

Copper(II)-catalyzed Alkynylation of 2*H*-Chromene Hemiketals with Terminal Alkynes to 2,2-Disubstituted 2-Alkynylated 2*H*-Chromenes

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1. General information:

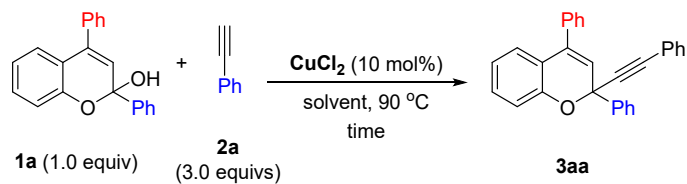
Reactions were monitored by thin layer chromatography using UV light to visualize the reaction course. Purification of reaction products were carried out by flash chromatography on silica gel H. Chemical yields refer to pure isolated substances. ^1H and ^{13}C NMR spectra were obtained using a Bruker 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.

All 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. 2*H*-chromene hemiacetals **1** were prepared according to the literature report.¹ CuCl_2 (99.999%) was purchased from Sigma-Aldrich and used as received.

1 a) Y.-C. Wu, H.-J. Li, L. Liu, N. Demoulin, Z. Liu, D. Wang and Y.-J. Chen, *Adv. Synth. Catal.*, 2011, **353**, 907; b) Y.-C. Wu, L. Liu, Y.-L. Liu, D. Wang and Y.-J. Chen, *J. Org. Chem.* 2007, **72**, 9383; c) M. Terada, T. Yamanaka and Y. Toda, *Chemical Engineering Journal.*, 2013, **19**, 13658.

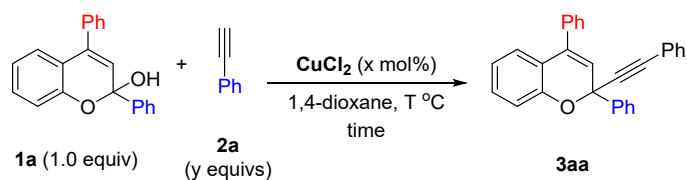
2. Condition optimization

2.1 Solvent screening



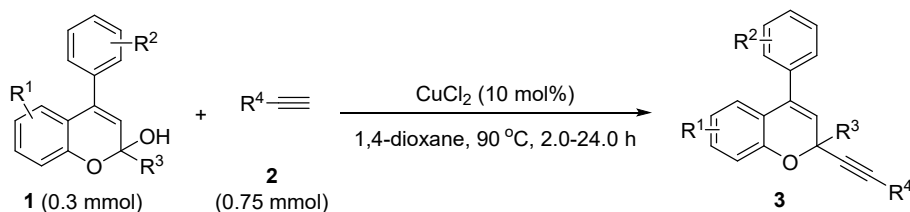
Entry	Solvent	Time (h)	Yield (%)
1	DCE	3	82
2	DCM	6	73
3	1,1,2-Trichloroethane	4	78
4	Toluene	4	53
5	CH_3CN	7	47
6	CH_3NO_2	10	40
7	DMF	10	30
8	$\text{CH}_3\text{CO}_2\text{Et}$	4	70
9	THF	4	72
10	1,4-Dioxane	1.5	83
11	DME	3	76
12	$\text{}^n\text{Bu}_2\text{O}$	24	21
13	18-Crown-6	6	61
14	Tetrahydropyran	4	68

2.2 Temperature, catalyst loading and the amount of ethynylbenzene screening

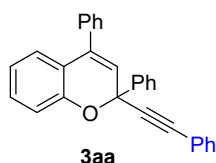


Entry	x	y	Temperature (°C)	Time (h)	Yield (%)
1	10	3.0	90	1.5	83
2	15	3.0	90	1.5	77
3	20	3.0	90	1.5	76
4	10	2.5	90	2.0	83
5	10	2.0	90	2.0	76
6	10	3.0	60	27	25
7	10	3.0	100	1	79
8	10	3.0	120	0.25	73

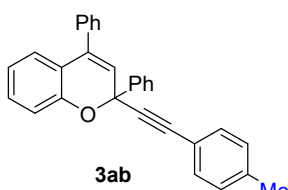
2. General procedure for the alkylation of 2*H*-chromene hemiketals with terminal alkynes to 2,2-disubstituted 2-alkynylated 2*H*-chromenes



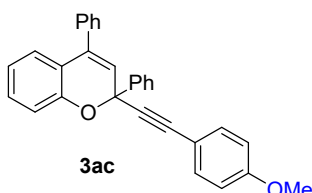
The reaction was carried out under an air atmosphere. To a 10-mL vial were added 2*H*-chromene hemiketals **1** (0.3 mmol, 1.0 equiv), alkynes **2** (0.75 mmol, 2.5 equivs) and 3.0 mL of anhydrous 1,4-dioxane. After adding CuCl₂ (4.0 mg, 10 mol%), the reaction mixture was stirred at 90 °C till almost full conversion of **1** by TLC analysis. The reaction mixture was directly subjected to column chromatography using petroleum ether as the eluent to afford the desired products **3**.



Column chromatography afforded the desired product **3aa** in 83% yield (95.7 mg) as yellow oil; ¹H NMR (400 MHz, CDCl₃): δ = 7.88-7.86 (m, 2H), 7.46-7.35 (m, 10H), 7.29-7.24 (m, 3H), 7.23-7.19 (m, 1H), 7.12-7.09 (m, 1H), 7.04-7.02 (m, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 5.92 (s, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃): δ = 152.5, 142.0, 137.6, 135.7, 131.9, 129.4, 128.8, 128.7, 128.52, 128.46, 128.4, 128.2, 128.1, 126.6, 125.9, 124.9, 122.3, 121.8, 121.5, 117.2, 88.12, 88.08, 76.1; HRMS (ESI): Exact mass calcd for C₂₈H₂₀O [M+H]⁺: 385.1587, Found: 385.1584.

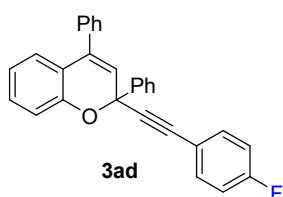


Column chromatography afforded product **3ab** in 71% yield (84.9 mg) as pale yellow oil; ¹H NMR (600 MHz, CDCl₃): δ = 7.88 (ABd, *J* = 7.2 Hz, 2H), 7.47-7.42 (m, 7H), 7.41-7.39 (m, 1H), 7.34 (ABd, *J* = 7.8 Hz, 2H), 7.24-7.21 (m, 1H), 7.13-7.10 (m, 3H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.92-6.90 (m, 1H), 5.93 (s, 1H), 2.34 (s, 3H); ¹³C {¹H} NMR (150 MHz, CDCl₃): δ = 152.5, 142.1, 138.8, 137.6, 135.6, 131.8, 129.7, 129.0, 128.8, 128.5, 128.43, 128.39, 128.0, 126.6, 125.9, 125.1, 121.8, 121.4, 119.2, 117.2, 88.4, 87.5, 76.2, 21.5; HRMS (ESI): Exact mass calcd for C₃₀H₂₂O [M+H]⁺: 399.1743, Found: 399.1744.



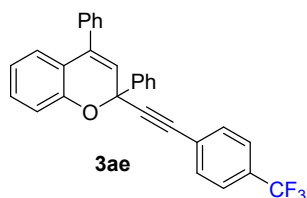
Column chromatography afforded **3ac** in 67% yield (83.3 mg) as yellow oil; ¹H NMR (600 MHz, CDCl₃): δ = 7.87-7.86 (m, 2H), 7.47-7.45 (m, 2H), 7.44-

7.40 (m, 5H), 7.39-7.37 (m, 3H), 7.23-7.20 (m, 1H), 7.12-7.10 (m, 1H), 7.03-7.02 (m, 1H), 6.92-6.89 (m, 1H), 6.82-6.81 (m, 2H), 5.92 (s, 1H), 3.80 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 159.9, 152.5, 142.2, 137.7, 135.5, 133.4, 129.7, 128.9, 128.42, 128.40, 128.0, 126.6, 125.9, 125.2, 121.8, 121.4, 117.2, 114.4, 113.8, 88.2, 86.8, 76.2, 55.3$; HRMS (ESI): Exact mass calcd for $\text{C}_{30}\text{H}_{22}\text{O}_2$ $[\text{M}+\text{H}]^+$: 415.1693, Found: 415.1694.

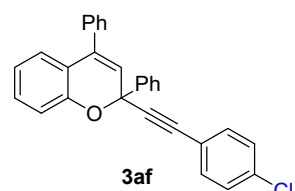


Column chromatography afforded **3ad** in 58% yield (70.0 mg) as yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.86-7.84$ (m, 2H), 7.46-7.44 (m, 3H), 7.43-7.40 (m, 6H), 7.38-7.35 (m, 1H), 7.24-7.21 (m, 1H), 7.12 (dd, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.03 (d, $J = 8.4$ Hz, 1H), 7.00-6.97 (m, 2H), 6.91 (t, $J = 7.8$ Hz, 1H), 5.92

(s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 162.7$ (d, $J_{\text{C-F}} = 249.0$ Hz), 152.4, 141.9, 137.6, 135.8, 133.9 (d, $J_{\text{C-F}} = 7.5$ Hz), 129.8, 128.8, 128.6, 128.5, 128.4, 128.1, 126.6, 126.0, 124.8, 121.8, 121.5, 118.4, 117.2, 115.5 (d, $J_{\text{C-F}} = 22.5$ Hz), 87.9, 87.0, 76.1; $^{19}\text{F}\{^1\text{H}\}$ NMR (565 MHz, CDCl_3): $\delta = -110.1$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{FO}$ $[\text{M}+\text{H}]^+$: 403.1493, Found: 403.1493.



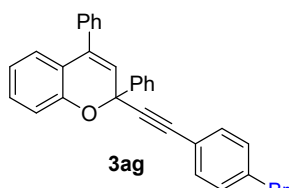
Column chromatography afforded the desired product **3ae** in 57% yield (77.4 mg) as yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.86-7.84$ (m, 2H), 7.56-7.52 (m, 4H), 7.47-7.44 (m, 4H), 7.43-7.40 (m, 3H), 7.39-7.38 (m, 1H), 7.25-7.23 (m, 1H), 7.13 (dd, $J = 7.8$ Hz, 1.8 Hz, 1H), 7.05 (dd, $J = 8.4$ Hz, 1.2 Hz, 1H), 6.93 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 5.93 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.4, 141.6, 137.5, 136.1, 132.1, 130.4$ (q, $J_{\text{C-F}} = 33.0$ Hz), 129.9, 128.8, 128.7, 128.6, 128.5, 128.2, 126.5, 126.12, 126.07, 125.2 (q, $J_{\text{C-F}} = 3.0$ Hz), 124.4, 121.8, 121.7, 117.2, 90.7, 86.6, 76.0; $^{19}\text{F}\{^1\text{H}\}$ NMR (565 MHz, CDCl_3): $\delta = -62.8$; HRMS (ESI): Exact mass calcd for $\text{C}_{30}\text{H}_{19}\text{F}_3\text{O}$ $[\text{M}+\text{H}]^+$: 453.1461, Found: 453.1462.



Column chromatography afforded the desired product **3af** in 75% yield (94.2 mg) as white solid; Mp: 99-101 °C; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.85$ (ABd, $J = 7.8$ Hz, 2H), 7.46-7.36 (m, 11H), 7.274-7.272 (m, 1H), 7.24-7.21 (m, 1H), 7.12-7.11 (m, 1H), 7.04-7.03 (m, 1H), 6.93-6.90 (m, 1H), 5.92 (s, 1H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.4, 141.8, 137.5, 135.9, 133.1, 129.8, 128.8, 128.6, 128.5, 128.4, 128.1, 126.5, 126.0, 124.7, 121.7, 121.6, 120.8, 117.1, 89.2, 86.9, 76.1$; HRMS (ESI): Exact mass

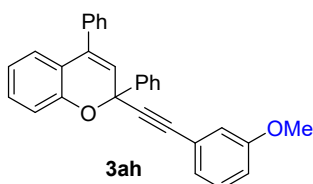
calcd for C₂₉H₁₉ClO [M+H]⁺: 419.1197, Found: 419.1197.



Product **3ag** was obtained in 67% yield (93.1 mg) as white solid; Mp: 42-44 °C;

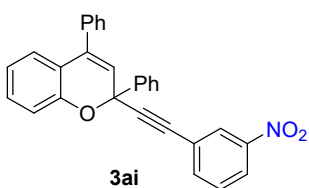
¹H NMR (600 MHz, CDCl₃): δ = 7.86-7.84 (m, 2H), 7.46-7.42 (m, 8H), 7.41-7.39 (m, 1H), 7.38-7.37 (m, 1H), 7.30-7.28 (m, 2H), 7.24-7.22 (m, 1H), 7.12 (dd, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.92 (td, *J* = 7.8 Hz, 1.2 Hz, 1H), 5.92 (s, 1H);

¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 152.5, 141.9, 137.6, 136.0, 133.4, 131.6, 129.9, 128.9, 128.7, 128.6, 128.5, 128.2, 126.6, 126.1, 124.7, 123.1, 121.8, 121.7, 121.3, 117.2, 89.4, 87.0, 76.2; HRMS (ESI): Exact mass calcd for C₂₉H₁₉BrO [M+H]⁺: 463.0692, Found: 463.0673.



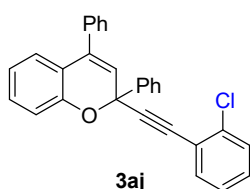
Column chromatography afforded product **3ah** in 67% yield (83.3 mg) as yellow oil; ¹H NMR (600 MHz, CDCl₃): δ = 7.88-7.86 (m, 2H), 7.47-7.42 (m, 7H), 7.41-7.37 (m, 2H), 7.23-7.19 (m, 2H), 7.13-7.11 (m, 1H), 7.05-7.03 (m, 2H), 6.97-6.96 (m, 1H), 6.92 (td, *J* = 7.8 Hz, 1.2 Hz, 1H), 6.88 (dd, *J* = 8.4 Hz, 3.0 Hz, 1H), 5.93 (s, 1H), 3.78 (s, 3H);

¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 159.2, 152.5, 142.0, 137.6, 135.7, 129.8, 129.3, 128.8, 128.53, 128.47, 128.4, 128.1, 126.6, 126.0, 124.9, 124.5, 123.3, 121.8, 121.5, 117.2, 116.6, 115.3, 88.04, 87.96, 76.2, 55.3; HRMS (ESI): Exact mass calcd for C₃₀H₂₂O₂ [M+H]⁺: 415.1693, Found: 415.1694.



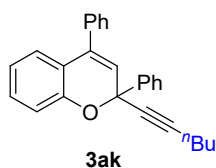
Column chromatography afforded the desired product **3ai** in 67% yield (86.3 mg) as yellow oil; ¹H NMR (600 MHz, CDCl₃): δ = 8.28-8.279 (m, 1H), 8.17-8.15 (m, 1H), 7.86-7.85 (m, 2H), 7.73-7.71 (m, 1H), 7.49-7.44 (m, 7H), 7.42-7.41 (m, 1H), 7.40-7.39 (m, 1H), 7.27-7.24 (m, 1H), 7.14 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.95-6.93 (m, 1H), 5.93 (s, 1H);

¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 152.3, 148.0, 141.4, 137.6, 137.4, 136.3, 130.0, 129.3, 128.81, 128.75, 128.6, 128.5, 128.2, 126.7, 126.5, 126.1, 124.2, 124.1, 123.4, 121.8, 121.7, 117.2, 90.9, 85.4, 75.9; HRMS (ESI): Exact mass calcd for C₂₉H₁₉NO₃ [M+H]⁺: 430.1438, Found: 430.1440.

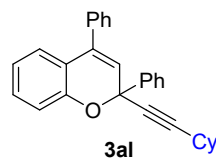


Column chromatography afforded the desired product **3aj** in 59% yield (74.1 mg) as yellow oil; ¹H NMR (600 MHz, CDCl₃): δ = 7.93-7.91 (m, 2H), 7.46-7.42 (m,

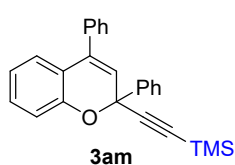
7H), 7.41-7.36 (m, 3H), 7.25-7.22 (m, 2H), 7.19-7.16 (m, 1H), 7.13-7.12 (m, 1H), 7.06-7.04 (m, 1H), 6.93 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 5.94 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.5, 141.6, 137.6, 136.4, 136.0, 133.4, 129.8, 129.6, 129.2, 128.9, 128.6, 128.5, 128.4, 128.1, 126.8, 126.3, 126.0, 124.9, 122.4, 122.0, 121.6, 117.3, 93.1, 85.1, 76.3$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{ClO}$ $[\text{M}+\text{H}]^+$: 419.1197, Found: 419.1199.



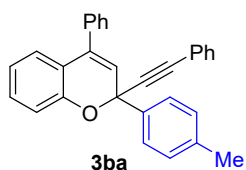
Column chromatography afforded the desired product **3ak** in 70% yield (76.5 mg) as pale yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.81$ -7.79 (m, 2H), 7.43-7.38 (m, 7H), 7.34-7.32 (m, 1H), 7.22-7.19 (m, 1H), 7.09-7.08 (m, 1H), 7.00-6.99 (m, 1H), 6.90-6.88 (m, 1H), 5.84 (s, 1H), 2.29-2.27 (m, 2H), 1.50-1.46 (m, 2H), 1.38-1.32 (m, 2H), 0.86 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.7, 142.4, 137.8, 135.2, 129.6, 128.9, 128.45, 128.39, 128.0, 126.7, 125.9, 122.0, 121.4, 117.2, 89.7, 79.5, 76.0, 30.6, 21.9, 18.8, 13.6$; HRMS (ESI): Exact mass calcd for $\text{C}_{27}\text{H}_{24}\text{O}$ $[\text{M}+\text{H}]^+$: 365.1900, Found: 365.1900.



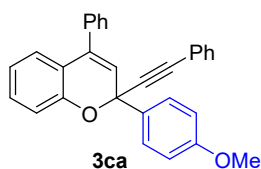
Column chromatography afforded the desired product **3al** in 75% yield (78.4 mg) as pale yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.77$ -7.75 (m, 2H), 7.42-7.37 (m, 7H), 7.33-7.31 (m, 1H), 7.21-7.18 (m, 1H), 7.08 (dd, $J = 7.8$ Hz, 1.8 Hz, 1H), 6.99-6.97 (m, 1H), 6.89 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 5.81 (s, 1H), 1.33-1.30 (m, 1H), 0.80-0.77 (m, 2H), 0.72-0.70 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.6, 142.5, 137.8, 135.1, 129.7, 128.9, 128.45, 128.39, 128.1, 126.6, 125.9, 125.6, 121.8, 121.4, 117.2, 92.6, 75.9, 74.5, 8.7, 0.1$; HRMS (ESI): Exact mass calcd for $\text{C}_{26}\text{H}_{20}\text{O}$ $[\text{M}+\text{H}]^+$: 349.1587, Found: 349.1588.



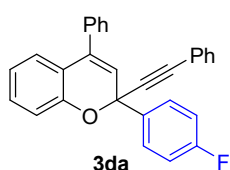
Column chromatography afforded **3am** in 52% yield (59.4 mg) as pale yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.79$ -7.78 (m, 2H), 7.43-7.42 (m, 4H), 7.41-7.40 (m, 1H), 7.39-7.38 (m, 2H), 7.35-7.34 (m, 1H), 7.21-7.18 (m, 1H), 7.08 (dd, $J = 7.8$ Hz, 1.2 Hz, 1H), 6.99-6.97 (m, 1H), 6.90-6.87 (m, 1H), 5.83 (s, 1H), 0.17 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.5, 141.8, 137.7, 135.6, 129.7, 128.9, 128.6, 128.48, 128.46, 128.1, 126.7, 125.9, 125.0, 121.8, 121.4, 117.2, 104.1, 93.4, 76.1, 0.1$; HRMS (ESI): Exact mass calcd for $\text{C}_{26}\text{H}_{24}\text{OSi}$ $[\text{M}+\text{H}]^+$: 381.1669, Found: 381.1670.



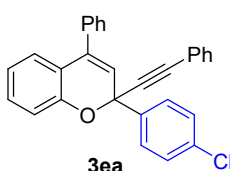
Column chromatography afforded product **3ba** in 67% yield (80.1 mg) as pale yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.77\text{-}7.75$ (m, 2H), 7.47-7.43 (m, 6H), 7.42-7.40 (m, 1H), 7.32-7.29 (m, 3H), 7.24-7.20 (m, 3H), 7.12 (dd, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.03 (d, $J = 7.8$ Hz, 1H), 6.91 (t, $J = 7.8$ Hz, 1H), 5.94 (s, 1H), 2.38 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.5, 139.0, 138.4, 137.7, 135.7, 131.9, 129.7, 129.1, 128.8, 128.6, 128.4, 128.2, 128.0, 126.6, 125.9, 125.0, 122.4, 121.8, 121.4, 117.2, 88.3, 87.9, 76.0, 21.2$; HRMS (ESI): Exact mass calcd for $\text{C}_{30}\text{H}_{22}\text{O}$ $[\text{M}+\text{H}]^+$: 399.1743, Found: 399.1745.



Column chromatography afforded the desired product **3ca** in 51% yield (63.4 mg) as pale yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.81\text{-}7.78$ (m, 2H), 7.47-7.43 (m, 6H), 7.41-7.38 (m, 1H), 7.32-7.29 (m, 3H), 7.21 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.11 (dd, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.05 (d, $J = 8.4$ Hz, 1H), 6.95-6.94 (m, 2H), 6.90 (td, $J = 7.2$ Hz, 1.2 Hz, 1H), 5.93 (s, 1H), 3.82 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 159.8, 152.6, 137.8, 135.8, 134.1, 132.0, 129.8, 128.9, 128.7, 128.5, 128.3, 128.2, 128.1, 126.0, 125.0, 122.4, 121.9, 121.5, 117.2, 113.8, 88.3, 88.1, 75.9, 55.4$; HRMS (ESI): Exact mass calcd for $\text{C}_{30}\text{H}_{22}\text{O}_2$ $[\text{M}+\text{H}]^+$: 415.1693, Found: 415.1693.

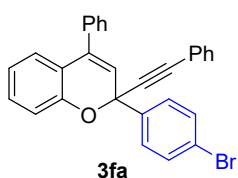


Column chromatography afforded the desired product **3da** in 62% yield (74.8 mg) as colorless oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.87\text{-}7.85$ (m, 2H), 7.47-7.41 (m, 7H), 7.33-7.28 (m, 3H), 7.23 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.13-7.09 (m, 3H), 7.04-7.02 (m, 1H), 6.93 (t, $J = 7.8$ Hz, 1H), 5.90 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 162.8$ (d, $J_{\text{C-F}} = 246.0$ Hz), 136.0, 131.9, 129.8, 128.81, 128.78, 128.6 (d, $J_{\text{C-F}} = 9.0$ Hz), 128.4, 128.24, 128.17, 126.0, 124.6, 122.1, 121.7, 121.6, 117.1, 115.3 (d, $J_{\text{C-F}} = 22.5$ Hz), 88.3, 87.8, 75.6; $^{19}\text{F}\{^1\text{H}\}$ NMR (565 MHz, CDCl_3): $\delta = -113.4$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{FO}$ $[\text{M}+\text{H}]^+$: 403.1493, Found: 403.1493.

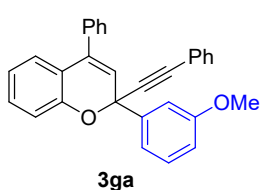


Column chromatography afforded the desired product **3ea** in 72% yield (90.5 mg) as pale yellow oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.81\text{-}7.79$ (m, 2H), 7.44-7.38 (m, 9H), 7.32-7.31 (m, 2H), 7.29-7.28 (m, 1H), 7.24-7.22 (m, 1H), 7.12-7.10 (m,

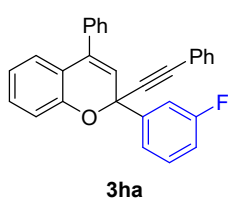
1H), 7.02 (d, $J = 7.8$ Hz, 1H), 6.93-6.91 (m, 1H), 5.89 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.2, 140.6, 137.4, 136.1, 134.5, 131.9, 129.9, 128.8, 128.6, 128.4, 128.25, 128.20, 128.1, 126.0, 124.3, 122.0, 121.7, 117.1, 88.3, 87.7, 75.6$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{ClO}$ $[\text{M}+\text{H}]^+$: 419.1197, Found: 419.1197.



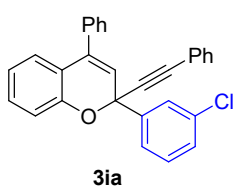
Column chromatography afforded product **3fa** in 52% yield (72.3 mg) as colorless oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.75\text{-}7.73$ (m, 2H), 7.56-7.54 (m, 2H), 7.44-7.41 (m, 7H), 7.33-7.28 (m, 3H), 7.23 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.11 (dd, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.03 (d, $J = 7.8$ Hz, 1H), 6.92 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 5.89 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.2, 141.1, 137.4, 136.1, 131.9, 131.6, 129.9, 128.8, 128.45, 128.4, 128.24, 128.20, 126.0, 124.3, 122.7, 122.0, 121.7, 117.1, 88.3, 87.7, 75.6$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{BrO}$ $[\text{M}+\text{H}]^+$: 463.0692, Found: 463.0692.



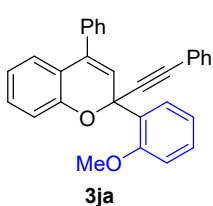
Column chromatography afforded the desired product **3ga** in 75% yield (93.3 mg) as colorless oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.47\text{-}7.43$ (m, 8H), 7.42-7.39 (m, 1H), 7.35 (t, $J = 7.8$ Hz, 1H), 7.32-7.28 (m, 3H), 7.25-7.22 (m, 1H), 7.12 (dd, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.06-7.04 (m, 1H), 6.93-6.90 (m, 2H), 5.93 (s, 1H), 3.84 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 159.6, 152.4, 143.5, 137.6, 135.7, 131.9, 129.7, 129.5, 128.8, 128.7, 128.4, 128.2, 128.1, 126.0, 124.9, 122.3, 121.8, 121.5, 119.0, 117.2, 114.0, 112.4, 88.04, 88.02, 76.0, 55.3$; HRMS (ESI): Exact mass calcd for $\text{C}_{30}\text{H}_{22}\text{O}_2$ $[\text{M}+\text{H}]^+$: 415.1693, Found: 415.1693.



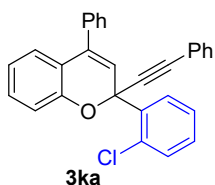
3ha was obtained in 68% yield (82.1 mg) as colorless oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.66\text{-}7.64$ (m, 1H), 7.60-7.57 (m, 1H), 7.46-7.44 (m, 6H), 7.42-7.41 (m, 1H), 7.40-7.39 (m, 1H), 7.33-7.29 (m, 3H), 7.25-7.23 (m, 1H), 7.13-7.12 (m, 1H), 7.08-7.04 (m, 2H), 6.95-6.92 (m, 1H), 5.90 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 162.7$ (d, $J_{\text{C-F}} = 244.5$ Hz), 152.4, 144.6 (d, $J_{\text{C-F}} = 7.5$ Hz), 137.4, 126.0, 131.9, 130.0 (d, $J_{\text{C-F}} = 7.5$ Hz), 129.9, 128.8, 128.4, 128.24, 128.2, 126.1, 124.3, 122.2 (d, $J_{\text{C-F}} = 3.0$ Hz), 121.71, 121.67, 117.1, 115.4 (d, $J_{\text{C-F}} = 21.0$ Hz), 113.9 (d, $J_{\text{C-F}} = 22.5$ Hz), 88.3, 87.6, 75.6; $^{19}\text{F}\{^1\text{H}\}$ NMR (565 MHz, CDCl_3): $\delta = -112.2$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{FO}$ $[\text{M}+\text{H}]^+$: 403.1493, Found: 403.1493.



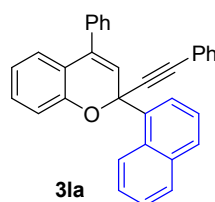
Column chromatography afforded **3ia** in 68% yield (85.4 mg) as colorless oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.86$ (t, $J = 1.8$ Hz, 1H), 7.76-7.74 (m, 1H), 7.45-7.44 (m, 6H), 7.42-7.40 (m, 1H), 7.36-7.31 (m, 5H), 7.26-7.23 (m, 1H), 7.13-7.12 (m, 1H), 7.06-7.04 (m, 1H), 6.95-6.92 (m, 1H), 5.88 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.2, 144.0, 137.3, 136.1, 134.4, 131.9, 129.9, 129.7, 128.84, 128.81, 128.7, 128.4, 128.24, 128.22, 126.9, 126.1, 124.8, 124.2, 122.0, 121.7, 121.66, 117.2, 88.4, 87.5, 75.6$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{ClO}$ $[\text{M}+\text{H}]^+$: 419.1197, Found: 419.1198.



Column chromatography afforded the desired product **3ja** in 59% yield (73.4 mg) as colorless oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.85$ -7.84 (m, 1H), 7.43-7.37 (m, 8H), 7.33 (td, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.28-7.26 (m, 2H), 7.24-7.21 (m, 1H), 7.13-7.11 (m, 1H), 7.07 (dd, $J = 7.8$ Hz, 1.2 Hz, 1H), 7.01-6.99 (m, 2H), 6.90-6.88 (m, 1H), 6.20 (s, 1H), 3.91 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 157.0, 152.8, 138.1, 134.1, 131.8, 129.6, 129.3, 128.9, 128.3, 128.1, 127.8, 127.2, 125.8, 124.9, 122.8, 122.0, 121.3, 120.4, 117.0, 112.4, 88.7, 86.0, 74.4, 55.9$; HRMS (ESI): Exact mass calcd for $\text{C}_{30}\text{H}_{22}\text{O}_2$ $[\text{M}+\text{H}]^+$: 415.1693, Found: 415.1694.

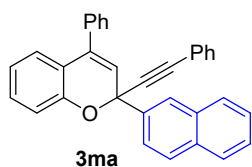


Column chromatography afforded the desired product **3ka** in 66% yield (82.9 mg) as white solid; Mp: 124-126°C; ^1H NMR (600 MHz, CDCl_3): $\delta = 8.00$ -7.99 (m, 1H), 7.47-7.46 (m, 1H), 7.44-7.38 (m, 7H), 7.32-7.28 (m, 5H), 7.27-7.24 (m, 2H), 7.13-7.10 (m, 2H), 6.94-6.91 (m, 1H), 6.18 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.4, 138.2, 137.7, 135.8, 132.8, 131.8, 131.7, 129.7, 129.6, 128.8, 128.6, 128.5, 128.4, 128.2, 128.0, 126.6, 126.1, 123.3, 122.3, 121.9, 121.6, 117.1, 88.0, 87.2, 75.2$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{ClO}$ $[\text{M}+\text{H}]^+$: 419.1197, Found: 419.1199.



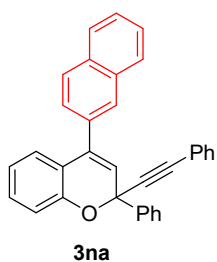
Column chromatography afforded the desired product **3la** in 66% yield (86.0 mg) as white solid; Mp: 59-61°C; ^1H NMR (600 MHz, CDCl_3): $\delta = 8.94$ (d, $J = 9.0$ Hz, 1H), 8.17-8.16 (m, 1H), 7.90-7.87 (m, 2H), 7.56-7.534 (m, 1H), 7.527-7.51 (m, 3H), 7.50-7.47 (m, 1H), 7.46-7.43 (m, 2H), 7.41-7.40 (m, 3H), 7.30-7.26 (m, 3H), 7.22-7.18 (m, 2H), 7.03-7.01 (m, 1H), 6.95-6.92 (m, 1H), 6.15 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.6, 137.7, 136.3, 135.7, 134.8, 131.8, 130.7, 130.2, 129.7, 128.85, 128.82, 128.6, 128.4, 128.2, 128.1, 126.6,$

126.1, 125.9, 125.8, 125.6, 125.3, 124.7, 122.4, 122.3, 121.7, 117.4, 89.0, 88.4, 76.6; HRMS (ESI): Exact mass calcd for C₃₃H₂₂O [M+H]⁺: 435.1743, Found: 435.1745.



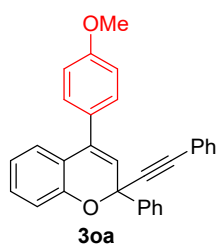
Column chromatography afforded product **3ma** in 52% yield (67.8 mg) as white solid; Mp: 46-48 °C; ¹H NMR (600 MHz, CDCl₃): δ = 8.32 (d, *J* = 1.2 Hz, 1H), 8.00-7.98 (m, 1H), 7.92-7.91 (m, 2H), 7.87-7.85 (m, 1H), 7.53-7.504 (m, 3H), 7.496-7.48 (m, 3H), 7.46-7.44 (m, 2H), 7.42-7.40 (m, 1H), 7.34-7.30 (m, 3H),

7.26-7.23 (m, 1H), 7.16-7.14 (m, 1H), 7.09-7.07 (m, 1H), 6.93 (td, *J* = 7.8 Hz, 1.2 Hz, 1H), 6.04 (s, 1H); ¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 152.5, 139.1, 137.6, 136.0, 133.2, 132.9, 131.9, 129.8, 128.9, 128.7, 128.5, 128.4, 128.2, 128.1, 127.6, 126.5, 126.3, 126.0, 125.6, 124.7, 124.5, 122.3, 121.8, 121.6, 117.2, 88.3, 88.1, 76.2; HRMS (ESI): Exact mass calcd for C₃₃H₂₂O [M+H]⁺: 435.1743, Found: 435.1747.



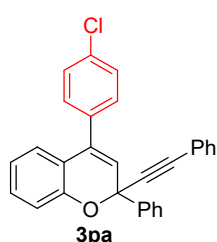
Column chromatography afforded **3na** in 74% yield (96.5 mg) as yellow solid; Mp: 51-53 °C; ¹H NMR (600 MHz, CDCl₃): δ = 7.95 (d, *J* = 1.8 Hz, 1H), 7.92-7.88 (m, 5H), 7.56-7.55 (m, 1H), 7.53-7.50 (m, 2H), 7.47-7.44 (m, 4H), 7.39-7.36 (m, 1H), 7.32-7.29 (m, 3H), 7.26-7.23 (m, 1H), 7.16-7.14 (m, 1H), 7.08-7.06 (m, 1H), 6.94-6.91 (m, 1H), 6.045-6.036 (m, 1H); ¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 152.5,

141.9, 135.7, 135.1, 133.3, 133.0, 131.9, 129.8, 128.7, 128.6, 128.5, 128.2, 128.0, 127.9, 127.8, 127.7, 126.8, 126.6, 126.3, 126.2, 126.1, 125.3, 122.3, 121.9, 121.6, 117.2, 88.2, 88.0, 76.2; HRMS (ESI): Exact mass calcd for C₃₃H₂₂O [M+H]⁺: 435.1743, Found: 435.1744.



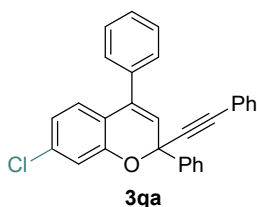
Column chromatography afforded **3oa** in 57% yield (70.9 mg) as colorless oil; ¹H NMR (600 MHz, CDCl₃): δ = 7.88-7.87 (m, 2H), 7.43-7.37 (m, 7H), 7.30-7.26 (m, 3H), 7.24-7.22 (m, 1H), 7.15-7.14 (m, 1H), 7.04-7.03 (m, 1H), 6.97-6.92 (m, 3H), 5.89 (s, 1H), 3.86 (s, 3H); ¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 159.5, 152.5, 142.0, 135.2, 131.9, 130.0, 129.9, 129.6, 128.6, 128.5, 128.4, 128.2, 126.6, 126.0, 124.2,

122.3, 122.0, 121.5, 117.1, 113.8, 88.2, 88.0, 76.1, 55.3; HRMS (ESI): Exact mass calcd for C₃₀H₂₂O₂ [M+H]⁺: 415.1693, Found: 415.1692.

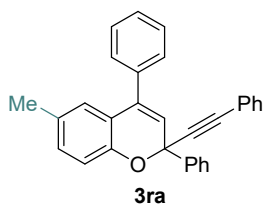


Column chromatography **3pa** in 57% yield (71.6 mg) as white solid; Mp: 105-107 °C; ¹H NMR (600 MHz, CDCl₃): δ = 7.86-7.85 (m, 2H), 7.44-7.42 (m, 4H), 7.40-7.37 (m,

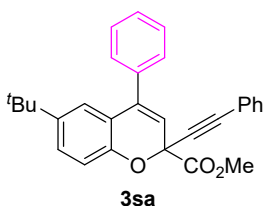
5H), 7.32-7.29 (m, 3H), 7.24-7.23 (m, 1H), 7.07-7.04 (m, 2H), 6.94-6.91 (m, 1H), 5.91 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 152.4, 141.7, 136.0, 134.7, 134.0, 131.9, 130.2, 130.0, 128.7, 128.63, 128.61, 128.5, 128.2, 126.6, 125.6, 125.2, 122.2, 121.6, 121.4, 117.3, 88.2, 87.8, 76.0$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{ClO}$ $[\text{M}+\text{H}]^+$: 419.1197, Found: 419.1196.



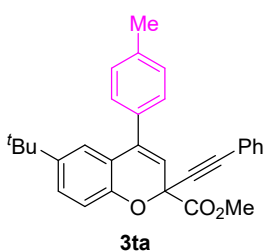
Column chromatography **3qa** in 64% yield (80.4 mg) as white solid; Mp: 40-42 °C; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.86-7.85$ (m, 2H), 7.47-7.43 (m, 9H), 7.42-7.39 (m, 2H), 7.33-7.31 (m, 2H), 7.06-7.04 (m, 2H), 6.90-6.89 (m, 1H), 5.93 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 153.1, 141.4, 137.1, 135.0, 134.7, 131.9, 128.8, 128.7, 128.5, 128.3, 128.2, 126.8, 126.6, 124.8, 122.0, 121.7, 120.4, 117.5, 88.5, 87.5, 76.6$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{19}\text{ClO}$ $[\text{M}+\text{H}]^+$: 419.1197, Found: 419.1198.



Column chromatography **3ra** in 67% yield (80.1 mg) as white solid; Mp: 34-35 °C; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.88-7.86$ (m, 2H), 7.46-7.44 (m, 7H), 7.42-7.41 (m, 2H), 7.37-7.36 (m, 1H), 7.32-7.29 (m, 3H), 7.03 (dd, $J = 7.8$ Hz, 1.8 Hz, 1H), 6.95-6.93 (m, 1H), 6.91 (d, $J = 1.8$ Hz, 1H), 5.92 (s, 1H), 2.22 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 150.2, 142.0, 137.7, 135.8, 131.9, 130.7, 130.2, 128.8, 128.6, 128.5, 128.42, 128.39, 128.2, 128.0, 126.6, 126.3, 125.0, 122.3, 121.5, 116.9, 88.2, 87.9, 75.9$; HRMS (ESI): Exact mass calcd for $\text{C}_{30}\text{H}_{22}\text{O}$ $[\text{M}+\text{H}]^+$: 399.1743, Found: 399.1744.

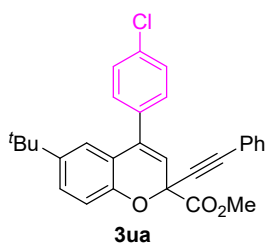


Column chromatography **3sa** in 76% yield (96.3 mg) as orange oil; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.45-7.42$ (m, 7H), 7.33-7.27 (m, 4H), 7.104-7.099 (m, 1H), 7.08 (d, $J = 8.4$ Hz, 1H), 6.02 (s, 1H), 3.90 (s, 3H), 1.21 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta = 168.6, 149.8, 144.6, 137.7, 137.2, 132.1, 129.0, 128.8, 128.4, 128.3, 128.2, 127.0, 123.2, 121.6, 120.3, 119.6, 116.4, 86.4, 85.1, 74.2, 53.6, 34.3, 31.4$; HRMS (ESI): Exact mass calcd for $\text{C}_{29}\text{H}_{26}\text{O}_3$ $[\text{M}+\text{H}]^+$: 423.1955, Found: 423.1960.

