Supporting Information

Silver-Catalyzed Pyrazole Migration and Cycloaddition Reaction of Diazo Pyrazoleamides with Ketimines

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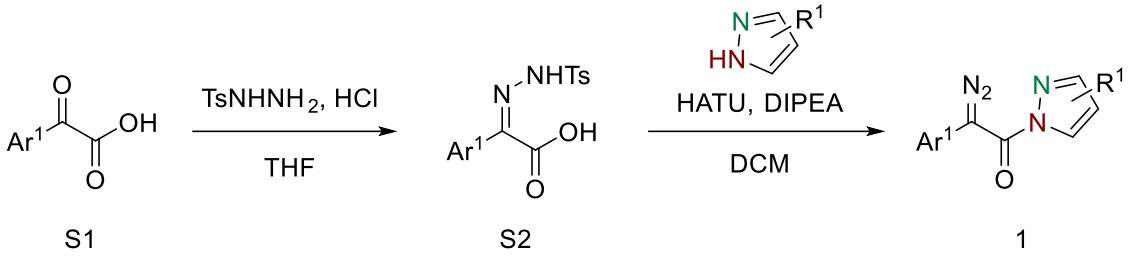
1. General information & materials

General information: All ^{1}H NMR (400 or 500 MHz) and ^{13}C NMR (100 or 125 MHz) and ^{19}F NMR (376 MHz) spectra were recorded on Brucker spectrometers in $CDCl_3$ or DMSO-d_6. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 or 500 MHz spectrometer; chemical shifts were reported in ppm with the solvent signal as reference, and coupling constants (*J*) were given in Hertz. The peak information was described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High-resolution mass spectrometry (HRMS) were recorded on a commercial apparatus (ESI or CI Source).

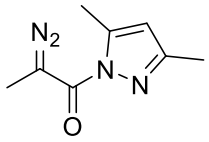
Materials: Solvent CH_2Cl_2 was distilled over calcium hydride. Isatin-derived ketimines were prepared according to the literature method. 4 Å molecular sieve was dried in a Muffle furnace at 250 ℃ over 5 h. All reactions were carried out under nitrogen atmosphere in a well-dried glassware.

2. General procedure for the synthesis and analytical data of diazo compounds 1 & 1'. [1]



Synthesis of S2: To a solution of corresponding acid (10 mmol, 1.0 equiv.) and 4-Methylbenzenesulfonhydrazide (1.86 g, 10 mmol, 1.0 equiv.) in THF (20 mL), was added a small amount of HCl. Then the reaction mixture was stirred at room temperature overnight. When the reaction was completed (monitored by TLC), the solvent was evaporated under vacuum to afford **S2** in > 80% yields, which was used in the next step without further purification.

Synthesis of 1: To a 50-mL oven-dried flask containing a magnetic stirring bar, **S2** (1.5 mmol) in DCM (10 mL), was added DIPEA (0.78 g, 6.0 mmol, 4.0 equiv.) and HATU (0.68 g, 1.8 mmol, 1.2 equiv.) slowly at 0 ℃, and the resulting reaction mixture was stirred at 0 ℃ for 20 min. Then corresponding pyrazole (1.6 mmol, 1.05 equiv.) was added. The reaction mixture was diluted with DCM (20 mL) and washed with 10 % citric acid solution (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and saturated aqueous NaCl (20 mL) in sequence, and the separated organic phase was dried with anhydrous Na_2SO_4. The solvent was evaporated in vacuo after filtration, and the residue was purified by column chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1/100~1/50) to provide diazo compounds **1**.

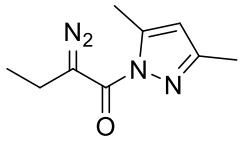


2-diazo-1-(3,5-dimethyl-1H-pyrazol-1-yl)propan-1-one

1a: Green oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (s, 1H), 2.51 (s, 3H), 2.20 (s, 3H), 2.14 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 150.2, 143.4, 109.8, 53.4, 13.9, 13.7, 11.1.

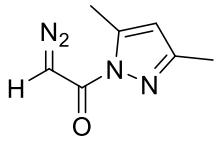


2-diazo-1-(3,5-dimethyl-1H-pyrazol-1-yl)butan-1-one.

1b: Green oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (s, 1H), 2.49 – 2.45 (m, 2H), 2.42 (s, 3H), 2.11 (s, 3H), 1.11 (t, J = 7.5 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 150.0, 143.4, 109.8, 60.8, 18.8, 13.9, 13.7, 11.5.

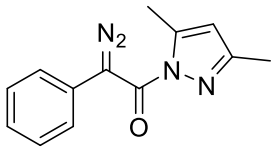


2-diazo-1-(3,5-dimethyl-1H-pyrazol-1-yl)ethan-1-one

1c: Green oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (s, 1H), 5.98 (s, 1H), 2.57 (s, 3H), 2.22 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 151.9, 143.7, 111.3, 49.8, 14.1, 13.8.

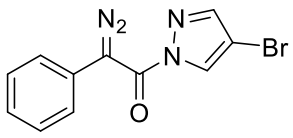


2-diazo-1-(3,5-dimethyl-1H-pyrazol-1-yl)-2-phenylethan-1-one.

1'a: Orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 7.6 Hz, 2H), 7.39 (m, 2H), 7.22 (m, 1H), 5.95 (s, 1H), 2.53 (s, 3H), 2.21 (s, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 150.3, 143.8, 128.9, 126.7, 126.6, 125.7, 110.3, 65.7, 13.9, 13.7.

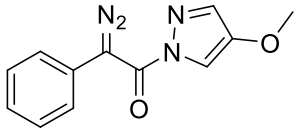


1-(4-bromo-1H-pyrazol-1-yl)-2-diazo-2-phenylethan-1-one.

1'b: Orange oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.60 (s, 1H), 7.55 (m, 2H), 7.43 (m, 2H), 7.28 (m, 1H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 142.8, 129.2, 129.2, 127.2, 125.9, 125.7, 98.2, 64.8.

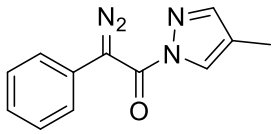


2-diazo-1-(4-methoxy-1H-pyrazol-1-yl)-2-phenylethan-1-one.

1'c: Orange oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 0.9 Hz, 1H), 7.58 – 7.54 (m, 2H), 7.46 – 7.42 (m, 3H), 7.29– 7.25 (m, 1H), 3.80 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 148.8, 133.2, 129.1, 126.9, 126.4, 125.8, 110.6, 64.2, 58.9.

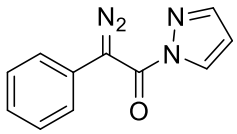


2-diazo-1-(4-methyl-1H-pyrazol-1-yl)-2-phenylethan-1-one.

1'd: Orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.60 – 7.55 (m, 2H), 7.50 (s, 1H), 7.46 – 7.41 (m, 2H), 7.29 – 7.25 (m, 1H), 2.14 (d, J = 0.5 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 143.7, 129.1, 127.2, 126.9, 126.4, 125.9, 119.5, 64.7, 9.0.

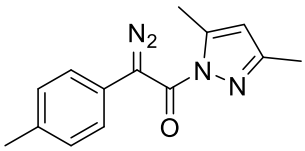


2-diazo-2-phenyl-1-(1H-pyrazol-1-yl)ethan-1-one.

1'e: Orange oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 2.6 Hz, 1H), 7.66 (d, J = 0.5 Hz, 1H), 7.57 (m, 2H), 7.42 (m, 2H), 7.26 (m, 1H), 6.42 (m, 1H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 142.4, 129.2, 129.1, 127.0, 126.2, 125.9, 108.7, 65.0.

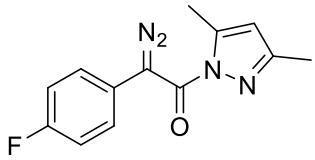


2-diazo-1-(3,5-dimethyl-1H-pyrazol-1-yl)-2-(p-tolyl)ethan-1-one

1'f: Orange oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 5.98 (s, 1H), 2.55 (s, 3H), 2.36 (s, 3H), 2.24 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 150.4, 143.9, 136.7, 129.8, 126.0, 123.5, 110.4, 65.6, 21.2, 14.0, 13.8.



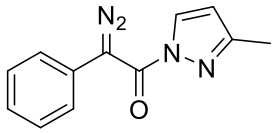
2-diazo-1-(3,5-dimethyl-1H-pyrazol-1-yl)-2-(4-fluorophenyl)ethan-1-one

1'g: Orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.48 (m, 2H), 7.15 – 7.10 (m, 2H), 5.98 (s, 1H), 2.54 (s, 3H), 2.24 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ161.9, 161.6 (d, *J* = 247.2 Hz), 150.5, 143.9, 127.9 (d, *J* = 8.1 Hz), 122.6, 116.0 (d, *J* = 22.0 Hz), 110.4, 60.4, 13.9, 13.7;

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.10.



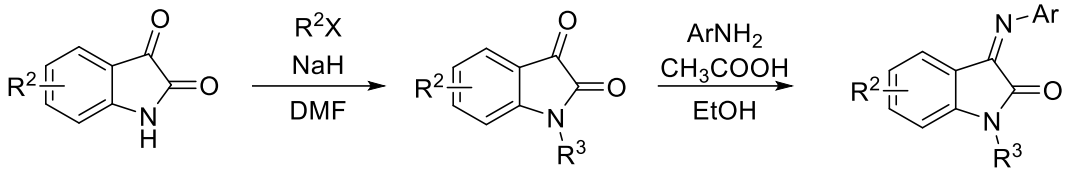
2-diazo-1-(5-methyl-1H-pyrazol-1-yl)-2-phenylethan-1-one

1'h: Orange oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J = 2.7 Hz, 1H), 7.51 – 7.48 (m, 2H), 7.37 – 7.34 (m, 2H), 7.20– 7.17 (m, 1H), 6.16 (d, J = 2.7 Hz, 1H), 2.24 (s, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 152.3, 129.8, 129.0, 126.8, 126.5, 125.8, 109.3, 64.7, 14.0.

3. General Procedure for the Synthesis of ketimine Compounds 2. [2]



Synthesis of S4: To a solution of corresponding isatin (10 mmol, 1.0 equiv.) in DMF (20 mL), was added NaH (12 mmol, 480 mg, 60% dispersion in mineral oil) slowly at 0 ℃. After stirred at 0 ℃ 10 minutes，the corresponding halide (15 mmol) was added in. The reaction mixture was then stirred at room temperature overnight. After the reaction go to completion (monitored by TLC), the mixture was quenched with saturated aqueous NH_4Cl (100 mL), and washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL) in sequence. The separated organic phase was dried with anhydrous Na_2SO_4 and evaporated in vacuo after filtration. The residue was then purified by column chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1/10~1/4) to provide compounds **S4** as dark red solid (90~95% yield).

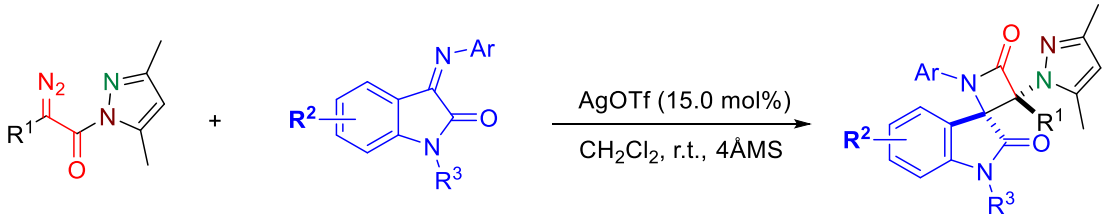
Synthesis of 2: To a solution of **S4** (10 mmol, 1.0 equiv.) in EtOH (20 mL), was added corresponding amine and 5 mol% catalytic amount of AcOH. The reaction mixture was then stirred at reflux temperature overnight. After the reaction go to completion (monitored by TLC), the solvent was evaporated and the residue was purified by column chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1/10~1/4) to provide ketimine compounds **2** as red solid (85~95% yield).

4. Experimental procedures

4.1 General procedure for optimization of conditions of cycloaddition reaction

To a 10 mL oven-dried Schlenk reaction tube equipped with a magnetic stir bar, was added metal catalyst, solvent (1.0 mL), 4 Å molecular sieve (100 mg), and isatin-derived ketimines **2a** (31.2 mg, 0.1 mmol). The Schlenk tube was sealed with a septum, evacuated and refilled with nitrogen (3 times). The solution of the diazo compound **1a** (26.7 mg, 0.15 mmol, 1.5 eq) in 1.0 mL solvent (same as above) was added to the mixture for 1 h via a syringe pump at indicate temperature. After completion of the addition, stirring was continued at indicate temperature until the diazo compound was consumed. The solvent was evaporated under vacuum after filtering through celite. The crude mixture was use directly for diastereoselectivities determination via crude ^{1}H NMR spectral analyses and then purified by column chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1/30~1/5) to give the product **3a**.

4.2 General procedure for the diastereoselective cycloaddition reaction

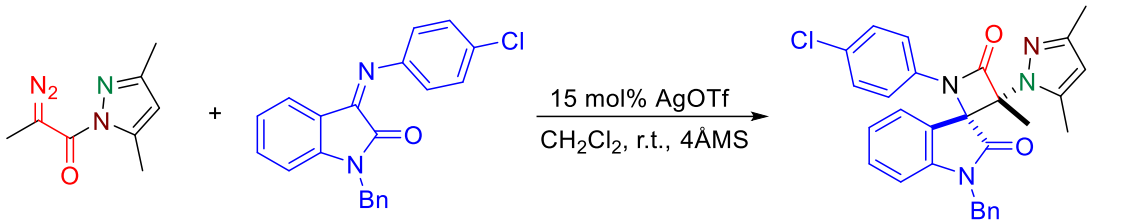


1 **2** **3 or 5**

To a 10 mL oven-dried Schlenk reaction tube equipped with a magnetic stir bar, was added AgOTf (7.7 mg, 15.0 mol %), CH_2Cl_2 (2.0 mL), isatin-derived ketimines **2** (0.2 mmol), and 4 Å molecular sieve (200 mg). The Schlenk tube was sealed with a septum, evacuated and refilled with nitrogen (3 times). The solution of the diazo compound **1** (0.3 mmol, 1.5 eq) in 2.0 mL CH_2Cl_2 was then added for 1 h via a syringe pump at room temperature. The reaction was then stirred at indicate temperature until the diazo compound was consumed completely. The solvent was evaporated under vacuum after filtering through celite. The crude mixture was use directly for diastereoselectivities determination via crude ^{1}H NMR spectral analyses

and then purified by column chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1/30~1/5) to give product **3** or **5**.

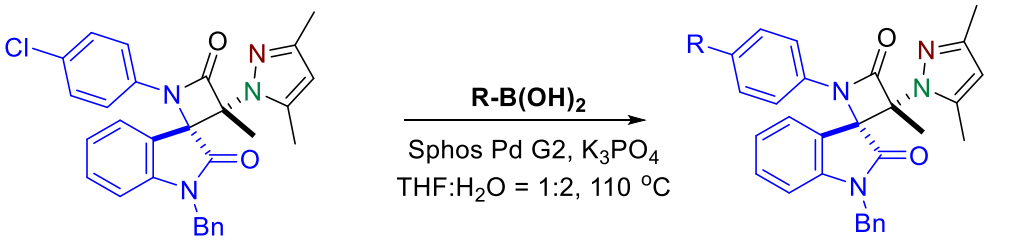
4.3 Procedure for the gram scale three-component reaction



1a (3.8 mmol) **2e** (2.5 mmol) **3e:** 93% yield (1.10 g), 90:10 *dr*

To a 100 mL oven-dried Schlenk reaction tube equipped with a magnetic stir bar, was added AgOTf (96.4 mg, 15.0 mol %), CH_2Cl_2 (25.0 mL), isatin-derived ketimines **2e** (865.2 mg, 2.5 mmol), and 4 Å molecular sieve (300 mg). The Schlenk tube was sealed with a septum, evacuated and refilled with nitrogen (3 times). The solution of the diazo compound **1a** (676.4 mg, 3.8 mmol, 1.5 eq) in 25.0 mL CH_2Cl_2 was then added to the reaction mixture for 1 h via a syringe pump at indicate temperature. The reaction was then stirred at indicate temperature until the diazo compound was consumed completely. The solvent was evaporated under vacuum after filtering through celite. The crude mixture was use directly for diastereoselectivities determination via crude ^{1}H NMR spectral analyses and then purified by column chromatography on silica gel (eluent: EtOAc/light petroleum ether = 1/30~1/5) to give the product **3e** (93% yield, 90:10 *dr*).

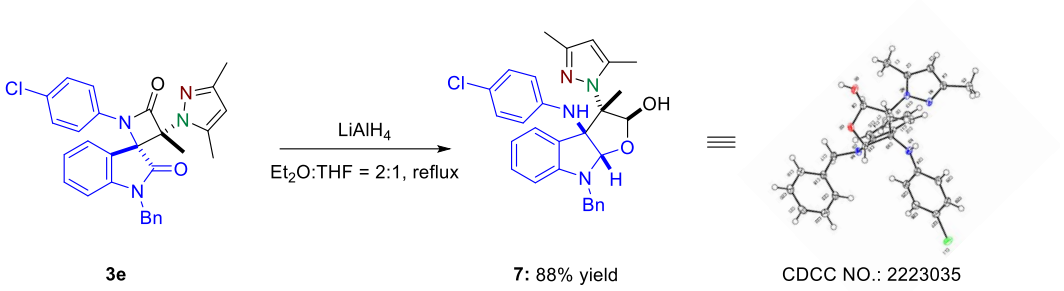
5. Product derivatizations



3e

6a: R = Ph, 84% yield
6b: R = Cyclopropane, 78% yield

Synthesis of 6: To a 25-mL flask containing a magnetic stirring bar, was added **3e** (100 mg, 0.2 mmol), 1.0 mL of THF, 2.0 mL of H_2O, boronic acid (0.4 mmol), Sphos Pd G2 (7.2 mg, 5 %), K_3PO_4 (127.2 mg, 0.6 mmol). The mixture was then reacted at indicate temperature until the compound **3e** was consumed completely. The solvent was evaporated under vacuum after filtering through Celite. Extracted with ethyl acetate (5 mL * 3). The organic phase was collected and washed with brine, dried over anhydrous Na_2SO_4. The solvent was removed in vacuo after filtration and the residue was purified by flash chromatography (eluent: EtOAc/light petroleum ether = 1/10~1/2) to give **6** as a white powder in corresponding yield.



3e **7:** 88% yield CDCC NO.: 2223035

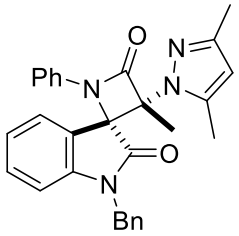
Synthesis of 7: To a 25-mL flask containing a magnetic stirring bar, was added **3e** (100 mg, 0.2 mmol), $LiAlH_4$ (38 mg, 1.0 mmol), THF (1.0 mL), Et_2O (2.0 mL) were added to the above reaction flask. The mixture was then reacted at indicate temperature until the compound **3e** was consumed completely. The reaction was quenched with wet Na_2SO_4 and extracted with ethyl acetate (5 mL * 2). The organic phase was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo after filtration and the residue was purified by flash chromatography (eluent: EtOAc/light petroleum ether = 1/10~1/2) to give **7** as a white powder (88 mg, 88% yield).

6. References

(1) R. M. Stephanie , Peter Wipf, *Synthesis* **2019**, 51, 213.

(2) (a) M. Rajopadhye, F. D. Dopp, *J. Heterocycl. Chem*. **1985**, 22, 93; (b) R. Bouhfid, N. Joly, M. Massoui, R. Cecchelli, V. Lequart, P. Martin, E. M. Assassi, *Heterocycles*, **2005**, 65, 2949.

7. Analytical data of compounds 3, 4, 5, 5', 6, 7, 8



3a

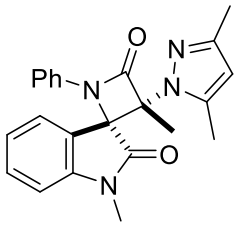
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3a: 91% yield, 93:7 *dr* (*cis:trans*), white solid, mp 164.6 - 166.5℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ7.35 – 7.26 (m, 7H), 7.20 (t, *J* = 7.8 Hz, 2H), 7.12 – 7.01 (m, 4H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.78 (s, 1H), 5.05 (d, *J* = 15.8 Hz, 1H), 4.62 (d, *J* = 15.8 Hz, 1H), 2.58 (s, 3H), 2.13 (s, 3H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 163.7, 149.1, 144.0, 136.0, 135.2, 130.9, 129.4(*two carbon signals overlapped*), 128.9, 127.8, 127.3, 126.3, 125.2, 122.7, 121.4, 117.7, 110.7, 107.0, 78.7, 70.8, 44.4, 22.2, 13.8, 13.4.

HRMS-ESI: calculated for $C_{29}H_{26}N_4O_2$ $[M + Na]^+$: 485.1948, found: 485.1949



3b

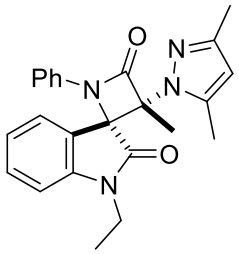
3-(3,5-dimethyl-1H-pyrazol-1-yl)-1',3-dimethyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3b: 86% yield, 93:7 *dr* (*cis:trans*), white solid, mp 147.9 - 150.5℃.

^{1}H NMR (400 MHz, $CDCl_3$)δ 7.43 (t, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 7.0 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 2H), 7.10 – 7.04 (m, 4H), 6.97 (d, *J* = 7.8 Hz, 1H), 5.76 (s, 1H), 3.12 (s, 3H), 2.52 (s, 3H), 2.10 (s, 3H), 1.99 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 163.5, 149.1, 144.9, 136.2, 131.2, 129.5 (*two carbon signals overlapped*), 126.3, 125.3, 122.7, 121.3, 117.8, 109.6, 107.1, 78.8, 70.7, 26.7, 22.3, 13.7, 13.3.

HRMS-ESI: calculated for $C_{23}H_{22}N_4O_2$ $[M + H]^+$: 387.1816, found: 387.1817



3c

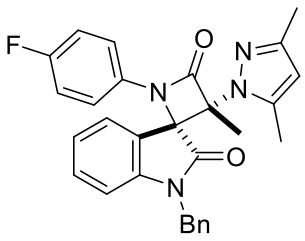
3-(3,5-dimethyl-1H-pyrazol-1-yl)-1'-ethyl-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3c: 88% yield, 90:10 *dr* (*cis:trans*), yellow solid, mp 156.7 - 159.2℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (td, *J* = 7.8, 1.0 Hz, 1H), 7.27 (d, *J* = 7.9 Hz, 1H), 7.24 – 7.15 (m, 2H), 7.14 – 7.01 (m, 4H), 6.98 (d, *J* = 7.9 Hz, 1H), 5.75 (s, 1H), 3.85 (dq, *J* = 14.5, 7.3 Hz, 1H), 3.46 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.54 (s, 3H), 2.08 (s, 3H), 2.01 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 163.6, 148.9, 144.0, 136.1, 131.0, 129.4 (*two carbon signals overlapped*), 126.5, 125.2, 122.4, 121.4, 117.7, 109.4, 106.9, 78.5, 70.7, 35.2, 22.3, 13.6, 13.3, 12.3.

HRMS-ESI: calculated for $C_{24}H_{24}N_4O_2$ $[M + H]^+$: 401.1972, found: 401.1971



3d

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-(4-fluorophenyl)-3-methylspiro[azetidine-2,3'-indoline]-2',4-dione

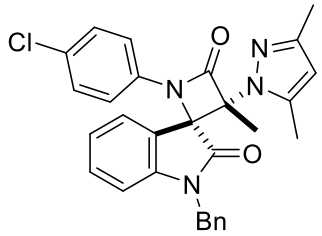
3d: 92% yield, 89:11 *dr* (*cis:trans*), white solid, mp 159.4 - 161.3℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 7H), 7.09 – 7.02 (m, 3H), 6.92 – 6.86 (m, 2H), 6.80 (d, *J* = 7.8 Hz, 1H), 5.77 (s, 1H), 5.03 (d, *J* = 15.8 Hz, 1H), 4.60 (d, *J* = 15.8 Hz, 1H), 2.55 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 163.5, 159.8 (d, *J* = 245.5 Hz), 149.2, 144.1, 135.2, 132.2 (d, *J* = 2.8 Hz), 131.1, 129.0 (*two carbon signals overlapped*), 127.9, 127.4, 126.3, 122.8, 121.1, 119.4 (d, *J* = 8.1 Hz), 116.3 (d, *J* = 22.9 Hz), 110.8, 107.1, 79.0, 71.0, 44.5, 22.3, 13.8, 13.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.91.

HRMS-ESI: calculated for $C_{29}H_{25}FN_4O_2$ $[M + Na]^+$: 503.1854, found: 503.1853



3e

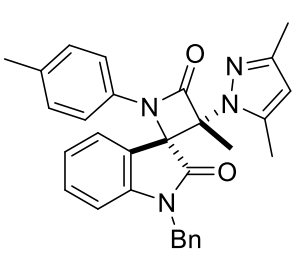
1'-benzyl-1-(4-chlorophenyl)-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methylspiro[azetidine-2,3'-indoline]-2',4-dione

3e: 90% yield, 90:10 *dr* (*cis:trans*), yellow solid, mp 167.3 - 169.4℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 7H), 7.16 (d, *J* = 8.7 Hz, 2H), 7.06 – 7.01 (m, 3H), 6.80 (d, *J* = 7.9 Hz, 1H), 5.77 (s, 1H), 5.02 (d, *J* = 15.7 Hz, 1H), 4.61 (d, *J* = 15.8 Hz, 1H), 2.54 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 163.6, 149.2, 144.0, 135.1, 134.5, 131.1, 130.5, 129.5, 129.0 (*two carbon signals overlapped*), 127.9, 127.4, 126.3, 122.8, 121.0, 118.9, 110.8, 107.1, 79.0, 70.9, 44.5, 22.2, 13.8, 13.4.

HRMS-ESI: calculated for $C_{29}H_{25}ClN_4O_2$ $[M + Na]^+$: 519.1558, found: 519.1557



3f

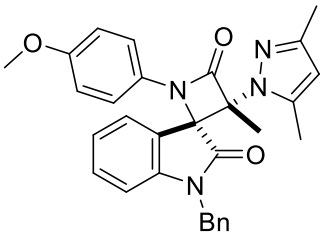
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-(p-tolyl)spiro[azetidine-2, 3'-indoline]-2',4-dione

3f: 89% yield, 93:7 *dr* (*cis:trans*), white solid, mp 206.8 - 208.9℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.29 – 7.26 (m, 5H), 7.04 – 6.97 (m, 5H), 6.77 (d, *J* = 8.1 Hz, 1H), 5.76 (s, 1H), 5.03 (d, *J* = 15.8 Hz, 1H), 4.60 (d, *J* = 15.8 Hz, 1H), 2.57 (s, 3H), 2.25 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 163.5, 149.1, 144.1, 135.3, 135.1, 133.6, 130.9, 129.9, 129.0 (*two carbon signals overlapped*), 127.8, 127.4, 126.3, 122.6, 121.6, 117.7, 110.6, 107.0, 78.7, 70.9, 44.4, 22.2, 21.0, 13.8, 13.4.

HRMS-ESI: calculated for $C_{30}H_{28}N_4O_2$ $[M + Na]^+$: 499.2104, found: 499.2105



3g

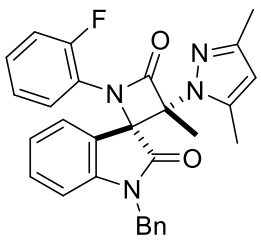
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-(4-methoxyphenyl)-3-methylspiro[azetidine-2,3'-indoline]-2',4-dione

3g: 88% yield, 90:10 *dr* (*cis:trans*), white solid, mp 171.5 - 174.5℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 7H), 7.06 – 7.02 (m, 3H), 6.75 (dd, *J* = 20.4, 8.4 Hz, 3H), 5.77 (s, 1H), 5.05 (d, *J* = 15.8 Hz, 1H), 4.59 (d, *J* = 15.8 Hz, 1H), 3.73 (s, 3H), 2.58 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 163.3, 157.1, 149.1, 144.1, 135.2, 130.9, 129.3, 129.0 (*two carbon signals overlapped*), 127.8, 127.3, 126.3, 122.7, 121.5, 119.4, 114.6, 110.6, 107.0, 78.7, 71.1, 55.6, 44.4, 22.2, 13.8, 13.4.

HRMS-ESI: calculated for $C_{30}H_{28}N_4O_3$ $[M + Na]^+$: 515.2054, found: 515.2054



3h

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-(2-fluorophenyl)-3-methylspiro[azetidine-2,3'-indoline]-2',4-dione

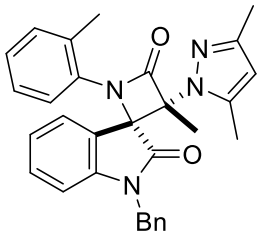
3h: 83% yield, 93:7 *dr* (*cis:trans*), white solid, mp 188.7 - 191.3℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.95 (m, 1H), 7.34 – 7.28 (m, 2H), 7.26 – 7.17 (m, 5H), 7.14 – 7.07 (m, 2H), 6.98 – 6.89 (m, 2H), 6.64 (d, *J* = 7.8 Hz, 1H), 5.77 (s, 1H), 5.09 (d, *J* = 15.9 Hz, 1H), 4.42 (d, *J* = 16.0 Hz, 1H), 2.57 (s, 3H), 2.12 (s, 3H), 2.05 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 164.9, 153.3 (d, *J* = 248.4 Hz) , 149.1, 144.6, 135.3, 130.7, 128.9 (*two carbon signals overlapped*), 127.6, 127.4 (d, *J* = 7.6 Hz), 127.1, 125.6, 124.9 (d, *J* = 3.5 Hz), 123.8, 123.0 (d, *J* = 11.8 Hz), 122.2, 122.1, 116.6 (d, *J* = 20.0 Hz), 110.4, 107.1, 79.1, 73.5, 44.4, 22.6, 13.8, 13.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -123.60.

HRMS-ESI: calculated for $C_{29}H_{25}N_4O_2$ $[M + Na]^+$: 503.1854, found: 503.1854



3i

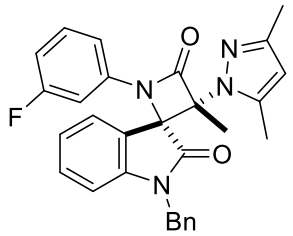
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-(o-tolyl)spiro[azetidine-2,3'-indoline]-2',4-dione

3i: 84% yield, 91:9 *dr* (*cis:trans*), white solid, mp 205.5 - 207.7℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.4 Hz, 1H), 7.32 – 7.27 (m, 3H), 7.23 – 7.15 (m, 5H), 7.10 (d, *J* = 7.8 Hz, 1H), 7.06 – 7.02 (m, 2H), 6.64 (d, *J* = 7.8 Hz, 1H), 5.79 (s, 1H), 5.09 (d, *J* = 15.9 Hz, 1H), 4.49 (d, *J* = 15.9 Hz, 1H), 2.62 (s, 3H), 2.55 (s, 3H), 2.15 (d, *J* = 10.7 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 164.4, 149.0, 144.7, 135.3, 135.1, 133.3, 131.6, 130.9, 128.9, 128.5, 127.7, 127.1, 126.8, 126.4, 124.8, 122.5, 121.7, 110.5, 106.9, 100.1, 78.0, 73.9, 44.4, 23.2, 19.3, 13.8, 13.5.

HRMS-ESI: calculated for $C_{30}H_{28}N_4O_2$ $[M + Na]^+$: 499.2104, found: 499.2103



3j

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-(3-fluorophenyl)-3-methylspiro[azetidine-2,3'-indoline]-2',4-dione

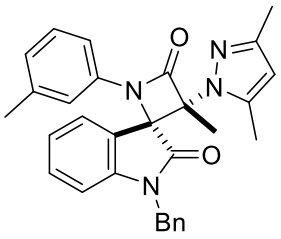
3j: 91% yield, 89:11 *dr* (*cis:trans*), yellow solid, mp 148.2 - 150.4℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 7H), 7.13 (td, *J* = 8.2, 6.4 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.96 (dt, *J* = 10.0, 2.1 Hz, 1H), 6.81 – 6.72 (m, 3H), 5.77 (s, 1H), 5.03 (d, *J* = 15.8 Hz, 1H), 4.62 (d, *J* = 15.8 Hz, 1H), 2.55 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 163.8, 163.0 (d, *J* = 247.0 Hz) , 149.2, 144.0, 137.3 (d, *J* = 10.3 Hz), 135.1, 131.2, 130.8 (d, *J* = 9.3 Hz), 129.0, 127.9, 127.3, 126.3, 122.8, 121.0, 113.0 (d, *J* = 3.0 Hz) , 112.2 (d, *J* = 21.3 Hz) , 110.9, 107.2, 105.6 (d, *J* = 26.3 Hz), 100.1, 79.0, 71.0, 44.5, 22.3, 13.8, 13.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -110.12.

HRMS-ESI: calculated for $C_{29}H_{25}N_4O_2$ $[M + Na]^+$: 503.1854, found: 503.1855



3k

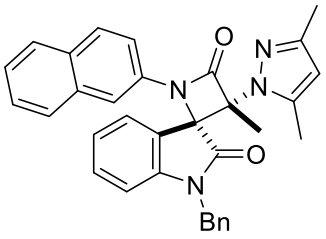
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-(m-tolyl)spiro[azetidine-2,3'-indoline]-2',4-dione

3k: 89% yield, 90:10 *dr* (*cis:trans*), white solid, mp 139.7 - 142.8℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 7H), 7.15 (s, 1H), 7.03 (t, *J* = 7.7 Hz, 2H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 5.77 (s, 1H), 4.98 (d, *J* = 15.8 Hz, 1H), 4.65 (d, *J* = 15.8 Hz, 1H), 2.57 (s, 3H), 2.22 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 163.7, 149.1, 144.0, 139.5, 136.0, 135.3, 130.9, 129.1, 129.0, 127.8, 127.4, 126.3, 126.2, 122.7, 121.5, 118.7, 114.4, 110.6, 107.0, 78.6, 70.8, 44.4, 22.3, 21.6, 13.8, 13.4.

HRMS-ESI: calculated for $C_{30}H_{28}N_4O_2$ $[M + Na]^+$: 499.2104, found: 499.2105



3l

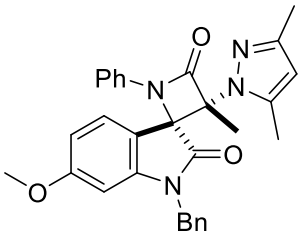
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-(naphthalen-2-yl)spiro[azetidine-2,3'-indoline]-2',4-dione

3l: 84% yield, 94:6 *dr* (*cis:trans*), yellow solid, mp 172.8 - 175.3℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 2H), 7.51 (d, *J* = 7.3 Hz, 1H), 7.41 – 7.29 (m, 11H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 5.79 (s, 1H), 4.99 (d, *J* = 15.7 Hz, 1H), 4.73 (d, *J* = 15.7 Hz, 1H), 2.60 (s, 3H), 2.14 (s, 3H), 2.11 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 163.9, 149.2, 144.1, 135.3, 133.7, 133.4, 131.0, 131.0, 129.6, 129.1 (*two carbon signals overlapped*), 127.9, 127.8, 127.7, 127.5, 126.9, 126.4, 125.7, 122.7, 121.4, 117.3, 114.9, 110.7, 107.1, 78.8, 71.0, 44.5, 22.3, 13.8, 13.4.

HRMS-ESI: calculated for $C_{33}H_{28}N_4O_2$ $[M + Na]^+$: 535.2104, found: 535.2103



3m

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-6'-methoxy-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

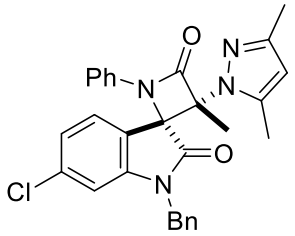
3m: 92% yield, 93:7 *dr* (*cis:trans*), yellow solid, mp 166.8 - 168.3℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.26 – 7.21 (m, 3H), 7.19 – 7.15 (m, 3H), 7.08 – 7.03 (m, 3H), 6.49 (d, *J* = 8.2 Hz, 1H), 6.35 (s, 1H), 5.74 (s, 1H), 4.96

(d, *J* = 15.7 Hz, 1H), 4.58 (d, *J* = 15.8 Hz, 1H), 3.72 (s, 3H), 2.53 (s, 3H), 2.10 (s, 3H), 2.03 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 163.9, 162.1, 149.0, 145.4, 136.2, 135.2, 129.4, 129.0 (*two carbon signals overlapped*), 127.9, 127.4, 127.3, 125.2, 117.7, 112.9, 107.0, 106.5, 98.8, 78.5, 70.6, 55.6, 44.5, 22.3, 13.8, 13.4.

HRMS-ESI: calculated for $C_{30}H_{28}N_4O_3$ $[M + Na]^+$: 515.2054, found: 515.2054



3n

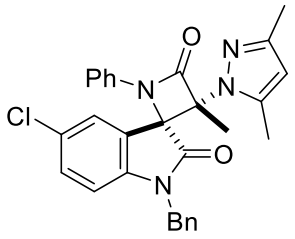
1'-benzyl-6'-chloro-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3n: 88% yield, 91:9 *dr* (*cis:trans*), white solid, mp 154.1 - 158.2℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 3H), 7.25 – 7.22 (m, 2H), 7.21 – 7.16 (m, 3H), 7.08 – 6.99 (m, 4H), 6.76 (s, 1H), 5.74 (s, 1H), 4.97 (d, *J* = 15.8 Hz, 1H), 4.57 (d, *J* = 15.8 Hz, 1H), 2.53 (s, 3H), 2.10 (s, 3H), 2.02 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 163.4, 149.3, 145.2, 136.9, 135.9, 134.7, 129.5, 129.1 (*two carbon signals overlapped*), 128.1, 127.3, 127.1, 125.5, 122.7, 119.8, 117.6, 111.4, 107.1, 78.9, 70.4, 44.6, 22.3, 13.8, 13.4.

HRMS-ESI: calculated for $C_{29}H_{25}N_4O_2$ $[M + Na]^+$: 519.1558, found: 519.1559



3o

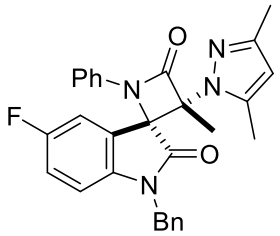
1'-benzyl-5'-chloro-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3o: 86% yield, 93:7 *dr* (*cis:trans*), white solid, mp 219.2 - 220.5℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.25 – 7.16 (m, 7H), 7.09 – 7.01 (m, 3H), 6.67 (d, *J* = 8.2 Hz, 1H), 5.73 (s, 1H), 4.96 (d, *J* = 15.8 Hz, 1H), 4.58 (d, *J* = 15.8 Hz, 1H), 2.51 (s, 3H), 2.08 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 163.2, 149.2, 142.4, 135.8, 134.7, 130.8, 129.5, 129.0 (*two carbon signals overlapped*), 128.2, 127.9, 127.2, 126.4, 125.4, 123.2, 117.5, 111.6, 107.0, 78.8, 70.5, 44.5, 22.3, 13.7, 13.3.

HRMS-ESI: calculated for $C_{29}H_{25}N_4O_2$ $[M + Na]^+$: 519.1558, found: 519.1558



3p

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-5'-fluoro-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

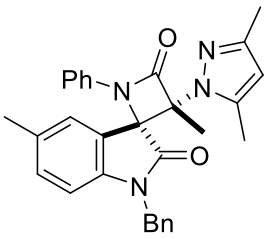
3p: 93% yield, 93:7 *dr* (*cis:trans*), white solid, mp 210.3 - 213.7℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ7.31 – 7.28 (m, 2H), 7.25 – 7.21 (m, 3H), 7.19 – 7.16 (m, 2H), 7.08 – 7.00 (m, 4H), 6.99 – 6.92 (m, 1H), 6.67 (dd, *J* = 8.5, 3.9 Hz, 1H), 5.73 (s, 1H), 4.99 (d, *J* = 15.8 Hz, 1H), 4.56 (d, *J* = 15.8 Hz, 1H), 2.52 (s, 3H), 2.09 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 163.4, 158.9 (d, *J* = 242.8 Hz), 149.3, 140.0, 135.9, 134.9, 129.5, 129.1 (*two carbon signals overlapped*), 128.0, 127.3, 125.5, 123.1 (d, *J* = 7.8 Hz), 117.6, 117.4 (d, *J* = 23.4 Hz), 114.3 (d, *J* = 25.5 Hz), 111.4 (d, *J* = 7.9 Hz), 107.1, 78.9, 70.8, 44.6, 22.3, 13.8, 13.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -119.44.

HRMS-ESI: calculated for $C_{29}H_{25}N_4O_2$ $[M + Na]^+$: 503.1854, found: 503.1854



3q

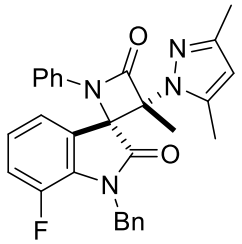
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3,5'-dimethyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3q: 90% yield, 94:6 *dr* (*cis:trans*), white solid, mp 204.5 - 206.8℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.30 (m, 2H), 7.27 – 7.26 (m, 3H), 7.22 – 7.19 (m, 2H), 7.11 – 7.06 (m, 7.6 Hz, 5H), 6.67 (d, *J* = 7.9 Hz, 1H), 5.76 (s, 1H), 5.01 (d, *J* = 15.8 Hz, 1H), 4.60 (d, *J* = 15.8 Hz, 1H), 2.56 (s, 3H), 2.27 (s, 3H), 2.12 (s, 3H), 2.07 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 163.7, 149.0, 141.6, 136.2, 135.4, 132.3, 131.3, 129.4, 128.9 (*two carbon signals overlapped*), 127.8, 127.4, 127.0, 125.2, 121.4, 117.7, 110.4, 107.0, 78.6, 70.9, 44.4, 22.3, 21.2, 13.8, 13.4.

HRMS-ESI: calculated for $C_{30}H_{28}N_4O_2$ $[M + Na]^+$: 499.2104, found: 499.2104



3r

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-7'-fluoro-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3r: 90% yield, 90:10 *dr* (*cis:trans*), white solid, mp 150.3 - 152.9℃.

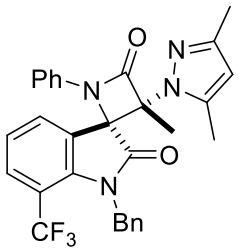
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 5H), 7.19 – 7.15 (m, 2H), 7.12 – 7.06 (m, 3H), 7.04 – 6.96 (m, 3H), 5.77 (s, 1H), 4.97 (d, *J* = 15.4 Hz, 1H), 4.89 (d, *J* = 15.4 Hz, 1H), 2.55 (s, 3H), 2.12 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 163.3, 149.3, 148.1 (d, *J* = 245.9 Hz), 136.5, 135.8, 130.7 (d, *J* = 9.3 Hz), 129.4, 128.7 (*two carbon signals overlapped*), 127.8 (d,

J = 3.9 Hz), 125.4, 124.5, 124.4, 123.4 (d, *J* = 6.4 Hz), 122.3 (d, *J* = 3.2 Hz), 119.3 (d, *J* = 19.6 Hz) , 117.7, 107.2, 79.0, 70.7, 46.0, 22.1, 13.8, 13.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -131.45.

HRMS-ESI: calculated for $C_{29}H_{25}FN_4O_2$ $[M + H]^+$: 481.2034, found: 481.2033



3s

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-phenyl-7'-(trifluoromethyl)spiro[azetidine-2,3'-indoline]-2',4-dione

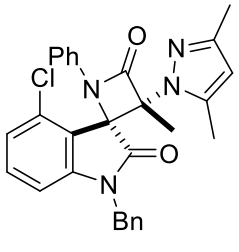
3s: 72% yield, 93:7 *dr* (*cis:trans*), white solid, mp 149.2 - 151.2℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.1 Hz, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.25 – 7.15 (m, 6H), 7.13 – 7.03 (m, 5H), 5.74 (s, 1H), 5.17 (d, *J* = 16.9 Hz, 1H), 4.89 (d, *J* = 16.9 Hz, 1H), 2.52 (s, 3H), 2.14 (s, 3H), 2.03 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 163.4, 149.4, 143.7, 142.6, 142.5, 135.8, 135.6, 129.6, 129.3 (q, *J* = 6.0 Hz), 128.4, 127.1, 126.0, 125.6, 124.6, 123.2(q, *J* = 270.1 Hz), 122.1, 117.8, 114.4 (q, *J* = 33.4 Hz), 107.3, 79.6, 69.4, 46.8 (q, *J* = 4.7 Hz), 22.0, 13.8, 13.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -54.68.

HRMS-ESI: calculated for $C_{30}H_{25}F_3N_4O_2$ $[M + Na]^+$: 553.1822, found: 553.1823



3t

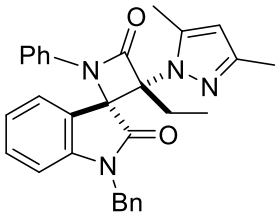
1'-benzyl-4'-chloro-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

3t: 61% yield, 87:13 *dr* (*cis:trans*), white solid, mp 178.2 - 181.1℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 5H), 7.25 – 7.21 (m, 2H), 7.19 – 7.17 (m, 1H), 7.14 – 7.10 (m, 3H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 5.77 (s, 1H), 5.02 (d, *J* = 15.8 Hz, 1H), 4.56 (d, *J* = 15.8 Hz, 1H), 2.56 (s, 3H), 2.18 (s, 3H), 2.12 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 162.5, 149.2, 145.7, 136.8, 134.9, 131.9, 131.8, 129.5, 129.1 (*two carbon signals overlapped*), 128.0, 127.4, 125.4, 124.6, 119.4, 117.0, 109.1, 107.2, 81.7, 72.0, 44.7, 19.9, 13.8, 13.4.

HRMS-ESI: calculated for $C_{29}H_{25}ClN_4O_2$ $[M + H]^+$: 497.1739, found: 497.1738



4a

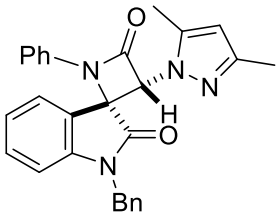
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-ethyl-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

4a: 65% yield, 90:10 *dr* (*cis:trans*), yellow solid, mp 197.9 - 200.5℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 7H), 7.18 (t, *J* = 7.8 Hz, 2H), 7.08 – 7.01 (m, 4H), 6.76 (d, *J* = 7.9 Hz, 1H), 5.75 (s, 1H), 5.05 (d, *J* = 15.9 Hz, 1H), 4.60 (d, *J* = 15.9 Hz, 1H), 2.60 – 2.53 (m, 4H), 2.41 (dt, *J* = 13.7, 6.9 Hz, 1H), 2.12 (s, 3H), 0.98 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 163.4, 149.3, 144.8, 144.2, 136.2, 135.3, 130.9, 129.4, 129.0, 127.8, 127.3, 126.6, 125.1, 122.6, 121.4, 117.7, 110.7, 106.6, 81.4, 70.5, 44.5, 29.8, 13.9, 13.4, 8.6.

HRMS-ESI: calculated for $C_{30}H_{28}N_4O_2$ $[M + H]^+$: 477.2285, found: 477.2284



4b

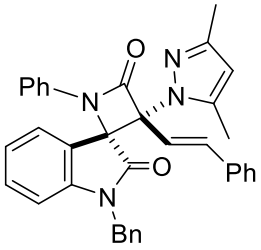
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

4b: 63% yield, 90:10 *dr* (*cis:trans*), yellow solid, mp 204.5 - 206.1℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 5H), 7.23 – 7.18 (m, 2H), 7.17 – 7.03 (m, 6H), 6.81 (d, *J* = 7.9 Hz, 1H), 6.00 (s, 1H), 5.84 (s, 1H), 5.12 (d, *J* = 15.7 Hz, 1H), 4.66 (d, *J* = 15.7 Hz, 1H), 2.45 (s, 3H), 2.17 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 159.8, 150.0, 143.0, 142.5, 136.0, 135.0, 131.0, 129.5, 129.0, 128.0, 127.3, 125.5, 123.9, 123.5, 123.3, 117.5, 110.5, 107.8, 76.2, 67.3, 44.4, 13.7, 12.3.

