Ligand-controlled Copper-catalyzed Carboamination Reactions of Styrenes and 1,3-Enynes to Access Diverse Imides

Authors: Qi-Xuan Jiang[1,3], Kai Xiao[1,3], Wei Huang[1,2,3], Feng-Hua Zhang[1,3]*

Affiliations: [1] Key Laboratory of Glyco-drug Research of Zhejiang Province, School of Pharmaceutical Science and Technology, Hangzhou Institute for Advanced Study, University of Chinese Academy of Sciences, Hangzhou 310024, China;

[2] State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China;

[3] University of Chinese Academy of Sciences, Beijing 101408, China;

Correspondence to: zhangfenghua01@ucas.ac.cn.

Supporting Information

Content

I. General Information

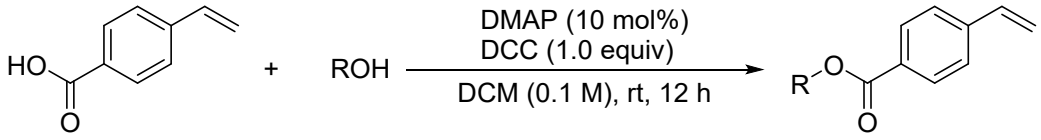
Unless otherwise noted, reagents were used as received from Leyan, TCI, Energy Chemical, J&K. All reactions were performed under an atmosphere of dry nitrogen gas in glove box. Anhydrous MeCN were purchased from J&K and stored under nitrogen gas. Other solvents were purified with activated aluminum oxide using a solvent-purification system.

NMR spectra were recorded on a Bruker spectrometer with a Prodigy broadband cryoprobe (600 MHz for ^{1}H and 151 MHz for ^{13}C); chemical shifts (δ) are reported in ppm downfield from tertramethylsilane, using the solvent resonance as the internal standard. High resolution mass spectrometric analysis was performed on ultra-performance liquid chromatography-time-of-flight mass spectrometer (Synapt-G2-Si, Waters, USA) with electron spray ionization (ESI) resource.

The alkenes were purchased from Leyan, Bidepharm, TCI, Energy Chemical, J&K and stored in glove box. The alkenes derived from drugs and 1,3-enynes were prepared according to the reported literatures.

II. Synthesis of 4-vinyl benzoate

2.1. General procedure A

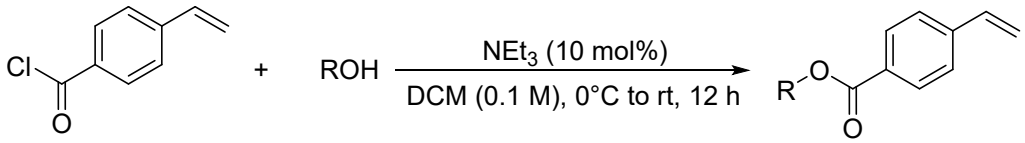


7 mmol 7.7 mmol

S1 as an example: Add 4-vinylbenzoic acid（1.03 g, 7 mmol, 1.0 equiv）, alcohol (7.7 mmol, 1.1 equiv), and 4-dimethylaminopyridine (85.5 mg, 0.7 mmol) to a 250 mL single mouthed bottle. Then, dichloromethane (70 mL, 0.1 M) was added, and dicyclohexylcarbodiimide (1.2 mL, 7 mmol, 1.0 equiv) was added to the solvent. Then, the reaction was stirred at room temperature for 12 hours.

Work-up: The reaction mixture was extracted with water and then concentrated organic phase. And the residue was purified by chromatography to provide the desired product.

2.2. General procedure B

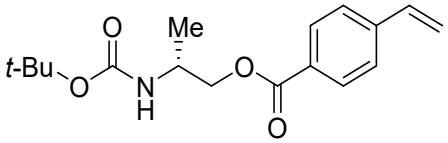


7 mmol 7.7 mmol

S6 as an example: Dissolve the alcohol (7.7 mmol, 1.1 equiv) in 70 mL DCM and added the triethylamine (90 μL, 0.7 mmol). Stir at 0 °C and slowly add 4-vinylbenzoyl chloride (1.2 g, 7 mmol, 1.0 equiv) dropwise. Then, the reaction was stirred at room temperature for 12 hours.

Work-up: The reaction mixture was extracted with water and then concentrated organic phase. And the residue was purified by chromatography to provide the desired product.

Data analysis of product **S1**



Method: General procedure A. Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 414.3 mg, 13% yield.

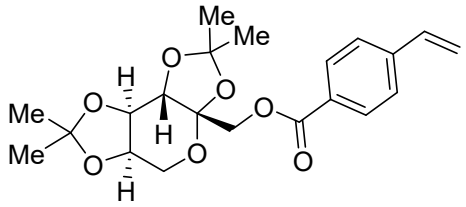
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 6.75 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.87 (d, *J* = 17.6 Hz, 1H), 5.39 (d, *J* = 10.9 Hz,

1H), 4.63 (s, 1H), 4.26 (d, *J* = 4.9 Hz, 2H), 4.17 – 4.05 (m, 1H), 1.43 (s, 9H), 1.25 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.2, 155.2, 142.1, 136.0, 130.0, 129.1, 126.1, 116.6, 79.5, 67.9, 45.6, 28.4, 17.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{17}H_{24}NO_4$: 306.1700, found: 306.1701.

Data analysis of product **S2**



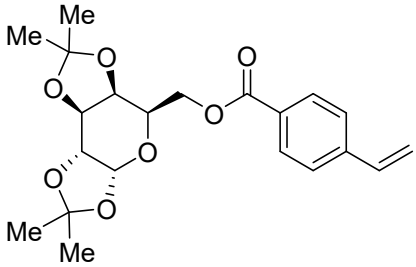
Method: General procedure A. Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 313.0 mg, 80% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 6.75 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.87 (d, *J* = 17.6 Hz, 1H), 5.39 (d, *J* = 10.9 Hz, 1H), 4.77 – 4.58 (m, 2H), 4.47 (d, *J* = 2.6 Hz, 1H), 4.33 (d, *J* = 11.8 Hz, 1H), 4.26 (d, *J* = 7.9 Hz, 1H), 3.96 (dd, *J* = 13.0, 1.5 Hz, 1H), 3.80 (d, *J* = 13.0 Hz, 1H), 1.55 (s, 3H), 1.47 (s, 3H), 1.36 (d, *J* = 13.7 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 161.8, 138.2, 132.1, 126.2, 125.1, 122.2, 112.7, 105.3, 104.9, 97.8, 66.9, 66.6, 66.2, 61.3, 57.4, 22.6, 22.0, 21.6, 20.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{27}O_7$: 391.1752, found: 391.1755.

Data analysis of product **S3**



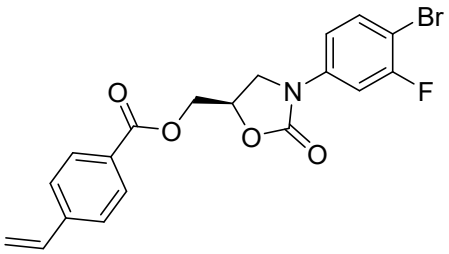
Method: General procedure A. Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 1190.7 mg, 31% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 6.74 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.85 (d, *J* = 17.6 Hz, 1H), 5.56 (d, *J* = 4.9 Hz, 1H), 5.37 (d, *J* = 10.9 Hz, 1H), 4.67 – 4.63 (m, 2H), 4.53 (dd, *J* = 11.5, 4.8 Hz, 1H), 4.42 (dd, *J* = 11.4, 7.6 Hz, 1H), 4.36 – 4.30 (m, 3H), 4.20 – 4.15 (m, 1H), 1.49 (d, *J* = 21.6 Hz, 6H), 1.34 (d, *J* = 13.9 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.2, 142.0, 136.1, 130.0, 126.1, 116.5, 109.7, 108.8, 96.4, 71.2, 70.8, 70.6, 66.2, 63.9, 26.02, 25.98, 25.0, 24.5.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{27}O_7$: 391.1752, found: 391.1755.

Data analysis of product **S4**



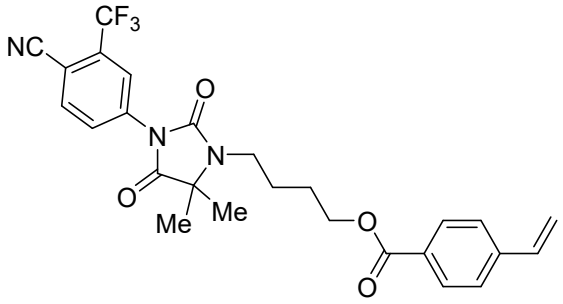
Method: General procedure B. Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 1.2 g, 29% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.1 Hz, 2H), 7.57 – 7.49 (m, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 1H), 6.74 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.87 (d, *J* = 17.6 Hz, 1H), 5.41 (d, *J* = 10.9 Hz, 1H), 5.02 (d, *J* = 4.0 Hz, 1H), 4.64 – 4.54 (m, 2H), 4.18 (t, *J* = 8.9 Hz, 1H), 3.93 – 3.87 (m, 1H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 159.2 (d, *J* = 246.7 Hz), 153.8, 142.7, 138.7 (d, *J* = 9.7 Hz), 135.8, 133.6, 130.1, 127.9, 126.3, 117.1, 114.4 (d, *J* = 3.2 Hz), 106.8 (d, *J* = 27.8 Hz), 103.5 (d, *J* = 21.1 Hz), 70.3, 64.5, 47.0.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{17}H_{16}BrFNO_4$: 420.0241, found: 420.0241.

Data analysis of product **S5**



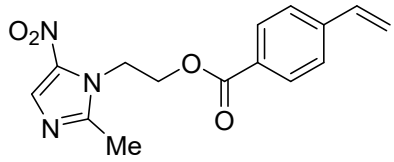
Method: General procedure A. Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 1.3 g, 27% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.99 (t, *J* = 9.4 Hz, 3H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 2H), 6.75 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.86 (d, *J* = 17.6 Hz, 1H), 5.39 (d, *J* = 10.9 Hz, 1H), 4.39 (s, 2H), 3.44 (s, 2H), 1.88 (s, 4H), 1.53 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.6, 166.3, 152.9, 142.1, 136.5, 136.0, 135.3, 133.6 (q, *J* = 33.0 Hz), 129.9, 129.2, 127.9, 126.2, 123.0 (q, *J* = 5.2 Hz), 122.0 (q, *J* = 272.0 Hz), 116.7, 115.0, 108.2, 64.0, 61.9, 40.0, 26.4, 26.2, 23.5.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{25}F_3N_3O_4$: 500.1792, found: 500.1790.

Data analysis of product **S6**



Method: General procedure B. Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 2.05 g, 68% yield.

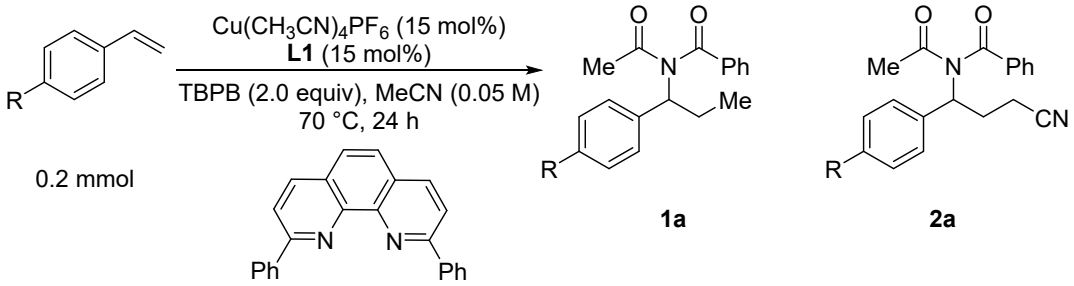
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 6.74 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.88 (d, *J* = 17.6 Hz, 1H), 5.41 (d, *J* = 10.9 Hz, 1H), 4.70 (dd, *J* = 18.2, 4.7 Hz, 6H), 2.49 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 150.8, 142.6, 138.6, 135.8, 133.3, 129.9, 128.1, 126.4, 117.1, 62.8, 45.3, 14.3.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{16}N_3O_4$: 302.1136, found: 302.1141.

III. Experimental Section and Data Analysis

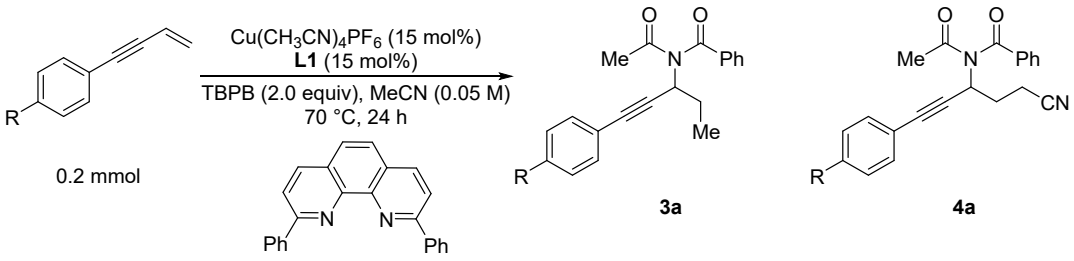
3.1 General procedure E



1a 2a as examples: In a nitrogen-filled glovebox, and oven-dried 8 mL vial with a magnetic stir bar, were charged the $Cu(CH_3CN)_4PF_6$ (11.2 mg, 0.03 mmol, 0.15 equiv), **L1** (10.0 mg, 0.03 mmol, 0.15 equiv), alkene (0.2 mmol, 1.0 equiv). Then 4.0 mL MeCN was added. To the solution were added the peroxide (78.0 μL, 0.4 mmol, 2.0 equiv) sequentially. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at 70 °C for 24 hours.

Work-up: The reaction mixture was concentrated. And the residue was purified by chromatography to provide the desired product.

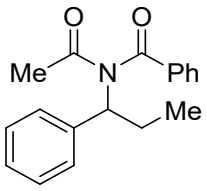
3.1 General procedure F



3a 4a as examples: In a nitrogen-filled glovebox, and oven-dried 8 mL vial with a magnetic stir bar, were charged the $Cu(CH_3CN)_4PF_6$ (11.2 mg, 0.03 mmol, 0.15 equiv), **L1** (10.0 mg, 0.03 mmol, 0.15 equiv), 1,3-enyne (0.2 mmol, 1.0 equiv). Then 4.0 mL MeCN was added. To the solution were added the peroxide (78.0 μL, 0.4 mmol, 2.0 equiv) sequentially. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at 70 °C for 24 hours.

Work-up: The reaction mixture was concentrated. And the residue was purified by chromatography to provide the desired product.

Data analysis of product **1a**



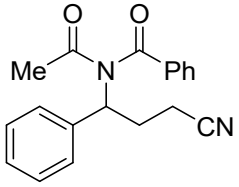
Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 30.9 mg, 50% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.62 – 7.58 (m, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 7.7 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 5.63 (t, *J* = 7.9 Hz, 1H), 2.45 – 2.34 (m, 1H), 2.26 (dp, *J* = 14.5, 7.3 Hz, 1H), 1.84 (s, 3H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 173.2, 139.9, 136.9, 132.8, 128.9, 128.9, 128.3, 128.3, 127.4, 62.2, 27.5, 25.2, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{20}NO_2$: 282.1489, found: 282.1489.

Data analysis of product **2a**



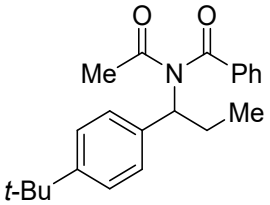
Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 26.3 mg, 43% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.55 (d, *J* = 7.6 Hz, 3H), 7.45 (d, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 5.82 – 5.77 (m, 1H), 2.89 – 2.79 (m, 1H), 2.62 (dq, *J* = 14.1, 7.1 Hz, 1H), 2.45 (hept, *J* = 9.1, 8.1 Hz, 2H), 1.85 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 172.7, 137.7, 136.3, 133.3, 129.1, 128.9, 128.7, 128.3, 128.3, 118.9, 59.1, 28.2, 27.3, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{19}N_2O_2$: 307.1441, found: 307.1441.

Data analysis of product **1b**



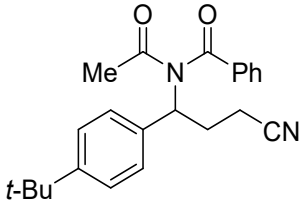
Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 11.6 mg, 17% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.60 (d, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.39 (dd, *J* = 22.0, 7.9 Hz, 4H), 7.32 – 7.28 (m, 2H), 5.59 (t, *J* = 8.0 Hz, 1H), 2.38 (tt, *J* = 15.2, 7.7 Hz, 1H), 2.24 (dp, *J* = 14.0, 7.1 Hz, 1H), 1.86 (s, 3H), 1.28 (d, *J* = 1.8 Hz, 10H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.6, 173.3, 150.2, 137.0, 136.8, 132.7, 128.9, 128.8, 127.9, 125.1, 61.9, 34.4, 31.3, 27.5, 25.2, 11.8.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{28}NO_2$: 338.2115, found: 338.2115.

Data analysis of product **2b**



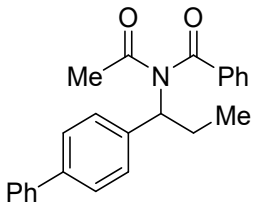
Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 27.1 mg, 37% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.54 (d, *J* = 7.9 Hz, 3H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 5.74 (s, 1H), 2.80 (dt, *J* = 15.6, 7.8 Hz, 1H), 2.62 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.50 – 2.37 (m, 2H), 1.85 (s, 3H), 1.27 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.6, 172.7, 151.2, 136.3, 134.6, 133.2, 128.99, 128.96, 128.0, 125.5, 119.0, 58.9, 34.5, 31.2, 28.3, 27.3, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{27}N_2O_2$: 363.2067, found: 363.2067.

Data analysis of product **1c**



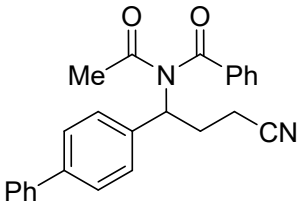
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 18.6 mg, 26% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.63 (d, *J* = 7.7 Hz, 2H), 7.55 (d, *J* = 12.0 Hz, 7H), 7.42 (dt, *J* = 9.2, 4.8 Hz, 4H), 7.32 (t, *J* = 7.3 Hz, 1H), 5.67 (t, *J* = 8.0 Hz, 1H), 2.42 (dt, *J* = 14.8, 7.5 Hz, 1H), 2.30 (dt, *J* = 14.1, 7.1 Hz, 1H), 1.87 (s, 3H), 1.03 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 173.3, 140.8, 140.2, 138.9, 136.9, 132.9, 128.9, 128.7, 127.3, 127.1, 127.0, 61.9, 27.6, 25.1, 11.8.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{24}NO_2$: 358.1802, found: 358.1802.

Data analysis of product **2c**



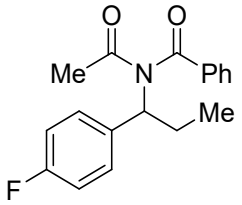
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 36.8 mg, 47% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.55 (td, *J* = 18.4, 16.8, 7.9 Hz, 9H), 7.42 (t, *J* = 7.5 Hz, 4H), 7.34 (t, *J* = 7.4 Hz, 1H), 5.83 (t, *J* = 7.9 Hz, 1H), 2.87 (dq, *J* = 15.6, 7.9 Hz, 1H), 2.67 (dq, *J* = 14.1, 7.2 Hz, 1H), 2.47 (s, 0H), 1.87 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 172.8, 141.1, 140.4, 136.7, 136.3, 133.4, 129.1, 129.0, 128.82, 128.79, 127.5, 127.3, 127.1, 119.0, 58.9, 28.2, 27.5, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{23}N_2O_2$: 383.1754, found: 383.1756.

Data analysis of product **1d**



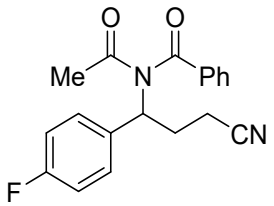
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 23.4 mg, 39% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.59 (d, *J* = 7.7 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.49 – 7.39 (m, 4H), 6.98 (t, *J* = 8.5 Hz, 2H), 5.60 (t, *J* = 7.9 Hz, 1H), 2.36 (dp, *J* = 15.3, 7.6 Hz, 1H), 2.23 (dp, *J* = 14.6, 7.4 Hz, 1H), 1.82 (s, 3H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 173.1, 162.0 (d, *J* = 246.3 Hz), 136.8, 135.6 (d, *J* = 3.3 Hz), 133.0, 130.2 (d, *J* = 7.7 Hz), 129.0, 128.9, 115.0 (d, *J* = 20.9 Hz), 61.5, 27.6, 25.3, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{19}FNO_2$: 300.1395, found: 300.1395.

Data analysis of product **2d**



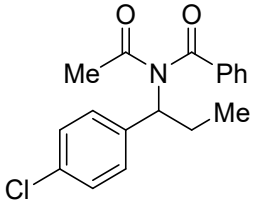
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 32.4 mg, 50% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.56 (dd, *J* = 16.8, 7.8 Hz, 3H), 7.47 – 7.40 (m, 4H), 7.01 (t, *J* = 8.5 Hz, 2H), 5.79 (t, *J* = 8.0 Hz, 1H), 2.82 (dt, *J* = 15.5, 7.8 Hz, 1H), 2.59 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.50 – 2.38 (m, 2H), 1.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 172.7, 162.4 (d, *J* = 247.6 Hz), 136.2, 133.6 (d, *J* = 2.9 Hz), 133.5, 130.3 (d, *J* = 8.3 Hz), 129.1, 128.9, 118.8, 115.6 (d, *J* = 21.0 Hz), 58.4, 28.3, 27.4, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{18}FN_2O_2$: 325.1352, found: 325.1347.

Data analysis of product **1e**



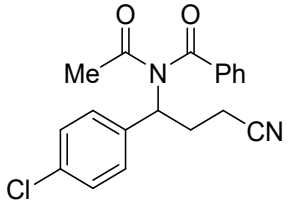
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Yellow liquid, 18.5 mg, 29% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.62 – 7.58 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (dd, *J* = 8.1, 5.4 Hz, 4H), 7.27 (d, *J* = 8.4 Hz, 2H), 5.59 (t, *J* = 7.9 Hz, 1H), 2.40 – 2.30 (m, 1H), 2.22 (dt, *J* = 14.1, 7.2 Hz, 1H), 1.82 (s, 3H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.3, 173.2, 138.4, 136.8, 133.3, 133.0, 129.8, 129.0, 128.9, 128.4, 61.5, 27.6, 25.1, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{19}ClNO_2$: 316.1099, found: 316.1099.

Data analysis of product **2e**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Yellow liquid, 34.4 mg, 51% yield.

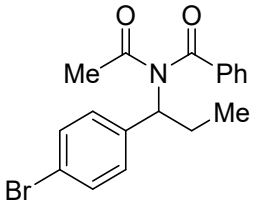
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.57 (dd, *J* = 14.3, 7.5 Hz, 3H), 7.43 (dd, *J* = 14.2, 7.6 Hz, 4H), 7.30 (d, *J* = 8.1 Hz, 2H), 5.77 (t, *J* = 7.9 Hz, 1H), 2.82 (dt, *J* = 15.5, 7.7 Hz, 1H), 2.57 (dq, *J* = 14.0, 7.1 Hz, 1H), 2.51 – 2.38 (m, 2H), 1.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.3, 172.8, 136.4, 136.1,

134.2, 133.5, 129.8, 129.2, 128.9, 128.9, 118.7, 58.5, 28.1, 27.5, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{18}ClN_2O_2$: 341.1052, found: 341.1052.

Data analysis of product **1f**



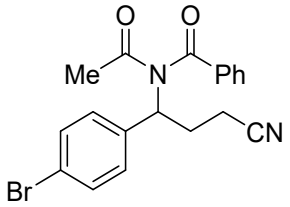
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 25.1 mg, 35% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.60 (d, *J* = 7.7 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.45 – 7.40 (m, 4H), 7.36 (d, *J* = 8.1 Hz, 2H), 5.57 (t, *J* = 7.9 Hz, 1H), 2.35 (dp, *J* = 15.3, 7.6 Hz, 1H), 2.21 (dp, *J* = 14.4, 7.3 Hz, 1H), 1.81 (s, 3H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 173.2, 138.9, 136.7, 133.1, 131.4, 130.2, 129.0, 128.9, 121.5, 61.6, 27.7, 25.0, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{19}BrNO_2$: 360.0594, found: 360.0593.

Data analysis of product **2f**



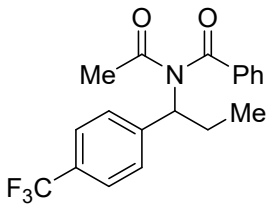
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 50.5 mg, 45% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.56 (dd, *J* = 14.4, 7.5 Hz, 3H), 7.44 (t, *J* = 8.0 Hz, 4H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.74 (t, *J* = 7.9 Hz, 1H), 2.81 (dq, *J* = 15.5, 7.8 Hz, 1H), 2.56 (dq, *J* = 14.0, 7.1 Hz, 1H), 2.49 – 2.37 (m, 2H), 1.82 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.3, 172.8, 136.9, 136.1, 133.5, 131.8, 130.1, 129.2, 128.9, 122.4, 118.7, 58.5, 28.0, 27.5, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{18}BrN_2O_2$: 385.0546, found: 385.0546.

Data analysis of product **1g**



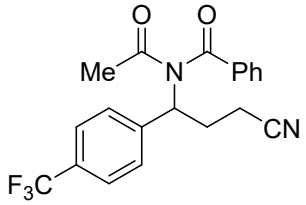
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 24.2 mg, 35% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.65 – 7.59 (m, 4H), 7.59 – 7.51 (m, 3H), 7.44 (t, *J* = 7.6 Hz, 2H), 5.66 (t, *J* = 7.9 Hz, 1H), 2.38 (dh, *J* = 14.3, 7.1, 6.6 Hz, 1H), 2.25 (dp, *J* = 15.0, 7.5 Hz, 1H), 1.83 (s, 3H), 1.01 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.1, 173.2, 144.0, 136.6, 133.1, 129.6 (q, *J* = 32.1, 31.7 Hz), 129.1, 128.9, 128.7, 125.2 (q, *J* = 3.4 Hz), 124.1 (q, *J* = 272.0 Hz), 61.7, 27.7, 24.9, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{19}F_3NO_2$: 350.1363, found: 350.1363.

Data analysis of product **2g**



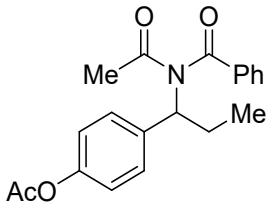
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 33.6 mg, 45% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.62 – 7.56 (m, 7H), 7.45 (t, *J* = 7.6 Hz, 2H), 5.84 (dd, *J* = 9.1, 6.7 Hz, 1H), 2.87 (ddd, *J* = 16.7, 14.4, 7.8 Hz, 1H), 2.60 (dq, *J* = 14.1, 7.0 Hz, 1H), 2.53 – 2.40 (m, 2H), 1.85 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 172.9, 142.0, 136.0, 133.6, 130.4 (q, *J* = 32.6 Hz), 129.2, 128.9, 128.7, 125.6 (q, *J* = 3.6 Hz), 123.9 (q, *J* = 272.1 Hz), 118.6, 58.6, 27.8, 27.5, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{18}F_3N_2O_2$: 375.1315, found: 375.1316.

Data analysis of product **1h**



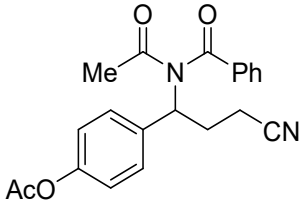
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 11.2 mg, 16% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.59 (d, *J* = 7.7 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 5.61 (t, *J* = 7.9 Hz, 1H), 2.37 (dp, *J* = 15.1, 7.5 Hz, 1H), 2.27 (s, 3H), 2.22 (dp, *J* = 14.5, 7.6 Hz, 1H), 1.83 (s, 3H), 0.99 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 173.2, 169.3, 149.9, 137.5, 136.8, 132.9, 129.5, 129.0, 128.9, 121.3, 61.6, 27.6, 25.2, 21.1, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{22}NO_4$: 340.1544, found: 340.1541.

Data analysis of product **2h**



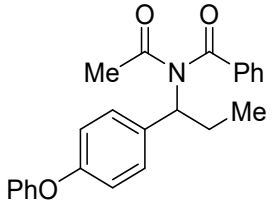
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 26.2 mg, 36% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.55 (dd, *J* = 10.1, 7.5 Hz, 3H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.05 (d, *J* = 8.3 Hz, 2H), 5.77 (t, *J* = 7.9 Hz, 1H), 2.81 (dt, *J* = 15.6, 7.8 Hz, 1H), 2.58 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.50 – 2.36 (m, 2H), 2.27 (s, 3H), 1.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 172.8, 169.2, 150.5, 136.2, 135.3, 133.4, 129.6, 129.1, 128.9, 121.8, 118.8, 58.6, 28.2, 27.4, 21.1, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{21}N_2O_4$: 365.1496, found: 365.1496.

Data analysis of product **1i**



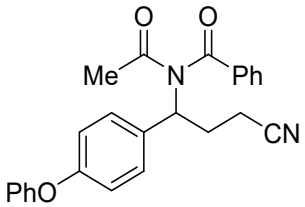
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 10.4 mg, 14 % yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.60 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.46 – 7.40 (m, 4H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.98 – 6.90 (m, 4H), 5.61 (t, *J* = 7.9 Hz, 1H), 2.37 (dq, *J* = 15.3, 7.6 Hz, 1H), 2.24 (dq, *J* = 14.2, 7.2 Hz, 1H), 1.84 (s, 3H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 173.1, 157.0, 156.5, 136.9, 134.6, 132.9, 129.9, 129.7, 129.0, 126.7, 123.3, 119.0, 118.4, 61.6, 27.6, 25.3, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{24}NO$: 374.1751., found: 374.1752.

Data analysis of product **2i**



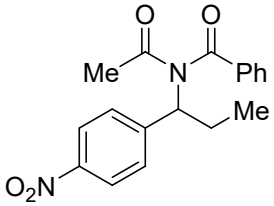
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 22.2 mg, 28% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.56 (d, *J* = 7.6 Hz, 3H), 7.43 (t, *J* = 8.6 Hz, 4H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 6.98 – 6.91 (m, 4H), 5.78 (t, *J* = 7.9 Hz, 1H), 2.86 – 2.77 (m, 1H), 2.60 (dq, *J* = 14.2, 7.2 Hz, 1H), 2.51 – 2.38 (m, 2H), 1.85 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 172.6, 157.4, 156.7, 136.3, 133.4, 132.3, 129.9, 129.8, 129.1, 129.0, 123.6, 119.2, 118.9, 118.6, 58.6, 28.4, 27.3, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{23}N_2O_3$: 399.1703, found: 399.1703.

Data analysis of product **1j**



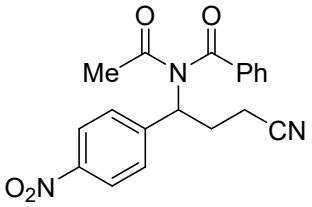
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 39.1 mg, 60% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 8.17 (d, *J* = 8.4 Hz, 2H), 7.65 (dd, *J* = 19.8, 8.1 Hz, 4H), 7.58 (q, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 5.69 (t, *J* = 7.9 Hz, 1H), 2.44 – 2.34 (m, 1H), 2.25 (dq, *J* = 16.9, 9.5, 8.3 Hz, 1H), 1.82 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.0, 172.1, 146.5, 146.3, 135.5, 132.3, 128.24, 128.16, 128.0, 122.5, 60.5, 26.7, 23.9, 10.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{19}N_2O_4$: 327.1340, found: 327.1340.

Data analysis of product **2j**



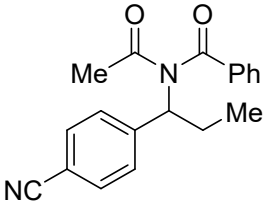
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 22.4 mg, 32% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 8.23 – 8.11 (m, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 7.60 (dd, *J* = 14.2, 7.5 Hz, 3H), 7.47 (t, *J* = 7.7 Hz, 2H), 5.89 (dd, *J* = 9.4, 6.3 Hz, 1H), 2.91 (ddt, *J* = 14.0, 9.3, 7.1 Hz, 1H), 2.59 (dq, *J* = 13.7, 6.9 Hz, 1H), 2.55 – 2.43 (m, 2H), 1.85 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.0, 171.9, 146.8, 144.3, 134.9, 132.8, 128.34, 128.31, 127.9, 122.9, 117.4, 57.4, 26.7, 26.6, 14.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{18}N_3O_4$: 352.1292, found: 352.1291

Data analysis of product **1k**



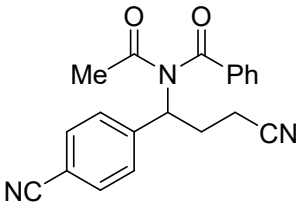
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 30.0 mg, 49% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.65 – 7.56 (m, 7H), 7.46 (t, *J* = 7.6 Hz, 2H), 5.64 (dd, *J* = 8.8, 7.0 Hz, 1H), 2.41 – 2.31 (m, 1H), 2.23 (dp, *J* = 14.4, 7.2 Hz, 1H), 1.83 (s, 3H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.0, 173.1, 145.5, 136.5, 133.3, 132.1, 129.13, 129.07, 128.9, 118.7, 111.3, 61.6, 27.7, 24.7, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{19}N_2O_2$: 307.1441 found: 307.1437.

Data analysis of product **2k**



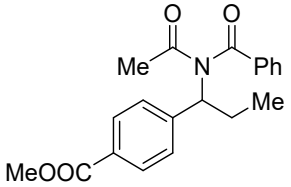
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 30.4 mg, 46% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.66 – 7.54 (m, 7H), 7.45 (t, *J* = 7.8 Hz, 2H), 5.82 (dd, *J* = 9.3, 6.4 Hz, 1H), 2.86 (ddt, *J* = 14.2, 9.6, 7.2 Hz, 1H), 2.55 (dq, *J* = 13.7, 6.8 Hz, 1H), 2.48 – 2.40 (m, 2H), 1.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.0, 172.8, 143.3, 135.9, 133.7, 132.5, 129.3, 129.1, 128.9, 118.5, 118.3, 112.2, 58.6, 27.6, 27.6, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{18}N_3O_2$: 332.1394, found: 332.1389.

Data analysis of product **1l**



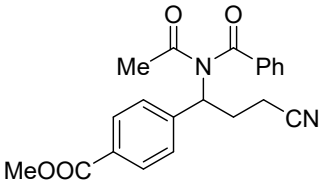
Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 25.8 mg, 38% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.99 – 7.95 (m, 2H), 7.60 (d, *J* = 7.8 Hz, 2H), 7.56 – 7.52 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 5.66 (t, *J* = 7.9 Hz, 1H), 3.90 – 3.87 (m, 3H), 2.39 (dp, *J* = 15.3, 7.7 Hz, 1H), 2.26 (dp, *J* = 14.5, 7.4 Hz, 1H), 1.83 (d, *J* = 1.4 Hz, 3H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 173.2, 166.9, 145.1, 136.6, 133.1, 129.6, 129.2, 129.0, 128.9, 128.3, 61.8, 52.1, 27.6, 24.9, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{22}NO_4$: 340.1544, found: 340.1544.

Data analysis of product **2l**



Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 32.0 mg, 44% yield.

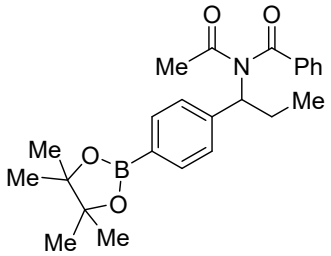
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.99 (d, *J* = 8.1 Hz, 2H), 7.54 (dd, *J* = 11.4, 7.9 Hz, 5H), 7.41 (t, *J* = 7.8 Hz, 2H), 5.84 (dd, *J* = 9.2, 6.6 Hz, 1H),

3.88 (s, 3H), 2.87 (ddt, *J* = 14.4, 9.4, 7.3 Hz, 1H), 2.60 (dq, *J* = 14.0, 7.0 Hz, 1H), 2.52 – 2.40 (m, 2H), 1.84 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 172.8, 166.5, 142.9, 136.1, 133.5, 130.1, 129.9, 129.2, 128.9, 128.3, 118.7, 58.7, 52.1, 27.9, 27.5, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{21}N_2O_4$: 365.1496, found: 365.1496.

Data analysis of product **1m**



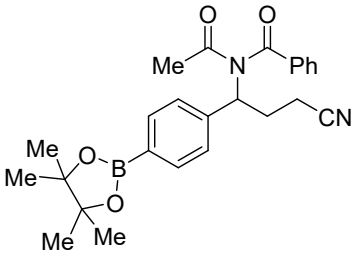
Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 15.0 mg, 19% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.75 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 5.64 (t, *J* = 7.8 Hz, 1H), 2.39 (dp, *J* = 15.0, 7.5 Hz, 1H), 2.34 – 2.22 (m, 1H), 1.83 (s, 3H), 1.32 (s, 12H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.3, 173.3, 142.9, 136.9, 134.8, 132.8, 128.92, 128.90, 127.6, 83.8, 62.1, 27.6, 25.0, 24.9, 24.8, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{31}BNO_4$: 408.2341, found: 408.2341.

Data analysis of product **2m**



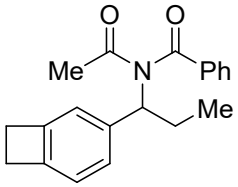
Purified by flash column chromatography on silica gel: 5 to 25% EtOAc in hexanes. Colorless liquid, 17.2 mg, 20% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.76 (d, *J* = 7.8 Hz, 2H), 7.55 (d, *J* = 7.9 Hz, 3H), 7.47 – 7.38 (m, 4H), 5.83 – 5.73 (m, 1H), 2.86 (dq, *J* = 15.9, 7.8 Hz, 1H), 2.63 (dq, *J* = 14.0, 7.0 Hz, 1H), 2.51 – 2.38 (m, 2H), 1.84 (s, 2H), 1.32 (s, 11H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 172.8, 140.7, 136.2, 135.1, 133.3, 129.1, 128.9, 127.6, 118.9, 83.9, 59.1, 28.0, 27.4, 24.9, 24.8, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{30}BN_2O_4$: 433.2293., found: 433.2298.

Data analysis of product **1n**



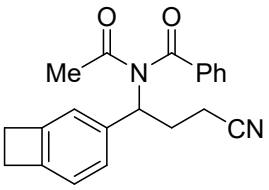
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 10.4 mg, 17% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.61 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.46 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.7 Hz, 1H), 7.19 (s, 1H), 6.97 (d, *J* = 7.6 Hz, 1H), 5.58 (t, *J* = 7.9 Hz, 1H), 3.11 (dq, *J* = 6.8, 3.9, 3.4 Hz, 4H), 2.35 (tt, *J* = 20.7, 10.2 Hz, 1H), 2.24 (dq, *J* = 14.2, 7.3 Hz, 1H), 1.83 (s, 3H), 0.99 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 173.3, 145.6, 145.0, 138.5, 137.0, 132.8, 128.95, 128.88, 127.2, 122.5, 122.3, 62.9, 29.4, 29.3, 27.6, 25.4, 11.8.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{22}NO_2$: 308.1645, found: 308.1650.

Data analysis of product **2n**



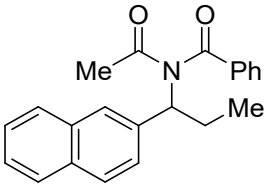
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 23.9 mg, 36% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.56 (d, *J* = 7.7 Hz, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 4.1 Hz, 1H), 7.17 (s, 1H), 5.74 (t, *J* = 7.9 Hz, 1H), 3.12 (s, 4H), 2.78 (dq, *J* = 15.6, 7.9 Hz, 1H), 2.62 (dq, *J* = 14.3, 7.2 Hz, 1H), 2.49 – 2.36 (m, 2H), 1.84 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 172.7, 146.1, 146.0, 136.4, 136.2, 133.3, 129.05, 128.99, 127.3, 122.7, 122.5, 119.0, 59.8, 29.4, 29.4, 28.5, 27.4, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{21}N_2O_2$: 333.1598, found: 333.1598.

Data analysis of product **1o**



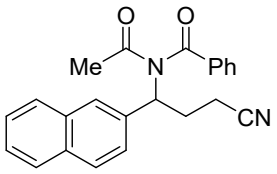
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 6.4 mg, 10% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.91 (s, 1H), 7.80 (dd, *J* = 17.8, 7.3 Hz, 3H), 7.66 – 7.57 (m, 3H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.48 – 7.36 (m, 4H), 5.80 (t, *J* = 7.9 Hz, 1H), 2.49 (dq, *J* = 15.3, 7.6 Hz, 1H), 2.39 (dp, *J* = 14.6, 7.3 Hz, 1H), 1.85 (s, 3H), 1.05 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 173.4, 137.2, 136.9, 133.2, 132.9, 132.8, 128.93, 128.91, 128.2, 128.0, 127.5, 127.4, 126.5, 126.0, 125.9, 62.3, 27.6, 25.2, 11.8.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{22}NO_2$: 332.1645, found: 332.1647.

Data analysis of product **2o**



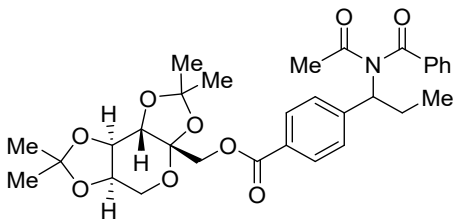
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 19.0 mg, 27% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.90 (s, 1H), 7.84 – 7.77 (m, 3H), 7.62 – 7.45 (m, 6H), 7.38 (t, *J* = 7.6 Hz, 2H), 5.97 (t, *J* = 7.9 Hz, 1H), 2.94 (dq, *J* = 15.6, 8.0 Hz, 1H), 2.76 (dq, *J* = 14.3, 7.4 Hz, 1H), 2.49 (qt, *J* = 16.7, 7.4 Hz, 2H), 1.86 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 172.9, 136.3, 135.0, 133.4, 133.1, 133.0, 129.1, 129.0, 128.6, 128.2, 127.7, 127.6, 126.5, 126.4, 126.0, 119.0, 59.2, 28.3, 27.5, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{21}N_2O_2$: 357.1598, found: 357.1598.

Data analysis of product **1p**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in

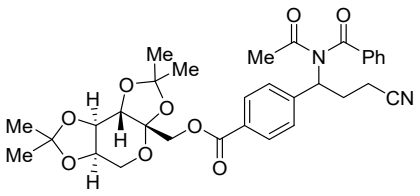
hexanes. Colorless liquid, 31.1 mg, 27% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 8.00 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 3H), 7.41 (t, *J* = 7.7 Hz, 2H), 5.68 – 5.63 (m, 1H), 4.64 – 4.59 (m, 2H), 4.44 (d, *J* = 2.6 Hz, 1H), 4.31 (d, *J* = 11.8 Hz, 1H), 4.24 (d, *J* = 7.9 Hz, 1H), 3.94 (d, *J* = 12.9 Hz, 1H), 3.78 (d, *J* = 13.0 Hz, 1H), 2.39 (dt, *J* = 15.4, 7.7 Hz, 1H), 2.26 (dq, *J* = 14.2, 7.2 Hz, 1H), 1.82 (s, 3H), 1.53 (s, 3H), 1.42 (d, *J* = 6.7 Hz, 3H), 1.36 (d, *J* = 2.8 Hz, 3H), 1.32 (s, 3H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.2, 173.1, 165.7, 145.31, 145.29, 136.6, 133.1, 129.8, 129.0, 128.9, 128.29, 128.27, 109.2, 108.8, 101.7, 70.8, 70.6, 70.1, 65.4, 61.7, 61.4, 27.6, 26.5, 25.9, 25.6, 24.9, 24.0, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{31}H_{38}NO_9$: 568.2541, found: 568.2541.

Data analysis of product **2p**



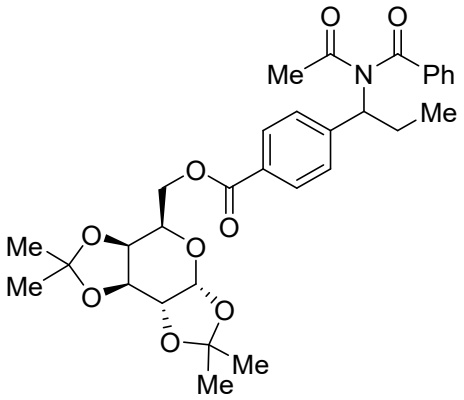
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 35.1 mg, 30% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.56 (dt, *J* = 14.2, 7.3 Hz, 5H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.88 – 5.83 (m, 1H), 4.65 – 4.60 (m, 2H), 4.43 (d, *J* = 2.3 Hz, 1H), 4.32 (dd, *J* = 11.8, 2.1 Hz, 1H), 4.25 (d, *J* = 7.9 Hz, 1H), 3.95 (d, *J* = 12.9 Hz, 1H), 3.79 (d, *J* = 13.0 Hz, 1H), 2.94 – 2.85 (m, 1H), 2.60 (dq, *J* = 14.0, 7.0 Hz, 1H), 2.47 (q, *J* = 7.8 Hz, 2H), 1.85 (s, 3H), 1.54 (s, 3H), 1.42 (d, *J* = 8.6 Hz, 3H), 1.37 – 1.31 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.2, 172.8, 165.4, 143.1, 143.0, 136.0, 133.5, 130.1, 129.8, 129.2, 128.9, 128.31, 128.30, 118.7, 109.2, 108.8, 101.6, 70.8, 70.6, 70.1, 65.6, 61.4, 58.6, 27.9, 27.4, 26.5, 25.84, 25.82, 25.5, 24.0, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{32}H_{37}N_2O_9$: 593.2494., found: 593.2499.

Data analysis of product **1q**



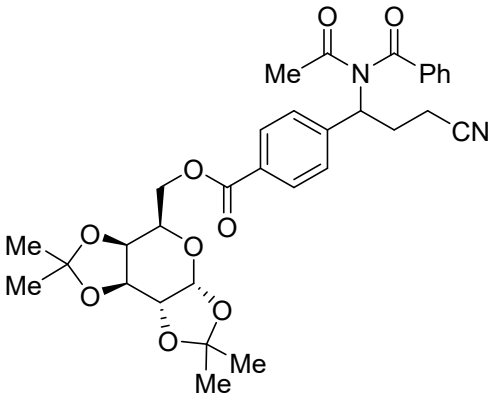
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 34.2 mg, 32% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.53 (d, *J* = 7.9 Hz, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 5.65 (t, *J* = 7.9 Hz, 1H), 5.56 – 5.53 (m, 1H), 4.64 (dd, *J* = 7.8, 2.3 Hz, 1H), 4.48 (dd, *J* = 11.5, 5.0 Hz, 1H), 4.40 (ddd, *J* = 11.7, 7.4, 4.5 Hz, 1H), 4.31 (s, 1H), 4.13 (dt, *J* = 31.9, 6.8 Hz, 1H), 2.38 (dp, *J* = 15.2, 7.5 Hz, 1H), 2.26 (dp, *J* = 14.5, 7.3 Hz, 1H), 1.83 (s, 3H), 1.50 (d, *J* = 3.6 Hz, 3H), 1.46 (s, 3H), 1.34 (s, 3H), 1.32 (s, 3H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.2, 173.2, 166.2, 145.18, 145.17, 136.7, 133.0, 129.7, 129.2, 129.0, 128.9, 128.2, 109.7, 108.8, 96.3, 71.2, 70.8, 70.6, 66.1, 63.8, 61.8, 27.6, 26.03, 25.97, 25.0, 24.9, 24.5, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{31}H_{38}NO_9$: 568.2541, found: 568.2541.

Data analysis of product **2q**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 37.0 mg, 31% yield.

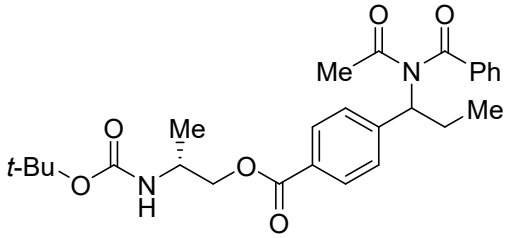
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 8.00 (d, *J* = 7.9 Hz, 2H), 7.53 (dd, *J* = 16.3, 7.8 Hz, 5H), 7.42 (t, *J* = 7.6 Hz, 2H), 5.82 (t, *J* = 7.9 Hz, 1H), 5.54 (t, *J* = 4.0 Hz, 1H), 4.63 (dd, *J* = 7.9, 2.4 Hz, 1H), 4.47 (dd, *J* = 11.5, 4.8 Hz, 1H), 4.40 (ddd, *J* = 11.6, 7.5, 3.9 Hz, 1H), 4.33 (dt, *J* = 4.7, 2.4 Hz, 1H),

4.30 (d, *J* = 7.9 Hz, 1H), 4.16 (d, *J* = 6.4 Hz, 1H), 2.91 – 2.82 (m, 1H), 2.59 (dq, *J* = 14.0, 7.0 Hz, 1H), 2.46 (tq, *J* = 16.9, 9.3, 8.2 Hz, 2H), 1.84 (s, 3H), 1.45 (m, 6H), 1.35 – 1.30 (m, 6H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.2, 172.8, 165.9, 142.9, 136.0, 133.5, 130.1, 130.0, 129.2, 128.9, 128.3, 118.7, 109.7, 108.8, 96.3, 71.1, 70.8, 70.5, 66.12, 66.10, 64.04, 64.01, 58.73, 58.71, 27.9, 27.5, 26.02, 25.96, 25.0, 24.5, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{32}H_{37}N_2O_9$: 593.2494, found: 593.2494.

Data analysis of product **1r**



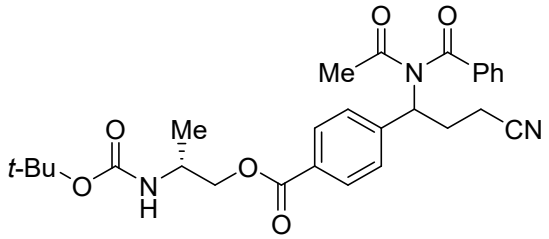
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 36,4 mg, 38% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 2H), 7.54 (dd, *J* = 7.9, 5.0 Hz, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 5.65 (t, *J* = 7.9 Hz, 1H), 4.63 (s, 1H), 4.24 (d, *J* = 5.1 Hz, 2H), 4.11 – 4.04 (m, 1H), 2.42 – 2.35 (m, 1H), 2.29 – 2.22 (m, 1H), 1.82 (s, 3H), 1.40 (d, *J* = 2.8 Hz, 9H), 1.22 (d, *J* = 7.0 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.1, 173.2, 166.2, 155.2, 145.3, 136.7, 133.1, 129.7, 129.0, 128.9, 128.3, 79.5, 67.8, 61.8, 45.6, 28.3, 27.6, 24.9, 17.7, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{35}N_2O_6$: 483.2490, found: 483.2490.

Data analysis of product **2r**



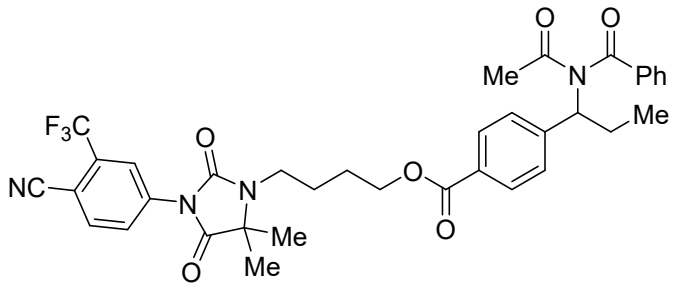
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 35.0 mg, 35% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 8.00 (d, *J* = 8.0 Hz, 2H), 7.54 (dd, *J* = 12.4, 7.9 Hz, 5H), 7.42 (t, *J* = 7.6 Hz, 2H), 5.83 (dd, *J* = 9.1, 6.7 Hz, 1H), 4.61 (s, 1H), 4.23 (t, *J* = 5.0 Hz, 2H), 4.09 (d, *J* = 7.2 Hz, 1H), 2.92 – 2.83 (m, 1H), 2.59 (dq, *J* = 13.9, 7.0 Hz, 1H), 2.46 (hept, *J* = 9.1, 8.1 Hz, 2H), 1.84 (s, 3H), 1.39 (d, *J* = 2.8 Hz, 9H), 1.22 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.2, 172.8, 165.9, 155.2, 143.1, 136.0, 133.5, 130.1, 129.9, 129.2, 128.9, 128.3, 118.7, 79.5, 68.0, 58.7, 45.5, 28.3, 27.8, 27.5, 17.7, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{34}N_3O_6$: 508.2442, found: 508.2442.

Data analysis of product **1s**



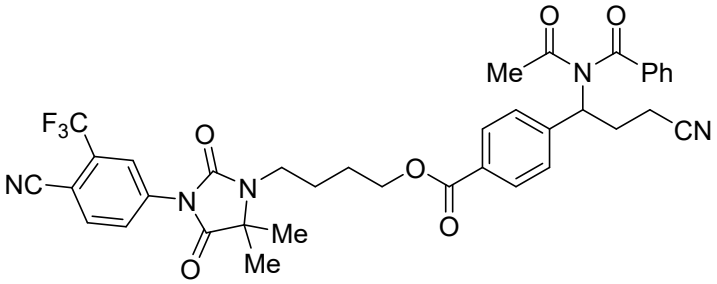
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 59 mg, 44% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 8.15 (s, 1H), 7.99 (dd, *J* = 19.4, 8.2 Hz, 3H), 7.91 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 2H), 7.55 (dd, *J* = 7.9, 4.1 Hz, 3H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.65 (t, *J* = 7.8 Hz, 1H), 4.37 (d, *J* = 5.5 Hz, 2H), 3.43 (d, *J* = 6.8 Hz, 2H), 2.39 (dp, *J* = 15.3, 7.5 Hz, 1H), 2.25 (ddq, *J* = 20.8, 14.8, 7.5 Hz, 1H), 1.89 – 1.84 (m, 4H), 1.83 (s, 3H), 1.52 (s, 6H), 1.00 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.6, 174.1, 173.2, 166.3, 152.9, 145.4, 136.6, 136.5, 135.3, 133.6 (q, *J* = 33.2 Hz), 133.1, 129.6, 129.2, 129.0, 128.9, 128.3, 127.9, 123.0 (q, *J* = 4.9 Hz), 122.0 (q, *J* = 273.3 Hz), 115.0, 108.3, 64.0, 61.9, 61.8, 40.0, 27.6, 26.4, 26.2, 24.9, 23.5, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{36}H_{36}F_3N_4O_6$: 677.2582, found: 677.2582.

Data analysis of product **2s**



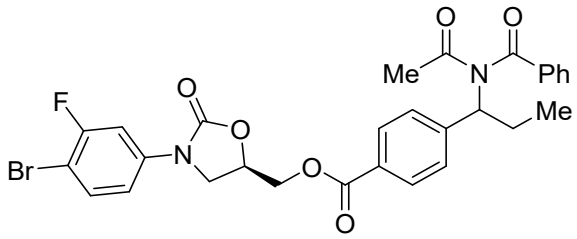
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 52 mg, 37% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 8.15 (s, 1H), 7.99 (d, *J* = 7.0 Hz, 3H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.55 (t, *J* = 8.6 Hz, 5H), 7.43 (t, *J* = 7.4 Hz, 2H), 5.84 (t, *J* = 7.6 Hz, 1H), 4.36 (s, 2H), 3.42 (s, 2H), 2.87 (dq, *J* = 15.2, 7.6 Hz, 1H), 2.60 (dt, *J* = 13.6, 6.7 Hz, 1H), 2.47 (hept, *J* = 9.5, 8.2 Hz, 2H), 1.84 (s, 7H), 1.52 (s, 6H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.5, 174.2, 172.9, 166.0, 152.9, 143.1, 136.5, 136.0, 135.3, 133.60 (q, *J* = 33.0 Hz), 133.5, 130.0, 129.9, 129.2, 128.9, 128.3, 127.9, 123.0 (q, *J* = 4.6 Hz), 122.0 (q, *J* = 274.8 Hz), 118.7, 115.0, 108.3, 64.2, 61.9, 58.7, 40.0, 27.8, 27.5, 26.4, 26.2, 23.5, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{37}H_{35}F_3N_5O_6$: 702.2534, found: 702.2534.

Data analysis of product **1t**



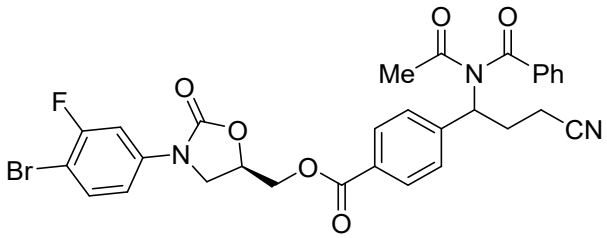
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 49.6 mg, 40% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 7.90 (d, *J* = 7.8 Hz, 2H), 7.60 (d, *J* = 7.3 Hz, 2H), 7.57 – 7.46 (m, 5H), 7.42 (t, *J* = 6.4 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 1H), 5.62 (t, *J* = 7.7 Hz, 1H), 5.00 – 4.96 (m, 1H), 4.54 (q, *J* = 12.2 Hz, 2H), 4.14 (t, *J* = 8.9 Hz, 1H), 3.87 (dt, *J* = 9.7, 5.5 Hz, 1H), 2.36 (dp, *J* = 15.1, 7.4 Hz, 1H), 2.24 (dq, *J* = 13.9, 6.9 Hz, 1H), 1.82 (s, 3H), 0.98 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.1, 173.2, 165.8, 159.2 (d, *J* = 246.5 Hz), 153.8, 146.1, 138.7 (d, *J* = 9.6 Hz), 136.6, 133.6, 133.1, 129.8, 129.1, 128.9, 128.4, 127.9, 114.4, 106.8 (d, *J* = 28.0 Hz), 103.4 (d, *J* = 21.2 Hz), 70.3, 64.4, 61.7, 47.0, 27.6, 24.8, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{29}H_{27}BrFN_2O_6$: 597.1031, found: 597.1031

Data analysis of product **2t**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 54.4 mg, 43% yield.

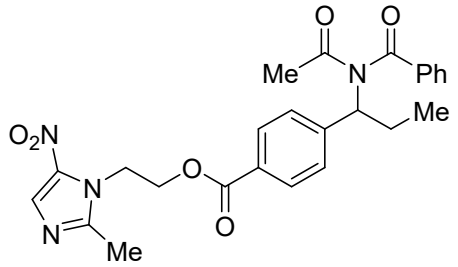
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 7.92 (d, *J* = 7.8 Hz, 2H), 7.58 – 7.47 (m, 7H), 7.45 – 7.37 (m, 2H), 7.13 (d, *J* = 8.4 Hz, 1H), 5.82 (t, *J* = 7.6 Hz, 1H), 4.99 (s, 1H), 4.61 – 4.48 (m, 2H), 4.15 (t, *J* = 8.7 Hz, 1H), 3.86 (d, *J* = 6.9 Hz, 1H), 2.84 (dt, *J* = 15.3, 7.6 Hz, 1H), 2.57 (dq, *J* = 13.4, 6.5

Hz, 1H), 2.46 (hept, *J* = 9.5, 8.2 Hz, 2H), 1.83 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *cis* and *trans*) δ 174.1, 172.9, 165.5, 159.2 (d, *J* = 246.5 Hz), 153.8, 143.8, 138.7 (d, *J* = 9.5 Hz), 136.0, 133.6, 130.1, 129.2, 128.9, 128.7, 128.4, 118.7, 114.4, 106.7 (d, *J* = 27.8 Hz), 103.4 (d, *J* = 21.1 Hz), 70.3, 64.6, 58.6, 47.0, 27.7, 27.5, 15.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{30}H_{26}BrFN_3O_6$: 622.0984, found: 622.0984.

Data analysis of product **1u**



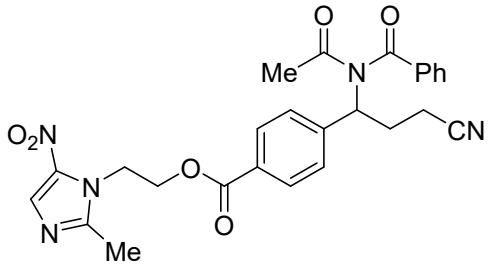
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 24.3 mg, 25% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.97 (s, 1H), 7.86 (d, *J* = 7.1 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 7.6 Hz, 3H), 7.43 (t, *J* = 7.1 Hz, 2H), 5.64 (t, *J* = 7.7 Hz, 1H), 4.70 – 4.67 (m, 3H), 4.65 (d, *J* = 4.6 Hz, 3H), 2.47 (s, 2H), 2.37 (dq, *J* = 14.6, 7.3 Hz, 1H), 2.24 (dt, *J* = 13.5, 6.8 Hz, 1H), 1.84 – 1.81 (m, 4H), 0.99 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.1, 173.2, 165.8, 150.8, 146.1, 138.6, 136.6, 133.3, 133.1, 129.6, 129.1, 128.9, 128.5, 128.0, 62.9, 61.7, 45.3, 27.7, 24.9, 14.4, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{27}N_4O_6$: 479.1925, found: 479.1925.

Data analysis of product **2u**



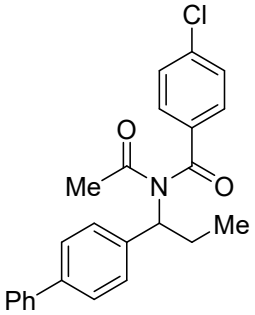
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 12.5 mg, 12% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 8.02 – 7.93 (m, 3H), 7.88 (d, *J* = 8.1 Hz, 3H), 7.55 (t, *J* = 7.9 Hz, 8H), 7.44 (t, *J* = 7.7 Hz, 3H), 5.88 – 5.79 (m, 1H), 4.72 – 4.69 (m, 5H), 4.66 (d, *J* = 4.6 Hz, 4H), 2.87 (dt, *J* = 15.9, 7.6 Hz, 2H), 2.61 – 2.57 (m, 2H), 2.47 (s, 5H), 1.84 (s, 4H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 172.9, 165.5, 143.8, 136.0, 133.6, 133.2, 130.2, 129.9, 129.7, 129.2, 128.9, 128.8, 128.6, 118.7, 62.9, 58.6, 45.2, 27.7, 27.6, 15.1, 14.3.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{26}N_5O_6$: 504.1878, found: 504.1878.

Data analysis of product **1v**



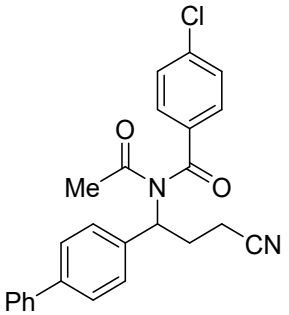
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 25.8 mg, 33% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.53 (dt, *J* = 24.0, 8.1 Hz, 8H), 7.45 – 7.37 (m, 4H), 7.33 (t, *J* = 7.3 Hz, 1H), 5.63 (t, *J* = 7.8 Hz, 1H), 2.39 (tq, *J* = 15.0, 7.6 Hz, 1H), 2.34 – 2.20 (m, 1H), 1.91 (s, 3H), 1.02 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.4, 173.0, 140.7, 140.4, 139.4, 138.6, 135.1, 130.3, 129.3, 128.8, 128.6, 127.3, 127.1, 127.0, 62.1, 27.5, 25.2, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{23}ClNO_2$: 392.1412, found: 392.1412.

Data analysis of product **2v**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 35.7 mg, 43% yield.

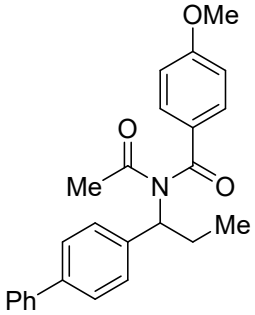
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.57 – 7.47 (m, 8H), 7.44 – 7.38 (m, 4H), 7.34 (t, *J* = 7.3 Hz, 1H), 5.80 (t, *J* = 7.8 Hz, 1H), 2.85 (dq, *J* = 15.6, 7.8 Hz, 1H), 2.65 (dq, *J* = 14.1, 7.0 Hz, 1H), 2.48 (tq, *J* = 17.1, 9.3, 8.1 Hz, 2H), 1.92 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.5, 172.5, 141.3, 140.2, 140.0, 136.5, 134.5, 130.3, 129.5, 128.8, 128.7, 127.6, 127.4, 127.0, 118.9, 59.0, 28.2,

27.3, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{22}ClN_2O_2$: 417.1365, found: 417.1365.

Data analysis of product **1w**



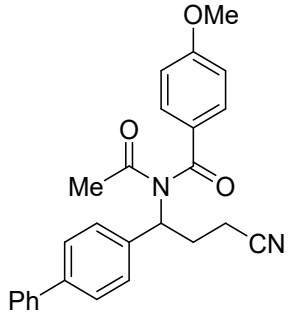
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 30.2 mg, 39% yield.

^1H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.62 (d, *J* = 8.6 Hz, 2H), 7.54 (dd, *J* = 18.2, 5.9 Hz, 6H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.65 (t, *J* = 7.8 Hz, 1H), 3.84 (s, 3H), 2.39 (dp, *J* = 15.3, 7.6 Hz, 1H), 2.26 (ddq, *J* = 21.7, 14.6, 7.5 Hz, 1H), 1.88 (s, 3H), 1.01 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.9, 172.7, 163.7, 140.8, 140.2, 139.0, 131.6, 129.0, 128.8, 128.7, 127.2, 127.1, 126.9, 114.2, 61.8, 55.5, 27.2, 25.3, 11.8.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{26}NO_3$: 388.1907, found: 388.1907.

Data analysis of product **2w**



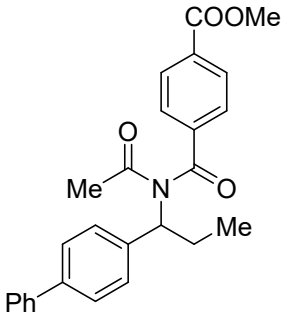
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 37.9 mg, 46% yield.

^1H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.54 (dq, *J* = 21.7, 8.2 Hz, 8H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.80 (t, *J* = 7.8 Hz, 1H), 3.83 (s, 3H), 2.85 (dq, *J* = 15.8, 7.9 Hz, 1H), 2.62 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.53 – 2.41 (m, *J* = 6.8 Hz, 2H), 1.89 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.9, 172.2, 164.1, 141.0, 140.4, 136.8, 131.7, 128.8, 128.8, 128.3, 127.5, 127.3, 127.0, 119.0, 114.4, 58.7, 55.6, 28.4, 26.9, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{25}N_2O_3$: 413.1860, found: 413.1861.

Data analysis of product **1x**



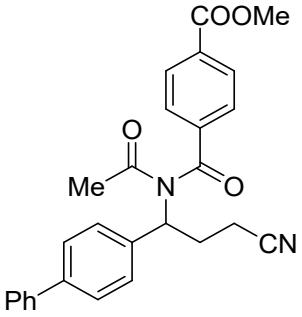
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 18.6 mg, 26% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 8.08 (d, *J* = 7.8 Hz, 2H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.58 – 7.49 (m, 6H), 7.42 (t, *J* = 7.3 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 5.64 (t, *J* = 7.8 Hz, 1H), 3.94 (s, 2H), 2.42 (dp, *J* = 15.0, 7.4 Hz, 1H), 2.31 (dp, *J* = 14.0, 7.0 Hz, 1H), 1.91 (s, 2H), 1.04 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.6, 173.3, 165.9, 140.65, 140.55, 140.4, 138.6, 133.7, 130.1, 128.8, 128.6, 127.3, 127.1, 62.1, 52.5, 27.6, 25.1, 11.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{26}NO_4$: 416.1857, found: 416.1857.

Data analysis of product **2x**



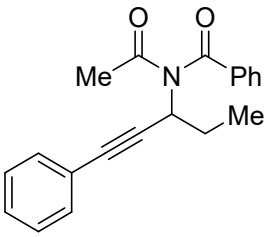
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 42.2 mg, 48% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 8.07 (d, *J* = 7.9 Hz, 2H), 7.63 (d, *J* = 7.9 Hz, 2H), 7.58 – 7.49 (m, 6H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H), 5.82 (t, *J* = 7.8 Hz, 1H), 3.93 (s, 2H), 2.87 (dq, *J* = 15.6, 7.8 Hz, 1H), 2.68 (dq, *J* = 14.0, 7.0 Hz, 1H), 2.48 (tq, *J* = 17.0, 8.9, 7.6 Hz, 2H), 1.91 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.7, 172.8, 165.7, 141.3, 140.2, 139.9, 136.4, 134.1, 130.2, 128.8, 128.69, 128.67, 127.6, 127.4, 127.1, 118.9, 59.1, 52.6, 28.1, 27.5, 15.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{25}N_2O_4$: 441.1809, found: 441.1809.

Data analysis of product **3a**



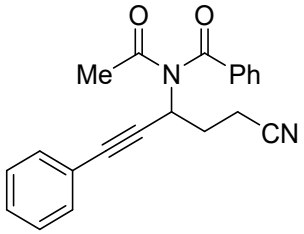
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 27.3 mg, 45% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.35 – 7.31 (m, 2H), 7.25 (d, *J* = 7.4 Hz, 3H), 5.34 (t, *J* = 7.8 Hz, 1H), 2.12 (ddd, *J* = 34.8, 13.6, 6.6 Hz, 2H), 2.05 (s, 3H), 1.04 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.1, 171.6, 136.0, 133.1, 131.8, 129.1, 129.0, 128.3, 128.2, 122.7, 86.7, 84.4, 50.8, 28.2, 26.5, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{20}NO_2$: 306.1489, found: 306.1489.

Data analysis of product **4a**



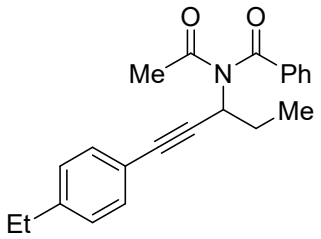
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 20.5 mg, 31% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.78 (d, *J* = 7.8 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.31 – 7.21 (m, 5H), 5.53 (t, *J* = 6.9 Hz, 1H), 2.53 (ddt, *J* = 16.1, 13.4, 8.7 Hz, 3H), 2.42 (dt, *J* = 12.7, 5.5 Hz, 1H), 1.98 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.8, 171.2, 135.5, 133.7, 131.8, 129.3, 129.2, 128.8, 128.3, 121.9, 118.6, 86.0, 84.2, 47.9, 30.5, 26.4, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{19}N_2O_2$: 331.1441, found: 331.1441.

Data analysis of product **3b**



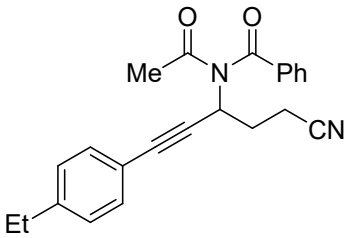
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 16.5 mg, 25% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 5.32 (t, *J* = 7.8 Hz, 1H), 2.61 (q, *J* = 7.6 Hz, 2H), 2.17 – 2.04 (m, 5H), 1.20 (t, *J* = 7.6 Hz, 3H), 1.03 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 171.6, 144.7, 136.1, 133.1, 131.8, 129.2, 128.9, 127.7, 119.9, 86.0, 84.5, 50.8, 28.8, 28.3, 26.4, 15.3, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{24}NO_2$: 334.1802, found: 334.1802.

Data analysis of product **4b**



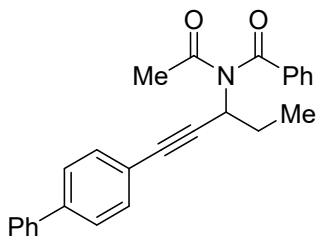
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 25.9 mg, 36% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.81 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.7 Hz, 2H), 5.55 (t, *J* = 6.9 Hz, 1H), 2.64 – 2.49 (m, 5H), 2.43 (dt, *J* = 13.1, 6.1 Hz, 1H), 2.01 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.9, 171.1, 145.3, 135.5, 133.6, 131.9, 129.3, 129.2, 127.8, 119.0, 118.7, 86.2, 83.4, 48.0, 30.5, 28.8, 26.4, 15.3, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{23}N_2O_2$: 359.1754, found: 359.1754.

Data analysis of product **3c**



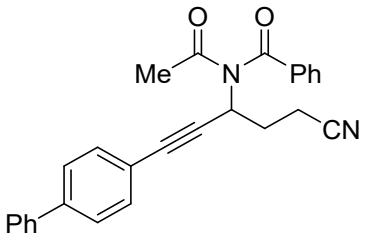
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 22.7 mg, 30% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.82 (d, *J* = 7.4 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.50 (dd, *J* = 7.7, 5.0 Hz, 6H), 7.45 – 7.39 (m, 5H), 7.35 (t, *J* = 7.3 Hz, 1H), 5.36 (t, *J* = 7.7 Hz, 1H), 2.18 (dt, *J* = 15.4, 7.7 Hz, 1H), 2.11 (dd, *J* = 13.9, 6.8 Hz, 1H), 2.07 (s, 3H), 1.06 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 171.6, 141.1, 140.4, 136.0, 133.2, 132.2, 129.2, 129.0, 128.8, 127.6, 127.0, 126.9, 121.6, 87.4, 84.2, 50.9, 28.3, 26.5, 11.3.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{26}H_{24}NO_2$: 382.1802, found: 382.1802.

Data analysis of product **4c**



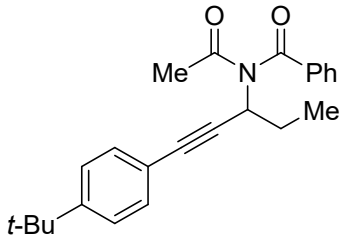
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 24.9 mg, 30% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.83 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.57 – 7.48 (m, 6H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 5.59 (t, *J* = 6.9 Hz, 1H), 2.59 (tdd, *J* = 18.5, 11.7, 5.0 Hz, 3H), 2.46 (dt, *J* = 12.6, 4.9 Hz, 1H), 2.03 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.9, 171.2, 141.6, 140.2, 135.5, 133.7, 132.3, 129.3, 129.2, 128.9, 127.8, 127.0, 127.0, 120.7, 118.6, 85.9, 84.8, 48.0, 30.5, 26.4, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{27}H_{23}N_2O_2$: 407.1754, found: 407.1754.

Data analysis of product **3d**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 28.0 mg, 39% yield.

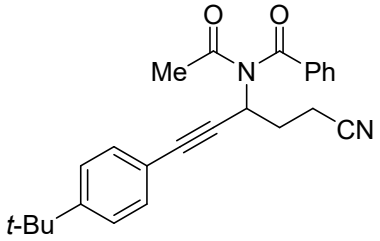
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.26 (s, 4H), 5.32 (t, *J* = 7.8 Hz, 1H), 2.17

– 2.06 (m, 2H), 2.04 (s, 3H), 1.27 (s, 9H), 1.02 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.2, 171.6, 151.6, 136.1, 133.1, 131.5, 129.2, 128.9, 125.2, 119.7, 86.0, 84.5, 50.8, 34.7, 31.1, 28.3, 26.4, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{28}NO_2$: 362.2115, found: 362.2115.

Data analysis of product **4d**



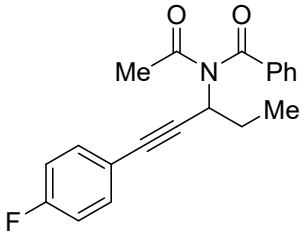
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 22.8 mg, 30% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.81 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.30 – 7.23 (m, 4H), 5.55 (t, *J* = 6.9 Hz, 1H), 2.64 – 2.50 (m, 3H), 2.44 (dt, *J* = 12.9, 5.9 Hz, 1H), 2.01 (s, 3H), 1.28 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.9, 171.1, 152.2, 135.5, 133.6, 131.6, 129.3, 129.2, 125.3, 118.8, 118.7, 86.1, 83.4, 48.0, 34.8, 31.1, 30.6, 26.4, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{27}N_2O_2$: 387.2067, found: 387.2067.