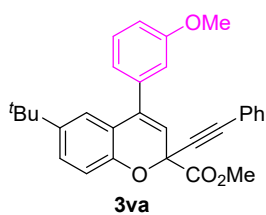


Column chromatography **3ta** in 76% yield (99.5 mg) as orange solid; Mp: 49-51 °C; ^1H NMR (600 MHz, CDCl_3): $\delta = 7.45-7.44$ (m, 2H), 7.33-7.26 (m, 6H), 7.25-7.24 (m, 2H), 7.13 (d, $J = 2.4$ Hz, 1H), 7.07 (d, $J = 8.4$ Hz, 1H), 5.99 (s, 1H), 3.89 (s, 3H), 2.42 (s, 3H), 1.22 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): $\delta =$

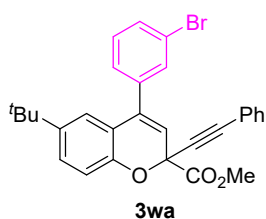
168.6, 149.8, 144.6, 138.2, 127.6, 134.2, 132.1, 129.1, 129.0, 128.6, 128.2, 126.9, 123.2, 121.6, 120.4, 119.2, 116.4, 86.3, 85.1, 74.1, 53.6, 34.3, 31.4, 21.3; HRMS (ESI): Exact mass calcd for C₃₀H₂₈O₂ [M+H]⁺: 437.2111, Found: 453.2060.



Column chromatography **3ua** in 68% yield (93.2 mg) as yellow solid; Mp: 48-50 °C; ¹H NMR (600 MHz, CDCl₃): δ = 7.45-7.43 (m, 2H), 7.42-7.41 (m, 2H), 7.37-7.36 (m, 2H), 7.33-7.32 (m, 1H), 7.30-7.28 (m, 3H), 7.08 (d, *J* = 3.0 Hz, 1H), 7.03 (d, *J* = 2.4 Hz, 1H), 6.01 (s, 1H), 3.90 (s, 3H), 1.22 (s, 9H); ¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 168.4, 149.7, 144.8, 136.7, 135.6, 134.3, 132.1, 130.1, 129.1, 128.7, 128.2, 127.3, 122.9, 121.5, 120.03, 119.95, 116.6, 86.5, 84.8, 74.0, 53.7, 34.3, 31.4; HRMS (ESI): Exact mass calcd for C₂₉H₂₅ClO₃ [M+H]⁺: 457.1565, Found: 457.1567.

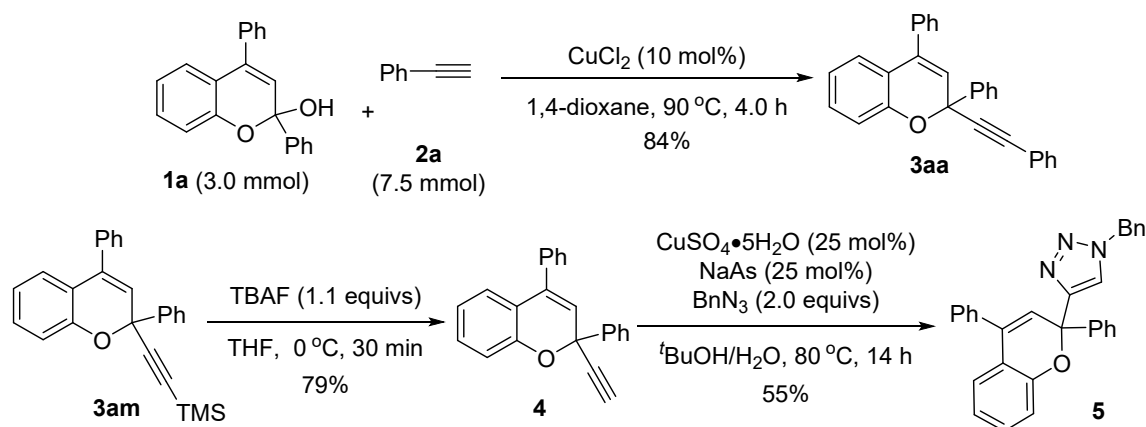


Column chromatography **3va** in 75% yield (101.8 mg) as colorless oil; ¹H NMR (600 MHz, CDCl₃): δ = 7.45-7.44 (m, 2H), 7.33-7.32 (m, 1H), 7.30-7.27 (m, 4H), 7.15-7.14 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 1H), 6.97-6.96 (m, 2H), 6.03 (s, 1H), 3.90 (s, 3H), 3.83 (s, 3H), 1.12 (s, 9H); ¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 168.5, 159.5, 149.7, 144.6, 138.5, 137.6, 132.1, 129.4, 129.0, 128.2, 127.92, 127.90, 127.0, 123.2, 121.6, 121.2, 120.2, 119.6, 116.4, 114.4, 113.8, 86.4, 85.0, 74.1, 55.3, 53.7, 34.3, 31.4; HRMS (ESI): Exact mass calcd for C₃₀H₂₈O₄ [M+H]⁺: 453.2060, Found: 453.2063.



Column chromatography **3wa** in 43% yield (64.7 mg) as yellow solid; Mp: 42-44 °C; ¹H NMR (600 MHz, CDCl₃): δ = 7.61-7.60 (m, 1H), 7.55-7.54 (m, 1H), 7.45-7.44 (m, 2H), 7.34-7.32 (m, 2H), 7.31-7.28 (m, 4H), 7.08 (d, *J* = 9.0 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 6.04 (s, 1H), 3.90 (s, 3H), 1.22 (s, 9H); ¹³C{¹H} NMR (150 MHz, CDCl₃): δ = 168.3, 149.7, 144.8, 139.2, 136.5, 132.1, 131.8, 131.4, 129.9, 129.1, 128.2, 127.4, 127.3, 122.9, 122.5, 121.5, 120.3, 119.9, 116.6, 86.6, 84.7, 74.0, 53.8, 34.3, 31.3; HRMS (ESI): Exact mass calcd for C₂₉H₂₅BrO₃ [M+H]⁺: 501.1060, Found: 501.1063.

3. Gram-scale synthesis and product elaboration



3.1 Gram-scale synthesis

To a 100 mL round bottom flask were added **1a** (0.90 g, 3.0 mmol, 1.0 equiv), phenylacetylene **2a** (0.77 g, 7.5 mmol, 2.5 equivs) and 30.0 mL of anhydrous 1,4-dioxane. After adding CuCl_2 (40.0 mg, 10 mol%), the reaction mixture was stirred at 90 °C till almost full conversion of **1a** by TLC analysis. The reaction mixture was directly subjected to column chromatography using petroleum ether as the eluent to afford the desired product **3aa** in 84% yield (0.97 g).

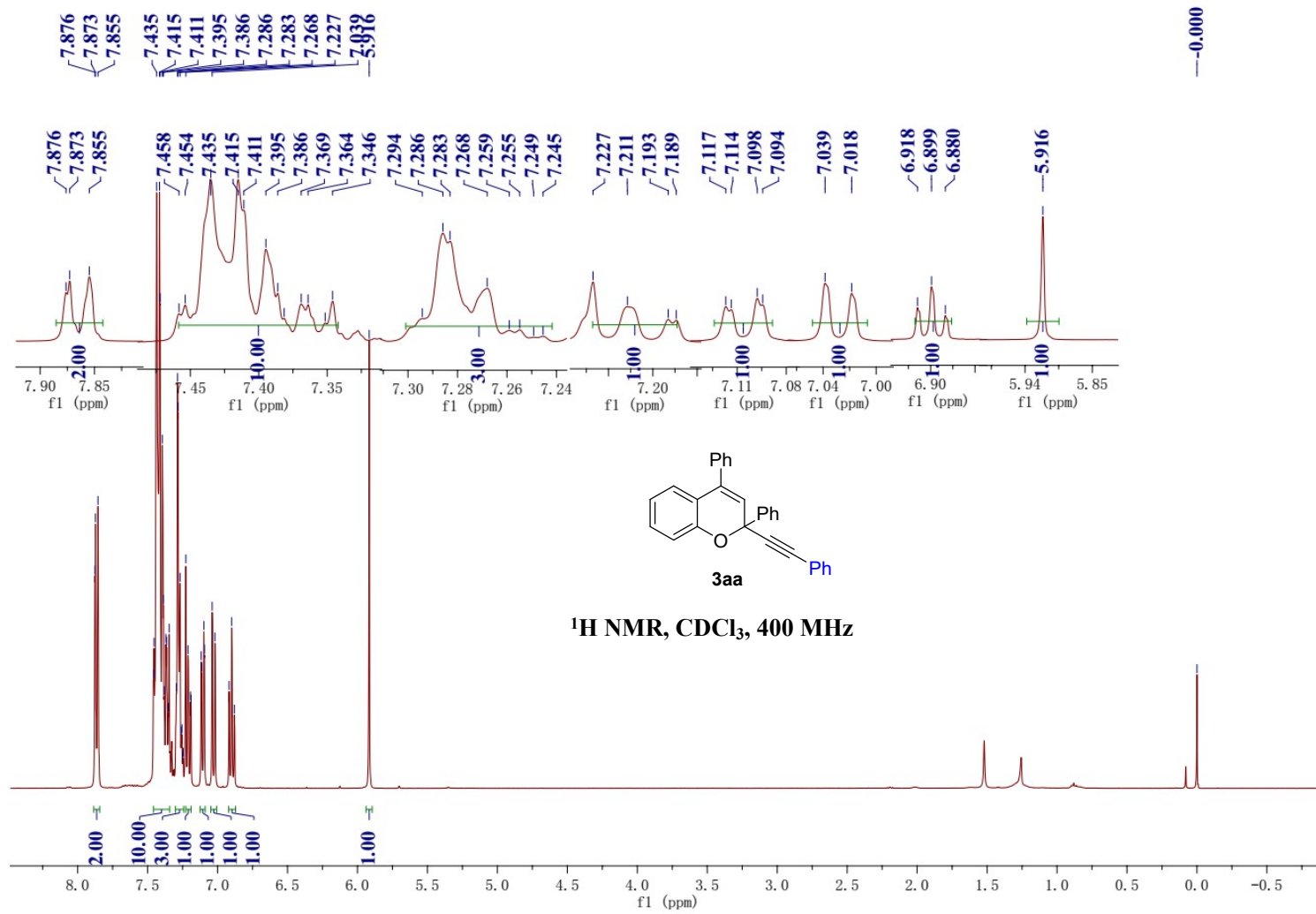
3.2 Product elaboration

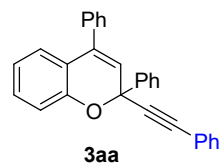
1) The synthesis of **4**

To a 10-mL round bottom flask were added sequentially **3am** (114.2 mg, 0.3 mmol), 5.0 mL of THF and TBAF (86.3 mg, 0.33 mmol, 1.1 equivs). The reaction mixture was stirred at 0 °C till almost full conversion of **3am** by TLC analysis. The reaction is terminated by the addition of 20 mL saturated aqueous NH_4Cl . The organic layer was extracted with ethyl acetate (3×10 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 40:1, v:v) as the eluent to afford the desired product **4** in 79% yield (73.1 mg) as colorless oil; $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 7.84\text{-}7.82$ (m, 2H), 7.44-7.37 (m, 8H), 7.25-7.23 (m, 1H), 7.14-7.12 (m, 1H), 7.04 (d, $J = 8.0$ Hz, 1H), 6.94 (t, $J = 7.6$ Hz, 1H), 5.86 (s, 1H), 2.82 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): $\delta = 152.2, 141.3, 137.4, 136.0, 129.8, 128.8, 128.6, 128.5, 128.4, 128.2, 126.5, 126.0, 124.6, 121.8, 121.7, 117.1, 82.7, 76.2, 75.4, 76.2, 75.4$; HRMS (ESI): Exact mass calcd for $\text{C}_{23}\text{H}_{16}\text{O}$ $[\text{M}+\text{H}]^+$: 309.1274, Found: 309.1268.

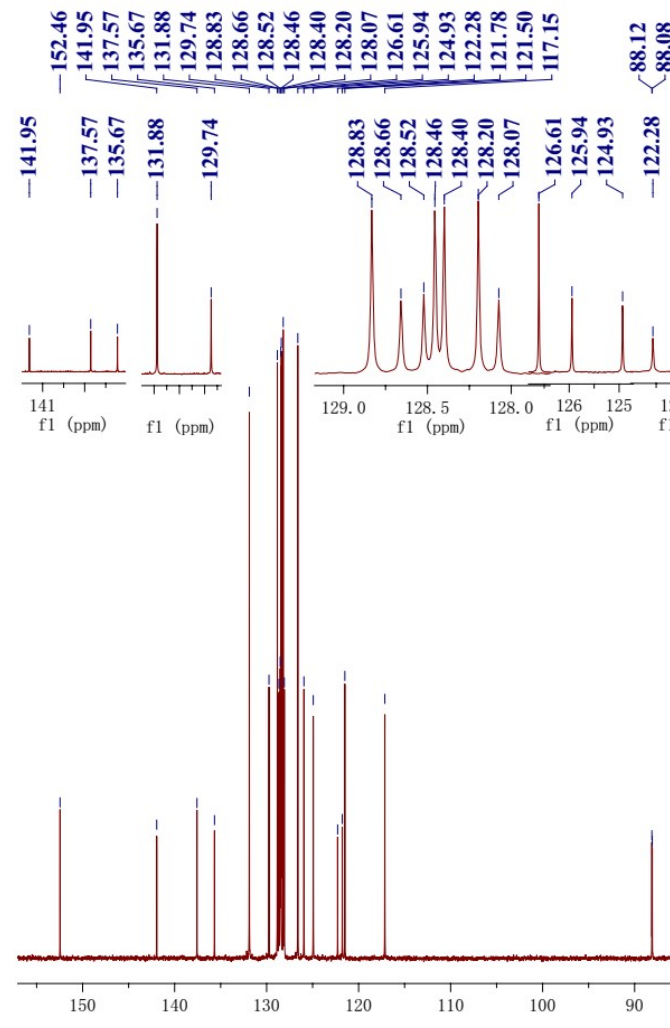
2) The synthesis of **5**

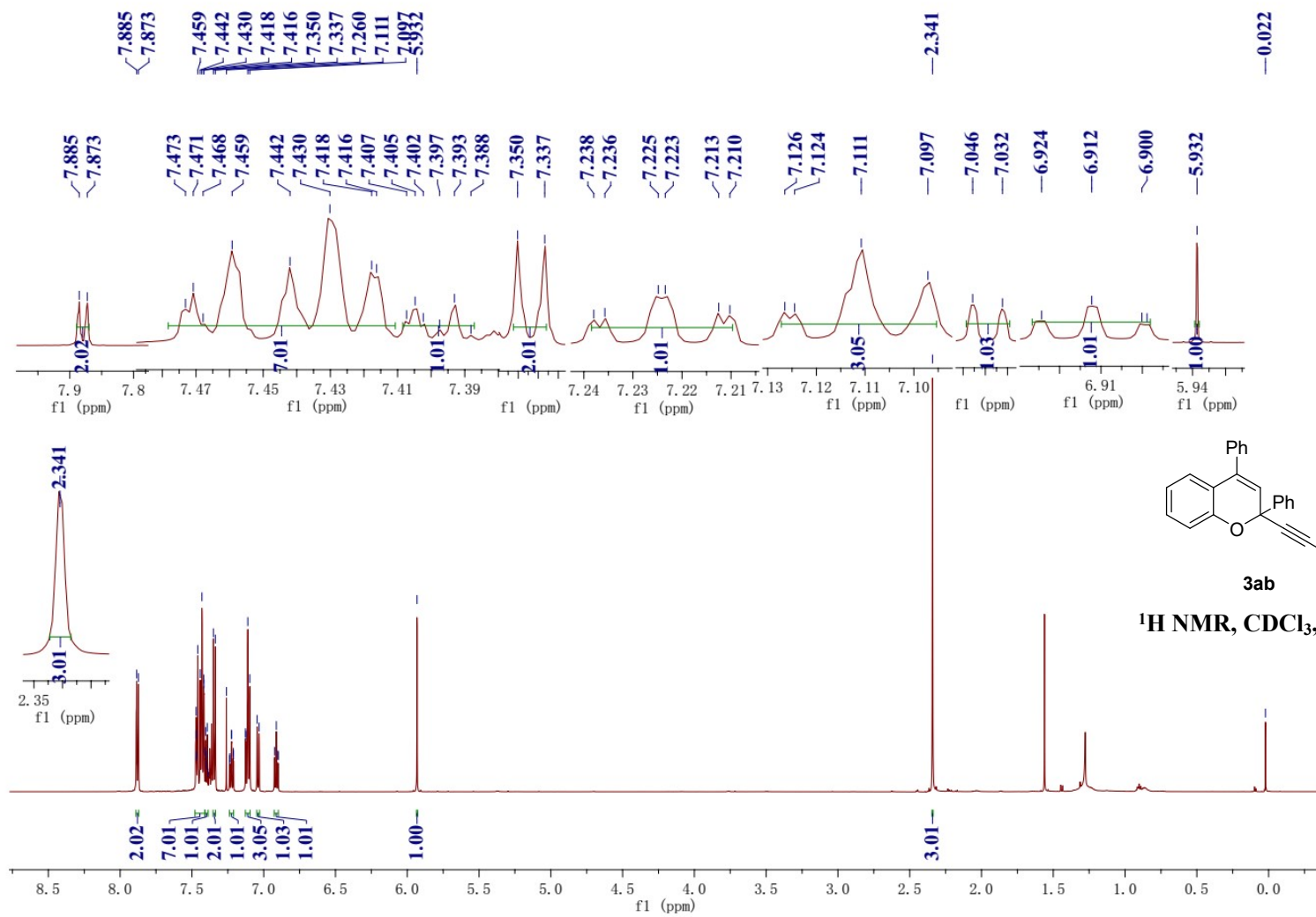
To a 25 mL of Schlenk tube were added sequentially **4** (61.7 mg, 0.2 mmol), CuSO₄·5H₂O (12.5 mg, 0.05 mmol, 0.25 equivs), sodium ascorbate (9.9 mg, 0.05 mmol, 0.25 equiv), and 4.0 mL H₂O and 4.0 mL *t*BuOH (4.0 mL). After adding BnN₃ (53.3 mg, 0.4 mmol, 2.0 equivs), the mixture was stirred at 80 °C under N₂ atmosphere till almost full conversion of **4** by TLC analysis. Then, the reaction is terminated by the addition of 20.0 mL saturated aqueous NH₄Cl. The organic layer was extract with ethyl acetate (3×10 mL) and then dried with Na₂SO₄. 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 **5** in 55% yield (73.1 mg) as white solid; ¹H NMR (400 MHz, CDCl₃): δ = 7.62-7.60 (m, 2H), 7.48 (s, 1H), 7.43-7.30 (m, 11H), 7.24-7.22 (m, 2H), 7.18-7.14 (m, 1H), 7.04-6.99 (m, 2H), 6.83 (t, *J* = 7.6 Hz, 1H), 6.47 (s, 1H), 5.50 (AB, *J* = 15.6 Hz, 1H), 5.46 (AB, *J* = 16.0 Hz, 1H); ¹³C {¹H} NMR (100 MHz, CDCl₃): δ = 152.5, 152.4, 143.4, 137.7, 135.7, 134.5, 129.6, 129.1, 128.8, 128.7, 128.34, 128.26, 128.03, 128.02, 127.8, 126.2, 126.1, 126.0, 122.3, 121.6, 121.4, 116.9, 78.2, 54.1; HRMS (ESI): Exact mass calcd for C₃₀H₂₃N₃O [M+H]⁺: 442.1914, Found: 442.1916.

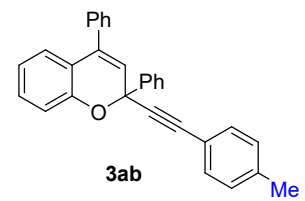
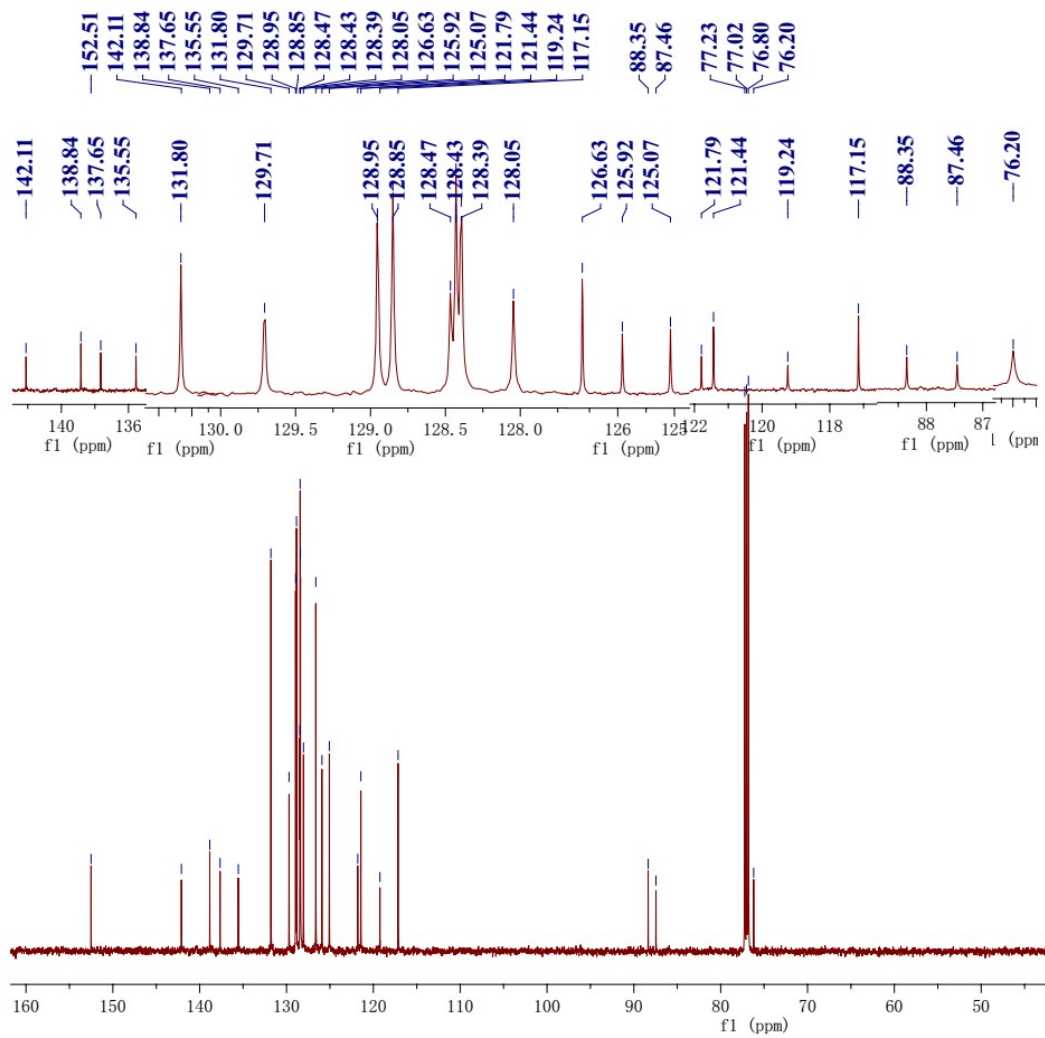




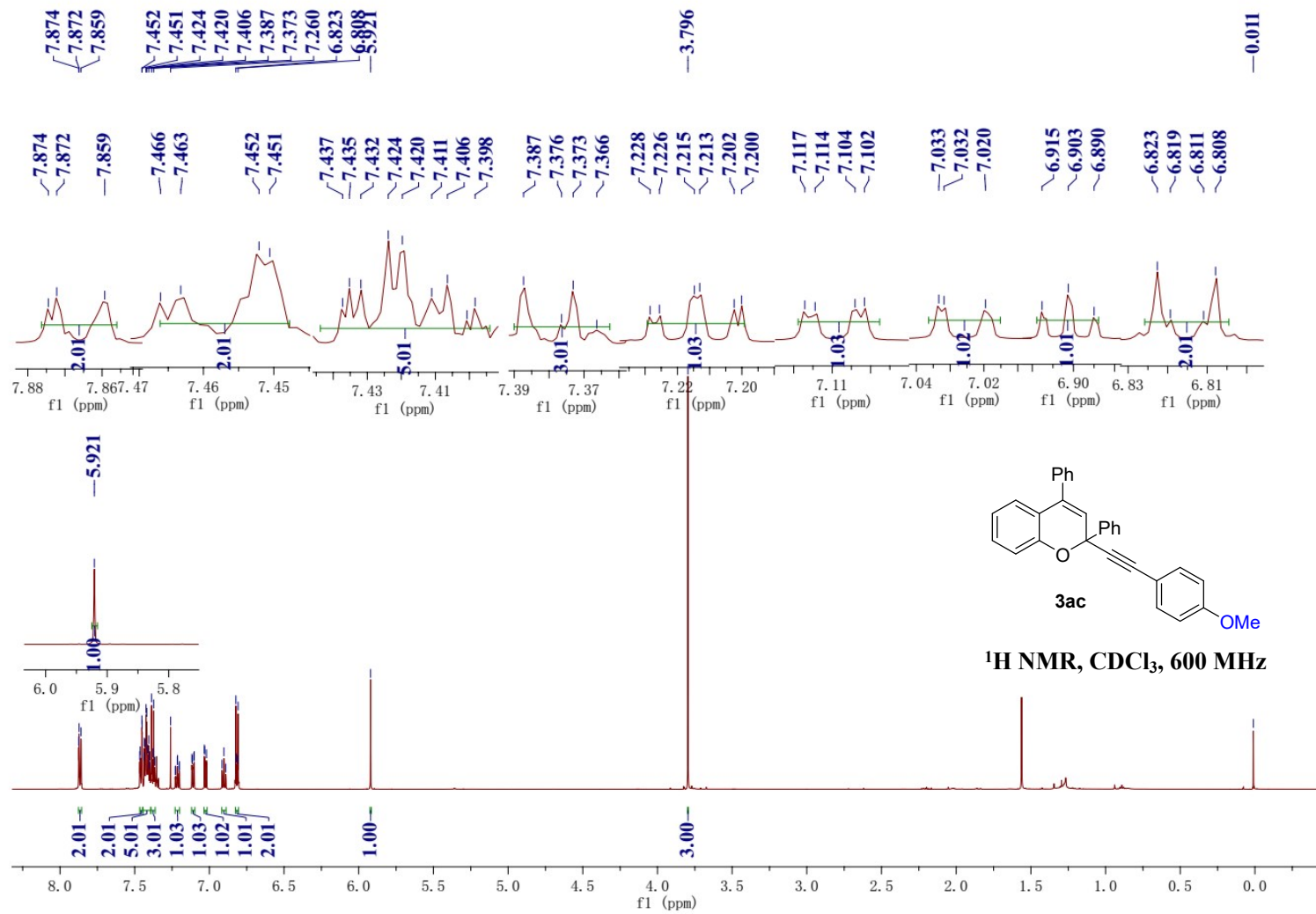
¹³C NMR, CDCl₃, 100 MHz

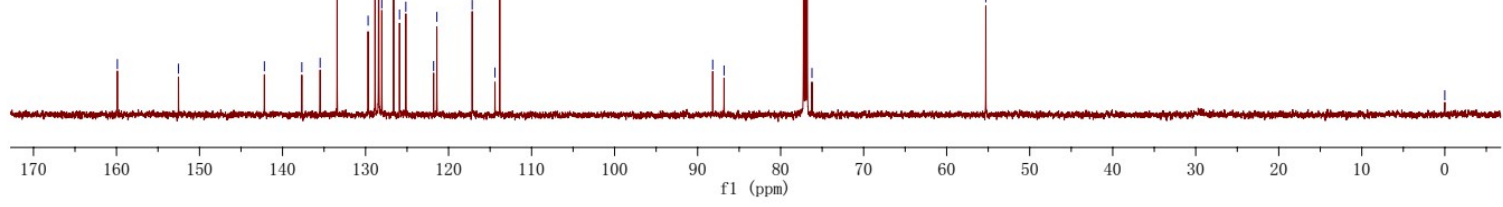
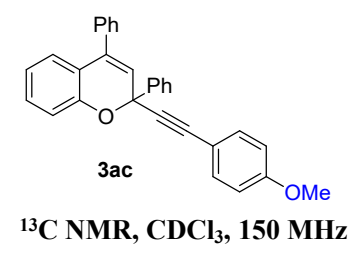
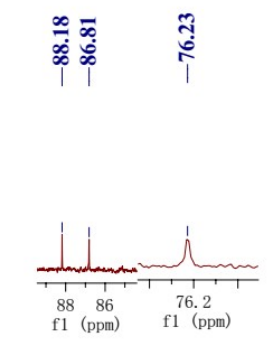
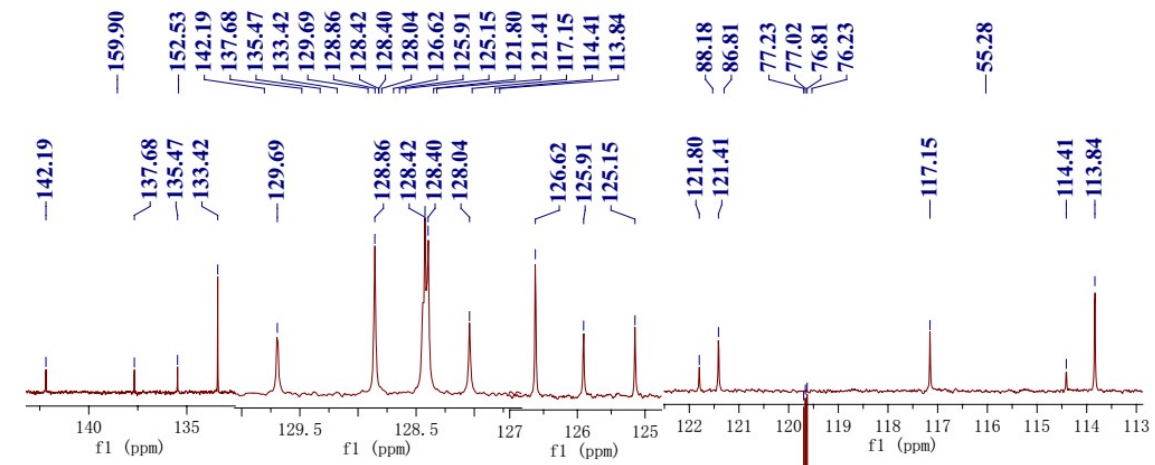


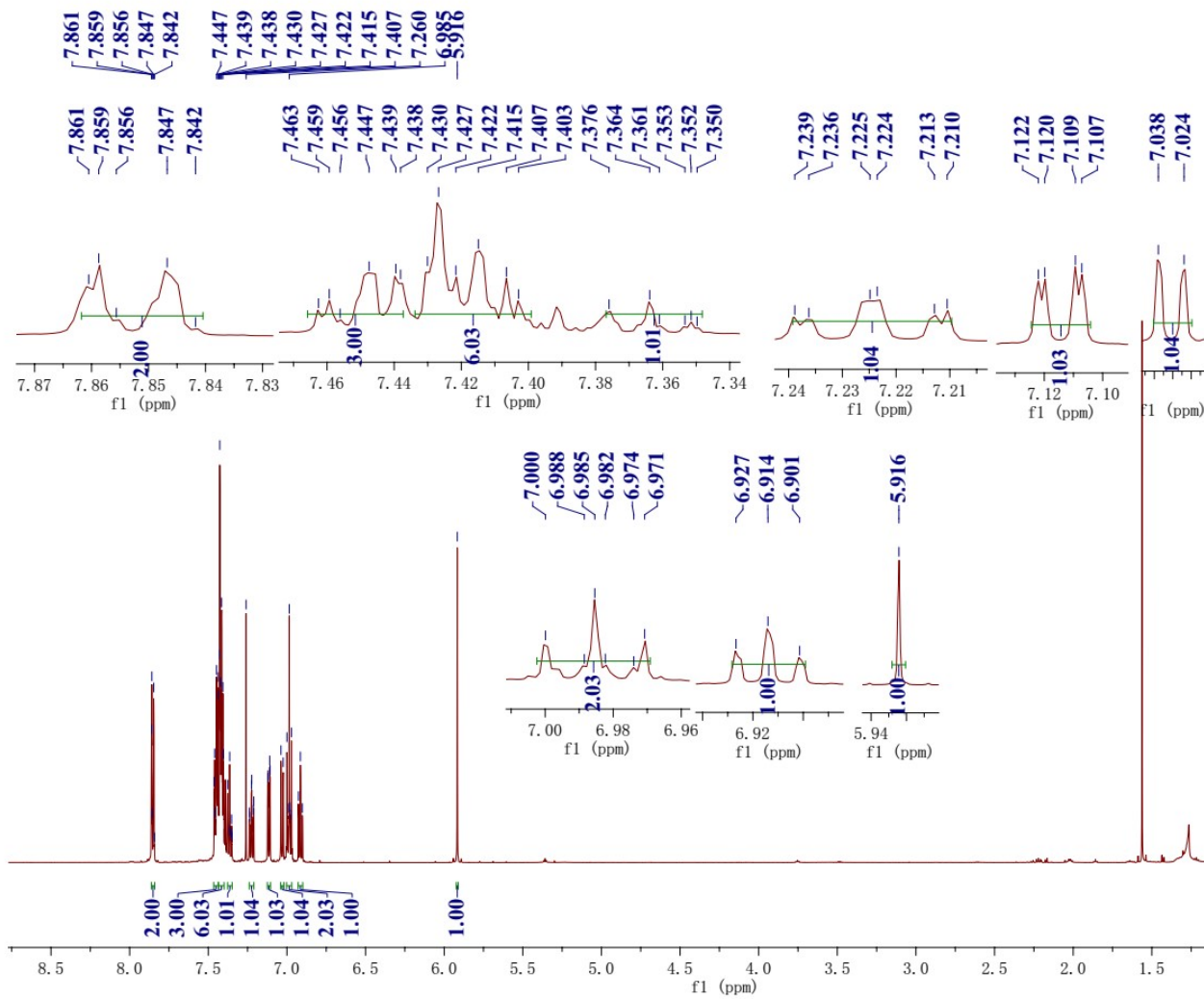


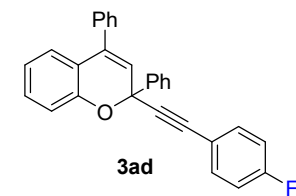
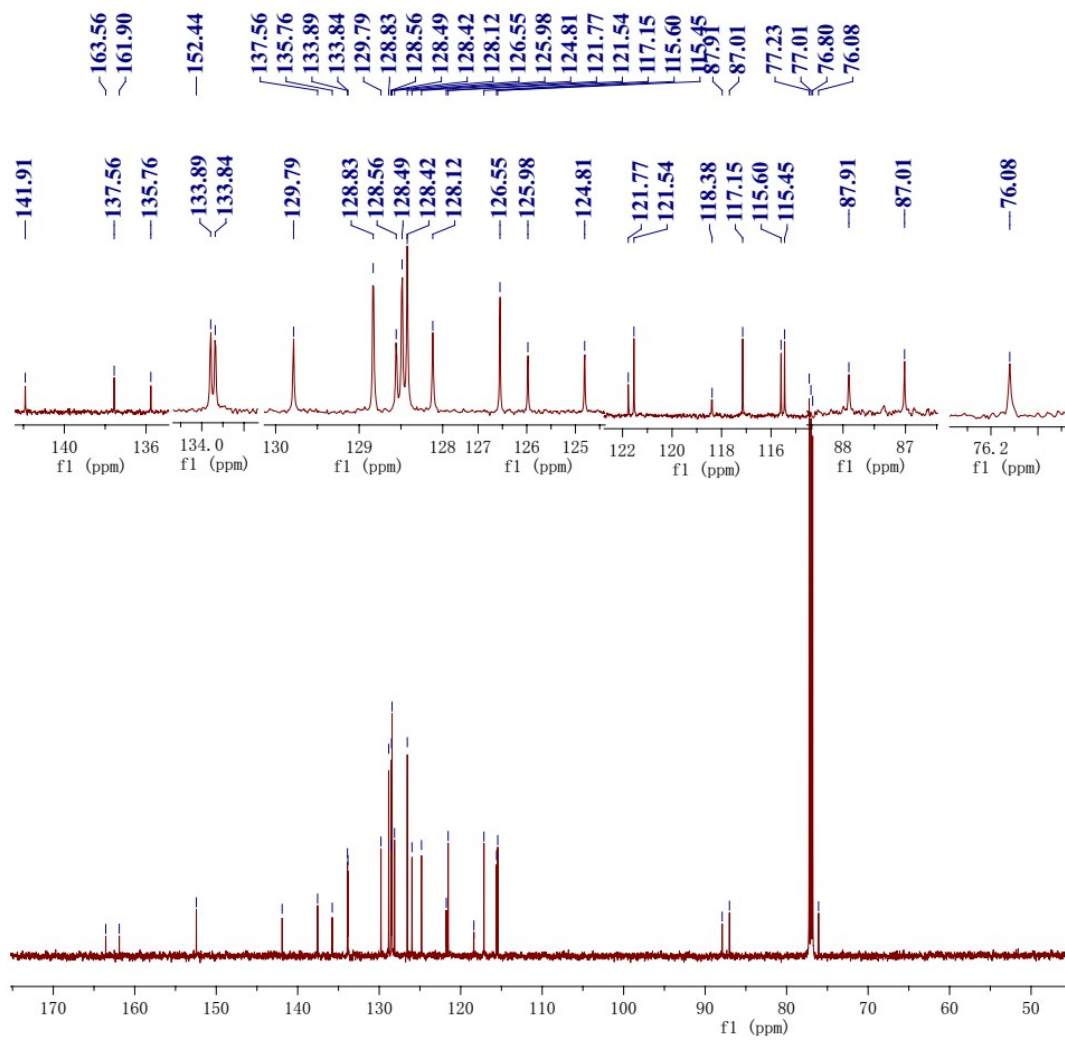