HRMS-ESI: calculated for $C_{28}H_{24}N_4O_2$ $[M + H]^+$: 449.1972, found: 449.1971



4c

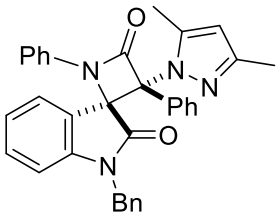
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-phenyl-3-((E)-styryl)spiro[azetidine-2,3'-indoline]-2',4-dione

4c: 85% yield, 70:30 *dr* (*cis:trans*), white solid, mp 164.2 - 166.3℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.37 (m, 2H), 7.35 – 7.32 (m, 4H), 7.31 – 7.26 (m, 5H), 7.21 – 7.12 (m, 6H), 7.09 – 7.05 (m, 1H), 6.97 – 6.93 (m, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 6.70 (d, *J* = 16.3 Hz, 1H), 5.78 (s, 1H), 5.02 (d, *J* = 15.7 Hz, 1H), 4.75 (d, *J* = 15.7 Hz, 1H), 2.57 (s, 3H), 2.12 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 160.7, 149.3, 144.1, 142.9, 136.2, 135.8, 135.4, 133.6, 131.1, 129.4, 129.0, 128.8, 128.7, 127.9, 127.6, 127.3, 127.2, 125.4, 124.6, 122.6, 121.0, 117.9, 110.6, 107.3, 82.1, 70.4, 44.6, 13.9, 13.2.

HRMS-ESI: calculated for $C_{36}H_{30}N_4O_2$ $[M + H]^+$: 551.2442, found: 551.2442



5a

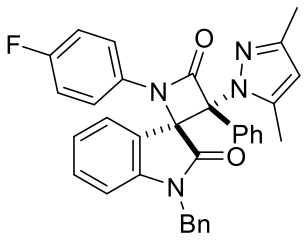
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1,3-diphenylspiro[azetidine-2,3'-indoline]-2',4-dione

5a: 92% yield, 90:10 *dr* (*trans:cis*), white solid, mp 199.2 - 201.8℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.51 (m, 2H), 7.40 – 7.36 (m, 2H), 7.35 – 7.27 (m, 4H), 7.25 – 7.18 (m, 3H), 7.15 – 7.08 (m, 4H), 7.06 – 6.94 (m, 2H), 6.76 (td, *J* = 7.6, 0.6 Hz, 1H), 6.35 – 6.30 (m, 1H), 5.63 (s, 1H), 5.10 (d, *J* = 15.2 Hz, 1H), 4.90 (d, *J* = 15.2 Hz, 1H), 2.16 (s, 3H), 1.38 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 161.0, 147.6, 143.1, 141.4, 136.7, 135.4, 132.0, 131.1, 129.5, 129.2, 129.1, 129.0, 128.4, 128.3, 127.9, 126.4, 125.1, 123.4, 122.6, 118.0, 109.5, 108.4, 86.5, 72.0, 44.8, 13.8, 12.8.

HRMS-ESI: calculated for $C_{34}H_{28}N_4O_2$ $[M + H]^+$: 525.2285, found: 525.2285



5b

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-(4-fluorophenyl)-3-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

5b: 92% yield, 89:11 *dr* (*trans:cis*), white solid, mp 216.8 - 218.6℃.

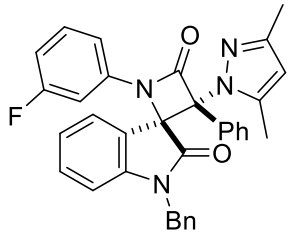
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 2H), 7.37 – 7.27 (m, 7H), 7.24 – 7.21 (m, 2H), 7.11 – 7.07 (m, 2H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.84 – 6.77 (m, 3H), 6.31 (d, *J* = 7.5 Hz, 1H), 5.65 (s, 1H), 5.10 (d, *J* = 15.2 Hz, 1H), 4.90 (d, *J* = 15.2 Hz, 1H), 2.18 (s, 3H), 1.36 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 161.0, 159.8 (d, *J* = 245.0 Hz), 147.7, 143.2, 141.4, 135.4, 132.9 (d, *J* = 2.8 Hz), 131.8, 131.3, 129.4, 129.1, 129.1, 128.4, 128.4,

127.9, 126.4, 123.5, 122.4, 120.0 (d, *J* = 8.1 Hz), 116.1 (d, *J* = 22.8 Hz), 109.6, 108.5, 86.8, 72.3, 44.8, 13.8, 12.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -116.22.

HRMS-ESI: calculated for $C_{34}H_{27}FN_4O_2$ $[M + H]^+$: 543.2191, found: 543.2191



5c

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-(3-fluorophenyl)-3-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

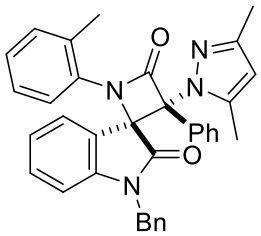
5c: 92% yield, 91:9 *dr* (*trans:cis*), yellow solid, mp 201.3 - 203.5℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.5 Hz, 2H), 7.41 – 7.38 (m, 2H), 7.37 – 7.27 (m, 5H), 7.24 – 7.20 (m, 2H), 7.08 – 7.04 (m, 1H), 7.03 – 6.98 (m, 2H), 6.81 – 6.77 (m, 2H), 6.75 – 6.71 (m, 1H), 6.30 (d, *J* = 7.4 Hz, 1H), 5.65 (s, 1H), 5.12 (d, *J* = 15.2 Hz, 1H), 4.92 (d, *J* = 15.2 Hz, 1H), 2.19 (s, 3H), 1.33 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 163.0 (d, *J* = 246.4 Hz), 161.2, 147.8, 143.2, 141.5, 138.1 (d, *J* = 10.5 Hz), 135.4, 131.8, 131.5, 130.7 (d, *J* = 9.2 Hz), 129.5, 129.3, 129.2, 128.5, 128.1, 126.5, 123.6, 122.2, 113.4 (d, *J* = 2.9 Hz), 112.1 (d, *J* = 21.3 Hz), 109.8, 108.6, 105.9 (d, *J* = 26.3 Hz), 100.2, 87.0, 72.3, 45.0, 13.9, 12.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -110.49.

HRMS-ESI: calculated for $C_{34}H_{27}FN_4O_2$ $[M + Na]^+$: 565.2010, found: 565.2010



5d

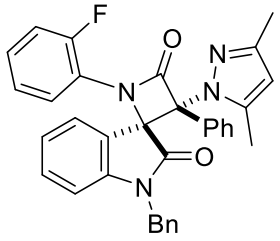
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-phenyl-1-(o-tolyl)spiro[azetidine-2,3'-indoline]-2',4-dione

5d: 91% yield, 93:7 *dr* (*trans:cis*), yellow solid, mp 153.4 - 155.6℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 2H), 7.29 – 7.17 (m, 10H), 7.15 – 7.10 (m, 1H), 6.98 – 6.89 (m, 2H), 6.85 – 6.78 (m, 2H), 6.35 (d, *J* = 7.4 Hz, 1H), 5.68 (s, 1H), 4.99 (d, *J* = 15.5 Hz, 1H), 4.92 (d, *J* = 15.5 Hz, 1H), 2.59 (s, 3H), 2.24 (s, 3H), 1.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.36, 161.69, 147.29, 143.71, 141.36, 136.89, 135.19, 133.81, 132.17, 131.57, 131.08, 129.67, 128.99, 128.93, 128.34, 128.04, 127.81, 126.74, 126.18, 125.17, 123.23, 123.01, 109.27, 108.42, 100.10, 86.43, 74.82, 44.53, 19.45, 13.76, 12.96.

HRMS-ESI: calculated for $C_{35}H_{30}N_4O_2$ $[M + H]^+$: 539.2442, found: 539.2442



5e

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-(2-fluorophenyl)-3-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

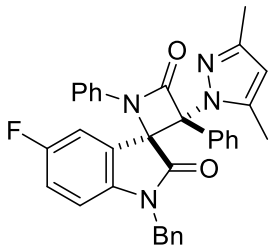
5e: 93% yield, 90:10 *dr* (*trans:cis*), yellow solid, mp 164.9 - 168.1℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 – 8.04 (m, 1H), 7.55 – 7.51 (m, 2H), 7.36 – 7.29 (m, 5H), 7.25 – 7.17 (m, 4H), 7.11 – 7.06 (m, 2H), 6.90 – 6.84 (m, 2H), 6.74 (t, *J* = 7.6 Hz, 1H), 6.37 (d, *J* = 7.4 Hz, 1H), 5.63 (s, 1H), 5.03 (d, *J* = 15.4 Hz, 1H), 4.84 (d, *J* = 15.4 Hz, 1H), 2.17 (s, 3H), 1.37 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.98, 162.20, 153.44 (d, *J* = 248.8 Hz), 147.58, 143.79, 141.41, 135.55, 132.20, 130.79, 129.42, 129.06, 128.98, 128.10, 128.06, 127.90, 127.34 (d, *J* = 7.6 Hz), 125.90, 125.04 (d, *J* = 1.8 Hz), 124.85 (d, *J* = 3.5 Hz), 123.82 (d, *J* = 2.1 Hz), 123.46, 122.97, 116.54 (d, *J* = 20.1 Hz), 109.06, 108.34, 87.65, 74.41, 44.81, 13.76, 12.76.

^{19}F NMR (376 MHz, $CDCl_3$) δ -121.85.

HRMS-ESI: calculated for $C_{34}H_{27}FN_4O_2$ $[M + Na]^+$: 565.2010, found: 565.2010



5f

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-5'-fluoro-1,3-diphenylspiro[azetidine-2,3'-indoline]-2',4-dione

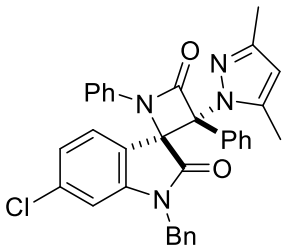
5f: 95% yield, 91:9 *dr* (*trans:cis*), white solid, mp 204.7 - 207.3℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.4 Hz, 2H), 7.38 – 7.32 (m, 5H), 7.30 – 7.24 (m, 3H), 7.17 – 7.10 (m, 4H), 7.05 (t, *J* = 7.1 Hz, 1H), 6.98 (td, *J* = 8.7, 2.5 Hz, 1H), 6.90 (dd, *J* = 8.6, 4.0 Hz, 1H), 6.11 (dd, *J* = 8.0, 2.4 Hz, 1H), 5.70 (s, 1H), 5.11 (d, *J* = 15.3 Hz, 1H), 4.89 (d, *J* = 15.3 Hz, 1H), 2.17 (s, 3H), 1.49 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 160.8, 159.3 (d, *J* = 242.8 Hz), 147.9, 141.5, 139.0, 139.0, 136.5, 135.1, 131.8, 129.4, 129.3, 129.2, 129.1, 128.4, 128.4, 128.0, 125.3, 124.5 (d, *J* = 8.5 Hz), 118.0, 117.4 (d, *J* = 23.8 Hz), 114.3 (d, *J* = 26.0 Hz), 110.2 (d, *J* = 7.8 Hz), 108.6, 86.8, 72.0, 44.9, 13.7, 13.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -119.24.

HRMS-ESI: calculated for $C_{34}H_{27}FN_4O_2$ $[M + H]^+$: 543.2191, found: 543.2191



5g

1'-benzyl-6'-chloro-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1,3-diphenylspiro[azetidine -2,3'-indoline]-2',4-dione

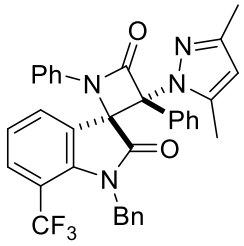
5g: 95% yield, 88:12 *dr* (*trans:cis*), white solid, mp 224.5 - 226.6℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.5 Hz, 2H), 7.40 – 7.35 (m, 5H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.18 – 7.14 (m, 2H), 7.13 – 7.09 (m, 2H), 7.08 –

7.04 (m, 1H), 6.99 (d, *J* = 1.3 Hz, 1H), 6.79 – 6.75 (m, 1H), 6.28 (d, *J* = 8.0 Hz, 1H), 5.70 – 5.66 (m, 1H), 5.07 (d, *J* = 15.3 Hz, 1H), 4.90 (d, *J* = 15.3 Hz, 1H), 2.16 (s, 3H), 1.51 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 160.8, 147.8, 144.3, 141.5, 137.0, 136.5, 134.9, 131.9, 129.4, 129.3, 129.2, 129.2, 128.5, 128.4, 128.0, 127.2, 125.3, 123.3, 121.2, 118.0, 110.2, 108.5, 86.7, 71.7, 44.9, 13.7, 13.1.

HRMS-ESI: calculated for $C_{34}H_{27}ClN_4O_2$ $[M + H]^+$: 559.1895, found: 559.1895



5h

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1,3-diphenyl-7'-(trifluoromethyl)spiro[azetidine-2,3'-indoline]-2',4-dione

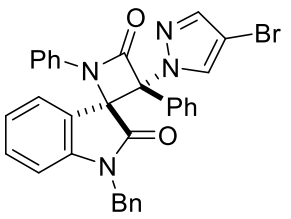
5h: 82% yield, 90:10 *dr* (*trans:cis*), white solid, mp 95.8 - 96.2℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.27 – 7.23 (m, 6H), 7.21 – 7.16 (m, 4H), 7.16 – 7.12 (m, 2H), 7.10 – 7.05 (m, 1H), 6.88 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 7.3 Hz, 1H), 5.66 (s, 1H), 5.27 – 5.20 (m, 2H), 2.09 (s, 3H), 1.69 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 160.7, 148.0, 141.9, 141.6, 135.9, 135.7, 132.1, 129.4, 129.3, 129.1, 129.0, 128.9 (q, *J* = 6.0 Hz), 128.5, 128.0, 127.6, 127.3, 126.5, 125.6, 123.5(q, *J* = 273.4 Hz), 122.6, 118.4, 113.3(q, *J* = 32.9 Hz), 108.2, 87.5, 70.4, 46.6, 13.6, 12.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -54.84.

HRMS-ESI: calculated for $C_{35}H_{27}F_3N_4O_2$ $[M + Na]^+$: 615.1978, found: 615.1978



5i

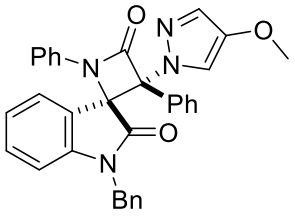
1'-benzyl-3-(4-bromo-1H-pyrazol-1-yl)-1,3-diphenylspiro[azetidine-2,3'-indoline]-2',4-dione

5i: 86% yield, > 95:5 *dr* (*trans:cis*), white solid, mp 194.3 - 196.1℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.61 (m, 2H), 7.51 (d, *J* = 12.6 Hz, 2H), 7.43 – 7.28 (m, 9H), 7.20 – 7.01 (m, 6H), 6.86 – 6.79 (m, 1H), 6.75 – 6.65 (m, 1H), 4.95 – 4.82 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 160.6, 143.3, 141.0, 136.2, 135.3, 132.5, 131.6, 130.0, 129.9, 129.4, 129.0, 128.8, 128.6, 128.3, 128.1, 125.6, 125.6, 123.5, 121.2, 118.0, 110.1, 94.5, 85.2, 72.7, 44.8.

HRMS-ESI: calculated for $C_{32}H_{23}BrN_4O_2$ $[M + Na]^+$: 597.0897, found: 597.0897



5j

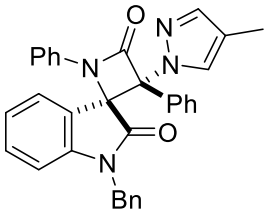
1'-benzyl-3-(4-methoxy-1H-pyrazol-1-yl)-1,3-diphenylspiro[azetidine-2,3'-indoline]-2',4-dione

5j: 91% yield, 95:5 *dr* (*trans:cis*), white solid, mp 196.6 - 199.1℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 2H), 7.38 – 7.27 (m, 10H), 7.19 – 7.12 (m, 5H), 7.08 – 7.03 (m, 1H), 7.03 – 6.98 (m, 1H), 6.83 – 6.78 (m, 1H), 6.76 – 6.69 (m, 1H), 4.93 – 4.83 (m, 2H), 3.60 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 161.1, 147.2, 143.1, 136.3, 135.8, 132.9, 131.2, 129.5, 129.2, 128.9, 128.8, 128.6, 128.4, 128.2, 127.9, 125.7, 125.3, 123.2, 121.5, 117.9, 114.0, 109.8, 85.3, 72.8, 58.9, 44.7.

HRMS-ESI: calculated for $C_{33}H_{26}N_4O_3$ $[M + H]^+$: 527.2078, found: 527.2078



5k

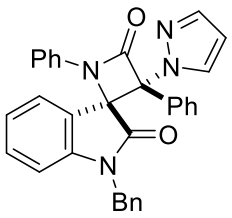
1'-benzyl-3-(4-methyl-1H-pyrazol-1-yl)-1,3-diphenylspiro[azetidine-2,3'-indoline]-2',4-dione

5k: 90% yield, 93:7 *dr* (*trans:cis*), yellow solid, mp 174.8 - 177.3℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.3 Hz, 2H), 7.38 – 7.29 (m, 10H), 7.18 – 7.13 (m, 4H), 7.08 – 7.04 (m, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.78 (t, *J* = 7.6 Hz, 1H), 6.70 (d, *J* = 7.4 Hz, 1H), 4.93 – 4.85 (m, 2H), 1.94 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 161.5, 143.2, 141.1, 136.5, 135.5, 133.2, 131.2, 129.5, 129.3, 129.0, 128.6, 128.6, 128.3, 128.2, 128.1, 125.9, 125.3, 123.2, 121.6, 117.9, 117.0, 109.9, 85.1, 72.9, 44.7, 8.9.

HRMS-ESI: calculated for $C_{33}H_{26}N_4O_2$ $[M + H]^+$: 511.2129, found: 511.2129



5l

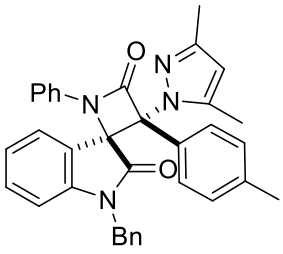
1'-benzyl-1,3-diphenyl-3-(1H-pyrazol-1-yl)spiro[azetidine-2,3'-indoline]-2',4-dione

5l: 90% yield, > 95:5 *dr* (*trans:cis*), yellow solid, mp 199.1 - 201.9℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.70 (m, 2H), 7.56 – 7.52 (m, 2H), 7.37 – 7.28 (m, 9H), 7.19 – 7.14 (m, 4H), 7.09 – 7.05 (m, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 6.62 (d, *J* = 7.4 Hz, 1H), 6.21 – 6.17 (m, 1H), 4.92 (d, *J* = 15.3 Hz, 1H), 4.87 (d, *J* = 15.2 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 161.3, 143.2, 140.5, 136.4, 135.5, 133.1, 131.3, 129.8, 129.6, 129.3, 129.0, 128.7, 128.5, 128.3, 128.2, 125.6, 125.4, 123.3, 121.5, 118.0, 109.9, 106.6, 85.0, 72.8, 44.8.

HRMS-ESI: calculated for $C_{32}H_{24}N_4O_2$ $[M + Na]^+$: 519.1791, found: 519.1792



5m

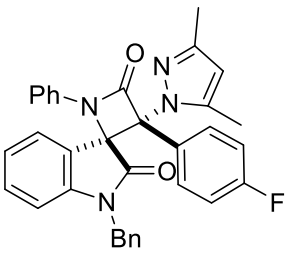
1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-1-phenyl-3-(p-tolyl)spiro[azetidine-2, 3'-indoline]-2',4-dione

5m: 95% yield, 90:10 *dr* (*trans:cis*), white solid, mp 180.0 - 182.3℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.43 (m, 2H), 7.43 – 7.39 (m, 2H), 7.38 – 7.33 (m, 3H), 7.32 – 7.28 (m, 1H), 7.16 – 7.12 (m, 4H), 7.07 – 7.02 (m, 3H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.35 (d, *J* = 7.3 Hz, 1H), 5.66 (s, 1H), 5.14 (d, *J* = 15.2 Hz, 1H), 4.93 (d, *J* = 15.2 Hz, 1H), 2.30 (s, 3H), 2.19 (s, 3H), 1.42 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 161.2, 147.5, 143.1, 141.3, 138.9, 136.8, 135.5, 131.0, 129.3, 129.2, 129.0, 129.0, 128.6, 128.4, 128.3, 126.3, 125.0, 123.3, 122.7, 118.0, 109.5, 108.3, 86.5, 72.0, 44.8, 21.3, 13.8, 12.8.

HRMS-ESI: calculated for $C_{35}H_{30}N_4O_2$ $[M + H]^+$: 539.2442, found: 539.2442



5n

1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-(4-fluorophenyl)-1-phenylspiro[azetidine-2,3'-indoline]-2',4-dione

5n: 93% yield, 88:12 *dr* (*trans:cis*), white solid, mp 218.1 - 223.2℃.

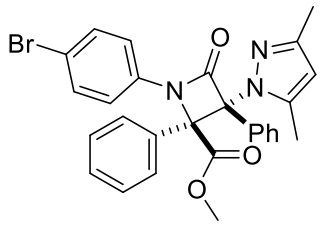
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 8.7, 5.2 Hz, 2H), 7.42 – 7.39 (m, 2H), 7.37 – 7.29 (m, 4H), 7.17 – 7.12 (m, 4H), 7.08 – 7.04 (m, 1H), 7.03 – 7.00 (m, 1H),

6.91 (t, *J* = 8.6 Hz, 2H), 6.79 (t, *J* = 7.6 Hz, 1H), 6.37 (d, *J* = 7.5 Hz, 1H), 5.67 (s, 1H), 5.10 (d, *J* = 15.2 Hz, 1H), 4.93 (d, *J* = 15.2 Hz, 1H), 2.15 (s, 3H), 1.51 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 162.9 (d, *J* = 249.2 Hz), 160.8, 147.8, 143.1, 141.3, 136.5, 135.4, 131.4 (d, *J* = 8.3 Hz), 131.2, 129.3, 129.1, 128.4, 128.4, 128.2 (d, *J* = 3.3 Hz), 126.2, 125.3, 123.4, 122.6, 118.0, 114.9 (d, *J* = 21.7 Hz), 109.5, 108.4, 85.7, 72.1, 44.8, 13.7, 12.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.13.

HRMS-ESI: calculated for $C_{34}H_{27}FN_4O_2$ $[M + H]^+$: 543.2191, found: 543.2191



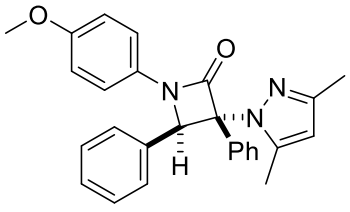
5'a

Methyl-1-(4-bromophenyl)-3-(3,5-dimethyl-1H-pyrazol-1-yl)-4-oxo-2,3-diphenylazetidine-2-carboxylate

5'a: 78% yield, 90:10 *dr* (*trans:cis*), light yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.33 (m, 3H), 7.32 – 7.27 (m, 8H), 7.18 – 7.15 (m, 1H), 7.09 – 7.06 (m, 2H), 5.40 (s, 1H), 3.44 (s, 3H), 1.98 (s, 3H), 1.76 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 160.0, 148.4, 141.2, 135.8, 134.1, 131.7, 130.5, 129.2, 129.0, 128.5, 128.3, 127.6, 127.3, 120.5, 117.6, 108.1, 100.0, 87.1, 78.8, 52.6, 29.7, 13.5, 13.0.



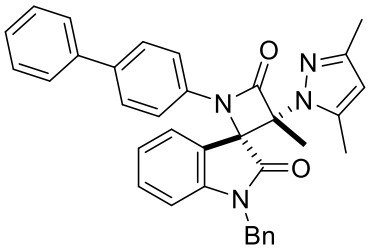
5'b

3(3,5-dimethyl-1H-pyrazol-1-yl)-1-(4-methoxyphenyl)-3,4-diphenylazetidin-2-one

5'b: 46% yield, >95:5 *dr* (*trans:cis*), light yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.37 (m, 2H), 7.19 – 7.16 (m, 2H), 7.06 – 7.03 (m, 3H), 7.03 – 7.01 (m, 4H), 6.89 – 6.86 (m, 2H), 6.83 – 6.80 (m, 2H), 5.88 (s, 1H), 3.75 (s, 3H), 2.32 (s, 3H), 2.10 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 162.3, 156.5, 147.4, 142.1, 135.3, 133.6, 130.8, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.3, 119.2, 114.3, 108.1, 83.0, 64.7, 55.4, 29.7, 13.8, 11.9.



6a

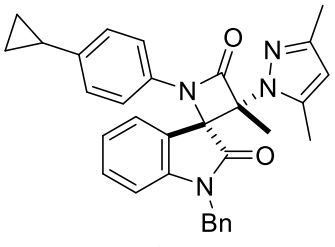
1-([1,1'-biphenyl]-4-yl)-1'-benzyl-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methylspiro [azetidine-2,3'-indoline]-2',4-dione

6a: 84% yield, yellow solid, mp 198.3 - 200.6℃.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.3 Hz, 2H), 7.44 – 7.37 (m, 4H), 7.35 – 7.28 (m, 8H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.9 Hz, 1H), 5.78 (s, 1H), 5.05 (d, *J* = 15.8 Hz, 1H), 4.63 (d, *J* = 15.8 Hz, 1H), 2.59 (s, 3H), 2.13 (s, 3H), 2.09 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 163.7, 149.2, 144.1, 140.3, 138.3, 135.2, 131.0, 129.0 (*two carbon signals overlapped*), 128.9, 128.1, 127.9, 127.5, 127.4, 127.0, 126.4, 122.8, 121.4, 118.0, 110.8, 107.1, 100.1, 78.8, 70.9, 44.5, 22.3, 13.8, 13.5.

HRMS-ESI: calculated for $C_{35}H_{30}N_4O_2$ $[M + Na]^+$: 561.2261, found: 561.2260



6b

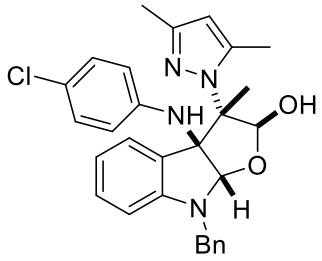
1'-benzyl-1-(4-cyclopropylphenyl)-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methylspiro[azetidine-2,3'-indoline]-2',4-dione

6b: 78% yield, white solid, mp 124.6 - 126.3℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.29 – 7.25 (m, 5H), 7.05 – 6.96 (m, 3H), 6.91 – 6.87 (m, 2H), 6.78 – 6.75 (m, 1H), 5.76 (s, 1H), 5.04 (d, *J* = 15.8 Hz, 1H), 4.59 (d, *J* = 15.8 Hz, 1H), 2.57 (s, 3H), 2.12 (s, 3H), 2.06 (s, 3H), 1.79 (td, *J* = 8.4, 4.2 Hz, 1H), 0.92 – 0.88 (m, 2H), 0.61 – 0.55 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 163.4, 149.1, 144.0, 141.3, 135.3, 133.5, 130.9, 129.0, 127.8, 127.4, 126.6, 126.3, 122.6, 121.6, 117.8, 110.6, 107.0, 78.7, 70.9, 44.4, 29.8, 22.2, 15.1, 13.8, 13.4, 9.2.

HRMS-ESI: calculated for $C_{32}H_{30}N_4O_2$ $[M + H]^+$: 503.2442, found: 503.2442



7

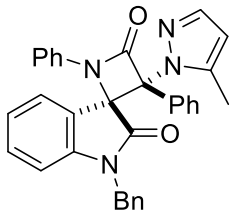
8-benzyl-3a-((4-chlorophenyl)amino)-3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-methyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indol-2-ol

7: 88% yield, yellow solid, mp 177.8 - 180.1℃.

^{1}H NMR (500 MHz, DMSO) δ 7.62 (s, 1H), 7.47 – 7.39 (m, 4H), 7.34 – 7.30 (m, 1H), 6.99 – 6.95 (m, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.53 (d, *J* = 7.9 Hz, 1H), 6.45 (d, *J* = 8.8 Hz, 2H), 6.25 (t, *J* = 7.4 Hz, 1H), 5.80 (s, 1H), 5.61 (d, *J* = 3.5 Hz, 1H), 5.38 (s, 1H), 5.17 (d, *J* = 7.0 Hz, 1H), 4.69 (d, *J* = 15.2 Hz, 1H), 4.50 (d, *J* = 15.2 Hz, 1H), 2.21 (s, 3H), 1.86 (s, 6H).

^{13}C NMR (125 MHz, DMSO) δ 152.0, 145.4, 141.3, 138.3, 130.1, 129.1 (*two carbon signals overlapped*), 128.7, 128.6, 127.8, 125.4, 124.8, 122.0, 118.1, 117.6, 107.3, 105.9, 94.7, 93.9, 75.6, 74.9, 48.0, 19.4, 13.8, 13.2.

HRMS-ESI: calculated for $C_{29}H_{29}ClN_4O_2$ $[M + H]^+$: 501.2052, found: 501.2052



8

1'-benzyl-3-(5-methyl-1H-pyrazol-1-yl)-1,3-diphenylspiro[azetidine-2,3'-indoline]-2',4-dione

8: 91% yield, 90:10 *dr* (*trans:cis*), white solid, mp 232.3 - 234.7℃.

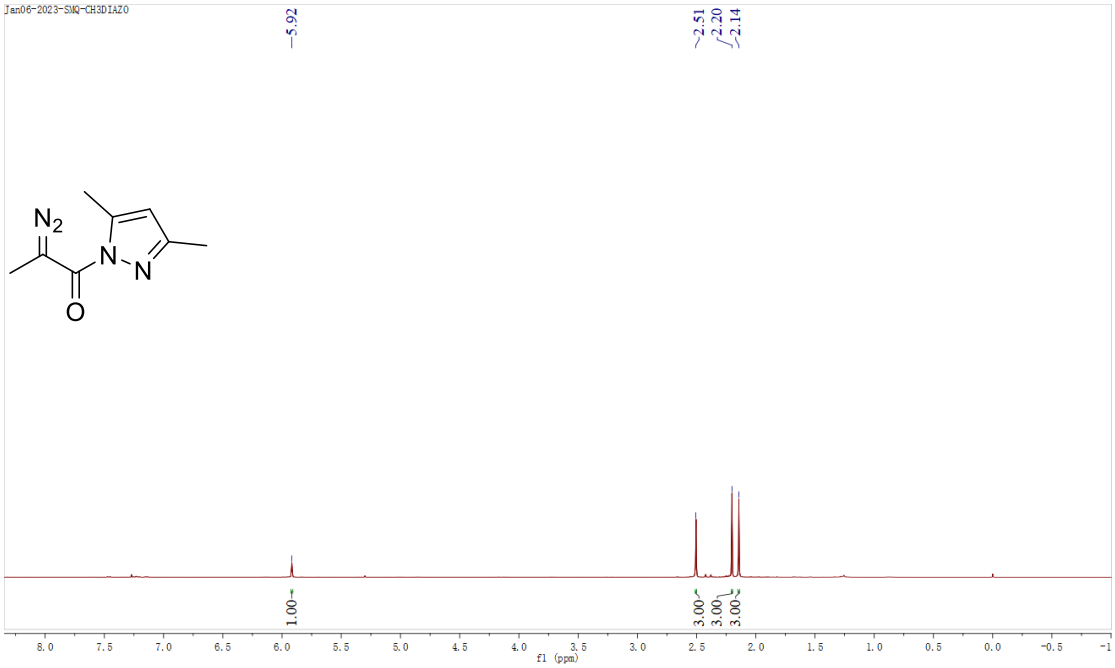
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, 2H), 7.47 (s, 1H), 7.44 – 7.40 (m, 2H), 7.38 – 7.28 (m, 5H), 7.26 – 7.22 (m, 2H), 7.16 – 7.12 (m, 4H), 7.07 – 7.02 (m, 2H), 6.77 (t, *J* = 7.6 Hz, 1H), 6.23 (d, *J* = 7.5 Hz, 1H), 5.88 (s, 1H), 5.15 (d, *J* = 15.1 Hz, 1H), 4.94 (d, *J* = 15.1 Hz, 1H), 1.44 (s, 3H).

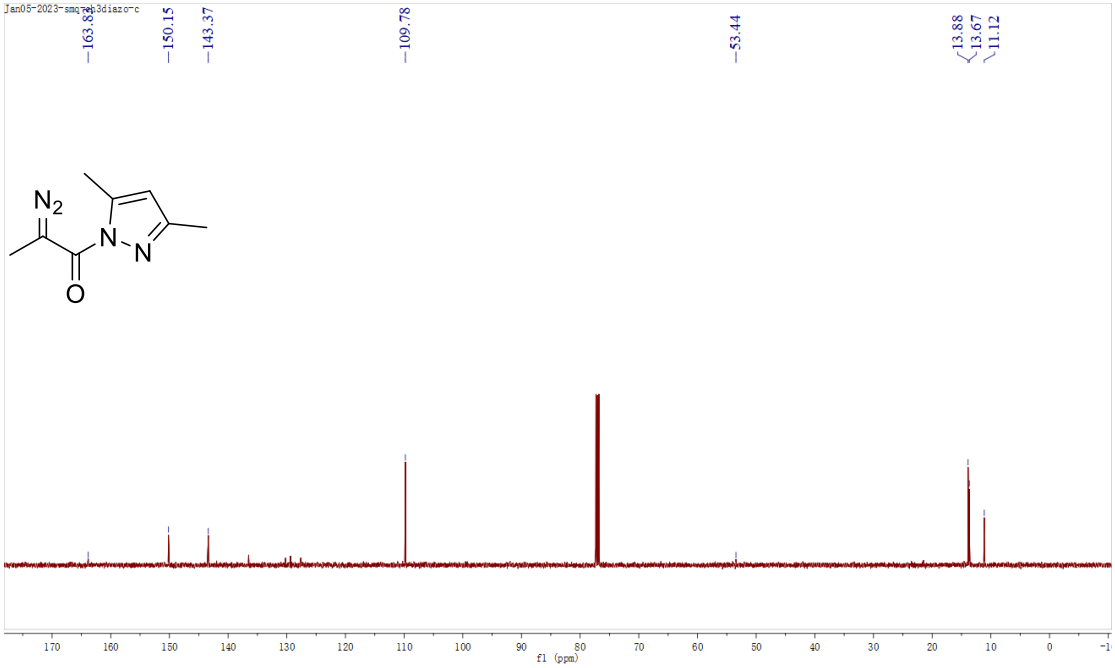
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 160.8, 143.1, 140.8, 138.7, 136.6, 135.4, 131.6, 131.3, 129.5, 129.2, 129.2, 129.1, 128.5, 128.4, 128.0, 126.3, 125.2, 123.5, 122.3, 118.0, 109.6, 108.4, 86.6, 71.9, 44.9, 12.8.

HRMS-ESI: calculated for $C_{33}H_{26}N_4O_2$ $[M + Na]^+$: 533.1948, found: 533.1948

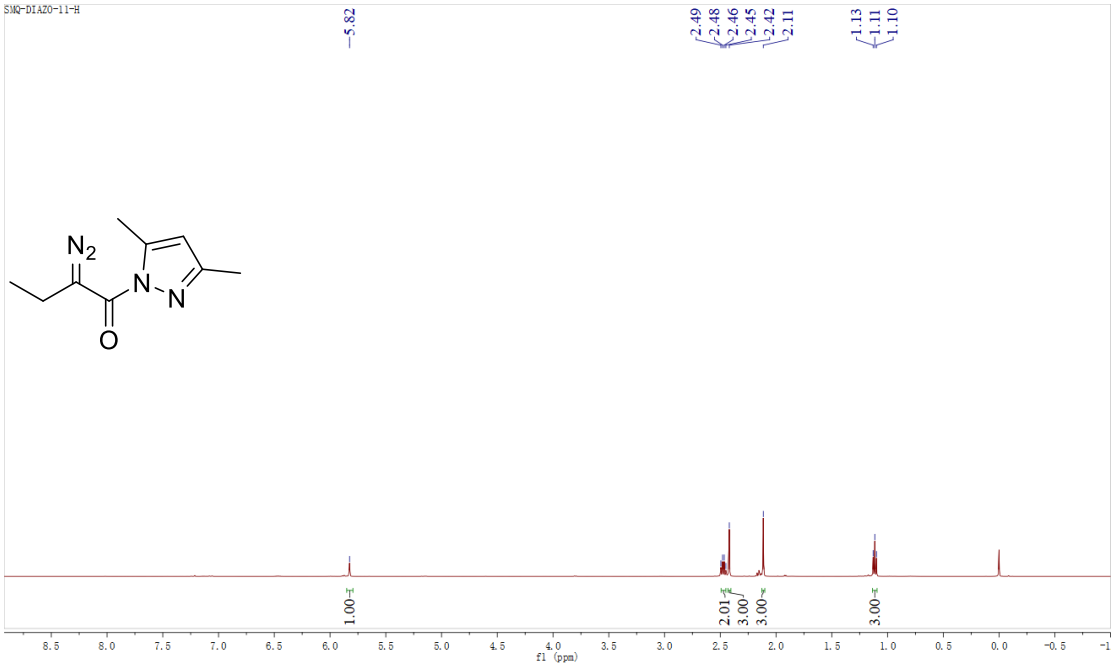
8. NMR spectra of compounds 1, 1', 3, 4, 5, 5', 6, 7, 8

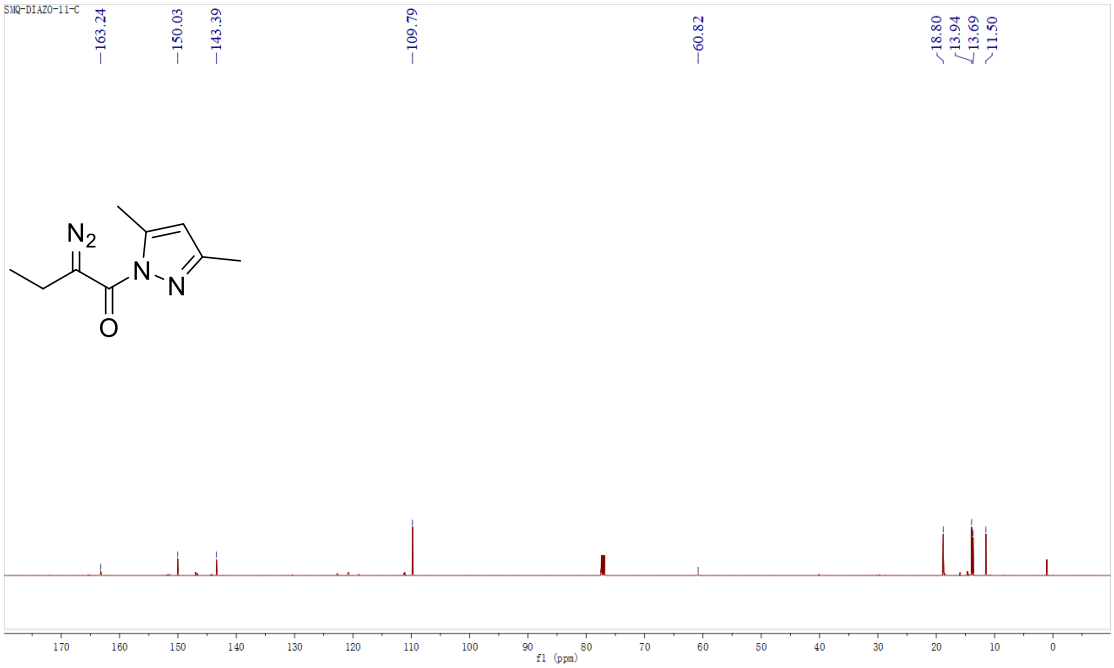
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1a



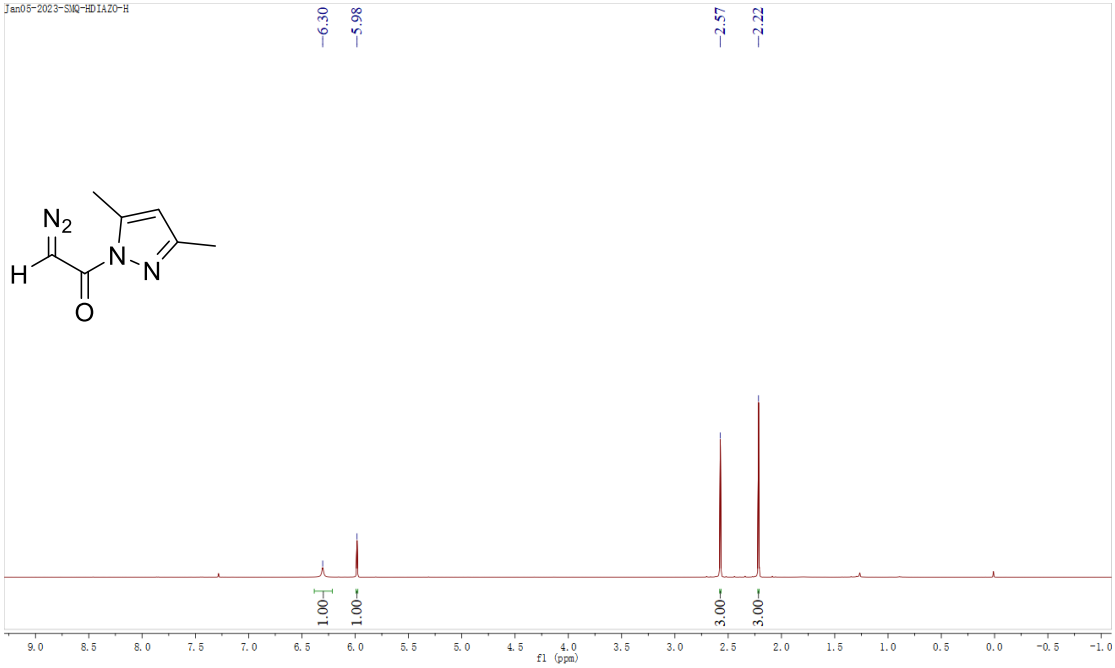


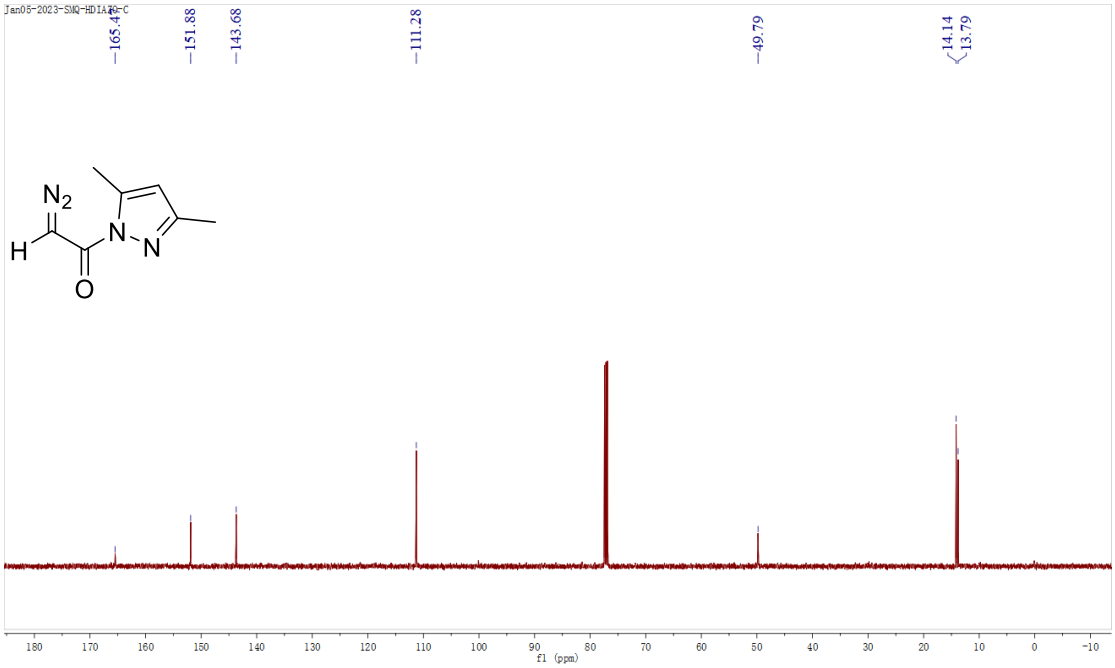
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1b



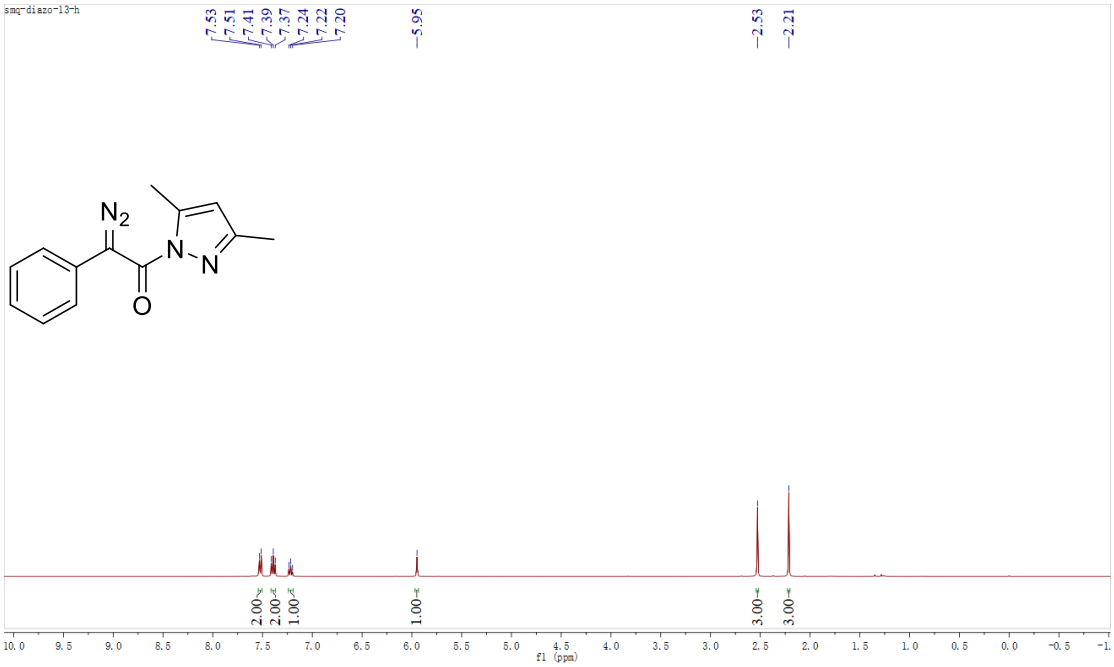


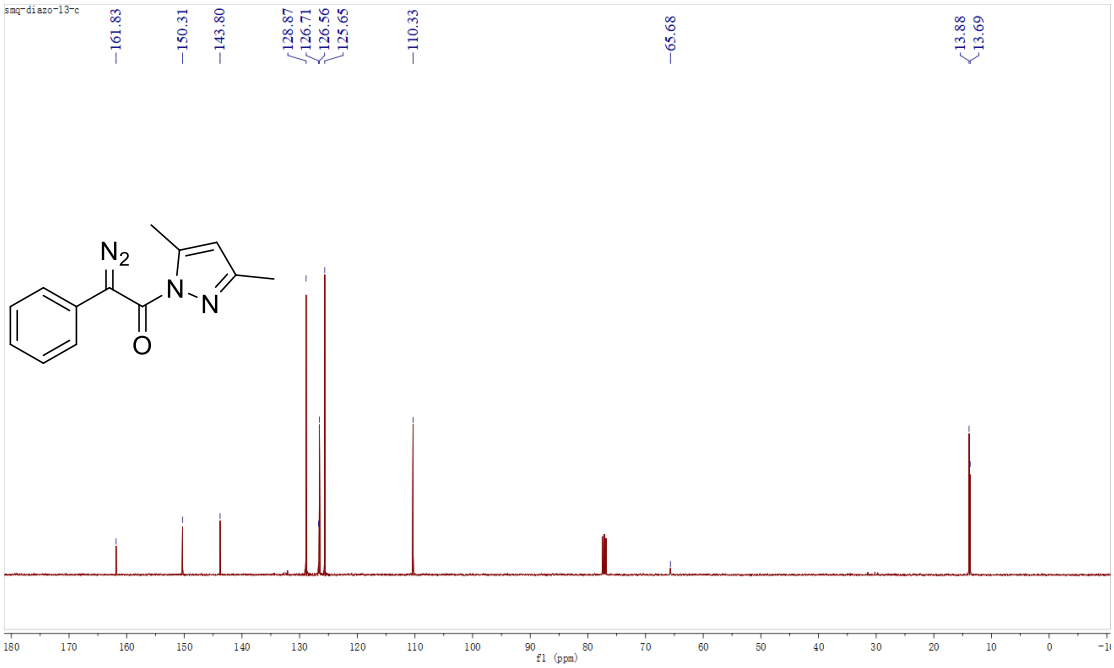
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1c



