H), 2.53 (s, 2H), 2.45 (d, *J* = 14.74 Hz, 3H), 2.30 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.2, 167.1, 163.9, 144.7, 144.4, 140.9, 136.9, 136.7, 135.7, 134.7, 130.2, 129.6, 129.4, 128.7, 128.6, 128.6, 128.5, 128.1, 127.5, 126.3, 125.2, 124.4, 124.2, 123.8, 123.6, 123.4, 123.1, 122.0, 118.2, 114.0, 105.7, 104.9, 44.7, 44.2, 25.6, 22.4. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ($[M+H]^+$): 423.1703, found 423.1703.

1-acetyl-2'-benzyl-6-fluoro-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6r)**



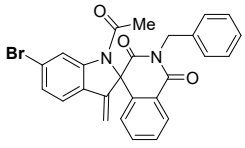
Pale yellow solid, 78 mg, 99% yield(mixture of rotamers≈2:1). Purification by silica gel flash column chromatography(PE:EA=4:1→3:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.27 (dd, *J* = 7.98, 1.43 Hz, 0.3H), 8.25 – 8.17 (m, 1H), 7.56 (td, *J* = 7.59, 1.43 Hz, 0.3H), 7.52 – 7.41 (m, 1H), 7.41 – 7.30 (m, 3H), 7.29 – 7.19 (m, 3H), 7.17 – 7.12 (m, 1H), 7.07 – 6.99 (m, 1.5H), 6.79 (td, *J* = 8.53, 1.99 Hz, 1H), 5.27 – 5.15 (m, 2H), 5.11 (dd, *J* = 14.02, 1.72 Hz, 1H), 4.40 (dd, *J* = 27.90, 2.55 Hz, 1H), 2.44 (s, 2H), 1.52 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.2, 168.9, 167.1, 165.5, 163.9, 163.3, 145.0, 144.3, 140.9, 136.7, 136.1, 135.7, 134.7, 130.1, 129.5, 129.4, 128.7, 128.6, 128.5, 128.1, 127.5, 124.2, 123.9, 123.8, 123.8, 123.6, 123.0, 122.4, 122.3, 120.8, 112.3, 112.1, 111.4, 111.2, 106.1, 105.9, 104.6, 104.6, 103.9, 102.0, 101.8, 44.7, 44.2. 25.5, 24.6. **HRMS** (ESI) calculated for $C_{26}H_{20}FN_2O_3^+$ ([M+H]$^+$): 427.1458, found 427.1460.

1-acetyl-2'-benzyl-6-chloro-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6s)**



Pale yellow solid, 71 mg, 95% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE:EA = 2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.60 (d, *J* = 1.93 Hz, 0.3H), 8.35 (dd, *J* = 7.89, 1.40 Hz, 0.3H), 8.27 (dd, *J* = 7.93, 1.45 Hz, 0.7H), 7.62 (td, *J* = 7.56, 1.39 Hz, 0.3H), 7.55 (t, *J* = 7.54 Hz, 0.3H), 7.51 (td, *J* = 7.59, 1.50 Hz, 0.7H), 7.47 – 7.41 (m, 1.3H), 7.41 – 7.36 (m, 2.6H), 7.33 – 7.24 (m, 3H), 7.24 – 7.18 (m, 1H), 7.13 (dd, *J* = 8.15, 1.63 Hz, 1H), 7.07 (dd, *J* = 7.84, 1.15 Hz, 0.7H), 5.35 (dd, *J* = 16.67, 2.52 Hz, 1H), 5.32 – 5.23 (m, 1H), 5.18 (d, *J* = 14.51 Hz, 1H), 4.52 (dd, *J* = 28.61, 2.54 Hz, 1H), 2.52 (s, 2H), 1.61 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.2, 167.1, 163.9, 144.7, 144.4, 140.9, 136.9, 136.7, 135.7, 134.7, 130.2, 129.6, 129.4, 128.7, 128.6, 128.6, 128.5, 128.1, 127.5, 126.3, 125.2, 124.4, 124.2, 123.8, 123.6, 123.4, 123.1, 122.0, 118.2, 114.0, 105.7, 104.9, 44.7, 44.2, 25.6, 24.6. **HRMS** (ESI) calculated for $C_{26}H_{20}ClN_2O_3^+$ ([M+H]$^+$): 443.1157, found 443.1159.

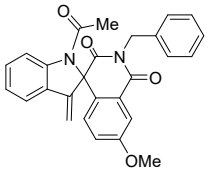
1-acetyl-2'-benzyl-6-bromo-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione **(6t)**



White solid, 55 mg, 97% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography(PE:EA=4:1→2:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.77 (d, *J* = 1.78 Hz, 0.3H), 8.35 (dd, *J* = 8.01, 1.40 Hz, 0.3H), 8.27 (dd, *J* = 7.91, 1.47 Hz, 0.6H), 7.63 (td, *J* = 7.59, 1.41 Hz, 0.3 H), 7.59 – 7.48 (m, 1.7H), 7.48 – 7.42 (m, 1.3H), 7.42 – 7.37 (m, 1.3H), 7.35 – 7.25 (m, 3.6H), 7.26 – 7.18 (m, 1.3H), 7.08 (dd, *J* = 7.79, 1.22 Hz, 0.7H), 5.38 (dd, *J* = 16.33, 2.52 Hz, 1H), 5.32 – 5.23 (m, 1H), 5.18

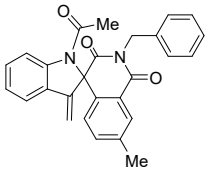
(dd, *J* = 13.86, 2.37 Hz, 1H), 4.54 (dd, *J* = 28.18, 2.53 Hz, 1H), 2.53 (s, 2H), 1.59 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.0, 167.0, 163.8, 144.7, 144.3, 140.8, 136.6, 135.6, 134.6, 130.0, 129.4, 129.3, 128.6, 128.5, 128.45, 128.43, 128.0, 127.4, 127.2, 126.6, 124.8, 124.1, 123.7, 123.6, 123.5, 122.9, 122.2, 120.9, 116.7, 105.7, 105.0, 44.6, 44.1, 25.5, 24.5. **HRMS** (ESI) calculated for $C_{26}H_{20}BrN_2O_3^+$ ($[M+H]^+$): 487.0657, found 487.0662.

1-acetyl-2'-benzyl-7'-methoxy-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6u)**



Pale yellow solid, 63 mg, 85% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 5: 1→4: 1).**^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.52 (d, *J* = 8.4 Hz, 0.2H), 7.76 (d, *J* = 3.0 Hz, 0.2H), 7.70 (d, *J* = 3.0 Hz, 0.8H), 7.47 – 7.45 (m, 0.8H), 7.43 – 7.41 (m, 0.5H), 7.39 – 7.37 (m, 3.8H), 7.36 – 7.35 (m, 0.2H), 7.28 – 7.26 (m, 0.7H), 7.25 – 7.24 (m, 0.7H), 7.23 – 7.22 (m, 0.2H), 7.21 – 7.18 (m, 1H), 7.13 – 7.12 (m, 0.2H), 7.12 – 7.10 (m, 1H), 7.08 (d, *J* = 9.0 Hz, 0.3H), 7.03 (d, *J* = 2.4 Hz, 0.3H), 7.01 (d, *J* = 3.0 Hz, 0.4H), 6.97 (s, 0.4H), 6.96 (s, 0.3H), 5.37 (d, *J* = 2.4 Hz, 0.8H), 5.34 (d, *J* = 2.4 Hz, 0.2H), 5.28 – 5.22 (m, 1H), 5.19 – 5.14 (m, 1H), 4.52 (d, *J* = 1.8 Hz, 0.8H), 4.47 (d, *J* = 2.4 Hz, 0.2H), 3.86 (s, 1H), 3.81 (s, 2H), 2.49 (s, 2H), 1.60 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 172.0, 171.1, 170.6, 169.4, 168.3, 167.8, 144.6, 143.0, 142.7, 141.5, 138.5, 136.6, 134.2, 133.7, 133.3, 133.0, 132.1, 131.9, 130.7, 130.4, 130.3, 130.0, 129.5, 129.2, 128.9, 128.7, 128.6, 128.5, 128.2, 128.1, 128.0, 127.9, 127.6, 127.4, 127.3, 123.5, 122.8, 82.6, 82.2, 80.1, 64.8, 59.7, 52.4, 52.3, 43.9, 43.7, 23.2, 21.6, 21.2. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_4^+$ ($[M+H]^+$): 439.1652, found 439.1651.

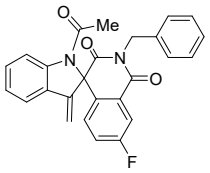
1-acetyl-2'-benzyl-7'-methyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6v)**



Pale white solid, 66 mg, 89% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.53 (d, *J* = 8.4 Hz, 0.2H), 8.15 – 8.12 (m, 0.2H), 8.08 – 8.05 (m, 0.8H), 7.47 – 7.42 (m, 1.3H), 7.41 – 7.36 (m, 4H), 7.29 – 7.27 (m, 1.5H), 7.25 – 7.23 (m, 1.2H), 7.22 – 7.18 (m, 0.8H), 7.14 – 7.10 (m, 1H), 7.08 (d, *J* = 7.8 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 0.8H), 5.37 (d, *J* = 2.4 Hz, 0.8H), 5.35 (d, *J* = 2.4 Hz, 0.2H), 5.27 (d, *J* = 12.6 Hz, 0.6H), 5.24 (s, 0.4H), 5.19 (s, 0.4H), 5.18 – 5.14 (m, 0.6H), 4.52 (d, *J* = 2.4 Hz, 0.8H), 4.48 (d, *J* = 2.4 Hz, 0.2H), 2.50 (s, 2.2H), 2.42 (s, 0.8H), 2.36 (s, 2.2H), 1.59 (s, 0.8H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.5, 169.4, 168.9, 167.2, 164.2, 163.6, 147.2, 146.2, 145.6, 143.8, 139.7, 138.6, 138.4, 137.7, 136.9, 136.6, 136.2, 135.6, 131.4, 131.0, 130.98, 129.5, 129.4, 128.6, 128.5, 128.5, 128.0, 127.7, 127.4, 124.9, 124.8, 124.2, 124.2, 123.6, 123.4, 123.1, 122.7, 121.3, 117.8, 113.4, 104.9, 104.1, 73.4, 72.9, 44.6, 44.1, 25.6, 24.7, 21.22, 21.17. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ($[M+H]^+$): 423.1709, found 423.1711.

1-acetyl-2'-benzyl-7'-fluoro-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione

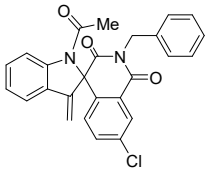
(6w)



Pale white solid, 66 mg, 89% yield (mixture of rotamers ≈ 6: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.52 (d, *J* = 7.0 Hz, 0.1H), 7.99 (dd, *J* = 9.0, 3.0 Hz, 0.1H), 7.90 (dd, *J* = 9.0, 3.0 Hz, 0.8H), 7.47 – 7.45 (m, 0.9H), 7.43 – 7.35 (m, 4H), 7.30 – 7.26 (m, 1H), 7.26 – 7.23 (m, 1.2H), 7.22 – 7.11 (m, 2.9H), 7.10 – 7.02 (m, 0.9H), 5.39 – 5.34 (m, 1H), 5.28 – 5.21 (m, 1H), 5.20 – 5.13 (m, 1H), 4.51 – 4.44 (m, 1H), 2.50 (s, 2.6H), 1.59 (s, 0.4H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.1, 168.9, 168.6, 167.4, 163.1, 163.0, 163.0, 161.4, 146.9, 146.1, 145.3, 143.6, 137.2, 137.2, 136.5, 136.3, 135.8, 131.5, 131.1, 129.4, 128.7, 128.5, 128.1, 127.5, 127.4, 125.9, 125.8, 125.6, 125.5, 125.1, 124.6, 124.4, 122.7, 122.3, 122.1, 121.4, 117.9, 115.6, 115.4, 113.5, 105.2, 104.4, 73.1, 72.5, 44.8, 44.3, 25.5, 24.7. **HRMS** (ESI) calculated for $C_{26}H_{20}FN_2O_3^+$ ([M+H]$^+$): 427.1458, found 427.1465.

1-acetyl-2'-benzyl-7'-chloro-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione

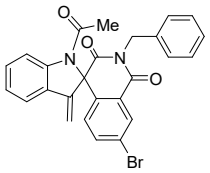
(6x)



White solid, 48 mg, 84% yield (mixture of rotamers ≈ 5: 1). Purification by silica gel flash column chromatography (PE: EA = 5: 1→2: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.53 (d, *J* = 8.29 Hz, 0.2H), 8.33 – 8.22 (m, 1H), 7.58 – 7.52 (m, 0.2H), 7.48 (dt, *J* = 7.81, 0.92 Hz, 1H), 7.46 – 7.35 (m, 5H), 7.32 – 7.27 (m, 2H), 7.25 – 7.21 (m, 0.8H), 7.16 (ddd, *J* = 7.96, 6.95, 1.34 Hz, 1H), 7.04 (d, *J* = 8.37 Hz, 0.8H), 5.43 – 5.37 (m, 1H), 5.25 (d, *J* = 14.11 Hz, 1H), 5.18 (d, *J* = 14.11 Hz, 1H), 4.54 – 4.47 (m, 1H), 2.53 (s, 2.5H), 1.61 (s, 0.5H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.0, 167.4, 162.9, 145.1, 143.7, 139.6, 136.5, 134.7, 131.2, 129.5, 129.1, 128.7, 128.6, 128.6, 127.6, 127.5, 125.4, 125.1, 124.9, 124.4, 122.8, 121.4, 113.5, 105.3, 72.6, 44.3, 25.6. **HRMS** (ESI) calculated for $C_{26}H_{20}ClN_2O_3^+$ ([M+H]$^+$): 443.1157, found 443.1158.

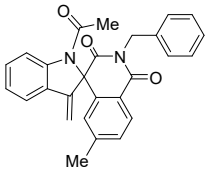
1-acetyl-2'-benzyl-7'-bromo-3-methylene-1'*H*-spiro[indoline-2,4'-isoquinoline]-1',3'(2'*H*)-dione

(6y)



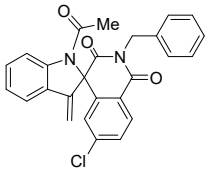
Pale yellow solid, 75 mg, 99% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE: EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.58 – 8.46 (m, 0.3H), 8.40 (d, *J* = 2.15 Hz, 0.8H), 7.71 (dd, *J* = 8.37, 2.16 Hz, 0.1H), 7.63 – 7.52 (m, 1H), 7.51 – 7.46 (m, 1H), 7.46 – 7.34 (m, 4H), 7.32 – 7.27 (m, 2H), 7.25 – 7.21 (m, 1H), 7.18 – 7.08 (m, 1H), 6.97 (d, *J* = 8.35 Hz, 0.7 H), 5.44 – 5.36 (m, 1H), 5.25 (d, *J* = 14.12 Hz, 1H), 5.18 (d, *J* = 14.09 Hz, 1H), 4.52 (d, *J* = 2.28 Hz, 1H), 2.53 (s, 2H), 1.61 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 168.9, 167.4, 162.8, 145.0, 143.7, 140.1, 138.6, 137.6, 136.5, 132.2, 131.2, 129.5, 128.7, 128.6, 128.6, 127.6, 127.5, 125.6, 125.1, 125.1, 124.6, 124.4, 124.1, 122.8, 122.5, 121.4, 119.2, 113.5, 105.4, 104.5, 72.6, 44.3, 25.6, 24.8. **HRMS** (ESI) calculated for $C_{26}H_{20}BrN_2O_3^+$ ($[M+H]^+$): 487.0657, found 487.0651.

1-acetyl-2'-benzyl-6'-methyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6z)**



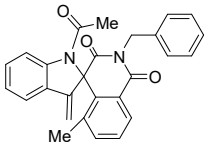
Pale yellow solid, 64 mg, 86% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1→3: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.55 (dt, *J* = 8.4, 0.6 Hz, 0.2H), 8.21 (d, *J* = 7.8 Hz, 0.2H), 8.14 (d, *J* = 8.4 Hz, 0.8H), 7.47 (dt, *J* = 7.2, 1.2 Hz, 0.8H), 7.44 – 7.42 (m, 0.6H), 7.43 – 7.39 (m, 1.6H), 7.40 – 7.37 (m, 2H), 7.34 – 7.30 (m, 0.3H), 7.30 – 7.25 (m, 0.8H), 7.25 – 7.24(m, 0.7H), 7.24 – 7.19 (m, 1.3H), 7.21 – 7.17 (m, 0.5H), 7.16 – 7.12 (m, 1.2H), 6.97 (s, 0.2H), 6.84 (s, 0.8H), 5.37 (d, *J* = 1.8 Hz, 0.7H), 5.35 (d, *J* = 2.4 Hz, 0.3H), 5.25 (s, 0.4H), 5.23 (s, 0.6H), 5.17 (d, *J* = 8.4 Hz, 0.7H), 5.15 (d, *J* = 8.4 Hz, 0.3H), 4.53 (d, *J* = 1.8 Hz, 0.7H), 4.49 (d, *J* = 2.4 Hz, 0.3H), 2.53 (s, 2H), 2.32 (s, 1H), 2.28 (s, 2H), 1.61 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.5, 169.3, 168.9, 167.3, 164.0, 163.4, 147.1, 147.0, 146.2, 145.7, 145.4, 143.9, 141.2, 140.4, 136.9, 136.3, 131.4, 131.0, 130.5, 130.0, 129.54, 129.48, 128.6, 128.5, 128.5, 128.0, 127.6, 127.4, 124.9, 124.8, 124.3, 124.2, 123.3, 122.7, 121.4, 121.3, 121.1, 117.8, 113.5, 105.0, 104.3, 73.5, 73.0, 44.5, 44.0, 25.6, 24.7, 22.0, 21.9. **HRMS** (ESI) calculated for $C_{26}H_{23}N_2O_3^+$ ($[M+H]^+$): 423.1709, found 423.1710.

1-acetyl-2'-benzyl-6'-chloro-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6aa)**



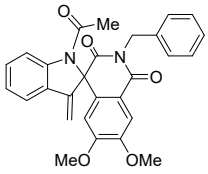
Pale white solid, 49 mg, 88% yield (mixture of rotamers ≈ 6: 1). Purification by silica gel flash column chromatography (PE/EA = 4:1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.42 (d, *J* = 8.4 Hz, 0.1H), 8.19 – 8.02 (m, 1H), 7.44 – 7.33 (m, 1H), 7.33 – 7.28 (m, 2H), 7.28 – 7.26 (m, 1H), 7.26 – 7.21 (m, 1.7H), 7.19 – 7.11 (m, 2.3H), 7.11 – 7.07 (m, 0.9H), 7.07 – 6.98 (m, 1.2H), 6.92 (d, *J* = 1.8 Hz, 0.8H), 5.30 – 5.24 (m, 1H), 5.16 – 5.08 (m, 1H), 5.07 – 5.01 (m, 1H), 4.42 – 4.33 (m, 1H), 2.42 (s, 2.6H), 1.50 (s, 0.4H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 168.9, 168.6, 167.5, 163.2, 162.6, 146.6, 146.1, 144.8, 143.6, 142.8, 142.4, 141.9, 141.1, 136.6, 135.9, 131.6, 131.6, 131.2, 130.1, 129.4, 129.0, 128.7, 128.5, 128.5, 128.1, 127.6, 127.4, 125.2, 124.4, 124.3, 124.1, 123.3, 122.8, 122.3, 122.0, 121.5, 118.0, 113.6, 105.4, 104.6, 72.7, 44.8, 44.2, 25.5, 24.7. **HRMS** (ESI) calculated for $C_{26}H_{20}ClN_2O_3^+$ ([M+H]$^+$): 443.1162, found 443.1160.

1-acetyl-2'-benzyl-5'-methyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6ab)**



Pale yellow solid, 69 mg, 93% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.42 (d, *J* = 8.4 Hz, 0.2H), 8.21 – 8.14 (m, 1H), 7.47 – 7.42 (m, 0.8H), 7.37 – 7.35 (m, 0.6H), 7.35 – 7.32 (m, 1.4H), 7.31 (d, *J* = 1.2 Hz, 0.4H), 7.29 (s, 0.6H), 7.28 – 7.27 (m, 1H), 7.26 – 7.23 (m, 1.6H), 7.21 – 7.18 (m, 0.8H), 7.18 – 7.17 (m, 0.9H), 7.17 – 7.15 (m, 0.7H), 7.13 – 7.10 (m, 0.8H), 7.08 – 7.04 (m, 1.2H), 5.37 – 5.35 (m, 1H), 5.19 – 5.11 (m, 1H), 5.11 – 5.04 (m, 1H), 4.48 (d, *J* = 1.8 Hz, 0.8H), 4.41 (d, *J* = 2.4 Hz, 0.2H), 2.40 (s, 2H), 1.94 (d, *J* = 4.8 Hz, 3H), 1.46 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.9, 169.4, 168.6, 167.7, 164.1, 163.4, 146.4, 146.0, 144.3, 144.1, 138.8, 138.2, 137.8, 137.3, 136.7, 136.2, 134.9, 131.5, 131.1, 129.2, 129.2, 128.8, 128.6, 128.4, 128.3, 128.23, 128.21, 128.1, 127.9, 127.8, 127.3, 126.4, 125.8, 125.4, 124.7, 124.5, 124.1, 124.0, 122.0, 120.6, 119.2, 118.1, 113.7, 105.3, 104.8, 73.9, 73.7, 44.8, 44.2, 25.2, 24.4, 20.5, 20.4. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ([M+H]$^+$): 423.1709, found 423.1717.

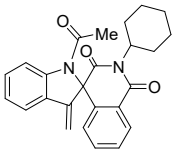
1-acetyl-2'-benzyl-6',7'-dimethoxy-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6ac)**



Pale yellow solid, 68 mg, 75% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 4: 1). **^{1}H NMR (600 MHz, CD_3Cl)** δ 8.39 (d, *J* = 8.4 Hz, 0.3H), 7.58 (s, 0.3H), 7.54 (s, 0.7H), 7.35 (d, *J* = 7.8 Hz, 0.7H), 7.30 – 7.26 (m, 2H),7.26 – 7.22 (m, 2H), 7.16 – 7.03 (m, 3H), 7.03 – 6.97 (m, 1H), 6.35 (s, 0.3H), 6.27 (s, 0.7H), 5.28 – 5.22 (m, 1H), 5.15 – 5.06 (m, 1H), 5.05 – 4.97 (m, 1H), 4.48 – 4.37 (m, 1H), 3.82 (s, 1H), 3.77 (s, 2H), 3.62 (s, 1H), 3.57 (s, 2H), 2.39 (s, 2H), 1.50 (s, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.7, 169.5, 169.1, 167.5, 163.7, 163.1, 155.5, 154.7, 150.0, 149.3, 146.9, 146.2, 145.3, 143.8, 136.9, 136.3, 135.4, 134.5, 131.3, 131.0, 129.3, 128.6, 128.5,

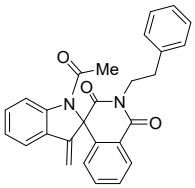
128.45, 128.41, 127.9, 127.6, 127.3, 124.91, 124.86, 124.2, 122.8, 121.4, 117.8, 116.8, 116.5, 113.4, 110.6, 110.4, 105.4, 105.0, 104.7, 104.3, 73.5, 73.1, 58.4, 56.6, 56.3, 56.2, 56.2, 44.5, 44.1, 25.6, 24.6. **HRMS** (ESI) calculated for $C_{28}H_{25}N_2O_5^+$ ($[M+H]^+$): 469.1758, found 469.1757.

1-acetyl-2'-cyclohexyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6ad)**



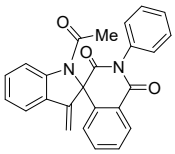
White solid, 56 mg, 76% yield (mixture of rotamers ≈ 2: 1). Purification by silica gel flash column chromatography (PE/EA = 5: 1→4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.57 – 8.54 (m, 0.3H), 8.32 (dd, *J* = 7.9, 1.5 Hz, 0.3H), 8.25 (dd, *J* = 7.7, 1.5 Hz, 0.7H), 7.59 (td, *J* = 7.6, 1.5 Hz, 0.3H), 7.55 – 7.50 (m, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 0.7H), 7.44 – 7.39 (m, 2.7H), 7.20 (dd, *J* = 7.7, 1.2 Hz, 0.3H), 7.17 – 7.12 (m, 1H), 7.06 (dd, *J* = 7.6, 1.3 Hz, 0.7H), 5.50 (d, *J* = 2.0 Hz, 0.7H), 5.49 (d, *J* = 2.4 Hz, 0.3H), 4.83 – 4.75 (m, 1H), 4.73 (d, *J* = 2.0 Hz, 0.7H), 4.70 (d, *J* = 2.4 Hz, 0.3H), 2.52 (s, 2H), 2.42 – 2.27 (m, 2H), 1.88 – 1.79 (m, 2H), 1.79 – 1.72 (m, 1H), 1.69 (s, 1H), 1.68 – 1.60 (m, 2H), 1.40 – 1.31 (m, 2H), 1.24 – 1.17 (m, 1H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.7, 169.7, 168.9, 167.2, 164.5, 163.9, 147.1, 146.2, 145.7, 143.9, 141.0, 140.3, 135.3, 134.2, 131.4, 131.0, 130.0, 129.4, 129.3, 128.3, 127.5, 124.9, 124.7, 124.4, 124.11, 124.06, 122.9, 122.7, 121.3, 117.8, 113.4, 104.6, 104.0, 74.0, 73.4, 54.9, 54.5, 29.4, 28.1, 27.8, 26.5, 26.4, 26.2, 25.7, 25.5, 25.3, 24.8. **HRMS** (ESI) calculated for $C_{25}H_{25}N_2O_3^+$ ($[M+H]^+$): 401.1865, found 401.1864.

1-acetyl-3-methylene-2'-phenethyl-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6ae)**



Pale white solid, 63 mg, 85% yield (mixture of rotamers ≈ 4: 1). Purification by silica gel flash column chromatography (PE/EA = 5: 1→4: 1).**^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.55 (d, *J* = 8.1 Hz, 0.2H), 8.33 (dd, *J* = 7.9, 1.4 Hz, 0.2H), 8.26 (dd, *J* = 7.8, 1.5 Hz, 0.8H), 7.61 – 7.57 (m, 0.2H), 7.56 – 7.52 (m, 0.3H), 7.51 – 7.45 (m, 1.6H), 7.45 – 7.39 (m, 2.8H), 7.31 – 7.28 (m, 1.6H), 7.28 – 7.26 (m, 1.3H), 7.26 – 7.24 (m, 0.9H), 7.23 (s, 0.2H), 7.22 – 7.19 (m, 0.6H), 7.19 – 7.17 (m, 0.6H), 7.16 – 7.12 (m, 1H), 7.08 (dd, *J* = 7.8, 1.2 Hz, 0.8H), 5.45 (d, *J* = 2.1 Hz, 0.8H), 5.42 (d, *J* = 2.5 Hz, 0.2H), 4.61 (d, *J* = 2.1 Hz, 0.8H), 4.58 (d, *J* = 2.5 Hz, 0.2H), 4.32 – 4.25 (m, 1.2H), 4.24 – 4.17 (m, 0.8H), 2.93 (t, *J* = 8.1 Hz, 2H), 2.51 (s, 2.4H), 1.59 (s, 0.6H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.5, 169.3, 168.8, 167.4, 164.0, 163.4, 147.0, 146.2, 145.6, 143.8, 141.2, 140.4, 138.7, 137.8, 135.6, 134.5, 131.4, 131.1, 129.8, 129.4, 129.3, 129.2, 129.1, 128.6, 128.5, 128.4, 127.6, 126.8, 126.5, 125.0, 124.7, 124.6, 124.3, 124.2, 124.1, 123.8, 123.6, 123.2, 122.7, 121.3, 117.9, 113.5, 105.0, 104.3, 73.6, 72.9, 42.5, 42.2, 33.8, 33.7, 25.6, 24.7. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ($[M+H]^+$): 423.1709, found 423.1711.

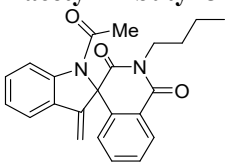
1-acetyl-3-methylene-2'-phenyl-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione **(6af)**



Yellow solid, 46 mg, 62% yield (mixture of rotamers ≈ 5: 1). Purification by silica gel flash column chromatography (PE/EA = 5: 1→4: 1). **^{1}H NMR (600 MHz, $CDCl_3$)** δ jj8.57 (d, *J* = 8.3 Hz, 0.15H), 8.39 (dd, *J* = 8.0, 1.4 Hz, 0.20H), 8.33 (dd, *J* = 7.9, 1.4 Hz, 0.80H) 7.62 – 7.45 (m, 5H), 7.44 – 7.33 (m, 3H), 7.28 (d, *J* = 7.8 Hz, 1.50H), 7.24 – 7.09 (m, 2.30H), 5.63 (d, *J* = 2.1 Hz, 1H), 4.97 (d, *J* = 2.1 Hz, 1H), 2.52 (s, 2.50H), 1.86 (s, 0.50H). **^{13}C NMR (151 MHz, $CDCl_3$)** δ 169.3, 167.4, 164.2, 145.9, 143.9, 141.3, 135.9, 135.1, 134.8, 131.5, 131.1, 130.2, 129.5, 129.5, 129.5, 129.2, 129.1, 129.0, 128.7, 128.4, 128.4, 128.0, 127.5, 125.0, 124.3, 124.2, 123.9, 123.3, 122.7, 121.4, 117.8, 113.4, 104.9, 104.1, 73.3, 25.5, 24.9. **HRMS** (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ($[M+H]^+$): 423.1709, found 423.1711.

HRMS (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ($[M+H]^+$): 423.1709, found 423.1721.

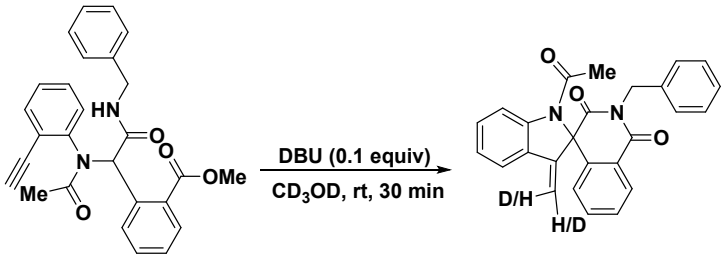
1-acetyl-2'-butyl-3-methylene-1'H-spiro[indoline-2,4'-isoquinoline]-1',3'(2'H)-dione (6ag)



White solid, 44 mg, 84% (mixture of rotamers≈3:1). Purification by silica gel flash column chromatography (PE:EA=5:1→2:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 8.62, 1.00 Hz, 0.2H), 8.36 – 8.25 (m, 1H), 7.62 (td, *J* = 7.68, 1.55 Hz, 0.3H), 7.60 – 7.52 (m, 0.3H), 7.54 – 7.46 (m, 1.6H), 7.47 – 7.38 (m, 2.8H), 7.25 – 7.21 (m, 0.2H), 7.16 (ddd, *J* = 7.60, 6.54, 1.74 Hz, 1H), 7.11 – 7.06 (m, 0.7H), 7.05 – 6.95 (m, 0.1H), 5.50 (d, *J* = 2.05 Hz, 0.7H), 5.48 (d, *J* = 2.41 Hz, 0.3H), 4.70 (d, *J* = 2.04 Hz, 0.7H), 4.66 (d, *J* = 2.43 Hz, 0.3H), 4.03 (pdd, *J* = 12.83, 8.70, 6.41 Hz, 2H), 2.52 (s, 2.3H), 1.70 (s, 0.7H), δ 1.66 – 1.59 (m, 2H), 1.45 – 1.35 (m, 2H), 0.94 (dt, *J* = 9.48, 7.37 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.5, 167.3, 164.1, 145.8, 144.0, 141.3, 135.5, 134.4, 131.5, 131.1, 129.9, 129.3, 129.3, 128.4, 127.6, 125.0, 124.2, 124.2, 124.0, 123.1, 122.7, 121.4, 117.9, 113.5, 104.8, 104.0, 41.2, 40.8, 29.7, 25.6, 24.8, 20.3, 13.9. HRMS (ESI) calculated for $C_{27}H_{23}N_2O_3^+$ ($[M+H]^+$): 423.1709, found 423.1721.

General procedure of deuterium exchange reaction

Preparation of 6a'



5a 6a'

To a solution of 5a (0.11 mmol, 1.0 equiv) in methanol (1.1 mL) was added DBU (0.01 mmol, 0.1 equiv). The reaction mixture was stirred at room temperature for 30 min. After completion, the reaction mixture was evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/Petroleum ether = 1: 2) to provide the 6a' as a pale-yellow solid (34 mg, 73%).

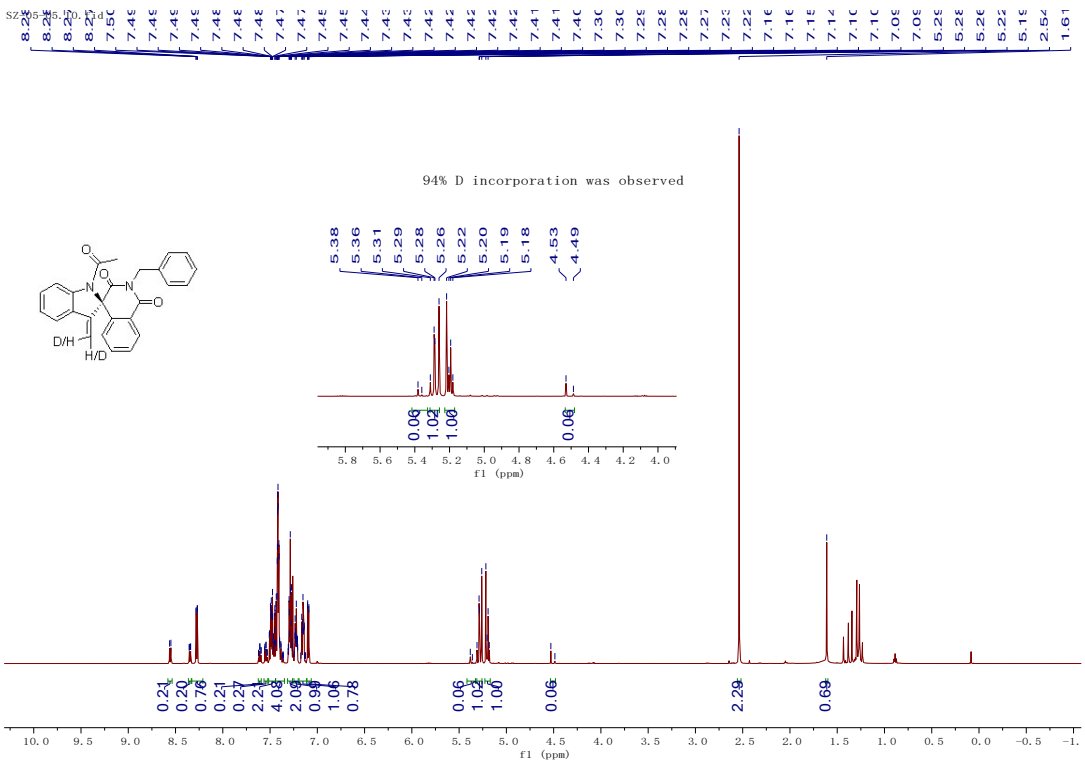
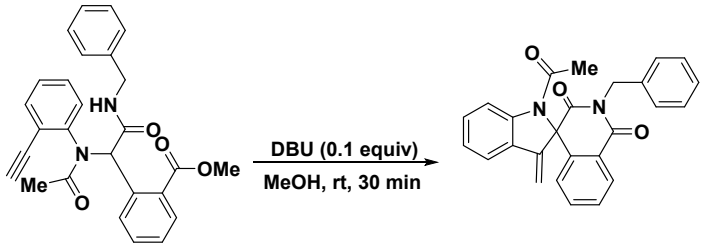


Figure S1. ^{1}H NMR spectrum of compound 6a'

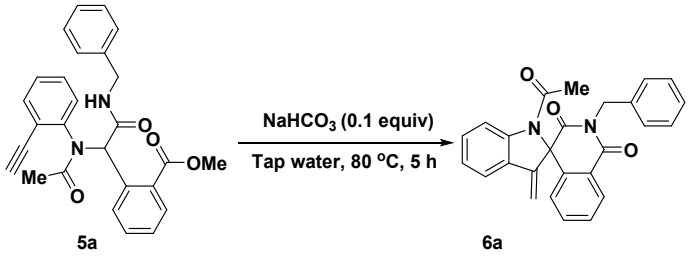
Scale-up synthesis of 6a



5a 6a

To a solution of 5a (1.67 g, 3.80 mmol) in methanol (19 mL) was added DBU (0.38 mmol, 0.1 equiv). The reaction mixture was stirred at room temperature for 30 min. After completion, the reaction mixture was evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/PE = 1: 2) to afford the desired 6a in 87% yield (1.34 g).

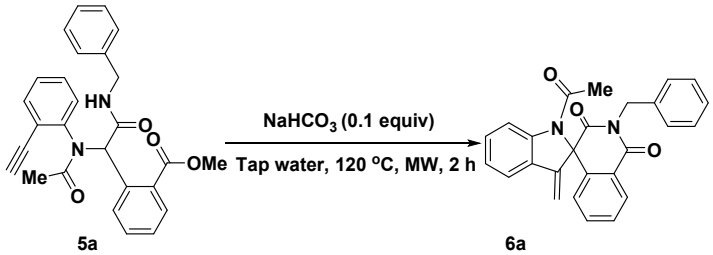
Synthesis of 6a in"Soda water"



5a 6a

To a solution of 5a (50 mg, 0.11 mmol) in tap water (1 mL) was added $NaHCO_3$ (0.01 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C for 5 h. After completion, the reaction mixture was extracted with EA, then evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/PE = 1: 2) to afford the desired 6a (24 mg,52%).

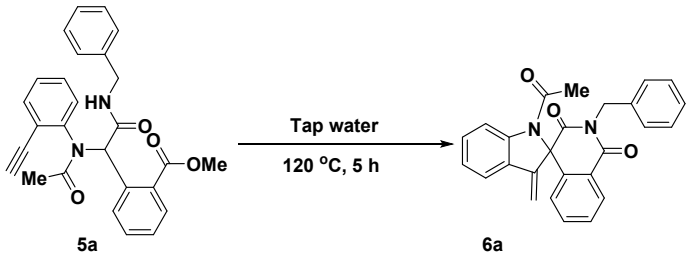
Synthesis of **6a** under microwave irradiation.



5a 6a

To a solution of 5a (50 mg, 0.11 mmol) in tap water (1 mL) was added $NaHCO_3$ (0.01 mmol, 0.1 equiv). The reaction mixture was stirred and under microwave irradiation at 120 °C for 2 h. After completion, the reaction mixture was extracted with EA, then evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/PE = 1: 2) to afford the desired 6a (42 mg, 84%).

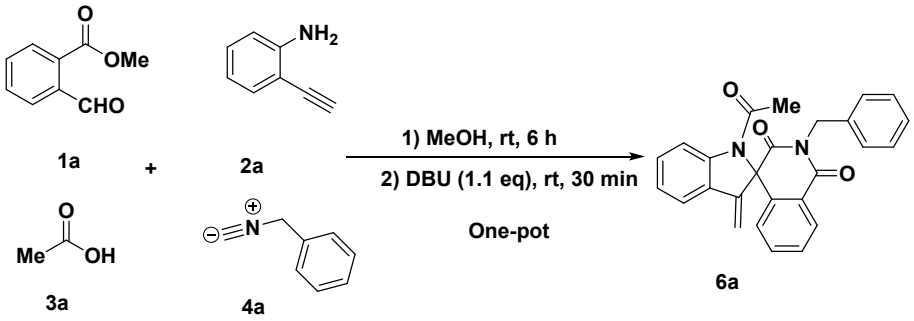
Synthesis of 6a in“High-temperature water”



5a 6a

To a solution of 5a (30 mg, 0.07 mmol) in tap water (0.6 mL). The reaction mixture was stirred at 120 °C for 6 h. After completion, the reaction mixture was extracted with EA, and then evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/PE = 1: 2) to afford the desired 6a (15 mg,53%).

One-pot synthesis of 6a



To a solution of aldehyde (1a, 0.30 mmol, 1.0 equiv) in methanol (3 mL) were added amine (2a, 0.34 mmol, 1.1 equiv), acid (3a, 0.34 mmol, 1.1 equiv) and isonitrile (4a, 0.30 mmol, 1.0 equiv) in a round bottom flask equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 6 h. After full consumption of the aldehydes, DBU (0.34 mmol, 1.1 equiv.) was subsequently added until the completion of the reaction. The reaction mixture was evaporated under reduced pressure to obtain a residue which was subjected to silica gel column chromatography (EtOAc/PE = 1: 2) to afford the desired 6a as yellow solid (48 mg, 39%).

Crystallographic data for compound 6a.

Single crystals suitable for X-ray diffraction were obtained by slow evaporation at room temperature from an Ether-EA mixture (1:1 v/v). The data were collected by a Bruker APEX-II CCD diffractometer equipped with a Mo radiation source (Kα = 1.54184 Å) at 293 K. CCDC 2330219 contains contain the supplementary crystallographic data for this paper and can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/getstructures or from the Cambridge Crystallographic Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033;

deposit@ccdc.cam.ac.uk

Table S6 Crystal data and structure refinement details for compound 6a

Identification code	**6a**
Empirical formula	**$C_{26}H_{20}N_2O_3$**
Formula weight	**408.44**
Temperature/K	**293(2)**
Crystal system	**monoclinic**
Space group	**I2/a**
a/Å	**15.6096(3)**
b/Å	**16.4461(3)**
c/Å	**16.1674(3)**
α/°	**90**
β/°	**96.743(10)**
γ/°	**90**
Volume/Å^3	**4121.74(13)**
Z	**8**
ρcalcg/cm^3	**1.316**
μ/mm-1	**0.700**
***F*(000)**	**1712.0**
Crystal size/mm^3	**0.29 × 0.28 × 0.26**
Radiation	**Cu Kα (λ = 1.54184)**
Index ranges	**$-16 \le h \le 18$, $-20 \le k \le 17$, $-19 \le l \le 19$**
Reflections collected	**11405**
Independent reflections	**3915 [R_{int} = 0.0186, R_{sigma} = 0.0175]**
Data/restraints/parameters	**3915/0/301**
Goodness-of-fit on F^2	**1.092**
Final R indexes [I>=2σ (I)]	**R_1 = 0.0415, wR_2 = 0.1204**
Final R indexes [all data]	**R1 = 0.0483, wR2 = 0.1337**
Largest diff. peak/hole / e Å^{-3}	**0.25/-0.20**

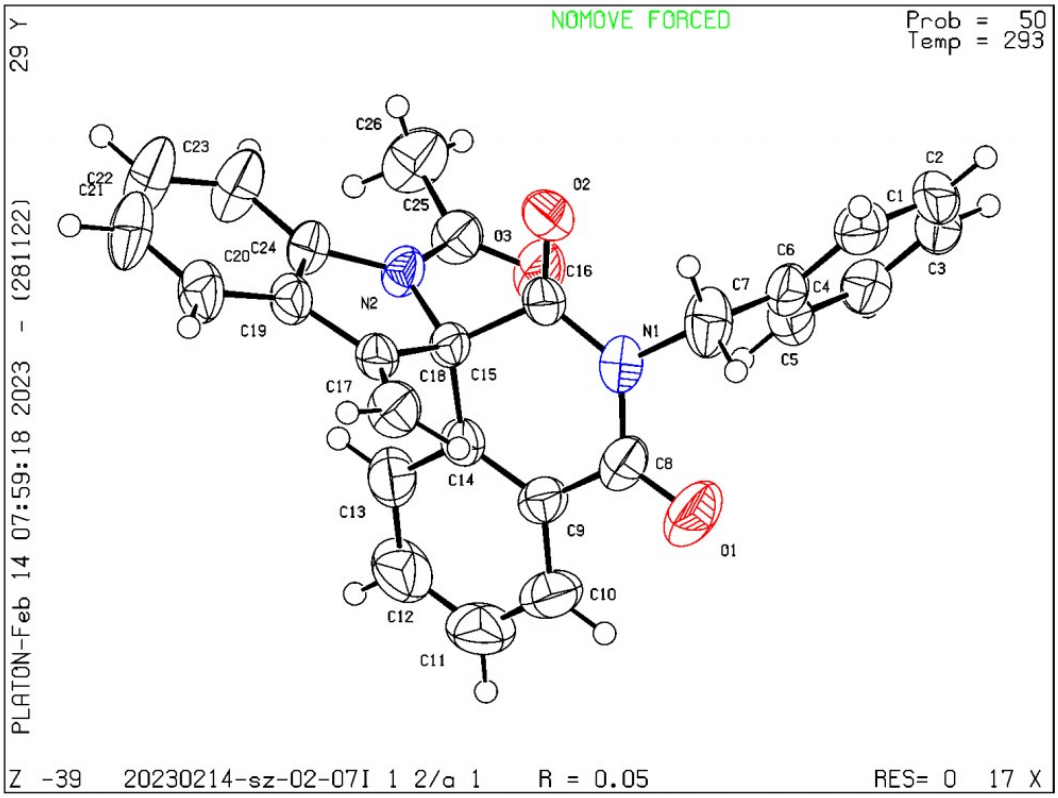


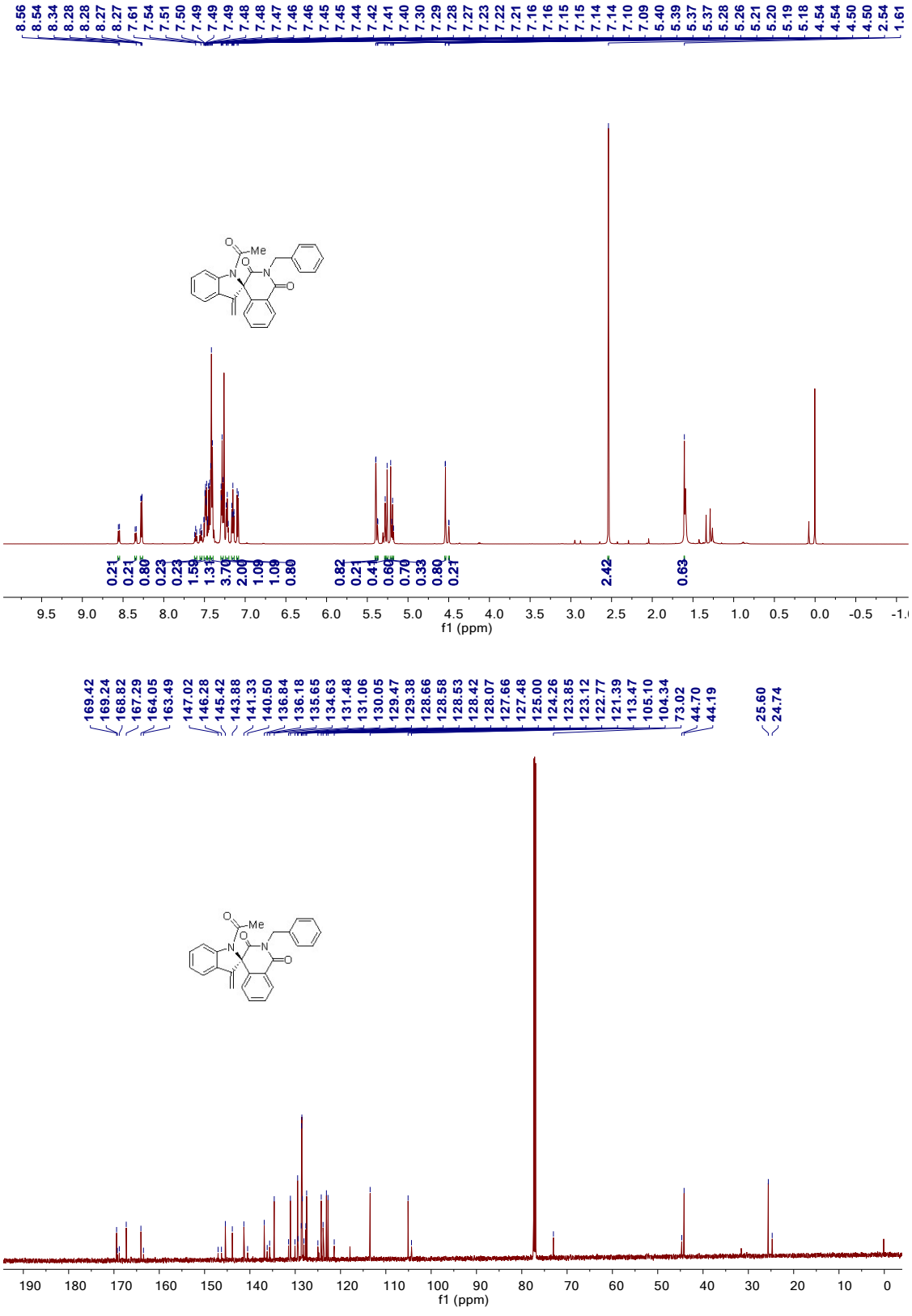
Figure S2 Crystal structure of compound 6a. Thermal ellipsoids are drawn at the 50% probability level.