3ab
¹³C NMR, CDCl₃, 150 MHz

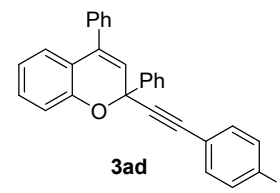




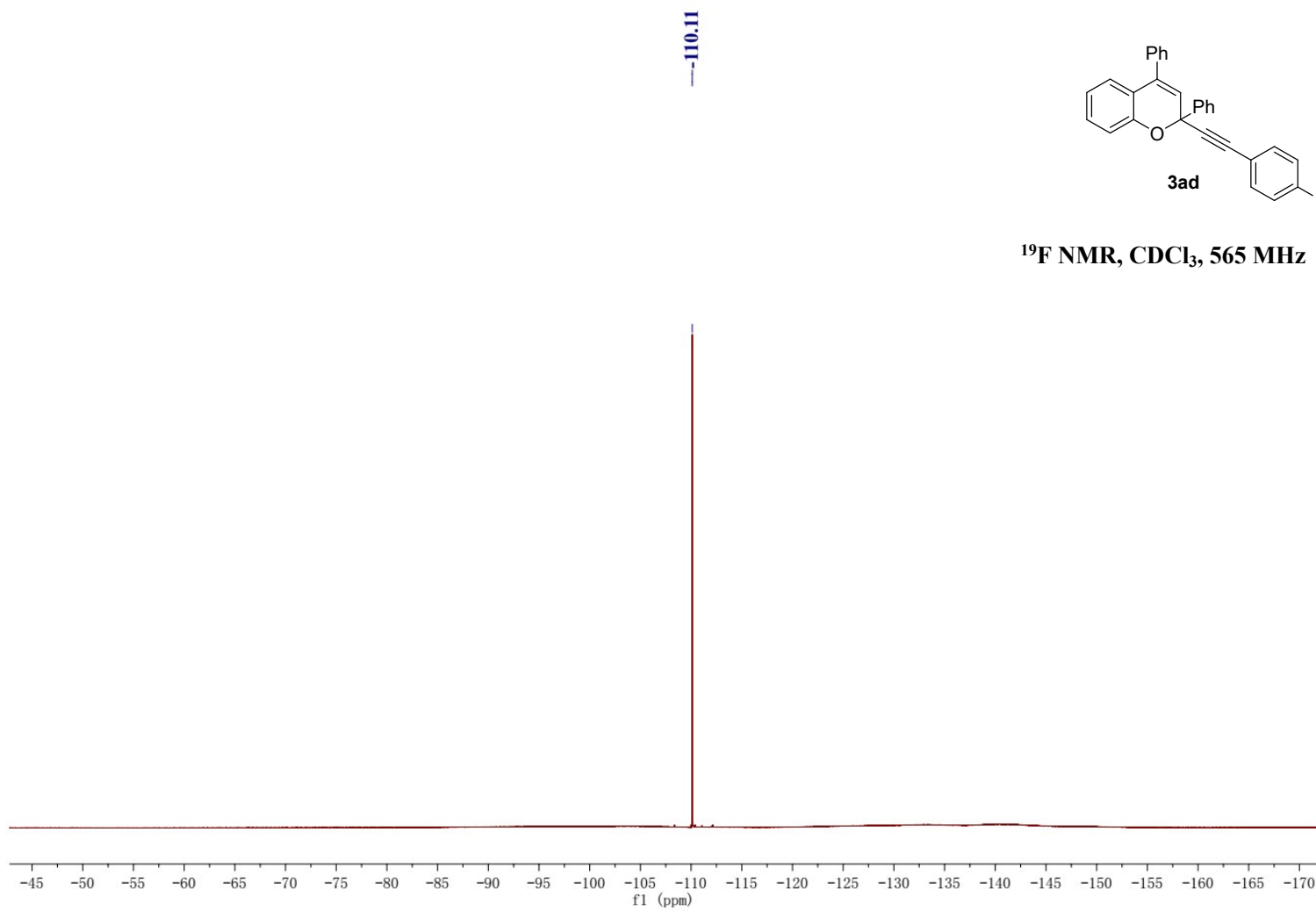


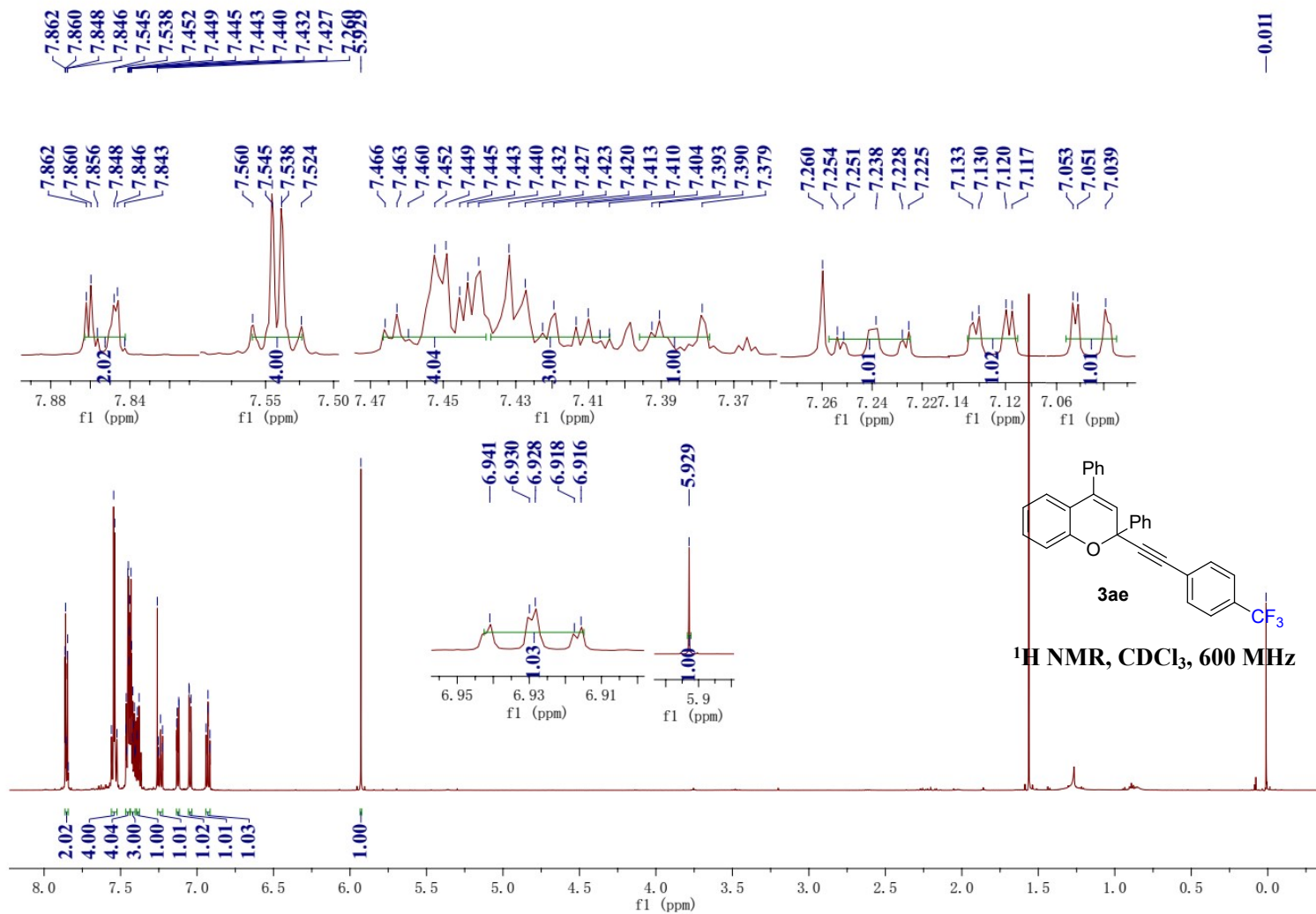


^{13}C NMR, CDCl_3 , 150 MHz

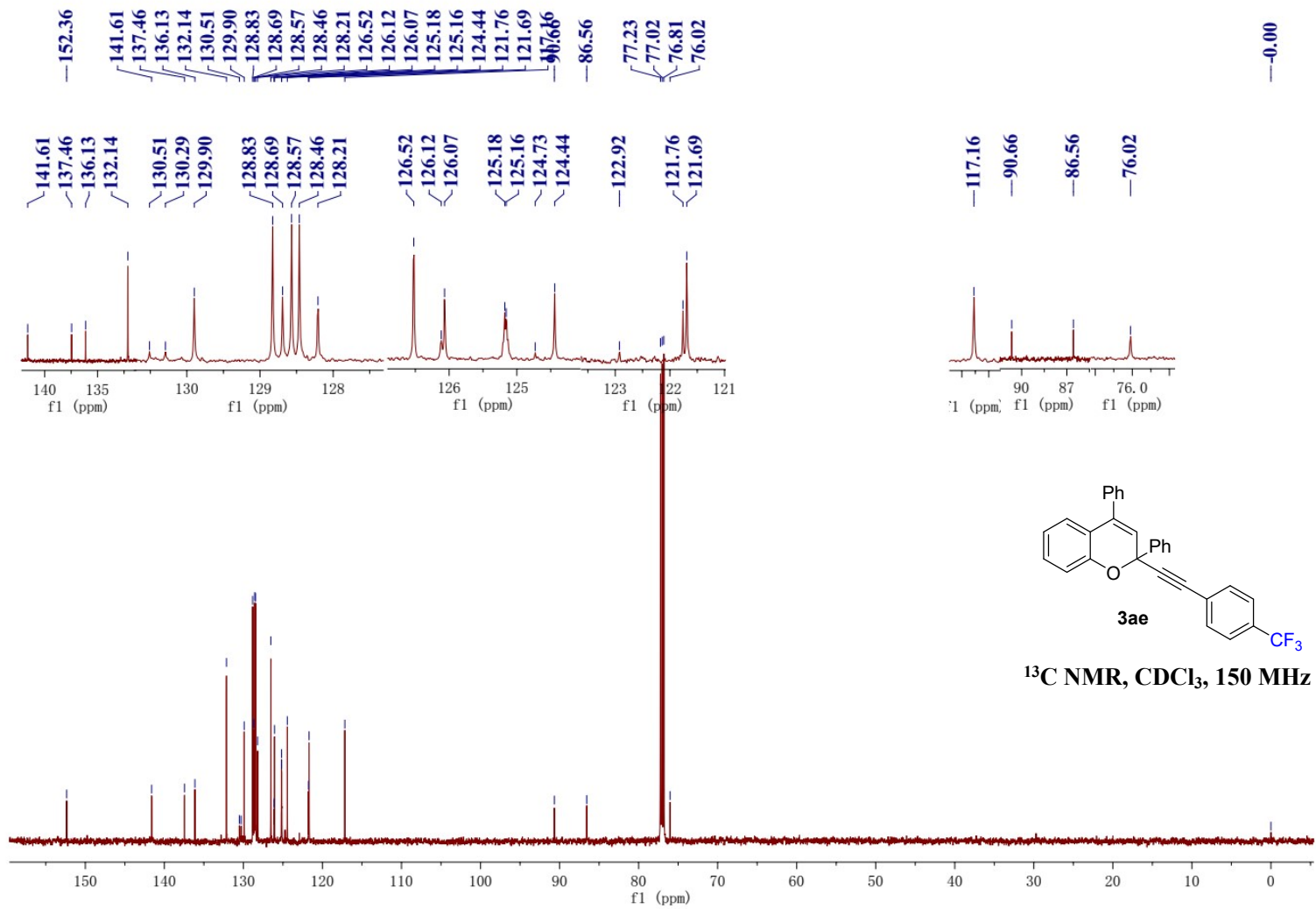


¹⁹F NMR, CDCl₃, 565 MHz

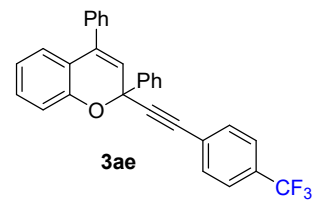




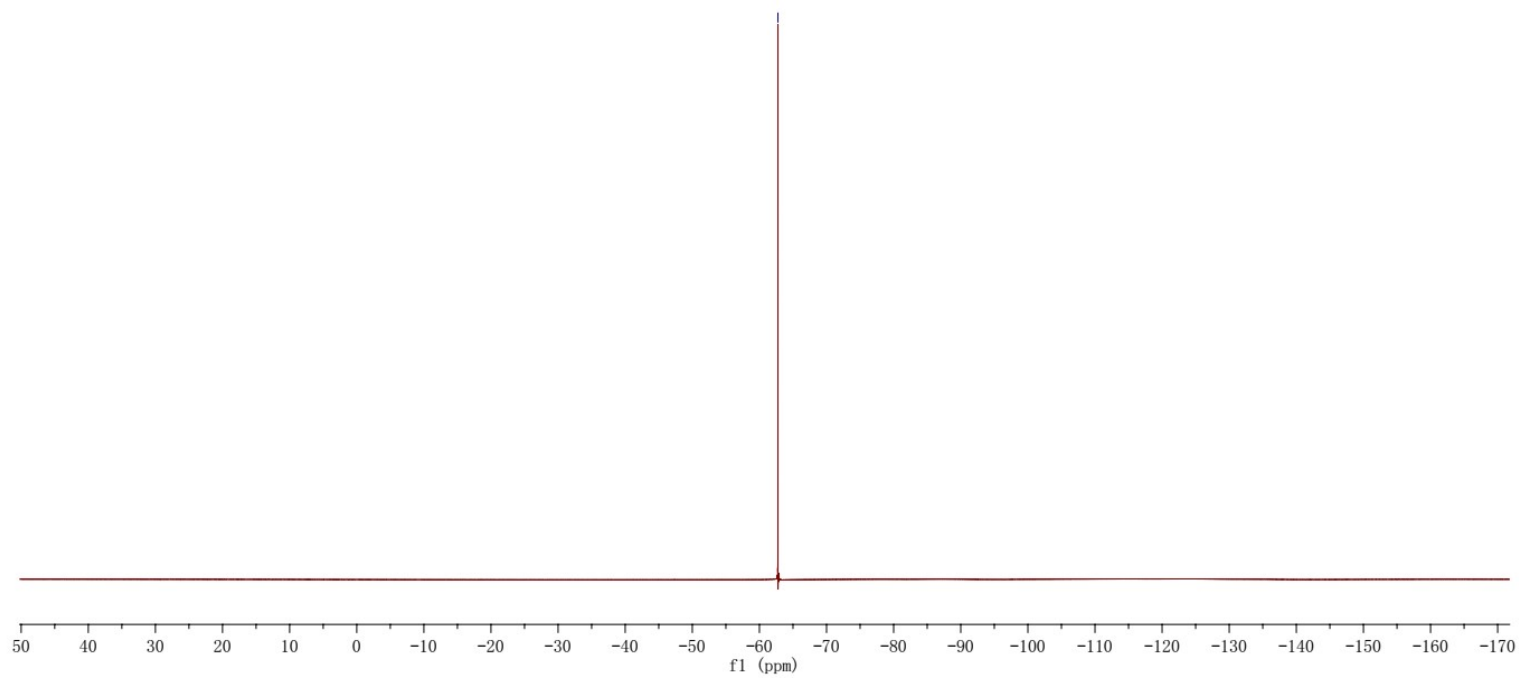
—0.011

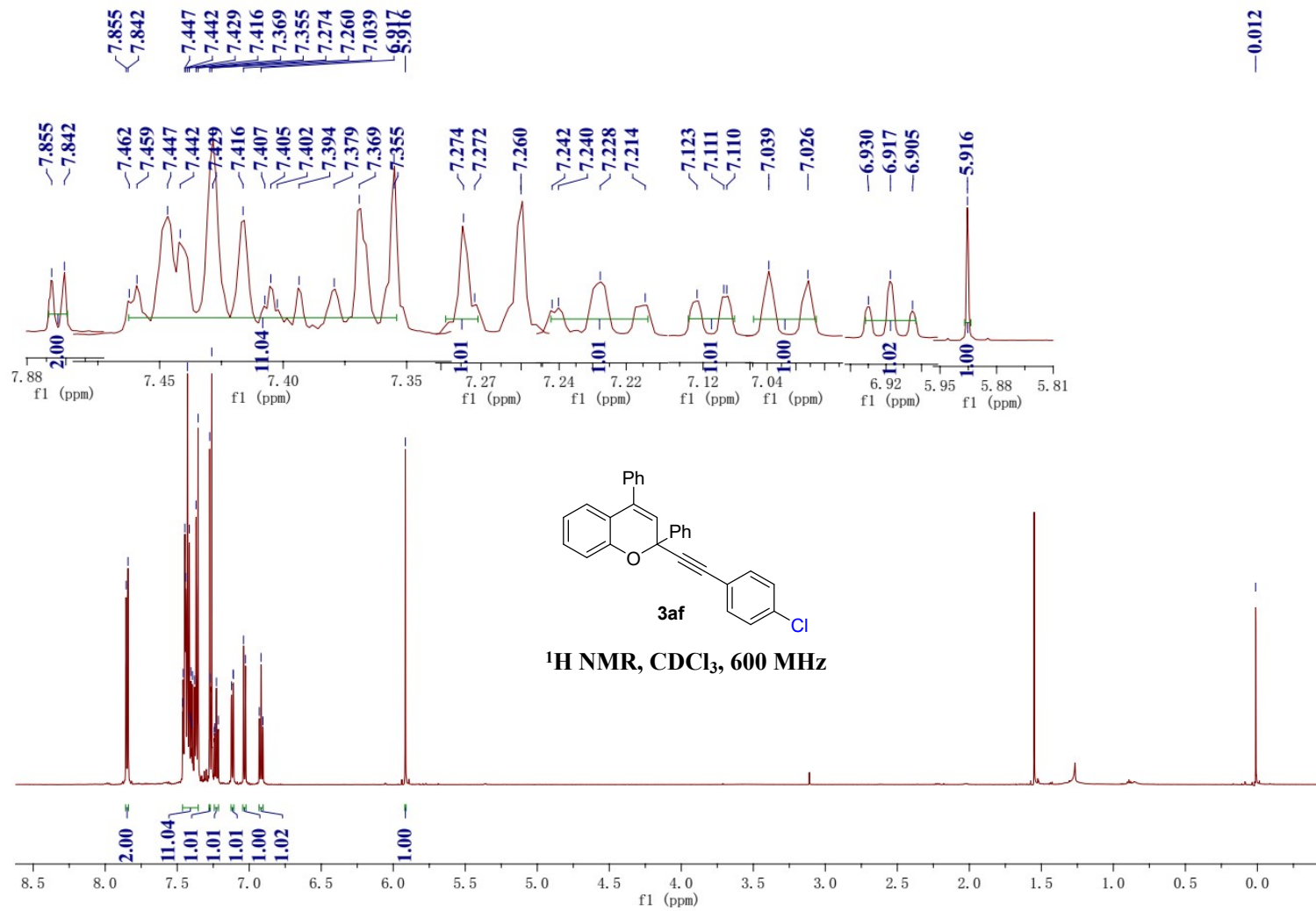


-62.76

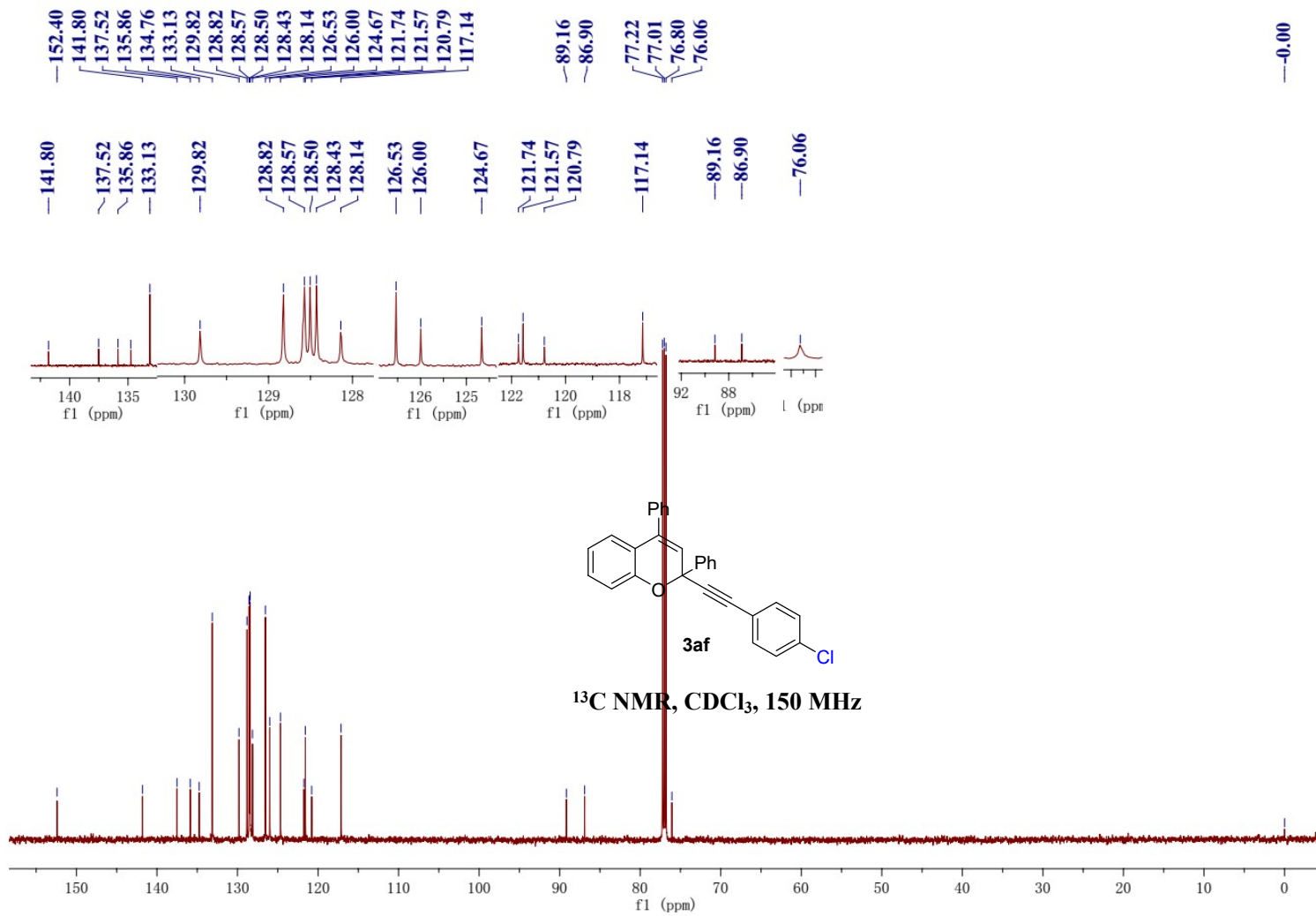


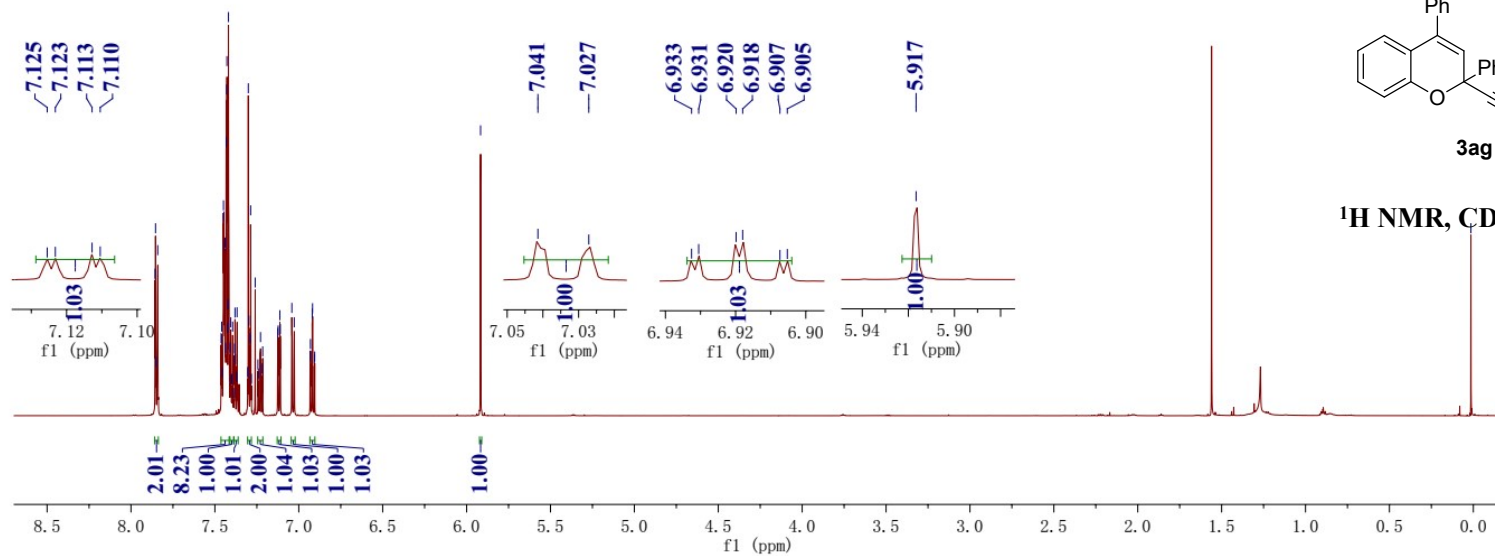
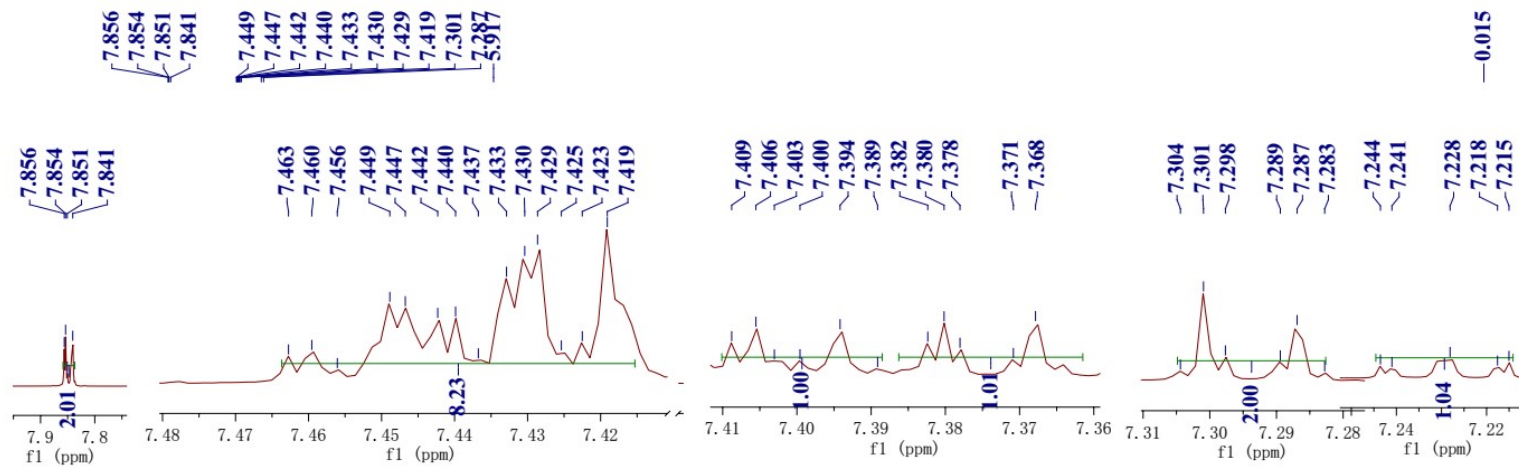
¹⁹F NMR, CDCl₃, 565 MHz

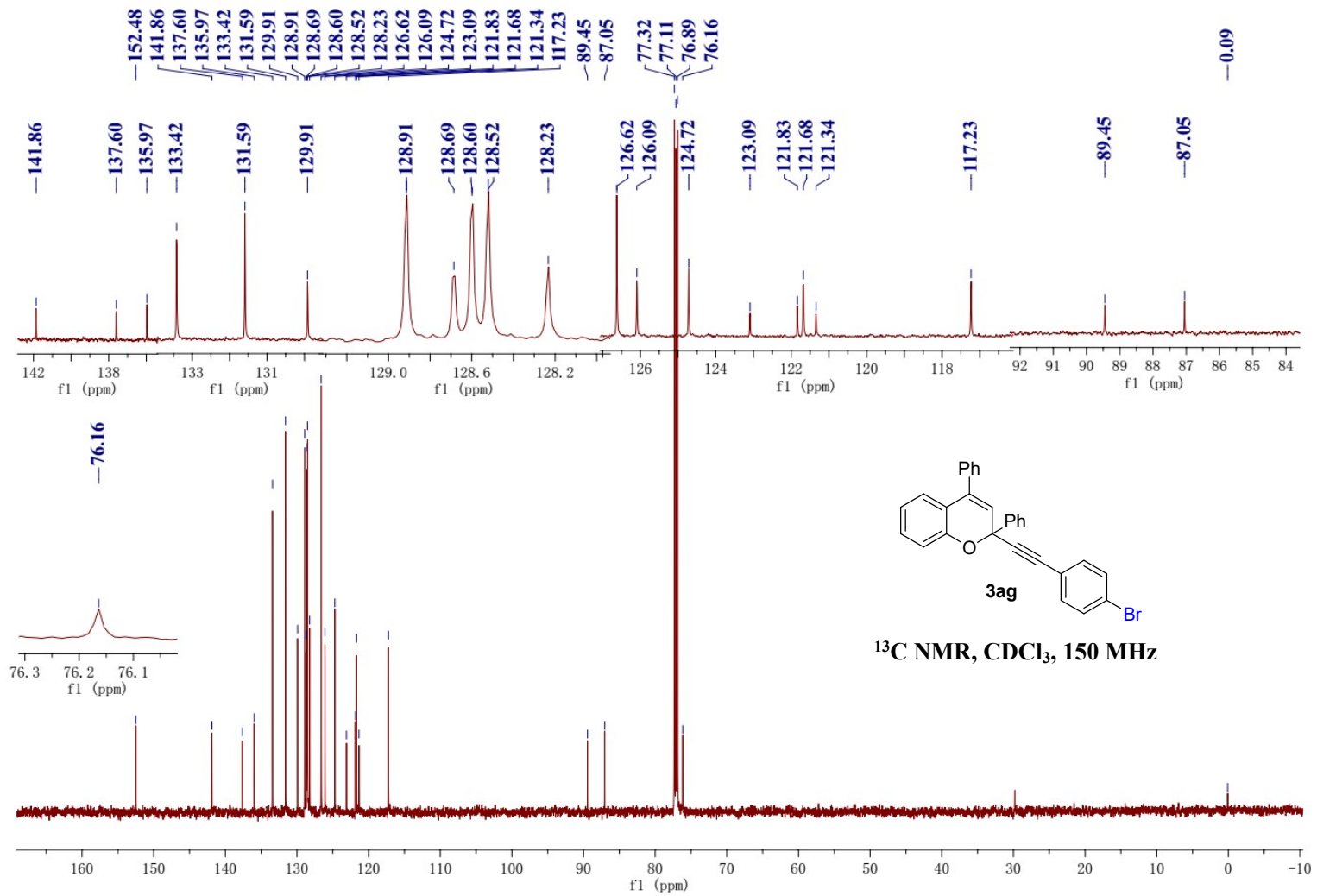


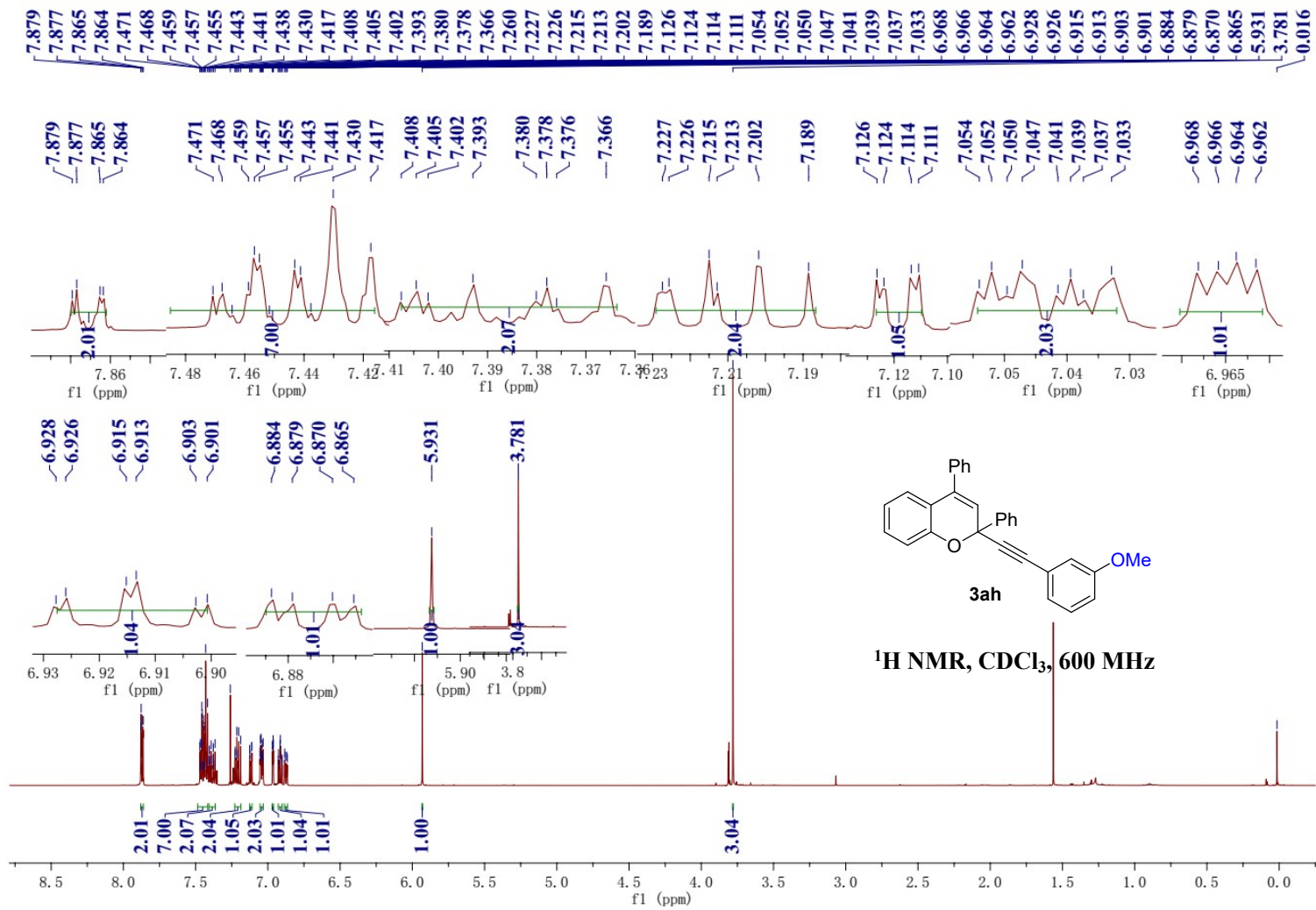


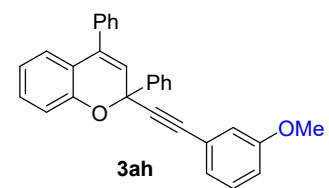
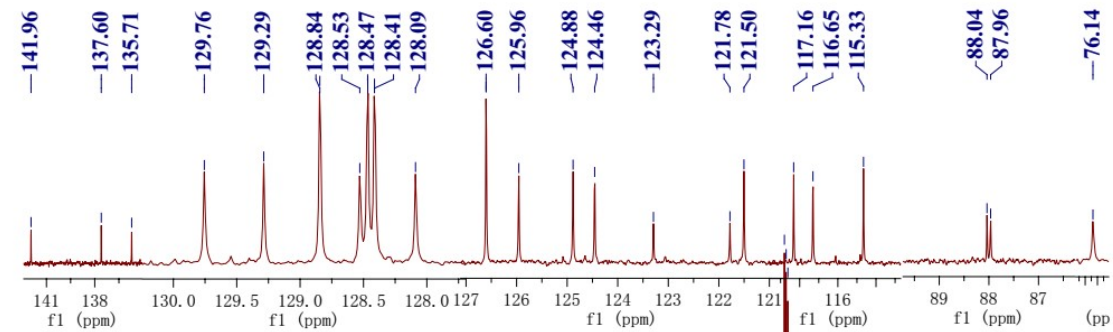
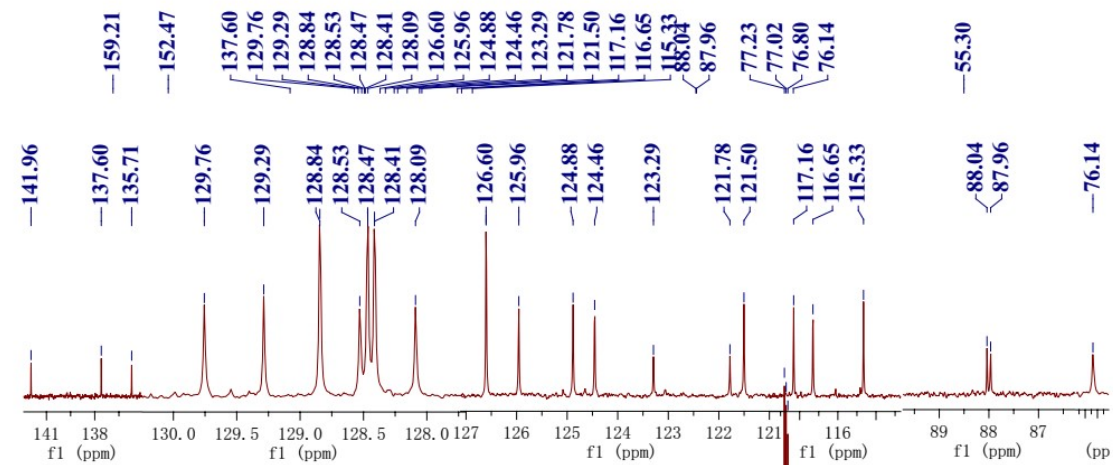
—0.012



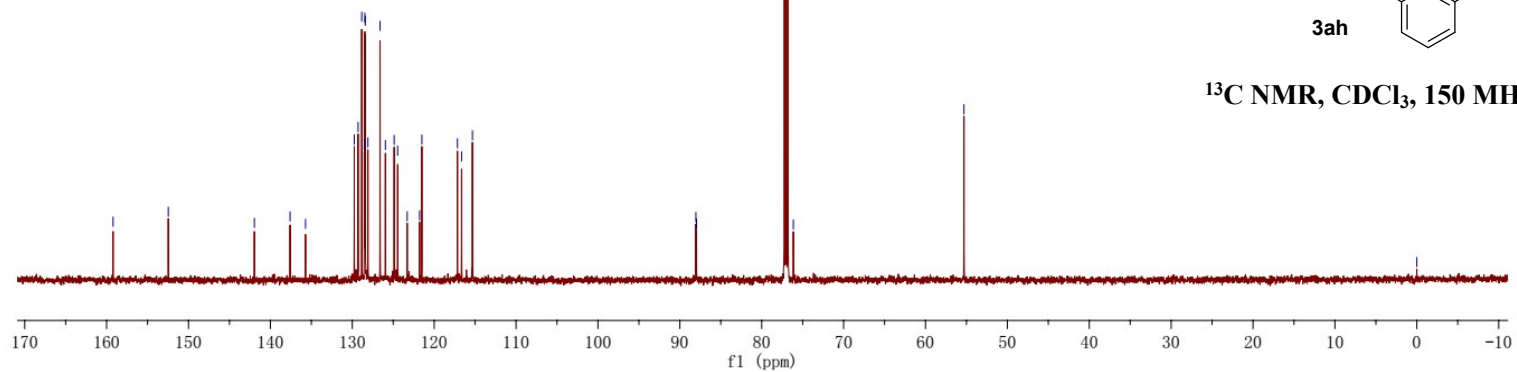


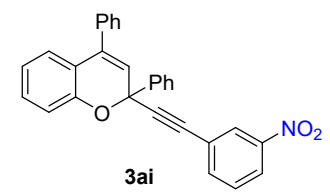




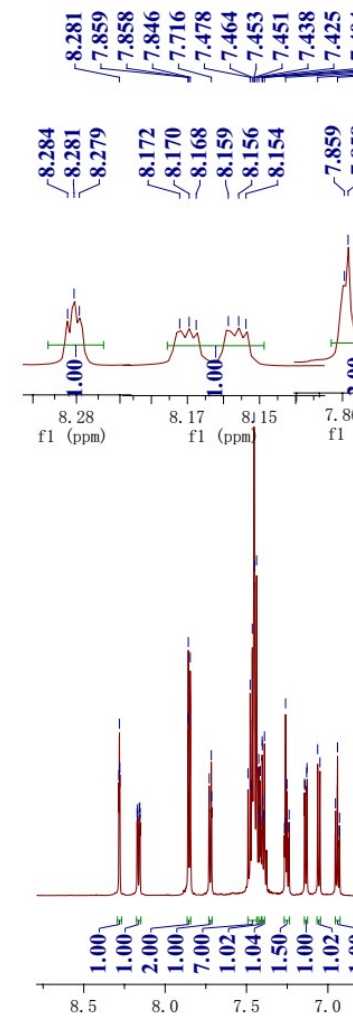


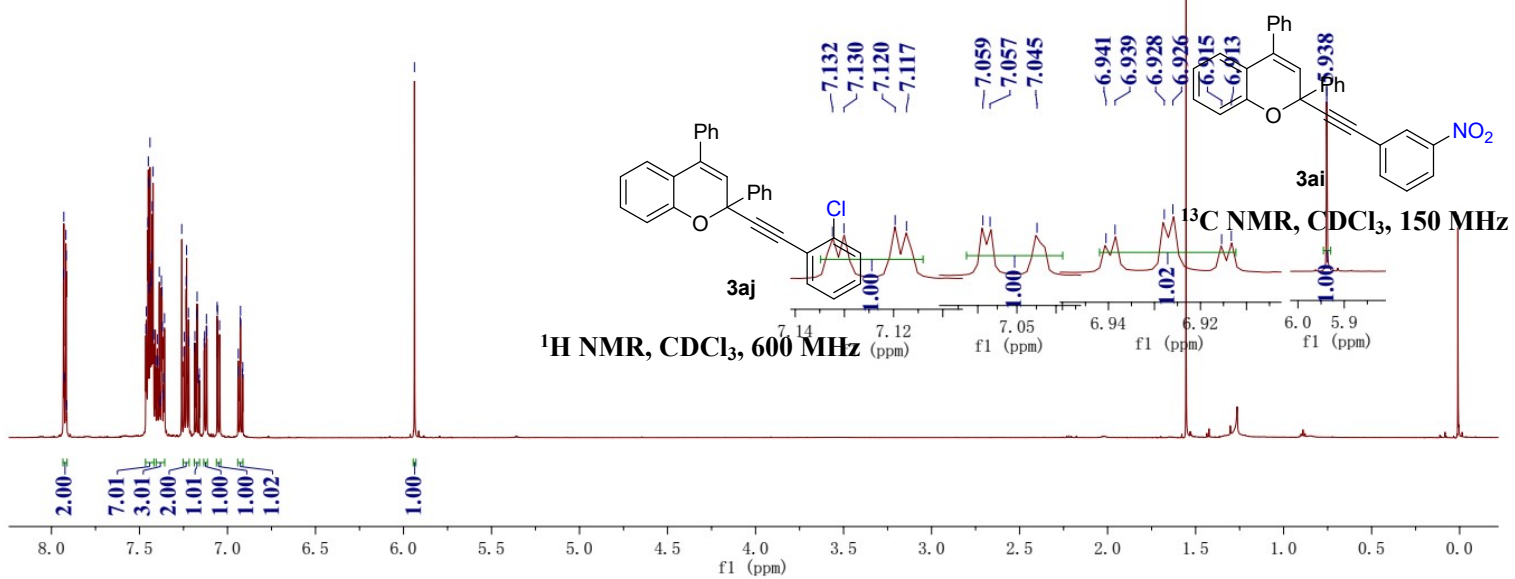
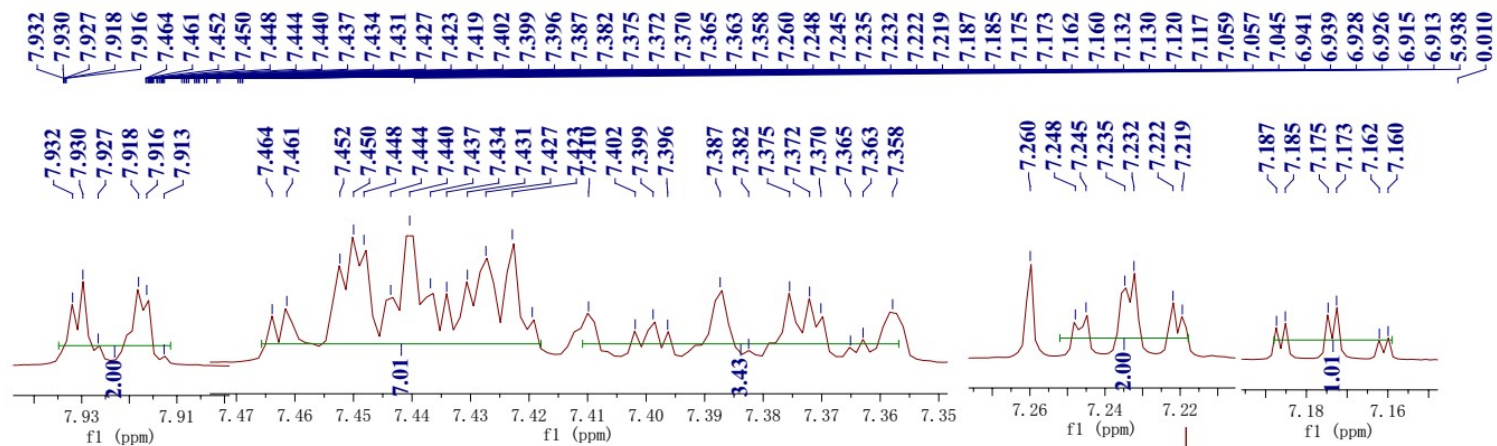
3ah
¹³C NMR, CDCl₃, 150 MHz