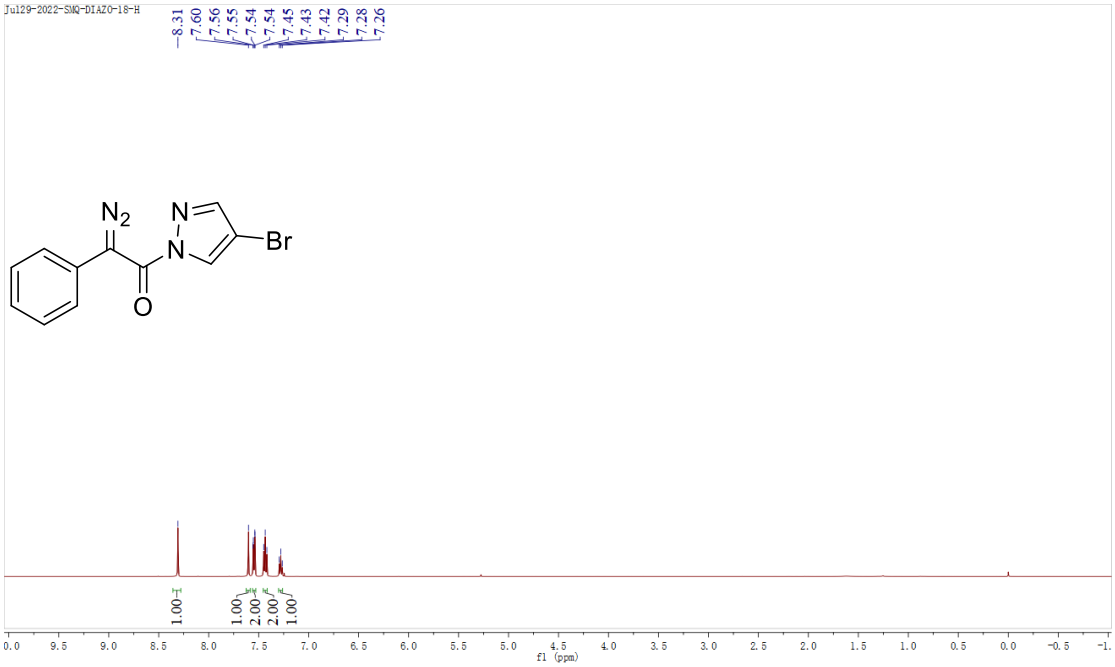


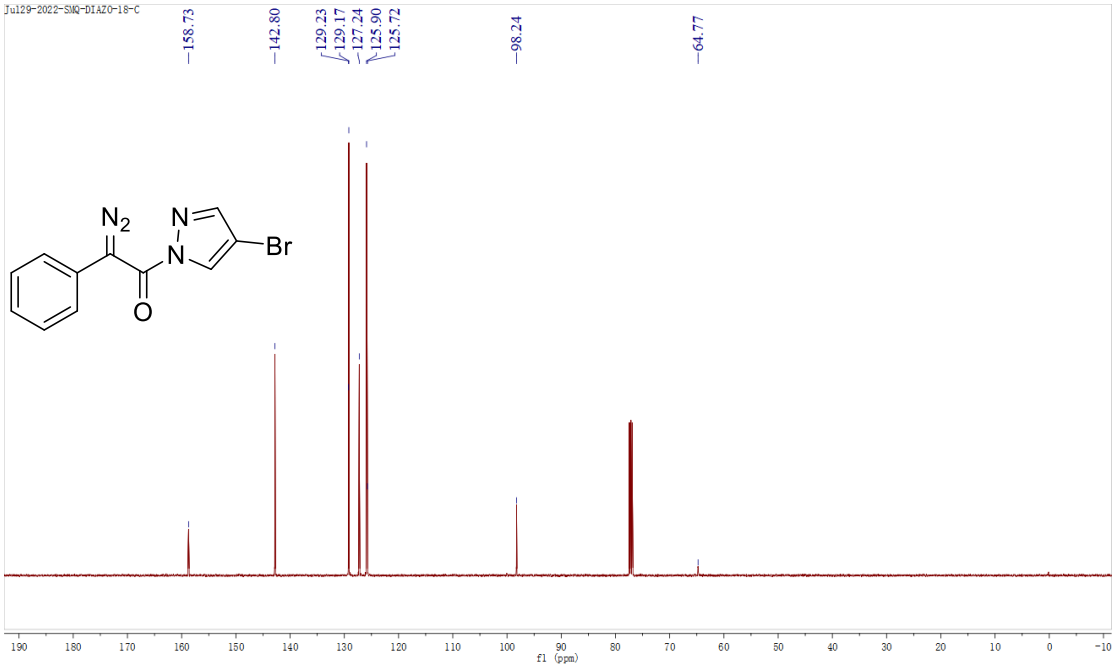
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 1'a



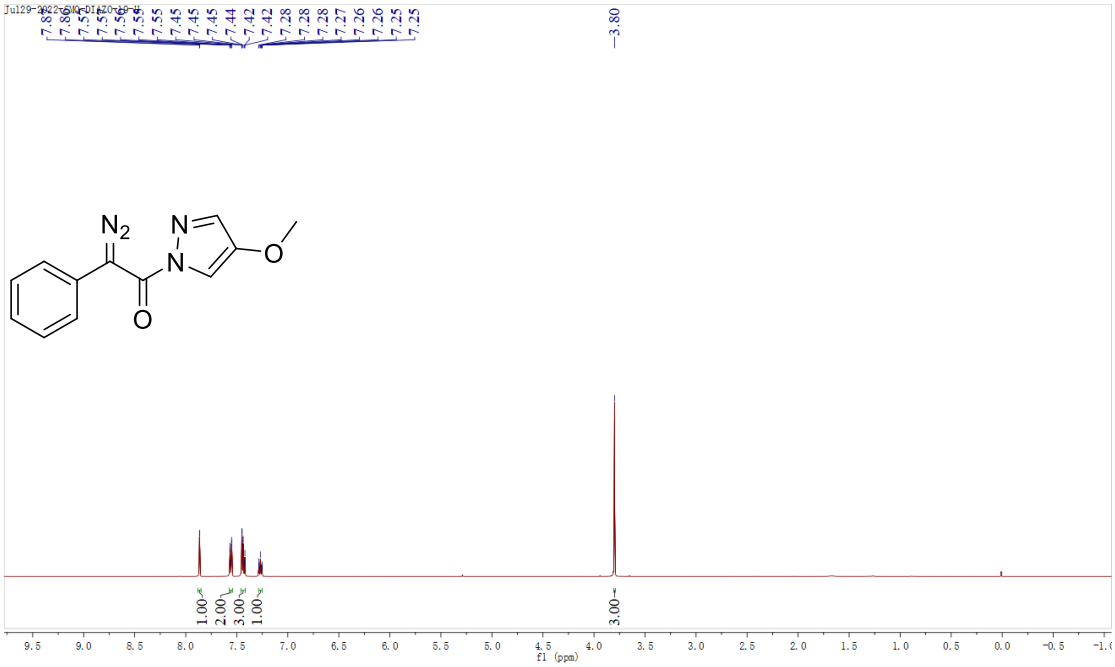


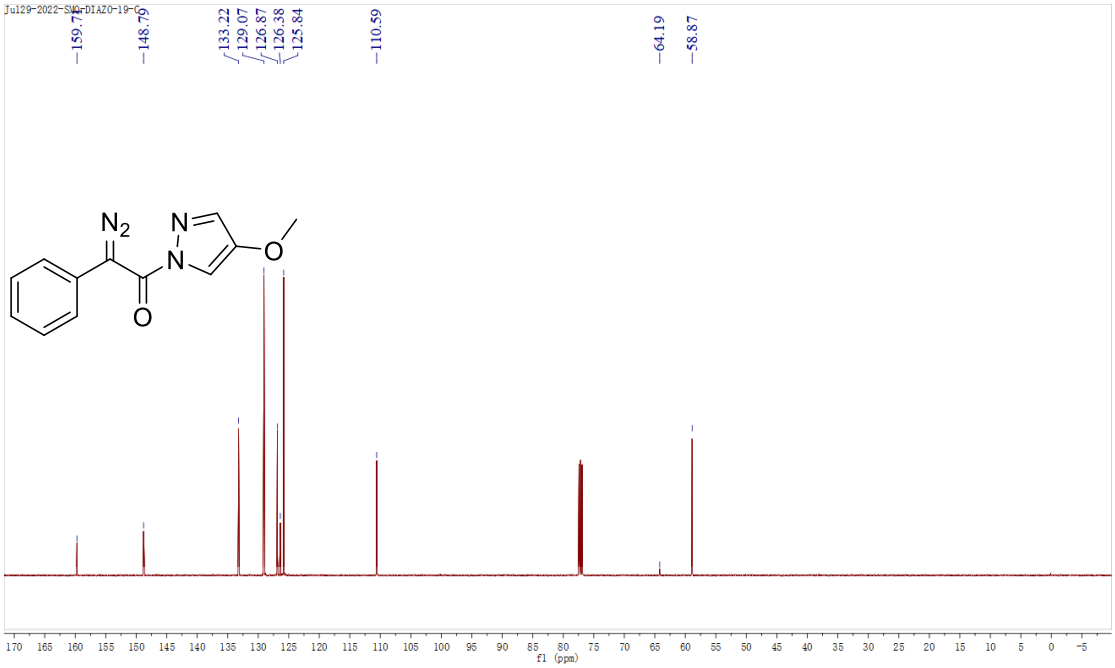
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1'b



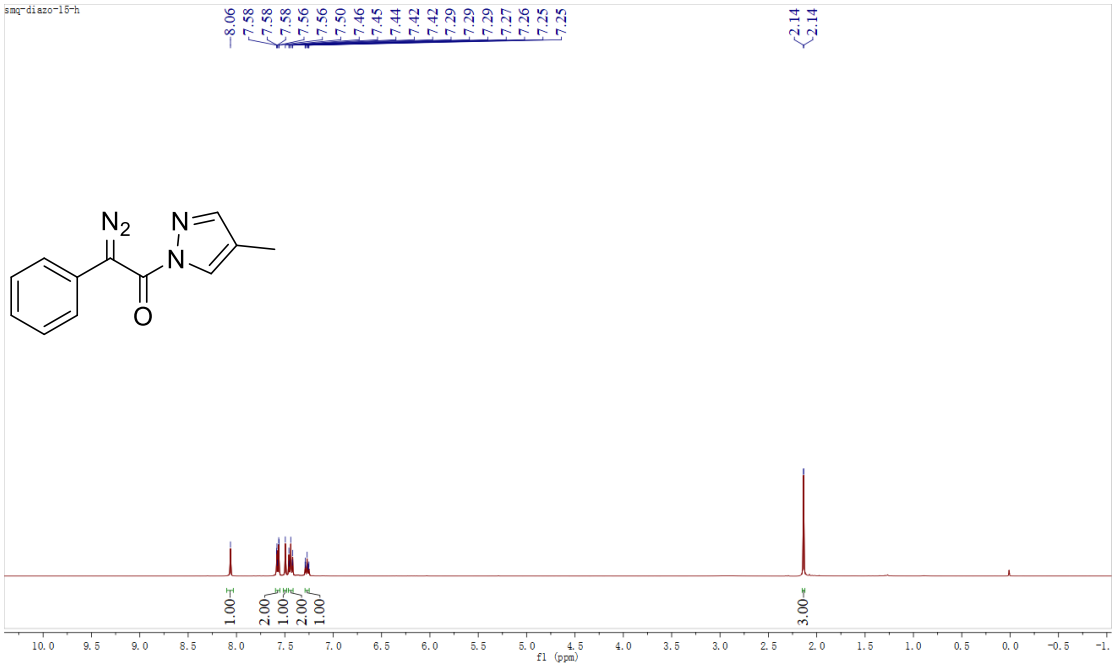


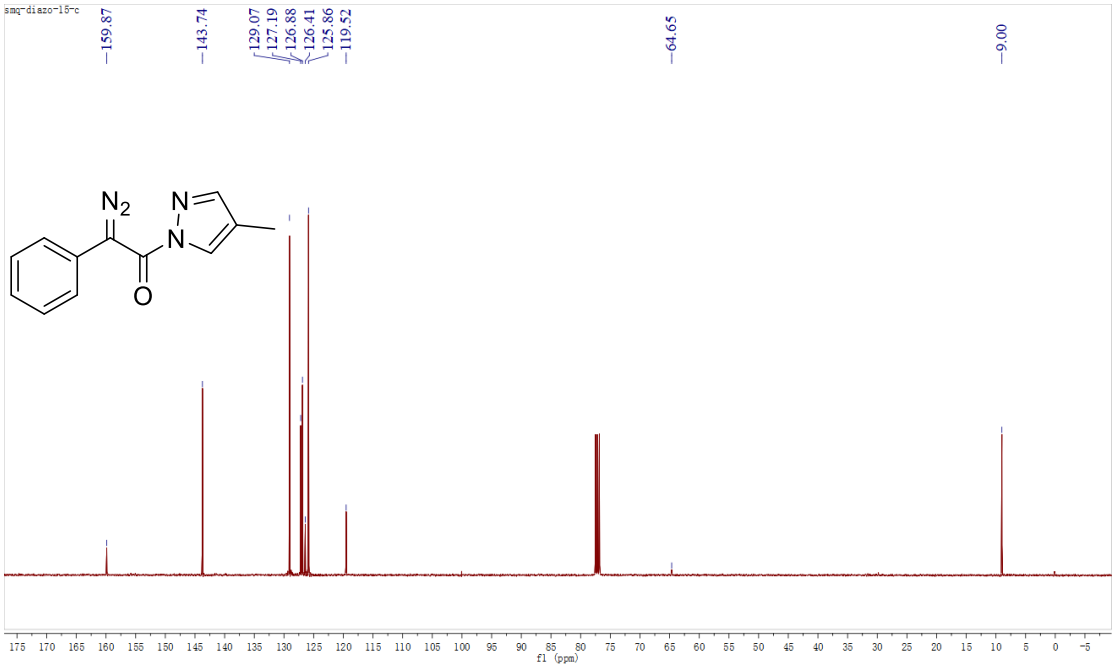
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1'c



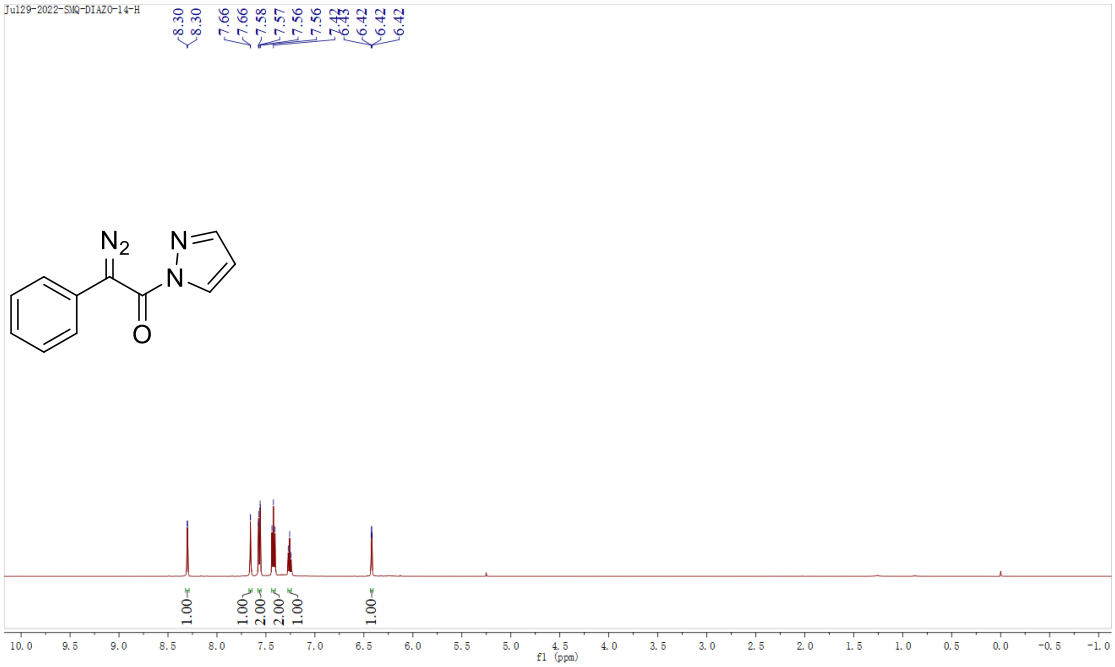


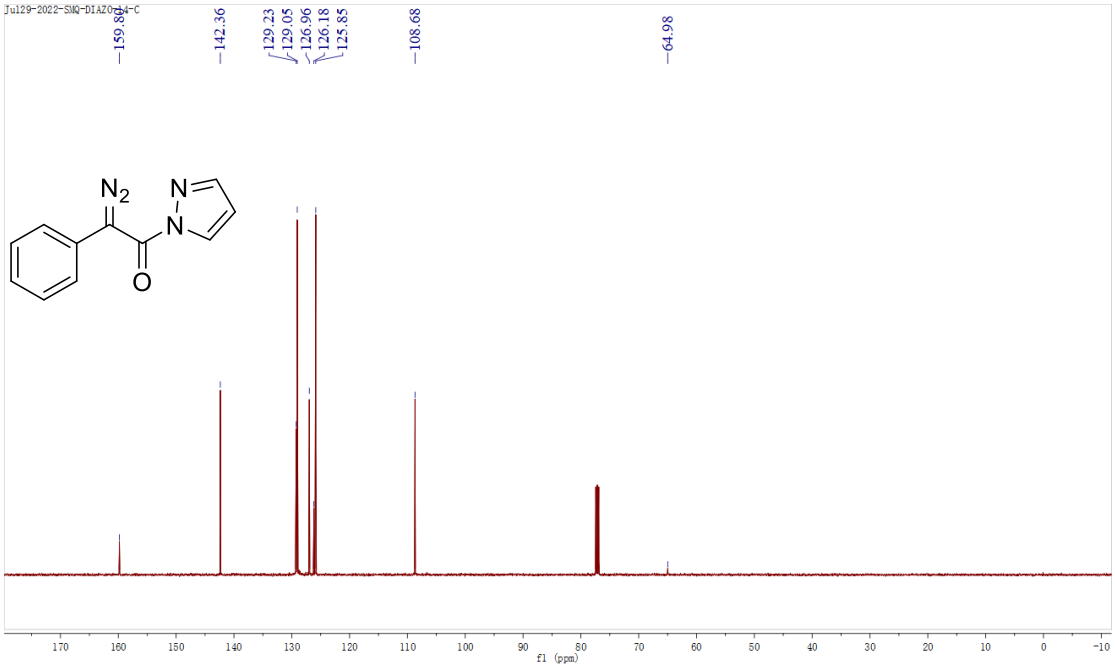
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 1'd



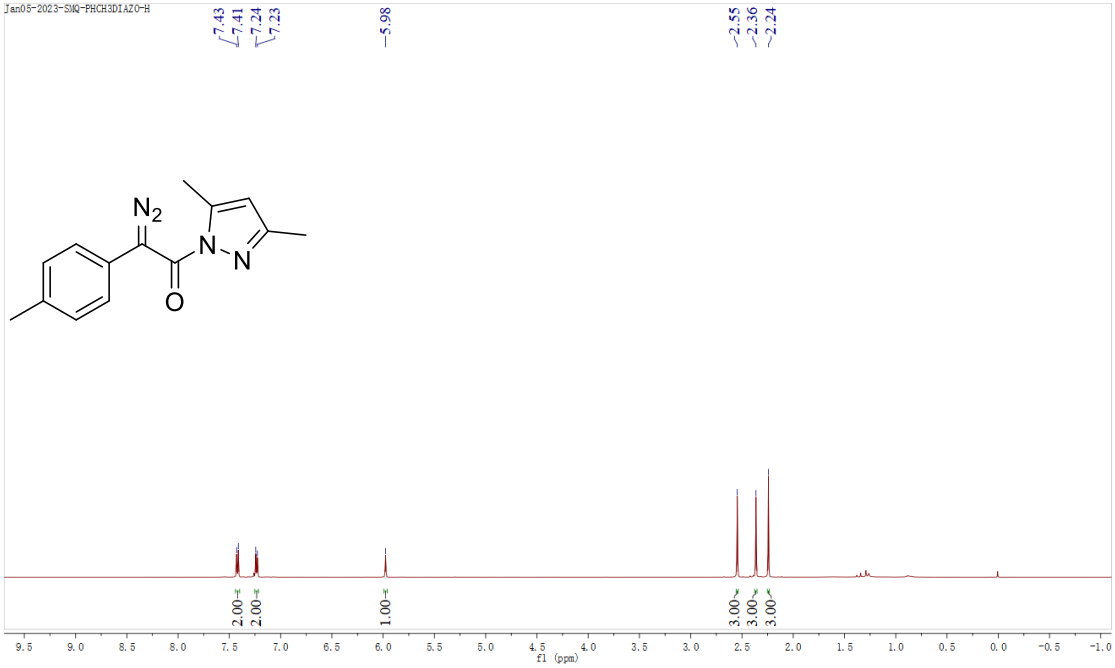


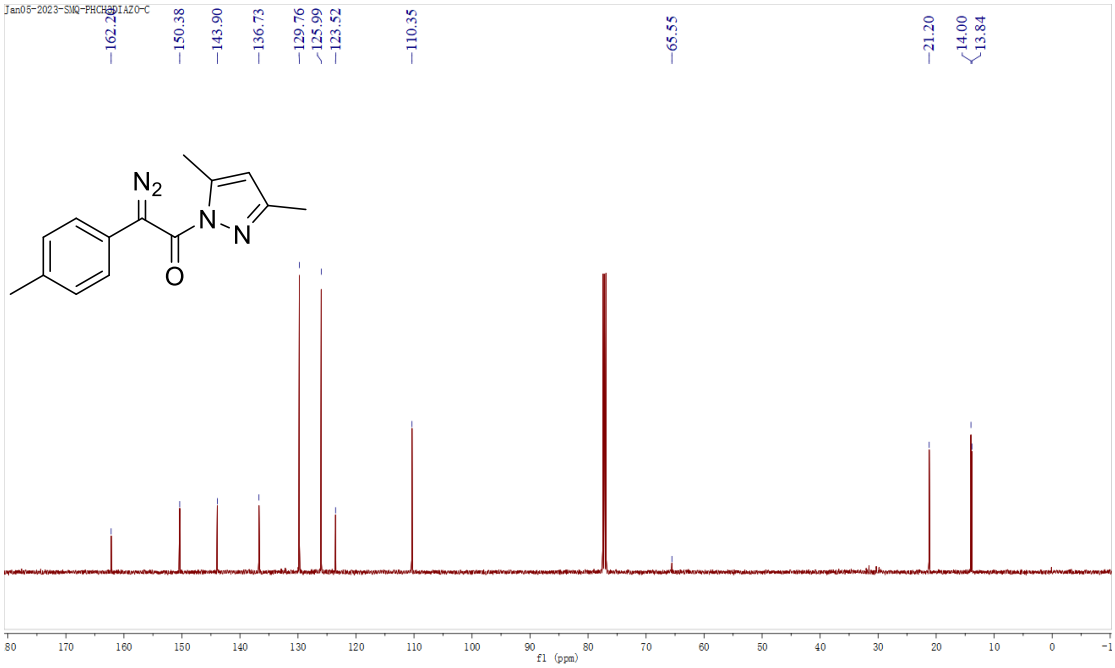
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1'e



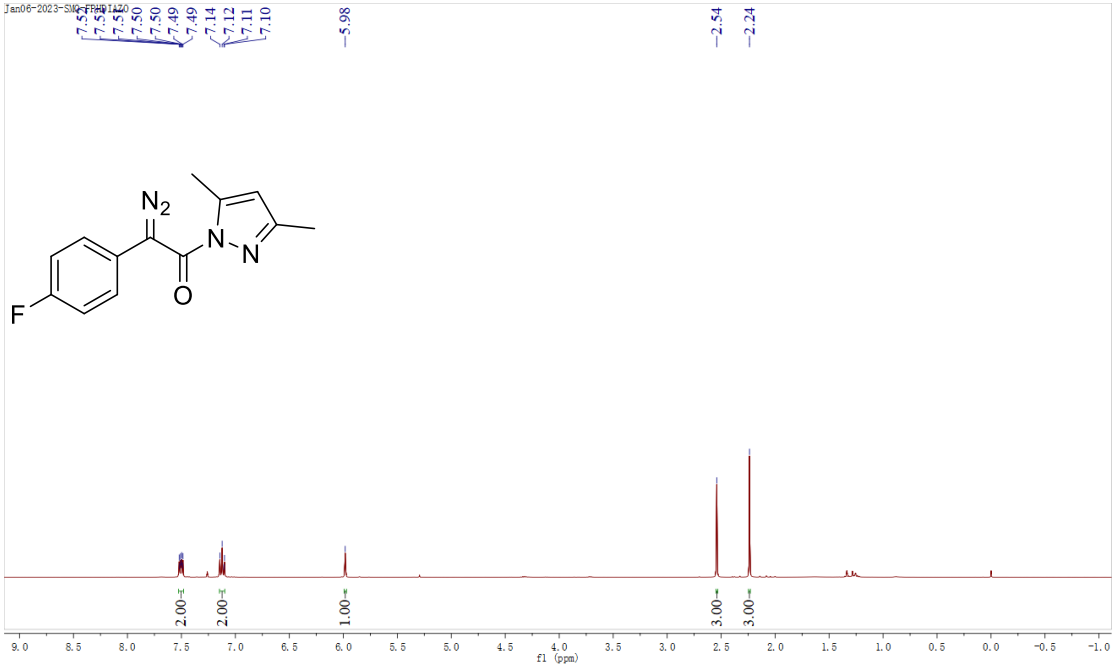


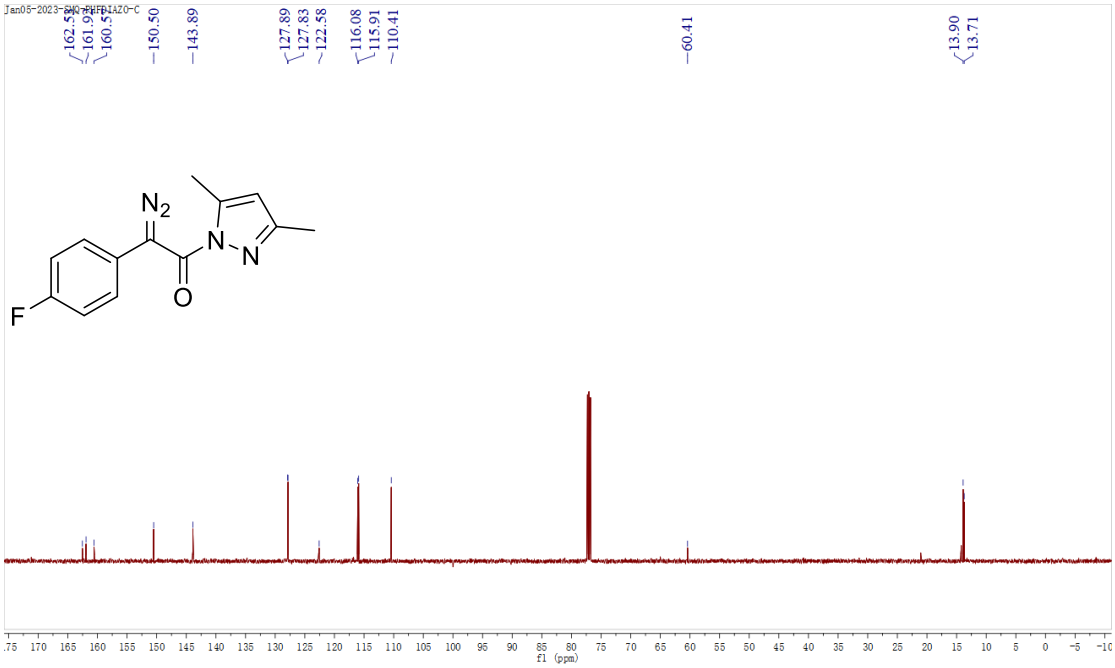
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1'f



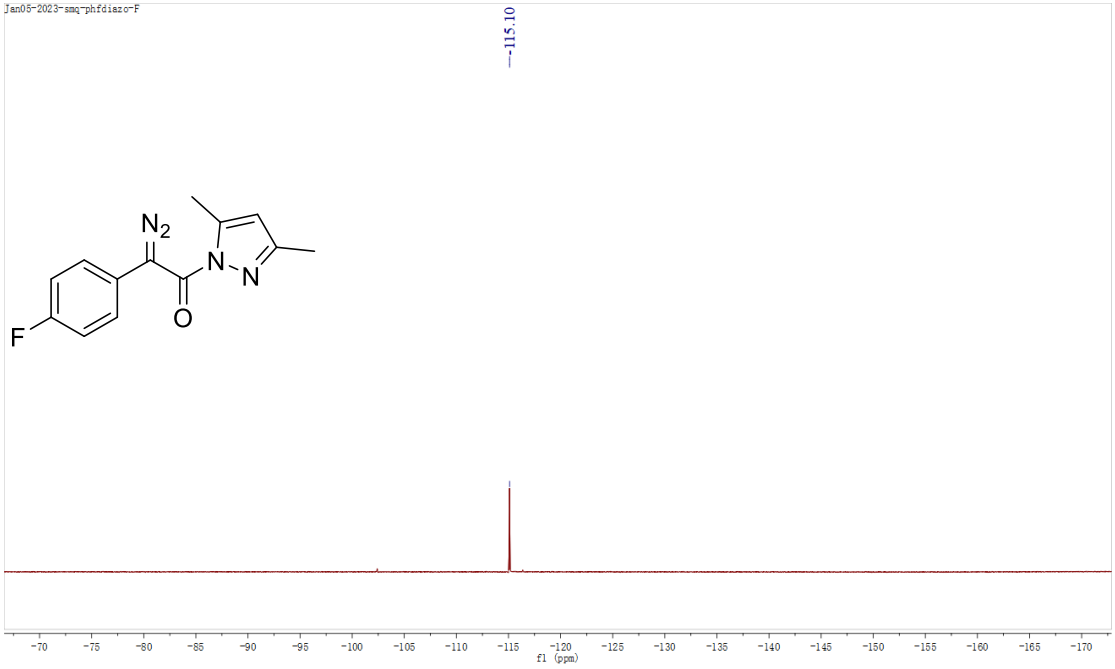


^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 1'g

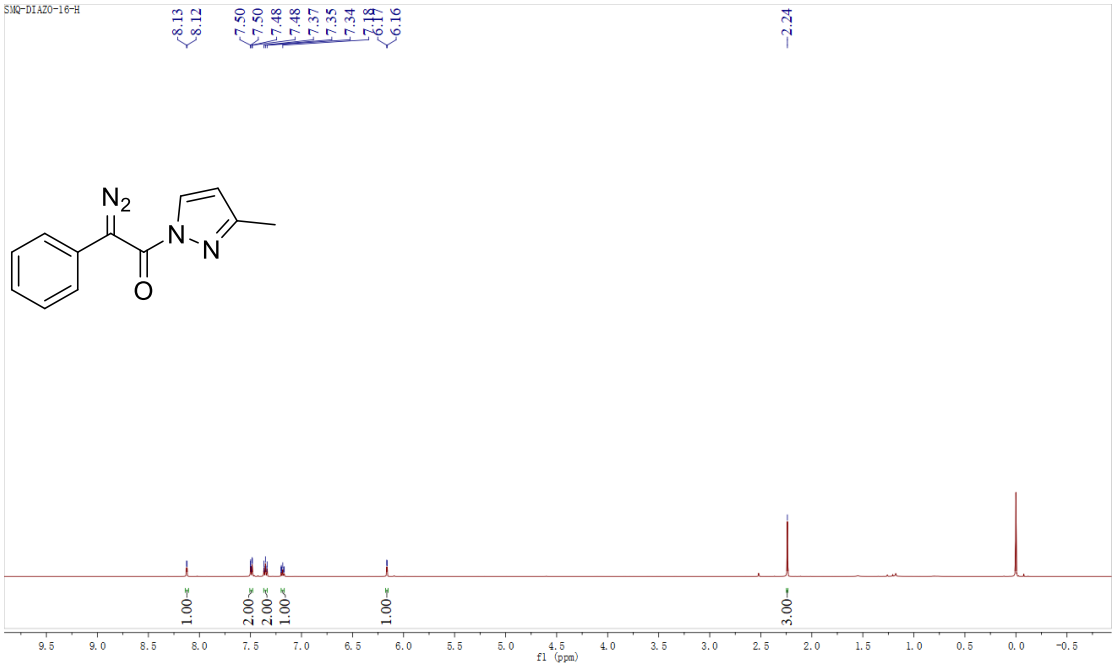


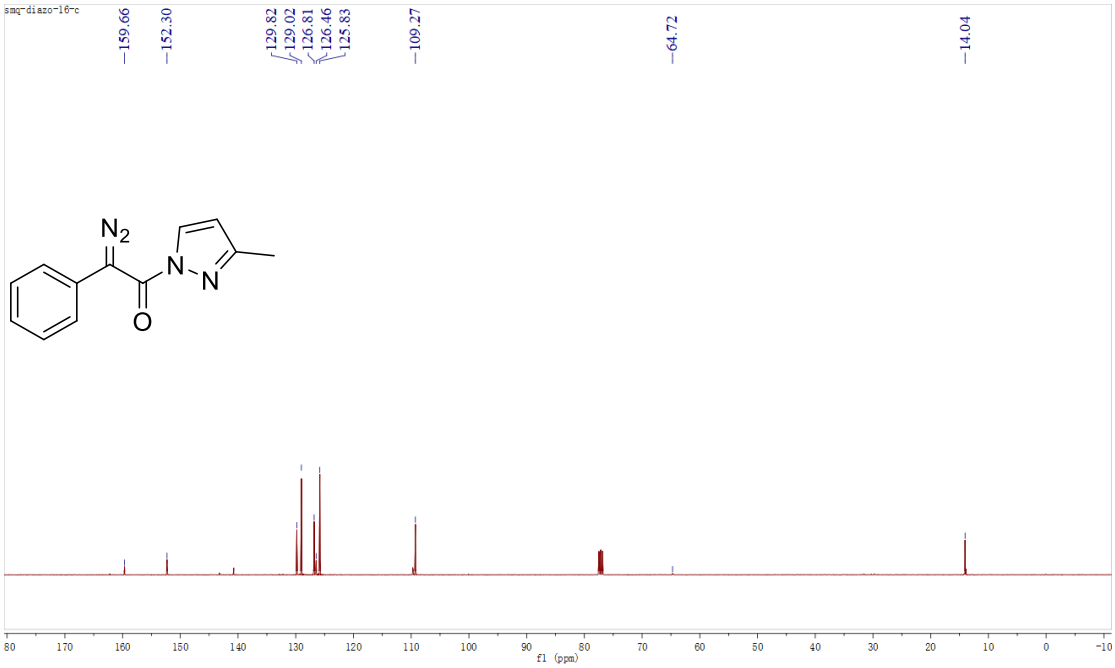


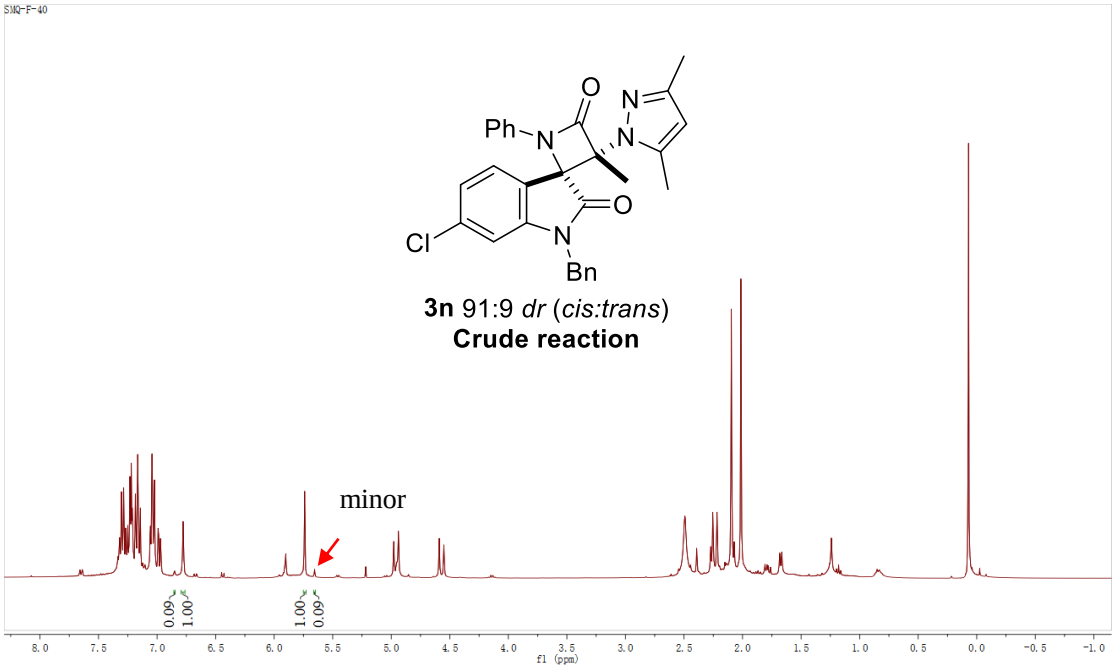
^{19}F NMR (376 MHz, $CDCl_3$) spectra for 1'g



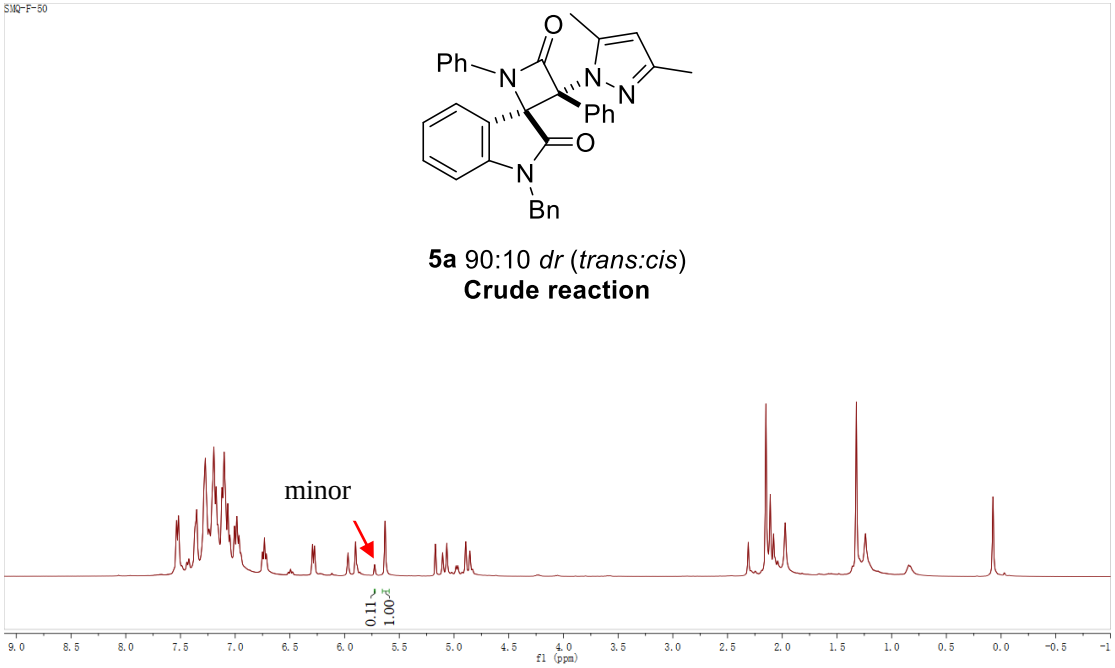
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 1'h





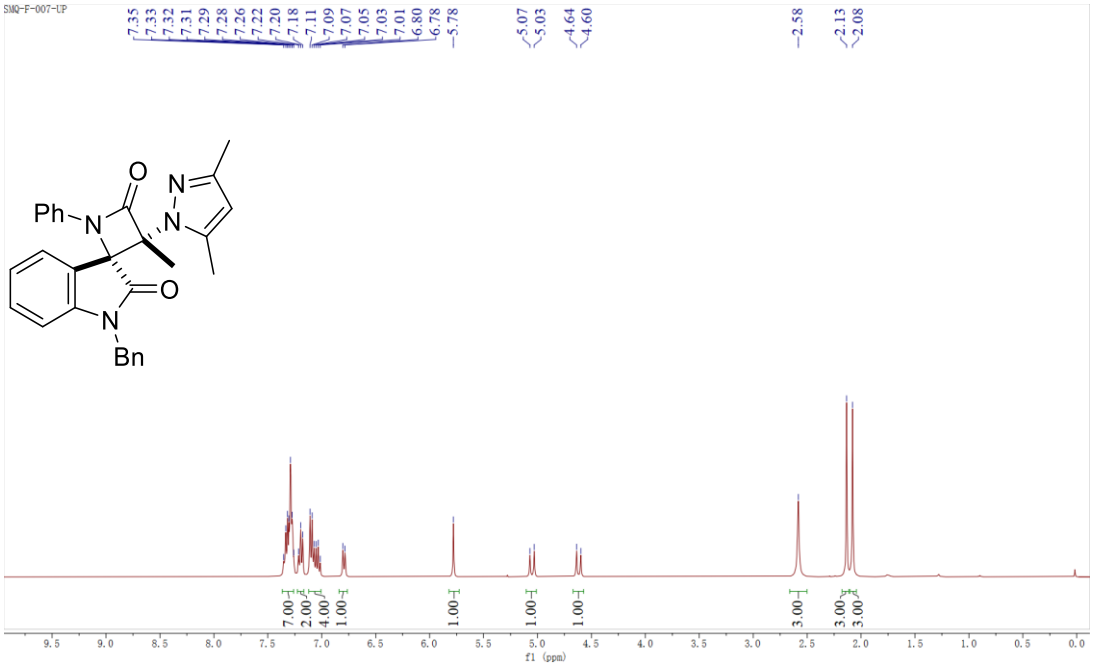


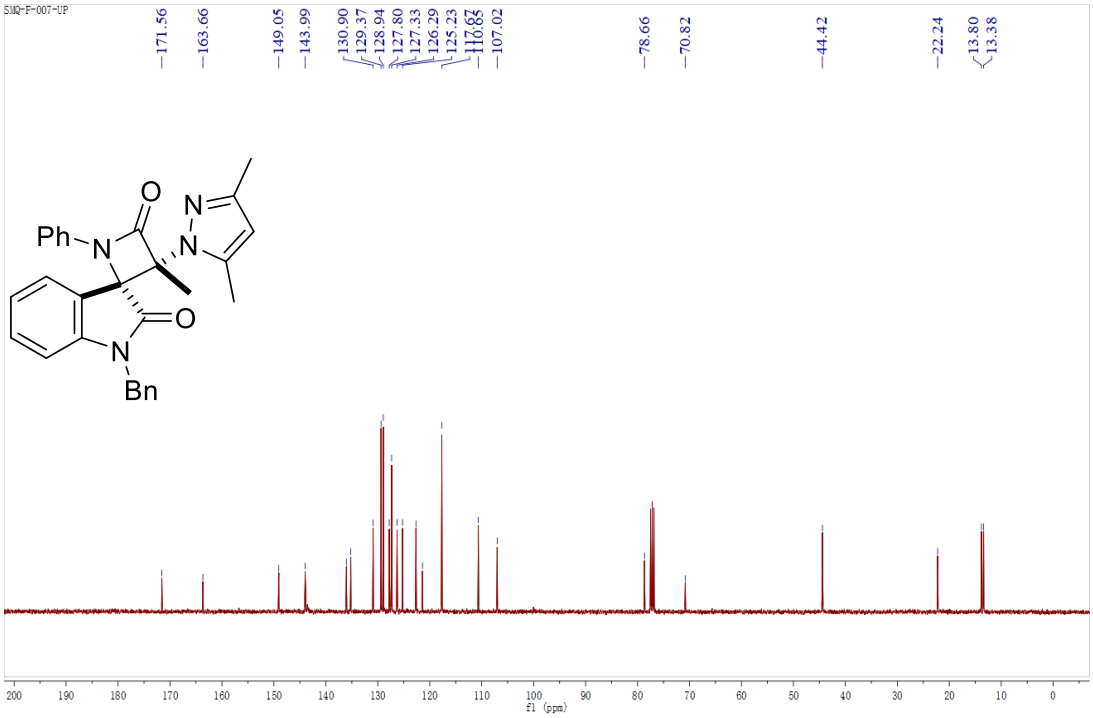
3n 91:9 *dr* (*cis:trans*)
Crude reaction



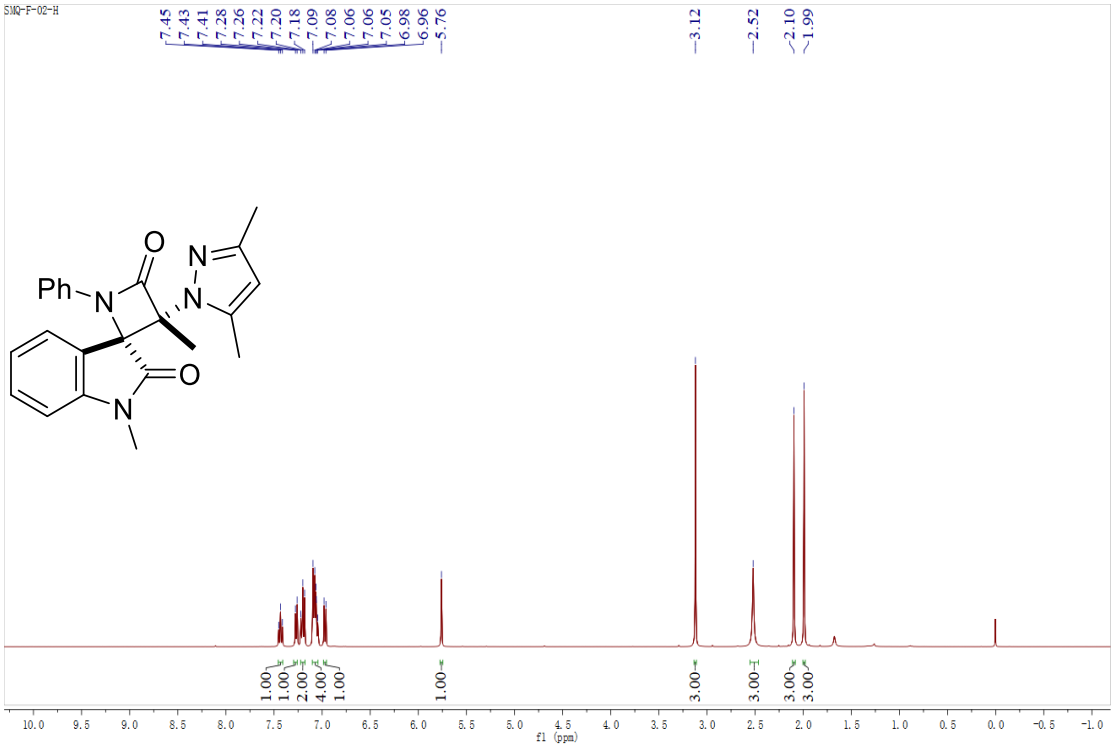
5a 90:10 *dr* (*trans:cis*)
Crude reaction