Measurement of cell viability and proliferation

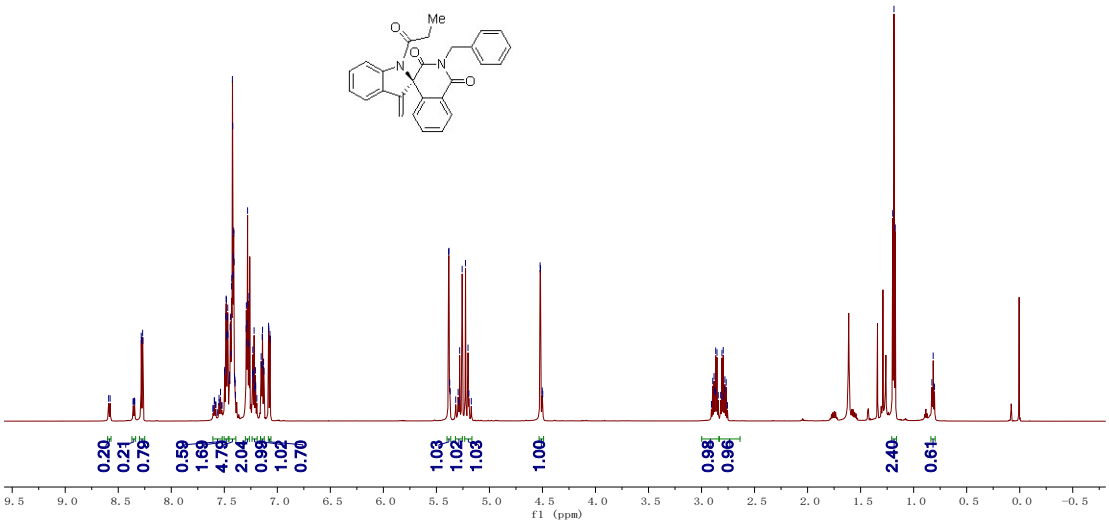
MCF7 (breast adenocarcinoma) and Jurkat (Clone E6-1, acute T cell leukemia) were purchased from American Type Culture Collection (ATCC, Manassas, VA, USA). MCF7 was cultured in high-glucose DMEM (Gibco, C11995500BT, USA) medium, Jurkat cells were cultured in RPMl medium modified (Gibco, C11875500BT, USA) medium with 10% bovine fetal serum (FBS, Biosera, 010321-UY, Uruguay Origin) and 1% penicillin/streptomycin (Thermo, 15140122, USA) at 37 ℃ in a humidified incubator containing 5% CO_2. The effects of compounds on the inhibition of cell proliferation were measured by CellTiter-Glo® luminescent cell viability assay (Promega, G7572, USA). Briefly, cancer cells were seeded on the 96 well-plates at a density of 1×10^3 cells per well with 200 μL complete medium. Then, cells were treated with compounds at a concentration of 40 μM for 72 h after incubating for 12-16 h. After that, 100 μL of the medium was removed, and each well was added 40 μL CellTiter-Glo® reagent. The 96 well-plates were then placed on an oscillator with gentle shaking to mix for 2 min and incubated for 10 min at room temperature. The chemiluminescent signals were detected using a multimode plate reader (EnSight™, PerkinElmer, USA). The luminescence value of the control wells was used as 100%, and the luminescence values of all compounds were calculated by GraphPad Prism 9, and the experiments were repeated three times.

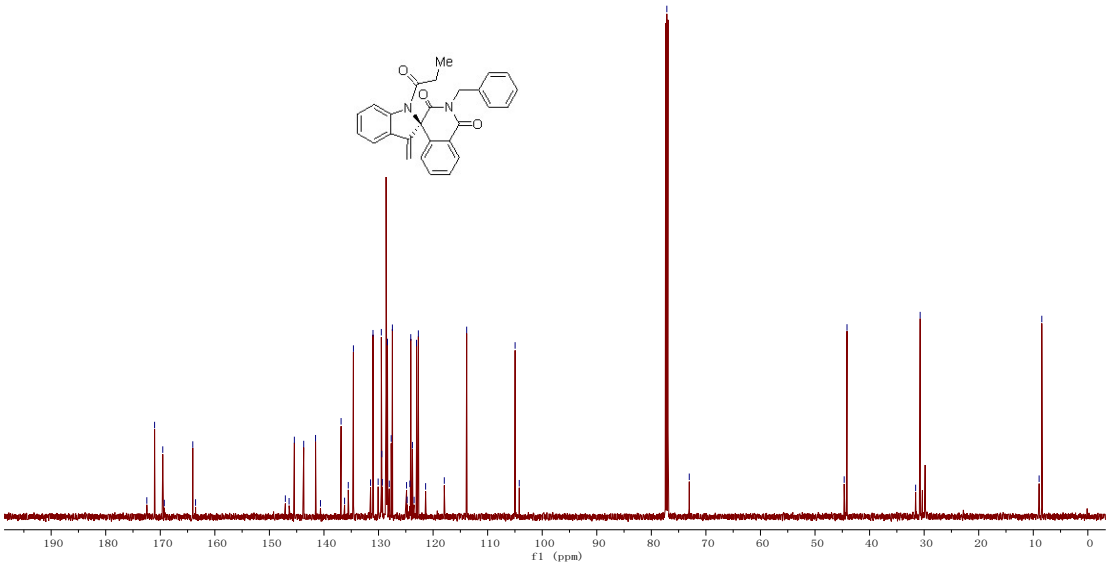
Copies of NMR spectra (6a-6ag)

^{1}H and ^{13}C NMR spectra of compound (6a)

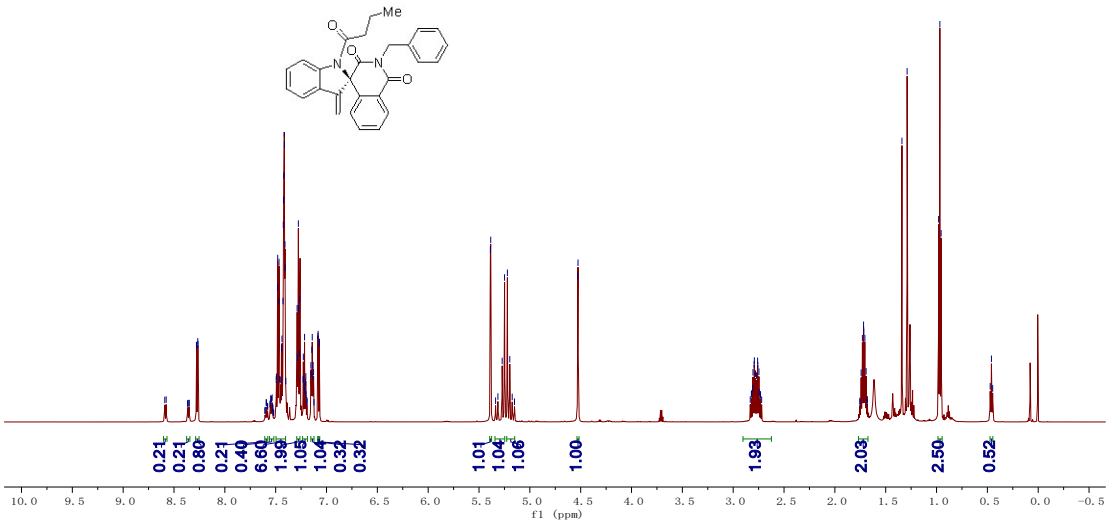


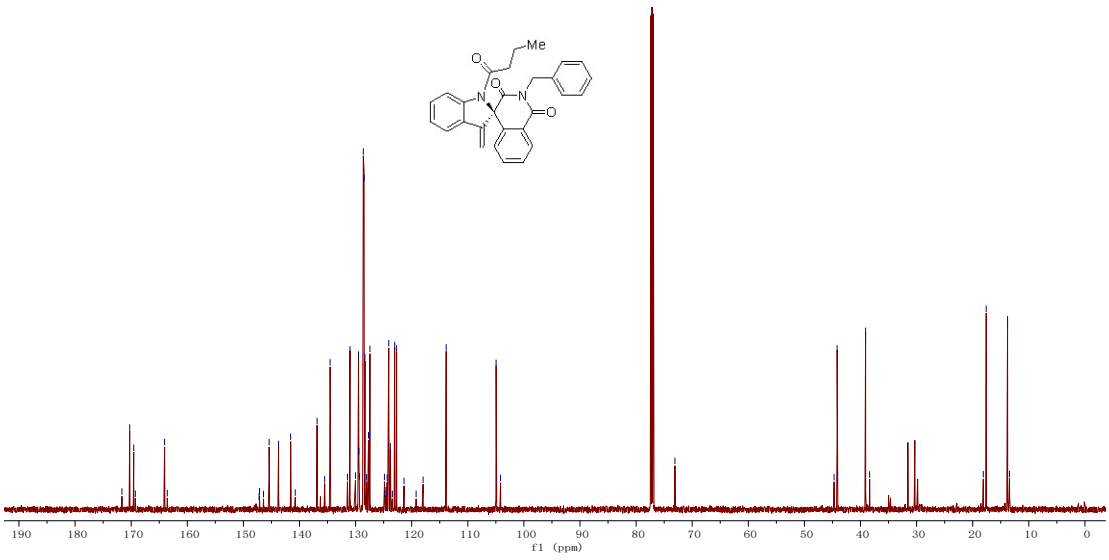
^{1}H and ^{13}C NMR spectra of compound (6b)



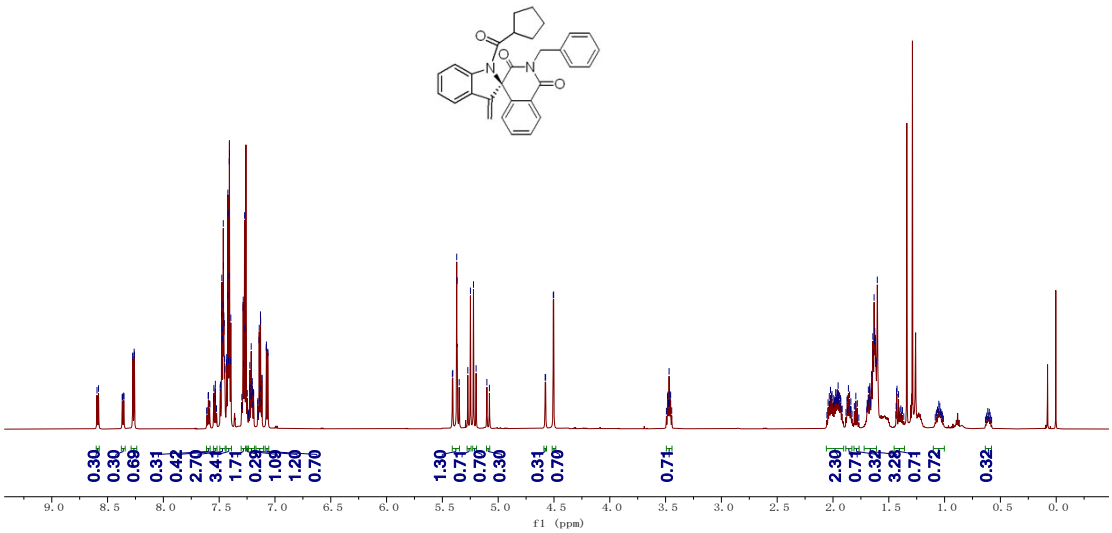


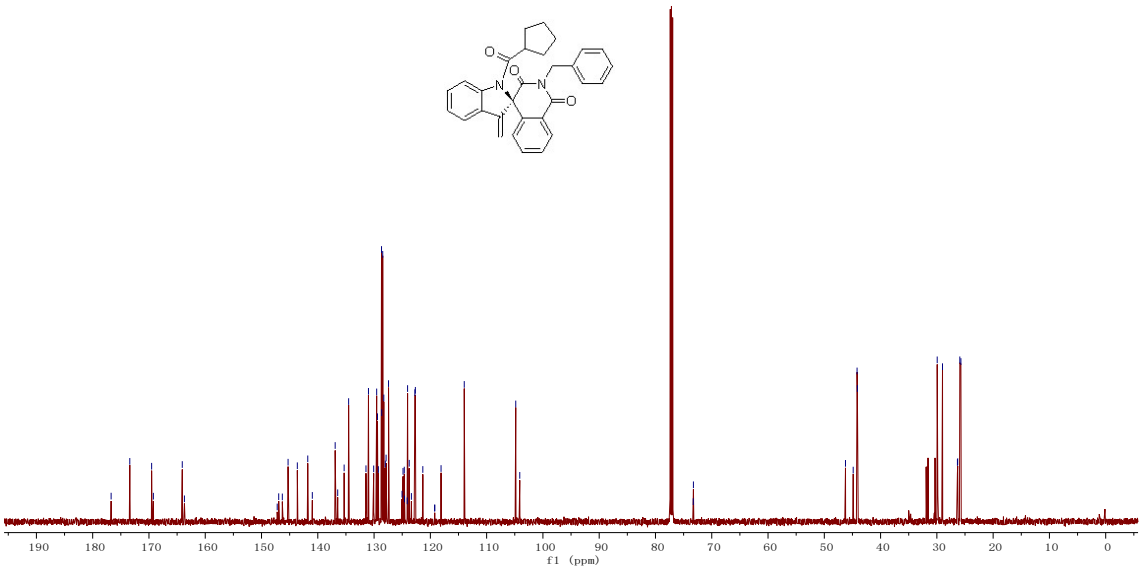
^{1}H and ^{13}C NMR spectra of compound (6c)



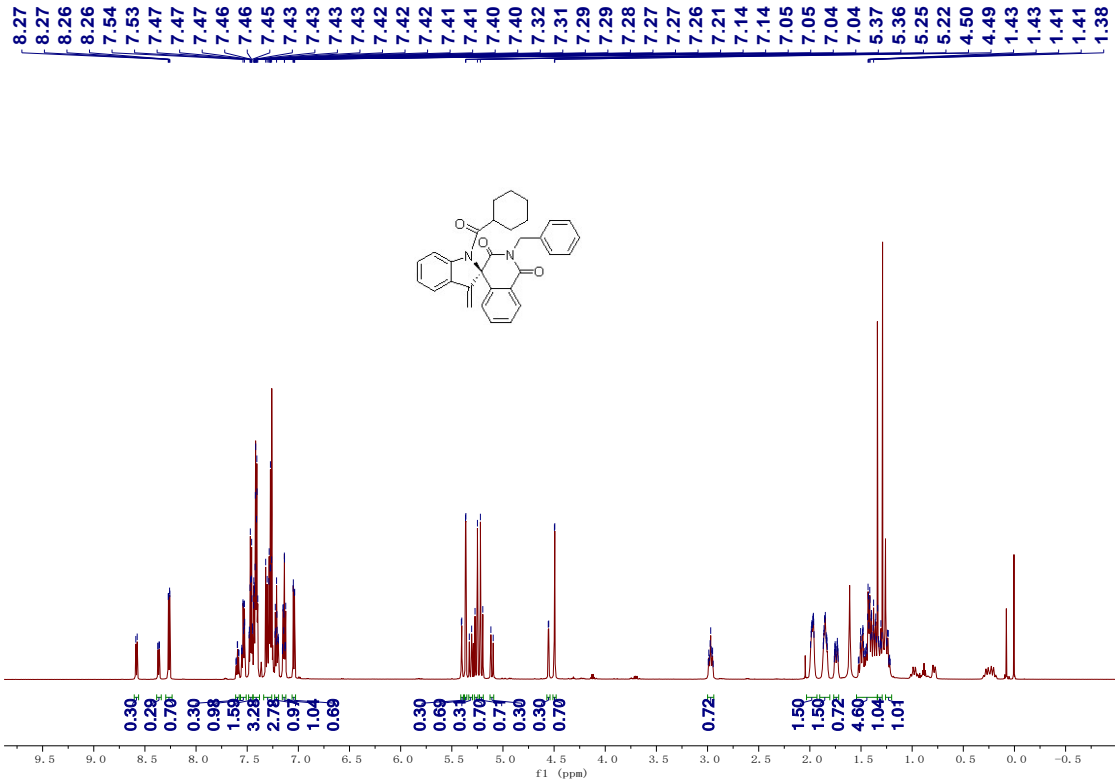


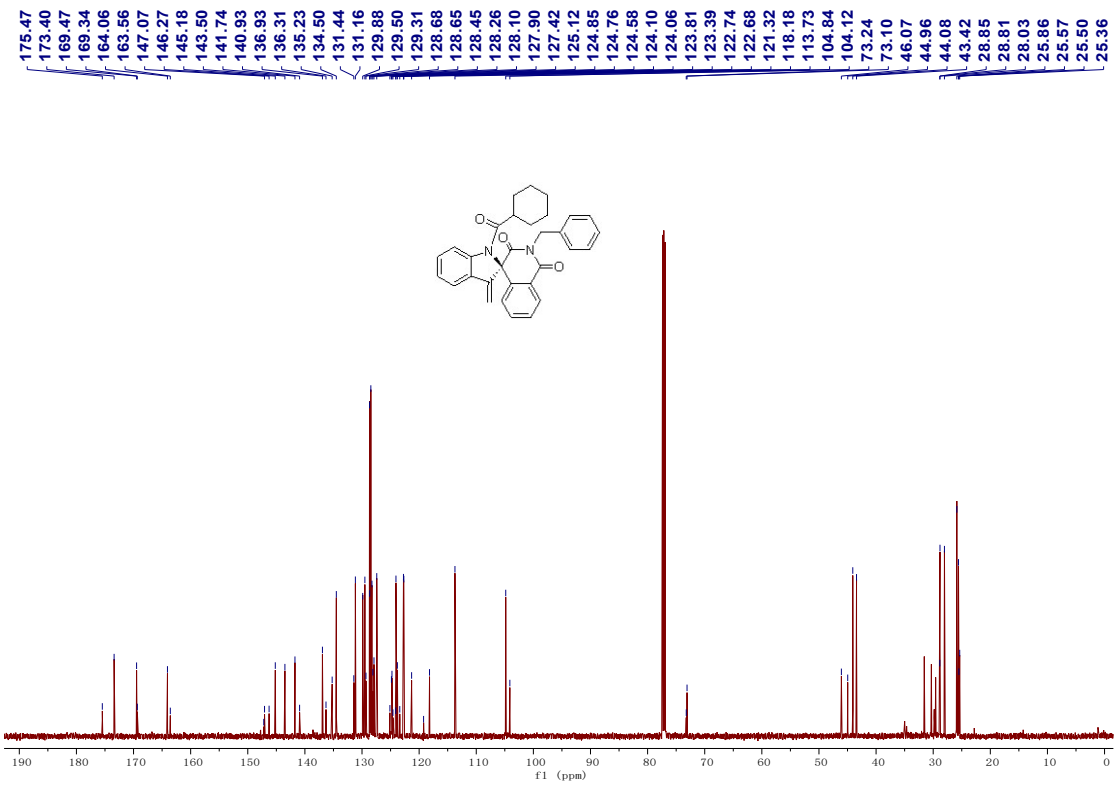
^{1}H and ^{13}C NMR spectra of compound (6d)



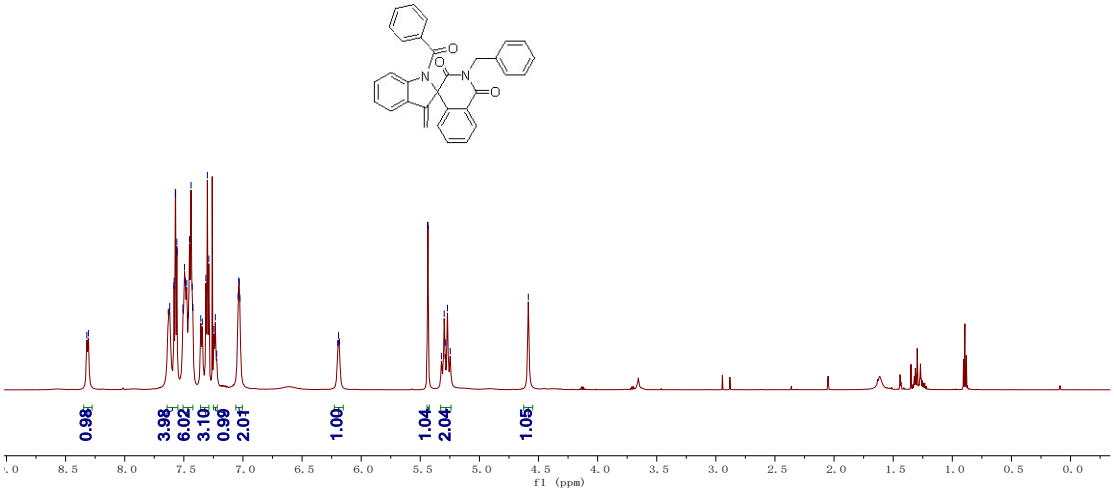


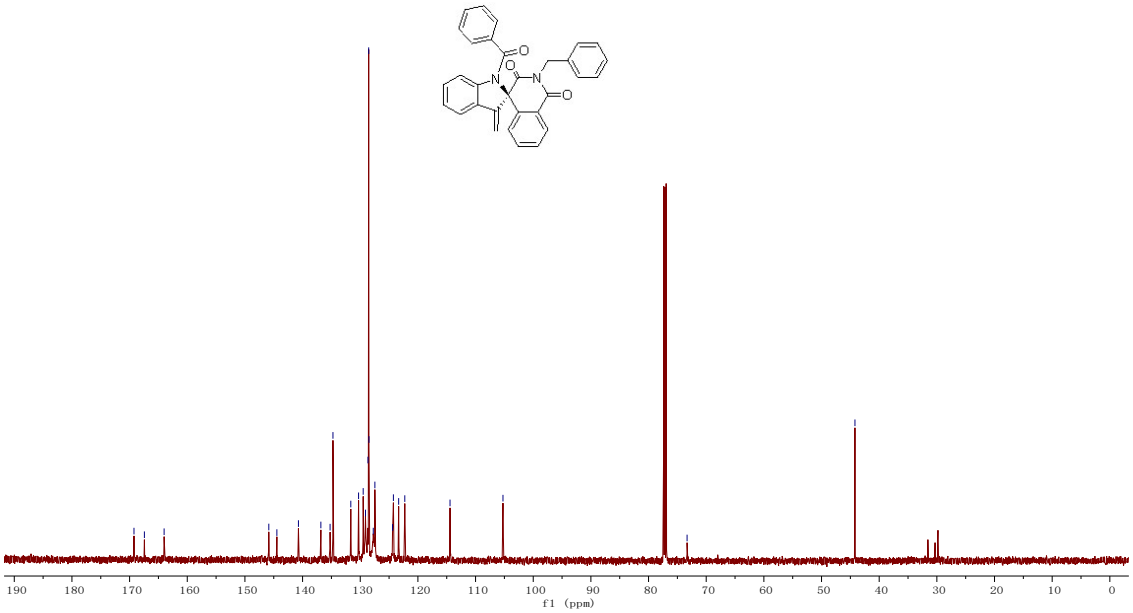
^{1}H and ^{13}C NMR spectra of compound (6e)



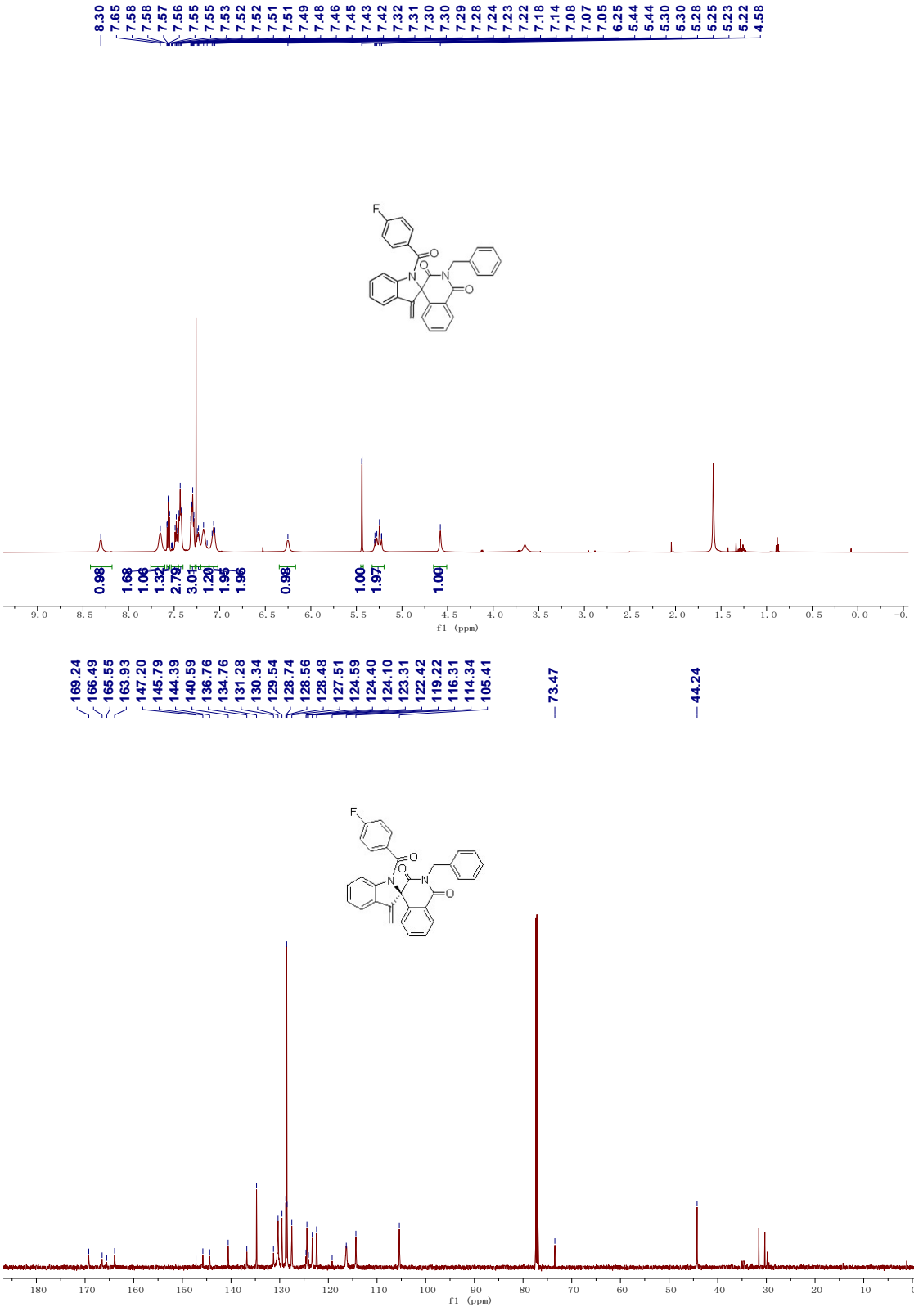


^{1}H and ^{13}C NMR spectra of compound (6f)

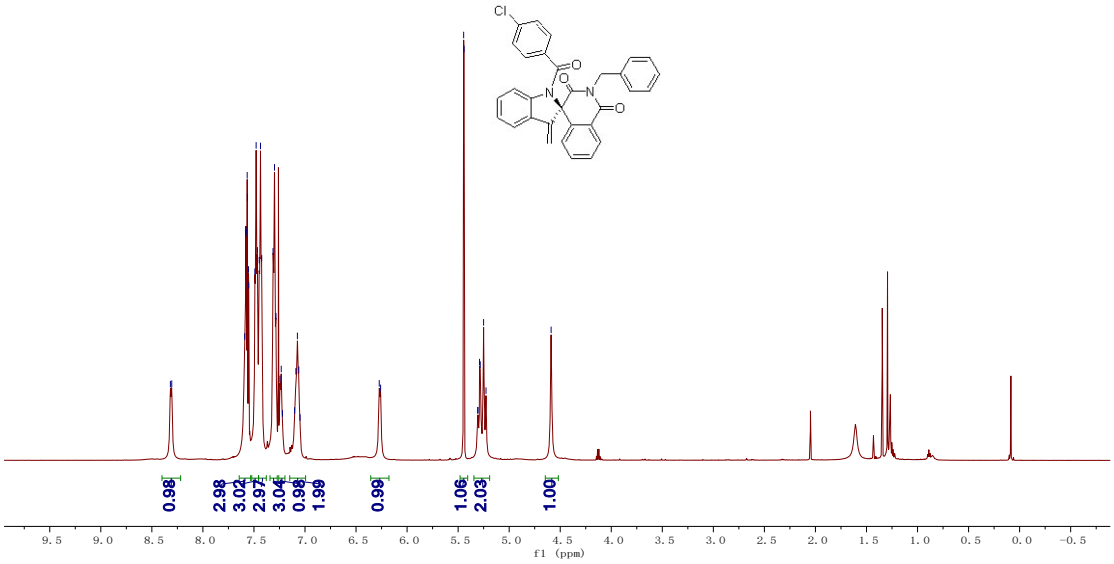


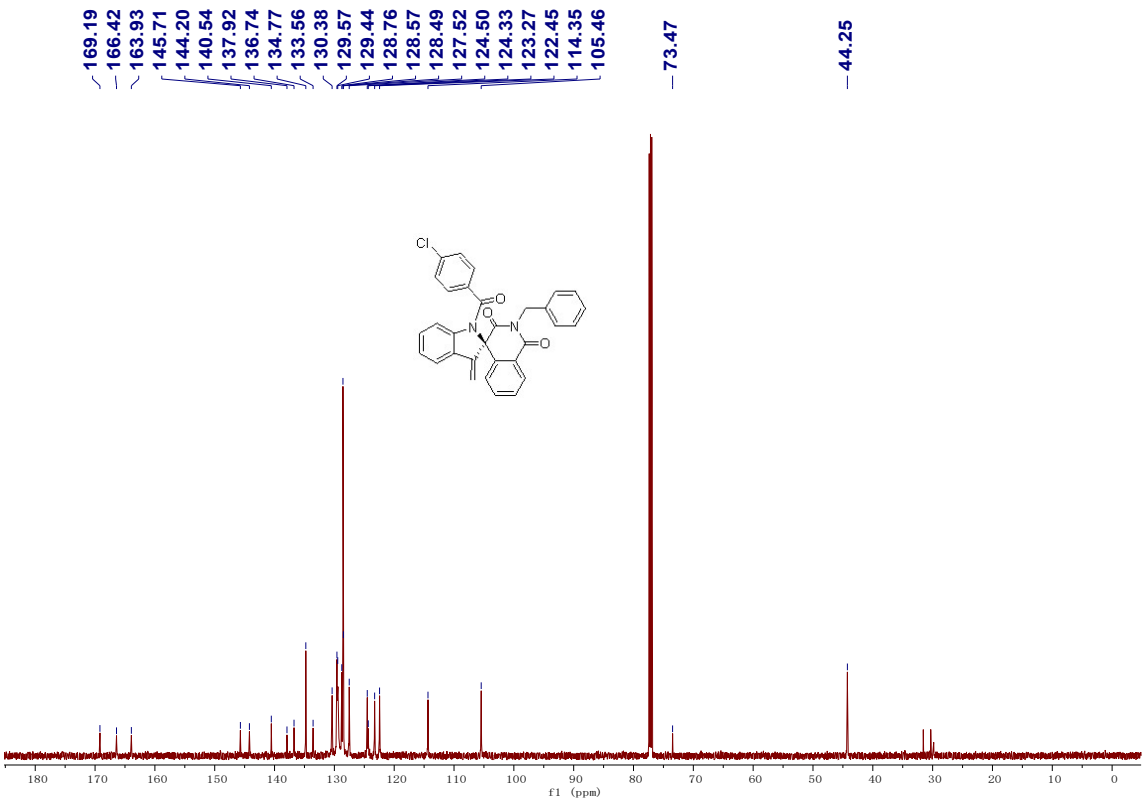


^{1}H and ^{13}C NMR spectra of compound (6g)

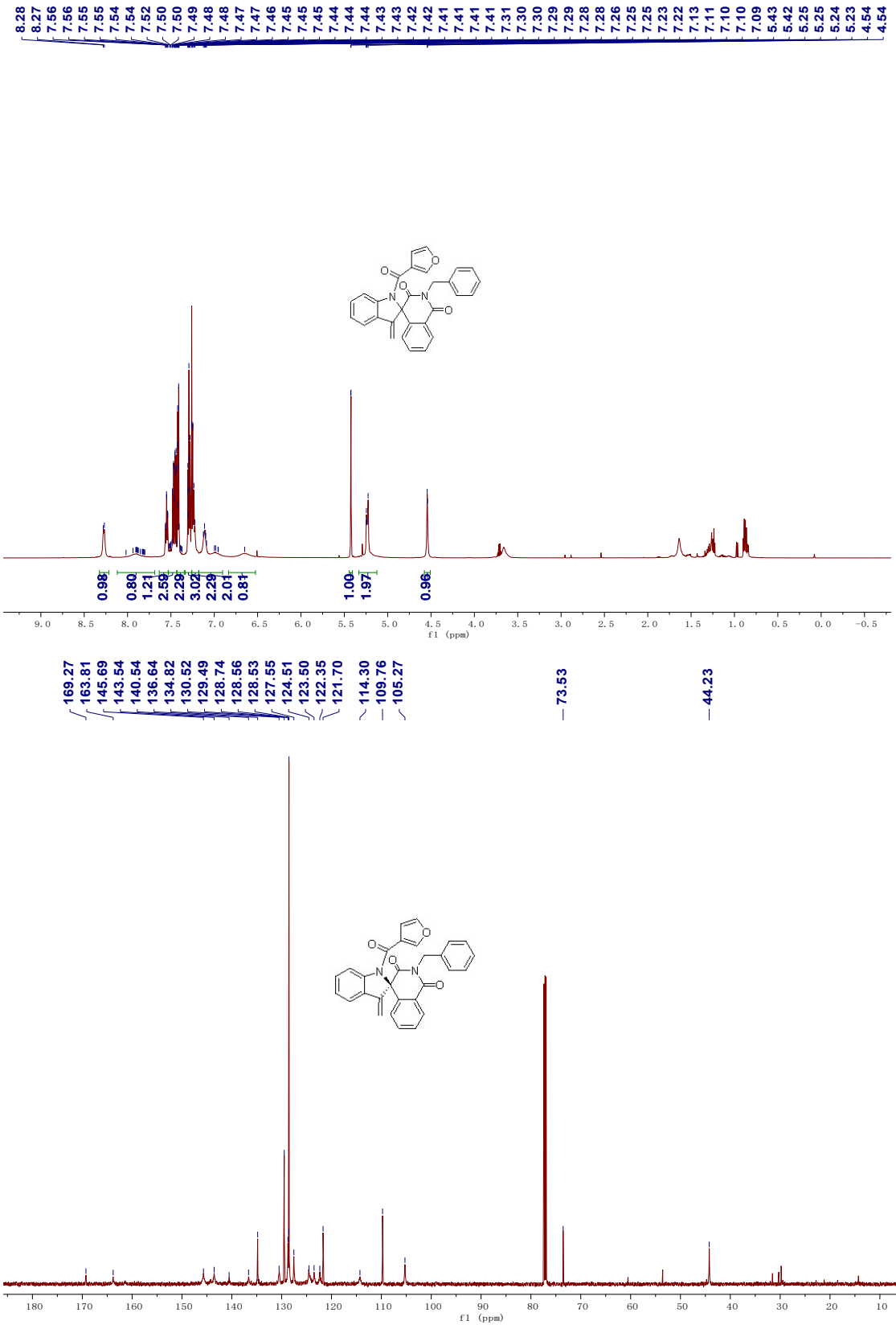


^{1}H and ^{13}C NMR spectra of compound (6h)

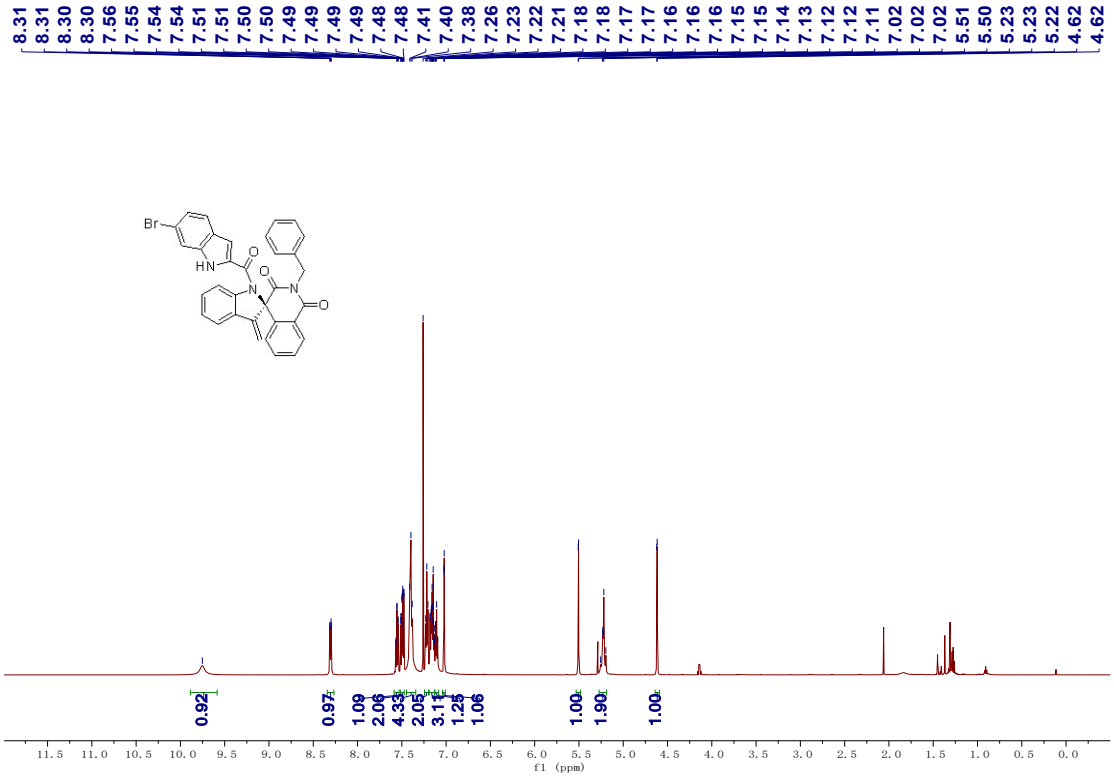


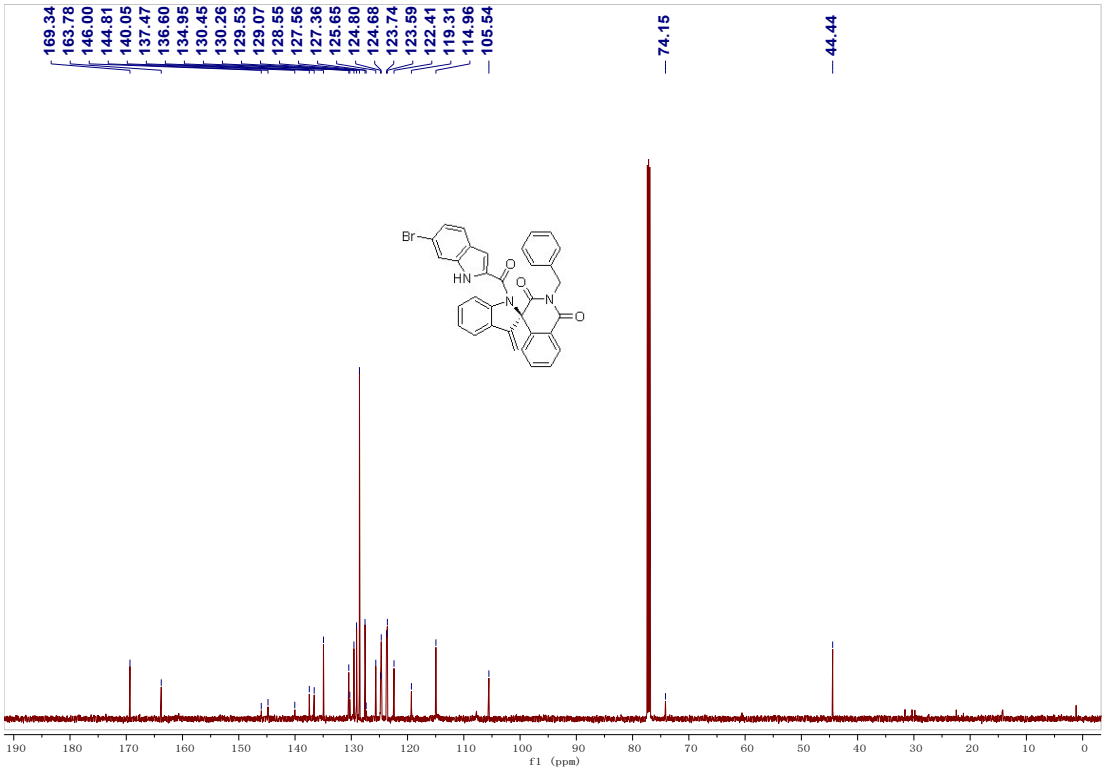


^{1}H and ^{13}C NMR spectra of compound (6i)

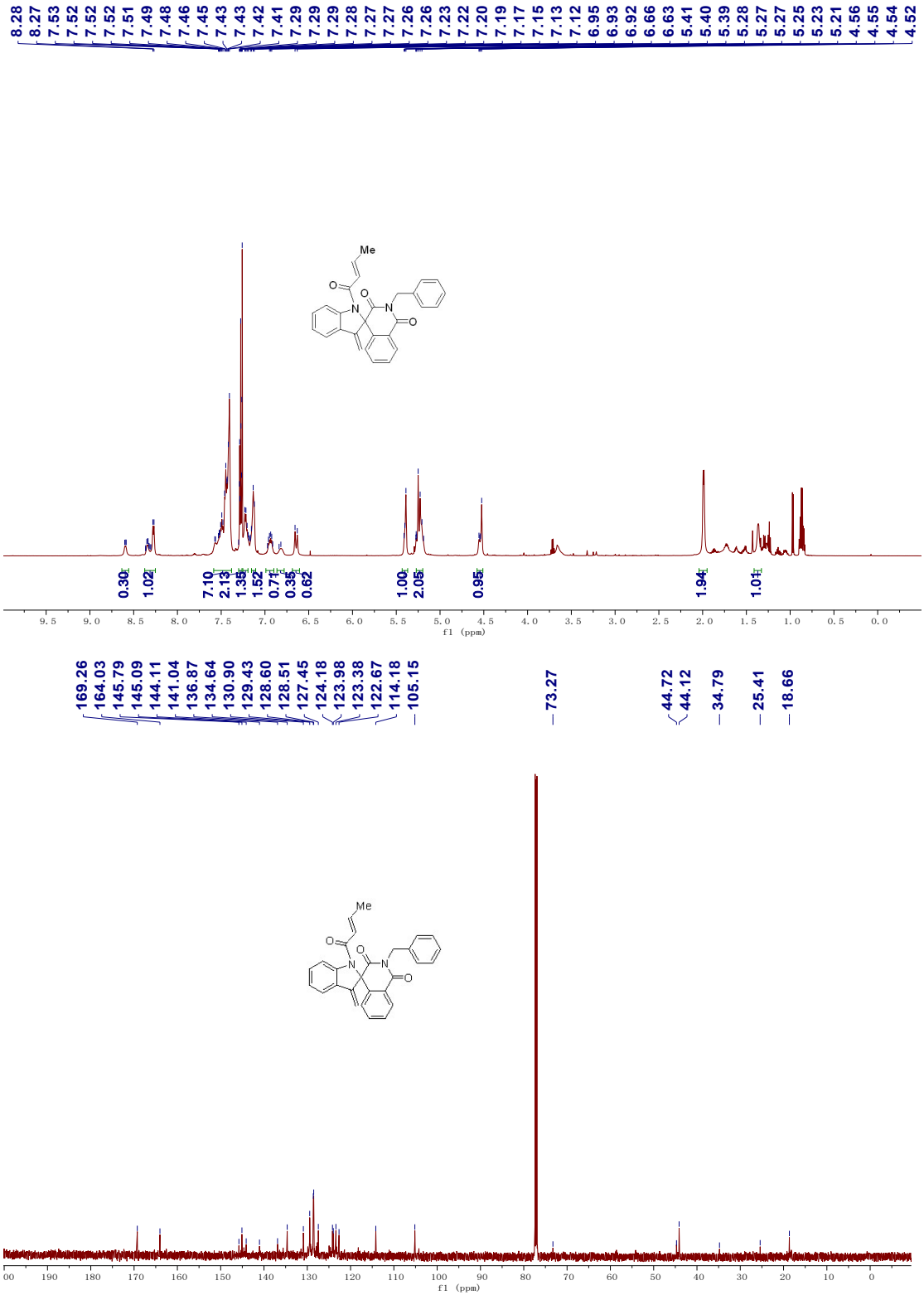


^{1}H and ^{13}C NMR spectra of compound (6j)