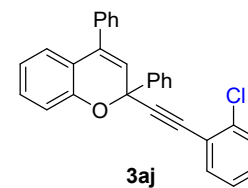
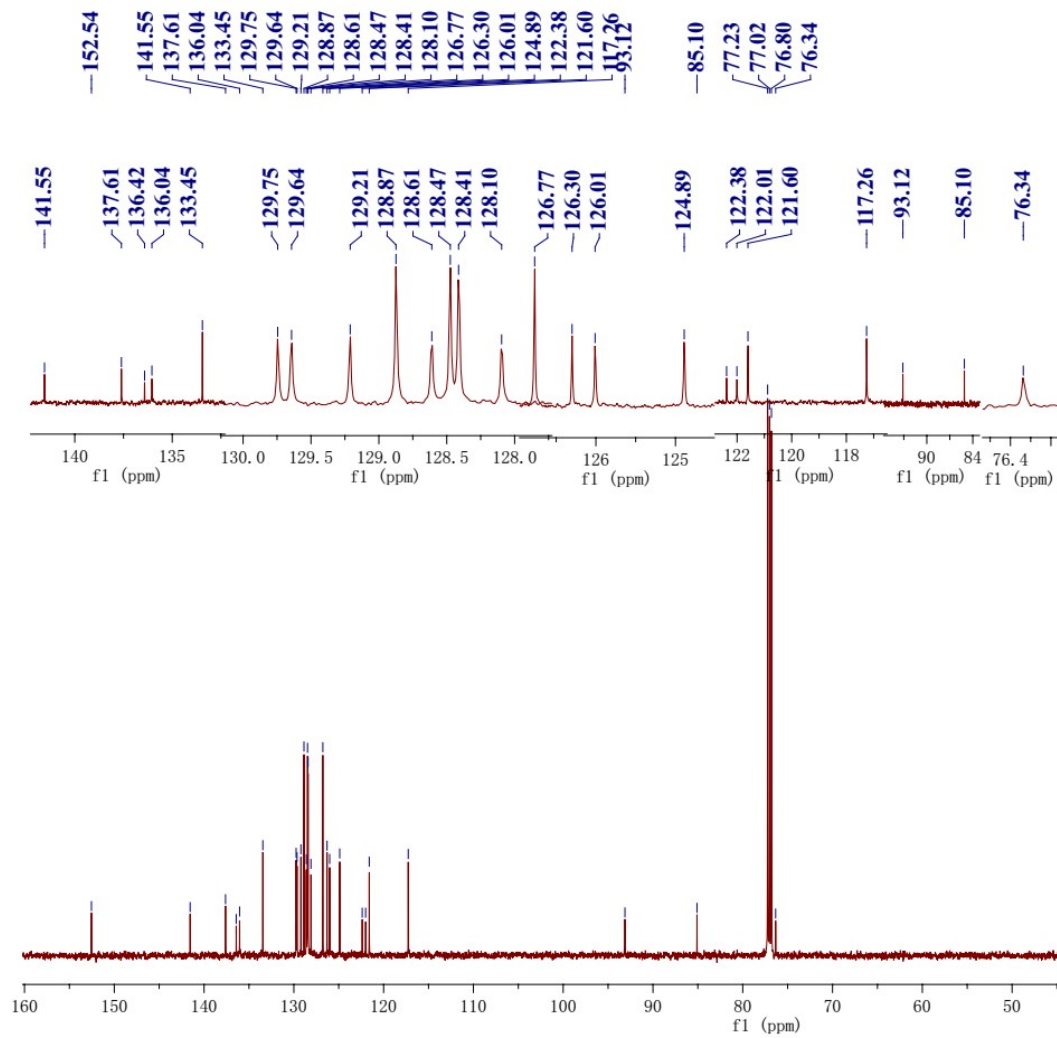




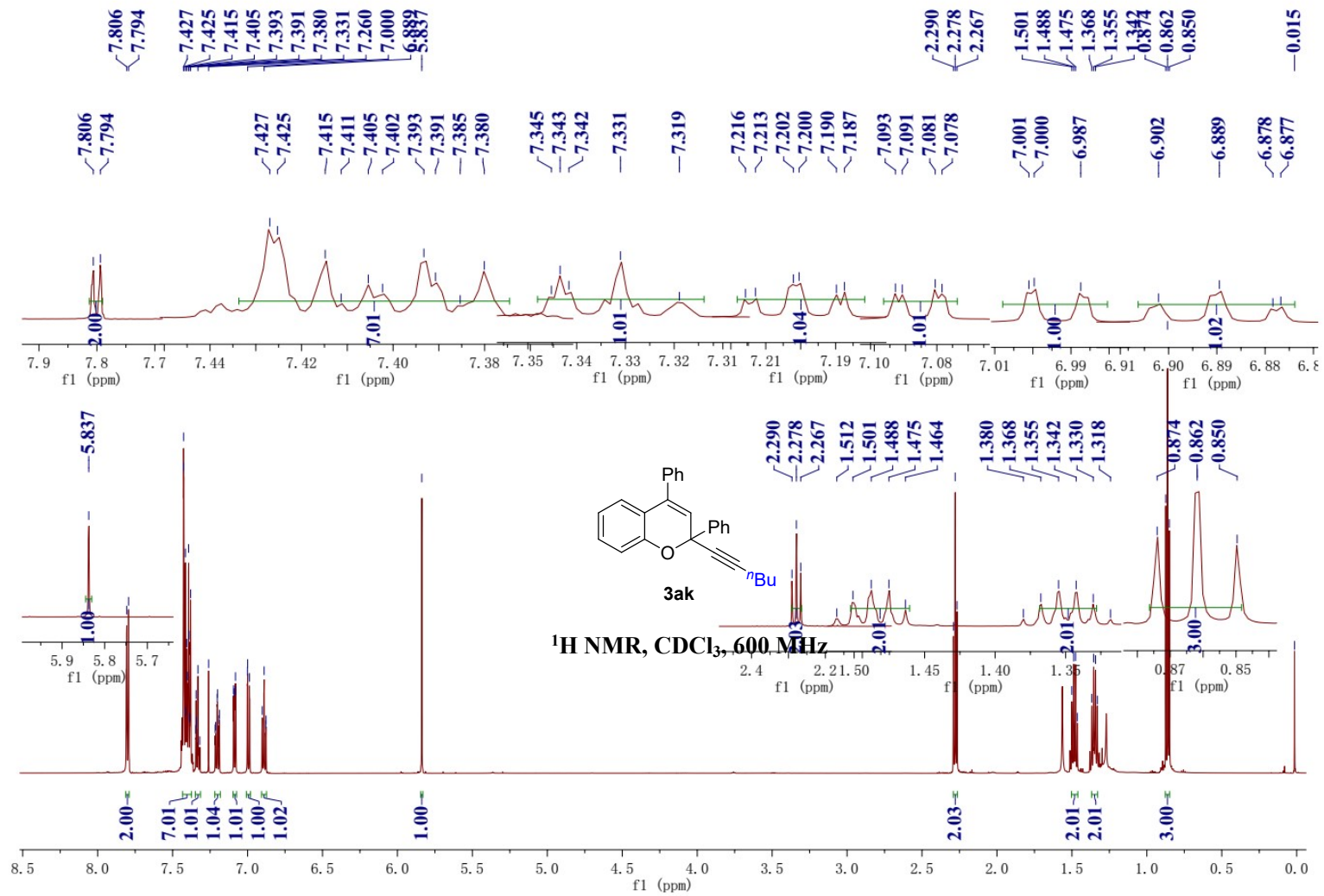
¹H NMR, CDCl₃, 600 MHz

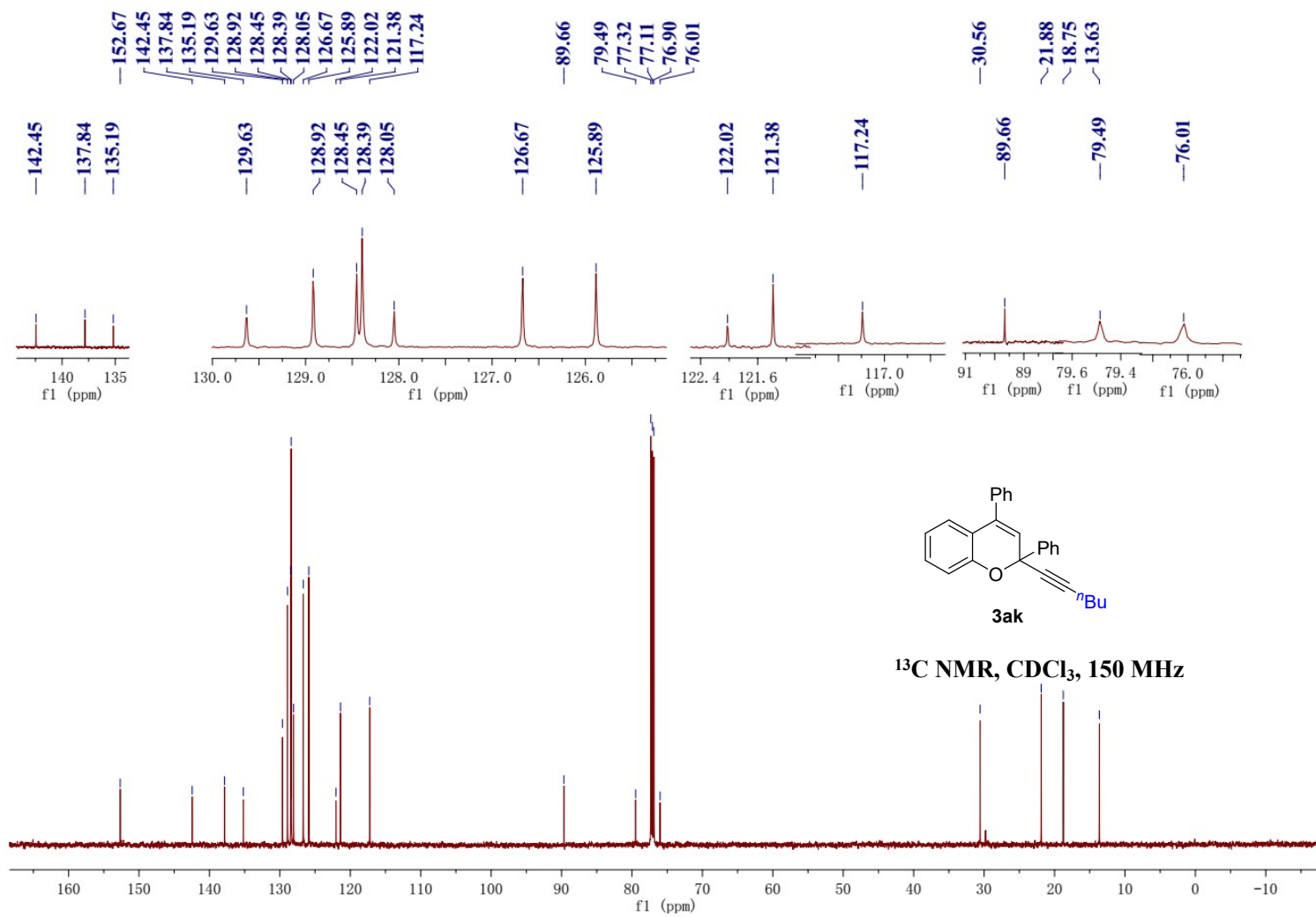


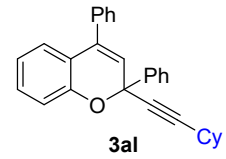
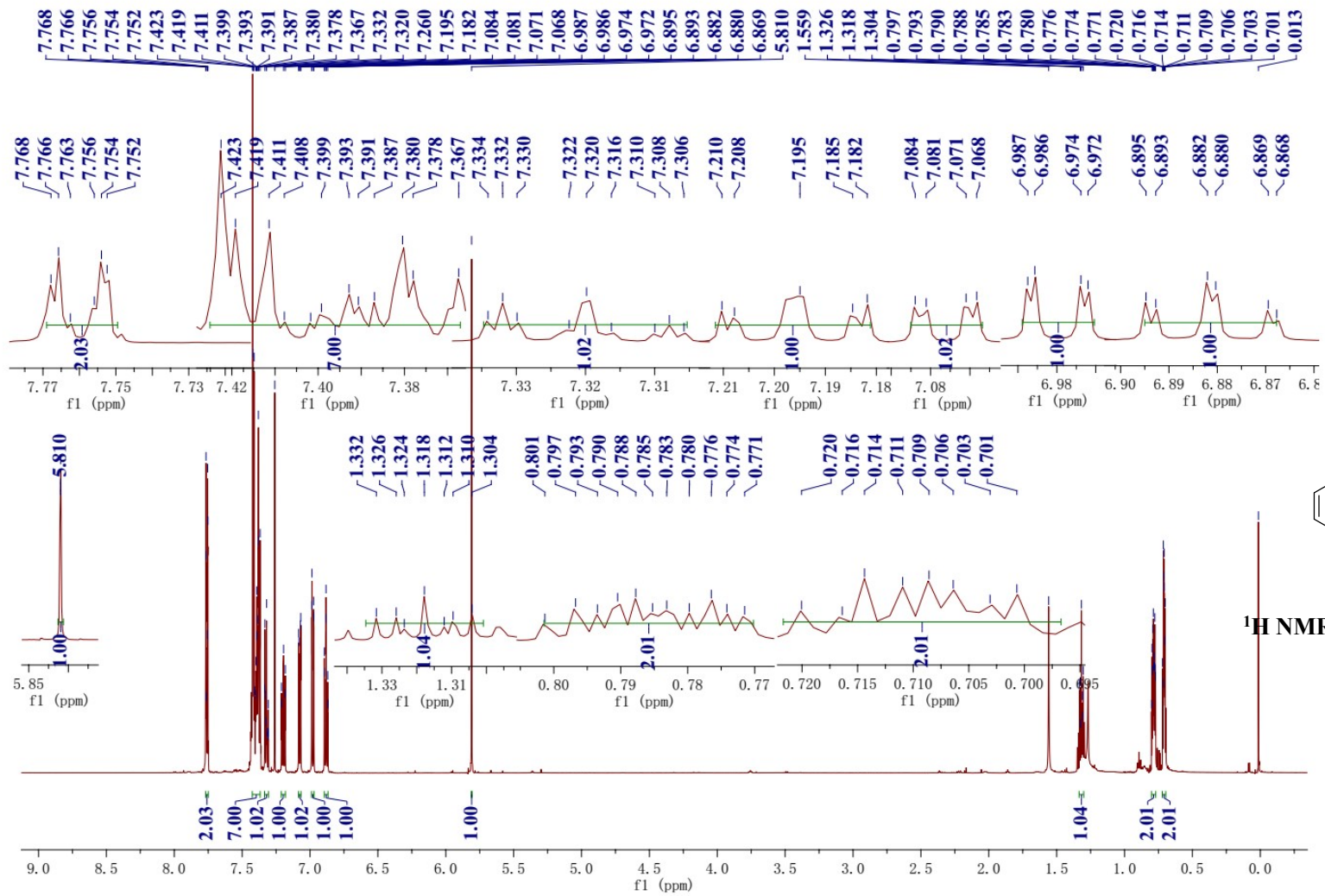




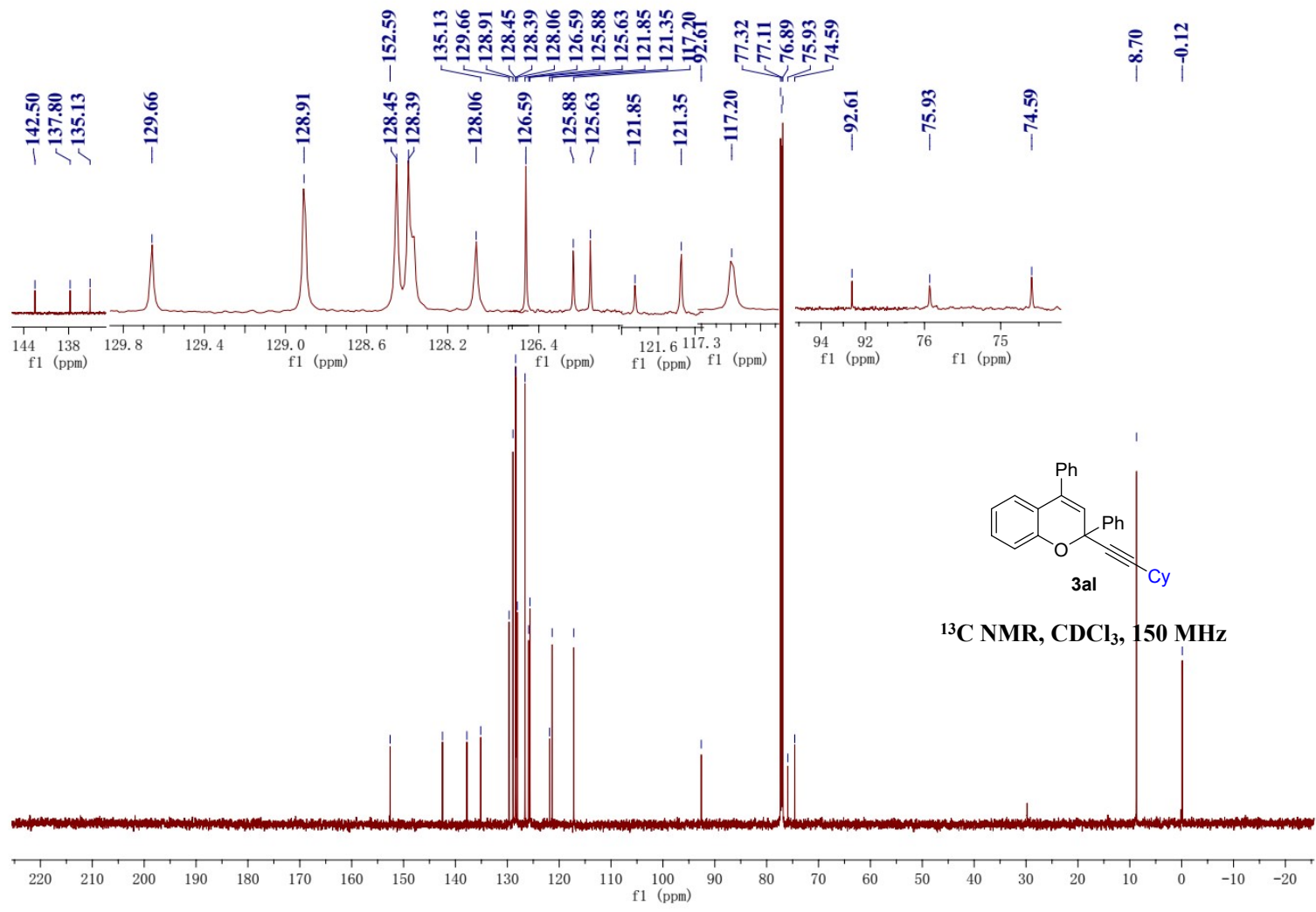
¹³C NMR, CDCl₃, 150 MHz

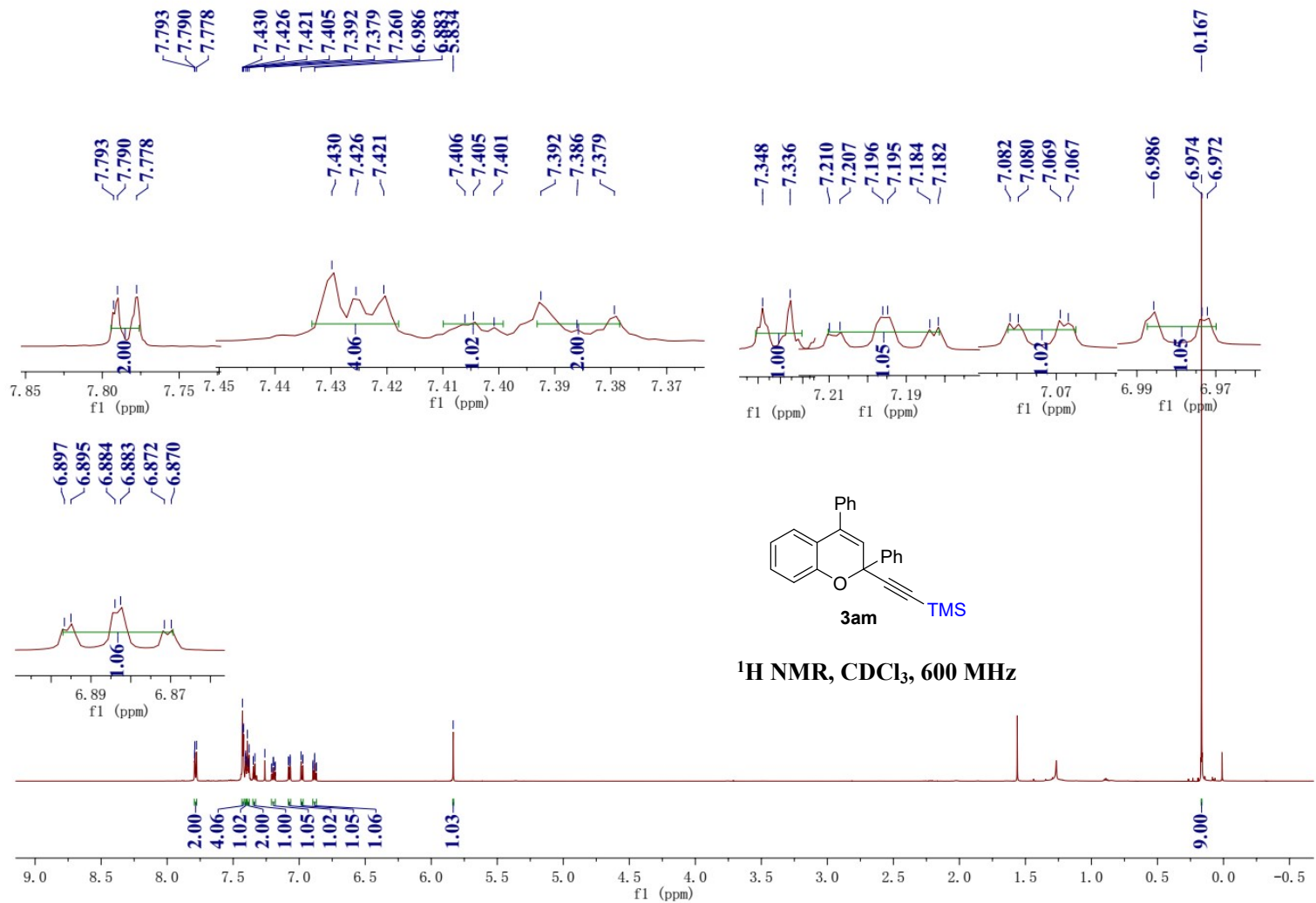


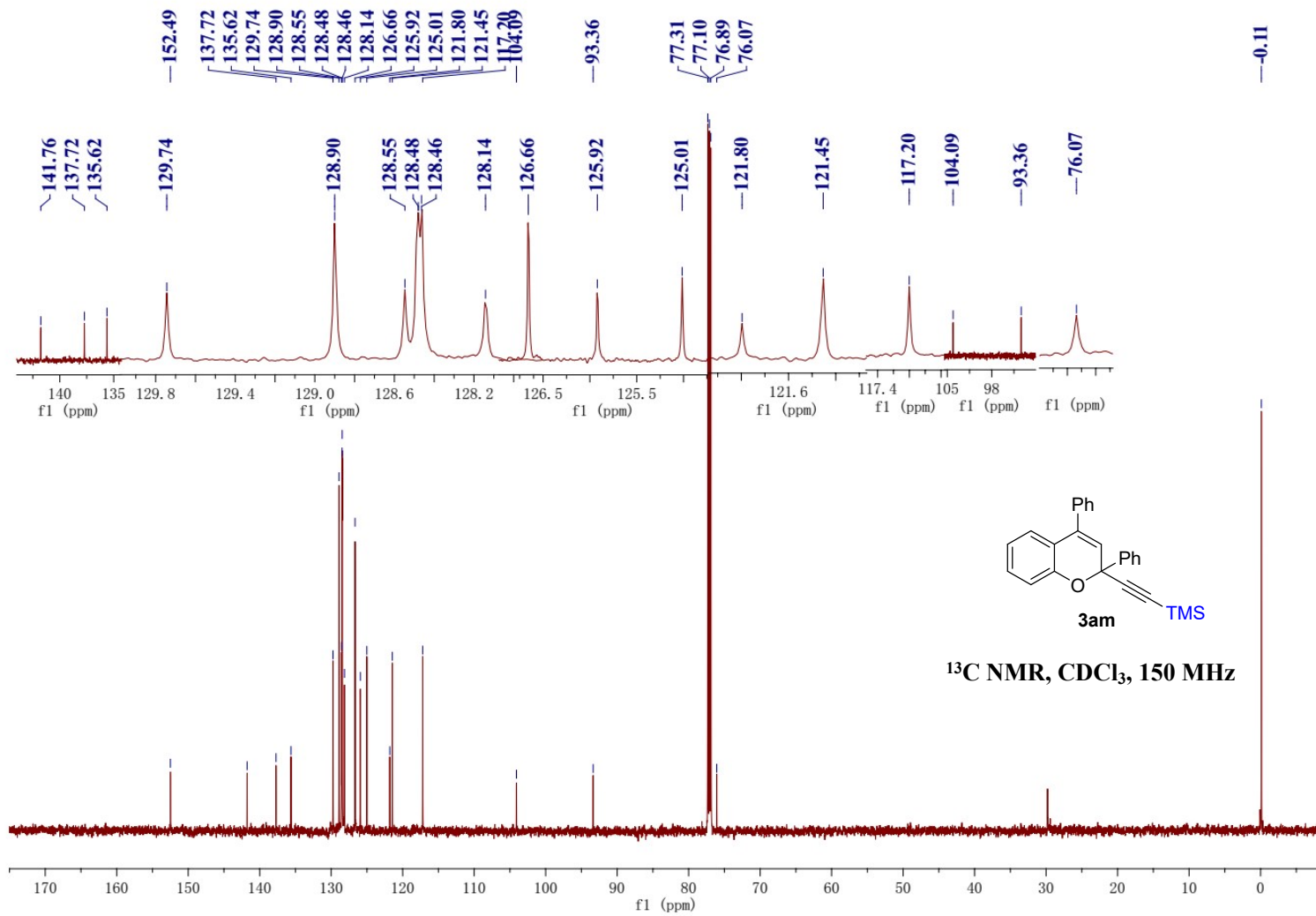


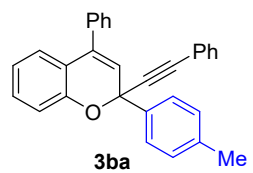
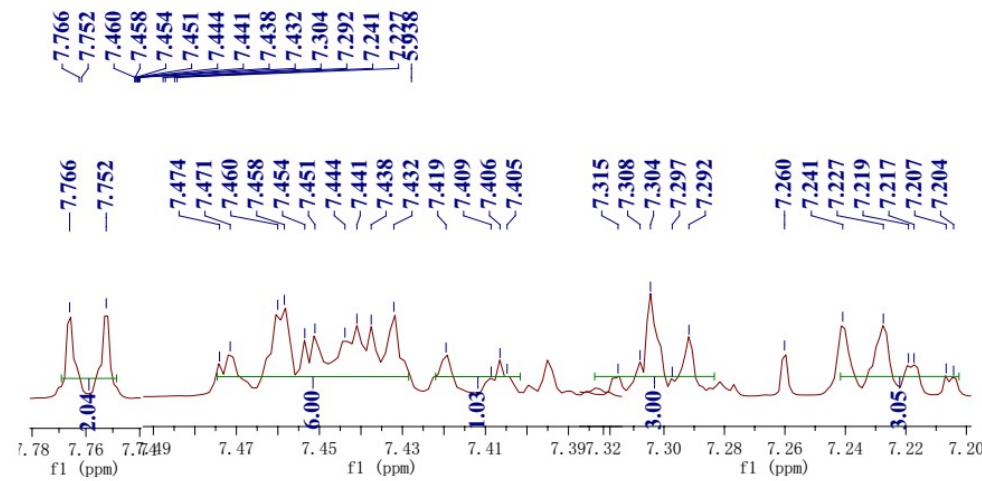


