

## Supplementary information

### **Catalytic system-controlled divergent reactions of pyrazolidinones with 3-alkynyl-3-hydroxyisoindolinones to construct diversified nitrogen-containing heterocyclic scaffolds**

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## I. General experimental information

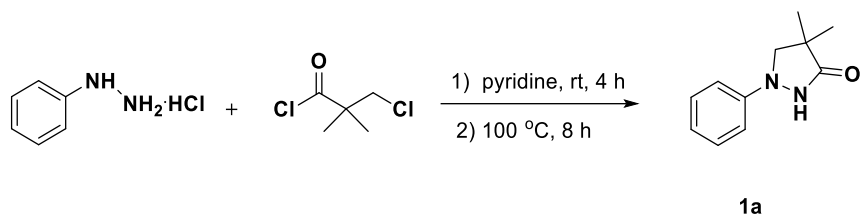
Unless otherwise specified, the reagents were purchased from commercial sources, and used without further purification. All products were characterized by their NMR and MS spectra.  $^1\text{H}$  and  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra were recorded on a 400, 500 or 600 MHz instrument. The chemical shifts were reported in parts per million (ppm,  $\delta$ ) downfield from tetramethylsilane (TMS). Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd), doublet of triplets (dt), triplet of doublets (td), doublet of doublet of doublets (ddd), doublet of doublet of triplets (ddt) and broad (br). High resolution mass spectra (HRMS) were measured on a Micromass Ultra Q-TOF spectrometer. Analytical thin-layer chromatography (TLC) was performed on HSGF 254 (0.2-0.3 mm thickness). Column chromatography was performed on silica gel (300-400 mesh) using ethyl acetate (EA)/petroleum ether (PE) or dichloromethane (DCM)/methanol (MeOH). HPLC analysis of target compounds was performed on an Agilent 1260 HPLC instrument with a binary pump and a photodiode array detector (DAD), using an Agilent Extend-C18 column (4.6 mm  $\times$  150 mm, 5  $\mu\text{m}$ ) at 1.0 mL/min flow monitored by UV absorption at 254 nm. Mobile phase A:  $\text{H}_2\text{O}$ , mobile phase B: MeOH.

| Time/min | %A | %B |
|----------|----|----|
| 0        | 20 | 80 |
| 10       | 20 | 80 |

## II. Synthesis of substrates

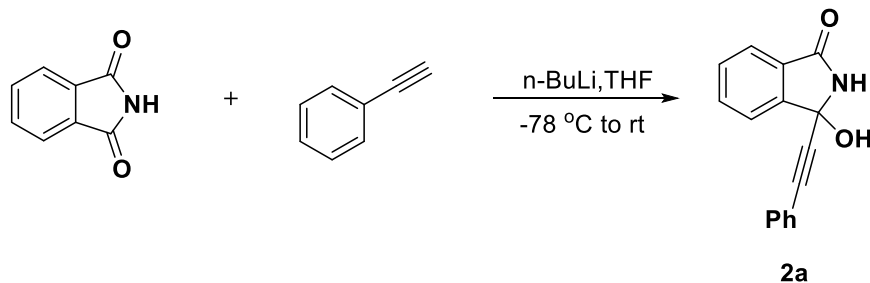
The pyrazolidinones **1a-1k**, 3-alkynyl-3-hydroxyisoindolinones **2a-2m**, and deuterated pyrazolidinone [**D**<sub>5</sub>]-**1a** were prepared based on literature procedures,<sup>[1-4]</sup> if needed, which were recrystallized before use. The detailed synthesis procedures of **1a**, **2a**, [**D**<sub>5</sub>]-**1a** are as follows:

### (1) Synthesis of pyrazolidinone (1a)



The 3-chloro-2,2-dimethylpropionyl chloride (1.06 g, 8.87 mmol, 1.0 eq.) was added dropwise to a solution of phenylhydrazine hydrochloride (1g, 6.87 mmol, 1.0 eq.) in pyridine (40 mL). The resulting mixture was stirred at room temperature for 4 h and then stirred at 100 °C for 8 h. The reaction mixture was poured into 200 mL aqueous HCl (2 M) and extracted with ethyl acetate (50 mL  $\times$  3). After then, the organic layer was washed with saturated sodium carbonate solution (100 mL  $\times$  3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtrated and concentrated in vacuo. The residue was purified by flash chromatography (PE/EA=3/1, v/v) to afford the corresponding pyrazolidinone **1a**.

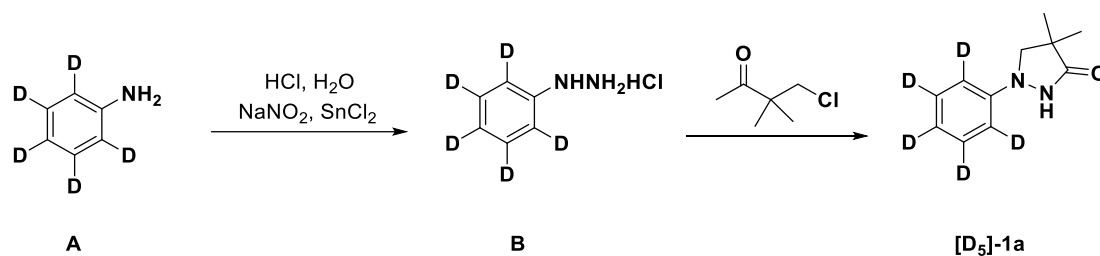
### (2) Synthesis of 3-hydroxy-3-(phenylethynyl) isoindolin-1-one (2a)



A solution of *N*-butyl lithium (2.61g, 40.78 mmol, 4.0 eq., 2.5 M in petroleum ether solution) was added dropwise to a solution of phenylacetylene (4.17g, 40.78 mmol, 4.0 eq.) in THF (30 mL) at -78 °C and then the reaction mixture was stirred for 30 min. After then, a solution of phthalimide (1.5 g, 10.19 mmol, 1.0 eq.) in THF (15 mL) was added to the reaction mixture. The resulting mixture was stirred at -78 °C for 30 min and stirred at room temperature for 4 h. Upon completion as indicated by TLC, the reaction mixture was quenched with saturated ammonium chloride and added 1N HCl to adjust pH=5.0. The aqueous solution was extracted with ethyl acetate (50 mL  $\times$  3), washed with saturated sodium chloride solution (100 mL  $\times$  3), dried over anhydrous

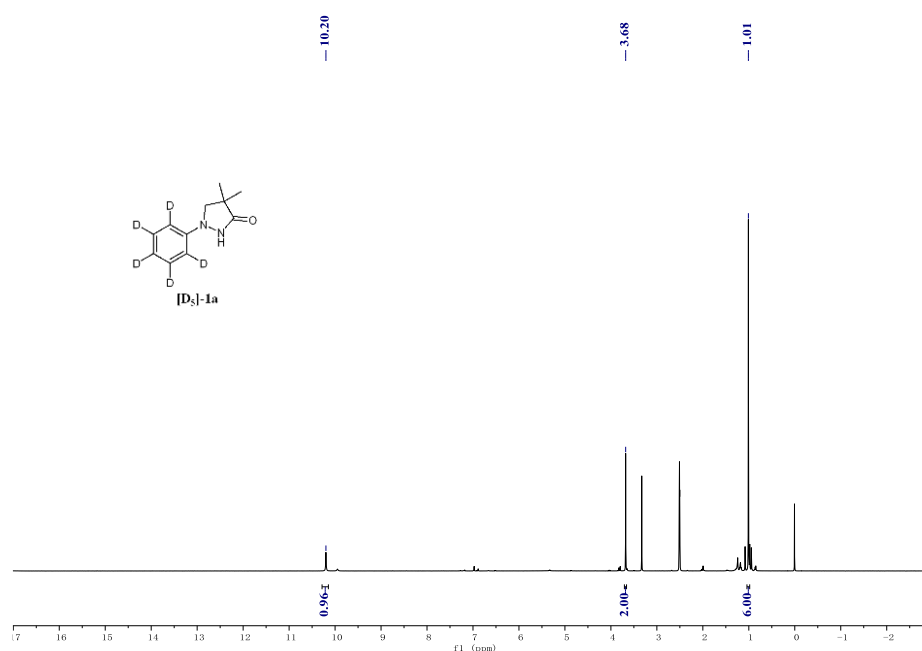
Na<sub>2</sub>SO<sub>4</sub>, filtrated and concentrated in vacuo. The residue was purified by flash chromatography over silica gel using PE/EA (1:1) to afford the corresponding pyrazolidinone **2a**.

### (3) Synthesis of [D<sub>5</sub>]-1a



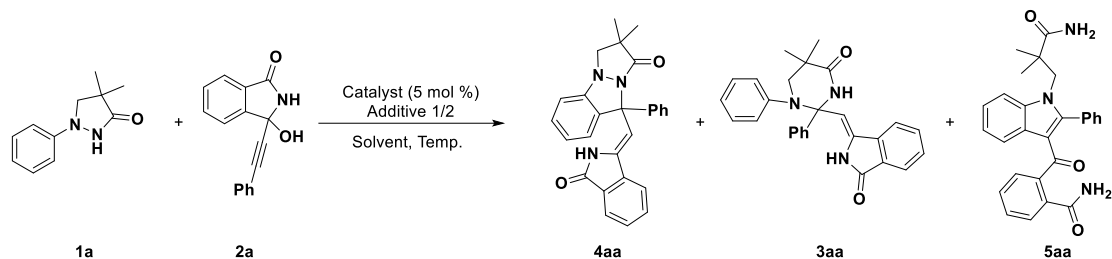
**Synthesis of phenylhydrazine hydrochloride D<sub>5</sub> (B):** A solution of NaNO<sub>2</sub> (718 mg, 10.4 mmol) in water (3 mL) was added dropwise to a solution of **A** (1.0 g, 10 mmol) in 37% HCl (5 mL). The resulting mixture was stirred at 0 °C for 20 min and added a saturated solution of tin(II) chloride dihydrate (2.67 g, 14 mmol) in 37% HCl. Then the mixture was stirred at 0 °C for 20 min and filtered to obtain **B** (1.5 g).

**Synthesis of [D<sub>5</sub>]-1a:** The pyrazolidinone **[D<sub>5</sub>]-1a** was prepared from deuterated phenylhydrazine hydrochloride according to the synthesis procedure of **1a**. <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.20 (s, 1H), 3.68 (s, 2H), 1.01 (s, 6H).



### III. Optimization of Reaction Conditions

**Table S1. Optimization of reaction conditions for 4aa<sup>[a]</sup>**



| Entry           | Catalyst                                                                  | Additive 1 | Additive 2   | Solvent            | Yield(%) <sup>b</sup><br><b>4aa (3aa/5aa)</b> |
|-----------------|---------------------------------------------------------------------------|------------|--------------|--------------------|-----------------------------------------------|
| 1               | [Cp*RhCl <sub>2</sub> ] <sub>2</sub>                                      | AgOAc      | AcOH         | DCE                | 8(nd/nd)                                      |
| 2               | [Cp*RhCl <sub>2</sub> ] <sub>2</sub>                                      | NaOAc      | AcOH         | DCE                | 24(nd/10)                                     |
| 3               | [Cp*RhCl <sub>2</sub> ] <sub>2</sub>                                      | LiOAc      | AcOH         | DCE                | 5(48/nd)                                      |
| 4               | [Cp*RhCl <sub>2</sub> ] <sub>2</sub>                                      | CsOPiv     | AcOH         | DCE                | 28(nd/10)                                     |
| 5               | [Cp*RhCl <sub>2</sub> ] <sub>2</sub>                                      | CsOPiv     | AcOH         | Dioxane            | nd(nd/50)                                     |
| 6               | [Cp*RhCl <sub>2</sub> ] <sub>2</sub>                                      | LiOAc      | AcOH         | CH <sub>3</sub> CN | 25(36/trace)                                  |
| 7               | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | AcOH         | CH <sub>3</sub> CN | 46(0/trace)                                   |
| 8               | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | AcOH         | Acetone            | 40(nd/12)                                     |
| 9               | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | AcOH         | MeOH               | nd(nd/10)                                     |
| 10              | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | AcOH         | CHCl <sub>3</sub>  | 37(nd/nd)                                     |
| 11              | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | PivOH        | CH <sub>3</sub> CN | 26(5/5)                                       |
| 12              | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | Benzoic acid | CH <sub>3</sub> CN | 52(nd/trace)                                  |
| 13 <sup>c</sup> | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | Benzoic acid | CH <sub>3</sub> CN | nd(nd/nd)                                     |
| 14 <sup>d</sup> | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | Benzoic acid | CH <sub>3</sub> CN | 55(nd/trace)                                  |
| 15 <sup>e</sup> | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | Benzoic acid | CH <sub>3</sub> CN | 22(nd/nd)                                     |
| 16 <sup>f</sup> | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | Benzoic acid | CH <sub>3</sub> CN | 57(nd/trace)                                  |
| 17 <sup>g</sup> | [Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub> | LiOAc      | Benzoic acid | CH <sub>3</sub> CN | 60(nd/trace)                                  |

<sup>a</sup>Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), catalyst (5 mol%), additive 1 (0.4 mmol), additive 2 (0.2 mmol) in solvent (4 mL), at 80 °C for 8 h. <sup>b</sup>Isolated yield. <sup>c</sup>rt. <sup>d</sup>100 °C. <sup>e</sup>120 °C. <sup>f</sup>**1a:2a**=1.2:1 <sup>g</sup>**1a:2a**=1.2:1, additive 1 (0.2 mmol), additive 2 (0.1 mmol), 100 °C. nd = not detected

**Table S2. Optimization of reaction conditions for 5aa<sup>[a]</sup>**

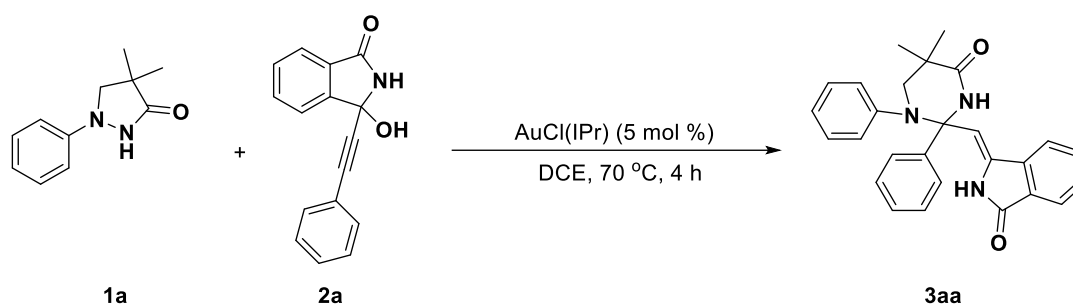
1a + 2a  $\xrightarrow[\text{Solvent, Temp}]{\text{Catalyst (5 mol %), Additives}}$  5aa

| Entry          | Catalyst                             | Additive 1                      | Additive 2 | Solvent | Yield(%) <sup>b</sup> 5aa |
|----------------|--------------------------------------|---------------------------------|------------|---------|---------------------------|
| 1              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | CsOPiv                          | AcOH       | Dioxane | 50                        |
| 2              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | Cs <sub>2</sub> CO <sub>3</sub> | AcOH       | Dioxane | 45                        |
| 3              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | CsF                             | AcOH       | Dioxane | 48                        |
| 4              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | CsOAc                           | AcOH       | Dioxane | 40                        |
| 5              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | Na <sub>2</sub> CO <sub>3</sub> | AcOH       | Dioxane | 31                        |
| 6              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | NaOPiv                          | AcOH       | Dioxane | 25                        |
| 7              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | CsOPiv                          | AcOH       | THF     | 41                        |
| 8              | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | CsOPiv                          | AcOH       | Diglyme | 75                        |
| 9 <sup>c</sup> | [Cp*RhCl <sub>2</sub> ] <sub>2</sub> | CsOPiv                          | AcOH       | Diglyme | 80                        |

<sup>a</sup>Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (5 mol%), additive 1 (0.4 mmol), additive 2 (0.2 mmol) in solvent (4 mL), at 80 °C for 8 h. <sup>b</sup>Isolated yield. <sup>c</sup>additive 1 (0.2 mmol), additive 2 (0.2 mmol), 2 h.

## IV. General procedure for the products

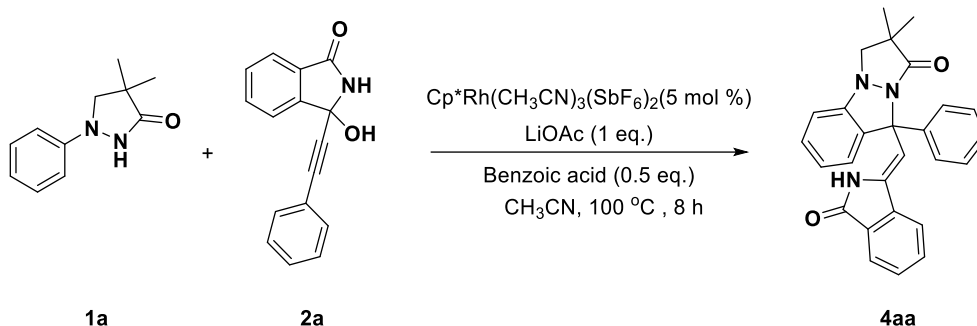
### (1) General procedure for the synthesis of 3 (Condition A)



The AuCl(IPr) (0.01 mmol, 0.05 eq.) was added to a solution of **1a** (0.24 mmol, 1.2 eq.) and **2a** (0.2 mmol, 1.0 eq.) in DCE (4.0 mL) and the reaction mixture was stirred at 70 °C for 4 h. Upon completion as indicated by TLC, the mixture was poured into water (30 mL) and extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine (10 mL × 3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtrated and

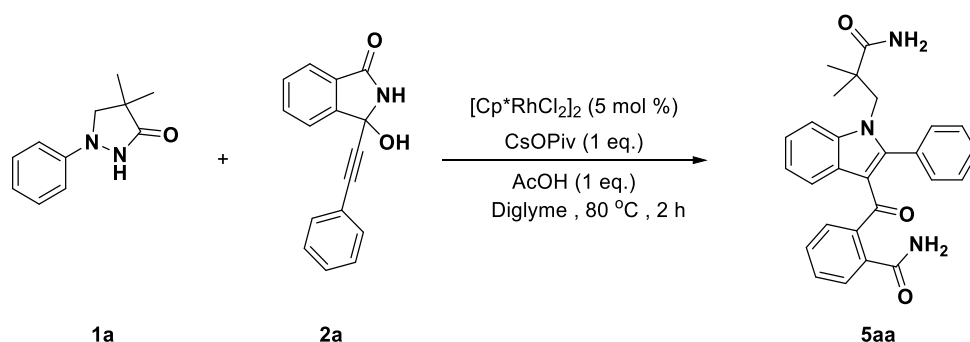
concentrated under vacuum. The residue was purified by column chromatography (PE/EA=1/1, v/v) to afford **3aa**.

## (2) General procedure for the synthesis of 4 (Condition B)



A suspension of **1a** (0.24 mmol, 1.2 eq.), **2a** (0.2 mmol, 1.0 eq.),  $[\text{Cp}^*\text{Rh}(\text{CH}_3\text{CN})_3](\text{SbF}_6)_2$  (0.01 mmol, 0.05 eq.), LiOAc (0.2 mmol, 1.0 eq.), benzoic acid (0.1 mmol, 0.5 eq.) in MeCN (4.0 mL) was stirred at 100 °C for 8 h. Upon completion as indicated by TLC, the reaction mixture was poured into water (30 mL) and extracted with ethyl acetate (10 mL  $\times$  3). The combined organic layer was washed with brine (10 mL  $\times$  3), dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtrated and concentrated under vacuum. The residue was purified by column chromatography (PE/EA=1/1, v/v) to afford **4aa**.

## (3) General procedure for the synthesis of 5 (Condition C)



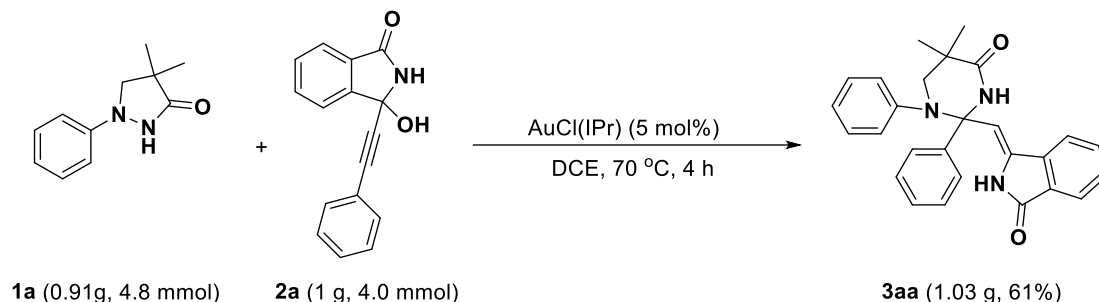
A suspension of **1a** (0.2 mmol, 1.0 eq.), **2a** (0.24 mmol, 1.2 eq.),  $[\text{Cp}^*\text{RhCl}_2]_2$  (0.01 mmol, 0.05 eq.), CsOPiv (0.2 mmol, 1.0 eq.), AcOH (0.2 mmol, 1.0 eq.) in diethylene glycol dimethyl ether (4.0 mL) was stirred at 80 °C for 2 h. Upon completion as indicated by TLC, the reaction mixture was poured into water (30 mL) and extracted

with ethyl acetate (10 mL  $\times$  3). The combined organic layer was washed with brine (10 mL  $\times$  3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtrated and concentrated under vacuum. The residue was purified by column chromatography (PE/EA=1/1, v/v) to afford **5aa**.

## V. Gram-scale preparations and conversions

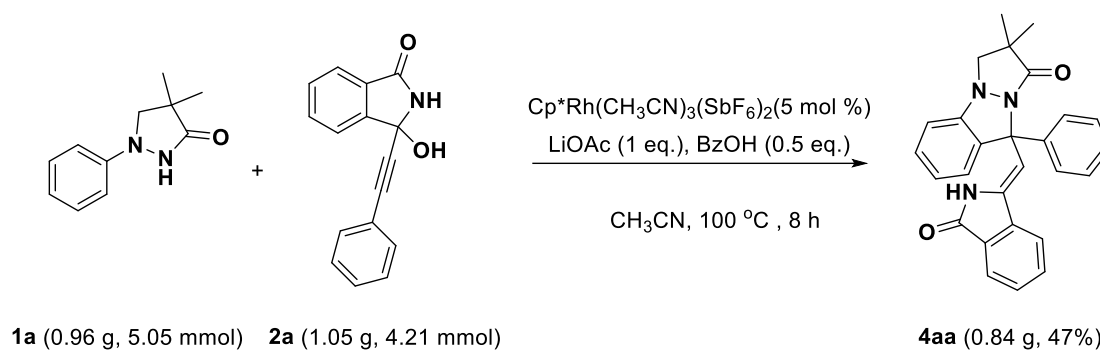
### (1) Gram-scale preparation

#### (a) Gram-scale preparation for 3aa



A suspension of **1a** (910 mg, 4.8 mmol), **2a** (1 g, 4.0 mmol), AuCl(IPr) (124.2 mg, 5 mol %) was combined in DCE (10 mL) was stirred at 70 °C for 4 h. Upon completion as indicated by TLC, the reaction mixture was poured into water (30 mL) and extracted with ethyl acetate (10 mL  $\times$  3). The combined organic layer was washed with brine (10 mL  $\times$  3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtrated and concentrated under vacuum. The residue was purified by column chromatography (PE/EA=1/1, v/v) to afford **3aa** as white solid (1.03 g, 61% yield).

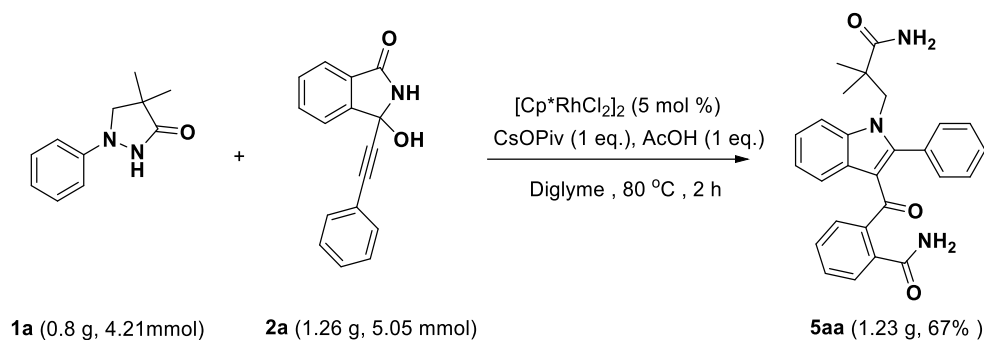
#### (b) Gram-scale preparation for 4aa



A suspension of **1a** (960 mg, 5.05 mmol), **2a** (1.05 g, 4.21 mmol), Cp\*Rh(CH<sub>3</sub>CN)<sub>3</sub>(SbF<sub>6</sub>)<sub>2</sub> (176.2 mg, 5 mol %), LiOAc (277.2 mg, 4.21 mmol), benzoic acid (256.2 mg, 2.1 mmol) in MeCN (10 mL) was stirred at 100 °C for 8 h. Upon completion as indicated by TLC, the reaction mixture was poured into water (50 mL) and extracted with ethyl acetate (30 mL  $\times$  3). The combined organic layer was washed with brine (20 mL  $\times$  3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtrated and concentrated under

vacuum. The residue was purified by column chromatography (PE/EA=1/1, v/v) to afford **4aa** as yellow oil (0.84 g, 47% yield).

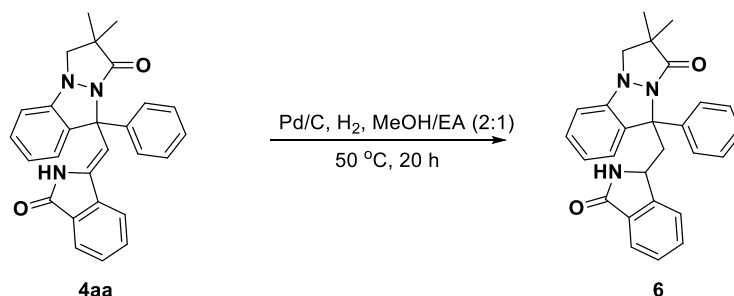
### (c) Gram-scale preparation for **5aa**



A suspension of **1a** (800 mg, 4.21 mmol), **2a** (1.26 g, 5.05 mmol),  $[\text{Cp}^*\text{RhCl}_2]_2$  (131.6 mg, 5 mol %), CsOPiv (982.8 mg, 4.21 mmol), HOAc (152 mg, 4.21 mmol) in diethylene glycol dimethyl ether (10 mL) was stirred at 80 °C for 2 h. Upon completion as indicated by TLC, the reaction was poured into water (50 mL) and extracted with ethyl acetate (30 mL  $\times$  3). The combined organic layer was washed with brine (20 mL  $\times$  3), dried over anhydrous  $\text{Na}_2\text{SO}_4$ , filtrated and concentrated under vacuum. The residue was purified by column chromatography (PE/EA = 1:1, v/v) to afford **5aa** as yellowish solid (1.23 g, 67% yield).

## (2) Conversions of **4aa** and **5aa**

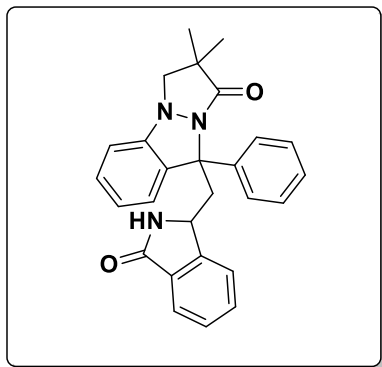
### (a) Procedure and Characterization of Compound **6**:



The 10 mol % Pd/C (10 mg) was added to a solution of **4aa** (100 mg, 0.24 mmol) in MeOH/EtOAc (v/v=2/1, 20 mL) under the hydrogen environment. The resulting

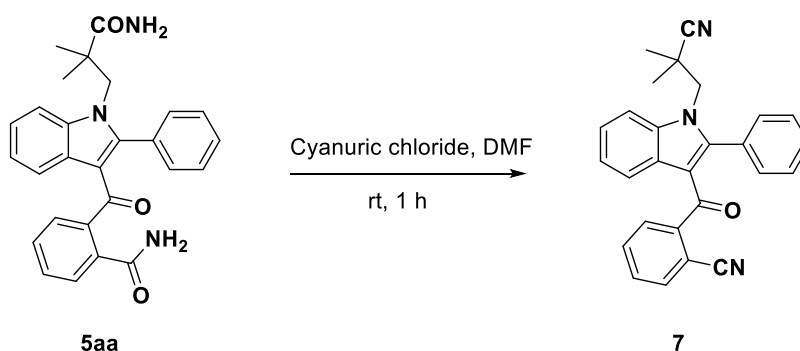
mixture was stirred at 50°C for 20 h. Upon completion as indicated by TLC, the mixture was filtered by suction and the filtrate was extracted with ethyl acetate (30 mL×3) and concentrated in vacuo. The residue was purified by column chromatography (PE/EA=1/1, v/v) to afford **6** as white solid (80 mg, 80% yield).

**(6) 2,2-dimethyl-9-((3-oxoisindolin-1-yl)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



**<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 7.83 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.60 – 7.51 (m, 1H), 7.49 – 7.42 (m, 4H), 7.42 – 7.30 (m, 5H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.20 – 7.14 (m, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 6.72 (s, 1H), 4.71 – 4.63 (m, 1H), 3.69 (d, *J* = 8.5 Hz, 1H), 3.54 (d, *J* = 8.5 Hz, 1H), 3.12 – 2.98 (m, 2H), 1.42 (d, *J* = 7.6 Hz, 6H). **<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, Chloroform-*d*)** δ 170.80, 170.05, 147.59, 147.16, 140.55, 133.40, 131.87, 129.57, 128.79, 128.34, 128.27, 126.47, 123.82, 123.61, 123.31, 122.42, 110.50, 70.40, 63.91, 54.25, 45.89, 43.69, 22.94, 22.90. **HRMS (ESI) *m/z***: calculated for C<sub>27</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub> [*M* + *H*]<sup>+</sup>: 424.2022, found: 424.2020.

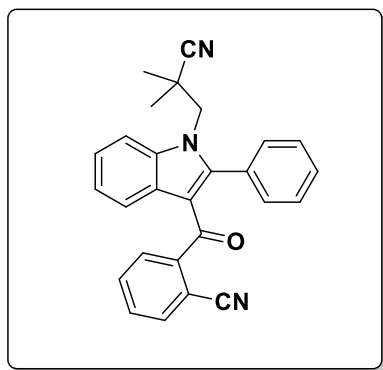
**(b) Procedure and Characterization of Compound 7:**



The solution of **5aa** (88 mg, 0.2 mmol) and cyanuric chloride (74 mg, 0.4 mmol) in DMF (3 mL) was stirred at room temperature for 1 h. Upon completion as indicated by TLC, the reaction mixture was quenched with water (30 mL), extracted with ethyl

acetate (15 mL × 3), washed with brine (15 mL × 3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum. The crude product was purified by column chromatography (PE/EA=2/1, v/v) to afford **7** as yellow oil (68 mg, 84% yield).

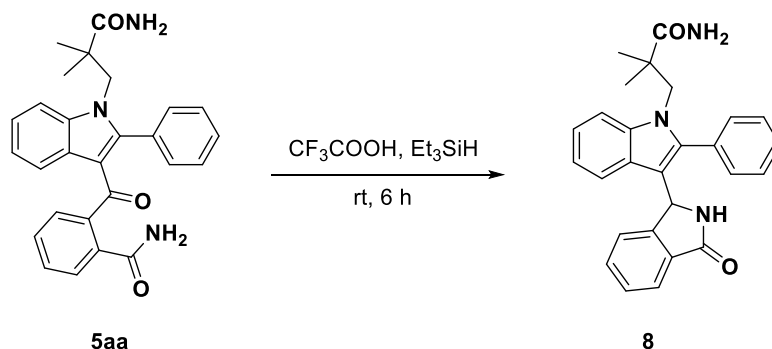
**(7) 2-(1-(2-cyano-2-methylpropyl)-2-phenyl-1*H*-indole-3-carbonyl)benzonitrile**



**<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)** δ 8.27 – 8.19 (m, 1H), 7.71 – 7.64 (m, 1H), 7.47 – 7.21 (m, 11H), 4.49 (s, 2H), 1.12 (s, 6H). **<sup>13</sup>C NMR (126 MHz, Chloroform-*d*)** δ 188.86, 146.07, 143.19, 136.06, 131.94, 130.74, 128.85, 128.54, 128.37, 128.30, 127.28, 123.14, 122.64, 122.41, 121.09, 116.31, 115.27, 110.52, 109.95, 49.42, 33.23, 24.68. **HRMS**

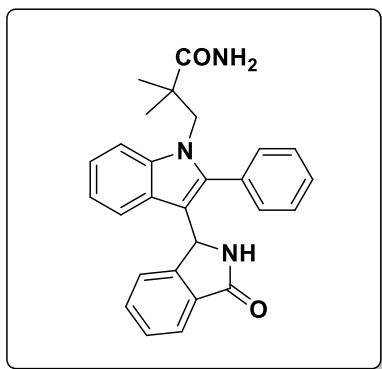
**(ESI) m/z:** calculated for C<sub>27</sub>H<sub>22</sub>N<sub>3</sub>O [M + H]<sup>+</sup>:404.1759, found: 404.1757.

**(c) Procedure and Characterization of Compound 8:**



The mixture of **5aa** (88 mg, 0.2 mmol), trifluoroacetic acid (2 mL) and triethylsilane (3 mL) was stirred at room temperature for 6 h. Upon completion as indicated by TLC, the mixture was quenched with 10 mL of saturated sodium carbonate solution, extracted with ethyl acetate (15 mL × 3), washed with brine (15 mL × 3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated under vacuum. The residue was purified by column chromatography (PE/EA=1/1, v/v) to afford **8** as yellow oil (59 mg, 70% yield).

**(8) 2,2-dimethyl-3-(3-(3-oxoisindolin-1-yl)-2-phenyl-1*H*-indol-1-yl)propanamide**



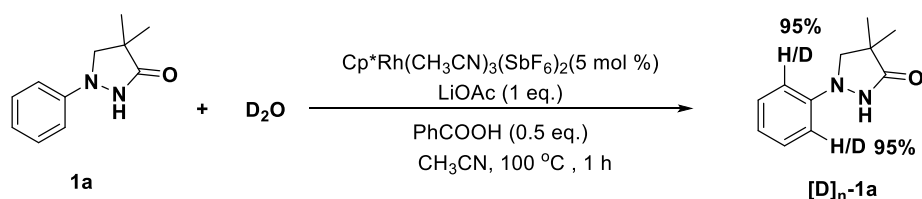
**$^1\text{H}$  NMR (400 MHz, Methanol- $d_4$ )**  $\delta$  7.91 – 7.82 (m, 1H), 7.64 – 7.49 (m, 8H), 7.29 – 7.20 (m, 1H), 7.12 – 7.03 (m, 1H), 6.78 (t,  $J$  = 7.5 Hz, 1H), 6.61 (s, 1H), 5.72 (s, 1H), 4.50 (d,  $J$  = 2.9 Hz, 2H), 0.90 (d,  $J$  = 2.1 Hz, 6H).  **$^{13}\text{C}$  NMR (126 MHz, Methanol- $d_4$ )**  $\delta$  180.15, 148.12, 140.59, 137.43, 131.57, 131.29, 130.92, 130.61, 128.08, 128.00, 127.46, 122.76, 122.28, 121.19, 118.95,

117.80, 110.86, 108.42, 54.18, 50.20, 43.77, 22.94, 22.81. **HRMS (EI)  $m/z$** : calculated for  $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_3$ : 423.1941, found: 423.1939.

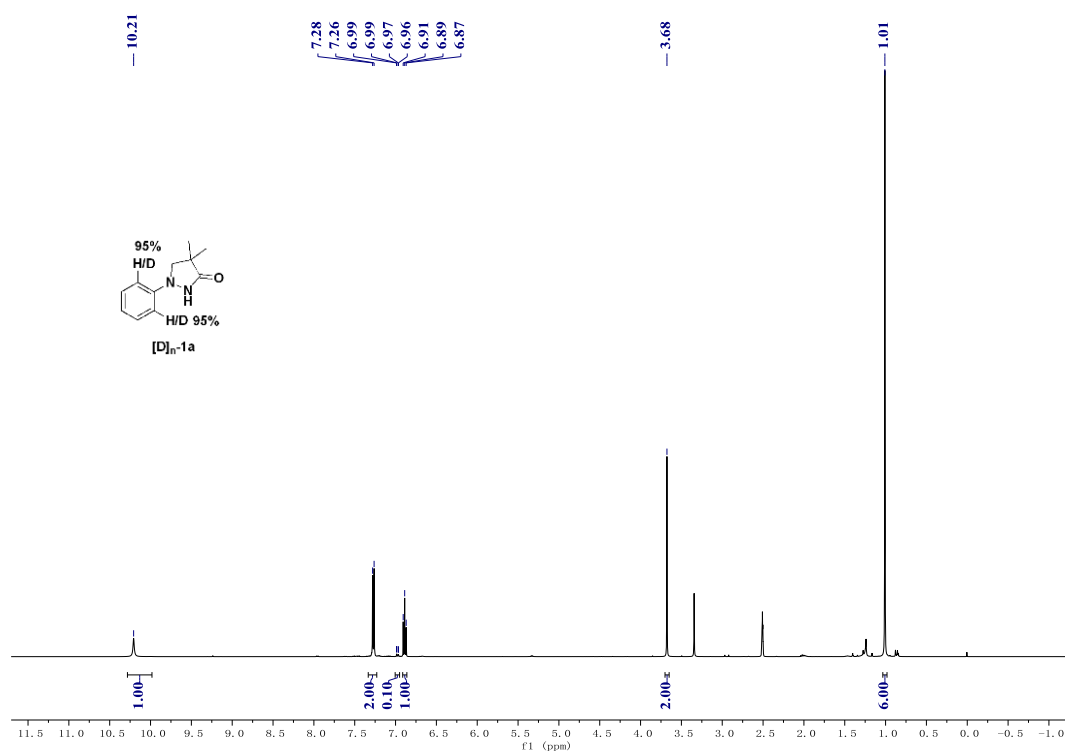
## VI. Mechanistic studies

### (1) H/D exchange experiment

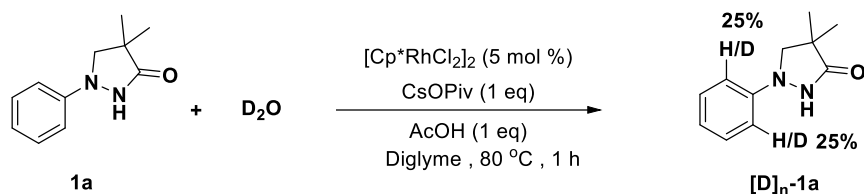
#### (a) H/D exchange experiment of 4aa



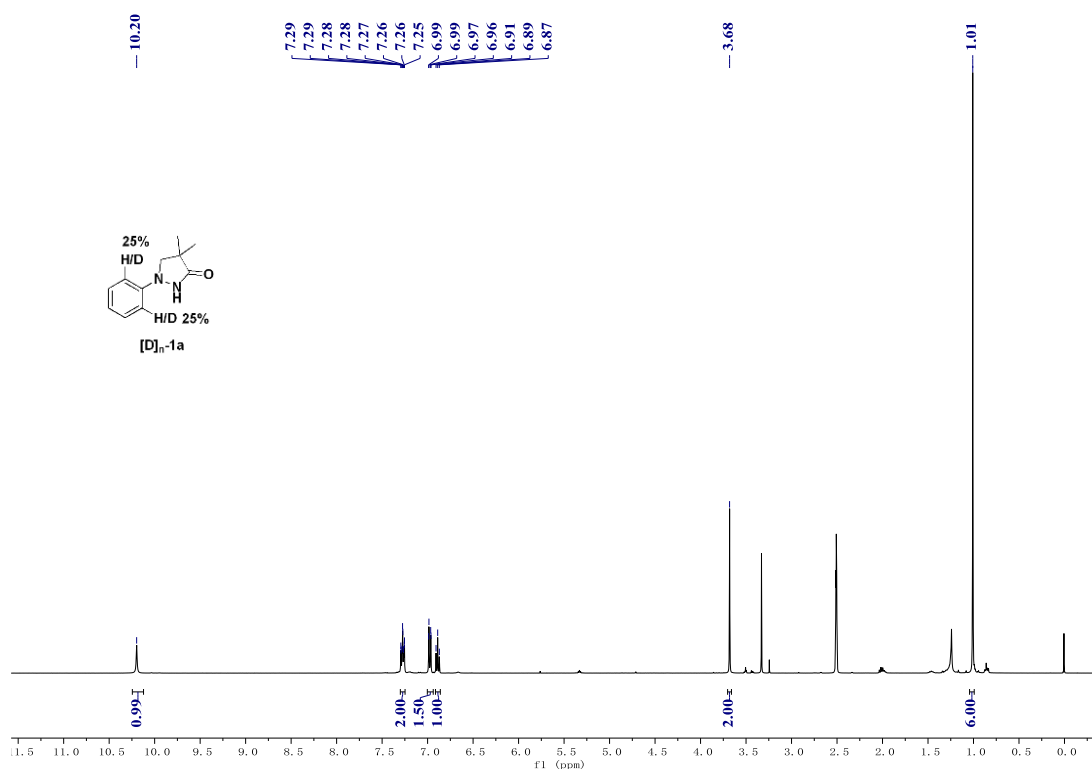
A pressure tube was charged with 4,4-Dimethyl-1-phenylpyrazolidine-3-one (**1a**, 57 mg, 0.3 mmol) and  $\text{D}_2\text{O}$  (0.3 ml),  $\text{Cp}^*\text{Rh}(\text{CH}_3\text{CN})_3(\text{SbF}_6)_2$  (12.4 mg, 5 mol %), LiOAc (19.8 mg, 0.3 mmol), benzoic acid (18.3 mg, 0.15 mmol) and MeCN (3 mL). The reaction mixture was stirred at 100 °C for 1 h. After that, the solvent was removed under vacuum and the resulting residue was purified by column chromatography (PE/EA=3/1, v/v) to afford the deuterium product [**D**]<sub>n</sub>-**1a**. The H/D exchange as follows figure.



**(b) H/D exchange experiment of 5aa**

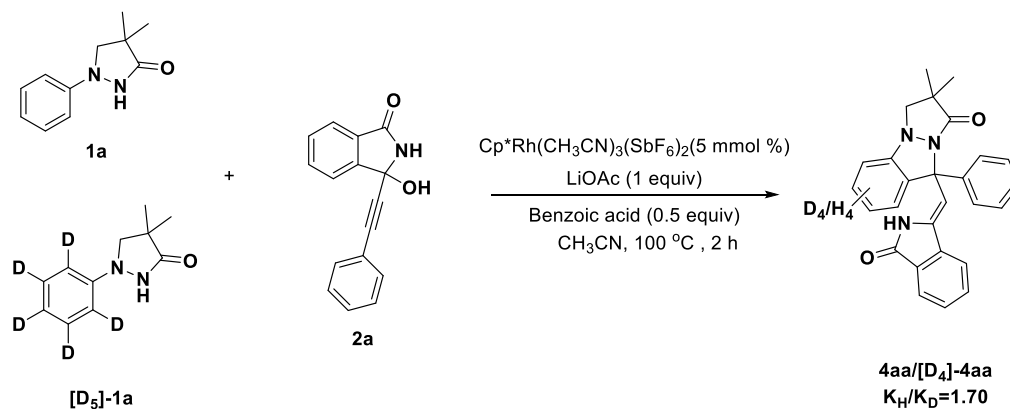


A pressure tube was charged with 4,4-dimethyl-1-phenylpyrazolidine-3-one (**1a**, 57 mg, 0.3 mmol) and D<sub>2</sub>O (0.3 ml), [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (9.3 mg, 5 mol %), CsOPiv (70.2 mg, 0.3 mmol), HOAc (7.5 mg, 0.15 mmol) and diethylene glycol dimethyl ether (3 mL). The reaction mixture was stirred at 80 °C for 1h. After that, the solvent was removed under vacuum and the residue was purified by column chromatography (PE/EA=3/1, v/v) to afford the deuterium product **[D]<sub>n</sub>-1a**. The H/D exchange as follows figure.



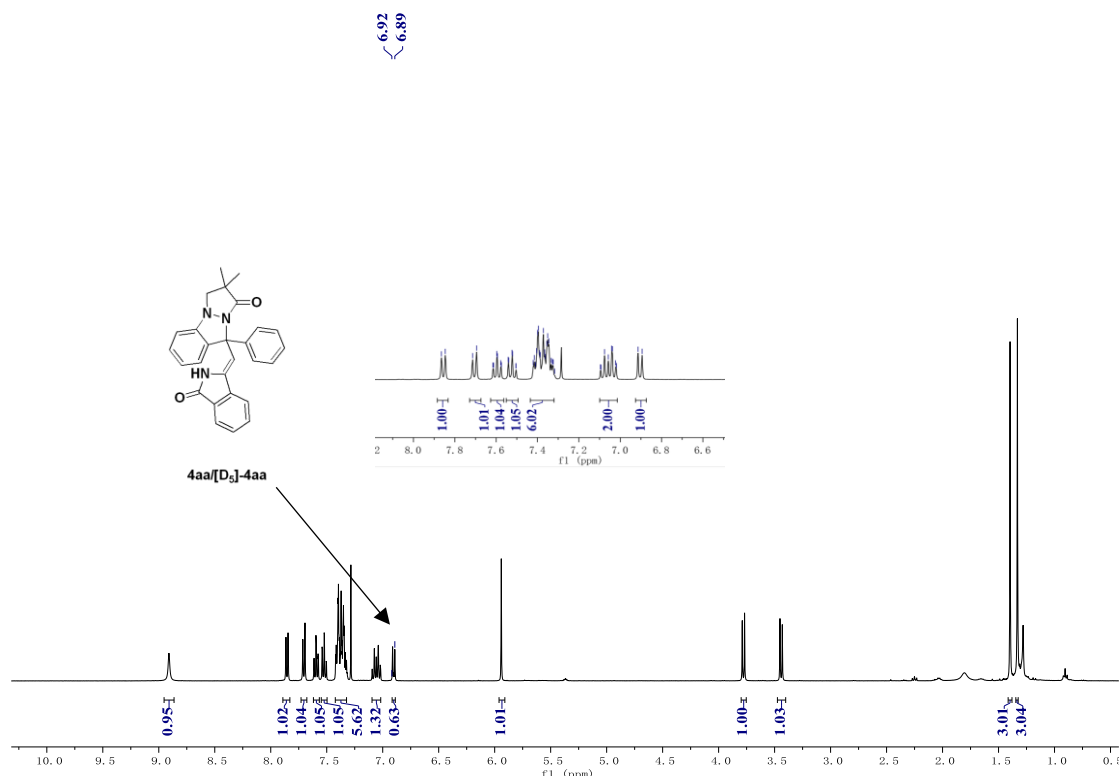
## (2) Kinetic isotope effect

### (a) KIE Experiments of **4aa**

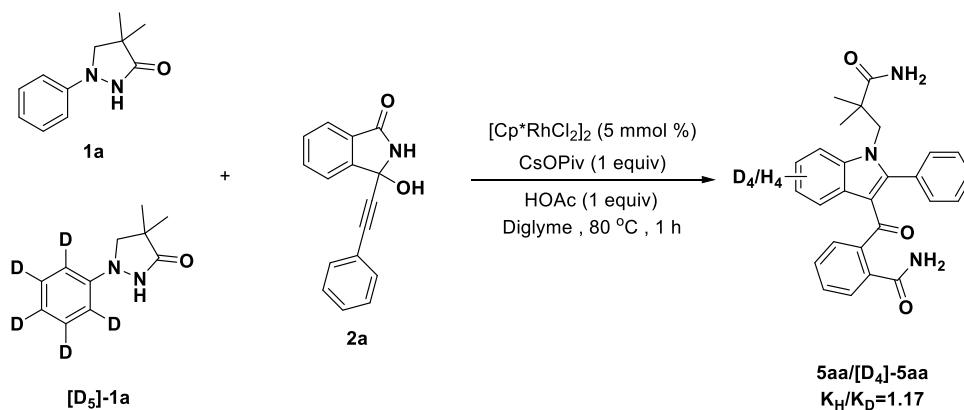


To a reaction tube were added **1a** (38 mg, 0.2 mmol), **[D<sub>5</sub>]-1a** (37 mg, 0.2 mmol), **2a** (24.9 mg, 0.2 mmol),  $\text{Cp}^*\text{Rh}(\text{CH}_3\text{CN})_3(\text{SbF}_6)_2$  (8.4 mg, 5 mol %), LiOAc (23.2 mg, 0.2 mmol), benzoic acid (12.2 mg, 0.1 mmol) and MeCN (4 mL). The resulting mixture was stirred at 100 °C for 2 h. Upon completion as indicated by TLC, the solvent was removed under vacuum and the residue was purified by column chromatography (PE/EA=1/1, v/v) to obtain a mixture of **4aa** and **[D<sub>4</sub>]-4aa**. According to the integral

value of characteristic peak in  $^1\text{H}$  NMR and the ratio of products **4aa** and **[D<sub>4</sub>]-4aa** was calculated. The ratio of **4aa**/**[D<sub>4</sub>]-4aa** was 1.70.

