# Supporting Information

# Paired Synthesis of Polycyclic Constitutional Isomers via Solvent-Controlled Skeletal Disproportionation

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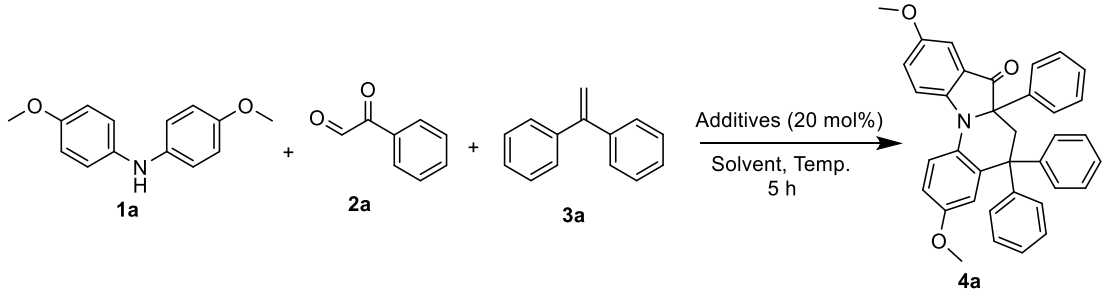
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## 1. General Information

NMR spectra were recorded on Bruker AVANCE III HD 600MHz. Chemical shifts ($\delta$) were reported in parts per million (ppm) relative to residual solvent peaks rounded to the nearest 0.01 for proton and 0.1 for carbon (*ref: $CDCl_3$[$^1$H: 7.26, $^{13}$C: 77.16]*, *DMSO-$d_6$ [$^1$H: 2.5,3.3, $^{13}$C:39.52]*). Coupling constants (*J*) were reported in Hz to the nearest 0.1 Hz. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet-doublet (dd), quintet (quint), sextet (sext), septet (sept), multiplet (m), and broad (b). High-resolution mass spectrometry (HRMS) data was obtained on Thermo Scientific Q Exactive instrument (ESI or APCI source, mass analyzer type is orbitrap). Enantiomeric excesses were measured on a SHIMADZU HPLC using CHIRALPAK columns.

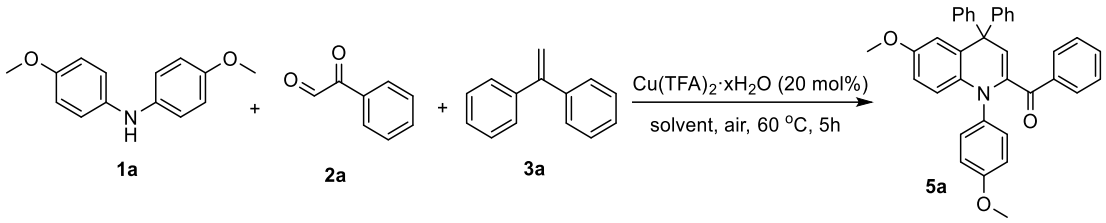
**Materials and Methods:** Unless otherwise stated, starting materials were purchased from commercial sources. Solvents were purchased in HPLC quality. Reactions were monitored by thin layer chromatography (TLC). Compounds were visualized by UV-light at 254 nm and 365 nm and by dipping the plates in a phosphomolybdic acid ethanol solution followed by heating. Flash column chromatography was performed over silica gel (300-400 mesh). The $CDCl_3$ used in the NMR experiments was stored over anhydrous $K_2CO_3$ before use.

## 2. Optimization of the reaction conditions




| Entry | Additives | Temp. (℃) | Solvent | Yield%(**4a**) [b] |
|---|---|---|---|---|
| 1 | $Cu(TFA)_2 \cdot xH_2O$ | 40 | DCE | 32 |
| 2 | $Cu(TFA)_2 \cdot xH_2O$ | 50 | DCE | 82 |
| **3** | **$Cu(TFA)_2 \cdot xH_2O$** | **60** | **DCE** | **88** |
| 4 | $Cu(TFA)_2 \cdot xH_2O$ | 80 | DCE | 81 |
| 5 | $Cu(TFA)_2 \cdot xH_2O$ | 100 | DCE | 70 |
| 6 | $Cu_2O$ | 60 | DCE | Not detected |
| 7 | $CuCO_3.Cu(OH)_2$ | 60 | DCE | Not detected |
| 8 | Copper(I) thiophene-2-carboxylate | 60 | DCE | Not detected |
| 9 | $CuBr_2$ | 60 | DCE | Not detected |
| 10 | Copper(II) hexafluoropentanedionate | 60 | DCE | Not detected |
| 11 | $Cu(OTf)_2$ | 60 | DCE | Not detected |
| **12** | **$Cu(TFA)_2 \bullet xH_2O$** | **60** | **DCE** | **88** |
| 13 | $Cu(TFA)_2 \bullet xH_2O$ | 60 | toluene | Not detected |
| 14 | $Cu(TFA)_2 \bullet xH_2O$ | 60 | 1, 4-dioxane | Not detected |
| 15 | $Cu(TFA)_2 \bullet xH_2O$ | 60 | MeCN | Not detected |
| 16 | $Cu(TFA)_2 \bullet xH_2O$ | 60 | DMF | Not detected |
| 17 | $Cu(TFA)_2 \bullet xH_2O$ | 60 | THF | Not detected |
| 18 | $Cu(TFA)_2 \bullet xH_2O$ | 60 | DMA | Not detected |
| **19** | **$Cu(TFA)_2 \bullet xH_2O$** | **60** | **DCE** | **88** |
| 20 | $Cu(TFA)_2 \bullet xH_2O$ | 60 | EA | Not detected |

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv), **3a** (0.4 mmol, 2.0 equiv), Additives (0.04 mmol, 0.2 equiv) and solvent (2.0 mL, *c* 0.1 M), Temp., 5 h, air atmosphere. [b] Isolated yield.

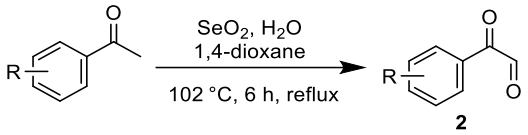



| Entry | Solvent | Yield%(**5a**)[b] |
|---|---|---|
| 1 | DCE | Trace |
| 2 | HFIP | 88% |
| 3 | DCE + MeOH (3:1) | Not detected |
| 4 | DCE + cyclohexanol (3:1) | Not detected |
| 5 | DCE + isopropanol (3:1) | Not detected |
| 6 | DCE + ethylene glycol (3:1) | Not detected |
| 7 | DCE + 2,2,2-Trifluoroethanol (3:1) | 81% |
| 8 | DCE + diethyl ether (3:1) | 30% |
| 9 | DCE + methyl tert-butyl ether (3:1) | Trace |
| 10 | DCE + diethylene glycol dimethyl ether (3:1) | Not detected |
| 11 | DCE + tris(perfluorobutyl)amine (3:1) | 48% |
| **12** | **DCE + HFIP (3:1)** | **89%** |

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv), **3a** (0.4 mmol, 2.0 equiv), $Cu(TFA)_2$•$xH_2O$ (0.04 mmol, 0.2 equiv) and solvent (2.0 mL, *c* 0.1 M),60 ℃, 5 h, air atmosphere.[b] Isolated yield.

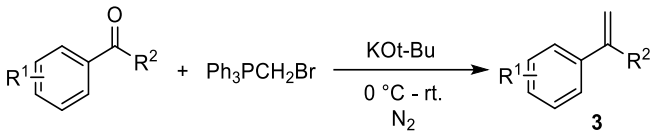
# 3. General procedure

## 3.1 General procedure for the synthesis of 2



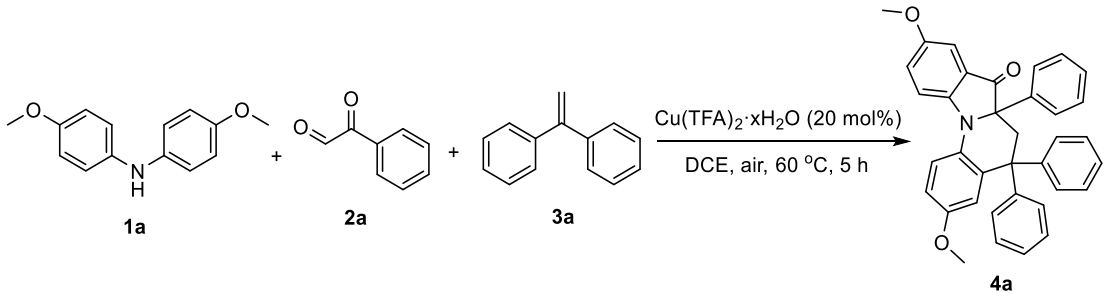

A 50 mL round-bottom flask was charged with acetophenone (10 mmol), tin dioxide (1.2 g, 11 mmol), $H_2O$ (200 μL), and 1,4-dioxane (4 mL). The reaction mixture was heated to reflux at 102 °C for 6 hours. After completion, the mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography eluting with dichloromethane to afford compound **2**.

## 3.2 General procedure for the synthesis of 3




A 30 mL pressure tube was charged with the aryl ketone (4 mmol), $Ph_3PCH_2Br$ (3572.2 mg, 10 mmol, 2.5 equiv), and potassium tert-butoxide (1122.12 mg, 10 mmol, 2.5 equiv). The tube was evacuated and backfilled with nitrogen. The pressure tube was then placed in an ice-water bath, and anhydrous THF (20 mL) was added under a nitrogen atmosphere. The tube was allowed to warm to room temperature and stirred overnight. The reaction progress was monitored by thin-layer chromatography (TLC). Upon complete consumption of the starting material (disappearance of the corresponding spot), the reaction was quenched by the slow addition of saturated aqueous $NH_4Cl$ solution. The mixture was extracted with ethyl acetate three times. The combined organic layers were dried over anhydrous $Na_2SO_4$, filtered to remove the drying agent, and concentrated under reduced pressure using a rotary evaporator to afford the crude product. The crude product was purified by silica gel column chromatography to yield compound **3**.

### 3.3 General procedure for the synthesis of 4

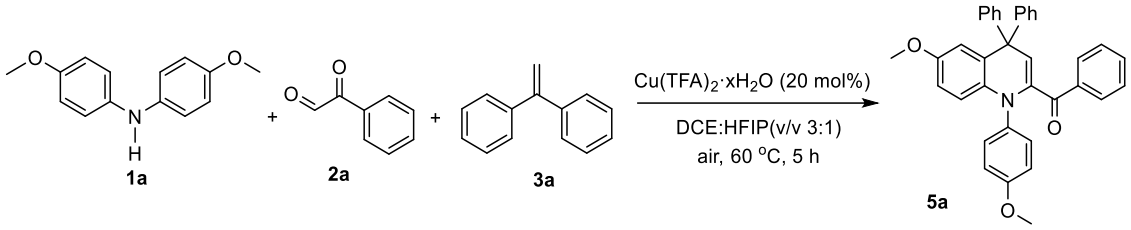



Take the synthesis of **4a** as an example, Bis(4-methoxyphenyl)amine (**1a**, 45.9 mg, 0.2 mmol), 2-oxo-2-phenylacetaldehyde (**2a**, 53.7 mg, 0.4 mmol), and copper(II) trifluoroacetate hydrate (12.4 mg, 0.04 mmol) were successively added to a dried, thick-walled 35 mL pressure tube. Subsequently, 1,2-dichloroethane (2.0 mL) and 1,1-diphenylethylene (**3a**, 72 μL, 0.4 mmol) were added sequentially using a micropipette, and the tube was quickly sealed. The reaction mixture was heated to 60 °C in an oil bath and stirred at this temperature for 5.0 hours. After the reaction was complete, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed successively with saturated sodium chloride solution, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: PE/DCM = 2:1) to afford compound **4a**.

**Experimental procedure for large-scale reactions**

Take the synthesis of **4a** as an example, Bis(4-methoxyphenyl)amine (**1a**, 687.8 mg, 3.0 mmol), 2-oxo-2-phenylacetaldehyde (**2a**, 804.8 mg, 6.0 mmol), and copper(II) trifluoroacetate hydrate (184.6 mg, 0.6 mmol) were successively added to a 100 mL dried, round-bottomed flask. Subsequently, 1,2-dichloroethane (30.0 mL) and 1,1-diphenylethylene (**3a**, 1.1 mL, 6.0 mmol) were added sequentially using a micropipette, and the flask was quickly sealed. The reaction mixture was heated to 60 °C in an oil bath and stirred at this temperature for 5.0 hours. After the reaction was complete, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed successively with saturated sodium chloride solution, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: PE/DCM = 2:1) to afford compound **4a** as a yellow oil (973.2 mg, 62%).

### 3.4 General procedure for the synthesis of 5

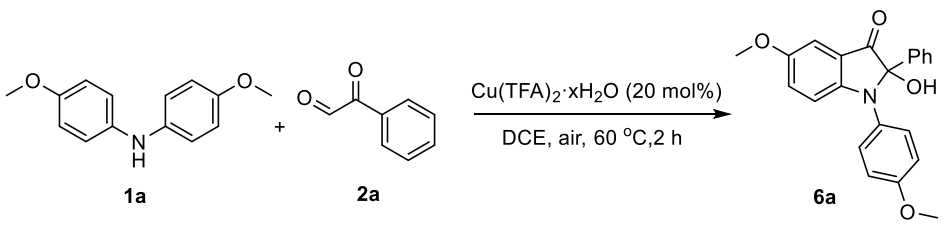



Take the synthesis of **5a** as an example, Bis(4-methoxyphenyl)amine (**1a**, 45.9 mg, 0.2 mmol), 2-oxo-2-phenylacetaldehyde (**2a**, 53.7 mg, 0.4 mmol), and copper(II) trifluoroacetate hydrate (12.3 mg, 0.04 mmol) were successively added to a dried, thick-walled 35 mL pressure tube. Subsequently, 1,2-dichloroethane (1.5 mL), hexafluoroisopropanol (0.5 mL), and 1,1-diphenylethylene (**3a**, 72 μL, 0.4 mmol) were added sequentially using a micropipette, and the tube was quickly sealed. The reaction mixture was heated to 60 °C in an oil bath and stirred at this temperature for 5.0 hours. After the reaction was complete, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed successively with saturated sodium chloride solution, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: PE/DCM = 3:1) to afford compound **5a**.

**Experimental procedure for large-scale reactions**

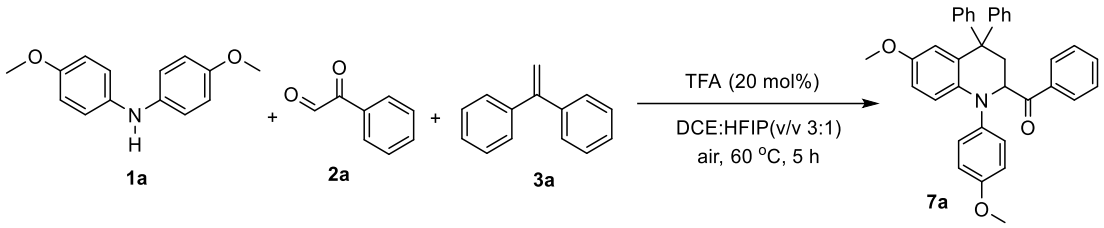
Take the synthesis of **5a** as an example, Bis(4-methoxyphenyl)amine (**1a**, 687.8 mg, 3.0 mmol), 2-oxo-2-phenylacetaldehyde (**2a**, 804.8 mg, 6.0 mmol), and copper(II) trifluoroacetate hydrate (184.6 mg, 0.6 mmol) were successively added to a 100 mL dried, round-bottomed flask. Subsequently, 1,2-dichloroethane (22.5 mL) hexafluoroisopropanol (7.5 mL), and 1,1-diphenylethylene (**3a**, 1.1 mL, 6.0 mmol) were added sequentially using a micropipette, and the flask was quickly sealed. The reaction mixture was heated to 60 °C in an oil bath and stirred at this temperature for 5.0 hours. After the reaction was complete, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed successively with saturated sodium chloride solution, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: PE/DCM = 3:1) to afford compound **5a** as a yellow oil (895.0 mg, 57%).

### 3.5 General procedure for the synthesis of 6a



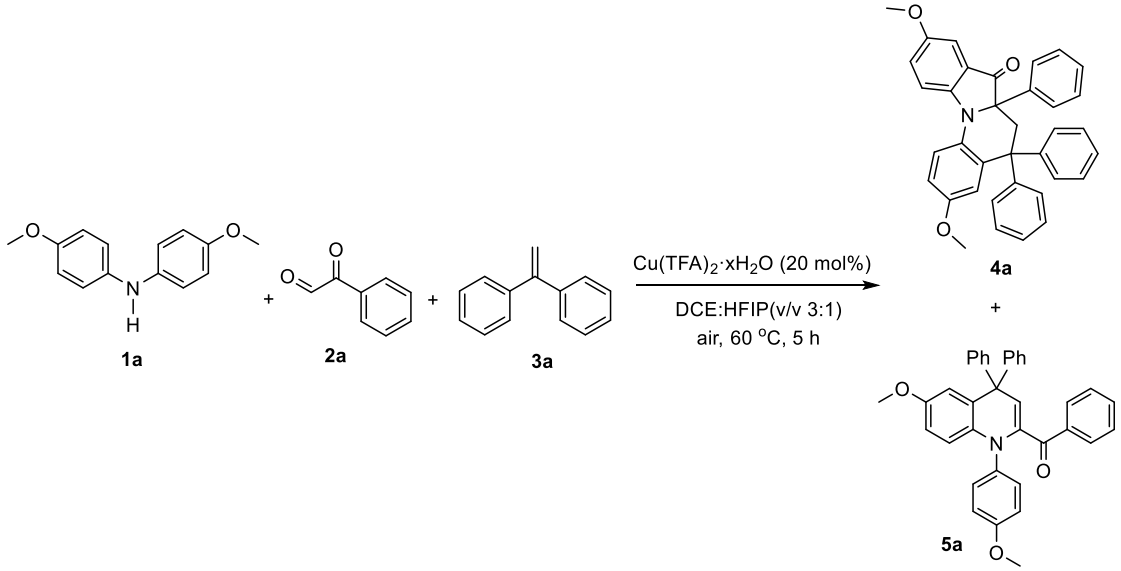
Bis(4-methoxyphenyl)amine (**1a**, 45.9 mg, 0.2 mmol), 2-oxo-2-phenylacetaldehyde (**2a**, 53.7 mg, 0.4 mmol), and copper(II) trifluoroacetate hydrate (12.3 mg, 0.04 mmol) were successively added to a dried, thick-walled 35 mL pressure tube. Subsequently, 1,2-dichloroethane (2.0 mL) was added using a micropipette, and the tube was quickly sealed. The reaction mixture was heated to 60 °C in an oil bath and stirred at this temperature for 2.0 hours. After the reaction was complete, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed successively with saturated sodium chloride solution, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: PE/EA = 6:1) to afford compound **6a**.

### 3.6 General procedure for the synthesis of 7a




Bis(4-methoxyphenyl)amine (**1a**, 45.9 mg, 0.2 mmol), 2-oxo-2-phenylacetaldehyde (**2a**, 53.7 mg, 0.4 mmol), and trifluoroacetic acid (15 μL, 0.04 mmol) were successively added to a dried, thick-walled 35 mL pressure tube. Subsequently, 1,2-dichloroethane (1.5 mL), hexafluoroisopropanol (0.5 mL), and 1,1-diphenylethylene (**3a**, 72 μL, 0.4 mmol) were added sequentially using a micropipette, and the tube was quickly sealed. The reaction mixture was heated to 60 °C in an oil bath and stirred at this temperature for 5.0 hours. After the reaction was complete, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed successively with saturated sodium chloride solution, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: PE/DCM = 2:1) to afford compound **7a**.

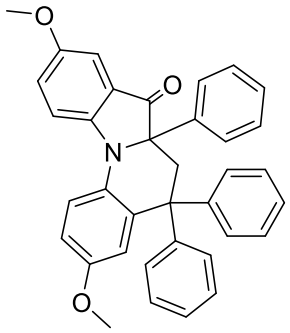
### 3.7 General procedure for scale-up reaction experiments yielding both 4a and 5a




Bis(4-methoxyphenyl)amine (**1a**, 687.8 mg, 3.0 mmol), 2-oxo-2-phenylacetaldehyde (**2a**, 804.8 mg, 6.0 mmol), and copper(II) trifluoroacetate hydrate (184.6 mg, 0.6 mmol) were successively added to a 100 mL dried, round-bottomed flask. Subsequently, 1,2-dichloroethane (29.0 mL) hexafluoroisopropanol (1.0 mL), and 1,1-diphenylethylene (**3a**, 1081.5 μL, 6.0 mmol) were added sequentially using a micropipette, and the flask was quickly sealed. The reaction mixture was heated to 60 °C in an oil bath and stirred at this temperature for 5.0 hours. After the reaction was complete, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was washed successively with saturated sodium chloride solution, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (eluent: PE/DCM/EA = 60:5:1) to afford compound **4a** as a yellow oil (675.0 mg, 43%) and compound **5a** as a yellow oil (612.2 mg, 39%).

## 4. Synthesis and characterization data of compounds

3,9-dimethoxy-5,5,6a-triphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4a**)



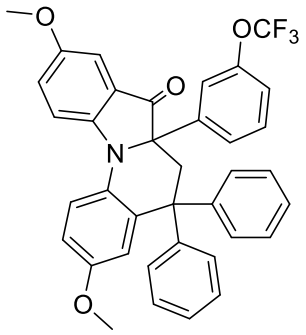
Compound **4a** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, ethene-1,1-diyldibenzene. **4a** was obtained in 88% yield (92.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.65 – 7.60 (m, 3H), 7.28 (t, *J* = 7.7 Hz, 3H), 7.26 – 7.19 (m, 3H), 7.03 – 6.97 (m, 4H), 6.94 (dd, *J* = 8.9, 2.7 Hz, 1H), 6.89 – 6.86 (m, 3H), 6.73 (dd, *J* = 6.7, 2.9 Hz, 2H), 6.57 (d, *J* = 2.7 Hz, 1H), 6.24 (d, *J* = 2.9 Hz, 1H), 4.12 (d, *J* = 13.9 Hz, 1H), 3.67 (s, 3H), 3.64 (s, 3H), 3.23 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.9, 156.7, 156.0, 153.5, 145.1, 144.8, 142.6, 142.6, 132.9, 129.7, 129.2, 128.8, 128.1, 127.8, 126.84, 126.81, 126.5, 126.4, 125.6, 120.3, 116.4, 112.0, 110.4, 105.5, 72.4, 56.0, 55.5, 52.5, 49.0.

**HRMS** (ESI) m/z calcd for $C_{36}H_{29}NO_3Na^+$ $(M+Na)^+$ 546.2040, found 546.2040.

3,9-dimethoxy-5,5-diphenyl-6a-(3-(trifluoromethoxy)phenyl)-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4b**)



Compound **4b** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-(3-(trifluoromethoxy)phenyl)acetaldehyde, ethene-1,1-diyldibenzene. **4b** was obtained in 94% yield (114.2 mg) as yellow solid.

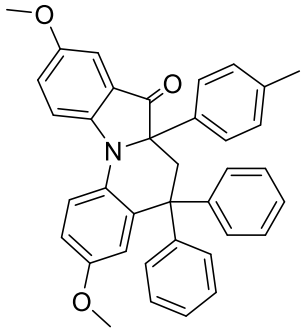
**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.59 (d, *J* = 8.5 Hz, 1H), 7.56 – 7.54 (m, 1H), 7.44 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.05 – 7.00 (m, 2H), 6.98 (dd, *J* = 8.6, 2.9 Hz, 1H), 6.95 (ddd, *J* = 8.9, 5.1, 2.2 Hz, 3H), 6.87 (dd, *J* = 5.1, 1.9 Hz, 3H), 6.72 – 6.68 (m, 2H), 6.56 (d, *J* = 2.7 Hz, 1H), 6.22 (d, *J* = 2.9 Hz, 1H), 4.01 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.17 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.2, 156.9, 156.1, 153.7, 149.5, 144.9, 144.8, 144.4, 142.6, 132.5, 130.1, 129.7, 129.2, 128.2, 127.8, 127.0, 126.9, 126.8, 126.5, 124.3, 120.2, 119.6, 118.2, 116.6, 112.2, 110.8, 105.4, 72.0, 56.0, 55.5, 52.4, 48.9.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -57.6.

**HRMS** (ESI) m/z calcd for $C_{37}H_{28}F_3NO_4Na^+$ $(M+Na)^+$ 630.1863, found 630.1862.

3,9-dimethoxy-5,5-diphenyl-6a-(p-tolyl)-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4c**)



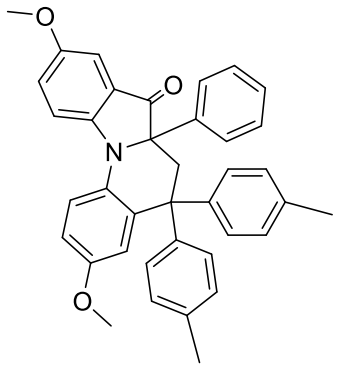

Compound **4c** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-(p-tolyl)acetaldehyde, ethene-1,1-diyldibenzene. **4c** was obtained in 94% yield (101.0 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.57 (d, *J* = 8.5 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.24 – 7.21 (m, 3H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.96 (ddd, *J* = 10.9, 7.9, 3.2 Hz, 4H), 6.90 (dd, *J* = 8.9, 2.7 Hz, 1H), 6.86 – 6.83 (m, 3H), 6.69 (dd, *J* = 6.4, 3.0 Hz, 2H), 6.54 (d, *J* = 2.7 Hz, 1H), 4.08 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 3.19 (d, *J* = 13.8 Hz, 1H), 2.26 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 202.2, 156.7, 156.0, 153.4, 145.2, 144.9, 142.6, 139.6, 137.2, 132.9, 129.7, 129.5, 129.2, 128.2, 127.8, 126.8, 126.5, 126.4, 125.5, 120.3, 116.4, 111.9, 110.4, 105.5, 72.3, 56.0, 55.5, 52.5, 49.0, 21.1.

**HRMS** (ESI) m/z calcd for $C_{37}H_{31}NO_3Na^+$ $(M+Na)^+$ 560.21962, found 560.21960.

3,9-dimethoxy-6a-phenyl-5,5-di-p-tolyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one (**4d**)



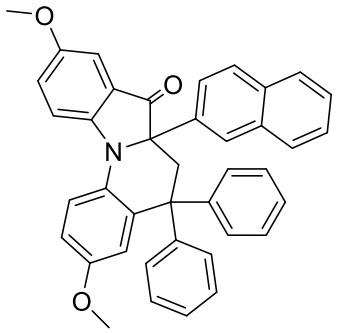
Compound **4d** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 4,4'-(ethene-1,1-diyl)bis(methylbenzene). **4d** was obtained in 58% yield (63.9 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.65 – 7.60 (m, 2H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.28 (s, 1H), 7.25 (s, 1H), 7.22 – 7.16 (m, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 7.00 – 6.91 (m, 3H), 6.89 (d, *J* = 7.9 Hz, 2H), 6.62 (d, *J* = 7.9 Hz, 2H), 6.56 – 6.51 (m, 3H), 6.23 (d, *J* = 2.9 Hz, 1H), 4.03 (d, *J* = 13.7 Hz, 1H), 3.67 (s, 3H), 3.64 (s, 3H), 3.15 (d, *J* = 13.7 Hz, 1H), 2.31 (s, 3H), 2.07 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 202.1, 156.8, 156.4, 153.5, 145.4, 142.7, 142.2, 139.6, 136.4, 135.8, 133.0, 129.7, 129.0, 128.9, 128.8, 128.3, 127.4, 126.9, 126.4, 125.6, 120.4, 116.5, 111.6, 110.7, 105.2, 72.6, 55.9, 55.5, 51.8, 49.3, 21.0, 20.7.

**HRMS (ESI)** m/z calcd for $C_{38}H_{33}NO_3Na^+$ $(M+Na)^+$ 574.2353, found 574.2353.

3,9-dimethoxy-6a-(naphthalen-2-yl)-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4e**)



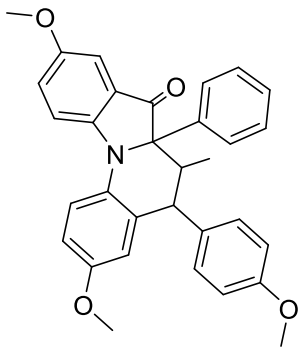
Compound **4e** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(naphthalen-2-yl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4e** was obtained in 94% yield (107.8 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 8.03 (s, 1H), 7.78 – 7.73 (m, 4H), 7.69 (d, *J* = 8.5 Hz, 1H), 7.40 (dd, *J* = 6.4, 2.8 Hz, 2H), 7.24 – 7.19 (m, 3H), 7.05 (d, *J* = 9.0 Hz, 1H), 7.01 – 6.97 (m, 3H), 6.95 (dt, *J* = 9.0, 1.6 Hz, 1H), 6.89 – 6.87 (m, 3H), 6.75 (dd, *J* = 6.6, 2.6 Hz, 2H), 6.57 (d, *J* = 2.7 Hz, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 4.18 (d, *J* = 14.0 Hz, 1H), 3.66 (d, *J* = 1.0 Hz, 3H), 3.65 – 3.62 (m, 3H), 3.29 (d, *J* = 14.0 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.9, 156.8, 156.0, 153.5, 145.1, 144.7, 142.7, 139.8, 133.3, 133.0, 132.8, 129.8, 129.2, 128.8, 128.3, 128.2, 127.8, 127.6, 126.9, 126.8, 126.6, 126.5, 126.1, 126.0, 124.1, 123.9, 120.4, 116.5, 112.0, 110.6, 105.5, 72.6, 56.0, 55.5, 52.5, 49.1.

**HRMS (ESI)** m/z calcd for $C_{40}H_{31}NO_3Na^+$ $(M+Na)^+$ 596.2196, found 596.2194.

3,9-dimethoxy-5-(4-methoxyphenyl)-6-methyl-6a-phenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4f**)



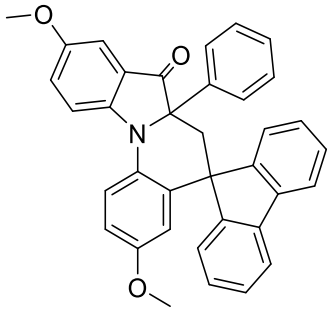
Compound **4f** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, (*E*)-1-methoxy-4-(prop-1-en-1-yl)benzene. **4f** was obtained in 94% yield (92.3 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.73 (d, *J* = 8.9 Hz, 1H), 7.67 (d, *J* = 9.1 Hz, 1H), 7.21 (dd, *J* = 9.1, 2.8 Hz, 1H), 7.09 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.05 – 6.99 (m, 2H), 6.94 – 6.90 (m, 1H), 6.87 (dd, *J* = 8.3, 7.0 Hz, 2H), 6.60 (d, *J* = 2.9 Hz, 1H), 6.39 – 6.25 (m, 4H), 4.06 (s, 1H), 3.76 (s, 3H), 3.70 (s, 3H), 3.68 (s, 3H), 3.41 – 3.36 (m, 1H), 1.03 (d, *J* = 6.9 Hz, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.0, 157.0, 154.7, 153.5, 152.7, 137.8, 136.0, 131.9, 129.6, 129.3, 128.0, 127.7, 127.0, 126.6, 121.2, 120.6, 116.9, 114.2, 113.1, 110.3, 105.9, 74.2, 55.9, 55.6, 55.4, 49.3, 43.8, 18.9.

**HRMS (ESI)** m/z calcd for $C_{32}H_{29}NO_4Na^+$ $(M+Na)^+$ 514.1989, found 514.1990.

3',9'-dimethoxy-6a'-phenyl-6',6a'-dihydro-7'H-spiro[fluorene-9,5'-indolo[1,2-a]quinolin]-7'-one(**4g**)



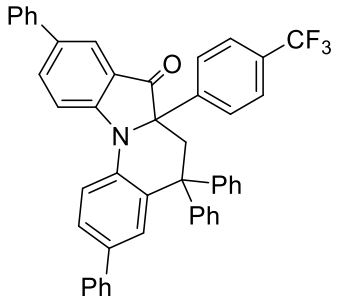

Compound **4g** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 9-methylene-9*H*-fluorene. **4g** was obtained in 94% yield (98.0 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)**δ 7.70 (d, *J* = 8.9 Hz, 1H), 7.65 (dd, *J* = 15.5, 8.0 Hz, 3H), 7.54 (d, *J* = 7.3 Hz, 2H), 7.32 – 7.27 (m, 4H), 7.19 – 7.07 (m, 4H), 6.93 – 6.89 (m, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 6.65 (t, *J* = 7.6 Hz, 1H), 5.75 – 5.72 (m, 1H), 5.32 (d, *J* = 7.8 Hz, 1H), 3.81 (s, 3H), 3.46 (s, 3H), 2.88 (d, *J* = 14.7 Hz, 1H), 2.74 (d, *J* = 14.7 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 199.8, 155.7, 154.5, 154.0, 153.1, 152.8, 140.1, 136.5, 134.5, 128.8, 128.1, 128.0, 127.9, 127.8, 127.7, 127.4, 127.1, 126.6, 124.2, 123.6, 119.9, 119.7, 119.5, 114.8, 113.6, 111.2, 106.2, 71.2, 56.1, 55.4, 53.3, 43.8.

**HRMS (ESI)** m/z calcd for $C_{36}H_{27}NO_3Na^+$ $(M+Na)^+$ 544.1883, found 544.1882.

3,5,5,9-tetraphenyl-6a-(4-(trifluoromethyl)phenyl)-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4h**)




Compound **4h** was synthesized according to general procedure 3.3 starting from di([1,1'-biphenyl]-4-yl)amine, 2-oxo-2-(4-(trifluoromethyl)phenyl)acetaldehyde, ethene-1,1-diyldibenzene. **4h** was obtained in 49% yield (67.0 mg) as yellow solid.

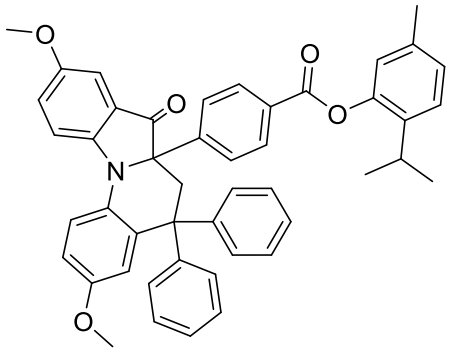
**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.85 (d, *J* = 8.1 Hz, 1H), 7.74 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.63 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.47 – 7.44 (m, 3H), 7.43 – 7.39 (m, 3H), 7.39 – 7.37 (m, 2H), 7.37 – 7.34 (m, 2H), 7.34 – 7.32 (m, 1H), 7.32 – 7.29 (m, 1H), 7.23 (dd, *J* = 5.0, 1.9 Hz, 3H), 6.99 (dd, *J* = 6.8, 2.9 Hz, 2H), 6.96 (d, *J* = 2.1 Hz, 1H), 6.93 – 6.86 (m, 3H), 6.85 – 6.81 (m, 2H), 4.06 (d, *J* = 14.0 Hz, 1H), 3.34 (d, *J* = 14.0 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.6, 158.6, 145.2, 144.7, 143.2, 142.4, 140.4, 140.1, 138.2, 138.1, 136.1, 133.7, 129.6, 129.4, 129.2, 129.0, 128.95, 128.2, 128.0, 127.5, 127.2, 127.1, 127.0, 126.7, 126.6, 126.62, 126.2, 125.7 (q, *J* = 3.3 Hz), 124.3 (q, *J* = 249.5 Hz), 120.6, 109.9, 72.2, 52.5, 49.0.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -62.63.

**HRMS (ESI)** m/z calcd for $C_{47}H_{32}F_3NONa^+$ $(M+Na)^+$ 706.2328, found 706.2325.

2-isopropyl-5-methylphenyl 4-(3,9-dimethoxy-7-oxo-5,5-diphenyl-5,6-dihydroindolo[1,2-a]quinolin-6a(7*H*)-yl)benzoate(**4i**)



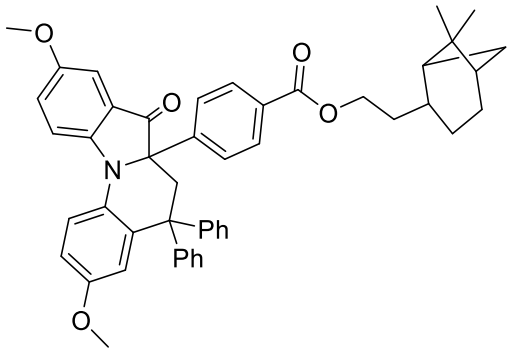
Compound **4i** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-ethyl-5-methylphenyl 4-(2-oxoacetyl)benzoate, ethene-1,1-diyldibenzene. **4i** was obtained in 76% yield (106.3 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 8.10 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.23 (t, *J* = 8.1 Hz, 4H), 7.05 (d, *J* = 8.7 Hz, 2H), 7.01 – 6.95 (m, 4H), 6.91 – 6.86 (m, 4H), 6.74 (dd, *J* = 6.4, 3.0 Hz, 2H), 6.59 (d, *J* = 2.7 Hz, 1H), 6.24 (d, *J* = 2.9 Hz, 1H), 4.08 (d, *J* = 13.9 Hz, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 3.23 (d, *J* = 13.8 Hz, 1H), 2.98 (p, *J* = 6.9 Hz, 1H), 2.33 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.1, 165.2, 156.9, 156.1, 153.7, 148.2, 148.2, 144.9, 144.3, 142.6, 137.3, 136.7, 132.5, 130.6, 129.7, 129.2, 128.7, 128.2, 127.9, 127.3, 127.0, 126.97, 126.8, 126.6, 126.56, 126.0, 123.0, 120.2, 116.7, 112.2, 110.8, 105.4, 72.6, 56.0, 55.5, 52.5, 48.9, 27.4, 23.1, 21.0.

**HRMS (ESI)** m/z calcd for $C_{47}H_{41}NO_5Na^+$ $(M+Na)^+$ 722.2877, found 722.2876.

2-(6,6-dimethylbicyclo[3.1.1]heptan-2-yl)ethyl 4-(3,9-dimethoxy-7-oxo-5,5-diphenyl-5,6-dihydroindolo[1,2-a]quinolin-6a(7*H*)-yl)benzoate(**4j**)



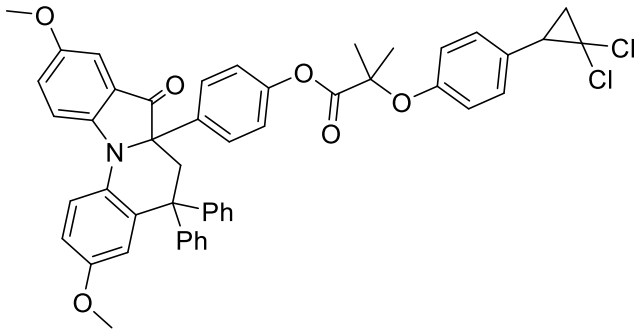
Compound **4j** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(6,6-dimethylbicyclo[3.1.1]heptan-2-yl)ethyl 4-(2-oxoacetyl)benzoate, ethene-1,1-diyldibenzene. **4j** was obtained in 53% yield (76.0 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.94 – 7.90 (m, 2H), 7.70 – 7.65 (m, 2H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.24 – 7.20 (m, 2H), 7.02 (d, *J* = 9.0 Hz, 1H), 6.99 – 6.93 (m, 4H), 6.87 (q, *J* = 3.0 Hz, 3H), 6.71 (dd, *J* = 6.5, 2.9 Hz, 2H), 6.56 (d, *J* = 2.7 Hz, 1H), 6.23 (d, *J* = 2.9 Hz, 1H), 4.28 (tq, *J* = 6.7, 3.6 Hz, 2H), 4.06 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.19 (d, *J* = 13.9 Hz, 1H), 2.38 – 2.29 (m, 1H), 2.20 – 2.10 (m, 1H), 2.01 – 1.91 (m, 2H), 1.89 (qd, *J* = 6.0, 3.8 Hz, 2H), 1.85 – 1.79 (m, 2H), 1.51 (ddt, *J* = 17.2, 10.9, 6.4 Hz, 1H), 1.18 (s, 3H), 1.02 (s, 3H), 0.89 (d, *J* = 9.6 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.2, 166.5, 156.8, 156.1, 153.7, 147.4, 144.9, 144.5, 142.6, 132.6, 130.0, 129.7, 129.6, 129.2, 128.2, 127.9, 127.8, 126.9, 126.9, 126.8, 126.5, 126.2, 125.6, 120.2, 116.6, 112.1, 110.7, 105.4, 72.5, 64.1, 56.0, 55.5, 52.5, 48.9, 46.4, 41.5, 38.8, 38.1, 36.5, 33.7, 28.3, 26.5, 23.4, 22.3.

**HRMS (ESI)** m/z calcd for $C_{48}H_{47}NO_5Na^+$ $(M+Na)^+$ 740.3347,found 740.3342.

4-(3,9-dimethoxy-7-oxo-5,5-diphenyl-5,6-dihydroindolo[1,2-a]quinolin-6a(7*H*)-yl)phenyl 2-(4-(2,2-dichlorocyclopropyl)phenoxy)-2-methylpropanoate(**4k**)



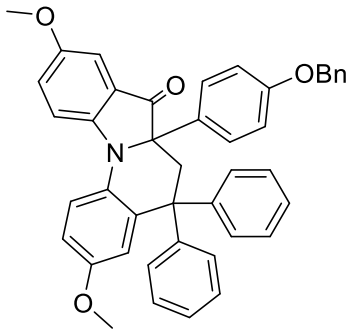

Compound **4k** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 4-(2-oxoacetyl)phenyl 2-(4-(2,2-dichlorocyclopropyl)phenoxy)-2-methylpropanoate, ethene-1,1-diyldibenzene. **4k** was obtained in 35% yield (56.6 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.58 (dd, *J* = 15.1, 8.5 Hz, 3H), 7.25 – 7.19 (m, 3H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.01 – 6.94 (m, 5H), 6.94 – 6.88 (m, 3H), 6.87 – 6.82 (m, 5H), 6.70 (dd, *J* = 6.7, 2.9 Hz, 2H), 6.55 (d, *J* = 2.7 Hz, 1H), 6.22 (d, *J* = 2.9 Hz, 1H), 4.03 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.17 (d, *J* = 13.8 Hz, 1H), 2.84 (dd, *J* = 10.7, 8.3 Hz, 1H), 1.95 (dd, *J* = 10.7, 7.4 Hz, 1H), 1.79 (t, *J* = 7.9 Hz, 1H), 1.72 (s, 6H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.7, 172.9, 156.8, 156.0, 155.1, 153.6, 150.0, 145.1, 144.6, 142.6, 140.4, 132.7, 129.9, 129.7, 129.2, 128.6, 128.2, 127.8, 126.9, 126.81, 126.80, 126.7, 126.5, 121. 5, 120.3, 118.7, 116.5, 112.1, 110.6, 105.5, 79.5, 72.1, 61.0, 56.0, 55.5, 52.5, 49.1, 35.0, 26.0, 25.7, 25.6.

**HRMS (ESI)** m/z calcd for $C_{49}H_{41}Cl_2NO_6Na^+$ $(M+Na)^+$ 832.2203, found 832.2204.

6a-(4-(benzyloxy)phenyl)-3,9-dimethoxy-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4m**)



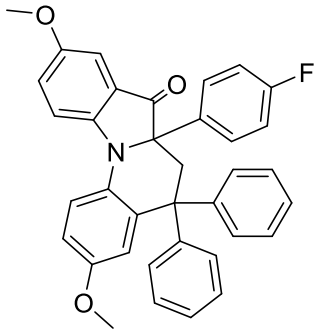

Compound **4m** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(4-(benzyloxy)phenyl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4m** was obtained in 69% yield (86.8 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.57 (d, *J* = 8.5 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.37 (dq, *J* = 15.2, 6.8 Hz, 5H), 7.30 (d, *J* = 6.9 Hz, 1H), 7.22 (dd, *J* = 11.1, 7.1 Hz, 3H), 7.00 – 6.94 (m, 4H), 6.91 (dd, *J* = 8.9, 2.7 Hz, 1H), 6.88 – 6.82 (m, 5H), 6.69 (dd, *J* = 6.6, 3.0 Hz, 2H), 6.56 (d, *J* = 2.6 Hz, 1H), 6.22 (d, *J* = 2.8 Hz, 1H), 5.00 (s, 2H), 4.04 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.18 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 202.2, 158.3, 156.7, 155.9, 153.4, 145.2, 144.7, 142.7, 137.2, 134.7, 132.9, 129.7, 129.2, 128.7, 128.2, 128.0, 127.8, 127.5, 126.8, 126.8, 126.5, 126.4, 120.3, 116.4, 115.2, 111.9, 110.4, 105.5, 72.0, 70.1, 56.0, 55.5, 52.4, 49.0.

**HRMS (ESI)** m/z calcd for $C_{43}H_{35}NO_4Na^+$ $(M+Na)^+$ 652.2459, found 652.2452.

6a-(4-fluorophenyl)-3,9-dimethoxy-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4n**)




Compound **4n** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(4-fluorophenyl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4n** was obtained in 94% yield (101.7 mg) as yellow solid.

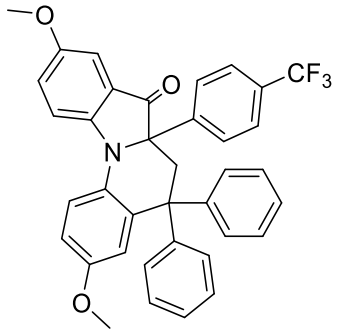
**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.61 – 7.55 (m, 3H), 7.23 (d, *J* = 7.7 Hz, 3H), 7.01 (d, *J* = 8.9 Hz, 1H), 7.00 – 6.96 (m, 3H), 6.94 (t, *J* = 8.7 Hz, 3H), 6.89 – 6.85 (m, 3H), 6.71 (dd, *J* = 6.7, 3.1 Hz, 2H), 6.58 (d, *J* = 2.7 Hz, 1H), 6.24 (d, *J* = 2.8 Hz, 1H), 4.02 (d, *J* = 13.9 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.17 (d, *J* = 13.9 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.8, 162.3 (d, *J* = 246.0 Hz), 156.8, 155.9, 153.6, 145.0, 144.5, 142.6, 138.01, 138.0, 132.7, 129.7, 129.2, 128.2, 127.8, 127.3 (d, *J* = 8.0 Hz), 126.9, 126.7 (d, *J* = 3.7 Hz), 126.5, 120.2, 116.5, 115.5 (d, *J* = 21.4 Hz), 112.1, 110.6, 105.4, 71.9, 56.0, 55.5, 52.4, 49.0.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -115.7.

**HRMS (ESI)** m/z calcd for $C_{36}H_{28}FNO_3Na^+$ $(M+Na)^+$ 564.1945, found 564.1946.

3,9-dimethoxy-5,5-diphenyl-6a-(4-(trifluoromethyl)phenyl)-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4o**)




Compound **4o** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-(4-(trifluoromethyl)phenyl)acetaldehyde, ethene-1,1-diyldibenzene. **4o** was obtained in 94% yield (111.1 mg) as yellow solid.

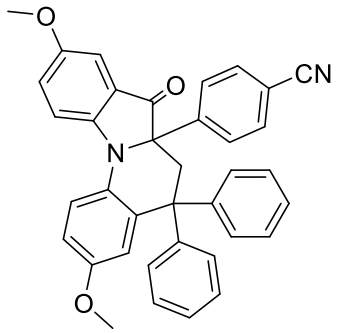
**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 6.4 Hz, 3H), 7.05 (d, *J* = 8.9 Hz, 1H), 7.00 – 6.96 (m, 2H), 6.95 – 6.93 (m, 2H), 6.91 – 6.87 (m, 3H), 6.75 – 6.71 (m, 2H), 6.59 (d, *J* = 2.6 Hz, 1H), 6.23 (d, *J* = 2.9 Hz, 1H), 4.01 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.19 (d, *J* = 13.9 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.1, 156.8, 156.0, 153.8, 146.1, 144.9, 144.1, 142.8, 132.5, 129.7, 129.2, 128.2, 127.9, 127.1, 127.0, 126.64, 126.6, 126.1, 125.6 (q, *J* = 3.8 Hz), 120.1, 116.7, 112.2, 110.8, 105.4, 72.3, 56.0, 55.5, 52.4, 48.9.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -62.6.

**HRMS (ESI)** m/z calcd for $C_{37}H_{28}F_3NO_3Na^+$ $(M+Na)^+$ 614.1913, found 614.1912.

4-(3,9-dimethoxy-7-oxo-5,5-diphenyl-5,6-dihydroindolo[1,2-a]quinolin-6a(7*H*)-yl)benzonitrile(**4p**)



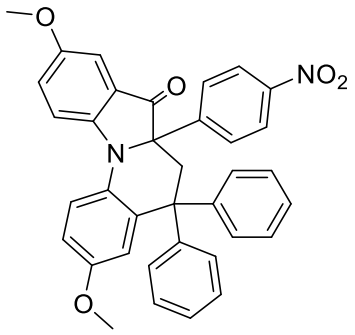
Compound **4p** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 4-(2-oxoacetyl)benzonitrile, ethene-1,1-diyldibenzene. **4p** was obtained in 53% yield (58.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.21 (dd, *J* = 5.2, 1.7 Hz, 3H), 7.05 (d, *J* = 9.0 Hz, 1H), 6.98 (ddd, *J* = 9.1, 7.6, 2.8 Hz, 2H), 6.92 (dd, *J* = 6.8, 2.8 Hz, 2H), 6.89 (dd, *J* = 5.1, 1.8 Hz, 3H), 6.74 – 6.69 (m, 2H), 6.58 (d, *J* = 2.7 Hz, 1H), 6.22 (d, *J* = 2.9 Hz, 1H), 3.97 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.15 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.6, 156.9, 156.0, 153.9, 147.5, 144.8, 143.9, 142.7, 132.5, 132.3, 129.6, 129.2, 128.2, 127.9, 127.2, 127.0, 126.7, 126.6, 120.1, 118.9, 116.8, 112.3, 111.2, 111.0, 105.4, 72.3, 56.0, 55.5, 52.4, 48.8.

**HRMS (ESI)** m/z calcd for $C_{37}H_{28}N_2O_3Na^+$ $(M+Na)^+$ 571.1992, found 571.1992.

3,9-dimethoxy-6a-(4-nitrophenyl)-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4q**)



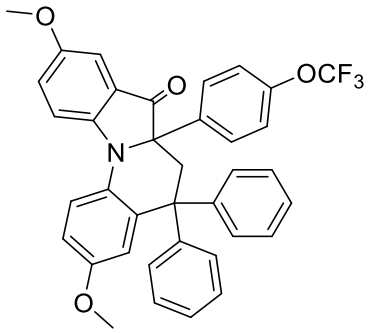

Compound **4q** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(4-nitrophenyl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4q** was obtained in 59% yield (67.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 8.07 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 1H), 7.23 – 7.19 (m, 3H), 7.08 (d, *J* = 9.0 Hz, 1H), 7.02 – 6.97 (m, 2H), 6.96 – 6.86 (m, 5H), 6.76 – 6.71 (m, 2H), 6.62 – 6.58 (m, 1H), 6.26 – 6.21 (m, 1H), 3.98 (d, *J* = 13.9 Hz, 1H), 3.69 – 3.64 (m, 6H), 3.18 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.4, 156.9, 156.0, 154.0, 149.3, 147.2, 144.7, 143.7, 142.7, 132.2, 129.6, 129.2, 128.2, 127.9, 127.3, 127.0, 126.7, 126.65, 126.6, 123.8, 120.1, 116.8, 112.4, 111.1, 105.4, 72.3, 56.0, 55.5, 52.4, 48.8.

**HRMS (ESI)** m/z calcd for $C_{36}H_{28}N2O_5Na^+$ $(M+Na)^+$ 591.1890, found 591.1892.

3,9-dimethoxy-5,5-diphenyl-6a-(4-(trifluoromethoxy)phenyl)-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4r**)




Compound **4r** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-(4-(trifluoromethoxy)phenyl)acetaldehyde, ethene-1,1-diyldibenzene. **4r** was obtained in 90% yield (109.3 mg) as yellow solid.

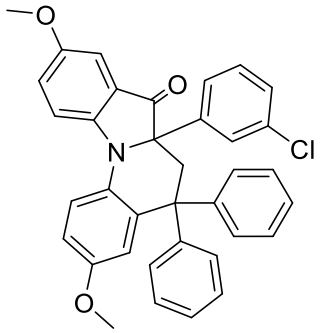
**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.60 (dd, *J* = 8.8, 2.6 Hz, 3H), 7.21 (d, *J* = 6.8 Hz, 3H), 7.07 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 9.0 Hz, 1H), 6.99 – 6.96 (m, 2H), 6.96 – 6.94 (m, 2H), 6.90 – 6.87 (m, 3H), 6.72 (dd, *J* = 6.6, 3.0 Hz, 2H), 6.59 (d, *J* = 2.7 Hz, 1H), 6.23 (d, *J* = 2.9 Hz, 1H), 3.98 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.18 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.5, 156.8, 155.9, 153.7, 148.6, 145.0, 144.1, 142.8, 140.8, 132.6, 129.7, 129.2, 128.2, 127.9, 127.2, 127.0, 126.9, 126.6, 126.5, 121.2, 120.2, 116.7, 112.2, 110.8, 105.4, 72.0, 56.0, 55.5, 52.4, 48.9.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -57.8.

**HRMS (ESI)** m/z calcd for $C_{37}H_{28}F3NO_4Na^+$ $(M+Na)^+$ 630.1863, found 630.1861.

6a-(3-chlorophenyl)-3,9-dimethoxy-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4s**)



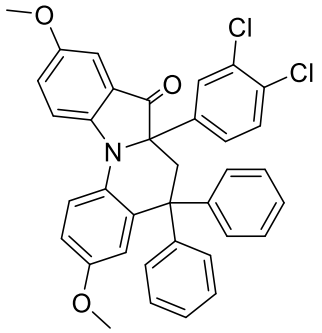

Compound **4s** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(3-chlorophenyl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4s** was obtained in 89% yield (99.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.58 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.24 – 7.19 (m, 5H), 7.01 (dd, *J* = 9.0, 1.6 Hz, 1H), 6.99 – 6.93 (m, 4H), 6.87 (dt, *J* = 5.5, 2.7 Hz, 3H), 6.73 – 6.68 (m, 2H), 6.57 (t, *J* = 2.2 Hz, 1H), 6.23 (d, *J* = 2.5 Hz, 1H), 4.01 (dd, *J* = 13.9, 1.7 Hz, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.16 (dd, *J* = 13.8, 1.7 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.5, 156.8, 156.0, 153.6, 145.0, 144.4, 142.6, 140.9, 133.4, 132.6, 129.7, 129.2, 128.8, 128.2, 127.8, 127.1, 126.9, 126.8, 126.7, 126.5, 120.2, 116.6, 112.1, 110.7, 105.4, 72.0, 56.0, 55.5, 52.4, 48.9.

**HRMS (ESI)** m/z calcd for $C_{36}H_{28}ClNO_3Na^+$ $(M+Na)^+$ 580.1650, found 580.1650.

6a-(3,4-dichlorophenyl)-3,9-dimethoxy-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4t**)



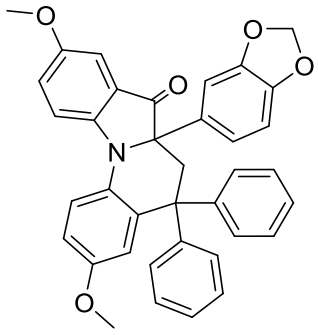
Compound **4t** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(3,4-dichlorophenyl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4t** was obtained in 81% yield (95.8 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.63 (d, *J* = 2.2 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.43 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 7.22 (d, *J* = 6.7 Hz, 3H), 7.04 (d, *J* = 9.0 Hz, 1H), 6.98 (ddd, *J* = 12.0, 8.7, 2.7 Hz, 2H), 6.95 – 6.93 (m, 2H), 6.88 (dd, *J* = 5.4, 1.8 Hz, 3H), 6.70 (dd, *J* = 6.8, 2.7 Hz, 2H), 6.58 (d, *J* = 2.7 Hz, 1H), 6.23 (d, *J* = 2.8 Hz, 1H), 3.93 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.66 (s, 3H), 3.14 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.9, 156.9, 155.9, 153.9, 144.8, 144.0, 142.6, 142.4, 132.6, 132.4, 131.6, 130.6, 129.7, 129.2, 128.2, 127.9, 127.7, 127.1, 127.0, 126.7, 126.6, 125.3, 120.2, 116.7, 112.3, 111.0, 105.4, 71.6, 56.0, 55.5, 52.4, 48.8.

**HRMS (ESI)** m/z calcd for $C_{36}H_{27}Cl2NO_3Na^+$ $(M+Na)^+$ 614.1260, found 614.1261.

6a-(benzo[d][1,3]dioxol-5-yl)-3,9-dimethoxy-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4u**)



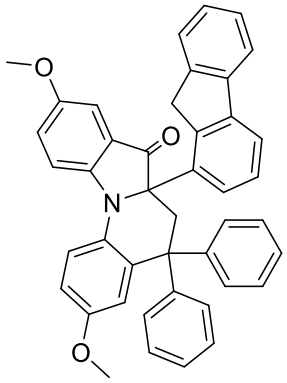

Compound **4u** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(benzo[d][1,3]dioxol-5-yl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4u** was obtained in 30% yield (34.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.57 (d, *J* = 8.5 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.11 – 7.06 (m, 2H), 6.97 (td, *J* = 8.6, 4.3 Hz, 4H), 6.92 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.88 – 6.83 (m, 3H), 6.69 (t, *J* = 7.6 Hz, 3H), 6.57 (d, *J* = 2.6 Hz, 1H), 6.22 (d, *J* = 2.8 Hz, 1H), 5.87 (s, 2H), 3.98 (d, *J* = 13.8 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.18 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.9, 156.7, 155.8, 153.5, 147.9, 147.0, 145.1, 144.5, 142.7, 136.2, 132.7, 129.7, 129.2, 128.1, 127.8, 126.8, 126.7, 126.6, 126.4, 120.2, 118.7, 116.5, 112.0, 110.5, 108.4, 106.6, 105.5, 101.1, 72.1, 56.0, 55.5, 52.4, 49.0.

**HRMS (ESI)** m/z calcd for $C_{37}H_{29}NO_5Na^+$ $(M+Na)^+$ 590.1938, found 590.1939.

6a-(9*H*-fluoren-1-yl)-3,9-dimethoxy-5,5-diphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4v**)



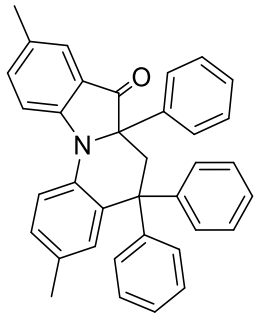

Compound **4v** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-(9H-fluoren-1-yl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **4v** was obtained in 58% yield (70.9 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.77 (s, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.68 – 7.64 (m, 2H), 7.62 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.34 (dt, *J* = 15.3, 7.5 Hz, 2H), 7.21 (dq, *J* = 14.0, 7.2 Hz, 3H), 7.05 (d, *J* = 9.0 Hz, 1H), 7.02 – 6.98 (m, 3H), 6.95 (dd, *J* = 9.0, 2.7 Hz, 1H), 6.90 – 6.86 (m, 3H), 6.74 (dd, *J* = 6.6, 3.0 Hz, 2H), 6.59 (d, *J* = 2.7 Hz, 1H), 6.24 (d, *J* = 2.9 Hz, 1H), 4.11 (d, *J* = 13.7 Hz, 1H), 3.83 (d, *J* = 7.7 Hz, 2H), 3.66 (s, 3H), 3.65 (s, 3H), 3.28 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 202.0, 156.7, 155.9, 153.5, 145.2, 144.6, 143.8, 143.6, 142.8, 141.4, 141.2, 140.9, 132.9, 129.7, 129.2, 128.1, 127.8, 126.8, 126.77, 126.7, 126.6, 126.4, 125.1, 124.2, 122.4, 120.3, 120.0, 119.98, 116.5, 112.0, 110.5, 105.6, 72.7, 56.0, 55.5, 52.5, 49.1, 37.1.

**HRMS (ESI)** m/z calcd for $C_{43}H_{33}NO_3Na^+$ $(M+Na)^+$ 634.2353, found 634.2351.

3,9-dimethyl-5,5,6a-triphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4w**)



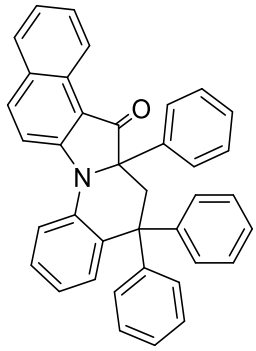
Compound **4w** was synthesized according to general procedure 3.3 starting from di-p-tolylamine, 2-oxo-2-phenylacetaldehyde, ethene-1,1-diyldibenzene. **4w** was obtained in 74% yield (72.7 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.58 (t, *J* = 7.9 Hz, 3H), 7.27 (d, *J* = 2.0 Hz, 1H), 7.23 (dt, *J* = 7.8, 4.1 Hz, 5H), 7.18 – 7.15 (m, 1H), 7.10 – 7.07 (m, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.99 – 6.96 (m, 2H), 6.94 (s, 1H), 6.85 (p, *J* = 3.7 Hz, 3H), 6.72 (dd, *J* = 6.9, 3.0 Hz, 2H), 6.49 – 6.45 (m, 1H), 4.07 (d, *J* = 13.8 Hz, 1H), 3.24 (d, *J* = 13.9 Hz, 1H), 2.23 (s, 3H), 2.15 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.9, 158.0, 145.4, 143.2, 142.7, 142.3, 137.6, 137.1, 134.4, 130.4, 129.6, 129.3, 128.73, 128.7, 128.3, 128.1, 127.7, 127.4, 126.7, 126.2, 125.6, 125.56, 124.6, 120.2, 108.9, 71.9, 52.3, 49.1, 21.5, 20.4.

**HRMS (ESI)** m/z calcd for $C_{36}H_{29}NONa^+$ $(M+Na)^+$ 514.2141, found 514.2144.

12,12,13a-triphenyl-13,13a-dihydrobenzo[4,5]indolo[1,2-a]quinolin-14(12*H*)-one(**4x**)



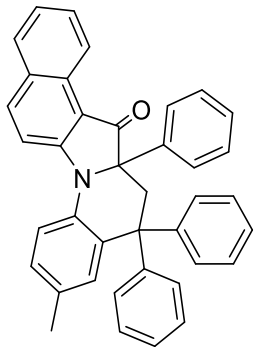
Compound **4x** was synthesized according to general procedure 3.3 starting from N-phenylnaphthalen-2-amine, 2-oxo-2-phenylacetaldehyde, ethene-1,1-diyldibenzene. **4x** was obtained in 71% yield (72.9 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 8.50 (d, *J* = 8.3 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.69 (d, *J* = 9.1 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.51 (td, *J* = 7.7, 1.5 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.30 – 7.27 (m, 2H), 7.25 (d, *J* = 7.6 Hz, 4H), 7.22 – 7.13 (m, 3H), 7.02 – 6.97 (m, 2H), 6.78 – 6.72 (m, 3H), 6.69 (t, *J* = 7.6 Hz, 2H), 6.42 (t, *J* = 7.2 Hz, 1H), 4.19 (d, *J* = 13.9 Hz, 1H), 3.31 (d, *J* = 13.8 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.8, 161.8, 145.0, 144.2, 142.9, 142.1, 138.6, 138.1, 130.4, 129.8, 129.3, 129.2, 129.1, 128.7, 128.2, 128.1, 128.0, 127.8, 127.7, 127.4, 126.7, 126.0, 125.98, 125.5, 125.4, 123.6, 122.8, 110.6, 110.57, 72.4, 52.4, 48.6.

**HRMS (ESI)** m/z calcd for $C_{38}H_{27}NONa^+$ $(M+Na)^+$ 536.1985, found 536.1986.

10-methyl-12,12,13a-triphenyl-13,13a-dihydrobenzo[4,5]indolo[1,2-a]quinolin-14(12*H*)-one(**4y**)



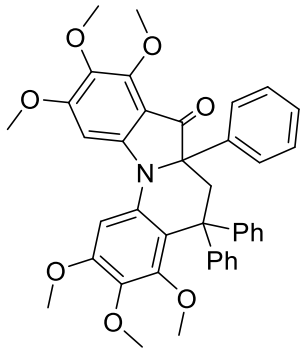

Compound **4y** was synthesized according to general procedure 3.3 starting from N-(p-tolyl)naphthalen-2-amine, 2-oxo-2-phenylacetaldehyde, ethene-1,1-diyldibenzene. **4y** was obtained in 91% yield (96.0 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 8.50 (d, *J* = 8.3 Hz, 1H), 7.69 – 7.62 (m, 4H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.47 – 7.42 (m, 1H), 7.38 (d, *J* = 6.3 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.25 – 7.22 (m, 4H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 7.2 Hz, 2H), 6.76 (d, *J* = 7.8 Hz, 2H), 6.70 (t, *J* = 7.6 Hz, 2H), 6.56 (s, 1H), 6.42 (t, *J* = 7.3 Hz, 1H), 4.17 (d, *J* = 13.9 Hz, 1H), 3.28 (d, *J* = 13.9 Hz, 1H), 2.28 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.9, 162.2, 145.1, 144.1, 143.0, 142.3, 138.2, 136.1, 135.3, 130.5, 130.48, 129.4, 129.3, 129.2, 128.8, 128.4, 128.2, 128.1, 128.08, 127.7, 127.4, 126.8, 126.0, 125.9, 125.4, 123.6, 122.8, 110.8, 110.6, 72.6, 52.5, 48.8, 21.5.

**HRMS (ESI)** m/z calcd for $C_{39}H_{29}NONa^+$ $(M+Na)^+$ 550.2141, found 550.2142.

2,3,4,8,9,10-hexamethoxy-5,5,6a-triphenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4z**)



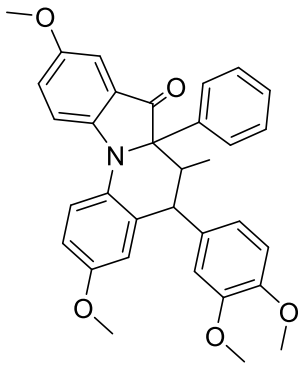

Compound **4z** was synthesized according to general procedure 3.3 starting from bis(3,4,5-trimethoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, ethene-1,1-diyldibenzene. **4z** was obtained in 29% yield (37.3 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.08 – 7.05 (m, 2H), 7.03 (t, *J* = 7.8 Hz, 2H), 6.99 (s, 1H), 6.96 – 6.92 (m, 3H), 6.89 – 6.83 (m, 3H), 6.81 – 6.79 (m, 1H), 6.79 – 6.68 (m, 5H), 3.94 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 3.68 (s, 3H), 3.65 (s, 3H), 3.37 (d, *J* = 14.4 Hz, 1H), 2.89 (d, *J* = 14.4 Hz, 1H), 2.59 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 195.0, 162. 0, 155. 5, 153.7, 153.3, 152.9, 147.6, 143.6, 139.5, 136. 3, 134.9, 134.2, 129.7, 129.4, 127.8, 127.5, 127.1, 126.4, 126.2, 125.9, 125.8, 123.8, 105.8, 102.2, 87.2, 71.6, 62.0, 61.7, 60.6, 58.7, 56.3, 56.3, 51.3, 50.9.

**HRMS (ESI)** m/z calcd for $C_{40}H_{37}NO_7Na^+$ $(M+Na)^+$ 666.2462, found 666.2460.

5-(3,4-dimethoxyphenyl)-3,9-dimethoxy-6-methyl-6a-phenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one (**4aa**)



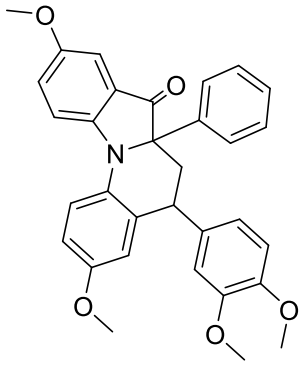
Compound **4aa** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, (E)-1,2-dimethoxy-4-(prop-1-en-1-yl)benzene. **4aa** was obtained in 92% yield (95.9 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.69 (t, *J* = 8.8 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.26 (m, 1H), 7.24 (dd, *J* = 9.1, 2.8 Hz, 1H), 7.08 (d, *J* = 2.8 Hz, 1H), 6.98 – 6.92 (m, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.68 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.61 (d, *J* = 2.0 Hz, 1H), 6.53 (dd, *J* = 3.0, 1.2 Hz, 1H), 4.00 (d, *J* = 5.3 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.63 (s, 3H), 3.02 – 2.95 (m, 1H), 0.59 (d, *J* = 6.7 Hz, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.0, 154.5, 153.5, 152.6, 148.7, 148.0, 137.6, 133.9, 132.2, 129.5, 129.2, 127.9, 127.8, 126.0, 122.7, 121.7, 120.1, 116.0, 113.6, 113.5, 111.1, 110.4, 105.7, 76.3, 56.1, 56.0, 55.9, 55.6, 46.0, 42.3, 11.1.

