Supporting Information

Copper-catalyzed [3 + 2] annulation of ethynyl epoxides with malononitrile to access highly substituted dihydrofurans with an all-carbon quaternary stereocenter

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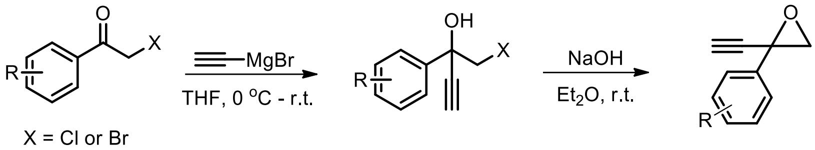
1. General Information

Reagents and Solvents: PE refers to petroleum ether b.p. 60 – 90 ^{o}C and EA refers to ethyl acetate. All other starting materials and solvents were commercially available and were used without further purification unless otherwise stated.

Chromatography: Flash column chromatography was carried out using commercially available 200 – 300 mesh under pressure unless otherwise indicated. Gradient flash chromatography was conducted eluting with PE/EA, they are listed as volumeratios.

Data collection: ^{1}H and ^{13}C NMR spectra were collected on BRUKER AV-300/500 (300/500 MHz) spectrometer using $CDCl_3$ or DMSO-d_6 as solvent. Chemical shifts of ^{1}H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ = 0.00 ppm) with the solvent resonance as an internal standard ($CDCl_3$: δ = 7.26 ppm, DMSO-d_6, δ = 2.50 ppm). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integration. Chemical shifts of ^{13}C NMR were reported in ppm with the solvent as the internal standard ($CDCl_3$: δ = 77.0 ppm, DMSO-d_6, δ = 39.5 ppm). High Resolution Mass measurement was performed on Agilent Q-TOF 6520 mass spectrometer with electron spray ionization (ESI) as the ion source. IR spectra were recorded on a FT-IR spectrometer. Melting point (m.p.) was measured on a microscopic melting point apparatus.

2. General Procedure for Preparation of Substituted Ethynyl Epoxides[1]

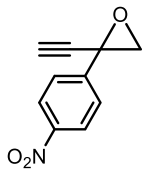


Substituted ethynyl epoxides were prepared in two steps from substituted phenacyl chloride/bromine. A typical experimental procedure for the preparation of ethynyl epoxide is described below.

Preparation of 2-ethynyl-2-(4-nitrophenyl)oxirane (**1e**) is used as an example:

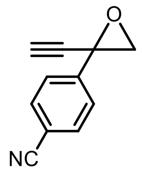
In a 100 mL round-bottomed flask were placed 2-chloro-1-(4-nitrophenyl)ethanone (10.0 mmol) and anhydrous THF (30 mL). Ethynylmagnesium bromide (0.5 M in THF; 11.0 mmol) was added to the solution at 0 °C, and the mixture was stirred at room temperature for 4 h. After that, the reaction was quenched slowly with sat. aq. NH_4Cl solution at 0 °C and extracted with EA (3 × 20 mL). The combined organic layers were washed with water and brine sequentially, dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by flash chromatography on silica gel (PE/EA = 200:1 ~ 100:1) to afford the 1-chloro-2-(4-nitrophenyl)but-3-yn-2-ol in 70% yield.
In a 100 mL round-bottomed flask were placed the 1-chloro-2-(4-nitrophenyl)-but-3-yn-2-ol and anhydrous diethyl ether (10 mL). Powdered NaOH (20.0 mmol) was added to the solution slowly, and the mixture was stirred at room temperature for 12 h. After that, the suspension was filtered through a pad of celite and washed by DCM (5 mL). Then the solvent was removed in vacuum and the crude product was purified by flash chromatography (PE/EA = 100:1) to afford the 2-ethynyl-2-(4-nitrophenyl)oxirane (**1e**) in 86% yield.

2-ethynyl-2-(4-nitrophenyl)oxirane (1e)



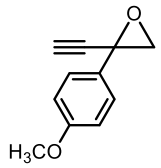
60% yield (1.13 g), yellow solid, m.p. 101 – 102 °C, R_f = 0.34 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 8.7 Hz, 2H), 7.67 (d, J = 8.8 Hz, 2H), 3.51 (d, J = 6.0 Hz, 1H), 3.01 (d, J = 6.0 Hz, 1H), 2.62 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0, 143.8, 126.5, 123.7, 79.9, 73.9, 59.2, 50.1 ppm; IR (KBr): $\tilde{\nu}$ = 2918, 2851, 2119, 1520, 1341, 847, 860, 748 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_7NO_3+H]^+$ 190.0499, found 190.0498.

4-(2-ethynyloxiran-2-yl)benzonitrile (1g)



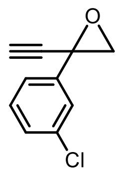
51% yield (0.86 g), yellow solid, m.p. 64 – 65 °C, R_f = 0.42 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.7 Hz, 2H), 7.60 (d, *J* = 8.7 Hz, 2H), 3.48 (d, *J* = 6.0 Hz, 1H), 2.98 (d, *J* = 6.1 Hz, 1H), 2.60 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 132.3, 126.3, 118.4, 112.4, 80.0, 73.8, 59.1, 50.2 ppm; IR (KBr): $\tilde{\nu}$ = 3063, 2992, 2922, 2230, 1506, 1417, 910, 842 cm^{-1}; HRMS (ESI) calcd for $[C_{11}H_7NO+H]^+$ 170.0600, found 170.0595.

2-ethynyl-2-(4-methoxyphenyl)oxirane(1i)



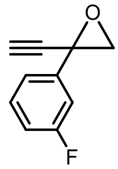
53% yield (0.93 g), yellow oil, R_f = 0.51 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 3.41 (d, *J* = 6.0 Hz, 1H), 3.01 (d, *J* = 6.0 Hz, 1H), 2.51 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 128.4, 126.9, 113.9, 81.4, 72.5, 58.6, 55.3, 50.5 ppm; IR (KBr): $\tilde{\nu}$ = 3296, 3065, 2987, 2124, 1576, 1473, 1269, 690, 785 cm^{-1}; HRMS (ESI) calcd for $[C_{11}H_{10}NO_2+H]^+$ 175.0754, found 175.0753.

2-(3-chlorophenyl)-2-ethynyloxirane(1j)



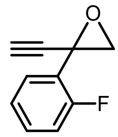
37% yield (0.66 g), yellow oil, R_f = 0.65 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 – 7.48 (m, 1H), 7.47 – 7.37 (m, 1H), 7.33 (dd, *J* = 4.9, 1.6 Hz, 2H), 3.46 (d, *J* = 6.1 Hz, 1H), 3.01 (d, *J* = 6.1 Hz, 1H), 2.59 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 141.3, 137.2, 132.4, 131.3, 128.4,126.3, 83.2, 80.1, 61.4, 52.8 ppm; IR (KBr): $\tilde{\nu}$ = 3063, 2988, 2123, 1599, 1427, 1267, 918, 785 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_7ClO+H]^+$ 179.0258, found 179.0248.

2-ethynyl-2-(3-fluorophenyl)oxirane(1k)



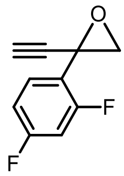
67% yield (1.09 g), yellow oil, R_f = 0.62 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 2H), 7.26 – 7.21 (m, 1H), 7.09 – 7.02 (m, 1H), 3.47 (d, *J* = 6.1 Hz, 1H), 3.01 (d, *J* = 6.1 Hz, 1H), 2.58 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9 (d, *J* = 246.2 Hz), 139.3 (d, *J* = 7.6 Hz), 130.0 (d, *J* = 8.3 Hz), 121.2 (d, *J* = 3.0 Hz), 115.4 (d, *J* = 21.1Hz), 112.7 (d, *J* = 23.5 Hz), 80.7, 72.9, 58.9, 50.2 ppm; IR (KBr): $\tilde{\nu}$ = 3067, 2989, 2909, 2126, 1593, 1487, 1279, 1188, 925, 785 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_7FO+H]^+$ 163.0554, found 163.0550.

2-ethynyl-2-(2-fluorophenyl)oxirane(1l)



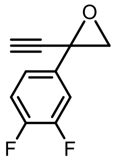
58% yield (0.94 g), yellow oil, R_f = 0.60 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.45 (m, 1H), 7.36 – 7.25 (m, 1H), 7.16 – 7.03 (m, 2H), 3.38 (d, *J* = 6.0 Hz, 1H), 3.06 (d, *J* = 6.1 Hz, 1H), 2.43 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5 (d, *J* = 249.6 Hz), 130.4 (d, *J* = 8.1 Hz), 128.3 (d, *J* = 3.0 Hz), 124.5 (d, *J* = 13.4 Hz), 124.2 (d, *J* = 3.7 Hz), 115.78 (d, *J* = 20.7 Hz), 81.3 , 71.7 (d, *J* = 1.6 Hz), 55.8 (d, *J* = 1.9 Hz), 47.5 ppm; IR (KBr): $\tilde{\nu}$ = 3067, 2926, 2855, 2124, 1491, 1456, 1220, 759 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_7FO+H]^+$ 163.0554, found 163.0558.

2-(2,4-difluorophenyl)-2-ethynyloxirane(1n)



50% yield (0.90 g), yellow oil, R_f = 0.63 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 – 7.41 (m, 1H), 6.93 – 6.77 (m, 2H), 3.37 (d, *J* = 5.9 Hz, 1H), 3.05 (d, *J* = 6.0 Hz, 1H), 2.44 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1 (dd, *J* = 248.9, 11.4 Hz), 160.7 (dd, *J* = 248.6, 12.0 Hz), 129.4 (dd, *J* = 9.9, 4.6 Hz), 120.8 (dd, *J* = 13.43, 3.7 Hz) 111.4 (dd, *J* = 21.5, 3.8 Hz), 104.6, 104.3, 103.9, 81.1, 71.9 (d, *J* = 1.5 Hz), 55.8 (d, *J* = 2.0 Hz), 47.1 ppm; IR (KBr): $\tilde{\nu}$ = 3082, 2995, 2916, 2122, 1616, 1506, 1142, 852 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_7F_2O+H]^+$ 181.0459, found 181.0463.

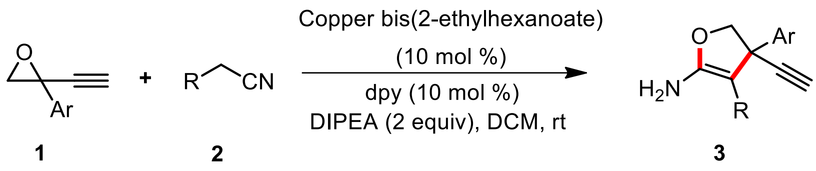
2-(3,4-difluorophenyl)-2-ethynyloxirane(1o)



45% yield (0.81 g), yellow oil, R_f = 0.62 (PE/EA = 20:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.19 (m, 2H), 7.16-7.09 (m, 1H), 3.42 (d, *J* = 6.0 Hz, 1H), 2.95 (d, *J* = 6.0 Hz, 1H), 2.56 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.98 (dd, *J* = 12.1, 7.4 Hz), 148.69 (dd, *J* = 12.1, 6.2 Hz), 133.78 (d, *J* = 2.2 Hz), 121.75 (dd, *J* = 6.6, 3.7 Hz), 117.31 (d, *J* = 17.7 Hz), 114.85 (d, *J* = 19.3 Hz), 80.4, 73.3, 58.8, 49.86 (d, *J* = 2.1 Hz) ppm; IR (KBr): $\tilde{\nu}$ = 3064, 2992, 2916, 2125, 1611, 1522, 1119, 771, 1770, 1558, 1521, 1508, 933, 769 cm^{-1}; HRMS (ESI) calcd for $[C_{10}H_7F_2O+H]^+$ 181.0459, found 181.0465.

3. General Procedure for Preparation of Substituted Dihydrofurans and Characterization

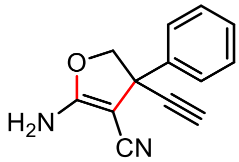
3.1 General procedure for Preparation of Substituted Dihydrofurans



A sealed tube were charged with Copper bis(2-ethylhexanoate) (0.01 mmol, 10 mol %), dpy (0.02 mmol, 20 mol %) and dry DCM (0.5 mL). The reaction mixture was stirred under at room temperature for 30 min. After that, **1** (0.1 mmol, 1.0 equiv), **2** (0.12 mmol, 1.2 equiv), DIPEA (0.2 mmol, 2.0 equiv) were dissolved in dry DCM (0.5 mL) and added to the tube via a syringe under argon. The reaction mixture was stirred at room temperature for 12 h. After the reaction was completed determined by TLC, the reaction mixture was diluted with EA (5 mL) and filtered through a plug of Celite. And then the solvent was removed under vacuum and the crude product was purified by flash chromatography on silica gel (PE/EA = 20:1 ~ 10:1) to afford the desired product **3**.

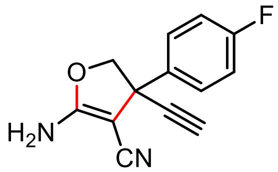
3.2 Characterization of the Products

2-amino-4-ethynyl-4-phenyl-4,5-dihydrofuran-3-carbonitrile (3aa)



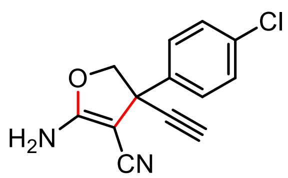
86% yield (18.1 mg), white solid, m.p. 144 – 145 ºC, R_f = 0.39 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.63 – 7.51 (m, 4H), 7.50 – 7.42 (m, 2H), 7.42 – 7.33 (m, 1H), 4.70 (d, J = 8.9 Hz, 1H), 4.40 (d, J = 8.9 Hz, 1H), 3.72 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.5, 142.3, 129.1, 128.1, 126.4, 118.7, 85.8, 83.4, 76.5, 59.2, 49.9 ppm. IR (KBr): $\tilde{\nu}$ = 2924, 2851, 2187, 1635, 1792, 1651, 1489, 1096, 827 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_{10}N_2O+H]^+$ 211.0866, found 211.0866.

2-amino-4-ethynyl-4-(4-fluorophenyl)-4,5-dihydrofuran-3-carbonitrile (3ba)



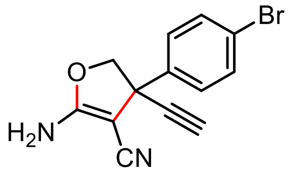
85% yield (19.4 mg), white solid, m.p. 174 – 175 ℃, R_f = 0.46 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.68 – 7.42 (m, 4H), 7.24 (t, J = 8.8 Hz, 2H), 4.65 (d, J = 8.9 Hz, 1H), 4.35 (d, J = 8.9 Hz, 1H), 3.70 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.5 , 161.9 (d, J = 244.3 Hz), 138.4 (d, J = 3.0 Hz), 128.6 (d, J = 8.4 Hz), 118.6 , 115.9 (d, J = 21.7 Hz), 85.6 , 83.3 , 76.7 , 59.1, 49.5 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2849, 2189, 1747, 1647, 1506, 1224, 835 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9FN_2O+H]^+$ 229.0772, found 229.0770.

2-amino-4-(4-chlorophenyl)-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3ca)



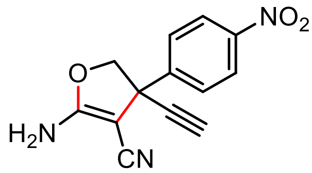
77% yield (18.8 mg), white solid, m.p. 111 – 112 ℃, R_f = 0.44 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.62 – 7.42 (m, 6H), 4.66 (d, J = 9.0 Hz, 1H), 4.37 (d, J = 9.0 Hz, 1H), 3.72 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.5, 141.3, 132.8, 129.1, 128.4, 118.5, 85.3, 83.1, 77.0, 59.0, 49.6 ppm; IR (KBr): $\tilde{\nu}$ = 2924, 2852, 2189, 1651, 1489, 1095, 1037, 827 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9ClN_2O+H]^+$ 245.0476, found 245.0476.

2-amino-4-(4-bromophenyl)-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3da)



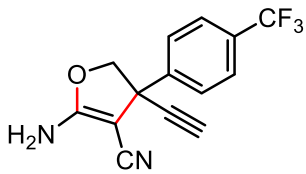
76% yield (21.9 mg), white solid, m.p. 149 – 150 °C, R_f = 0.47 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 7.60 (d, *J* = 8.6 Hz, 2H), 7.52 (s, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 4.64 (d, *J* = 9.0 Hz, 1H), 4.34 (d, *J* = 9.0 Hz, 1H), 3.71 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-*d*$_6$) δ 168.5, 141.8, 132.0, 128.8, 121.3, 118.5, 85.2, 83.1, 77.0, 59.0, 49.6 ppm; IR (KBr): $\tilde{\nu}$ = 2922, 2191, 1653, 1593, 1473, 1037, 1008, 821 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9BrN_2O+H]^+$ 288.9971, found 288.9970.

2-amino-4-ethynyl-4-(4-nitrophenyl)-4,5-dihydrofuran-3-carbonitrile (3ea)



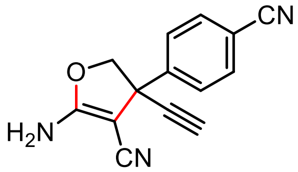
71% yield (18.1 mg), green solid, m.p. 219 – 220 °C, R_f = 0.21 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 8.30 (d, *J* = 8.9 Hz, 2H), 7.79 (d, *J* = 9.0 Hz, 2H), 7.64 (s, 2H), 4.73 (d, *J* = 9.1 Hz, 1H), 4.49 (d, *J* = 9.1 Hz, 1H), 3.84 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-*d*$_6$) δ 168.1, 149.2, 146.9, 127.4, 123.9, 117.8, 84.1, 82.2, 77.1, 58.5, 49.5 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2849, 2187, 1647, 1541, 1339, 931, 657 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9N_3O_3+H]^+$ 256.0717, found 466.256.0721.

2-amino-4-ethynyl-4-(4-(trifluoromethyl)phenyl)-4,5-dihydrofuran-3-carbonitrile (3fa)



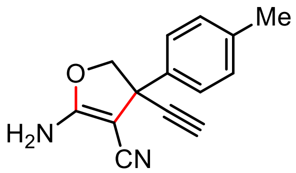
86% yield (23.9 mg), white solid, m.p. 115 – 116 °C, R_f = 0.59 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ 7.94 – 7.68 (m, 4H), 7.58 (s, 2H), 4.71 (d, *J* = 9.0 Hz, 1H), 4.45 (d, *J* = 9.1 Hz, 1H), 3.77 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-*d*$_6$) δ 168.6 , 146.9 , 128.8 (d, *J* = 31.6 Hz), 127.4 , 126.2, 126.1, 118.4 , 84.9 , 82.9 , 77.2 , 59.0 , 49.9 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2851, 2187, 1747, 1647, 1506, 1039 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_9F_3N_2O+H]^+$ 279.0740, found 279.0743.

2-amino-4-(4-cyanophenyl)-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3ga)



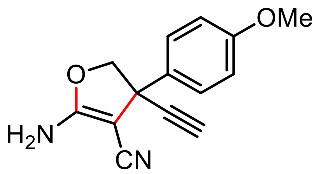
87% yield (20.5 mg), white solid, m.p. 201 – 202 °C, R_f = 0.38 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.07 – 7.85 (m, 2H), 7.81 – 7.65 (m, 2H), 7.59 (s, 2H), 4.70 (d, J = 9.1 Hz, 1H), 4.45 (d, J = 9.1 Hz, 1H), 3.78 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.6, 147.8, 133.2, 127.6, 119.0, 118.3, 111.0, 84.6, 82.7, 77.5, 58.9, 50.1 ppm; IR (KBr): $\tilde{\nu}$ = 2926, 2191, 1647, 1327, 1068, 1039, 1124, 810 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_9N_3O+H]^+$ 236.0818, found 236.0821.

2-amino-4-ethynyl-4-(p-tolyl)-4,5-dihydrofuran-3-carbonitrile (3ha)



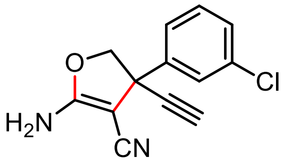
72% yield (16.1 mg), white solid, m.p. 140 – 141 °C, R_f = 0.45 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.58 – 7.30 (m, 4H), 7.21 (d, J = 8.0 Hz, 2H), 4.63 (d, J = 8.9 Hz, 1H), 4.30 (d, J = 8.8 Hz, 1H), 3.64 (s, 1H), 2.30 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 167.9, 138.8, 136.8, 129.1, 125.9, 118.2, 85.5, 83.0, 75.9, 58.8, 49.2, 20.5 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2851, 2180, 1600, 1471, 1037, 815, 727 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{12}N_2O+H]^+$ 225.1022, found 225.1026.

2-amino-4-ethynyl-4-(4-methoxyphenyl)-4,5-dihydrofuran-3-carbonitrile (3ia)



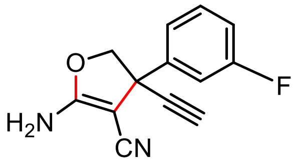
58% yield (13.9 mg), white solid, m.p. 115 – 117 °C, R_f = 0.37 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.53 – 7.34 (m, 4H), 6.97 (d, J = 8.8 Hz, 2H), 4.62 (d, J = 8.8 Hz, 1H), 4.29 (d, J = 8.8 Hz, 1H), 3.76 (s, 3H), 3.65 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.3, 159.1, 134.0, 127.7, 118.8, 114.4, 86.1, 83.6, 76.3, 59.3, 55.6, 49.4 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2849, 2187, 1645, 1508, 1252, 1035, 831 cm^{-1}; HRMS (ESI) calcd for $[C_{14}H_{12}N_2O_2+H]^+$ 241.0972, found 241.0976.

2-amino-4-(3-chlorophenyl)-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3ja)



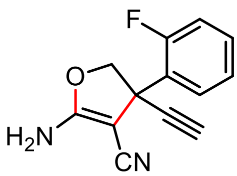
81% yield (19.8 mg), white solid, m.p. 137 – 138 ºC, R_f = 0.50 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.57 (s, 2H), 7.53 – 7.46 (m, 3H), 7.45 – 7.40 (m, 1H) 4.66 (d, *J* = 9.1 Hz, 1H), 4.42 (d, *J* = 9.1 Hz, 1H), 3.75 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.6, 144.8, 133.7, 131.2, 128.1, 126.3, 125.3, 118.5, 85.0, 83.0, 77.1, 58.8, 49.7 ppm; IR (KBr): $\tilde{\nu}$ = 2922, 2851, 2185, 1660, 1598, 1473, 1041, 937 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9ClN_2O+H]^+$ 245.0476, found 245.0481.

2-amino-4-ethynyl-4-(3-fluorophenyl)-4,5-dihydrofuran-3-carbonitrile (3ka)



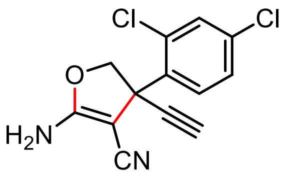
71% yield (16.2 mg), white solid, m.p.140 – 141 ºC, R_f = 0.49 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.76 – 7.41 (m, 3H), 7.38 – 7.35 (m, 1H), 7.33 – 7.09 (m, 2H), 4.67 (d, *J* = 9.0 Hz, 1H), 4.41 (d, *J* = 9.0 Hz, 1H), 3.71 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.6 , 162.7 (d, *J* = 244.2 Hz), 145.3 (d, *J* = 6.6 Hz), 131.2 (d, *J* = 8.1 Hz), 122.6 (d, *J* = 2.7 Hz), 118. 4, 114.9 (d, *J* = 21.0 Hz), 113.4 (d, *J* = 23.0 Hz), 85.2, 83.0, 76.8, 58.9, 49.8 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2848, 2187, 1653, 1338, 1041, 758 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9N_2FO+H]^+$ 229.0772, found 229.0772.

2-amino-4-ethynyl-4-(2-fluorophenyl)-4,5-dihydrofuran-3-carbonitrile (3la)



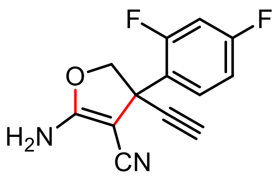
63% yield (14.3 mg), white solid, m.p. 131 – 132 ºC, R_f = 0.51 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.59 – 7.38 (m, 3H), 7.38 – 7.26 (m, 1H), 7.25 – 7.07 (m, 2H), 4.65 (dd, *J* = 10.1, 1.3 Hz, 1H), 4.45 (dd, *J* = 10.4,1.5 Hz, 1H), 3.52 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.6, 160.5 (d, *J* = 247.7 Hz), 130.6 (d, *J* = 8.6 Hz), 129.6 (d, *J* = 11.4 Hz), 128.2 (d, *J* = 3.3 Hz), 124.7 (d, *J* = 3.5 Hz), 118.9 , 116.9 (d, *J* = 21.5 Hz), 85.0, 81.7 (d, *J* = 3.5 Hz), 56.4, 46.7 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2851, 2187, 1506, 1259, 1034, 934, 750 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_9N_2FO+H]^+$ 229.0772, found 229.0775.

2-amino-4-(2,4-dichlorophenyl)-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3ma)



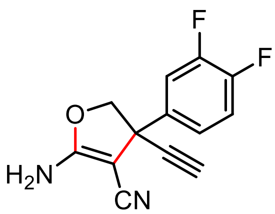
64% yield (25.0 mg), white solid, m.p. 195 – 196 ^{o}C, R_f = 0.56 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.68 (d, J = 2.2 Hz, 1H), 7.65 – 7.56 (m, 3H), 7.56 – 7.52 (m, 1H), 4.84 (d, J = 9.3 Hz, 1H), 4.59 (d, J = 9.3 Hz, 1H), 3.59 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.9, 138.7, 133.9, 133.7, 131.1, 129.8, 127.8, 119.1, 84.5, 81.0, 75.8, 56.0, 48.8 ppm; IR (KBr): $\tilde{v}$ = 2922, 2951, 2185, 1651, 1499, 1275, 1041, 966 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_8Cl_2N_2O+H]^+$ 279.0086, found 279.0090.

2-amino-4-(2,4-difluorophenyl)-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3na)



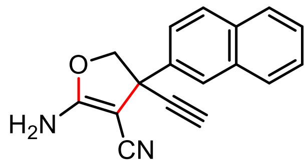
71% yield (17.5 mg), white solid, m.p. 155 – 156 ^{o}C, R_f = 0.48 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.70 – 7.40 (m, 3H), 7.35 – 7.27 (m, 1H), 7.22 – 7.02 (m, 1H), 4.72 (dd, J = 9.1, 1.2 Hz, 1H), 4.54 (dd, J = 9.1, 1.6 Hz, 1H), 3.63 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.97 (dd, J = 244.7, 12.05 Hz), 160.0 (dd, J = 249.15, 12.25 Hz), 128.9 (dd, J = 9.8, 4.7 Hz), 125.6 (dd, J = 11.9, 3.5 Hz), 118.3, 111.02 (dd, J = 21.1, 3.3 Hz), 105.4, 105.1, 104.7, 84.2, 81.0, 75.5, 55.8, 45.9 ppm; IR (KBr): $\tilde{v}$ = 2926, 2189, 1661, 1593, 1518, 1285, 1040, 773 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_8F_2N_2O+H]^+$ 247.0677, found 247.0678.

2-amino-4-(3,4-difluorophenyl)-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3oa)



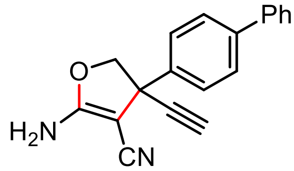
64% yield (15.7 mg), white solid, m.p. 118 – 119 ^{o}C, R_f = 0.53 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.73 – 7.40 (m, 4H), 7.39 – 7.34 (m, 1H), 4.66 (d, J = 9.0 Hz, 1H), 4.40 (d, J = 9.0 Hz, 1H), 3.72 (s, 1H). ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.1, 150.60 (dd, J = 32.7, 12.7 Hz), 147.34 (dd, J = 33.0, 12.8 Hz), 139.5, 122.88 (dd, J = 6.7, 3.3 Hz), 117.9, 117.8, 117.5, 115.25 (d, J = 18.6 Hz), 84.5, 82.4, 76.6, 58.4, 49.0 ppm; IR (KBr): $\tilde{\nu}$ = 2924, 2853, 2187, 1651, 1435, 1040, 937, 817 cm^{-1}; HRMS (ESI) calcd for $[C_{13}H_8F_2N_2O+H]^+$ 247.0677, found 247.0680.

2-amino-4-ethynyl-4-(naphthalen-2-yl)-4,5-dihydrofuran-3-carbonitrile (3pa)



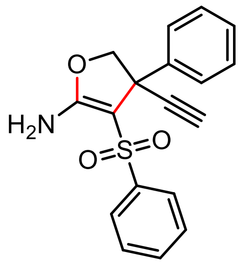
80% yield (20.8mg), white solid, m.p. 149 – 150 °C, R_f = 0.47 (PE/EA = 2:1); ^1H NMR (300 MHz, DMSO-d_6) δ 8.20 – 7.82 (m, 4H), 7.74 – 7.44 (m, 5H), 4.74 (d, J = 9.0 Hz, 1H), 4.50 (d, J = 9.0 Hz, 1H), 3.77 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.0, 139.1, 132.5, 132.2, 128.6, 128.0, 127.4, 126.5, 126.3, 124.5, 124.1, 118.2, 85.2, 82.7, 76.4, 59.0, 58.9, 49.6 ppm; IR (KBr): $\tilde{\nu}$ = 2924, 2855, 2189, 1645, 1489, 1095, 827 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{12}N_2O+H]^+$ 261.1022, found 261.1028.