¹H NMR, CDCl₃, 600 MHz

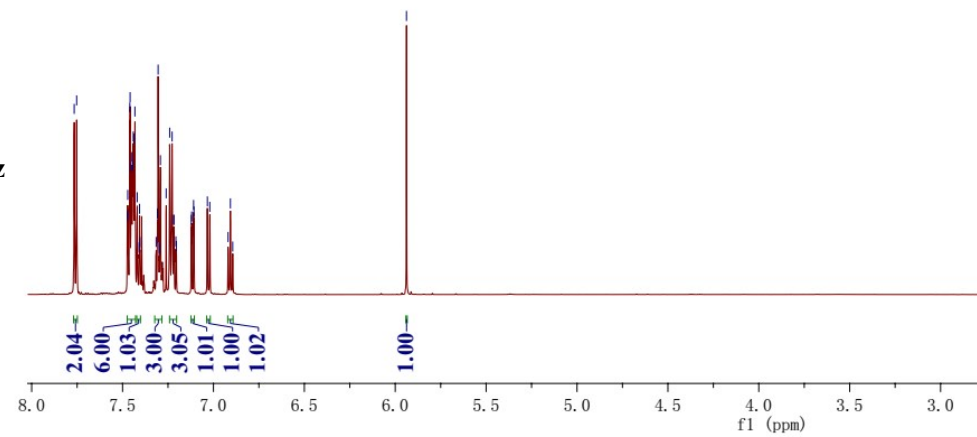


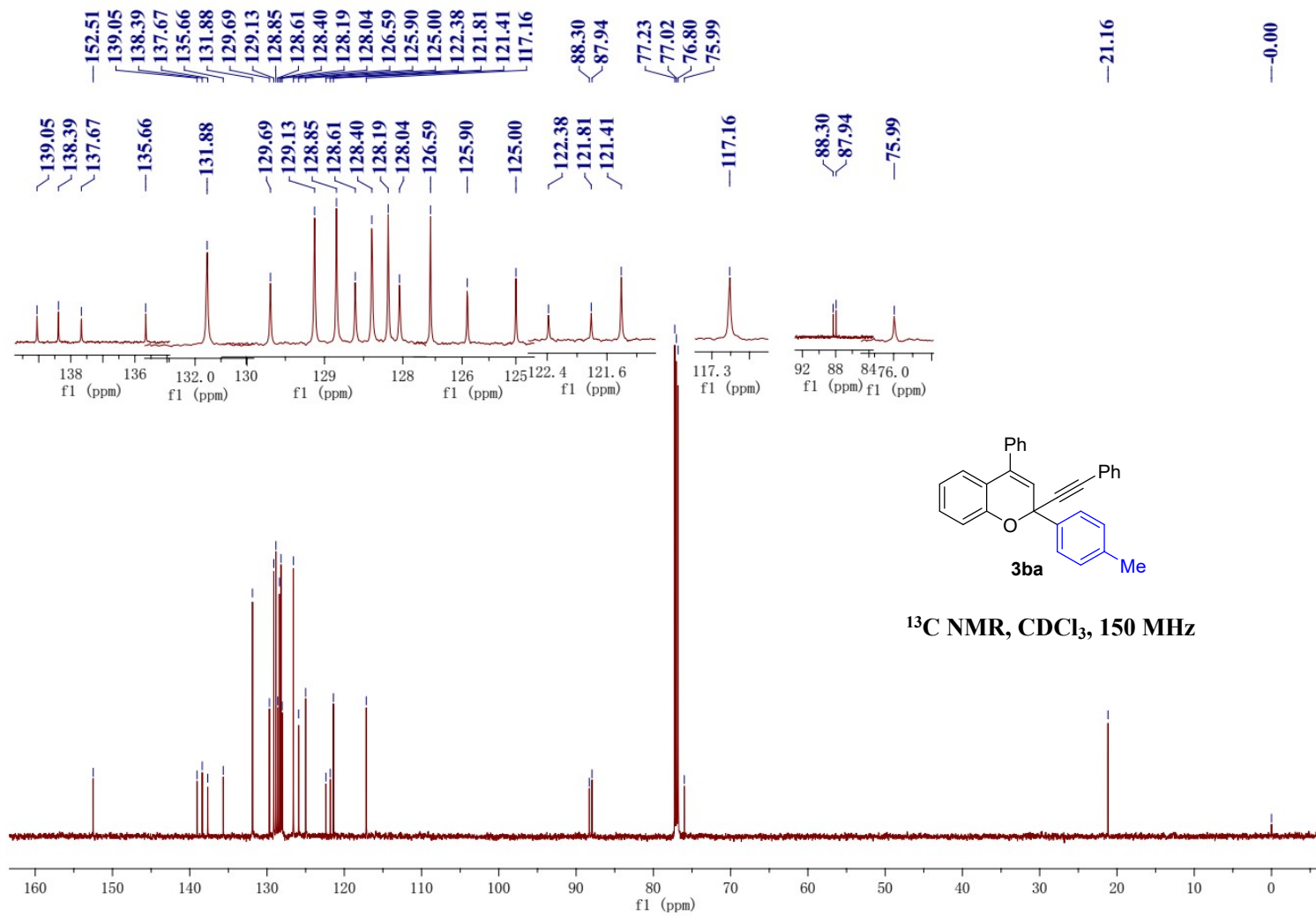


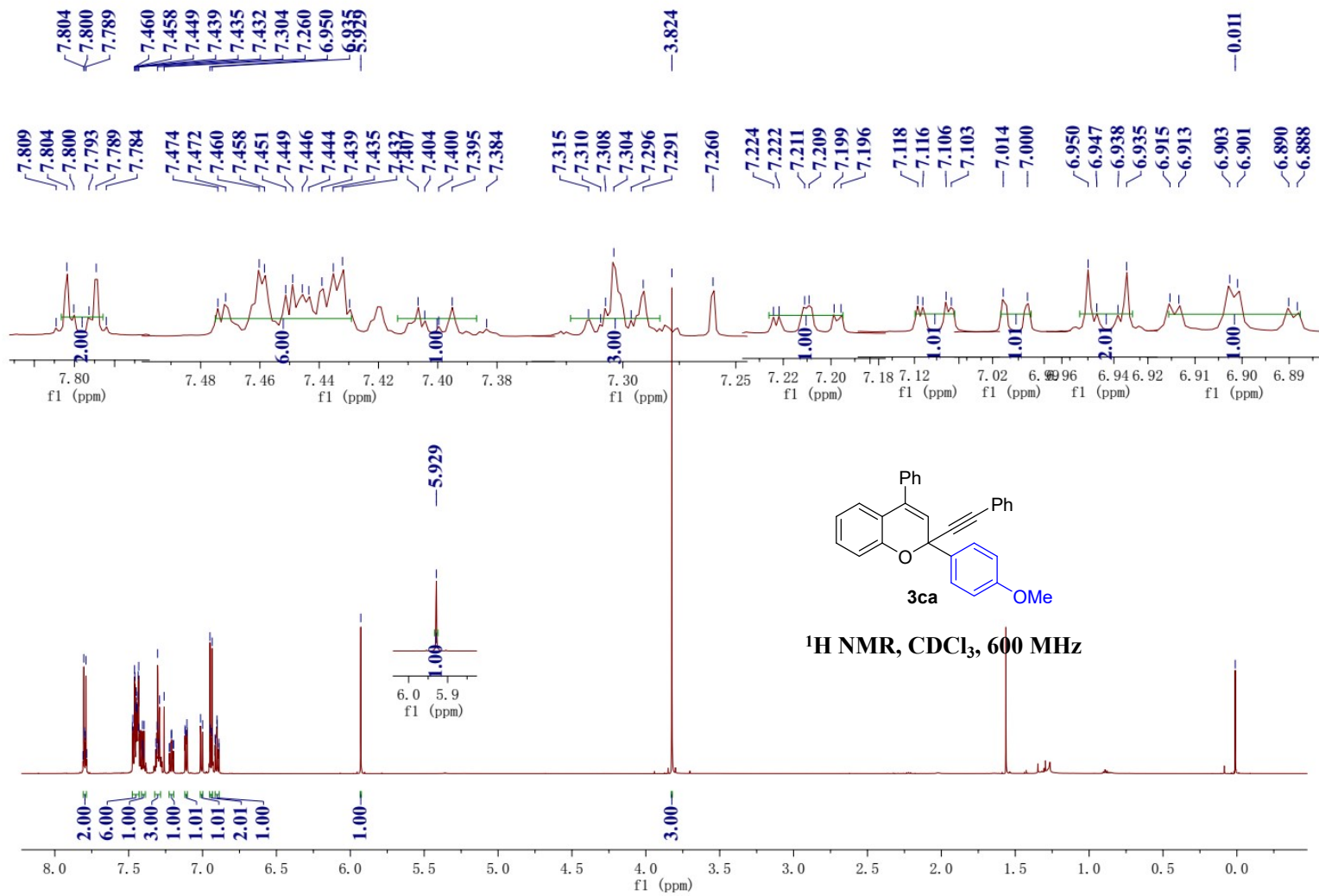


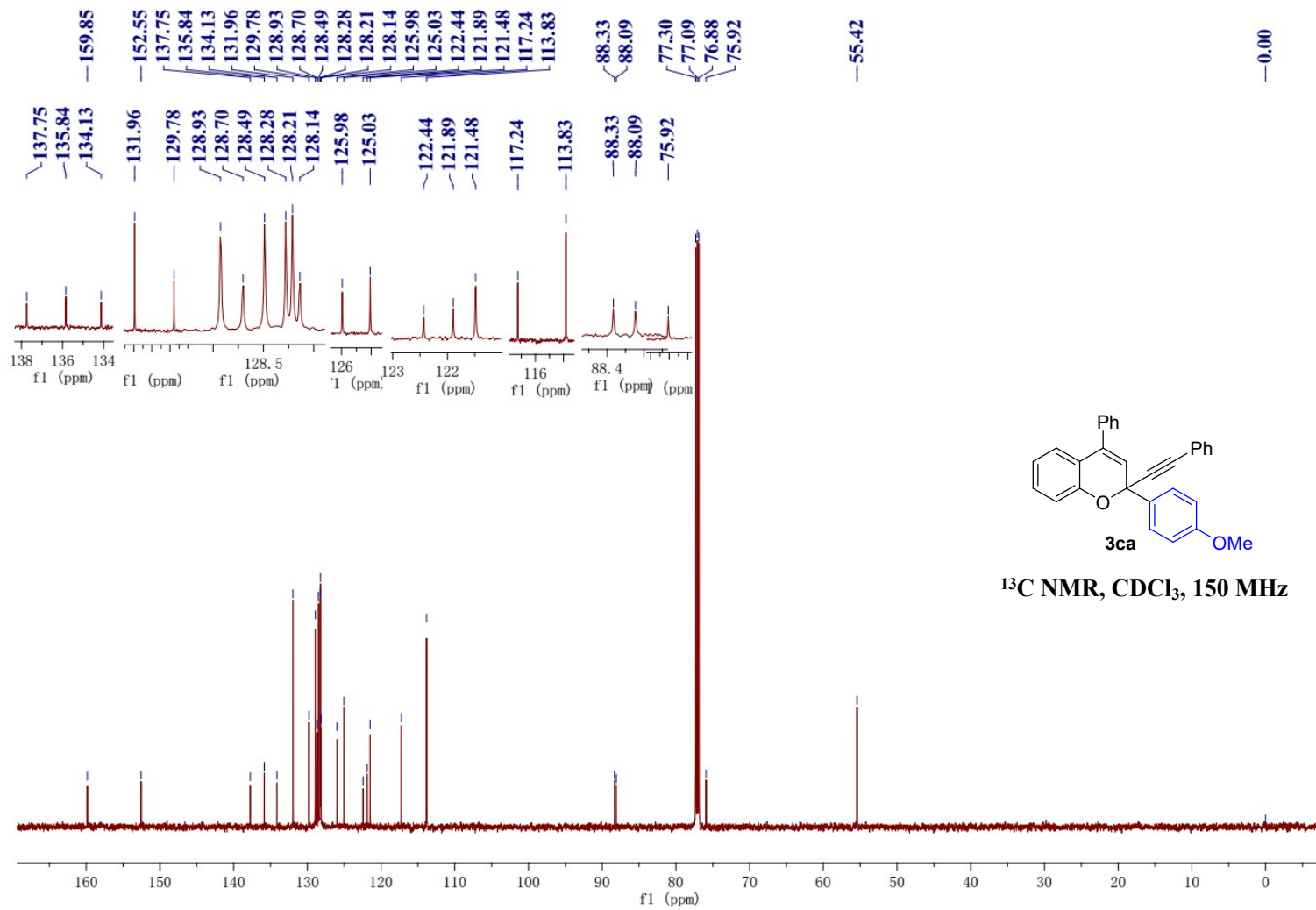


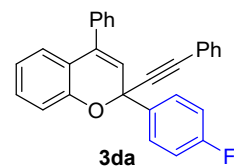
$^1\text{H NMR}$, CDCl_3 , 600 MHz



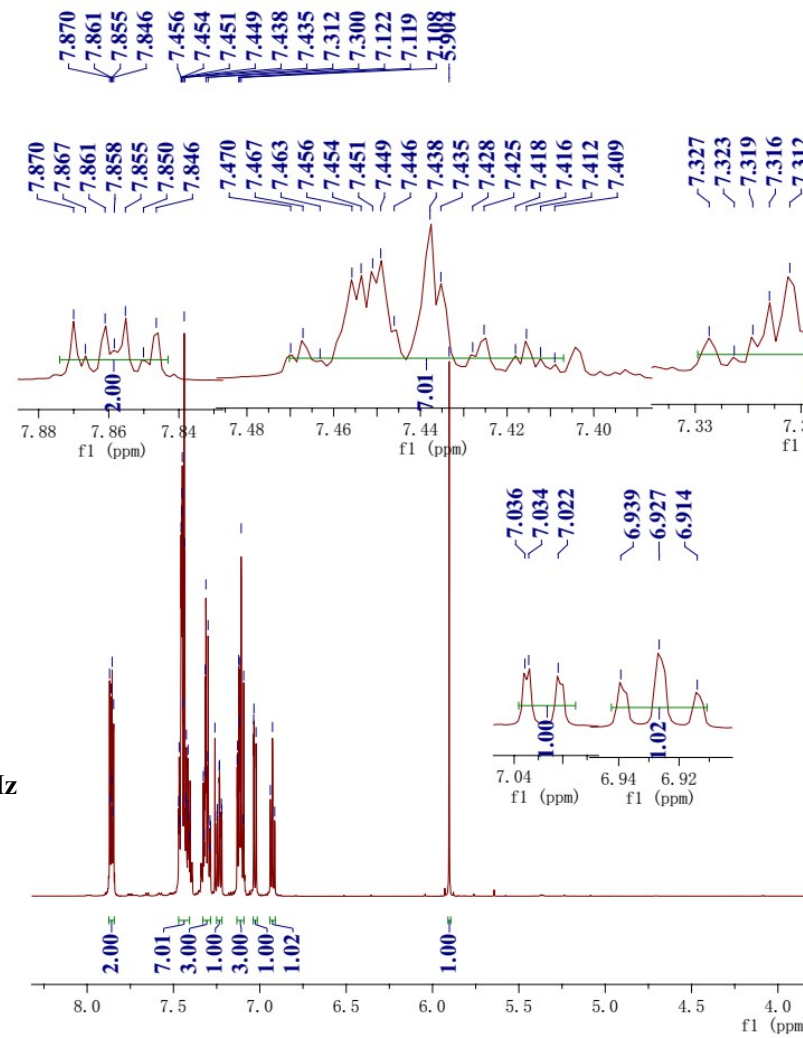


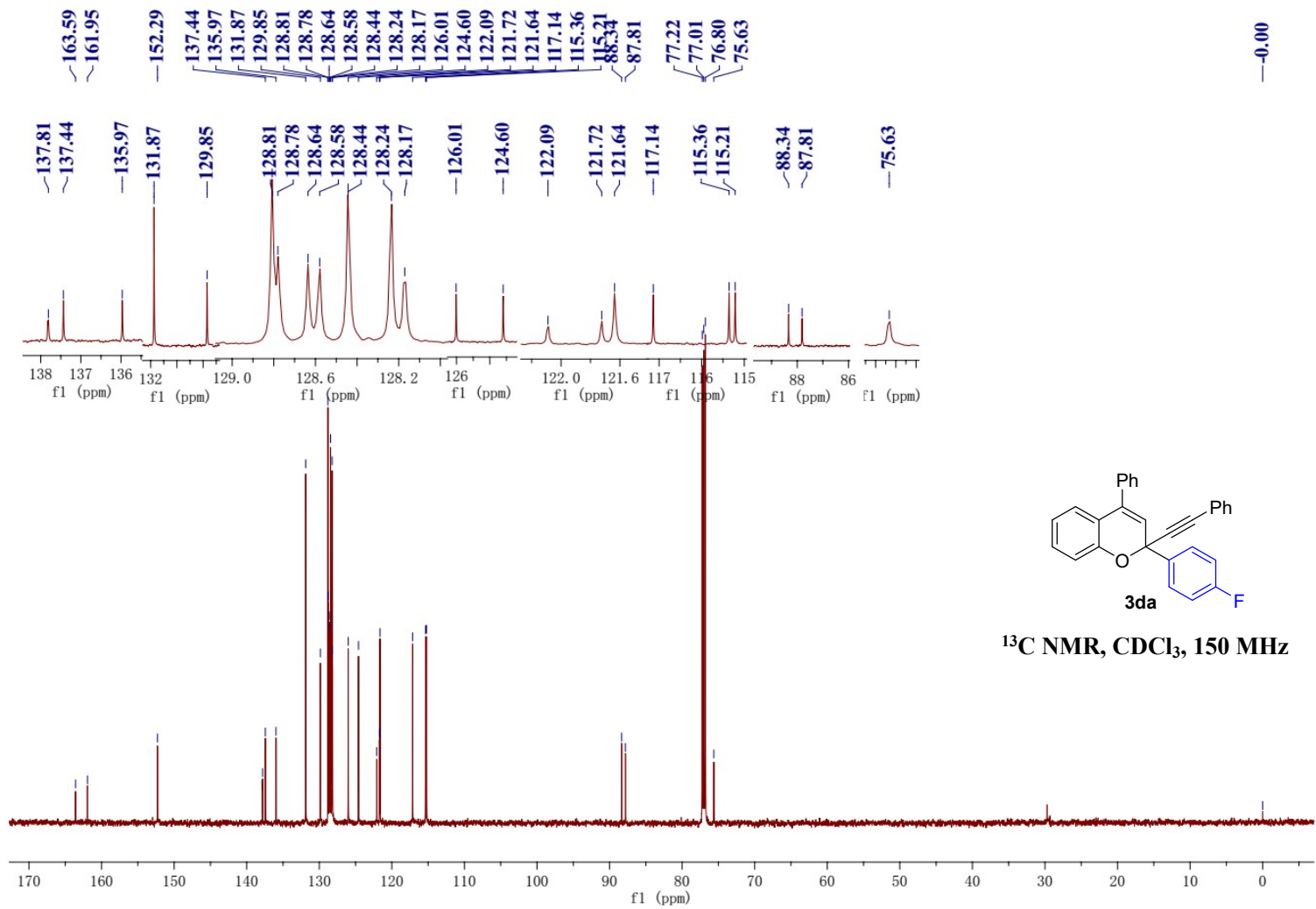




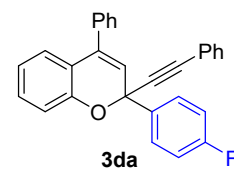


¹H NMR, CDCl₃, 600 MHz

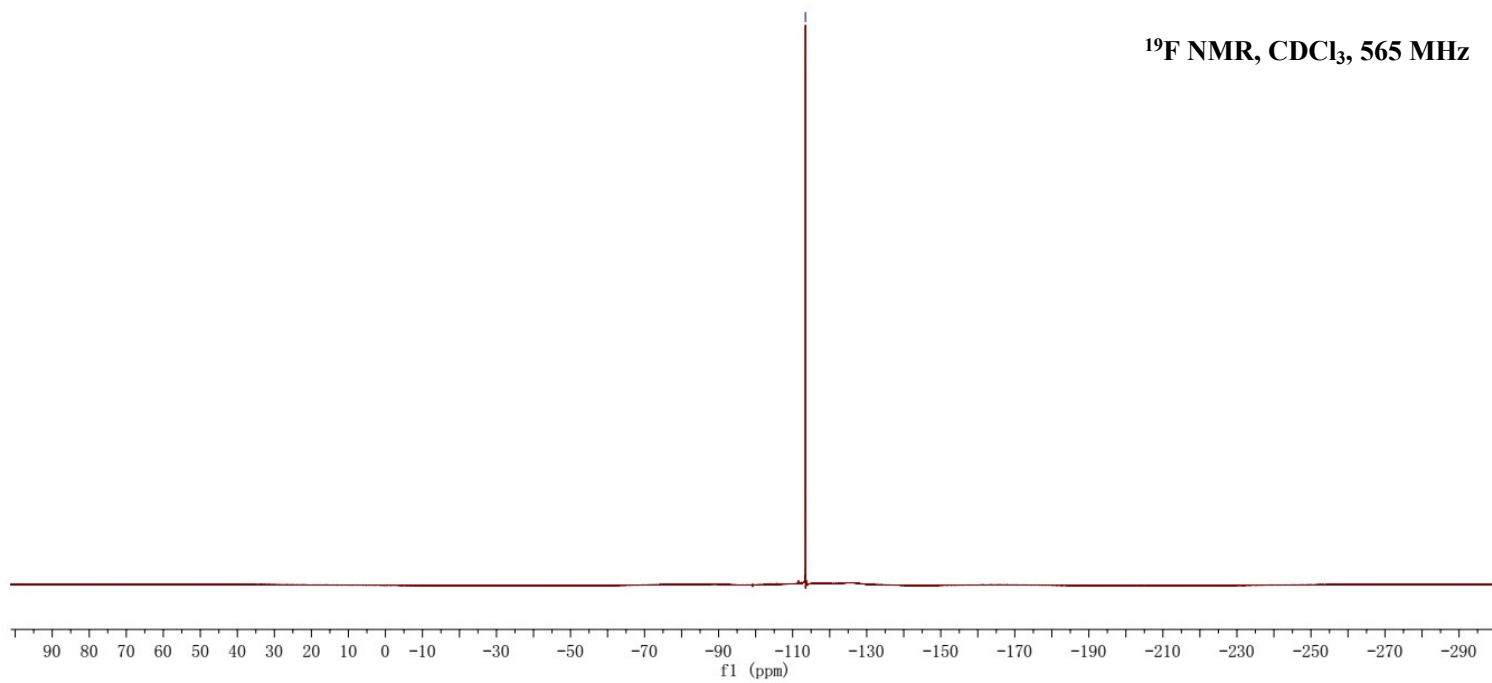


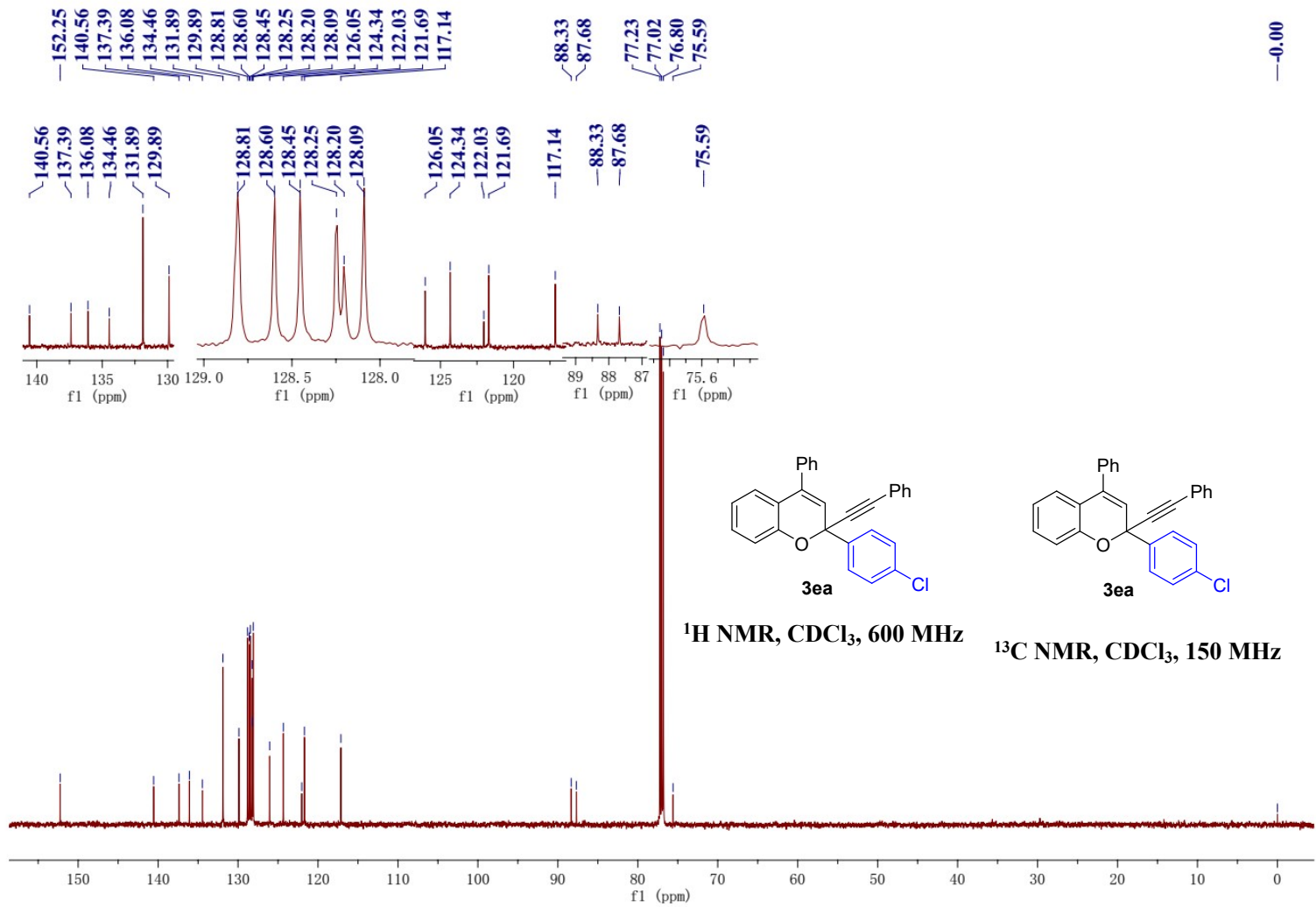


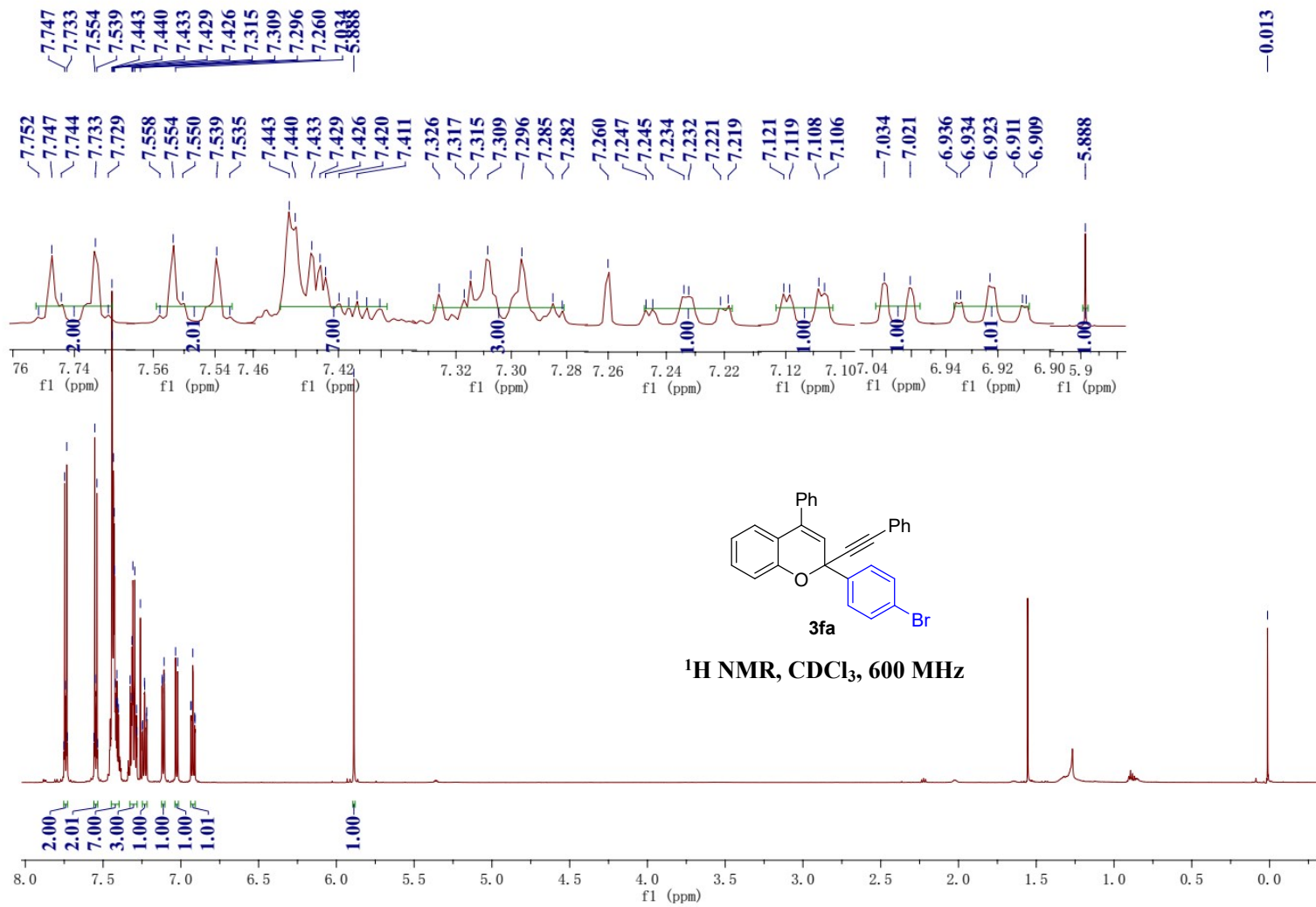
-113.44



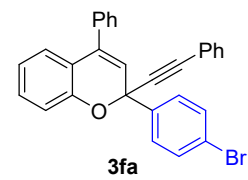
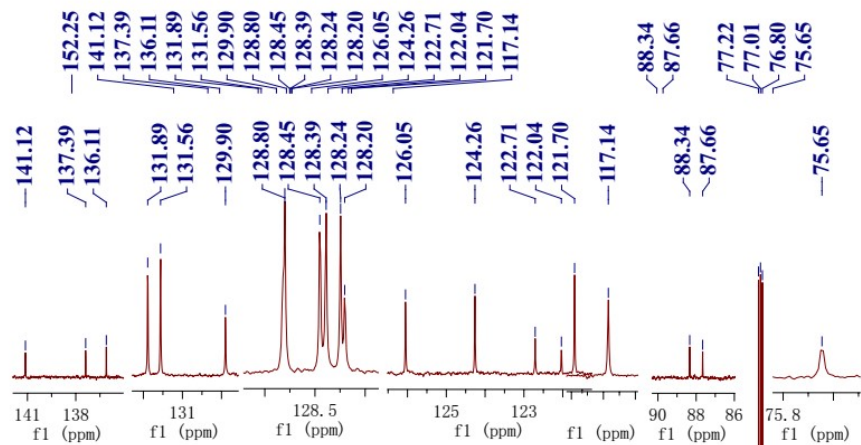
¹⁹F NMR, CDCl₃, 565 MHz



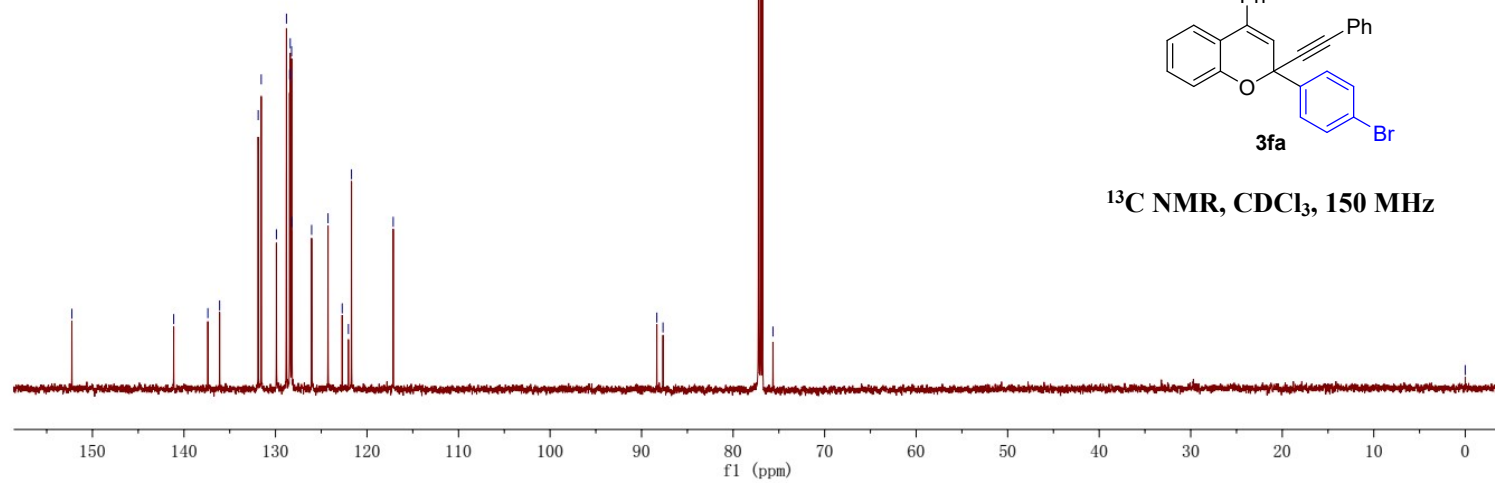


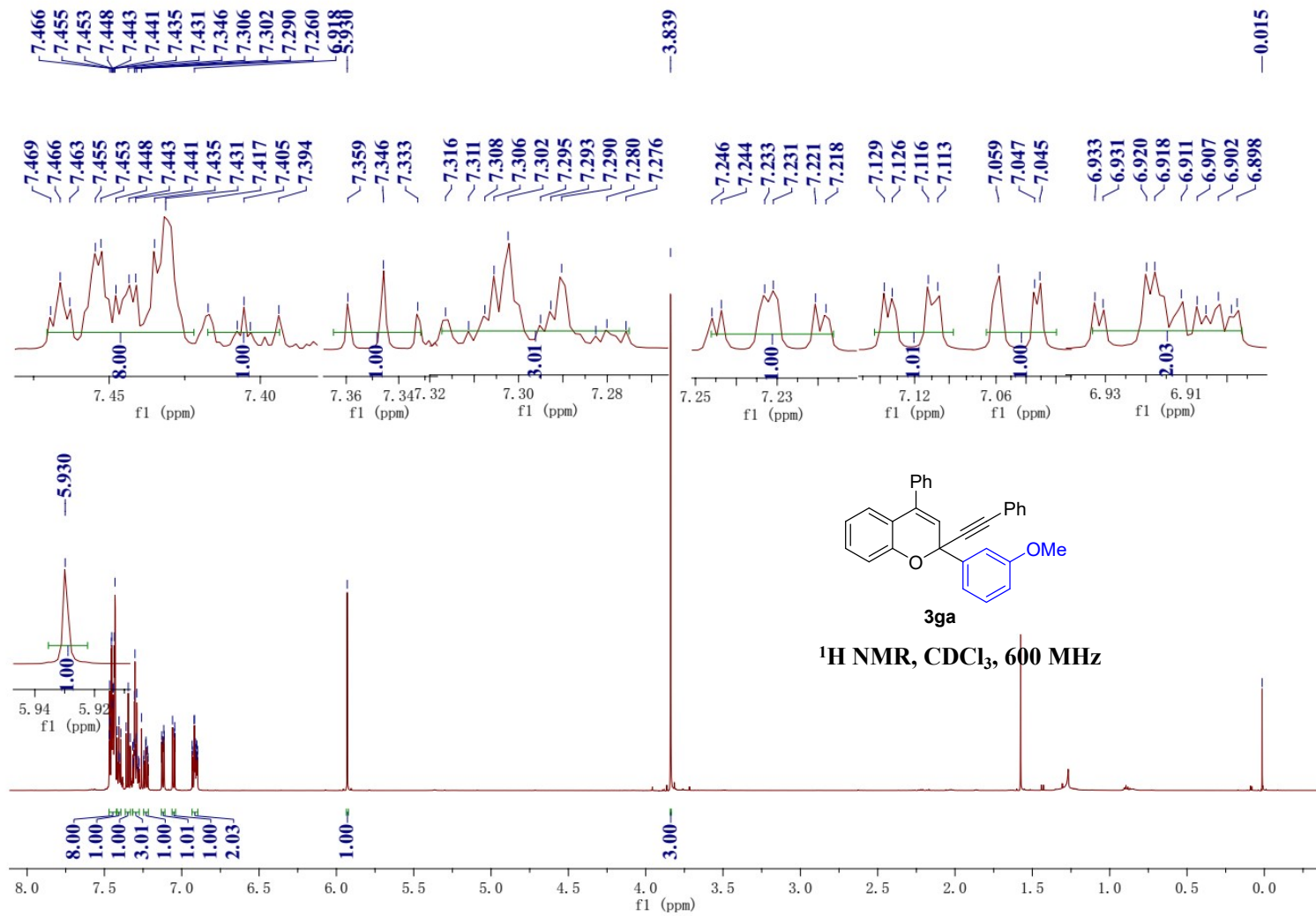


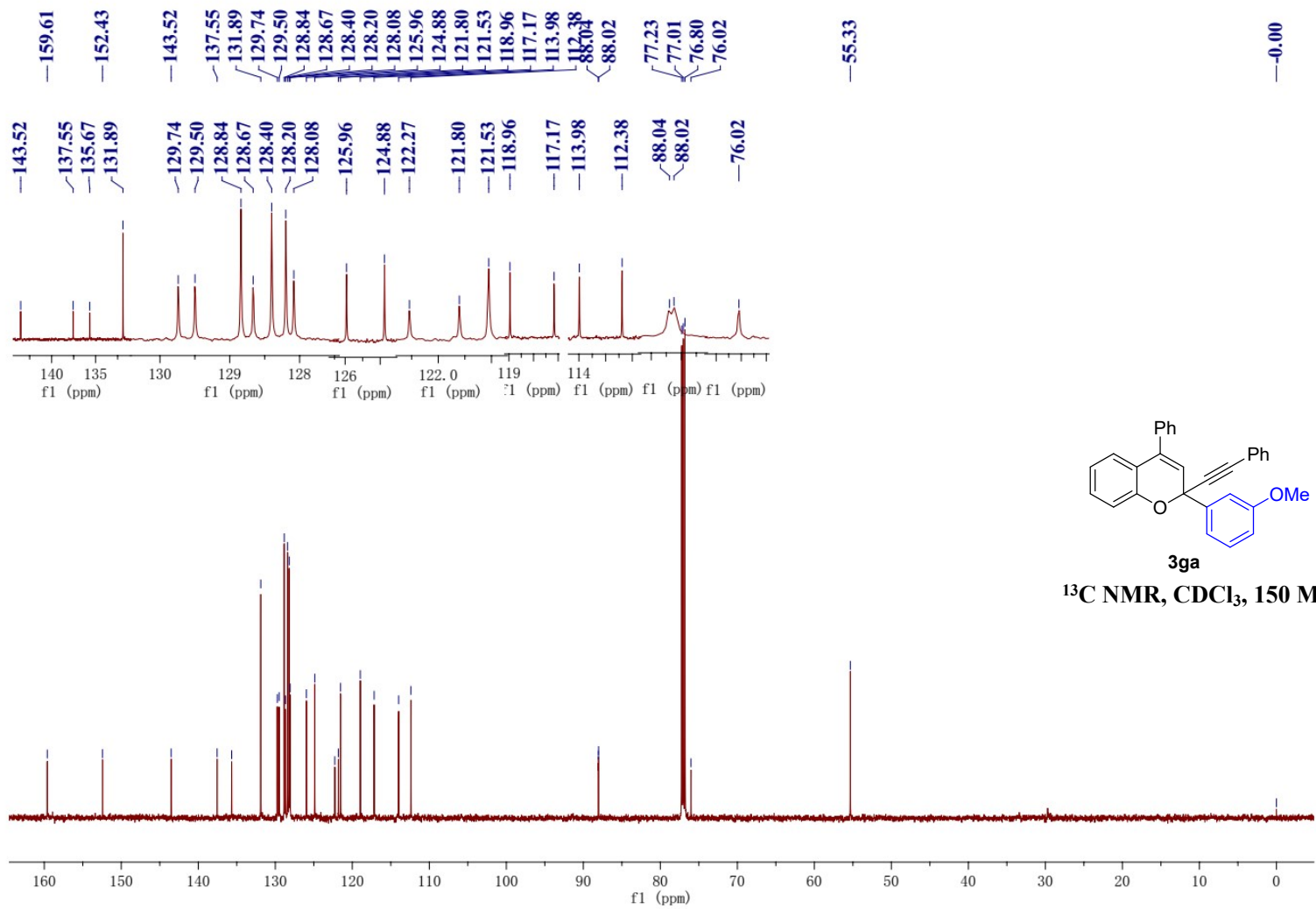
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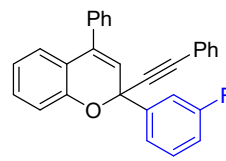