**HRMS (ESI)** m/z calcd for $C_{33}H_{31}NO_5Na^+$ $(M+Na)^+$ 544.2094, found 544.2095.

5-(3,4-dimethoxyphenyl)-3,9-dimethoxy-6a-phenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one(**4ab**)



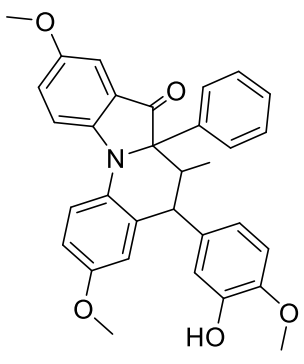
Compound **4ab** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 1,2-dimethoxy-4-vinylbenzene. **4ab** was obtained in 40% yield (40.6 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.63 (dd, *J* = 14.4, 8.9 Hz, 2H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 3.0 Hz, 1H), 7.13 (d, *J* = 2.8 Hz, 1H), 6.91 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.66 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.57 (d, *J* = 2.0 Hz, 1H), 6.33 (d, *J* = 2.9 Hz, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.61 (s, 3H), 2.93 (dd, *J* = 13.6, 5.6 Hz, 1H), 2.05 (t, *J* = 13.1 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 199.4, 155.1, 153.9, 152.8, 149.2, 148.1, 136.3, 136.3, 133.0, 132.1, 129.0, 127.8, 127.75, 126.5, 122.3, 121.2, 120.2, 115.5, 113.3, 111.7, 111.6, 111.4, 105.9, 72.7, 56.1, 56.0, 55.99, 55.5, 41.6, 40.5.

**HRMS (ESI)** m/z calcd for $C_{32}H_{29}NO_5Na^+$ $(M+Na)^+$ 530.1938, found 530.1937.

5-(3-hydroxy-4-methoxyphenyl)-3,9-dimethoxy-6-methyl-6a-phenyl-6,6a-dihydroindolo[1,2-a]quinolin-7(5*H*)-one (**4ac**)



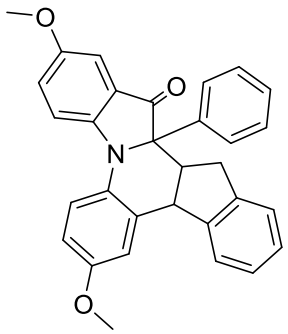
Compound **4ac** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, (E)-5-ethylidene-2-methoxycyclohexa-1,3-dien-1-ol. **4ac** was obtained in 95% yield (96.4 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.69 (t, *J* = 8.9 Hz, 2H), 7.57 (d, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.26 (m, 1H), 7.26 – 7.22 (m, 1H), 7.08 (d, *J* = 2.8 Hz, 1H), 6.97 – 6.92 (m, 1H), 6.85 (d, *J* = 8.1 Hz, 1H), 6.64 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.59 (d, *J* = 1.9 Hz, 1H), 6.54 (dd, *J* = 3.0, 1.2 Hz, 1H), 3.98 (d, *J* = 5.2 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.64 (s, 3H), 2.97 (dd, *J* = 6.8, 5.3 Hz, 1H), 0.58 (d, *J* = 6.7 Hz, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200.1, 154.5, 153.4, 152.6, 146.4, 144.6, 137.6, 133.3, 132.2, 129.6, 129.1, 127.9, 127.8, 126.0, 123.4, 121.7, 120.1, 116.0, 114.3, 113.6, 112.8, 110.4, 105.7, 76.3, 56.2, 55.9, 55.6, 46.1, 42.3, 11.1.

HRMS (ESI) m/z calcd for $C_{32}H_{29}NO_5Na^+$ $(M+Na)^+$ 530.1939, found 530.1937.

2,8-dimethoxy-14b-phenyl-9b,14,14a,14b-tetrahydro-15*H*-indeno[2,1-c]indolo[1,2-a]quinolin-15-one(**4ad**)




Compound **4ad** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 1*H*-indene. **4ad** was obtained in 88% yield (80.8 mg) as yellow solid.

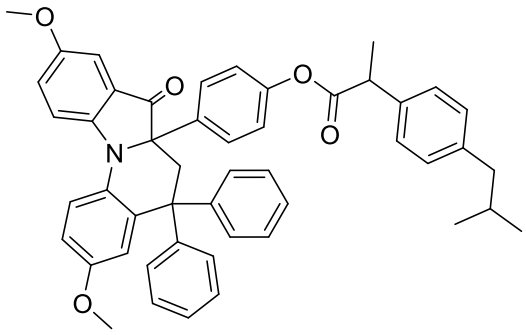
**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.58 – 7.51 (m, 4H), 7.47 (d, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.21 (m, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.15 – 7.11 (m, 2H), 7.05 (d, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 2.9 Hz, 1H), 6.83 (dd, *J* = 8.8, 2.9 Hz, 1H), 4.11 (d, *J*

= 7.6 Hz, 1H), 3.95 (dt, *J* = 11.2, 7.3 Hz, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 2.80 (dd, *J* = 15.3, 7.1 Hz, 1H), 2.55 (dd, *J* = 15.4, 11.2 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 199.2, 155.1, 153.6, 153.1, 145.1, 141.9, 136.9, 131.1, 130.4, 129.0, 128.0, 127.9, 127.6, 127.0, 126.5, 125.0, 124.7, 120.8, 120.75, 115.2, 112.9, 110.1, 106.0, 73.4, 56.0, 55.5, 47.8, 44.3, 32.7.

**HRMS (ESI)** m/z calcd for $C_{31}H_{25}NO_3Na^+$ $(M+Na)^+$ 482.1727, found 482.1727.

4-(3,9-dimethoxy-7-oxo-5,5-diphenyl-5,6-dihydroindolo[1,2-a]quinolin-6a(7*H*)-yl)phenyl 2-(4-isobutylphenyl)propanoate(**4ae**)



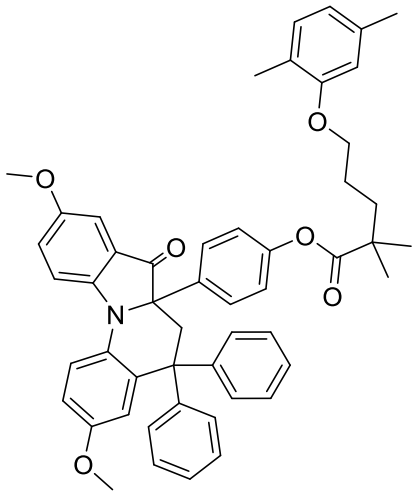
Compound **4ae** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 4-(2-oxoacetyl)phenyl 2-(4-isobutylphenyl)propanoate, ethene-1,1-diyldibenzene. **4ae** was obtained in 57% yield (82.9 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.60 – 7.55 (m, 3H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.12 (dd, *J* = 8.1, 2.6 Hz, 2H), 6.97 (tt, *J* = 8.5, 4.6 Hz, 4H), 6.94 – 6.88 (m, 4H), 6.86 (q, *J* = 3.0 Hz, 3H), 6.70 (dd, *J* = 6.7, 3.0 Hz, 2H), 6.55 (d, *J* = 2.7 Hz, 1H), 6.23 (d, *J* = 2.9 Hz, 1H), 4.04 (dd, *J* = 13.8, 2.1 Hz, 1H), 3.90 (q, *J* = 7.1 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.18 (d, *J* = 13.8 Hz, 1H), 2.47 (dd, *J* = 7.3, 2.3 Hz, 2H), 1.86 (td, *J* = 6.8, 2.3 Hz, 1H), 1.58 (d, *J* = 7.2 Hz, 3H), 0.92 (d, *J* = 2.0 Hz, 3H), 0.90 (d, *J* = 2.1 Hz, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.73, 201.7, 173.3, 156.7, 156.0, 153.5, 150.3, 145.0, 144.7, 144.6, 142.5, 140.9, 140.86, 139.9, 139.89, 137.3, 132.7, 129.7, 129.6, 129.1, 128.2, 127.7, 127.3, 126.9, 126.8, 126.6, 126.4, 121.6, 120.2, 116.5, 112.0, 110.5, 105.4, 72.1, 55.9, 55.5, 52.4, 49.0, 45.3, 45.1, 30.3, 22.5, 18.6, 18.6.

**HRMS (ESI)** m/z calcd for $C_{49}H_{45}NO_5Na^+$ $(M+Na)^+$ 750.3190, found 750.3185.

4-(3,9-dimethoxy-7-oxo-5,5-diphenyl-5,6-dihydroindolo[1,2-a]quinolin-6a(7*H*)-yl)phenyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate(**4af**)



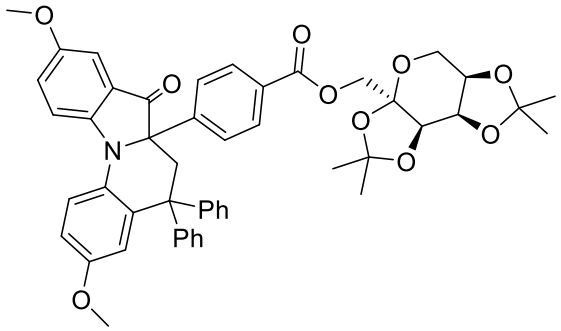
Compound **4af** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, 4-(2-oxoacetyl)phenyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate, ethene-1,1-diyldibenzene. **4af** was obtained in 34% yield (52.5 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.63 – 7.59 (m, 2H), 7.57 (d, *J* = 8.5 Hz, 1H), 7.25 – 7.19 (m, 3H), 6.98 (tt, *J* = 8.4, 5.0 Hz, 5H), 6.94 – 6.91 (m, 3H), 6.87 – 6.85 (m, 3H), 6.70 (dd, *J* = 6.4, 2.9 Hz, 2H), 6.67 – 6.64 (m, 1H), 6.61 (d, *J* = 1.6 Hz, 1H), 6.55 (d, *J* = 2.7 Hz, 1H), 6.22 (d, *J* = 2.9 Hz, 1H), 4.05 (d, *J* = 13.8 Hz, 1H), 3.97 – 3.92 (m, 2H), 3.67 (s, 3H), 3.64 (s, 3H), 3.19 (d, *J* = 13.9 Hz, 1H), 2.29 (s, 3H), 2.16 (s, 3H), 1.85 – 1.82 (m, 4H), 1.33 (s, 6H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.8, 176.4, 157.0, 156.8, 156.0, 153.5, 150.4, 145.1, 144.7, 142.5, 139.9, 136.6, 132.8, 130.5, 129.7, 129.2, 128.2, 127.8, 126.9, 126.8, 126.7, 126.66, 126.4, 123.7, 121.7, 120.9, 120.3, 116.5, 112.1, 112.0, 110.6, 105.4, 72.1, 67.9, 56.0, 55.5, 52.5, 49.1, 42.5, 37.3, 25.4, 25.3, 21.5, 16.0.

**HRMS (ESI)** m/z calcd for $C_{51}H_{49}NO_6Na^+$ $(M+Na)^+$ 794.3452, found 794.3450.

((3aR,5aR,8aR,8bR)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl 4-(3,9-dimethoxy-7-oxo-5,5-diphenyl-5,6-dihydroindolo[1,2-a]quinolin-6a(7*H*)-yl)benzoate(**4ag**)



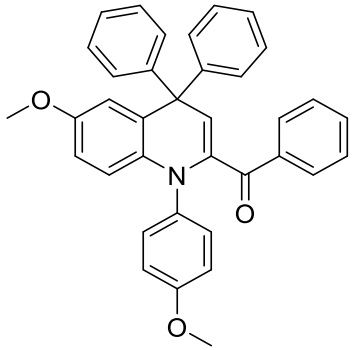

Compound **4ag** was synthesized according to general procedure 3.3 starting from bis(4-methoxyphenyl)amine, ((3aR,5aR,8aR,8bR)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-3a-yl)methyl 4-(2-oxoacetyl)benzoate, ethene-1,1-diyldibenzene. **4ag** was obtained in 32% yield (52.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.85 (dt, *J* = 8.4, 1.4 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.51 (dt, *J* = 8.5, 1.3 Hz, 1H), 7.12 (q, *J* = 6.1 Hz, 3H), 6.92 (d, *J* = 9.0 Hz, 1H), 6.88 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.85 (dt, *J* = 8.8, 2.8 Hz, 3H), 6.79 – 6.74 (m, 3H), 6.64 – 6.57 (m, 2H), 6.45 (d, *J* = 2.6 Hz, 1H), 6.12 (d, *J* = 2.8 Hz, 1H), 4.54 – 4.53 (m, 1H), 4.51 (dd, *J* = 5.4, 2.2 Hz, 2H), 4.33 – 4.29 (m, 1H), 4.15 (d, *J* = 7.9 Hz, 1H), 3.95 (dd, *J* = 13.9, 2.5 Hz, 1H), 3.68 (d, *J* = 12.9 Hz, 2H), 3.56 (s, 3H), 3.54 (s, 3H), 3.07 (d, *J* = 13.8 Hz, 1H), 1.43 (s, 3H), 1.36 (d, *J* = 4.7 Hz, 3H), 1.24 (s, 6H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 201.1, 165.8, 165.7, 156.9, 156.1, 153.7, 147.8, 144.9, 144.5, 144.4, 142.5, 132.63, 132.6, 130.2, 129.7, 129.2, 129.0, 128.2, 127.8, 127.0, 126.9, 126.8, 126.5, 125.7, 120.3, 120.2, 116.6, 112.1, 110.8, 108.7, 105.4, 101.8, 71.2, 70.5, 70.2, 70.19, 65.7, 25.9, 25.9, 24.2, 24.1.

**HRMS (ESI)** m/z calcd for $C_{49}H_{47}NO_{10}Na^+$ $(M+Na)^+$ 832.3092, found 832.3093.

(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)(phenyl)methanone (**5a**)



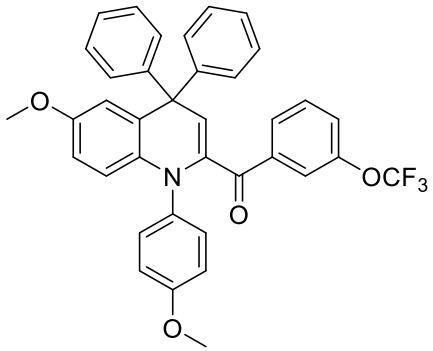
Compound **5a** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, ethene-1,1-diyldibenzene. **5a** was obtained in 89% yield (103.8 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, CDCl3)** δ 7.60 – 7.57 (d, 2H), 7.46 – 7.43 (m, 1H), 7.36 – 7.32 (m, 4H), 7.30 – 7.28 (m, 2H), 7.25 (s, 1H), 7.25 – 7.22 (m, 5H), 7.02 – 6.99 (m, 2H), 6.76 – 6.74 (m, 2H), 6.64 (dd, *J* = 2.5, 1.6 Hz, 1H), 6.39 (dd, *J* = 2.5, 0.8 Hz, 1H), 5.65 (s, 1H), 3.73 (s, 3H), 3.60 (s, 4H).

**$^{13}$C NMR (151 MHz, CDCl$_3$)** δ 192.5, 158.6, 154.7, 148.9, 140.1, 137.8, 136.5, 135.0, 132.9, 131.6, 129.8, 129.3, 128.2, 128.18, 127.5, 126.4, 116.6, 116.5, 116.1, 114.5, 112.8, 55.5, 55.4, 52.5.

**HRMS (ESI)** m/z calcd for $C_{36}H_{29}NO_3Na^+$ $(M+Na)^+$ 546.2040, found 546.2040.

(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)(3-(trifluoromethoxy)phenyl)methanone(**5b**)




Compound **5b** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-(3-(trifluoromethoxy)phenyl)acetaldehyde, ethene-1,1-diyldibenzene. **5b** was obtained in 79% yield (95.9 mg) as yellow solid.

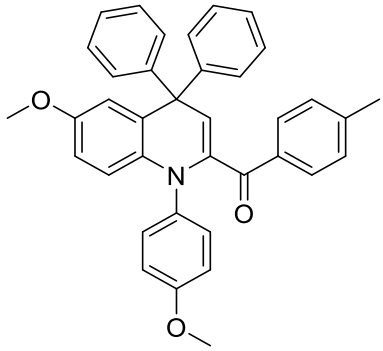
**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.47 (dt, *J* = 7.2, 1.7 Hz, 1H), 7.39 – 7.34 (m, 5H), 7.32 – 7.27 (m, 4H), 7.26 – 7.23 (m, 4H), 7.01 – 6.97 (m, 2H), 6.78 – 6.74 (m, 2H), 6.67 (dd, *J* = 9.1, 2.7 Hz, 1H), 6.64 (d, *J* = 9.0 Hz, 1H), 6.40 (d, *J* = 2.7 Hz, 1H), 5.71 (s, 1H), 3.74 (s, 3H), 3.60 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.0, 158.7, 154.9, 149.0, 148.6, 140.0, 139.7, 136.2, 134.8, 131.5, 129.7, 129.2, 128.3, 127.8, 127.5, 126.5, 125.2, 122.1, 116.8, 116.4, 116.1, 114.6, 112.9, 55.5, 55.4, 52.5.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -57.8.

**HRMS (ESI)** m/z calcd for $C_{37}H_{28}F_3NO_4Na^+$ $(M+Na)^+$ 630.1863, found 630.1860.

(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)(p-tolyl)methanone(**5c**)

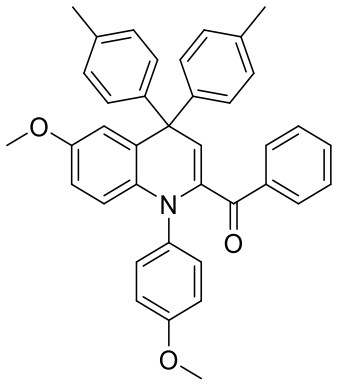


Compound **5c** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-(p-tolyl)acetaldehyde, ethene-1,1-diyldibenzene. **5c** was obtained in 65% yield (69.8 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.55 – 7.50 (m, 2H), 7.37 – 7.30 (m, 5H), 7.26 – 7.21 (m, 6H), 7.09 (d, *J* = 7.7 Hz, 2H), 7.04 – 7.01 (m, 2H), 6.76 (dd, *J* = 8.9, 2.2 Hz, 2H), 6.64 (tt, *J* = 9.2, 4.8 Hz, 2H), 6.39 (t, *J* = 2.4 Hz, 1H), 5.60 (s, 1H), 3.73 (s, 3H), 3.60 (s, 3H), 2.34 (s, 3H).
**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.1, 158.6, 154.6, 148.9, 143.8, 140.0, 136.6, 135.2, 135.0, 131.6, 130.1, 129.3, 128.9, 128.2, 127.5, 126.4, 116.4, 116.1, 115.9, 114.5, 112.8, 55.5, 55.4, 52.5, 21.8.

**HRMS (ESI)** m/z calcd for $C_{37}H_{31}NO_3Na^+$ $(M+Na)^+$ 560.2196, found 560.2194.

(6-methoxy-1-(4-methoxyphenyl)-4,4-di-p-tolyl-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5d**)



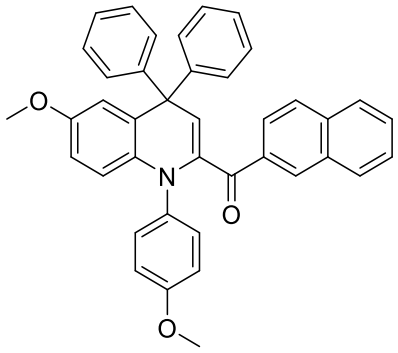
Compound **5d** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 4,4'-(ethene-1,1-diyl)bis(methylbenzene). **5d** was obtained in 72% yield (79.4 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.62 – 7.59 (m, 2H), 7.44 (ddt, *J* = 8.7, 7.3, 1.3 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.13 (d, *J* = 8.7 Hz, 4H), 7.11 (d, *J* = 8.4 Hz, 4H), 7.02 – 7.00 (m, 2H), 6.77 – 6.74 (m, 2H), 6.63 (d, *J* = 2.2 Hz, 2H), 6.41 (dd, *J* = 2.2, 1.0 Hz, 1H), 5.63 (s, 1H), 3.73 (s, 3H), 3.60 (s, 3H), 2.36 (s, 6H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.5, 158.5, 154.6, 146.1, 139.8, 137.9, 136.5, 135.8, 135.3, 132.8, 131.6, 129.8, 129.1, 128.9, 128.1, 128.0, 117.5, 116.4, 116.1, 114.5, 112.7, 55.5, 55.4, 51.9, 21.1.

**HRMS (ESI)** m/z calcd for $C_{38}H_{33}NO_3Na^+$ $(M+Na)^+$ 574.2353, found 574.2351.

(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)(naphthalen-2-yl)methanone(**5e**)



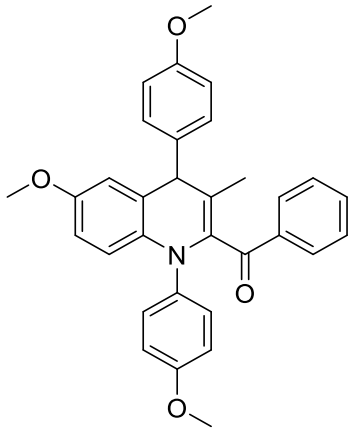
Compound **5e** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-(naphthalen-2-yl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **5e** was obtained in 91% yield (104.3 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 8.02 – 8.00 (m, 1H), 7.80 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.75 – 7.67 (m, 3H), 7.55 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.52 – 7.49 (m, 1H), 7.37 (dd, *J* = 8.2, 7.1 Hz, 4H), 7.32 – 7.27 (m, 5H), 7.08 – 7.03 (m, 2H), 6.75 – 6.72 (m, 2H), 6.66 (dd, *J* = 3.7, 1.6 Hz, 2H), 6.40 (dd, *J* = 2.5, 0.7 Hz, 1H), 5.71 (s, 1H), 3.70 (s, 3H), 3.61 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.3, 158.6, 154.8, 148.9, 140.0, 136.6, 135.6, 135.1, 134.9, 132.4, 132.2, 131.7, 129.6, 129.4, 128.5, 128.3, 128.1, 127.8, 127.5, 126.7, 126.4, 125.0, 116.4, 116.3, 116.1, 114.6, 112.8, 55.5, 55.4, 52.6.

**HRMS (ESI)** m/z calcd for $C_{40}H_{31}NO_3Na^+$ $(M+Na)^+$ 596.2196, found 596.2194.

(6-methoxy-1,4-bis(4-methoxyphenyl)-3-methyl-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5f**)



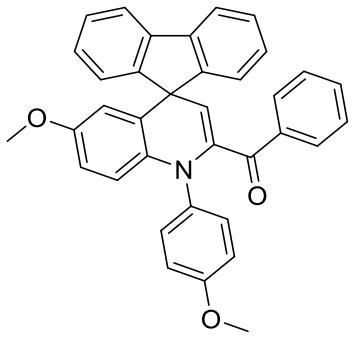
Compound **5f** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, (*E*)-1-methoxy-4-(prop-1-en-1-yl)benzene. **5f** was obtained in 81% yield (79.6 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.74 (d, *J* = 7.6 Hz, 2H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.3 Hz, 2H), 6.54 (dd, *J* = 9.0, 2.7 Hz, 1H), 6.51 – 6.46 (m, 2H), 5.10 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.64 (s, 3H), 1.92 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.7, 158.5, 157.8, 154.8, 142.9, 138.9, 137.6, 135.6, 135.4, 132.8, 131.4, 130.7, 129.7, 128.6, 128.2, 117.0, 116.4, 114.6, 114.3, 113.6, 112.3, 55.6, 55.5, 55.4, 41.7, 31.3.

**HRMS (ESI)** m/z calcd for $C_{32}H_{29}NO_4Na^+$ $(M+Na)^+$ 514.1989, found 514.1990.

(6'-methoxy-1'-(4-methoxyphenyl)-1'H-spiro[fluorene-9,4'-quinolin]-2'-yl)(phenyl)methanone(**5g**)



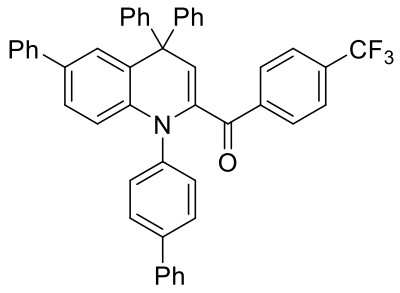

Compound **5g** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 9-methylene-9*H*-fluorene. **5g** was obtained in 57% yield (59.4 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.83 (d, *J* = 7.5 Hz, 2H), 7.56 – 7.52 (m, 2H), 7.34 (t, *J* = 7.9 Hz, 4H), 7.23 (dd, *J* = 8.3, 3.4 Hz, 3H), 7.21 – 7.17 (m, 2H), 7.09 (d, *J* = 3.6 Hz, 3H), 6.80 – 6.75 (m, 2H), 6.63 (d, *J* = 9.1 Hz, 1H), 6.52 (dd, *J* = 9.1, 3.0 Hz, 1H), 5.93 (d, *J* = 2.9 Hz, 1H), 3.77 (s, 3H), 3.42 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 182.3, 158.8, 153.9, 153.8, 144.1, 141.3, 138.2, 138.0, 136.1, 135.1, 131.7, 130.7, 130.5, 130.4, 129.4, 128.9, 128.0, 127.8, 127.7, 127.5, 127.4, 124.3, 120.1, 116.7, 115.0, 113.7, 112.8, 55.7, 55.3, 53.3.

**HRMS (APCI)** m/z calcd for $C_{36}H_{28}NO_3^+(M+H)^+$ 522.2064, found 522.2065.

(1-([1,1'-biphenyl]-4-yl)-4,4,6-triphenyl-1,4-dihydroquinolin-2-yl)(4-(trifluoromethyl)phenyl)methanone(**5h**)




Compound **5h** was synthesized according to general procedure 3.4 starting from di([1,1'-biphenyl]-4-yl)amine, 2-oxo-2-(4-(trifluoromethyl)phenyl)acetaldehyde, ethene-1,1-diyldibenzene. **5h** was obtained in 50% yield (68.3 mg) as yellow solid.

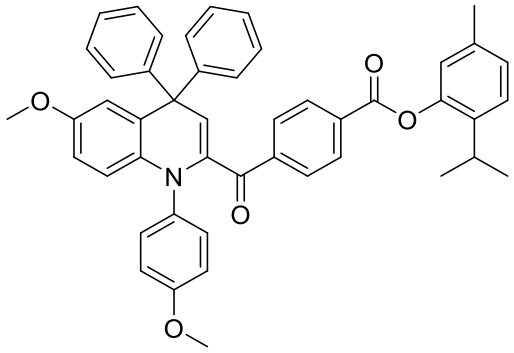
**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.55 – 7.51 (m, 4H), 7.47 – 7.41 (m, 3H), 7.40 (dd, *J* = 6.6, 2.0 Hz, 4H), 7.38 – 7.35 (m, 4H), 7.35 – 7.33 (m, 3H), 7.33 – 7.30 (m, 5H), 7.21 – 7.19 (m, 2H), 7.15 (d, *J* = 2.2 Hz, 1H), 5.89 (s, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.0, 171.3, 148.6, 140.9, 140.7, 140.68, 140.66, 140.6, 140.1, 139.4, 135.0, 130.5, 129.8 (q, *J* = 27.6 Hz), 129.3, 128.9, 128.8, 128.4, 128.2, 127.7, 127.2, 126.9, 126.7, 126.6, 126.6, 126.1, 125.3 (q, *J* = 3.9 Hz), 119.4, 115.8, 60.5, 52.5.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -63.01.

**HRMS (ESI)** m/z calcd for $C_{47}H_{32}F_3NONa^+$ $(M+Na)^+$ 706.2328, found 706.2325.

2-isopropyl-5-methylphenyl 4-(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinoline-2-carbonyl)benzoate(**5i**)



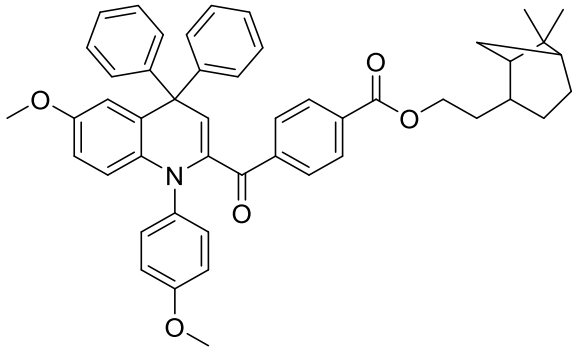
Compound **5i** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-ethyl-5-methylphenyl 4-(2-oxoacetyl)benzoate, ethene-1,1-diyldibenzene. **5i** was obtained in 63% yield (88.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 8.10 (dd, *J* = 8.4, 1.6 Hz, 2H), 7.70 – 7.62 (m, 2H), 7.36 (t, *J* = 7.7 Hz, 4H), 7.30 – 7.27 (m, 2H), 7.25 – 7.21 (m, 5H), 7.08 (d, *J* = 8.1 Hz, 1H), 7.03 – 6.98 (m, 2H), 6.93 (s, 1H), 6.79 – 6.74 (m, 2H), 6.66 (d, *J* = 1.6 Hz, 2H), 6.42 – 6.35 (m, 1H), 5.73 (d, *J* = 1.3 Hz, 1H), 3.75 (s, 3H), 3.60 (s, 3H), 2.35 (s, 3H), 1.21 (s, 3H), 1.20 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.8, 171.3, 164.7, 158.7, 154.9, 148.7, 148.1, 141.9, 140.1, 137.2, 136.9, 136. 3, 134.9, 132.9, 131.6, 129.9, 129.7, 129.3, 128.3, 127.6, 127.5, 126.7, 126.6, 122.8, 117. 7, 116.6, 116.1, 114.6, 113.0, 60.5, 55.5, 55.48, 52.6, 27. 4, 23.2, 21.0.

**HRMS (ESI)** m/z calcd for $C_{47}H_{41}NO_5Na^+$ $(M+Na)^+$ 722.2877, found 722.2873.

2-(6,6-dimethylbicyclo[3.1.1]heptan-2-yl)ethyl 4-(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinoline-2-carbonyl)benzoate(**5j**)



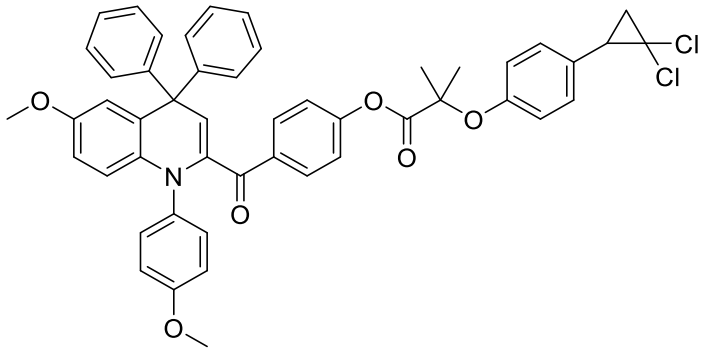
Compound **5j** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-(6,6-dimethylbicyclo[3.1.1]heptan-2-yl)ethyl 4-(2-oxoacetyl)benzoate, ethene-1,1-diyldibenzene. **5j** was obtained in 65% yield (93.2 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.92 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 4H), 7.27 (s, 1H), 7.25 – 7.21 (m, 5H), 6.98 – 6.93 (m, 2H), 6.75 – 6.71 (m, 2H), 6.67 – 6.63 (m, 2H), 6.38 (d, *J* = 2.6 Hz, 1H), 5.68 (s, 1H), 4.32 (q, *J* = 6.5 Hz, 2H), 3.73 (s, 3H), 3.59 (s, 3H), 2.35 (ddt, *J* = 8.5, 6.2, 3.1 Hz, 1H), 2.17 (dd, *J* = 9.6, 6.9 Hz, 1H), 1.93 – 1.90 (m, 2H), 1.88 – 1.85 (m, 2H), 1.53 (ddd, *J* = 14.6, 7.3, 4.7 Hz, 1H), 1.20 (s, 3H), 1.04 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.9, 166.0, 158.7, 154.9, 148. 7, 141.3, 140.2, 136.3, 134.9, 133.9, 131.5, 129.4, 129.3, 129.3, 129.3, 128.3, 127.6, 126.5, 117.1, 116.5, 116.1, 114.6, 112.9, 64.7, 55.5, 55.46, 52.6, 46.4, 41.5, 38.8, 38.2, 36.5, 33.7, 28.3, 26.5, 23.4, 22.4.

**HRMS (ESI)** m/z calcd for $C_{48}H_{47}NO_5Na^+$ $(M+Na)^+$ 740.3346, found 740.3343.

4-(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinoline-2-carbonyl)phenyl 2-(4-(2,2-dichlorocyclopropyl)phenoxy)-2-methylpropanoate(**5k**)



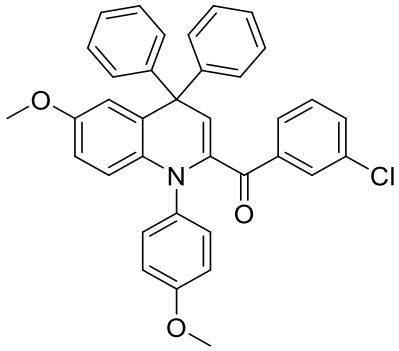

Compound **5k** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 4-(2-oxoacetyl)phenyl 2-(4-(2,2-dichlorocyclopropyl)phenoxy)-2-methylpropanoate, ethene-1,1-diyldibenzene. **5k** was obtained in 31% yield (50.2 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.62 – 7.53 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 4H), 7.24 (d, *J* = 7.3 Hz, 2H), 7.23 – 7.21 (m, 4H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.98 – 6.94 (m, 2H), 6.93 – 6.86 (m, 4H), 6.76 – 6.73 (m, 2H), 6.64 (dd, *J* = 9.0, 2.8 Hz, 1H), 6.61 (d, *J* = 9.0 Hz, 1H), 6.38 (d, *J* = 2.7 Hz, 1H), 5.63 (s, 1H), 3.73 (s, 3H), 3.59 (s, 3H), 2.86 (dd, *J* = 10.6, 8.3 Hz, 1H), 1.96 (dd, *J* = 10.7, 7.4 Hz, 1H), 1.82 – 1.77 (m, 1H), 1.74 (s, 6H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.17, 172.48, 158.68, 154.98, 154.80, 154.01, 148.78, 139.98, 136.38, 135.66, 134.88, 131.54, 131.31, 130.00, 129.27, 128.82, 128.26, 127.53, 126.45, 121.20, 118.79, 116.45, 116.15, 116.10, 114.64, 112.91, 79.45, 60.95, 55.54, 55.47, 52.54, 34.95, 25.99, 25.59, 25.55.

**HRMS (ESI)** m/z calcd for $C_{49}H_{41}Cl_2NO_6Na^+$ $(M+Na)^+$ 832.2203, found 832.2206.

(3-chlorophenyl)(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)methanone(**5m**)



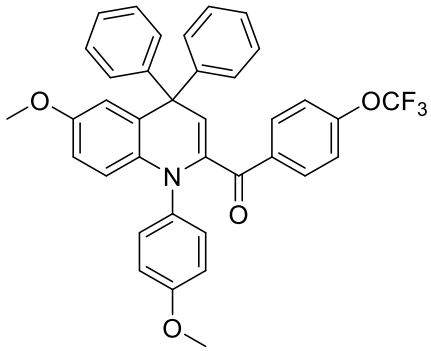

Compound **5m** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-(3-chlorophenyl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **5m** was obtained in 87% yield (97.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.50 (t, *J* = 1.9 Hz, 1H), 7.44 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.40 (ddd, *J* = 8.0, 2.2, 1.1 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 5H), 7.23 – 7.20 (m, 6H), 7.00 – 6.97 (m, 2H), 6.78 – 6.75 (m, 2H), 6.66 – 6.64 (m, 2H), 6.36 (dd, *J* = 2.0, 1.3 Hz, 1H), 5.68 (s, 1H), 3.74 (s, 3H), 3.59 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.0, 158.7, 154.9, 148.7, 139.8, 139.4, 136.4, 134.9, 134.4, 132.7, 131.5, 129.8, 129.5, 129.3, 128.3, 127.7, 127.5, 126.5, 117.6, 116.5, 116.0, 114.6, 112.9, 55.5, 55.48, 52.6.

**HRMS (ESI)** m/z calcd for $C_{36}H_{28}ClNO_3Na^+$ $(M+Na)^+$ 580.1650, found 580.1648.

(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)(4-(trifluoromethoxy)phenyl)methanone(**5n**)



Compound **5n** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-(4-(trifluoromethoxy)phenyl)acetaldehyde, ethene-1,1-diyldibenzene. **5n** was obtained in 85% yield (102.6 mg) as yellow solid.

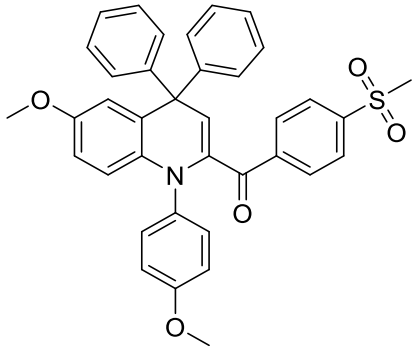
**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.45 (dt, *J* = 7.2, 1.6 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 5H), 7.28 – 7.26 (m, 2H), 7.25 (d, *J* = 4.8 Hz, 2H), 7.24 – 7.21 (m, 4H), 6.97 – 6.94 (m, 2H), 6.75 – 6.72 (m, 2H), 6.64 – 6.59 (m, 2H), 6.37 (d, *J* = 2.7 Hz, 1H), 5.69 (s, 1H), 3.72 (s, 3H), 3.58 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.0, 158.7, 154.9, 148.9, 148.6, 140.0, 139.7, 136.2, 134.8, 131.5, 129.7, 129.2, 128.3, 127.8, 127.5, 126.5, 125.2, 122.1, 116.8, 116.4, 116.1, 114.6, 112.9, 55.5, 55.4, 52.5.

**$^{19}$F NMR (565 MHz, $CDCl_3$)** δ -57.9.

**HRMS (ESI)** m/z calcd for $C_{37}H_{28}F_3NO_4Na^+$ $(M+Na)^+$ 630.1863, found 630.1861.

(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)(4-(methylsulfonyl)phenyl)methanone(**5o**)



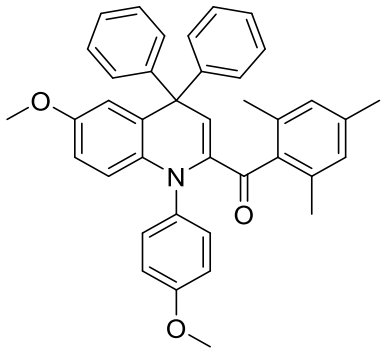

Compound **5o** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-(4-(methylsulfonyl)phenyl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **5o** was obtained in 94% yield (114.9 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.85 – 7.80 (m, 2H), 7.65 – 7.60 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 4H), 7.30 – 7.27 (m, 2H), 7.23 – 7.19 (m, 4H), 6.96 – 6.93 (m, 2H), 6.76 – 6.71 (m, 2H), 6.68 – 6.62 (m, 2H), 6.37 (d, *J* = 2.7 Hz, 1H), 5.72 (s, 1H), 3.73 (s, 3H), 3.59 (s, 3H), 3.01 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 191.0, 158.8, 155.0, 148.4, 143.6, 142.3, 140.1, 136.1, 134.7, 131.5, 130.2, 129.2, 128.3, 127.5, 127.3, 126.6, 117.7, 116.5, 116.0, 114.7, 113.0, 55.5, 55.48, 52.6, 44.4.

**HRMS (ESI)** m/z calcd for $C_{37}H_{31}NO_5SNa^+$ $(M+Na)^+$ 624.1815, found 624.1813.

mesityl(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)methanone(**5p**)



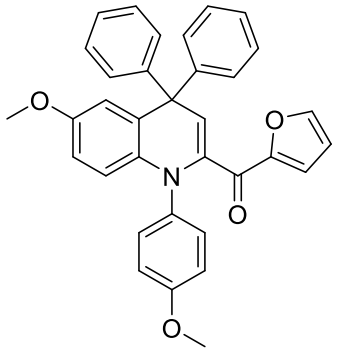

Compound **5p** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-mesityl-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **5p** was obtained in 31% yield (35.2 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.30 (t, *J* = 7.6 Hz, 4H), 7.26 – 7.23 (m, 2H), 7.08 – 7.05 (m, 4H), 7.03 – 6.99 (m, 2H), 6.83 – 6.78 (m, 3H), 6.72 (s, 2H), 6.68 (dd, *J* = 9.1, 2.9 Hz, 1H), 6.22 (d, *J* = 2.9 Hz, 1H), 6.06 (s, 1H), 3.79 (s, 3H), 3.58 (s, 3H), 2.24 (s, 3H), 1.95 (s, 6H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 196.1, 158.6, 154.8, 148.2, 141.2, 138.7, 137.5, 136.8, 136.1, 135.3, 132.1, 129.3, 128.8, 128.4, 128.3, 126.6, 124.9, 117.9, 115.6, 114.0, 113.0, 55.51, 55.5, 52.5, 21.2, 19.3.

**HRMS (ESI)** m/z calcd for $C_{39}H_{35}NO_3Na^+$ $(M+Na)^+$ 588.2509, found 588.2509.

furan-2-yl(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)methanone(**5q**)



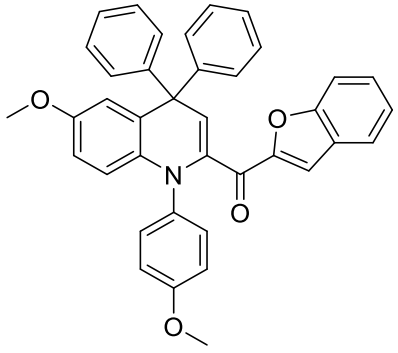
Compound **5q** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-(furan-2-yl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **5q** was obtained in 75% yield (77.2 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.55 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.36 (dd, *J* = 8.6, 6.9 Hz, 4H), 7.29 – 7.27 (m, 5H), 7.11 – 7.09 (m, 2H), 6.92 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.83 – 6.81 (m, 2H), 6.68 – 6.66 (m, 2H), 6.42 (dd, *J* = 3.6, 1.7 Hz, 1H), 6.39 (d, *J* = 2.5 Hz, 1H), 5.86 (s, 1H), 3.77 (s, 3H), 3.60 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 178.8, 158.7, 154.7, 152.4, 148.9, 147.6, 138.9, 136.6, 134.9, 131.5, 129.2, 128.3, 127.5, 126.4, 121.0, 116.8, 116.0, 114.6, 112.9, 112.1, 55.5, 55.4, 52.6.

**HRMS (ESI)** m/z calcd for $C_{34}H_{27}NO_4Na^+$ $(M+Na)^+$ 536.1832, found 536.1832.

benzofuran-2-yl(6-methoxy-1-(4-methoxyphenyl)-4,4-diphenyl-1,4-dihydroquinolin-2-yl)methanone(**5r**)



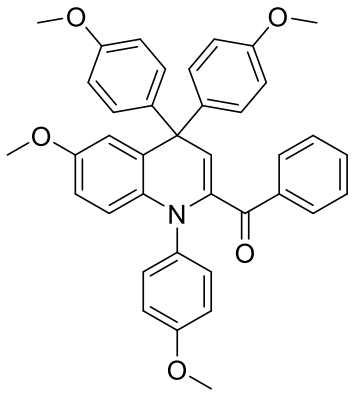
Compound **5r** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-(benzofuran-2-yl)-2-oxoacetaldehyde, ethene-1,1-diyldibenzene. **5r** was obtained in 68% yield (77.2 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.61 – 7.59 (m, 1H), 7.49 (dt, *J* = 8.5, 1.0 Hz, 1H), 7.42 (tt, *J* = 8.3, 1.2 Hz, 2H), 7.39 – 7.34 (m, 4H), 7.29 – 7.27 (m, 4H), 7.27 (d, *J* = 1.2 Hz, 2H), 7.19 (t, *J* = 1.0 Hz, 1H), 7.13 – 7.09 (m, 2H), 6.70 – 6.64 (m, 2H), 6.38 (dd, *J* = 2.7, 1.0 Hz, 1H), 5.94 (s, 1H), 3.73 (s, 3H), 3.60 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 180.6, 158.8, 156.1, 154.8, 152.5, 148.8, 139.0, 136.5, 134.9, 131.6, 129.3, 128.7, 128.3, 127.5, 126.9, 126.5, 124.0, 123.5, 117.4, 117.0, 116.9, 116.0, 114.7, 113.0, 112.7, 55.5, 55.4, 52.7.

**HRMS (ESI)** m/z calcd for $C_{38}H_{29}NO_4Na^+$ $(M+Na)^+$ 586.1989, found 586.1986.

(6-methoxy-1,4,4-tris(4-methoxyphenyl)-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5s**)



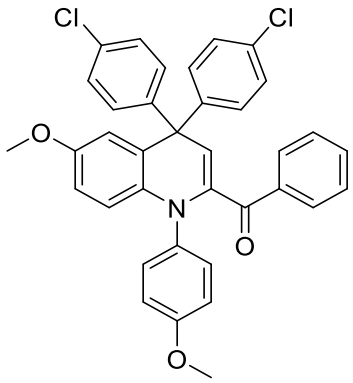

Compound **5s** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 4,4'-(ethene-1,1-diyl)bis(methoxybenzene). **5s** was obtained in 94% yield (109.6 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.62 – 7.59 (m, 2H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 4H), 7.02 – 6.98 (m, 2H), 6.86 (d, *J* = 8.7 Hz, 4H), 6.75 (d, *J* = 8.5 Hz, 2H), 6.63 (d, *J* = 1.9 Hz, 2H), 6.40 – 6.37 (m, 1H), 5.63 (d, *J* = 1.8 Hz, 1H), 3.82 (s, 6H), 3.73 (d, *J* = 1.9 Hz, 3H), 3.61 (d, *J* = 1.8 Hz, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.5, 158.5, 158.0, 154.6, 141.4, 139.7, 137.9, 136.5, 135.2, 132.8, 131.5, 130.2, 129.8, 128.3, 128.2, 117.5, 116.4, 116.0, 114.5, 113.5, 112.6, 55.5, 55.43, 55.4, 51.1.

**HRMS (ESI)** m/z calcd for $C_{38}H_{33}NO_5Na^+$ $(M+Na)^+$ 606.2251, found 606.2250.

(4,4-bis(4-chlorophenyl)-6-methoxy-1-(4-methoxyphenyl)-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5t**)



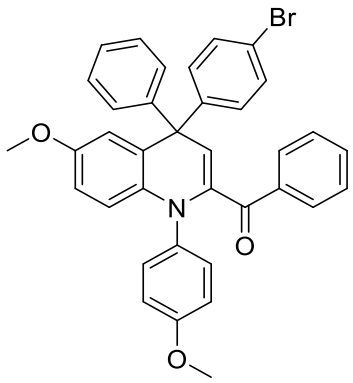

Compound **5t** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 4,4'-(ethene-1,1-diyl)bis(chlorobenzene). **5t** was obtained in 68% yield (80.4 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.58 – 7.55 (m, 2H), 7.46 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.33 – 7.30 (m, 4H), 7.30 – 7.28 (m, 2H), 7.18 – 7.14 (m, 4H), 6.99 – 6.96 (m, 2H), 6.77 – 6.74 (m, 2H), 6.66 (dd, *J* = 9.1, 2.9 Hz, 1H), 6.61 (d, *J* = 9.0 Hz, 1H), 6.33 (d, *J* = 2.8 Hz, 1H), 5.47 (s, 1H), 3.73 (s, 3H), 3.62 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.3, 158.8, 154.9, 147.1, 140.6, 137.5, 136.2, 134.4, 133.1, 132.5, 131.5, 130.5, 129.7, 128.5, 128.3, 126.5, 116.6, 115.9, 114.6, 113.8, 113.0, 55.6, 55.5, 51.7.

**HRMS (ESI)** m/z calcd for $C_{36}H_{27}Cl_2NO_3Na^+$ $(M+Na)^+$ 614.1260, found 614.1261.

(4-(4-bromophenyl)-6-methoxy-1-(4-methoxyphenyl)-4-phenyl-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5u**)



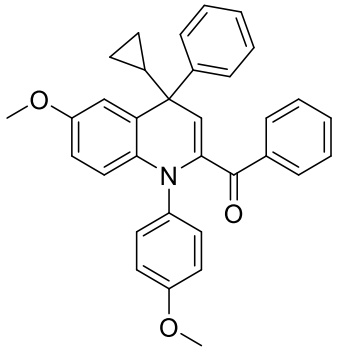

Compound **5u** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 1-bromo-4-(1-phenylvinyl)benzene. **5u** was obtained in 68% yield (81.9 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.58 – 7.56 (m, 2H), 7.47 – 7.44 (m, 3H), 7.34 (t, *J* = 7.7 Hz, 2H), 7.31 – 7.27 (m, 3H), 7.23 – 7.20 (m, 2H), 7.12 – 7.09 (m, 2H), 7.00 – 6.97 (m, 2H), 6.77 – 6.73 (m, 2H), 6.65 (dd, *J* = 9.1, 2.8 Hz, 1H), 6.61 (d, *J* = 9.0 Hz, 1H), 6.35 (d, *J* = 2.8 Hz, 1H), 5.54 (s, 1H), 3.73 (s, 3H), 3.61 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.4, 158.7, 154.8, 148.4, 148.0, 140.4, 137.7, 136.3, 134.7, 133.0, 131.5, 131.3, 131.0, 129.7, 129.2, 128.4, 128.2, 126.9, 126.6, 120.5, 116.5, 116.0, 115.0, 114.6, 113.0, 55.6, 55.5, 52.2.

**HRMS (ESI)** m/z calcd for $C_{36}H_{28}BrNO_3Na^+$ $(M+Na)^+$ 624.1145, found 624.1141.

(4-cyclopropyl-6-methoxy-1-(4-methoxyphenyl)-4-phenyl-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5v**)



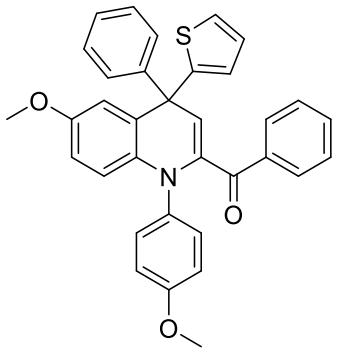
Compound **5v** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, (1-cyclopropylvinyl)benzene. **5v** was obtained in 94% yield (104.2 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.76 – 7.72 (m, 2H), 7.68 – 7.64 (m, 2H), 7.48 – 7.45 (m, 1H), 7.33 (ddd, *J* = 8.3, 7.3, 2.2 Hz, 4H), 7.22 – 7.18 (m, 1H), 7.15 – 7.12 (m, 2H), 6.82 – 6.78 (m, 2H), 6.55 (dd, *J* = 9.1, 2.9 Hz, 1H), 6.50 (d, *J* = 9.0 Hz, 1H), 6.38 (d, *J* = 2.9 Hz, 1H), 4.76 (s, 1H), 3.76 (s, 3H), 3.61 (s, 3H), 1.28 – 1.24 (m, 1H), 0.77 – 0.72 (m, 1H), 0.65 (dddd, *J* = 14.3, 6.0, 4.3, 1.3 Hz, 2H), 0.52 – 0.47 (m, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.6, 158.6, 154.4, 150.7, 140.5, 137.6, 135.8, 135.2, 132.9, 131.3, 129.7, 128.8, 128.5, 128.3, 128.2, 126.3, 116.0, 115.6, 114.6, 112.3, 111.6, 55.6, 55.5, 46.8, 23.2, 2.3, 1.7.

**HRMS (ESI)** m/z calcd for $C_{33}H_{29}NO_3Na^+$ $(M+Na)^+$ 510.2040, found 510.2040.

(6-methoxy-1-(4-methoxyphenyl)-4-phenyl-4-(thiophen-2-yl)-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5w**)



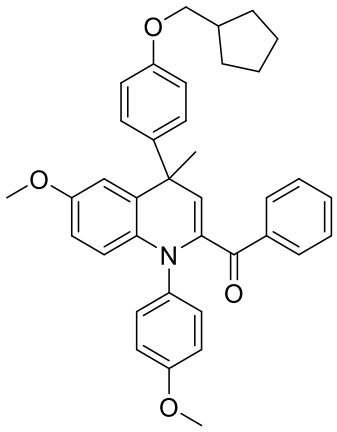

Compound **5w** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 2-(1-phenylvinyl)thiophene. **5w** was obtained in 94% yield (105.1 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$)** δ 7.73 – 7.69 (m, 2H), 7.48 – 7.44 (m, 1H), 7.34 – 7.32 (m, 4H), 7.32 – 7.30 (m, 4H), 7.05 – 7.02 (m, 2H), 6.99 (ddd, *J* = 5.1, 3.6, 0.7 Hz, 1H), 6.76 (ddt, *J* = 4.8, 2.3, 1.2 Hz, 2H), 6.74 (d, *J* = 0.6 Hz, 1H), 6.64 (ddd, *J* = 9.0, 2.9, 0.7 Hz, 1H), 6.59 – 6.55 (m, 2H), 5.57 (s, 1H), 3.73 – 3.72 (s, 3H), 3.62 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.4, 158.6, 155.0, 154.7, 148.8, 139. 7, 137.5, 135.8, 134.8, 133.0, 131.5, 129.9, 128.7, 128.3, 128.2, 127.6, 126.7, 126.7, 126.1, 125.5, 116.6, 115.6, 114.9, 114.6, 113.3, 55.6, 55.4, 49.7.

**HRMS (ESI)** m/z calcd for $C_{34}H_{27}NO_3SNa^+$ $(M+Na)^+$ 552.1604, found 552.1603.

(4-(4-(cyclopentylmethoxy)phenyl)-6-methoxy-1-(4-methoxyphenyl)-3-methyl-1,4-dihydroquinolin-2-yl)(phenyl)methanone(**5x**)

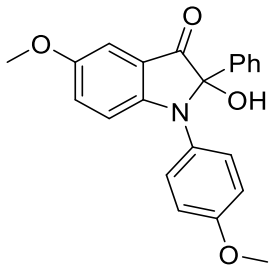


Compound **5x** was synthesized according to general procedure 3.4 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, 1-(cyclopentylmethoxy)-4-(prop-1-en-2-yl)benzene. **5x** was obtained in 94% yield (104.8 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.75 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.46 (tt, *J* = 7.8, 1.3 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.15 – 7.12 (m, 2H), 6.90 – 6.87 (m, 2H), 6.82 – 6.78 (m, 2H), 6.55 (dd, *J* = 9.1, 2.8 Hz, 1H), 6.52 – 6.47 (m, 2H), 5.11 (s, 1H), 3.83 (dd, *J* = 7.0, 1.7 Hz, 2H), 3.76 (s, 3H), 3.64 (s, 3H), 2.37 (p, *J* = 7.4 Hz, 1H), 1.92 (s, 3H), 1.88 – 1.81 (m, 2H), 1.69 – 1.62 (m, 2H), 1.62 (s, 2H), 1.37 (dq, *J* = 13.7, 7.0 Hz, 2H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 192.7, 158.5, 157.6, 154.7, 142.6, 138.9, 137.6, 135.7, 135.4, 132.8, 131.4, 130.8, 129.7, 128.6, 128.2, 117.2, 116.3, 114.6, 114.3, 114.2, 112.3, 72.3, 55.5, 55.4, 41.7, 39.2, 31.3, 29.6, 25.5.

**HRMS (ESI)** m/z calcd for $C_{37}H_{37}NO_4Na^+$ $(M+Na)^+$ 582.2615, found 582.2612.

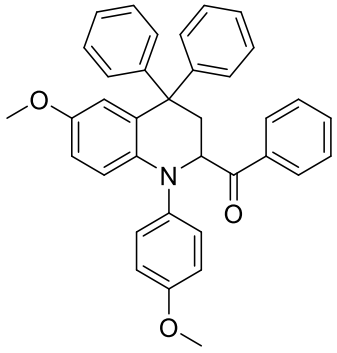



Compound **6a** was synthesized according to general procedure 3.5 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde. **6a** was obtained in 94% yield (91.4 mg) as yellow solid.

**$^1$H NMR (600 MHz, $CDCl_3$):** δ 7.42 (dd, J = 7.6, 2.2 Hz, 2H), 7.27 (dd, J = 5.9, 4.1 Hz, 3H), 7.15 (dd, J = 9.0, 3.4 Hz, 3H), 7.08 (d, J = 2.8 Hz, 1H), 6.88 (d, J = 8.9 Hz, 1H), 6.80 – 6.75 (m, 2H), 3.79 (s, 3H), 3.74 (s, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 200.0, 157.6, 156.0, 153.5, 137.1, 131.2, 128.7, 128.6, 128.5, 127.0, 126.1, 117.7, 114.5, 112.1, 106.0, 92.0, 56.0, 55.4.

**HRMS (ESI):** m/z calcd for $C_{22}H_{20}NO_4^+$ $(M+H)^+$ 362.1387, found 362.1381.




Compound **7a** was synthesized according to general procedure 3.6 starting from bis(4-methoxyphenyl)amine, 2-oxo-2-phenylacetaldehyde, ethene-1,1-diyldibenzene. **7a** was obtained in 87% yield (91.4 mg) as yellow solid.

**$^{1}$H NMR (600 MHz, $CDCl_3$)** δ 7.85 – 7.82 (m, 2H), 7.55 – 7.51 (m, 1H), 7.39 (td, *J* = 7.8, 2.4 Hz, 4H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.25 – 7.22 (m, 2H), 7.20 (dd, *J* = 7.7, 1.6 Hz, 3H), 7.08 – 7.05 (m, 2H), 6.84 – 6.79 (m, 2H), 6.74 (d, *J* = 8.9 Hz, 1H), 6.69 – 6.65 (m, 3H), 6.15 (d, *J* = 2.9 Hz, 1H), 4.72 (dd, *J* = 12.0, 5.0 Hz, 1H), 3.68 (s, 3H), 3.59 (s, 3H), 3.05 (dd, *J* = 13.4, 5.0 Hz, 1H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 200. 7, 156.4, 152.5, 146.4, 145.4, 141.4, 139.9, 135.6, 133.8, 133.5, 129.3, 129.2, 129.15, 128.8, 128.6, 128.2, 128.18, 127.1, 126.8, 126.7, 120.1, 115.9, 114.6, 112.9, 63.7, 55.6, 55.5, 51.9, 42.0.

**HRMS (ESI)** m/z calcd for $C_{36}H_{31}NO_3Na^+$ $(M+Na)^+$ 548.2196, found 548.2194.

## 5. Computational Details

All DFT calculations were performed with Gaussian09 package and the default grid (int = fine) was used for all calculations[1]. A careful conformational searching was conducted by CREST[2] to capture the lowest energy conformer of key transition states. The ensemble of structures created by CREST at the GFN2-xTB level was first optimized using the B3LYP-D3[3, 4] functional in combination with the def2-SVP[5] basis set. The reaction conditions of liquid phase were simulated in the optimization of all structures by introducing the SMD[6] solvation model (in DCE). Vibrational frequency analysis was used to identify the nature of each optimized structure, as the intermediates show no imaginary frequency while transition states show only one imaginary frequency. Thermal correction of free energy ($G_{therm}$) was performed under experimental conditions (333.15 K and 1 atm). The single-point energy ($E$) of each optimized structure was further refined using the ωB97XD[7] functional in combination with a triple-ζ basis set def2-TZVPP[5], as the ωB97XD/def2-TZVPP level was considered to be suitable for the computation of organic systems, which was recommended by Houk and co-workers.[8] Solvation effects ($G_{sol}$) were incorporated into single-point energy calculations by using the SMD model (DCE as the solvent). The contribution ($G_{std}$) originating from the change of the standard state from 1 atm gas phase to 1 mol/L solution environment was also included. As such, the relative Gibbs free energy ($\Delta G$) is given by $\Delta G = \Delta E + \Delta G_{therm} + \Delta G_{sol} + \Delta G_{std}$. The 3D images of DFT-derived structure were created with CYLview.[9]

### 5.1 Conformational searching

**Table 1.** Various conformers of selectivity-determining TS created by CREST.

| Structure | Number of conformers [a] |
|---|---|
| **TSA** | 13 |
| **TSB** | 29 |
| **TSA-HFIP** | 119 |
| **TSB-HFIP** | 66 |
| **TSA0** | 13 |
| **TSB0** | 13 |

[a] CREST was utilized to generate an ensemble of conformers for catalytic model. It is worth noting that the atoms involving in the reaction coordinate of a structure must remain frozen when applying CREST.

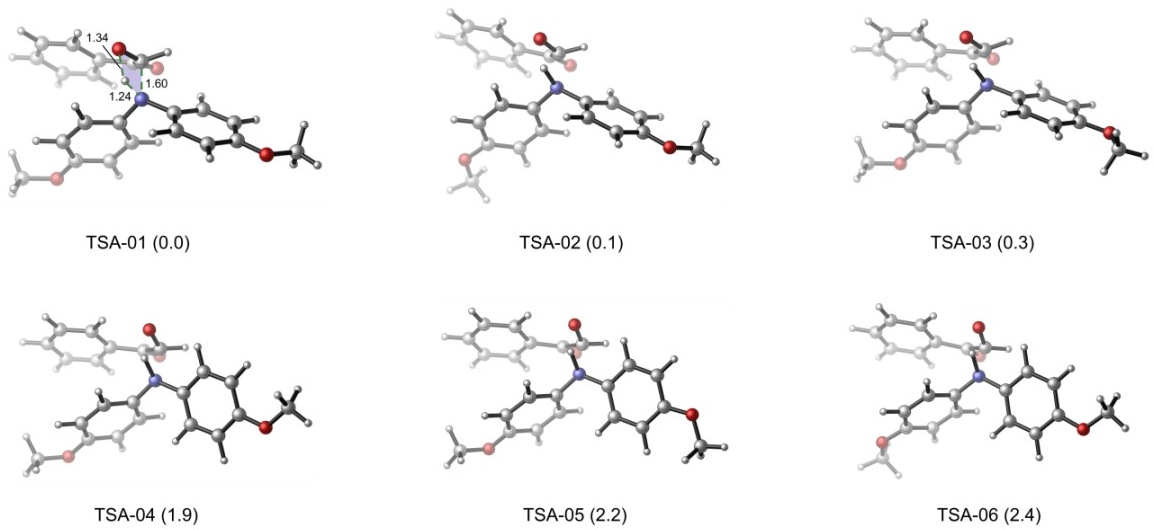



Figure 5.1 3D structures of the 6 lowest transition-state conformations for the TSA ensemble. Relative free energies in kcal/mol.

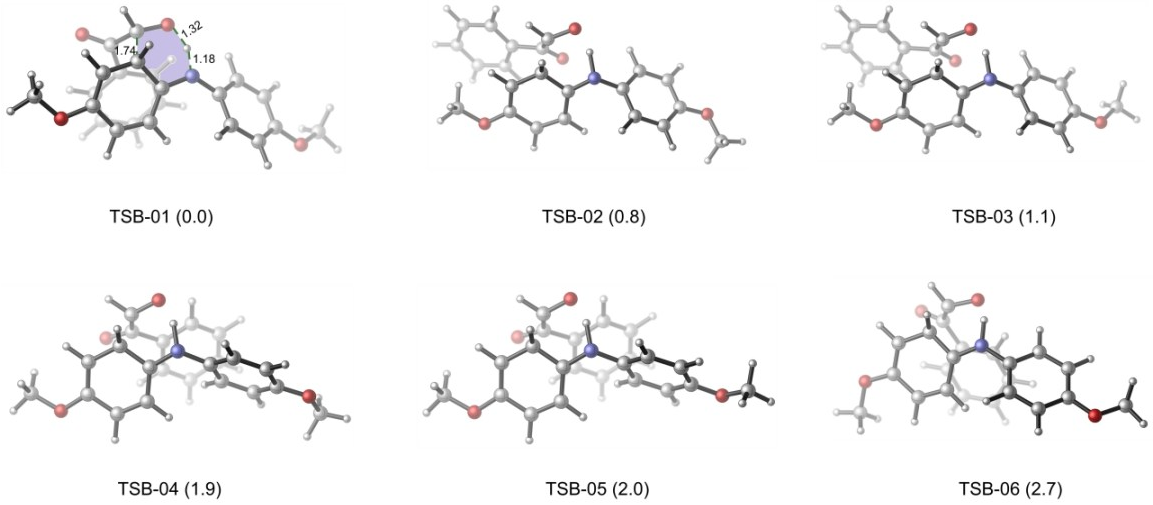



Figure 5.2 3D structures of the 6 lowest transition-state conformations for the TSB ensemble. Relative free energies in kcal/mol.

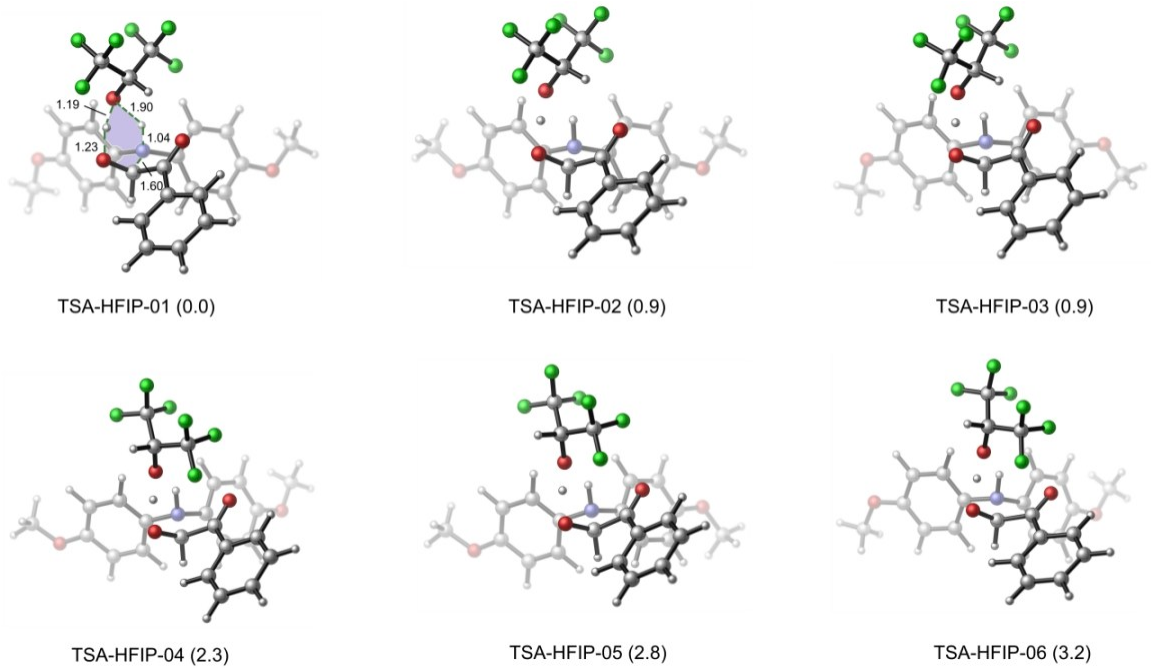



Figure 5.3 3D structures of the 6 lowest transition-state conformations for the TSA-HFIP ensemble. Relative free energies in kcal/mol.

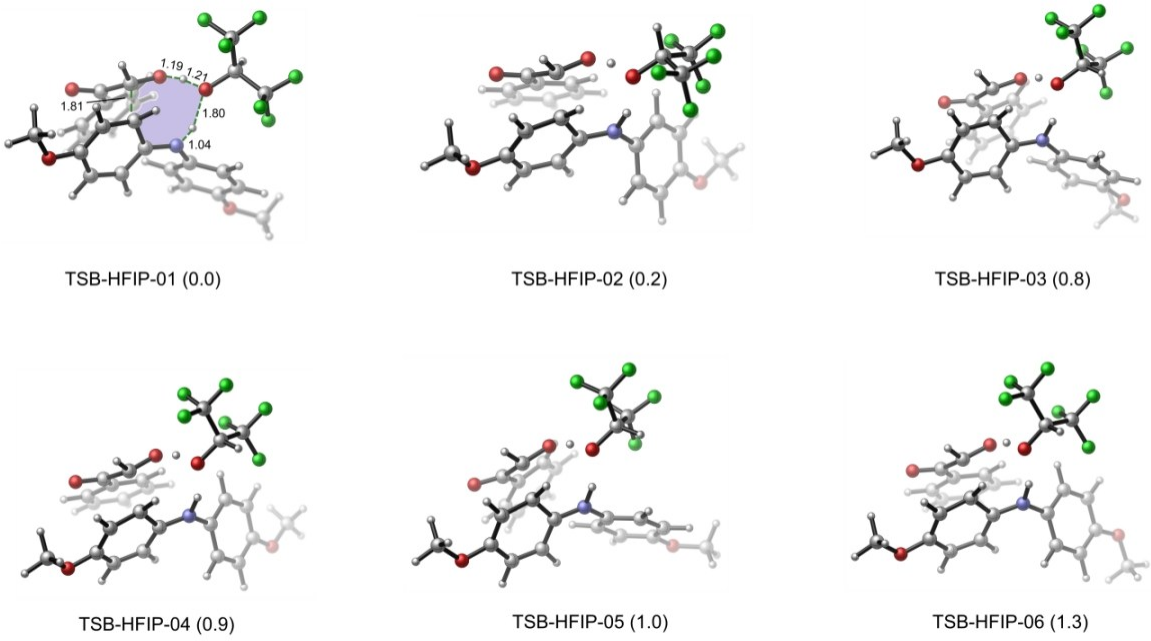



Figure 5.4 3D structures of the 6 lowest transition-state conformations for the TSB-HFIP ensemble. Relative free energies in kcal/mol.