4-([1,1'-biphenyl]-4-yl)-2-amino-4-ethynyl-4,5-dihydrofuran-3-carbonitrile (3qa)



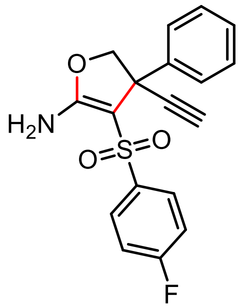
76% yield (21.7 mg), white solid, m.p. 210 – 212 °C, R_f = 0.42 (PE/EA = 2:1); ^1H NMR (300 MHz, DMSO-d_6) δ 7.85 – 7.53 (m, 6H), 7.55 – 7.28 (m, 5H), 4.69 (d, J = 8.9 Hz, 1H), 4.42 (d, J = 8.9 Hz, 1H), 3.69 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.0, 141.0, 139.5, 139.5, 128.9, 127.5, 127.0, 126.6, 126.6, 118.2, 85.2, 82.8, 76.1, 58.8, 49.3 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2851, 2187, 1635, 1506, 1033, 765 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{14}N_2O+H]^+$ 287.1179, found 287.1182.

4-ethynyl-4-phenyl-3-(phenylsulfonyl)-4,5-dihydrofuran-2-amine (3ab)



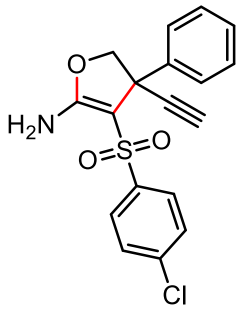
41% yield (13.3 mg), white solid, m.p. 187 – 188 °C, R_f = 0.40 (PE/EA = 2:1); ^1H NMR (300 MHz, DMSO-d_6) δ 7.60 – 7.57 (m, 2H), 7.52 – 7.47 (m, 1H), 7.41 – 7.35 (m, 6H), 7.25 – 7.20 (m, 3H), 4.55 (d, J = 8.6 Hz, 1H), 4.35 (d, J = 8.8 Hz, 1H), 3.39 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.6, 145.5, 142.1, 132.0, 128.8, 128.4, 127.4, 126.8, 126.3, 84.6, 83.9, 82.1, 76.9, 49.8 ppm; IR (KBr): $\tilde{\nu}$ = 2922, 2311, 1770, 1506, 1489, 1271, 1124, 723 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{15}NO_3S+H]^+$ 326.0845, found 326.0842.

4-ethynyl-3-((4-fluorophenyl)sulfonyl)-4-phenyl-4,5-dihydrofuran-2-amine (3ac)



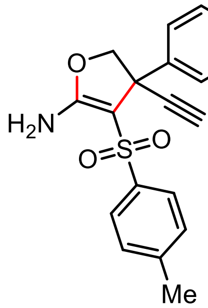
48% yield (16.5 mg), white solid, m.p. 197 – 198 °C, R$_f$ = 0.44 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-*d$_6$*) δ 7.68 – 7.53 (m, 2H), 7.52 – 7.29 (m, 4H), 7.24 – 7.17 (m, 5H), 4.57 (d, *J* = 8.8 Hz, 1H), 4.36 (d, *J* = 8.8 Hz, 1H), 3.42 (s, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-*d$_6$*) δ 165.6, 164.14 (d, *J* = 247.9 Hz), 141.93 (d, *J* = 3.4 Hz),, 129.3 (d, *J* = 9.3 Hz), 128.4, 127.5, 126.8, 115.8 (d, *J* = 22.4 Hz), 84.6, 83.9, 81.9, 77.0, 49.8 ppm; IR (KBr): $\tilde{\nu}$ = 2924, 2852, 2320, 1749, 1714, 1636, 1128, 833 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{14}FNO_3S+H]^+$ 344.0751, found 344.0754.

3-((4-chlorophenyl)sulfonyl)-4-ethynyl-4-phenyl-4,5-dihydrofuran-2-amine (3ad)



51% yield (18.3 mg), white solid, m.p. 164 – 165 °C, R$_f$ = 0.42 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-*d$_6$*) δ 7.60 – 7.52 (m, 2H), 7.52 – 7.34 (m, 6H), 7.23 (dd, *J* = 5.2, 2.1 Hz, 3H), 4.57 (d, *J* = 8.8 Hz, 1H), 4.37 (d, *J* = 8.8 Hz, 1H), 3.46 (s, 1H) ppm; ^{13}C NMR (75 MHz,DMSO-*d$_6$*) δ 165.8, 144.3, 142.0, 136.8, 128.9, 128.4, 128.2, 127.5, 126.8, 84.5, 83.9, 81.6, 77.1, 49.7 ppm; IR (KBr): $\tilde{\nu}$ = 2924, 2853, 2310, 1635, 1417, 1274, 754 cm^{-1}; HRMS (ESI) calcd for $[C_{18}H_{14}ClNO_3S+H]^+$ 360.0456, found 360.0454.

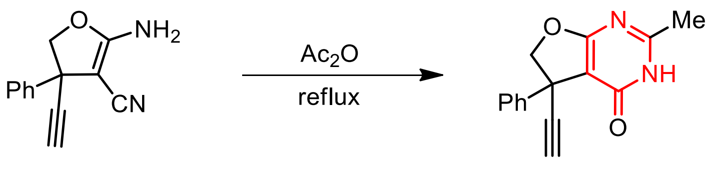
4-ethynyl-4-phenyl-3-tosyl-4,5-dihydrofuran-2-amine (3ae)



37% yield (12.6 mg), white solid, m.p. 197 – 199 °C, R_f = 0.41 (PE/EA = 2:1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.45 (d, J = 7.9 Hz, 2H), 7.37 (d, J = 6.8 Hz, 2H), 7.32 – 7.03 (m, 7H), 4.50 (d, J = 8.8 Hz, 1H), 4.29 (d, J = 8.8 Hz, 1H), 3.35 (s, 1H), 2.30 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.3, 143.7, 143.2, 143.1, 130.1, 129.3, 128.3, 127.7, 127.3, 85.6, 84.8, 83.3, 77.8, 50.8, 22.3 ppm; IR (KBr): $\tilde{\nu}$ = 2922, 2850, 1634, 1429, 1278, 1128, 835 cm^{-1}; HRMS (ESI) calcd for $[C_{19}H_{17}NO_3S+H]^+$ 340.1002, found 340.1002.

4. Further Study of the Reaction

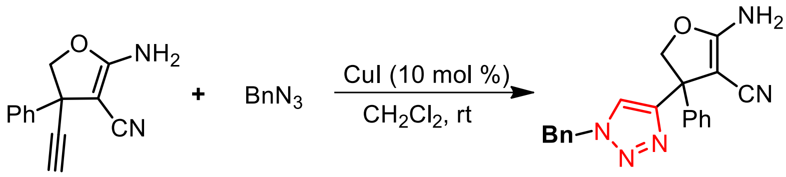
4.1 Preparation of 4 and Characterization[2]:



A solution of **3aa** (0.1 mmol) in acetic anhydride (1 mL) was refluxed for 6 h. Then the reaction mixture was concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (PE/EA = 50:1) to give dihydrofuran derivative **4** in 56% yield.

5-ethynyl-2-methyl-5-phenyl-5,6-dihydrofuro[2,3-d]pyrimidin-4(3H)-one (4)
56% yield (14.1 mg), colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.75 – 7.51 (m, 2H), 7.49 – 7.08 (m, 3H), 4.92 (d, J = 9.1 Hz, 1H), 4.60 (d, J = 9.1 Hz, 1H), 2.77 (s, 1H), 2.19 (s, 3H) ppm; ^{13}C NMR (75 MHz, CDCl3) δ 167.6, 159.8, 139.7, 129.0, 128.3, 126.1, 114.6, 84.8, 82.9, 75.5, 49.9, 29.7, 24.0 ppm; IR (KBr): $\tilde{\nu}$ = 2982, 1760, 1729, 1446, 1180, 1025, 995, 818, 700 cm^{-1}; HRMS (ESI) calcd for $[C_{15}H_{12}N_2O_2+Na]^+$ 275.0791, found 275.0810.

4.2 Preparation of 5 and Characterization[3]:



3aa **5**, 75% yield

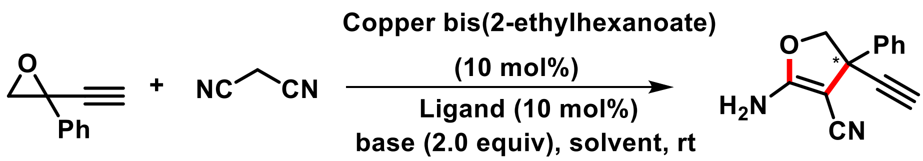
To a solution of **3aa** (0.1 mmol, 1.0 equiv) in DCM was added CuI (10 mol %), benzyl azid (0.1 mmol, 1.0 equiv) under air. The mixture was stirred at room temperature for 24 h. After the reaction was completed determined by TLC, the reaction mixture was diluted with EA (5 mL) and filtered through a plug of Celite. And then the solvent was removed under vacuum and the crude product was purified by flash chromatography on silica gel (PE/EA = 2:1) to afford dihydrofuran derivative **5** in 75% yield.

2-amino-4-(1-benzyl-1H-1,2,3-triazol-4-yl)-4-phenyl-4,5-dihydrofuran-3-carbonitrile (5)

75% yield (25.7 mg), white solid, m.p. 267 – 268 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.88 (s, 1H), 7.38 – 7.26 (m, 12H), 5.61 (s, 2H), 5.14 (d, J = 8.9 Hz, 1H), 4.54 (d, J = 8.9 Hz, 1H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.0, 139.1, 132.5, 132.2, 128.6, 128.0, 127.4, 126.5, 126.3, 124.5, 124.1, 118.2, 85.2, 82.7, 76.4, 59.0, 58.9, 49.6 ppm; IR (KBr): $\tilde{\nu}$ = 2920, 2175, 1697, 1681, 1506, 1456, 1039, 912 cm^{-1}; HRMS (ESI) calcd for $[C_{20}H_{17}N_5O+Na]^+$ 366.1325, found 366.1338.

4.3 Optimization of reaction conditions for asymmetric version of the reaction

Table S1: Optimization of the reaction conditions.[a]

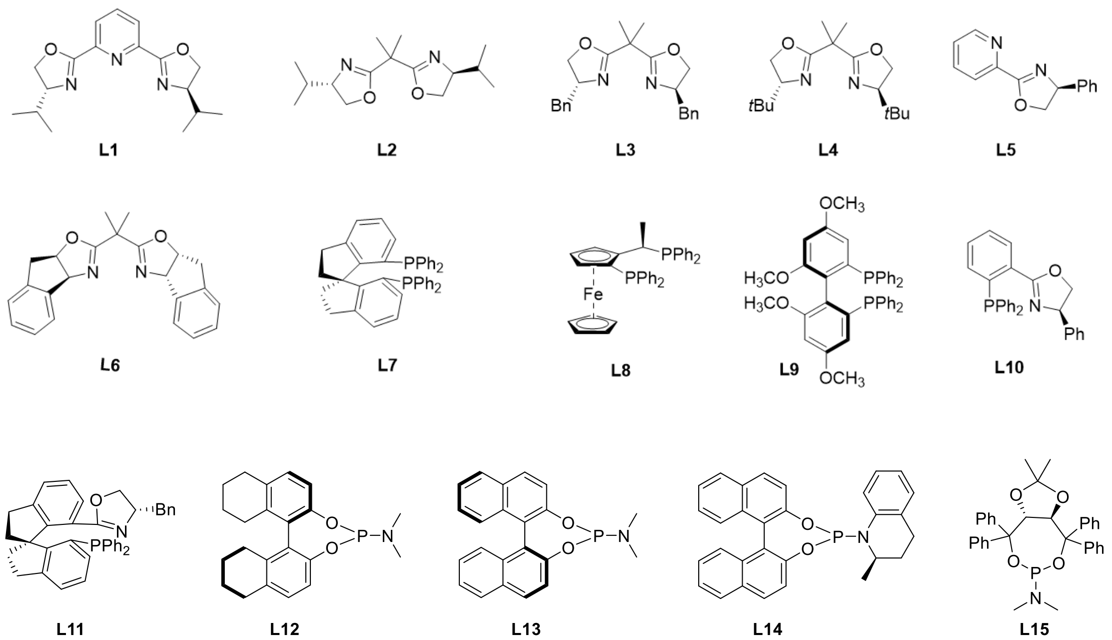


1a **2a** **3aa**

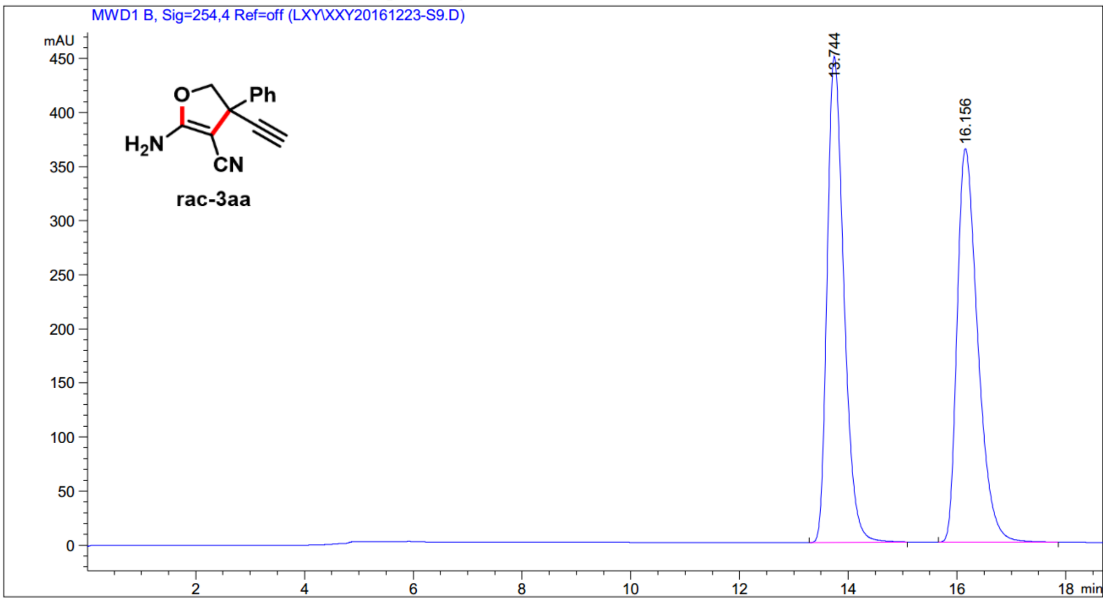
Entry	Ligand	Base	Solvent	Yield (%)	Er[b]
1	L1	DIPEA	DCM	71	50:50
2	L2	DIPEA	DCM	72	53:47

3	L3	DIPEA	DCM	67	52:48
4	L4	DIPEA	DCM	90	46:54
5	L5	DIPEA	DCM	57	50:50
6	L6	DIPEA	DCM	62	44:56
7	L7	DIPEA	DCM	91	55:45
8	L8	DIPEA	DCM	24	50:50
9	L9	DIPEA	DCM	10	50:50
10	L10	DIPEA	DCM	26	50:50
11	L11	DIPEA	DCM	34	52:48
12	L12	DIPEA	DCM	81	50:50
13	L13	DIPEA	DCM	67	50:50
14	L14	DIPEA	DCM	43	50:50
15	L15	DIPEA	DCM	86	50:50
16[c]	L7	DIPEA	DCM	52	55:44
17	L7	DBU	DCM	27	50:50
18	L7	K_2CO_3	DCM	26	56:44
19	L7	NaOH	DCM	NR	-
20	L7	DIPEA	THF	48	55:45
21	L7	DIPEA	DCE	78	60:40
22	L7	DIPEA	Toluene	50	56:44

[a]Reaction conditions: 1a (0.1 mmol, 1.0 equiv), 2a (0.1 mmol, 1 equiv), Copper bis(2-ethylhexanoate) (10 mol%), ligand (10 mol%), base (0.2 mmol, 2.0 equiv) in solvent (1.0 mL) for 12 h. [b] The er valure was determined by HPLC, using CHIRALCEL OD-H, i-PrOH: Hexane =20:80, v = 0.5 mL/min, λ = 254 nm. [c]$CuCl_2$ instead of Copper bis(2-ethylhexanoate).



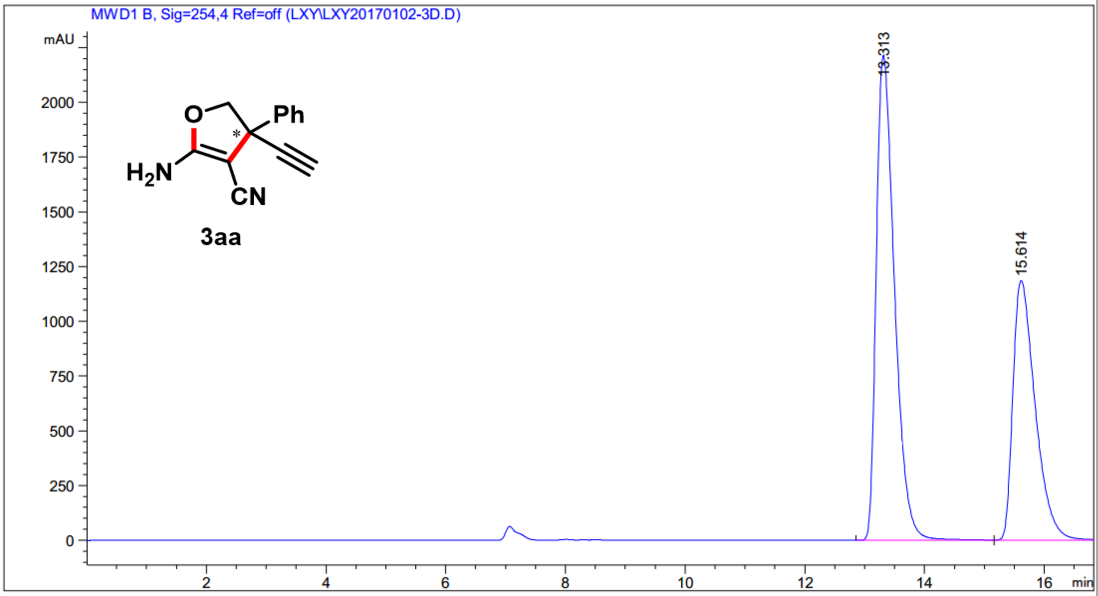
Additional Info : Peak(s) manually integrated



Signal 1: MWD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.744	BB	0.3286	9571.21777	449.17276	49.9634
2	16.156	BB	0.4051	9585.25195	364.09885	50.0366

Additional Info : Peak(s) manually integrated

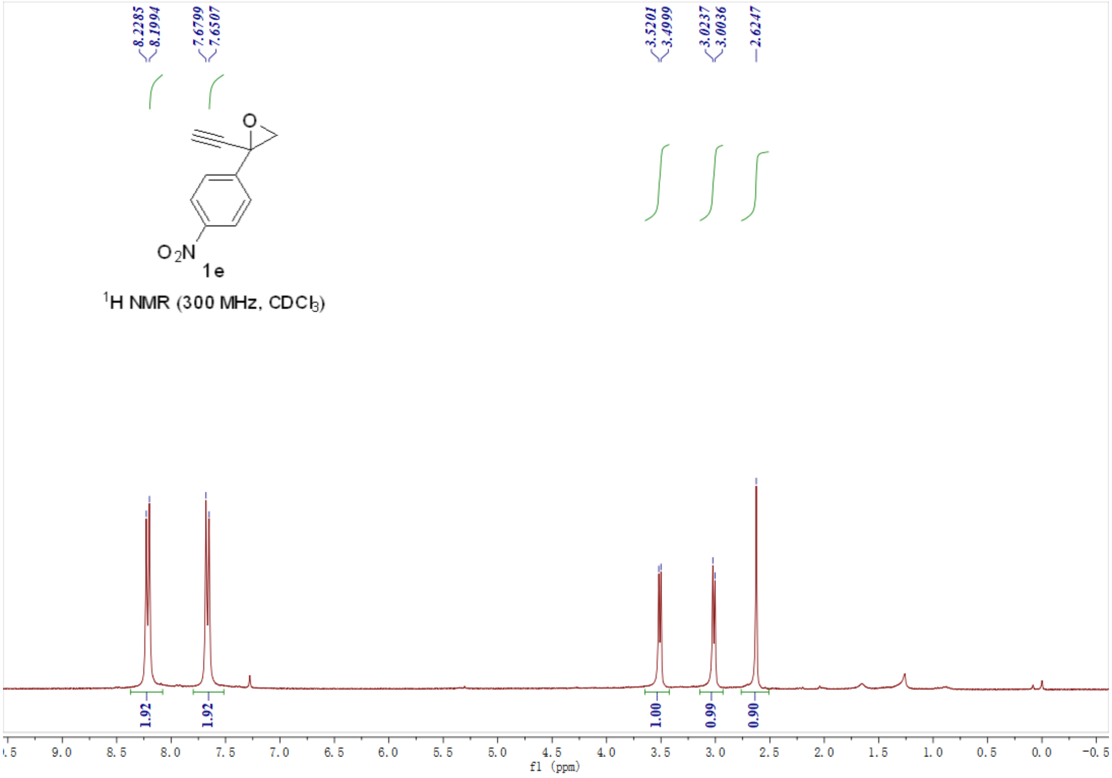


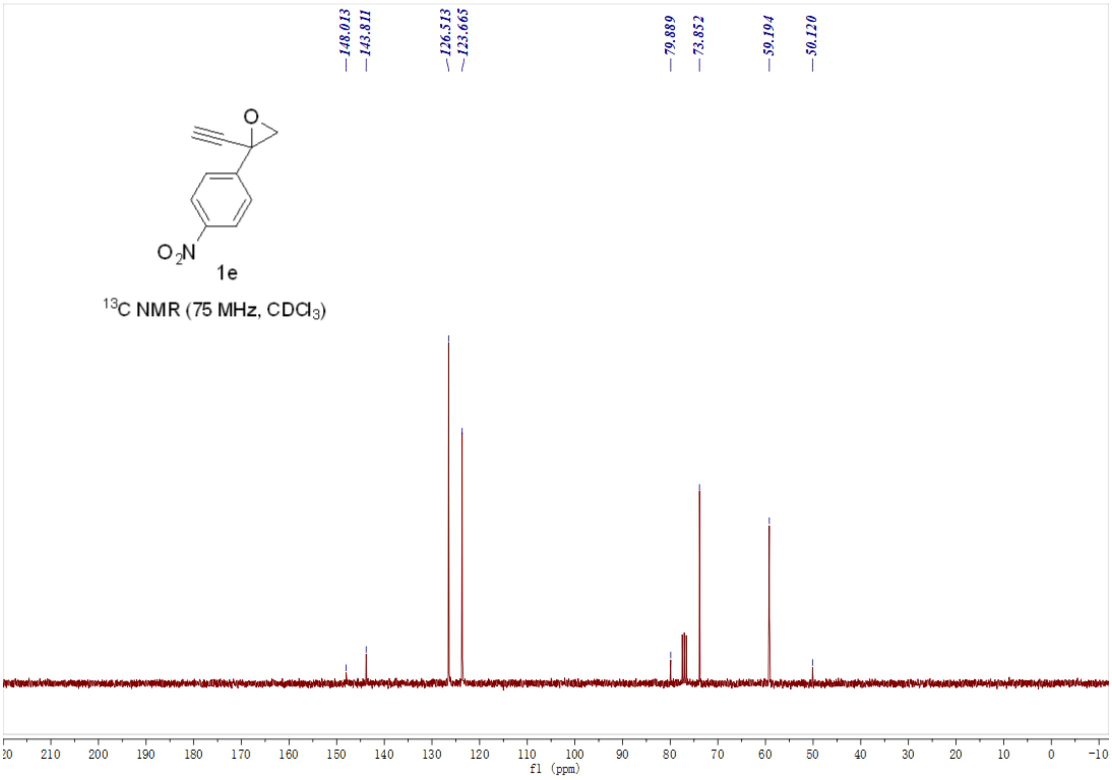
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.313	BV	0.3253	4.69414e4	2214.14209	60.4997
2	15.614	VBA	0.3931	3.06482e4	1187.40088	39.5003

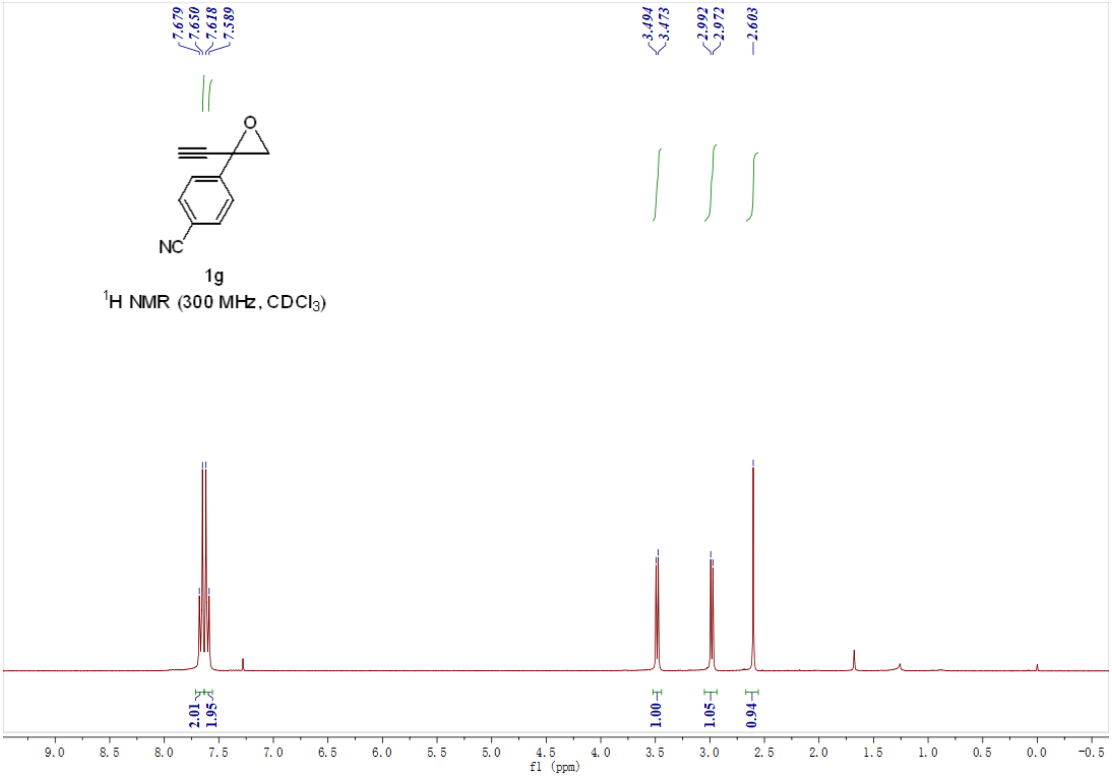
5. Reference

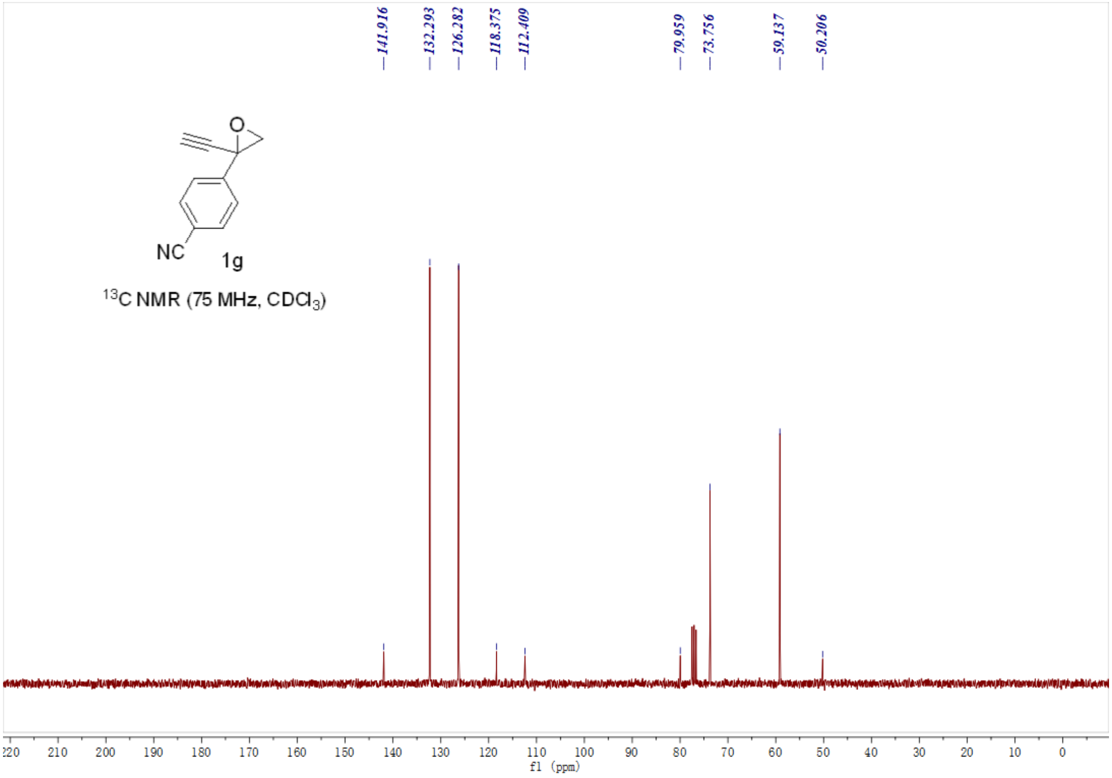
1. Hattori, G.; Yoshida, A.; Miyake, Y.; Nishibayashi, Y. *J. Org. Chem.*, **2009**, *74*, 7603.
2. Solhy, A.; Elmakssoudi, A.; Tahir, R.; Karkouri, M.; Larzek, M.; Bousmina, M.; Zahouily, M. *Green Chem.*, **2010**, *12*, 2261.
3. Vidala, C.; García-Álvarez, J. *Green Chem.*, **2014**, *16*, 3515.

