Rhodium(III)-catalysed redox neutral alkylation of 3-arylbenzo[*d*]isoxazoles: Easy access to substituted succinimides

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Supporting Information Placeholder

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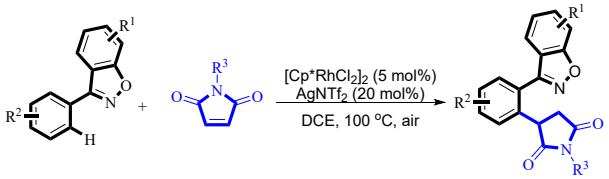
1. General information

Unless otherwise stated, all commercial materials and solvents were used directly without further purification. ^{1}H and ^{13}C NMR spectra were measured on a 400 MHz Bruker spectrometer (^{1}H 400MHz, ^{13}C 100MHz, ^{19}F NMR 376 MHz), using $CDCl_3$ (spectra were referenced to the solvent peaks ^{1}H: residual $CDCl_3$ = 7.26 ppm, ^{13}C: $CDCl_3$ = 77.0 ppm) or DMSO-d_6 (spectra were referenced to the solvent peaks ^{1}H: residual DMSO-d_6 = 2.50 ppm, ^{13}C: DMSO-d_6 = 39.5 ppm) as the solvent (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublet, m = multiplet). High-resolution mass spectra (HRMS) were measured on ESI-TOF. Column chromatography was performed on silica gel (70-230 mesh ASTM) using the reported eluent. Thin-layer chromatography (TLC) was carried out on 4×5 cm plates with a layer thickness of 0.2 mm (silica gel 60 F254). Starting materials 3-phenylbenzo[*d*]isoxazoles **1** [1-2] were prepared according to the literatures, maleimides **2** are commercially available.

2. General procedure for the synthesis of 3

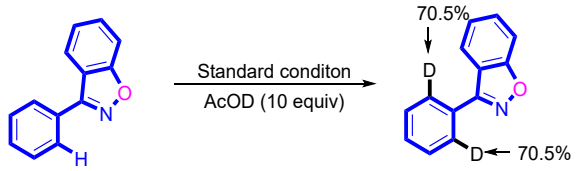


1 **2** **3**

A reaction tube (25 mL) equipped with a magnetic stirrer bar was charged with 3-phenylbenzo[*d*]isoxazoles **1** (0.2 mmol, 1.0 eq), maleimides **2** (0.24 mmol, 1.2 eq), $[RhCp^*Cl_2]_2$ (0.0050 mmol, 5 mol%), $AgNTf_2$ (0.02 mmol, 20 mol%), DCE (2 mL). The reaction mixture was stirred at 100 °C (metal module heating) for 12 h under air. After cooled to room temperature, the resulting mixture was diluted by DCM, then was concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluent: petroleum ether/ethyl acetate = 5:1) to afford the desired product **3**.

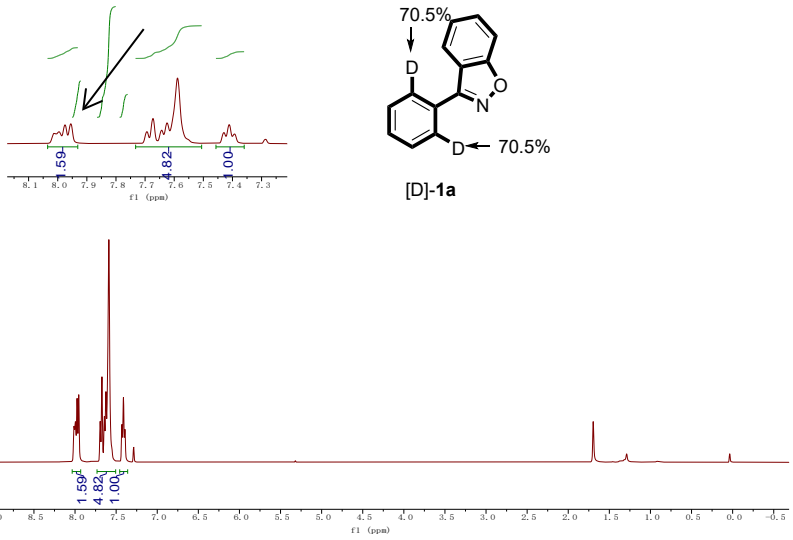
3. Mechanism experiments

(1) H/D exchange

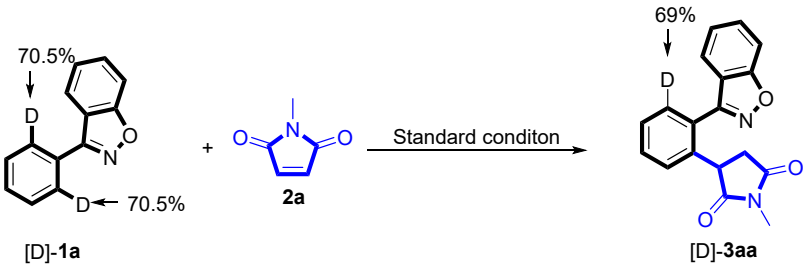


1a **[D]-1a**

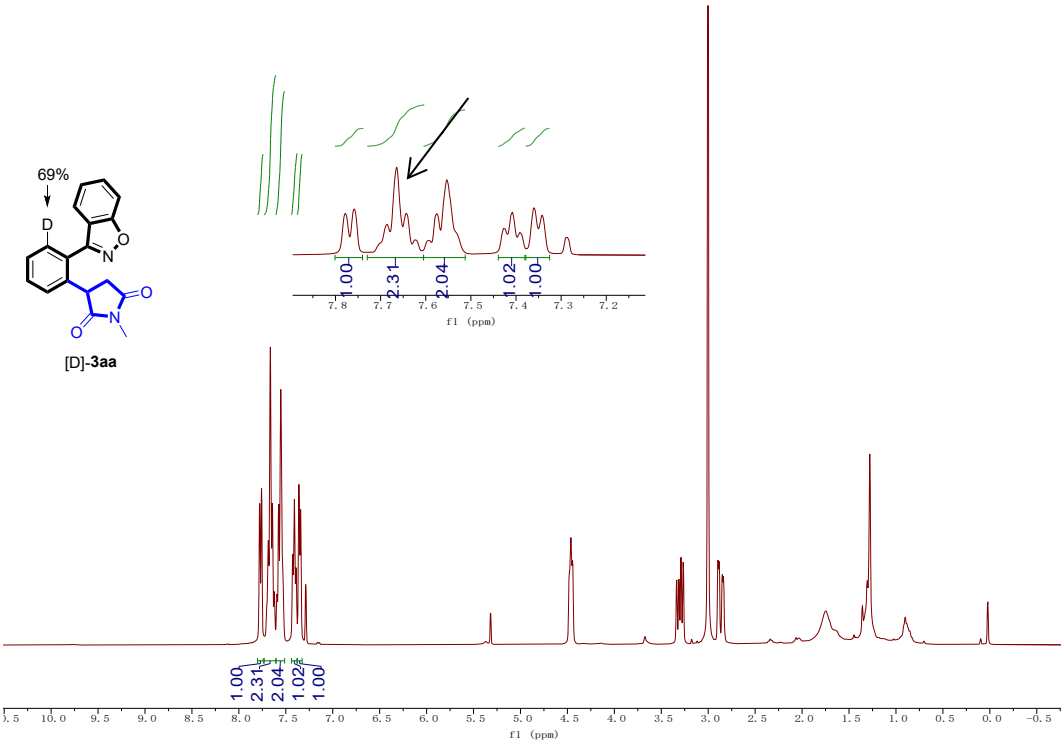
A reaction tube (25 mL) equipped with a magnetic stirrer bar was charged with **1a** (0.2 mmol, 39 mg, 1.0 eq), $[RhCp^*Cl_2]_2$ (0.0050 mmol, 6.18 mg, 5 mol%), $AgNTf_2$ (0.02 mmol, 11.5 mg, 20 mol%), AcOD (2 mmol, 120 mg, 10 eq), DCE (2 mL). The reaction mixture was stirred at 100 °C (metal module heating) for 12 h under air. After cooled to room temperature, the resulting mixture was diluted by DCM, then concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluent: petroleum ether/ethyl acetate = 20:1) to afford the desired product [D]-**1a**. The deuterium incorporation was calculated based on the ^1H NMR spectrum.



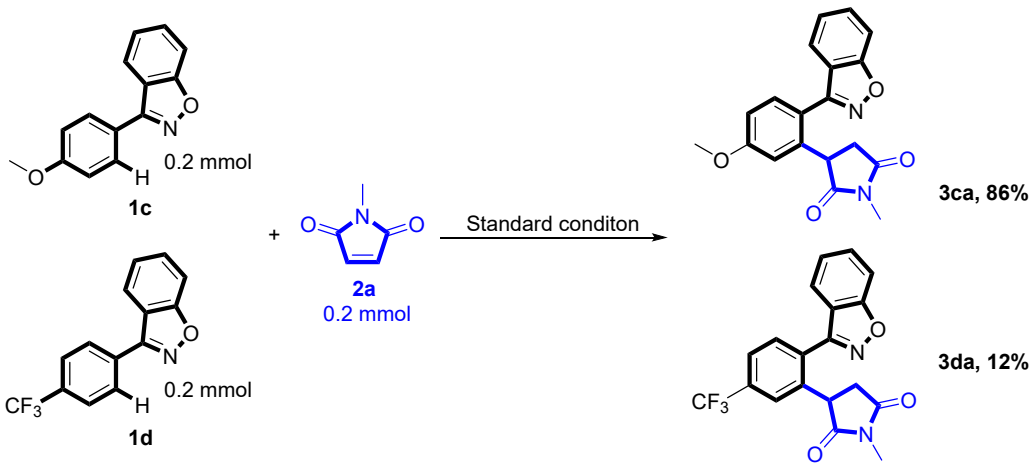
(2) KIE experiment



A reaction tube (25 mL) equipped with a magnetic stirrer bar was charged with [D]-**1a** (0.2 mmol, 39 mg, 1.0 eq), maleimide **2a** (26.6 mg, 0.24 mmol, 1.2 eq), $[RhCp^*Cl_2]_2$ (0.0050 mmol, 6.18 mg, 5 mol%), $AgNTf_2$ (0.02 mmol, 11.5 mg, 20 mol%), DCE (2 mL). The reaction mixture was stirred at 100 °C (metal module heating) for 12 h under air. After cooled to room temperature, the resulting mixture was diluted by DCM, then concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluent: petroleum ether/ethyl acetate = 5:1) to afford the desired product [D]-**3aa**. The value of K_H/K_D was calculated according to the ratio (70.5% D) of deuterated initial substrate [D]-**1a** and the ratio (69% D) of deuterated products [D]-**3aa**. K_H/K_D = (31%/69%)/(29.5%/70.5%) = 1.07



(3) Competition experiment



A reaction tube (25 mL) equipped with a magnetic stirrer bar was charged with **1c** (0.2 mmol, 39.0 mg, 1.0 eq), **1d** (0.2 mmol, 52.6 mg, 1.0 eq), maleimide **2a** (22.2 mg, 0.2 mmol, 1.0 eq), $[RhCp^*Cl_2]_2$ (0.0050 mmol, 6.18 mg, 5 mol%), $AgNTf_2$ (0.02 mmol, 11.5 mg, 20 mol%), DCE (2 mL). The reaction mixture was stirred at 100 ^oC (metal module heating) for 12 h under air. After cooled to room temperature, the resulting mixture was diluted by DCM, then concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluent: petroleum ether/ethyl acetate = 5:1) to afford the desired products **3ca** and **3da** with ~7:1 ratio.

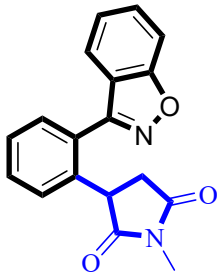
4. References：

1. Duan, P.; Yang, Y.; Ben, R.; Yan, Y.; Dai, L.; Hong, M.; Wu, Y.-D.; Wang, D.; Zhang, X.; Zhao, J., Palladium-catalyzed benzo [*d*] isoxazole synthesis by C-H activation/ 4+1 annulation. *Chem. Sci.* **2014,** *5* (4), 1574-1578.

2. Noguchi, T.; Nishii, Y.; Miura, M., Rhodium-catalyzed Synthesis of 1-Arylisoquinoline Derivatives through Annulative Coupling of 3-Aryl-1,2-benzisoxazoles and Alkynes. *Chem. Lett.* **2017,** *46* (10), 1512-1514.

5. Characterization of compounds 3

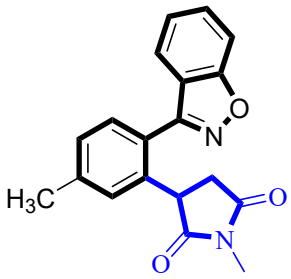
3-(2-(Benzo[*d*]isoxazol-3-yl)phenyl)-1-methylpyrrolidine-2,5-dione (3aa)



White solid, 93% yield, 57.0 mg, m.p.: 58-59 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.1 Hz, 1H), 7.73 – 7.58 (m, 3H), 7.60 – 7.50 (m, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 7.35 (d, *J* = 7.3 Hz, 1H), 4.45 (dd, *J* = 9.5, 6.5 Hz, 1H), 3.29 (dd, *J* = 18.3 Hz, 9.6 Hz, 1H), 2.99 (s, 3H), 2.86 (dd, *J* = 18.2, 5.3 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 178.0, 176.1, 163.4, 157.1, 137.4, 130.8, 130.3, 129.1, 128.2, 128.0, 124.3, 122.3, 121.5, 110.0, 44.5, 39.0, 25.1. HRMS (ESI) calcd for $C_{18}H_{15}N_2O_3$ $[M + H]^+$ 307.1077; found: 307.1076.

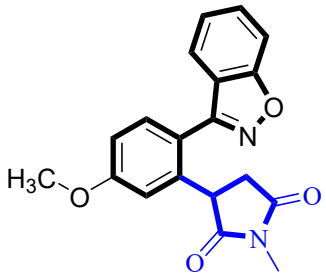
3-(2-(Benzo[*d*]isoxazol-3-yl)-5-methylphenyl)-1-methylpyrrolidine-2,5-dione (3ba)



White solid, 94% yield, 60.2 mg, m.p.: 82-83 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.8 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 7.3 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.13 (s, 1H), 4.45 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.29 (dd, *J* = 18.5, 9.8 Hz, 1H), 3.02 (s, 3H), 2.85 (dd, *J* = 18.5, 5.6 Hz, 1H), 2.46 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 178.2, 176.2, 163.4, 157.1, 141.0, 137.2, 130.6, 130.2, 129.7, 129.1, 125.0, 124.1, 122.3, 121.6, 109.9, 44.4, 39.0, 25.1, 21.4. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3$ $[M + H]^+$ 321.1234; found: 321.1231.

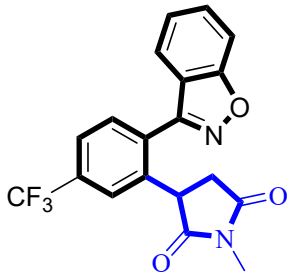
3-(2-(Benzo[*d*]isoxazol-3-yl)-5-methoxyphenyl)-1-methylpyrrolidine-2,5-dione (3ca)



Colorless oil, 99% yield, 66.6 mg, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 7.9 Hz, 1H), 7.68 – 7.61 (m, 3H), 7.39 (t, *J* = 7.1 Hz, 1H), 7.05 (d, *J* = 8.5 Hz, 1H), 6.84 (s, 1H), 4.46 (dd, *J* = 9.5, 5.9 Hz, 1H), 3.90 (s, 3H), 3.29 (dd, *J* = 18.6, 9.7 Hz, 1H), 3.00 (s, 3H), 2.86 (dd, *J* = 18.6, 5.6 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.9, 176.1, 163.3, 161.2, 156.9, 138.9, 132.1, 130.2, 124.1, 122.3, 121.6, 120.1, 115.3, 113.2, 110.0, 55.5, 44.6, 38.8, 25.1. HRMS (ESI) calcd for $C_{19}H_{17}N_2O4$ [M + H]$^{+}$ 337.1183; found: 337.1182.

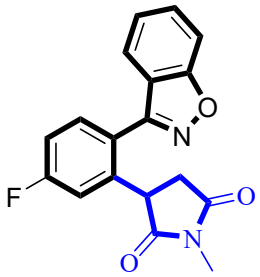
3-(2-(Benzo[*d*]isoxazol-3-yl)-5-(trifluoromethyl)phenyl)-1-methylpyrrolidine-2,5-dione (3da)



White solid, 81% yield, 60.6 mg, m.p.: 83-84 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 - 7.78 (m, 2H), 7.76 – 7.65 (m, 3H), 7.63 (s, 1H), 7.44 (t, *J* = 7.3 Hz, 1H), 4.50 (dd, *J* = 9.8, 6.0 Hz, 1H), 3.32 (dd, *J* = 18.4, 9.8 Hz, 1H), 2.99 (s, 3H), 2.91 (dd, *J* = 18.4, 6.0 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.1, 175.4, 163.5, 156.2, 138.3, 132.8 (q, $J_{C\text{-}F}$ = 33.1 Hz), 131.8, 131.4, 130.7, 126.5 (q, $J_{C\text{-}F}$ = 3.7 Hz), 125. 2 (q, $J_{C\text{-}F}$ = 3.5 Hz), 124.6, 123.4 (q, $J_{C\text{-}F}$ = 272.8 Hz), 121.9, 121.0, 110.2, 44.7, 38.6, 25.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.07. HRMS (ESI) calcd for $C_{19}H_{14}F_3N_2O_3$ [M + H]$^{+}$ 375.0591; found: 375.0592.

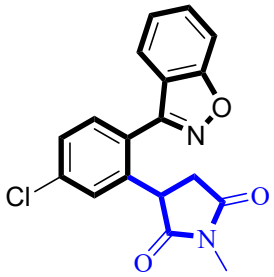
3-(2-(Benzo[*d*]isoxazol-3-yl)-5-fluorophenyl)-1-methylpyrrolidine-2,5-dione (3ea)



Colorless oil, 91% yield, 59.0 mg, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.1 Hz, 1H), 7.71 – 7.62 (m, 3H), 7.41 (t, *J* = 7.1 Hz, 1H), 7.30 – 7.21 (m, 1H), 7.08 (d, *J* = 9.8 Hz, 1H), 4.46 (dd, *J* = 9.7, 5.8 Hz, 1H), 3.30 (dd, *J* = 18.5, 9.7 Hz, 1H), 3.00 (s, 3H), 2.84 (dd, *J* = 18.5, 5.7 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.3, 175.6, 163.7 (d, $J_{C\text{-}F}$ = 251.6 Hz), 163.4, 156.41, 139.9 (d, $J_{C\text{-}F}$ = 8.2 Hz), 132.6 (d, $J_{C\text{-}F}$ = 9.4 Hz), 130.4, 124.4, 124.1 (d, $J_{C\text{-}F}$ = 3.1 Hz), 122.0, 121.4, 116.4 (d, $J_{C\text{-}F}$ = 23.2 Hz), 115.6 (d, $J_{C\text{-}F}$ = 21.6 Hz), 110.1, 44.4, 38.7, 25.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -108.89. HRMS (ESI) calcd for $C_{18}H_{14}FN_2O_3$ $[M + H]^+$ 325.0983; found: 325.0983.

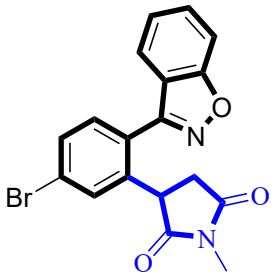
3-(2-(Benzo[*d*]isoxazol-3-yl)-5-chlorophenyl)-1-methylpyrrolidine-2,5-dione (3fa)



White solid, 89% yield, 60.6 mg, m.p.: 87-88 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.71 – 7.59 (m, 3H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.35 (s, 1H), 4.44 (t, *J* = 7.7 Hz, 1H), 3.30 (dd, *J* = 18.6, 9.7 Hz, 1H), 3.00 (s, 3H), 2.86 (dd, *J* = 18.5, 5.7 Hz, 1H).

