Dehydrative Alkynylation of 3-Hydroxyisoindolinones with Terminal Alkynes for the Synthesis of 3-Alkynylated 3,3-Disubstituted Isoindolinones

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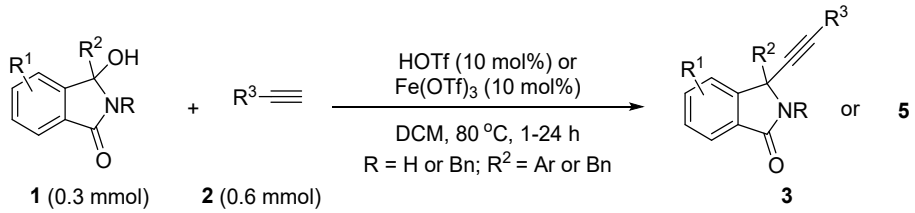
1. General information:

Reactions were monitored by thin layer chromatography using UV light to visualize the reaction course. Purification of reaction products were carried out by flash chromatography on silica gel H. Chemical yields refer to pure isolated substances. ^{1}H and ^{13}C NMR spectra were obtained using a Bruker DPX-600 or DPX-400 spectrometer. The ^{19}F NMR spectra was recorded at JEOL 565 MHz. HRMS data were collected on a on a Thermo Scientific LTQ Orbitrap Discovery (Bremen, Germany). The linear ion trap (LTQ) part of the hybrid MS system was equipped with electrospray ionization (ESI) probe and operated in both positive and negative ion modes. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, m = multiplet, br = broad.

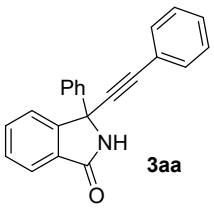
Unless noted, reactions were run under an atmosphere of air. Anhydrous THF, toluene and 1,4-dioxane were prepared by distillation over sodium-benzophenone ketyl prior to use. Anhydrous acetone was distilled over anhydrous $CaSO_4$ and stored over MS 4Å. Anhydrous halogenated solvents and CH_3CN were prepared by first distillation over P_2O_5 and then from CaH_2. Anhydrous ethyl acetate was prepared by first dried in anhydrous Na_2SO_4 and then distilled over P_2O_5 and stored over MS 4Å. Anhydrous CH_3NO_2 was prepared by first dried in anhydrous Na_2SO_4 and then distilled under reduced pressure. 3-Hydroxyisoindoliones **1** were prepared according to the literature report.[1]

1 J. Sućˊ, Josipa, I. Dokli and M. Grediˇcak, *Chem. Commun*., 2016, **52**, 2071.

2. General procedure for the direct alkynylation of 3-hydroxyisoindoliones with terminal alkynes to 3-alkylated 3,3-disubstituted isoindolinones

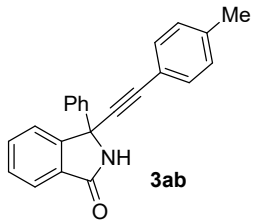


To a 10 mL vial were added 3-hydroxyisoindoliones **1** (0.3 mmol, 1.0 equiv), terminal alkynes **2** (0.6 mmol, 2.0 equivs) and 3.0 mL of anhydrous DCM. After adding HOTf (4.5 mg, 10 mol%) or $Fe(OTf)_3$ (6.2 mg, 10 mol%), the reaction mixture was stirred at 80 °C till almost full conversion of **1** by TLC analysis. The reaction mixture was directly subjected to column chromatography using petroleum ether/ethyl acetate as the eluent to afford products **3** or **5**. In the following, unless noted, HOTf was used as the catalyst.



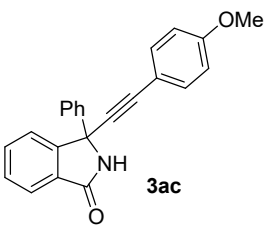
3aa

Column chromatography afforded the desired product **3aa** in 84% yield (77.9 mg) as yellow solid; Mp: 168-170 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.89-7.88 (m, 1H), 7.63-7.61 (m, 2H), 7.55 (td, *J* =7.2 Hz, 1.2 Hz, 1H), 7.51-7.47 (m, 3H), 7.39-7.31 (m, 7H), 6.72 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.3, 139.7, 133.2, 131.8, 129.2, 128.94, 128.90, 128.88, 128.6, 128.4, 125.9, 124.0, 123.2, 121.9, 86.6, 86.0, 61.9; HRMS (ESI): Exact mass calcd for $C_{22}H_{15}NO$ $[M+H]^+$: 310.1227, Found: 310.1230.



3ab

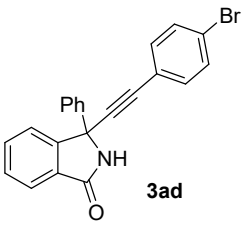
Column chromatography afforded the desired product **3ab** in 42% yield (40.7 mg) or 69% yield (67.2 mg, $Fe(OTf)_3$ used as the catalyst) as pale yellow solid; Mp: 216-218 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.63-7.61 (m, 2H), 7.55 (t, *J* =7.2 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.38-7.35 (m, 5H), 7.34-7.33 (m, 1H), 7.13 (d, *J* = 7.8 Hz, 2H), 6.57 (s, 1H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.4, 139.8, 139.1, 133.1, 131.7, 129.2, 129.1, 128.8, 128.5, 125.9, 124.0, 123.2, 118.8, 86.2, 85.9, 61.9, 21.5; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO$ $[M+H]^+$: 324.1383, Found: 324.1385.



3ac

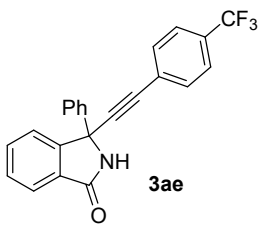
Column chromatography afforded the desired product **3ac** in 56% yield (57.0 mg)

as pale yellow solid; Mp: 172-174 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 6.6 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.38-7.32 (m, 4H), 6.84 (d, *J* = 7.8 Hz, 2H), 6.72 (s, 1H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.9, 160.0, 150.4, 139.9, 133.3, 133.1, 129.2, 128.8, 128.5, 125.9, 124.0, 123.2, 114.0, 113.9, 86.0, 85.2, 62.0, 55.3; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO_2$ [M+H]$^+$: 340.1333, Found: 340.1333.



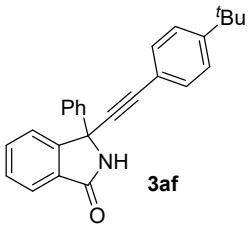
3ad

Column chromatography afforded the desired product **3ad** in 74% yield (86.2 mg) as pale yellow solid; Mp: 143-145 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.61-7.58 (m, 2H), 7.56 (td, *J* =7.2 Hz, 1H), 7.50 (td, *J* = 7.2 Hz, 1H), 7.47-7.45 (m, 2H), 7.38-7.31 (m, 6H), 6.81 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.8, 150.0, 139.4, 133.3, 133.2, 131.7, 129.2, 129.0, 128.9, 128.7, 125.8, 124.1, 123.3, 123.1, 120.8, 87.8, 84.9, 61.9; HRMS (ESI): Exact mass calcd for $C_{22}H_{14}BrNO$ [M+H]$^+$: 388.0332, Found: 388.0329.



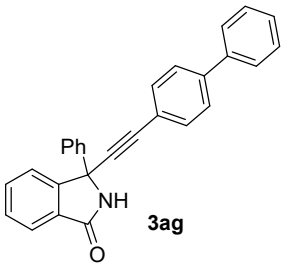
3ae

Column chromatography afforded the desired product **3ae** in 59% yield (66.8 mg) as pale yellow solid; Mp: 186-188 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.62-7.61 (m, 2H), 7.58-7.55 (m, 5H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.40-7.33 (m, 4H), 7.23-7.20 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 170.0, 149.8, 139.3, 133.3, 132.2, 130.7 (q, $J_{C\text{-}F}$ = 33.0 Hz), 129.3, 129.1, 129.0, 128.8, 126.5, 125.8, 125.7, 125.3 (q, $J_{C\text{-}F}$ = 3.0 Hz), 124.7, 124.1, 123.8 (q, $J_{C\text{-}F}$ = 271.5 Hz), 123.1, 89.2, 84.4, 61.9; ^{19}F{^{1}H} NMR (565 MHz, $CDCl_3$): *δ* = -62.9; HRMS (ESI): Exact mass calcd for $C_{23}H_{14}F_3NO$ [M+H]$^+$: 378.1101, Found: 378.1100.



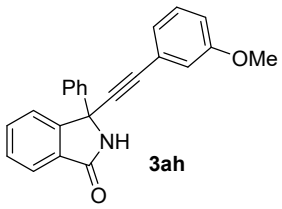
3af

Column chromatography afforded the desired product **3af** in 46% yield (50.4 mg) or 72% yield (79.0 mg, $Fe(OTf)_3$ used as the catalyst) as pale yellow solid; Mp: 151-153 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.63-7.61 (m, 2H), 7.56-7.53 (m, 1H), 7.50-7.47 m, 1H), 7.42-7.40 (m, 2H), 7.38-7.37 (m, 1H), 7.36-7.31 (m, 5H), 6.75-6.74 (m, 1H), 1.31 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.8, 152.3, 150.4, 139.8, 133.1, 131.6, 129.2, 128.8, 128.6, 125.9, 125.4, 124.0, 123.2, 118.8, 86.2, 85.9, 61.9, 34.8, 31.1; HRMS (ESI): Exact mass calcd for $C_{26}H_{23}NO$ [M+H]$^+$: 366.1853, Found: 366.1857.



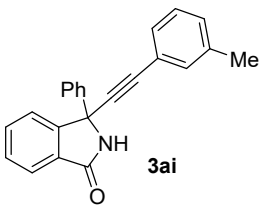
3ag

Column chromatography afforded **3ag** in 51% yield (59.0 mg) as pale yellow solid; Mp: 160-162 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.2 Hz 1H), 7.66-7.64 (m, 2H), 7.59-7.57 (m, 3H), 7.56-7.55 (m, 4H), 7.51-7.48 (m, 1H), 7.46-7.44 (m, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.39-7.34 (m, 4H), 7.02 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.2, 141.7, 140.1, 139.7, 133.2, 132.3, 129.2, 128.92, 128.89, 128.6, 127.8, 127.0, 125.9, 124.0, 123.2, 120.7, 87.2, 85.9, 61.9; HRMS (ESI): Exact mass calcd for $C_{28}H_{19}NO$ $[M+H]^+$: 386.1540, Found: 386.1542.



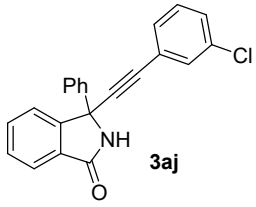
3ah

Column chromatography afforded the desired product **3ah** in 64% yield (65.2 mg) as pale yellow solid; Mp: 171-173 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.63-7.61 (m, 2H), 7.55 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.49 (td, *J* = 7.8 Hz, 0.6 Hz, 1H), 7.39-7.33 (m, 4H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.08-7.06 (m, 1H), 6.99-6.98 (m, 1H), 6.94 (s, 1H), 6.91-6.89 (m, 1H), 3.79 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.9, 159.3, 150.2, 139.6, 133.2, 129.5, 129.2, 128.91, 128.88, 128.6, 125.9, 124.4, 124.0, 123.2, 122.9, 116.6, 115.6, 86.4, 85.9, 61.9, 55.3; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO_2$ $[M+H]^+$: 340.1333, Found: 340.1332.



3ai

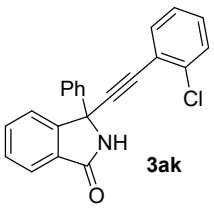
Column chromatography afforded the desired product **3ai** in 73% yield (70.8 mg) as pale yellow solid; Mp: 189-191 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.39-7.27 (m, 6H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.16-7.15 (m, 1H), 6.96 (s, 1H), 2.32 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.3, 139.8, 138.1, 133.1, 132.4, 129.8, 129.3, 128.9, 128.8, 128.6, 128.3, 125.9, 124.0, 123.1, 121.7, 86.23, 86.17, 61.9, 21.2; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO$ $[M+H]^+$: 324.1383, Found: 324.1383.



3aj

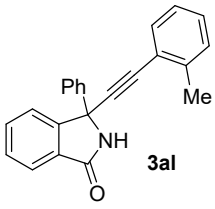
Column chromatography afforded **3aj** in 37% yield (38.2 mg) or 62% yield (63.5 mg, $Fe(OTf)_3$ used as the catalyst) as pale yellow solid; Mp: 173-175 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.61-7.59 (m, 2H), 7.56 (td, *J* =

7.2 Hz, 1.2 Hz, 1H), 7.51-7.48 (m, 1H), 7.46 (t, *J* = 1.8 Hz, 1H), 7.38-7.32 (m, 6H), 7.25 (t, *J* = 7.8 Hz, 1H), 6.97 (s, 1H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): δ = 170.0, 150.0, 139.4, 133.2, 131.7, 130.0, 129.6, 129.3, 129.2, 129.0, 128.9, 128.7, 125.8, 124.1, 123.6, 123.1, 88.0, 84.4, 61.8; HRMS (ESI): Exact mass calcd for $C_{22}H_{14}ClNO$ $[M+H]^+$: 344.0837, Found: 344.0839.



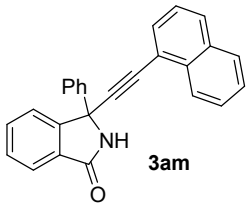
3ak

Product **3ak** was obtained in 41% yield (42.3 mg) or 53% yield (54.3 mg, $Fe(OTf)_3$ used as the catalyst) as pale yellow solid; Mp: 188-190 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.70-7.68 (m, 2H), 7.55 (td, *J* = 7.2 Hz, 0.6 Hz, 1H), 7.49 (td, *J* = 7.2 Hz, 0.6 Hz, 1H), 7.46 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.38-7.35 (m, 2H), 7.34-7.32 (m, 1H), 7.28 (td, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.20 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 6.92 (s, 1H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.1, 139.4, 136.4, 133.4, 133.2, 129.9, 129.3, 129.2, 129.0, 128.9, 128.6, 126.5, 126.0, 124.0, 123.3, 121.9, 91.7, 82.9, 62.0; HRMS (ESI): Exact mass calcd for $C_{22}H_{14}ClNO$ $[M+H]^+$: 344.0837, Found: 344.0840.



3al

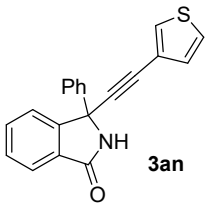
Column chromatography afforded the desired product **3al** in 66% yield (64 mg) as pale yellow solid; Mp: 153-155 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.66-7.64 (m, 2H), 7.55 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.38-7.31 (m, 3H), 7.24 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.20-7.19 (m, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 7.07 (s, 1H), 2.42 (s, 3H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.5, 140.5, 139.8, 133.1, 132.1, 129.5, 129.2, 128.91, 128.86, 128.6, 125.9, 125.6, 124.0, 123.1, 121.7, 90.5, 85.0, 62.1, 20.8; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO$ $[M+H]^+$: 324.1383, Found: 324.1382.



3am

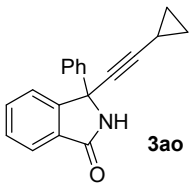
Product **3am** was obtained in 45% yield (48.5 mg) or 62% yield (66.8 mg, $Fe(OTf)_3$ used as the catalyst) as pale yellow solid; Mp: 180-182 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.87-7.85 (m, 2H), 7.73-7.71 (m, 3H), 7.61-7.58 (m, 1H), 7.56-7.54 (m, 2H), 7.53-7.52 (m, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.41-7.39 (m, 2H), 7.37-7.36 (m, 1H), 6.72 (s, 1H); $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.4, 139.8, 133.32, 133.26, 133.1, 131.0, 129.4, 129.3, 128.99, 128.97, 128.7, 128.4, 127.1, 126.6, 126.0, 125.8, 125.1, 124.1, 123.2, 119.5, 91.4, 84.3,

62.2; HRMS (ESI): Exact mass calcd for $C_{26}H_{17}NO$ $[M+H]^+$: 360.1383, Found: 360.1386.



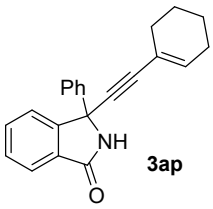
3an

Column chromatography afforded the desired product **3an** in 42% yield (39.7 mg) or 62% yield (58.7 mg, $Fe(OTf)_3$ used as the catalyst) as pale yellow solid; Mp: 161-163 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 7.8 Hz, 1H), 7.62-7.60 (m, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.50-7.47 (m, 2H), 7.38-7.31 (m, 4H), 7.28-7.27 (m, 1H), 7.13 (d, *J* = 4.8 Hz, 1H), 6.92 (brs, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.8, 150.2, 139.6, 133.2, 129.85, 129.79, 129.2, 128.91, 128.88, 128.6, 125.9, 125.6, 124.0, 123.2, 120.9, 86.2, 81.2, 61.9; HRMS (ESI): Exact mass calcd for $C_{20}H_{13}NOS$ $[M+H]^+$: 316.0791, Found: 316.0791.



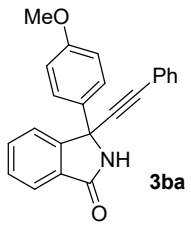
3ao

Column chromatography afforded **3ao** in 40% yield (32.8 mg) as pale yellow solid; Mp: 190-192 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.8 Hz, 1H), 7.53-7.50 (m, 3H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.33-7.31 (m, 2H), 7.30-7.28 (m, 2H), 6.66 (s, 1H), 1.34-1.31 (m, 1H), 0.82-0.80 (m, 2H), 0.74-0.71 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 170.3, 151.1, 140.6, 133.5, 129.6, 129.2, 129.1, 128.8, 126.3, 124.3, 123.5, 90.4, 73.2, 62.0, 8.8, 0.5; HRMS (ESI): Exact mass calcd for $C_{19}H_{15}NO$ $[M+H]^+$: 274.1227, Found: 274.1228.



3ap

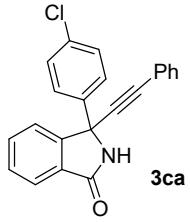
Column chromatography afforded **3ap** in 24% yield (22.6 mg) as pale yellow solid; Mp: 178-180 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 7.2 Hz, 1H), 7.56-7.54 (m, 2H), 7.52 (td, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.48-7.45 (m, 1H), 7.35-7.32 (m, 2H), 7.32-7.30 (m, 2H), 6.46 (s, 1H), 6.20-6.18 (m, 1H), 2.15-2.13 (m, 2H), 2.11-2.08 (m, 2H), 1.65-1.62 (m, 2H), 1.59-1.56 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.8, 150.6, 140.0, 136.5, 133.1, 129.2, 128.8, 128.7, 128.4, 125.9, 123.9, 123.1, 119.7, 87.9, 83.8, 61.9, 29.0, 25.6, 22.1, 21.4; HRMS (ESI): Exact mass calcd for $C_{22}H_{19}NO$ $[M+H]^+$: 314.1540, Found: 314.1544.



3ba

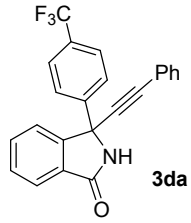
Column chromatography afforded the desired product **3ba** in 52% yield (52.9 mg) as pale yellow solid; Mp: 176-178 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.57-7.54 (m, 1H), 7.53-7.51 (m, 2H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.48-7.46 (m, 2H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.35-7.31 (m, 3H), 6.88-6.87 (m, 2H), 6.56 (s, 1H), 3.80 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.8, 159.8, 150.5, 133.1, 131.8,

131.6, 129.3, 128.9, 128.8, 128.4, 127.3, 123.9, 123.1, 122.0, 114.1, 86.8, 85.8, 61.5, 55.4; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO_2$ $[M+H]^+$: 340.1333, Found: 340.1333.



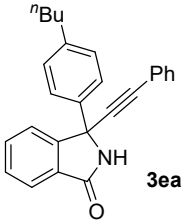
3ca

Column chromatography afforded the desired product **3ca** in 69% yield (71.2 mg) as pale yellow solid; Mp: 173-175 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 7.8 Hz, 1H), 7.57-7.55 (m, 3H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.46-7.45 (m, 2H), 7.36-7.34 (m, 2H), 7.33-7.30 (m, 4H), 7.24-7.23 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 170.0, 149.9, 138.4, 134.6, 133.3, 131.8, 129.2, 129.08, 129.06, 129.0, 128.4, 127.4, 124.1, 123.0, 121.6, 86.3, 86.1, 61.4; HRMS (ESI): Exact mass calcd for $C_{22}H_{14}ClNO$ $[M+H]^+$: 344.0837, Found: 344.0839.



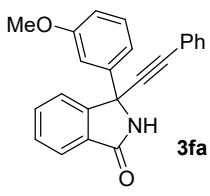
3da

Column chromatography afforded the desired product **3da** in 58% yield (65.7 mg) as pale yellow solid; Mp: 178-180 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.57 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.48-7.46 (m, 2H), 7.38-7.32 (m, 4H), 7.11 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.9, 149.6, 143.9, 133.4, 131.9, 130.9 (q, J_{C-F} = 33.0 Hz), 129.3, 129.2, 129.1, 128.5, 126.4, 125.9 (q, J_{C-F} = 4.5 Hz), 124.8 (q, J_{C-F} = 271.5 Hz), 124.2, 123.1, 121.5, 86.7, 85.8, 61.5; ^{19}F{^{1}H} NMR (565 MHz, $CDCl_3$): δ = -62.6; HRMS (ESI): Exact mass calcd for $C_{23}H_{14}F_3NO$ $[M+H]^+$: 378.1101, Found: 378.1100.



3ea

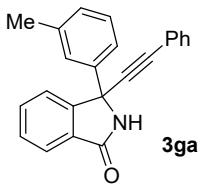
Column chromatography afforded the desired product **3ea** in 59% yield (64.7 mg) as pale yellow solid; Mp: 175-177 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.56-7.54 (m, 1H), 7.52-7.50 (m, 2H), 7.50-7.46 (m, 3H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.35-7.31 (m, 3H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.60 (s, 1H), 2.59 (t, *J* = 7.8 Hz, 2H), 1.60-1.54 (m, 2H), 1.37-1.31 (m, 2H), 0.91 (t, *J* = 7.8 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.7, 150.4, 143.6, 136.8, 133.1, 131.8, 129.2, 128.9, 128.8, 128.4, 125.8, 124.0, 123.2, 122.0, 86.8, 85.8, 61.7, 35.2, 33.5, 22.3, 13.9; HRMS (ESI): Exact mass calcd for $C_{26}H_{23}NO$ $[M+H]^+$: 366.1853, Found: 366.1859.



3fa

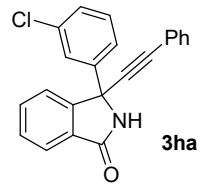
Column chromatography afforded **3fa** in 48% yield (48.9 mg) or 67% yield (67.9 mg, $Fe(OTf)_3$ used as the catalyst) as pale yellow solid; Mp: 196-198 °C; ^{1}H NMR (600

MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.56-7.54 (m, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.47-7.46 (m, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.34-7.30 (m, 3H), 7.8 (t, *J* = 7.8 Hz, 1H), 7.21-7.19 (m, 2H), 6.89 (s, 1H), 6.86 (dd, *J* = 7.8 Hz, 2.4 Hz, 1H), 3.78 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.9, 159.9, 150.1, 141.4, 133.1, 131.8, 130.0, 129.2, 128.9, 128.4, 124.0, 123.1, 121.9, 118.2, 113.6, 112.0, 86.6, 85.8, 61.8, 55.3; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO_2$ $[M+H]^+$: 340.1333, Found: 340.1333.



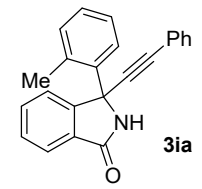
3ga

Column chromatography afforded the desired product **3ga** in 70% yield (67.9 mg) as pale yellow solid; Mp: 186-188 °C; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.2 Hz, 1H), 7.56-7.53 (m, 1H), 7.50-7.46 (m, 4H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.37 (s, 1H), 7.35-7.30 (m, 3H), 7.27-7.24 (m, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.87 (s, 1H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.9, 150.3, 139.6, 138.7, 133.1, 131.8, 129.4, 129.2, 128.9, 128.83, 128.75, 128.4, 126.3, 124.0, 123.1, 122.0, 86.8, 85.8, 61.9, 21.5; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO$ $[M+H]^+$: 324.1383, Found: 324.1384.



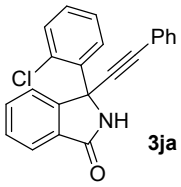
3ha

Column chromatography afforded the desired product **3ha** in 58% yield (59.8 mg) as pale yellow solid; Mp: 186-188 °C; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.633-7.630 (m, 1H), 7.57 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.52-7.50 (m, 2H), 7.47 (dd, *J* = 7.8 Hz, 1.2 Hz, 2H), 7.38 (d, *J* = 7.2 Hz, 1H), 7.36-7.32 (m, 3H), 7.31-7.28 (m, 2H), 7.10 (s, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.9, 149.7, 141.9, 134.8, 133.3, 131.9, 130.2, 129.2, 129.1, 128.8, 128.4, 126.3, 124.2, 123.1, 121.6, 86.4, 85.9, 61.5; HRMS (ESI): Exact mass calcd for $C_{22}H_{14}ClNO$ $[M+H]^+$: 344.0837, Found: 344.0836.



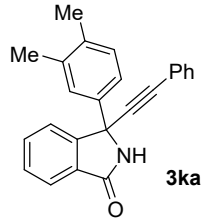
3ia

Column chromatography afforded the desired product **3ia** in 55% yield (53.4 mg) as pale yellow solid; Mp: 175-177 °C; ^1H NMR (600 MHz, $CDCl_3$): δ = 8.03-8.02 (m, 1H), 7.89 (d, *J* = 7.2 Hz ,1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.43-7.41 (m, 2H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.32-7.25 (m, 5H), 7.12-7.10 (m, 1H), 6.88-6.85 (m, 1H), 2.01 (s, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 169.9, 149.0, 136.7, 135.6, 133.1, 133.0, 131.7, 130.8, 129.00, 128.95, 128.81, 128.79, 128.3, 126.2, 124.0, 123.5, 122.1, 87.9, 86.3, 62.8, 20.3; HRMS (ESI): Exact mass calcd for $C_{23}H_{17}NO$ $[M+H]^+$: 324.1383, Found: 324.1385.



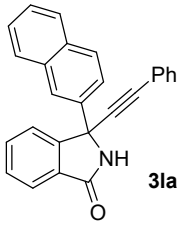
3ja

Column chromatography afforded the desired product **3ja** in 46% yield (47.4 mg) as pale yellow solid; Mp: 145-147 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 7.8 Hz, 1H), 7.69-7.65 (m, 2H), 7.61-7.60 (m, 1H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.44-7.41 (m, 3H), 7.32-7.30 (m, 2H), 7.29-7.28 (m, 2H), 7.24 (td, *J* = 7.8 Hz, 0.6 Hz, 1H), 7.07 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.3, 147.4, 135.8, 133.7, 132.7, 132.0, 131.8, 131.2, 130.1, 129.3, 128.89, 128.87, 128.3, 126.9, 124.2, 122.0, 86.7, 85.7, 61.2; HRMS (ESI): Exact mass calcd for $C_{22}H_{14}ClNO$ [M+H]$^+$: 344.0837, Found: 344.0836.



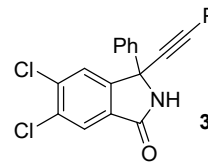
3ka

Column chromatography afforded the desired product **3ka** in 58% yield (58.7 mg) as pale yellow solid; Mp: 188-190 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.8 Hz, 1H), 7.56-7.53 (m, 1H), 7.50-7.46 (m, 3H), 7.41-7.39 (m, 2H), 7.35-7.30 (m, 4H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.68 (s, 1H), 2.24 (s, 3H), 2.23 (s, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.8, 150.4, 137.25, 137.20, 137.0, 133.1, 131.8, 130.1, 129.2, 128.85, 128.77, 128.4, 126.8, 124.0, 123.4, 123.1, 122.0, 86.9, 85.7, 61.7, 20.0, 19.4; HRMS (ESI): Exact mass calcd for $C_{24}H_{19}NO$ [M+H]$^+$: 338.1540, Found: 338.1541.



3la

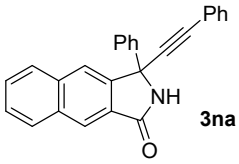
Column chromatography afforded the desired product **3la** in 64% yield (69.0 mg) as pale yellow solid; Mp: 205-207 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 1.8 Hz, 1H), 7.92-7.87 (m, 2H), 7.82-7.78 (m, 2H), 7.54-7.50 (m, 6H), 7.45 (dd, *J* = 8.4 Hz, 1.8 Hz, 1H), 7.41-7.40 (m, 1H), 7.38-7.34 (m, 3H), 7.02 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 170.0, 150.2, 136.8, 133.2, 133.1, 133.0, 131.9, 129.4, 129.0, 128.9, 128.4, 128.3, 127.6, 126.7, 126.6, 125.4, 124.1, 123.3, 123.2, 121.9, 86.5, 86.3, 62.0; HRMS (ESI): Exact mass calcd for $C_{26}H_{17}NO$ [M+H]$^+$: 360.1383, Found: 360.1385.



3ma

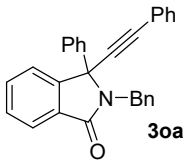
Column chromatography afforded the desired product **3ma** in 52% yield (56.8 mg) as pale yellow solid; Mp: 204-206 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.94 (s, 1H), 7.61-7.59 (m, 2H), 7.49-7.47 (m, 2H), 7.45 (s, 1H), 7.41-7.33 (m, 6H), 6.94 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 167.6, 149.2, 138.5, 137.7, 134.0, 131.9, 129.2, 129.13, 129.10, 129.06, 128.5, 125.9, 125.8, 125.4, 121.4, 86.8, 85.3, 61.5; HRMS (ESI): Exact mass calcd for

$C_{22}H_{13}Cl_2NO$ $[M+H]^+$: 378.0447, Found: 378.0445.



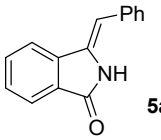
3na

Column chromatography afforded the desired product **3na** in 70% yield (78.5 mg) as pale yellow solid; Mp: 213-215 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 8.03-8.02 (m, 1H), 7.85-7.84 (m, 1H), 7.82 (s, 1H), 7.71-7.70 (m, 2H), 7.58-7.53 (m, 2H), 7.49-7.47 (m, 2H), 7.39-7.37 (m, 2H), 7.35-7.29 (m, 4H), 6.98 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.6, 145.4, 140.6, 136.0, 133.2, 131.9, 129.7, 128.94, 128.91, 128.6, 128.44, 128.39, 128.1, 127.3, 126.8, 126.0, 124.8, 122.5, 121.9, 87.3, 86.1, 61.8; HRMS (ESI): Exact mass calcd for $C_{26}H_{17}NO$ $[M+H]^+$: 360.1383, Found: 360.1377.



3oa

Column chromatography afforded the desired product **3oa** in 36% yield (43.4 mg) as pale yellow solid; Mp: 109-111 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.95-7.94 (m, 1H), 7.52-7.47 (m, 2H), 7.39-7.38 (m, 2H), 7.31-7.28 (m, 4H), 7.27-7.23 (m, 5H), 7.17-7.10 (m, 5H), 4.97 (d, *J* = 15.0 Hz, 1H), 4.29 (d, *J* = 15.6 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 168.4, 149.4, 138.0, 137.5, 132.8, 131.8, 130.1, 128.9, 128.85, 128.78, 128.7, 128.6, 128.2, 128.1, 127.0, 123.9, 123.0, 121.9, 88.6, 85.3, 66.8, 44.5; HRMS (ESI): Exact mass calcd for $C_{29}H_{21}NO$ $[M+H]^+$: 400.1696, Found: 400.1691.

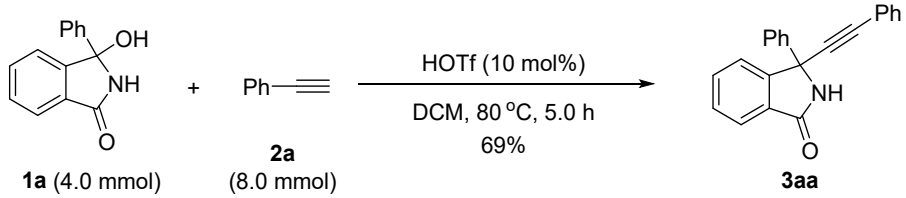


5aa

Column chromatography afforded the desired product **5aa**[2] in 87% yield (58.0 mg) as pale yellow-green solid; Mp: 177-179 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37 (s, 1H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.47-7.43 (m, 4H), 7.33-7.30 (m, 1H), 6.56 (s, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 169.1, 138.3, 135.1, 133.2, 132.4, 129.3, 128.8, 128.6, 127.8, 123.7, 119.9, 106.0.

3. Scaled synthesis and product elaboration

3.1 Scaled synthesis

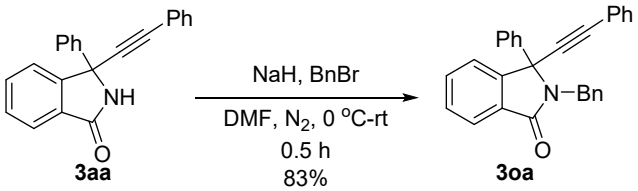


[2] M. Hellal and G. D. Cuny, *Tetrahedron Lett.*, 2011, **52**, 5508.

To a 100 mL of sealed tube were added **1a** (0.90 g, 4.0 mmol, 1.0 equiv), phenylacetylene **2a** (0.82 g, 8.0 mmol, 2.0 equivs) and 30.0 mL of CH_2Cl_2. After adding HOTf (100 mg, 10 mol%), the reaction mixture was stirred at 80 °C till almost full conversion of **1a** by TLC analysis. The residue was directly subjected to column chromatography using petroleum ether/ethyl acetate (10:1, v:v) as the eluent to afford the desired product **3aa** in 69% yield (0.86 g).

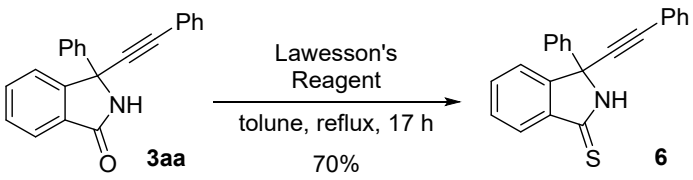
3.2 Product elaboration

1) Synthesis of 3oa



Under the N_2 atmosphere, to a 25 mL dried Schlenk tube were sequentially added **3aa** (92.8 mg, 0.3 mmol) and 3.0 mL of anhydrous DMF. After cooling to 0 °C, NaH (0.02 g, 0.45 mmol, 1.5 equivs) was added portion wise into the reaction mixture. The resulting solution was stirred at the same temperature till there was no obvious gas generating. Then, BnBr (43 μL, 0.36 mmol) was added in the tube. Upon the completion of the reaction (monitored by TLC), the reaction mixture was quenched with H_2O and extracted with ethyl acetate (4×15 mL). The combined organic layers were then washed with H_2O, dried over anhydrous Na_2SO_4. After removing the solvent, the residue was then subjected to column chromatography using petroleum ether/ethyl acetate (generally 5:1, v:v) as the eluent to afford the desired product **3oa** in 83% yield (99.6 mg) as colorless oil.

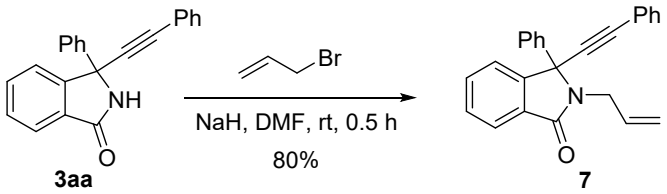
2) Synthesis of 6



To a 25 mL of sealed tube were sequentially added **3aa** (61.8 mg, 0.2 mmol), Lawesson's reagent

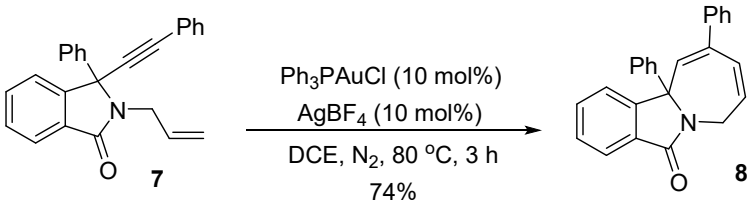
(80.9 mg, 0.2 mmol) and 3.0 mL of toluene. The reaction mixture was then refluxed for 17 h till almost full conversion of **3aa** by TLC analysis. Then, the reaction mixture was quenched with water and extracted with ethyl acetate (3× 15 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified over silica gel by column chromatography to afford compound **6** in 70% yield (45.1 mg) as pale yellow solid; Mp: 141-143 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.47 (brs, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.58 (td, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.55-7.51 (m, 3H), 7.49-7.47 (m, 2H), 7.38-7.31 (m, 7H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 195.4, 148.4, 137.9, 136.0, 133.1, 131.9, 129.2, 129.1, 129.05, 129.02, 128.4, 125.9, 125.8, 122.5, 121.6, 87.4, 84.1, 68.7; HRMS (ESI): Exact mass calcd for $C_{22}H_{15}NS$ $[M+H]^+$: 326.0998, Found: 326.1000.

3) Synthesis of 7



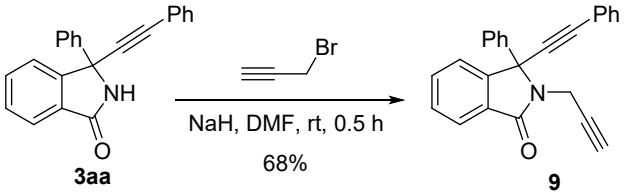
Under the N_2 atmosphere, to a 25 mL dried Schlenk tube were sequentially added **3aa** (0.31 g, 1.0 mmol) and 5.0 mL of anhydrous DMF. After cooling to 0 °C, NaH (0.06 g, 1.5 mmol, 1.5 equivs) was added portion wise. The resulting solution was stirred at the same temperature till there was no obvious gas generating. Then, allyl bromide (101 μL, 1.2 mmol) was added. Upon the completion of the reaction (monitored by TLC), the reaction mixture was quenched with H_2O and extracted with ethyl acetate (4×15 mL). The combined organic layers were then washed with H_2O, dried over anhydrous Na_2SO_4. After removing the solvent, the residue was then subjected to column chromatography using petroleum ether/ethyl acetate (generally 5:1, v:v) as the eluent to afford the desired product **7** in 80% yield (277.4 mg) as white solid; Mp: 91-93 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.50-7.46 (m, 5H), 7.36-7.32 (m, 7H), 5.85-5.79 (m, 1H), 5.16 (dd, *J* = 16.8 Hz, 1.2 Hz, 1H), 5.03-5.01 (m, 1H), 4.29 (dd, *J* = 15.6 Hz, 6.0 Hz, 1H), 3.90 (dd, *J* = 15.6 Hz, 6.6 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 168.0, 149.2, 138.3, 133.3, 132.7, 131.8, 130.3, 129.0, 128.9, 128.8, 128.7, 128.5, 126.9, 123.8, 123.0, 122.1, 117.3, 88.0, 85.6, 66.7, 43.7; HRMS (ESI): Exact mass calcd for $C_{25}H_{19}NO$ $[M+H]^+$: 350.1539, Found: 350.1541.