¹³C NMR, CDCl₃, 150 MHz



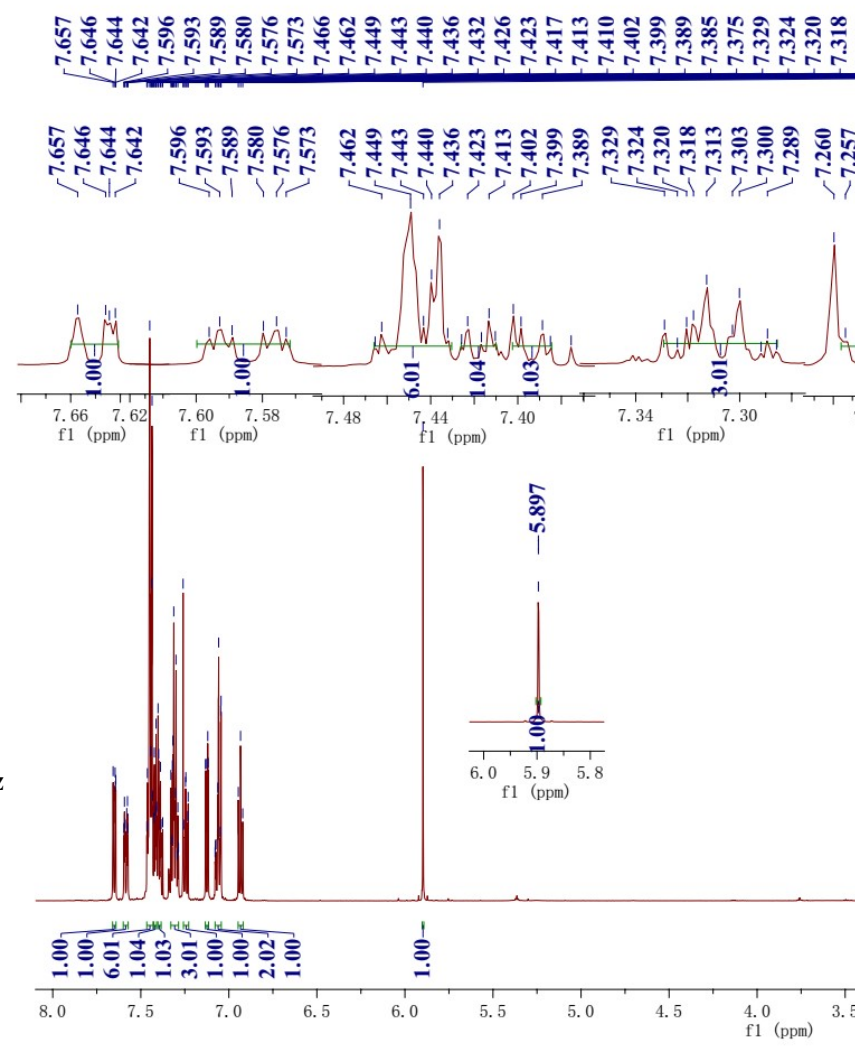


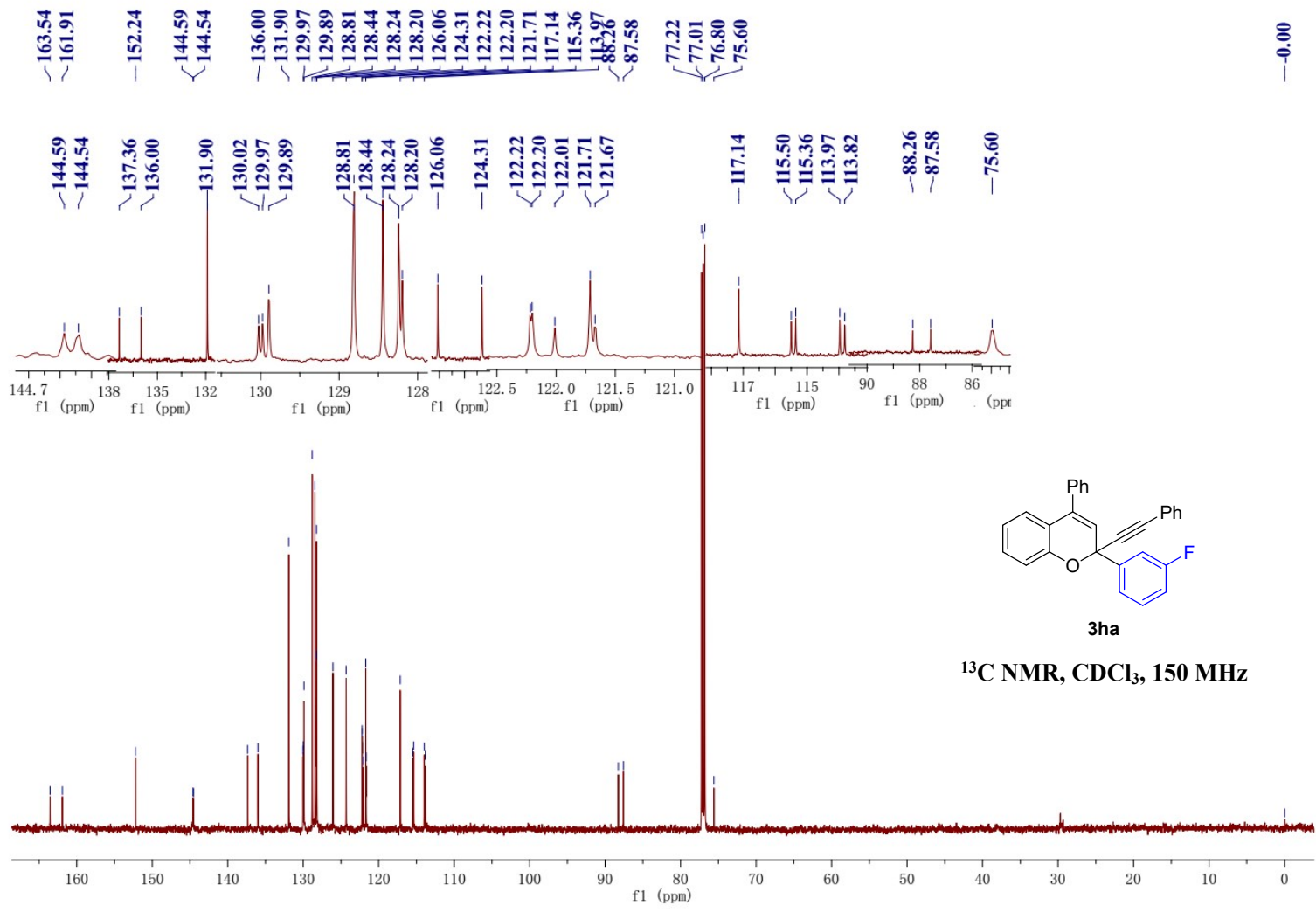




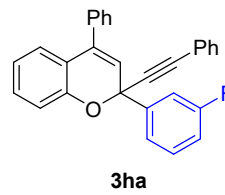
3ha

¹H NMR, CDCl₃, 600 MHz

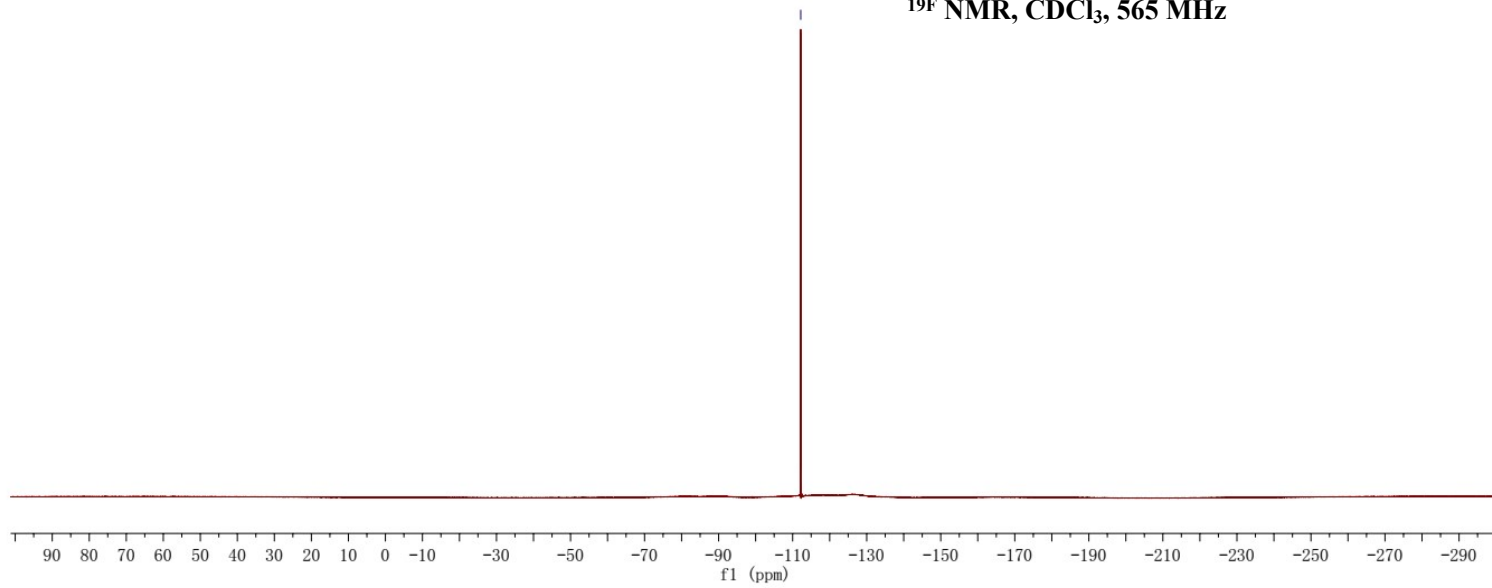


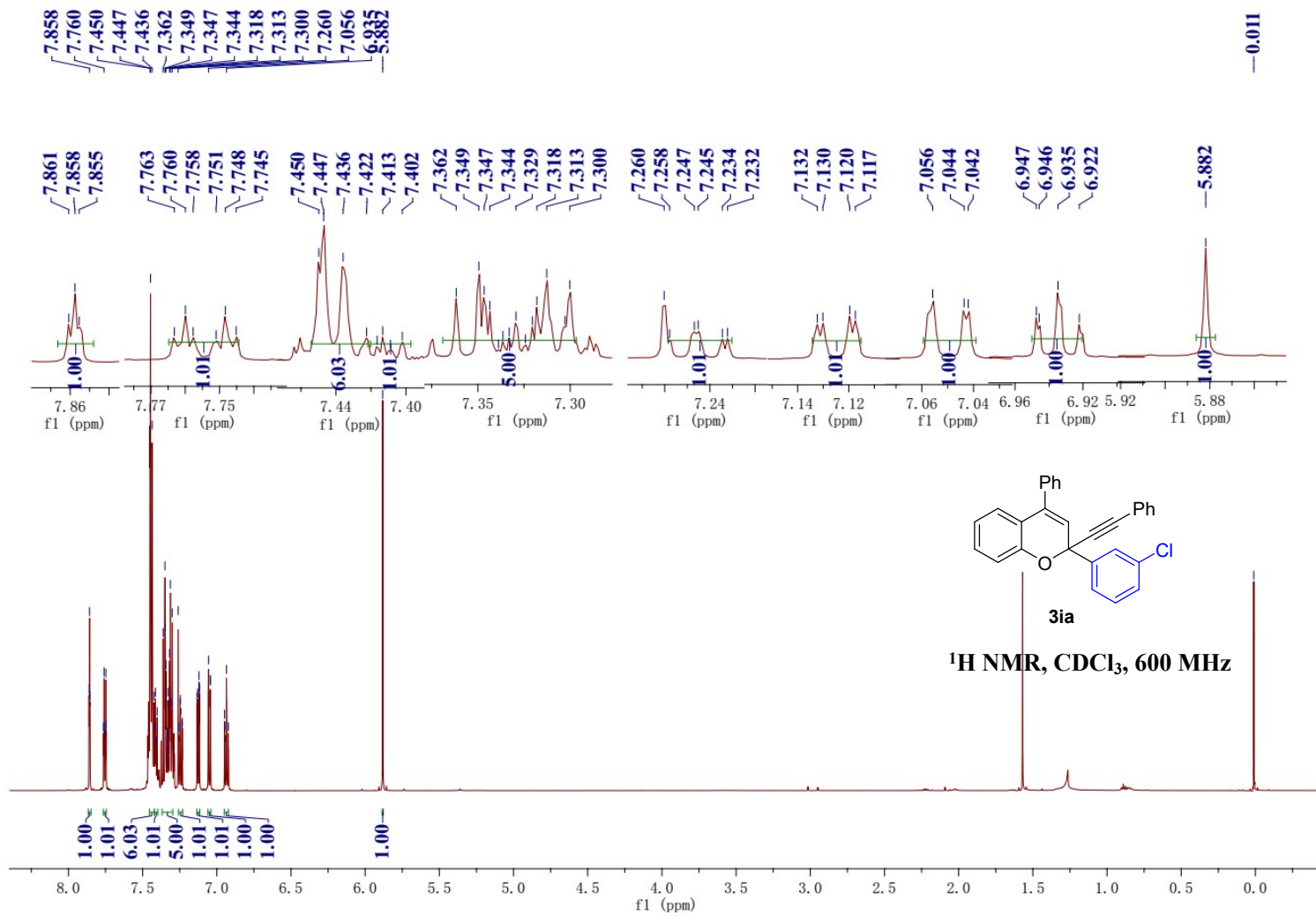


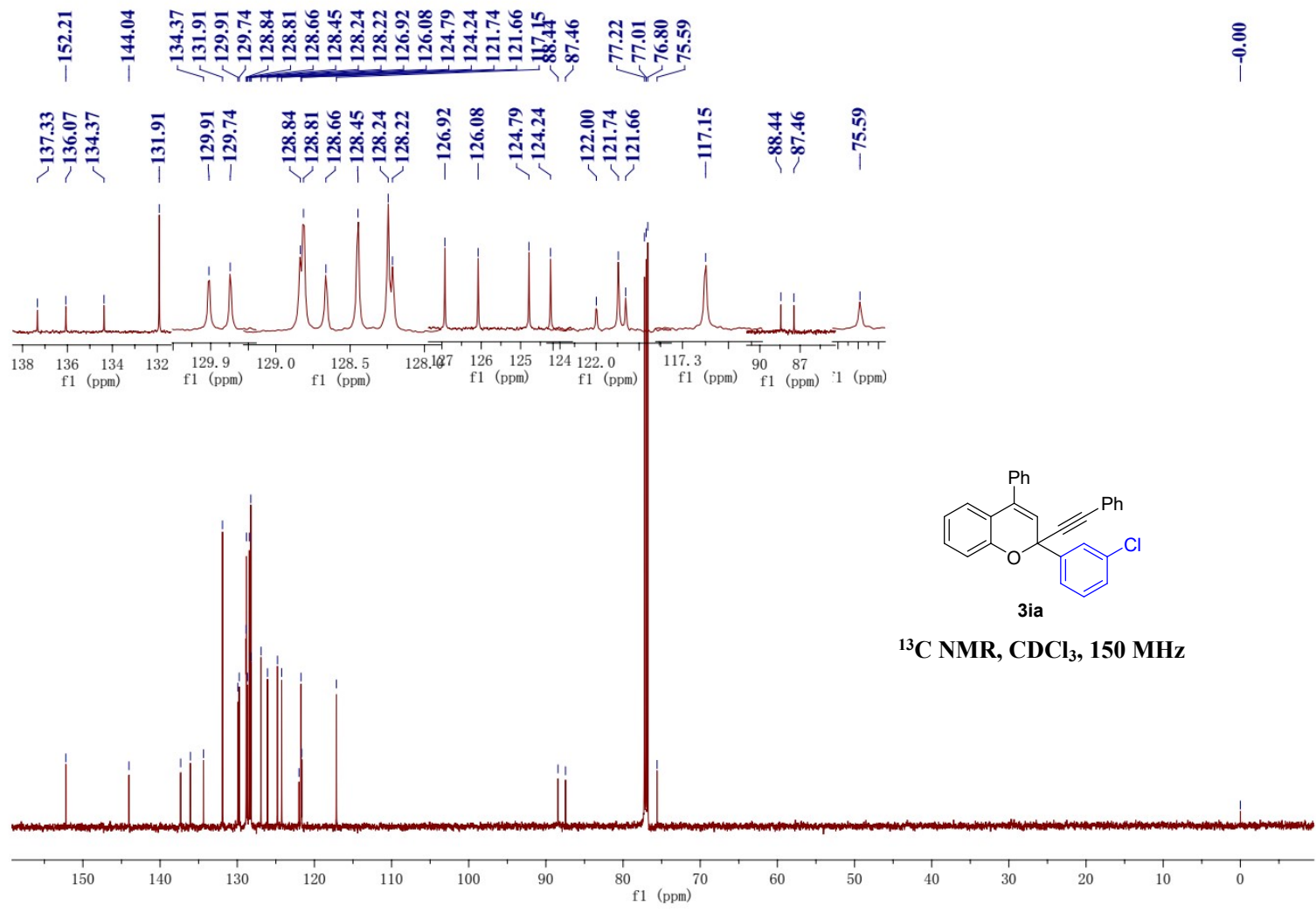
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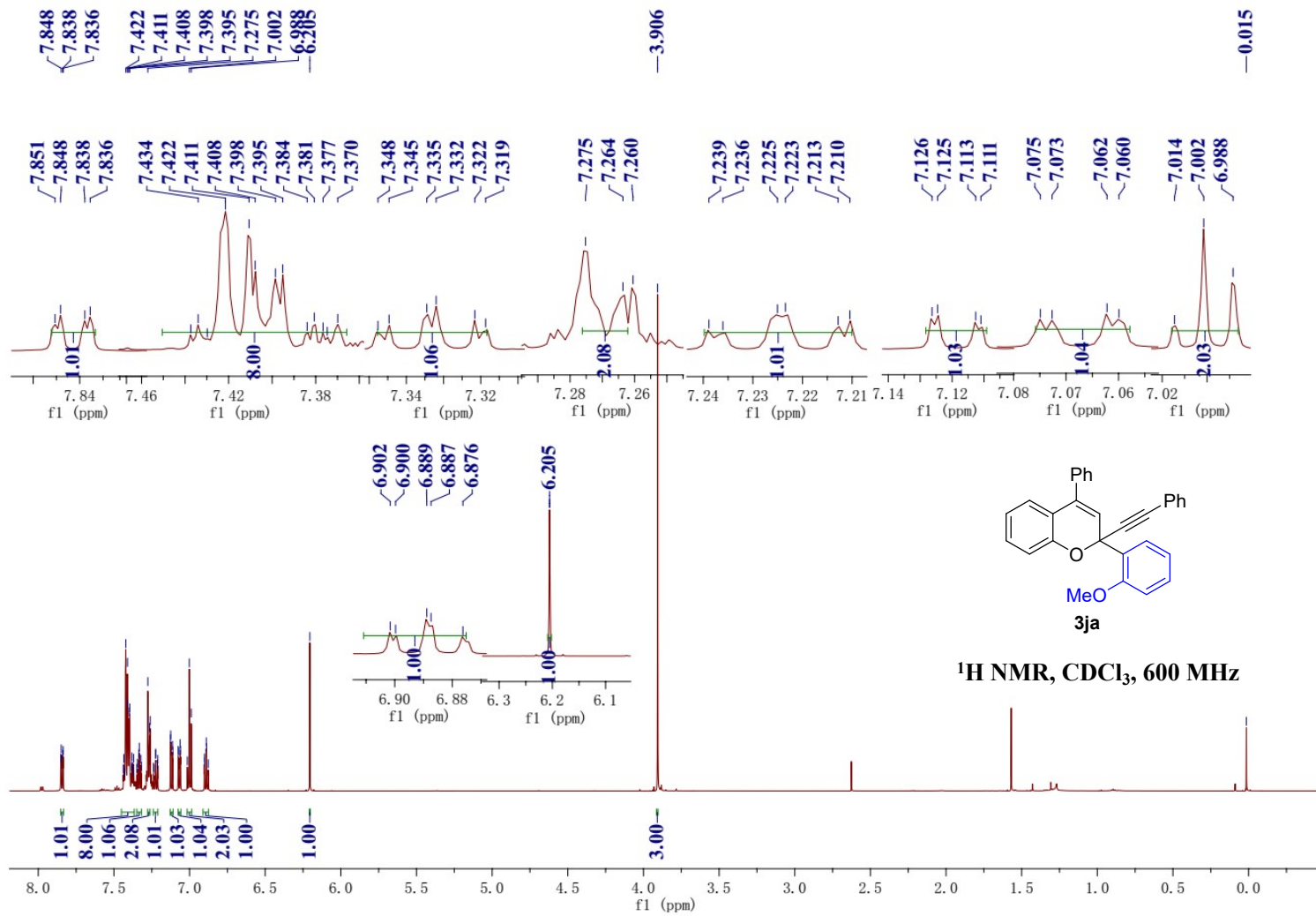


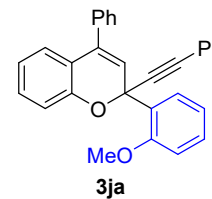
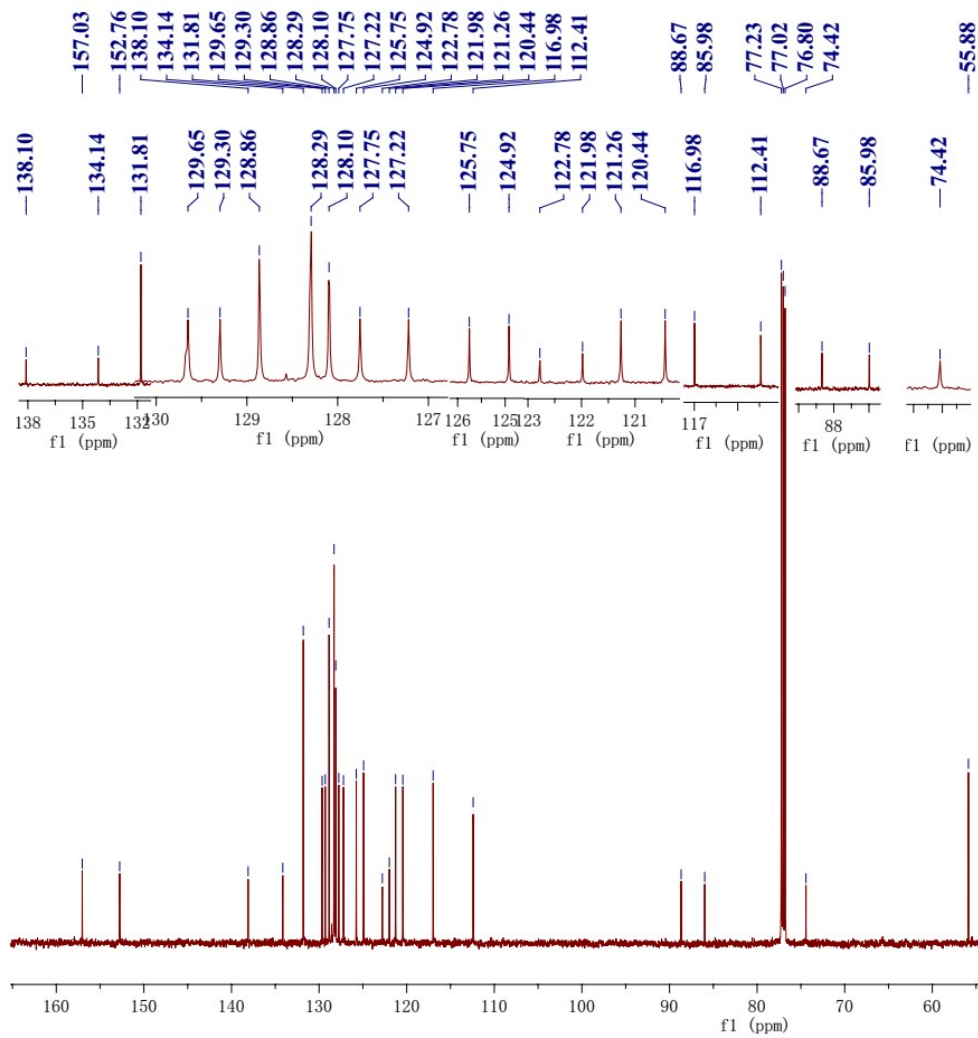
¹⁹F NMR, CDCl₃, 565 MHz



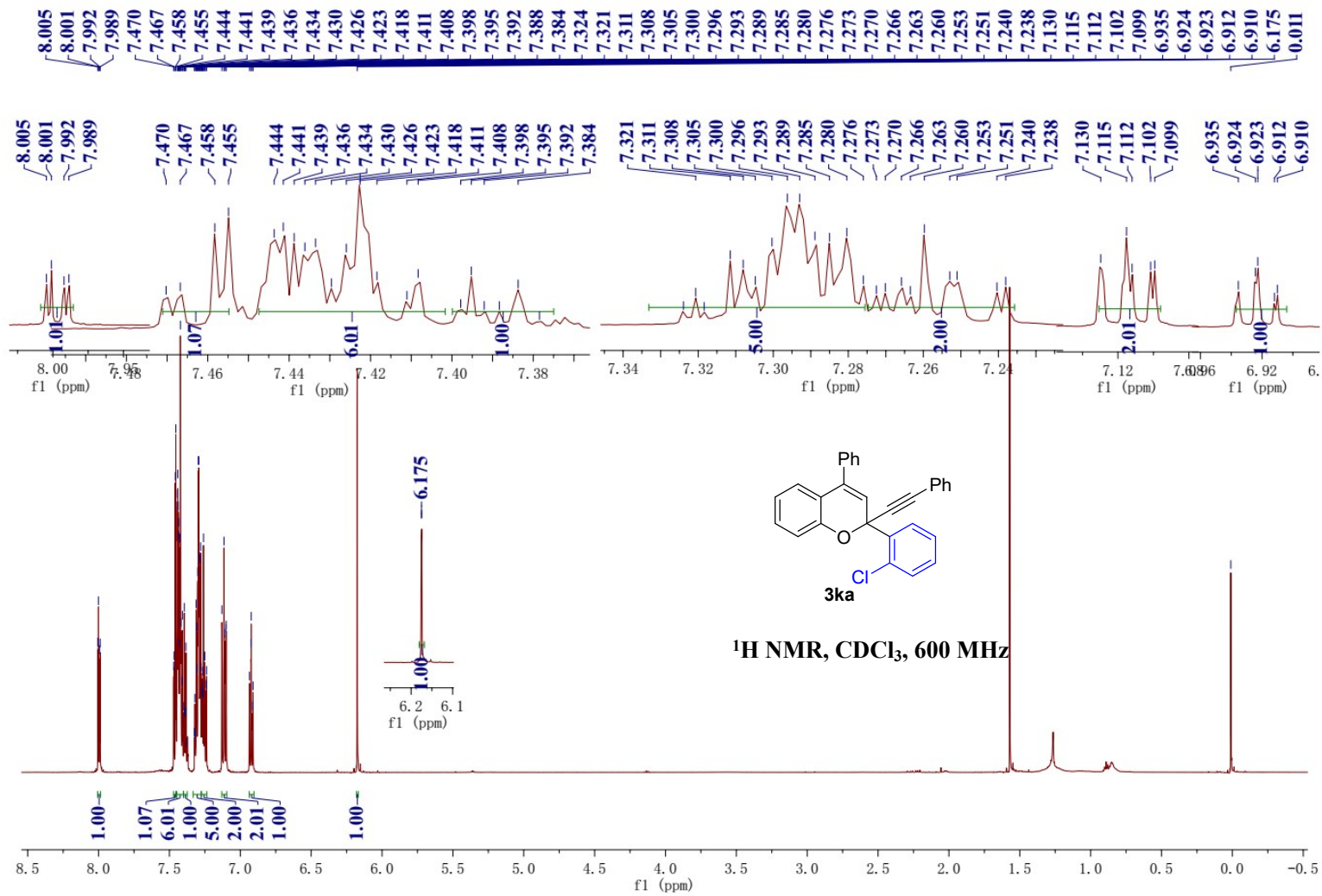


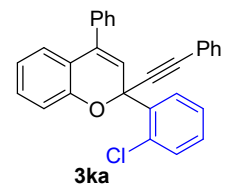
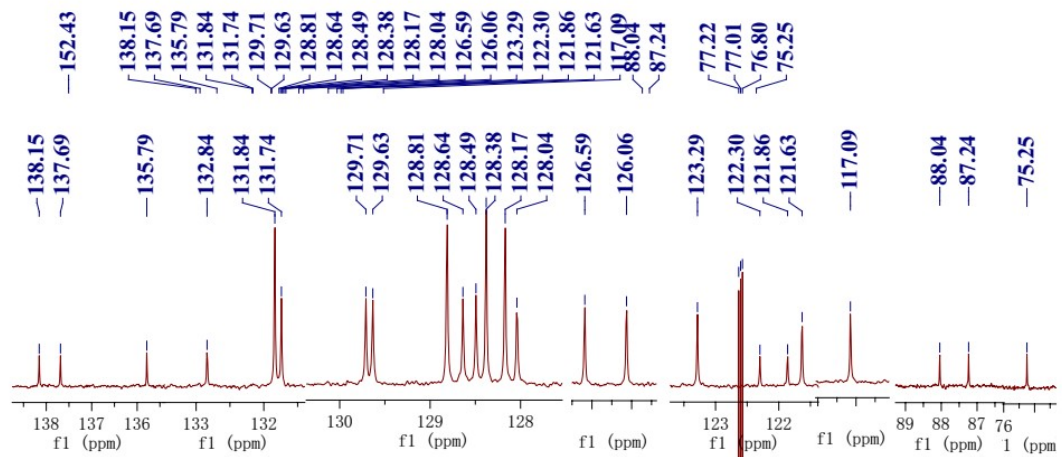




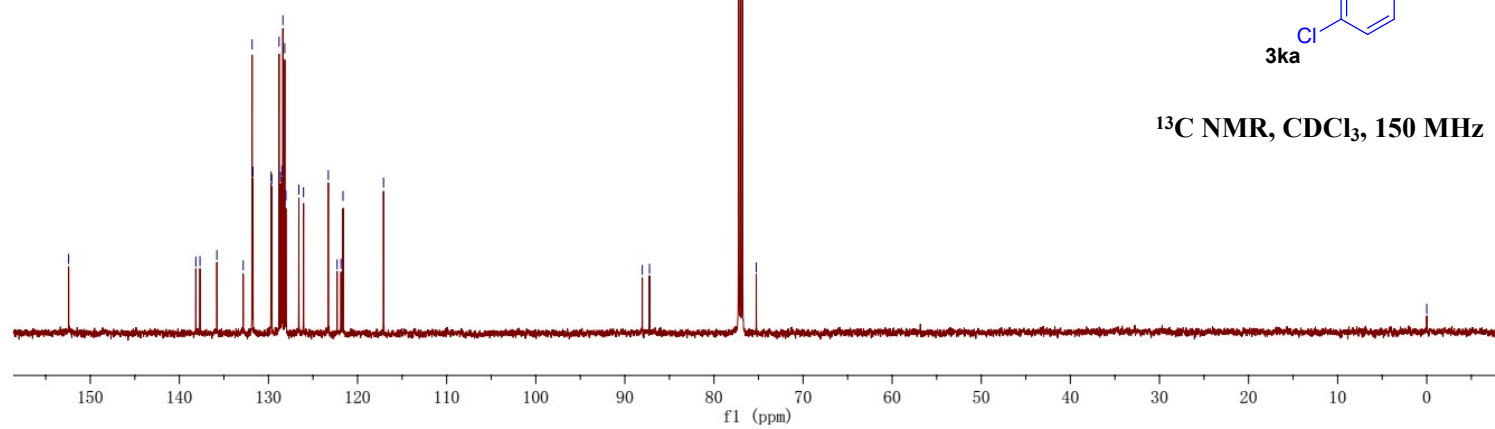


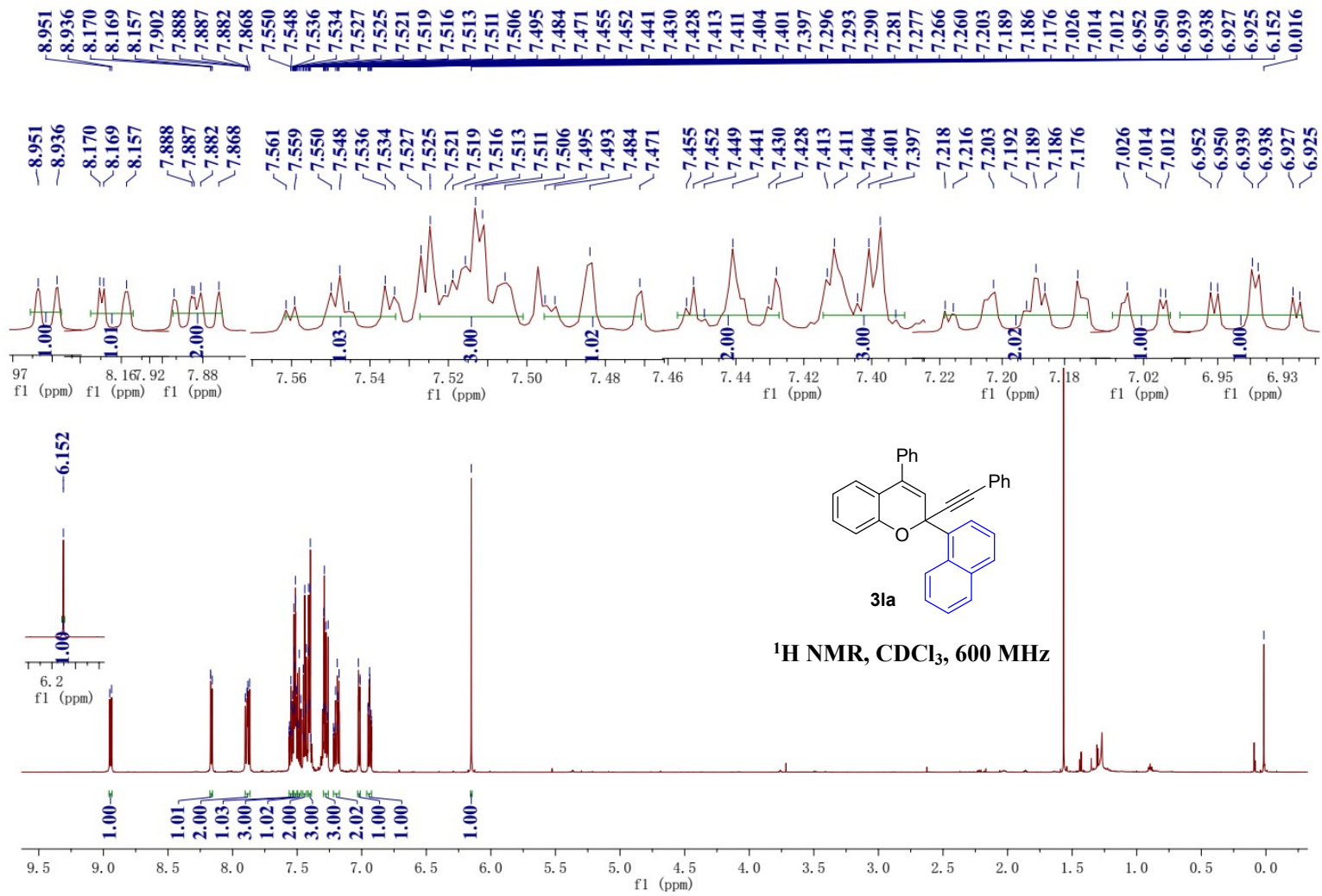
¹³C NMR, CDCl₃, 150 MHz

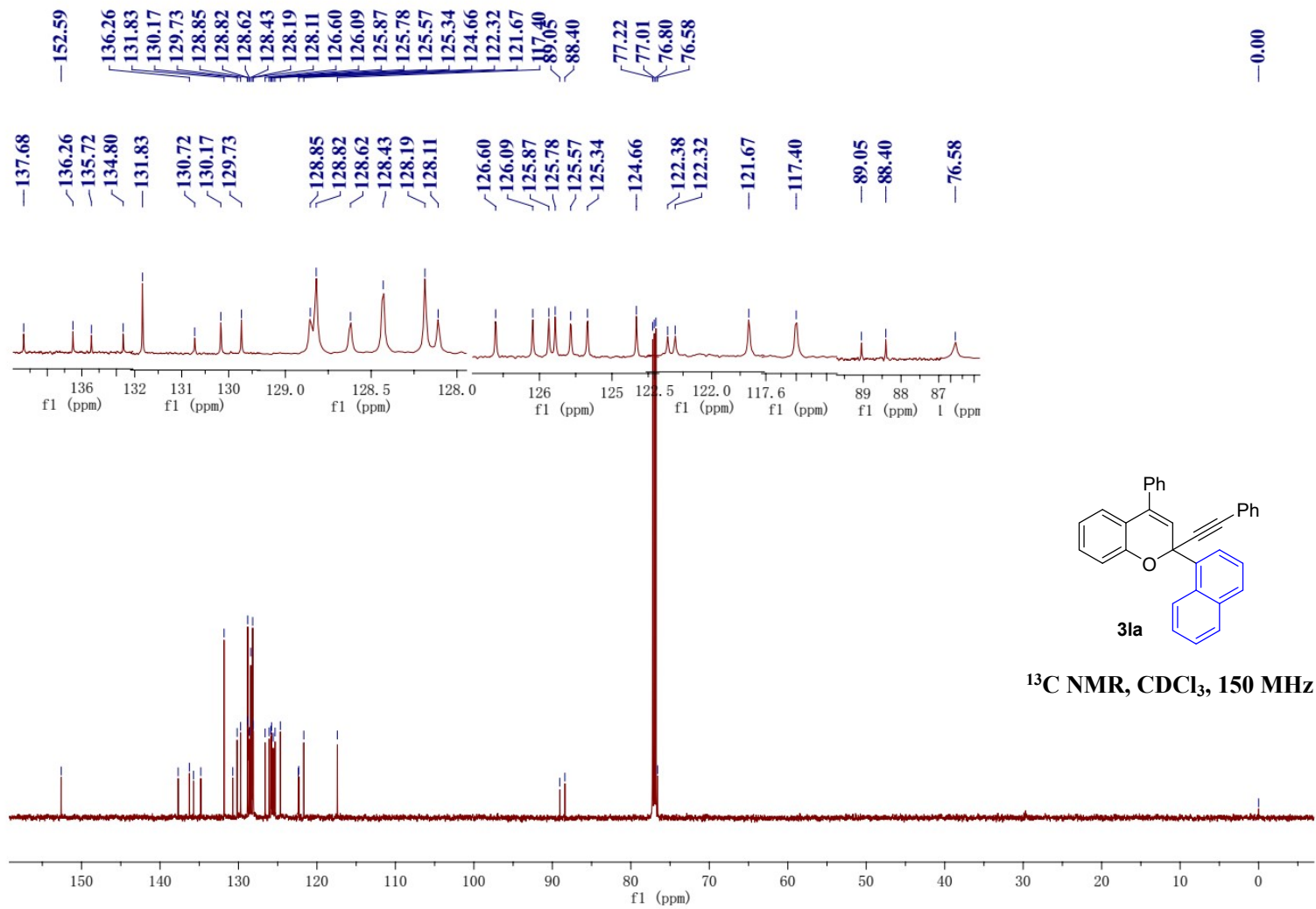


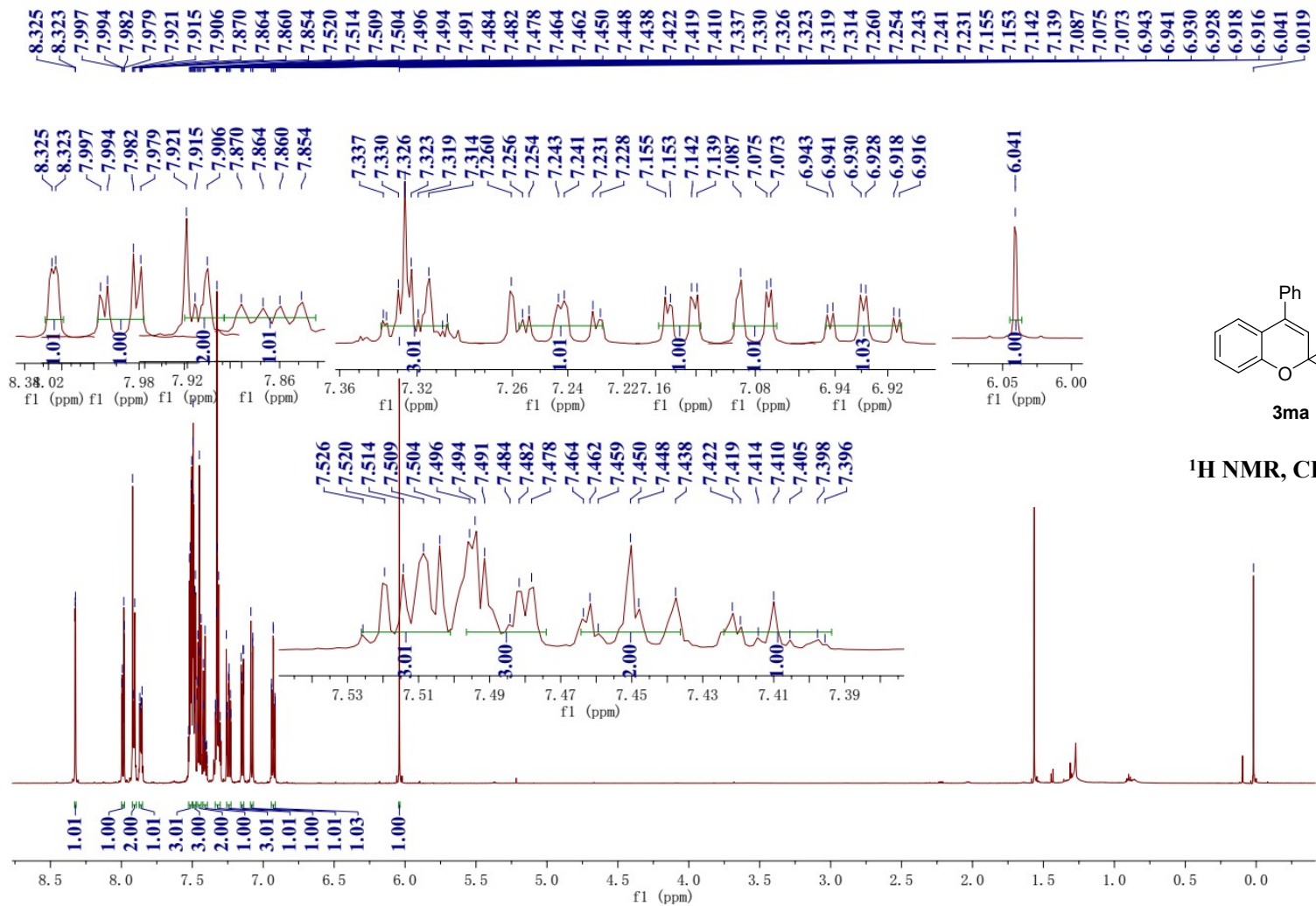


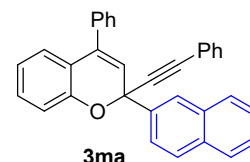
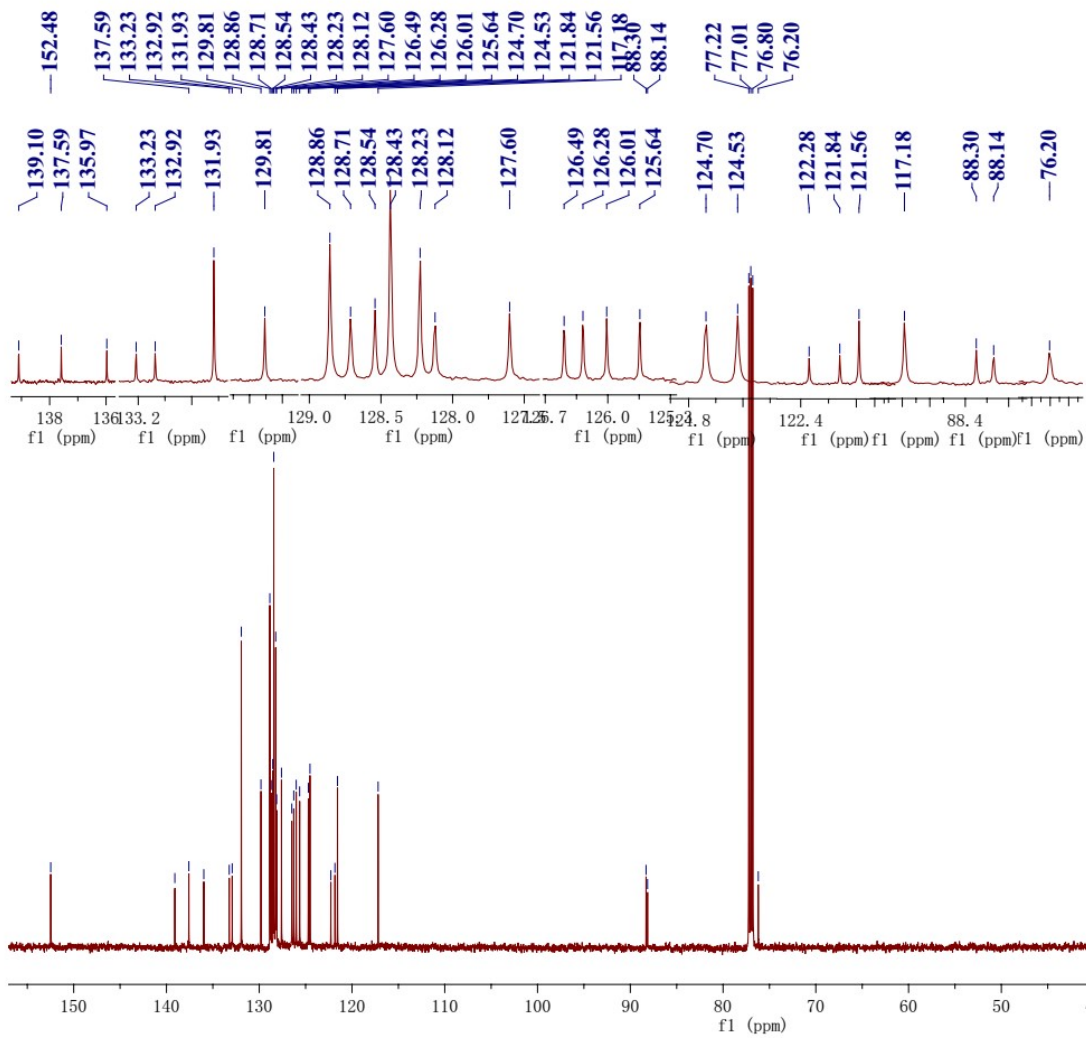
¹³C NMR, CDCl₃, 150 MHz