Data analysis of product **3e**



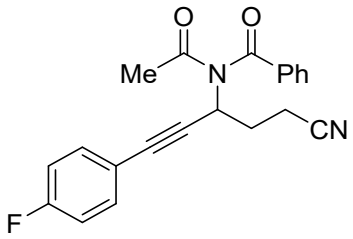
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 22.1 mg, 34% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.31 (dd, *J* = 8.5, 5.4 Hz, 2H), 6.94 (t, *J* = 8.5 Hz, 2H), 5.32 (t, *J* = 7.8 Hz, 1H), 2.18 – 2.06 (m, 2H), 2.04 (s, 3H), 1.03 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.1, 171.6, 162.5 (d, *J* = 249.6 Hz), 136.0, 133.7 (d, *J* = 8.6 Hz), 133.2, 129.1, 129.0, 118.8 (d, *J* = 3.7 Hz), 115.4 (d, *J* = 22.7 Hz), 86.4, 83.3, 50.7, 28.2, 26.5, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{19}FNO_2$: 324.1395, found: 324.1395.

Data analysis of product **4e**



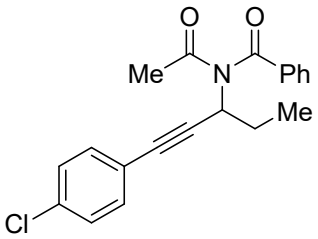
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 22.2 mg, 32% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.30 (dd, *J* = 8.4, 5.4 Hz, 2H), 6.95 (t, *J* = 8.5 Hz, 2H), 5.54 (t, *J* = 6.1 Hz, 1H), 2.61 – 2.50 (m, 3H), 2.47 – 2.39 (m, 1H), 2.00 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.8, 171.2, 162.8 (d, *J* = 250.4 Hz), 135.5, 133.8 (d, *J* = 8.7 Hz), 133.7, 129.3, 129.2, 118.6, 118.0 (d, *J* = 3.3 Hz), 115.6 (d, *J* = 21.9 Hz), 84.9, 83.9, 47.9, 30.4, 26.5, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{18}FN_2O_2$: 349.1347, found: 349.1347.

Data analysis of product **3f**



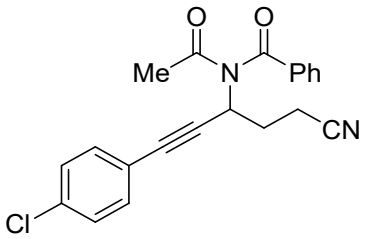
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 23.7 mg, 35% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.78 (d, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.24 (q, *J* = 8.1 Hz, 4H), 5.32 (t, *J* = 7.8 Hz, 1H), 2.12 (dq, *J* = 35.2, 6.6 Hz, 1H), 2.04 (s, 3H), 1.03 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.0, 171.6, 136.0, 134.3, 133.2, 133.0, 129.1, 129.0, 128.5, 121.2, 87.8, 83.2, 50.7, 28.1, 26.5, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{19}ClNO_2$: 340.1099, found: 340.1099.

Data analysis of product **4f**



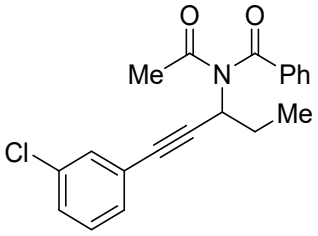
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 20.6 mg, 28% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.24 (s, 4H), 5.55 (t, *J* = 5.9 Hz, 1H), 2.61 – 2.50 (m, 3H), 2.44 (ddd, *J* = 12.0, 7.2, 4.4 Hz, 1H), 2.00 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.8, 171.2, 135.4, 134.9, 133.7, 133.1, 129.24, 129.20, 128.6, 120.4, 118.5, 85.2, 84.8, 47.9, 30.3, 26.5, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{18}ClN_2O_2$: 365.1052, found: 365.1052.

Data analysis of product **3g**



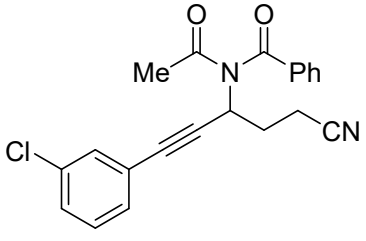
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 22.0 mg, 32% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 2.2 Hz, 1H), 7.27 – 7.15 (m, 3H), 5.32 (t, *J* = 7.8 Hz, 1H), 2.12 (ddt, *J* = 36.9, 13.9, 7.1 Hz, 2H), 2.04 (s, 3H), 1.03 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.0, 171.6, 135.9, 134.0, 133.2, 131.7, 129.9, 129.4, 129.1, 129.0, 128.6, 124.4, 88.1, 83.0, 50.7, 28.0, 26.5, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{19}ClNO_2$: 340.1099, found: 340.1099.

Data analysis of product **4g**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in

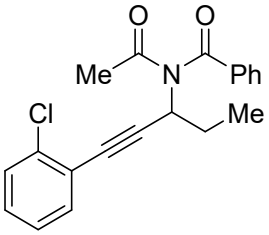
hexanes. Colorless liquid, 16.4 mg, 23% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 9.5 Hz, 2H), 7.20 (d, *J* = 6.3 Hz, 2H), 5.55 (t, *J* = 6.7 Hz, 1H), 2.62 – 2.49 (m, 3H), 2.44 (dt, *J* = 12.1, 5.5 Hz, 1H), 2.01 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.7, 171.2, 135.4, 134.2, 133.8, 131.7, 130.0, 129.5, 129.25, 129.24, 129.1, 123.6, 118.5, 85.5, 84.5, 47.8, 30.3, 26.5, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{18}ClN_2O_2$: 365.1052, found: 365.1052.

Data analysis of product **3h**



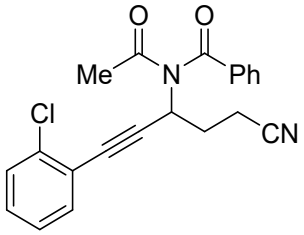
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 25.8 mg, 38% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.87 – 7.78 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.39 – 7.31 (m, 2H), 7.20 (td, *J* = 7.7, 1.8 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 5.34 (t, *J* = 7.9 Hz, 1H), 2.16 (ddd, *J* = 46.2, 13.7, 7.1 Hz, 2H), 2.08 (s, 2H), 1.06 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.1, 171.6, 136.0, 135.9, 133.5, 133.1, 129.3, 129.2, 129.1, 129.0, 126.3, 122.7, 92.1, 81.1, 51.1, 28.1, 26.5, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{19}ClNO_2$: 340.1099, found: 340.1099.

Data analysis of product **4h**



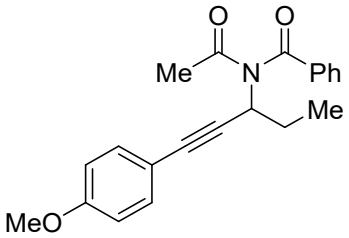
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 18.0 mg, 25% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.83 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.35 (dd, *J* = 7.8, 5.7 Hz, 2H), 7.20 (dt, *J* = 41.9, 7.6 Hz, 2H), 5.58 (t, *J* = 7.0 Hz, 1H), 2.67 – 2.54 (m, 3H), 2.49 – 2.41 (m, 1H), 2.03 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.8, 171.2, 136.0, 135.3, 133.7, 133.5, 129.8, 129.3, 129.24, 129.17, 126.4, 121.9, 118.6, 89.4, 82.7, 48.1, 30.3, 26.4, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{18}ClN_2O_2$: 365.1052, found: 365.1052.

Data analysis of product **3i**



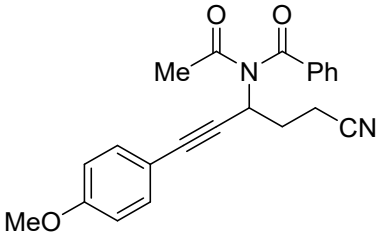
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 21.2 mg, 32% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.93 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 7.4 Hz, 2H), 7.61 (q, *J* = 7.1 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 5.35 (t, *J* = 7.7 Hz, 1H), 3.90 (s, 3H), 2.17 (dd, *J* = 14.4, 6.8 Hz, 1H), 2.10 (dt, *J* = 13.5, 7.3 Hz, 1H), 2.05 (s, 3H), 1.05 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.0, 171.6, 166.5, 135.9, 133.3, 131.7, 129.3, 129.1, 129.0, 127.4, 89.9, 83.6, 52.2, 50.7, 28.0, 26.6, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{22}NO_3$: 336.1594, found: 336.1594.

Data analysis of product **4i**



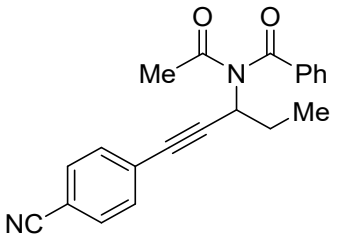
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 17.3 mg, 24% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.93 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 5.58 (t, *J* = 7.0 Hz, 1H), 3.90 (s, 3H), 2.61 – 2.52 (m, 3H), 2.50 – 2.43 (m, 1H), 2.01 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 172.7, 170.2, 165.4, 134.3, 132.8, 130.8, 129.1, 128.4, 128.2, 125.5, 117.5, 86.2, 84.1, 51.2, 46.9, 29.2, 25.5, 13.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_3$: 361.1547, found: 361.1547.

Data analysis of product **3j**



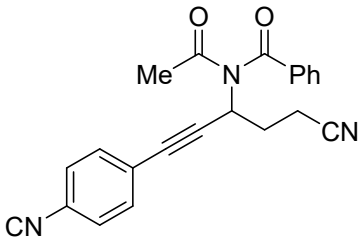
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 20.3 mg, 31% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.78 (d, *J* = 7.3 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.50 (t, *J* = 7.7 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 5.36 (t, *J* = 7.7 Hz, 1H), 2.18 (dt, *J* = 15.4, 7.7 Hz, 1H), 2.09 (dt, *J* = 13.5, 7.3 Hz, 1H), 2.03 (s, 3H), 1.04 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.8, 171.6, 135.9, 133.3, 132.3, 131.9, 129.09, 129.08, 127.7, 118.4, 111.7, 91.5, 82.7, 50.6, 27.9, 26.7, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{19}N_2O_2$: 331.1441, found: 331.1441.

Data analysis of product **4j**



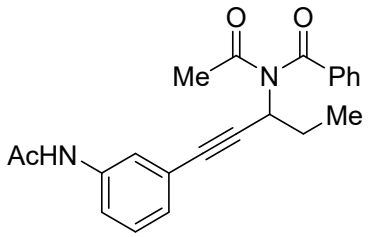
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 11.3 mg, 16% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.78 (d, *J* = 7.7 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.58 – 7.50 (m, 4H), 7.42 (d, *J* = 8.1 Hz, 2H), 5.59 (t, *J* = 6.6 Hz, 1H), 2.56 (s, 3H), 2.48 – 2.42 (m, 1H), 2.00 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.6, 171.3, 135.3, 133.9, 132.4, 132.0, 129.3, 129.2, 126.8, 118.4, 118.2, 112.3, 88.7, 84.1, 47.8, 30.1, 26.6, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{18}N_3O_2$: 356.1394, found: 356.1394.

Data analysis of product **3k**



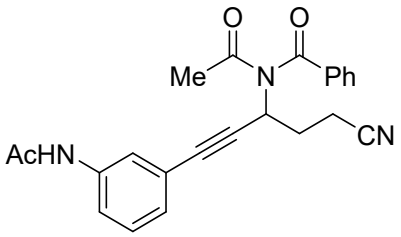
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 20.3 mg, 31% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.78 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 3H), 7.43 (s, 1H), 7.27 (s, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 5.29 (t, *J* = 7.7 Hz, 1H), 2.24 – 2.04 (m, 8H), 1.02 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.1, 171.8, 168.3, 137.8, 135.9, 133.2, 129.1, 129.0, 128.9, 127.7, 123.4, 122.9, 119.9, 87.0, 83.9, 50.9, 28.1, 26.5, 24.6, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{23}N_2O_3$: 363.1703, found: 363.1703.

Data analysis of product **4k**



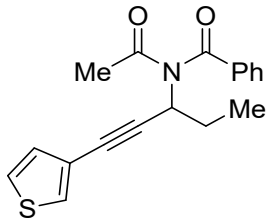
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 20.3 mg, 31% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.80 (d, *J* = 7.7 Hz, 3H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.55 – 7.48 (m, 5H), 7.46 (s, 1H), 7.26 (s, 2H), 7.21 (t, *J* = 7.9 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 5.53 (d, *J* = 7.1 Hz, 1H), 2.62 – 2.50 (m, 5H), 2.42 (td, *J* = 12.3, 11.2, 5.5 Hz, 2H), 2.15 (s, 3H), 2.01 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.8, 171.3, 168.3, 137.9, 135.4, 133.7, 129.3, 129.2, 129.0, 127.7, 122.9, 122.6, 120.4, 118.6, 85.5, 84.4, 48.0, 30.3, 26.5, 24.6, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{22}N_3O_3$: 388.1656, found: 388.1656.

Data analysis of product **3l**



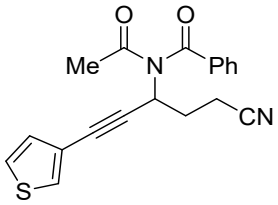
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 15.7 mg, 25% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 3.0 Hz, 1H), 7.20 (t, *J* = 4.0 Hz, 1H), 7.01 (d, *J* = 4.9 Hz, 1H), 5.31 (t, *J* = 7.8 Hz, 1H), 2.20 – 2.07 (m, 2H), 2.05 (s, 3H), 1.02 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.1, 171.6, 136.0, 133.1, 130.0, 129.1, 129.0, 128.9, 125.1, 121.7, 86.3, 79.4, 50.8, 28.2, 26.5, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{18}NO_2S$: 312.1053, found: 312.1053.

Data analysis of product **4l**



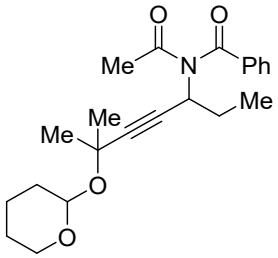
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 16.2 mg, 24% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.80 (d, *J* = 7.7 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 3.1 Hz, 1H), 7.21 (dd, *J* = 5.1, 3.0 Hz, 1H), 6.99 (d, *J* = 5.0 Hz, 1H), 5.53 (t, *J* = 6.8 Hz, 1H), 2.54 (ddd, *J* = 15.6, 8.4, 4.2 Hz, 3H), 2.42 (dt, *J* = 12.5, 5.5 Hz, 1H), 2.00 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.8, 171.2, 135.5, 133.7, 129.9, 129.7, 129.3, 129.2, 125.4, 120.9, 118.6, 83.8, 81.1, 48.0, 30.4, 26.4, 14.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{17}N_2O_2S$: 337.1005, found: 337.1005.

Data analysis of product **3m**



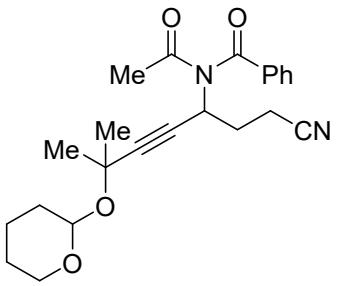
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 10.2 mg, 14% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *trans* and *cis*) δ 7.76 (dd, *J* = 7.1, 3.9 Hz, 2H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.48 (t, *J* = 6.5 Hz, 2H), 5.16 (t, *J* = 6.8 Hz, 1H), 4.95 – 4.80 (m, 1H), 3.92 – 3.81 (m, 1H), 3.47 – 3.31 (m, 1H), 2.09 – 2.03 (m, 1H), 1.98 (s, 4H), 1.50 – 1.31 (m, 12H), 0.98 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *trans* and *cis*) δ 174.02, 174.01, 171.18, 171.16, 136.10, 136.07, 133.2, 129.2, 129.0, 96.44, 96.41, 87.0, 86.9, 81.3, 81.2, 71.1, 63.62, 63.56, 50.1, 32.0, 30.51, 30.48, 29.7, 29.8, 28.39, 28.37, 26.3, 25.3, 20.72, 20.68, 11.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{30}NO_4$: 372.2170, found: 372.2170.

Data analysis of product **4m**



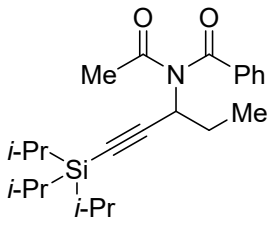
Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 19.9 mg, 25% yield.

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture of *trans* and *cis*) δ 8.09 – 8.04 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 5.77 (q, *J* = 3.9, 2.8 Hz, 1H), 4.96 (q, *J* = 4.4 Hz, 1H), 3.93 (tt, *J* = 11.4, 4.4 Hz, 1H), 3.47 (ddt, *J* = 16.4, 10.9, 5.2 Hz, 1H), 2.65 (t, *J* = 7.4 Hz, 2H), 2.31 – 2.22 (m, 2H), 1.85 – 1.79 (m, 1H), 1.74 – 1.60 (m, 2H), 1.57 – 1.43 (m, 12H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture of *trans* and *cis*) δ 165.1, 133.5, 129.9, 129.3, 128.5, 118.8, 96.2, 90.17, 90.16, 79.0, 78.9, 70.7, 63.44, 63.41, 62.8, 62.7, 32.0, 30.73, 30.71, 30.00, 29.99, 29.81, 29.77, 25.3, 20.4, 13.0.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{29}N_2O_4$: 397.2122, found: 397.2122.

Data analysis of product **3n**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 26.7 mg, 35% yield.

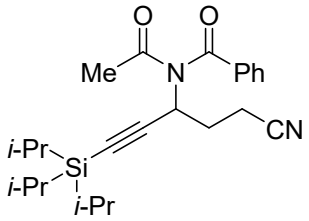
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.55 (dt, *J* = 28.0, 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 5.16 (t, *J* = 7.8 Hz, 1H), 2.11 (dt,

J = 13.0, 7.7 Hz, 1H), 2.00 (s, 4H), 0.97 (d, *J* = 4.6 Hz, 24H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.0, 171.0, 136.0, 133.1, 129.3, 128.9, 104.5, 85.4, 51.0, 28.6, 26.2, 18.4, 11.14, 11.06.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{36}NO_2Si$: 386.2510, found: 386.2510.

Data analysis of product **4n**



Purified by flash column chromatography on silica gel: 5 to 50% EtOAc in hexanes. Colorless liquid, 26.7 mg, 35% yield.

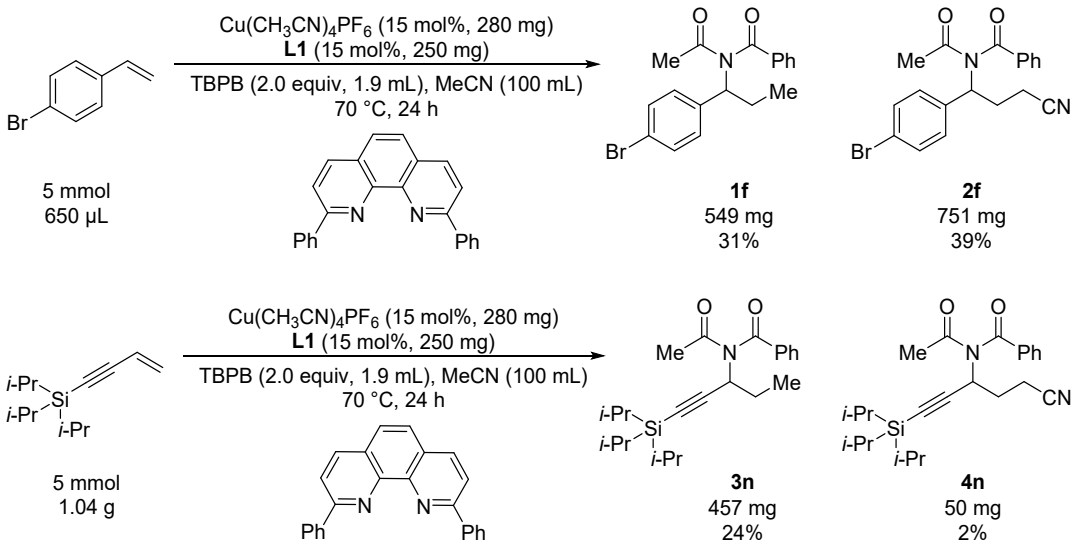
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.80 (d, *J* = 7.5 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 5.40 (t, *J* = 7.3 Hz, 1H), 2.59 – 2.37 (m, 4H), 1.96 (s, 3H), 0.95 (s, 21H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.7, 170.6, 135.4, 133.7, 129.5, 129.1, 118.7, 101.8, 87.8, 48.0, 30.7, 26.1, 18.4, 14.6, 10.9.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{35}N_2O_2Si$: 411.2463, found: 411.2463.

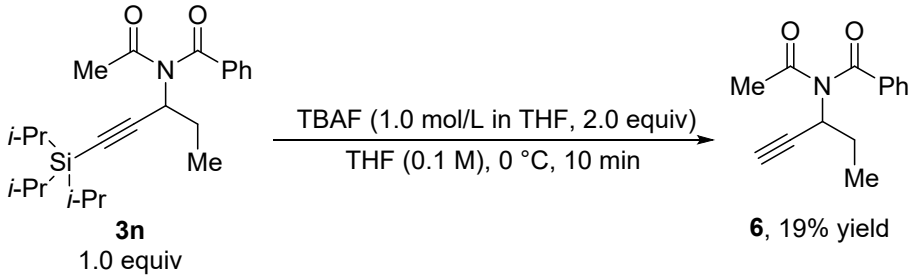
IV. Synthetic application

4.1 Large-scale synthesis (5.0 mmol scale)



In a nitrogen-filled glovebox, and oven-dried 250 mL round bottom flask vial with a magnetic stir bar, were charged the $Cu(CH_3CN)_4PF_6$ (280 mg, 0.75 mmol, 0.15 equiv), **L1** (250 mg, 0.75 mmol, 0.15 equiv), 4-bromostyrene (or 3-buten-1-yn-1-yltris(1-methylethyl)silane) (5.0 mmol, 1.0 equiv). Then 70 mL MeCN was added. To the solution were added the peroxide TBPB (1.9 mL, 10.0 mmol, 2.0 equiv) sequentially. Then, the reactions were stirred at 70 °C for 24 hours. The reaction mixture was concentrated. And the residue was purified by flash chromatography to provide separately the desired product **1f** (549 mg, 31% yield), **2f** (751 mg, 39% yield), **3n** (457 mg, 24% yield) and **4n** (50 mg, 2% yield).

4.2 Desilication reaction



Dissolved the **3n** (1.0 mmol, 1.0 equiv) in 10 mL THF and stirred continuously at 0 °C. Then slowly dripped TBAF (2.0 mL, 2.0 equiv, 1.0 M in THF). Ten minutes later, TLC showed that the materials had been consumed, and the reaction was quenched with ice water. Use EA extraction reaction, then concentrate the organic phase and residue was purified by flash

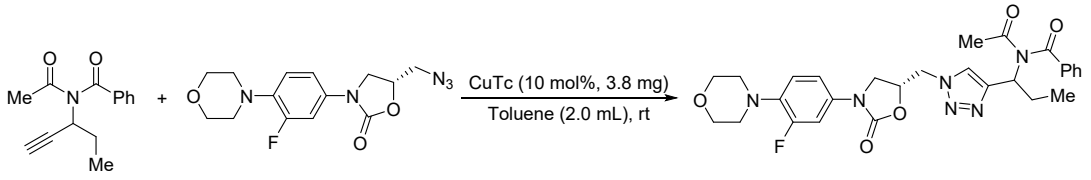
chromatography to provide separately the desired product **6** (55 mg, 19% yield).

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.75 (d, *J* = 7.7 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 5.14 – 5.00 (m, 1H), 2.34 (d, *J* = 2.0 Hz, 1H), 2.10 (dd, *J* = 14.3, 6.8 Hz, 1H), 2.05 – 2.00 (m, 4H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.9, 171.8, 135.9, 133.2, 129.0, 81.2, 72.2, 50.3, 27.7, 26.7, 11.1.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{16}NO_2$: 230.1176., found: 230.1181.

4.3 Cu-catalyzed Click reaction



6
1.0 equiv
0.2 mmol
45.8 mg

7
1.1 equiv

8
105.3 mg
96% yield

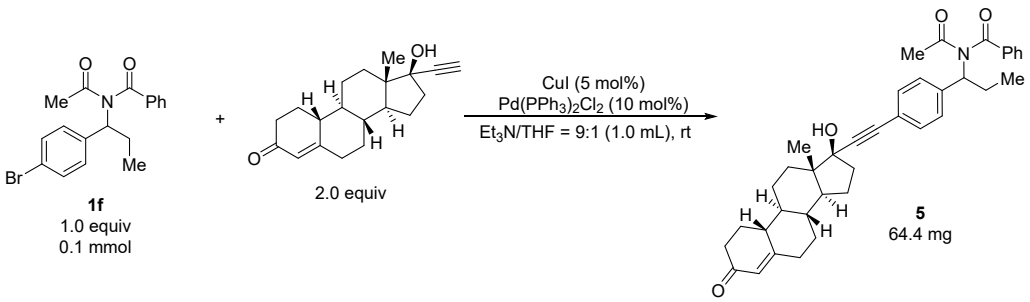
In a nitrogen-filled glovebox, and oven-dried 4 mL vial with a magnetic stir bar, were charged the CuTc (3.8 mg, 0.02 mmol), azide **7** (70.6 mg, 0.22 mmol, 1.1 equiv), **6** (45.8 mg, 0.2 mmol, 1.0 equiv). Then 2.0 mL toluene was added. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at rt for 12 hours. After the reaction is completed the mixture was concentrated. And the residue was purified by chromatography to provide the product **8** (105.3 mg, 96% yield).

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C, mixture *cis* and *trans*) δ 7.83 (d, *J* = 16.7 Hz, 1H), 7.72 (dd, *J* = 28.2, 7.5 Hz, 2H), 7.53 (q, *J* = 7.9 Hz, 1H), 7.42 (dt, *J* = 14.3, 7.6 Hz, 2H), 7.31 (dd, *J* = 21.0, 14.4 Hz, 1H), 6.97 (dd, *J* = 20.1, 8.6 Hz, 1H), 6.87 (t, *J* = 8.9 Hz, 1H), 5.54 (dt, *J* = 15.1, 8.0 Hz, 1H), 5.10 – 4.94 (m, 1H), 4.69 (qd, *J* = 16.7, 14.6, 4.5 Hz, 2H), 4.10 (q, *J* = 9.1, 8.1 Hz, 1H), 3.92 – 3.73 (m, 5H), 3.10 – 2.91 (m, 4H), 2.34 (dq, *J* = 14.0, 8.4, 6.6 Hz, 1H), 2.14 (dd, *J* = 6.7, 4.0 Hz, 1H), 1.98 (d, *J* = 18.8 Hz, 3H), 0.96 (dt, *J* = 11.5, 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C, mixture *cis* and *trans*) δ 174.52, 174.46, 173.2, 156.2, 154.5, 153.5, 153.4, 148.2, 148.1, 136.7, 136.6, 136.0, 136.0, 132.8, 132.7, 132.53, 132.46, 132.44, 132.37, 129.0, 128.93, 128.90, 128.88, 124.3, 124.2, 118.8, 114.31, 114.29, 114.27, 114.2, 107.9, 107.8, 107.7, 107.6, 70.5, 70.2, 66.9, 55.8, 55.7, 52.3, 52.1, 50.93, 50.92, 47.6, 47.4, 27.01, 26.99, 25.7, 25.6, 14.2, 11.3, 11.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{32}FN_6O_5$: 551.2413., found: 551.2413.

4.4 Sonogashira coupling reaction



In a nitrogen-filled glovebox, and oven-dried 4 mL vial with a magnetic stir bar, were charged the copper catalyst CuI (1.9 mg, 0.005 mmol), palladium catalyst $Pd(PPh_3)_2Cl_2$ (7.0 mg, 0.01 mmol), Norethisterone (59.6 mg, 0.2 mmol, 2.0 equiv), **1f** (35.9 mg, 0.1 mmol, 1.0 equiv). Then 900 μL triethylamine and 100 μL THF was added. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at rt for 12 hours. After the reaction is completed the mixture was concentrated. And the residue was purified by chromatography to provide the product **5** (64.4 mg, 55% yield).

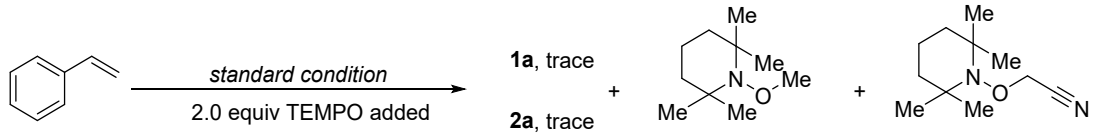
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.58 (d, *J* = 7.4 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.44 – 7.39 (m, 4H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.82 (s, 1H), 5.59 (t, *J* = 7.8 Hz, 1H), 2.50 – 2.18 (m, 10H), 2.11 – 2.03 (m, 2H), 1.91 (d, *J* = 12.9 Hz, 1H), 1.85 – 1.65 (m, 9H), 1.60 – 1.52 (m, 2H), 1.35 (ddd, *J* = 32.0, 16.1, 5.2 Hz, 3H), 1.07 (q, *J* = 11.8, 11.4 Hz, 1H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.87 (dt, *J* = 10.1, 5.3 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 200.0, 174.2, 173.2, 166.7, 140.2, 136.7, 133.0, 131.5, 129.0, 128.9, 128.3, 124.6, 121.9, 92.7, 85.8, 80.1, 61.8, 49.5, 49.2, 47.4, 42.6, 41.1, 39.0, 36.5, 35.5, 32.8, 30.7, 27.6, 26.5, 26.3, 24.9, 23.0, 12.9, 11.6.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{38}H_{44}NO_4$: 578.3265., found: 578.3265.

V. Mechanistic experiments

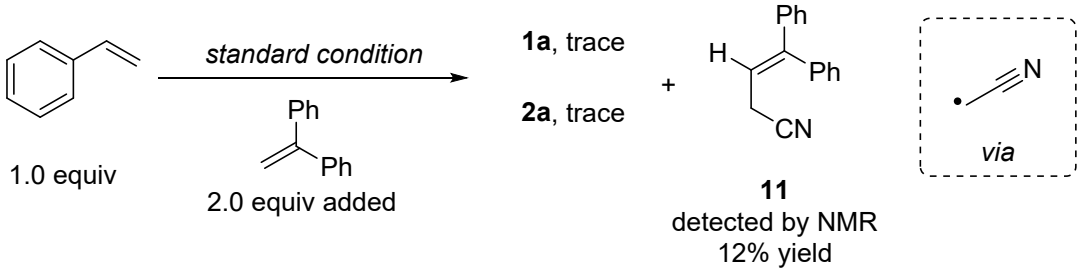
5.1 Radical trapping experiment by TEMPO



In a nitrogen-filled glovebox, and oven-dried 8 mL vial with a magnetic stir bar, were charged the copper catalyst $Cu(CH_3CN)_4PF_6$ (11.2 mg, 0.03 mmol), **L1** (10.0 mg, 0.03 mmol), alkene (23.0 μL, 0.2 mmol, 1.0 equiv) and TEMPO (0.4 mmol, 62.4 mg, 2.0 equiv). Then 4.0 mL MeCN was added. To the solution were added the peroxide TBPB (78.0 μL, 0.4 mmol, 2.0 equiv) sequentially. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at 70 °C for 24 hours. The product **9** was detected by GC-MS. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{110}H_{22}NO_2$: 172.1696, found: 172.1696.

The product **10** was detected by GC-MS. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{11}H_{21}N_2O$: 197.1649, found: 197.1649.

5.2 Radical trapping experiment by 1,1-diphenylethylene



In a nitrogen-filled glovebox, and oven-dried 8 mL vial with a magnetic stir bar, were charged the copper catalyst $Cu(CH_3CN)_4PF_6$ (11.2 mg, 0.03 mmol), **L1** (10.0 mg, 0.03 mmol), alkene (23.0 μL, 0.2 mmol, 1.0 equiv) and 1,1-diphenylethylene (0.4 mmol, 72 mg, 2.0 equiv). Then 4.0 mL MeCN was added. To the solution were added the peroxide TBPB (78.0 μL, 0.4 mmol, 2.0 equiv) sequentially. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at 70 °C for 24 hours. The reaction mixture was concentrated. And the residue was purified by chromatography to provide the desired product **11** (12% yield).

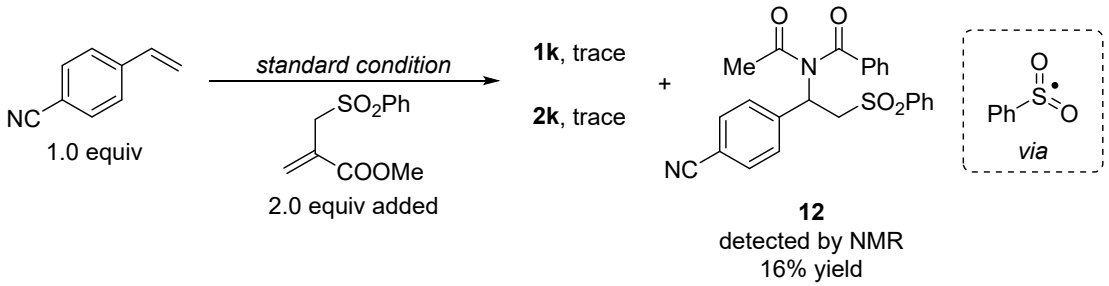
^1H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.41 (dt, J = 28.5, 7.3 Hz, 4H), 7.29 (s, 2H), 7.25 – 7.20 (m, 3H), 7.18 (d, J = 7.3 Hz, 2H), 6.04 (t, J = 7.3 Hz, 1H),

3.15 (d, *J* = 7.3 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 147.6, 140.7, 138.0, 129.4, 128.8, 128.4, 128.1, 127.4, 126.1, 118.1, 115.5, 18.4.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_4N$: 220.1121, found: 220.1121.

5.3 Radical trapping experiment by methyl 2-[(phenylsulfonyl)methyl]acrylate



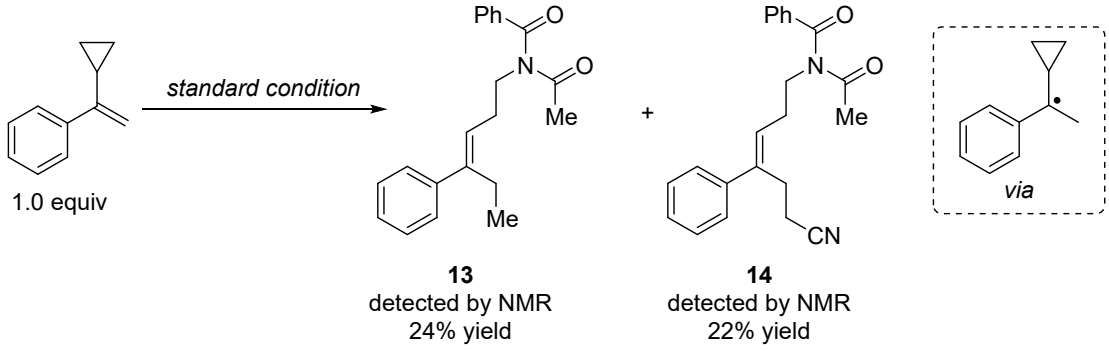
In a nitrogen-filled glovebox, and oven-dried 8 mL vial with a magnetic stir bar, were charged the copper catalyst $Cu(CH_3CN)_4PF_6$ (11.2 mg, 0.03 mmol), **L1** (10.0 mg, 0.03 mmol), alkene (23.0 μL, 0.2 mmol, 1.0 equiv) and methyl 2-[(phenylsulfonyl)methyl]acrylate (0.4 mmol, 96 mg, 2.0 equiv). Then 4.0 mL MeCN was added. To the solution were added the peroxide TBPB (78.0 μL, 0.4 mmol, 2.0 equiv) sequentially. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at 70 °C for 24 hours. The reaction mixture was concentrated. And the residue was purified by chromatography to provide the desired product **12** (16% yield).

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.91 (d, *J* = 7.6 Hz, 2H), 7.65 (dd, *J* = 15.7, 7.5 Hz, 3H), 7.59 – 7.51 (m, 7H), 7.45 (t, *J* = 7.7 Hz, 2H), 6.33 (dd, *J* = 9.7, 3.5 Hz, 1H), 4.66 (dd, *J* = 14.6, 9.8 Hz, 1H), 3.76 (dd, *J* = 14.6, 3.7 Hz, 1H), 1.82 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 173.9, 173.6, 142.7, 139.1, 136.0, 134.2, 133.3, 132.4, 129.5, 129.1, 128.90, 128.88, 128.2, 118.2, 112.3, 56.6, 53.5, 28.2.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{21}N_2O_4S$: 433.1217, found: 433.1217.

5.4 Radical ring-opening experiment



In a nitrogen-filled glovebox, and oven-dried 8 mL vial with a magnetic

stir bar, were charged the copper catalyst $Cu(CH_3CN)_4PF_6$ (11.2 mg, 0.03 mmol), **L1** (10.0 mg, 0.03 mmol), α-cyclopropylstyrene (28.8 mg, 0.2 mmol, 1.0 equiv). Then 4.0 mL MeCN was added. To the solution were added the peroxide TBPB (78.0 μL, 0.4 mmol, 2.0 equiv) sequentially. Then the vial was closed with a PTFE septum cap, and taken out of the glovebox. Then, the reaction was stirred at 70 °C for 24 hours. The reaction mixture was concentrated. And the residue was purified by chromatography to provide the desired product **13**.

13 (24% yield, reported in the form of a mixture of *Z*/*E* isomers).

^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.57 – 7.39 (m, 5H), 7.26 – 6.97 (m, 5H), 5.46 (t, *J* = 7.6 Hz, 0.73H, major), 5.28 (t, *J* = 7.4 Hz, 0.23H, minor), 3.87 (t, *J* = 7.2 Hz, 1.49H, major), 3.73 (t, *J* = 7.1 Hz, 0.46H, minor), 2.50 (dd, *J* = 14.6, 7.4 Hz, 1.50H, major), 2.40 (q, *J* = 7.5 Hz, 1.50H, major), 2.27 (dd, *J* = 14.4, 7.3 Hz, 0.52H, minor), 2.21 – 2.17 (m, 2.72 H), 2.12 (s, 0.74 H, minor), 0.91 – 0.86 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 173.4, 173.2, 145.9, 144.8, 142.5, 140.8, 135.8, 135.7, 132.3, 132.1, 128.8, 128.7, 128.4, 128.3, 128.2, 128.12, 128.08, 126.8, 126.6, 126.3, 123.3, 121.2, 46.35, 46.30, 32.1, 29.7, 28.6, 28.1, 26.3, 26.0, 22.8, 13.5, 12.7.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{21}H_{24}NO_2$: 322.1802, found: 322.1802.

14 (22% yield, reported in the form of a mixture of *Z*/*E* isomers).

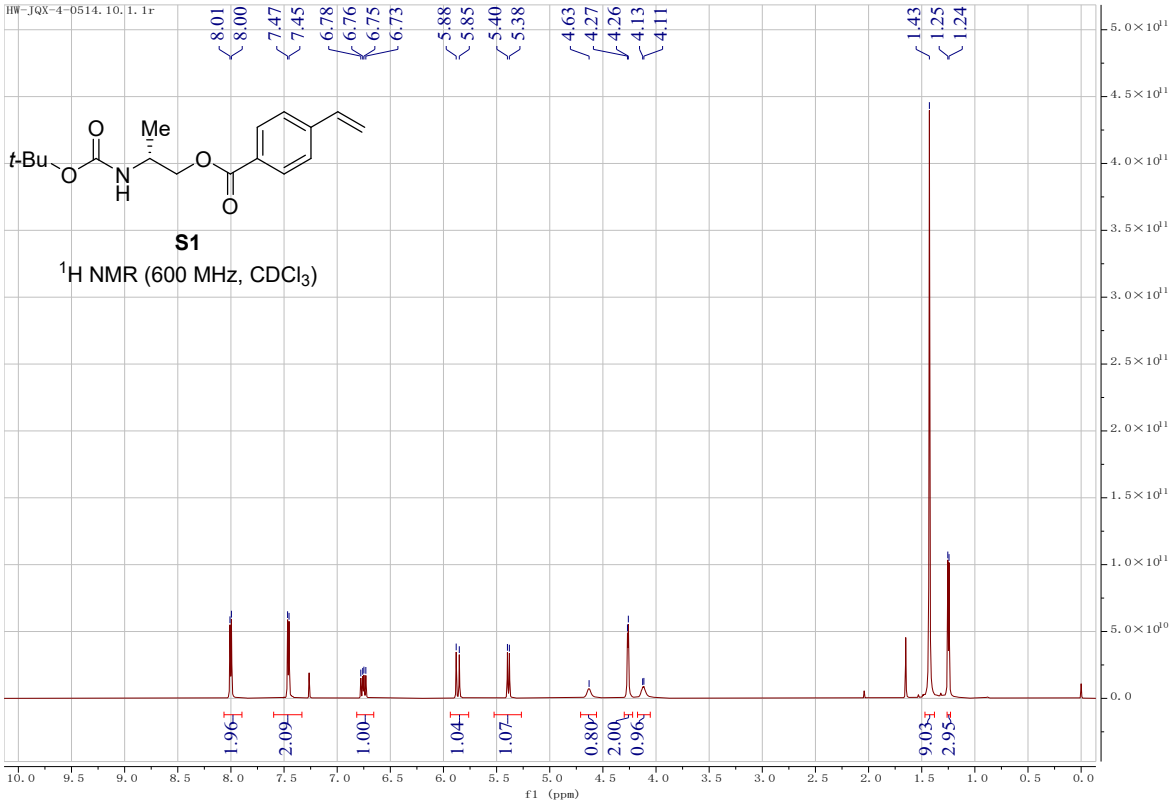
^{1}H NMR (600 MHz, $CDCl_3$, sample at 25 °C) δ 7.58 – 7.42 (m, 5H), 7.33 – 7.03 (m, 5H), 5.66 (t, *J* = 7.7 Hz, 0.71H, major), 5.51 (t, *J* = 7.4 Hz, 0.23H, minor), 3.90 (t, *J* = 7.2 Hz, 1.48H, major), 3.78 (t, *J* = 7.1 Hz, 0.47H, minor), 2.79 (t, *J* = 7.4 Hz, 1.45H, major), 2.62 (t, *J* = 7.2 Hz, 0.49H, minor), 2.57 (dd, *J* = 14.7 Hz, 7.5 Hz, 1.50H, major), 2.29 – 2.24 (m, 2.36H), 2.18 (s, 2.11H, major), 2.11 (s, 0.70 H, minor).

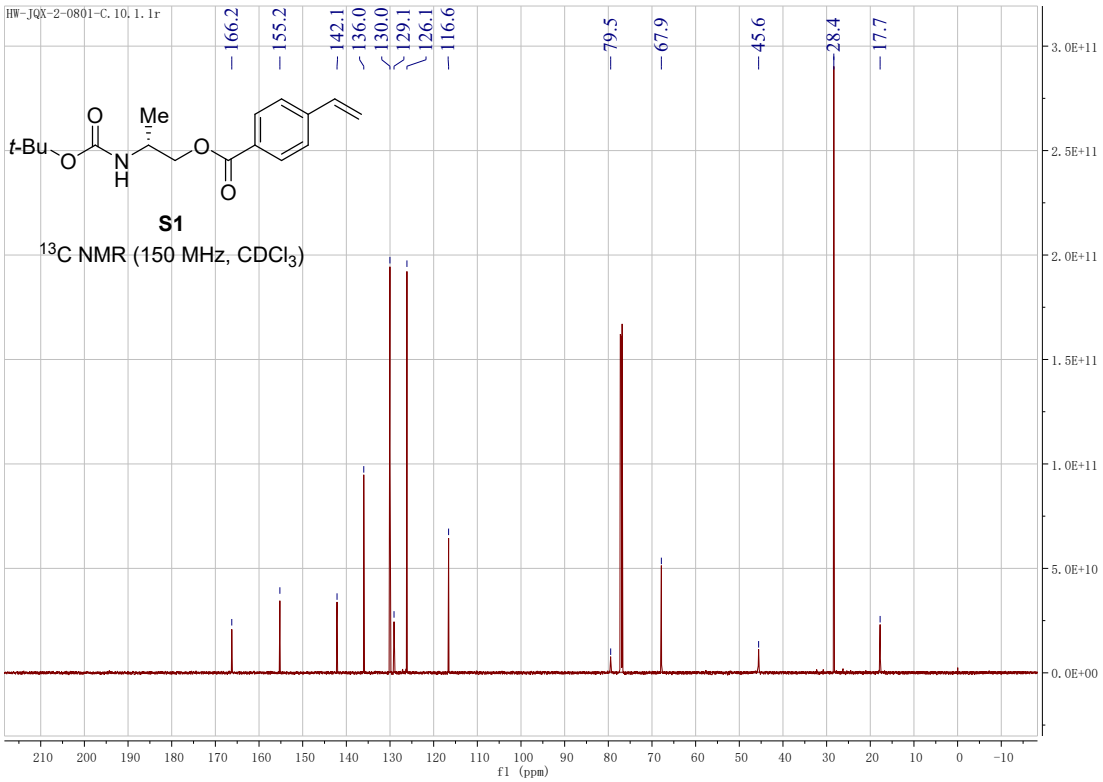
^{13}C NMR (151 MHz, $CDCl_3$, sample at 25 °C) δ 174.4, 174.3, 173.4, 173.1, 140.6, 140.0, 139.5, 138.1, 135.6, 132.5, 132.3, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 127.7, 127.6, 127.4, 126.4, 126.0, 119.0, 118.9, 46.0, 45.9, 35.0, 28.7, 28.3, 26.3, 26.0, 25.5, 16.31, 16.26.

HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{23}N_2O_2$: 347.1754, found: 347.1754.

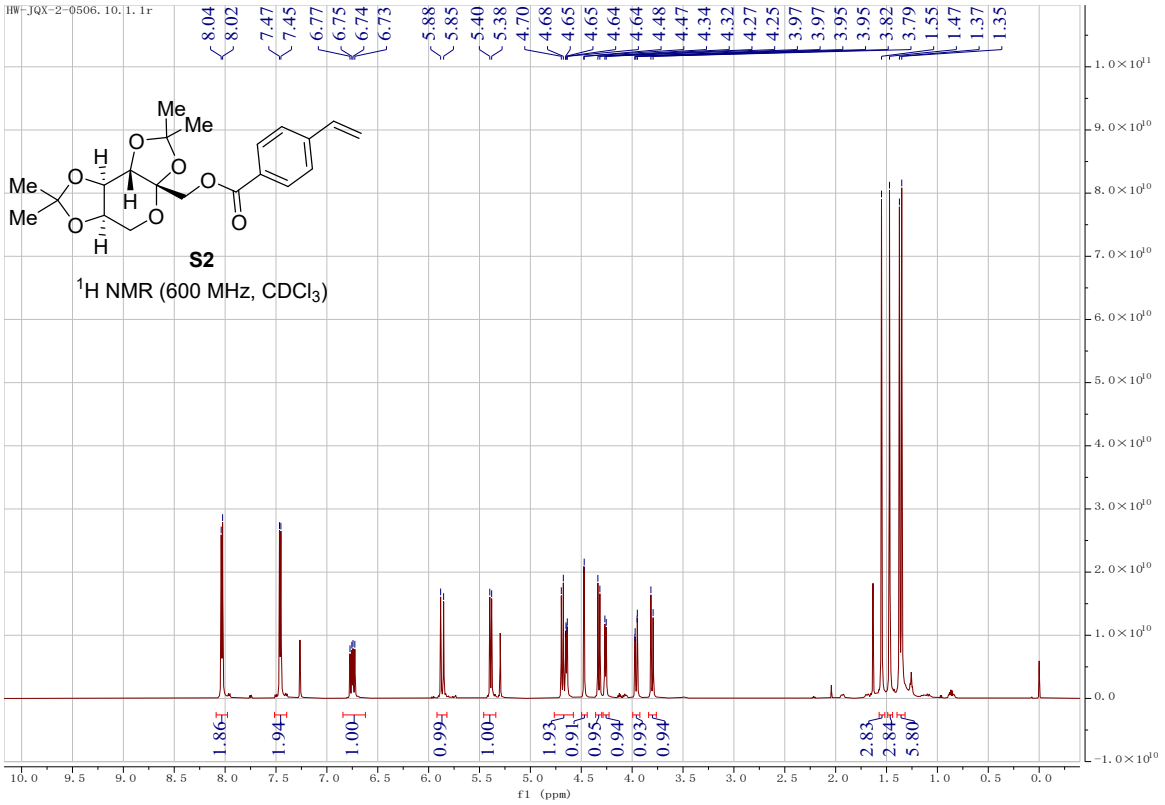
VI. NMR Spectra

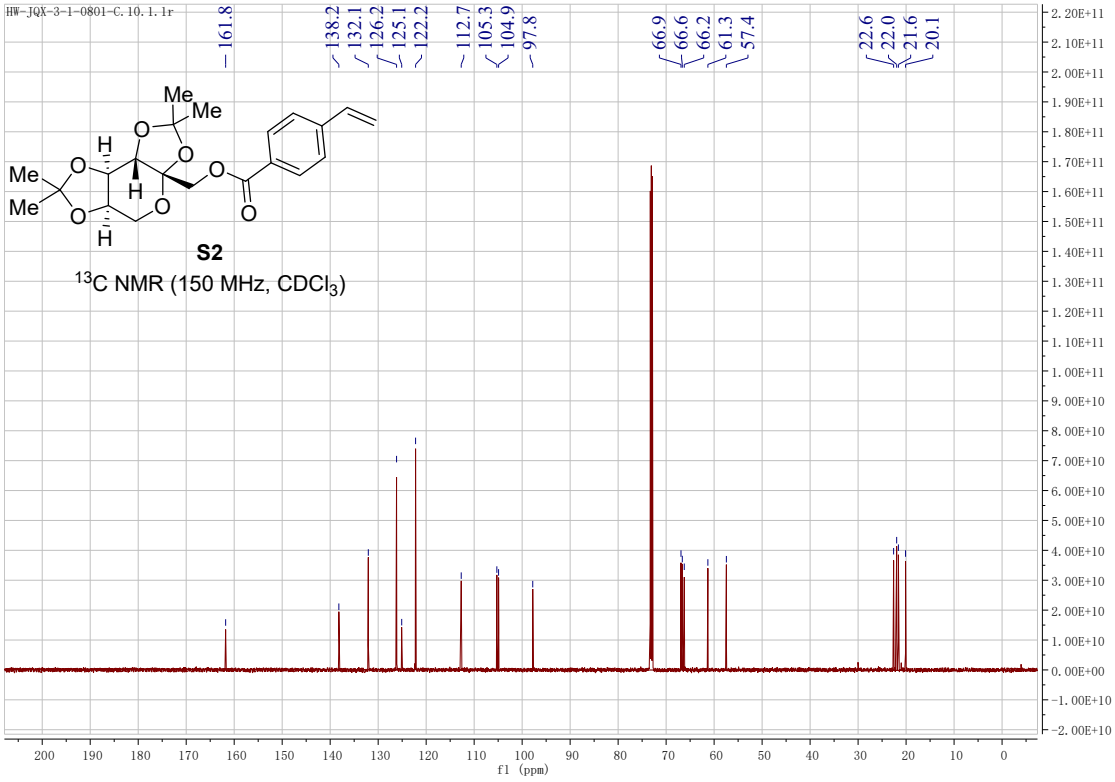
^{1}H and ^{13}C Spectrum for Compound S1 at 25 ℃



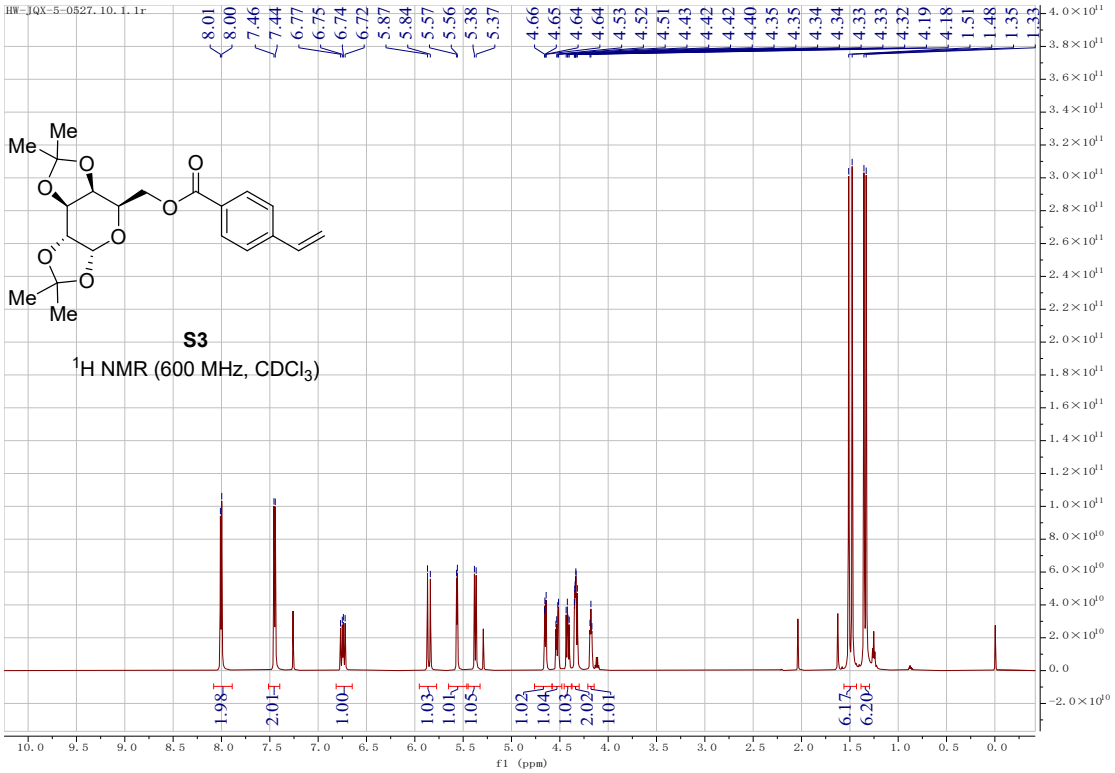


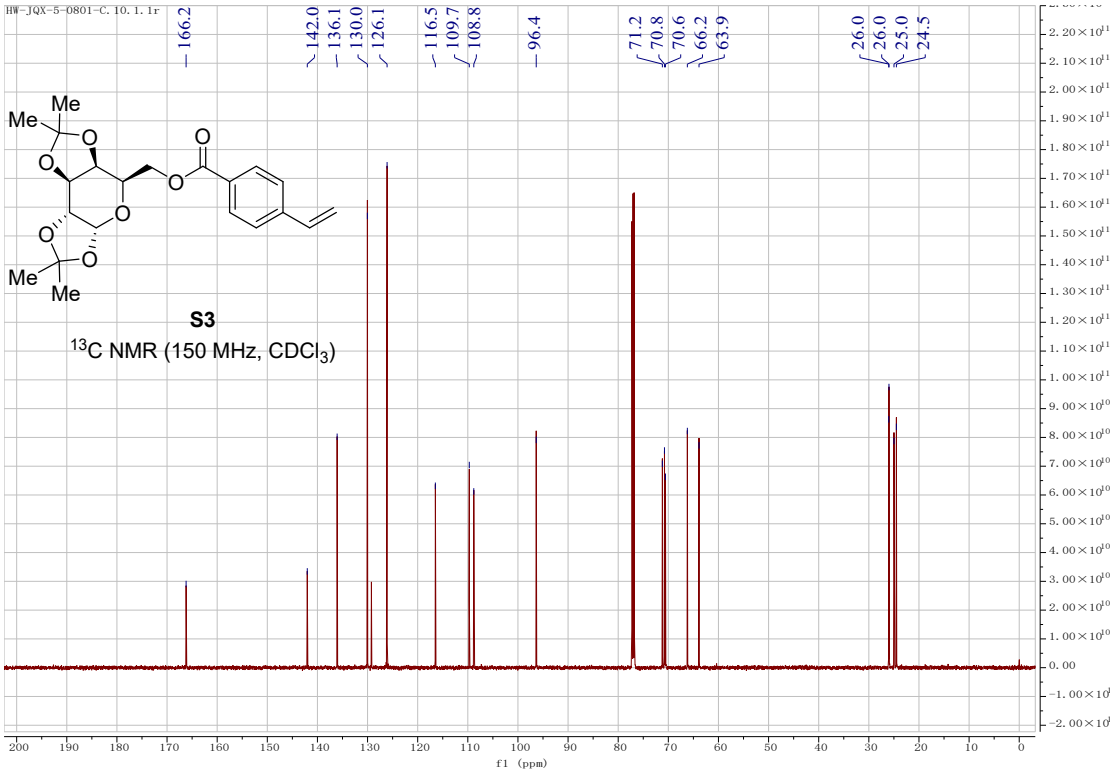
^{1}H and ^{13}C Spectrum for Compound S2 at 25 ℃



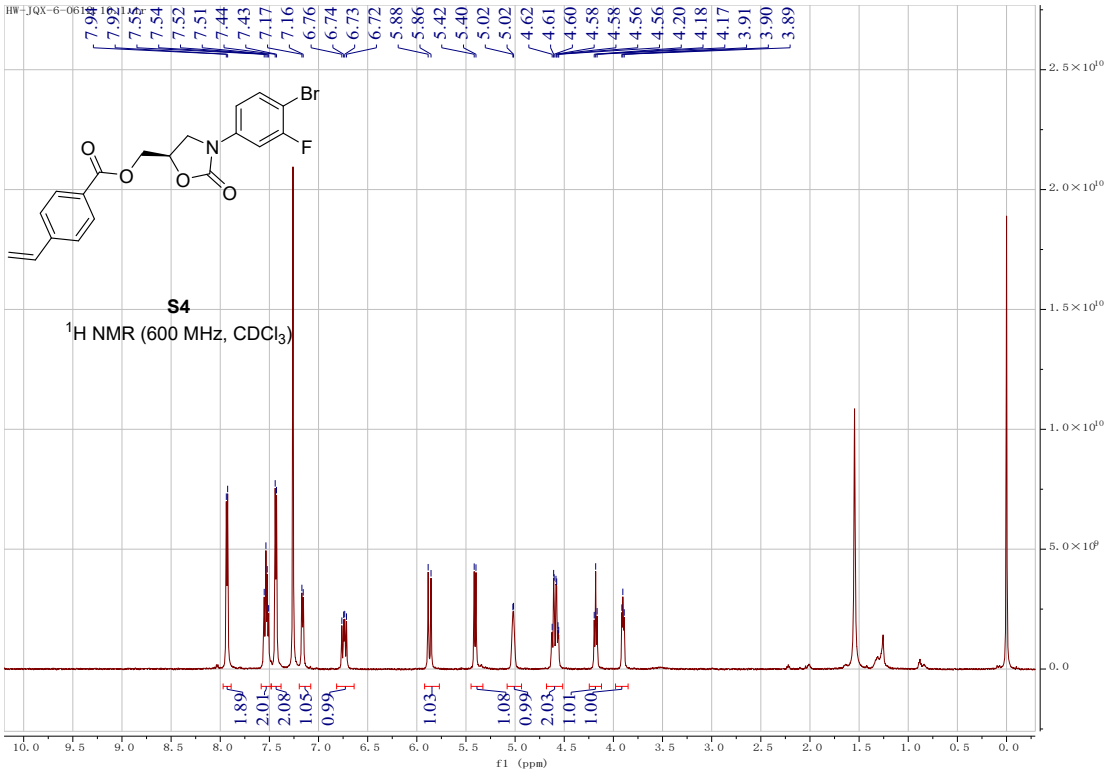


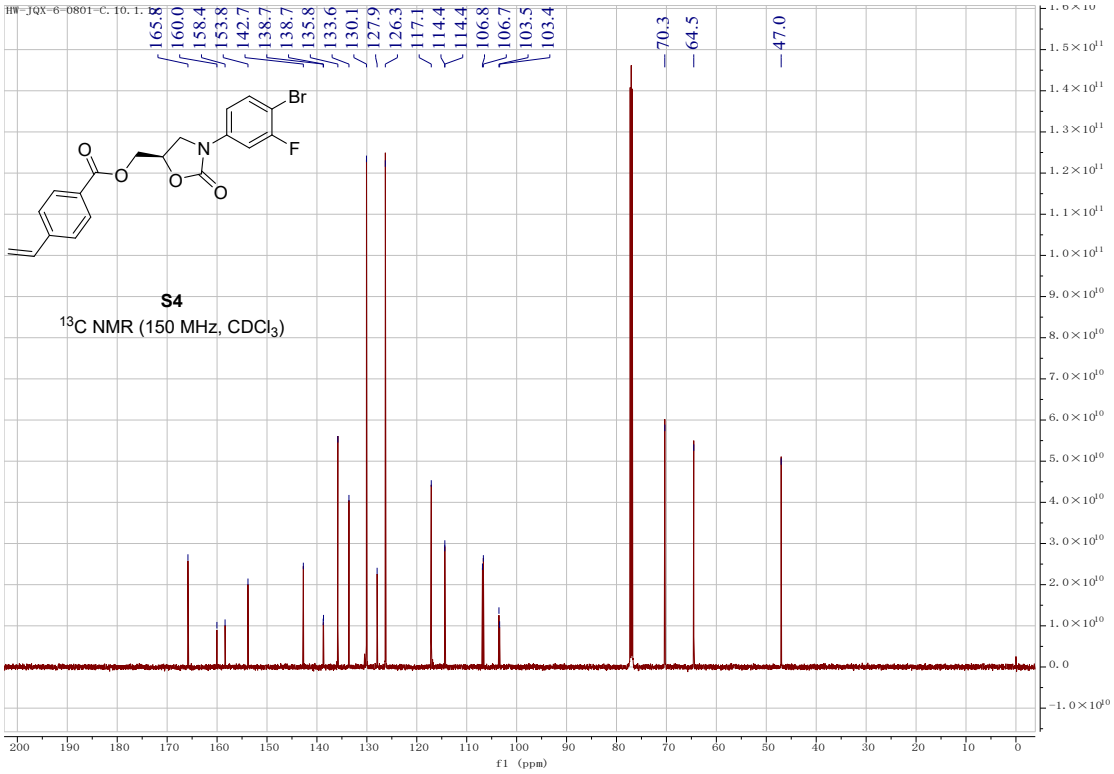
^{1}H and ^{13}C Spectrum for Compound S3 at 25 ℃



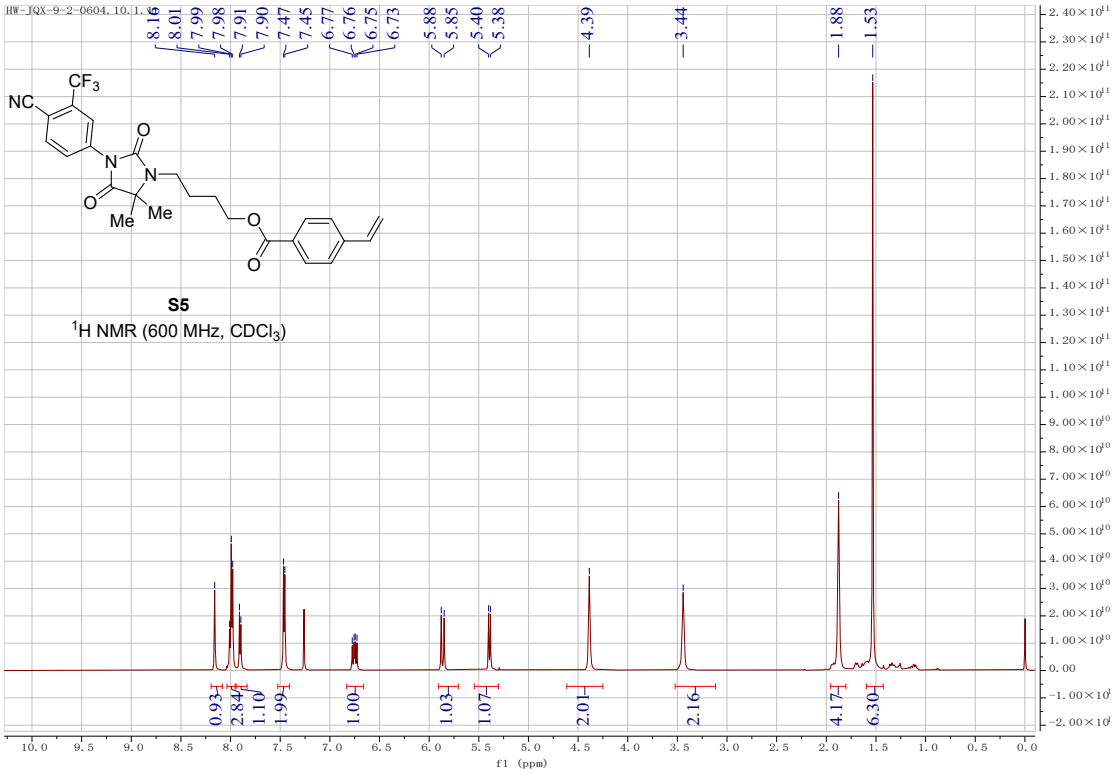


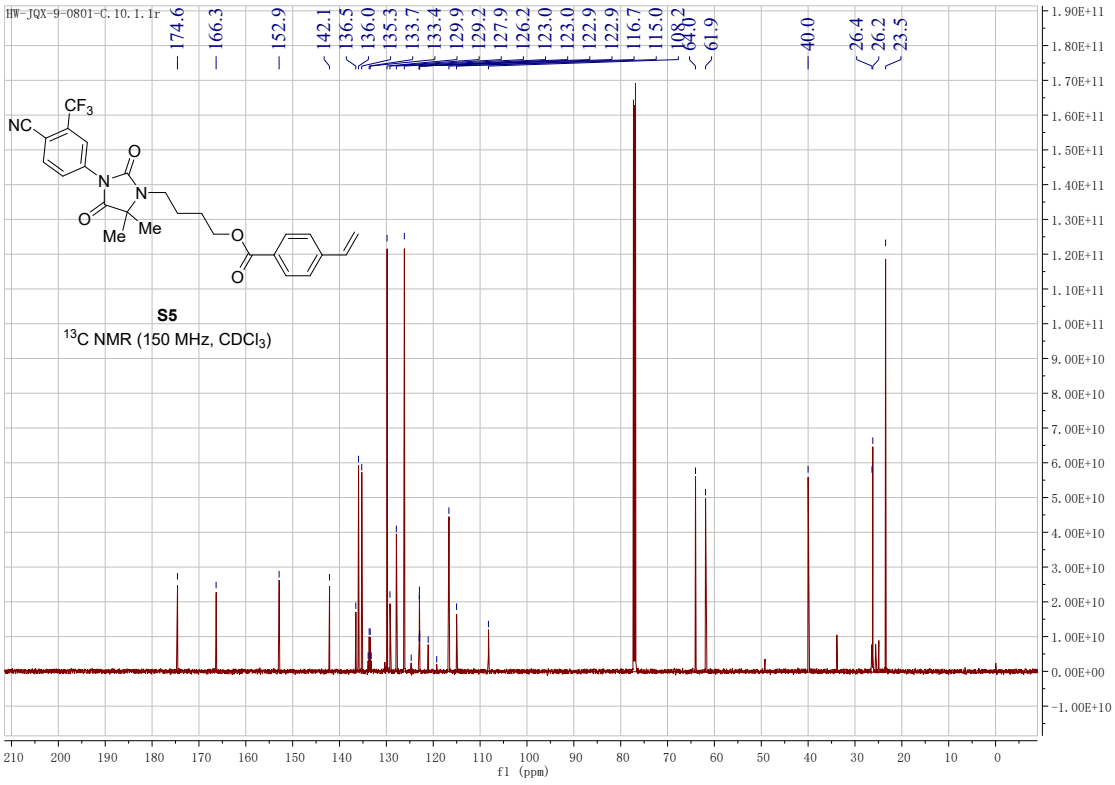
^{1}H and ^{13}C Spectrum for Compound S4 at 25 ℃



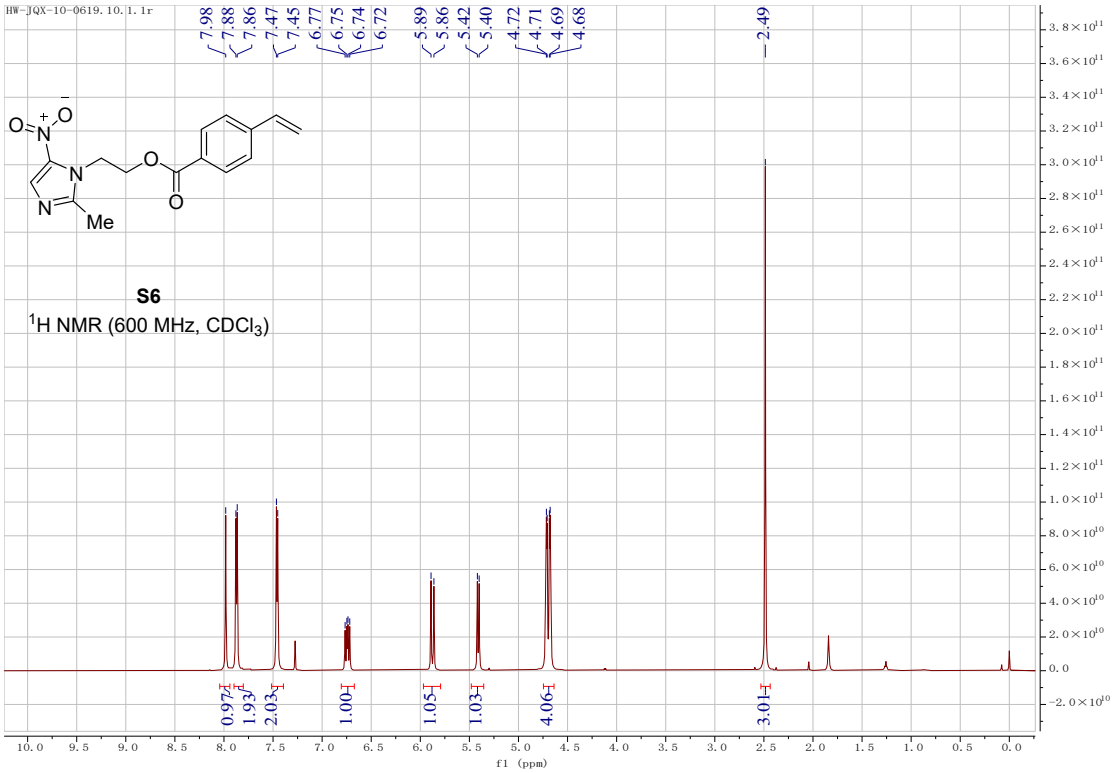


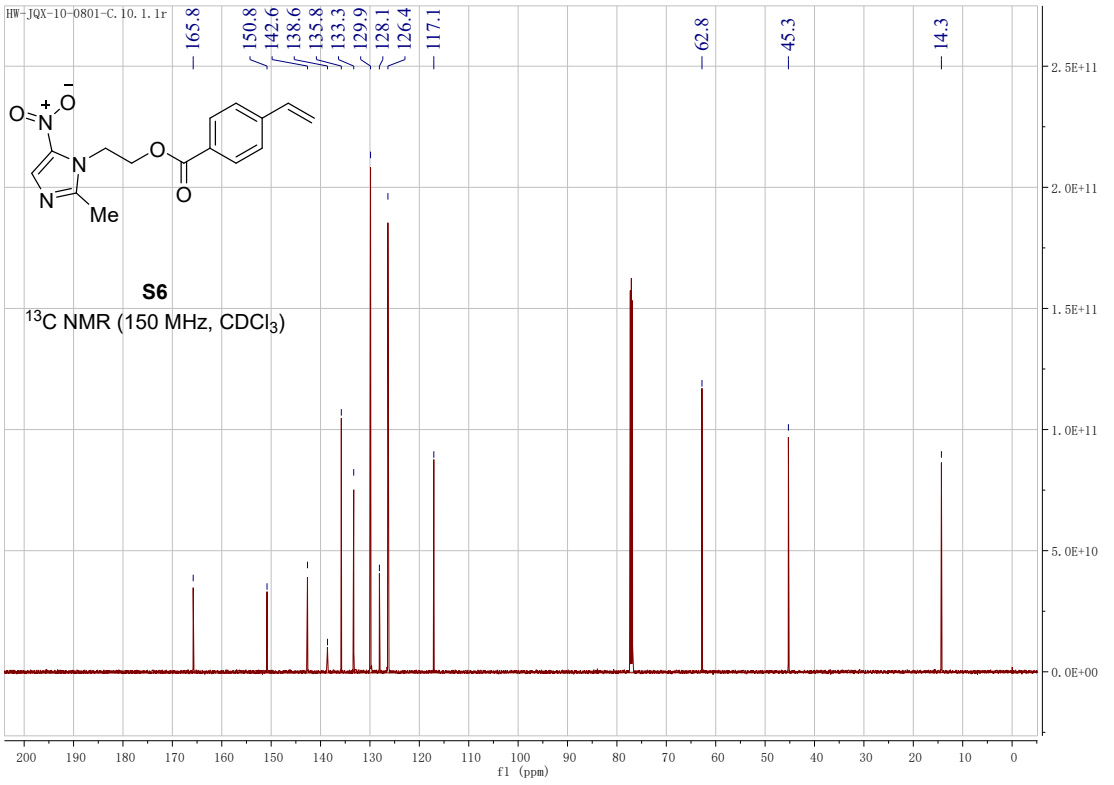
^{1}H and ^{13}C Spectrum for Compound S5 at 25 ℃