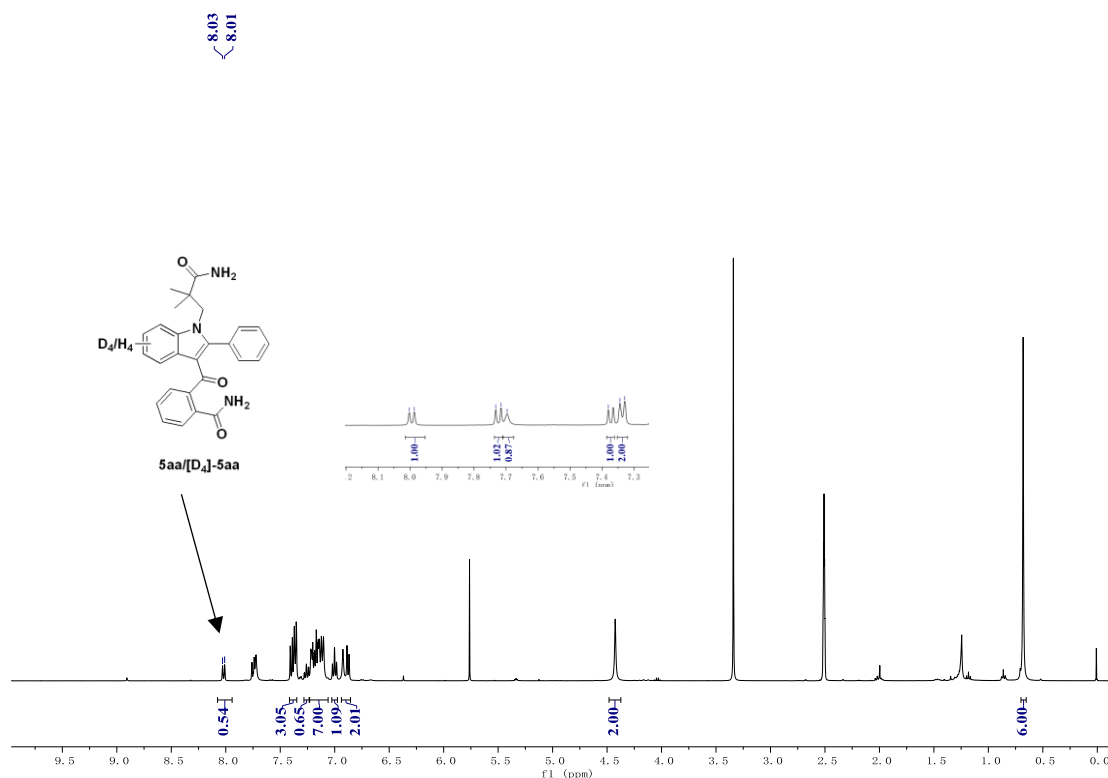


## (b) KIE Experiments of **5aa**

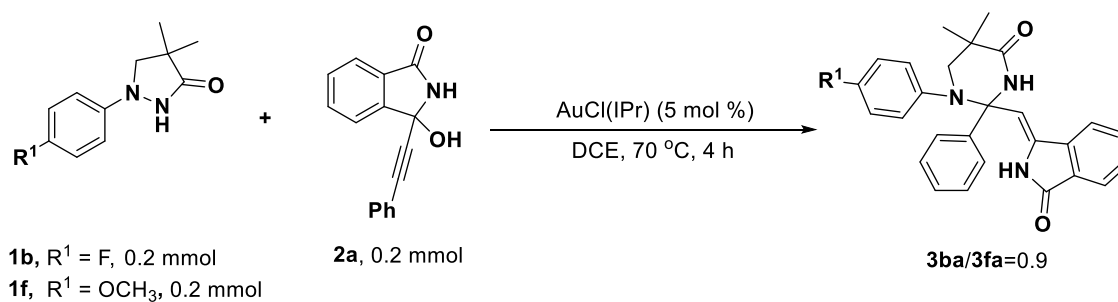


To a reaction tube were added **1a** (38 mg, 0.2 mmol), **[D<sub>5</sub>]-1a** (37 mg, 0.2 mmol), **2a** (24.9 mg, 0.1 mmol),  $[\text{Cp}^*\text{RhCl}_2]_2$  (6.28 mg, 5 mol %), CsOPiv (46.8 mg, 0.2 mmol), AcOH (12.0 mg, 0.2 mmol) and diglyme (4 mL). The resulting mixture was stirred at 80 °C for 1 h. Upon completion as indicated by TLC, the solvent was removed under vacuum and the residue was purified by column chromatography (PE/EA = 1/1, v/v) to obtain a mixture of **5aa** and **[D<sub>4</sub>]-5aa**. According to the integral value of characteristic

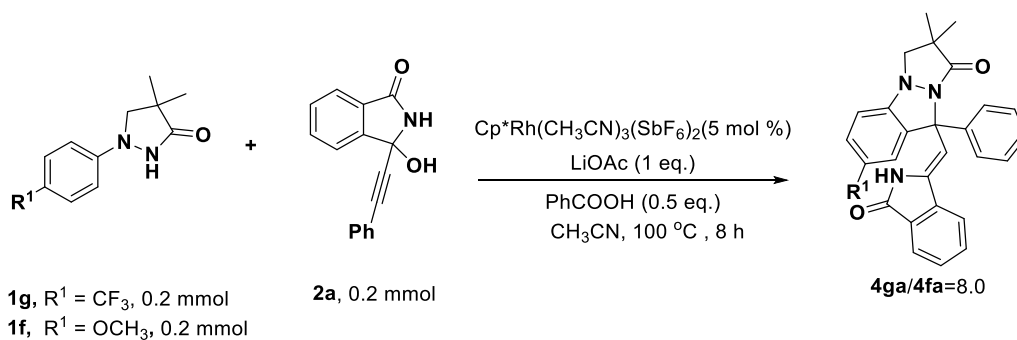
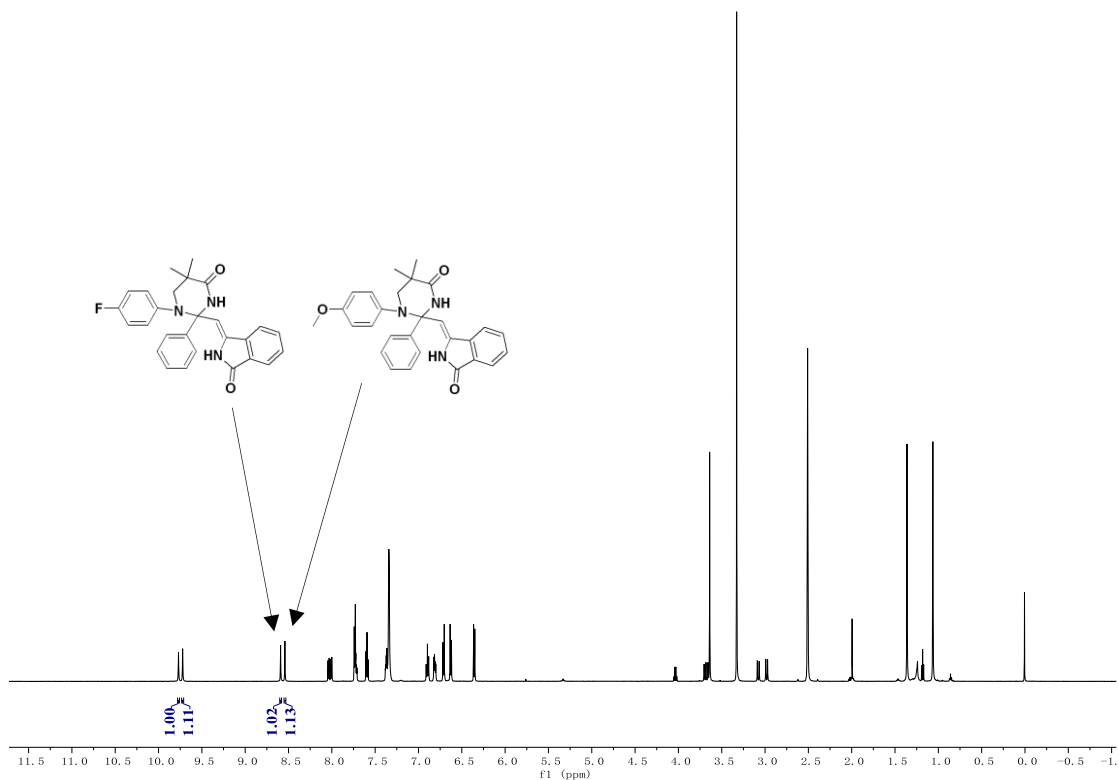
peak in  $^1\text{H}$  NMR and the ratio of products **5aa** and **[D<sub>4</sub>]-5aa** was calculated. The ratio of **5aa**/ **[D<sub>4</sub>]-5aa** was 1.17.



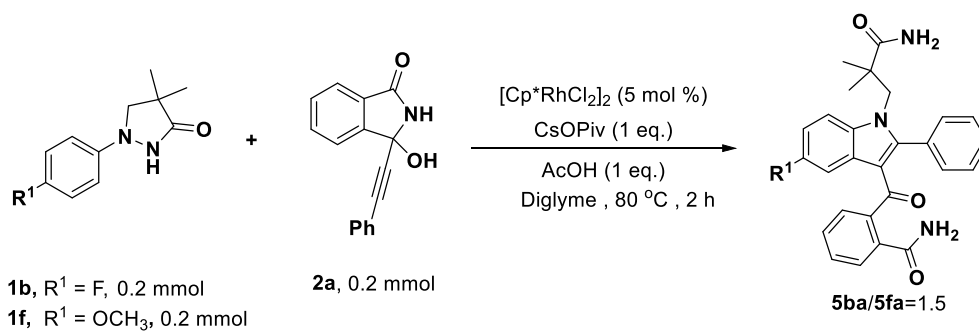
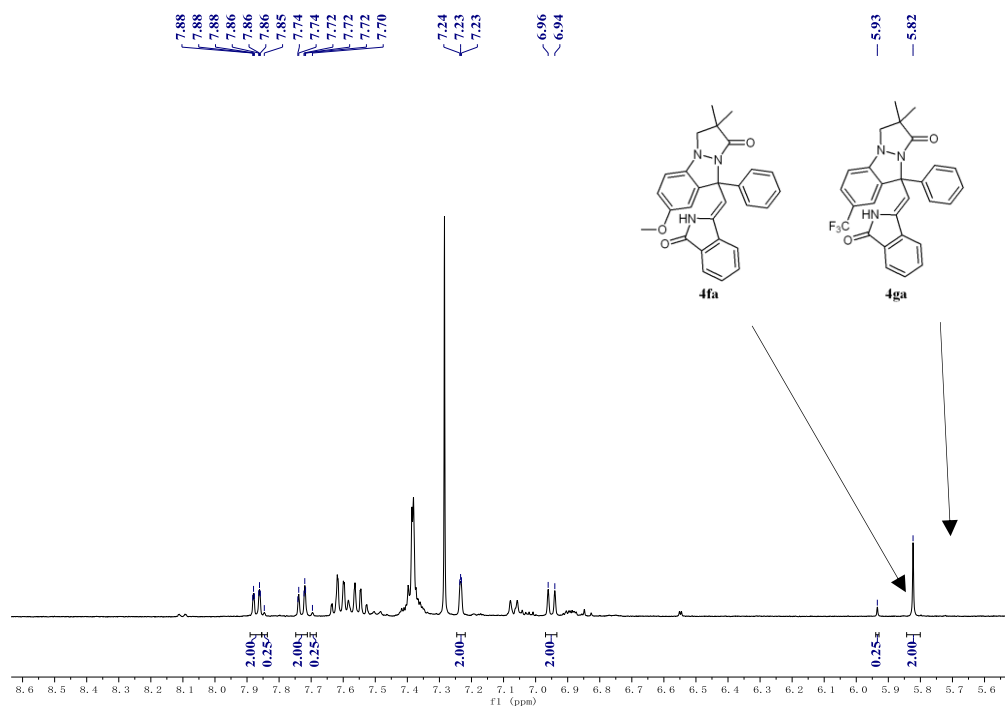
### (3) Competition experiment



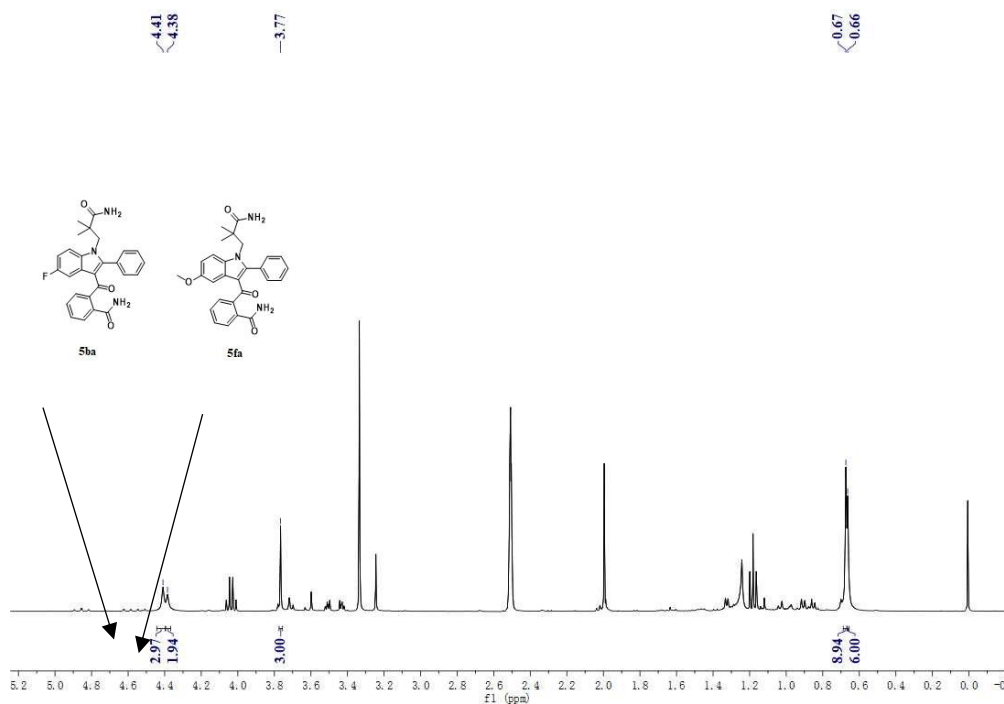
To a reaction tube were added **1b** (42 mg, 0.2 mmol), **1f** (44 mg, 0.2 mmol), **2a** (49.8 mg, 0.2 mmol),  $\text{AuCl(IPr)}$  (6.2 mg, 5 mol%) and DCE (4 mL). The mixture was stirred at 70 °C for 4 h. Upon completion as indicated by TLC,, the solvent was removed under vacuum and the resulting residue was purified by column chromatography (PE/EA=1/1, v/v) to obtain a mixture of **3ba** and **3fa**. The ratio of **3ba/3fa** was 0.90 based on  $^1\text{H}$  NMR.



To a reaction tube equipped were added **1g** (52 mg, 0.2 mmol), **1f** (44 mg, 0.2 mmol), **2a** (49.8 mg, 0.2 mmol),  $\text{Cp}^*\text{Rh}(\text{CH}_3\text{CN})_3(\text{SbF}_6)_2$  (8.39 mg, 5 mol %),  $\text{LiOAc}$  (13.2 mg, 0.2 mmol), benzoic acid (12.2 mg, 0.1 mmol) and  $\text{MeCN}$  (4 mL). The reaction mixture was stirred at 100 °C for 8 h. Upon completion as indicated by TLC, the solvent was removed under vacuum and the residue was purified by column chromatography (PE/EA=1/1, v/v) to obtain a mixture of **4ga** and **4fa**. The ratio of **4ga/4fa** was 8.0 based on  $^1\text{H}$  NMR.

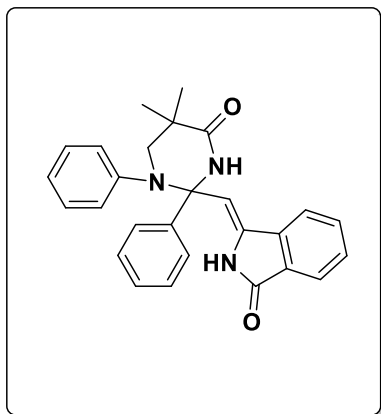


To a reaction tube were added **1b** (42 mg, 0.2 mmol), **1f** (44 mg, 0.2 mmol), **2a** (49.8 mg, 0.2 mmol), Cy-[Cp\*RhCl<sub>2</sub>]<sub>2</sub> (6.28 mg, 5 mol %), CsOPiv (46.8 mg, 0.2 mmol), HOAc (12 mg, 0.2 mmol) and diglyme (4 mL). The reaction mixture was stirred at 80 °C (oil bath) for 2 h. Upon completion as indicated by TLC, the solvent was removed under vacuum and the residue was purified by column chromatography (PE/EA=1/1, v/v) to obtain a mixture of **5ba** and **5fa**. The ratio of **5ba/5fa** was 1.5 based on <sup>1</sup>H NMR.



## VII. Characterization of the products

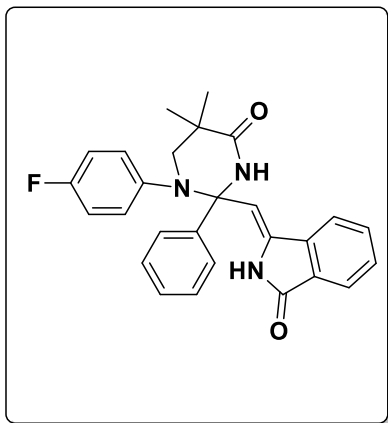
**(3aa)**                      **(Z/E)-3-((5,5-dimethyl-4-oxo-1,2-diphenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 61 mg, yield: 65%. <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 9.85 (s, 1H), 8.56 (s, 1H), 8.02 – 7.92 (m, 1H), 7.78 – 7.67 (m, 2H), 7.58 (td, *J* = 7.4, 0.7 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.32 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.05 (dd, *J* = 8.5, 7.2 Hz, 2H), 6.89 (t, *J* = 7.3 Hz, 1H), 6.82 – 6.71 (m, 2H), 6.35 (s, 1H), 3.71 (d, *J* = 13.0 Hz, 1H), 3.19 (d, *J* = 13.0 Hz,

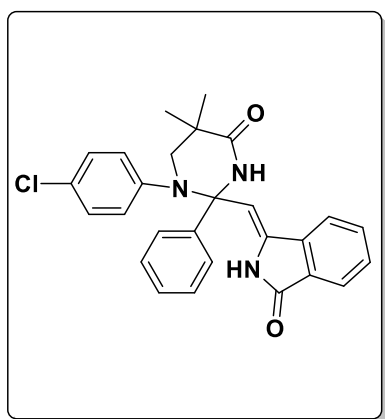
1H), 1.38 (s, 3H), 1.05 (s, 3H). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>) δ 174.9, 168.2, 147.5, 142.0, 136.1, 132.5, 129.7, 128.6, 128.2, 128.2, 128.0, 128.0, 124.8, 123.0, 122.7, 120.6, 106.2, 77.6, 58.9, 25.9, 23.4. HRMS (ESI) *m/z*: calculated for C<sub>27</sub>H<sub>24</sub>N<sub>3</sub>O<sub>2</sub> [M- H]<sup>-</sup>: 422.1874, found:422.1879.

**(3ba)** **(Z/E)-3-((1-(4-fluorophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl) methylene)isoindolin-1-one**



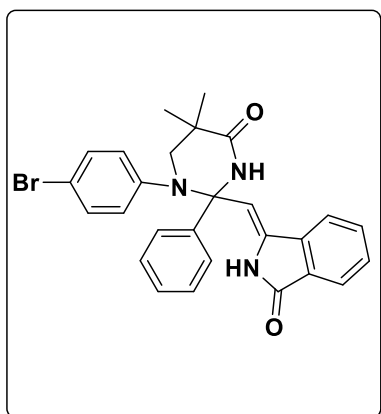
Following by general procedure for the synthesis of **3aa**. White solid, 56 mg, yield: 64%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.80 (s, 1H), 8.60 (s, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.40 – 7.30 (m, 5H), 6.94 – 6.85 (m, 2H), 6.85 – 6.77 (m, 2H), 6.36 (s, 1H), 3.70 (d, *J* = 12.8 Hz, 1H), 3.08 (d, *J* = 12.9 Hz, 1H), 1.36 (s, 3H), 1.06 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)** δ 175.0, 175.0, 168.2, 168.0, 158.5 (d, *J* = 240.9 Hz), 143.8, 141.8, 141.8, 137.7, 137.6, 136.0, 135.9, 132.5, 129.7, 128.8, 128.3, 128.2, 128.0, 127.4 (d, *J* = 8.1 Hz), 122.7, 120.7, 114.6 (d, *J* = 22.1 Hz), 105.9, 105.8, 77.6, 77.5, 59.0, 26.0, 23.4, 23.4. **HRMS (ESI) m/z**: calculated for C<sub>27</sub>H<sub>23</sub>FN<sub>3</sub>O<sub>2</sub> [M- H]<sup>-</sup>:440.1780, found: 440.1783.

**(3ca)** **(Z/E)-3-((1-(4-chlorophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



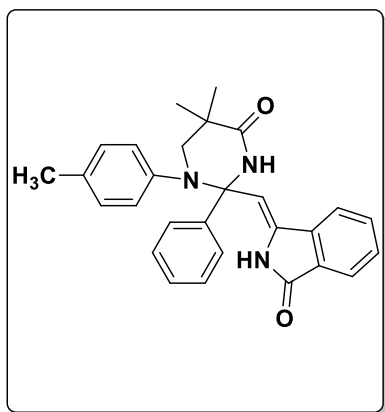
Following by general procedure for the synthesis of **3aa**. White solid, 42 mg, yield: 46%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.88 (s, 1H), 8.60 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.77 – 7.67 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 – 7.37 (m, 2H), 7.38 – 7.31 (m, 3H), 7.14 – 7.07 (m, 2H), 6.86 – 6.75 (m, 2H), 6.32 (s, 1H), 3.71 (d, *J* = 13.1 Hz, 1H), 3.20 (d, *J* = 13.1 Hz, 1H), 1.37 (s, 3H), 1.05 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, DMSO-*d*<sub>6</sub>)** δ 175.3, 168.7, 146.8, 142.2, 138.1, 136.6, 133.0, 130.2, 129.2, 128.8, 128.5, 128.4, 128.3, 127.4, 126.8, 123.1, 121.2, 106.4, 78.0, 59.3, 26.3, 23.8. **HRMS (ESI) m/z**: calculated for C<sub>27</sub>H<sub>23</sub>ClN<sub>3</sub>O<sub>2</sub> [M- H]<sup>-</sup>:456.1484, found: 456.1487.

**(3da) (Z/E)-3-((1-(4-bromophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



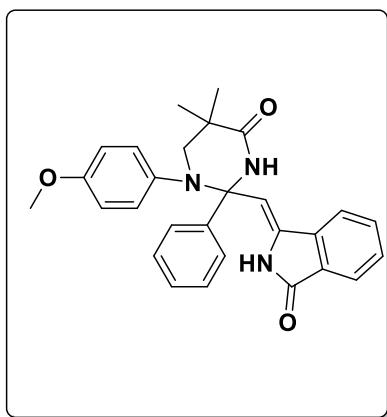
Following by general procedure for the synthesis of **3aa**. White solid, 36 mg, yield: 36%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.89 (s, 1H), 8.60 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.78 – 7.67 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.46 – 7.29 (m, 5H), 7.25 – 7.17 (m, 2H), 6.79 – 6.71 (m, 2H), 6.32 (s, 1H), 3.71 (d, *J* = 13.1 Hz, 1H), 3.21 (d, *J* = 13.1 Hz, 1H), 1.37 (s, 3H), 1.05 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, DMSO-*d*<sub>6</sub>)** δ 175.2, 168.7, 147.3, 142.2, 138.1, 136.7, 133.0, 131.2, 130.2, 129.2, 128.8, 128.5, 128.4, 127.0, 123.1, 121.3, 115.4, 106.4, 77.9, 59.3, 26.3, 23.8. **HRMS (ESI) *m/z***: calculated for C<sub>27</sub>H<sub>23</sub>BrN<sub>3</sub>O<sub>2</sub> [*M* - H]<sup>-</sup>: 500.0979, found: 500.0981.

**(3ea) (Z/E)-3-((5,5-dimethyl-4-oxo-2-phenyl-1-(*p*-tolyl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



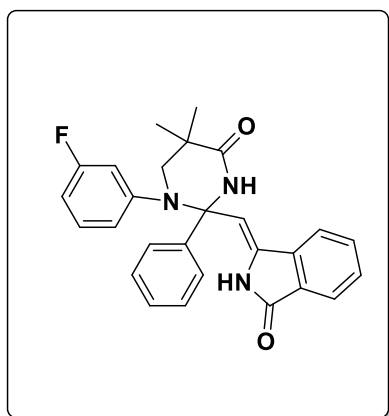
Following by general procedure for the synthesis of **3aa**. White solid, 52 mg, yield: 60%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.83 (s, 1H), 8.56 (s, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.77 – 7.68 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.42 – 7.29 (m, 5H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.66 (d, *J* = 8.1 Hz, 2H), 6.34 (s, 1H), 3.68 (d, *J* = 12.9 Hz, 1H), 3.09 (d, *J* = 12.8 Hz, 1H), 2.14 (s, 3H), 1.37 (s, 3H), 1.05 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)** δ 175.0, 168.2, 144.9, 142.11, 137.7, 136.0, 136.0, 132.5, 132.3, 129.7, 128.6, 128.5, 128.3, 128.1, 128.0, 125.2, 122.7, 120.6, 106.1, 77.6, 77.5, 59.0, 25.9, 23.4, 23.4, 20.2. **HRMS (ESI) *m/z***: calculated for C<sub>28</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub> [*M* - H]<sup>-</sup>: 436.2031, found: 436.2035.

**(3fa) (Z/E)-3-((1-(4-methoxyphenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 36 mg, yield: 41%. **<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)** δ 9.71 (s, 1H), 8.54 (s, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.34 (d, *J* = 2.1 Hz, 5H), 6.71 (d, *J* = 8.9 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 6.36 (s, 1H), 3.66 (s, 1H), 3.64 (s, 3H), 2.98 (d, *J* = 12.6 Hz, 1H), 1.36 (s, 3H), 1.06 (s, 3H). **<sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>)** δ 175.0, 168.1, 155.7, 142.0, 140.3, 137.7, 135.8, 132.5, 129.6, 128.6, 128.3, 128.0, 127.2, 122.7, 120.6, 113.1, 106.0, 77.7, 59.0, 55.0, 26.0, 23.5. **HRMS (ESI) *m/z***: calculated for C<sub>28</sub>H<sub>26</sub>N<sub>3</sub>O<sub>3</sub> [*M* - *H*]<sup>-</sup>: 452.1980, found: 452.1979. HPLC purity: 92.4%; *t<sub>R</sub>* = 2.728 min, MeOH-H<sub>2</sub>O (80:20).

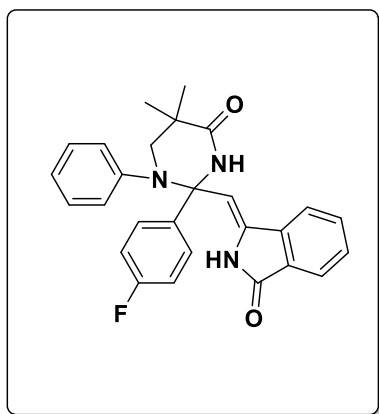
**(3ia) (Z/E)-3-((1-(3-fluorophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 22 mg, yield: 25%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.95 (s, 1H), 8.60 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 1H), 7.78 – 7.68 (m, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.40 – 7.31 (m, 3H), 7.09 (q, *J* = 7.9 Hz, 1H), 6.74 – 6.62 (m, 2H), 6.51 (dt, *J* = 12.1, 2.4 Hz, 1H), 6.33 (s, 1H), 3.74 (d, *J* = 13.3 Hz, 1H), 3.31 (d, *J* = 16.2 Hz, 3H), 1.38 (s, 3H), 1.06 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)** δ 174.7, 174.7, 168.3, 161.7 (d, *J* = 241.9 Hz), 149.4 (d, *J* = 9.6 Hz), 141.7, 137.7, 136.3, 132.5, 129.8, 129.3 (d, *J* = 9.8 Hz), 128.8, 128.4, 128.0, 122.7, 120.8, 119.9, 111.0 (d, *J* = 23.6 Hz), 109.1 (d, *J* = 20.9 Hz),

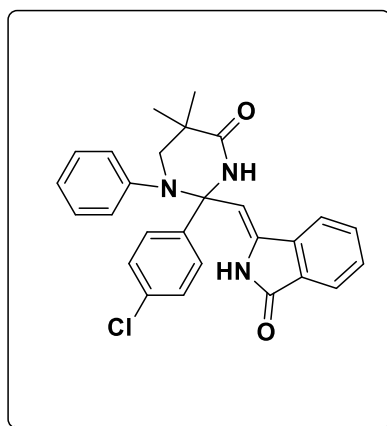
106.0, 77.5, 77.5, 58.7, 25.7, 23.2, 23.2. **HRMS (ESI) m/z**: calculated for C<sub>27</sub>H<sub>23</sub>FN<sub>3</sub>O<sub>2</sub> [M- H]<sup>-</sup>:440.1780, found:440.1783.

**(3ab) (Z/E)-3-((2-(4-fluorophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 51 mg, yield: 58%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.89 (s, 1H), 8.58 (s, 1H), 8.02 (d, *J* = 7.7 Hz, 1H), 7.80 – 7.68 (m, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 6.9 Hz, 2H), 7.12 (dt, *J* = 22.8, 8.1 Hz, 4H), 6.92 (t, *J* = 7.1 Hz, 1H), 6.80 (d, *J* = 7.9 Hz, 2H), 6.39 (s, 1H), 3.74 (d, *J* = 13.0 Hz, 1H), 3.18 (d, *J* = 13.3 Hz, 1H), 1.40 (s, 3H), 1.06 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)** δ 175.3, 175.3, 168.7, 168.6, 162.4 (d, *J* = 245.3 Hz), 147.8, 138.6, 138.1, 136.8, 133.0, 131.0 (d, *J* = 8.6 Hz), 130.2, 128.6, 128.5, 125.5, 123.6, 123.2, 121.2, 115.4 (d, *J* = 21.5 Hz), 106.3, 77.5, 77.5, 59.4, 26.3, 23.7. **HRMS (ESI) m/z**: calculated for C<sub>27</sub>H<sub>23</sub>FN<sub>3</sub>O<sub>2</sub> [M- H]<sup>-</sup>:440.1780, found:440.1782.

**(3ac) (Z/E)-3-((2-(4-chlorophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**

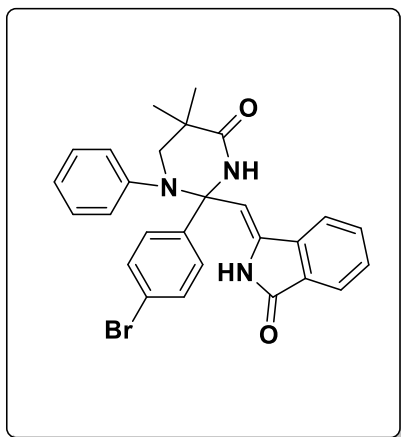


Following by general procedure for the synthesis of **3aa**. White solid, 63 mg, yield: 70%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.88 (s, 1H), 8.58 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.80 – 7.69 (m, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.40 (s, 4H), 7.17 – 7.05 (m, 2H), 6.92 (t, *J* = 7.3 Hz, 1H), 6.87 – 6.78 (m, 2H), 6.38 (s, 1H), 3.73 (d, *J* = 13.1 Hz, 1H), 3.20 (d, *J* = 13.1 Hz, 1H), 1.39 (s, 3H), 1.06 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)** δ 175.3, 168.7, 147.7, 141.4, 141.3, 138.0, 136.8, 133.6, 133.0, 130.6, 130.2,

128.7, 128.6, 128.4, 125.4, 123.6, 123.2, 121.2, 106.2, 77.5, 77.4, 59.4, 26.3, 23.7, 23.7.

**HRMS (ESI) m/z:** calculated for  $C_{27}H_{23}ClN_3O_2$   $[M - H]^-$ :456.1484, found:456.1489.

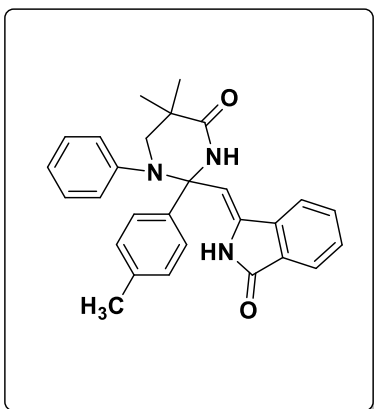
**(3ad) (Z/E)-3-((2-(4-bromophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 72 mg, yield: 72%.  **$^1H$  NMR (400 MHz, DMSO- $d_6$ )**  $\delta$  9.88 (s, 1H), 8.57 (s, 1H), 8.03 (d,  $J = 7.8$  Hz, 1H), 7.77 – 7.67 (m, 2H), 7.64 – 7.49 (m, 3H), 7.34 (d,  $J = 8.4$  Hz, 2H), 7.10 (t,  $J = 7.7$  Hz, 2H), 6.96 – 6.76 (m, 3H), 6.38 (s, 1H), 3.73 (d,  $J = 13.1$  Hz, 1H), 3.20 (d,  $J = 13.0$  Hz, 1H), 1.39 (s, 3H), 1.06 (s, 3H).  **$^{13}C\{^1H\}$  NMR (151 MHz, DMSO- $d_6$ )**

$\delta$  175.3, 175.2, 168.7, 147.7, 141.8, 141.8, 138.1, 133.0, 131.6, 131.0, 130.3, 128.7, 128.4, 125.3, 123.6, 123.2, 122.3, 121.2, 106.1, 77.6, 77.5, 59.5, 26.3, 26.3, 23.7, 23.7. **HRMS (ESI) m/z:** calculated for  $C_{27}H_{23}BrN_3O_2$   $[M - H]^-$ :500.0979, found:500.0984.

**(3ae) (Z/E)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(p-tolyl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one**

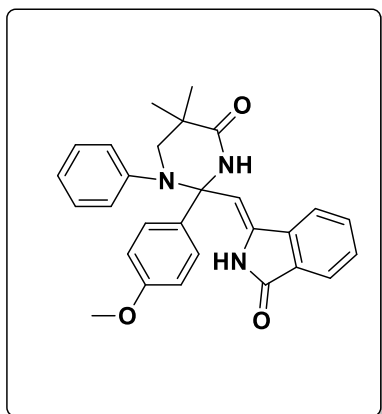


Following by general procedure for the synthesis of **3aa**. White solid, 46 mg, yield: 53%.  **$^1H$  NMR (400 MHz, DMSO- $d_6$ )**  $\delta$  9.85 (s, 1H), 8.53 (s, 1H), 7.99 (d,  $J = 7.8$  Hz, 1H), 7.77 – 7.67 (m, 2H), 7.59 (t,  $J = 7.4$  Hz, 1H), 7.27 (d,  $J = 8.1$  Hz, 2H), 7.13 (d,  $J = 8.0$  Hz, 2H), 7.07 (t,  $J = 7.7$  Hz, 2H), 6.89 (t,  $J = 7.3$  Hz, 1H), 6.81 (d,  $J = 8.0$  Hz, 2H), 6.35 (s, 1H), 3.70 (d,  $J = 13.0$  Hz, 1H), 3.19 (d,  $J = 13.0$  Hz, 1H), 2.29 (s, 3H), 1.37

(s, 3H), 1.05 (s, 3H).  **$^{13}C\{^1H\}$  NMR (126 MHz, DMSO- $d_6$ )**  $\delta$  175.3, 148.0, 138.3, 133.0,

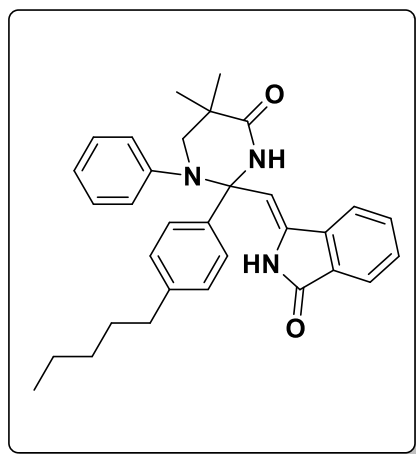
130.1, 129.2, 128.5, 128.4, 125.2, 123.3, 123.2, 121.1, 107.0, 77.8, 77.8, 59.4, 26.3, 26.3, 23.8, 23.8, 21.2. **HRMS (ESI) m/z**: calculated for C<sub>28</sub>H<sub>26</sub>N<sub>3</sub>O<sub>2</sub> [M- H]<sup>-</sup>:436.2031, found:436.2034.

**(3af)** **(Z/E)-3-((2-(4-methoxyphenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 51 mg, yield: 56%. **<sup>1</sup>H NMR (600 MHz, Acetic acid -d<sub>4</sub>)** δ 7.89 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.20 (dd, *J* = 8.7, 7.1 Hz, 2H), 7.07 (d, *J* = 7.8 Hz, 3H), 6.99 – 6.95 (m, 2H), 6.28 (s, 1H), 3.85 (s, 3H), 3.57 (d, *J* = 13.3 Hz, 1H), 3.36 (d, *J* = 13.2 Hz, 1H), 1.39 (s, 3H), 1.28 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (151 MHz, Acetic acid -d<sub>4</sub>)** δ 179.9, 170.2, 160.1, 147.5, 137.8, 134.7, 133.0, 132.9, 129.8, 128.9, 128.3, 128.0, 125.8, 124.3, 123.6, 120.0, 113.7, 107.9, 78.4, 58.6, 54.6, 39.2, 24.5, 24.1. **HRMS (ESI) m/z**: calculated for C<sub>28</sub>H<sub>26</sub>N<sub>3</sub>O<sub>3</sub> [M- H]<sup>-</sup>:452.1980, found:452.1981.

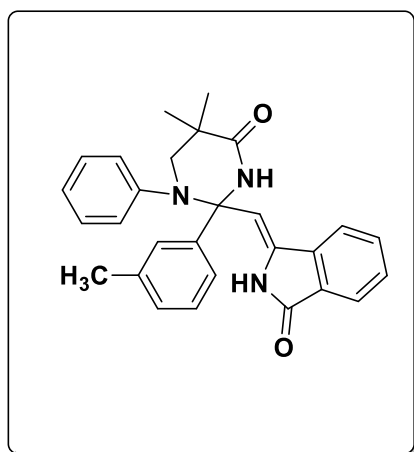
**(3ag)** **(Z/E)-3-((5,5-dimethyl-4-oxo-2-(4-pentylphenyl)-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 48 mg, yield: 49%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 9.86 (s, 1H), 8.54 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.76 – 7.69 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.04 (t, *J* = 7.8 Hz, 2H), 6.89 (t, *J* = 7.3 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 2H), 6.34 (s, 1H), 3.71 (d, *J* = 13.0 Hz, 1H), 3.17 (d, *J* = 12.9 Hz, 1H), 2.59

– 2.52 (m, 2H), 1.55 (q,  $J = 7.4$  Hz, 2H), 1.37 (s, 3H), 1.29 – 1.21 (m, 4H), 1.05 (s, 3H), 0.85 (t,  $J = 7.1$  Hz, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  175.3, 168.6, 148.0, 143.2, 138.2, 133.0, 130.1, 128.6, 128.5, 128.5, 128.4, 125.3, 123.4, 123.2, 121.1, 106.8, 106.8, 77.9, 59.3, 35.1, 31.2, 31.0, 26.3, 23.8, 23.8, 22.4, 14.4. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{32}\text{H}_{34}\text{N}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 492.2657, found: 492.2657.

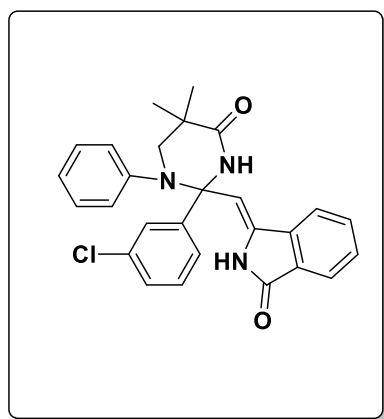
**(3ai) (Z/E)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(*m*-tolyl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 60 mg, yield: 69%.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  9.81 (s, 1H), 8.55 (s, 1H), 7.98 (d,  $J = 7.7$  Hz, 1H), 7.76 – 7.67 (m, 2H), 7.59 (t,  $J = 7.4$  Hz, 1H), 7.26 – 7.12 (m, 4H), 7.07 (t,  $J = 7.7$  Hz, 2H), 6.90 (t,  $J = 7.3$  Hz, 1H), 6.81 (d,  $J = 8.0$  Hz, 2H), 6.32 (s, 1H), 3.68 (d,  $J = 13.0$  Hz, 1H), 3.18 (d,  $J = 13.0$  Hz, 1H), 2.26 (s, 3H), 1.36 (s, 3H),

1.05 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  168.1, 147.5, 142.1, 137.2, 132.5, 129.7, 129.2, 128.8, 128.5, 128.0, 125.4, 124.9, 123.0, 122.7, 120.6, 112.3, 106.4, 106.3, 77.6, 77.5, 58.9, 25.9, 23.5, 23.5, 21.2. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{28}\text{H}_{26}\text{N}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 436.2031, found: 436.2032. HPLC purity: 95.1%;  $t_R = 2.568$  min, MeOH- $\text{H}_2\text{O}$  (80:20).

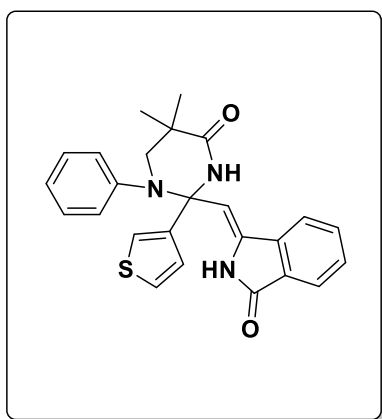
**(3ak) (Z/E)-3-((2-(3-chlorophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 65 mg, yield: 72%.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  9.80 (s, 1H), 8.63 (s, 1H), 8.02 (d,  $J = 7.7$  Hz, 1H), 7.77 – 7.68 (m, 2H), 7.59 (t,  $J = 7.4$  Hz, 1H), 7.45 – 7.32 (m, 4H), 7.11 (t,  $J = 7.7$  Hz, 2H), 6.94 (t,  $J = 7.3$  Hz, 1H), 6.87 (d,  $J = 8.0$  Hz, 2H), 6.36 (s, 1H), 3.70 (d,  $J = 13.1$  Hz, 1H), 3.20 (d,  $J = 13.1$  Hz,

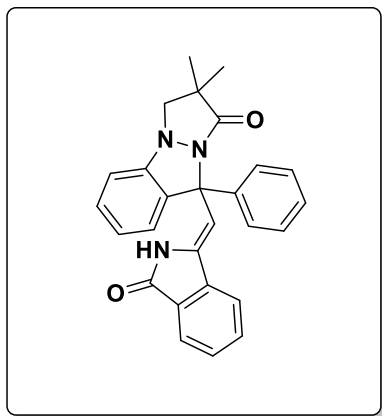
1H), 1.35 (s, 3H), 1.05 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  175.43, 168.63, 147.63, 144.97, 138.09, 136.56, 133.29, 133.04, 130.55, 130.27, 129.03, 128.65, 128.41, 128.21, 127.37, 125.43, 123.79, 123.19, 121.24, 106.07, 77.60, 59.44, 26.28, 23.96. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{25}\text{ClN}_3\text{O}_2$   $[\text{M}+\text{H}]^+$ :458.1630, found: 458.1634.

**(3al) (Z/E)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(thiophen-3-yl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one**



Following by general procedure for the synthesis of **3aa**. White solid, 56 mg, yield: 66%.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  9.79 (s, 1H), 8.62 (s, 1H), 7.94 (d,  $J$  = 7.7 Hz, 1H), 7.77 – 7.68 (m, 2H), 7.61 – 7.51 (m, 2H), 7.25 (d,  $J$  = 2.8 Hz, 1H), 7.11 (t,  $J$  = 7.3 Hz, 3H), 6.94 (t,  $J$  = 7.3 Hz, 1H), 6.86 (d,  $J$  = 8.0 Hz, 2H), 6.30 (s, 1H), 3.64 (d,  $J$  = 12.9 Hz, 1H), 3.16 (d,  $J$  = 12.9 Hz, 1H), 1.33 (s, 3H), 1.05 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  175.3, 175.3, 168.5, 148.1, 144.1, 144.0, 138.3, 132.9, 130.1, 128.5, 128.1, 127.2, 126.4, 126.3, 125.2, 123.7, 123.1, 121.1, 107.2, 107.2, 75.3, 75.2, 59.0, 26.2, 26.2, 24.0, 23.9. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{25}\text{H}_{22}\text{N}_3\text{O}_2\text{S}$   $[\text{M}-\text{H}]^-$ :428.1438, found:428.1441. HPLC purity: 92.8%;  $t_R$  = 2.484 min, MeOH- $\text{H}_2\text{O}$  (80:20).

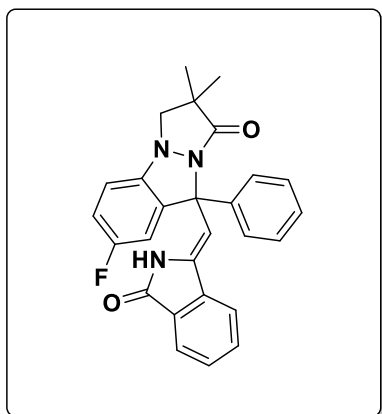
**(4aa) (Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow oil, 25 mg, yield: 60%.  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  8.93 (s, 1H), 7.86 (d,  $J$  = 7.4 Hz, 1H), 7.70 (d,  $J$  = 7.6 Hz, 1H), 7.60 (td,  $J$  = 7.6, 1.2 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.43 – 7.32 (m, 6H), 7.11 – 7.01 (m, 2H), 6.90 (d,  $J$  = 7.9 Hz, 1H), 5.94 (s, 1H), 3.78 (d,  $J$  = 8.3 Hz, 1H), 3.44 (d,  $J$  = 8.3 Hz, 1H),

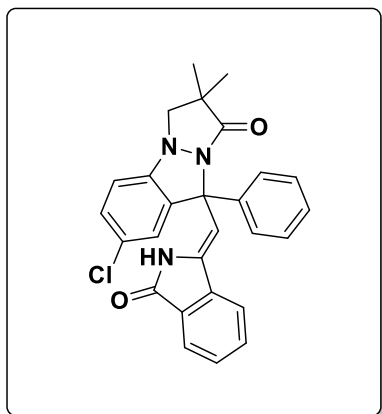
1.40 (s, 3H), 1.33 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, Chloroform-*d*)  $\delta$  169.8, 168.4, 138.9, 137.7, 137.0, 135.9, 132.0, 129.6, 129.5, 129.4, 128.8, 128.5, 127.8, 123.8, 123.5, 120.1, 110.3, 104.9, 69.1, 64.3, 46.0, 22.8, 22.7. HRMS (ESI) *m/z*: calculated for  $\text{C}_{27}\text{H}_{22}\text{N}_3\text{O}_2$  [*M* - *H*] $^-$ : 420.1718, found: 420.1716.

**(4ba) (Z/E)-7-fluoro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow oil, 44 mg, yield: 51%.  $^1\text{H}$  NMR (500 MHz, Chloroform-*d*)  $\delta$  9.05 (s, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 7.7 Hz, 1H), 7.58 (td, *J* = 7.5, 1.2 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.37 – 7.31 (m, 5H), 7.02 (td, *J* = 8.6, 2.5 Hz, 1H), 6.82 (dd, *J* = 8.7, 4.1 Hz, 1H), 6.70 (dd, *J* = 7.9, 2.5 Hz, 1H), 5.85 (s, 1H), 3.76 (d, *J* = 8.2 Hz, 1H), 3.35 (d, *J* = 8.2 Hz, 1H), 1.37 (s, 3H), 1.29 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform-*d*)  $\delta$  169.6, 167.9, 159.2 (d, *J* = 242.6 Hz), 141.8, 137.6, 137.1, 137.0, 131.7, 129.3, 129.1, 128.4, 128.3, 127.3, 123.1, 119.6, 115.9 (d, *J* = 24.0 Hz), 110.8 (d, *J* = 8.5 Hz), 110.6 (d, *J* = 25.0 Hz), 103.5, 68.8, 64.3, 45.7, 22.3, 22.1. HRMS (ESI) *m/z*: calculated for  $\text{C}_{27}\text{H}_{21}\text{FN}_3\text{O}_2$  [*M* - *H*] $^-$ : 438.1623, found: 438.1628.

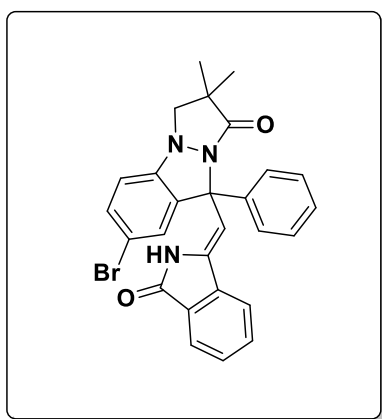
**(4ca) (Z/E)-7-chloro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow oil, 42 mg, yield: 47%.  $^1\text{H}$  NMR (400 MHz, Chloroform-*d*)  $\delta$  9.00 (s, 1H), 7.86 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.72 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.61 (td, *J* = 7.4, 1.1 Hz, 1H), 7.54 (td, *J* = 7.3, 0.8 Hz, 1H), 7.43 – 7.32 (m, 5H), 7.30 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.97 (d, *J* = 2.0 Hz, 1H), 6.83 (d, *J* = 8.4 Hz, 1H), 5.85 (s, 1H),

3.79 (d,  $J = 8.3$  Hz, 1H), 3.39 (d,  $J = 8.3$  Hz, 1H), 1.39 (s, 3H), 1.32 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.4, 167.9, 144.2, 137.5, 137.3, 137.0, 131.65, 129.31, 129.02, 128.48, 128.33, 127.31, 123.40, 123.12, 119.6, 110.8, 103.5, 68.7, 63.8, 45.7, 22.4, 22.2. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{21}\text{ClN}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 454.1328, found: 454.1326.

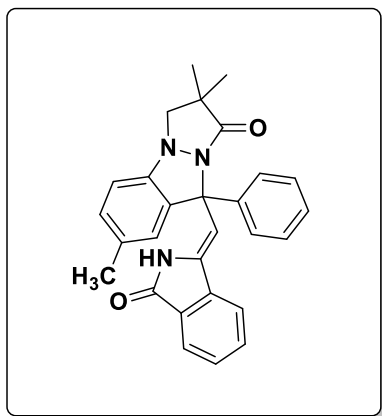
**(4da) (Z/E)-7-bromo-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow oil, 57 mg, yield: 56%.  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  8.99 (s, 1H), 7.86 (dt,  $J = 7.5$ , 1.1 Hz, 1H), 7.72 (dt,  $J = 7.8$ , 1.0 Hz, 1H), 7.61 (td,  $J = 7.5$ , 1.2 Hz, 1H), 7.54 (td,  $J = 7.4$ , 1.0 Hz, 1H), 7.45 (dd,  $J = 8.4$ , 1.9 Hz, 1H), 7.42 – 7.32 (m, 5H), 7.11 (d,  $J = 1.8$  Hz, 1H), 6.78 (d,  $J = 8.4$  Hz, 1H), 5.85 (s, 1H), 3.78 (d,  $J = 8.3$  Hz, 1H), 3.39 (d,  $J = 8.3$  Hz, 1H), 1.39

(s, 3H), 1.32 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.3, 167.9, 144.6, 137.7, 137.5, 137.1, 137.0, 131.8, 131.7, 129.3, 128.5, 128.3, 127.3, 126.2, 123.1, 119.6, 115.4, 111.3, 103.6, 68.6, 63.7, 45.7, 22.4, 22.2. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{22}\text{BrN}_3\text{NaO}_2$   $[\text{M} + \text{Na}]^+$ : 522.0788, found: 522.0790.

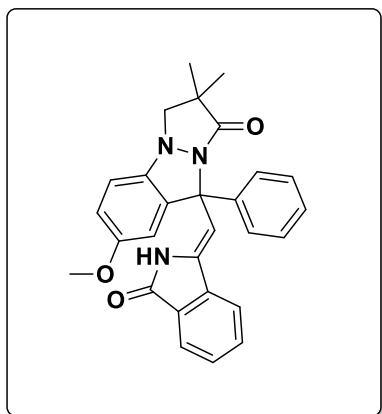
**(4ea) (Z/E)-2,2,7-trimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow oil, 47 mg, yield: 54%.  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  8.79 (s, 1H), 7.59 (td,  $J = 7.5$ , 1.2 Hz, 1H), 7.52 (td,  $J = 7.4$ , 1.0 Hz, 1H), 7.38 – 7.30 (m, 1H), 7.28 – 7.23 (m, 1H), 7.21 – 7.12 (m, 3H), 7.10 – 7.03 (m, 2H), 6.90 (d,  $J = 7.9$  Hz, 1H), 5.95 (s, 1H), 3.74 (d,  $J = 8.3$  Hz, 1H), 3.47 (d,  $J = 8.3$  Hz, 1H), 2.34 (s, 3H), 1.39 (s, 3H), 1.34 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126

**MHz, Chloroform-*d***)  $\delta$  169.4, 167.9, 143.5, 138.5, 137.2, 136.5, 135.5, 133.2, 131.6, 129.6, 129.1, 128.3, 128.0, 127.3, 123.6, 123.0, 119.6, 109.7, 104.7, 68.6, 64.3, 45.6, 22.3, 22.2, 20.6. **HRMS (ESI) *m/z***: calculated for C<sub>28</sub>H<sub>25</sub>N<sub>3</sub>NaO<sub>2</sub> [M + Na]<sup>+</sup>: 458.1839, found: 458.1841.

