Synthesis of fungicidal morpholines and isochromenopyridinones by acid-catalyzed intramolecular reactions of isoindolinones

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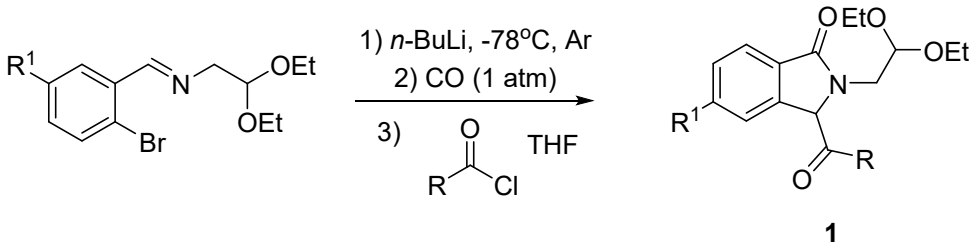
Supporting Information

2. General Information

Nuclear magnetic resonance (NMR) spectra for ^{1}H NMR (400 MHz or 600 MHz), ^{13}C NMR (101 MHz or 151 MHz) were taken on Bruker Avance 400 MHz or 600 MHz spectrometer in Chloroform-*d* or DMSO-d_6 solution with TMS as internal standard. High resolution mass spectra (HRMS) were recorded with an Agilent 6520 Q-TOF LC/MS instrument (Agilent Technologies Inc. State of California, United States of America). The crystal structure was recorded on a Rigaku 007 Saturn 70 diffractometer (Rigaku, Tokyo, Japan). Conversion was monitored by thin layer chromatography (TLC). Flash column chromatography was performed over silica gel (60-100 mesh). IR spectra was recorded on Bruker TENSOR 27.

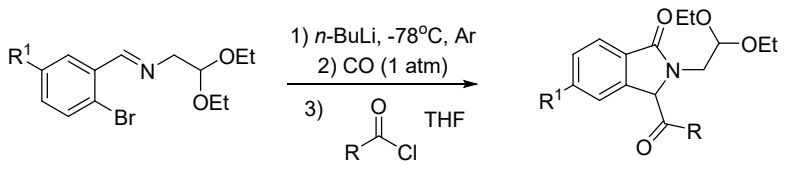
3. General Procedure for the Preparation of 3-Acyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones (1).

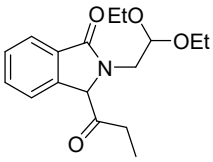


1

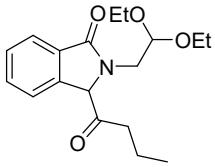
The procedures were according to the reported method.[1]A hexane solution of *n*-BuLi (1.6 M, 1.0 equiv) was slowly added to the stirred solution of aromatic imine (1.0 equiv) in THF (0.08 M) at -78 ℃ under argon atmosphere. After continuously stirring for 30 min, carbon monoxide was bubbled into the solution. The carbon monoxide atmosphere was kept with a balloon at the exit. The reaction mixture was continuously stirred at low temperature for 30 min, then acyl chloride (1.0 equiv) was slowly added dropwise with syringe. The reaction mixture was allowed to reach room temperature slowly and stirred for 1 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:1~1:5) as the eluent to afford products **1a**-**1q**.

Table S1. Synthesis of 3-Acyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones 1.

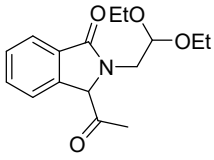




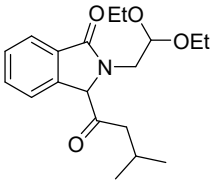
1a 52%



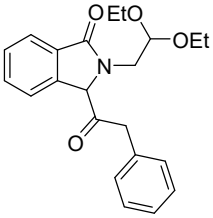
1b 51%



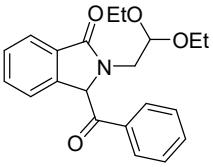
1c 70%



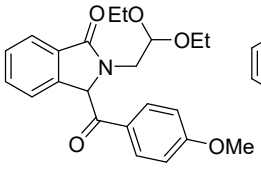
1d 69%



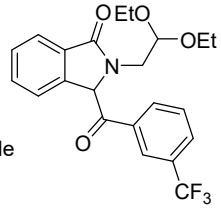
1e 70%



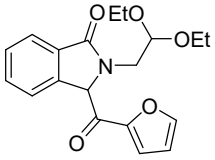
1f 74%



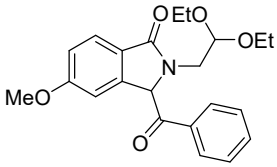
1g 62%



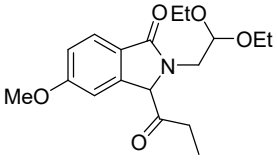
1h 54%



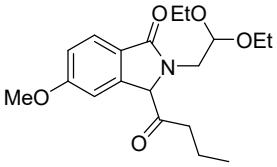
1i 60%



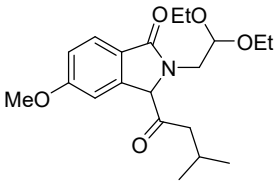
1j 45%



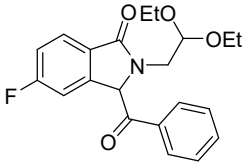
1k 71%



1l 45%



1m 50%



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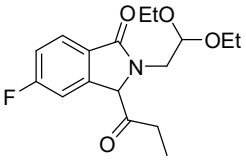
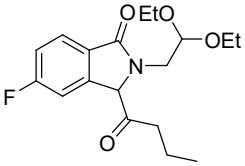
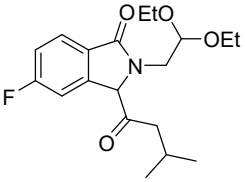


1o 64%



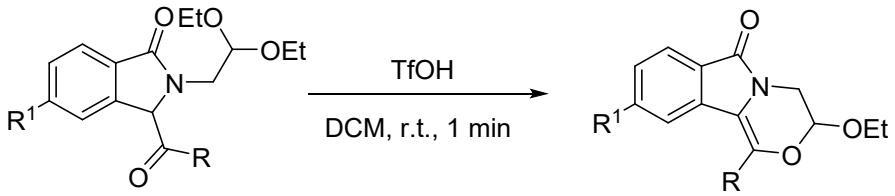
1p 45%



1q 58%

4. General Procedure for the Preparation of 2-5

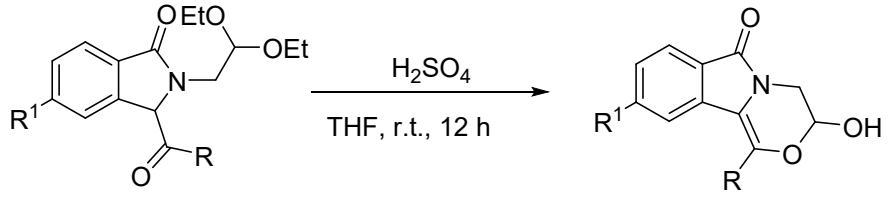
4.1 Typical procedure for the synthesis of 3-ethoxy-3,4-dihydro-6*H*-[1,4]-oxazino- [3,4-*a*]-isoindol-6-ones (2).



1 **2**

Trifluoromethanesulfonic acid (1.0 equiv) was added to a solution of the 3-acyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones **1** (1.0 equiv) in dichloromethane (0.05 M). After stirred for 1 min., the reaction mixture was diluted with 10 mL saturated sodium bicarbonate solution, and extracted with DCM (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 3:2~1:3) as the eluent to afford 3-ethoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-ones **2a**-**2q**.

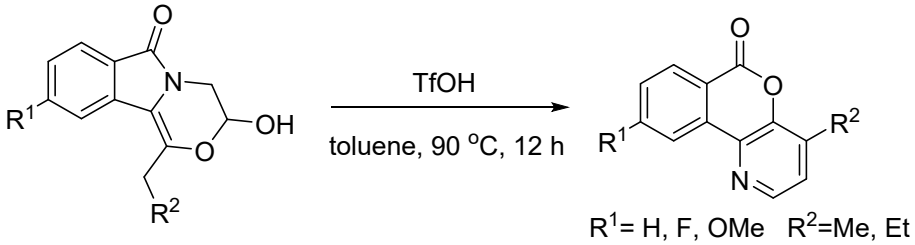
4.2 Typical procedure for the synthesis of 3-hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino -[3,4-*a*]-isoindol-6-ones (3).



1 **3**

Concentrated sulfuric acid (8.0 equiv) was added to a solution of the 3-acyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones **1** (1.0 equiv) in THF (0.025 M). After stirred for 12 h, the reaction mixture was diluted with 10 mL saturated sodium bicarbonate solution, and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 4:1~1:1) as the eluent to afford 3-ethoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]isoindol-6-ones **3a**-**3q**.

4.3 Typical procedure for the synthesis of 6*H*-isochromeno-[4,3-*b*]-pyridin-6-ones (4).

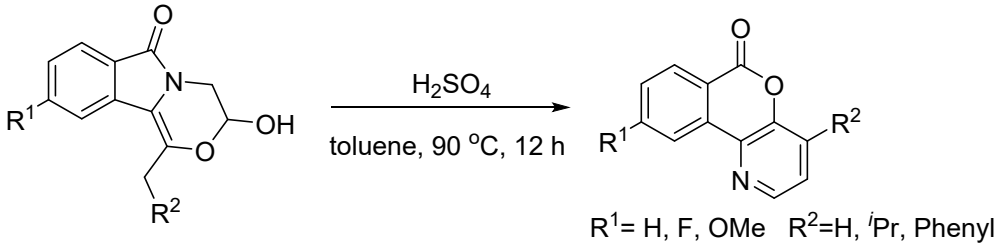


3

R^1= H, F, OMe R^2=Me, Et

4a-**4f**

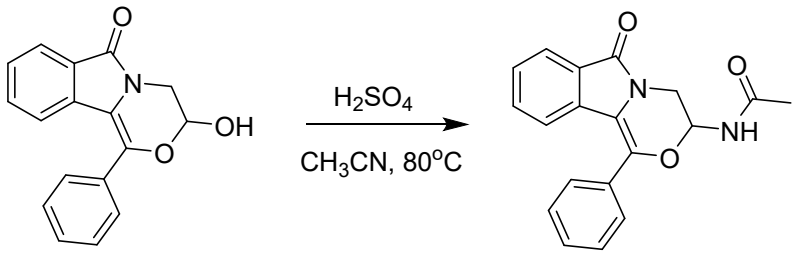
Trifluoromethanesulfonic acid (1.5 equiv) was added to a solution of the 3-ethoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-ones **3** (1.0 equiv) in toluene (0.03 M). The mixture was stirred at 90 ℃ for 9 h under air atmosphere. After reaching room temperature, the reaction mixture was diluted with 10 mL saturated sodium bicarbonate solution, and extracted with DCM (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:3~1:10) as the eluent to afford 6*H*-isochromeno[4,3-*b*]pyridin-6-ones **4a**-**4f**.



3 **4g-4k**

Concentrated sulfuric acid (2.0 equiv) was added to a solution of the 3-ethoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-ones **3** (1.0 equiv) in toluene (0.03 M). The mixture was stirred at 90 ℃ for 9 h under air atmosphere. After reaching room temperature, the reaction mixture was diluted with 10 mL saturated sodium bicarbonate solution, and extracted with DCM (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:3~1:10) as the eluent to afford 6*H*-isochromeno-[4,3-*b*]-pyridin-6-ones **4g**-**4k**.

4.4 Procedure for the synthesis of *N*-(6-oxo-1-phenyl-3,4-dihydro-6*H*-[1,4]oxazino [3,4-*a*]isoindol-3-yl)acetamide (5).

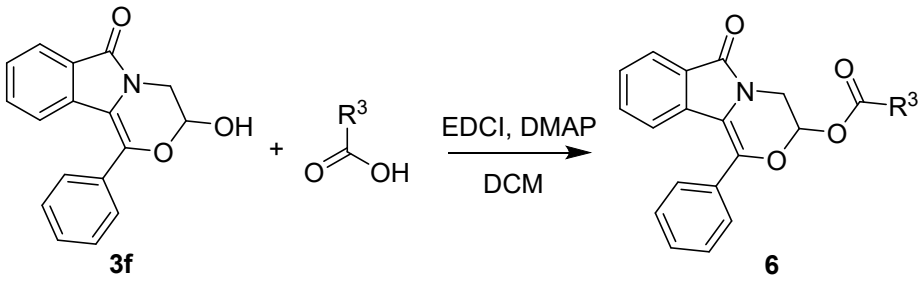


3f **5** 68%

Concentrated sulfuric acid (0.02 mL, 0.4 mmol, 0.8 equiv) was added to a solution of the 3-hydroxy-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one **3f** (140 mg, 1.0 equiv) in acetonitrile (10 mL). The mixture was stirred at 80 ℃ for 7 h under air atmosphere. After reaching room temperature, the reaction mixture was diluted with 10 mL saturated sodium bicarbonate

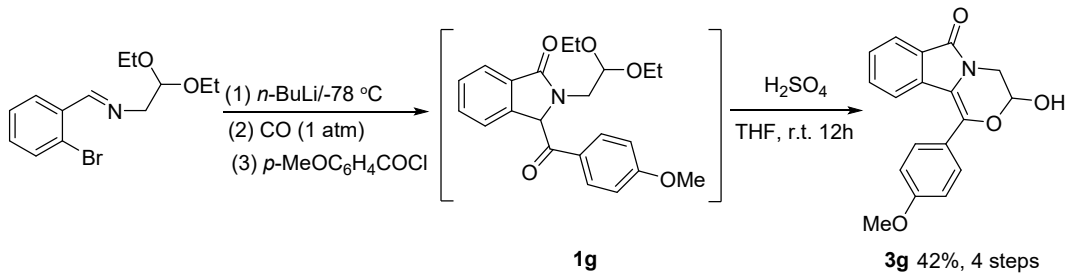
solution, and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with MeOH/CH_2Cl_2 (v/v = 1:15) as the eluent to afford 108 mg of white solid **5** in yield of 68%.