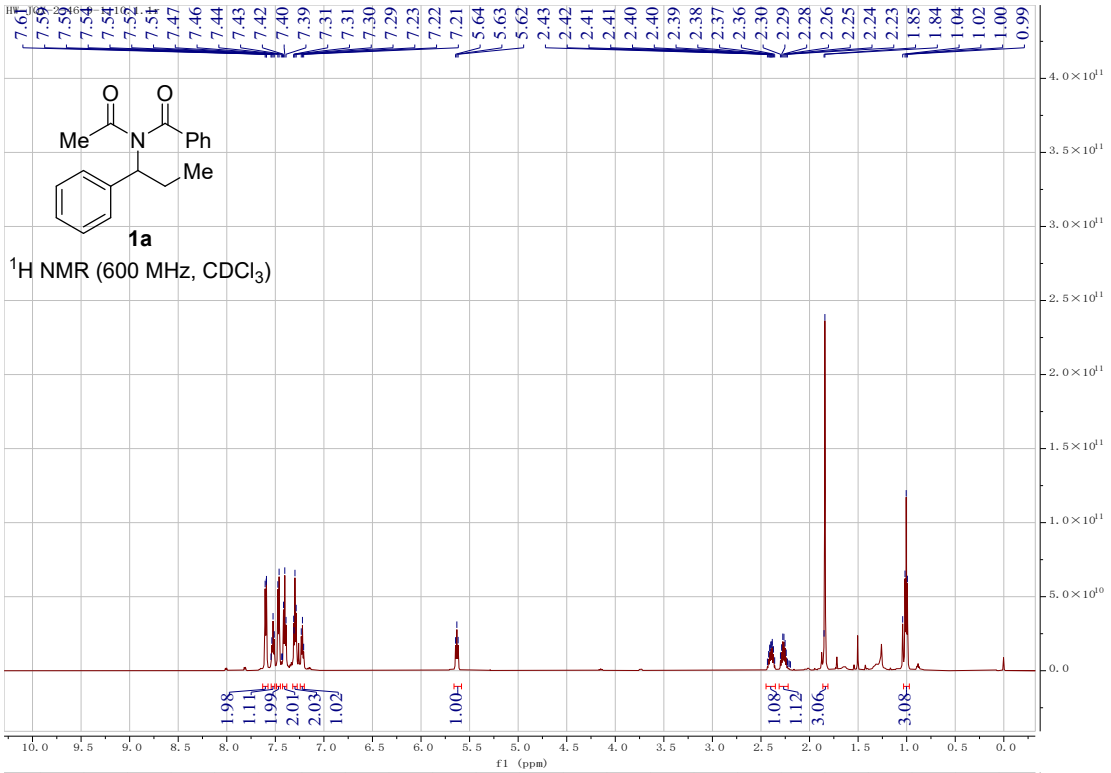


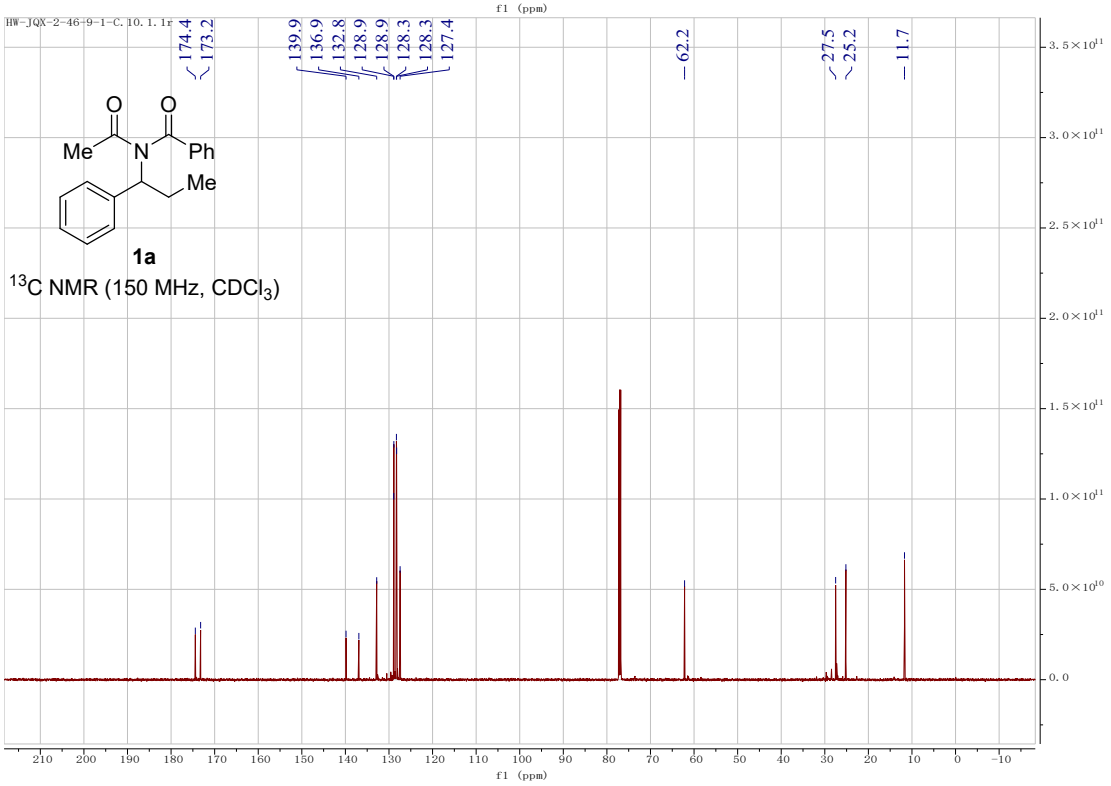
^{1}H and ^{13}C Spectrum for Compound S6 at 25 ℃



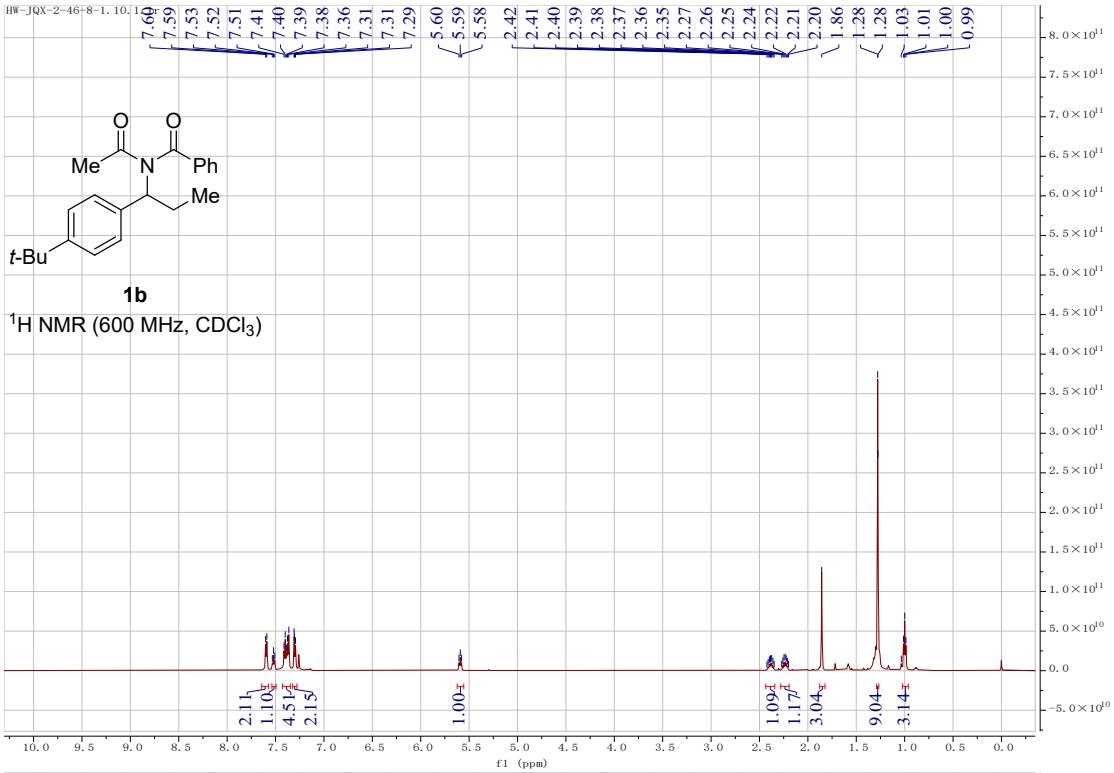


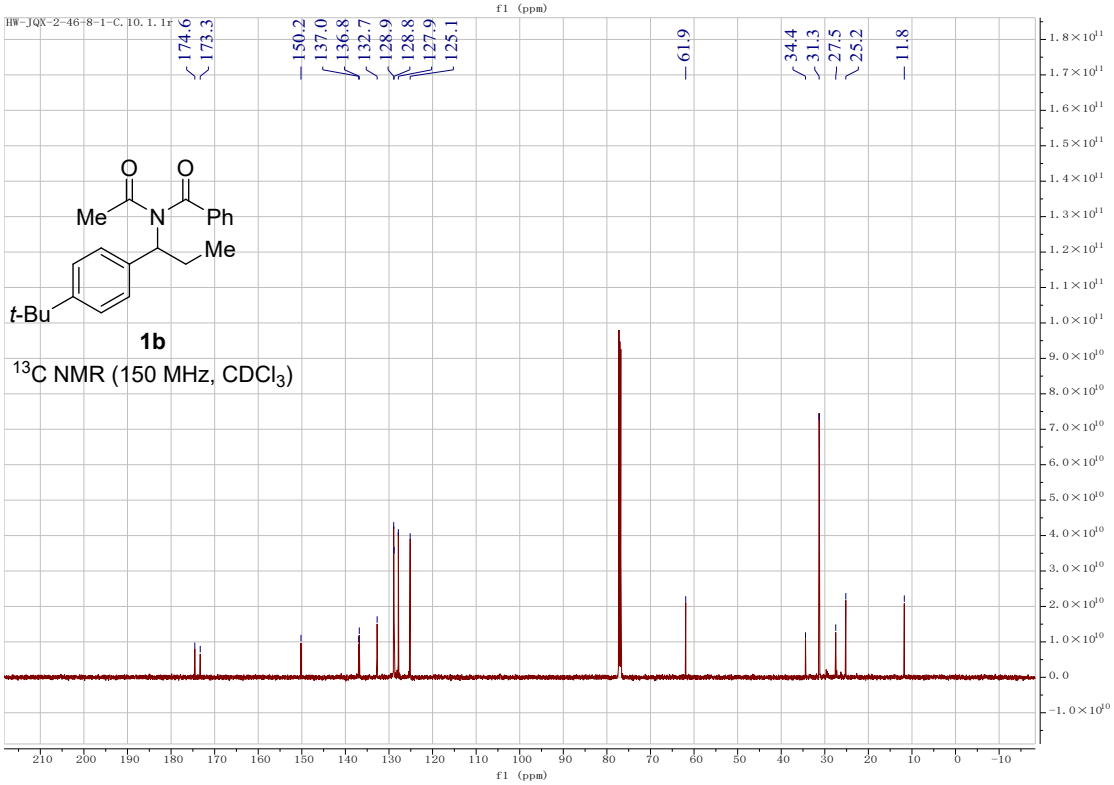
^{1}H and ^{13}C Spectrum for Compound 1a at 25 ℃



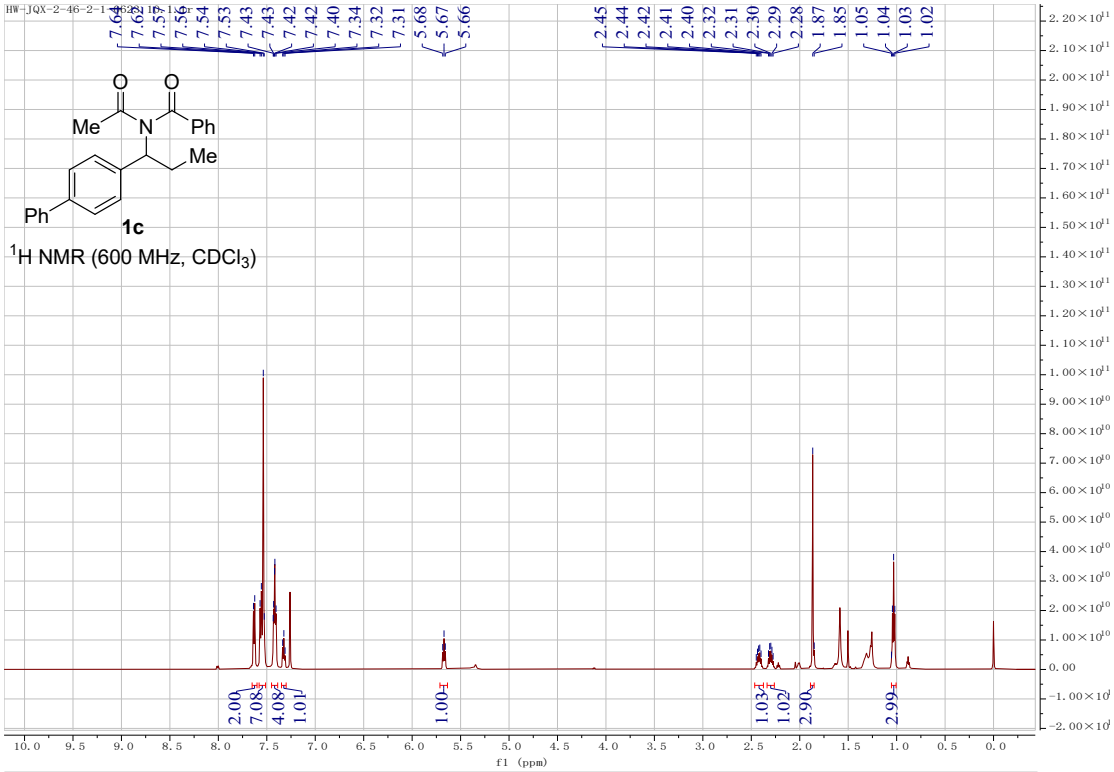


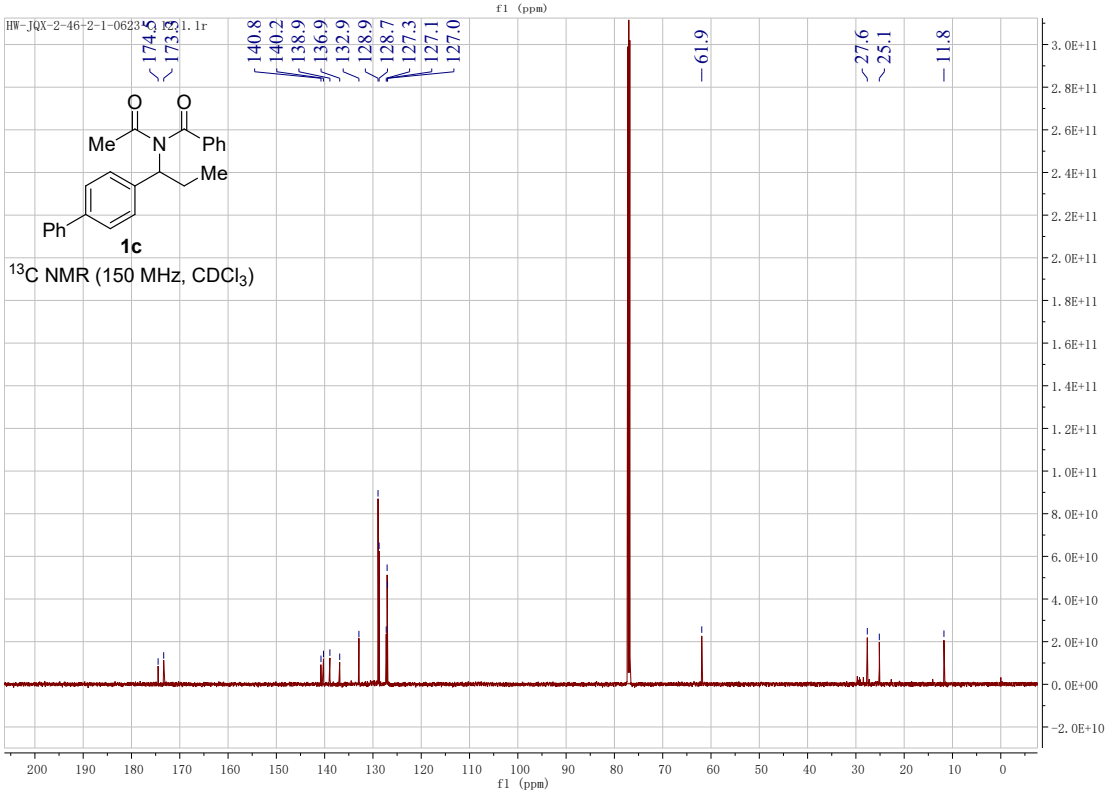
^{1}H and ^{13}C Spectrum for Compound 1b at 25 ℃



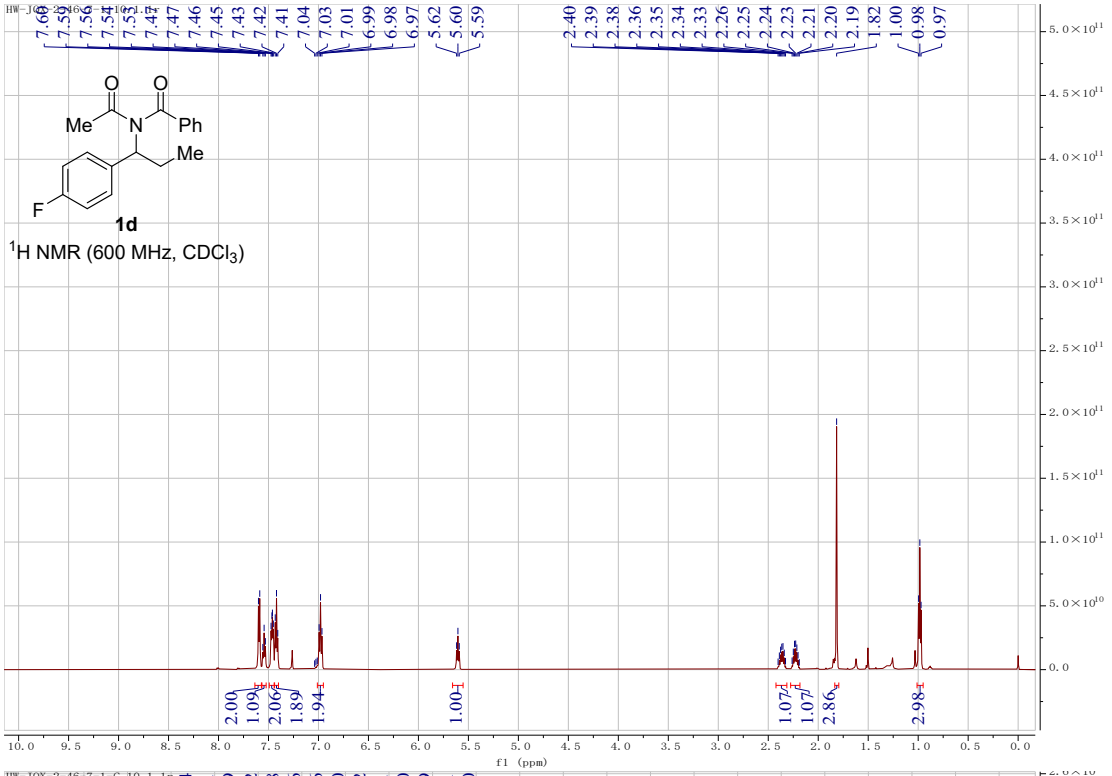


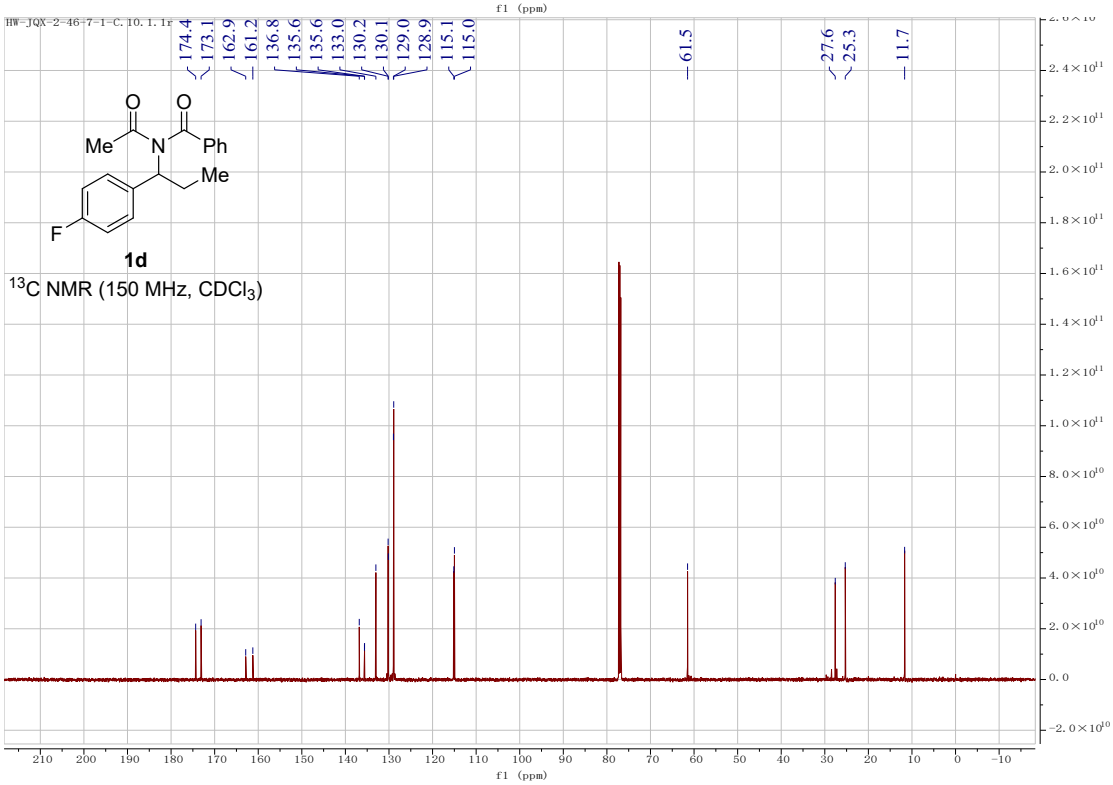
^{1}H and ^{13}C Spectrum for Compound 1c at 25 ℃



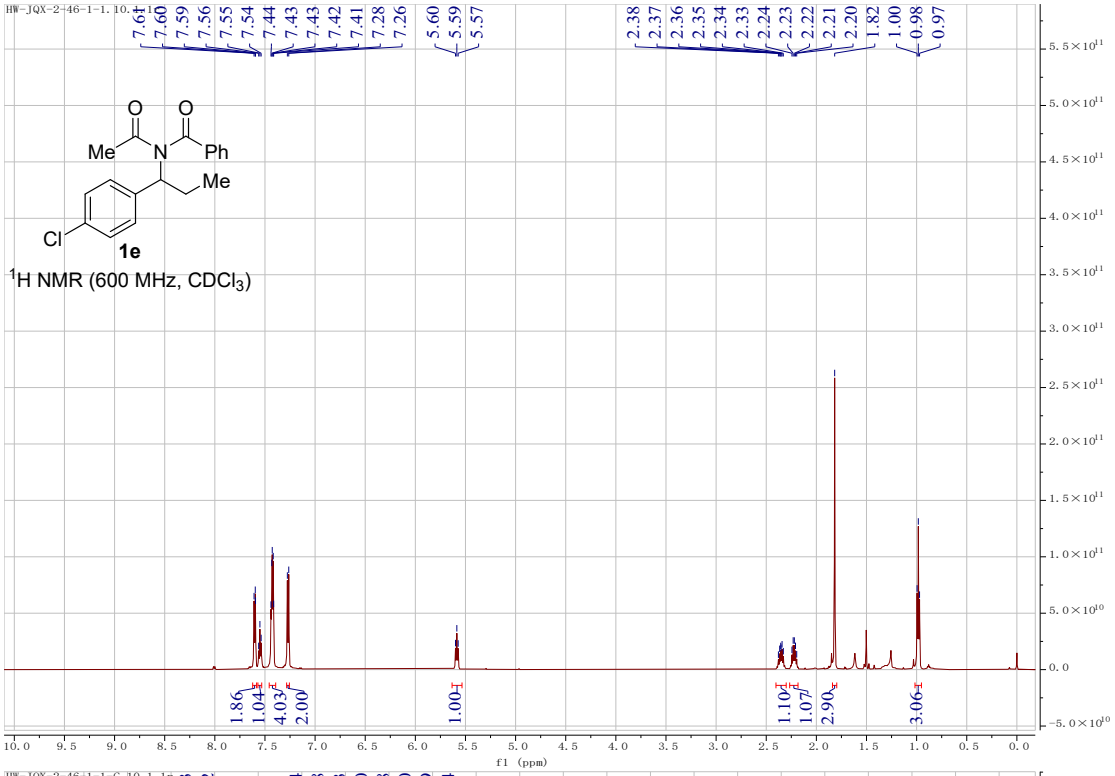


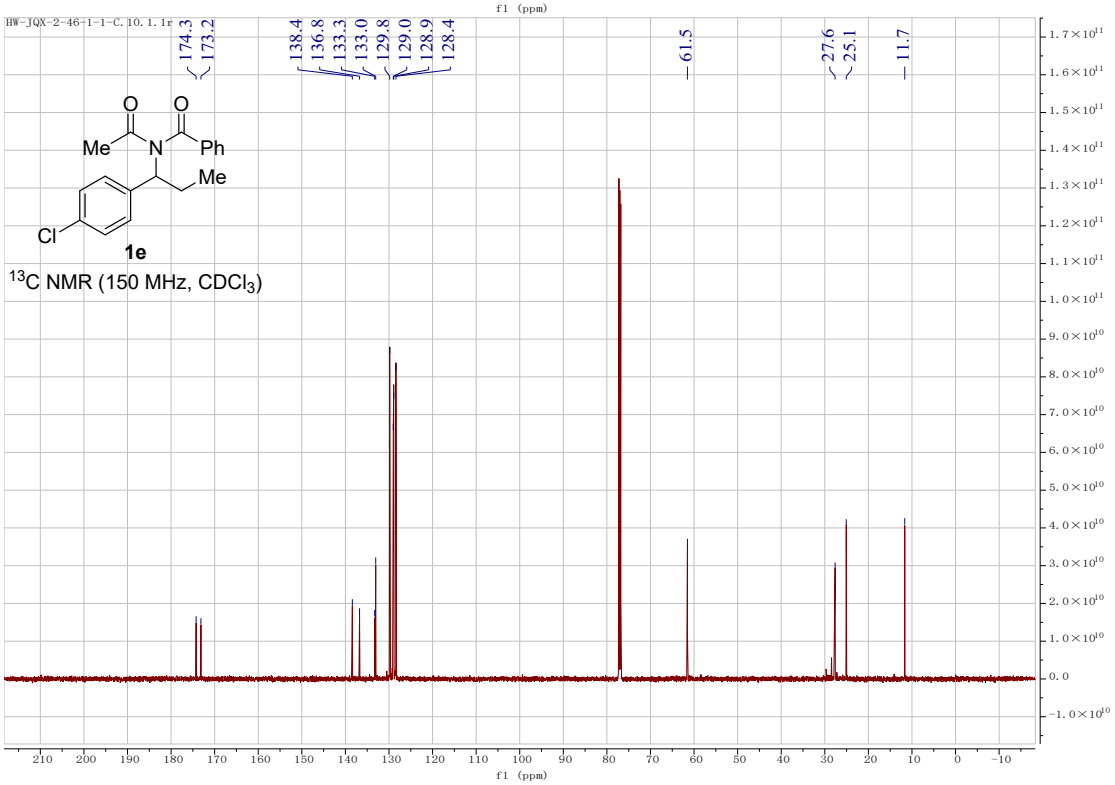
^{1}H and ^{13}C Spectrum for Compound 1d at 25 ℃



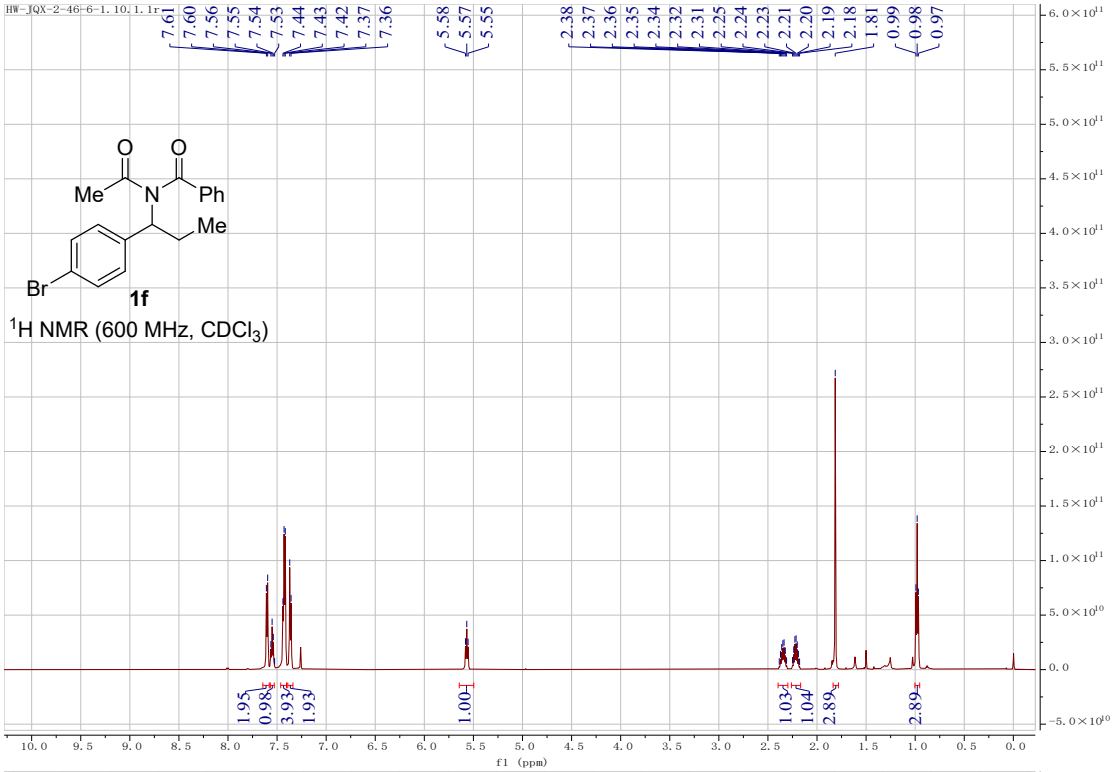


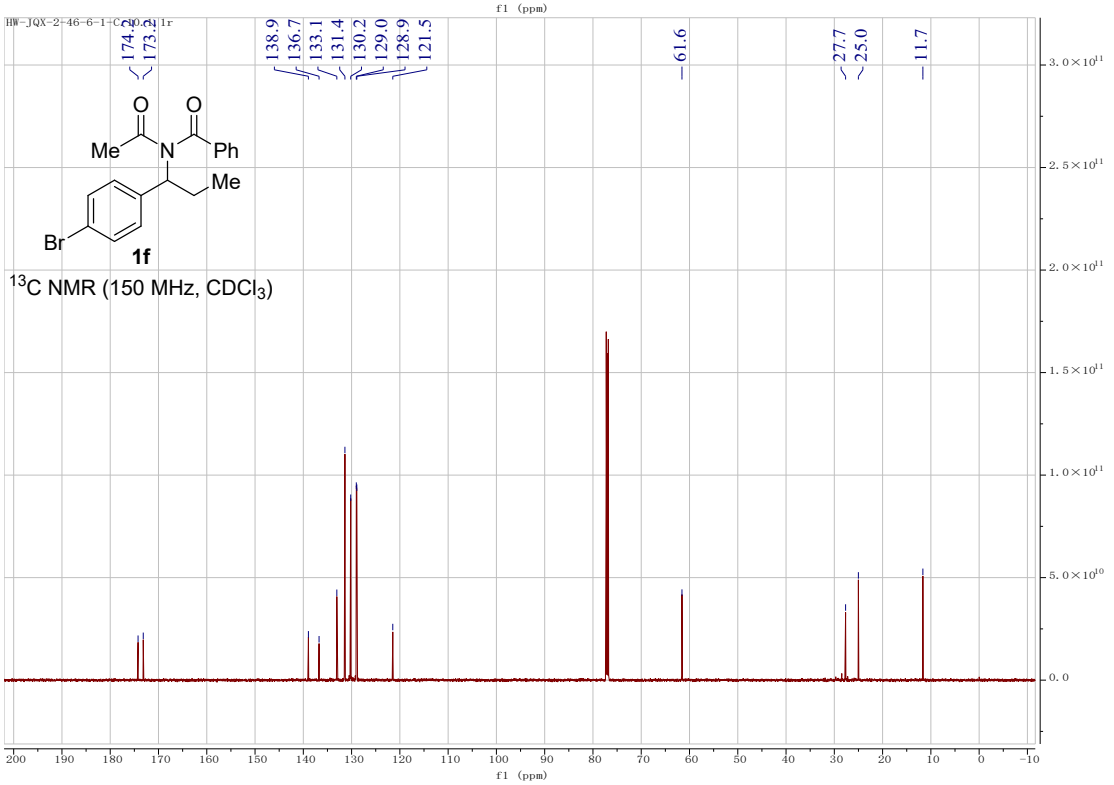
^{1}H and ^{13}C Spectrum for Compound 1e at 25 ℃



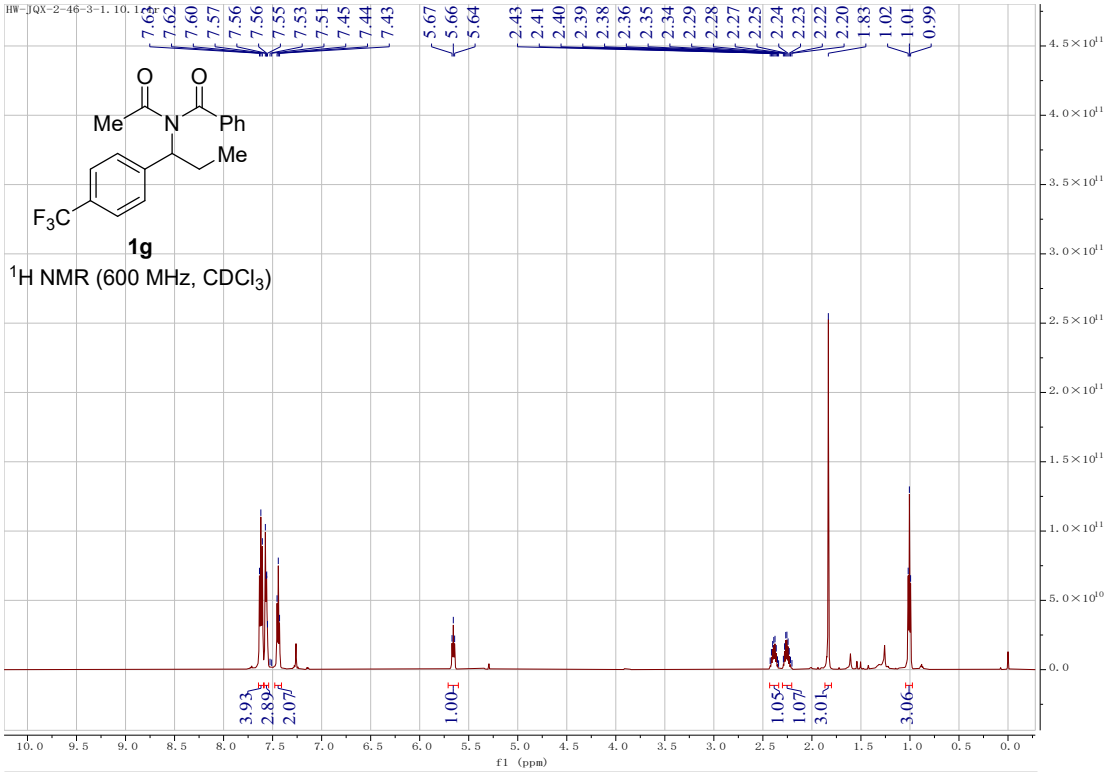


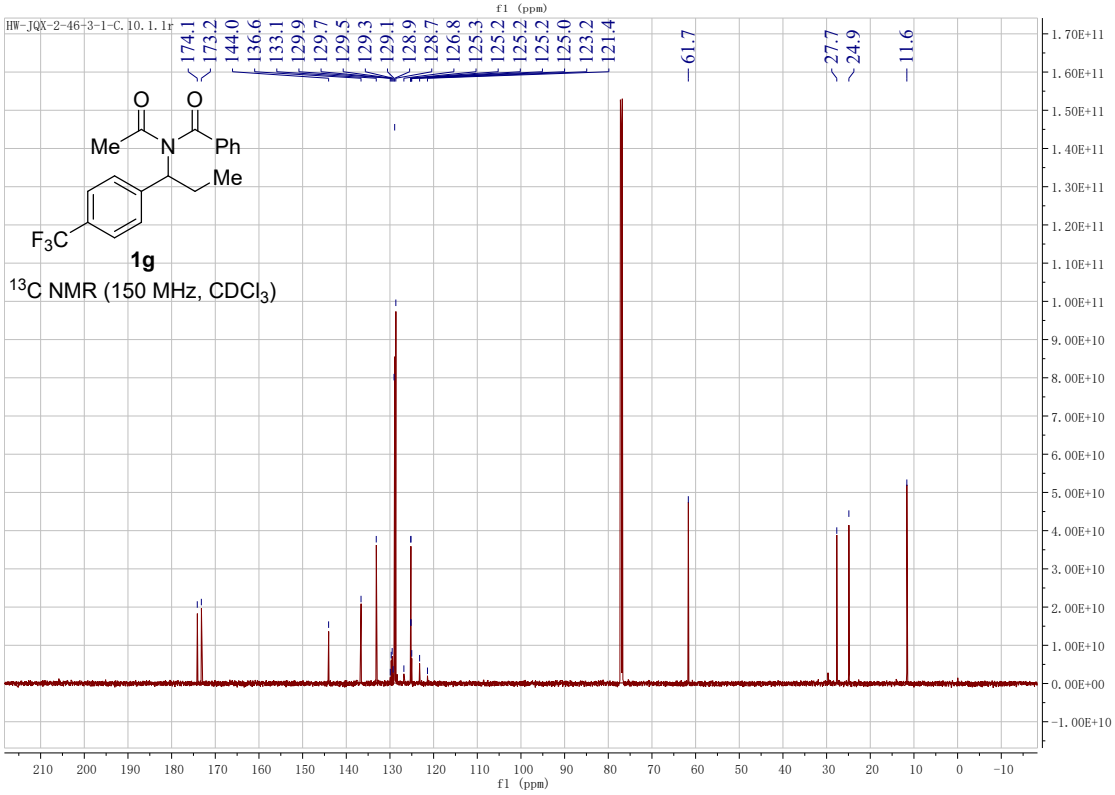
^{1}H and ^{13}C Spectrum for Compound 1f at 25 ℃



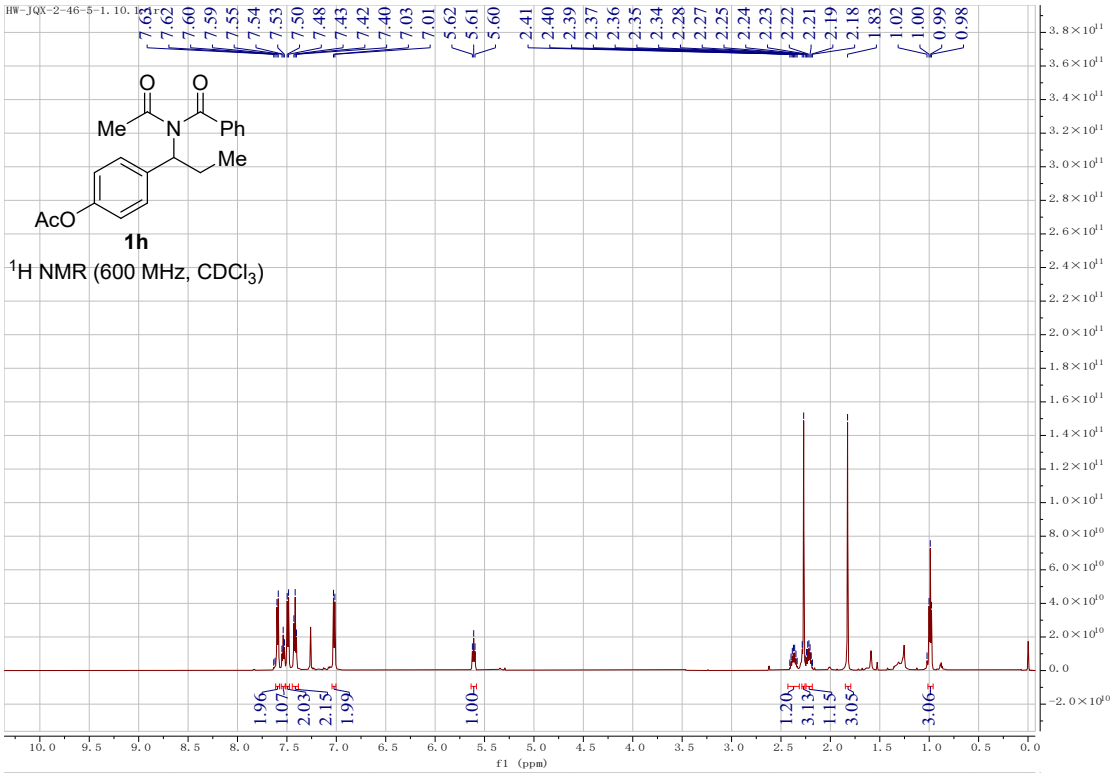


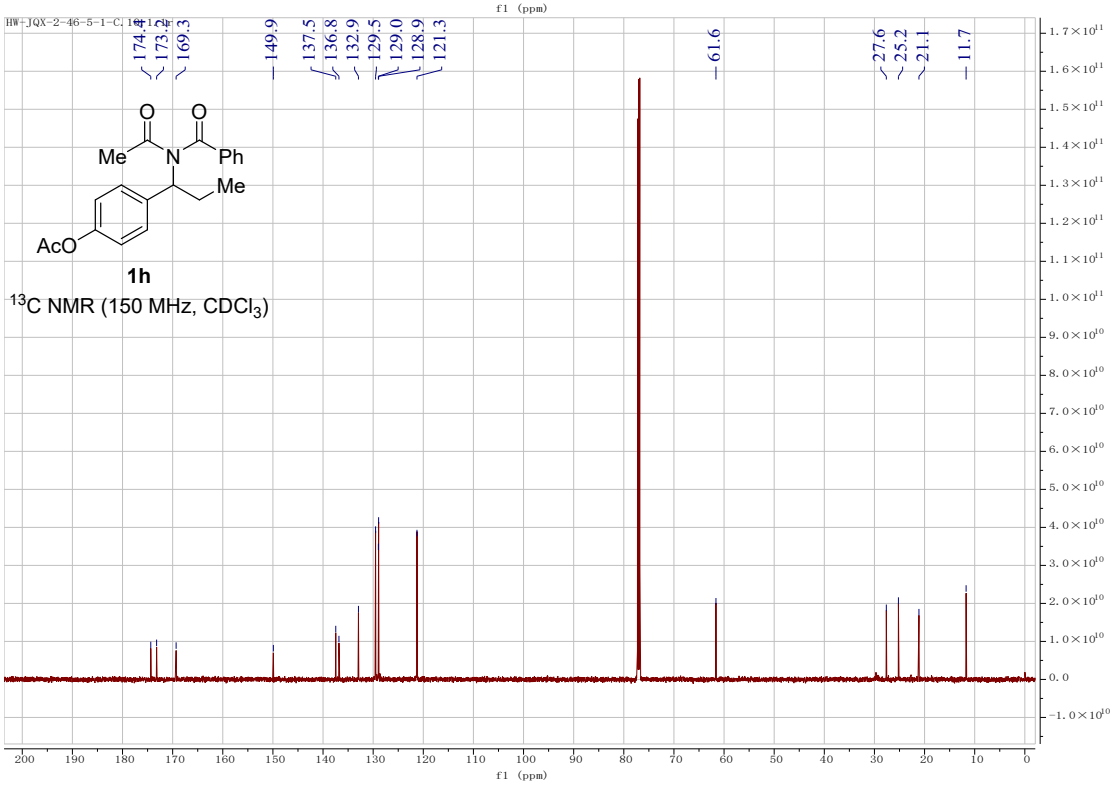
^{1}H and ^{13}C Spectrum for Compound 1g at 25 ℃



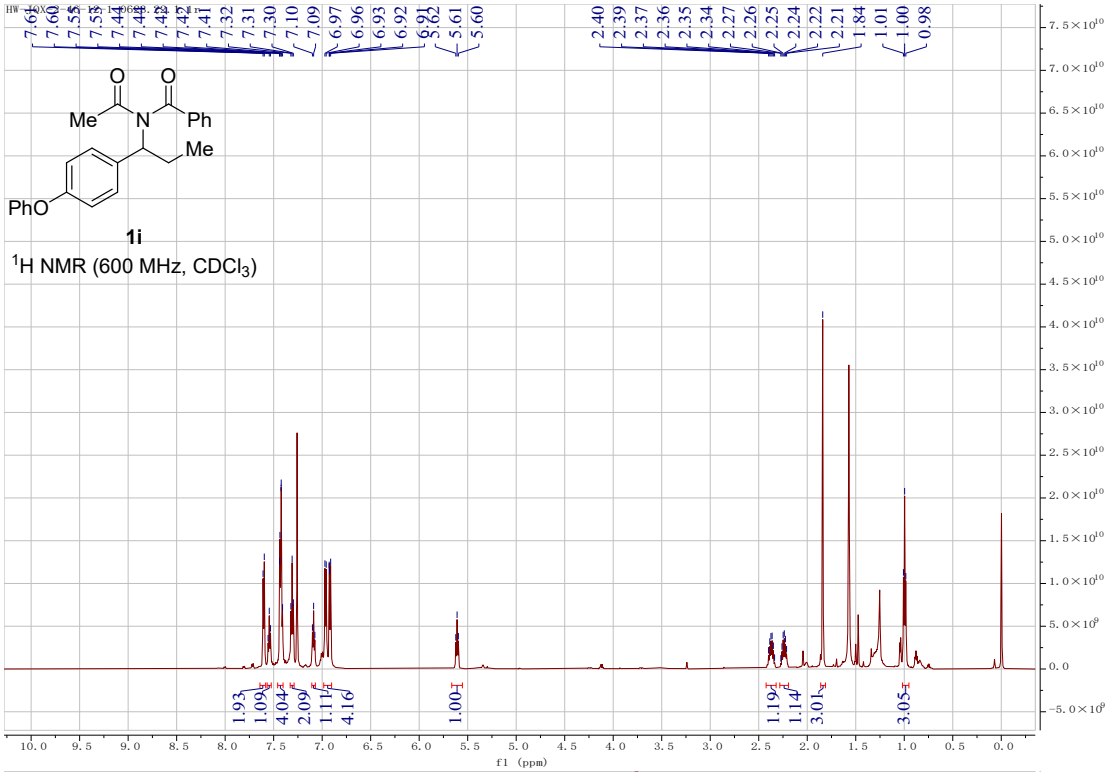


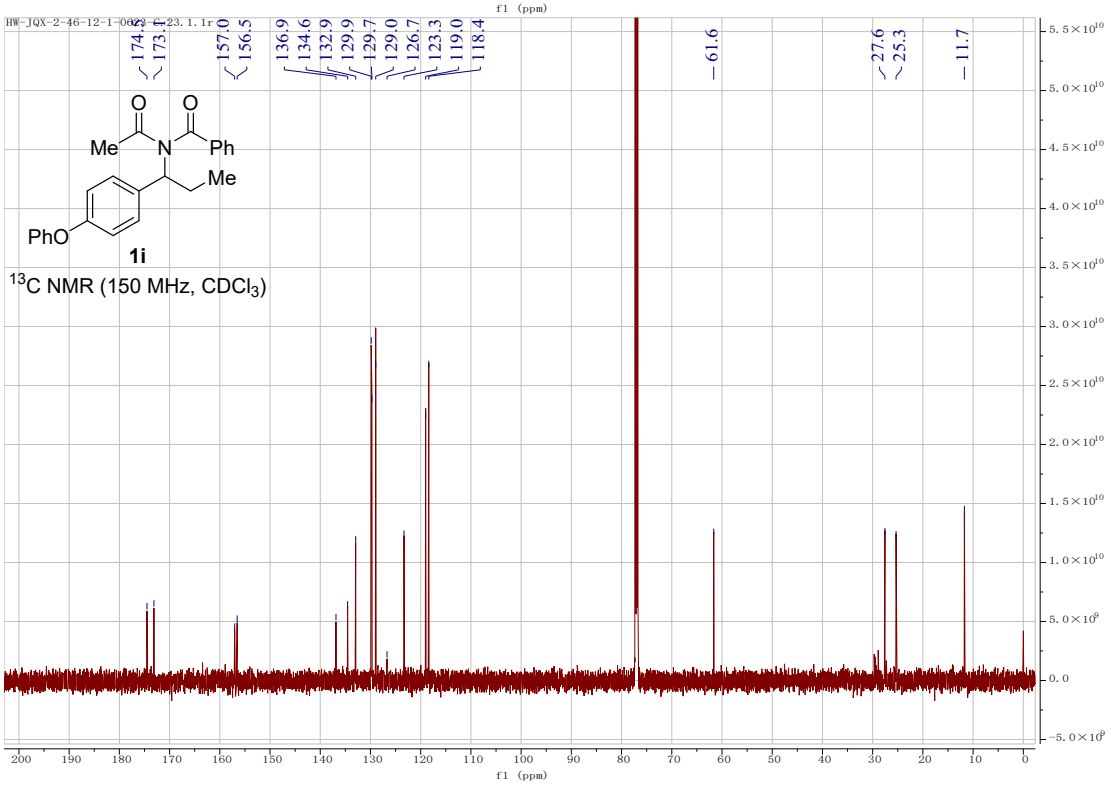
^{1}H and ^{13}C Spectrum for Compound 1h at 25 ℃



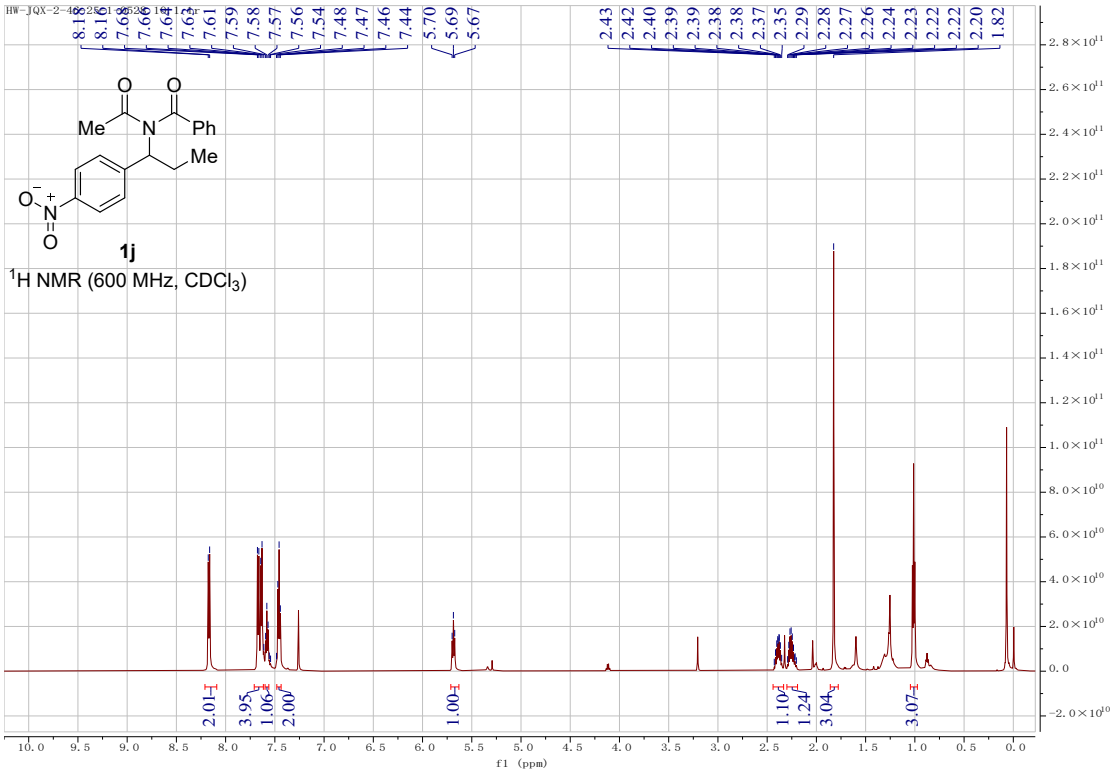


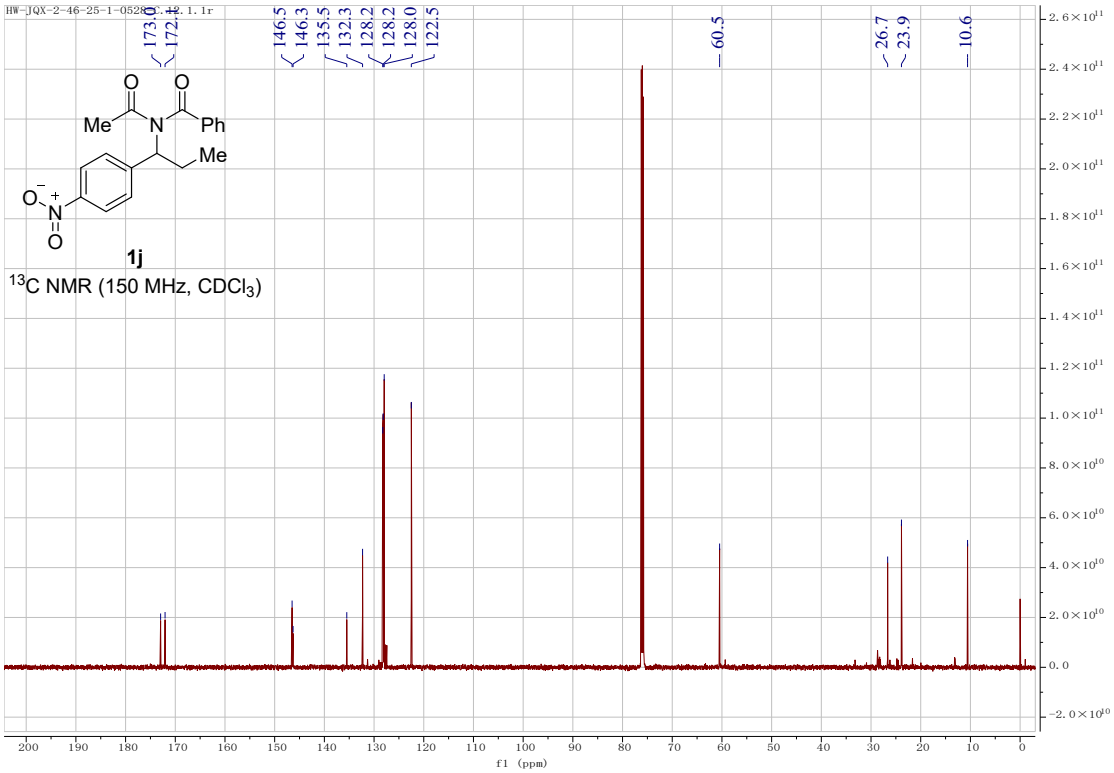
^{1}H and ^{13}C Spectrum for Compound 1i at 25 ℃



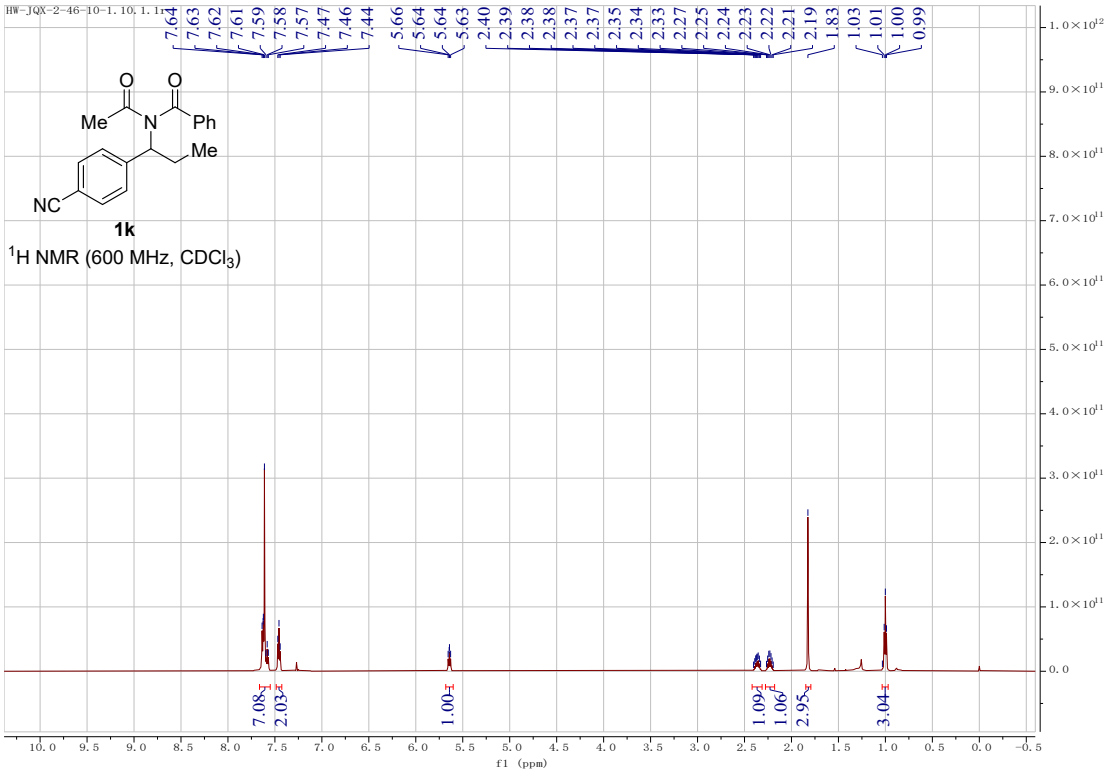


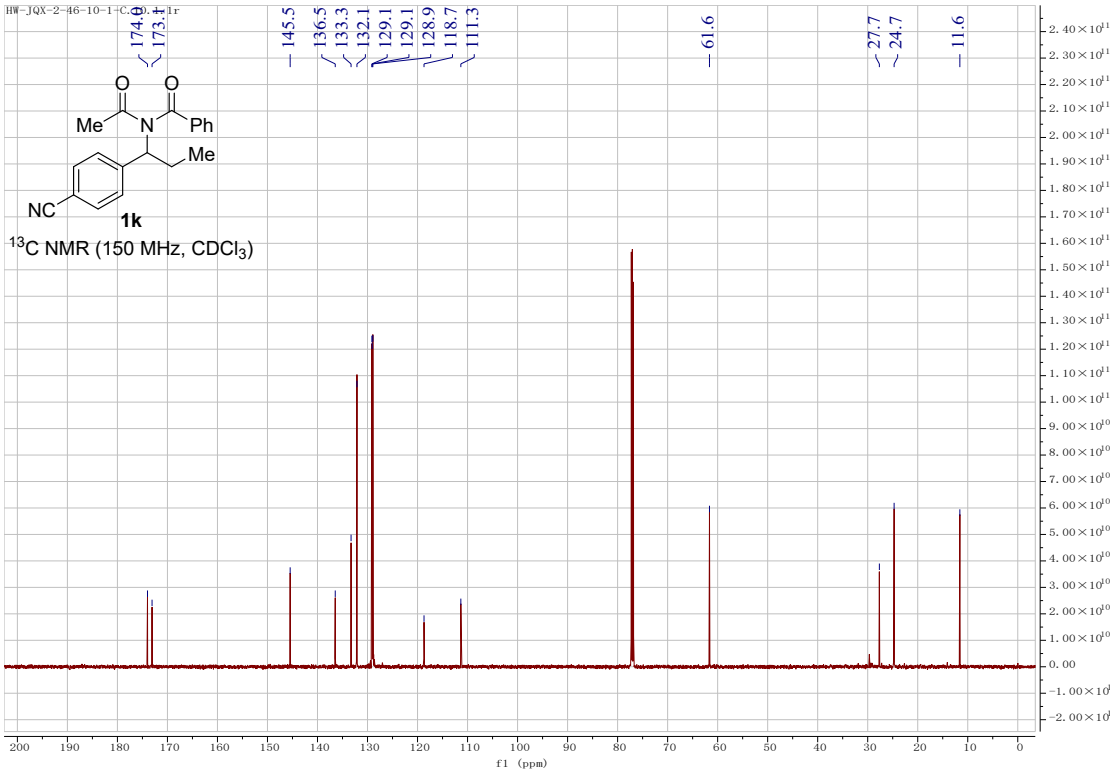
^{1}H and ^{13}C Spectrum for Compound 1j at 25 ℃



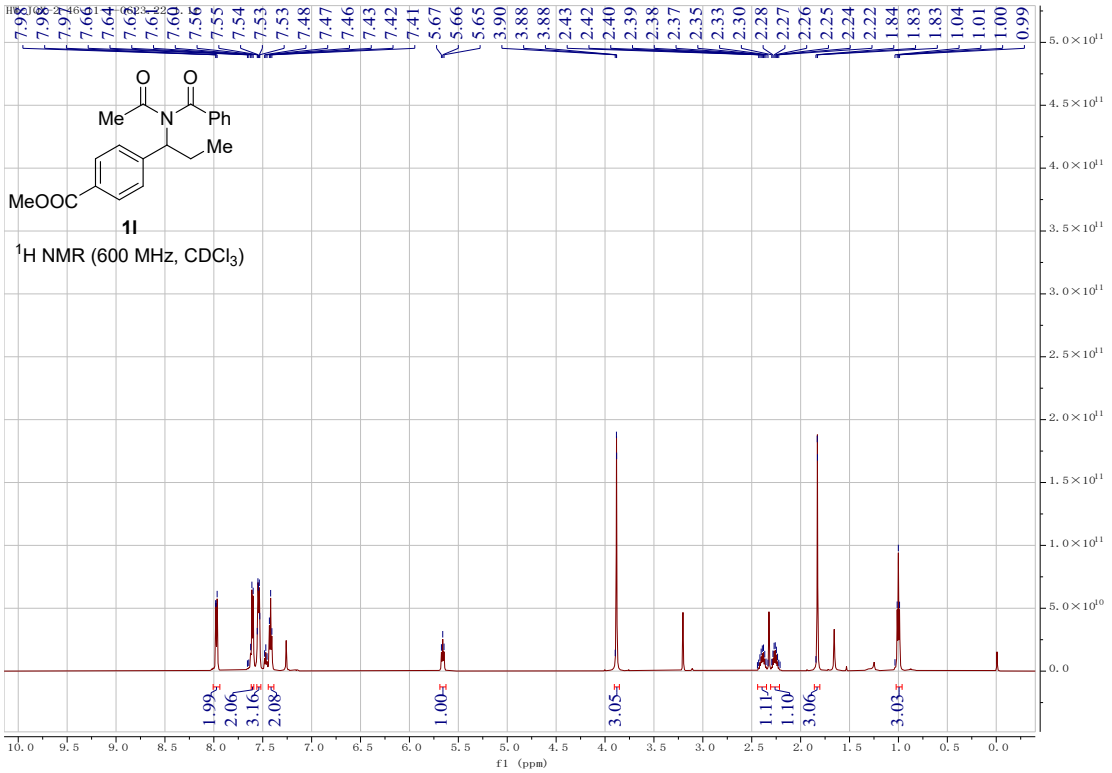


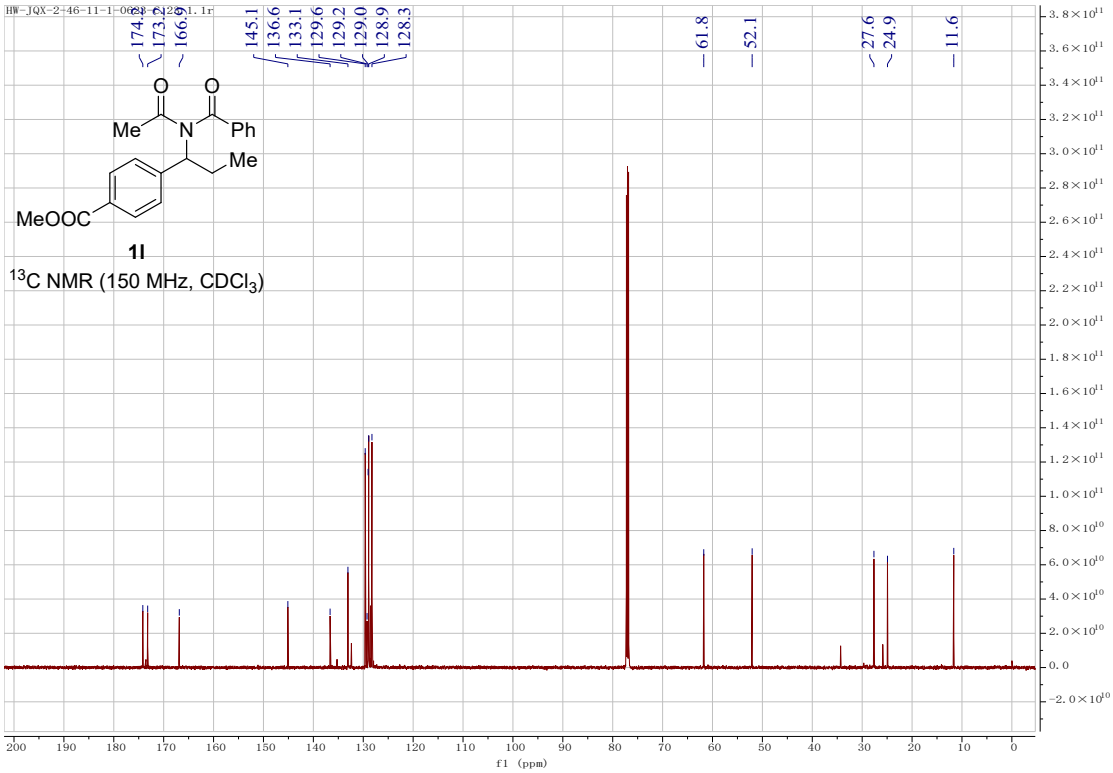
^{1}H and ^{13}C Spectrum for Compound 1k at 25 ℃



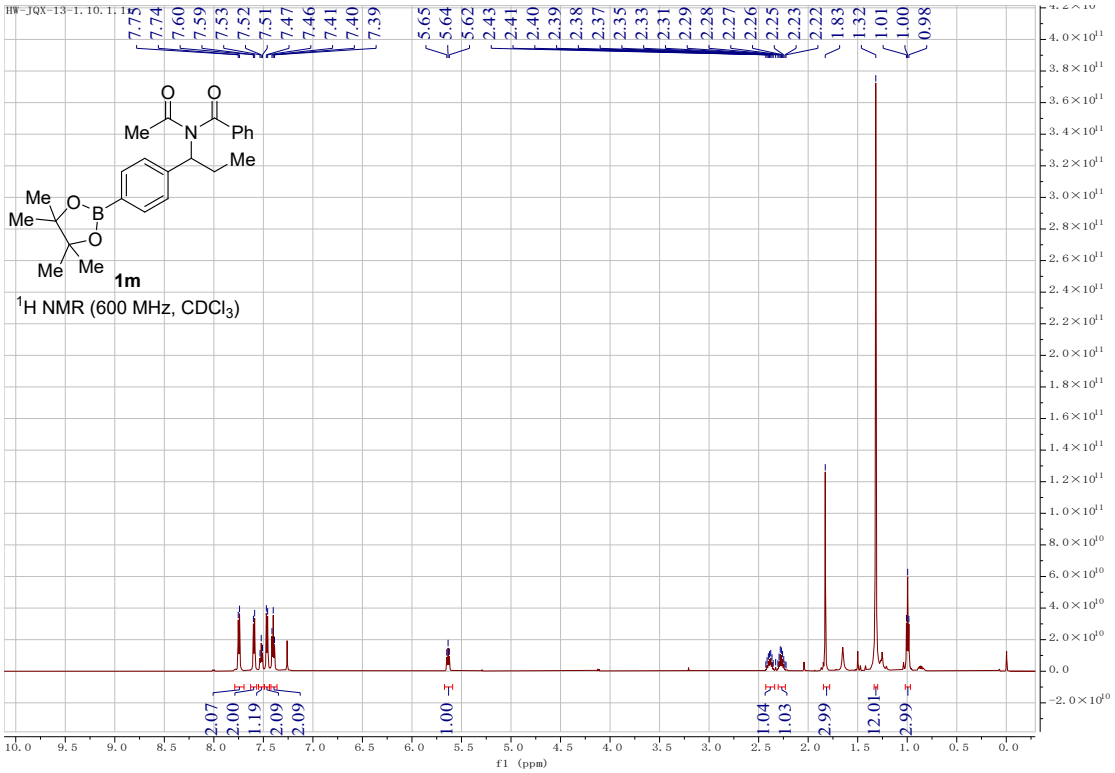


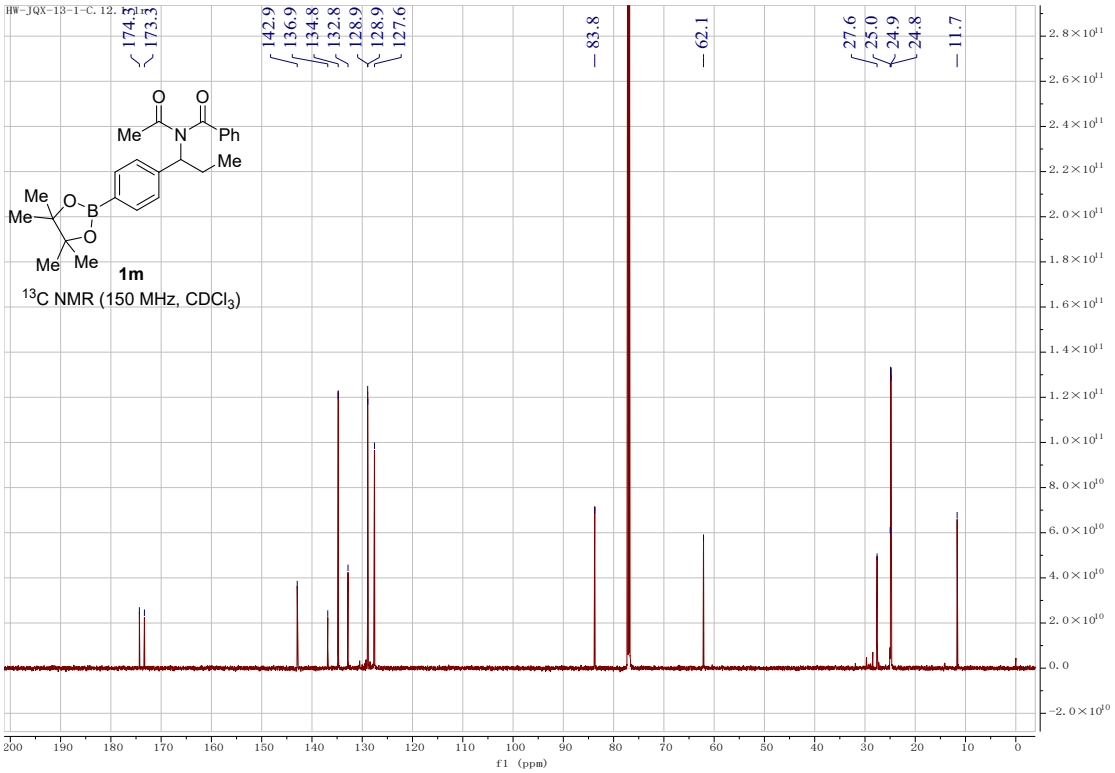
^{1}H and ^{13}C Spectrum for Compound 1l at 25 ℃



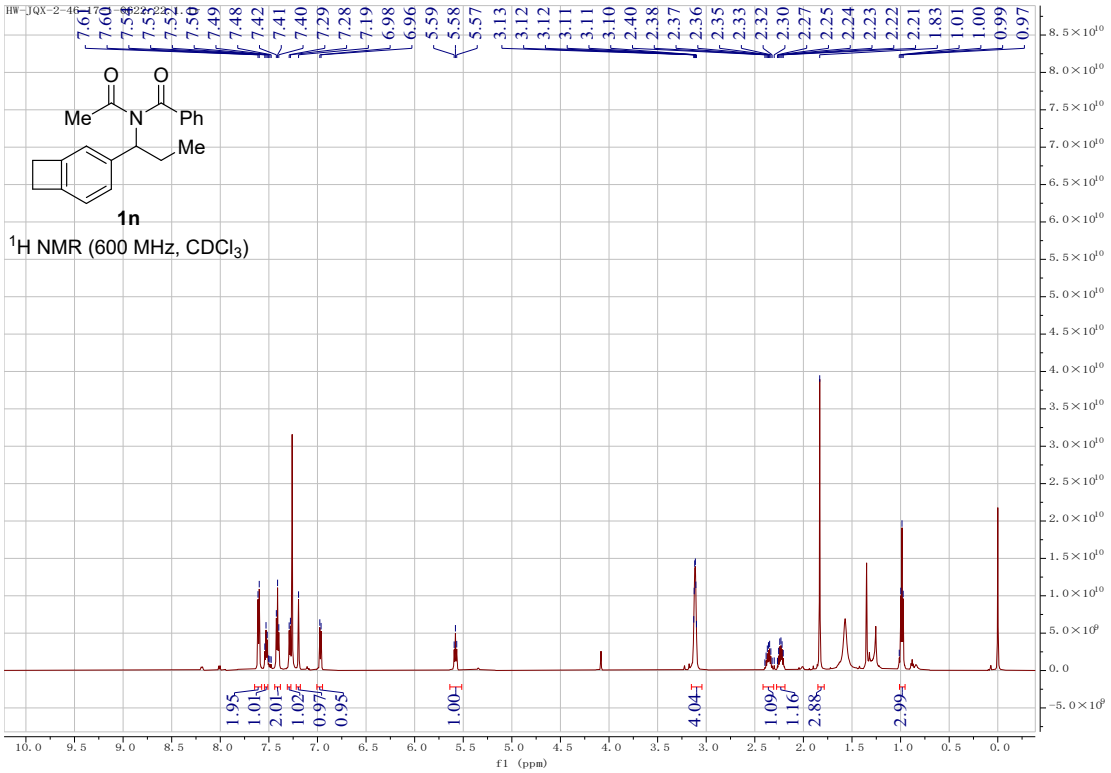


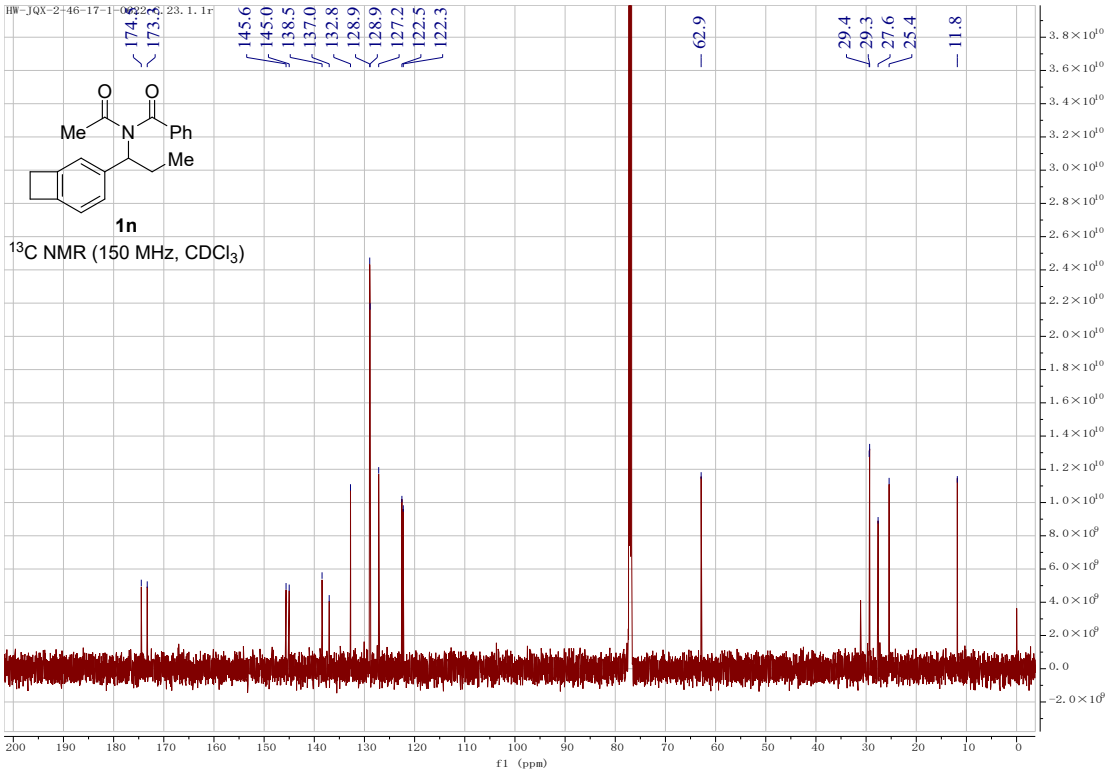
^{1}H and ^{13}C Spectrum for Compound 1m at 25 ℃