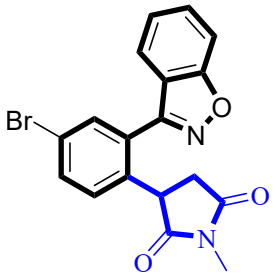
^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.3, 175.6, 163.5, 156.3, 139.1, 136.8, 131.9, 130.5, 129.5, 128.6, 126.6, 124.5, 122.0, 121.2, 110.1, 44.4, 38.7, 25.2. HRMS (ESI) calcd for $C_{18}H_{14}ClN_2O_3$ $[M + H]^+$ 341.0687; found: 341.0685.

3-(2-(Benzo[*d*]isoxazol-3-yl)-5-bromophenyl)-1-methylpyrrolidine-2,5-dione (3ga)



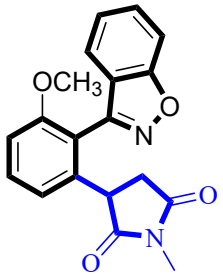
White solid, 91% yield, 70.1 mg, m.p.: 88-89 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.71 – 7.61 (m, 3H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.50 (s, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 4.43 (dd, *J* = 9.8, 5.8 Hz, 1H), 3.30 (dd, *J* = 18.5, 9.7 Hz, 1H), 3.00 (s, 3H), 2.86 (dd, *J* = 18.5, 5.9 Hz, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.3, 175.6, 163.5, 156.4, 139.3, 132.4, 132.1, 131.5, 130.5, 127.0, 125.0, 124.5, 122.0, 121.2, 110.1, 44.3, 38.7, 25.2. HRMS (ESI) calcd for $C_{18}H_{14}BrN_2O_3$ [M + H]$^+$ 385.0182; found: 385.0183.

3-(2-(Benzo[*d*]isoxazol-3-yl)-4-bromophenyl)-1-methylpyrrolidine-2,5-dione (3ha)



White solid, 87% yield, 67.0 mg, m.p.: 85-86 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.73 – 7.60 (m, 3H), 7.48 – 7.41 (m, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 4.40 (dd, *J* = 9.5, 6.2 Hz, 1H), 3.29 (dd, *J* = 18.7, 9.7 Hz, 1H), 2.99 (s, 3H), 2.84 (dd, *J* = 18.5, 5.4 Hz, 1H). ^{13}C NMR (100 MHz, Chloroform-d_3) δ 177.5, 175.7, 163.5, 156.0, 136.4, 133.7, 133.4, 130.8, 130.6, 130.1, 124.6, 122.1, 122.0, 121.1, 110.1, 44.2, 38.7, 25.2. HRMS (ESI) calcd for $C_{18}H_{14}BrN_2O_3$ [M + H]$^+$ 385.0182; found: 385.0181.

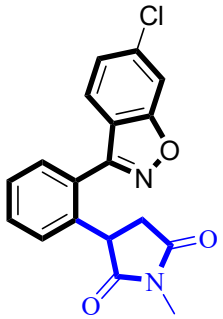
3-(2-(Benzo[*d*]isoxazol-3-yl)-3-methoxyphenyl)-1-methylpyrrolidine-2,5-dione (3ia)



White solid, 85% yield, 57.0 mg, m.p.: 89-90 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.48 (m, 4H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 4.07 (dd, *J* = 9.7, 5.4 Hz, 1H), 3.76 (s, 3H), 3.15 (dd, *J* = 18.6, 9.7 Hz, 1H), 2.95-2.85 (m, 4H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.6, 176.0, 163.0, 158.6, 155.2, 139.5, 131.9, 129.9, 123.7, 123.0, 122.5, 120.5, 117.1, 110.6, 109.8, 55.8, 44.5, 38.8, 25.0. HRMS (ESI) calcd for $C_{18}H_{17}N_2O_4$ [M + H]$^{+}$ 337.1183; found: 337.1180.

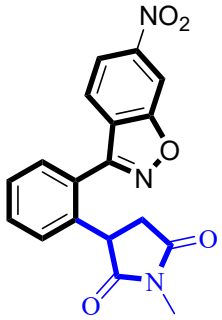
3-(2-(6-Chlorobenzo[*d*]isoxazol-3-yl)phenyl)-1-methylpyrrolidine-2,5-dione (3ja)



Colorless oil, 88% yield, 59.9 mg, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.74 (s, 1H), 7.65 (d, *J* = 6.6 Hz, 1H), 7.62 – 7.51 (m, 4H), 7.36 (d, *J* = 6.4 Hz, 1H), 4.44 (dd, *J* = 9.2, 5.4 Hz, 1H), 3.29 (dd, *J* = 18.4, 9.6 Hz, 1H), 3.00 (s, 3H), 2.87 (dd, *J* = 18.3, 3.1 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.9, 176.0, 162.0, 156.8, 137.3, 131.0, 130.9, 130.6, 130.0, 129.4, 128.4, 127.3, 122.9, 121.7, 111.1, 44.5, 38.8, 25.1. HRMS (ESI) calcd for $C_{18}H_{14}ClN_2O_3$ [M + H]$^{+}$ 341.0687; found: 341.0686.

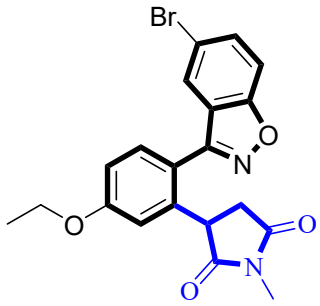
1-Methyl-3-(2-(6-nitrobenzo[*d*]isoxazol-3-yl)phenyl)pyrrolidine-2,5-dione (3ka)



White solid, 51% yield, 35.8 mg, m.p.: 227-228 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 – 8.49 (m, 2H), 8.12 (d, J = 9.3 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.71 – 7.52 (m, 3H), 4.42 (t, J = 7.6 Hz, 1H), 3.13 (dd, J = 18.2, 9.7 Hz, 1H), 2.83 – 2.70 (m, 4H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 178.4, 176.4, 165.4, 158.9, 145.3, 138.3, 131.8, 131.2, 130.7, 128.8, 126.7, 126.3, 122.5, 120.0, 111.7, 44.3, 38.6, 25.1. HRMS (ESI) calcd for $C_{18}H_{14}N_3O_5$ $[M + H]^+$ 352.0928; found: 352.0930.

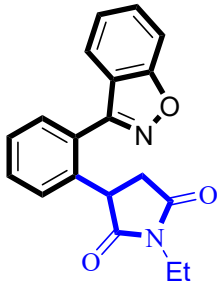
3-(2-(5-Bromobenzo[*d*]isoxazol-3-yl)-5-ethoxyphenyl)-1-methylpyrrolidine-2,5-dione (3la)



White solid, 93% yield, 80.5 mg, m.p.: 121-122 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.90 (s, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.59 (d, J = 8.5 Hz, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.05 (d, J = 8.5 Hz, 1H), 6.84 (s, 1H), 4.45 (dd, J = 9.7, 5.7 Hz, 1H), 4.13 (q, J = 6.9 Hz, 2H), 3.29 (dd, J = 18.5, 9.6 Hz, 1H), 3.01 (s, 3H), 2.85 (dd, J = 18.5, 5.6 Hz, 1H), 1.48 (t, J = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.8, 176.0, 162.2, 160.8, 156.4, 138.9, 133.3, 132.0, 124.9, 123.7, 119.1, 117.0, 116.1, 113.6, 111.4, 63.9, 44.5, 38.8, 25.2, 14.7. HRMS (ESI) calcd for $C_{20}H_{18}BrN_2O_4$ $[M + H]^+$ 429.0444; found: 429.0444.

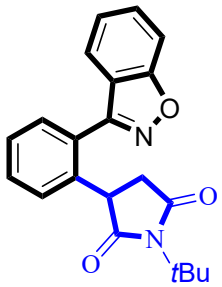
3-(2-(Benzo[*d*]isoxazol-3-yl)phenyl)-1-ethylpyrrolidine-2,5-dione (3ab)



White solid, 90% yield, 57.7 mg, m.p.: 59-60 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.1 Hz, 1H), 7.71 – 7.61 (m, 3H), 7.60 – 7.50 (m, 2H), 7.41 (t, *J* = 6.8 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 4.44 (dd, *J* = 9.6, 5.7 Hz, 1H), 3.65 – 3.51 (m, 2H), 3.28 (dd, *J* = 18.5, 9.6 Hz, 1H), 2.86 (dd, *J* = 18.5, 5.5 Hz, 1H), 1.18 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.8, 175.9, 163.4, 157.2, 137.5, 130.8, 130.8, 130.3, 129.0, 128.2, 128.1, 124.2, 122.3, 121.5, 110.0, 44.4, 39.0, 34.0, 13.0. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3$ [M + H]$^+$ 321.1234; found: 321.1234.

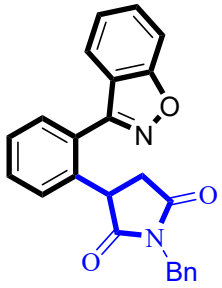
3-(2-(Benzo[*d*]isoxazol-3-yl)phenyl)-1-(tert-butyl)pyrrolidine-2,5-dione (3ac)



White solid, 89% yield, 62.0 mg, m.p.: 140-141 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.61 (m, 3H), 7.60 – 7.49 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 7.7 Hz, 1H), 4.30 (dd, *J* = 10.1, 6.2 Hz, 1H), 3.14 (dd, *J* = 18.2, 10.0 Hz, 1H), 2.77 (dd, *J* = 18.2, 6.1 Hz, 1H), 1.58 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 178.9, 177.0, 163.4, 157.3, 138.2, 130.7, 130.2, 128.9, 128.02, 127.98, 124.2, 122.3, 121.7, 110.0, 58.7, 44.4, 39.3, 28.3. HRMS (ESI) calcd for $C_{19}H_{17}N_2O_3$ [M + H]$^+$ 349.1547; found: 349.1546.

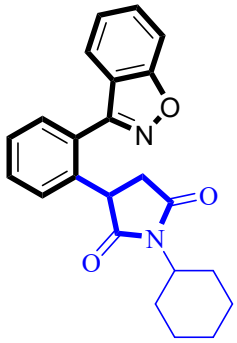
3-(2-(Benzo[*d*]isoxazol-3-yl)phenyl)-1-benzylpyrrolidine-2,5-dione (3ad)



White solid, 70% yield, 53.5 mg, m.p.: 69-70 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.72 – 7.63 (m, 3H), 7.53 (t, *J* = 4.3 Hz, 2H), 7.45 – 7.37 (m, 3H), 7.36 – 7.30 (m, 3H), 7.26 – 7.20 (m, 1H), 4.74 (d, *J* = 14.0 Hz, 1H), 4.64 (d, *J* = 14.4 Hz, 1H), 4.48 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.31 (dd, *J* = 18.6, 9.7 Hz, 1H), 2.84 (dd, *J* = 18.6, 5.6 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.7, 175.7, 163.4, 157.1, 137.5, 135.8, 130.8, 130.7, 130.3, 128.9, 128.7, 128.2, 128.1, 128.0, 124.2, 122.3, 121.5, 110.0, 44.2, 42.7, 39.1. HRMS (ESI) calcd for $C_{24}H_{19}N_2O_3$ $[M + H]^+$ 383.1390; found: 383.1393.

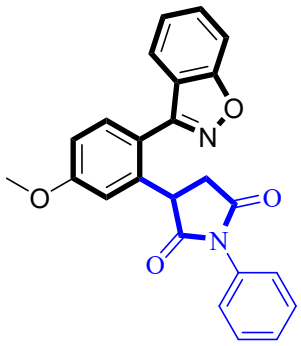
3-(2-(Benzo[*d*]isoxazol-3-yl)phenyl)-1-cyclohexylpyrrolidine-2,5-dione (3ae)



White solid, 80% yield, 59.9 mg, m.p.: 156-157 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.71 – 7.61 (m, 3H), 7.60 – 7.49 (m, 2H), 7.41 (t, *J* = 7.4 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 4.38 (dd, *J* = 9.8, 5.7 Hz, 1H), 4.02 (t, *J* = 12.5 Hz, 1H), 3.22 (dd, *J* = 18.4, 9.7 Hz, 1H), 2.79 (dd, *J* = 18.4, 5.6 Hz, 1H), 2.25 – 2.05 (m, 1H), 1.83 (d, *J* = 12.6 Hz, 2H), 170 – 1.55 (m, 4H), 1.41 – 1.25 (m, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 178.0, 176.2, 163.4, 157.2, 137.9, 130.8, 130.7, 130.2, 128.7, 128.1, 124.2, 122.3, 121.6, 110.0, 52.0, 44.0, 38.9, 28.72, 28.68, 25.8, 25.0. HRMS (ESI) calcd for $C_{23}H_{23}N_2O_3$ $[M + H]^+$ 375.1703; found: 375.1701.

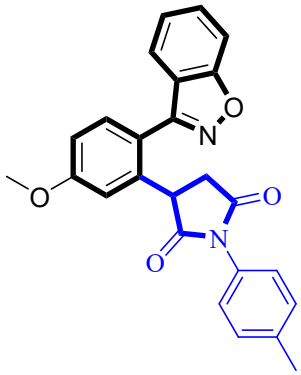
3-(2-(Benzo[*d*]isoxazol-3-yl)-5-methoxyphenyl)-1-phenylpyrrolidine-2,5-dione (3af)



White solid, 61% yield, 48.6 mg, m.p.: 89-91 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.73 – 7.59 (m, 3H), 7.52 – 7.43 (m, 2H), 7.44 – 7.35 (m, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 8.6 Hz, 1H), 7.00 (s, 1H), 4.66 – 4.57 (m, 1H), 3.92 (s, 3H), 3.44 (dd, *J* = 18.5, 9.8 Hz, 1H), 3.08 (dd, *J* = 18.6, 6.1 Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 176.7, 175.0, 163.4, 161.2, 157.0, 138.6, 132.3, 132.0, 130.2, 129.1, 128.6, 126.5, 124.2, 122.4, 121.6, 120.0, 116.2, 113.3, 110.0, 55.6, 45.2, 38.7. HRMS (ESI) calcd for $C_{24}H_{19}N_2O_4$ $[M + H]^+$ 399.1339; found: 399.1336.

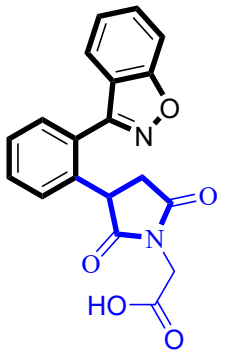
3-(2-(Benzo[*d*]isoxazol-3-yl)-5-methoxyphenyl)-1-(p-tolyl)pyrrolidine-2,5-dione (3ag)



White solid, 55% yield, 45.3 mg, m.p.: 99-100 °C, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.73 – 7.59 (m, 3H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.5 Hz, 1H), 6.99 (s, 1H), 4.60 (dd, *J* = 9.8, 6.1 Hz, 1H), 3.92 (s, 3H), 3.43 (dd, *J* = 18.6, 9.9 Hz, 1H), 3.07 (dd, *J* = 18.5, 6.0 Hz, 1H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 176.8, 175.2, 163.4, 161.2, 157.0, 138.7, 132.3, 130.2, 129.8, 129.4, 126.3, 124.2, 122.4, 121.6, 120.1, 116.1, 113.3, 110.0, 55.6, 45.2, 38.8, 21.2. HRMS (ESI) calcd for $C_{25}H_{21}N_2O_4$ $[M + H]^+$ 413.1496; found: 413.1496.

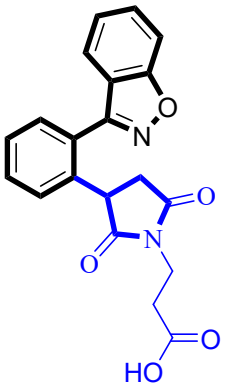
2-(3-(2-(Benzo[*d*]isoxazol-3-yl)phenyl)-2,5-dioxopyrrolidin-1-yl)acetic acid (3ah)



Colorless oil, 71% yield, 49.7 mg, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.71 – 7.63 (m, 3H), 7.60 –7.50 (m, 2H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 4.59 (dd, *J* = 9.8, 5.4 Hz, 1H), 4.41 – 4.22 (m, 2H), 3.40 (dd, *J* = 18.7, 9.6 Hz, 1H), 2.93 – 2.84 (m, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.5, 175.4, 163.4, 157.1, 137.3, 131.1, 130.5, 130.4, 128.9, 128.3, 128.0, 124.3, 122.3, 121.5, 110.0, 44.1, 39.6, 39.1. HRMS (ESI) calcd for $C_{19}H_{15}N_2O_5$ $[M + H]^+$ 351.0975; found: 351.0978.

3-(3-(2-(Benzo[*d*]isoxazol-3-yl)phenyl)-2,5-dioxopyrrolidin-1-yl)propanoic acid (3ai)

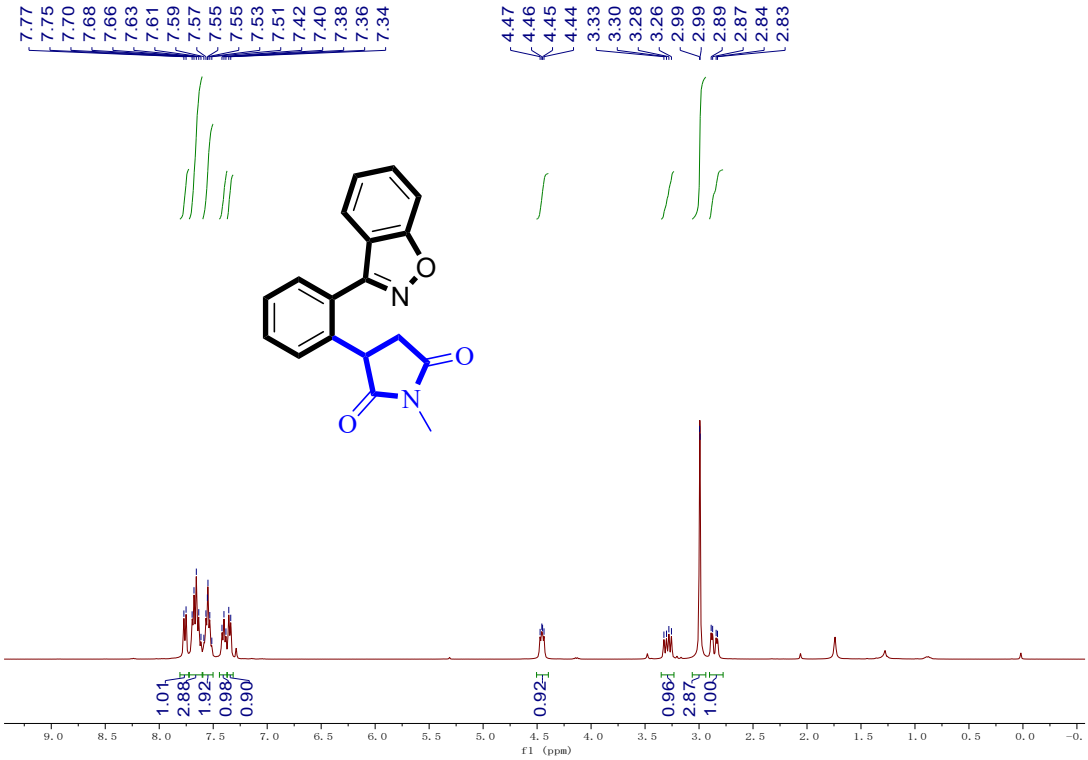


Colorless oil, 88% yield, 64.1 mg, ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.73 – 7.61 (m, 3H), 7.60 – 7.50 (m, 2H), 7.45 – 7.34 (m, 2H), 4.52 – 4.38 (m, 1H), 3.90 – 3.72 (m, 2H), 3.29 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.88 (dd, *J* = 18.2, 4.1 Hz, 1H), 2.76 – 2.58 (m, 2H).