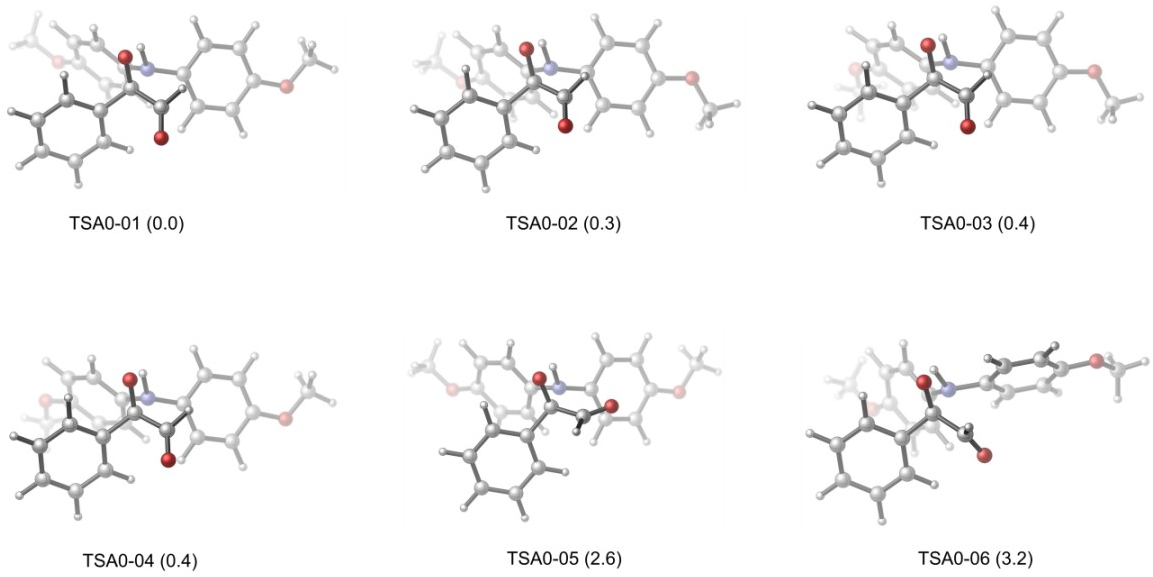



Figure 5.5 3D structures of the 6 lowest transition-state conformations for the TSA0 ensemble. Relative free energies in kcal/mol.

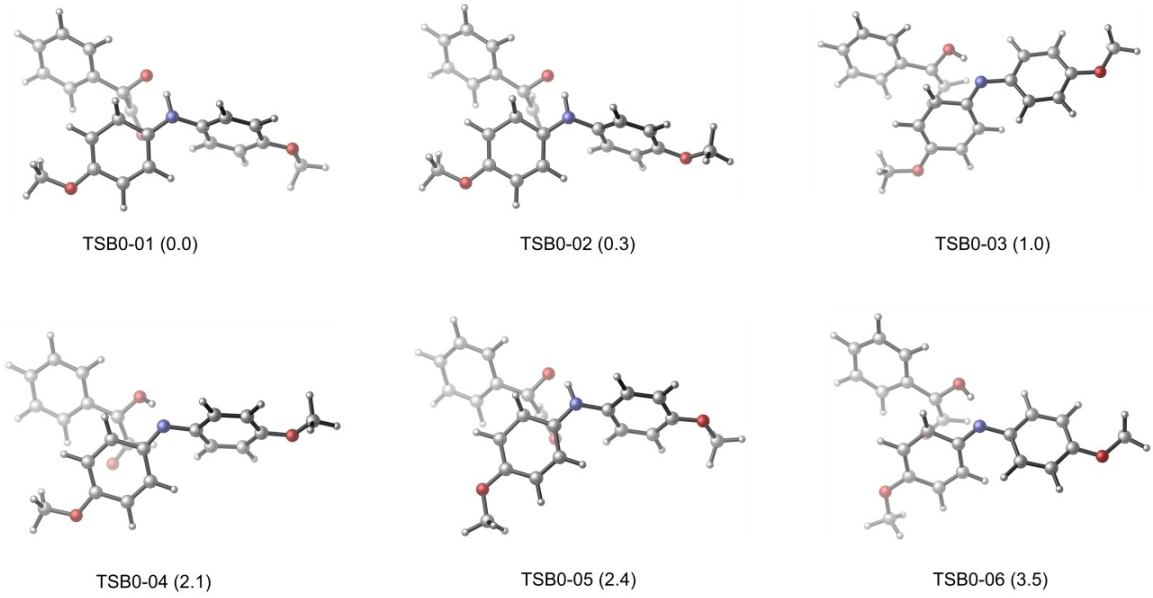



Figure 5.6 3D structures of the 6 lowest transition-state conformations for the TSB0 ensemble. Relative free energies in kcal/mol.

## 5.2 DFT investigation of regioselectivity in phenylglyoxal substrate

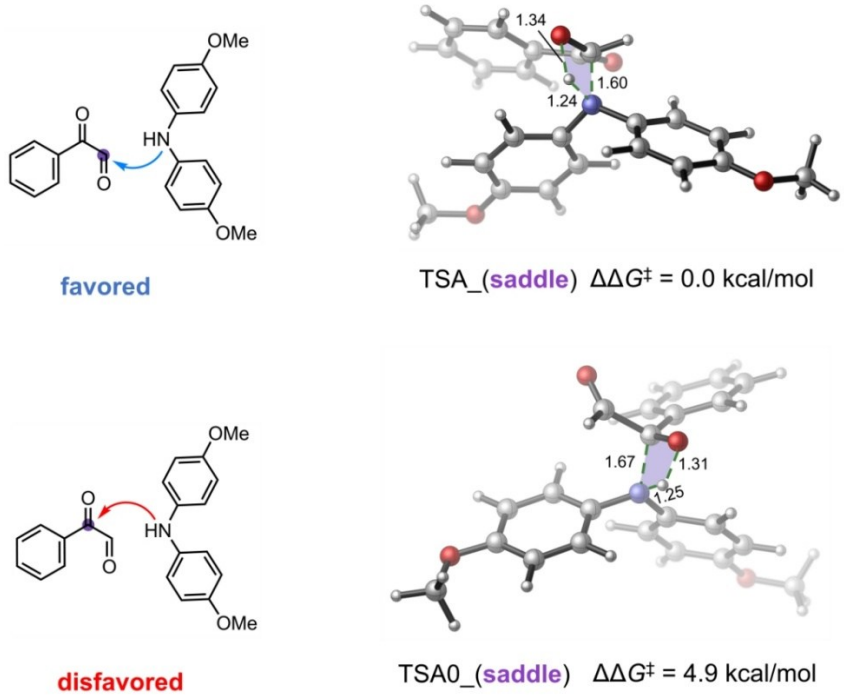



Figure 5.7 Relative Gibbs free energies of different carbon sites in phenylglyoxal substrate during the first C-N bond formation stage.

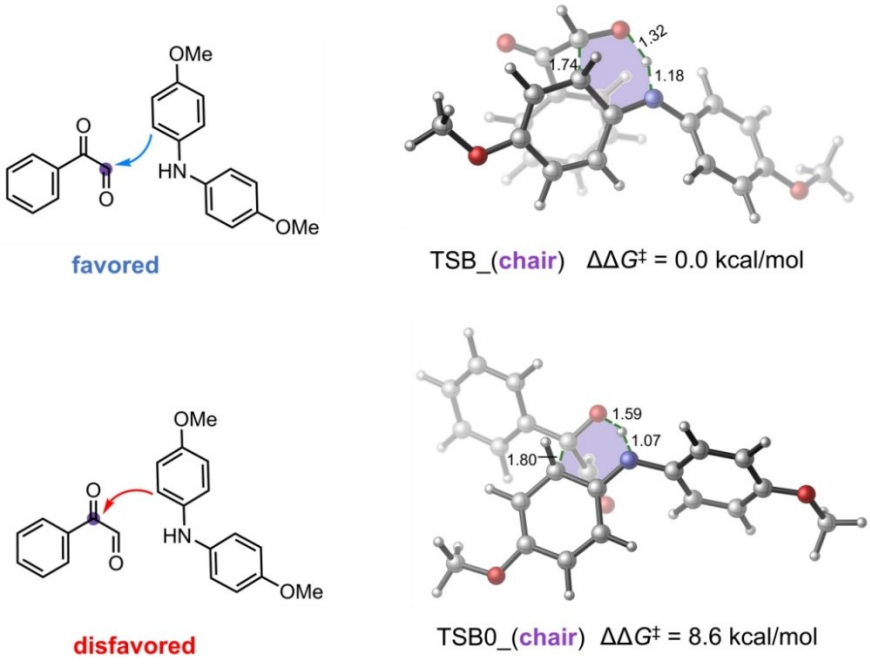



Figure 5.8 Relative Gibbs free energies of different carbon sites in phenylglyoxal substrate during the first C-C bond formation stage.

## 5.3 List of Cartesian Coordinates

Phenylglyoxal

| | | | |
|---|---|---|---|
| O | -2.493373 | -1.546364 | -0.000228 |
| C | -2.550684 | -0.343047 | 0.000005 |
| H | -3.520993 | 0.213900 | 0.000174 |
| C | -1.373471 | 0.654978 | 0.000066 |
| O | -1.713951 | 1.827202 | 0.000118 |
| C | 0.050663 | 0.230876 | 0.000033 |
| C | 0.463144 | -1.117081 | 0.000136 |
| C | 1.027202 | 1.249457 | -0.000092 |
| C | 1.824471 | -1.430453 | 0.000112 |
| H | -0.278224 | -1.913759 | 0.000236 |
| C | 2.382211 | 0.930683 | -0.000123 |
| H | 0.698979 | 2.290675 | -0.000168 |
| C | 2.783614 | -0.412546 | -0.000020 |
| H | 2.137525 | -2.477441 | 0.000196 |
| H | 3.130875 | 1.726904 | -0.000223 |
| H | 3.847528 | -0.664183 | -0.000045 |

A

| | | | |
|---|---|---|---|
| N | 0.927529 | 0.091478 | 1.135963 |
| H | 0.833099 | 0.417827 | 2.094096 |
| C | 2.283661 | -0.098205 | 0.763224 |
| C | 3.250415 | -0.362880 | 1.752174 |
| C | 2.709094 | 0.028255 | -0.566960 |
| C | 4.593779 | -0.504388 | 1.419055 |
| H | 2.937349 | -0.458504 | 2.795731 |
| C | 4.055258 | -0.136618 | -0.913501 |
| H | 1.986288 | 0.289811 | -1.339992 |
| C | 5.011101 | -0.405735 | 0.079335 |
| H | 5.344496 | -0.706466 | 2.186560 |
| H | 4.344891 | -0.033942 | -1.959565 |
| C | -0.141284 | -0.749921 | 0.761648 |
| C | -1.310685 | -0.731109 | 1.540980 |
| C | -0.131174 | -1.557036 | -0.391033 |
| C | -2.446095 | -1.458930 | 1.179008 |
| H | -1.340851 | -0.112986 | 2.442961 |
| C | -1.262991 | -2.284178 | -0.756384 |
| H | 0.757615 | -1.614971 | -1.018274 |
| C | -2.439073 | -2.230375 | 0.007314 |
| H | -3.333757 | -1.395024 | 1.808258 |
| H | -1.257035 | -2.897003 | -1.660931 |
| O | 6.337006 | -0.577030 | -0.150013 |
| O | -3.504091 | -2.935472 | -0.463589 |
| C | -4.714826 | -2.912916 | 0.267733 |
| H | -5.124121 | -1.890549 | 0.356614 |
| H | -5.430422 | -3.533628 | -0.289926 |
| H | -4.592618 | -3.336015 | 1.281737 |
| C | 6.826009 | -0.490669 | -1.476559 |
| H | 6.369684 | -1.253106 | -2.133433 |
| H | 6.652342 | 0.508618 | -1.915168 |
| H | 7.908823 | -0.670931 | -1.422769 |
| O | -0.112073 | 3.201453 | 1.334708 |
| C | 0.284966 | 2.651623 | 0.333796 |
| H | 1.361012 | 2.640202 | 0.038639 |
| C | -0.572836 | 1.982079 | -0.756127 |
| O | 0.035540 | 1.646536 | -1.761589 |
| C | -2.030854 | 1.738134 | -0.598350 |
| C | -2.799750 | 2.259160 | 0.461303 |
| C | -2.653406 | 0.916577 | -1.559736 |
| C | -4.160249 | 1.958244 | 0.550776 |
| H | -2.327778 | 2.891015 | 1.210912 |
| C | -4.007796 | 0.609628 | -1.459682 |
| H | -2.048732 | 0.509995 | -2.371610 |
| C | -4.764975 | 1.131182 | -0.402531 |
| H | -4.751317 | 2.367376 | 1.373974 |
| H | -4.474172 | -0.047757 | -2.197384 |
| H | -5.828294 | 0.890259 | -0.321191 |

TSA

| | | | |
|---|---|---|---|
| N | 0.811211 | -0.502851 | -0.840396 |
| H | 0.499233 | -1.059189 | -1.901861 |
| C | 2.204412 | -0.217712 | -0.567387 |
| C | 2.956380 | 0.456228 | -1.540099 |
| C | 2.804242 | -0.600893 | 0.633906 |
| C | 4.296960 | 0.741167 | -1.308440 |
| H | 2.482016 | 0.754899 | -2.477878 |
| C | 4.154611 | -0.319865 | 0.871982 |
| H | 2.211056 | -1.119023 | 1.390326 |

| | | | |
|---|---|---|---|
| C | 4.910945 | 0.355064 | -0.100636 |
| H | 4.898761 | 1.261359 | -2.056734 |
| H | 4.600217 | -0.630905 | 1.816679 |
| C | -0.131640 | 0.560567 | -0.513798 |
| C | -1.165550 | 0.837921 | -1.410142 |
| C | -0.086281 | 1.224523 | 0.720457 |
| C | -2.169263 | 1.752987 | -1.080278 |
| H | -1.204564 | 0.315443 | -2.367160 |
| C | -1.078679 | 2.137937 | 1.054598 |
| H | 0.715938 | 1.013850 | 1.428626 |
| C | -2.139319 | 2.400622 | 0.165682 |
| H | -2.969103 | 1.941932 | -1.795631 |
| H | -1.063047 | 2.656259 | 2.015632 |
| O | 6.219005 | 0.673418 | 0.028893 |
| O | -3.068642 | 3.283417 | 0.593023 |
| C | -4.203498 | 3.544601 | -0.217776 |
| H | -4.784666 | 2.625482 | -0.410694 |
| H | -4.829142 | 4.252911 | 0.342542 |
| H | -3.921363 | 4.002819 | -1.182175 |
| C | 6.907468 | 0.316108 | 1.216271 |
| H | 6.466246 | 0.799105 | 2.106290 |
| H | 6.919271 | -0.777764 | 1.369379 |
| H | 7.940616 | 0.669685 | 1.094816 |
| O | -0.121565 | -2.246527 | -1.798921 |
| C | 0.279512 | -1.984558 | -0.542404 |
| H | 1.162723 | -2.546219 | -0.169790 |
| C | -0.703210 | -1.923815 | 0.653590 |
| O | -0.202674 | -1.925562 | 1.768783 |
| C | -2.173539 | -1.781417 | 0.463794 |
| C | -2.839388 | -2.159106 | -0.717957 |
| C | -2.911376 | -1.213473 | 1.521595 |
| C | -4.218352 | -1.965905 | -0.833137 |
| H | -2.256257 | -2.586972 | -1.531736 |
| C | -4.283609 | -1.006258 | 1.393955 |
| H | -2.384879 | -0.922571 | 2.432527 |
| C | -4.940126 | -1.383404 | 0.214459 |
| H | -4.732288 | -2.266179 | -1.750055 |
| H | -4.845385 | -0.548216 | 2.212103 |
| H | -6.017030 | -1.222630 | 0.113933 |

B

| | | | |
|---|---|---|---|
| N | 0.362760 | -1.650016 | 0.783084 |
| H | 0.293614 | -1.772334 | 1.788503 |
| C | 1.656436 | -1.383800 | 0.314956 |
| C | 2.623995 | -0.904148 | 1.214613 |
| C | 2.055492 | -1.623438 | -1.016521 |
| C | 3.940058 | -0.656263 | 0.812358 |
| H | 2.337542 | -0.714613 | 2.252420 |
| C | 3.358808 | -1.357379 | -1.426927 |
| H | 1.346212 | -2.036684 | -1.734708 |
| C | 4.317532 | -0.867679 | -0.523401 |
| H | 4.654828 | -0.286136 | 1.547804 |
| H | 3.663156 | -1.540351 | -2.460248 |
| C | -0.858121 | -1.478741 | 0.139624 |
| C | -2.025196 | -1.970549 | 0.764673 |
| C | -1.016709 | -0.782976 | -1.081941 |
| C | -3.294081 | -1.778560 | 0.212025 |
| H | -1.930458 | -2.517907 | 1.706150 |
| C | -2.276055 | -0.599722 | -1.635564 |
| H | -0.153304 | -0.342201 | -1.578203 |
| C | -3.434059 | -1.079720 | -0.994664 |
| H | -4.163073 | -2.163500 | 0.745407 |
| H | -2.392414 | -0.040970 | -2.566895 |
| O | 5.561043 | -0.641522 | -1.023703 |
| O | -4.614530 | -0.823621 | -1.612416 |
| C | -5.819464 | -1.165148 | -0.952848 |
| H | -5.916733 | -2.256240 | -0.805925 |
| H | -5.902244 | -0.663270 | 0.028234 |
| H | -6.639559 | -0.822116 | -1.599263 |
| C | 6.567335 | -0.144588 | -0.162014 |
| H | 6.300266 | 0.842200 | 0.258499 |
| H | 6.778492 | -0.840245 | 0.670587 |
| H | 7.476011 | -0.035463 | -0.770723 |
| O | -0.541055 | 0.170443 | 2.981590 |
| C | -1.628107 | 0.381275 | 2.490071 |
| H | -2.568356 | -0.050222 | 2.909252 |
| C | -1.950919 | 1.276164 | 1.286506 |
| O | -3.139457 | 1.350052 | 1.006152 |
| C | -0.905639 | 2.008476 | 0.520087 |
| C | -1.336457 | 2.805309 | -0.559740 |
| C | 0.472412 | 1.902794 | 0.786974 |
| C | -0.412471 | 3.470360 | -1.361767 |

| | | | |
|---|---|---|---|
| H | -2.406532 | 2.875471 | -0.763361 |
| C | 1.396344 | 2.565513 | -0.024389 |
| H | 0.818053 | 1.285944 | 1.611847 |
| C | 0.959339 | 3.346827 | -1.098763 |
| H | -0.756754 | 4.081422 | -2.200152 |
| H | 2.464714 | 2.460529 | 0.180089 |
| H | 1.686370 | 3.859949 | -1.733977 |

TSB

| | | | |
|---|---|---|---|
| N | 0.668097 | -1.253963 | 0.931247 |
| H | 0.347432 | -0.764491 | 1.954330 |
| C | 1.969131 | -1.029173 | 0.445996 |
| C | 2.801284 | -0.129791 | 1.131909 |
| C | 2.501709 | -1.731524 | -0.654018 |
| C | 4.115717 | 0.100931 | 0.717501 |
| H | 2.412795 | 0.404139 | 2.001967 |
| C | 3.810177 | -1.508470 | -1.068174 |
| H | 1.893469 | -2.475919 | -1.170959 |
| C | 4.630902 | -0.583979 | -0.395971 |
| H | 4.726288 | 0.814095 | 1.271405 |
| H | 4.227745 | -2.055291 | -1.916600 |
| C | -0.454916 | -1.324815 | 0.224259 |
| C | -1.670940 | -1.498780 | 1.050828 |
| C | -0.593313 | -1.087322 | -1.184167 |
| C | -2.958164 | -1.592688 | 0.343702 |
| H | -1.535904 | -2.320232 | 1.767284 |
| C | -1.833739 | -1.095746 | -1.753430 |
| H | 0.283420 | -0.861533 | -1.789569 |
| C | -3.037542 | -1.353806 | -0.996019 |
| H | -3.843981 | -1.790976 | 0.946641 |
| H | -1.954413 | -0.881467 | -2.818434 |
| O | 5.887014 | -0.433926 | -0.880184 |
| O | -4.167775 | -1.329478 | -1.742992 |
| C | -5.410614 | -1.480867 | -1.078642 |
| H | -5.501951 | -2.475338 | -0.605599 |
| H | -5.550727 | -0.703809 | -0.305748 |
| H | -6.191862 | -1.375826 | -1.843940 |
| C | 6.772044 | 0.469461 | -0.240264 |
| H | 6.390280 | 1.505846 | -0.266911 |
| H | 6.960720 | 0.184043 | 0.810240 |
| H | 7.718768 | 0.425237 | -0.796273 |
| O | -0.446403 | -0.040134 | 2.727623 |
| C | -1.662234 | -0.201790 | 2.216855 |
| H | -2.433816 | -0.576785 | 2.923068 |
| C | -2.317799 | 0.989965 | 1.492694 |
| O | -3.510313 | 1.186839 | 1.664957 |
| C | -1.543035 | 1.804508 | 0.503134 |
| C | -2.259055 | 2.355191 | -0.577215 |
| C | -0.152704 | 2.002859 | 0.576587 |
| C | -1.595208 | 3.059645 | -1.580952 |
| H | -3.338527 | 2.198210 | -0.625826 |
| C | 0.508033 | 2.719635 | -0.424893 |
| H | 0.393979 | 1.594094 | 1.422465 |
| C | -0.207512 | 3.240330 | -1.508262 |
| H | -2.157452 | 3.467408 | -2.425190 |
| H | 1.589208 | 2.866840 | -0.359048 |
| H | 0.314332 | 3.790453 | -2.296019 |

A-HFIP

| | | | |
|---|---|---|---|
| N | 0.131935 | 0.989237 | 0.244262 |
| H | -0.589800 | 0.281225 | 0.374120 |
| C | -0.407478 | 2.294117 | 0.215948 |
| C | 0.305039 | 3.448779 | 0.574044 |
| C | -1.746768 | 2.448147 | -0.210540 |
| C | -0.281163 | 4.718797 | 0.488660 |
| H | 1.327912 | 3.377365 | 0.941356 |
| C | -2.329934 | 3.706088 | -0.291924 |
| H | -2.335182 | 1.565423 | -0.462020 |
| C | -1.603758 | 4.862243 | 0.046784 |
| H | 0.311745 | 5.586623 | 0.779089 |
| H | -3.366952 | 3.817028 | -0.617450 |
| C | 1.377913 | 0.618214 | 0.800687 |
| C | 2.583340 | 1.226980 | 0.397404 |
| C | 1.446505 | -0.460615 | 1.692275 |
| C | 3.803572 | 0.780839 | 0.889615 |
| H | 2.567670 | 2.031613 | -0.338414 |
| C | 2.674089 | -0.930575 | 2.174147 |
| H | 0.524870 | -0.954041 | 2.006323 |
| C | 3.866472 | -0.308821 | 1.776732 |
| H | 4.738159 | 1.243282 | 0.565399 |
| H | 2.681897 | -1.781876 | 2.854833 |
| O | -2.259506 | 6.045907 | -0.076637 |

| | | | |
|---|---|---|---|
| O | 5.107838 | -0.691595 | 2.169889 |
| C | 5.242696 | -1.809353 | 3.028508 |
| H | 4.839832 | -2.730425 | 2.569316 |
| H | 6.319587 | -1.941778 | 3.203441 |
| H | 4.741523 | -1.646172 | 3.999715 |
| C | -1.588347 | 7.242477 | 0.269761 |
| H | -0.692410 | 7.409055 | -0.355904 |
| H | -2.299049 | 8.062598 | 0.095417 |
| H | -1.286398 | 7.253437 | 1.332954 |
| O | -1.205404 | 0.271860 | -2.519231 |
| C | 0.000927 | 0.294951 | -2.370044 |
| H | 0.592589 | 1.193796 | -2.632294 |
| C | 0.737698 | -0.951230 | -1.854138 |
| O | 0.062601 | -1.829222 | -1.336362 |
| C | 2.210187 | -1.039048 | -1.973825 |
| C | 2.875050 | -2.035477 | -1.231554 |
| C | 2.962749 | -0.166904 | -2.785788 |
| C | 4.261813 | -2.142360 | -1.278641 |
| H | 2.283804 | -2.703498 | -0.603647 |
| C | 4.352161 | -0.289178 | -2.843518 |
| H | 2.476483 | 0.604015 | -3.385045 |
| C | 5.003192 | -1.267500 | -2.084418 |
| H | 4.772041 | -2.901237 | -0.680671 |
| H | 4.930049 | 0.386763 | -3.478262 |
| H | 6.092717 | -1.348653 | -2.118533 |
| C | -2.859821 | -1.929498 | 1.614176 |
| C | -2.617118 | -2.072975 | 0.110537 |
| C | -3.724489 | -2.860905 | -0.604332 |
| H | -1.689719 | -2.656610 | -0.008967 |
| O | -2.529852 | -0.791262 | -0.415081 |
| H | -2.019009 | -0.794856 | -1.255341 |
| F | -3.463393 | -2.879143 | -1.922364 |
| F | -4.934458 | -2.308775 | -0.439992 |
| F | -3.789460 | -4.131564 | -0.180377 |
| F | -2.968952 | -3.124972 | 2.210170 |
| F | -3.966038 | -1.227321 | 1.887725 |
| F | -1.824192 | -1.282268 | 2.180483 |

TSA-HFIP

| | | | |
|---|---|---|---|
| N | 0.894029 | 0.063406 | 0.184532 |
| H | 0.246838 | -0.470026 | -0.437256 |
| C | 1.976862 | -0.864934 | 0.564651 |
| C | 3.058987 | -0.412676 | 1.317640 |
| C | 1.893395 | -2.207592 | 0.179365 |
| C | 4.078071 | -1.295415 | 1.684119 |
| H | 3.126775 | 0.632404 | 1.622504 |
| C | 2.906622 | -3.088916 | 0.540772 |
| H | 1.026768 | -2.557124 | -0.383488 |
| C | 4.009314 | -2.644884 | 1.294077 |
| H | 4.916505 | -0.919105 | 2.269483 |
| H | 2.861522 | -4.140418 | 0.249786 |
| C | 1.358190 | 1.254850 | -0.541628 |
| C | 1.710749 | 2.427875 | 0.134077 |
| C | 1.433508 | 1.193023 | -1.931375 |
| C | 2.144391 | 3.533508 | -0.591354 |
| H | 1.644481 | 2.495467 | 1.220738 |
| C | 1.869902 | 2.298418 | -2.664029 |
| H | 1.137789 | 0.279905 | -2.451784 |
| C | 2.230364 | 3.481626 | -1.994954 |
| H | 2.420242 | 4.460249 | -0.084355 |
| H | 1.917293 | 2.227941 | -3.750306 |
| O | 4.941407 | -3.575090 | 1.591946 |
| O | 2.659988 | 4.605004 | -2.607735 |
| C | 2.762705 | 4.630789 | -4.023497 |
| H | 1.785013 | 4.457881 | -4.506870 |
| H | 3.120192 | 5.634762 | -4.289885 |
| H | 3.485677 | 3.882610 | -4.393746 |
| C | 6.081481 | -3.203977 | 2.351587 |
| H | 5.801546 | -2.830649 | 3.352553 |
| H | 6.686833 | -4.113415 | 2.466849 |
| H | 6.683438 | -2.435496 | 1.835114 |
| O | -0.605749 | -0.830323 | 1.831372 |
| C | -0.074410 | 0.326517 | 1.432541 |
| H | 0.581710 | 0.800038 | 2.183251 |
| C | -1.191264 | 1.278613 | 0.953702 |
| O | -1.517457 | 1.318890 | -0.221064 |
| C | -1.908839 | 2.051456 | 2.005688 |
| C | -2.754735 | 3.099733 | 1.598346 |
| C | -1.768789 | 1.766774 | 3.377281 |
| C | -3.433639 | 3.864535 | 2.545727 |
| H | -2.860907 | 3.304694 | 0.530930 |
| C | -2.459766 | 2.528110 | 4.322283 |

| | | | |
|---|---|---|---|
| H | -1.154055 | 0.927020 | 3.705153 |
| C | -3.285772 | 3.579997 | 3.909685 |
| H | -4.081042 | 4.684278 | 2.224059 |
| H | -2.357101 | 2.296807 | 5.385433 |
| H | -3.819761 | 4.177781 | 4.653123 |
| C | -2.024780 | -1.569037 | -2.446142 |
| C | -2.285163 | -1.623554 | -0.935930 |
| C | -3.274367 | -2.735784 | -0.557002 |
| H | -2.799726 | -0.672701 | -0.691741 |
| O | -1.090200 | -1.811783 | -0.296181 |
| H | -1.003629 | -1.392473 | 0.809921 |
| F | -3.457022 | -2.731387 | 0.775151 |
| F | -2.834931 | -3.958108 | -0.897015 |
| F | -4.481485 | -2.566888 | -1.128214 |
| F | -3.150754 | -1.378089 | -3.155104 |
| F | -1.441899 | -2.689278 | -2.904545 |
| F | -1.194644 | -0.547601 | -2.729349 |

B-HFIP

| | | | |
|---|---|---|---|
| N | 0.054672 | -0.276880 | -1.348403 |
| H | 0.731963 | -1.030624 | -1.399381 |
| C | 0.596442 | 1.017901 | -1.297602 |
| C | 1.844408 | 1.265843 | -1.893421 |
| C | -0.030806 | 2.076054 | -0.609505 |
| C | 2.455081 | 2.522586 | -1.811134 |
| H | 2.353680 | 0.460844 | -2.426834 |
| C | 0.560061 | 3.332538 | -0.545112 |
| H | -0.973202 | 1.905229 | -0.092792 |
| C | 1.809821 | 3.575324 | -1.143854 |
| H | 3.427583 | 2.666548 | -2.282599 |
| H | 0.070190 | 4.147702 | -0.007305 |
| C | -1.266929 | -0.673373 | -1.442091 |
| C | -1.574773 | -2.041858 | -1.256076 |
| C | -2.339710 | 0.204894 | -1.730617 |
| C | -2.881572 | -2.521092 | -1.357077 |
| H | -0.761275 | -2.740522 | -1.043183 |
| C | -3.640474 | -0.271110 | -1.810486 |
| H | -2.152488 | 1.263092 | -1.908735 |
| C | -3.937060 | -1.632599 | -1.606837 |
| H | -3.064802 | -3.583630 | -1.198958 |
| H | -4.465064 | 0.412464 | -2.024302 |
| O | 2.304470 | 4.833417 | -1.018572 |
| O | -5.245128 | -1.980324 | -1.680615 |
| C | -5.620527 | -3.300204 | -1.330964 |
| H | -6.717268 | -3.340630 | -1.389864 |
| H | -5.200926 | -4.048009 | -2.028130 |
| H | -5.305713 | -3.551359 | -0.302521 |
| C | 3.558249 | 5.140313 | -1.600410 |
| H | 4.372923 | 4.531542 | -1.167859 |
| H | 3.549536 | 4.997077 | -2.696142 |
| H | 3.753656 | 6.199726 | -1.382780 |
| O | -0.313155 | -0.633225 | 1.531523 |
| C | -1.377432 | -1.233987 | 1.518184 |
| H | -1.430837 | -2.343477 | 1.516454 |
| C | -2.762384 | -0.605419 | 1.524540 |
| O | -3.694335 | -1.379822 | 1.350266 |
| C | -2.967179 | 0.855346 | 1.715985 |
| C | -2.003712 | 1.704159 | 2.293473 |
| C | -4.210757 | 1.390685 | 1.324582 |
| C | -2.280220 | 3.063450 | 2.461993 |
| H | -1.039552 | 1.306878 | 2.606022 |
| C | -4.475386 | 2.749423 | 1.480047 |
| H | -4.953851 | 0.721463 | 0.887240 |
| C | -3.508584 | 3.589981 | 2.049196 |
| H | -1.528188 | 3.715380 | 2.913388 |
| H | -5.437023 | 3.158326 | 1.159670 |
| H | -3.716045 | 4.656123 | 2.173540 |
| C | 3.661699 | -1.474830 | 1.833195 |
| C | 2.867238 | -1.401551 | 0.520349 |
| C | 3.642064 | -1.957165 | -0.676723 |
| H | 2.714071 | -0.326141 | 0.316128 |
| O | 1.692133 | -2.130337 | 0.629117 |
| H | 1.000969 | -1.562559 | 1.052626 |
| F | 2.900994 | -1.822812 | -1.796180 |
| F | 3.924827 | -3.257882 | -0.542189 |
| F | 4.792159 | -1.299277 | -0.873431 |
| F | 3.998446 | -2.730413 | 2.157323 |
| F | 2.900400 | -0.989479 | 2.828264 |
| F | 4.786700 | -0.745340 | 1.783276 |

TSB-HFIP

| | | | |
|---|---|---|---|
| N | -0.186818 | 0.433159 | -0.864886 |

| | | | |
|---|---|---|---|
| H | 0.806173 | 0.280750 | -0.606203 |
| C | -0.620013 | 1.780129 | -0.824218 |
| C | 0.277674 | 2.777393 | -1.228276 |
| C | -1.882780 | 2.155750 | -0.329577 |
| C | -0.074482 | 4.127421 | -1.169129 |
| H | 1.266519 | 2.493431 | -1.592679 |
| C | -2.241041 | 3.496659 | -0.276886 |
| H | -2.573558 | 1.401759 | 0.046375 |
| C | -1.346374 | 4.498779 | -0.699078 |
| H | 0.648484 | 4.876124 | -1.492735 |
| H | -3.215395 | 3.796154 | 0.114877 |
| C | -0.884469 | -0.666493 | -1.156671 |
| C | -0.284783 | -1.962908 | -0.807219 |
| C | -2.193544 | -0.659553 | -1.729353 |
| C | -0.907866 | -3.168973 | -1.341598 |
| H | 0.809289 | -1.964349 | -0.885341 |
| C | -2.788858 | -1.841265 | -2.083225 |
| H | -2.697589 | 0.281549 | -1.942375 |
| C | -2.154155 | -3.118436 | -1.901585 |
| H | -0.382020 | -4.111244 | -1.191587 |
| H | -3.777286 | -1.836248 | -2.549654 |
| O | -1.789087 | 5.771959 | -0.605255 |
| O | -2.879658 | -4.169495 | -2.345895 |
| C | -2.366050 | -5.474426 | -2.134792 |
| H | -3.120950 | -6.174896 | -2.517298 |
| H | -1.419267 | -5.632877 | -2.681917 |
| H | -2.198458 | -5.670096 | -1.060846 |
| C | -0.938304 | 6.835994 | -1.001765 |
| H | -0.014308 | 6.866661 | -0.397596 |
| H | -0.668154 | 6.766156 | -2.070365 |
| H | -1.503262 | 7.763594 | -0.836313 |
| O | 0.375260 | -0.984151 | 1.484855 |
| C | -0.306567 | -2.005305 | 1.000851 |
| H | 0.144725 | -3.010115 | 1.120362 |
| C | -1.789995 | -2.094613 | 1.358855 |
| O | -2.354575 | -3.165938 | 1.199793 |
| C | -2.562742 | -0.886385 | 1.800369 |
| C | -2.015049 | 0.159208 | 2.565961 |
| C | -3.927975 | -0.839979 | 1.454907 |
| C | -2.820543 | 1.228654 | 2.969384 |
| H | -0.962034 | 0.128351 | 2.835049 |
| C | -4.720107 | 0.242318 | 1.834789 |
| H | -4.350367 | -1.660782 | 0.871982 |
| C | -4.167081 | 1.279892 | 2.597945 |
| H | -2.387281 | 2.033800 | 3.568207 |
| H | -5.772716 | 0.277533 | 1.542044 |
| H | -4.787856 | 2.127159 | 2.901464 |
| C | 4.280896 | -1.282148 | 1.087783 |
| C | 3.439562 | -0.094409 | 0.591210 |
| C | 4.167474 | 0.715954 | -0.488979 |
| H | 3.351573 | 0.588315 | 1.463403 |
| O | 2.252361 | -0.545614 | 0.087487 |
| H | 1.401120 | -0.810252 | 0.906811 |
| F | 3.421595 | 1.785100 | -0.829997 |
| F | 4.378744 | 0.005887 | -1.606748 |
| F | 5.357945 | 1.178735 | -0.069495 |
| F | 4.582519 | -2.142597 | 0.101865 |
| F | 3.582295 | -1.963953 | 2.012805 |
| F | 5.436787 | -0.898308 | 1.658506 |

TSA0

| | | | |
|---|---|---|---|
| N | 0.404682 | -0.148505 | 0.801797 |
| H | 0.300774 | -0.513265 | 1.993636 |
| C | -0.621503 | 0.797677 | 0.416188 |
| C | -1.634511 | 1.084947 | 1.337449 |
| C | -0.663948 | 1.392164 | -0.853883 |
| C | -2.681792 | 1.948691 | 1.009130 |
| H | -1.606570 | 0.619168 | 2.323925 |
| C | -1.700185 | 2.257534 | -1.187345 |
| H | 0.111256 | 1.182119 | -1.590750 |
| C | -2.722772 | 2.543225 | -0.263538 |
| H | -3.452725 | 2.151542 | 1.752141 |
| H | -1.741037 | 2.727293 | -2.172409 |
| C | 1.747871 | 0.123682 | 0.337980 |
| C | 2.198957 | -0.269773 | -0.931689 |
| C | 2.626977 | 0.779474 | 1.203834 |
| C | 3.508939 | -0.009714 | -1.320260 |
| H | 1.526507 | -0.785433 | -1.618127 |
| C | 3.943405 | 1.049781 | 0.820446 |
| H | 2.275440 | 1.083239 | 2.192640 |
| C | 4.394942 | 0.653469 | -0.450646 |
| H | 3.872739 | -0.315734 | -2.303288 |

| | | | |
|---|---|---|---|
| H | 4.605394 | 1.560647 | 1.519360 |
| O | -3.685534 | 3.394298 | -0.682586 |
| O | 5.645503 | 0.860061 | -0.918066 |
| C | 6.596780 | 1.518317 | -0.096361 |
| H | 6.788680 | 0.958388 | 0.836092 |
| H | 7.526893 | 1.569557 | -0.678764 |
| H | 6.276767 | 2.544253 | 0.158315 |
| C | -4.751052 | 3.726143 | 0.193372 |
| H | -5.334818 | 2.834578 | 0.483354 |
| H | -4.387512 | 4.231392 | 1.105736 |
| H | -5.404117 | 4.415659 | -0.359067 |
| O | -0.163779 | -1.702836 | 2.274404 |
| C | -0.085574 | -1.738743 | 0.923467 |
| C | 1.102908 | -2.640401 | 0.528641 |
| O | 1.079534 | -3.517244 | -0.299758 |
| H | 1.975726 | -2.482153 | 1.207788 |
| C | -1.352469 | -2.002299 | 0.150550 |
| C | -1.372713 | -2.001634 | -1.252849 |
| C | -2.538034 | -2.247683 | 0.854211 |
| C | -2.566048 | -2.233587 | -1.940052 |
| H | -0.453639 | -1.813529 | -1.809715 |
| C | -3.732196 | -2.486680 | 0.167255 |
| H | -2.501265 | -2.247547 | 1.944837 |
| C | -3.749206 | -2.476949 | -1.231234 |
| H | -2.574202 | -2.224003 | -3.033213 |
| H | -4.652717 | -2.677820 | 0.725515 |
| H | -4.682807 | -2.658897 | -1.770540 |

TSB0

| | | | |
|---|---|---|---|
| N | 1.111430 | -0.399282 | -1.004589 |
| H | 0.607717 | -1.326947 | -0.833853 |
| C | 2.502748 | -0.373228 | -0.697903 |
| C | 3.416494 | -0.871727 | -1.640100 |
| C | 2.972772 | 0.065261 | 0.546819 |
| C | 4.775433 | -0.910435 | -1.349108 |
| H | 3.048627 | -1.225606 | -2.606104 |
| C | 4.337668 | 0.033298 | 0.846638 |
| H | 2.258339 | 0.419539 | 1.292846 |
| C | 5.251317 | -0.454570 | -0.104251 |
| H | 5.497029 | -1.292114 | -2.074754 |
| H | 4.673001 | 0.378768 | 1.824566 |
| C | 0.257919 | 0.608551 | -0.803283 |
| C | -1.176045 | 0.269032 | -0.821291 |
| C | 0.663317 | 1.960347 | -0.563412 |
| C | -2.116265 | 1.375389 | -0.621190 |
| H | -1.445022 | -0.340872 | -1.693615 |
| C | -0.274825 | 2.928931 | -0.346767 |
| H | 1.722984 | 2.214844 | -0.574868 |
| C | -1.684662 | 2.640769 | -0.339869 |
| H | -3.176943 | 1.148613 | -0.712172 |
| H | 0.027081 | 3.965609 | -0.176519 |
| O | 6.588095 | -0.530065 | 0.084866 |
| O | -2.471015 | 3.718838 | -0.094232 |
| C | -3.875645 | 3.539011 | -0.096496 |
| H | -4.245204 | 3.220347 | -1.088135 |
| H | -4.192839 | 2.793977 | 0.655567 |
| H | -4.318639 | 4.512829 | 0.153887 |
| C | 7.143143 | -0.102577 | 1.318200 |
| H | 6.755690 | -0.692655 | 2.167630 |
| H | 8.227970 | -0.258863 | 1.241405 |
| H | 6.948075 | 0.968354 | 1.505559 |
| O | -0.543625 | -2.066554 | -0.020011 |
| C | -1.380386 | -1.108572 | 0.317932 |
| C | -0.934589 | -0.633663 | 1.707249 |
| O | -0.173204 | 0.277451 | 1.940236 |
| C | -2.859952 | -1.466326 | 0.241370 |
| C | -3.820813 | -0.810863 | 1.026141 |
| C | -3.268217 | -2.488020 | -0.626005 |
| C | -5.171916 | -1.163052 | 0.934421 |
| H | -3.516369 | -0.013242 | 1.710471 |
| C | -4.618301 | -2.834197 | -0.727977 |
| H | -2.503989 | -3.008849 | -1.207152 |
| C | -5.574659 | -2.172240 | 0.052397 |
| H | -5.911553 | -0.647887 | 1.553415 |
| H | -4.927112 | -3.629266 | -1.412498 |
| H | -6.630395 | -2.446835 | -0.021865 |
| H | -1.267677 | -1.328853 | 2.520352 |

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## 6. Compound similarity heatmap of the isomeric products.

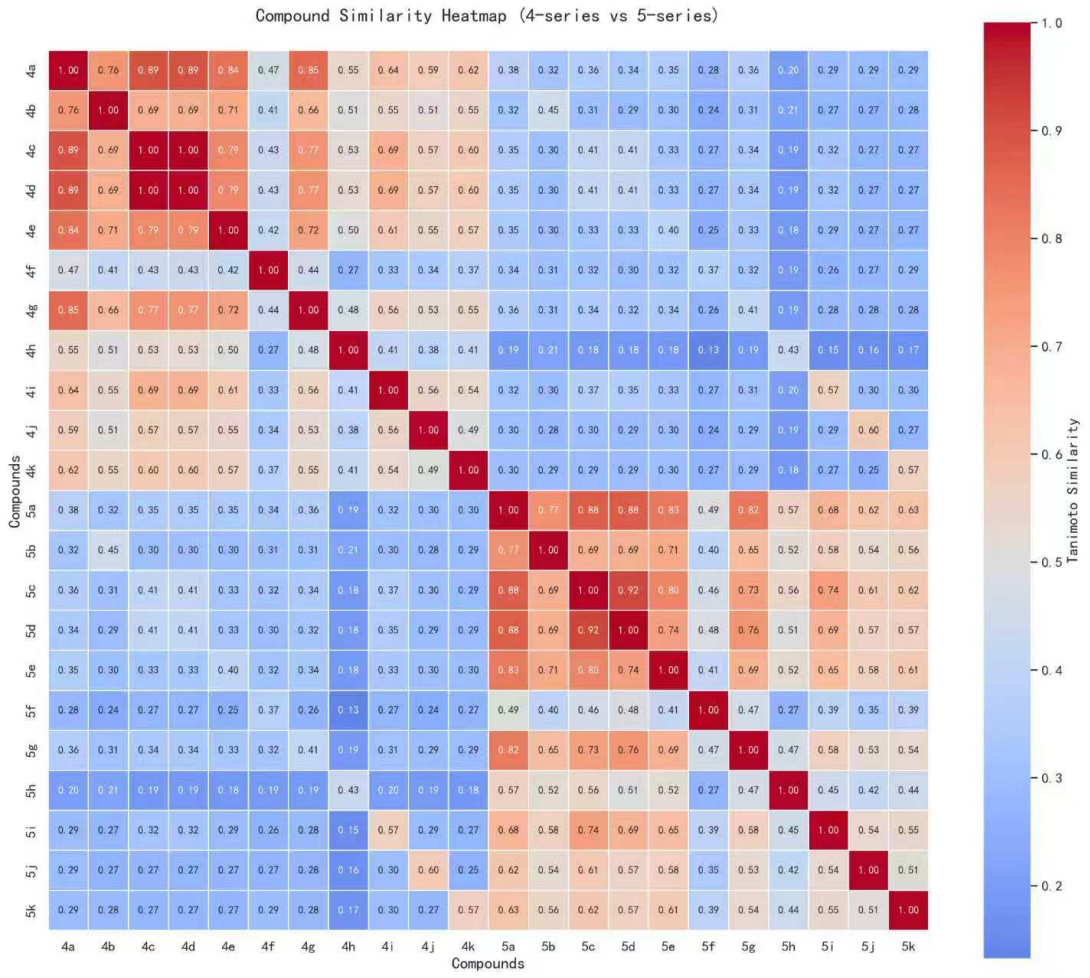



Figure 6.1 Compound similarity heatmap of the isomeric products.

The molecular similarity heatmap reveals two broadly distinct clusters corresponding to the indolo[1,2-a]quinoline series (4a–k) and the 2-acyl-1,4-dihydroquinoline series (5a–k) (Figure 6.1). Compounds within each series generally exhibit higher Tanimoto similarities than compounds from different series, consistent with their shared core scaffolds. The matched constitutional isomer pairs display similarities ranging from approximately 0.37 to 0.60, indicating that changes in core connectivity substantially alter the molecular fingerprints despite identical molecular formulas and closely related peripheral groups. For example, the similarity between 4a and 5a is 0.38, whereas the higher similarities of 4i/5i and 4j/5j (0.57 and 0.60, respectively) are consistent with the greater contribution of their shared peripheral fragments. Within-series variation is also evident, as illustrated by the relatively low similarity between 4f and 4h (0.27). Together, these results illustrate structural diversification through both skeletal disproportionation and peripheral substitution, providing a basis for comparing the biological activities of the paired compound libraries.

## 7. 3D Scatter plot for all the synthetic products.

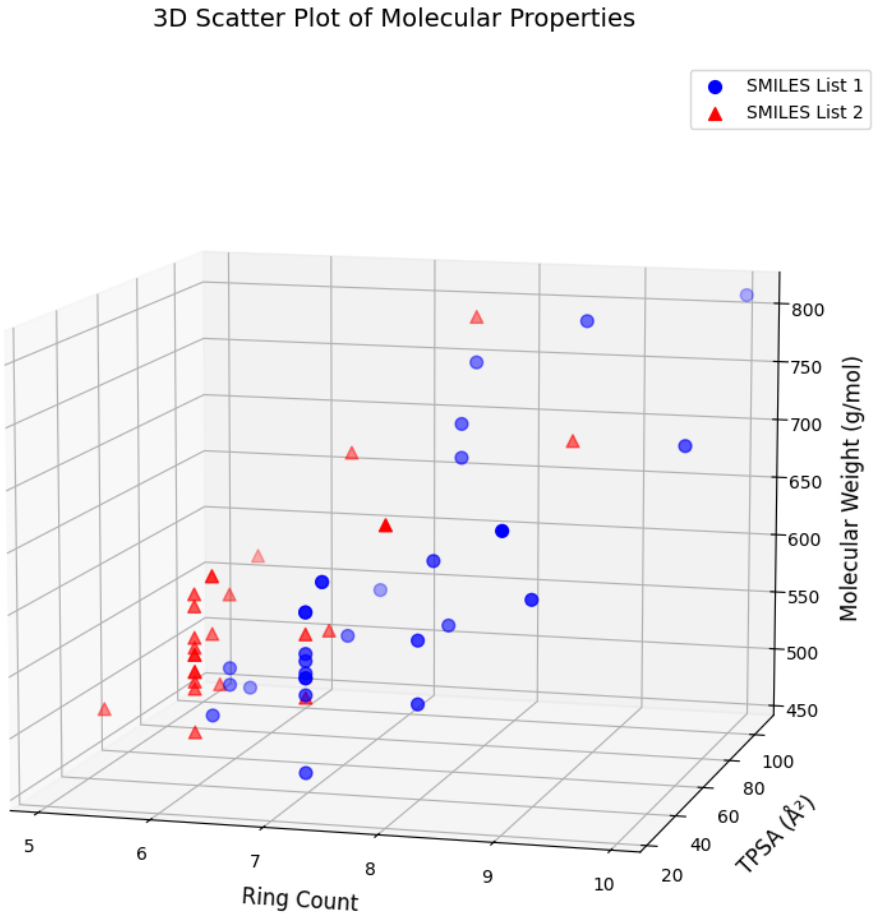



Figure 7.1 3D Scatter plot for all the synthetic products.

A three-dimensional chemical space plot is generated by calculating and mapping the molecular descriptors of compounds (such as bond lengths, bond angles, electronegativity, etc.) onto a high-dimensional space, converting each compound into a point, and using three-dimensional visualisation techniques to present their relative positions and distribution patterns. These plots are primarily used to intuitively compare the similarities and differences in the chemical properties of two compounds, revealing their clustering patterns or dispersion trends within a multidimensional property space. This provides a visual basis for drug molecule design, activity prediction and structure-activity relationship studies, thereby aiding the understanding of their potential chemical behaviour and biological activity.

Findings that can be demonstrated or observed from this plot:
1. Molecular similarities and differences: If two compounds exhibit significant spatial clustering (close proximity) in the plot, this indicates that they are highly similar in key chemical properties and may possess similar biological activities or reactivity; conversely, if they are dispersed or located in different clusters, this suggests significant

differences in their properties, which can serve as a reference for differentiated applications or structural modification design.

2. Localisation of active regions: By combining the distribution of known active molecules, it is possible to identify whether specific regions in the plot are enriched with the target activity, thereby determining whether the two compounds lie within a potential space of pharmacological activity. This provides direction for screening candidate molecules or optimising structures in drug development.

3. Insights into structure-activity relationships: By comparing the coordinate differences between the two compounds in a multidimensional space, one can correlate the patterns of variation in their structural features (such as functional group positions and molecular conformations) with their chemical properties (such as polarity and hydrophilicity), thereby revealing key factors influencing activity and aiding rational drug design.

4. Potential for Multi-Target Action: If the two compounds are distributed in the intersection of multiple distinct activity clusters, this may suggest their potential to regulate multiple biological targets, providing clues for the development of multi-functional drugs or combination therapies.

5. Synthetic feasibility and optimisation pathways: By combining the theoretical distribution of compounds within chemical space, it is possible to assess the scope for both molecules in terms of synthetic feasibility and structural optimisation, thereby guiding experimental design to balance therapeutic efficacy with synthesis costs.

In drug R&D, this diagram assists researchers in rapidly screening candidate molecules similar to lead compounds, whilst simultaneously identifying sites requiring structural modification through spatial distribution differences, thereby accelerating the drug discovery process.

# 8. Antiproliferative activities of isomeric pairs against PANC-1, MDA-MB-231, and MCF-7 cells.

## 8.1. Cell culture and antiproliferative activity assay

The human pancreatic carcinoma cell line (PANC-1) and the human breast adenocarcinoma cell lines (MCF-7 and MDA-MB-231) were purchased from Wuhan Servicebio Technology Co., Ltd. (Wuhan, China). All cells were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and 1% antibiotics (penicillin/streptomycin). Cells were maintained at 37 °C in a humidified incubator with 5% $CO_2$. When cells reached approximately 80-90% confluence, they were subcultured during the logarithmic growth phase. Cells were detached using 0.25% trypsin-EDTA solution, and the digestion was terminated by the addition of complete DMEM medium.

The antiproliferative activities of **4a-k** and **5a-k** was evaluated using the Cell Counting Kit-8 (CCK-8) assay. PANC-1, MCF-7, and MDA-MB-231 cells were seeded in 96-well plates at a density of $5\times10^3$ cells per well and allowed to attach for 24 h. The cells were then treated with increasing concentrations of **4a-k** and **5a-k** for 72 h. After treatment, the culture medium was removed, and 100 μL of fresh complete DMEM containing 10% (v/v) CCK-8 reagent was added to each well. After incubation at 37°Cfor 2 h, the absorbance was measured at 450 nm using a microplate reader. Cell viability was calculated according to:

$$\text{Cell viability (\%)} = \frac{\mathrm{OD_{sample}} - \mathrm{OD_{blank}}}{\mathrm{OD_{control}} - \mathrm{OD_{blank}}} \times 100\%$$

where $OD_{sample}$ represents the absorbance of cells treated with **4a-k** and **5a-k**; $OD_{control}$ represents the absorbance of untreated control cells; and $OD_{blank}$ represents the absorbance of the corresponding cell-free blank.

Dose–response curves based on cell viability following treatment with different concentrations of each compound were fitted using GraphPad Prism 10.0 software (GraphPad Software, San Diego, CA, USA), and the half-maximal inhibitory concentration ($IC_{50}$) values were calculated. The resulting $IC_{50}$ values are presented in Table 8.1.

## 8.2. Calculation of molecular descriptors and QED values

The molecular descriptors and quantitative estimate of drug-likeness (QED) values of the synthesized compounds were calculated using the RDKit cheminformatics toolkit (Release_2025.09.4) in Python[1, 2]. The molecular structures were provided as simplified molecular input line entry system (SMILES) strings and converted into RDKit molecular objects. As shown in Table 8.2, molecular formula, molecular weight (MW), octanol–water partition coefficient (logP), numbers of hydrogen-bond donors (HBD) and acceptors (HBA), topological polar surface area (TPSA), number of rotatable bonds (ROTB), number of aromatic rings (AROM), and number of structural alerts (ALERTS) were calculated. The overall QED score was subsequently determined using the default

average-weighted QED algorithm implemented in RDKit.

### 8.3. Visualization of antiproliferative activity

The $IC_{50}$ values were converted into reverse min–max normalized activity scores ranging from 1 to 5 using $S = 1 + [(50 - IC_{50})/(50 - 3)] \times 4$. Under this transformation, lower $IC_{50}$ values corresponded to higher normalized scores. The resulting scores were visualized using a bubble plot with color mapping (Figure 4C), in which both bubble size and color represented antiproliferative potency, thereby facilitating comparison between the isomeric pairs.

The concentration–viability data for the isomeric pairs **4b**/**5b** against MCF-7 cells and **4c**/**5c** against MDA-MB-231 cells are presented in Table 8.3. The corresponding concentration–viability curves were constructed (Figure 4D) to directly compare the concentration-dependent antiproliferative responses of the isomeric pairs in the selected cell lines.

## References

(1) Bickerton, G. R.; Paolini, G. V.; Besnard, J.; Muresan, S.; Hopkins, A. L. Quantifying the Chemical Beauty of Drugs. *Nature Chemistry* **2012**, *4*, 90–98.

(2) Greg Landrum, Paolo Tosco, Brian Kelley, Ricardo Rodriguez, David Cosgrove, Riccardo Vianello, sriniker, Peter Gedeck, Gareth Jones, Dan Nealschneider, Eisuke Kawashima, NadineSchneider, tadhurst-cdd, Andrew Dalke, Niels Maeder, Matt Swain, Brian Cole, Aleksandr Savelev, Samo Turk, … guillaume godin. (2026). rdkit/rdkit: 2025_09_4 (Q3 2025) Release (Versions Release_2025_09_4) [Computer software]. Zenodo.

Table 8.1 Antiproliferative activities of isomeric pairs with $IC_{50}$ values

| **Cell** | **PANC-1** | | **MCF-7** | | **MDA-MB-231** | |
|---|---|---|---|---|---|---|
| **Compounds** [α] | **4** [β] | **5** [β] | **4** [β] | **5** [β] | **4** [β] | **5** [β] |
| **a** | ＞50 | 13.24±0.84 | 15.54±1.33 | 18.72±0.65 | > 50 | 18.74±0.19 |
| **b** | ＞50 | ＞50 | 7.84±0.74 | ＞50 | > 50 | > 50 |
| **c** | ＞50 | ＞50 | 37.43±6.64 | > 50 | 51.26±0.93 | 3.36±0.40 |
| **d** | ＞50 | 6.42±0.18 | > 50 | 18.61±3.48 | > 50 | 10.28±0.99 |
| **e** | ＞50 | 6.83±0.67 | > 50 | 31.33±5.63 | > 50 | 10.67±0.20 |
| **f** | ＞50 | ＞50 | > 50 | > 50 | > 50 | > 50 |
| **g** | ＞50 | ＞50 | > 50 | > 50 | > 50 | > 50 |
| **h** | ＞50 | ＞50 | > 50 | > 50 | > 50 | > 50 |
| **i** | ＞50 | 14.54±1.09 | > 50 | 11.82±0.65 | > 50 | 6.19±0.28 |
| **j** | ＞50 | 8.07±0.43 | > 50 | 22.32±0.59 | > 50 | 5.15±0.07 |
| **k** | ＞50 | ＞50 | > 50 | > 50 | > 50 | 46.27±1.36 |

[α] Compound identities are defined by combining the column number and row letter, corresponding to compounds 4a–4k and 5a–5k. [β] $IC_{50}$ values are expressed in μM. The values presented are the mean ± SD of triplicate experiments. [γ] Colchicine was used as the positive control, with an $IC_{50}$ value of <0.1953 μM. Values reported as >50 indicate that the $IC_{50}$ was higher than the highest tested concentration.

Table 8.2 Calculated physicochemical descriptors and quantitative estimate of drug-likeness (QED) values of compounds **4a**–**5k**

| Compound | Formula | MW | logP | HBD | HBA | TPSA | ROTB | AROM | ALERTS | QED |
|---|---|---|---|---|---|---|---|---|---|---|
| 4a | C36H29NO3 | 523.63 | 7.672 | 0 | 4 | 38.77 | 5 | 5 | 0 | 0.237 |
| 5a | C36H29NO3 | 523.63 | 7.957 | 0 | 4 | 38.77 | 7 | 5 | 1 | 0.203 |
| 4b | C37H28F3NO4 | 607.63 | 8.57 | 0 | 5 | 48 | 6 | 5 | 0 | 0.194 |
| 5b | C37H28F3NO4 | 607.63 | 8.855 | 0 | 5 | 48 | 8 | 5 | 1 | 0.165 |
| 4c | C37H31NO3 | 537.66 | 7.98 | 0 | 4 | 38.77 | 5 | 5 | 0 | 0.228 |
| 5c | C37H31NO3 | 537.66 | 8.265 | 0 | 4 | 38.77 | 7 | 5 | 1 | 0.196 |
| 4d | C38H33NO3 | 551.69 | 8.289 | 0 | 4 | 38.77 | 5 | 5 | 0 | 0.22 |
| 5d | C38H33NO3 | 551.69 | 8.574 | 0 | 4 | 38.77 | 7 | 5 | 1 | 0.19 |
| 4e | C40H31NO3 | 573.69 | 8.825 | 0 | 4 | 38.77 | 5 | 6 | 0 | 0.207 |
| 5e | C40H31NO3 | 573.69 | 9.11 | 0 | 4 | 38.77 | 7 | 6 | 1 | 0.179 |
| 4f | C32H29NO4 | 491.59 | 6.724 | 0 | 5 | 48 | 5 | 4 | 0 | 0.31 |
| 5f | C32H29NO4 | 491.59 | 7.153 | 0 | 5 | 48 | 7 | 4 | 1 | 0.257 |
| 4g | C36H27NO3 | 521.62 | 7.652 | 0 | 4 | 38.77 | 3 | 5 | 0 | 0.244 |
| 5g | C36H27NO3 | 521.62 | 7.937 | 0 | 4 | 38.77 | 5 | 5 | 1 | 0.22 |
| 4h | C47H32F3NO | 683.77 | 12.007 | 0 | 2 | 20.31 | 5 | 7 | 0 | 0.18 |
| 5h | C47H32F3NO | 683.77 | 12.292 | 0 | 2 | 20.31 | 7 | 7 | 1 | 0.156 |
| 4i | C47H41NO5 | 699.85 | 10.323 | 0 | 6 | 65.07 | 8 | 6 | 2 | 0.116 |
| 5i | C47H41NO5 | 699.85 | 10.608 | 0 | 6 | 65.07 | 10 | 6 | 3 | 0.081 |
| 4j | C48H47NO5 | 717.91 | 10.291 | 0 | 6 | 65.07 | 9 | 5 | 1 | 0.142 |
| 5j | C48H47NO5 | 717.91 | 10.576 | 0 | 6 | 65.07 | 11 | 5 | 2 | 0.1 |
| 4k | C49H41Cl2NO6 | 810.77 | 11.096 | 0 | 7 | 74.3 | 10 | 6 | 3 | 0.077 |
| 5k | C49H41Cl2NO6 | 810.77 | 11.381 | 0 | 7 | 74.3 | 12 | 6 | 4 | 0.053 |
| Colchicine | C22H25NO6 | 399.44 | 2.872 | 1 | 6 | 83.09 | 5 | 2 | 0 | 0.833 |

Table 8.3 Concentration-dependent effects of compounds **4b**/**5b** and **4c**/**5c** on cell viability.

| **Cell** | **MCF-7 cell viability (%)** | | | | | | **MDA-MB-231 cell viability (%)** | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Concentration (μM)** | **4b** | | | **5b** | | | **4c** | | | **5c** | | |
| 100 | 34.34 | 38.01 | 35.47 | 54.94 | 59.45 | 51.69 | 1.81 | 1.81 | 1.31 | 2.97 | 1.97 | 1.56 |
| 50 | 39.84 | 41.11 | 27.01 | 79.20 | 68.19 | 82.72 | 59.92 | 53.79 | 53.21 | 3.13 | 2.22 | 2.22 |
| 25 | 36.18 | 40.69 | 38.29 | 84.98 | 81.73 | 79.48 | 103.21 | 101.72 | 101.64 | 21.76 | 21.01 | 17.37 |
| 12.5 | 44.64 | 40.13 | 47.74 | 88.93 | 80.47 | 83.15 | 100.65 | 105.95 | 98.66 | 33.60 | 31.61 | 32.52 |
| 6.25 | 53.53 | 51.27 | 47.74 | 88.36 | 91.47 | 87.09 | 102.47 | 101.81 | 100.40 | 38.07 | 35.09 | 34.84 |
| 3.125 | 60.58 | 57.90 | 59.03 | 90.48 | 91.47 | 87.94 | 102.39 | 97.92 | 99.32 | 42.95 | 39.31 | 38.23 |
| 1.5625 | 60.72 | 58.18 | 63.26 | 96.97 | 92.88 | 100.78 | 100.90 | 98.33 | 101.89 | 65.88 | 64.39 | 60.50 |
| 0.78125 | 63.68 | 64.81 | 64.95 | 101.20 | 103.74 | 93.44 | 101.48 | 101.31 | 99.74 | 87.16 | 82.11 | 81.61 |
| 0.39063 | 70.73 | 70.73 | 71.86 | 98.38 | 102.75 | 94.01 | 100.98 | 101.56 | 103.96 | 95.10 | 90.38 | 91.13 |
| 0.19531 | 79.62 | 79.90 | 81.03 | 108.53 | 114.46 | 114.17 | 106.69 | 103.79 | 104.04 | 98.66 | 99.82 | 96.01 |

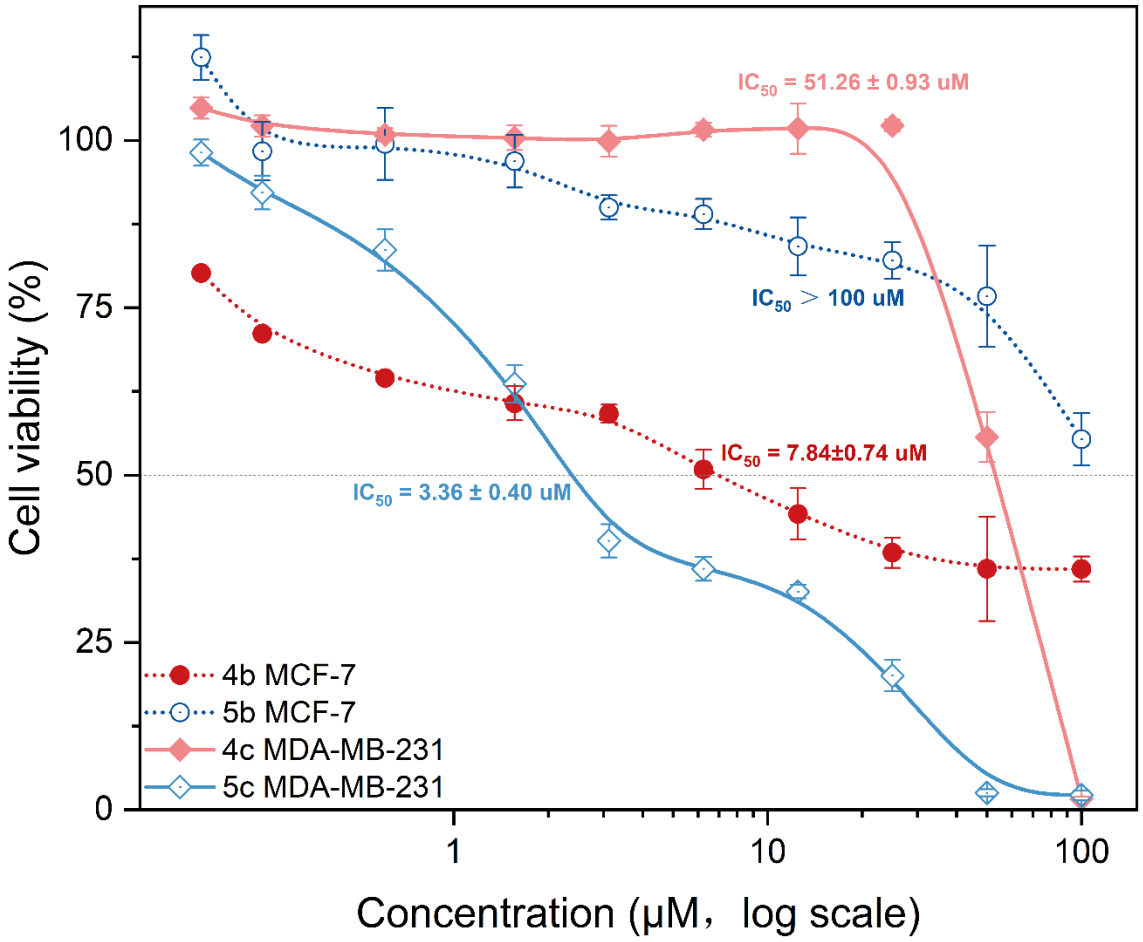
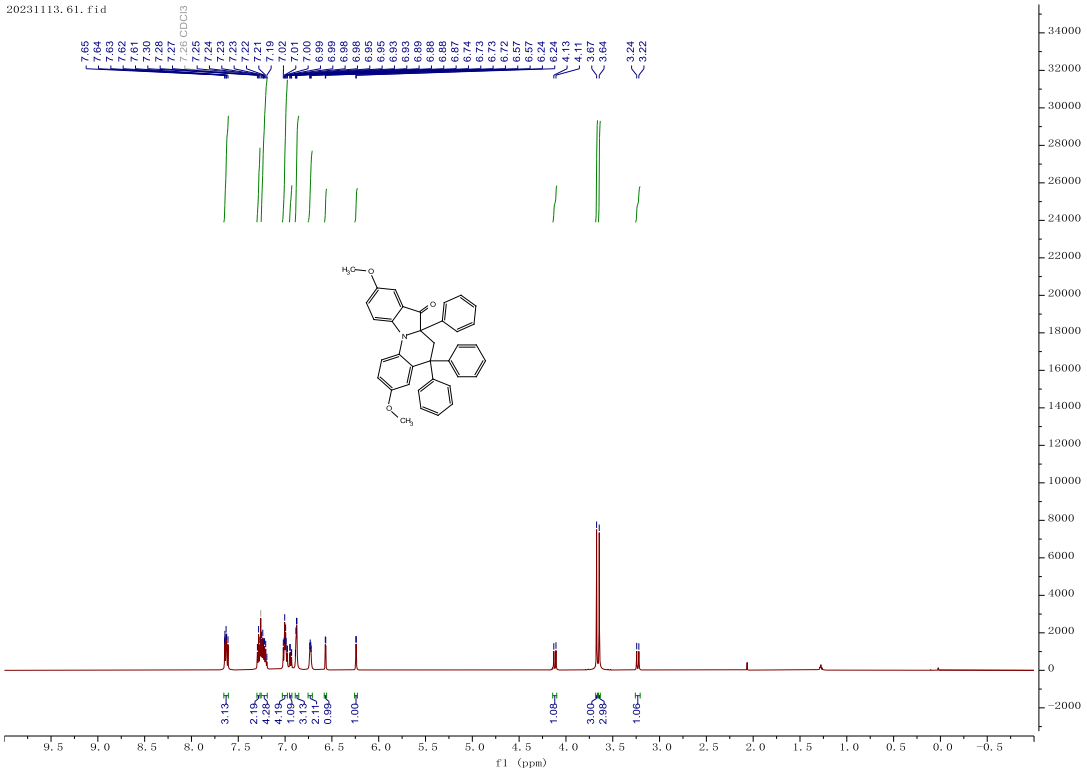