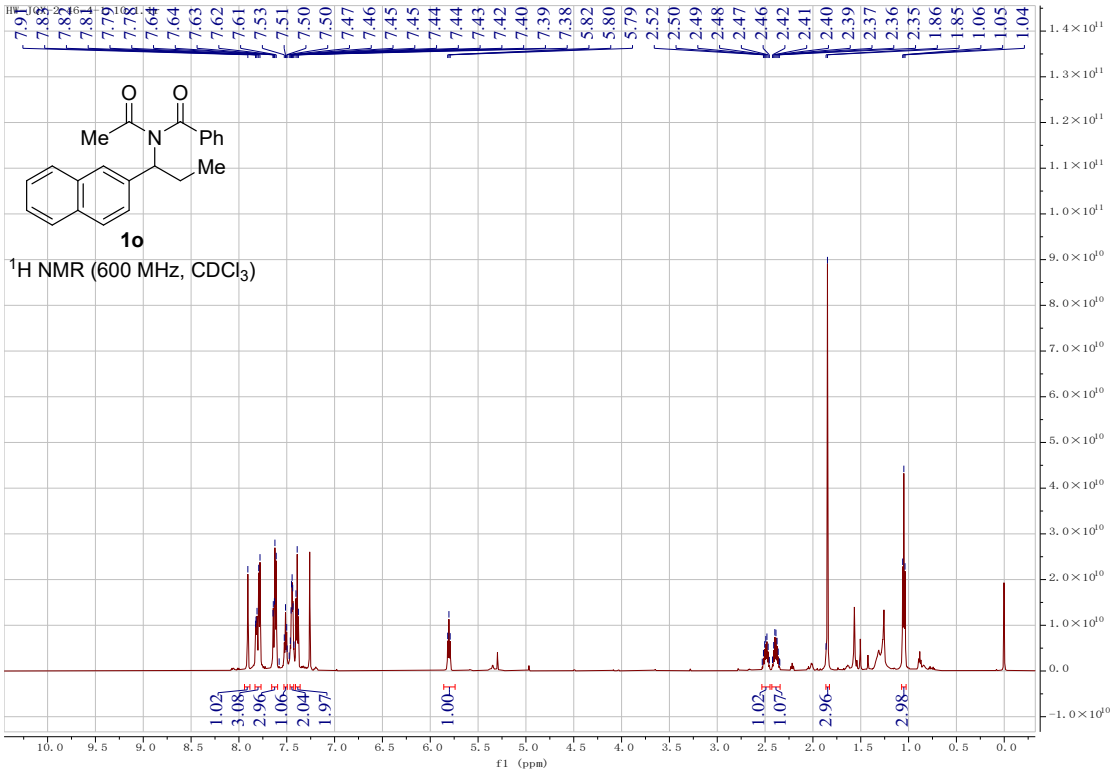


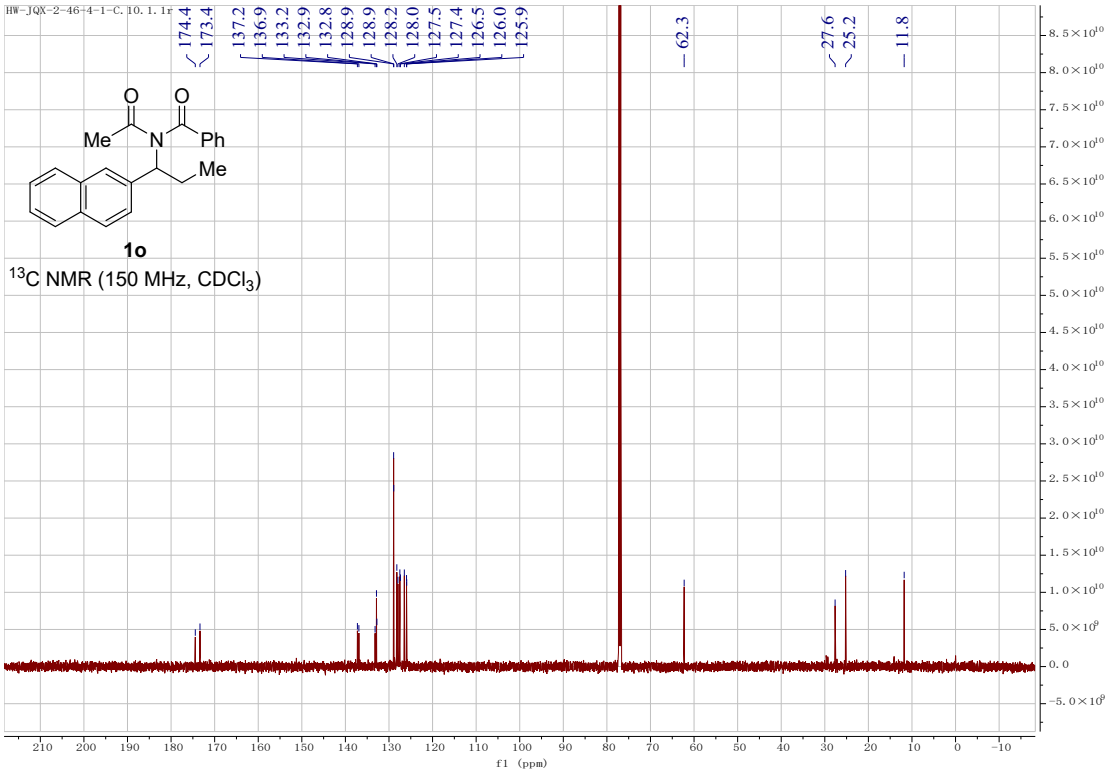
^{1}H and ^{13}C Spectrum for Compound 1n at 25 ℃



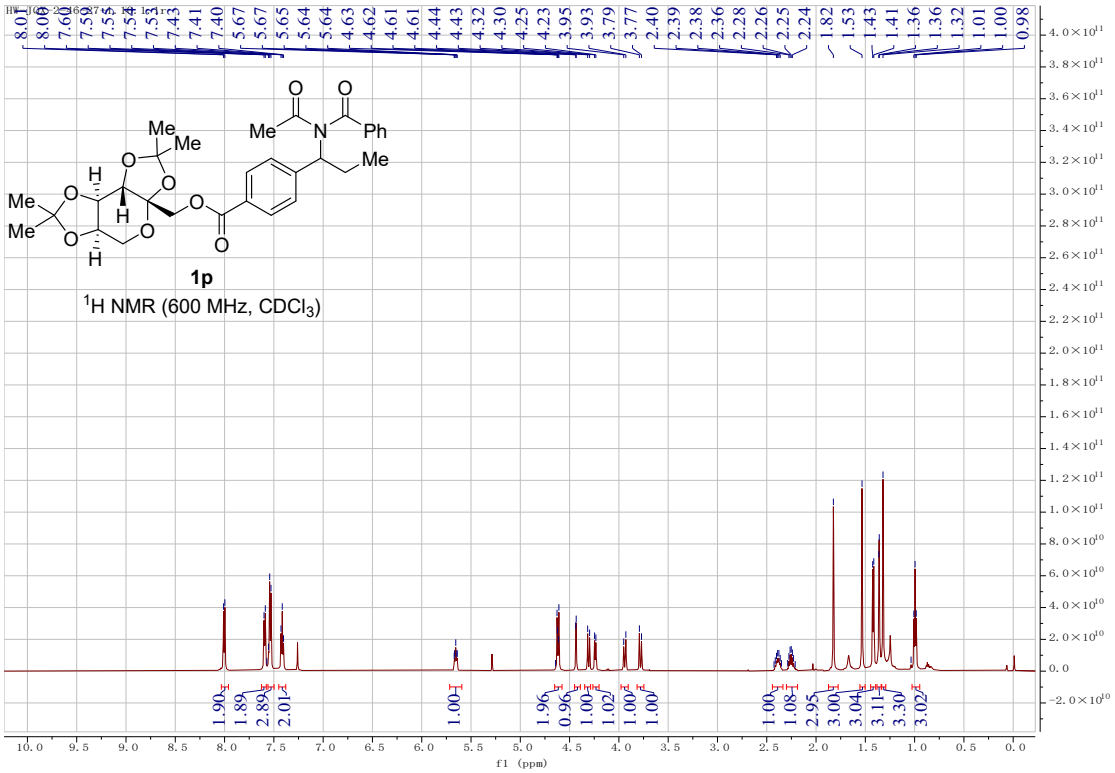


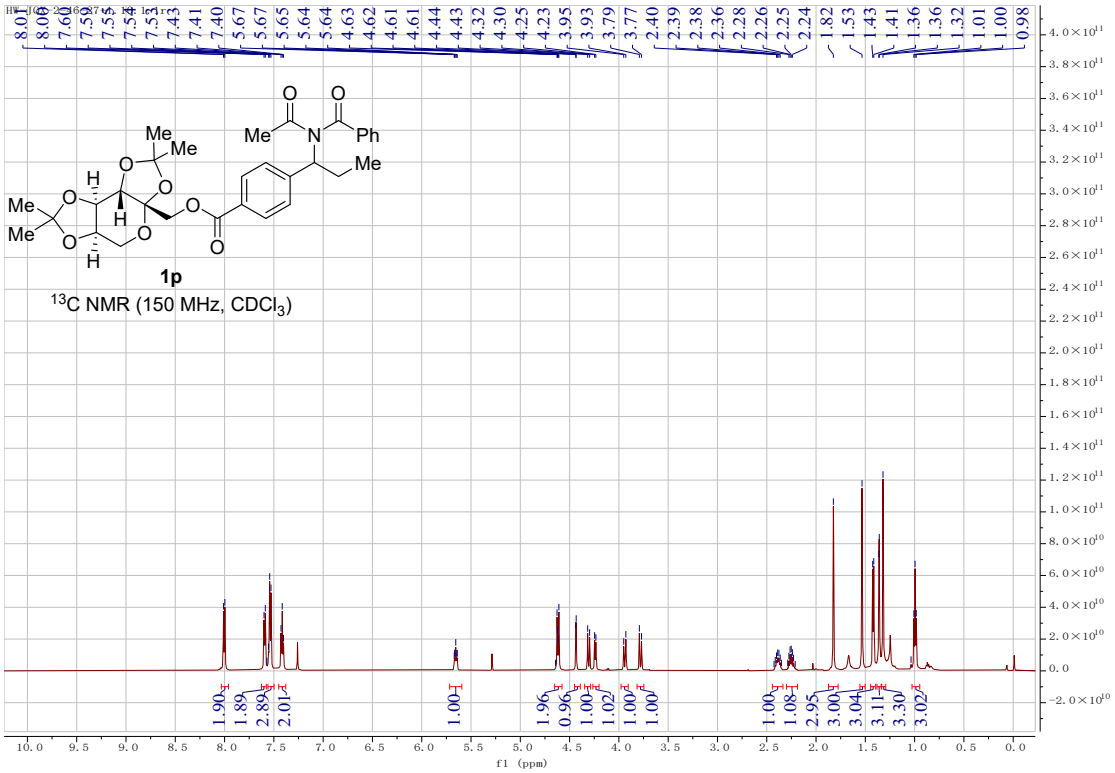
^{1}H and ^{13}C Spectrum for Compound 1o at 25 ℃



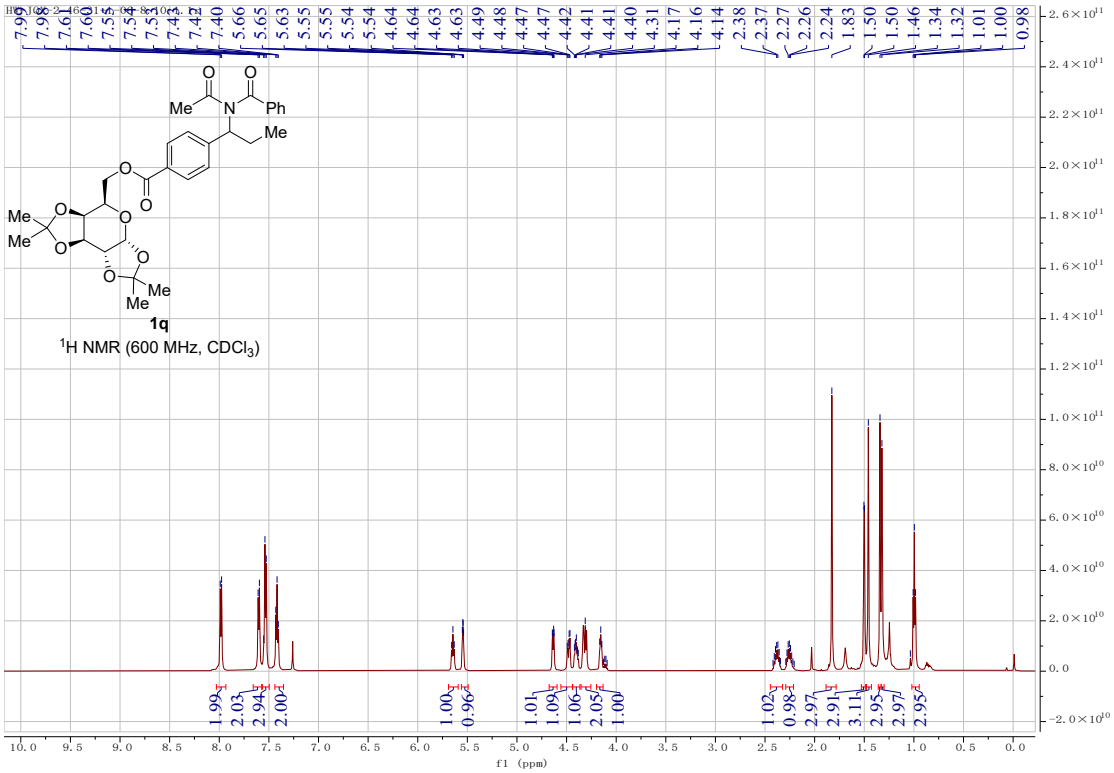


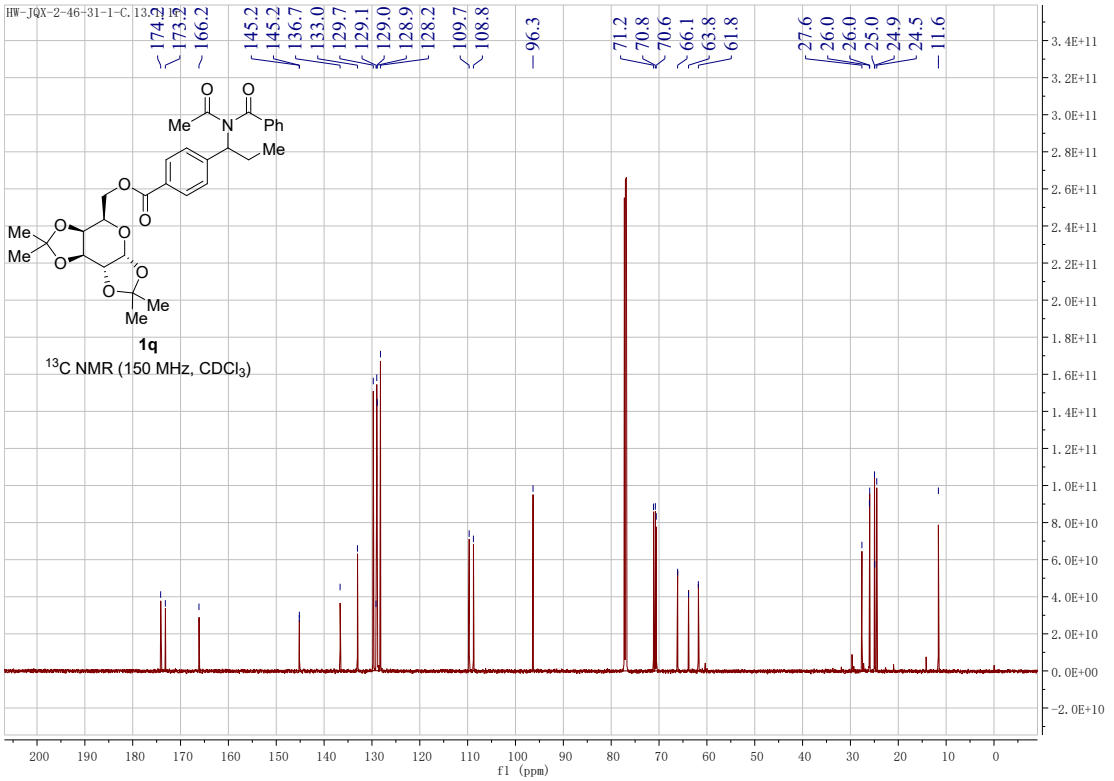
^{1}H and ^{13}C Spectrum for Compound 1p at 25 ℃



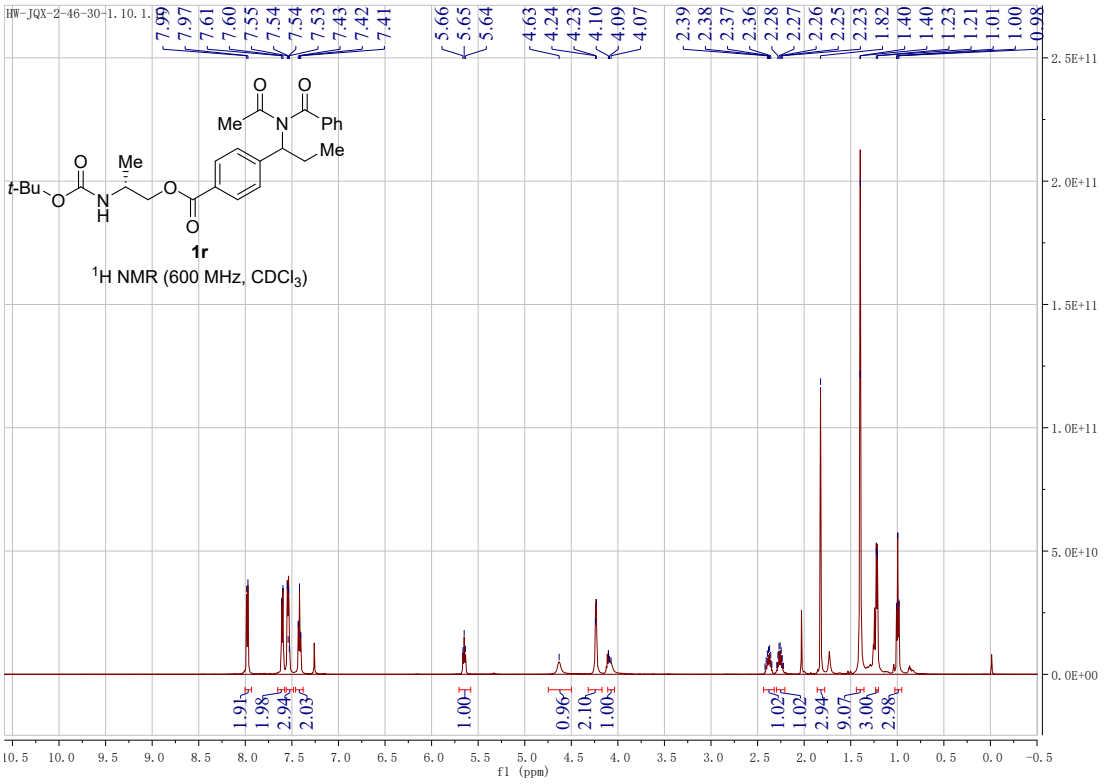


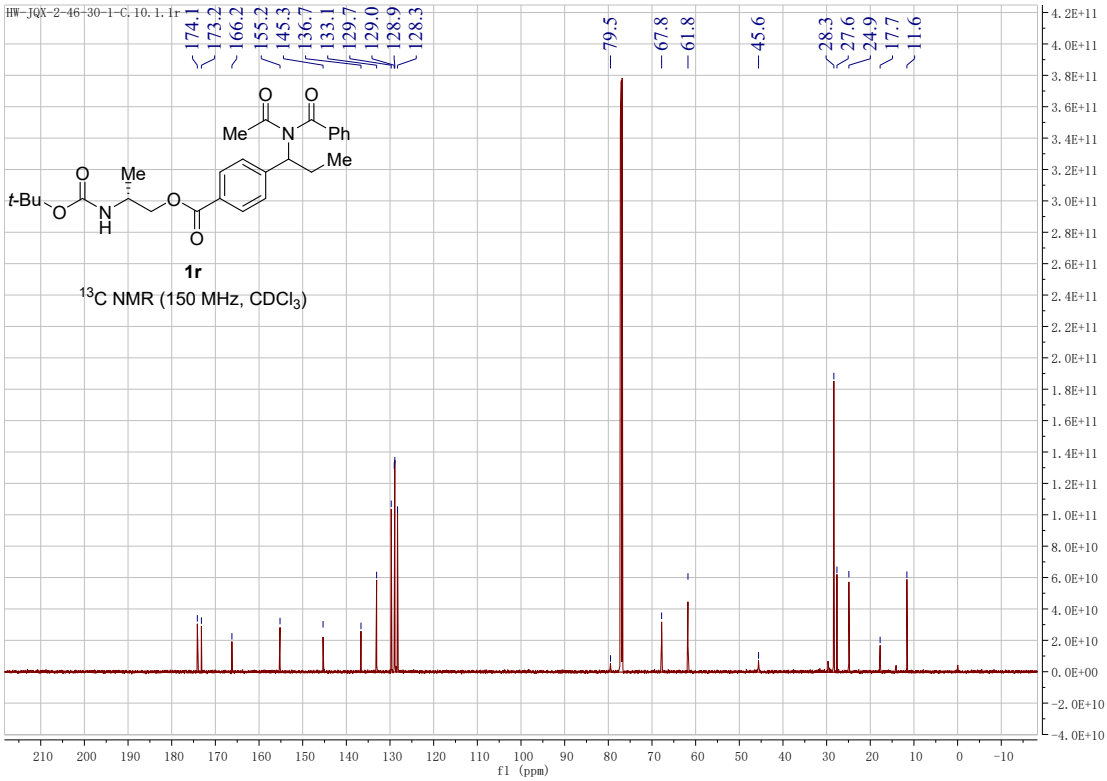
^{1}H and ^{13}C Spectrum for Compound 1q at 25 ℃



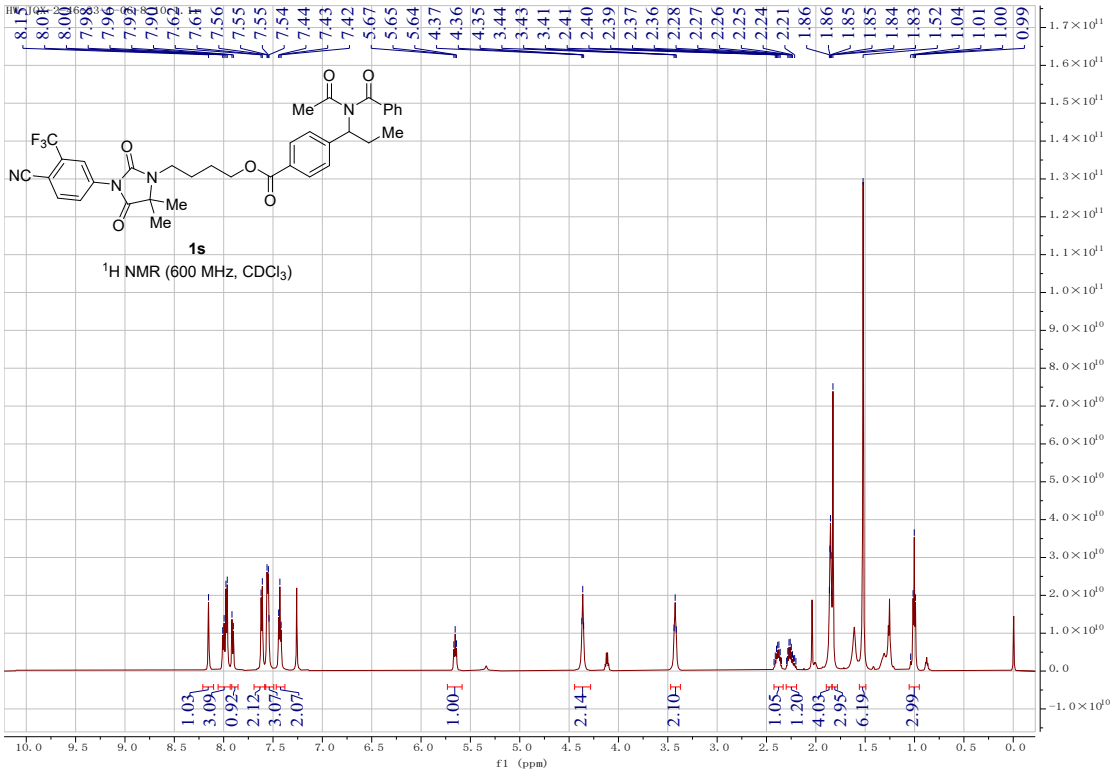


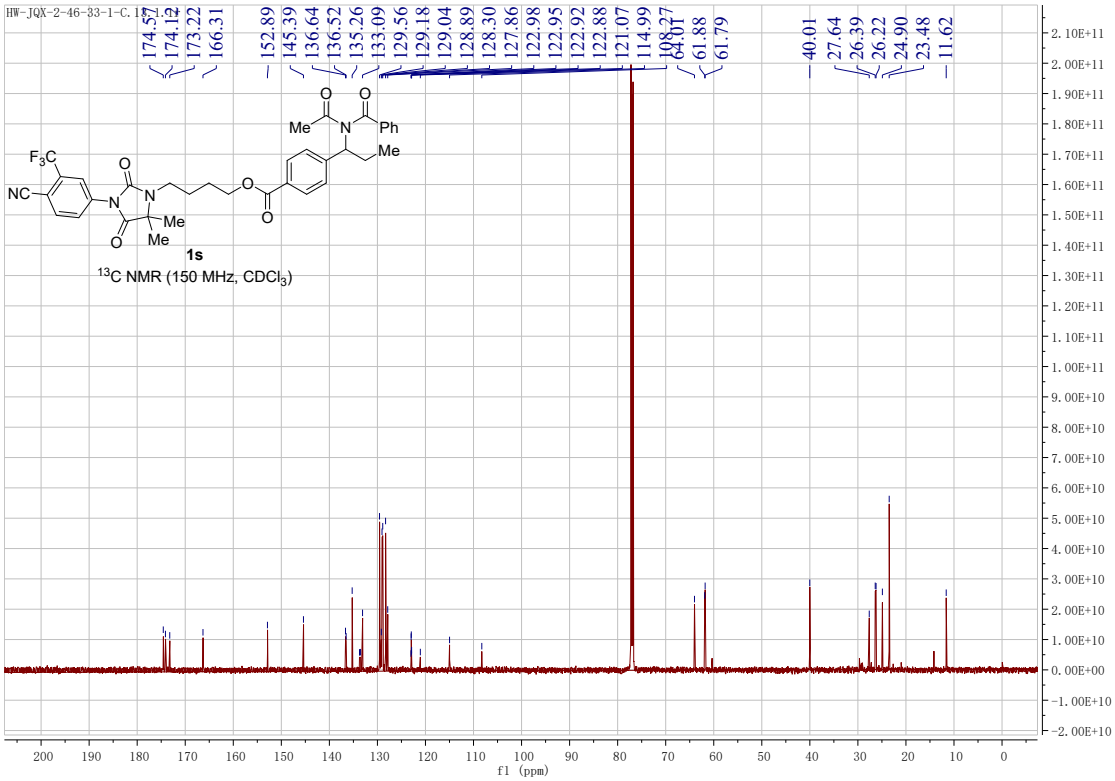
^{1}H and ^{13}C Spectrum for Compound 1r at 25 ℃



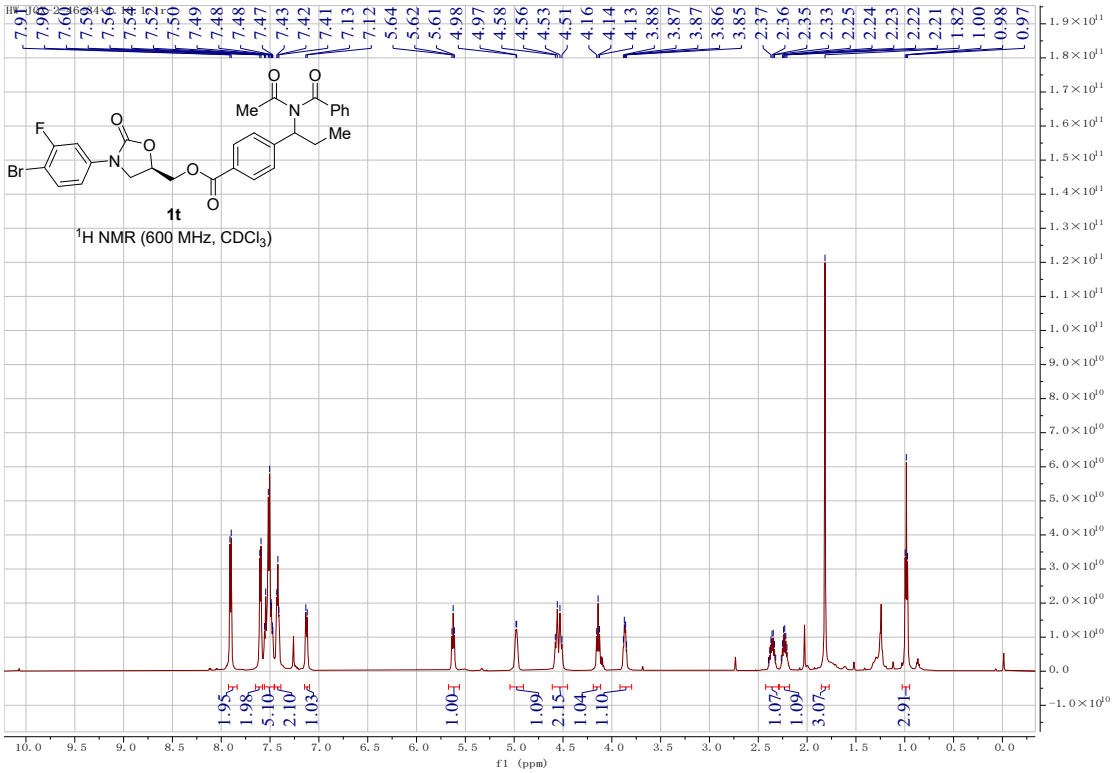


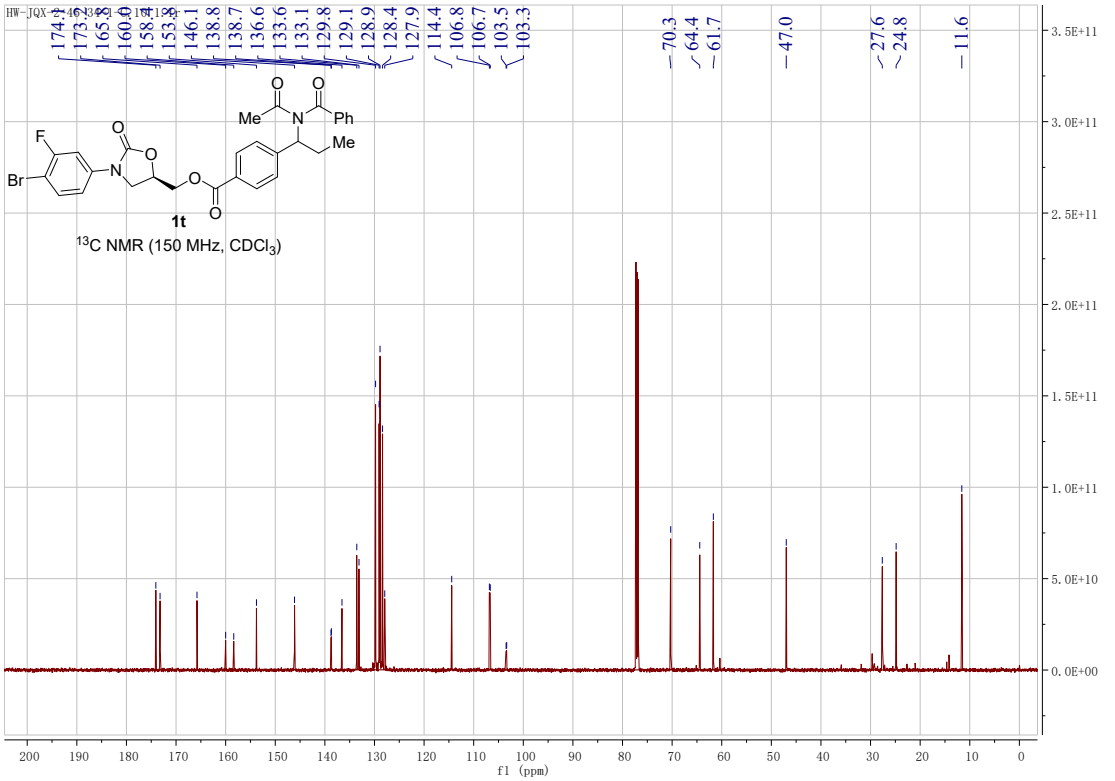
^{1}H and ^{13}C Spectrum for Compound 1s at 25 ℃



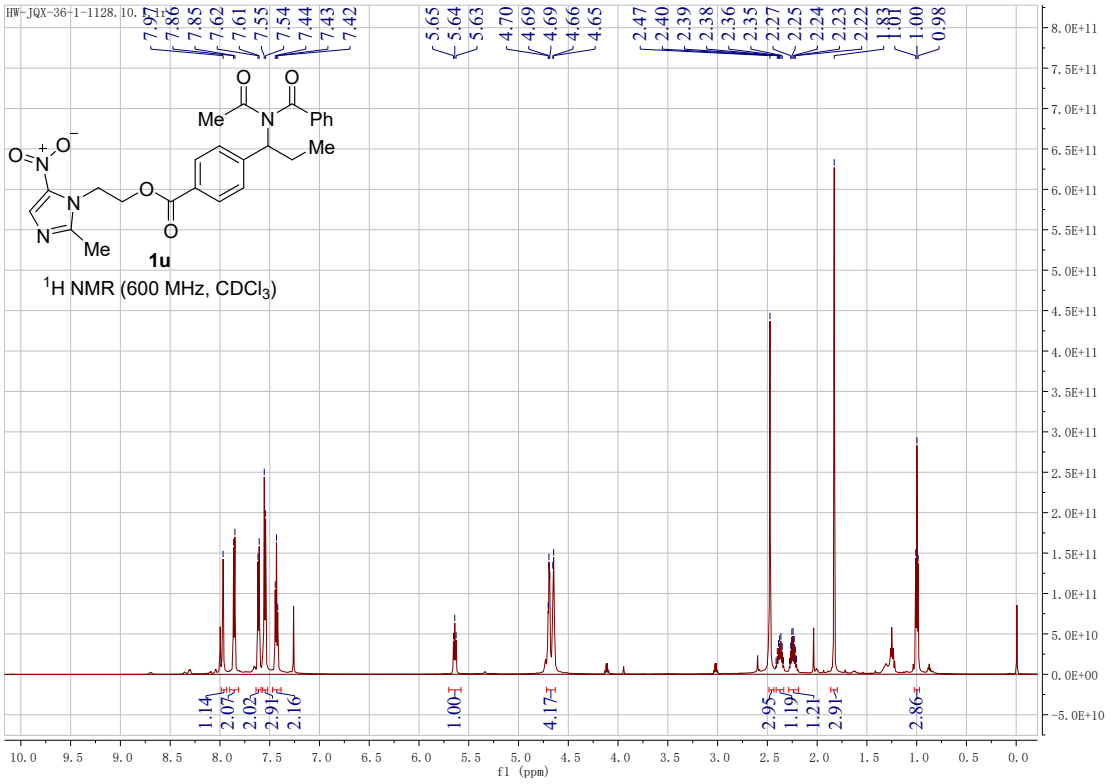


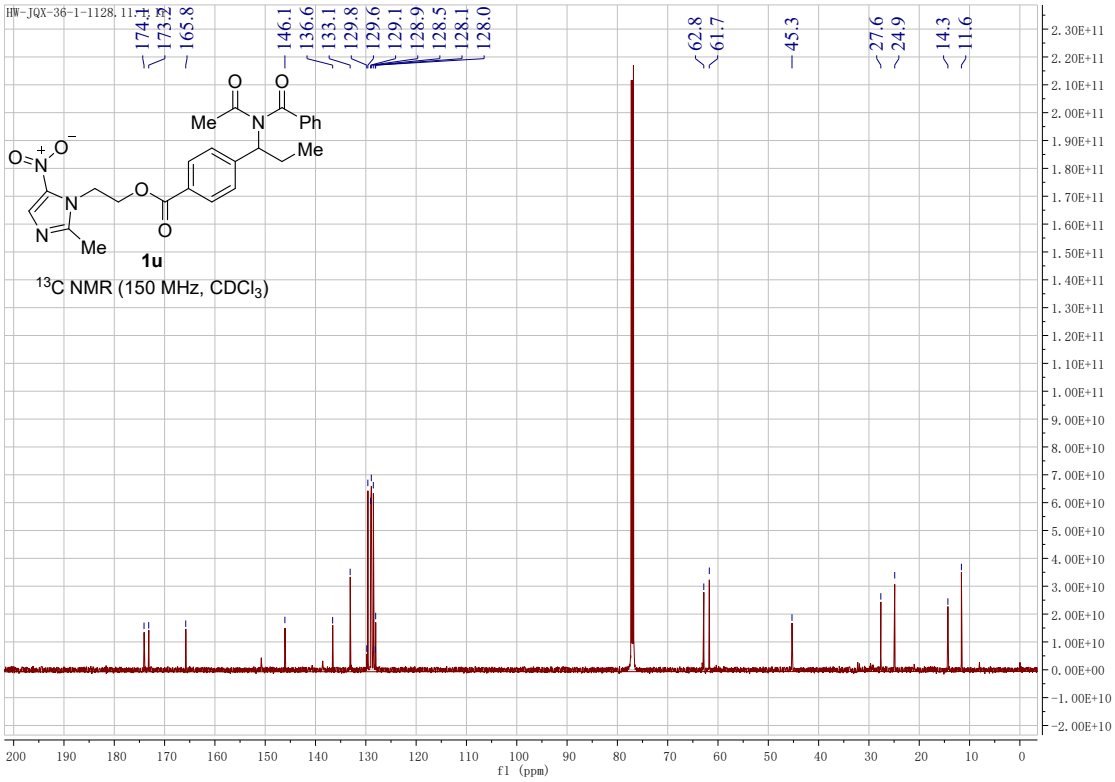
^{1}H and ^{13}C Spectrum for Compound 1t at 25 ℃



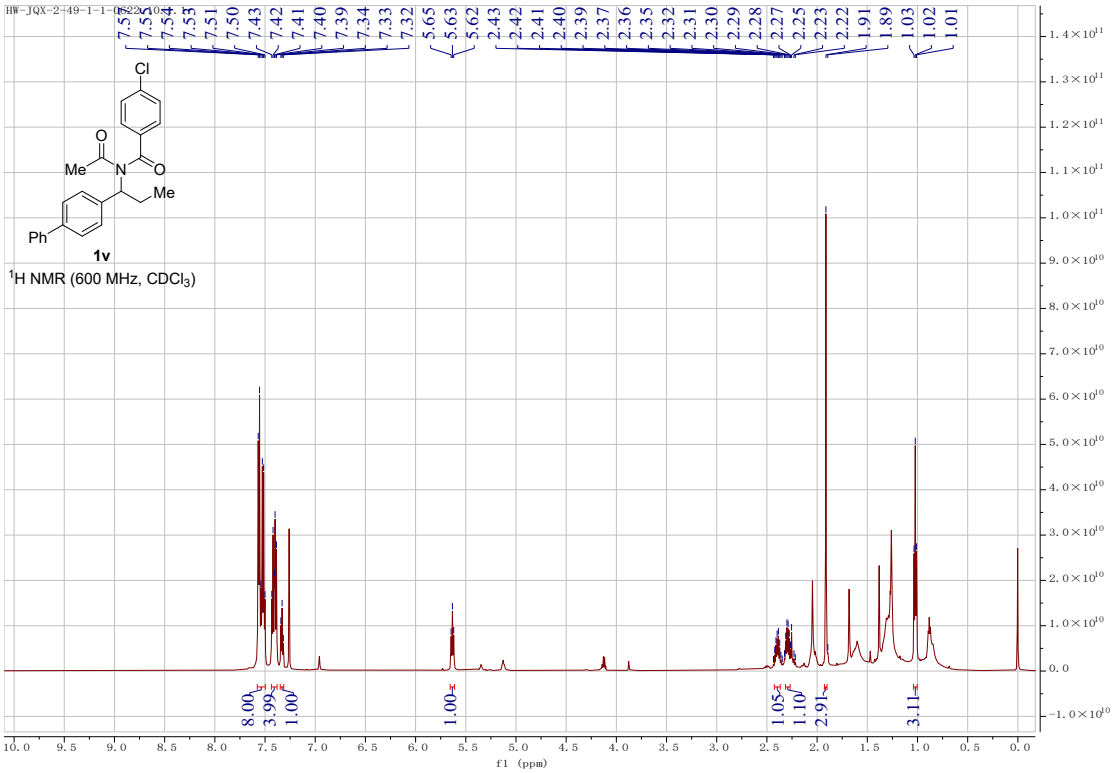


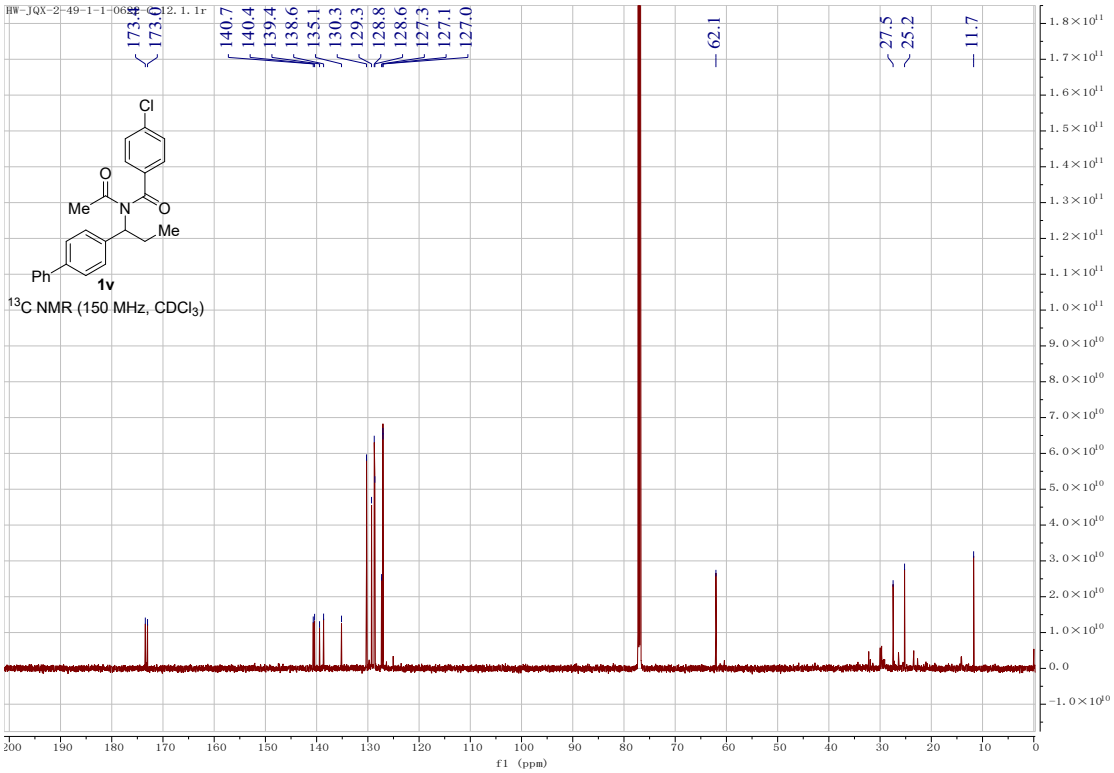
^{1}H and ^{13}C Spectrum for Compound 1u at 25 ℃



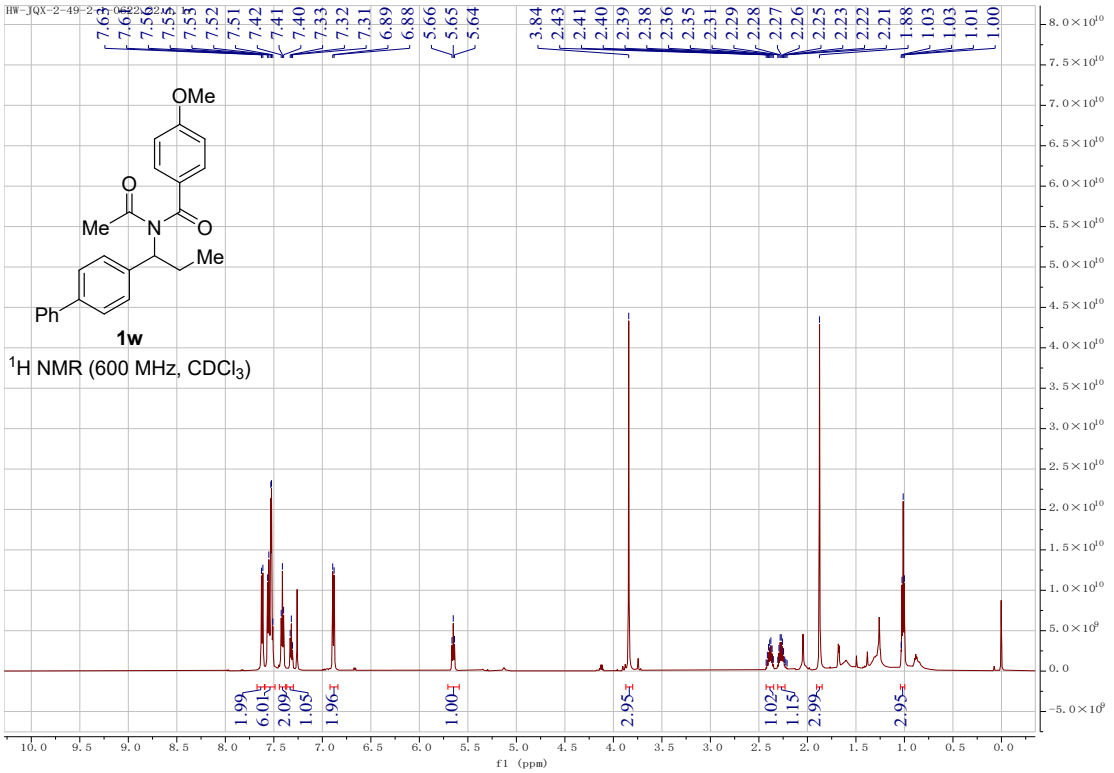


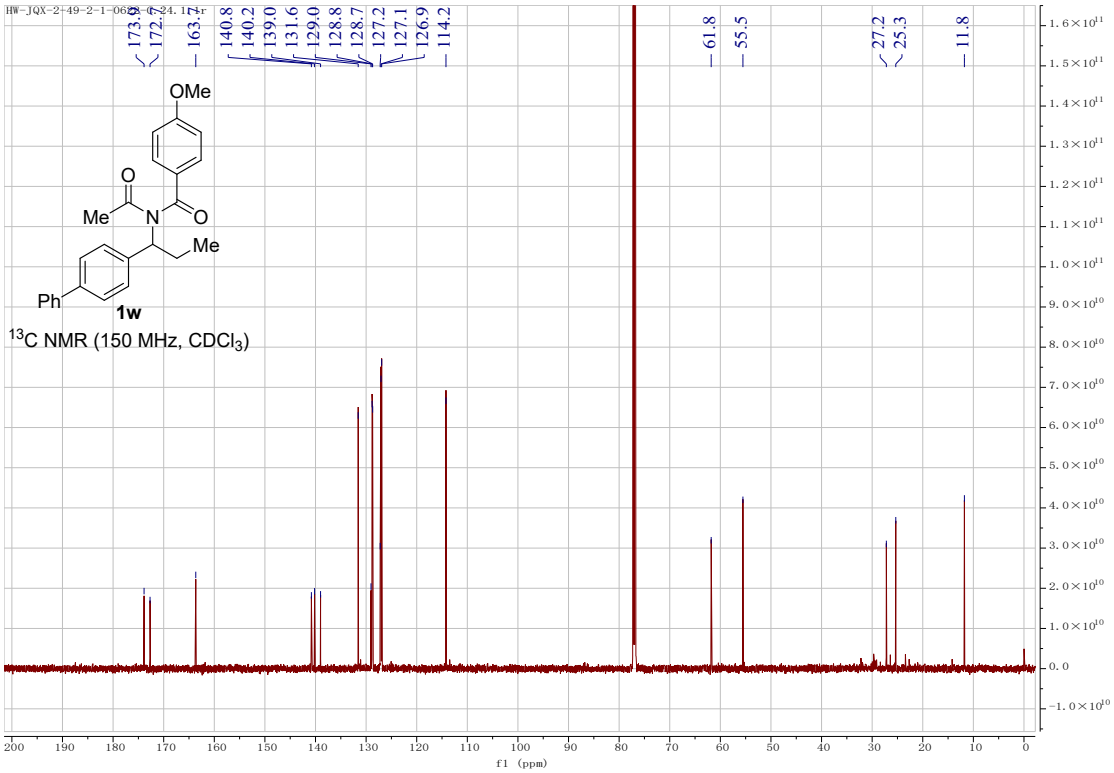
^{1}H and ^{13}C Spectrum for Compound 1v at 25 ℃



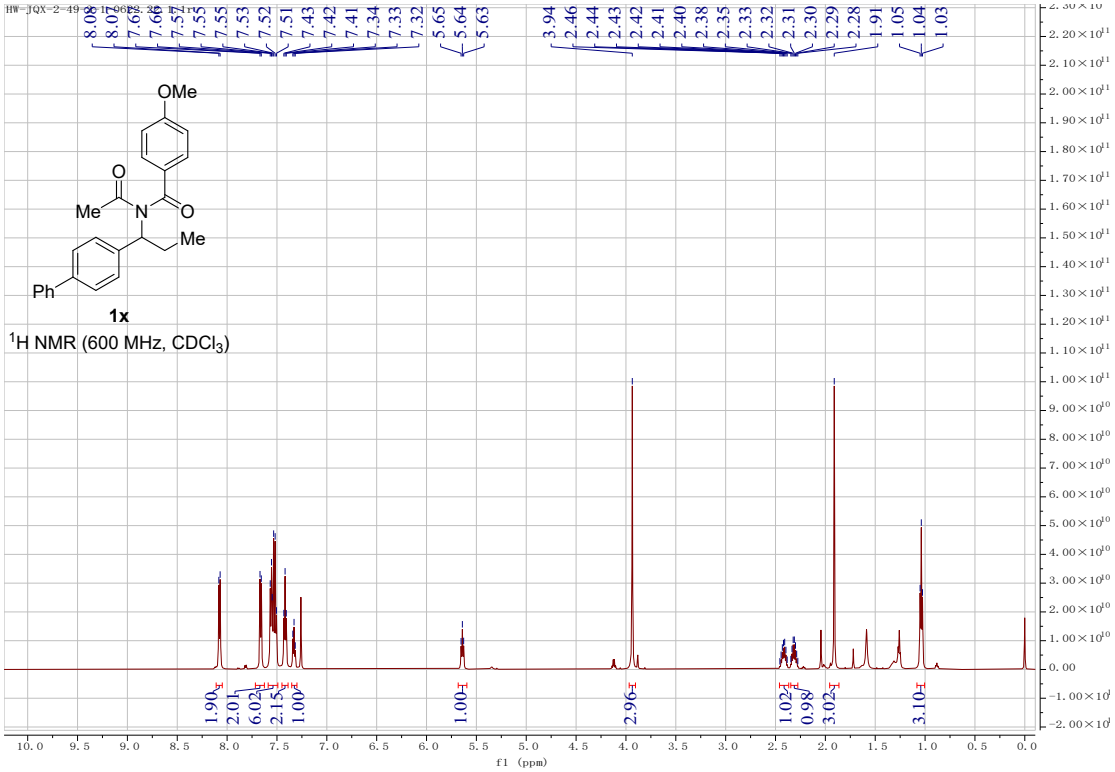


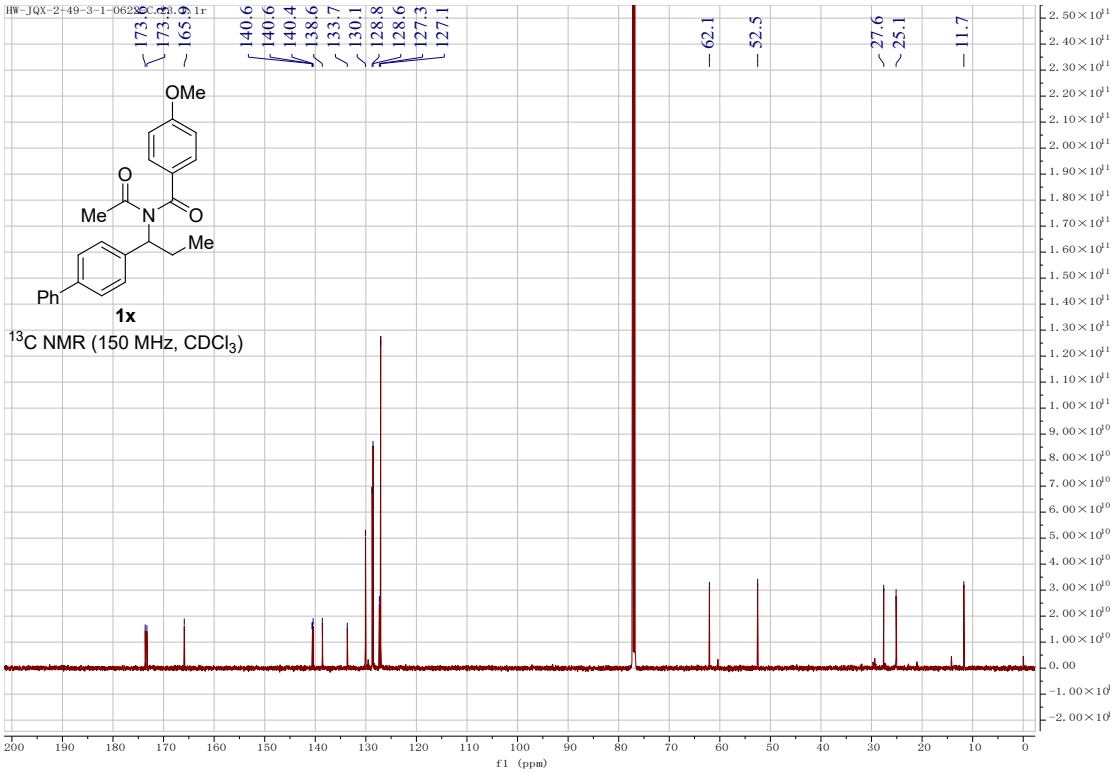
^{1}H and ^{13}C Spectrum for Compound 1w at 25 ℃



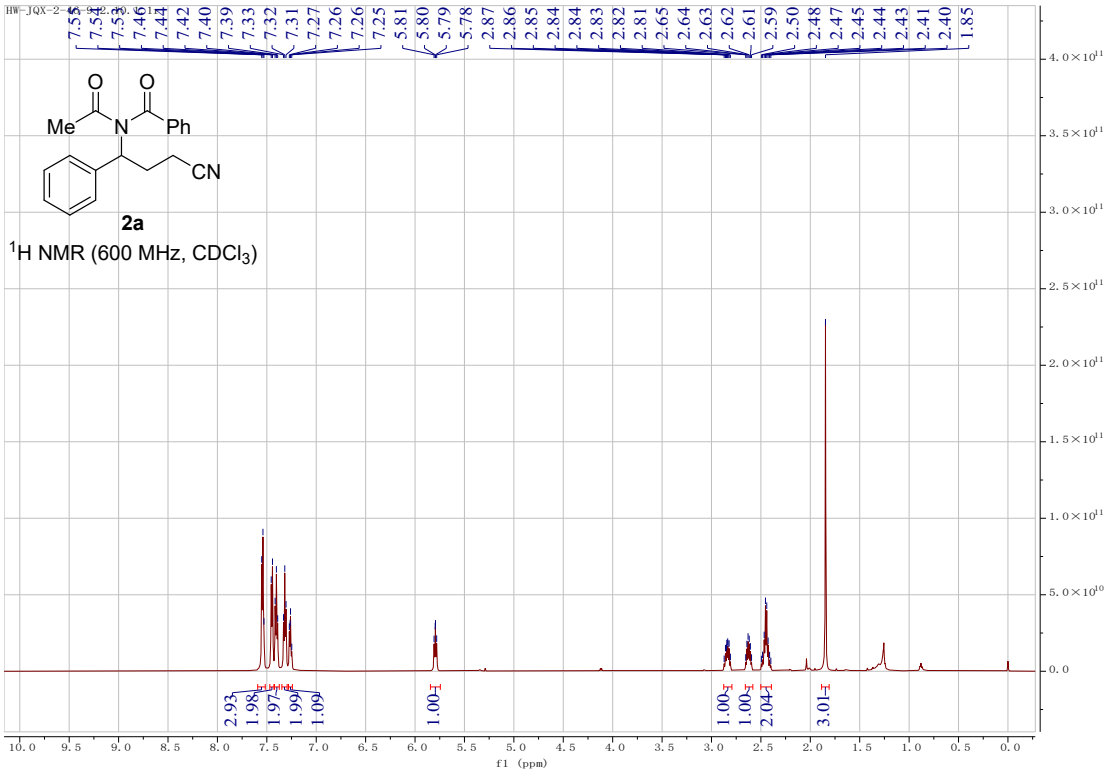


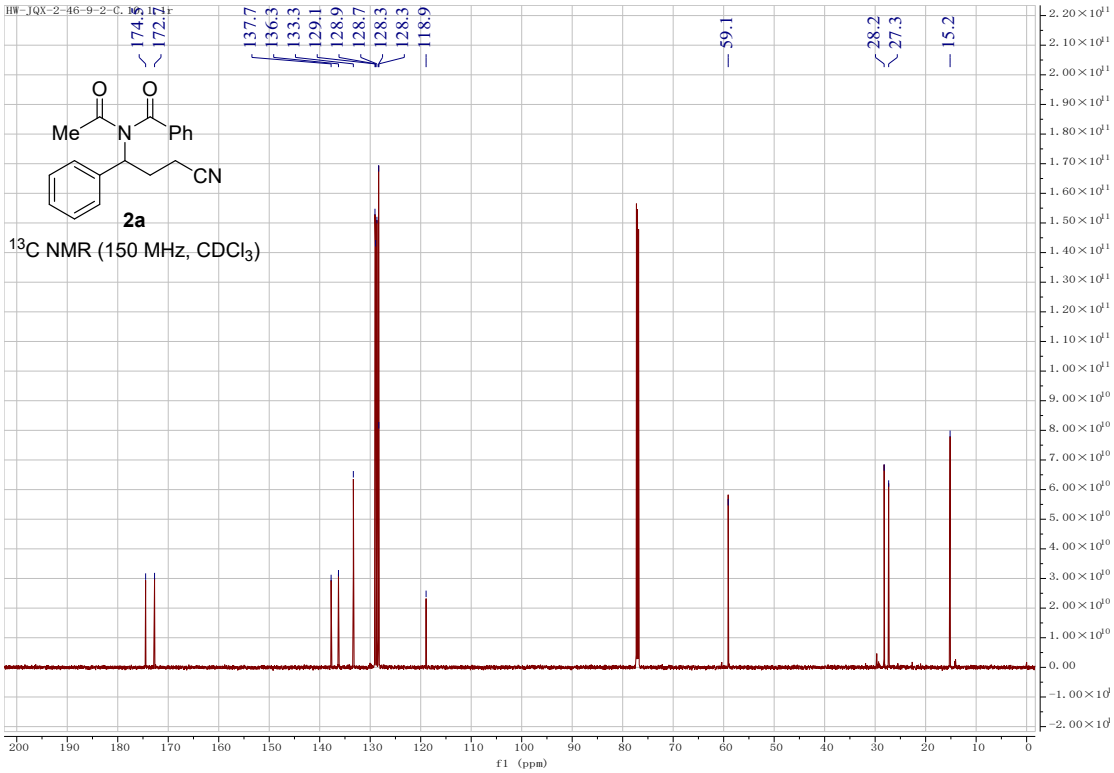
^{1}H and ^{13}C Spectrum for Compound 1x at 25 ℃



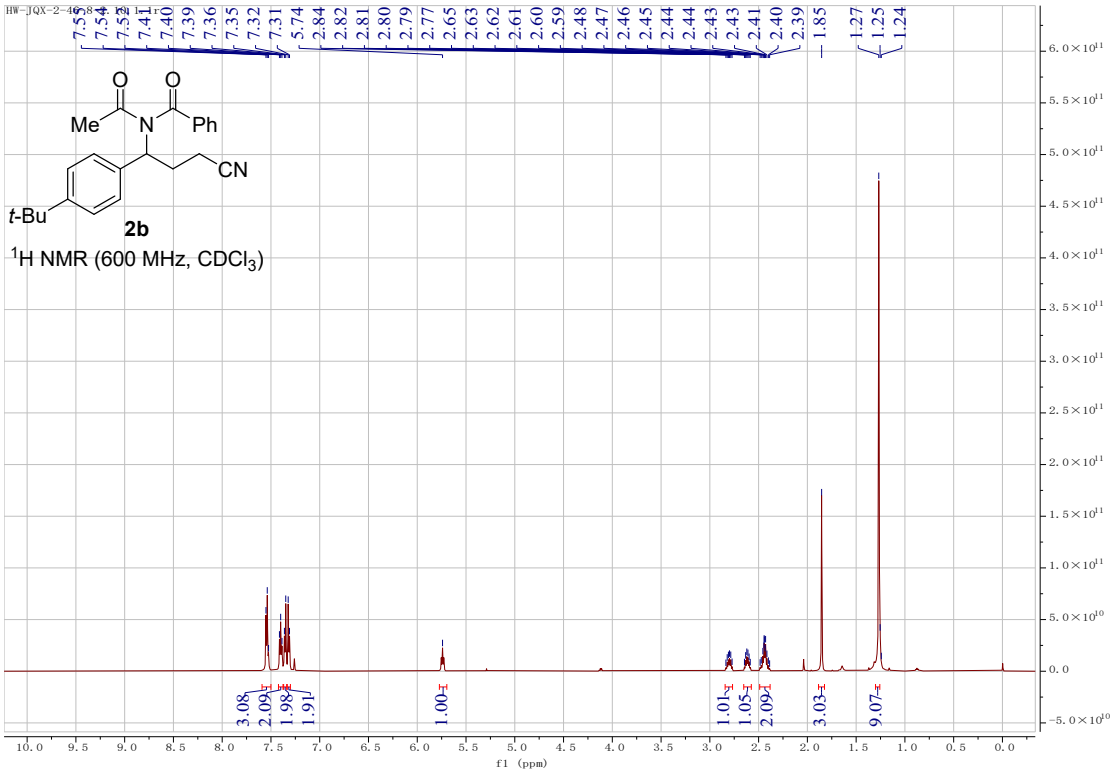


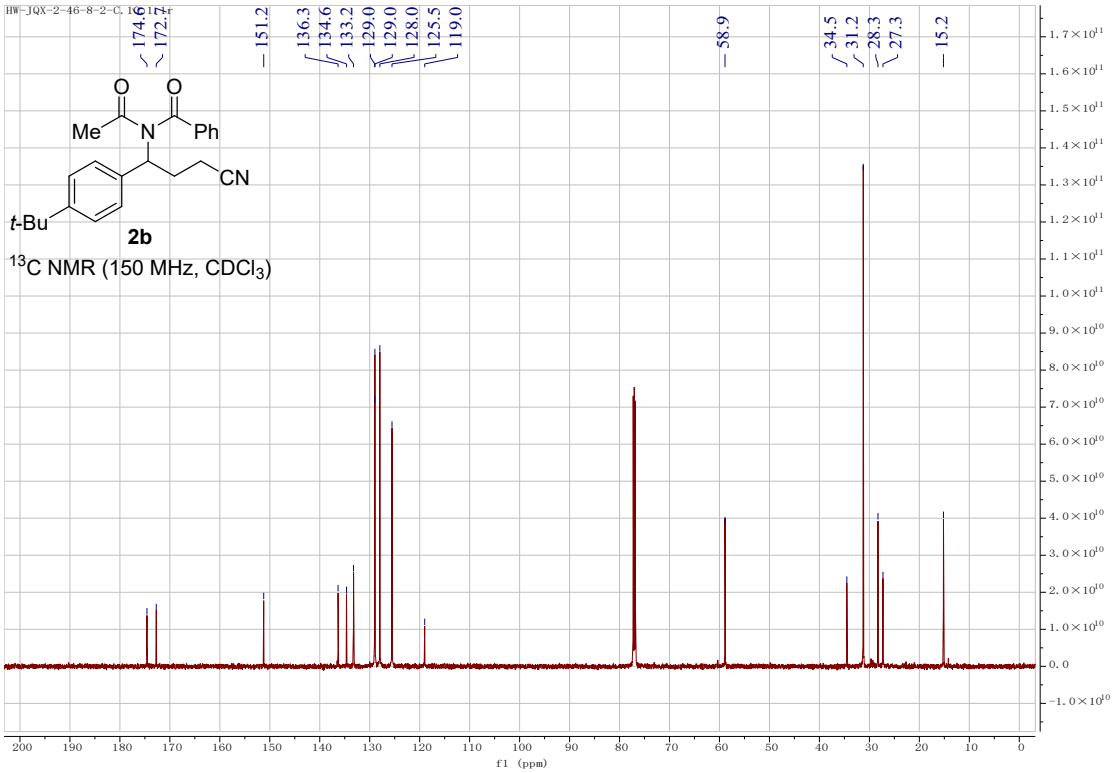
^{1}H and ^{13}C Spectrum for Compound 2a at 25 ℃



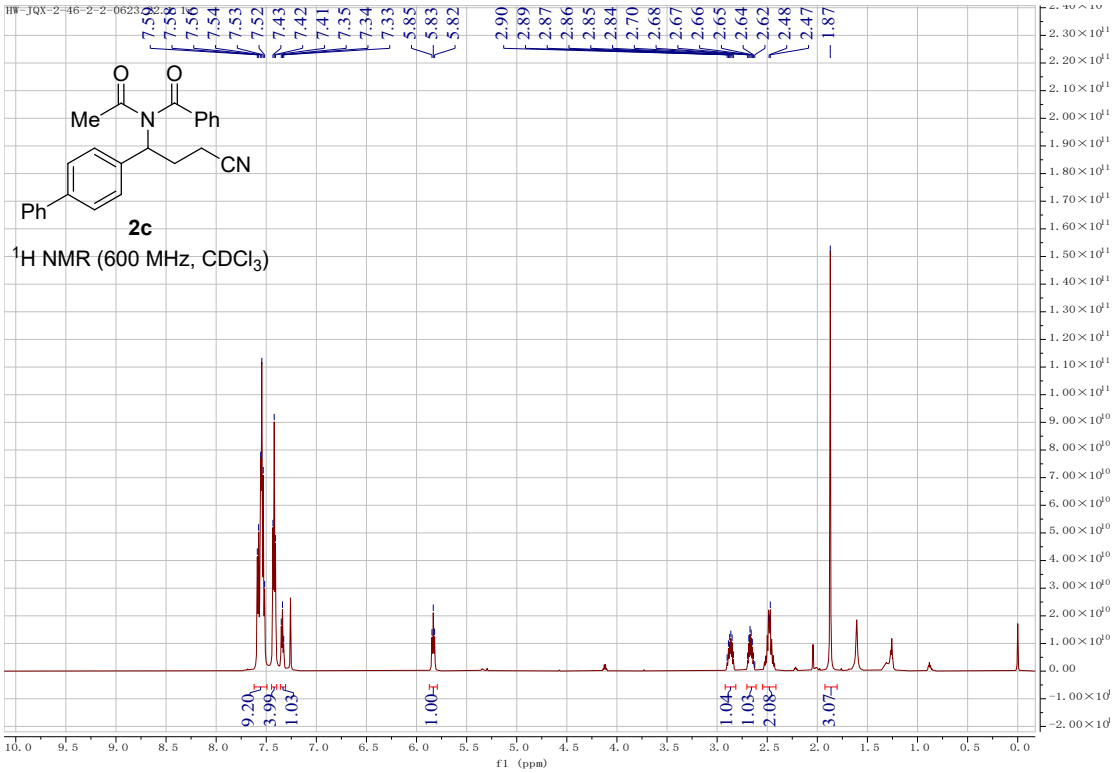


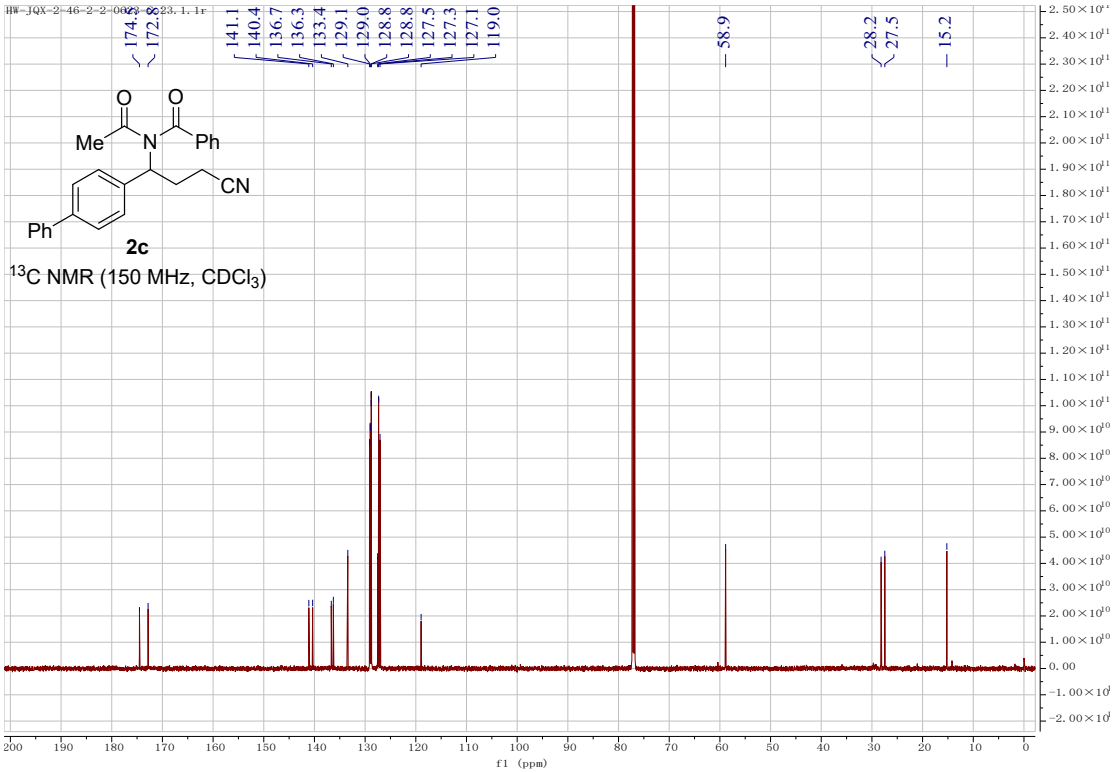
^{1}H and ^{13}C Spectrum for Compound 2b at 25 ℃



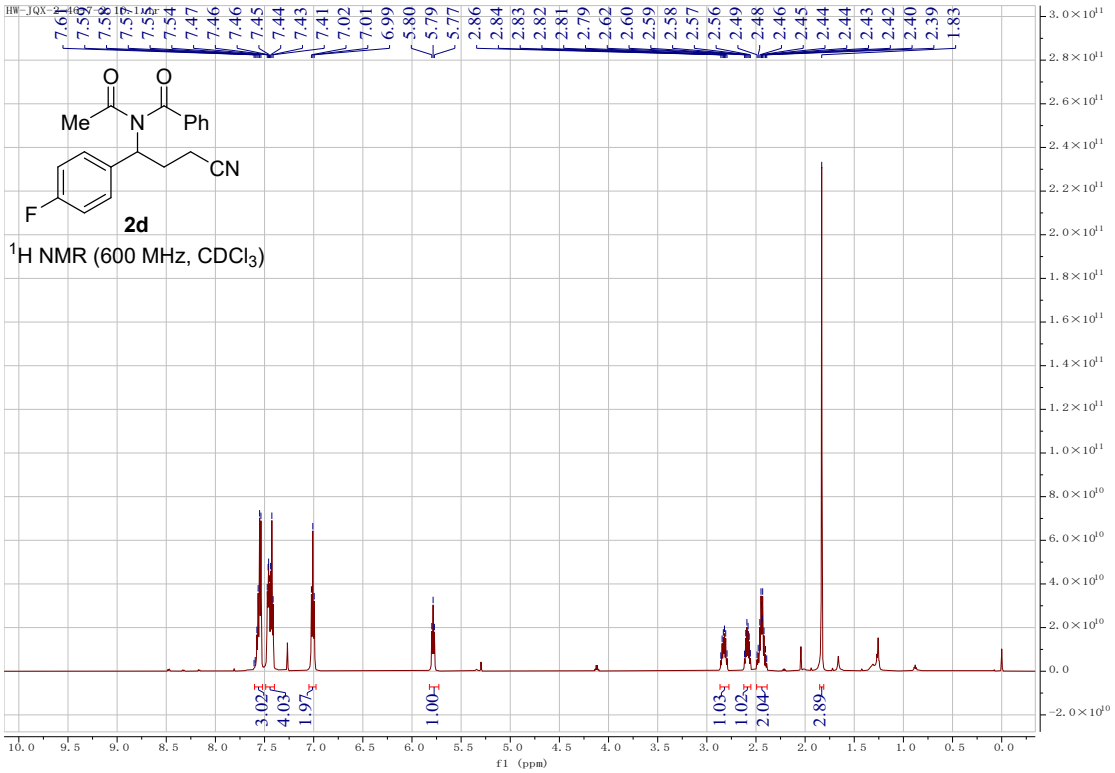


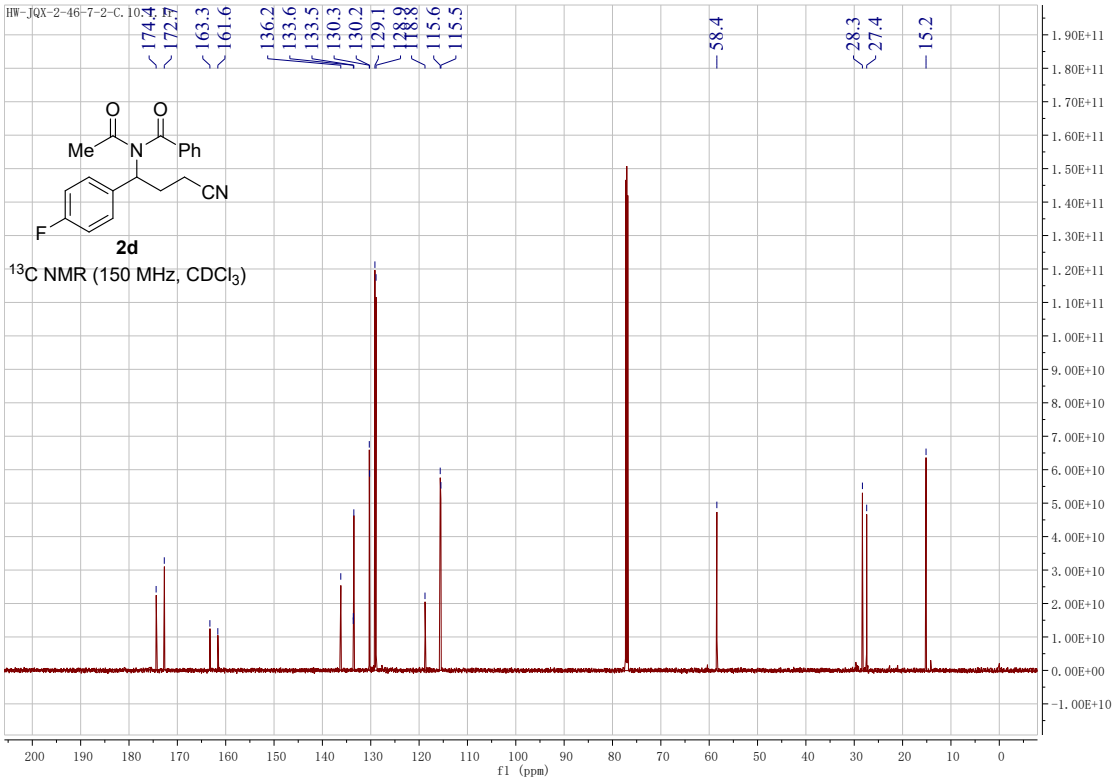
^{1}H and ^{13}C Spectrum for Compound 2c at 25 ℃