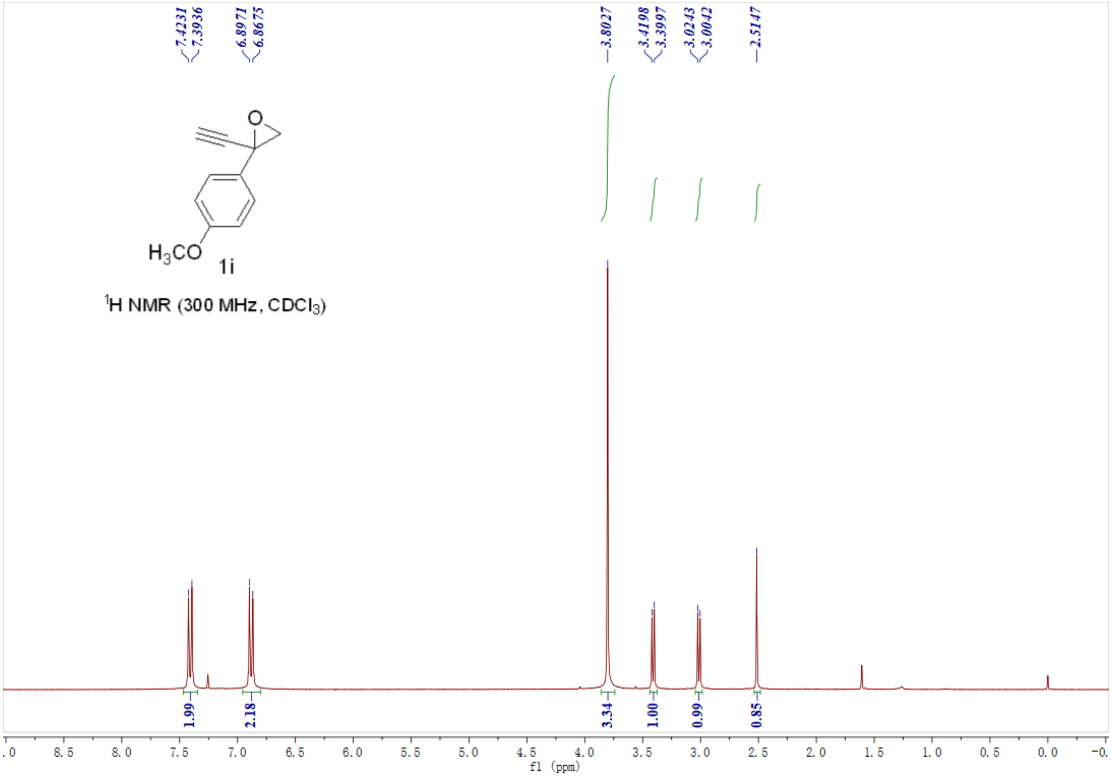
6 ^{1}H and ^{13}C NMR Spectra of Title Compounds

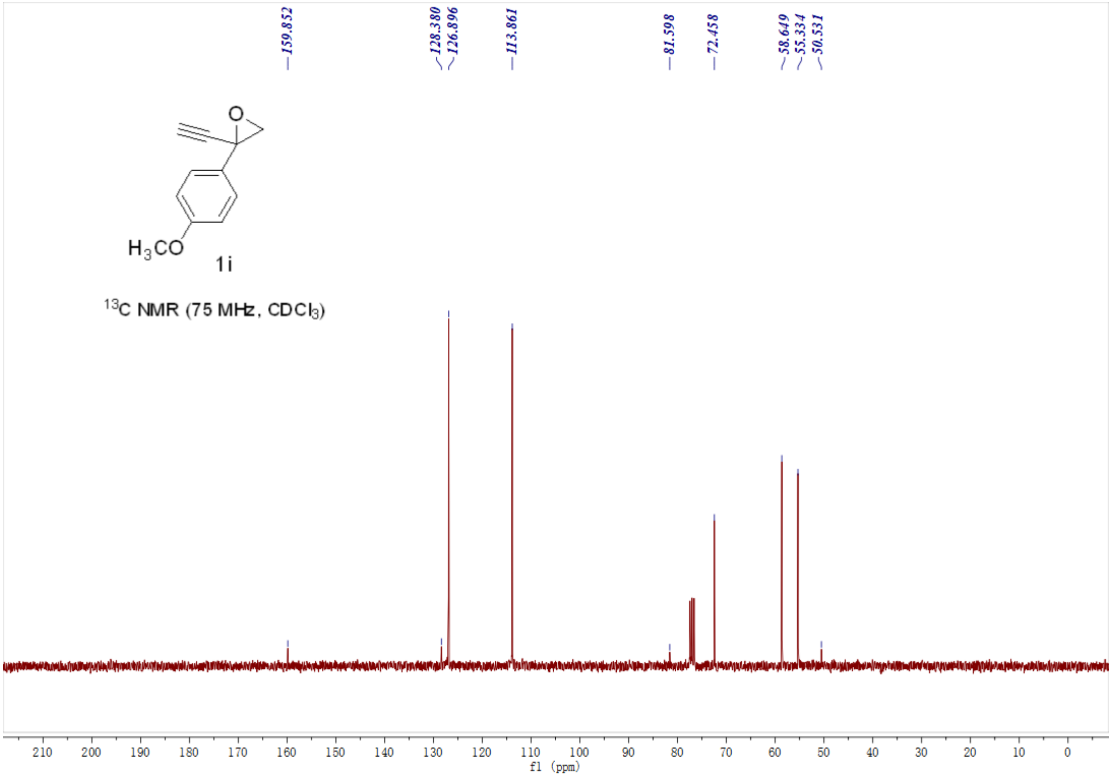


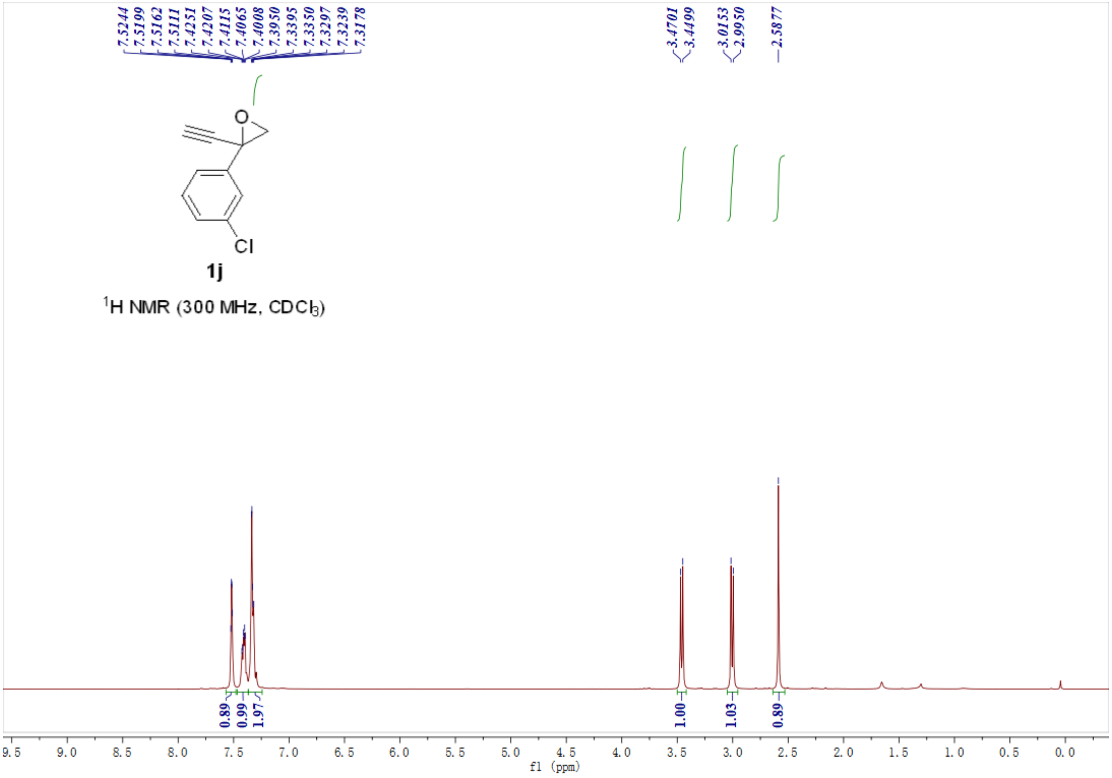


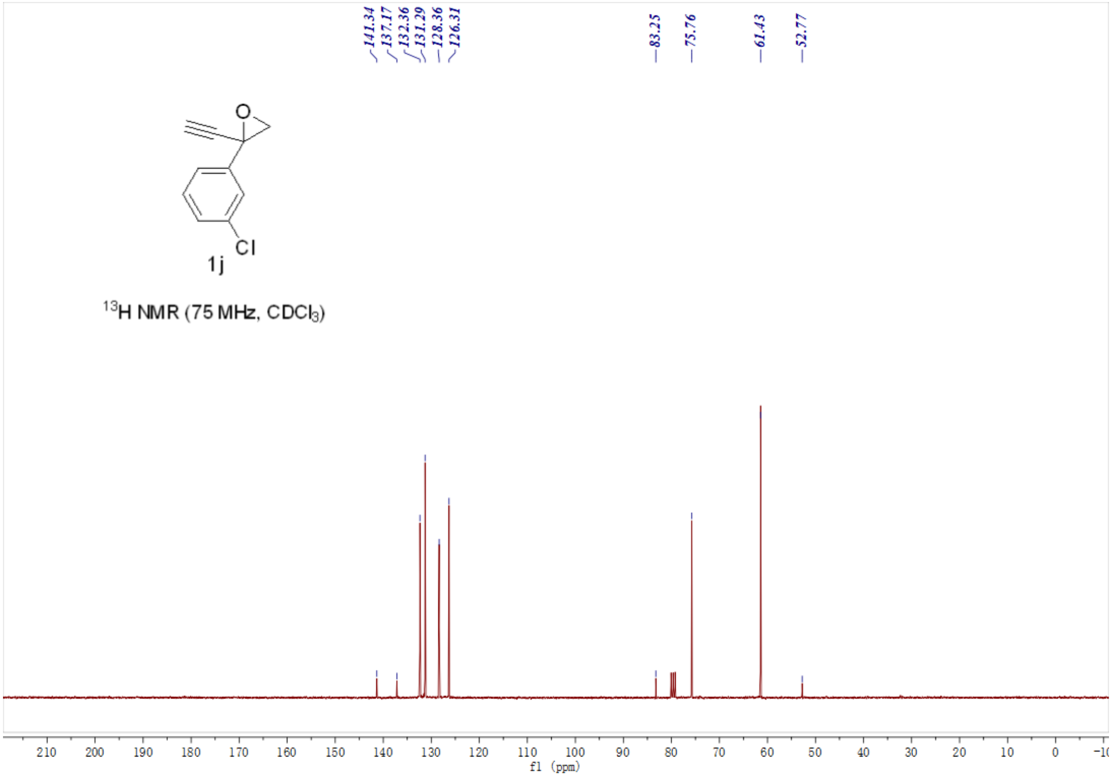

7.679
7.650
7.618
7.589
3.494
3.473
2.992
2.972
2.603
NC
1g
¹H NMR (300 MHz, CDCl₃)
2.01
1.95
1.00
1.05
0.94
f1 (ppm)

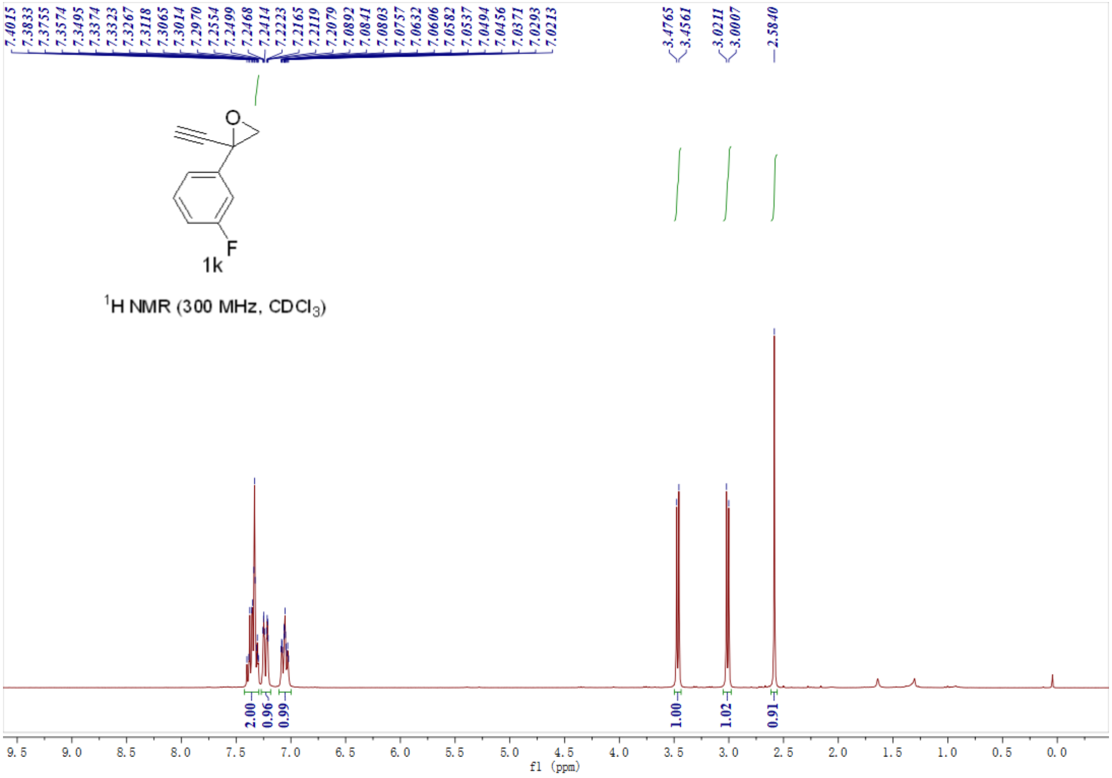

141.916
132.293
126.282
118.375
112.409
79.959
73.756
59.137
50.206
NC
1g
¹³C NMR (75 MHz, CDCl₃)
f1 (ppm)

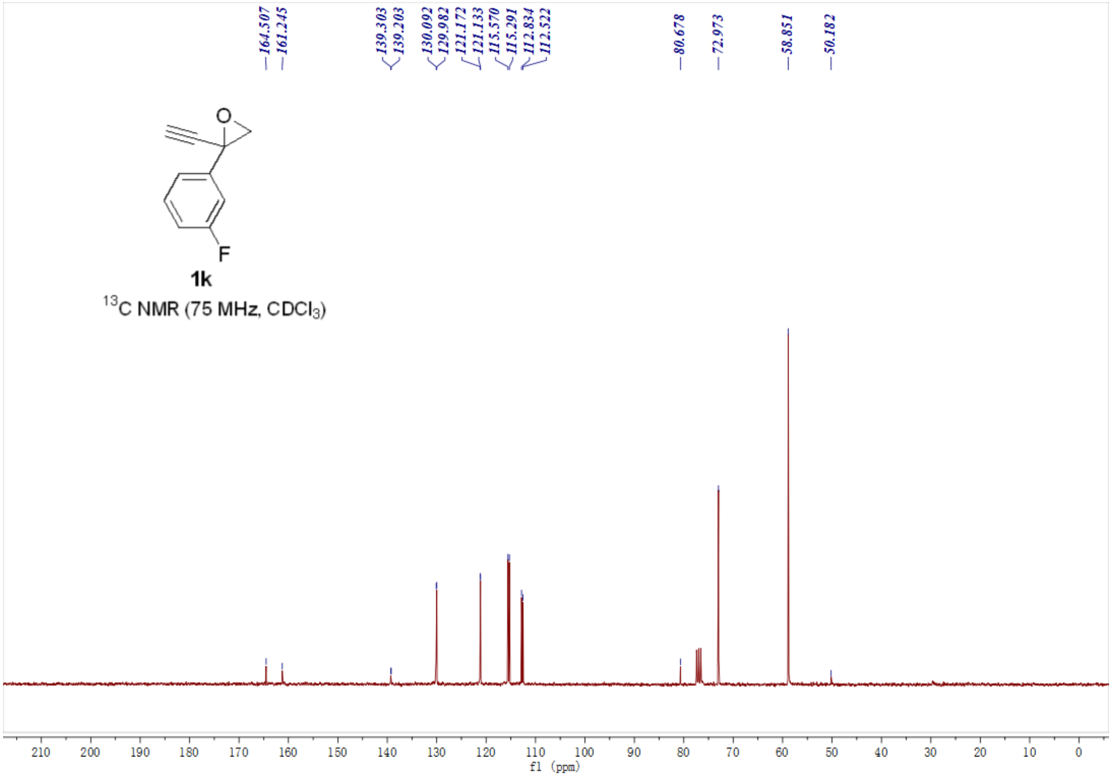

7.4231
7.3936
6.8971
6.8675
3.8027
3.4198
3.3997
3.0243
3.0042
2.5147
H3CO
1i
1H NMR (300 MHz, CDCl3)
1.99
2.18
3.34
1.00
0.99
0.85
f1 (ppm)

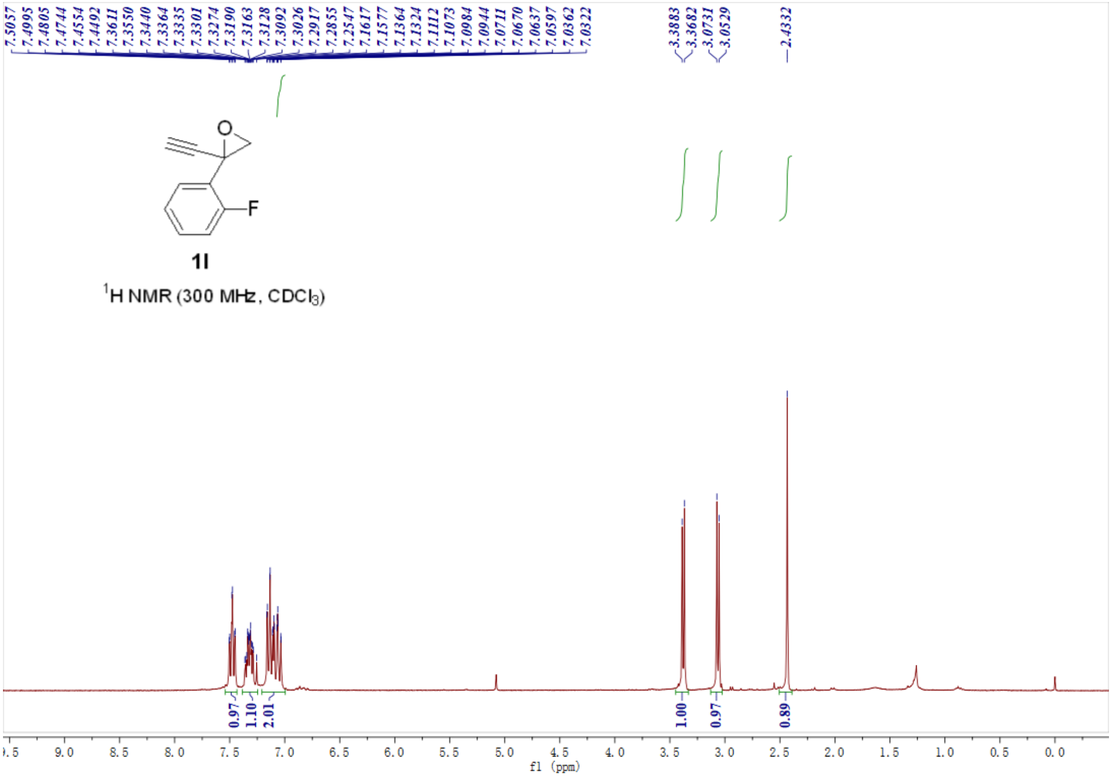

159.852
128.380
126.896
113.861
81.598
72.458
58.649
55.334
50.531
H3CO
1i
13C NMR (75 MHz, CDCl3)
f1 (ppm)


7.5244
7.5199
7.5162
7.5111
7.4251
7.4207
7.4115
7.4065
7.4008
7.3950
7.3395
7.3350
7.3297
7.3239
7.3178
3.4701
3.4499
3.0153
2.9950
2.5877
O
Cl
1j
1H NMR (300 MHz, CDCl3)
0.89
0.99
1.97
1.00
1.03
0.89
f1 (ppm)


141.34
137.17
132.36
131.29
128.36
126.31
83.25
75.76
61.43
52.77
O
Cl
1j
13H NMR (75 MHz, CDCl3)
f1 (ppm)

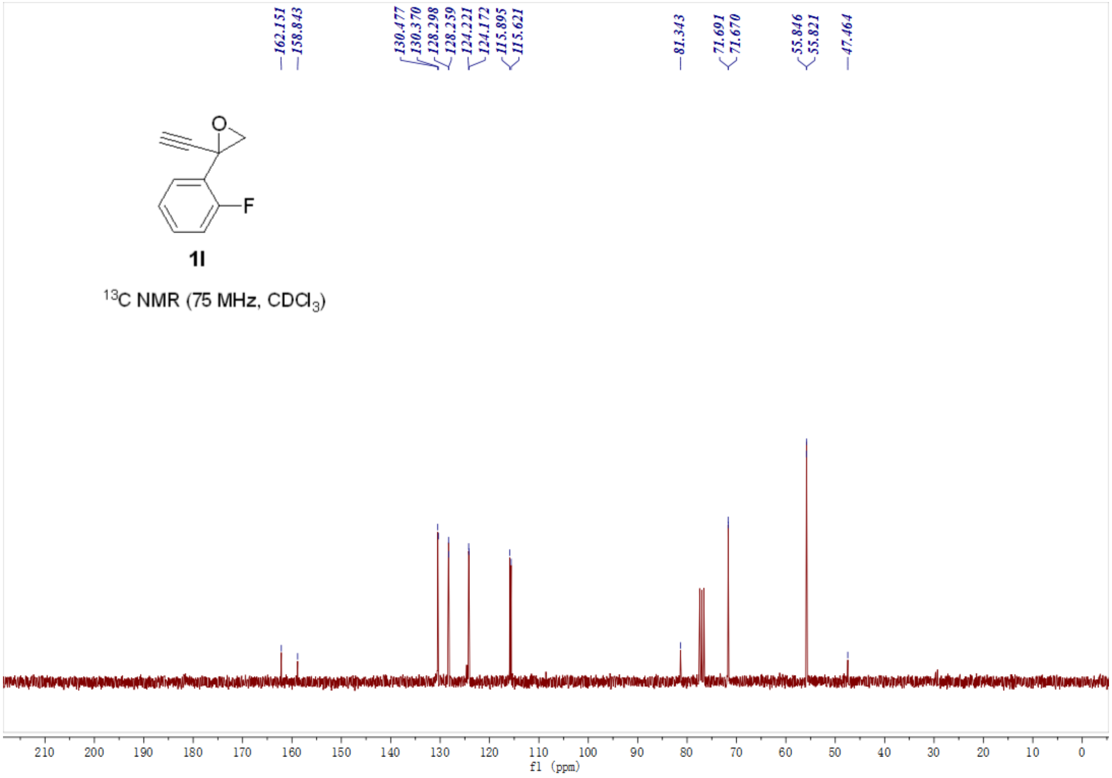

7.4015
7.3833
7.3755
7.3574
7.3495
7.3374
7.3323
7.3267
7.3118
7.3065
7.3014
7.2970
7.2554
7.2499
7.2468
7.2414
7.2223
7.2165
7.2119
7.2079
7.0892
7.0841
7.0803
7.0757
7.0632
7.0606
7.0582
7.0537
7.0494
7.0456
7.0371
7.0293
7.0213
3.4765
3.4561
3.0211
3.0007
2.5840
O
F
1k
^{1}H NMR (300 MHz, CDCl$_3$)
2.00
0.96
0.99
1.00
1.02
0.91
f1 (ppm)


164.507
161.245
139.303
139.203
130.092
129.982
121.172
121.133
115.570
115.291
112.834
112.522
80.678
72.973
58.851
50.182
O
F
1k
^{13}C NMR (75 MHz, CDCl$_3$)
f1 (ppm)



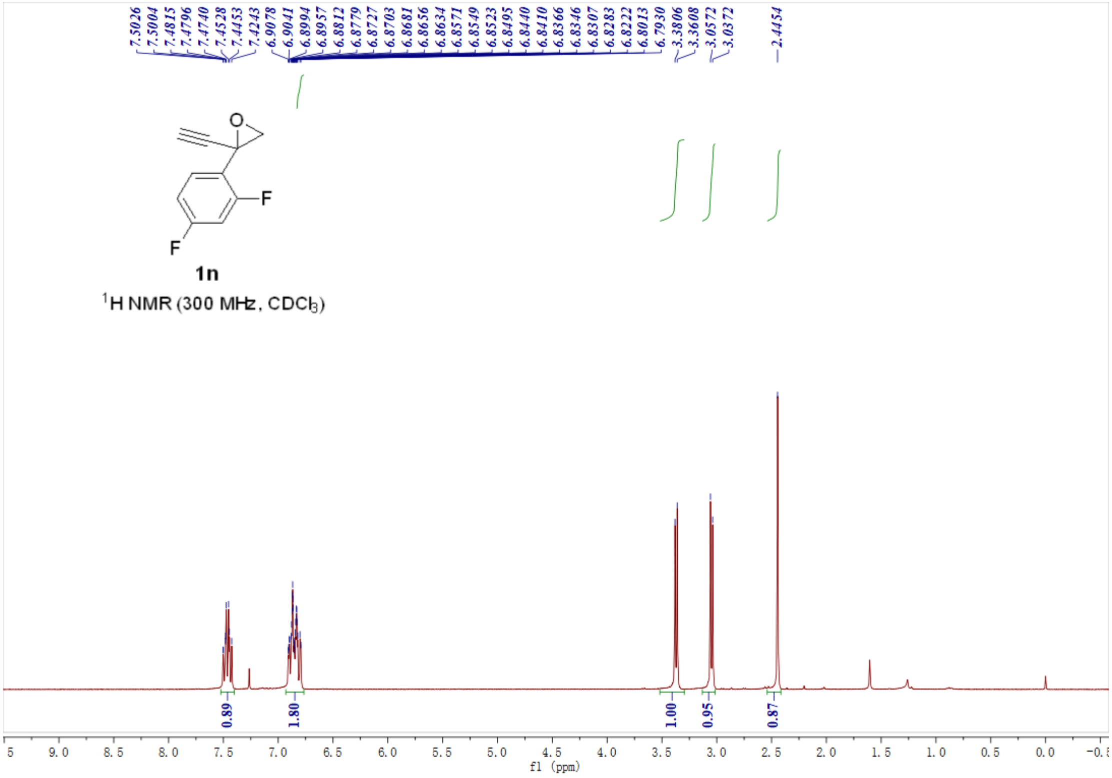
1l

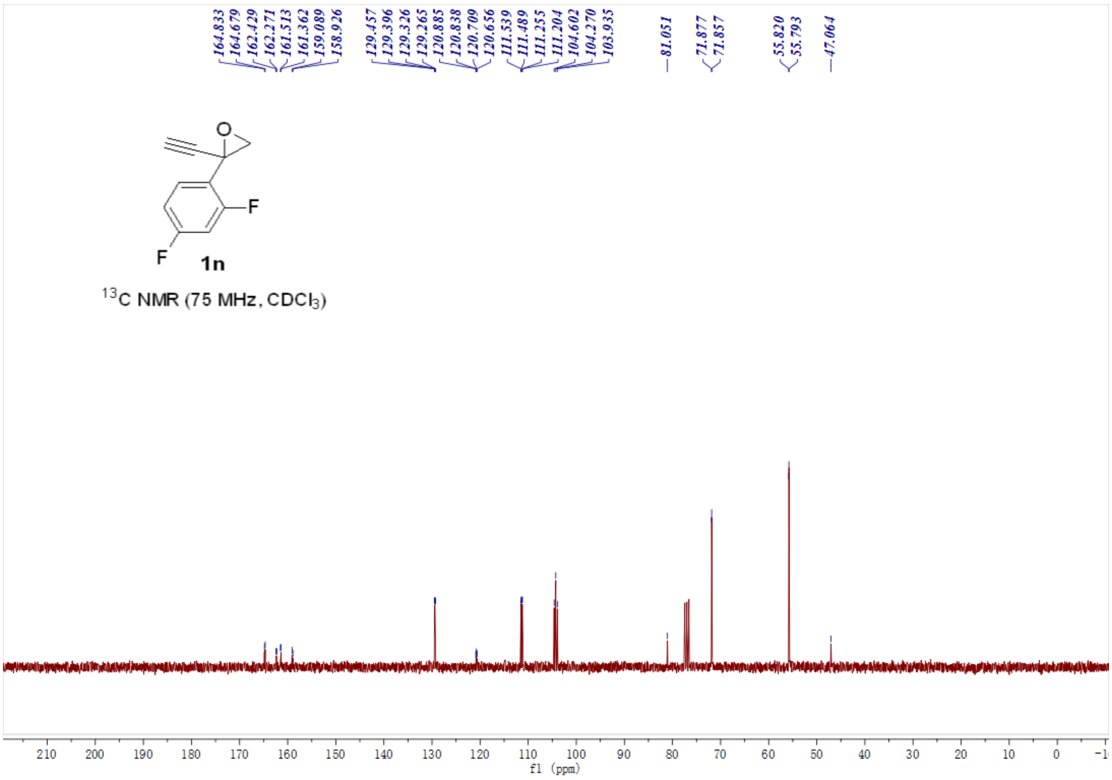
^{1}H NMR (300 MHz, $CDCl_3$)