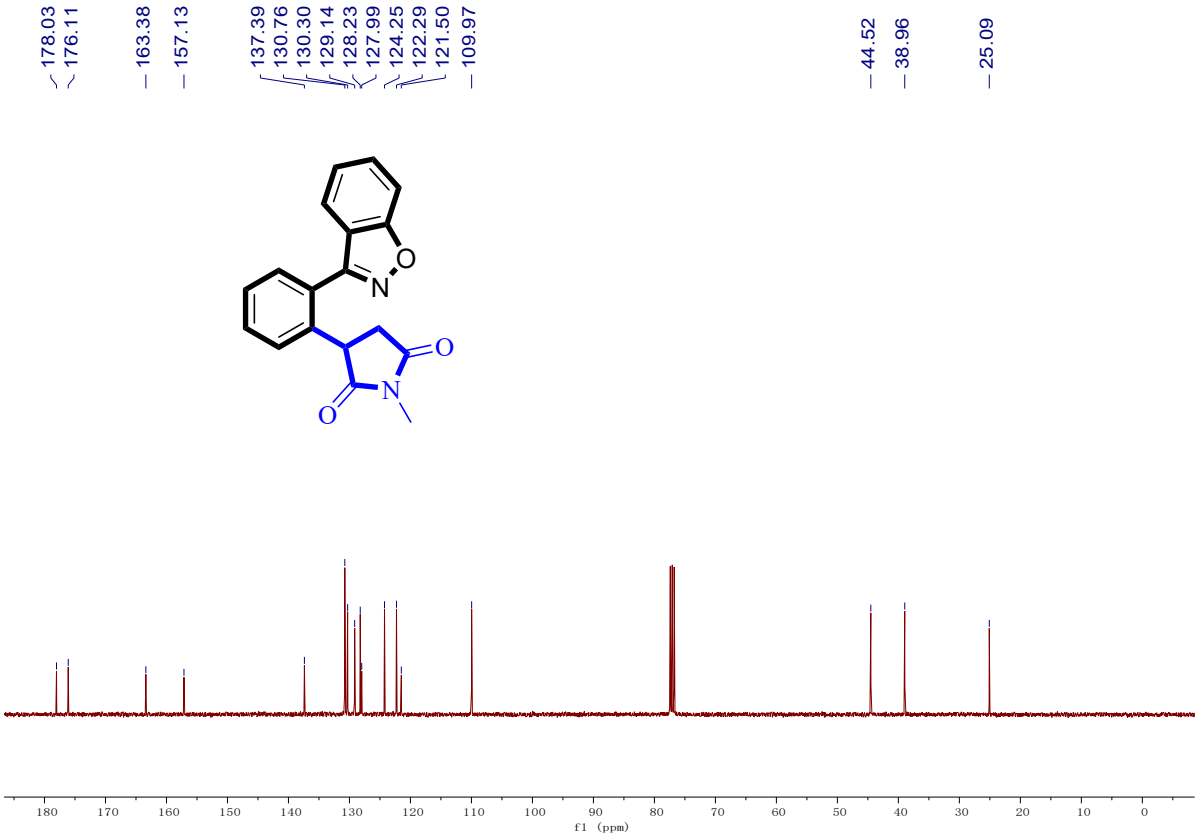
^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.7, 175.8, 163.4, 157.2, 137.1, 130.83, 130.75, 130.4, 129.5, 128.3, 127.9, 124.3, 122.3, 121.4, 110.0, 44.6, 38.8, 34.5, 31.5. HRMS (ESI) calcd for $C_{20}H_{17}N_2O_5$ $[M + H]^+$ 365.1132; found: 365.1135.

6. NMR spectra of products

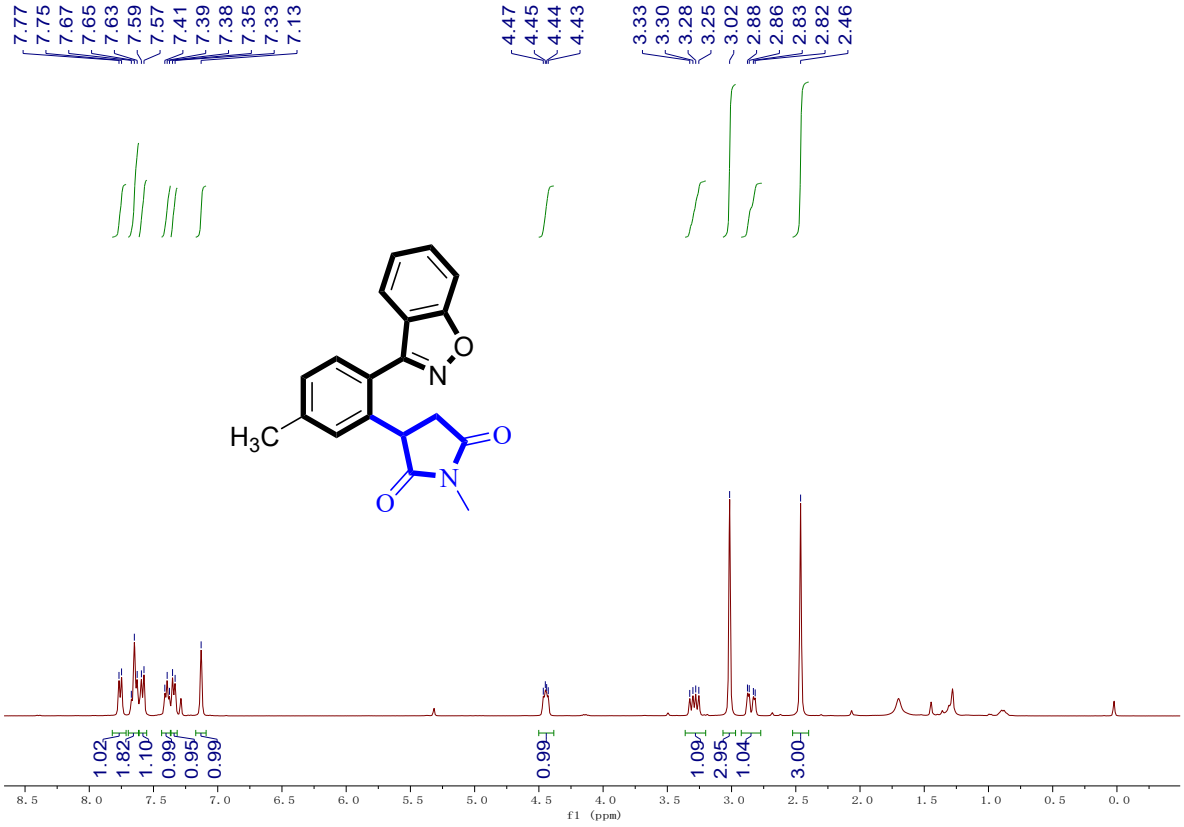
^{1}H NMR (Chloroform-*d*) spectrum of **3aa**



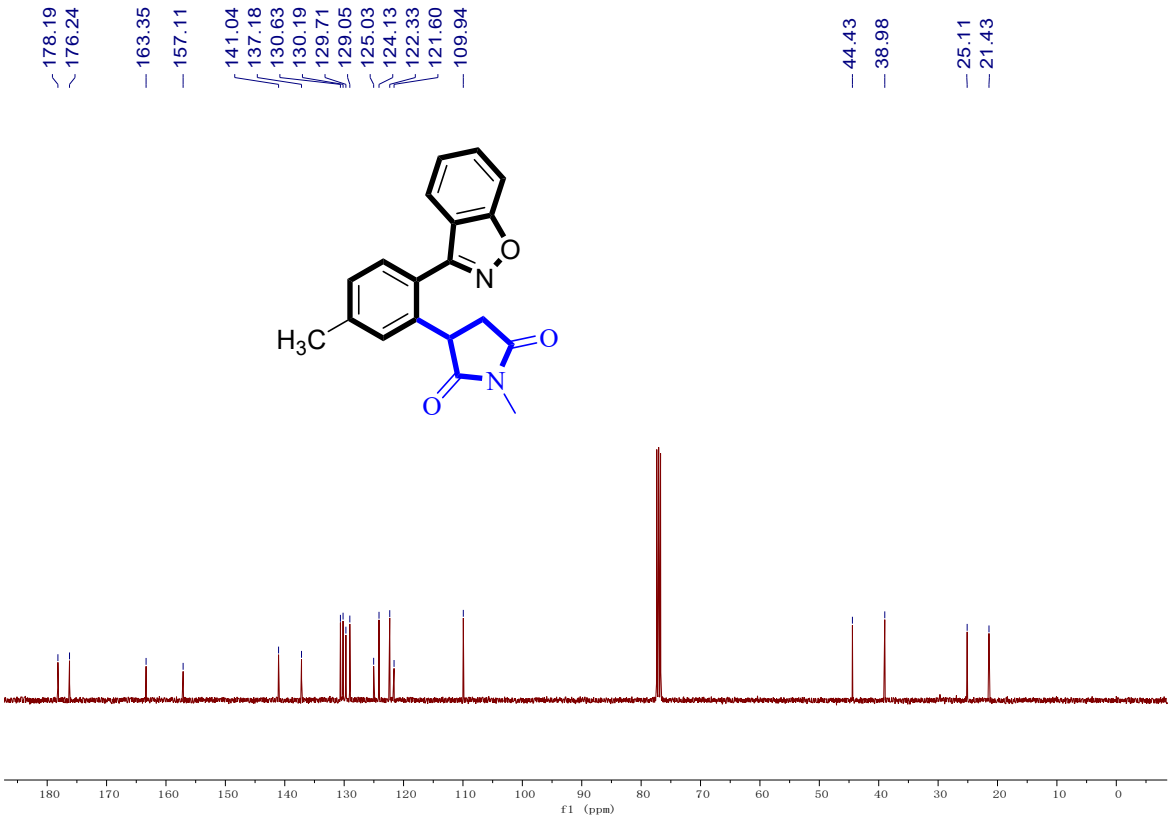
^{13}C NMR (Chloroform-*d*) spectrum of **3aa**



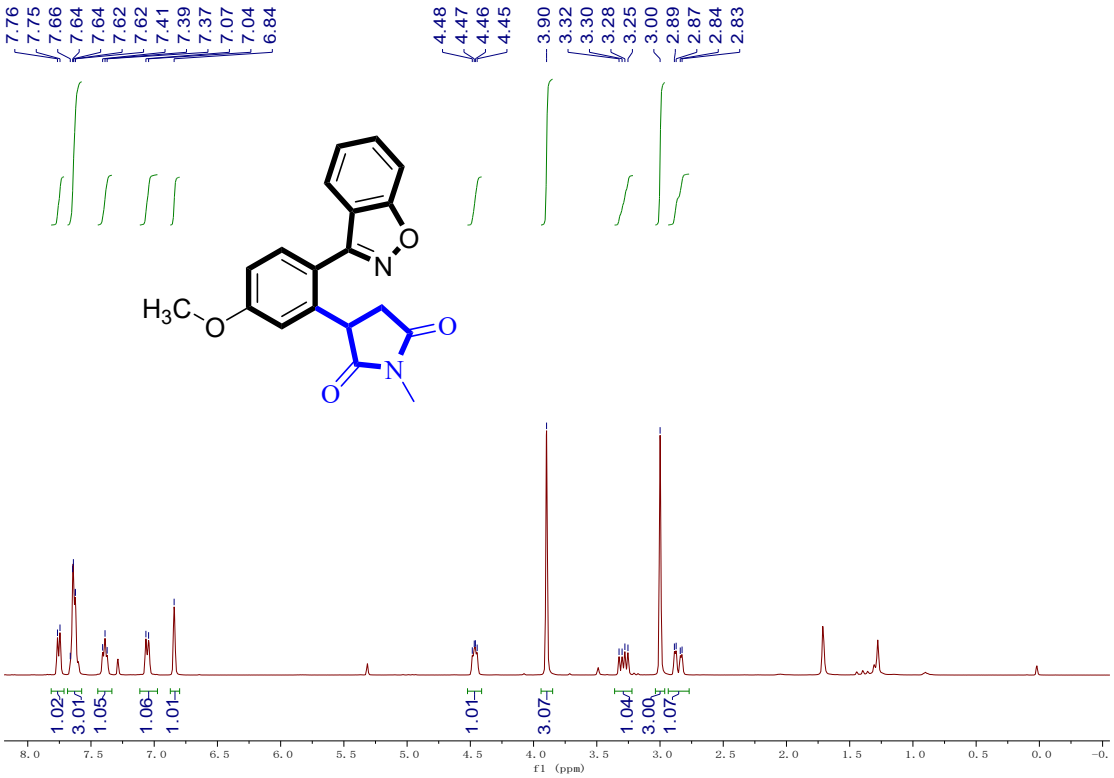
^{1}H NMR (Chloroform-*d*) spectrum of **3ba**



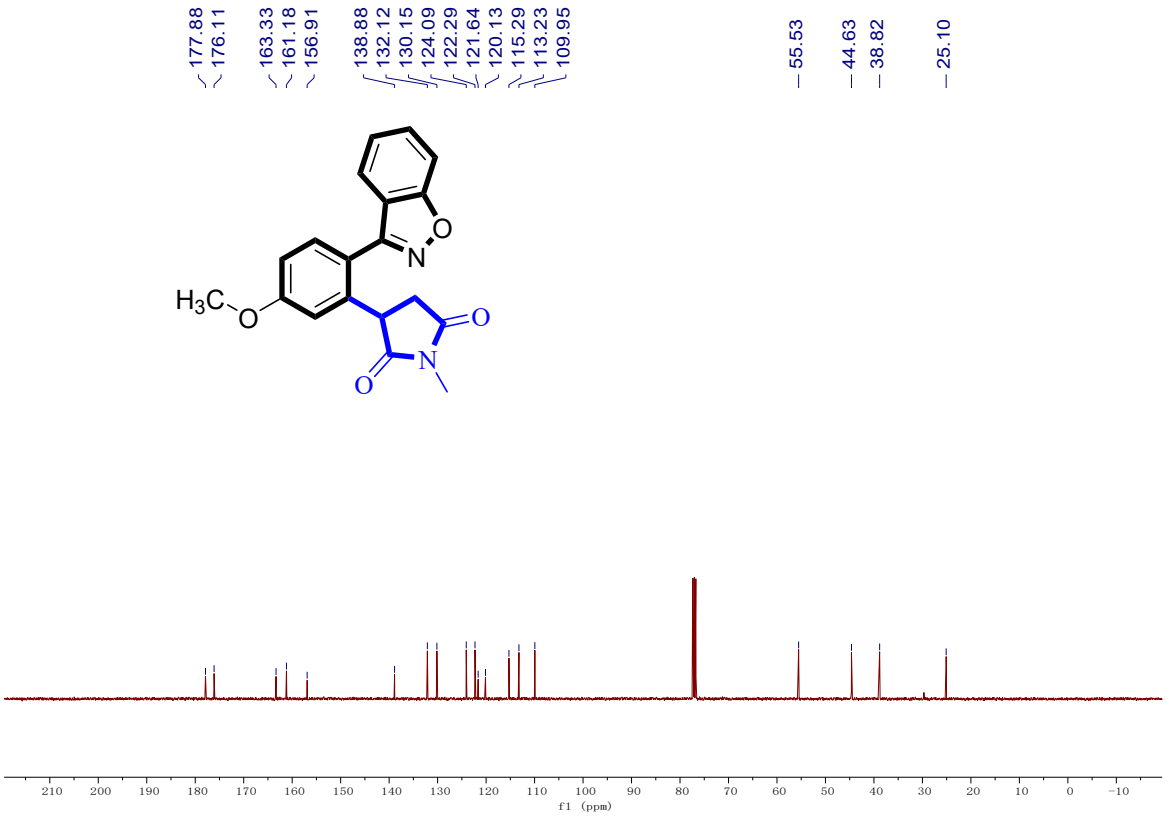
^{13}C NMR (Chloroform-*d*) spectrum of **3ba**



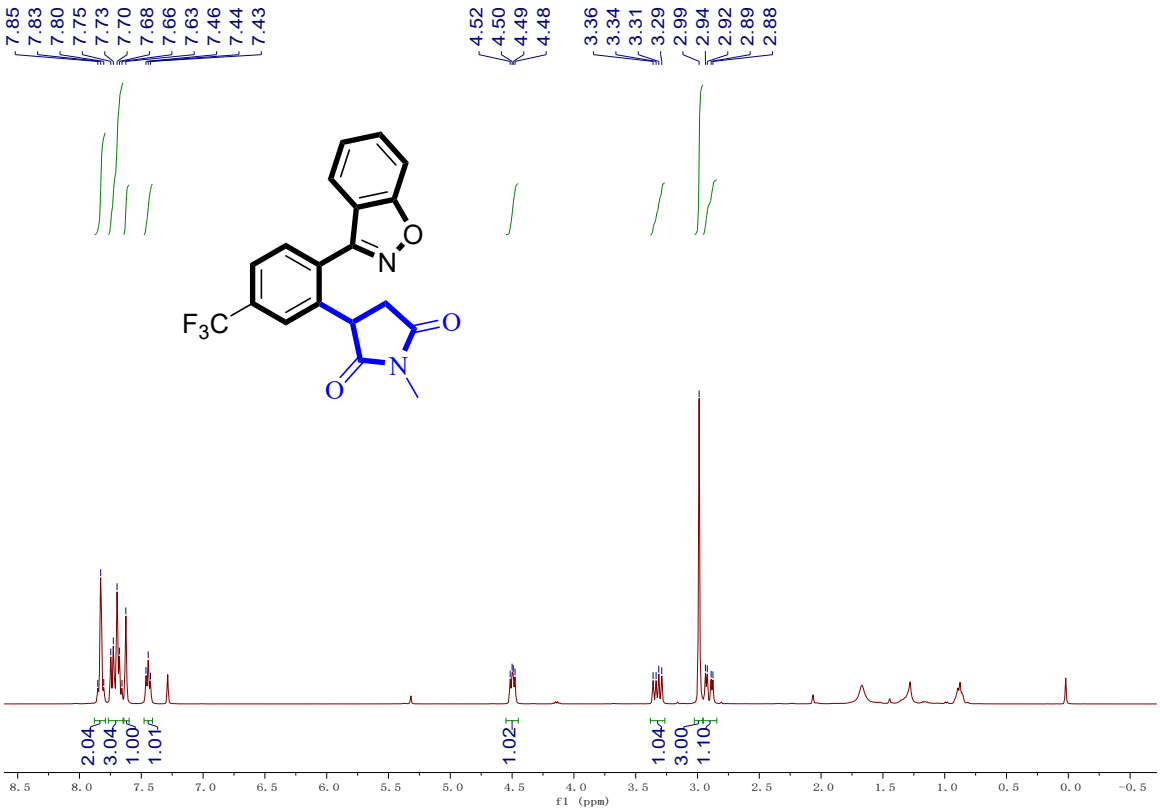
^{1}H NMR (Chloroform-*d*) spectrum of **3ca**