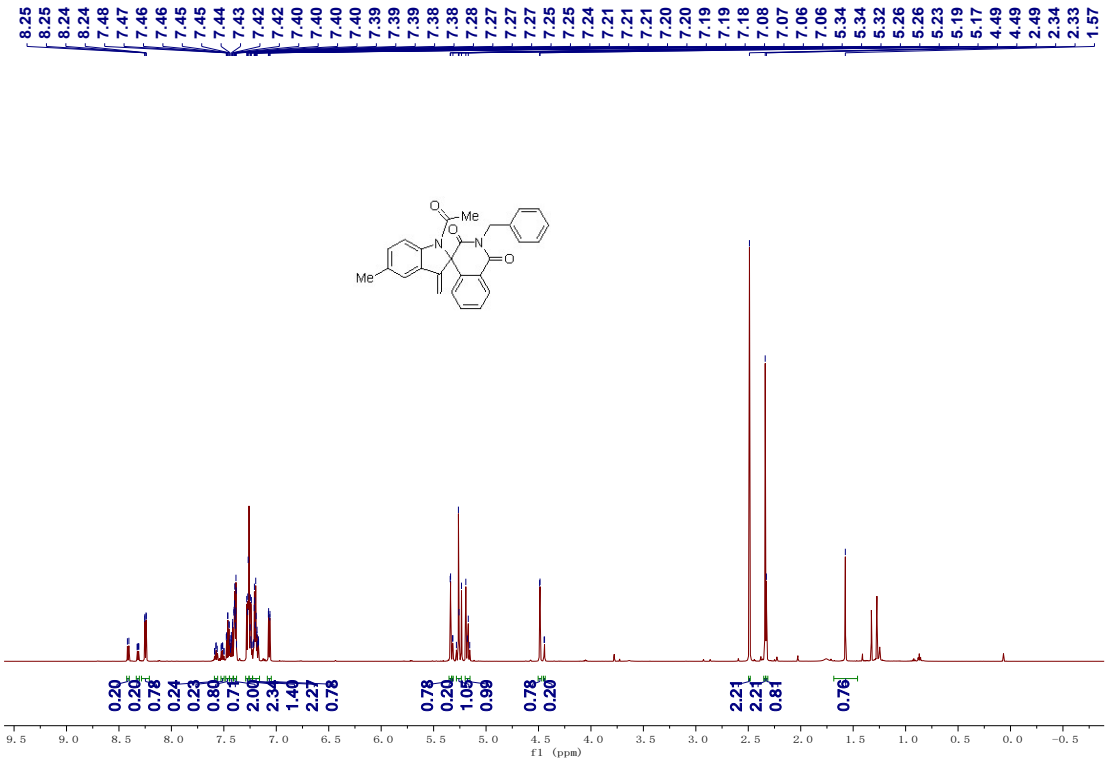


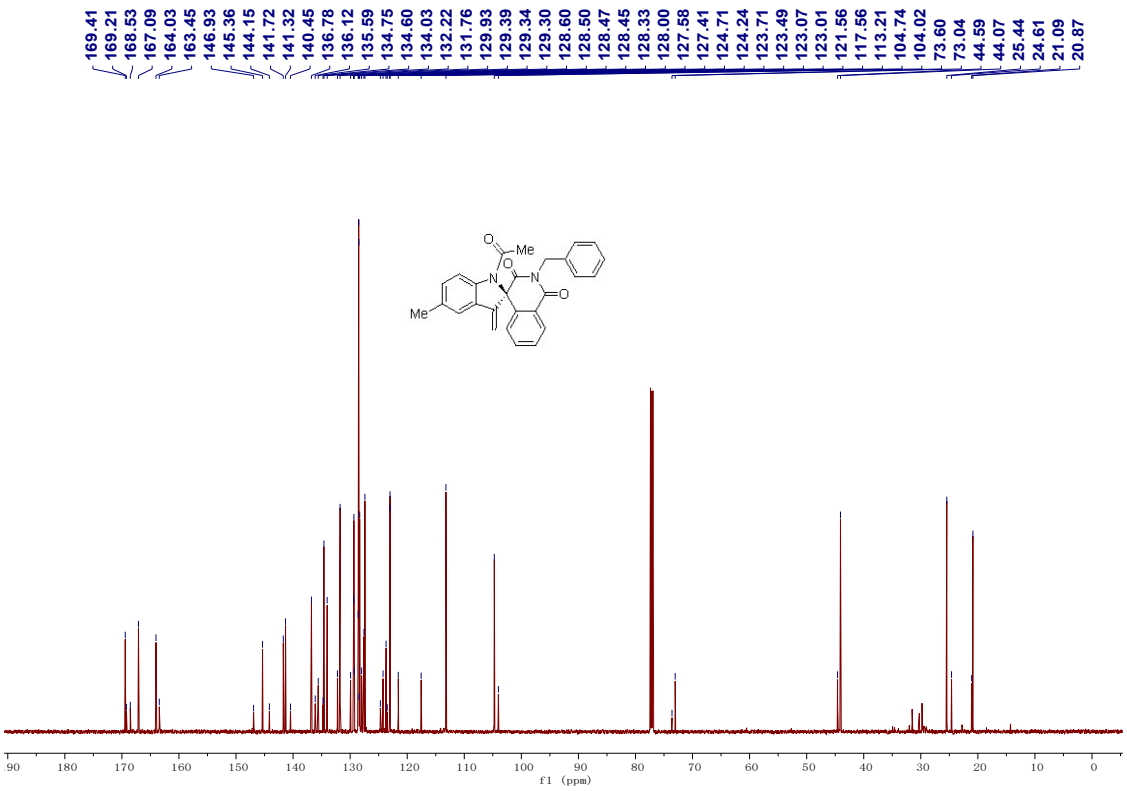


^{1}H and ^{13}C NMR spectra of compound (6k)

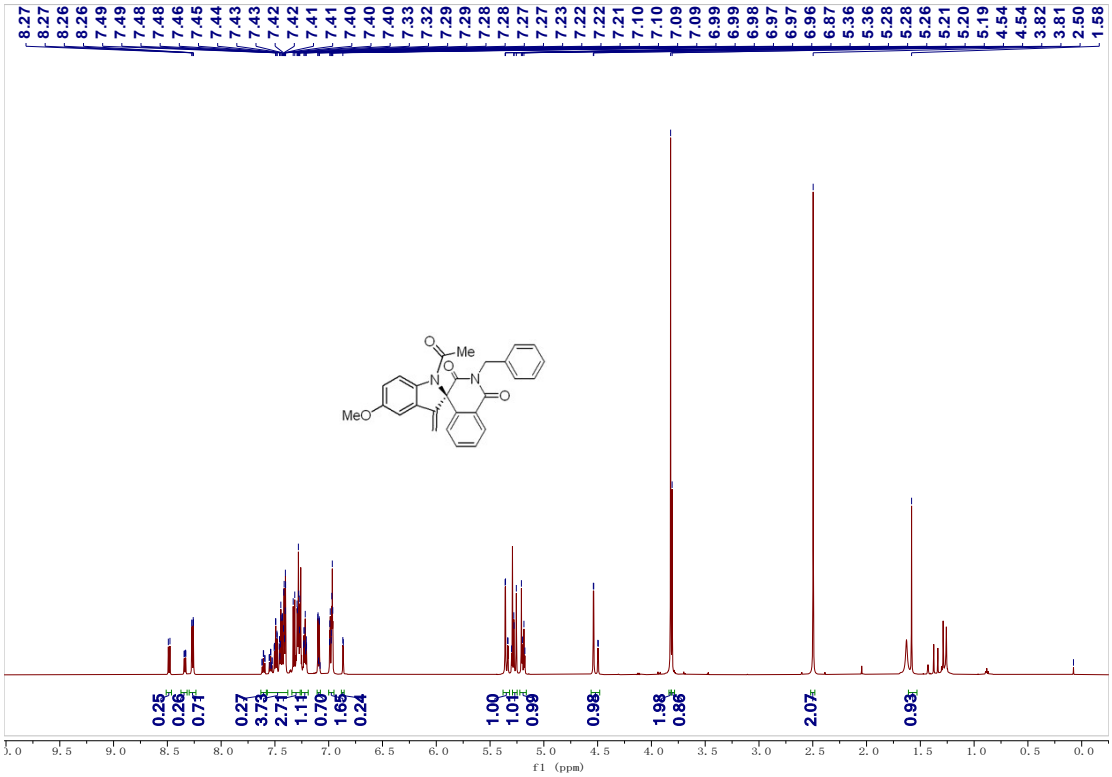


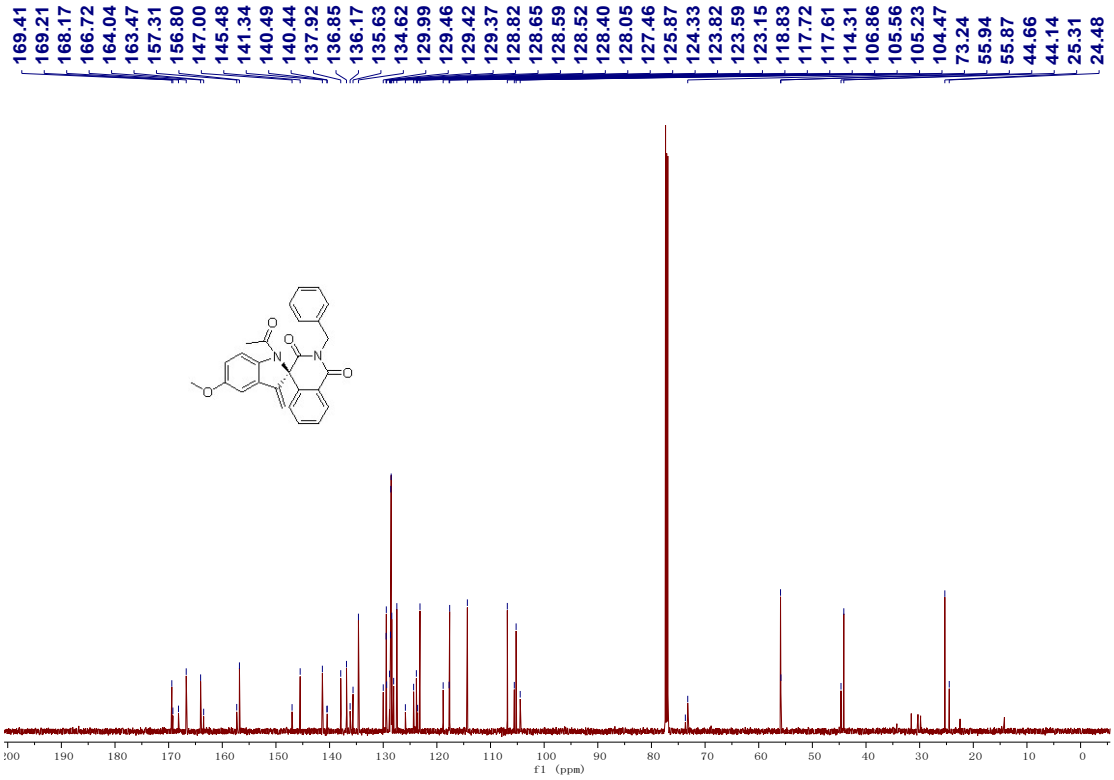
^{1}H and ^{13}C NMR spectra of compound (6l)



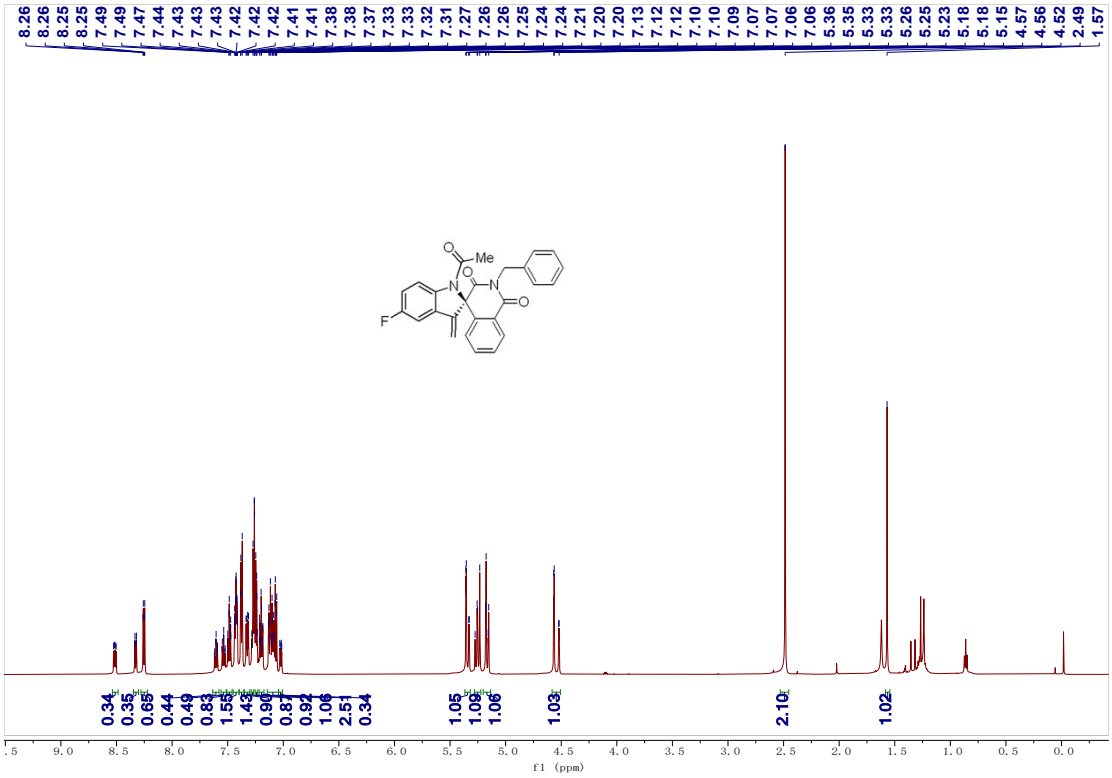


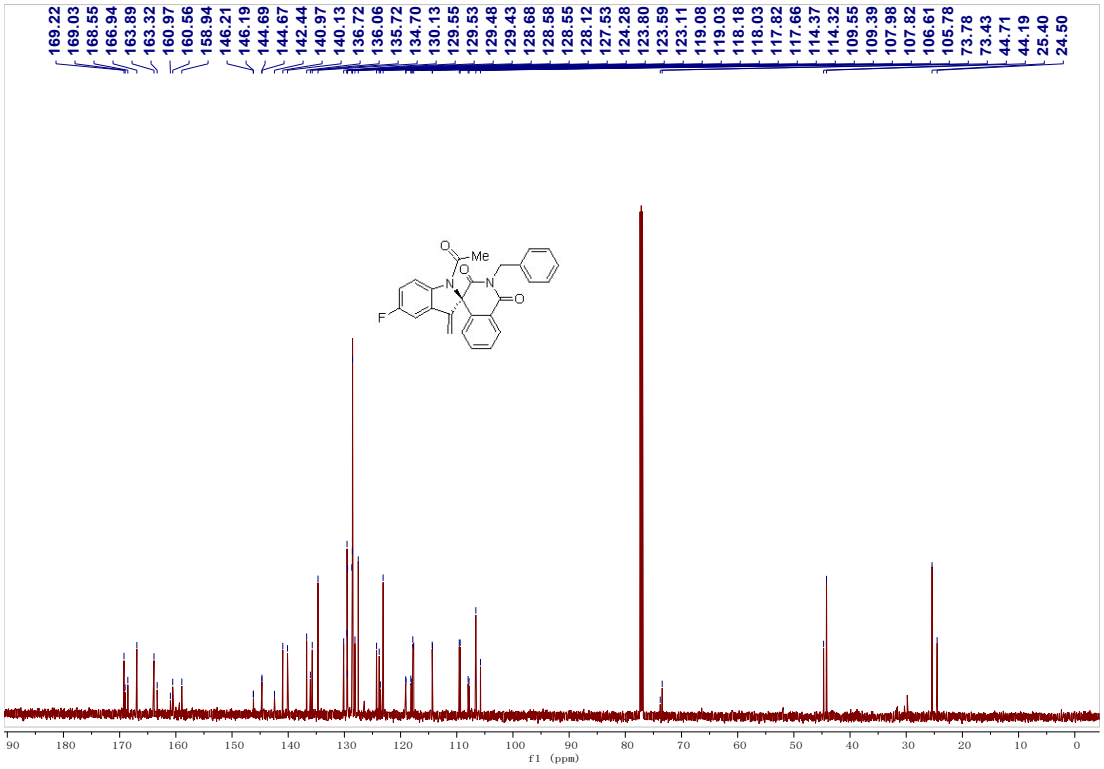
^{1}H and ^{13}C NMR spectra of compound (6m)



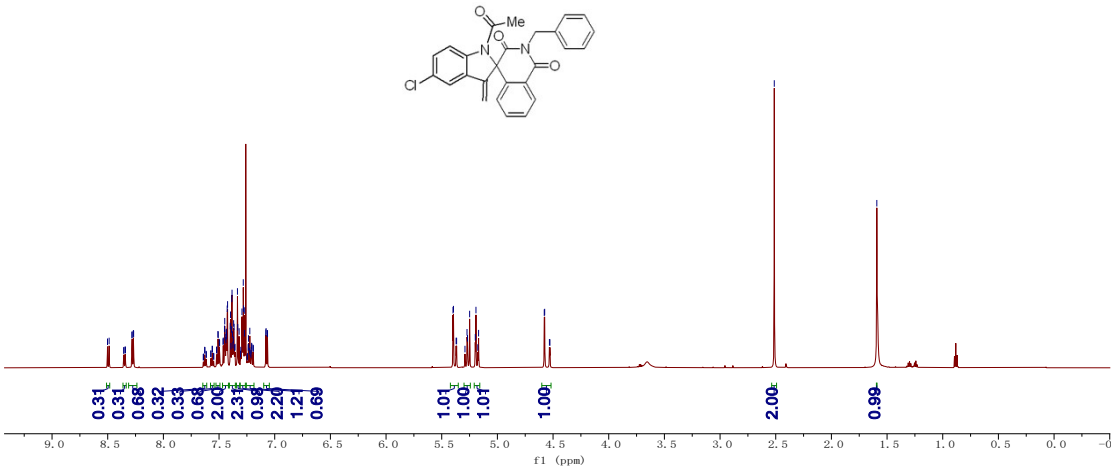


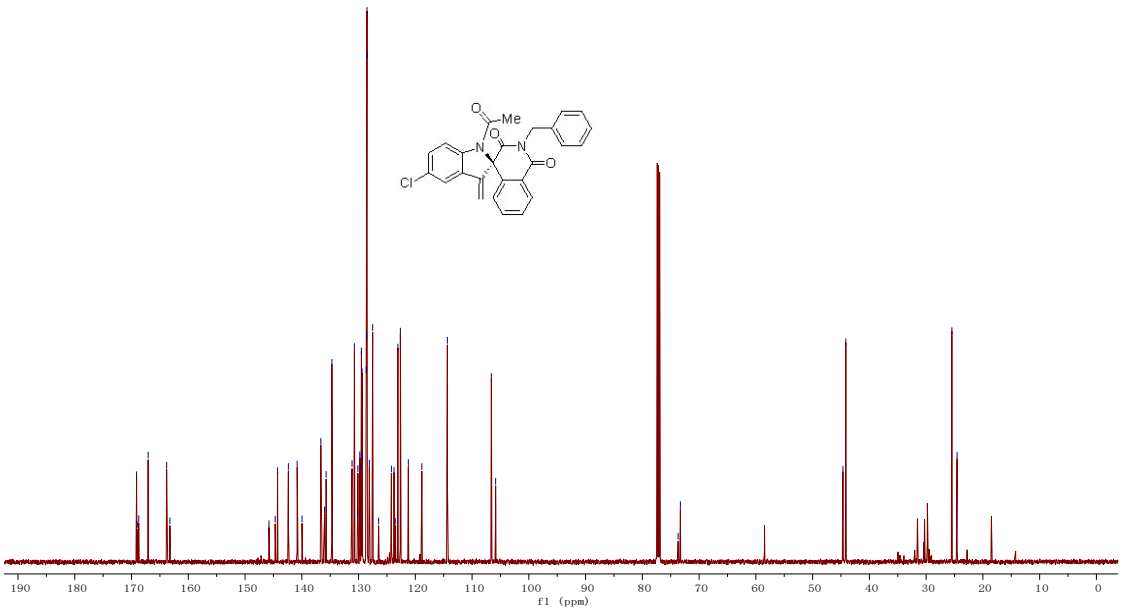
^{1}H and ^{13}C NMR spectra of compound (6n)



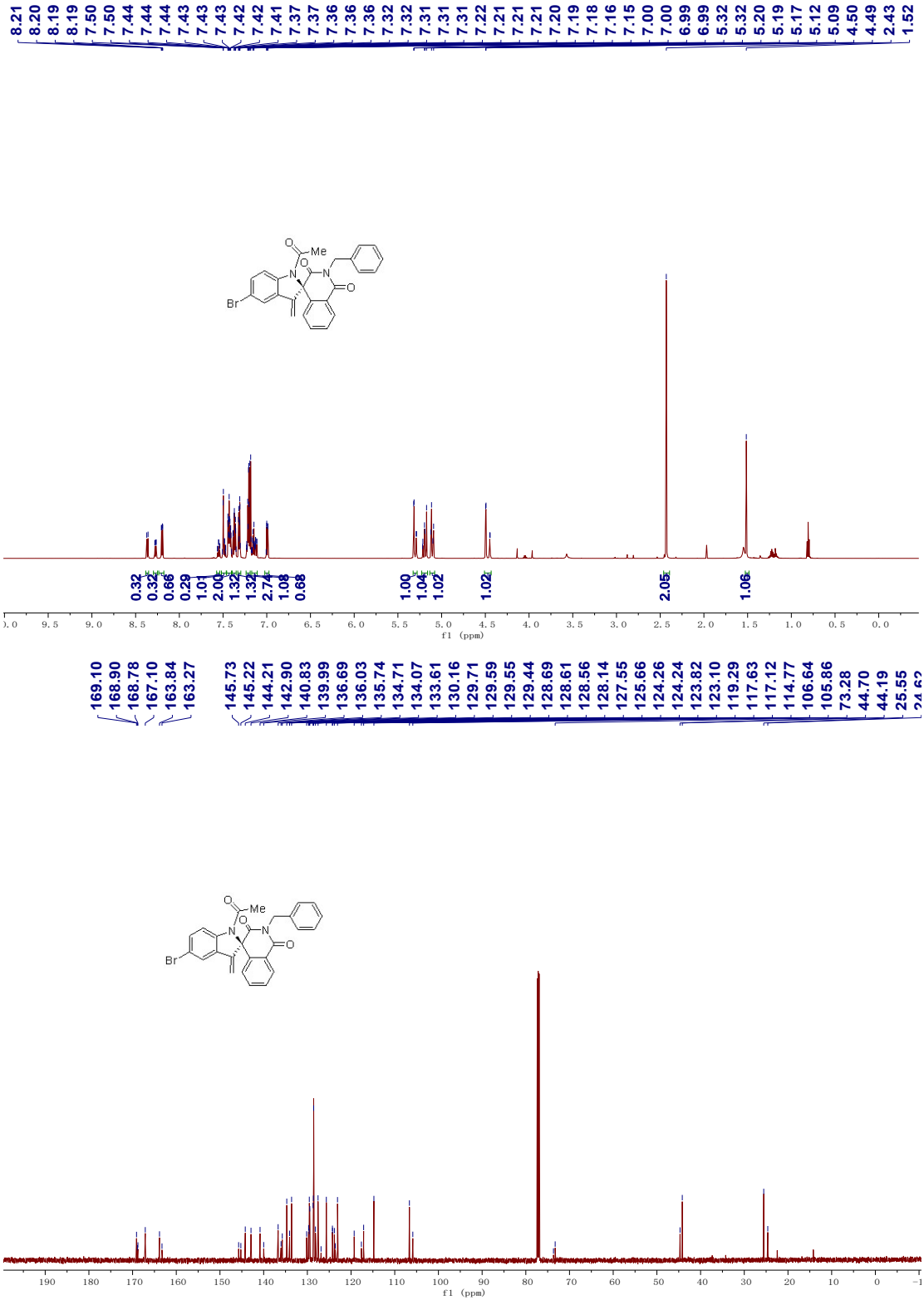


^{1}H and ^{13}C NMR spectra of compound (6o)

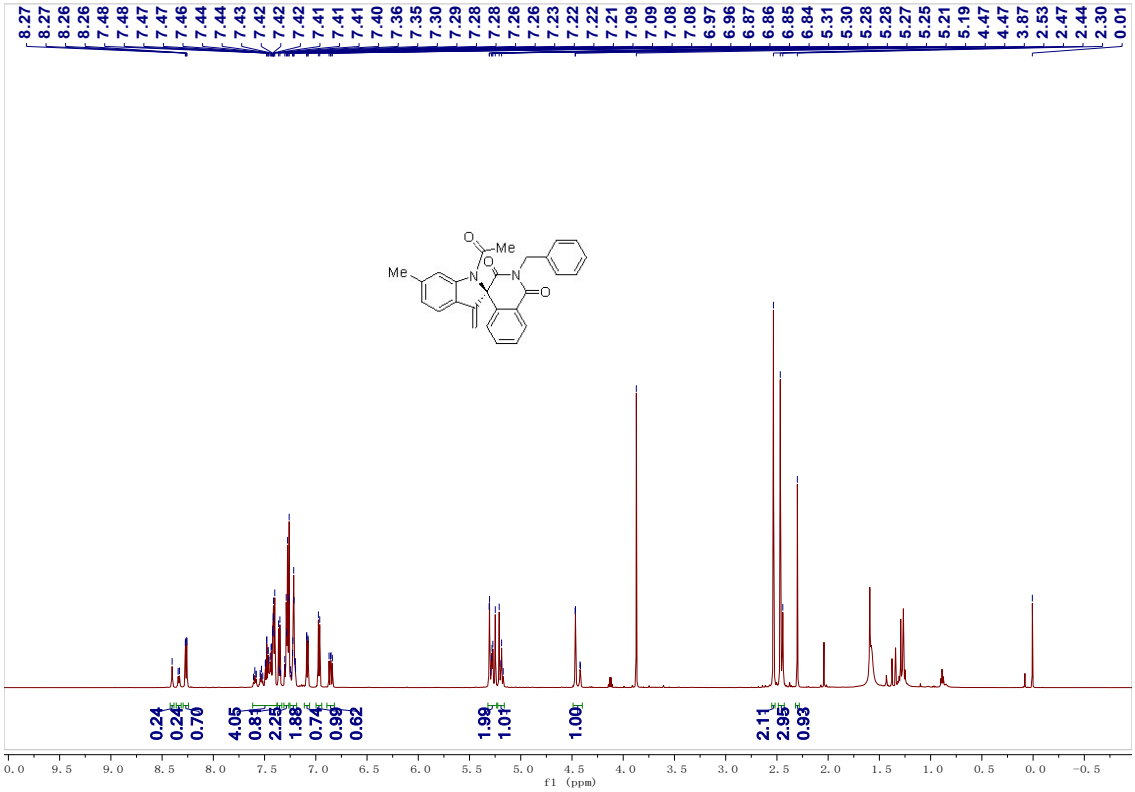


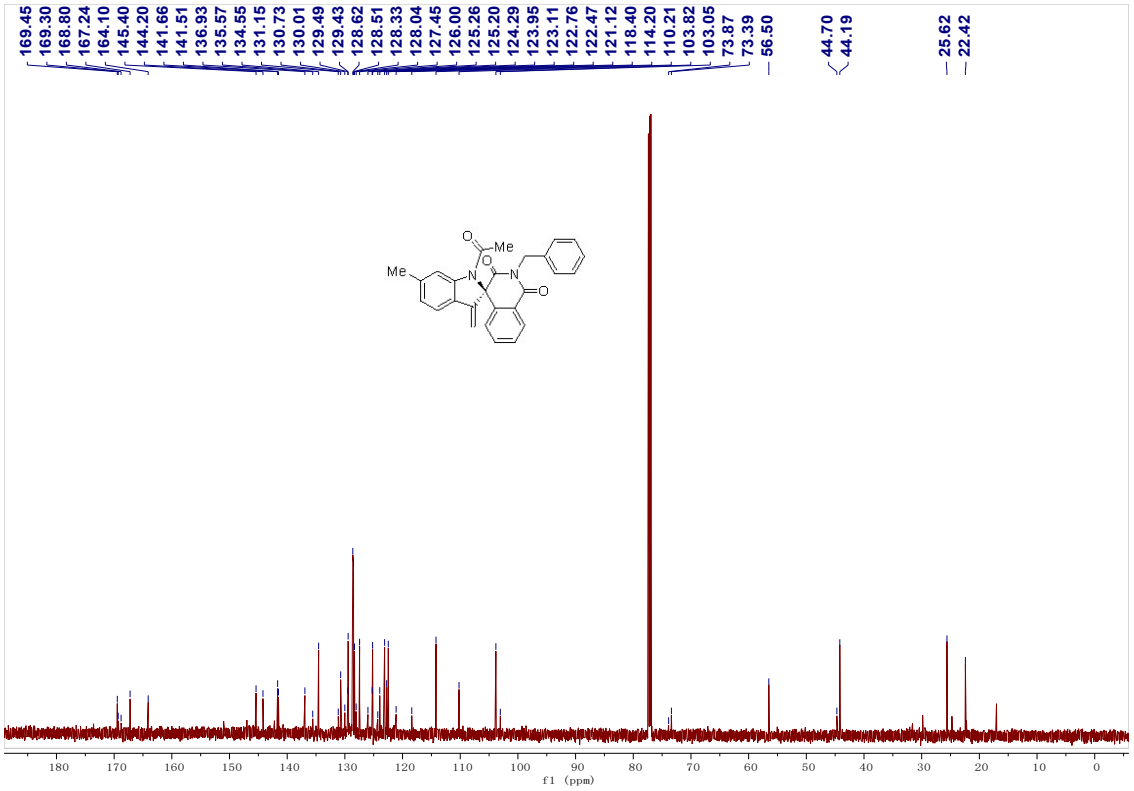


^{1}H and ^{13}C NMR spectra of compound (6p)

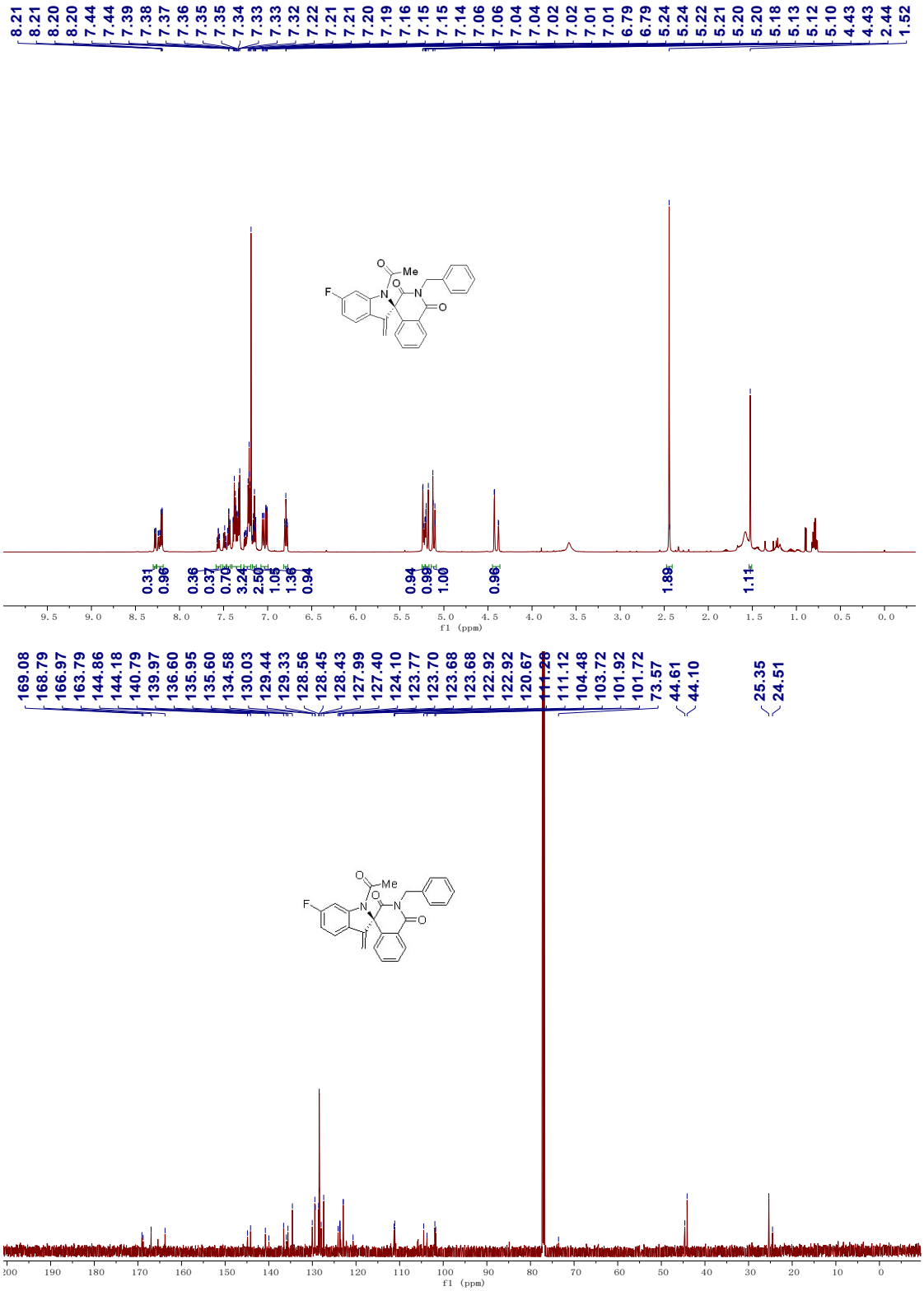


^{1}H and ^{13}C NMR spectra of compound (6q)

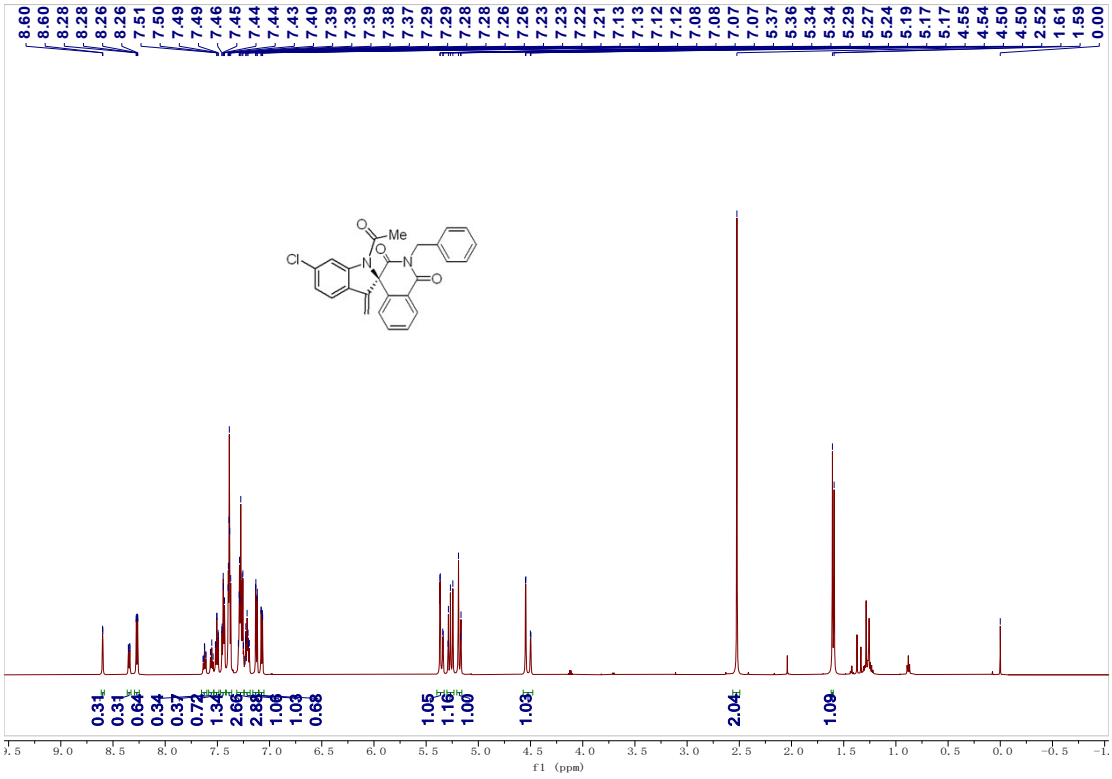


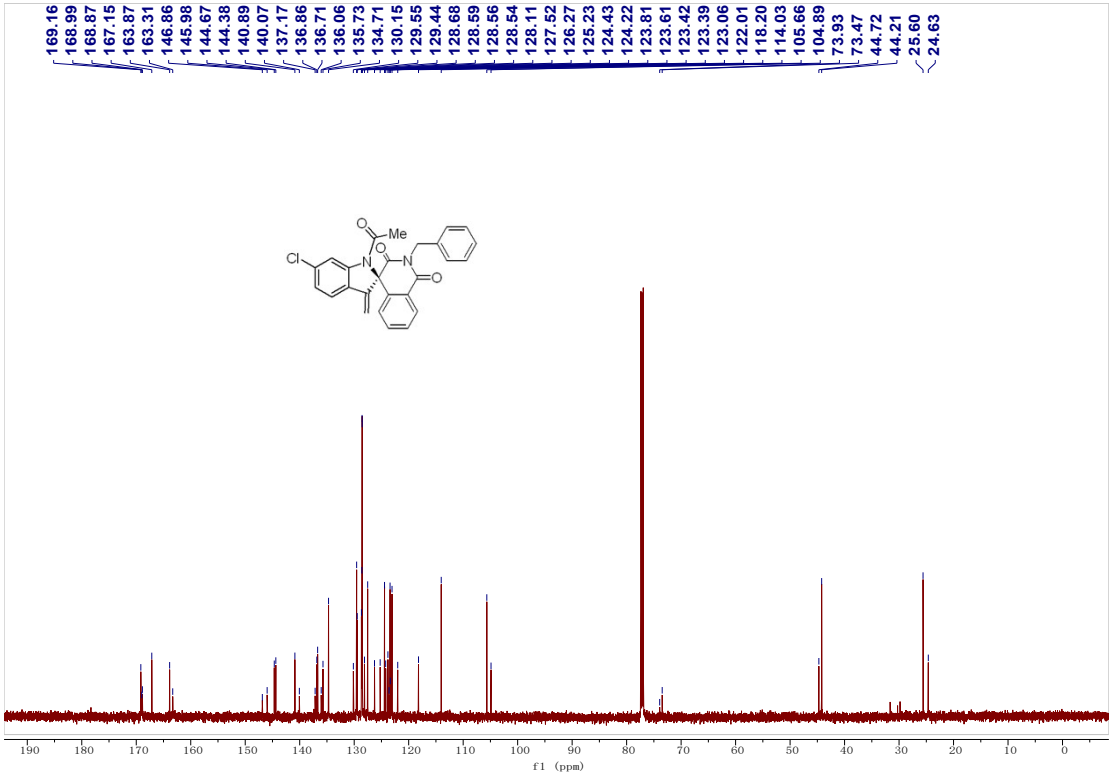


^{1}H and ^{13}C NMR spectra of compound (6r)

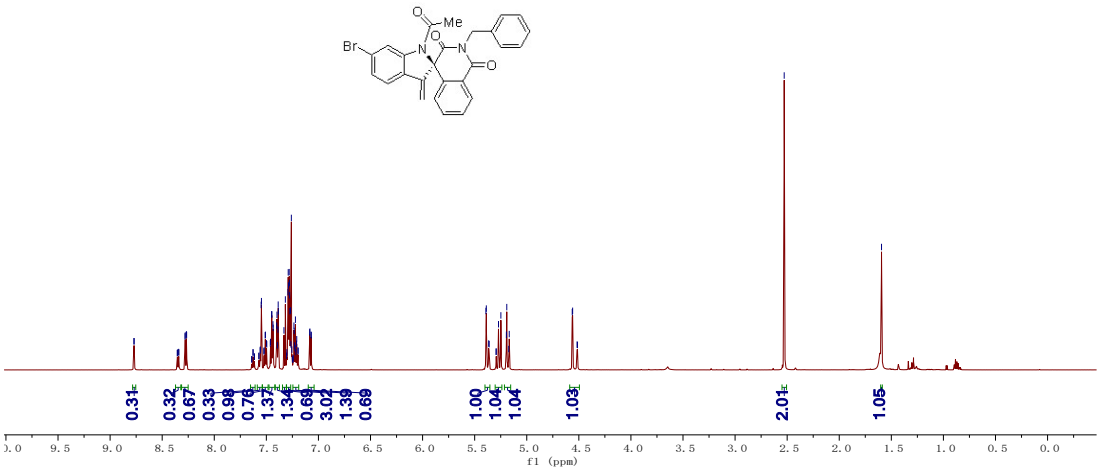


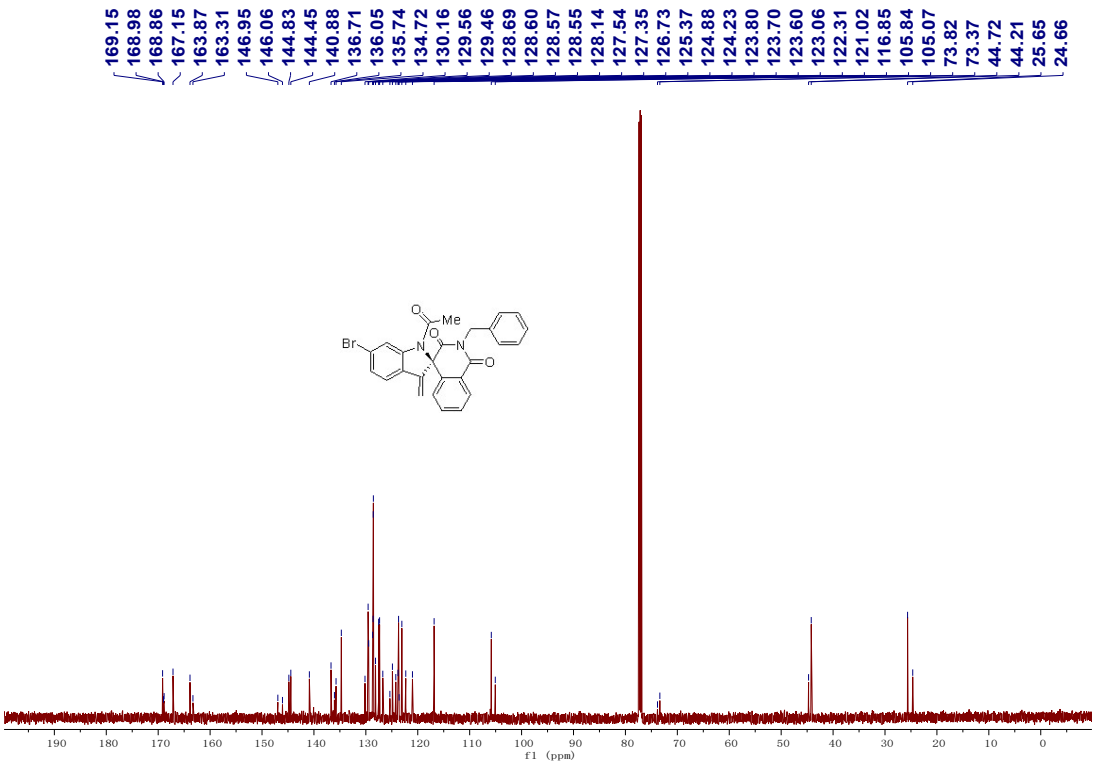
^{1}H and ^{13}C NMR spectra of compound (6s)



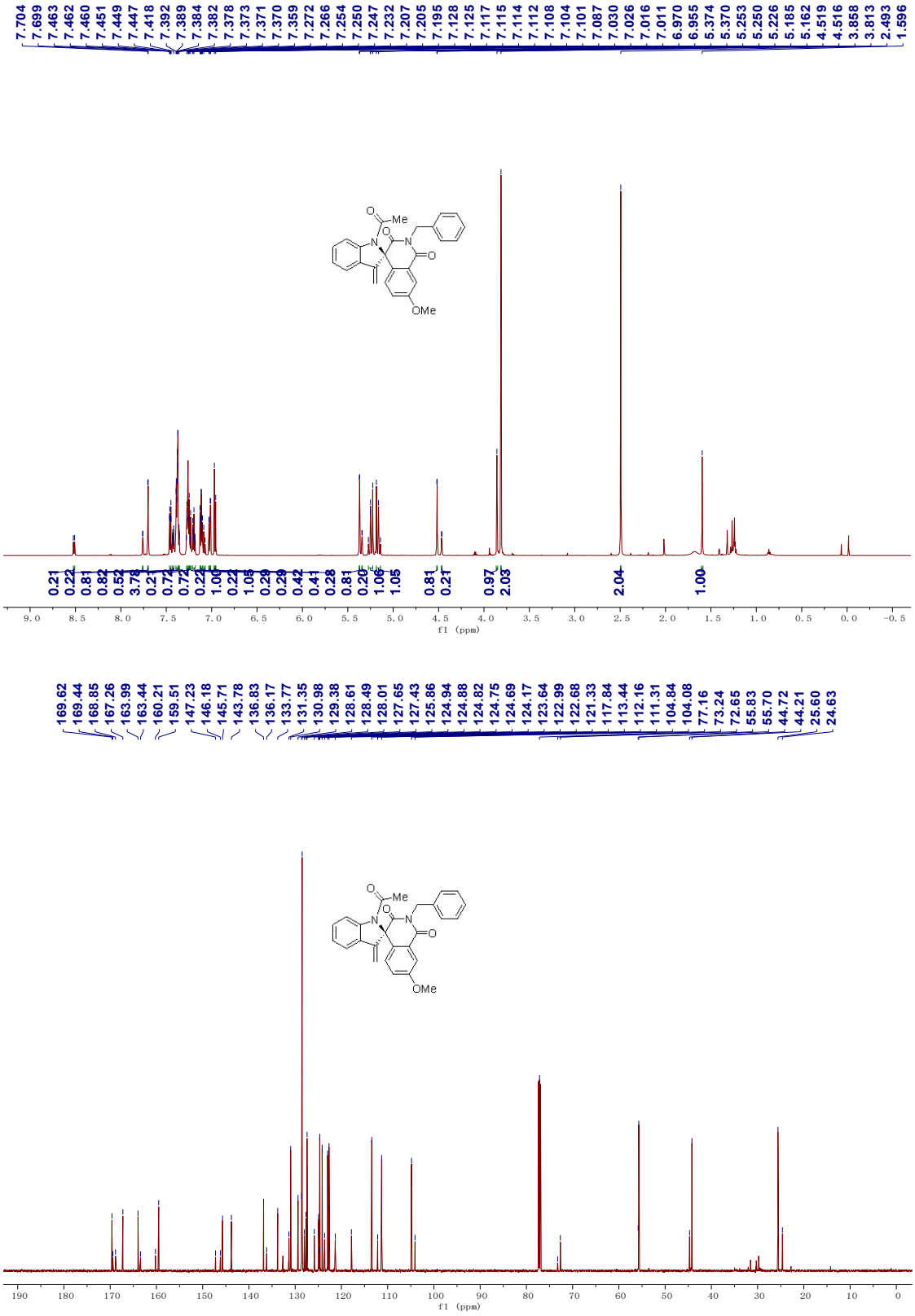


^{1}H and ^{13}C NMR spectra of compound (6t)