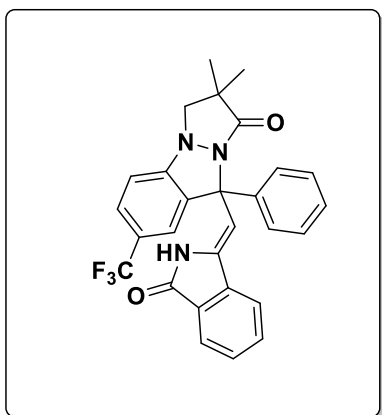
**(4fa) (Z/E)-7-methoxy-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow oil, 45 mg, yield: 50%. **<sup>1</sup>H NMR (500 MHz, Chloroform-*d*)**  $\delta$  9.01 (s, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.40 – 7.31 (m, 5H), 6.87 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 1H), 6.52 (d, *J* = 2.4 Hz, 1H), 5.91 (s, 1H), 3.73 (d, *J* = 6.4 Hz, 4H), 3.33 (d, *J* = 8.2 Hz, 1H), 1.36 (s, 3H), 1.28 (s, 3H).

**<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, Chloroform-*d*)**  $\delta$  169.6, 167.9, 156.5, 139.5, 138.1, 136.7, 131.6, 129.2, 128.3, 128.1, 127.4, 123.1, 119.6, 114.6, 110.7, 109.0, 104.2, 68.8, 64.8, 55.4, 45.6, 22.3, 22.2. **HRMS (ESI) *m/z***: calculated for C<sub>28</sub>H<sub>25</sub>N<sub>3</sub>NaO<sub>3</sub> [M + Na]<sup>+</sup>: 474.1788, found: 474.1790.

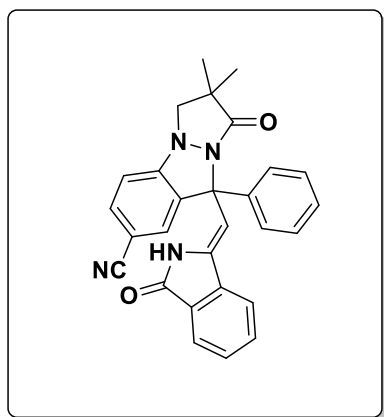
**(4ga) (Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-7-(trifluoromethyl)-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow oil, 65 mg, yield: 71%. **<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)**  $\delta$  9.00 (s, 1H), 7.87 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.73 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.62 (td, *J* = 7.6, 1.3 Hz, 2H), 7.55 (td, *J* = 7.3, 1.2 Hz, 1H), 7.43 – 7.34 (m, 5H), 7.23 (s, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 5.83 (s, 1H), 3.85 (d, *J* = 8.4 Hz, 1H), 3.46 (d, *J* = 8.4 Hz, 1H), 1.41 (s, 3H), 1.34 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126**

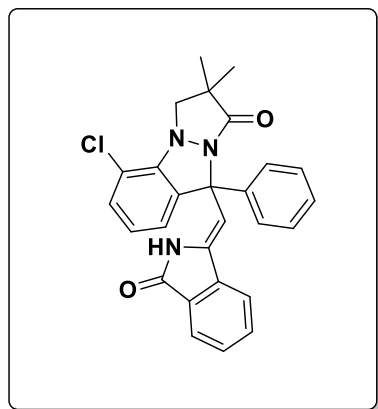
**MHz, Chloroform-*d***)  $\delta$  169.3, 167.9, 148.0, 137.3, 137.2, 137.0, 136.4, 131.7, 129.4, 129.1, 128.6, 128.4, 127.3, 126.6, 126.6, 123.1, 120.5, 120.4, 119.7, 68.7, 63.0, 45.6, 22.5, 22.2. **HRMS (ESI) *m/z***: calculated for C<sub>28</sub>H<sub>21</sub>F<sub>3</sub>N<sub>3</sub>O<sub>2</sub> [M - H]<sup>-</sup>: 488.1591, found: 488.1595.

**(4ha) (Z/E)-2,2-dimethyl-1-oxo-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazole-7-carbonitrile**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 55 mg, yield: 62%. **<sup>1</sup>H NMR (500 MHz, Chloroform-*d*)**  $\delta$  8.93 (s, 1H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.54 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.40 – 7.32 (m, 5H), 7.24 (d, *J* = 1.5 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 5.75 (s, 1H), 3.83 (d, *J* = 8.5 Hz, 1H), 3.47 (d, *J* = 8.5 Hz, 1H), 1.38 (s, 3H), 1.33 (s, 3H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, Chloroform-*d*)**  $\delta$  169.1, 167.8, 148.3, 137.5, 137.0, 137.0, 136.9, 133.6, 131.8, 129.5, 129.1, 128.7, 128.6, 127.2, 127.1, 123.2, 119.6, 109.7, 105.9, 102.8, 68.6, 62.4, 45.7, 22.6, 22.2. **HRMS (ESI) *m/z***: calculated for C<sub>28</sub>H<sub>22</sub>N<sub>4</sub>NaO<sub>2</sub> [M + Na]<sup>+</sup>: 469.1635, found: 469.163.

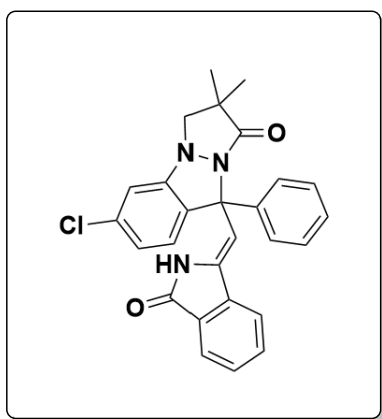
**(4ia) (Z/E)-5-chloro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 40 mg, yield: 45%. **<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  9.51 (s, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.70 (t, *J* = 7.5 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.41 – 7.35 (m, 4H), 7.33 (t, *J* = 6.7 Hz, 1H), 7.03 (d, *J* = 9.9 Hz, 1H), 7.02 – 6.99 (m, 1H), 6.86 (t, *J* = 8.0 Hz, 1H), 6.16 (s, 1H), 3.99 (d, *J* = 8.7 Hz, 1H), 3.54 (d, *J* = 8.7 Hz, 1H), 1.25 (s,

3H), 1.23 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  169.9, 167.5, 163.5, 162.1, 147.3, 147.2, 139.0, 137.3, 136.4, 132.6, 131.7, 130.0, 129.7, 128.8, 128.7, 128.1, 127.5, 125.2, 125.2, 122.9, 121.2, 110.1, 110.0, 105.6, 98.5, 98.3, 68.4, 62.7, 45.6, 22.5, 22.1. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{22}\text{FN}_3\text{NaO}_2$   $[\text{M} + \text{Na}]^+$ : 462.1588, found: 462.1591. HPLC purity: 93.2%;  $t_R$  = 3.055 min, MeOH- $\text{H}_2\text{O}$  (80:20).

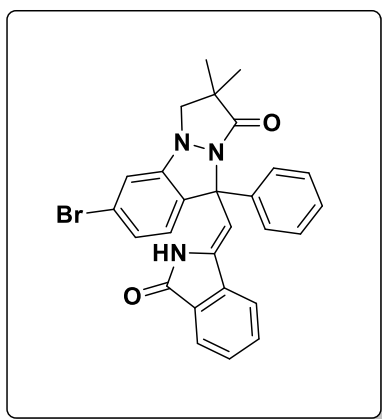
**(4ja) (Z/E)-6-chloro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 43 mg, yield: 47%.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  9.52 (s, 1H), 8.07 (d,  $J$  = 7.7 Hz, 1H), 7.75 (d,  $J$  = 7.5 Hz, 1H), 7.70 (t,  $J$  = 7.5 Hz, 1H), 7.60 (t,  $J$  = 7.4 Hz, 1H), 7.40 – 7.35 (m, 4H), 7.33 (t,  $J$  = 7.4 Hz, 1H), 7.25 (d,  $J$  = 1.7 Hz, 1H), 7.08 (dd,  $J$  = 8.2, 1.8 Hz, 1H), 7.01 (d,  $J$  = 8.2 Hz, 1H), 6.15 (s, 1H), 4.01 (d,  $J$  = 8.7 Hz, 1H), 3.56 (d,  $J$  = 8.7 Hz, 1H), 1.24

(s, 3H), 1.23 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (201 MHz, DMSO- $d_6$ ) 169.3, 166.9, 146.4, 138.3, 136.6, 135.9, 134.0, 133.1, 132.0, 129.4, 128.1, 127.5, 126.9, 124.5, 122.5, 122.2, 120.6, 110.1, 104.5, 67.8, 62.0, 44.9, 21.9, 21.5. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{21}\text{ClN}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 454.1328, found: 454.1328. HPLC purity: 93.4%;  $t_R$  = 3.054 min, MeOH- $\text{H}_2\text{O}$  (80:20).

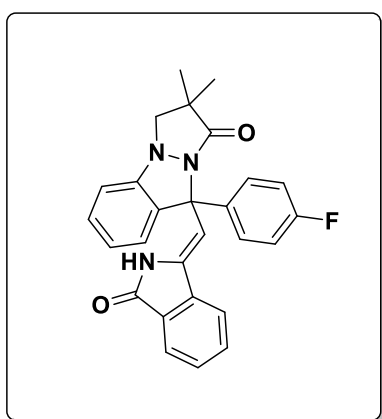
**(4ka) (Z/E)-6-bromo-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 67 mg, yield: 68%.  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  8.90 (s, 1H), 7.86 (dt,  $J$  = 7.4, 1.1 Hz, 1H), 7.70 (dt,  $J$  = 7.8, 1.0 Hz, 1H), 7.61 (td,  $J$  = 7.5, 1.2 Hz, 1H), 7.53 (td,  $J$  = 7.4, 1.1 Hz, 1H), 7.42 – 7.33 (m, 5H), 7.18 (dd,  $J$  = 8.1, 1.7 Hz, 1H), 7.04 (d,  $J$  = 1.7 Hz, 1H), 6.88 (d,  $J$  = 8.2 Hz, 1H), 5.85 (s, 1H),

3.76 (d,  $J = 8.3$  Hz, 1H), 3.43 (d,  $J = 8.3$  Hz, 1H), 1.39 (s, 3H), 1.33 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.3, 167.9, 146.9, 137.8, 137.1, 136.9, 134.7, 131.7, 129.3, 129.1, 128.5, 128.3, 127.2, 126.2, 124.6, 123.1, 122.5, 119.6, 113.1, 103.7, 68.6, 63.5, 45.6, 22.4, 22.2. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{21}\text{BrN}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 498.0823, found:498.0822.

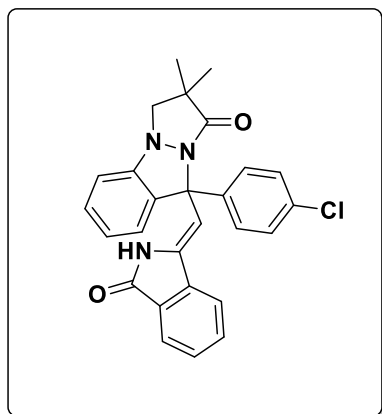
**(4ab) (Z/E)-9-(4-fluorophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 52 mg, yield: 60%.  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  9.10 (s, 1H), 7.86 (dt,  $J = 7.4$ , 1.0 Hz, 1H), 7.69 (dd,  $J = 7.6$ , 1.0 Hz, 1H), 7.60 (td,  $J = 7.5$ , 1.2 Hz, 1H), 7.52 (td,  $J = 7.4$ , 1.0 Hz, 1H), 7.40 – 7.34 (m, 3H), 7.10 – 6.98 (m, 4H), 6.91 (d,  $J = 7.9$  Hz, 1H), 5.90 (s, 1H), 3.83 (d,  $J = 8.3$  Hz, 1H), 3.38 (d,  $J = 8.4$  Hz, 1H), 1.40 (s, 3H), 1.31 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$

NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.4, 168.0, 162.1 (d,  $J = 248.5$  Hz), 145.6, 137.1, 136.7, 135.3, 134.1, 134.1, 131.7, 129.4 (d,  $J = 8.5$  Hz), 129.2 (d,  $J = 26.0$  Hz), 123.5, 123.2, 123.1, 119.6, 115.4, 115.2, 109.9, 104.2, 68.1, 63.9, 45.6, 22.4, 22.1. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{22}\text{FN}_3\text{NaO}_2$   $[\text{M} + \text{Na}]^+$ : 462.1588, found:462.1588.

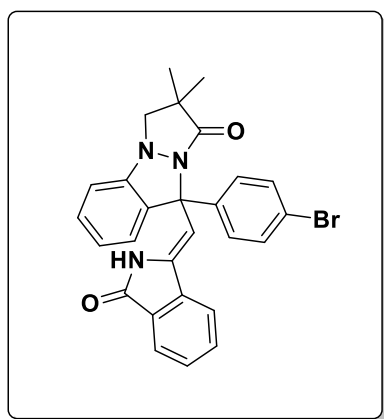
**(4ac) (Z/E)-9-(4-chlorophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 47 mg, yield: 52%.  $^1\text{H}$  NMR (500 MHz, Chloroform- $d$ )  $\delta$  9.06 (s, 1H), 7.83 (d,  $J = 7.5$  Hz, 1H), 7.66 (d,  $J = 7.7$  Hz, 1H), 7.57 (t,  $J = 7.5$  Hz, 1H), 7.50 (t,  $J = 7.4$  Hz, 1H), 7.36 – 7.27 (m, 5H), 7.05 (t,  $J = 7.5$  Hz, 1H), 6.96 (d,  $J = 7.7$  Hz, 1H), 6.88 (d,  $J = 7.9$  Hz, 1H), 5.85 (s, 1H), 3.80 (d,  $J = 8.3$  Hz, 1H),

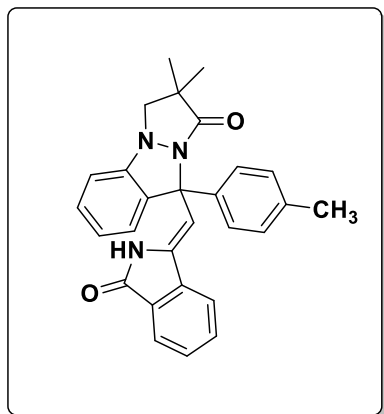
3.36 (d,  $J = 8.4$  Hz, 1H), 1.37 (s, 3H), 1.28 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.4, 167.9, 145.5, 136.9, 135.1, 134.1, 131.7, 129.3, 129.1, 129.1, 128.8, 128.5, 123.5, 123.1, 119.6, 110.0, 103.8, 68.1, 63.9, 45.6, 22.4, 22.1. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{21}\text{ClN}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 454.1328, found:454.1329.

**(4ad) (Z/E)-9-(4-bromophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 40 mg, yield: 40%.  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  9.08 (s, 1H), 7.86 (dt,  $J = 7.5$ , 1.0 Hz, 1H), 7.69 (dt,  $J = 7.7$ , 1.0 Hz, 1H), 7.60 (td,  $J = 7.5$ , 1.2 Hz, 1H), 7.53 (td,  $J = 7.4$ , 1.1 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.36 (td,  $J = 7.6$ , 1.2 Hz, 1H), 7.31 – 7.23 (m, 3H), 7.08 (td,  $J = 7.6$ , 1.0 Hz, 1H), 6.98 (dd,  $J = 7.8$ , 1.2 Hz, 1H), 6.91 (dt,  $J = 7.9$ , 0.8 Hz, 1H), 5.86 (s, 1H), 3.83 (d,  $J = 8.3$  Hz, 1H), 3.38 (d,  $J = 8.3$  Hz, 1H), 1.40 (s, 3H), 1.31 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, Chloroform- $d$ )  $\delta$  169.8, 168.4, 146.0, 137.9, 137.5, 137.4, 135.6, 132.1, 131.9, 129.8, 129.6, 129.6, 124.0, 123.6, 123.6, 122.9, 120.1, 110.4, 104.1, 68.5, 64.4, 46.1, 22.8, 22.6. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{21}\text{BrN}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 498.0823, found:498.0825.

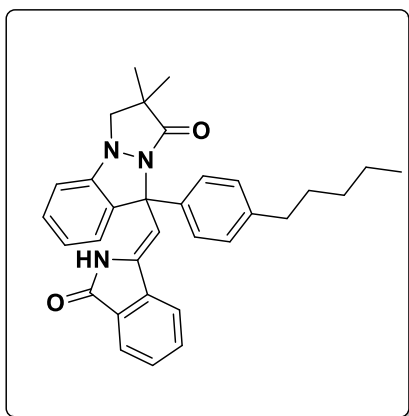
**(4ae) (Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(p-tolyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 37 mg, yield: 43%.  $^1\text{H}$  NMR (500 MHz, Chloroform- $d$ )  $\delta$  8.97 (s, 1H), 7.83 (d,  $J = 7.5$  Hz, 1H), 7.67 (d,  $J = 7.6$  Hz, 1H), 7.59 – 7.53 (m, 1H), 7.49 (t,  $J = 7.4$  Hz, 1H), 7.31 (td,  $J = 7.6$ , 1.3 Hz, 1H), 7.25 (d,  $J = 8.3$  Hz, 2H), 7.13 (d,  $J = 8.0$  Hz, 2H), 7.07 – 6.97 (m, 2H), 6.87 (d,  $J = 7.9$

Hz, 1H), 5.90 (s, 1H), 3.76 (d,  $J = 8.3$  Hz, 1H), 3.39 (d,  $J = 8.2$  Hz, 1H), 2.32 (s, 3H), 1.37 (s, 3H), 1.29 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.3, 167.9, 145.7, 137.9, 137.2, 136.4, 135.6, 135.4, 131.5, 129.1, 129.1, 128.8, 127.3, 123.3, 123.0, 119.6, 109.8, 104.8, 68.6, 63.9, 45.6, 22.4, 22.2, 20.7. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{28}\text{H}_{25}\text{N}_3\text{NaO}_2$   $[\text{M}^+ \text{Na}]^+$ : 458.1839, found: 458.1841.

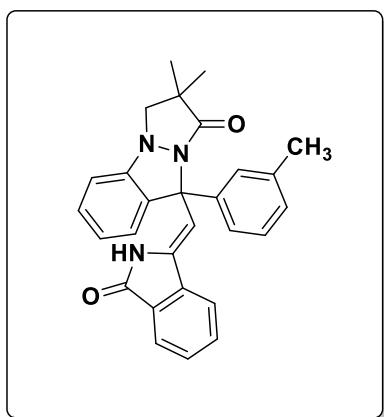
**(4ag) (Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(4-pentylphenyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 47 mg, yield: 48%.  $^1\text{H}$  NMR (500 MHz, Chloroform- $d$ )  $\delta$  8.86 (s, 1H), 7.83 (dt,  $J = 7.6$ , 1.0 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.56 (td,  $J = 7.5$ , 1.2 Hz, 1H), 7.49 (td,  $J = 7.5$ , 1.0 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.30 – 7.24 (m, 3H), 7.16 – 7.12 (m, 2H), 7.07 – 7.00 (m, 2H), 6.87 (d,  $J = 7.9$  Hz, 1H), 5.92 (s, 1H), 3.73 (d,  $J = 8.3$  Hz, 1H), 3.41 (d,  $J = 8.3$  Hz, 1H),

2.61 – 2.55 (m, 2H), 1.63 – 1.55 (m, 2H), 1.37 (s, 3H), 1.34 – 1.30 (m, 7H), 0.91 – 0.87 (m, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  145.7, 142.8, 136.3, 135.6, 135.5, 131.5, 129.1, 129.1, 128.8, 128.3, 127.1, 123.4, 123.2, 123.0, 119.6, 109.8, 104.9, 68.6, 63.8, 45.6, 35.1, 31.2, 30.4, 22.4, 22.3, 22.1, 13.6. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{32}\text{H}_{32}\text{N}_3\text{O}_2$   $[\text{M} - \text{H}]^-$ : 490.2500, found: 490.2503.

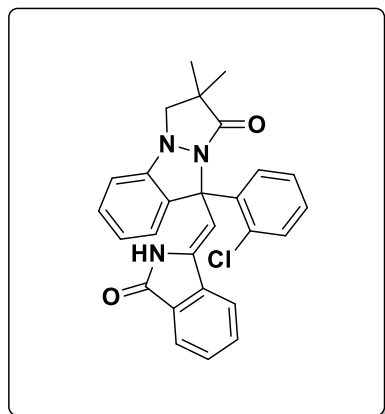
**(4ai) (Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(*m*-tolyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 46 mg, yield: 54%.  $^1\text{H}$  NMR (500 MHz, Chloroform- $d$ )  $\delta$  8.83 (s, 1H), 7.85 (d,  $J = 7.5$  Hz, 1H), 7.71 (d,  $J = 7.7$  Hz, 1H), 7.62 – 7.56 (m, 1H), 7.52 (t,  $J = 7.4$  Hz, 1H), 7.37 – 7.31 (m, 1H), 7.26 (dd,  $J = 15.7$ , 8.0 Hz, 1H), 7.19 (d,  $J = 7.9$  Hz, 2H), 7.14 (d,  $J = 7.5$  Hz, 1H), 7.11 – 7.03 (m, 2H), 6.90 (d,  $J =$

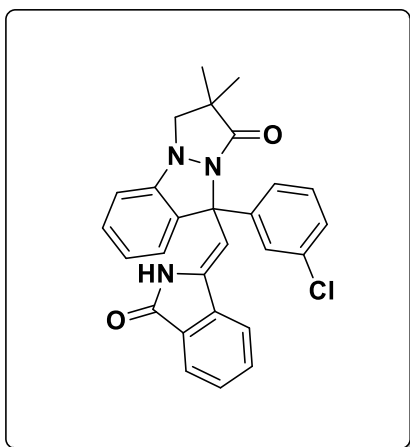
7.9 Hz, 1H), 5.95 (s, 1H), 3.75 (d,  $J = 8.3$  Hz, 1H), 3.47 (d,  $J = 8.3$  Hz, 1H), 2.34 (s, 3H), 1.39 (s, 3H), 1.34 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.2, 167.8, 145.6, 138.5, 137.9, 137.2, 136.3, 135.3, 131.5, 129.1, 129.0, 128.9, 128.8, 128.2, 127.7, 124.4, 123.3, 123.2, 123.0, 119.6, 109.8, 104.6, 68.6, 63.8, 45.5, 22.3, 22.3, 21.2. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{28}\text{H}_{25}\text{N}_3\text{NaO}_2$   $[\text{M}^+ \text{Na}]^+$ : 458.1839, found: 458.1841.

**(4aj) (Z/E)-9-(2-chlorophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 47 mg, yield: 52%.  $^1\text{H}$  NMR (500 MHz, Chloroform- $d$ )  $\delta$  9.38 (s, 1H), 7.86 (dt,  $J = 7.5$ , 1.1 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.68 – 7.64 (m, 1H), 7.57 (td,  $J = 7.5$ , 1.2 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.36 – 7.26 (m, 4H), 7.02 (td,  $J = 7.6$ , 1.0 Hz, 1H), 6.86 (dd,  $J = 7.6$ , 1.2 Hz, 1H), 6.82 (d,  $J = 7.8$  Hz, 1H), 5.71 (s, 1H), 3.85 (d,  $J = 8.1$  Hz, 1H), 3.61 (d,  $J = 8.1$  Hz, 1H), 1.40 (s, 3H), 1.34 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, Chloroform- $d$ )  $\delta$  169.5, 168.0, 146.6, 137.1, 136.9, 134.3, 133.2, 132.0, 131.9, 131.6, 130.7, 130.1, 129.4, 129.3, 129.0, 126.7, 123.2, 122.8, 121.5, 119.7, 109.0, 104.6, 67.7, 62.4, 45.5, 23.5, 22.1. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{22}\text{ClN}_3\text{NaO}_2$   $[\text{M}^+ \text{Na}]^+$ : 478.1293, found: 478.1295.

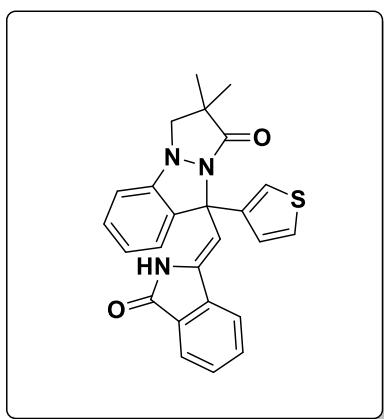
**(4ak) (Z/E)-9-(3-chlorophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 42 mg, yield: 46%.  $^1\text{H}$  NMR (600 MHz, DMSO- $d_6$ )  $\delta$  9.51 (s, 1H), 8.08 (d,  $J = 7.7$  Hz, 1H), 7.75 (d,  $J = 7.4$  Hz, 1H), 7.71 (t,  $J = 7.4$  Hz, 1H), 7.61 (t,  $J = 7.4$  Hz, 1H), 7.41 (s, 2H), 7.37 (t,  $J = 6.4$  Hz, 1H), 7.34 (s, 2H), 7.13 – 7.02 (m, 3H), 6.17 (s, 1H), 4.00 (d,  $J =$

8.6 Hz, 1H), 3.52 (d,  $J = 8.6$  Hz, 1H), 1.26 (s, 3H), 1.23 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (201 MHz, DMSO- $d_6$ )  $\delta$  169.4, 166.9, 145.0, 140.9, 136.6, 135.9, 134.5, 132.6, 132.0, 129.5, 128.9, 128.1, 127.6, 126.6, 126.0, 123.0, 123.0, 122.2, 120.7, 110.0, 104.4, 67.4, 62.4, 45.0, 21.8, 21.4. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{22}\text{ClN}_3\text{NaO}_2$   $[\text{M}^+ \text{Na}]^+$ : 478.1293, found:478.1294.

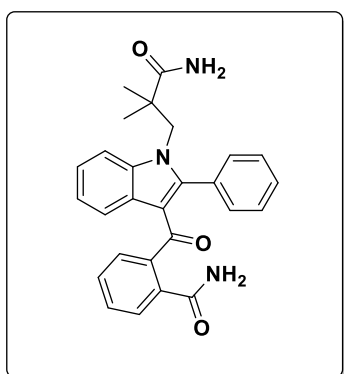
**(4al) (Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(thiophen-3-yl)-2,3-dihydro-1H,9H-pyrazolo[1,2-*a*]indazol-1-one**



Following by general procedure for the synthesis of **4aa**. Yellow solid, 17 mg, yield: 21%.  $^1\text{H}$  NMR (400 MHz, Chloroform- $d$ )  $\delta$  9.28 (s, 1H), 7.86 (dt,  $J = 7.4$ , 1.1 Hz, 1H), 7.67 (dt,  $J = 7.8$ , 1.0 Hz, 1H), 7.59 (td,  $J = 7.5$ , 1.3 Hz, 1H), 7.52 (td,  $J = 7.4$ , 1.0 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.12 – 7.05 (m, 2H), 6.90 (dd,  $J = 7.9$ , 0.8 Hz, 1H), 6.87 – 6.83 (m, 1H), 5.94 (s, 1H), 3.82 (d,  $J = 8.3$  Hz, 1H), 3.33 (d,  $J = 8.3$  Hz, 1H), 1.40 (s, 3H),

1.31 (s, 3H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, Chloroform- $d$ )  $\delta$  170.0, 168.4, 146.1, 140.0, 137.6, 137.0, 135.3, 132.0, 129.7, 129.5, 127.1, 127.1, 124.7, 123.8, 123.5, 123.5, 120.0, 110.4, 105.4, 66.0, 64.6, 46.1, 22.9, 22.7. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{25}\text{H}_{20}\text{N}_3\text{O}_2\text{S}[\text{M} - \text{H}]^-$ : 426.1282, found:426.1284. HPLC purity: 98.6%;  $t_R = 2.443$  min, MeOH- $\text{H}_2\text{O}$  (80:20).

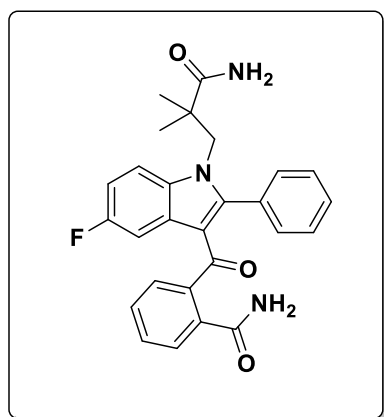
**(5aa) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-phenyl-1H-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 72 mg, yield: 80%.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.02 (d,  $J = 7.2$  Hz, 1H), 7.75 (d,  $J = 8.2$  Hz, 1H), 7.72 (s, 1H), 7.43 – 7.33 (m, 3H), 7.28 – 7.24 (m, 1H), 7.22 – 7.09 (m, 7H), 7.02 – 6.98 (m, 1H), 6.92 (s, 1H), 6.88 (dd,  $J = 7.7$ , 1.2 Hz, 1H), 4.42 (s, 2H), 0.68

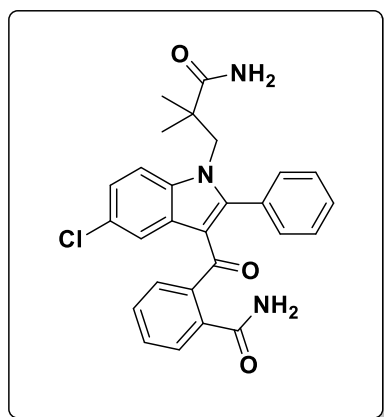
(s, 6H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  192.8, 178.2, 169.7, 147.8, 142.4, 137.6, 135.6, 130.9, 129.3, 128.8, 128.6, 128.2, 127.8, 127.5, 127.3, 123.1, 122.4, 121.8, 115.2, 112.7, 50.5, 44.0, 24.7. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{24}\text{N}_3\text{O}_3$   $[\text{M} - \text{H}]^-$ : 438.1823, found: 438.1824.

**(5ba) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5-fluoro-2-phenyl-1H-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 76 mg, yield: 85%.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  7.78 (dd,  $J = 9.1, 4.5$  Hz, 1H), 7.75 (s, 1H), 7.70 (dd,  $J = 10.1, 2.7$  Hz, 1H), 7.40 (dd,  $J = 7.7, 1.2$  Hz, 1H), 7.37 – 7.32 (m, 2H), 7.25 – 7.10 (m, 7H), 7.01 (td,  $J = 7.5, 1.2$  Hz, 1H), 6.94 (s, 1H), 6.91 – 6.86 (m, 1H), 4.41 (s, 2H), 0.68 (s, 6H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  192.7, 178.2, 169.6, 159.1 (d,  $J = 234.6$  Hz), 149.2, 142.1, 135.5, 134.2, 131.9, 130.6, 129.4, 129.0, 128.7, 128.1, 128.0 (d,  $J = 11.0$  Hz), 127.9, 127.5, 115.2, 114.1 (d,  $J = 9.7$  Hz), 111.2 (d,  $J = 25.9$  Hz), 106.5 (d,  $J = 24.8$  Hz), 50.9, 43.9, 24.6. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{23}\text{FN}_3\text{O}_3$   $[\text{M} - \text{H}]^-$ : 456.1729, found: 456.1732.

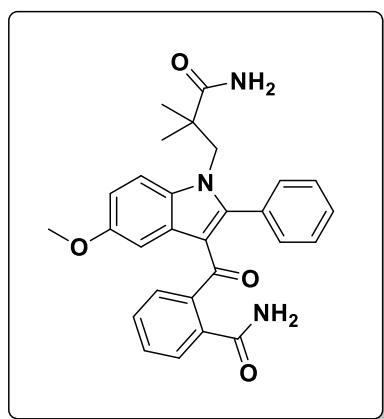
**(5ca) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5-chloro-2-phenyl-1H-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 86 mg, yield: 91%.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  8.05 (d,  $J = 2.2$  Hz, 1H), 7.79 (d,  $J = 8.9$  Hz, 1H), 7.75 (s, 1H), 7.40 (dd,  $J = 7.7, 1.1$  Hz, 1H), 7.36 – 7.31 (m, 2H), 7.28 (dd,  $J = 8.9, 2.2$  Hz, 1H), 7.23 (s, 1H), 7.20 – 7.07 (m, 5H), 7.02 (td,  $J = 7.5, 1.2$  Hz, 1H), 6.96 – 6.83 (m, 2H), 4.40 (s, 2H),

0.67 (s, 6H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  177.6, 169.0, 148.4, 141.5, 135.6, 134.9, 129.8, 128.9, 128.5, 128.2, 128.0, 127.6, 127.4, 127.0, 126.7, 122.6, 120.3, 114.4, 113.9, 50.4, 43.4, 24.1. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{27}\text{H}_{23}\text{ClN}_3\text{O}_3$   $[\text{M} - \text{H}]^-$ : 472.1433, found: 472.1434.

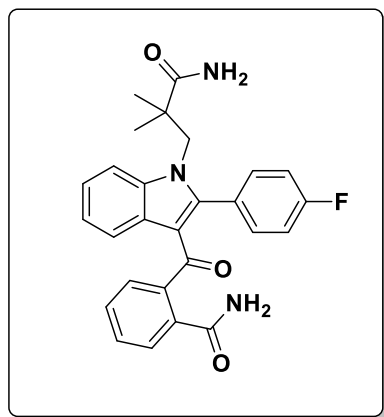
**(5fa) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5-methoxy-2-phenyl-1H-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 76 mg, yield: 81%.  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  7.72 (s, 1H), 7.64 (d,  $J = 9.0$  Hz, 1H), 7.57 (d,  $J = 2.6$  Hz, 1H), 7.42 – 7.31 (m, 3H), 7.21 (s, 1H), 7.18 – 7.07 (m, 5H), 7.00 – 6.95 (m, 1H), 6.91 (s, 1H), 6.88 (dd,  $J = 9.0, 2.6$  Hz, 1H), 6.84 (d,  $J = 7.5$  Hz, 1H), 4.38 (s, 2H), 3.76 (s, 3H), 0.66 (s, 6H).

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz, DMSO- $d_6$ )  $\delta$  178.2, 169.8, 155.9, 148.1, 142.4, 135.6, 132.6, 131.1, 129.2, 128.7, 128.5, 128.2, 128.1, 127.8, 127.5, 114.9, 113.5, 112.8, 103.5, 55.7, 50.7, 44.0, 24.6. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{28}\text{H}_{26}\text{N}_3\text{O}_4$   $[\text{M} - \text{H}]^-$ : 468.1929, found: 468.1928.

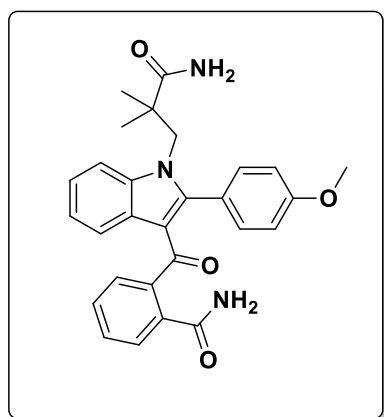
**(5ab) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(4-fluorophenyl)-1H-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 65 mg, yield: 72%.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ )  $\delta$  8.03 (d,  $J = 2.3$  Hz, 1H), 7.76 (d,  $J = 8.8$  Hz, 1H), 7.73 (s, 1H), 7.38 (d,  $J = 7.7$  Hz, 1H), 7.33 – 7.30 (m, 2H), 7.26 (dd,  $J = 8.8, 2.3$  Hz, 1H), 7.21 (s, 1H), 7.18 – 7.11 (m, 3H), 7.12 – 7.06 (m, 3H), 6.99 (t,  $J = 7.5$  Hz, 1H), 6.91 (s, 1H), 6.86 (d,  $J = 7.5$  Hz, 1H), 4.38 (s, 2H), 0.65 (s, 6H).  $^{13}\text{C}\{^1\text{H}\}$  NMR

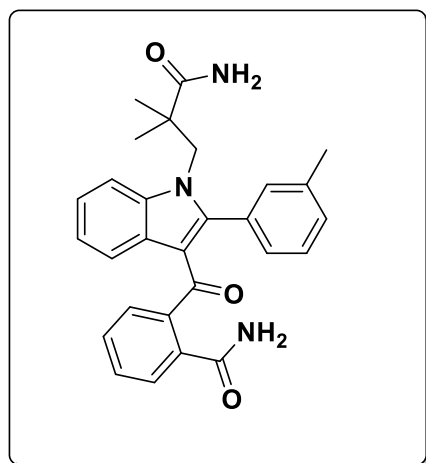
(126 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  192.7, 178.1, 169.7, 162.3 (d,  $J$  = 246.3 Hz), 146.7, 142.4, 137.7, 135.6, 129.4, 128.5, 128.2, 127.6, 127.2, 123.3, 122.5, 121.8, 115.4, 114.9, 114.7, 112.7, 50.6, 44.1, 24.7. **HRMS (ESI)  $m/z$ :** calculated for C<sub>27</sub>H<sub>23</sub>FN<sub>3</sub>O<sub>3</sub> [M - H]<sup>-</sup>: 456.1729, found: 456.1733.

**(5af) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(4-methoxyphenyl)-1*H*-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 68 mg, yield: 72%. **<sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  8.02 (d,  $J$  = 7.9 Hz, 1H), 7.71 (d,  $J$  = 8.9 Hz, 2H), 7.39 (d,  $J$  = 7.7 Hz, 1H), 7.23 (t,  $J$  = 6.3 Hz, 3H), 7.16 (dd,  $J$  = 14.1, 7.4 Hz, 3H), 7.08 (s, 1H), 6.99 (t,  $J$  = 7.8 Hz, 1H), 6.90 (s, 1H), 6.81 (d,  $J$  = 7.6 Hz, 1H), 6.62 (d,  $J$  = 8.3 Hz, 2H), 4.40 (s, 2H), 3.67 (s, 3H), 0.68 (s, 6H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  192.4, 177.8, 169.3, 159.1, 147.6, 142.0, 137.1, 135.1, 128.8, 127.9, 127.7, 127.1, 127.0, 122.6, 122.5, 121.9, 121.2, 112.9, 112.1, 55.1, 50.0, 43.6, 24.2. **HRMS (ESI)  $m/z$ :** calculated for C<sub>28</sub>H<sub>26</sub>N<sub>3</sub>O<sub>4</sub> [M - H]<sup>-</sup>: 468.1929, found: 468.1927. HPLC purity: 95.4%, MeOH-H<sub>2</sub>O (80:20).

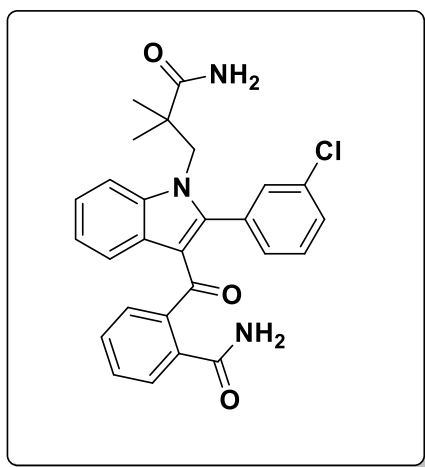
**(5ai) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(3-methylphenyl)-1*H*-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 56 mg, yield: 62%. **<sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>)**  $\delta$  8.12 (d,  $J$  = 7.7 Hz, 1H), 7.74 (d,  $J$  = 8.2 Hz, 1H), 7.70 (s, 1H), 7.42 (d,  $J$  = 7.6 Hz, 1H), 7.26 (t,  $J$  = 7.4 Hz, 1H), 7.23 – 7.19 (m, 2H), 7.18 (s, 1H), 7.14 (d,  $J$  = 7.5 Hz, 1H), 7.13 – 7.09 (m, 2H), 7.05 (t,  $J$  = 7.4 Hz, 1H), 6.98 (t,  $J$  = 7.2 Hz, 1H), 6.96 – 6.91 (m, 2H), 6.83 (d,  $J$  = 7.2

Hz, 1H), 4.44 (s, 2H), 2.08 (s, 3H), 0.69 (s, 6H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  192.9, 178.3, 169.7, 148.1, 142.4, 137.6, 136.9, 135.4, 130.7, 129.4, 129.2, 128.4, 127.7, 127.4, 127.3, 123.1, 122.4, 121.8, 115.1, 112.6, 50.6, 44.0, 21.1. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{28}\text{H}_{28}\text{N}_3\text{O}_3$   $[\text{M} + \text{H}]^+$ : 454.2125, found: 454.2129. HPLC purity: 95.2%, MeOH-H<sub>2</sub>O (80:20).

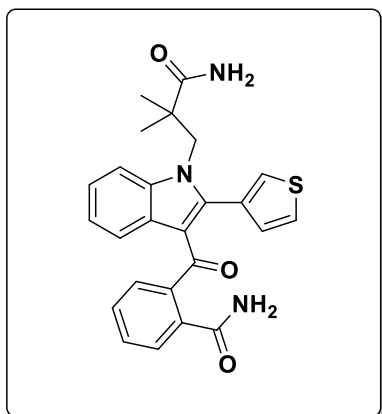
**(5ak) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(3-chlorophenyl)-1H-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 67 mg, yield: 71%.  $^1\text{H}$  NMR (600 MHz, DMSO)  $\delta$   $^1\text{H}$  NMR (600 MHz, DMSO)  $\delta$  8.06 (d,  $J$  = 7.9 Hz, 1H), 7.77 (d,  $J$  = 8.4 Hz, 2H), 7.49 (s, 1H), 7.47 (d,  $J$  = 7.7 Hz, 1H), 7.35 – 7.31 (m, 1H), 7.28 (t,  $J$  = 7.6 Hz, 1H), 7.24 (s, 1H), 7.23 – 7.18 (m, 4H), 7.11 (s, 1H), 7.04 (t,  $J$  = 7.4 Hz, 1H), 6.91 (s, 1H), 6.88 (d,  $J$  = 7.3 Hz, 1H),

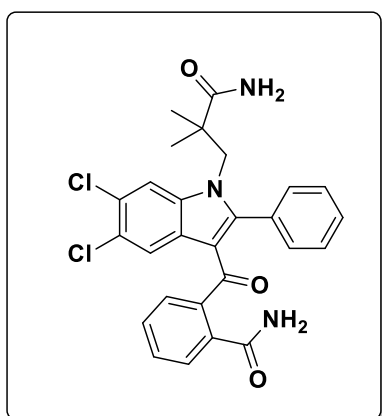
4.41 (d,  $J$  = 72.9 Hz, 2H), 0.87 – 0.85 (m, 3H), 0.71 (s, 6H).  $^{13}\text{C}\{^1\text{H}\}$  NMR (151 MHz, DMSO- $d_6$ )  $\delta$  194.6, 179.9, 171.5, 147.8, 144.2, 139.6, 137.3, 134.8, 134.6, 131.5, 131.3, 130.7, 130.5, 129.5, 129.0, 125.3, 124.5, 123.8, 117.3, 114.7, 114.5, 52.6, 46.0. HRMS (ESI)  $m/z$ : calculated for  $\text{C}_{28}\text{H}_{25}\text{ClN}_3\text{O}_3$   $[\text{M} + \text{H}]^+$ : 474.1579, found: 474.1579. HPLC purity: 99.4%, MeOH-H<sub>2</sub>O (80:20).

**(5al) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(thiophen-3-yl)-1H-indole-3-carbonyl)benzamide**



Following by general procedure for the synthesis of **5aa**. White solid, 66 mg, yield: 75%. **<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>)** δ 8.08 (d, *J* = 7.5 Hz, 1H), 7.80 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.62 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.43 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.32 – 7.18 (m, 5H), 7.15 – 7.03 (m, 3H), 6.94 (s, 1H), 6.88 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.47 (s, 2H), 0.71 (s, 6H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)** δ 192.2, 177.7, 169.7, 142.7, 141.7, 137.3, 135.5, 130.5, 129.7, 128.7, 128.2, 127.4, 127.2, 126.9, 125.4, 122.8, 122.0, 121.2, 114.9, 112.0, 50.3, 43.6, 24.0. **HRMS (ESI) *m/z***: calculated for C<sub>25</sub>H<sub>22</sub>N<sub>3</sub>O<sub>3</sub>S [M - H]<sup>-</sup>: 444.1387, found: 444.1389.

**(5am) 2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5,6-dichloro-2-phenyl-1H-indole-3-carbonyl)benzamide**



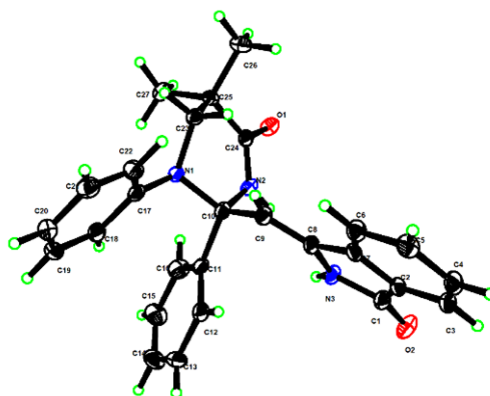
Following by general procedure for the synthesis of **5aa**. White solid, 62 mg, yield: 61%. **<sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)** δ 8.24 (d, *J* = 7.1 Hz, 1H), 7.90 (s, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.54 (s, 1H), 7.42 (s, 1H), 7.34 – 7.25 (m, 4H), 7.21 – 7.12 (m, 3H), 7.09 (s, 1H), 6.98 (s, 1H), 6.91 (s, 1H), 4.39 (s, 2H), 0.68 (s, 6H). **<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, DMSO-*d*<sub>6</sub>)** δ 177.7, 167.0, 148.1, 141.5, 137.3, 135.2, 131.6, 131.4, 130.5, 130.3, 129.9, 129.0, 128.3, 127.4, 126.8, 123.1, 122.4, 121.4, 114.5, 112.3, 50.3, 43.5, 24.2. **HRMS (ESI) *m/z***: calculated for C<sub>27</sub>H<sub>22</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>3</sub> [M - H]<sup>-</sup>: 506.1044, found: 506.1048.

## VIII. X-ray Crystallographic Data

Single Crystal X-ray Diffraction (SCXRD): X-ray diffractions of all single crystals were carried out at 100(2) K on a Bruker D8 VENTURE diffractometer using Mo-K $\alpha$  radiation ( $\lambda = 0.71073$  Å). Integration and scaling of intensity data was performed using the SAINT program. Data were corrected for the effects of absorption using SADABS. The structures were solved by direct method and refined with full-matrix least-squares technique using SHELX-2014 software. Non-hydrogen atoms were refined with anisotropic displacement parameters, and hydrogen atoms were placed in calculated positions and refined with a riding model.

### (1) The Single Crystal Structure of 3aa (Deposition Data: CCDC 2410303)

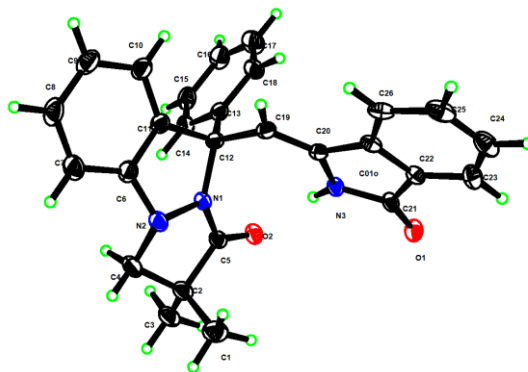
Crystal Data for C<sub>54</sub>H<sub>52</sub>N<sub>6</sub>O<sub>5</sub> (M = 865.01 g/mol): monoclinic, space group P2<sub>1</sub>/c (no. 14),  $a = 10.9888(2)$  Å,  $b = 18.4115(5)$  Å,  $c = 12.1884(3)$  Å,  $\alpha = 90^\circ$ ,  $\beta = 109.3740(10)^\circ$ ,  $\gamma = 90^\circ$ ,  $V = 2326.32(10)$  Å<sup>3</sup>,  $Z = 2$ ,  $T = 170(2)$  K,  $\mu(\text{CuK}\alpha) = 0.640$  mm<sup>-1</sup>,  $D_{\text{calc}} = 1.235$  g/cm<sup>3</sup>, 22292 reflections measured ( $8.53^\circ \leq 2\theta \leq 149.236^\circ$ ), 4691 unique ( $R_{\text{int}} = 0.0599$ ,  $R_{\text{sigma}} = 0.0412$ ) which were used in all calculations. The final  $R_1$  was 0.1018 ( $I > 2\sigma(I)$ ) and  $wR_2$  was 0.2367 (all data).



### (2) The Single Crystal Structure of 4aa (Deposition Data: CCDC 2410625)

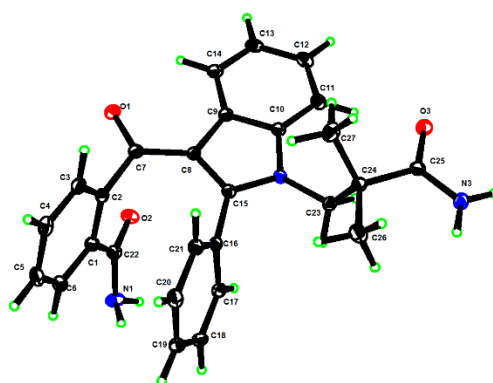
Crystal Data for C<sub>55</sub>H<sub>48</sub>Cl<sub>2</sub>N<sub>6</sub>O<sub>4</sub> (M = 927.89 g/mol): monoclinic, space group Pn (no. 7),  $a = 14.0724(3)$  Å,  $b = 41.3599(10)$  Å,  $c = 16.7154(4)$  Å,  $\alpha = 90^\circ$ ,  $\beta = 102.8130(10)^\circ$ ,  $\gamma = 90^\circ$ ,  $V = 9486.7(4)$  Å<sup>3</sup>,  $Z = 8$ ,  $T = 170(2)$  K,  $\mu(\text{CuK}\alpha) = 1.662$  mm<sup>-1</sup>,  $D_{\text{calc}} = 1.299$  g/cm<sup>3</sup>, 150635 reflections measured ( $4.272^\circ \leq 2\theta \leq 149.836^\circ$ ), 36461 unique ( $R_{\text{int}} =$

0.0557,  $R_{\text{sigma}} = 0.0449$ ) which were used in all calculations. The final  $R_1$  was 0.0526 ( $I > 2\sigma(I)$ ) and  $wR_2$  was 0.1531 (all data).