4) Synthesis of 8



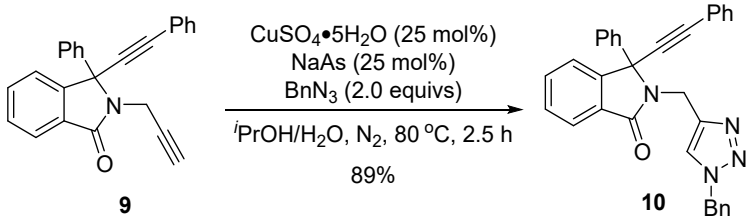
Under the N_2 atmosphere, to a 25 mL dried Schlenk tube were sequentially added **6** (34.9 mg, 0.1 mmol), Ph_3PAuCl (5.0 mg, 0.01 mmol), $AgBF_4$ (2.0 mg, 0.01 mmol) and 1.0 mL of anhydrous DCE. Then the reaction mixture was stirred at 80 °C till almost full conversion of **6** by TLC analysis. The reaction mixture was directly subjected to column chromatography using petroleum ether/ethyl acetate (generally 8:1, v:v) as the eluent to afford the desired product **8** in 74% yield (25.8 mg) as white solid; Mp: 231-233 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 7.2 Hz, 1H), 7.50-7.48 (m, 1H), 7.47-7.44 (m, 1H), 7.43-7.42 (m, 2H), 7.38-7.35 (m, 4H), 7.34-7.32 (m, 3H), 7.32-7.29 (m, 2H), 5.74 (s, 1H), 5.52 (s, 1H), 5.24 (s, 1H), 4.99 (dd, *J* = 19.8 Hz, 4.2 Hz, 1H), 3.83 (dd, *J* = 19.8 Hz, 2.4 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 167.3, 148.3, 141.8, 140.1, 138.9, 138.4, 131.5, 130.8, 129.2, 128.9, 128.4, 128.2, 127.8, 125.6, 124.85, 124.76, 124.3, 116.5, 69.7, 39.0; HRMS (ESI): Exact mass calcd for $C_{25}H_{19}NO$ $[M+H]^+$: 350.1539, Found: 350.1538.

5) Synthesis of 9



Under the N_2 atmosphere, to a 25 mL dried Schlenk tube were sequentially added **3aa** (0.31 g, 1.0 mmol) and 5.0 mL of anhydrous DMF. After cooling to 0 °C, NaH (0.06 g, 1.5 mmol, 1.5 equivs) was added portion wise. The resulting solution was stirred at the same temperature till there was no obvious gas generating. Then, propargyl bromide (103 μL, 1.2 mmol) was added. Upon the completion of the reaction (monitored by TLC), the reaction mixture was quenched with H_2O and extracted with ethyl acetate (4×15 mL). The combined organic layers were then washed with H_2O, dried over anhydrous Na_2SO_4. After removing the solvent, the residue was then subjected to column chromatography using petroleum ether/ethyl acetate (generally 5:1, v:v) as the eluent to afford product **9** in 68% yield (236.9 mg) as pale yellow solid; Mp: 140-143 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 7.2 Hz, 1H), 7.55-7.53 (m, 1H), 7.52-7.48 (m, 5H), 7.37-7.32 (m, 7H), 4.41 (dd, *J* = 17.4 Hz, 2.4 Hz, 1H), 4.15 (dd, *J* = 17.4 Hz, 2.4 Hz, 1H), 2.00 (t, *J* = 2.4 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 167.6, 149.2, 137.7, 133.1, 131.9, 129.6, 129.1, 129.0, 128.9, 128.8, 128.5, 127.0, 124.0, 123.1, 122.0, 88.4, 84.7, 78.4, 71.2, 66.6, 29.5; HRMS (ESI): Exact mass calcd for $C_{25}H_{17}NO$ $[M+H]^+$: 348.1383, Found: 348.1384.

6) Synthesis of 10



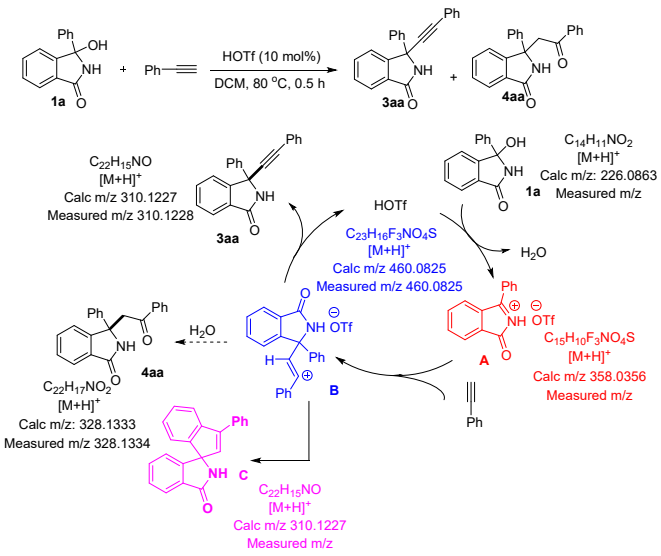
Under N_2 atmosphere, to a 25 mL dried Schlenk tube were sequentially added **9** (69.5 mg, 0.2 mmol), $CuSO_4$•$5H_2O$ (12.5 mg, 0.05 mmol, 0.25 equiv), sodium ascorbate (9.9 mg, 0.05 mmol, 0.25 equiv), and H_2O (2.0 mL) and ^{i}PrOH (2.0 mL). After adding BnN_3 (53.3 mg, 0.4 mmol, 2.0 equivs), the mixture was stirred at 80 °C till almost full convertion of **9** by TLC analysis. Then, the reaction is terminated by the addition of 20.0 mL saturated aqueous NH_4Cl. The organic layer was extracted with

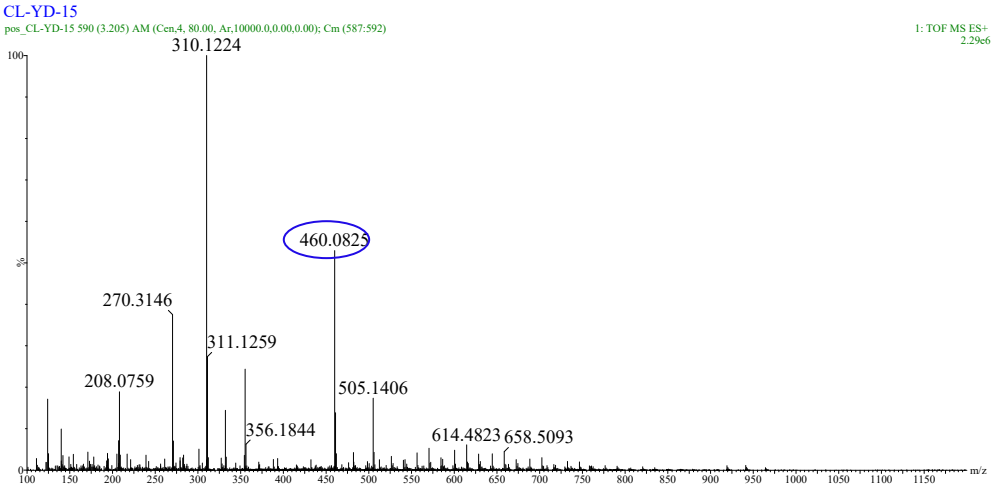
ethyl acetate (3×15 mL) and then dried with Na_2SO_4. After removing the solvent, the residue was then subjected to column chromatography using petroleum ether/ethyl acetate (generally 4:1, v:v) as the eluent to afford the desired product **10** in 89% yield (85.5 mg) as sticky pale yellow oil; Mp: 131-133 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 7.8 Hz, 1H), 7.57-7.51 (m, 2H), 7.40-7.33 (m, 9H), 7.32-7.27 (m, 4H), 7.26-7.24 (m, 2H), 7.10 (d, *J* = 7.2 Hz, 2H), 5.33 (d, *J* = 8.4 Hz, 1H), 5.28-5.26 (m, 1H), 4.98 (d, *J* = 16.2 Hz, 1H), 4.65 (d, *J* = 16.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 168.1, 149.2, 144.8, 137.6, 134.6, 133.0, 131.9, 129.9, 129.03, 128.96, 128.8, 128.6, 128.4, 128.1, 126.9, 123.8, 123.2, 122.9, 121.7, 88.4, 84.9, 66.7, 54.0, 36.3; HRMS (ESI): Exact mass calcd for $C_{32}H_{24}N_4O$ $[M+H]^+$: 481.2023, Found: 481.2028.

4. Mechanistic sdudy

To explore the reaction mechanism, we have tried to detect the possible intermediates during the reaction course by MS. To a 10-mL vial were added 3-hydroxyisoindoliones **1** (0.3 mmol, 1.0 equiv), terminal alkynes **2** (0.6 mmol, 2.0 equivs) and 3.0 mL of anhydrous DCM. After adding HOTf (4.5 mg, 10 mol%), the reaction mixture was stirred at 80 °C for about 0.5 h. After the HOTf was removed by extraction, the sample was sent to mass spectrometry for detection.

We believe that the process of formation of intermediate **A** from **1a** and HOTf is reversible, so we did not find directly the possible peak signal of intermediate **A** from the mass spectrum. However, we successfully found the presence of intermediate **B** from the results of mass spectrometry, which can prove that the reaction proceeded *via* the formation of intermediate **B**.

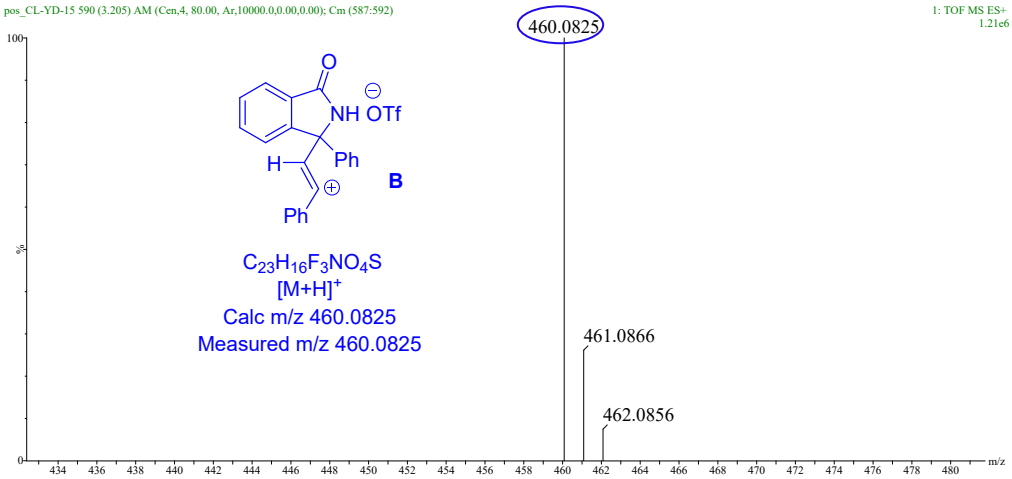




CL-YD-15

pos_CL-YD-15 590 (3.205) AM (Cen,4, 80.00, Ar,10000.0,0.00,0.00); Cm (587:592)

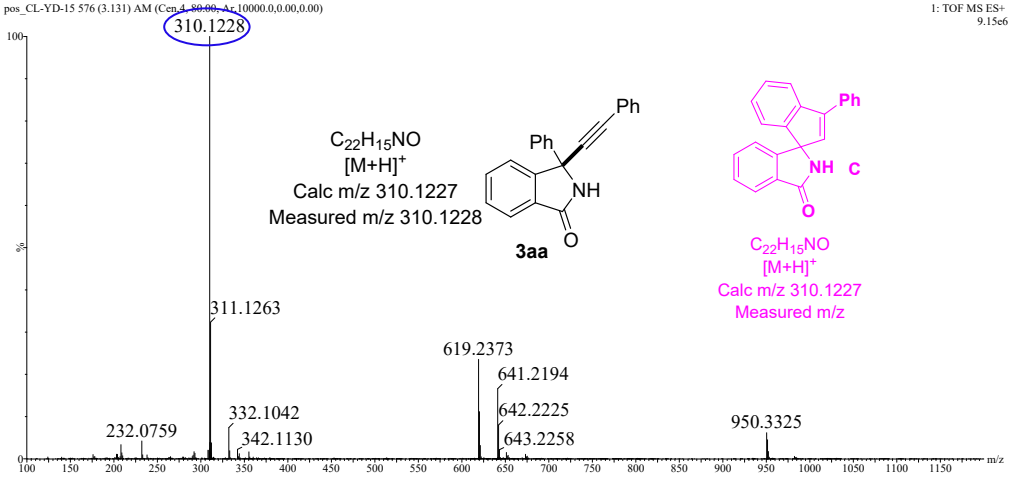
1: TOF MS ES+
1.21e6



CL-YD-15

pos_CL-YD-15 576 (3.131) AM (Cen,4, 80.00, Ar,10000.0,0.00,0.00)

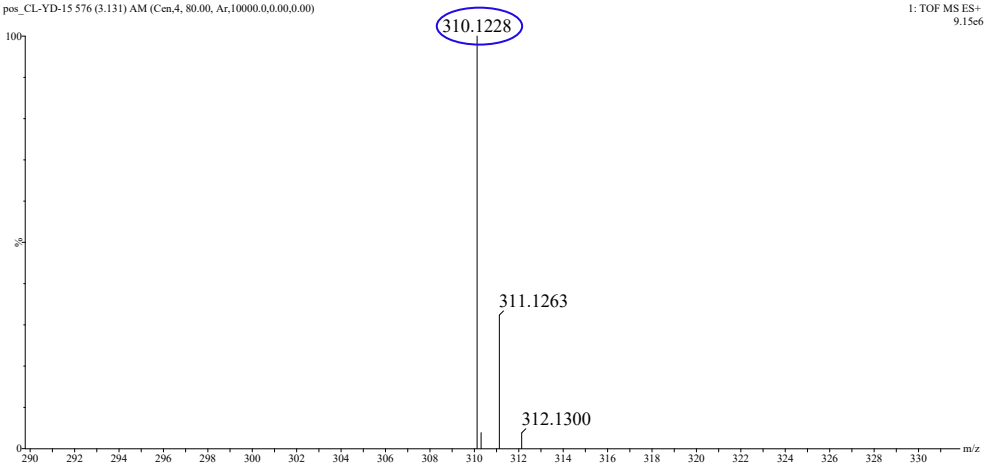
1: TOF MS ES+
9.15e6



CL-YD-15

pos_CL-YD-15 576 (3.131) AM (Cen,4, 80.00, Ar,10000.0,0.00,0.00)

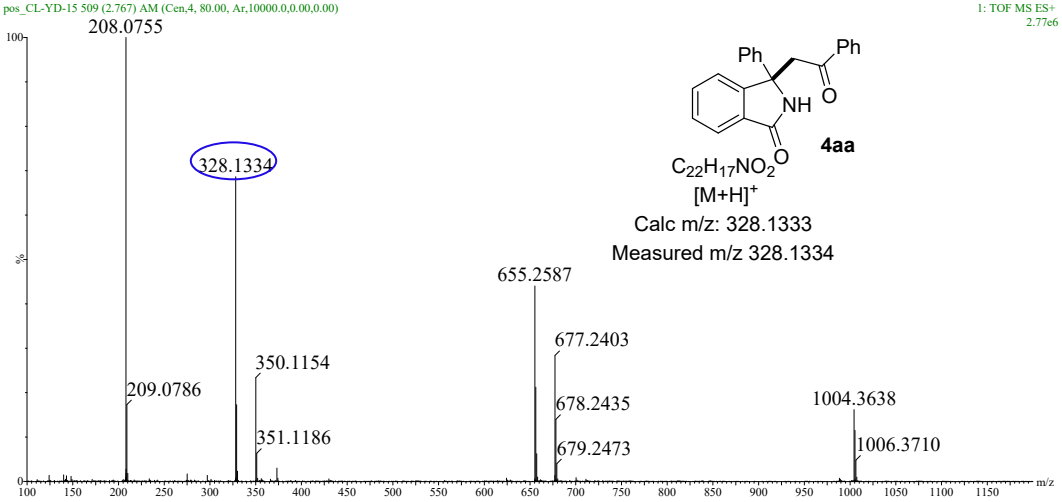
1: TOF MS ES+
9.15e6



CL-YD-15

pos_CL-YD-15 509 (2.767) AM (Cen,4, 80.00, Ar,10000.0,0.00,0.00)

1: TOF MS ES+
2.77e6



4aa

$C_{22}H_{17}NO_2$

$[M+H]^+$

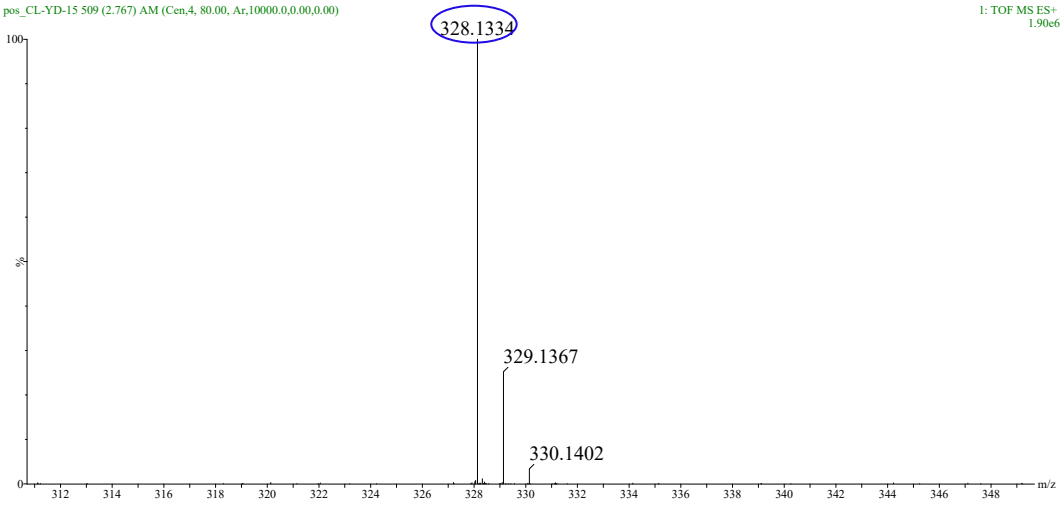
Calc m/z: 328.1333

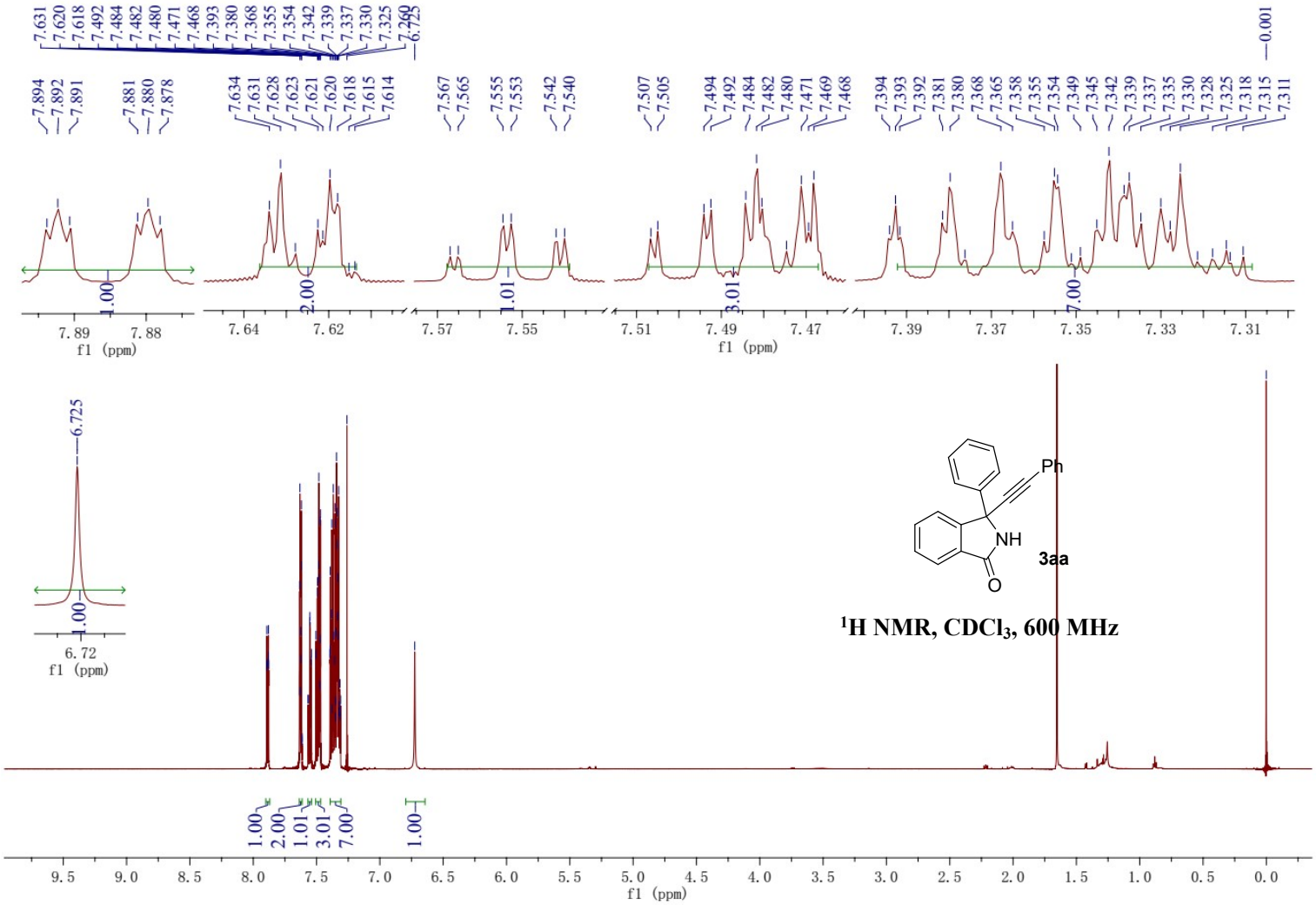
Measured m/z 328.1334

CL-YD-15

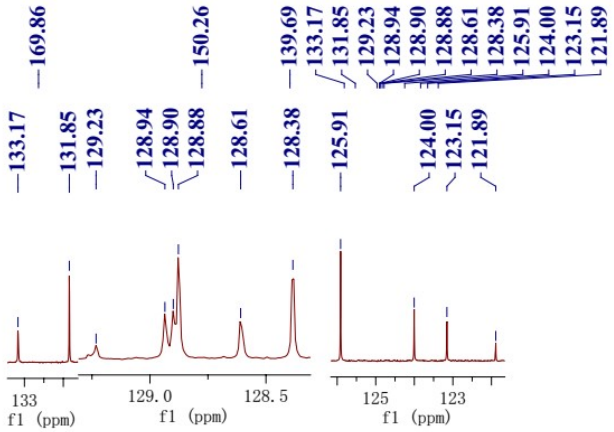
pos_CL-YD-15 509 (2.767) AM (Cen,4, 80.00, Ar,10000.0,0.00,0.00)