4.5 Typical procedure for the synthesis of 6.



The acid (0.5 mmol, 1.0 equiv), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (0.75 mmol, 144 mg, 1.5 equiv) and 4-dimethylaminopyridine (0.1 mmol, 12 mg, 0.2 equiv) were added to a solution of **3f** (140 mg, 1.0 equiv) in dichloromethane (20 mL). After stirred for 12 h, the reaction mixture was diluted with 10 mL saturated sodium bicarbonate solution, and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (v/v = 1:3) as the eluent to afford compounds **6**.

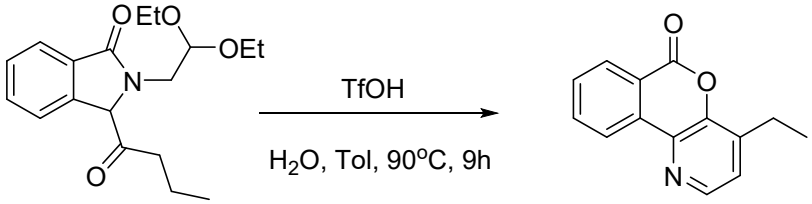
5. One-pot Synthesis of 3g



1g **3g** 42%, 4 steps

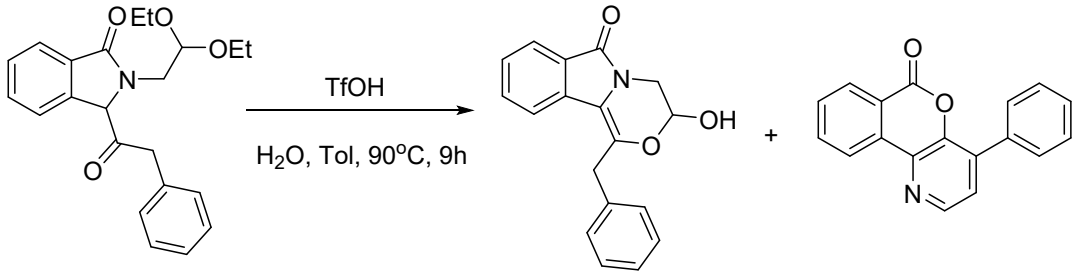
A hexane solution of *n*-BuLi (1.6 M, 1.25 mL, 2.0 mmol) was slowly added to the stirred solution of 1-(2-bromophenyl)-*N*-(2,2-diethoxyethyl)methanimine (600 mg, 2.0 mmol) in THF (25 mL) at -78 ℃ under argon atmosphere. After continuously stirring for 30 minutes, carbon monoxide was bubbled into the solution. The carbon monoxide atmosphere was kept with a balloon at the exit. The reaction mixture was continuously stirred at low temperature for 0.5 h, then 4-methoxybenzoyl chloride (0.27 mL, 2.0 mmol) was slowly added dropwise with syringe. The reaction mixture was allowed to reach room temperature slowly and stirred for 2 h. Then, concentrated sulfuric acid (0.87 mL, 16.0 mmol, 8.0 equiv) was added to the reaction system. After stirred for 12 h, the reaction mixture was diluted with 50 mL saturated sodium bicarbonate solution, and extracted with ethyl acetate (3 × 30 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 2:1) as the eluent to afford product 3-ethoxy-1-(4-methoxyphenyl)-3,4-dihydro-6*H*-[1,4]oxazino[3,4-*a*]isoindol-6-one **3g** in yield of 42% (361 mg).

6. Intramolecular rearrangement of 1b and 1e



1b **4b** 40%

H_2O (50 μL, 2.82 mmol, 5.0 equiv) and trifluoromethanesulfonic acid (0.08 mL, 0.85 mmol, 1.5 equiv) were added to a solution of the 3-butyryl-2-(2,2-diethoxyethyl)isoindolin-1-one **1b** (180 mg, 0.56 mmol, 1.0 equiv) in toluene (25 mL). The mixture was stirred at 90 ℃ for 9 h under air atmosphere. After reaching room temperature, the reaction mixture was diluted with 20 mL saturated sodium bicarbonate solution, and extracted with DCM (3 × 10 mL). The combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:7) as the eluent to afford product 4-ethyl-6*H*-isochromeno[4,3-*b*]pyridin-6-one **4b** in yield of 40% (51 mg).

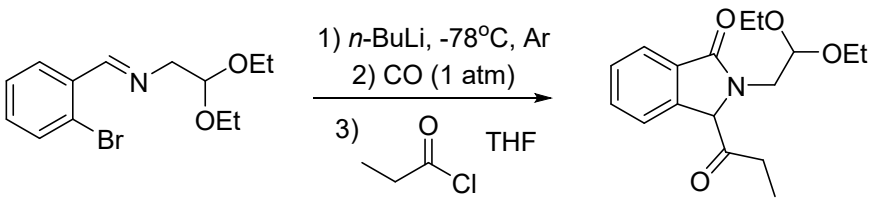


1e **3e** 53% **4i** 10%

H_2O (0.12 mL, 6.51 mmol, 5.0 equiv) and trifluoromethanesulfonic acid (0.17 mL, 1.95 mmol, 1.5 equiv) were added to a solution of the 2-(2,2-diethoxyethyl)-3-(2-phenylacetyl) isoindolin-1-one **1e** (478 mg, 1.30 mmol, 1.0 equiv) in toluene (25 mL). The mixture was stirred at 90 ℃ for 9 h under air atmosphere. After reaching room temperature, the reaction mixture was diluted with 20 mL saturated sodium bicarbonate solution, and extracted with DCM (3 × 15 mL). The combined organic extracts were washed with brine (30 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:7) as the eluent to afford product 4-phenyl-6*H*-benzo[*c*]chromen-6-one **4i** in yield of 10% (35 mg). Meanwhile, 1-benzyl-3-hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one **3e** (189 mg, 53% yield) was also separated by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:7).

7. Gram-scale Synthesis

7.1 Gram-scale synthesis of 2-(2,2-diethoxyethyl)-3-propionylisoindolin-1-one (1a).



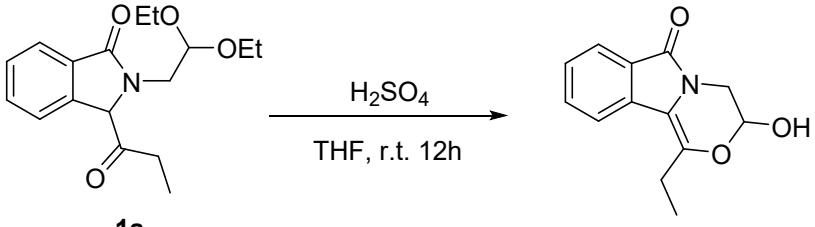
4.8 g, 16.0 mmol

1a

41%, 2.02 g

A hexane solution of *n*-BuLi (1.6 M, 10.0 mL, 16.0 mmol) was slowly added to the stirred solution of 1-(2-bromophenyl)-*N*-(2,2-diethoxyethyl)methanimine (4.8 g, 16.0 mmol) in THF (200 mL) at -78 ℃ under argon atmosphere. After continuously stirring for 30 minutes, carbon monoxide was bubbled into the solution. The carbon monoxide atmosphere was kept with a balloon at the exit. The reaction mixture was continuously stirred at low temperature for 1 h, then acetyl chloride (1.36 mL, 16.0 mmol) was slowly added dropwise with syringe. The reaction mixture was allowed to reach room temperature slowly and stirred for 2 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:3) as the eluent to afford product 2-(2,2-diethoxyethyl)-3-propionylisoindolin-1-one **1a** in yield of 41% (2.02g).

7.2 Gram-scale synthesis of 1-ethyl-3-hydroxy-3,4-dihydro-6*H*-[1,4]oxazino[3,4-*a*]isoindol-6-one (2a).



1a

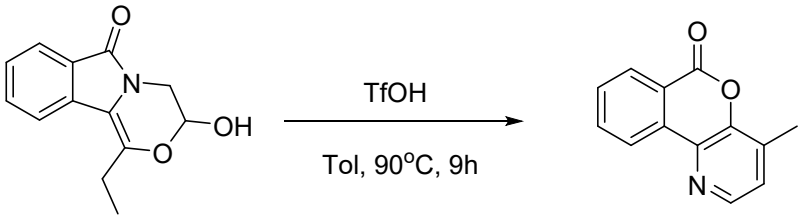
3.5 g, 11.5 mmol

3a

65%, 1.73 g

Concentrated sulfuric acid (5.0 mL, 91.7 mmol, 8.0 equiv) was added to a solution of the 2-(2,2-diethoxyethyl)-3-propionylisoindolin-1-one **1a** (3.5 g, 11.5 mmol, 1.0 equiv) in THF (50 mL). After stirred for 12 h, the reaction mixture was diluted with 300 mL saturated sodium bicarbonate solution, and extracted with ethyl acetate (3 × 150 mL). The combined organic extracts were washed with brine (200 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 3:1) as the eluent to afford product 1-ethyl-3-hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one **3a** in yield of 65% (1.73 g).

7.3 Gram-scale synthesis of 4-methyl-6*H*-isochromeno[4,3-*b*]pyridin-6-one 4a.



3a
1.73 g, 7.49 mmol

4a
73%, 1.16 g

Trifluoromethanesulfonic acid (1.0 mL, 11.23 mmol, 1.5 equiv) was added to a solution of **3a** (1.73g, 7.49 mmol, 1.0 equiv) in toluene (50 mL). The mixture was stirred at 90 ℃ for 9 h under air atmosphere. After reaching room temperature, the reaction mixture was diluted with 200 mL saturated sodium bicarbonate solution, and extracted with DCM (3 × 150 mL). The combined organic extracts were washed with brine (200 mL), dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica with ethyl acetate/petroleum ether (*v*/*v* = 1:7) as the eluent to afford product **4a** in yield of 73% (1.16 g).

8. Bioactivity Test Procedure

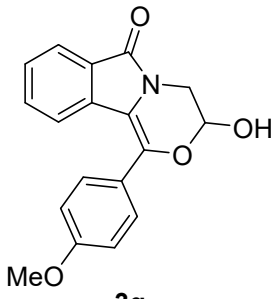
The *in vitro* fungicidal activity of compounds **2**, **3**, **4** and **6** against *Alternaria solani* (*A. s*), *B. cinerea* (*B. c*), *Cercospora arachidicola* (*C. a*), *F. graminearum* (*F. g*), *Physalospora piricola* (*P. p*), *R. solani* (*R. s*), and *Sclerotinia sclerotiorum* (*S. s*) was assessed at a concentration of 50 μg/mL using the mycelium growth-inhibition method.[2] Generally, a mother solution of the test compound (25000 μg/mL) was prepared with N, N-dimethylformamide (DMF) as a solvent, then a test solution (500 μg/mL) was made by adding 100 μL mother solution to 4900 μL sterile water with 0.1% Tween 80. Finally, the culture with 50 μg/mL of the test compound was prepared by mixing 4 mL of the test solution with 36 mL of potato dextrose agar (PDA). Each treatment included three replicates. Pure DMF without the target compound was added into PDA medium as a blank control, BTH was used as a positive control. Their relative inhibitory rate I (%) was calculated according to the following equation:

$$I\ (\%) = [(C-T)/(C-4)]\times 100$$

Where I is the inhibitory rate, C is the colony diameter of the control (mm), T is the colony diameter of treatment (mm), and the diameter of the colony cake inoculated on the medium is 4 (mm).

The immune-inducing activity of compounds **6** was tested as follows according to our previous work[3]: *Arabidopsis thaliana* (Col-0) seeds were sown in soil in a growth chamber on a 16 h light (22 ℃)/8 h dark (20 ℃) cycle for 2 weeks. Twenty seedlings of *A. thaliana* were sprayed with 1 mL of 100 μM of **6a**, **6b**, **6c** or BTH respectively; 0.2% DMF (*N*, *N*-Dimethylformamide) without test compound was used as control. Twenty-four hours after the chemical treatment, seedlings were inoculated with *Hyaloperonospora arabidopsidis* isolate Noco2 with 5×10^4 spores/mL according to the description of Mcdowell et al.[4] After inoculation, seedlings were placed in an incubator at 18 ℃ with 80–100% humidity and were monitored for 7 days. To determine the number of spores, collected seedlings were vortexed in sterile water and counted in a hemocytometer.[5] Each treatment included three replicates.

9. X-ray Structure of 3g and 4b (displacement ellipsoids are drawn at the 30% probability level)



3g

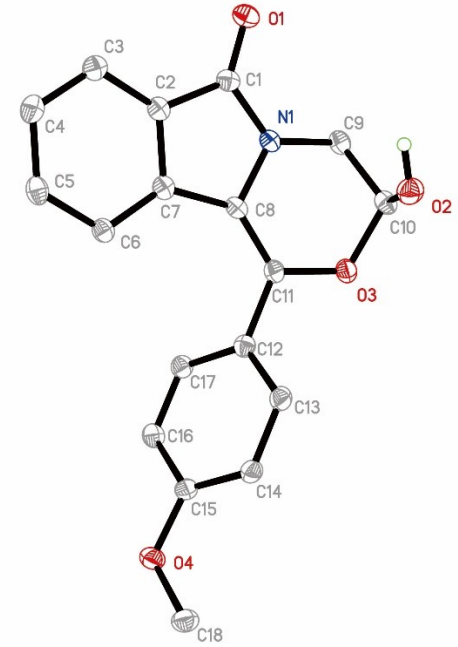


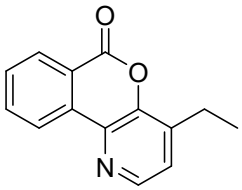
Figure S2. X-ray Structure of Compound 3g.

Single crystal of compound **3g** [$C_{18}H_{15}NO_4$] was cultivated from the mixture solvent system of petroleum hexane/tetrahydrofuran (*v*/*v* = 2:1), and the crystal was obtained when the solvent evaporated slowly. CCDC: 2298279 contains the supplementary crystallographic data which can be obtained free of charge from the Cambridge Crystallographic Data Center via https://www.ccdc.cam.ac.uk/structures/.