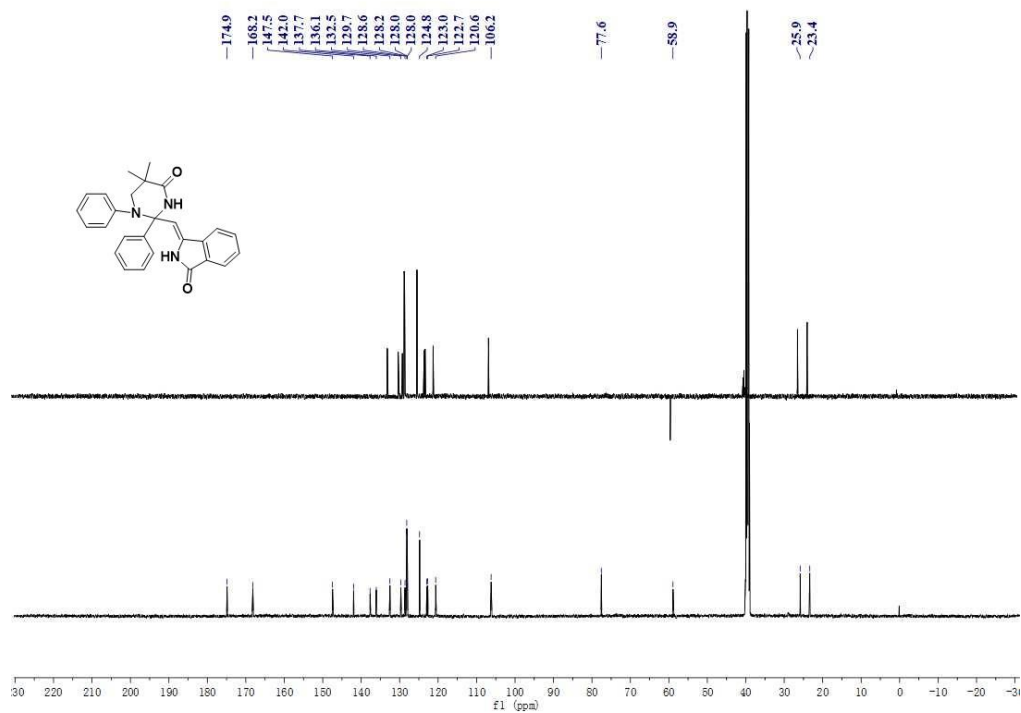
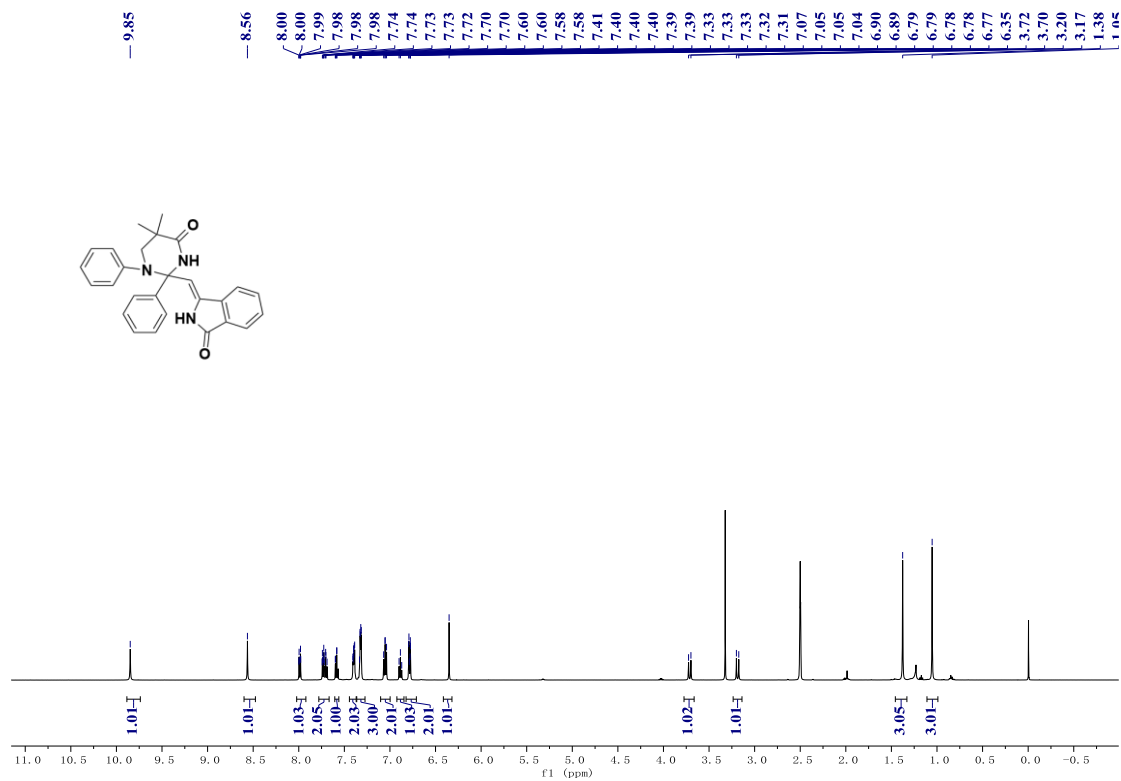
### (3) The Single Crystal Structure of 5aa (Deposition Data: CCDC 2410305)

Crystal Data for  $\text{C}_{27}\text{H}_{25}\text{N}_3\text{O}_3$  ( $M = 439.50$  g/mol): orthorhombic, space group  $Pbca$  (no. 61),  $a = 19.2491(12)$  Å,  $b = 9.9787(4)$  Å,  $c = 22.4268(14)$  Å,  $\alpha = 90^\circ$ ,  $\beta = 90^\circ$ ,  $\gamma = 90^\circ$ ,  $V = 4307.8(4)$  Å<sup>3</sup>,  $Z = 8$ ,  $T = 170.00$  K,  $\mu(\text{MoK}\alpha) = 0.720$  mm<sup>-1</sup>,  $D_{\text{calc}} = 1.355$  g/cm<sup>3</sup>, 18845 reflections measured ( $7.884^\circ \leq 2\theta \leq 127.572^\circ$ ), 3488 unique ( $R_{\text{int}} = 0.0995$ ,  $R_{\text{sigma}} = 0.0666$ ) which were used in all calculations. The final  $R_1$  was 0.0590 ( $I > 2\sigma(I)$ ) and  $wR_2$  was 0.1477 (all data).

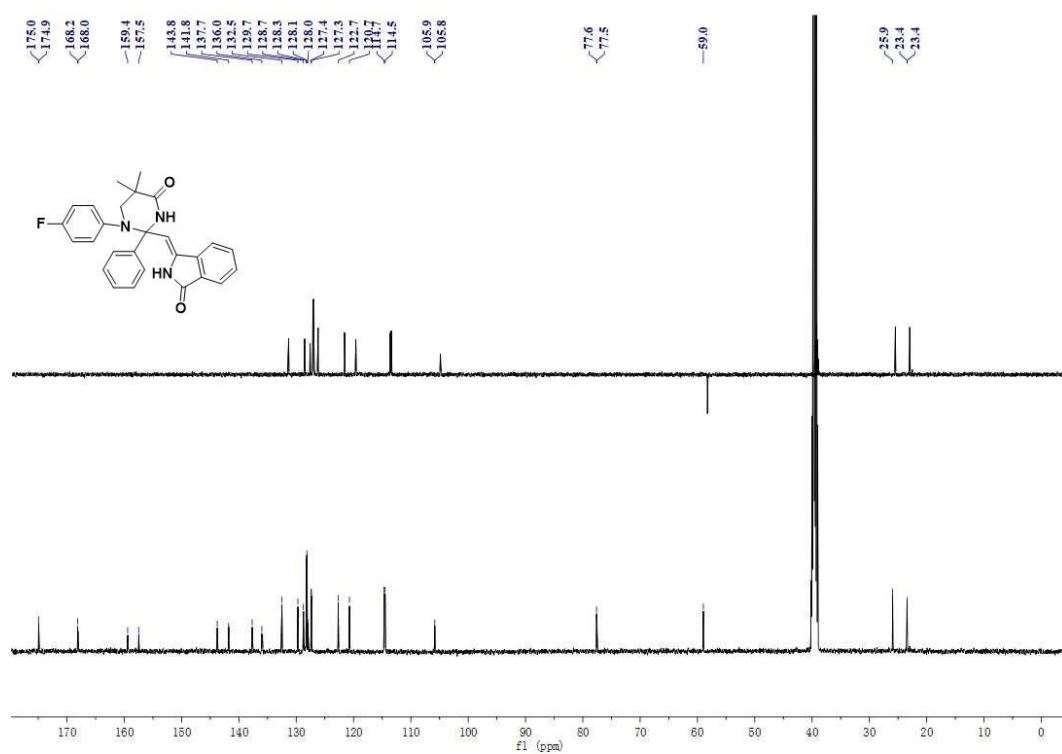
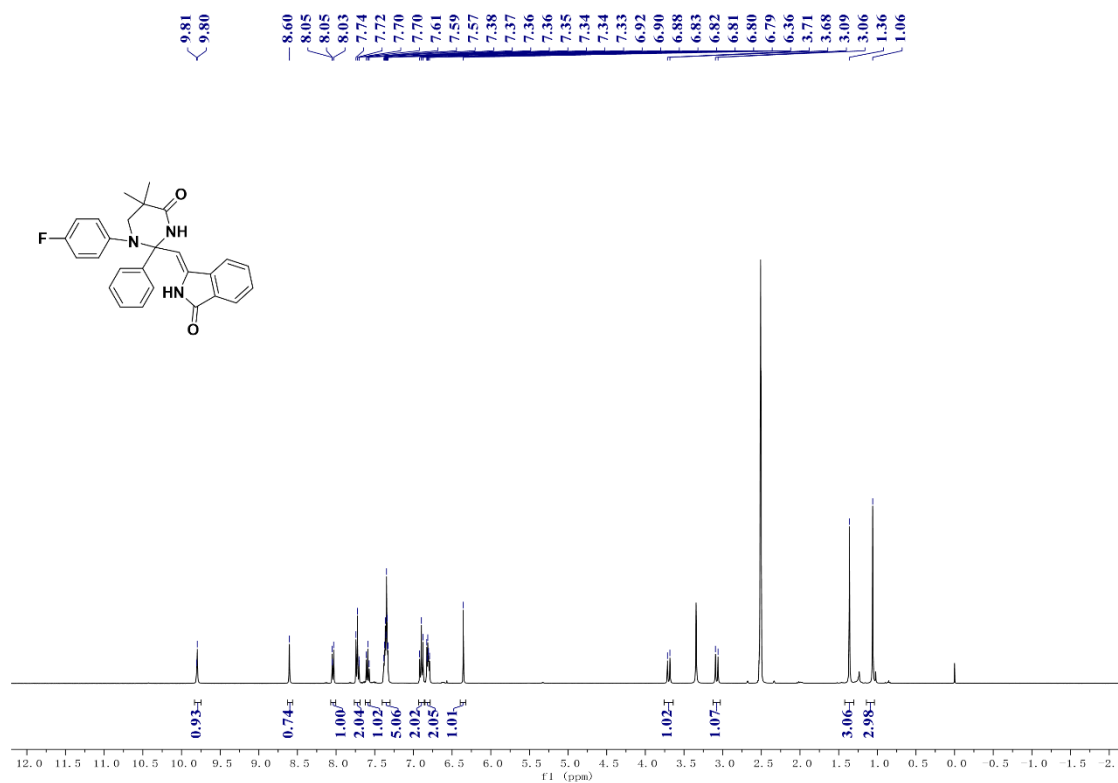


## IX. NMR Spectra of Products

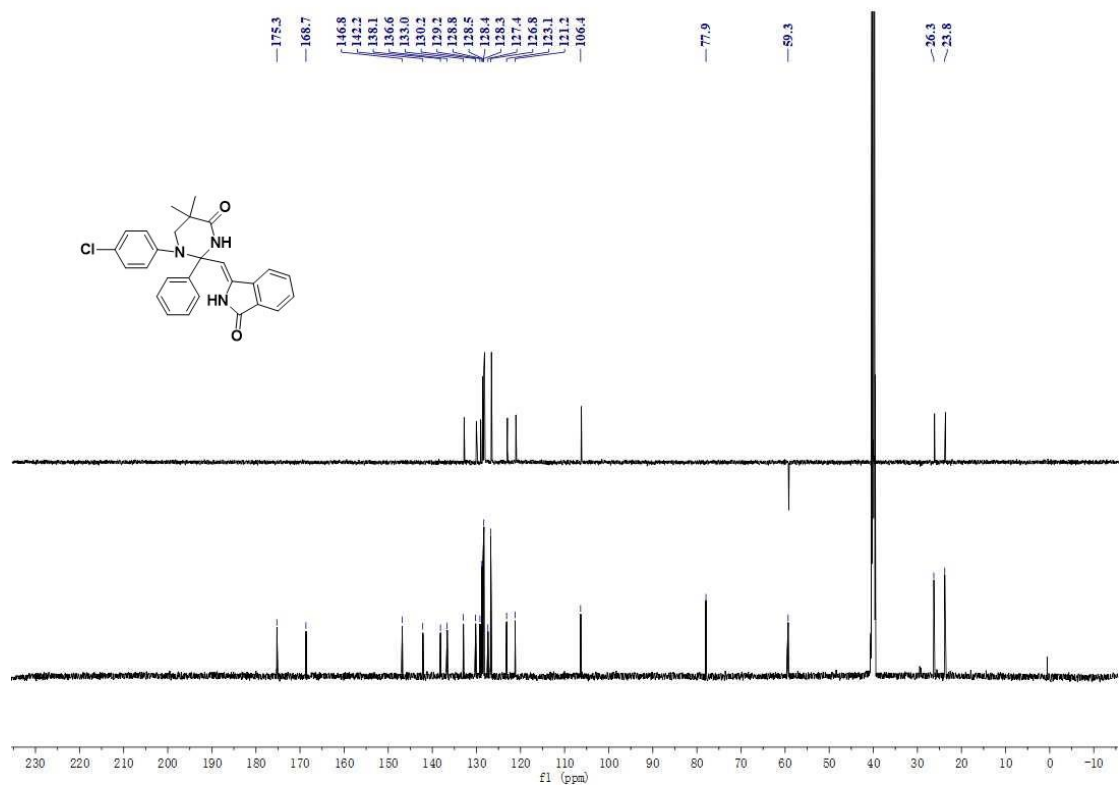
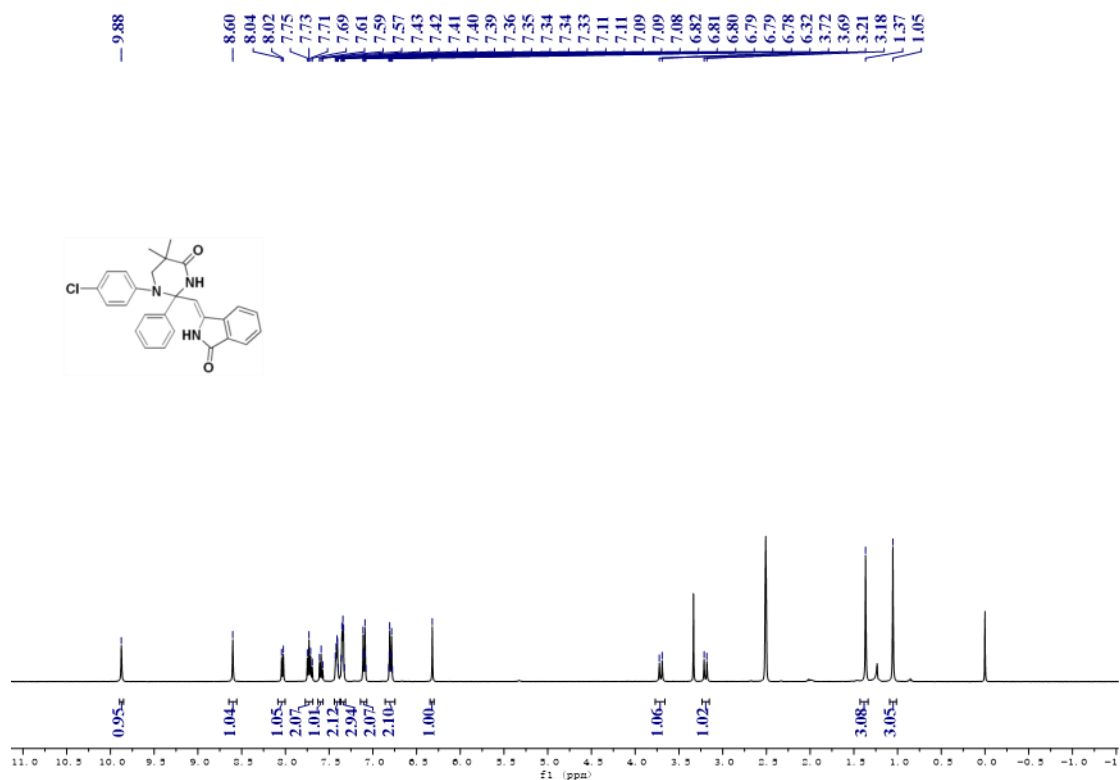
(*Z/E*)-3-((5,5-dimethyl-4-oxo-1,2-diphenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3aa)



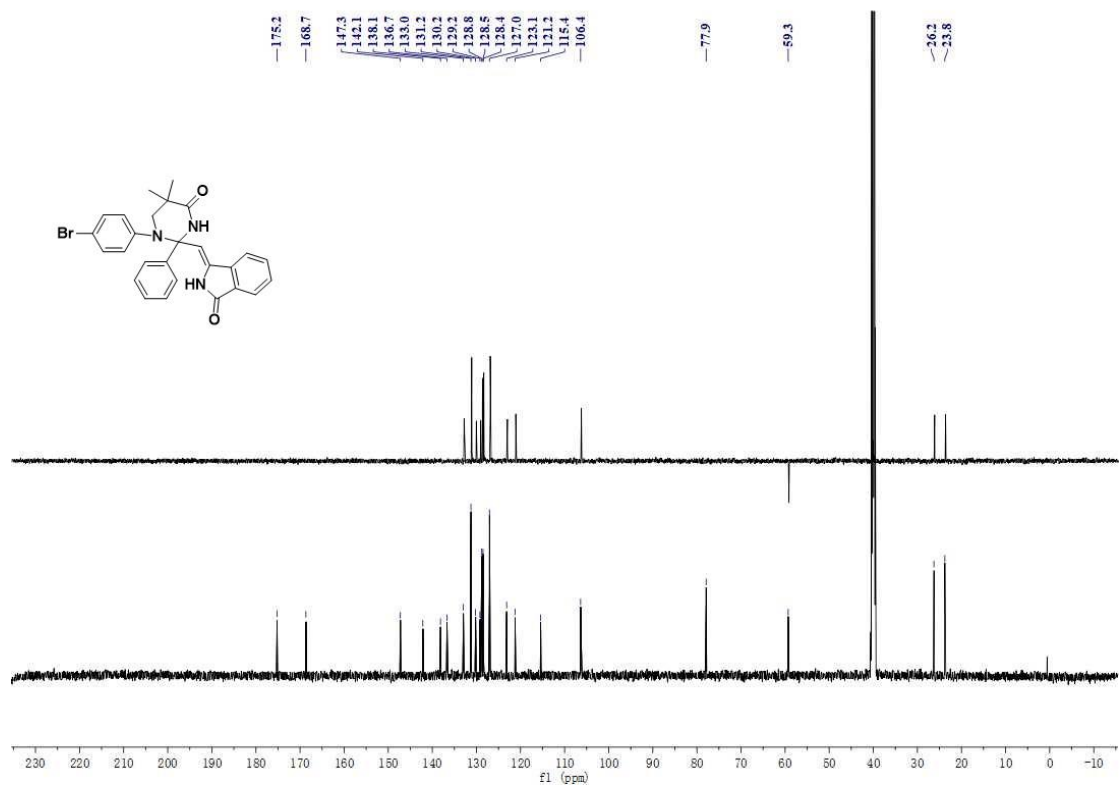
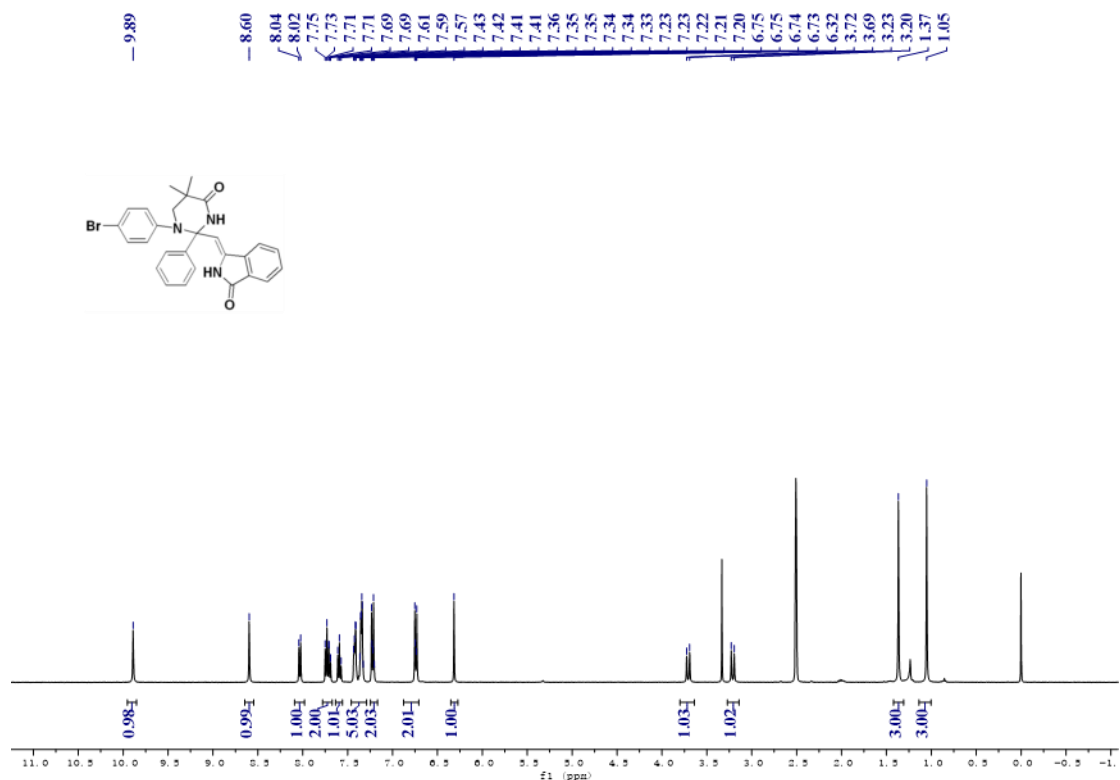
**(*Z/E*)-3-((1-(4-fluorophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ba)**



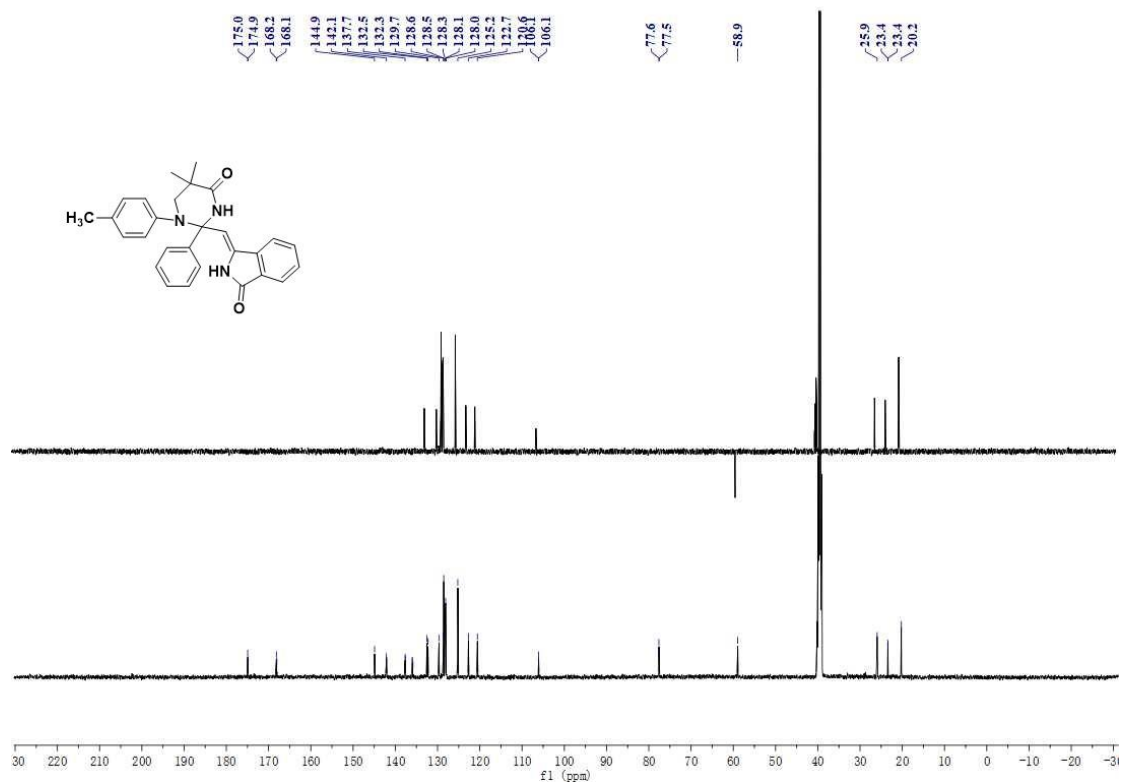
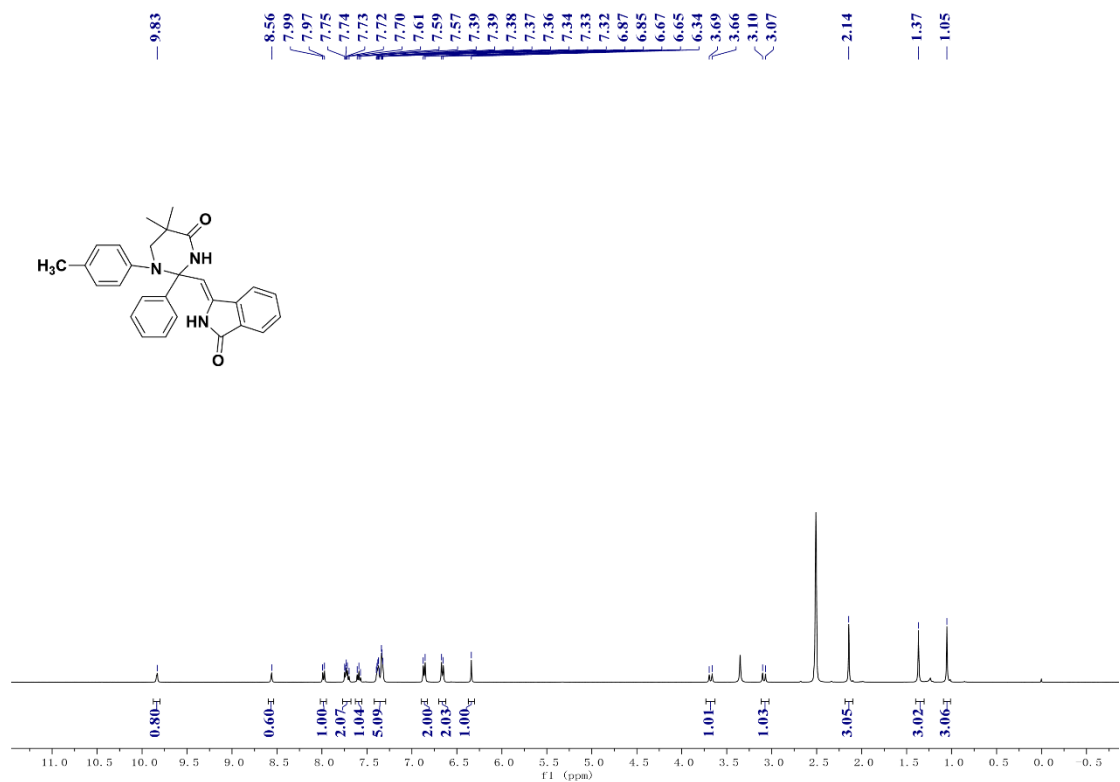
**(Z/E)-3-((1-(4-chlorophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ca)**



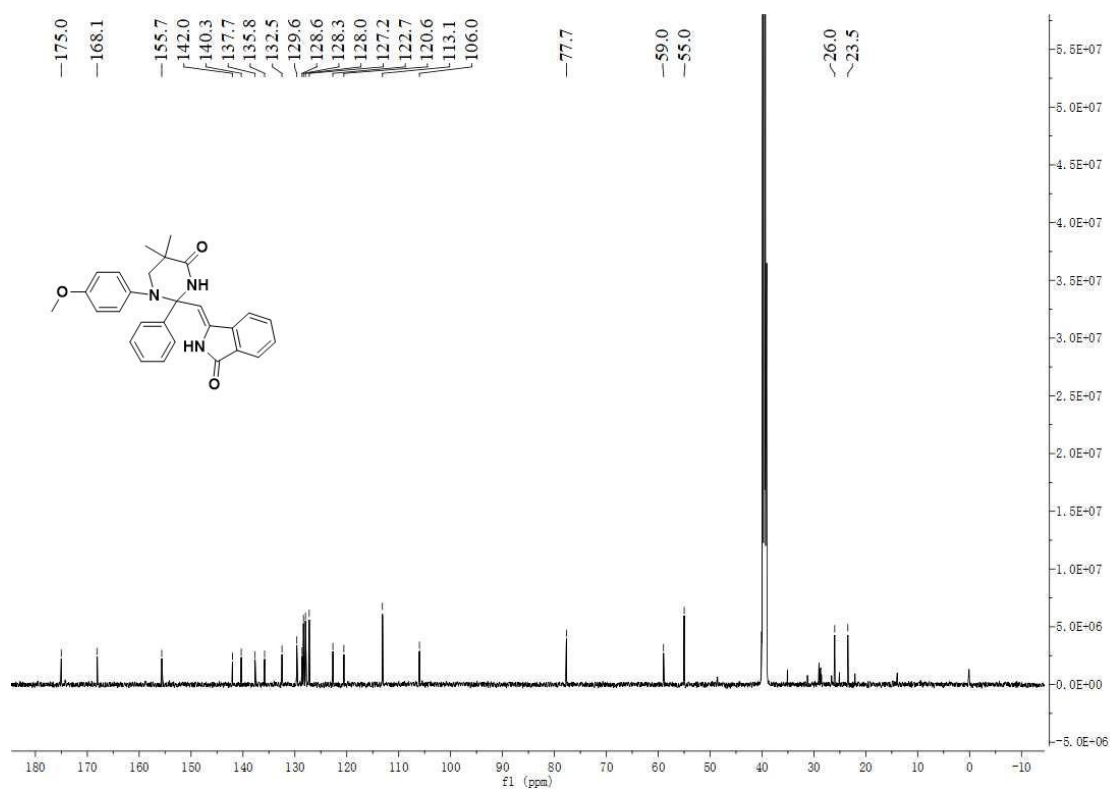
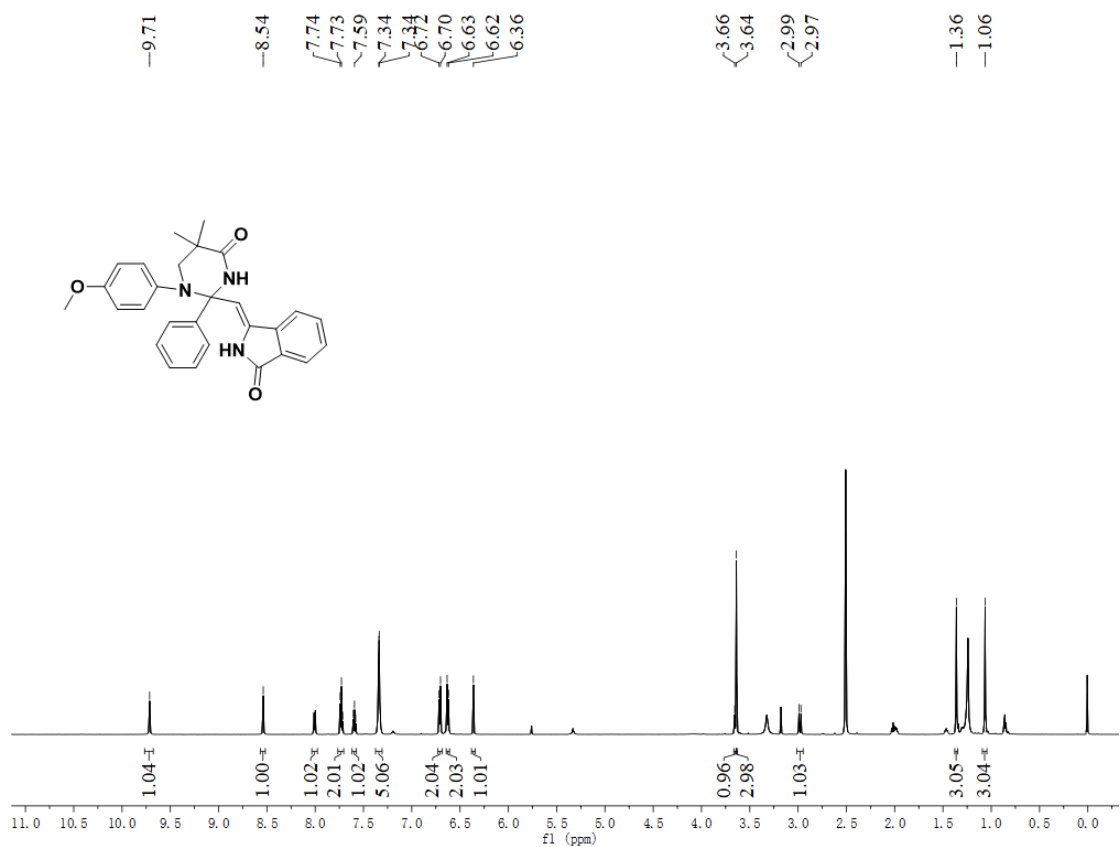
**(*Z/E*)-3-((1-(4-bromophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3da)**



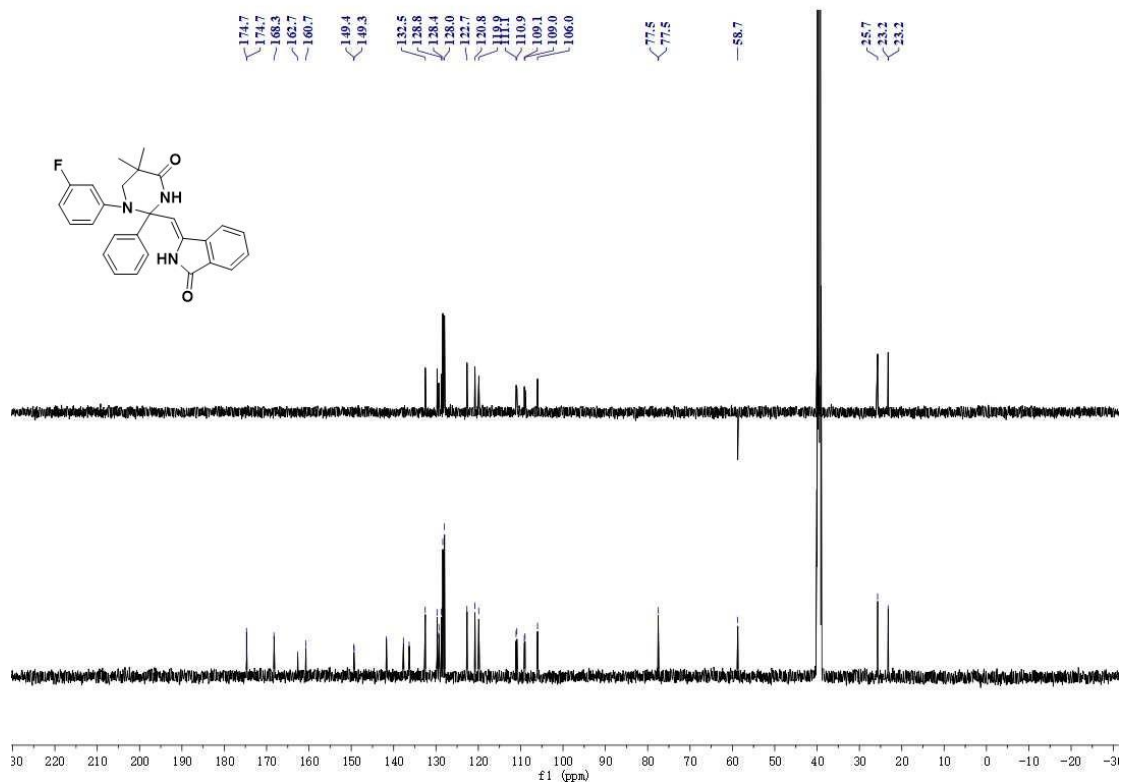
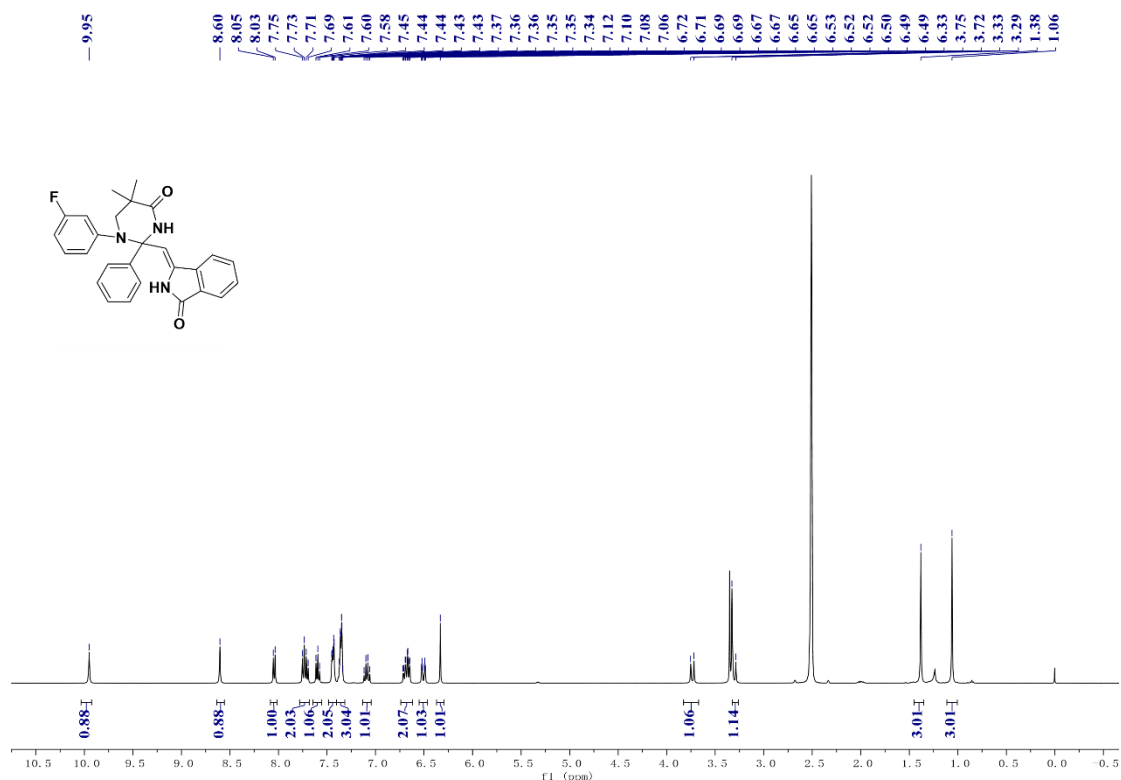
**(*Z/E*)-3-((5,5-dimethyl-4-oxo-2-phenyl-1-(*p*-tolyl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ea)**



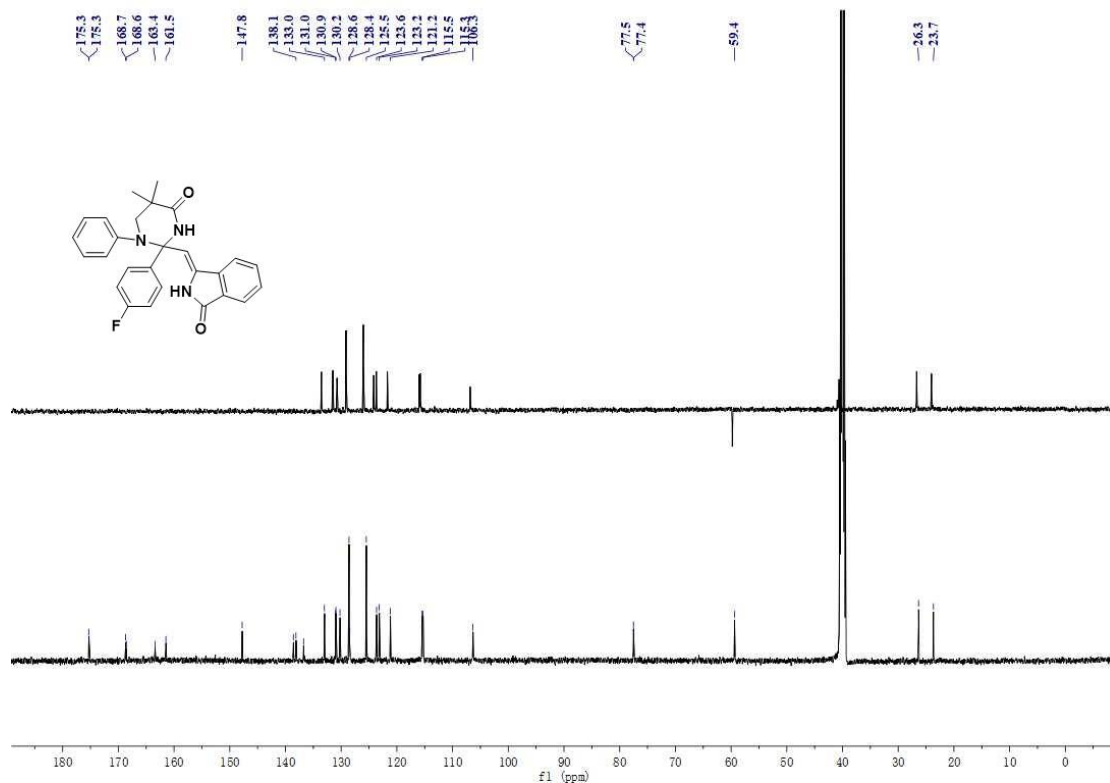
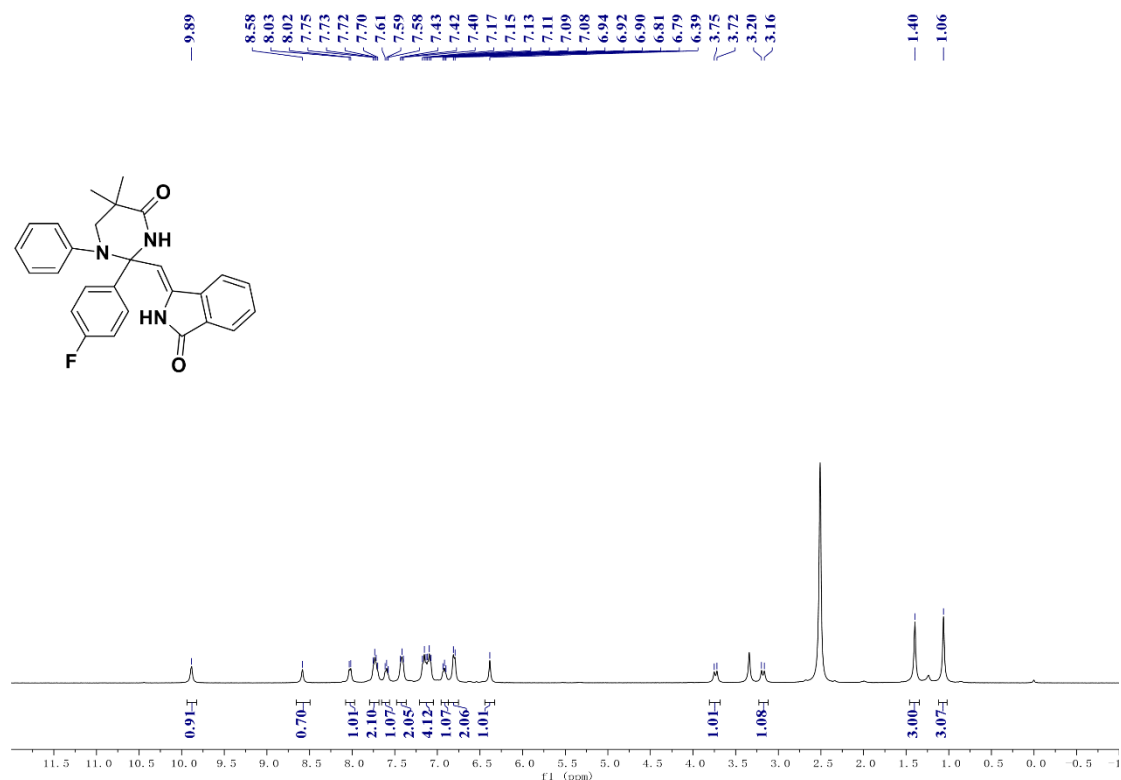
**(Z/E)-3-((1-(4-methoxyphenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3fa)**



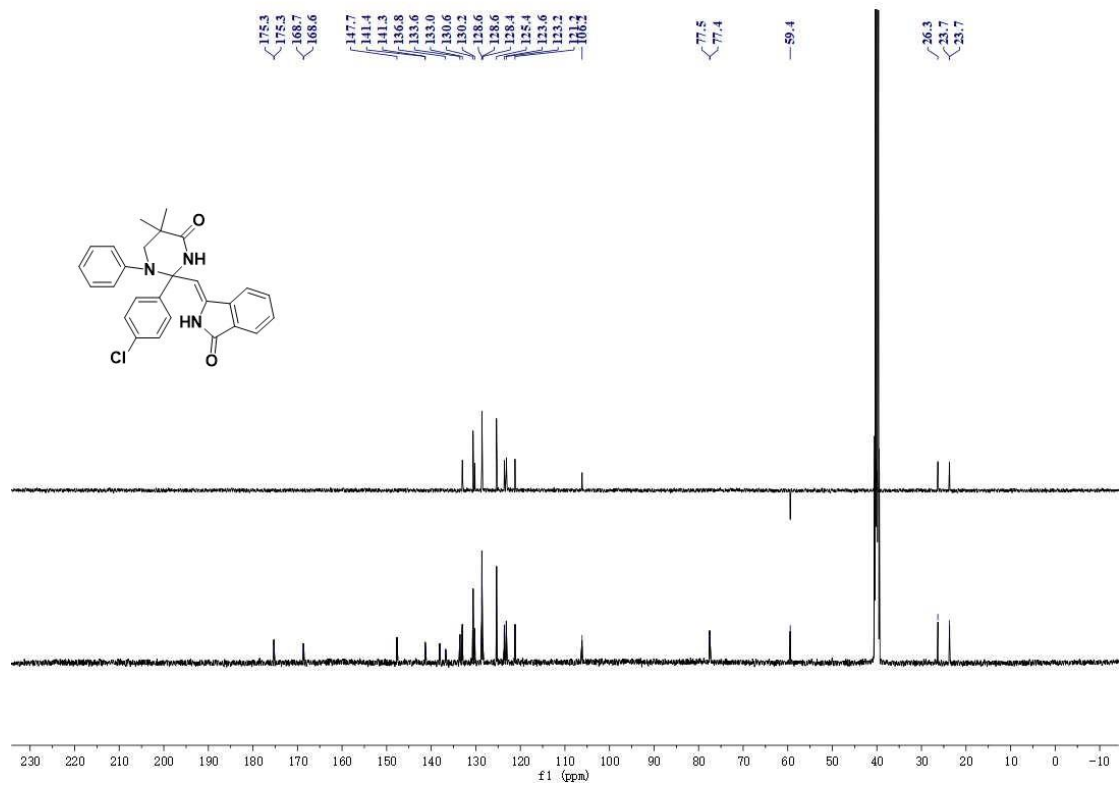
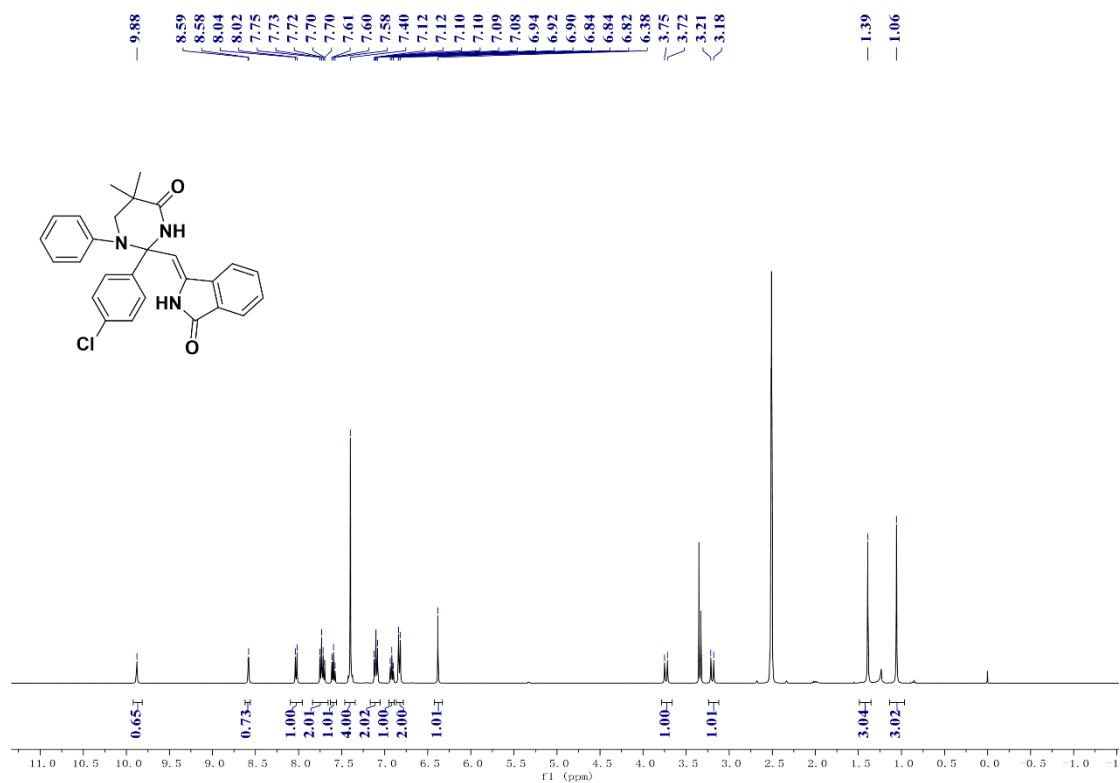
**(Z/E)-3-((1-(3-fluorophenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ia)**



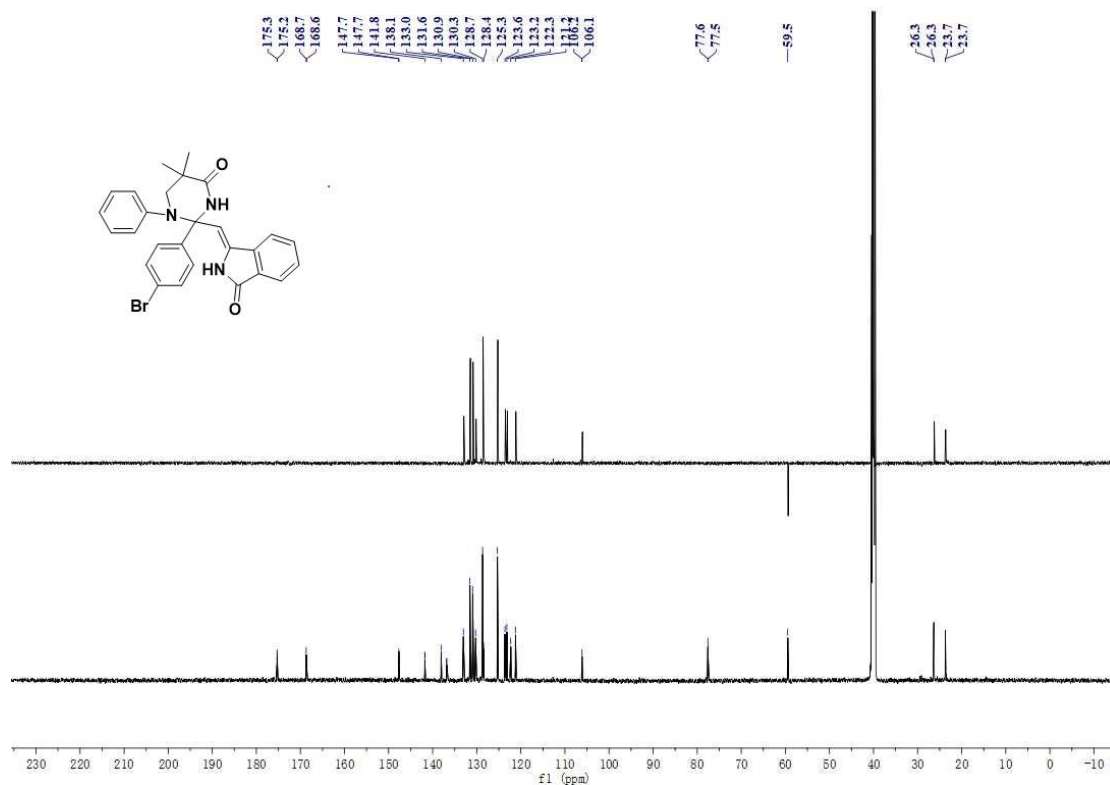
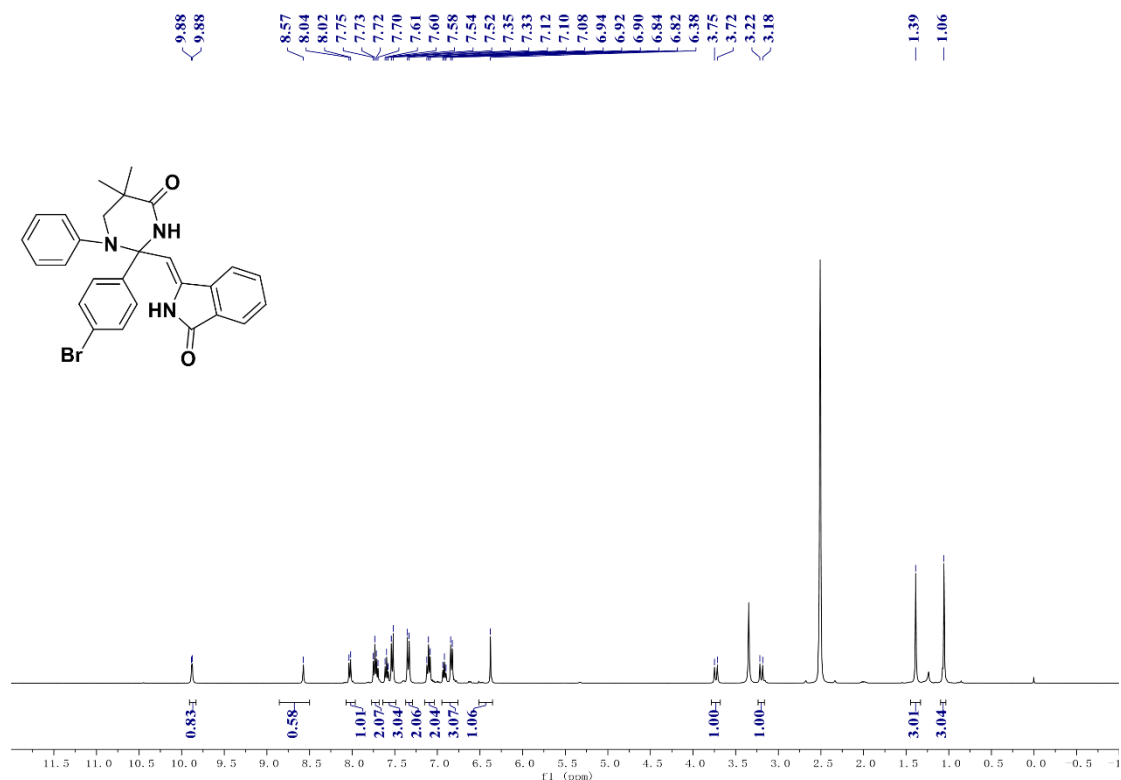
**(Z/E)-3-((2-(4-fluorophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ab)**