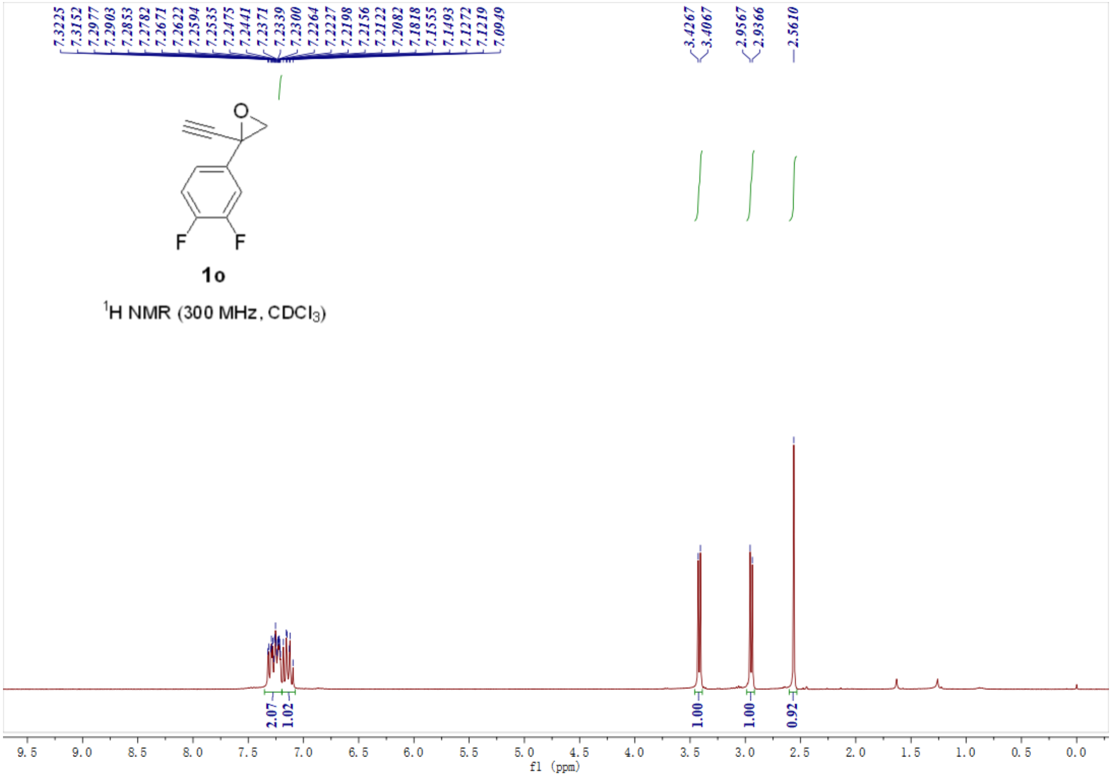


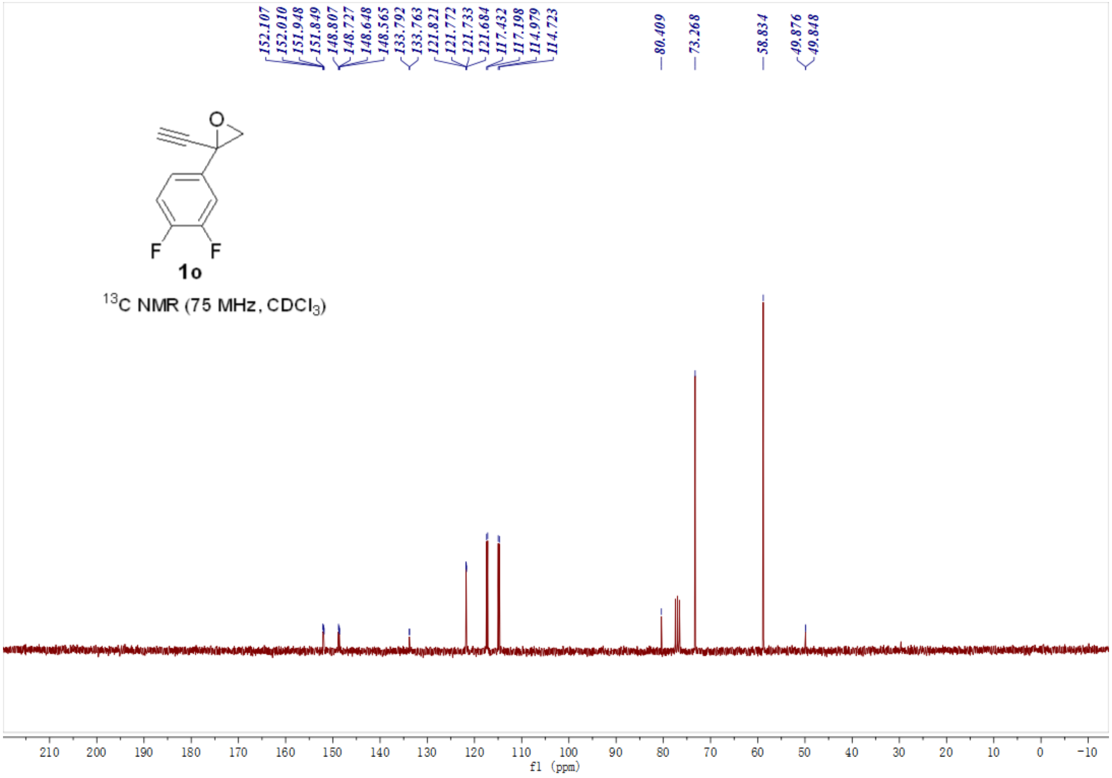
1l

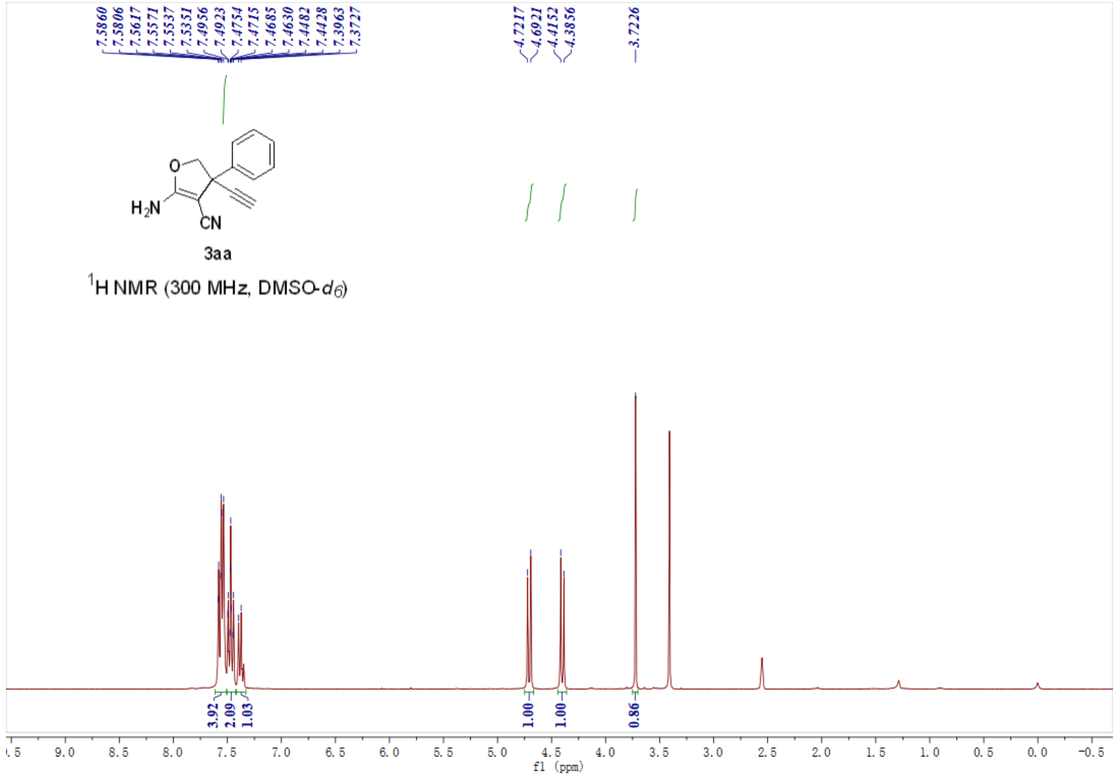
^{13}C NMR (75 MHz, $CDCl_3$)

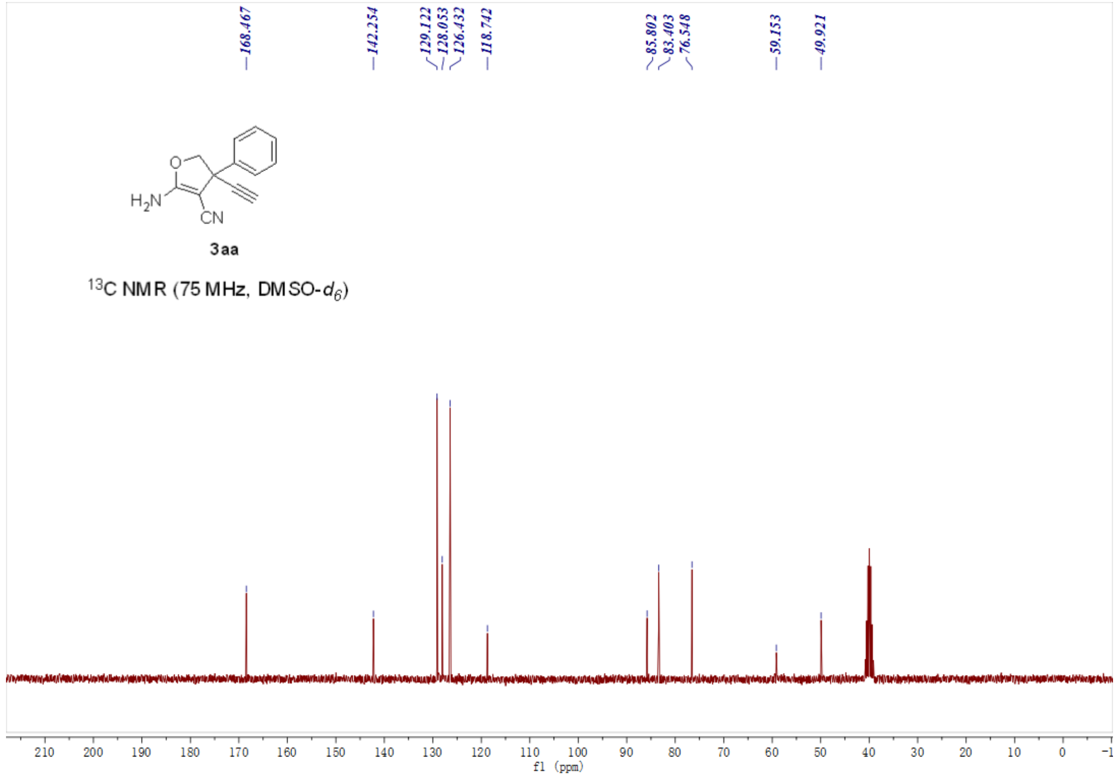


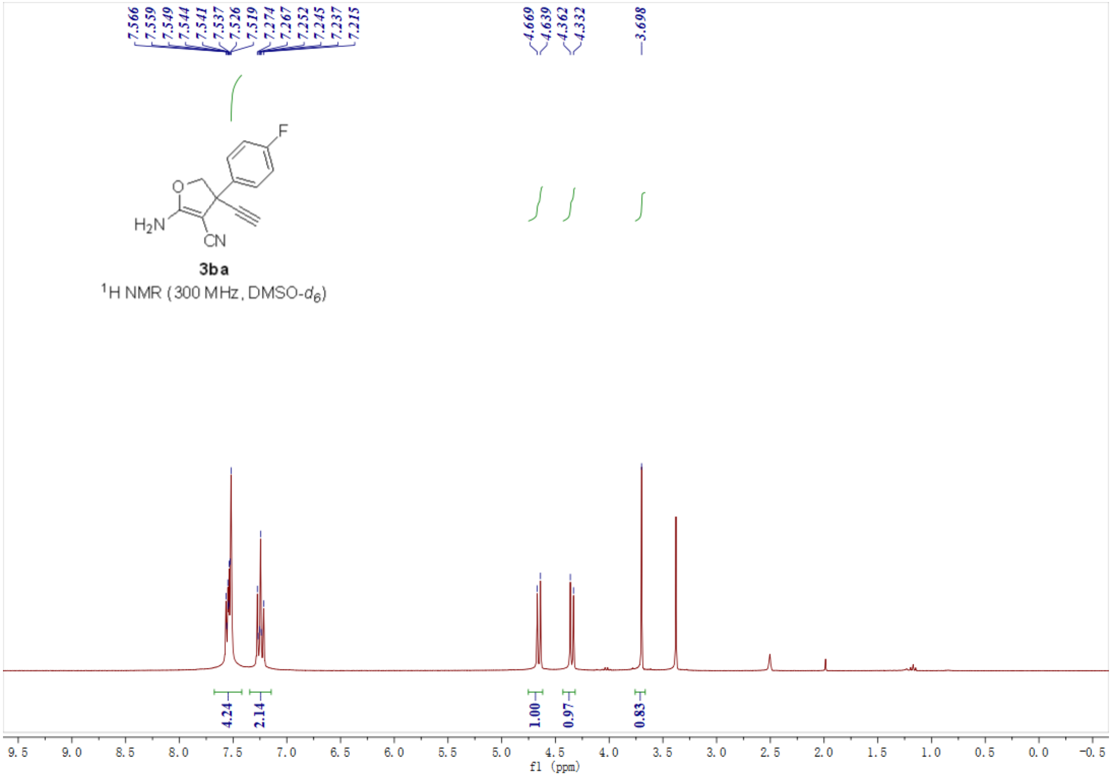


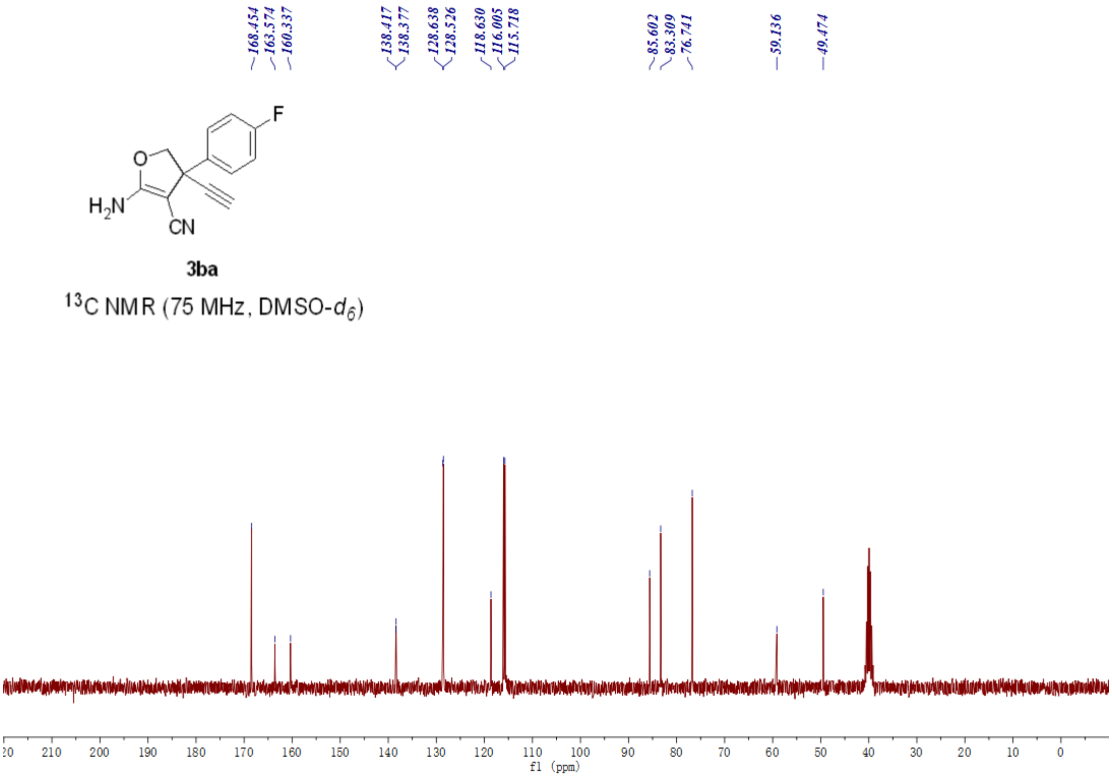

7.3225
7.3152
7.2977
7.2903
7.2853
7.2782
7.2671
7.2622
7.2594
7.2535
7.2475
7.2441
7.2371
7.2339
7.2300
7.2264
7.2227
7.2198
7.2156
7.2122
7.2082
7.1818
7.1555
7.1493
7.1272
7.1219
7.0949
3.4267
3.4067
2.9567
2.9366
2.5610
F
F
1o
¹H NMR (300 MHz, CDCl₃)
2.07
1.02
1.00
1.00
0.92
f1 (ppm)

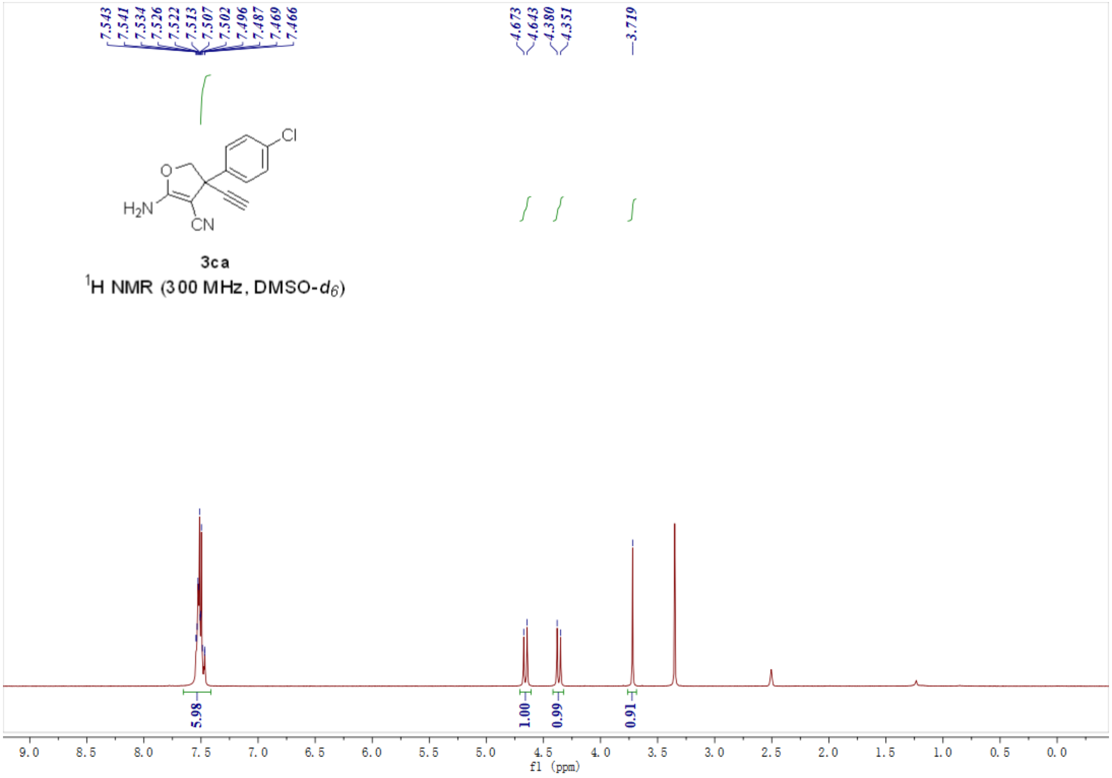

152.107
152.010
151.948
151.849
148.807
148.727
148.648
148.565
133.792
133.763
121.821
121.772
121.733
121.684
117.432
117.198
114.979
114.723
80.409
73.268
58.834
49.876
49.848
F
F
1o
¹³C NMR (75 MHz, CDCl₃)
f1 (ppm)

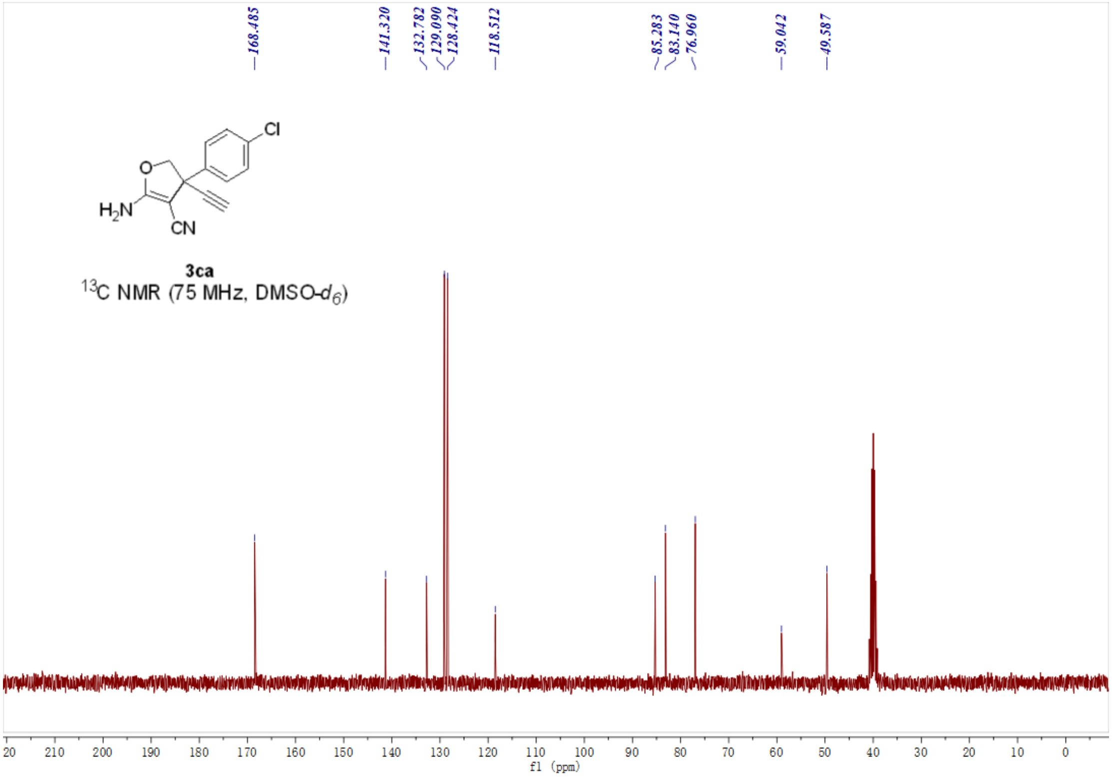

3aa
^{1}H NMR (300 MHz, DMSO-d_6)

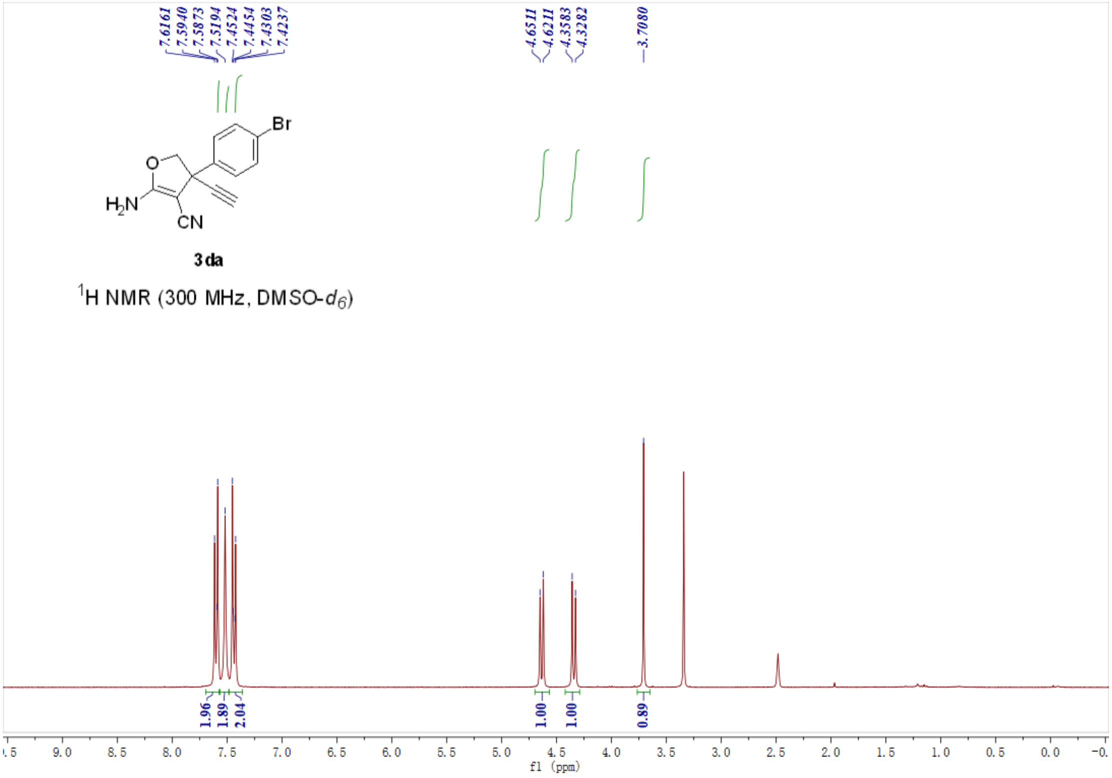

3aa
^{13}C NMR (75 MHz, DMSO-d_6)


7.566
7.559
7.549
7.544
7.541
7.537
7.526
7.519
7.274
7.267
7.252
7.245
7.237
7.215
4.669
4.639
4.362
4.332
3.698
3ba
^{1}H NMR (300 MHz, DMSO-d_6)
4.24
2.14
1.00
0.97
0.83
f1 (ppm)


168.454
163.574
160.337
138.417
138.377
128.638
128.526
118.630
116.005
115.718
85.602
83.309
76.741
59.136
49.474
3ba
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