Table S1 Crystal Data and Structure Refinement for r20210103b.

Identification code	r20210103b
Empirical formula	$C_{18}H_{15}NO_4$
Formula weight	309.31
Temperature/K	113.15
Crystal system	triclinic
Space group	Pī
a/Å	4.6598(3)
b/Å	14.0337(7)

c/Å	13.5783(16)
α/°	115.794(11)
β/°	93.082(7)
γ/°	94.546(7)
Volume/Å^3	715.88(14)
Z	2
ρ_{calc}g/cm^3	1.435
μ/mm^{-1}	0.102
F(000)	324.0
Crystal size/mm^3	0.22 × 0.18 × 0.16
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.674 to 52.744
Index ranges	-5 ≤ h ≤ 5, -15 ≤ k ≤ 15, -16 ≤ l ≤ 16
Reflections collected	7528
Independent reflections	2915 [Rint = 0.0515, Rsigma = 0.0639]
Data/restraints/parameters	2915/0/211
Goodness-of-fit on F^2	1.033
Final R indexes [I>=2σ (I)]	R_1 = 0.0834, wR_2 = 0.2180
Final R indexes [all data]	R_1 = 0.1115, wR_2 = 0.2424
Largest diff. peak/hole / e Å^{-3}	0.62/-0.28



4b

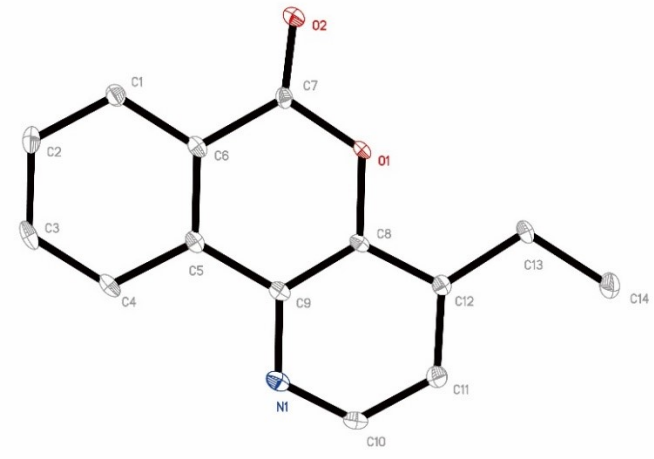


Figure S3. **X-ray Structure of Compound 4b.**

Single crystal of compound **4b** [$C_{14}H_{11}NO_2$] was cultivated from the mixture solvent system of petroleum hexane/dichloromethane (*v*/*v* = 2:1), and the crystal was obtained when the solvent evaporated slowly. CCDC: 2298345 contains the supplementary crystallographic data which can be obtained free of charge from the Cambridge Crystallographic Data Center via https://www.ccdc.cam.ac.uk/structures/.

Table S2 Crystal Data and Structure Refinement for P200907a9.

Identification code	P200907a9
Empirical formula	$C_{14}H_{11}NO_2$
Formula weight	225.24
Temperature/K	136.2(3)
Crystal system	monoclinic
Space group	P2/n
a/Å	6.6228(5)
b/Å	8.4131(6)
c/Å	18.9386(13)
α/°	90
β/°	93.381(6)
γ/°	90
Volume/Å^3	1053.39(13)
Z	4
ρ_{calc}g/cm^3	1.420
μ/mm^{-1}	0.096
F(000)	472.0
Crystal size/mm^3	1 × 0.5 × 0.2
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.408 to 52.998
Index ranges	$-8 \le h \le 8$, $-10 \le k \le 10$, $-22 \le l \le 23$
Reflections collected	6655
Independent reflections	2163 [R_{int} = 0.0351, R_{sigma} = 0.0378]
Data/restraints/parameters	2163/0/155
Goodness-of-fit on F^2	1.023
Final R indexes [I>=2σ (I)]	R_1 = 0.1122, wR_2 = 0.2190
Final R indexes [all data]	R_1 = 0.1231, wR_2 = 0.2236
Largest diff. peak/hole / e Å^{-3}	0.67/-0.46

10. Reference

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11. Product Characterization

11.1 Product Characterization of 3-Acyl-*N*-(2,2-diethoxyethyl)isoindolin-1-ones 1

2-(2,2-Diethoxyethyl)-3-propionylisoindolin-1-one(1a)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (891 mg, 58%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.75 (m, 1H), 7.49 (td, J = 7.4, 1.4 Hz, 1H), 7.44 (t, J = 7.0 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 5.32 (s, 1H), 4.60 (dd, J = 6.3, 3.5 Hz, 1H), 4.17 (dd, J = 14.4, 3.5 Hz, 1H), 3.64 (dqd, J = 9.4, 7.0, 4.5 Hz, 2H), 3.52 (dq, J = 9.3, 7.0 Hz, 1H), 3.40 (dq, J = 9.4, 7.0 Hz, 1H), 3.11 (dd, J = 14.4, 6.3 Hz, 1H), 2.38 (dq, J = 18.4, 7.3 Hz, 1H), 2.17 (dq, J = 18.4, 7.2 Hz, 1H), 1.14 (t, J = 7.0 Hz, 3H), 1.08 (t, J = 7.0 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 169.4, 139.6, 132.1, 131.5, 129.1, 124.2, 122.4, 100.8, 70.8, 63.3, 62.9, 44.5, 31.0, 15.27, 15.24, 7.4.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_4$ 328.1519; Found 328.1523.

3-Butyryl-2-(2,2-diethoxyethyl)isoindolin-1-one (1b)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (1.249 g, 51%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92–7.86 (m, 1H), 7.57 (td, J = 7.4, 1.4 Hz, 1H), 7.52 (t, J = 7.0 Hz, 1H), 7.49–7.44 (m, 1H), 5.39 (s, 1H), 4.69 (dd, J = 6.4, 3.5 Hz, 1H), 4.27 (dd, J = 14.4, 3.5 Hz, 1H), 3.72 (dqd, J = 9.4, 7.0, 4.6 Hz, 2H), 3.60 (dq, J = 9.3, 7.0 Hz, 1H), 3.48 (dq, J = 9.4, 7.0 Hz, 1H), 3.17 (dd, J = 14.4, 6.4 Hz, 1H), 2.37 (ddd, J = 17.8, 7.9, 6.4 Hz, 1H), 2.21 (ddd, J = 17.8, 7.7, 6.8 Hz, 1H), 1.50 (dt, J = 22.2, 7.4 Hz, 2H), 1.23 (t, J = 7.0 Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H), 0.78 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.8, 169.4, 139.4, 132.1, 131.5, 129.1, 124.2, 122.4, 100.7, 70.9, 63.3, 62.89, 44.5, 39.4, 16.6, 15.3, 15.2, 13.5.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{25}NNaO_4$ 342.1676; Found 342.1678.

3-Acetyl-2-(2,2-diethoxyethyl)isoindolin-1-one (1c)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 5:2) to give the product as a yellow oil (610 mg, 70%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.1 Hz, 1H), 7.49 (td, J = 7.4, 1.3 Hz, 1H), 7.44 (t, J = 7.1 Hz, 1H), 7.39 (d, J = 7.2 Hz, 1H), 5.25 (s, 1H), 4.61 (dd, J = 6.1, 3.7 Hz, 1H), 4.12 (dd, J = 14.4, 3.7 Hz, 1H), 3.63 (dqd, J = 9.4, 7.0, 4.8 Hz, 2H), 3.58–3.48 (m, 1H), 3.41 (dq, J = 9.3, 7.0 Hz, 1H), 3.19 (dd, J = 14.4, 6.1 Hz, 1H), 1.92 (s, 3H), 1.14 (t, J = 7.0 Hz, 3H), 1.07 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.8, 169.3, 139.3, 132.2, 131.5, 129.2, 124.1, 122.5, 100.7, 71.2, 63.2, 62.8, 44.5, 24.8, 15.23, 15.20.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{21}NNaO_4$ 314.1363; Found 314.1359.

2-(2,2-Diethoxyethyl)-3-(3-methylbutanoyl)isoindolin-1-one (1d)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash

chromatography (petroleum ether/ethyl acetate = 4:1) to give the product as a yellow oil (460 mg, 69%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.3 Hz, 1H), 7.53–7.41 (m, 2H), 7.38 (t, J = 7.8 Hz, 1H), 5.29 (s, 1H), 4.59 (dd, J = 6.0, 3.2 Hz, 1H), 4.20 (dd, J = 14.3, 3.0 Hz, 1H), 3.63 (tt, J = 14.0, 6.9 Hz, 2H), 3.54–3.44 (m, 1H), 3.38 (td, J = 14.3, 7.0 Hz, 1H), 3.05 (dd, J = 14.3, 6.4 Hz, 1H), 2.17 (dd, J = 16.3, 5.3 Hz, 1H), 2.10–1.90 (m, 2H), 1.13 (t, J = 7.0 Hz, 3H), 1.06 (t, J = 7.0 Hz, 3H), 0.74 (d, J = 6.2 Hz, 3H), 0.60 (d, J = 6.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.1, 169.3, 139.2, 132.0, 131.5, 129.0, 124.1, 122.4, 100.7, 71.0, 63.2, 62.8, 46.3, 44.4, 23.5, 22.4, 22.1, 15.22, 15.18.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{27}NNaO_4$ 356.1832; Found 356.1836.

2-(2,2-Diethoxyethyl)-3-(2-phenylacetyl)isoindolin-1-one (1e)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (773 mg, 70%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 4.8 Hz, 1H), 7.55–7.47 (m, 2H), 7.36 (d, J = 6.7 Hz, 1H), 7.21 (d, J = 7.0 Hz, 3H), 6.96 (d, J = 7.1 Hz, 2H), 5.44 (s, 1H), 4.72–4.61 (m, 1H), 4.16 (dd, J = 14.4, 2.5 Hz, 1H), 3.68 (ddd, J = 15.1, 10.4, 6.1 Hz, 2H), 3.63–3.53 (m, 2H), 3.53–3.40 (m, 1H), 3.17 (dd, J = 14.3, 5.9 Hz, 1H), 1.21 (t, J = 6.8 Hz, 3H), 1.14 (t, J = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 203.3, 169.5, 139.4, 132.7, 132.2, 131.7, 129.4, 129.3, 128.5, 127.1, 124.2, 122.7, 100.6, 71.0, 63.3, 62.8, 44.7, 44.3, 15.31, 15.25.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{25}NNaO_4$ 390.1676; Found 390.1675.

3-Benzoyl-2-(2,2-diethoxyethyl)isoindolin-1-one (1f)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give the product as a yellow oil (520 mg, 74%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–8.01 (m, 2H), 7.89 (d, J = 7.4 Hz, 1H), 7.72–7.65 (m, 1H), 7.57 (t, J = 7.7 Hz, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.38 (td, J = 7.5, 1.2 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 6.55 (s, 1H), 4.70–4.62 (m, 1H), 4.37 (dd, J = 14.6, 3.4 Hz, 1H), 3.74–3.64 (m, 2H), 3.52 (ddq, J = 14.0, 9.3, 7.0 Hz, 2H), 3.25 (dd, J = 14.6, 5.7 Hz, 1H), 1.16 (t, J = 7.0 Hz, 3H), 1.08 (t, J = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 169.2, 140.1, 135.9, 134.1, 131.7, 131.6, 129.1, 128.9, 128.8, 124.3, 122.5, 101.3, 66.2, 63.1, 63.0, 43.6, 15.3, 15.2.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{23}NNaO_4$ 376.1519; Found 376.1519.

2-(2,2-Diethoxyethyl)-3-(4-methoxybenzoyl)isoindolin-1-one (1g)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a yellow oil (478 mg, 62%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.01 (m, 2H), 7.88 (d, J = 7.1 Hz, 1H), 7.49–7.35 (m, 2H), 7.17 (d, J = 7.6 Hz, 1H), 7.08–7.00 (m, 2H), 6.49 (s, 1H), 4.71–4.61 (m, 1H), 4.35 (dd, J = 14.6, 3.4 Hz, 1H), 3.91 (s, 3H), 3.75–3.63 (m, 2H), 3.60–3.44 (m, 2H), 3.24 (dd, J = 14.6, 5.9 Hz, 1H), 1.16 (t, J = 7.0 Hz, 3H), 1.10 (t, J = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 169.2, 164.3, 140.5, 131.8, 131.5, 131.3, 128.73, 128.67, 124.2, 122.4, 114.3, 101.3, 65.89, 63.0, 62.9, 55.6, 43.6, 15.3, 15.2.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{25}NNaO_5$ 406.1625; Found 406.1630.

2-(2,2-Diethoxyethyl)-3-(3-(trifluoromethyl)benzoyl)isoindolin-1-one (1h)
According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 5:2) to give the product as a yellow oil (459 mg, 54%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.18 (d, J = 7.9 Hz, 1H), 7.94 (t, J = 8.6 Hz, 2H), 7.72 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.42 (td, J = 7.5, 1.2 Hz, 1H), 7.10–7.03 (m, 1H), 6.55 (s, 1H), 4.64 (dd, J = 5.3, 3.3 Hz, 1H), 4.45–4.33 (m, 1H), 3.69 (dq, J = 9.0, 7.2 Hz, 2H), 3.62–3.44 (m, 3H), 3.23 (dd, J = 14.6, 5.4 Hz, 1H), 1.18 (t, J = 7.0 Hz, 3H), 1.07 (t, J = 7.0 Hz, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 192.6, 169.2, 139.6, 136.6, 131.9, 131.81, 131.79 (q, J = 30.6 Hz), 131.7, 130.4 (q, J = 3.2 Hz), 129.8, 129.1, 125.8 (q, J = 3.3 Hz), 124.5, 123.5 (q, J = 272.7 Hz), 122.2, 101.4, 66.2, 63.30, 63.27, 43.5, 15.2, 15.1.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{22}F_3NNaO_4$ 444.1393; Found 444.1396.