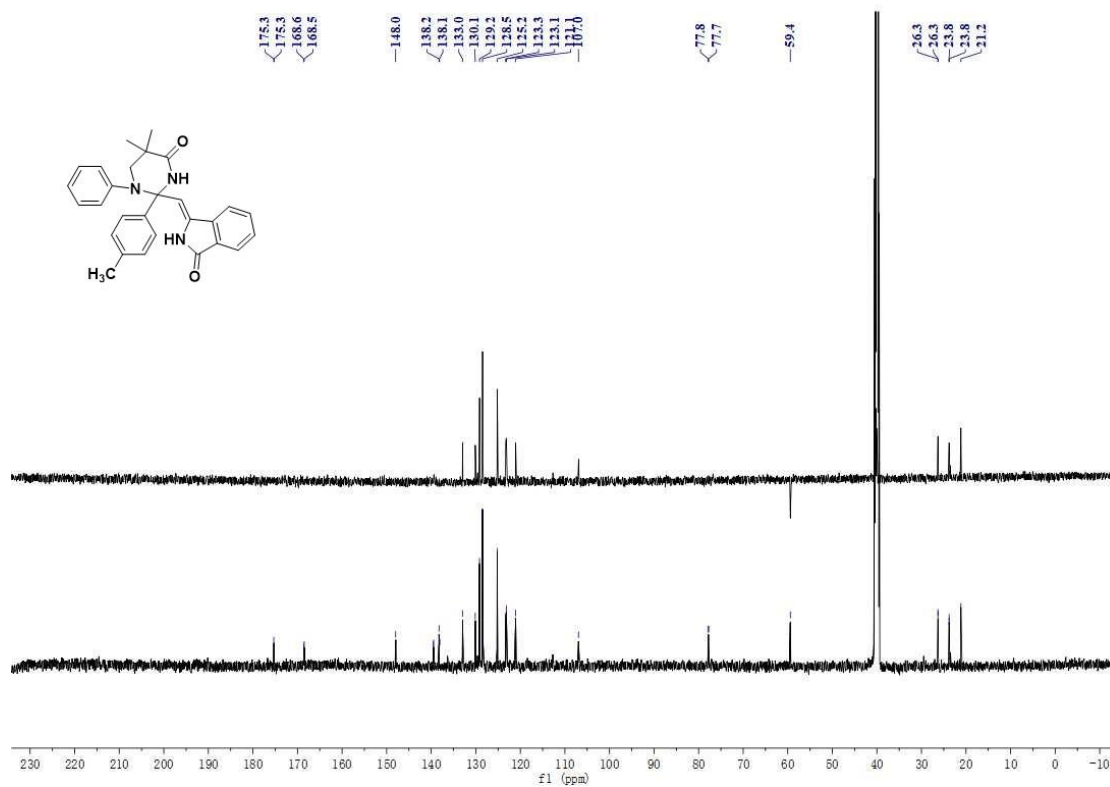
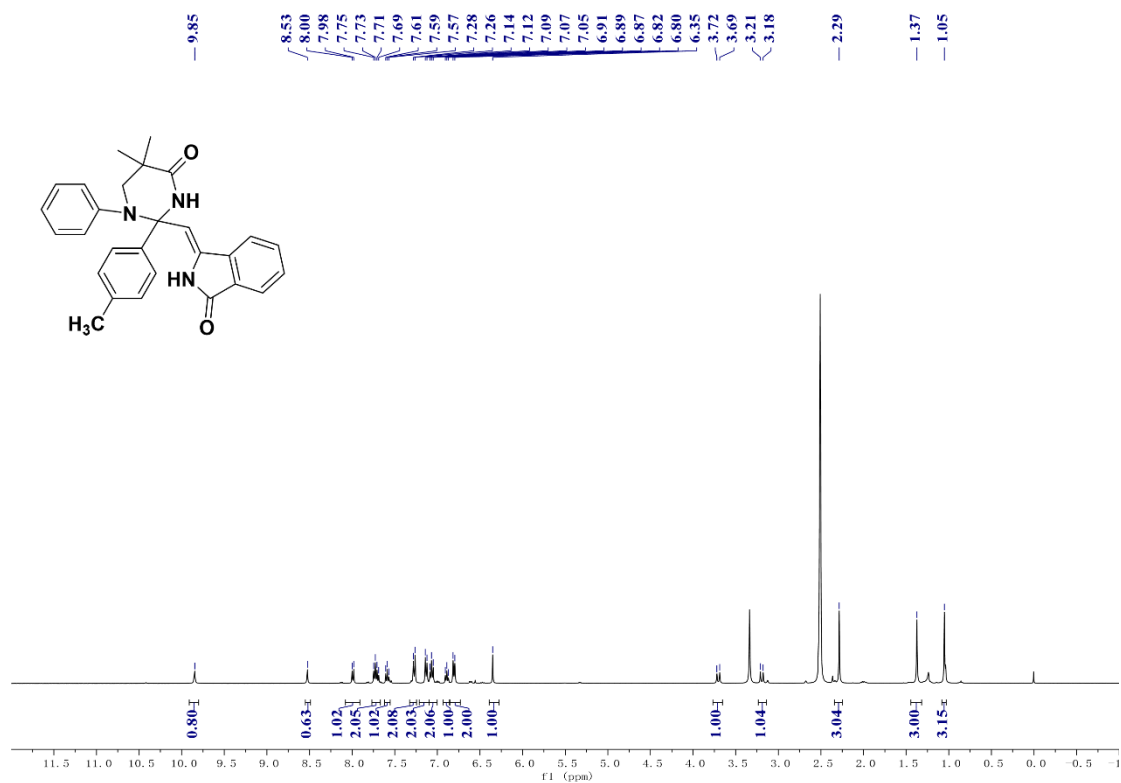
**(*Z/E*)-3-((2-(4-chlorophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ac)**



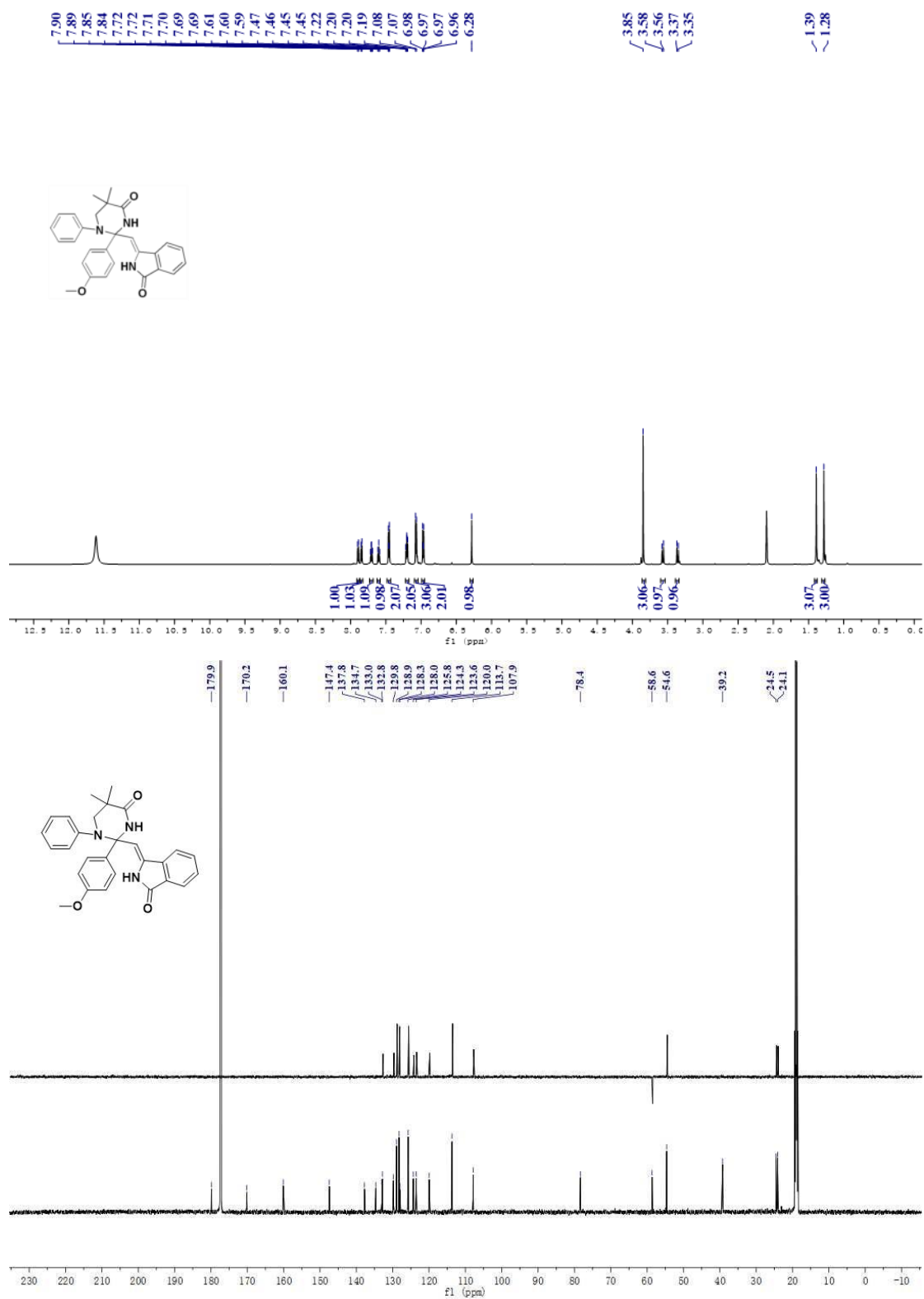
**(Z/E)-3-((2-(4-bromophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ad)**



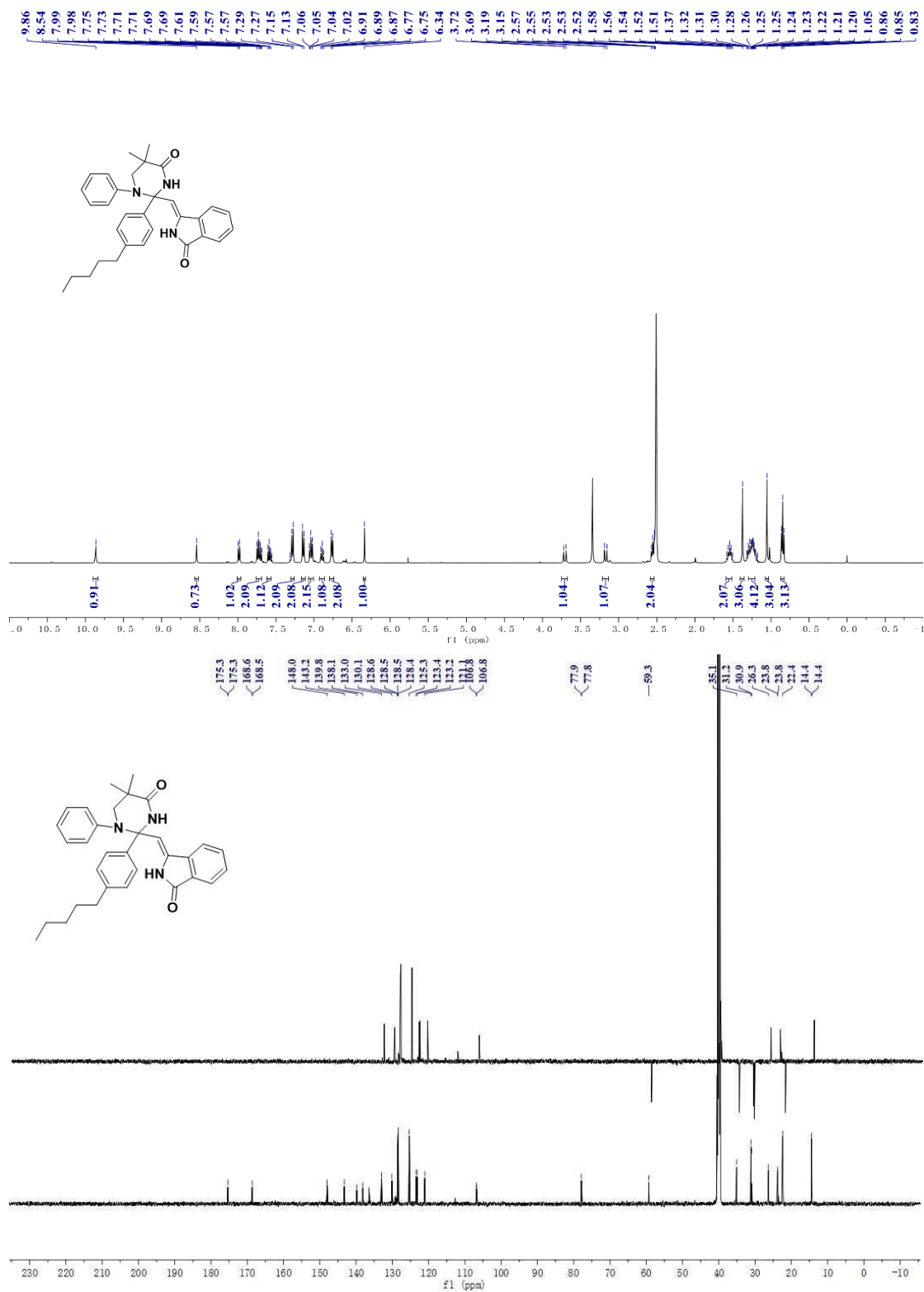
**(Z/E)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(p-tolyl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ae)**



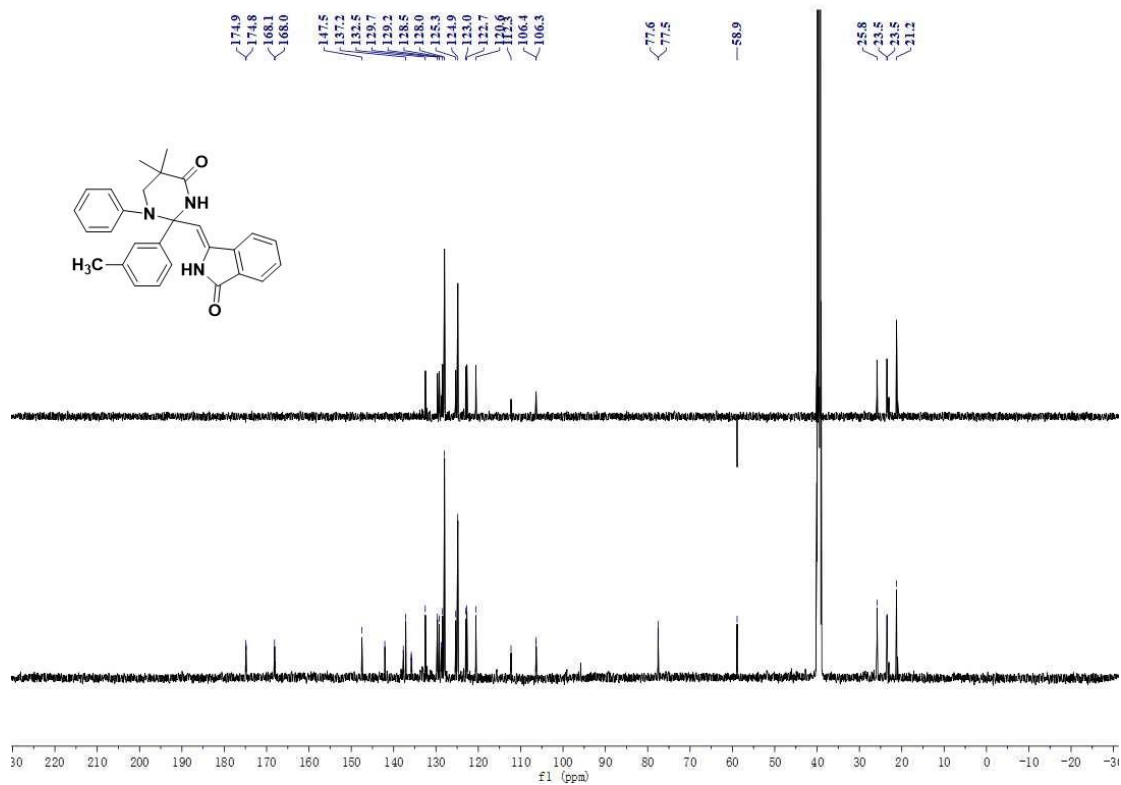
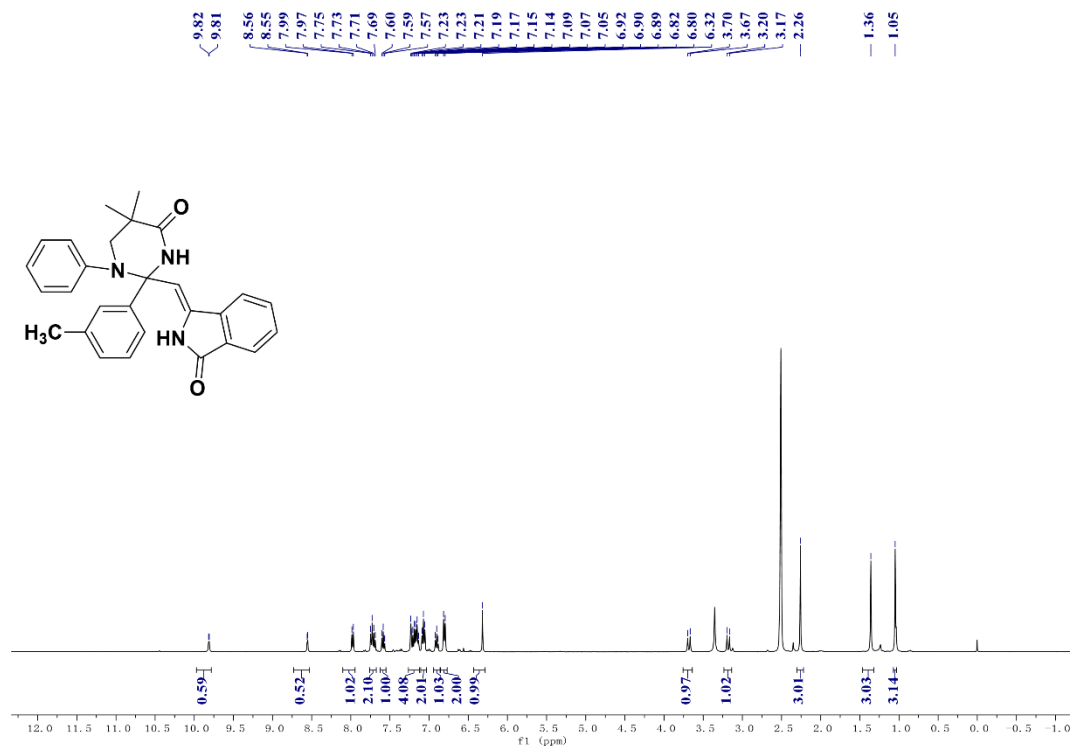
**(Z/E)-3-((2-(4-methoxyphenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3af)**



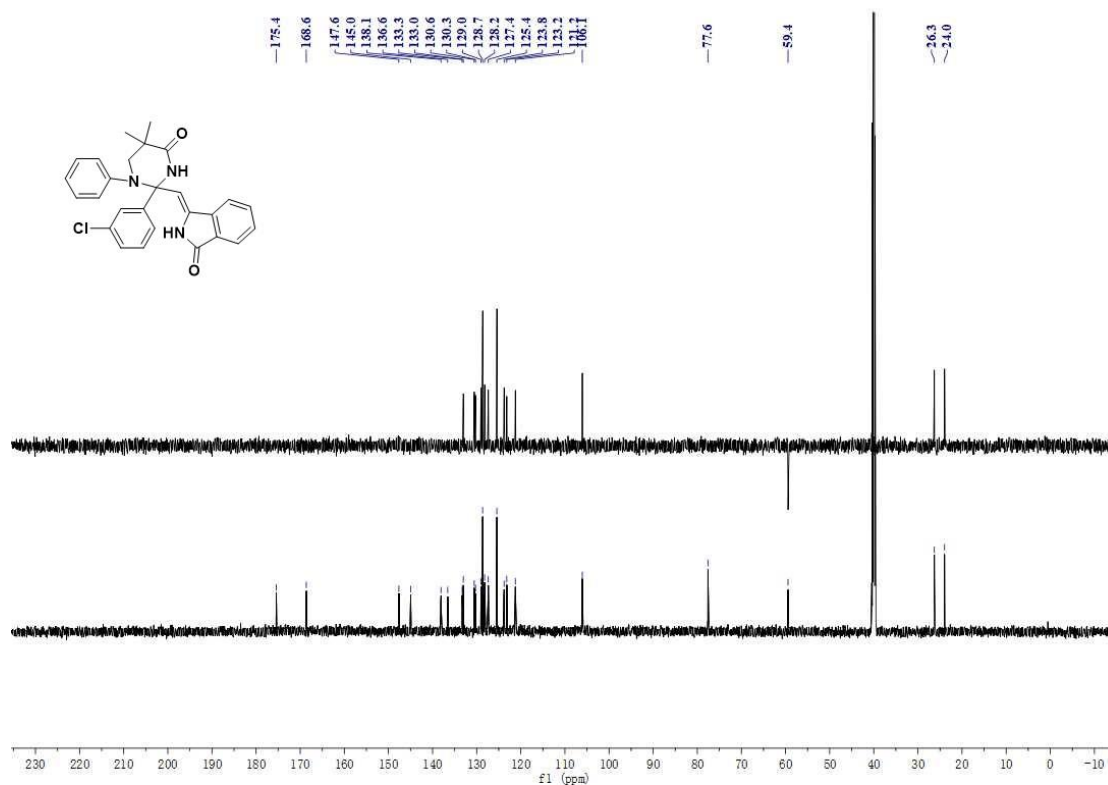
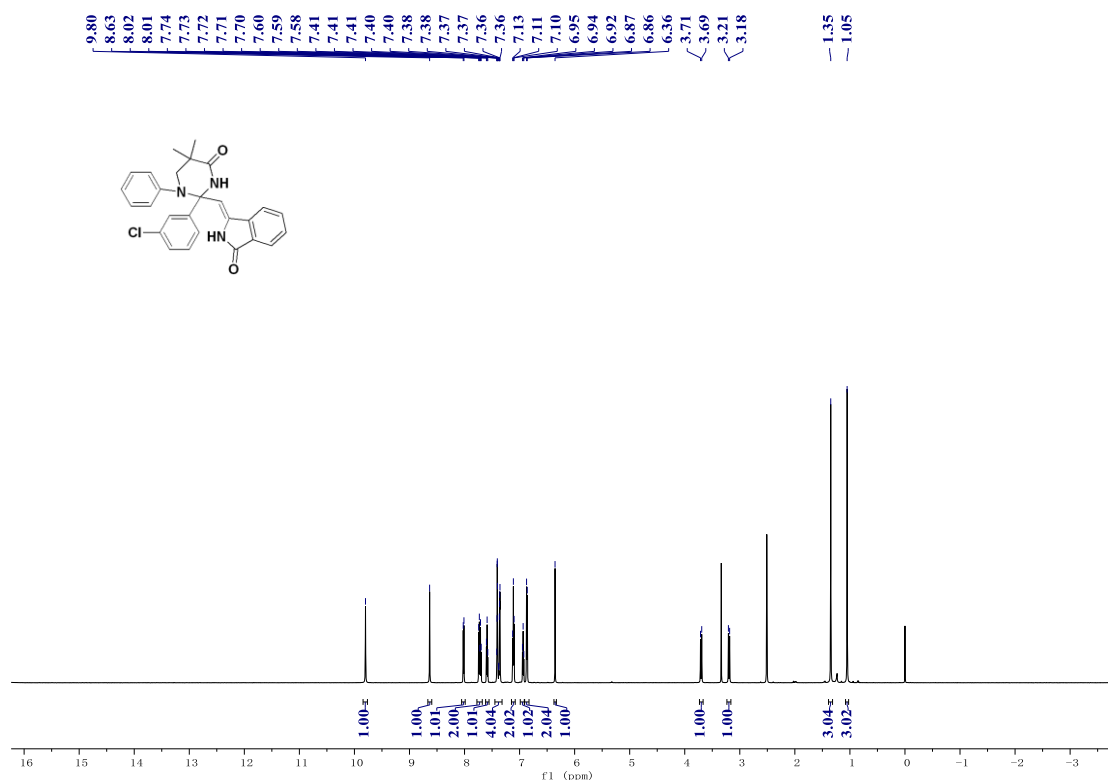
**(Z/E)-3-((5,5-dimethyl-4-oxo-2-(4-pentylphenyl)-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ag)**



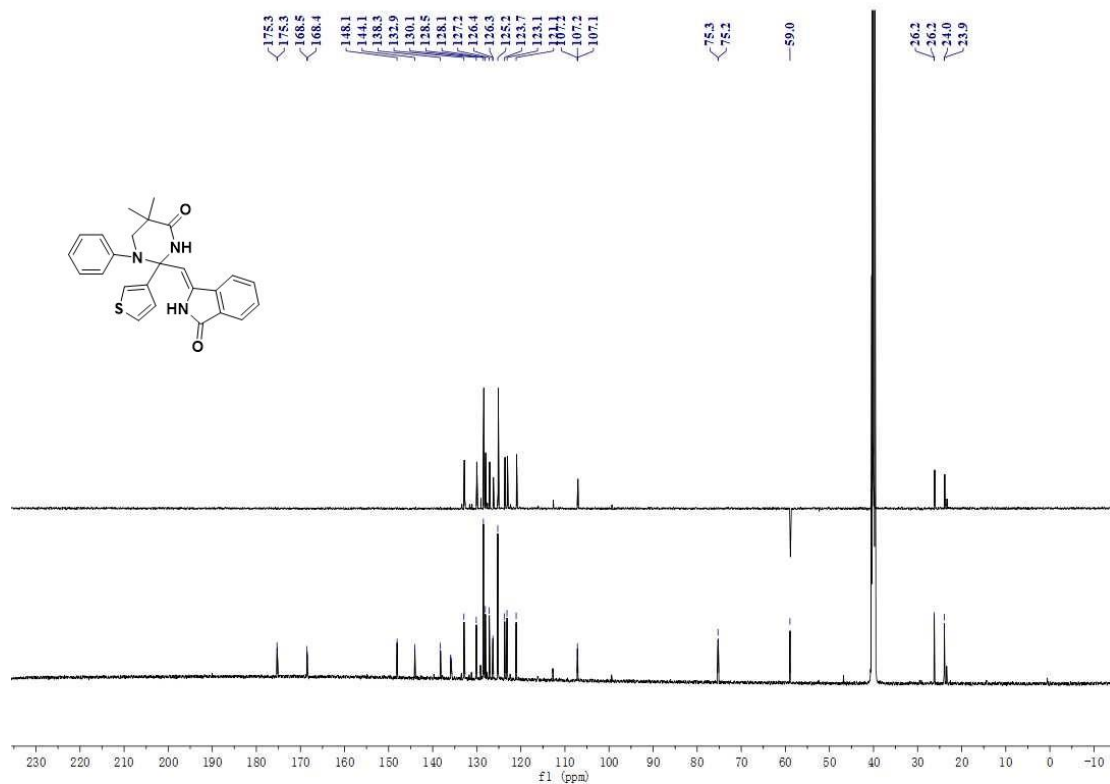
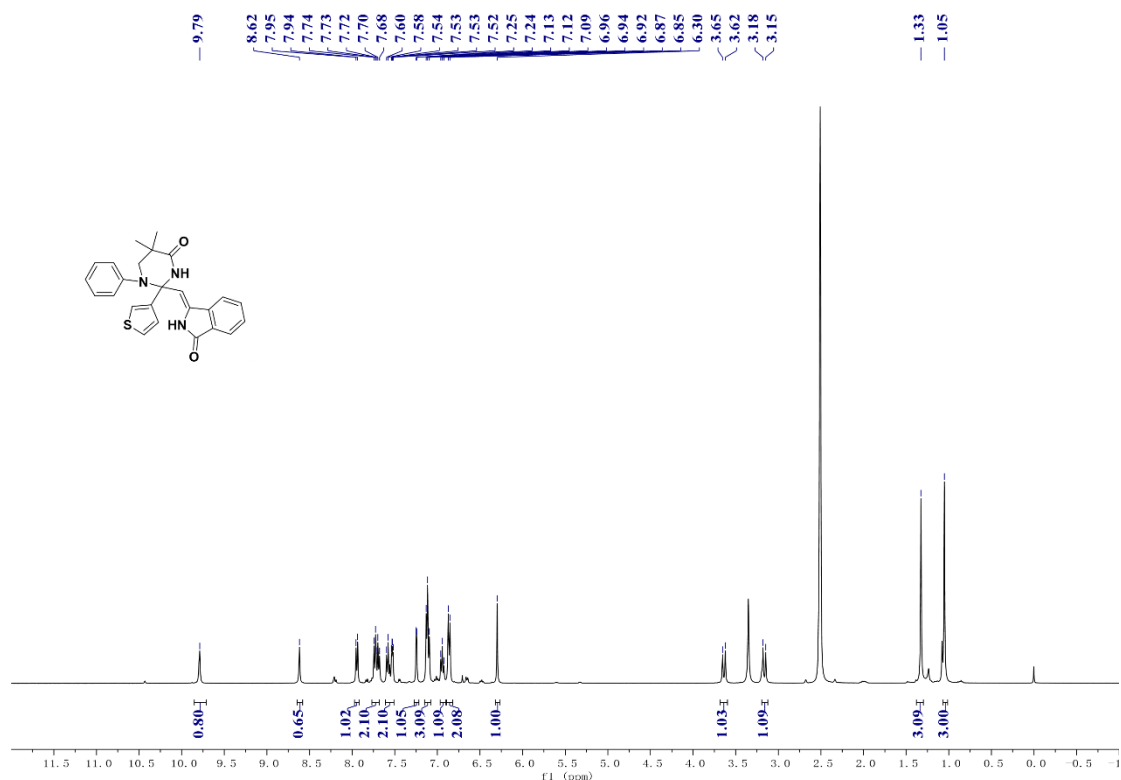
**(*Z/E*)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(*m*-tolyl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ai)**



**(*Z/E*)-3-((2-(3-chlorophenyl)-5,5-dimethyl-4-oxo-1-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ak)**

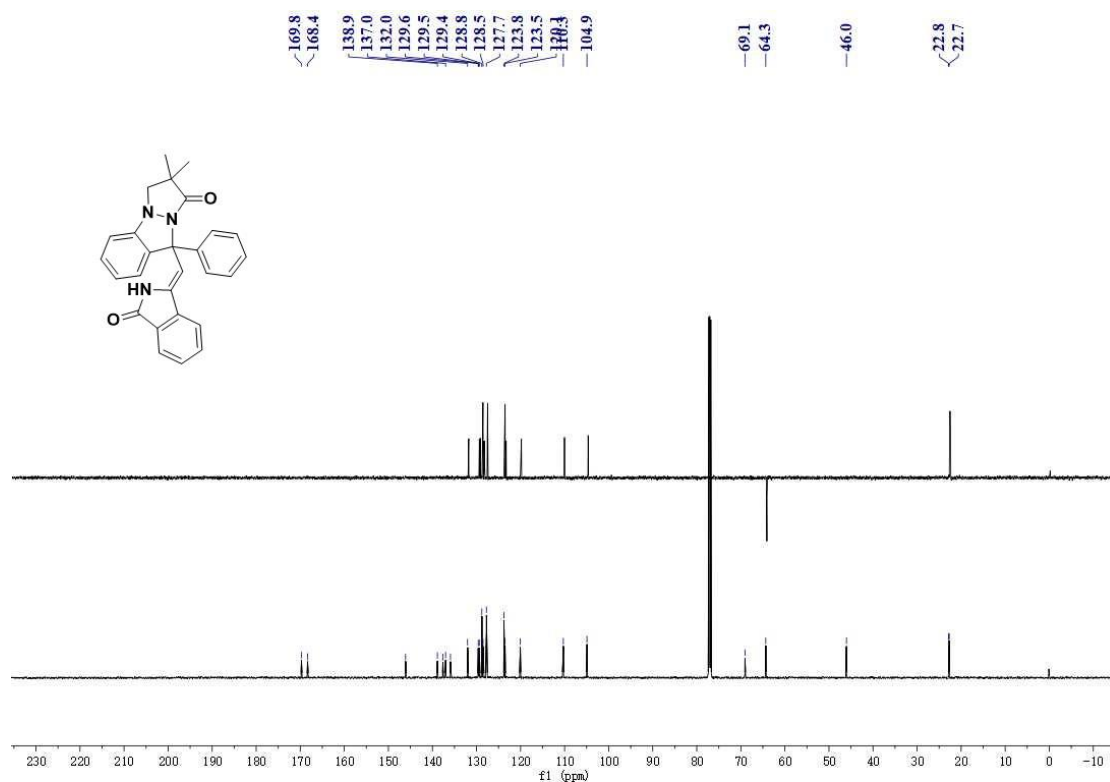
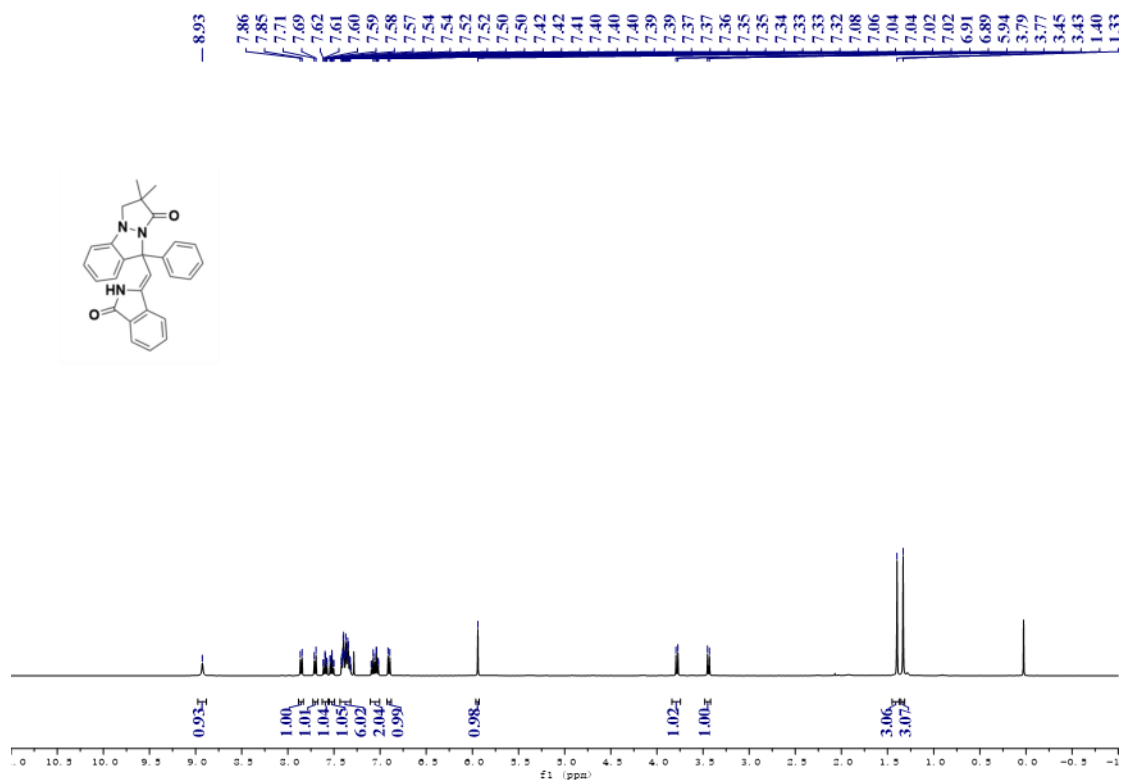


**(Z/E)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(thiophen-3-yl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3al)**



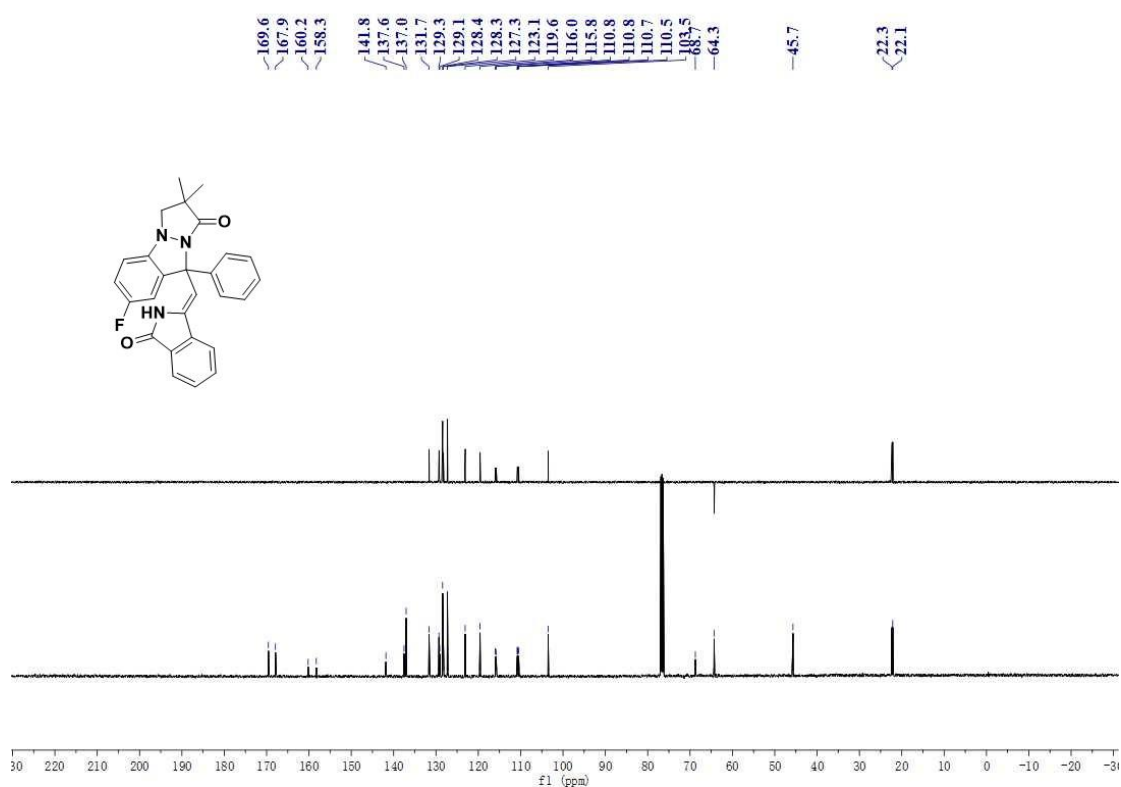
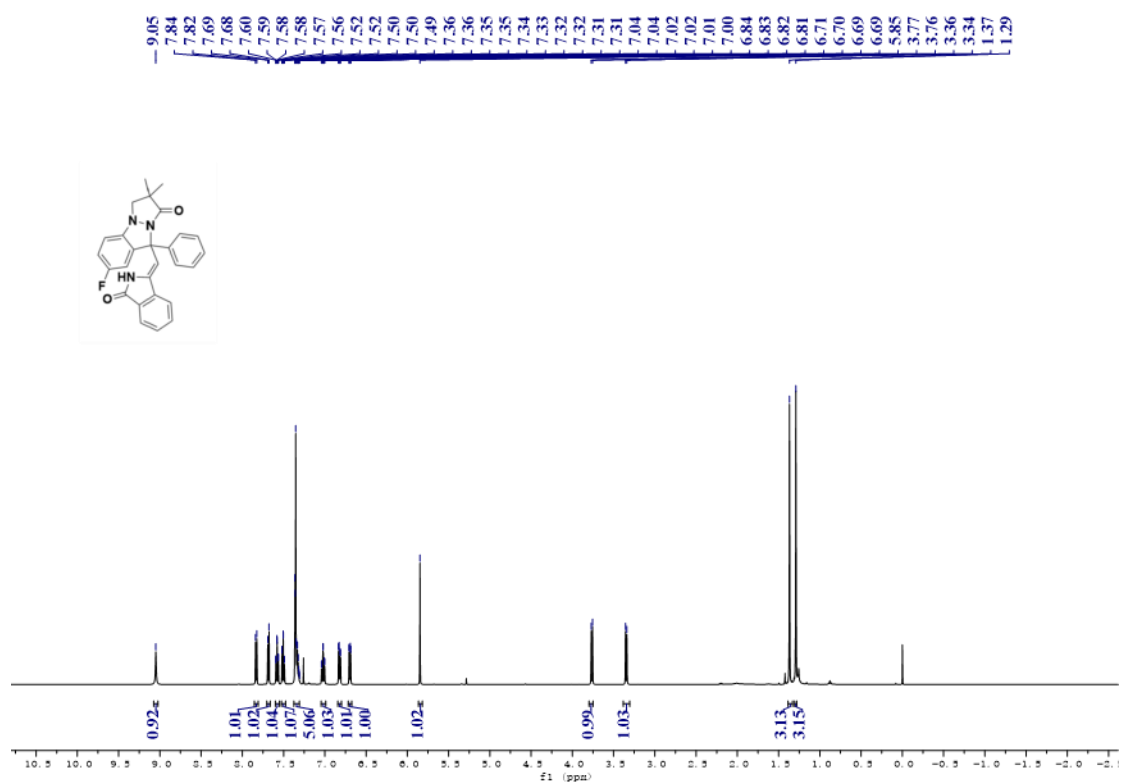
**(Z/E)-2,2-dimethyl-9-((3-oxoisoindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-**

pyrazolo[1,2-*a*]indazol-1-one (4aa)



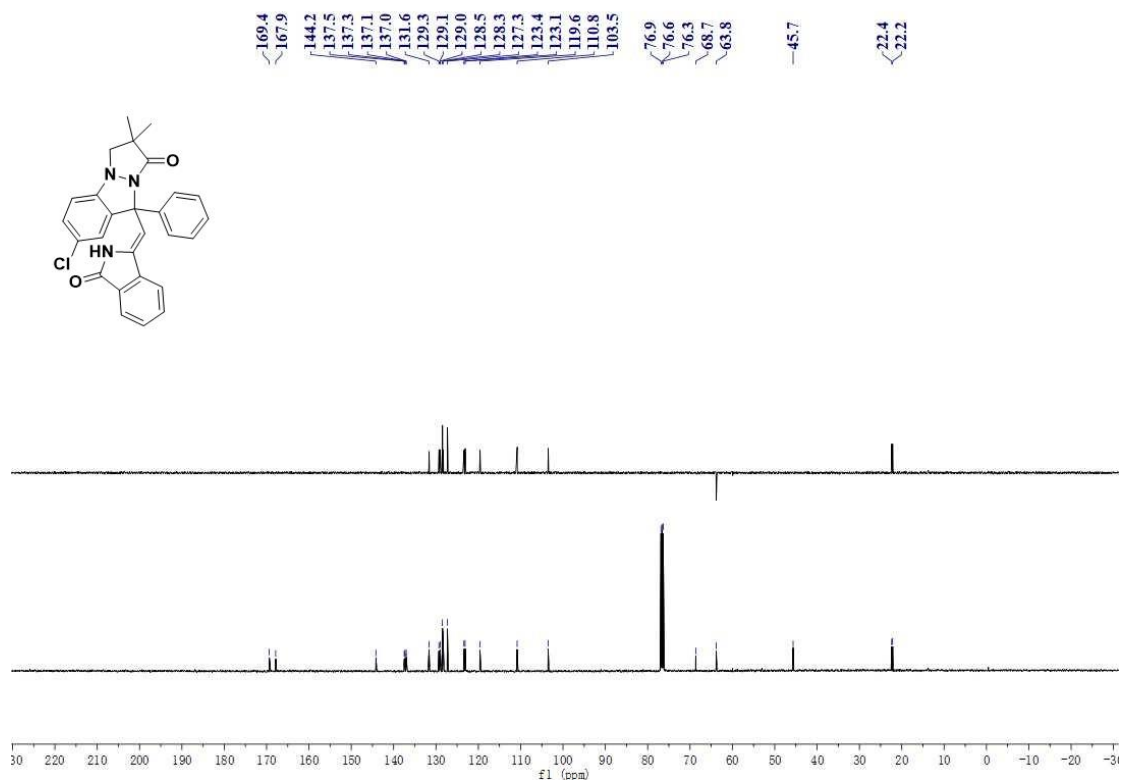
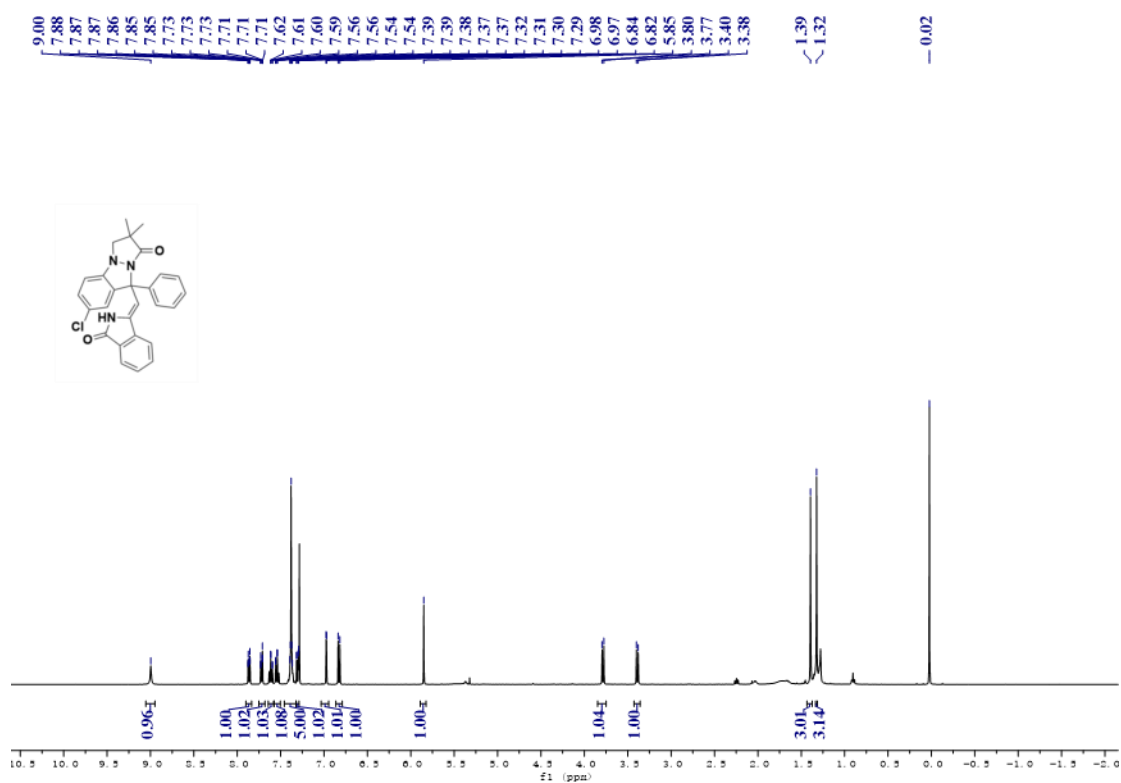
(*Z/E*)-7-fluoro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-