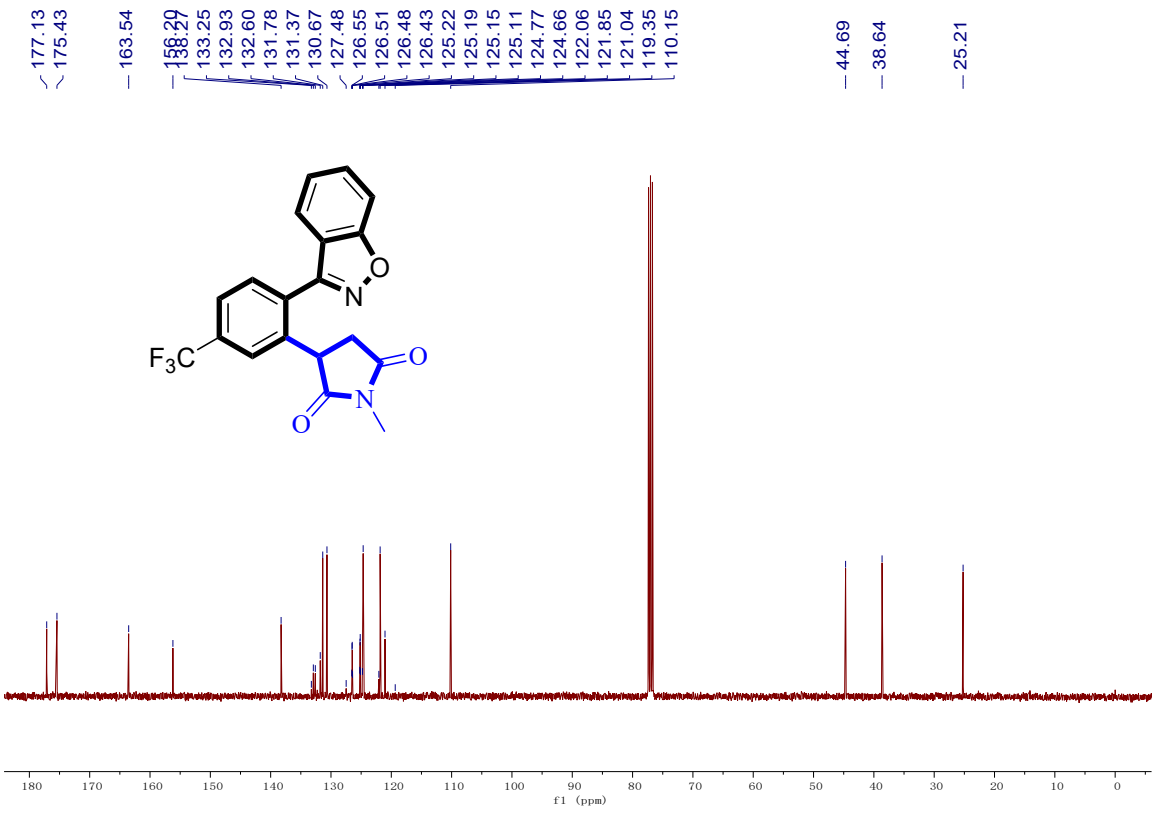
^{13}C NMR (Chloroform-*d*) spectrum of **3ca**



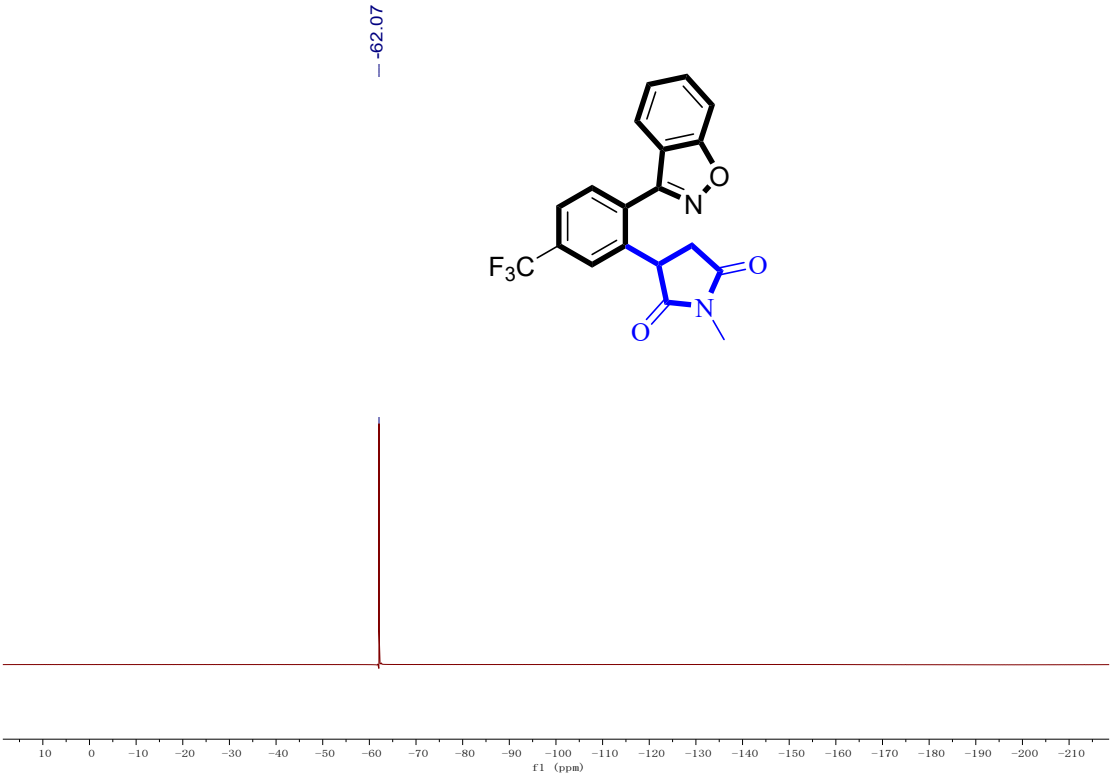
^{1}H NMR (Chloroform-*d*) spectrum of **3da**



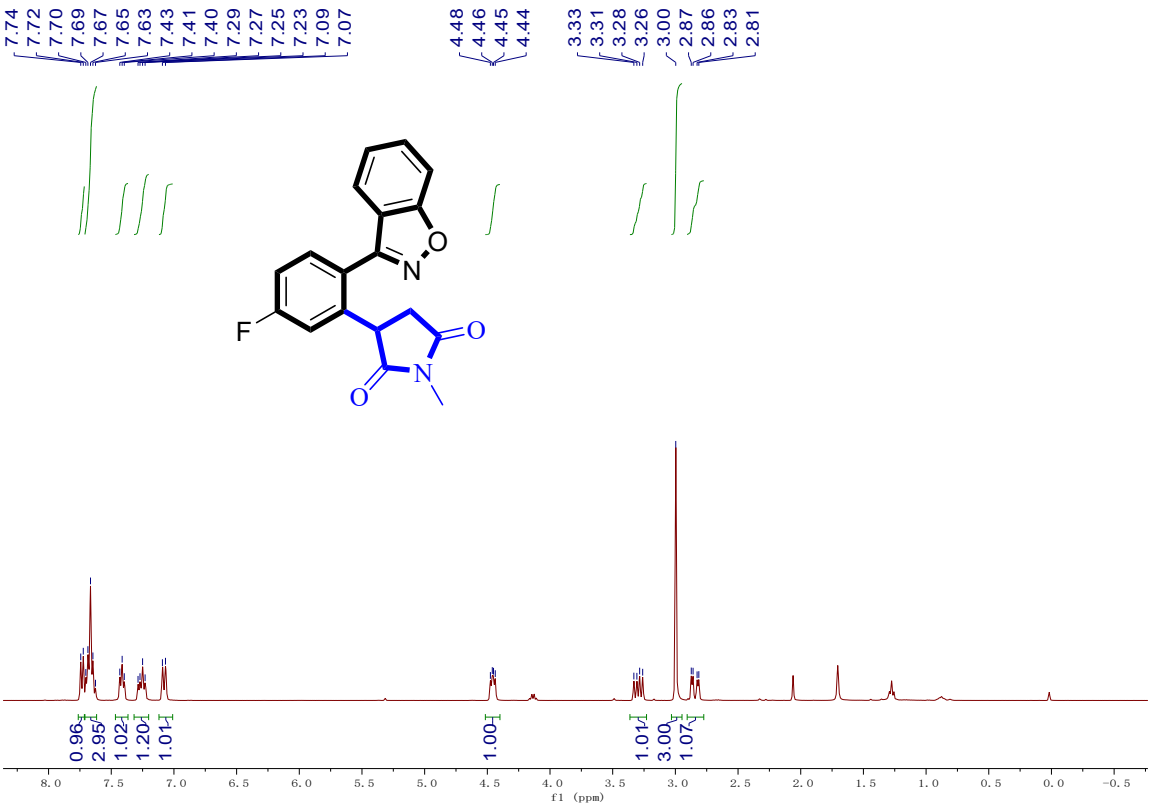
^{13}C NMR (Chloroform-*d*) spectrum of **3da**



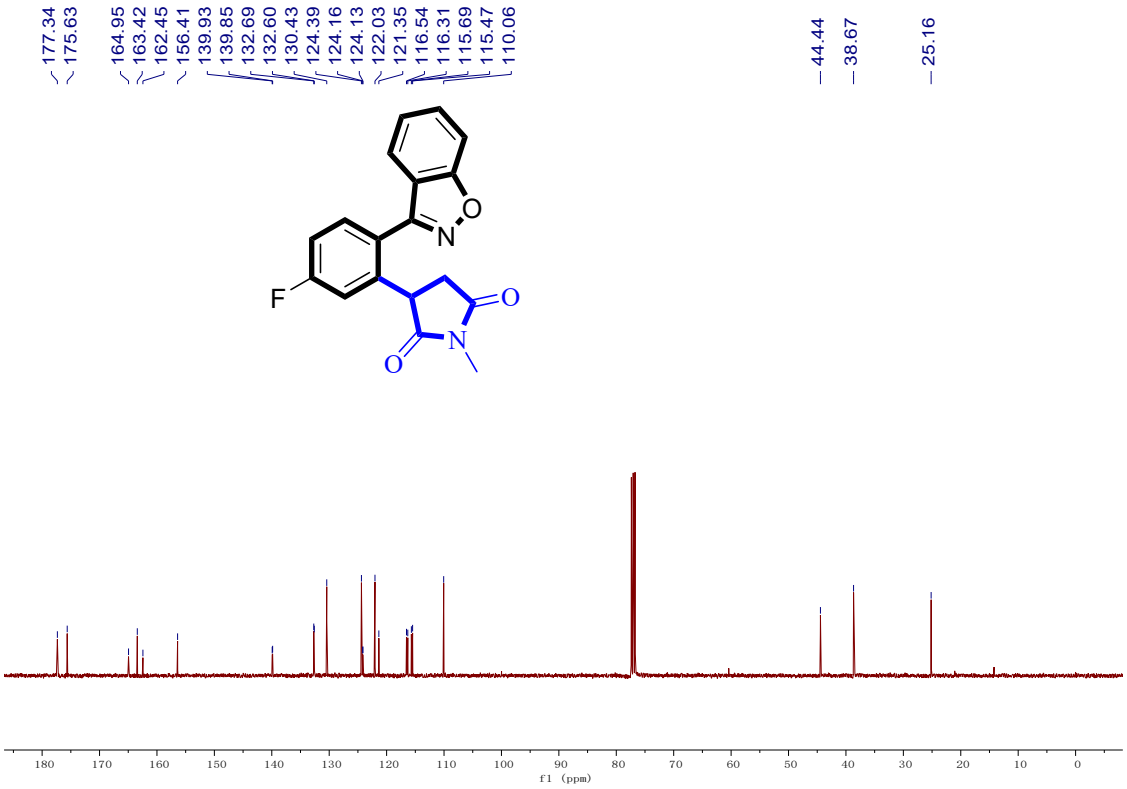
^{19}F NMR (DMSO-d_6) spectrum of **3da**



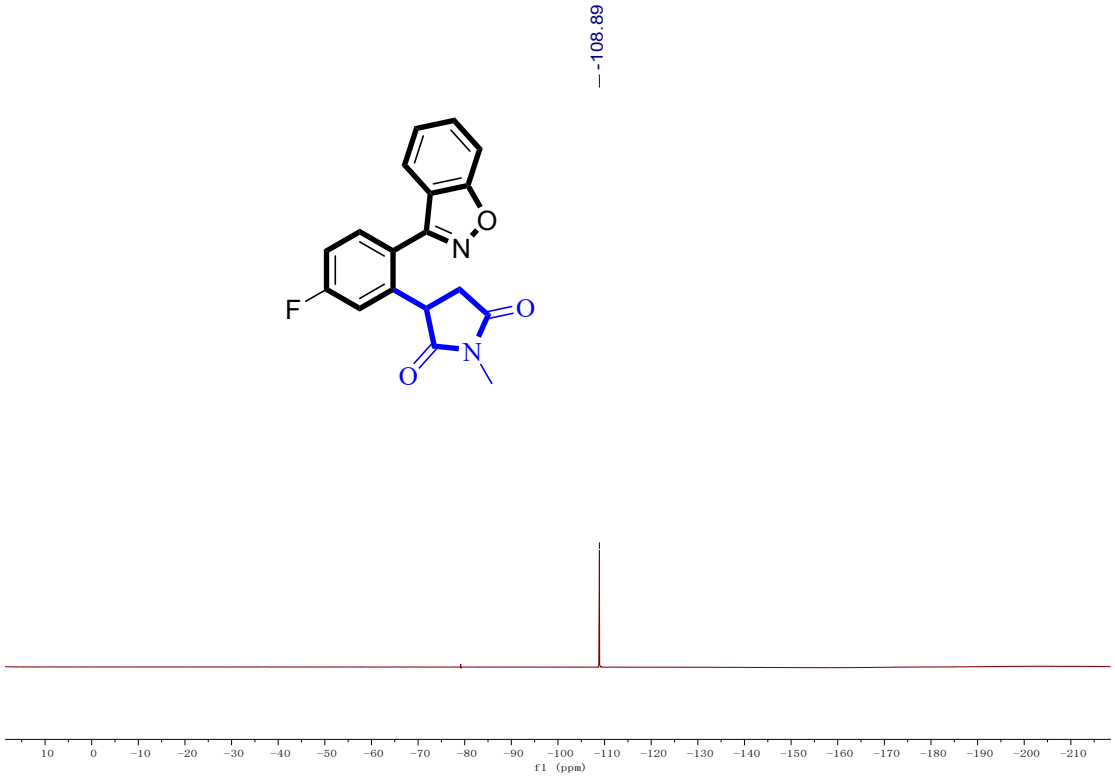
^{1}H NMR (Chloroform-*d*) spectrum of **3ea**



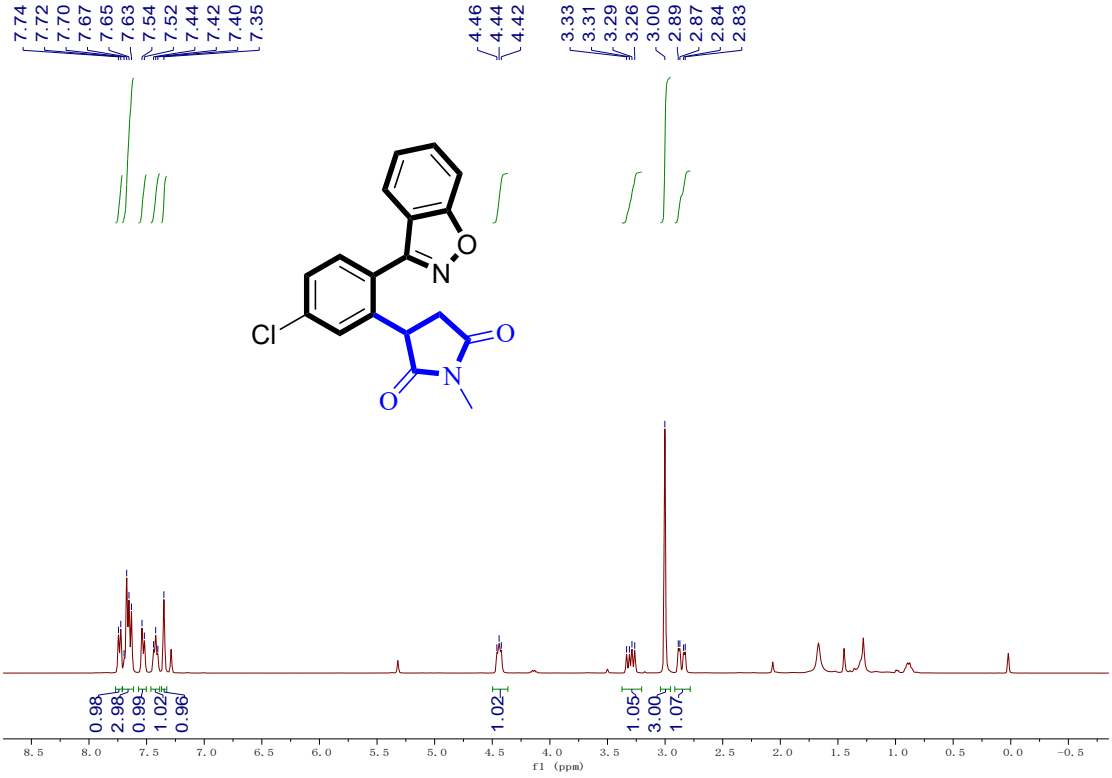
^{13}C NMR (Chloroform-*d*) spectrum of **3ea**



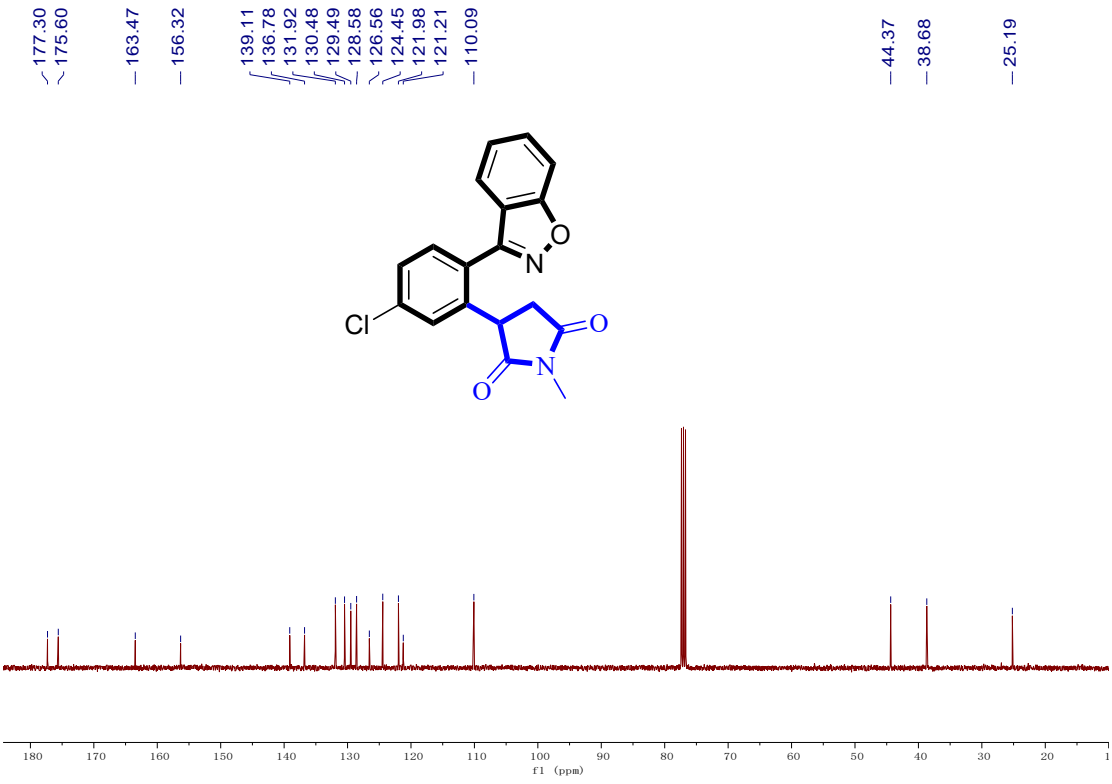
^{19}F NMR (DMSO-d_6) spectrum of **3ea**