2-(2,2-Diethoxyethyl)-3-(furan-2-carbonyl)isoindolin-1-one (1i)
According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 4:1) to give the product as a yellow oil (622 mg, 60%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92–7.86 (m, 1H), 7.76 (d, J = 1.1 Hz, 1H), 7.46 (dd, J = 5.6, 3.1 Hz, 2H), 7.35 (d, J = 3.6 Hz, 1H), 7.34–7.29 (m, 2H), 6.66 (dd, J = 3.6, 1.6 Hz, 1H), 6.26 (s, 1H), 4.65 (dd, J = 5.9, 3.6 Hz, 1H), 4.30 (dd, J = 14.5, 3.5 Hz, 1H), 3.74–3.64 (m, 2H), 3.51 (dqd, J = 14.0, 7.0, 3.5 Hz, 2H), 3.27 (dd, J = 14.5, 6.0 Hz, 1H), 1.12 (dt, J = 14.0, 7.0 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 182.4, 169.3, 151.3, 147.5, 140.3, 131.8, 131.6, 128.9, 124.2, 122.6, 119.4, 113.1, 101.1, 66.6, 63.1, 62.7, 43.8, 15.2, 15.1.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{21}NNaO_5$ 366.1312; Found 366.1310.

3-Benzoyl-2-(2,2-diethoxyethyl)-5-methoxyisoindolin-1-one (1j)
According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a yellow oil (346 mg, 45%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–7.95 (m, 2H), 7.81 (d, J = 8.4 Hz, 1H), 7.67 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.7 Hz, 2H), 7.05–6.91 (m, 1H), 6.63 (t, J = 5.6 Hz, 1H), 6.41 (s, 1H), 4.70–4.57 (m, 1H), 4.29 (dd, J = 14.6, 3.4 Hz, 1H), 3.82–3.62 (m, 6H), 3.59–3.43 (m, 3H), 3.20 (dd, J = 14.6, 5.9 Hz, 1H), 1.17 (t, J = 7.0 Hz, 3H), 1.09 (t, J = 7.0 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 169.1, 162.7, 142.3, 135.9, 134.0, 129.1, 128.8, 125.6, 124.2, 114.6, 108.2, 101.3, 66.3, 63.1, 63.0, 55.5, 43.7, 15.3, 15.2.
HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{25}NNaO_5$ 406.1625; Found 406.1623.

2-(2,2-Diethoxyethyl)-5-methoxy-3-propionylisoindolin-1-one (1k)
According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a yellow oil (473 mg,

71%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 1H), 7.01 (dd, J = 8.4, 2.1 Hz, 1H), 6.89 (d, J = 1.5 Hz, 1H), 5.27 (s, 1H), 4.66 (dd, J = 6.3, 3.6 Hz, 1H), 4.17 (dd, J = 14.4, 3.6 Hz, 1H), 3.84 (s, 3H), 3.73–3.64 (m, 2H), 3.61–3.51 (m, 1H), 3.45 (dq, J = 9.3, 7.0 Hz, 1H), 3.15 (dd, J = 14.4, 6.4 Hz, 1H), 2.40 (dq, J = 18.5, 7.2 Hz, 1H), 2.19 (dq, J = 18.5, 7.2 Hz, 1H), 1.20 (t, J = 7.0 Hz, 3H), 1.13 (t, J = 7.0 Hz, 4H), 0.95 (t, J = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.0, 169.4, 163.2, 142.0, 125.4, 124.0, 115.9, 107.1, 100.8, 70.8, 63.3, 62.9, 55.7, 44.7, 30.5, 15.25, 15.23, 7.4.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{25}NNaO_5$ 358.1625; Found 358.1630.

3-Butyryl-2-(2,2-diethoxyethyl)-5-methoxyisoindolin-1-one (1l)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (229 mg, 84%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (t, J = 7.5 Hz, 1H), 7.02 (dd, J = 8.4, 1.6 Hz, 1H), 6.90 (s, 1H), 5.26 (s, 1H), 4.67 (dd, J = 6.4, 3.5 Hz, 1H), 4.20 (dd, J = 14.4, 3.4 Hz, 1H), 3.84 (s, 3H), 3.70 (ddd, J = 13.6, 6.9, 3.4 Hz, 2H), 3.62–3.56 (m, 1H), 3.46 (dd, J = 9.1, 6.9 Hz, 1H), 3.20–3.09 (m, 1H), 2.36–2.27 (m, 1H), 2.15 (dt, J = 17.8, 7.2 Hz, 1H), 1.56–1.41 (m, 2H), 1.21 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H), 0.75 (dd, J = 15.9, 8.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 206.4, 169.4, 163.2, 141.8, 125.4, 124.1, 116.0, 107.1, 100.8, 70.9, 63.3, 62.9, 55.7, 44.7, 38.9, 16.6, 15.25, 15.22, 13.5.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{27}NNaO_5$ 372.1781; Found 372.1781.

2-(2,2-Diethoxyethyl)-5-methoxy-3-(3-methylbutanoyl)isoindolin-1-one (1m)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 5:2) to give the product as a yellow oil (841 mg, 50%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4 Hz, 1H), 6.96 (dd, J = 8.4, 2.0 Hz, 1H), 6.84 (s, 1H), 5.20 (s, 1H), 4.60 (dd, J = 6.5, 3.4 Hz, 1H), 4.16 (dd, J = 14.4, 3.3 Hz, 1H), 3.78 (s, 3H), 3.64 (dqd, J = 14.0, 7.0, 4.0 Hz, 2H), 3.57–3.46 (m, 1H), 3.44–3.32 (m, 1H), 3.04 (dd, J = 14.4, 6.6 Hz, 1H), 2.19–2.08 (m, 1H), 2.06–1.94 (m, 2H), 1.15 (t, J = 7.0 Hz, 3H), 1.08 (t, J = 7.0 Hz, 3H), 0.77 (d, J = 6.3 Hz, 3H), 0.61 (d, J = 6.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.8, 169.3, 163.1, 141.5, 125.4, 124.0, 115.9, 107.0, 100.8, 71.0, 63.3, 62.8, 55.7, 45.9, 44.5, 23.5, 22.5, 22.1, 15.23, 15.20.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{29}NNaO_5$ 386.1938; Found 386.1939.

3-Benzoyl-2-(2,2-diethoxyethyl)-5-fluoroisoindolin-1-one (1n)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give the product as a yellow oil (379 mg, 40%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06–7.99 (m, 2H), 7.88 (dd, J = 8.3, 5.0 Hz, 1H), 7.71 (t, J = 7.4 Hz, 1H), 7.58 (t, J = 7.3 Hz, 2H), 7.15 (t, J = 8.7 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 6.52 (s, 1H), 4.66–4.60 (m, 1H), 4.34 (dd, J = 14.6, 3.2 Hz, 1H), 3.74–3.64 (m, 2H), 3.59–3.43 (m, 2H), 3.23 (dd, J = 14.6, 5.5 Hz, 1H), 1.17 (t, J = 7.0 Hz, 3H), 1.07 (t, J = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.9, 168.2, 164.9 (d, J = 251.8 Hz), 142.3 (d, J = 10.0 Hz), 135.71, 134.4, 129.2, 128.9, 127.8, 126.3 (d, J = 9.8 Hz), 116.5 (d, J = 23.4 Hz), 110.1 (d, J = 25.0 Hz), 101.3, 65.8, 63.2, 43.6, 15.3, 15.1.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{22}FNNaO_4$ 394.1425; Found 394.1425.

2-(2,2-Diethoxyethyl)-5-fluoro-3-propionylisoindolin-1-one (1o)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (416 mg, 64%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91–7.77 (m, 1H), 7.18 (td, J = 8.7, 2.1 Hz, 1H), 7.12 (dd, J = 7.9, 1.8 Hz, 1H), 5.33 (s, 1H), 4.67–4.60 (m, 1H), 4.26–4.17 (m, 1H), 3.73–3.62 (m, 2H), 3.55 (dq, J = 9.3, 7.0 Hz, 1H), 3.44 (dq, J = 9.4, 7.0 Hz, 1H), 3.12 (dt, J = 15.2, 7.6 Hz, 1H), 2.41–2.27 (m, 1H), 2.25–2.13 (m, 1H), 1.56–1.42 (m, 2H), 1.21–1.16 (m, 3H), 1.11 (t, J = 7.0 Hz, 3H), 0.76 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.2, 168.4, 165.2 (d, J = 252.7 Hz), 141.8 (d, J = 10.1 Hz), 127.6 (s), 126.2 (d, J = 9.7 Hz), 116.9 (d, J = 23.6 Hz), 109.9 (d, J = 24.8 Hz), 100.7, 70.5 (d, J = 2.2 Hz), 63.4, 63.0, 44.5, 39.6, 16.5, 15.24, 15.20, 13.4.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{22}FNNaO_4$ 346.1425; Found 346.1427.

3-Butyryl-2-(2,2-diethoxyethyl)-5-fluoroisoindolin-1-one (1p)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (304 mg, 45%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 8.4, 5.0 Hz, 1H), 7.18 (td, J = 8.7, 2.1 Hz, 1H), 7.12 (dd, J = 7.9, 1.8 Hz, 1H), 5.33 (s, 1H), 4.63 (dd, J = 6.2, 3.4 Hz, 1H), 4.21 (dd, J = 14.4, 3.4 Hz, 1H), 3.73–3.62 (m, 2H), 3.55 (dq, J = 9.3, 7.0 Hz, 1H), 3.44 (dq, J = 9.4, 7.0 Hz, 1H), 3.13 (dd, J = 14.4, 6.2 Hz, 1H), 2.41–2.28 (m, 1H), 2.25–2.13 (m, 1H), 1.49 (tt, J = 14.7, 7.4 Hz, 2H), 1.18 (t, J = 7.0 Hz, 3H), 1.11 (t, J = 7.0 Hz, 3H), 0.76 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.2, 168.4, 165.2 (d, J = 252.7 Hz), 141.8 (d, J = 10.1 Hz), 127.6, 126.2 (d, J = 9.7 Hz), 116.9 (d, J = 23.6 Hz), 109.9 (d, J = 24.8 Hz), 100.7, 70.5 (d, J = 2.2 Hz), 44.5, 39.6, 16.5, 15.24, 15.20, 13.4.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{24}FNNaO_4$ 360.1582; Found 360.1584.

2-(2,2-Diethoxyethyl)-5-fluoro-3-(3-methylbutanoyl)isoindolin-1-one (1q)

According to the *general procedure* (**3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 4:1) to give the product as a yellow oil (407 mg, 58%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 8.4, 5.0 Hz, 1H), 7.21 (td, J = 8.7, 2.1 Hz, 1H), 7.15 (d, J = 7.9 Hz, 1H), 5.34 (s, 1H), 4.71–4.61 (m, 1H), 4.27 (dd, J = 14.4, 3.3 Hz, 1H), 3.76–3.66 (m, 2H), 3.59 (dq, J = 9.3, 7.0 Hz, 1H), 3.47 (dq, J = 9.4, 7.0 Hz, 1H), 3.11 (dt, J = 13.7, 6.9 Hz, 1H), 2.30–2.20 (m, 1H), 2.16–2.03 (m, 2H), 1.25–1.20 (m, 3H), 1.15 (t, J = 7.0 Hz, 3H), 0.86 (d, J = 6.4 Hz, 3H), 0.72 (d, J = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8, 168.4, 165.2 (d, J = 253.5 Hz), 141.6 (d, J = 10.0 Hz), 127.6, 126.2 (d, J = 9.9 Hz), 116.9 (d, J = 23.5 Hz), 110.0 (d, J = 24.8 Hz), 100.8, 70.8 (d, J = 2.3 Hz), 63.4, 63.1, 46.5, 44.6, 23.6, 22.5, 22.2, 15.28, 15.24.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{26}FNNaO_4$ 374.1738; Found 374.1741.

11.2 Product Characterization of 3-Ethoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-ones (2)

3-Ethoxy-1-ethyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2a)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give the product as a yellow oil (400 mg, 71%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.56–7.51 (m, 1H), 7.41–7.35 (m, 1H), 5.36–5.21 (m, 1H), 4.01–3.84 (m, 3H), 3.77–3.64 (m, 1H), 2.69 (tt, J = 14.8, 7.3 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 140.5, 134.1, 131.3, 129.1, 126.8, 123.7, 120.7, 113.9, 96.3, 64.9, 42.0, 24.2, 15.0, 11.7.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}NO_3$ 260.1281; Found 260.1285.

3-Ethoxy-1-propyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2b)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give the product as a yellow oil (252 mg, 74%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.4 Hz, 1H), 5.27 (s, 1H), 4.04–3.85 (m, 3H), 3.77–3.65 (m, 1H), 2.67 (t, J = 7.4 Hz, 2H), 1.76 (dq, J = 14.8, 7.2 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H), 1.06 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 139.3, 134.3, 131.2, 129.2, 126.7, 123.7, 120.7, 114.7, 96.3, 64.9, 42.1, 32.6, 20.6, 15.0, 13.7.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}NO_3$ 274.1438; Found 274.1444.

3-Ethoxy-1-methyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2c)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:1) to give the product as a yellow oil (143 mg, 94%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 1H), 7.63 (d, J = 7.9 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.4 Hz, 1H), 5.27 (t, J = 3.4 Hz, 1H), 4.00–3.85 (m, 3H), 3.71 (dq, J = 9.6, 7.1 Hz, 1H), 2.34 (s, 3H), 1.25 (t, J = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 135.2, 134.3, 131.2, 129.1, 126.8, 123.7, 120.6, 114.5, 96.4, 65.0, 42.0, 16.9, 15.0.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{16}NO_3$ 246.1125; Found 246.1123.

3-Ethoxy-1-isobutyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2d)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (102 mg, 89%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 7.4 Hz, 1H), 5.24 (d, J = 2.9 Hz, 1H), 4.00–3.83 (m, 3H), 3.69 (dq, J = 14.3, 7.1 Hz, 1H), 2.58 (dd, J = 14.3, 6.7 Hz, 1H), 2.51 (dd, J = 14.2, 8.0 Hz, 1H), 2.12 (tt, J = 13.4, 6.7 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H), 1.03 (d, J = 6.6 Hz, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7, 138.9, 134.3, 131.2, 129.3, 126.8, 123.7, 120.8, 115.2, 96.3, 65.0, 42.1, 39.6, 27.4, 22.7, 22.1, 15.0.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{22}NO_3$ 288.1594; Found 288.1592.