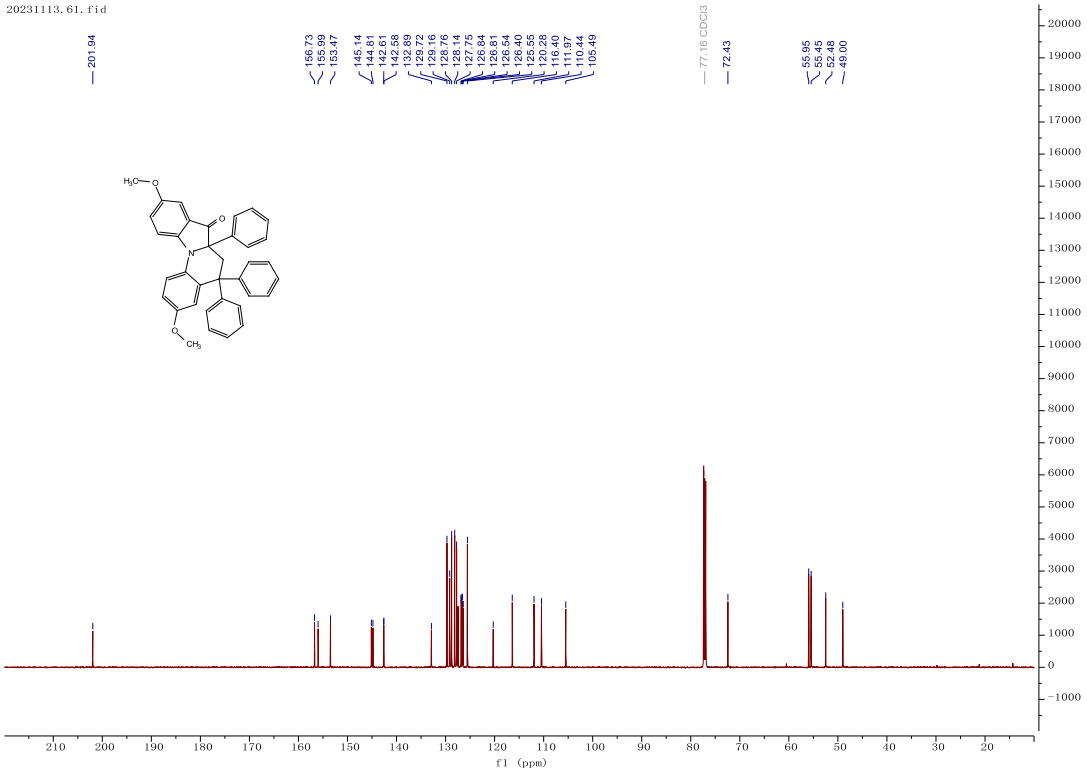

Figure 8.1 Concentration–viability curves for the isomeric pairs **4b**/**5b** against MCF-7 cells and **4c**/**5c** against MDA-MB-231 cells

# 9. Copies of the $^{1}$H, $^{13}$C and $^{19}$F spectra

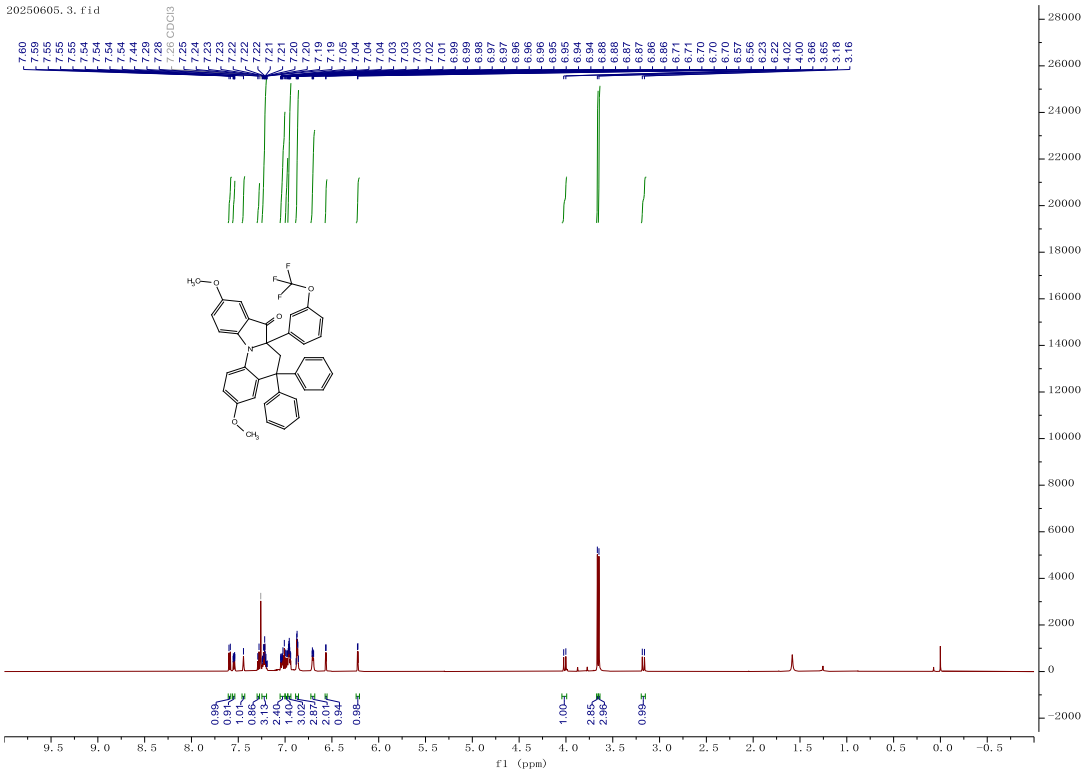
$^{1}$H NMR of compound **4a** (in $CDCl_3$)



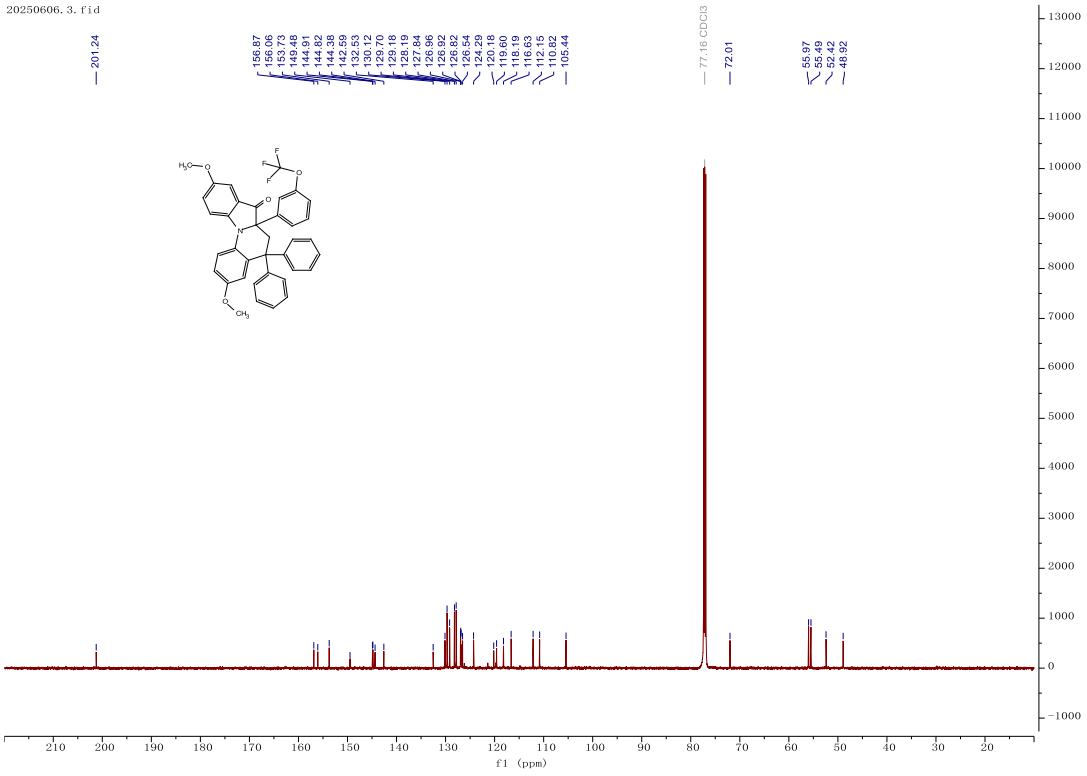

$^{13}$C NMR of compound **4a** (in $CDCl_3$)



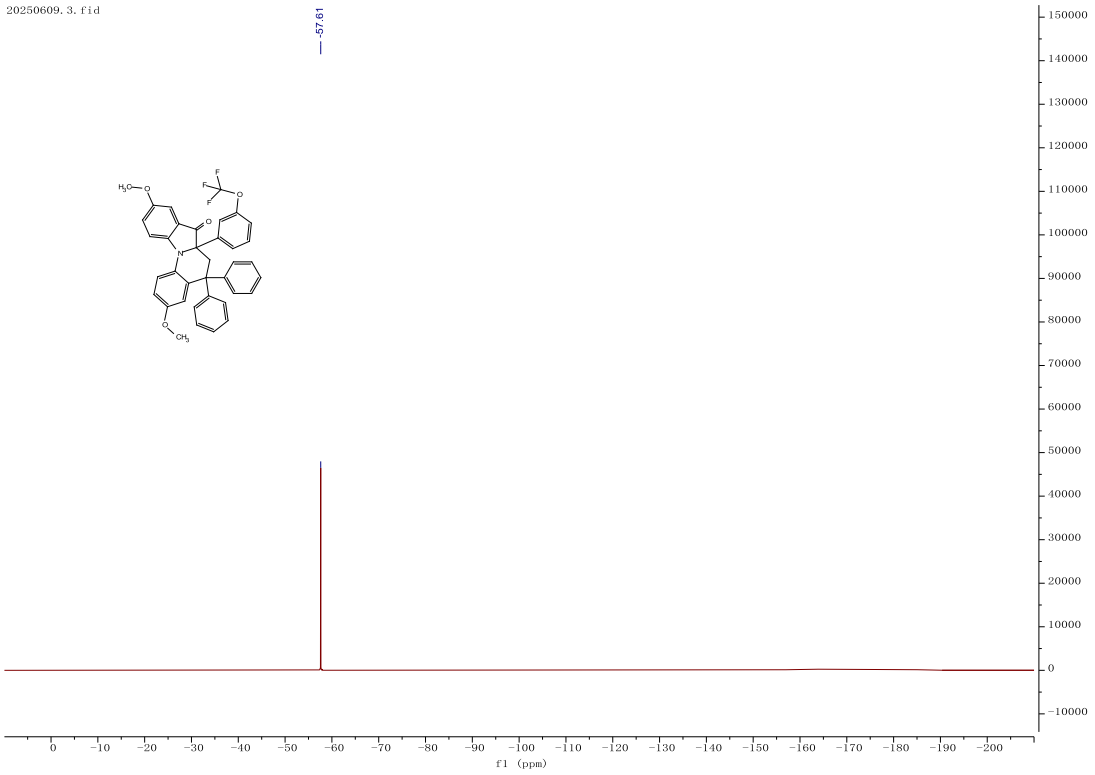

$^{1}$H NMR of compound **4b** (in $CDCl_3$)



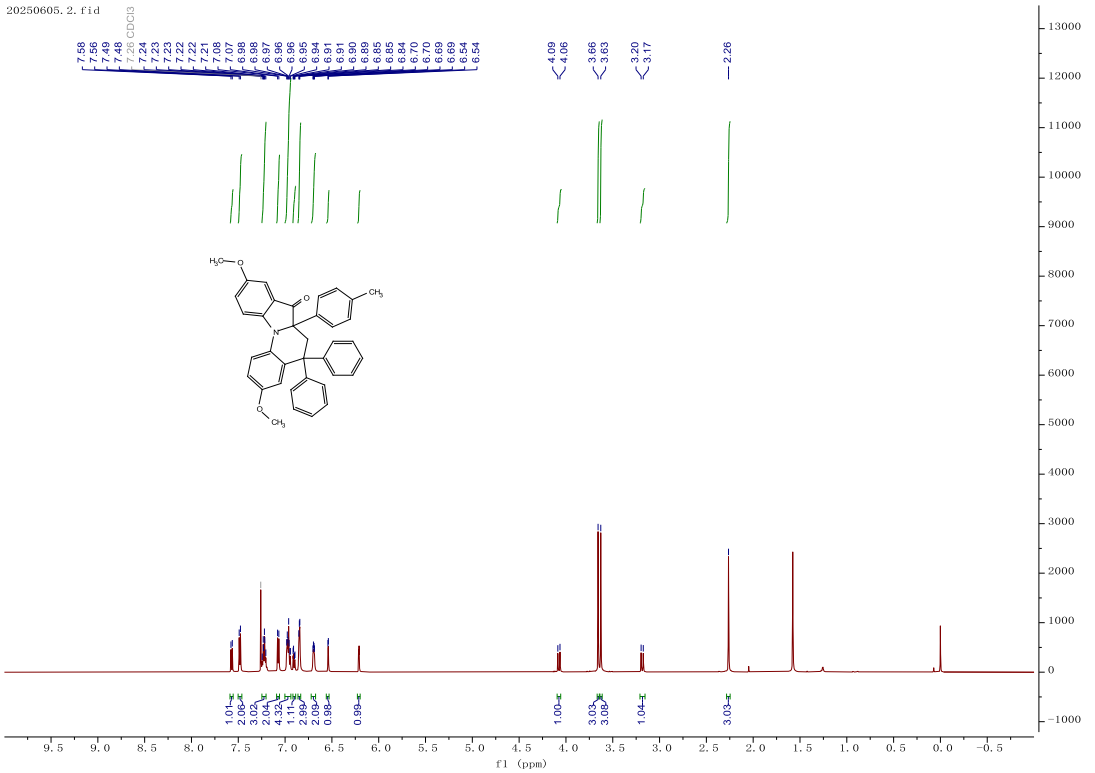

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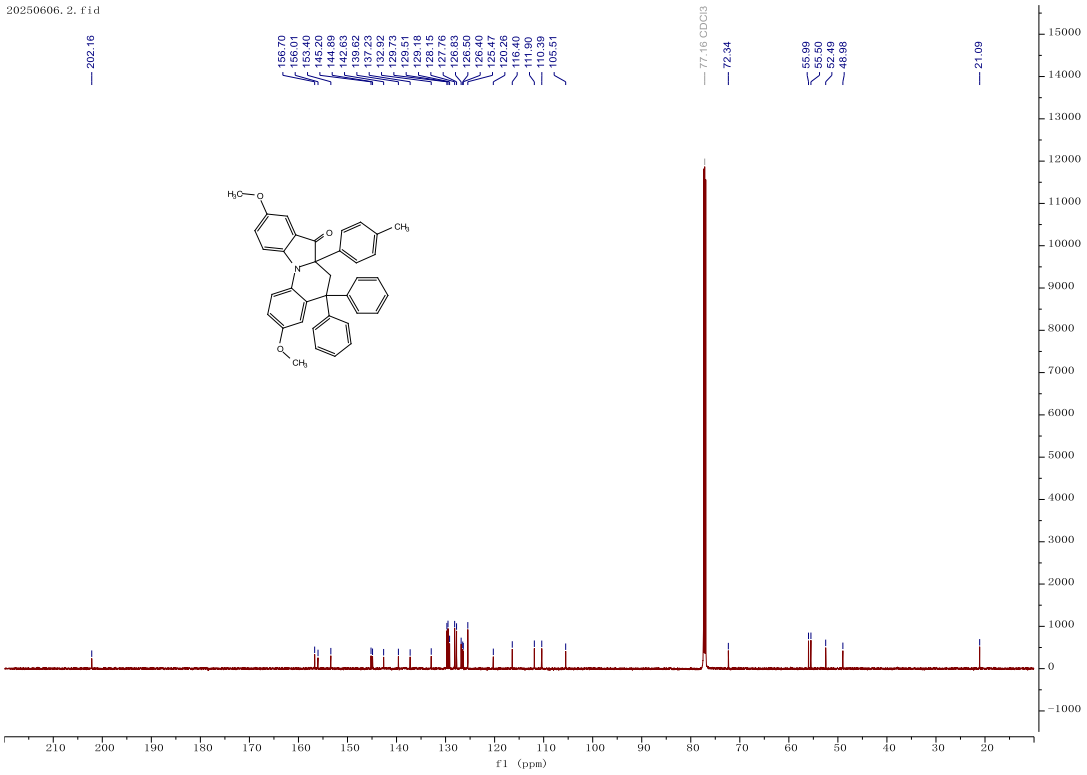

$^{19}$F NMR of compound **4b** (in $CDCl_3$)



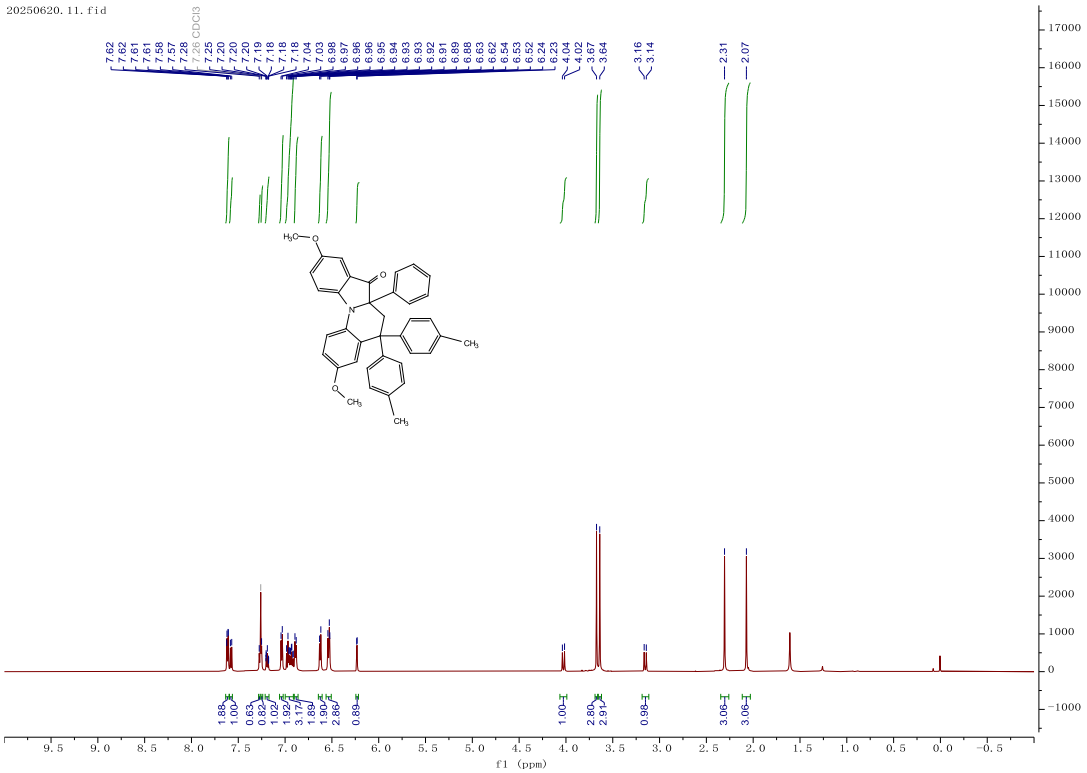

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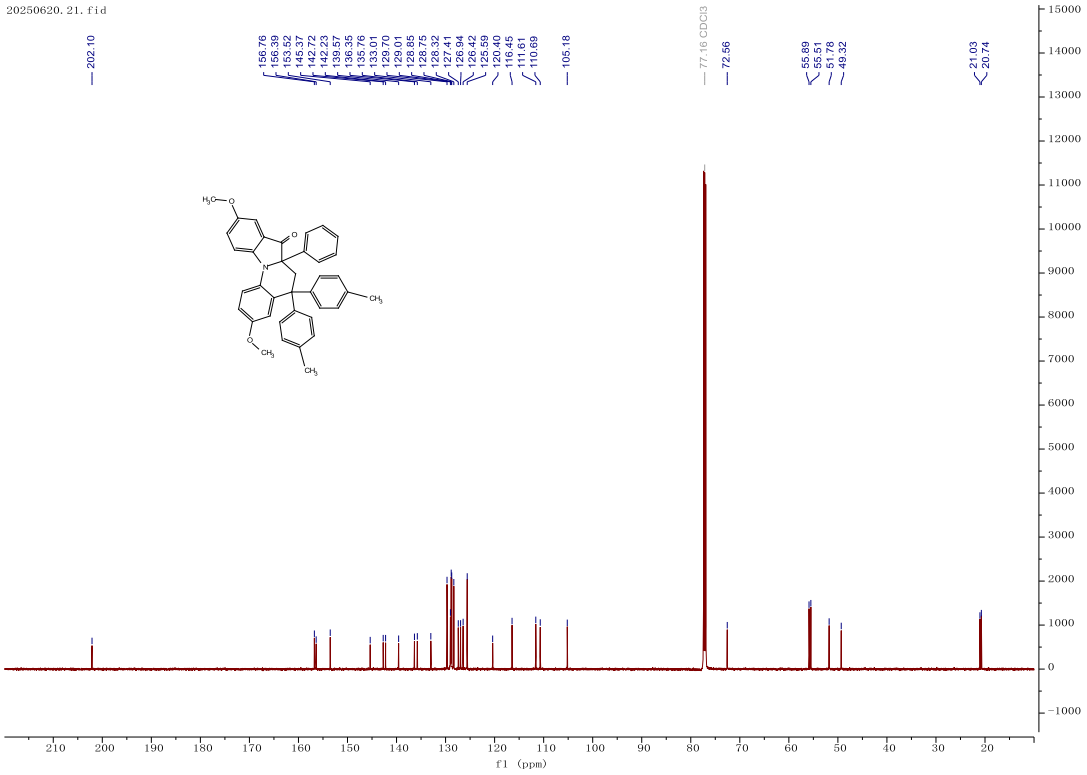

$^{13}$C NMR of compound **4c** (in $CDCl_3$)



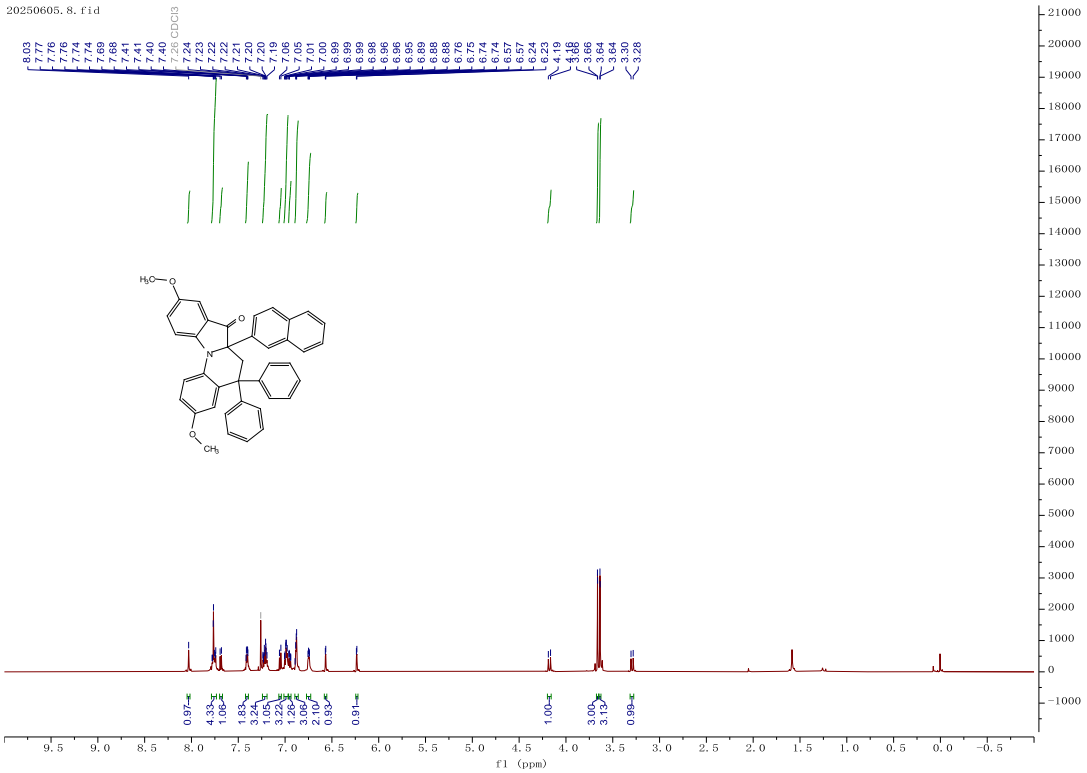

$^{1}$H NMR of compound **4d** (in $CDCl_3$)



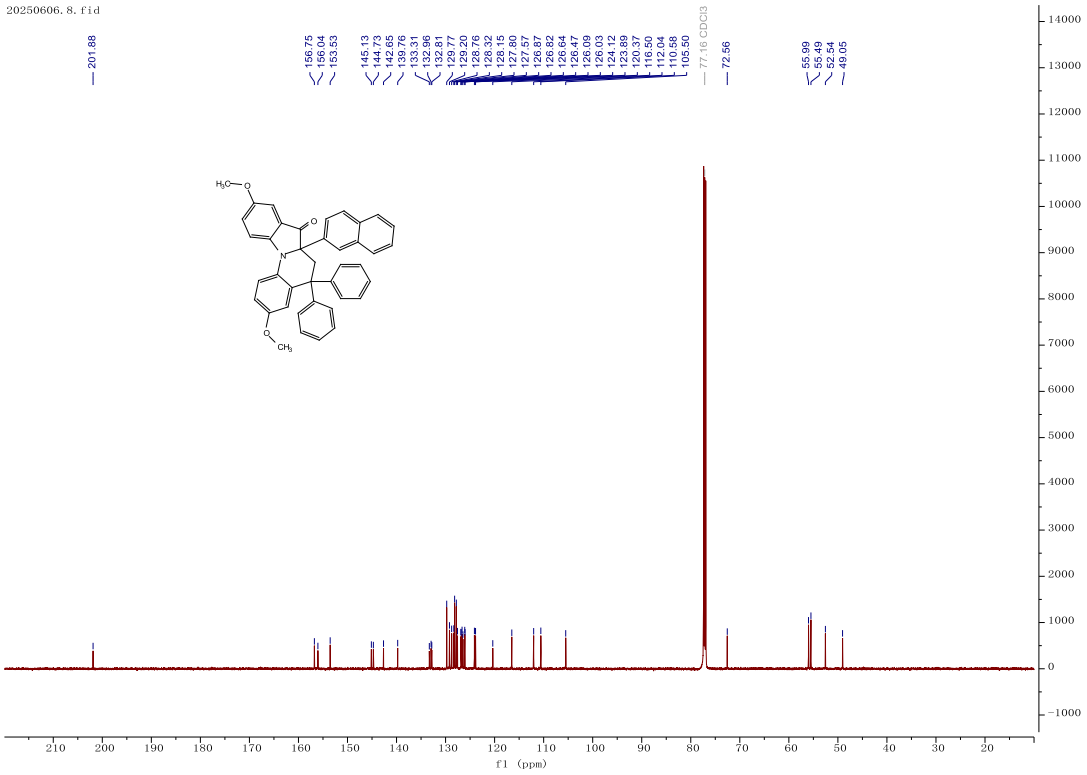

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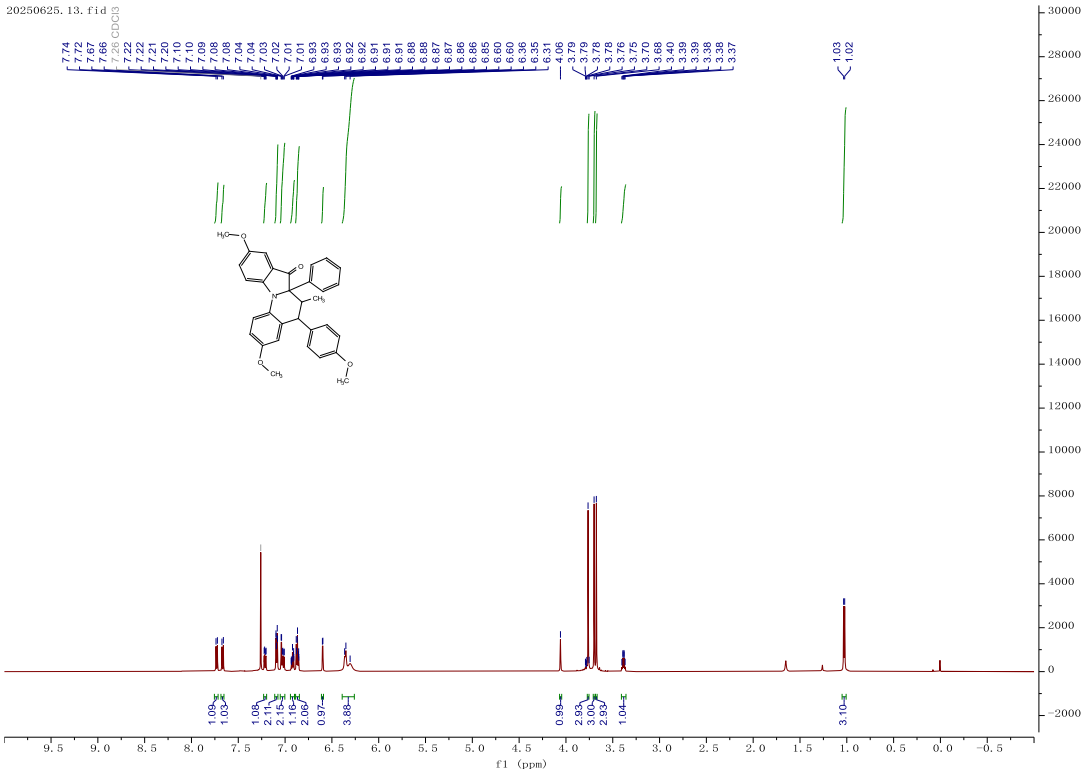

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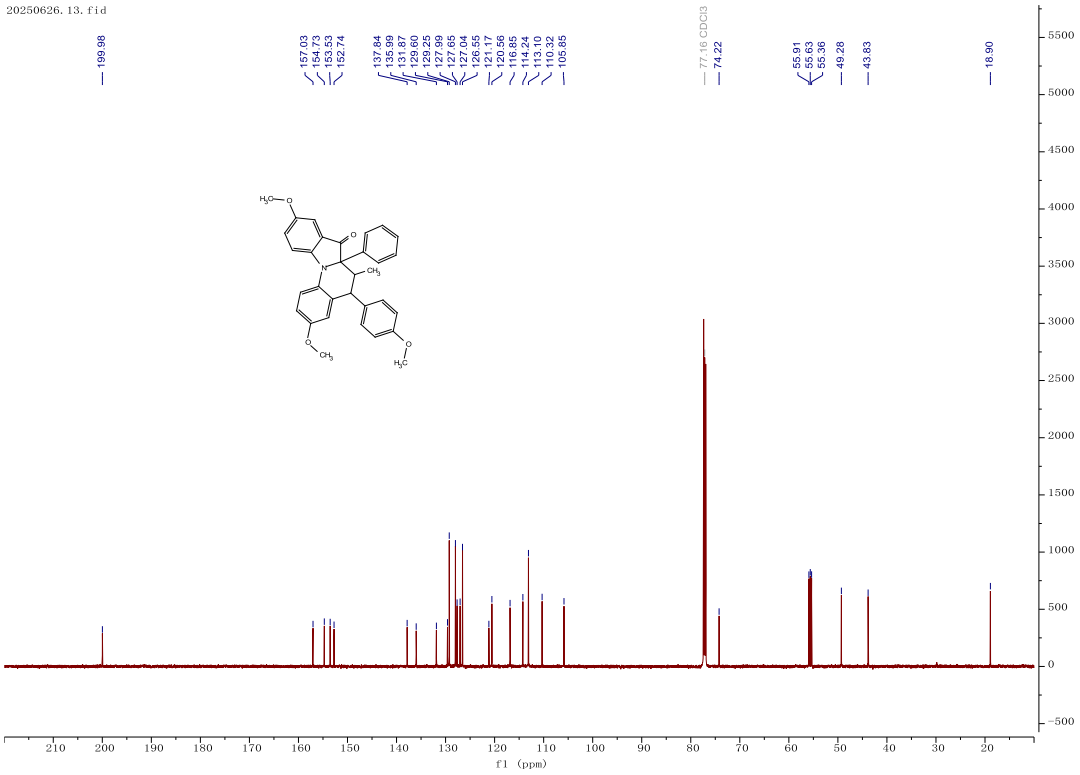

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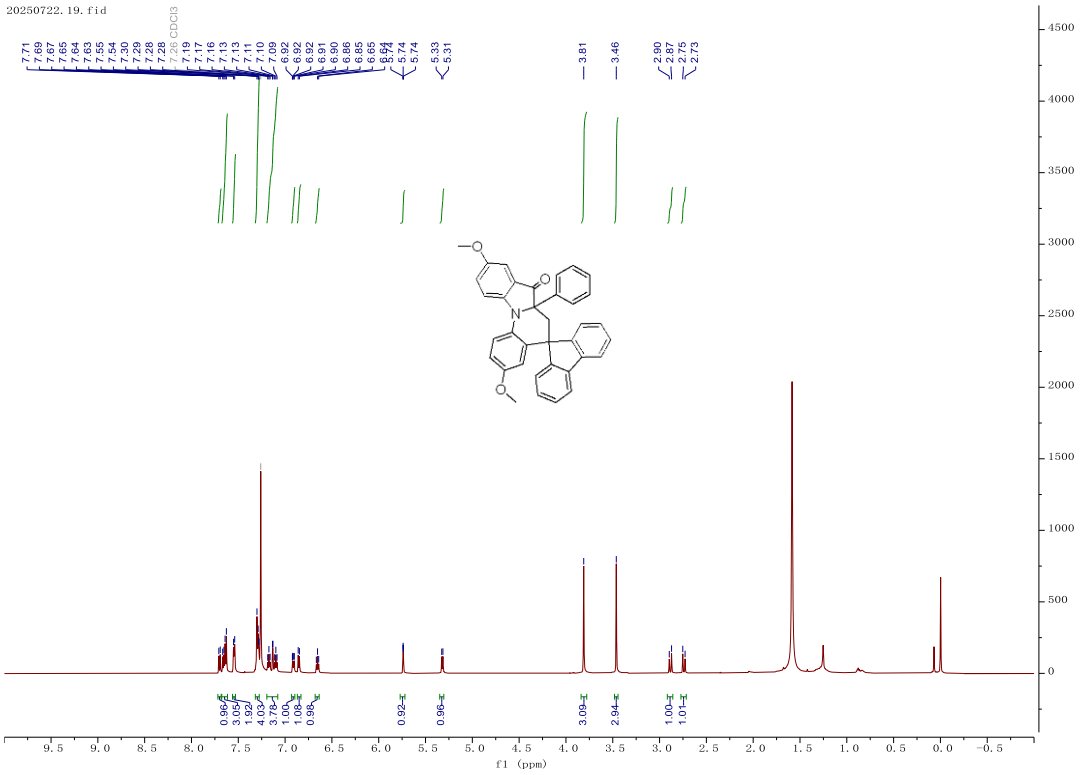

$^{1}$H NMR of compound **4f** (in $CDCl_3$)



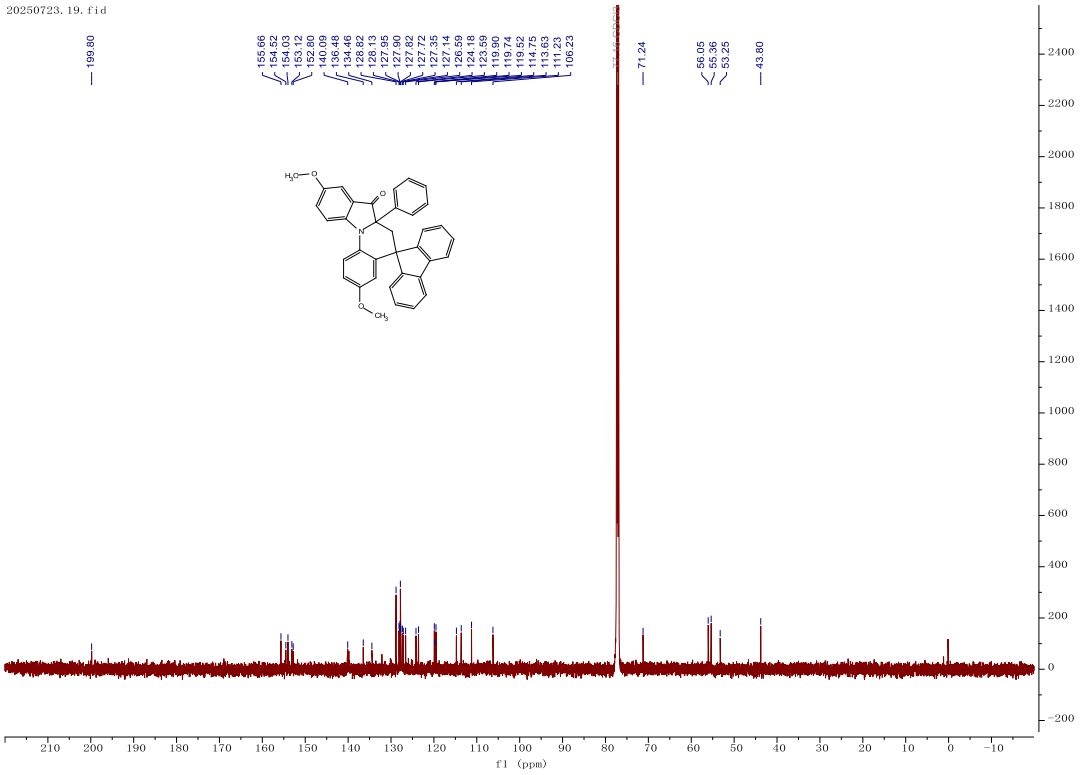

$^{13}$C NMR of compound **4f** (in $CDCl_3$)



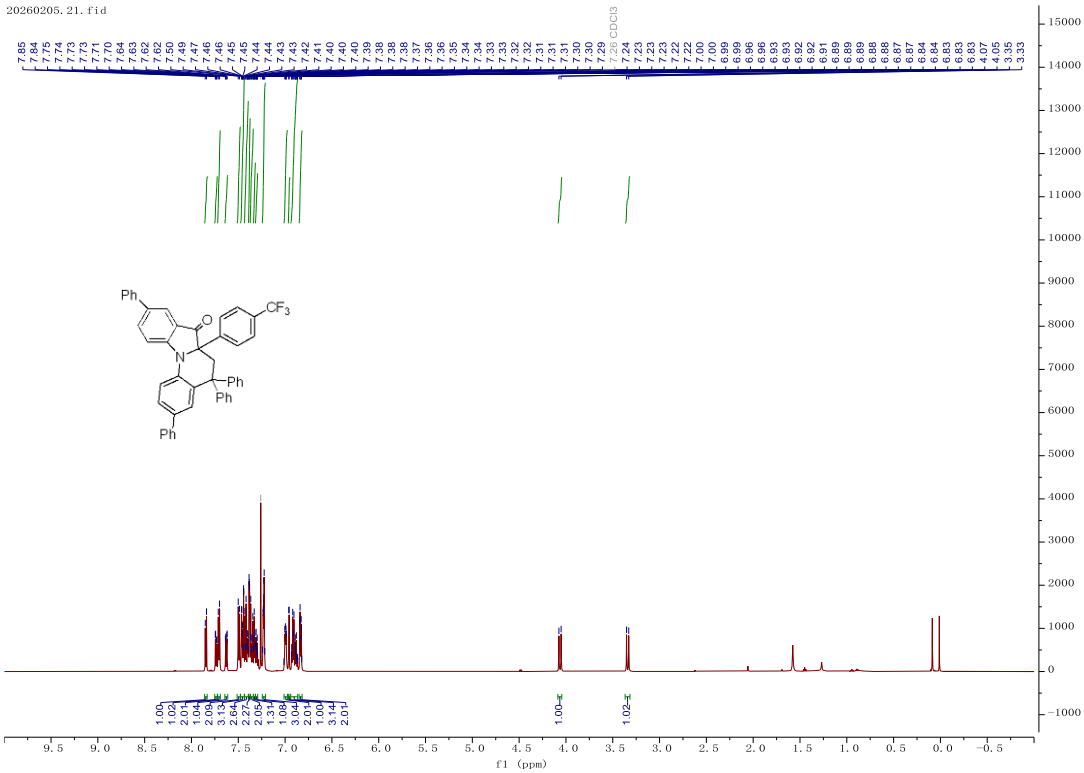

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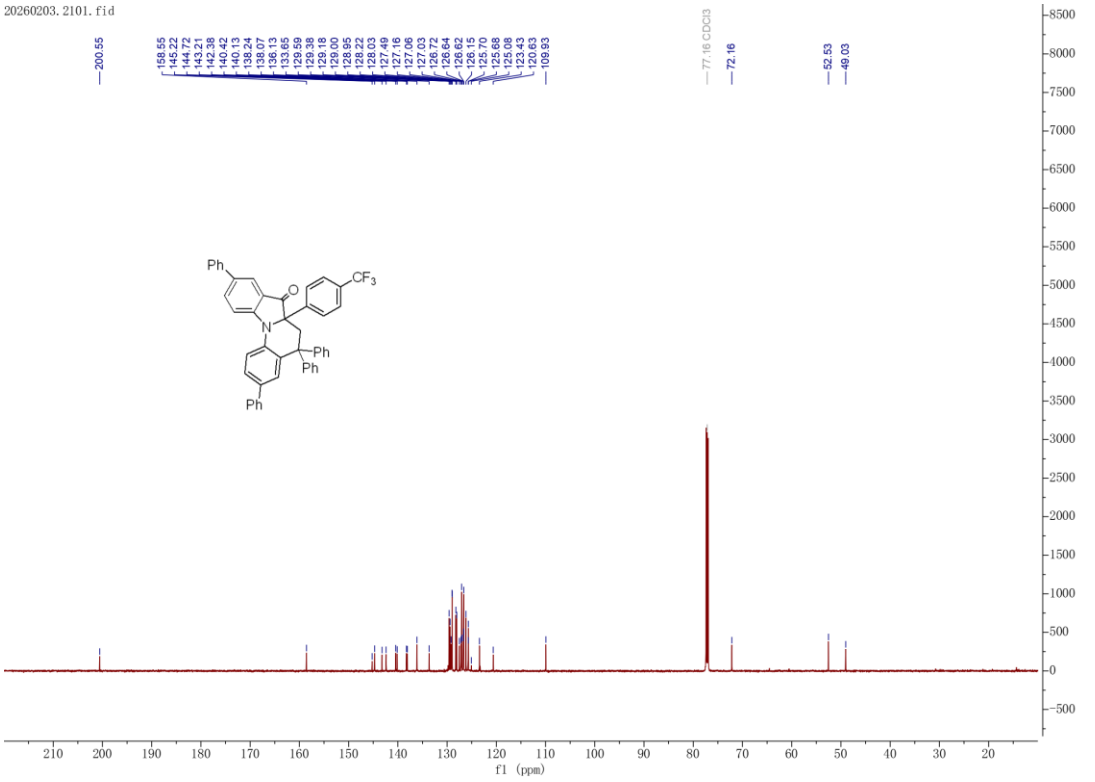

$^{13}$C NMR of compound **4g** (in $CDCl_3$)



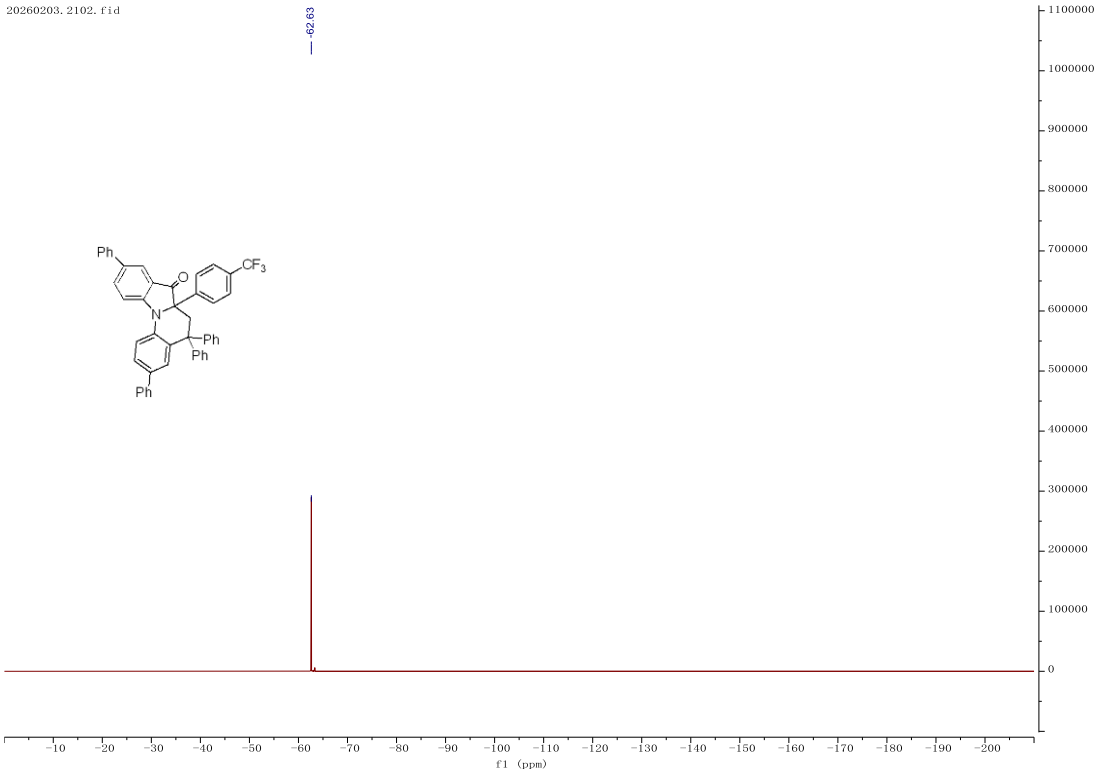

$^{1}$H NMR of compound **4h** (in $CDCl_3$)



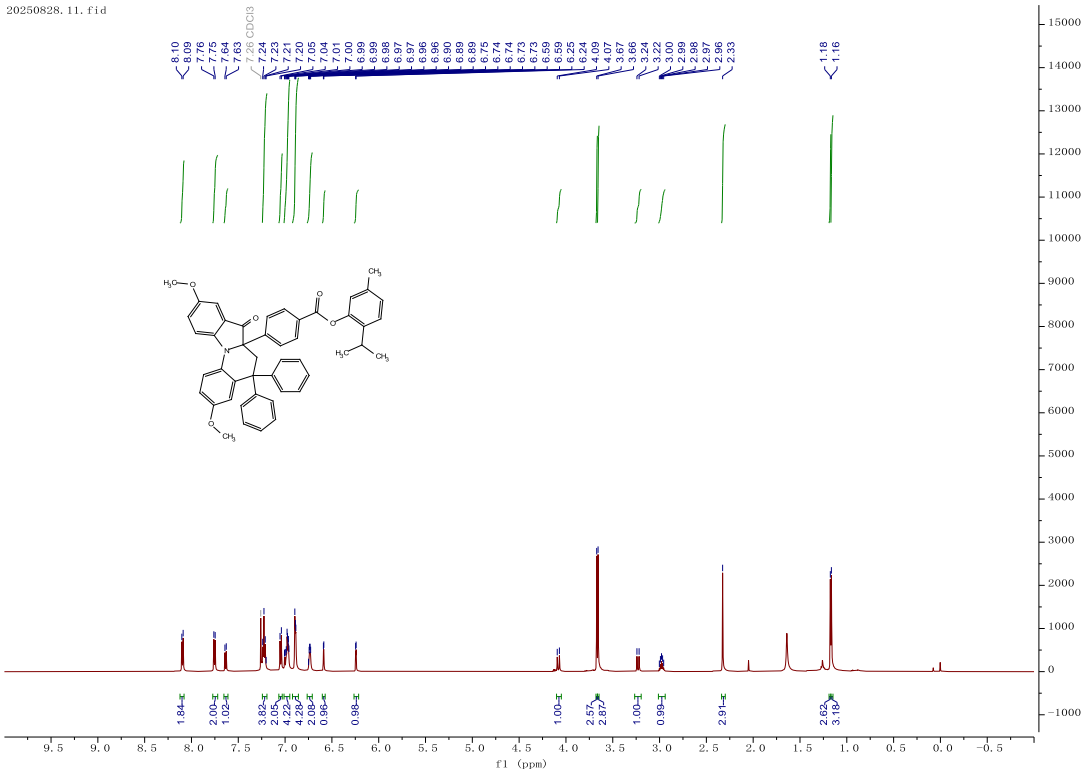

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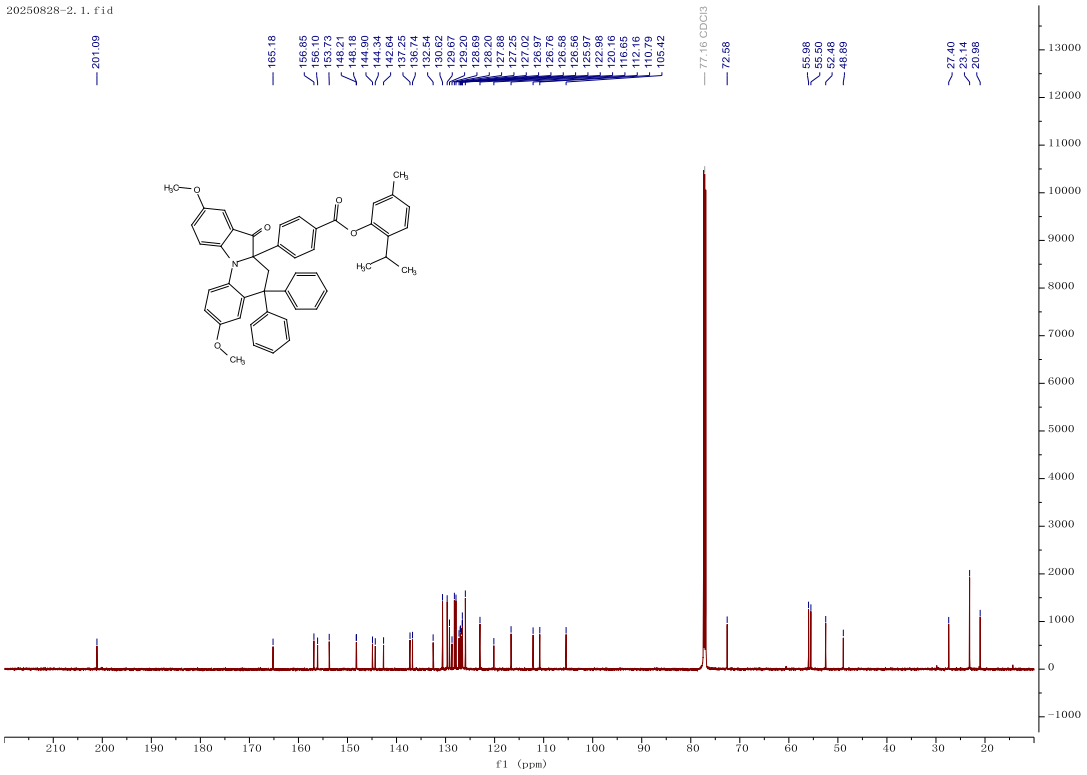

$^{19}F$ NMR of compound **4h** (in $CDCl_3$)



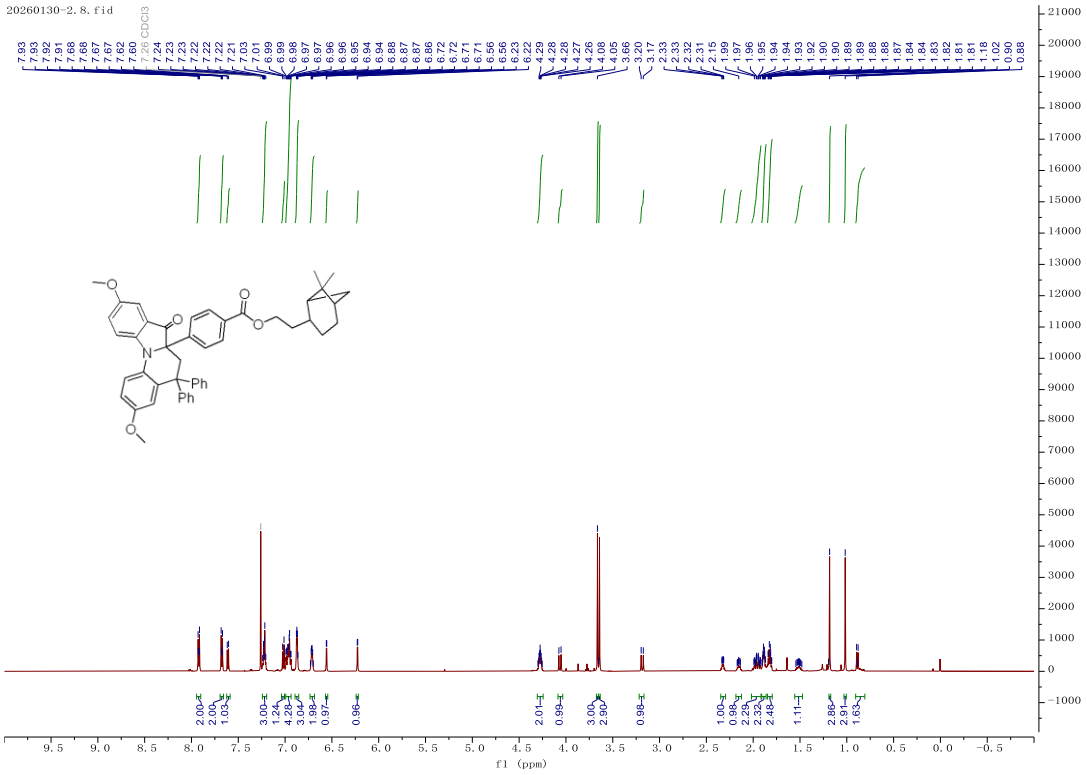

$^{1}H$ NMR of compound **4i** (in $CDCl_3$)



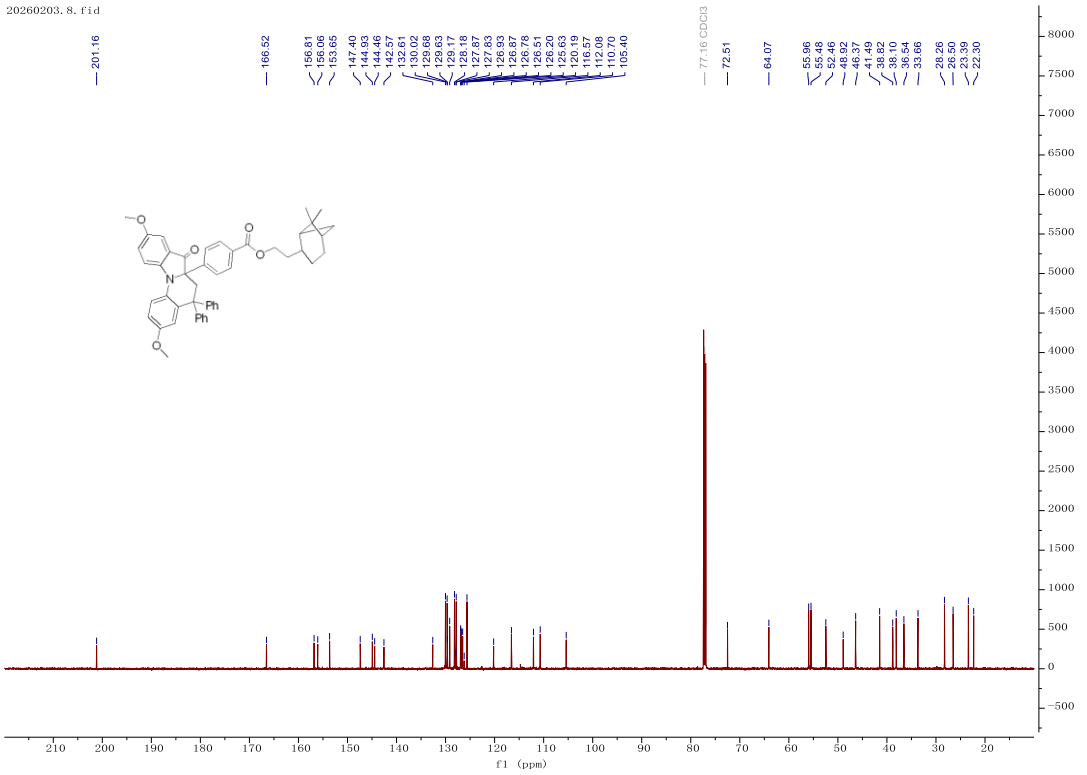

$^{13}$C NMR of compound **4i** (in $CDCl_3$)



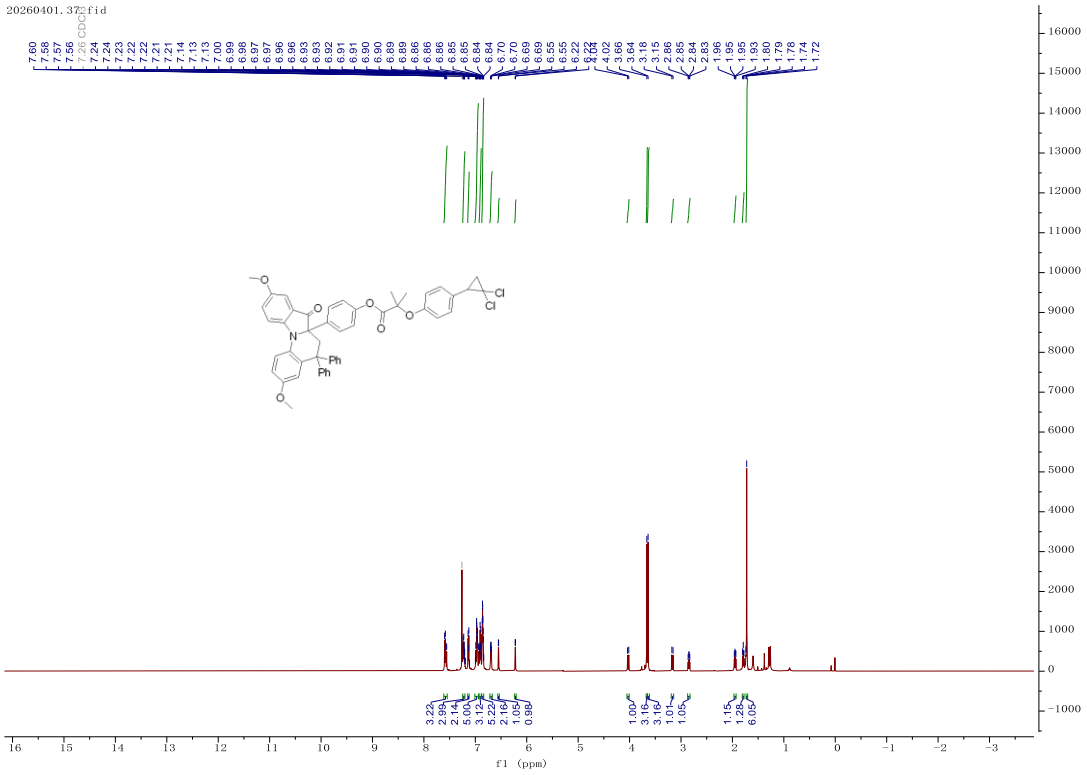

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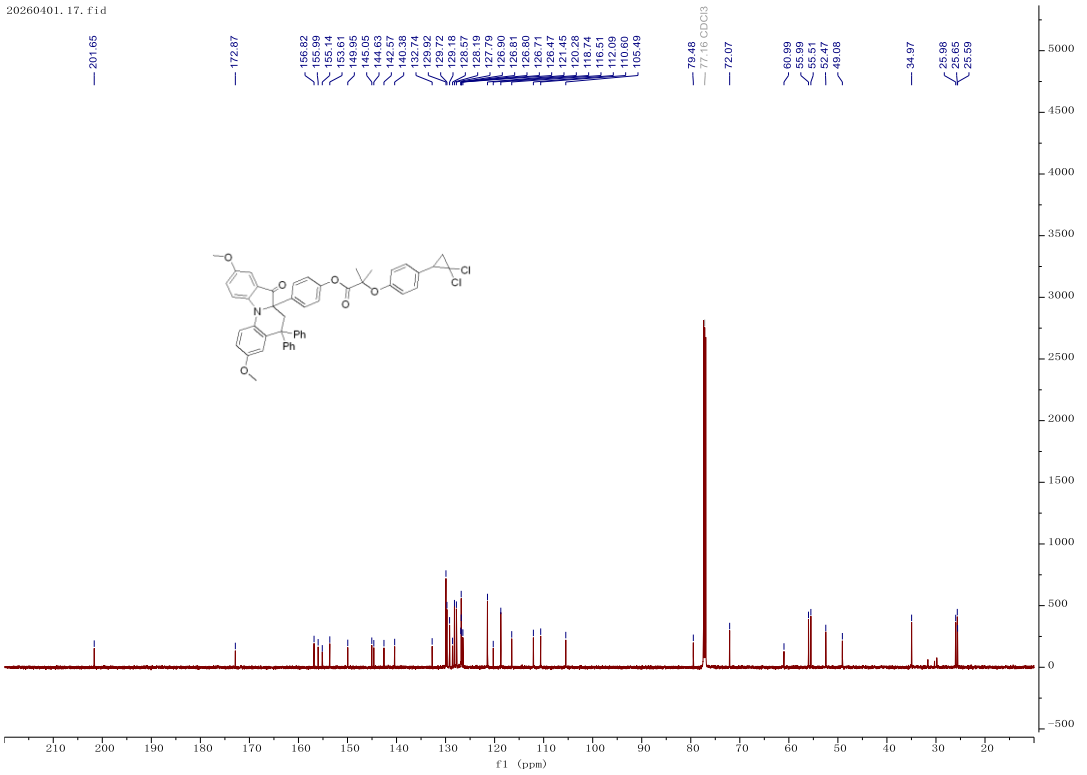

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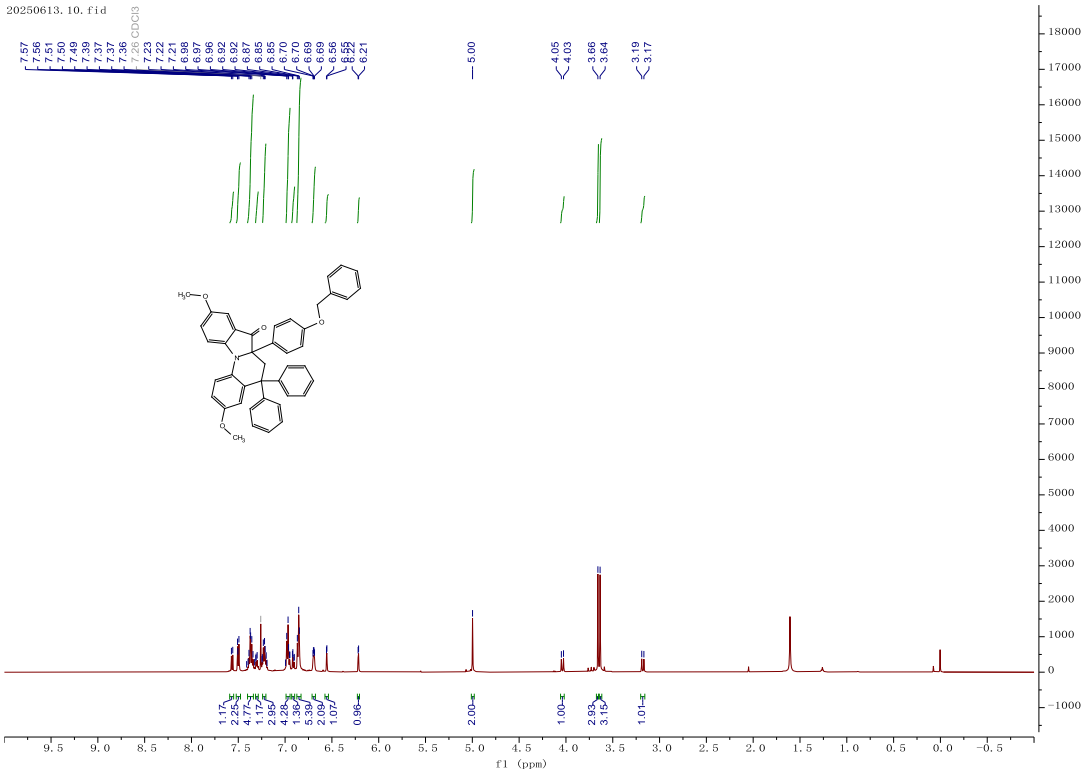