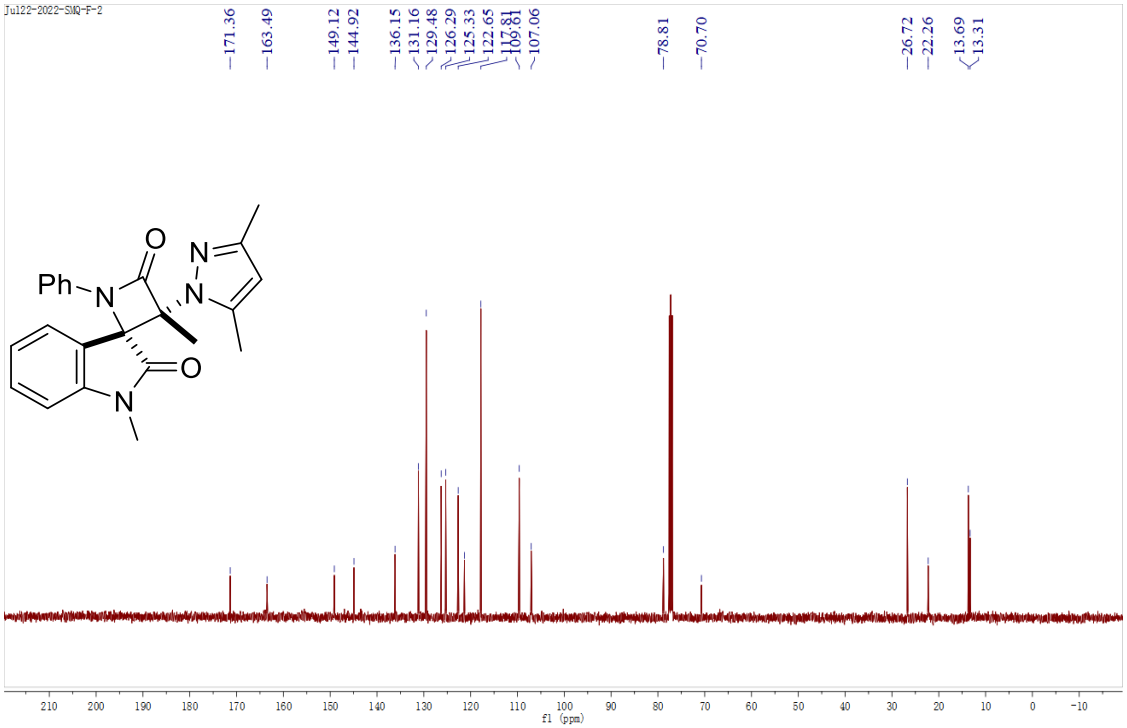
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 3a



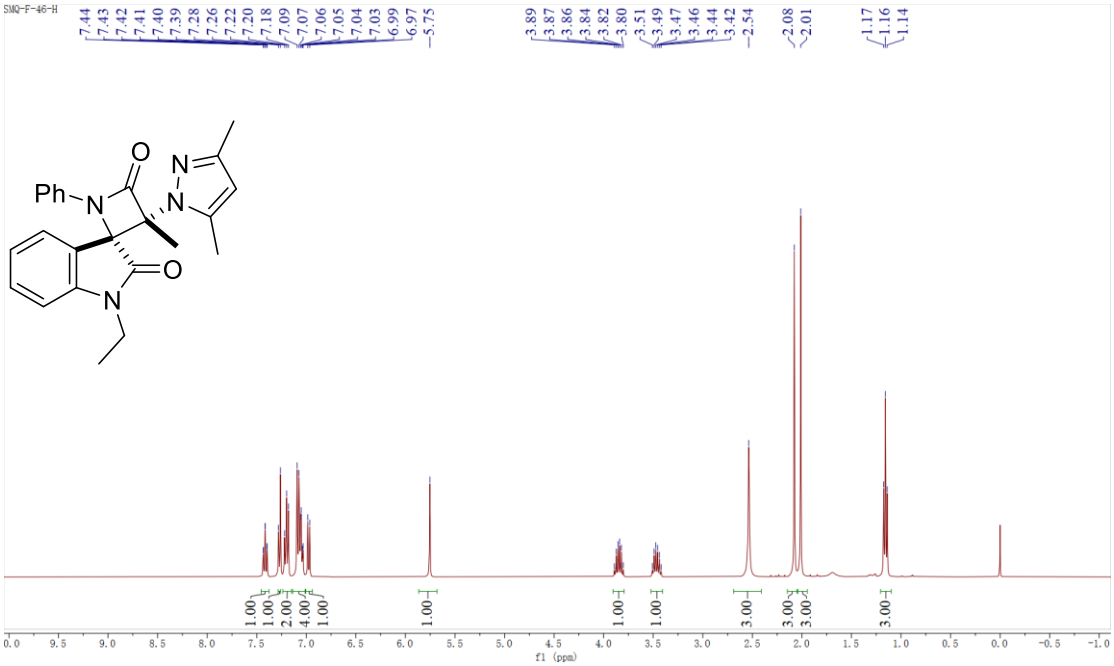


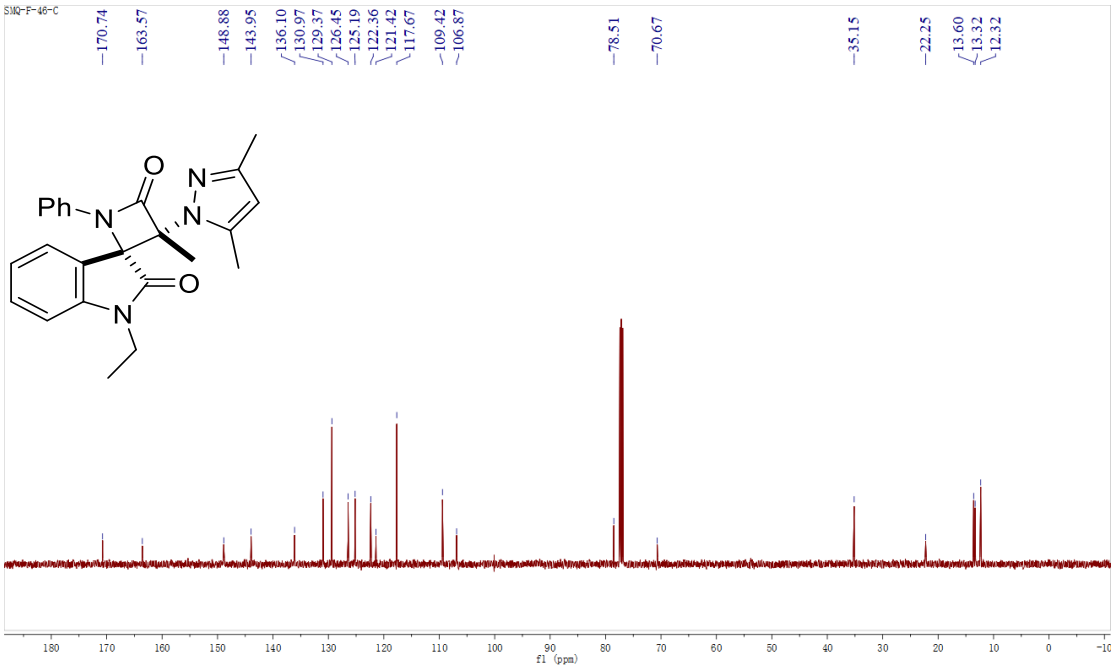
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 3b



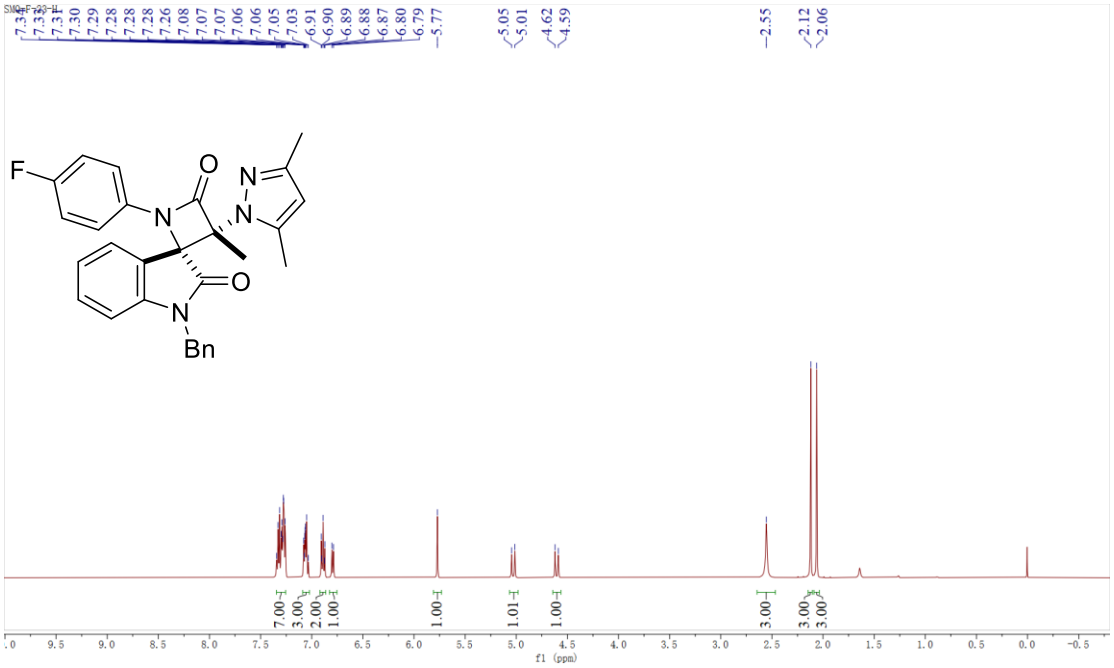


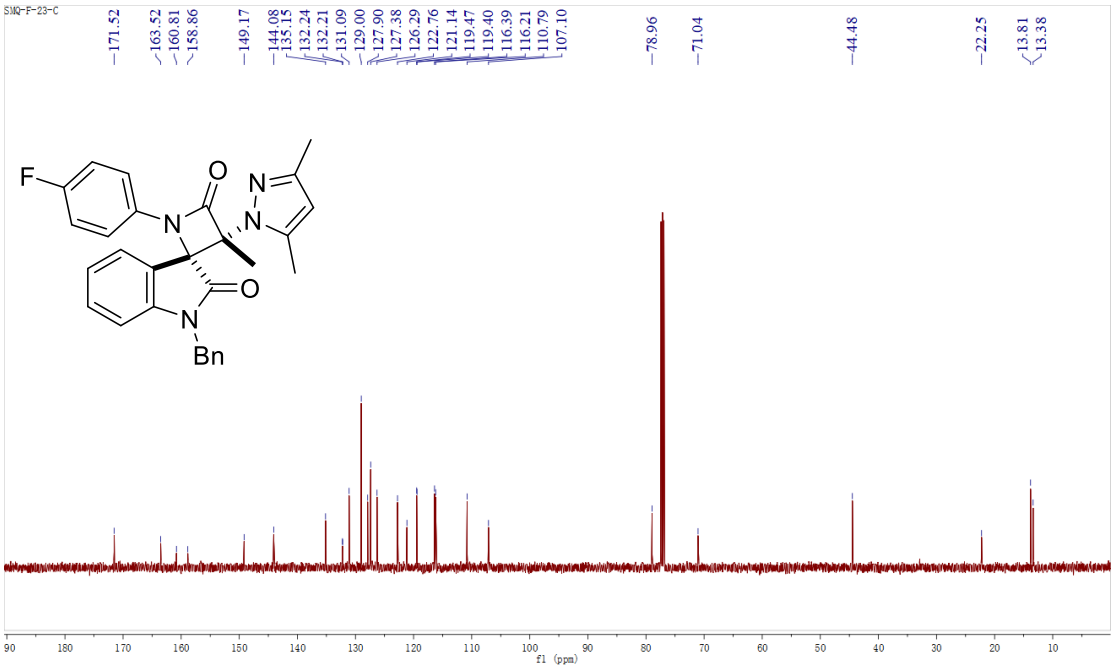
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3c



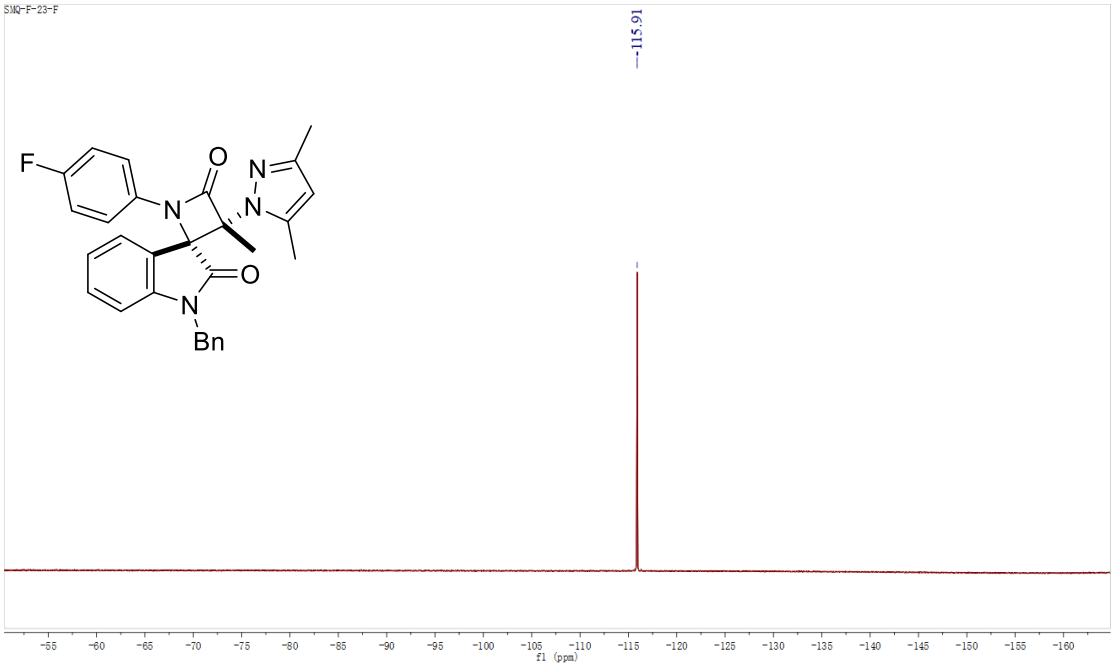


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3d

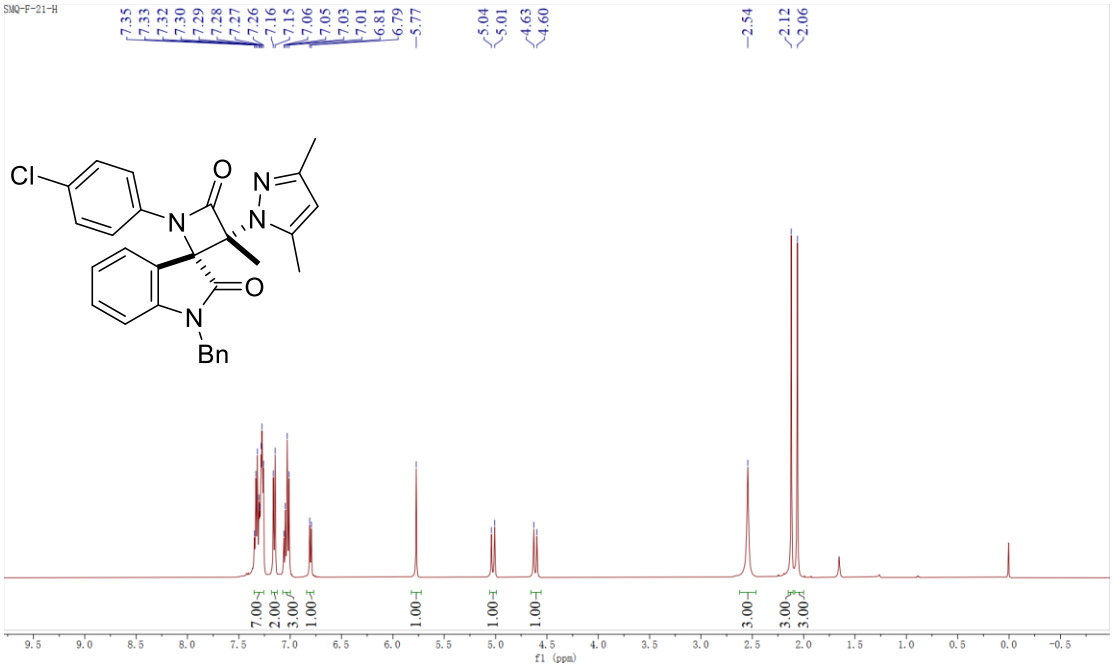


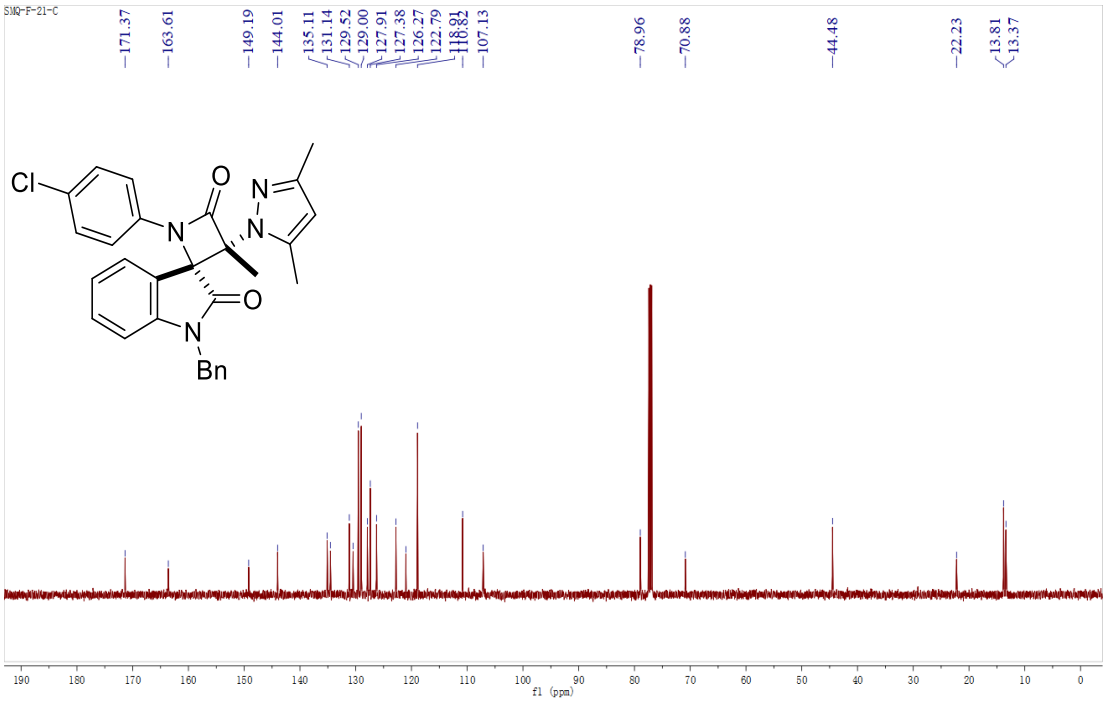


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 3d

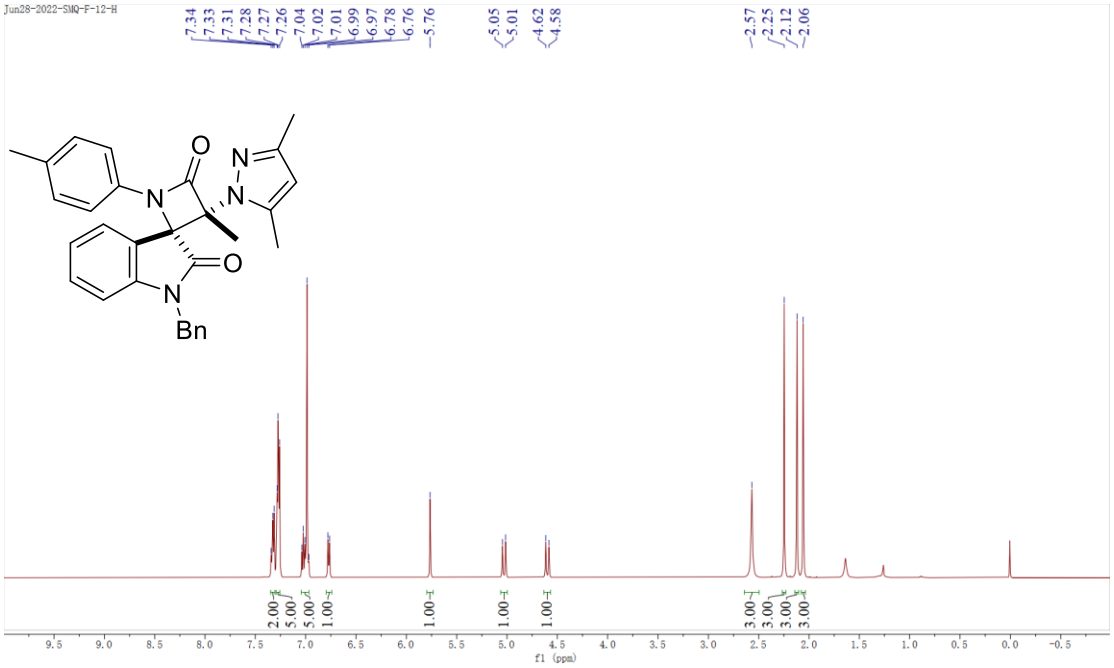


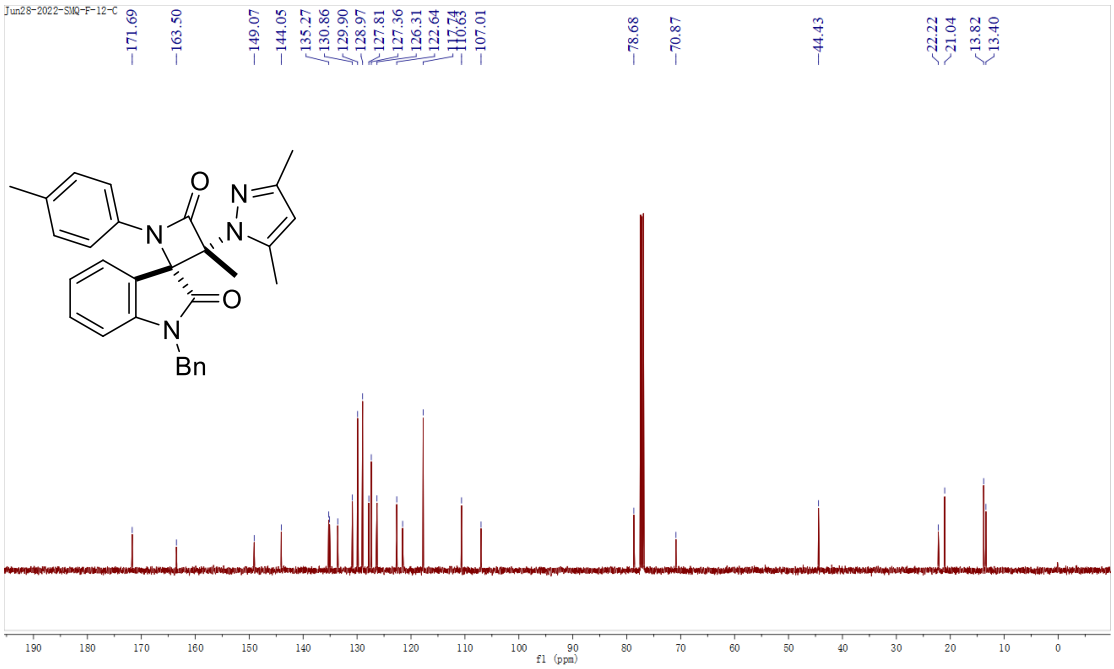
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3e



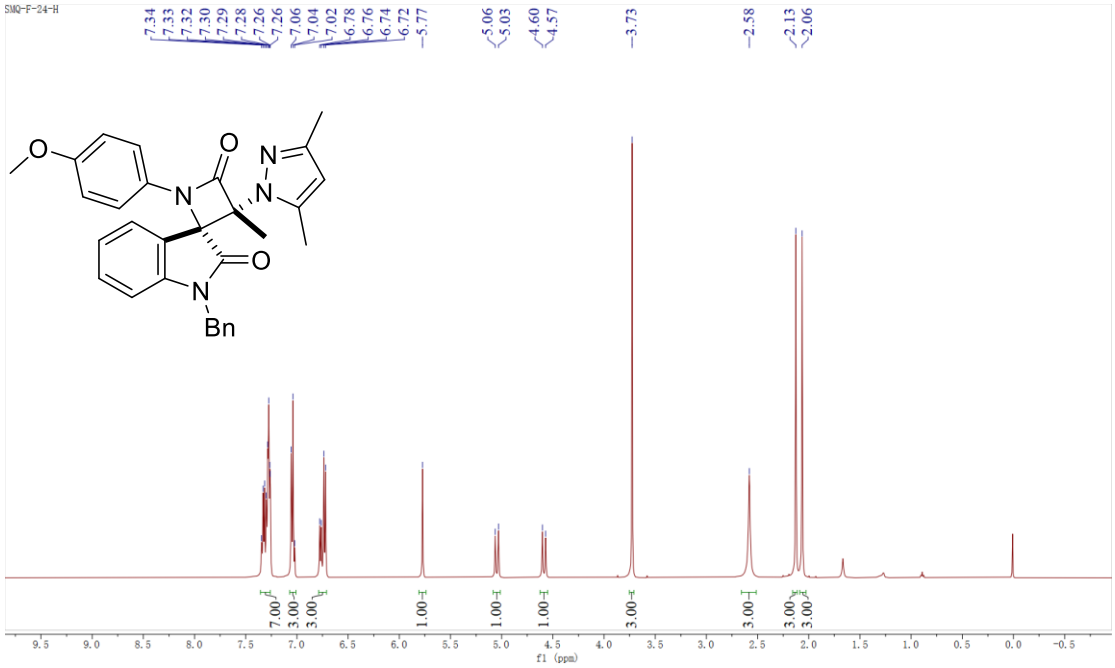


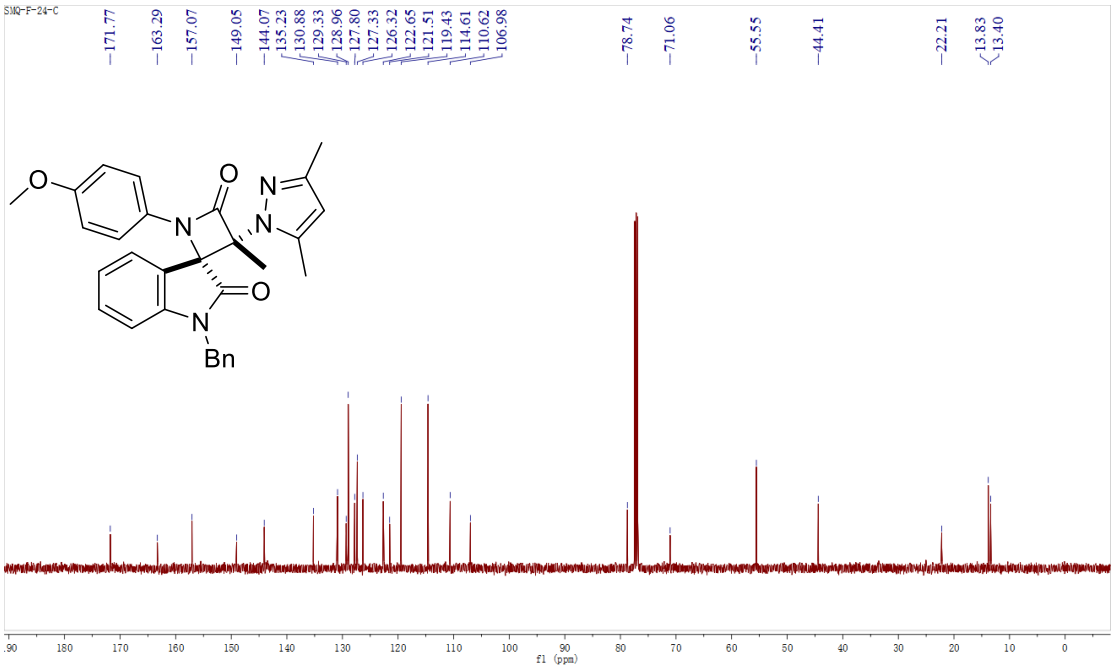
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3f



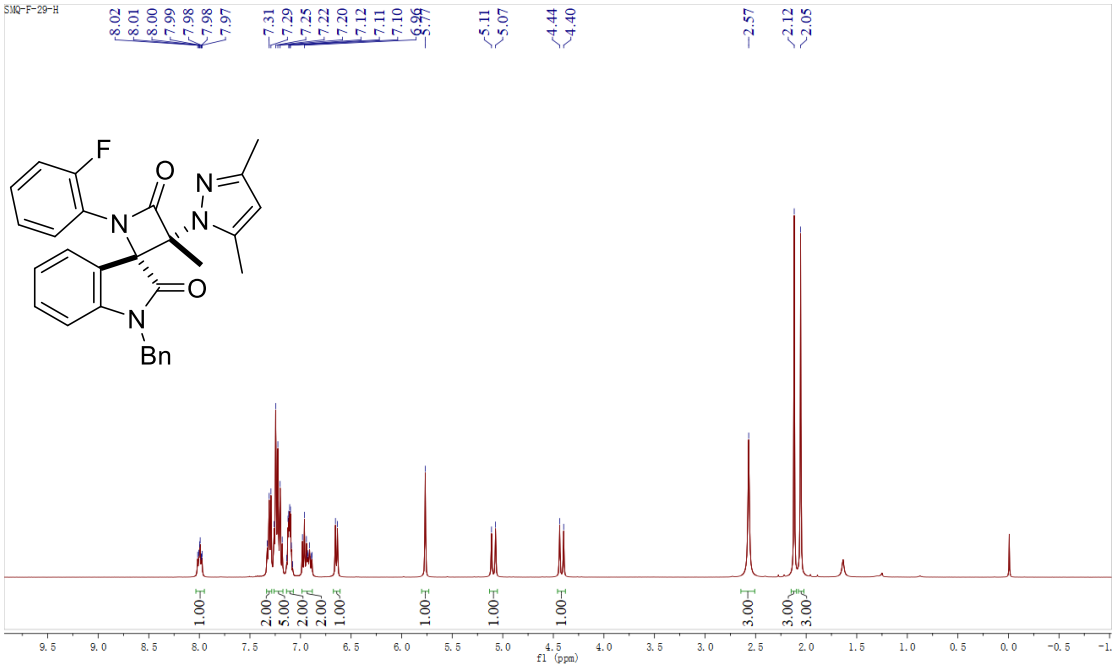


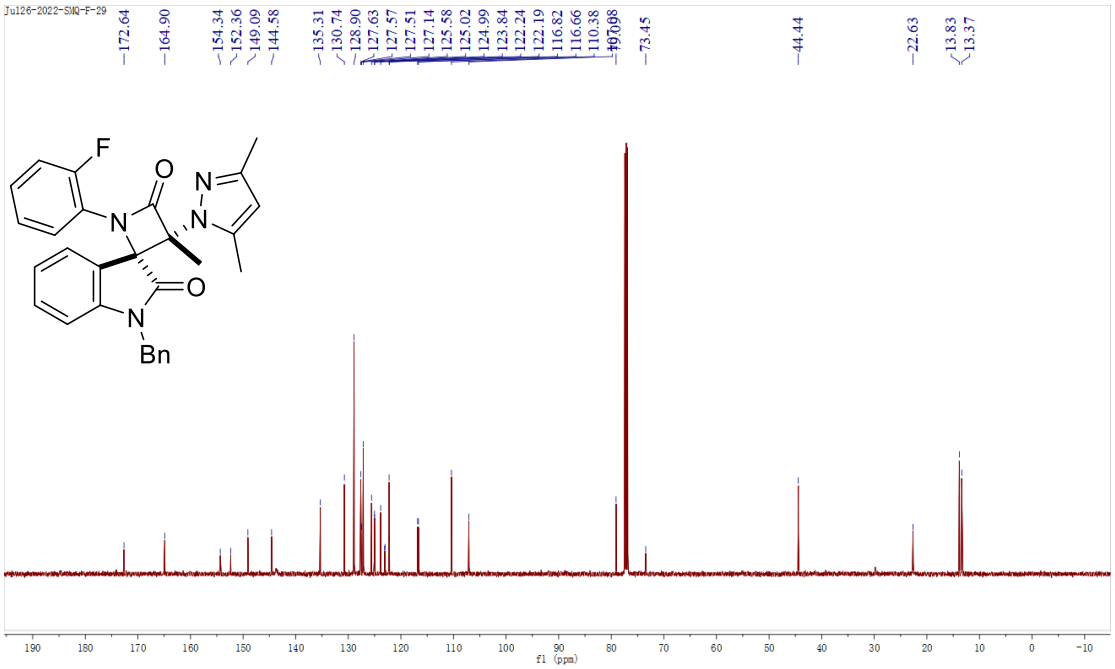
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3g



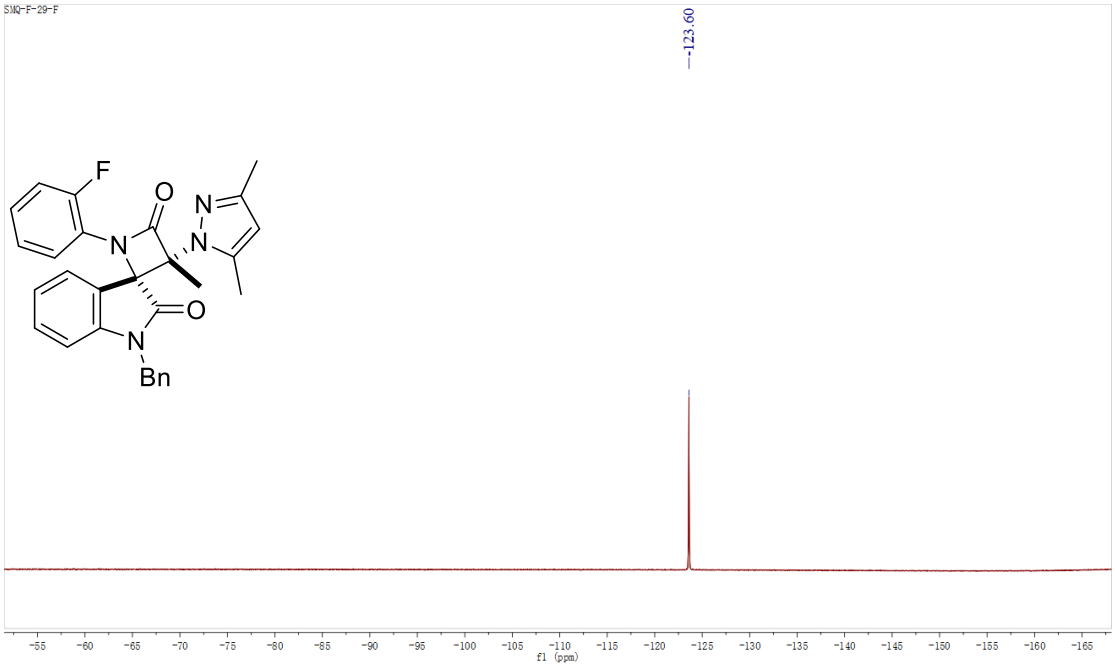


^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3h

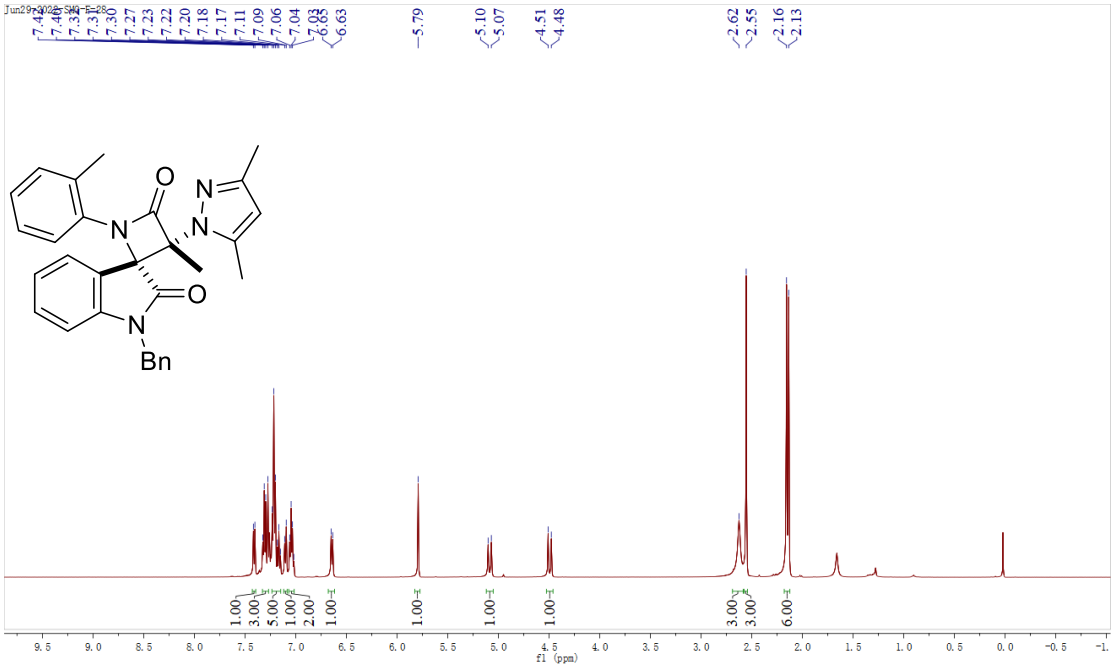


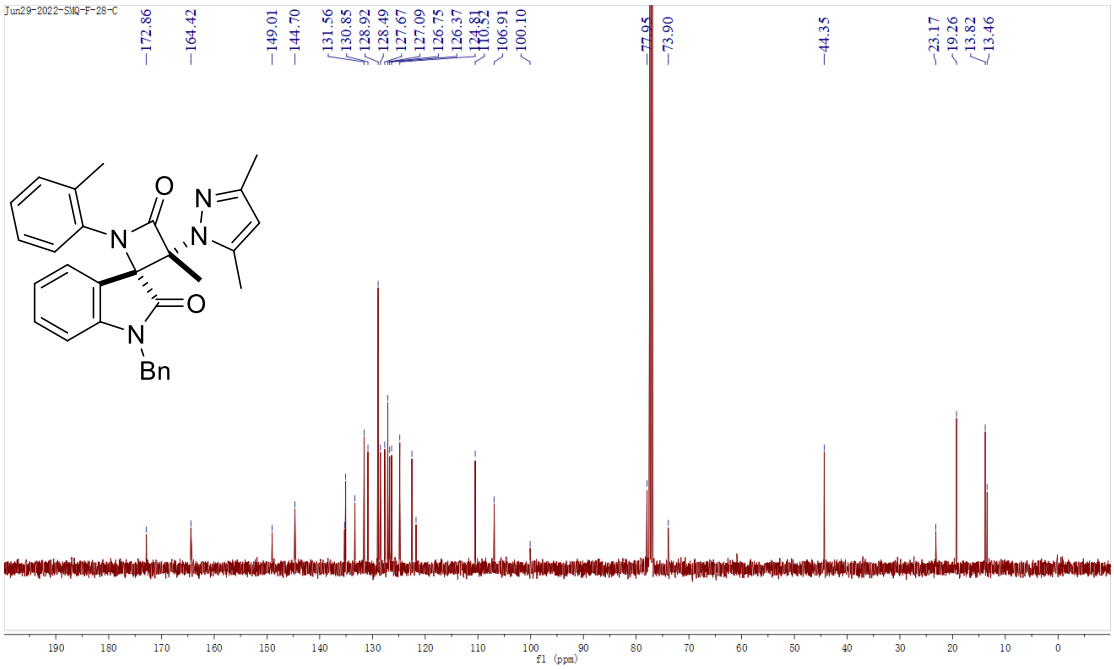


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 3h

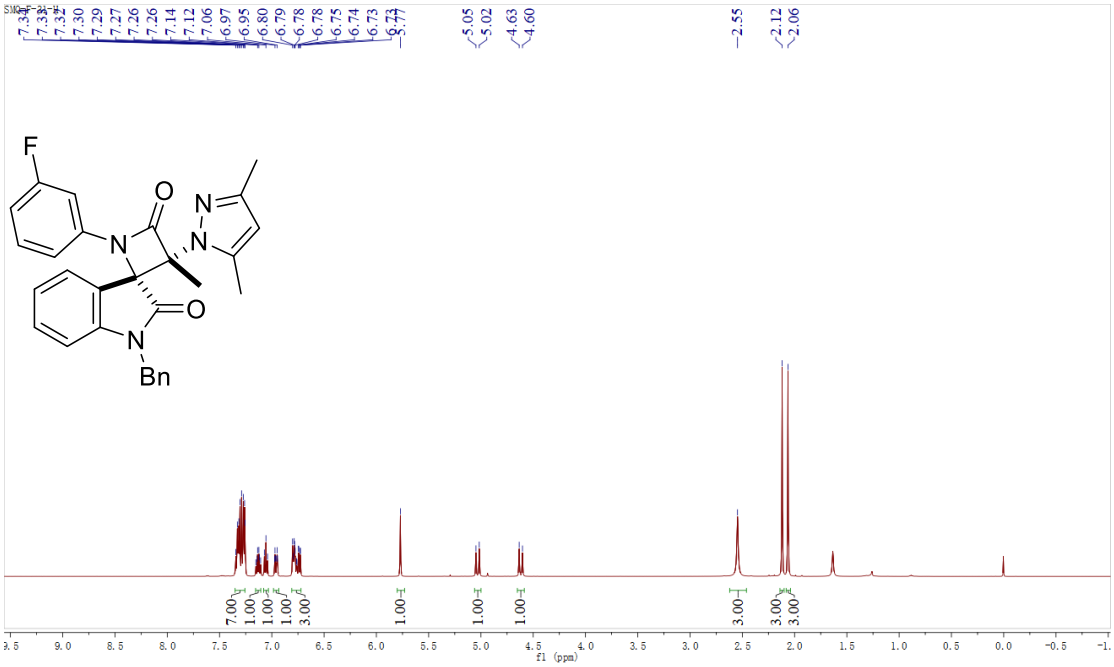


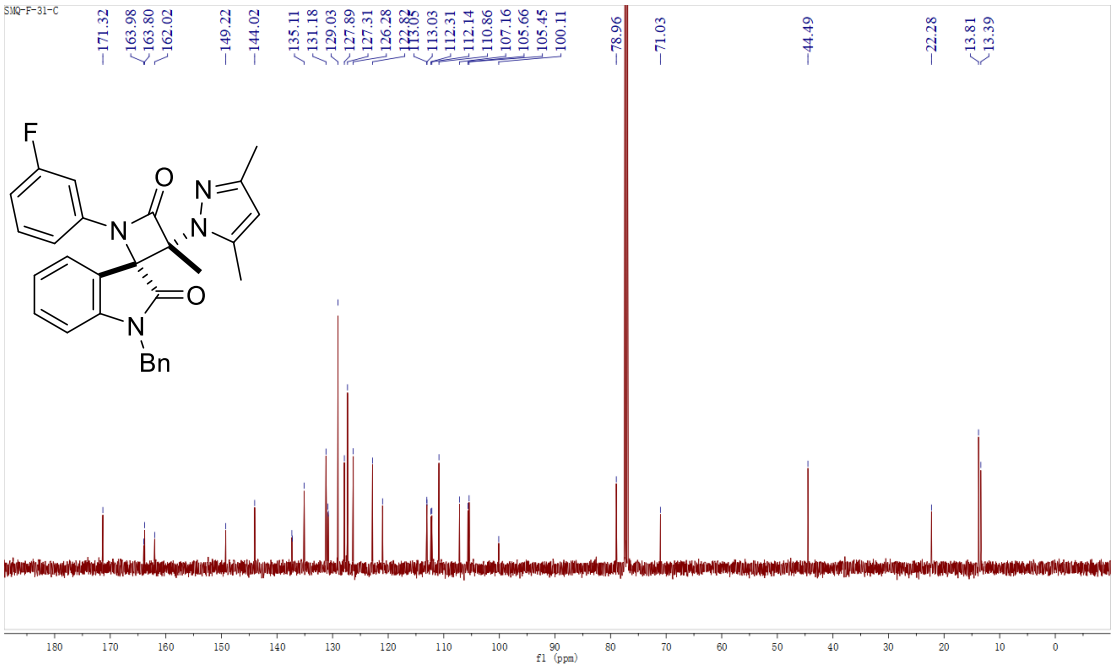
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3i