1-Benzyl-3-ethoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2e)
According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a white solid (371 mg, 97%), m.p.: 160-161 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 7.9 Hz, 1H), 7.64–7.52 (m, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.37–7.31 (m, 4H), 7.30–7.26 (m, 1H), 5.25 (t, J = 2.8 Hz, 1H), 4.18–4.08 (m, 2H), 3.92 (d, J = 15.6 Hz, 1H), 3.83 (dd, J = 13.0, 2.8 Hz, 1H), 3.49–3.38 (m, 2H), 1.05 (t, J = 7.1 Hz, 3H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 164.0, 136.9, 136.7, 134.1, 131.6, 129.4, 128.7, 128.5, 127.2, 127.0, 123.8, 120.5, 115.7, 95.9, 64.6, 42.1, 36.7, 14.7.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}NO_3$ 322.1438; Found 322.1435.

3-Ethoxy-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2f)
According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give the product as a yellow oil (353 mg, 78%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, J = 4.3, 3.7 Hz, 1H), 7.69–7.61 (m, 2H), 7.53–7.46 (m, 3H), 7.33 (ddt, J = 14.5, 13.6, 4.5 Hz, 3H), 5.44 (t, J = 3.1 Hz, 1H), 4.17–4.10 (m, 1H), 4.09–4.01 (m, 1H), 4.01–3.94 (m, 1H), 3.80 (dq, J = 9.6, 7.1 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 136.7, 134.1, 133.1, 131.1, 130.0, 129.4, 129.0, 128.7, 127.5, 123.4, 120.6, 115.7, 96.7, 65.1, 42.2, 15.1.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}NO_3$ 308.1281; Found 308.1286.

3-Ethoxy-1-(4-methoxyphenyl)-3,4-dihydro-6*H*-[1,4]oxazino[3,4-*a*]isoindol-6-one (2g)
According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a yellow solid (168 mg, 57%), m.p.: 165-166 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.84 (m, 1H), 7.61–7.54 (m, 2H), 7.37–7.29 (m, 3H), 7.05–6.98 (m, 2H), 5.42 (dd, J = 3.6, 2.8 Hz, 1H), 4.12–3.95 (m, 3H), 3.90 (s, 3H), 3.83–3.74 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 161.0, 136.8, 134.2, 131.0, 130.9, 129.0, 127.3, 125.3, 123.4, 120.5, 115.0, 114.1, 96.8, 65.0, 55.4, 42.2, 15.1.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}NO_4$ 338.1387; Found 338.1390.

3-Ethoxy-1-(3-(trifluoromethyl)phenyl)-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2h)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (152 mg, 78%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.90–7.84 (m, 2H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 5.48 (s, 1H), 4.14 (dt, *J* = 14.2, 7.1 Hz, 1H), 4.06 (dt, *J* = 14.4, 7.3 Hz, 1H), 3.98 (dd, *J* = 12.9, 1.6 Hz, 1H), 3.86 – 3.76 (m, 1H), 1.29 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) *δ* 164.1, 134.9, 134.1, 133.6, 132.7, 131.4, 131.2 (q, *J* = 32.6 Hz), 129.3, 129.1, 128.0, 126.5 (d, *J* = 3.3 Hz), 126.2 (q, *J* = 3.4 Hz), 123.8 (q, *J* = 272.6 Hz), 123.6, 120.3, 116.7, 96.8, 65.3, 42.2, 15.0.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{17}F_3NO_3$ 376.1155; Found 376.1161.

3-Ethoxy-1-(furan-2-yl)-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2i)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give the product as a yellow oil (60 mg, 76%)

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.16 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.65 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.56–7.48 (m, 1H), 7.42 (td, *J* = 7.5, 0.8 Hz, 1H), 6.81 (dd, *J* = 3.5, 0.7 Hz, 1H), 6.59 (dd, *J* = 3.4, 1.8 Hz, 1H), 5.42 (t, *J* = 3.0 Hz, 1H), 4.15–4.06 (m, 1H), 4.01–3.93 (m, 1H), 3.93–3.88 (m, 1H), 3.74 (tt, *J* = 7.1, 4.1 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) *δ* 164.3, 147.6, 143.4, 133.4, 131.5, 129.0, 127.8, 127.1, 123.4, 122.4, 116.6, 111.85, 111.79, 96.1, 65.0, 42.4, 15.0.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}NO_4$ 298.1074; Found 298.1071.

3-Ethoxy-9-methoxy-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2j)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a yellow oil (164 mg, 72%)

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.74 (t, *J* = 12.7 Hz, 1H), 7.66 (s, 2H), 7.49 (s, 3H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.75 (s, 1H), 5.43 (s, 1H), 4.08 (d, *J* = 9.2 Hz, 2H), 4.00–3.88 (m, 1H), 3.81 (dd, *J* = 20.2, 12.9 Hz, 1H), 3.64 (s, 3H), 1.28 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) *δ* 164.0, 162.3, 136.5, 136.1, 133.1, 130.1, 129.5, 128.6, 124.7, 122.2, 115.8, 114.6, 105.1, 96.8, 65.0, 55.3, 42.2, 15.1.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{20}NO_4$ 338.1387; Found 338.1394.

3-Ethoxy-1-ethyl-9-methoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2k)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:1) to give the product as a yellow oil (65 mg, 75%)

^{1}H NMR (600 MHz, $CDCl_3$) *δ* 7.80 (d, *J* = 8.4 Hz, 1H), 7.06 (s, 1H), 6.93 (d, *J* = 7.4 Hz, 1H), 5.25 (s, 1H), 3.97–3.83 (m, 6H), 3.70 (dq, *J* = 14.4, 7.1 Hz, 1H), 2.73–2.58 (m, 2H), 1.27 (t, *J* = 7.6 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) *δ* 163.7, 162.6, 140.4, 136.0, 125.0, 122.4, 113.9, 112.9, 106.1, 96.3, 64.9, 55.7, 42.0, 24.2, 15.0, 11.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}NO_4$ 290.1387; Found 290.1381.

3-Ethoxy-9-methoxy-1-propyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2l)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a yellow oil (130 mg, 86%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 1H), 7.08 (s, 1H), 6.92 (d, J = 8.3 Hz, 1H), 5.23 (s, 1H), 3.96–3.83 (m, 6H), 3.69 (td, J = 14.5, 7.1 Hz, 1H), 2.61 (t, J = 7.4 Hz, 2H), 1.73 (dt, J = 14.5, 7.2 Hz, 2H), 1.23 (t, J = 7.0 Hz, 3H), 1.04 (t, J = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.6, 162.5, 139.3, 136.2, 125.0, 122.4, 114.6, 112.9, 106.2, 96.3, 64.9, 55.7, 42.0, 32.6, 20.6, 15.0, 13.7.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{22}NO_4$ 304.1543; Found 304.1548.

3-Ethoxy-1-isobutyl-9-methoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2m)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 5:4) to give the product as a yellow oil (112 mg, 75%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 1H), 7.10 (d, J = 2.1 Hz, 1H), 6.93 (dd, J = 8.5, 2.2 Hz, 1H), 5.22 (t, J = 3.5 Hz, 1H), 3.98 – 3.91 (m, 1H), 3.90 – 3.87 (m, 5H), 3.68 (dq, J = 9.6, 7.1 Hz, 1H), 2.55 (dd, J = 14.2, 6.8 Hz, 1H), 2.47 (dd, J = 14.2, 7.8 Hz, 1H), 2.11 (dp, J = 20.3, 6.7 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.05 (d, J = 6.7 Hz, 3H), 1.03 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 162.4, 138.9, 136.2, 125.0, 122.5, 115.1, 112.9, 106.4, 96.3, 65.0, 55.6, 42.0, 39.6, 27.4, 22.7, 22.2, 15.0.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{24}NO_4$ 318.1700; Found 318.1694.

3-Ethoxy-9-fluoro-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2n)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (83 mg, 78%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.4, 5.2 Hz, 1H), 7.65–7.60 (m, 2H), 7.54–7.49 (m, 3H), 7.03 (td, J = 8.7, 2.2 Hz, 1H), 6.92 (dd, J = 9.5, 2.2 Hz, 1H), 5.46 (q, J = 2.9 Hz, 1H), 4.13 (dd, J = 13.0, 3.5 Hz, 1H), 4.09–4.02 (m, 1H), 3.94 (dd, J = 13.0, 2.6 Hz, 1H), 3.80 (dq, J = 9.6, 7.1 Hz, 1H), 1.28 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7 (d, J = 248.8 Hz), 163.2, 137.8, 136.0 (d, J = 11.3 Hz), 132.6, 130.4, 129.3, 128.9, 125.4 (d, J = 10.3 Hz), 125.1 (d, J = 1.2 Hz), 115.3 (d, J = 24.3 Hz), 107.5 (d, J = 26.1 Hz), 96.7, 65.1, 42.2, 15.1.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{17}FNO_3$ 326.1187; Found 326.1192.

3-Ethoxy-1-ethyl-9-fluoro-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2o)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give the product as a yellow oil (149 mg, 97%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 (dd, J = 8.1, 5.3 Hz, 1H), 7.26 (d, J = 9.7 Hz, 1H), 7.08 (t, J = 8.5 Hz, 1H), 5.28 (s, 1H), 3.98 (dd, J = 13.0, 3.3 Hz, 1H), 3.93 (dd, J = 15.6, 8.2 Hz, 1H), 3.84

(dd, *J* = 12.9, 1.8 Hz, 1H), 3.75 – 3.65 (m, 1H), 2.71–2.55 (m, 2H), 1.28 (t, *J* = 7.5 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0 (d, *J* = 248.7 Hz), 162.9, 141.5, 136.0 (d, *J* = 10.9 Hz), 125.6 (d, *J* = 10.7 Hz), 125.2, 114.5 (d, *J* = 24.3 Hz), 113.4 (d, *J* = 3.7 Hz), 107.7 (d, *J* = 26.0 Hz), 96.3, 64.9, 42.0, 24.1, 15.0, 11.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}FNO_3$ 278.1187; Found 278.1183.

3-Ethoxy-9-fluoro-1-propyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2p)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:2) to give the product as a yellow oil (118 mg, 83%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.2, 5.2 Hz, 1H), 7.31–7.20 (m, 1H), 7.08 (t, *J* = 8.7 Hz, 1H), 5.27 (s, 1H), 4.00–3.78 (m, 3H), 3.76–3.62 (m, 1H), 2.60 (t, *J* = 7.4 Hz, 2H), 1.74 (dd, *J* = 14.5, 7.3 Hz, 2H), 1.24 (t, *J* = 7.0 Hz, 3H), 1.04 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0 (d, *J* = 248.9 Hz), 162.9, 140.4, 136.1 (d, *J* = 10.6 Hz), 125.6 (d, *J* = 10.2 Hz), 125.3, 114.5 (d, *J* = 24.3 Hz), 114.2 (d, *J* = 3.8 Hz), 107.7 (d, *J* = 25.6 Hz), 96.3, 65.0, 42.1, 32.6, 20.6, 15.0, 13.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}FNO_3$ 292.1343; Found 292.1342.

3-Ethoxy-9-fluoro-1-isobutyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (2q)

According to the *general procedure* (**4.1**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (130 mg, 90%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.4, 5.3 Hz, 1H), 7.32–7.28 (m, 1H), 7.08 (td, *J* = 8.8, 2.2 Hz, 1H), 5.26 (dd, *J* = 3.8, 2.9 Hz, 1H), 3.99–3.84 (m, 3H), 3.69 (dq, *J* = 9.5, 7.1 Hz, 1H), 2.53 (dd, *J* = 14.3, 6.8 Hz, 1H), 2.45 (dd, *J* = 14.3, 7.9 Hz, 1H), 2.17–2.06 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.06 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9 (d, *J* = 248.8 Hz), 162.8, 140.0, 136.2 (d, *J* = 11.0 Hz), 125.6 (d, *J* = 10.2 Hz), 125.4 (d, *J* = 1.6 Hz), 114.8 (s), 114.6 (d, *J* = 23.8 Hz), 107.8 (d, *J* = 26.1 Hz), 96.3, 65.1, 42.1, 39.6, 27.4, 22.6, 22.1, 14.9.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{21}FNO_3$ 306.1500; Found 306.1497.

11.3 Product Characterization of 3-Hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-ones (3)

1-Ethyl-3-hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3a)

According to the *Gram-scale synthesis* (**7.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:3) to give the product as a yellow oil (1.73 g, 65%)

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.75 (d, *J* = 7.0 Hz, 2H), 7.66 (s, 1H), 7.60 (t, *J* = 6.9 Hz, 1H), 7.41 (t, *J* = 7.0 Hz, 1H), 5.57 (s, 1H), 3.81 (d, *J* = 12.6 Hz, 1H), 3.74–3.65 (m, 1H), 2.64 (td, *J* = 14.9, 7.1 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 142.4, 134.0, 131.4, 128.5, 126.6, 123.5, 120.5, 113.2, 91.5, 43.0, 24.3, 11.5.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}NO_3$ 232.0968; Found 232.0973.

3-Hydroxy-1-propyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3b)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:3) to give the product as a yellow oil (147 mg, 60%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.27 (t, J = 7.3 Hz, 1H), 6.69 (s, 1H), 5.63 (s, 1H), 3.94 (d, J = 3.0 Hz, 2H), 2.59 (dd, J = 11.1, 6.9 Hz, 2H), 1.71 (dd, J = 14.7, 7.3 Hz, 2H), 1.00 (t, J = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 141.2, 134.1, 131.4, 128.5, 126.6, 123.5, 120.6, 113.9, 91.4, 43.0, 32.7, 20.5, 13.7.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{16}NO_3$ 246.1125; Found 246.1127.