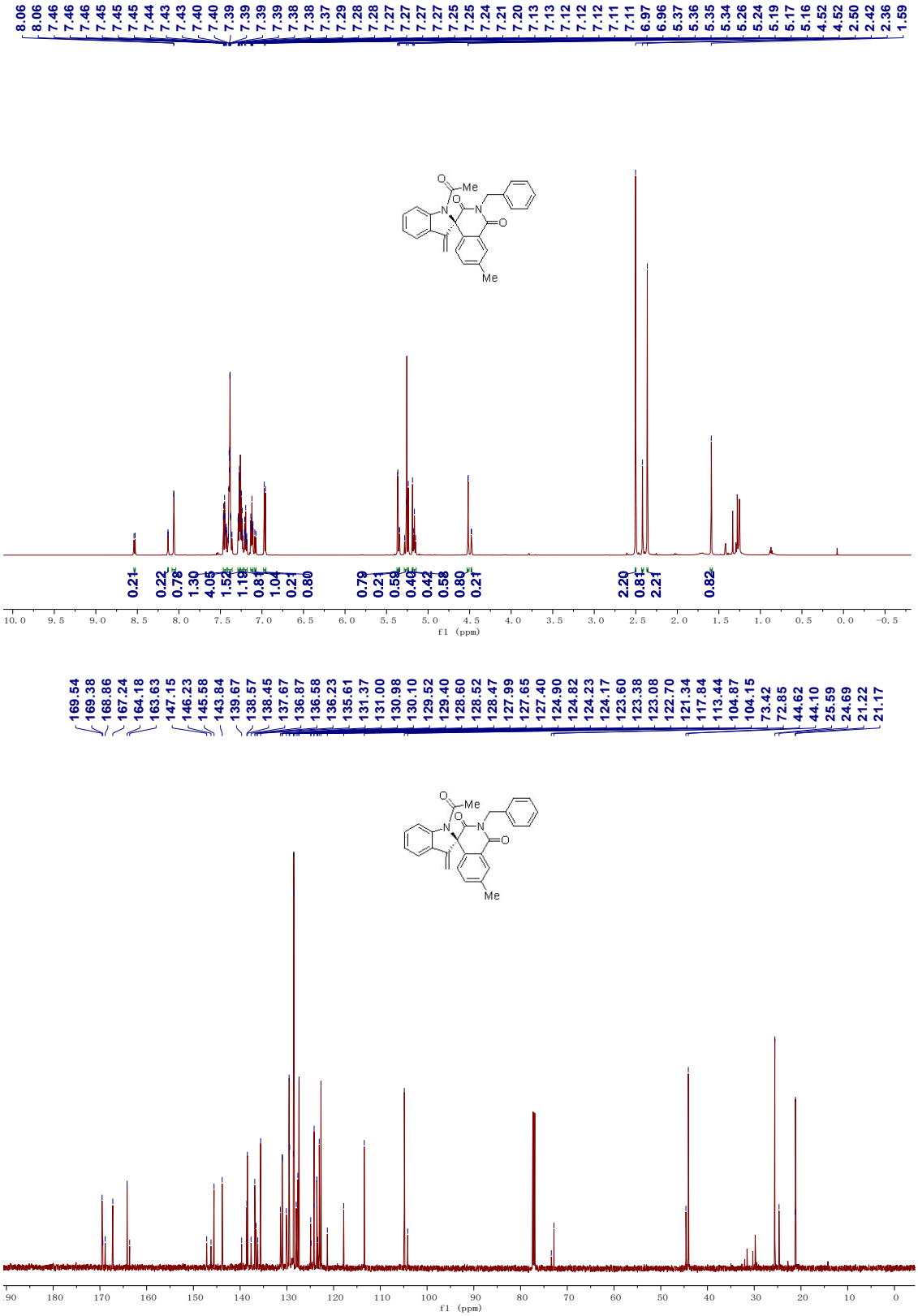




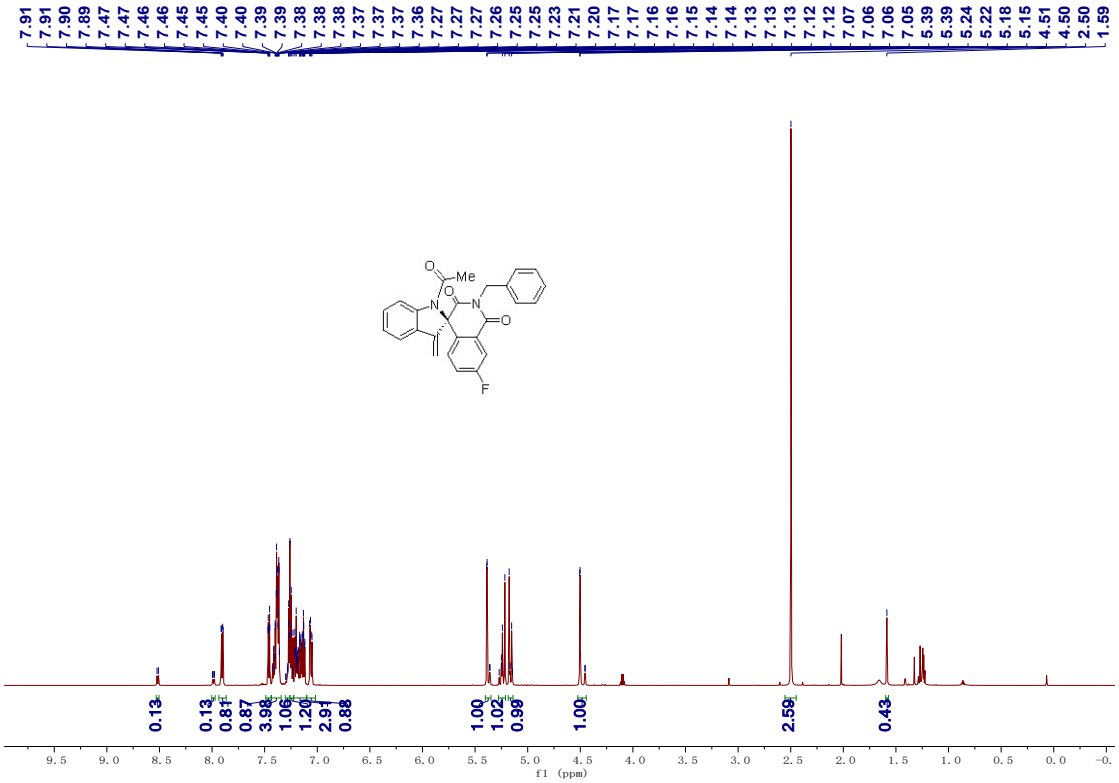
^{1}H and ^{13}C NMR spectra of compound (6u)

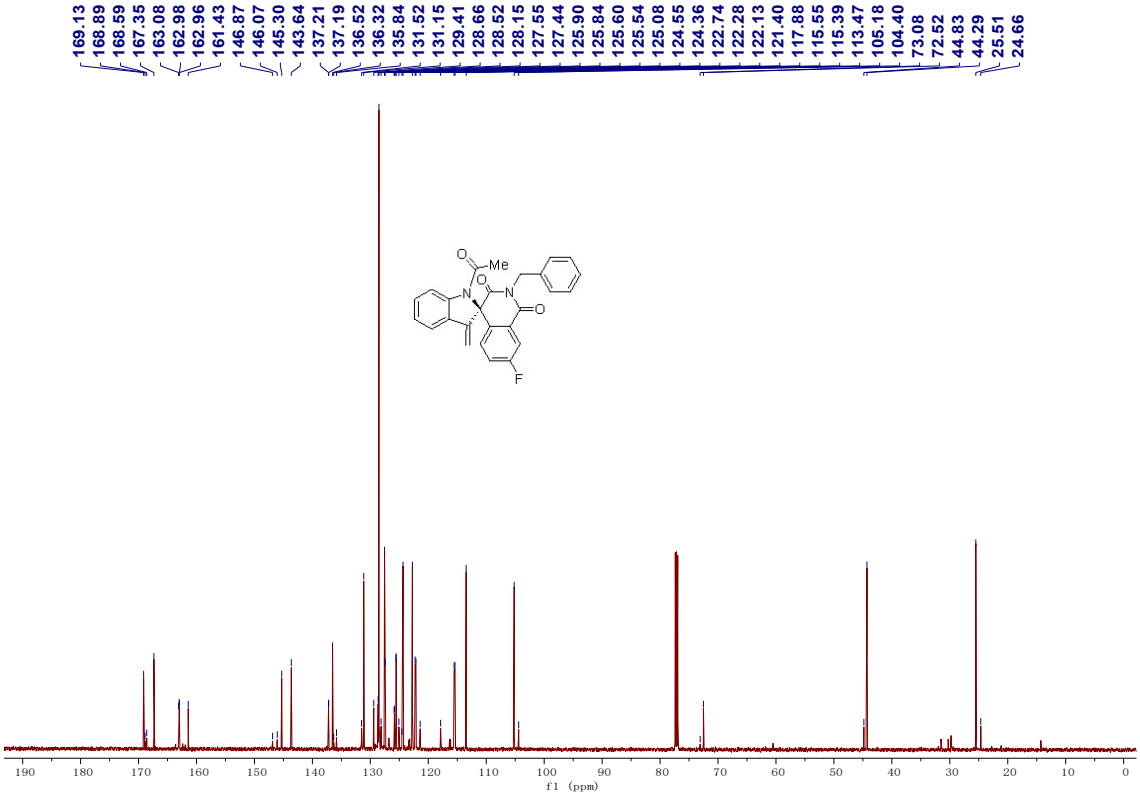


^{1}H and ^{13}C NMR spectra of compound (6v)

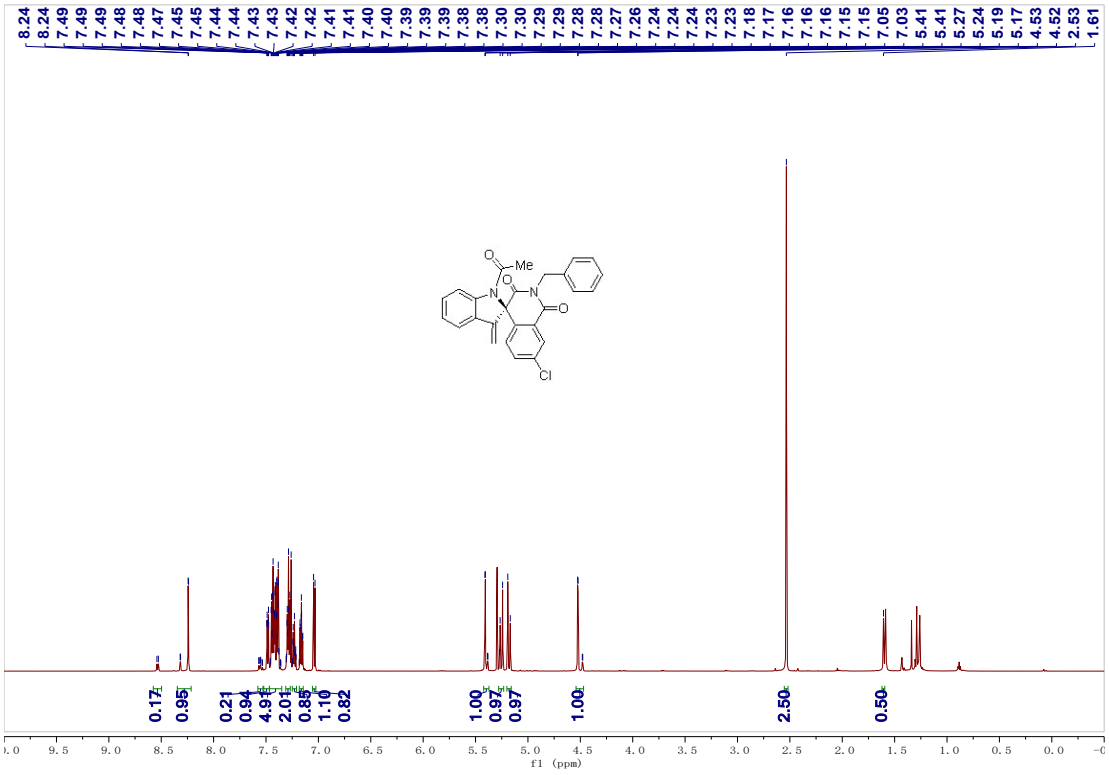


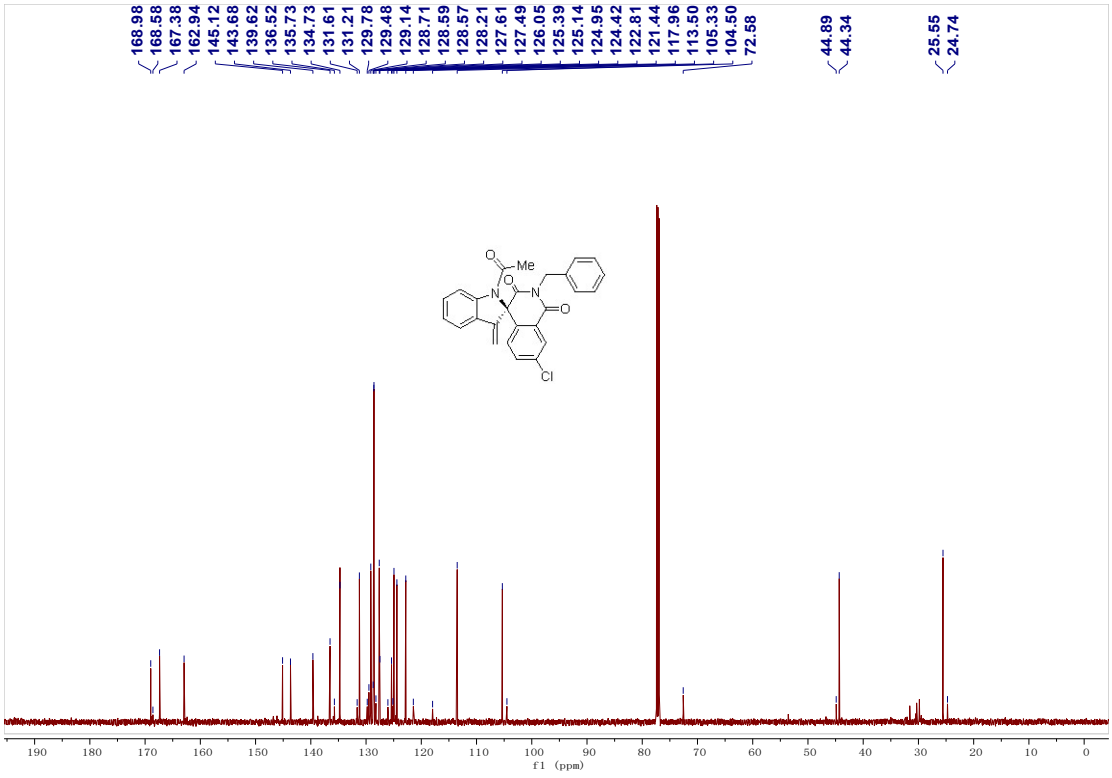
^{1}H and ^{13}C NMR spectra of compound (6w)



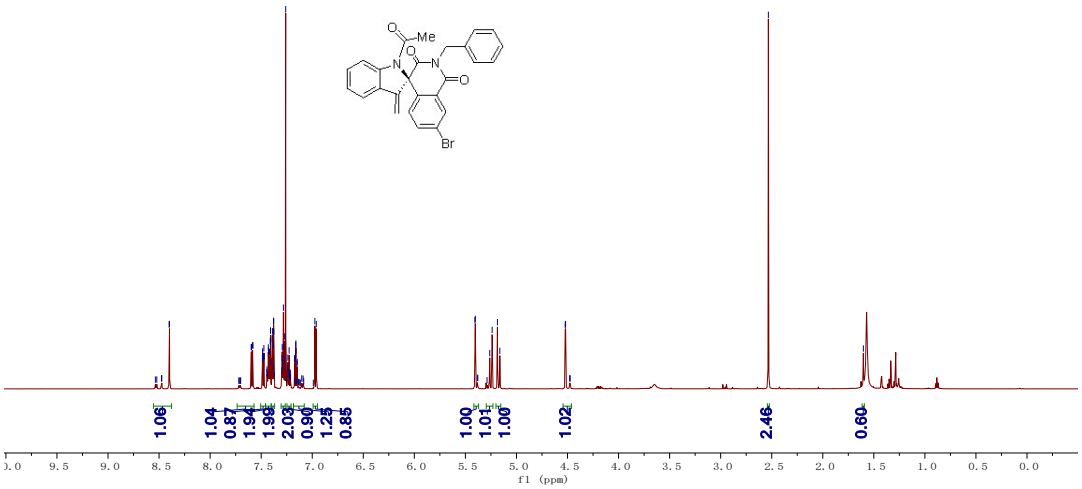


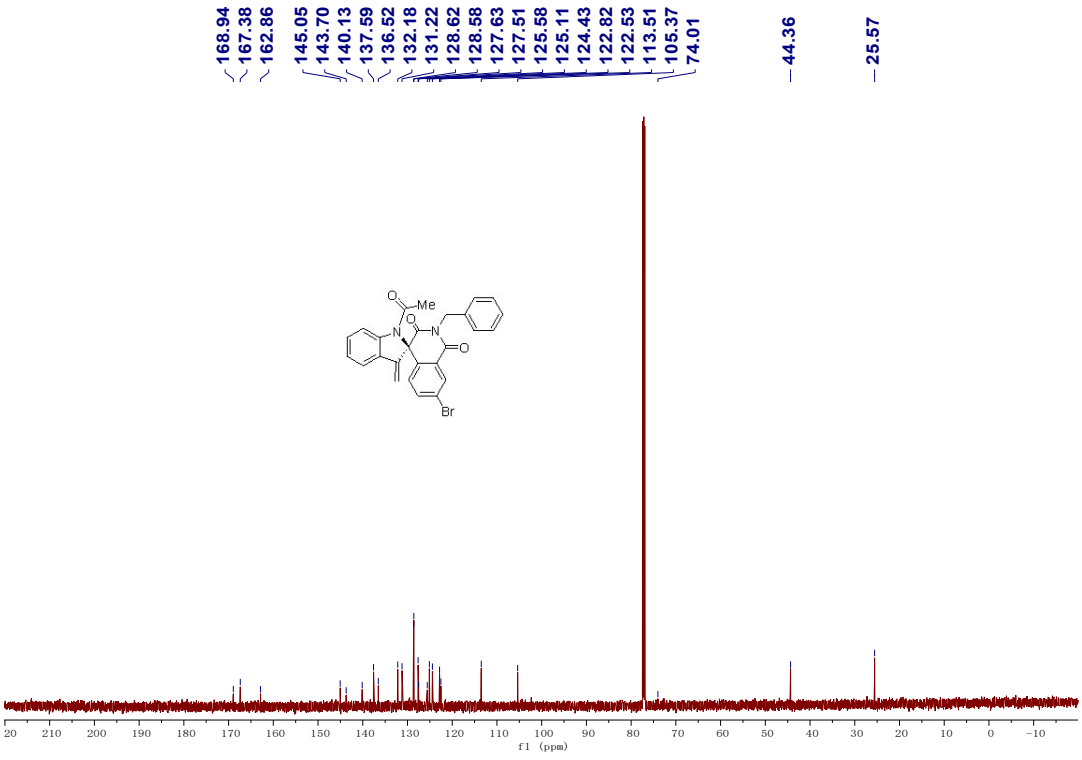
^{1}H and ^{13}C NMR spectra of compound (6x)



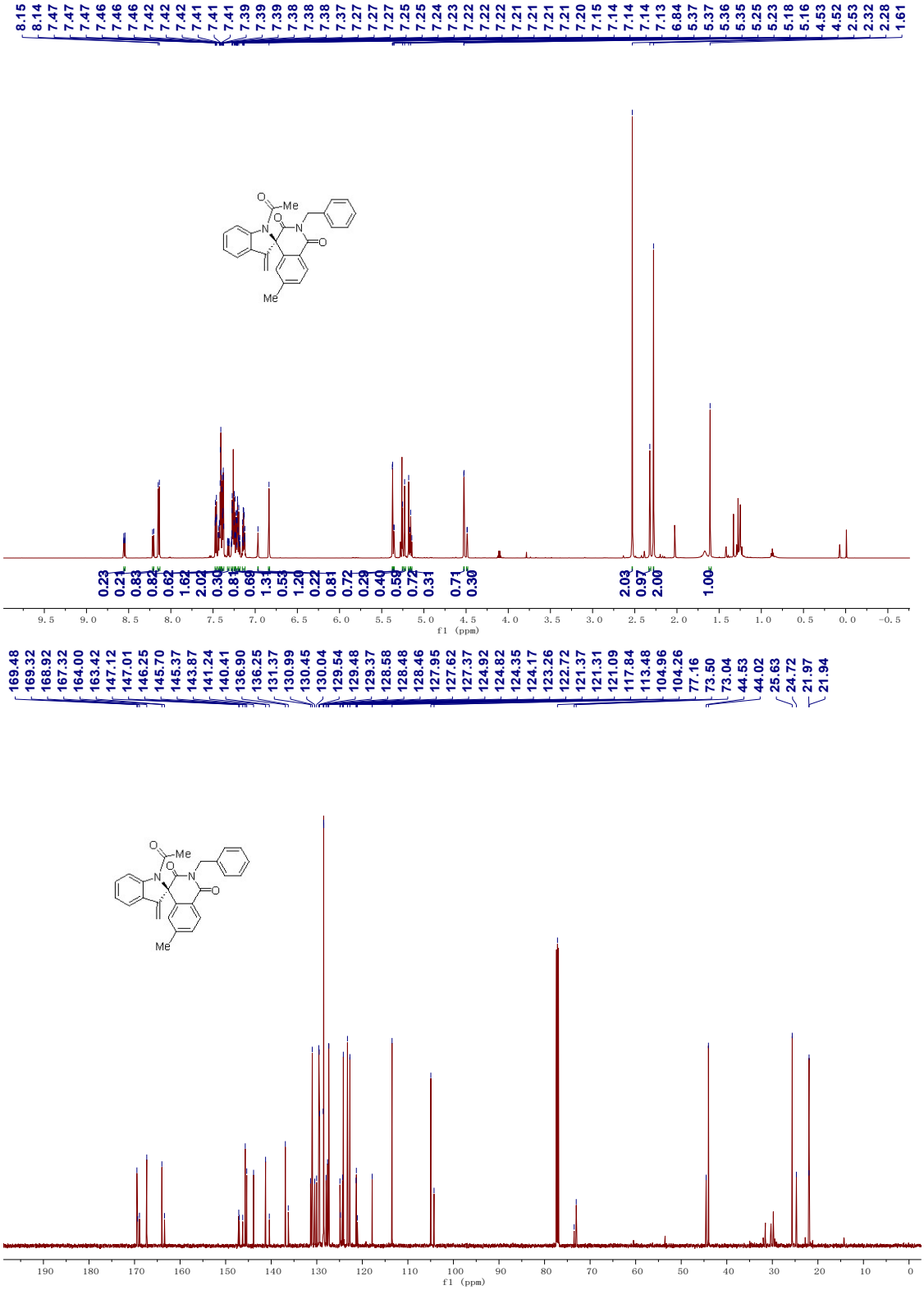


^{1}H and ^{13}C NMR spectra of compound (6y)

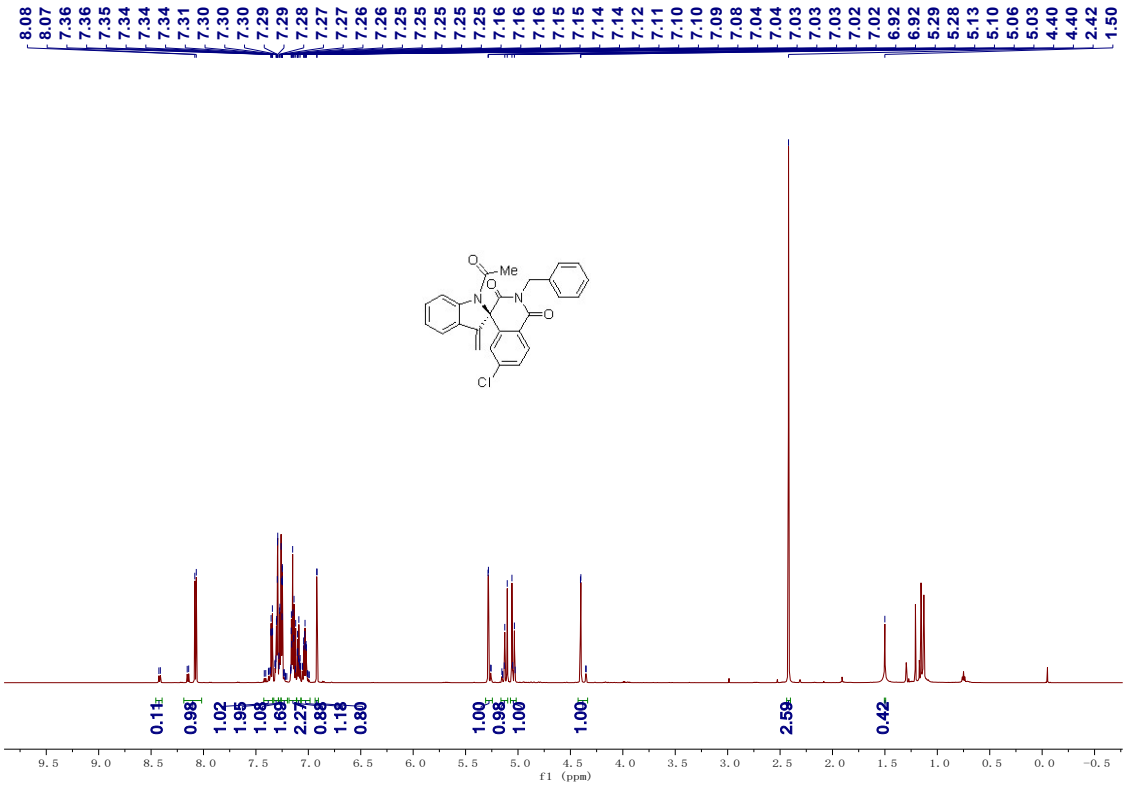


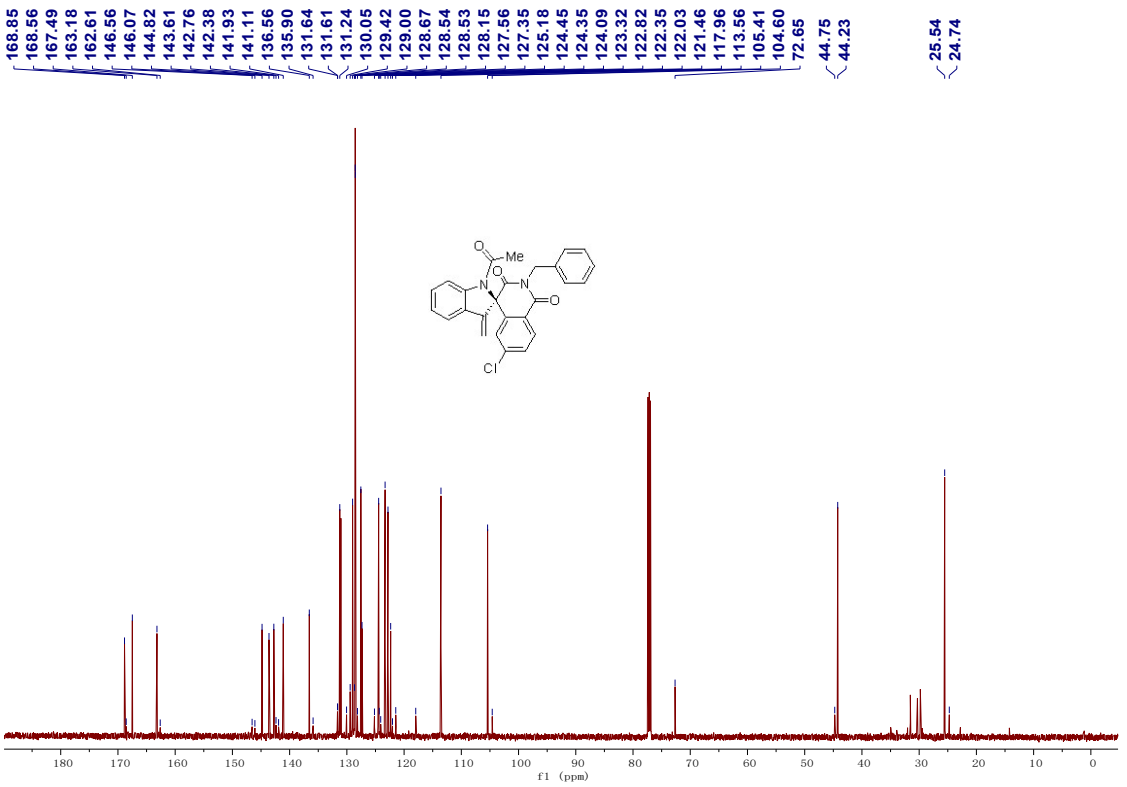


^{1}H and ^{13}C NMR spectra of compound (6z)

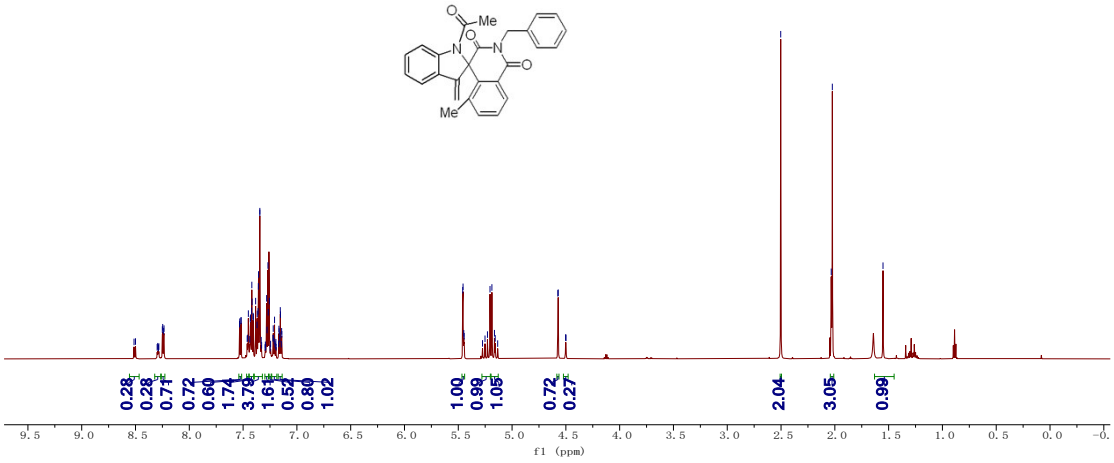


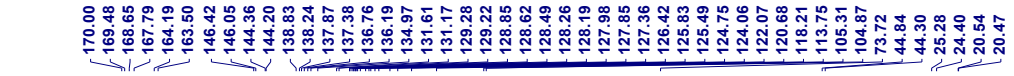
^{1}H and ^{13}C NMR spectra of compound (6aa)

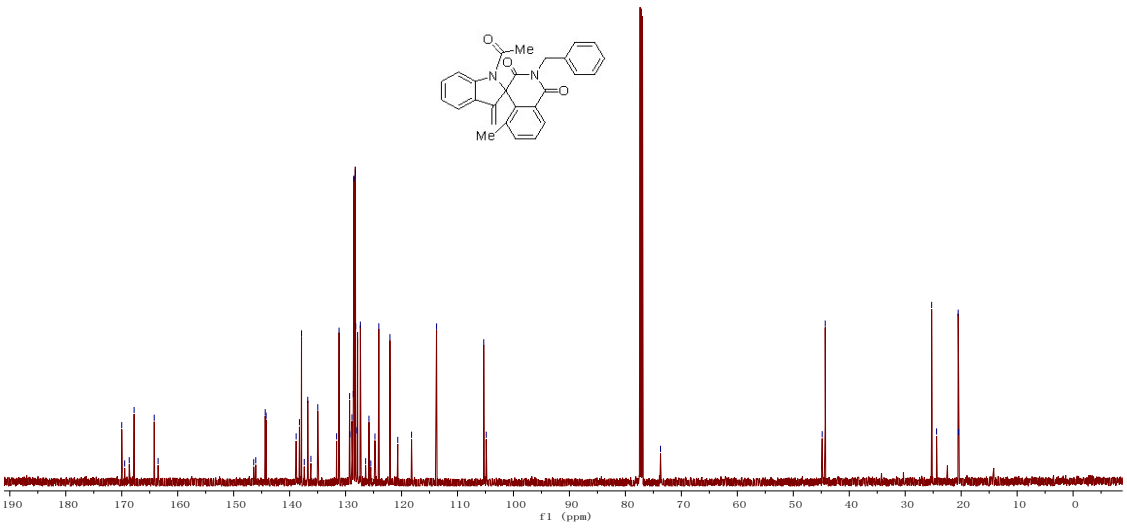




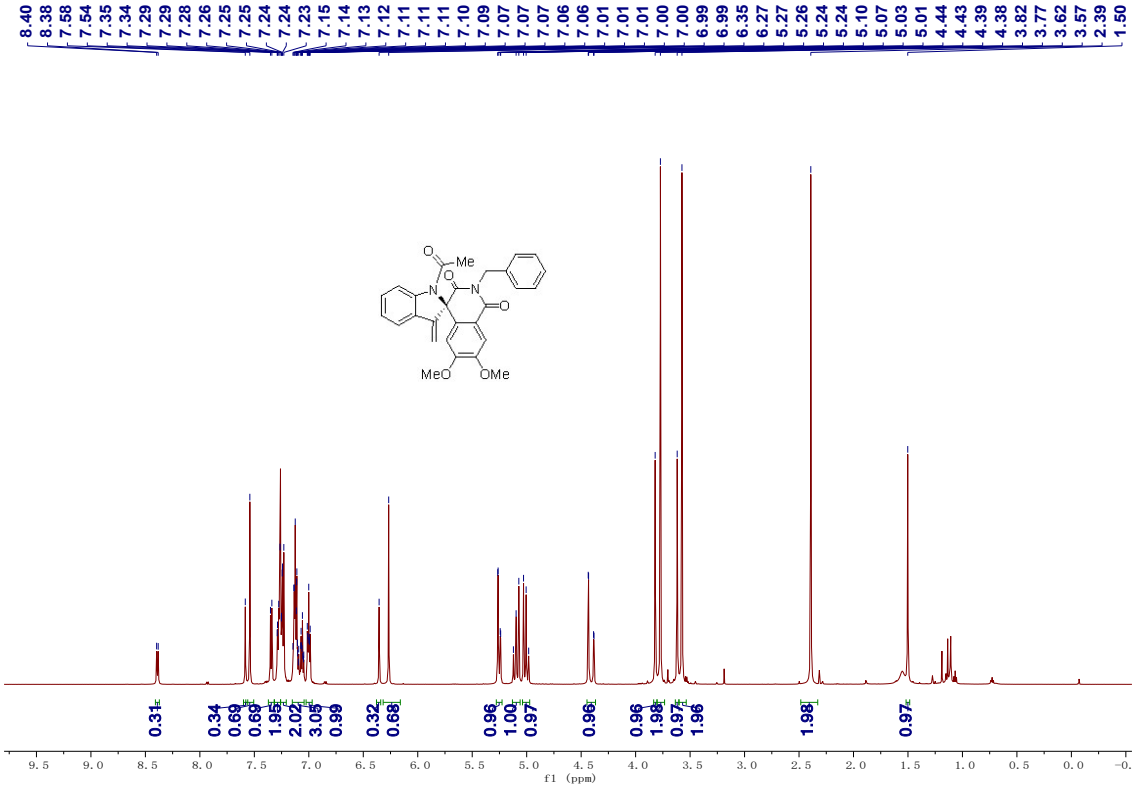
^{1}H and ^{13}C NMR spectra of compound (6ab)

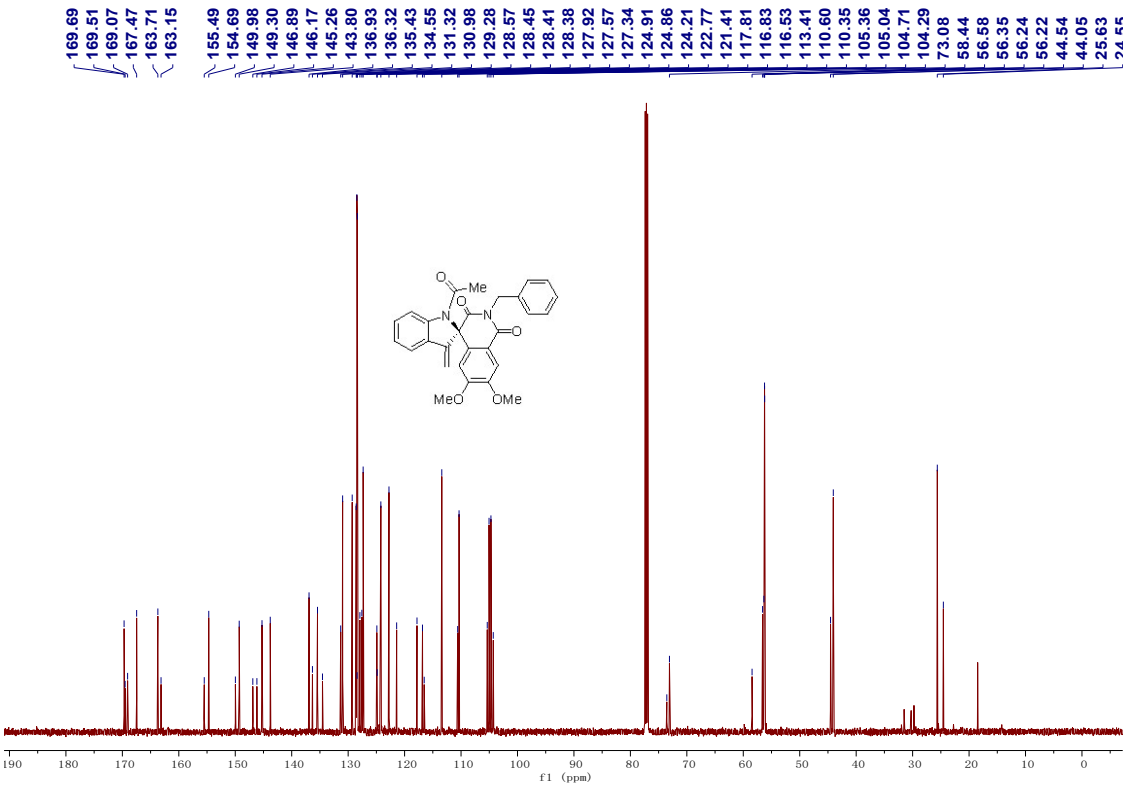




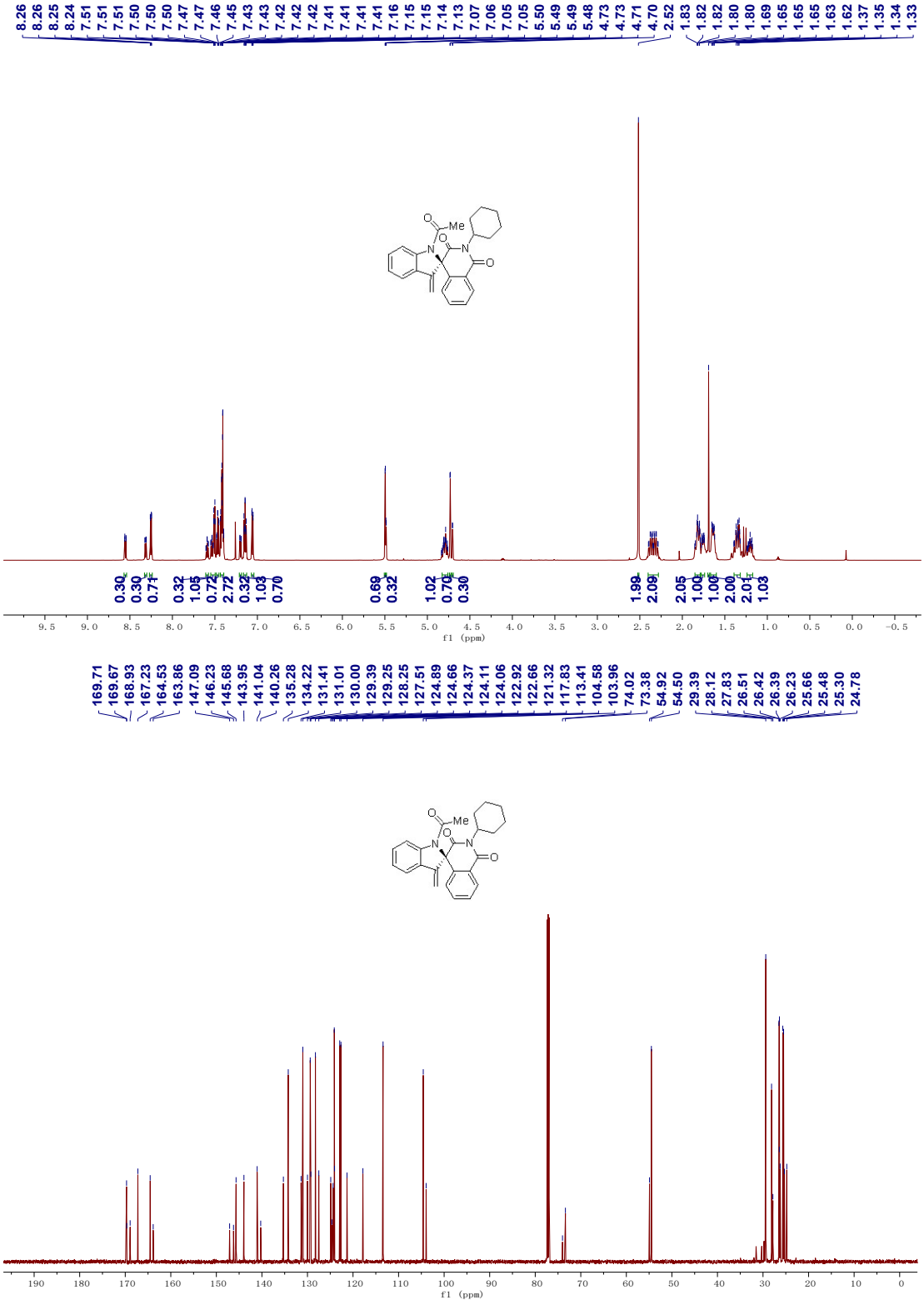


^{1}H and ^{13}C NMR spectra of compound (6ac)

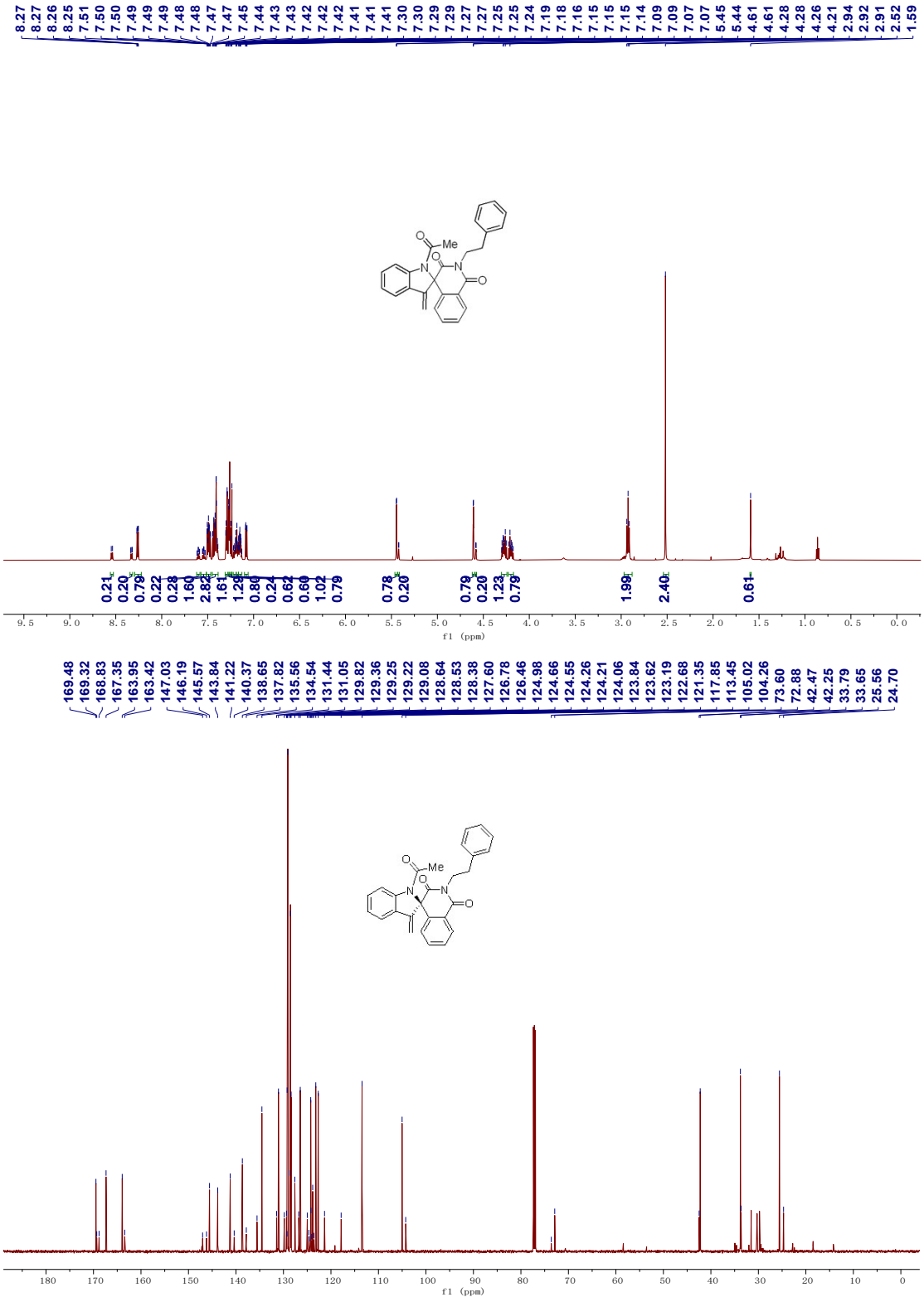




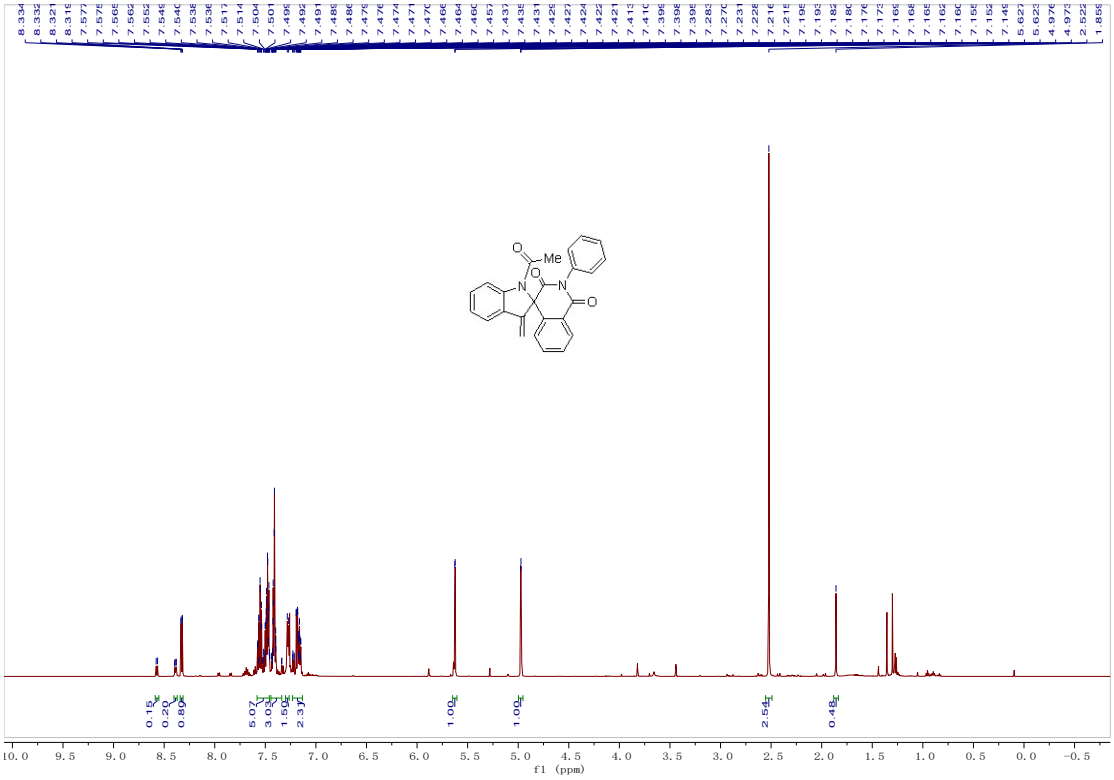
^{1}H and ^{13}C NMR spectra of compound (6ad)