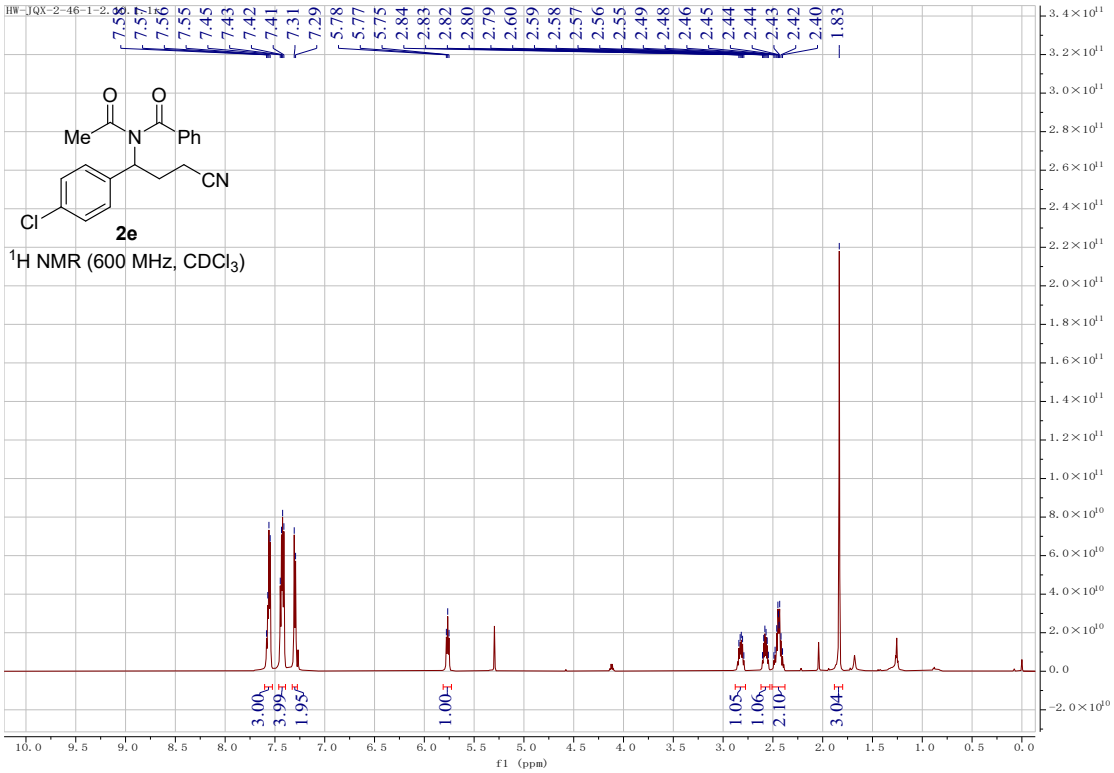


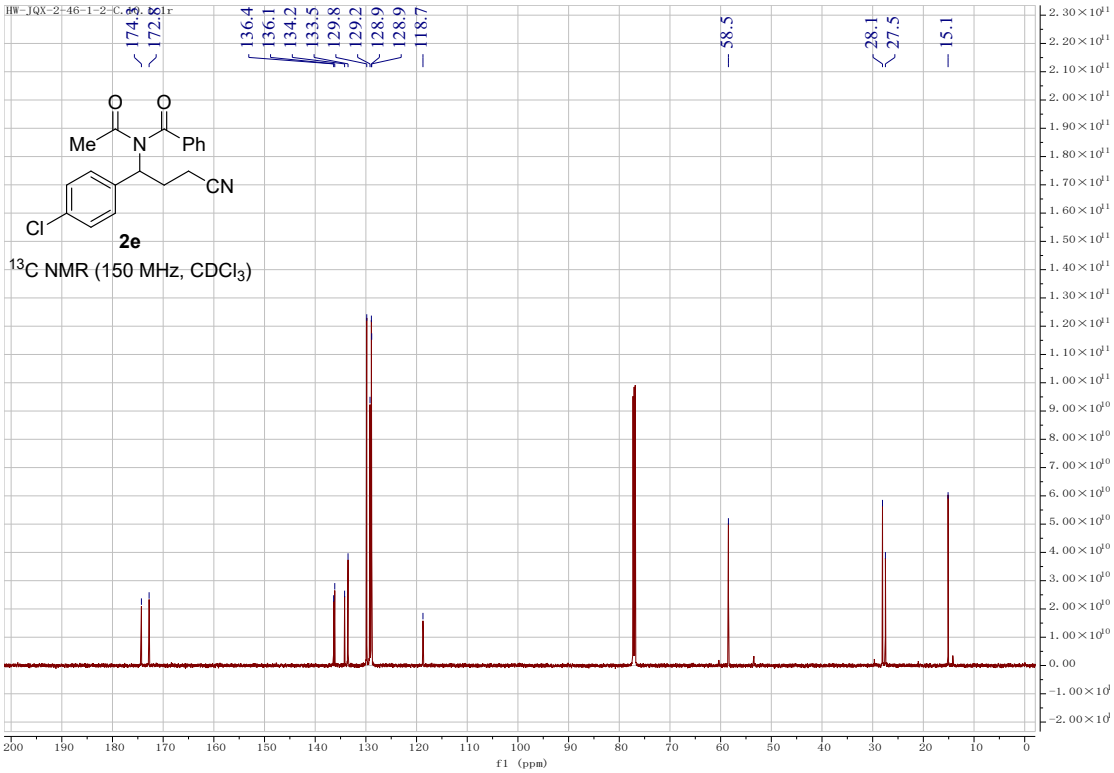
^{1}H and ^{13}C Spectrum for Compound 2d at 25 ℃



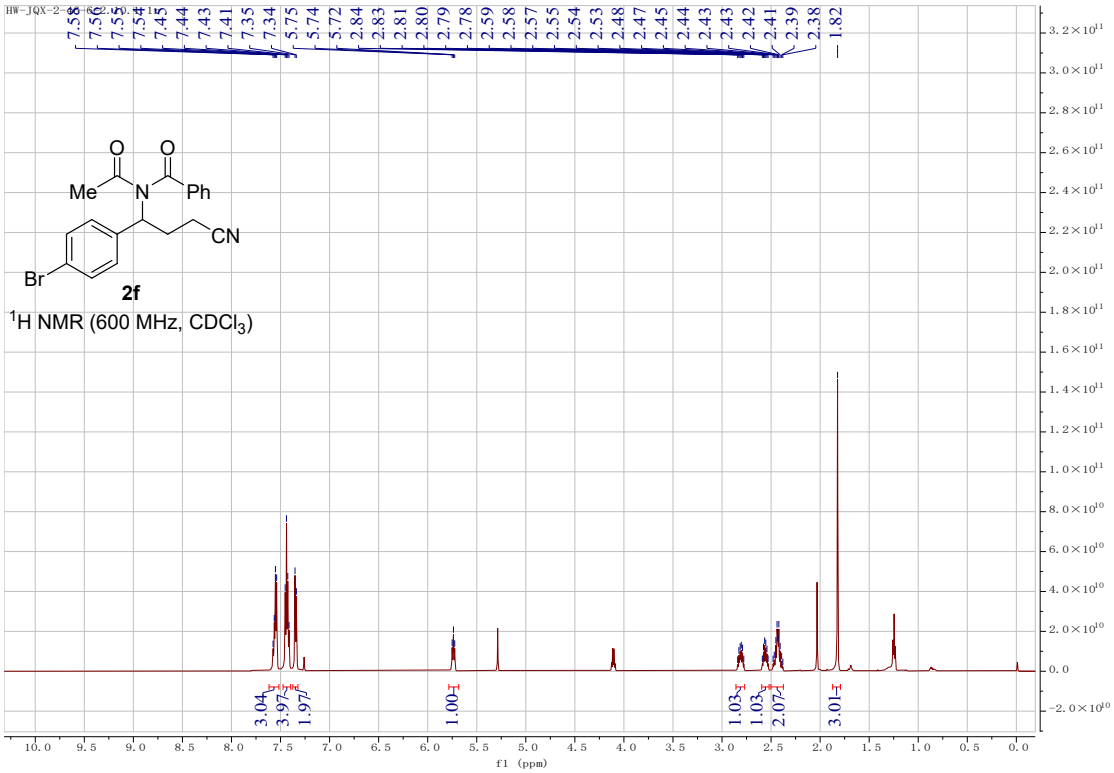


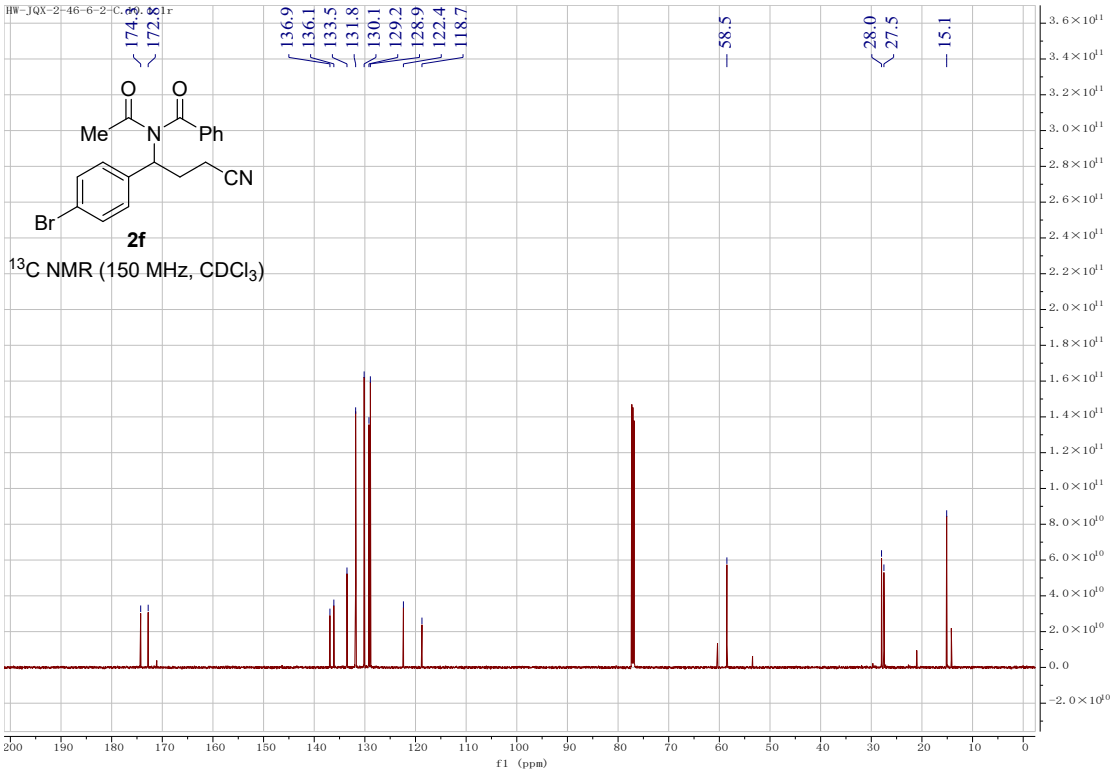
^{1}H and ^{13}C Spectrum for Compound 2e at 25 ℃



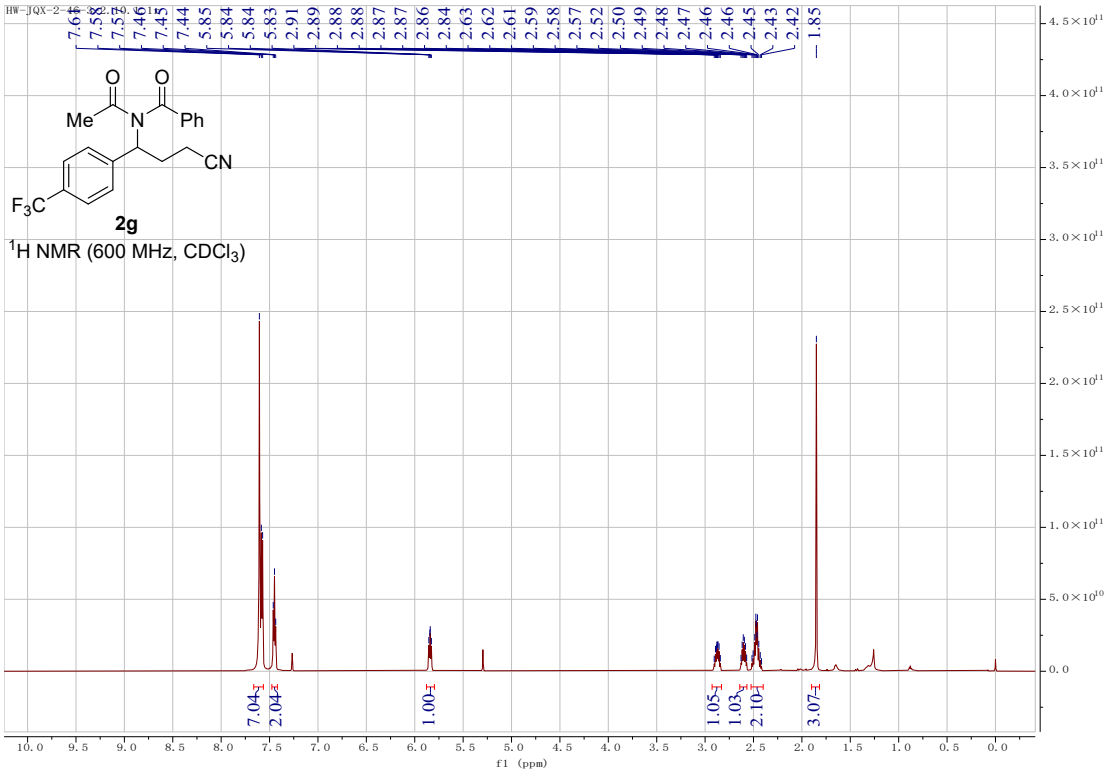


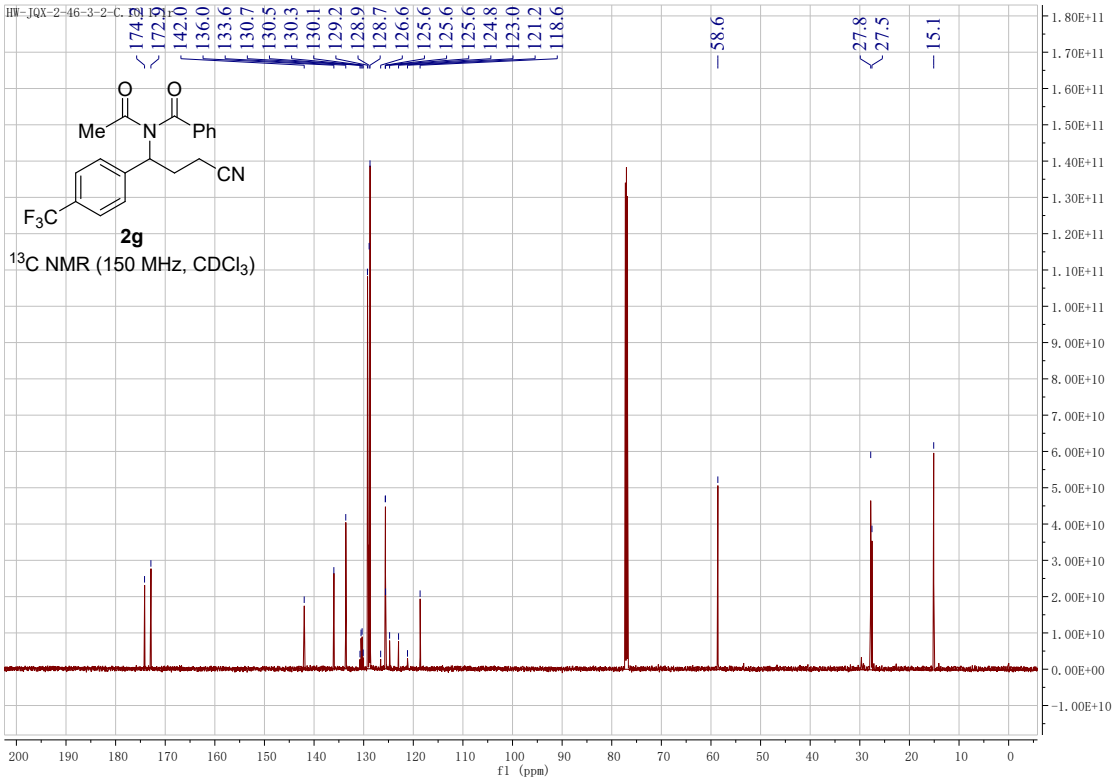
^{1}H and ^{13}C Spectrum for Compound 2f at 25 ℃



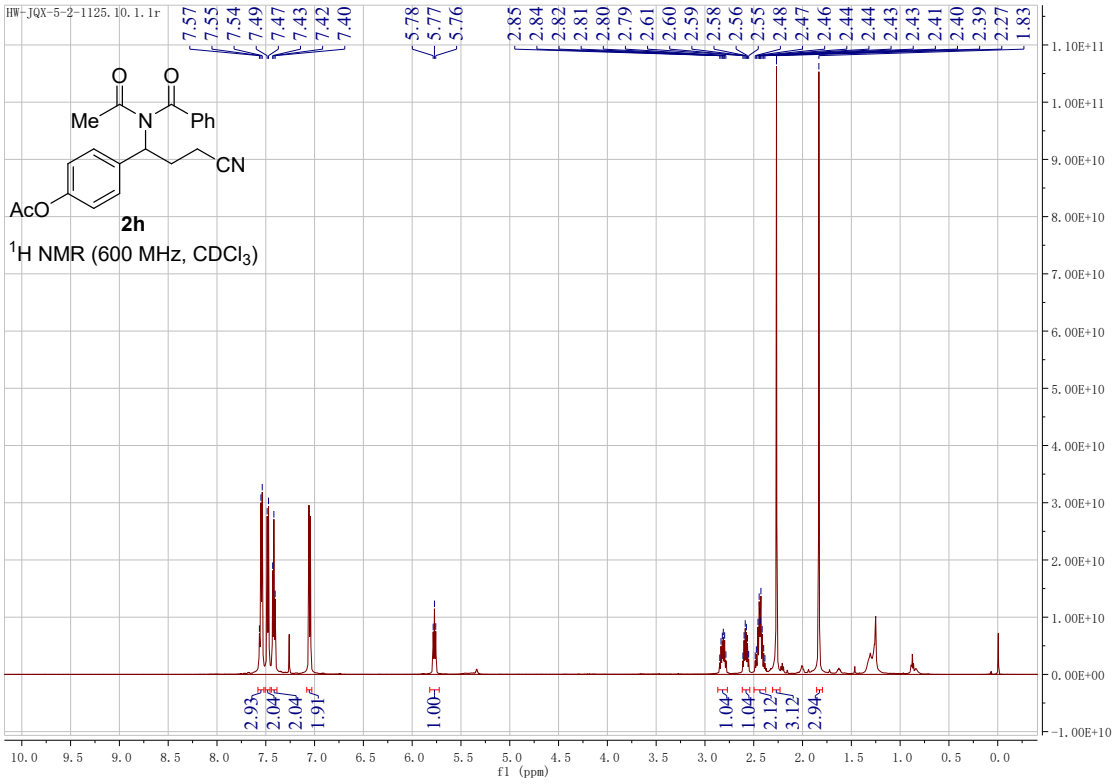


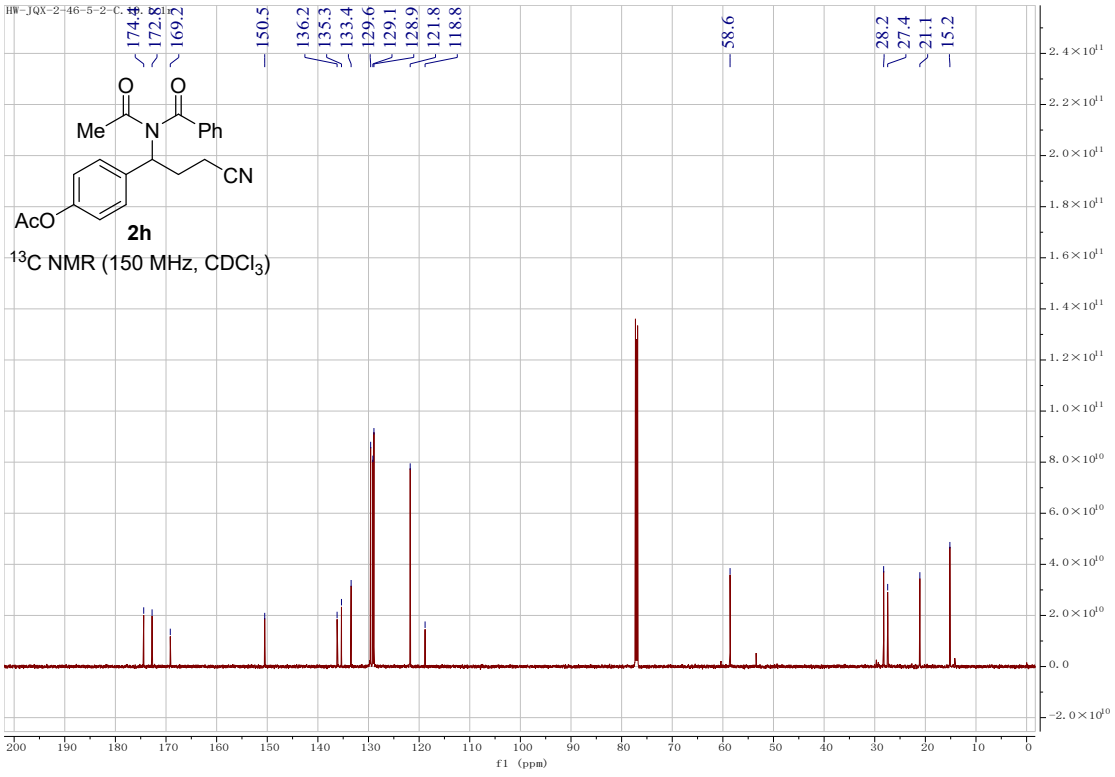
^{1}H and ^{13}C Spectrum for Compound 2g at 25 ℃



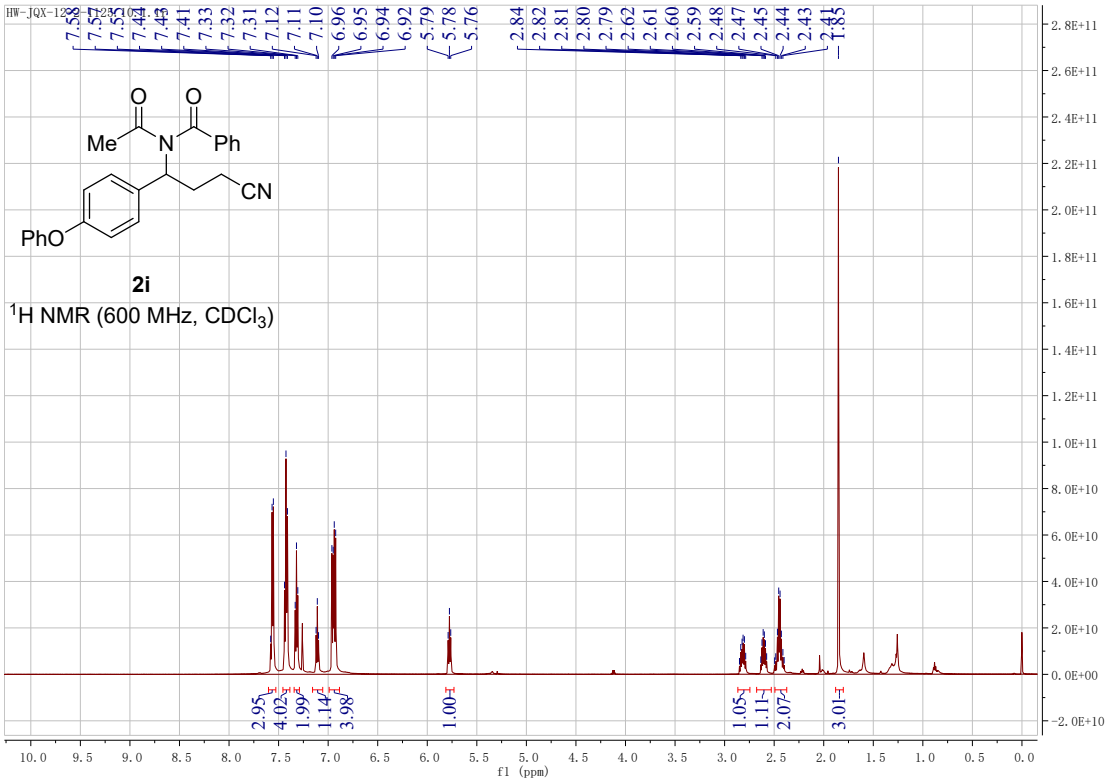


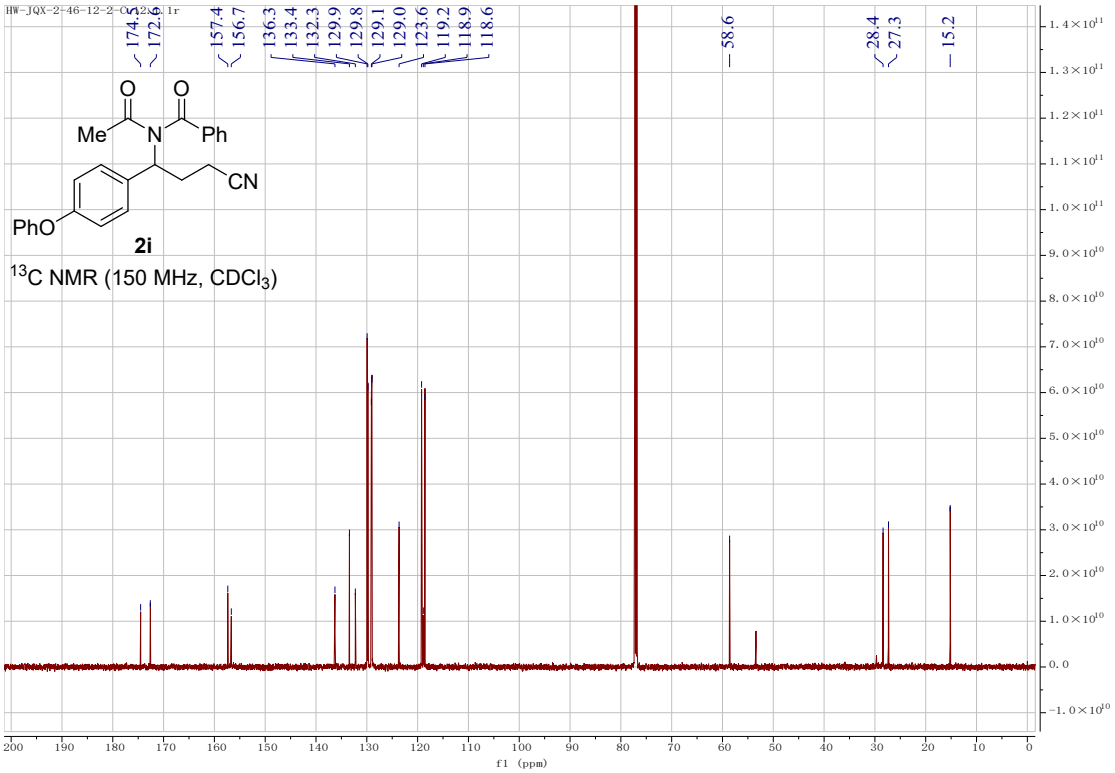
^{1}H and ^{13}C Spectrum for Compound 2h at 25 ℃



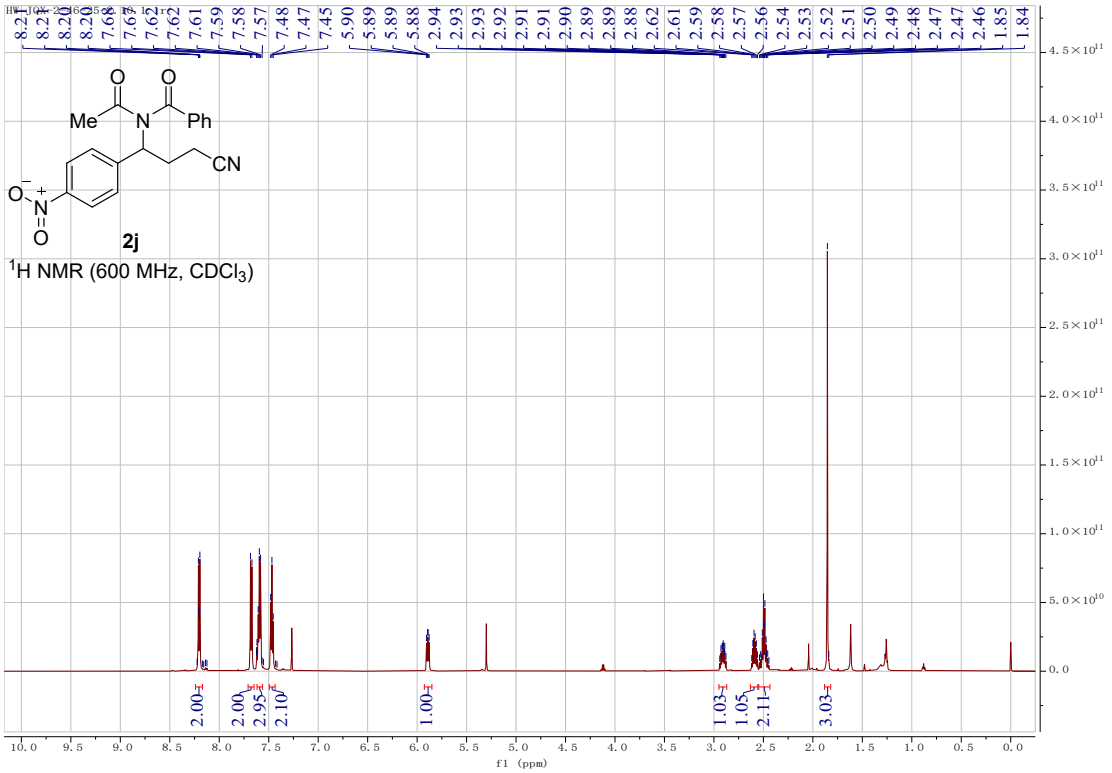


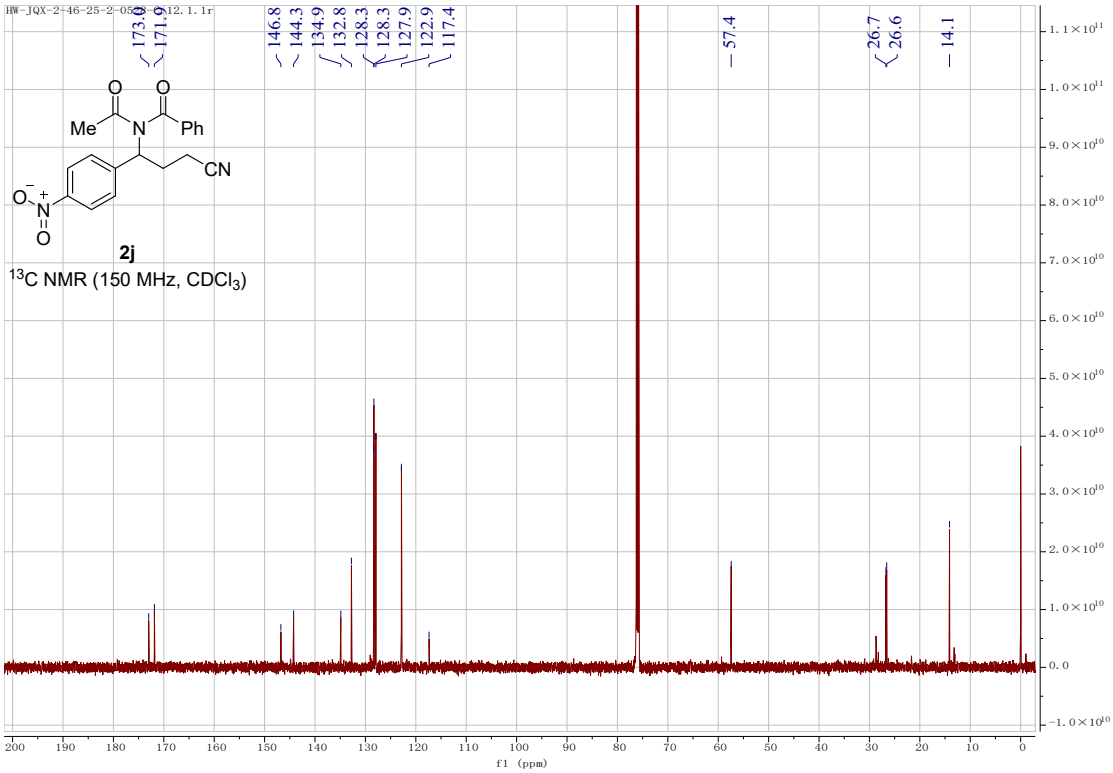
^{1}H and ^{13}C Spectrum for Compound 2i at 25 ℃



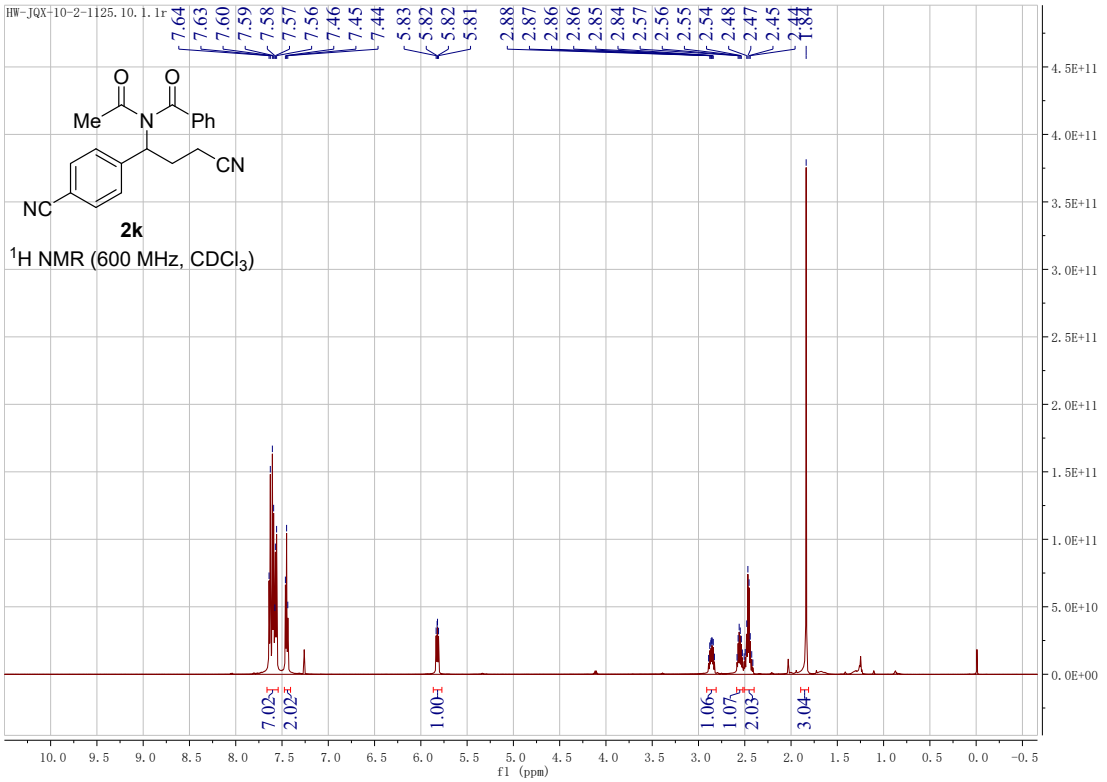


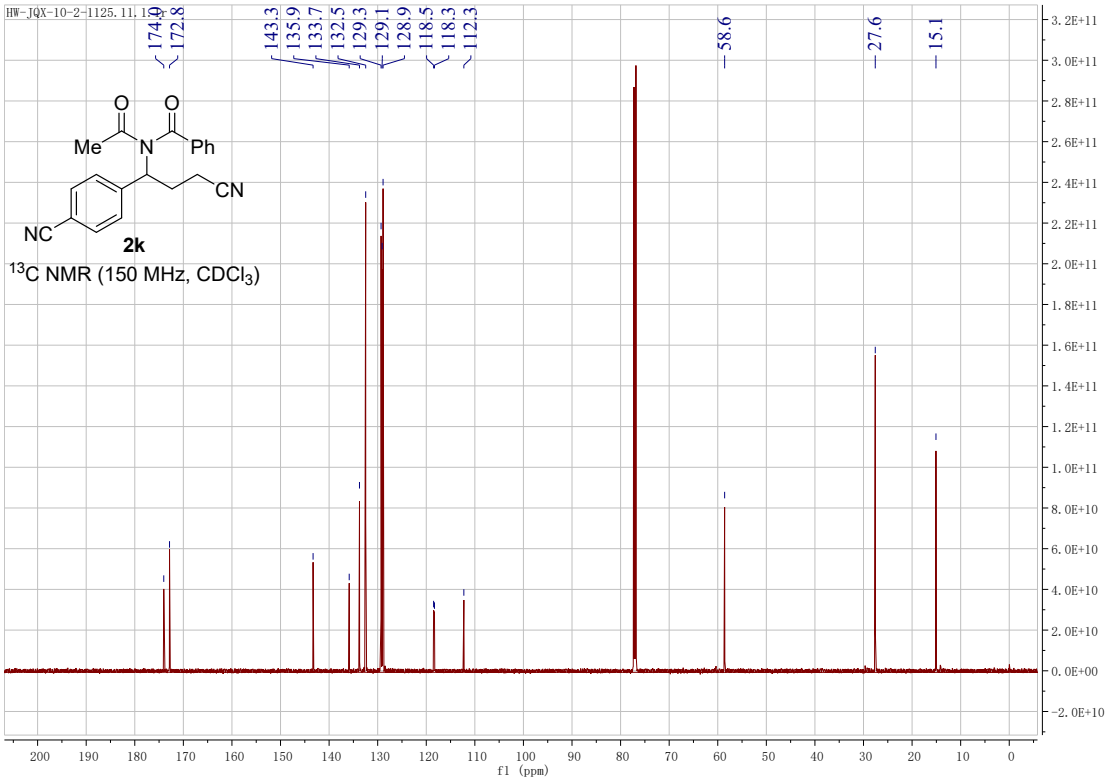
^{1}H and ^{13}C Spectrum for Compound 2j at 25 ℃



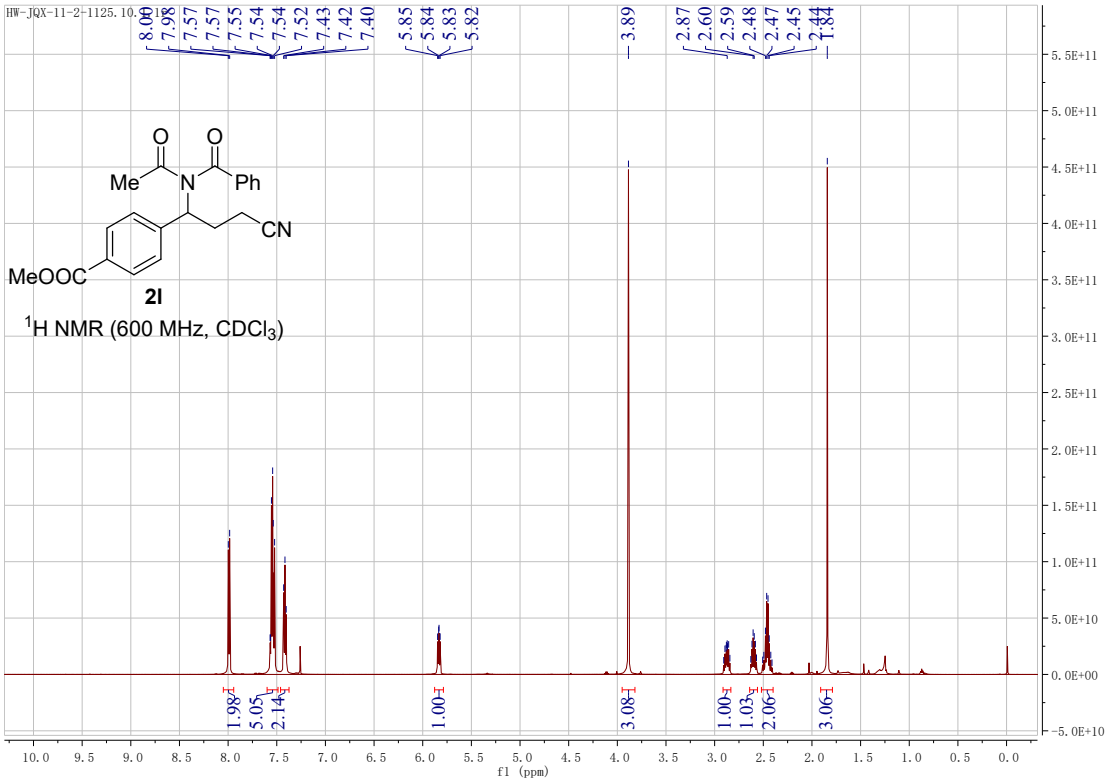


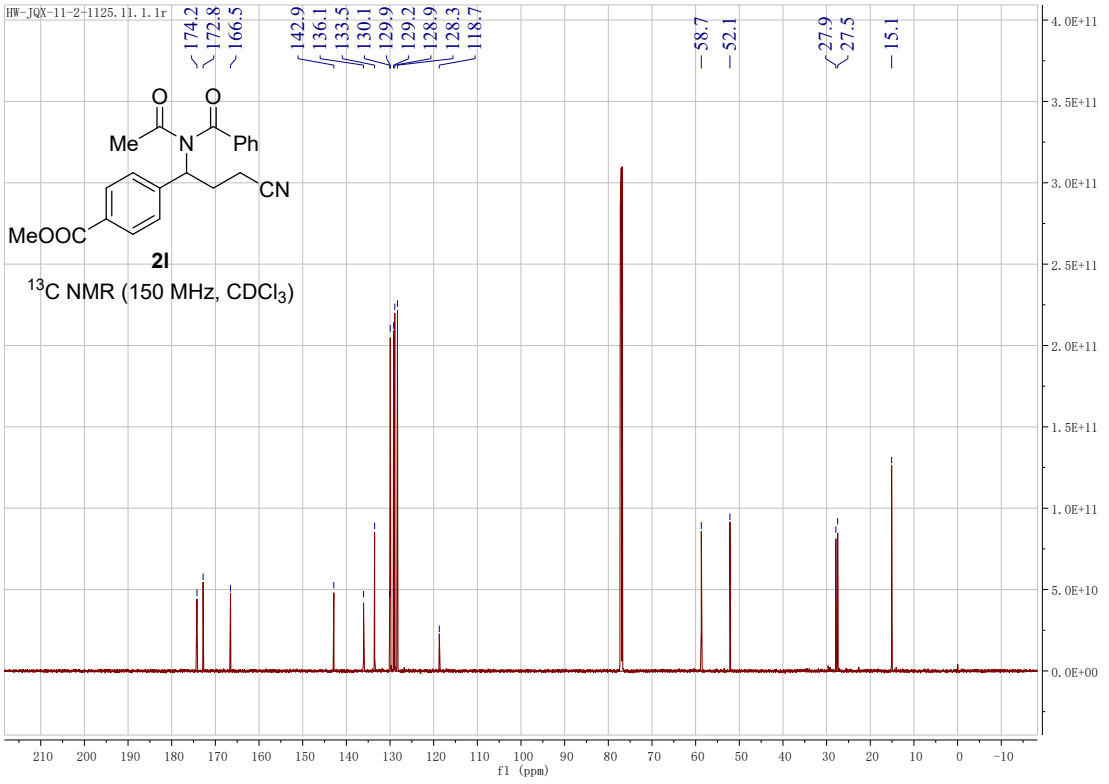
^{1}H and ^{13}C Spectrum for Compound 2k at 25 ℃



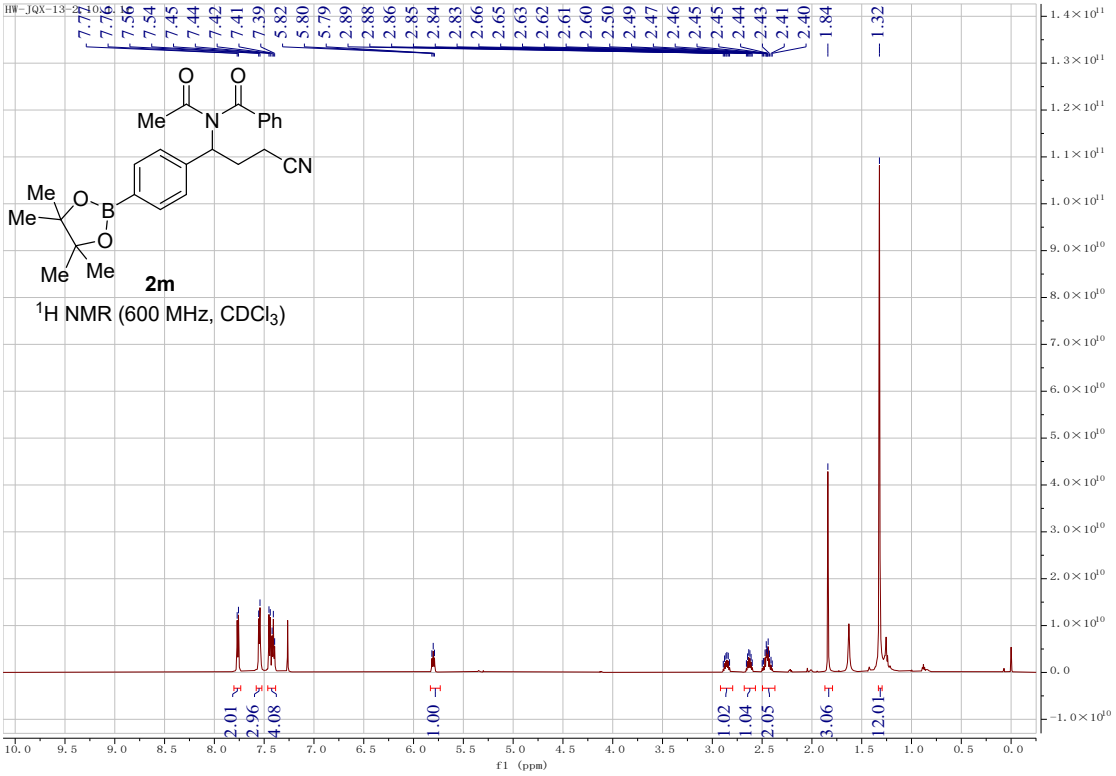


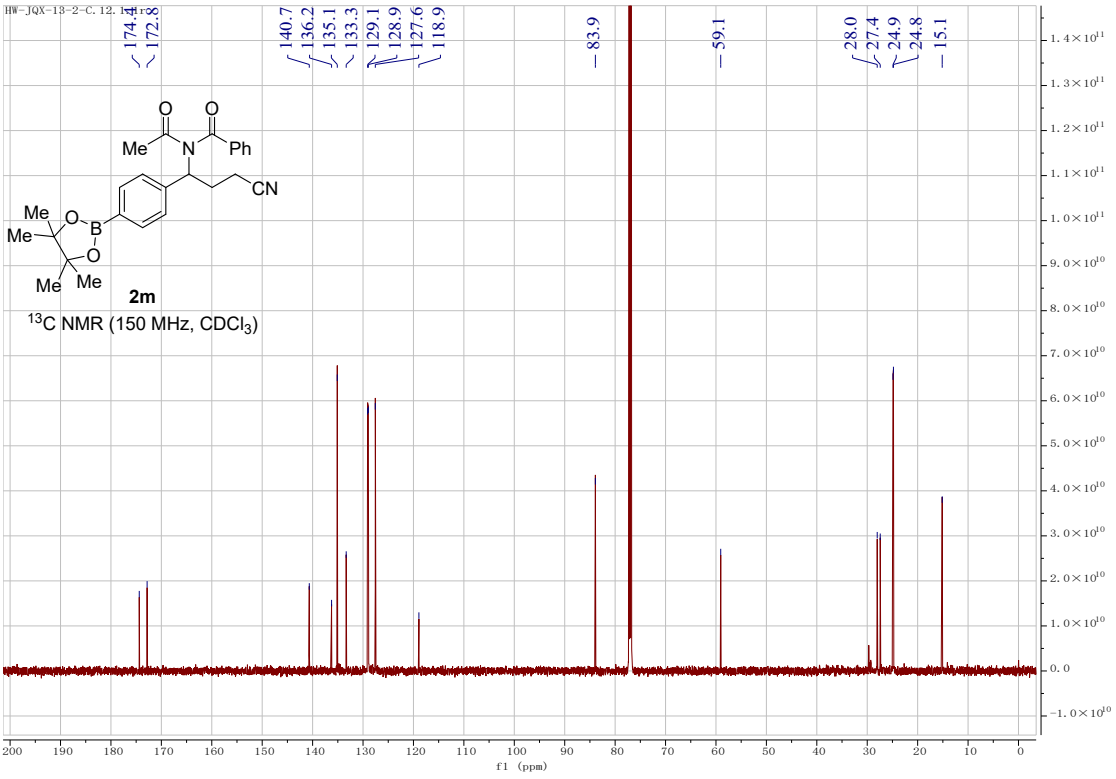
^{1}H and ^{13}C Spectrum for Compound 2l at 25 ℃



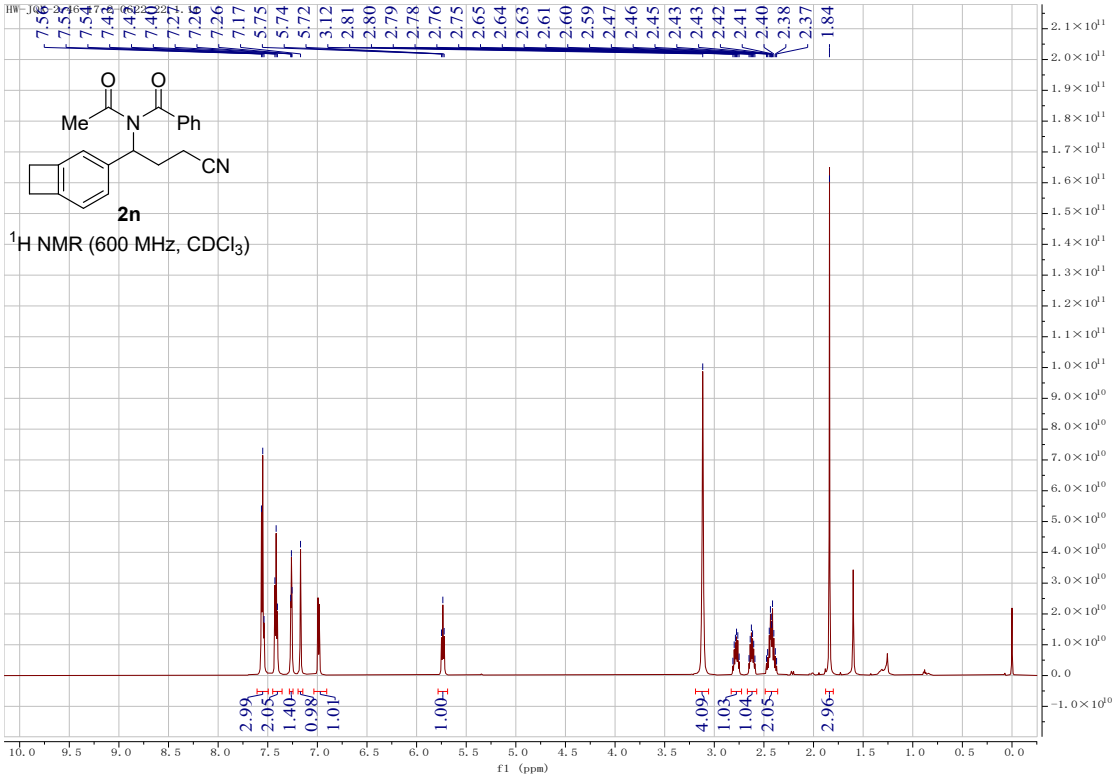


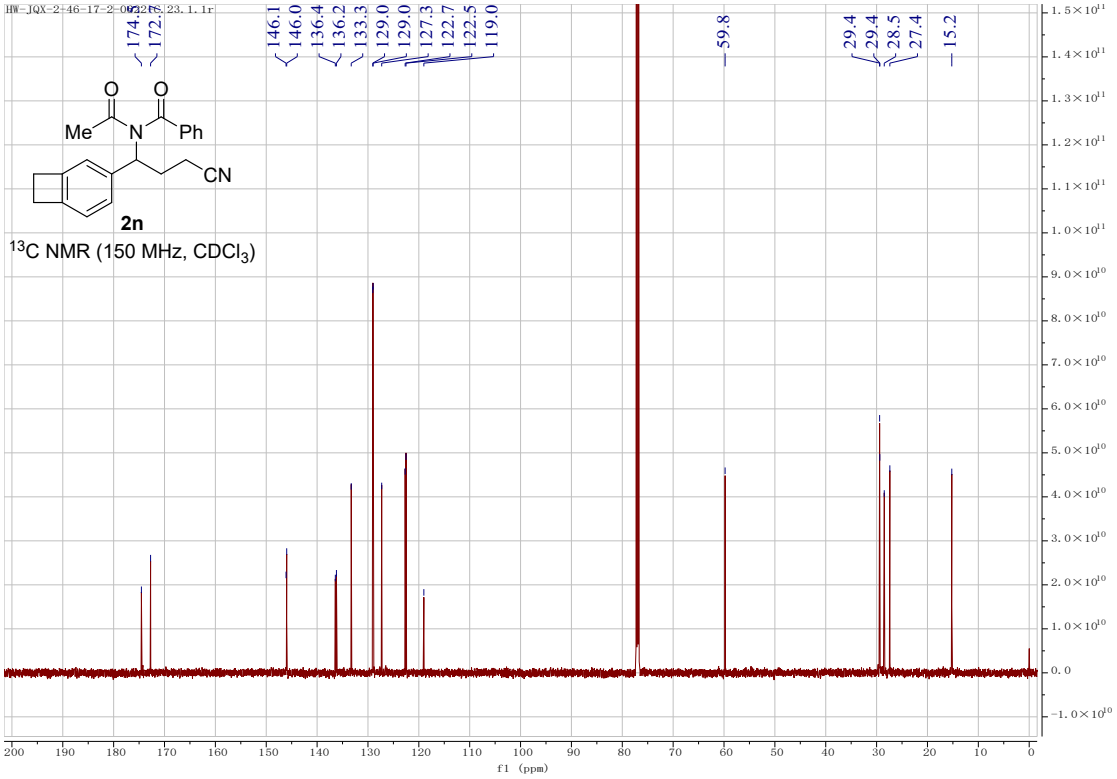
^{1}H and ^{13}C Spectrum for Compound 2m at 25 ℃



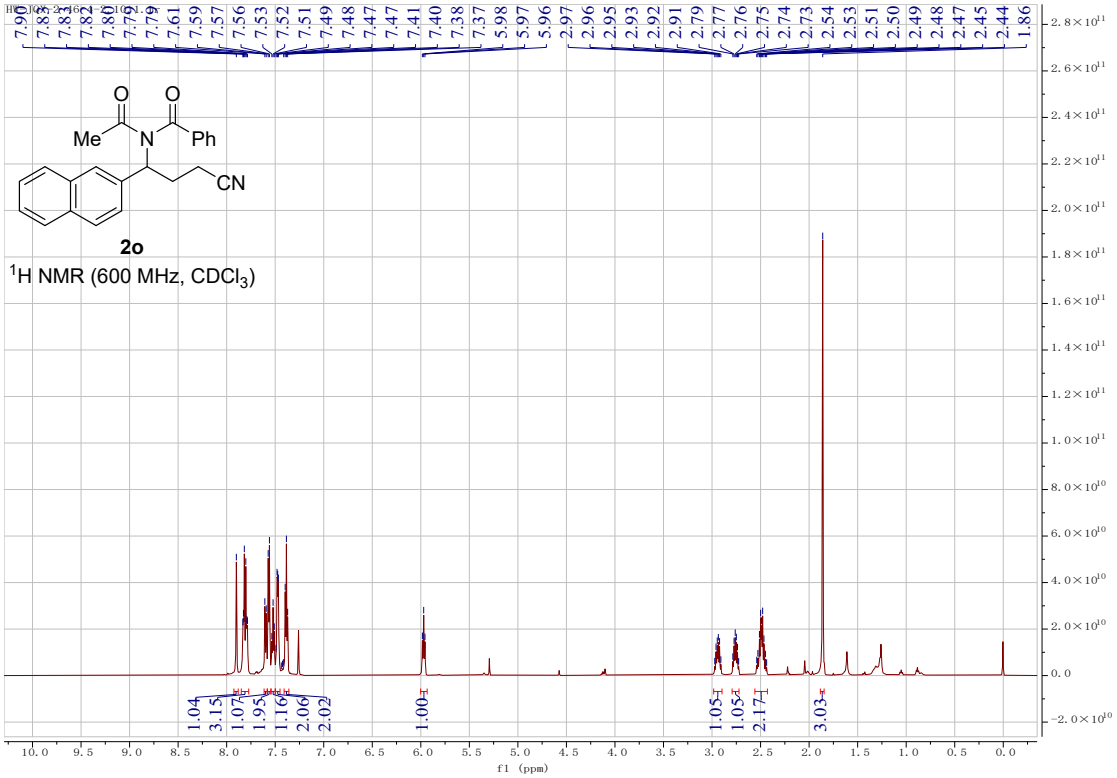


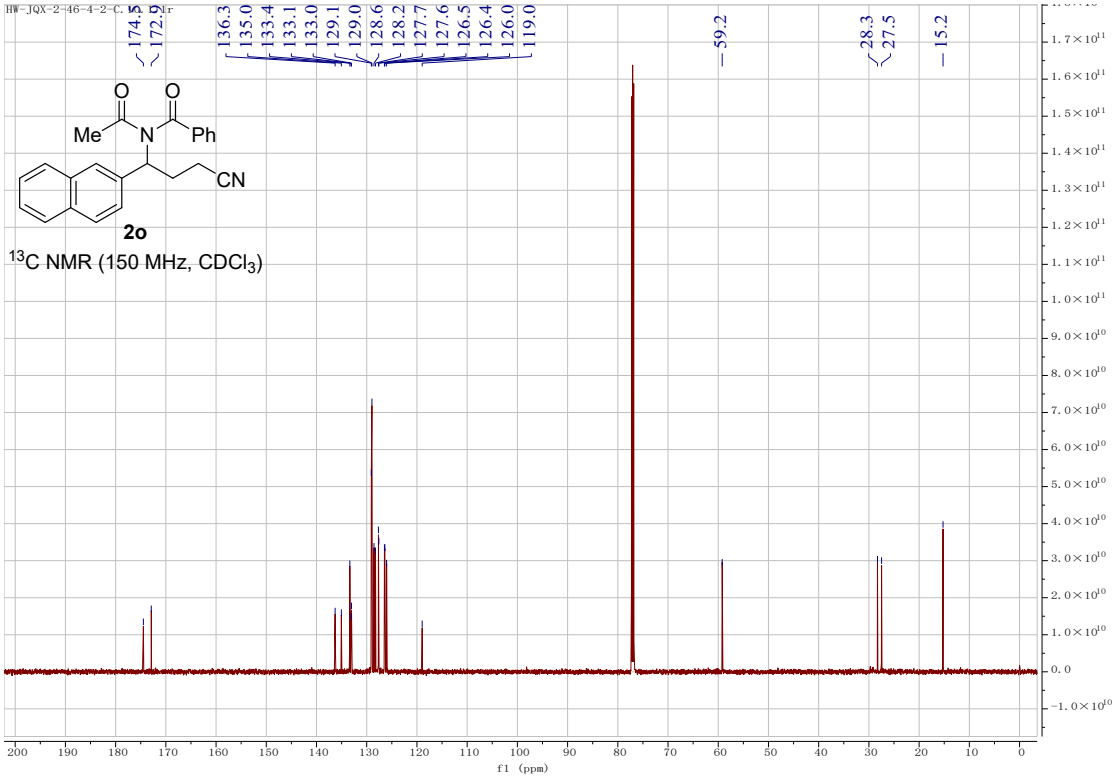
^{1}H and ^{13}C Spectrum for Compound 2n at 25 ℃



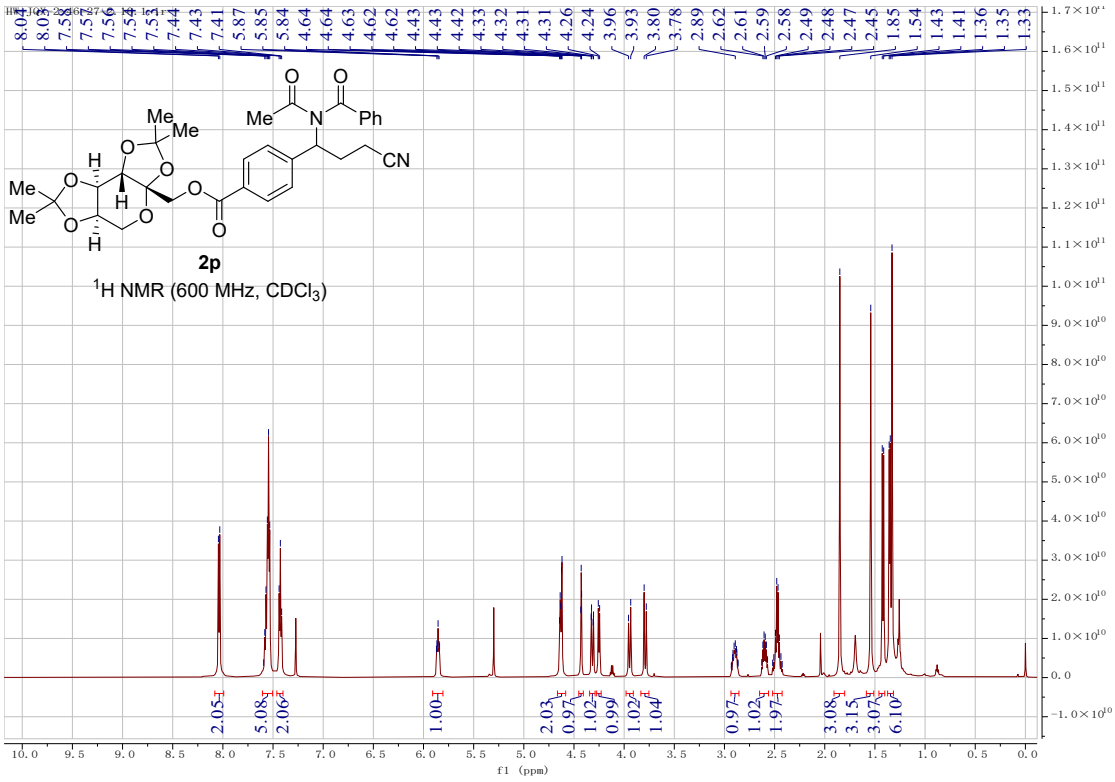


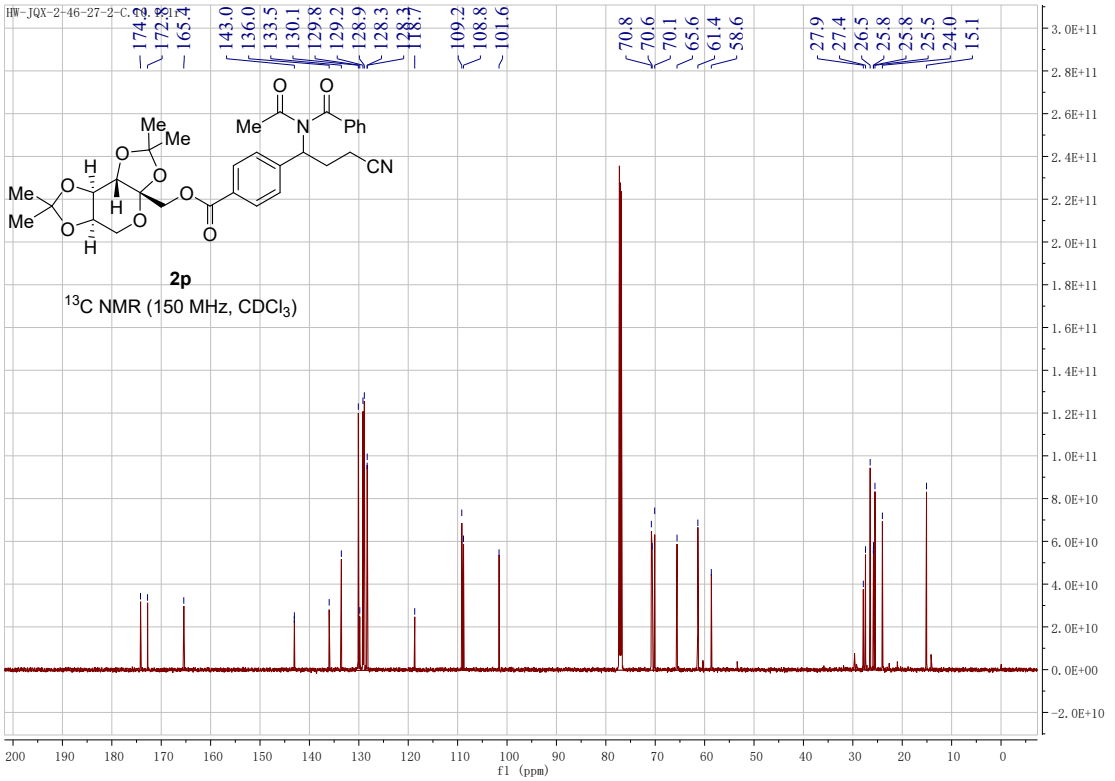
^{1}H and ^{13}C Spectrum for Compound 2o at 25 ℃



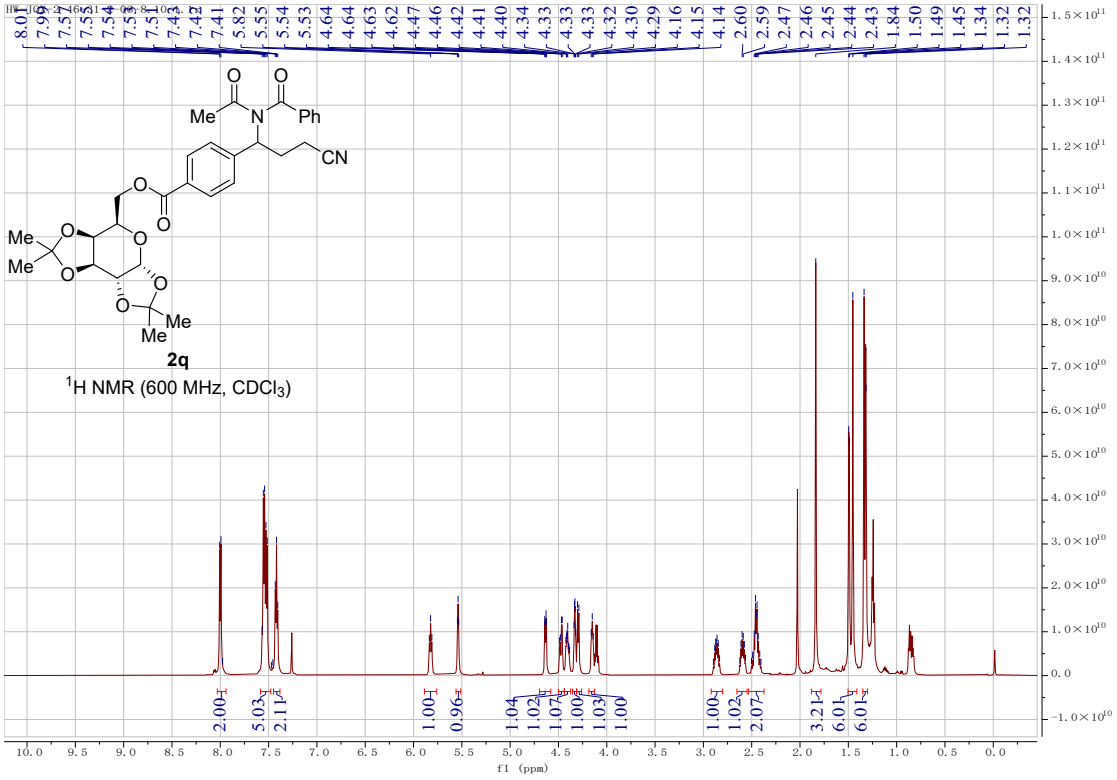


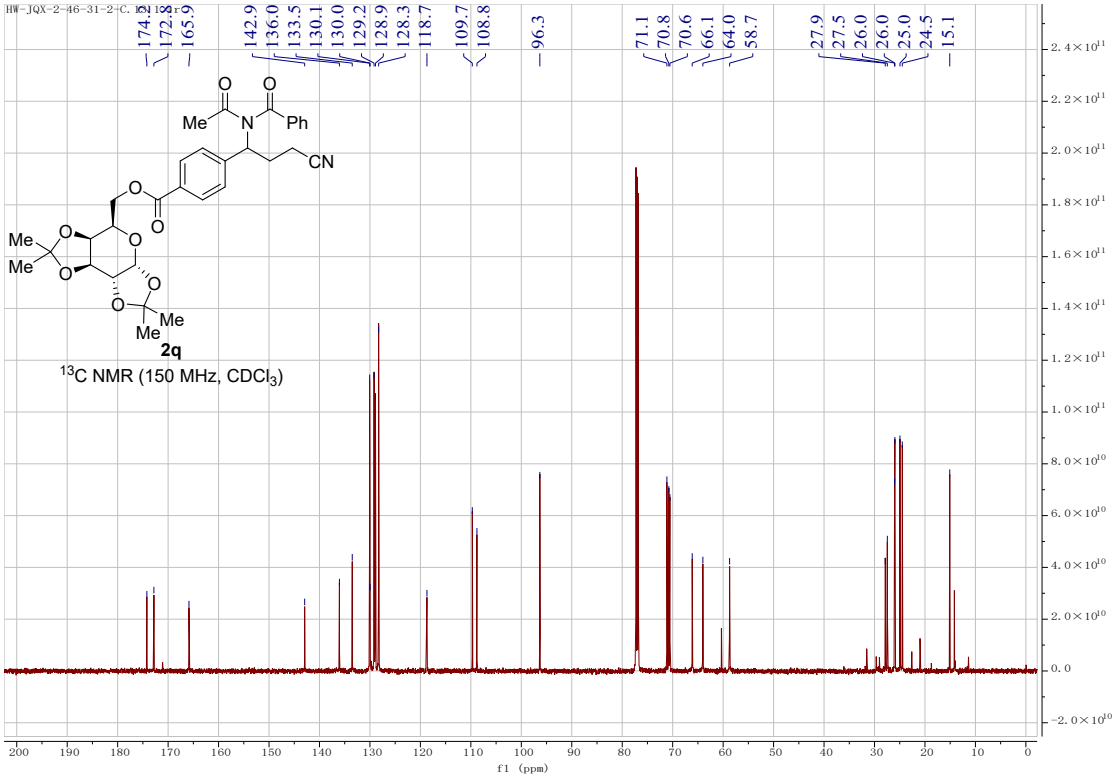
^{1}H and ^{13}C Spectrum for Compound 2p at 25 ℃



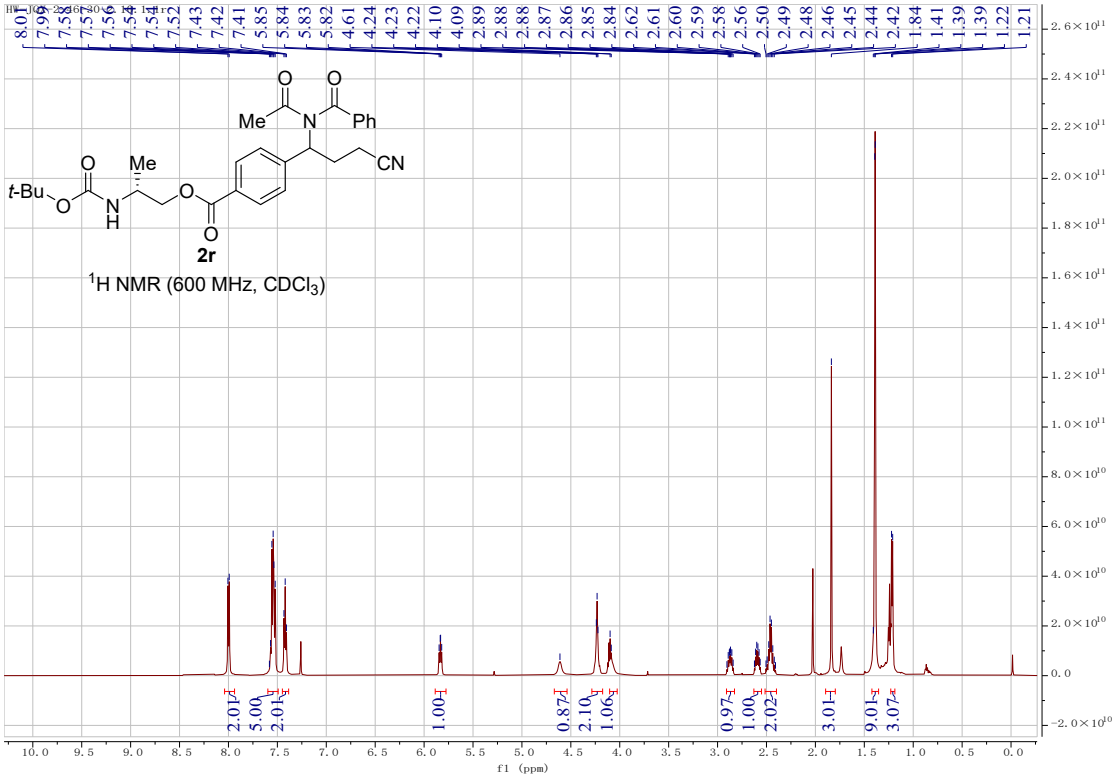


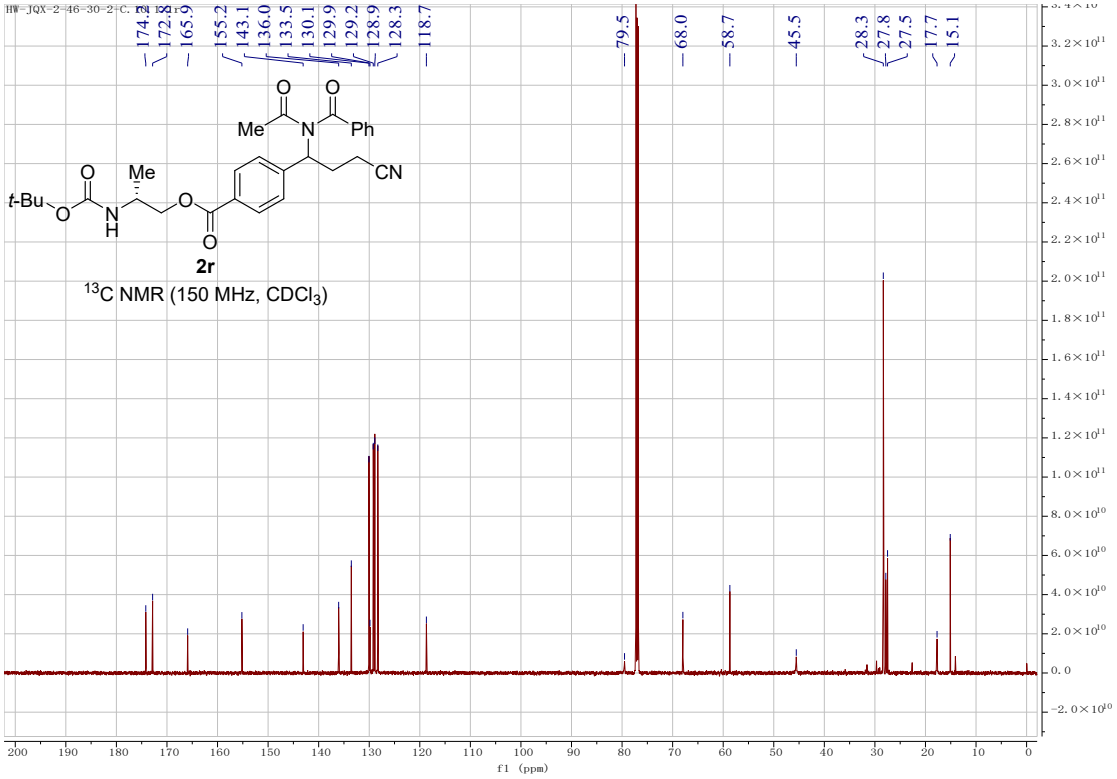
^{1}H and ^{13}C Spectrum for Compound 2q at 25 ℃