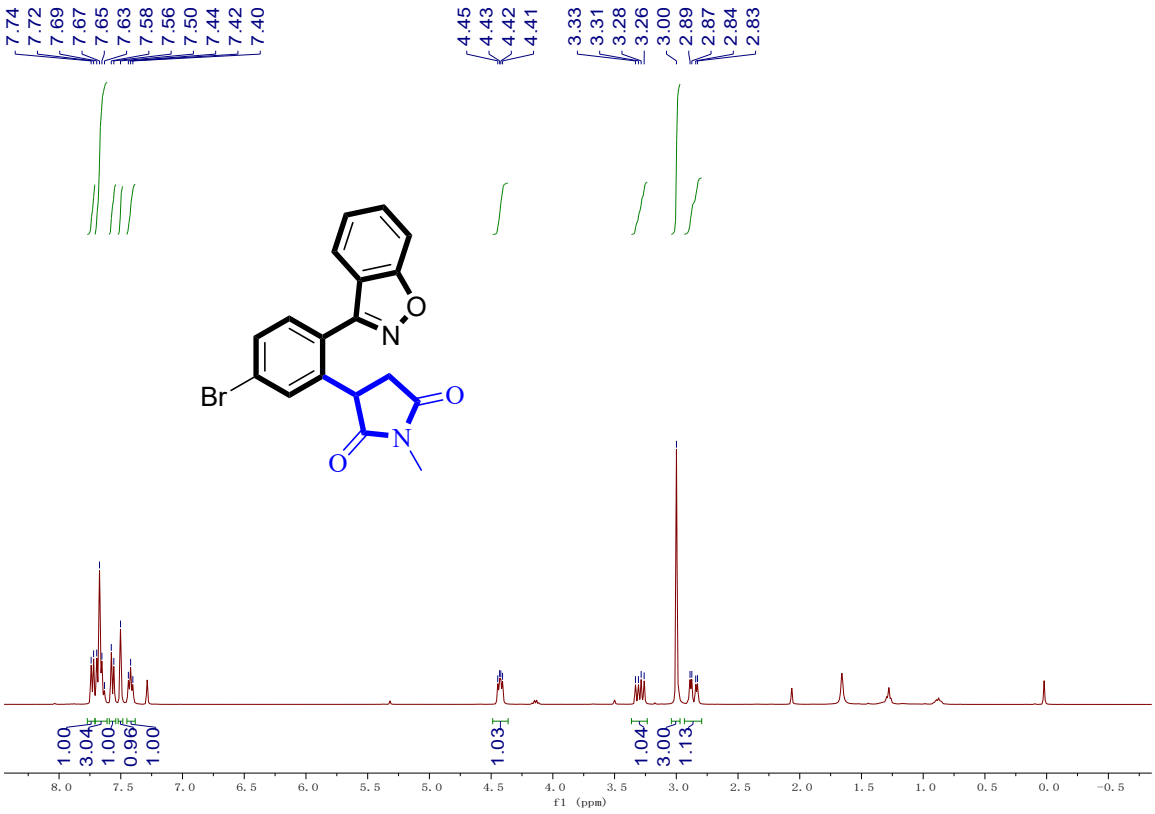
[1]H NMR (Chloroform-*d*) spectrum of **3fa**



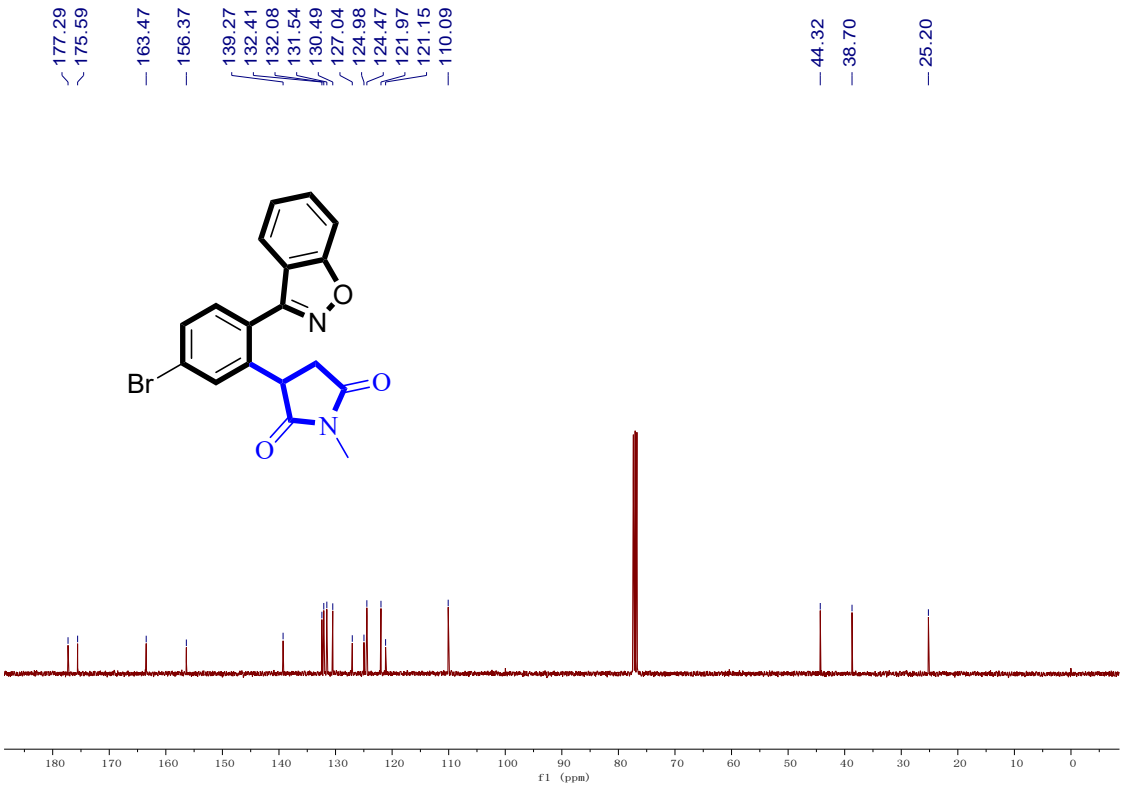
[13]C NMR (Chloroform-*d*) spectrum of **3fa**



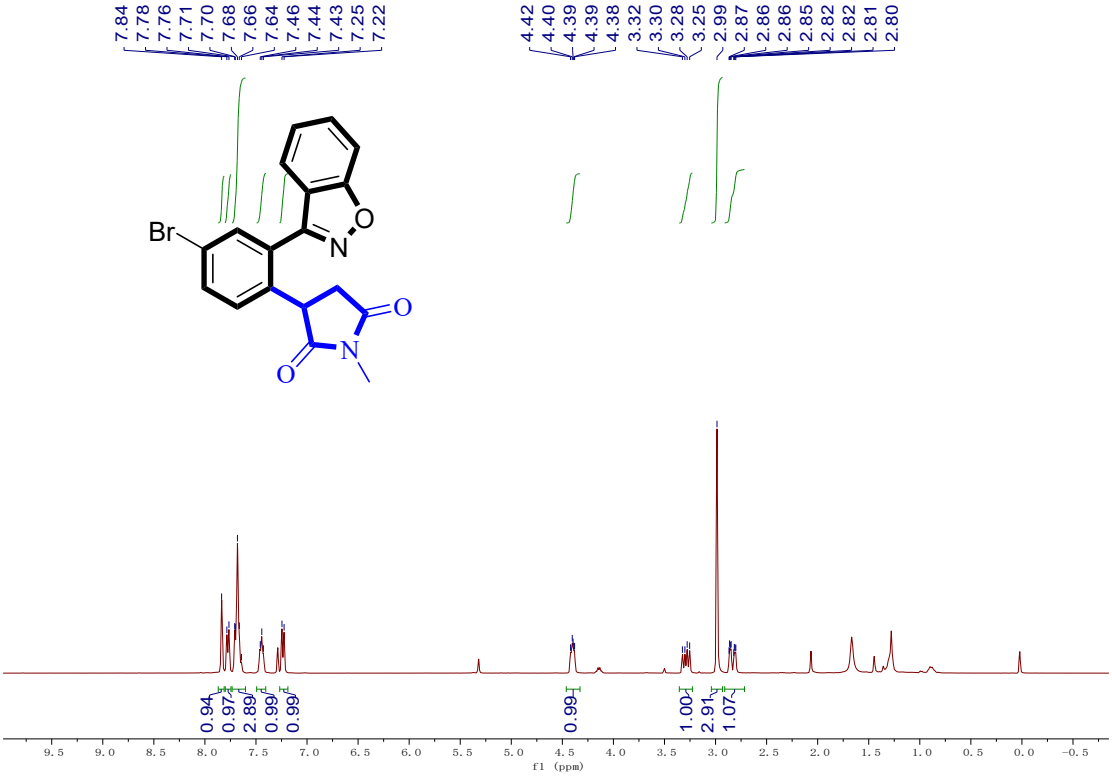
^{1}H NMR (Chloroform-*d*) spectrum of **3ga**



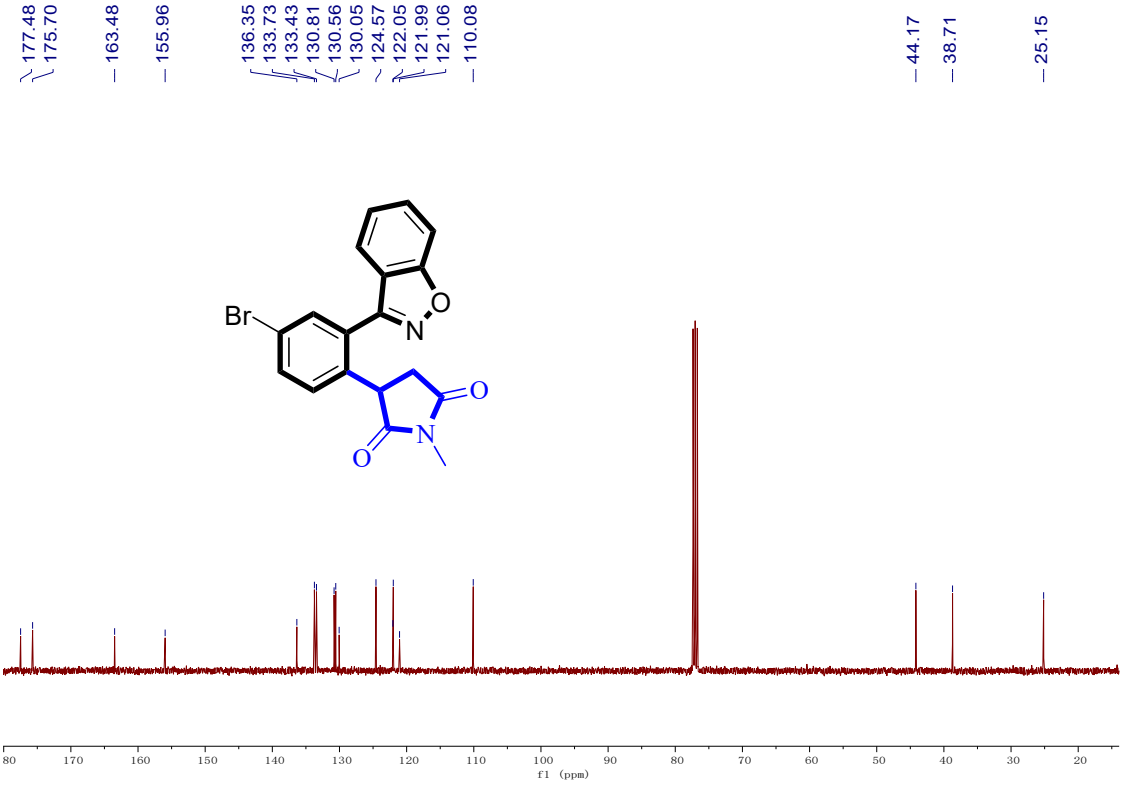
^{13}C NMR (Chloroform-*d*) spectrum of **3ga**



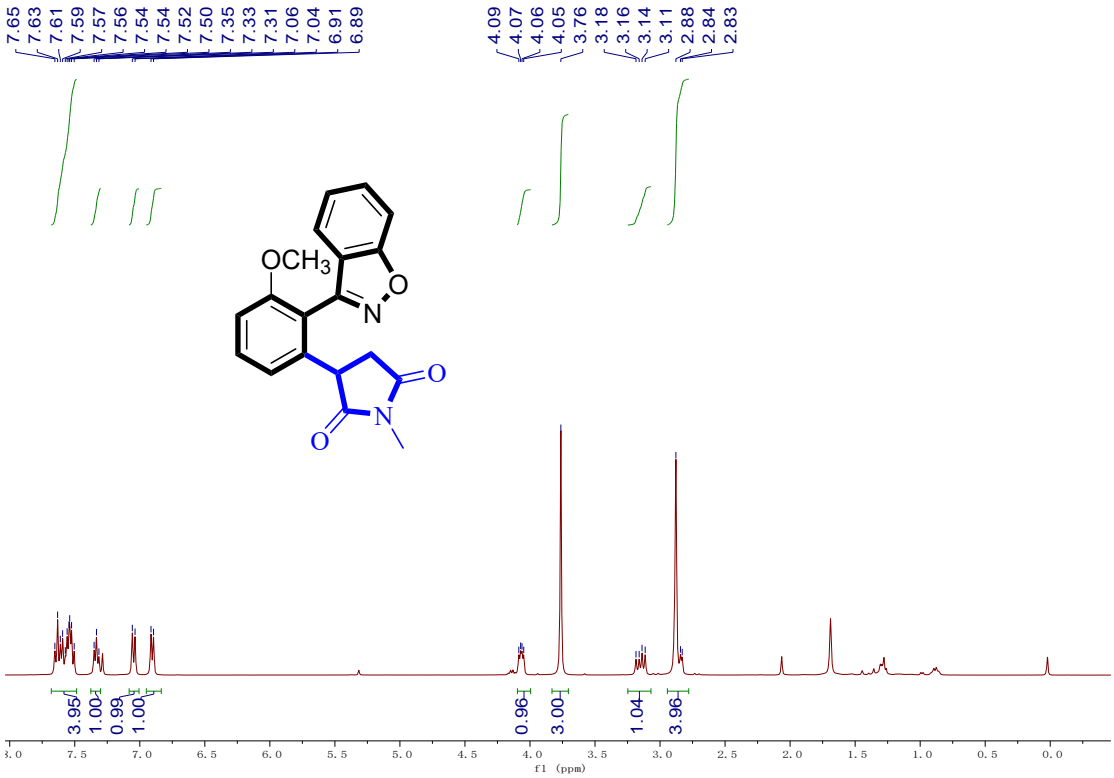
^{1}H NMR (Chloroform-*d*) spectrum of **3ha**



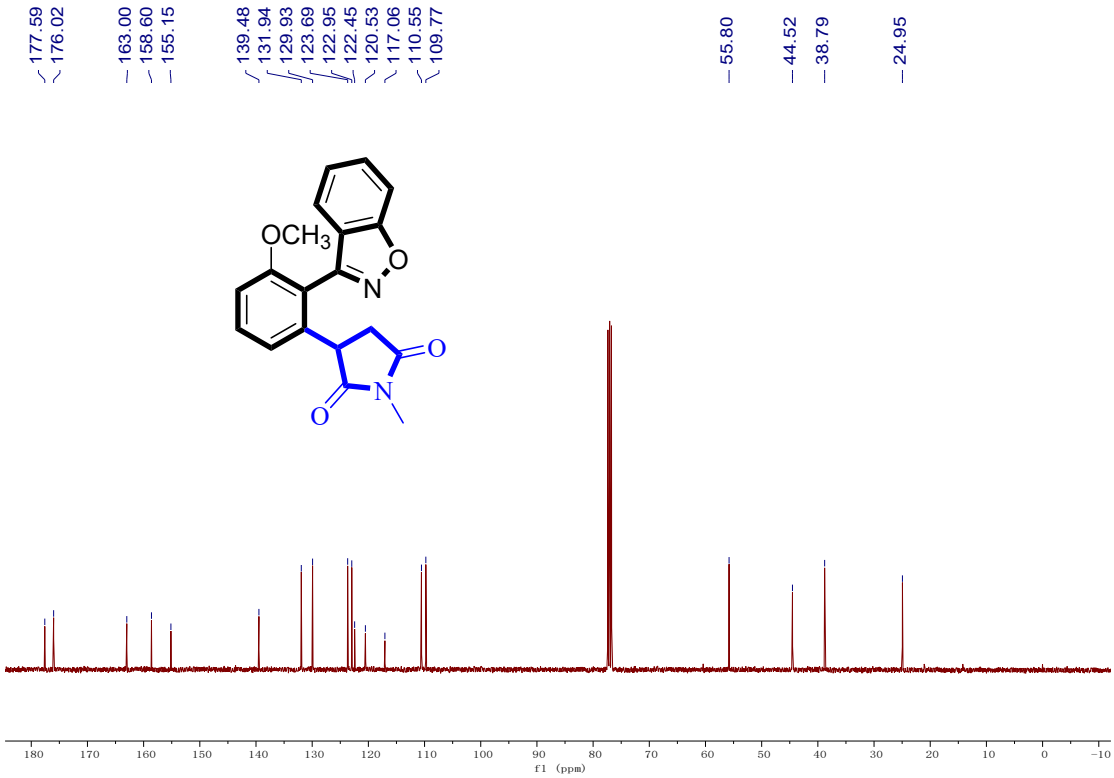
^{13}C NMR (Chloroform-*d*) spectrum of **3ha**



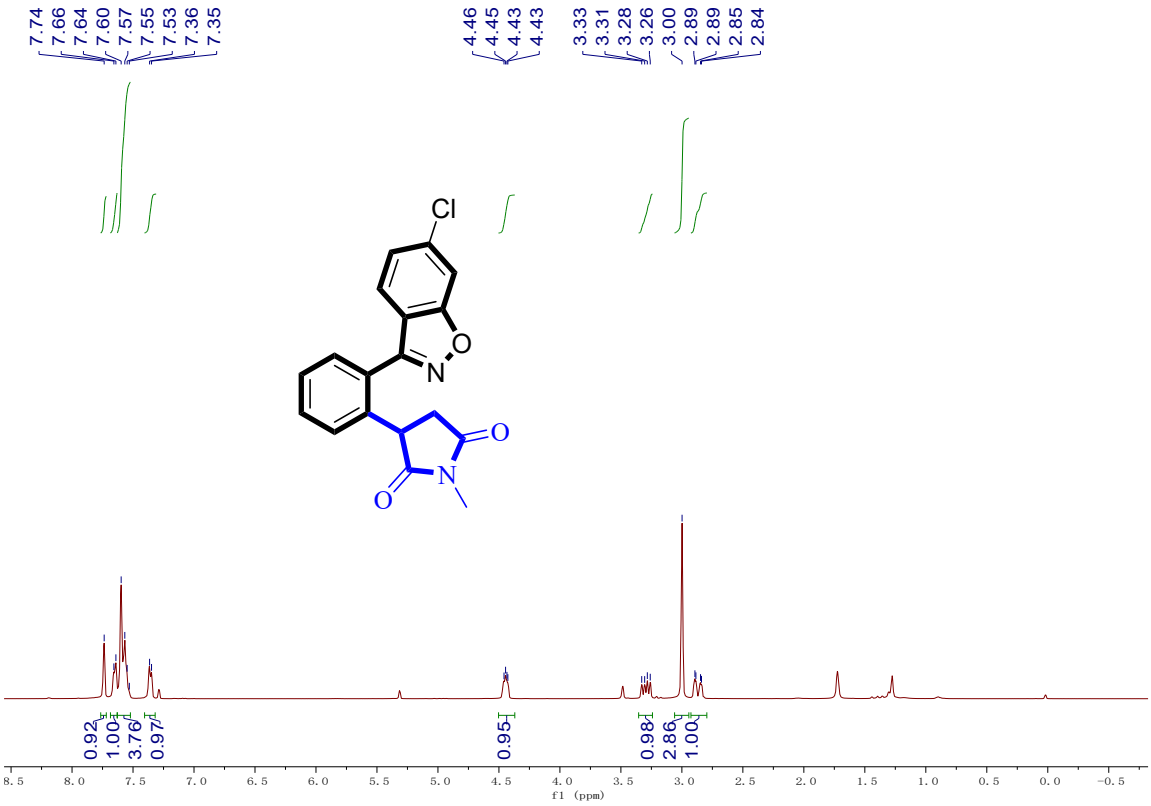
^{1}H NMR (Chloroform-*d*) spectrum of **3ia**