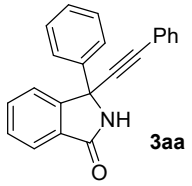
1: TOF MS ES+
1.90e6





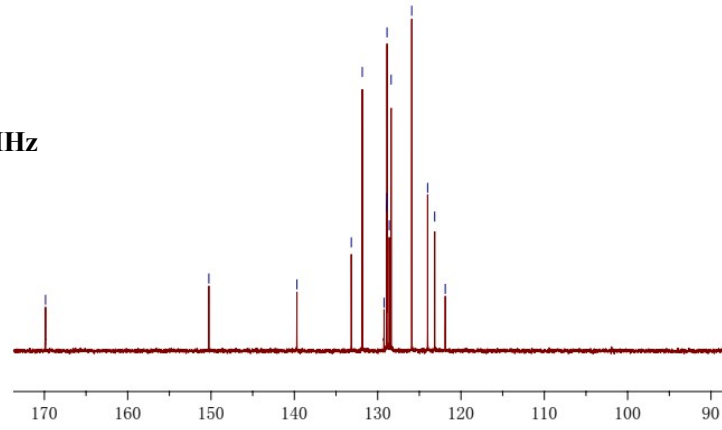
^{1}H NMR, $CDCl_3$, 600 MHz

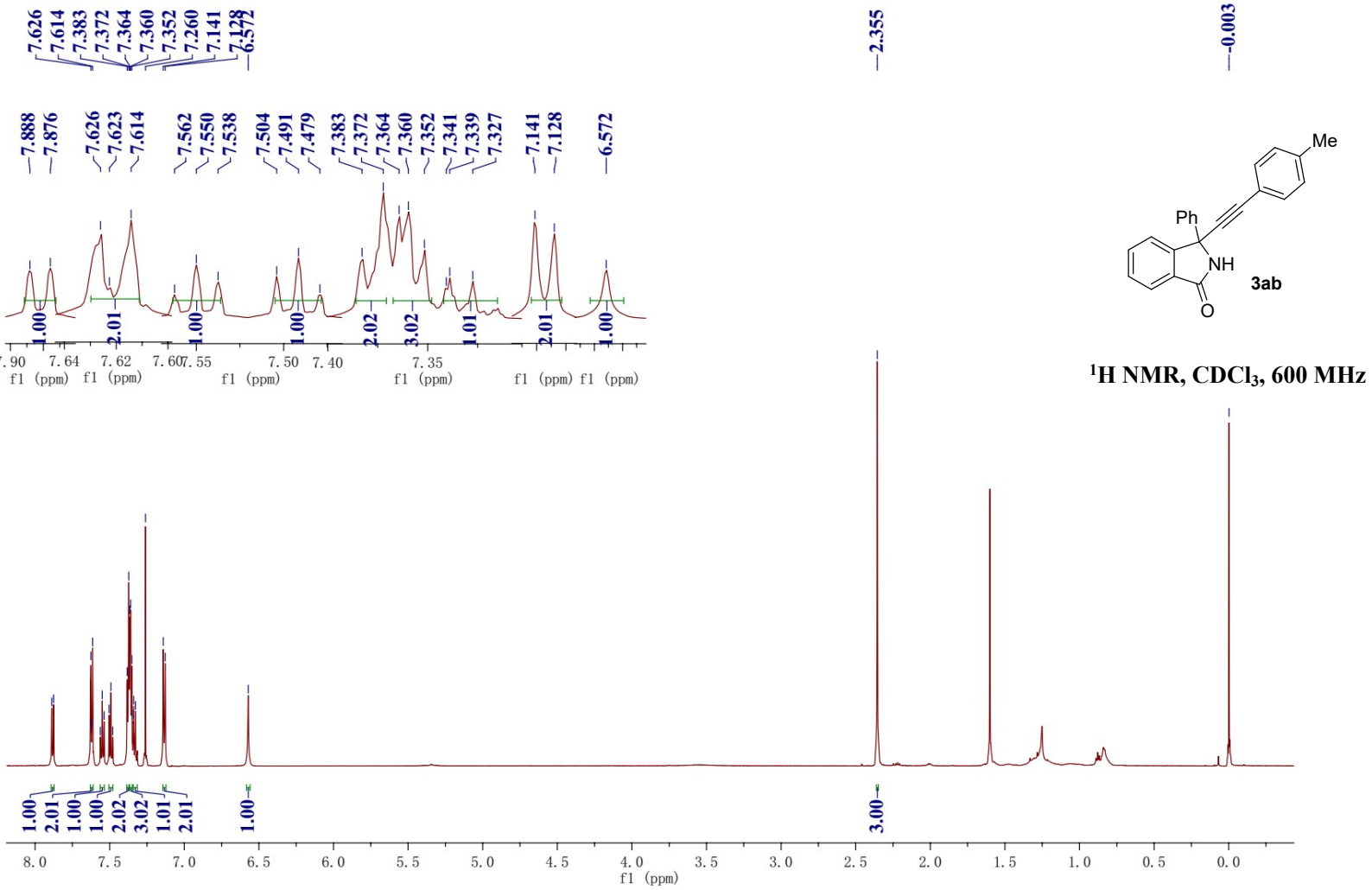




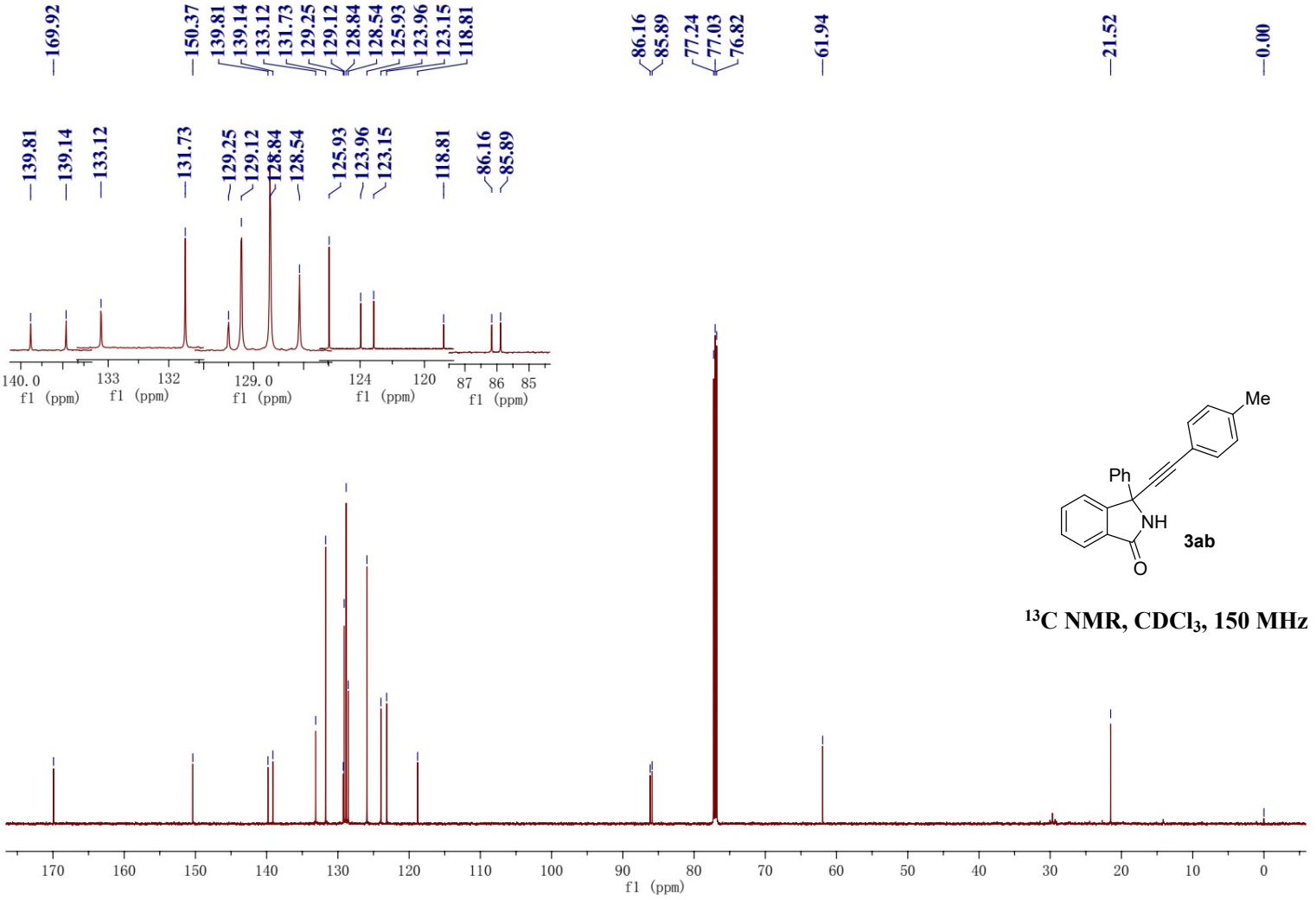
3aa

^{13}C NMR, $CDCl_3$, 150 MHz

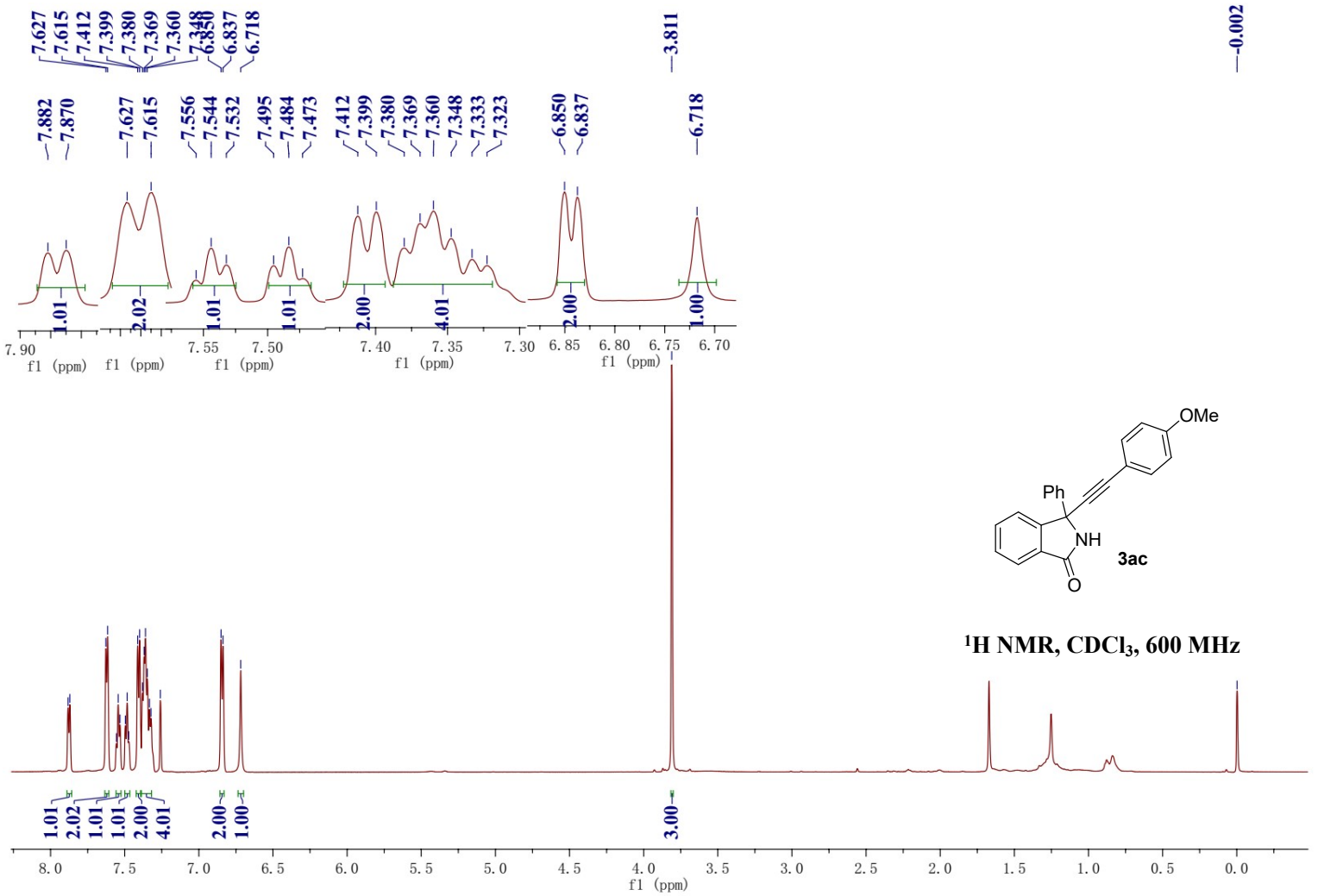




^{1}H NMR, $CDCl_3$, 600 MHz

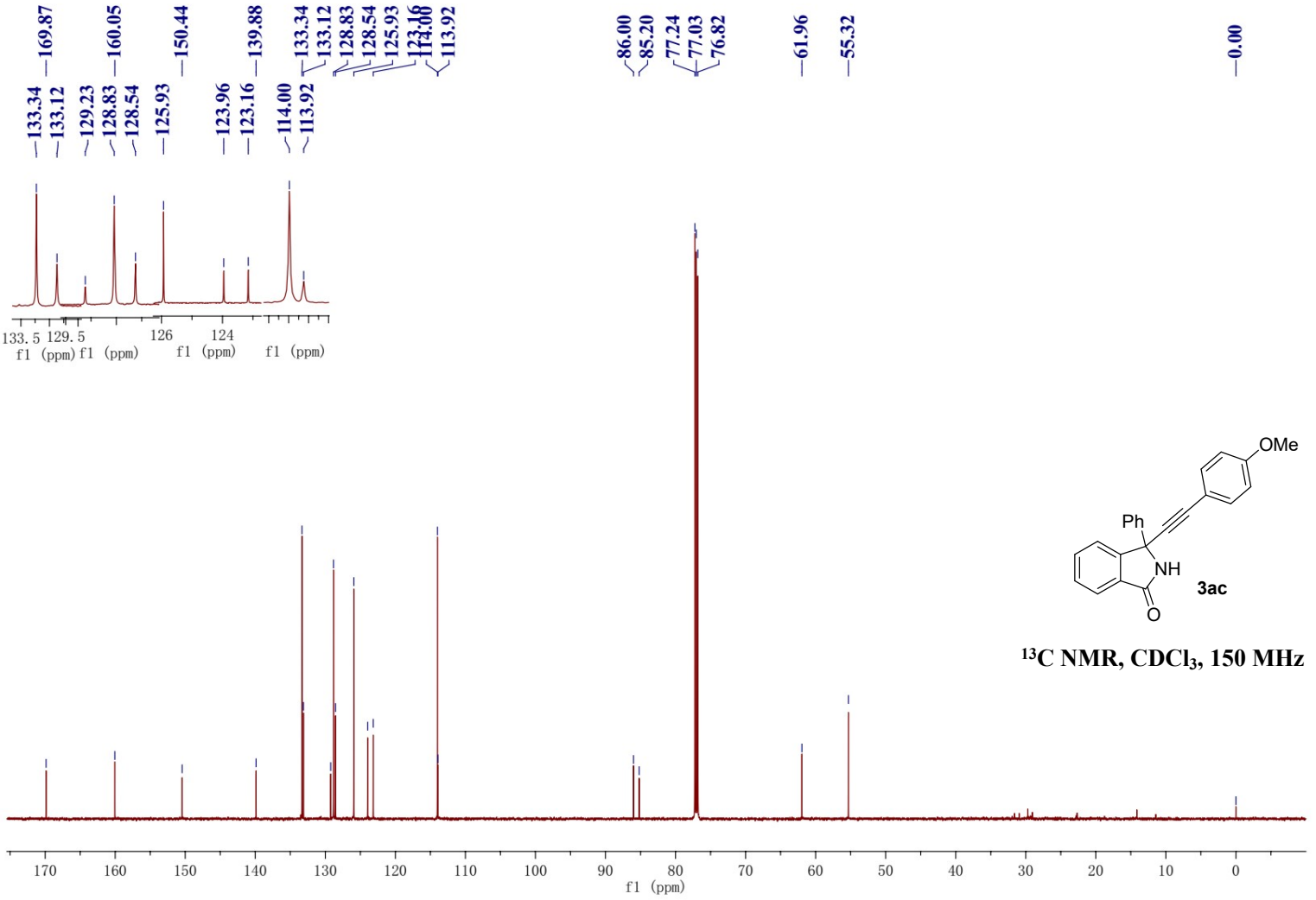


^{13}C NMR, $CDCl_3$, 150 MHz



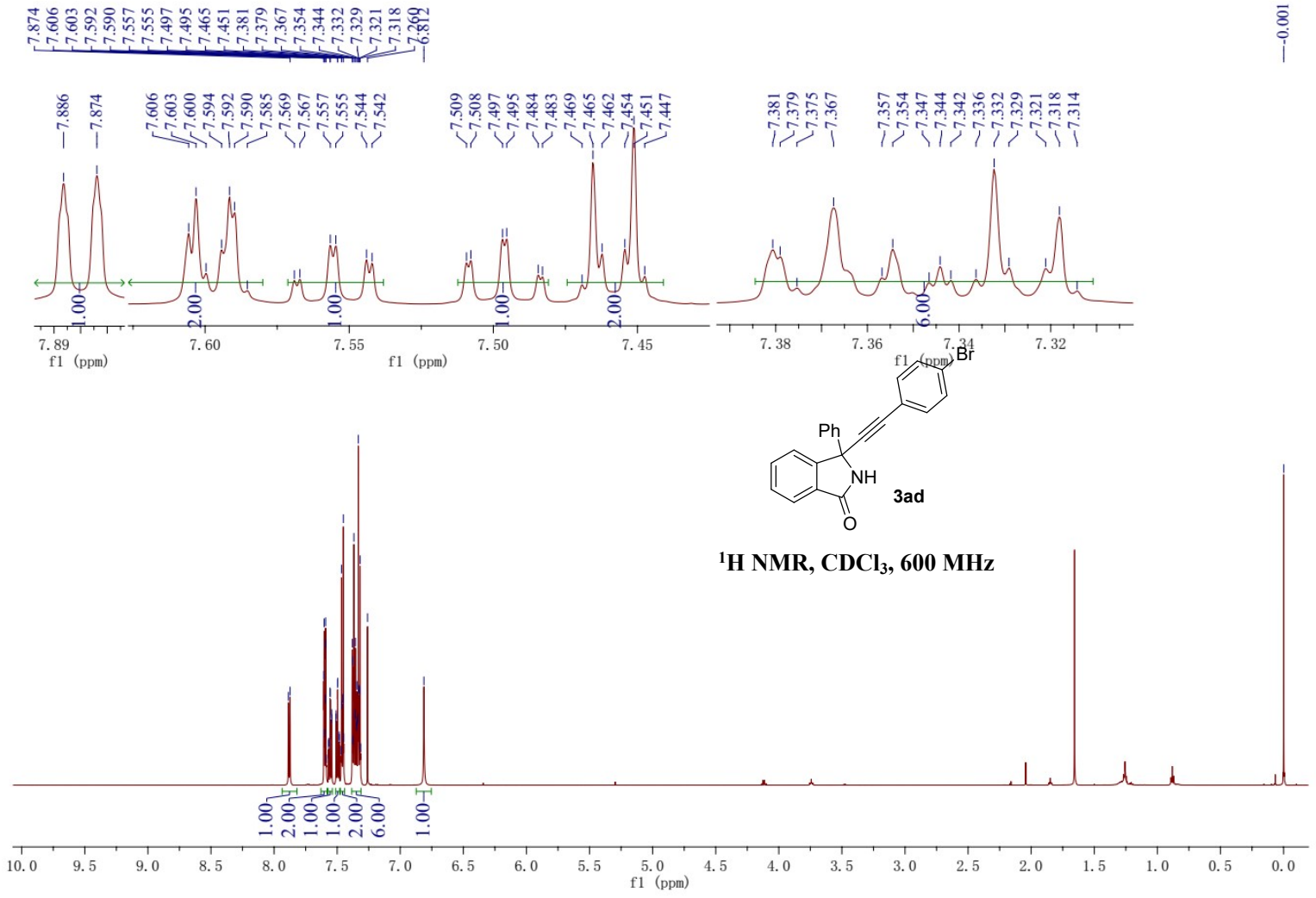
3ac

^{1}H NMR, $CDCl_3$, 600 MHz

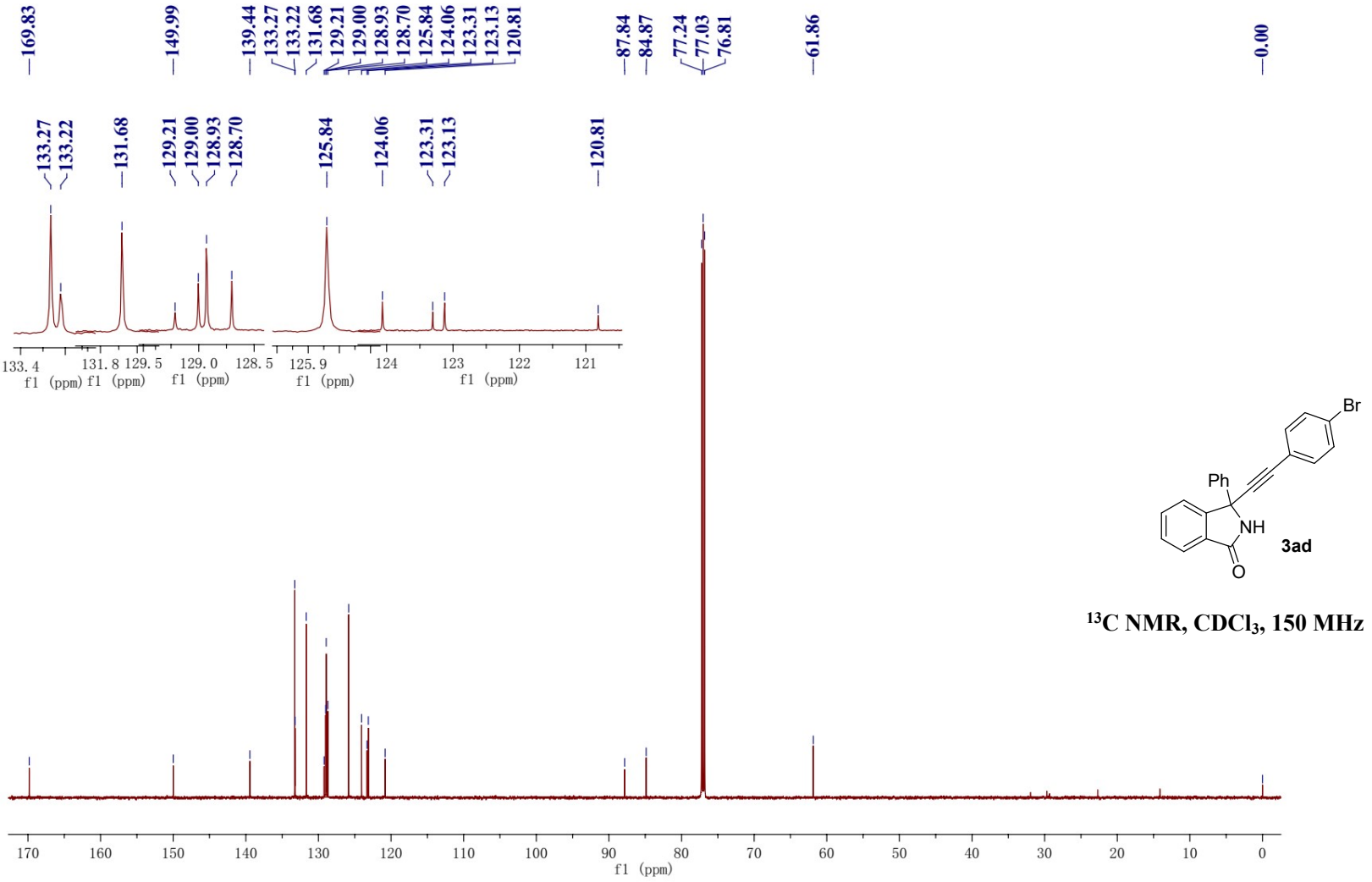


3ac

^{13}C NMR, $CDCl_3$, 150 MHz

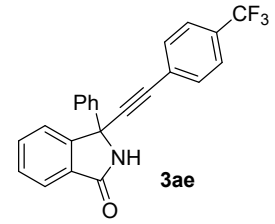


^{1}H NMR, $CDCl_3$, 600 MHz



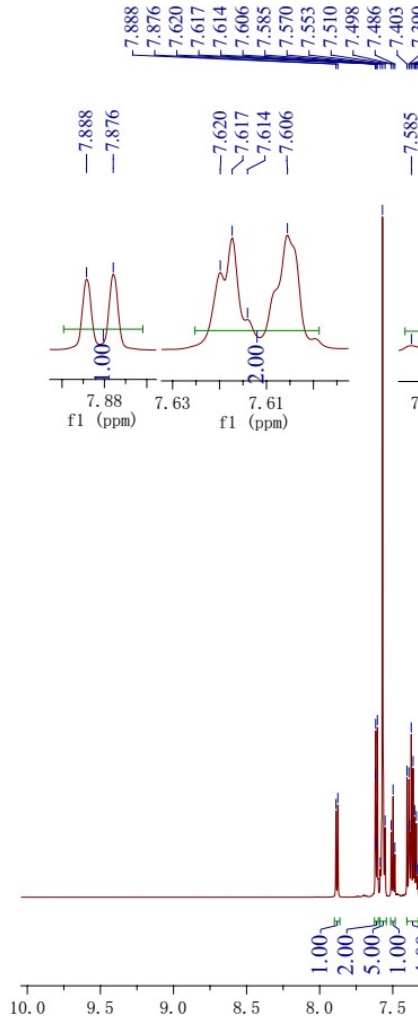
3ad

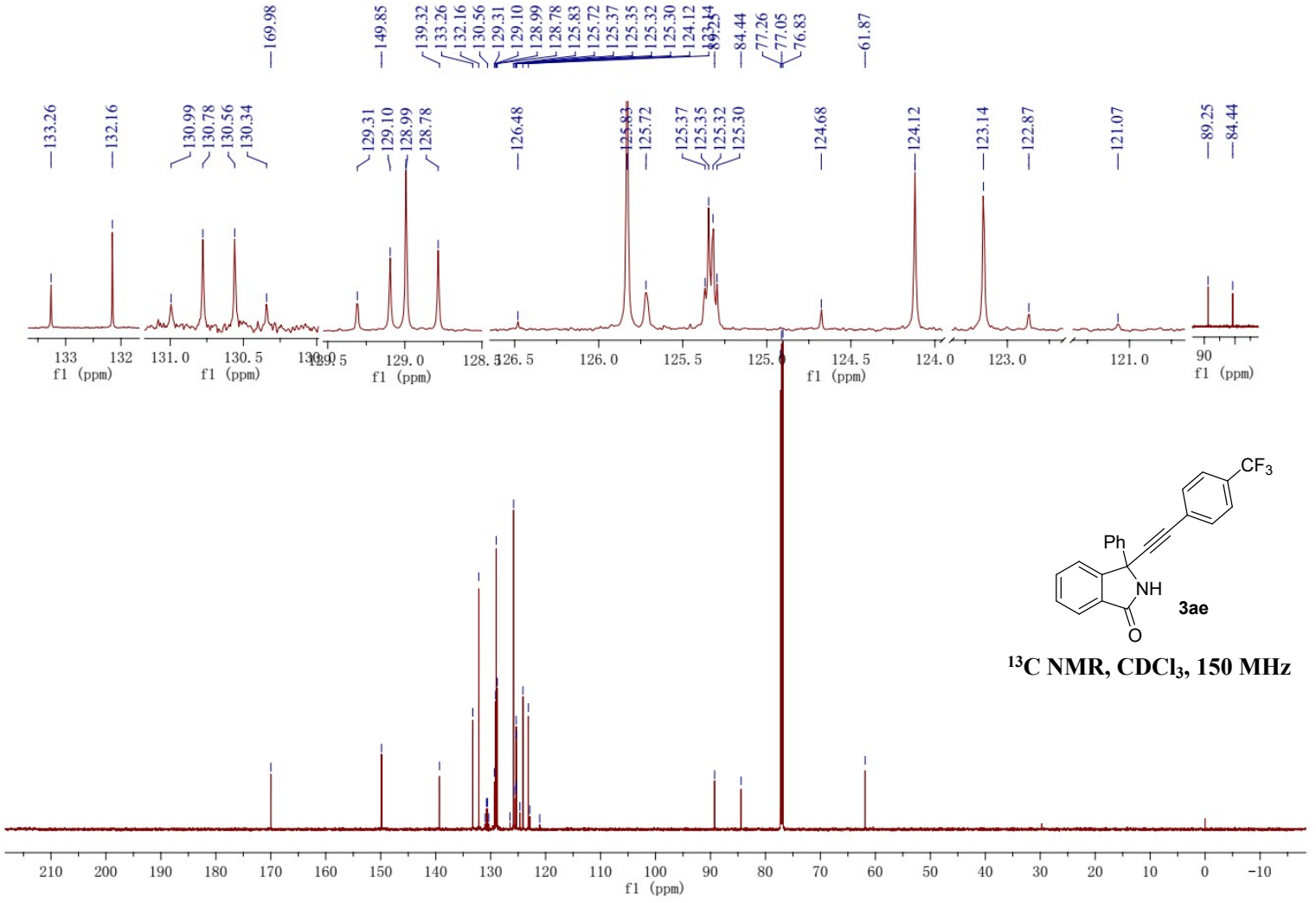
^{13}C NMR, $CDCl_3$, 150 MHz



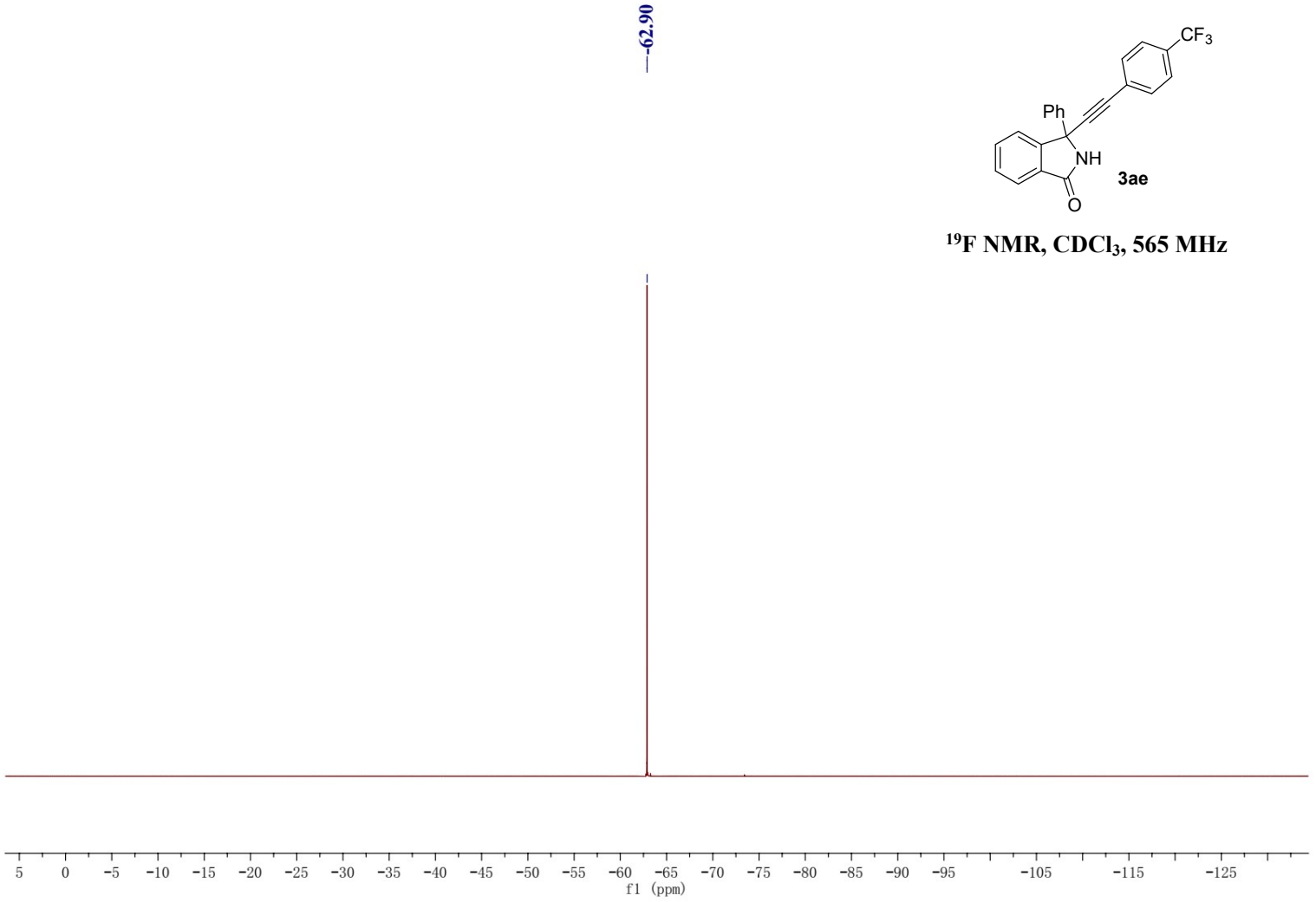
3ae

^{1}H NMR, $CDCl_3$, 600 MHz

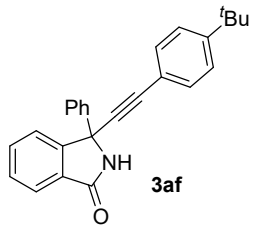




^{13}C NMR, $CDCl_3$, 150 MHz

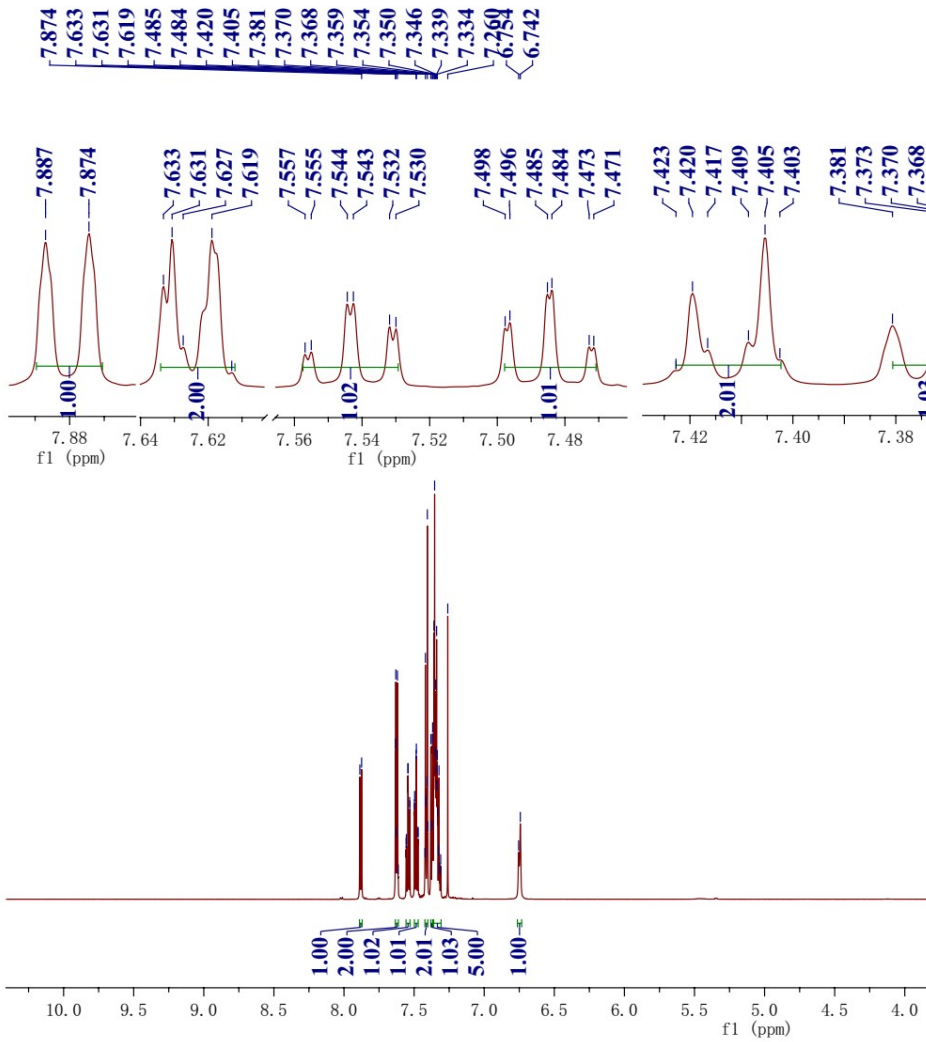


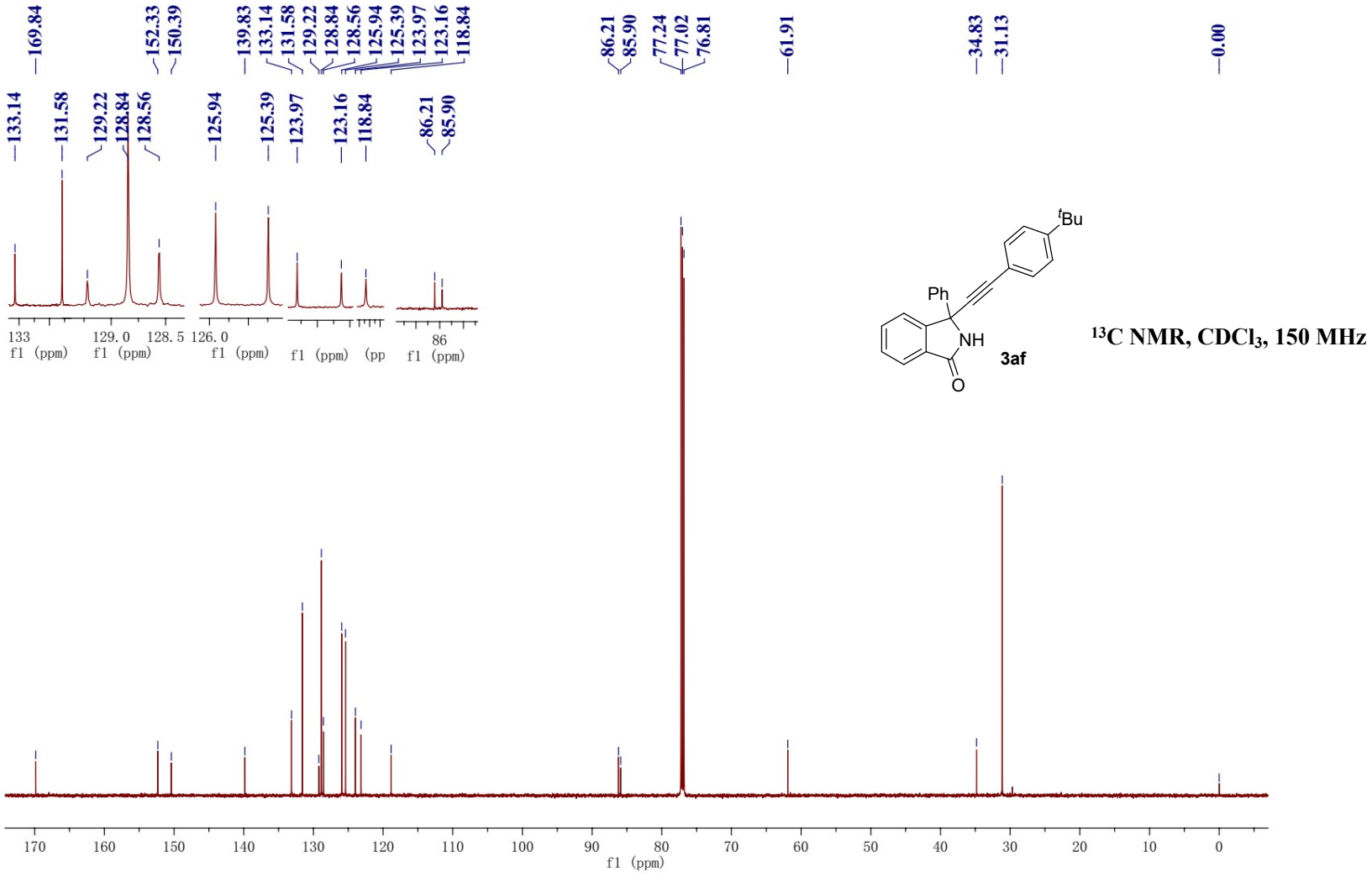
^{19}F NMR, $CDCl_3$, 565 MHz



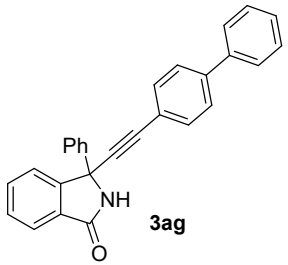
3af

^{1}H NMR, $CDCl_3$, 600 MHz



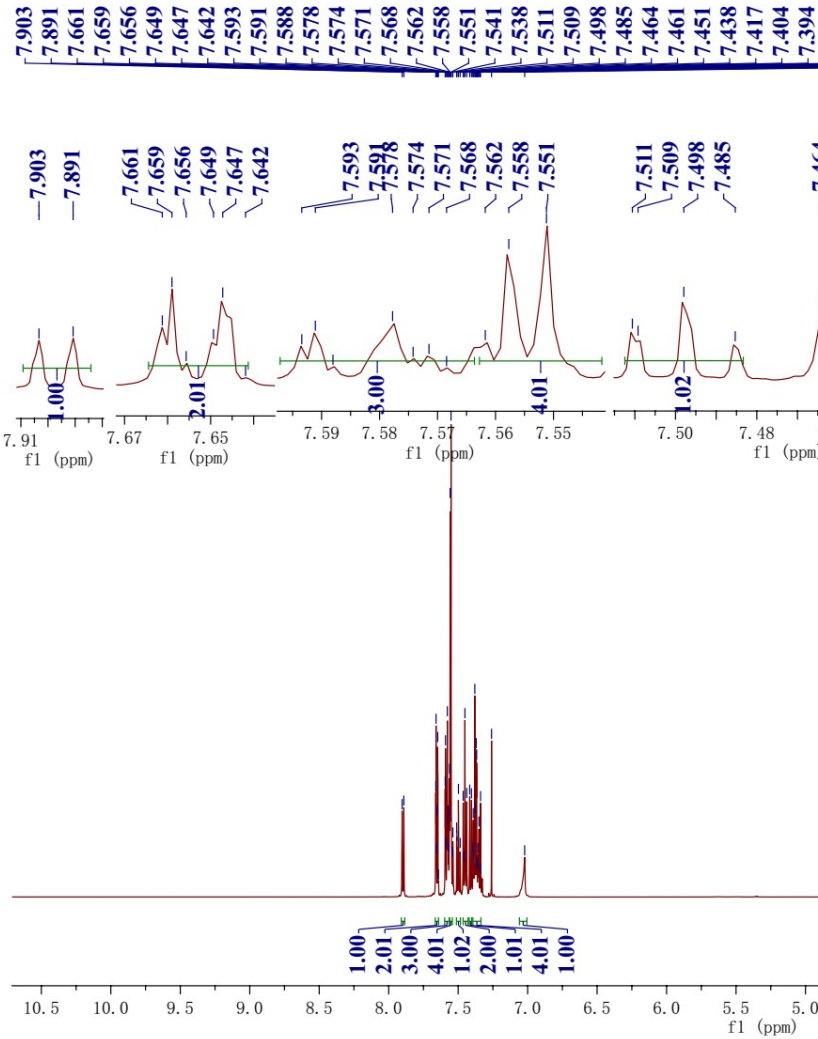


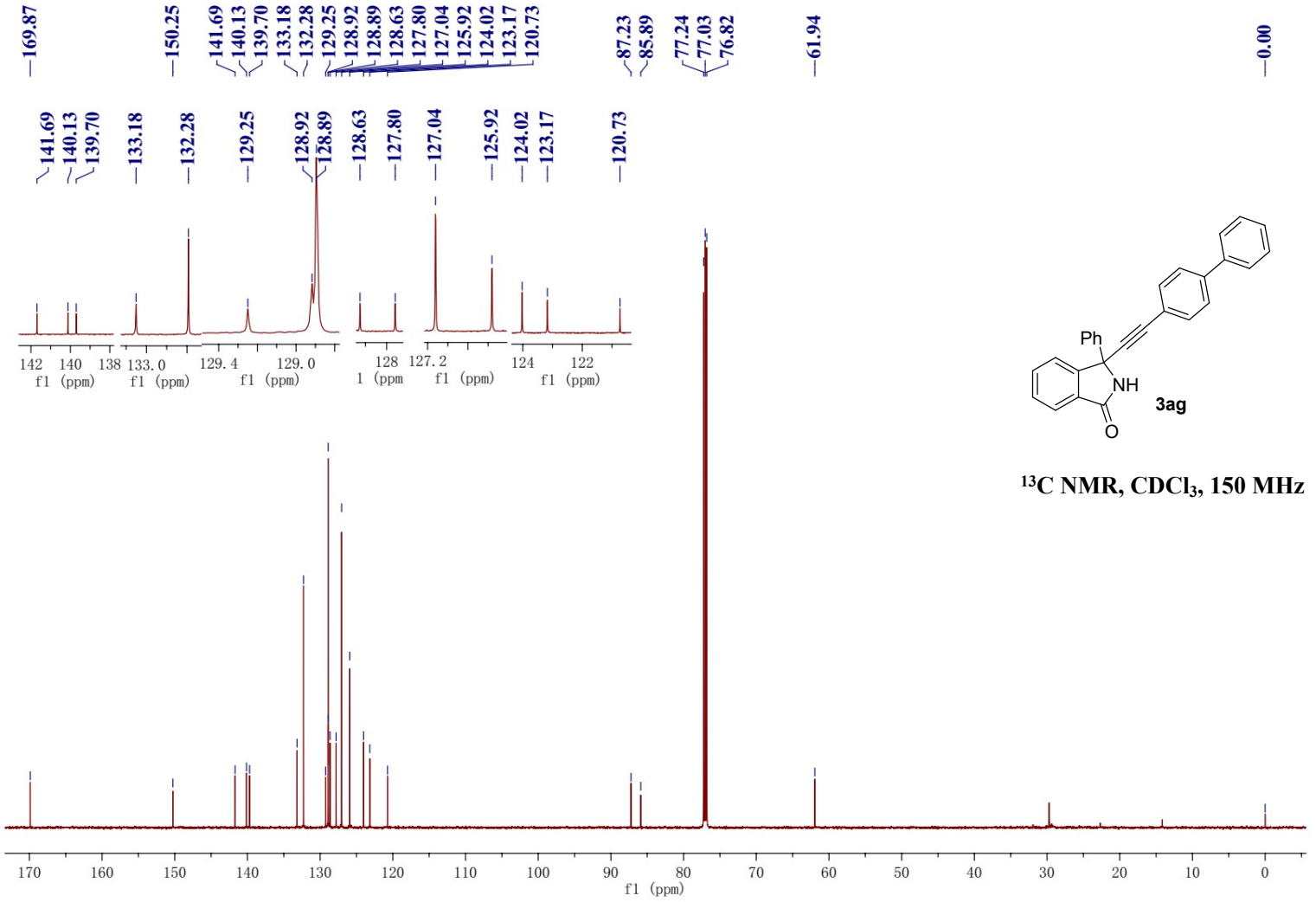
^{13}C NMR, $CDCl_3$, 150 MHz



3ag

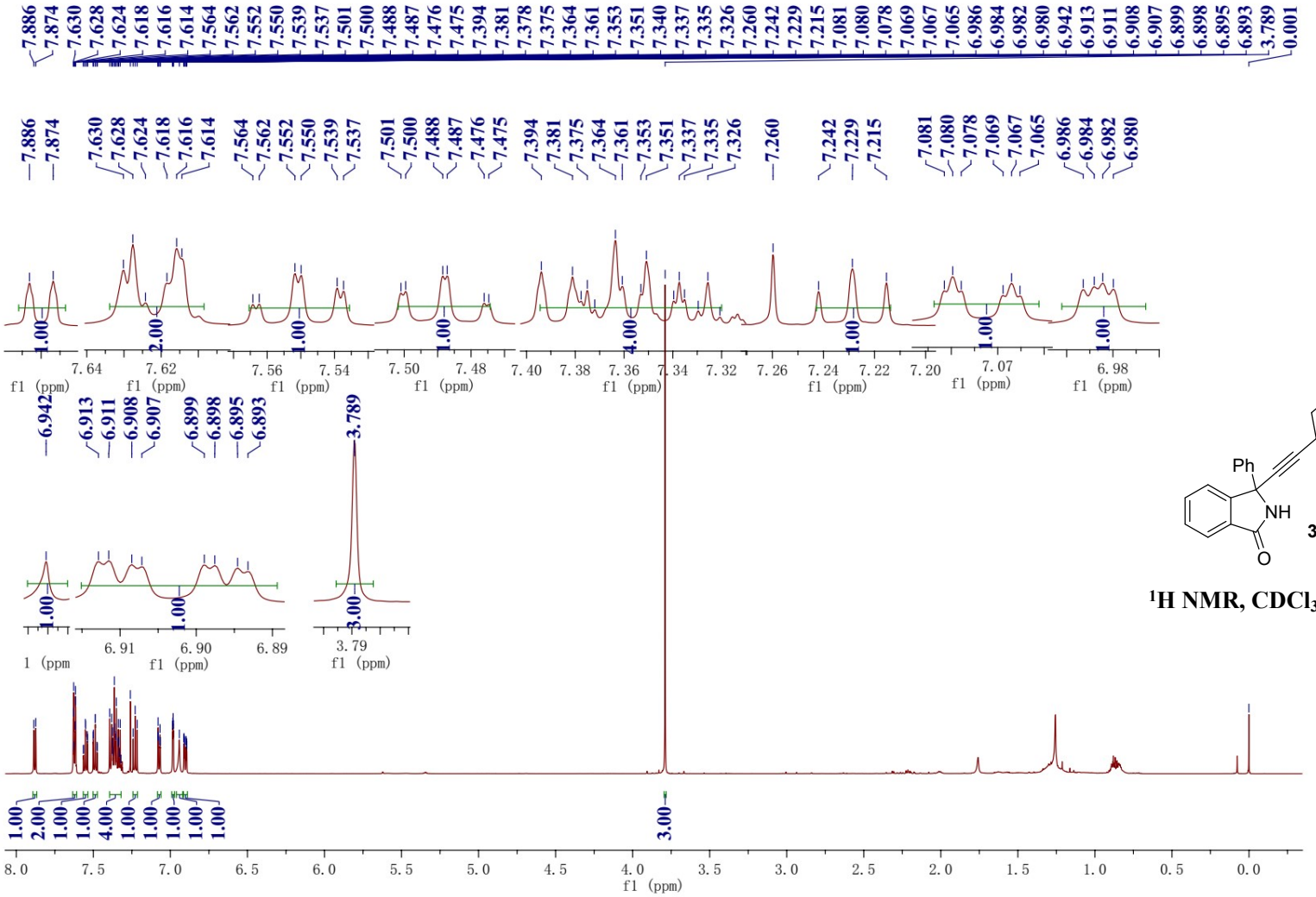
^{1}H NMR, $CDCl_3$, 600 MHz