3-Hydroxy-1-methyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3c)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:2) to give the product as a white solid (94 mg, 82%), m.p.: 137-138 °C

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.81 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 7.5 Hz, 1H), 7.67 (d, J = 5.5 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 7.4 Hz, 1H), 5.55 (s, 1H), 3.82 (d, J = 12.0 Hz, 1H), 3.67 (dd, J = 12.8, 4.4 Hz, 1H), 2.30 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.3, 136.2, 133.80, 131.4, 128.3, 126.6, 122.8, 120.9, 113.1, 91.2, 42.5, 16.9.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{12}NO_3$ 218.0812; Found 218.0813.

3-Hydroxy-1-isobutyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3d)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:3) to give the product as a white solid (149 mg, 65%), m.p.: 120-121 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 5.9 Hz, 1H), 7.63–7.58 (m, 1H), 7.42 (t, J = 7.3 Hz, 1H), 5.61–5.49 (m, 1H), 3.81 (dd, J = 12.8, 2.6 Hz, 1H), 3.70 (dd, J = 12.9, 4.4 Hz, 1H), 2.53 (s, 2H), 2.09–1.95 (m, 1H), 1.00 (d, J = 6.7 Hz, 3H), 0.98 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.8, 140.0, 134.3, 132.0, 129.0, 127.1, 123.3, 121.6, 114.4, 91.40, 43.1, 39.4, 27.4, 22.6, 22.5.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}NO_3$ 260.1281; Found 260.1278.

1-Benzyl-3-hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3e)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:2) to give the product as a white solid (109 mg, 75%), m.p.: 154-155 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.89 (d, J = 7.9 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 6.0 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.4 Hz, 1H), 7.42–7.30 (m, 4H), 7.26 (t, J = 6.9 Hz, 1H), 5.58 (s, 1H), 4.15–3.97 (m, 2H), 3.90 (d, J = 12.4 Hz, 1H), 3.73 (dd, J = 12.8, 4.4 Hz, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.5, 137.9, 137.0, 133.6, 131.6, 128.6, 128.5, 128.2, 127.0, 126.5, 122.9, 120.8, 114.4, 91.4, 42.6, 35.9.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_3$ 294.1125; Found 294.1129.

3-Hydroxy-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3f)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:3) to give the product as a yellow solid (690 mg, 66%), m.p.: 168-169 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77 (dd, J = 9.7, 4.5 Hz, 2H), 7.66 (d, J = 3.6 Hz, 2H), 7.56 (d, J = 3.4 Hz, 3H), 7.44–7.39 (m, 2H), 7.24–7.19 (m, 1H), 5.77 (s, 1H), 3.89 (s, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 163.3, 137.6, 134.1, 133.5, 131.8, 130.5, 129.8, 129.2, 128.8, 128.0, 123.3, 120.4, 115.0, 91.7, 43.2.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{14}NO_3$ 280.0968; Found 280.0970.

3-Hydroxy-1-(4-methoxyphenyl)-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3g)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:2) to give the product as a white solid (158 mg, 75%), m.p.: 179-180 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84–7.74 (m, 2H), 7.62 (d, J = 8.7 Hz, 2H), 7.51–7.38 (m, 2H), 7.29 (d, J = 7.1 Hz, 1H), 7.14 (d, J = 8.7 Hz, 2H), 5.78 (dt, J = 5.8, 3.1 Hz, 1H), 3.92 (dd, J = 14.6, 3.6 Hz, 3H), 3.89 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.6, 160.5, 137.2, 133.7, 131.2, 130.8, 128.2, 127.2, 125.1, 122.8, 119.8, 114.1, 113.7, 91.2, 55.3, 42.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_3$ 310.1074; Found 310.1074.

3-Hydroxy-1-(3-(trifluoromethyl)phenyl)-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3h)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:2) to give the product as a white solid (132 mg, 70%), m.p.: 191-192 °C

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06–7.98 (m, 2H), 7.96–7.91 (m, 1H), 7.86–7.81 (m, 2H), 7.81–7.75 (m, 1H), 7.50–7.42 (m, 2H), 7.24–7.17 (m, 1H), 5.87–5.79 (m, 1H), 3.91 (ddd, J = 15.0, 13.0, 2.7 Hz, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.9, 135.0, 134.2, 133.3, 133.2, 131.6, 129.9, 129.6 (q, J = 31.8 Hz), 128.4, 127.9, 126.4 (q, J = 3.5 Hz), 125.8 (q, J = 3.7 Hz), 123.9 (q, J = 272.3 Hz), 123.0, 119.7, 115.6, 91.2, 42.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{13}F_3NO_3$ 348.0842; Found 348.0846.

1-(Furan-2-yl)-3-hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3i)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:1) to give the product as a yellow oil (245 mg, 61%)

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06 (d, J = 8.0 Hz, 1H), 7.99 (dd, J = 1.8, 0.8 Hz, 1H), 7.83 (d, J = 5.9 Hz, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.60 (td, J = 7.7, 1.2 Hz, 1H), 7.48 (td, J = 7.5, 0.8 Hz, 1H), 6.88 (dd, J = 3.4, 0.7 Hz, 1H), 6.74 (dd, J = 3.4, 1.8 Hz, 1H), 5.72 (dt, J = 6.2, 3.3 Hz, 1H), 3.88 – 3.83 (m, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.9, 146.9, 144.4, 132.9, 131.7, 128.4, 127.8, 127.7, 122.8, 121.8, 115.3, 112.3, 112.1, 91.1, 79.1, 42.9.

HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{11}NNaO_4$ 292.0580; Found 292.0575.

3-Hydroxy-9-methoxy-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3j)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 2:5) to give the product as a white solid (140 mg, 58%), m.p.: 180-181 ^oC

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77 (t, J = 6.8 Hz, 1H), 7.71–7.63 (m, 3H), 7.60–7.53 (m, 3H), 6.99 (dd, J = 8.5, 2.2 Hz, 1H), 6.67 (t, J = 4.6 Hz, 1H), 5.82–5.72 (m, 1H), 3.89–3.81 (m, 2H), 3.65 (d, J = 13.4 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.6, 161.8, 136.9, 135.5, 132.9, 130.1, 129.3, 128.6, 124.3, 121.4, 114.5, 114.1, 104.6, 91.2, 55.2, 42.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{16}NO_4$ 310.1074; Found 310.1076.

1-Ethyl-3-hydroxy-9-methoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3k)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:3) to give the product as a yellow oil (105 mg, 63%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, J = 8.5 Hz, 1H), 6.88 (s, 1H), 6.80 (d, J = 8.4 Hz, 1H), 5.63 (s, 1H), 3.90 (d, J = 2.7 Hz, 2H), 3.84 (s, 3H), 2.58 (dt, J = 14.1, 7.0 Hz, 2H), 1.24 (t, J = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 162.7, 141.6, 136.1, 124.8, 122.0, 114.0, 113.1, 105.9, 91.5, 79.6, 56.1, 43.0, 24.2, 11.9.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{16}NO_4$ 262.1074; Found 262.1079.

3-Hydroxy-9-methoxy-1-propyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3l)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:2) to give the product as a yellow oil (123 mg, 51%)

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.66 (d, J = 8.4 Hz, 1H), 7.17 (s, 1H), 7.01 (d, J = 8.3 Hz, 1H), 5.53 (s, 1H), 3.88 (s, 3H), 3.77 (d, J = 12.4 Hz, 1H), 3.65 (dd, J = 12.7, 4.1 Hz, 1H), 2.60 (dt, J = 14.8, 7.4 Hz, 2H), 1.66 (dd, J = 14.5, 7.2 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 162.5, 141.0, 136.1, 124.8, 121.7, 113.9, 113.0, 105.7, 91.3, 55.6, 42.9, 32.7, 20.4, 13.8.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}NO_4$ 276.1230; Found 276.1233.

3-Hydroxy-1-isobutyl-9-methoxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3m)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:4) to give the product as a yellow oil (129 mg, 77%)

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.67 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 5.6 Hz, 1H), 7.17 (s, 1H), 7.01 (d, J = 8.3 Hz, 1H), 5.53 (s, 1H), 3.88 (s, 3H), 3.76 (d, J = 11.5 Hz, 1H), 3.64 (dd, J = 12.7, 4.1 Hz, 1H), 2.49 (s, 2H), 2.07–2.00 (m, 1H), 1.01 (d, J = 6.7 Hz, 3H), 0.99 (d, J = 6.6 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 162.7, 162.6, 140.0, 136.2, 124.8, 122.1, 114.4, 113.9, 106.2, 91.4, 56.1, 43.1, 39.4, 27.5, 22.7, 22.6.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}NO_4$ 290.1387; Found 290.1383.

9-Fluoro-3-hydroxy-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3n)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:4) to give the product as yellow solid (63 mg, 47%), m.p.: 191-192 °C

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.86 (s, 1H), 7.84–7.78 (m, 1H), 7.67 (d, J = 1.6 Hz, 2H), 7.59 (s, 3H), 7.26 (t, J = 8.3 Hz, 1H), 6.81 (d, J = 9.2 Hz, 1H), 5.80 (s, 1H), 3.89 (s, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 163.9 (d, J = 246.3 Hz), 161.8, 138.3, 135.6 (d, J = 11.4 Hz), 132.6, 130.4, 129.2, 128.8, 125.3 (d, J = 10.3 Hz), 124.8, 115.1 (d, J = 24.0 Hz), 114.0, 106.4 (d, J = 26.2 Hz), 91.4, 42.70.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{13}FNO_3$ 298.0874; Found 298.0873.

1-Ethyl-9-fluoro-3-hydroxy-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3o)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (ethyl acetate) to give the product as a yellow oil (144 mg, 95%)

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.78 (dd, J = 7.4, 5.7 Hz, 1H), 7.71 (d, J = 5.3 Hz, 1H), 7.60 (d, J = 9.3 Hz, 1H), 7.25 (t, J = 8.5 Hz, 1H), 5.59 (s, 1H), 3.79 (d, J = 12.4 Hz, 1H), 3.70 (dd, J = 12.7, 3.6 Hz, 1H), 2.72–2.64 (m, 1H), 2.64–2.57 (m, 1H), 1.18 (t, J = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 165.2 (d, J = 288.5 Hz), 162.0, 143.1, 136.0 (d, J = 11.1 Hz), 125.6 (d, J = 10.2 Hz), 125.3, 114.8 (d, J = 23.9 Hz), 112.7, 108.3 (d, J = 25.5 Hz), 91.6, 79.6, 43.1, 24.1, 12.0.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{13}FNO_3$ 250.0874; Found 250.0879.

9-Fluoro-3-hydroxy-1-propyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3p)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:2) to give the product as a yellow solid (207 mg, 87%), m.p.: 127-128 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, J = 8.5, 5.2 Hz, 1H), 7.16 (dd, J = 9.3, 2.1 Hz, 1H), 6.97 (td, J = 8.7, 2.1 Hz, 1H), 6.36 (s, 1H), 5.68–5.62 (m, 1H), 3.99 (dd, J = 13.1, 3.9 Hz, 1H), 3.87 (dd, J = 13.1, 2.7 Hz, 1H), 2.64–2.49 (m, 2H), 1.79–1.67 (m, 2H), 1.03 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0 (d, J = 249.6 Hz), 163.3, 142.4, 136.0 (d, J = 11.1 Hz), 125.5(d, J = 10.1 Hz), 124.6, 114.4 (d, J = 24.3 Hz), 113.5, 107.5 (d, J = 25.9 Hz), 91.3, 43.0, 32.7, 20.4, 13.7.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{15}FNO_3$ 264.1030; Found 264.1032.

9-Fluoro-3-hydroxy-1-isobutyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-6-one (3q)

According to the *general procedure* (**4.2**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 1:1) to give the product as a yellow solid (116 mg, 84%), m.p.: 145-146 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 8.5, 5.2 Hz, 1H), 7.12 (dd, J = 9.3, 2.1 Hz, 1H), 6.90 (td, J = 8.7, 2.1 Hz, 1H), 5.95 (d, J = 6.3 Hz, 1H), 5.57 (s, 1H), 3.92 (dt, J = 11.9, 5.9 Hz, 1H), 3.82–3.73 (m, 1H), 2.38 (t, J = 6.8 Hz, 2H), 2.08–1.99 (m, 1H), 0.95 (d, J = 6.7 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0 (d, J = 249.9 Hz), 163.3, 141.8, 136.1 (d, J = 10.8 Hz), 125.5 (d, J = 10.6 Hz), 124.7, 114.5 (d, J = 23.8 Hz), 114.1 (d, J = 3.8 Hz), 107.7 (d, J = 26.0 Hz), 91.2, 43.0, 39.7, 27.3, 22.5, 22.4.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{17}FNO_3$ 278.1187; Found 278.1186.

11.4 Product Characterization of 6*H*-isochromeno-[4,3-*b*]-pyridin-6-ones 4

4-Methyl-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4a)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (39 mg, 81%), m.p.: 97-98 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 8.0 Hz, 1H), 8.45 (d, J = 4.7 Hz, 1H), 8.37 (dd, J = 7.9, 0.6 Hz, 1H), 7.94–7.84 (m, 1H), 7.75–7.64 (m, 1H), 7.27 (d, J = 4.6 Hz, 1H), 2.52 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 146.8, 145.4, 135.9, 135.8, 135.7, 135.1, 130.3, 129.9, 126.4, 123.6, 122.3, 15.4.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{10}NO_2$ 212.0706; Found 212.0703.

IR (C=O): υ 1732 cm^{-1}

4-Ethyl-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4b)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 6:1) to give the product as a yellow solid (32 mg, 67%), m.p.: 96-97 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (t, J = 9.9 Hz, 1H), 8.51 (d, J = 4.7 Hz, 1H), 8.38 (dd, J = 8.0, 0.7 Hz, 1H), 7.95–7.87 (m, 1H), 7.73–7.65 (m, 1H), 7.30 (d, J = 4.7 Hz, 1H), 2.96 (q, J = 7.6 Hz, 2H), 1.36 (t, J = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3, 146.3, 145.8, 141.3, 136.0, 135.1, 130.3, 129.9, 124.5, 123.6, 122.3, 22.2, 13.3.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}NO_2$ 226.0863; Found 226.0859.