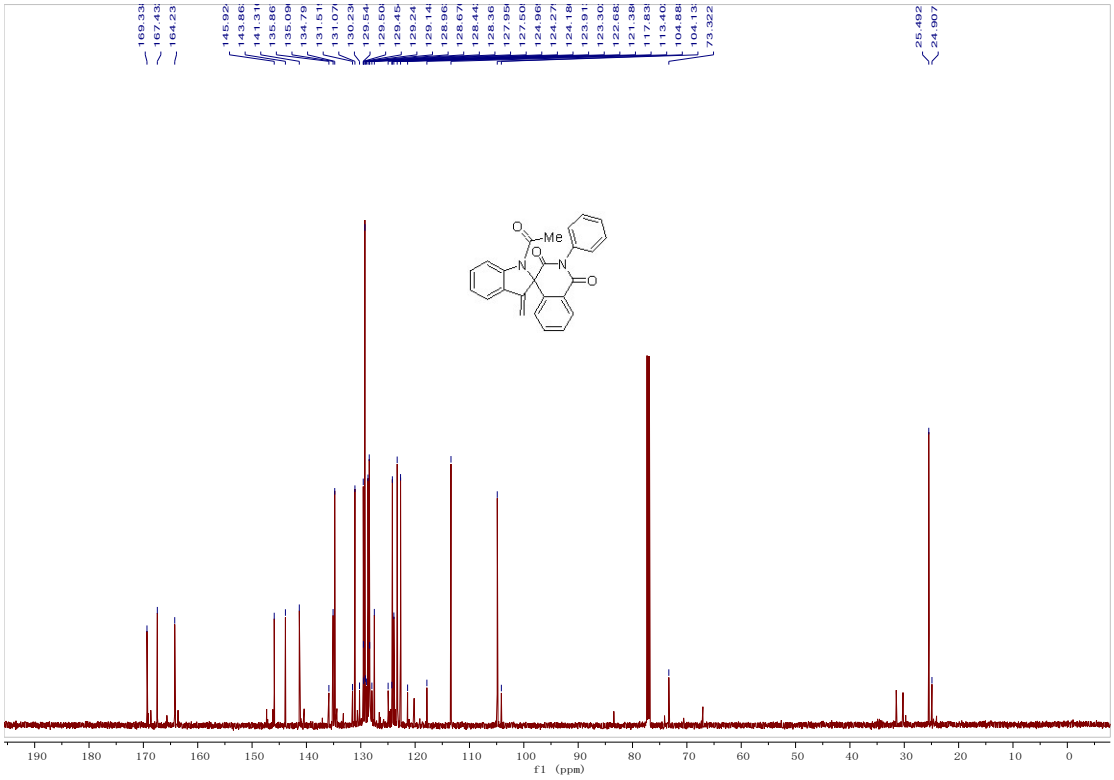


^{1}H and ^{13}C NMR spectra of compound (6ae)

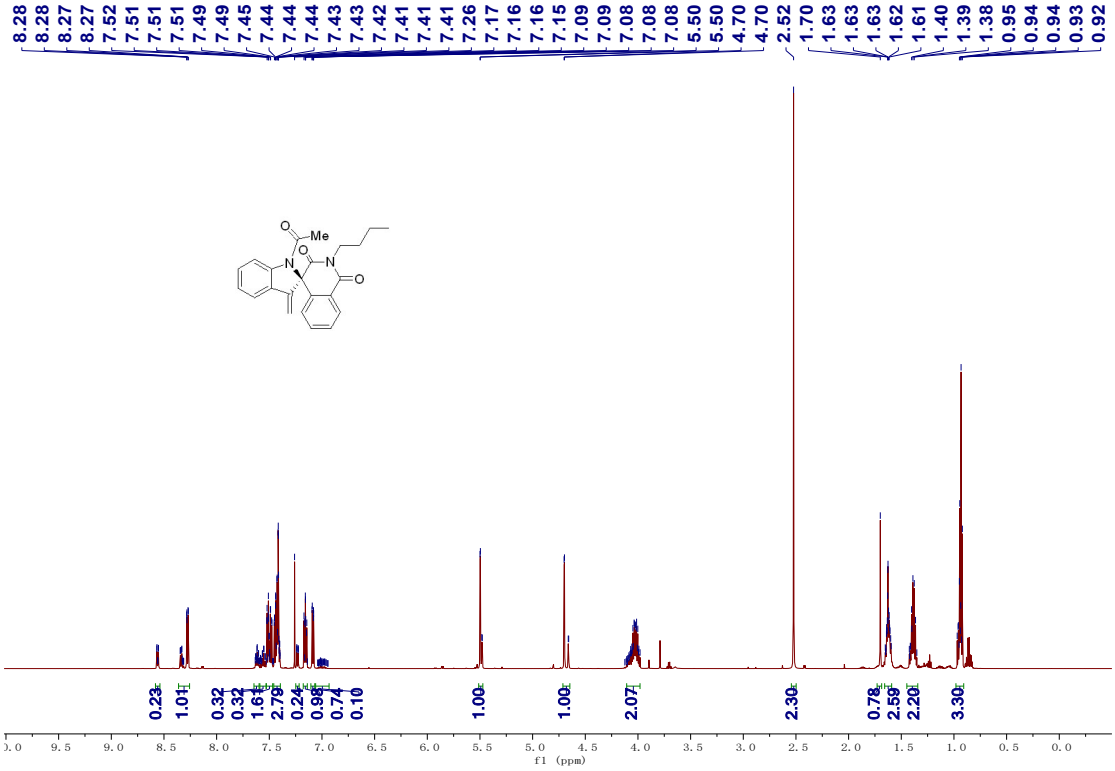


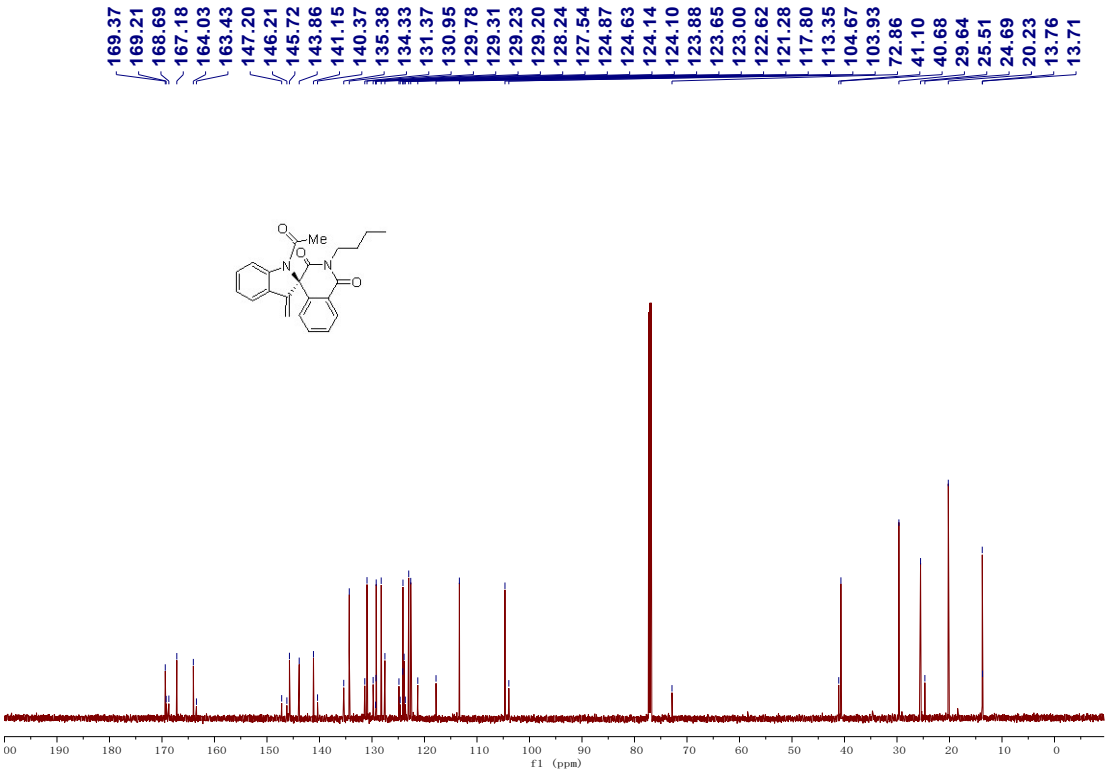
^{1}H and ^{13}C NMR spectra of compound (6af)





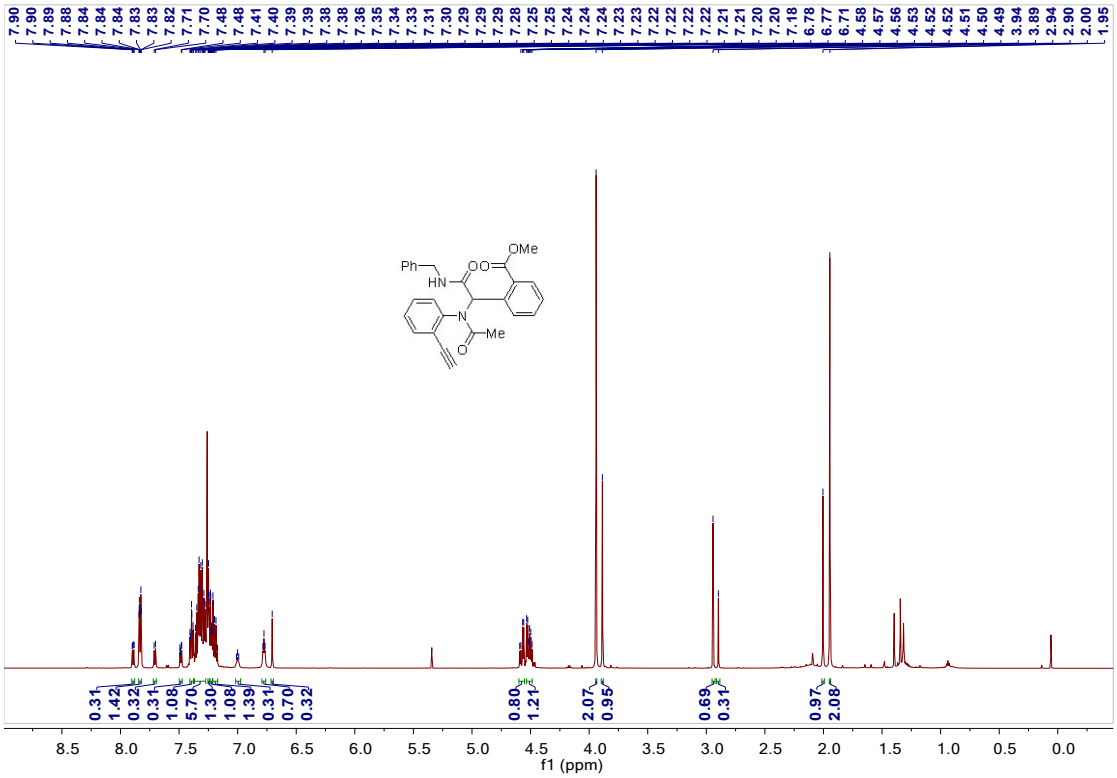
^{1}H and ^{13}C NMR spectra of compound (6ag)

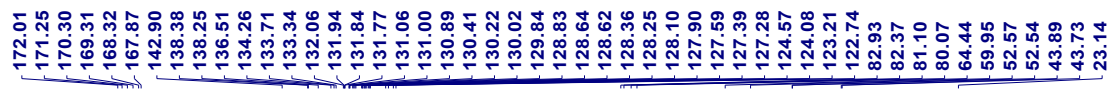


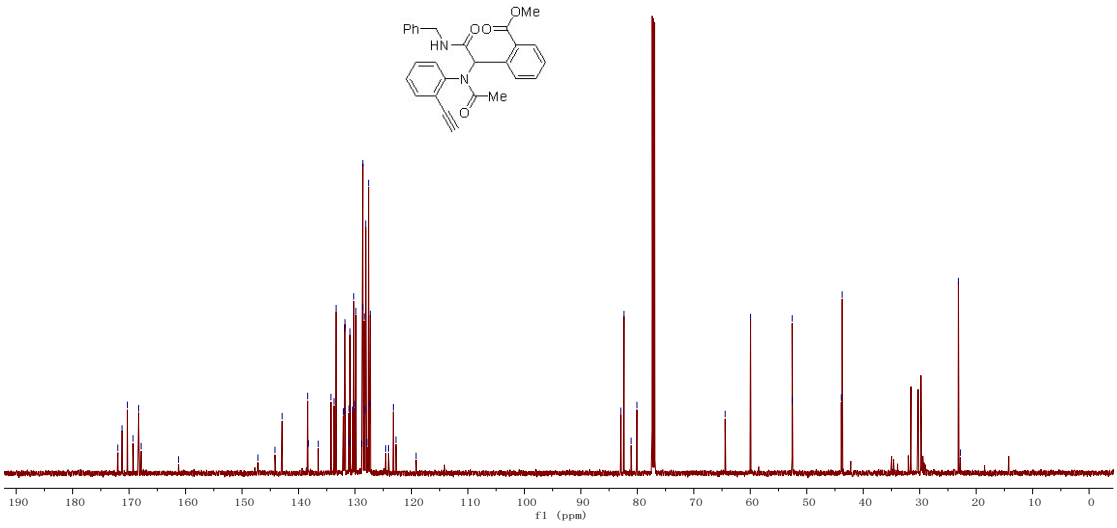


Copies of NMR spectra (Ugi product 5a-5ak)

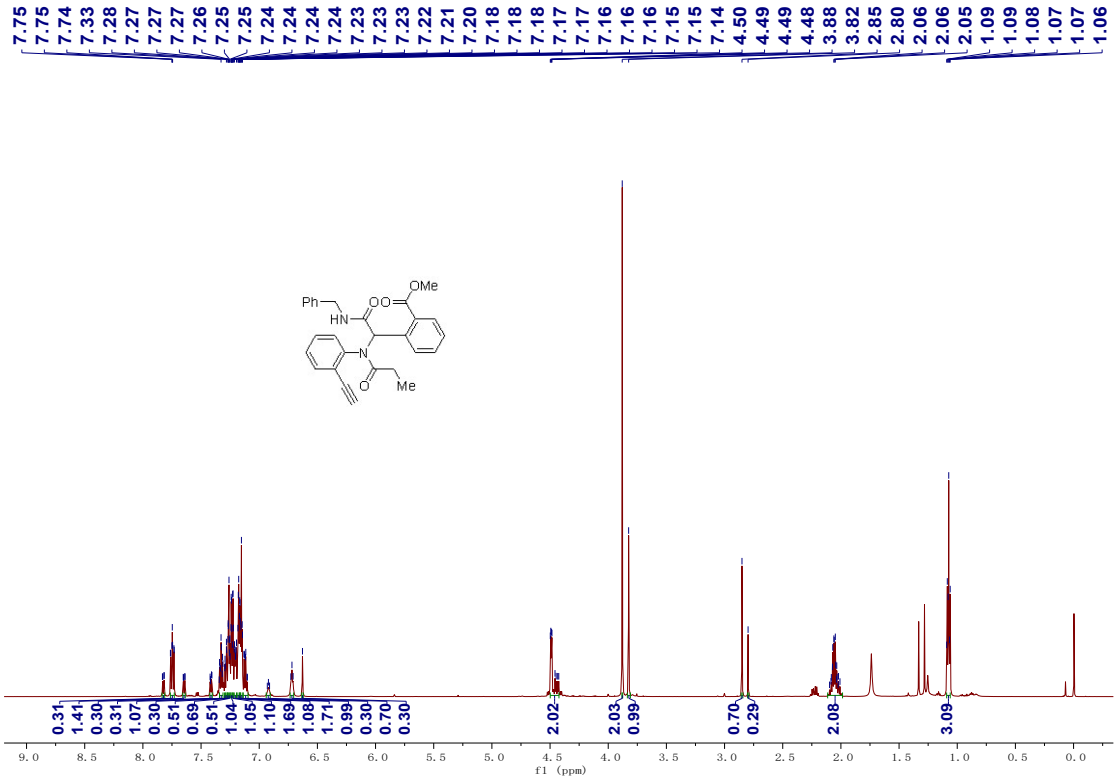
^{1}H and ^{13}C NMR spectra of compound (5a)

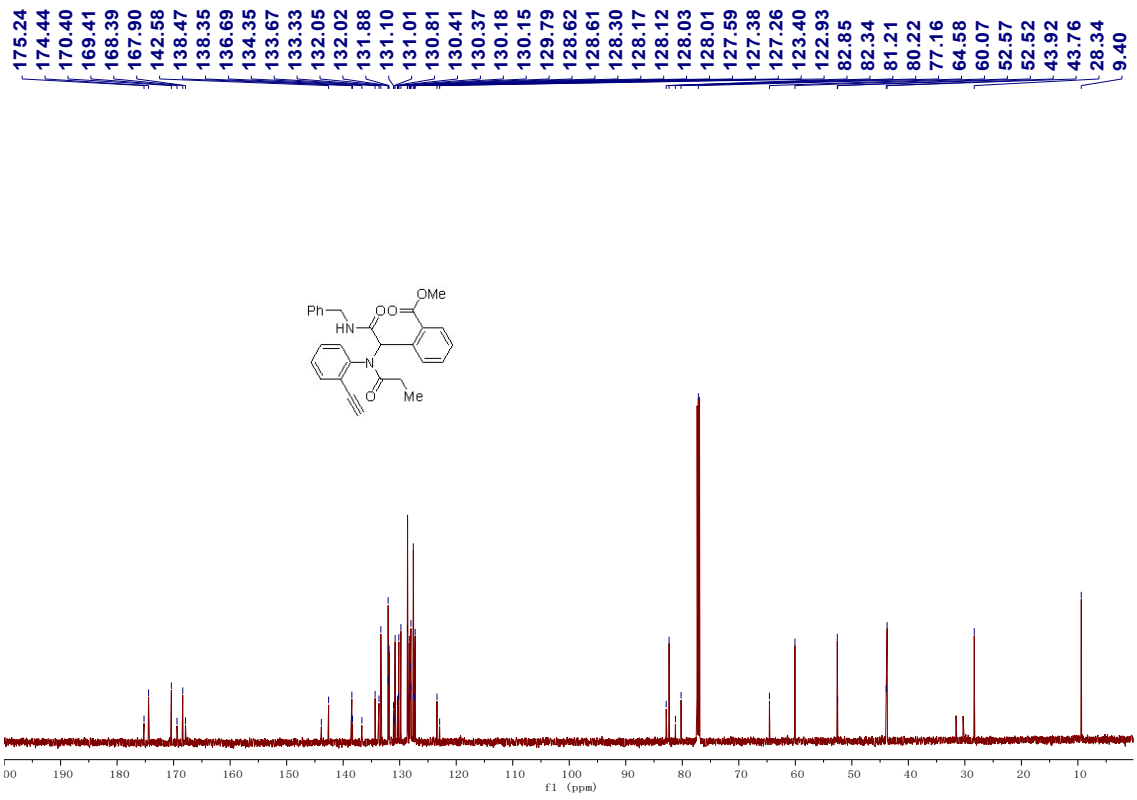




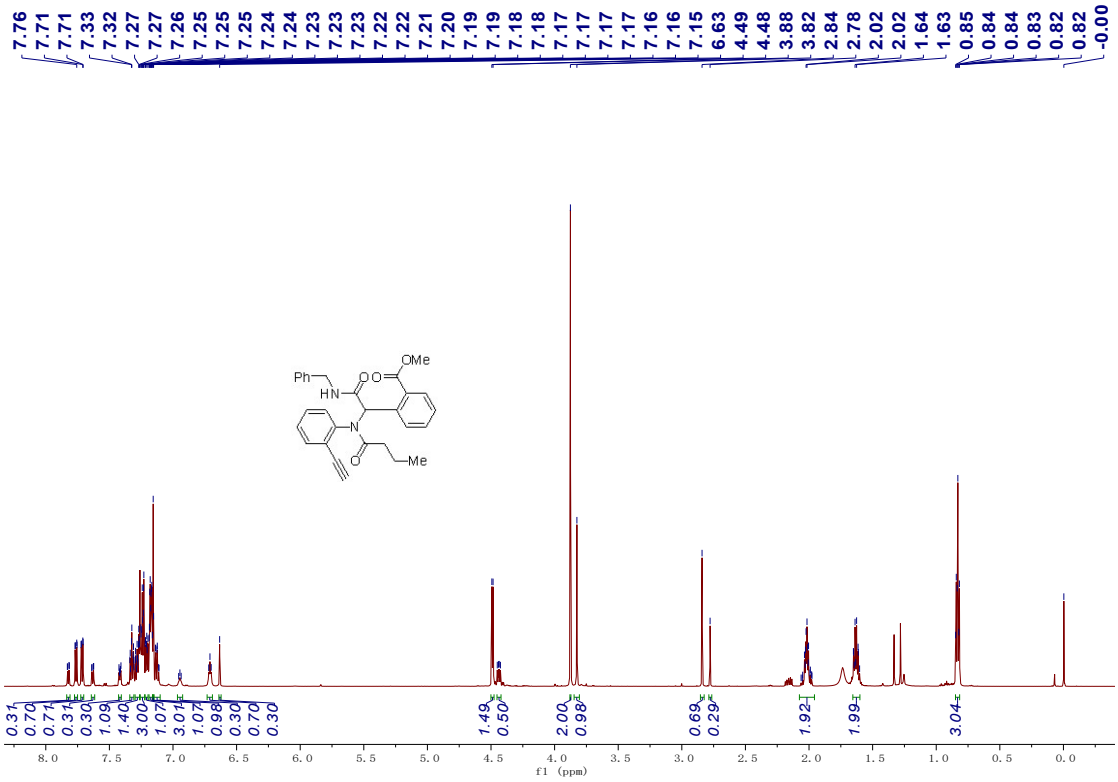


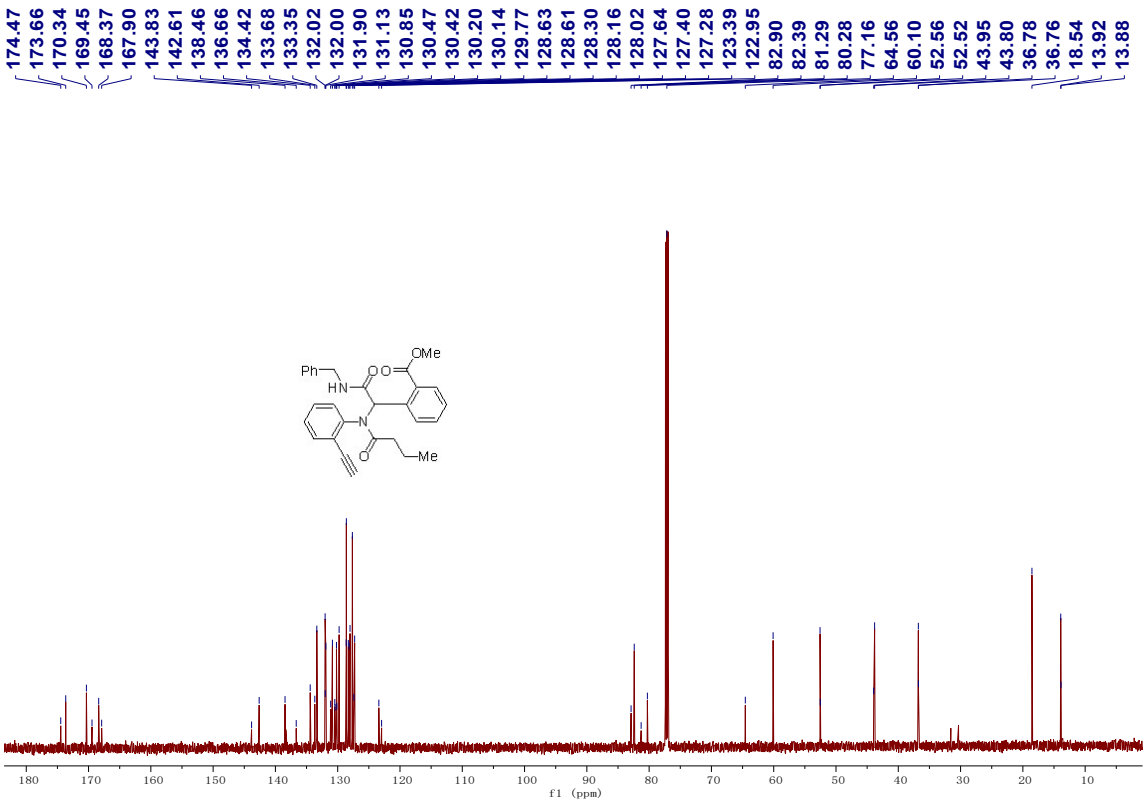
^{1}H and ^{13}C NMR spectra of compound (5b)



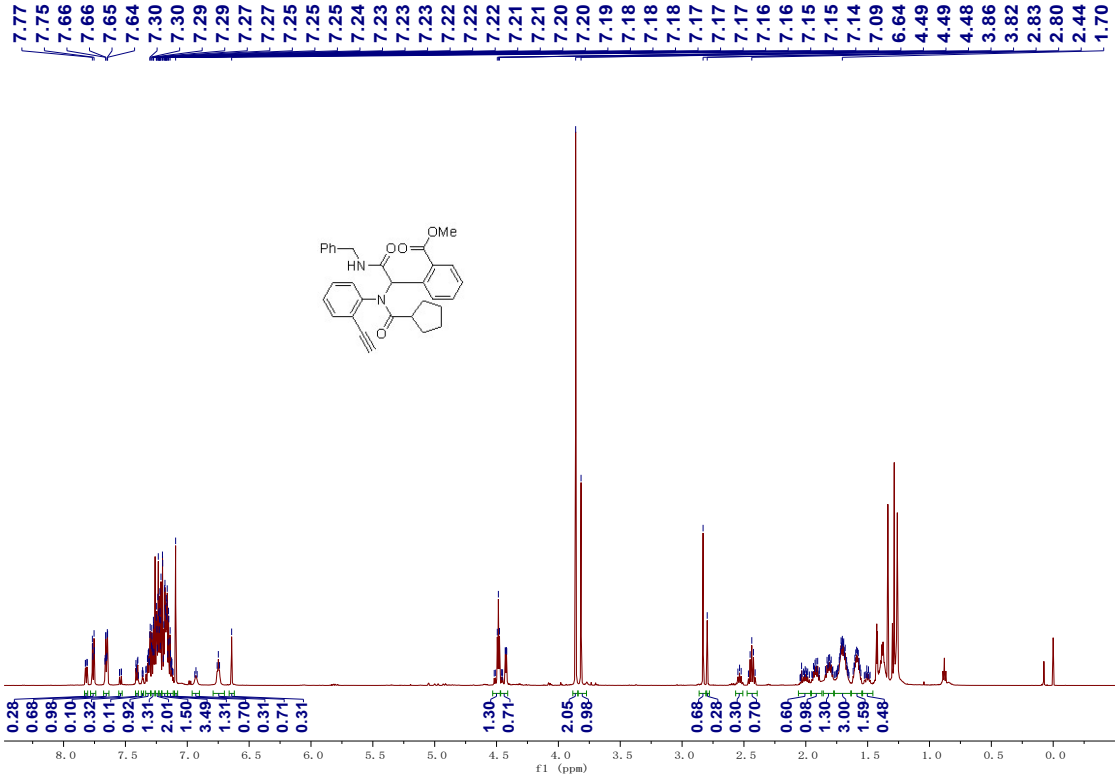


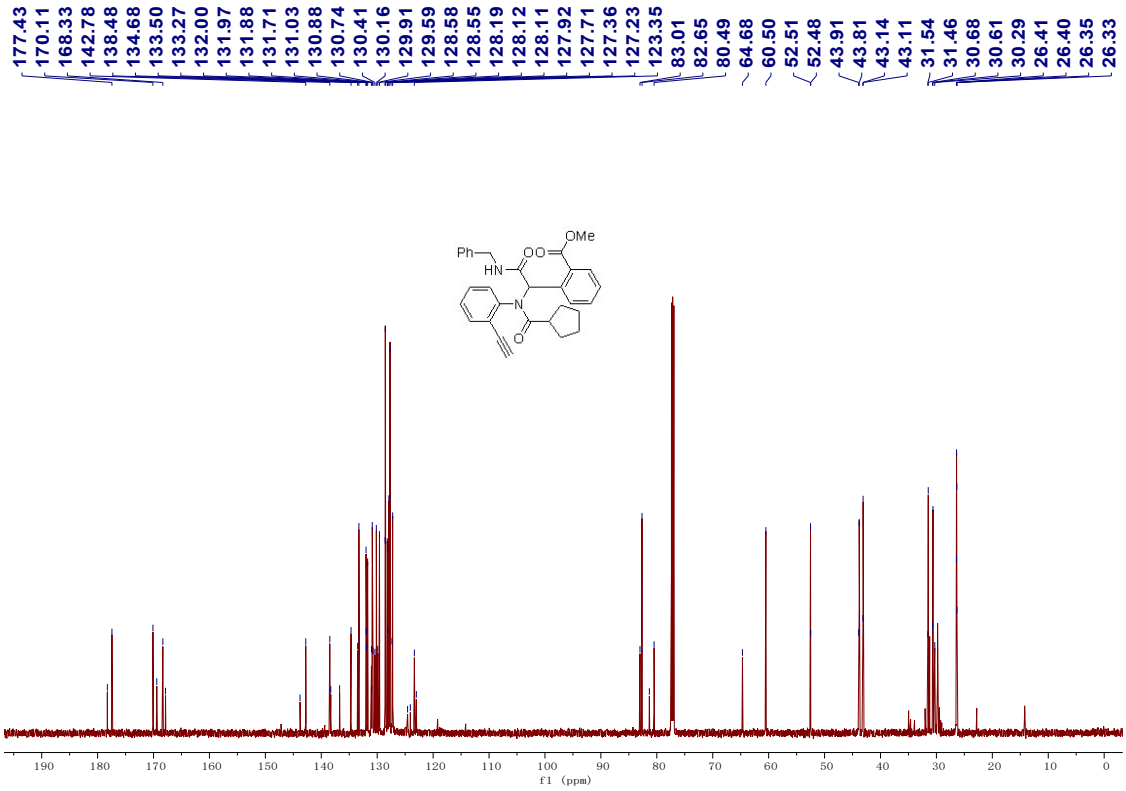
^{1}H and ^{13}C NMR spectra of compound (5c)



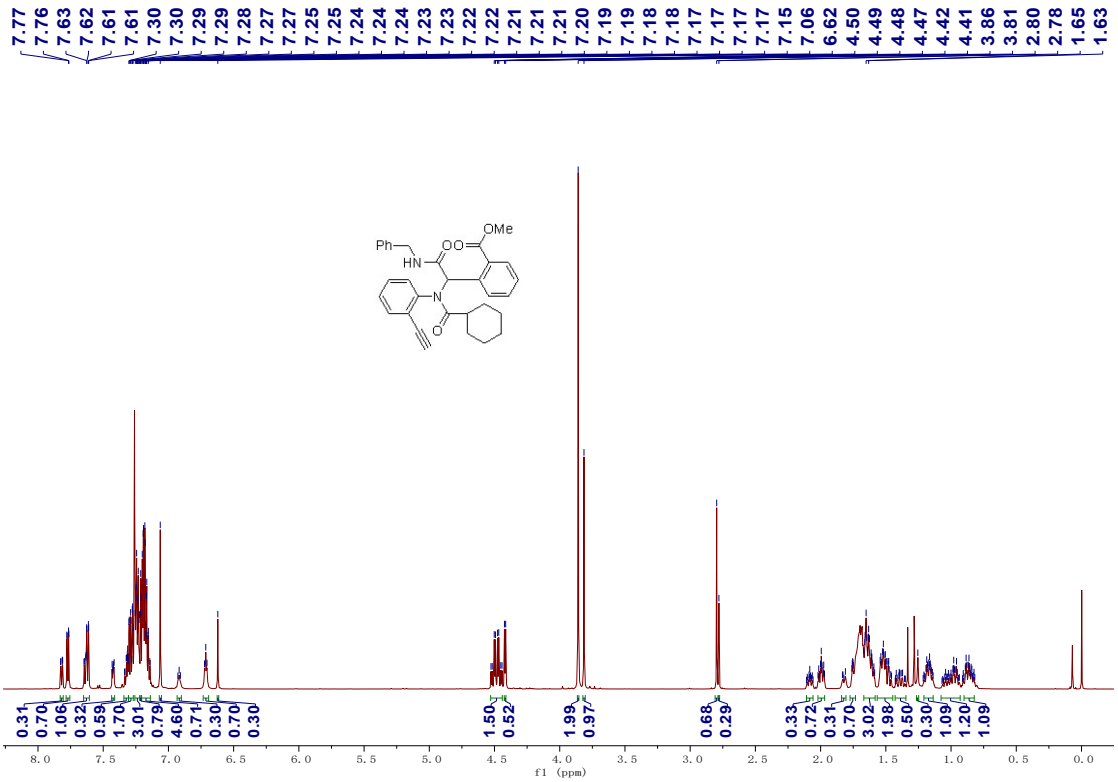


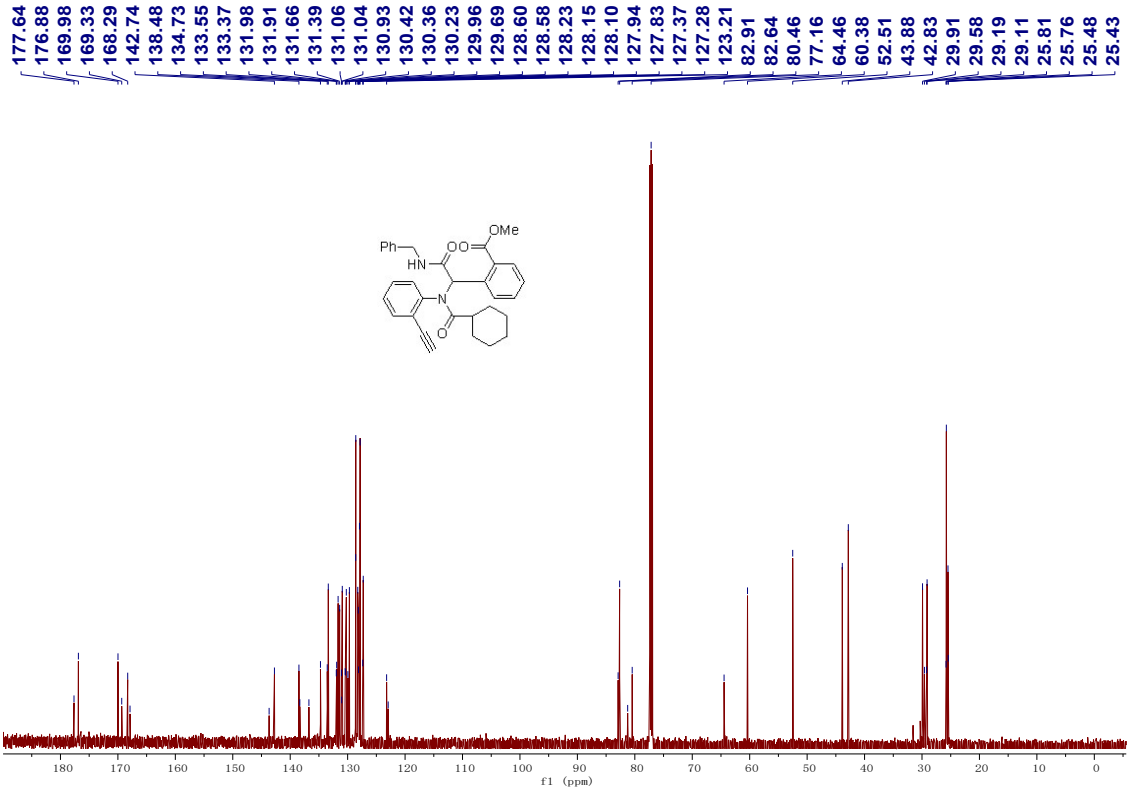
^{1}H and ^{13}C NMR spectra of compound (5d)



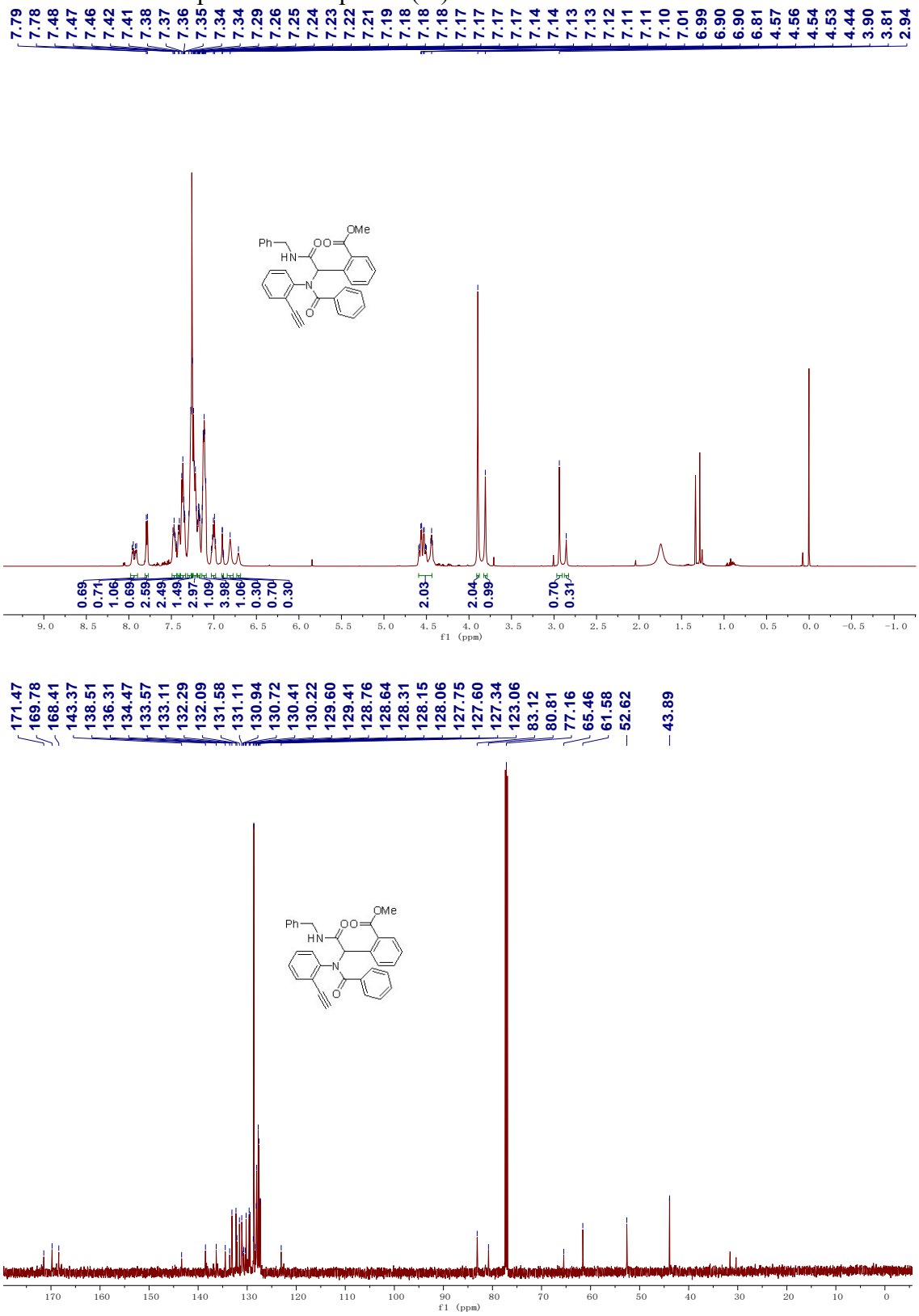


^{1}H and ^{13}C NMR spectra of compound (5e)

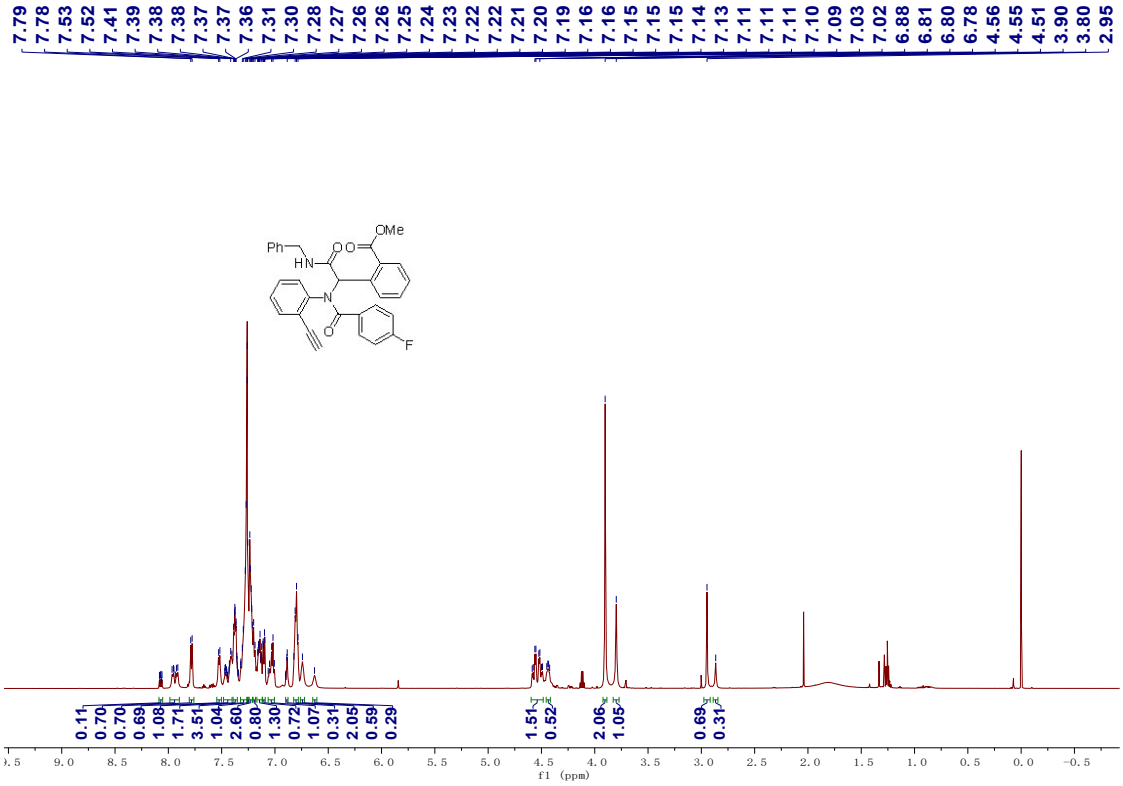


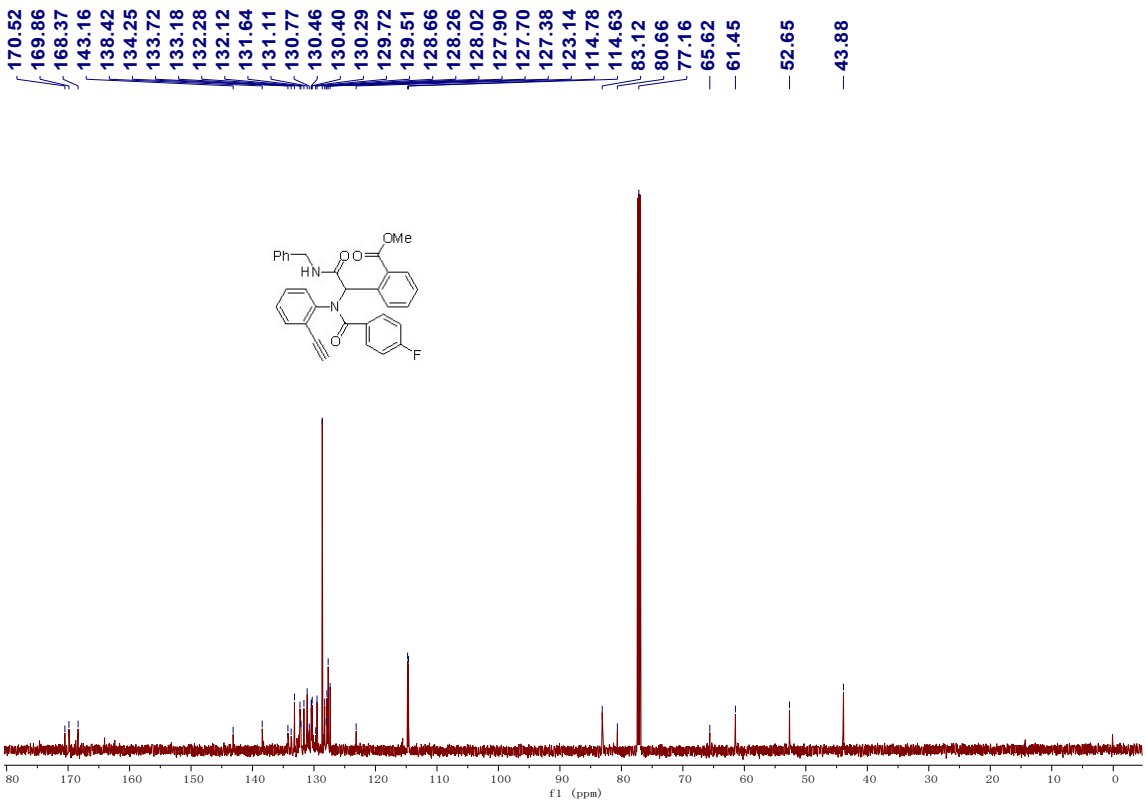


^{1}H and ^{13}C NMR spectra of compound (5f)