**1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ba)**

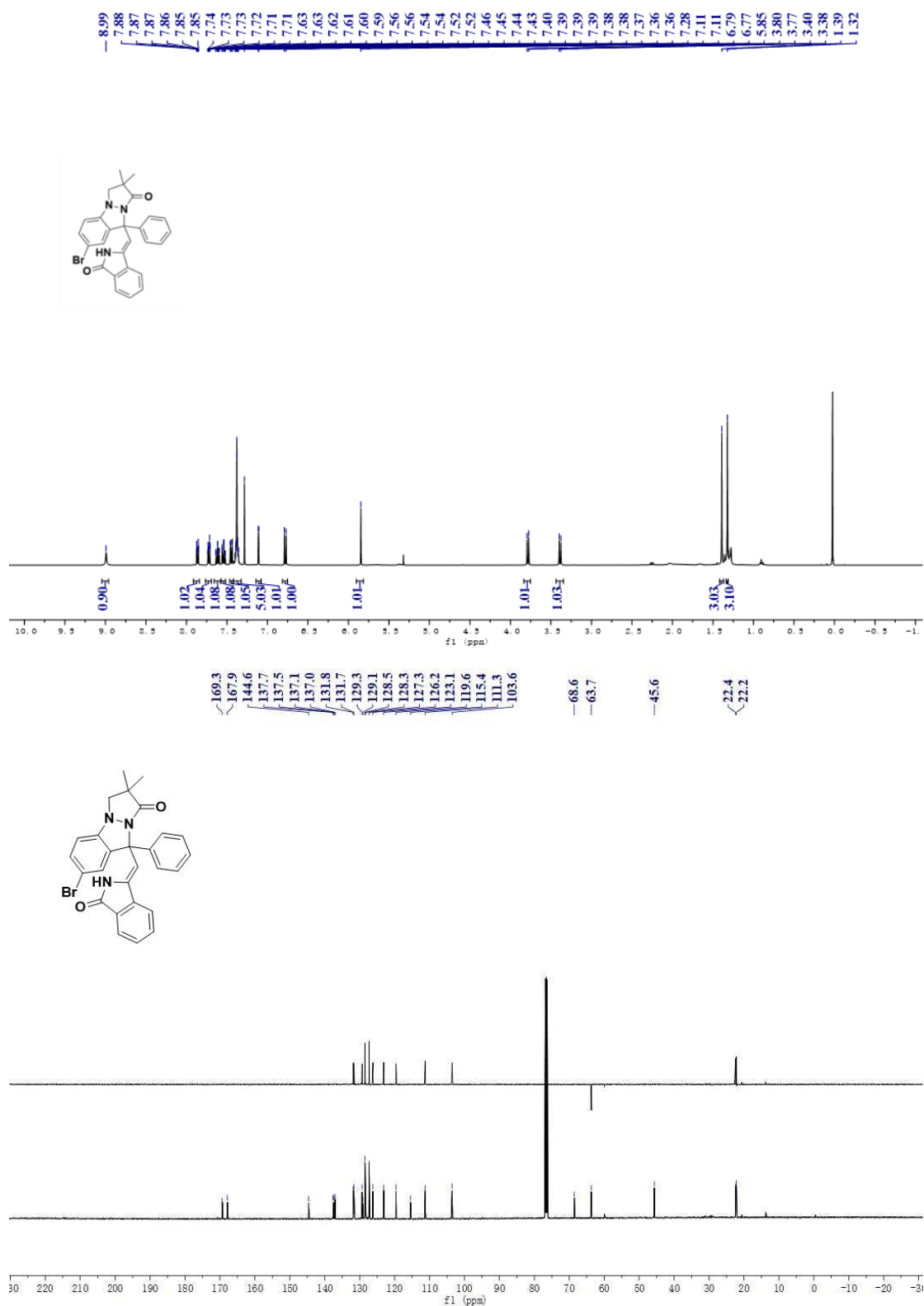


**(*Z/E*)-7-chloro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-**

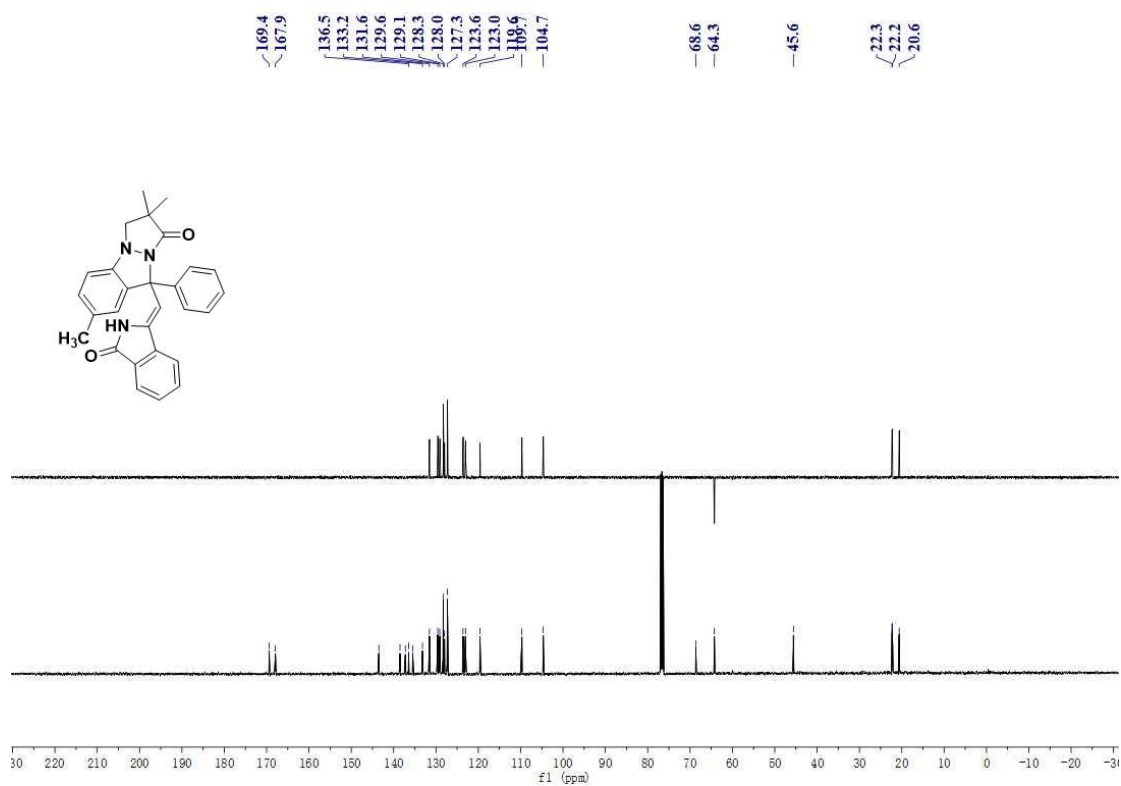
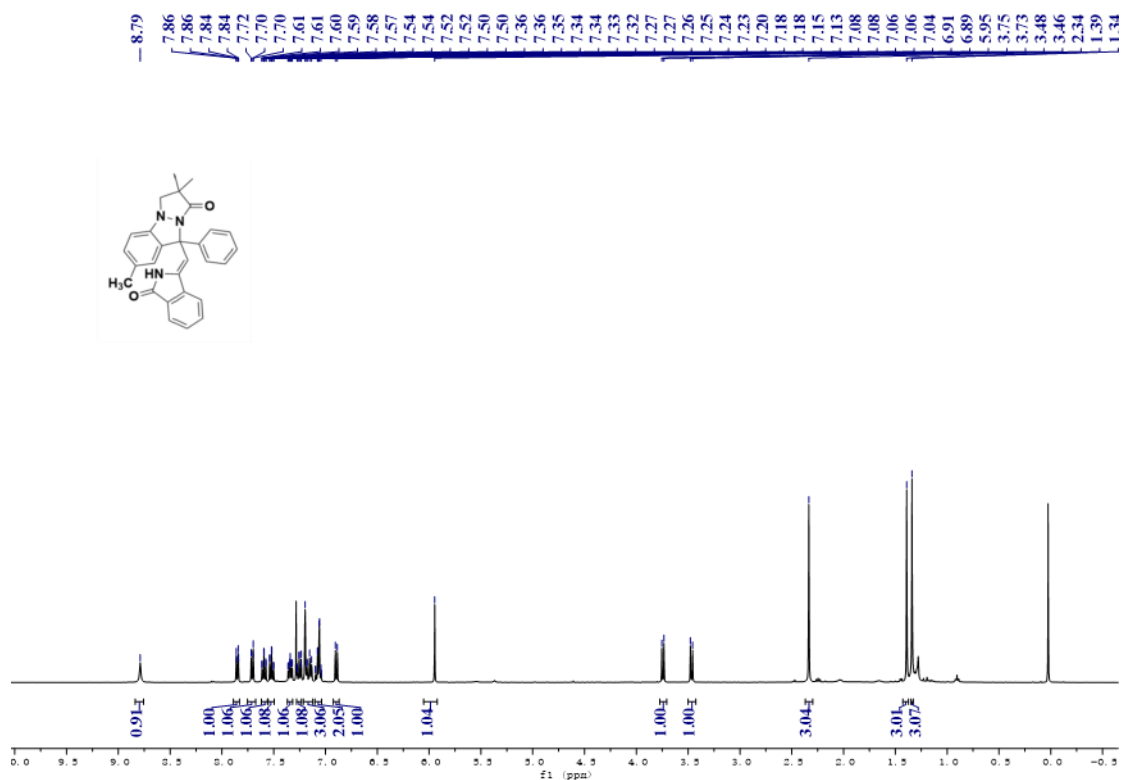
**dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ca)**



**(*Z/E*)-7-bromo-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4da)**



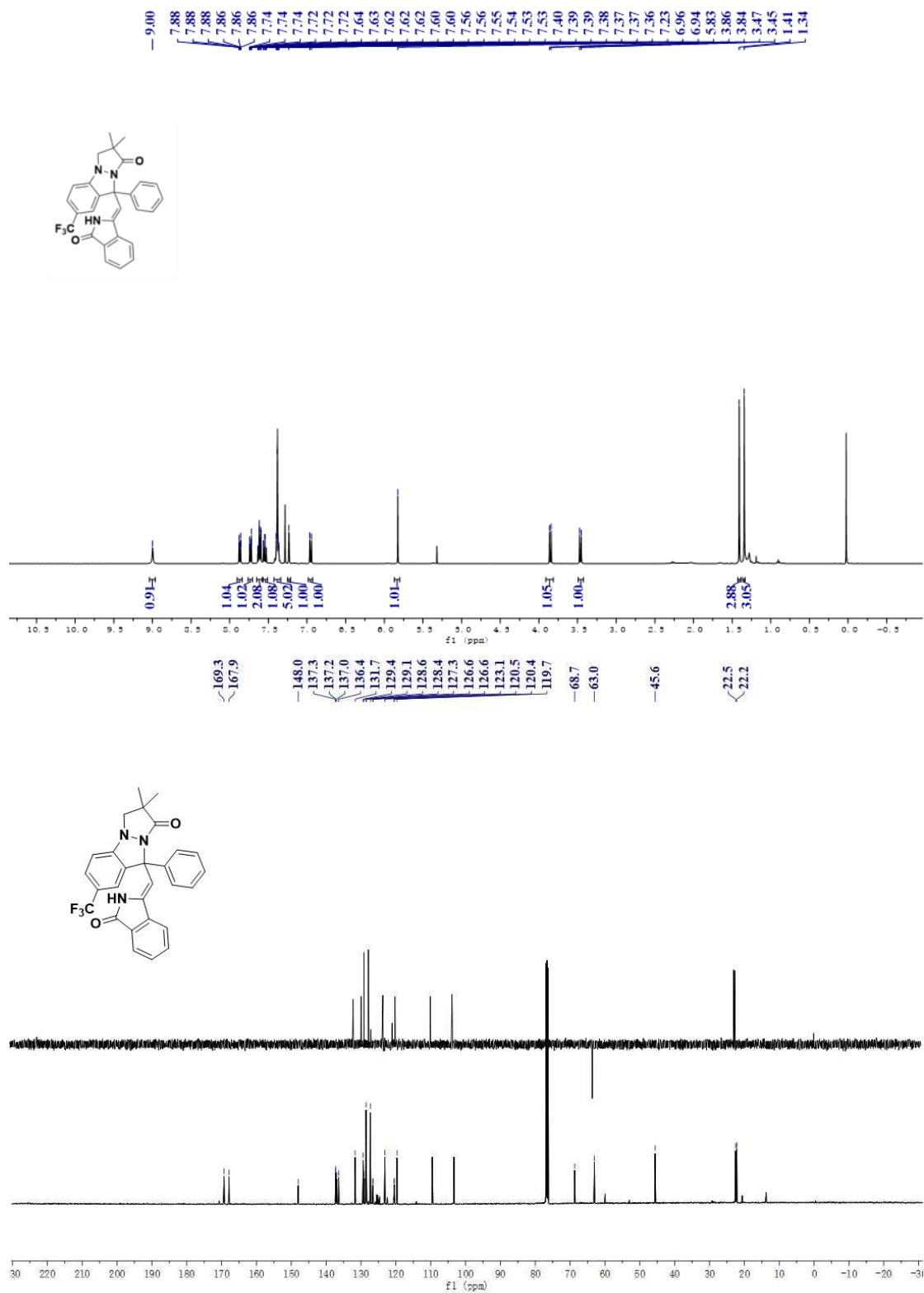
**(*Z/E*)-2,2,7-trimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ea)**



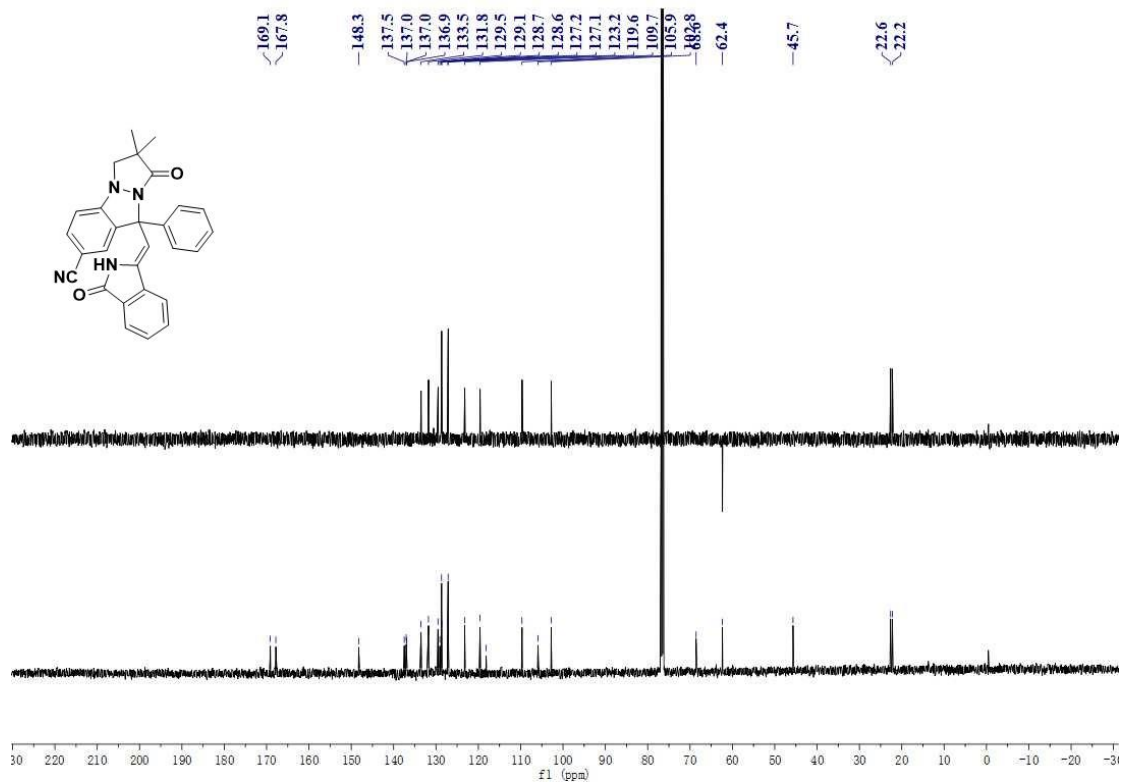
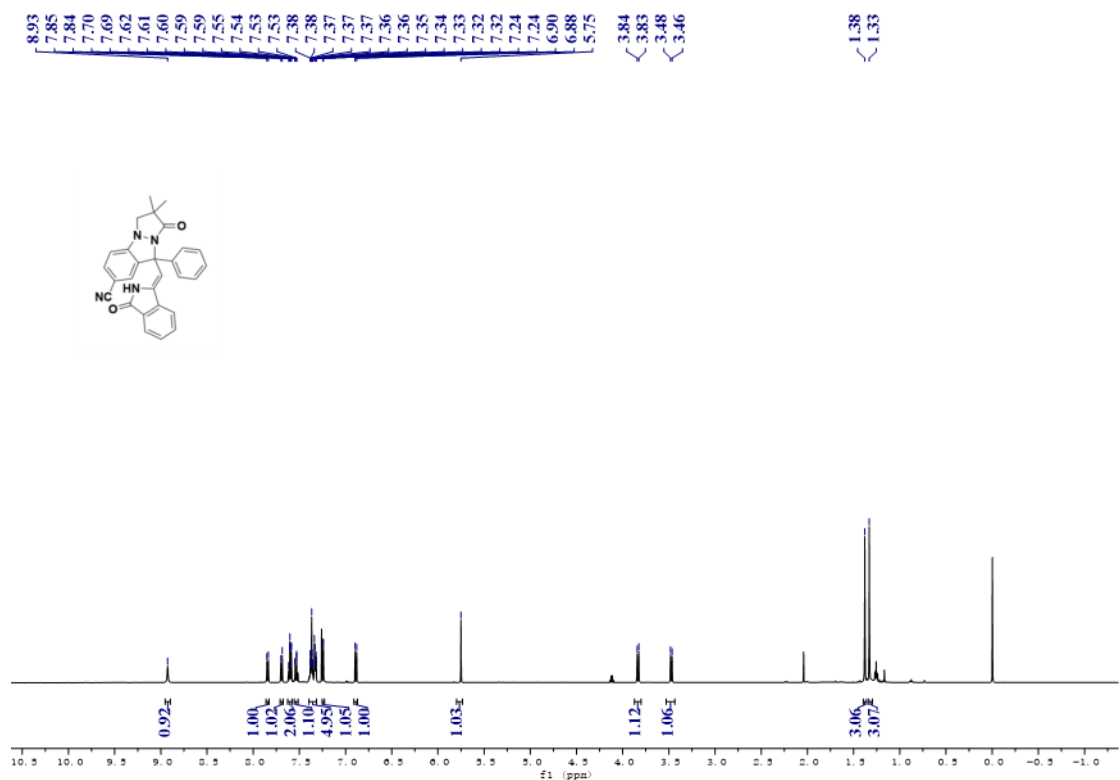
Chemical structure of compound 10 is shown in the top left corner. The <sup>1</sup>H NMR spectrum (CDCl<sub>3</sub>) displays peaks from 1.28 to 7.84 ppm. Integration values are provided below the baseline: 0.94, 1.03, 1.06, 1.09, 1.08, 5.09, 1.01, 1.00, 1.03, 1.06, 4.13, 1.01, 3.12, 3.08.



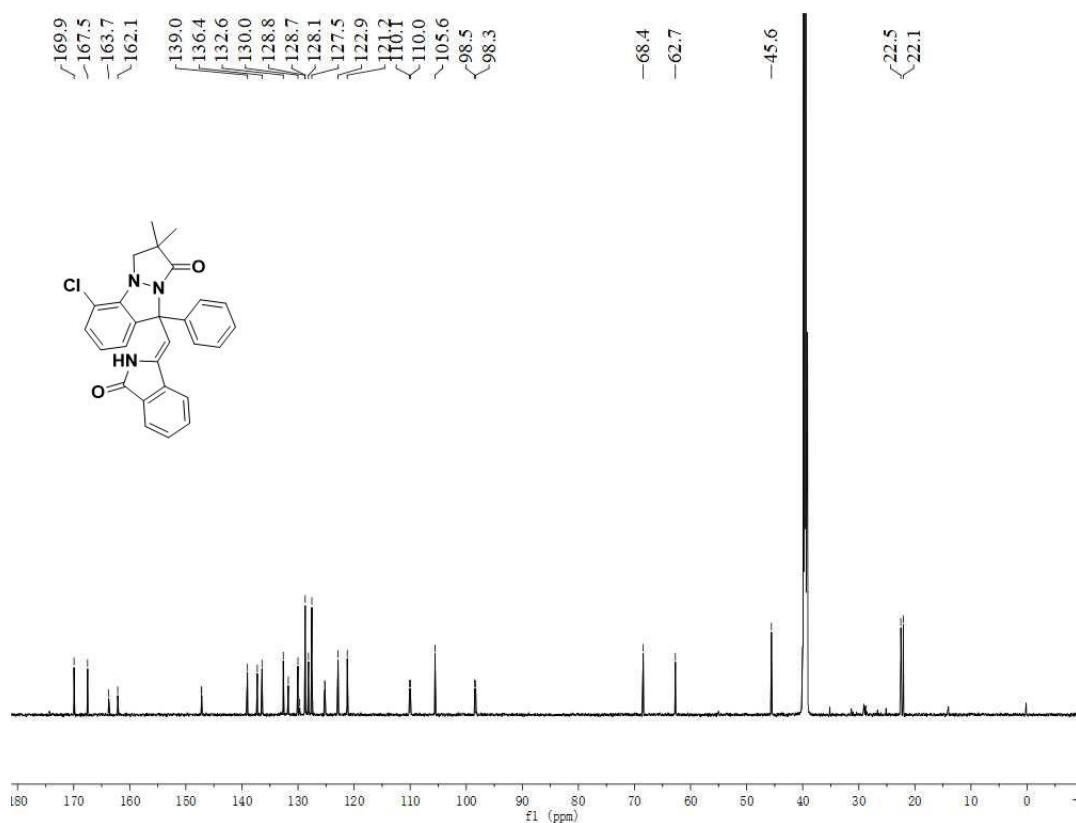
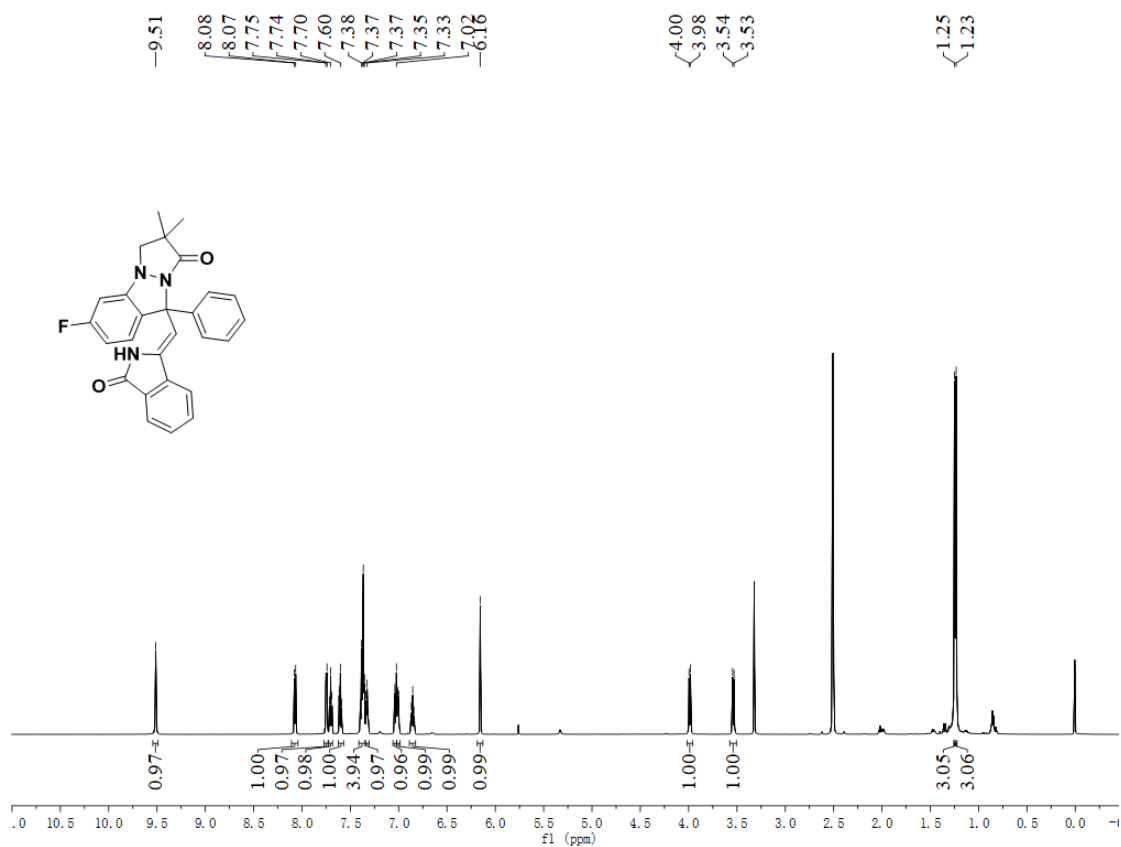
**(*Z/E*)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-7-(trifluoromethyl)-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ga)**



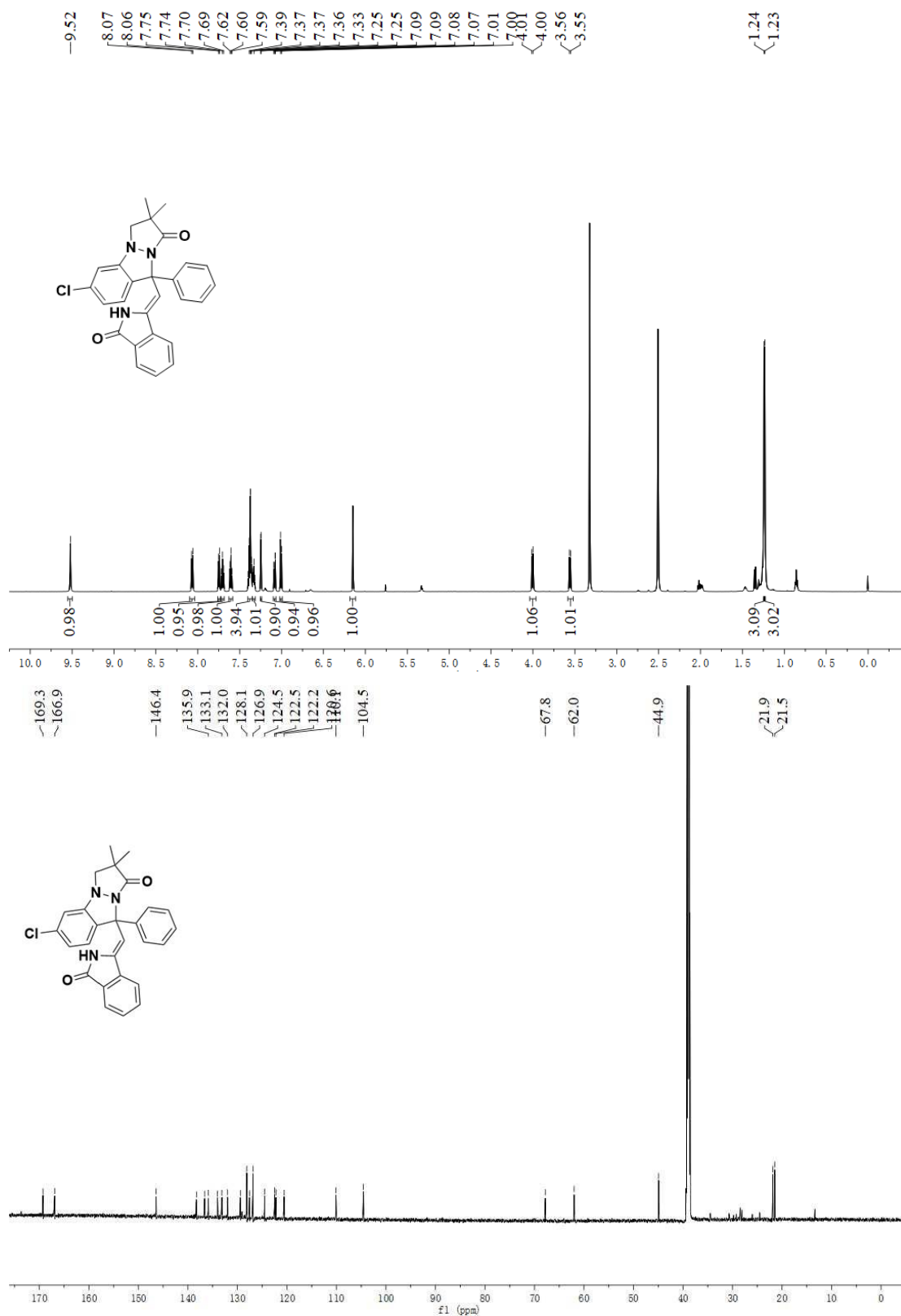
**(*Z/E*)-2,2-dimethyl-1-oxo-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazole-7-carbonitrile (4ha)**



**(Z/E)-6-fluoro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4ia)**

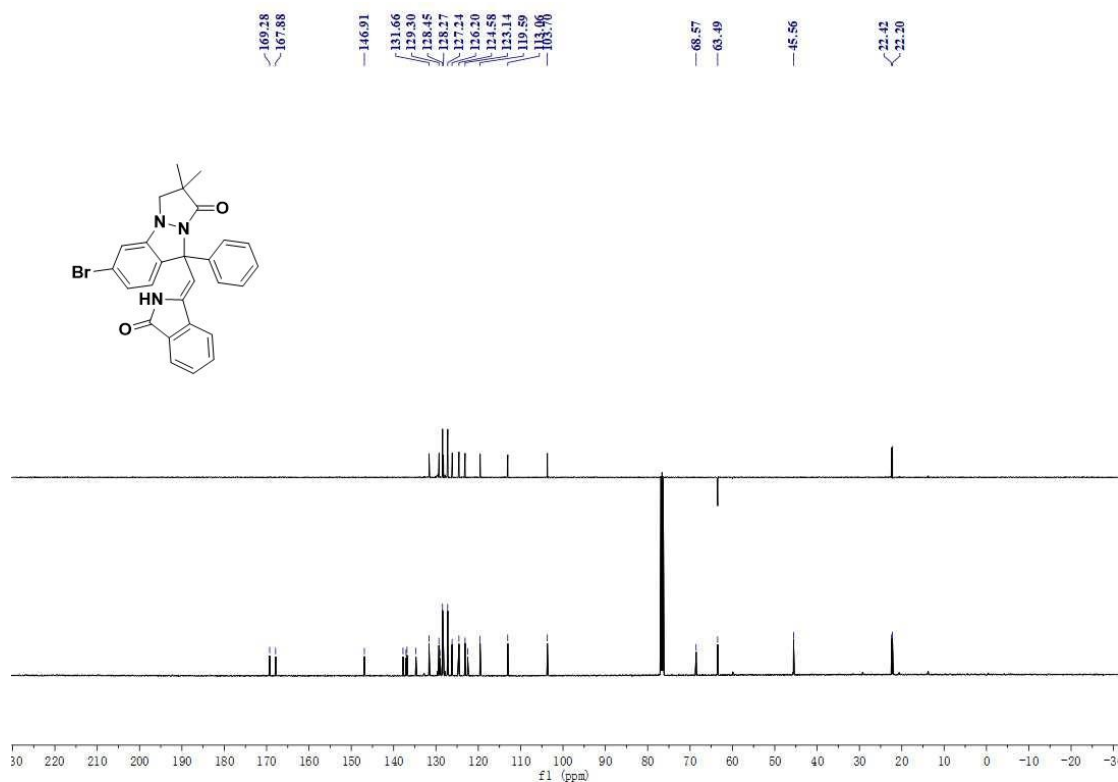
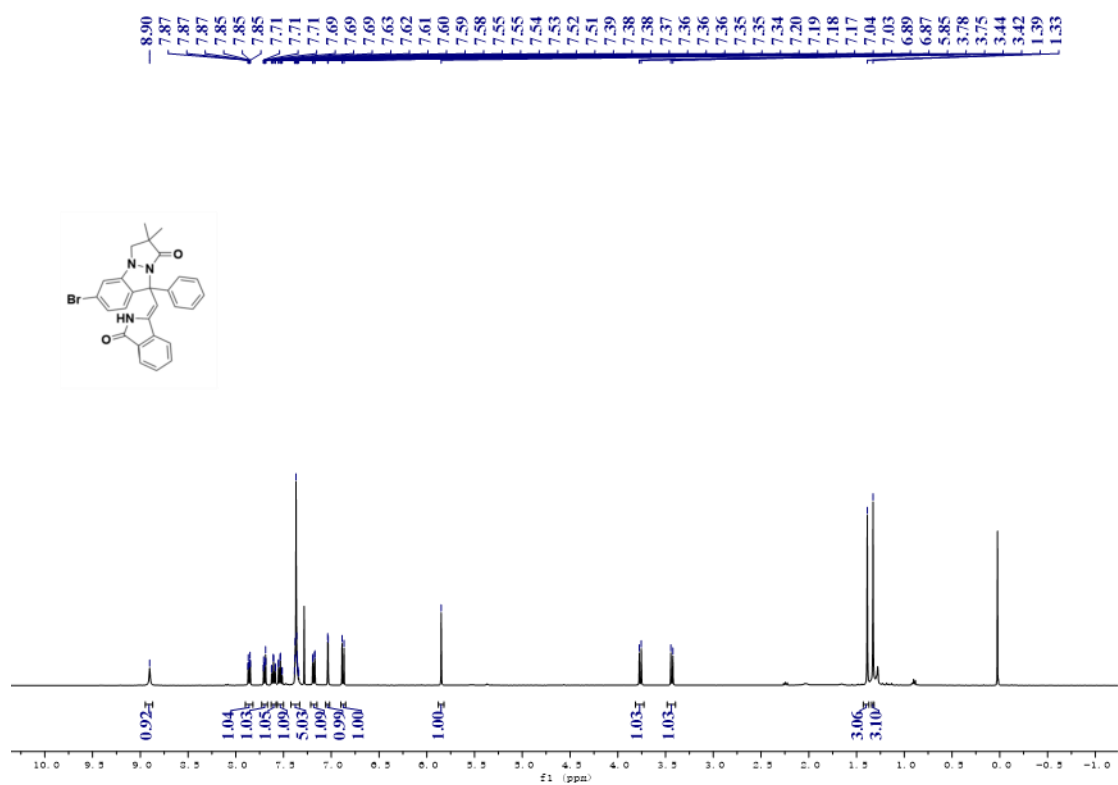


**(Z/E)-6-chloro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4ja)**

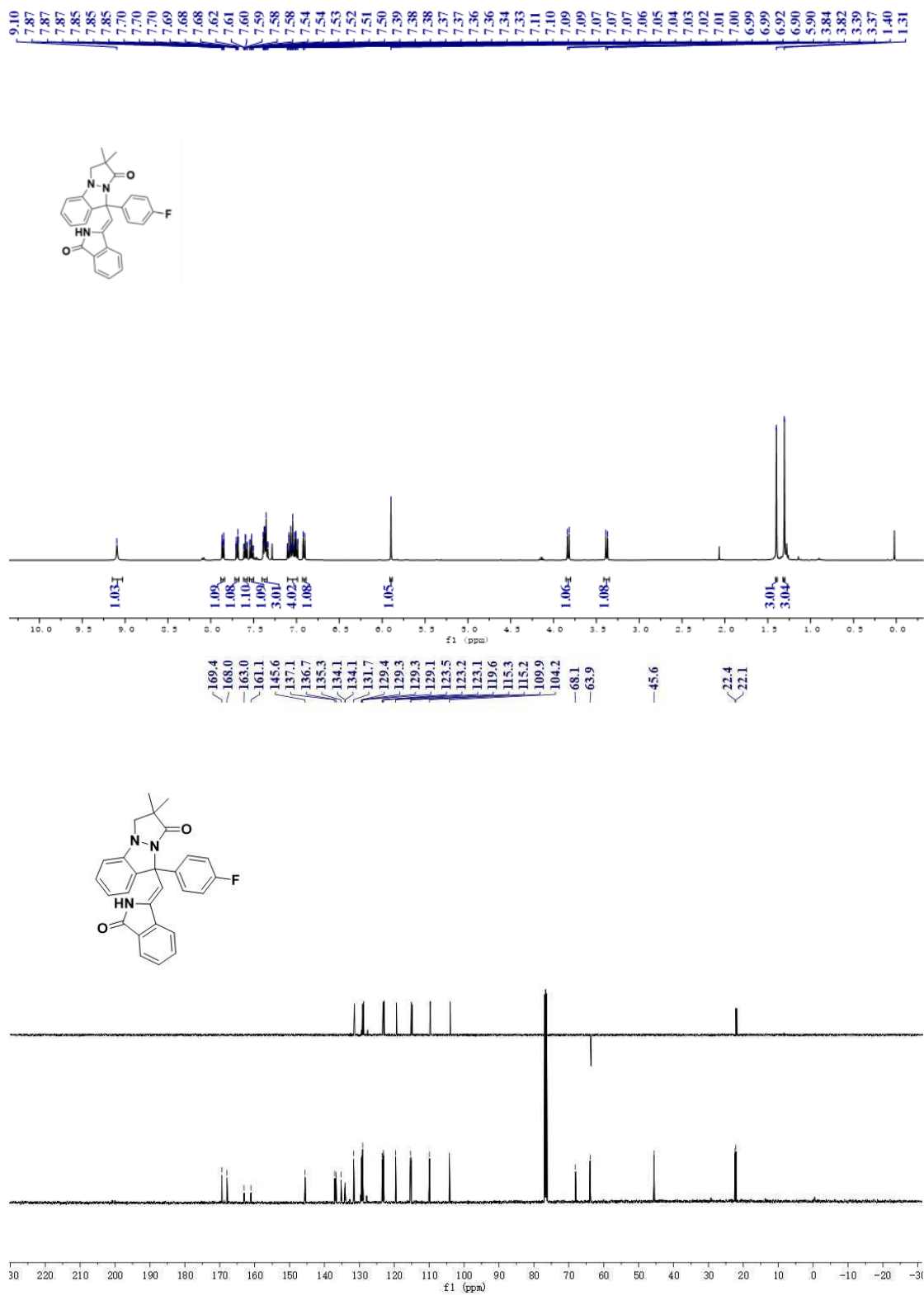


**(Z/E)-6-bromo-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-**

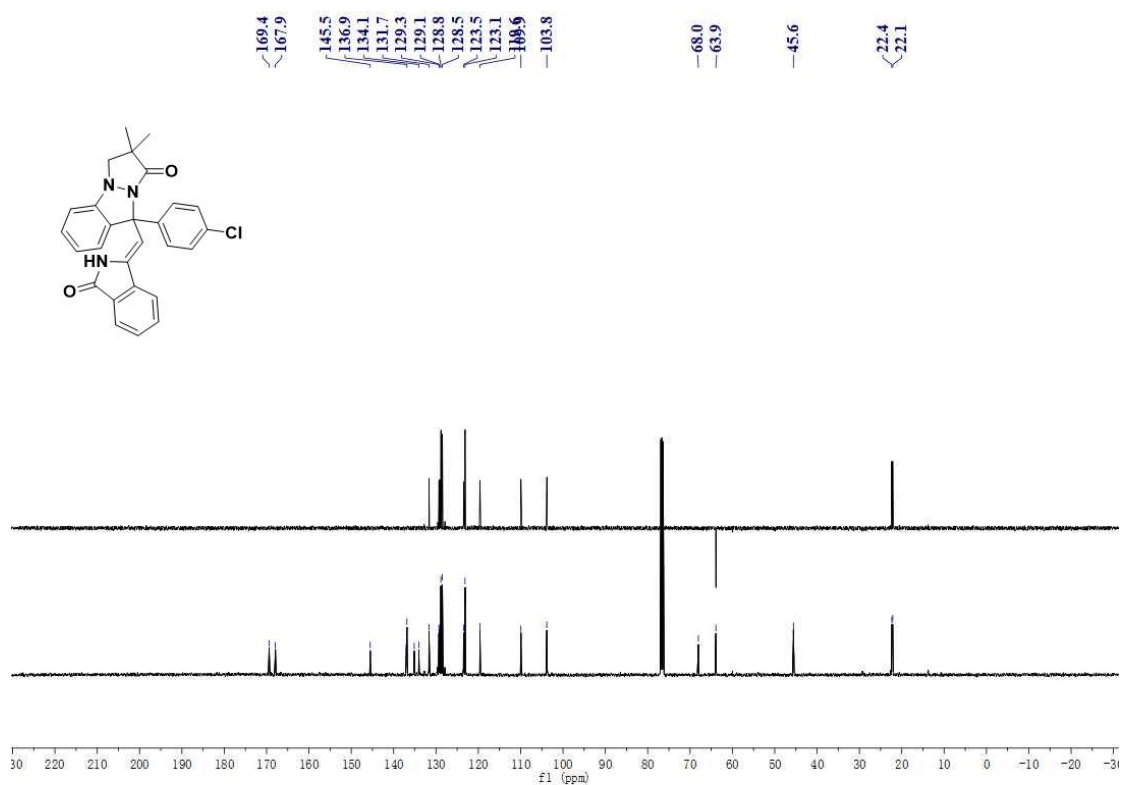
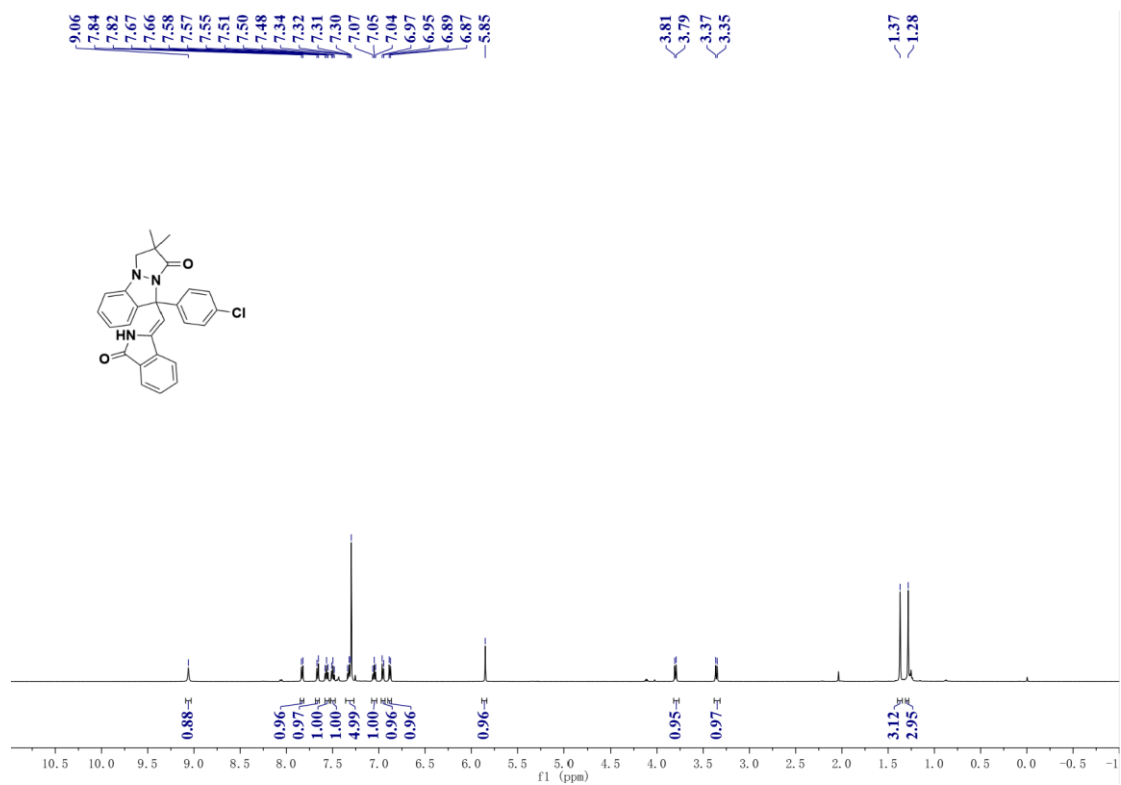
**dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ka)**

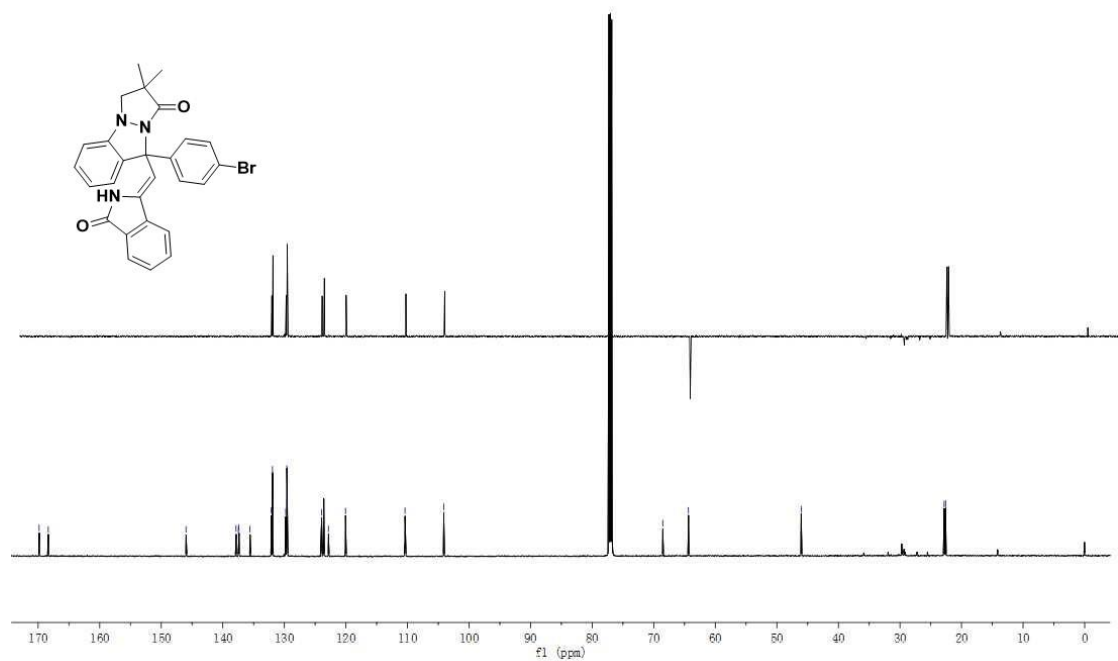


**(*Z/E*)-6-bromo-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ab)**

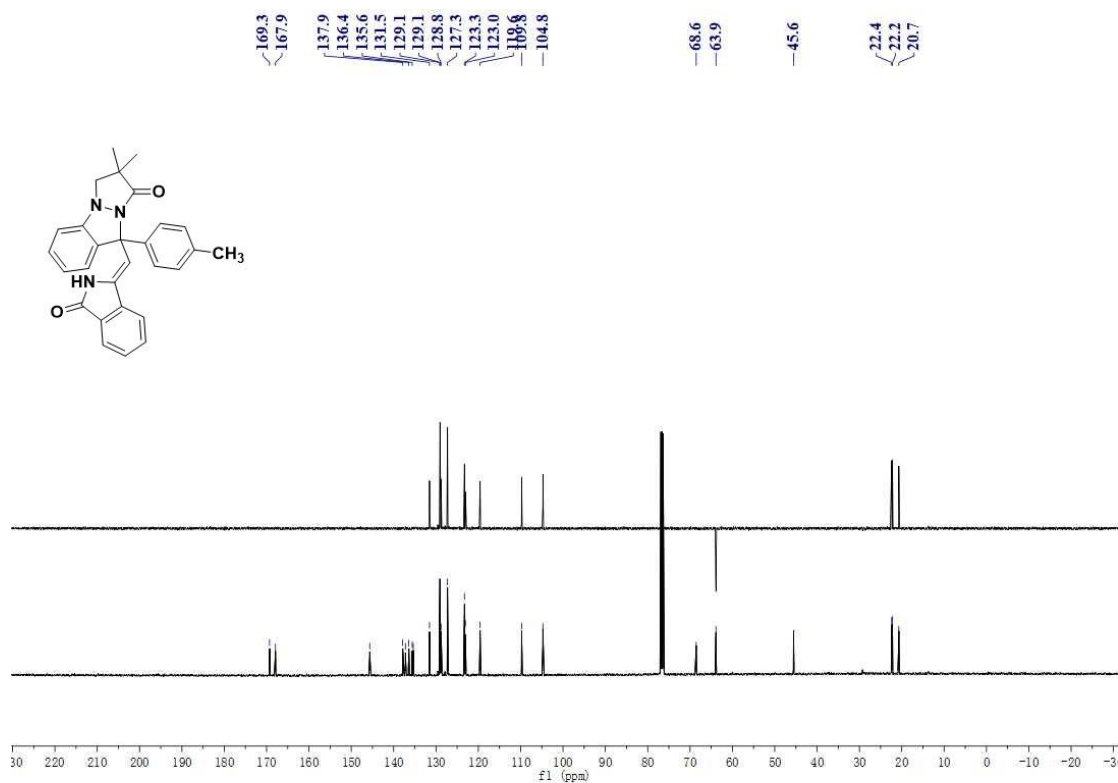
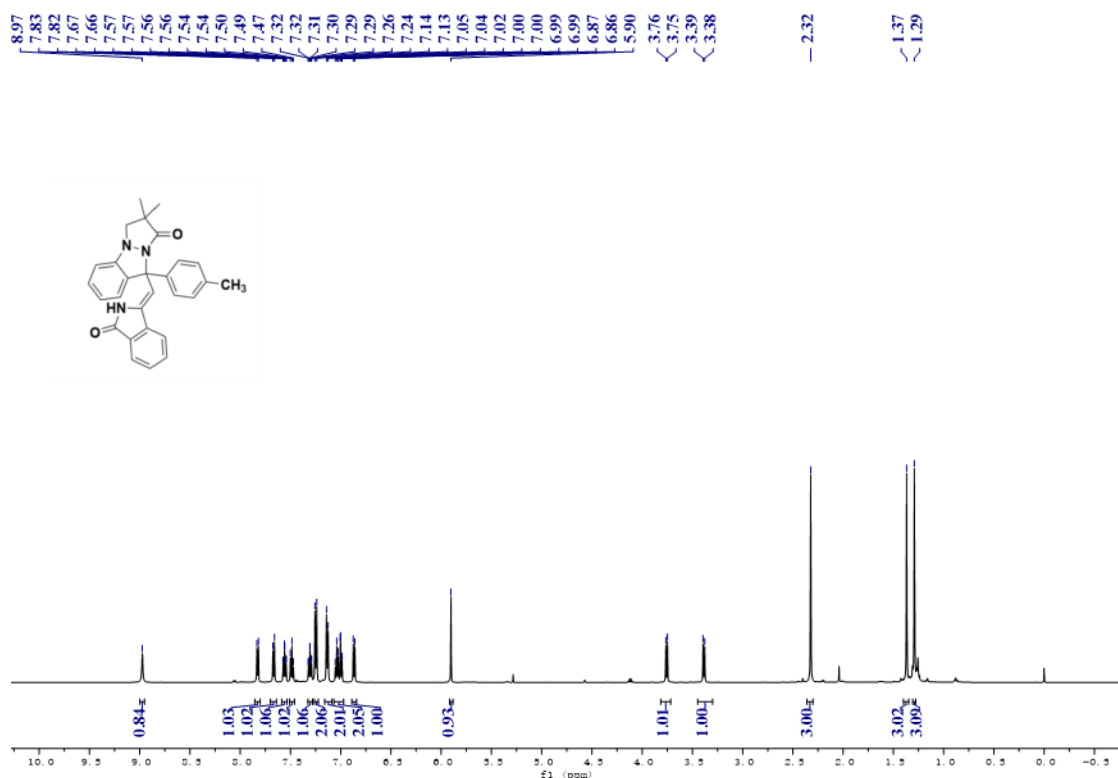


**(*Z/E*)-9-(4-chlorophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ac)**

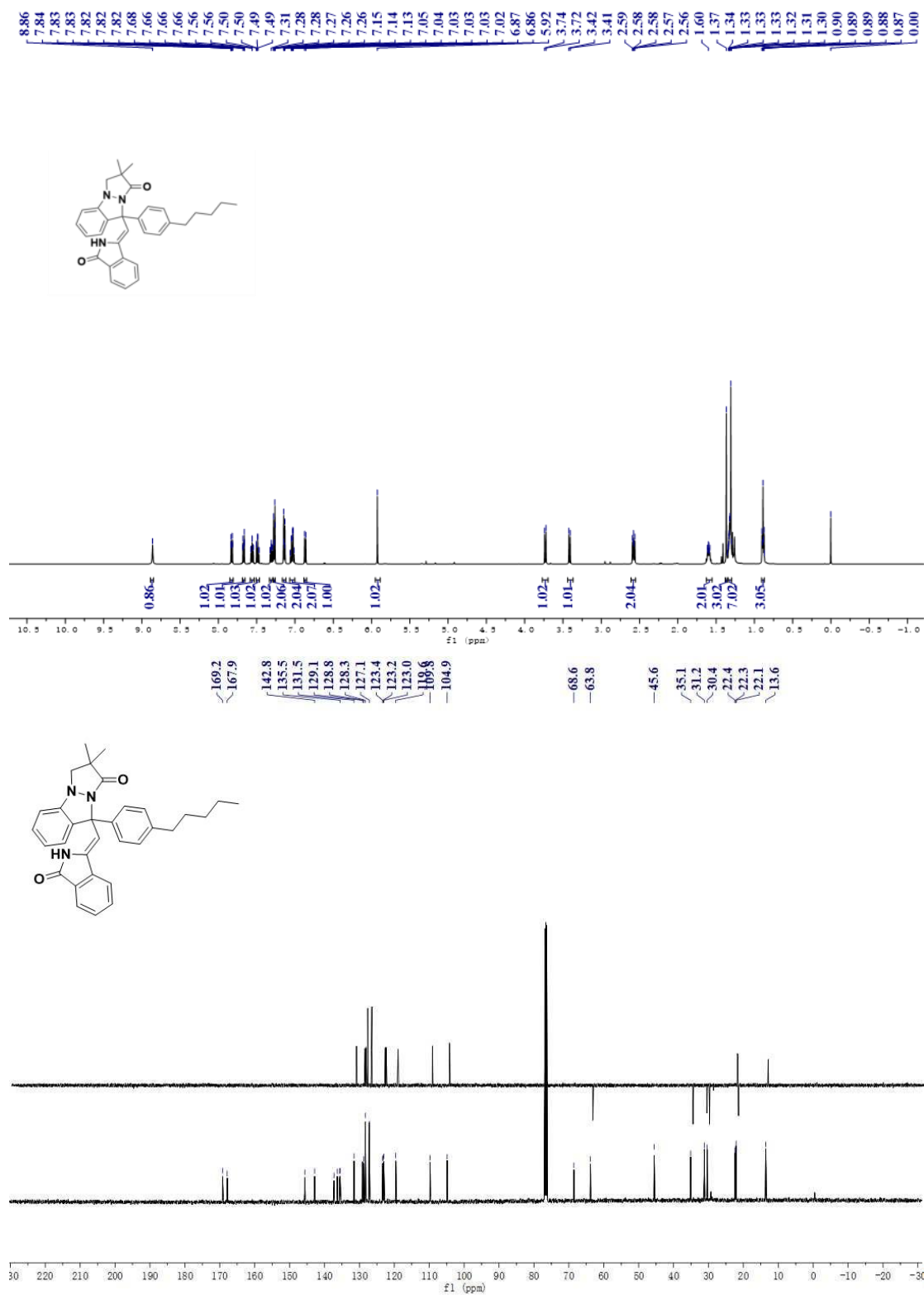


[illegible]