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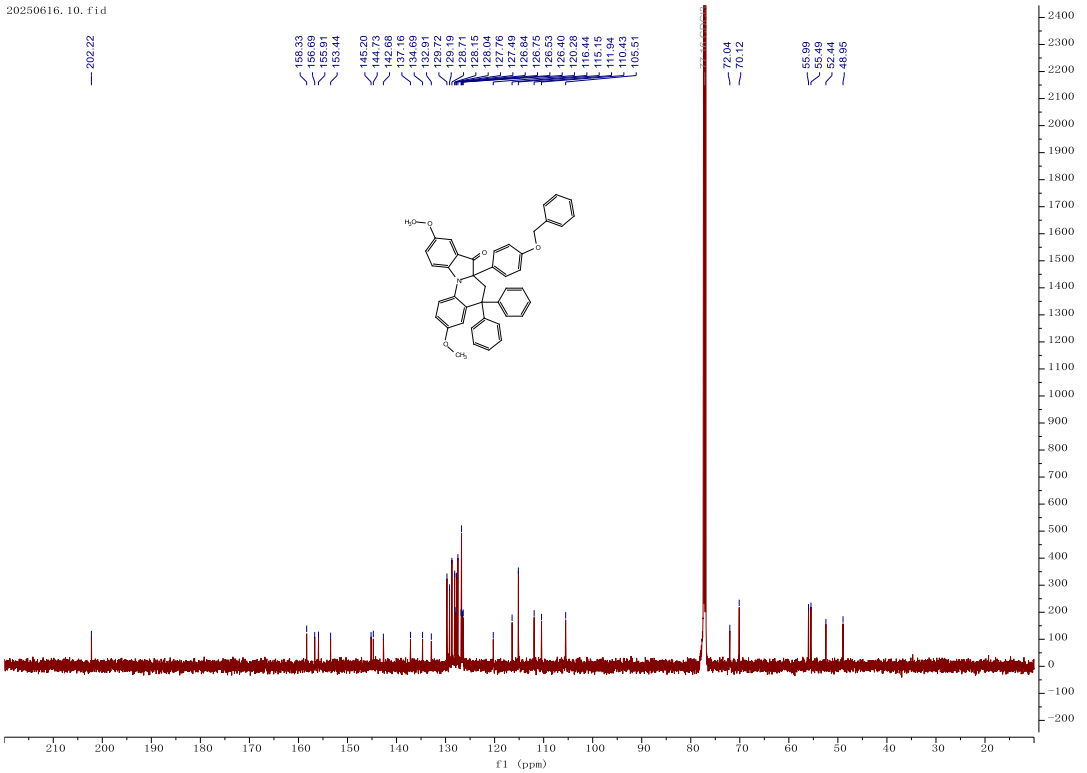
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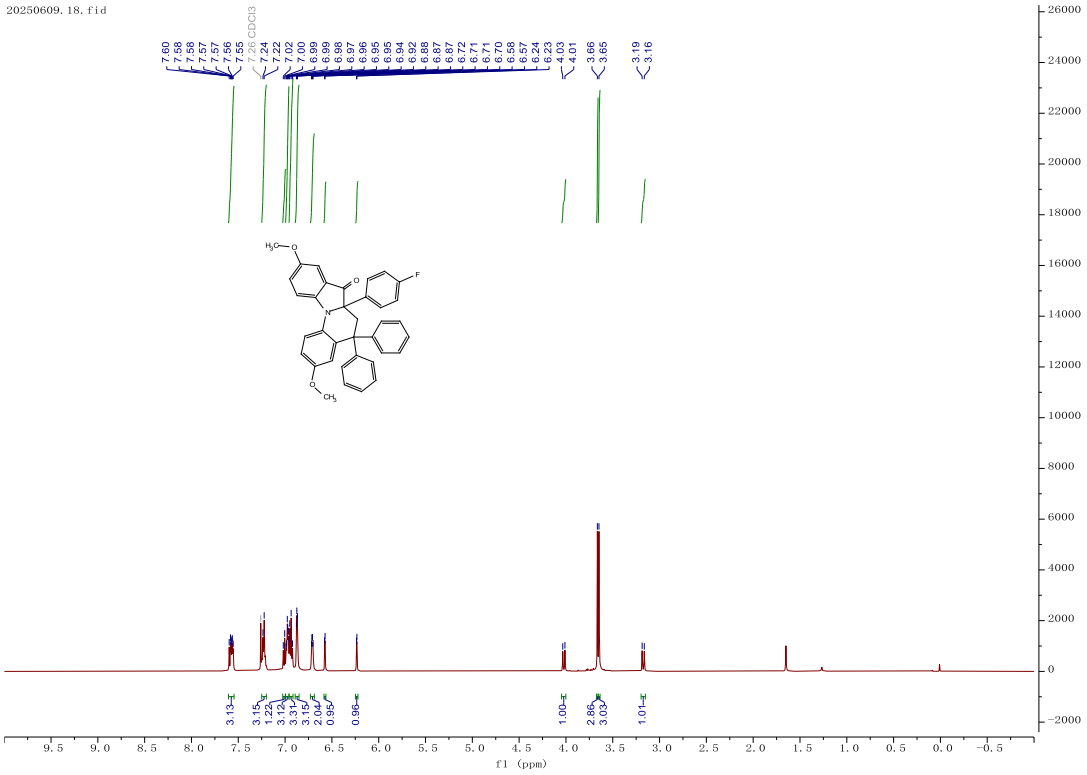
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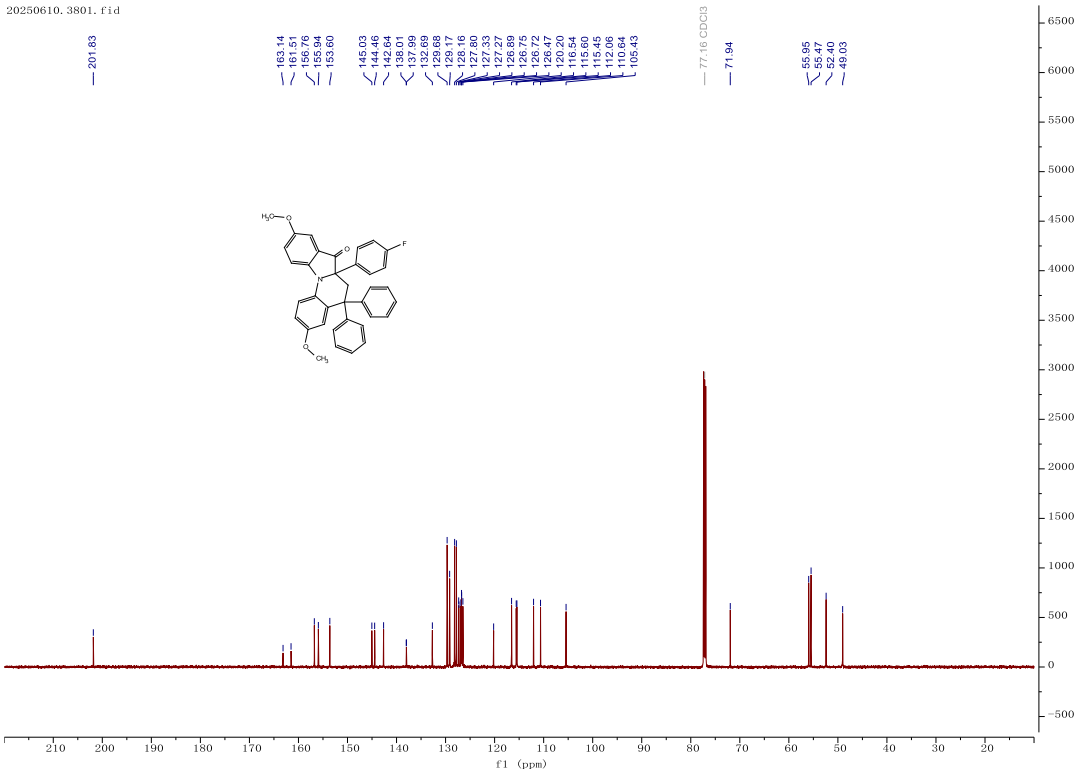
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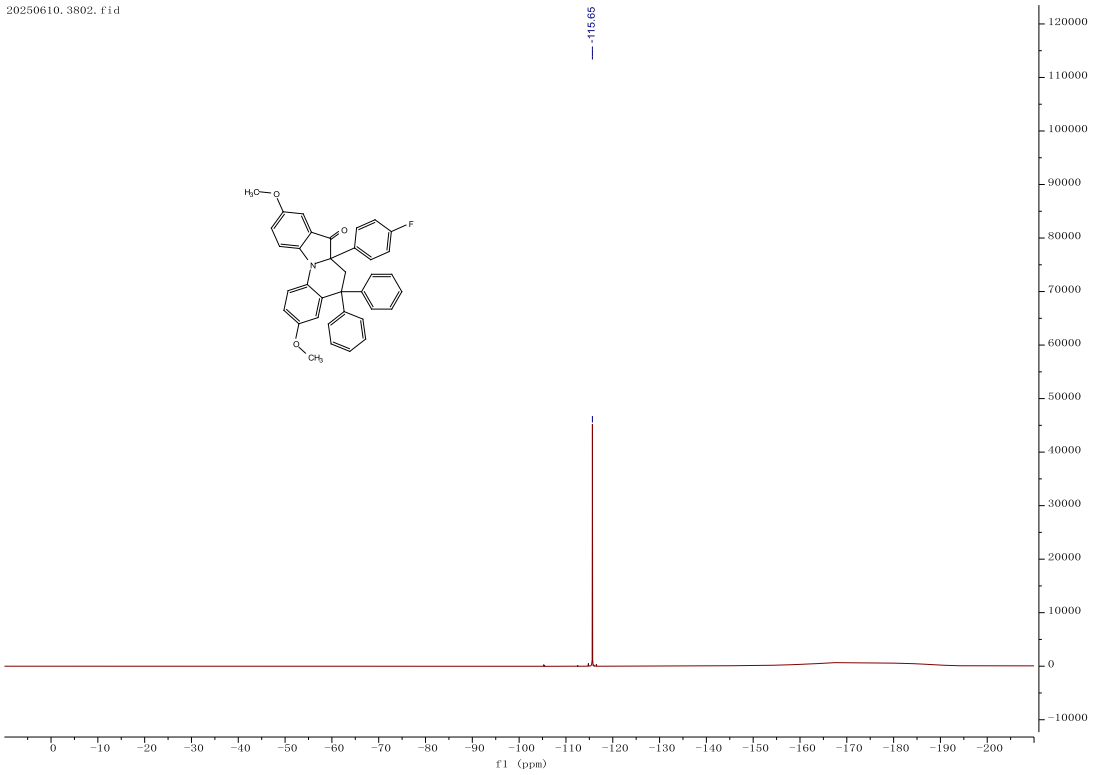
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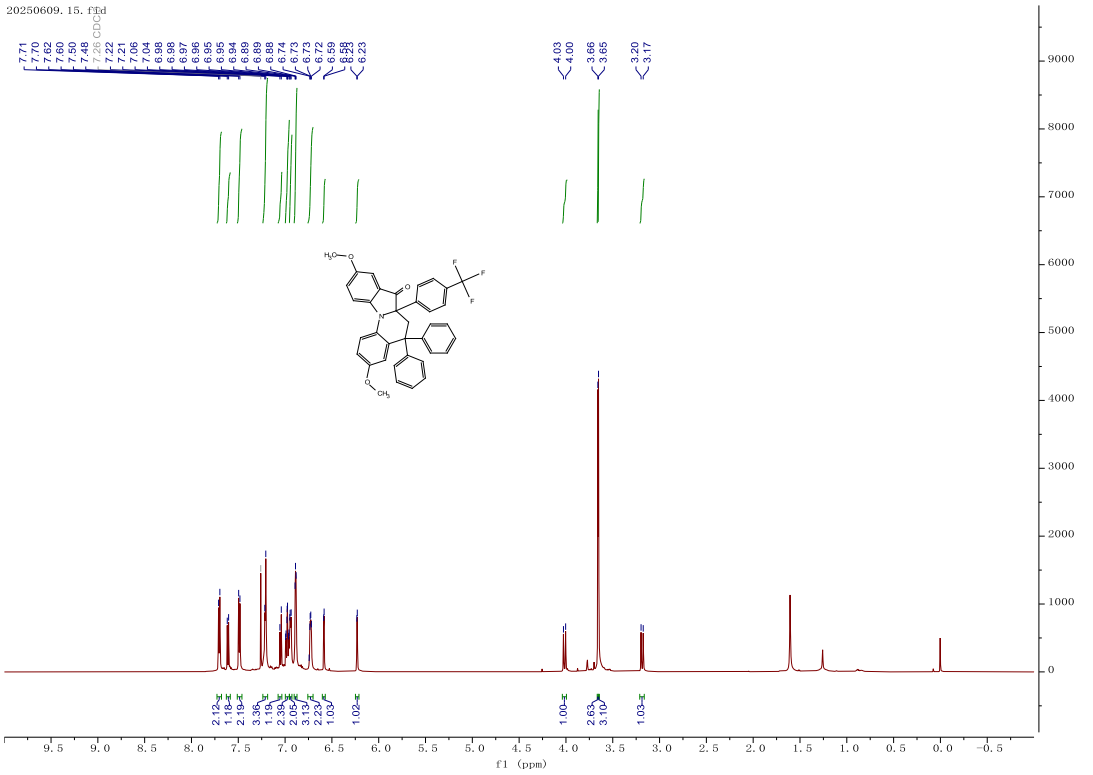

$^{13}$C NMR of compound **4n** (in $CDCl_3$)



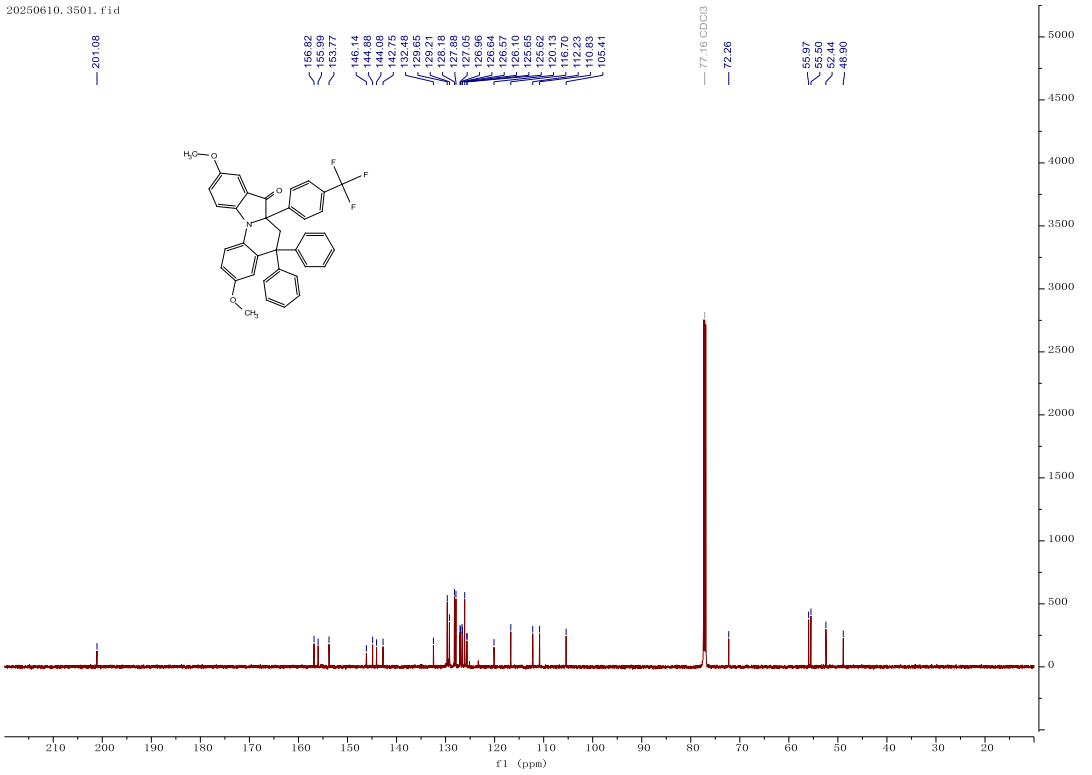

$^{19}$F NMR of compound **4n** (in $CDCl_3$)



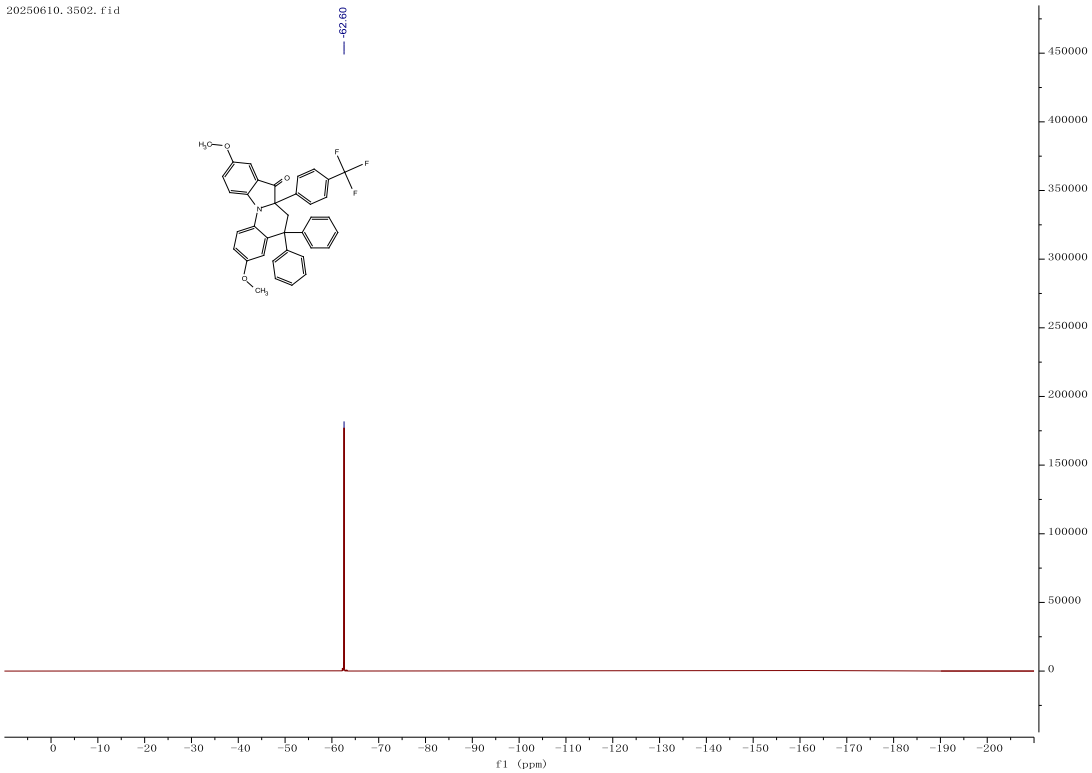

$^{1}$H NMR of compound **4o** (in $CDCl_3$)



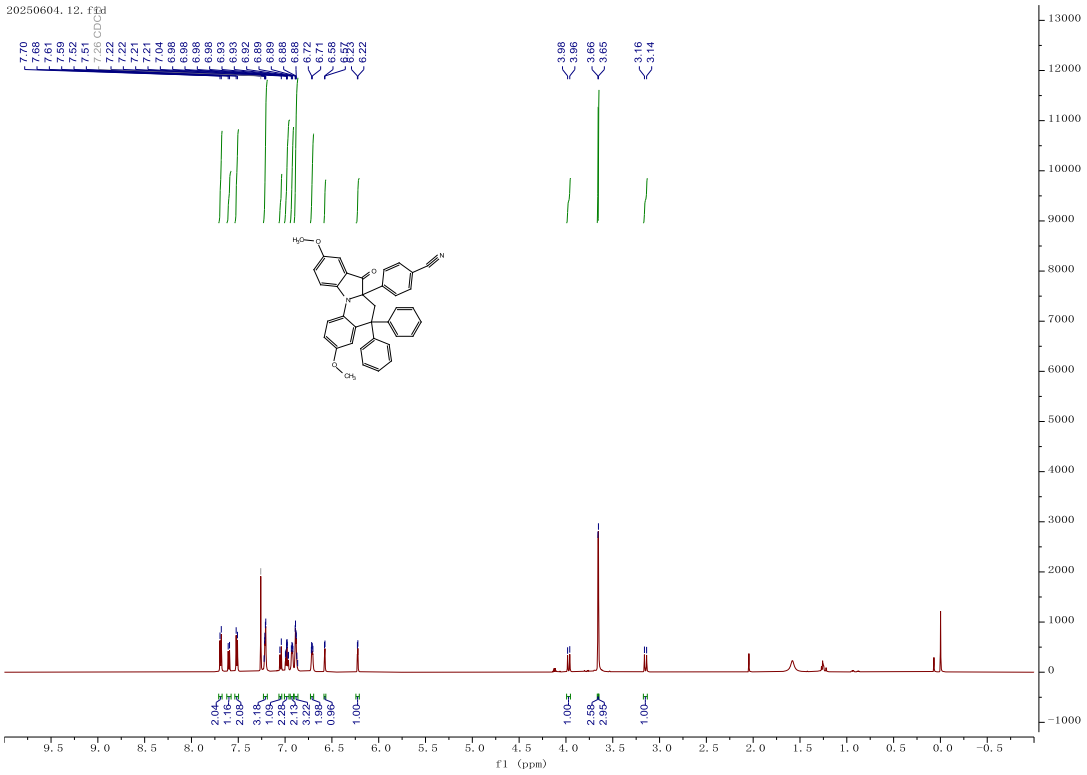

$^{13}$C NMR of compound **4o** (in $CDCl_3$)



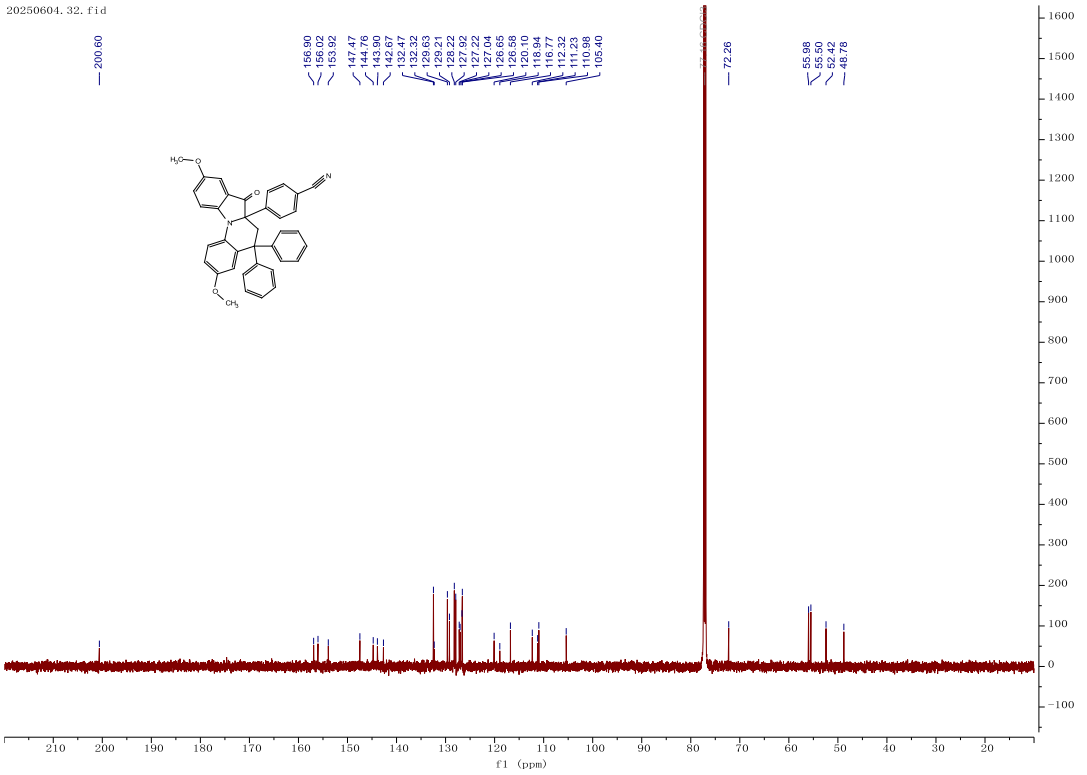

$^{19}$F NMR of compound **4o** (in $CDCl_3$)



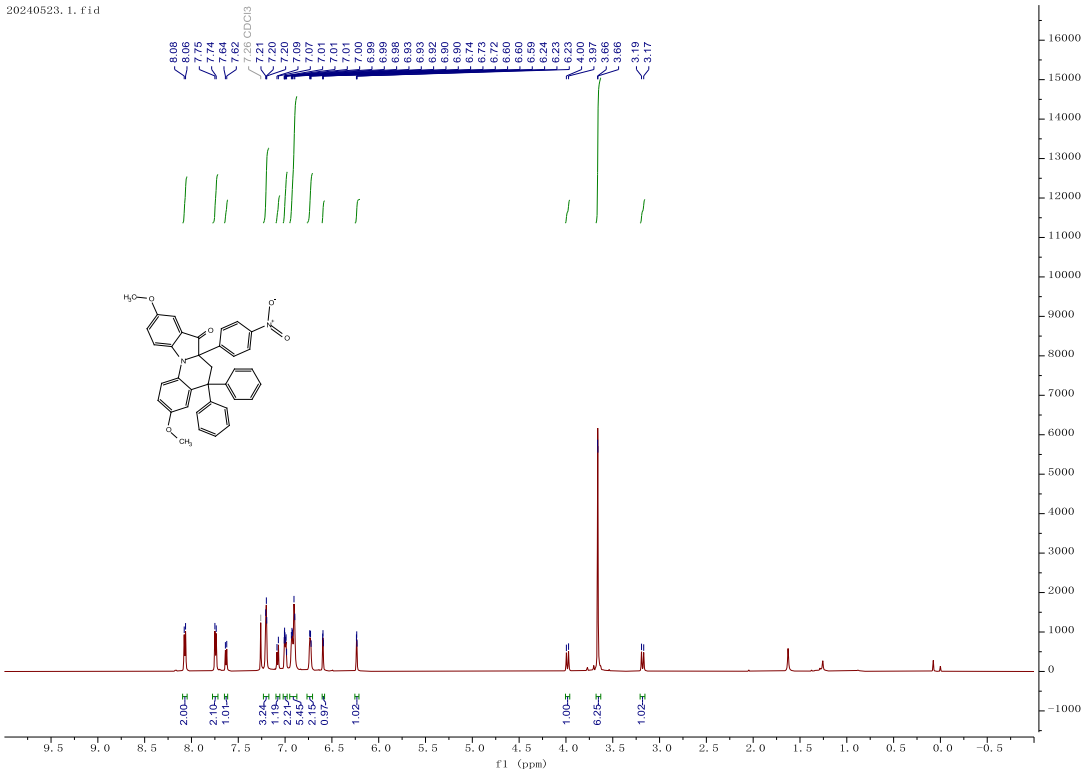

$^{1}$H NMR of compound **4p** (in $CDCl_3$)



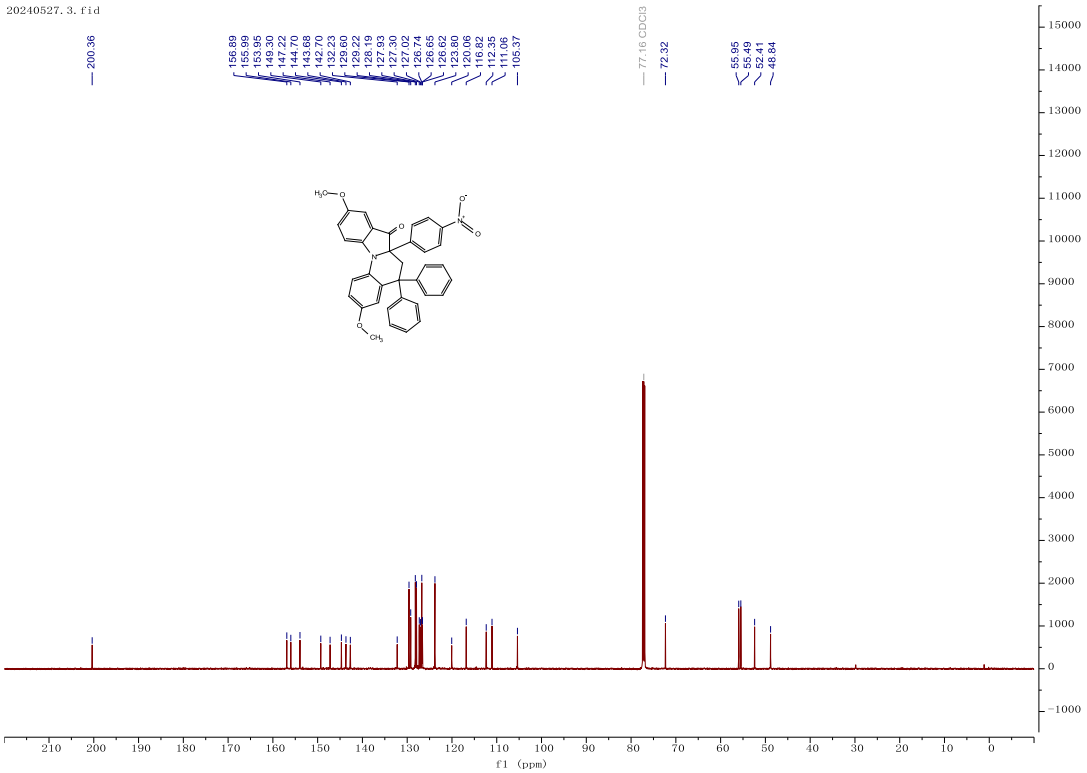

$^{13}C$ NMR of compound **4p** (in $CDCl_3$)



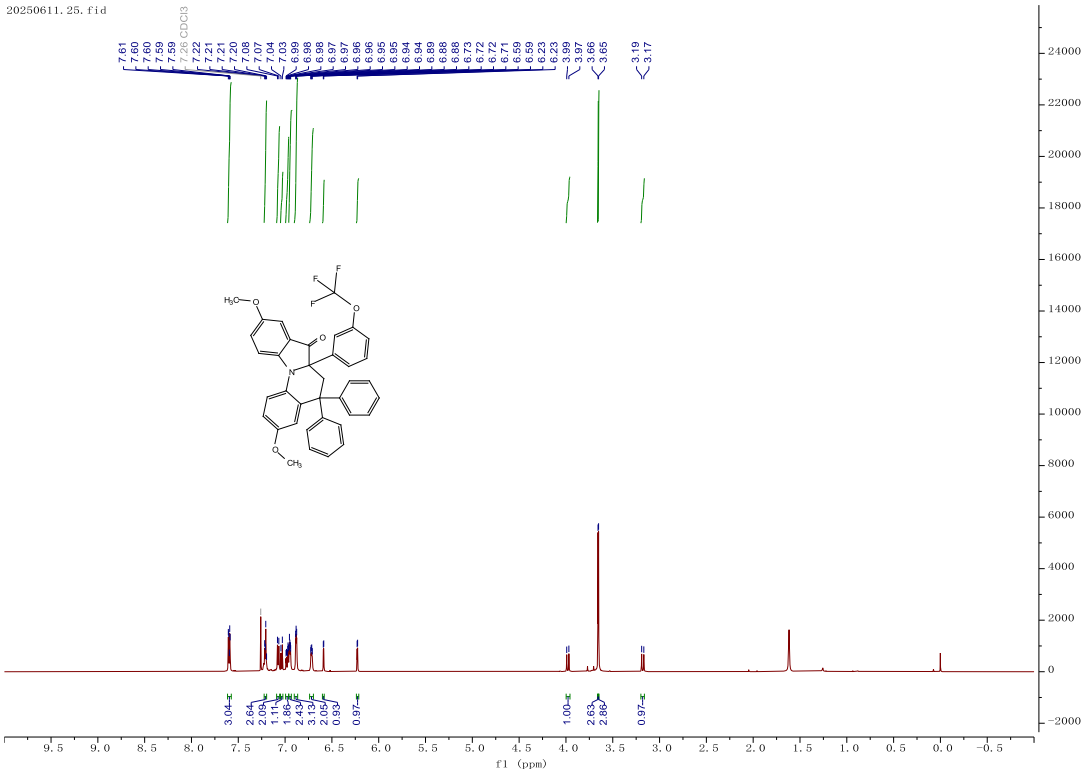

$^{1}H$ NMR of compound **4q** (in $CDCl_3$)



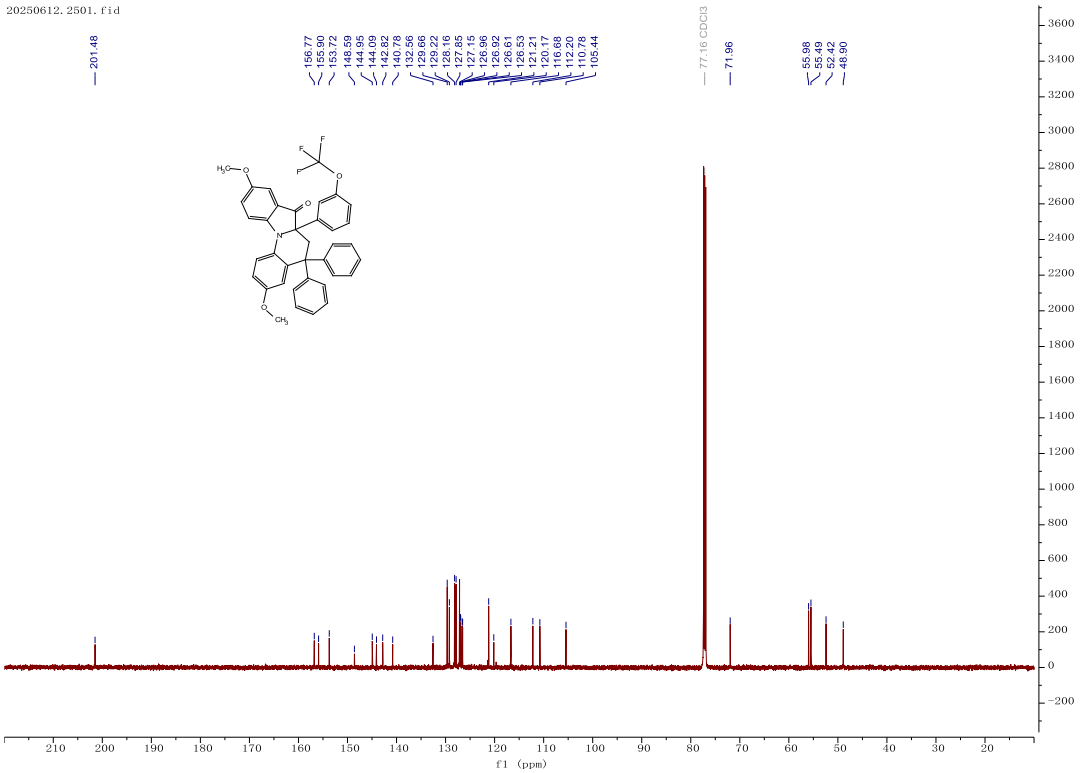

$^{13}$C NMR of compound **4q** (in $CDCl_3$)



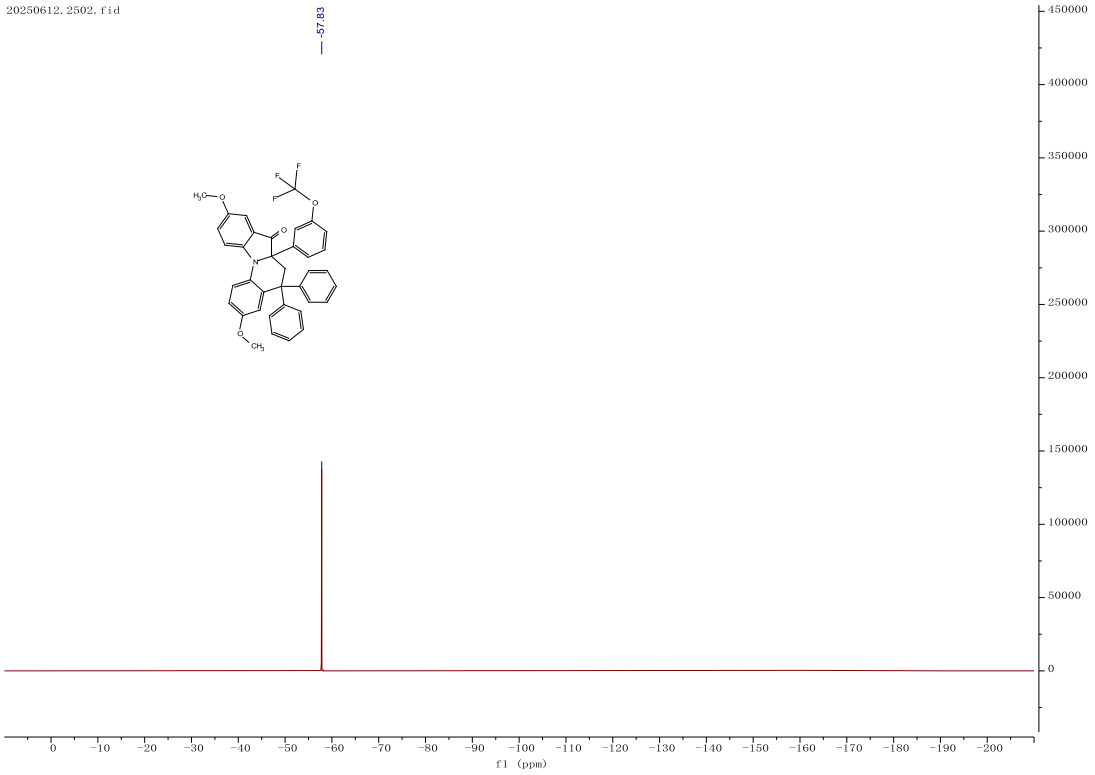

$^{1}$H NMR of compound **4r** (in $CDCl_3$)



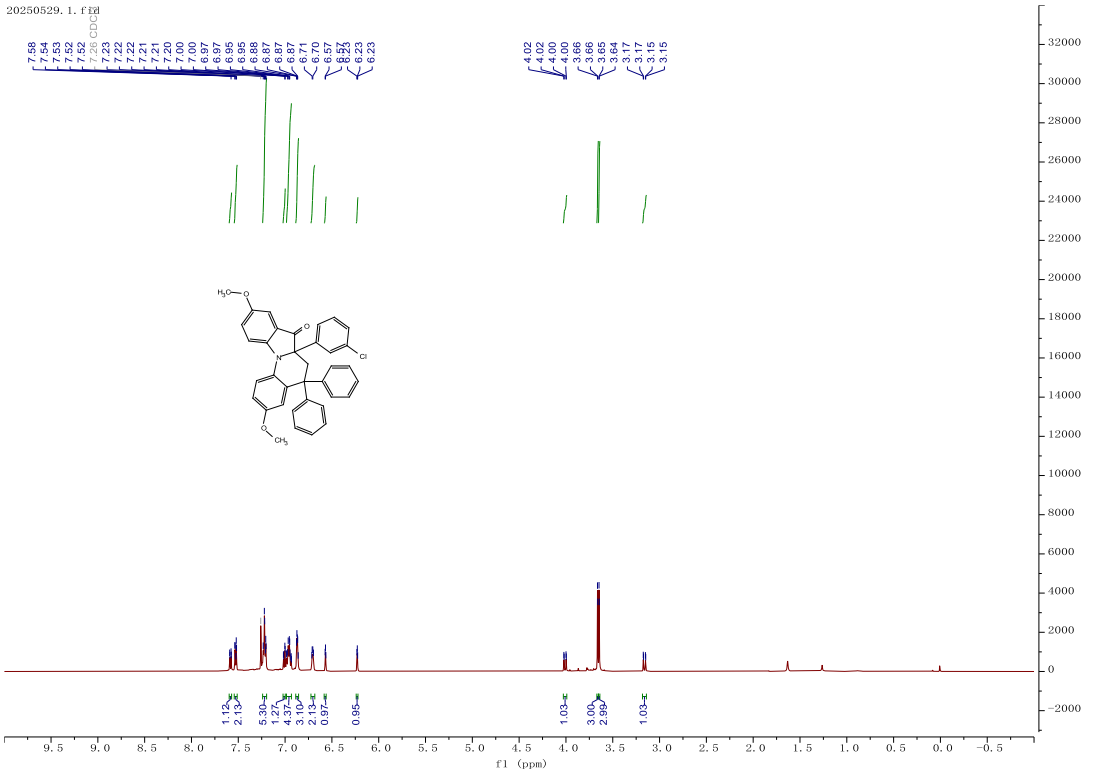

$^{13}$C NMR of compound **4r** (in $CDCl_3$)



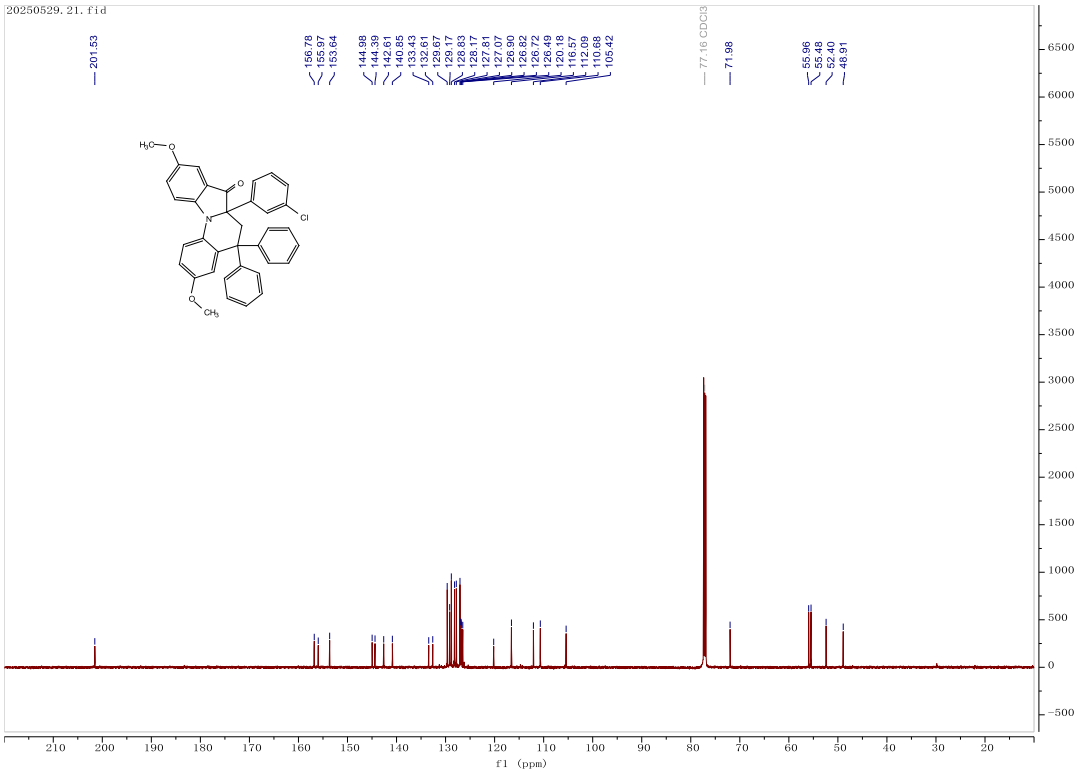

$^{19}$F NMR of compound **4r** (in $CDCl_3$)



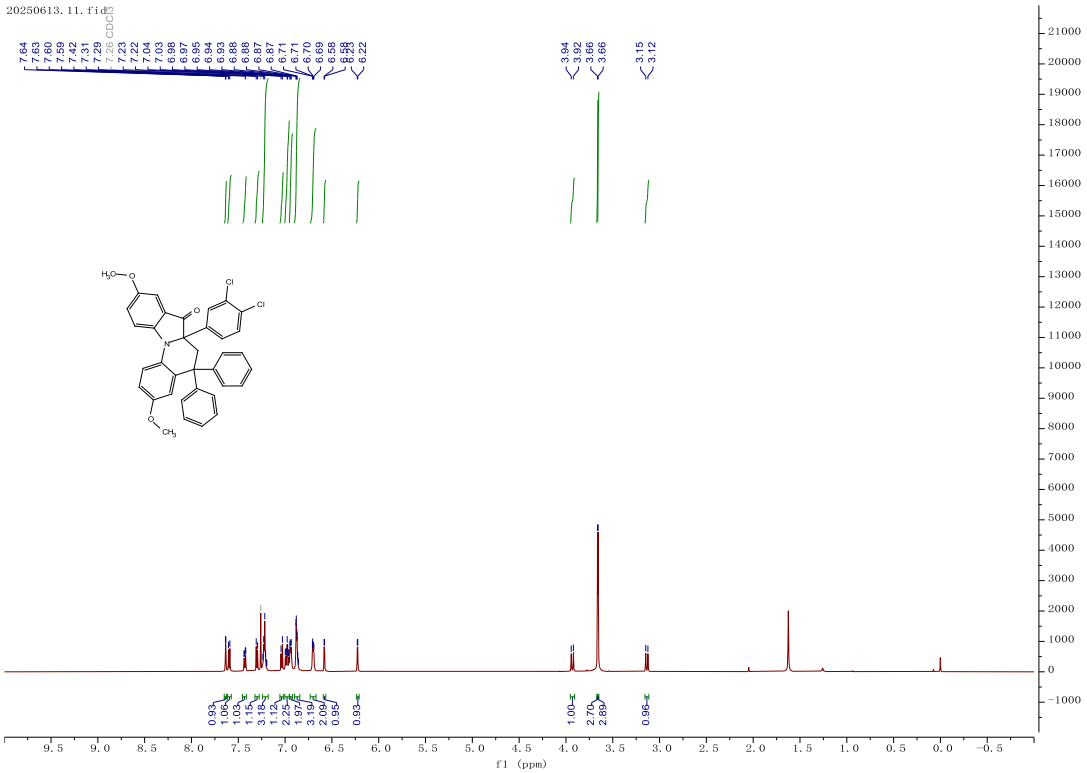

$^{1}$H NMR of compound **4s** (in $CDCl_3$)



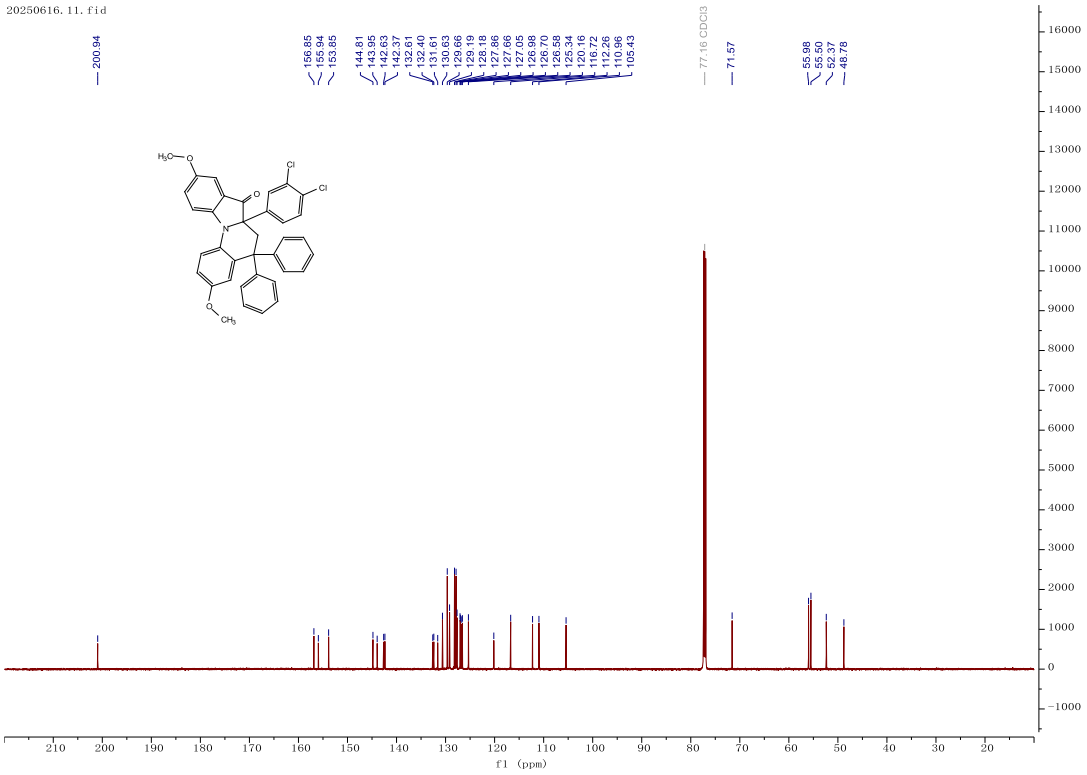

$^{13}$C NMR of compound **4s** (in $CDCl_3$)



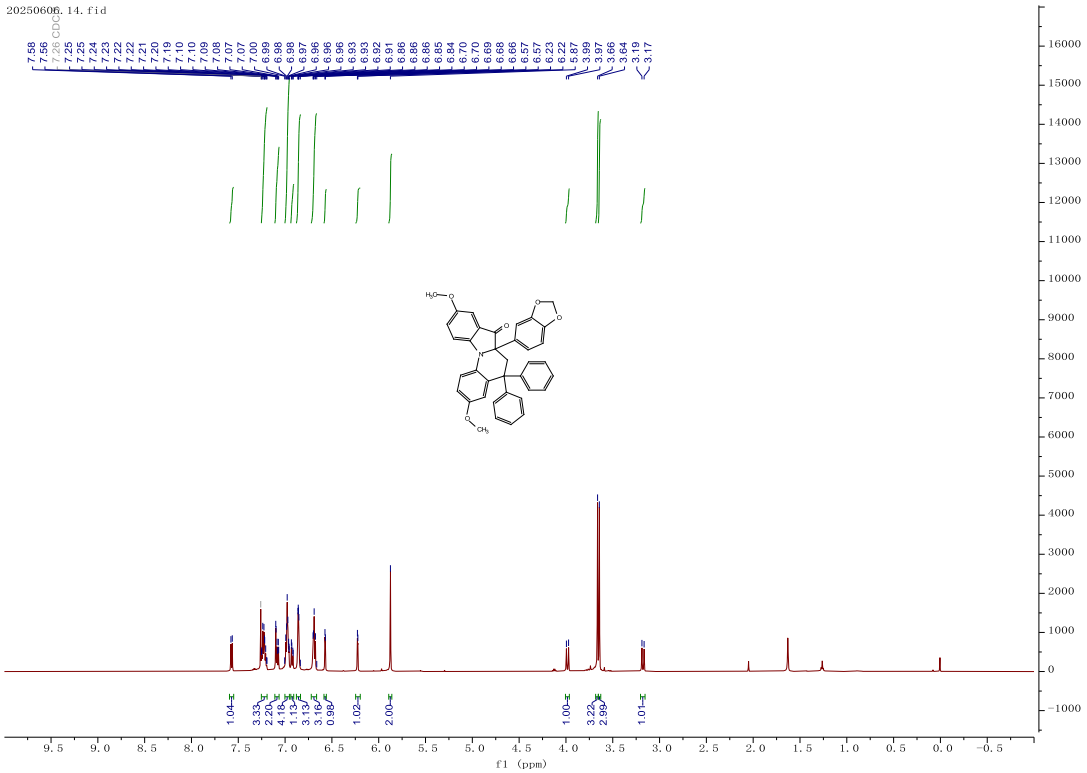

$^{1}$H NMR of compound **4t** (in $CDCl_3$)



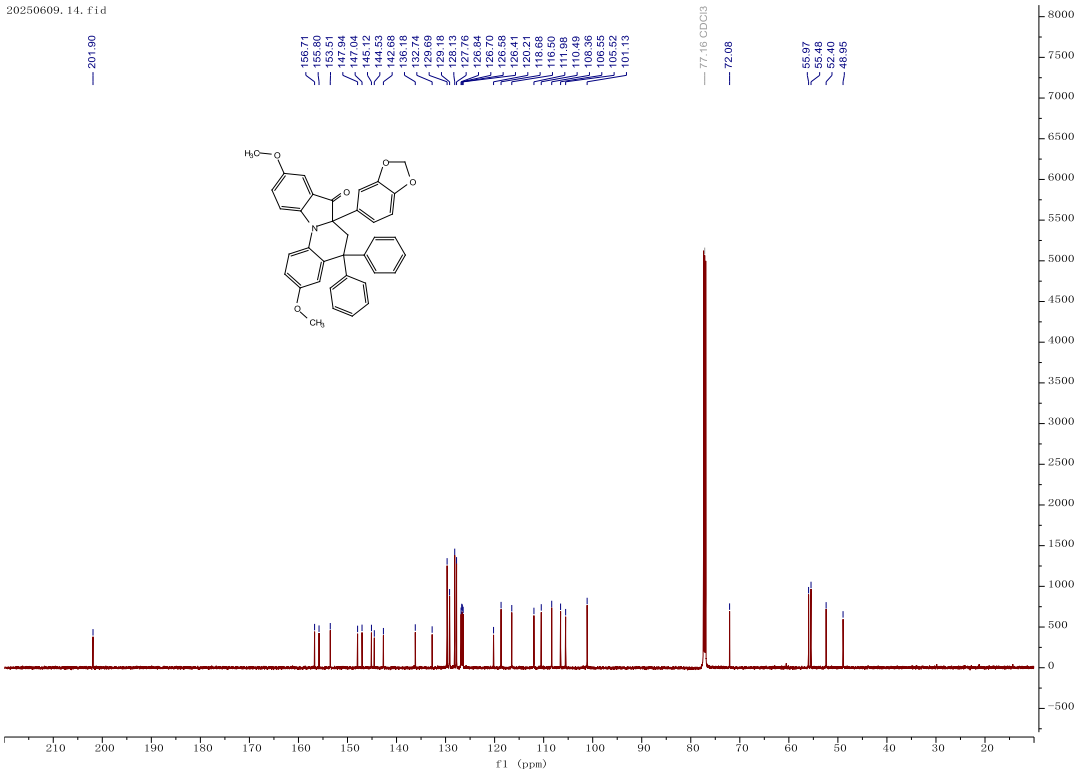

$^{13}$C NMR of compound **4t** (in $CDCl_3$)



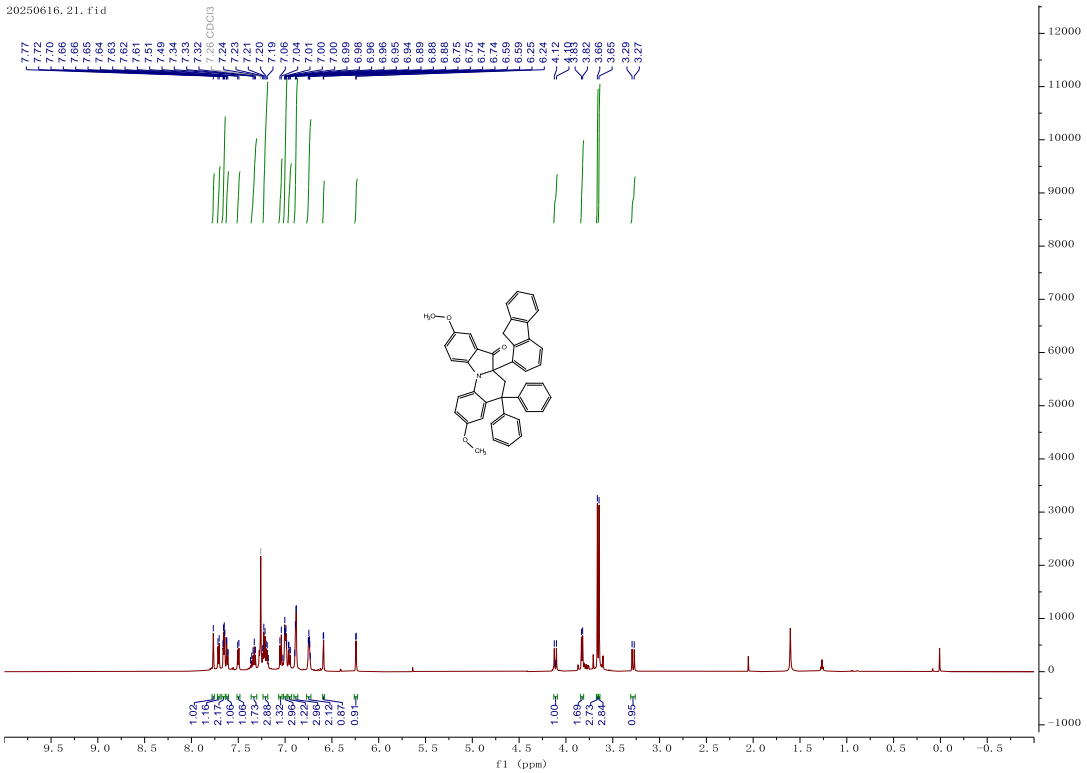

$^{1}$H NMR of compound **4u** (in $CDCl_3$)



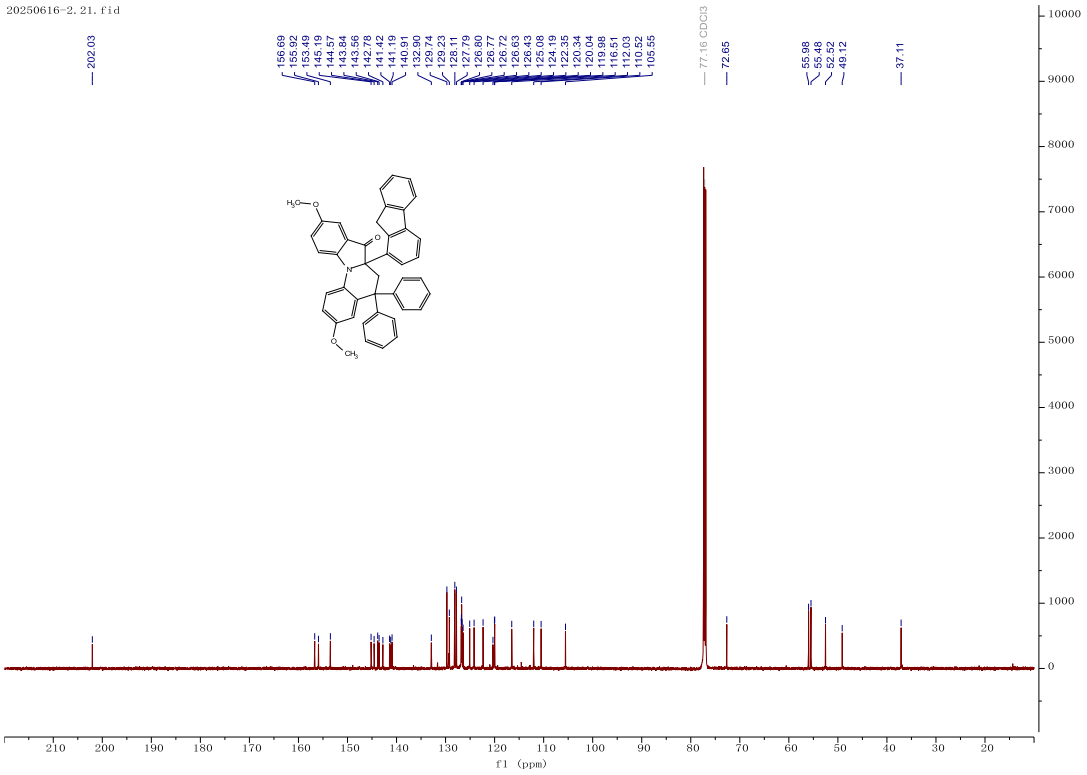

$^{13}$C NMR of compound **4u** (in $CDCl_3$)



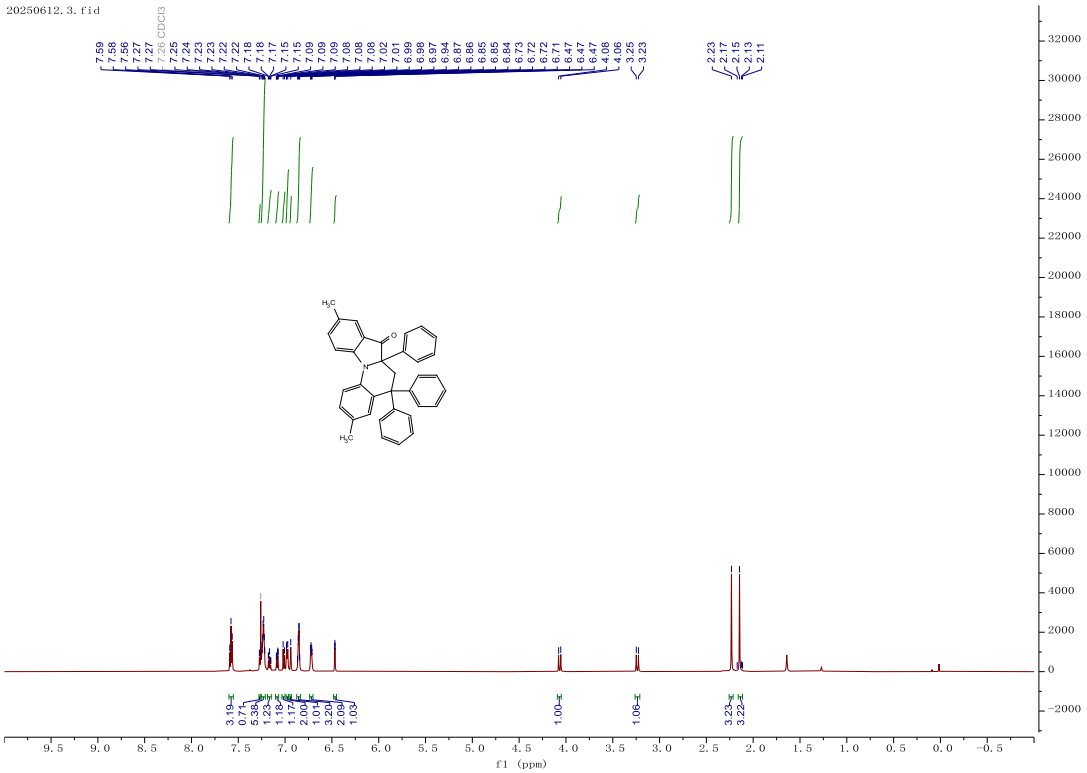

$^{1}$H NMR of compound **4v** (in $CDCl_3$)



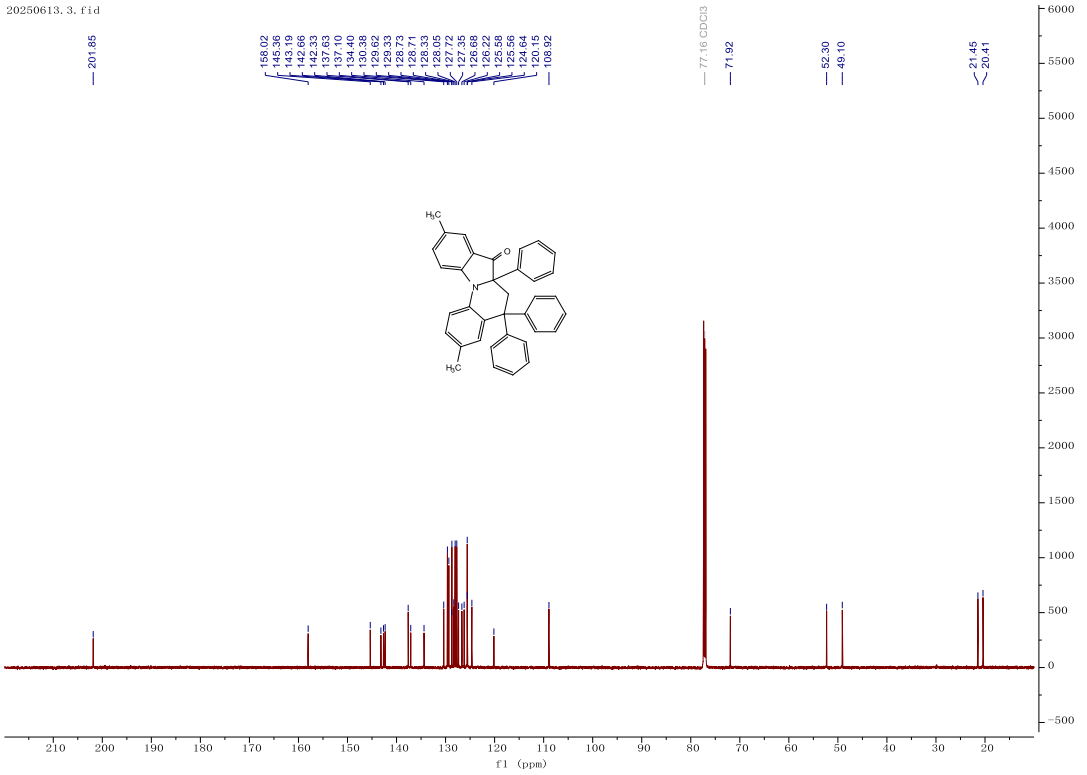

$^{13}$C NMR of compound **4v** (in $CDCl_3$)



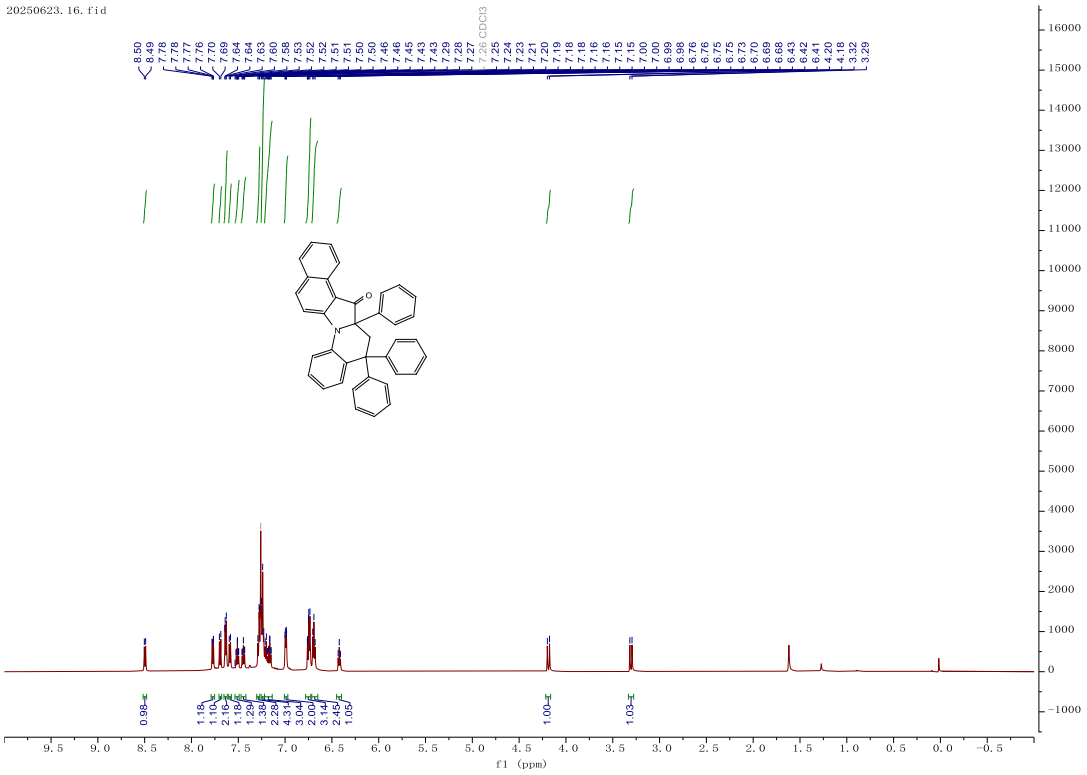

$^{1}$H NMR of compound **4w** (in $CDCl_3$)



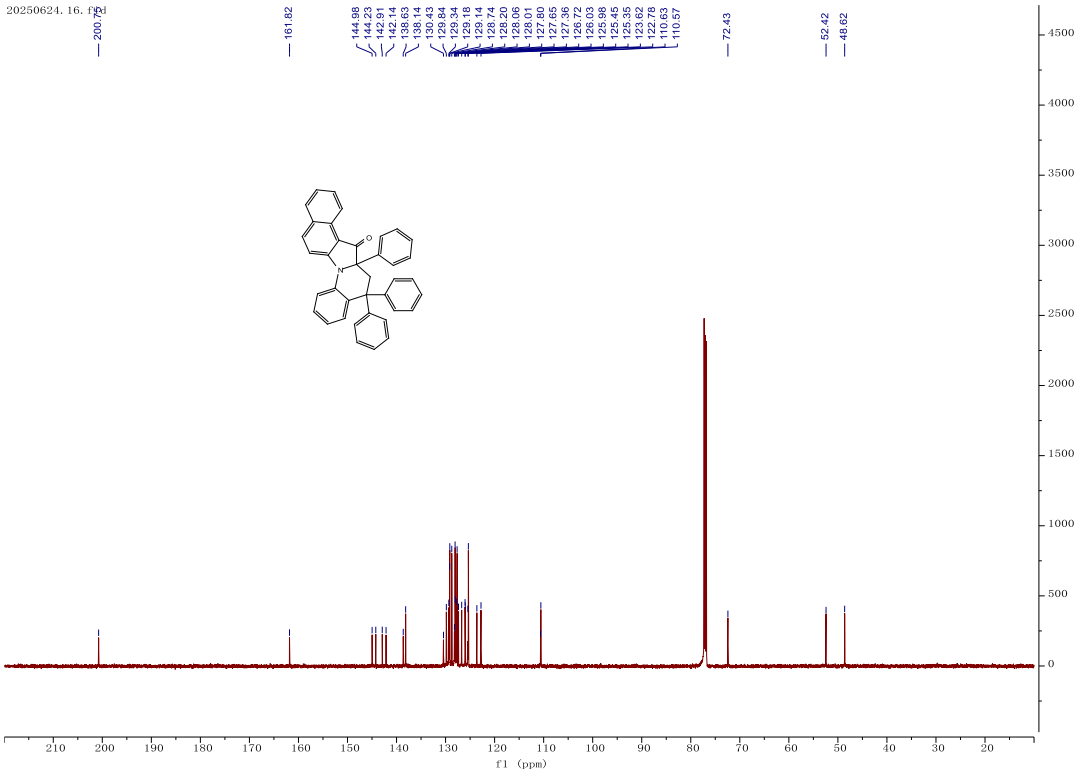

$^{13}$C NMR of compound **4w** (in $CDCl_3$)



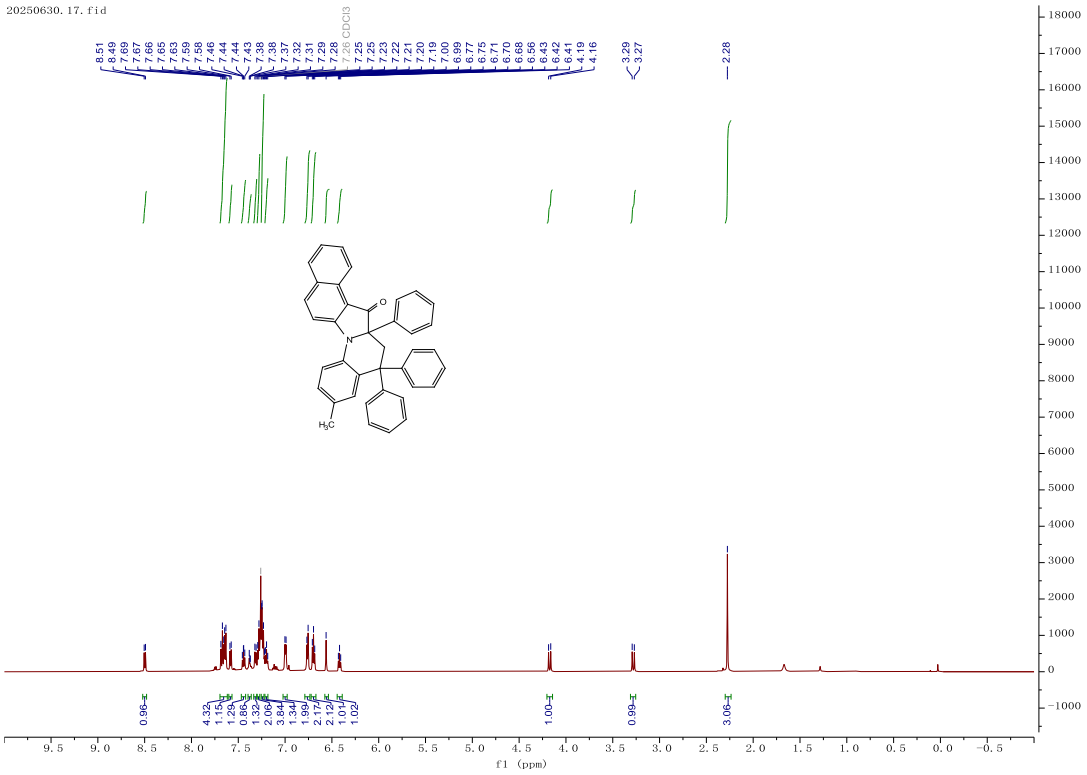

$^{1}$H NMR of compound **4x** (in $CDCl_3$)