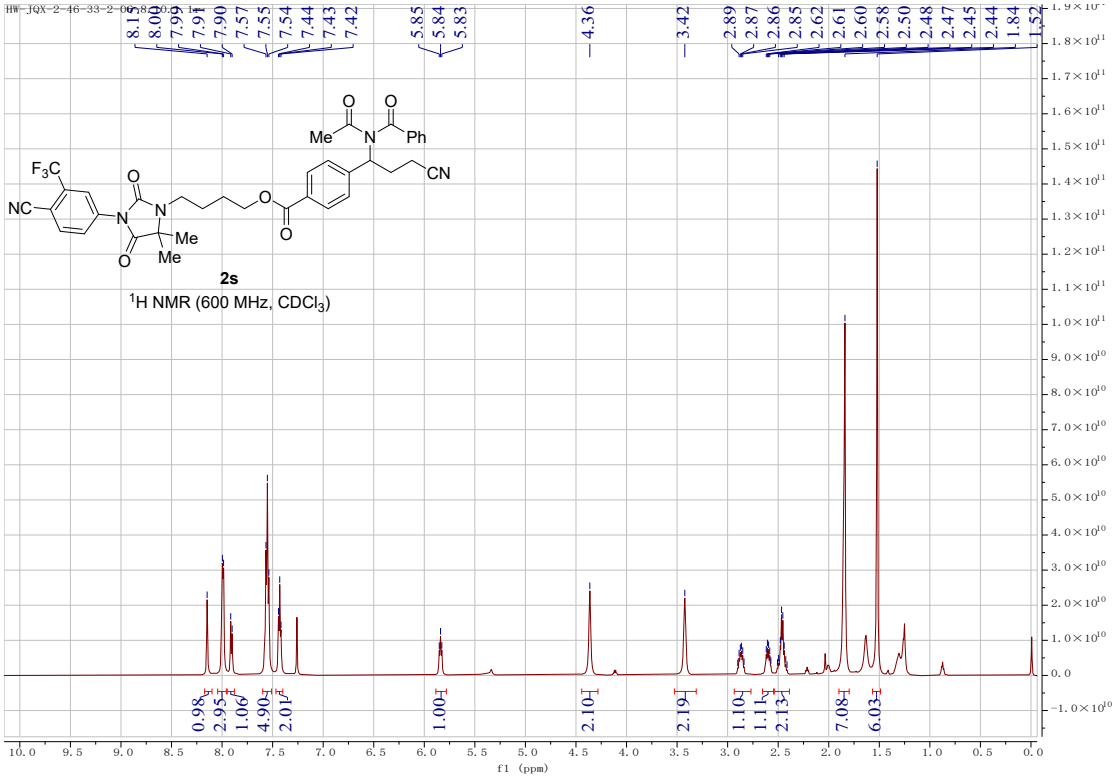


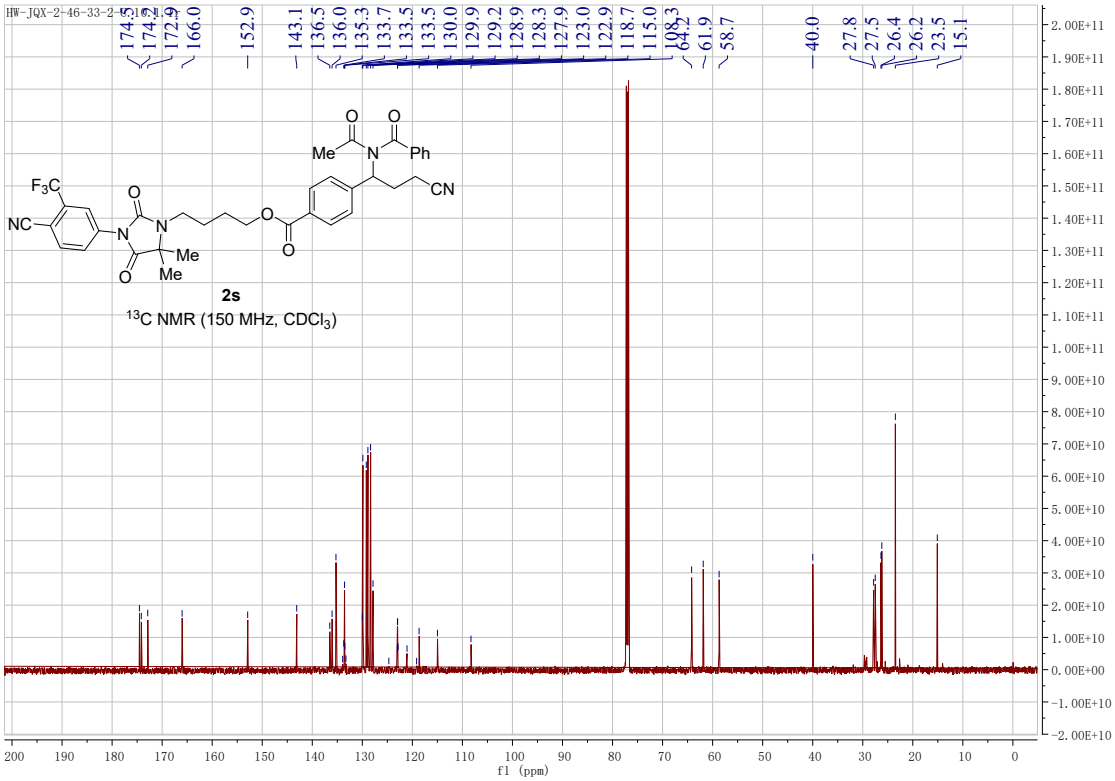
^{1}H and ^{13}C Spectrum for Compound 2r at 25 ℃



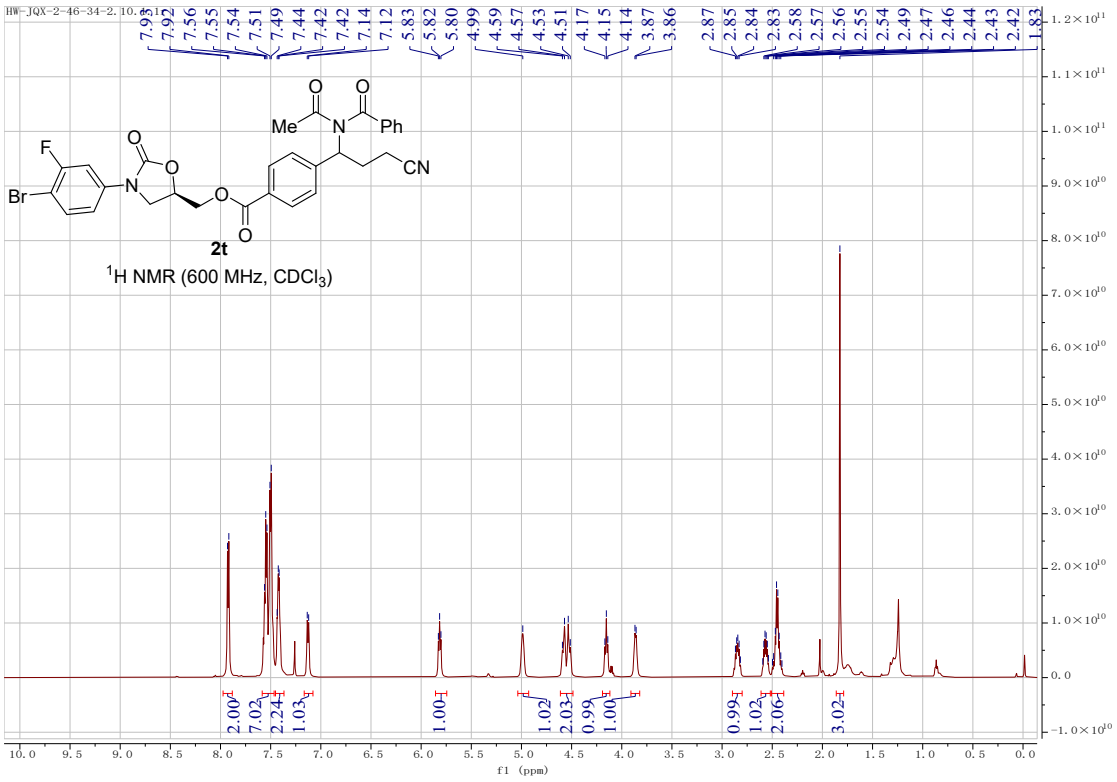


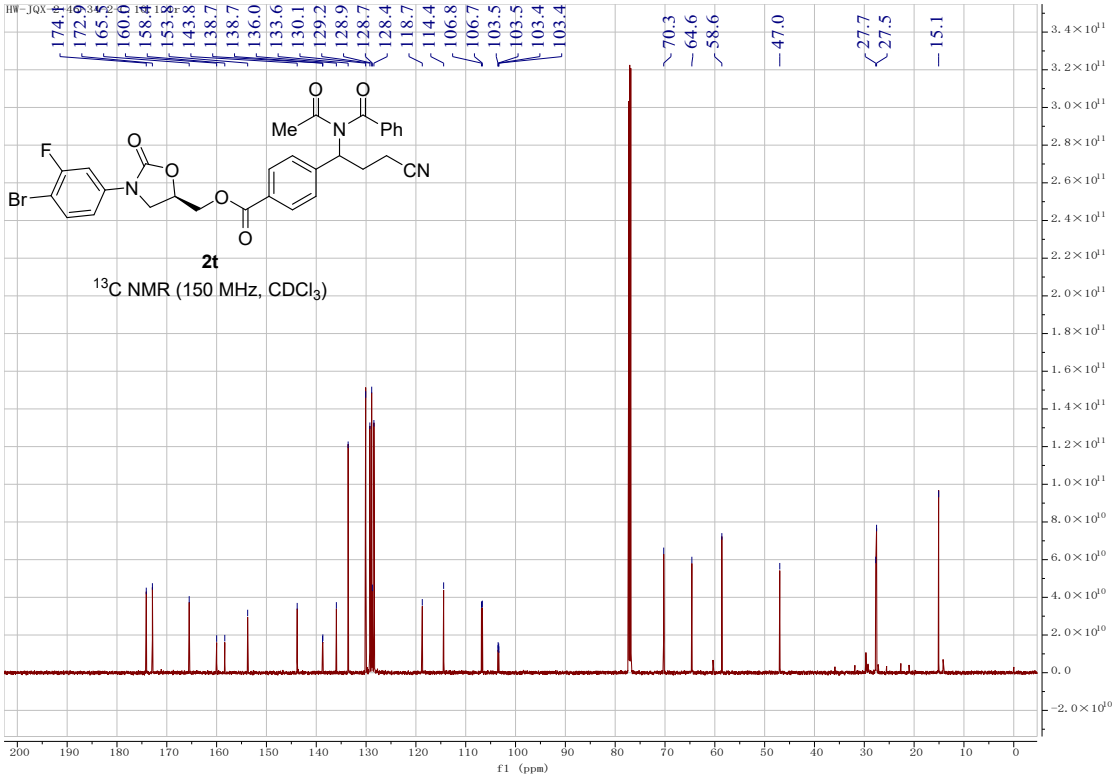
^{1}H and ^{13}C Spectrum for Compound 2s at 25 ℃



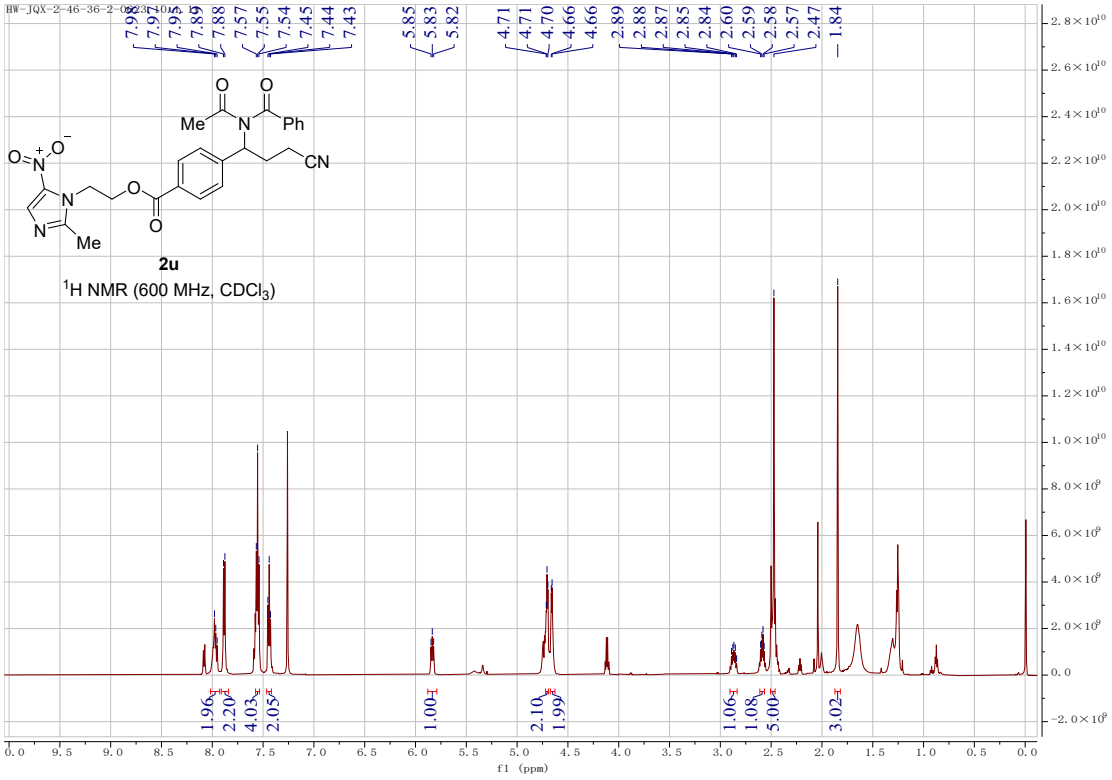


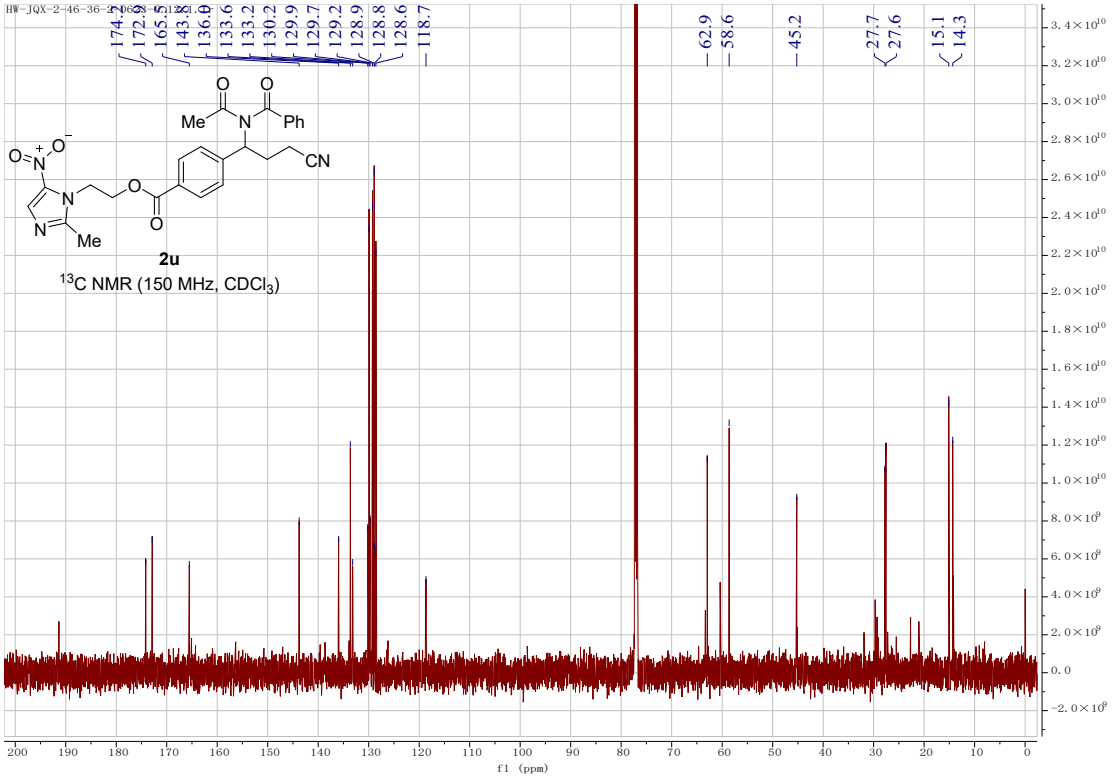
^{1}H and ^{13}C Spectrum for Compound 2t at 25 ℃



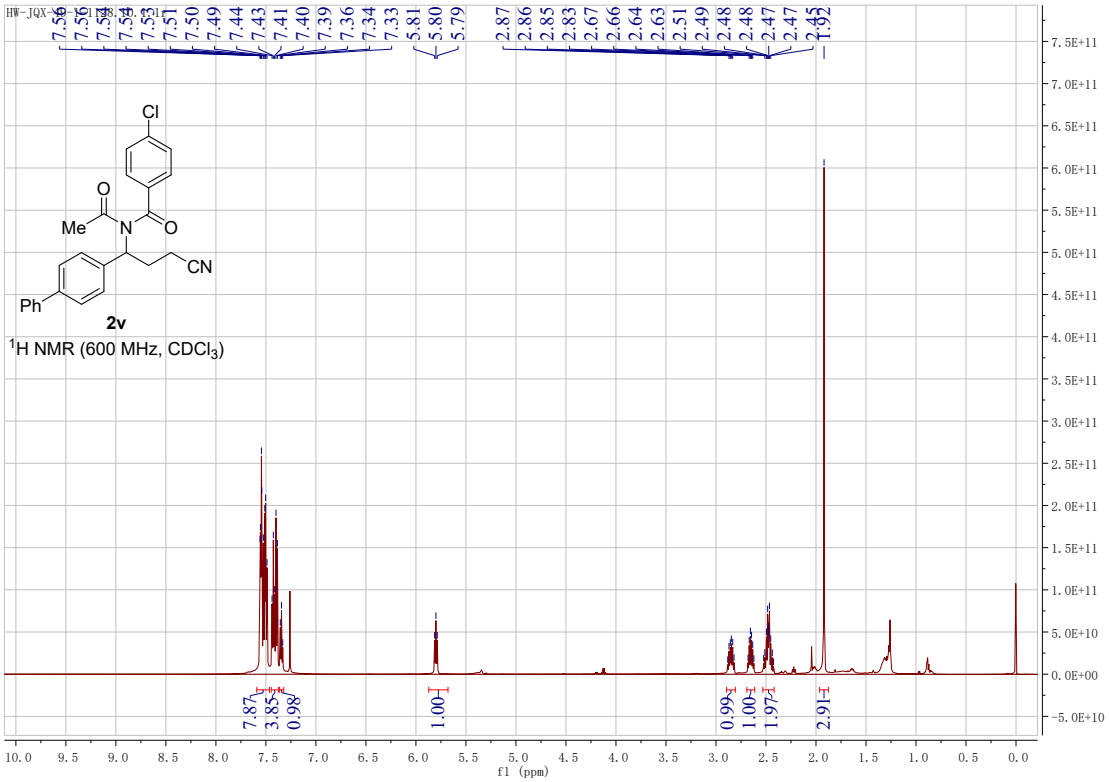


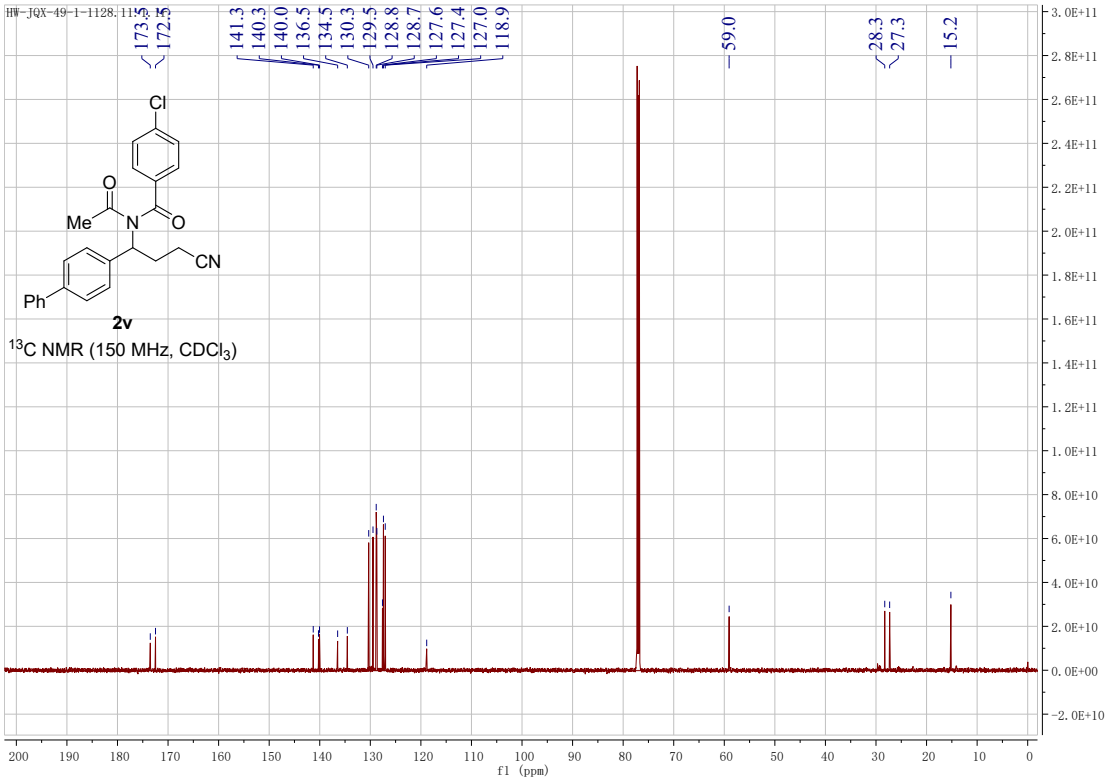
^{1}H and ^{13}C Spectrum for Compound 2u at 25 ℃



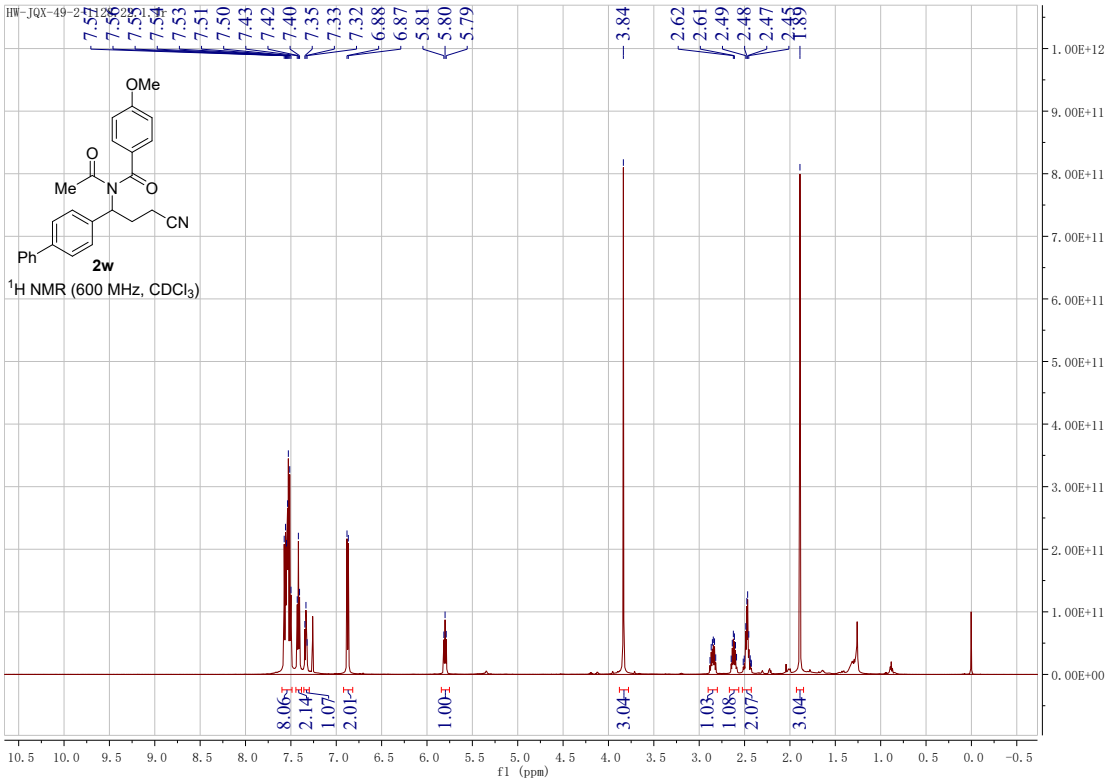


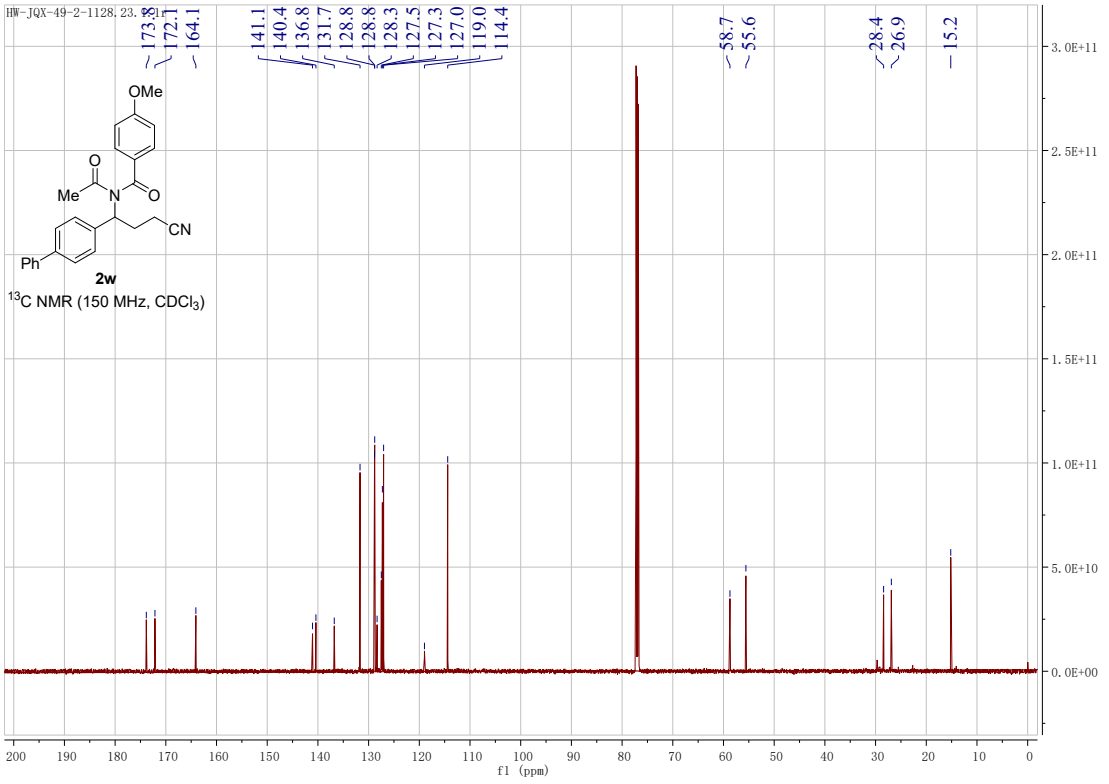
^{1}H and ^{13}C Spectrum for Compound 2v at 25 ℃



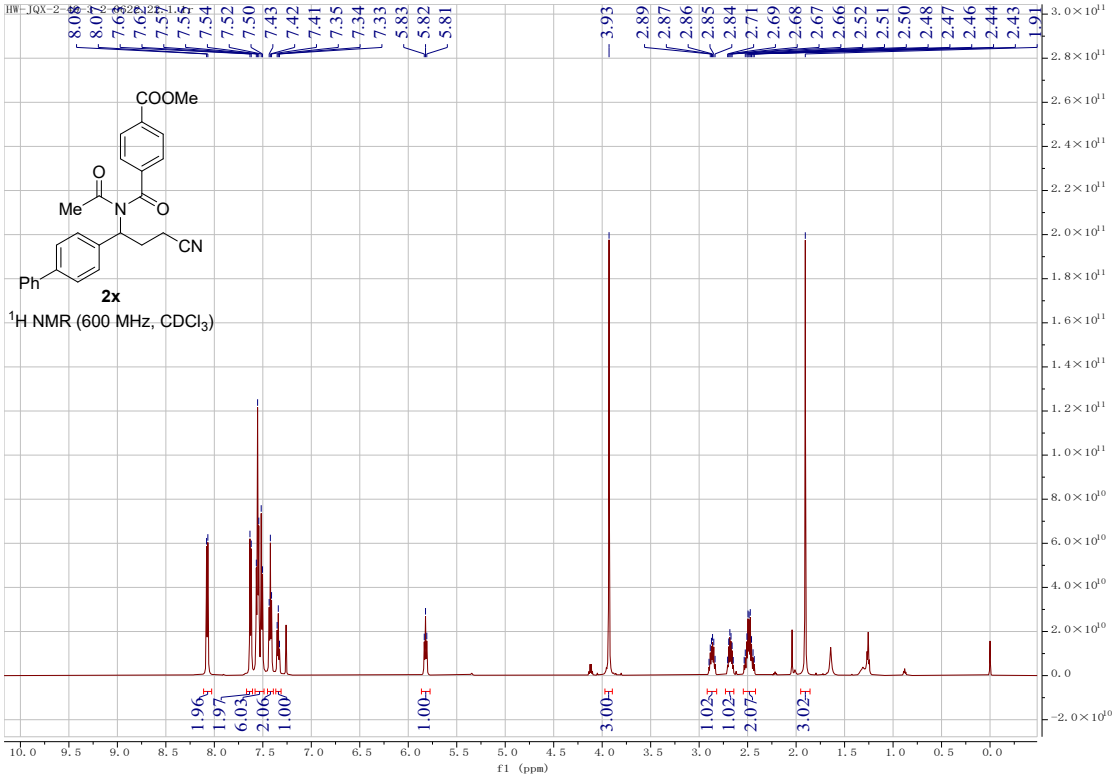


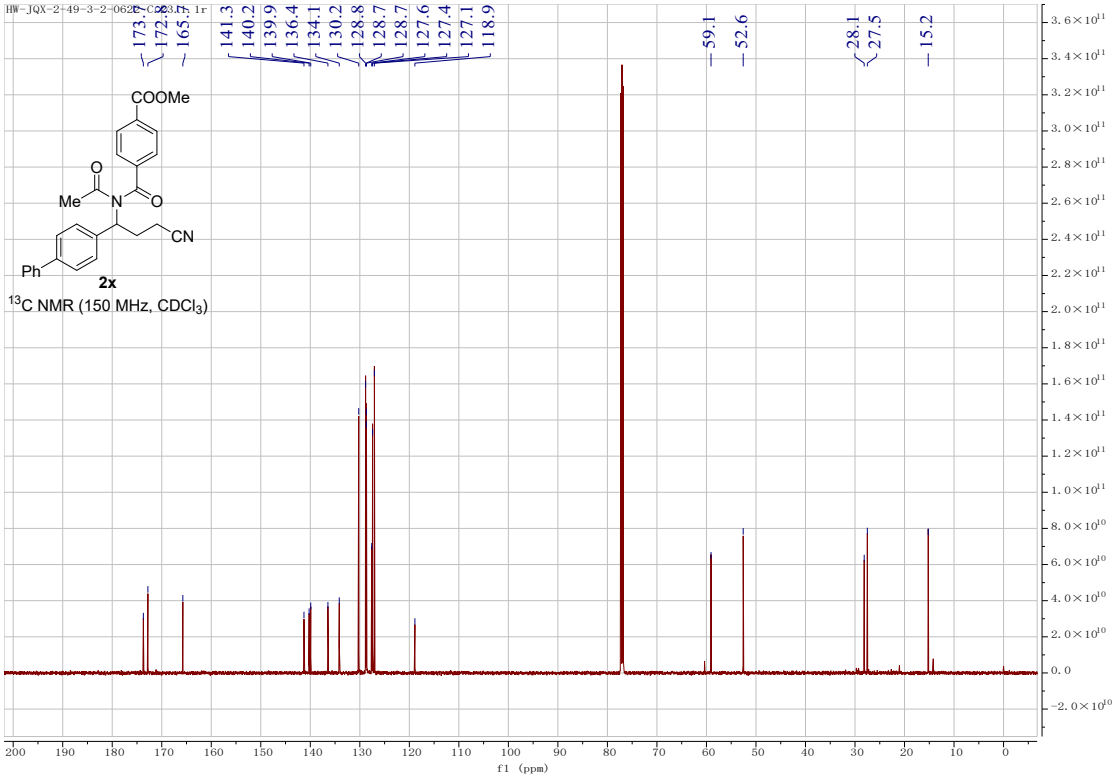
^{1}H and ^{13}C Spectrum for Compound 2w at 25 ℃



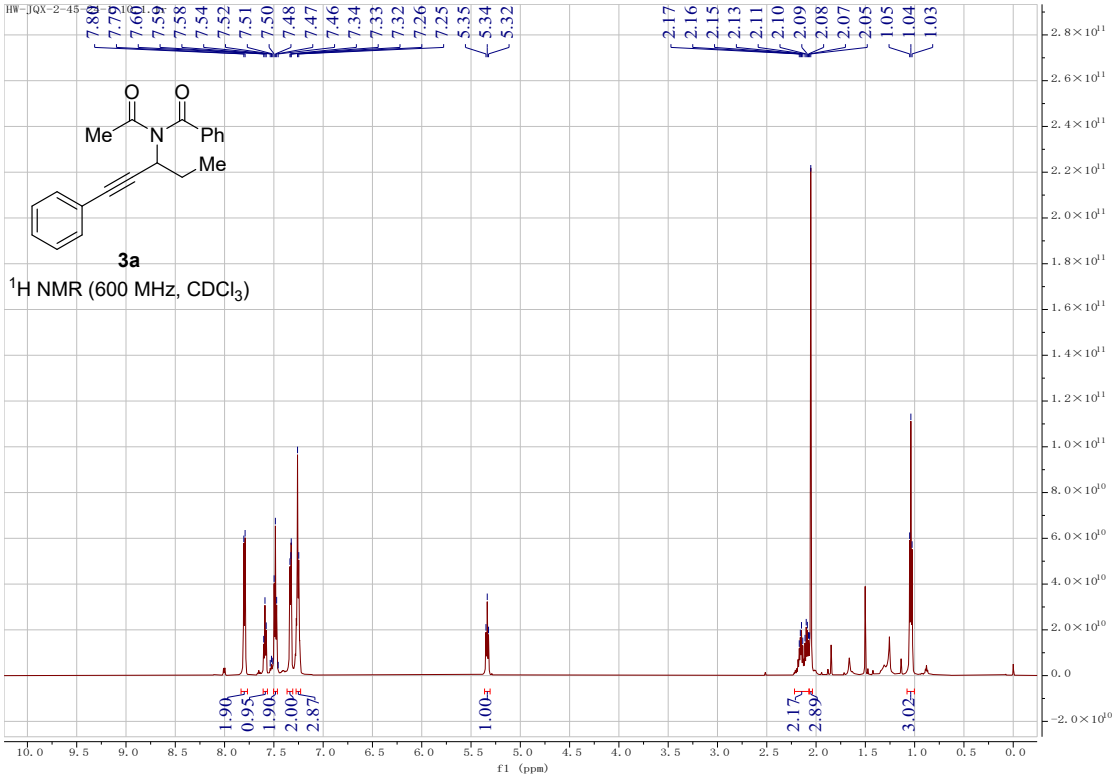


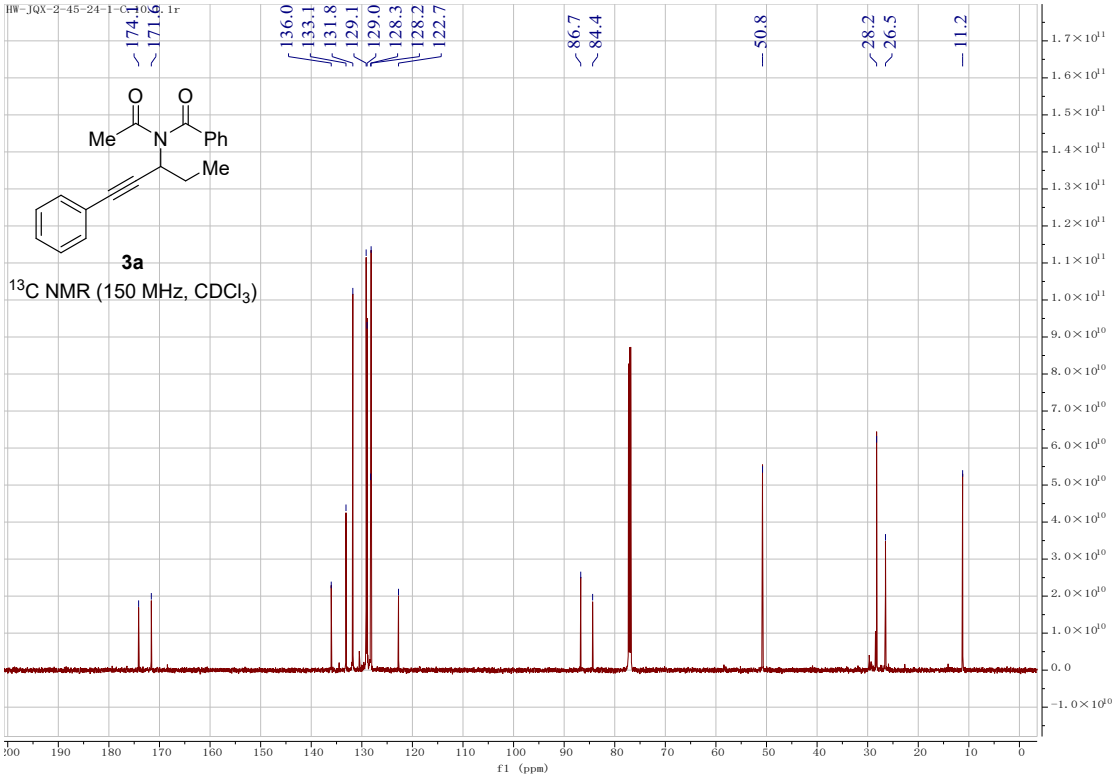
^{1}H and ^{13}C Spectrum for Compound 2x at 25 ℃



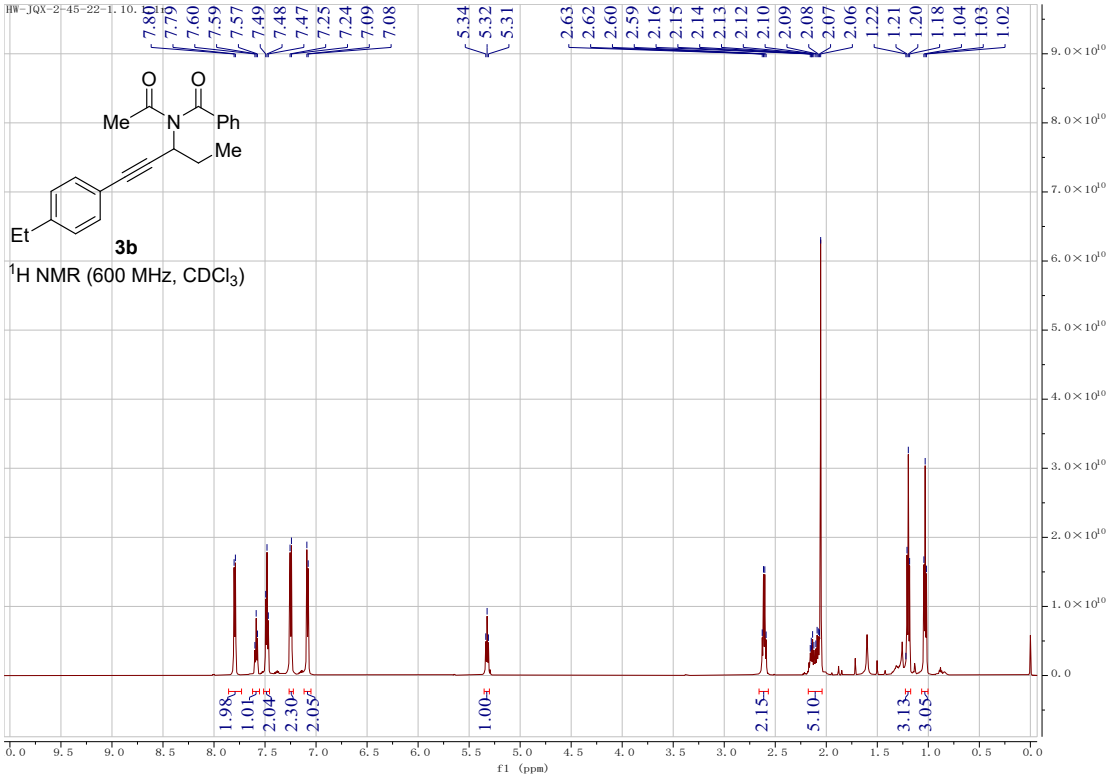


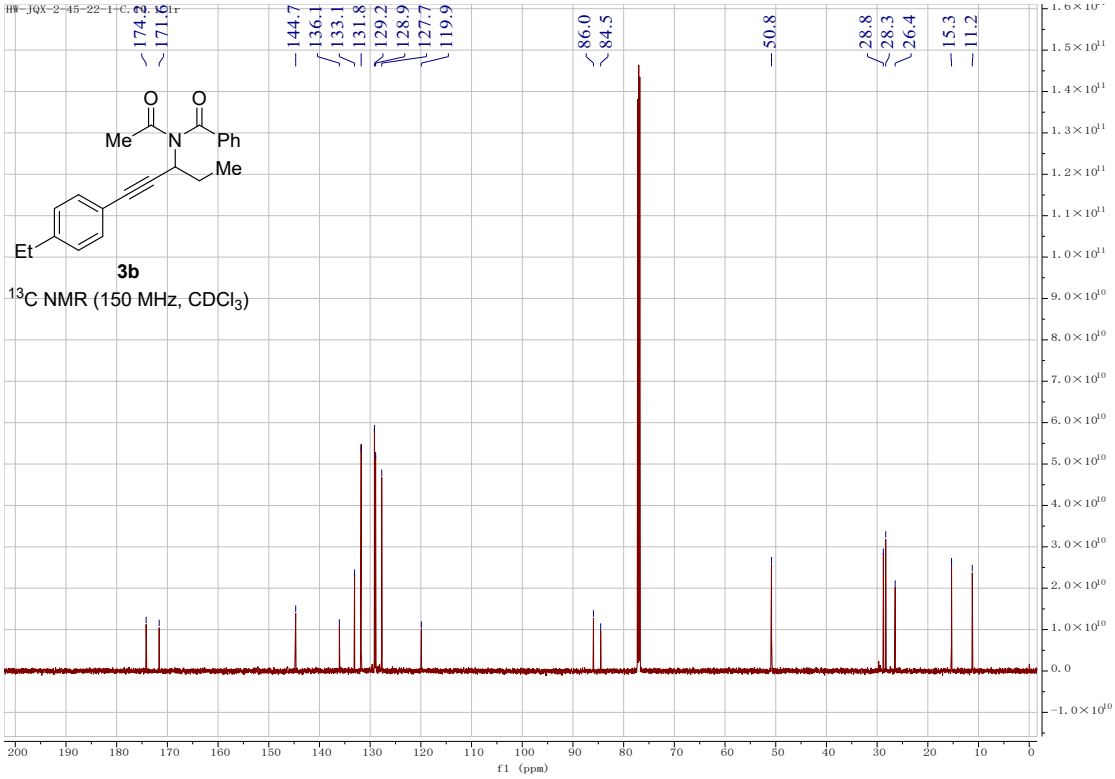
^{1}H and ^{13}C Spectrum for Compound 3a at 25 ℃



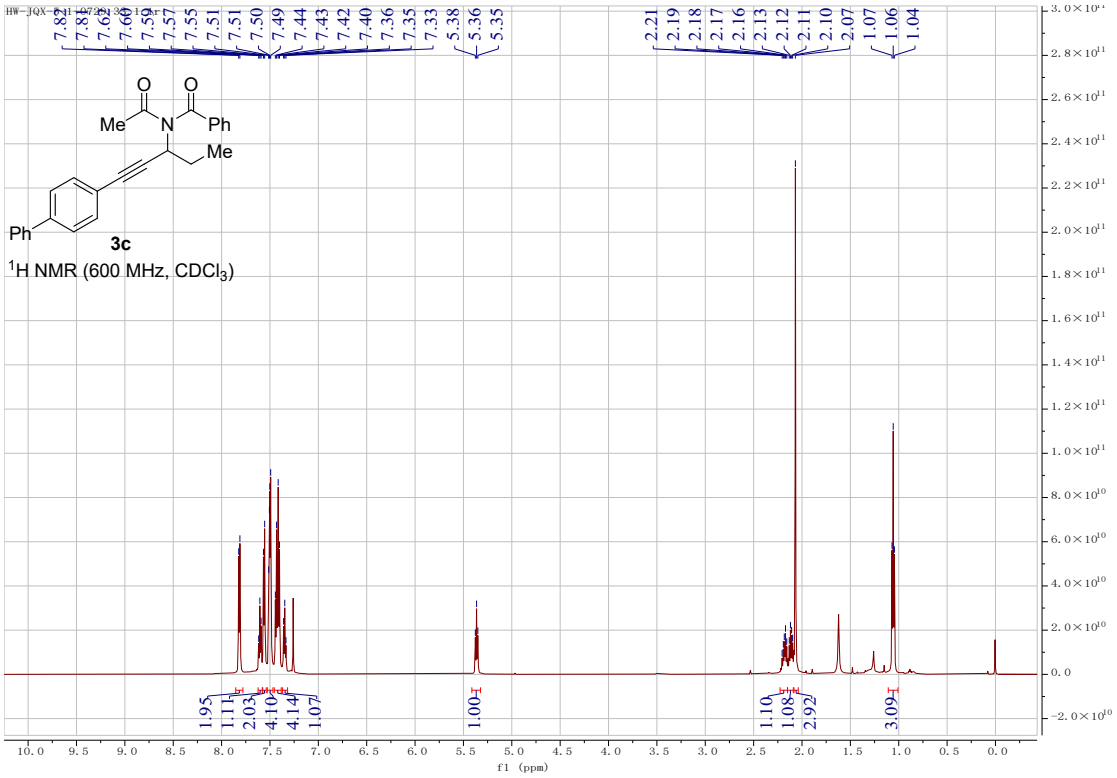


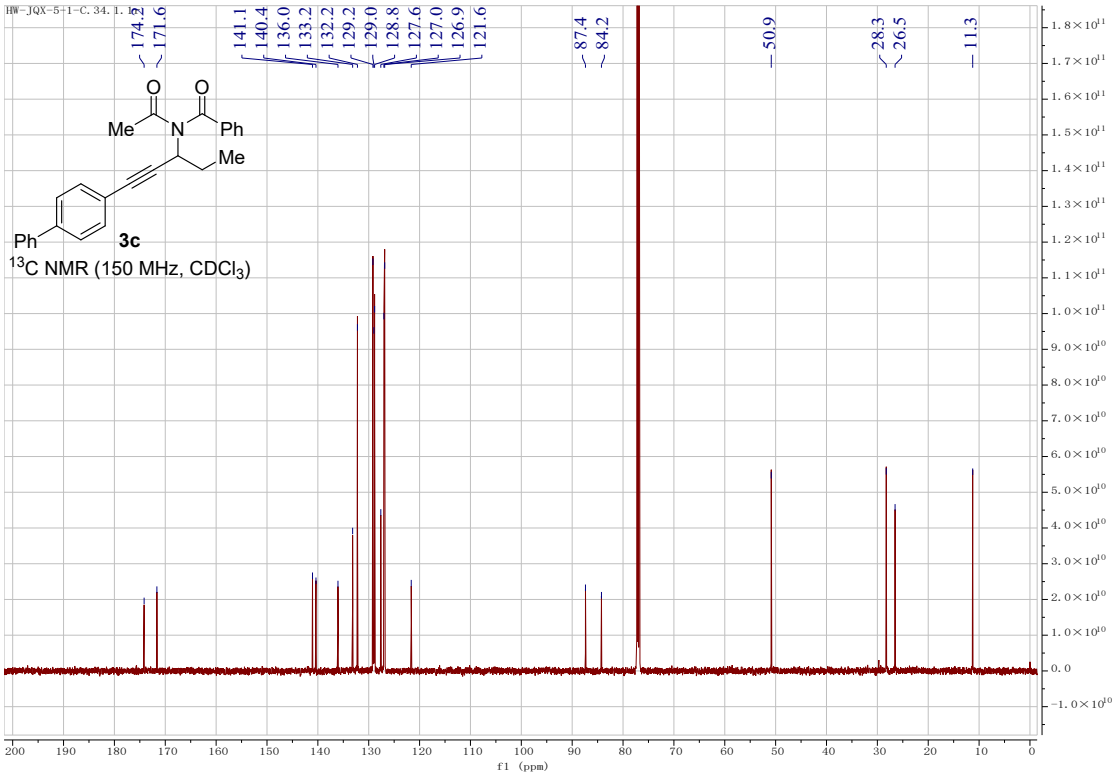
^{1}H and ^{13}C Spectrum for Compound 3b at 25 ℃



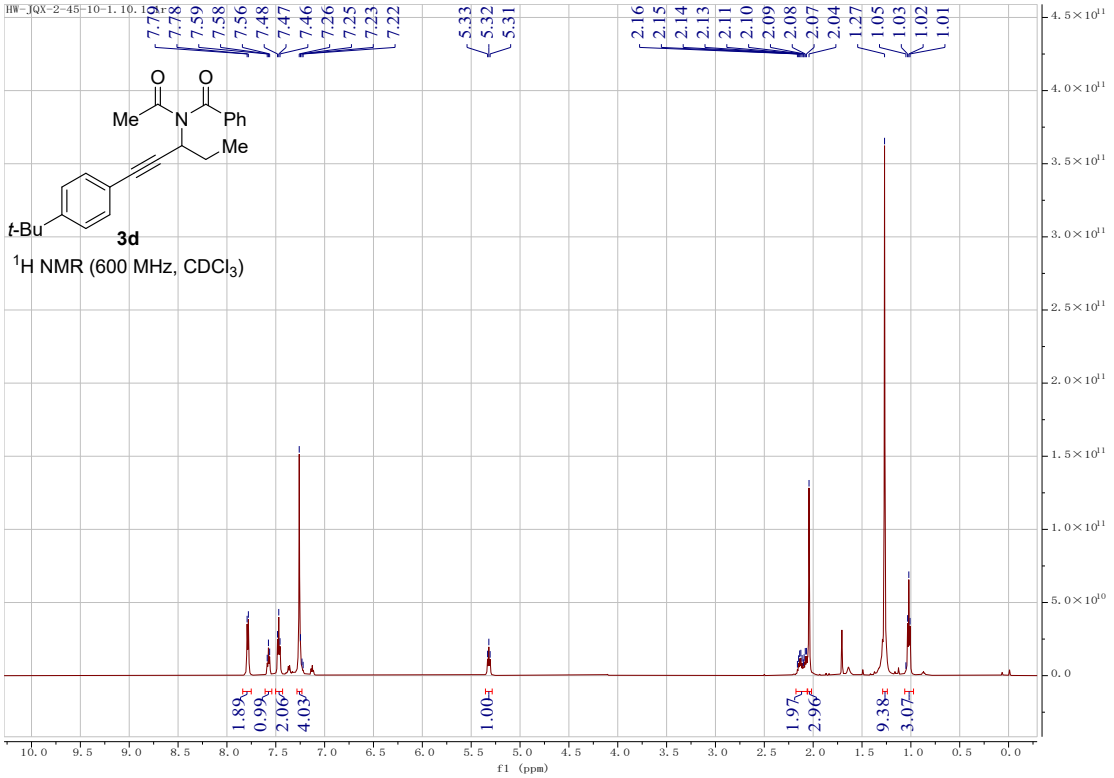


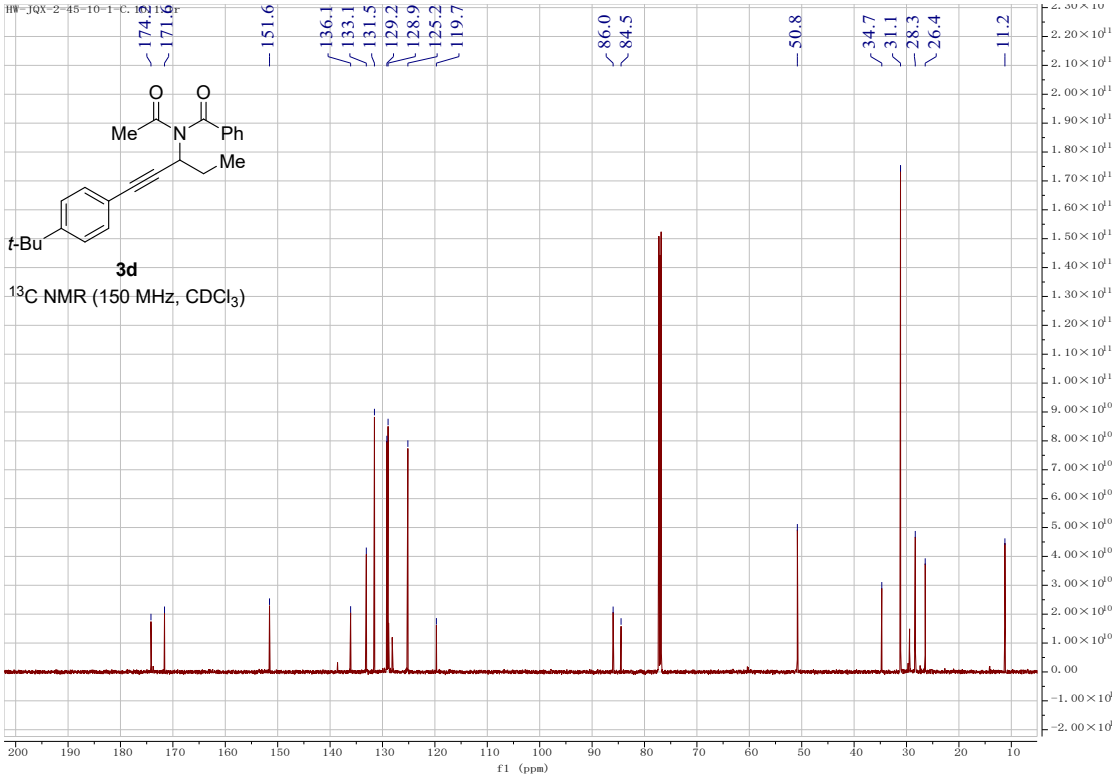
^{1}H and ^{13}C Spectrum for Compound 3c at 25 ℃



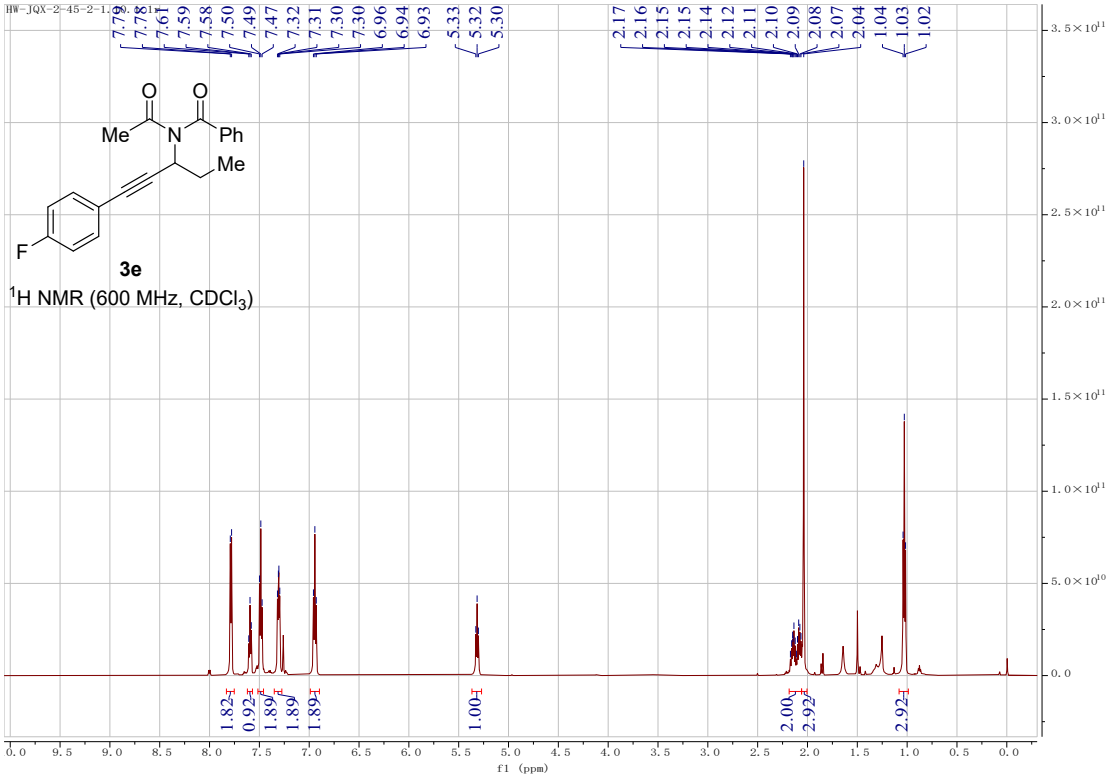


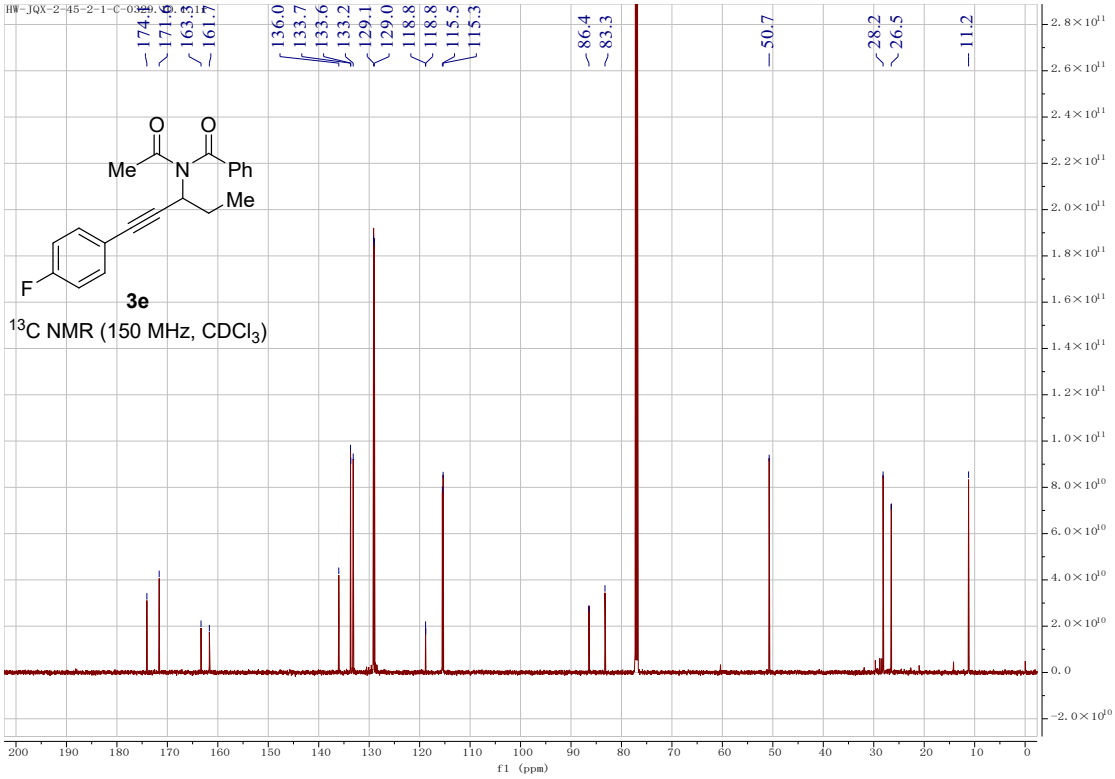
^{1}H and ^{13}C Spectrum for Compound 3d at 25 ℃



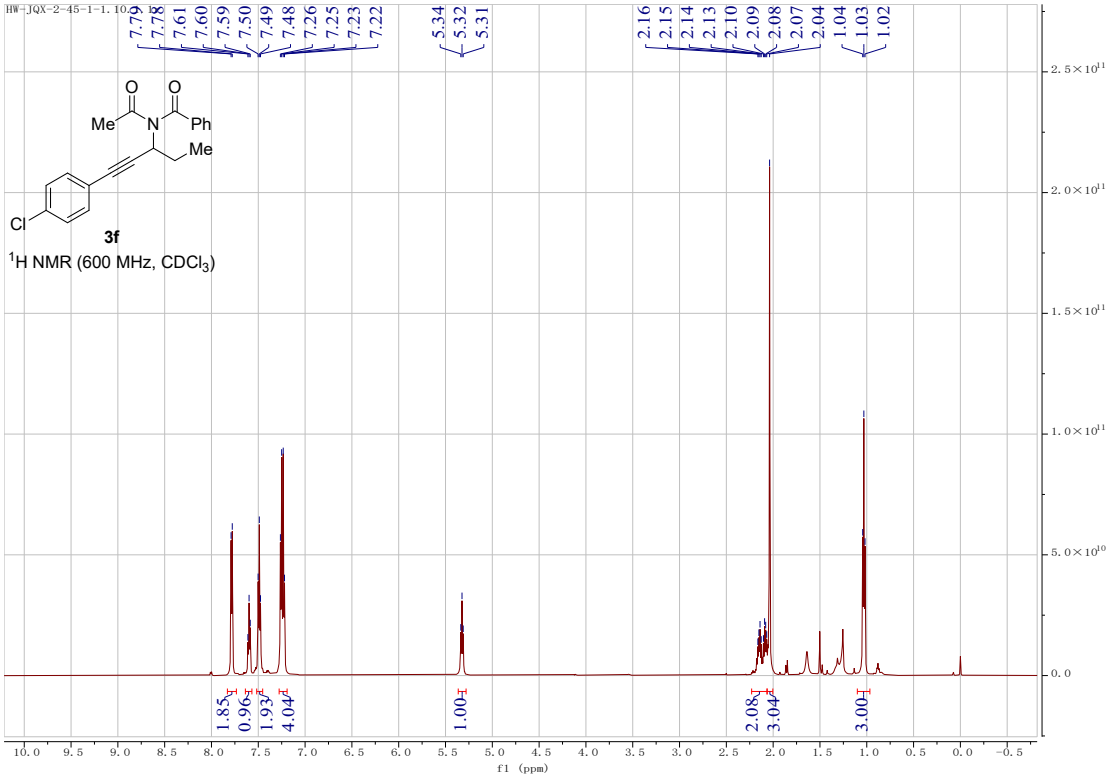


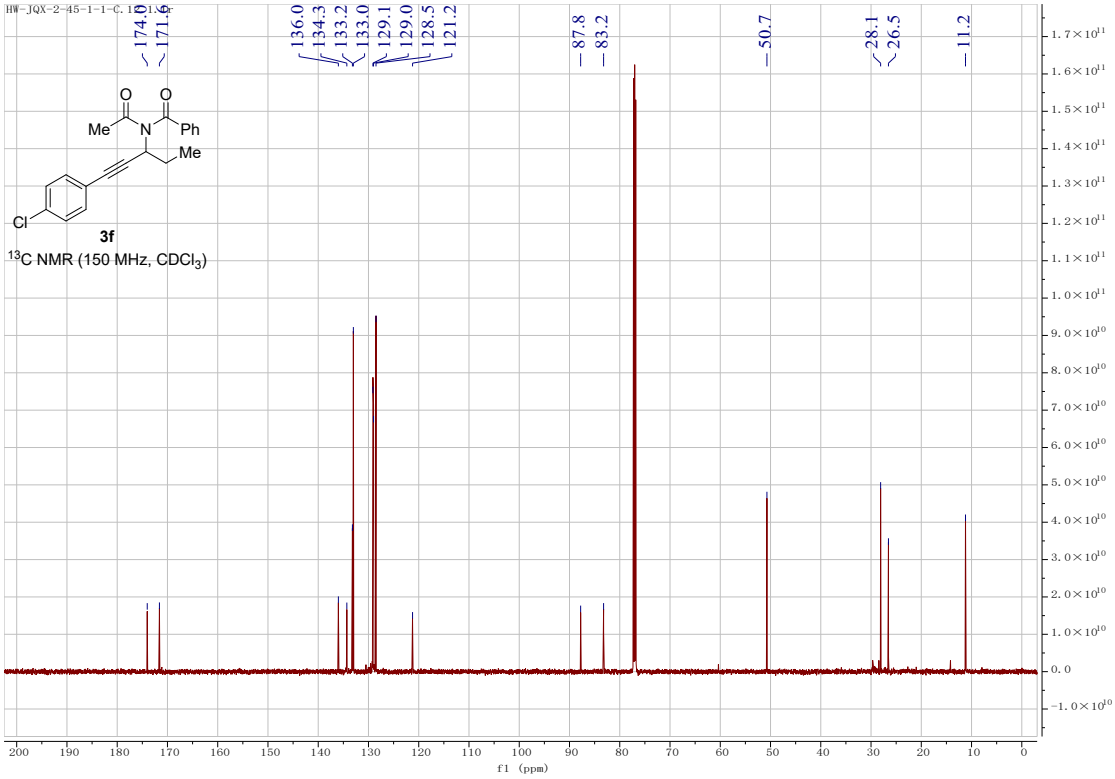
^{1}H and ^{13}C Spectrum for Compound 3e at 25 ℃



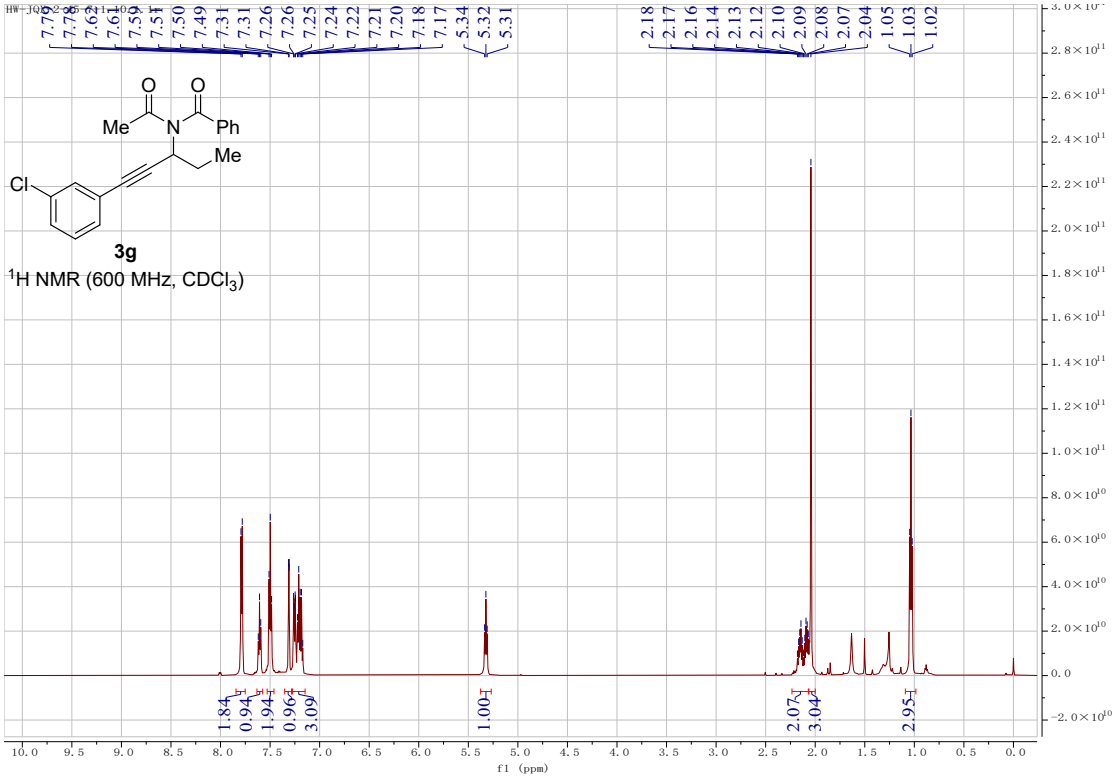


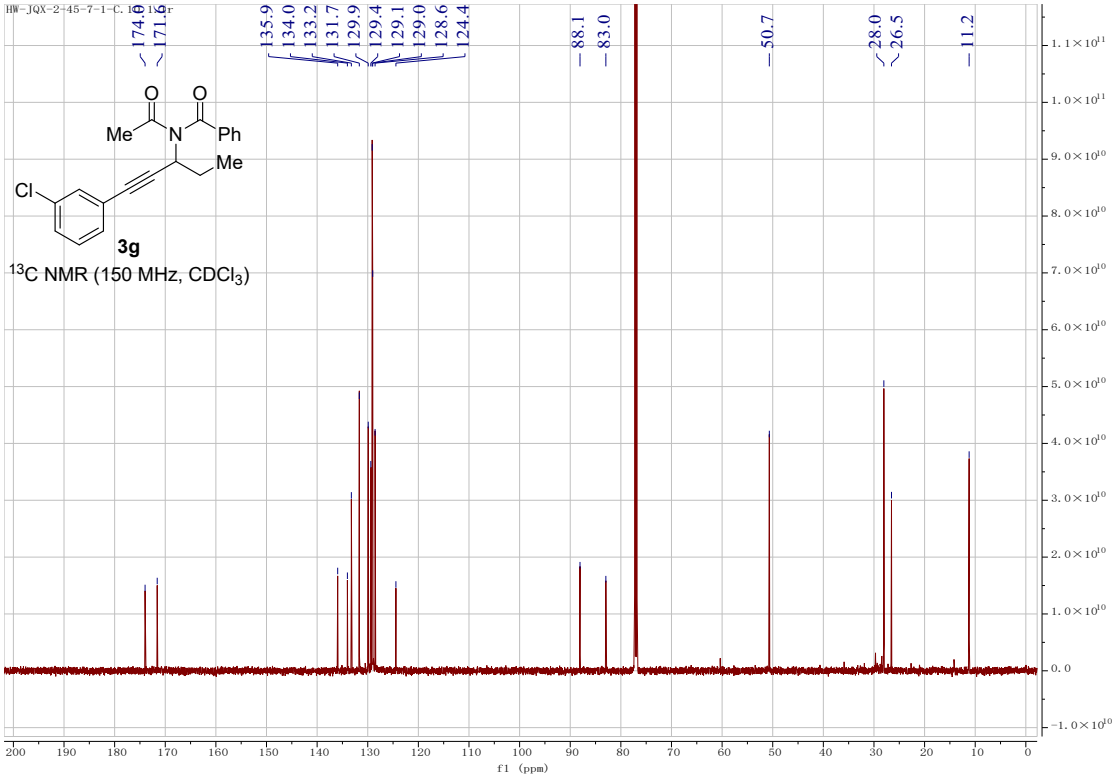
^{1}H and ^{13}C Spectrum for Compound 3f at 25 ℃



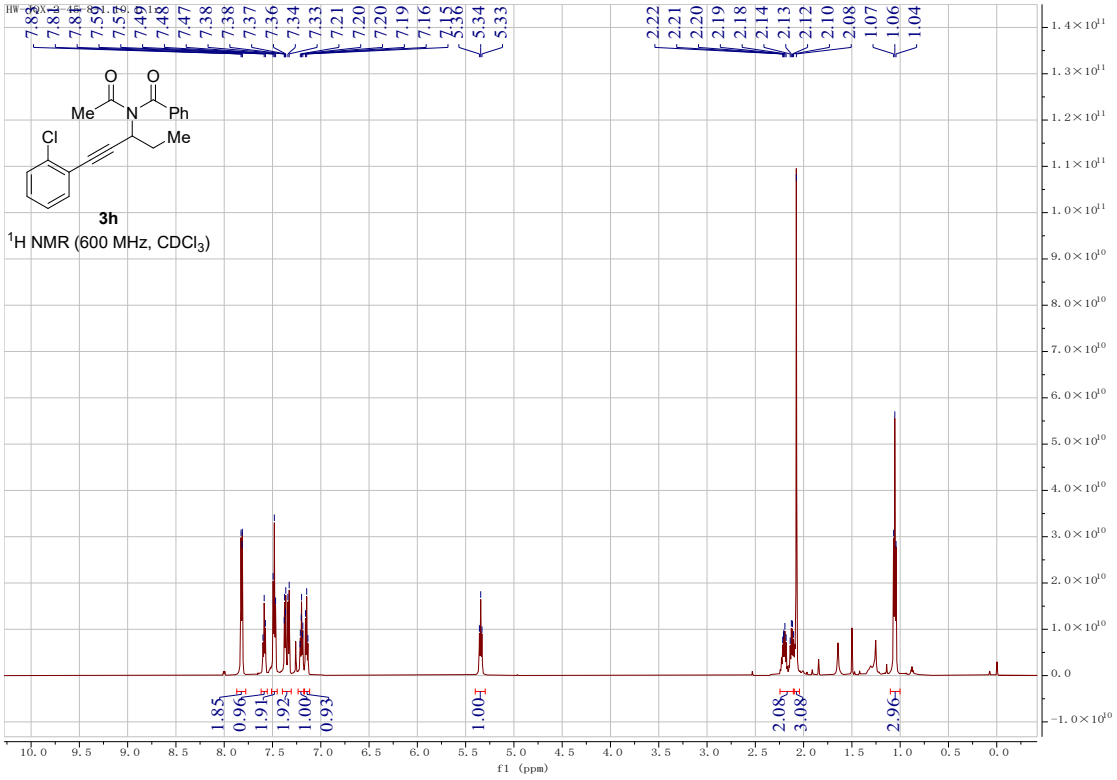


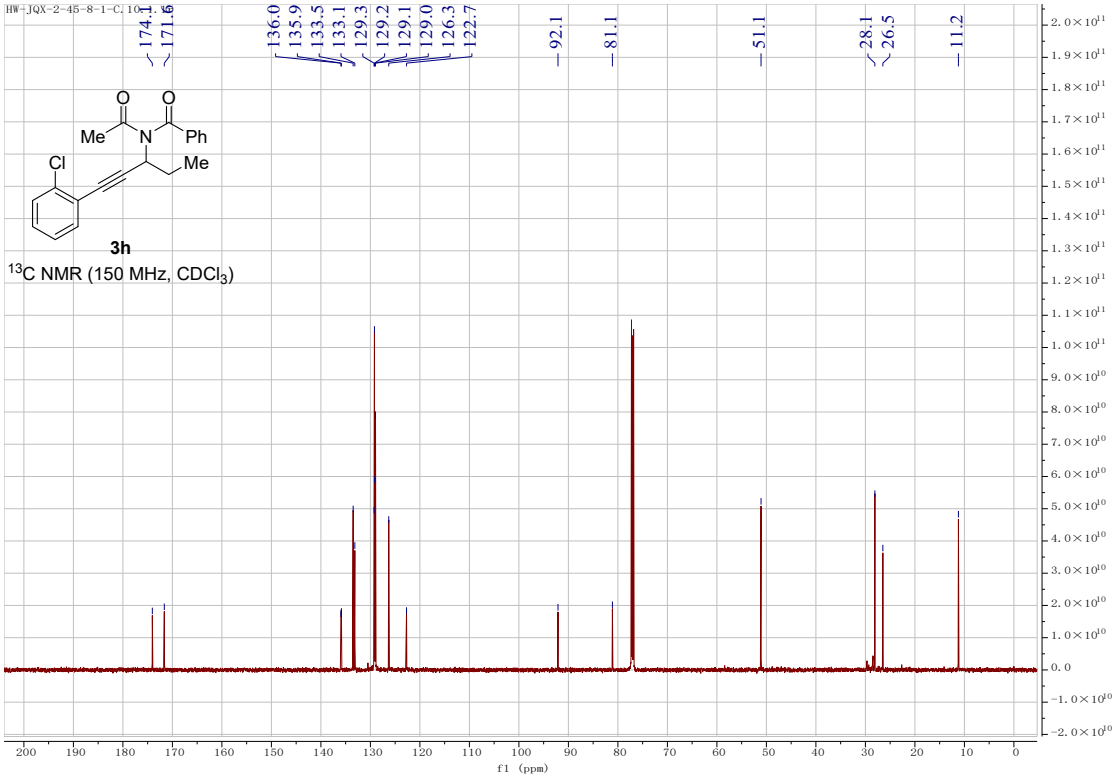
^{1}H and ^{13}C Spectrum for Compound 3g at 25 ℃