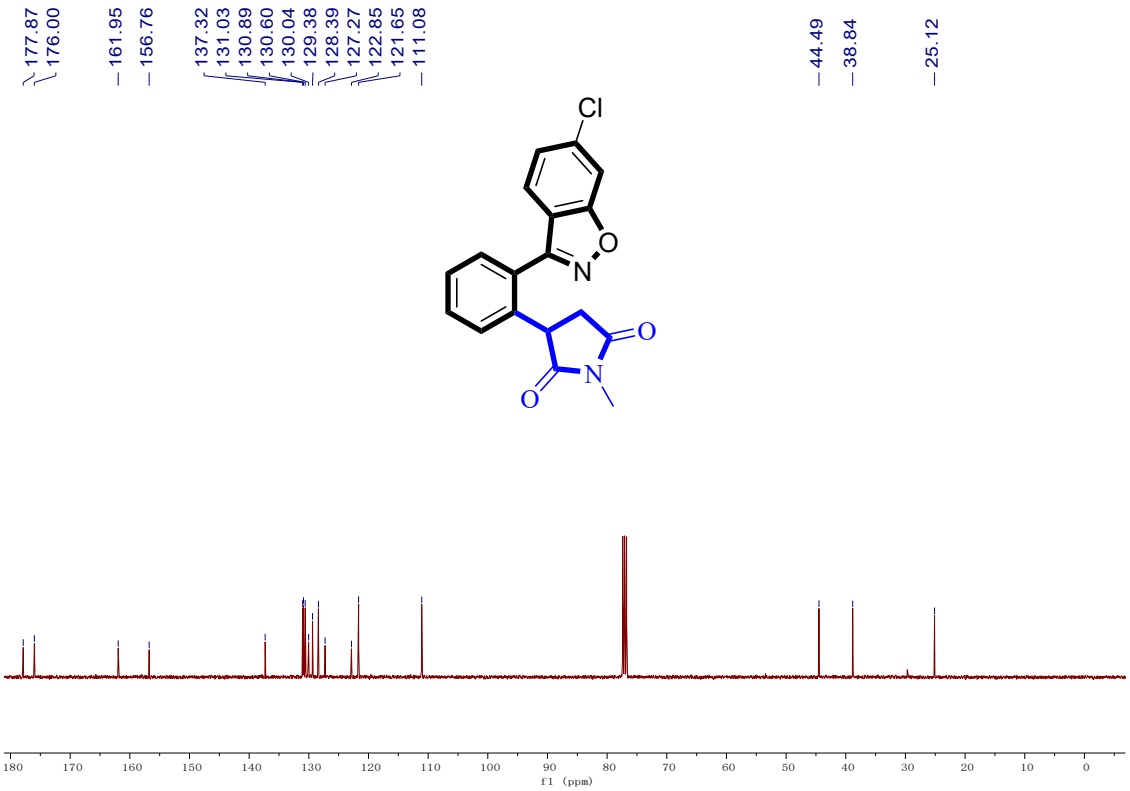
^{13}C NMR (Chloroform-*d*) spectrum of **3ia**



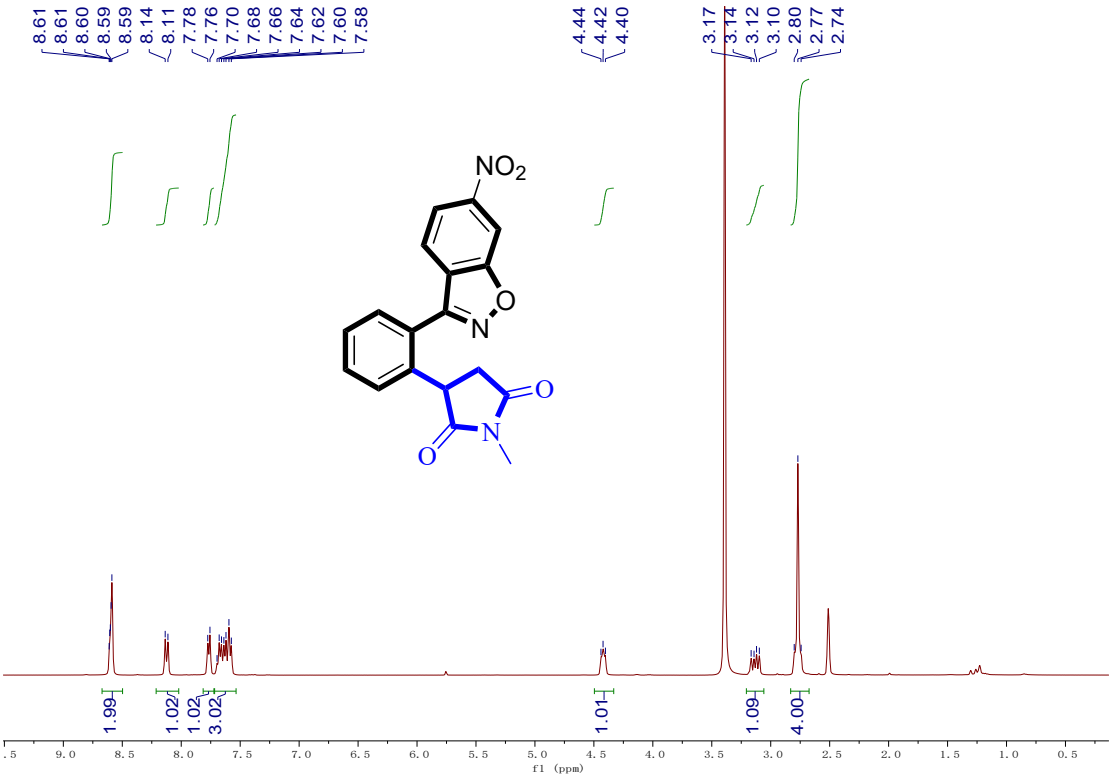
^{1}H NMR (Chloroform-*d*) spectrum of **3ja**



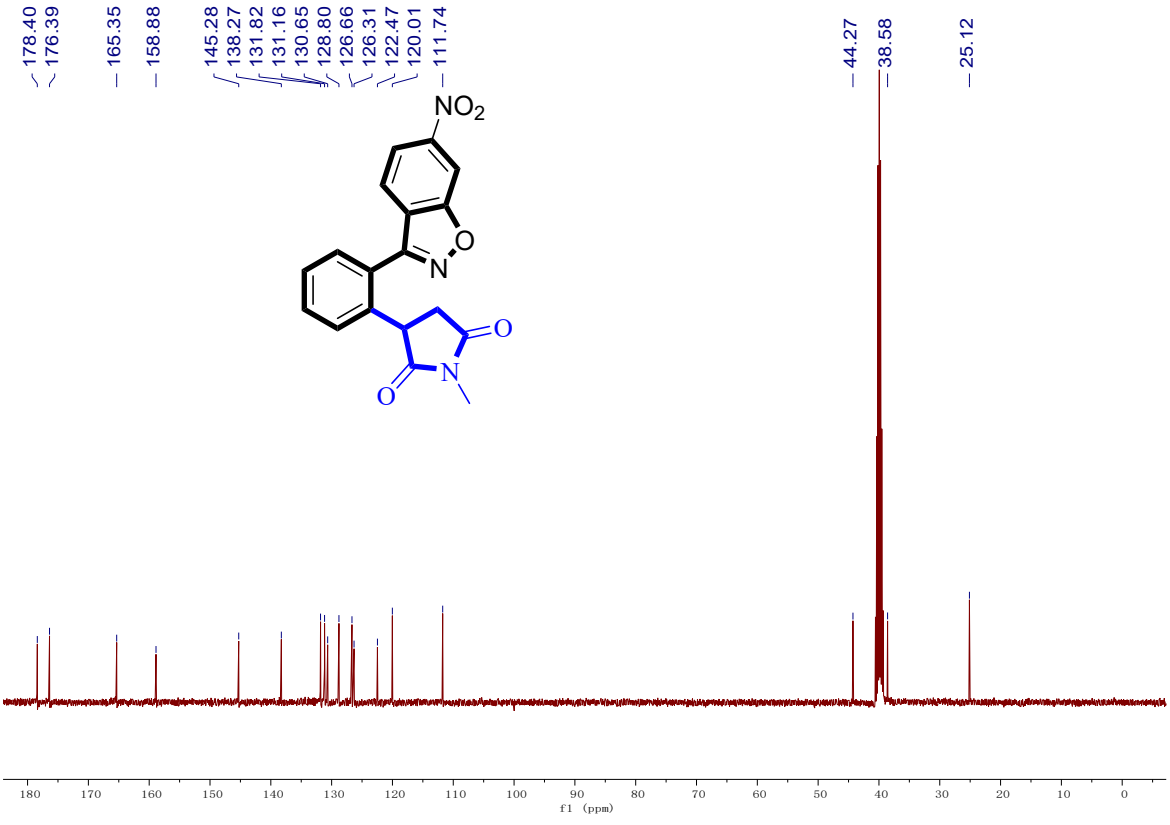
^{13}C NMR (Chloroform-*d*) spectrum of **3ja**



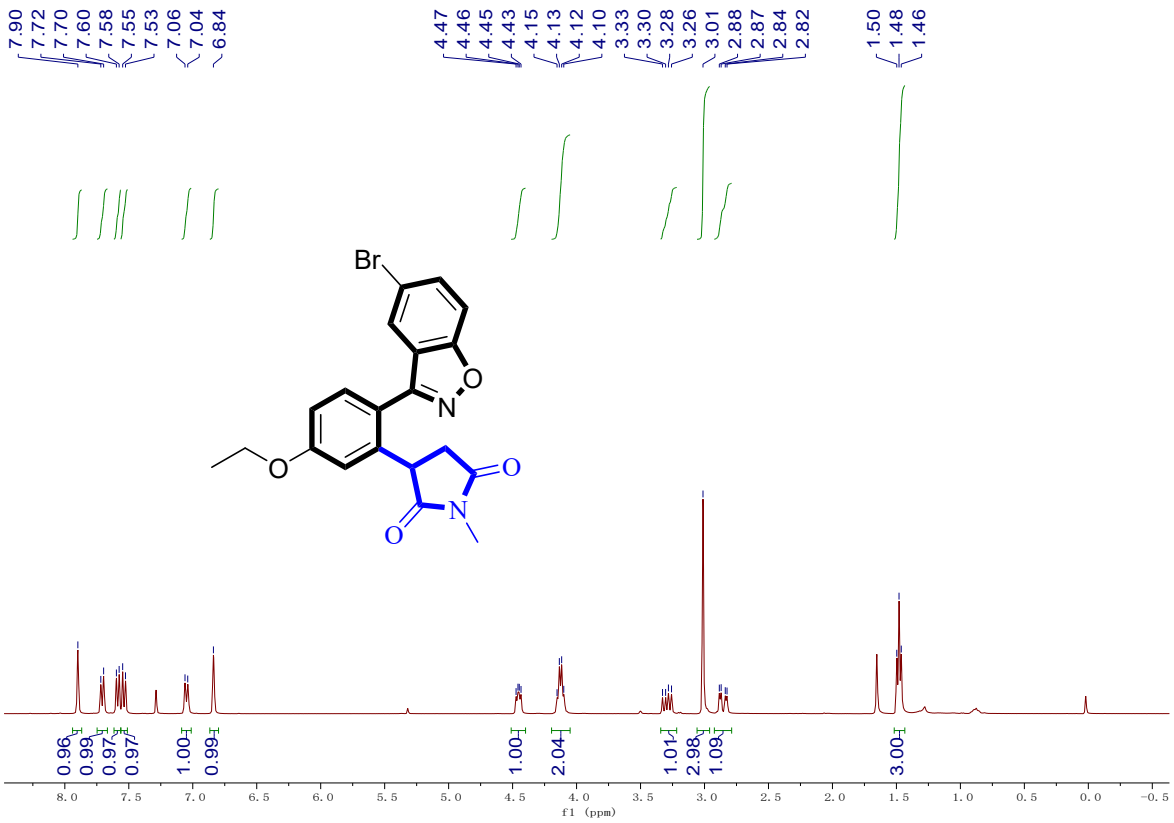
^{1}H NMR (DMSO-d_6) spectrum of **3ka**



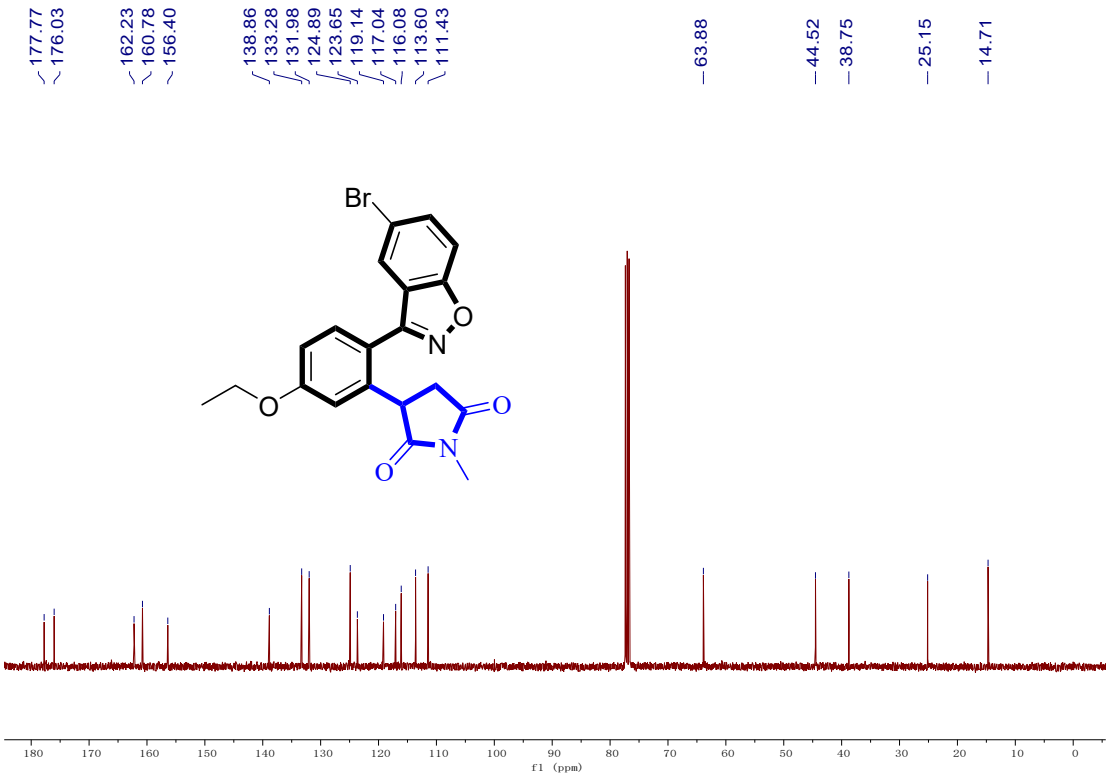
^{13}C NMR (DMSO-d_6) spectrum of **3ka**



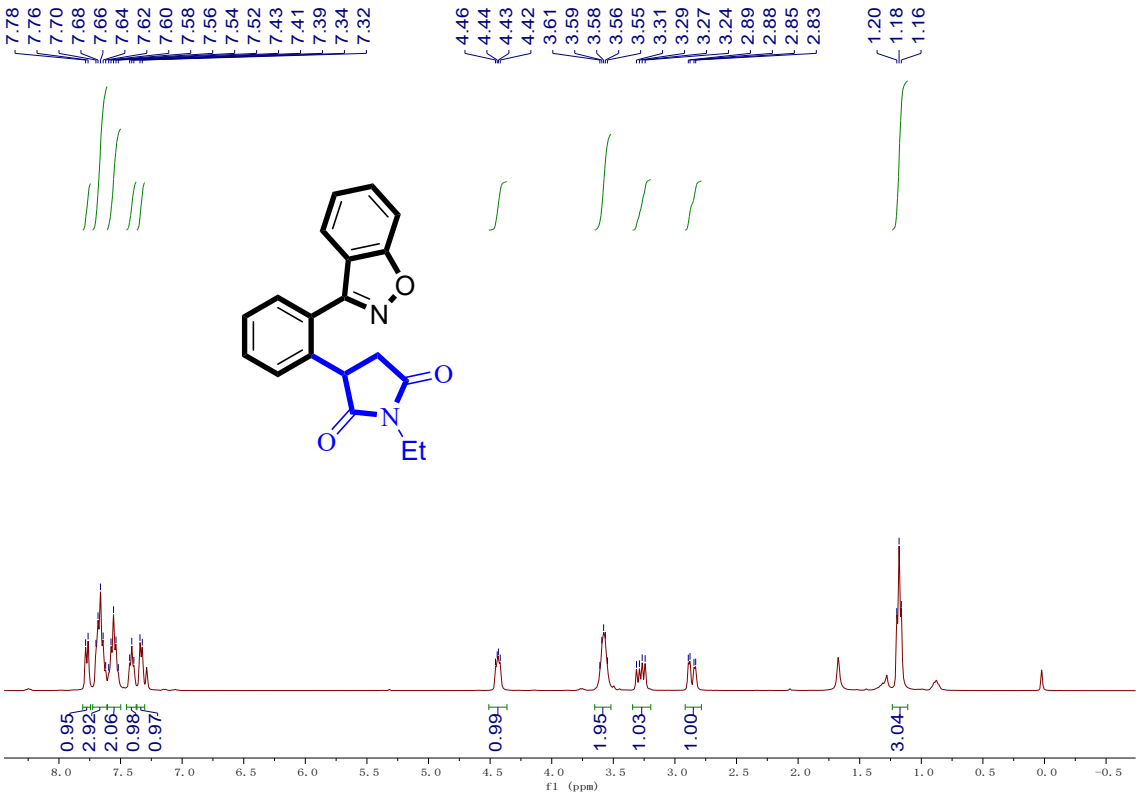
^{1}H NMR (Chloroform-*d*) spectrum of **3la**



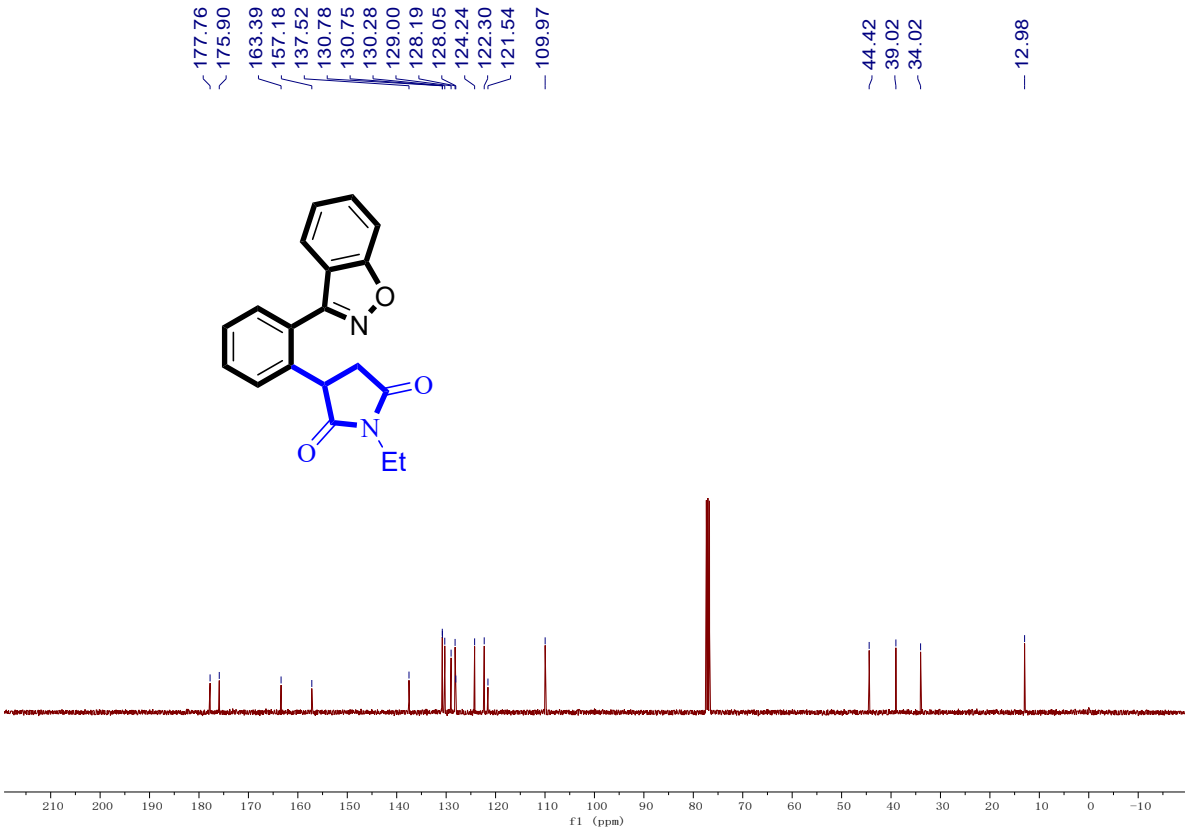
^{13}C NMR (Chloroform-*d*) spectrum of **3la**