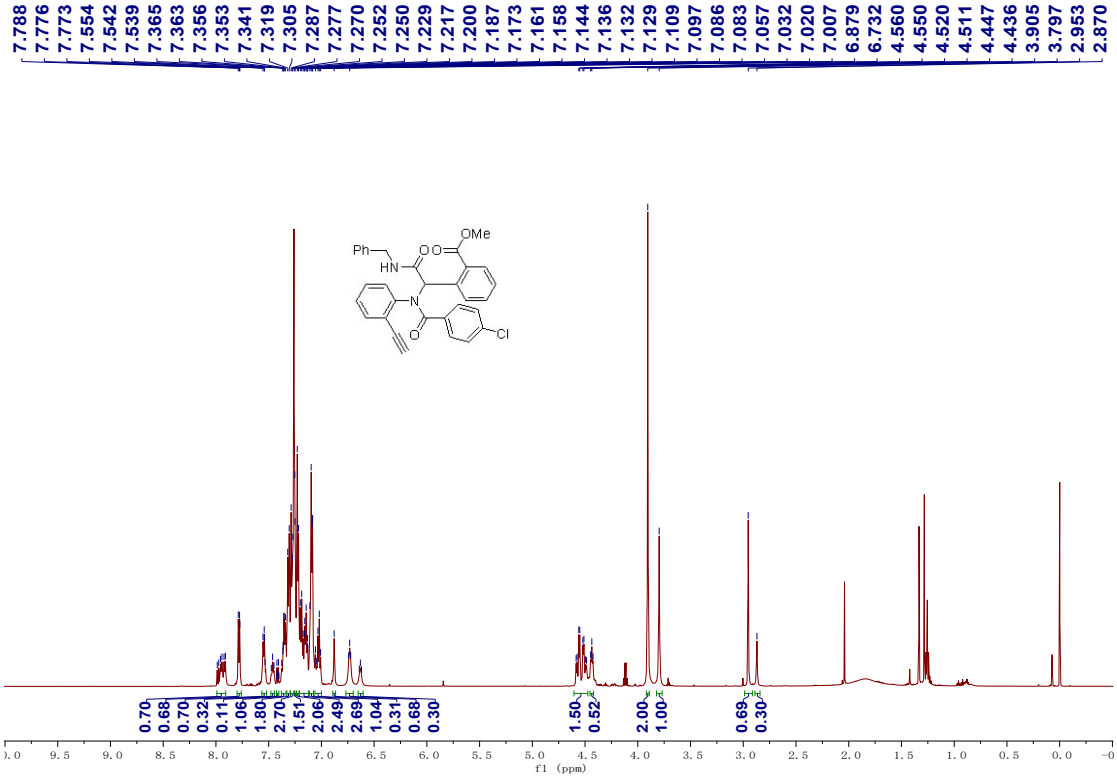


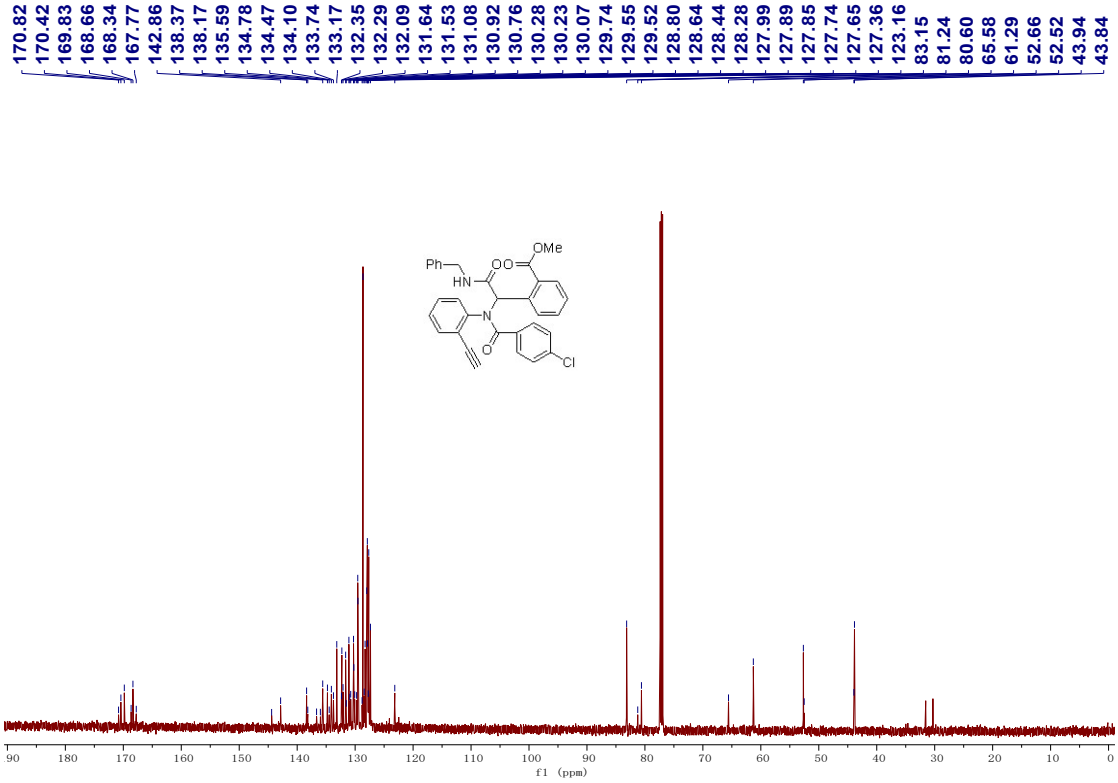
^{1}H and ^{13}C NMR spectra of compound (5g)



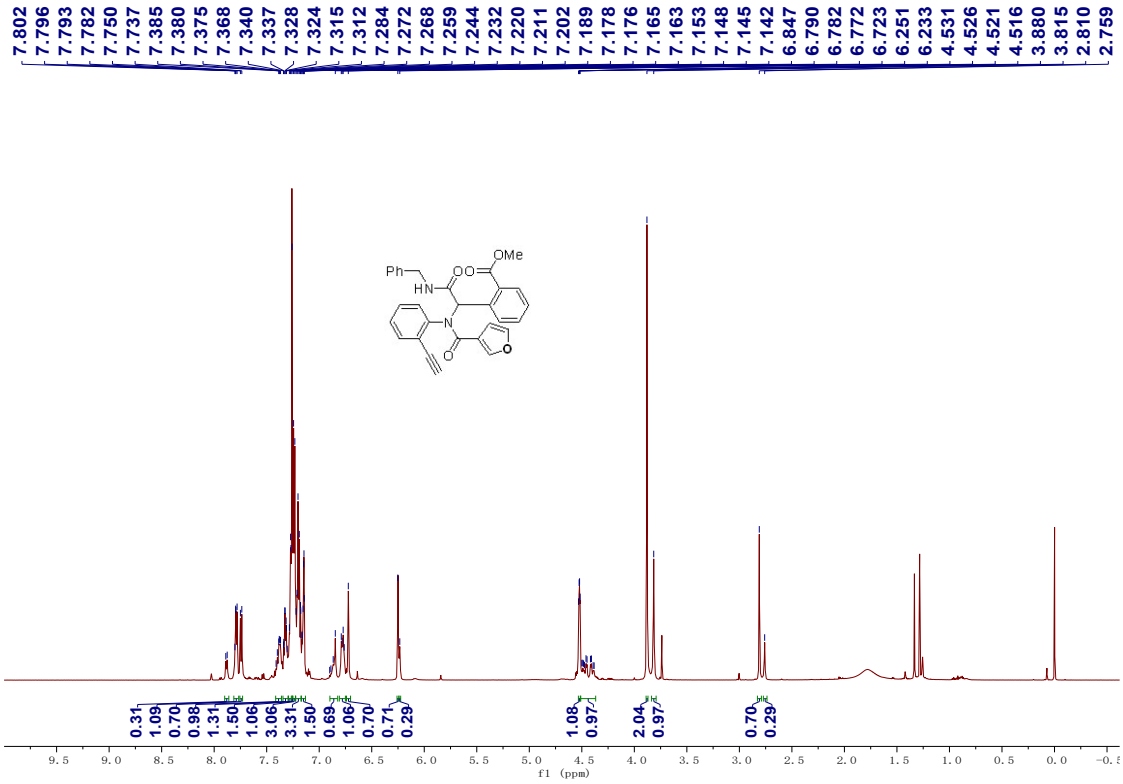


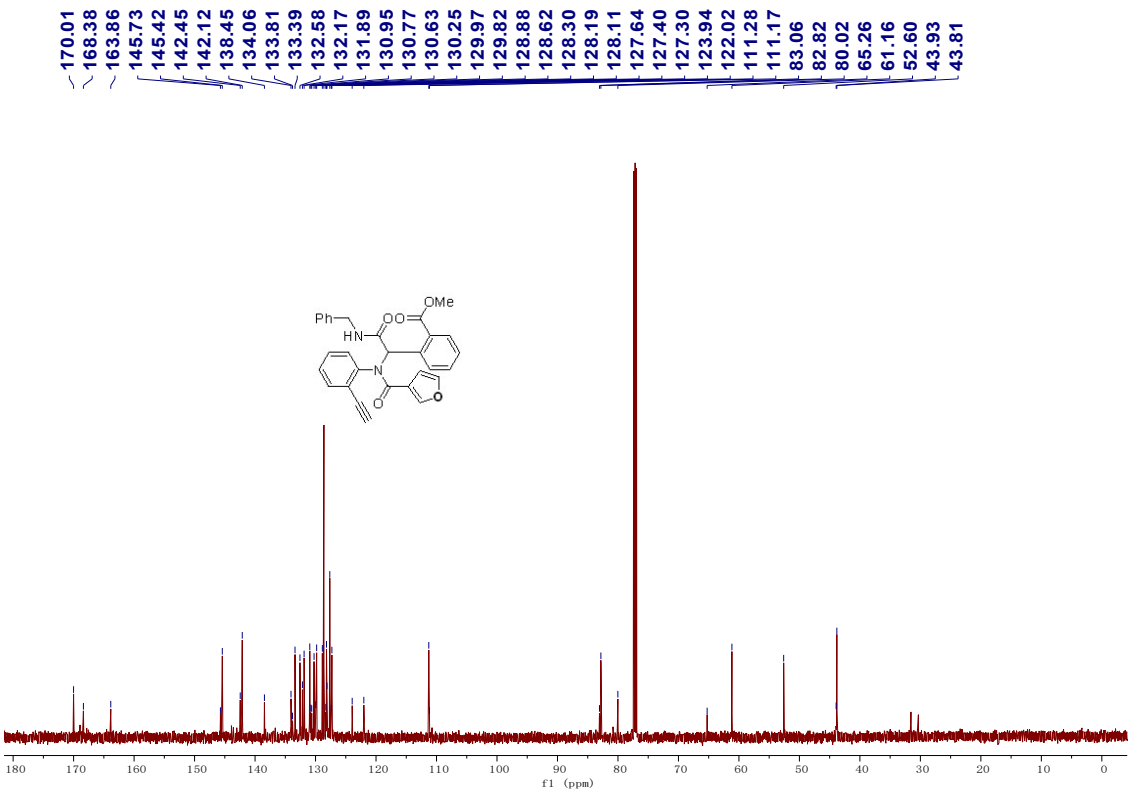
^{1}H and ^{13}C NMR spectra of compound (5h)



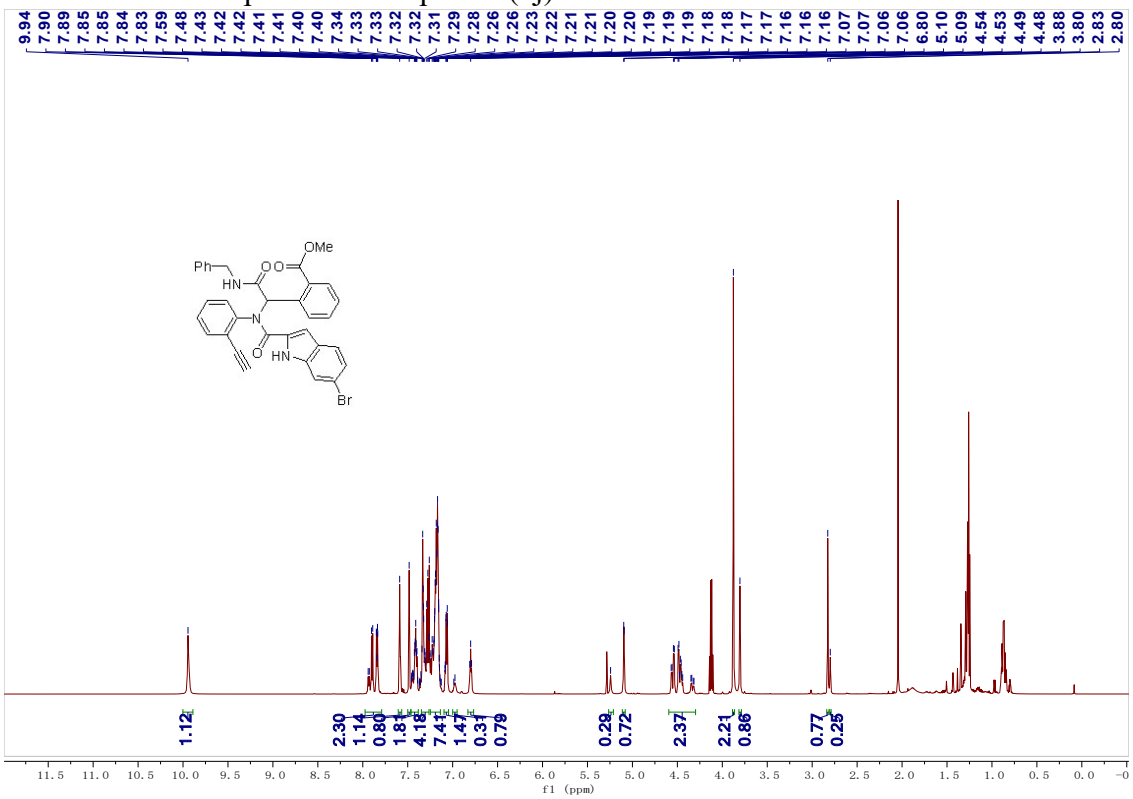


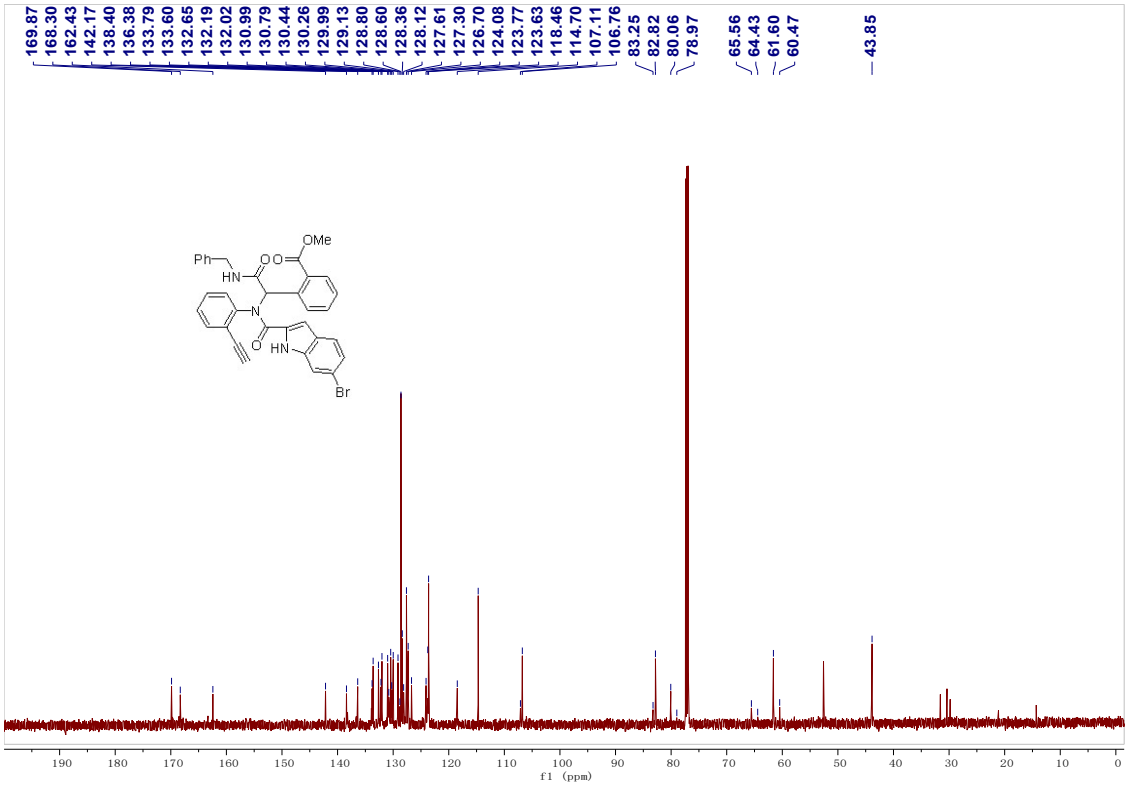
^{1}H and ^{13}C NMR spectra of compound (5i)



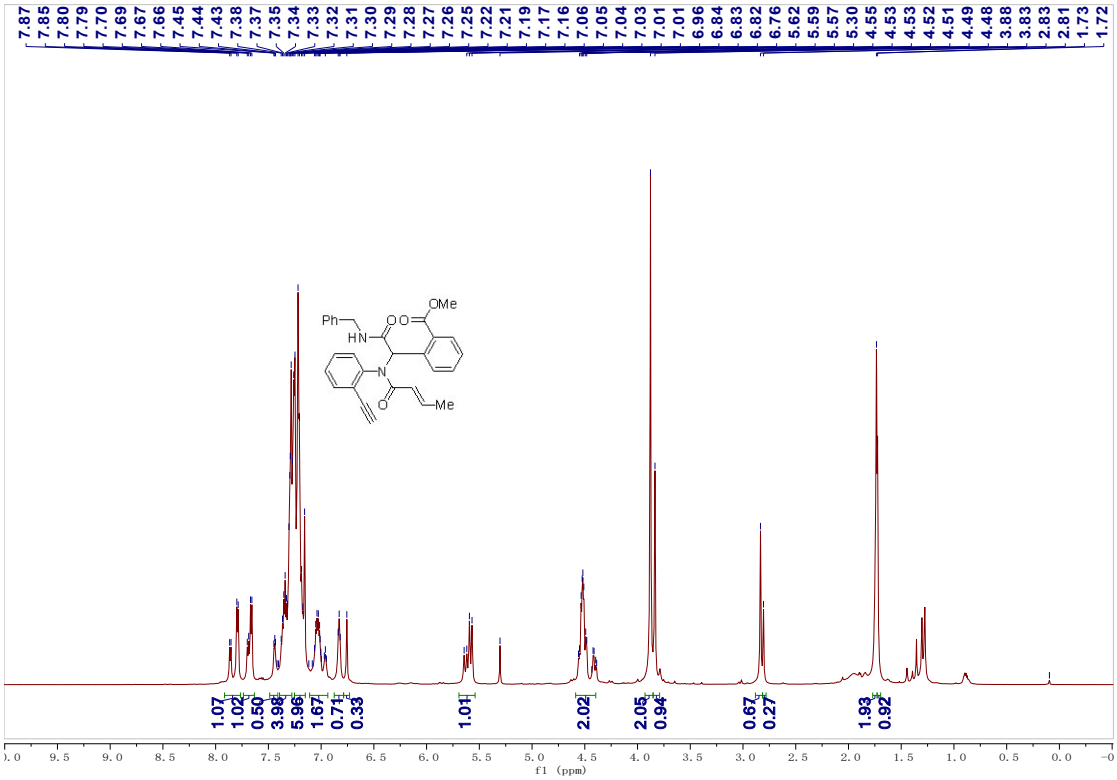


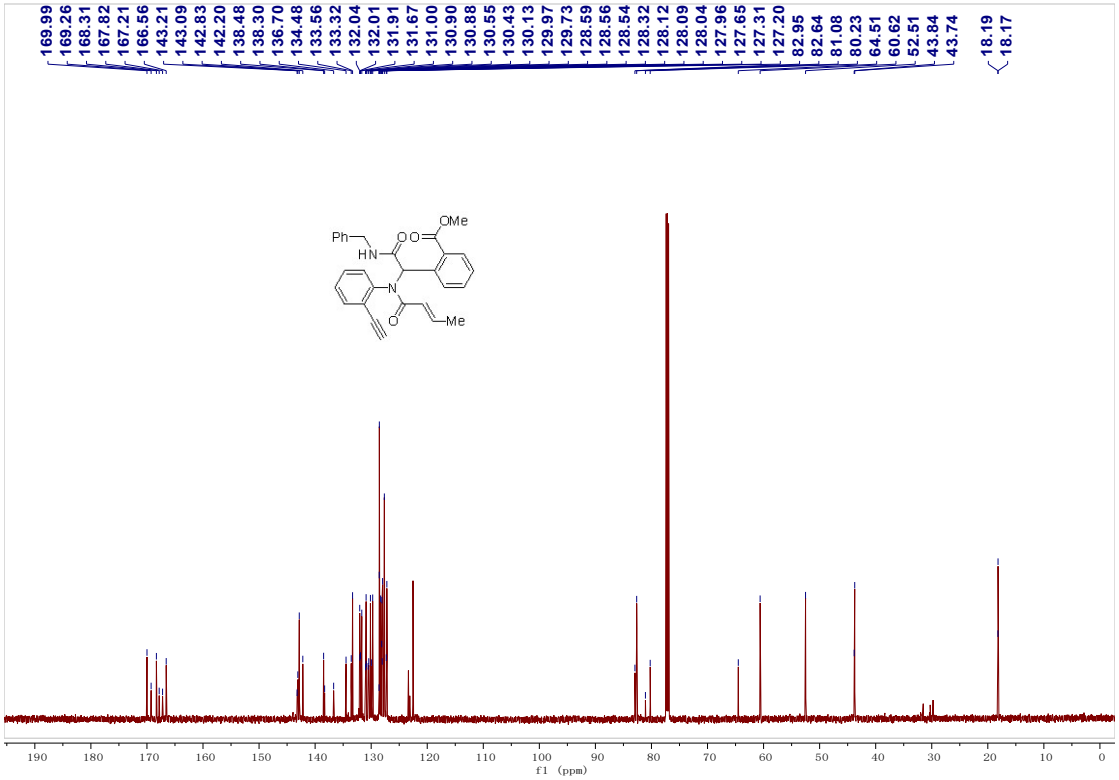
^{1}H and ^{13}C NMR spectra of compound (5j)



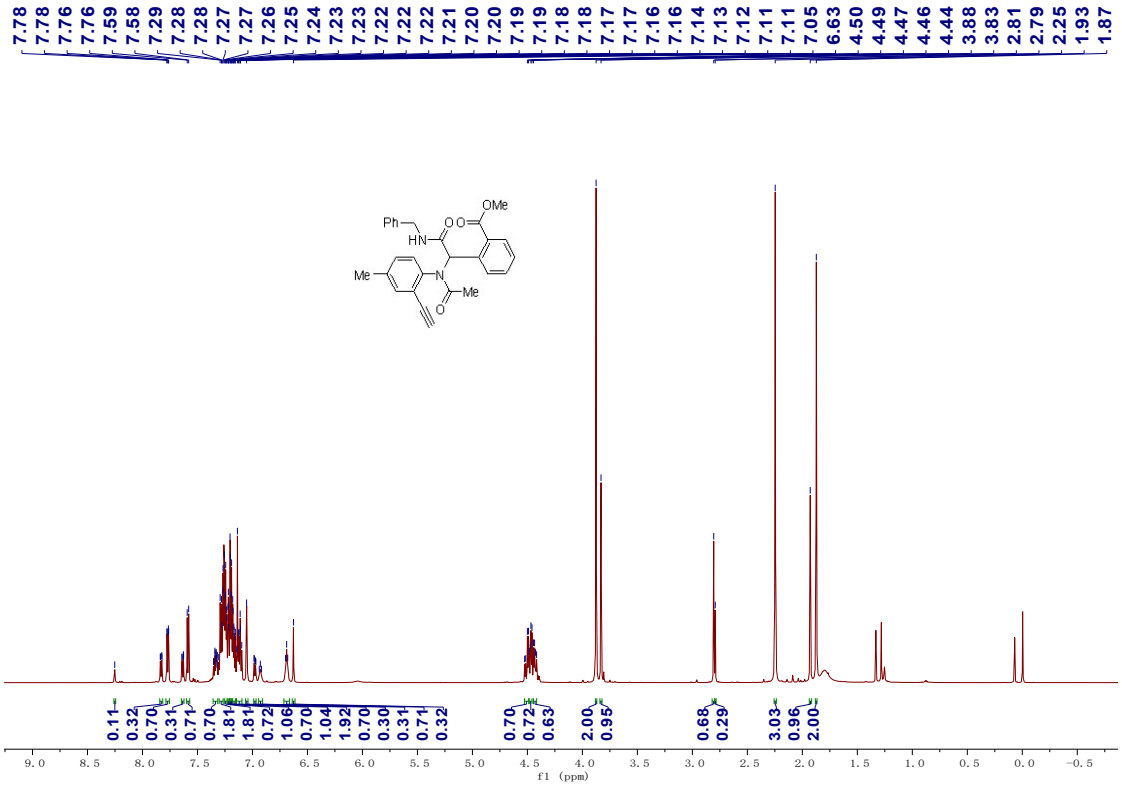


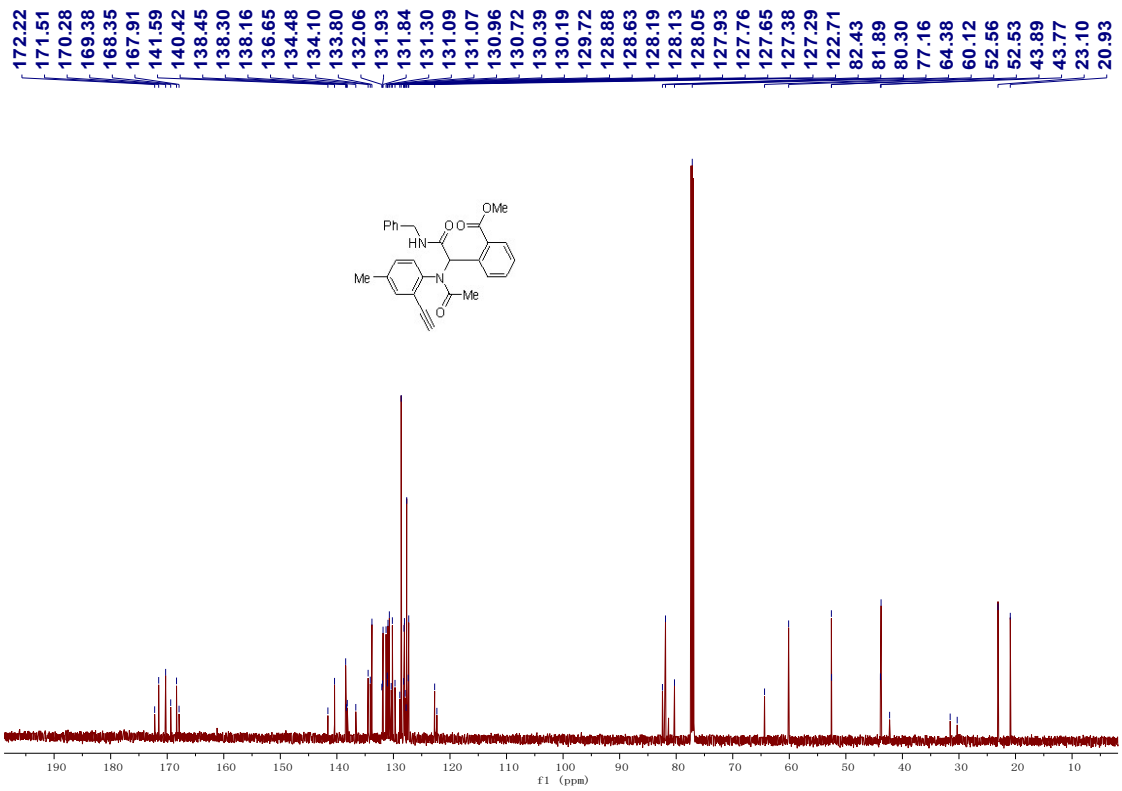
^{1}H and ^{13}C NMR spectra of compound (5k)



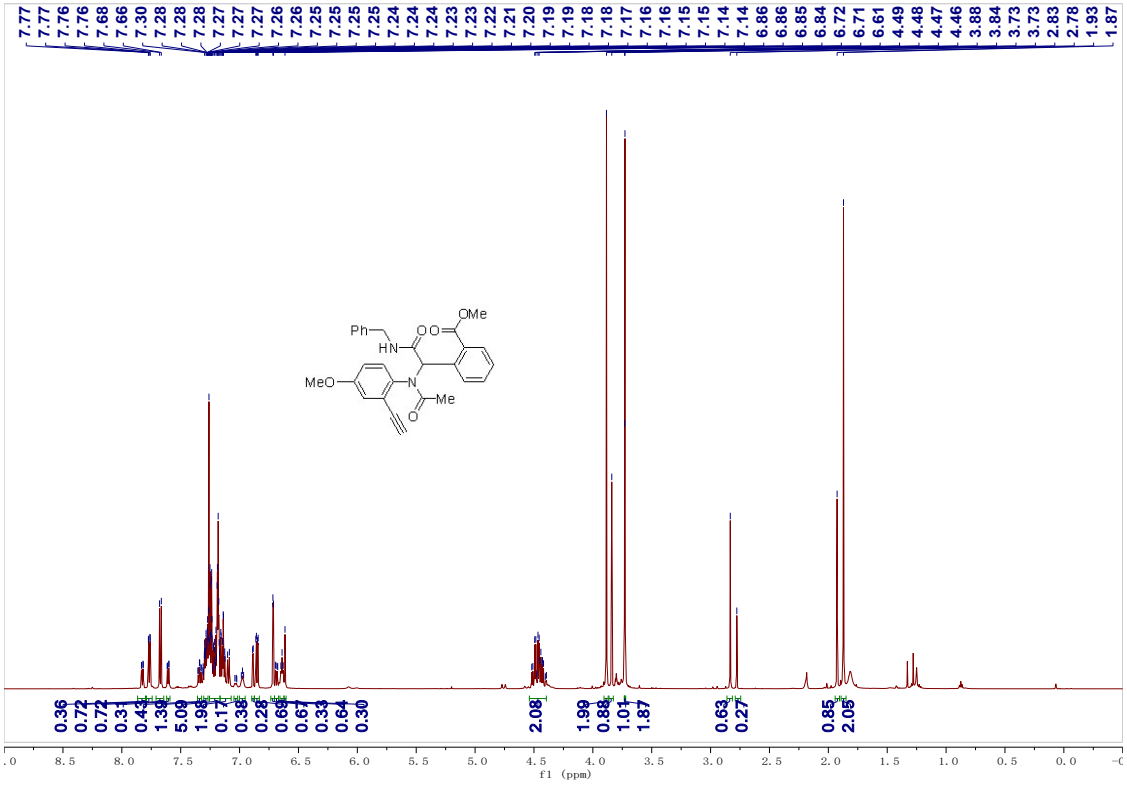


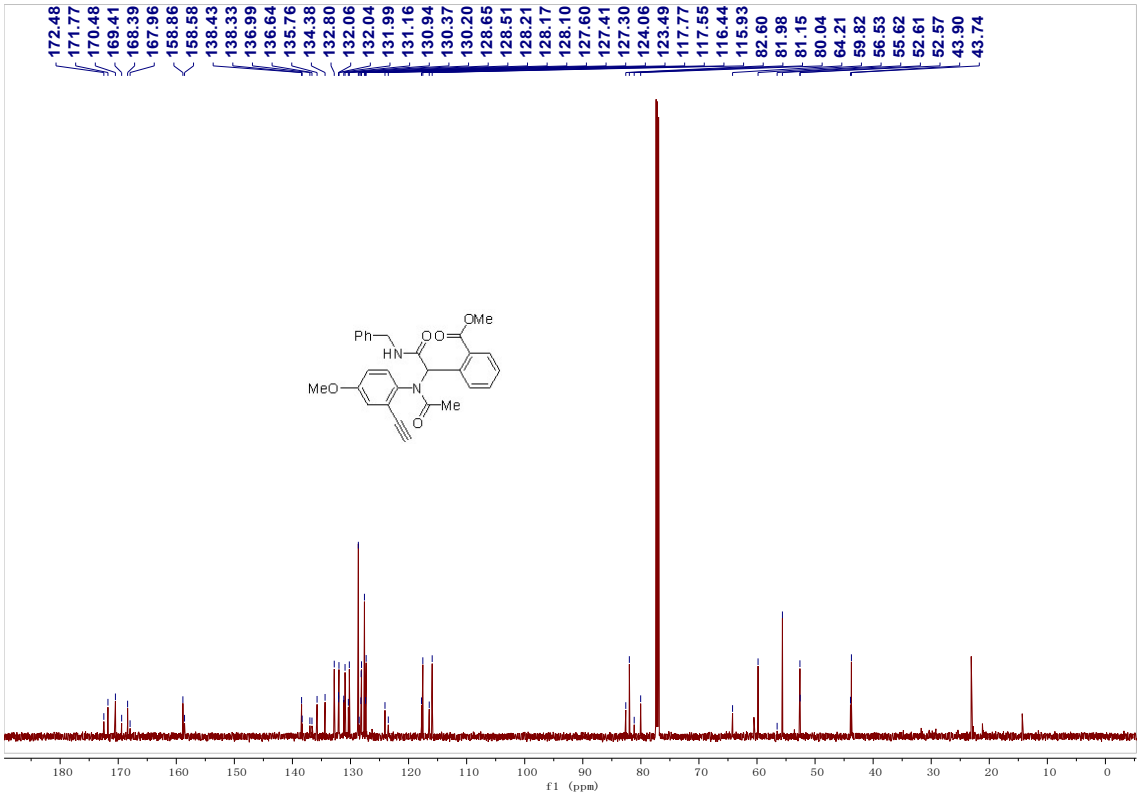
^{1}H and ^{13}C NMR spectra of compound (5l)



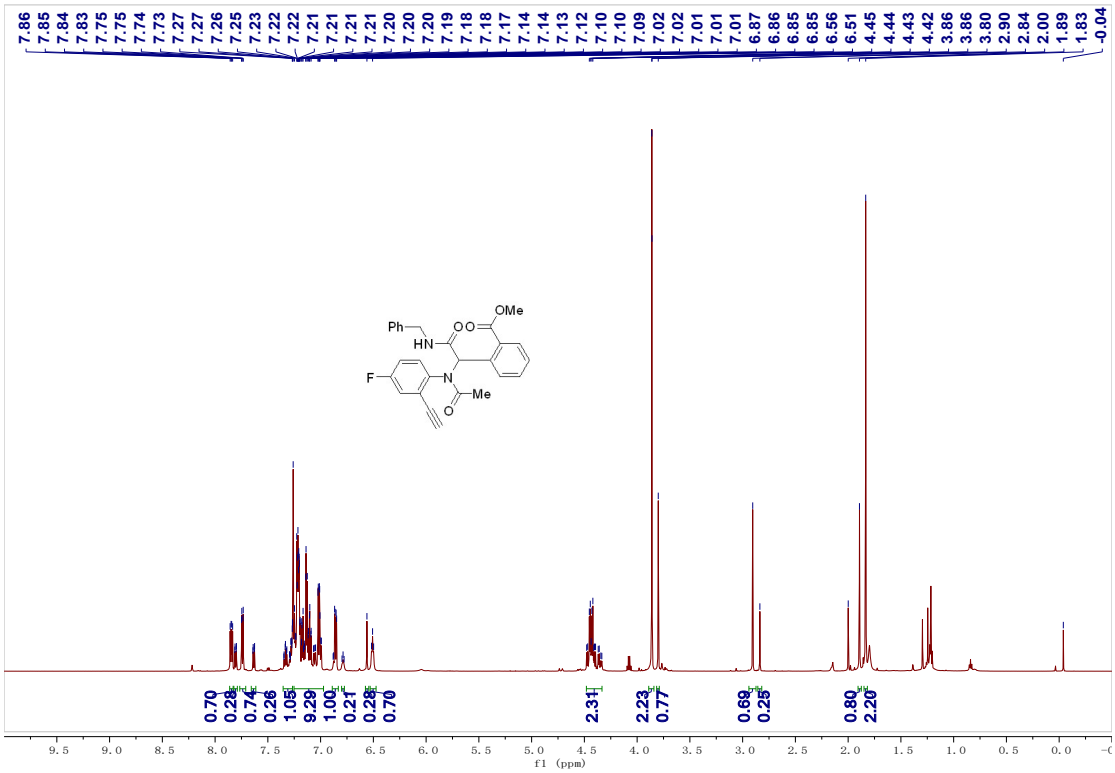


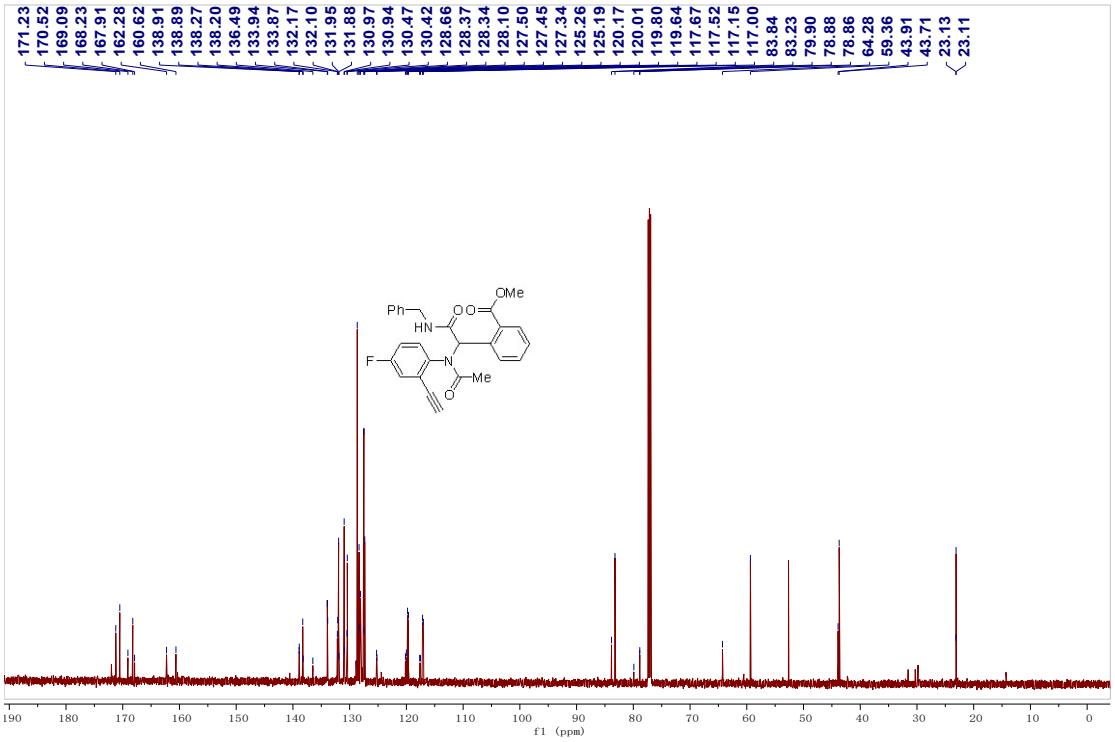
^{1}H and ^{13}C NMR spectra of compound (5m)



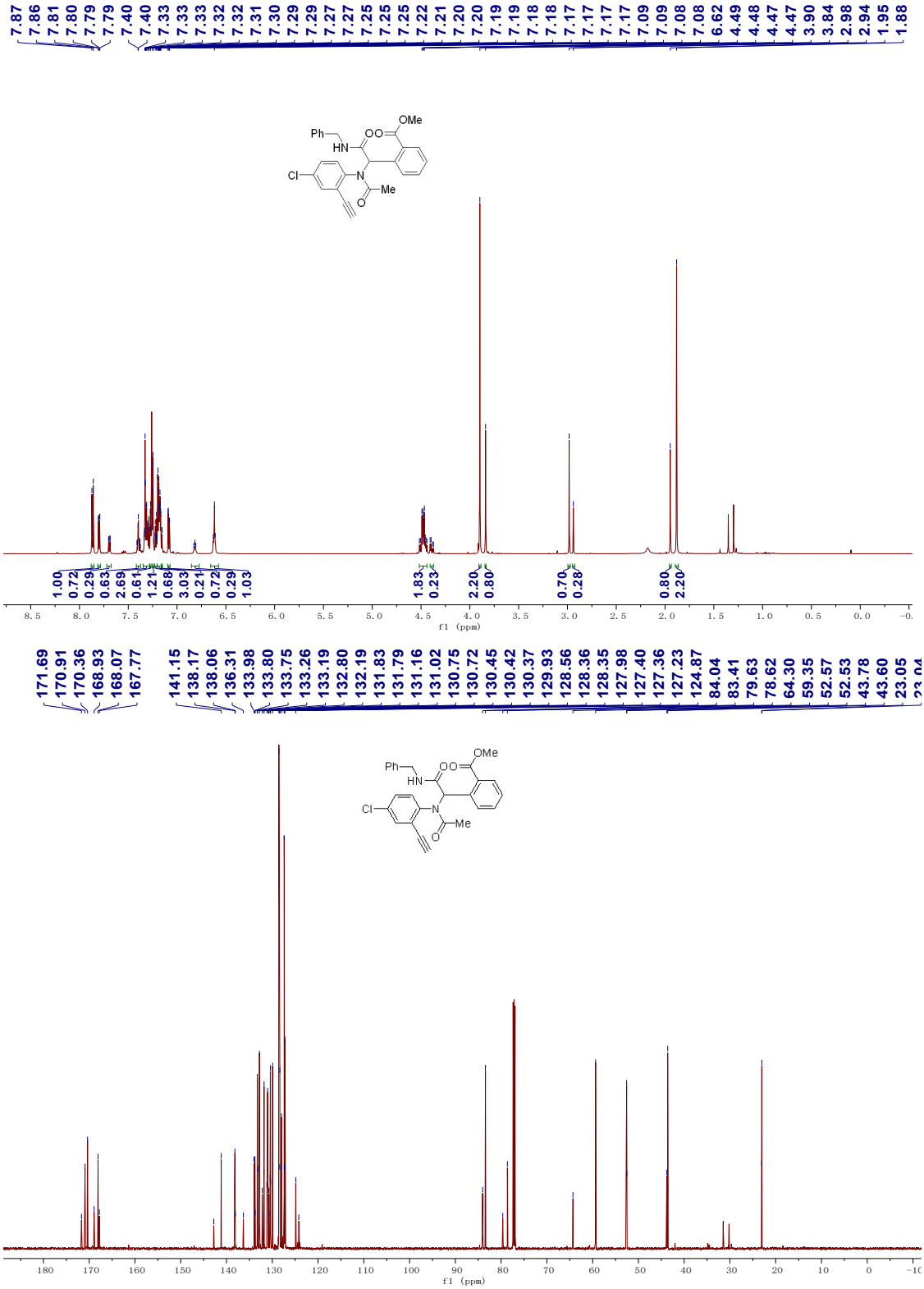


^{1}H and ^{13}C NMR spectra of compound (5n)

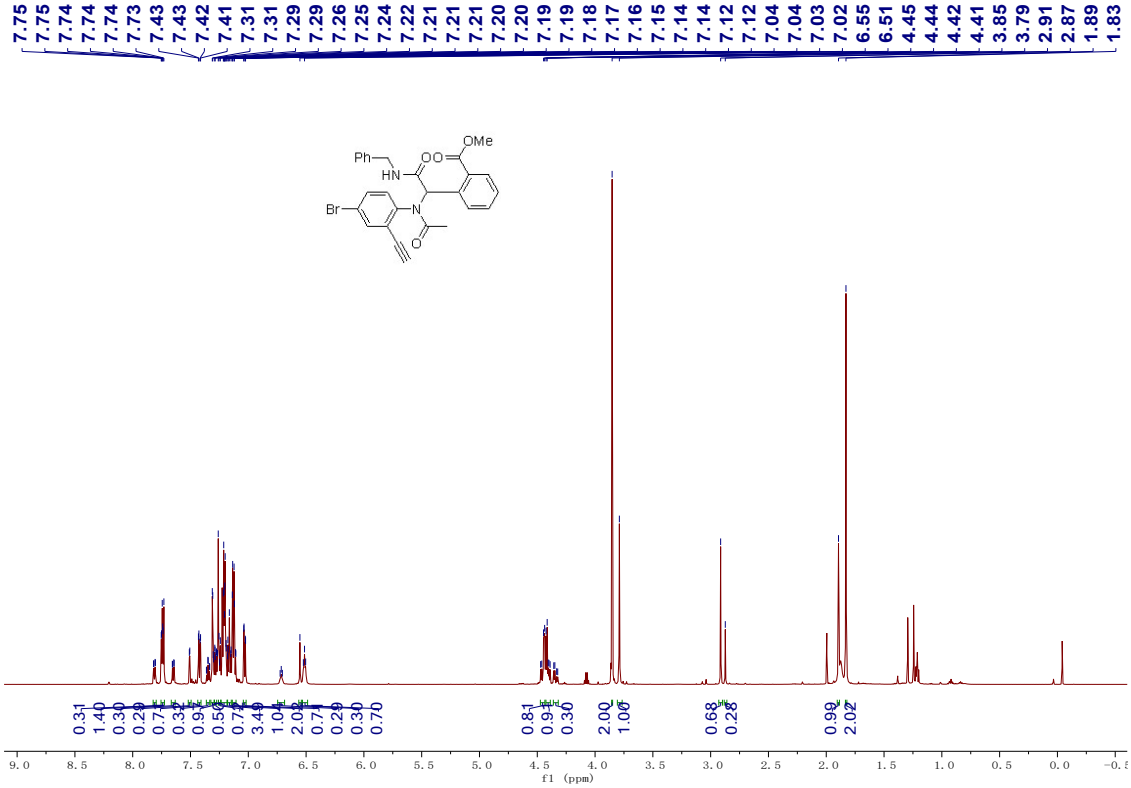


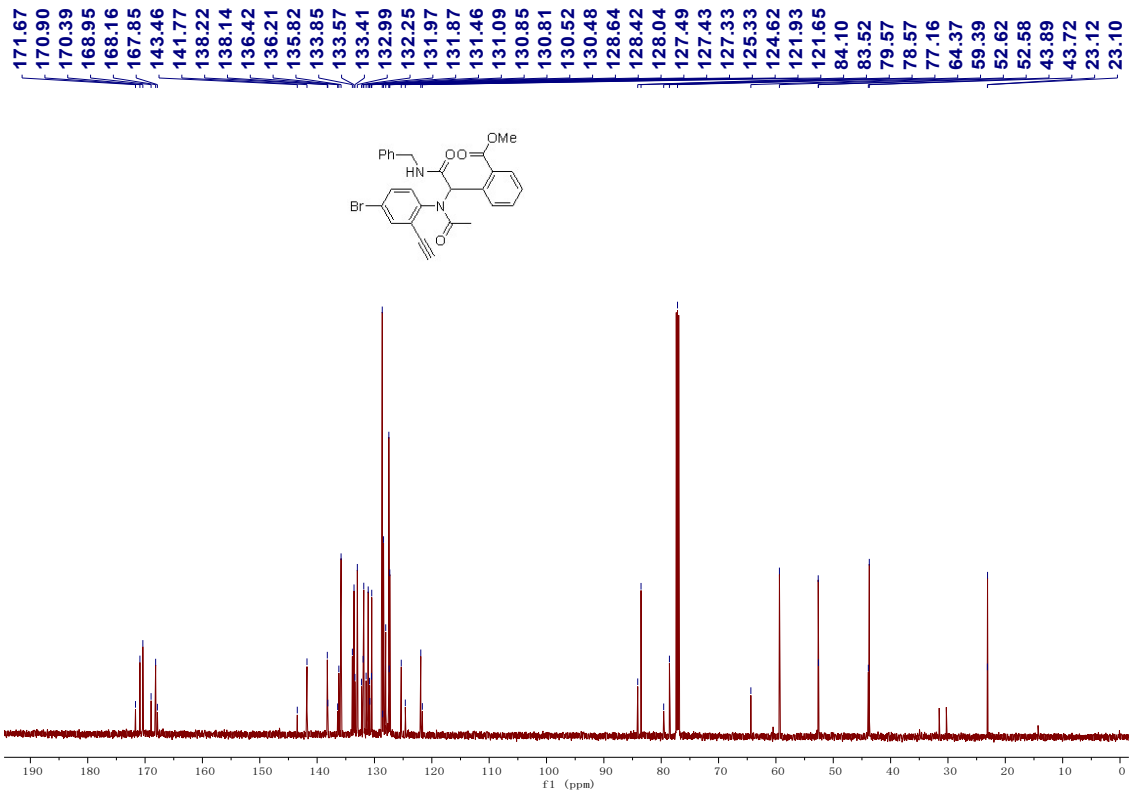


^{1}H and ^{13}C NMR spectra of compound (5o)