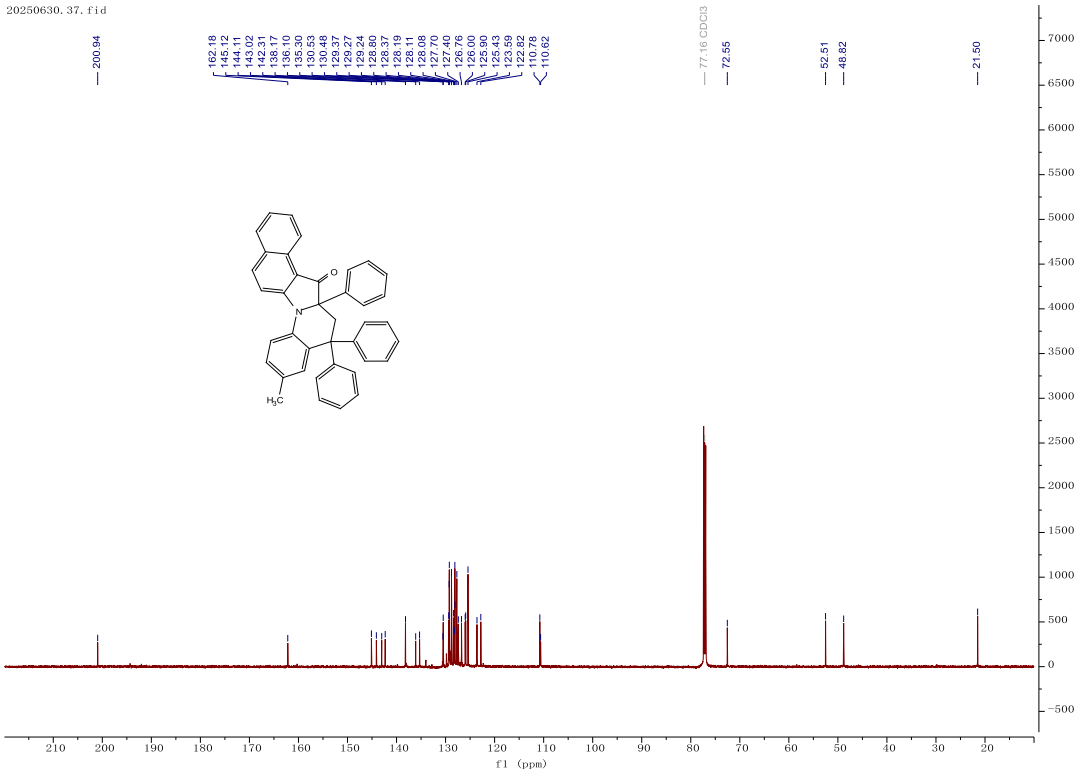

$^{13}$C NMR of compound **4x** (in $CDCl_3$)



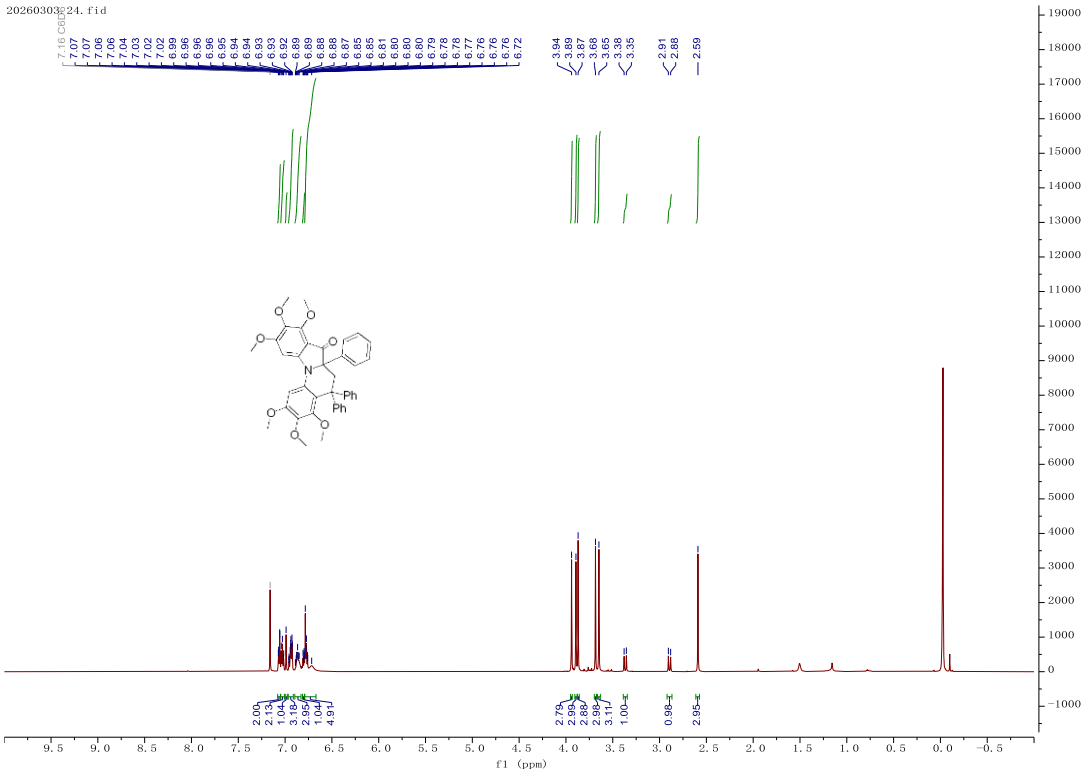

$^{1}$H NMR of compound **4y** (in $CDCl_3$)



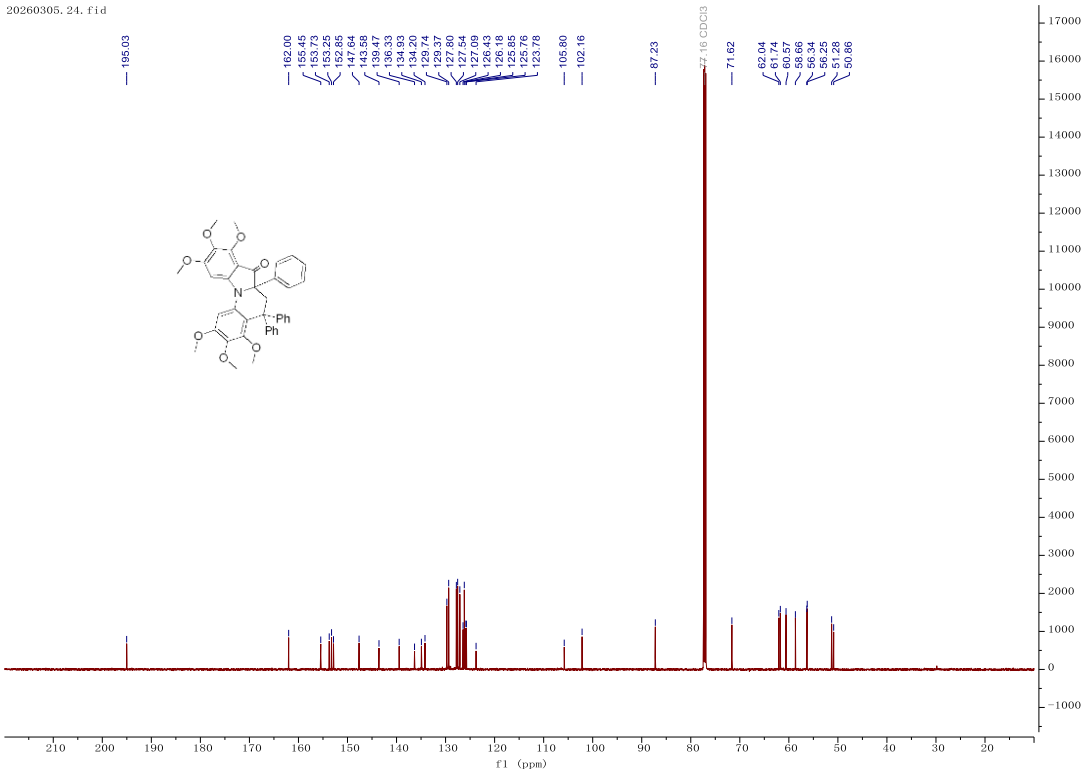

$^{13}$C NMR of compound **4y** (in $CDCl_3$)



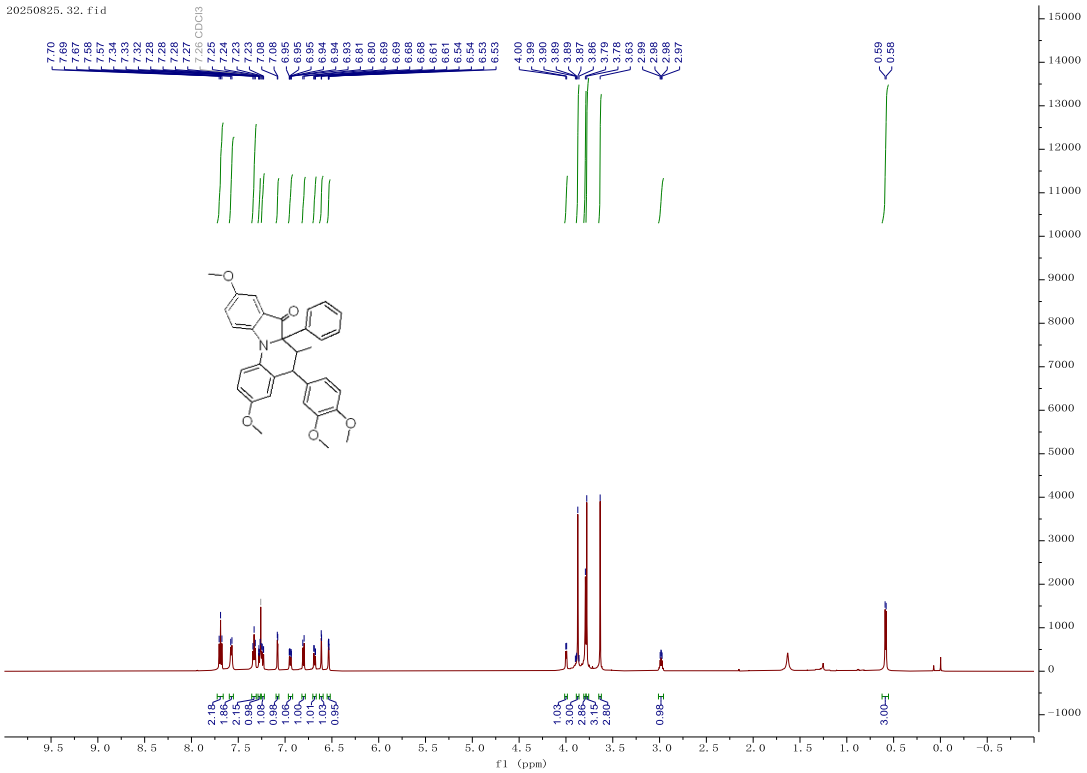
$^{1}$H NMR of compound **4z** (in $CDCl_3$)



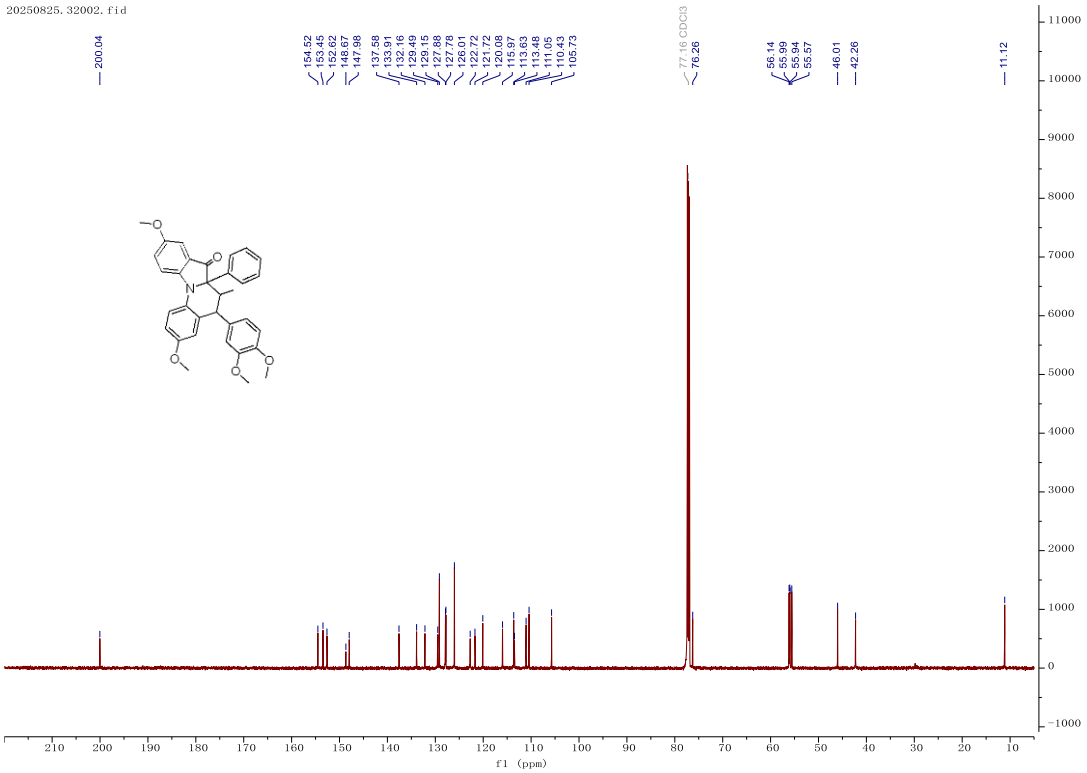
$^{13}$C NMR of compound **4z** (in $CDCl_3$)



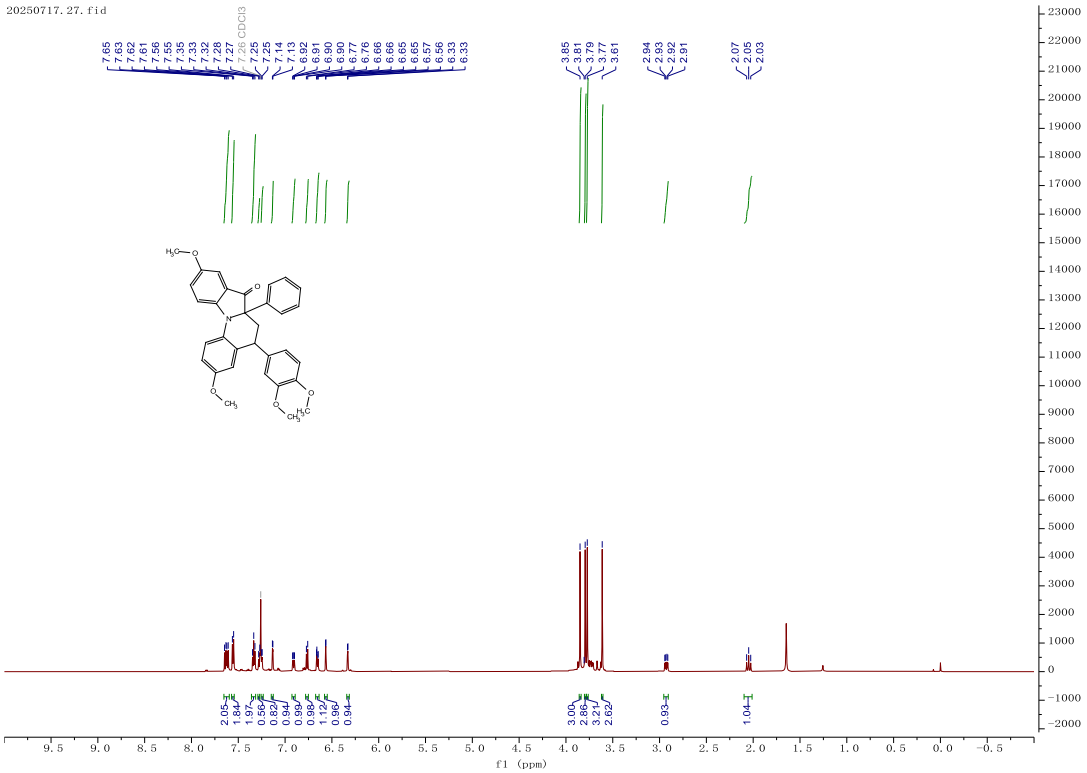

$^{1}$H NMR of compound **4aa** (in $CDCl_3$)



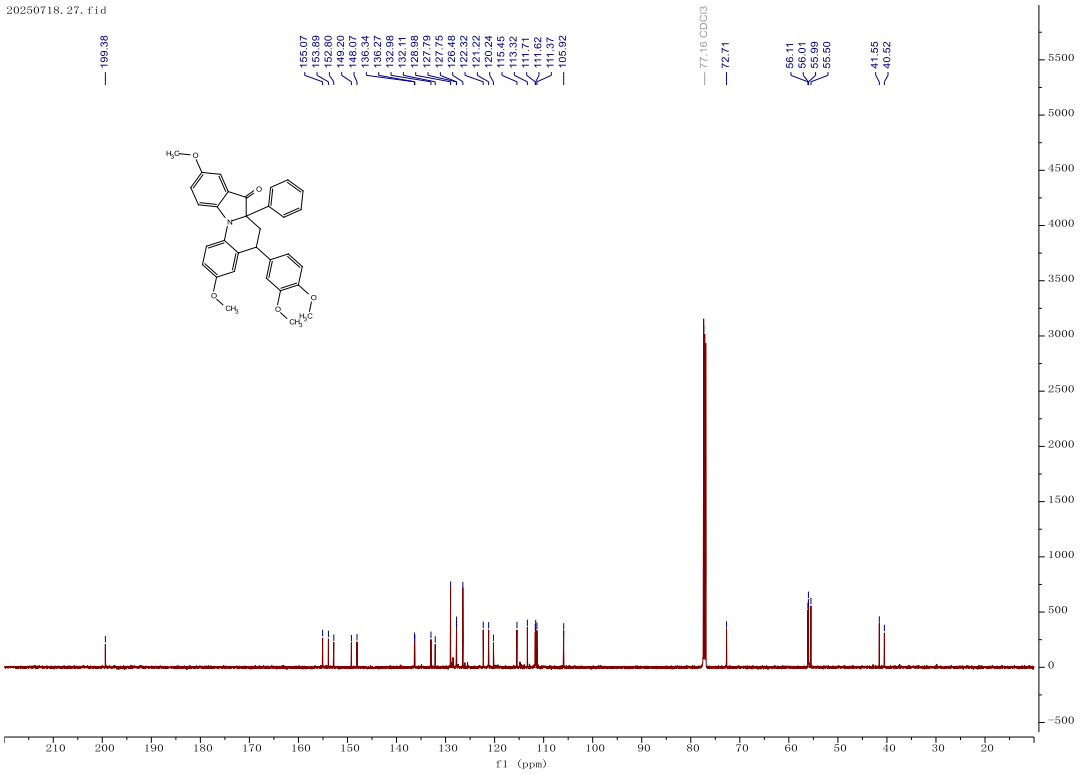

$^{13}$C NMR of compound **4aa** (in $CDCl_3$)



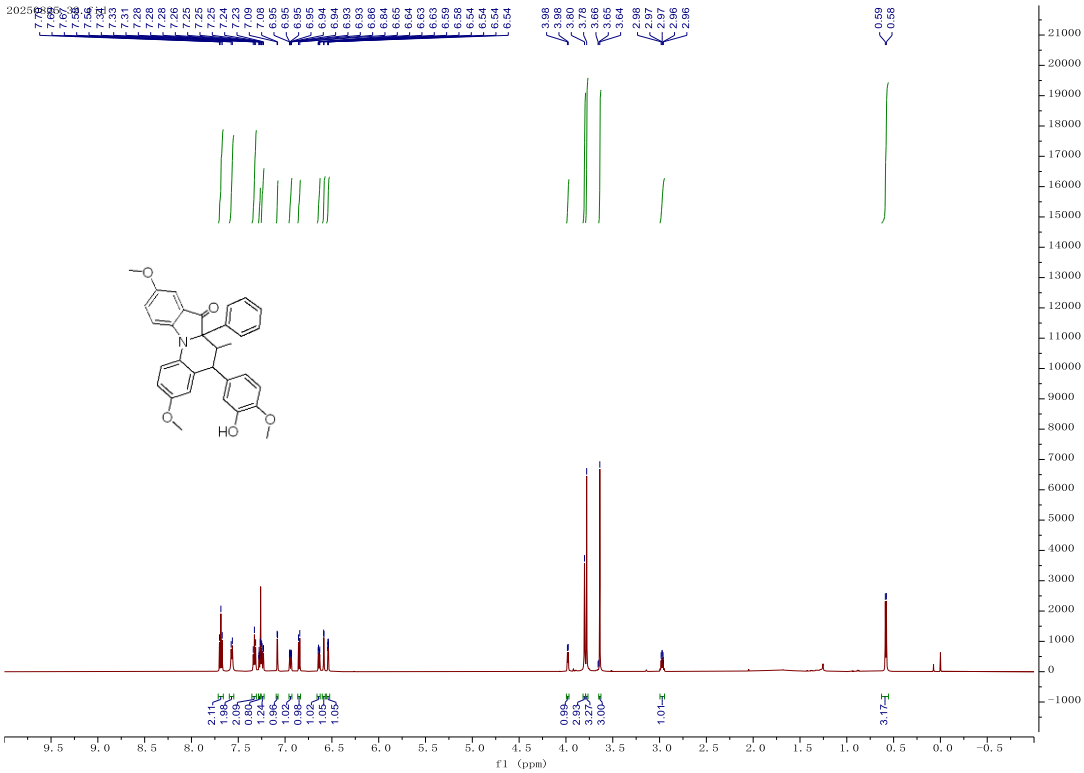

$^{1}$H NMR of compound **4ab** (in $CDCl_3$)



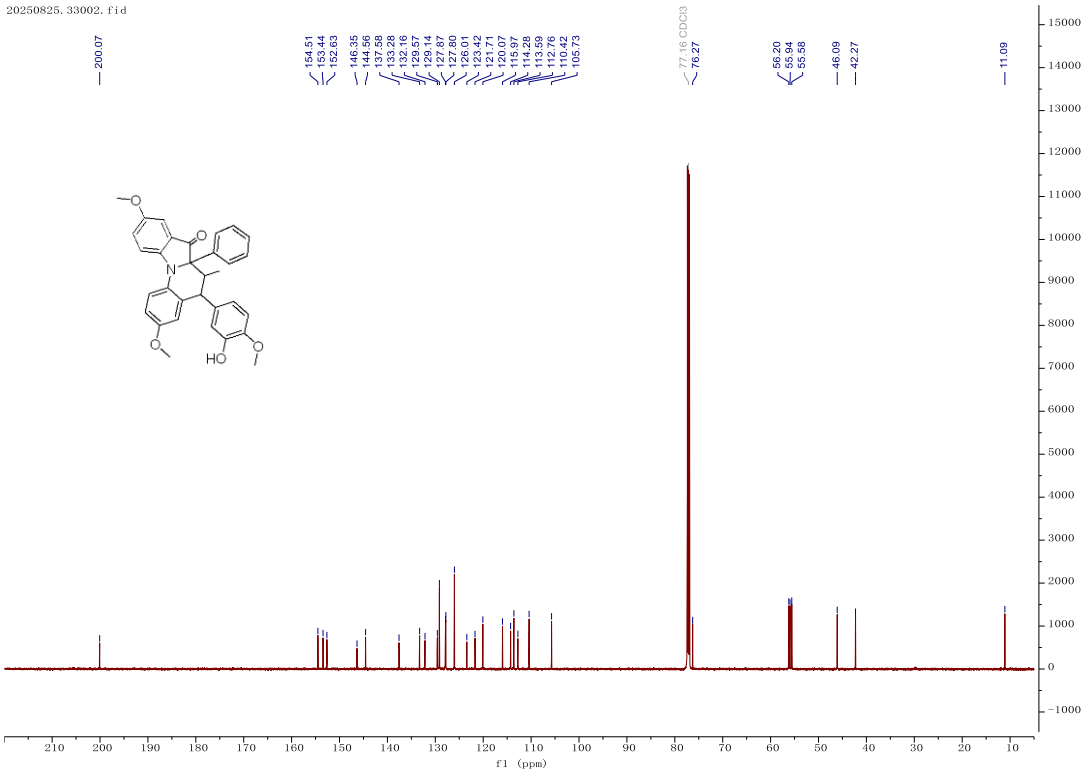

$^{13}$C NMR of compound **4ab** (in $CDCl_3$)



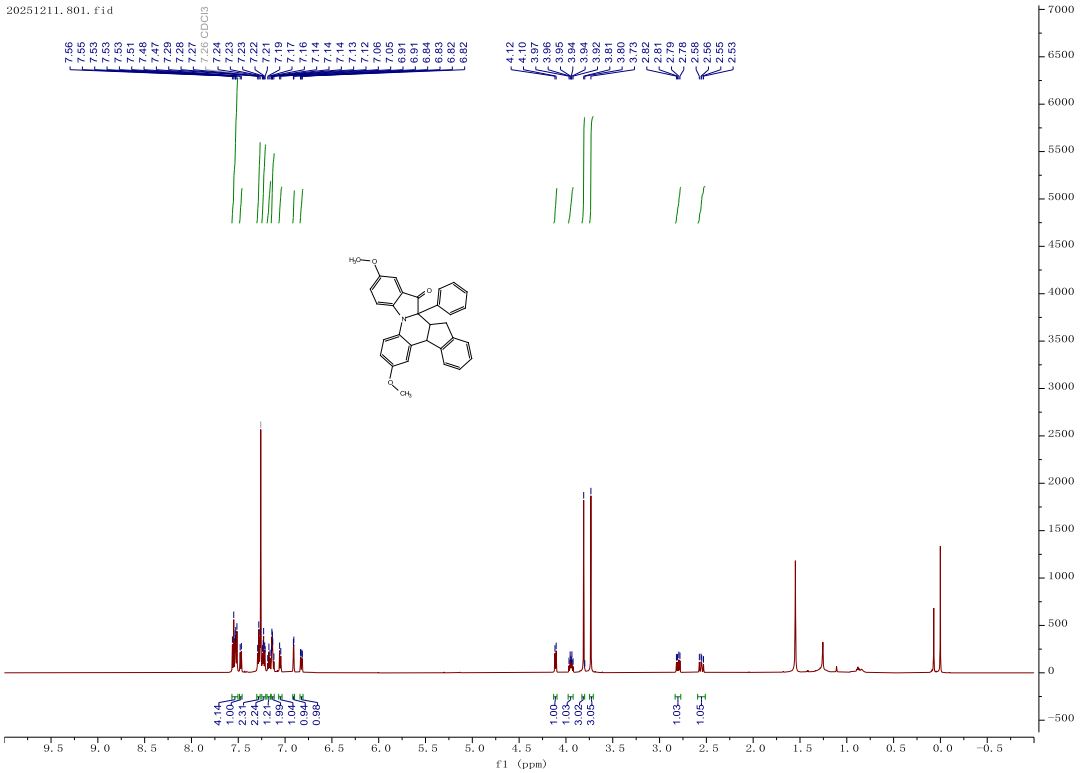

$^{1}$H NMR of compound **4ac** (in $CDCl_3$)



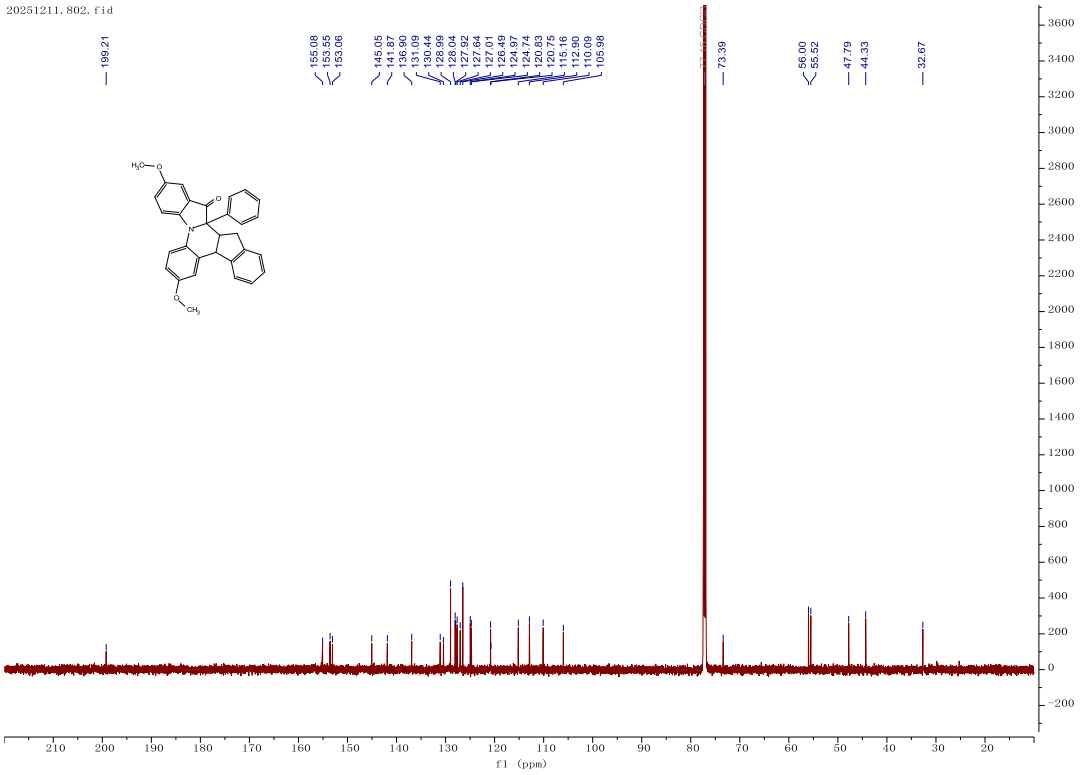

$^{13}$C NMR of compound **4ac** (in $CDCl_3$)



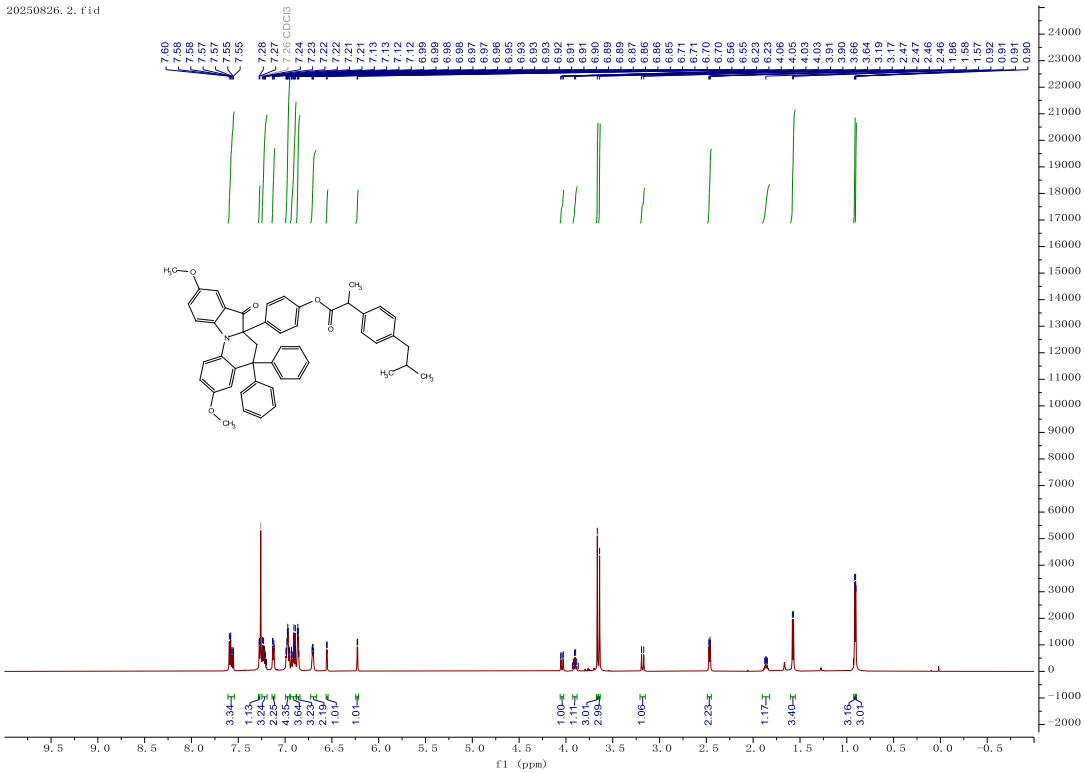

$^{1}$H NMR of compound **4ad** (in $CDCl_3$)



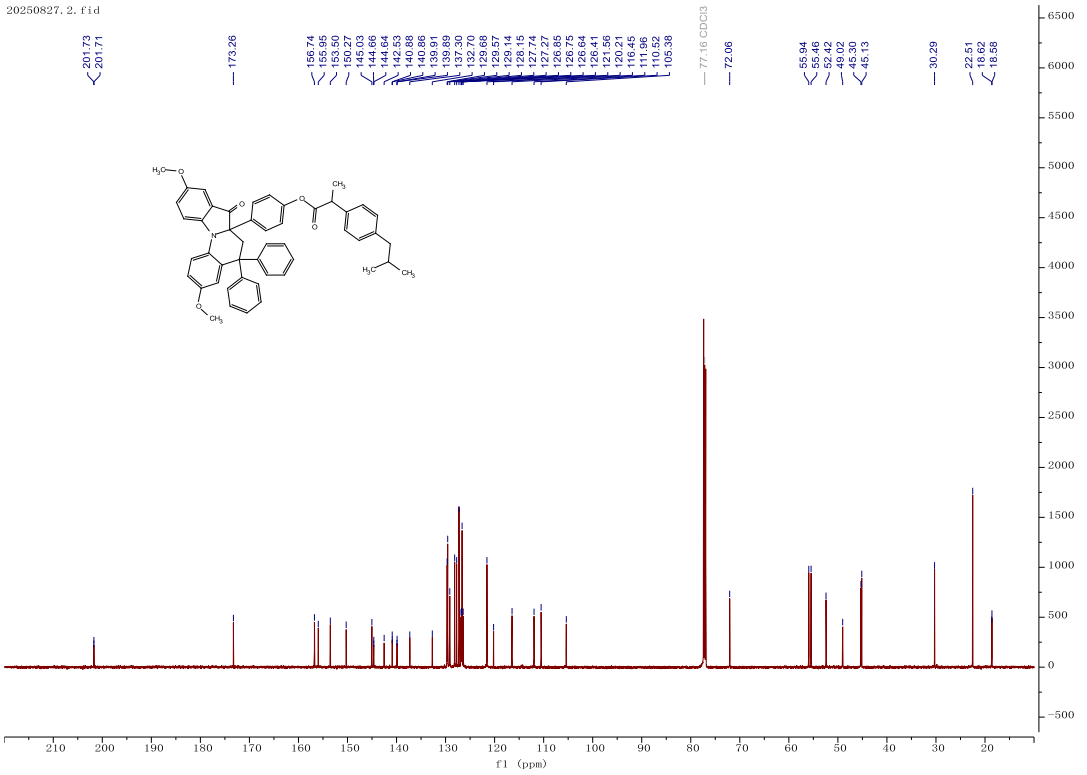

$^{13}$C NMR of compound **4ad** (in $CDCl_3$)



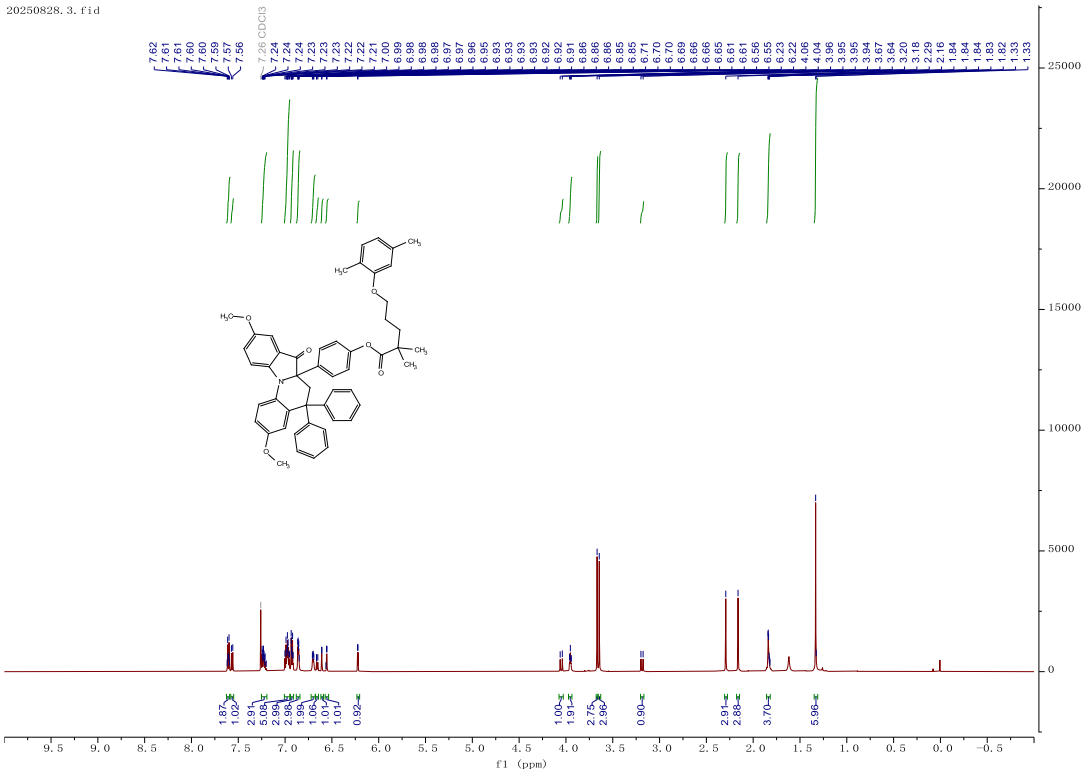

$^{1}$H NMR of compound **4ae** (in $CDCl_3$)



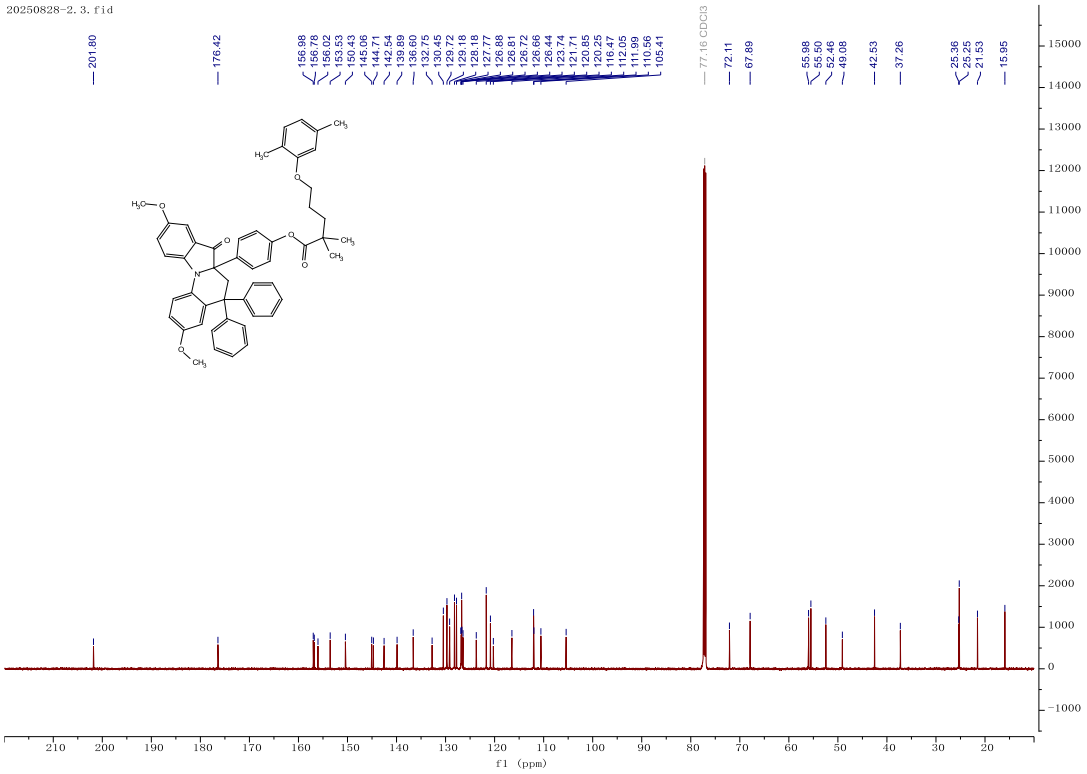

$^{13}$C NMR of compound **4ae** (in $CDCl_3$)



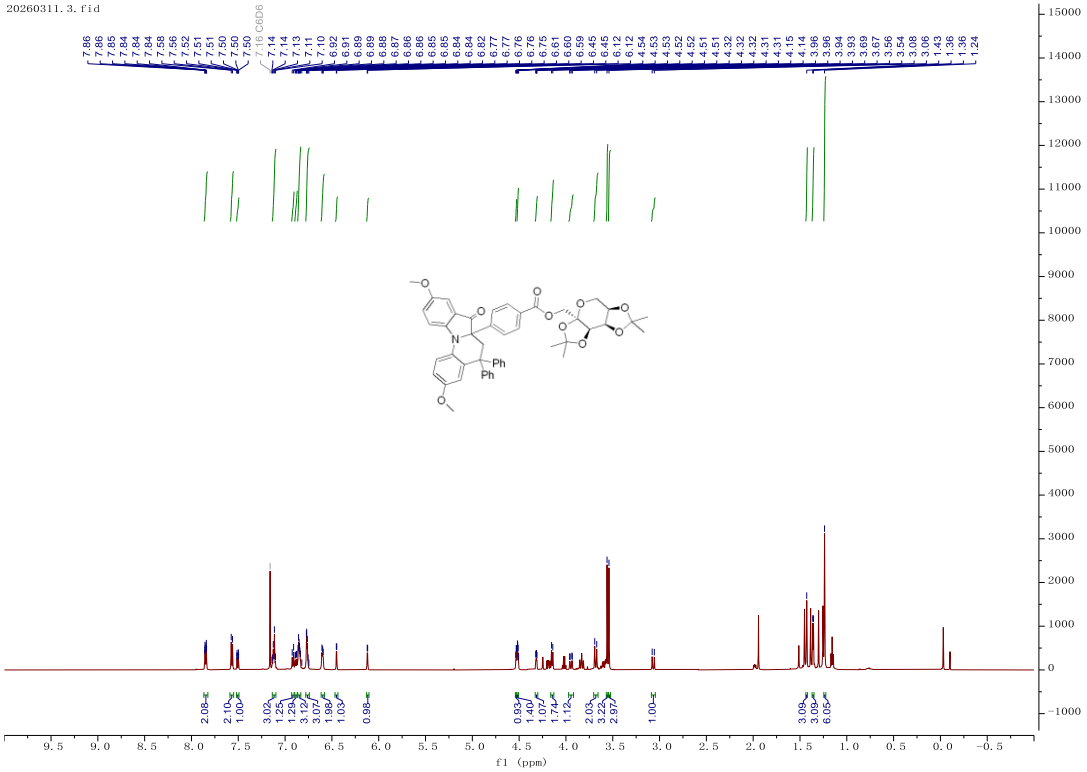

$^{1}$H NMR of compound **4af** (in $CDCl_3$)



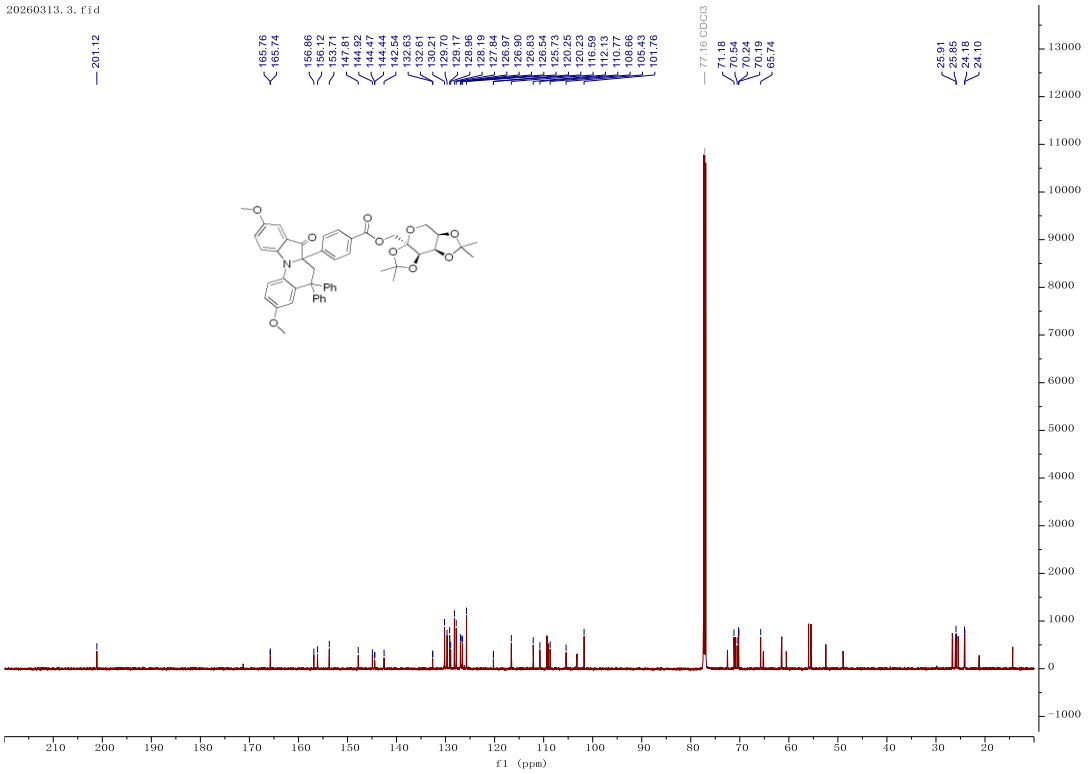
$^{13}$C NMR of compound **4af** (in $CDCl_3$)



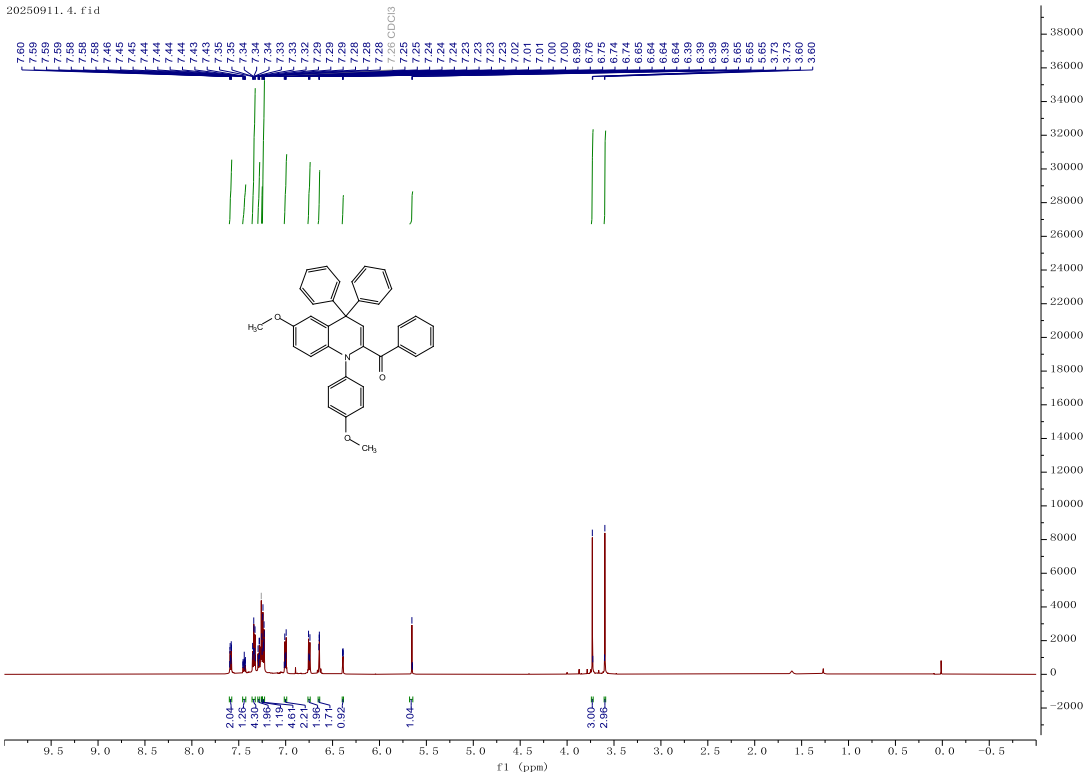

$^{1}$H NMR of compound **4ag** (in $CDCl_3$)



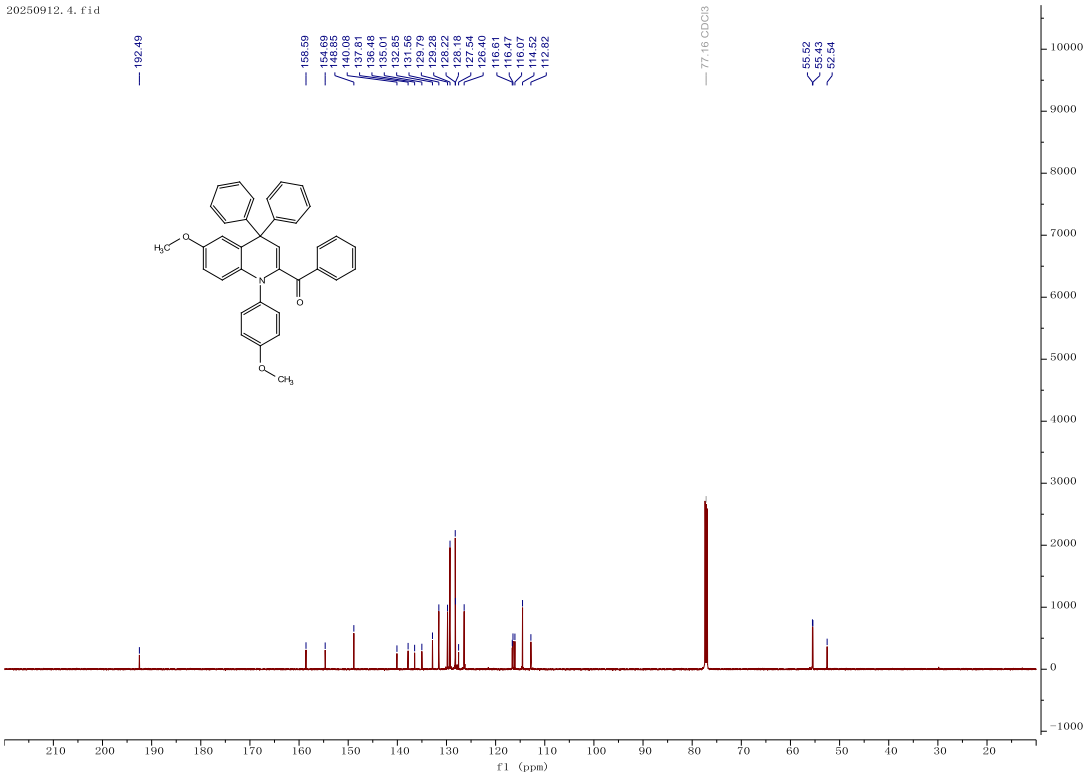
$^{13}$C NMR of compound **4ag**(in $CDCl_3$)



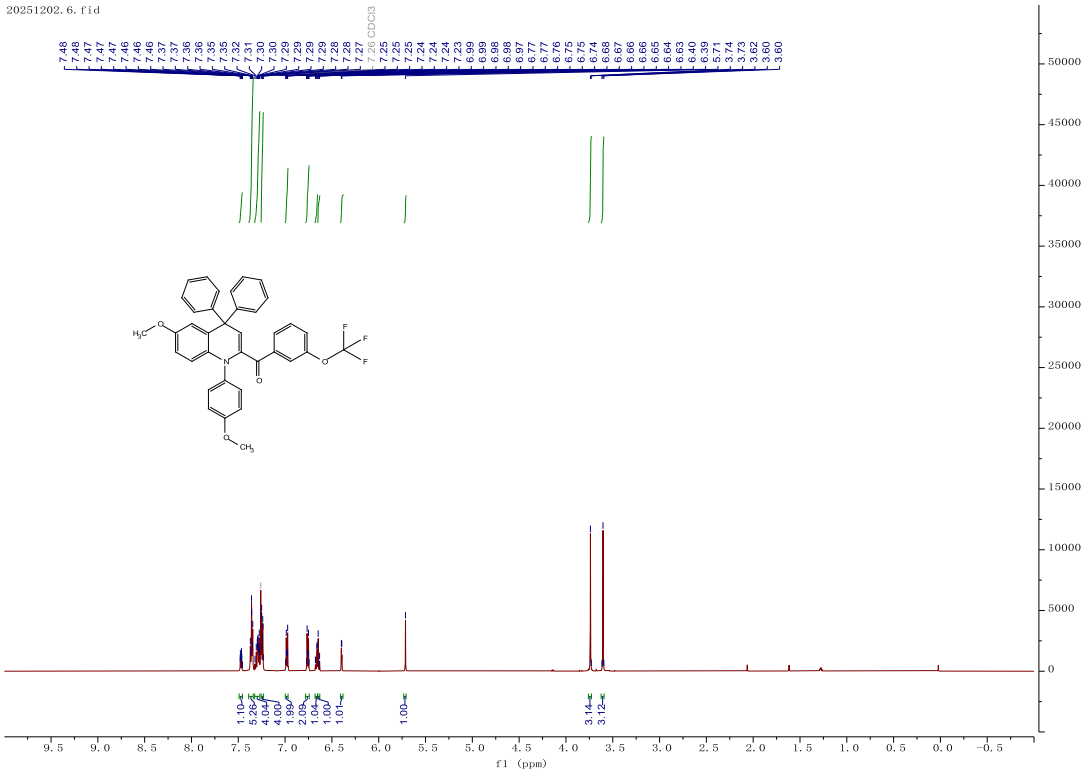

$^{1}$H NMR of compound **5a** ($CDCl_3$)



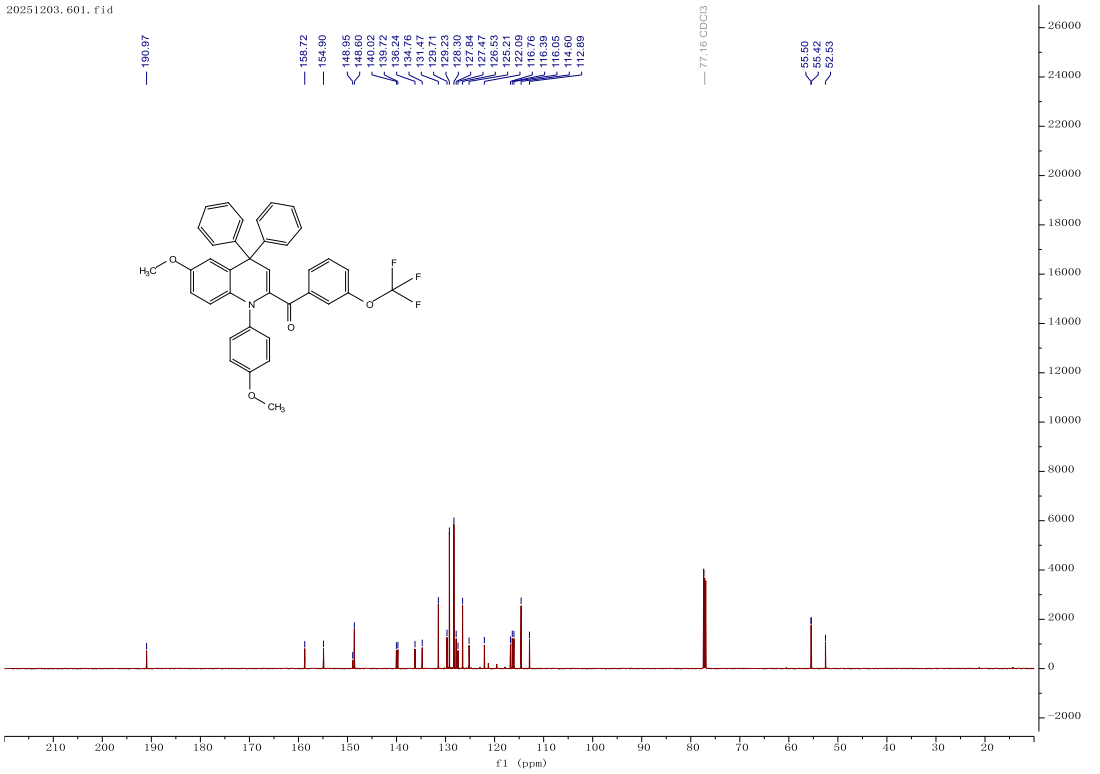
$^{13}$C NMR of compound **5a** (in $CDCl_3$)



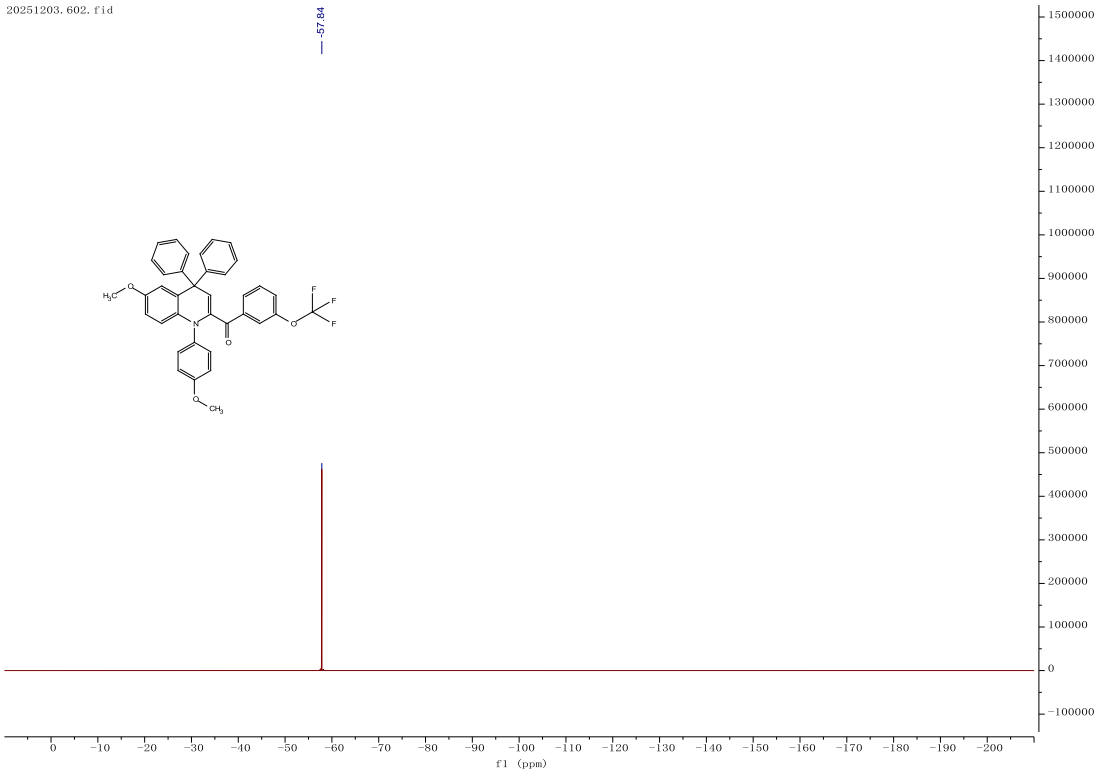

$^{1}$H NMR of compound **5b** (in $CDCl_3$)



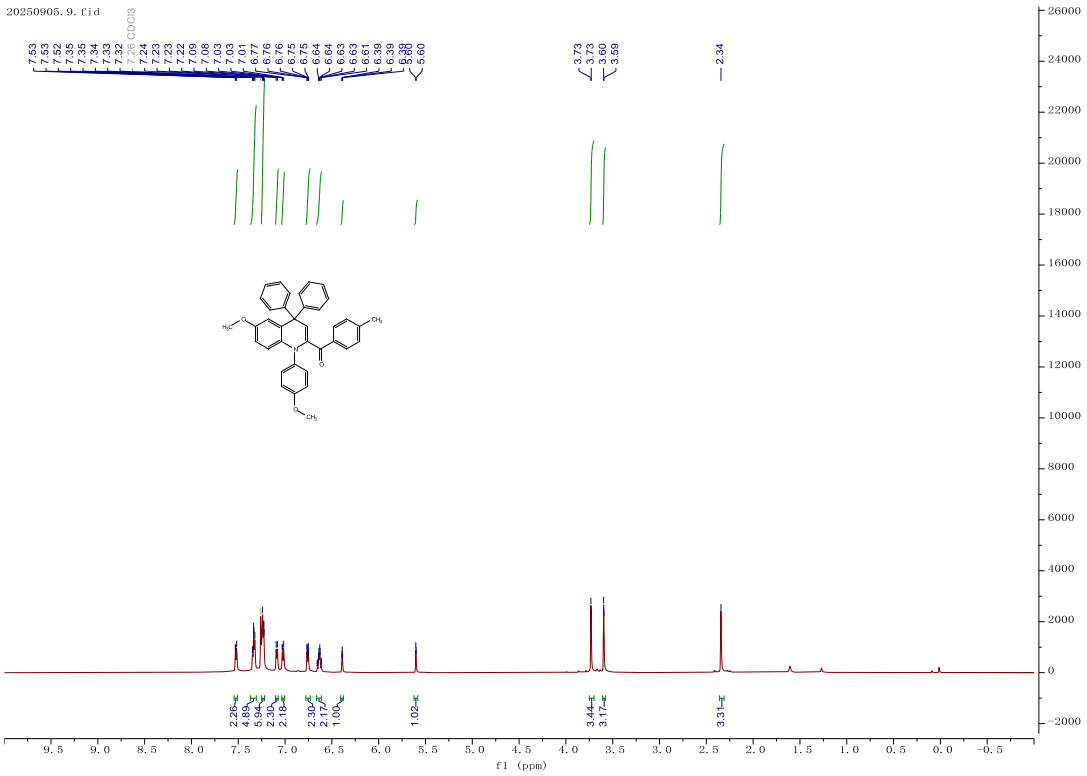
## $^{13}C$ NMR of compound **5b** (in $CDCl_3$)



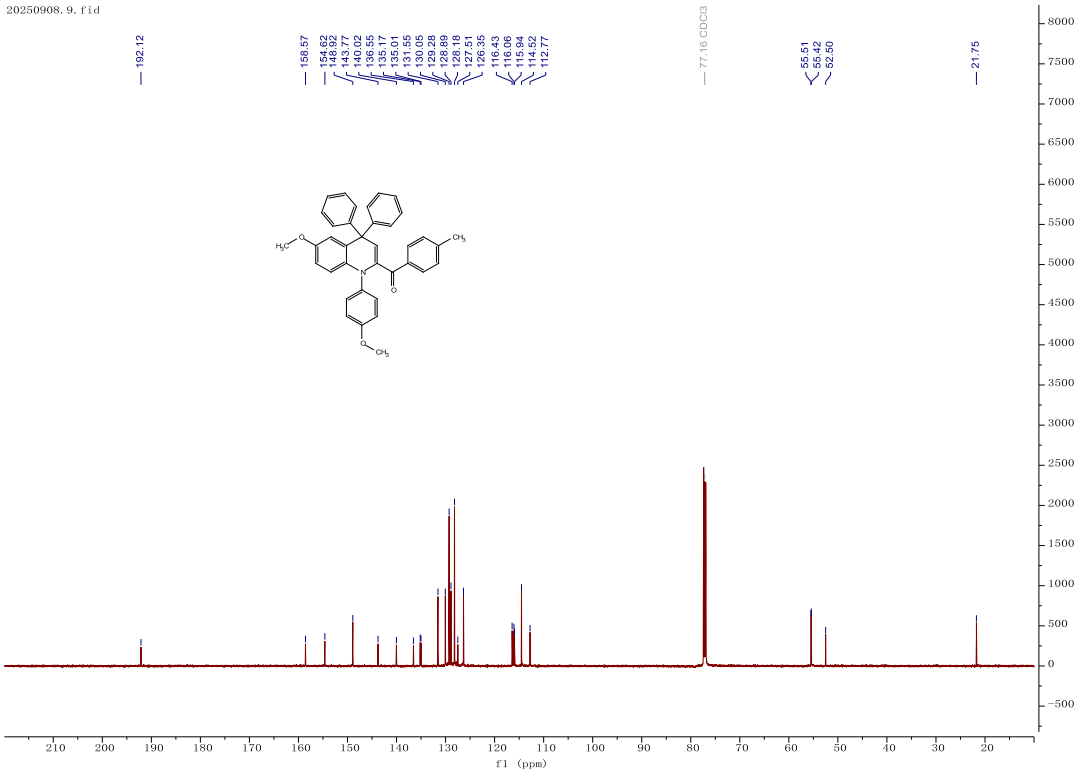

## $^{19}F$ NMR of compound **5b** (in $CDCl_3$)



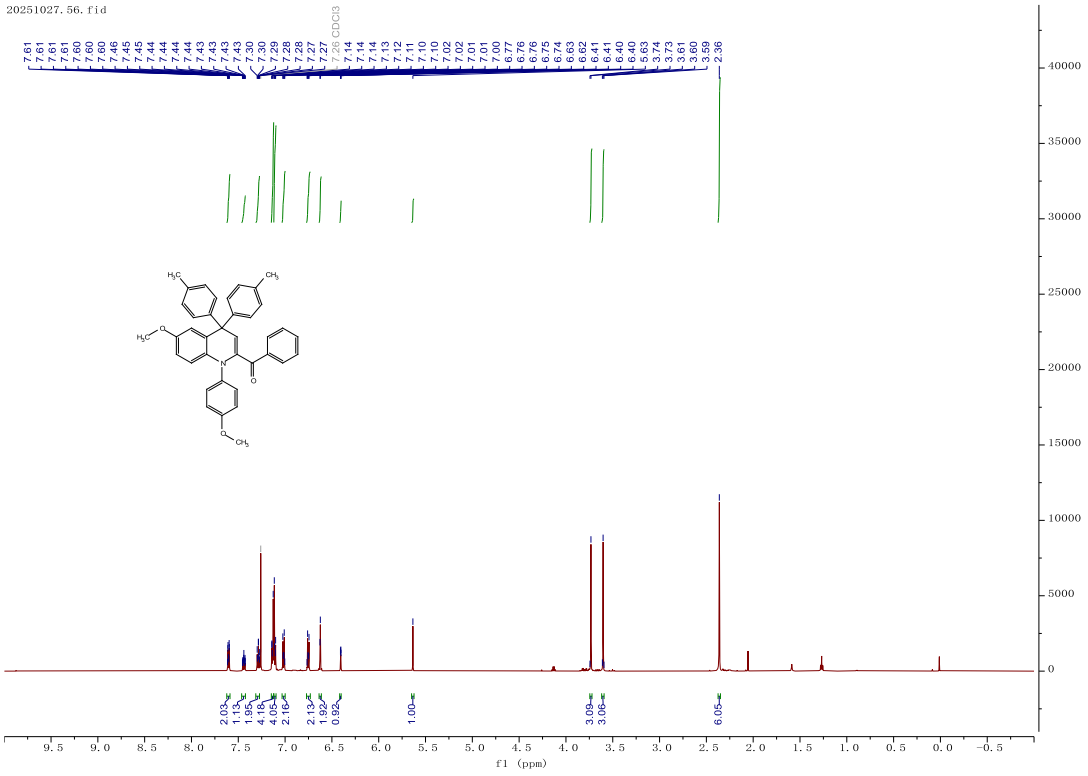
## $^{1}$H NMR of compound **5c** (in $CDCl_3$)