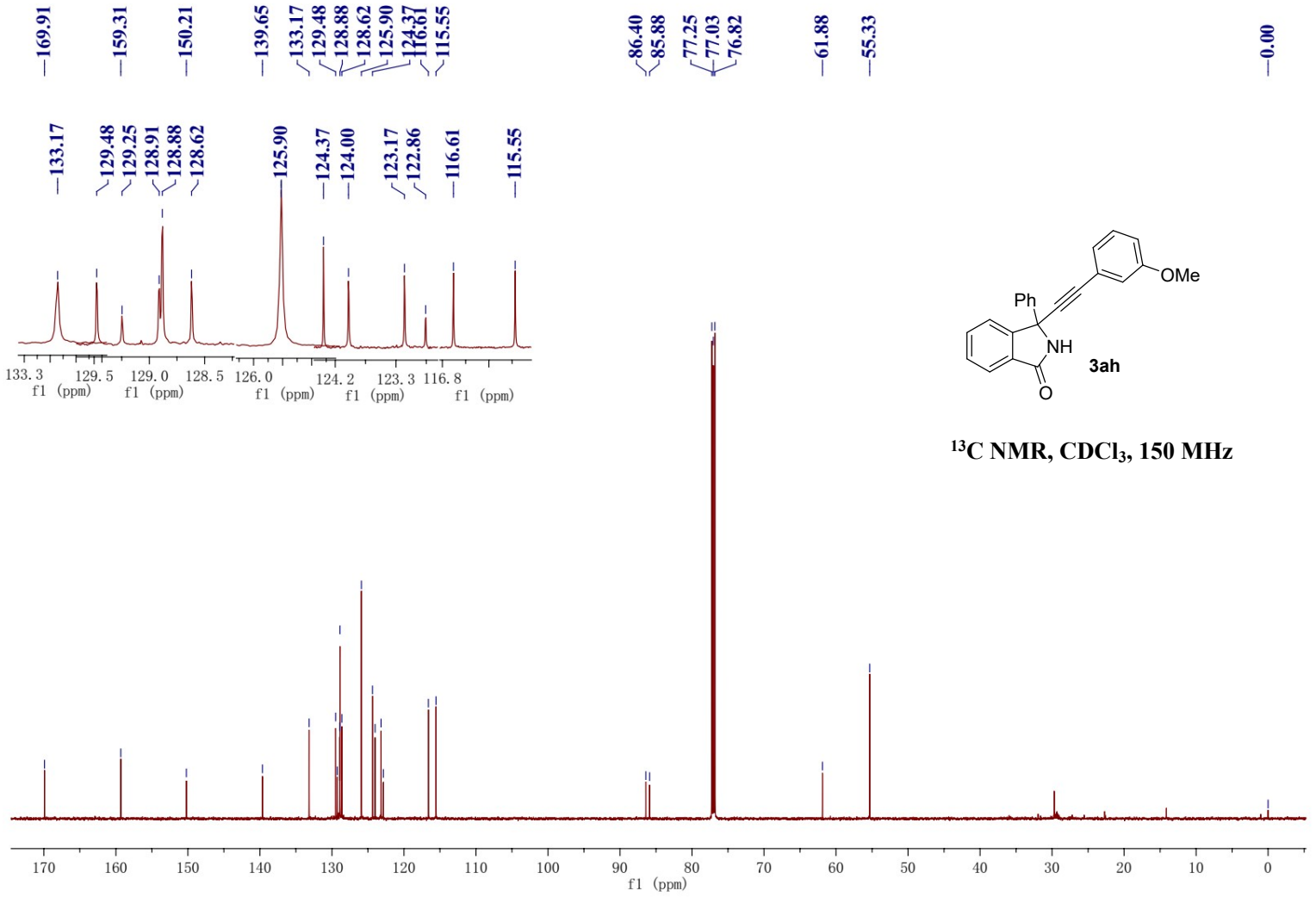
3ag

^{13}C NMR, $CDCl_3$, 150 MHz

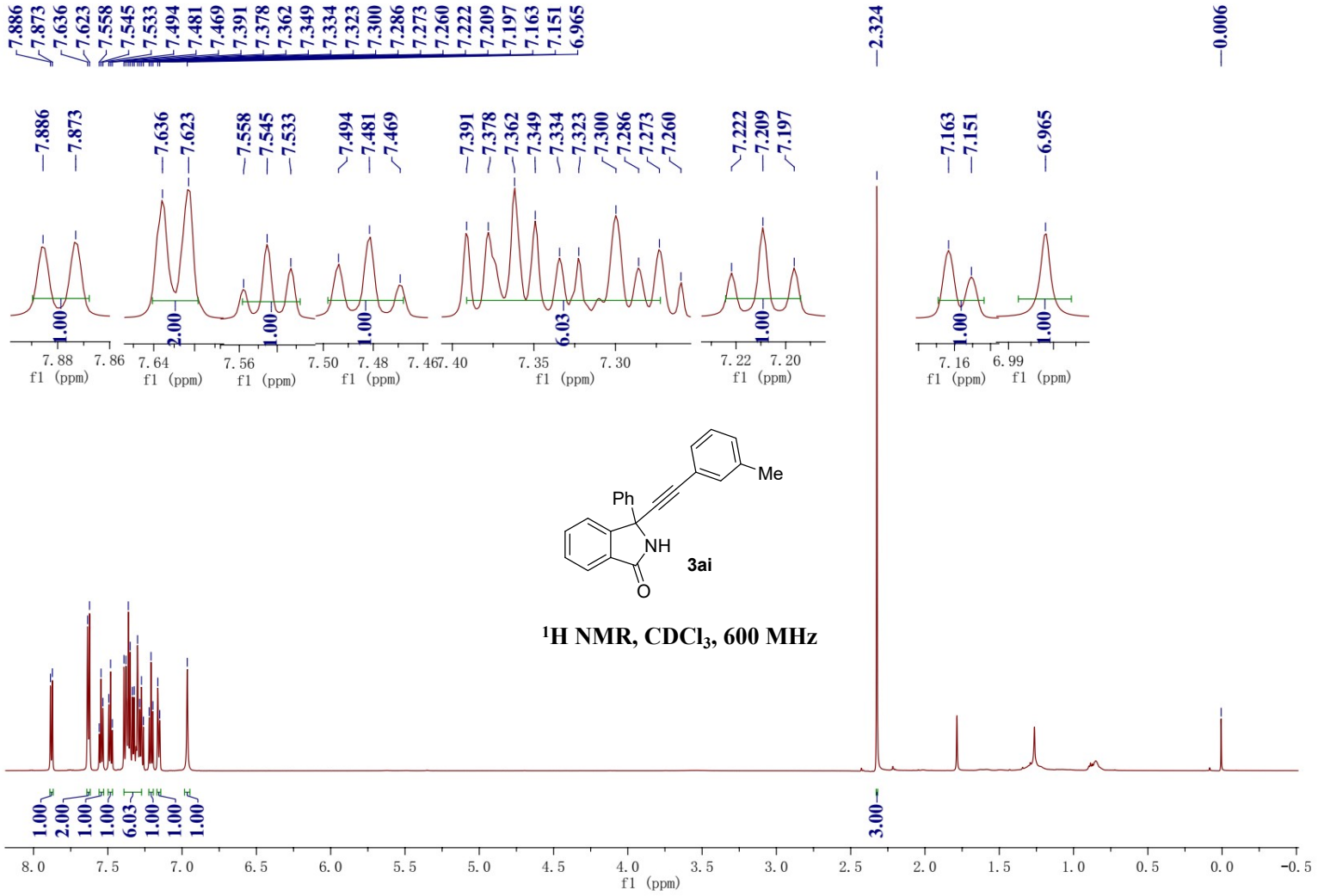


3ah

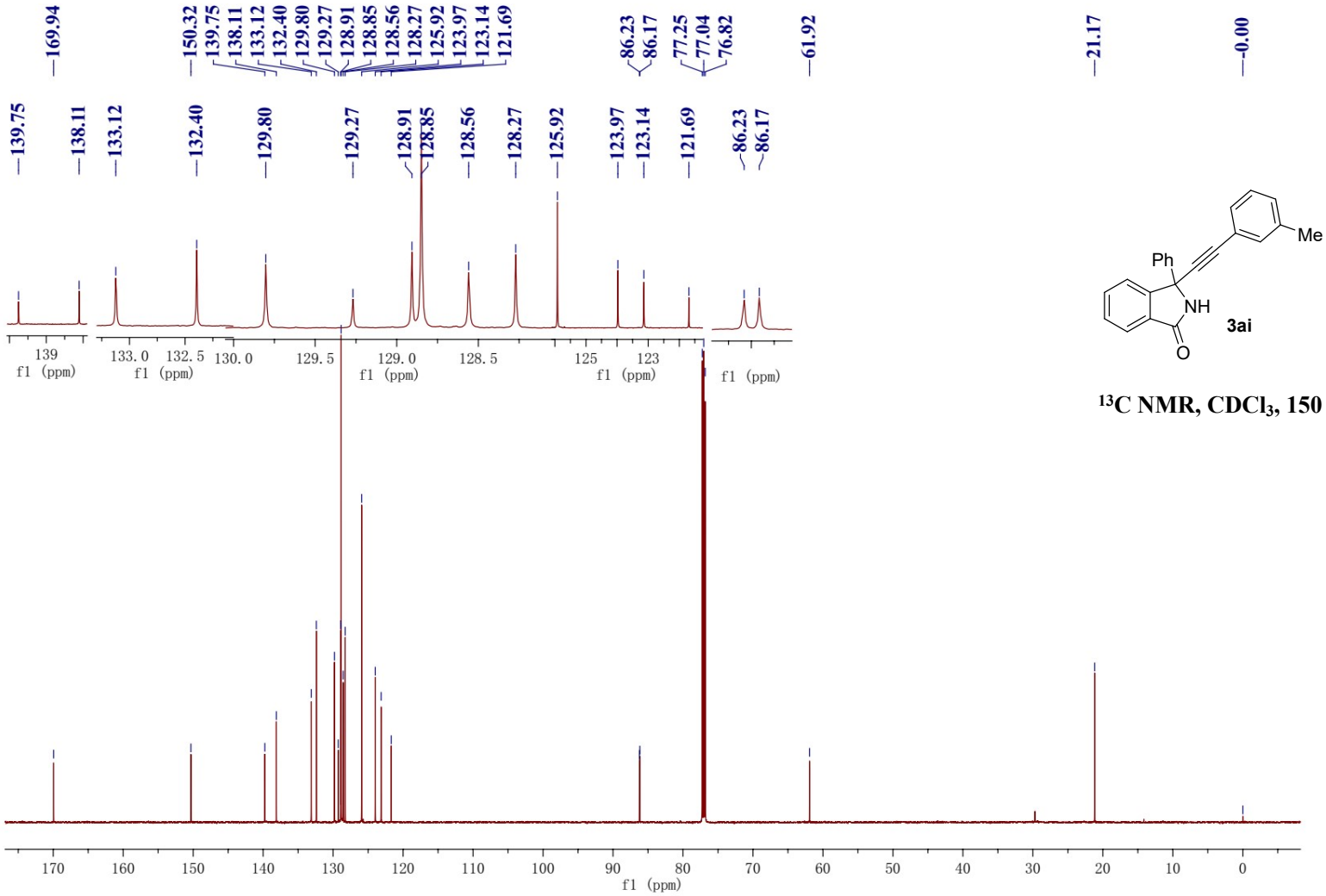
^{1}H NMR, $CDCl_3$, 600 MHz



^{13}C NMR, $CDCl_3$, 150 MHz

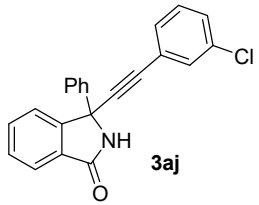


^{1}H NMR, $CDCl_3$, 600 MHz



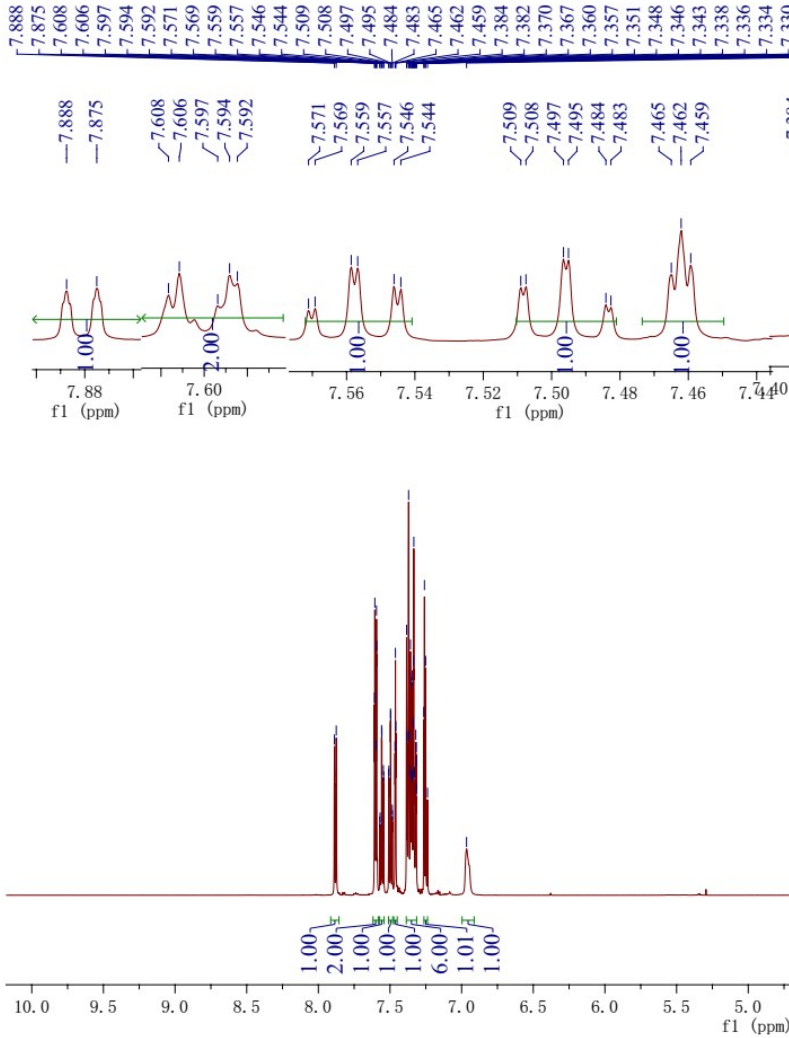
3ai

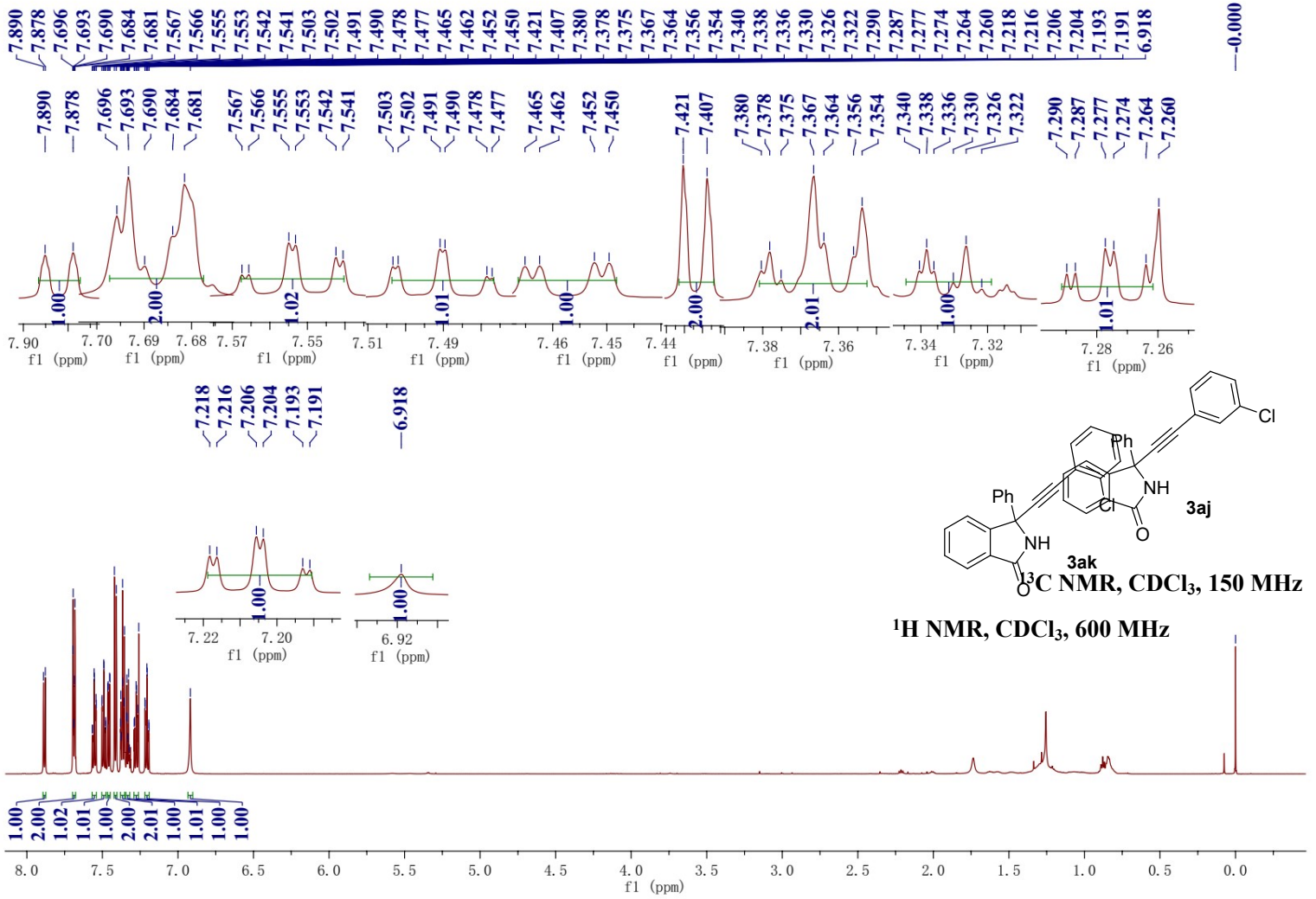
^{13}C NMR, $CDCl_3$, 150 MHz



3aj

^{1}H NMR, $CDCl_3$, 600 MHz



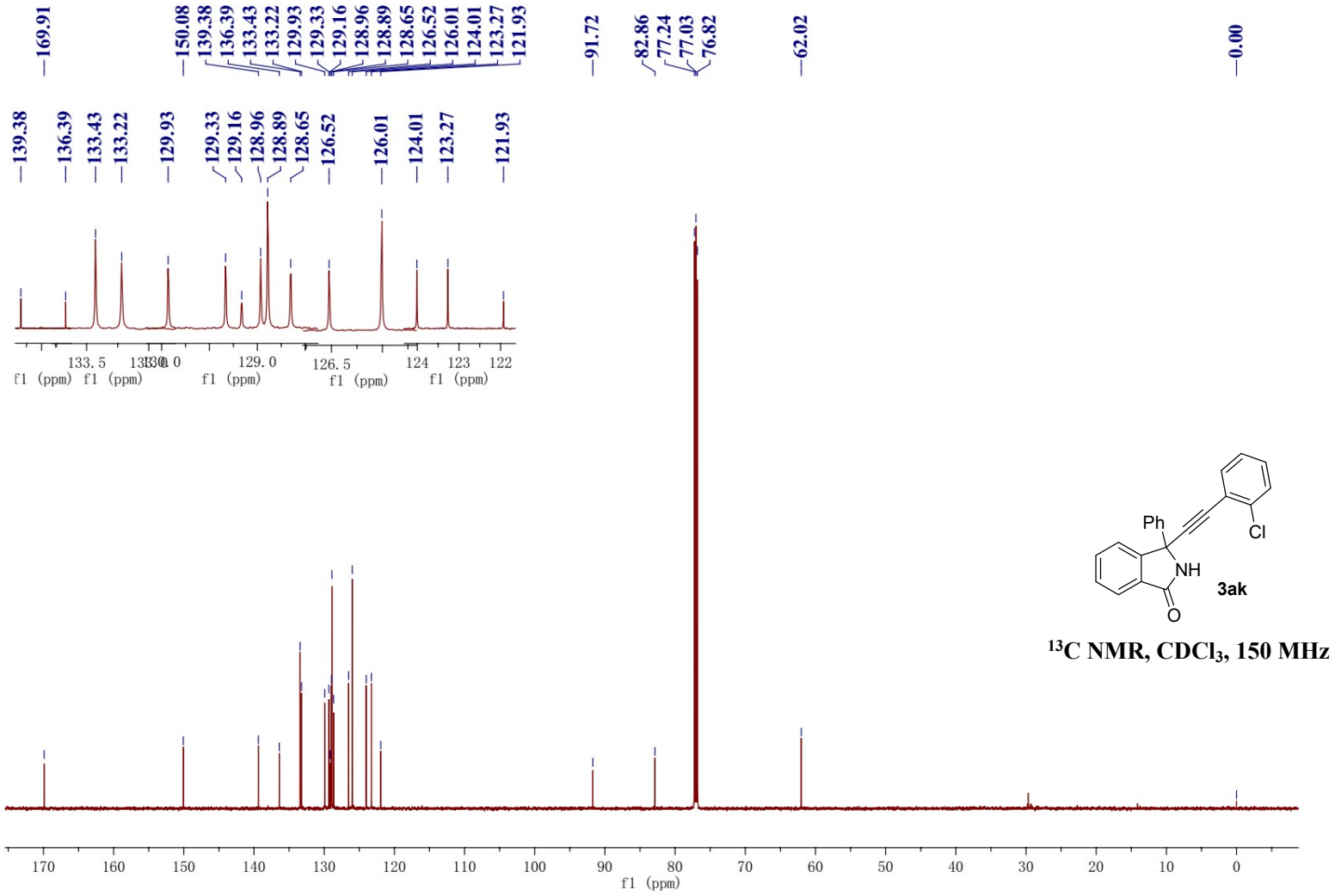


3aj

3ak

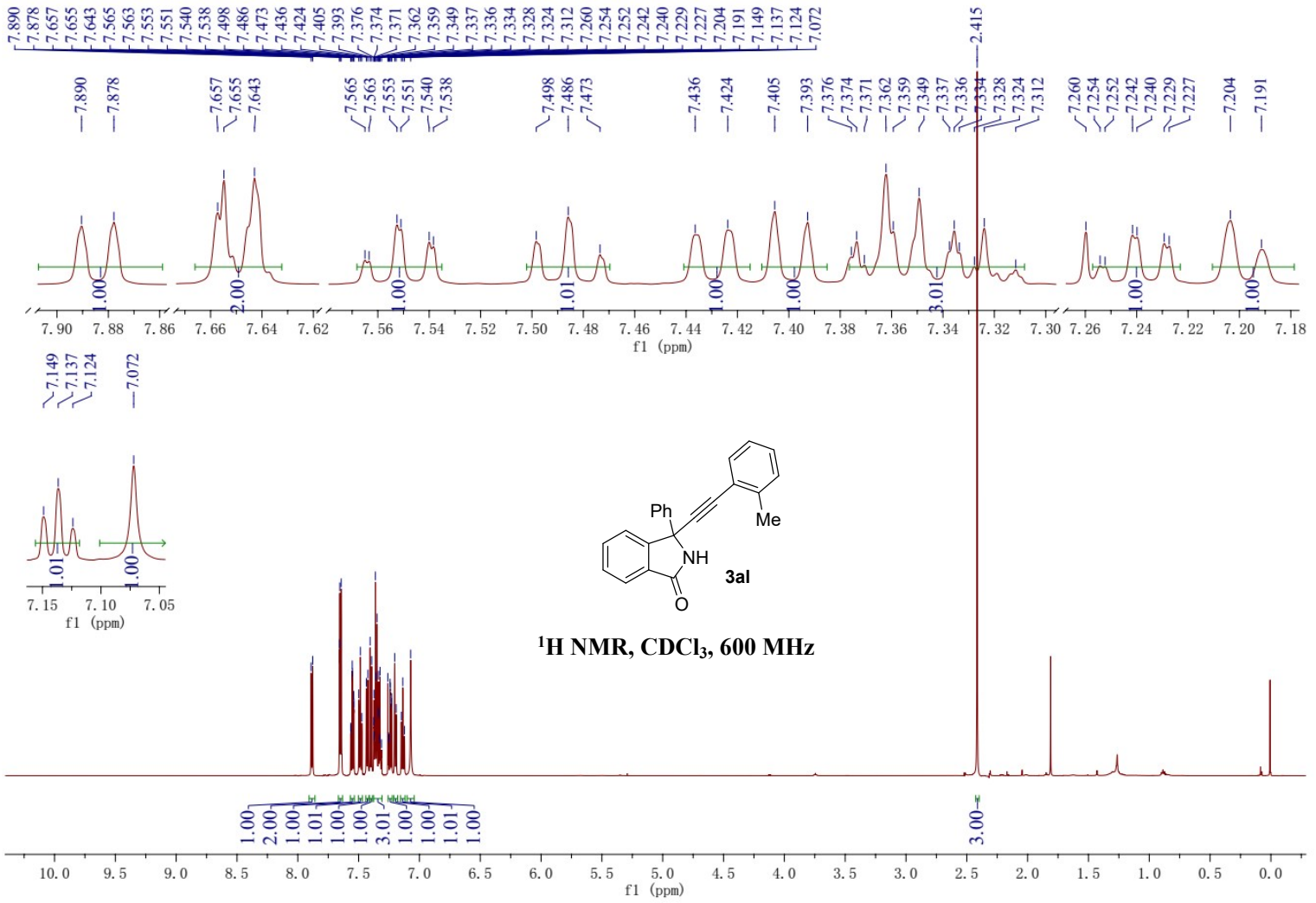
^{13}C NMR, $CDCl_3$, 150 MHz

^{1}H NMR, $CDCl_3$, 600 MHz

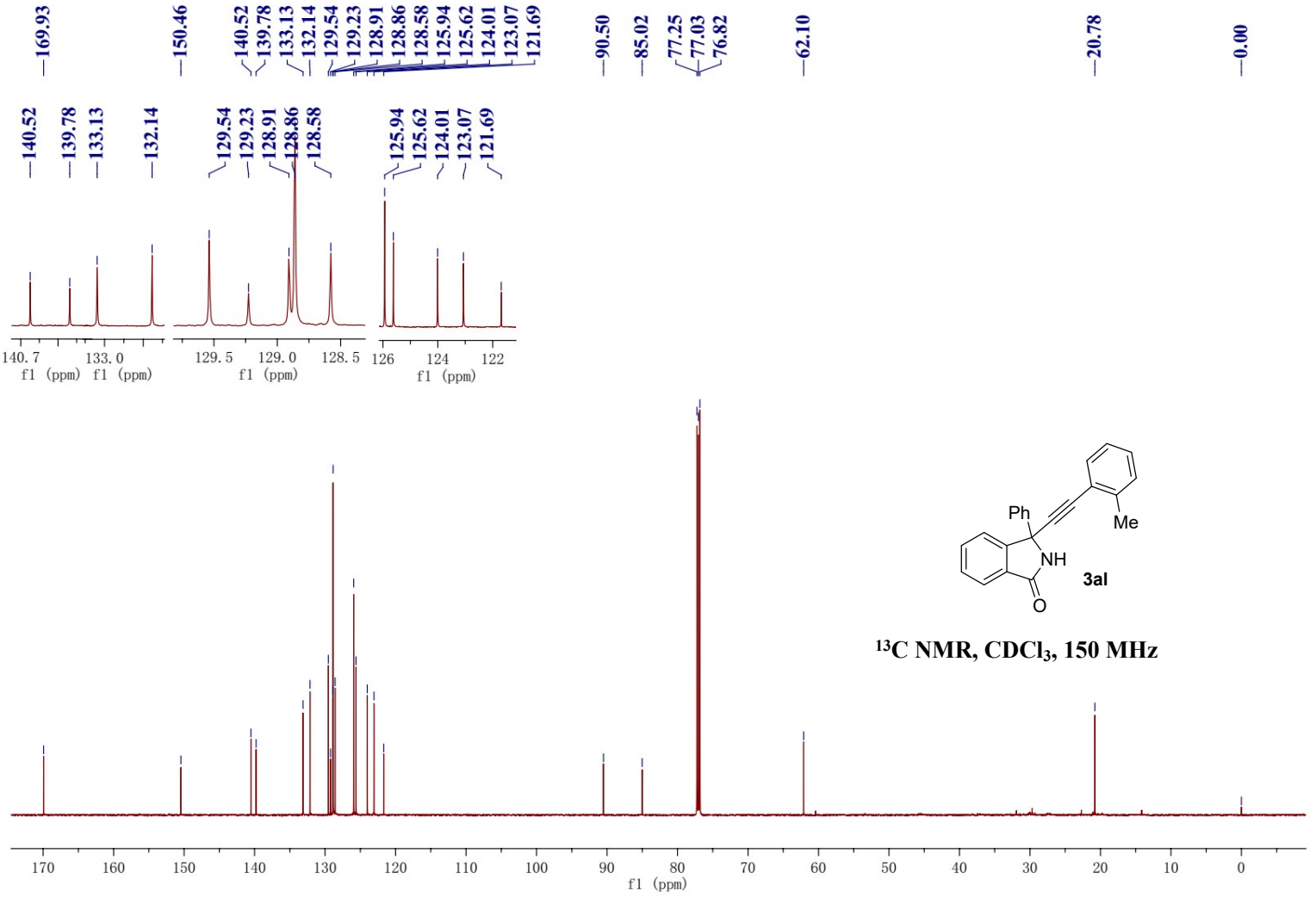


3ak

^{13}C NMR, $CDCl_3$, 150 MHz

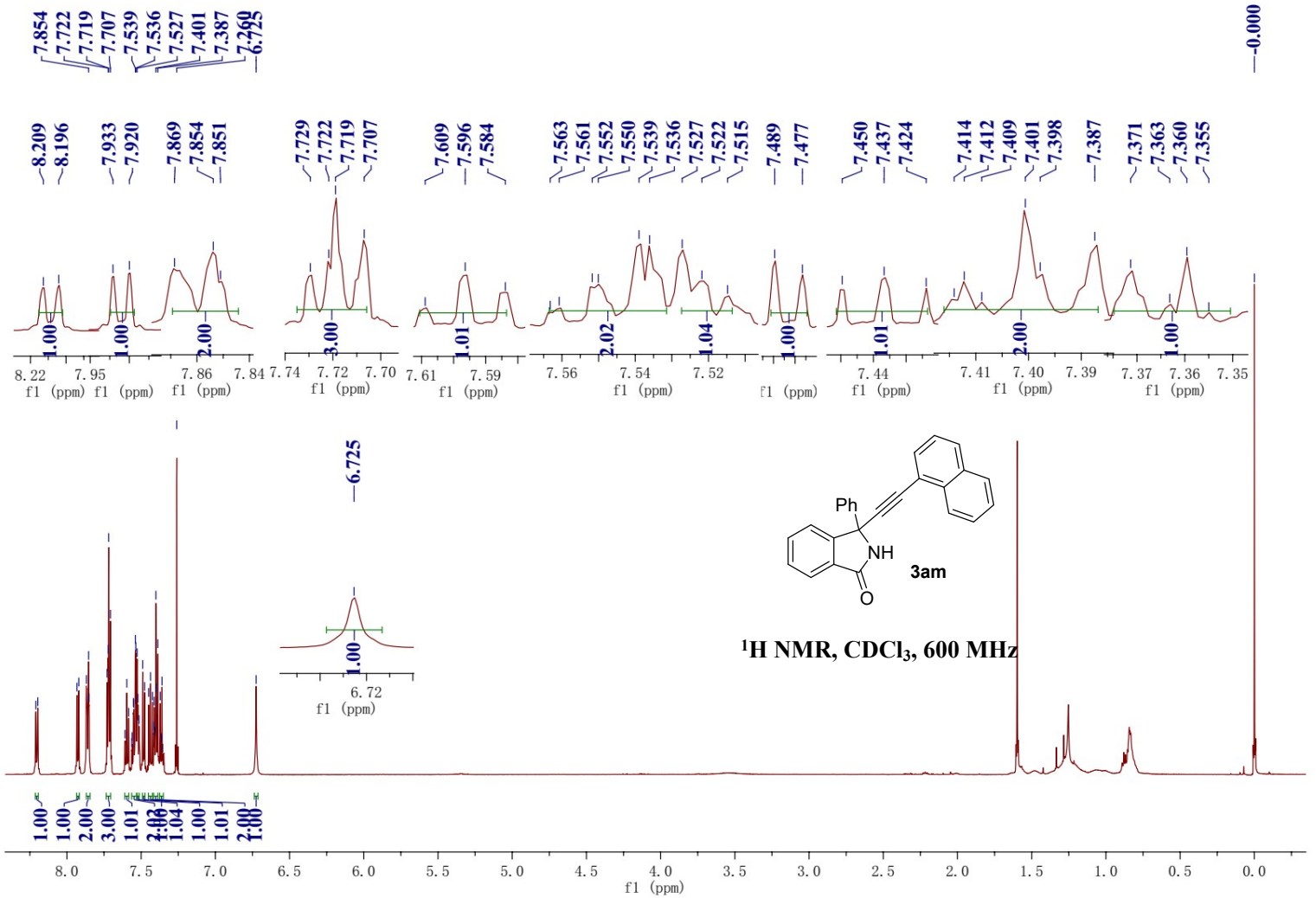


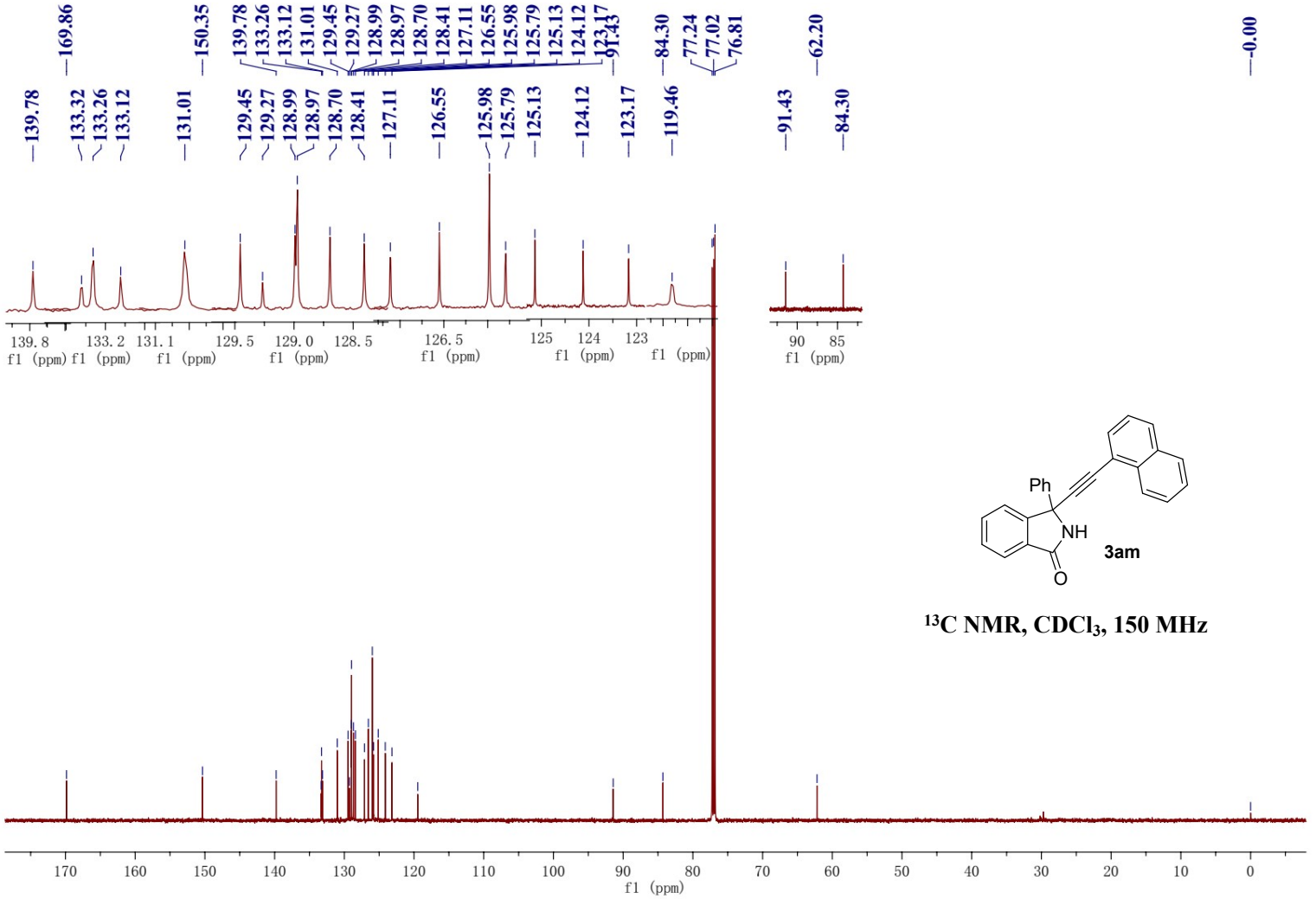
^{1}H NMR, $CDCl_3$, 600 MHz



3al

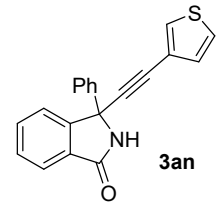
^{13}C NMR, $CDCl_3$, 150 MHz


7.854
7.722
7.719
7.707
7.539
7.536
7.527
7.401
7.387
7.260
6.725
0.000
8.209
8.196
7.933
7.920
7.869
7.854
7.851
7.729
7.722
7.719
7.707
7.609
7.596
7.584
7.563
7.561
7.552
7.550
7.539
7.536
7.527
7.522
7.515
7.489
7.477
7.450
7.437
7.424
7.414
7.412
7.409
7.401
7.398
7.387
7.371
7.363
7.360
7.355
1.00
1.00
2.00
3.00
1.01
2.02
1.04
1.00
1.01
2.00
1.00
f1 (ppm)
Ph
NH
O
3am
1H NMR, CDCl3, 600 MHz