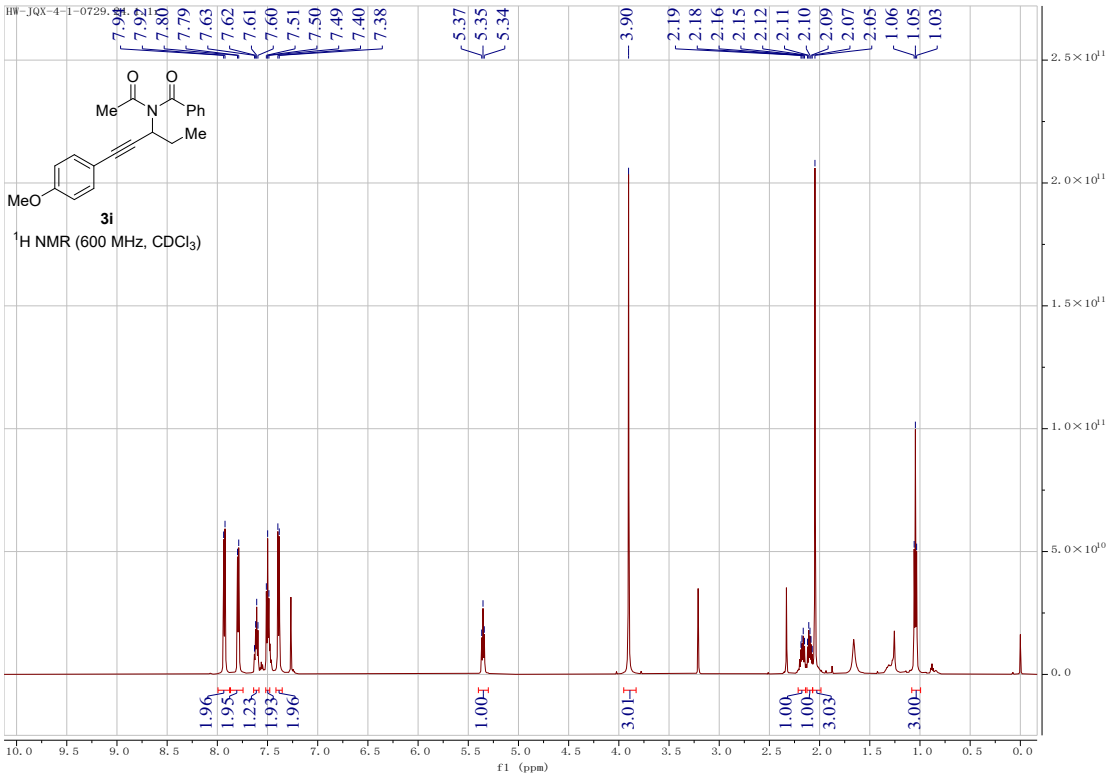


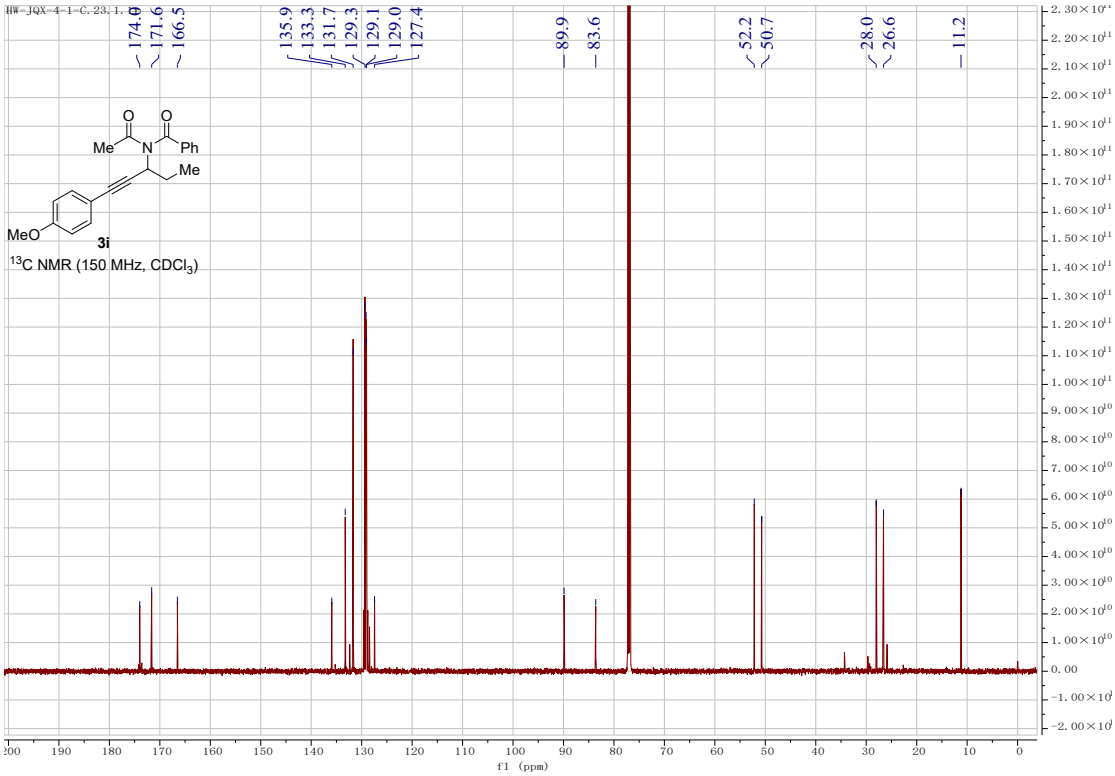
^{1}H and ^{13}C Spectrum for Compound 3h at 25 ℃



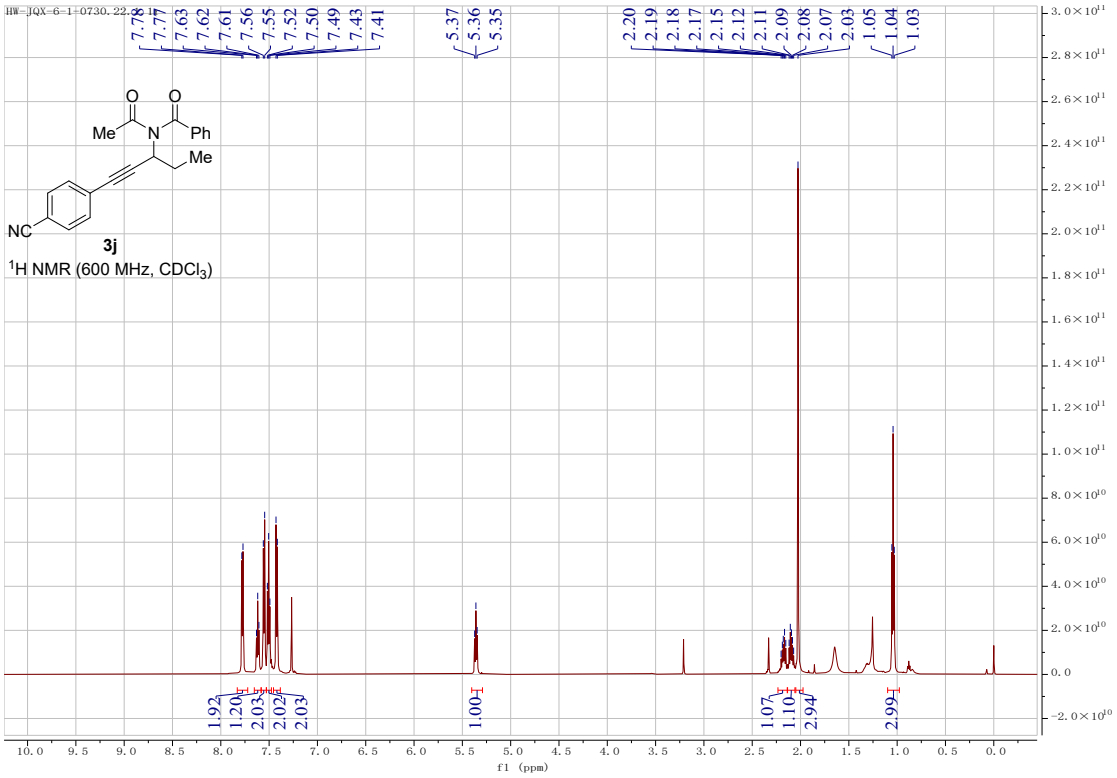


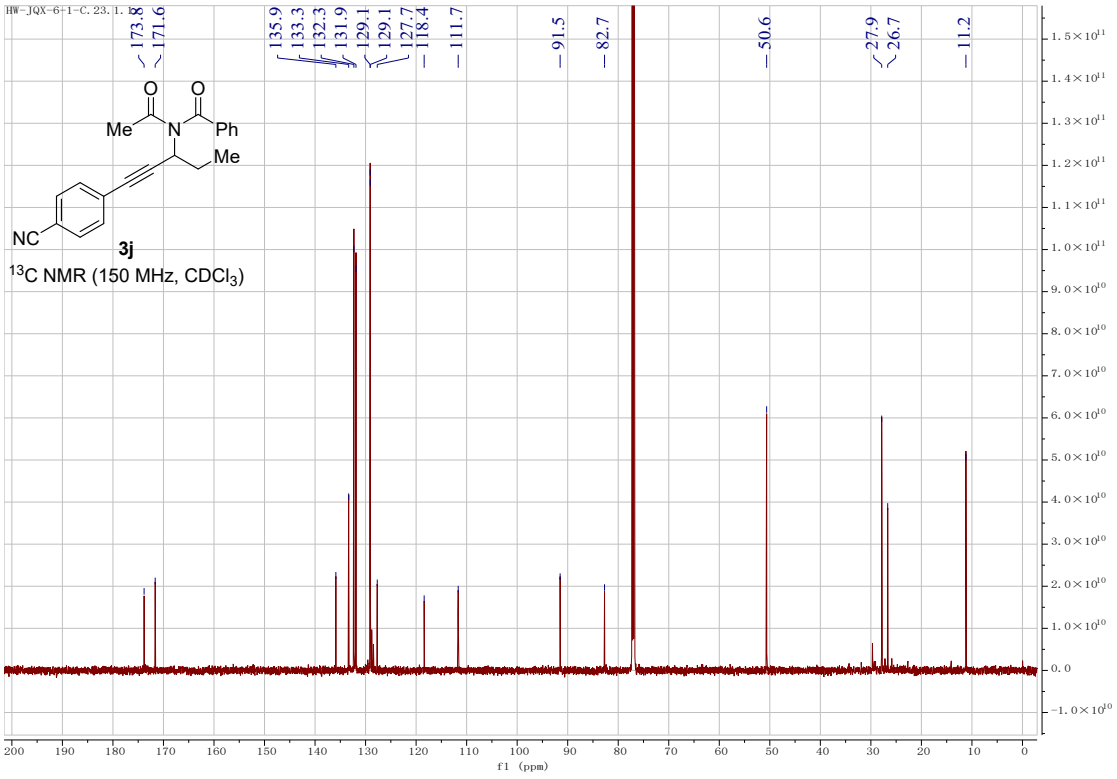
^{1}H and ^{13}C Spectrum for Compound 3i at 25 ℃



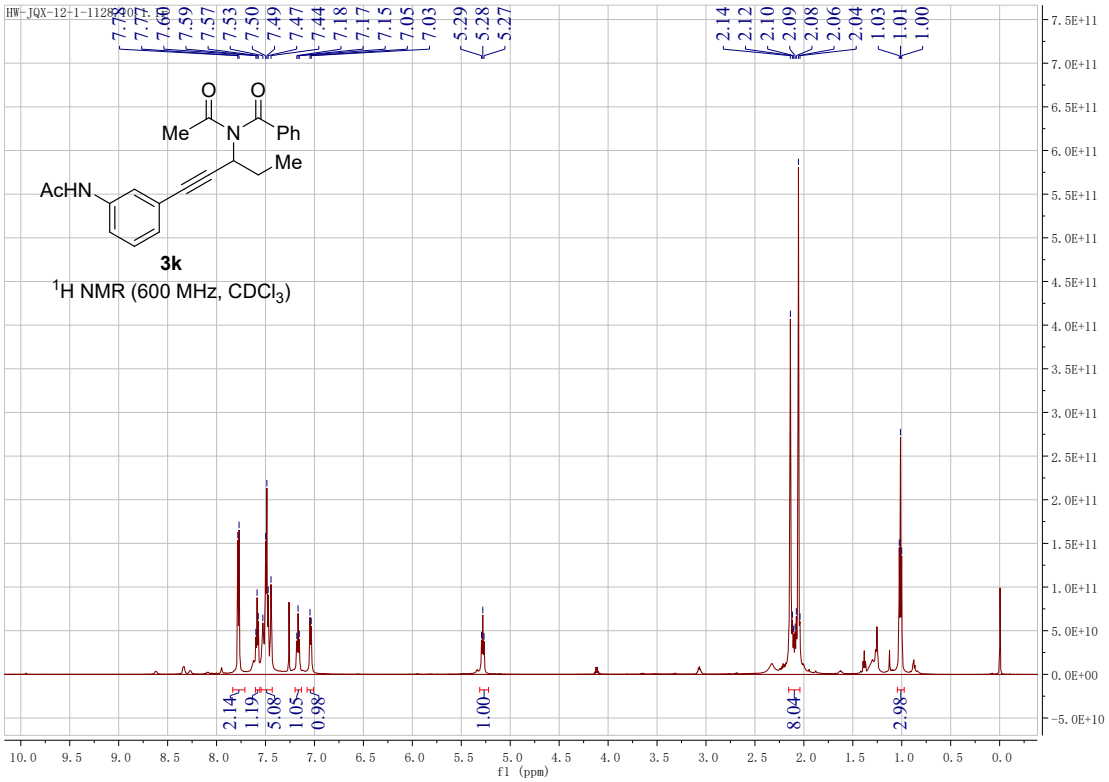


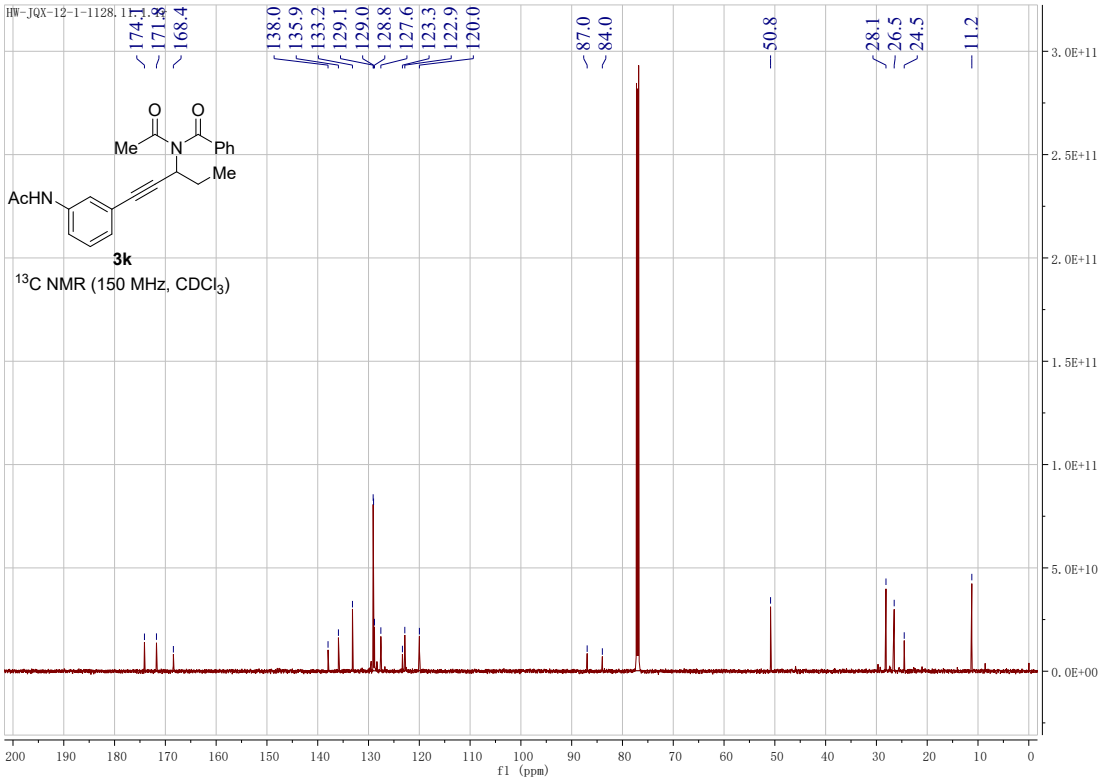
^{1}H and ^{13}C Spectrum for Compound 3j at 25 ℃



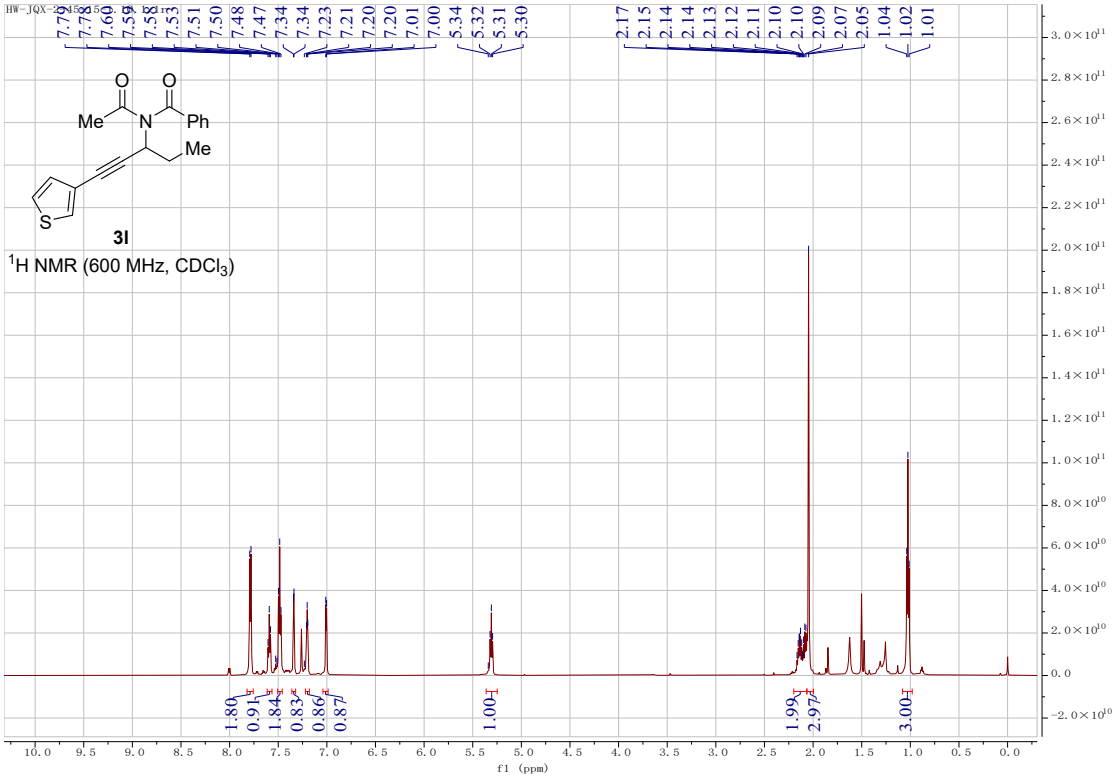


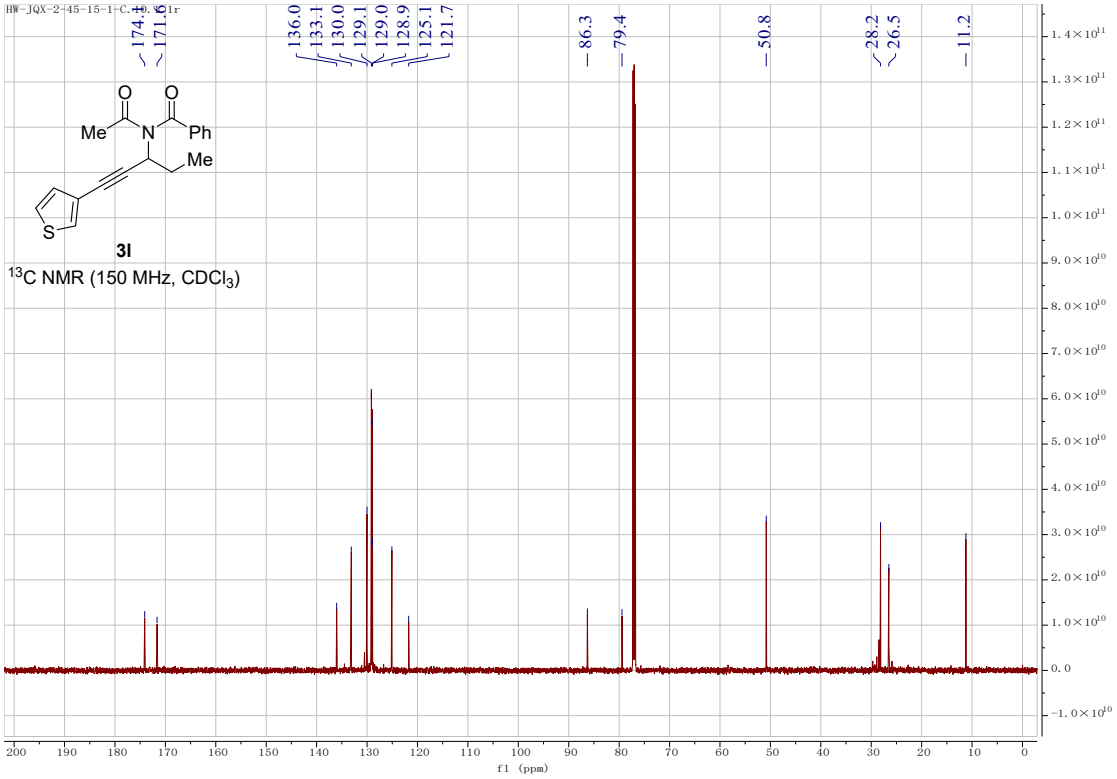
^{1}H and ^{13}C Spectrum for Compound 3k at 25 ℃



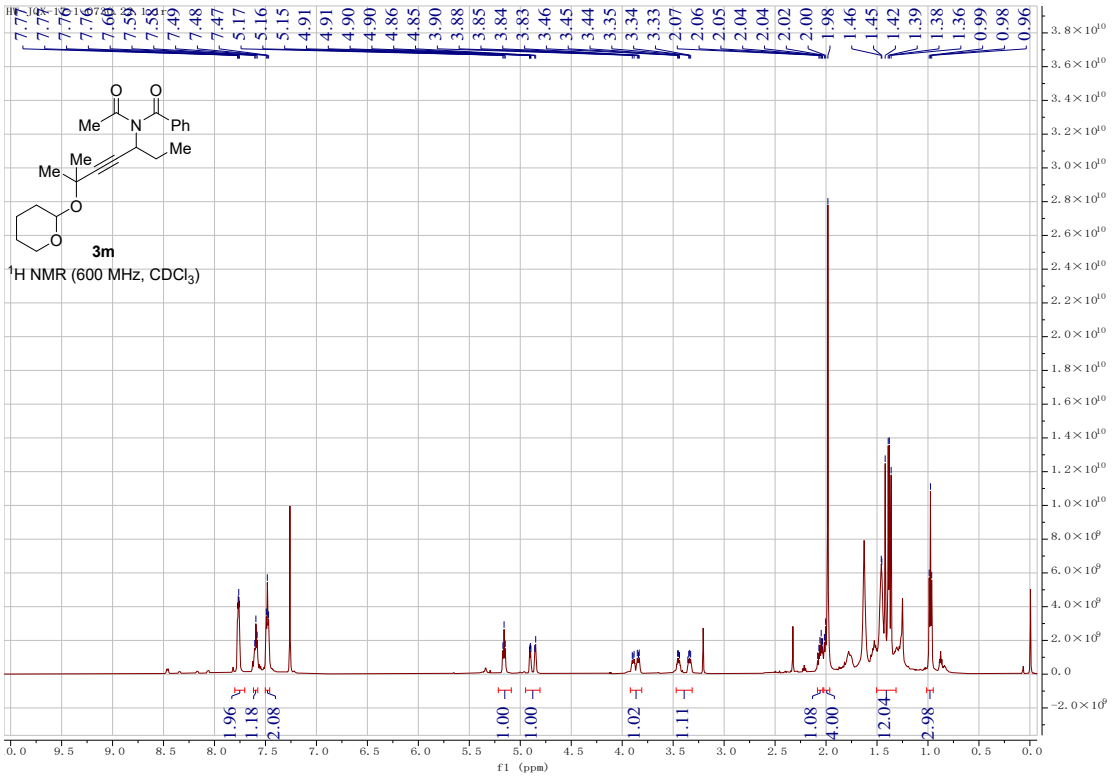


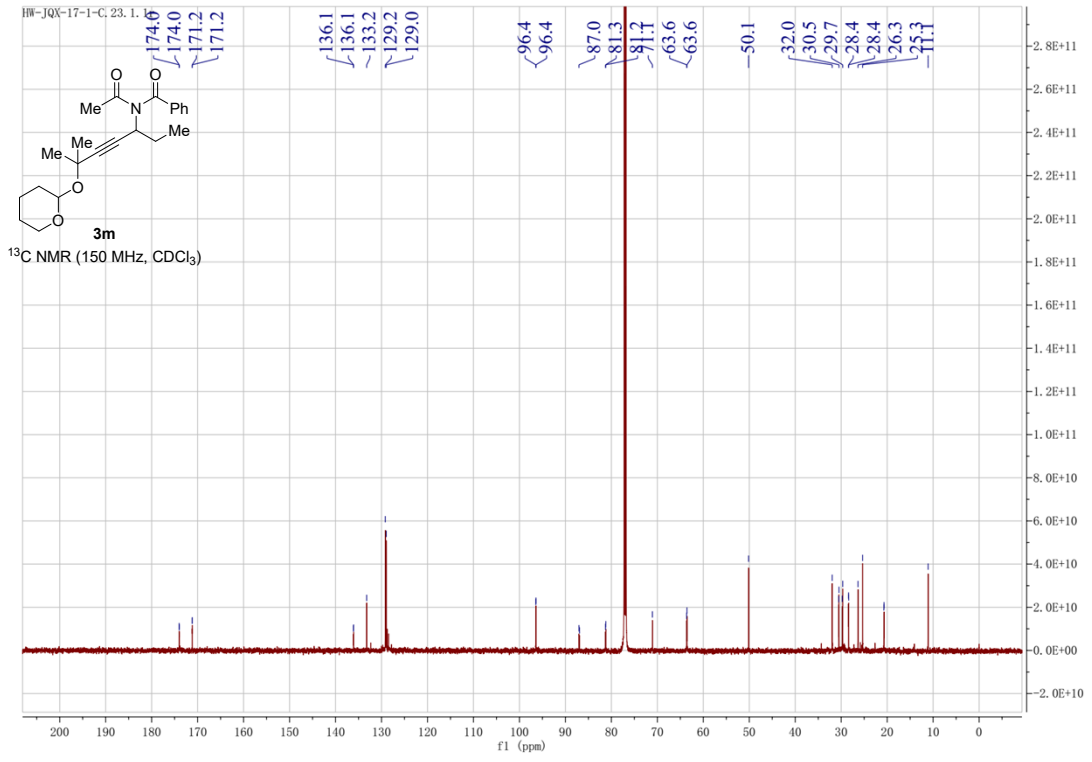
^{1}H and ^{13}C Spectrum for Compound 3l at 25 ℃



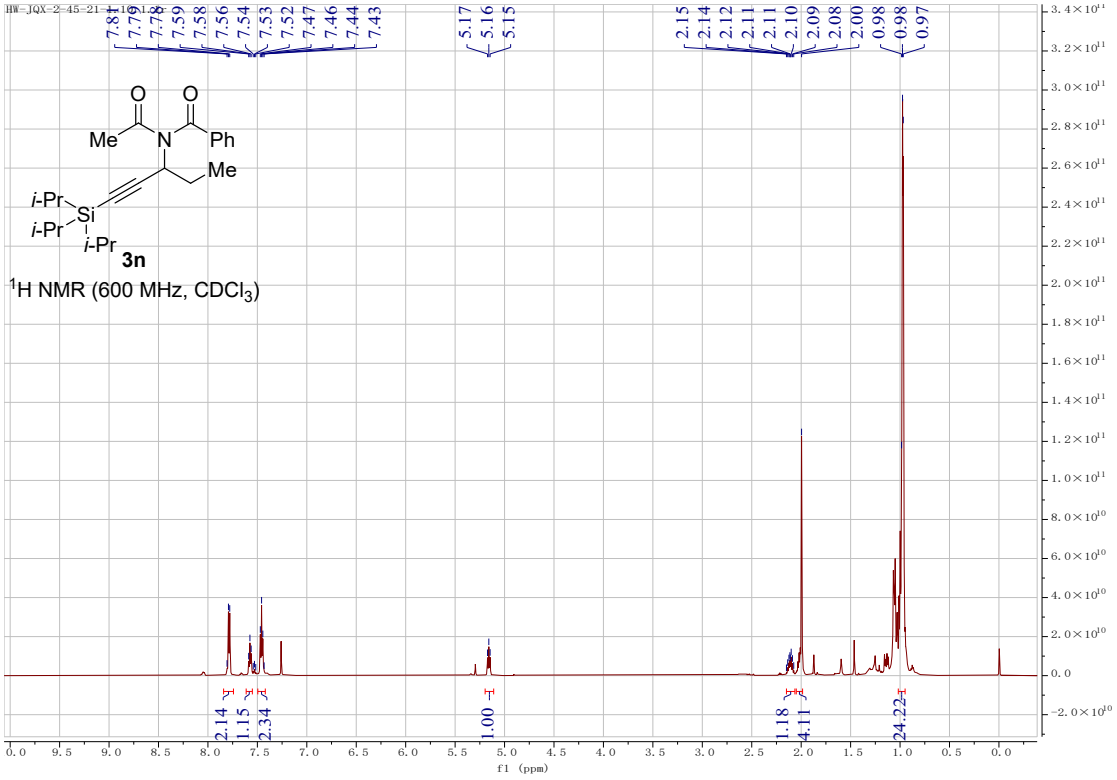


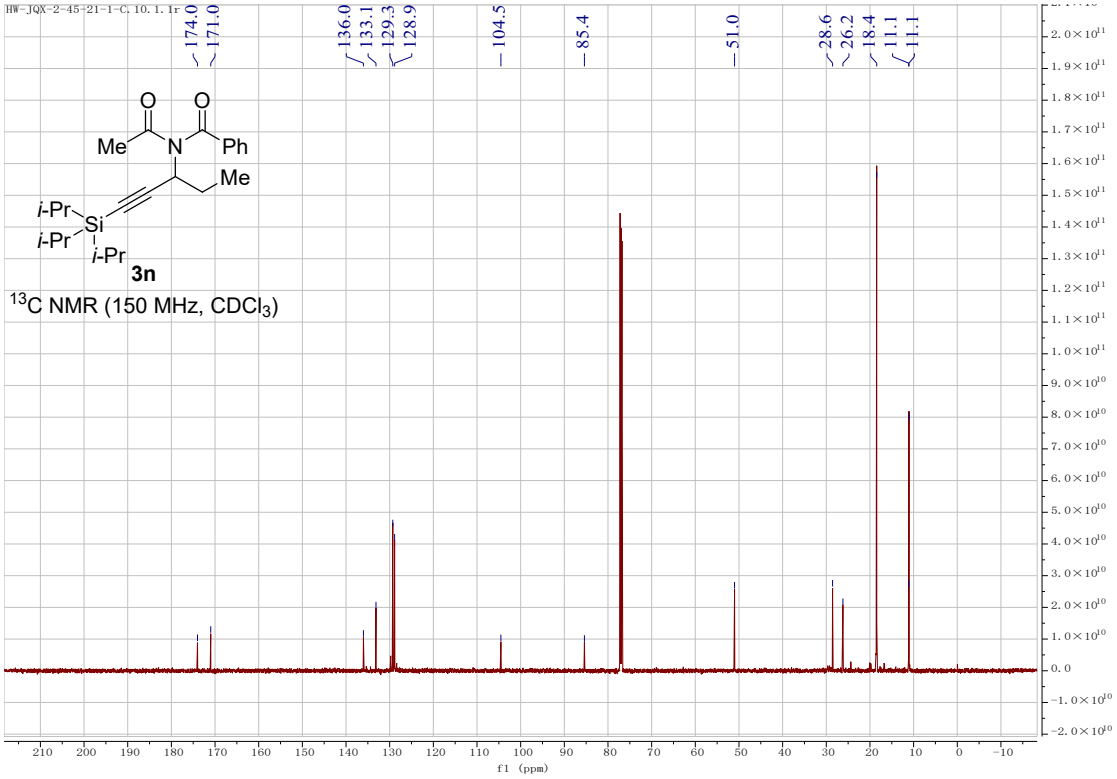
^{1}H and ^{13}C Spectrum for Compound 3m at 25 ℃



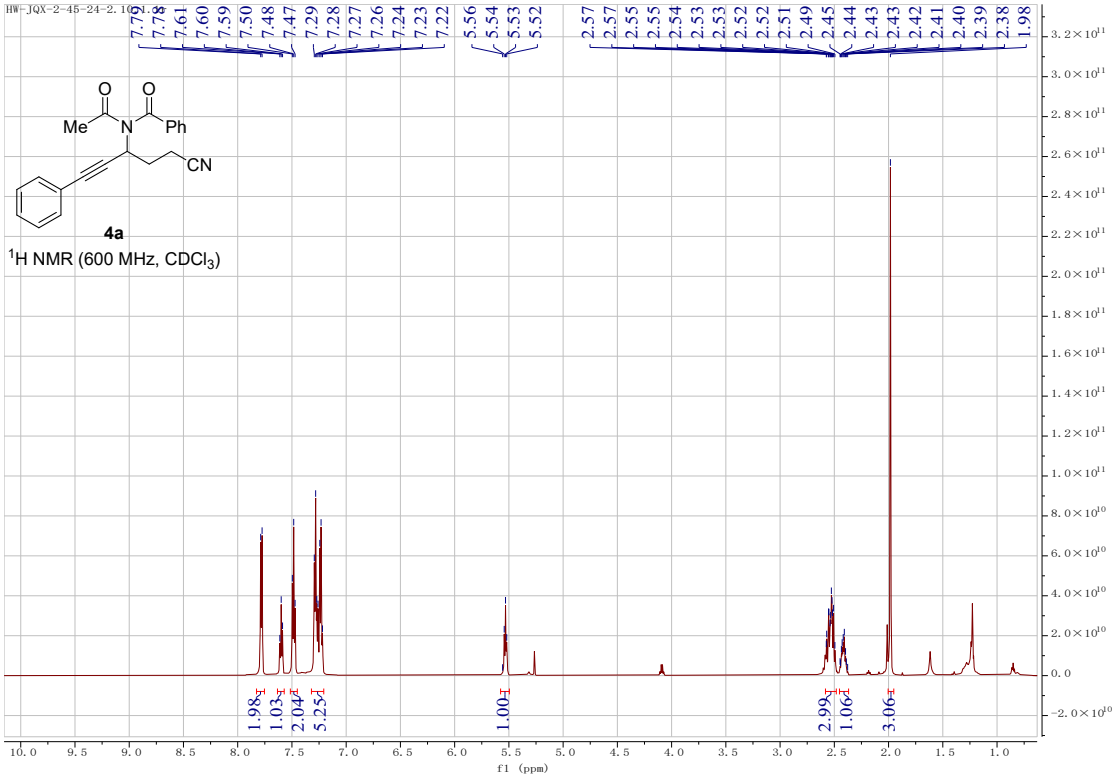


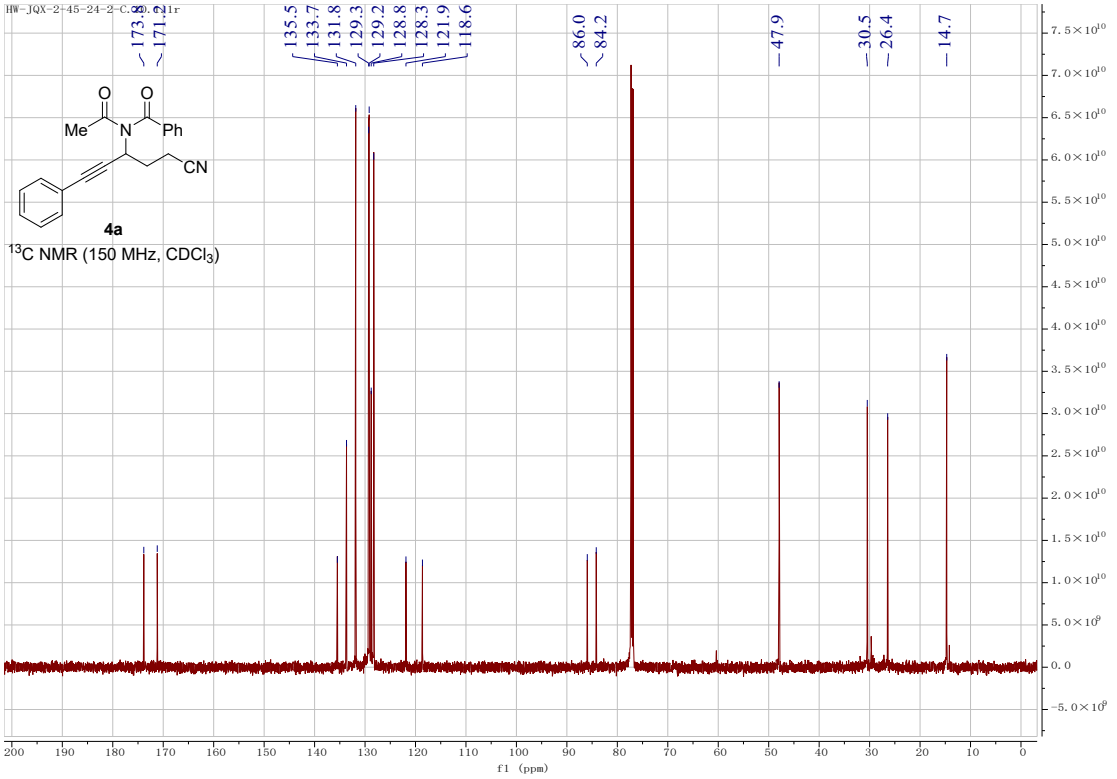
^{1}H and ^{13}C Spectrum for Compound 3n at 25 ℃



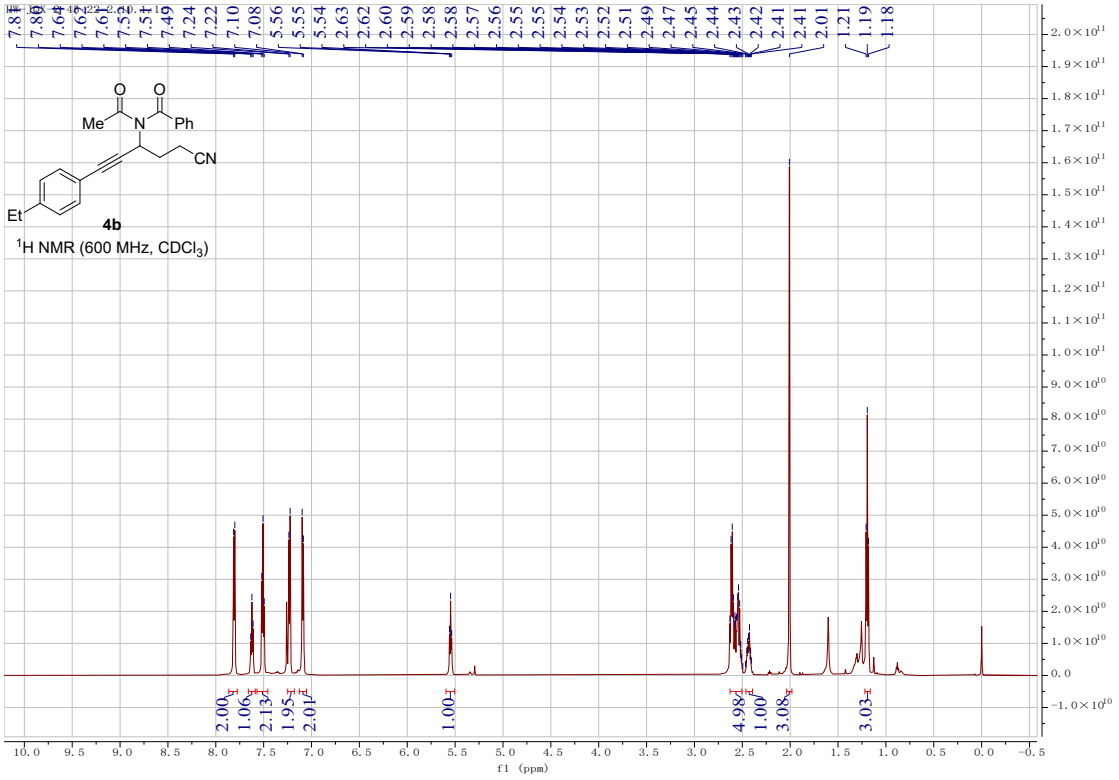


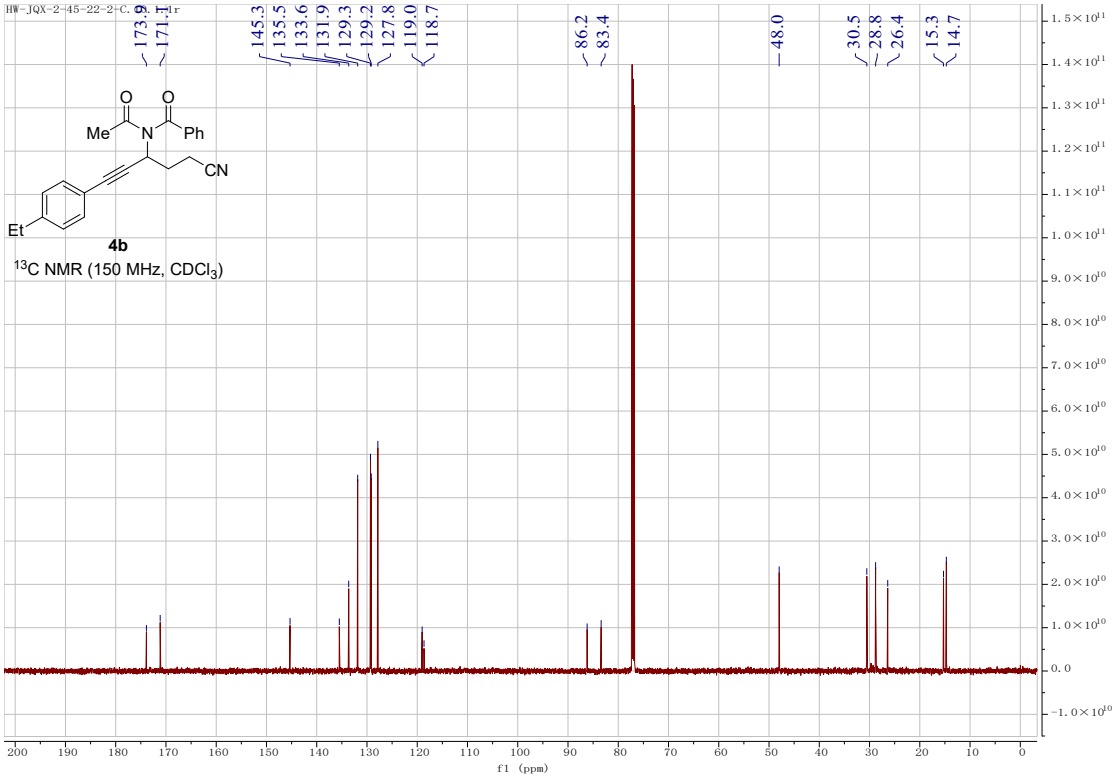
^{1}H and ^{13}C Spectrum for Compound 4a at 25 ℃



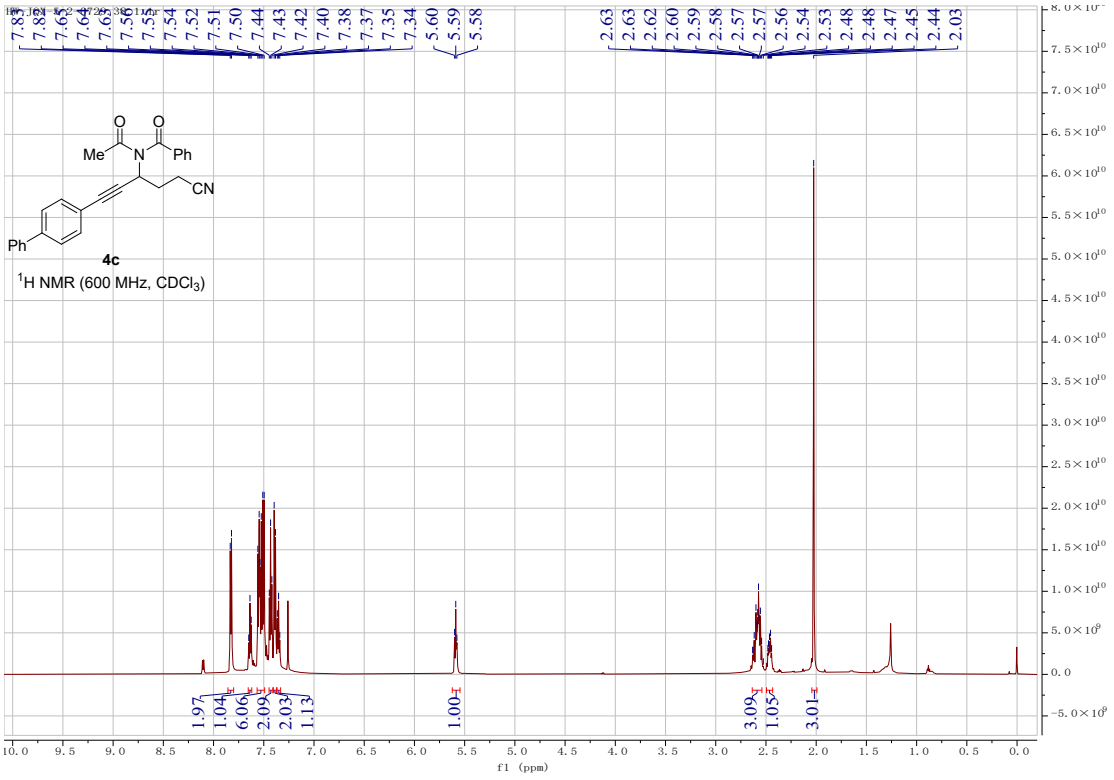


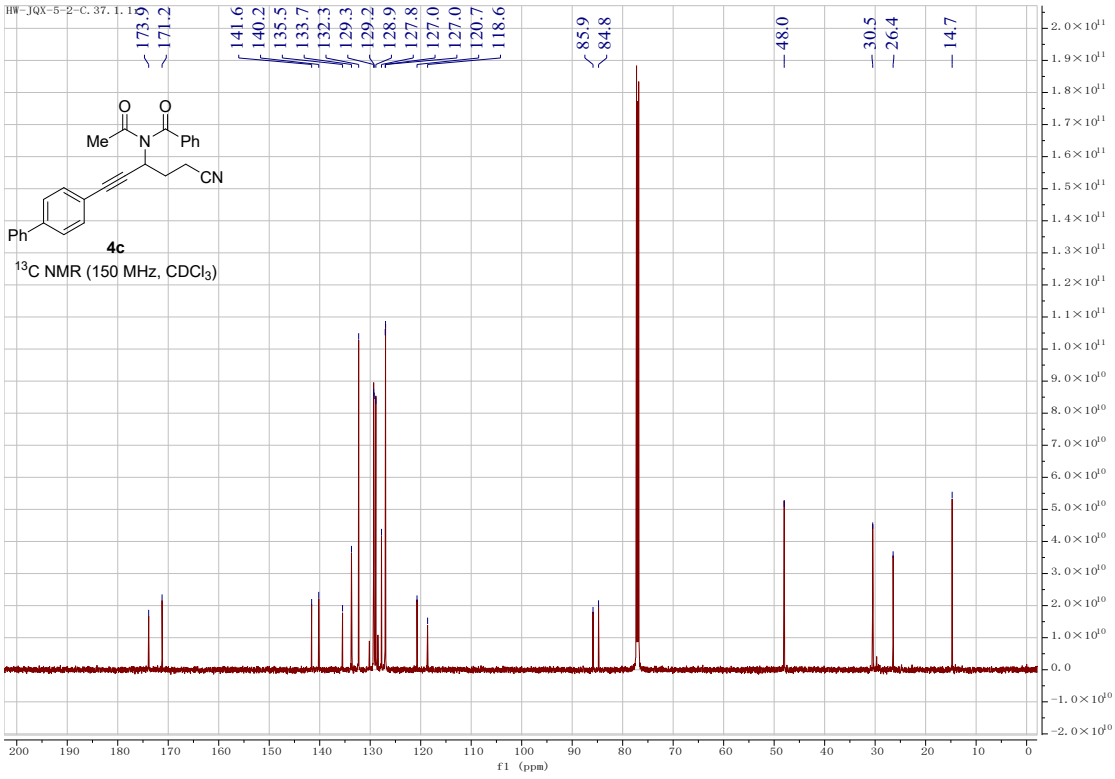
^{1}H and ^{13}C Spectrum for Compound 4b at 25 ℃



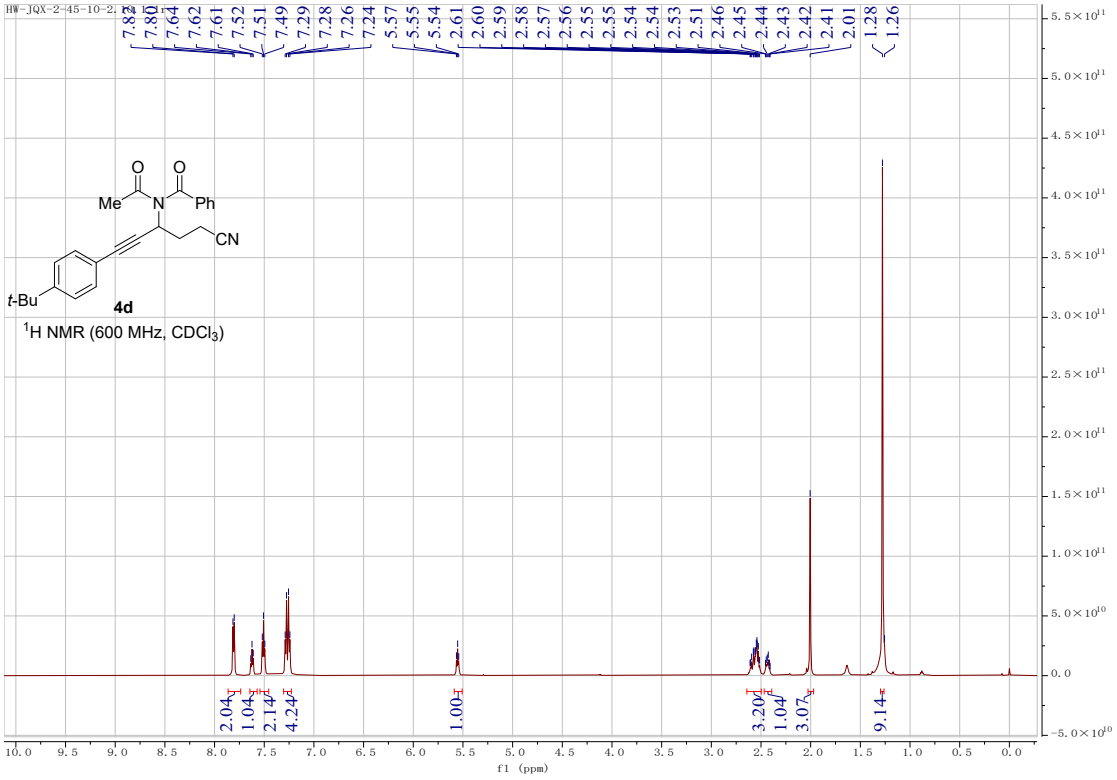


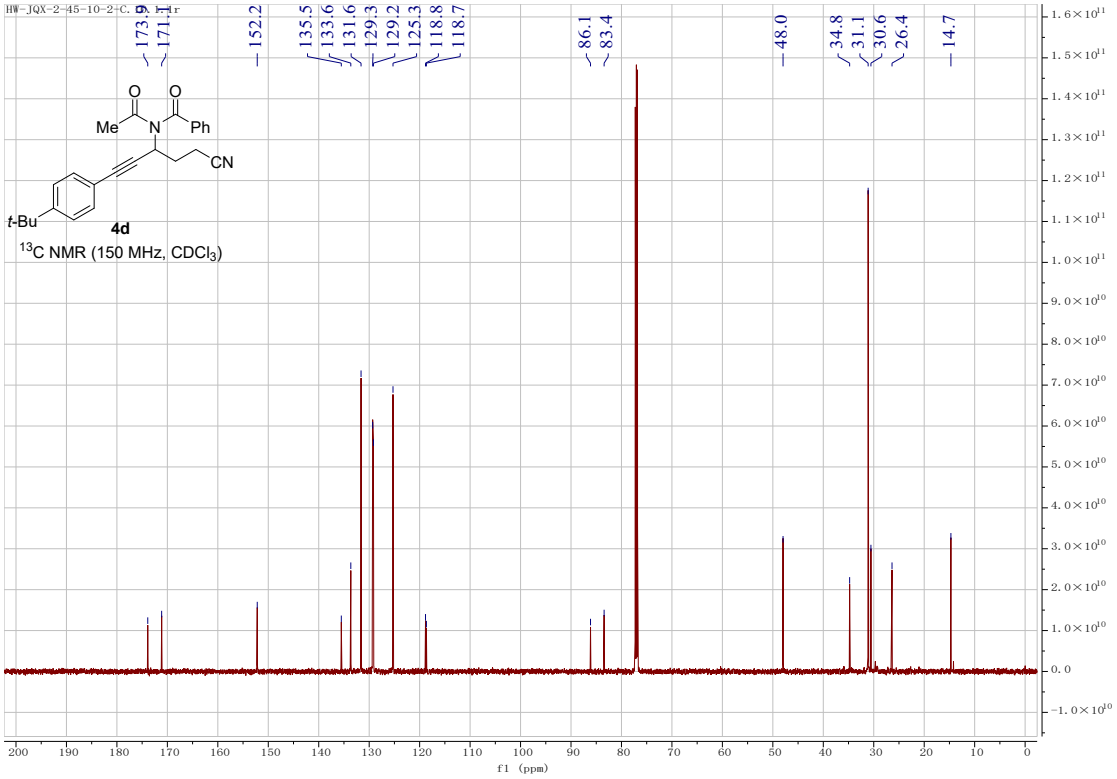
^{1}H and ^{13}C Spectrum for Compound 4c at 25 ℃



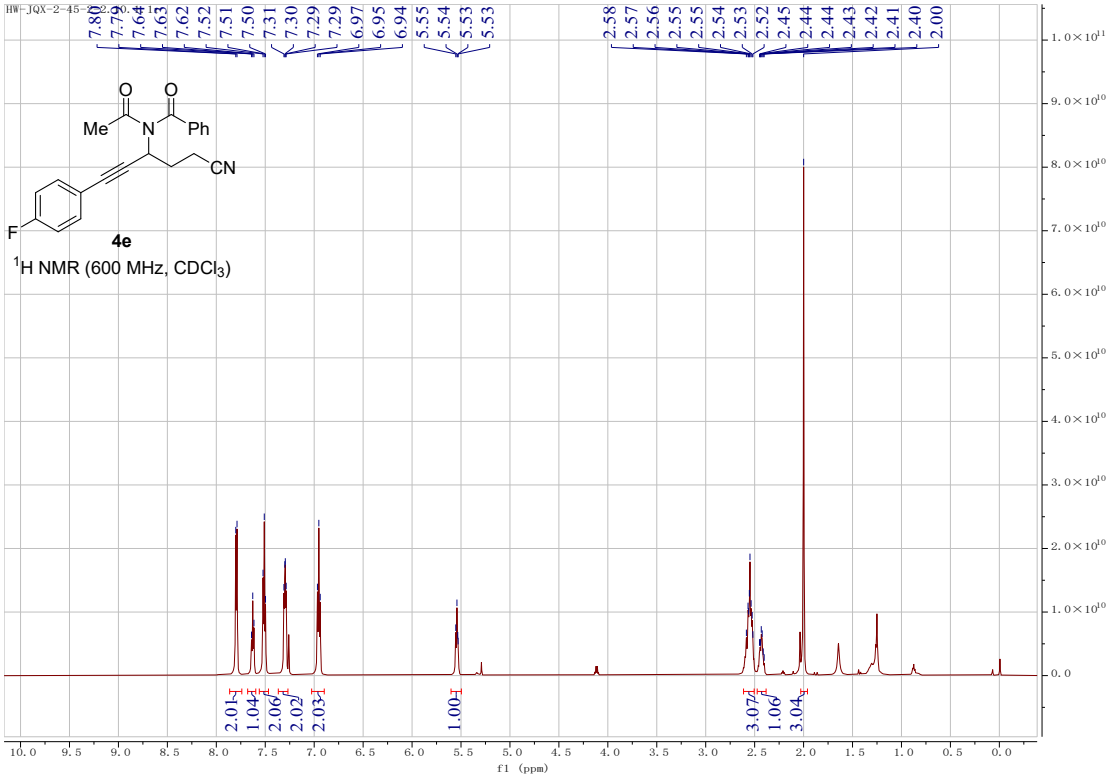


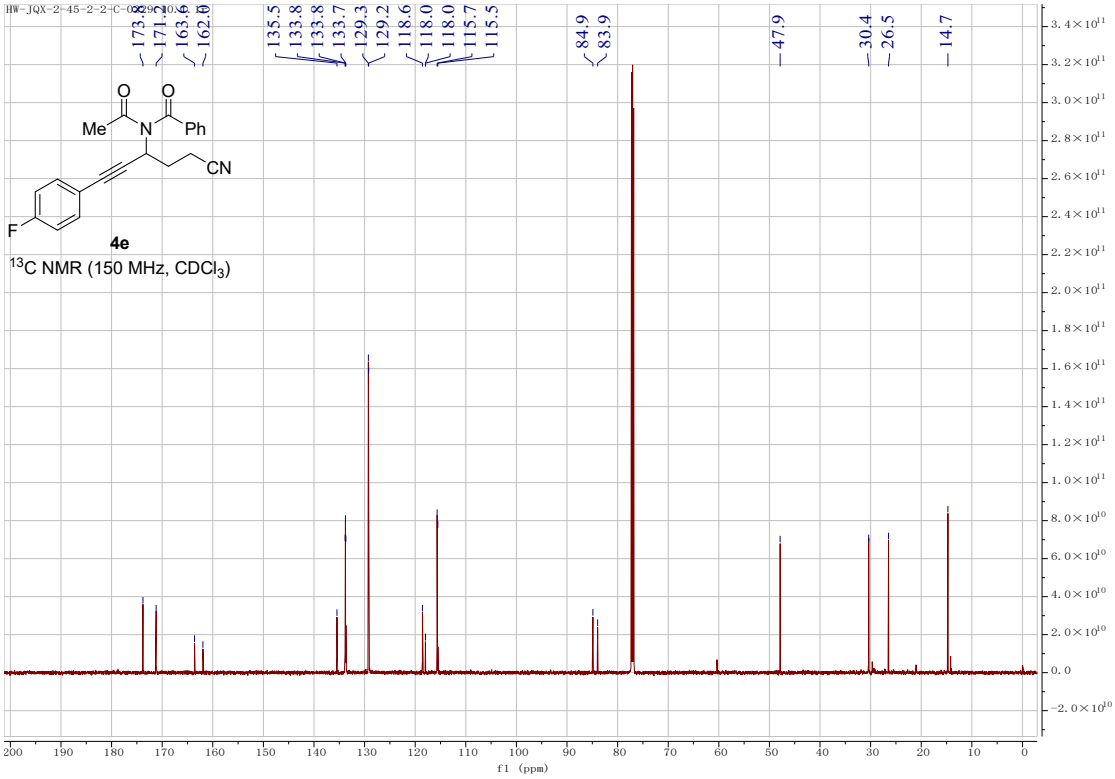
^{1}H and ^{13}C Spectrum for Compound 4d at 25 ℃



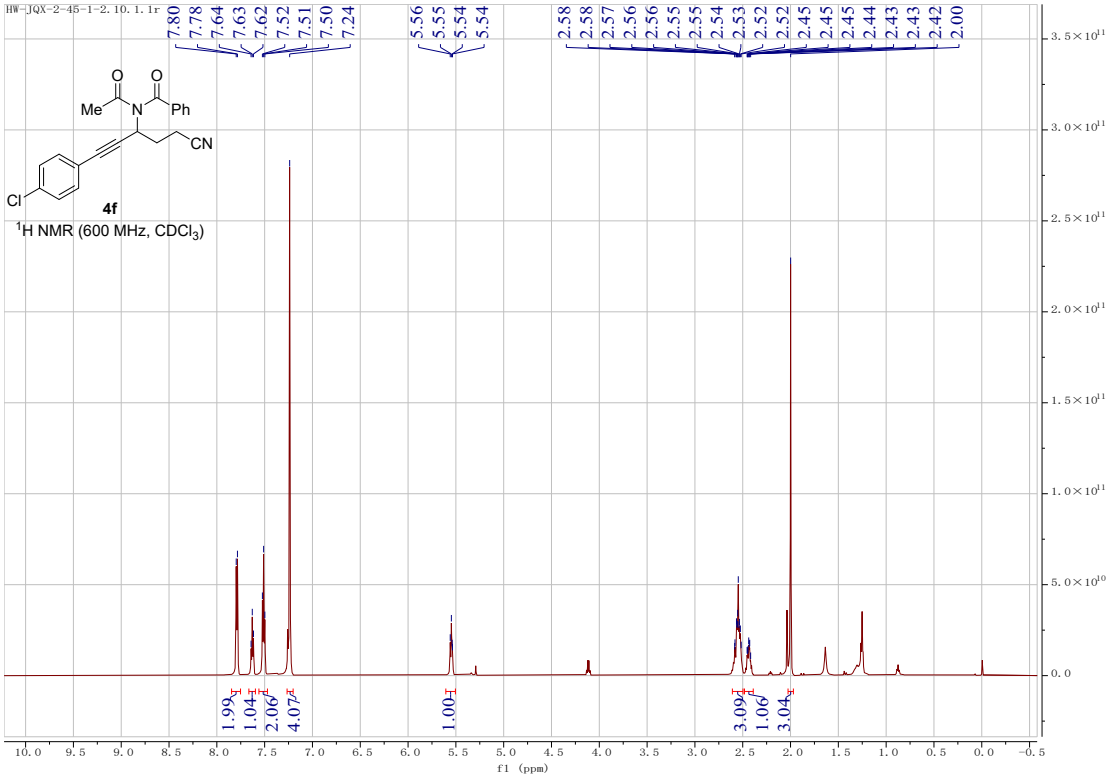


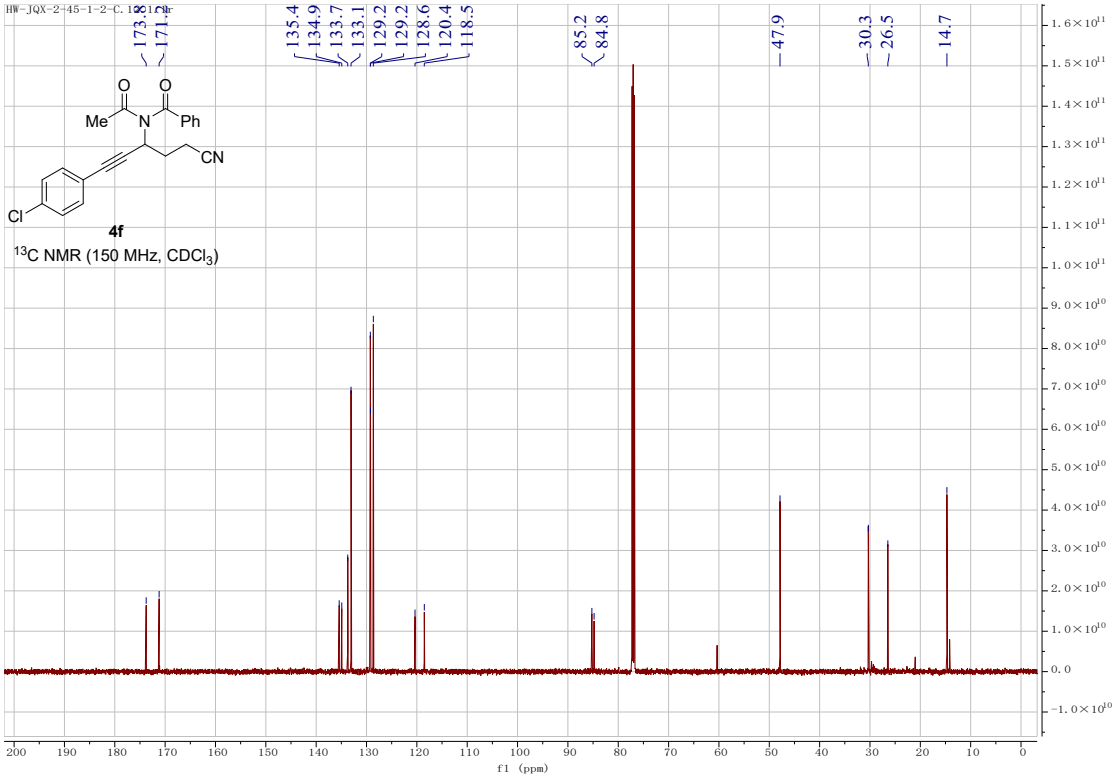
^{1}H and ^{13}C Spectrum for Compound 4e at 25 ℃



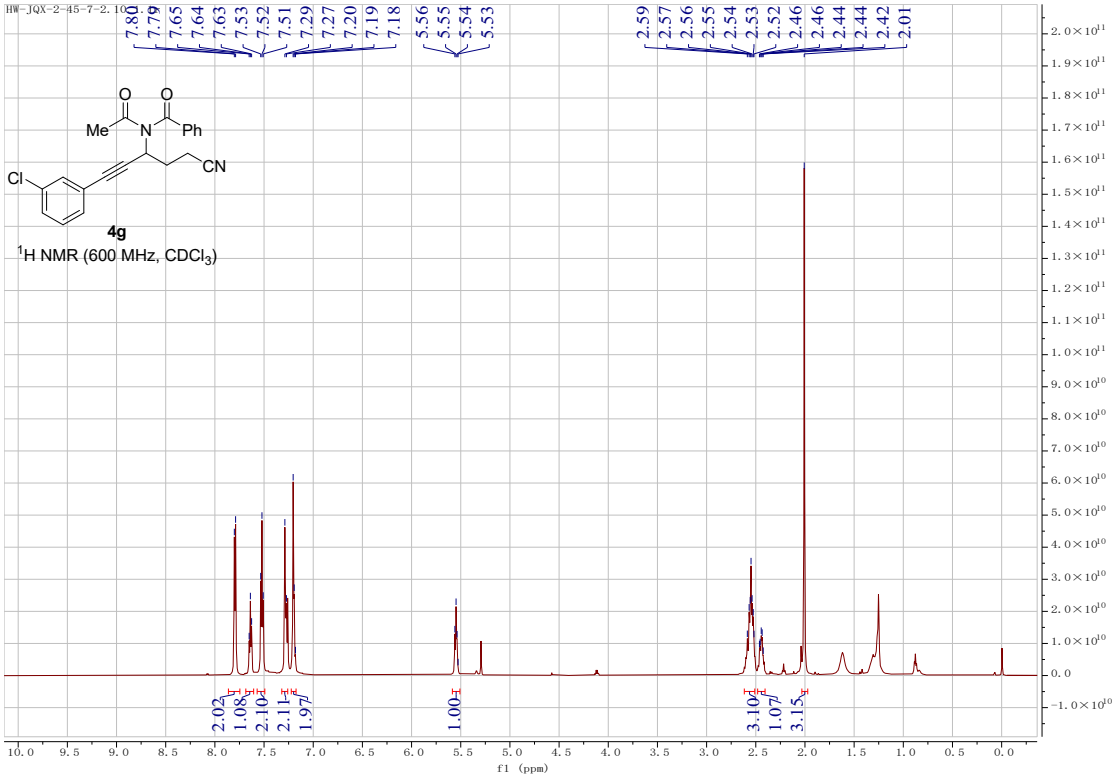


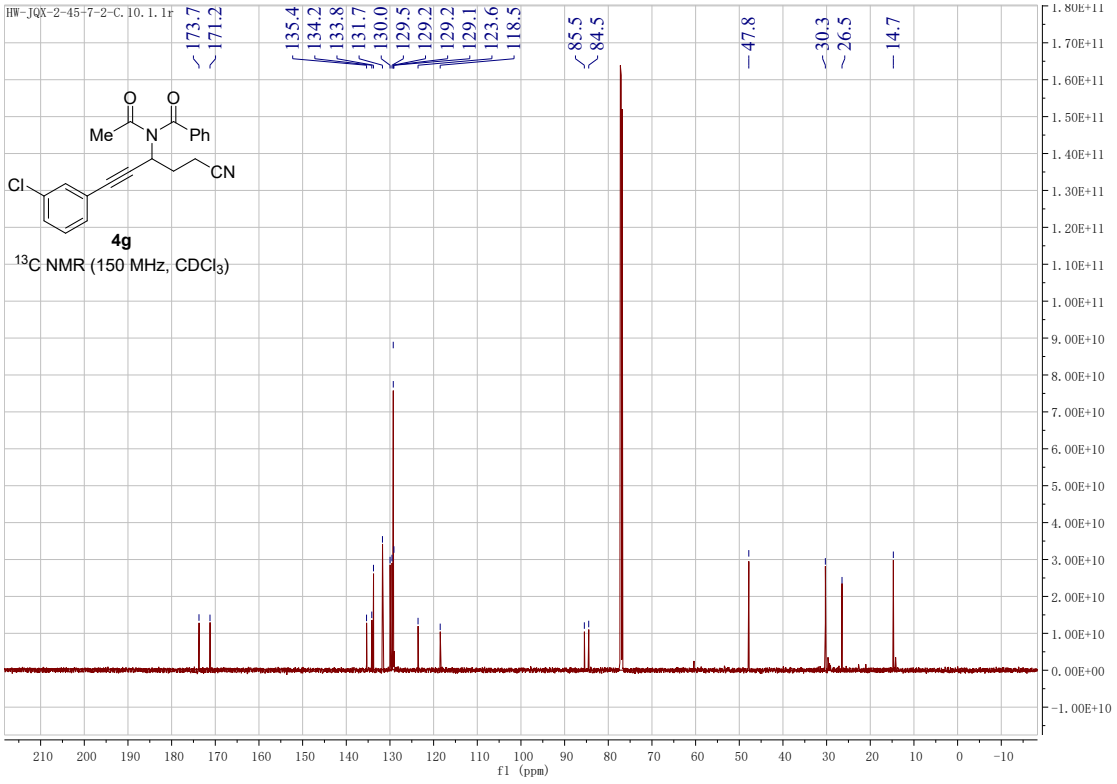
^{1}H and ^{13}C Spectrum for Compound 4f at 25 ℃



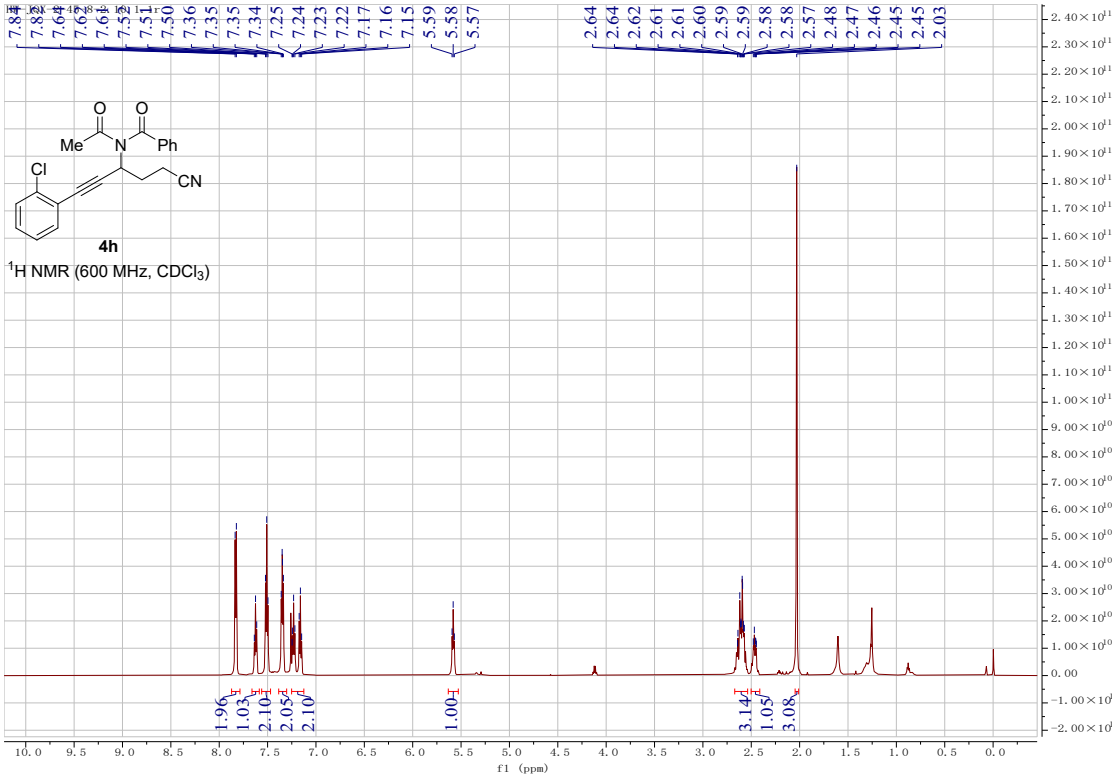


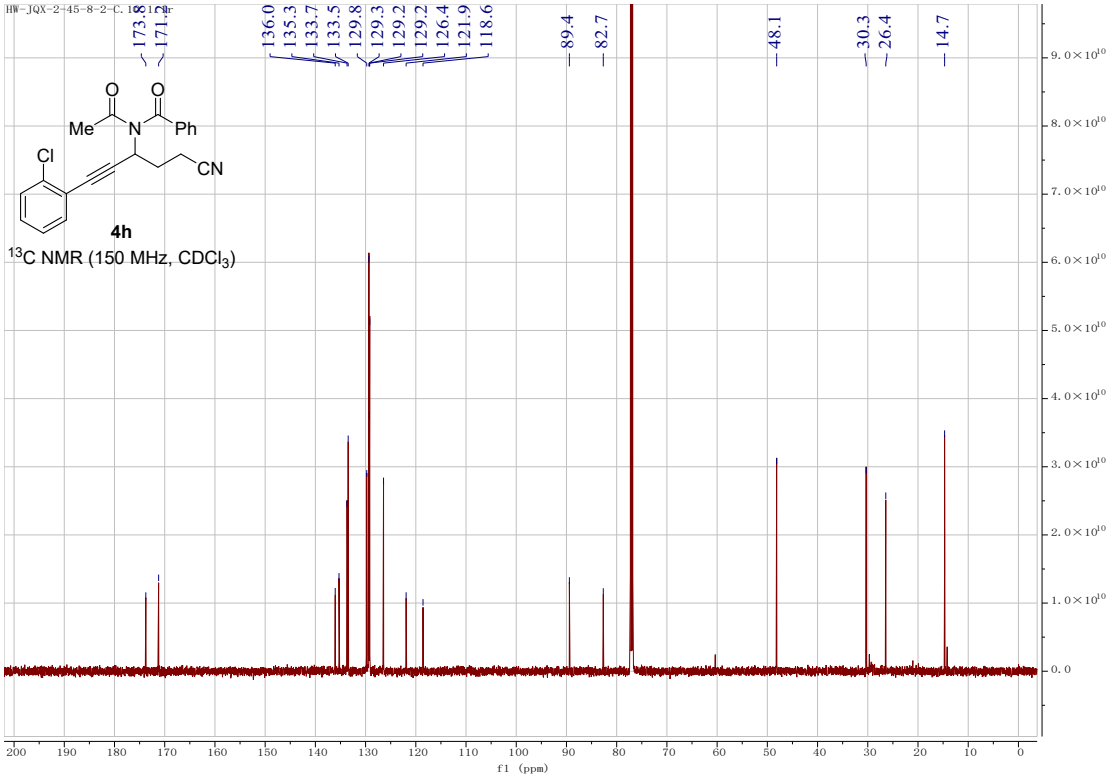
^{1}H and ^{13}C Spectrum for Compound 4g at 25 ℃