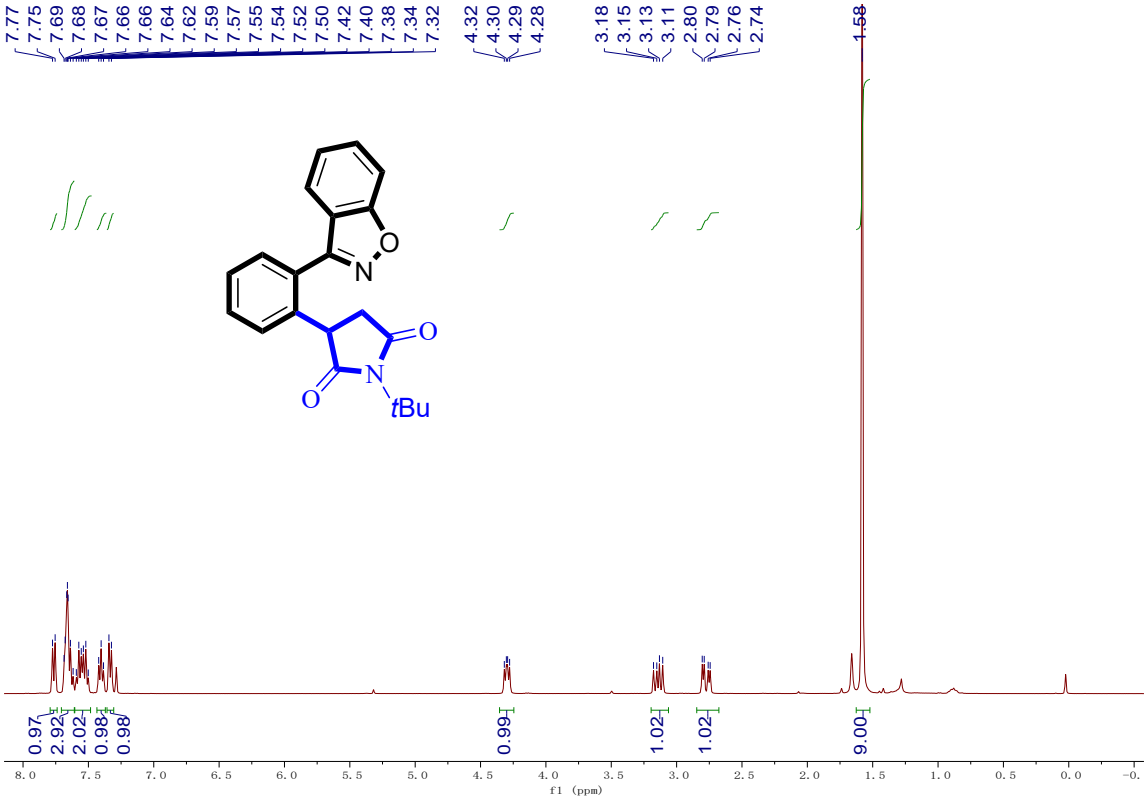
^{1}H NMR (Chloroform-*d*) spectrum of **3ab**



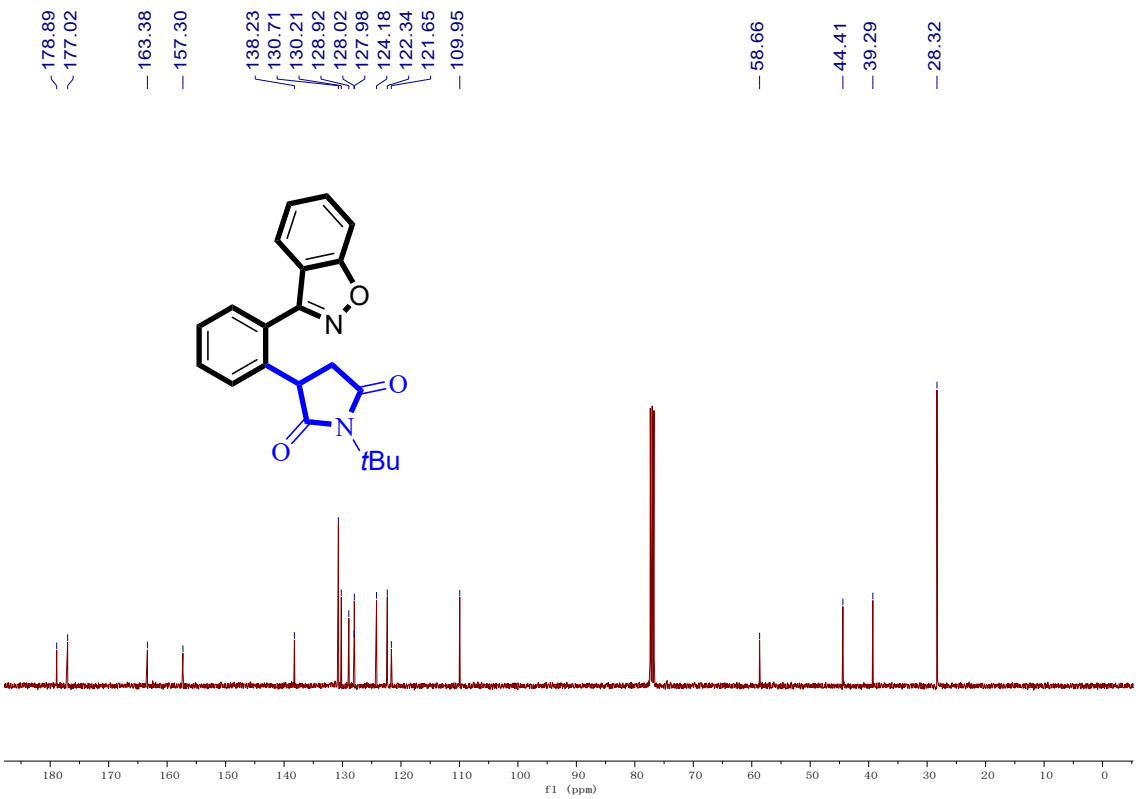
^{13}C NMR (Chloroform-*d*) spectrum of **3ab**



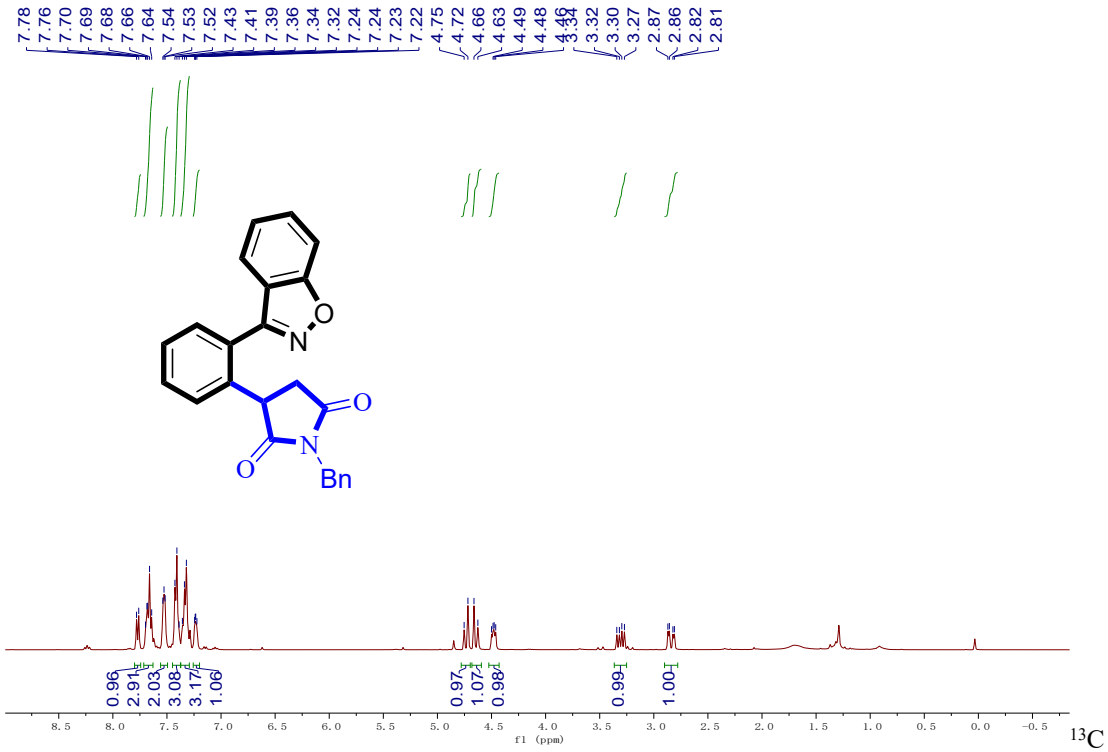
^{1}H NMR (Chloroform-*d*) spectrum of **3ac**



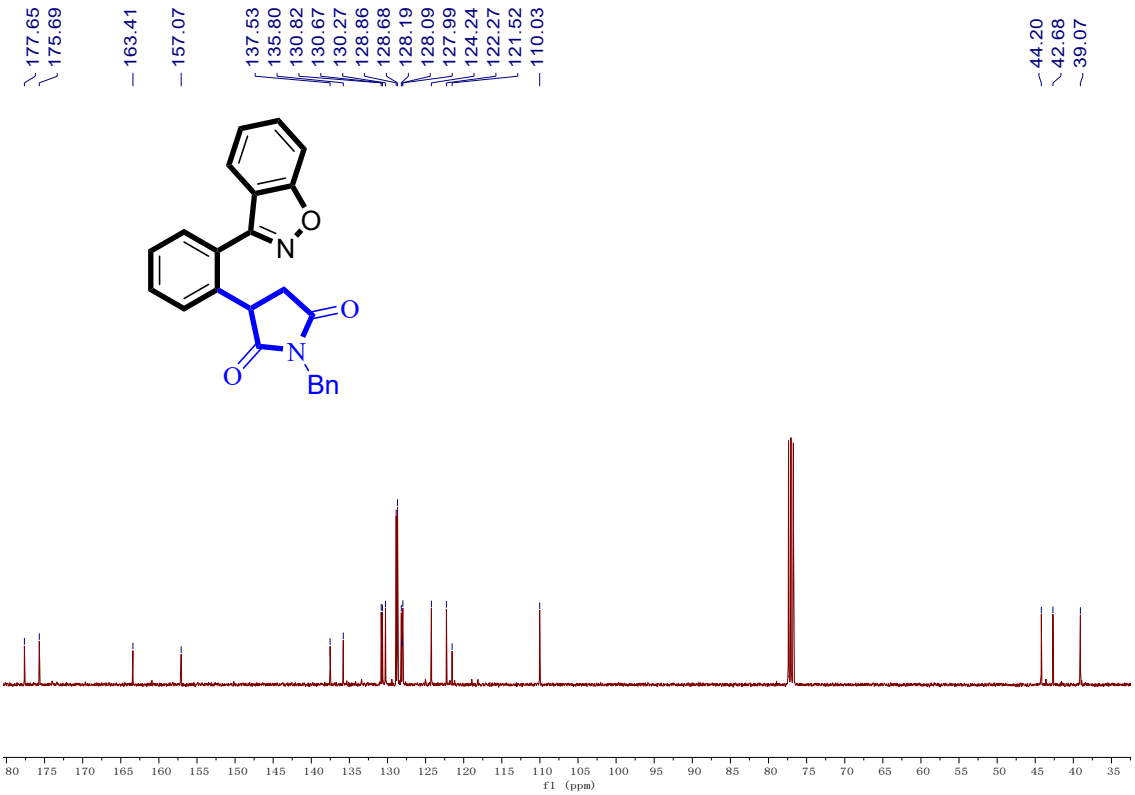
^{13}C NMR (Chloroform-*d*) spectrum of **3ac**



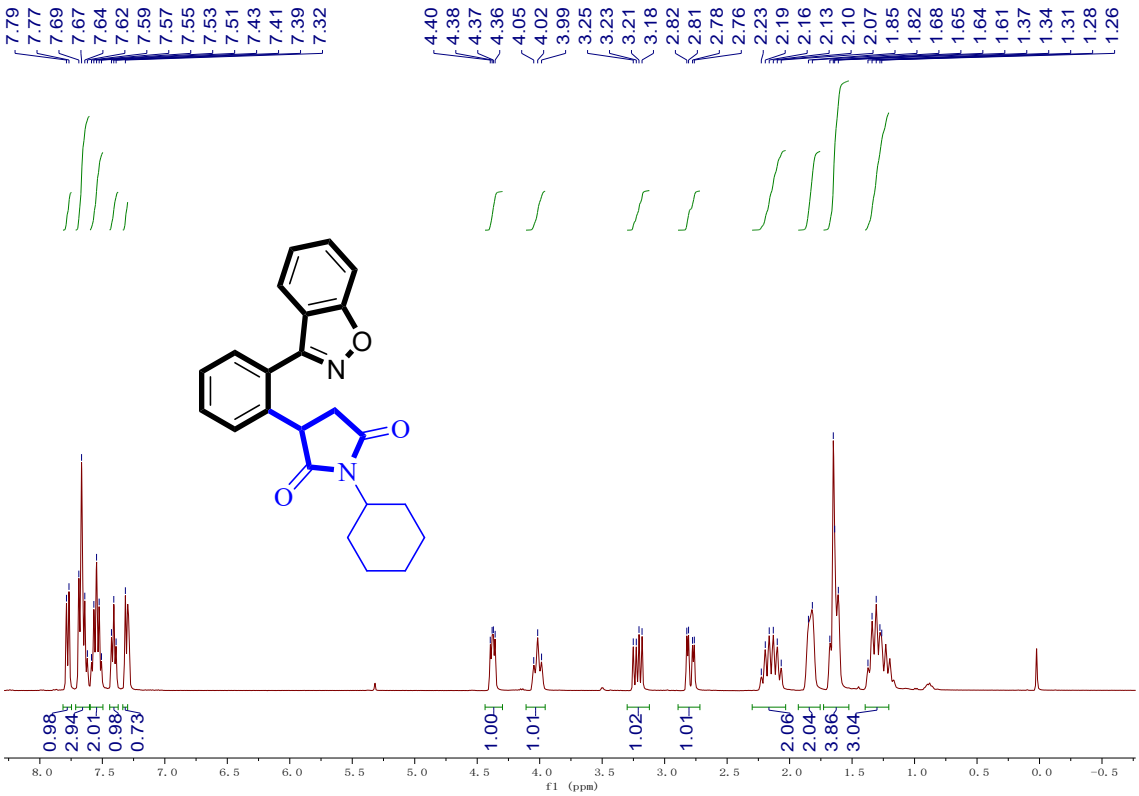
^{1}H NMR (Chloroform-*d*) spectrum of **3ad**



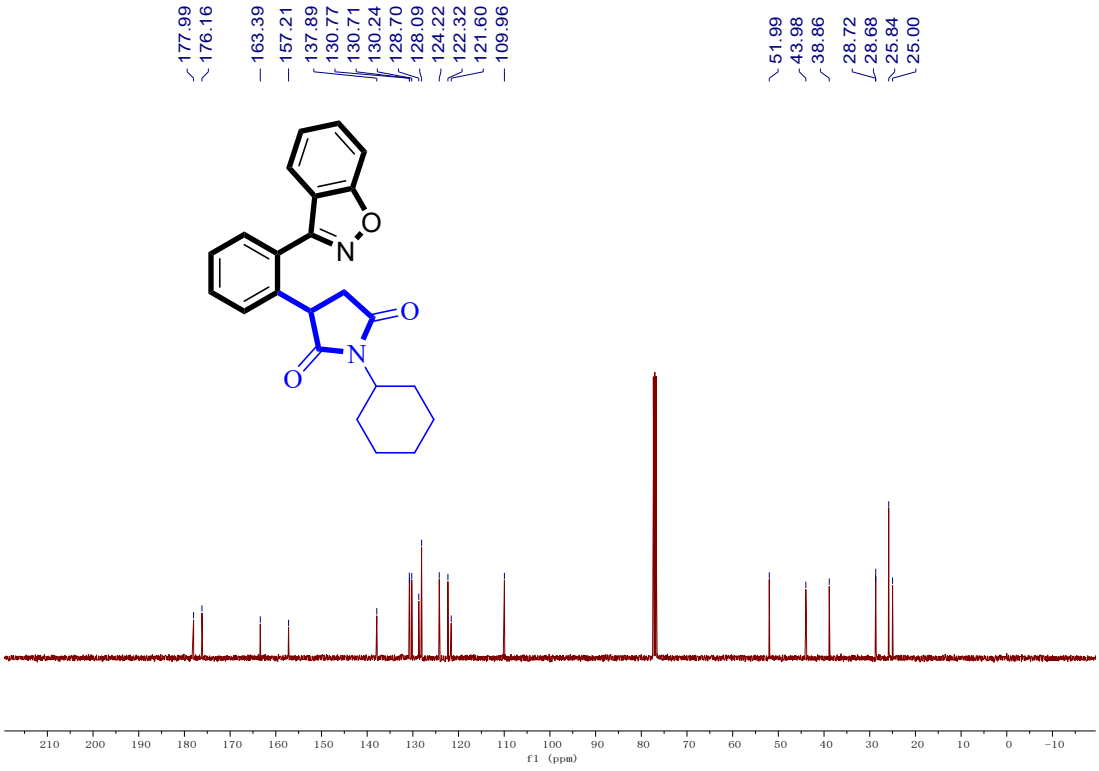
^{13}C NMR (Chloroform-*d*) spectrum of **3ad**