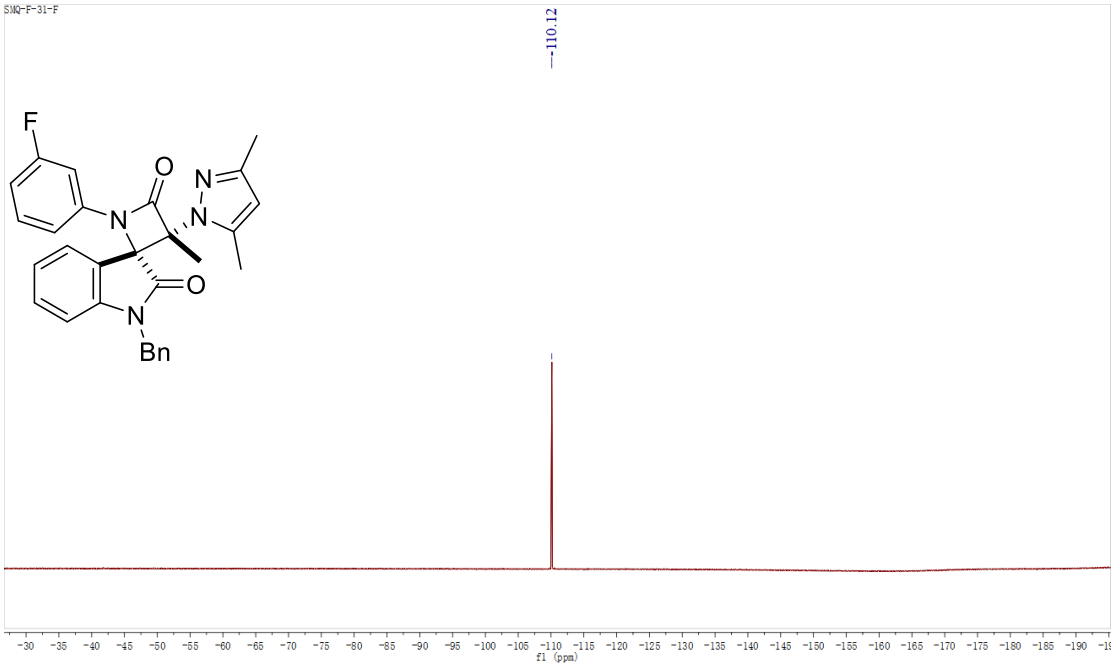


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3j

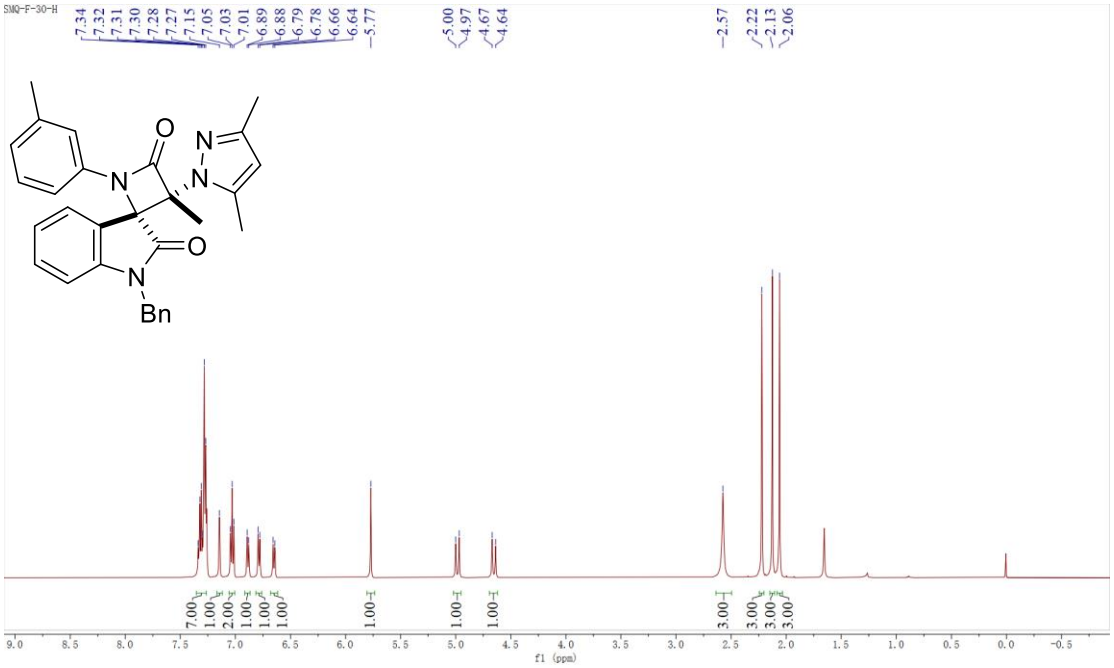


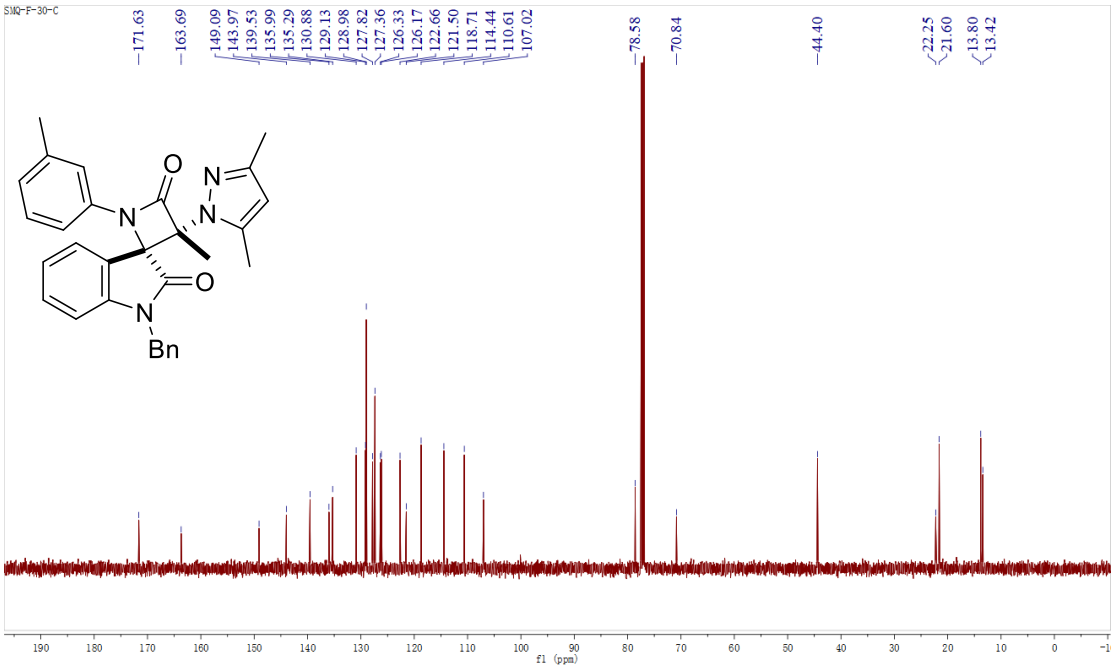


^{19}F NMR (376 MHz, $CDCl_3$) and spectra for 3j

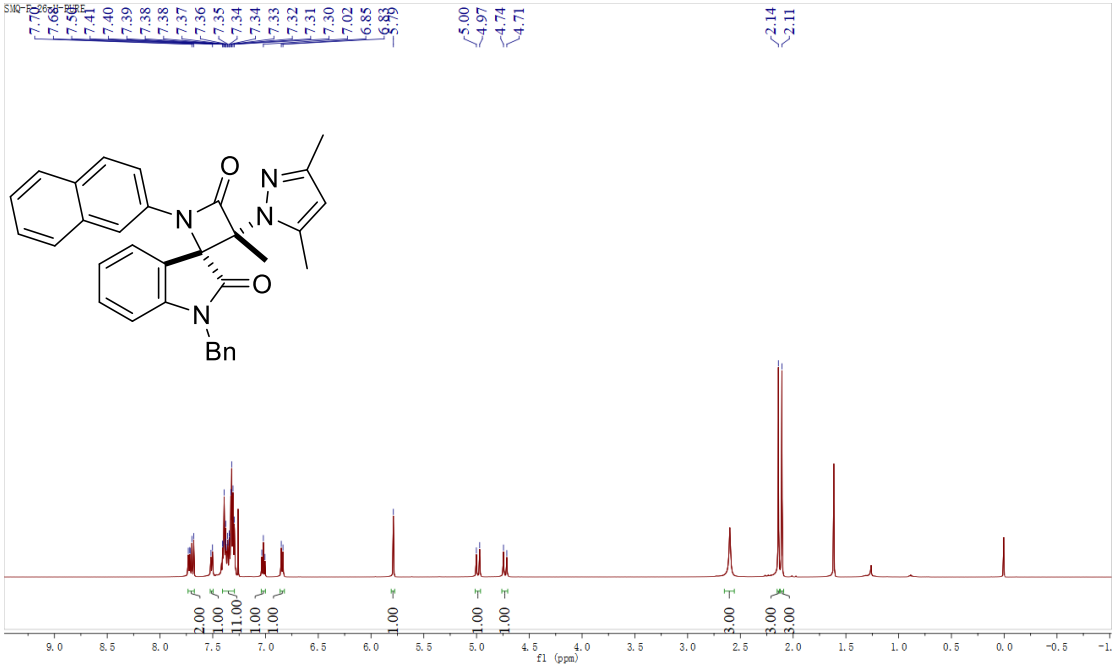


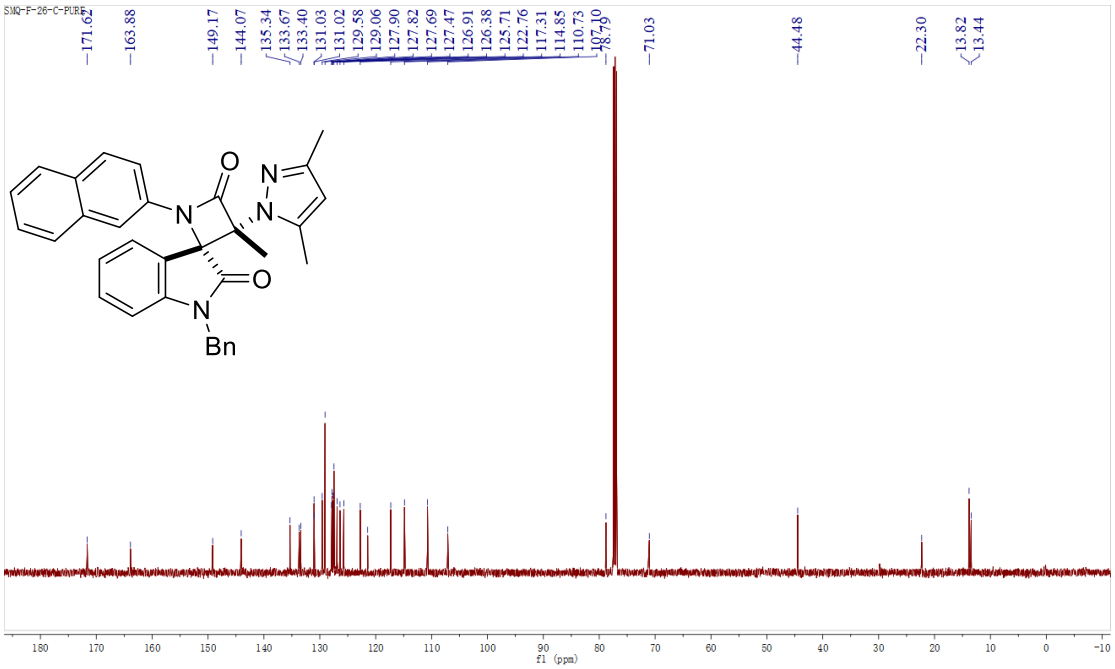
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3k



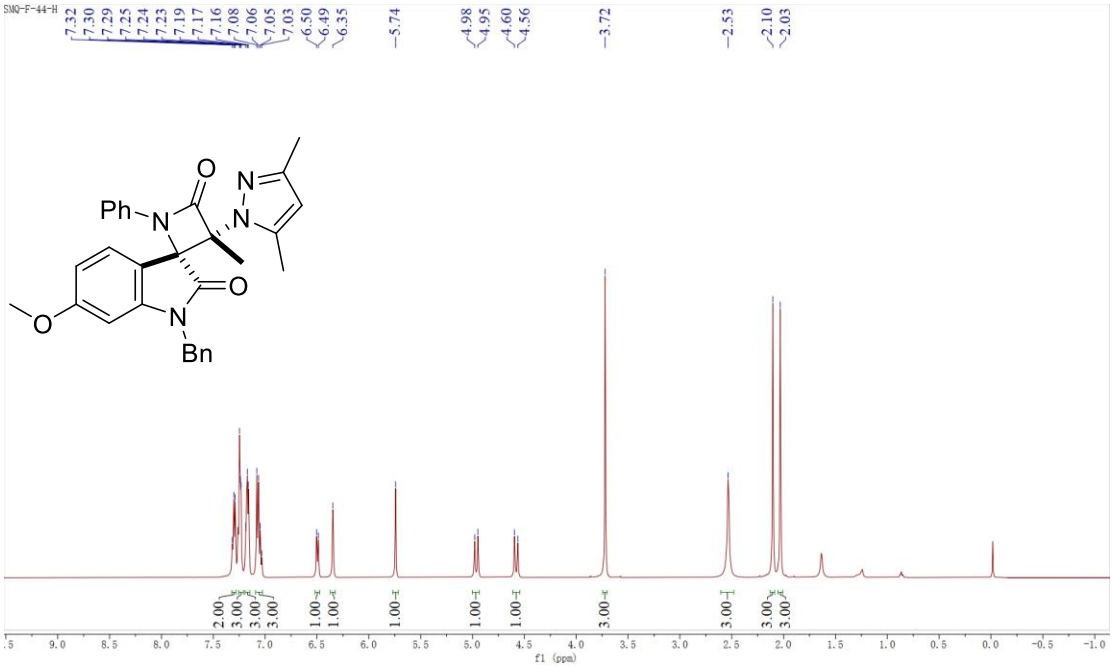


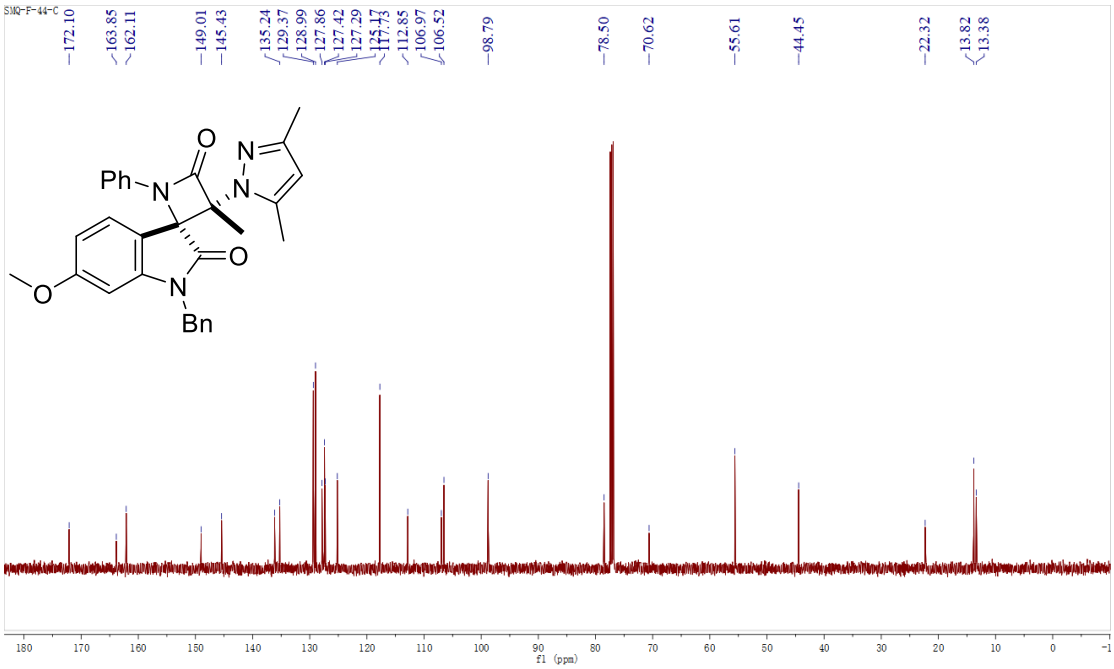
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3l



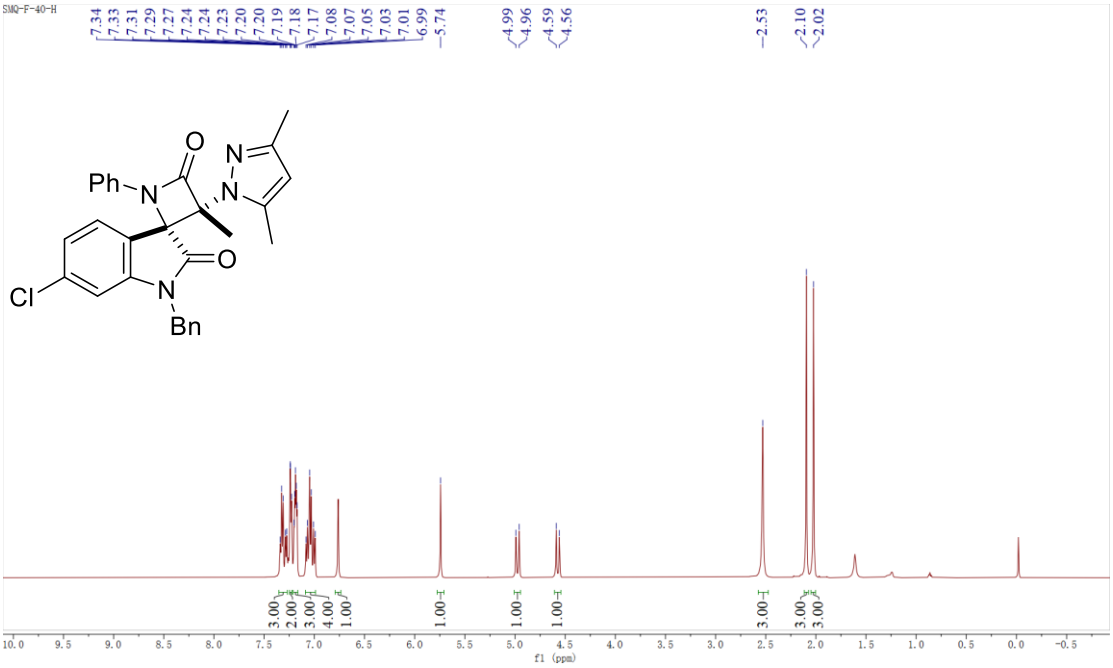


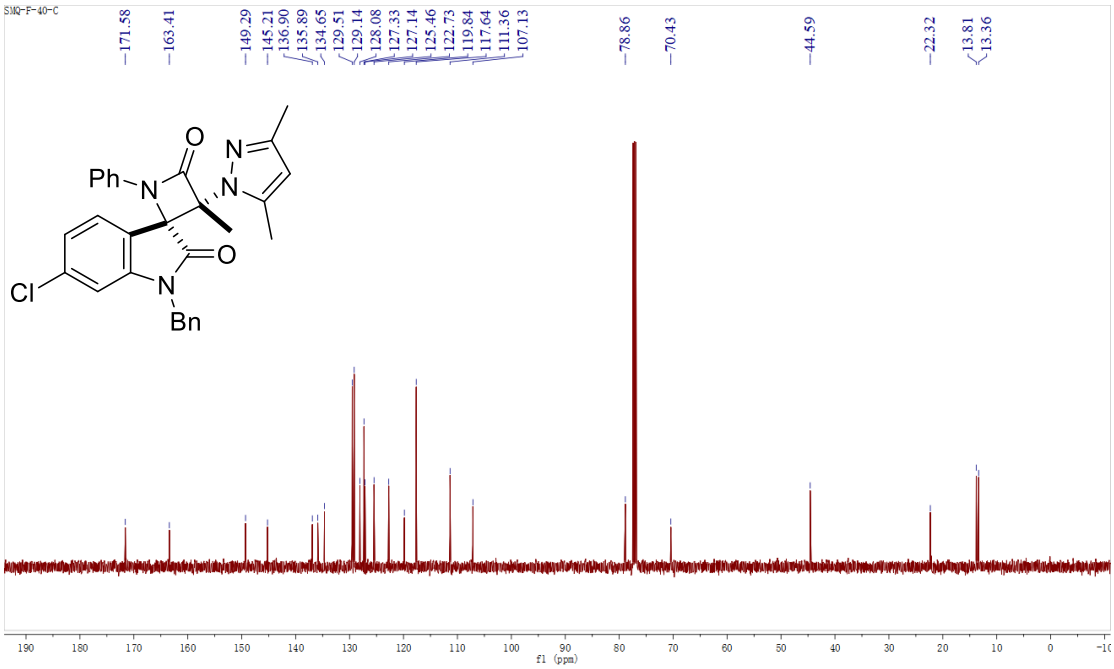
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3m



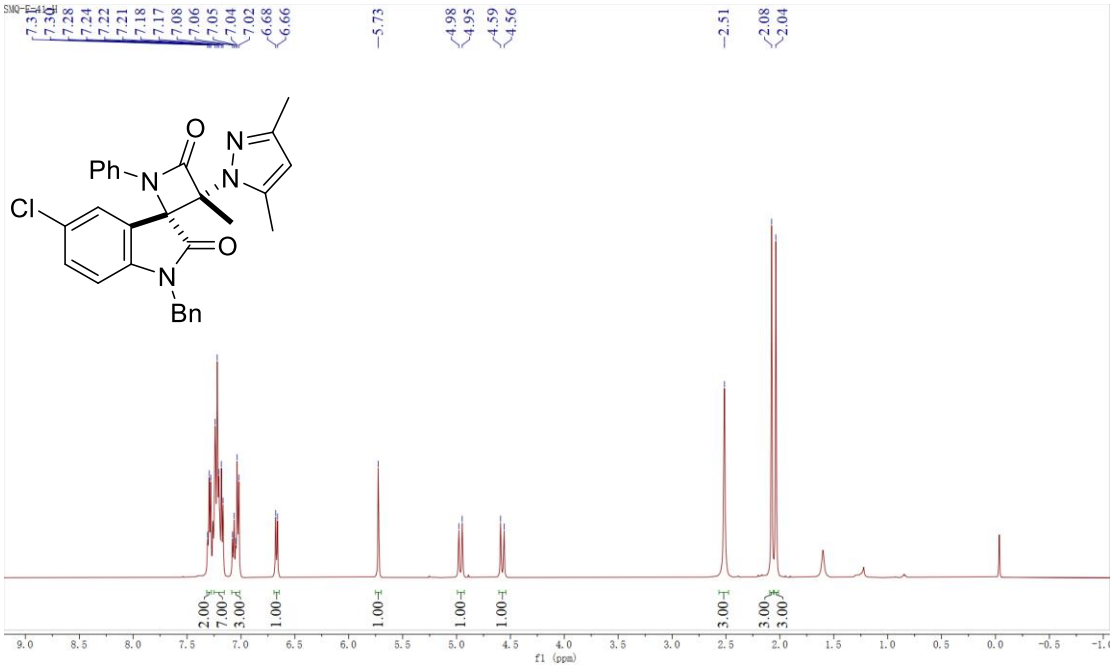


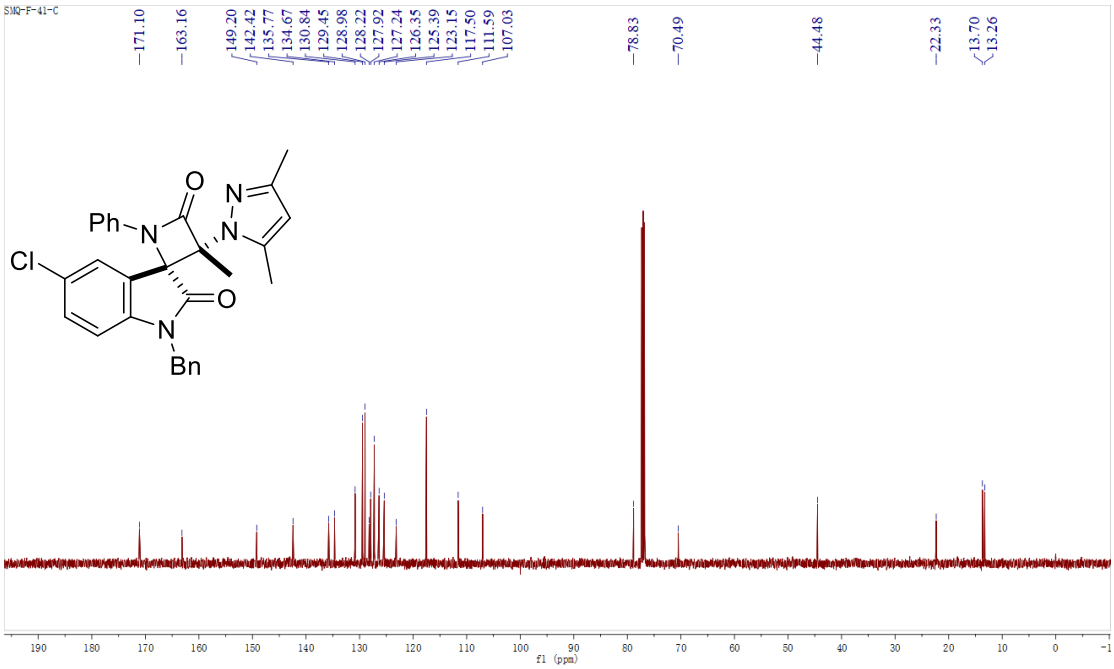
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3n



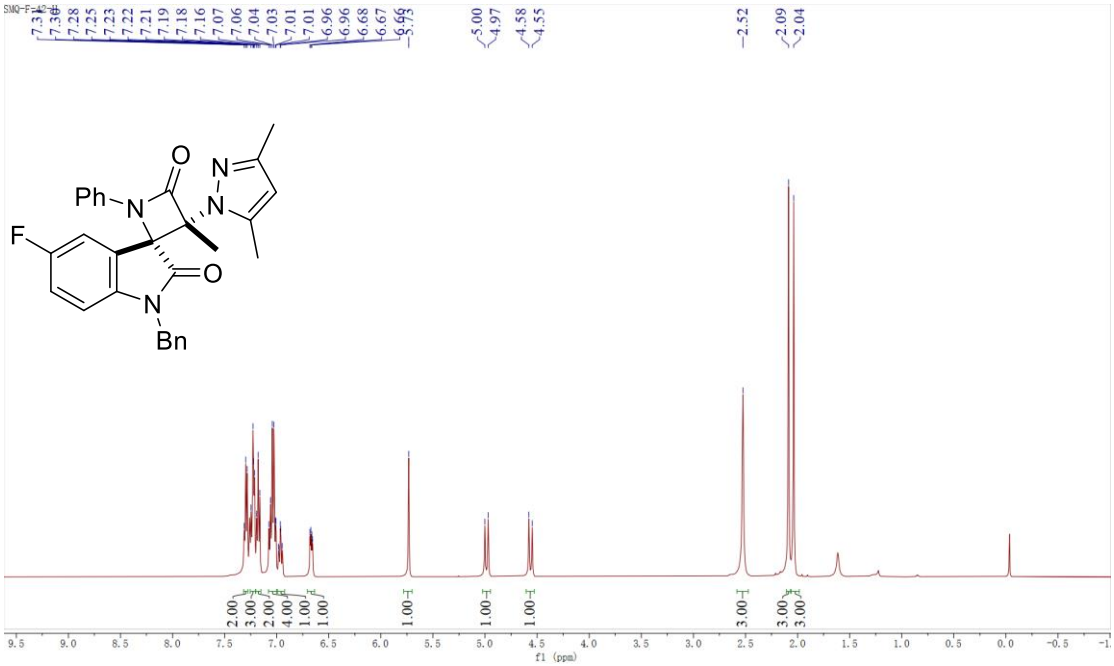


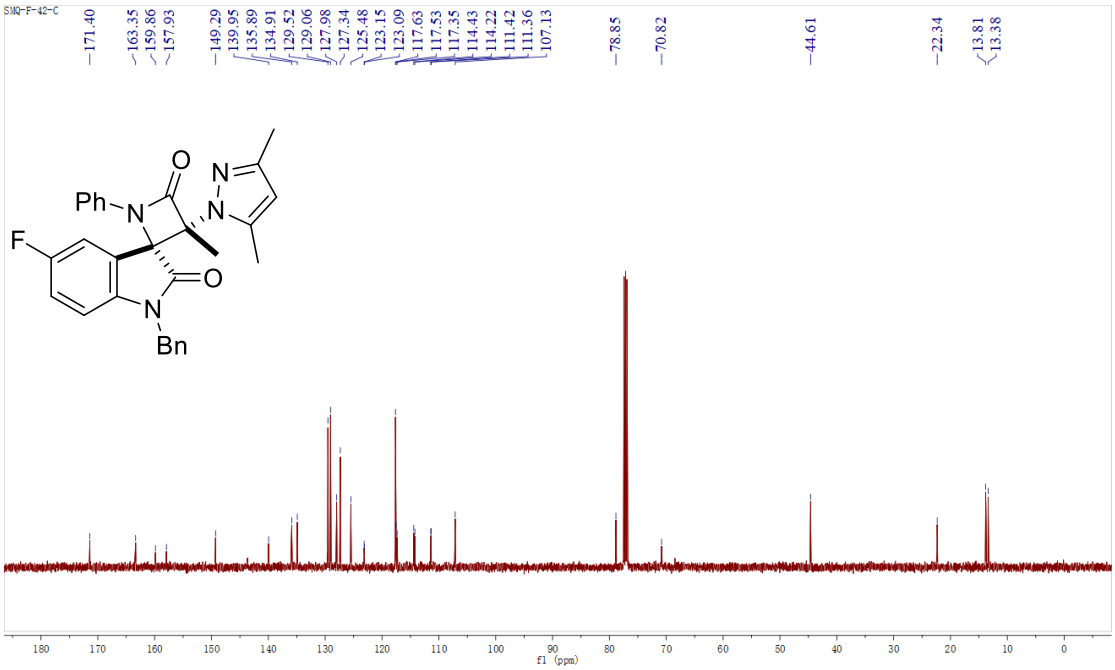
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3o



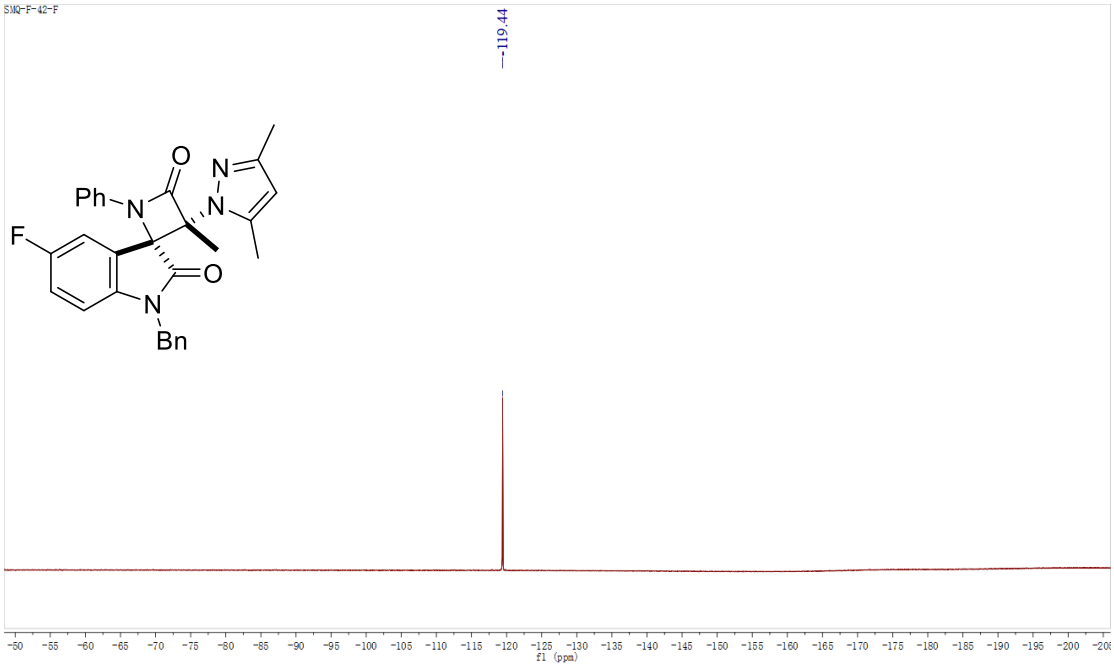


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3p

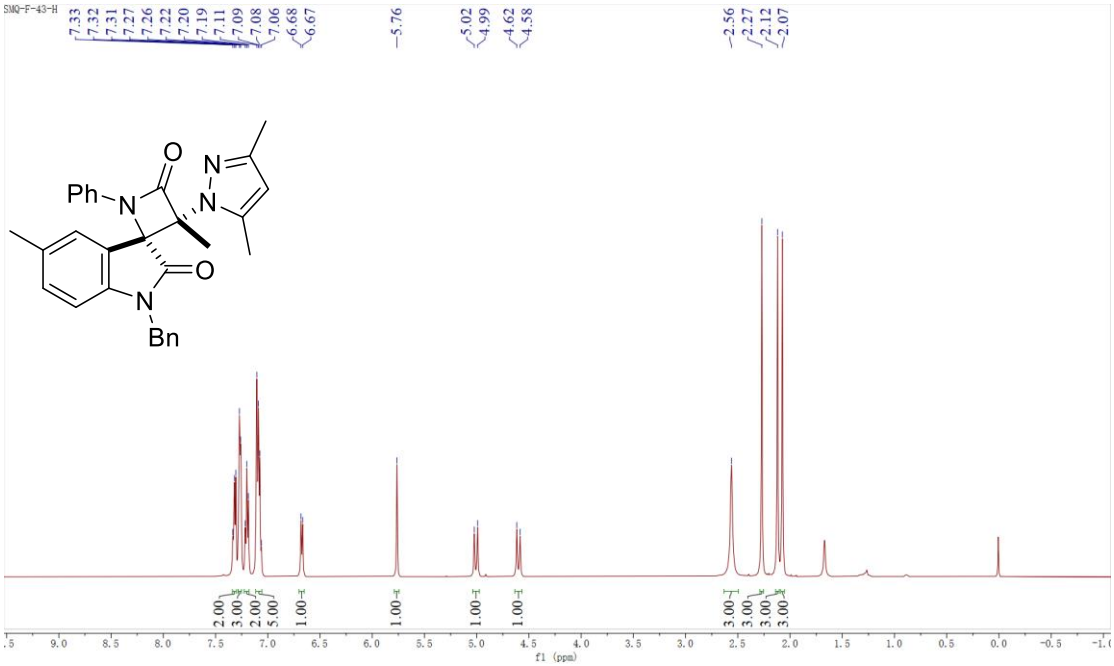


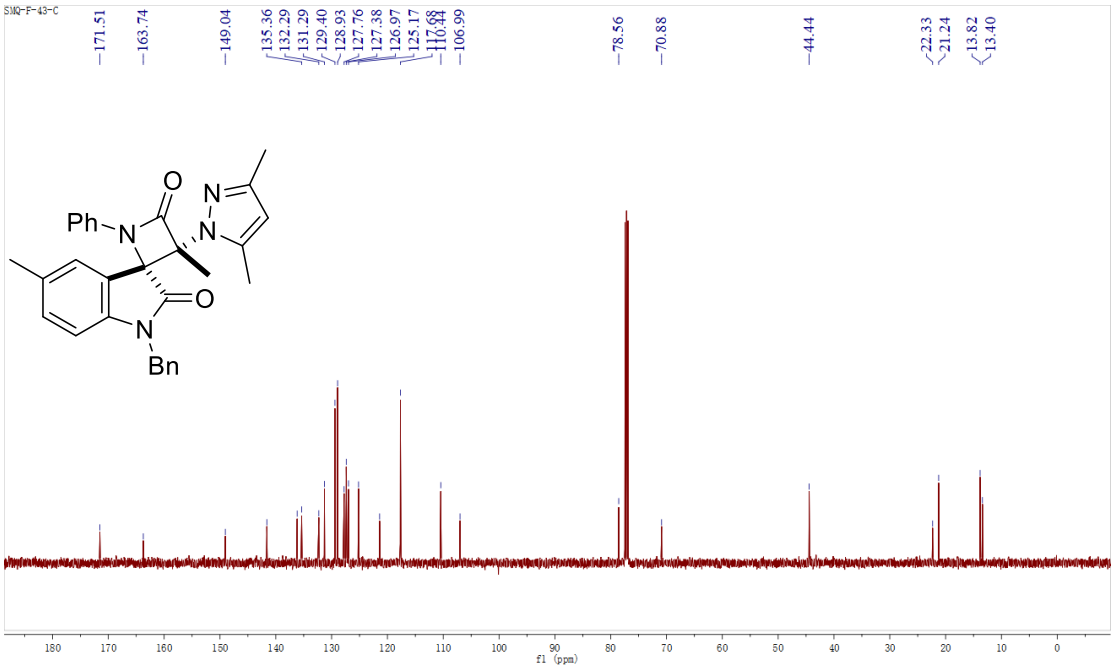


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 3p

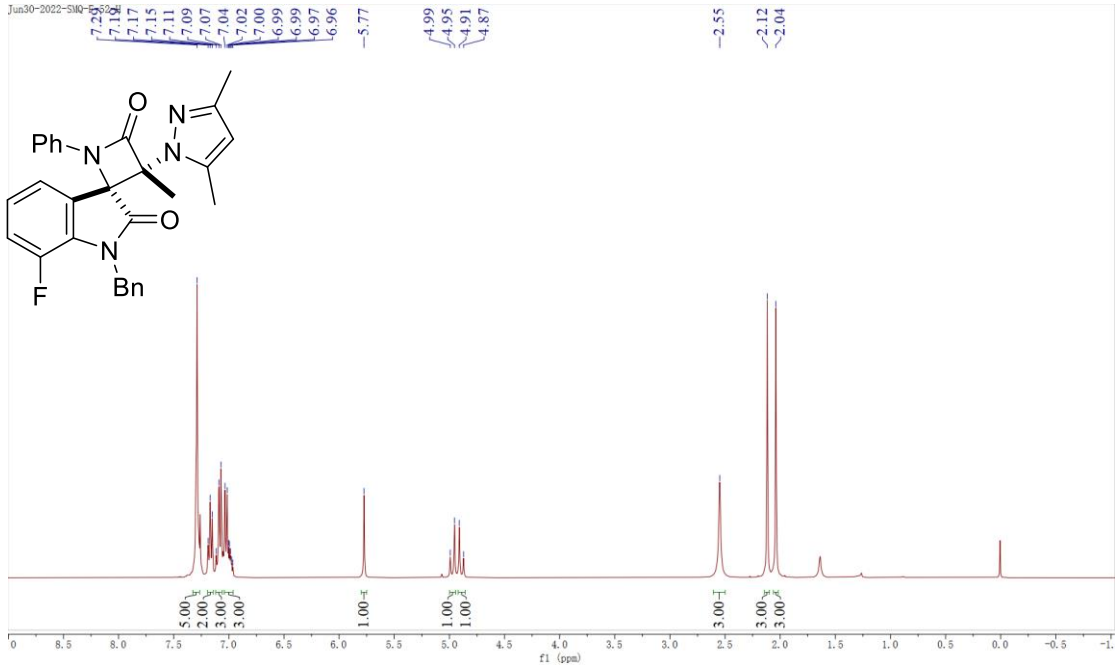


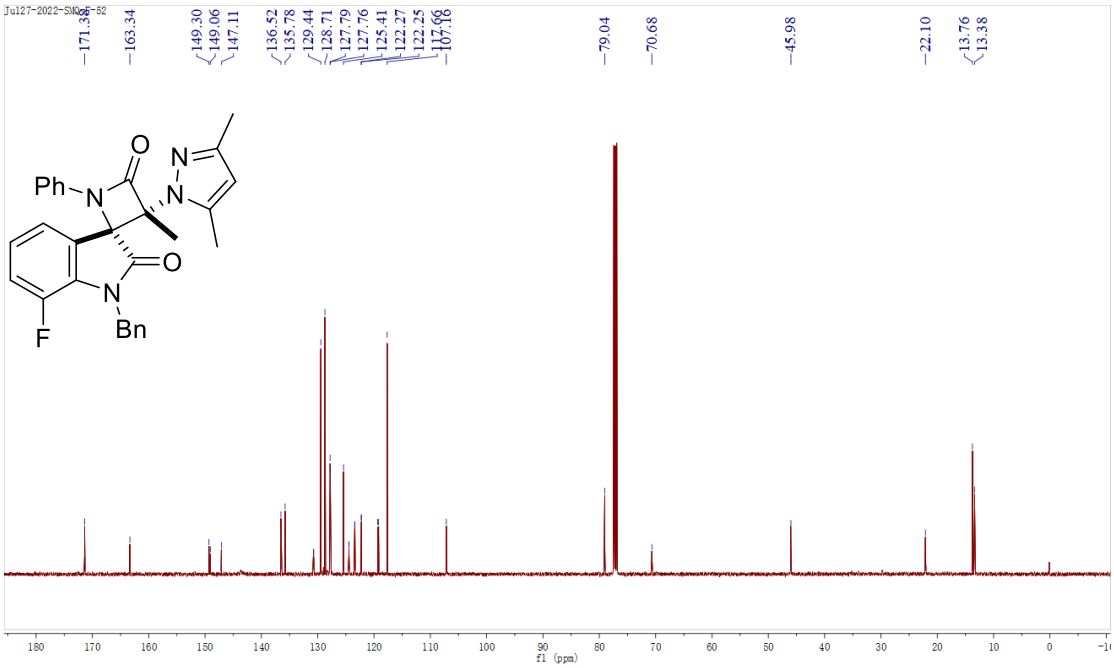
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3q