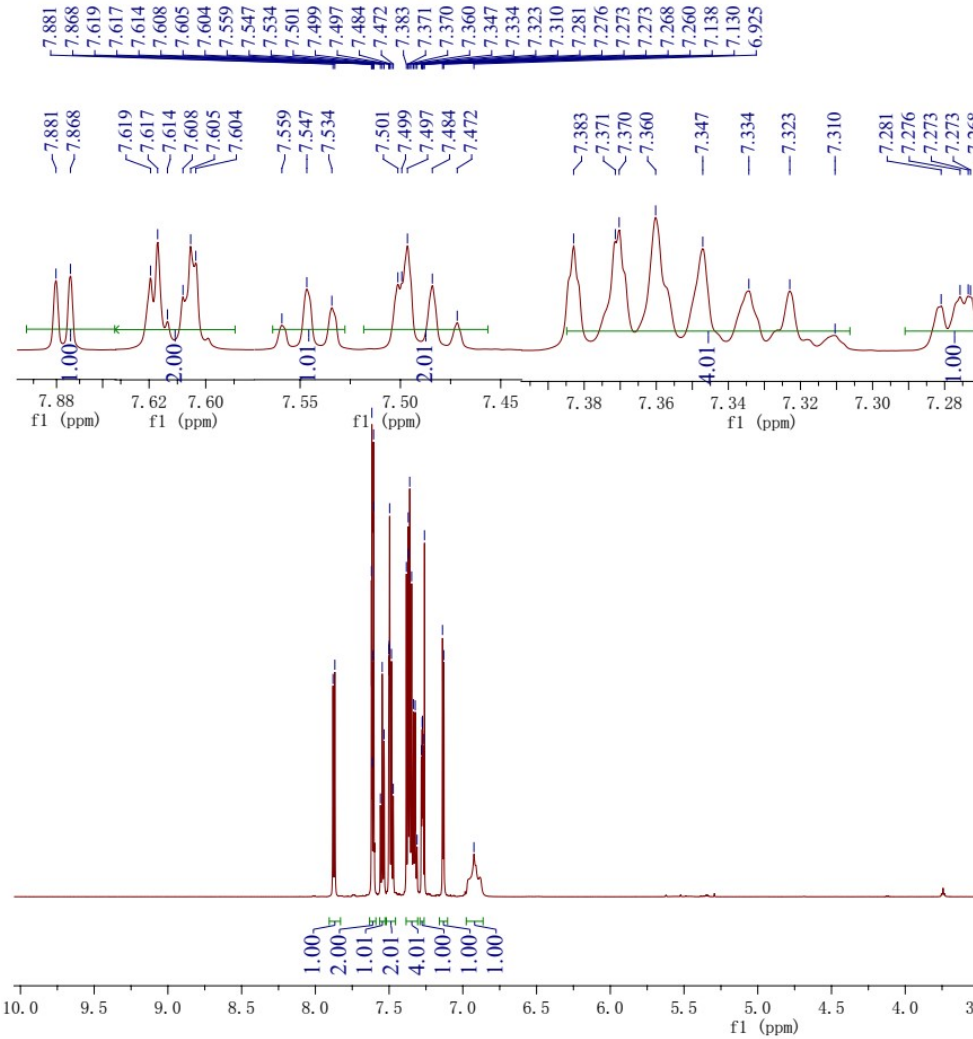
3am

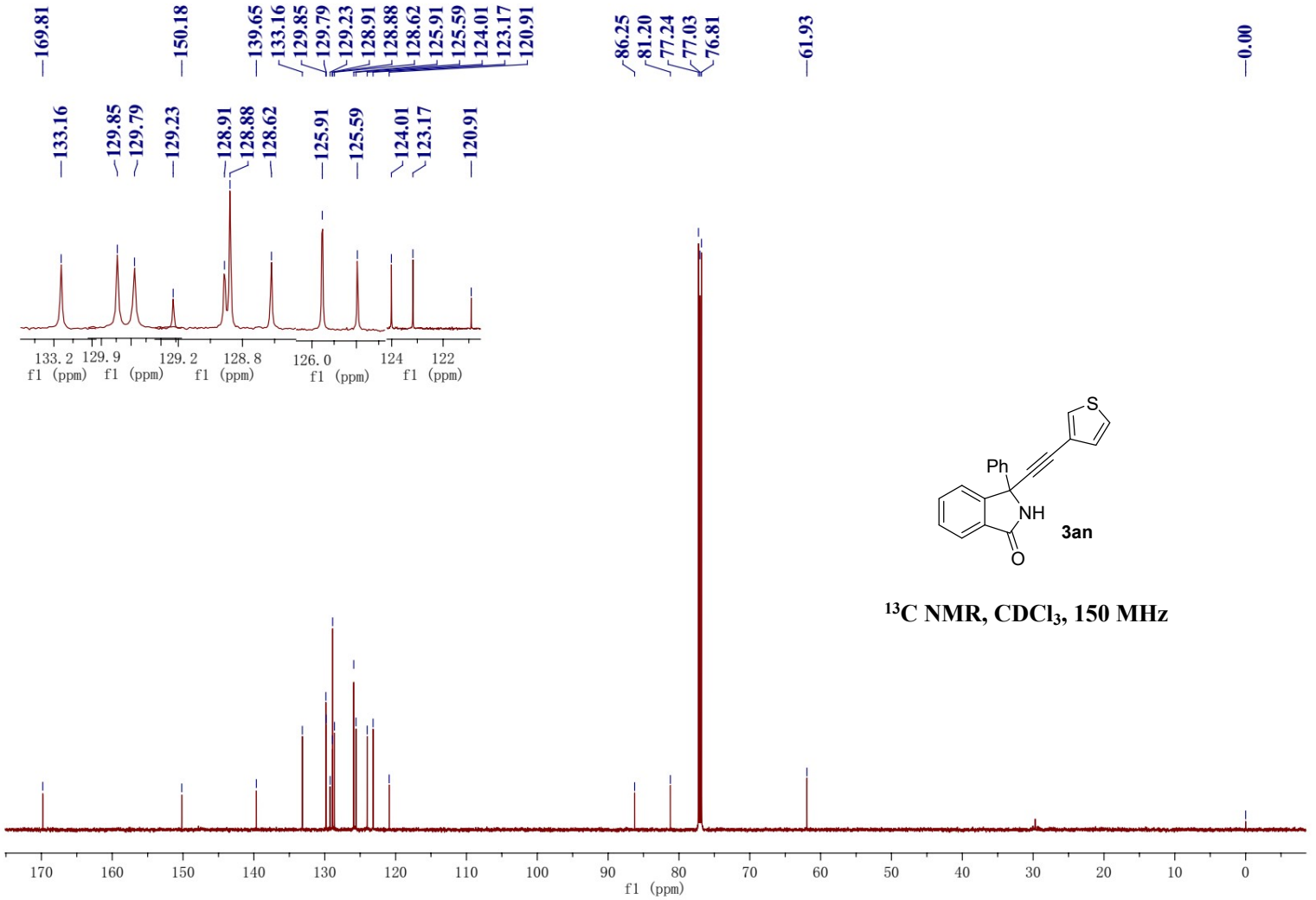
^{13}C NMR, $CDCl_3$, 150 MHz



3an

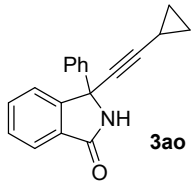
^{1}H NMR, $CDCl_3$, 600 MHz





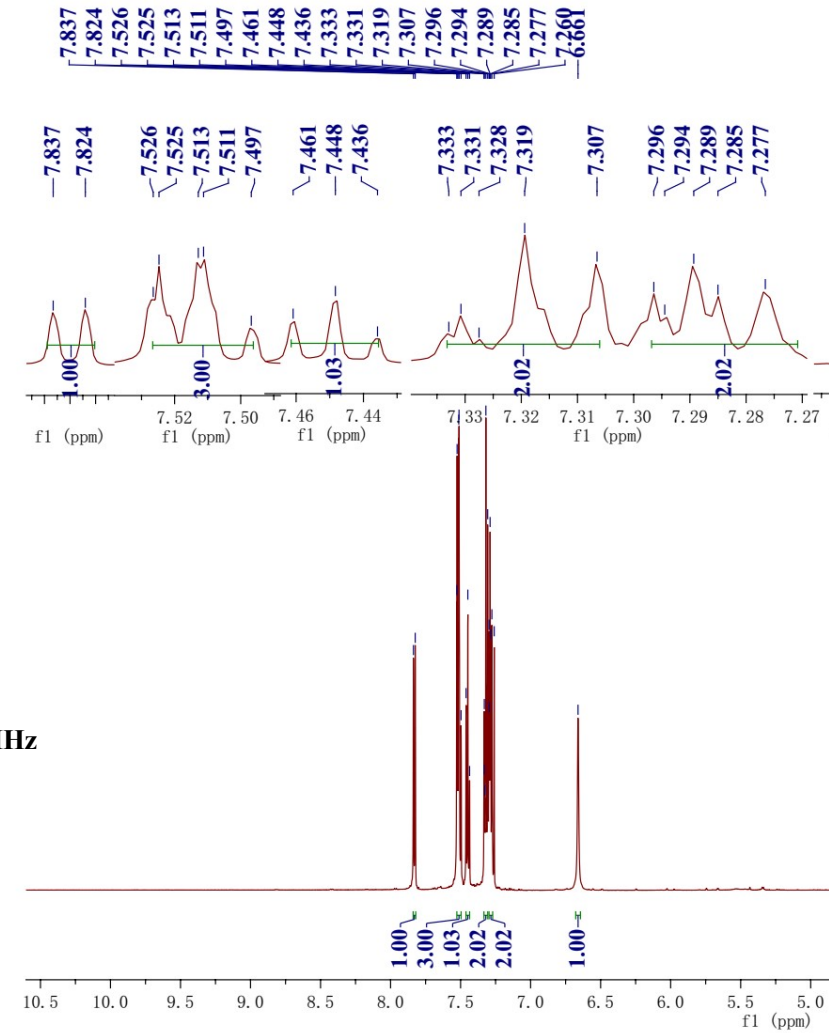
3an

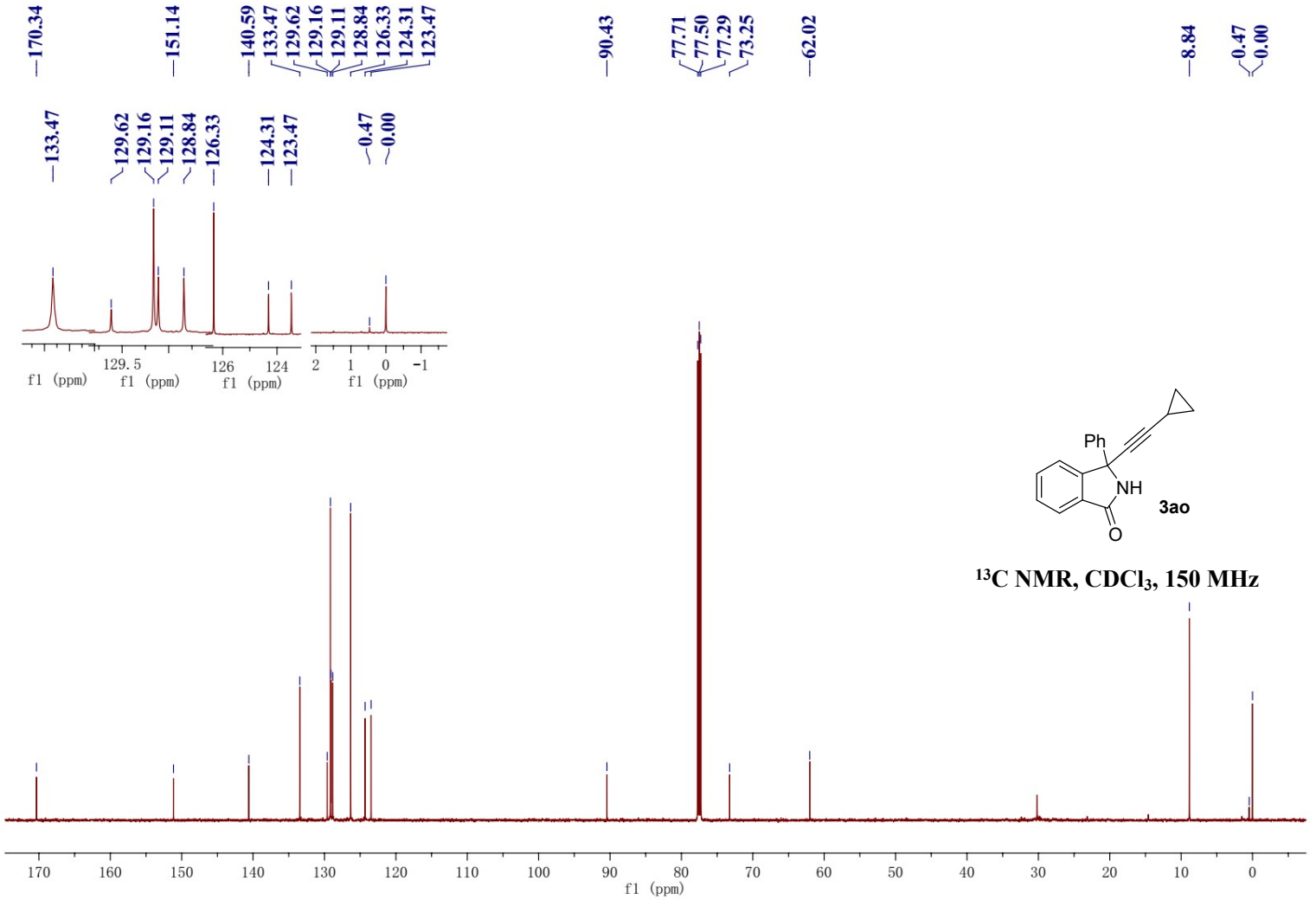
^{13}C NMR, $CDCl_3$, 150 MHz



3ao

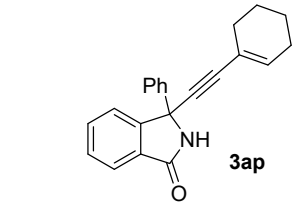
^{1}H NMR, $CDCl_3$, 600 MHz





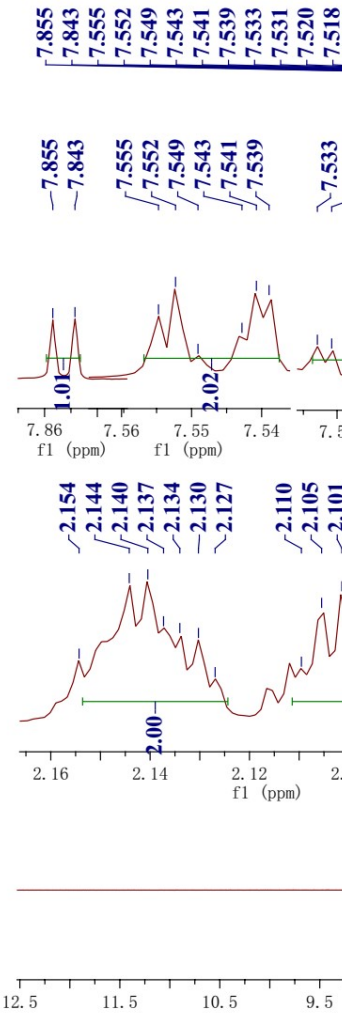
3ao

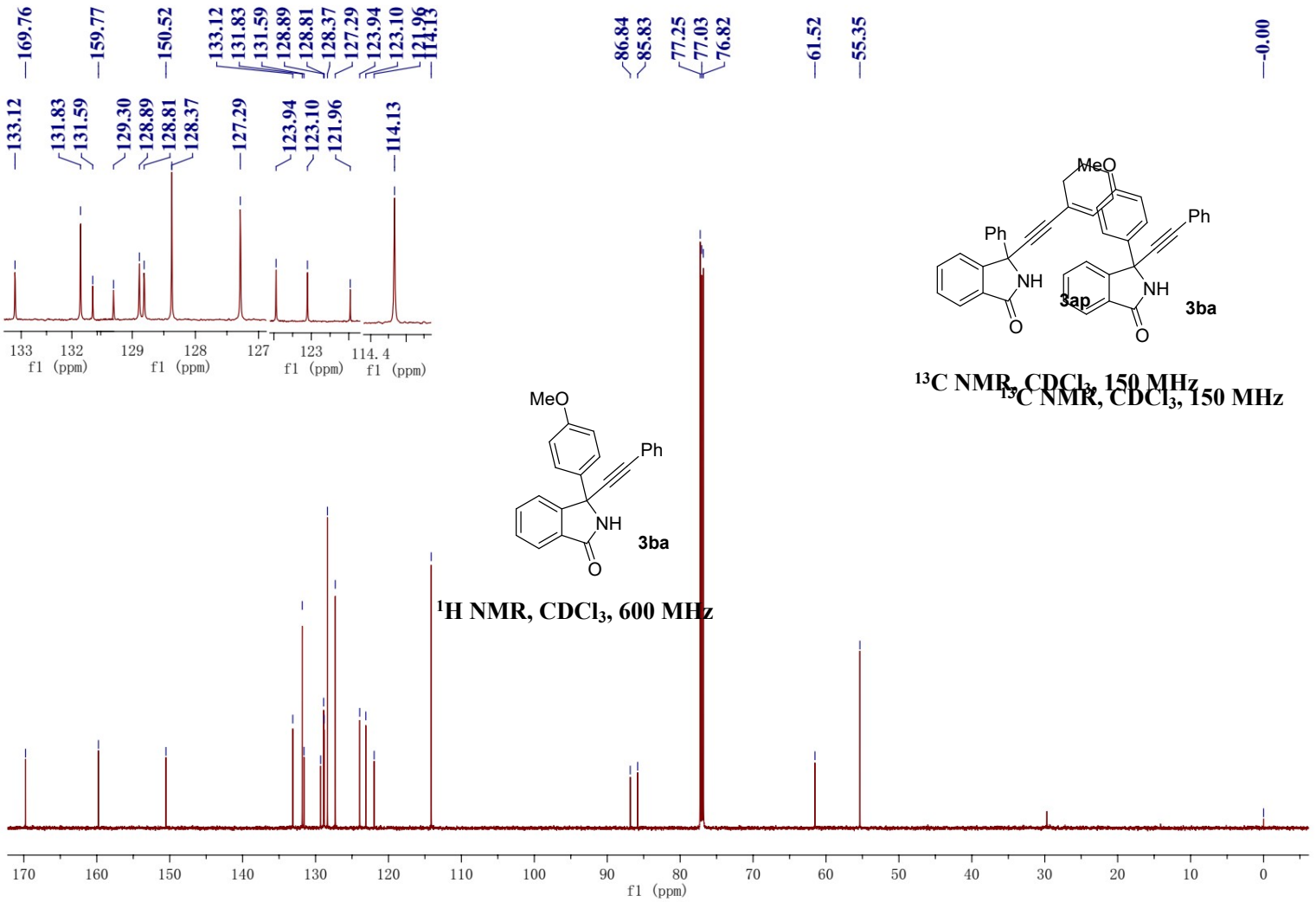
^{13}C NMR, $CDCl_3$, 150 MHz

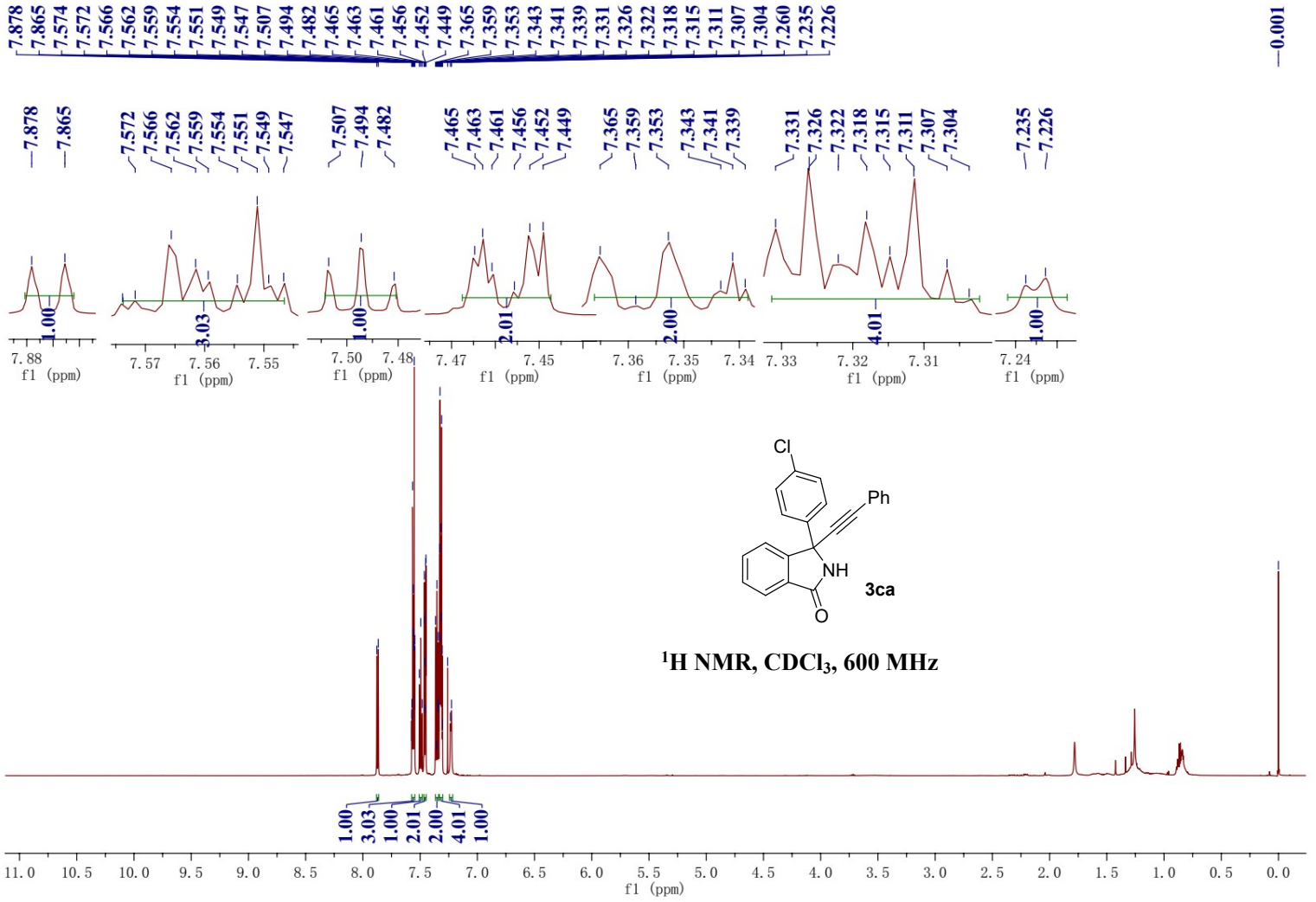


3ap

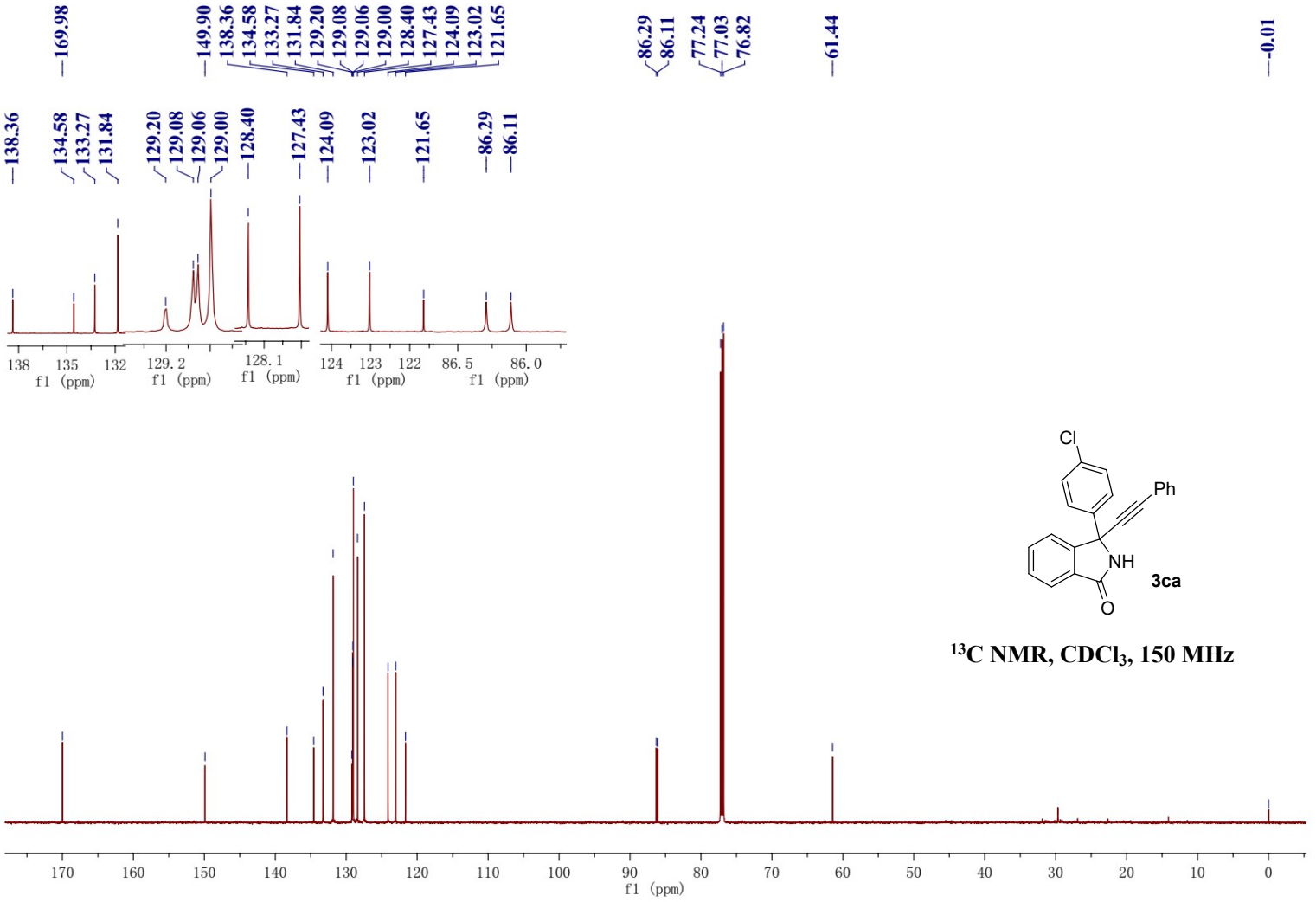
^{1}H NMR, $CDCl_3$, 600 MHz




169.76
159.77
150.52
133.12
131.83
131.59
128.89
128.81
128.37
127.29
123.94
123.10
121.96
114.13
86.84
85.83
77.25
77.03
76.82
61.52
55.35
0.00
MeO
Ph
NH
O
3ba
3ap
^{1}H NMR, CDCl$_3$, 600 MHz
^{13}C NMR, CDCl$_3$, 150 MHz
f1 (ppm)

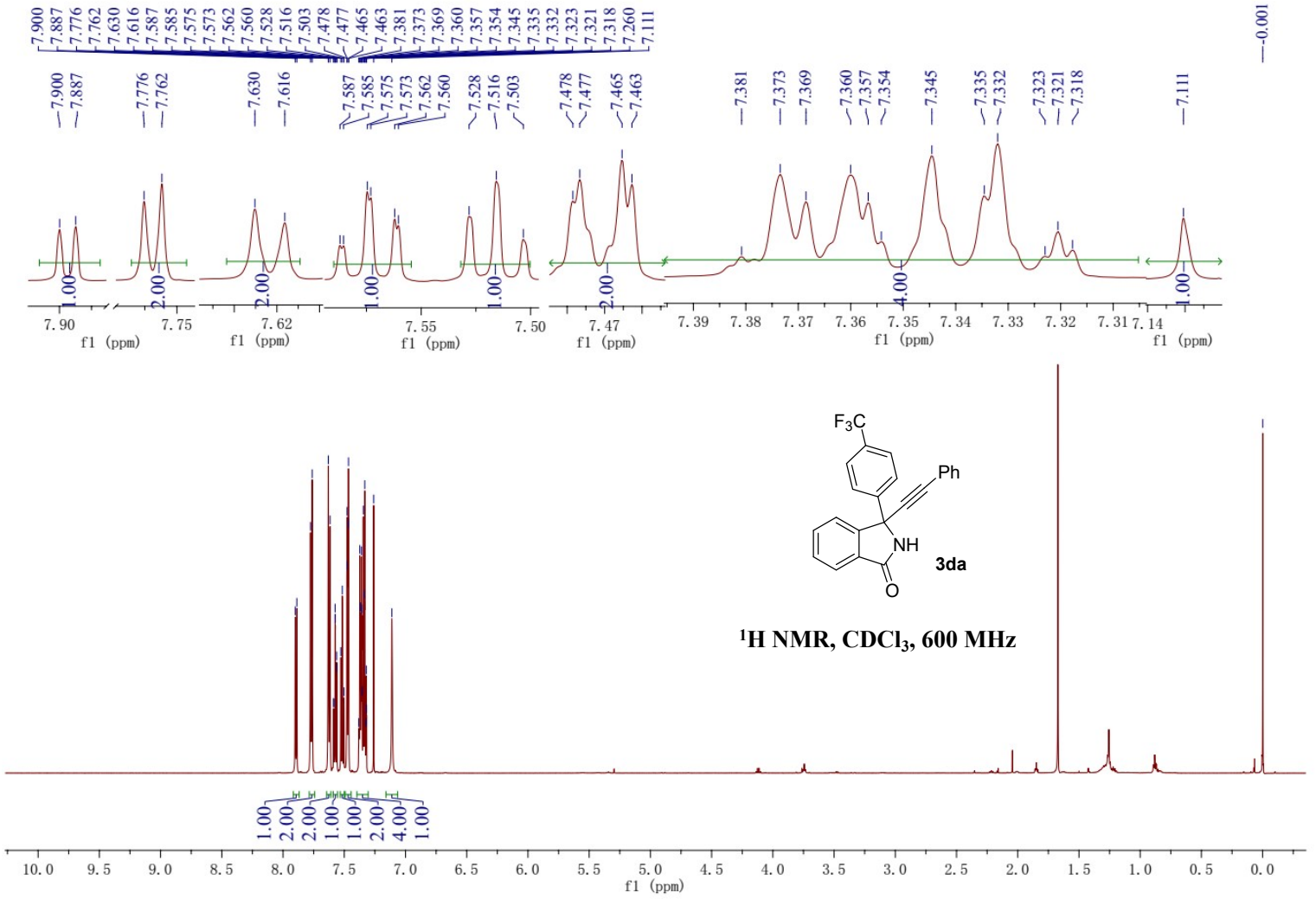


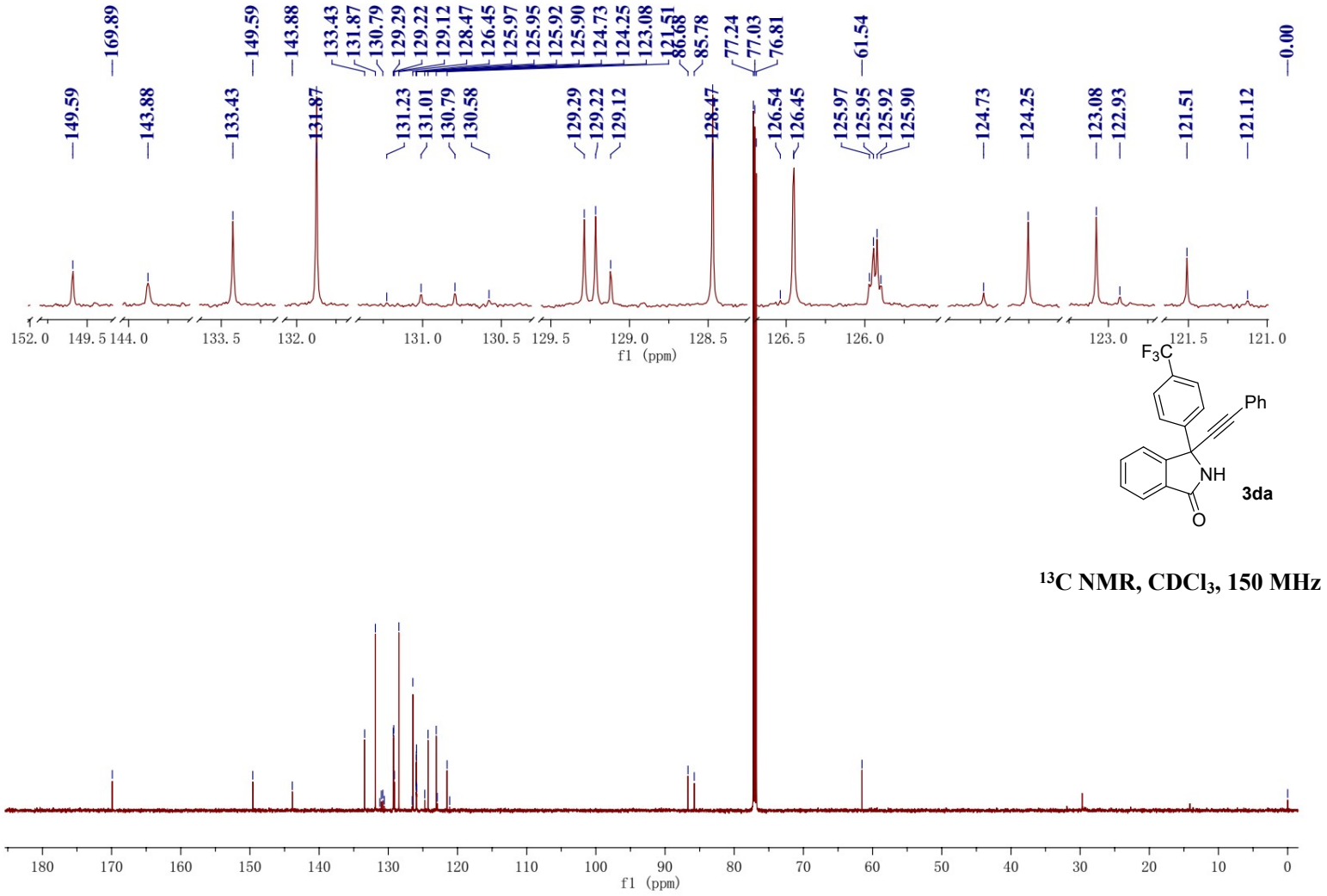
^{1}H NMR, $CDCl_3$, 600 MHz



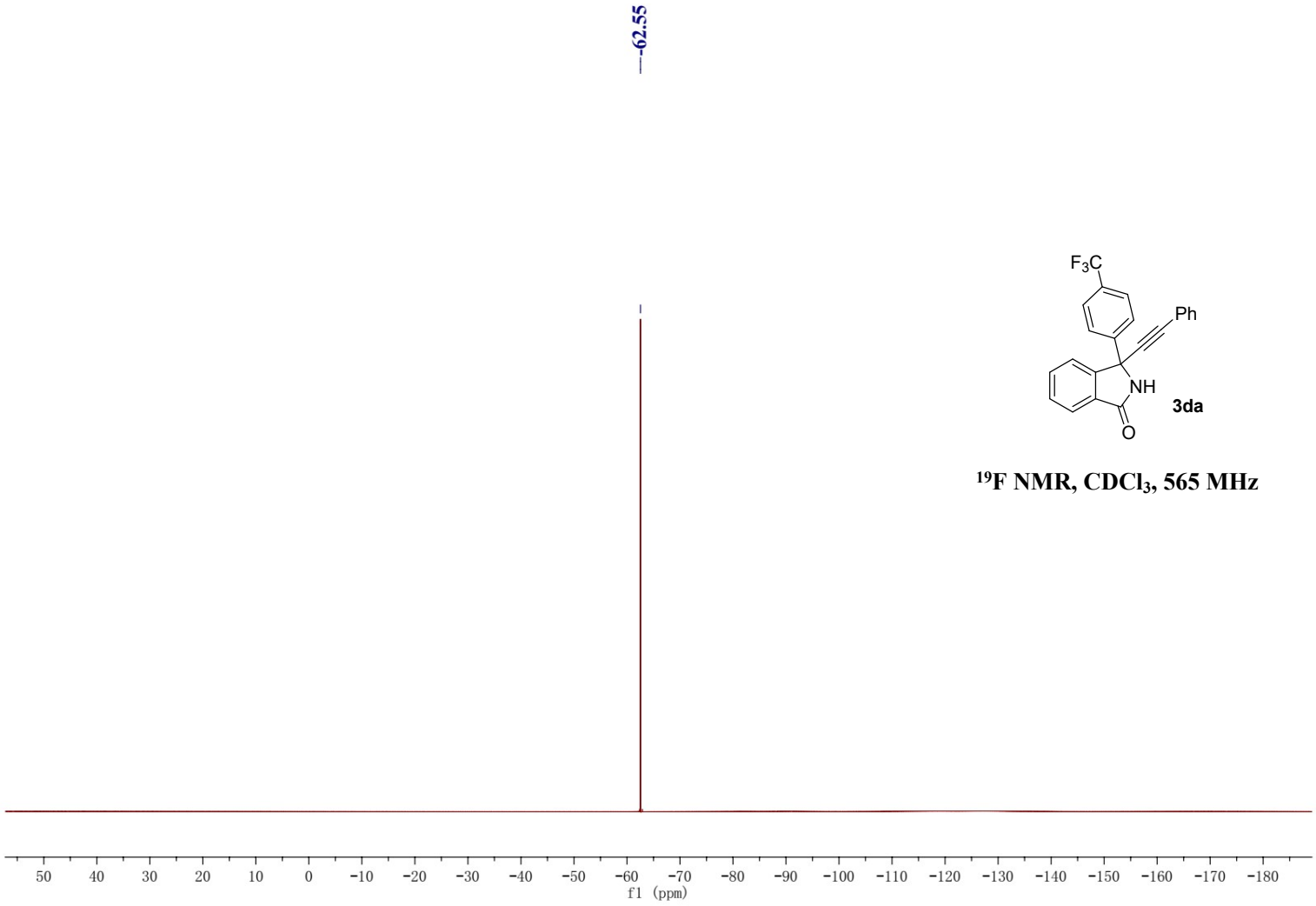
3ca

^{13}C NMR, $CDCl_3$, 150 MHz

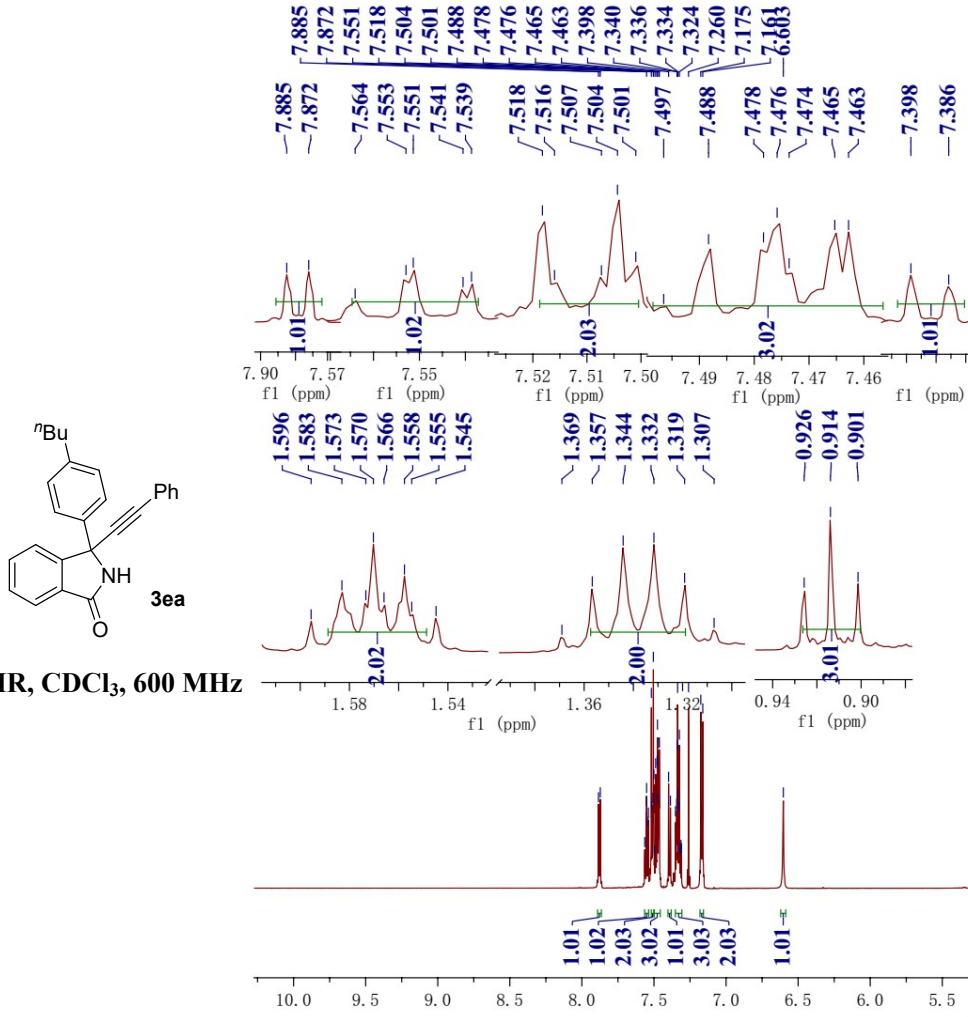

7.900
7.887
7.776
7.762
7.630
7.616
7.587
7.585
7.575
7.573
7.562
7.560
7.528
7.516
7.503
7.478
7.477
7.465
7.463
7.381
7.373
7.369
7.360
7.357
7.354
7.345
7.335
7.332
7.323
7.321
7.318
7.260
7.111
-0.001
1.00
2.00
2.00
1.00
1.00
2.00
4.00
1.00
f1 (ppm)
F3C
Ph
NH
O
3da
1H NMR, CDCl3, 600 MHz