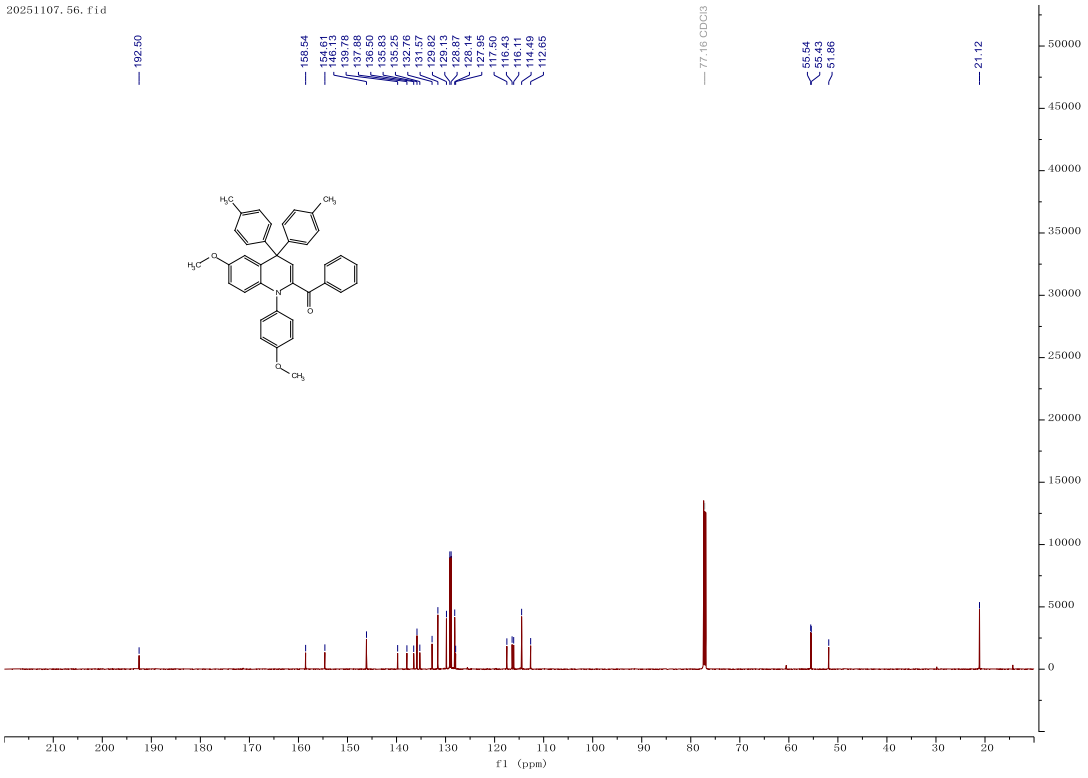

## $^{13}$C NMR of compound **5c** (in $CDCl_3$)



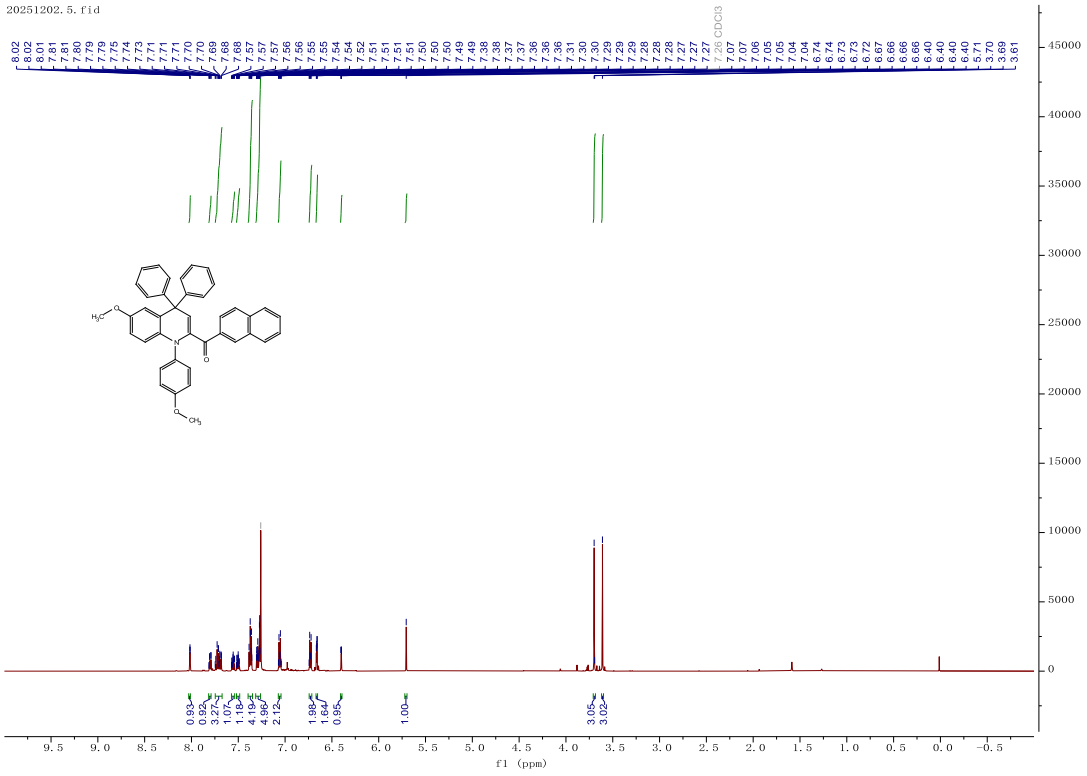
$^{1}$H NMR of compound **5d**(in $CDCl_3$)



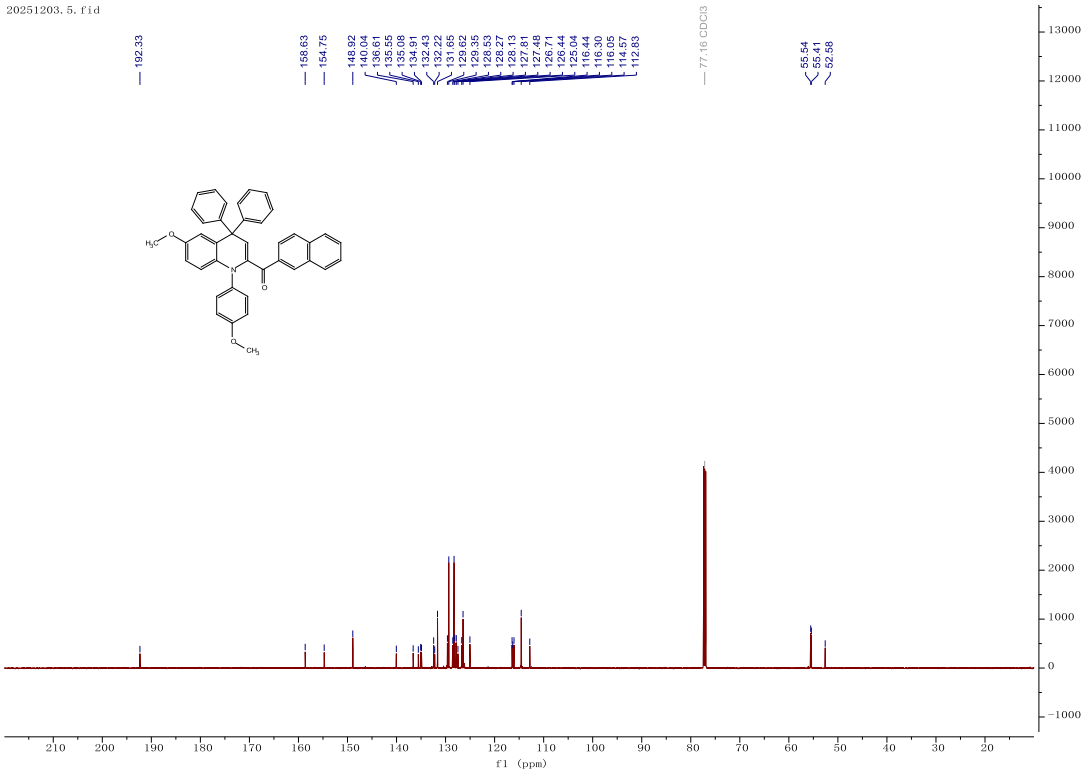

$^{13}$C NMR of compound **5d** (in $CDCl_3$)



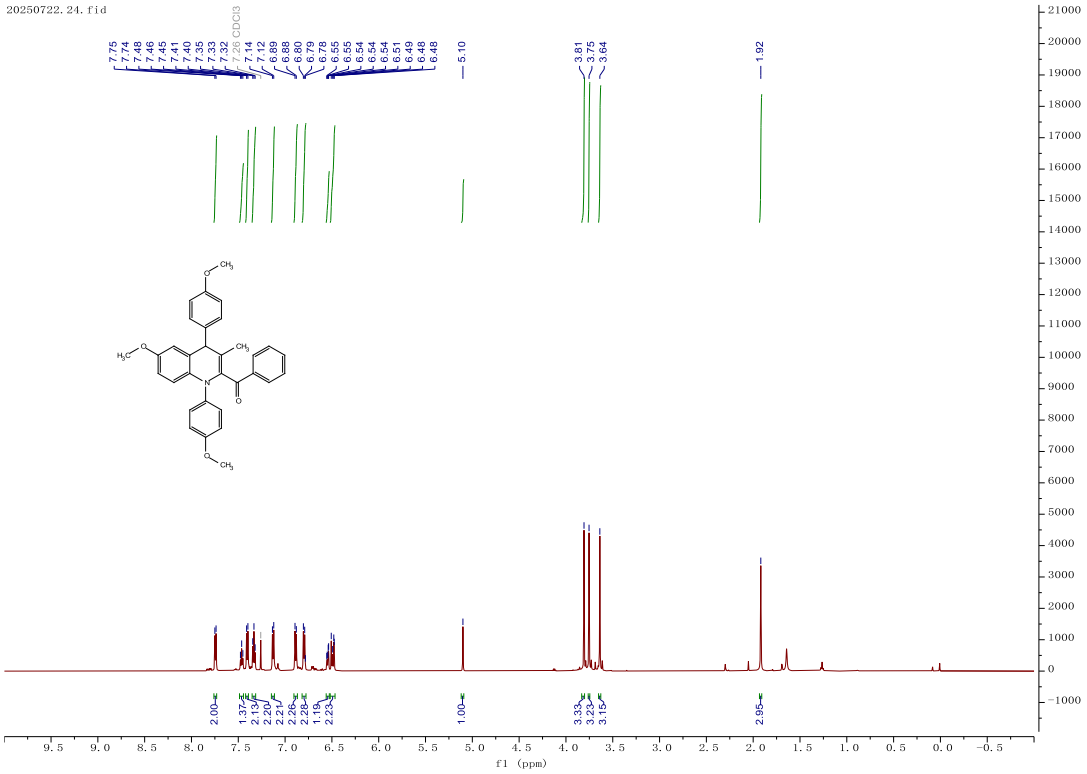
$^{1}$H NMR of compound **5e** (in $CDCl_3$)



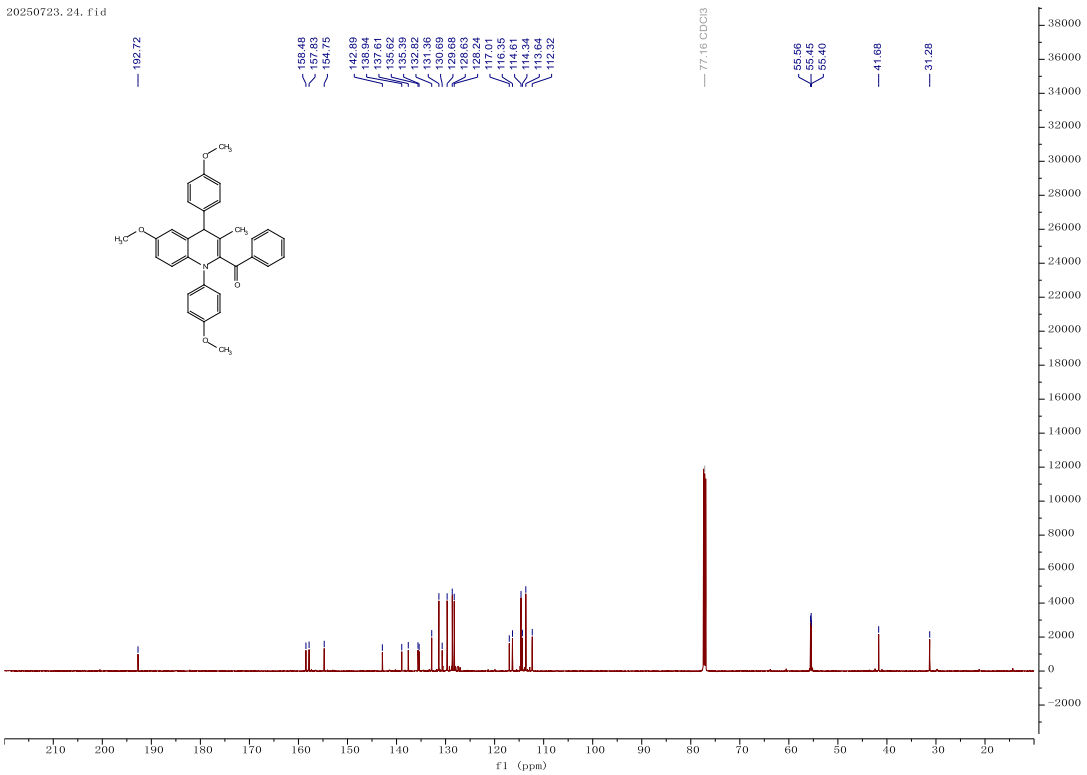

$^{13}$C NMR of compound **5e** (in $CDCl_3$)



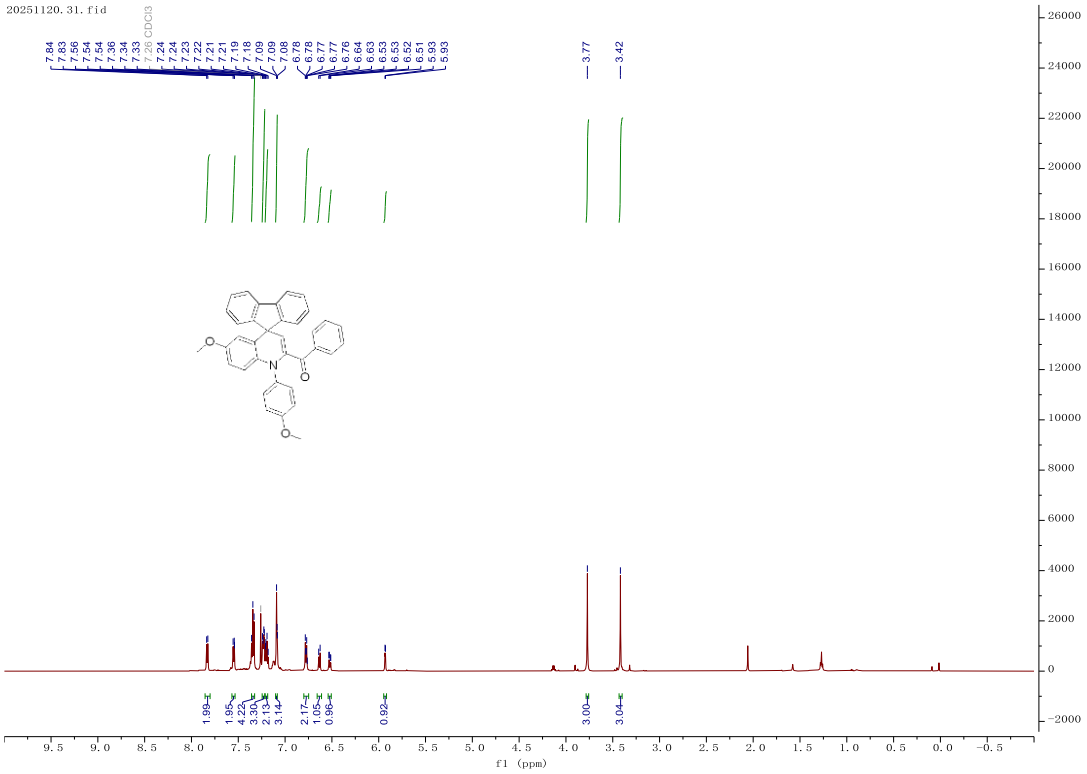
$^{1}$H NMR of compound **5f** (in $CDCl_3$)



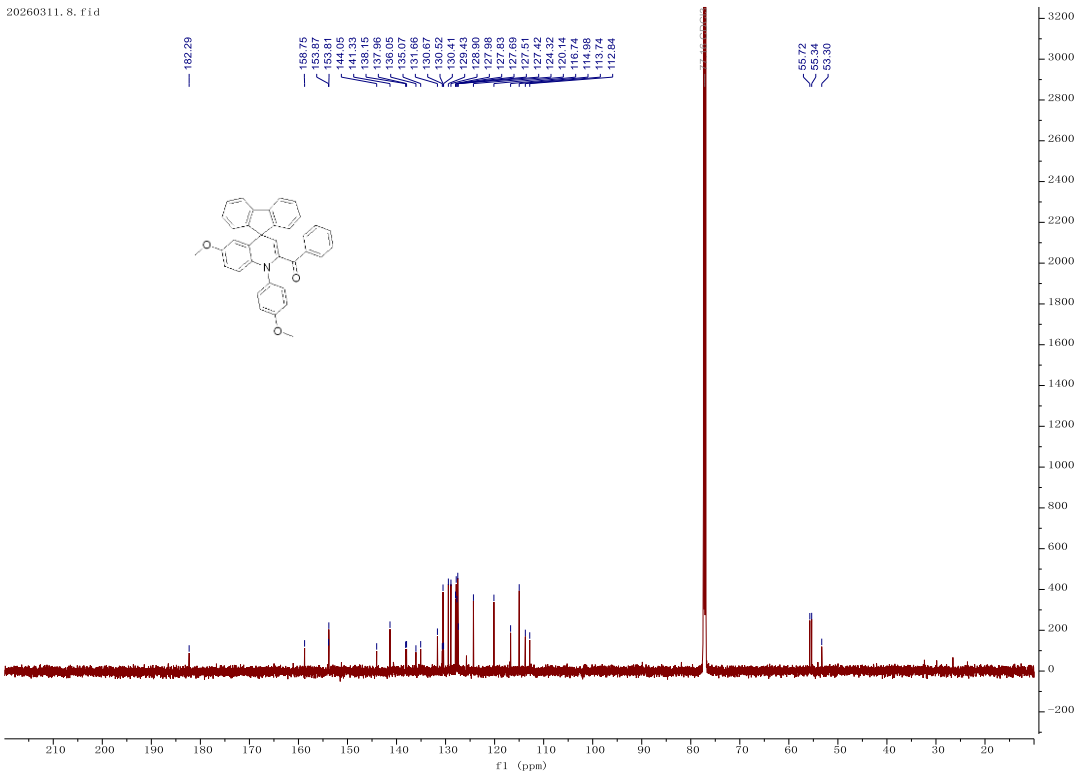

$^{13}$C NMR of compound **5f** (in $CDCl_3$)



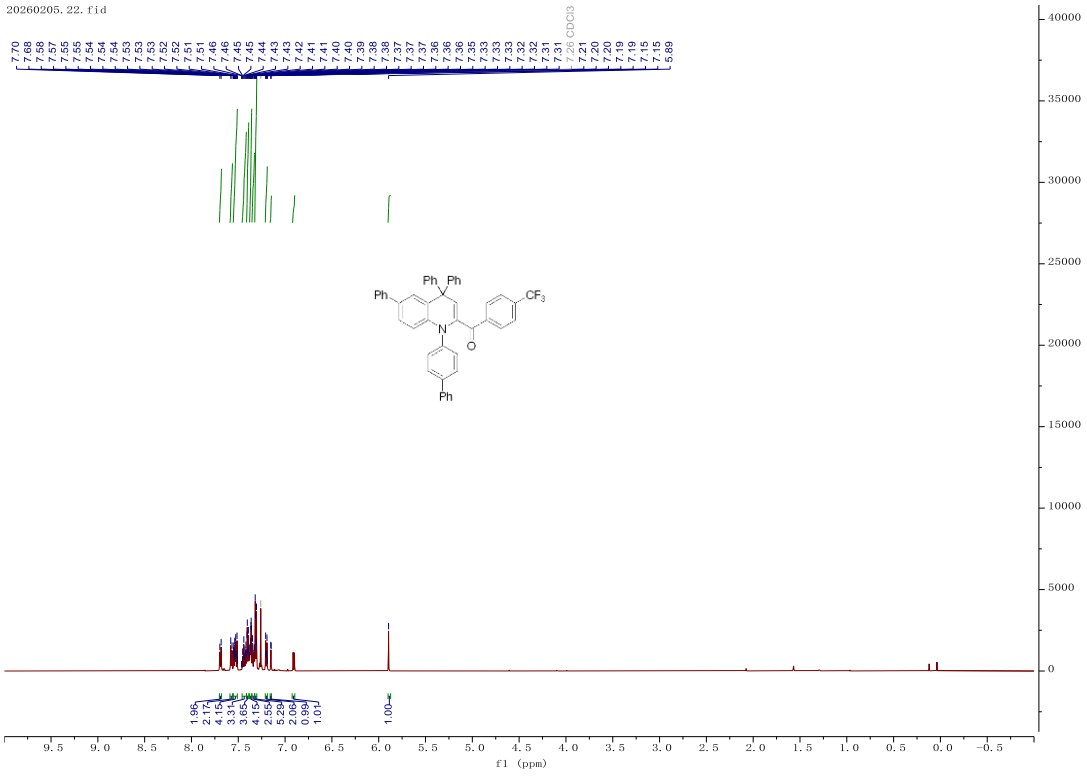
$^{1}$H NMR of compound **5g** (in $CDCl_3$)



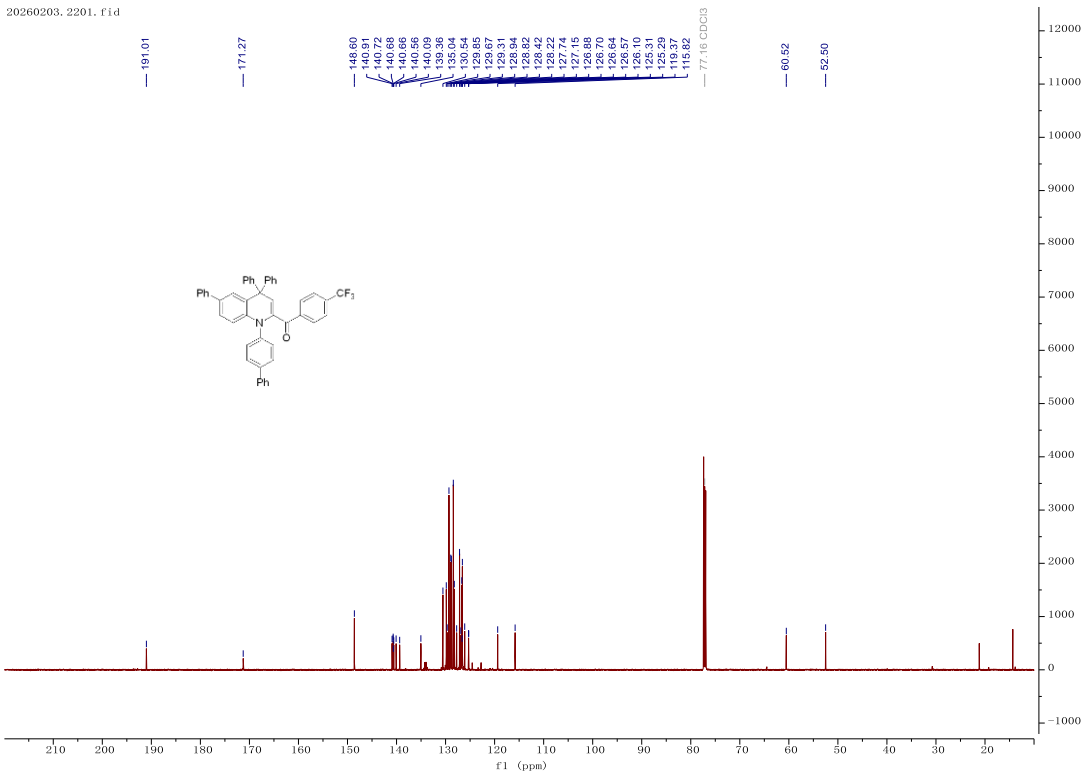

$^{13}$C NMR of compound **5g** (in $CDCl_3$)



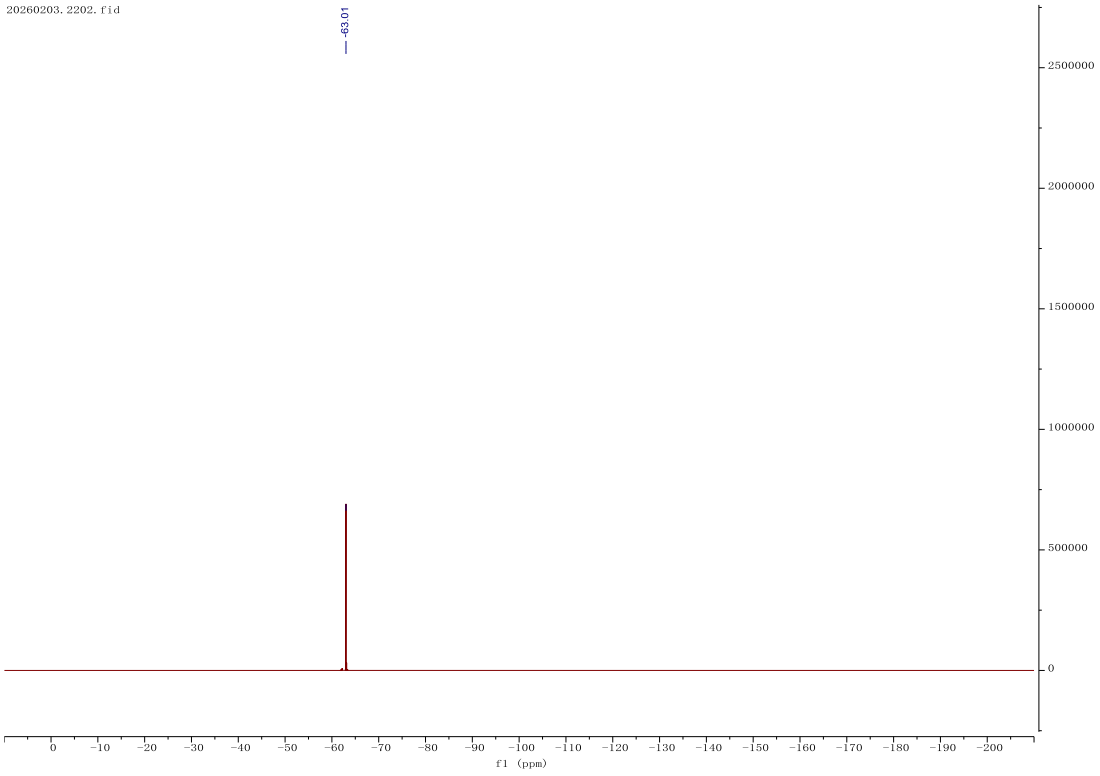
$^{1}$H NMR of compound **5h** (in $CDCl_3$)



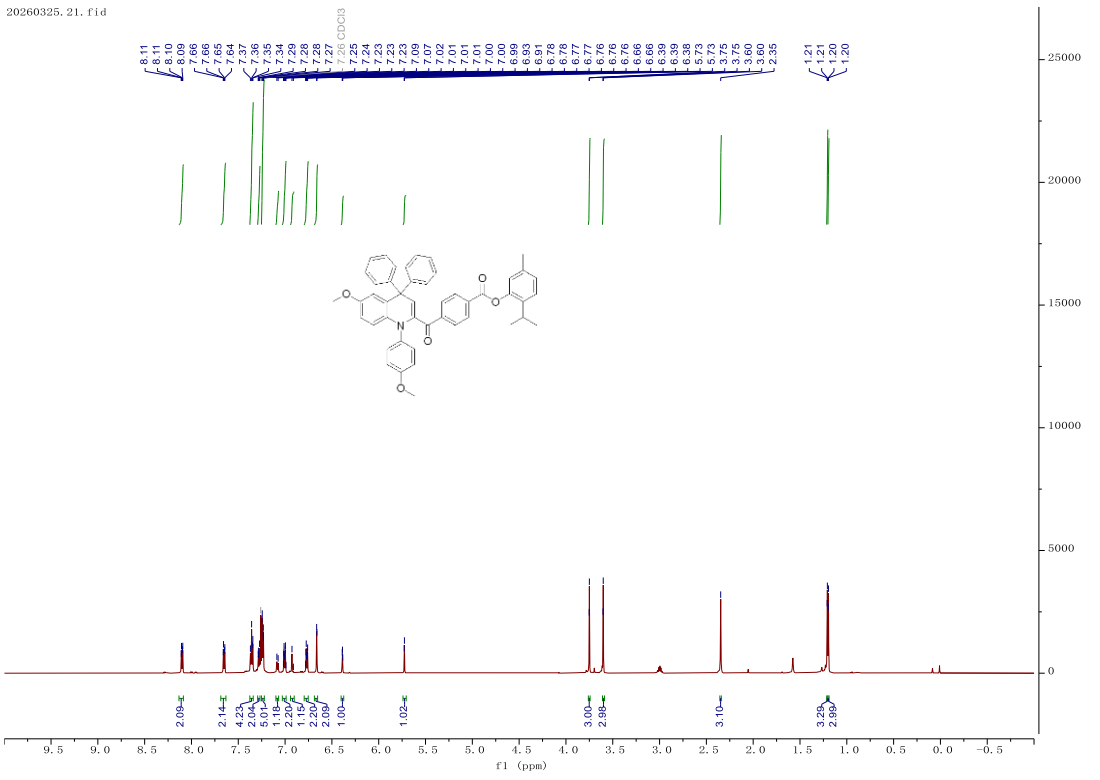

$^{13}$C NMR of compound **5h** (in $CDCl_3$)



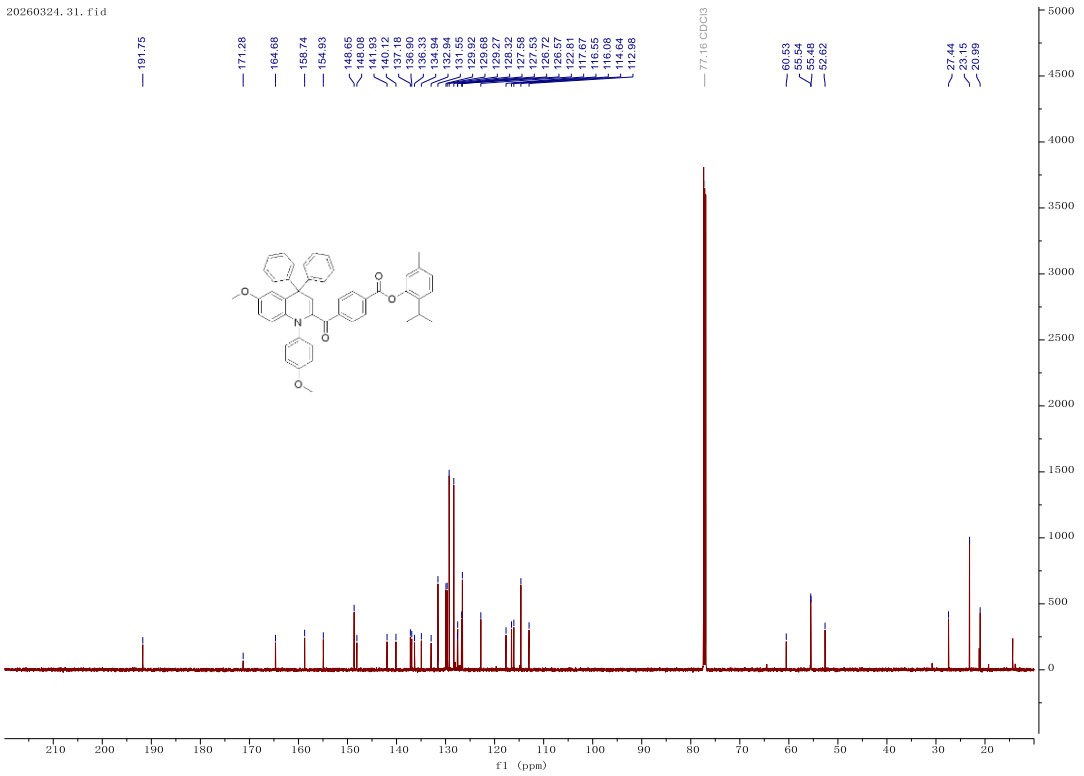
$^{19}$F NMR of compound **5h** (in $CDCl_3$)



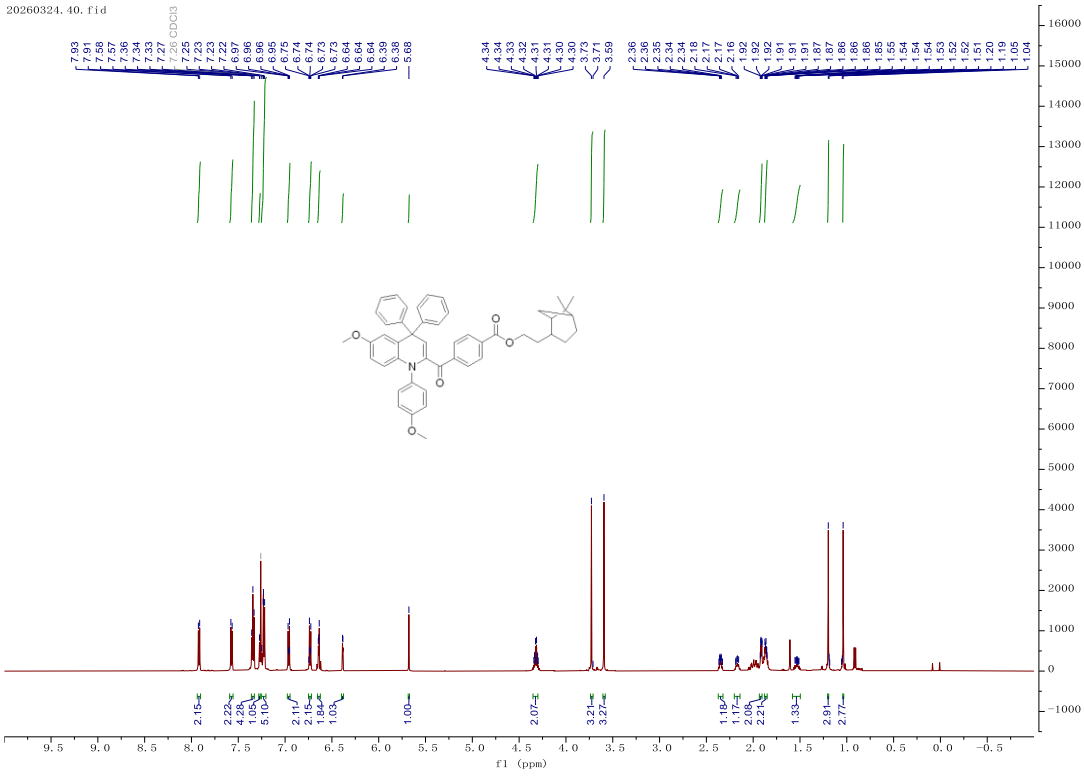

$^{1}$H NMR of compound **5i** (in $CDCl_3$)



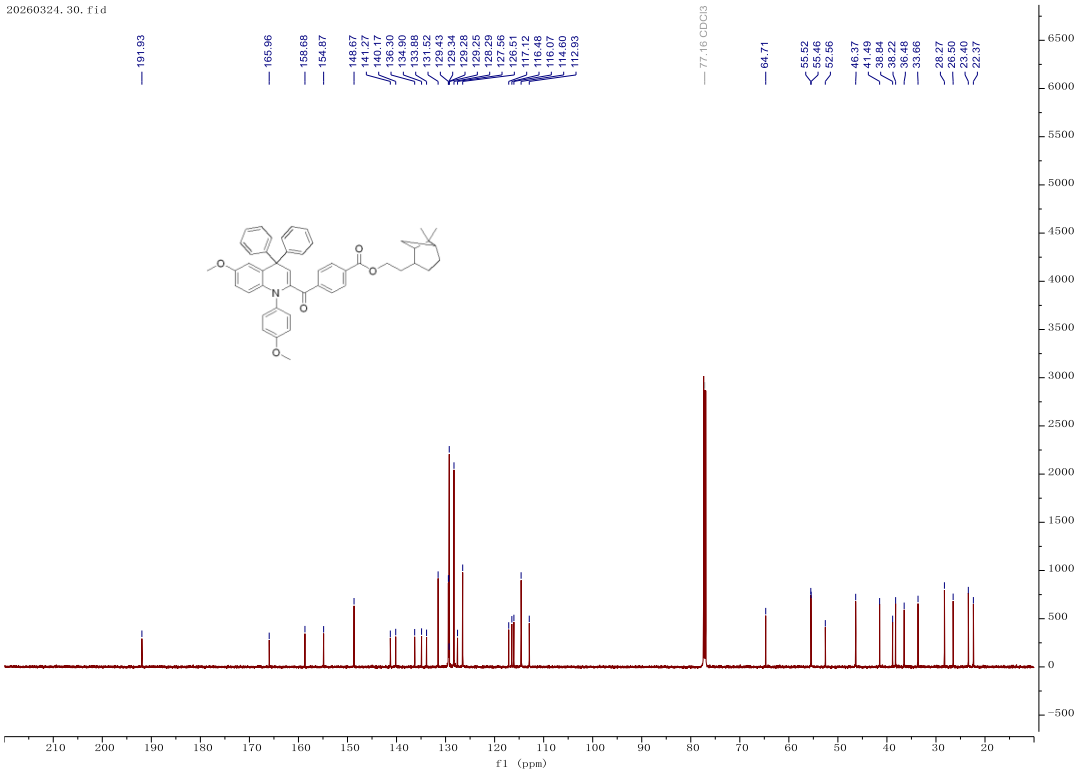
$^{13}$C NMR of compound **5i** (in $CDCl_3$)



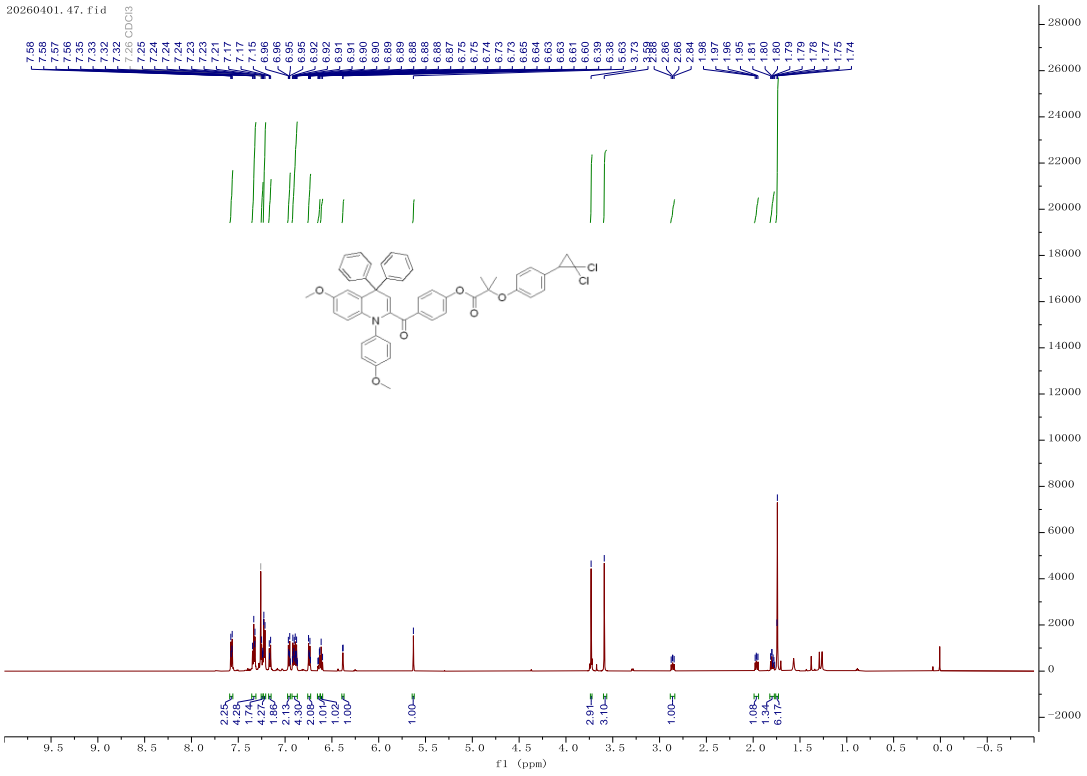

$^{1}$H NMR of compound **5j** (in $CDCl_3$)



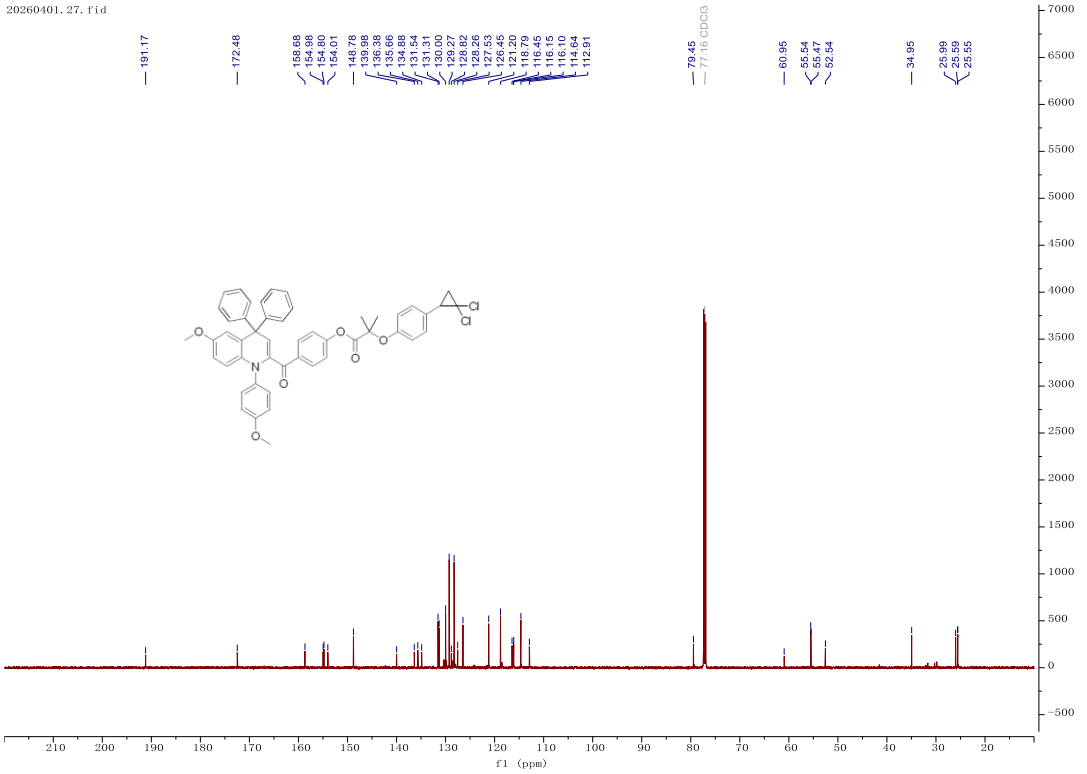
$^{13}$C NMR of compound **5j** (in $CDCl_3$)



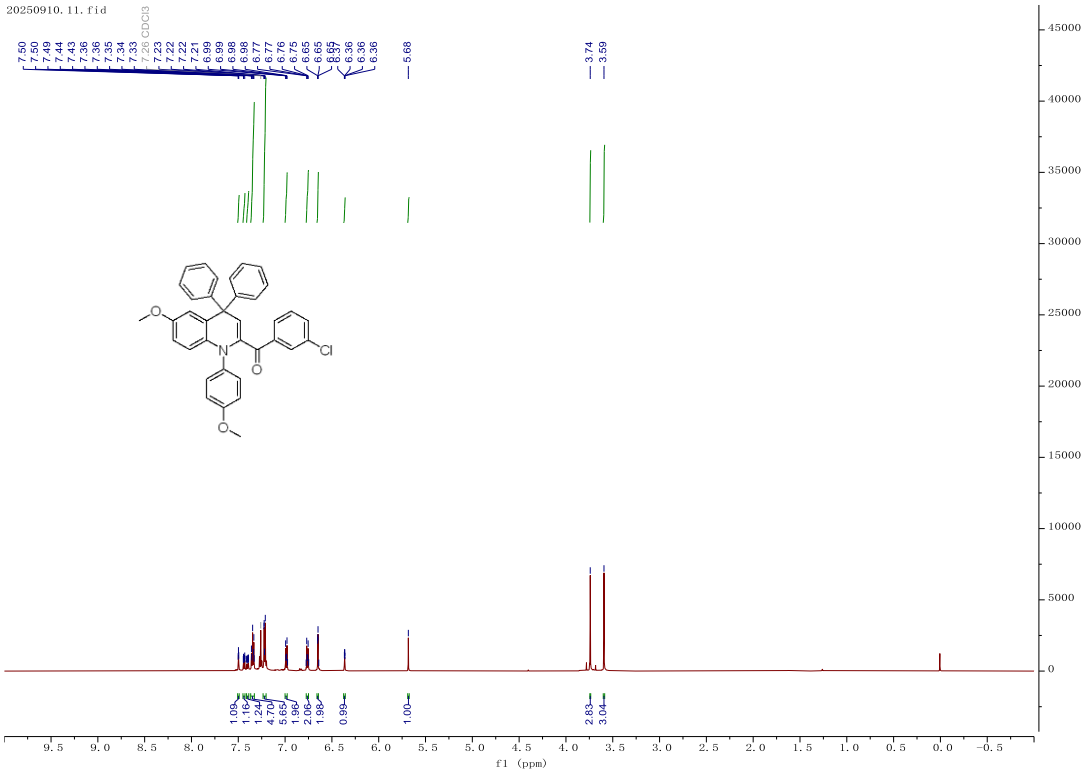

$^{1}$H NMR of compound **5k** (in $CDCl_3$)



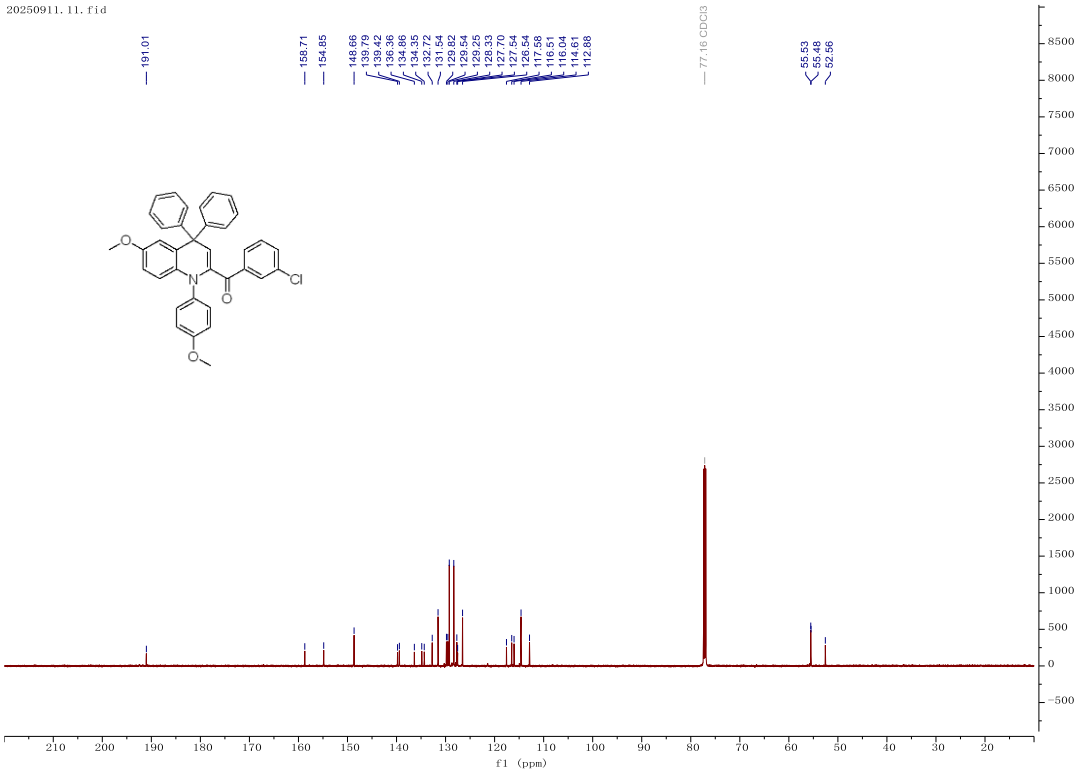
$^{13}$C NMR of compound **5k** (in $CDCl_3$)



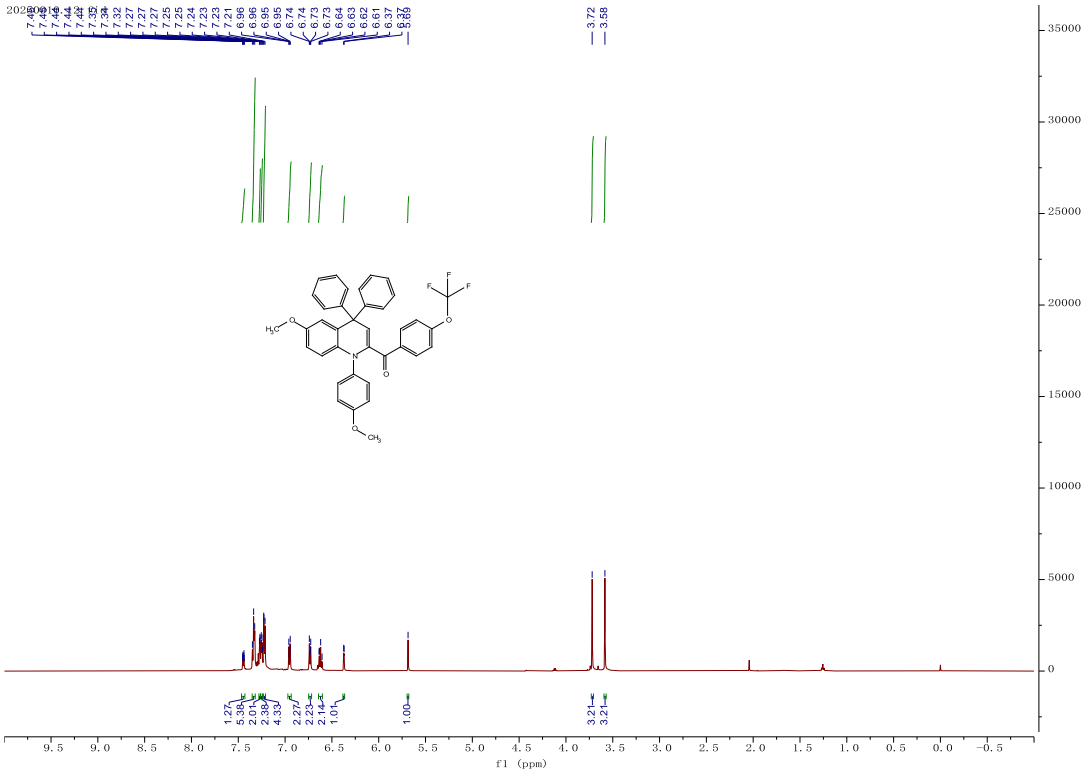

$^{1}$H NMR of compound **5m** (in $CDCl_3$)



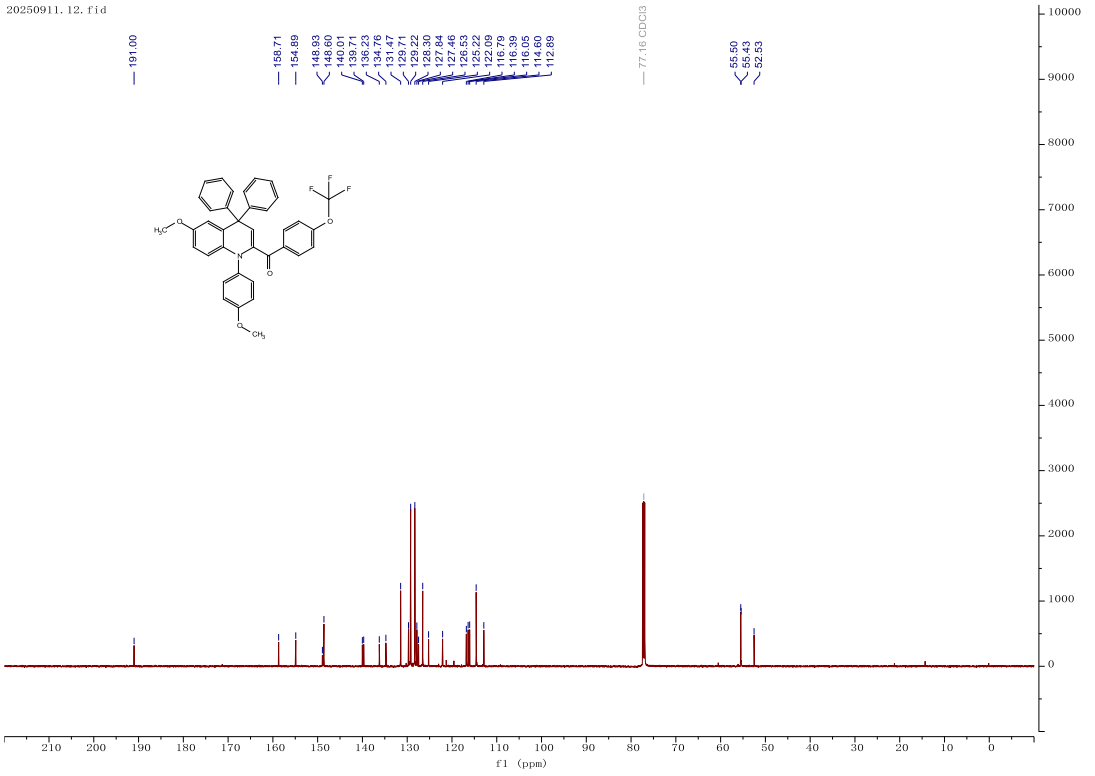
$^{13}$C NMR of compound **5m** (in $CDCl_3$)



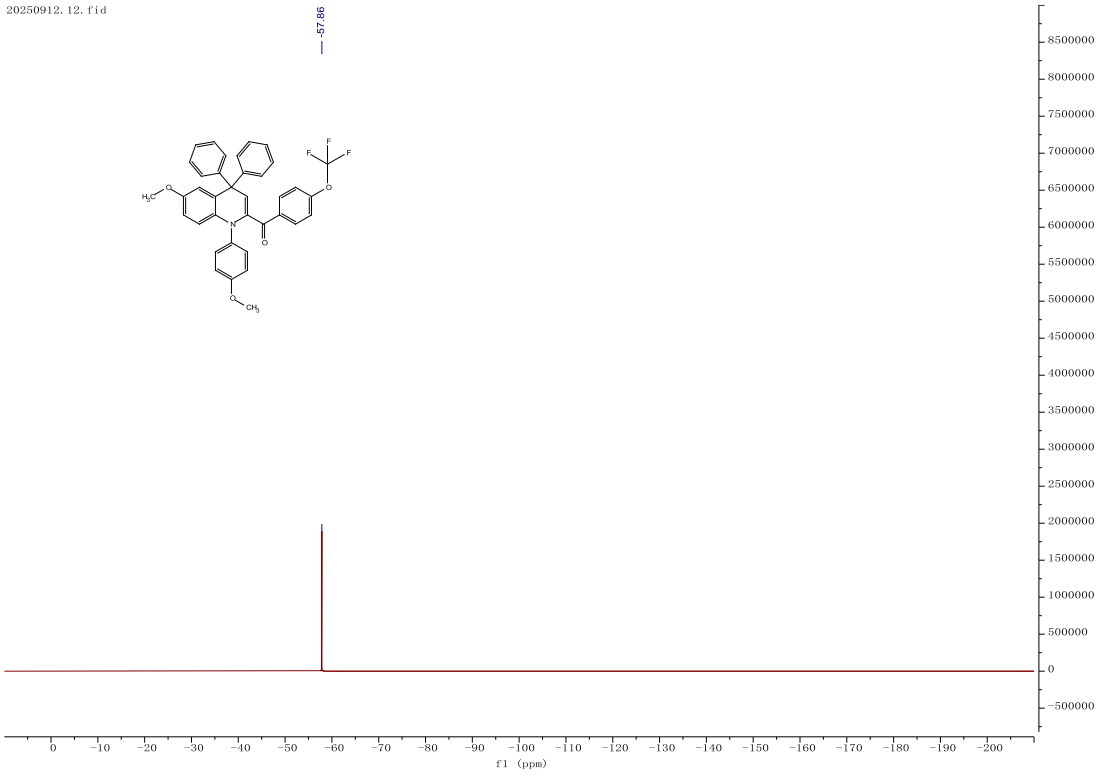

$^{1}$H NMR of compound **5n** (in $CDCl_3$)



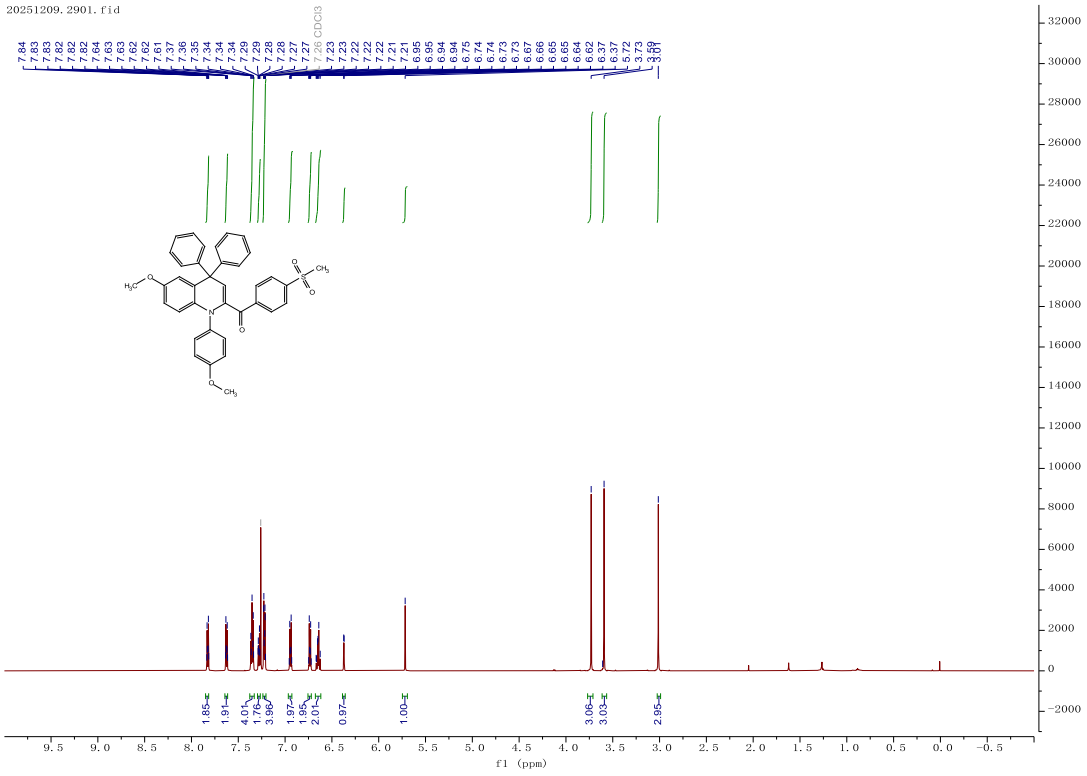
$^{13}$C NMR of compound **5n** (in $CDCl_3$)



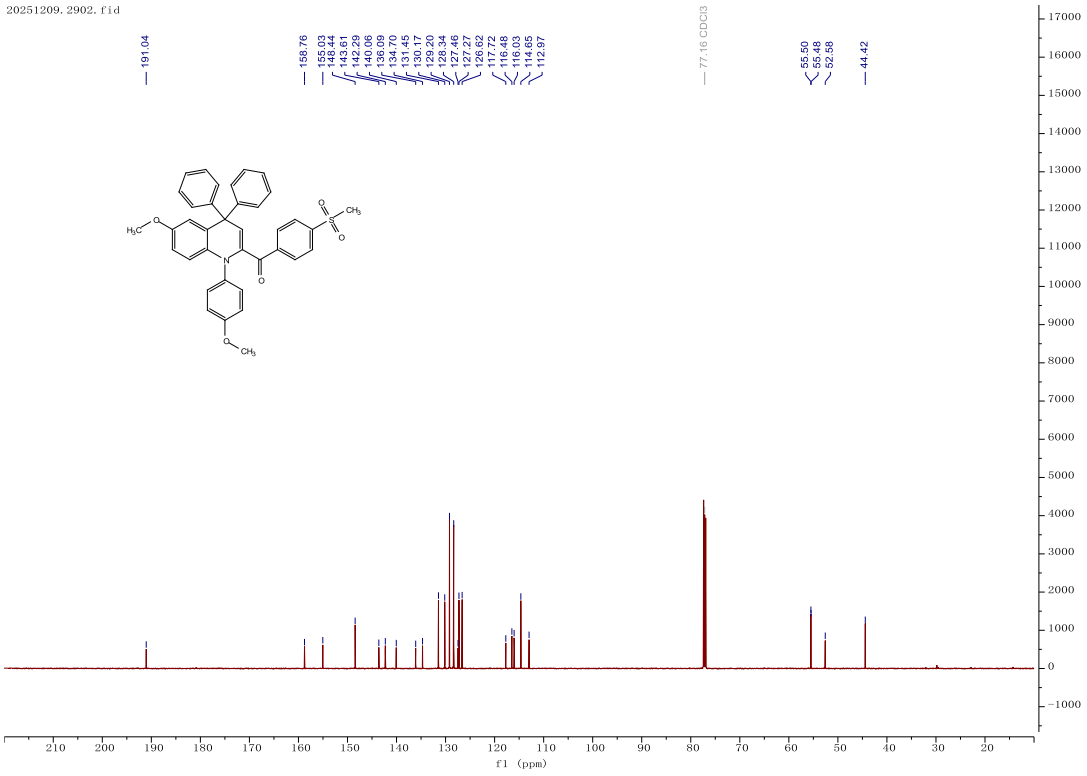

$^{19}$F NMR of compound **5n** (in $CDCl_3$)



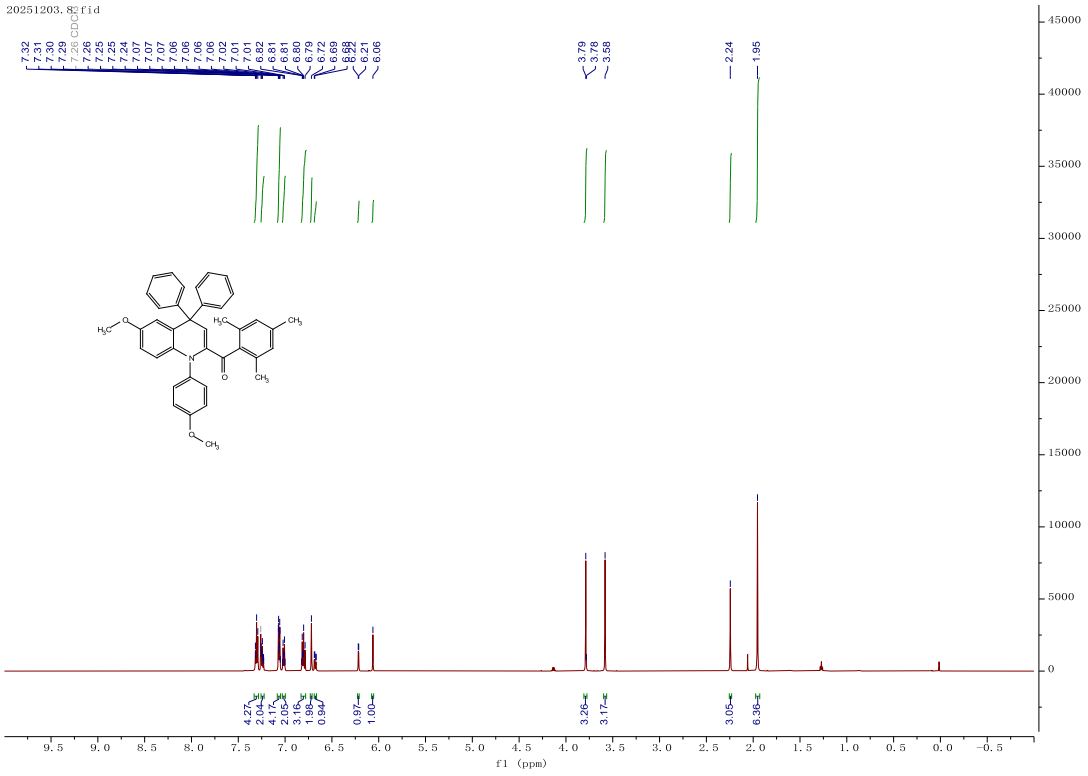
## $^{1}$H NMR of compound **5o** (in $CDCl_3$)



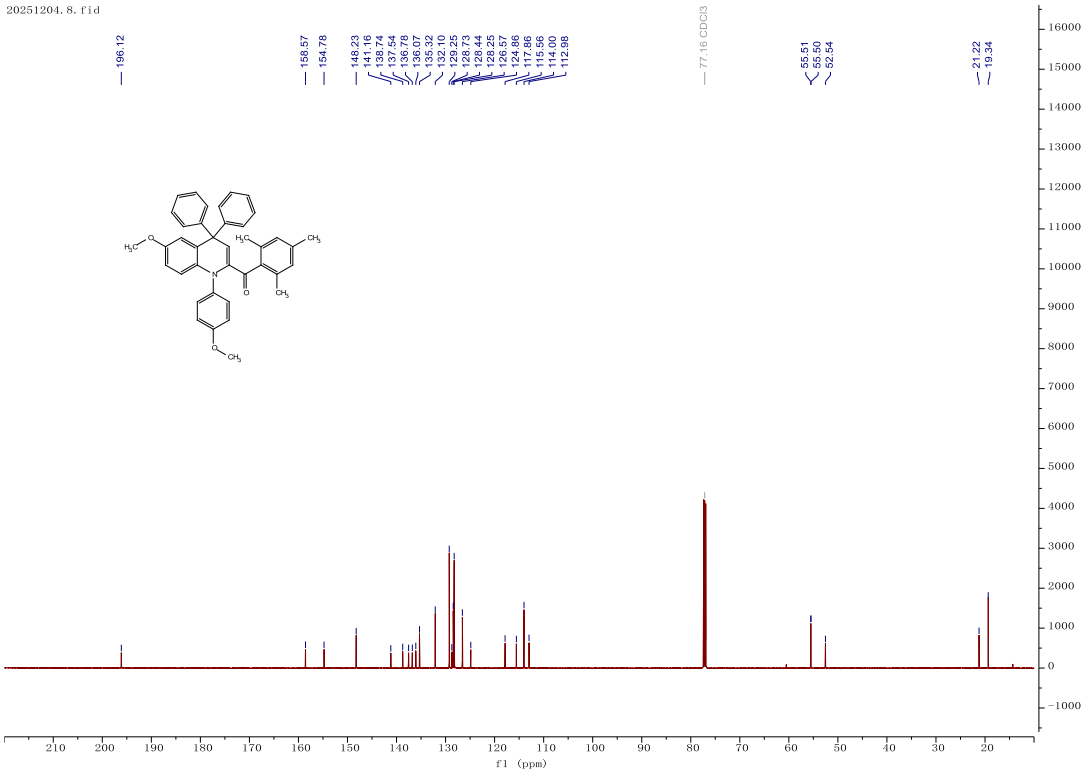

## $^{13}$C NMR of compound **5o** (in $CDCl_3$)



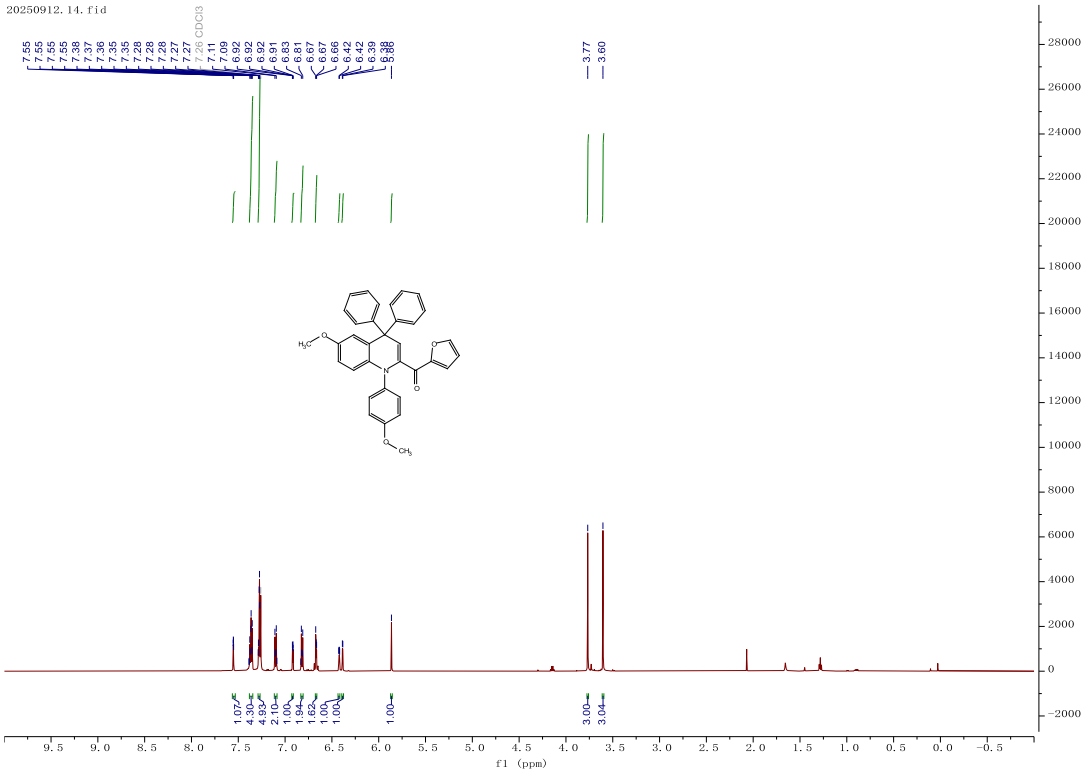
$^{1}$H NMR of compound **5p** (in $CDCl_3$)