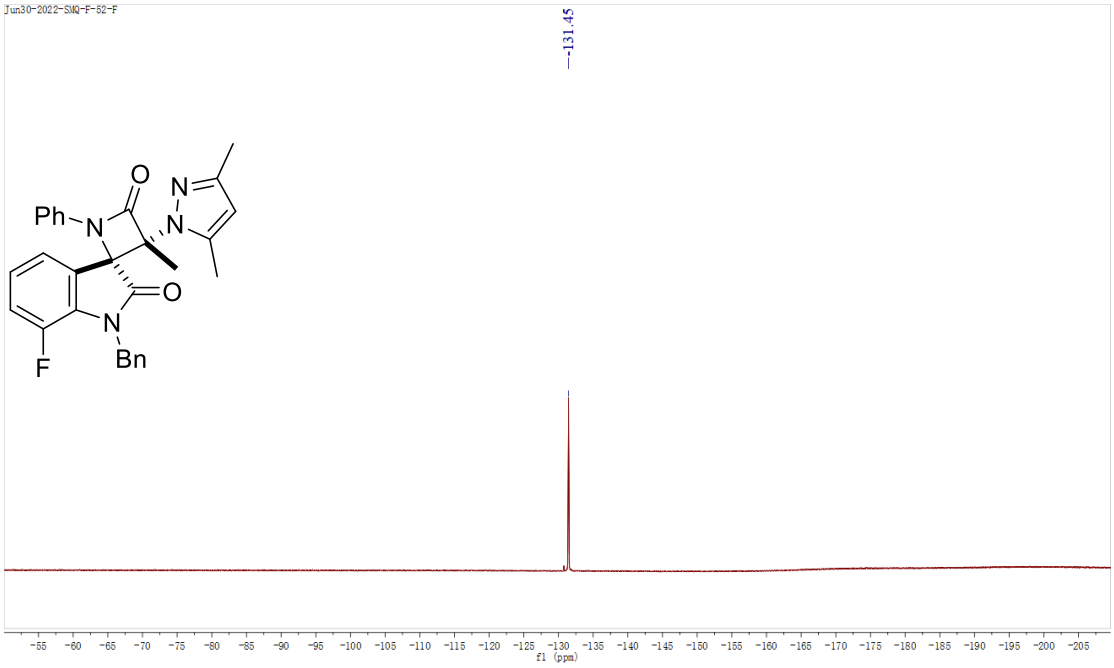


^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3r

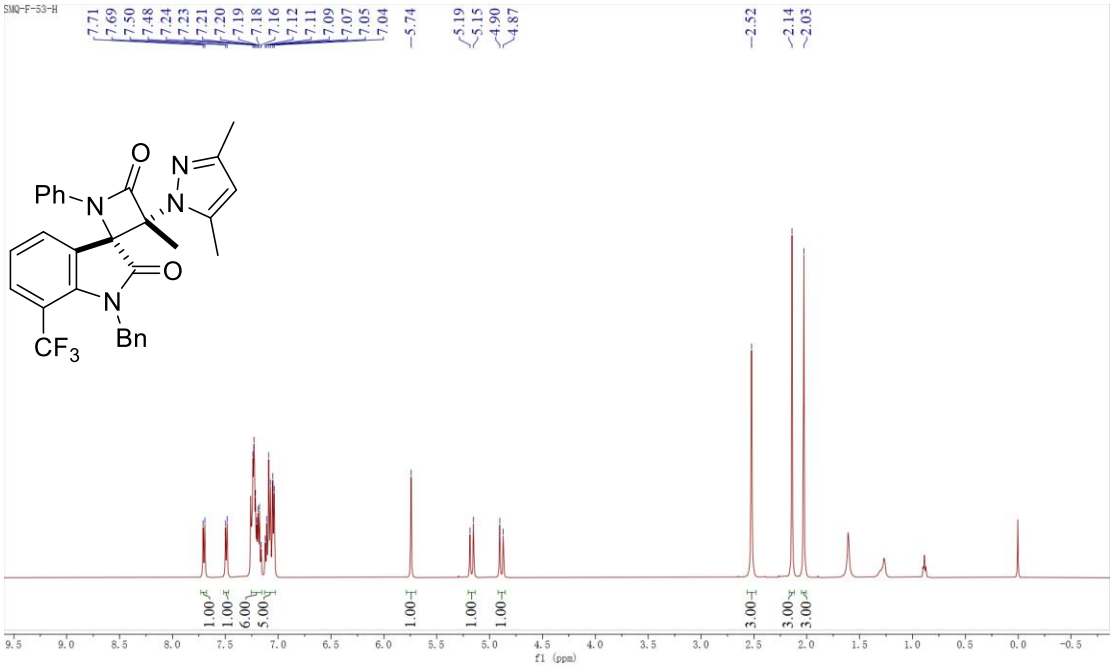


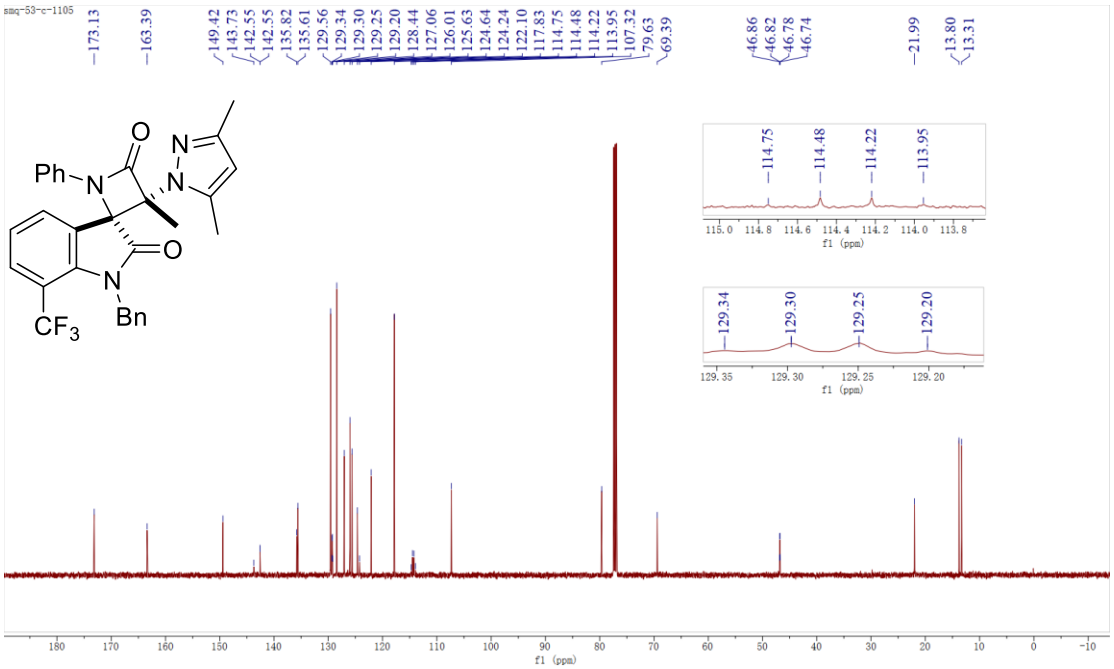


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 3r

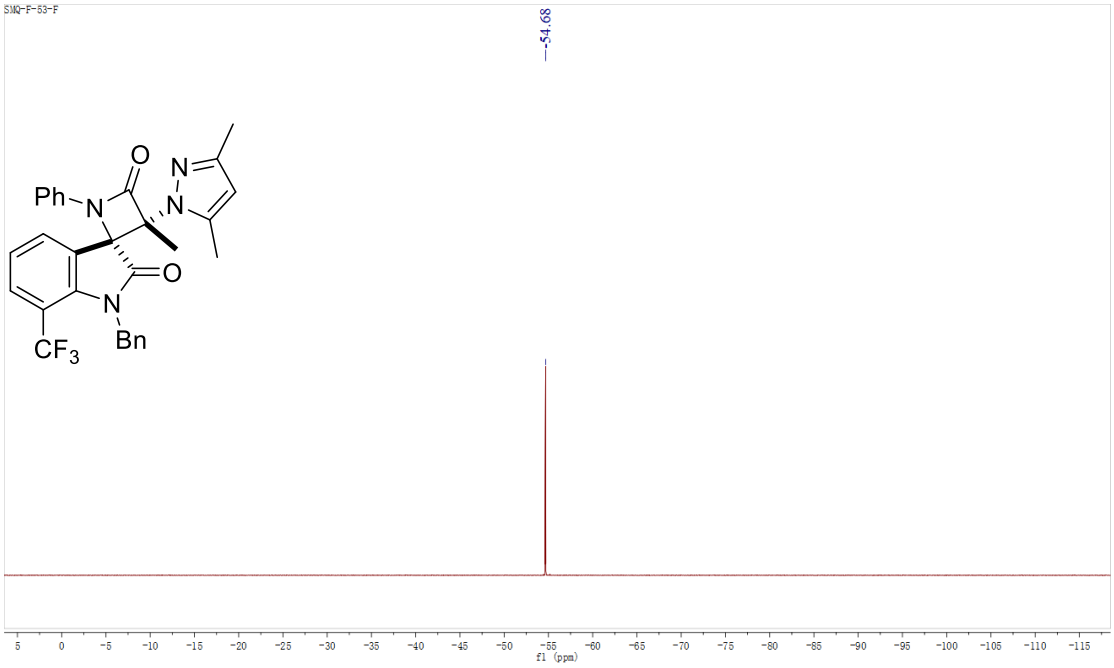


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 3s

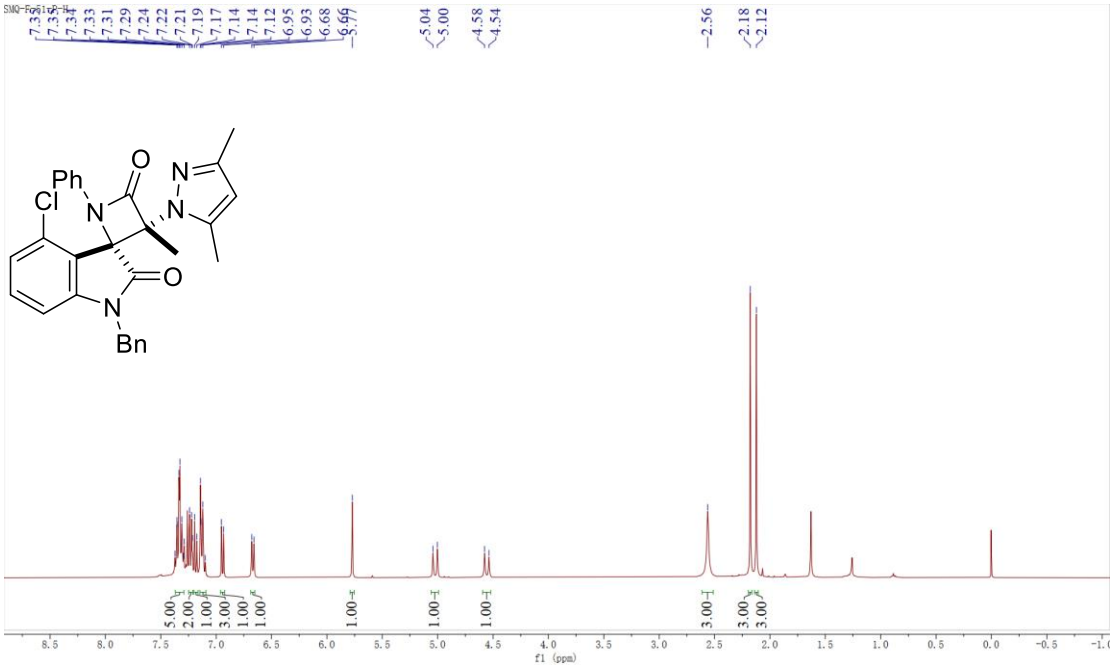


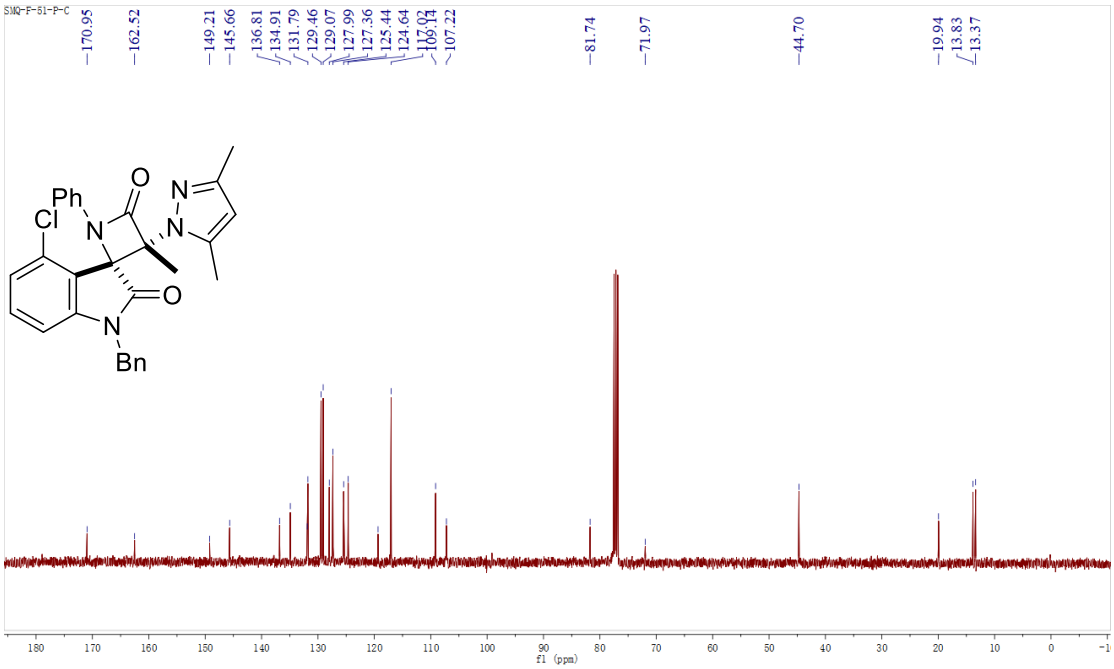


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 3s

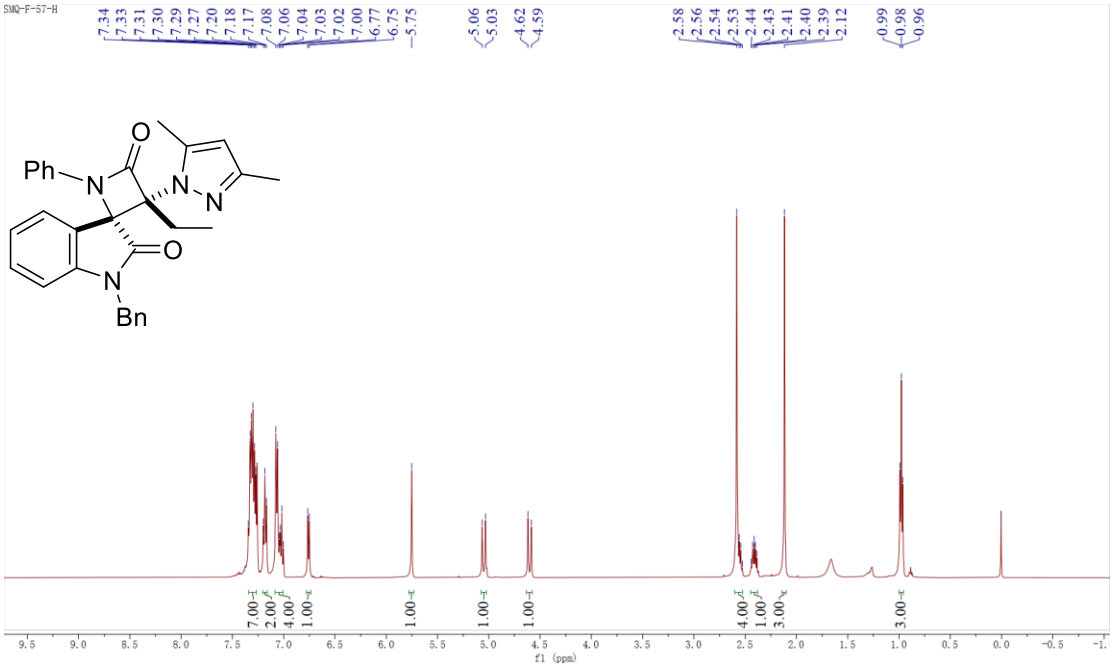


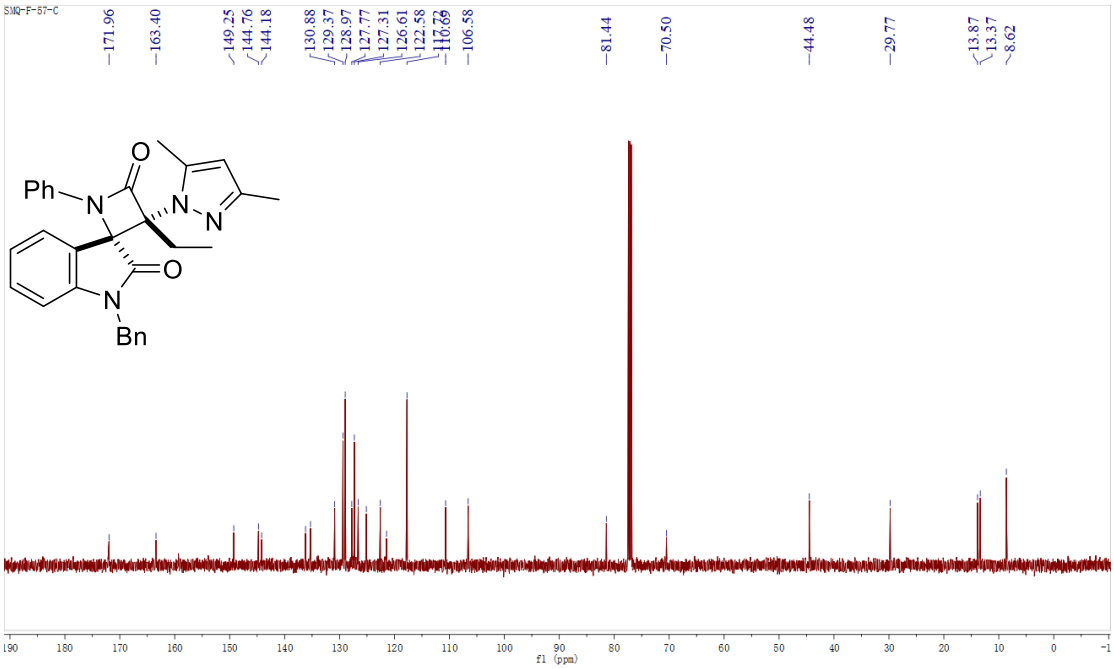
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 3t



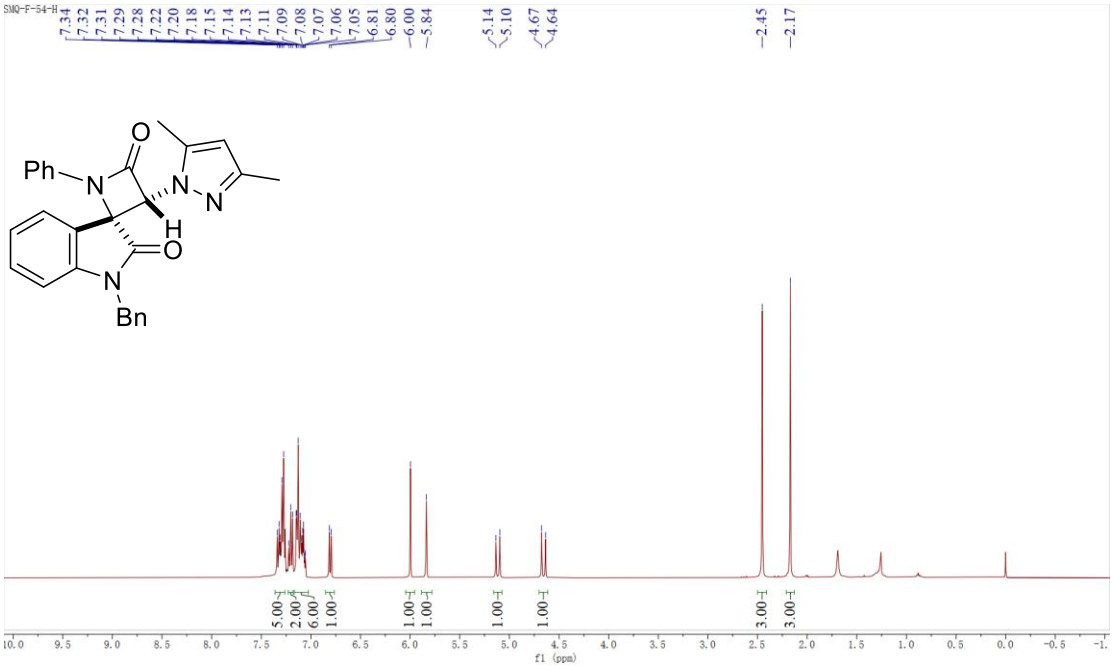


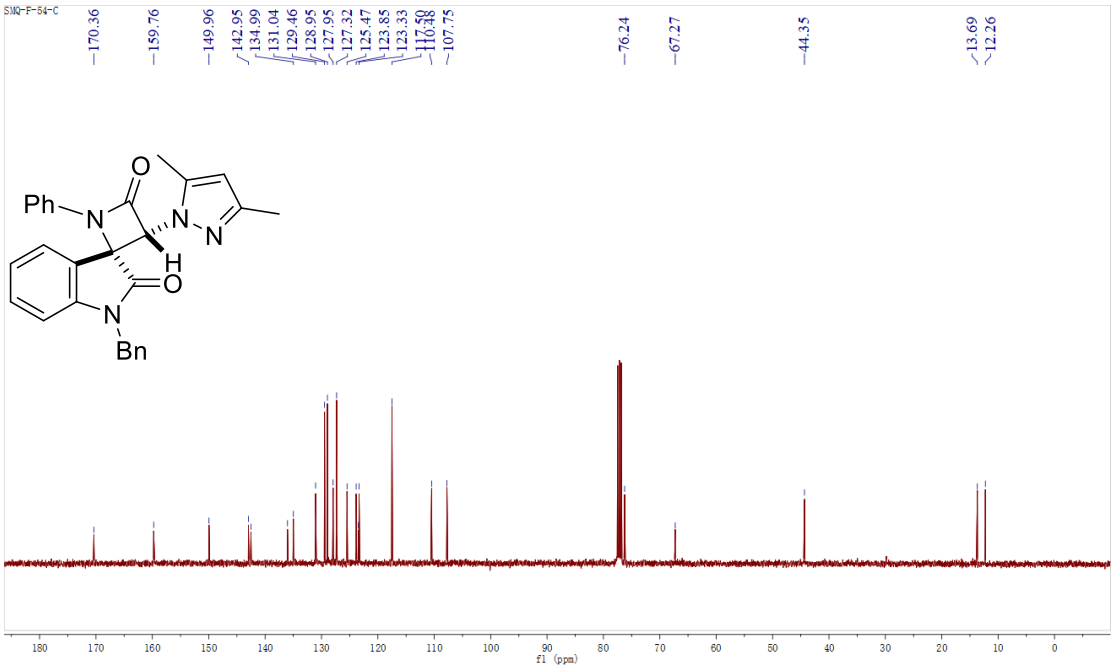
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 4a



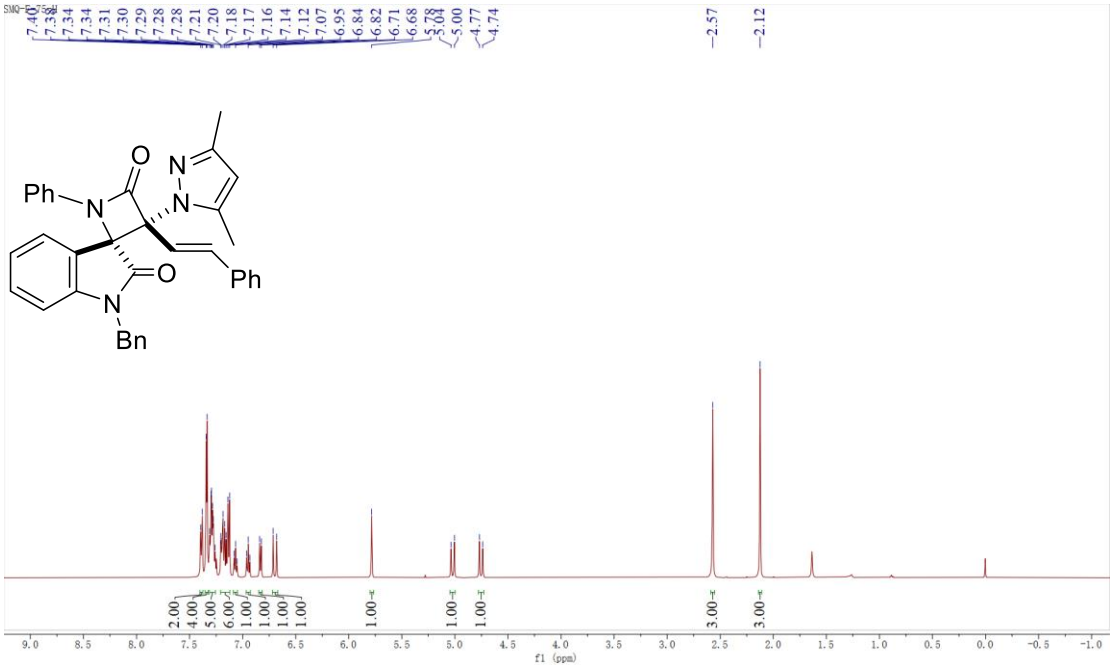


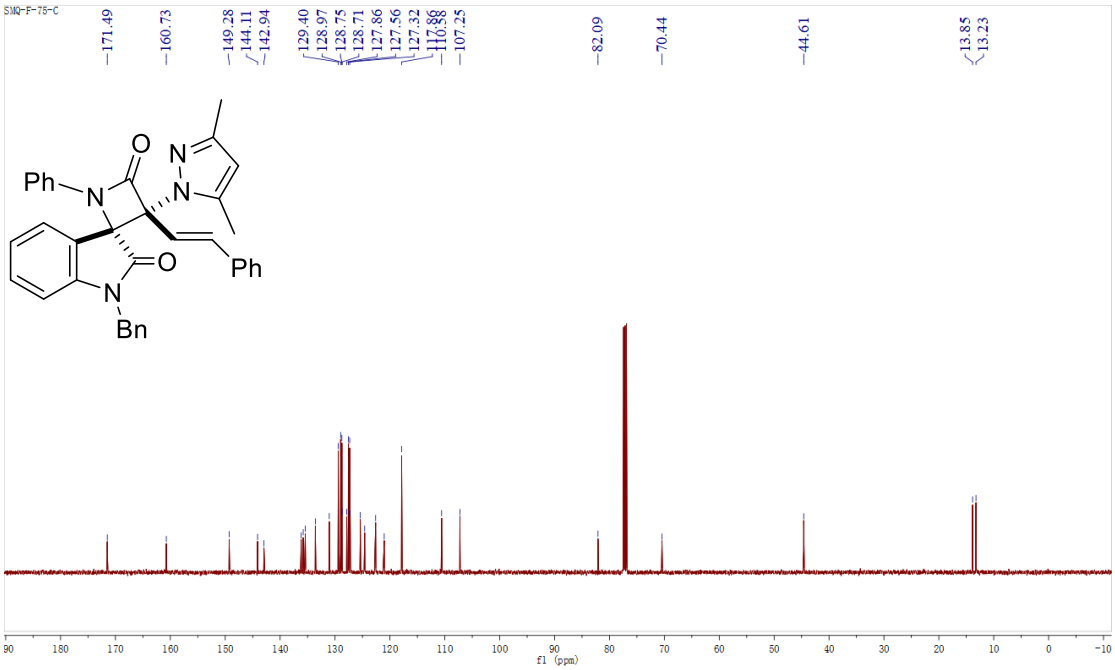
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 4b



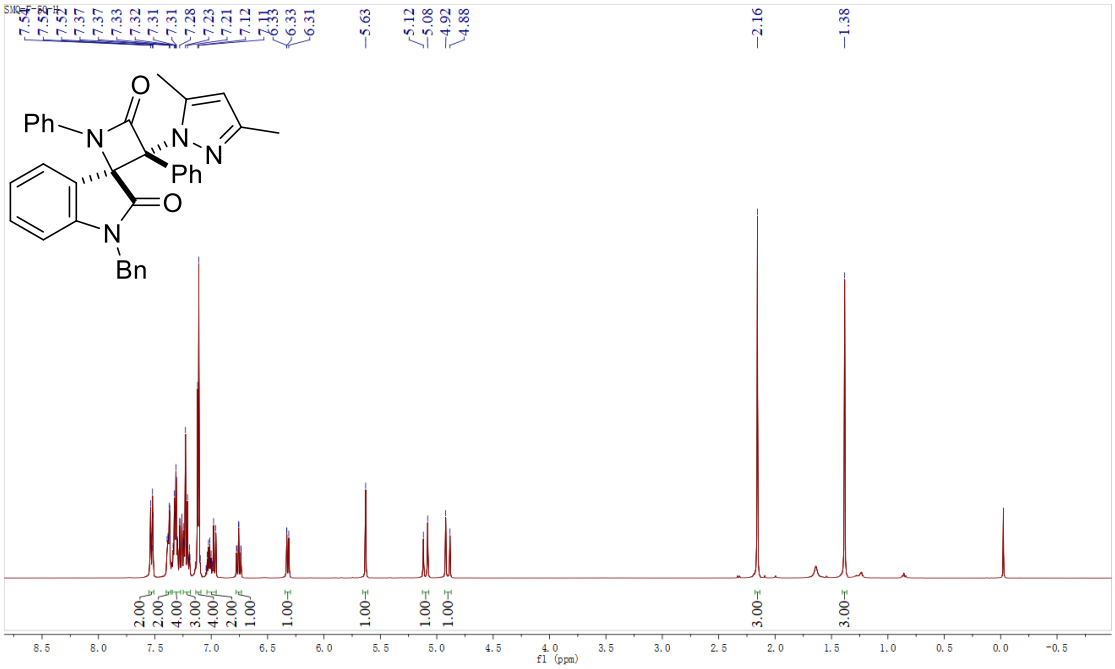


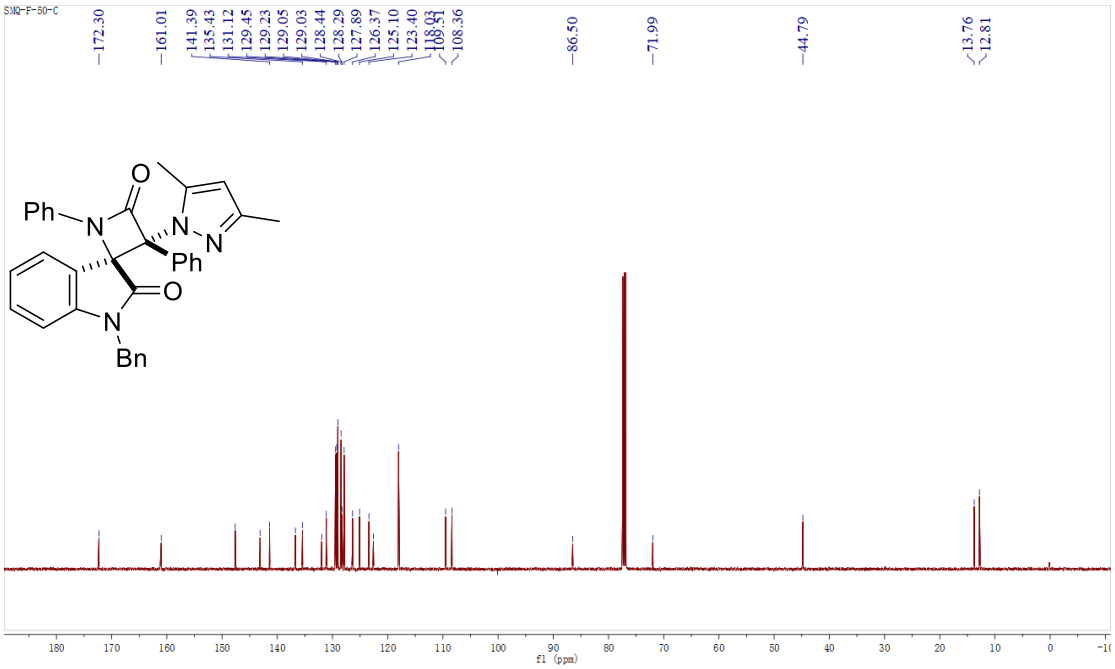
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 4c



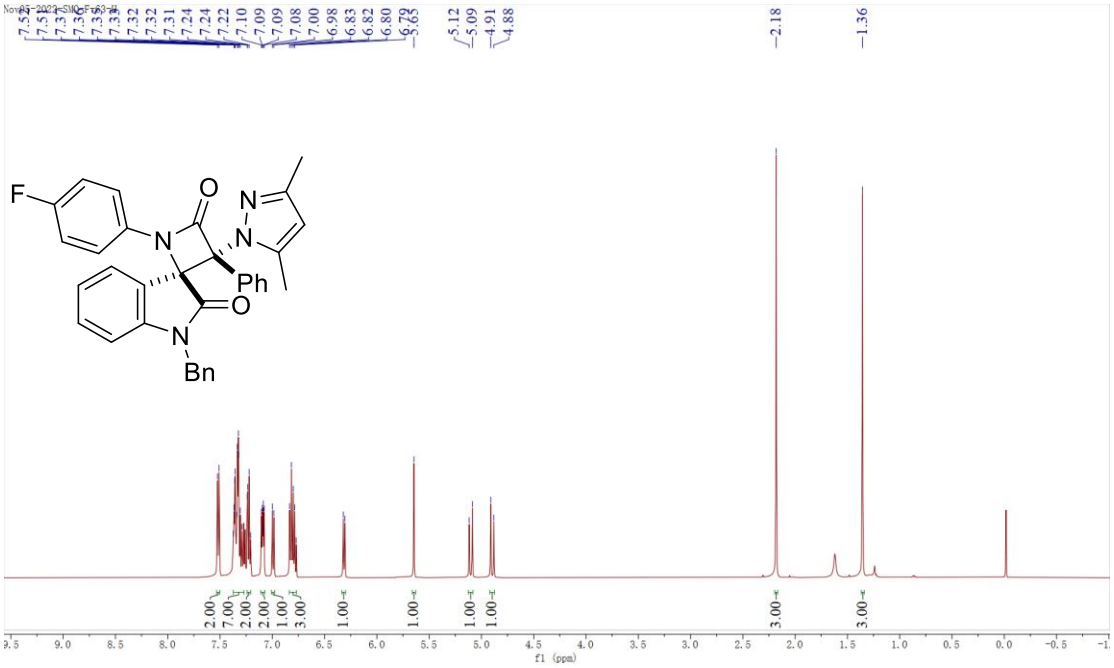


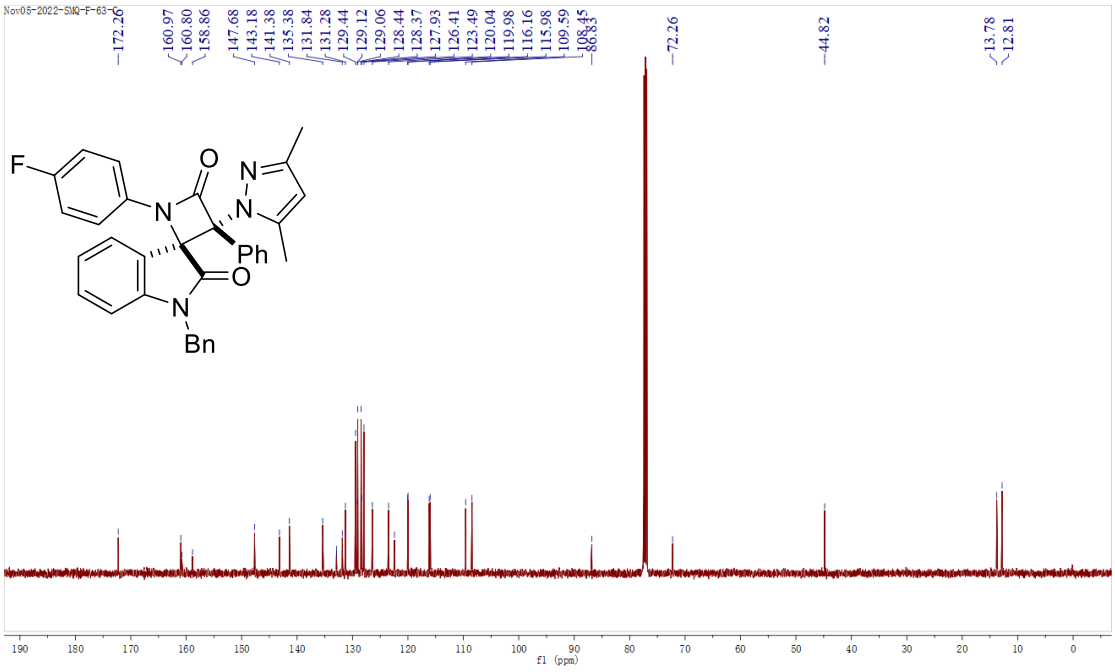
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5a



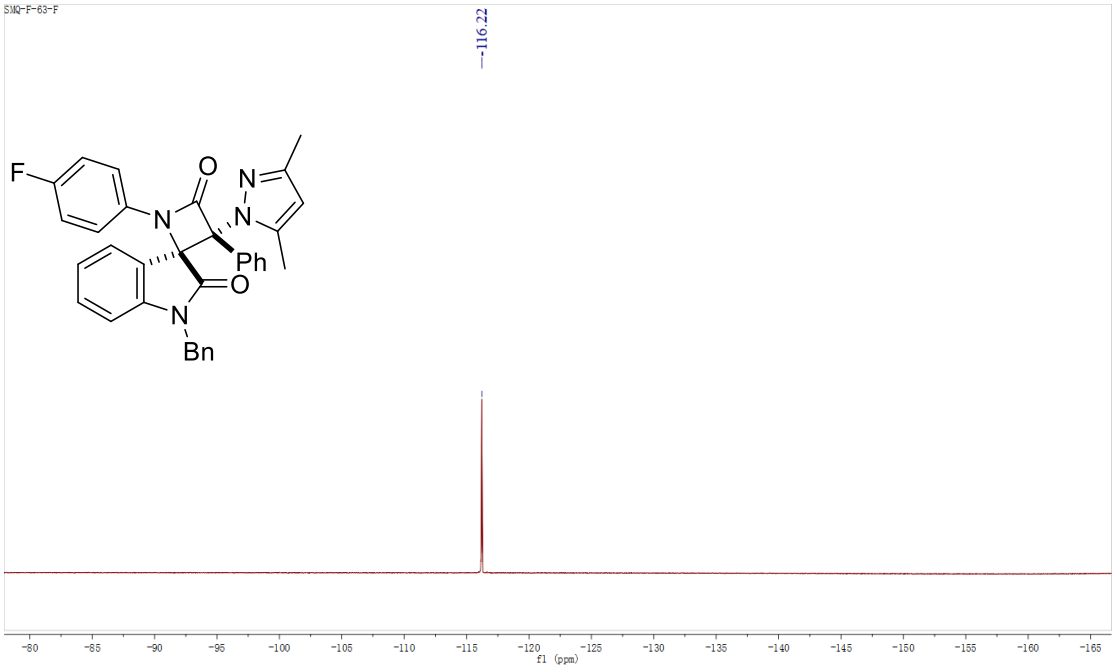


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5b

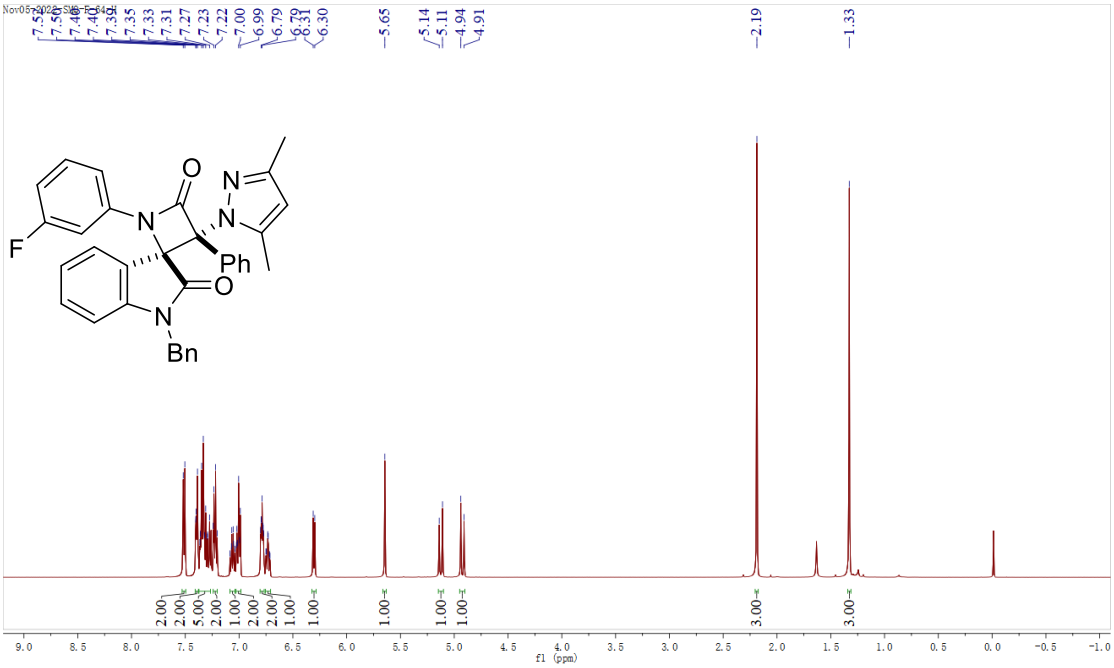


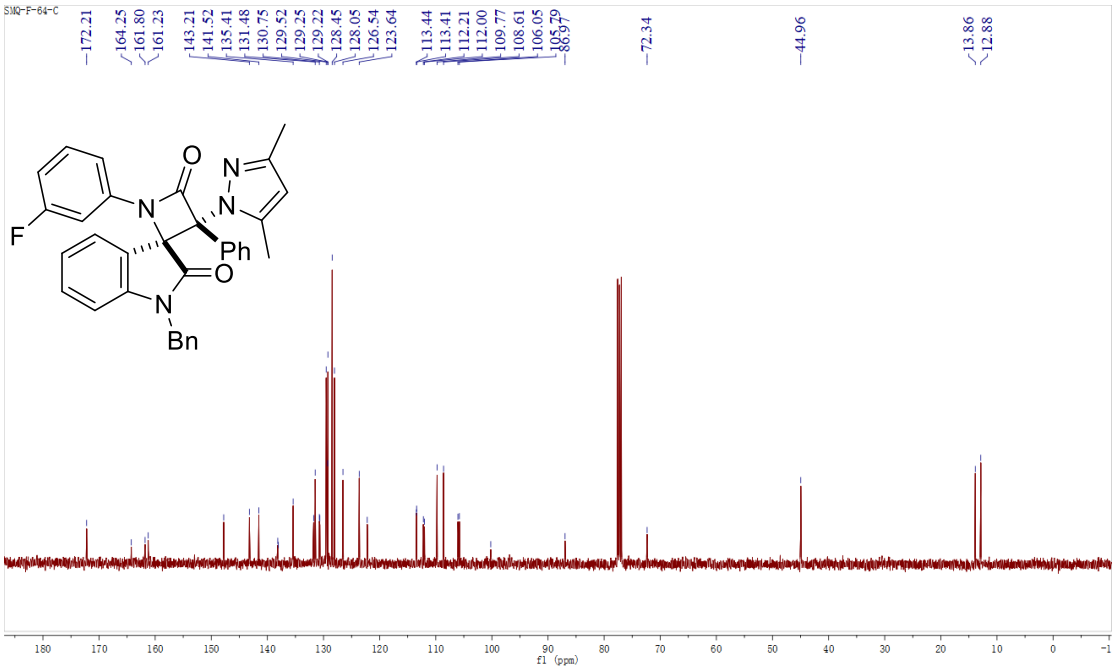


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 5b

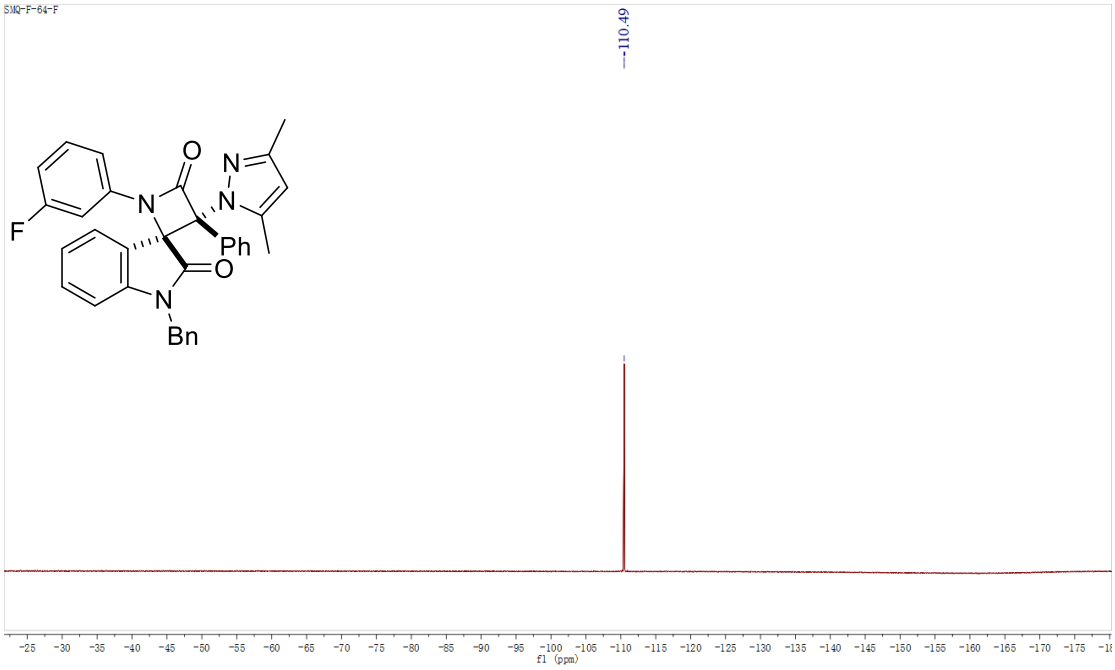


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 5c

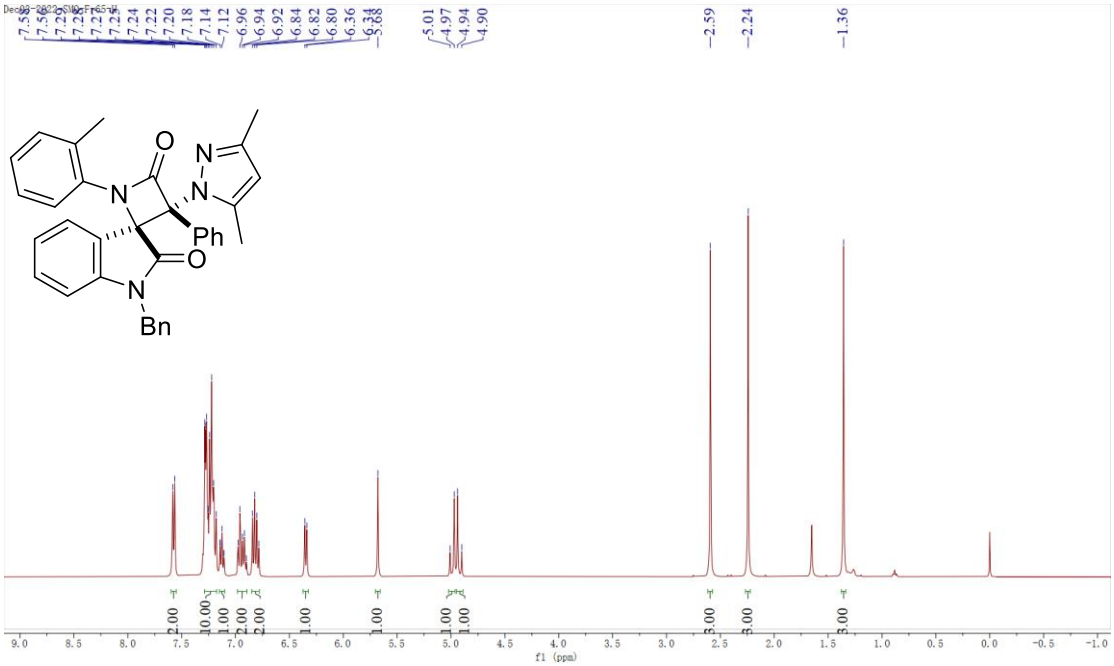


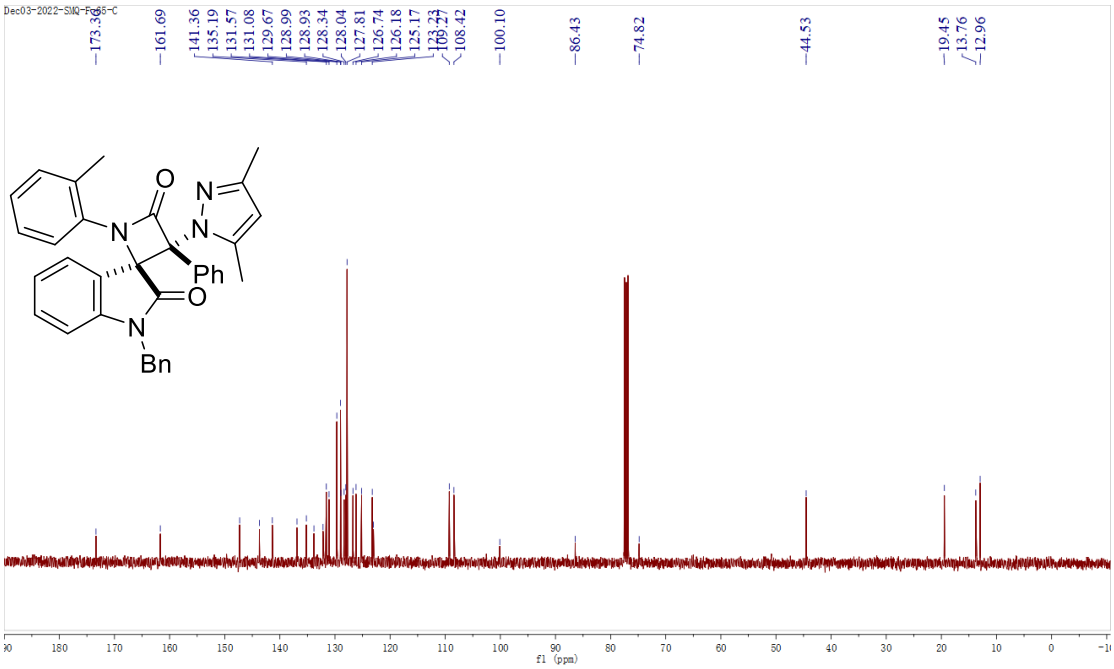


^{19}F NMR (500 MHz, $CDCl_3$) spectra for 5c

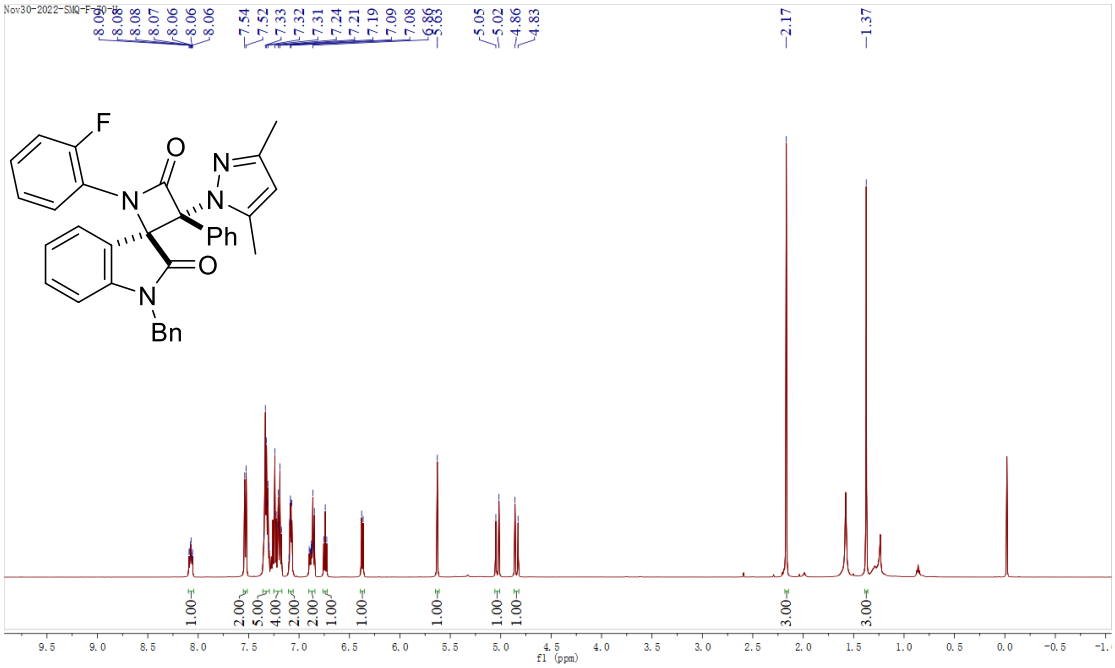


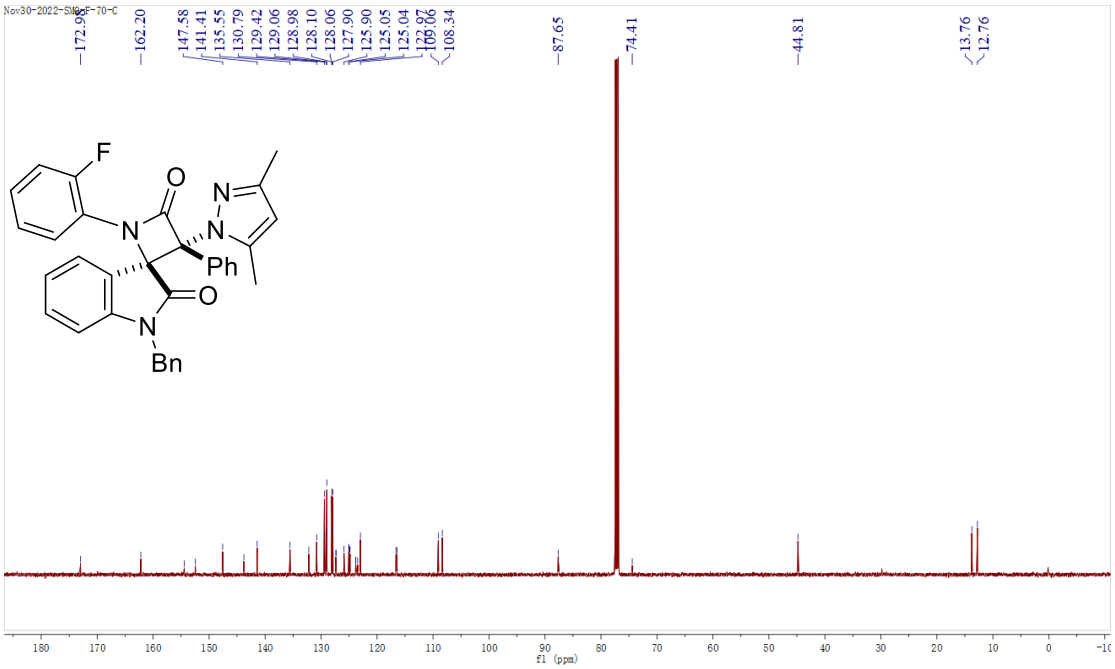
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 5d