IR (C=O): υ 1729 cm^{-1}

9-Methoxy-4-methyl-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4c)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 5:2) to give the product as a yellow solid (73 mg, 80%), m.p.: 209-210 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, J = 4.6 Hz, 1H), 8.26 (d, J = 8.8 Hz, 1H), 8.04 (d, J = 2.5 Hz, 1H), 7.29–7.24 (m, 1H), 7.17 (dd, J = 8.8, 2.5 Hz, 1H), 4.02 (s, 3H), 2.51 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 160.0, 147.2, 145.1, 138.3, 135.9, 135.8, 132.1, 126.5, 119.3, 115.3, 105.0, 56.0, 15.4.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}NO_3$ 242.0812; Found 242.0811.

IR (C=O): υ 1720 cm^{-1}

4-Ethyl-9-methoxy-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4d)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (67 mg, 82%), m.p.: 107-108 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J = 4.7 Hz, 1H), 8.27 (d, J = 8.8 Hz, 1H), 8.06 (d, J = 2.6 Hz, 1H), 7.28 (t, J = 9.2 Hz, 1H), 7.17 (dt, J = 14.5, 7.2 Hz, 1H), 4.03 (s, 3H), 2.94 (q, J = 7.6 Hz, 2H), 1.35 (t, J = 7.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 160.0, 146.7, 145.4, 141.3, 138.4, 135.9, 132.1, 124.6, 119.2, 115.3, 105.0, 56.0, 22.2, 13.3.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}NO_3$ 256.0968; Found 256.0974.
IR (C=O): υ 1735 cm^{-1}

9-Fluoro-4-methyl-6*H*-isochromeno[4,3-*b*]pyridin-6-one (4e)
According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (99 mg, 98%), m.p.: 159-160 °C
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, J = 4.5 Hz, 1H), 8.38 (dd, J = 8.5, 5.5 Hz, 1H), 8.26 (d, J = 9.2 Hz, 1H), 7.34 (dd, J = 11.5, 4.9 Hz, 1H), 7.30 (d, J = 4.3 Hz, 1H), 2.51 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2 (d, J = 257.6 Hz), 159.4, 147.2, 145.6, 139.1 (d, J = 10.3 Hz), 136.0, 135.1, 133.4 (d, J = 9.9 Hz), 127.0, 118.8 (d, J = 2.1 Hz), 118.5 (d, J = 23.5 Hz), 109.9 (d, J = 24.1 Hz), 15.4.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_9FNO_2$ 230.0612; Found 230.0617.
IR (C=O): υ 1747 cm^{-1}

4-Ethyl-9-fluoro-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4f)
According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (45 mg, 61%), m.p.: >250 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, J = 4.7 Hz, 1H), 8.40 (dd, J = 8.8, 5.4 Hz, 1H), 8.31 (dd, J = 9.3, 2.6 Hz, 1H), 7.39–7.35 (m, 1H), 7.35–7.31 (m, 1H), 2.95 (q, J = 7.6 Hz, 2H), 1.36 (t, J = 7.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2 (d, J = 257.4 Hz), 159.4, 146.8, 145.9, 141.5, 139.2 (d, J = 10.1 Hz), 135.1, 133.3 (d, J = 10.0 Hz), 125.1, 118.8 (d, J = 2.0 Hz), 118.4(d, J = 23.6 Hz), 109.9 (d, J = 23.9 Hz), 22.2, 13.2.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}FNO_2$ 244.0768; Found 244.0773.
IR (C=O): υ 1743 cm^{-1}

4-Isopropyl-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4g)
According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (28 mg, 61%), m.p.: 100-101 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, J = 7.9 Hz, 1H), 8.55 (d, J = 4.8 Hz, 1H), 8.39 (dd, J = 7.9, 0.6 Hz, 1H), 7.96–7.88 (m, 1H), 7.69 (dt, J = 11.8, 2.4 Hz, 1H), 7.36 (d, J = 4.8 Hz, 1H), 3.75–3.63 (m, 1H), 1.37 (s, 3H), 1.36 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3, 146.0, 145.7, 136.1, 135.1, 130.3, 129.9, 123.7, 122.3, 122.0, 26.5, 22.1.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}NO_3$ 270.1125; Found 270.1123.
IR (C=O): υ 1741 cm^{-1}

6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4h)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (40 mg, 73%), m.p.: 137-138 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (dd, J = 8.0, 0.5 Hz, 1H), 8.59 (dd, J = 4.5, 1.4 Hz, 1H), 8.35 (dd, J = 7.9, 0.7 Hz, 1H), 7.94–7.85 (m, 1H), 7.71–7.66 (m, 1H), 7.64 (dd, J = 8.3, 1.4 Hz, 1H), 7.42 (dd, J = 8.3, 4.5 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 147.8, 146.1, 136.8, 135.6, 135.2, 130.6, 130.1, 124.84, 124.81, 123.4, 122.5.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_8NO_2$ 198.0550; Found 198.0550.

IR (C=O): υ 1741 cm^{-1}

4-Phenyl-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4i)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (54 mg, 32%), m.p.: 141-142 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 8.0 Hz, 1H), 8.66 (d, J = 4.7 Hz, 1H), 8.40 (d, J = 7.9 Hz, 1H), 7.95 (t, J = 7.4 Hz, 1H), 7.73 (dd, J = 10.5, 3.8 Hz, 3H), 7.56 (t, J = 7.3 Hz, 2H), 7.52 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 4.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 145.9, 144.9, 137.9, 137.2, 135.9, 135.2, 133.8, 130.6, 130.0, 129.4, 129.2, 128.8, 125.3, 123.8, 122.3.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{12}NO_2$ 274.0863; Found 274.0859.

IR (C=O): υ 1746 cm^{-1}

4-Isopropyl-9-methoxy-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4j)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 7:1) to give the product as a yellow solid (37 mg, 61%), m.p.: 156-157 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.8 Hz, 1H), 8.29 (d, J = 8.8 Hz, 1H), 8.09 (d, J = 2.6 Hz, 1H), 7.35 (d, J = 4.8 Hz, 1H), 7.19 (dd, J = 8.8, 2.6 Hz, 1H), 4.05 (s, 3H), 3.75–3.61 (m, 1H), 1.37 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 160.1, 146.1, 145.8, 145.6, 138.5, 136.0, 132.1, 122.1, 119.3, 115.3, 105.1, 56.0, 26.5, 22.1.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{16}NO_3$ 270.1125; Found 270.1123.

IR (C=O): υ 1728 cm^{-1}

9-Fluoro-4-isopropyl-6*H*-isochromeno-[4,3-*b*]-pyridin-6-one (4k)

According to the *general procedure* (**4.3**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 12:1) to give the product as a yellow solid (84 mg, 61%), m.p.: 101-102 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 4.9 Hz, 1H), 8.42 (ddd, J = 11.9, 9.1, 4.0 Hz, 2H), 7.44–7.35 (m, 2H), 3.70 (dt, J = 13.8, 6.9 Hz, 1H), 1.38 (d, J = 6.9 Hz, 6H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.1 (d, J = 257.5 Hz), 159.4, 146.2, 146.1, 145.9, 139.0(d, J = 10.3 Hz), 135.0 , 133.3 (d, J = 10.0 Hz), 122.7, 118.6 (d, J = 23.0 Hz), 110.1 (d, J = 24.1 Hz), 26.5, 22.1.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}FNO_2$ 258.0925; Found 258.0928.
IR (C=O): υ 1741 cm^{-1}

11.5 Product Characterization of Compounds 5

***N*-(6-oxo-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-3-yl)acetamide (5)**

According to the *general procedure* (**4.4**). The crude reaction mixture was purified by flash chromatography (CH_2Cl_2/MeOH = 15:1) to give the product as a white solid (108 mg, 68%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4 Hz, 1H), 7.67 – 7.63 (m, 2H), 7.60 (d, J = 7.5 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.32 (d, J = 7.7 Hz, 1H), 7.28 (d, J = 5.5 Hz, 1H), 7.21 (dd, J = 10.7, 4.0 Hz, 1H), 6.33 – 6.19 (m, 1H), 4.12 (dd, J = 13.1, 3.9 Hz, 1H), 4.05 (dd, J = 13.1, 3.2 Hz, 1H), 2.13 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 164.1, 138.6, 133.9, 132.6, 131.4, 130.3, 129.5, 128.6, 128.3, 127.6, 123.1, 120.6, 114.8, 74.6, 41.5, 23.2.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{29}H_{17}N_2O_3$ 321.1234; Found 321.1234.

11.6 Product Characterization of compounds 6

6-Oxo-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-3-yl 4-methyl-1,2,3-thiadiazole-5-carboxylate (6a)

According to the *general procedure* (**4.5**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (100 mg, 49%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.4 Hz, 1H), 7.67–7.59 (m, 2H), 7.56–7.49 (m, 3H), 7.49–7.44 (m, 1H), 7.42 (d, J = 3.2 Hz, 2H), 6.93 (d, J = 1.8 Hz, 1H), 4.59 (d, J = 13.7 Hz, 1H), 4.03 (d, J = 13.6 Hz, 1H), 2.87 (d, J = 1.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 162.9, 158.0, 138.2, 135.4, 133.6, 131.8, 131.7, 130.5, 129.4, 128.8, 128.6, 128.4, 123.8, 120.9, 116.3, 89.7, 41.0, 14.1.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{16}N_3O_4S$ 406.0856; Found 406.0853.

6-Oxo-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-3-yl 3,4-dichloroisothiazole-5-carboxylate (6b)

According to the *general procedure* (**4.5**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (163 mg, 71%)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.4 Hz, 1H), 7.67–7.59 (m, 2H), 7.52 (d, J = 1.7 Hz, 2H), 7.51–7.47 (m, 1H), 7.47–7.42 (m, 1H), 7.40 (d, J = 5.5 Hz, 2H), 6.95 (t, J = 2.0 Hz, 1H), 4.63 (dd, J = 13.7, 1.9 Hz, 1H), 4.01 (dd, J = 13.7, 2.2 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.30, 156.2, 150.6, 148.6, 135.4, 133.7, 131.80, 131.75, 130.5, 129.4, 128.8, 128.6, 128.4, 126.9, 123.7, 120.9, 116.4, 89.7, 41.0.
HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{13}Cl_2N_2O_4S$ 458.9968; Found 458.9976.

6-Oxo-1-phenyl-3,4-dihydro-6*H*-[1,4]-oxazino-[3,4-*a*]-isoindol-3-yl benzo[*d*][1,2,3]-thiadiazole-7-carboxylate (6c)

According to the *general procedure* (**4.5**). The crude reaction mixture was purified by flash chromatography (petroleum ether/ethyl acetate = 3:1) to give the product as a yellow oil (138 mg, 63%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (d, J = 8.2 Hz, 1H), 8.34 (d, J = 7.3 Hz, 1H), 7.96 (d, J = 7.4 Hz, 1H), 7.73–7.67 (m, 1H), 7.62 (d, J = 1.7 Hz, 1H), 7.61 (d, J = 2.3 Hz, 1H), 7.48 (d, J = 4.7 Hz, 2H), 7.47–7.43 (m, 2H), 7.43–7.37 (m, 2H), 7.07 (t, J = 2.0 Hz, 1H), 4.69 (dd, J = 13.7, 1.9 Hz, 1H), 4.06 (dd, J = 13.7, 2.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 162.9, 158.9, 140.7, 135.7, 133.8, 131.9, 131.81, 131.75, 130.4, 129.6, 129.5, 128.8, 128.4, 127.3, 123.8, 121.7, 120.9, 116.3, 89.7, 41.2.

HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{16}N_3O_4S$ 444.0856; Found 444.0854.