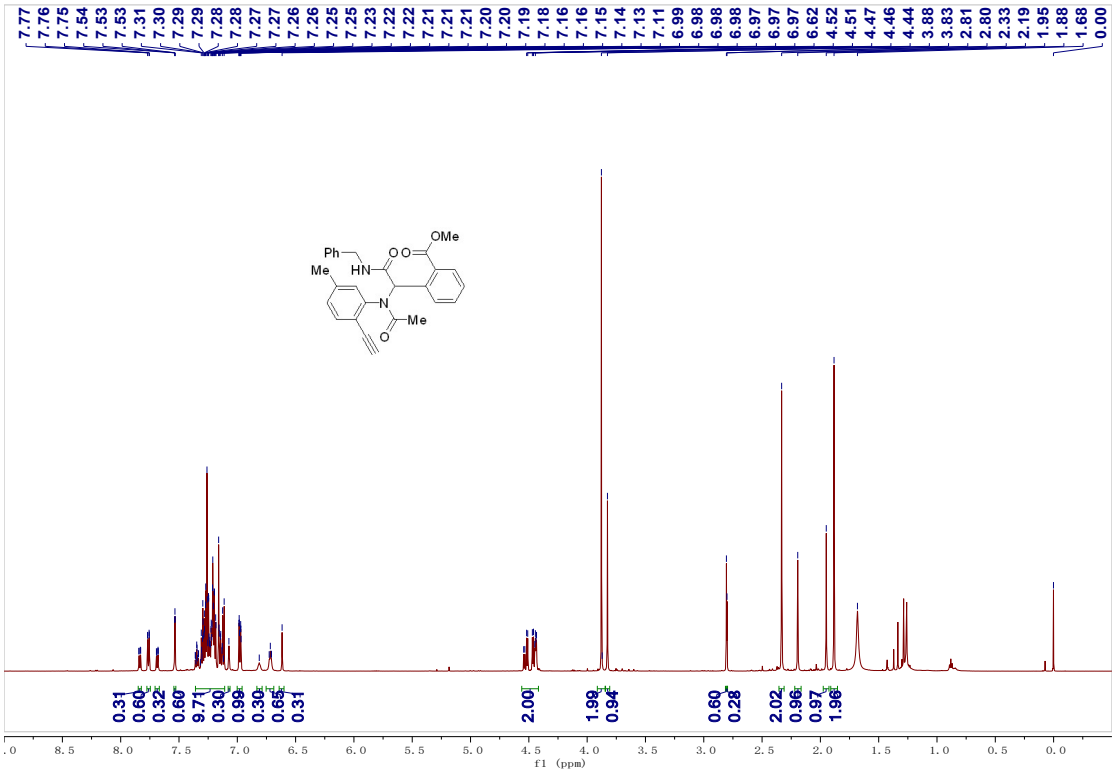


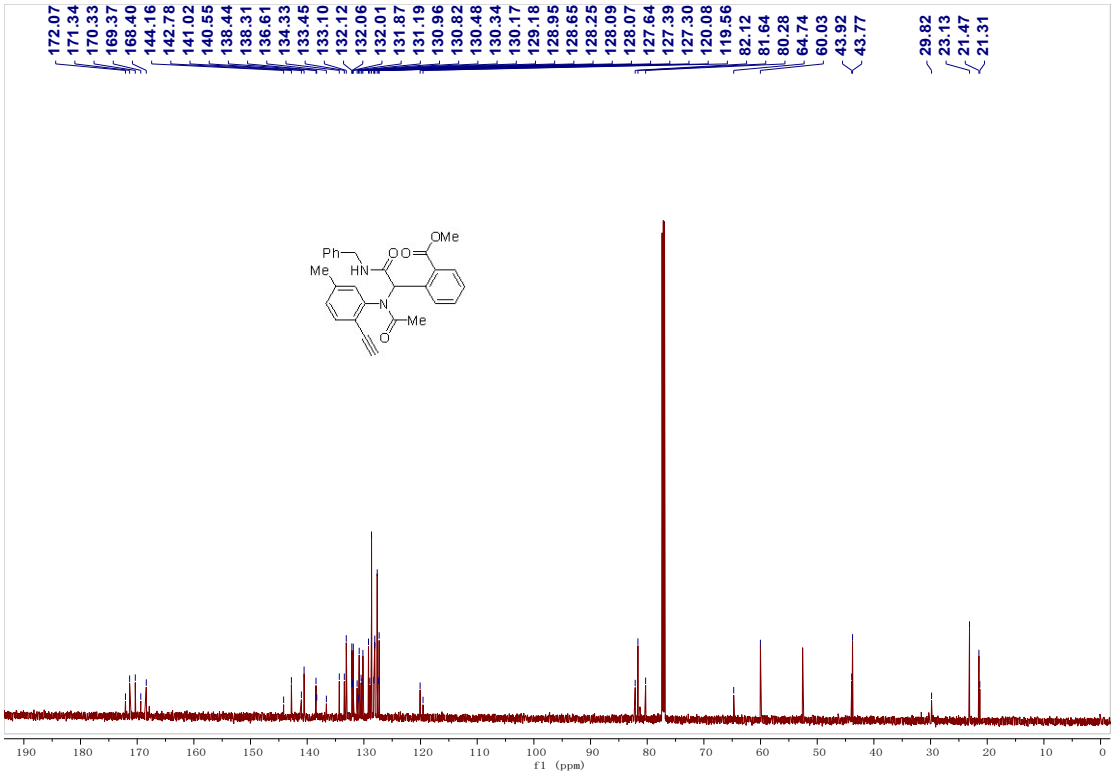
^{1}H and ^{13}C NMR spectra of compound (5p)



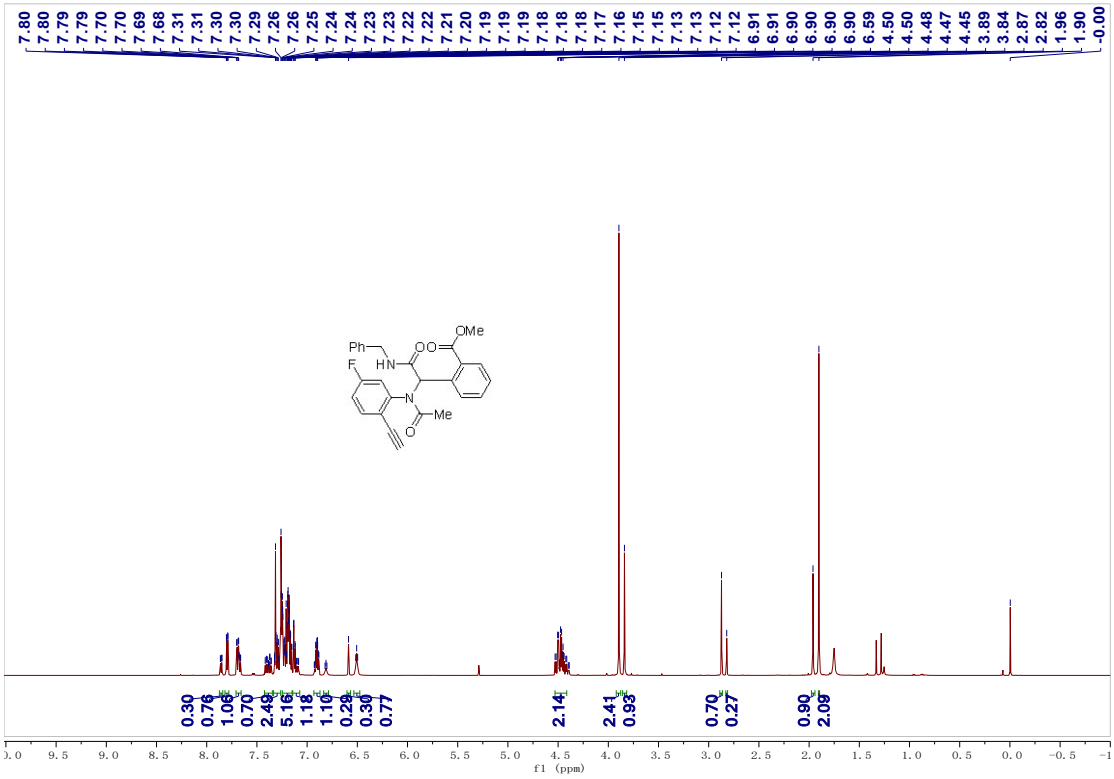


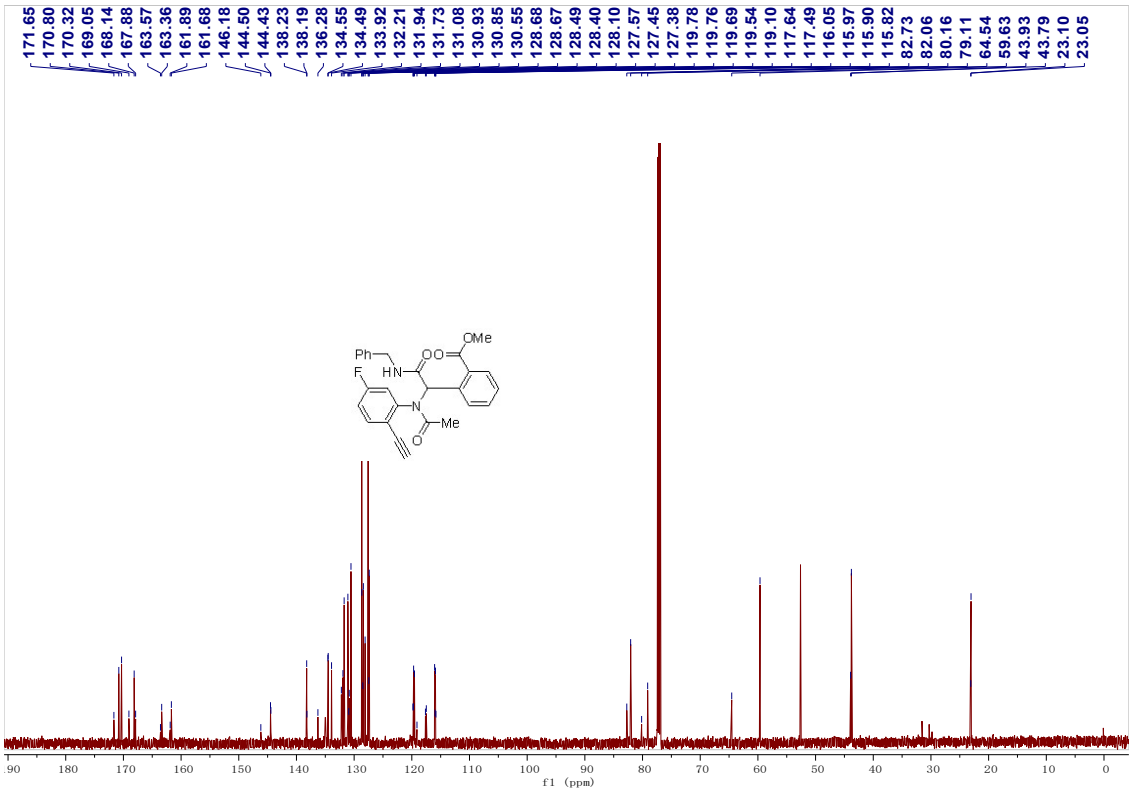
^{1}H and ^{13}C NMR spectra of compound (5q)



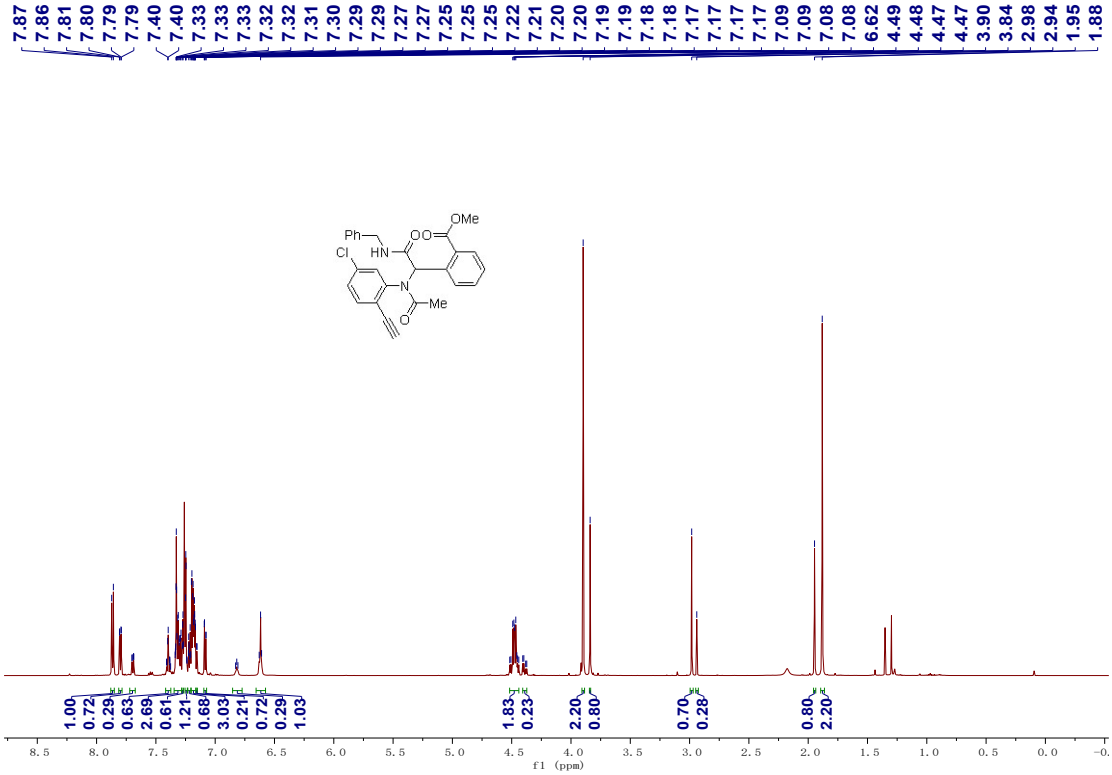


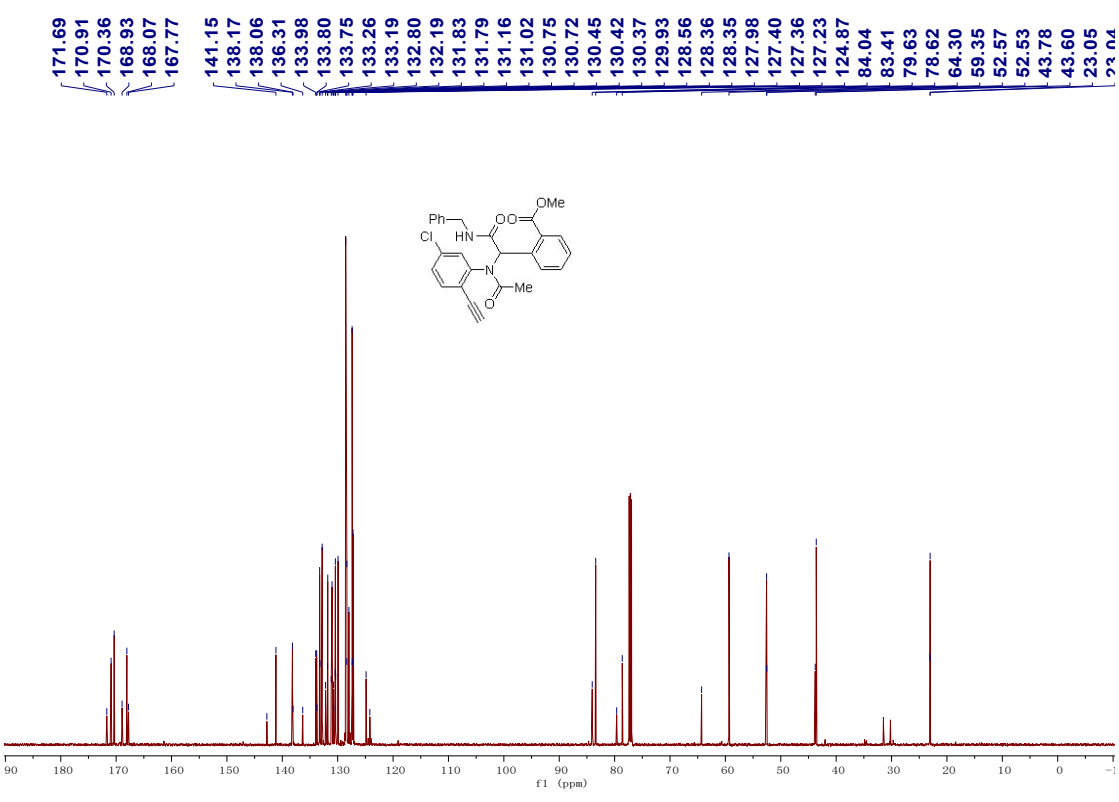
^{1}H and ^{13}C NMR spectra of compound (5r)



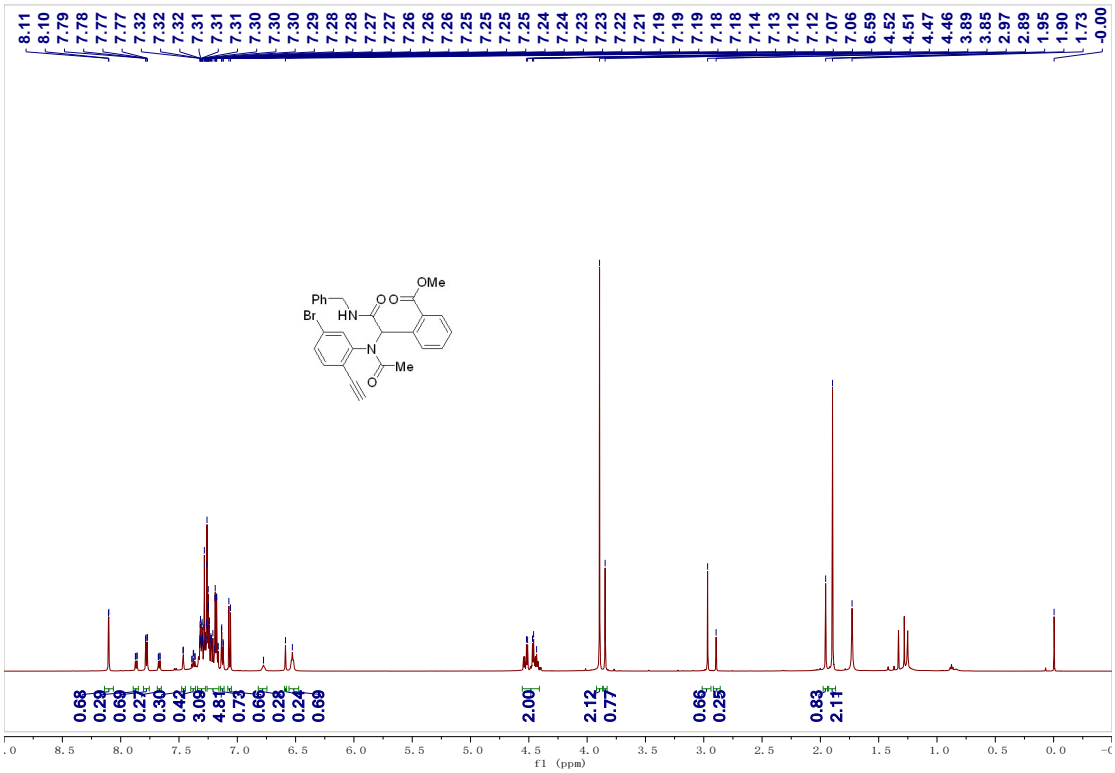


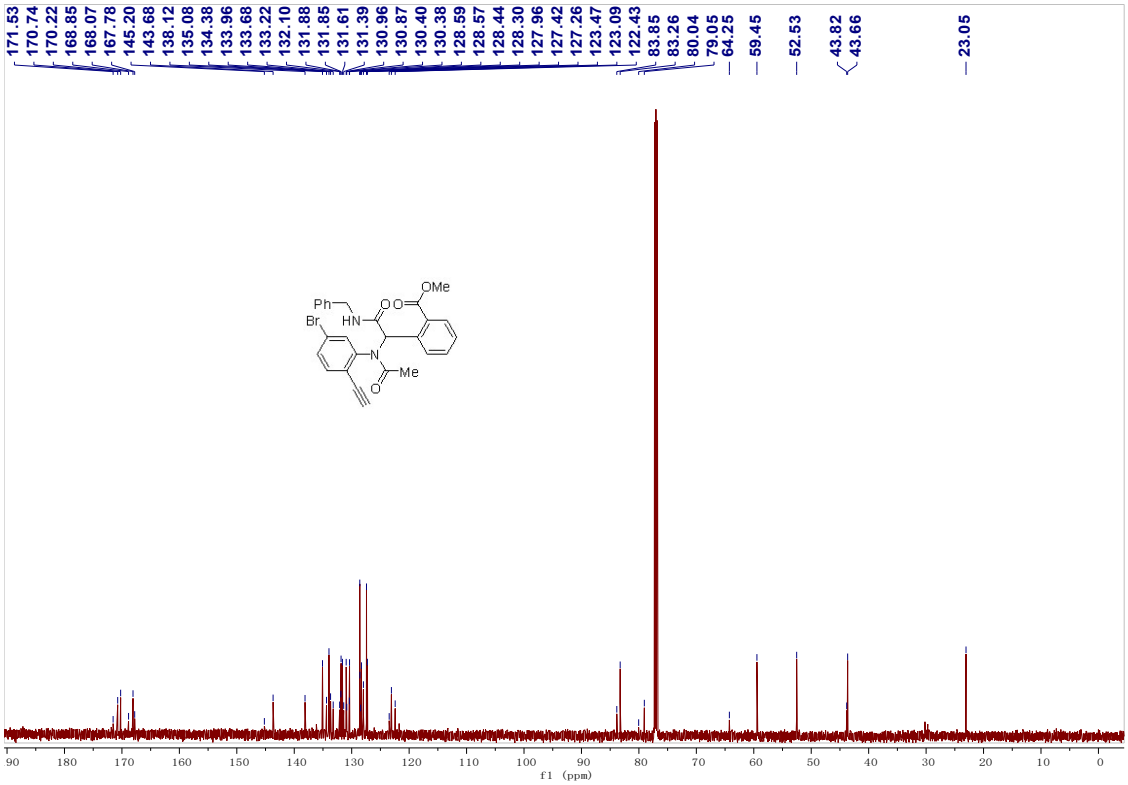
^{1}H and ^{13}C NMR spectra of compound (5s)



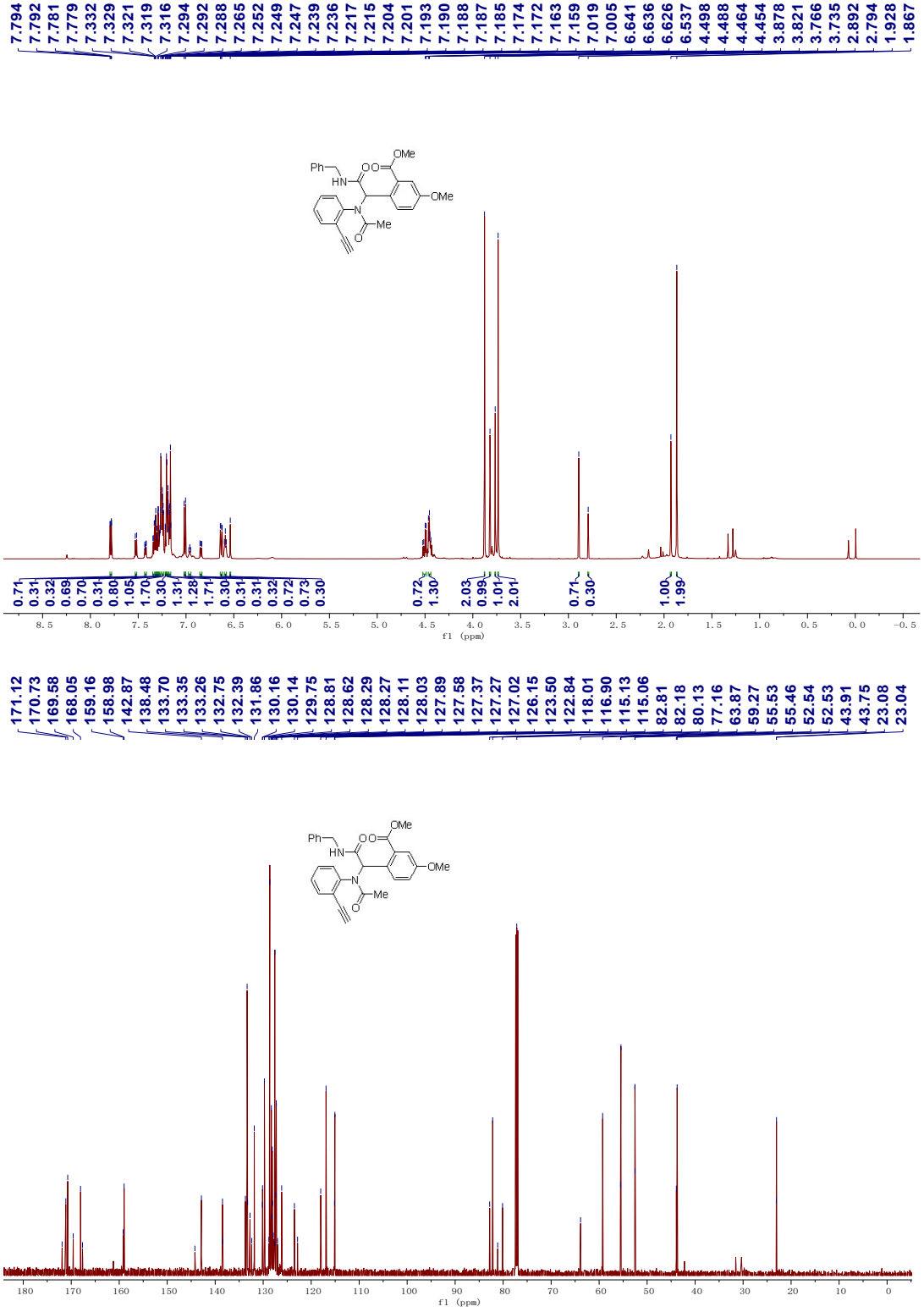


^{1}H and ^{13}C NMR spectra of compound (5t)

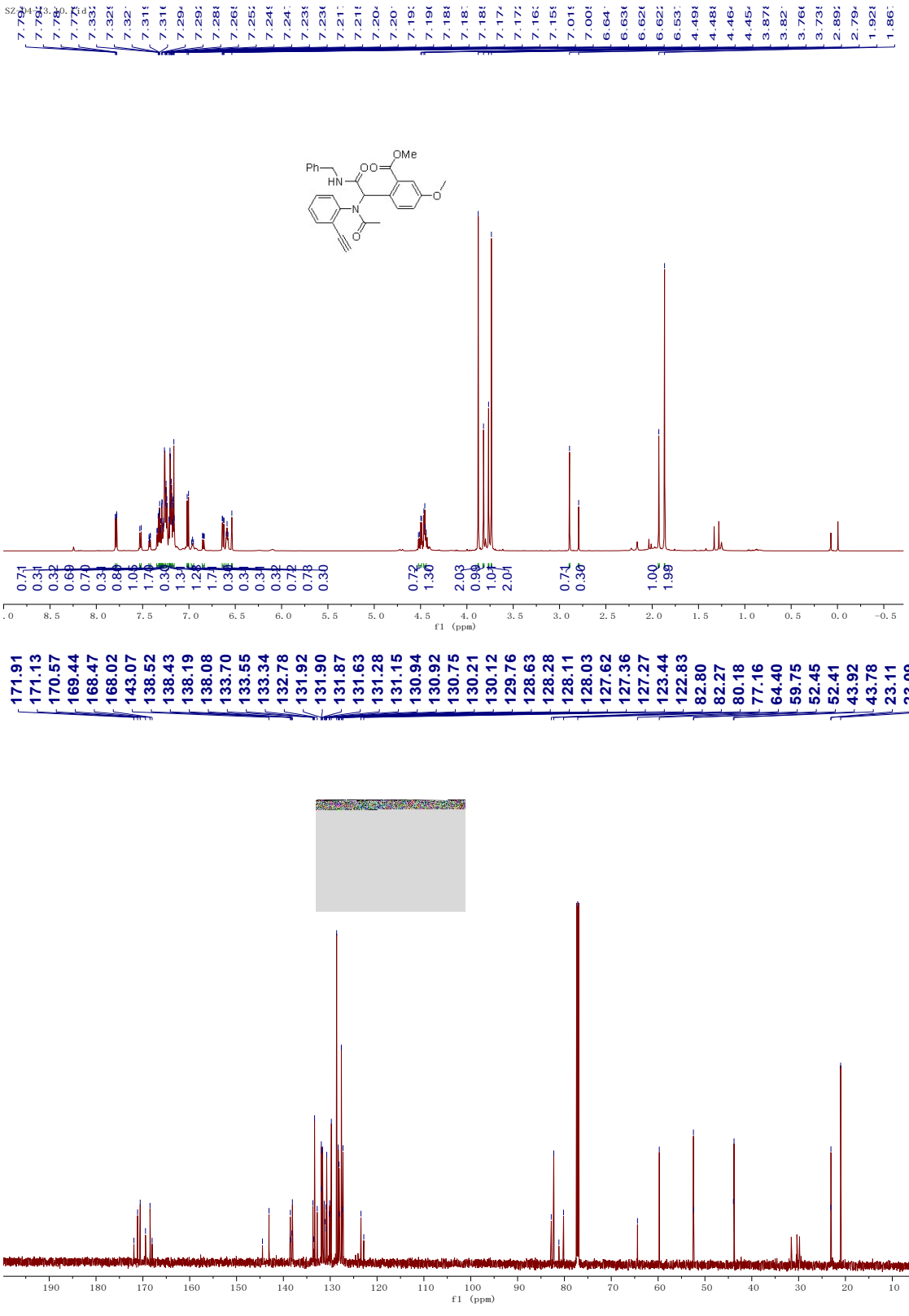




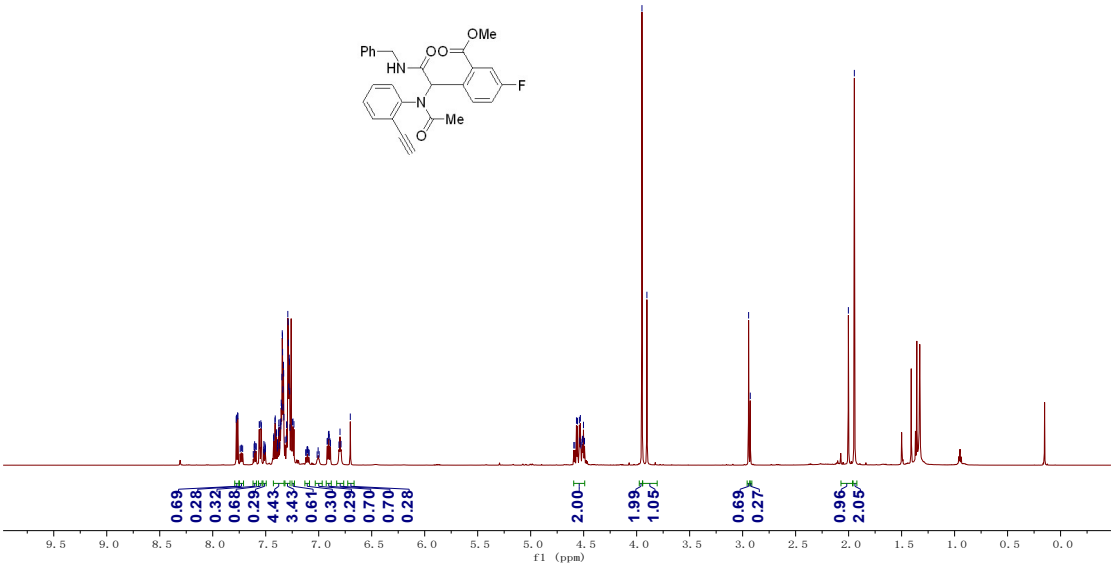
^{1}H and ^{13}C NMR spectra of compound (5u)

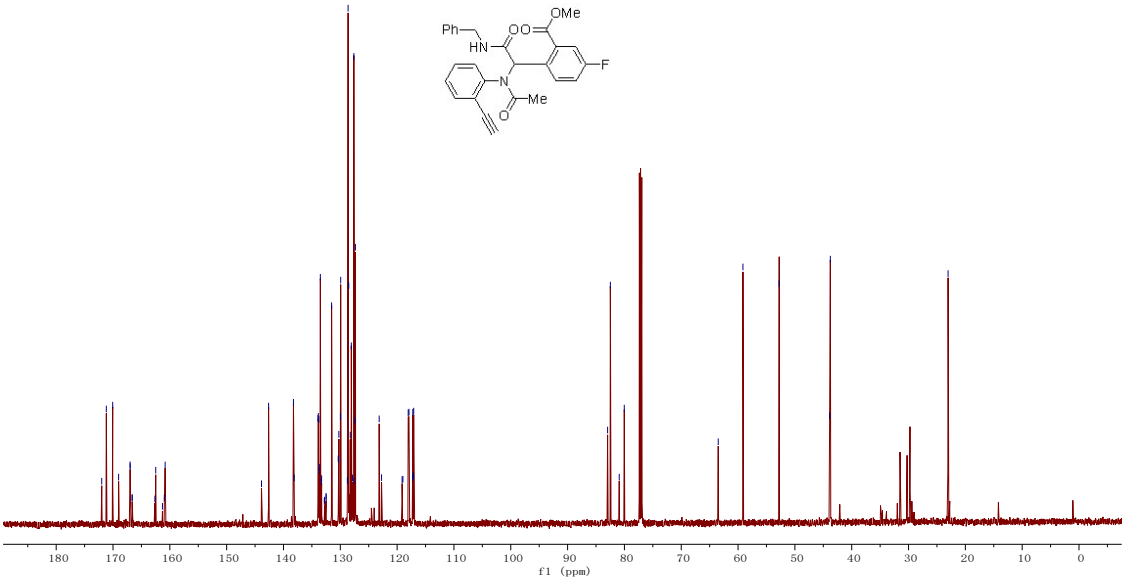


^{1}H and ^{13}C NMR spectra of compound (5v)

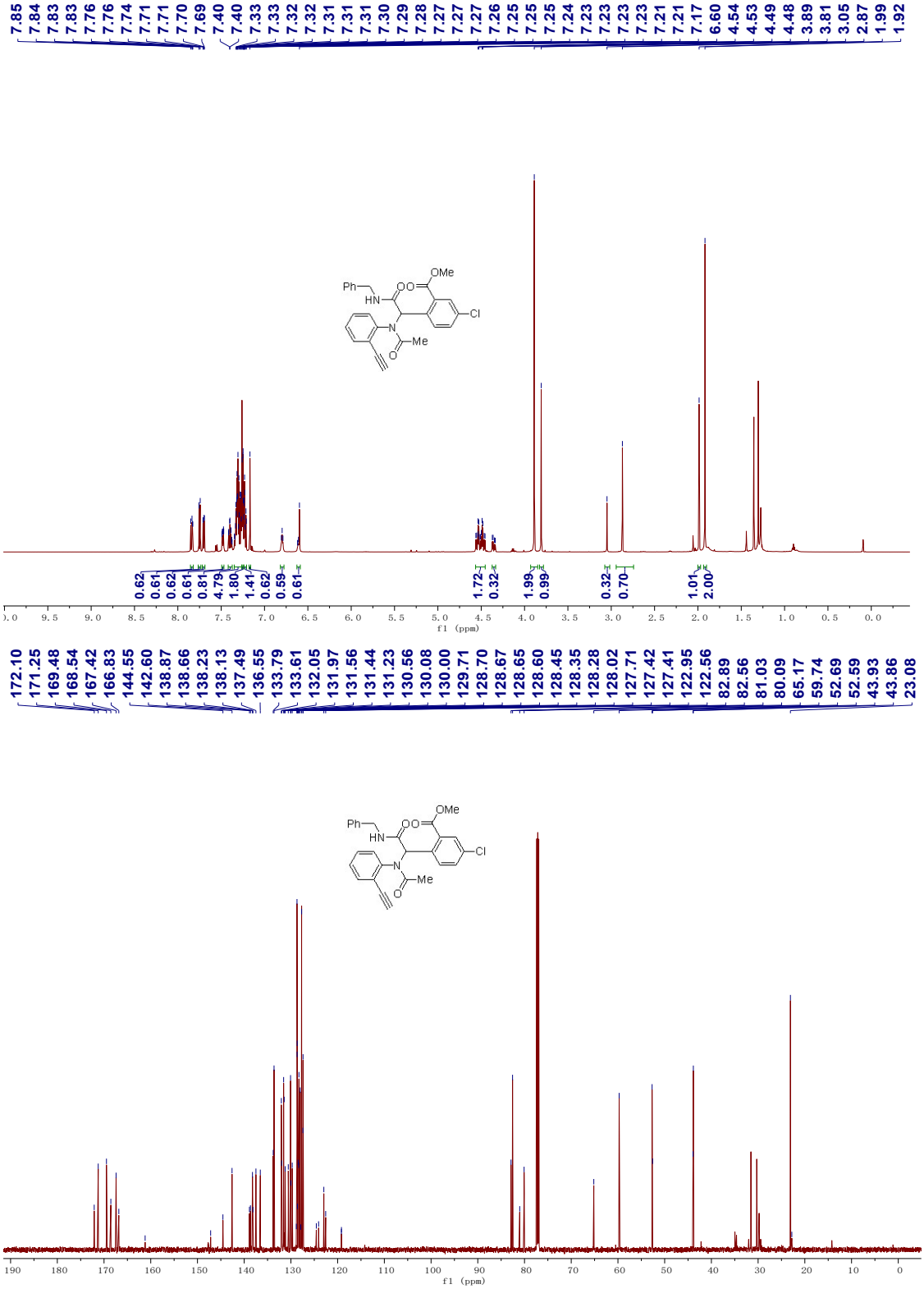


^{1}H and ^{13}C NMR spectra of compound (5w)

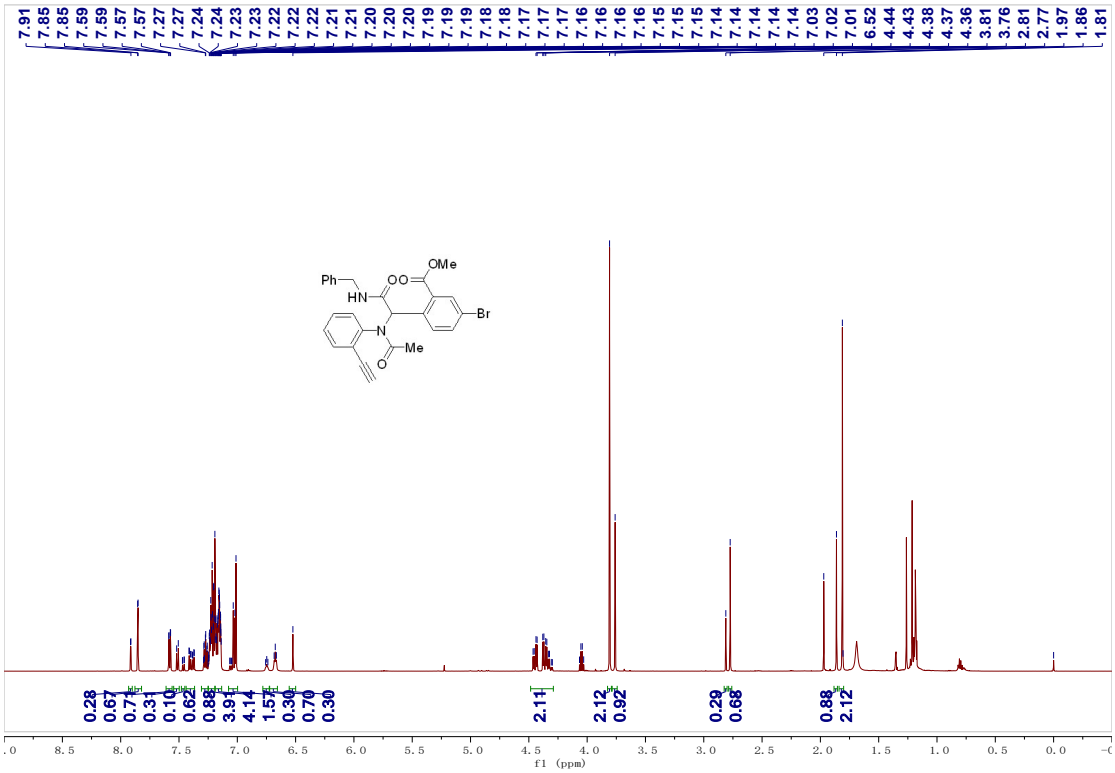


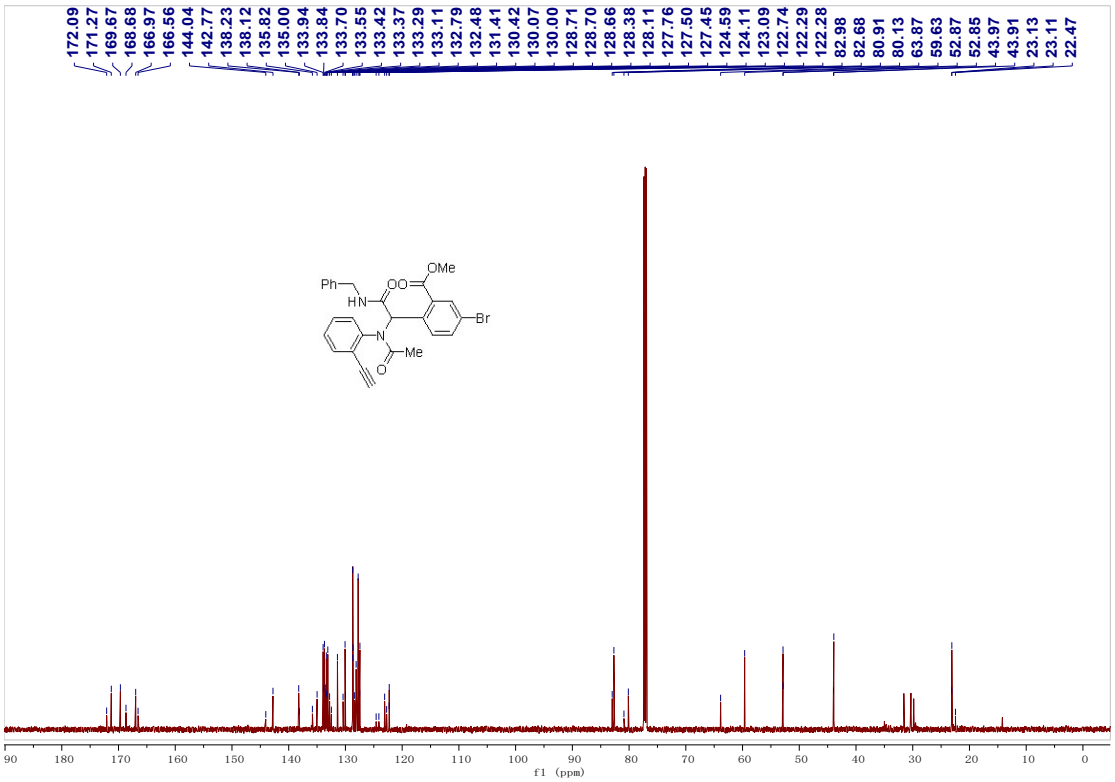


^{1}H and ^{13}C NMR spectra of compound (5x)

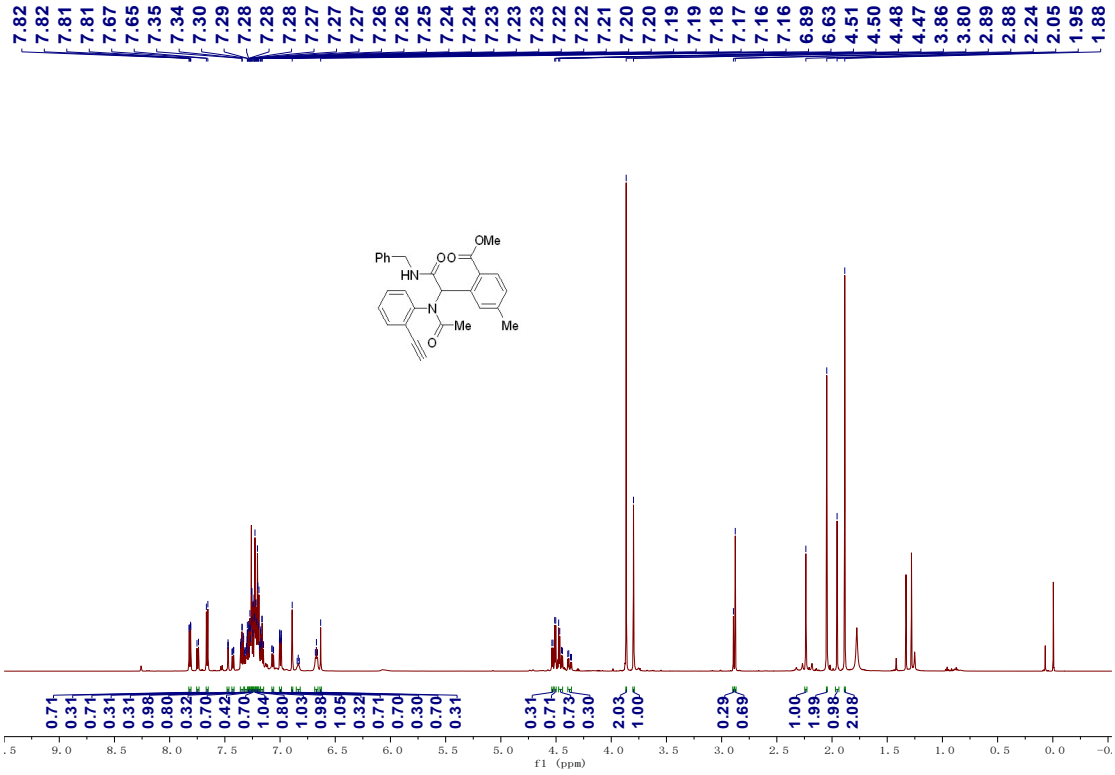


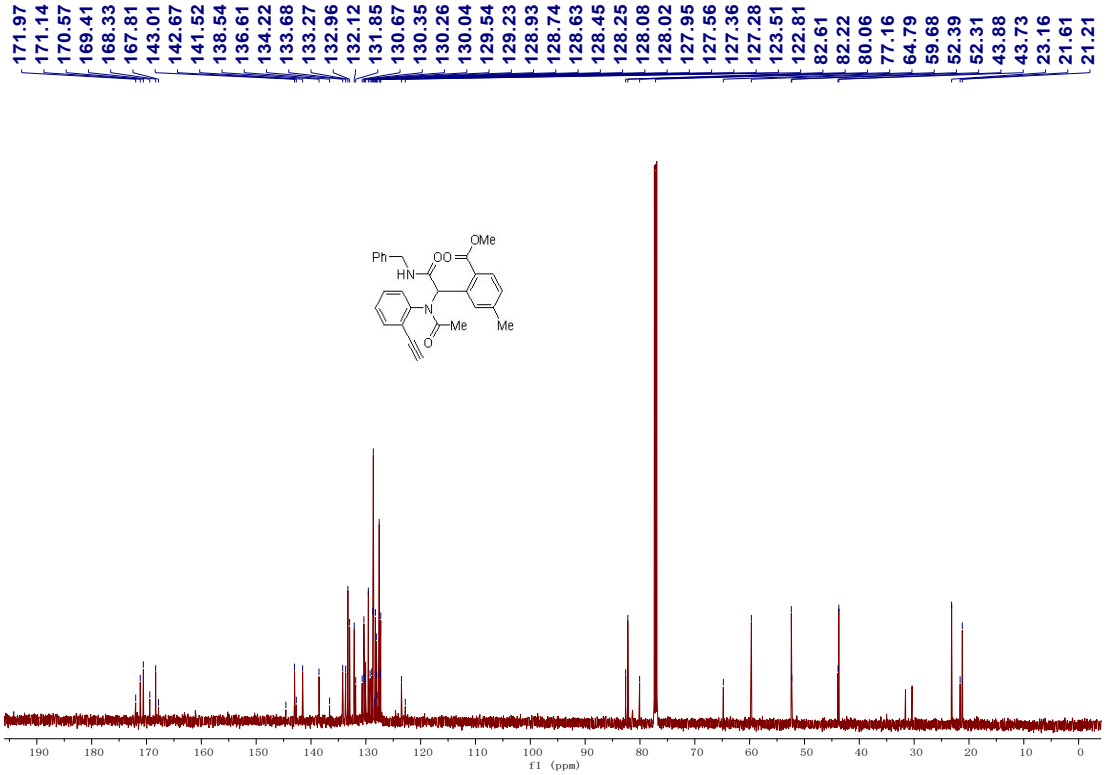
^{1}H and ^{13}C NMR spectra of compound (5y)