^{13}C NMR, $CDCl_3$, 150 MHz

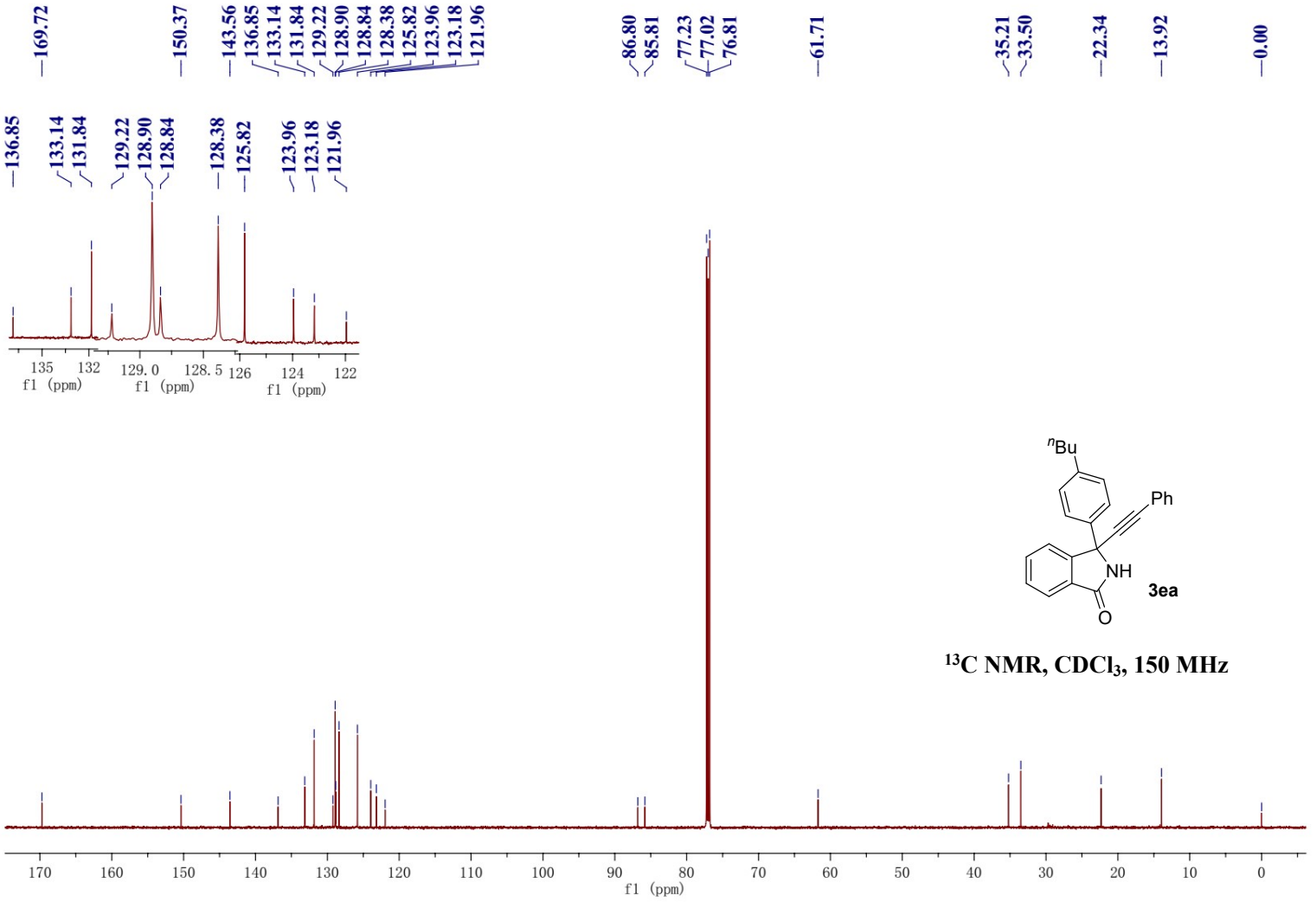


^{19}F NMR, $CDCl_3$, 565 MHz



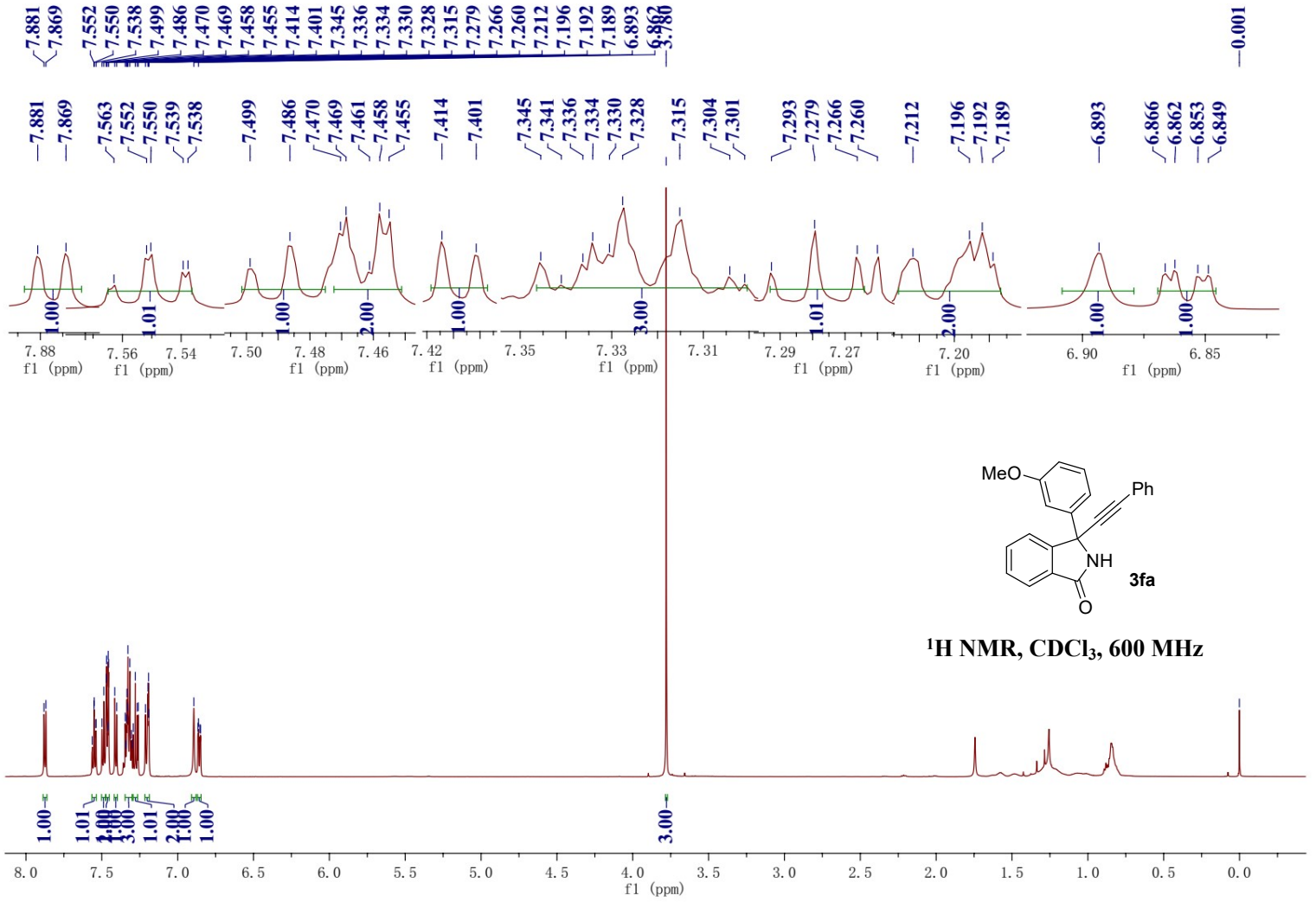
3ea

^{1}H NMR, $CDCl_3$, 600 MHz

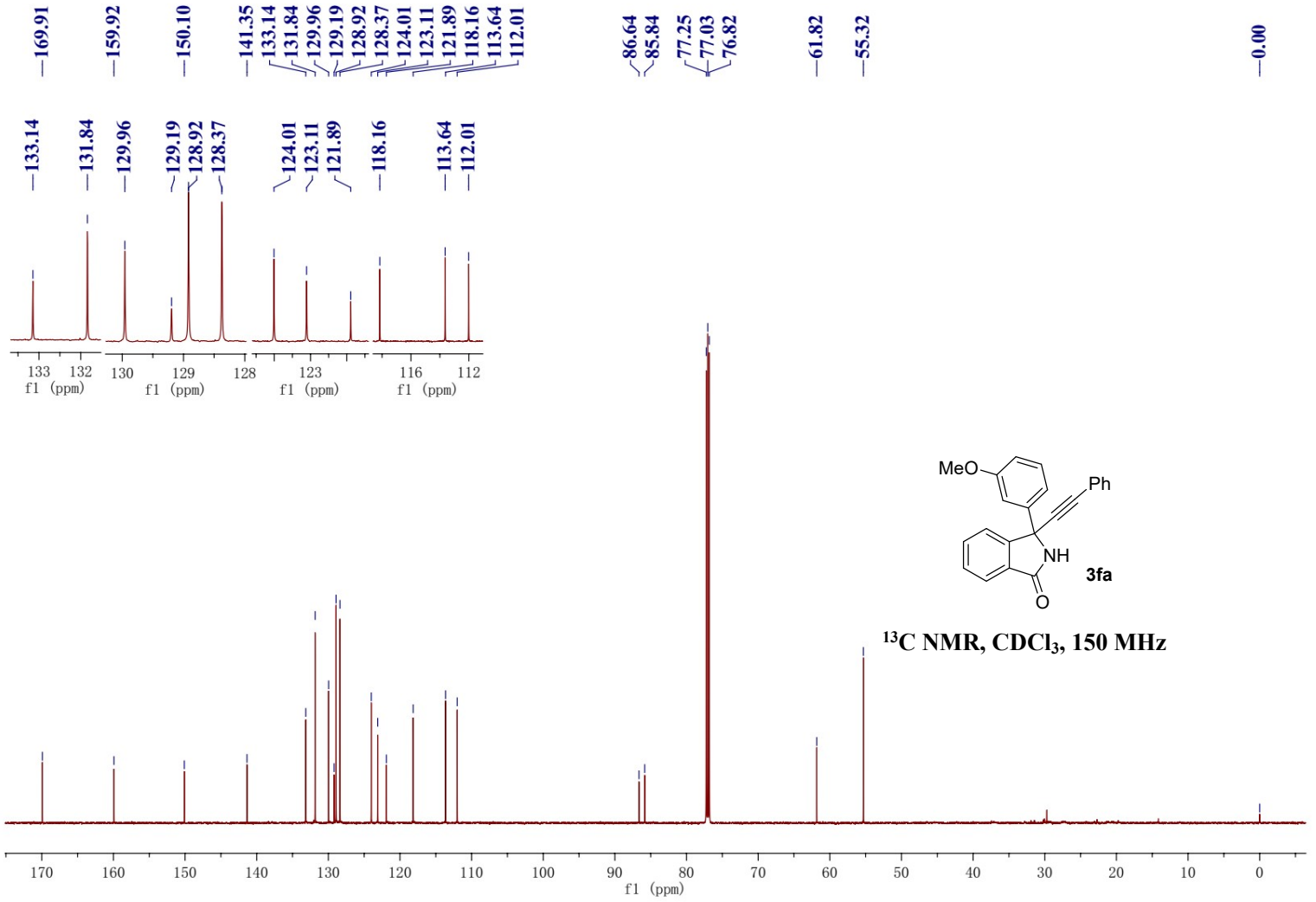


3ea

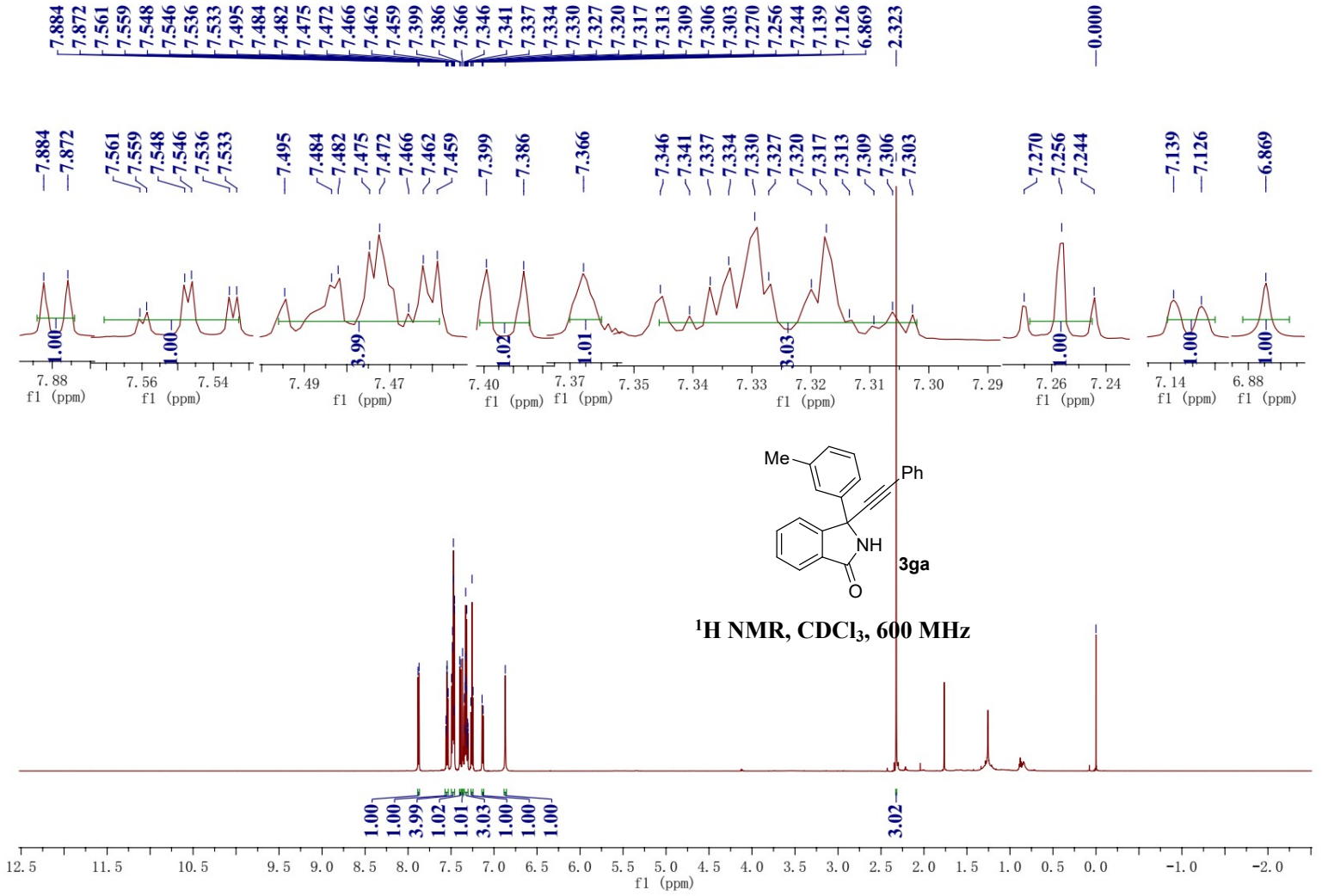
^{13}C NMR, $CDCl_3$, 150 MHz

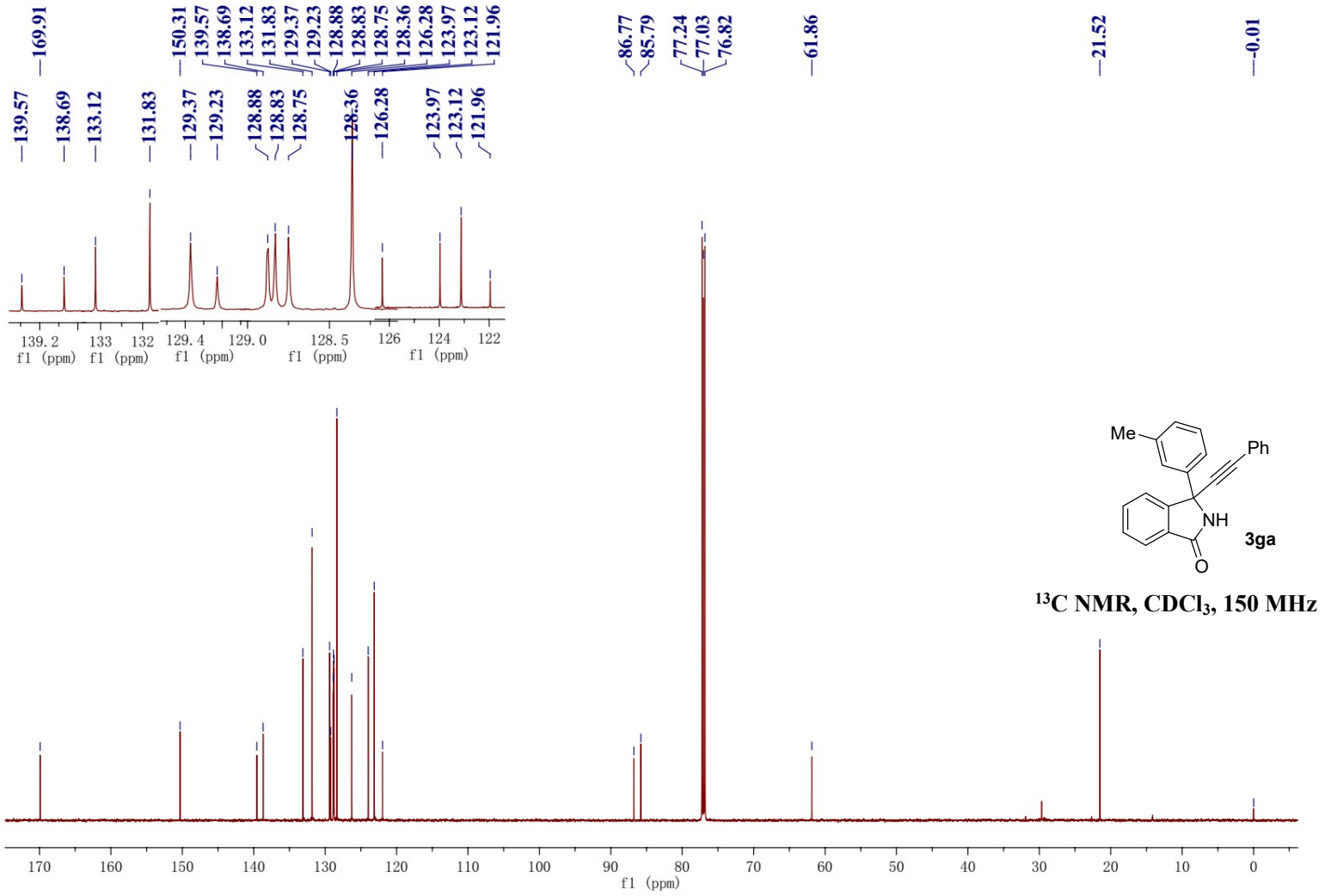


^{1}H NMR, $CDCl_3$, 600 MHz



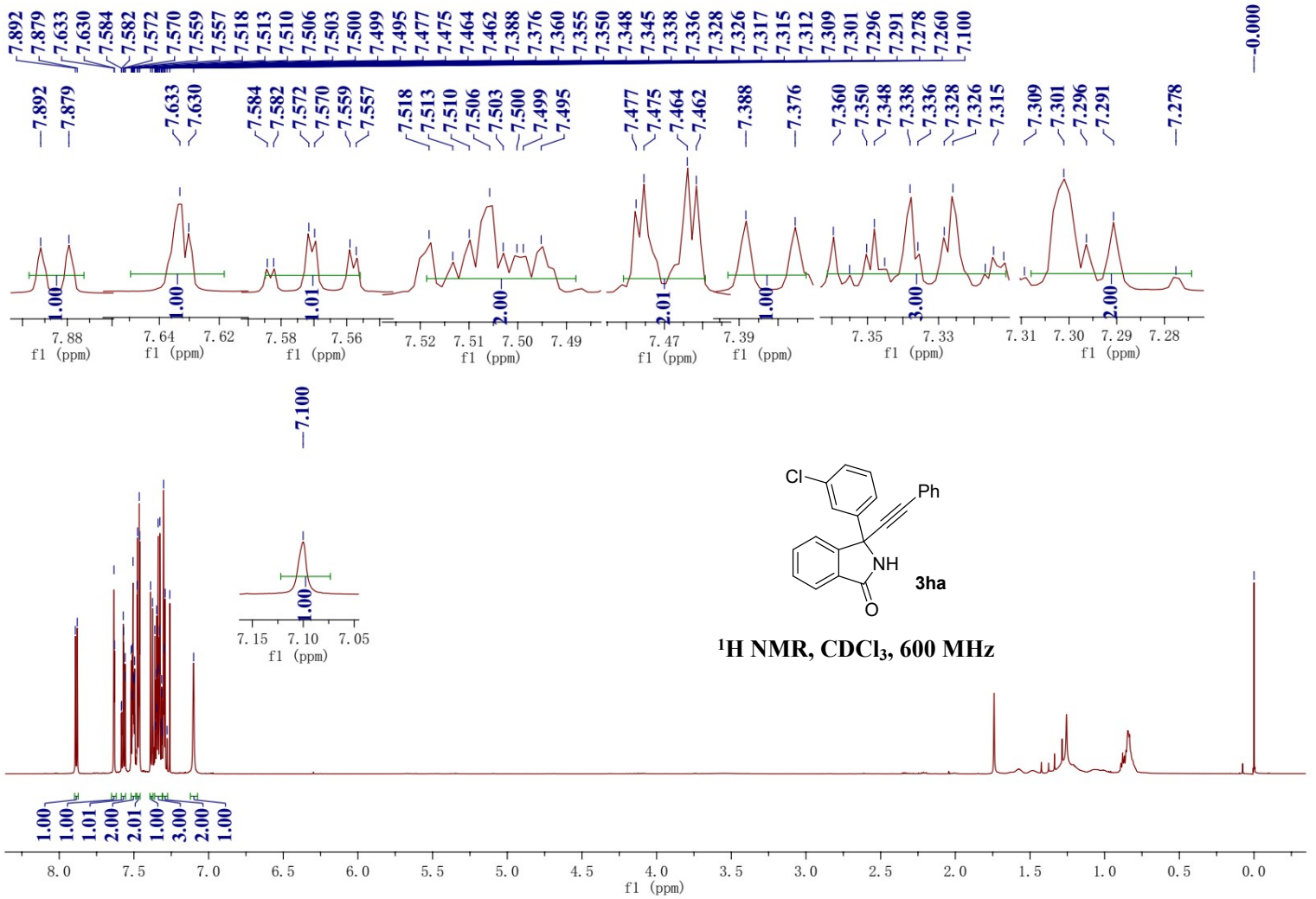
^{13}C NMR, $CDCl_3$, 150 MHz


7.884
7.872
7.561
7.559
7.548
7.546
7.536
7.533
7.495
7.484
7.482
7.475
7.472
7.466
7.462
7.459
7.399
7.386
7.366
7.346
7.341
7.337
7.334
7.330
7.327
7.320
7.317
7.313
7.309
7.306
7.303
7.270
7.256
7.244
7.139
7.126
6.869
2.323
0.000
Me
Ph
NH
O
3ga
1H NMR, CDCl3, 600 MHz
f1 (ppm)