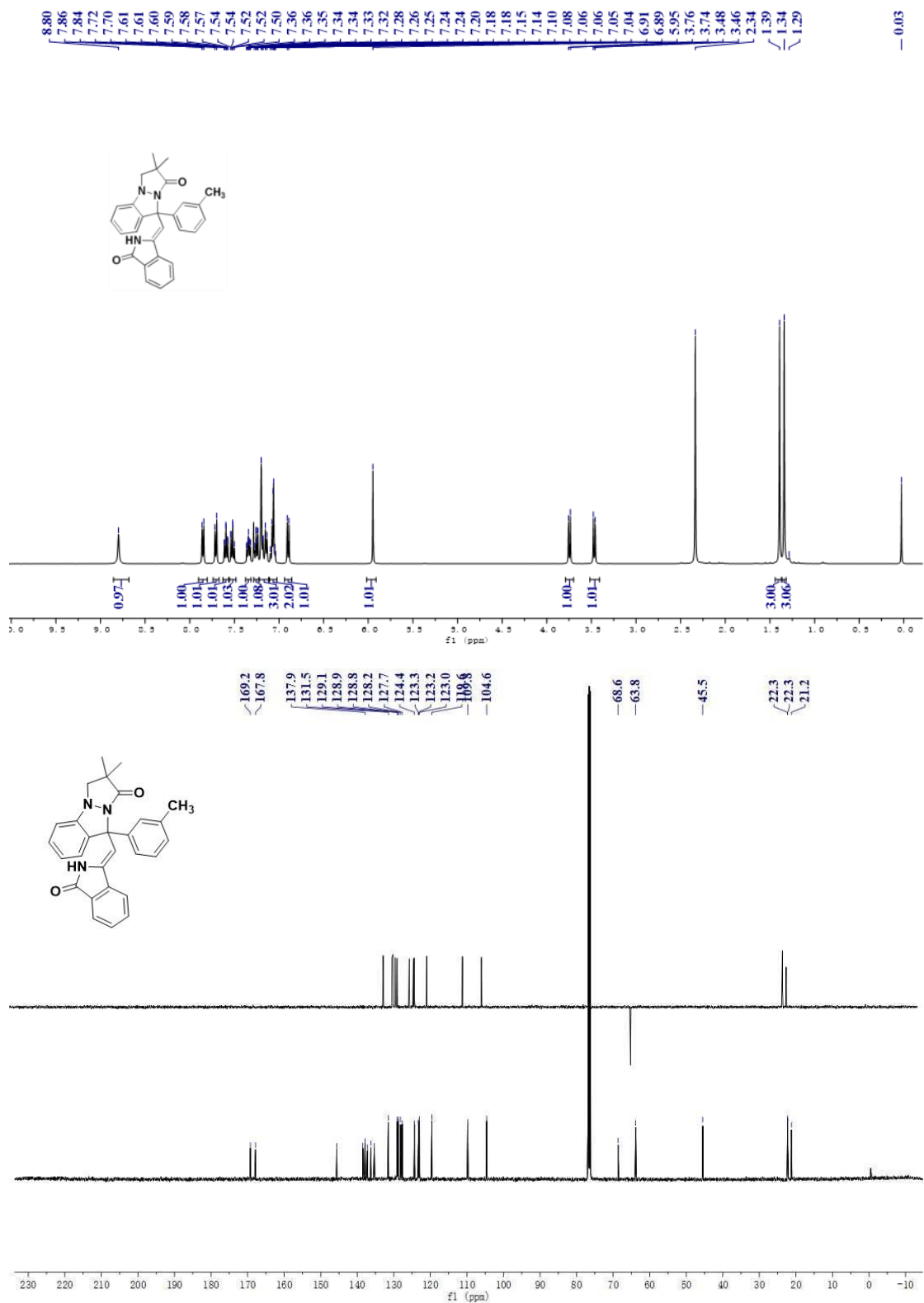
**(*Z/E*)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(*p*-tolyl)-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ae)**



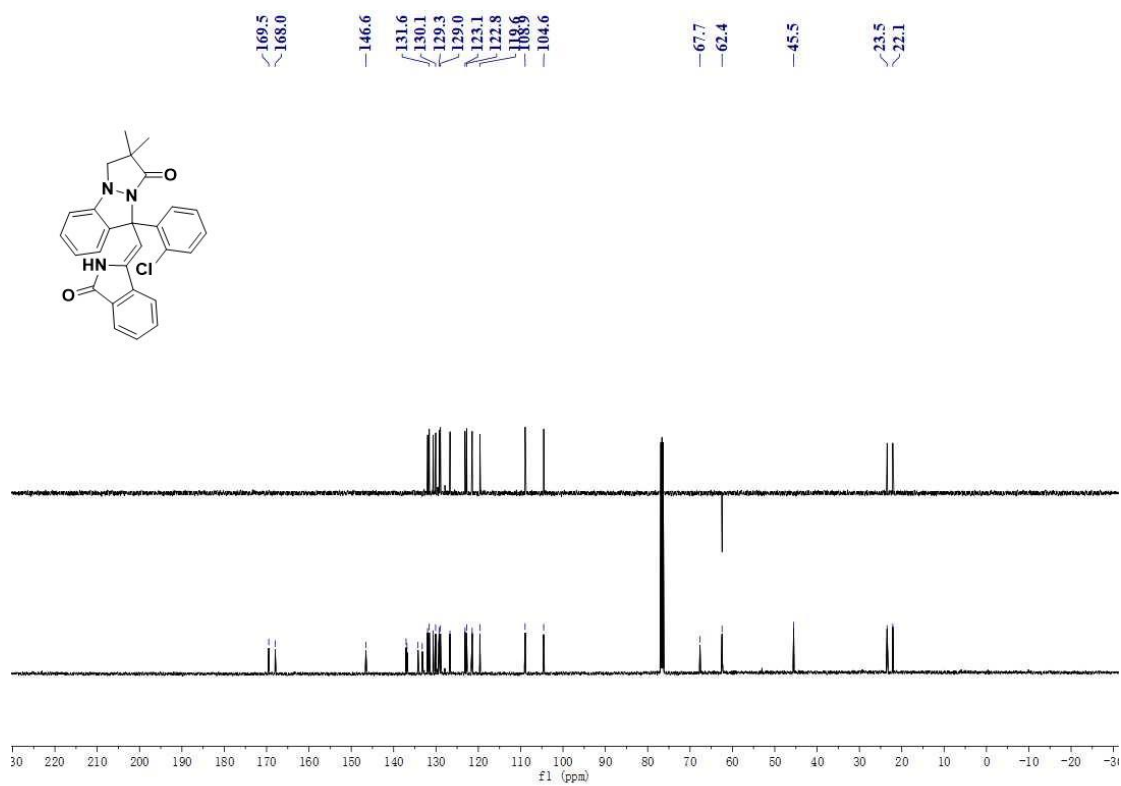
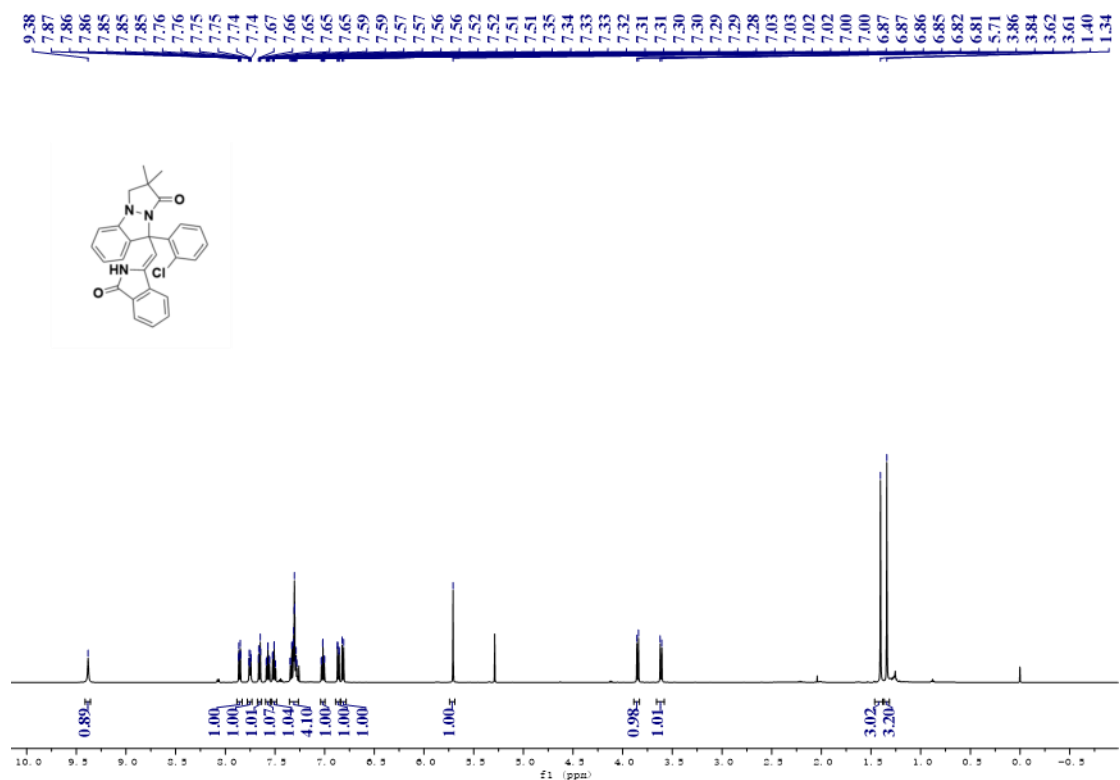
**(Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(4-pentylphenyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4ag)**



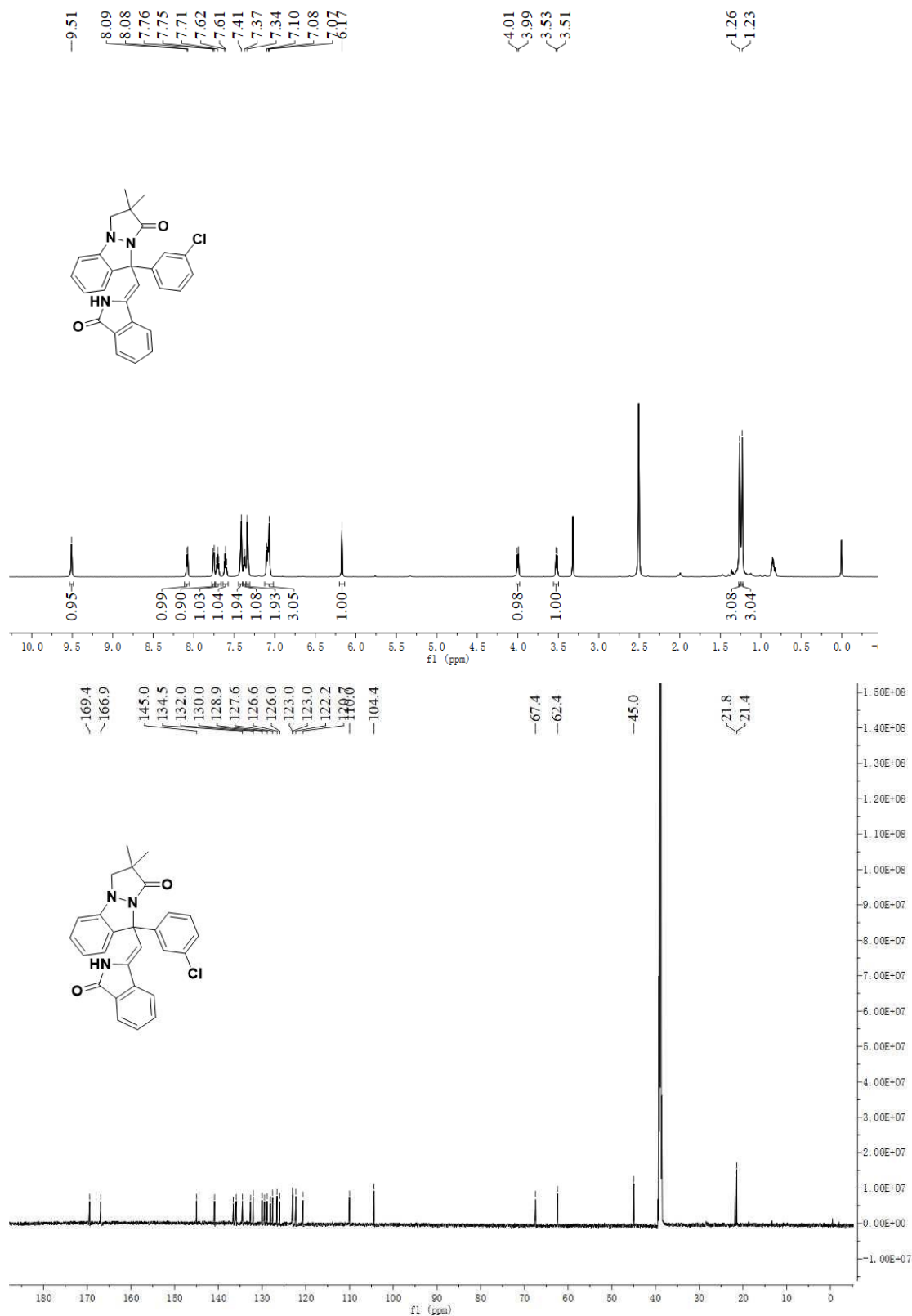
**(Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(m-tolyl)-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4ai)**



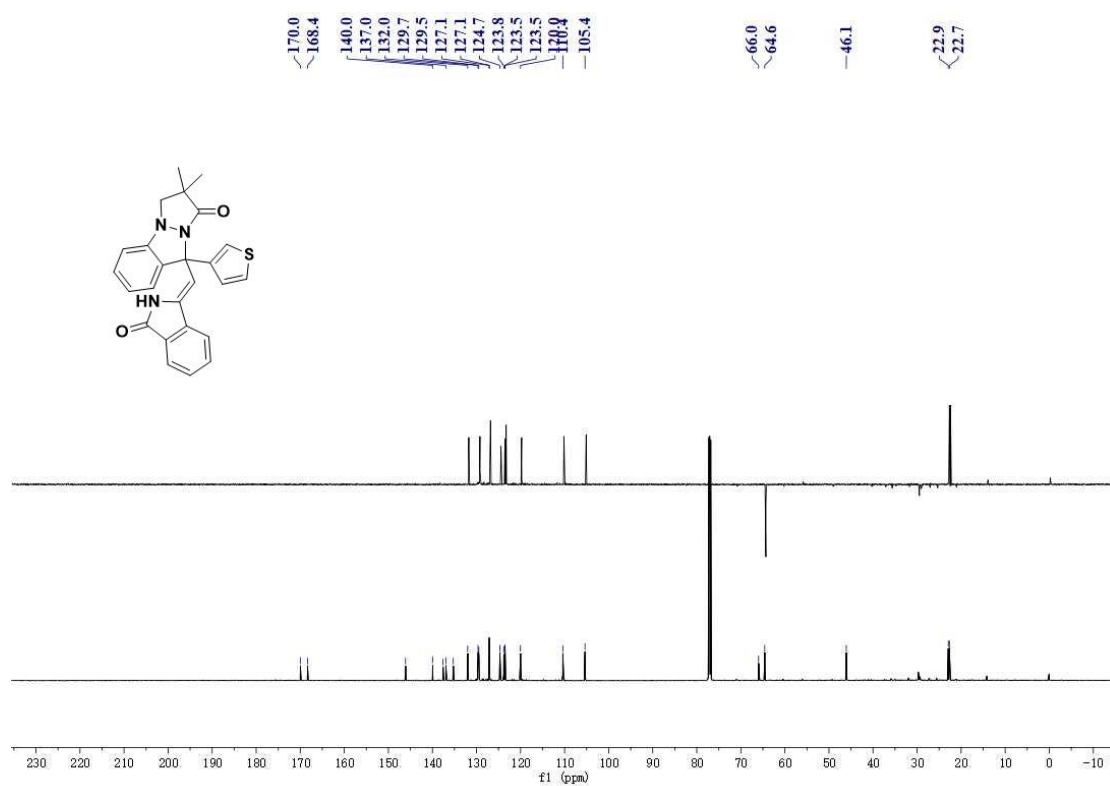
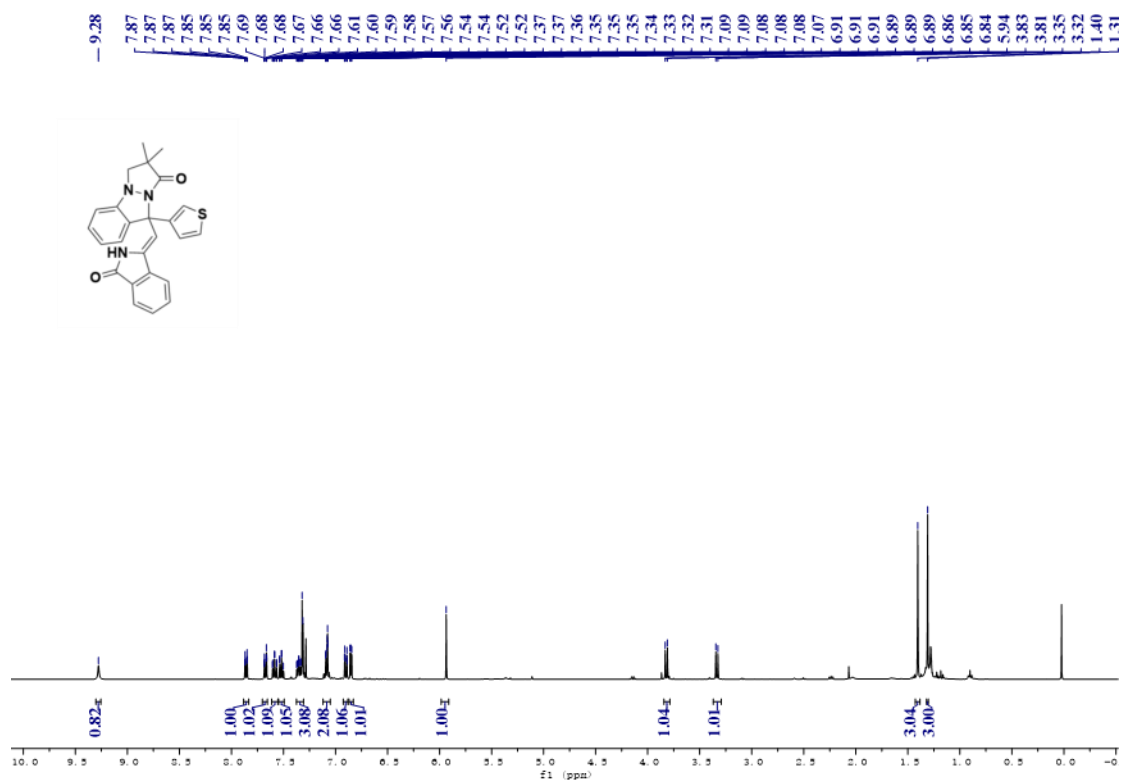
**(Z/E)-9-(2-chlorophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4aj)**



**(Z/E)-9-(3-chlorophenyl)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4ak)**

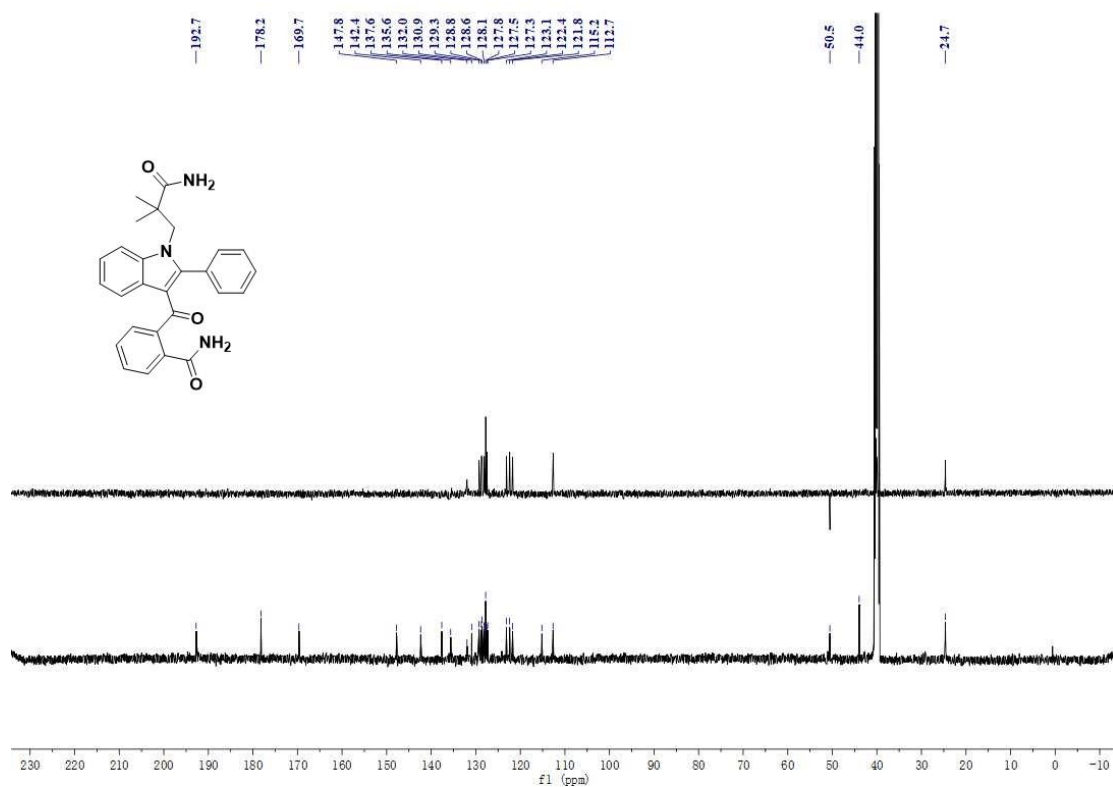
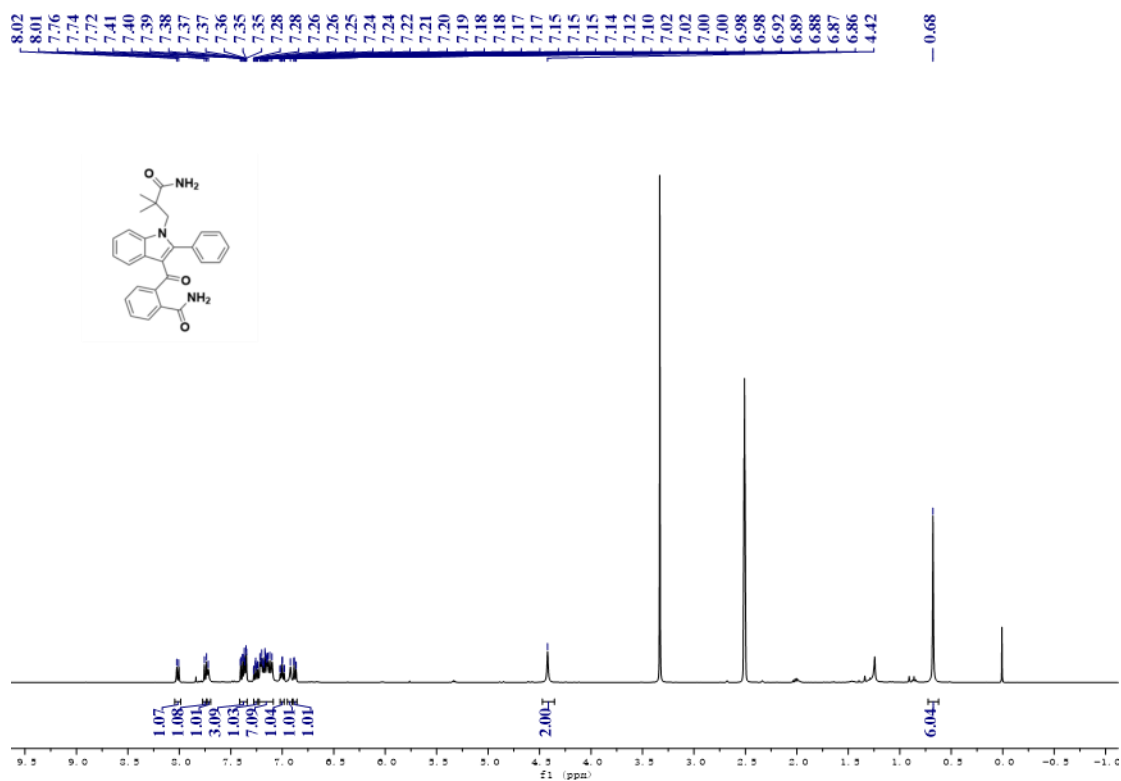


**(Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(thiophen-3-yl)-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-*a*]indazol-1-one (4a)**



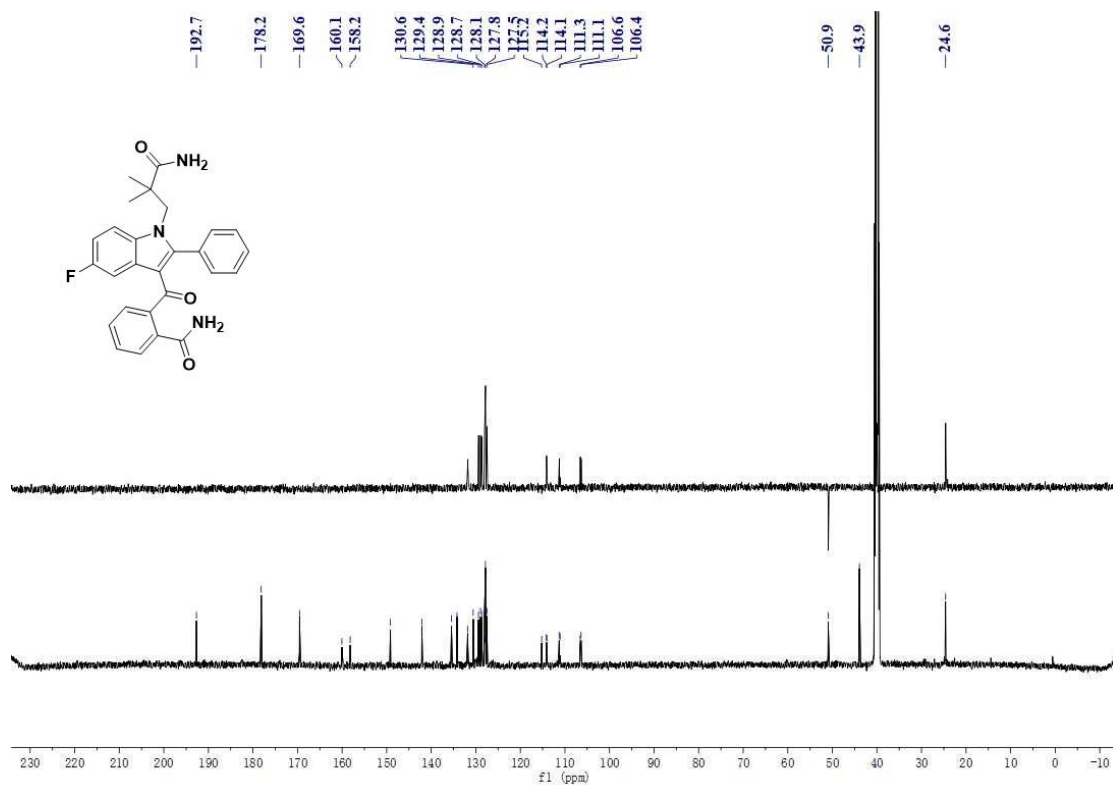
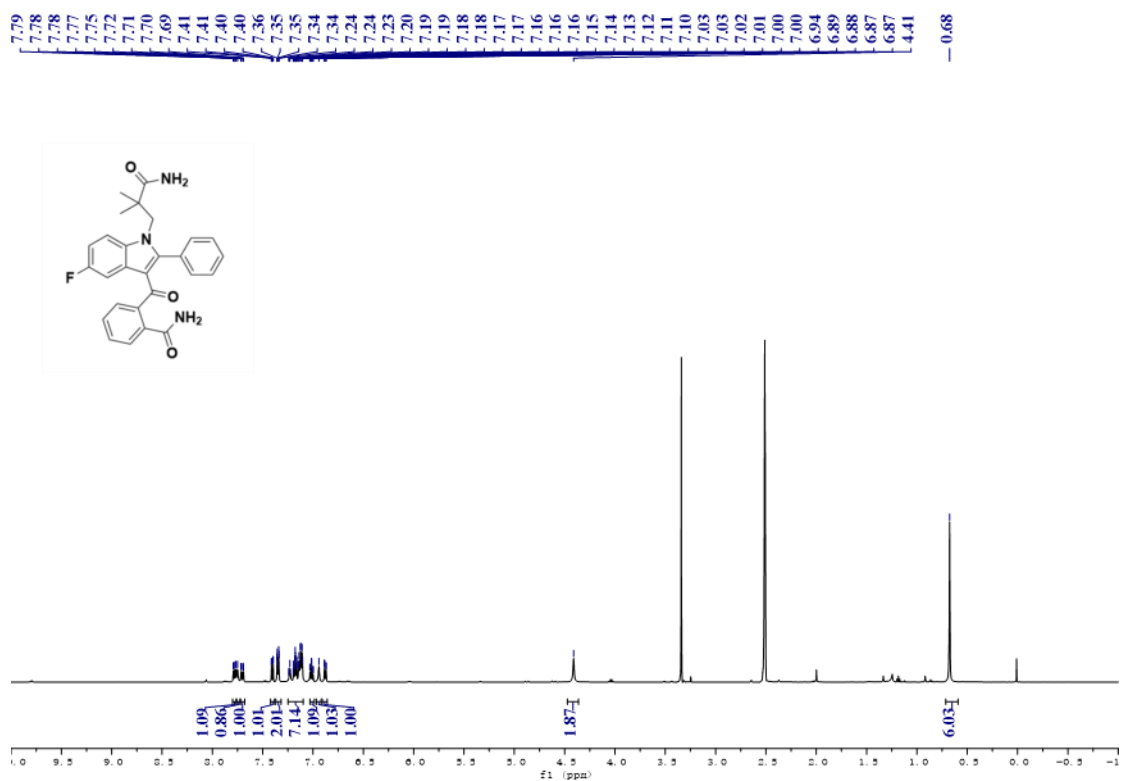
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-phenyl-1*H*-indole-3-carbonyl)benzamide**

(5aa)

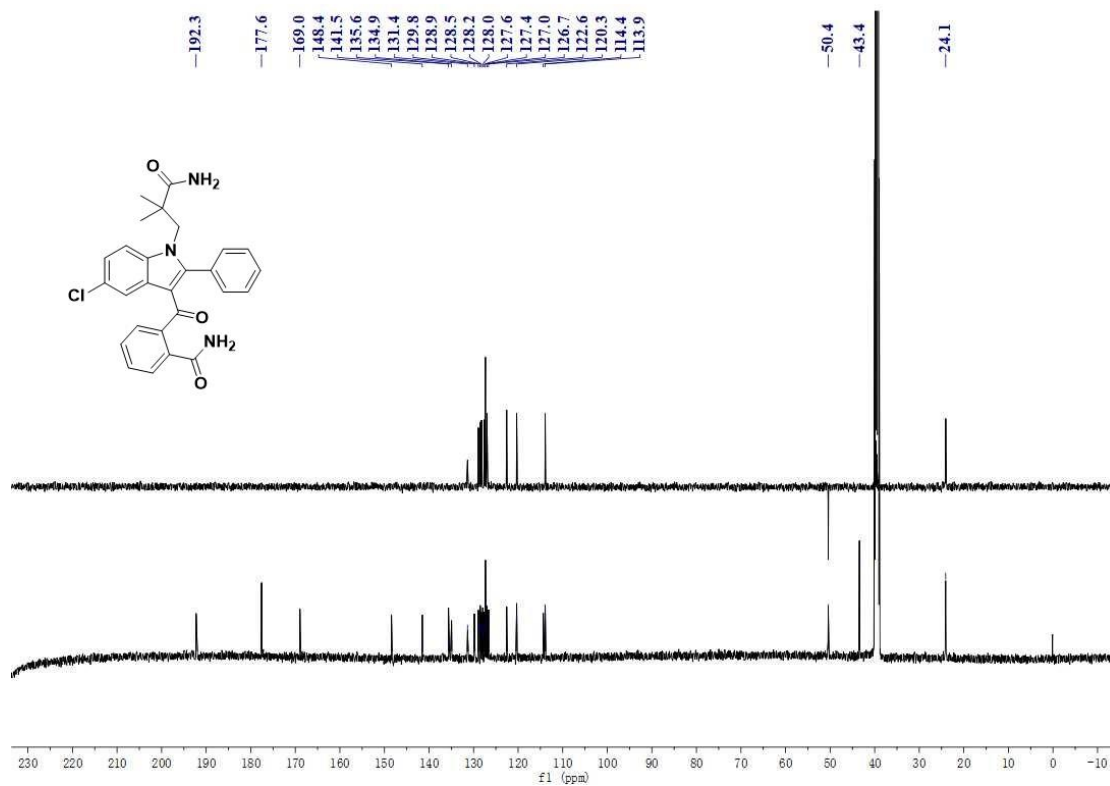
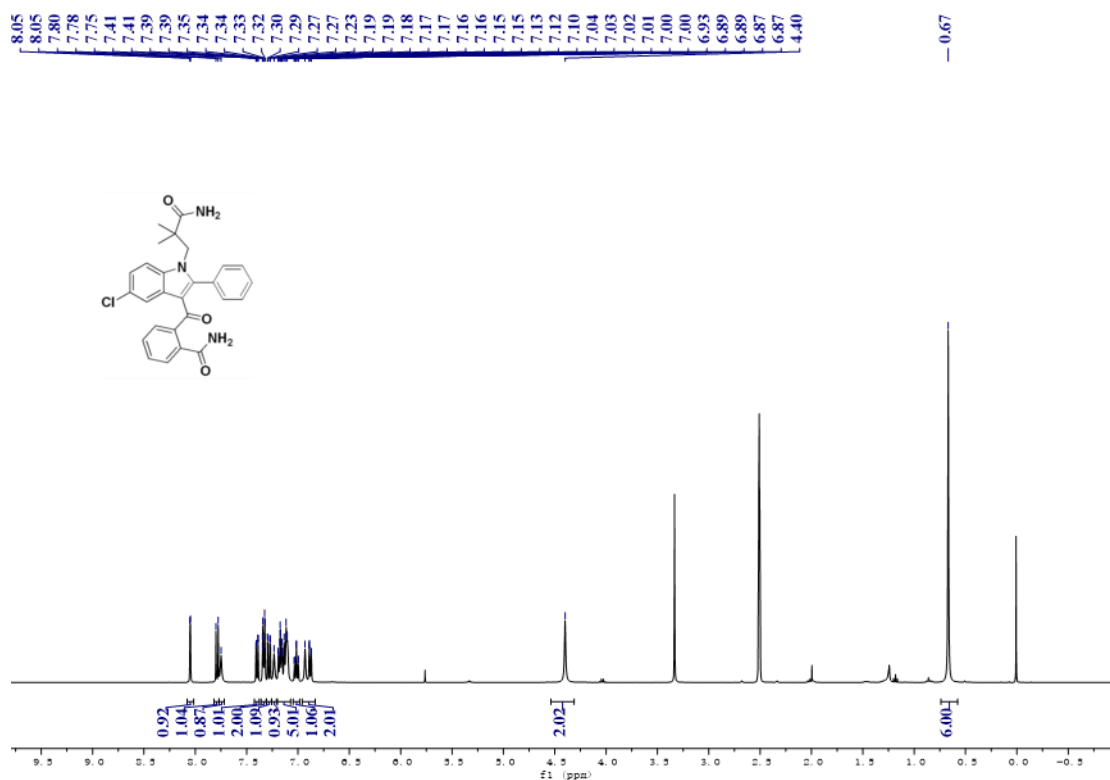


2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5-fluoro-2-phenyl-1H-indole-3-

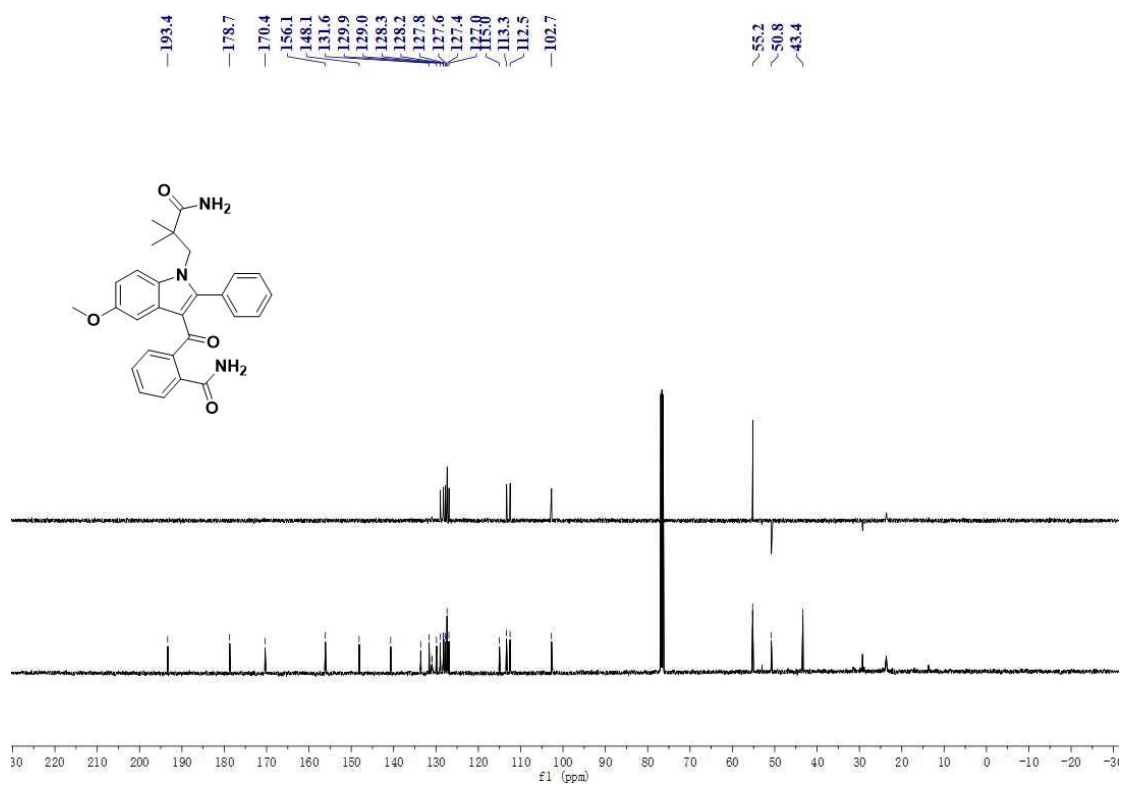
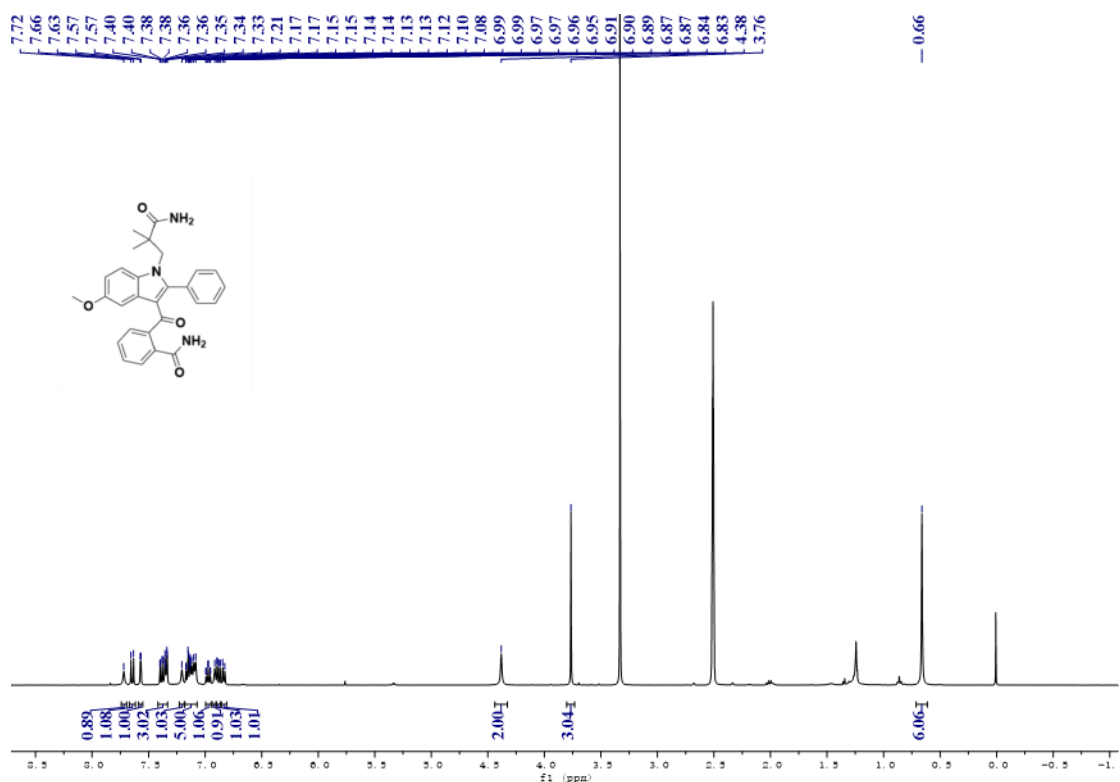
carbonyl)benzamide (5ba)



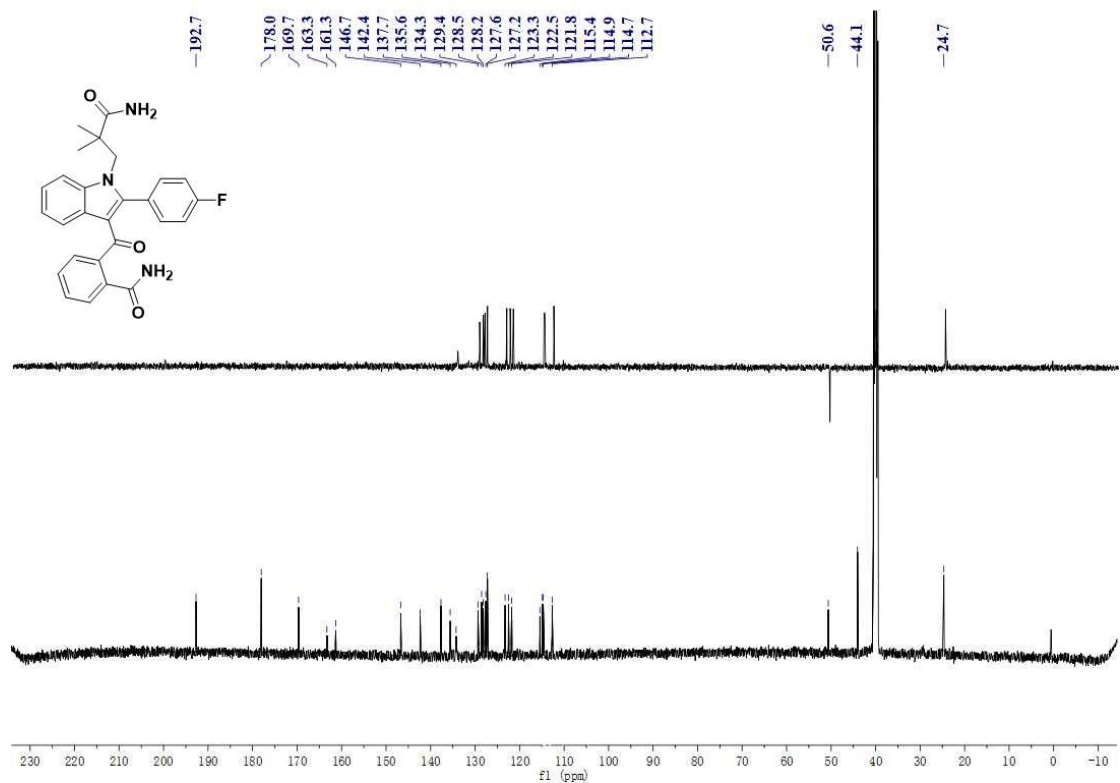
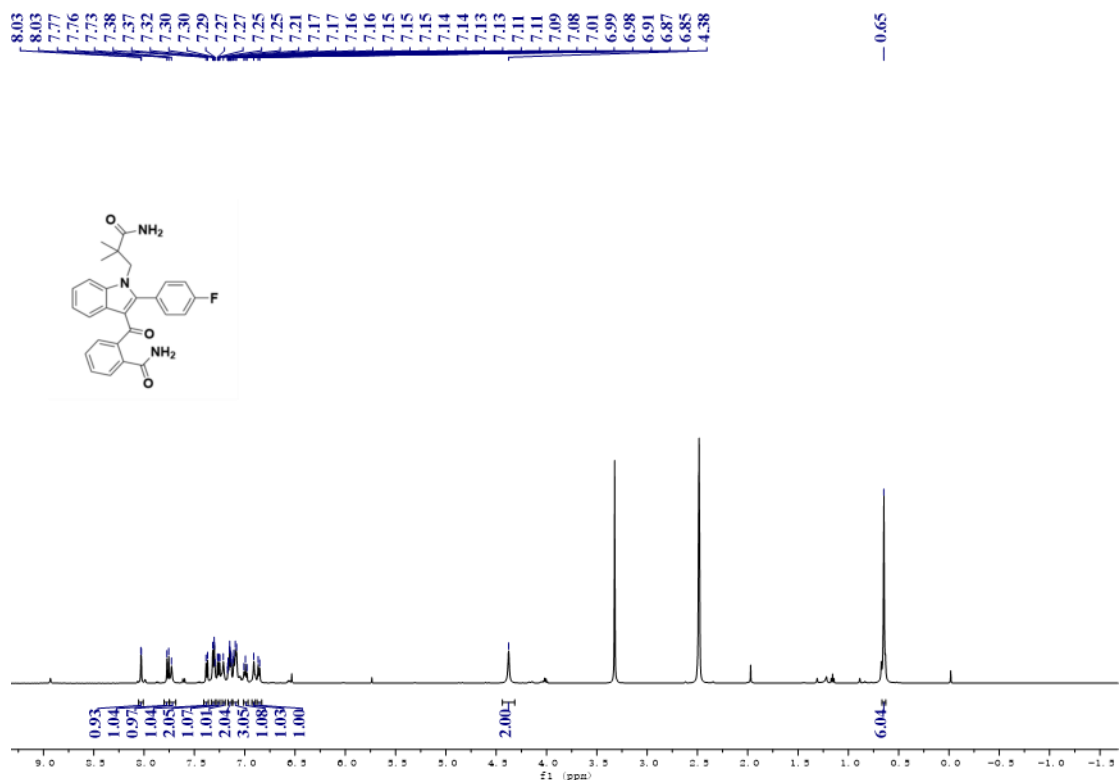
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5-chloro-2-phenyl-1*H*-indole-3-carbonyl)benzamide (5ca)**



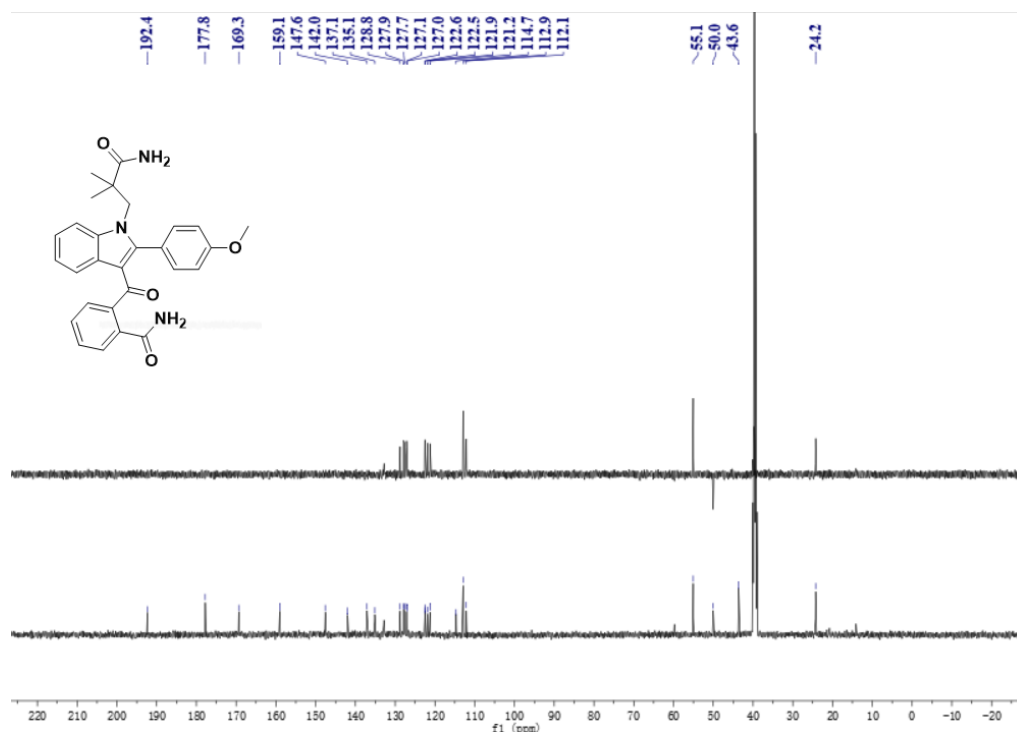
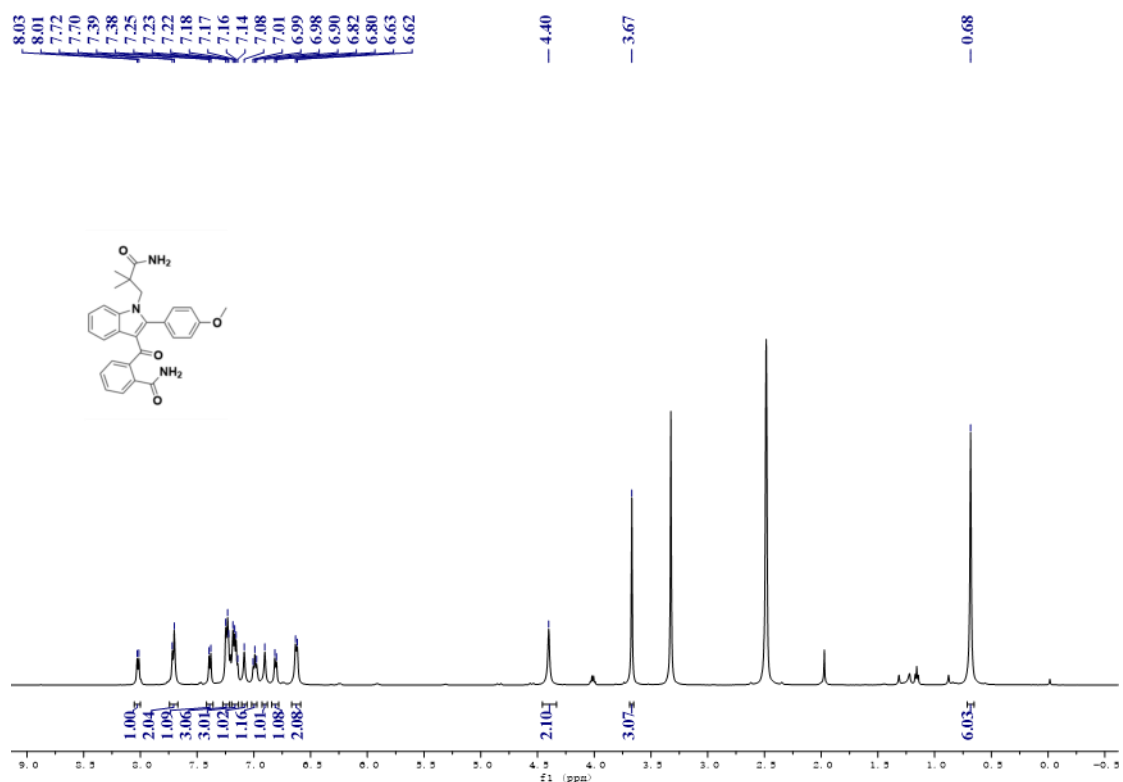
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5-methoxy-2-phenyl-1*H*-indole-3-carbonyl)benzamide (5fa)**