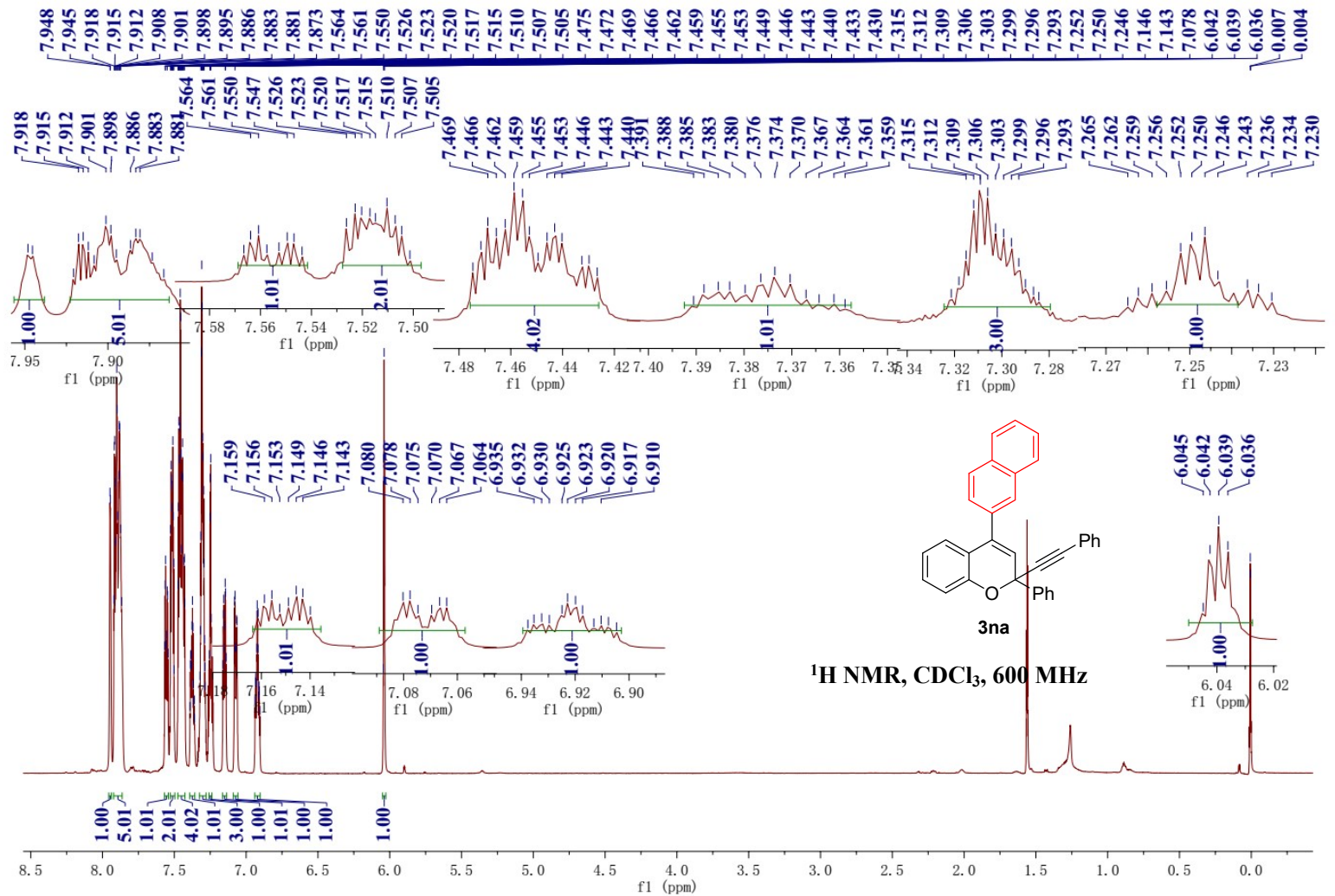


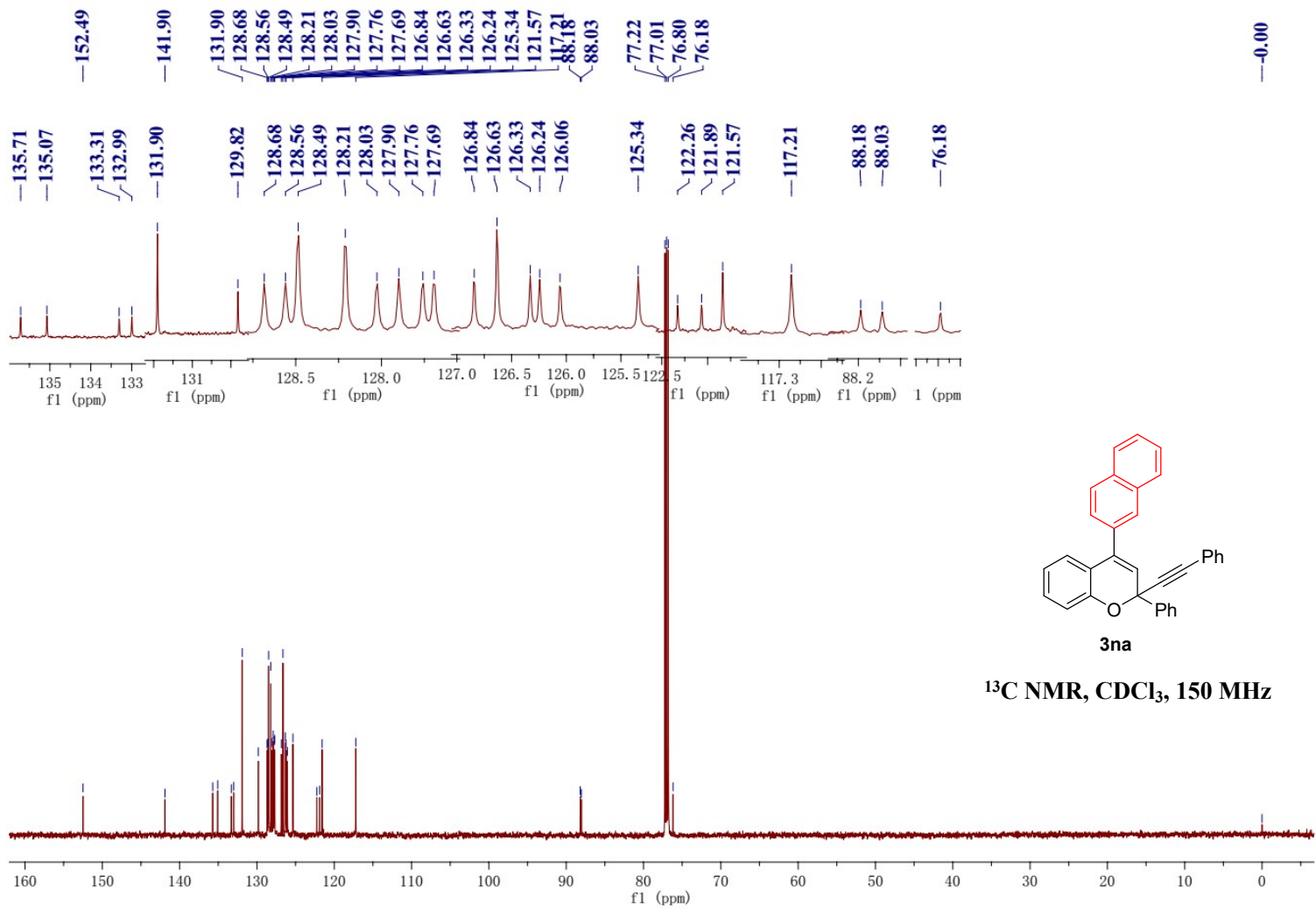


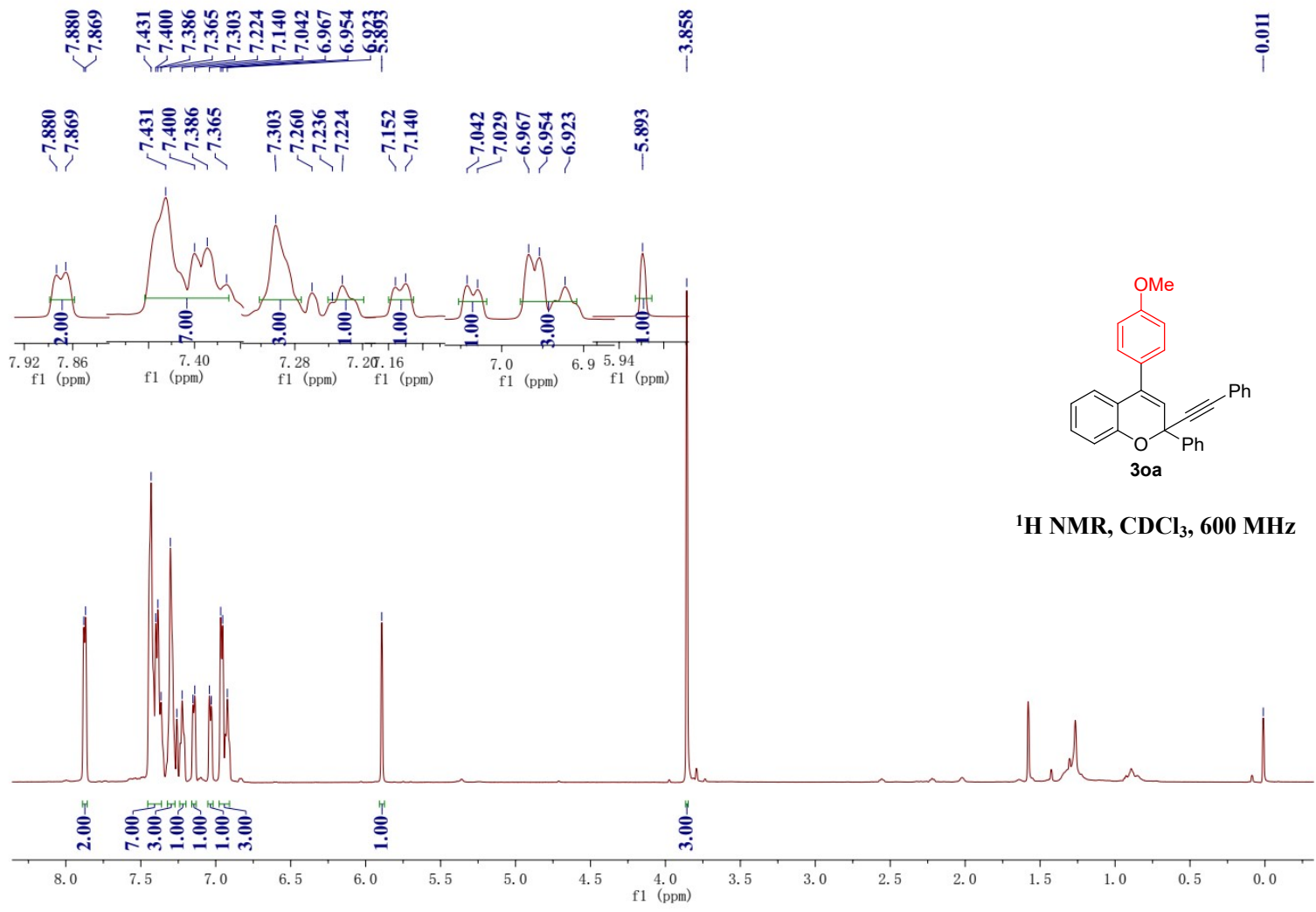


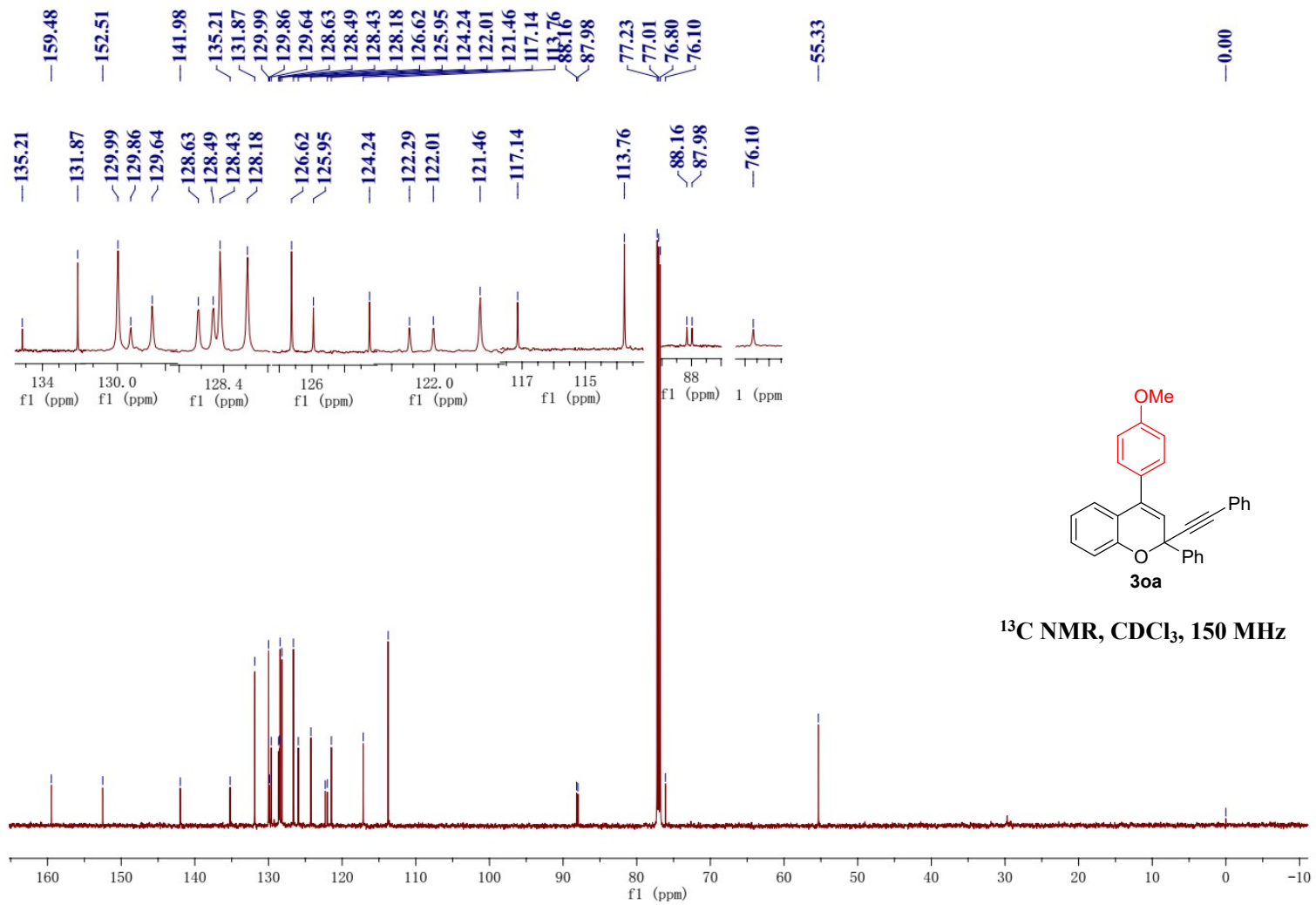


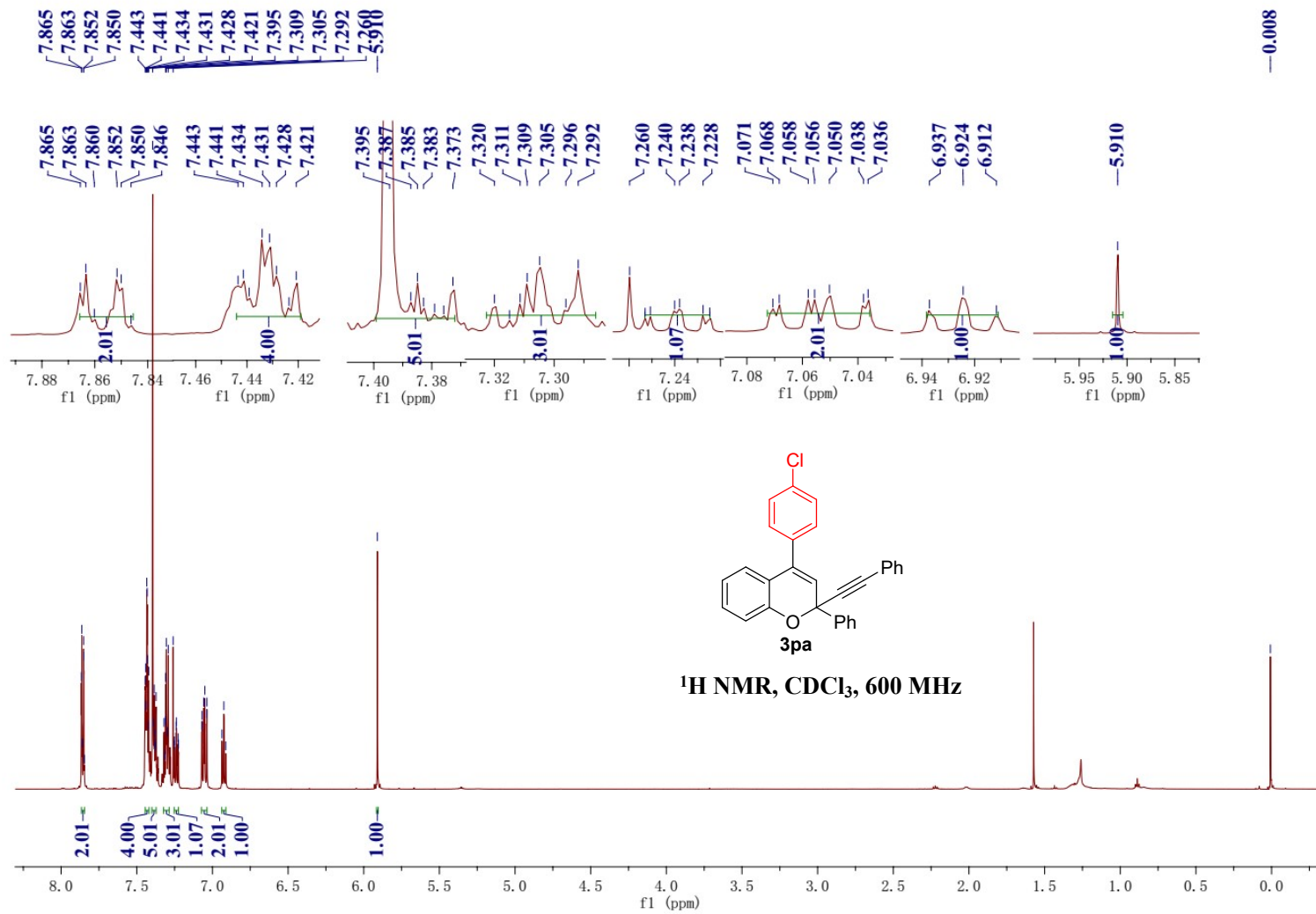
¹³C NMR, CDCl₃, 150 MHz

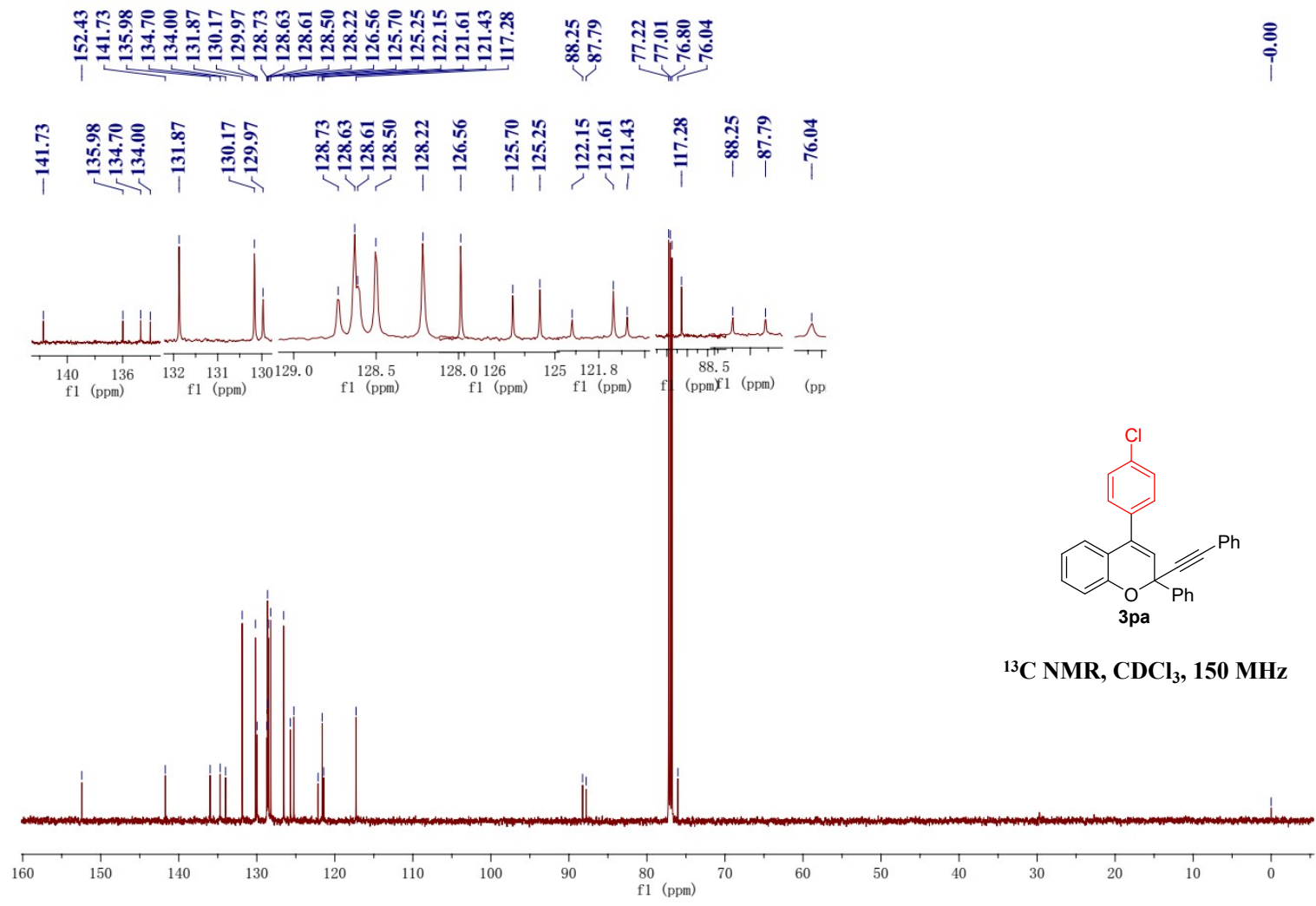


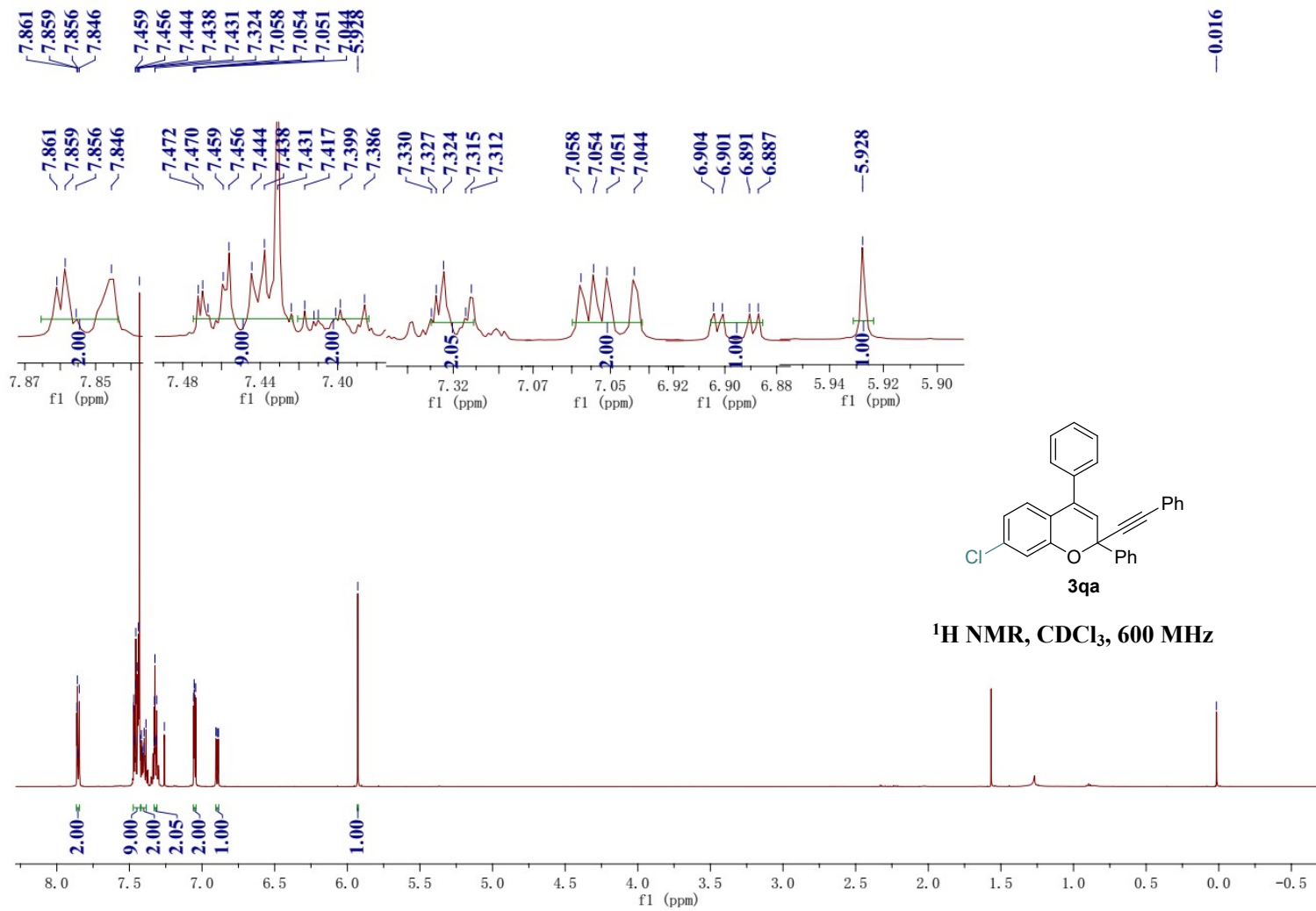


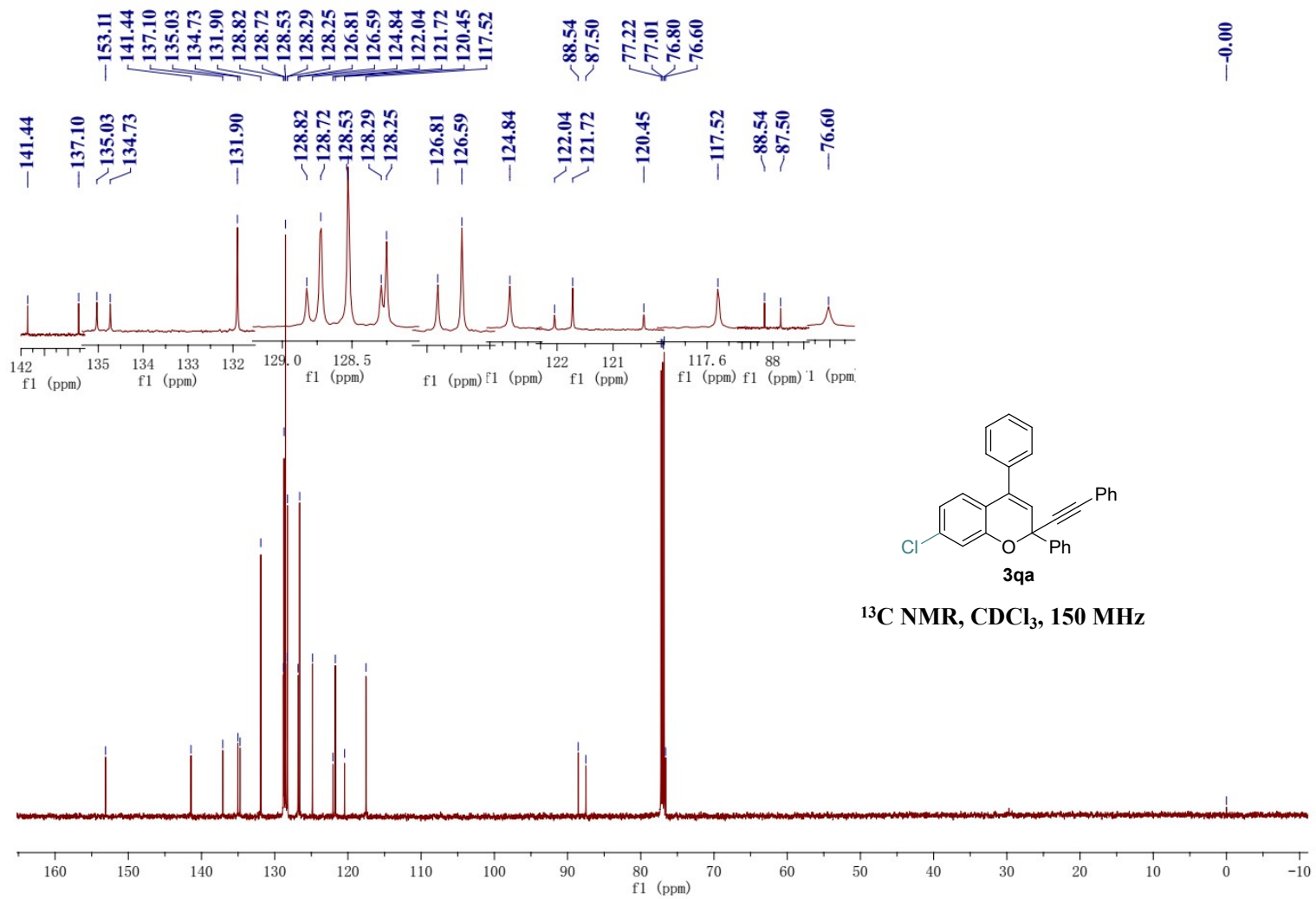


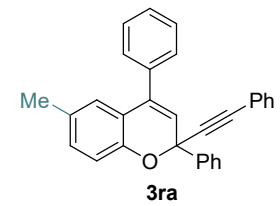
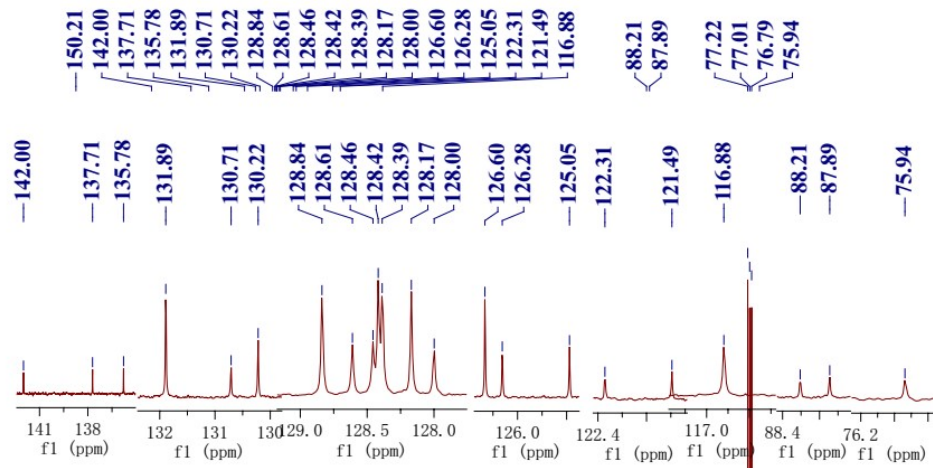




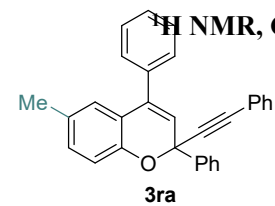




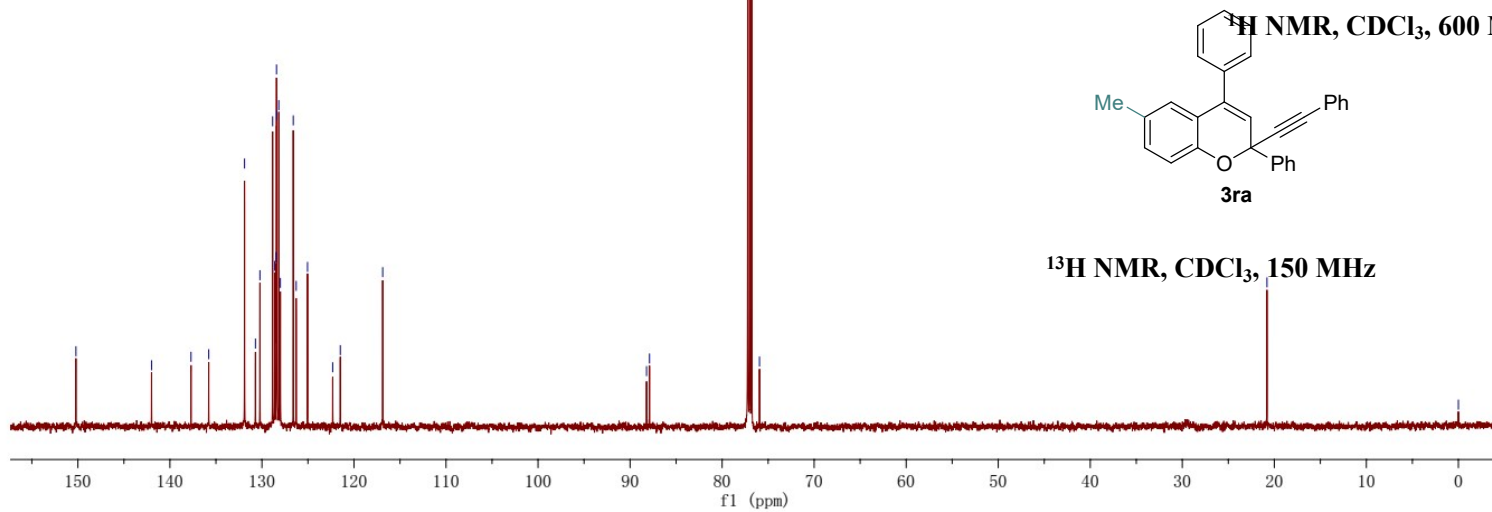


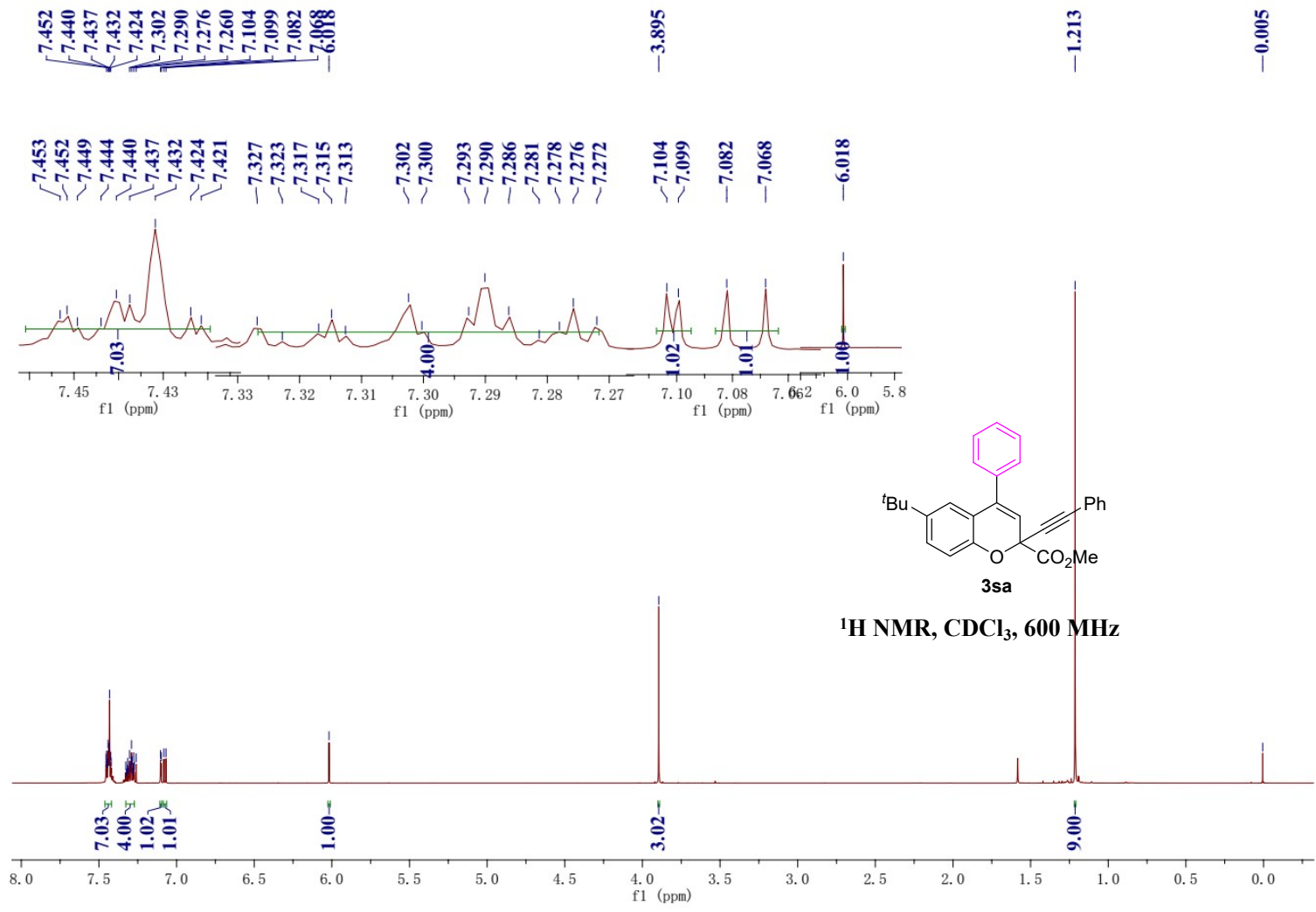


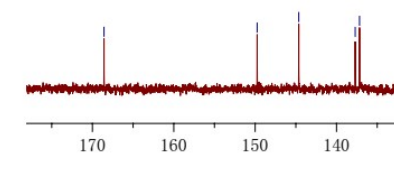
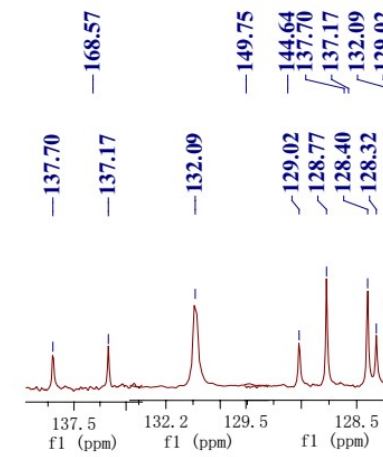
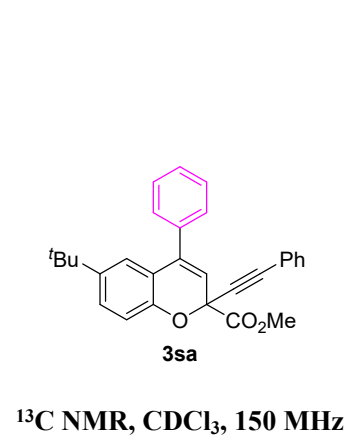
¹H NMR, CDCl₃, 600 MHz