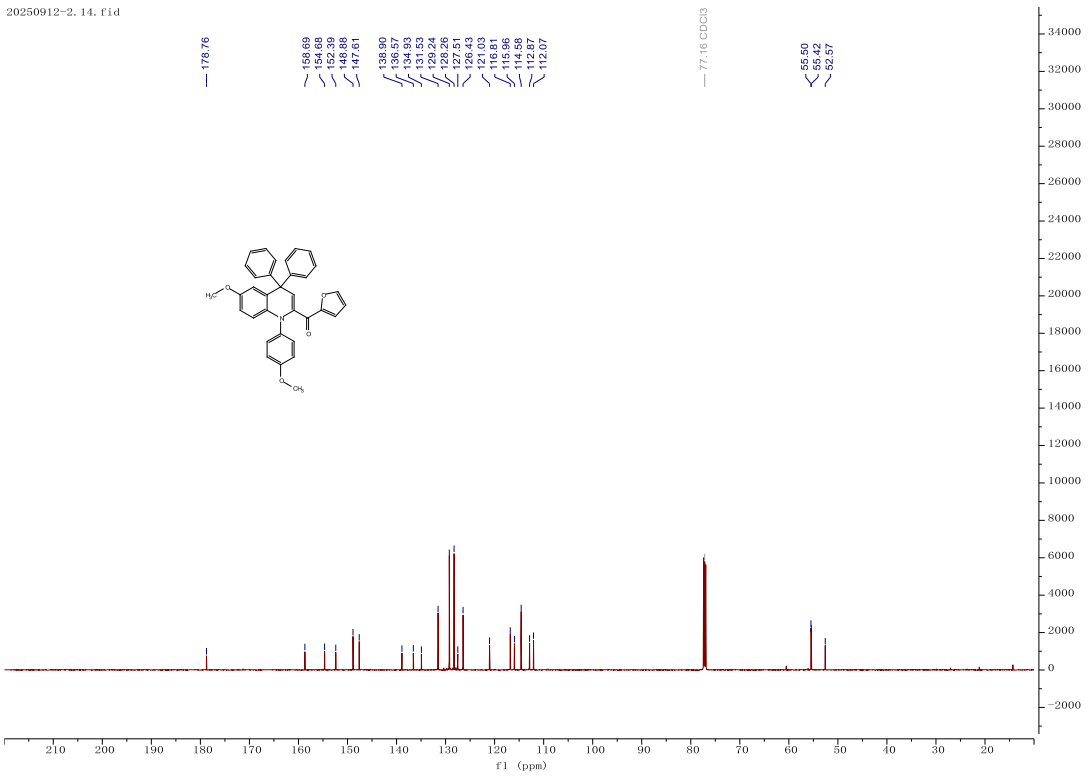

$^{13}$C NMR of compound **5p** (in $CDCl_3$)



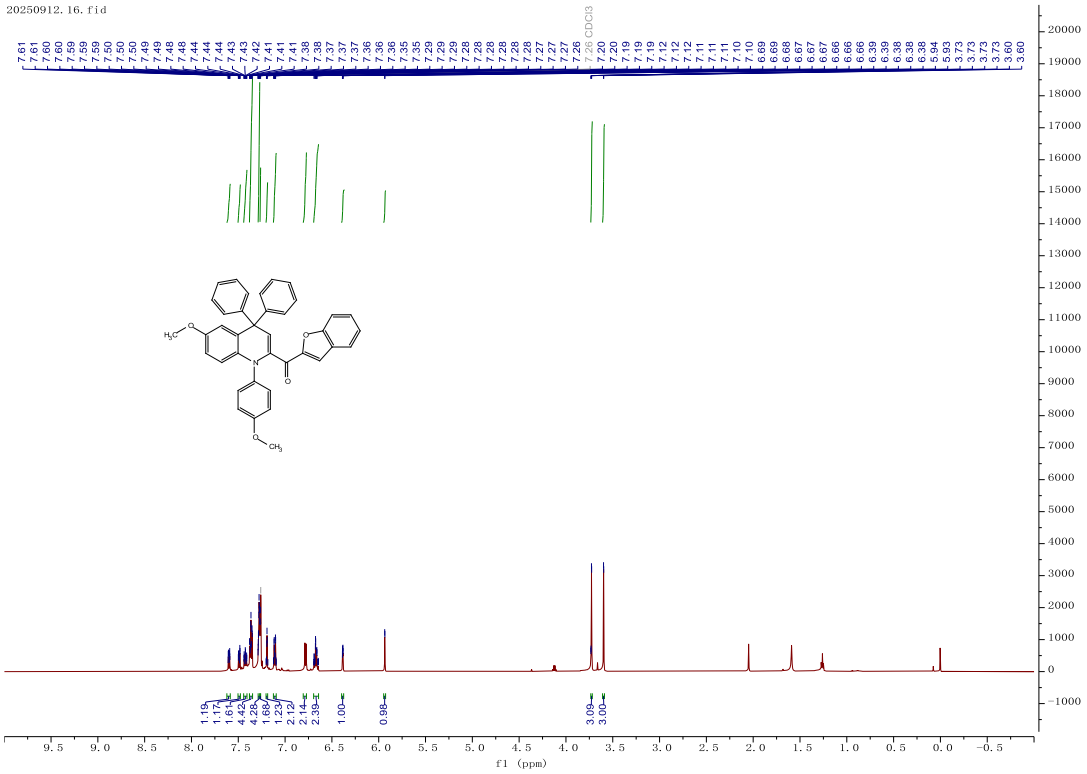
$^{1}$H NMR of compound **5q** (in $CDCl_3$)



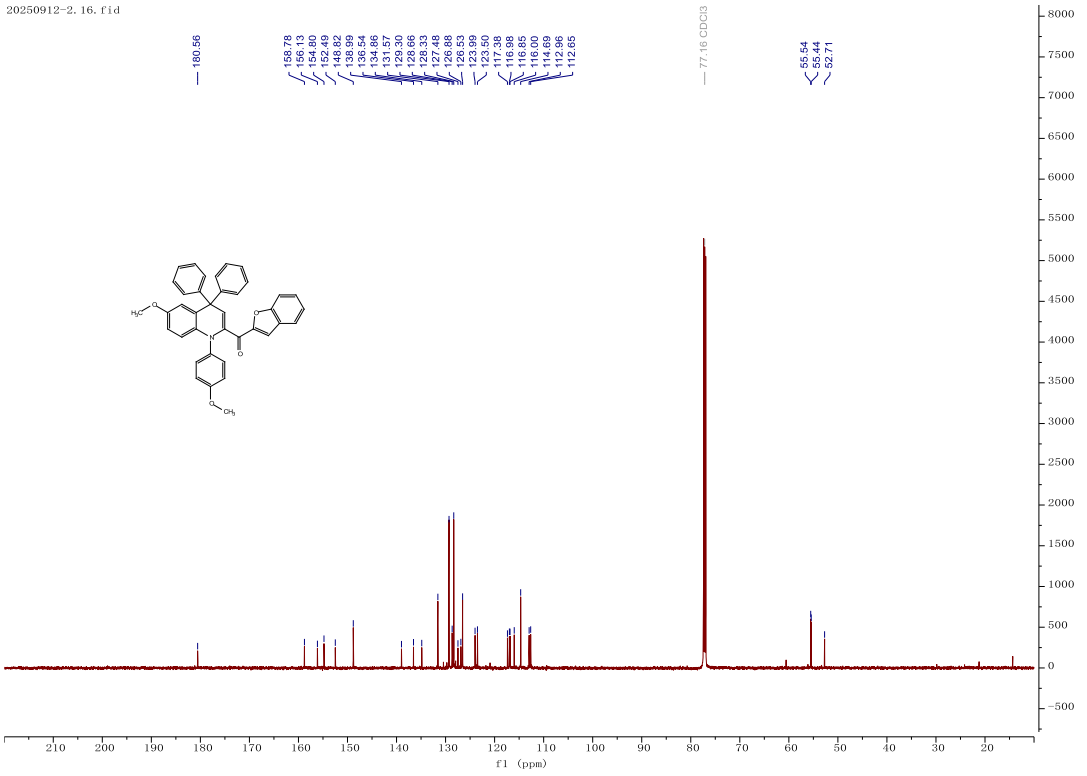

$^{13}$C NMR of compound **5q** (in $CDCl_3$)



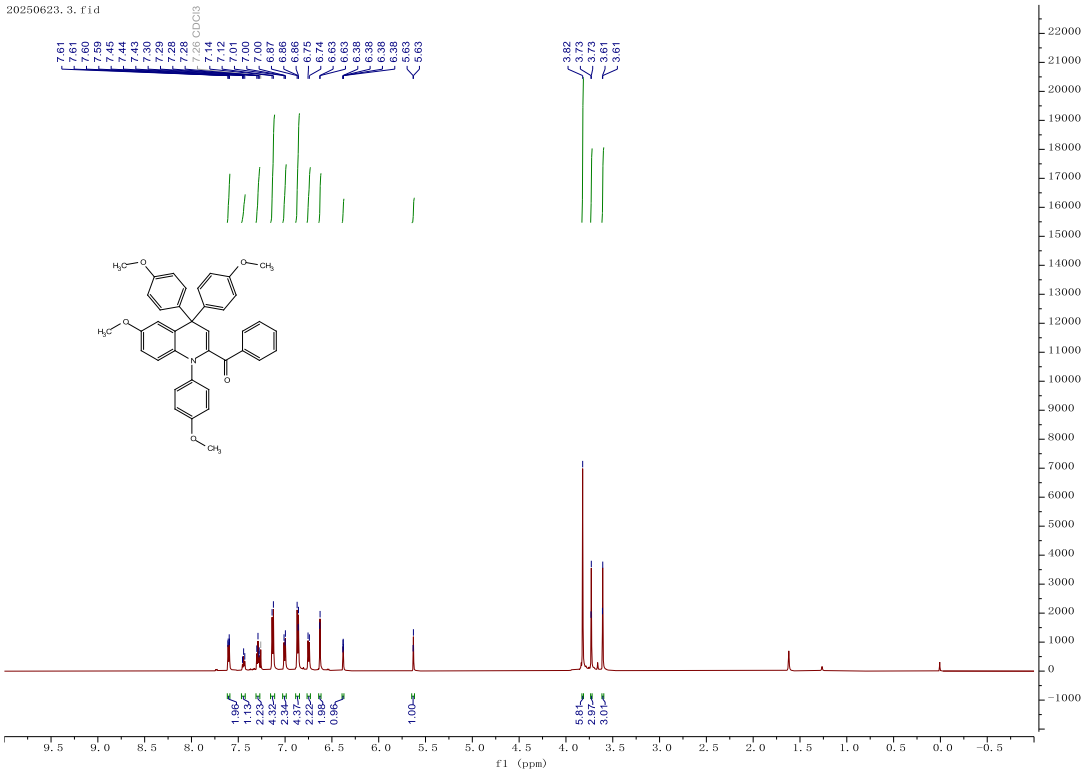
$^{1}$H NMR of compound **5r** (in $CDCl_3$)



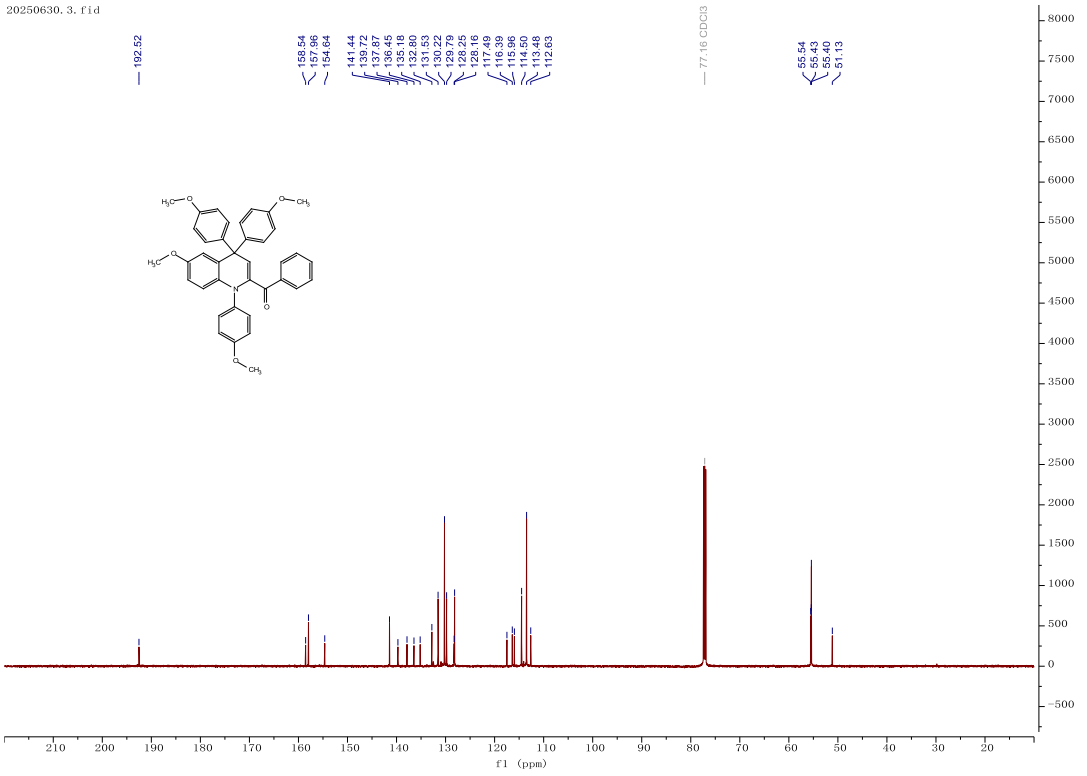

$^{13}$C NMR of compound **5r** (in $CDCl_3$)



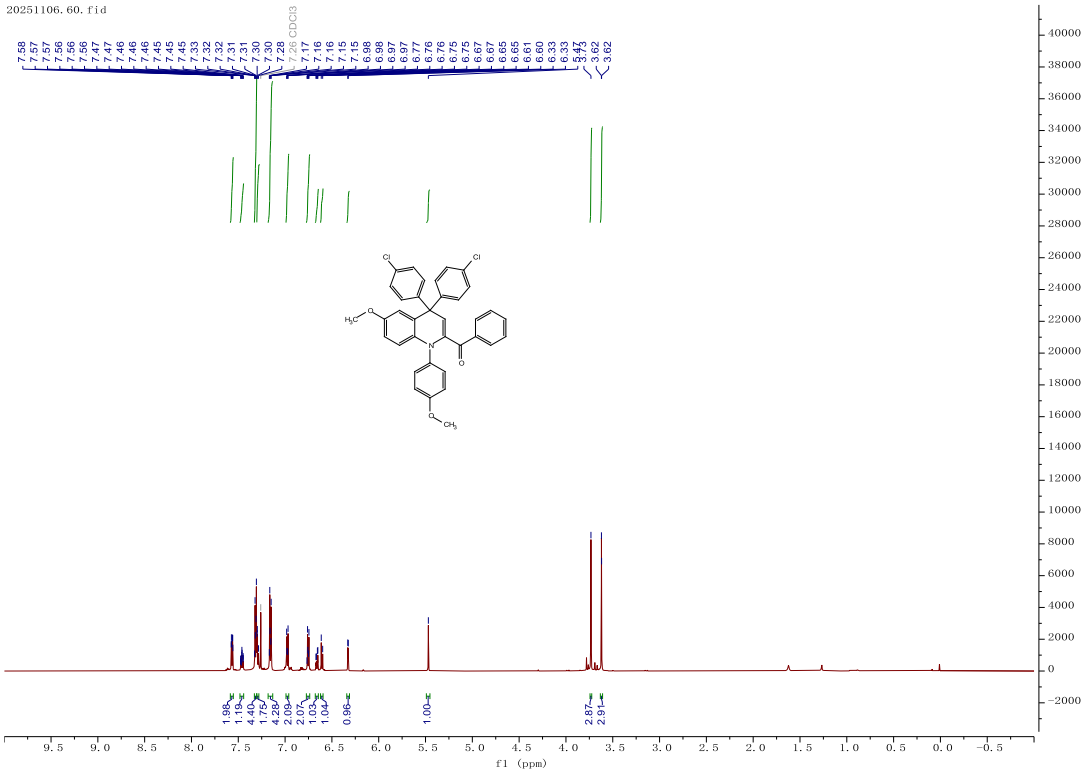
$^{1}$H NMR of compound **5s** (in $CDCl_3$)



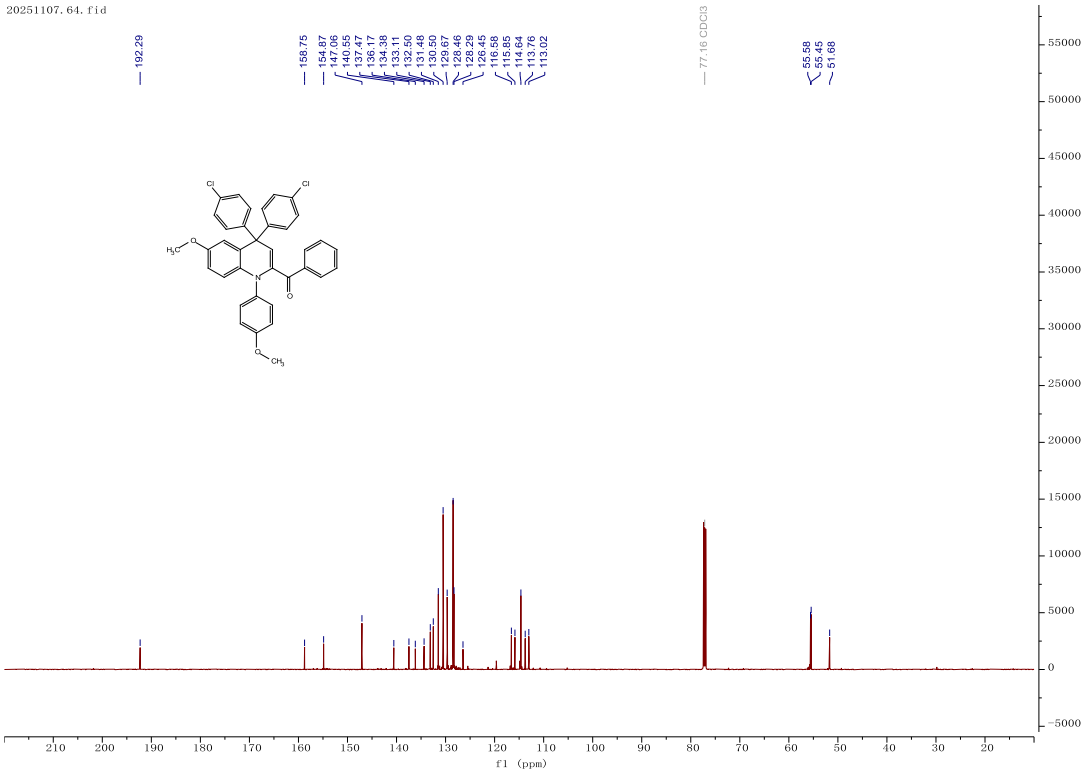

$^{13}$C NMR of compound **5s** (in $CDCl_3$)



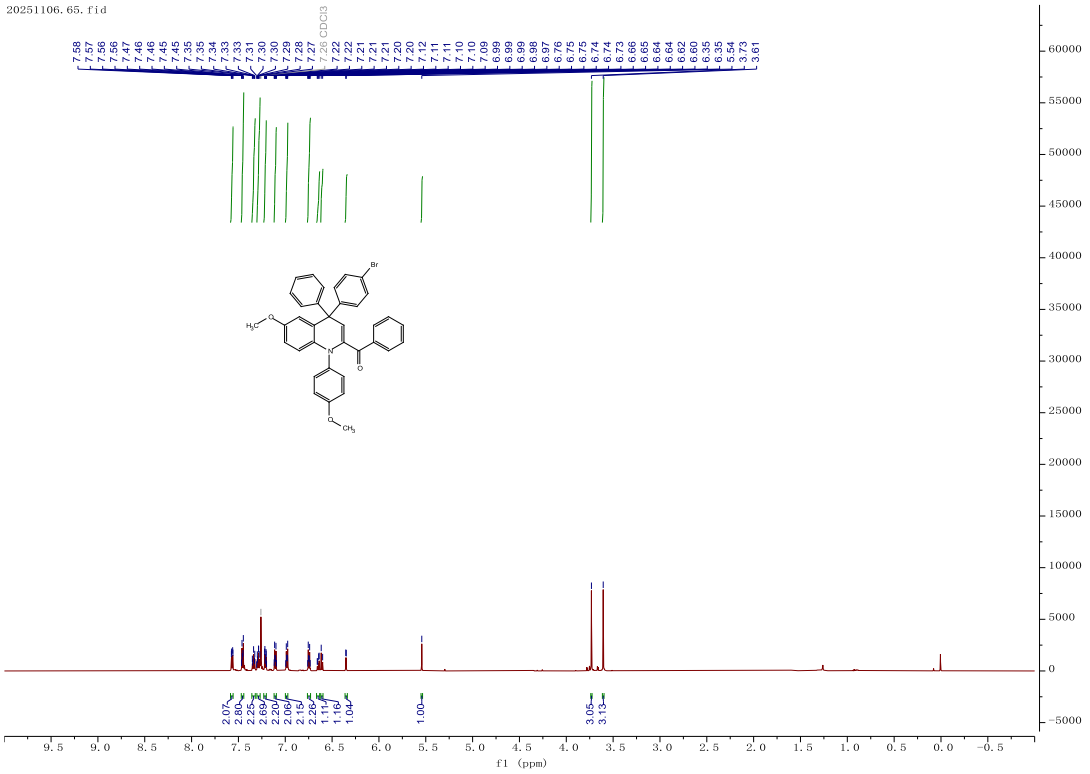
## $^{1}$H NMR of compound **5t** (in $CDCl_3$)



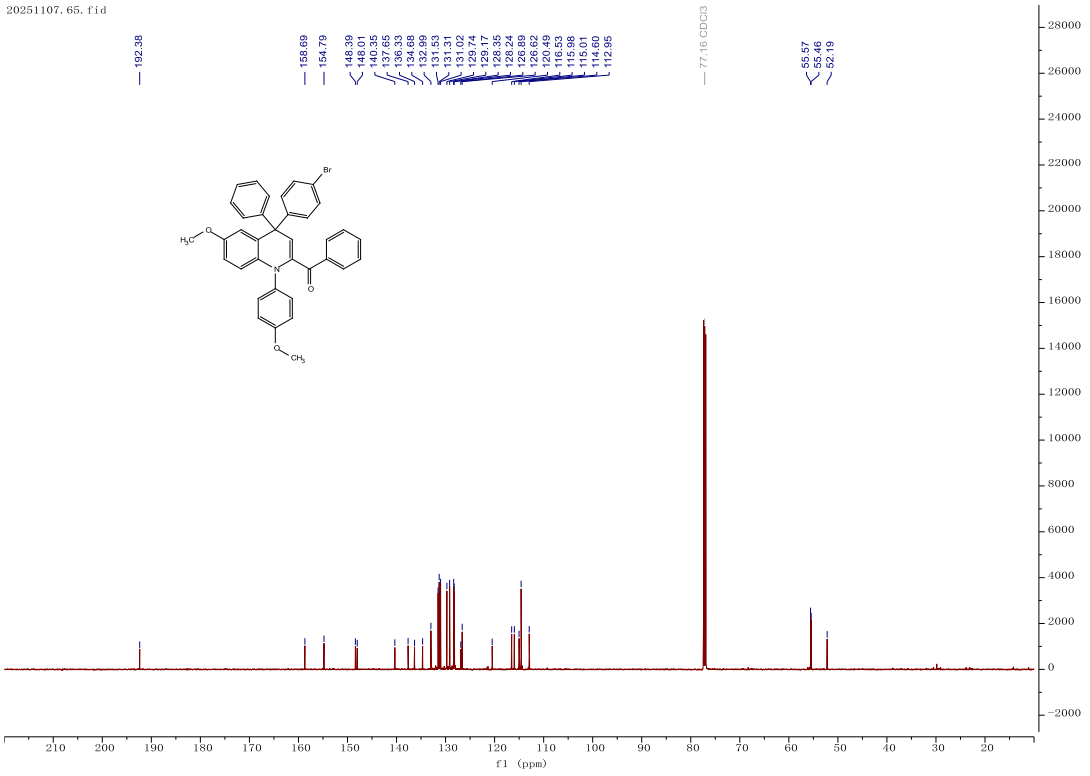

## $^{13}$C NMR of compound **5t** (in $CDCl_3$)



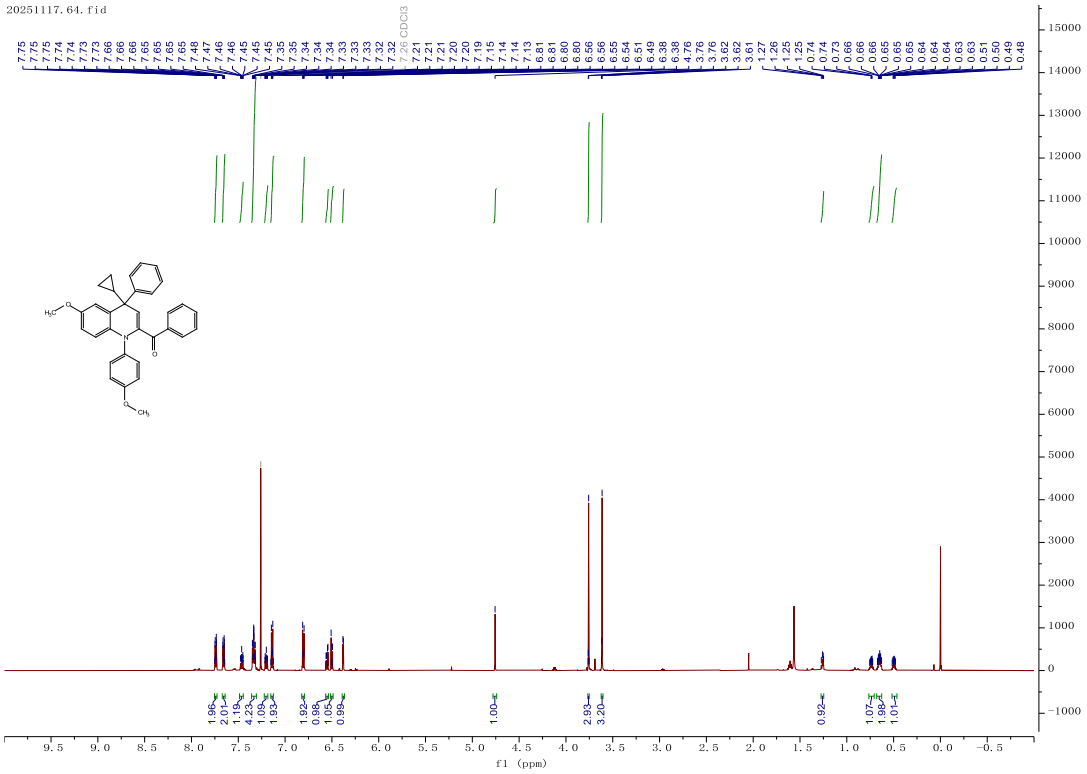
$^{1}$H NMR of compound **5u** (in $CDCl_3$)



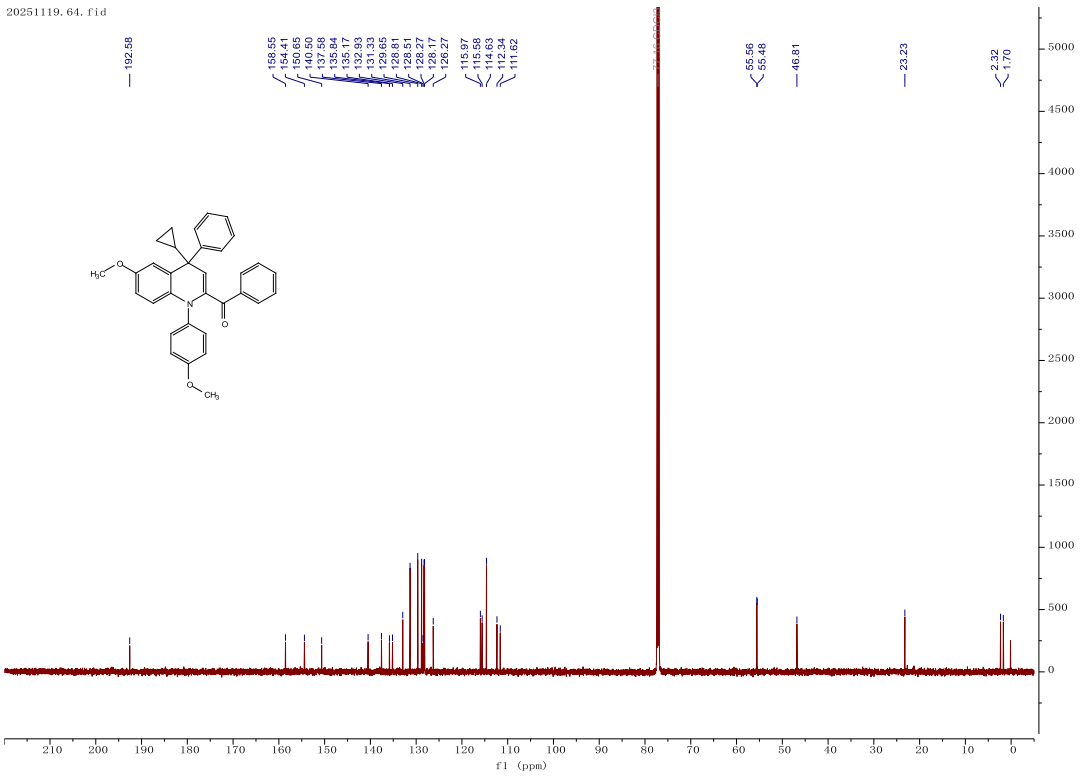

$^{13}$C NMR of compound **5u** (in $CDCl_3$)



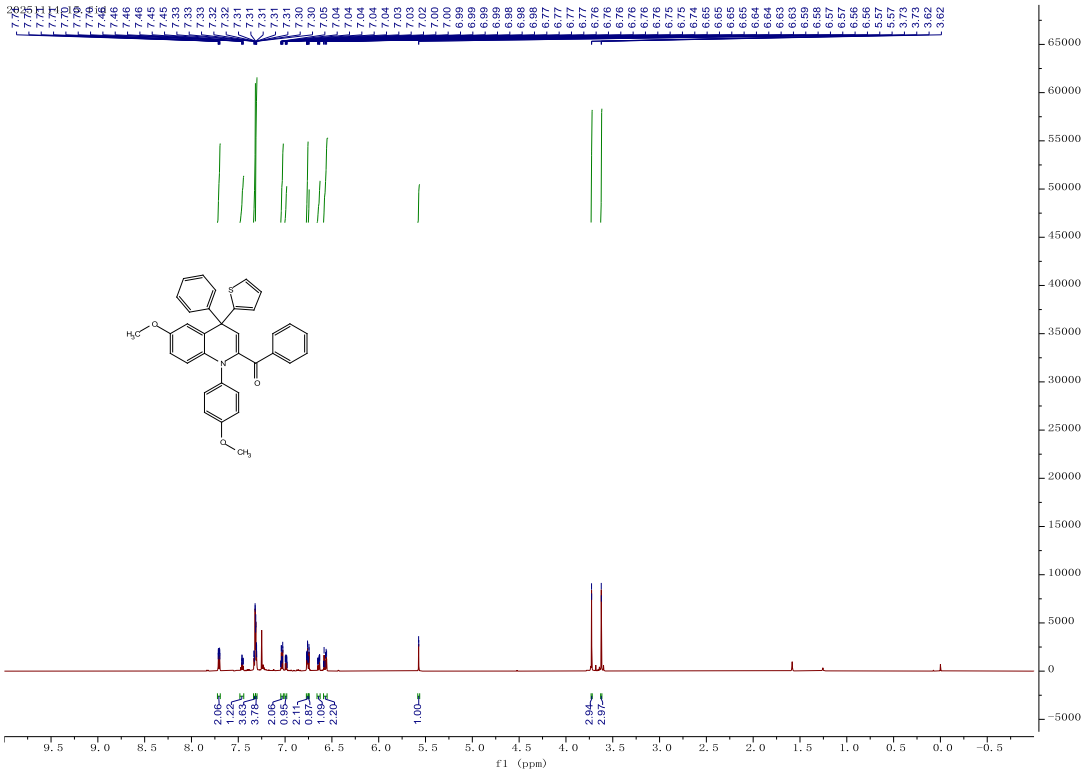
## $^{1}$H NMR of compound **5v** (in $CDCl_3$)



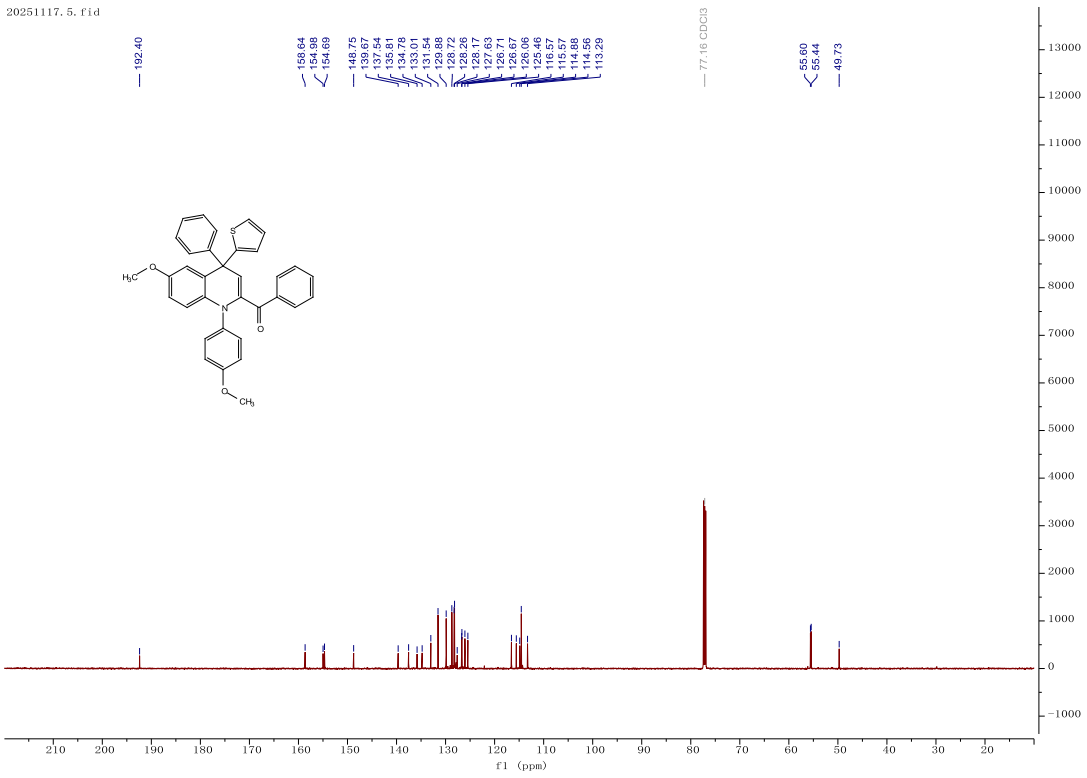

## $^{13}$C NMR of compound **5v** (in $CDCl_3$)



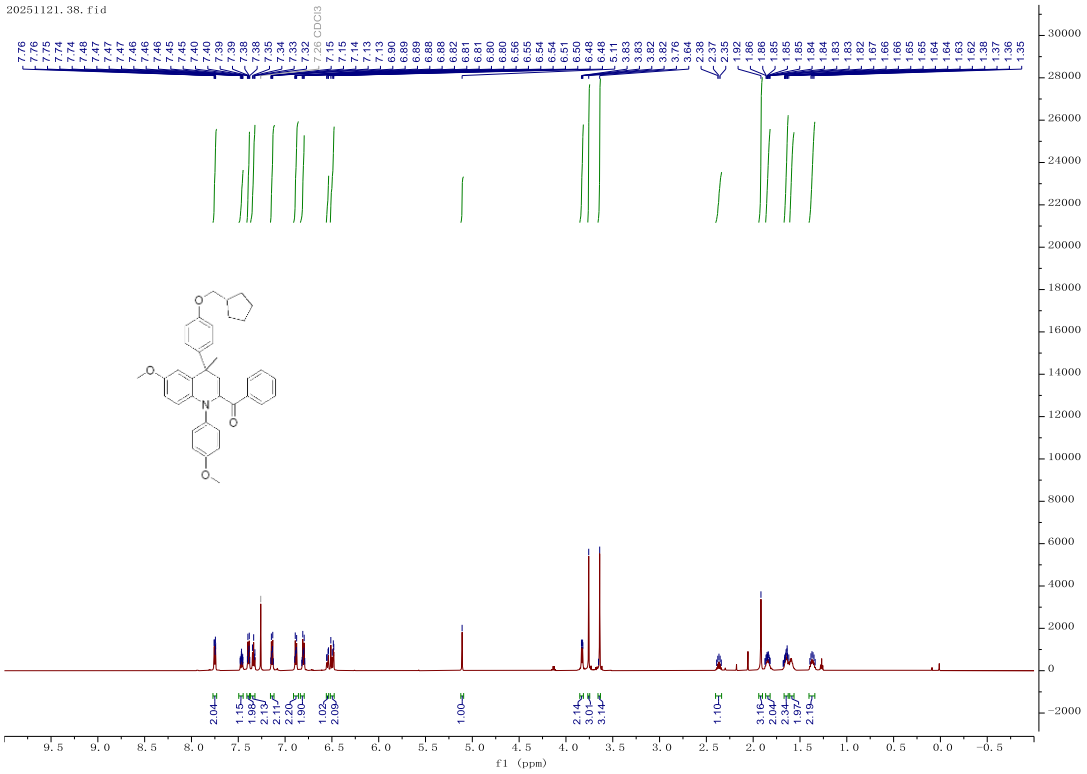
$^{1}$H NMR of compound **5w** (in $CDCl_3$)



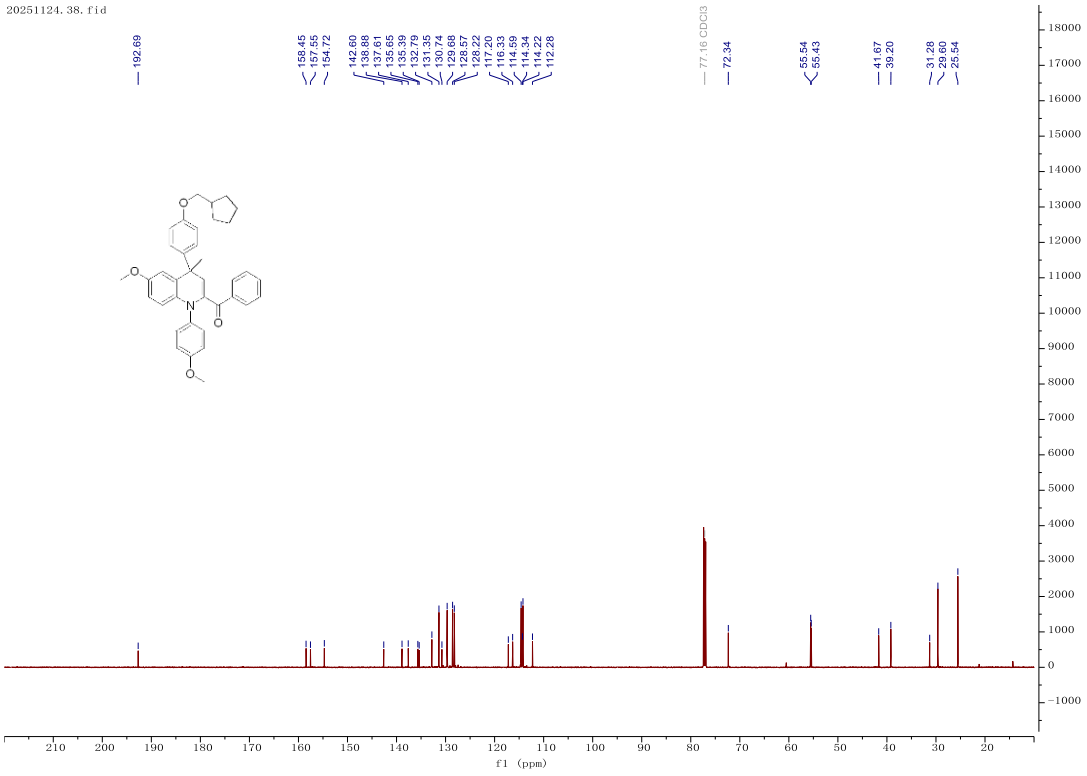
$^{13}$C NMR of compound **5w** (in $CDCl_3$)



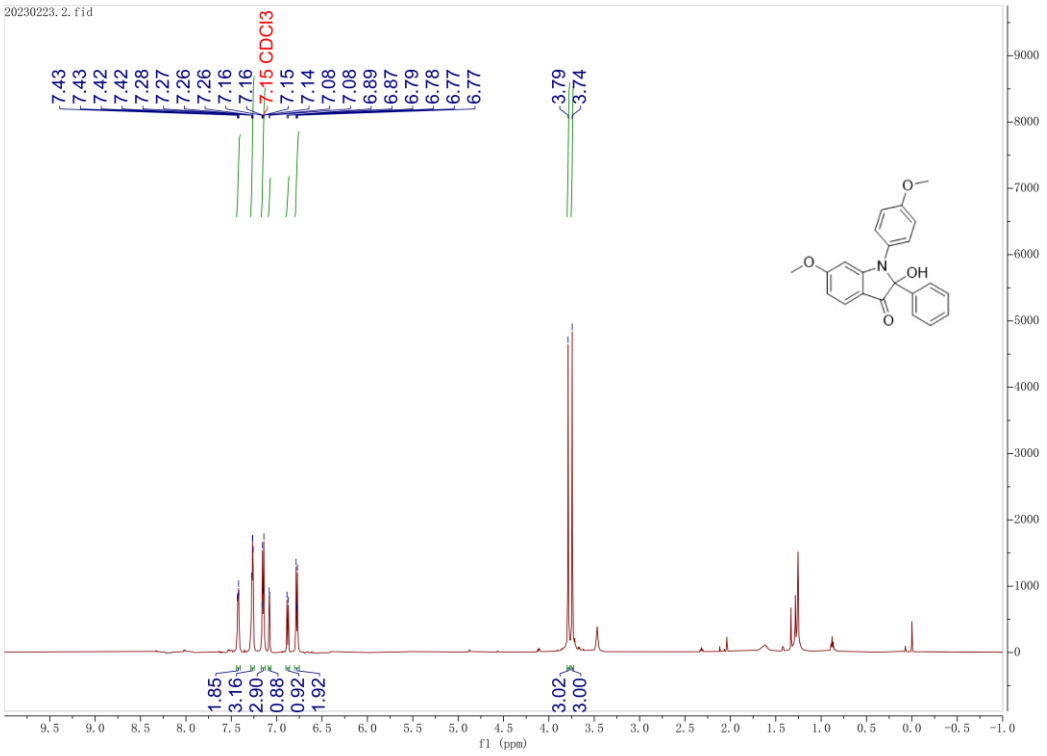
$^{1}$H NMR of compound **5x** (in $CDCl_3$)



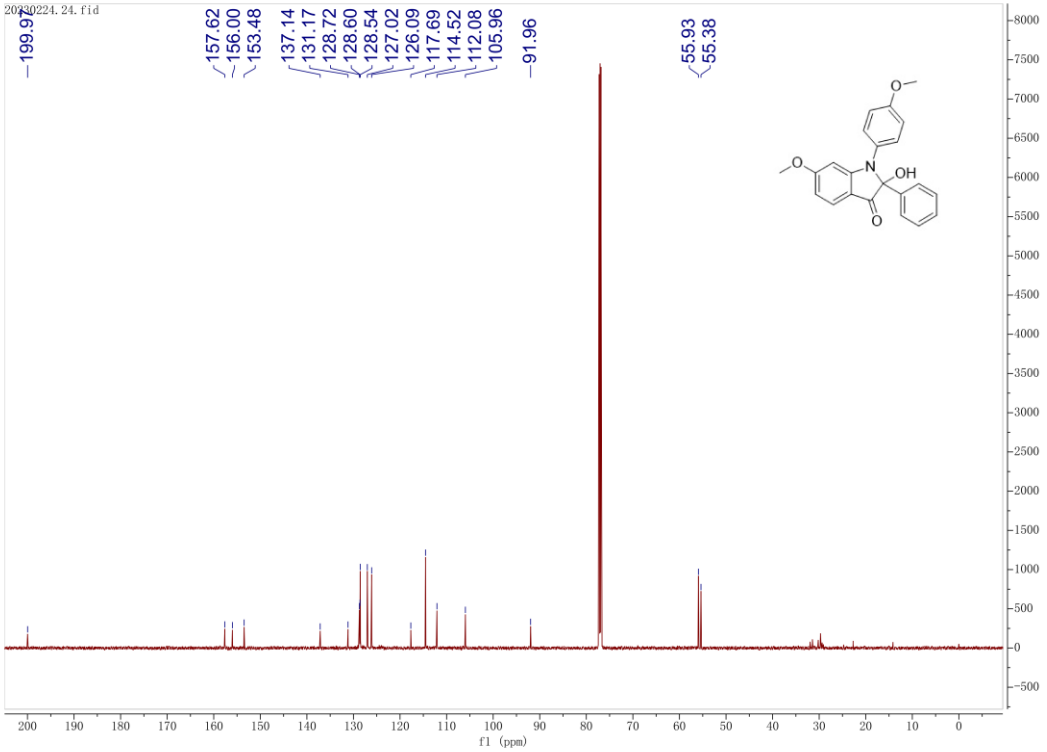

$^{13}$C NMR of compound **5x** (in $CDCl_3$)



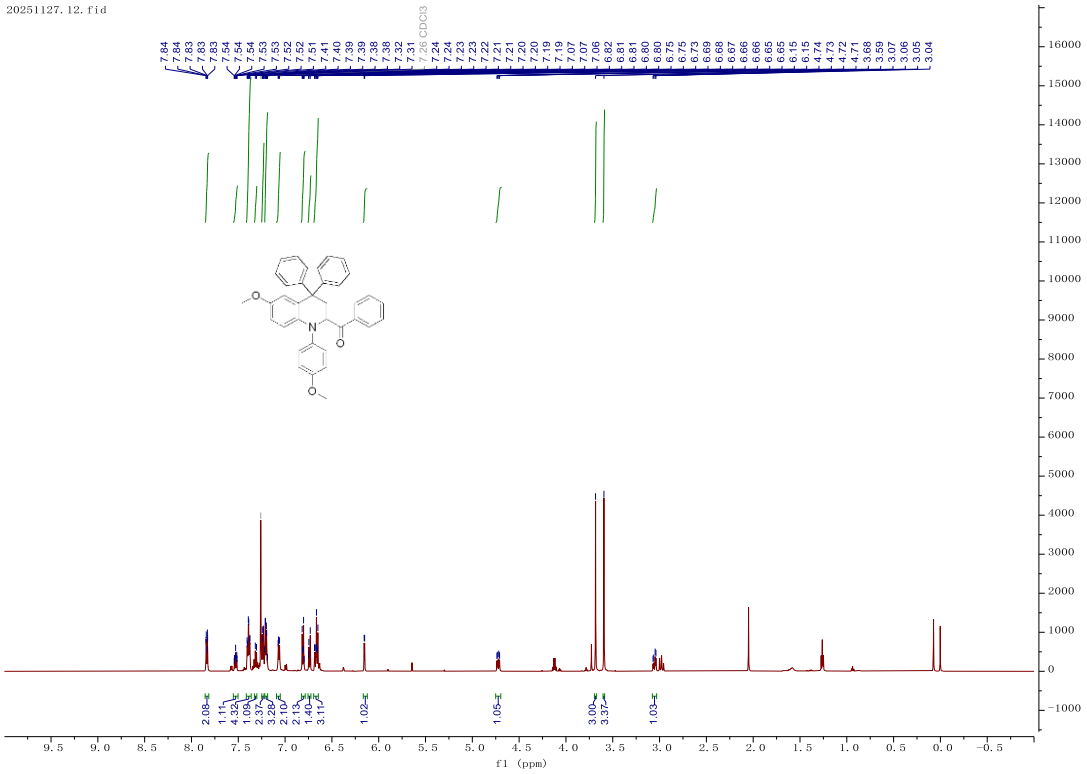
$^{1}$H NMR of compound **6a** (in $CDCl_3$)



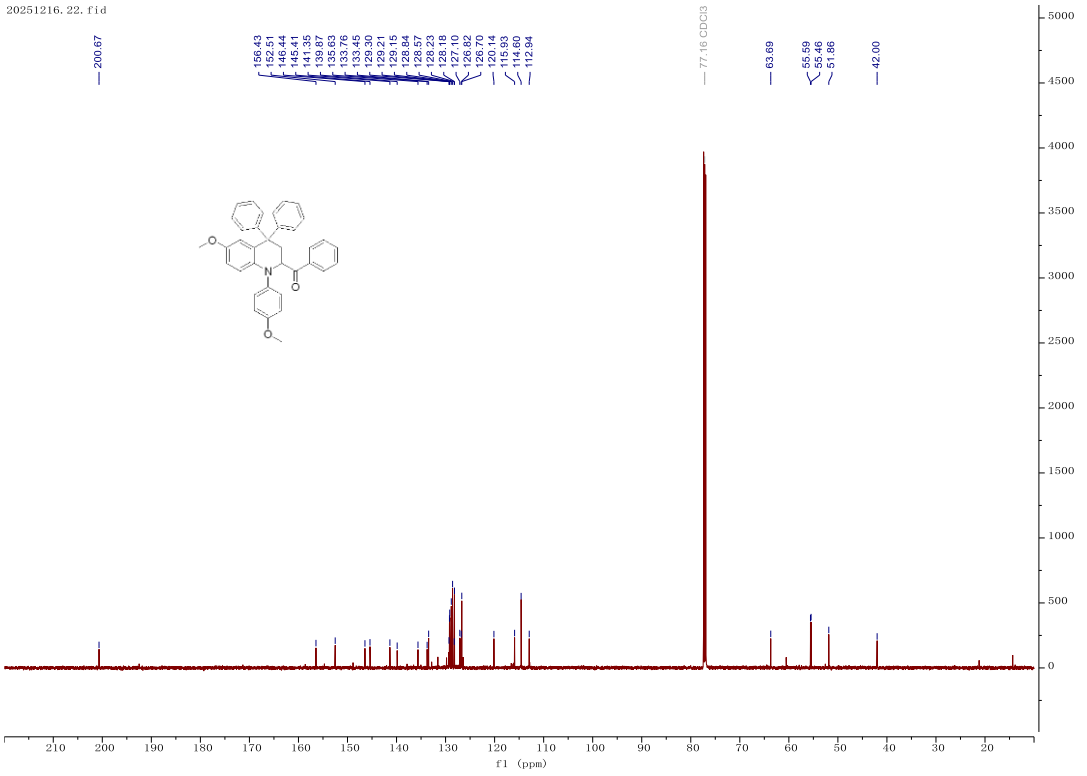

$^{13}$C NMR of compound **6a** (in $CDCl_3$)



## $^{1}$H NMR of compound **7a** (in $CDCl_3$)

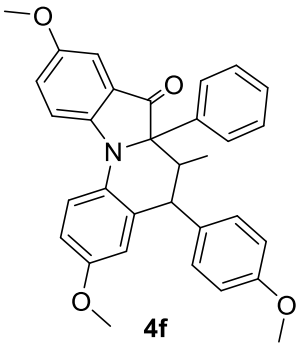



## $^{13}$C NMR of compound **7a** (in $CDCl_3$)



## 10. Crystallographic data

X-ray Crystallographic Data for **4f** (CCDC: 2525034)



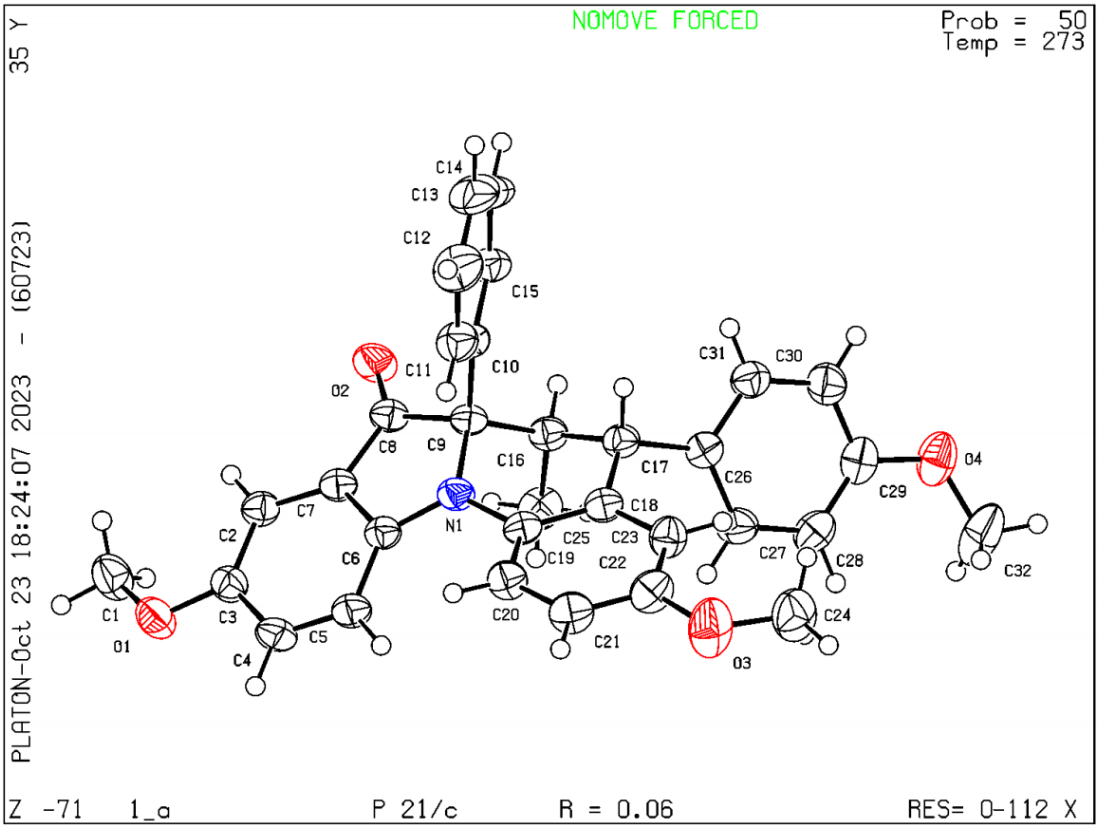



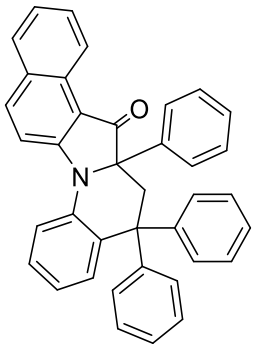

Figure 10.1 Molecular structure of **4f** with 50% probability ellipsoids

Crystal Data for Compound **4f**: CCDC 2525034 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic.

| CCDC number | 2525034 |
|---|---|
| Empirical formula | $C_{32}H_{29}NO_4$ |
| Formula weight | 491.56 |
| Temperature [K] | 273(2) |
| Crystal system | monoclinic |
| Space group (number) | $P2_1/c$(14) |
| *a* [Å] | 10.13290(10) |
| *b* [Å] | 9.62230(10) |
| *c* [Å] | 26.3148(4) |
| α [°] | 90 |
| β [°] | 97.6560(10) |
| γ [°] | 90 |
| Volume [Å$^3$] | 2542.87(5) |
| *Z* | 4 |
| $\rho_{calc}$ [gcm$^{-3}$] | 1.284 |
| $\mu$ [mm$^{-1}$] | 0.674 |
| *F*(000) | 1040 |
| Crystal size [mm$^3$] | 0.080×0.100×0.120 |
| Crystal colour | colorless |
| Crystal shape | Block |
| Radiation | $_{CuK\alpha}$ (λ=1.54178 Å) |
| 2θ range [°] | 6.78 to 144.18 (0.81 Å) |
| Index ranges | −12 ≤ h ≤ 12 |
| | −11 ≤ k ≤ 10 |
| | −32 ≤ l ≤ 32 |
| Reflections collected | 18055 |
| Independent reflections | 4949 |
| | $R_{int}$ = 0.0893 |
| | $R_{sigma}$ = 0.0601 |
| Completeness to θ = 67.679° | 98.9 % |
| Data / Restraints / Parameters | 4949 / 0 / 338 |
| Absorption correction $T_{min}/T_{max}$ (method) | ? / ? (multi-scan) |
| Goodness-of-fit on $F^2$ | 1.050 |
| Final *R* indexes [$I \geq 2\sigma(I)$] | $R_1$ = 0.0564 |
| | w$R_2$ = 0.1551 |
| Final *R* indexes [all data] | $R_1$ = 0.0611 |
| | w$R_2$ = 0.1605 |
| Largest peak/hole [eÅ$^{-3}$] | 0.29/−0.28 |

Table 10.1 Crystal data and structure refinement for **4f**

X-ray Crystallographic Data for **4x** (CCDC: 2525032)




**4x**

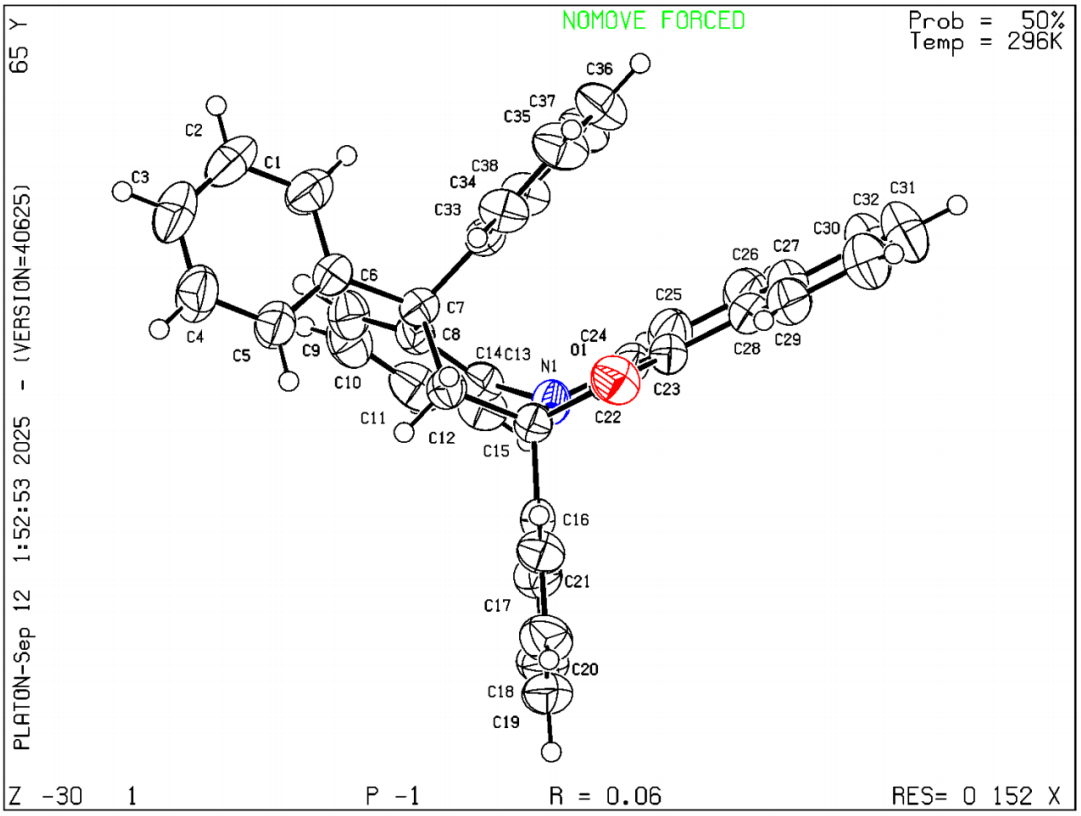


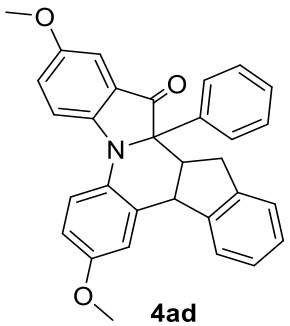

Figure 10.2 Molecular structure of **4x** with 50% probability ellipsoids

Crystal Data for Compound **4x**: CCDC 2525032 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic.

| CCDC number | 2525032 |
|---|---|
| Empirical formula | C38H27NO |
| Formula weight | 513.60 |
| Temperature [K] | 296.15 |
| Crystal system | triclinic |
| Space group (number) | $P\bar{1}$ (2) |
| $a$ [Å] | 10.0302(8) |
| $b$ [Å] | 11.1190(9) |
| $c$ [Å] | 12.7187(9) |
| α [°] | 81.403(2) |
| β [°] | 78.605(2) |
| γ [°] | 79.420(2) |
| Volume [Å$^3$] | 1357.40(18) |
| $Z$ | 2 |
| $\rho_{calc}$ [gcm$^{-3}$] | 1.257 |
| $\mu$ [mm$^{-1}$] | 0.075 |
| $F$(000) | 540 |
| Crystal size [mm$^3$] | 0.18×0.2×0.22 |
| Crystal colour | clear whiteish colourless |
| Crystal shape | block |
| Radiation | $MoK\alpha$ (λ=0.71073 Å) |
| 2θ range [°] | 5.17 to 50.04 (0.84 Å) |
| Index ranges | −11 ≤ h ≤ 11 |
| | −13 ≤ k ≤ 13 |
| | −15 ≤ l ≤ 15 |
| Reflections collected | 17990 |
| Independent reflections | 4739 |
| | $R_{int}$ = 0.0638 |
| | $R_{sigma}$ = 0.0761 |
| Completeness to θ = 25.019° | 99.0 % |
| Data / Restraints / Parameters | 4739 / 0 / 361 |
| Absorption correction $T_{min}/T_{max}$ (method) | 0.6199 / 0.7452 (none) |
| Goodness-of-fit on $F^2$ | 1.041 |
| Final $R$ indexes [$I$≥2σ($I$)] | $R_1$ = 0.0569 |
| | w$R_2$ = 0.1073 |
| Final $R$ indexes [all data] | $R_1$ = 0.1285 |
| | w$R_2$ = 0.1355 |
| Largest peak/hole [eÅ$^{-3}$] | 0.14/−0.18 |

Table 10.2 Crystal data and structure refinement for **4x**

X-ray Crystallographic Data for **4ad** (CCDC: 2525033)



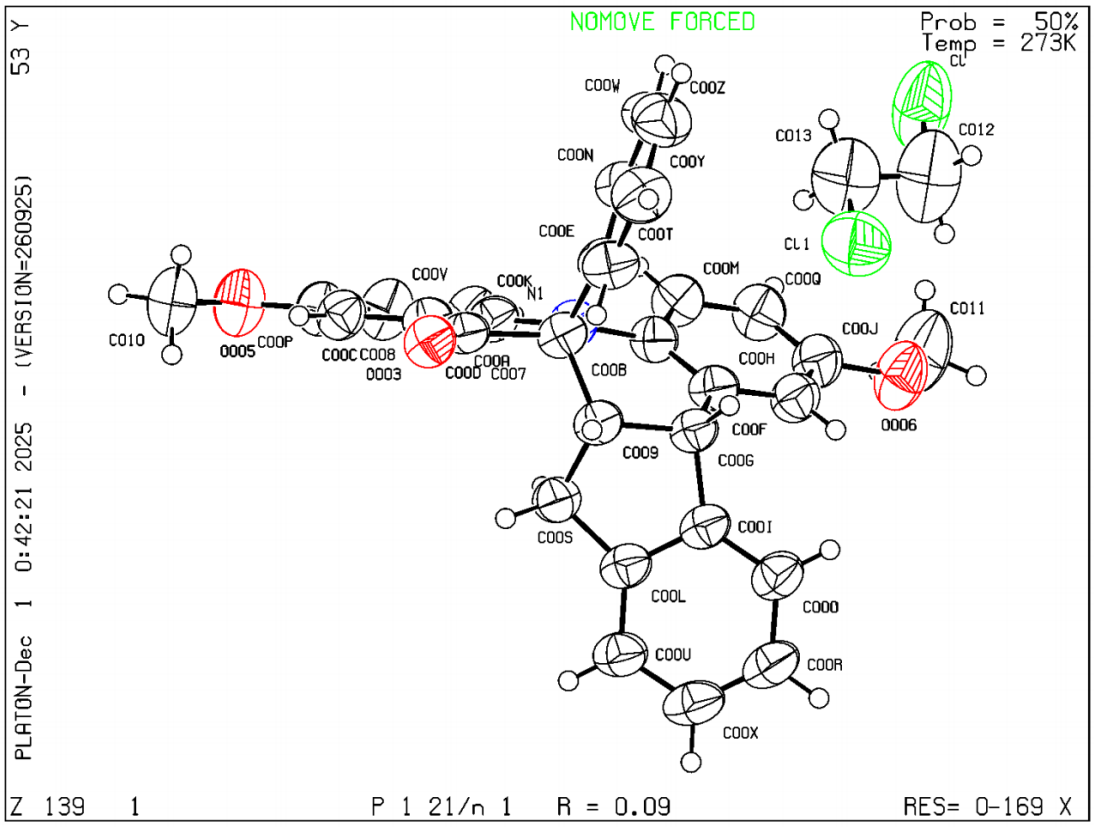




Figure 10.3 Molecular structure of **4ad** with 50% probability ellipsoids

Crystal Data for Compound **4ad**: CCDC 2525033 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic.

| CCDC number | 2525033 |
|---|---|
| Empirical formula | $C_{31}H_{25}NO_3$ |
| Formula weight | 558.47 |
| Temperature [K] | 273.15 |
| Crystal system | monoclinic |
| Space group (number) | $P2_1/n$(14) |
| *a* [Å] | 10.117 |
| *b* [Å] | 10.501 |
| *c* [Å] | 25.999 |
| α [°] | 90 |
| β [°] | 94.44 |
| γ [°] | 90 |
| Volume [Å$^3$] | 2753.6 |
| *Z* | 4 |
| $\rho_{calc}$ [gcm$^{-3}$] | 1.347 |
| $\mu$ [mm$^{-1}$] | 2.404 |
| *F*(000) | 1168 |
| Crystal size [mm$^3$] | 0.18×0.2×0.22 |
| Crystal colour | clear whiteish colourless |
| Crystal shape | block |
| Radiation | *CuKα* (λ=1.54178 Å) |
| 2θ range [°] | 6.82 to 133.24 (0.84 Å) |
| Index ranges | −12 ≤ h ≤ 12 |
| | 0 ≤ k ≤ 10 |
| | 0 ≤ l ≤ 30 |
| Reflections collected | 4863 |
| Independent reflections | 4863 |
| | $R_{int}$ = 0 |
| | $R_{sigma}$ = 0.1255 |
| Completeness to θ = 66.618° | 99.8 % |
| Data / Restraints / Parameters | 4863 / 1 / 354 |
| Absorption correction $T_{min}/T_{max}$ (method) | 0.2447 / 0.7528 (multi-scan) |
| Goodness-of-fit on $F^2$ | 1.092 |
| Final *R* indexes [$I \geq 2\sigma(I)$] | $R_1$ = 0.0896 |
| | w$R_2$ = 0.2457 |
| Final *R* indexes [all data] | $R_1$ = 0.1005 |
| | w$R_2$ = 0.2577 |
| Largest peak/hole [eÅ$^{-3}$] | 0.63/−0.52 |

Table 10.3 Crystal data and structure refinement for **4ad**