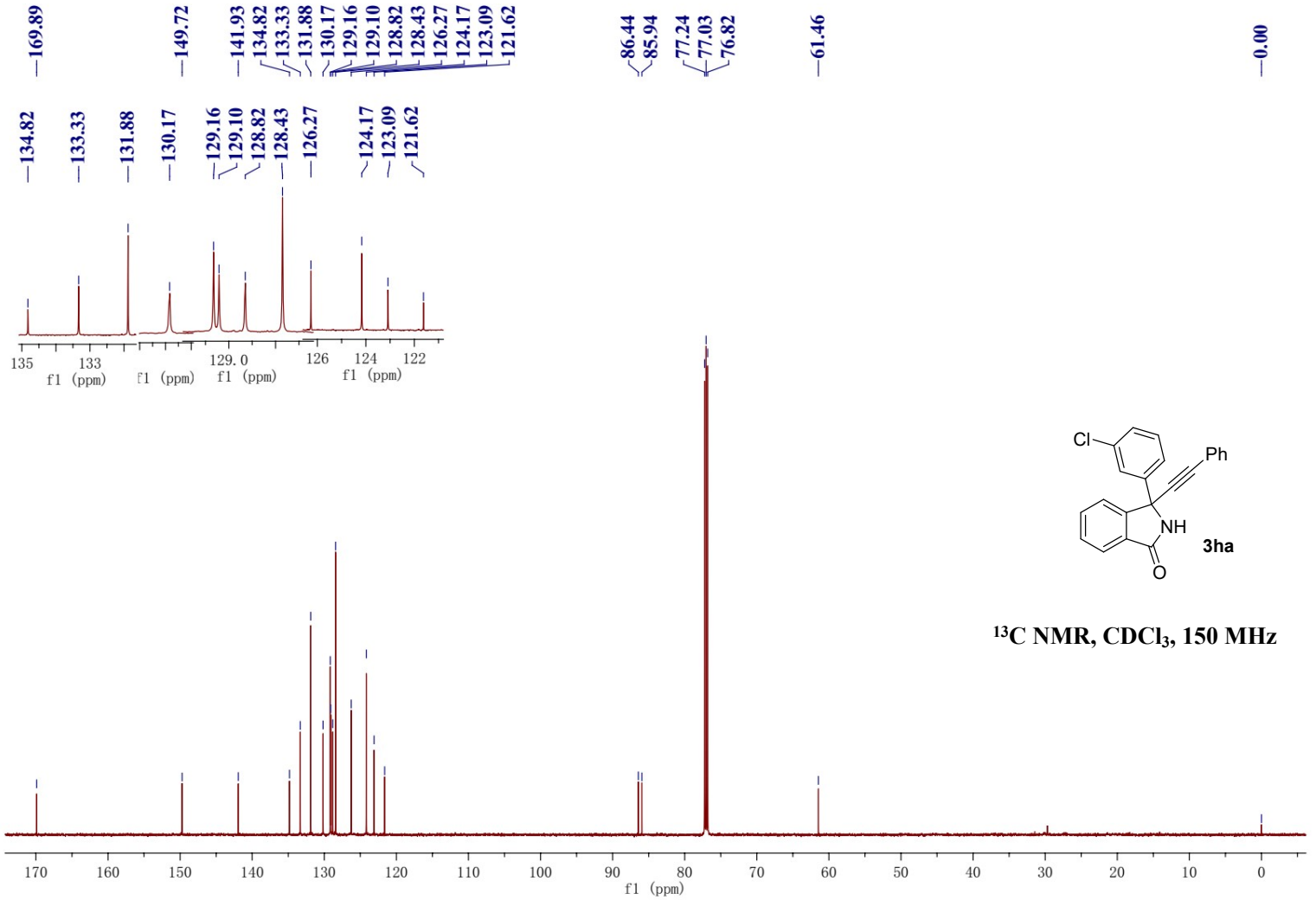


3ga

^{13}C NMR, $CDCl_3$, 150 MHz

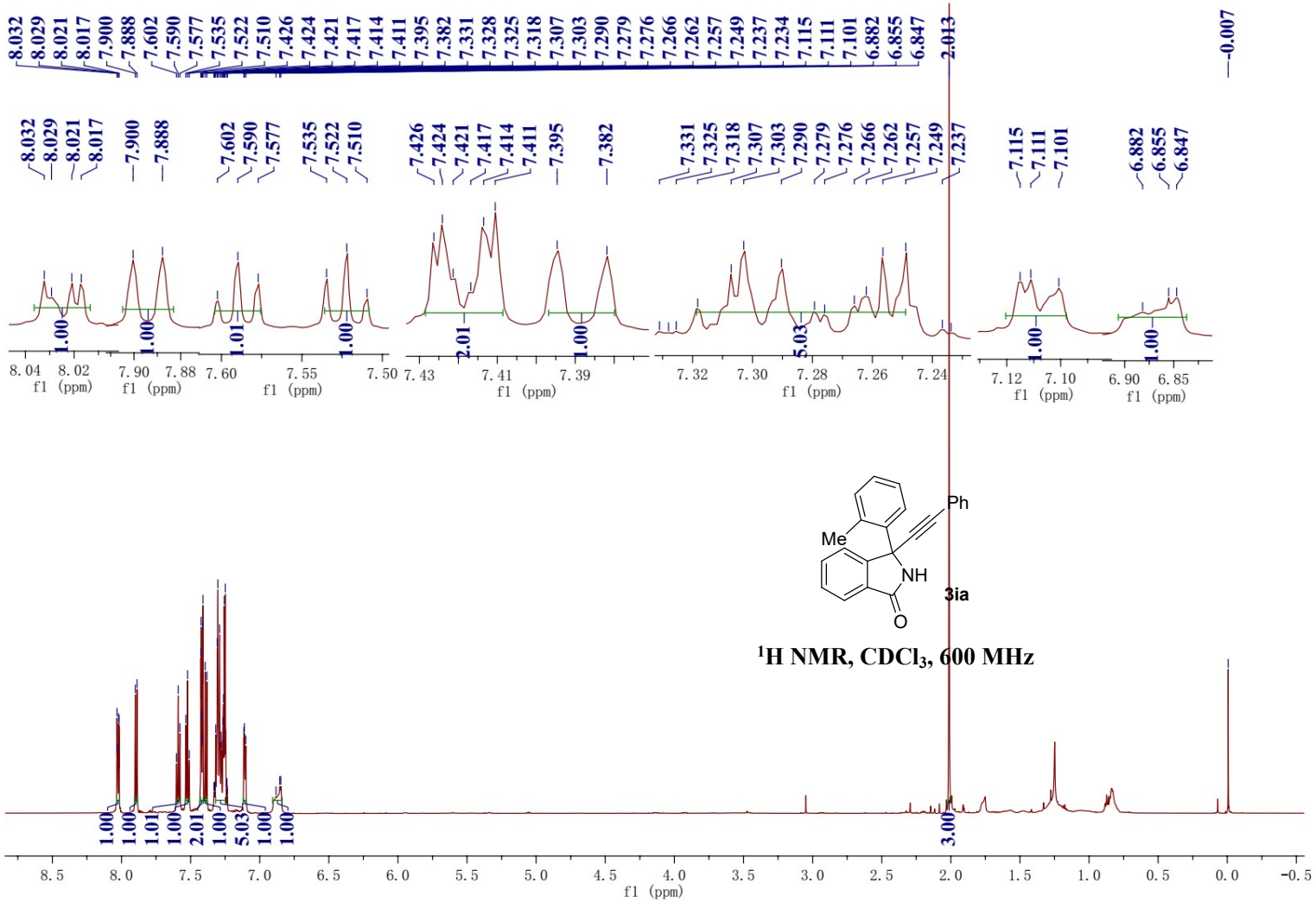


^{1}H NMR, $CDCl_3$, 600 MHz

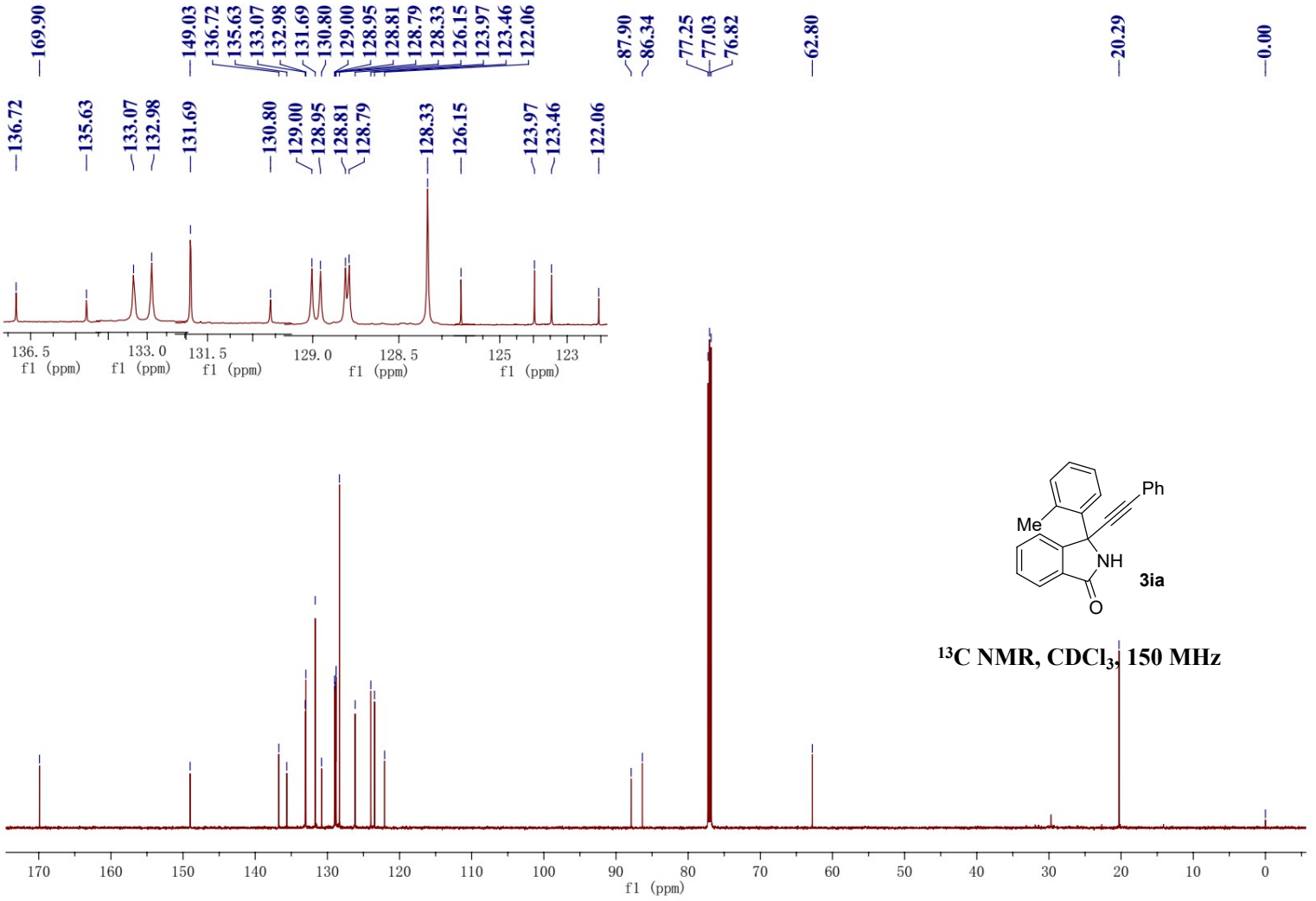


3ha

^{13}C NMR, $CDCl_3$, 150 MHz

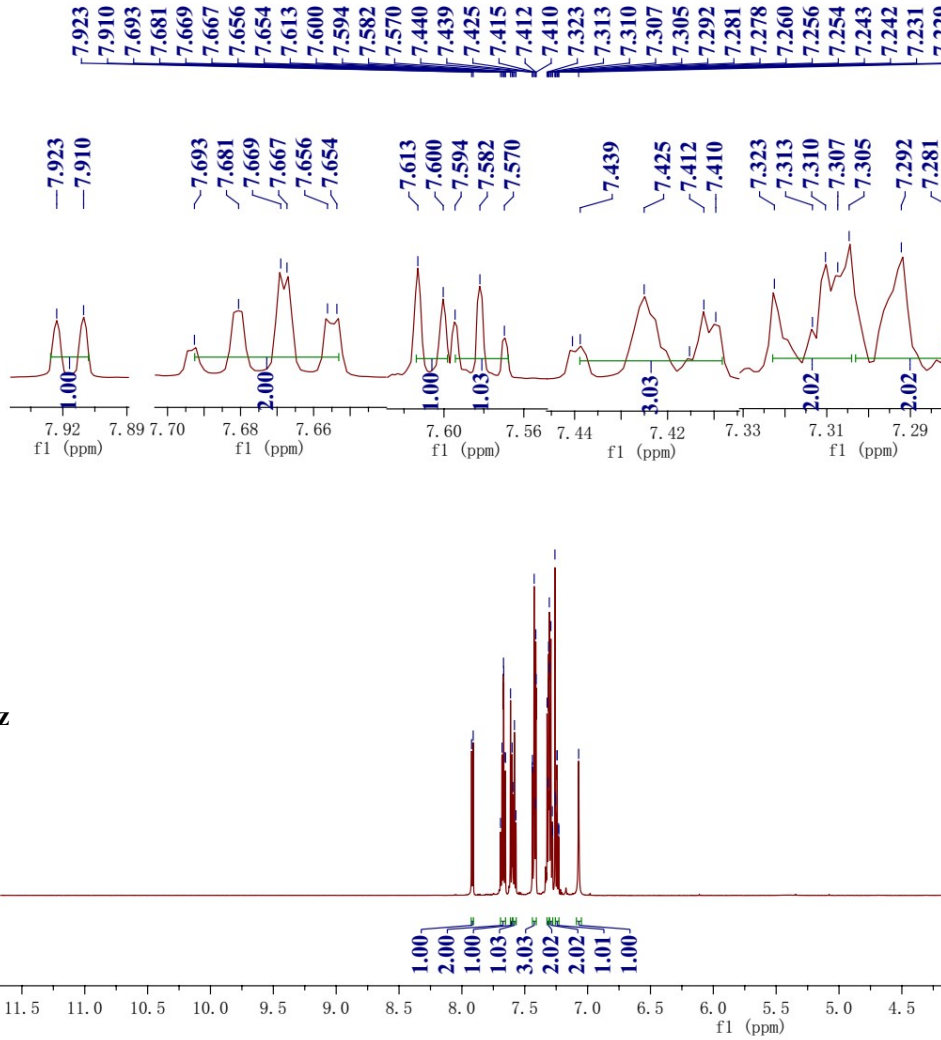


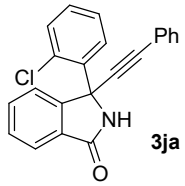
^{1}H NMR, $CDCl_3$, 600 MHz



3ia

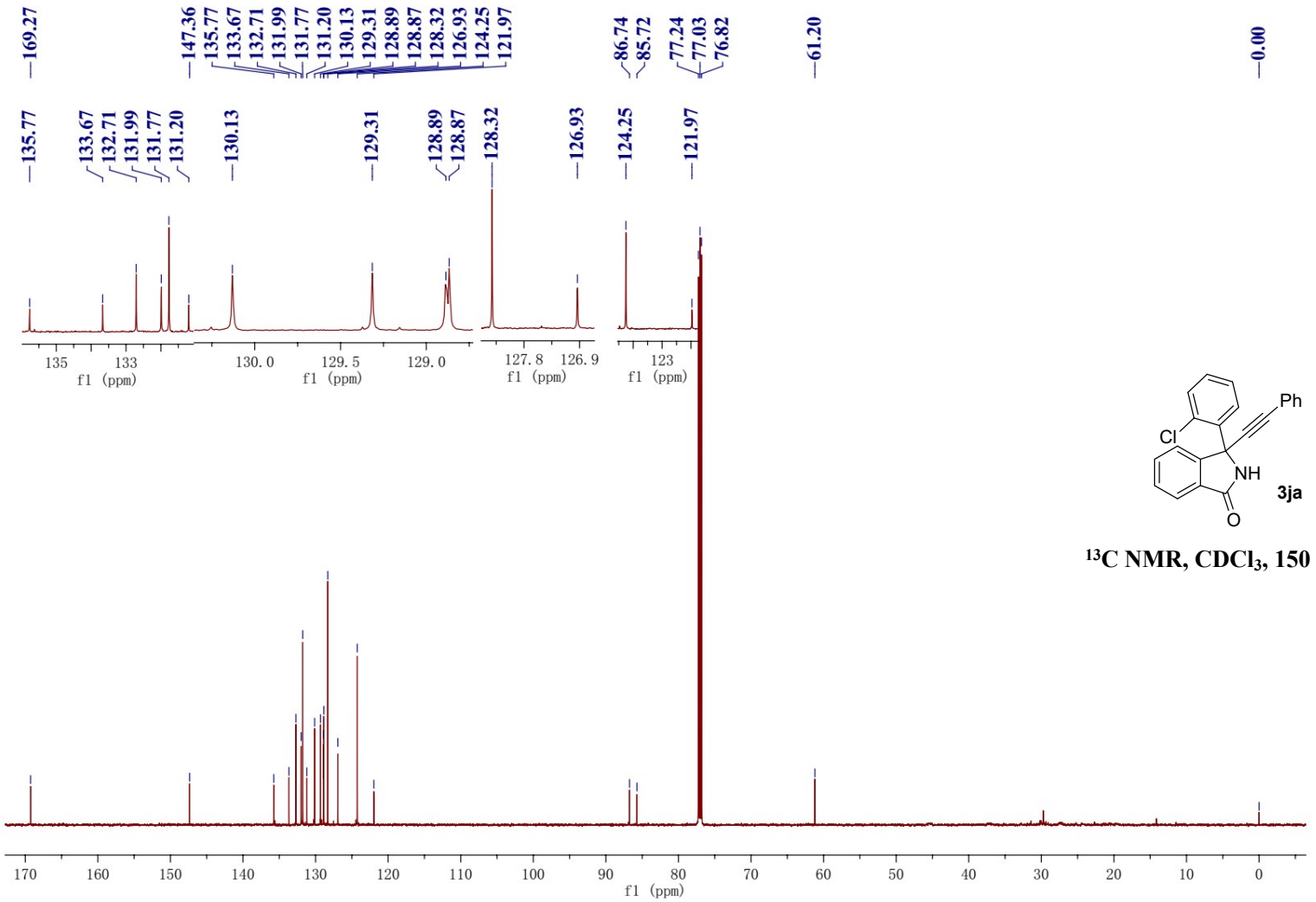
^{13}C NMR, $CDCl_3$, 150 MHz





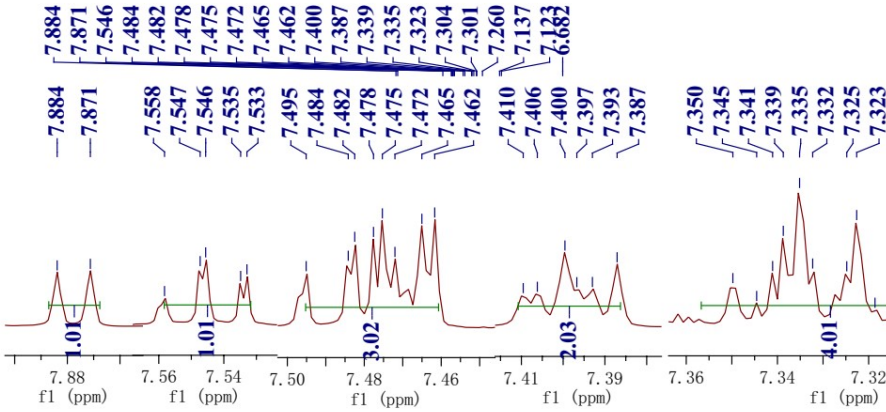
3ja

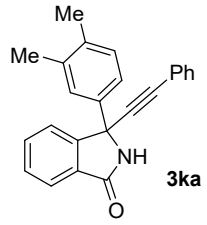
^{1}H NMR, $CDCl_3$, 600 MHz



3ja

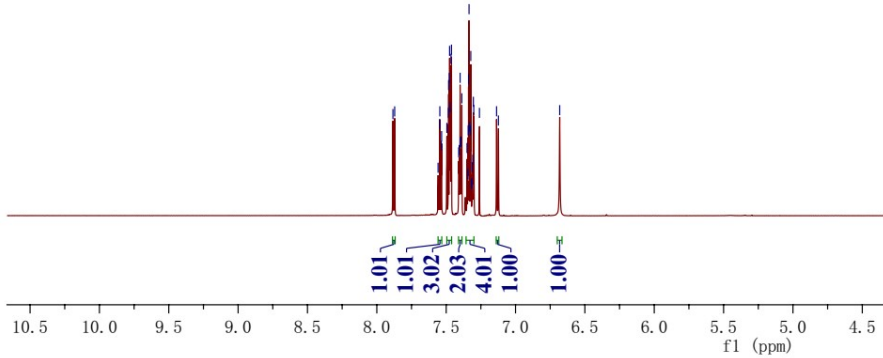
^{13}C NMR, $CDCl_3$, 150 MHz

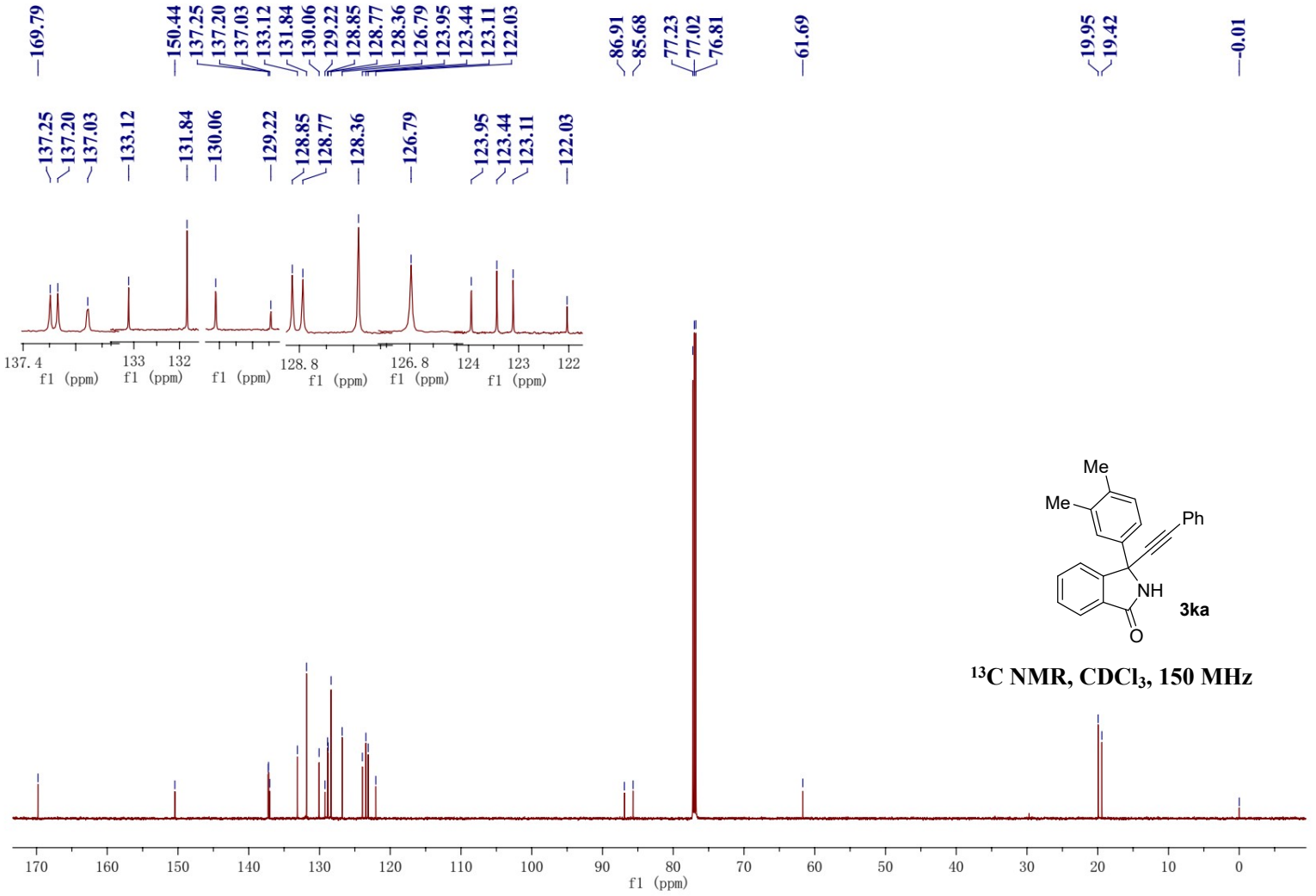




3ka

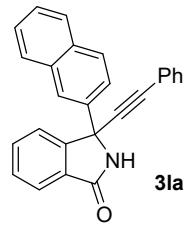
^{1}H NMR, $CDCl_3$, 600 MHz





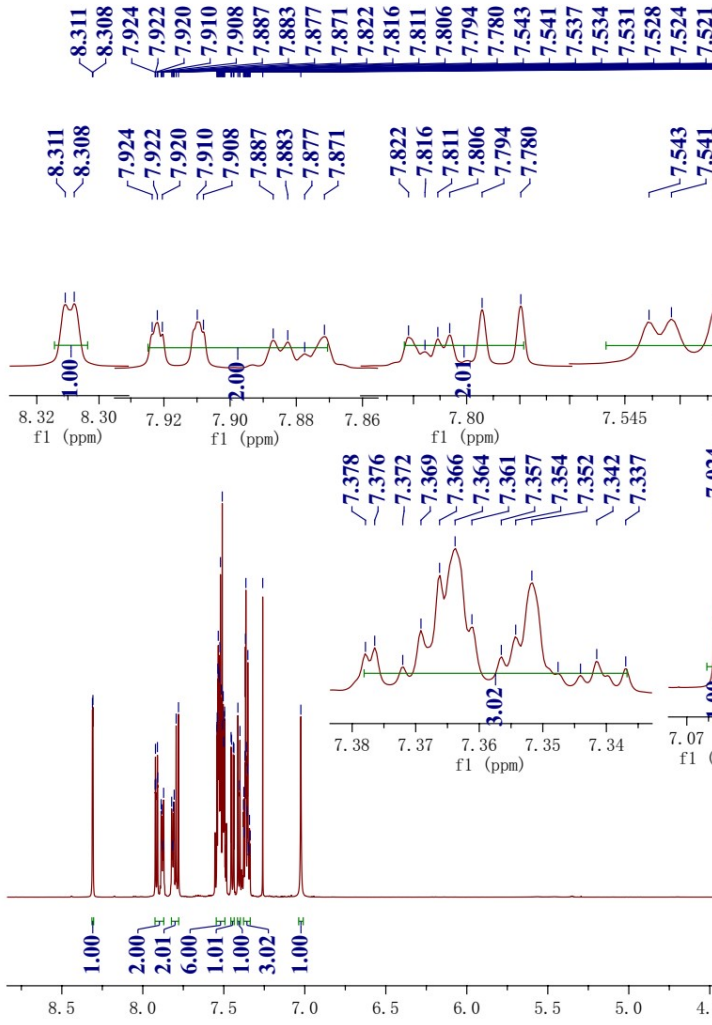
3ka

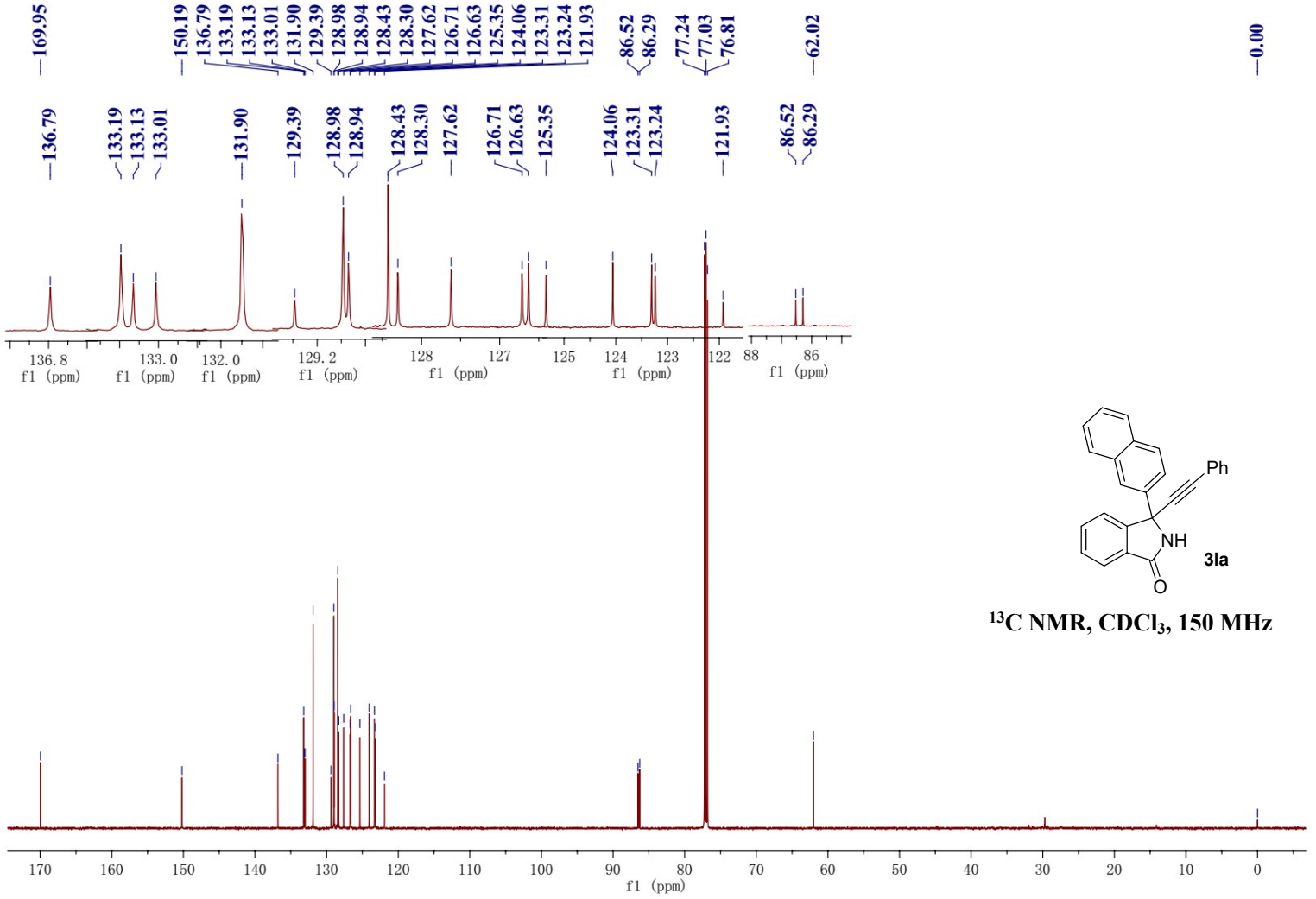
^{13}C NMR, $CDCl_3$, 150 MHz



3la

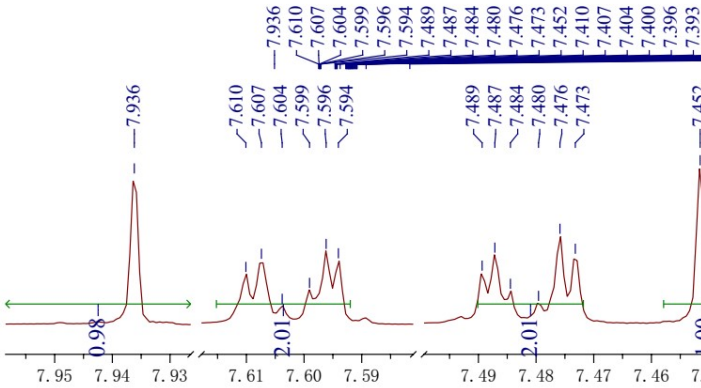
^{1}H NMR, $CDCl_3$, 600 MHz

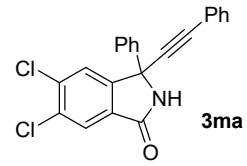




3la

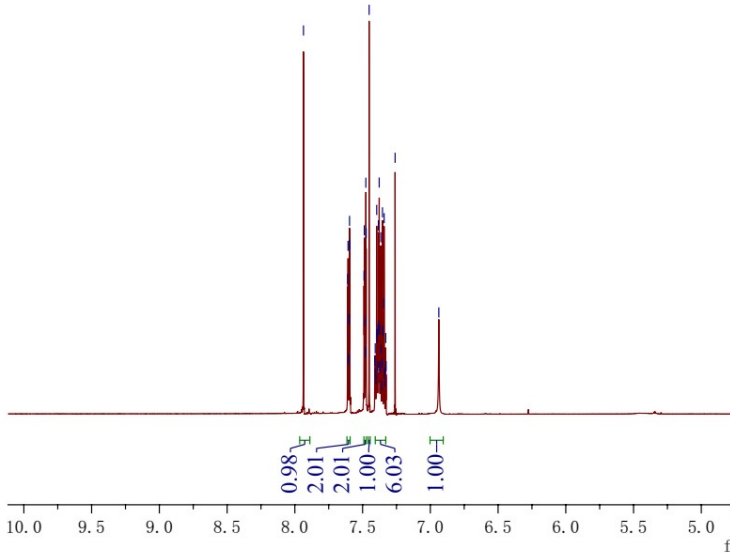
^{13}C NMR, $CDCl_3$, 150 MHz

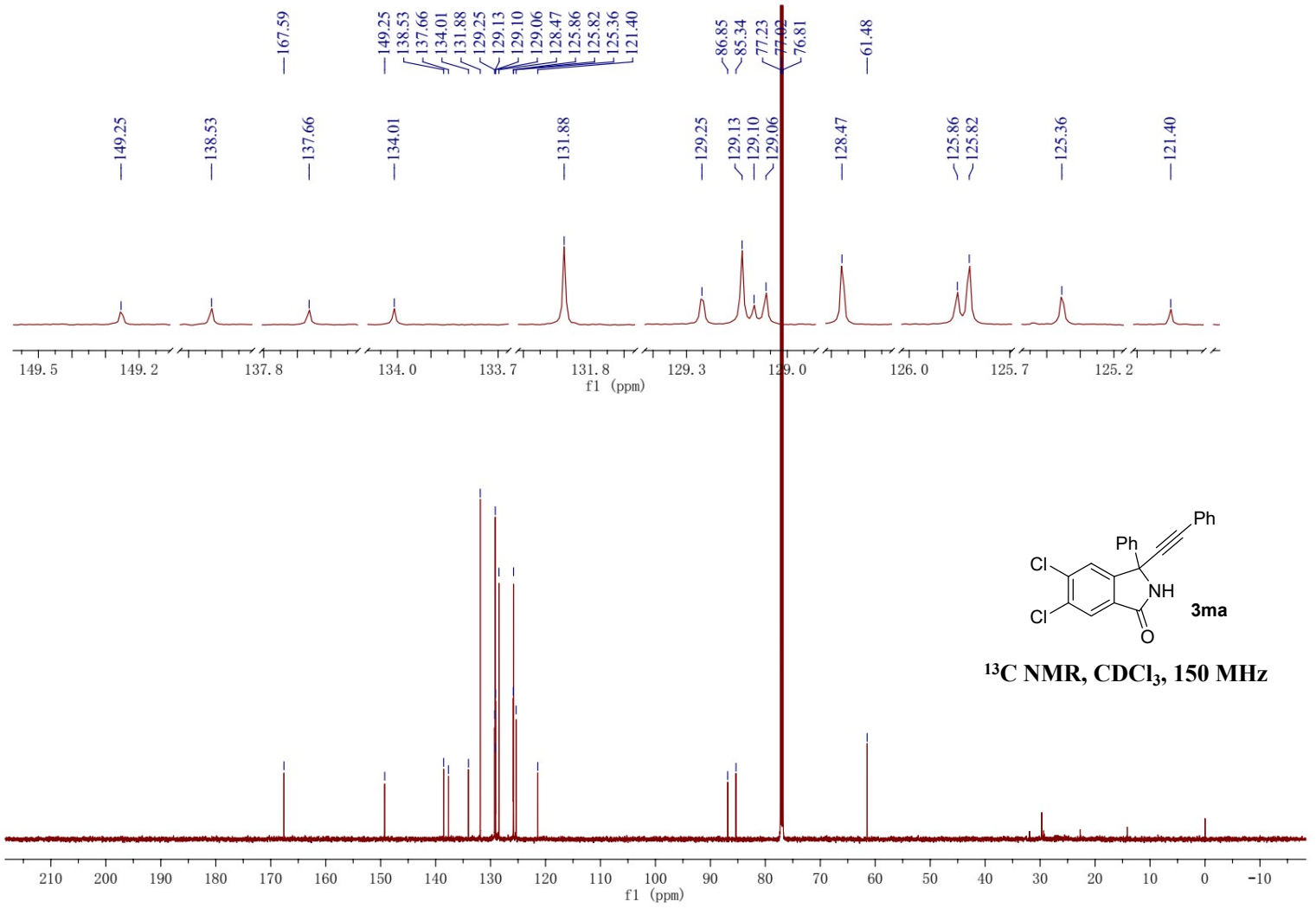




3ma

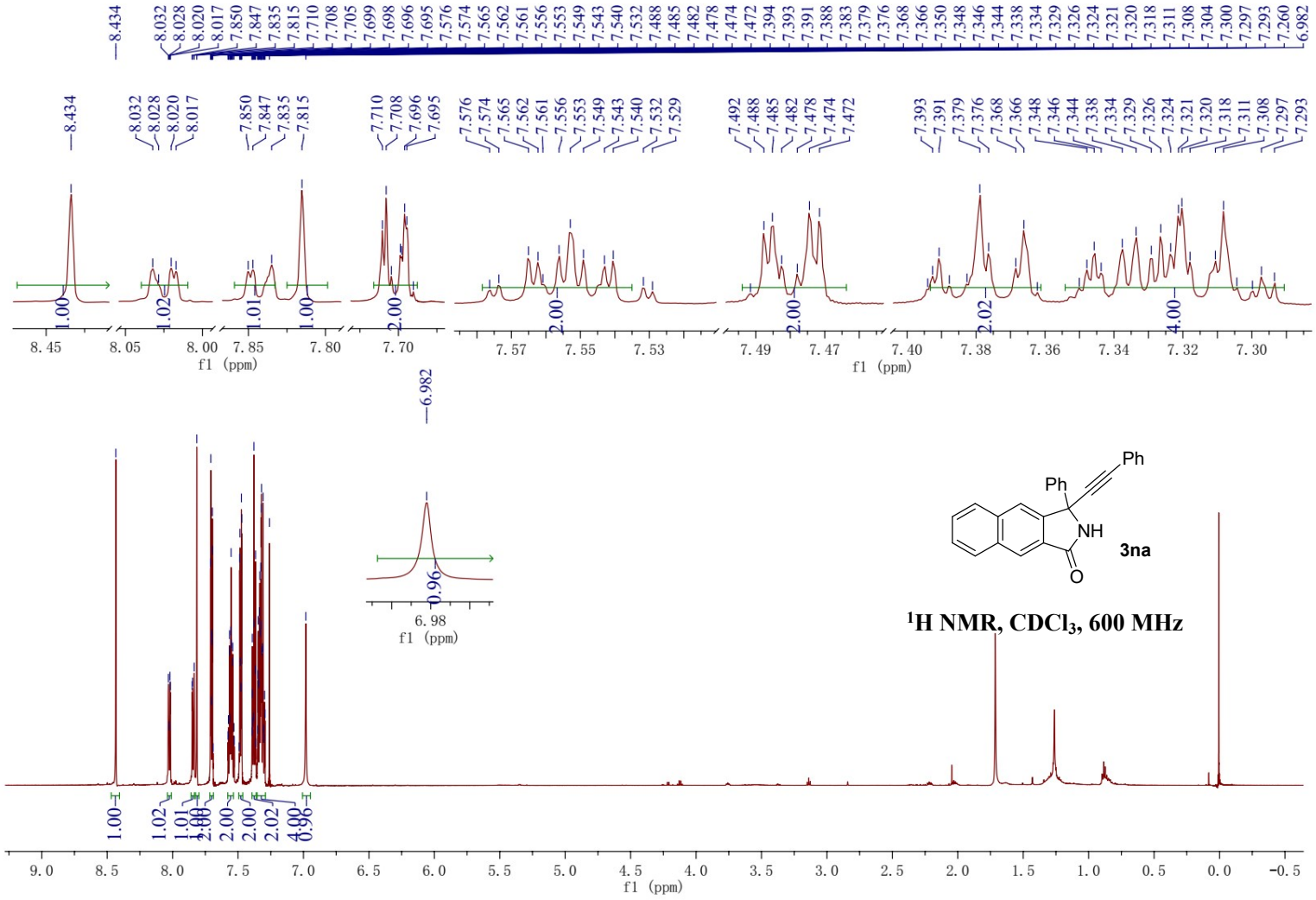
^{1}H NMR, $CDCl_3$, 600 MHz

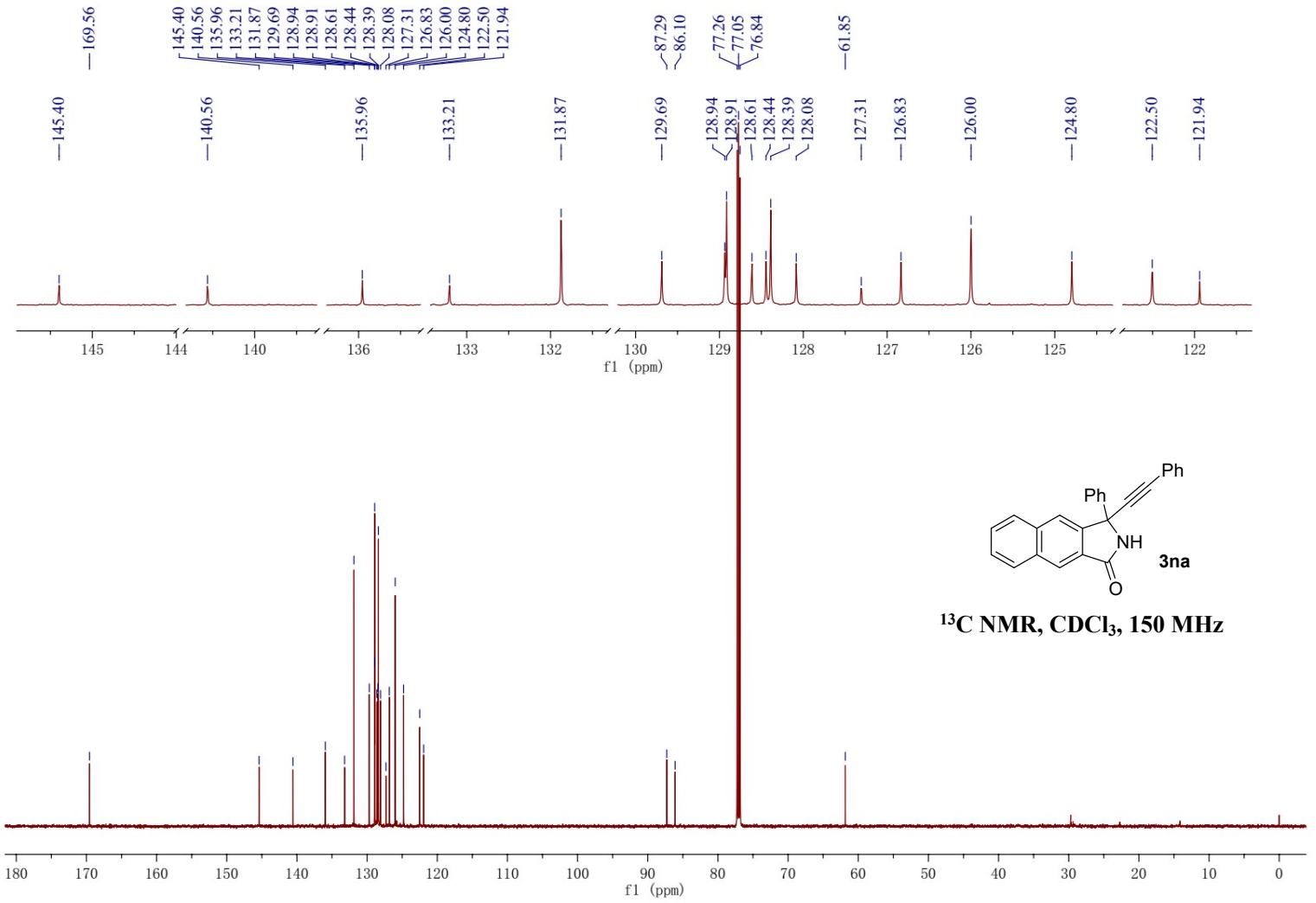




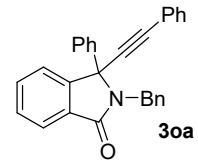
3ma

^{13}C NMR, $CDCl_3$, 150 MHz


Ph
Ph
NH
O
3na
^{1}H NMR, CDCl$_3$, 600 MHz

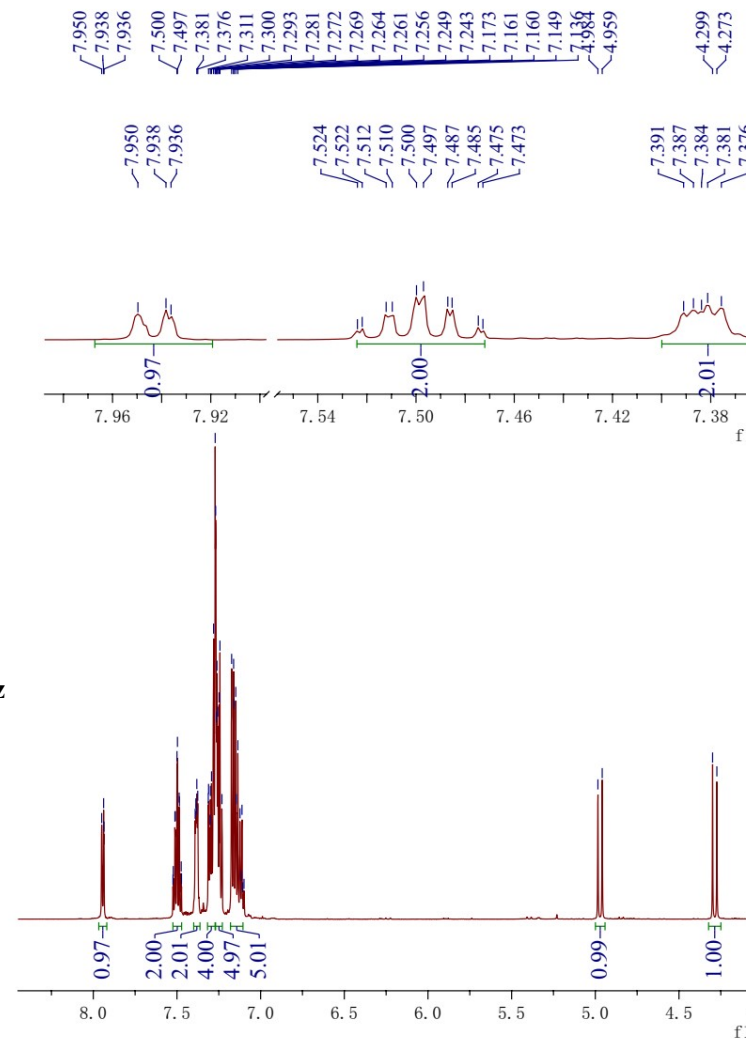


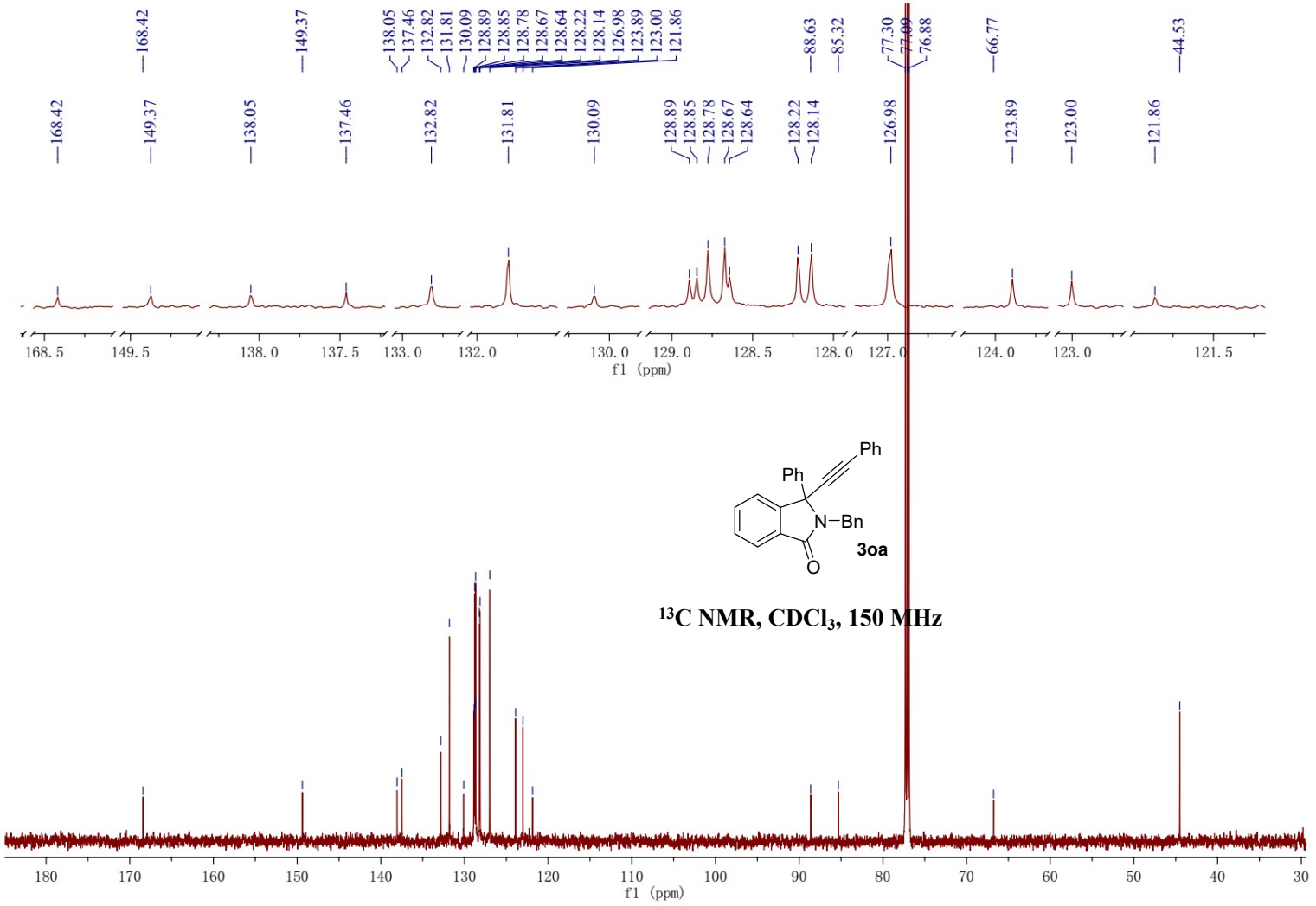
^{13}C NMR, $CDCl_3$, 150 MHz



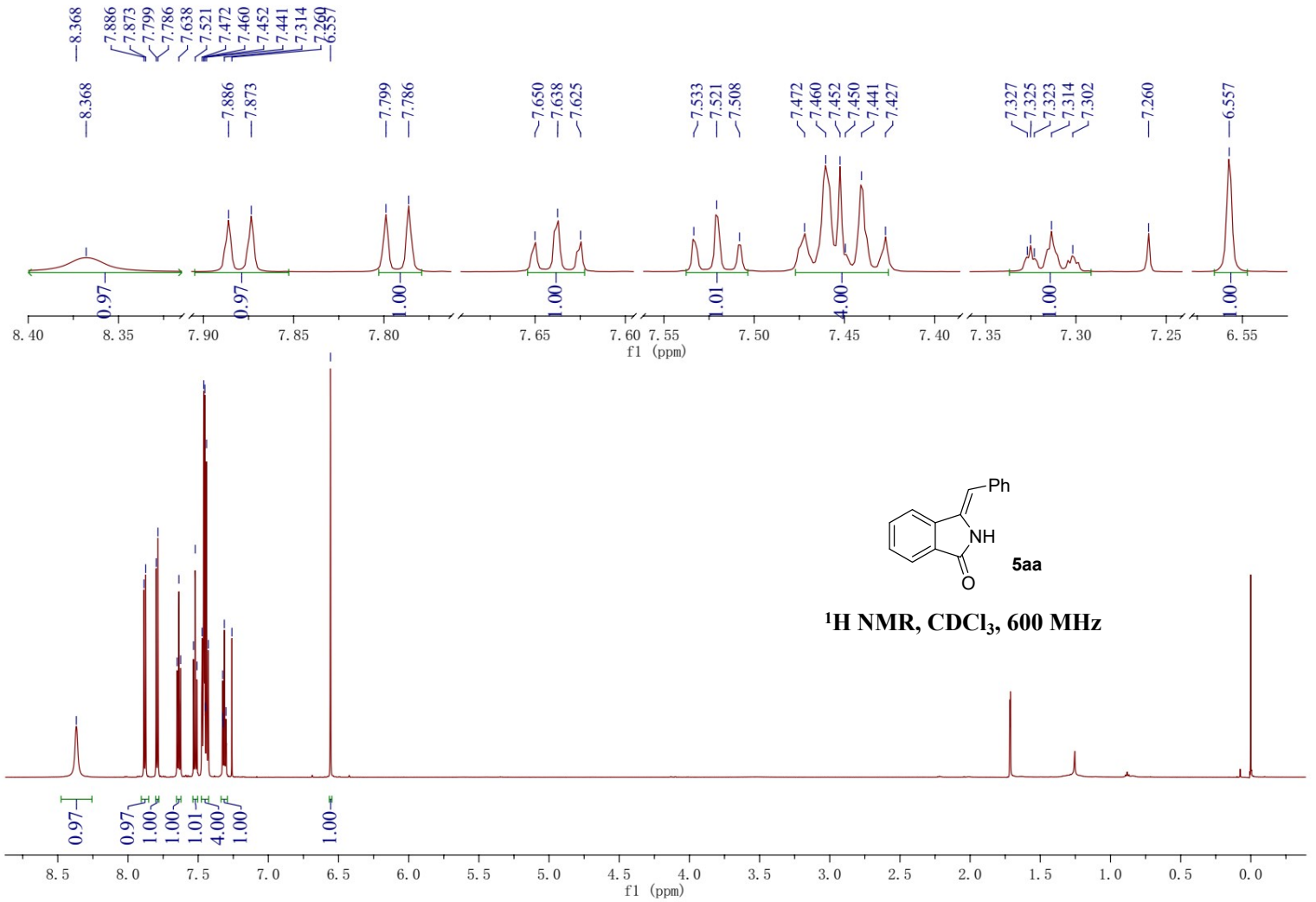
3oa

^{1}H NMR, $CDCl_3$, 600 MHz

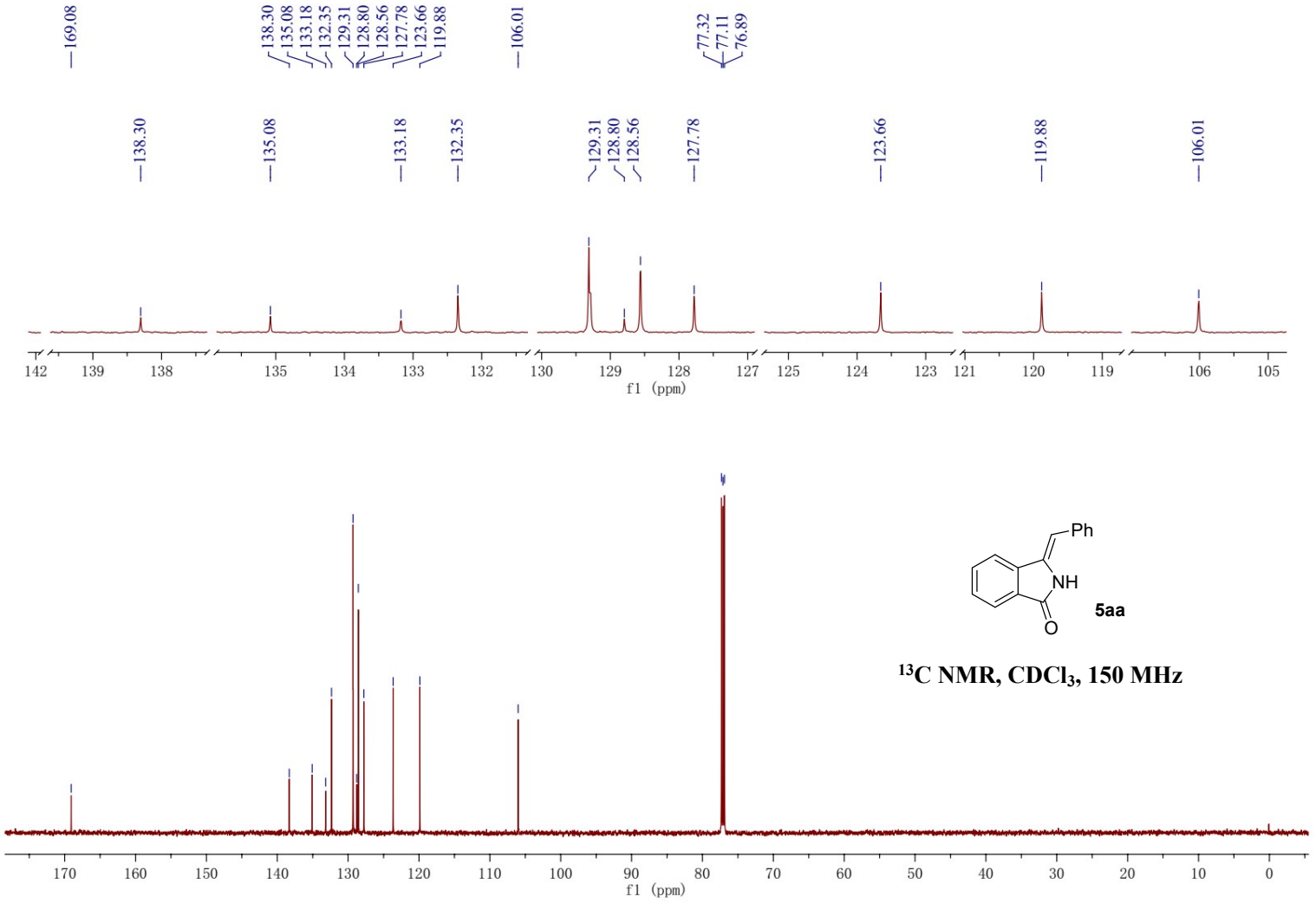




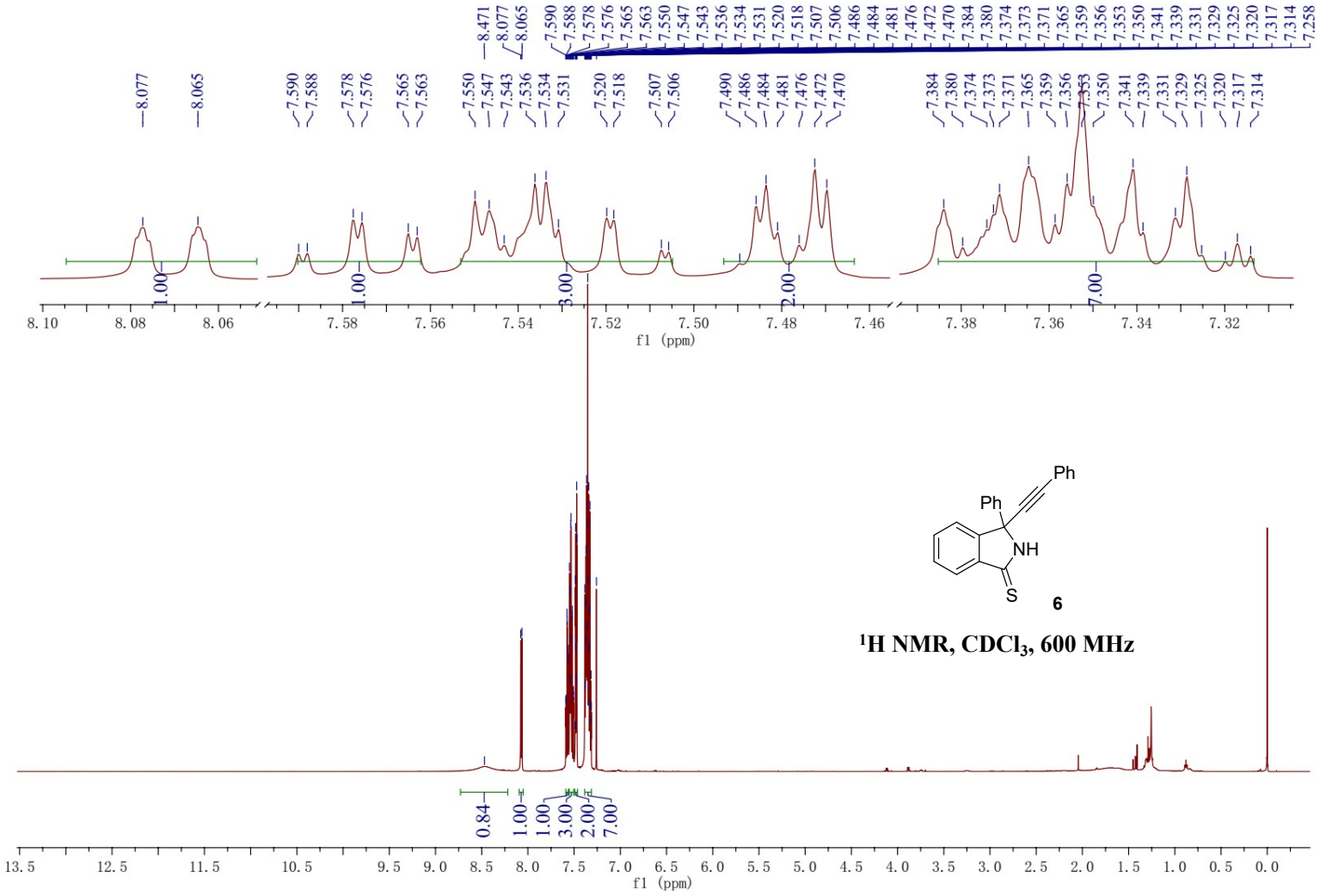
^{13}C NMR, $CDCl_3$, 150 MHz

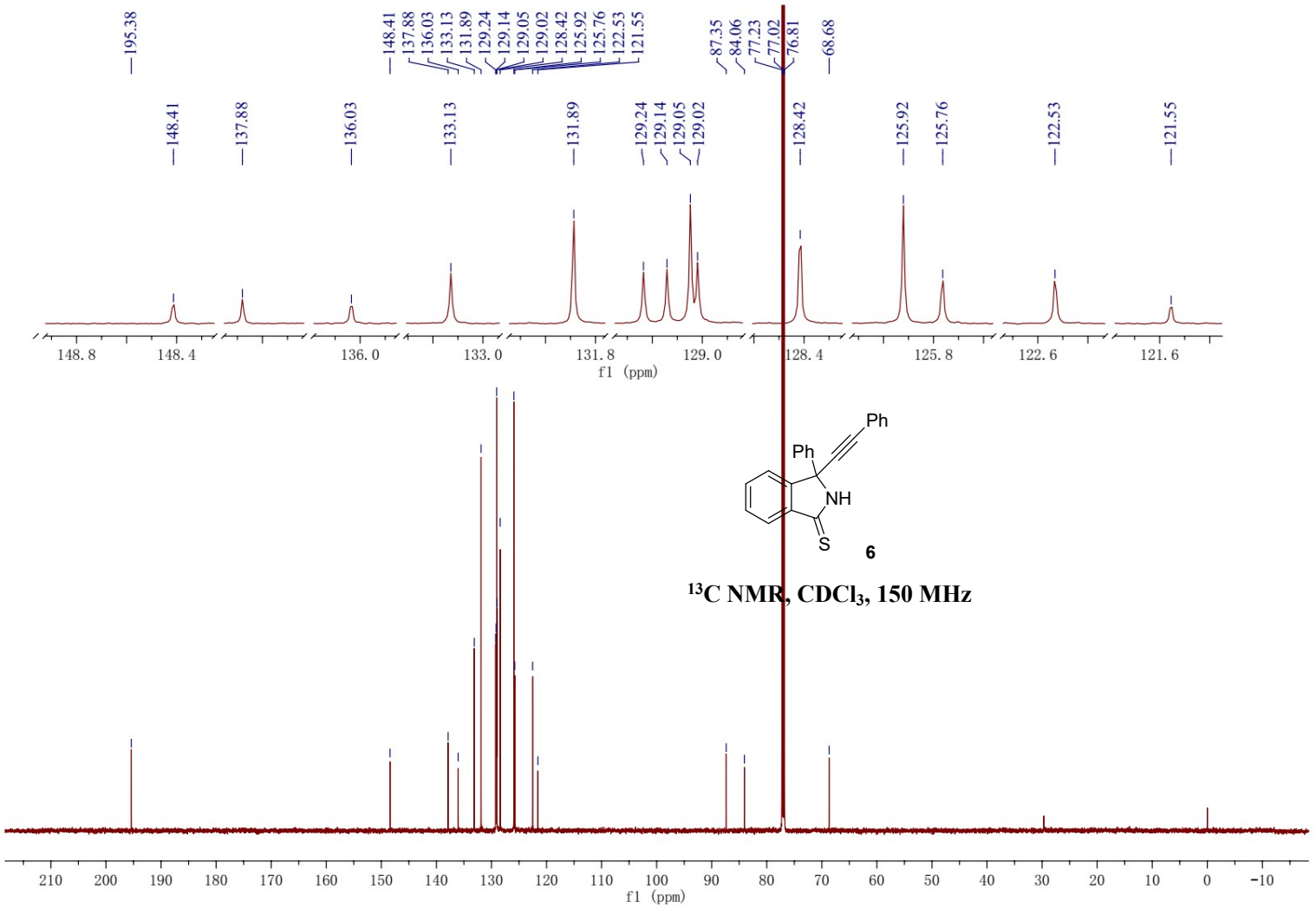


^{1}H NMR, $CDCl_3$, 600 MHz