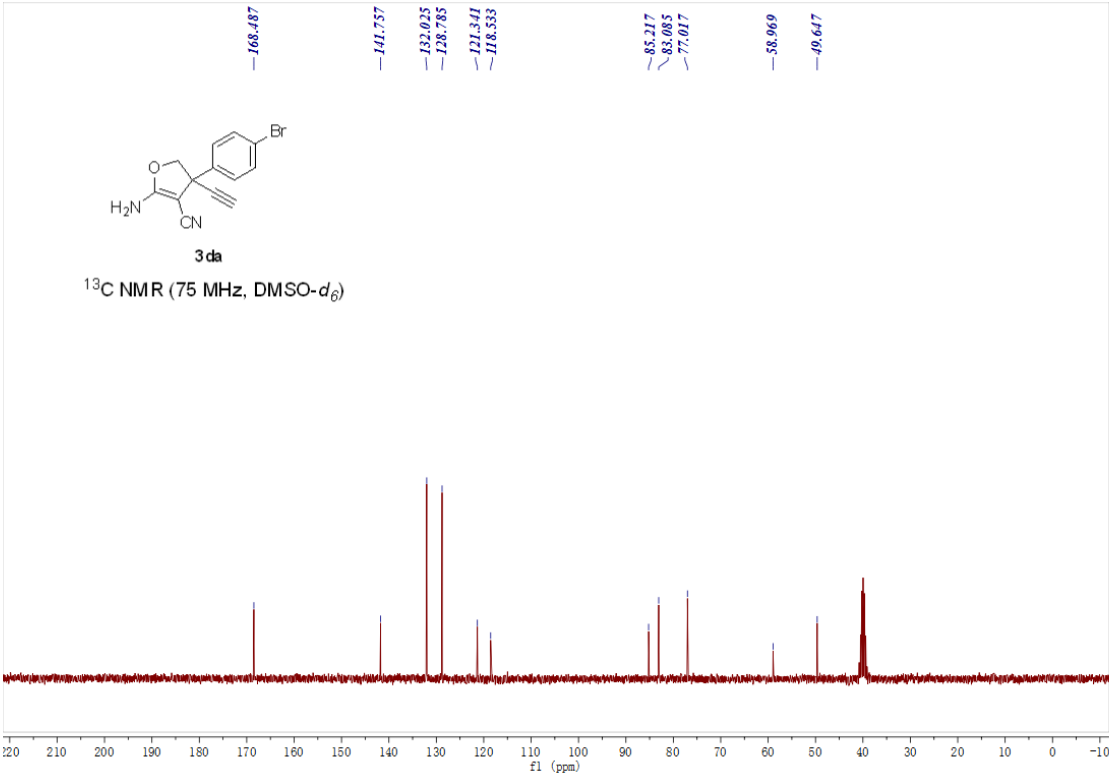

3ca
^{1}H NMR (300 MHz, DMSO-d_6)
7.543 7.541 7.534 7.526 7.522 7.513 7.507 7.502 7.496 7.487 7.469 7.466
4.673 4.643 4.380 4.351
3.719
5.98
1.00
0.99
0.91
f1 (ppm)


3ca
^{13}C NMR (75 MHz, DMSO-d_6)
168.485
141.320 132.782 129.090 128.424
118.512
85.283 83.140 76.960
59.042
49.587
f1 (ppm)



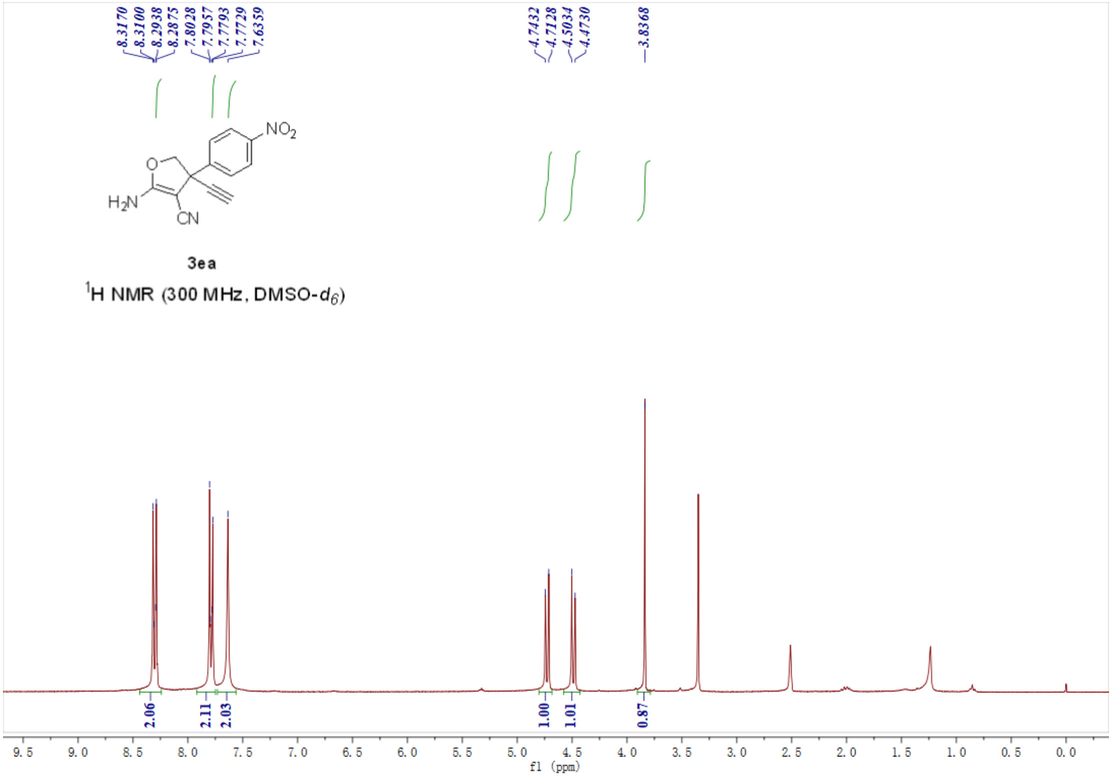
3da

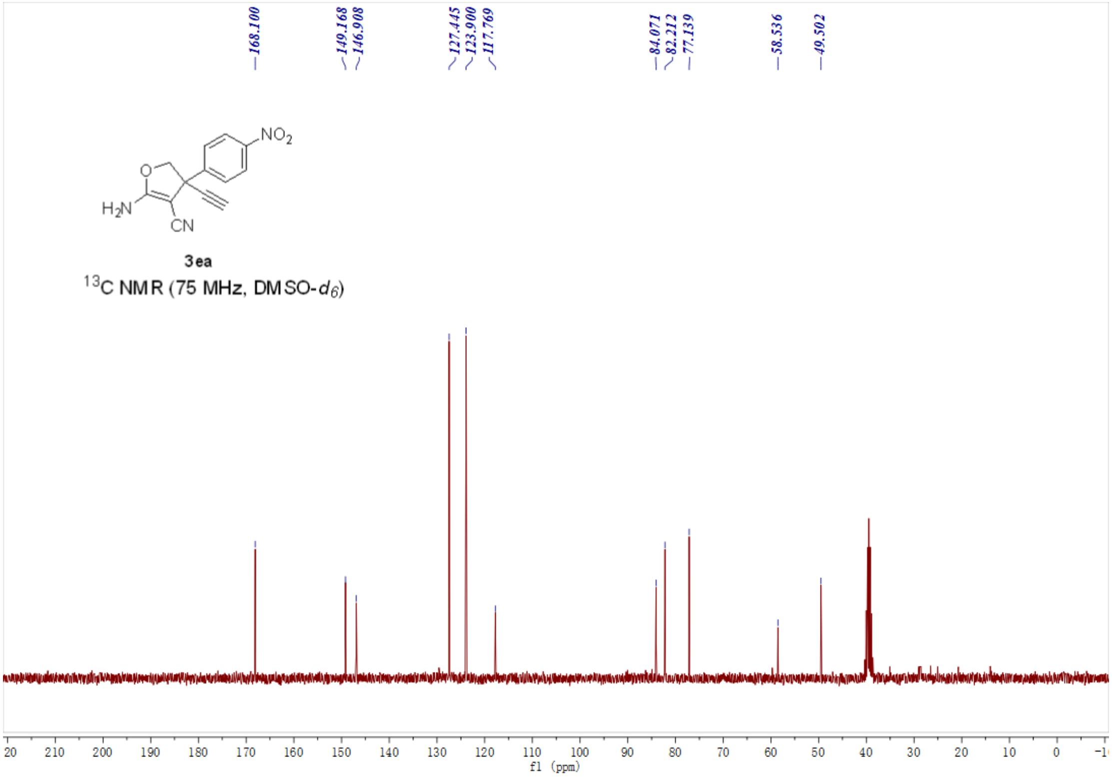
^{1}H NMR (300 MHz, DMSO-d_6)

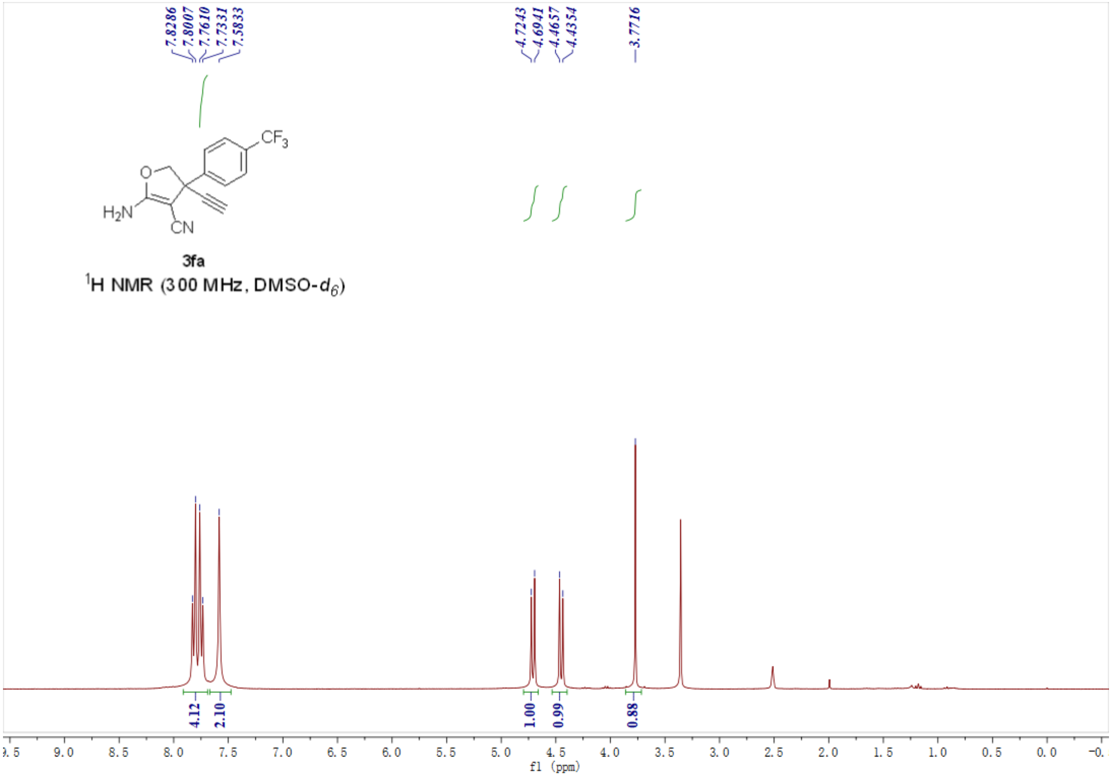


3da

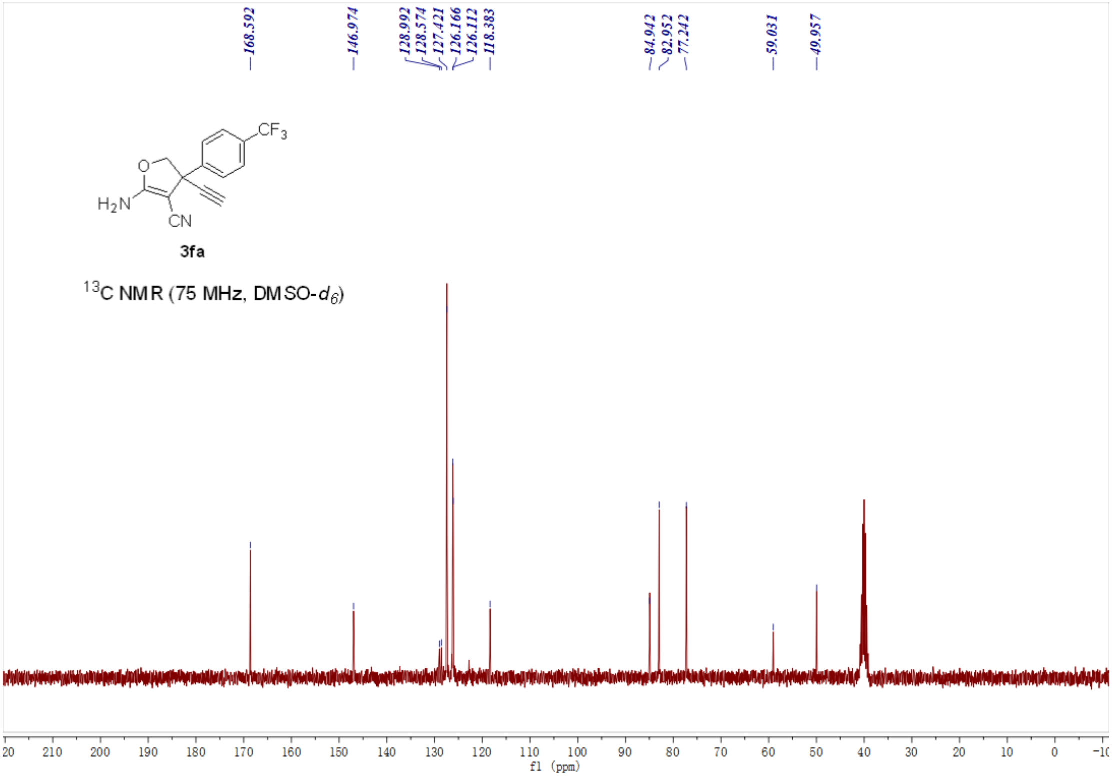
^{13}C NMR (75 MHz, DMSO-d_6)


8.3170
8.3100
8.2938
8.2875
7.8028
7.7957
7.7793
7.7729
7.6359
4.7432
4.7128
4.5034
4.4730
3.8368
NO2
O
H2N
CN
3ea
1H NMR (300 MHz, DMSO-d6)
2.06
2.11
2.03
1.00
1.01
0.87
f1 (ppm)

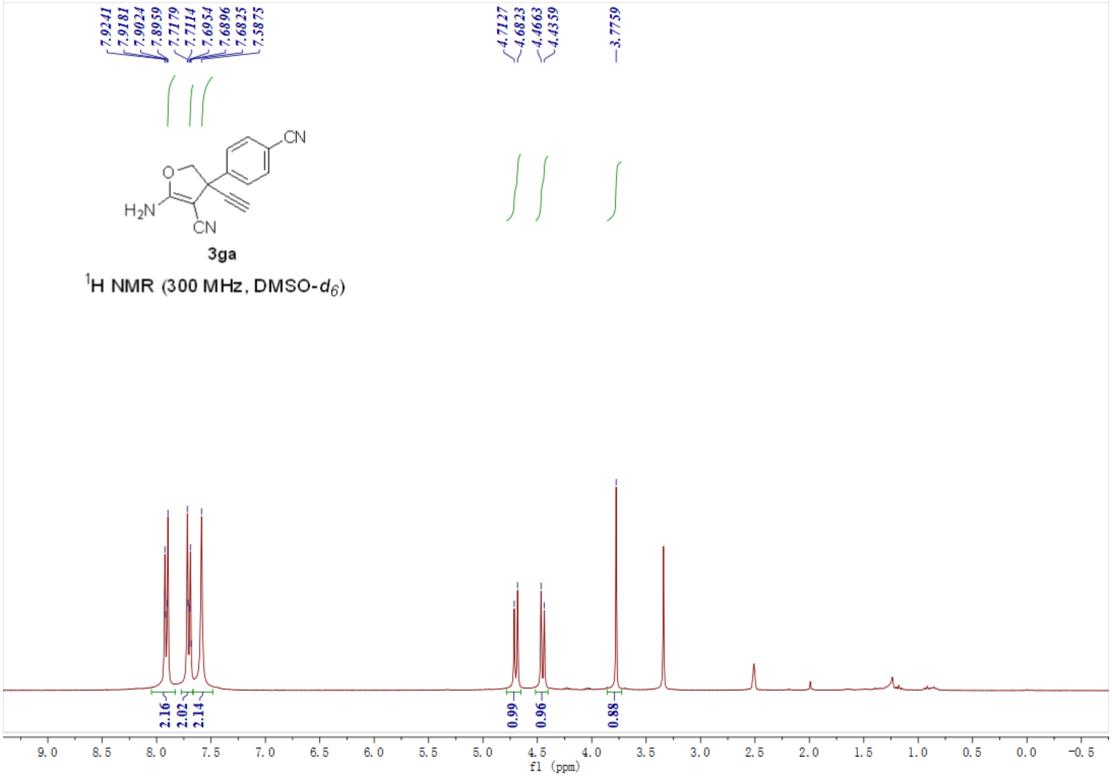

168.100
149.168
146.908
127.445
123.900
117.769
84.071
82.212
77.139
58.536
49.502
NO2
O
H2N
CN
3ea
13C NMR (75 MHz, DMSO-d6)
f1 (ppm)



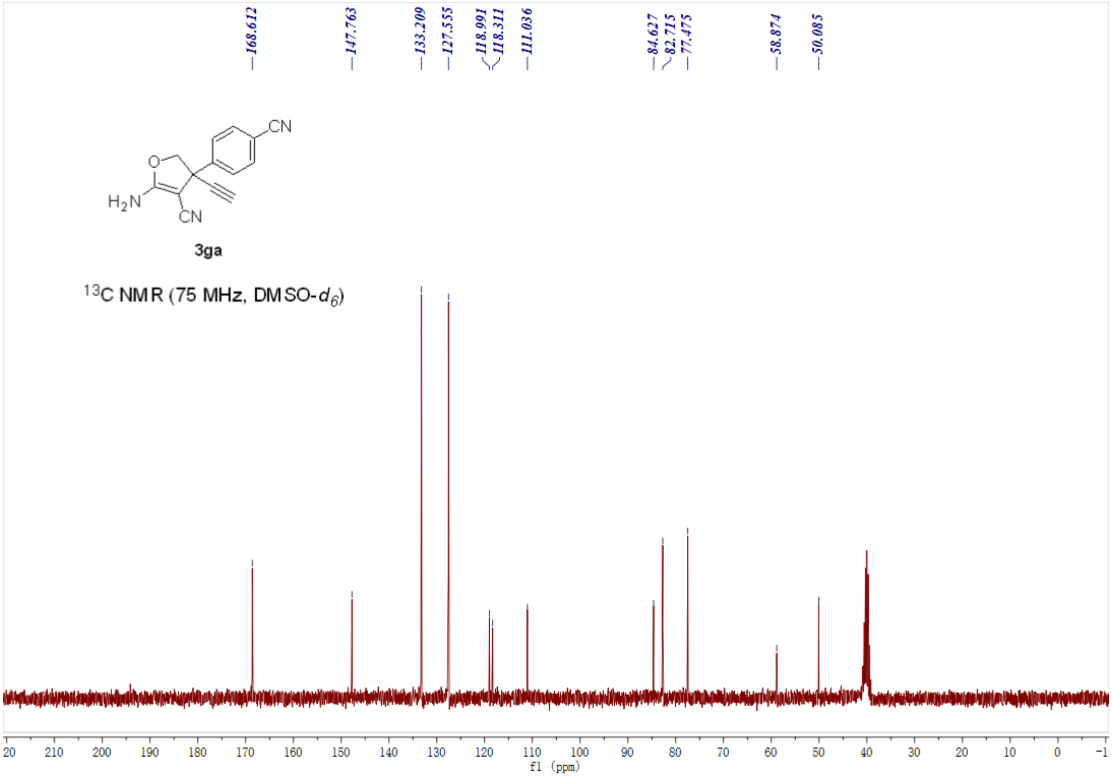
7.8286
7.8007
7.7610
7.7331
7.5833
4.7243
4.6941
4.4657
4.4354
3.7716
CF3
O
H2N
CN
3fa
1H NMR (300 MHz, DMSO-d6)
4.12
2.10
1.00
0.99
0.88
f1 (ppm)



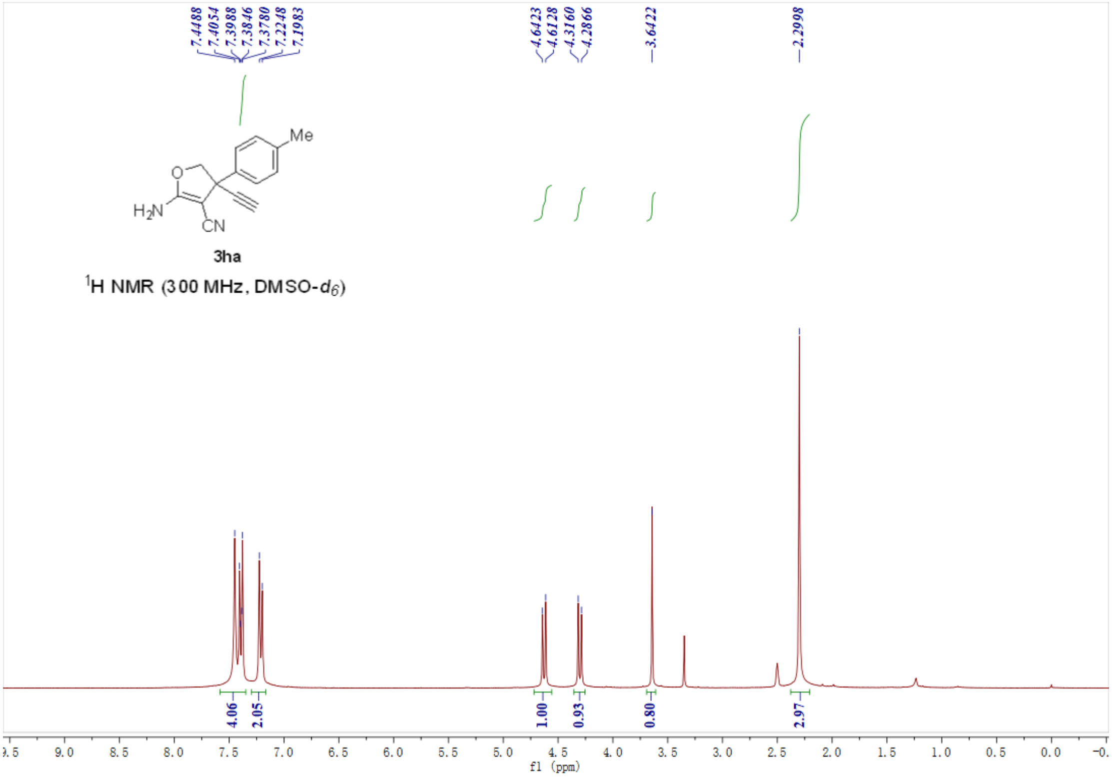
168.592
146.974
128.992
128.574
127.421
126.166
126.112
118.383
84.942
82.952
77.242
59.031
49.957
CF3
O
H2N
CN
3fa
13C NMR (75 MHz, DMSO-d6)
f1 (ppm)

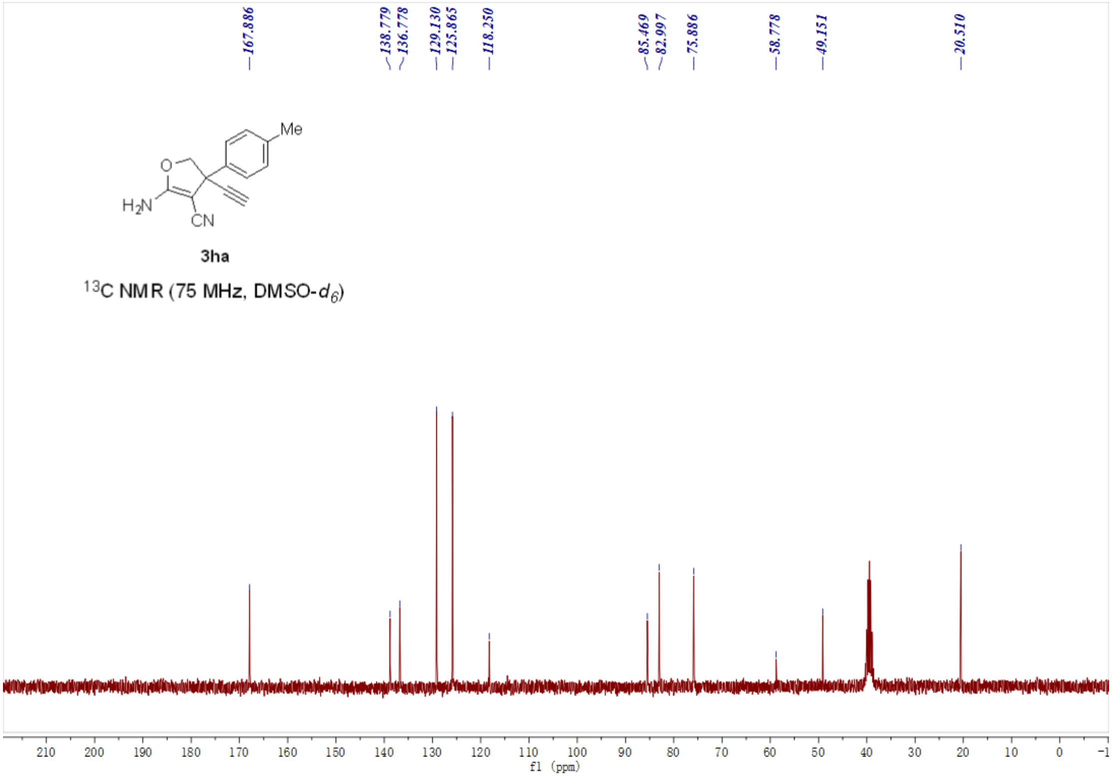


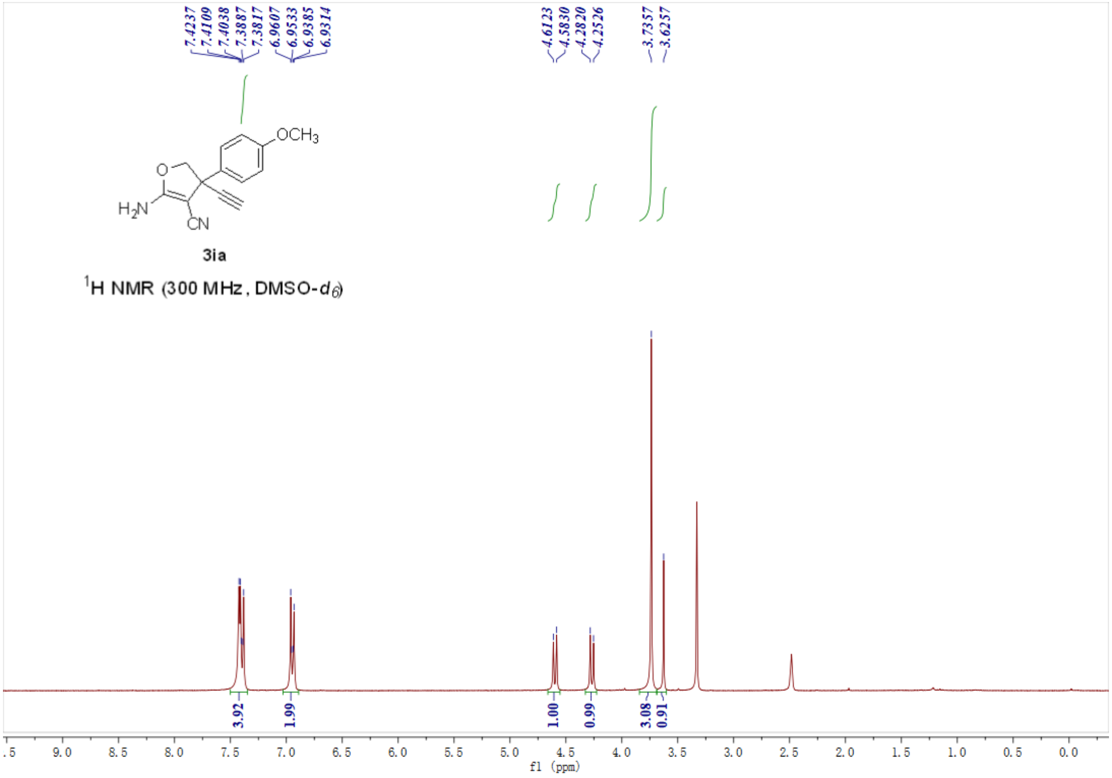
7.9241
7.9181
7.9024
7.8959
7.7179
7.7114
7.6954
7.6896
7.6825
7.5875
4.7127
4.6823
4.4663
4.4359
3.7759
3ga
^{1}H NMR (300 MHz, DMSO-d_6)
2.16
2.02
2.14
0.99
0.96
0.88
f1 (ppm)