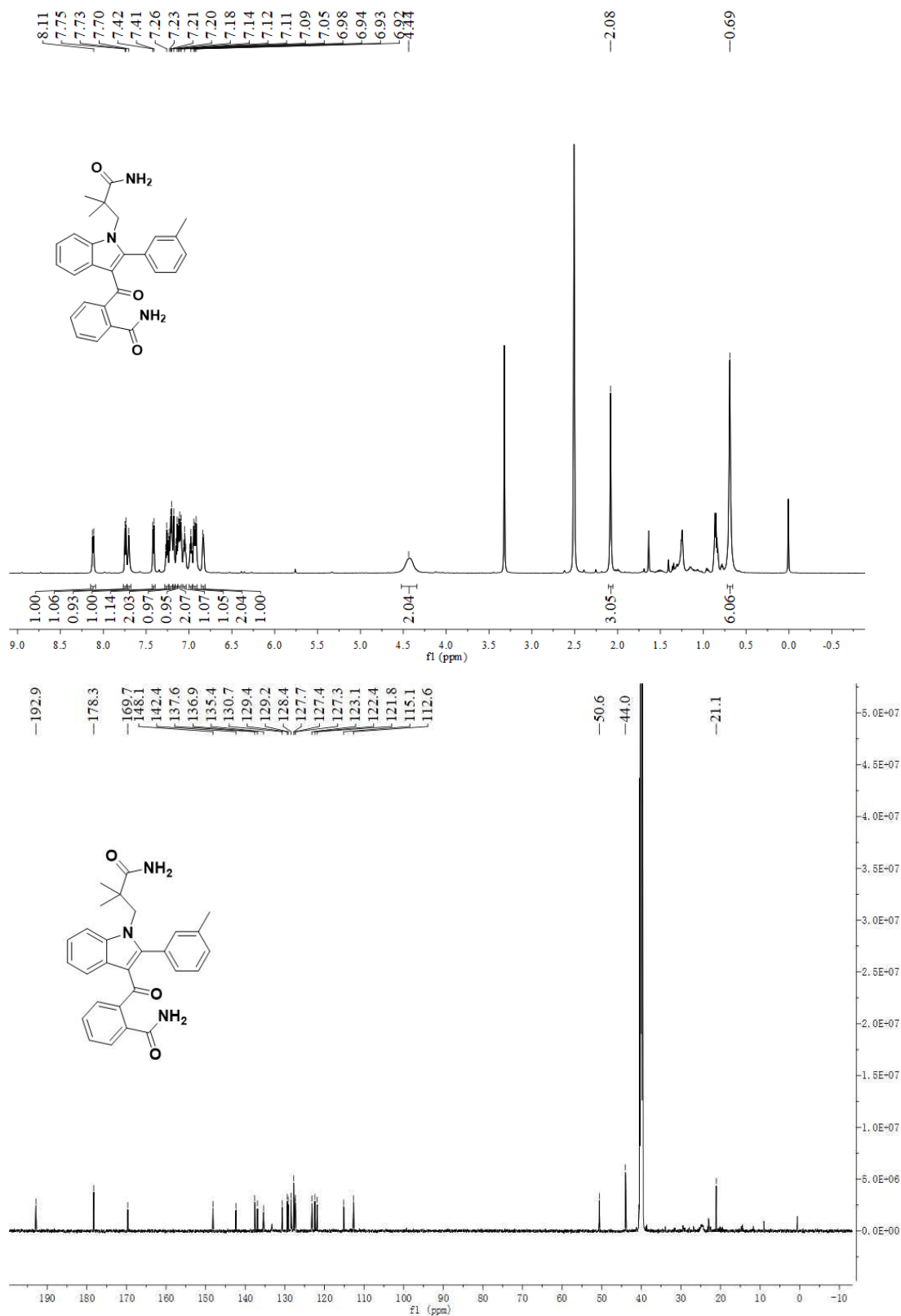
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(4-fluorophenyl)-1*H*-indole-3-carbonyl)benzamide (5ab)**



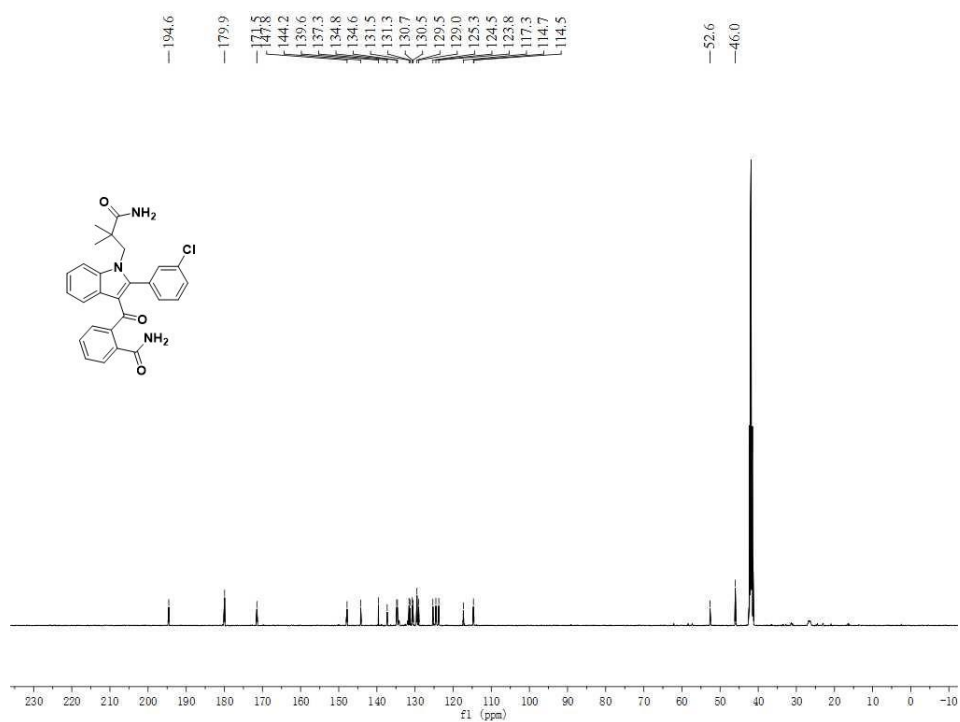
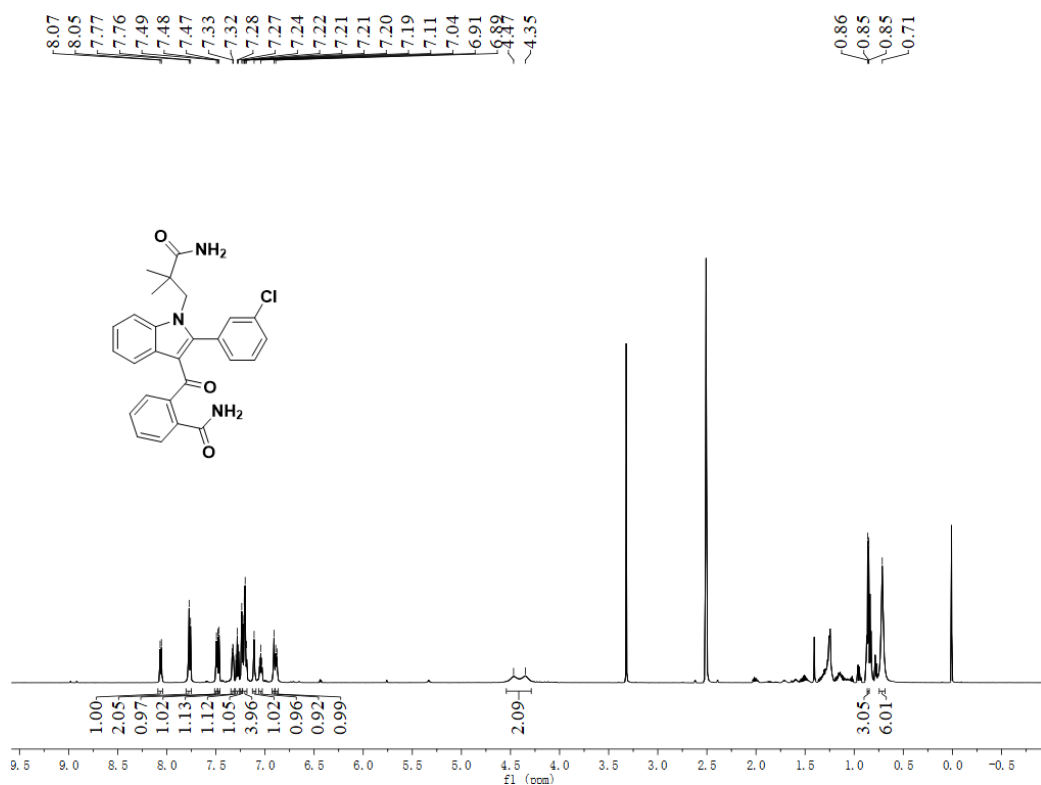
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(4-methoxyphenyl)-1*H*-indole-3-carbonyl)benzamide (5af)**



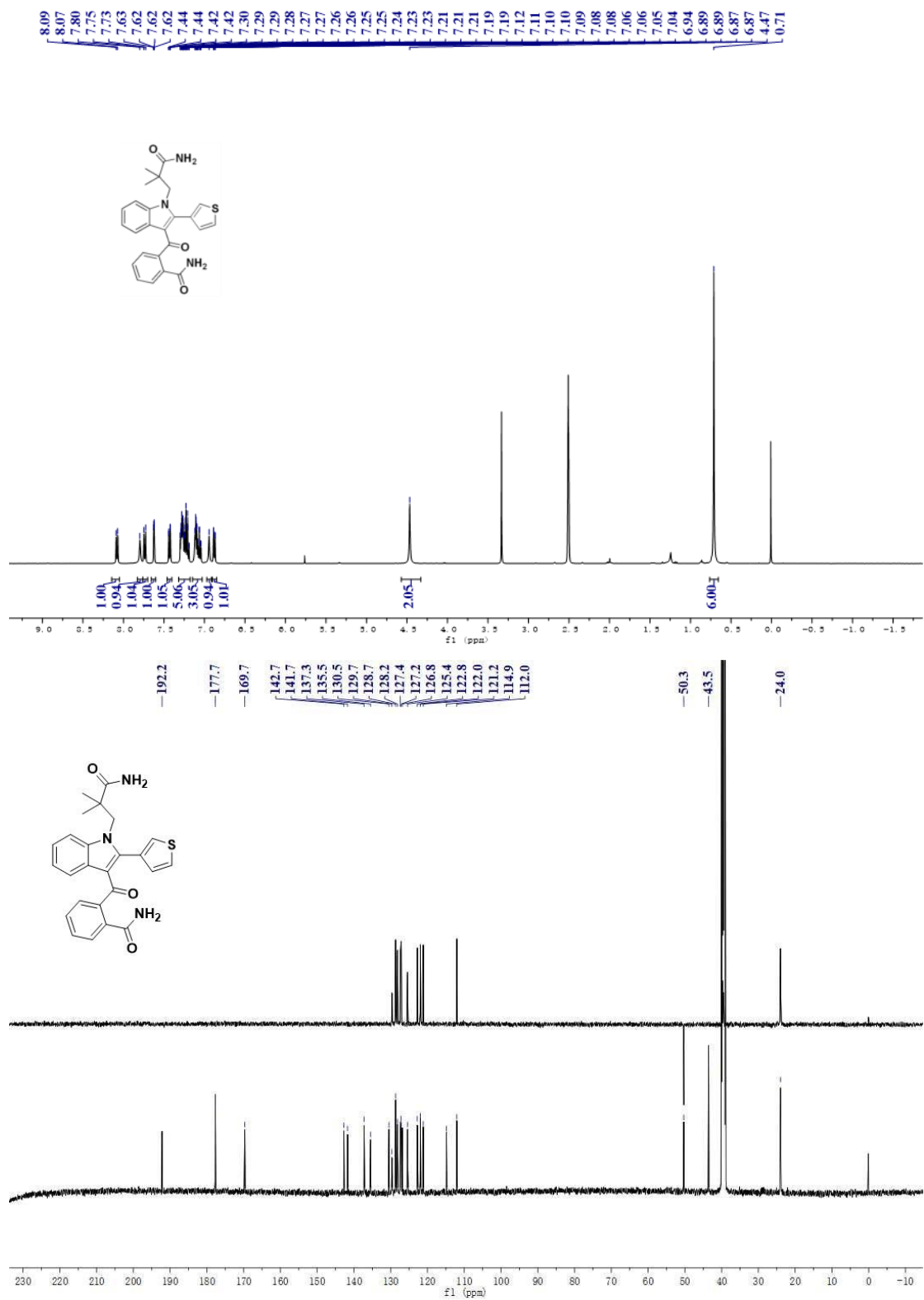
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(3-methylphenyl)-1*H*-indole-3-carbonyl)benzamide (5ai)**



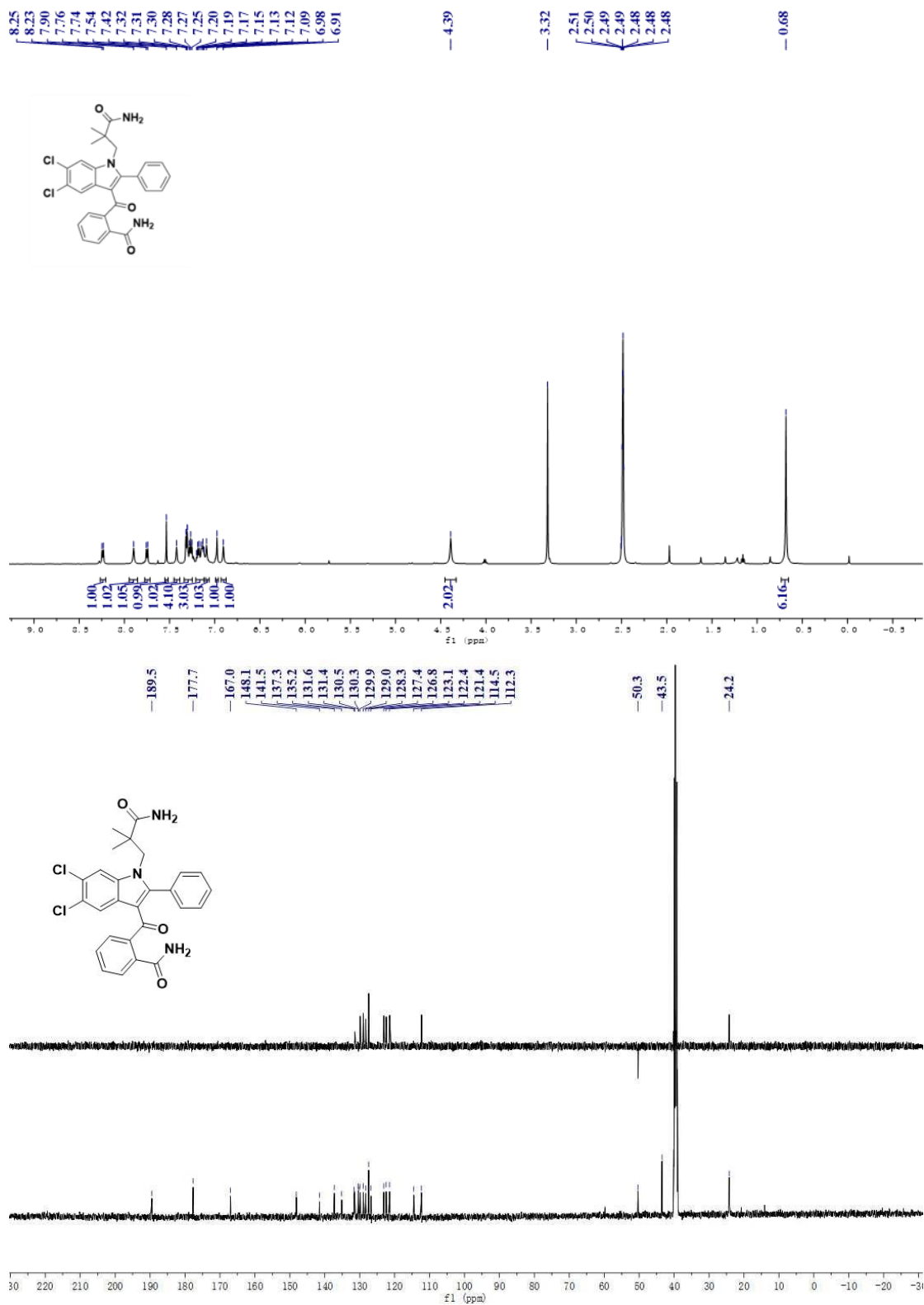
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(3-chlorophenyl)-1*H*-indole-3-carbonyl)benzamide (5ak)**



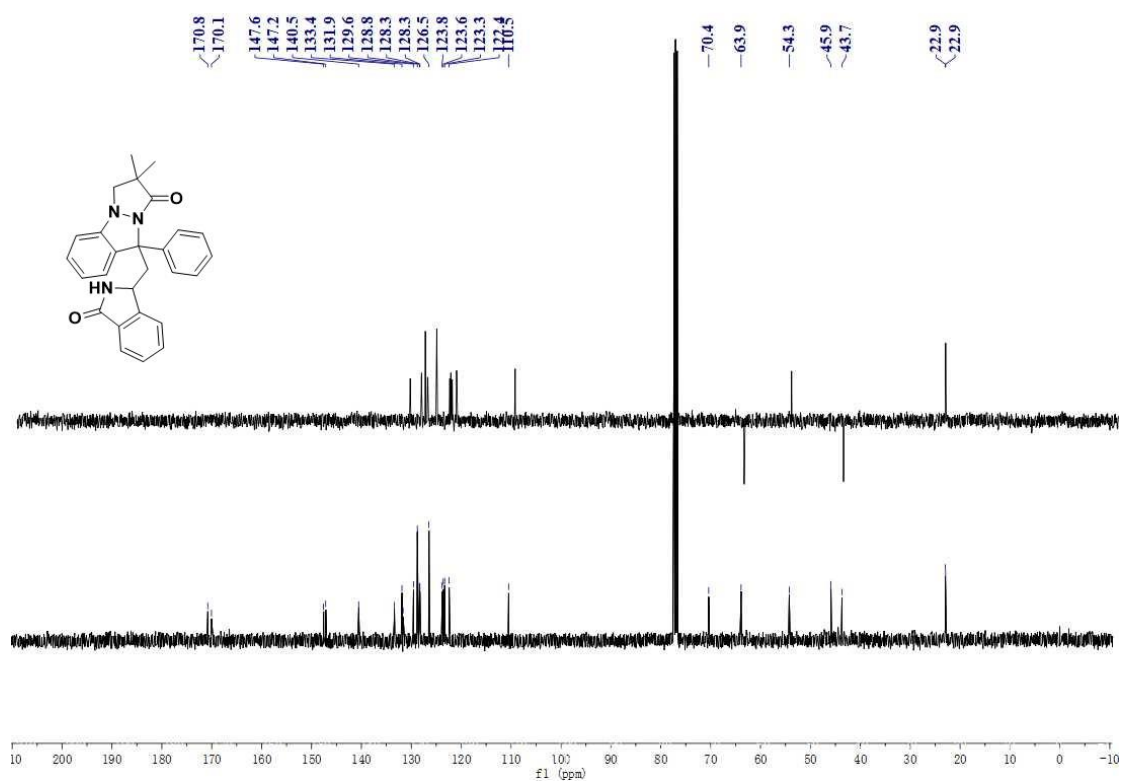
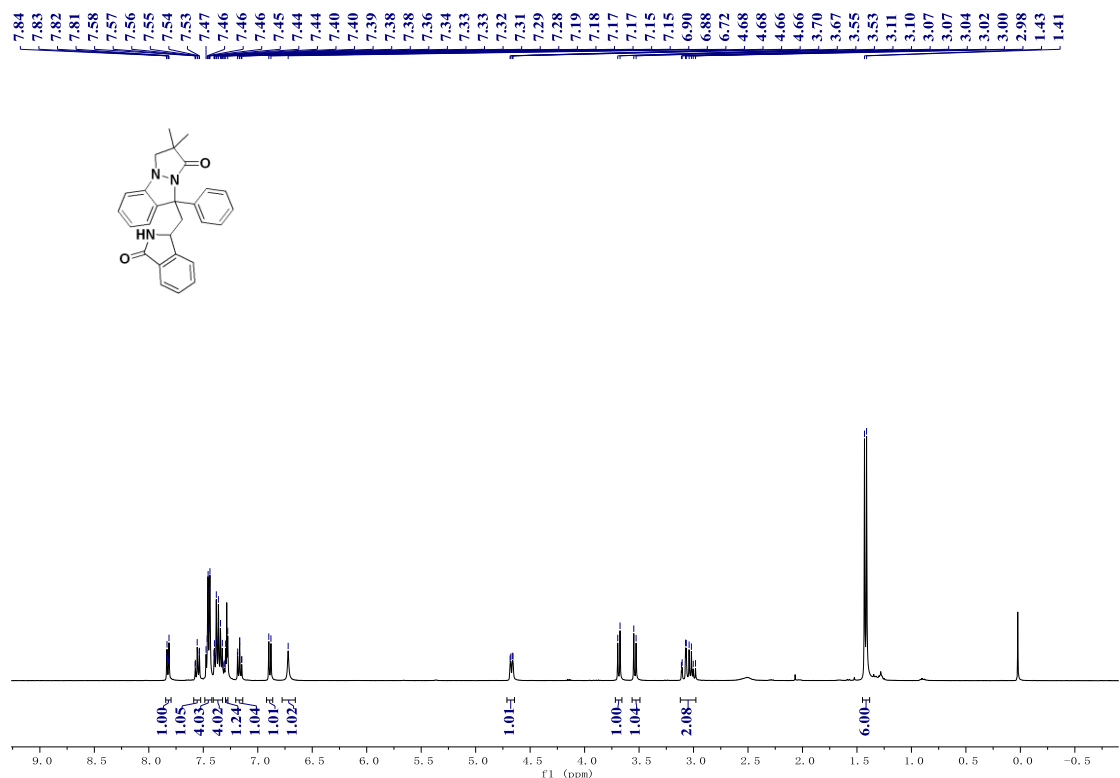
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(thiophen-3-yl)-1H-indole-3-carbonyl)benzamide (5aI)**



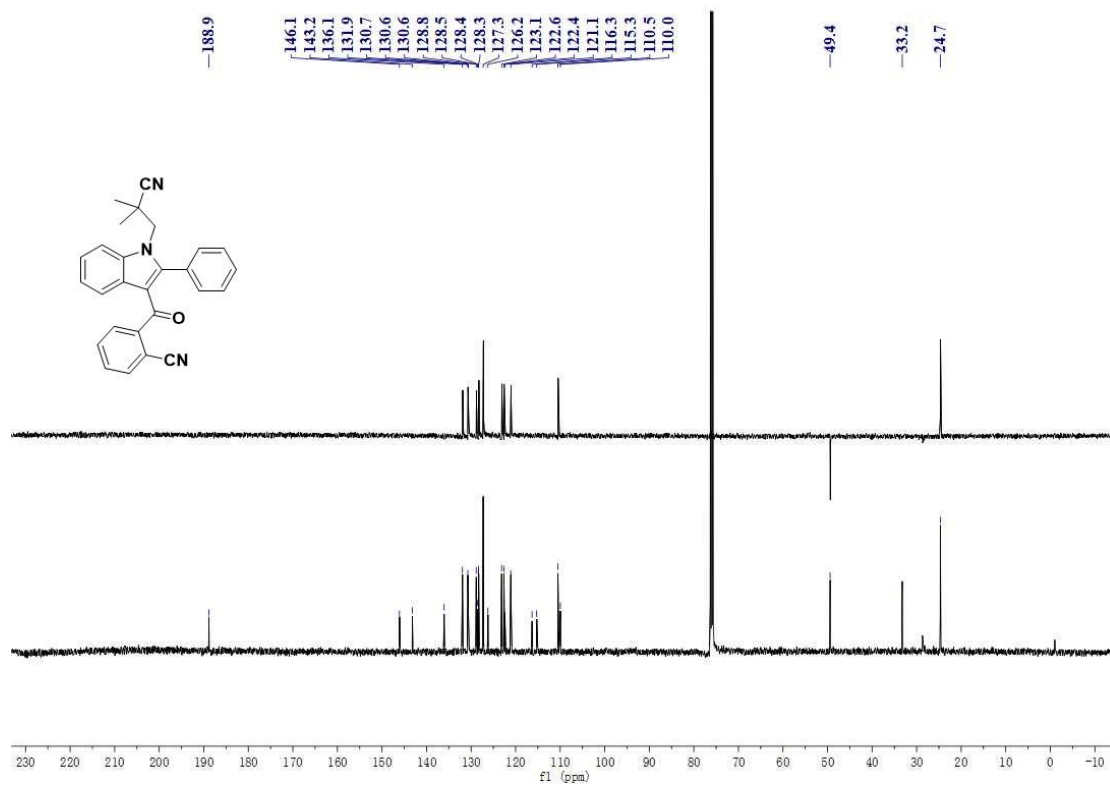
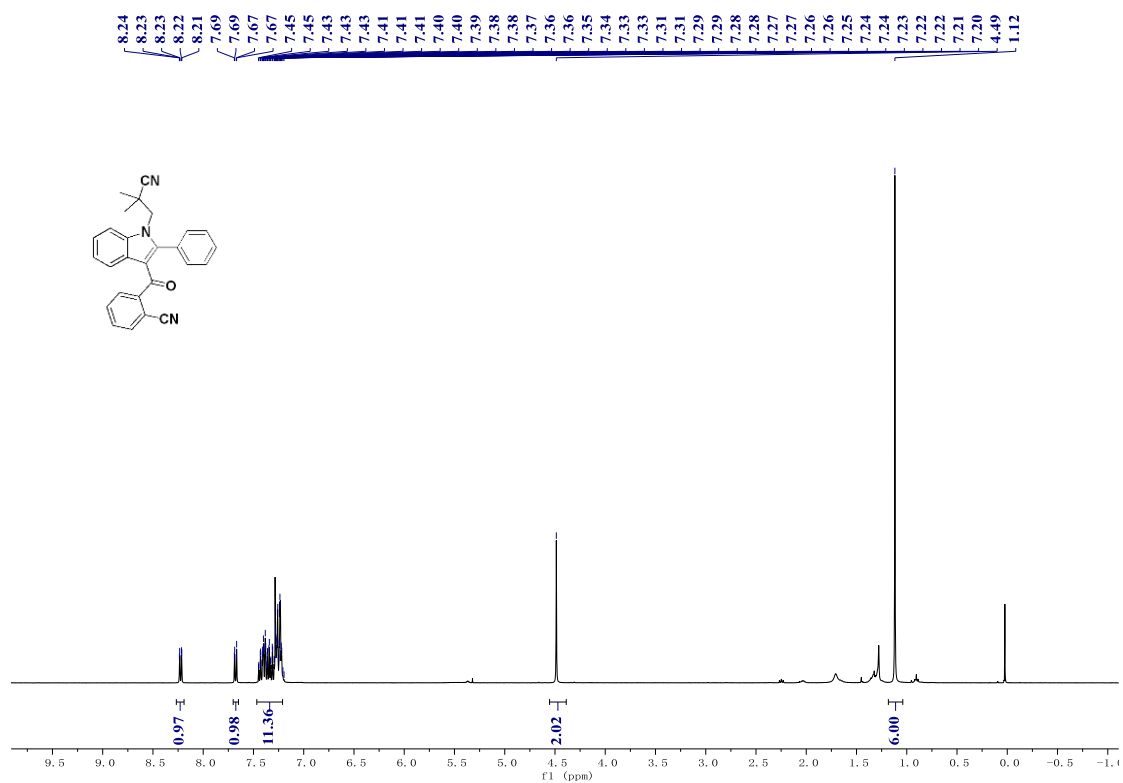
**2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-5,6-dichloro-2-phenyl-1H-indole-3-carbonyl)benzamide (5am)**



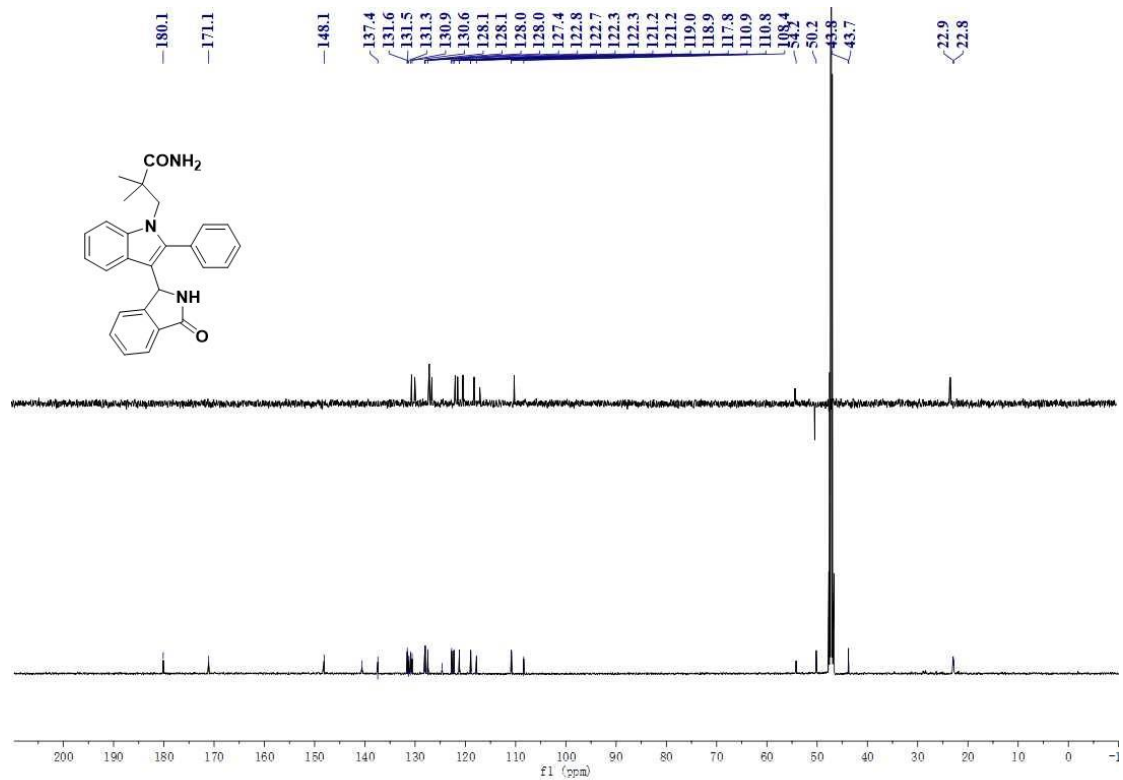
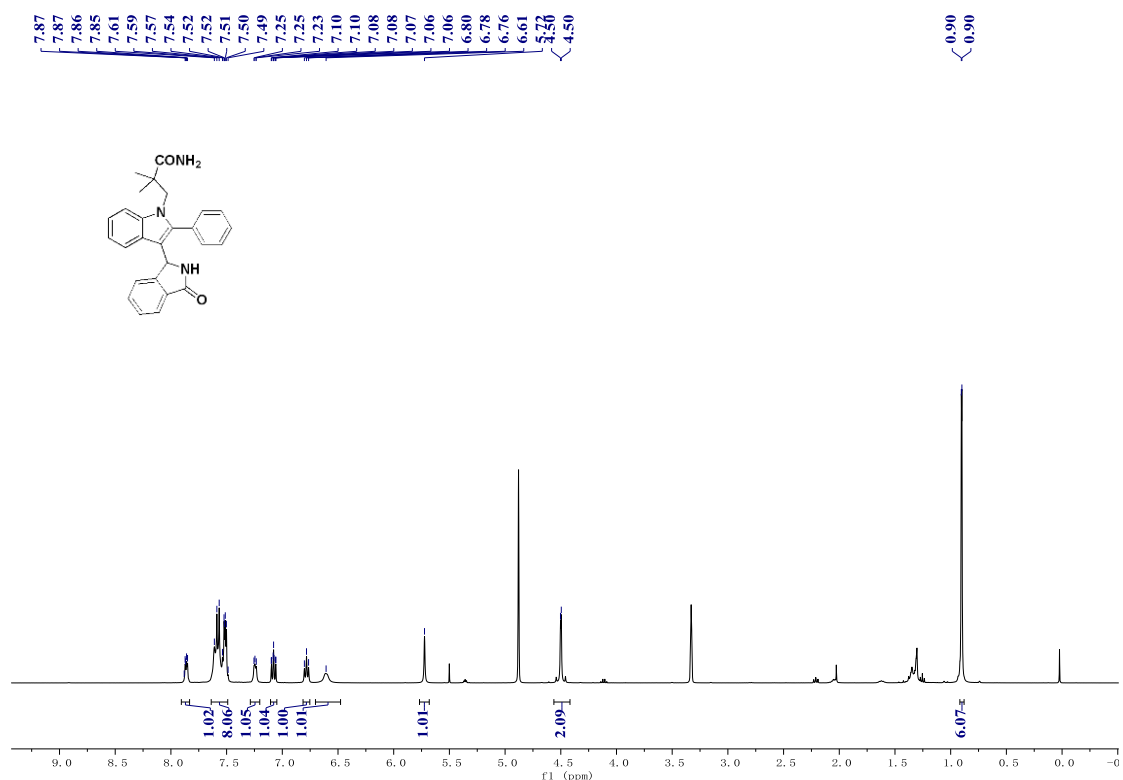
**2,2-dimethyl-9-((3-oxoisindolin-1-yl)methyl)-9-phenyl-2,3-dihydro-1*H*,9*H*-pyrazolo[1,2-  
a]indazol-1-one (6)**



**2-(1-(2-cyano-2-methylpropyl)-2-phenyl-1*H*-indole-3-carbonyl)benzonitrile (7)**

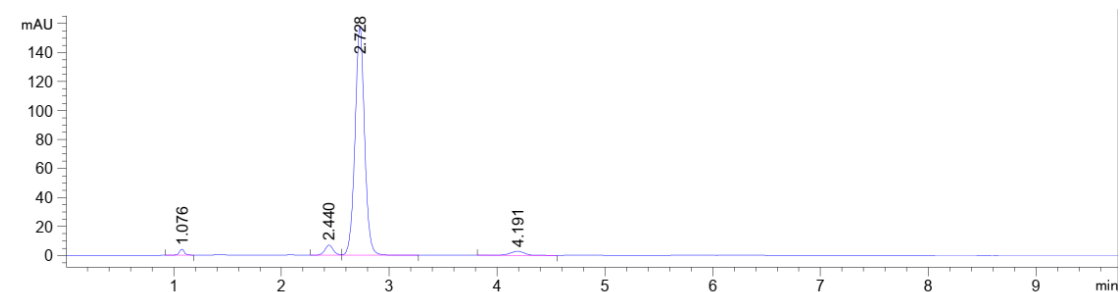


2,2-dimethyl-3-(3-(3-oxoisoindolin-1-yl)-2-phenyl-1*H*-indol-1-yl)propenamide (8)



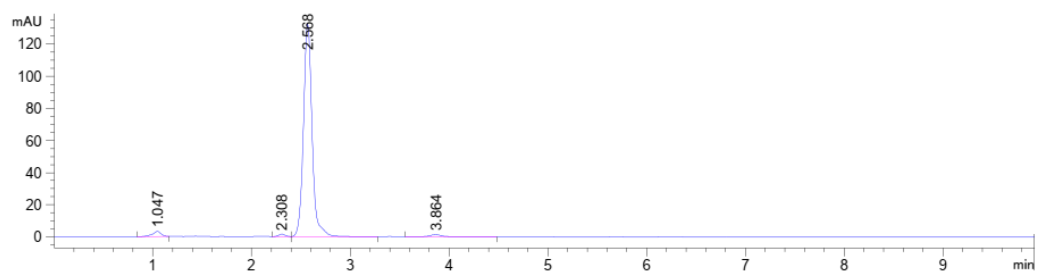
## X. HPLC Data of Products

### (*Z/E*)-3-((1-(4-methoxyphenyl)-5,5-dimethyl-4-oxo-2-phenylhexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3fa)



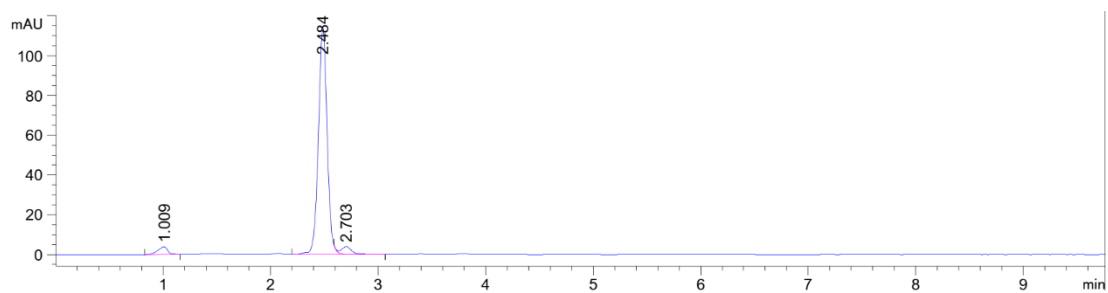
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]  | 峰面积 %   |
|-----|------------|----|----------|-------------|-----------|---------|
| 1   | 1.076      | BB | 0.0543   | 14.04102    | 4.06391   | 1.3356  |
| 2   | 2.440      | BV | 0.0840   | 38.33609    | 6.98852   | 3.6466  |
| 3   | 2.728      | VB | 0.0938   | 971.08032   | 157.76369 | 92.3719 |
| 4   | 4.191      | BB | 0.1447   | 27.81449    | 2.87882   | 2.6458  |

### (*Z/E*)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(*m*-tolyl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3ai)



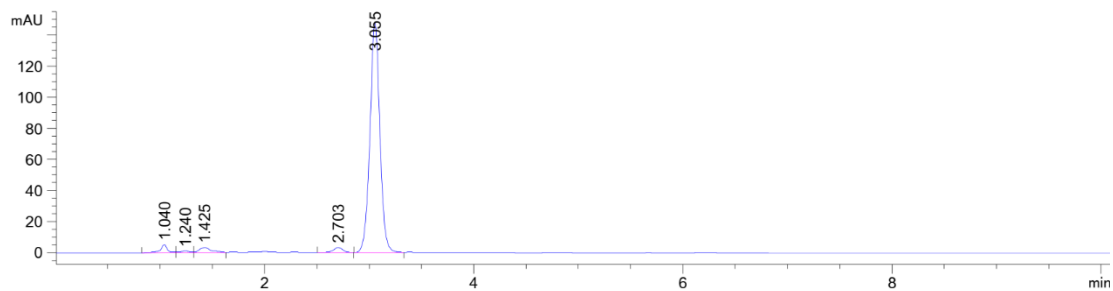
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]  | 峰面积 %   |
|-----|------------|----|----------|-------------|-----------|---------|
| 1   | 1.047      | BB | 0.0873   | 19.97430    | 3.18078   | 2.3687  |
| 2   | 2.308      | BV | 0.0747   | 7.43303     | 1.52927   | 0.8815  |
| 3   | 2.568      | VB | 0.0927   | 802.23846   | 132.39668 | 95.1352 |
| 4   | 3.864      | BB | 0.1411   | 13.61569    | 1.40390   | 1.6146  |

**(Z/E)-3-((5,5-dimethyl-4-oxo-1-phenyl-2-(thiophen-3-yl)hexahydropyrimidin-2-yl)methylene)isoindolin-1-one (3al)**



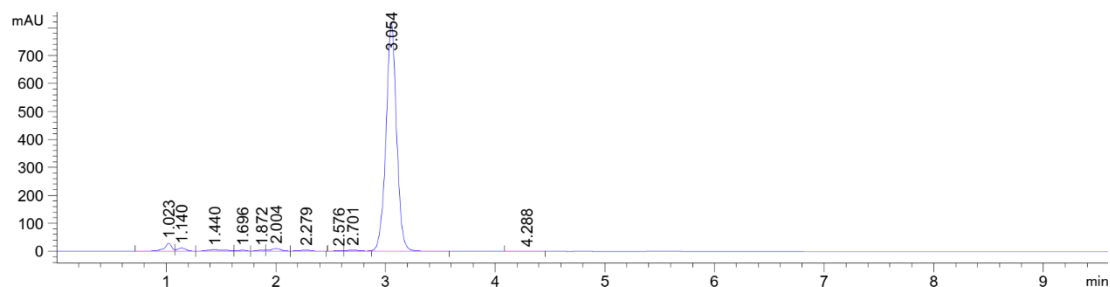
| 峰 # | 保留时间 [min] | 类型   | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]  | 峰面积 %   |
|-----|------------|------|----------|-------------|-----------|---------|
| 1   | 1.009      | BB   | 0.0908   | 24.35287    | 3.79697   | 3.4850  |
| 2   | 2.484      | BV R | 0.0861   | 648.51910   | 114.44514 | 92.8065 |
| 3   | 2.703      | VB E | 0.0984   | 25.91402    | 3.85796   | 3.7084  |

**(Z/E)-6-fluoro-2,2-dimethyl-9-((3-oxoisoindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4ia)**



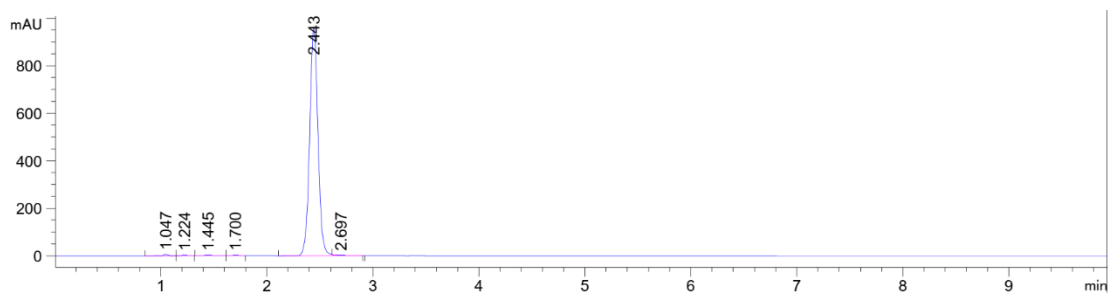
| 峰 # | 保留时间 [min] | 类型 | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]  | 峰面积 %   |
|-----|------------|----|----------|-------------|-----------|---------|
| 1   | 1.040      | BV | 0.0634   | 22.78896    | 5.17395   | 2.1785  |
| 2   | 1.240      | VV | 0.0759   | 5.87707     | 1.07313   | 0.5618  |
| 3   | 1.425      | VB | 0.1164   | 22.80117    | 3.00785   | 2.1796  |
| 4   | 2.703      | BB | 0.0927   | 19.26088    | 3.17848   | 1.8412  |
| 5   | 3.055      | BB | 0.1010   | 975.37708   | 147.83421 | 93.2389 |

**(Z/E)-6-chloro-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-phenyl-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4ja)**



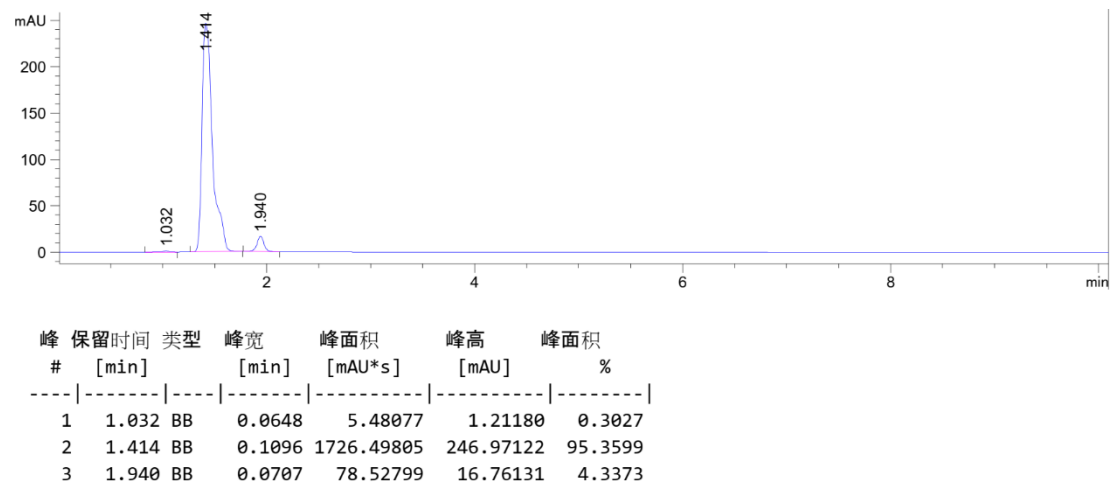
| 峰 # | 保留时间 [min] | 类型   | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]  | 峰面积 %   |
|-----|------------|------|----------|-------------|-----------|---------|
| 1   | 1.023      | BV   | 0.0665   | 132.13000   | 28.26178  | 2.2374  |
| 2   | 1.140      | VB   | 0.0751   | 57.38038    | 11.31824  | 0.9716  |
| 3   | 1.440      | BV   | 0.1365   | 46.54298    | 4.43126   | 0.7881  |
| 4   | 1.696      | VB   | 0.0671   | 12.11019    | 2.76519   | 0.2051  |
| 5   | 1.872      | BV   | 0.0746   | 12.96139    | 2.66935   | 0.2195  |
| 6   | 2.004      | VB   | 0.0832   | 50.64160    | 8.79382   | 0.8575  |
| 7   | 2.279      | BB   | 0.0945   | 23.67161    | 3.61219   | 0.4008  |
| 8   | 2.576      | BV E | 0.0807   | 9.51313     | 1.82884   | 0.1611  |
| 9   | 2.701      | VV E | 0.1082   | 32.24899    | 4.36544   | 0.5461  |
| 10  | 3.054      | VB R | 0.1029   | 5517.39697  | 815.78876 | 93.4267 |
| 11  | 4.288      | BB   | 0.1353   | 10.99170    | 1.24193   | 0.1861  |

**(Z/E)-2,2-dimethyl-9-((3-oxoisindolin-1-ylidene)methyl)-9-(thiophen-3-yl)-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (4al)**

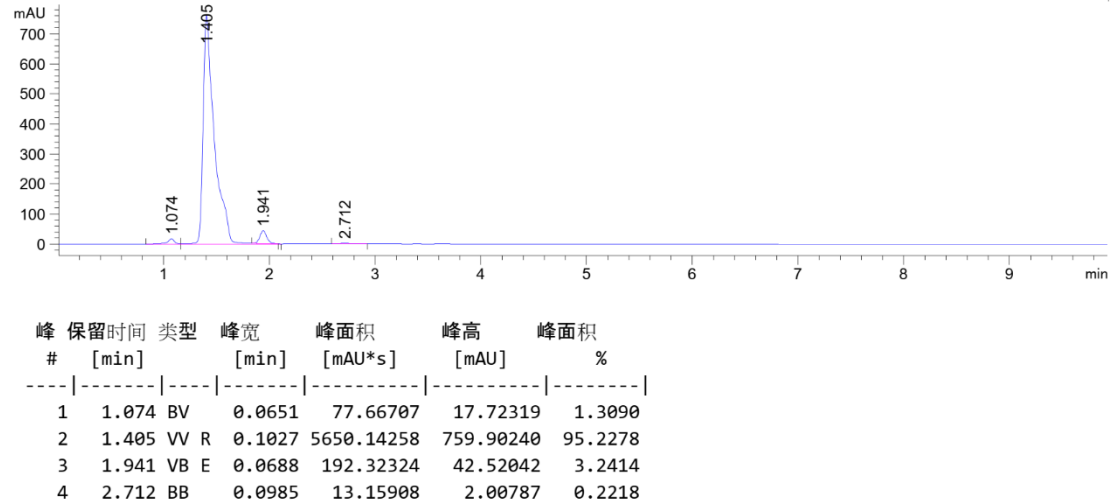


| 峰 # | 保留时间 [min] | 类型   | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]  | 峰面积 %   |
|-----|------------|------|----------|-------------|-----------|---------|
| 1   | 1.047      | BV   | 0.0610   | 21.83553    | 5.19918   | 0.4130  |
| 2   | 1.224      | VB   | 0.0526   | 12.57133    | 3.61460   | 0.2378  |
| 3   | 1.445      | BB   | 0.0983   | 18.15282    | 2.63877   | 0.3434  |
| 4   | 1.700      | BV   | 0.0918   | 9.08126     | 1.61106   | 0.1718  |
| 5   | 2.443      | VB R | 0.0812   | 5210.88867  | 961.96759 | 98.5612 |
| 6   | 2.697      | VB E | 0.0905   | 14.42750    | 2.32060   | 0.2729  |

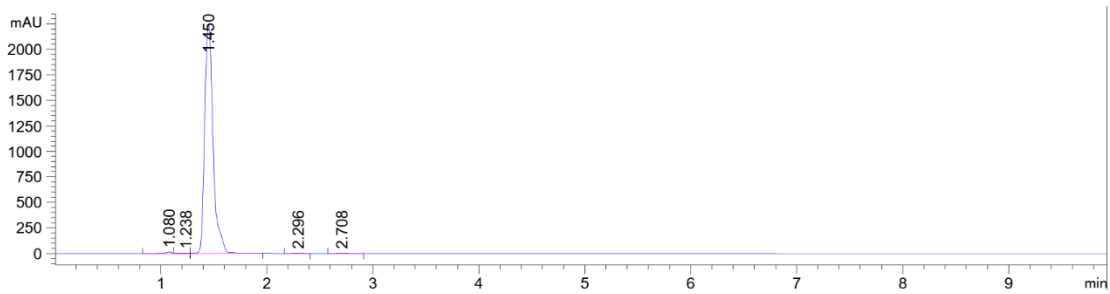
2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(4-methoxyphenyl)-1*H*-indole-3-carbonyl)benzamide (5af)



2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(3-methylphenyl)-1*H*-indole-3-carbonyl)benzamide (5ai)



2-(1-(3-amino-2,2-dimethyl-3-oxopropyl)-2-(3-chlorophenyl)-1*H*-indole-3-carbonyl)benzamide (5ak)



| 峰 # | 保留时间 [min] | 类型   | 峰宽 [min] | 峰面积 [mAU*s] | 峰高 [mAU]   | 峰面积 %   |
|-----|------------|------|----------|-------------|------------|---------|
| 1   | 1.080      | BV R | 0.0554   | 45.99453    | 12.35875   | 0.3714  |
| 2   | 1.238      | VV E | 0.0829   | 12.61239    | 2.19988    | 0.1018  |
| 3   | 1.450      | VB   | 0.0862   | 1.23102e4   | 2238.36646 | 99.4051 |
| 4   | 2.296      | BB   | 0.0757   | 6.71095     | 1.35656    | 0.0542  |
| 5   | 2.708      | BB   | 0.0967   | 8.34928     | 1.30432    | 0.0674  |