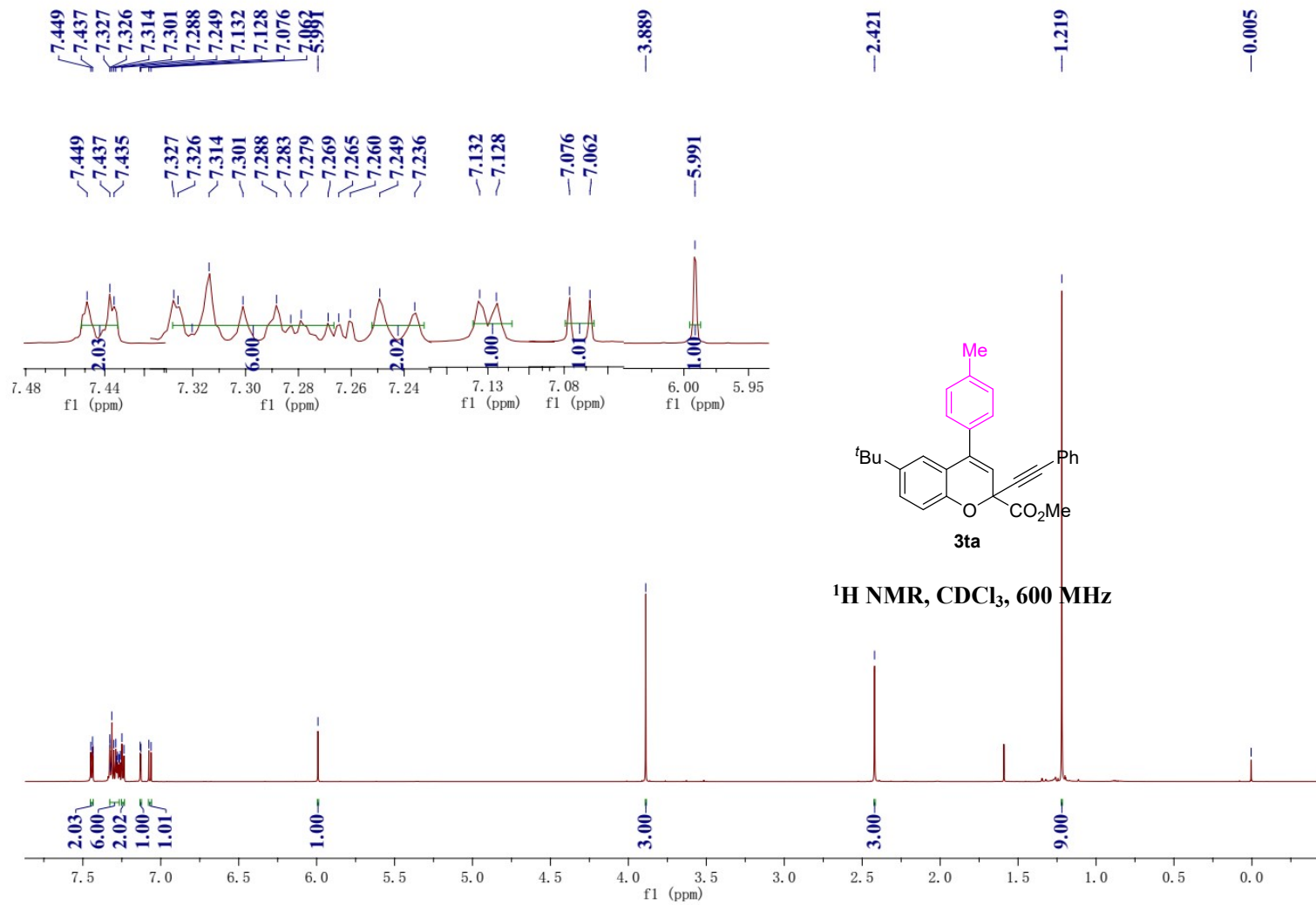


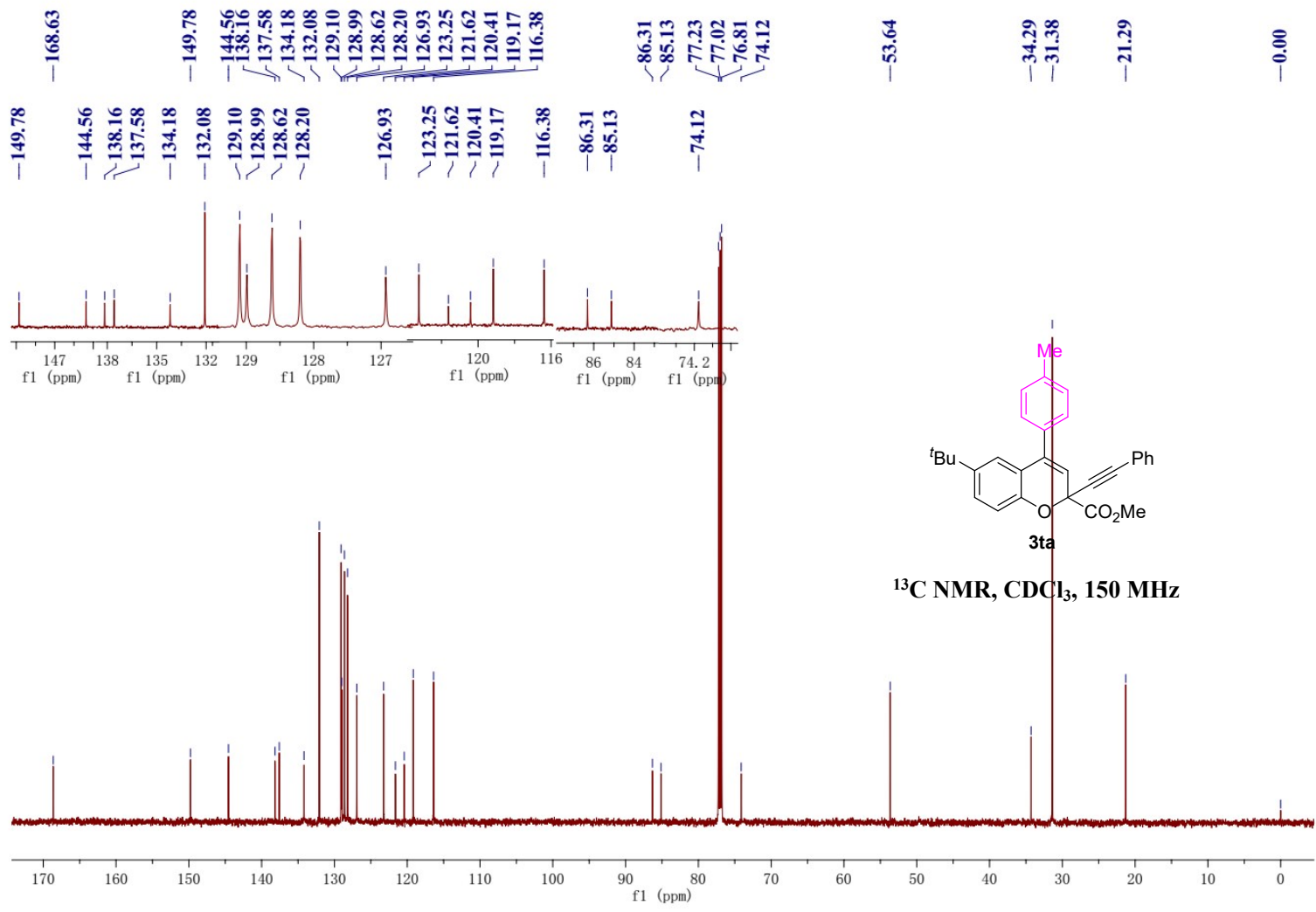
¹³H NMR, CDCl₃, 150 MHz

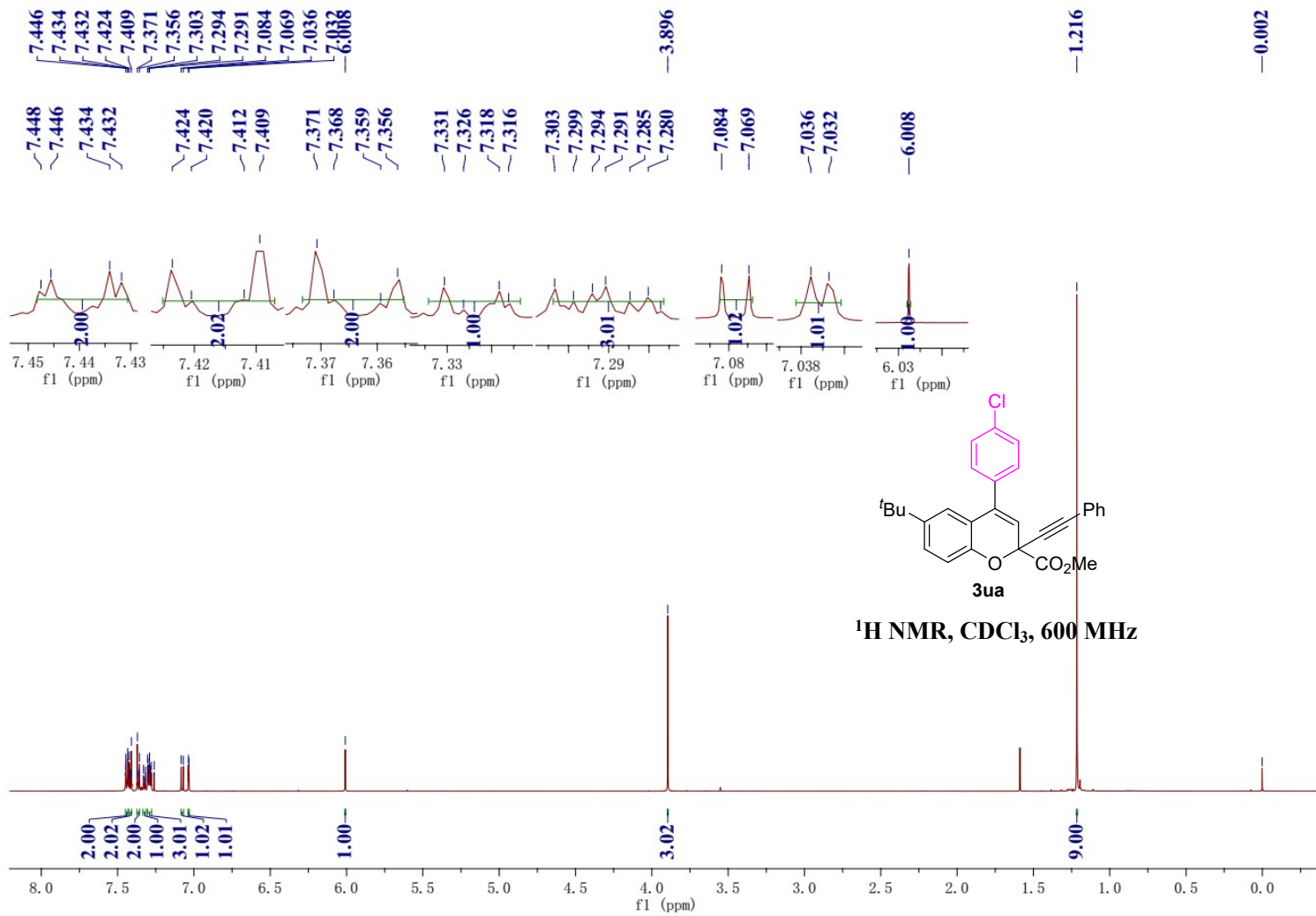


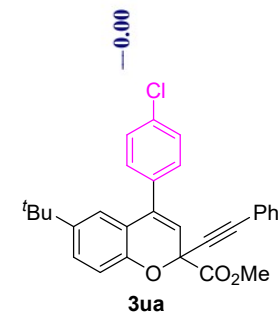
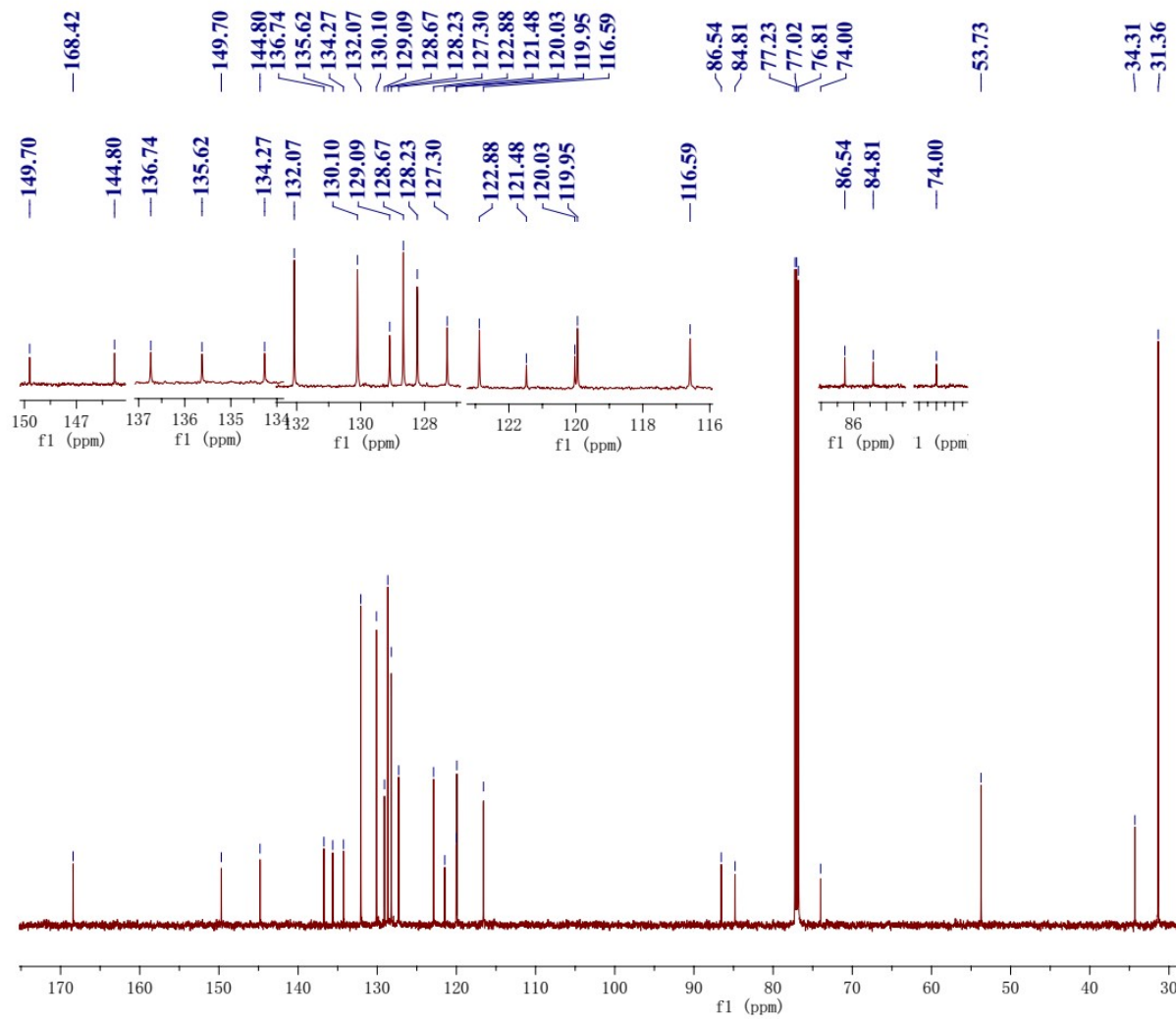




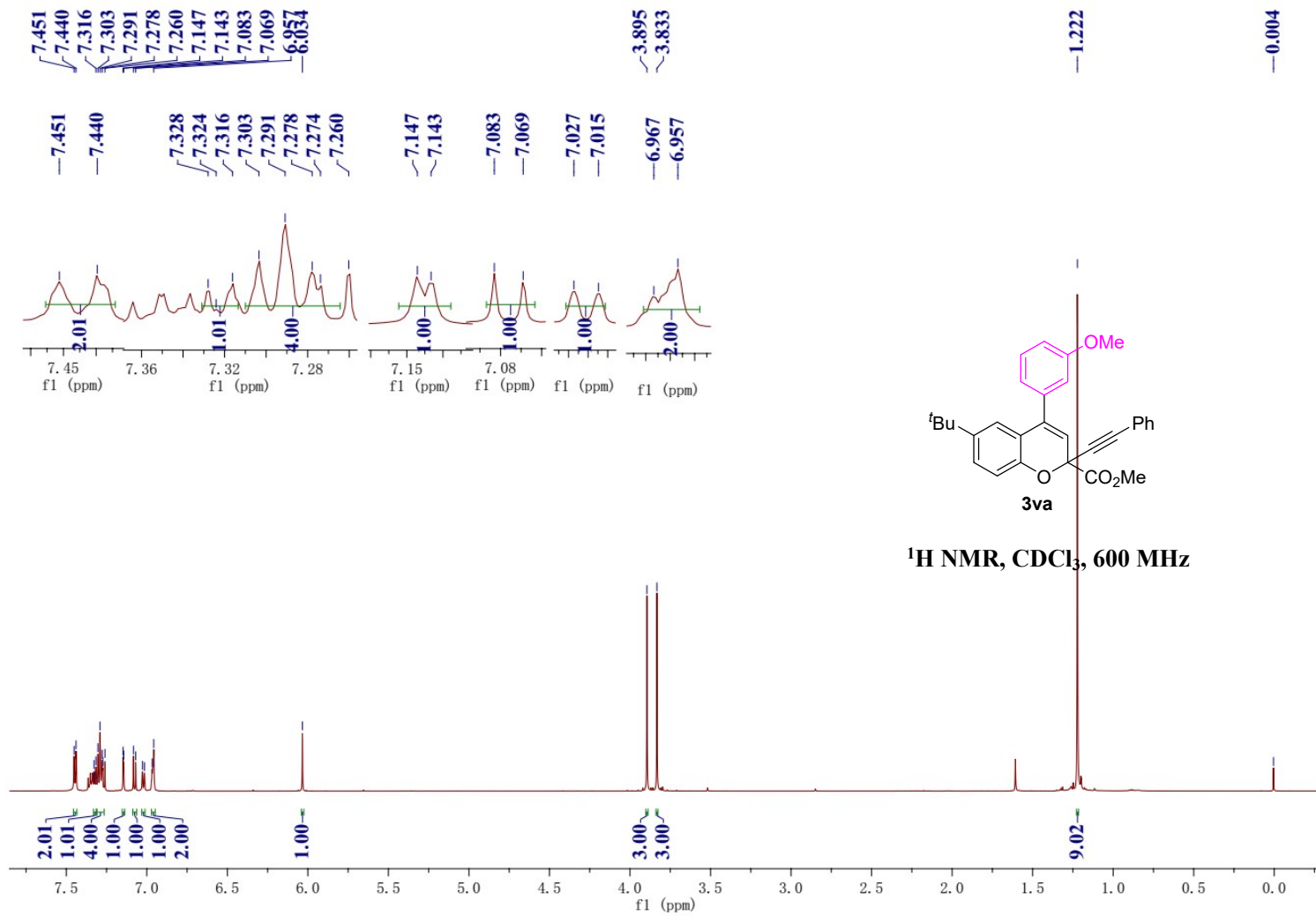


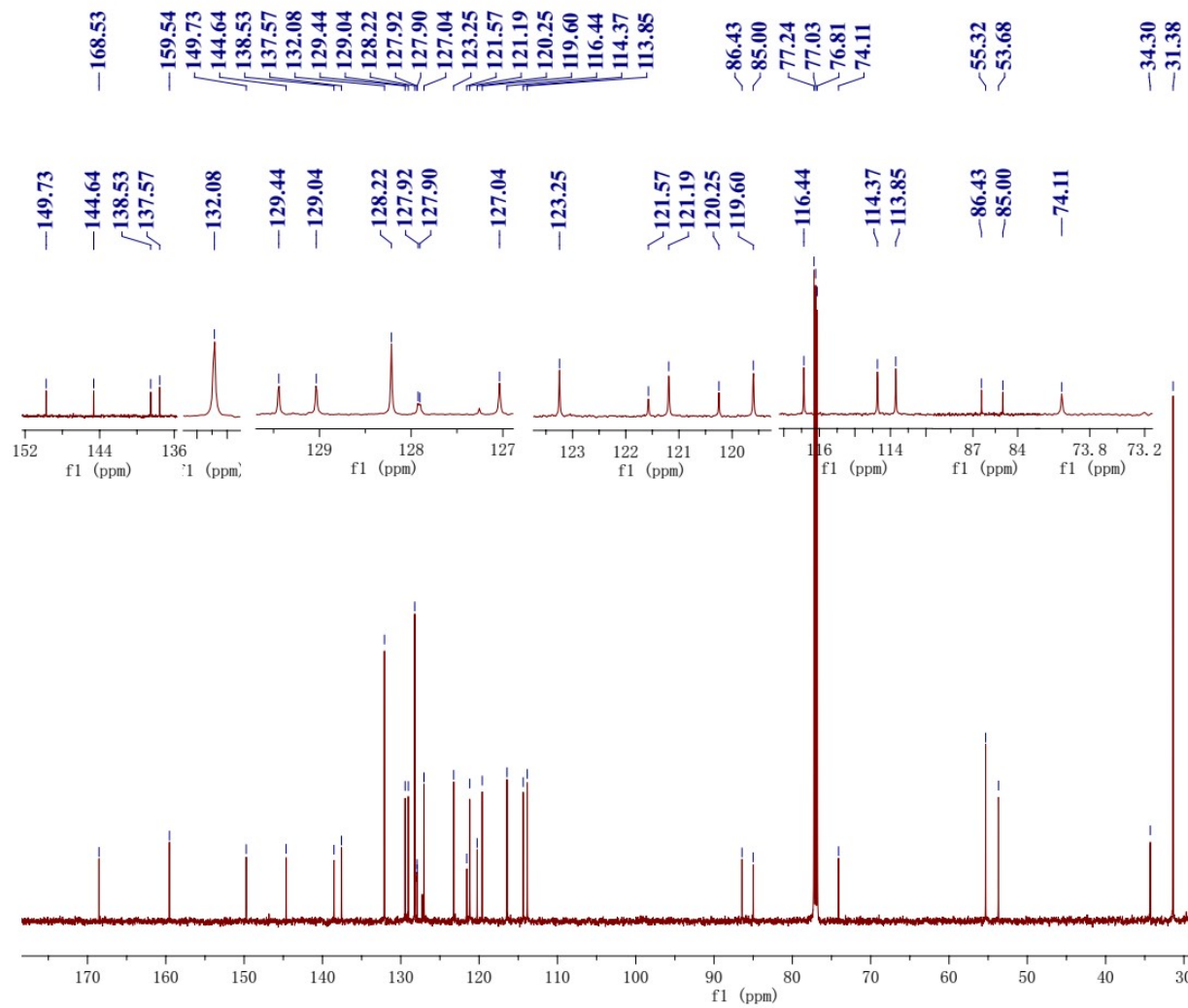


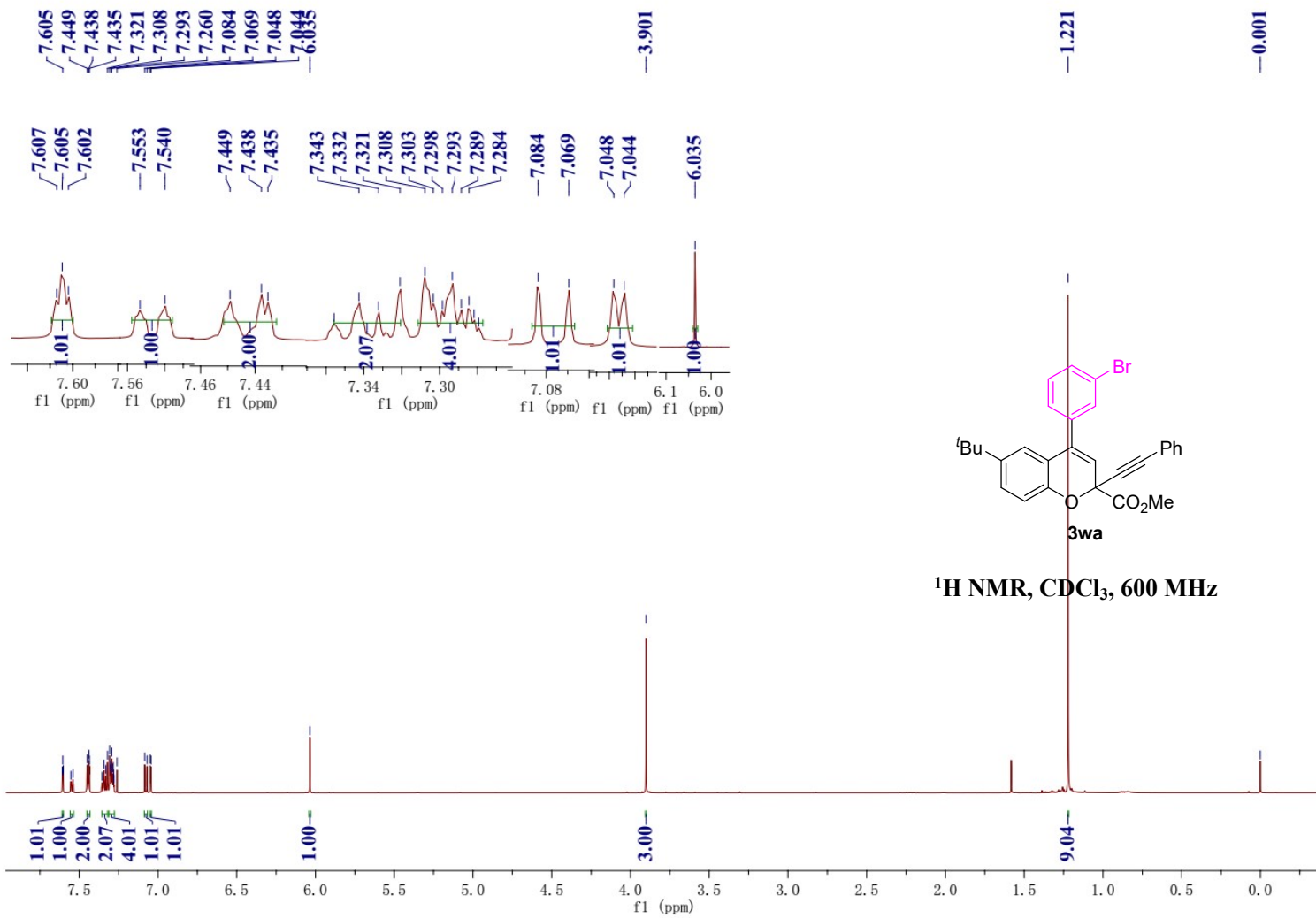


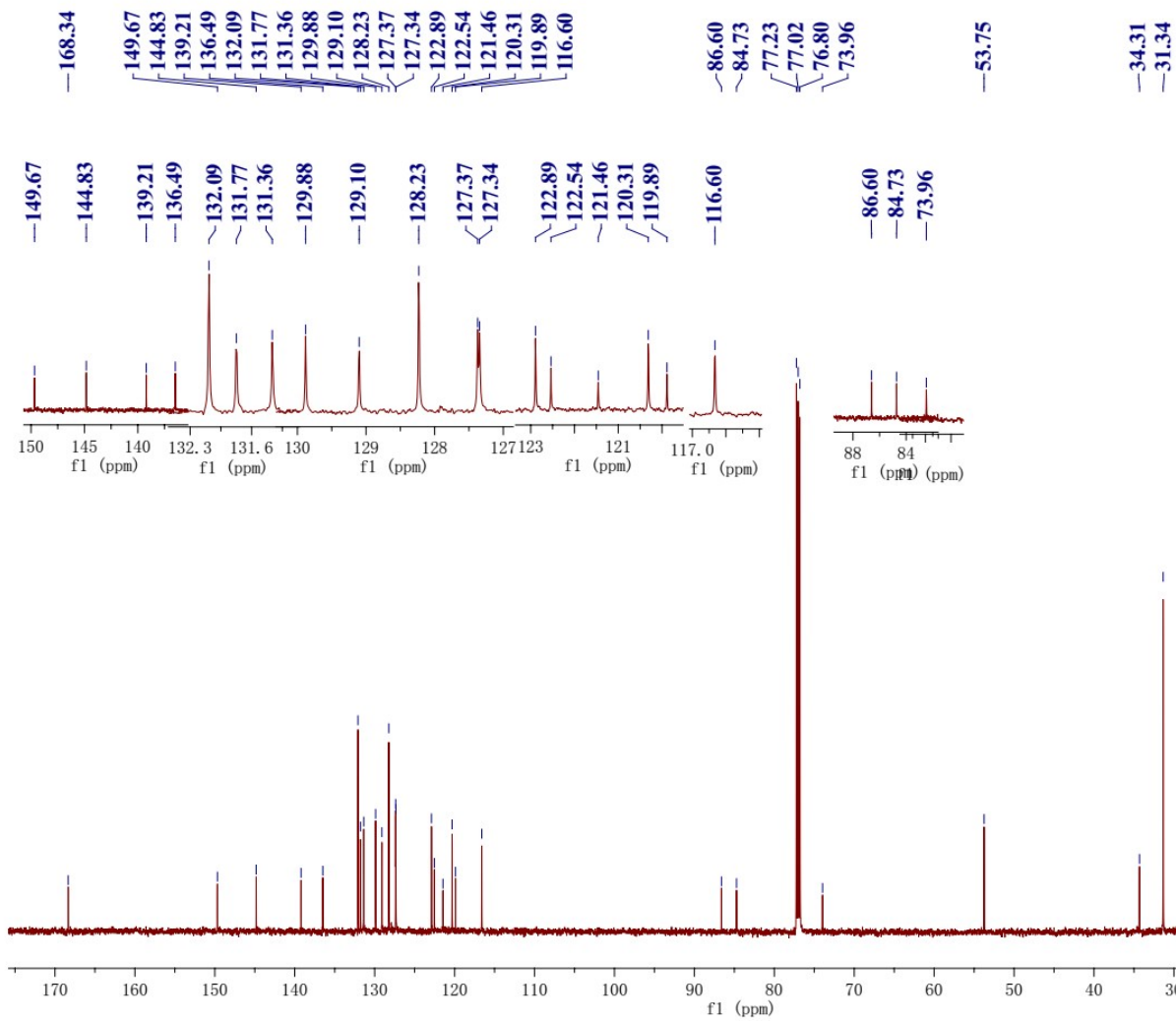


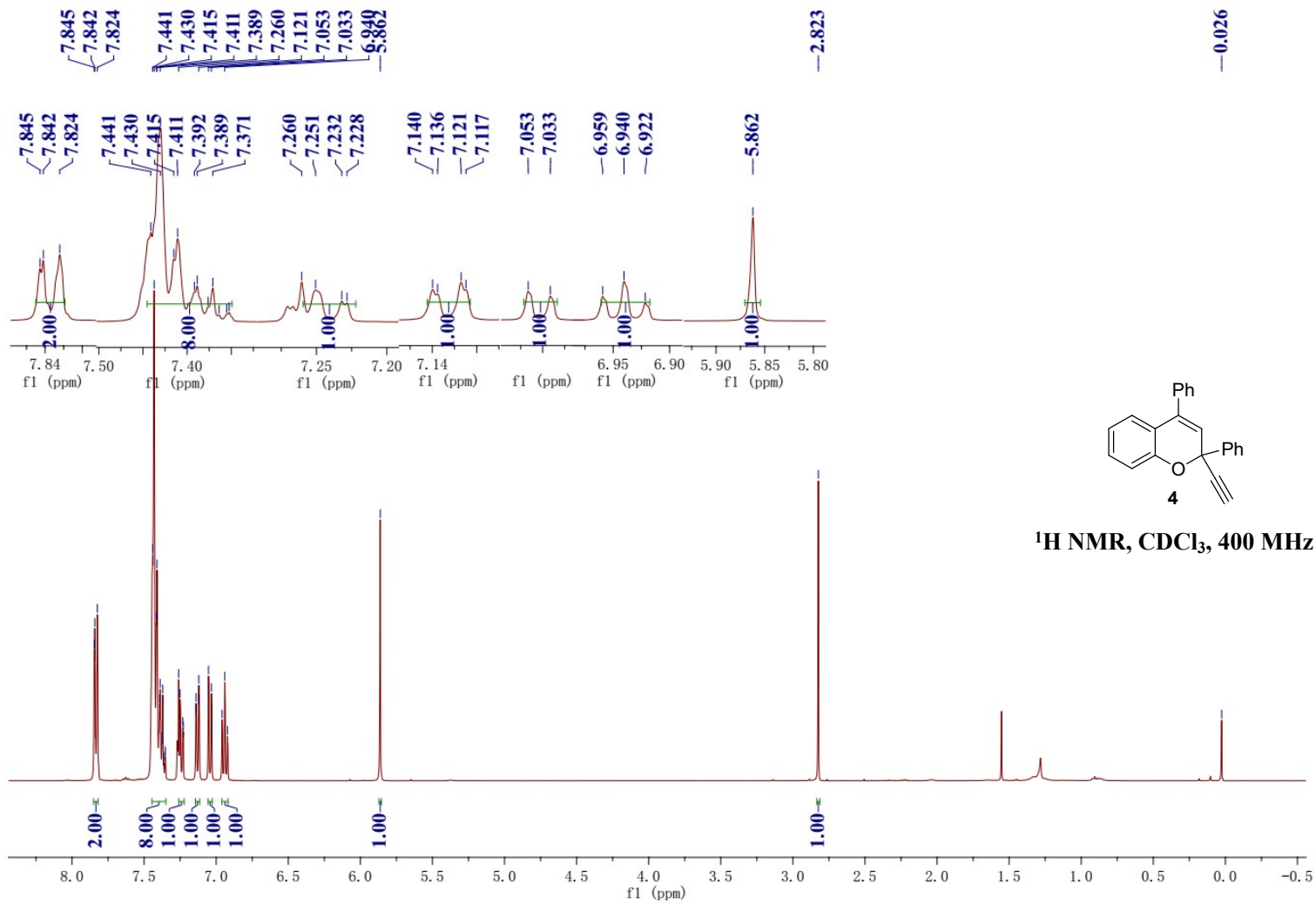
^{13}C NMR, CDCl_3 , 150 MHz

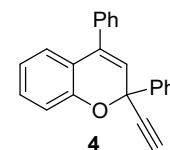
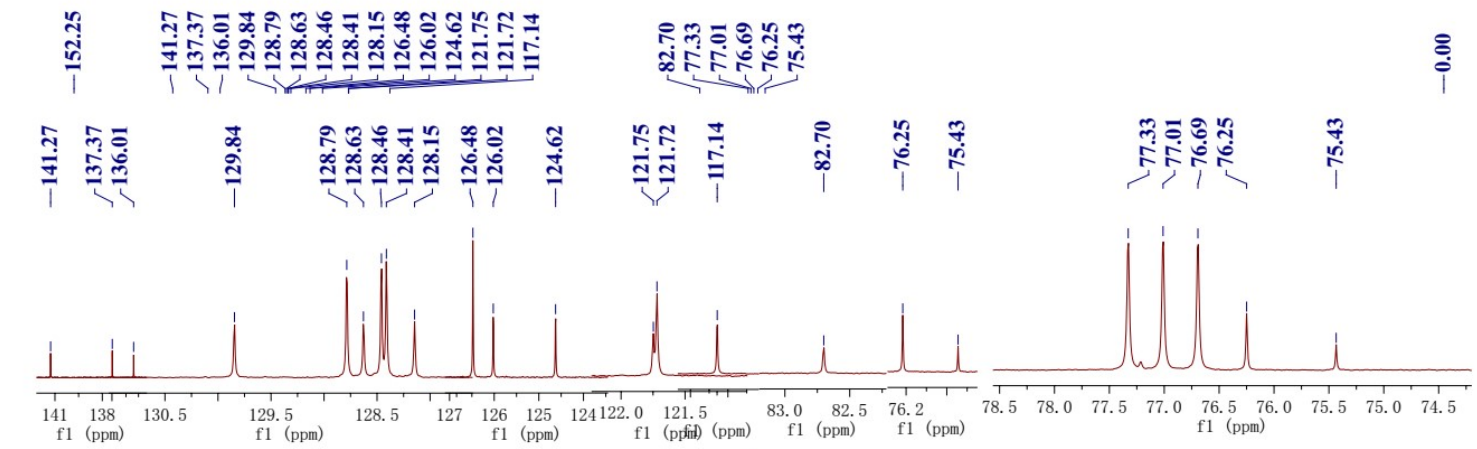




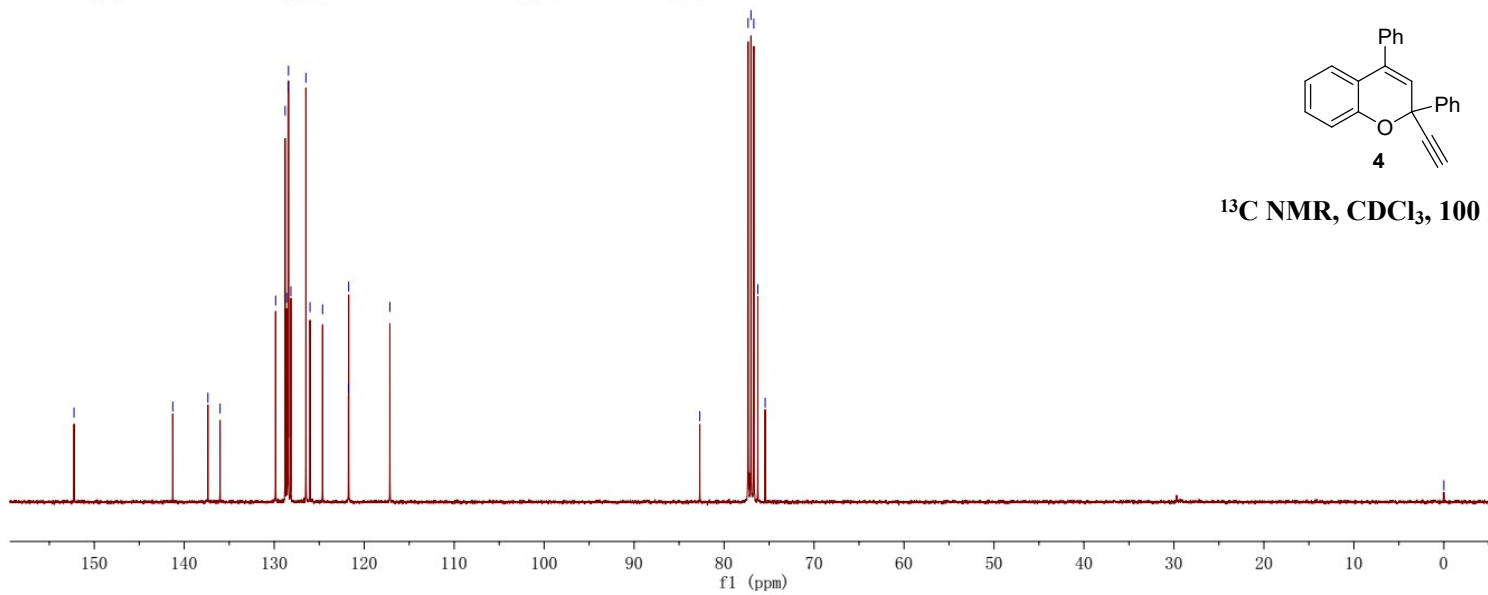


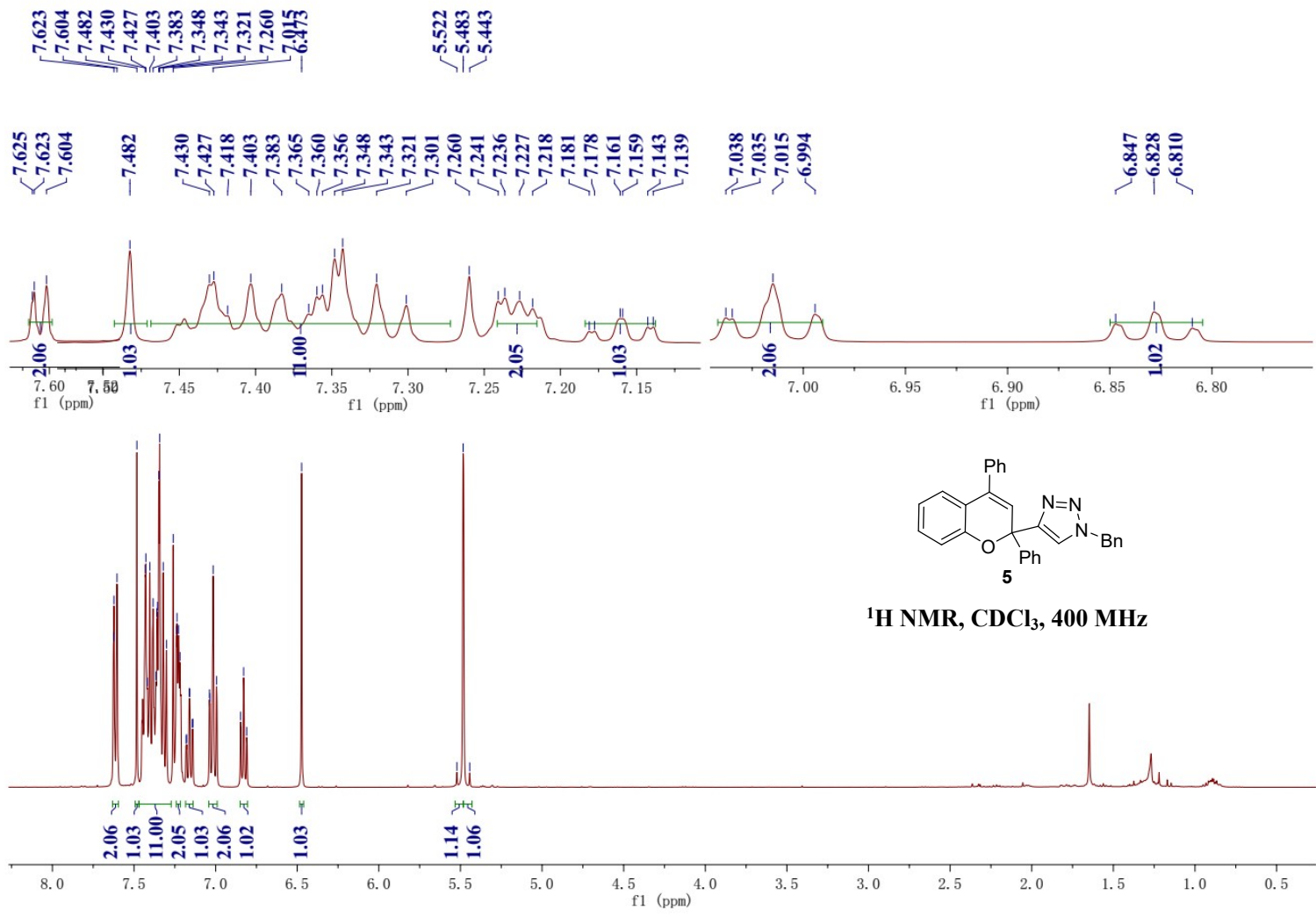


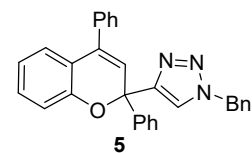
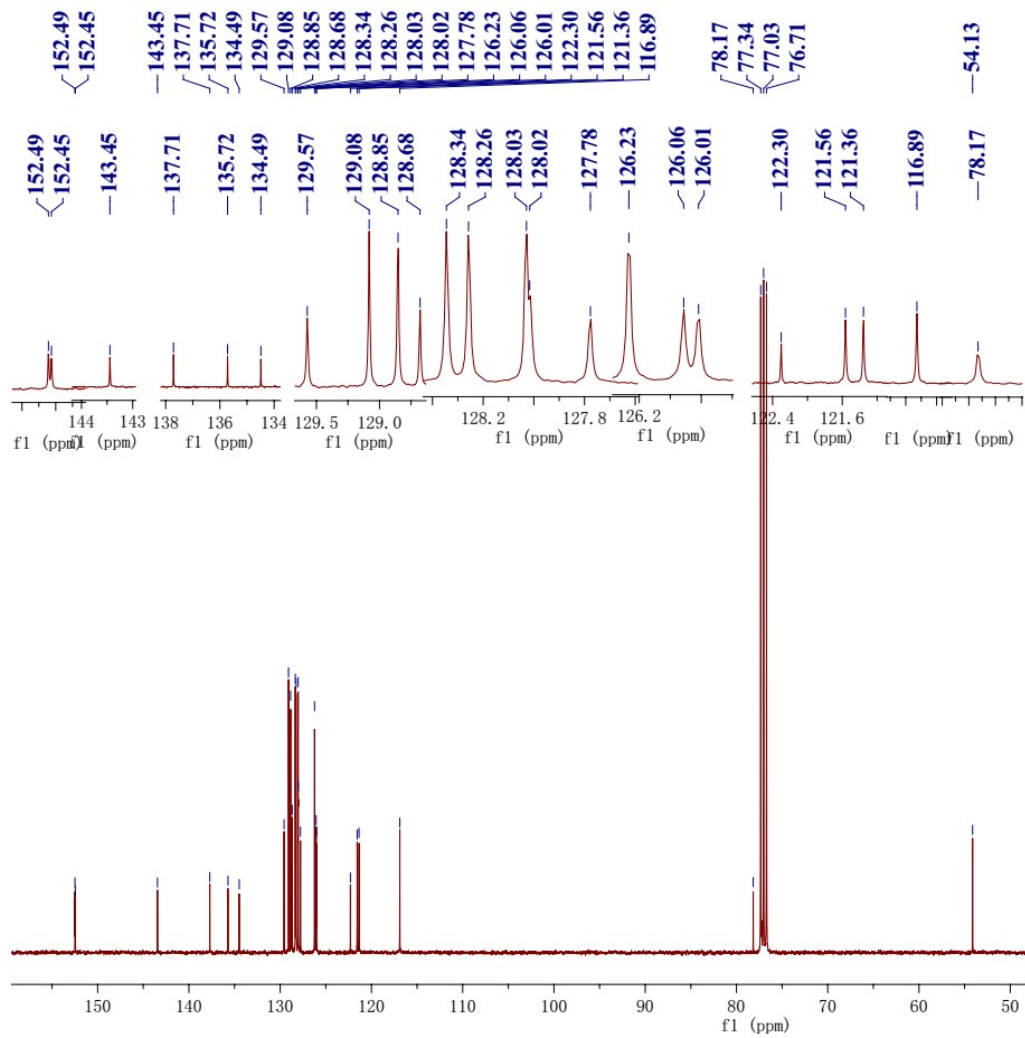




¹³C NMR, CDCl₃, 100 MHz







¹³C NMR, CDCl₃, 100 MHz