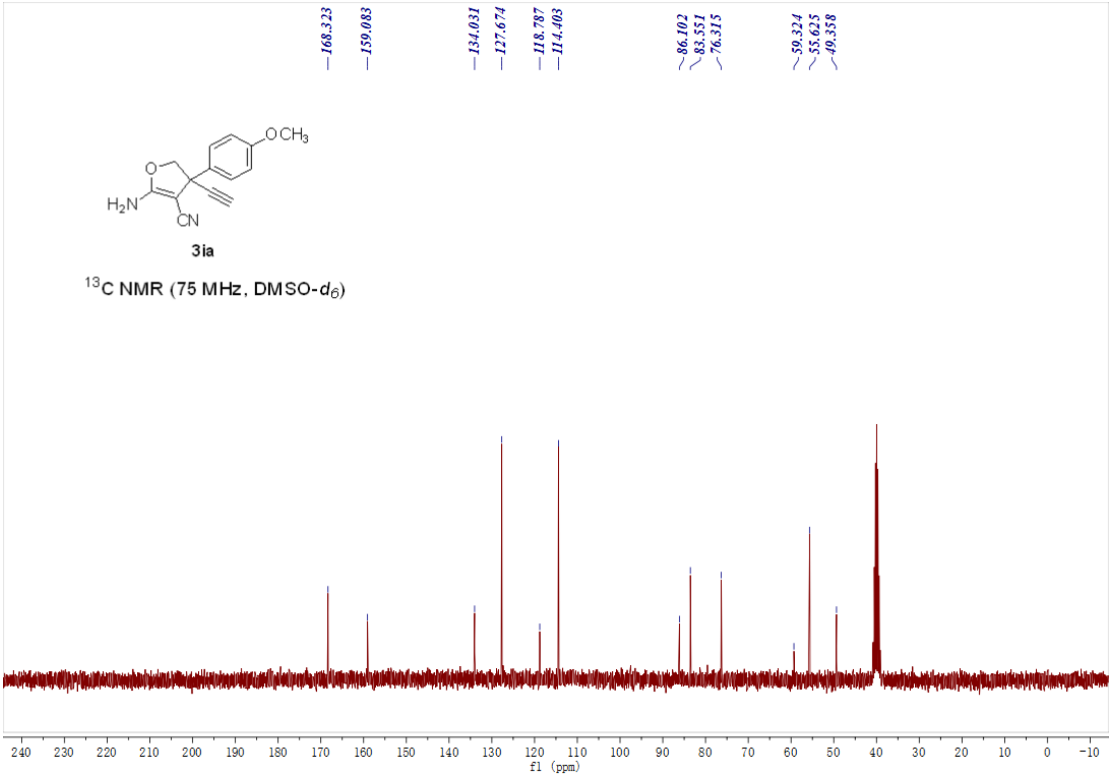


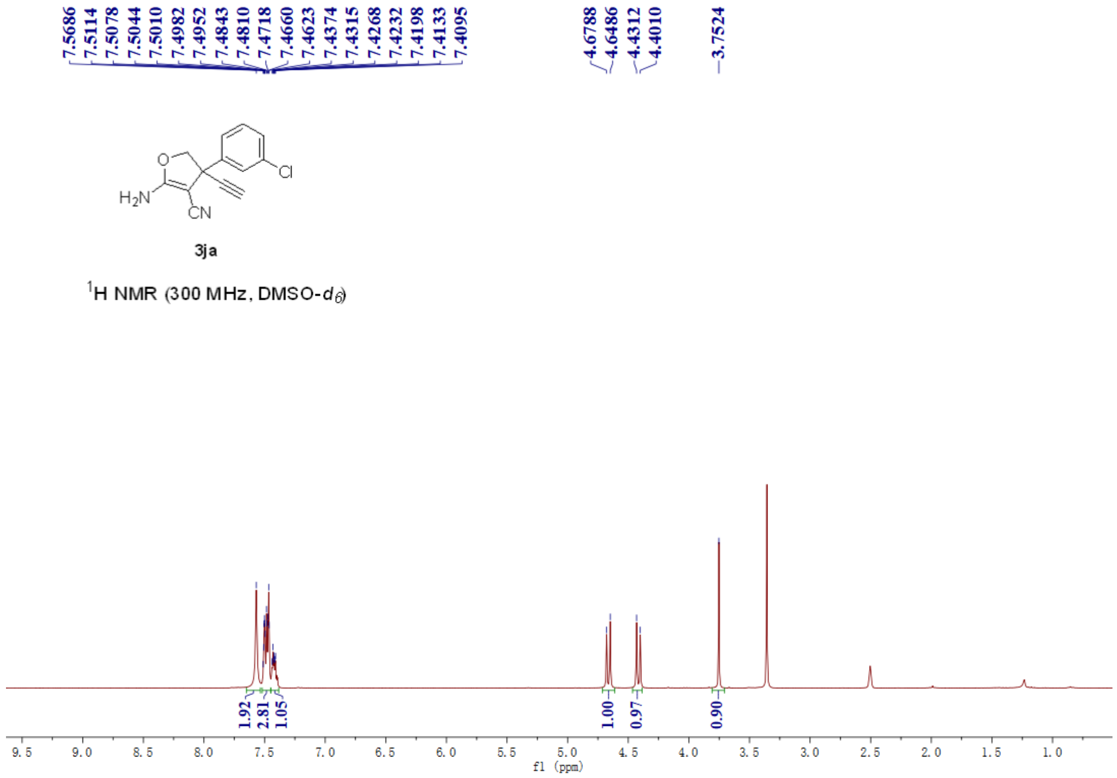
168.612
147.763
133.209
127.555
118.991
118.311
111.036
84.627
82.715
77.475
58.874
50.085
3ga
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)


7.4488
7.4054
7.3988
7.3846
7.3780
7.2248
7.1983
4.6423
4.6128
4.3160
4.2866
3.6422
2.2998
Me
O
H2N
CN
3ha
1H NMR (300 MHz, DMSO-d6)
4.06
2.05
1.00
0.93
0.80
2.97
f1 (ppm)


167.886
138.779
136.778
129.130
125.865
118.250
85.469
82.997
75.886
58.778
49.151
20.510
Me
O
H2N
CN
3ha
13C NMR (75 MHz, DMSO-d6)
f1 (ppm)

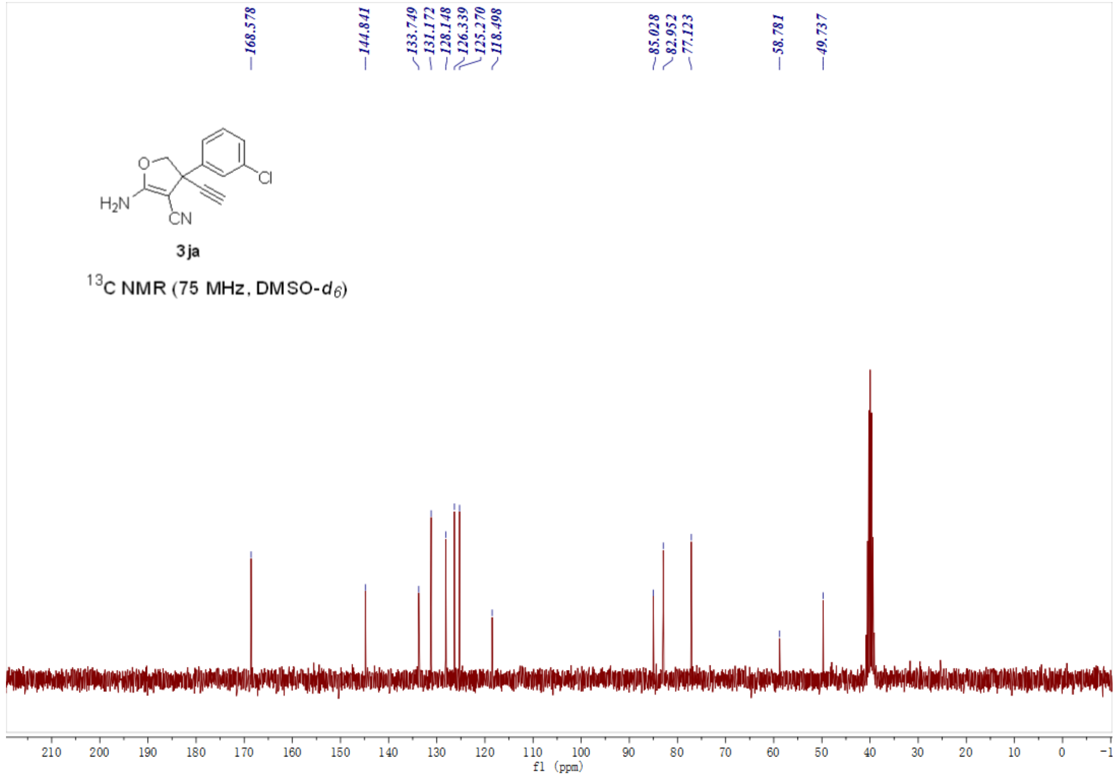

7.4237
7.4109
7.4038
7.3887
7.3817
6.9607
6.9533
6.9385
6.9314
4.6123
4.5830
4.2820
4.2526
3.7357
3.6257
OCH3
O
H2N
CN
3ia
1H NMR (300 MHz, DMSO-d6)
3.92
1.99
1.00
0.99
3.08
0.91
f1 (ppm)


168.323
159.083
134.031
127.674
118.787
114.403
86.102
83.551
76.315
59.324
55.625
49.358
OCH3
O
H2N
CN
3ia
13C NMR (75 MHz, DMSO-d6)
f1 (ppm)



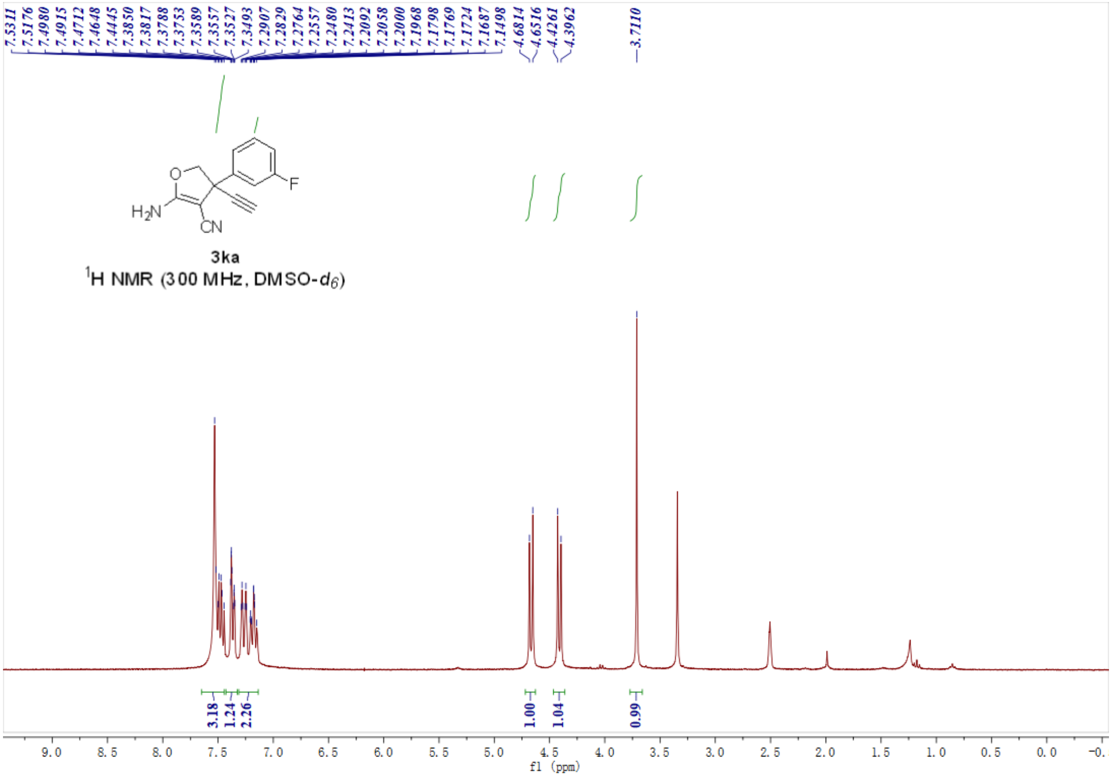
3ja

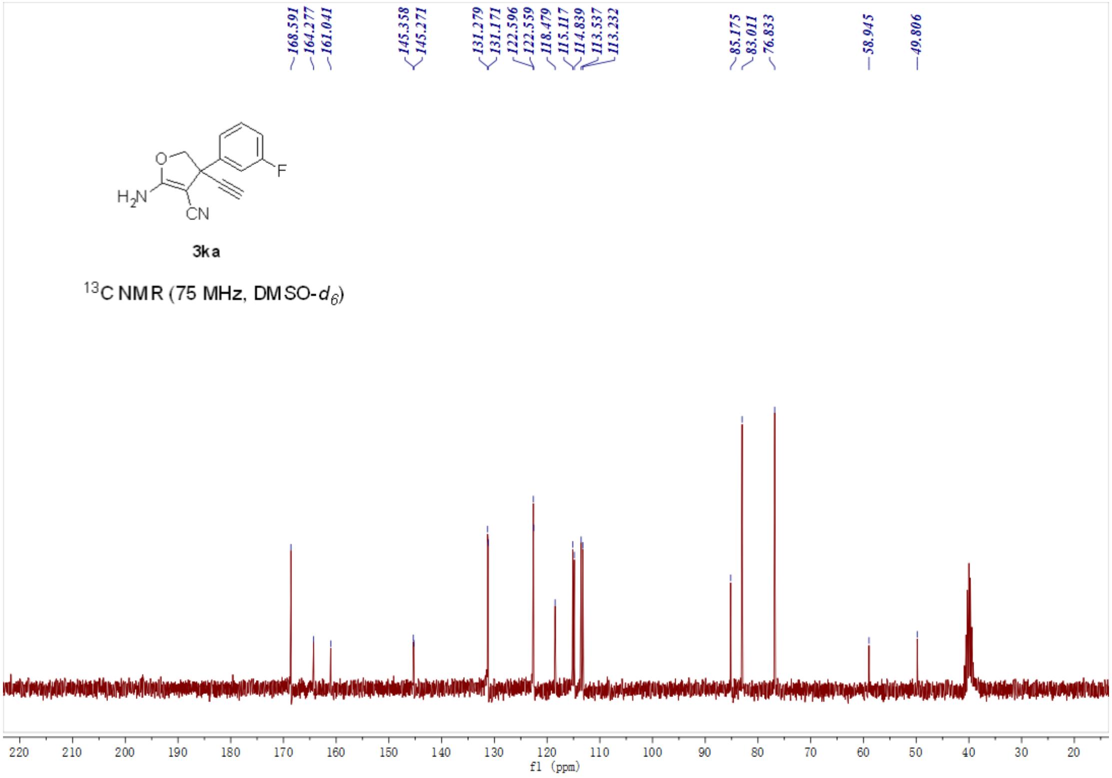
^{1}H NMR (300 MHz, DMSO-d_6)

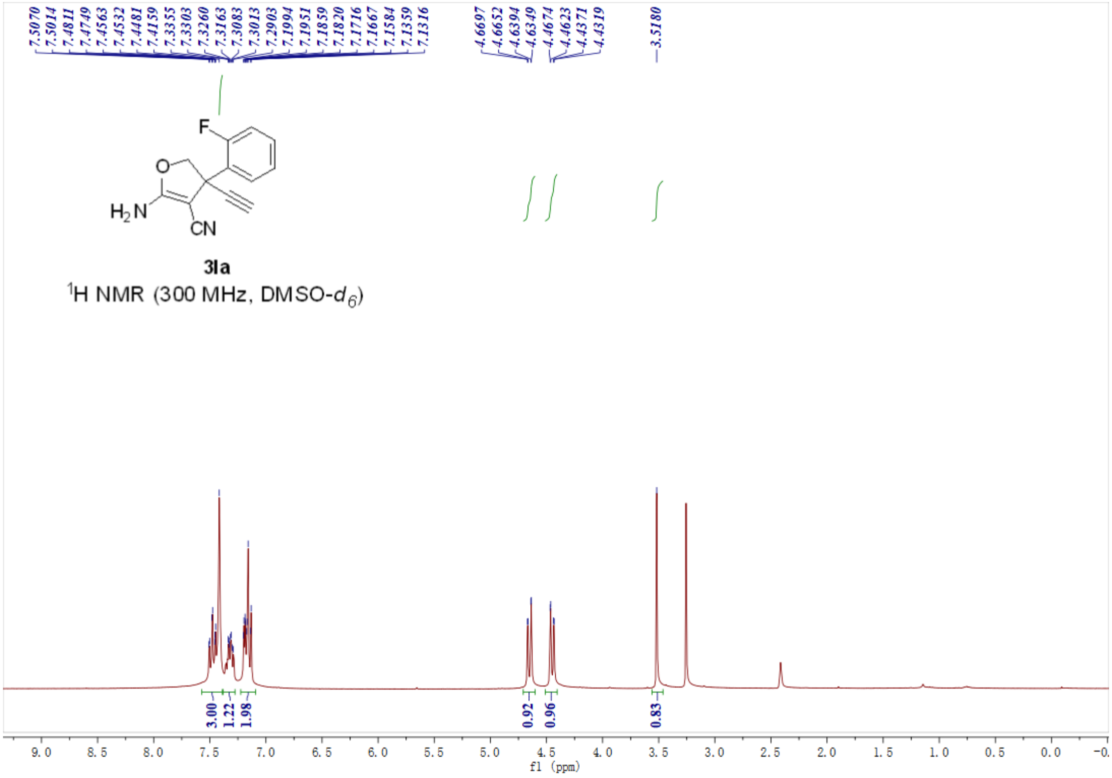


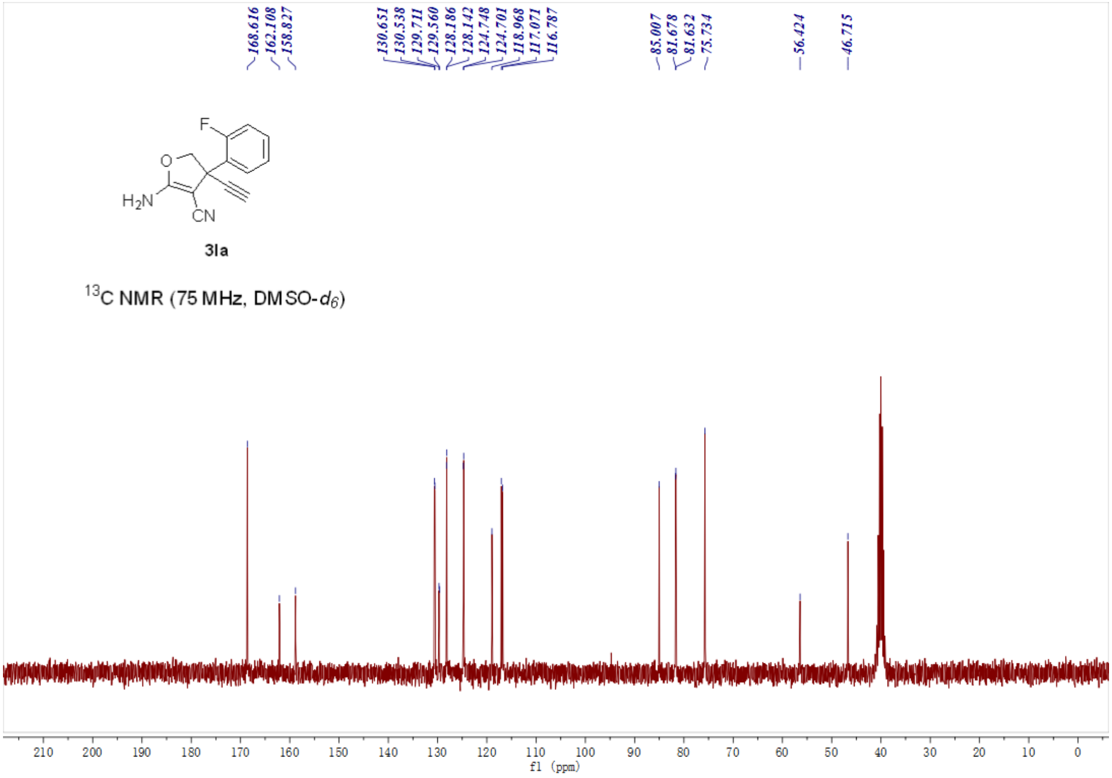
3ja

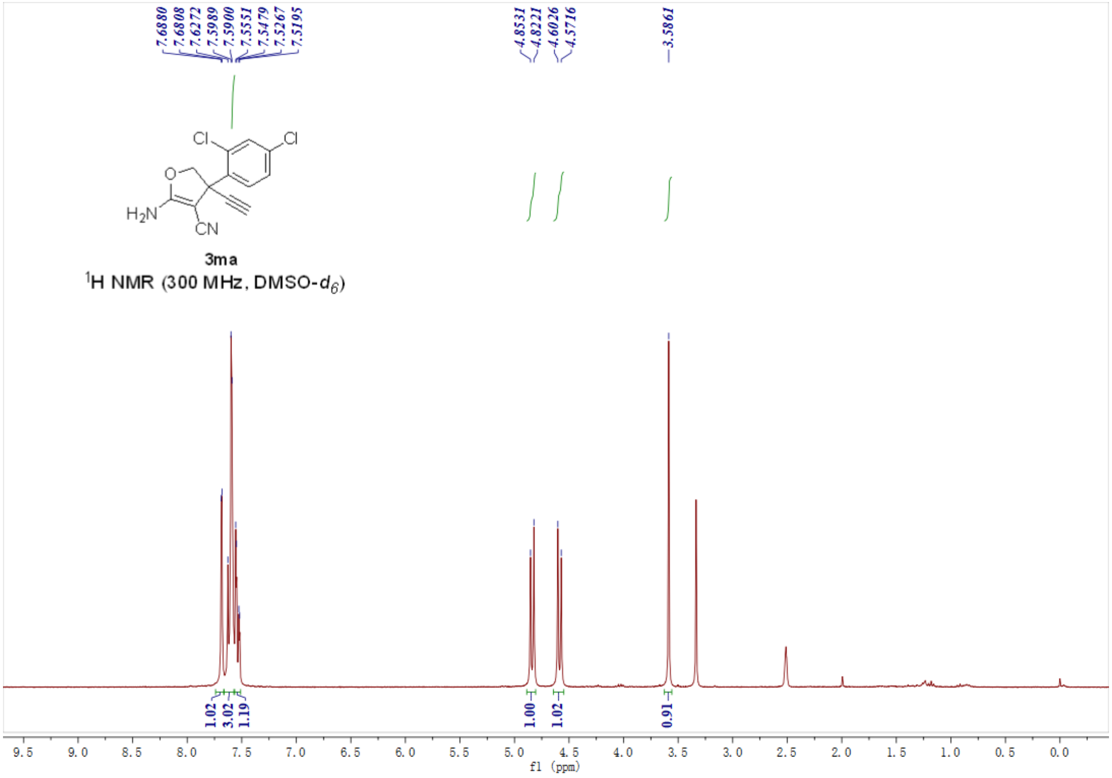
^{13}C NMR (75 MHz, DMSO-d_6)

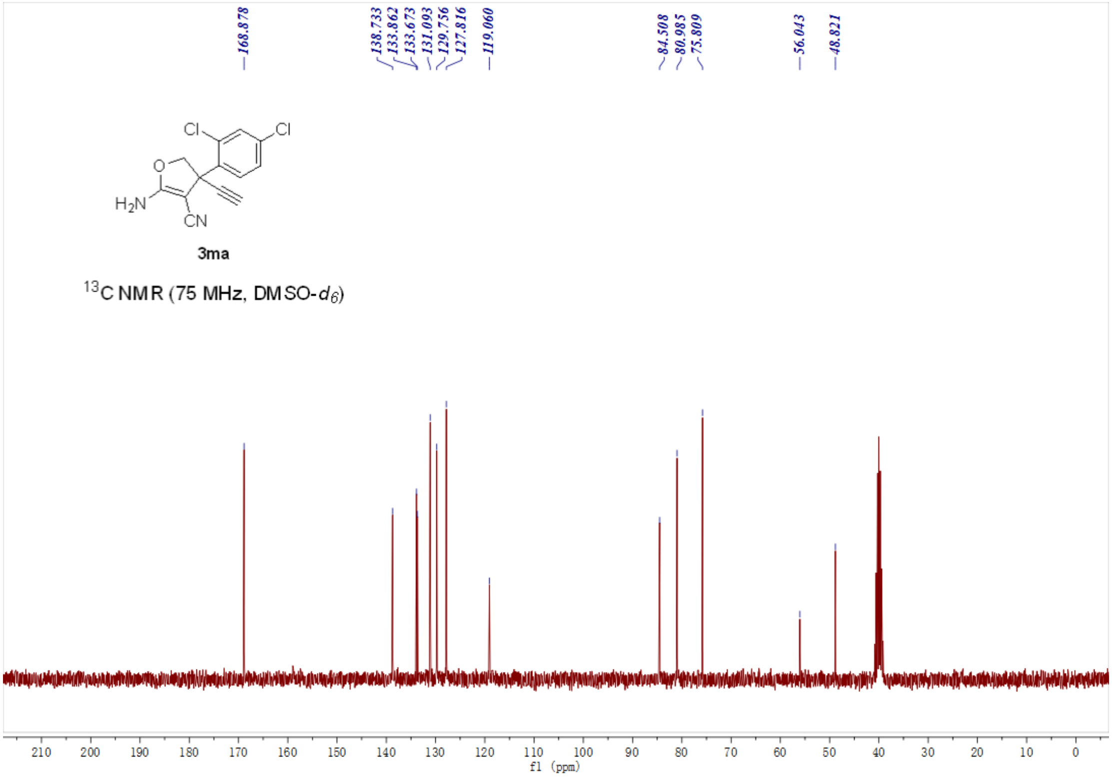

7.5311
7.5176
7.4980
7.4915
7.4712
7.4648
7.4445
7.3850
7.3817
7.3788
7.3753
7.3589
7.3557
7.3527
7.3493
7.2907
7.2829
7.2764
7.2557
7.2480
7.2413
7.2092
7.2058
7.2000
7.1968
7.1798
7.1769
7.1724
7.1687
7.1498
4.6814
4.6516
4.4261
4.3962
3.7110
3ka
^{1}H NMR (300 MHz, DMSO-d_6)
3.18
1.24
2.26
1.00
1.04
0.99
f1 (ppm)

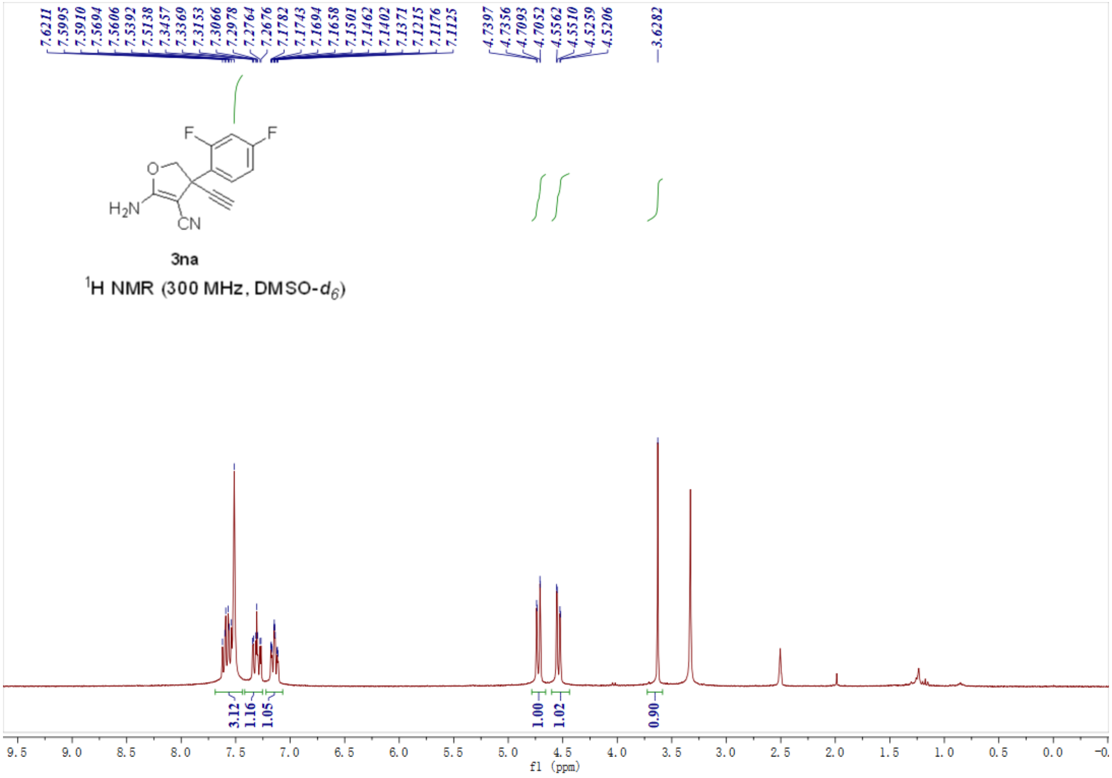

168.591
164.277
161.041
145.358
145.271
131.279
131.171
122.596
122.559
118.479
115.117
114.839
113.537
113.232
85.175
83.011
76.833
58.945
49.806
3ka
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