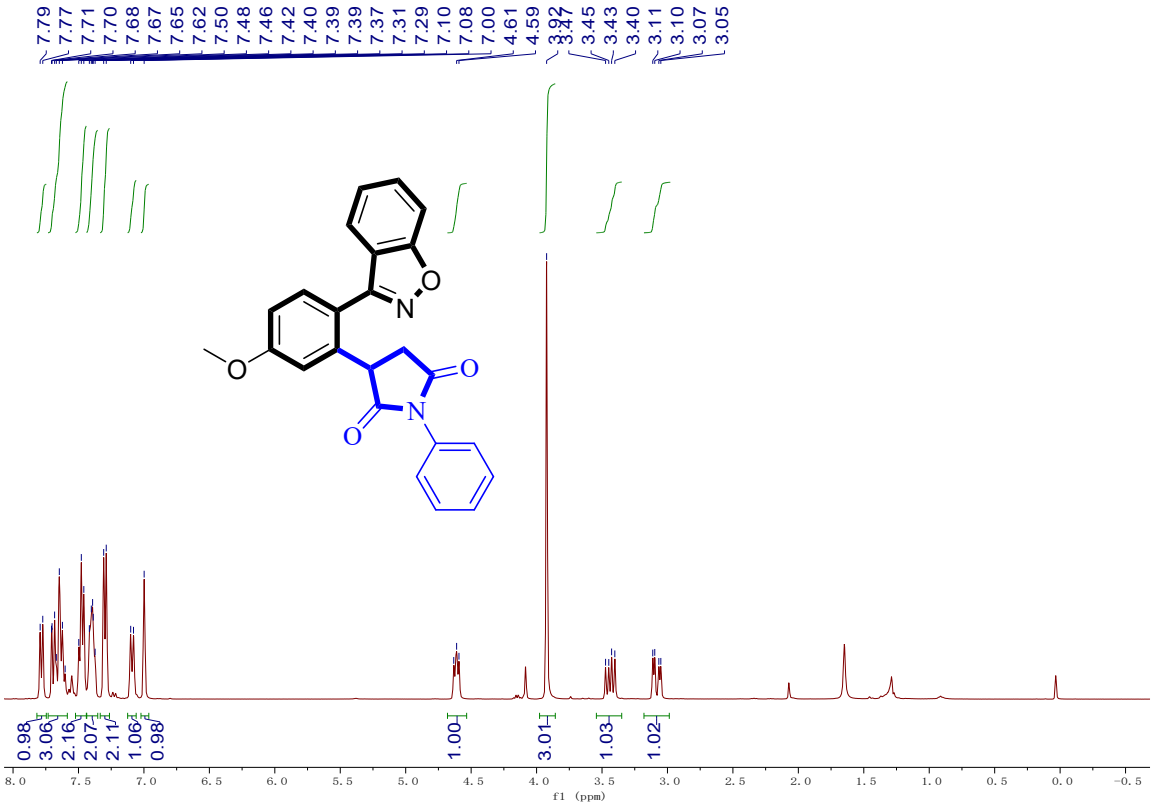
^{1}H NMR (Chloroform-*d*) spectrum of **3ae**



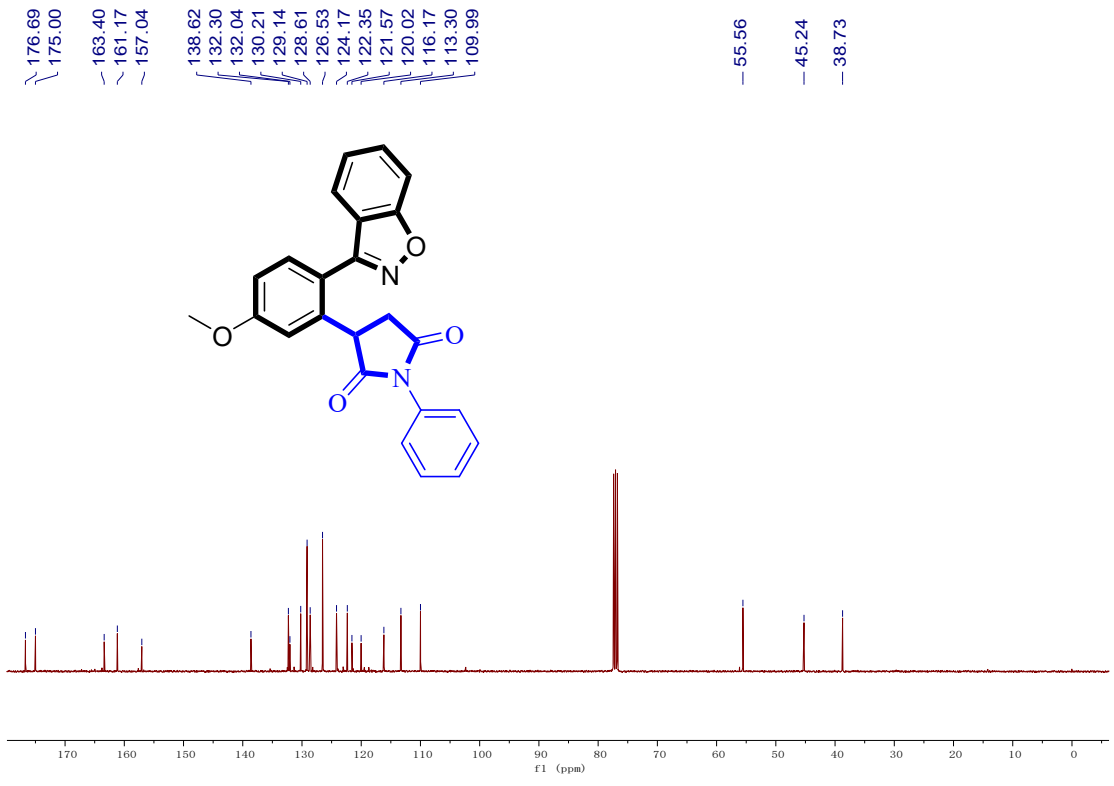
^{13}C NMR (Chloroform-*d*) spectrum of **3ae**



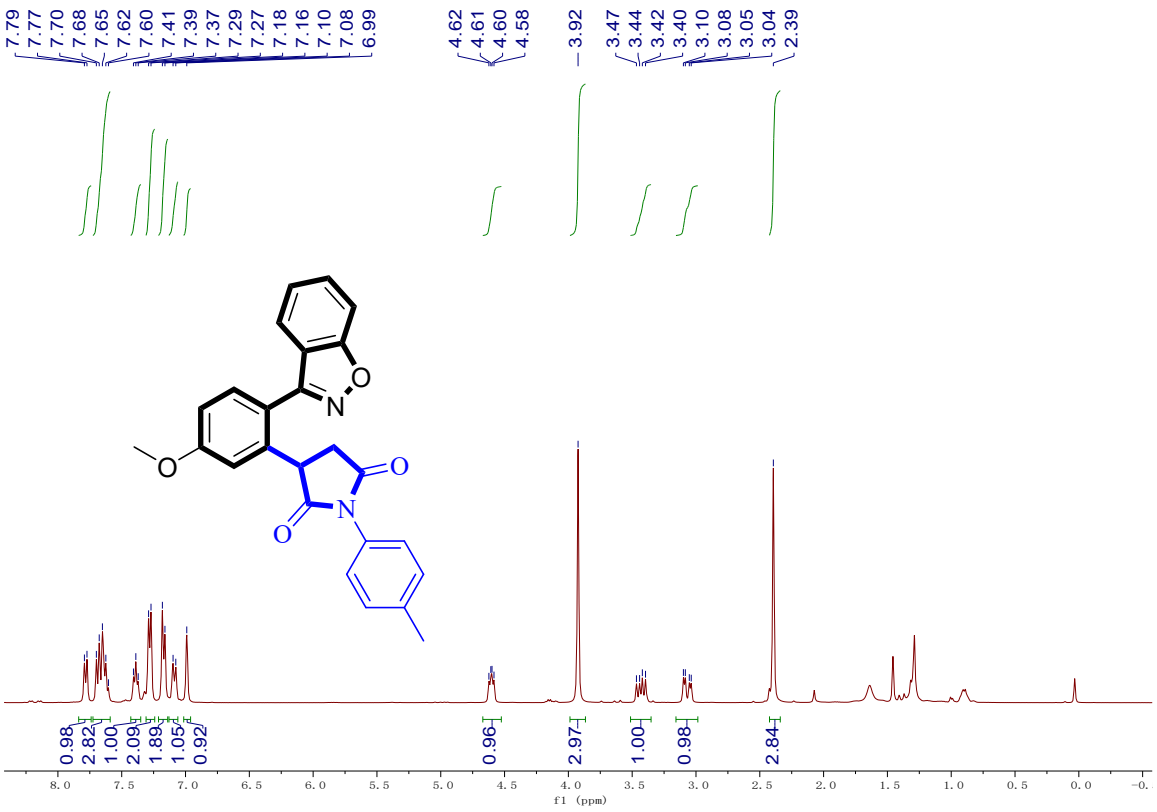
^{1}H NMR (Chloroform-*d*) spectrum of **3af**



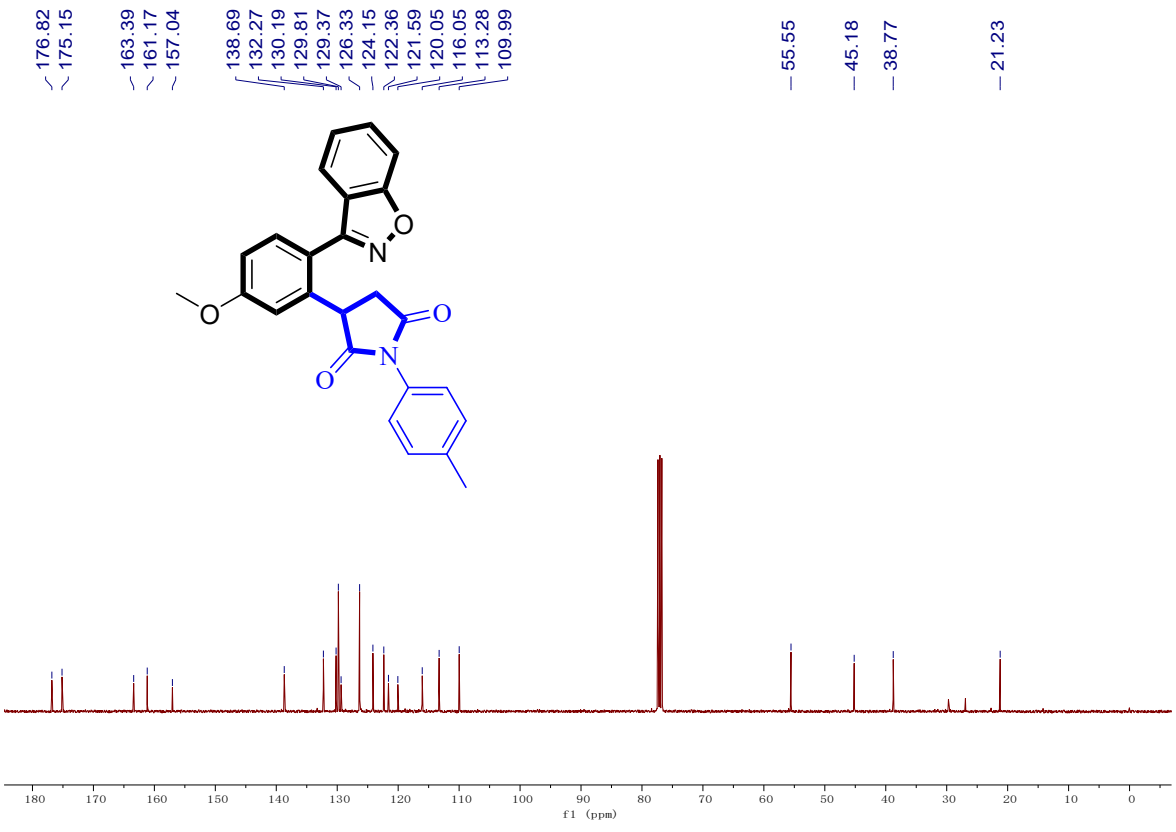
^{13}C NMR (Chloroform-*d*) spectrum of **3af**



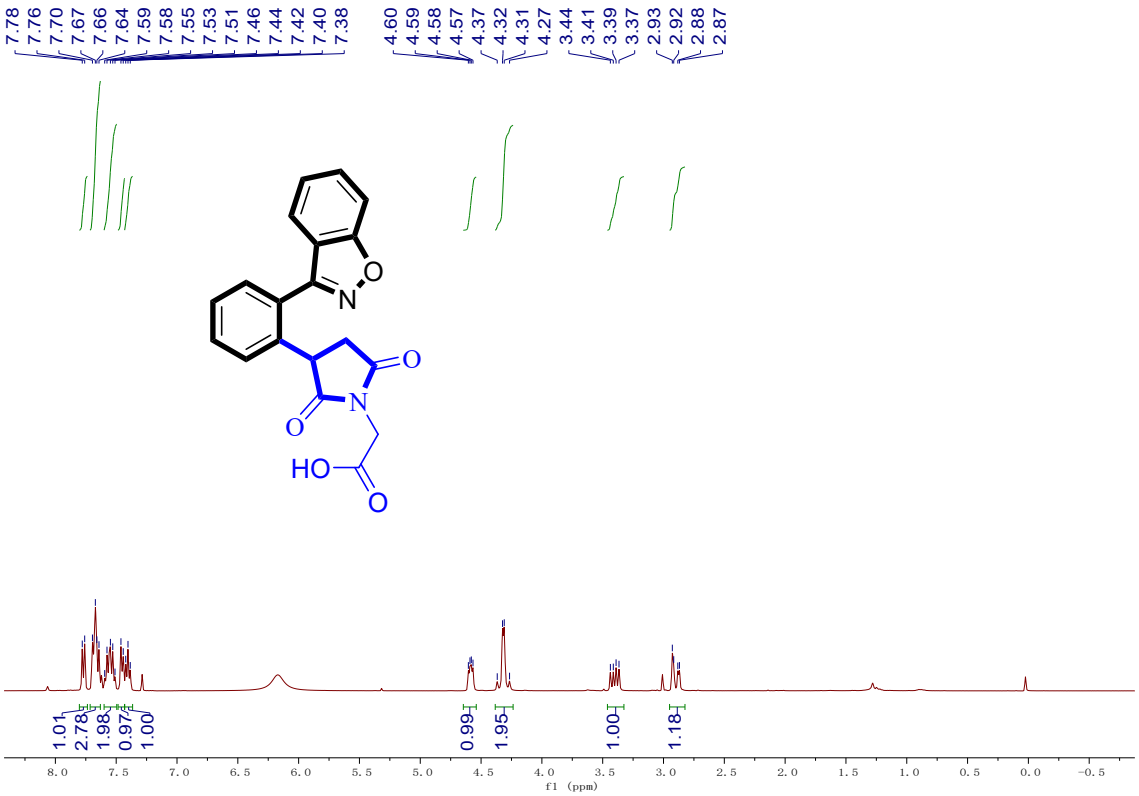
^{1}H NMR (Chloroform-*d*) spectrum of **3ag**



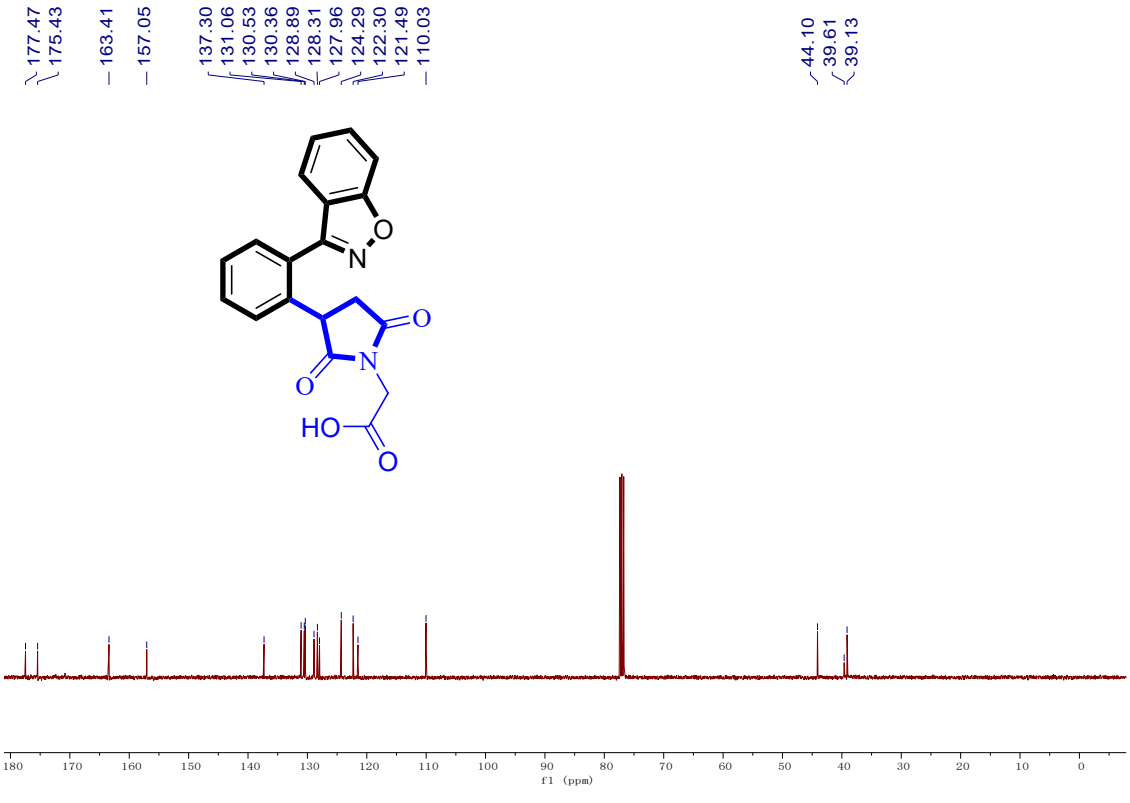
^{13}C NMR (Chloroform-*d*) spectrum of **3ag**



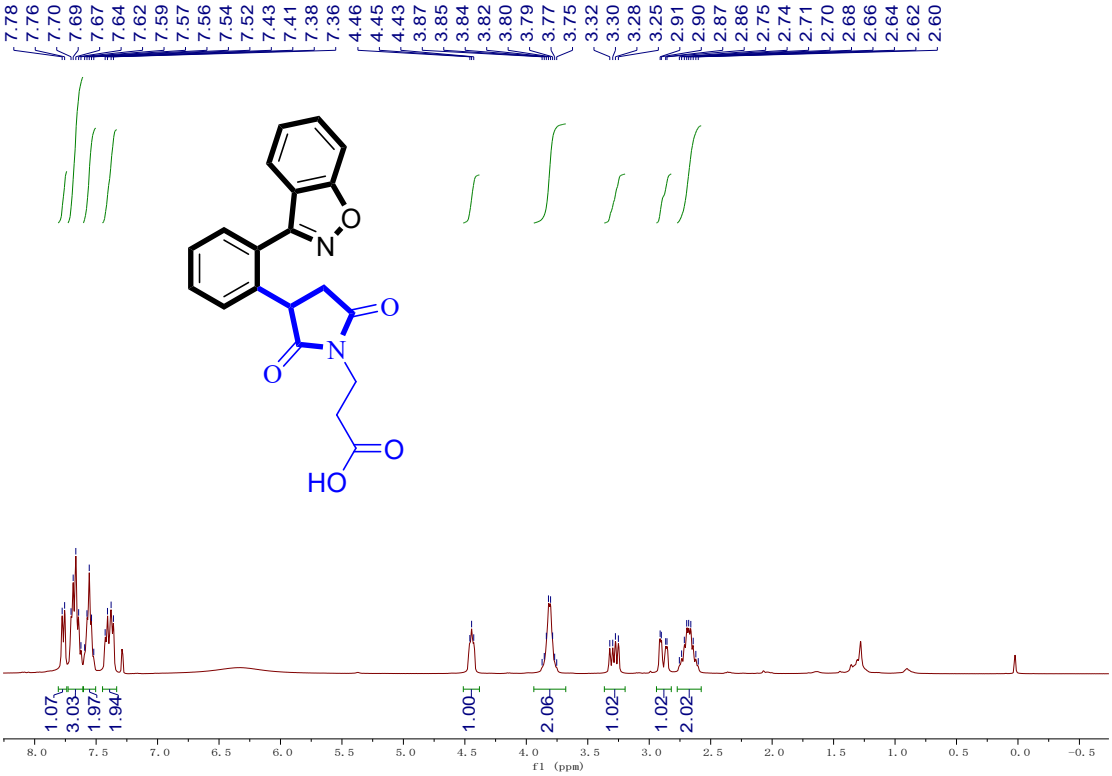
^{1}H NMR (Chloroform-*d*) spectrum of **3ah**



^{13}C NMR (Chloroform-*d*) spectrum of **3ah**



^{1}H NMR (Chloroform-*d*) spectrum of **3ai**



^{13}C NMR (Chloroform-*d*) spectrum of **3ai**