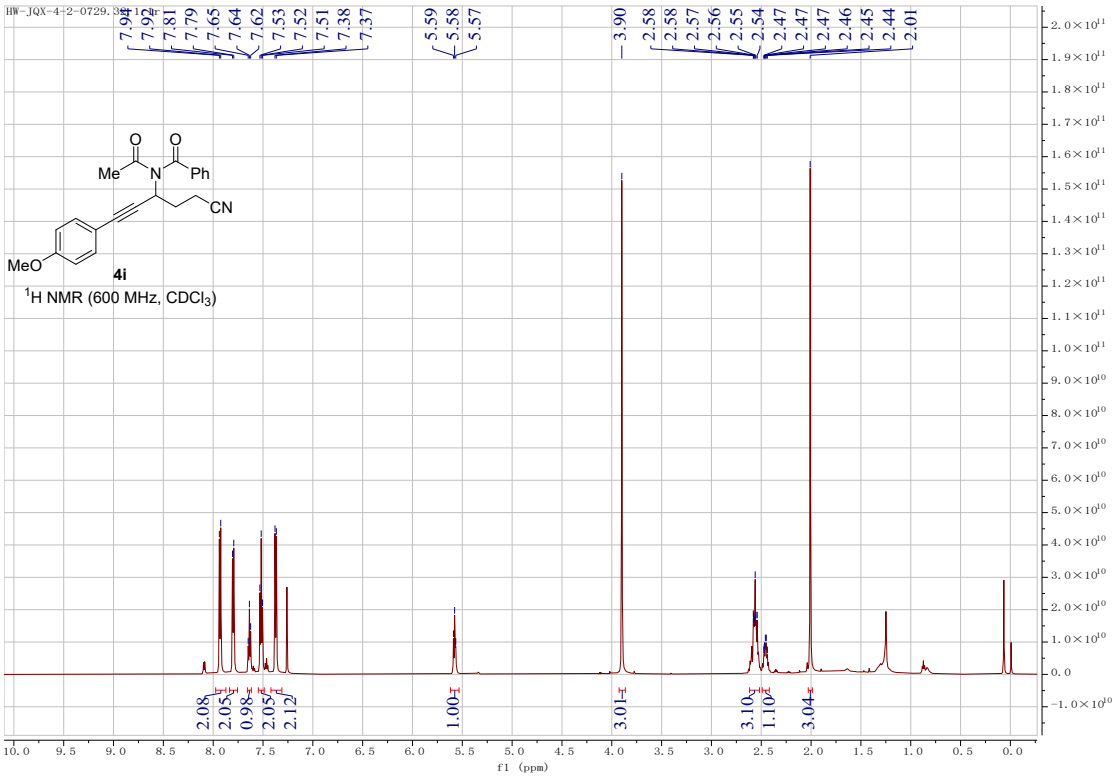


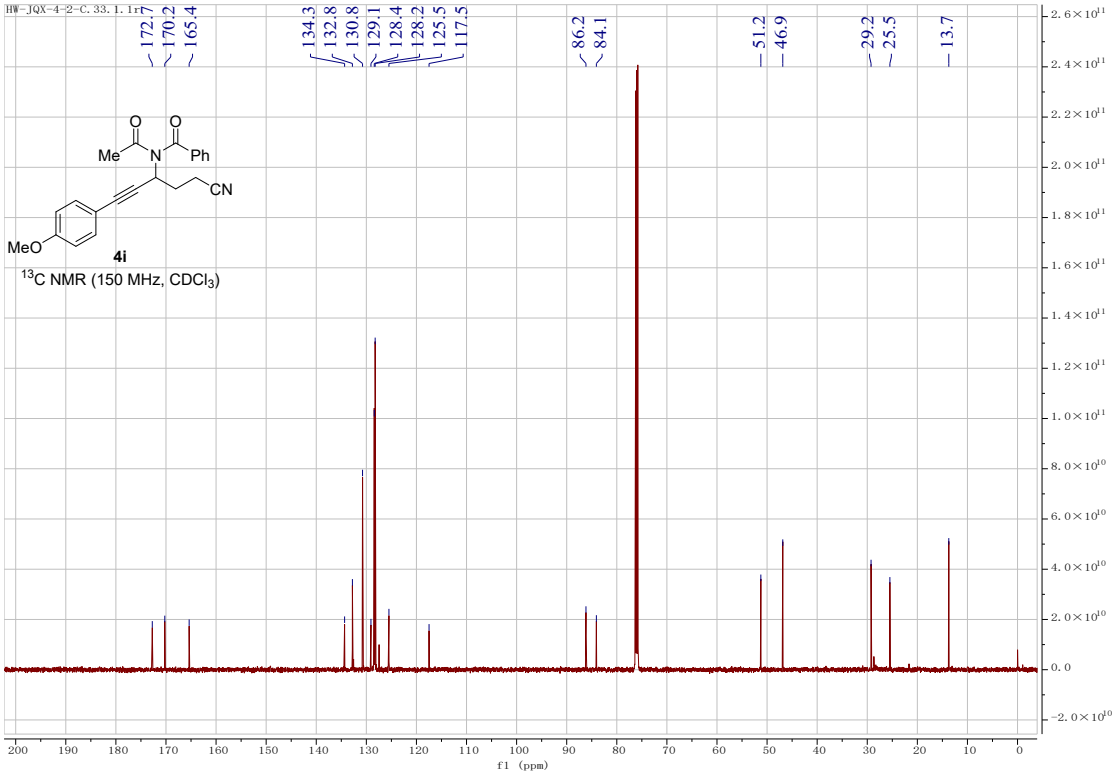
^{1}H and ^{13}C Spectrum for Compound 4h at 25 ℃



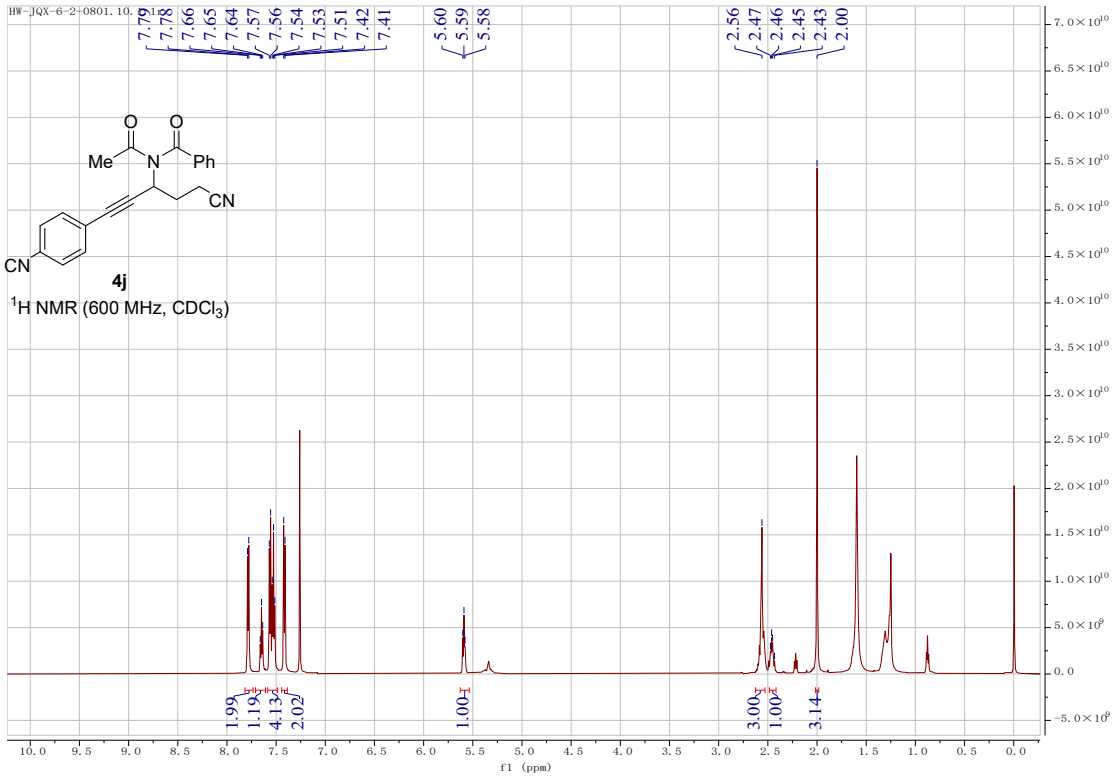


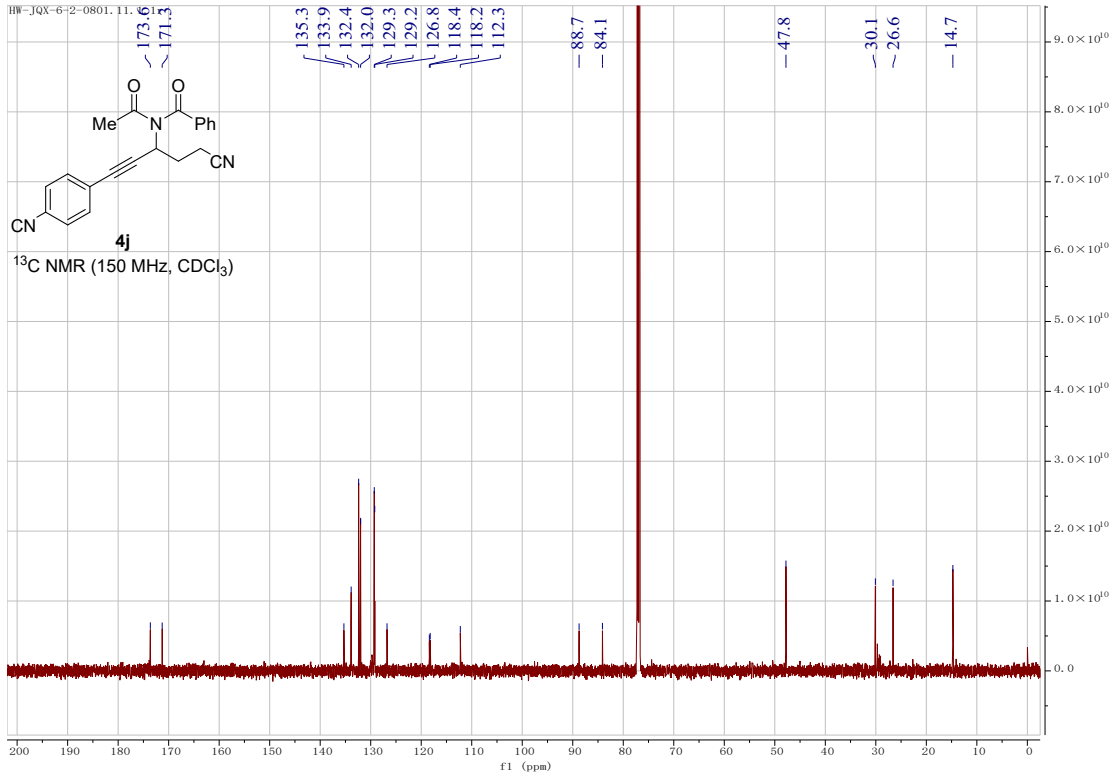
^{1}H and ^{13}C Spectrum for Compound 4i at 25 ℃



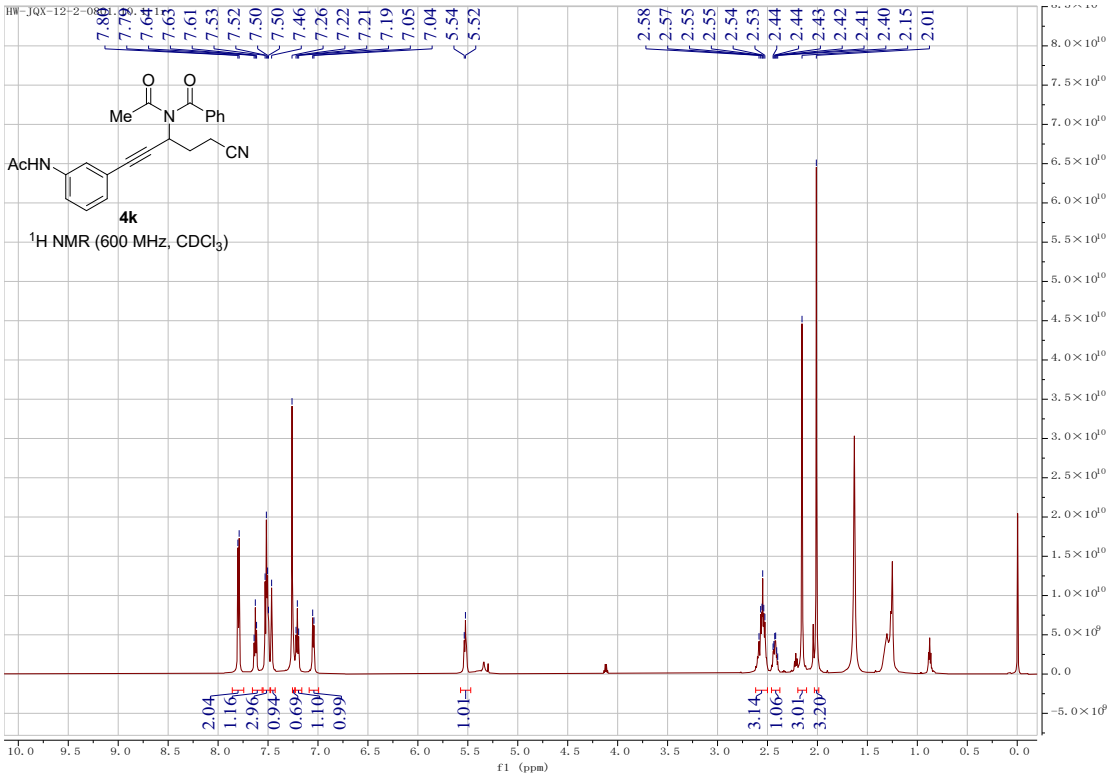


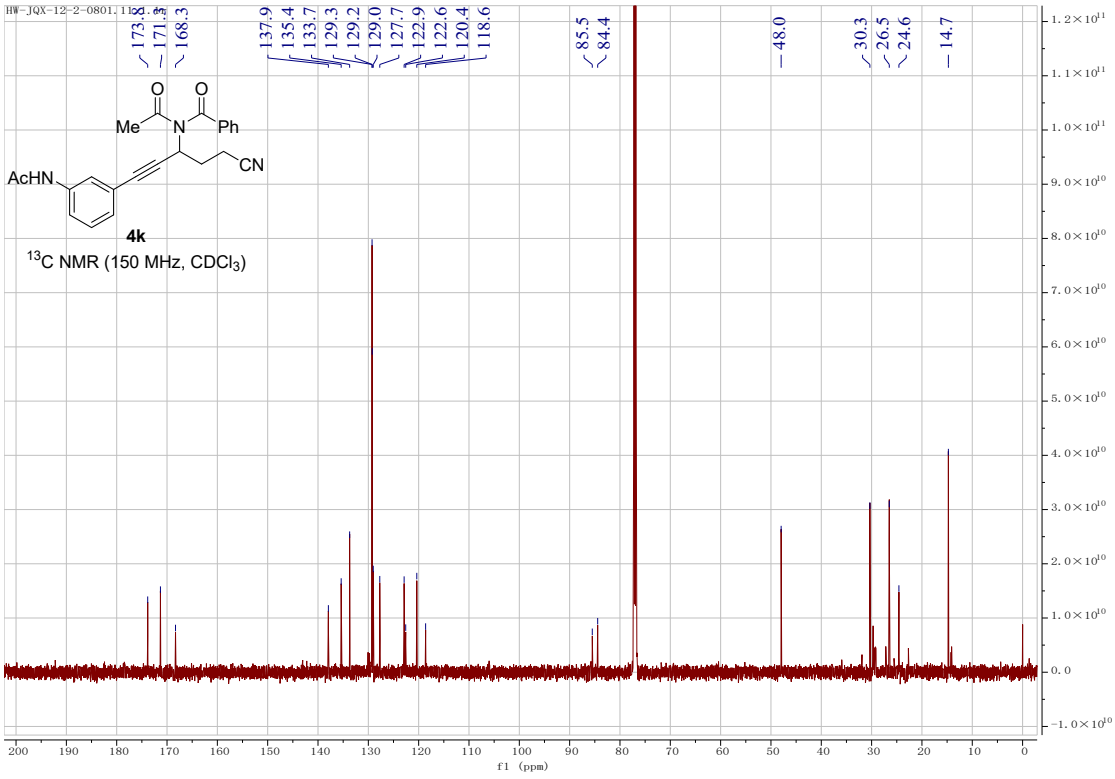
^{1}H and ^{13}C Spectrum for Compound 4j at 25 ℃



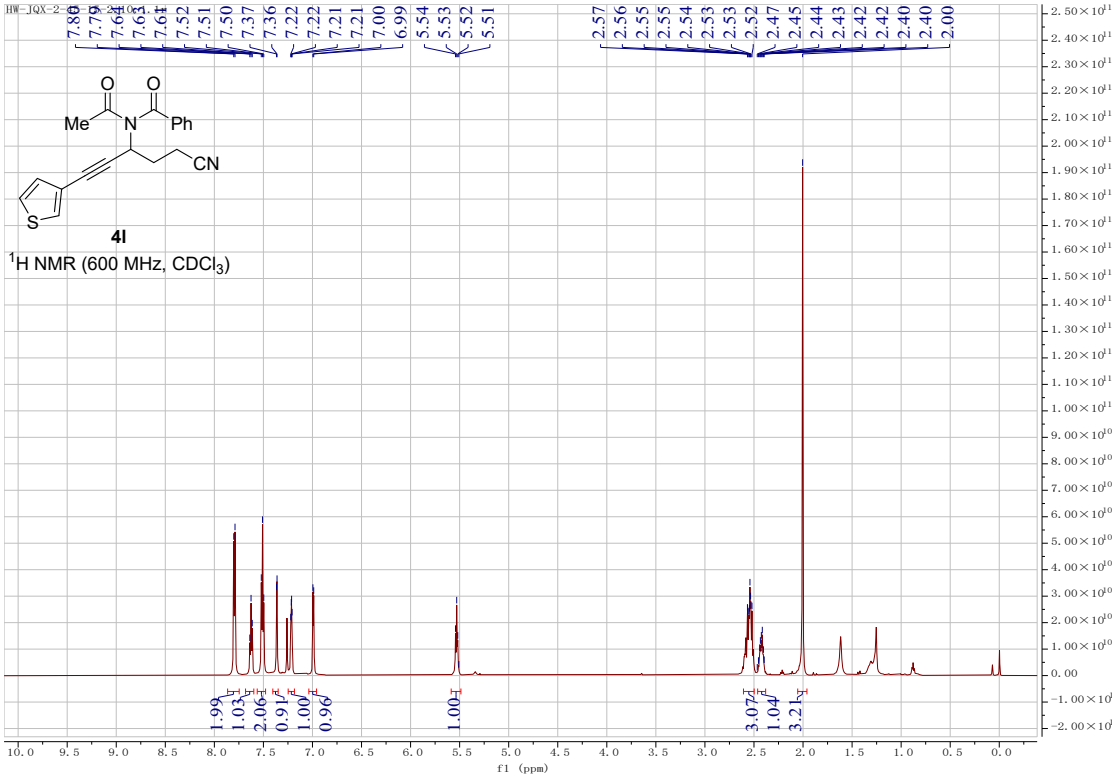


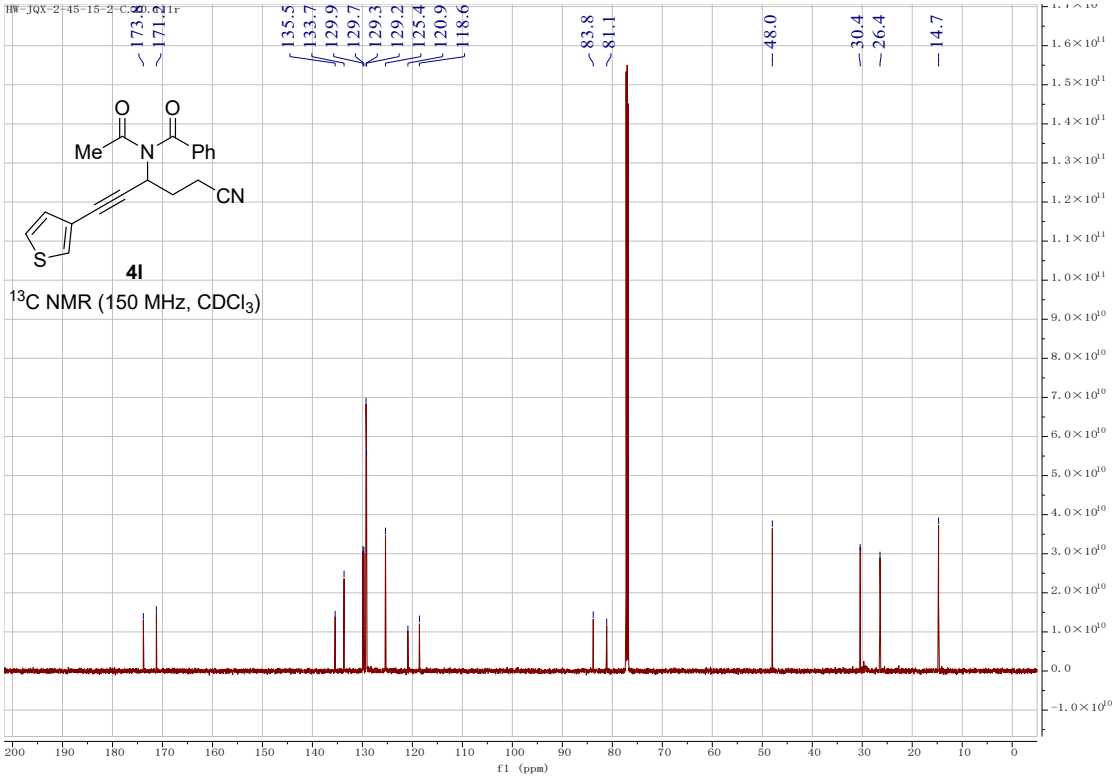
^{1}H and ^{13}C Spectrum for Compound 4k at 25 ℃



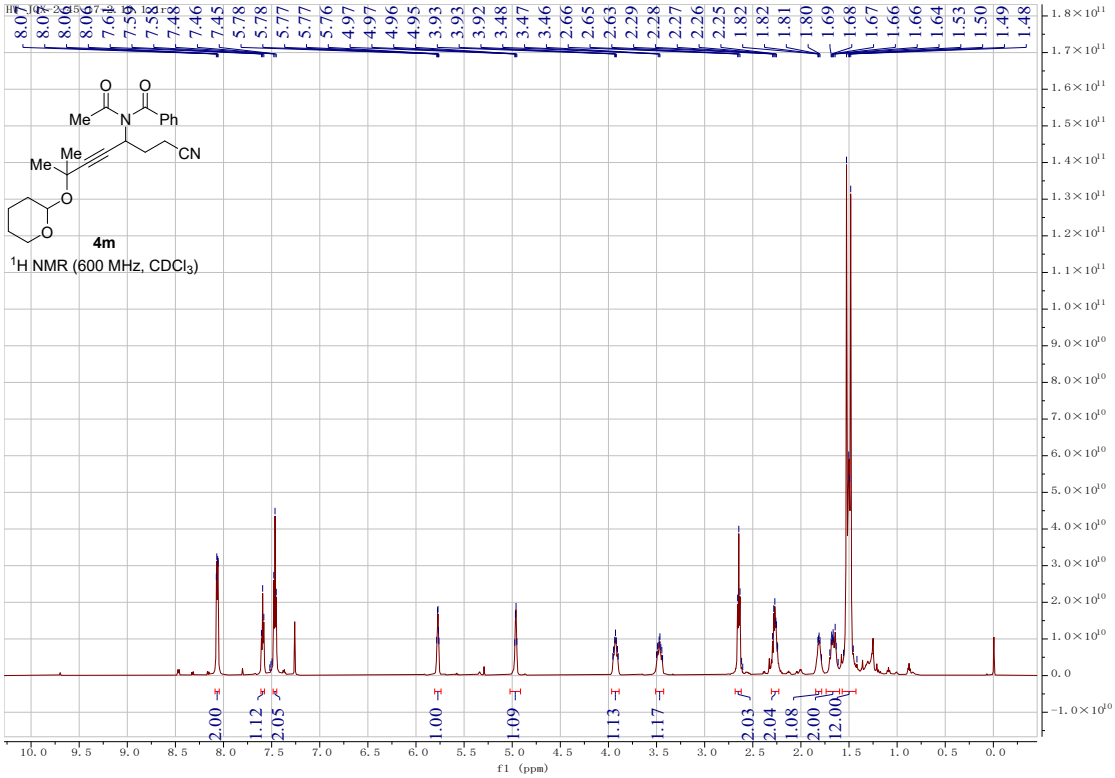


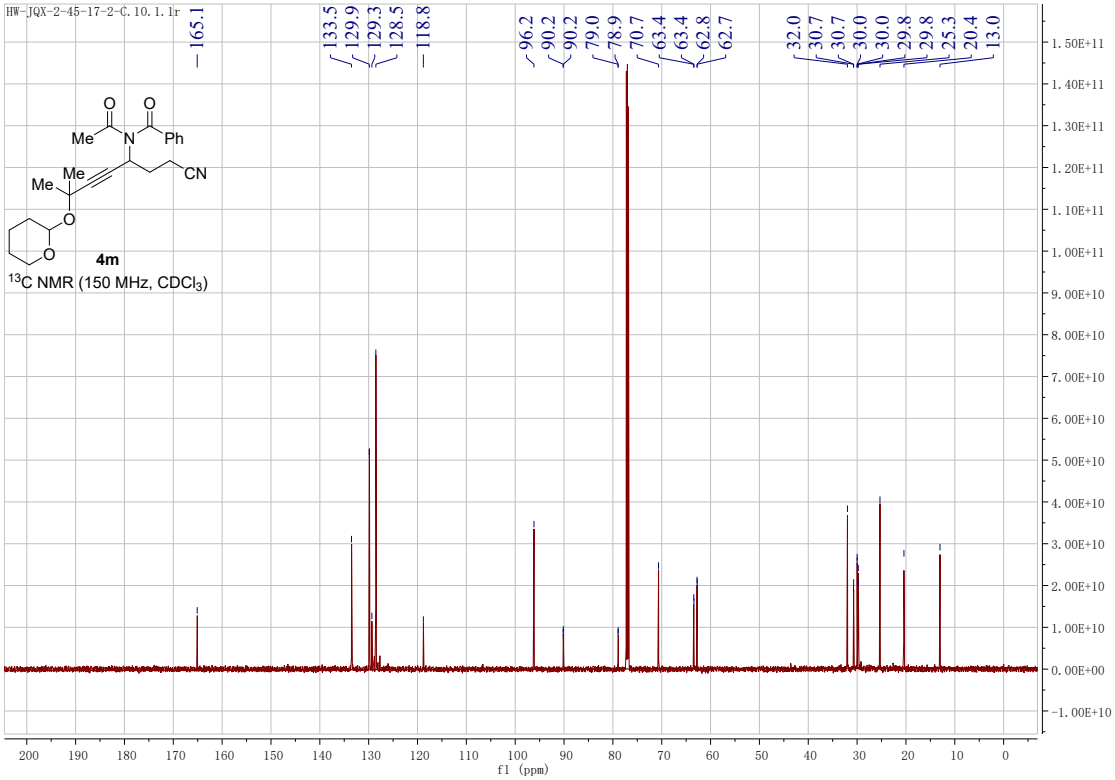
^{1}H and ^{13}C Spectrum for Compound 4l at 25 ℃



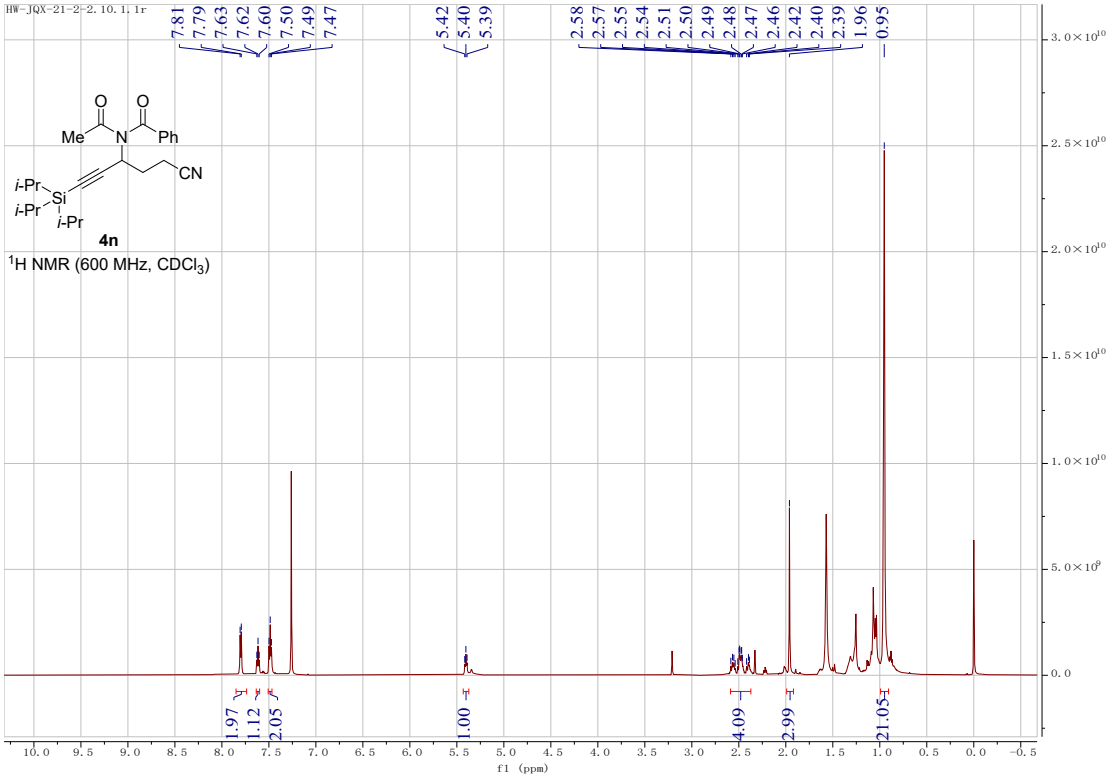


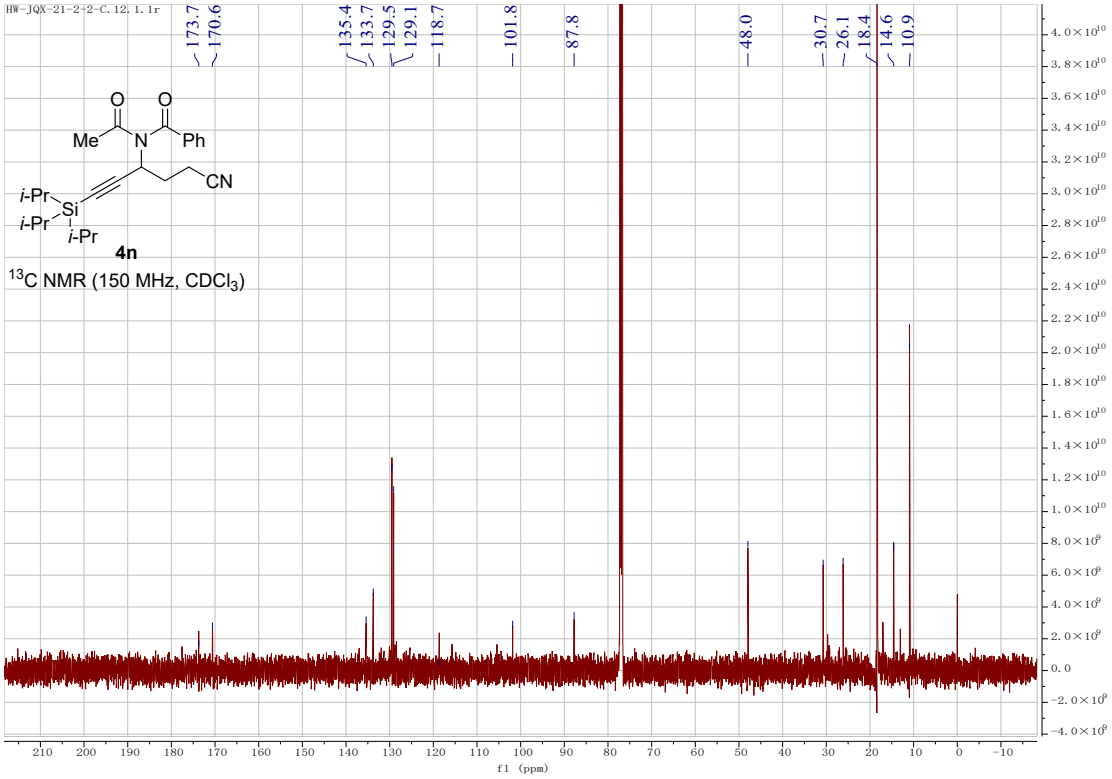
^{1}H and ^{13}C Spectrum for Compound 4m at 25 ℃



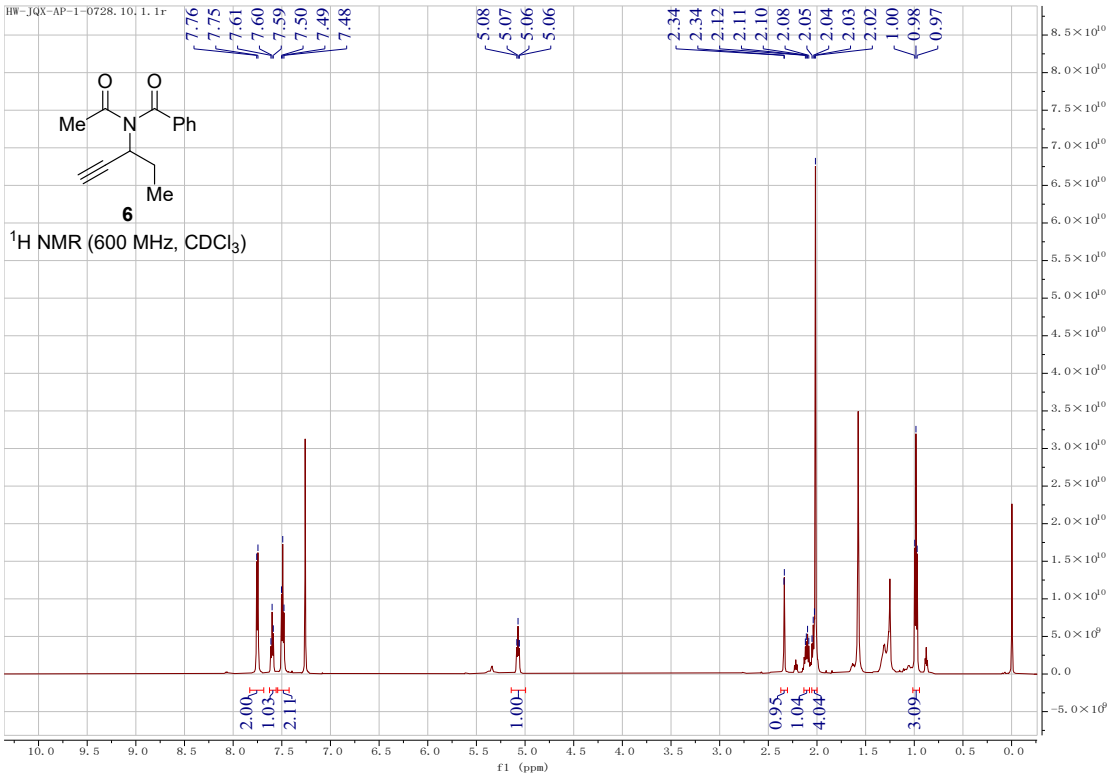


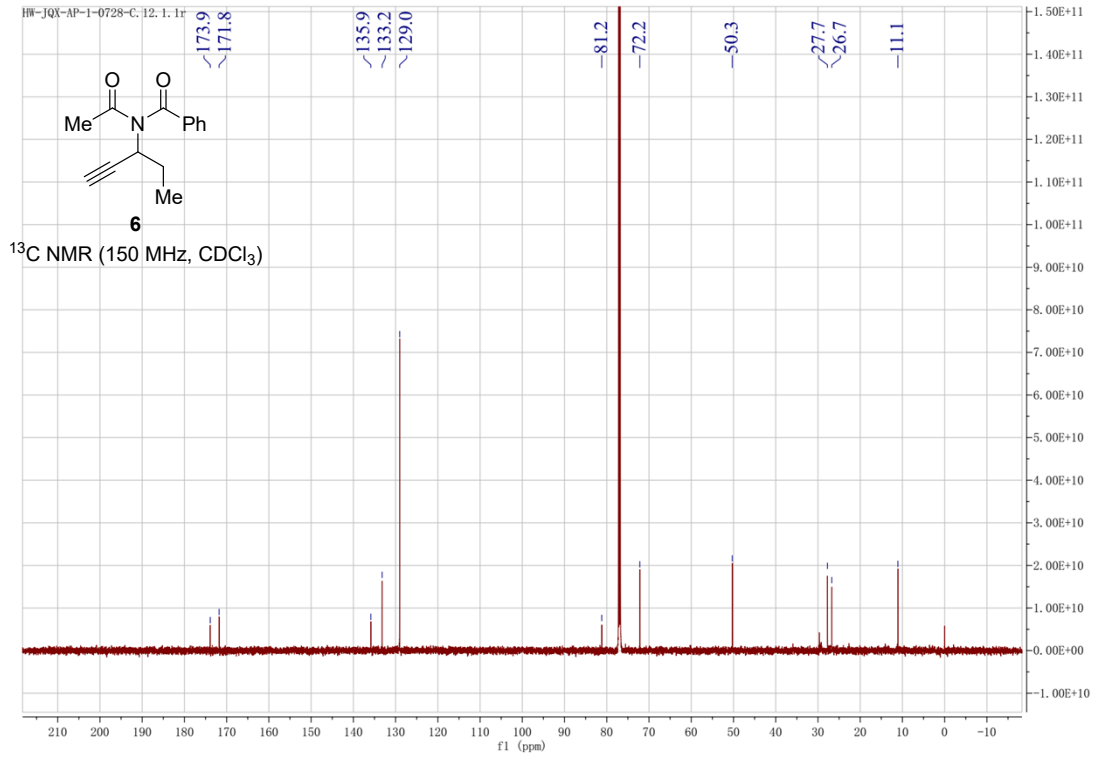
^{1}H and ^{13}C Spectrum for Compound 4n at 25 ℃



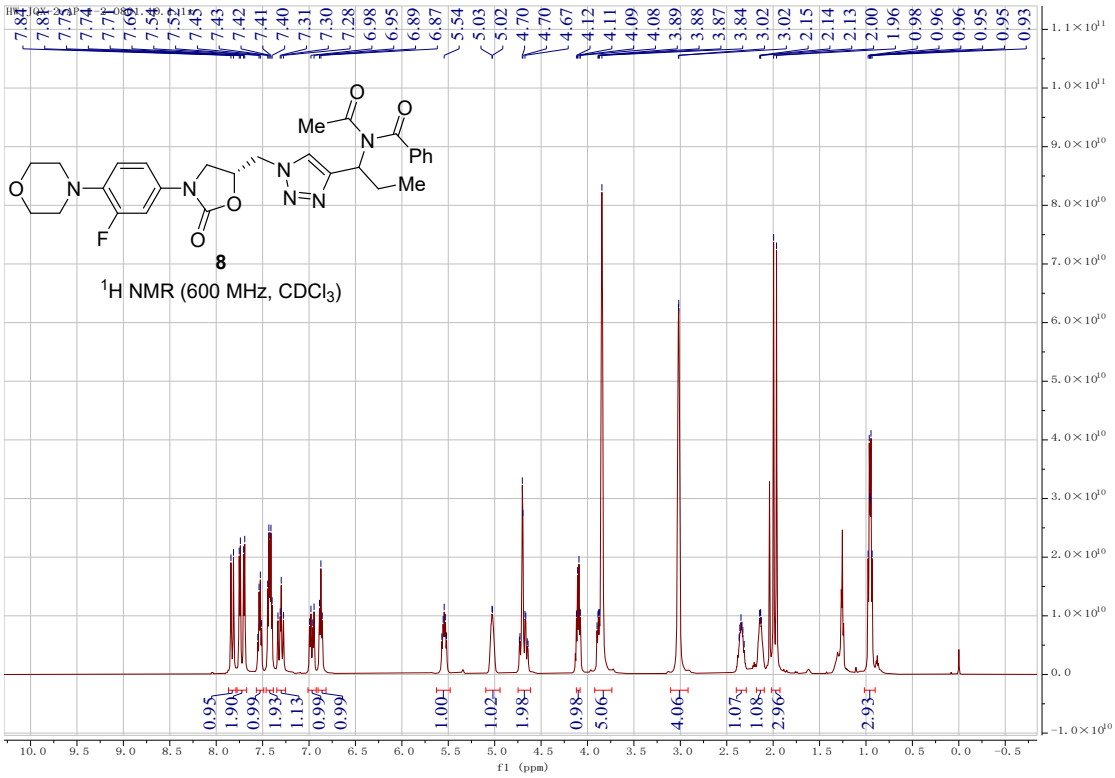


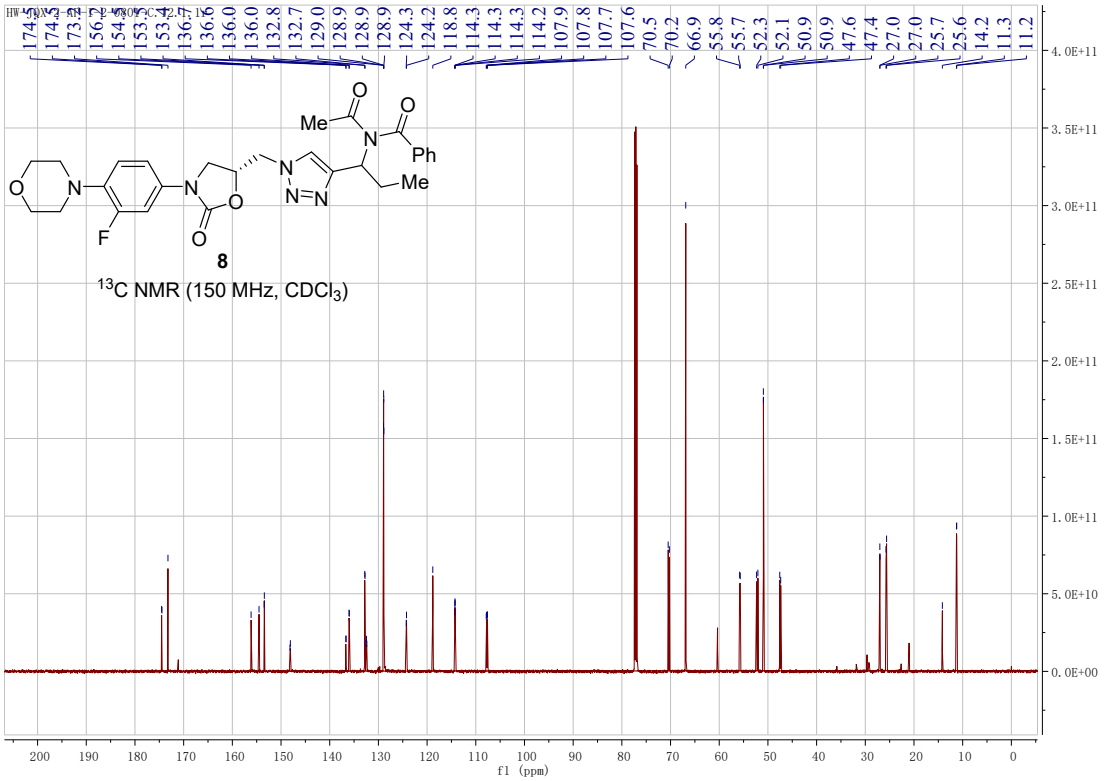
^{1}H and ^{13}C Spectrum for Compound 6 at 25 ℃



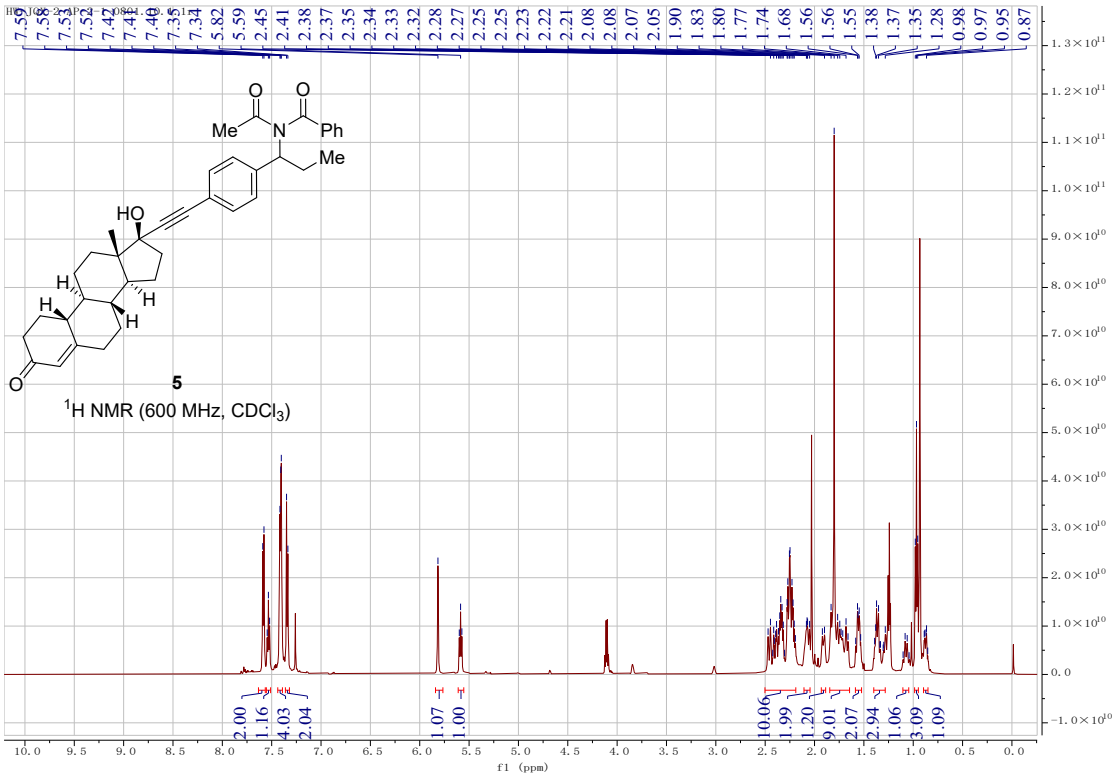


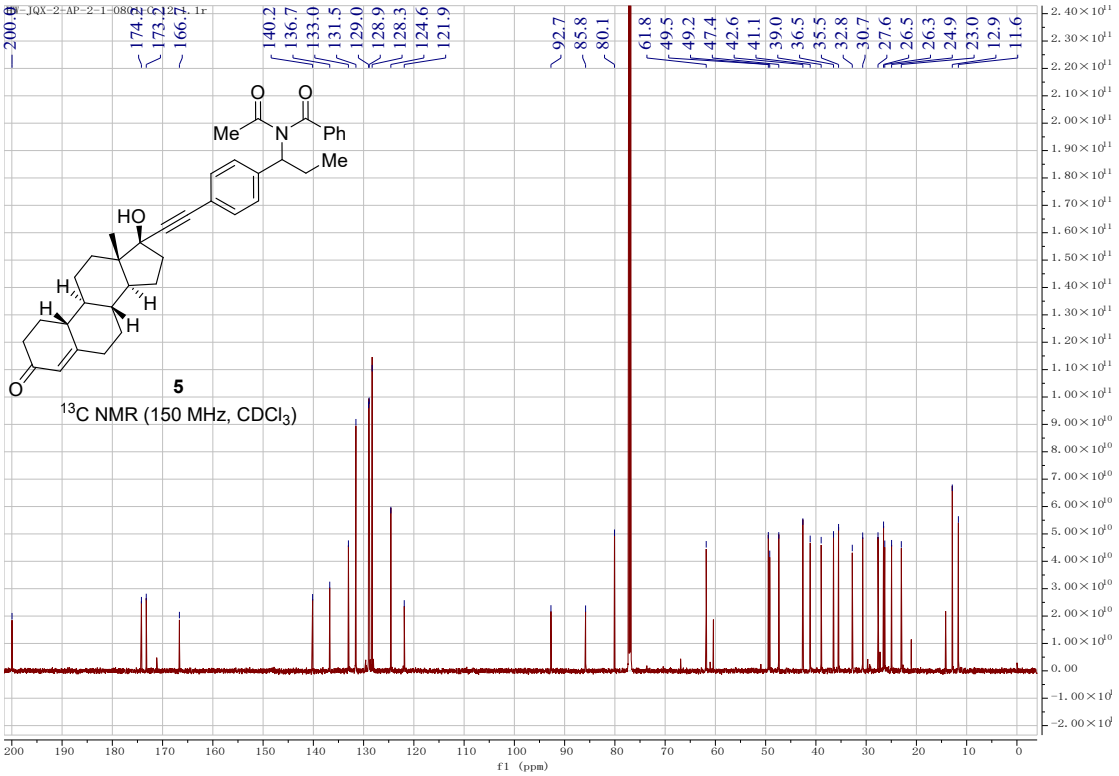
^{1}H and ^{13}C Spectrum for Compound 8 at 25 ℃



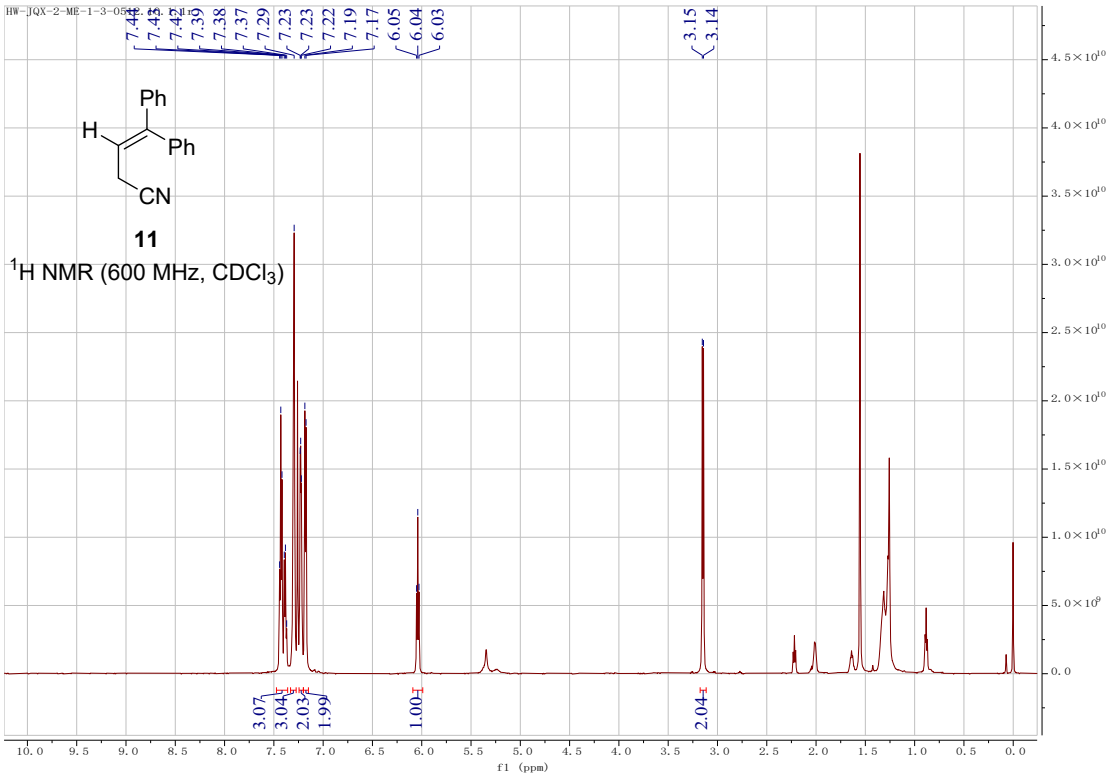


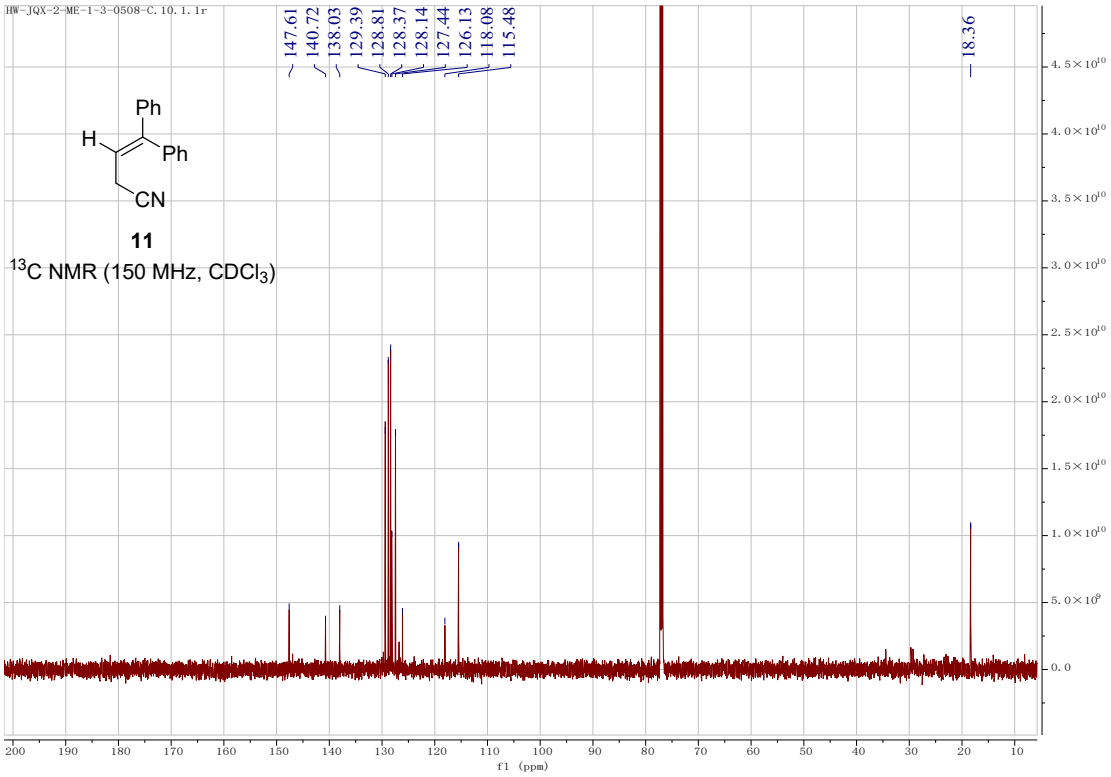
^{1}H and ^{13}C Spectrum for Compound 5 at 25 ℃



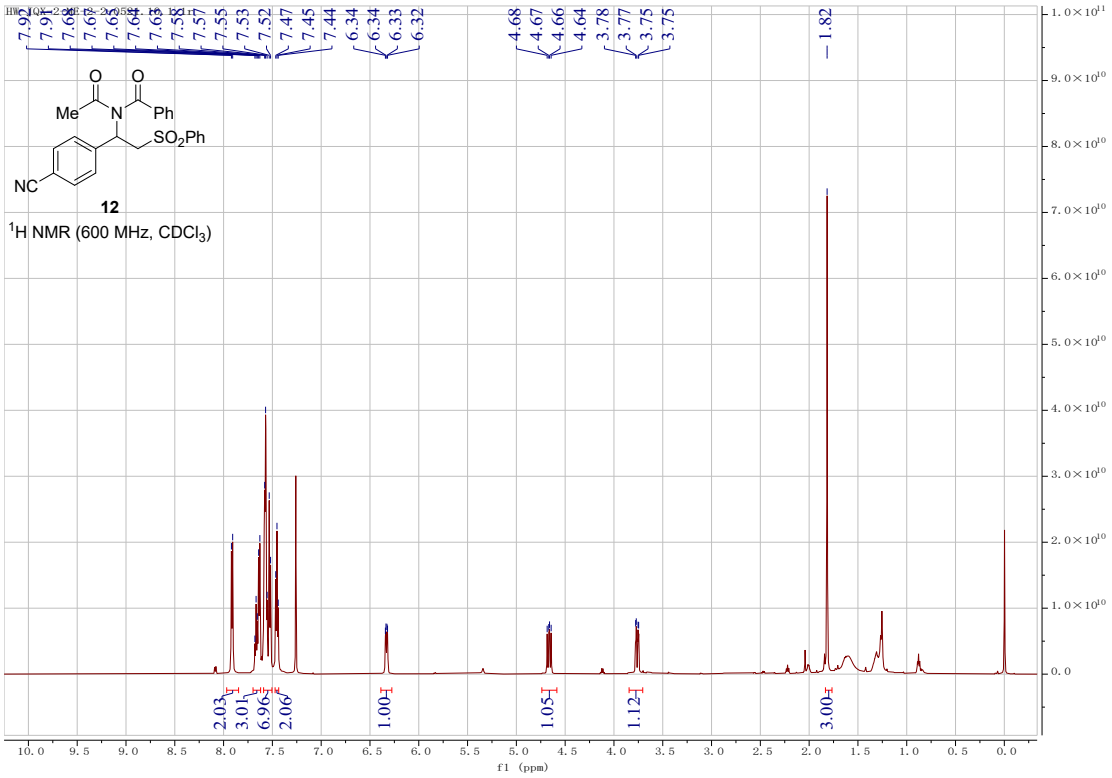


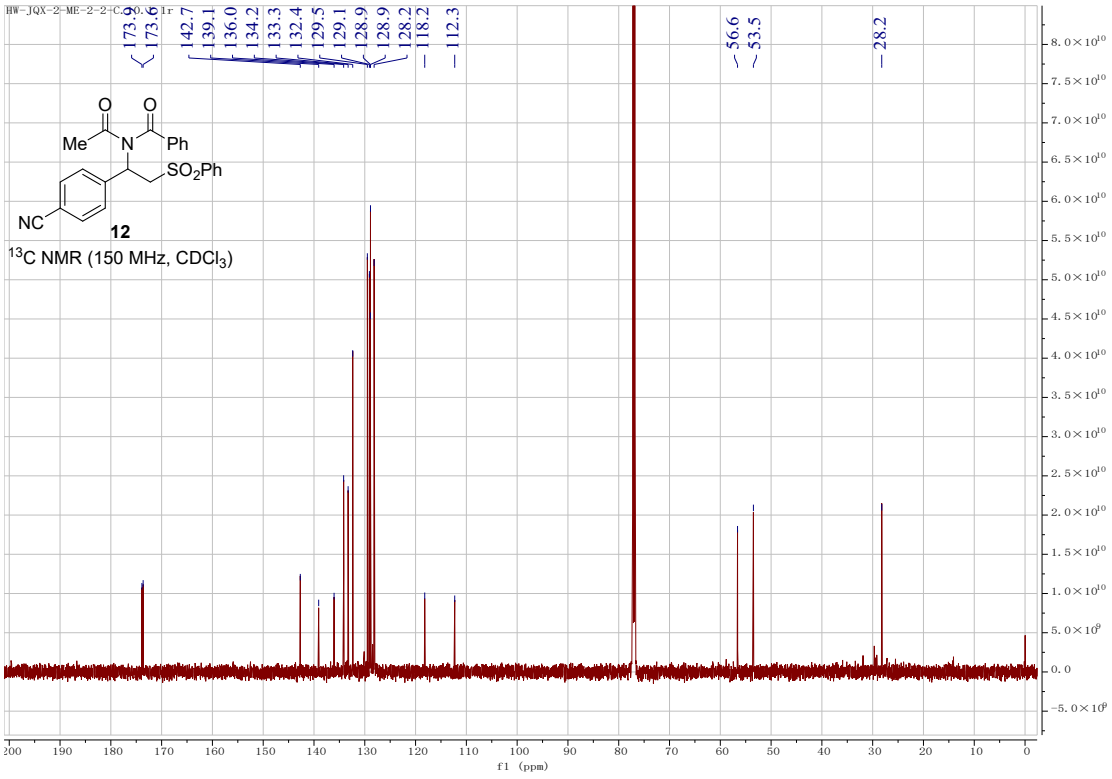
^{1}H and ^{13}C Spectrum for Compound 11 at 25 ℃



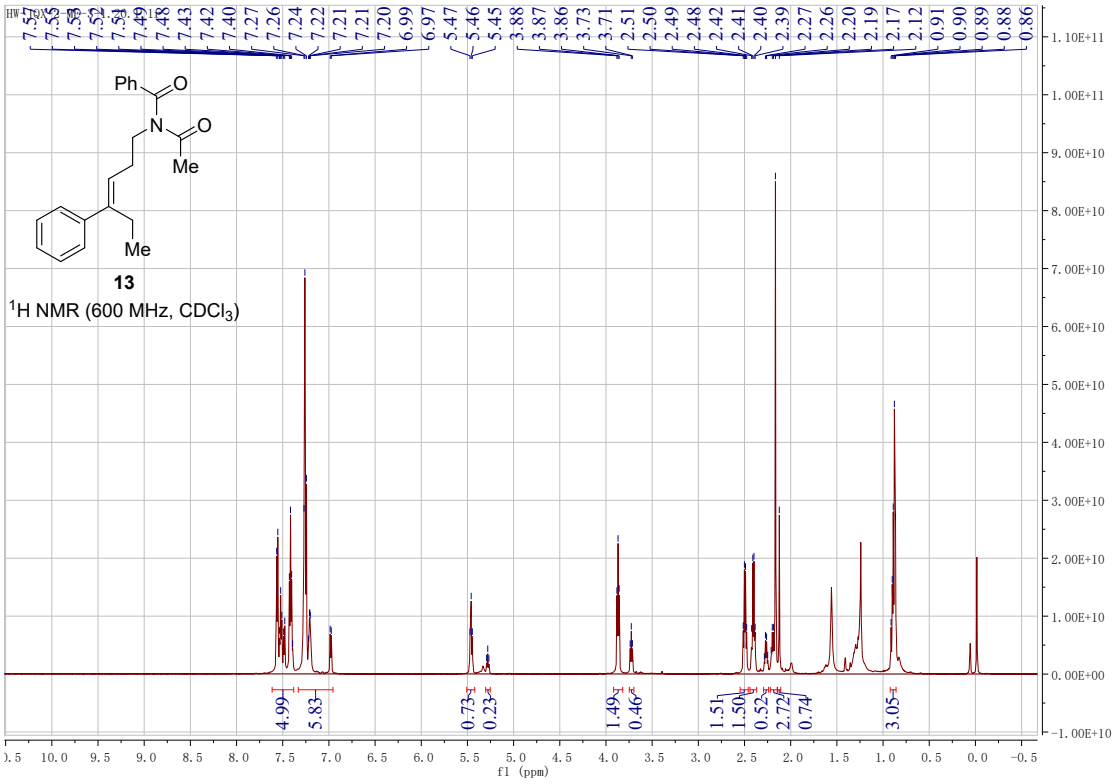


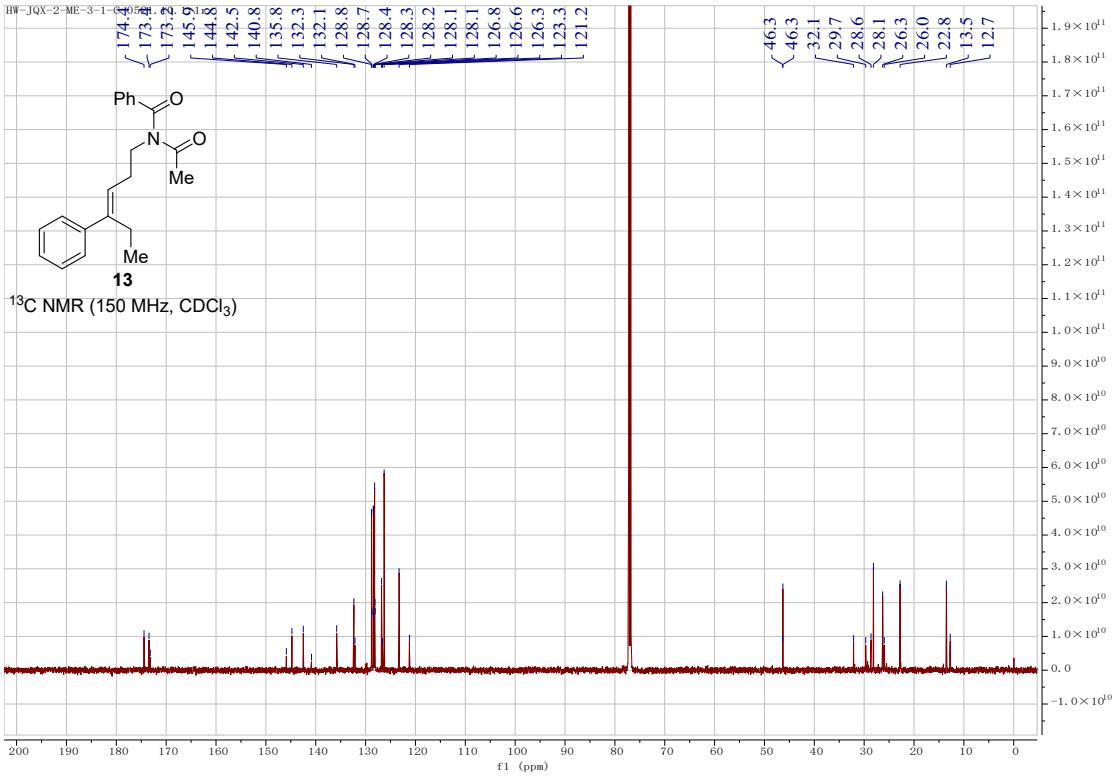
^{1}H and ^{13}C Spectrum for Compound 12 at 25 ℃



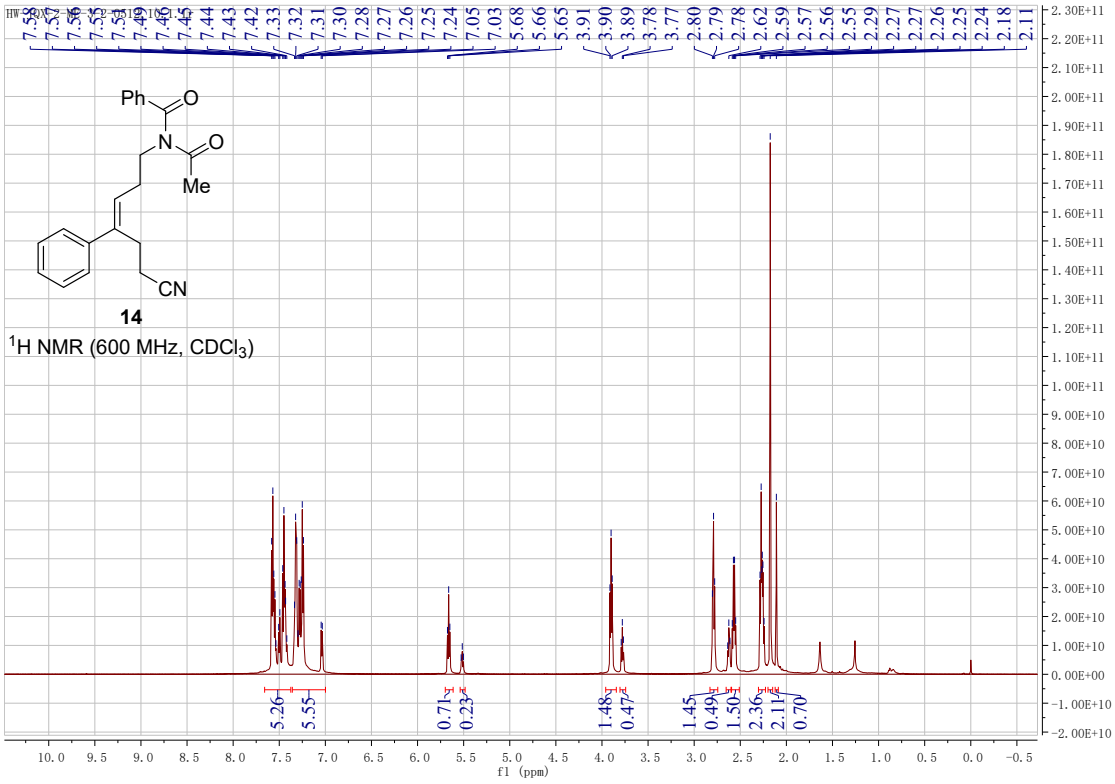


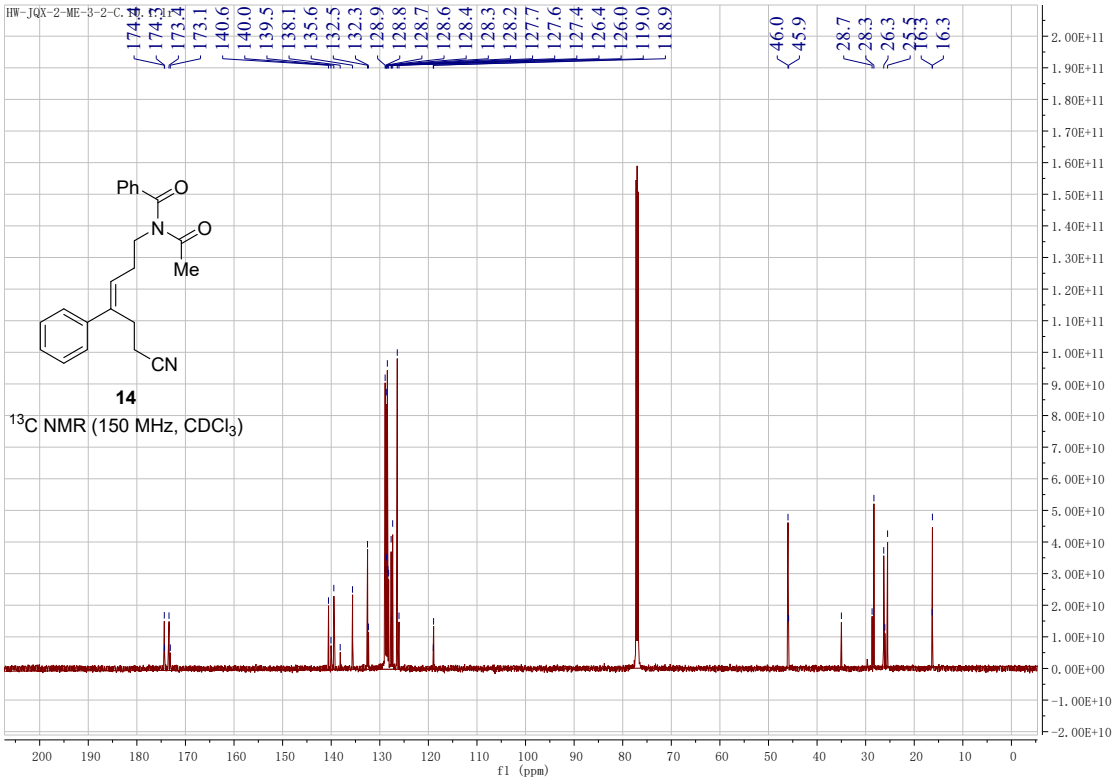
^{1}H and ^{13}C Spectrum for Compound 13 at 25 ℃





^{1}H and ^{13}C Spectrum for Compound 14 at 25 ℃





VII. Ligand effect and by-product analysis (Figure S1 and S2)

4-vinylbiphenyl was selected as the substrate. And under standard conditions, ligand **L1** and **L2** were evaluated. And the results were showed as the following figure. When **L1** was used, target imides **1c** and **2c** were obtained in 26% yield and 47% yield respectively. The by-products **B-1** and **B-2** resulting from carboxylate anion attack were not detected according to the TLC analysis. And when the ligand **L2** was used, target imides **1c** and **2c** were only detected in trace amount according to the TLC analysis. And the by-products **B-1** and **B-2** resulting from carboxylate anion attack were obtained in 34% yield and 31% yield respectively. These results indicated that the significant influence of ligand to the reaction.

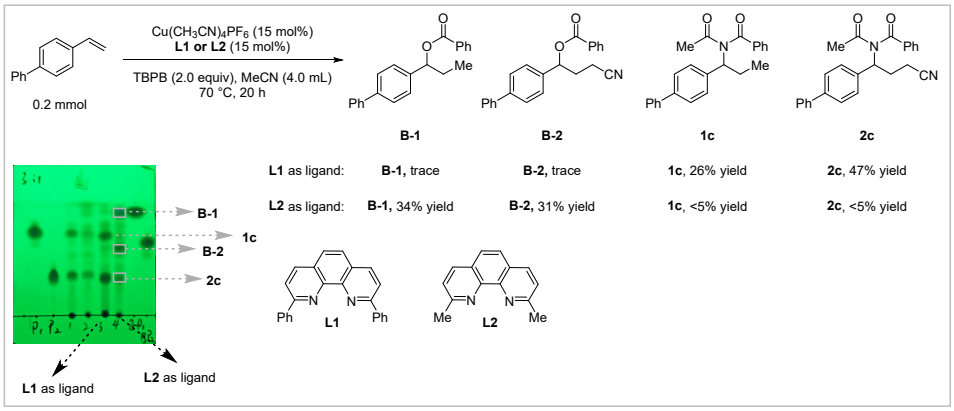


Figure S1 Ligand effect to the reaction with 4-vinylbiphenyl.

In the reaction of 1,3-enyne, when **L1** was used as ligand, the target imides **3a** and **4a** were obtained in 45% yield and 31% yield respectively. Although other trace amount of by-products cannot be isolated in the reaction with **L1**, the by-product **B-3** and **B-4** could be isolated in 34% yield and 40% yield respectively when the ligand **L2** was applied.

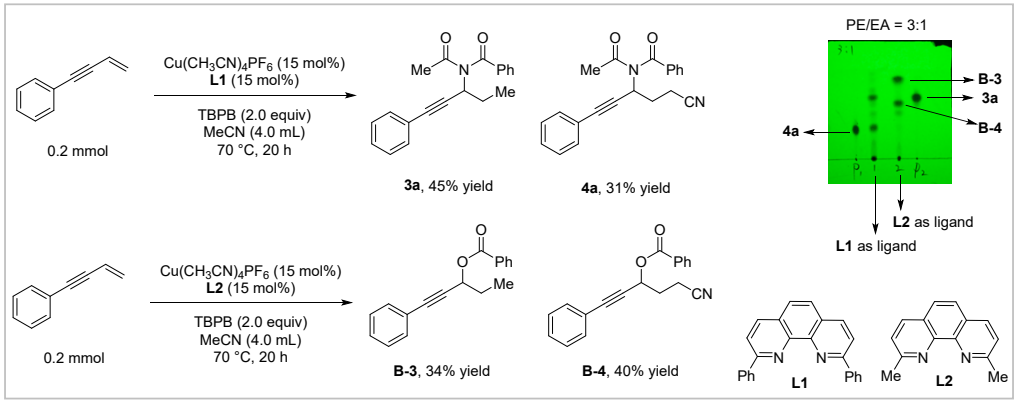


Figure S2 Ligand effect to the reaction with 1,3-enyne.