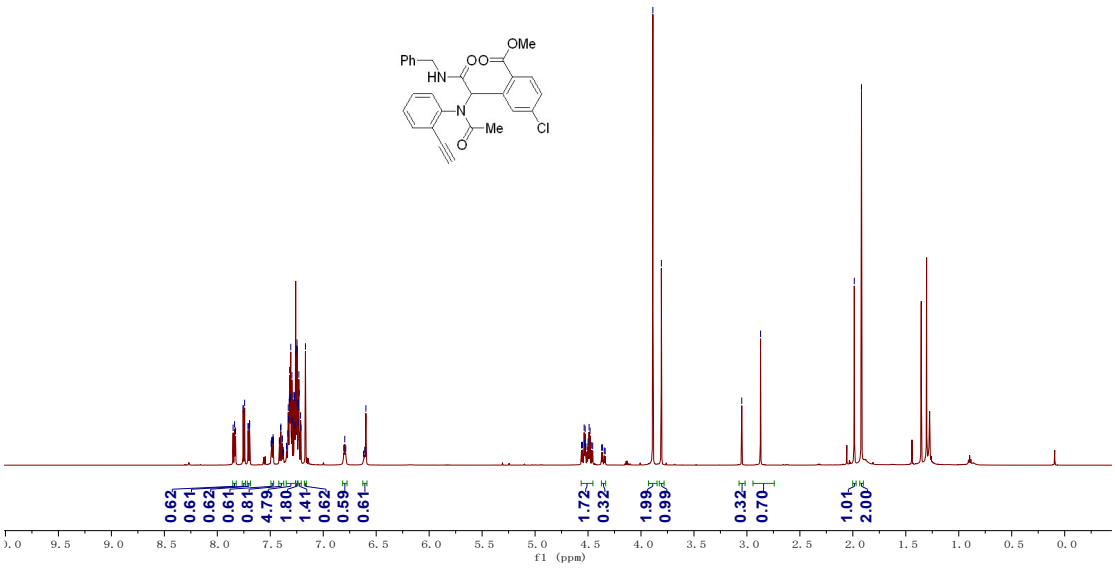


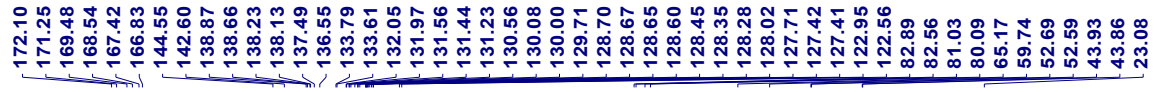
^{1}H and ^{13}C NMR spectra of compound (5z)

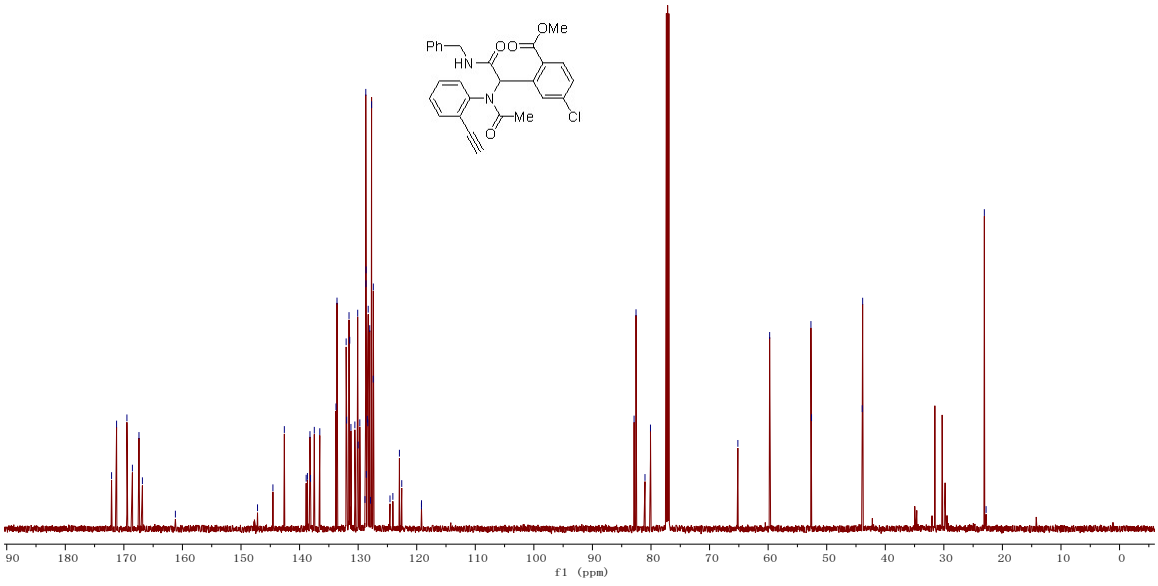




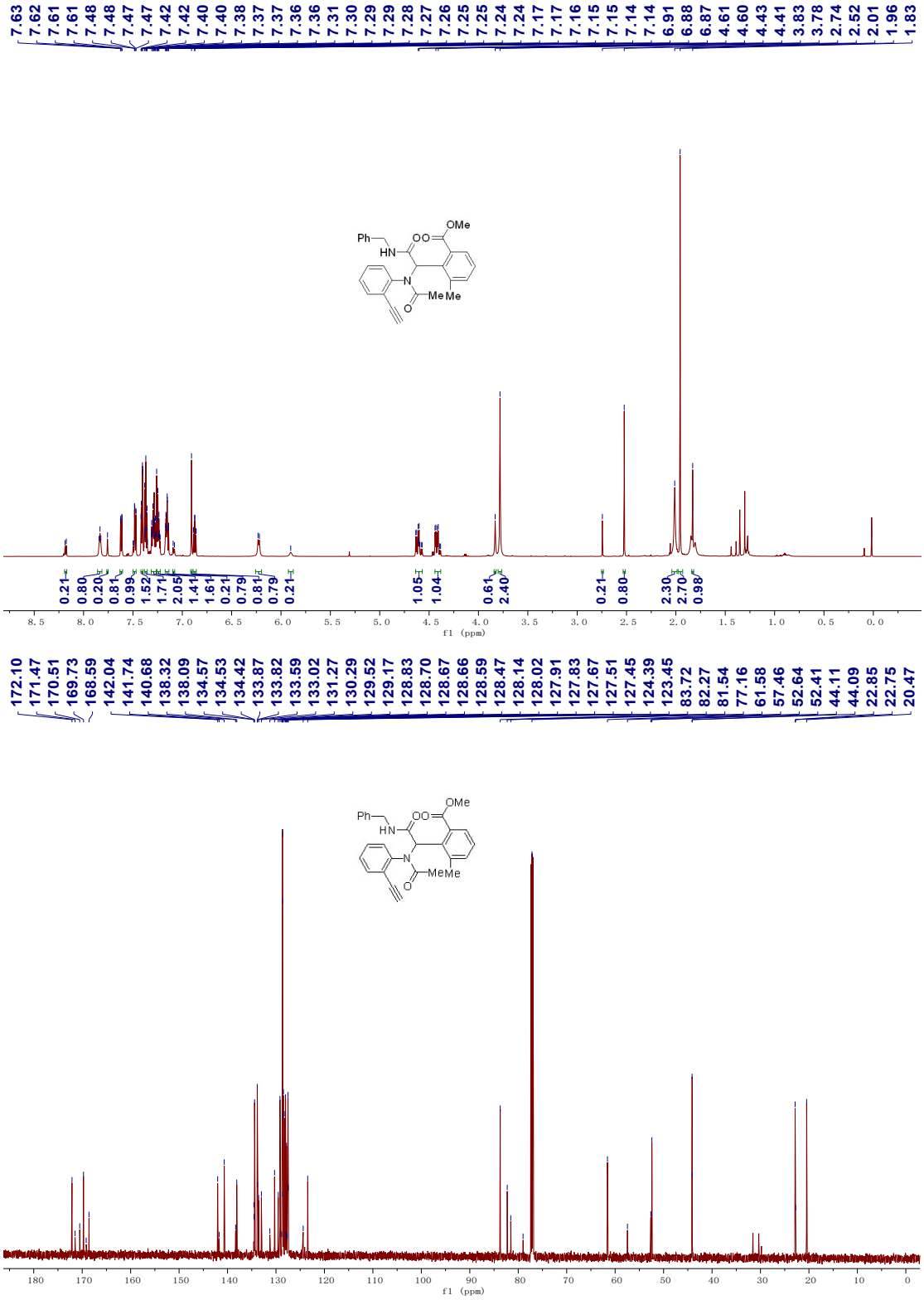
^{1}H and ^{13}C NMR spectra of compound (5aa)



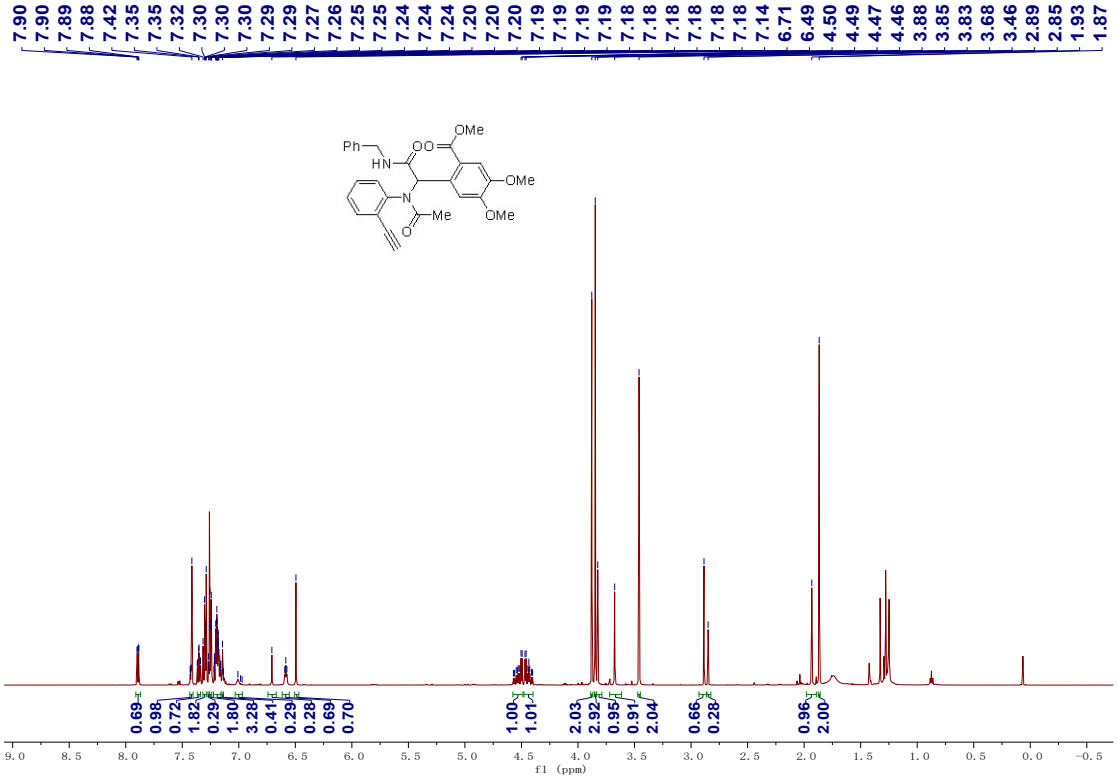


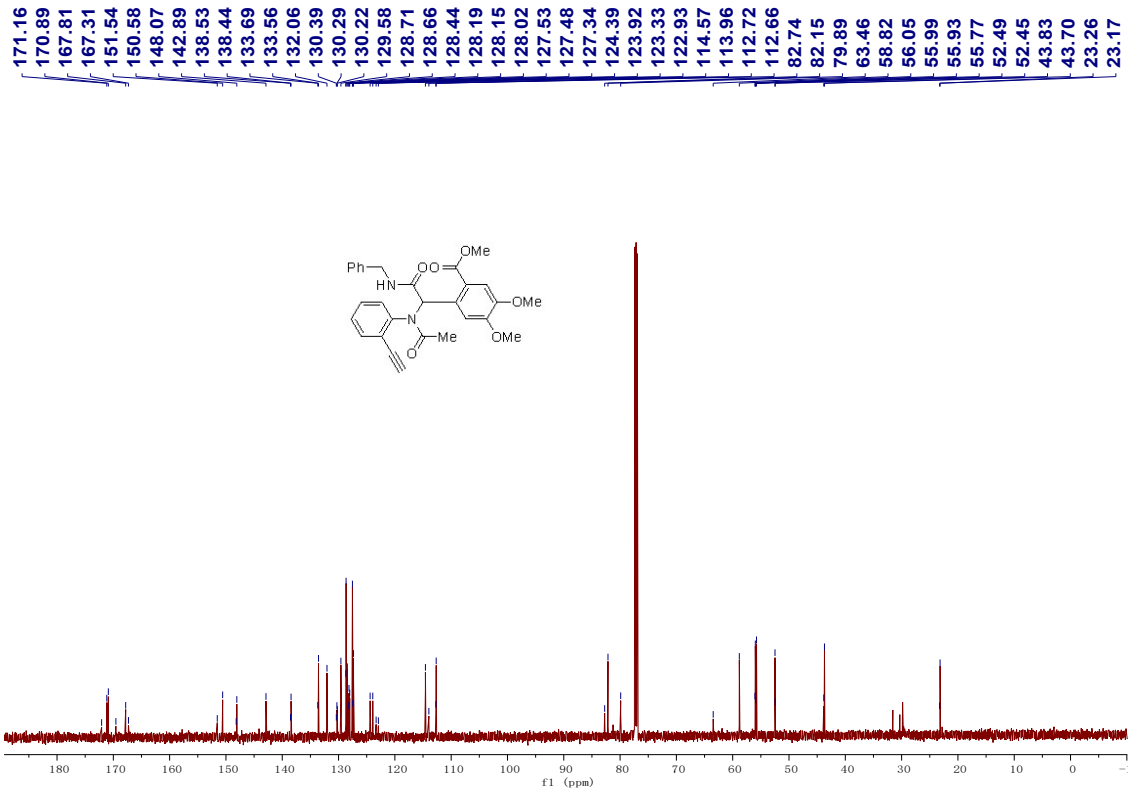


^{1}H and ^{13}C NMR spectra of compound (5ab)

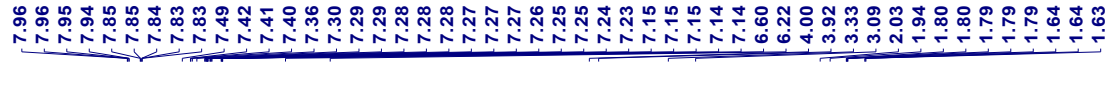


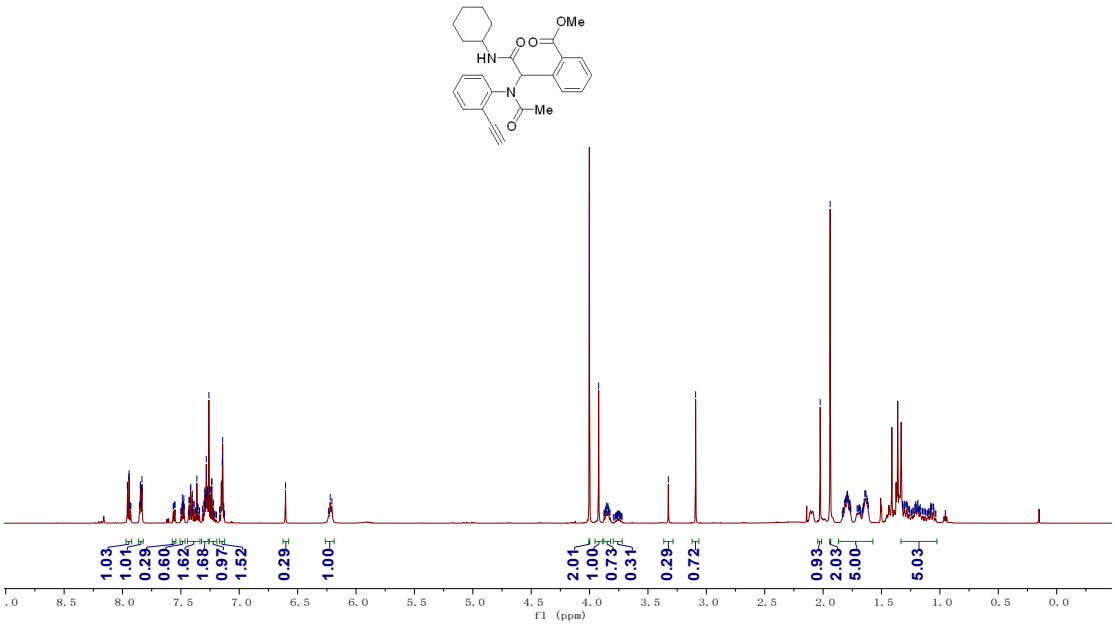
^{1}H and ^{13}C NMR spectra of compound (5ac)

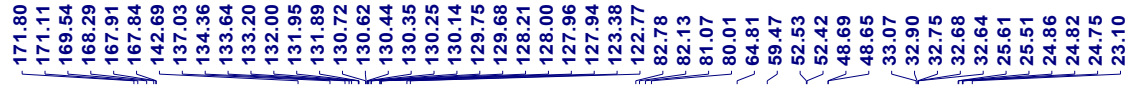


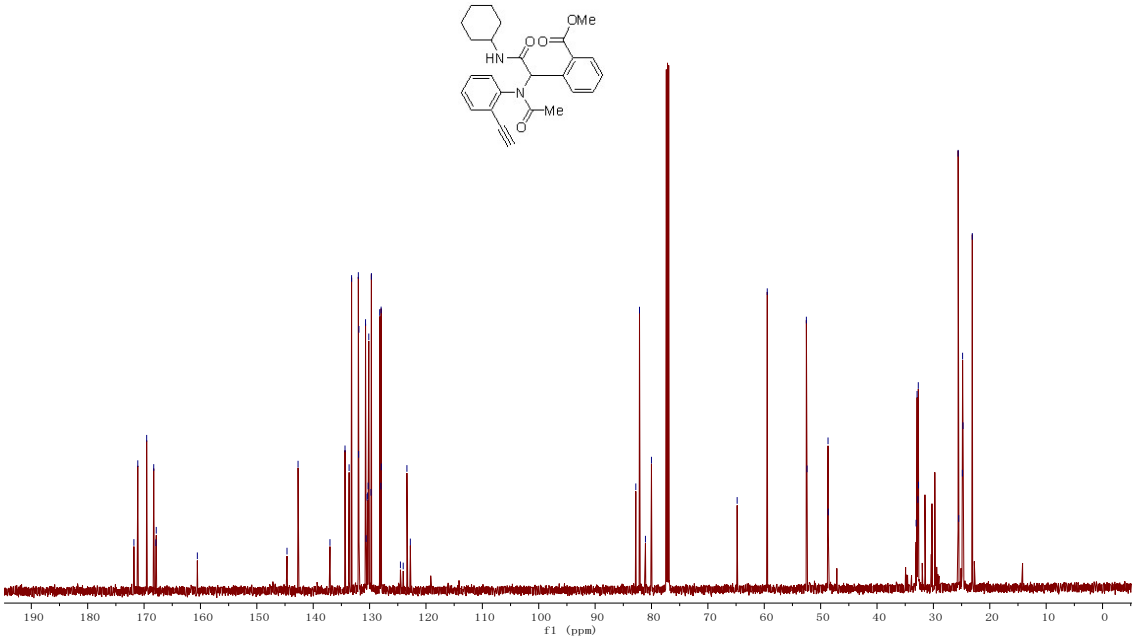


^{1}H and ^{13}C NMR spectra of compound (5ad)

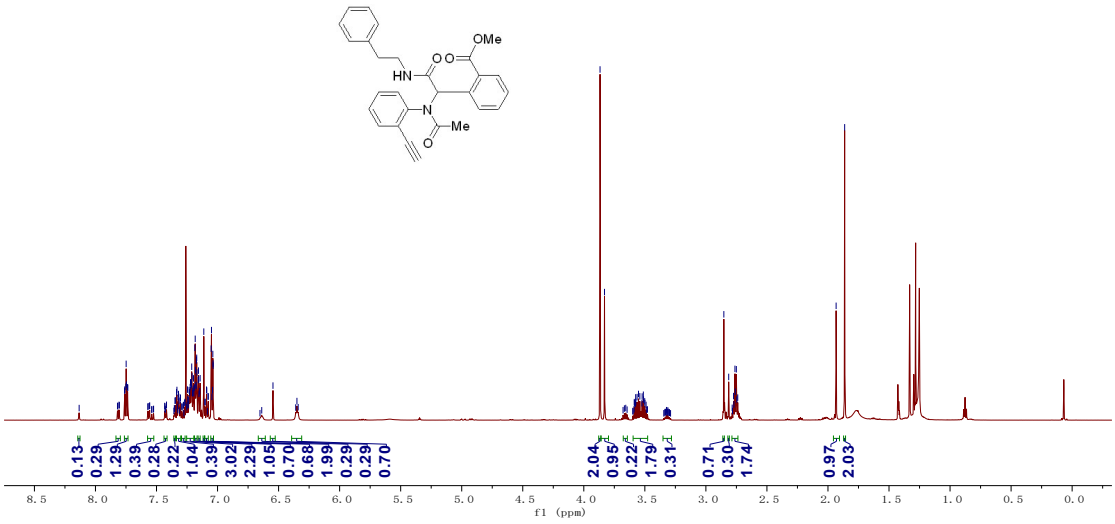


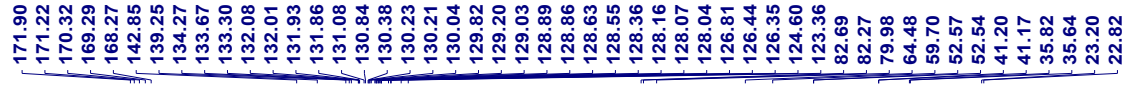


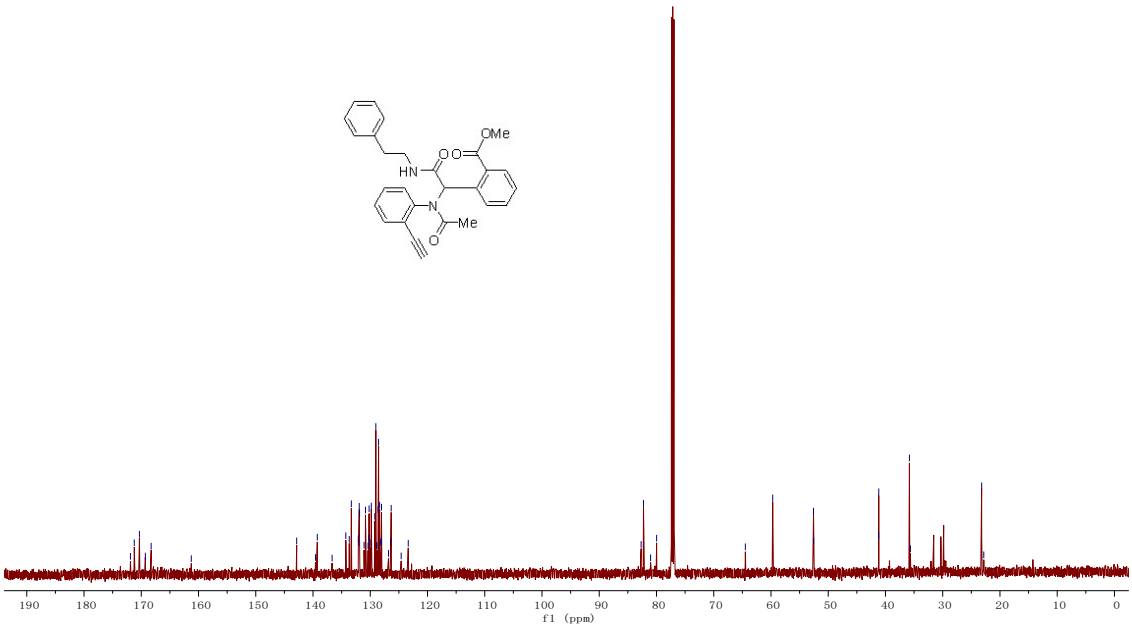




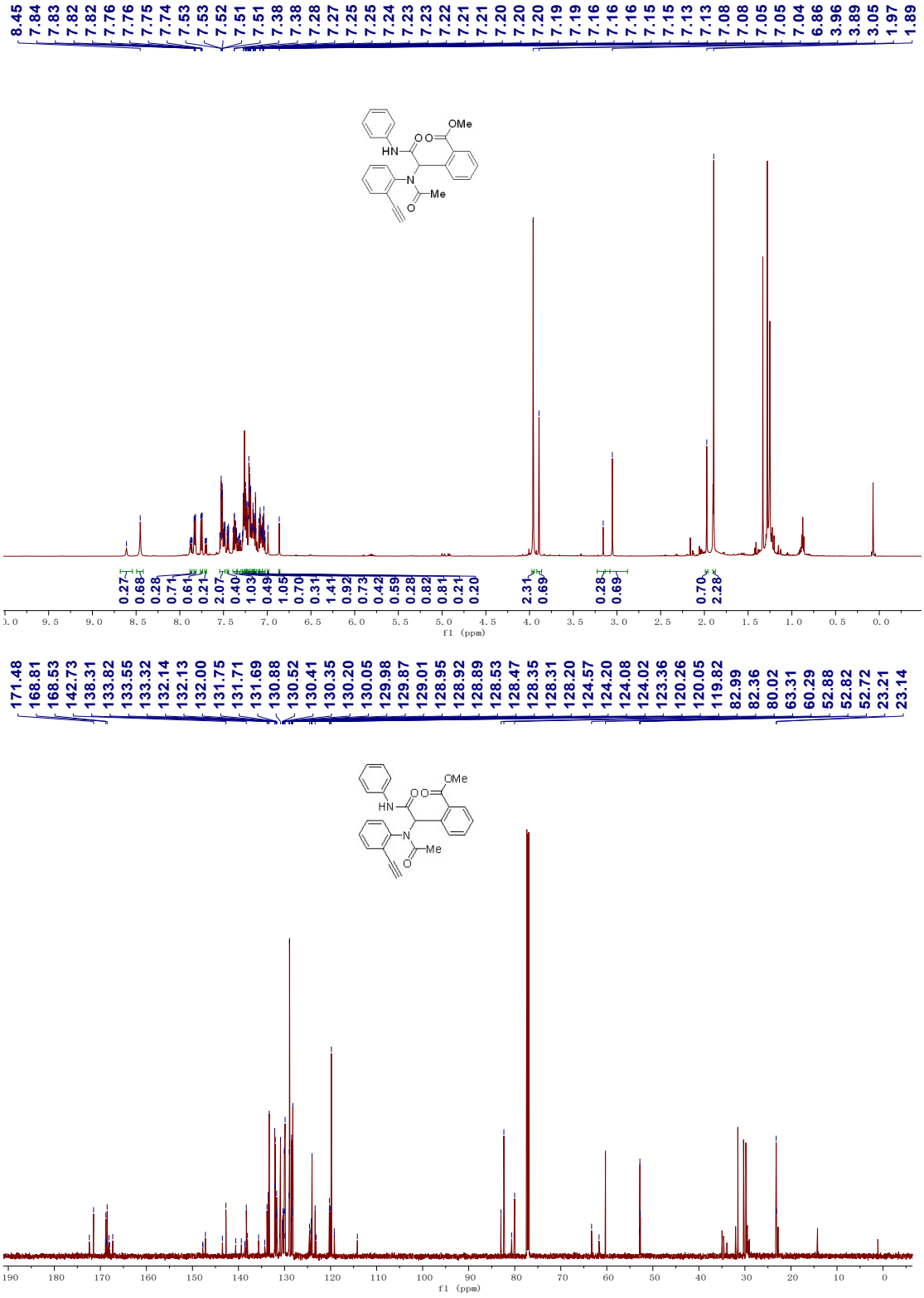
^{1}H and ^{13}C NMR spectra of compound (5ae)



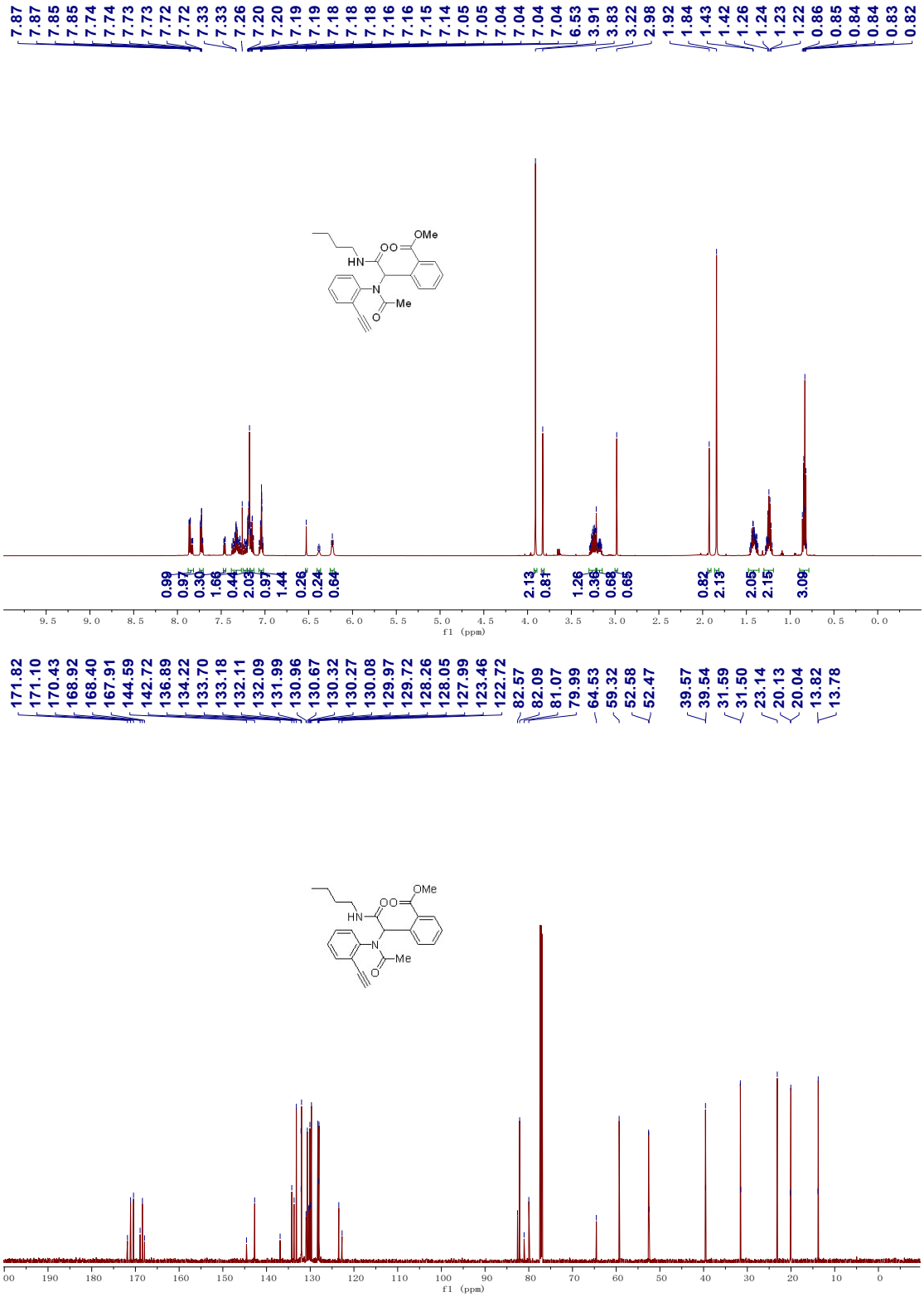




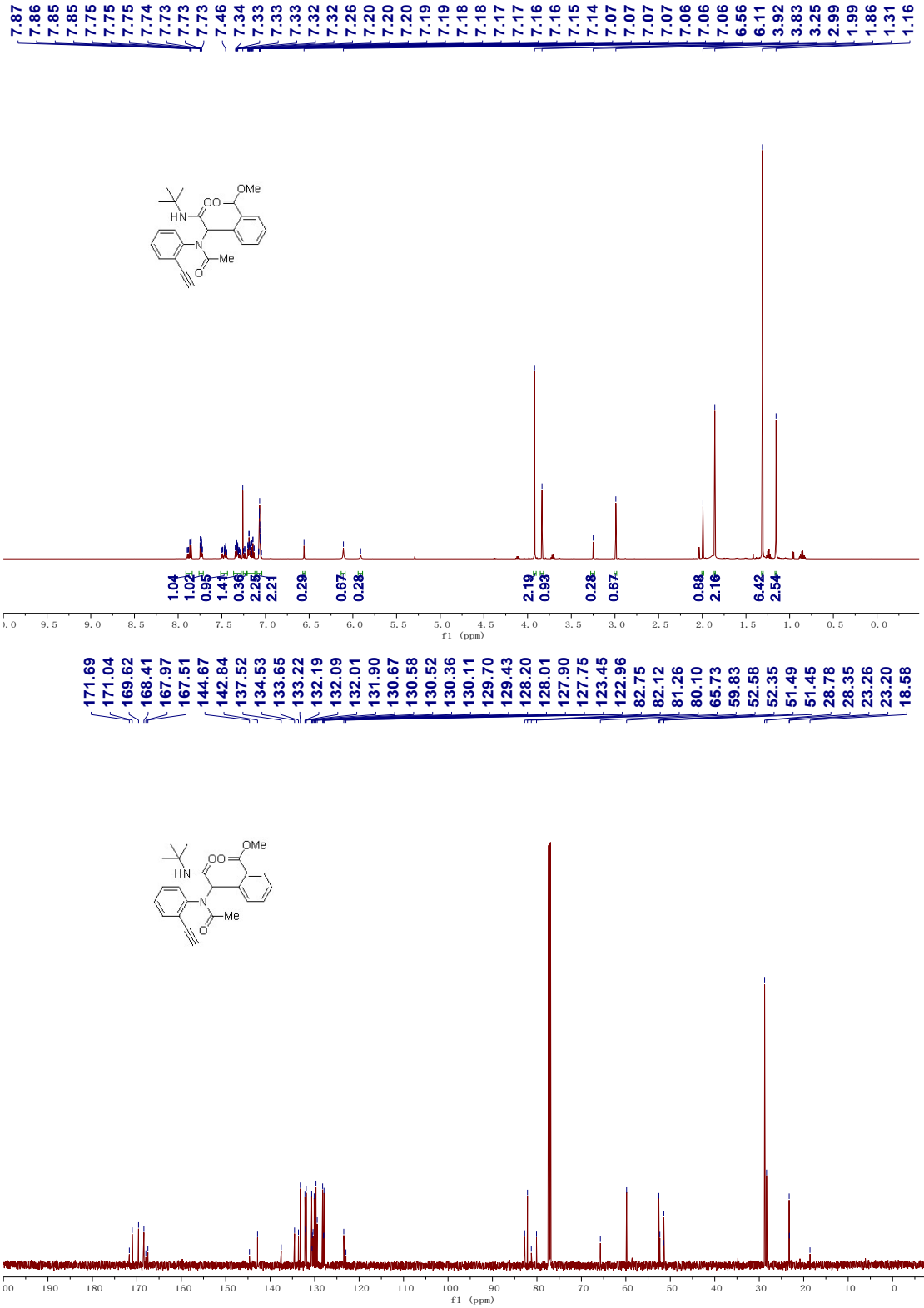
^{1}H and ^{13}C NMR spectra of compound (5af)



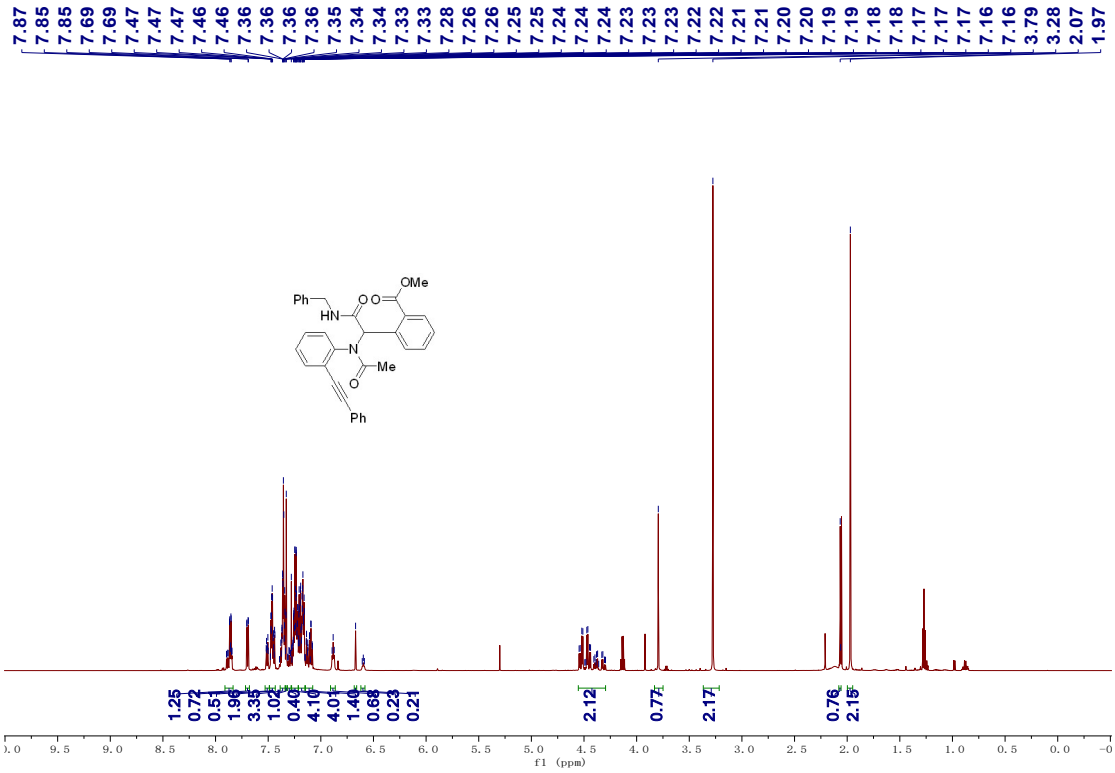
^{1}H and ^{13}C NMR spectra of compound (5ag)

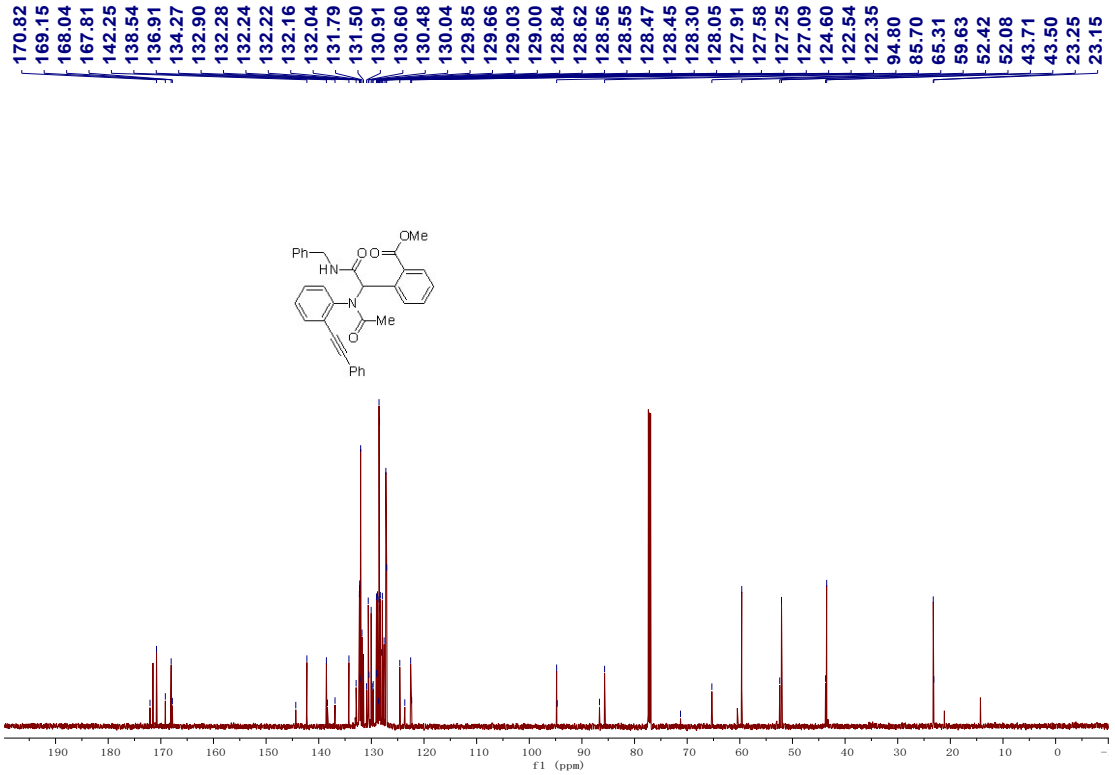


^{1}H and ^{13}C NMR spectra of compound (5ah)

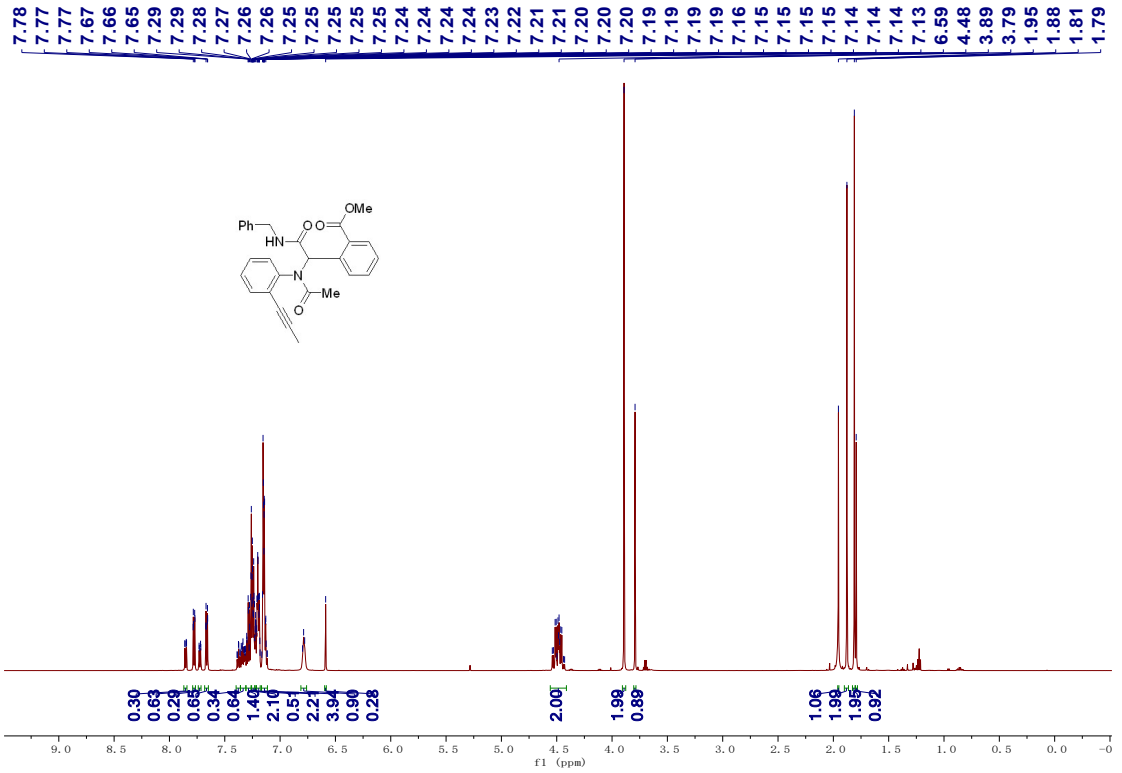


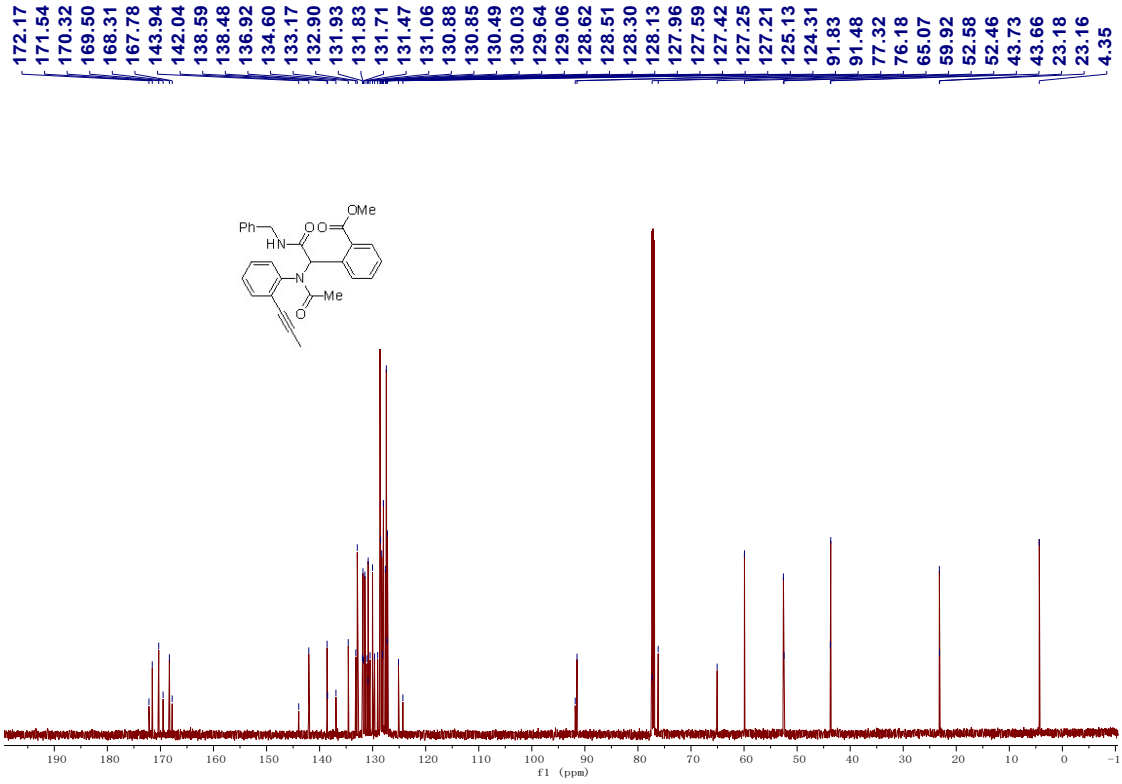
^{1}H and ^{13}C NMR spectra of compound (5ai)





^{1}H and ^{13}C NMR spectra of compound (5aj)





^{1}H and ^{13}C NMR spectra of compound (5ak)