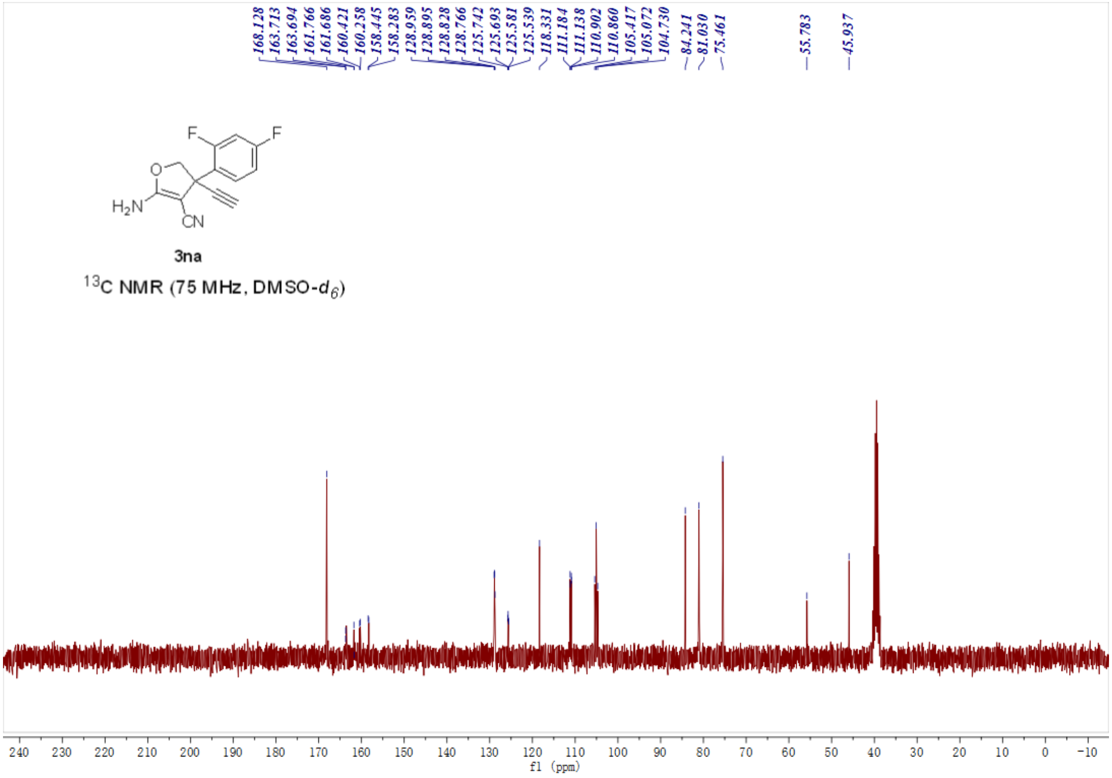

7.5070
7.5014
7.4811
7.4749
7.4563
7.4532
7.4481
7.4159
7.3355
7.3303
7.3260
7.3163
7.3083
7.3013
7.2903
7.1994
7.1951
7.1859
7.1820
7.1716
7.1667
7.1584
7.1359
7.1316
4.6697
4.6652
4.6394
4.6349
4.4674
4.4623
4.4371
4.4319
3.5180
F
O
H_2N
CN
3la
^1H NMR (300 MHz, DMSO-d_6)
3.00
1.22
1.98
0.92
0.96
0.83
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

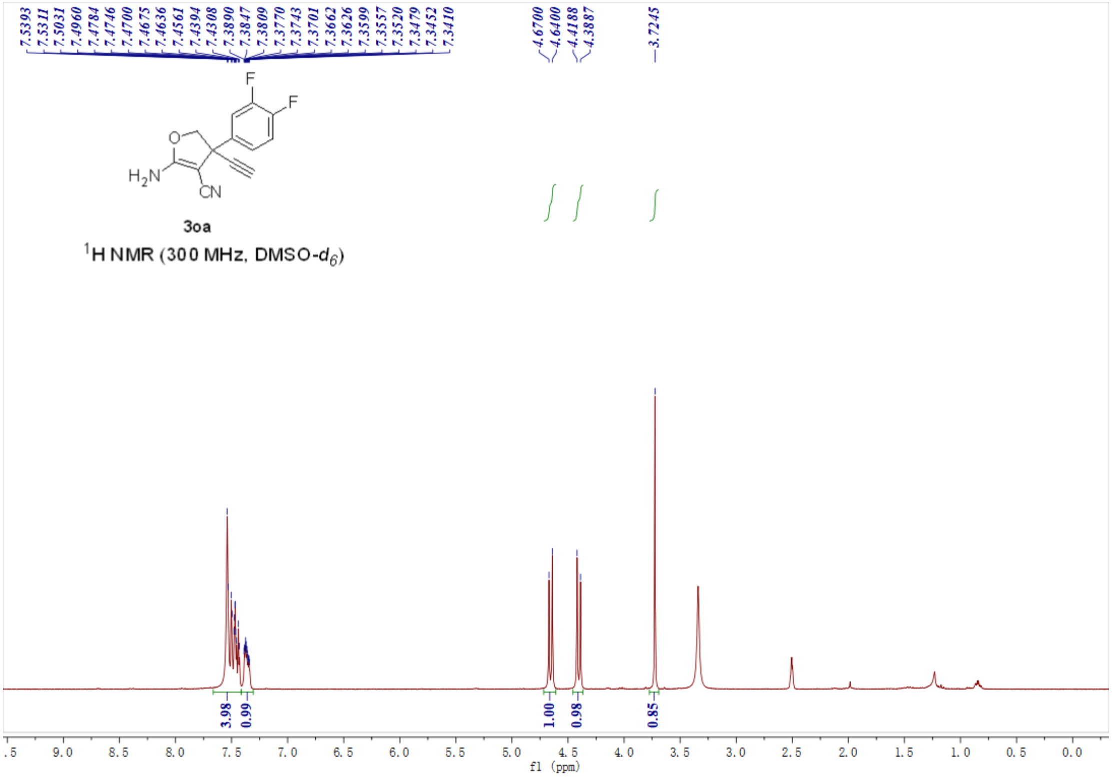

168.616
162.108
158.827
130.651
130.538
129.711
129.560
128.186
128.142
124.748
124.701
118.968
117.071
116.787
85.007
81.678
81.632
75.734
56.424
46.715
F
O
H_2N
CN
3la
^{13}C NMR (75 MHz, DMSO-d_6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

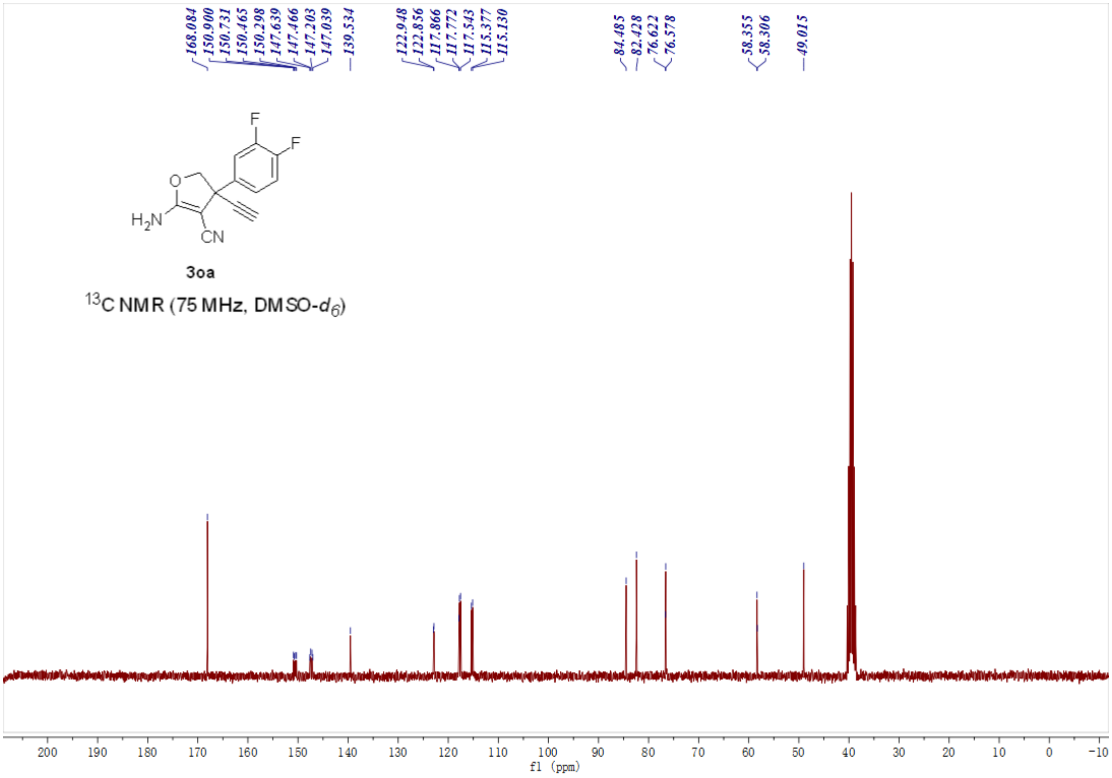

7.6880
7.6808
7.6272
7.5989
7.5900
7.5551
7.5479
7.5267
7.5195
4.8531
4.8221
4.6026
4.5716
3.5861
3ma
^{1}H NMR (300 MHz, DMSO-d_6)
1.02
3.02
1.19
1.00
1.02
0.91
f1 (ppm)

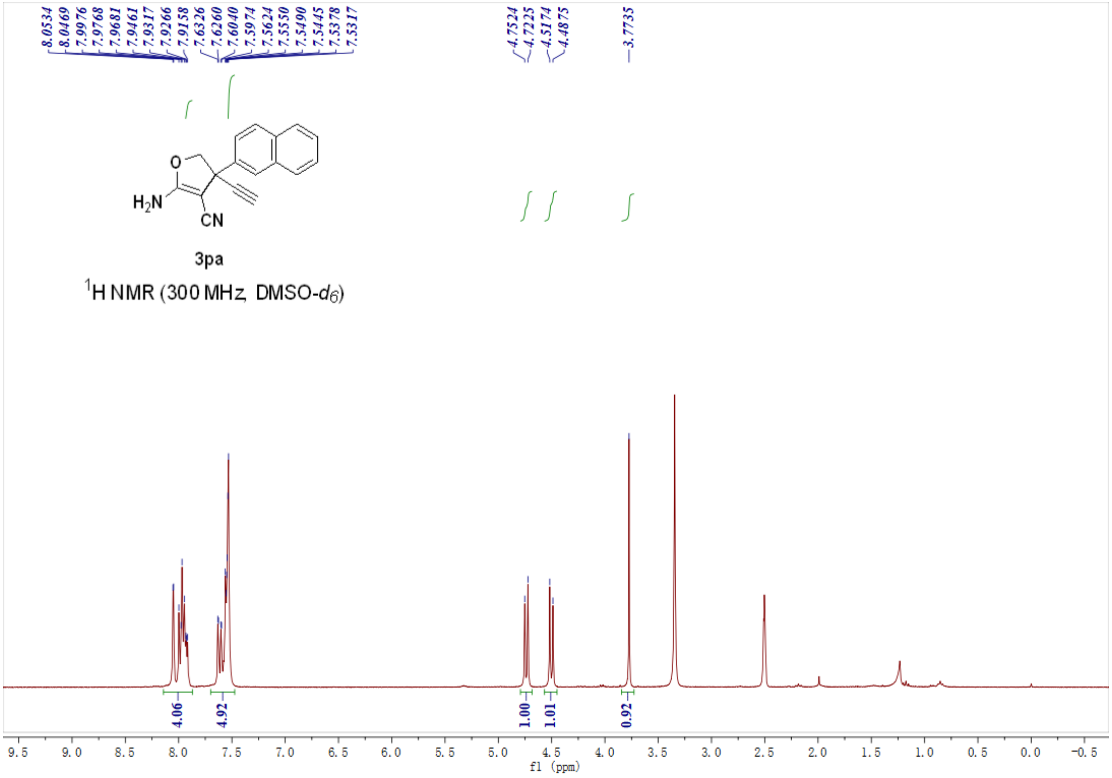

168.878
138.733
133.862
133.673
131.093
129.756
127.816
119.060
84.508
80.985
75.809
56.043
48.821
3ma
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

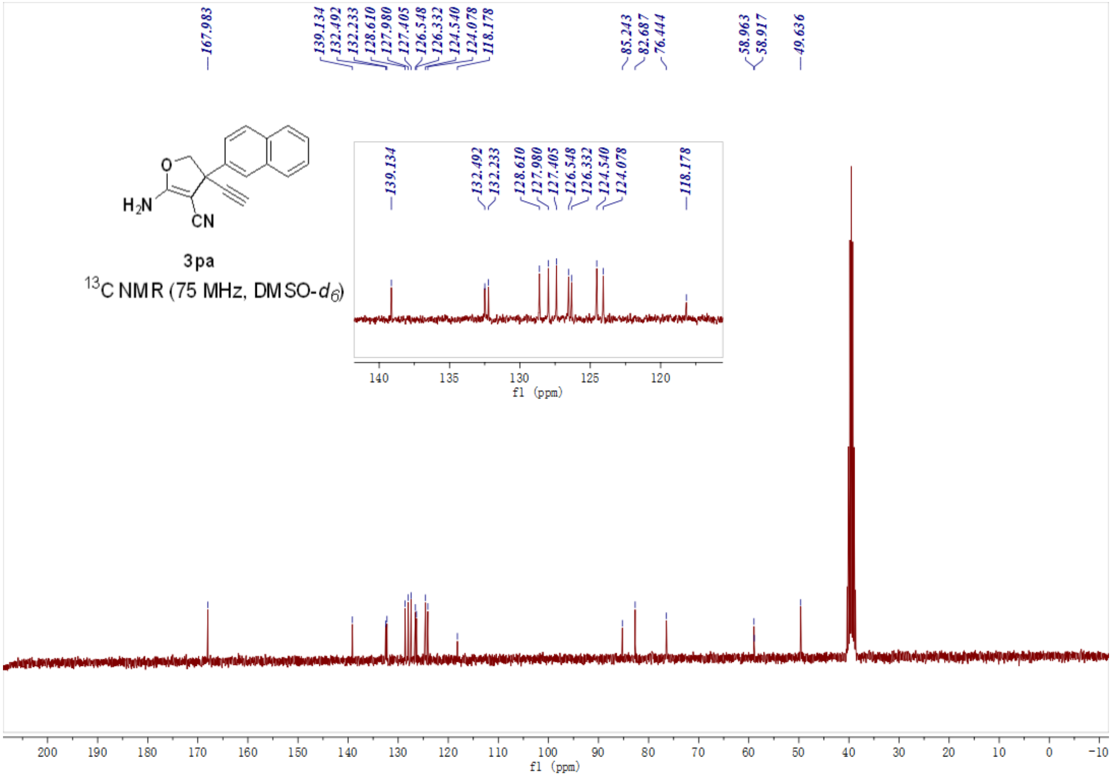

7.6211
7.5995
7.5910
7.5694
7.5606
7.5392
7.5138
7.3457
7.3369
7.3153
7.3066
7.2978
7.2764
7.2676
7.1782
7.1743
7.1694
7.1658
7.1501
7.1462
7.1402
7.1371
7.1215
7.1176
7.1125
4.7397
4.7356
4.7093
4.7052
4.5562
4.5510
4.5259
4.5206
3.6282
F
F
O
H_2N
CN
3na
^{1}H NMR (300 MHz, DMSO-d_6)
3.12
1.16
1.05
1.00
1.02
0.90
f1 (ppm)

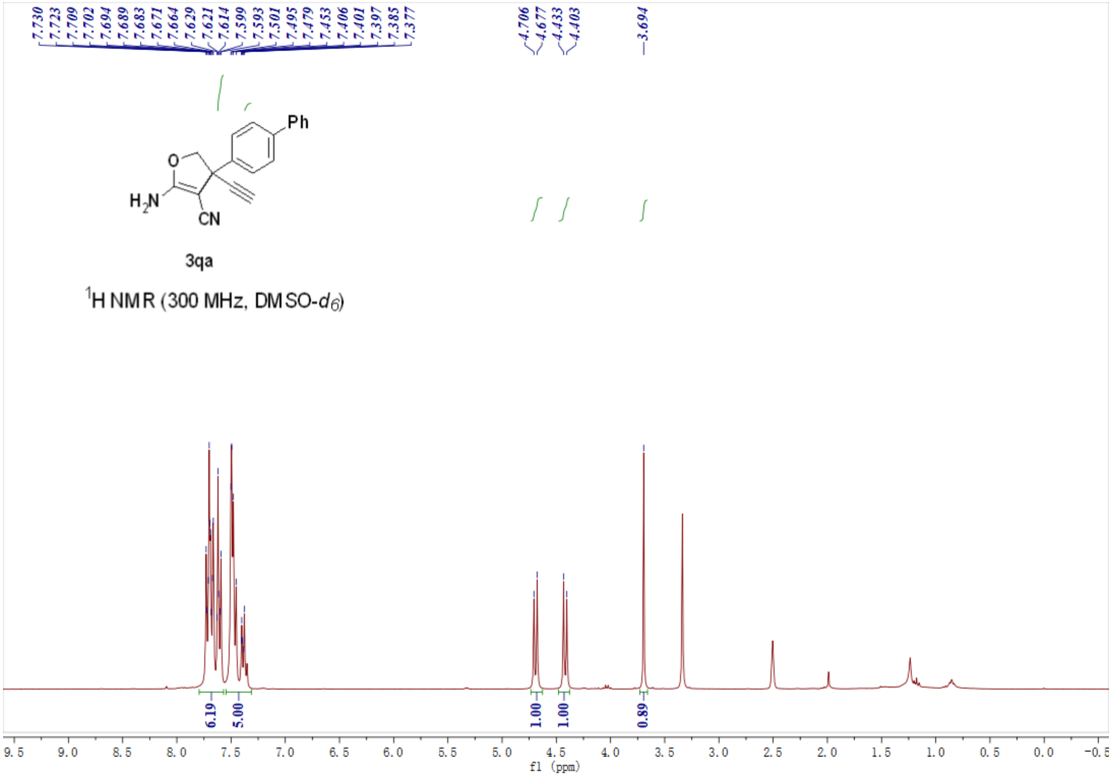

168.128
163.713
163.694
161.766
161.686
160.421
160.258
158.445
158.283
128.959
128.895
128.828
128.766
125.742
125.693
125.581
125.539
118.331
111.184
111.138
110.902
110.860
105.417
105.072
104.730
84.241
81.030
75.461
55.783
45.937
F
F
O
H_2N
CN
3na
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

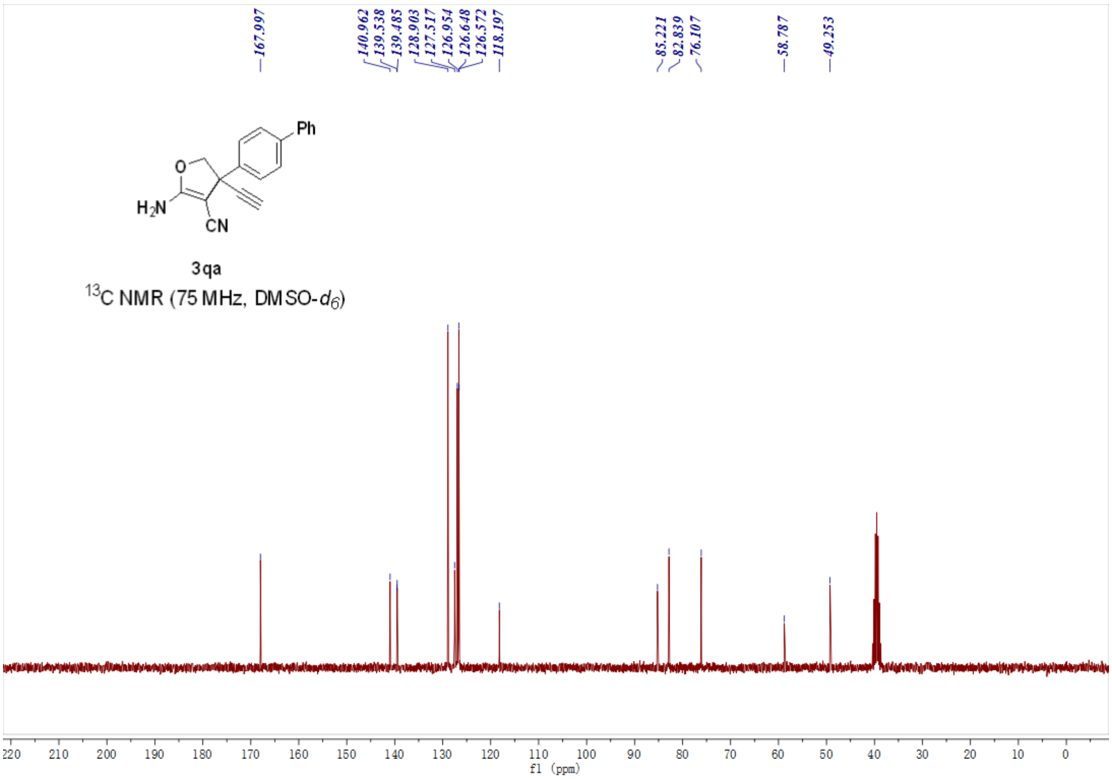

7.5393
7.5311
7.5031
7.4960
7.4784
7.4746
7.4700
7.4675
7.4636
7.4561
7.4394
7.4308
7.3890
7.3847
7.3809
7.3770
7.3743
7.3701
7.3662
7.3626
7.3599
7.3557
7.3520
7.3479
7.3452
7.3410
4.6700
4.6400
4.4188
4.3887
3.7245
3oa
^{1}H NMR (300 MHz, DMSO-d_6)
3.98
0.99
1.00
0.98
0.85
f1 (ppm)

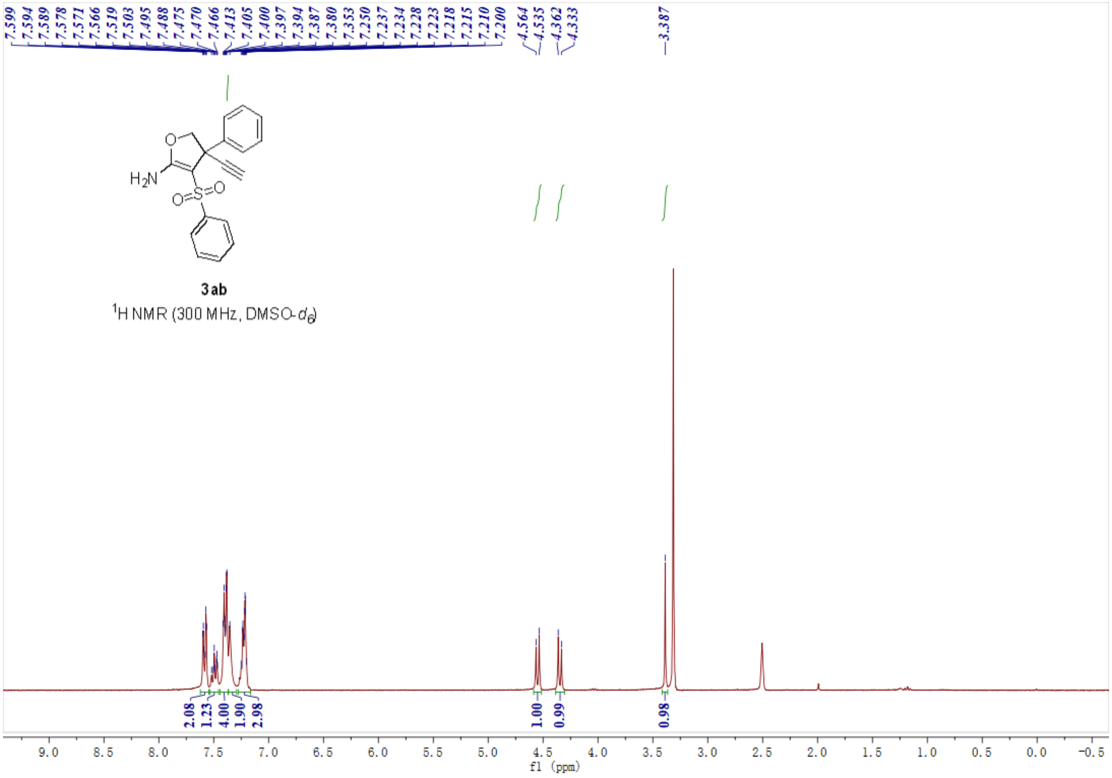

168.084
150.900
150.731
150.465
150.298
147.639
147.466
147.203
147.039
139.534
122.948
122.856
117.866
117.772
117.543
115.377
115.130
84.485
82.428
76.622
76.578
58.355
58.306
49.015
3oa
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

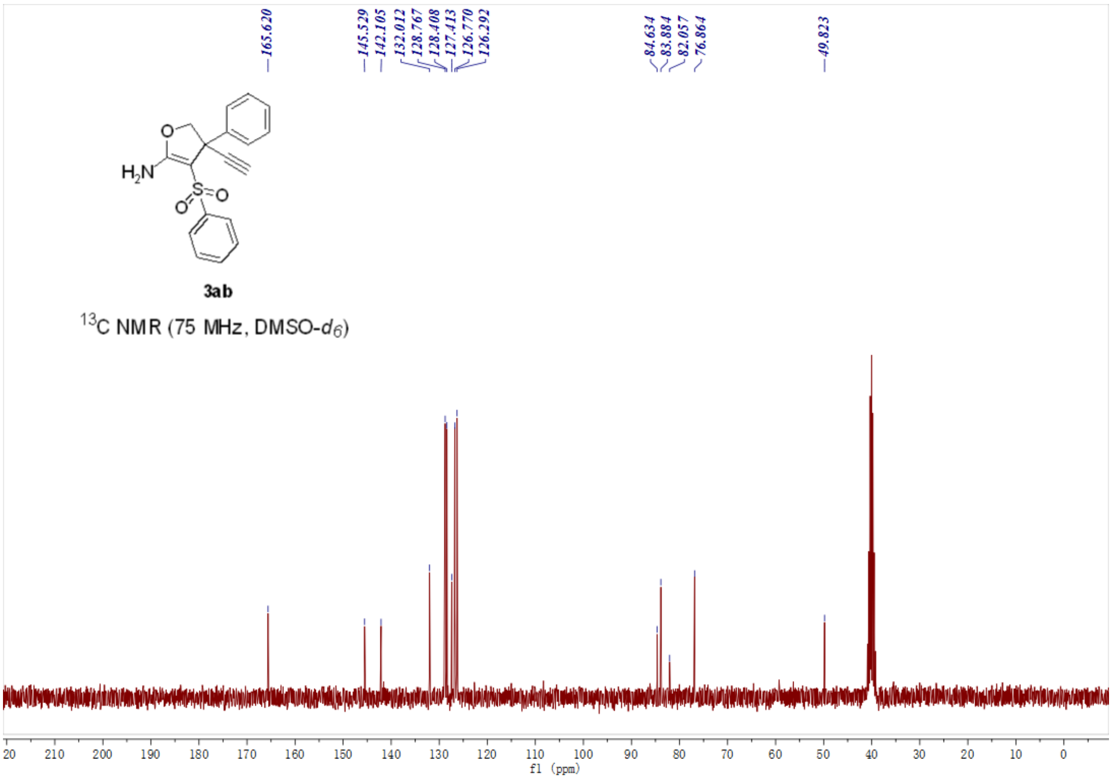

8.0534
8.0469
7.9976
7.9768
7.9681
7.9461
7.9317
7.9266
7.9158
7.6326
7.6260
7.6040
7.5974
7.5624
7.5550
7.5490
7.5445
7.5378
7.5317
4.7524
4.7225
4.5174
4.4875
3.7735
O
H_2N
CN
3pa
^{1}H NMR (300 MHz, DMSO-d_6)
4.06
4.92
1.00
1.01
0.92
f1 (ppm)

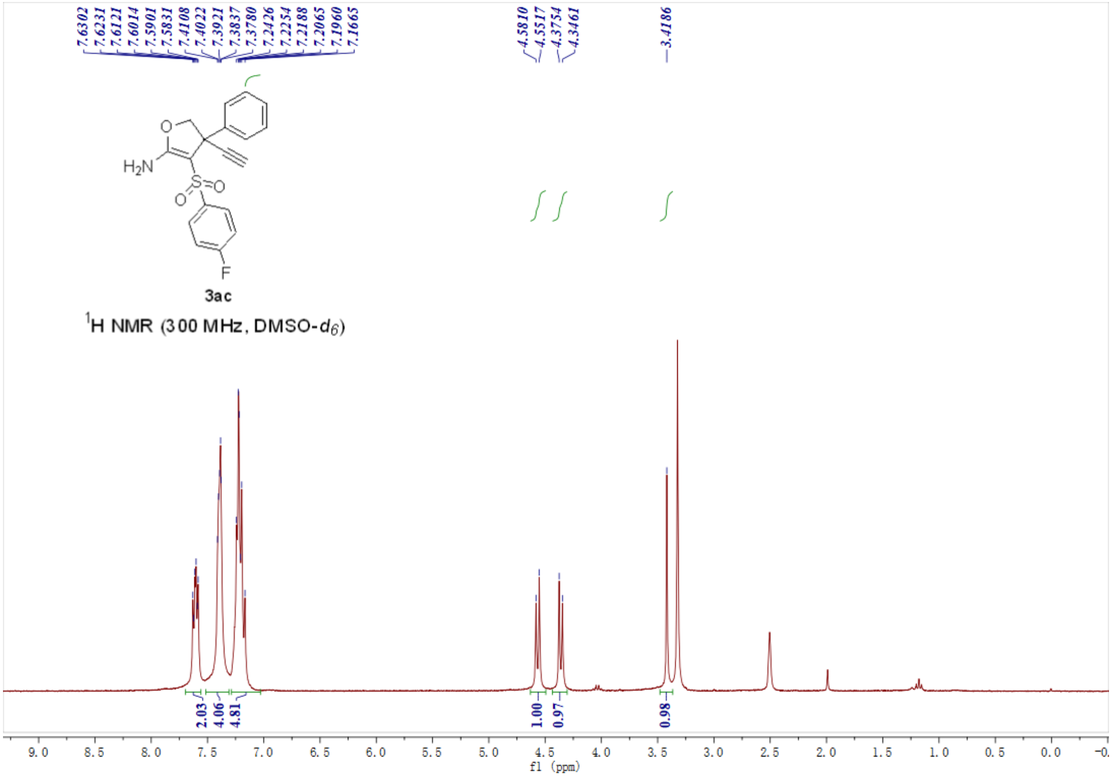

167.983
139.134
132.492
132.233
128.610
127.980
127.405
126.548
126.332
124.540
124.078
118.178
85.243
82.687
76.444
58.963
58.917
49.636
O
H_2N
CN
3pa
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