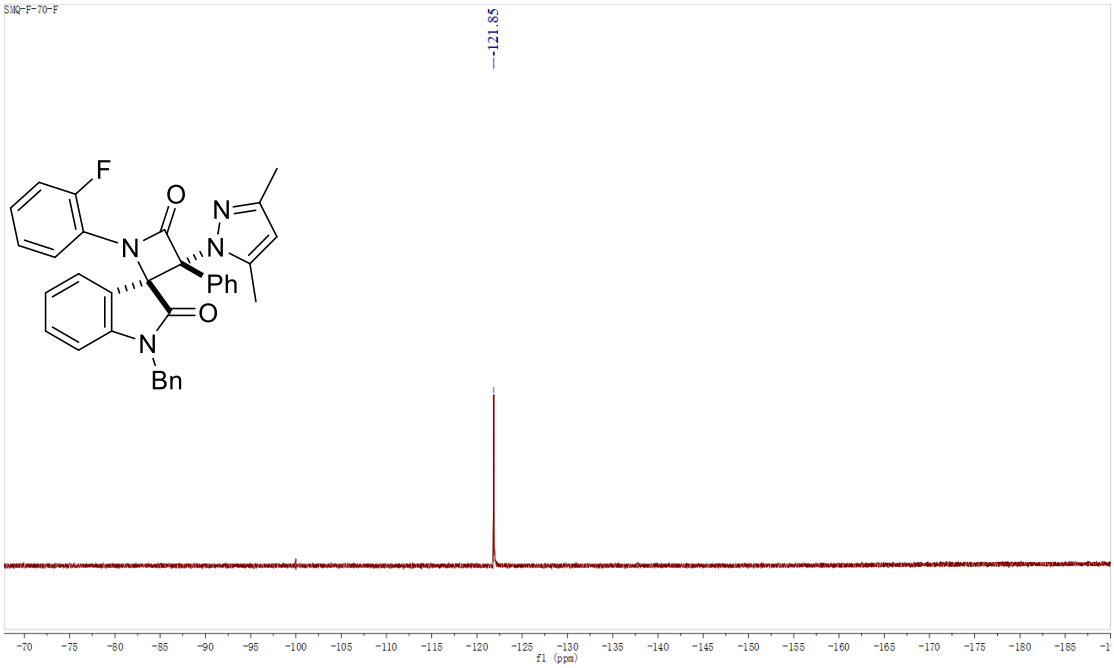


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5e

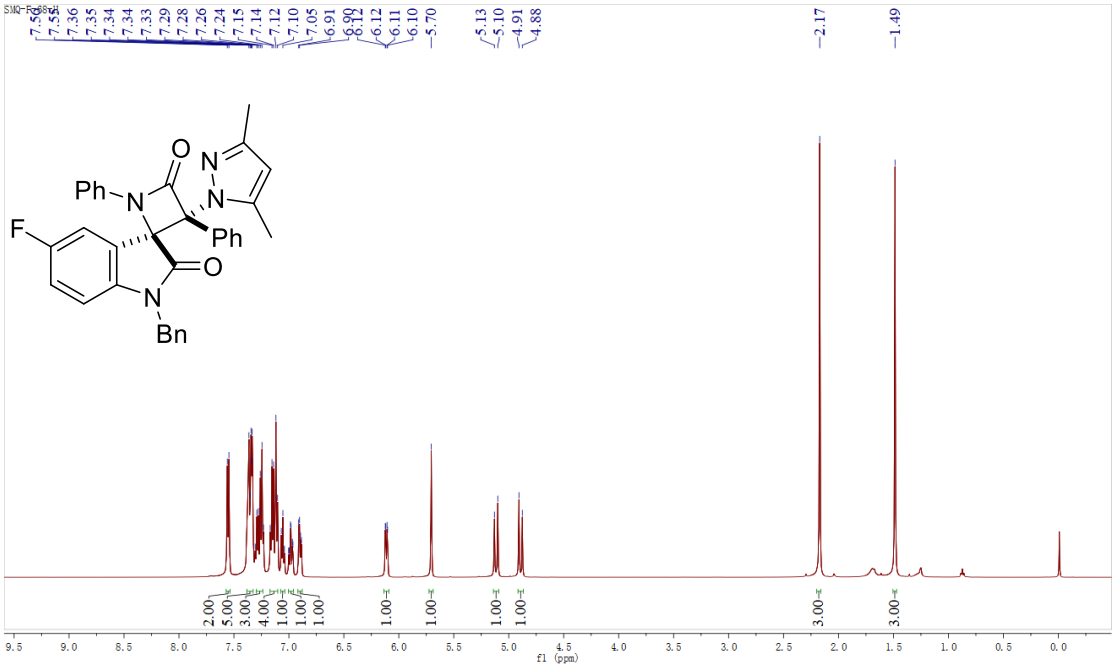


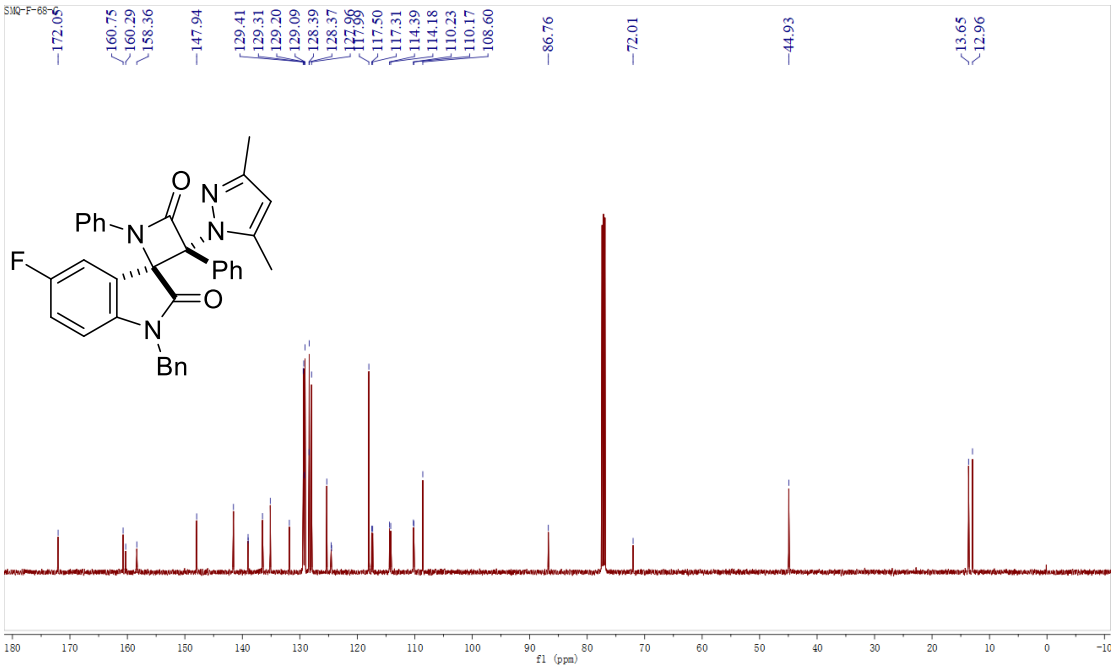


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 5e

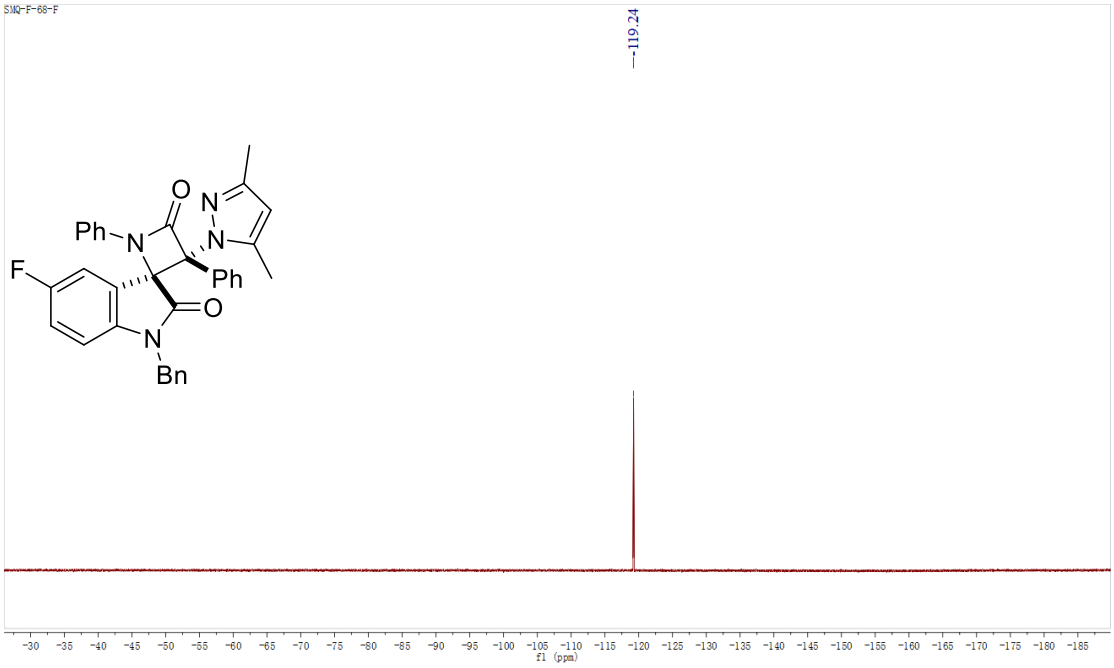


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5f

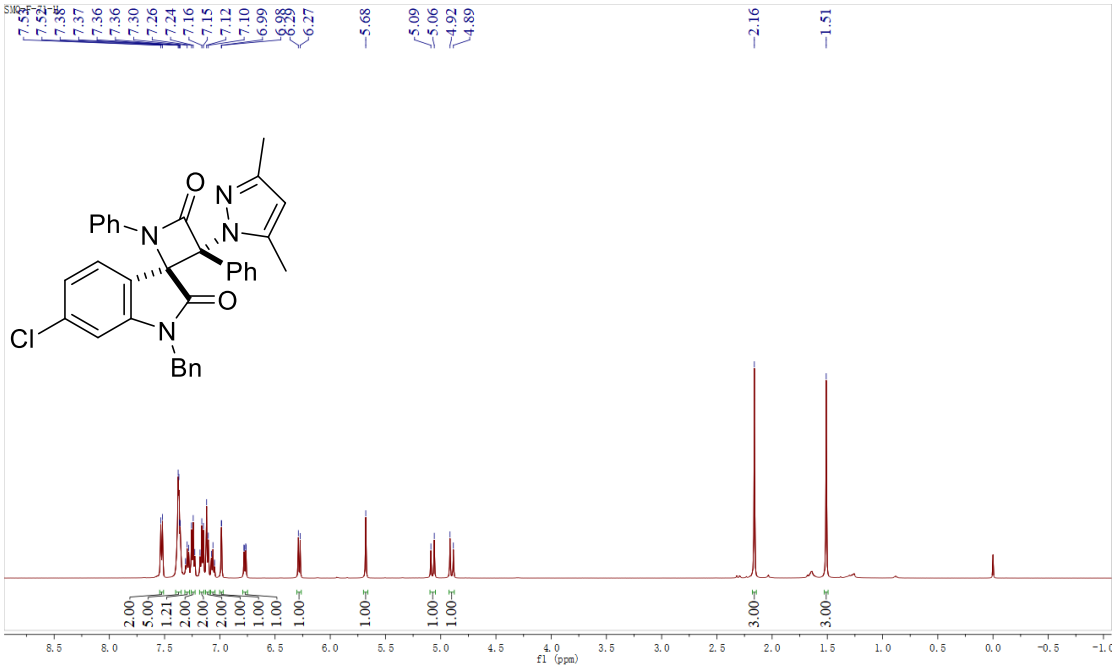


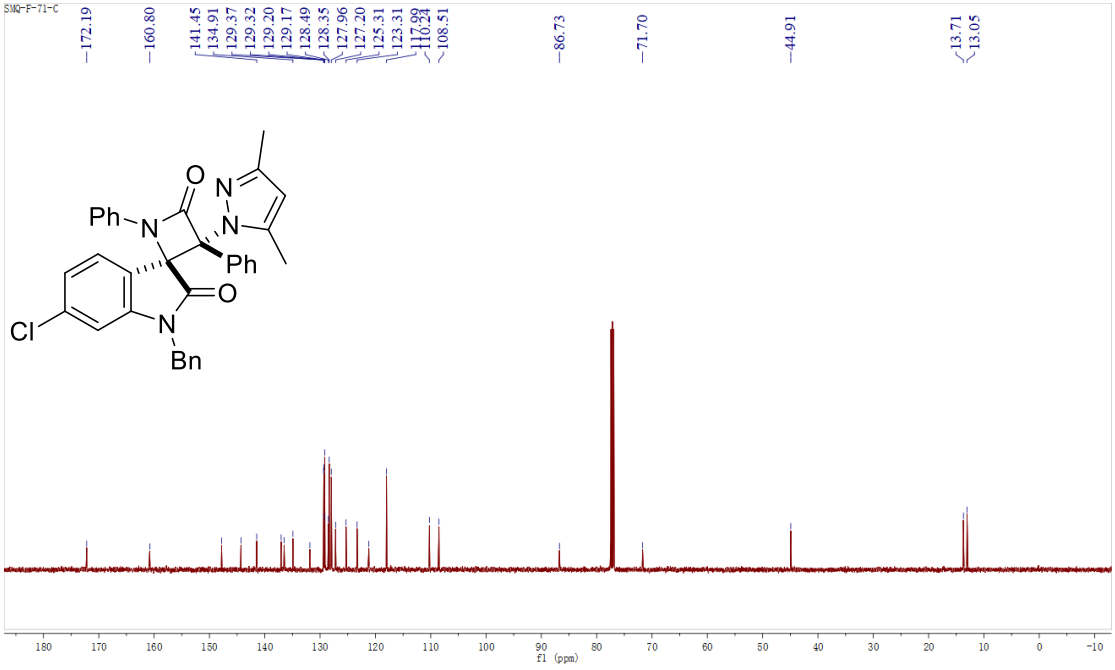


^{19}F NMR (376 MHz, $CDCl_3$) spectra for 5f

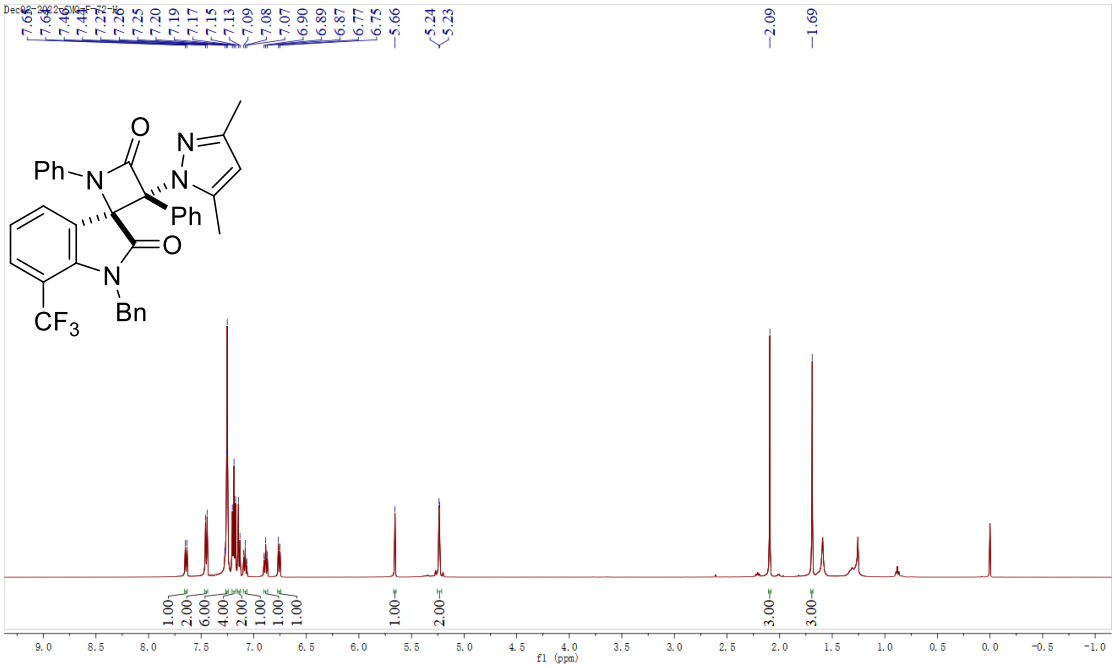


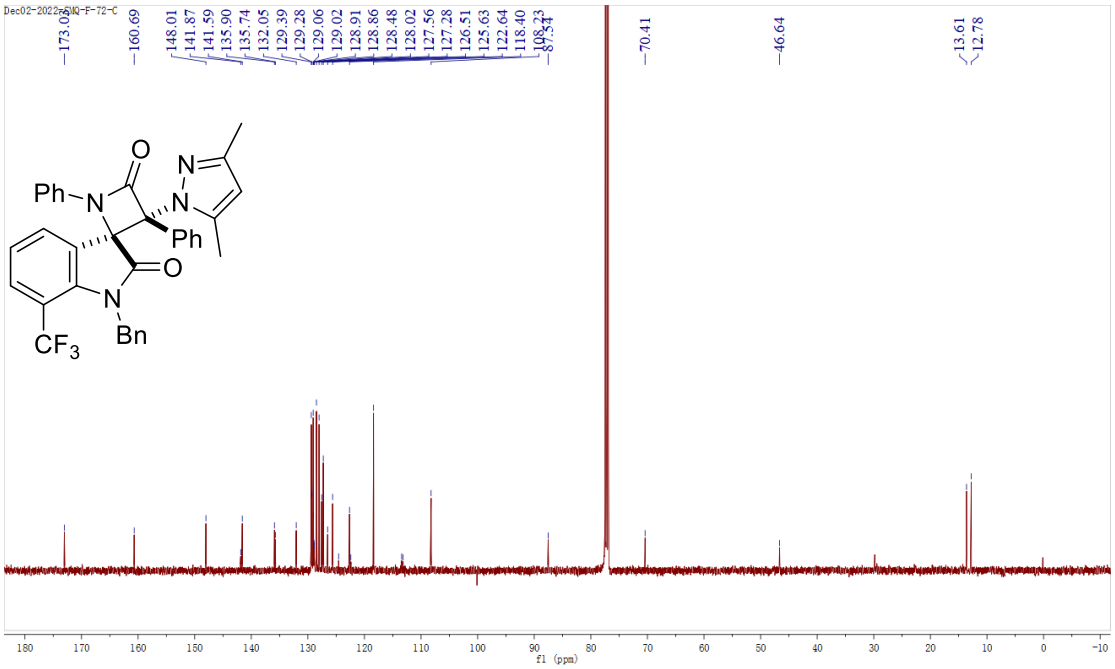
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5g



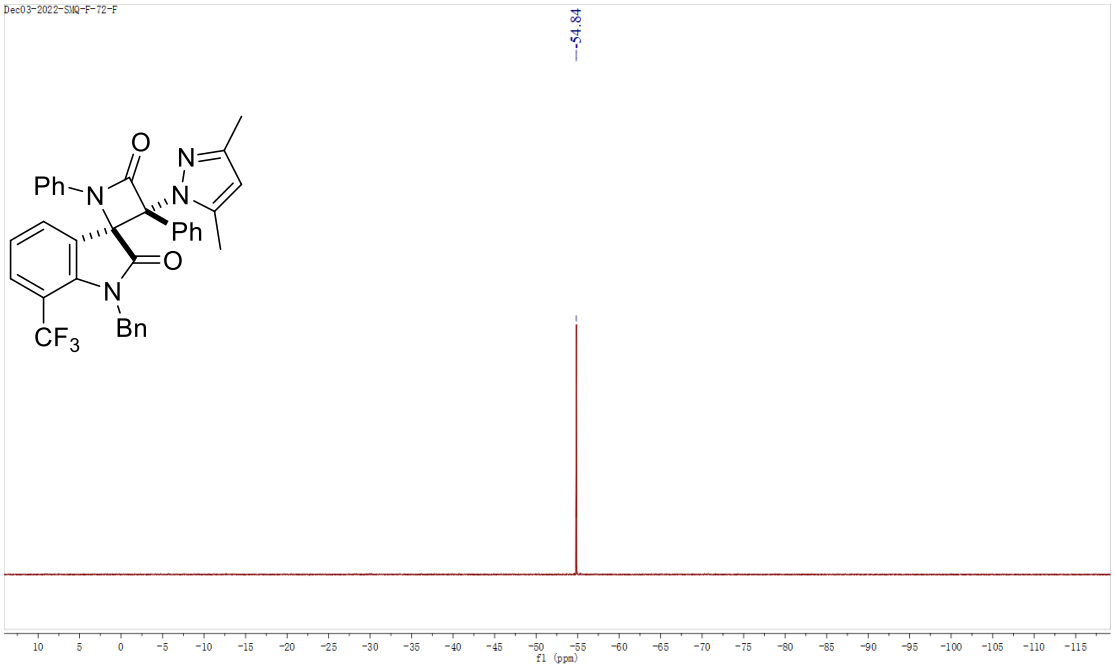


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5h

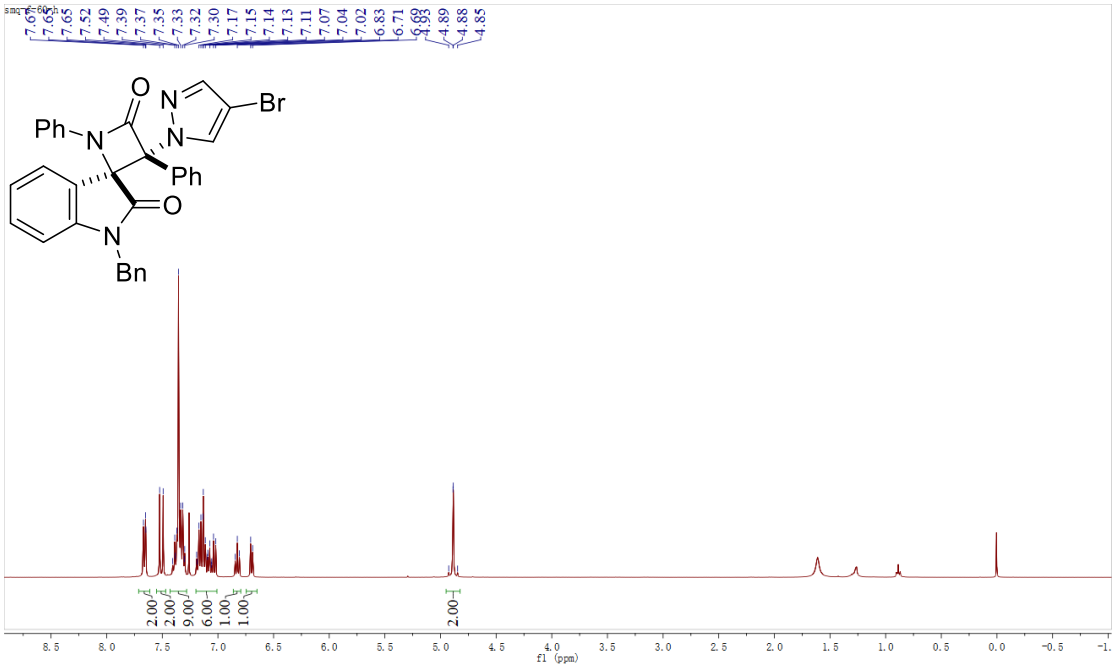


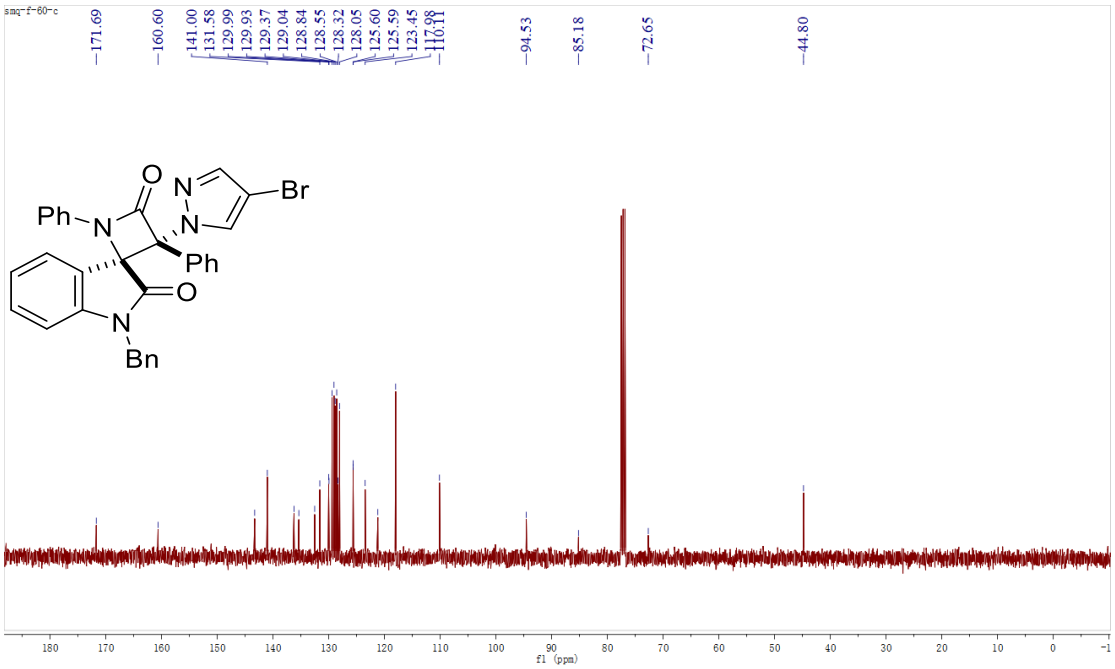


^{19}F NMR (376MHz, $CDCl_3$) spectra for 5h

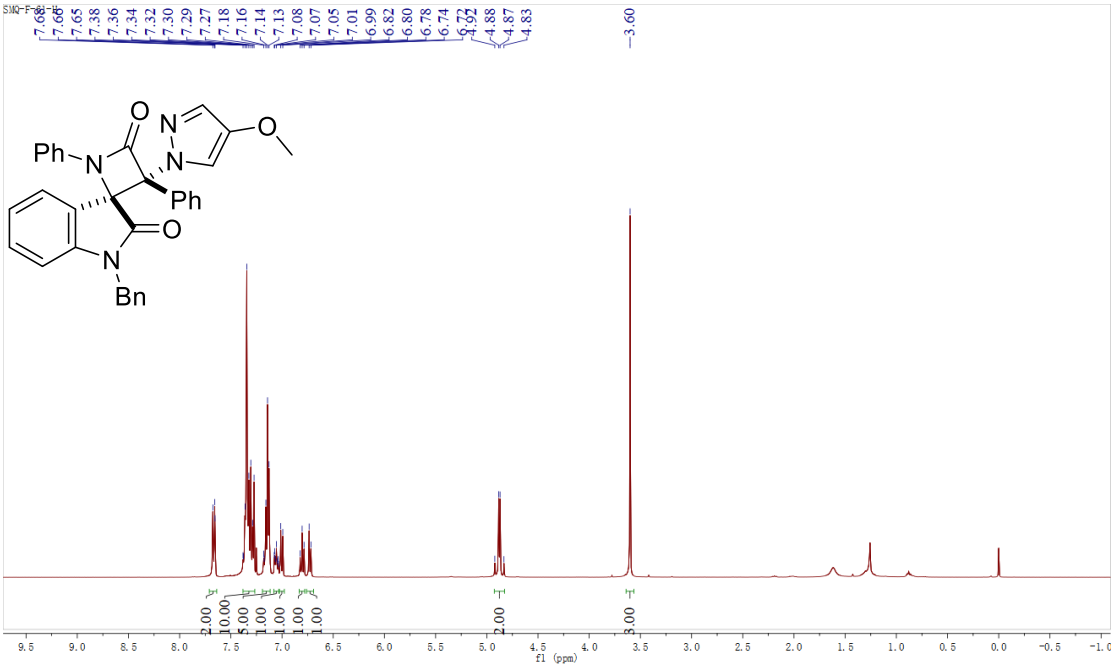


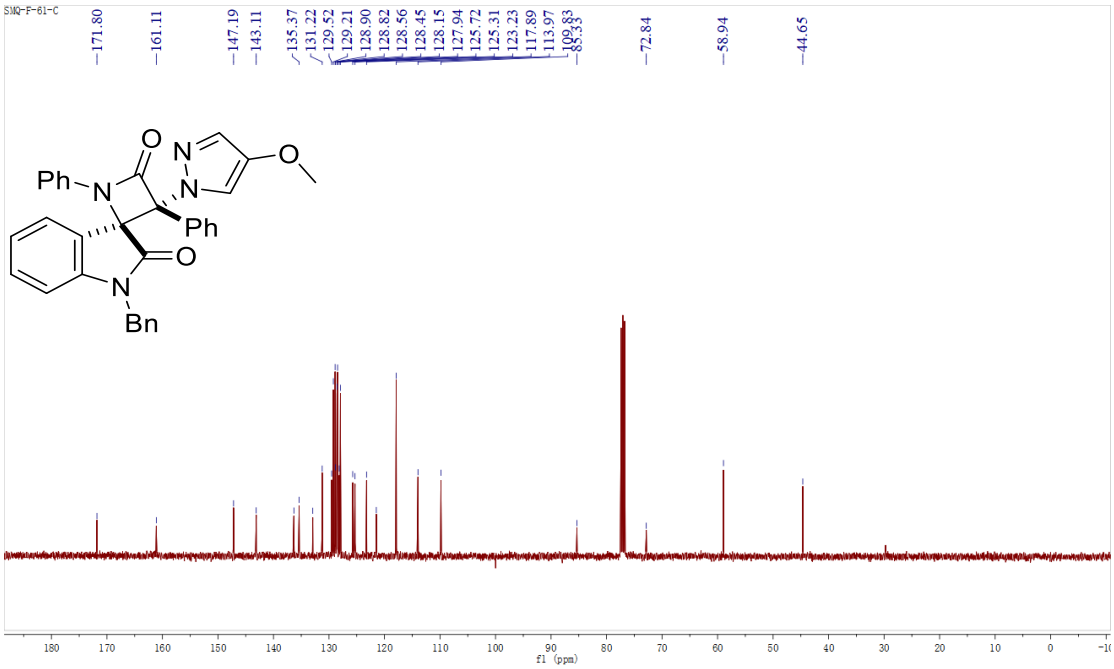
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 5i



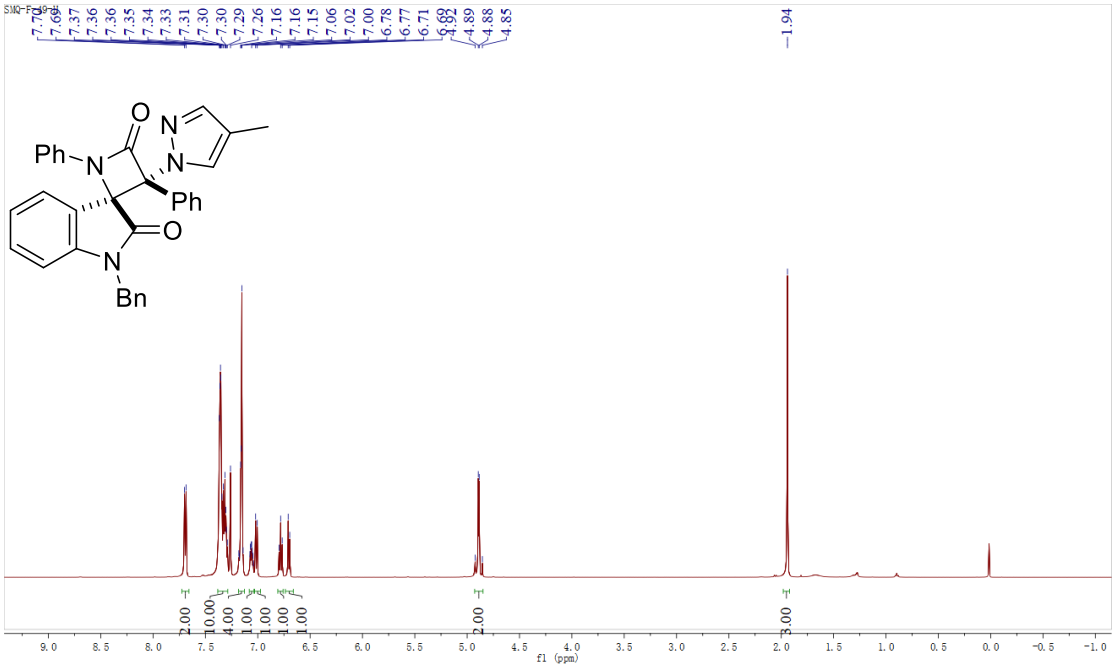


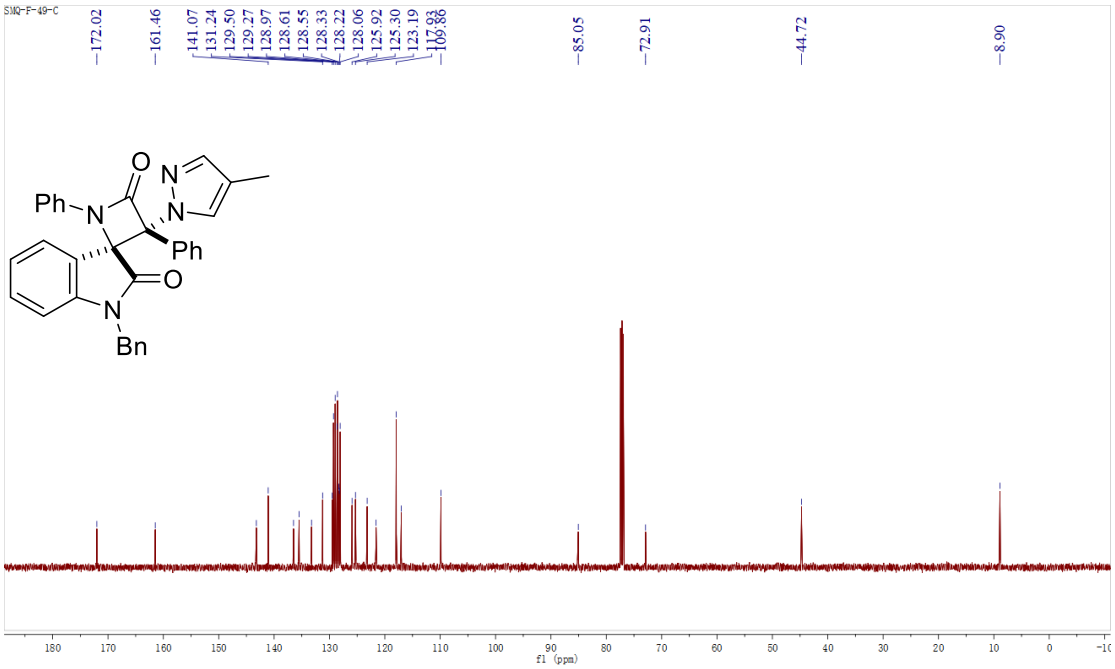
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 5j



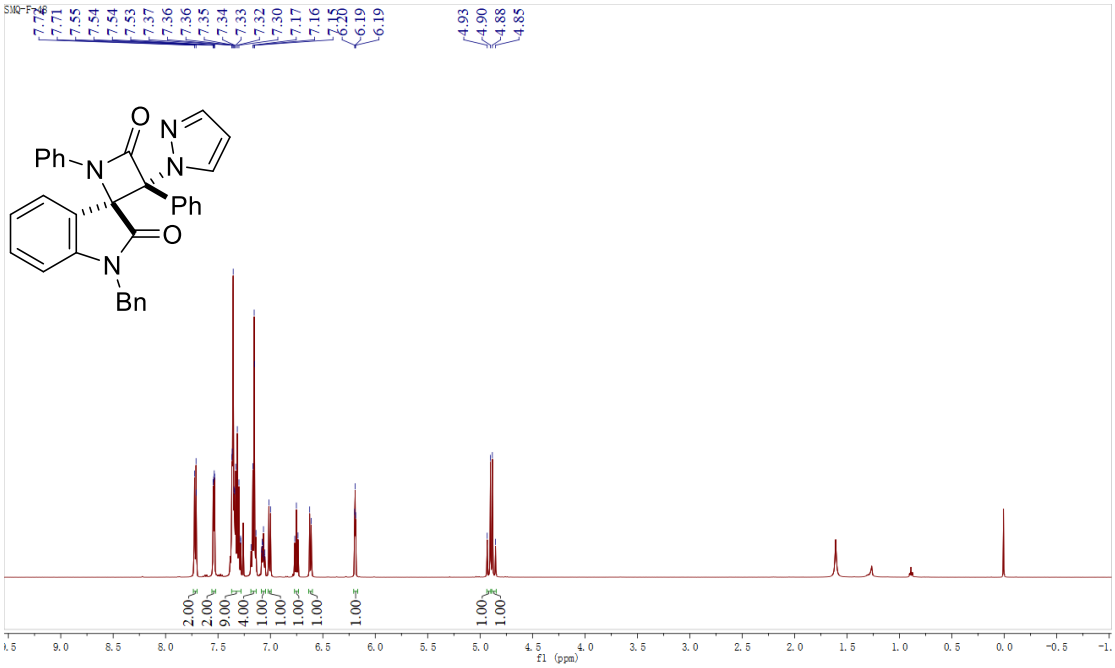


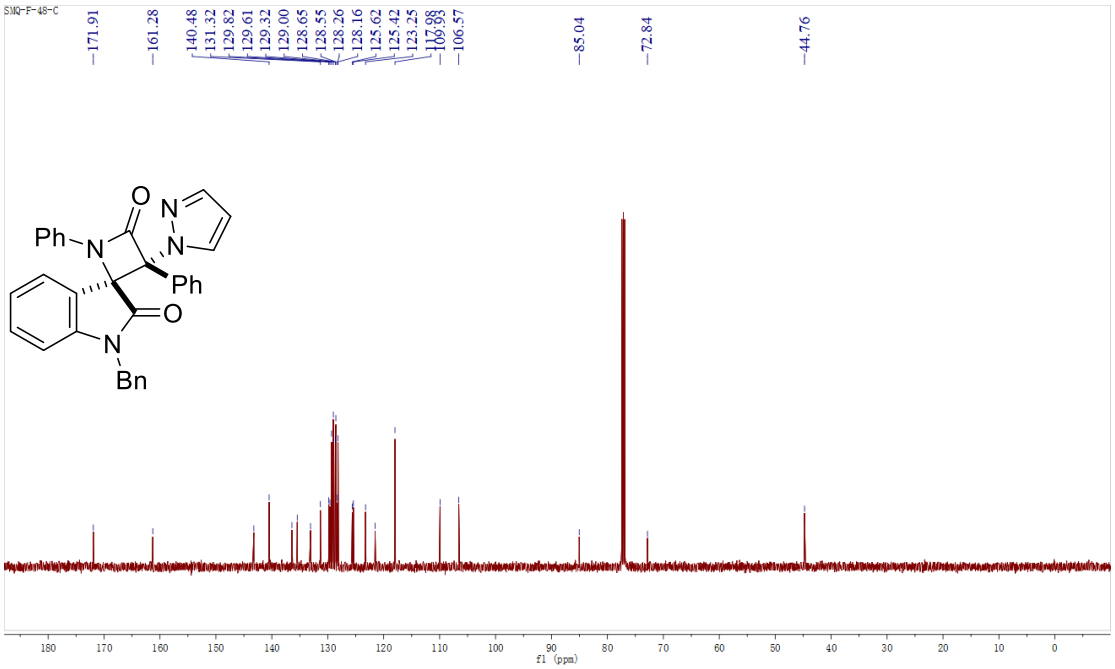
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5k



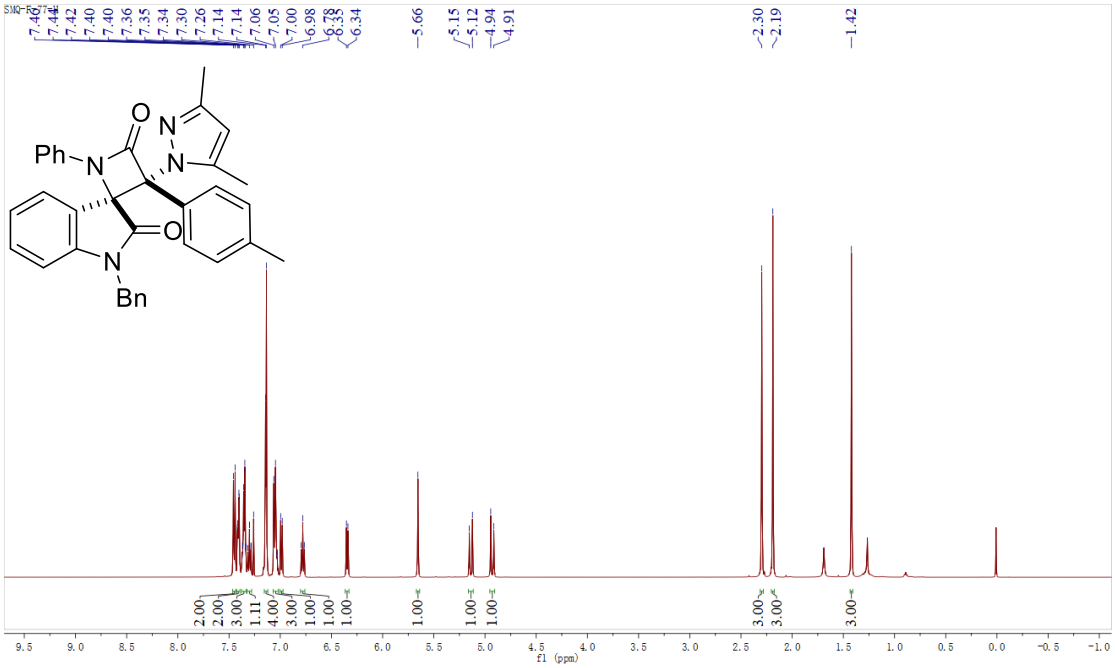


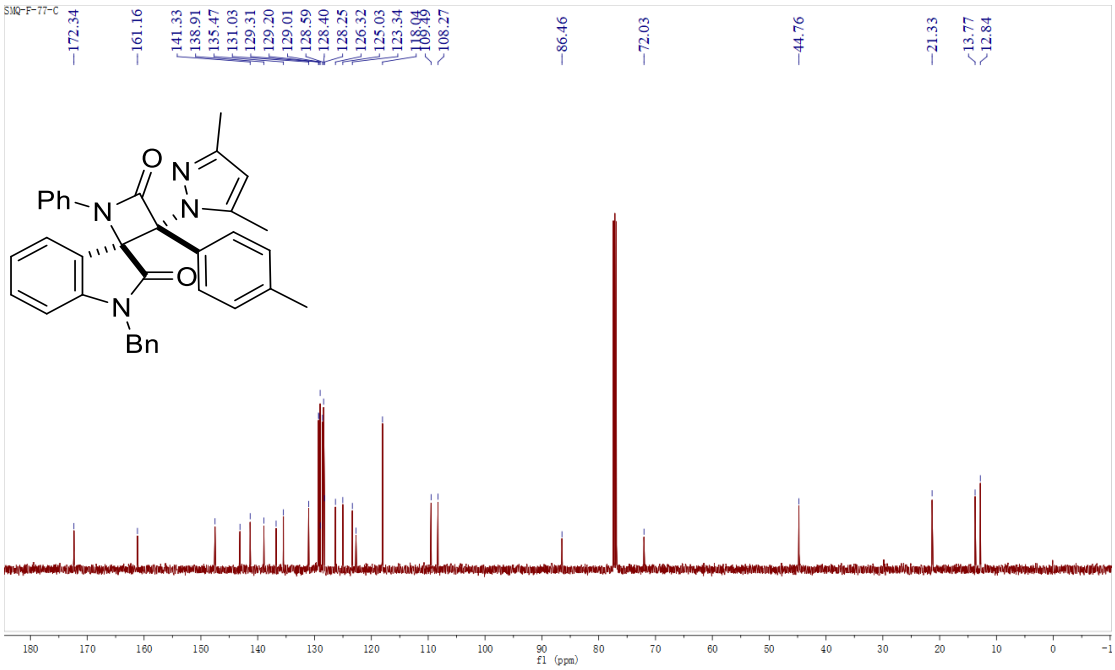
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5l



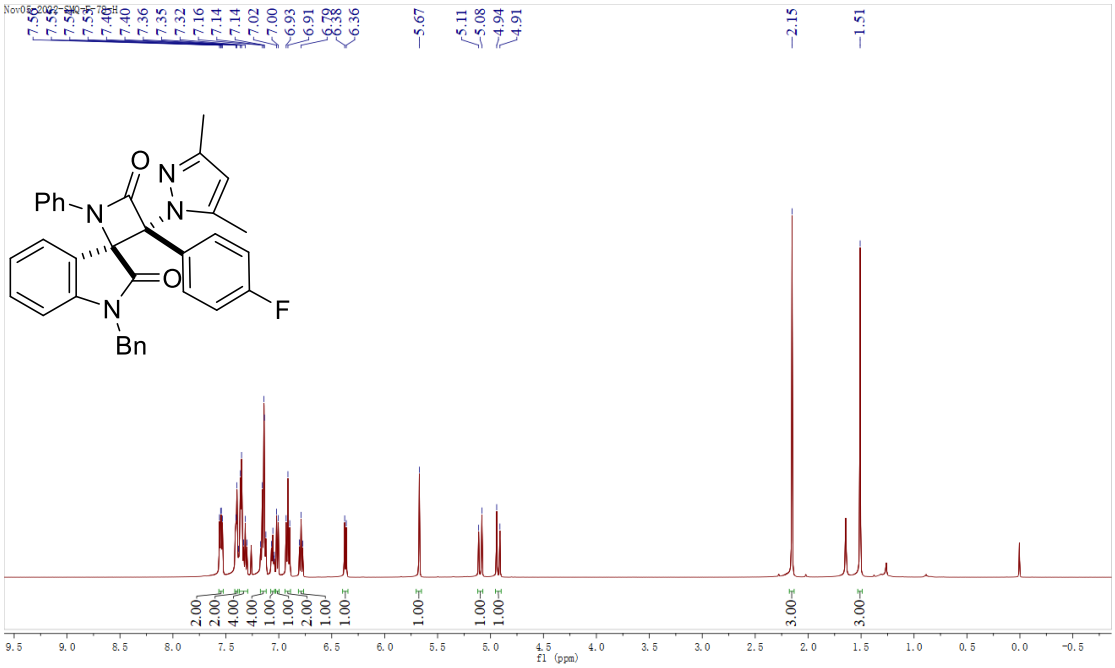


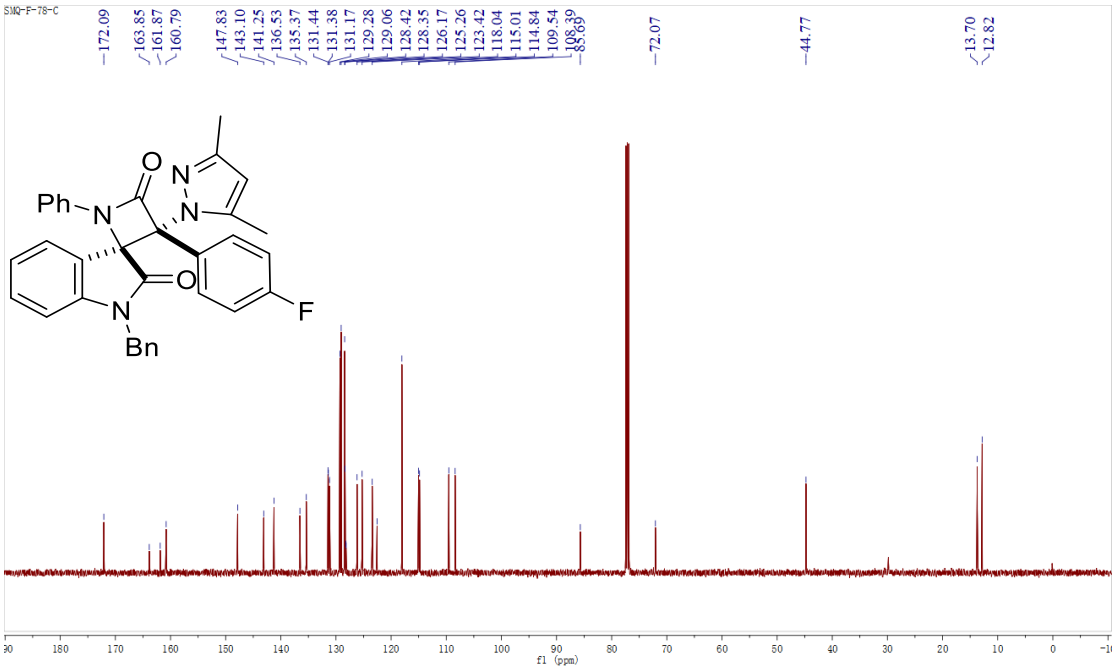
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5m