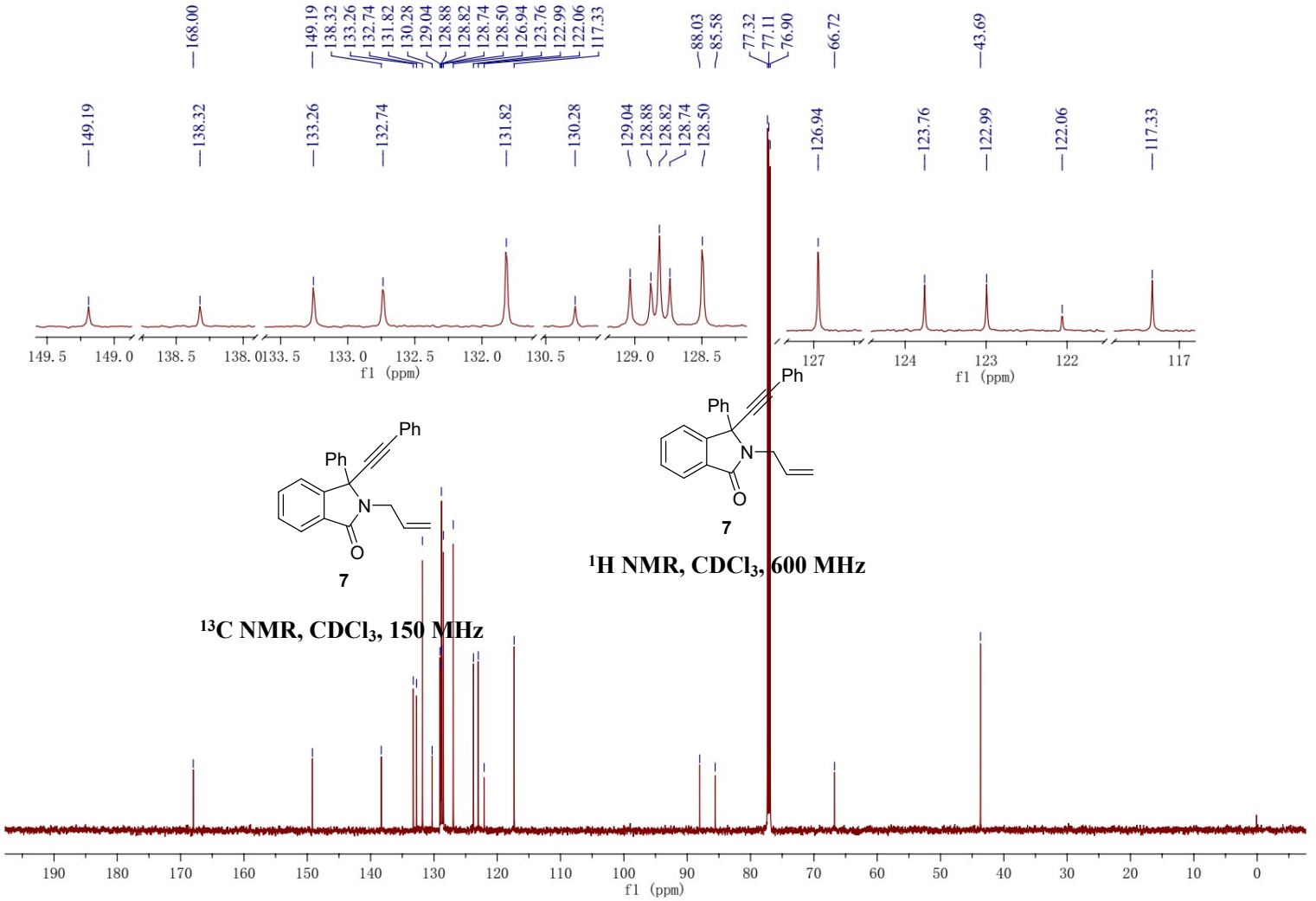
^{13}C NMR, $CDCl_3$, 150 MHz

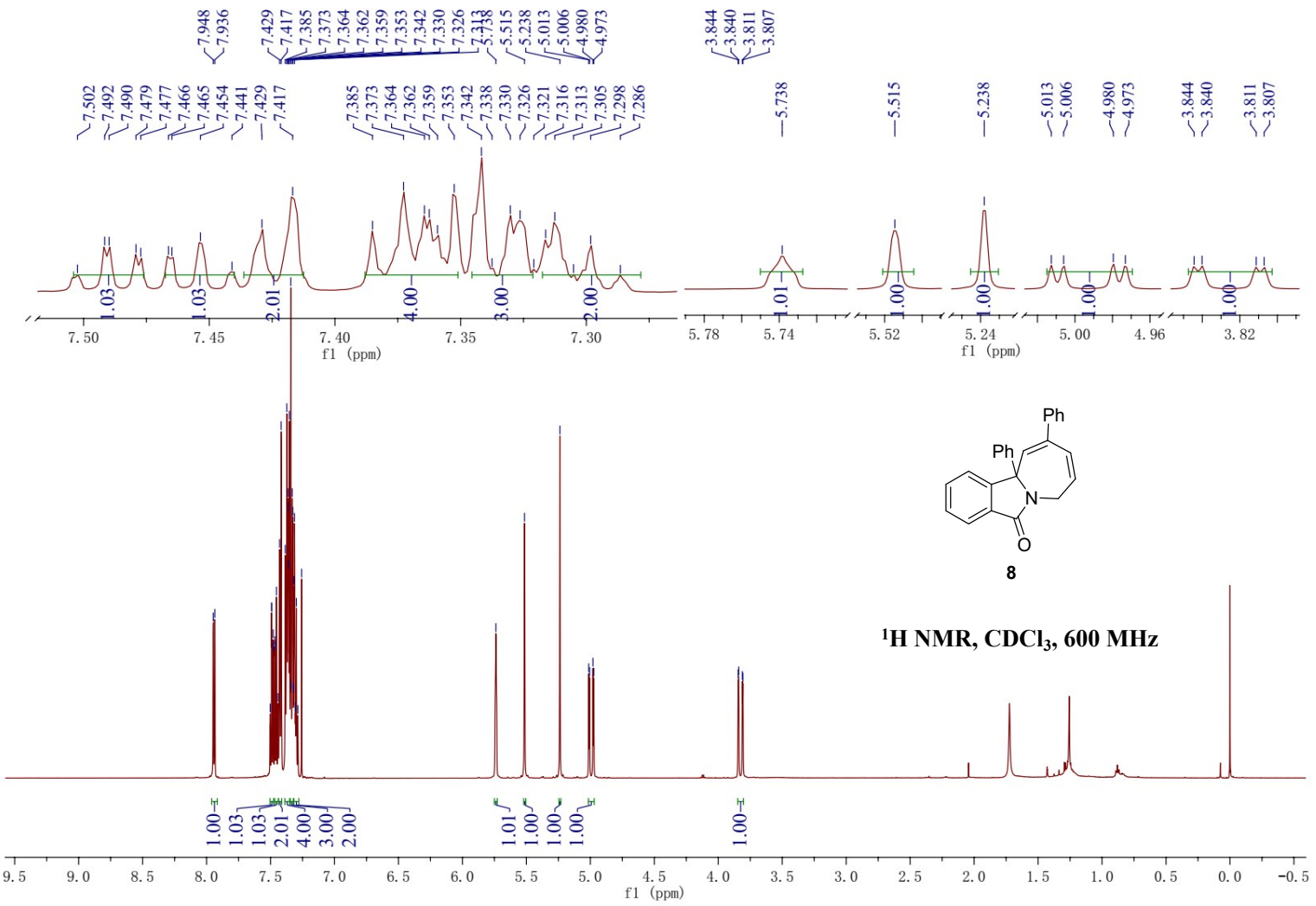

8.471
8.077
8.065
7.590
7.588
7.578
7.576
7.565
7.563
7.550
7.547
7.543
7.536
7.534
7.531
7.520
7.518
7.507
7.506
7.490
7.486
7.484
7.481
7.476
7.472
7.470
7.384
7.380
7.374
7.373
7.371
7.365
7.359
7.356
7.353
7.350
7.341
7.339
7.331
7.329
7.325
7.320
7.317
7.314
7.258
1.00
1.00
3.00
2.00
7.00
f1 (ppm)
0.84
1.00
1.00
3.00
2.00
7.00
f1 (ppm)
Ph
Ph
NH
S
6
^{1}H NMR, CDCl$_3$, 600 MHz

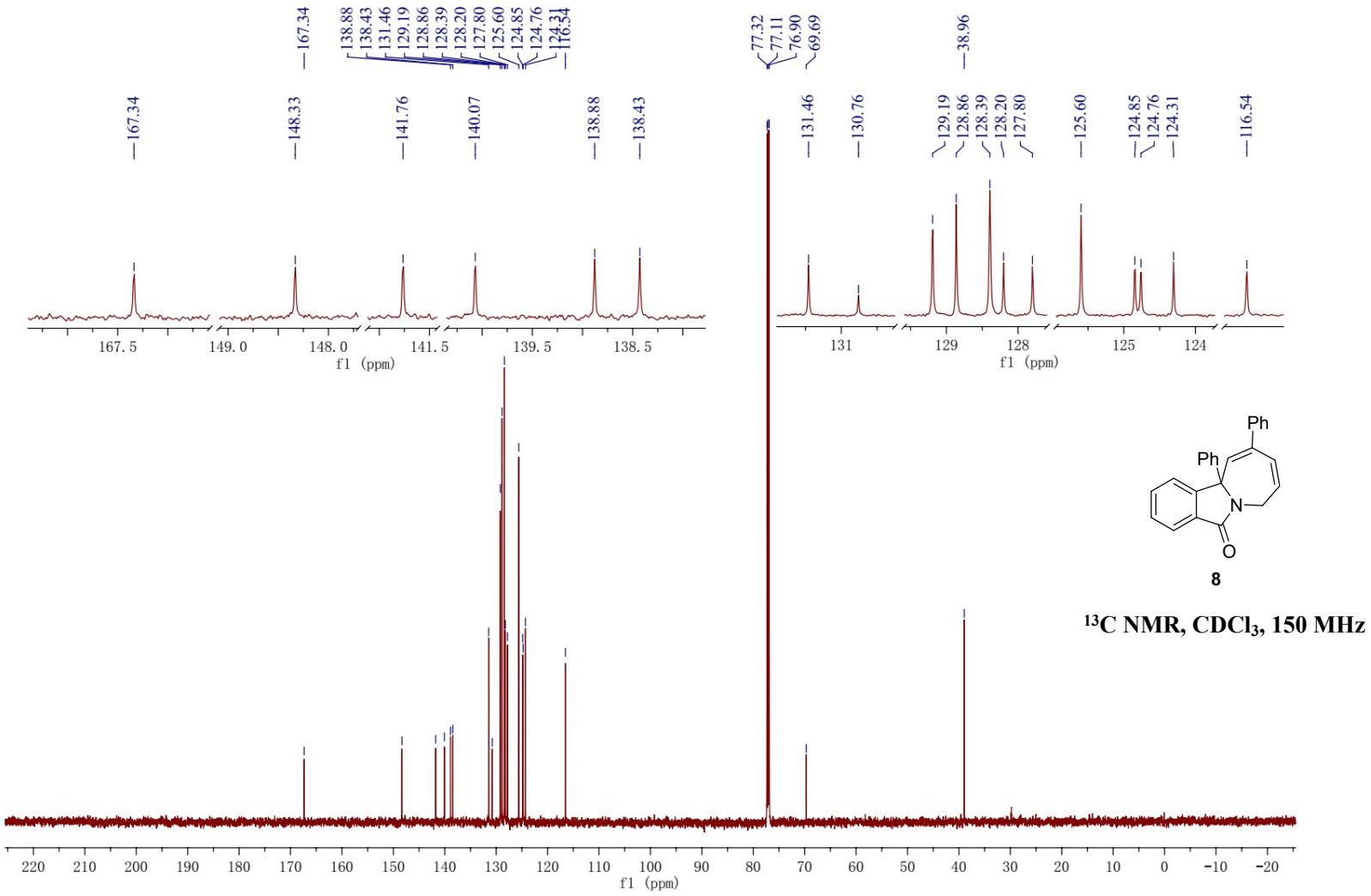


6

^{13}C NMR, $CDCl_3$, 150 MHz

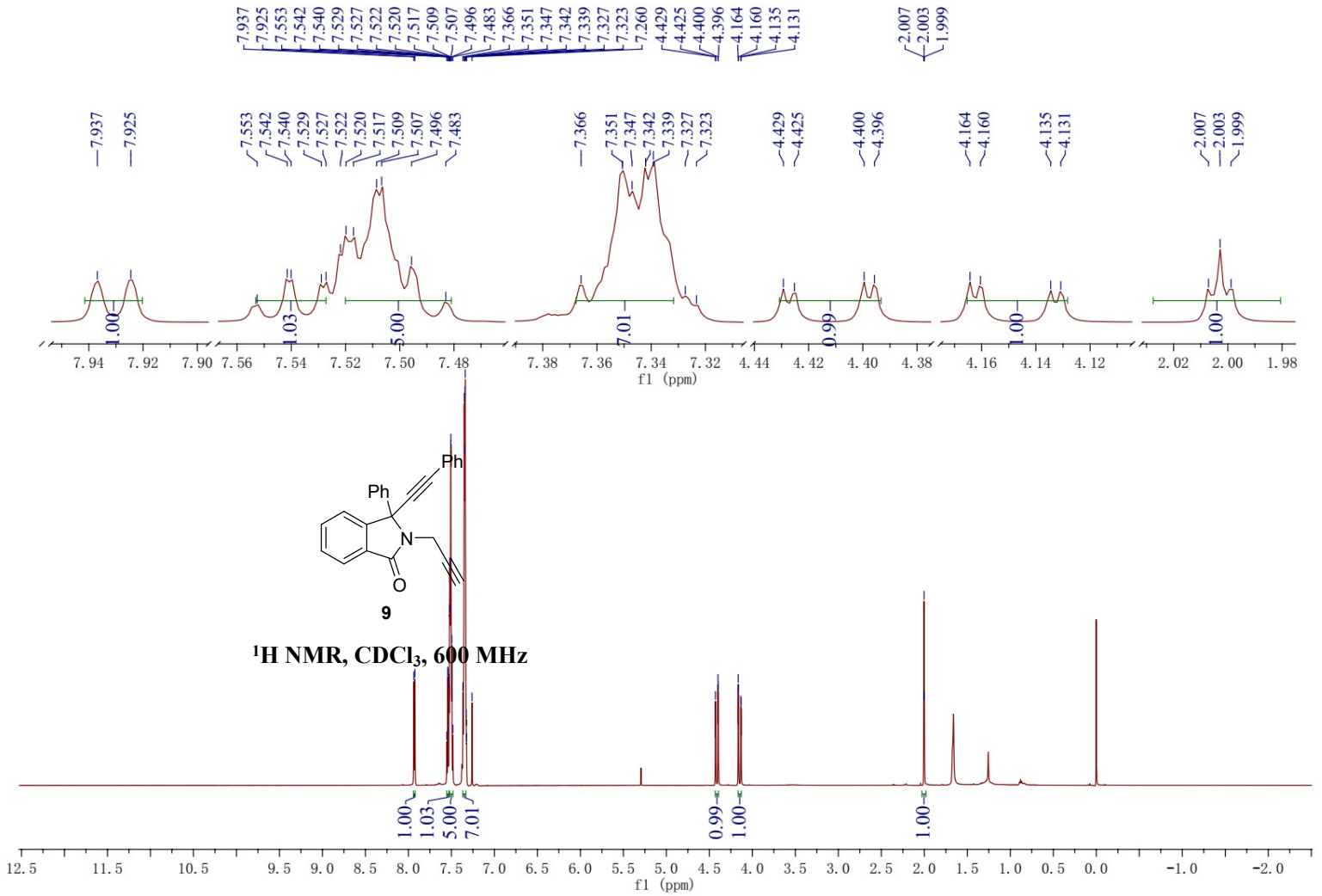

168.00
149.19
138.32
133.26
132.74
131.82
130.28
129.04
128.88
128.82
128.74
128.50
126.94
123.76
122.99
122.06
117.33
88.03
85.58
77.32
77.11
76.90
66.72
43.69
f1 (ppm)
Ph
Ph
N
O
7
13C NMR, CDCl3, 150 MHz
1H NMR, CDCl3, 600 MHz

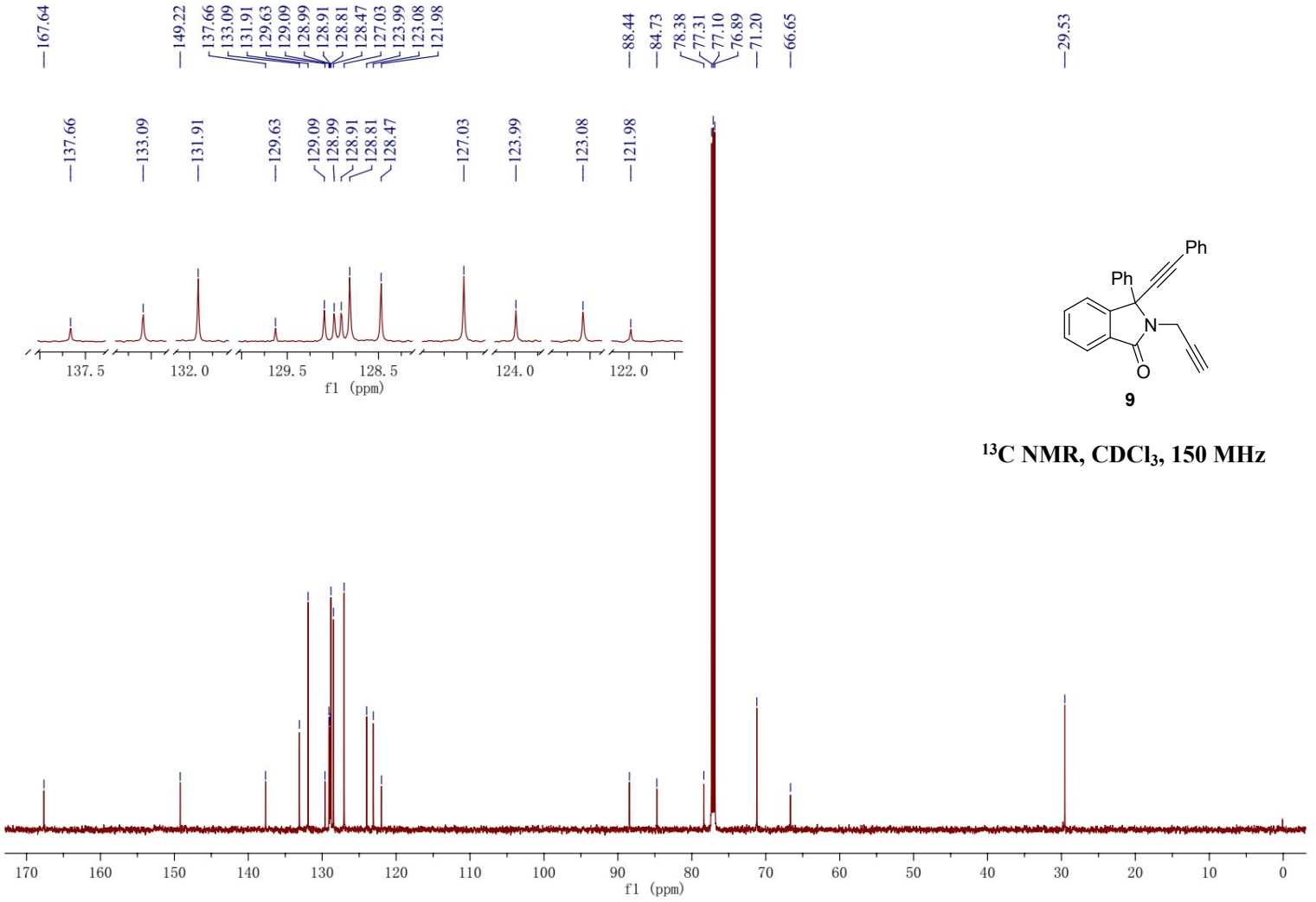

Ph
Ph
N
O
8
^{1}H NMR, $CDCl_3$, 600 MHz
f1 (ppm)



8

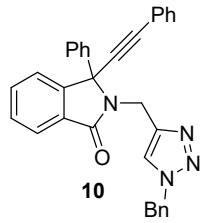
^{13}C NMR, $CDCl_3$, 150 MHz


7.937
7.925
7.553
7.542
7.540
7.529
7.527
7.522
7.520
7.517
7.509
7.507
7.496
7.483
7.366
7.351
7.347
7.342
7.339
7.327
7.323
7.260
4.429
4.425
4.400
4.396
4.164
4.160
4.135
4.131
2.007
2.003
1.999
1.00
1.03
5.00
7.01
0.99
1.00
1.00
f1 (ppm)
Ph
Ph
N
O
9
1H NMR, CDCl3, 600 MHz
1.00
1.03
5.00
7.01
0.99
1.00
1.00
f1 (ppm)



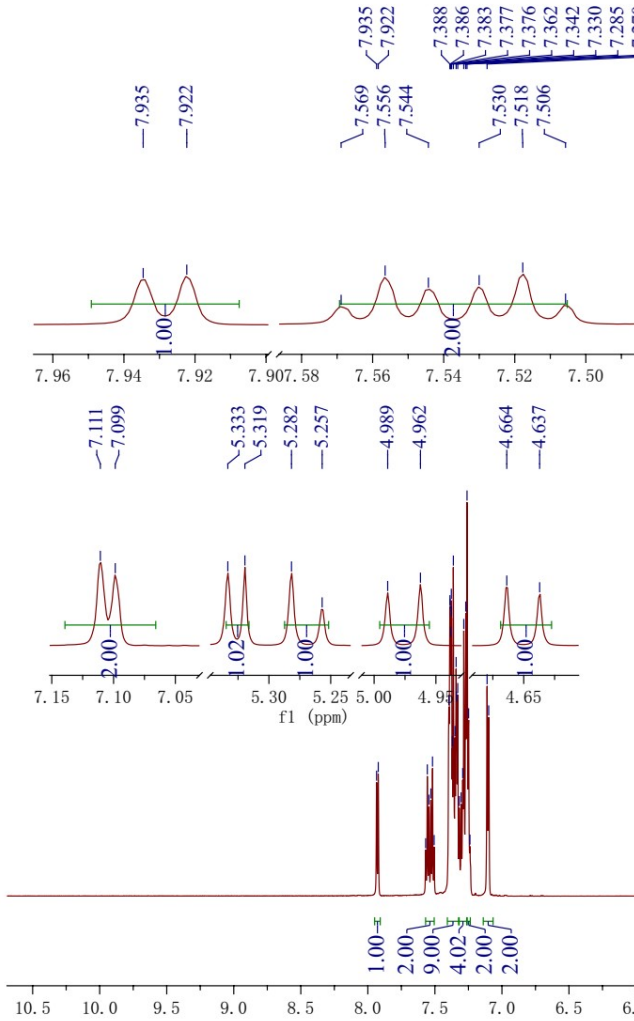
9

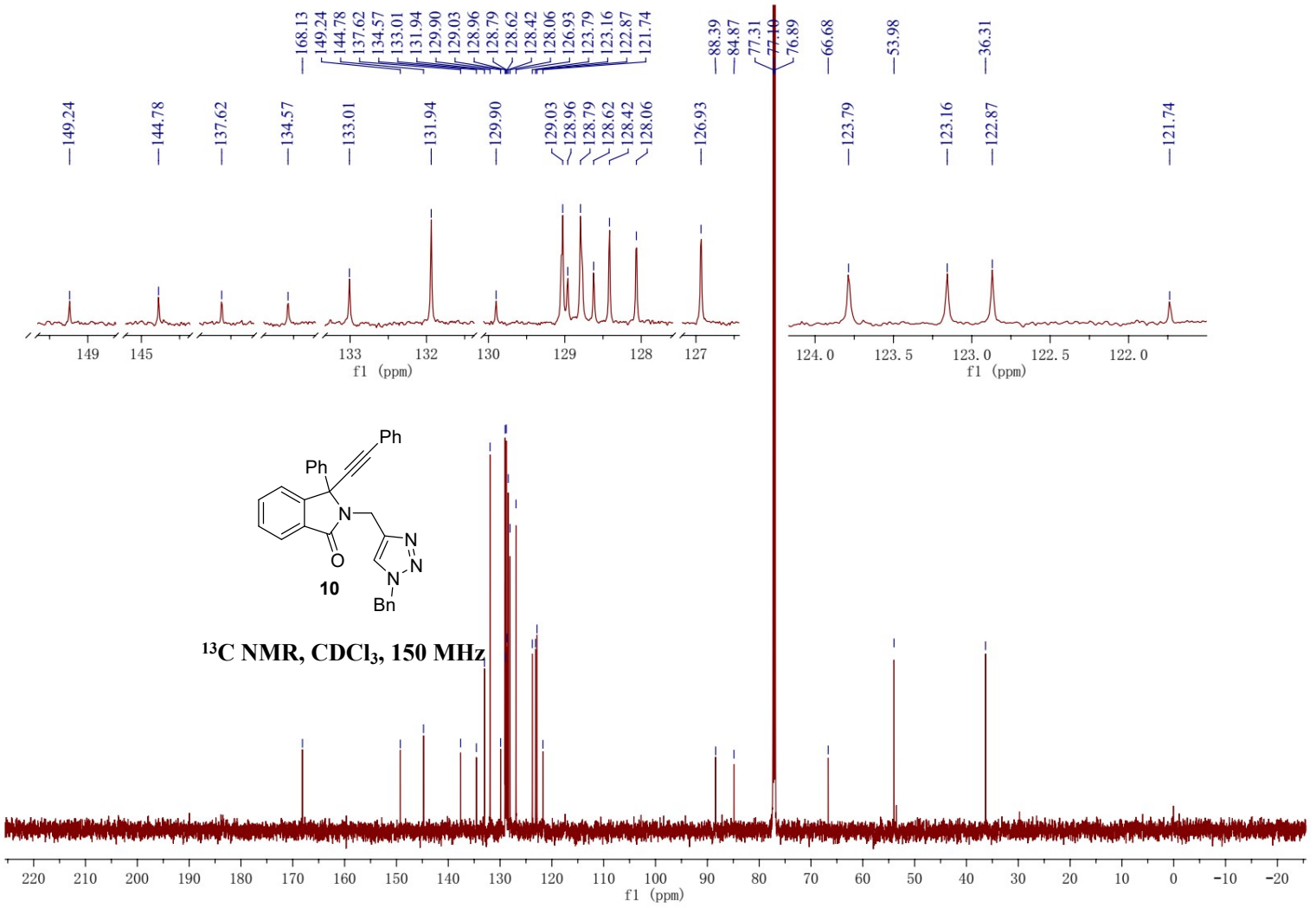
^{13}C NMR, $CDCl_3$, 150 MHz



10

^{1}H NMR, $CDCl_3$, 600 MHz




168.13
149.24
144.78
137.62
134.57
133.01
131.94
129.90
129.03
128.96
128.79
128.62
128.42
128.06
126.93
123.79
123.16
122.87
121.74
88.39
84.87
77.31
77.10
76.89
66.68
53.98
36.31
f1 (ppm)
Ph
Ph
N
O
N
N
N
Bn
10
13C NMR, CDCl3, 150 MHz