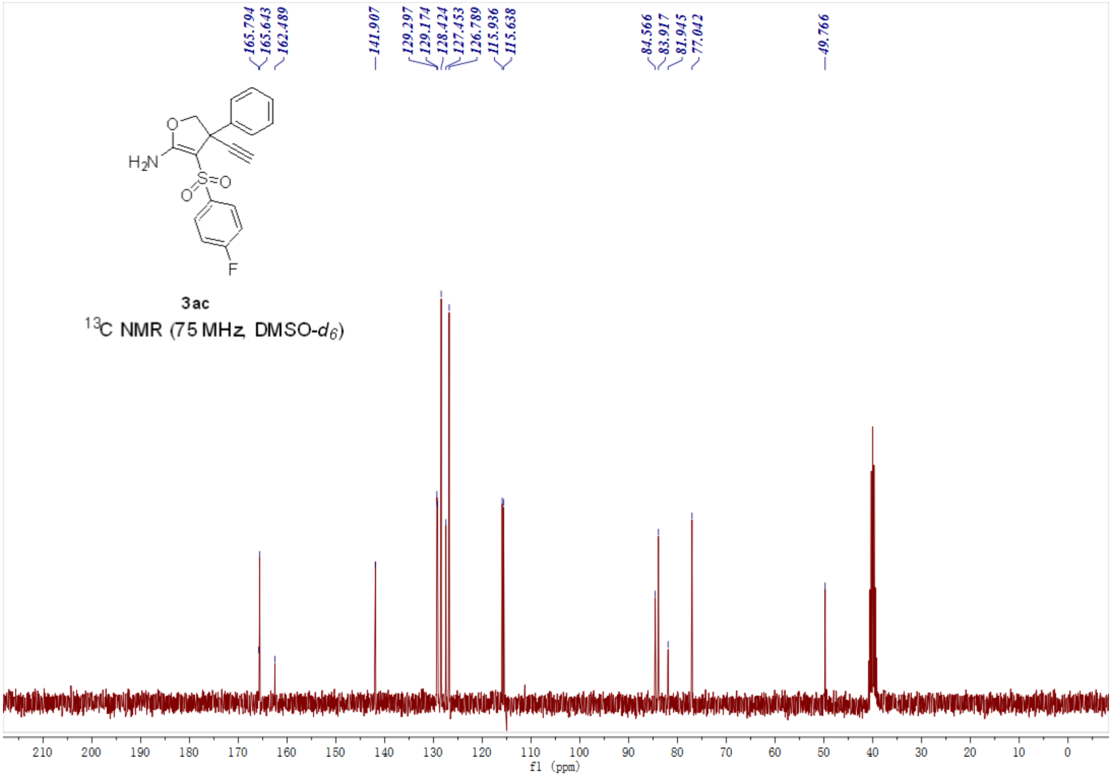


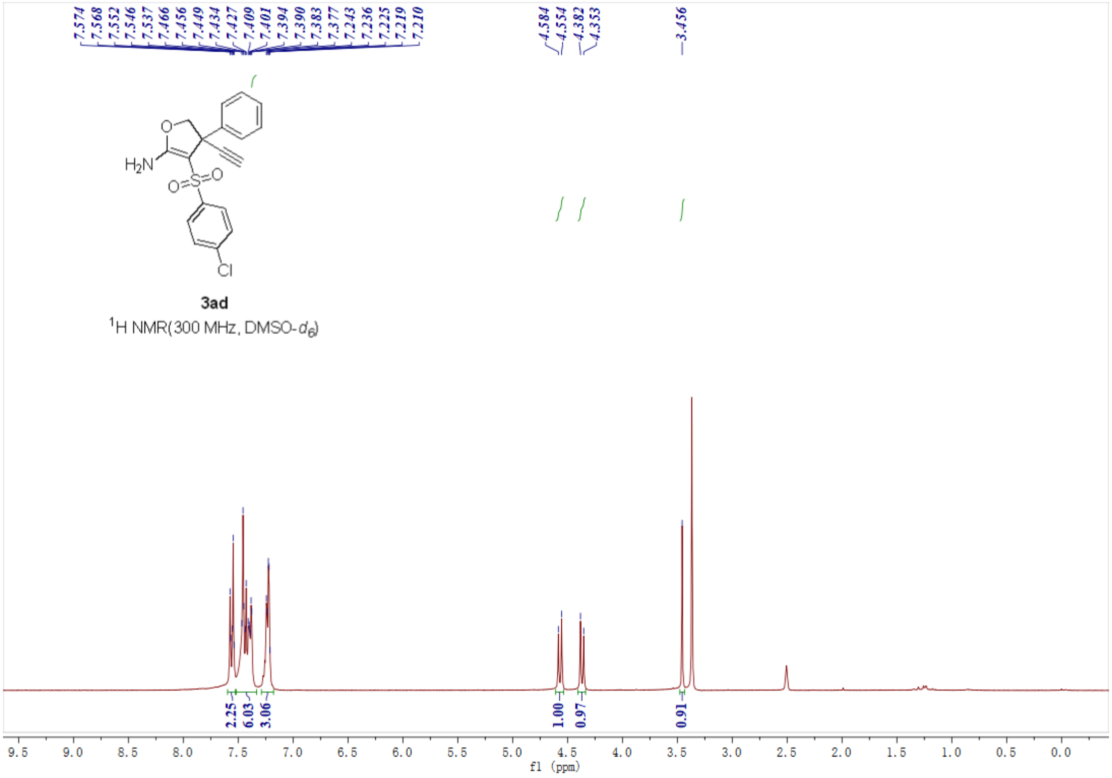


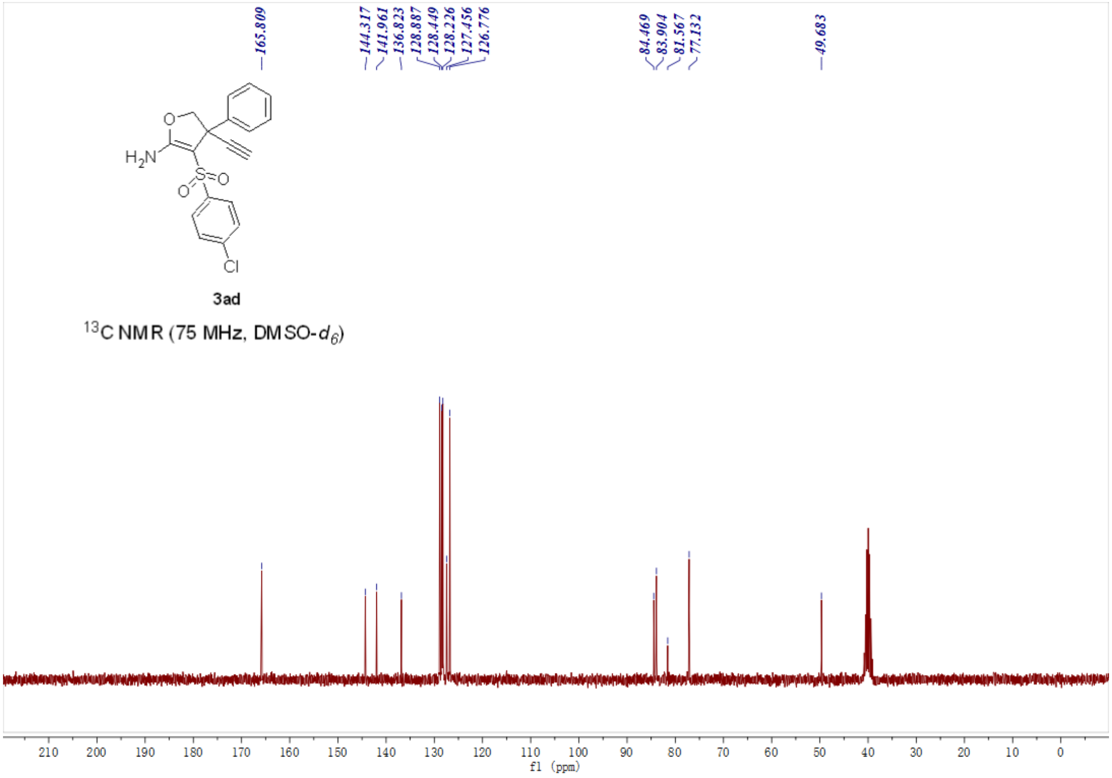

7.599
7.594
7.589
7.578
7.571
7.566
7.519
7.503
7.495
7.488
7.475
7.470
7.466
7.413
7.405
7.400
7.397
7.394
7.387
7.380
7.353
7.250
7.237
7.234
7.228
7.223
7.218
7.215
7.210
7.200
4.564
4.535
4.362
4.333
3.387
3ab
^{1}H NMR (300 MHz, DMSO-d_6)
2.08
1.23
4.00
1.90
2.98
1.00
0.99
0.98
f1 (ppm)

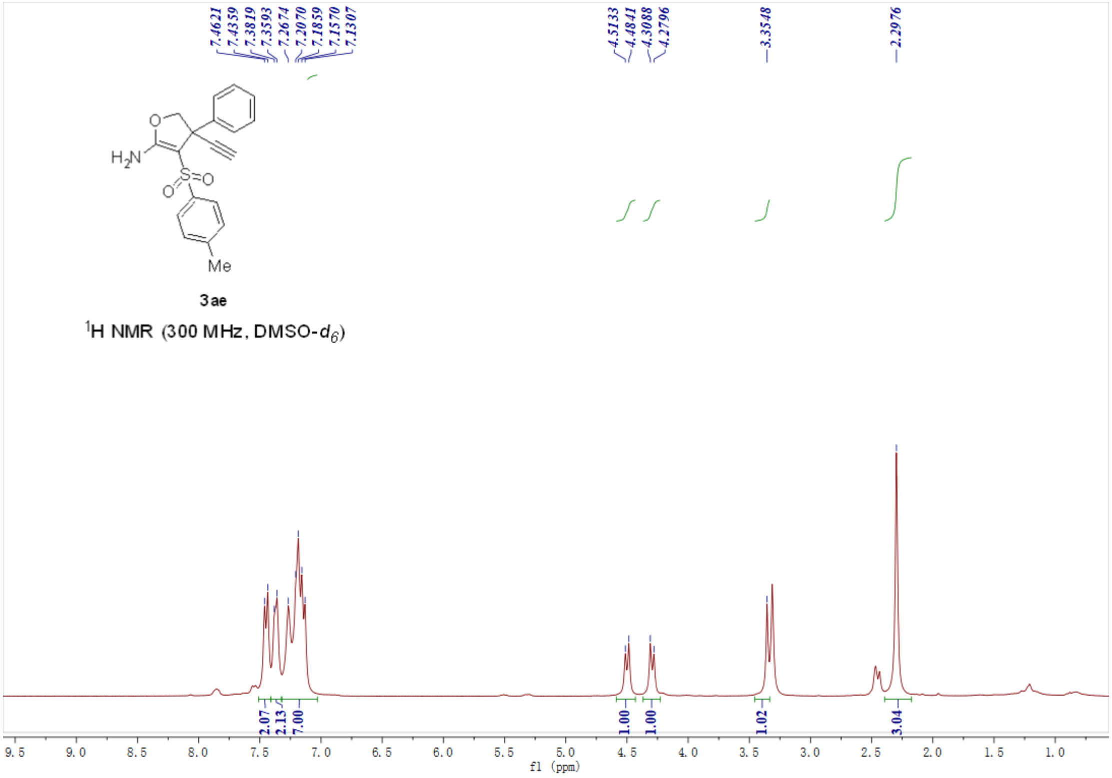

165.620
145.529
142.105
132.012
128.767
128.408
127.413
126.770
126.292
84.634
83.884
82.057
76.864
49.823
3ab
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

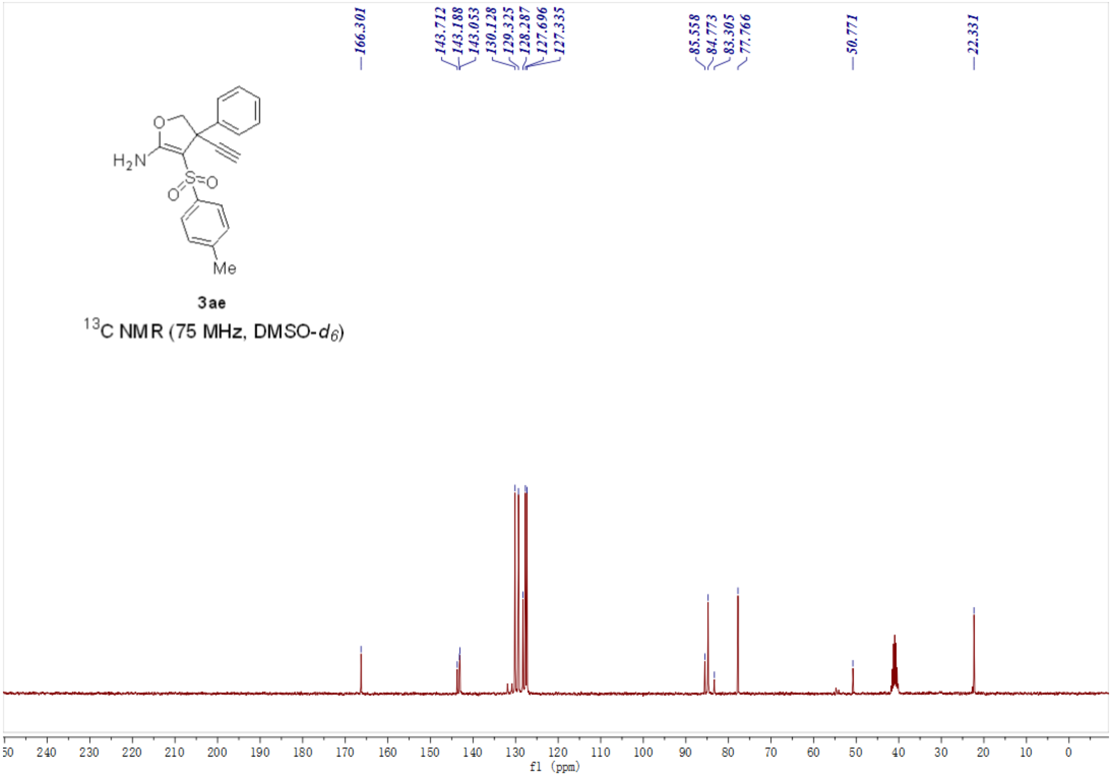

7.6302
7.6231
7.6121
7.6014
7.5901
7.5831
7.4108
7.4022
7.3921
7.3837
7.3780
7.2426
7.2254
7.2188
7.2065
7.1960
7.1665
4.5810
4.5517
4.3754
4.3461
3.4186
O
H_2N
S
O
O
F
3ac
^{1}H NMR (300 MHz, DMSO-d_6)
2.03
4.06
4.81
1.00
0.97
0.98
f1 (ppm)

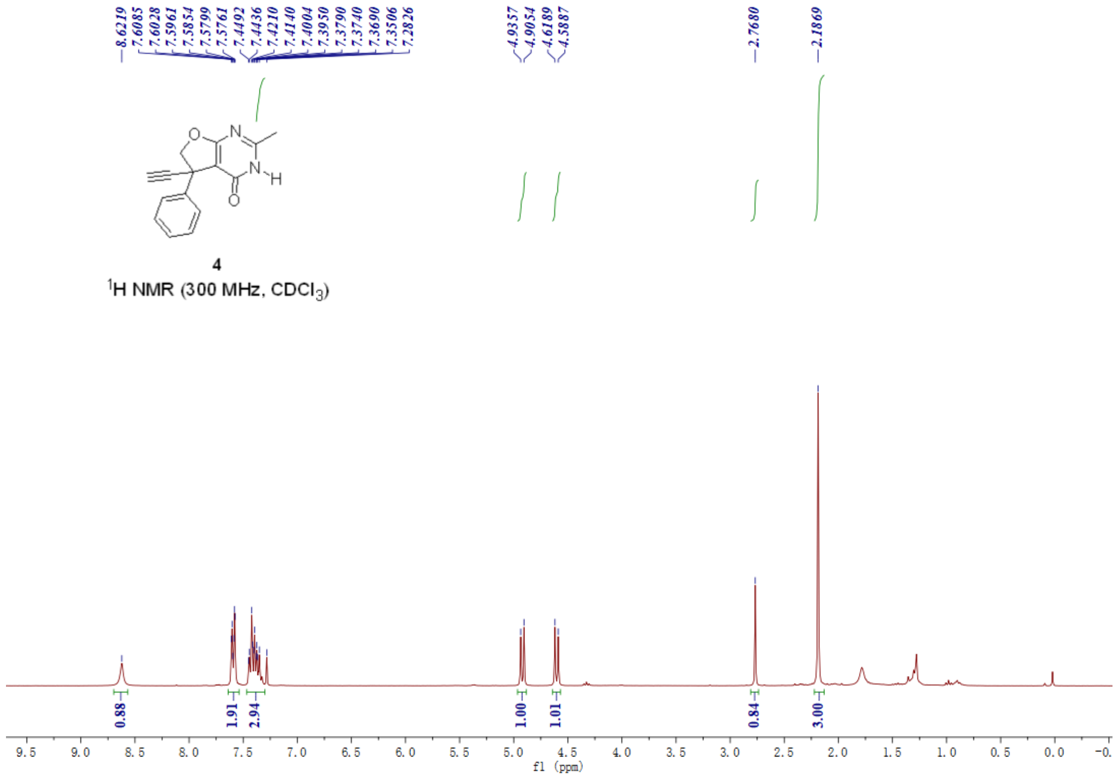

165.794
165.643
162.489
141.907
129.297
129.174
128.424
127.453
126.789
115.936
115.638
84.566
83.917
81.945
77.042
49.766
O
H_2N
S
O
O
F
3ac
^{13}C NMR (75 MHz, DMSO-d_6)
f1 (ppm)

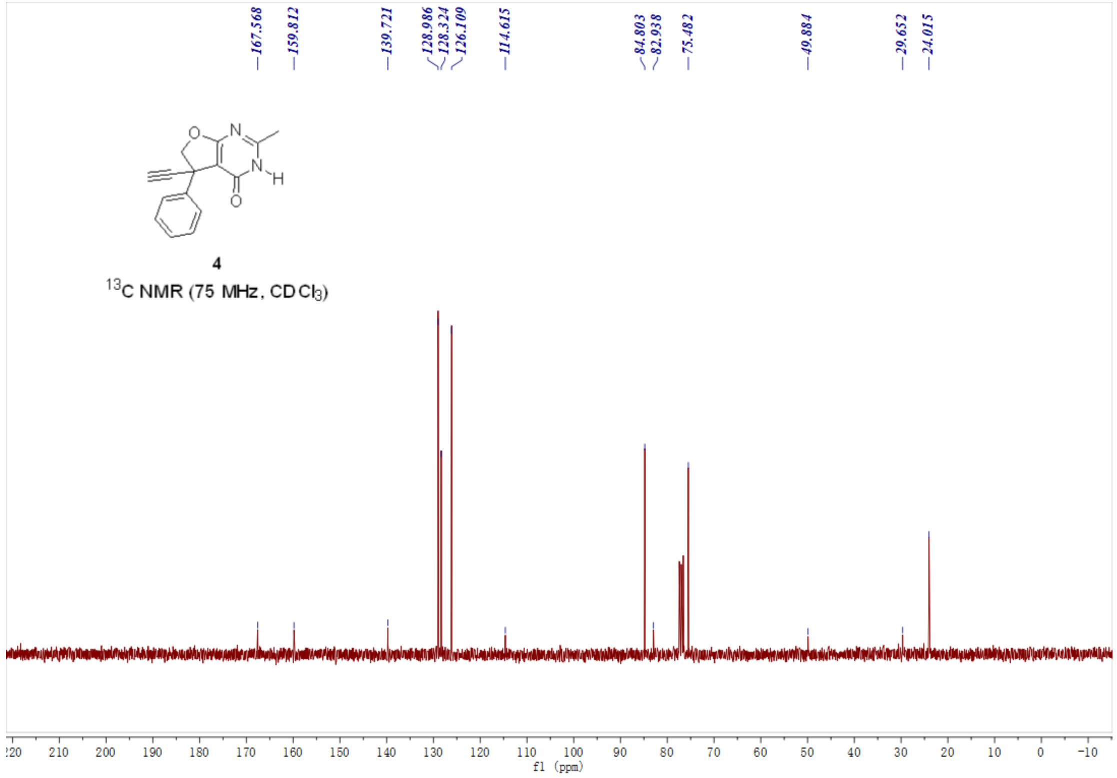

7.574 7.568 7.552 7.546 7.537 7.466 7.456 7.449 7.434 7.427 7.409 7.401 7.394 7.390 7.383 7.377 7.243 7.236 7.225 7.219 7.210
4.584 4.554 4.382 4.353
3.456
H2N
O
S
O
O
Cl
3ad
1H NMR(300 MHz, DMSO-d6)
2.25 6.03 3.06
1.00 0.97
0.91
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

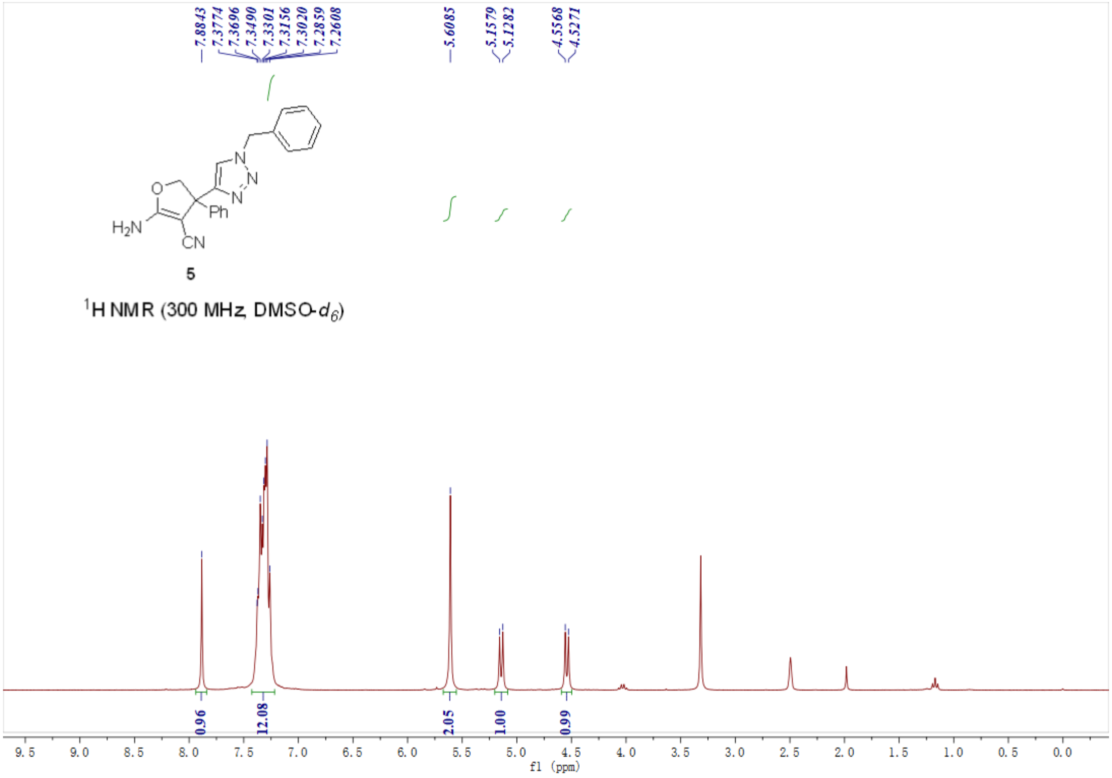

165.809
144.317 141.961 136.823 128.887 128.449 128.226 127.456 126.776
84.469 83.904 81.567 77.132
49.683
H2N
O
S
O
O
Cl
3ad
13C NMR (75 MHz, DMSO-d6)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

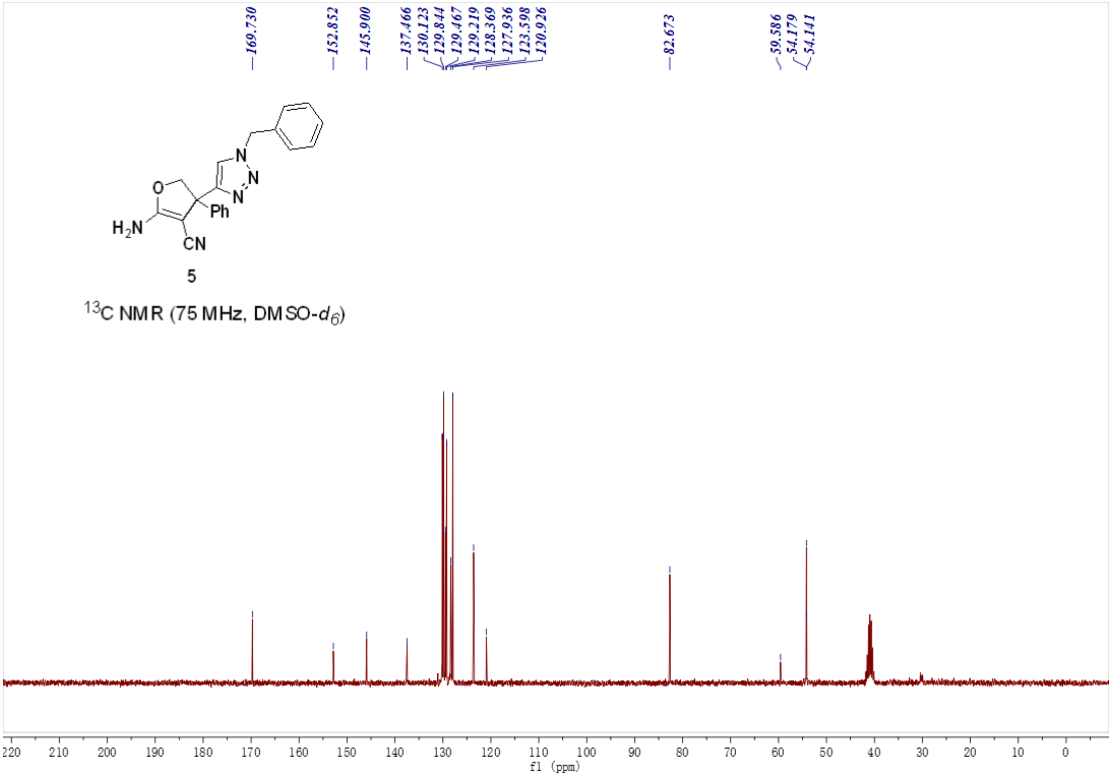

7.4621
7.4359
7.3819
7.3593
7.2674
7.2070
7.1859
7.1570
7.1307
4.5133
4.4841
4.3088
4.2796
3.3548
2.2976
H2N
O
S
O
O
Me
3ae
1H NMR (300 MHz, DMSO-d6)
2.07
2.13
7.00
1.00
1.00
1.02
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)


166.301
143.712
143.188
143.053
130.128
129.325
128.287
127.696
127.335
85.558
84.773
83.305
77.766
50.771
22.331
H2N
O
S
O
O
Me
3ae
13C NMR (75 MHz, DMSO-d6)
50 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.6219
7.6085
7.6028
7.5961
7.5854
7.5799
7.5761
7.4492
7.4436
7.4210
7.4140
7.4004
7.3950
7.3790
7.3740
7.3690
7.3506
7.2826
4.9357
4.9054
4.6189
4.5887
2.7680
2.1869
4
^{1}H NMR (300 MHz, CDCl$_3$)
0.88
1.91
2.94
1.00
1.01
0.84
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


167.568
159.812
139.721
128.986
128.324
126.109
114.615
84.803
82.938
75.482
49.884
29.652
24.015
4
^{13}C NMR (75 MHz, CDCl$_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.8843
7.3774
7.3696
7.3490
7.3301
7.3156
7.3020
7.2859
7.2608
5.6085
5.1579
5.1282
4.5568
4.5271
N
N
N
O
Ph
H2N
CN
5
1H NMR (300 MHz, DMSO-d6)
0.96
12.08
2.05
1.00
0.99
f1 (ppm)


169.730
152.852
145.900
137.466
130.123
129.844
129.467
129.219
128.369
127.936
123.598
120.926
82.673
59.586
54.179
54.141
N
N
N
O
Ph
H2N
CN
5
13C NMR (75 MHz, DMSO-d6)
f1 (ppm)