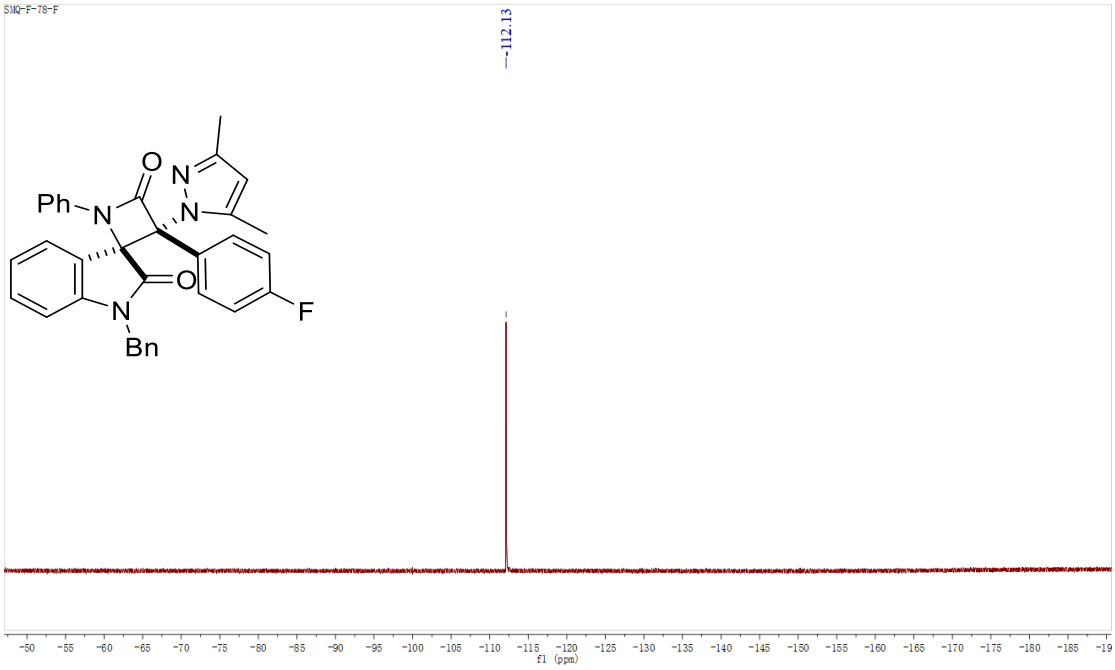


^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5n

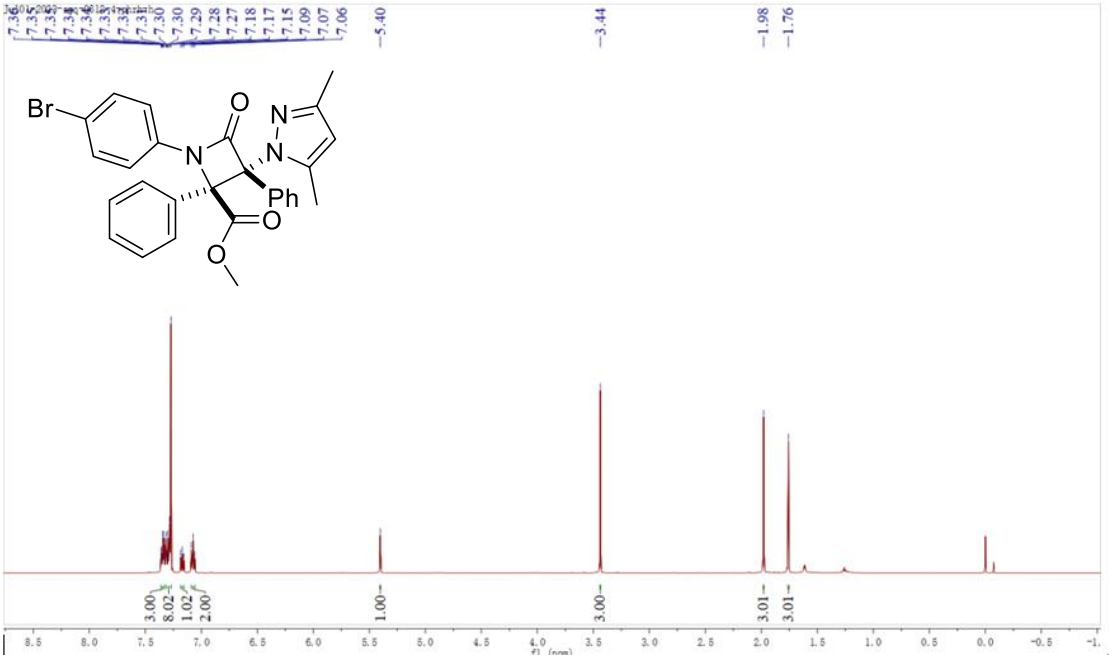




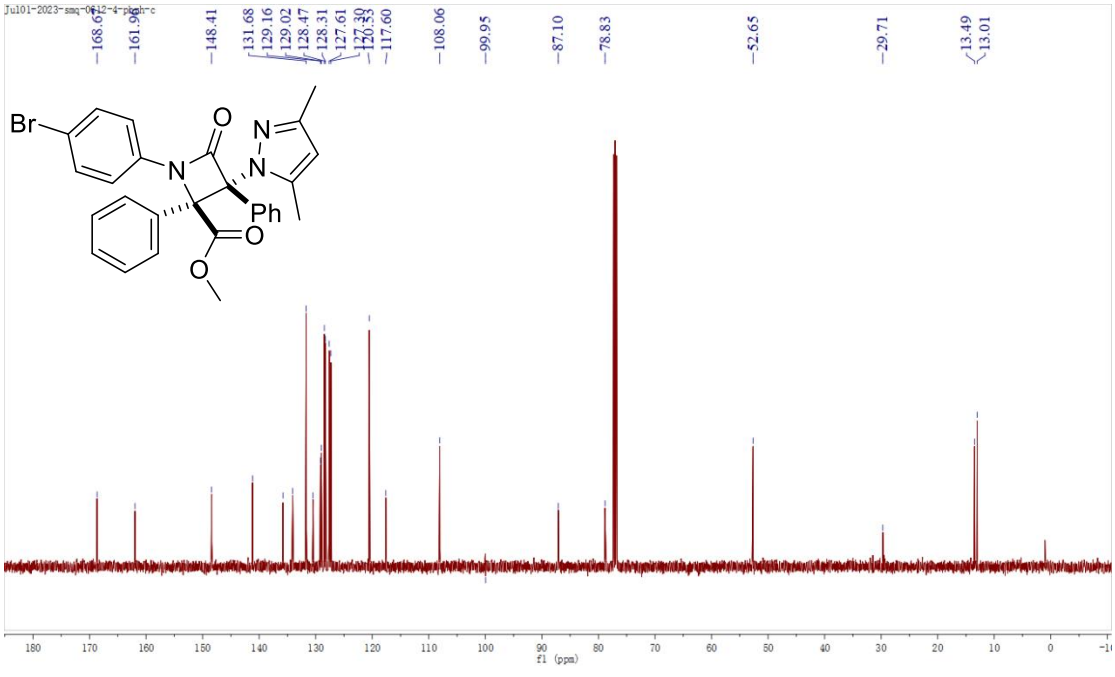
^{19}F NMR (376 MHz, $CDCl_3$) spectra for 5n



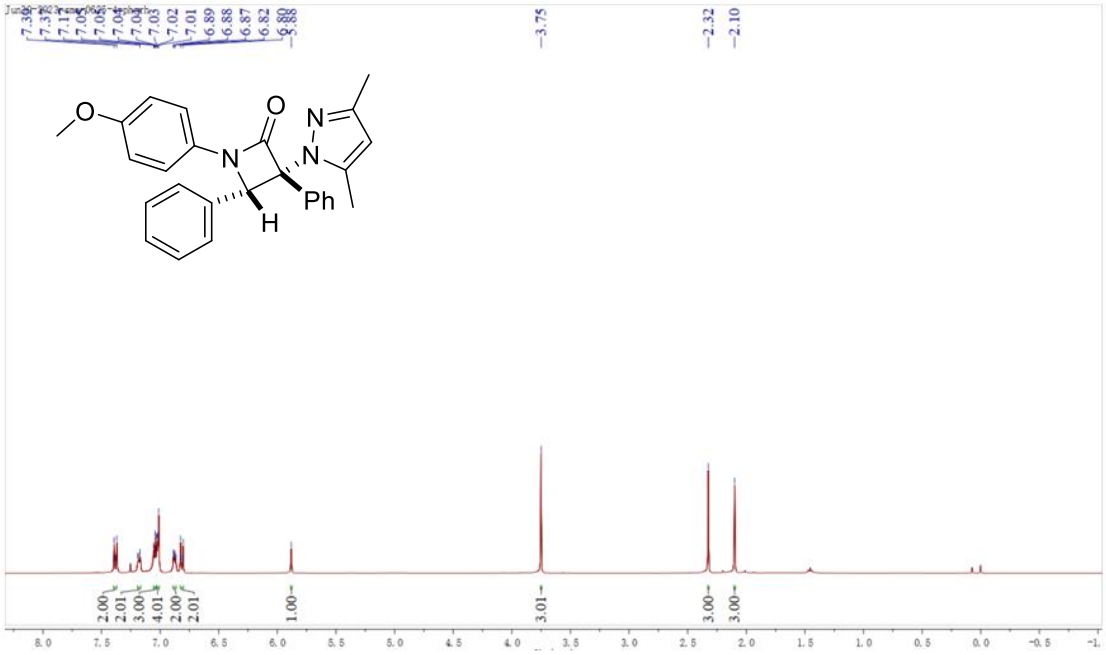
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5'a

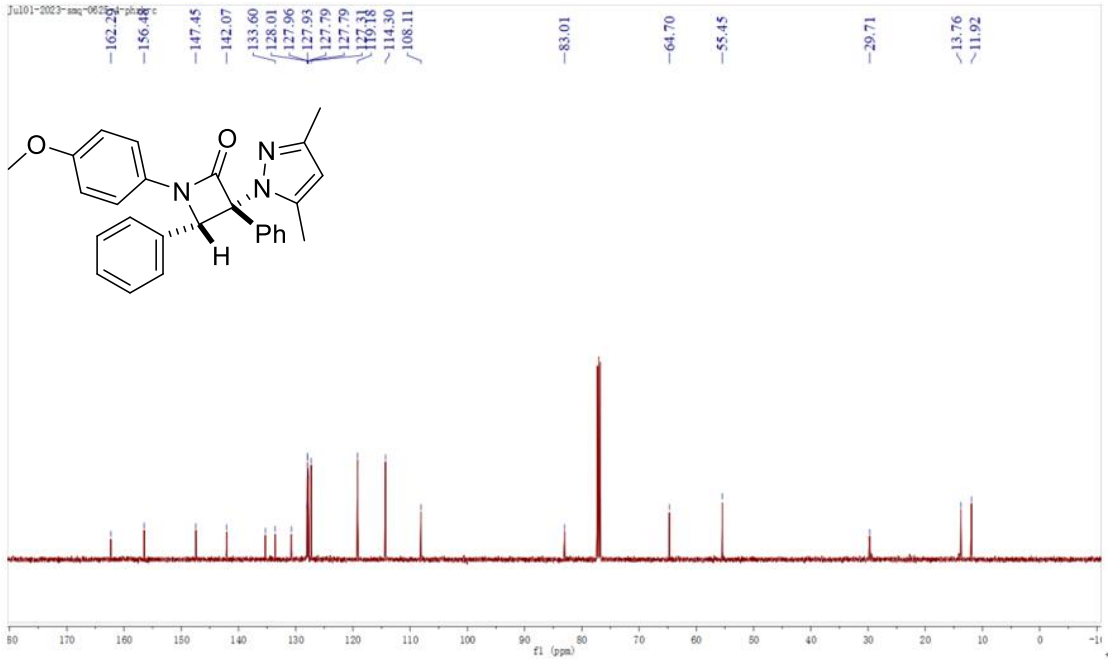


^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 160.0, 148.4, 141.2, 135.8, 134.1, 131.7, 130.5, 129.2, 129.0, 128.5, 128.3, 127.6, 127.3, 120.5, 117.6, 108.1, 100.0, 87.1, 78.8, 52.6, 29.7, 13.5, 13.0.

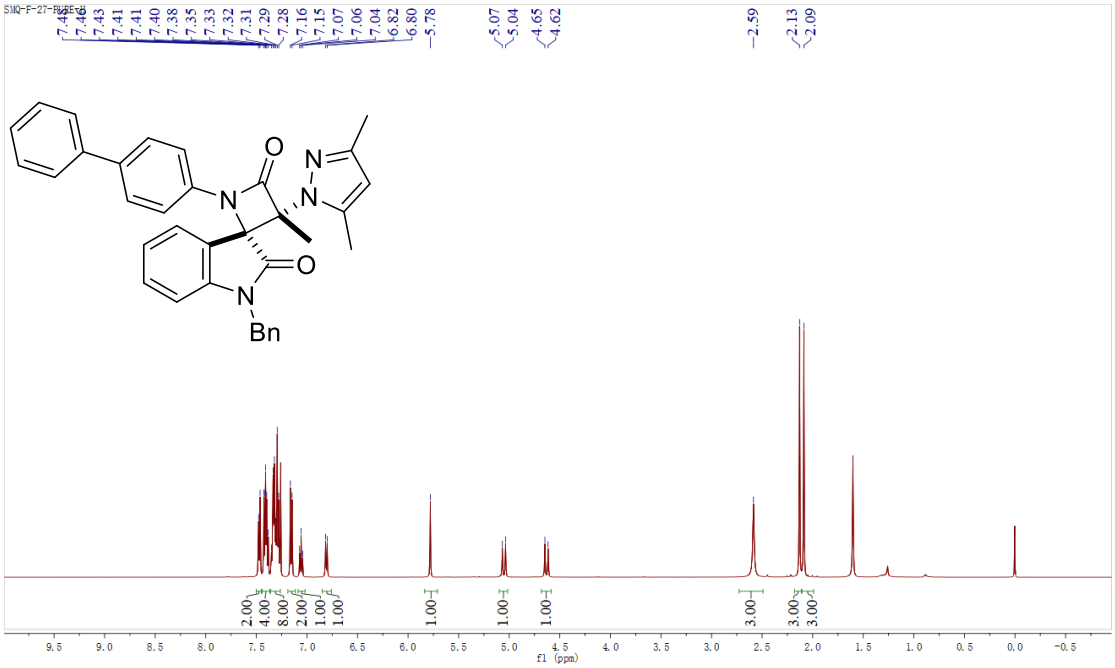


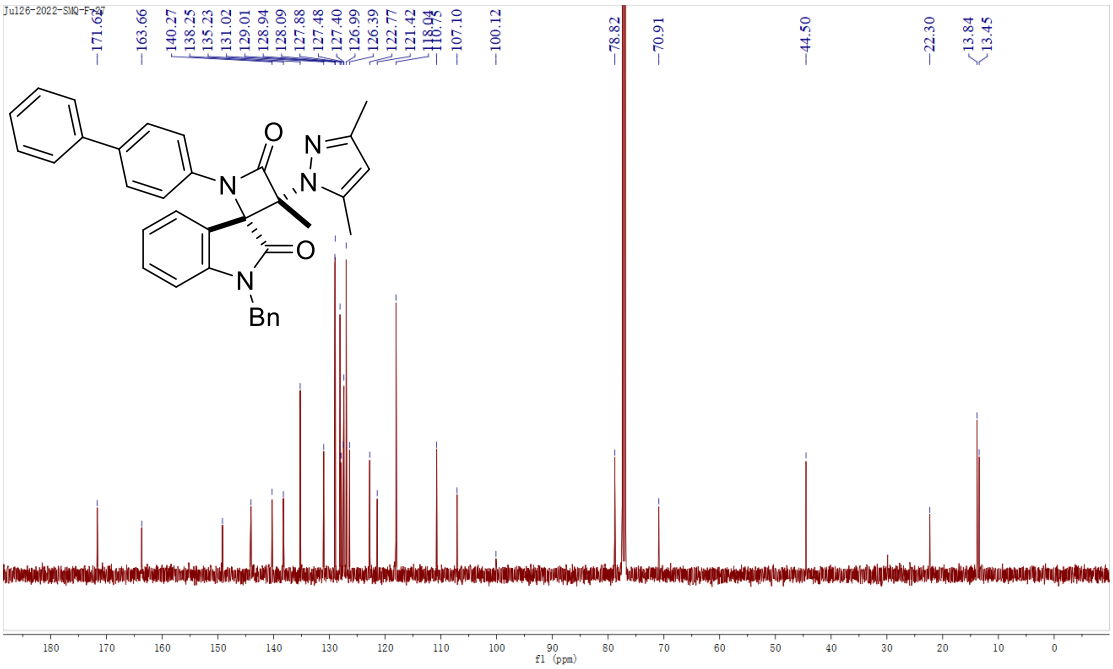
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 5'b



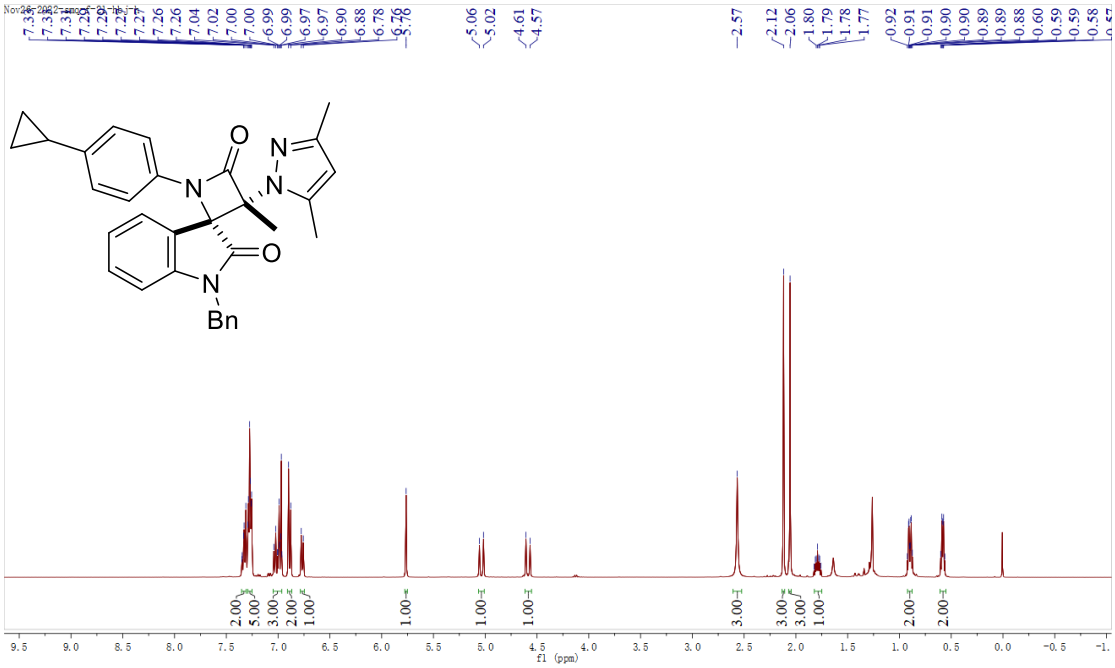


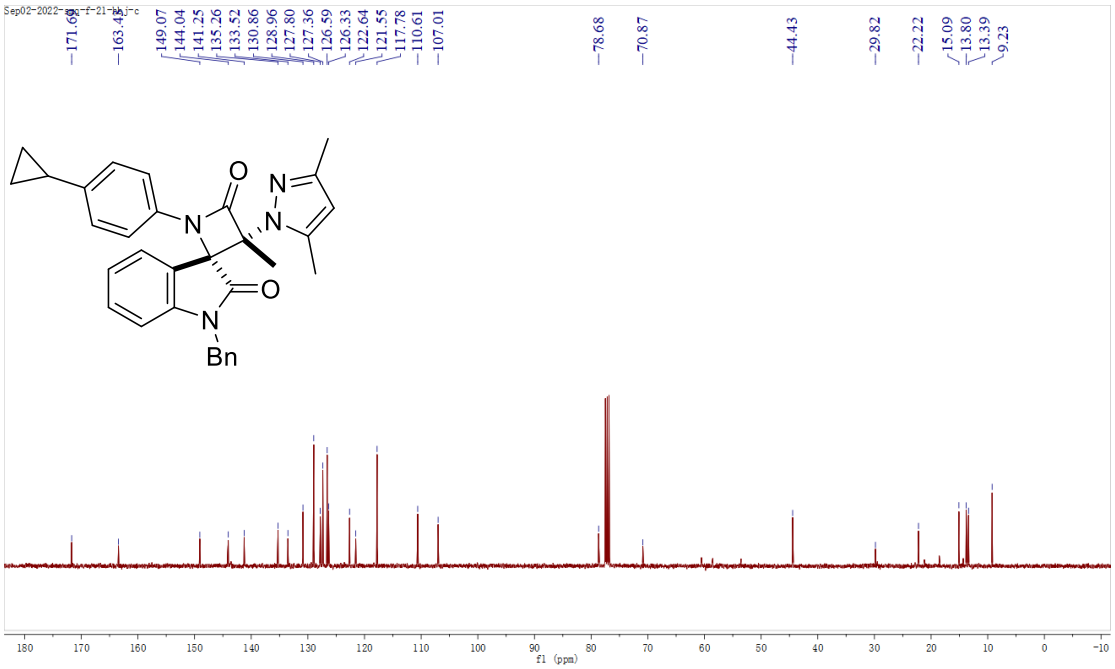
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 6a



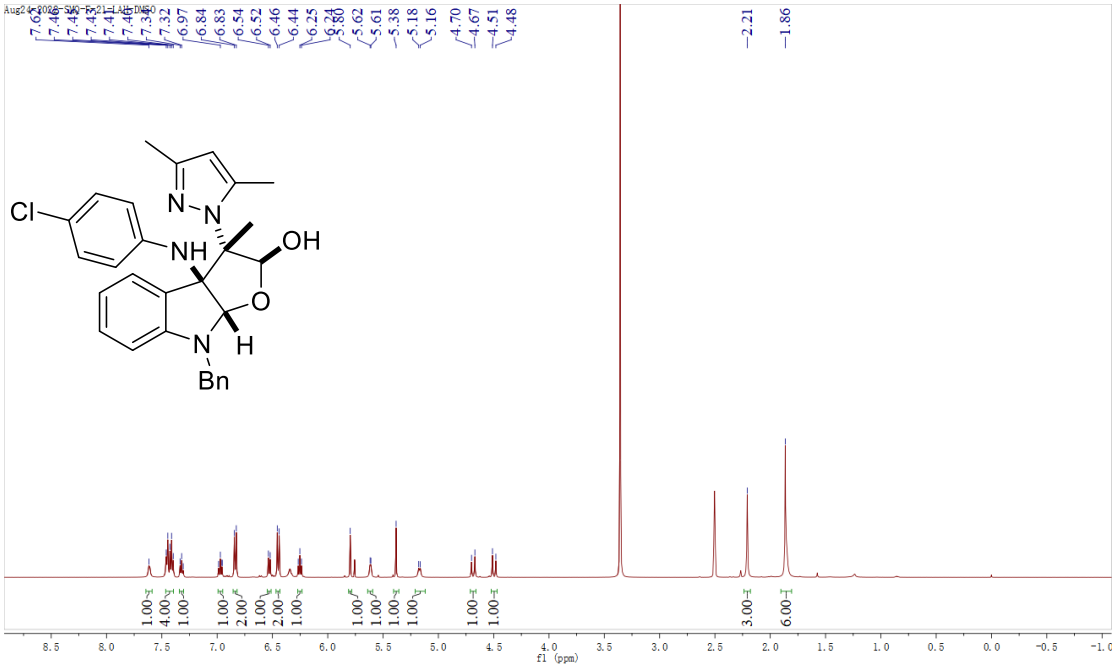


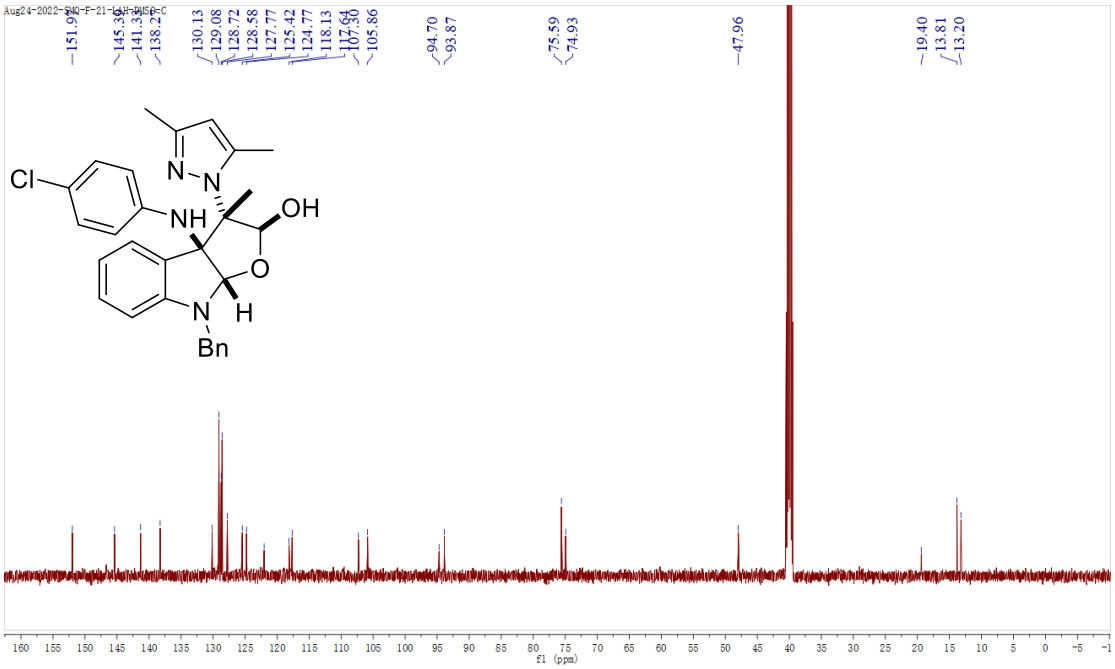
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra for 6b



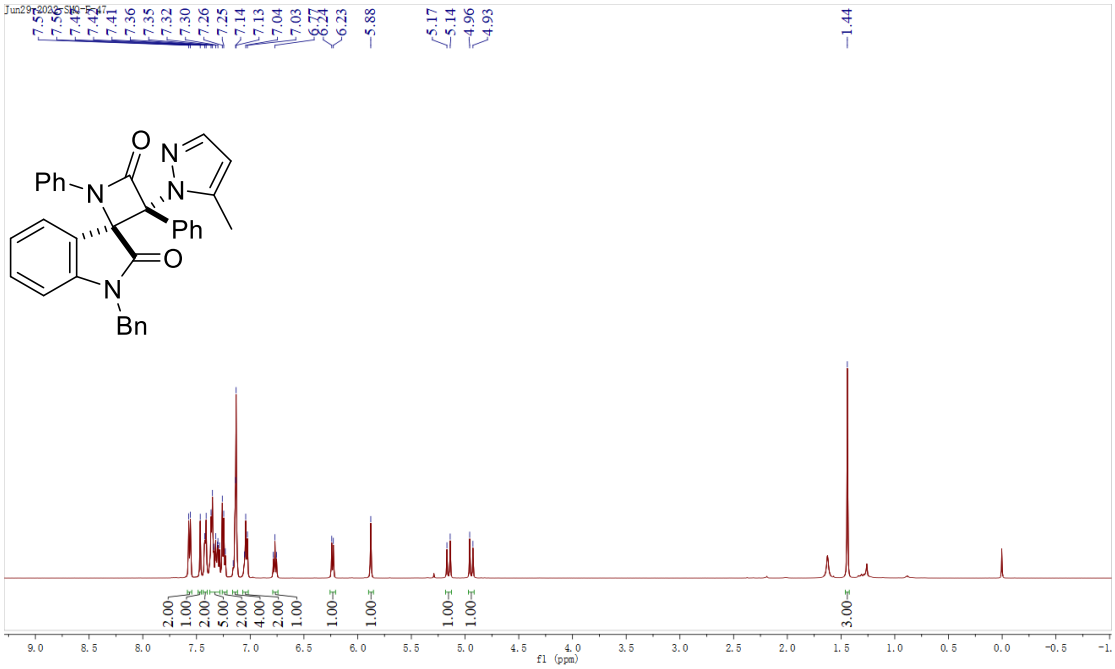


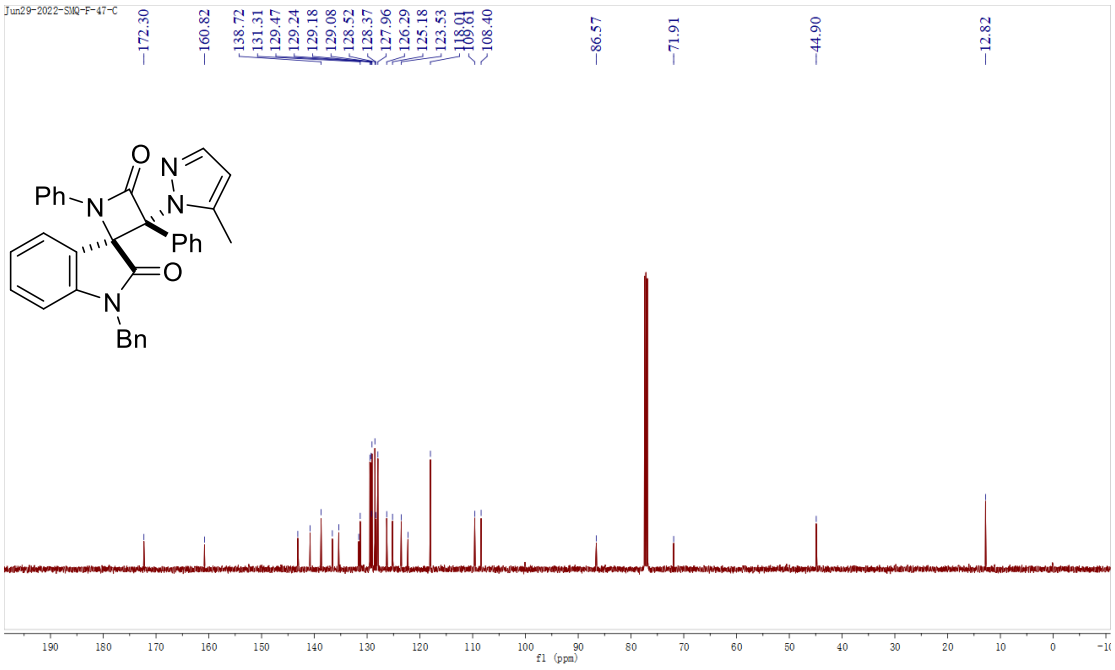
^{1}H NMR (500 MHz, DMSO-d_6) and ^{13}C NMR (125 MHz, DMSO-d_6) spectra for 7





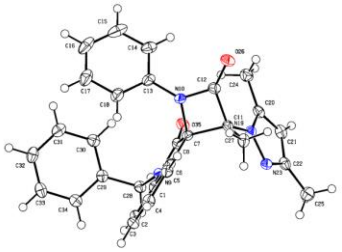
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) spectra for 8





9. Single crystal X-ray diffraction data

Single crystal X-ray diffraction data of 3a (CDCC No.: 2173515)



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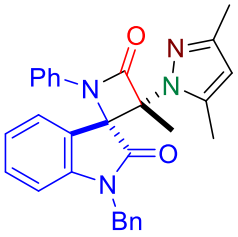


3a

Bond precision: C-C = 0.0019 A Wavelength=1.54184

Cell: a=12.0222(2) b=8.7354(2) c=22.4535(3)
alpha=90 beta=95.275(1) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	2348.05(7)	2348.05(7)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C29 H26 N4 O2	C29 H26 N4 O2
Sum formula	C29 H26 N4 O2	C29 H26 N4 O2
Mr	462.54	462.54
Dx,g cm-3	1.308	1.308
Z	4	4
Mu (mm-1)	0.668	0.668
F000	976.0	976.0
F000'	978.80	
h,k,lmax	15,10,28	15,10,27
Nref	4854	4632
Tmin,Tmax	0.792,0.818	0.530,1.000
Tmin'	0.792	

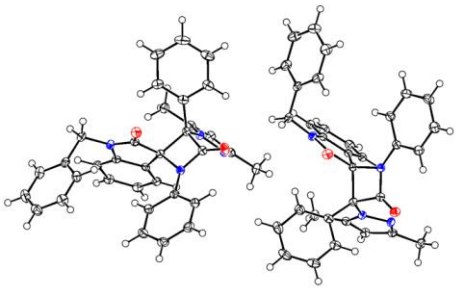
Correction method= # Reported T Limits: Tmin=0.530 Tmax=1.000
AbsCorr = MULTI-SCAN

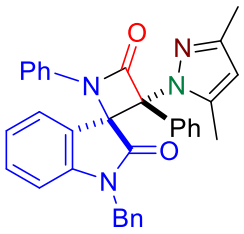
Data completeness= 0.954 Theta(max)= 75.300

R(reflections)= 0.0392(4098) wR2(reflections)= 0.1041(4632)

S = 1.065 Npar= 320

Single crystal X-ray diffraction data of 5a (CDCC No.: 2223042)





5a

Bond precision: C-C = 0.0020 A Wavelength=1.54184

Cell: a=16.8499(1) b=16.0418(1) c=19.5299(1)
alpha=90 beta=90.450(1) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	5278.82(5)	5278.82(5)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C34 H28 N4 O2	C34 H28 N4 O2
Sum formula	C34 H28 N4 O2	C34 H28 N4 O2
Mr	524.60	524.60
Dx,g cm-3	1.320	1.320
Z	8	8
Mu (mm-1)	0.663	0.663
F000	2208.0	2208.0
F000'	2214.30	
h,k,lmax	21,20,24	21,19,24
Nref	10972	10510
Tmin,Tmax	0.820,0.876	0.848,1.000
Tmin'	0.767	

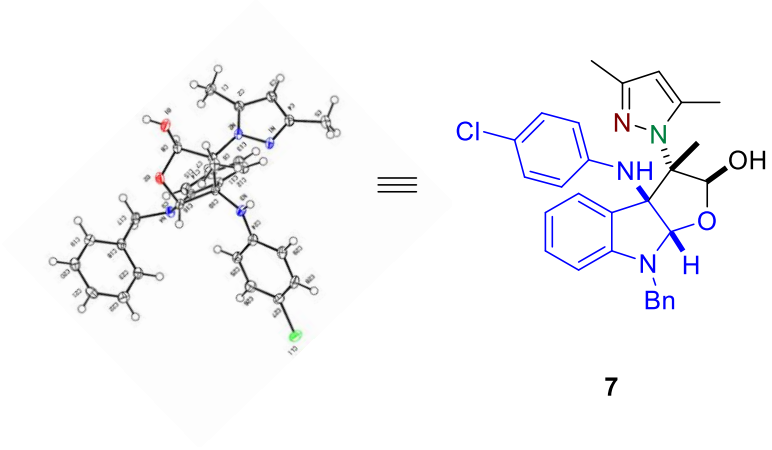
Correction method= # Reported T Limits: Tmin=0.848 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.958 Theta(max)= 75.668

R(reflections)= 0.0404(10252) wR2(reflections)= 0.0943(10510)

S = 1.146 Npar= 725

Single crystal X-ray diffraction data of 7 (CDCC No.: 2223035)



7

Bond precision: C-C = 0.0069 A Wavelength=1.54184

Cell: a=9.9599(5) b=11.0330(3) c=11.8000(5)
alpha=86.694(3) beta=71.741(4) gamma=86.666(3)
Temperature: 100 K

	Calculated	Reported
Volume	1228.24(9)	1228.24(9)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C29 H29 Cl N4 O2	C29 H29 Cl N4 O2
Sum formula	C29 H29 Cl N4 O2	C29 H29 Cl N4 O2
Mr	501.01	501.01
Dx,g cm-3	1.355	1.355
Z	2	2
Mu (mm-1)	1.655	1.655
F000	528.0	528.0
F000'	530.13	
h,k,lmax	12,13,14	12,13,14
Nref	5082	4815
Tmin,Tmax	0.652,0.847	0.339,1.000
Tmin'	0.570	

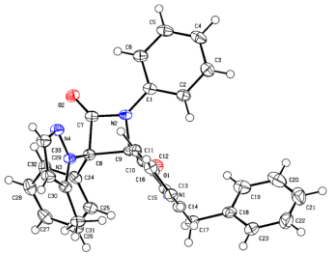
Correction method= # Reported T Limits: Tmin=0.339 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.947 Theta(max)= 75.346

R(reflections)= 0.0841(4534) wR2(reflections)= 0.2461(4815)

S = 1.020 Npar= 329

Single crystal X-ray diffraction data of 8 (CDCC No.: 2209013)



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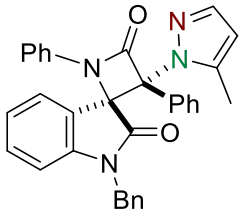


8

Bond precision: C-C = 0.0029 A Wavelength=1.54184

Cell: a=13.1778(4) b=14.3635(4) c=13.5804(4)
alpha=90 beta=96.473(3) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	2554.10(13)	2554.10(13)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C33 H26 N4 O2	C33 H26 N4 O2
Sum formula	C33 H26 N4 O2	C33 H26 N4 O2
Mr	510.58	510.58
Dx,g cm-3	1.328	1.328
Z	4	4
Mu (mm-1)	0.671	0.671
F000	1072.0	1072.0
F000'	1075.08	
h,k,lmax	16,18,17	16,17,16
Nref	5311	4962
Tmin,Tmax		0.189,1.000
Tmin'		

Correction method= # Reported T Limits: Tmin=0.189 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.934 Theta(max)= 75.695

R(reflections)= 0.0564(4171) wR2(reflections)= 0.1628(4962)

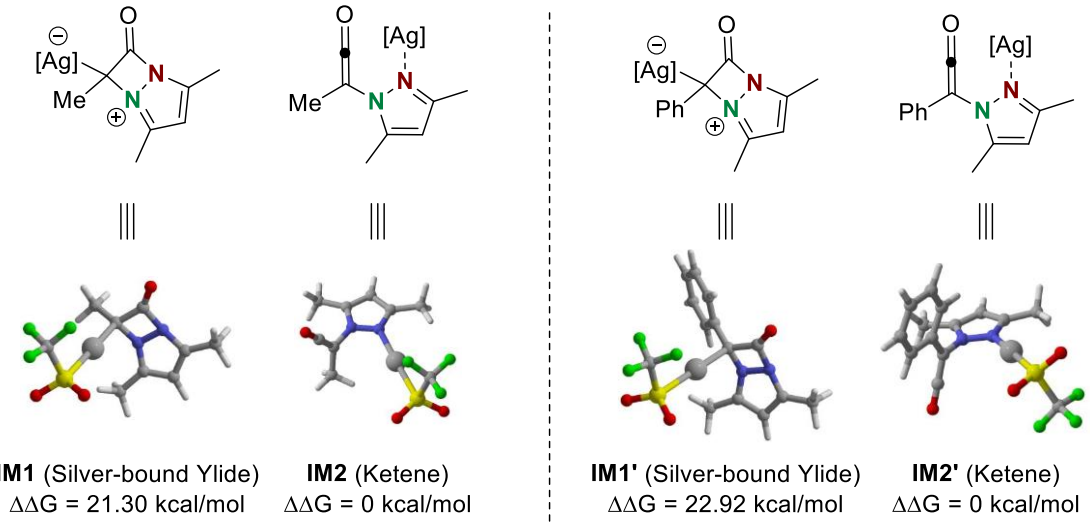
S = 1.048 Npar= 353

10. Computational Studies

Method

We performed calculations with Gaussian 09 program, We ran the geometry optimization, frequency and structures with m062x/6-31G(d)/Lanl2dz (6-31G(d) is applied to nonmetal elements such as C, H, O, N and Lanl2dz is used for silver element). We added Solvent effect with self-consistent reaction field (SCRF) method based on SMD model in dichloromethane (ε=9.1). The 3D optimized structures were displayed by CYLview visualization program.

DFT studies of intermediate stability ([Ag] = AgOTf)



IM1 (Silver-bound Ylide) ΔΔG = 21.30 kcal/mol

IM2 (Ketene) ΔΔG = 0 kcal/mol

IM1' (Silver-bound Ylide) ΔΔG = 22.92 kcal/mol

IM2' (Ketene) ΔΔG = 0 kcal/mol

Reference:

1. Gaussian 09, Revision D.01,
M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski,
and D. J. Fox, Gaussian, Inc., Wallingford CT, 2013.

Calculated Enthalpy and Gibbs Free Energy

Structures	*H* (Hartree)	*G* (Hartree)	*ΔΔH* (Kcal/mol)	*ΔΔG* (Kcal/mol)
Me-ketene	-1526.86	-1526.94	0	0
Me-ylide	-1526.82	-1526.90	21.30	23.82
Ph-ketene	-1718.47	-1718.56	0	0
Ph-ylide	-1718.44	-1718.52	22.92	24.23

Cartesian Coordinates

IM2:ketene

Imaginary sequence 0

0 1

O	-2.32766400	-2.98004000	1.69258900
C	-5.25805600	-0.36027100	0.28088100
C	-1.62269800	3.27465900	0.18185800
C	-2.24818900	-1.90688600	-1.69126200
C	-2.48223500	-1.46281800	-0.27286100
N	-2.79488000	-0.10587600	0.00443800
C	-2.38608500	-2.26635000	0.77756200
N	-1.81888400	0.83574600	-0.02938900
C	-2.41335000	2.00833100	0.15803900
C	-3.80297100	1.81878500	0.31387300
C	-4.01606400	0.45952400	0.20318800
H	-6.12442200	0.29749700	0.36885500
H	-5.37812400	-0.97903100	-0.61408100
H	-5.23748400	-1.02520500	1.15044900
H	-1.96627700	3.96178500	-0.59688800
H	-1.72948600	3.78146600	1.14545100
H	-0.56135700	3.06245500	0.01582700
H	-3.16045600	-1.78765400	-2.28539100
H	-1.45417200	-1.30389000	-2.14829300
H	-1.94361100	-2.95553100	-1.72248000
H	-4.55269500	2.57815400	0.48232500
Ag	0.30489900	0.27265000	-0.38038600
S	2.74347000	-0.30486200	-0.76901400
O	3.51376400	0.62519100	-1.63453500
O	3.04978700	-1.75292800	-0.90268700
C	3.43766300	0.06669500	0.90785500
F	4.72015900	-0.27083600	1.00454200
F	2.74739800	-0.61103600	1.83432300
F	3.31505100	1.37034900	1.17930100

IM1: ylide

Imaginary sequence 0

0 1

N	-3.26952100	-0.63588500	0.25169200
C	-3.81863600	0.07168900	1.27214400
C	-3.73820700	1.40975300	0.89643100
C	-3.02428300	1.47643600	-0.31885800
N	-2.78303500	0.21753600	-0.68297600
C	-1.68164300	-0.69777400	-1.13857300
C	-2.22760900	-1.66263400	-0.16060100
O	-2.07512000	-2.75849200	0.26960400
C	-1.67519700	-1.04886200	-2.61099500
C	-4.41762200	-0.58622600	2.46275500
C	-2.53916700	2.63482200	-1.11296000
Ag	0.30022000	0.04172500	-0.35871200
S	2.55351800	0.90775800	0.46591100
O	2.68552000	1.13206400	1.93035000
O	3.24117400	1.88590900	-0.41890300
C	3.59555700	-0.60430800	0.22569100
F	4.86097600	-0.39947000	0.58200500
F	3.56799200	-0.97549400	-1.06010600
F	3.10665100	-1.61648400	0.95207900
H	-4.14519700	2.25036900	1.44067700
H	-3.75367300	-1.36786700	2.84261100
H	-4.59119900	0.15185900	3.24679600
H	-5.37257600	-1.05120600	2.19820400
H	-2.66673600	3.55862300	-0.54746300
H	-1.47681100	2.50432400	-1.35240300
H	-3.09140800	2.71612200	-2.05404800
H	-0.97390300	-1.87212100	-2.77602900
H	-2.66560200	-1.35686500	-2.96958000
H	-1.33394700	-0.20020900	-3.20931600

IM2':ketene

Imaginary sequence 0

0 1

O	1.86801500	-0.19113500	3.44799100
C	4.80687000	1.28784700	0.74991100
C	0.83780100	3.55898800	-1.60401200
C	2.20838300	-1.52554700	0.18918400
C	2.22422800	-0.28132900	0.98321000
N	2.36564000	0.98331000	0.36039500
C	2.02163100	-0.23802200	2.30149800
N	1.30243200	1.55712300	-0.26111100
C	1.75169200	2.66842000	-0.82976100
C	3.13316600	2.81414200	-0.57099000

C	3.49842300	1.71930200	0.18351900
C	2.29502000	-1.44513100	-1.20607900
C	2.26727500	-2.60780500	-1.97438300
C	2.15061700	-3.85397600	-1.36558700
C	2.06507300	-3.93399600	0.02497100
C	2.09521800	-2.78125800	0.80014100
H	5.57302900	2.02536500	0.50559700
H	4.75147400	1.18756200	1.83849300
H	5.10773600	0.31949500	0.33647600
H	1.24104500	3.75165900	-2.60207500
H	-0.14760500	3.09374500	-1.70897700
H	0.71687000	4.52259300	-1.09988500
H	3.77746000	3.61798600	-0.89642300
H	2.38952400	-0.47748700	-1.69166800
H	2.33771100	-2.53220000	-3.05527000
H	2.12766700	-4.75708400	-1.96681400
H	1.97511600	-4.90060600	0.51095000
H	2.03483100	-2.85961800	1.88343800
Ag	-0.62094700	0.42938100	-0.39453700
S	-2.88087700	-0.73159900	-0.43730100
O	-2.97881000	-2.03008500	0.27826500
O	-3.65490200	-0.60378900	-1.69956800
C	-3.82512900	0.39492300	0.68993500
F	-5.09816500	0.02865800	0.80663400
F	-3.78211700	1.64651100	0.21464400
F	-3.26848100	0.40160500	1.90631800

IM1’-ylide

Imaginary sequence 0

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N	-2.83825600	-1.35866900	-0.76545700
C	-3.04268600	-2.67254300	-0.48996700
C	-2.91450800	-2.80269300	0.89064400
C	-2.50716400	-1.55618000	1.40616600
N	-2.50613000	-0.70230500	0.37901600
C	-1.61369100	0.28218800	-0.30278600
C	-1.99165300	-0.38369300	-1.56278100
O	-1.82533800	-0.34391000	-2.73729600
C	-3.40191400	-3.65751300	-1.54248100
C	-2.10745500	-1.14291900	2.77515600
Ag	0.56579400	-0.19758800	0.12853000
S	2.99383200	-0.74026600	0.70711600
O	3.46884800	-2.10527000	0.35768900
O	3.51699400	-0.15916700	1.97221800

C	3.86030500	0.29358400	-0.56331600
F	5.18355500	0.20006300	-0.46542400
F	3.51088300	1.57790400	-0.42048600
F	3.49362500	-0.09402900	-1.79100100
H	-3.08645800	-3.70284100	1.46396500
H	-2.77703000	-3.51694900	-2.42879300
H	-3.27149300	-4.67130100	-1.16203400
H	-4.44709400	-3.52401800	-1.83962700
H	-1.82989400	-2.01859900	3.36353000
H	-1.25667200	-0.45341400	2.72656400
H	-2.93336000	-0.63164600	3.28002100
C	-1.87058500	1.72856800	-0.09455200
C	-2.62986900	2.18792100	0.98497500
C	-1.33093800	2.65561700	-0.99745200
C	-2.84448400	3.55384300	1.15935300
H	-3.05658700	1.47655700	1.68720800
C	-1.55926700	4.01596000	-0.82361800
H	-0.73163600	2.30479000	-1.83465700
C	-2.31403900	4.47299100	0.25741400
H	-3.43528700	3.89666100	2.00372600
H	-1.14178600	4.72302600	-1.53417700
H	-2.48453300	5.53600100	0.39538400