12. Copies of ^{1}H NMR, ^{13}C NMR Spectra for New Compounds

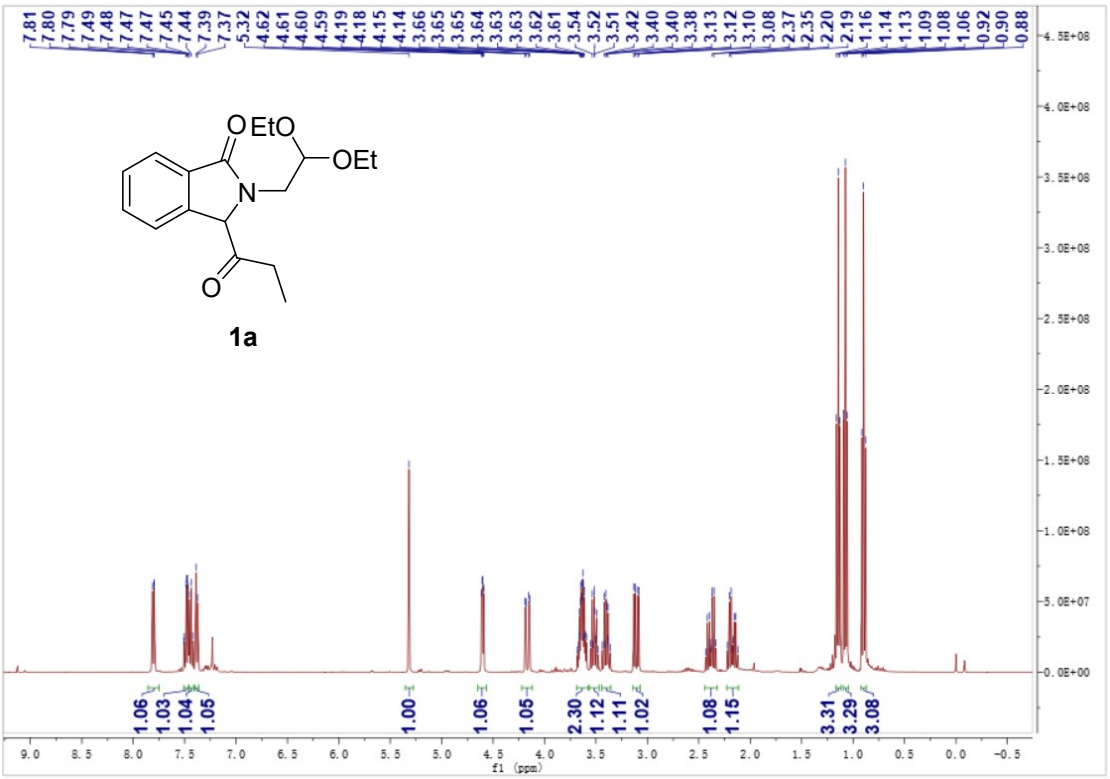

Figure S4. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1a**

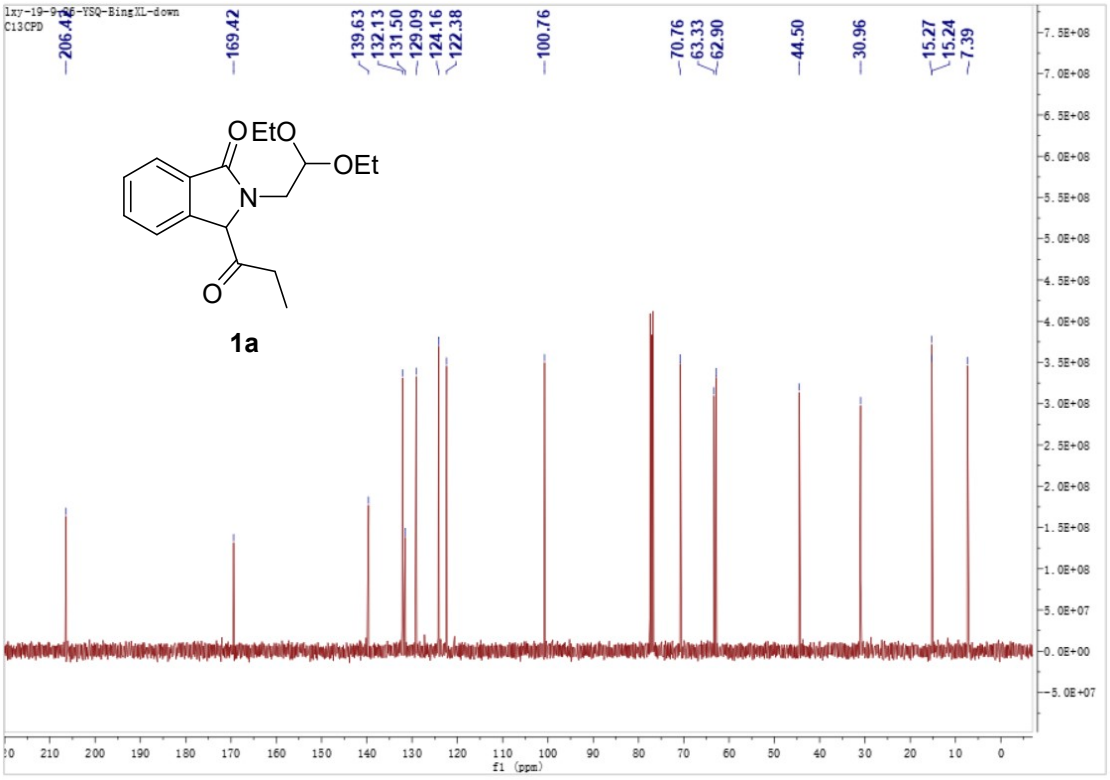

Figure S5. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1a**

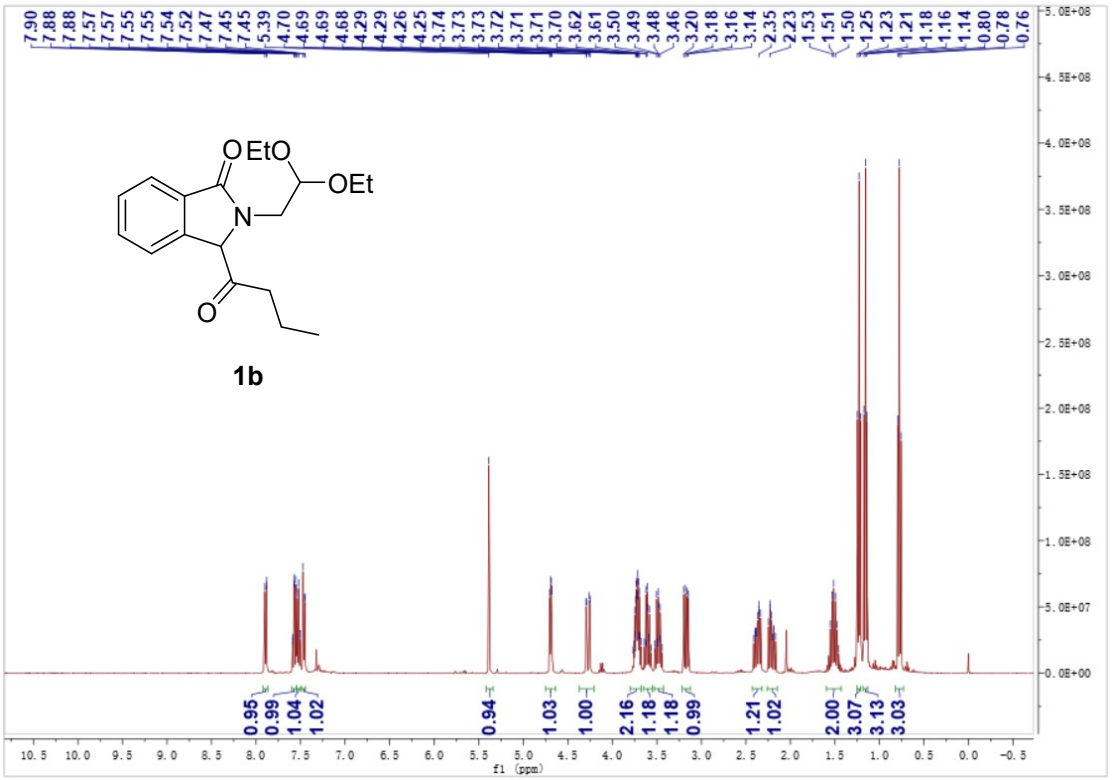

Figure S6. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1b**

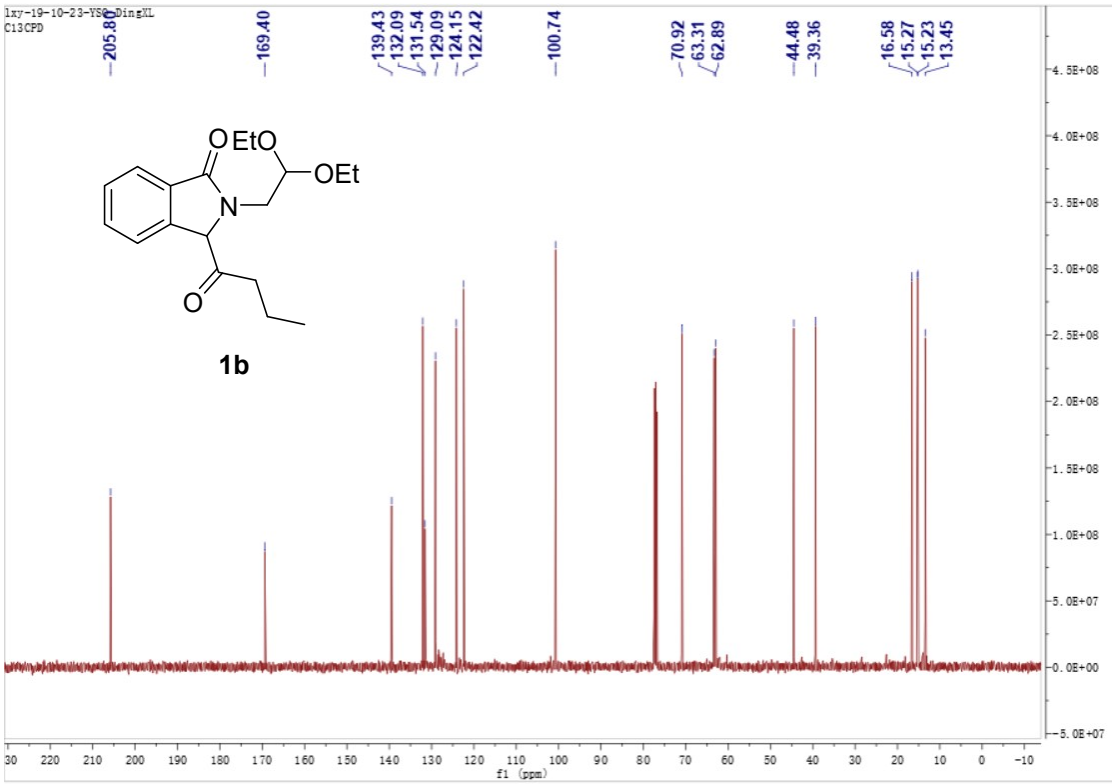

Figure S7. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1b**

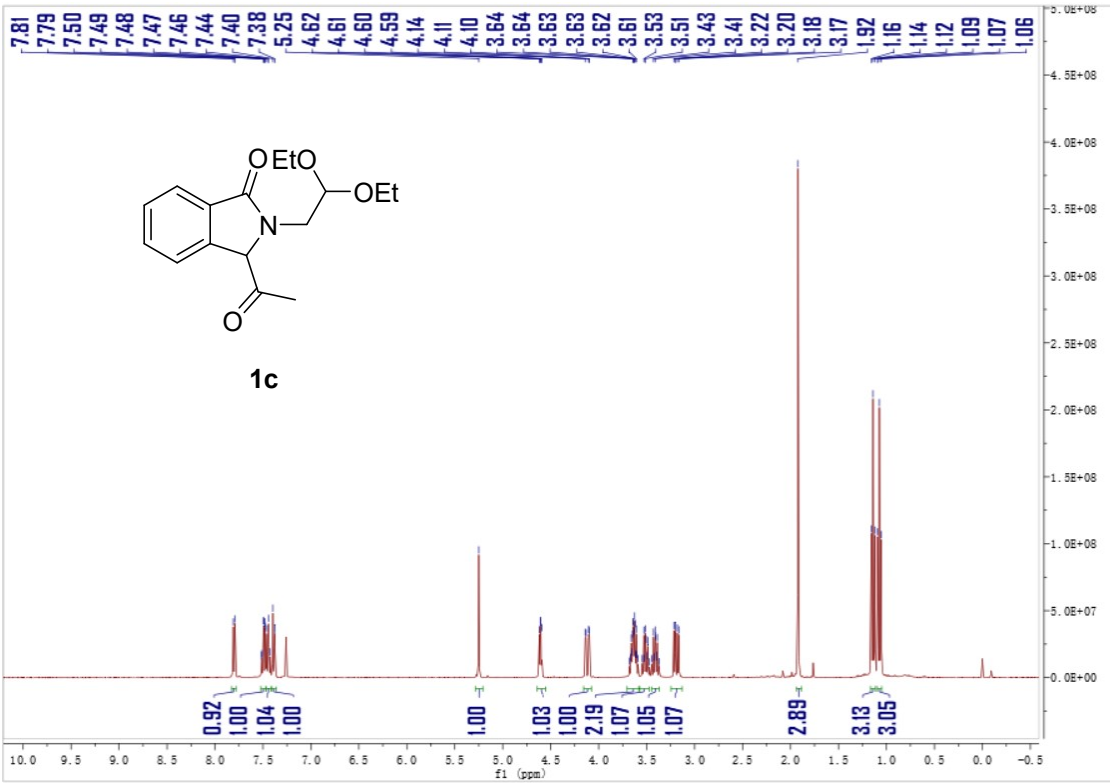

Figure S8. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1c**

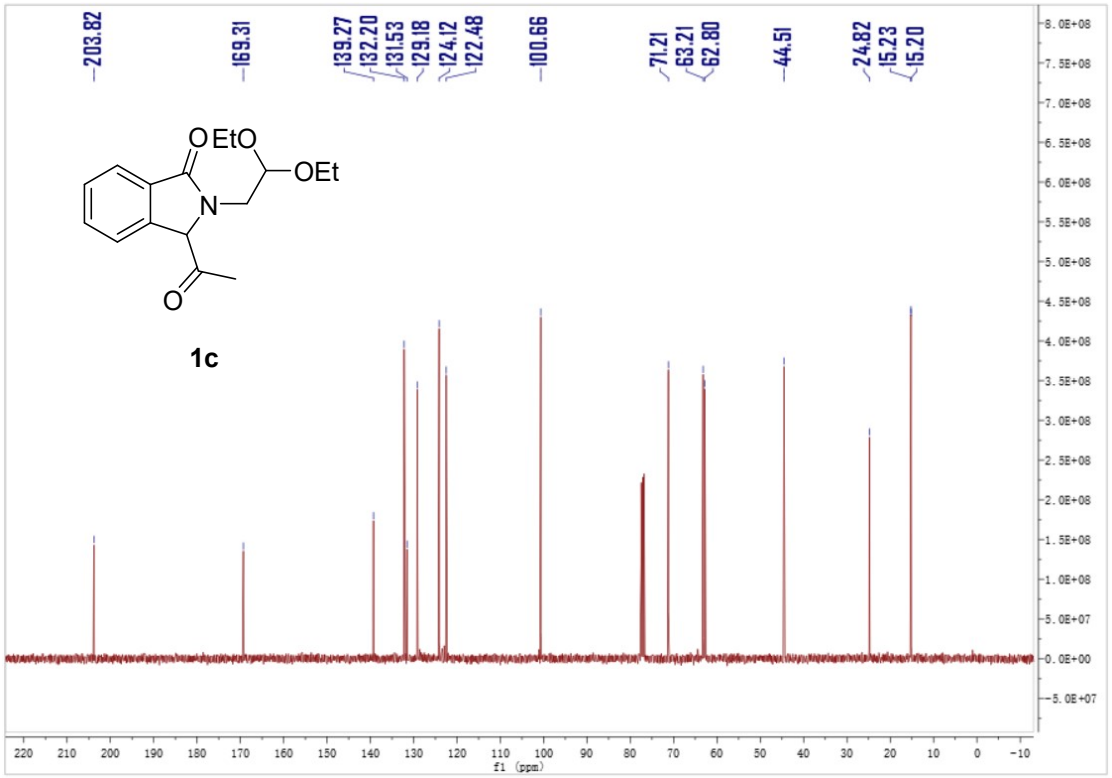

Figure S9. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1c**

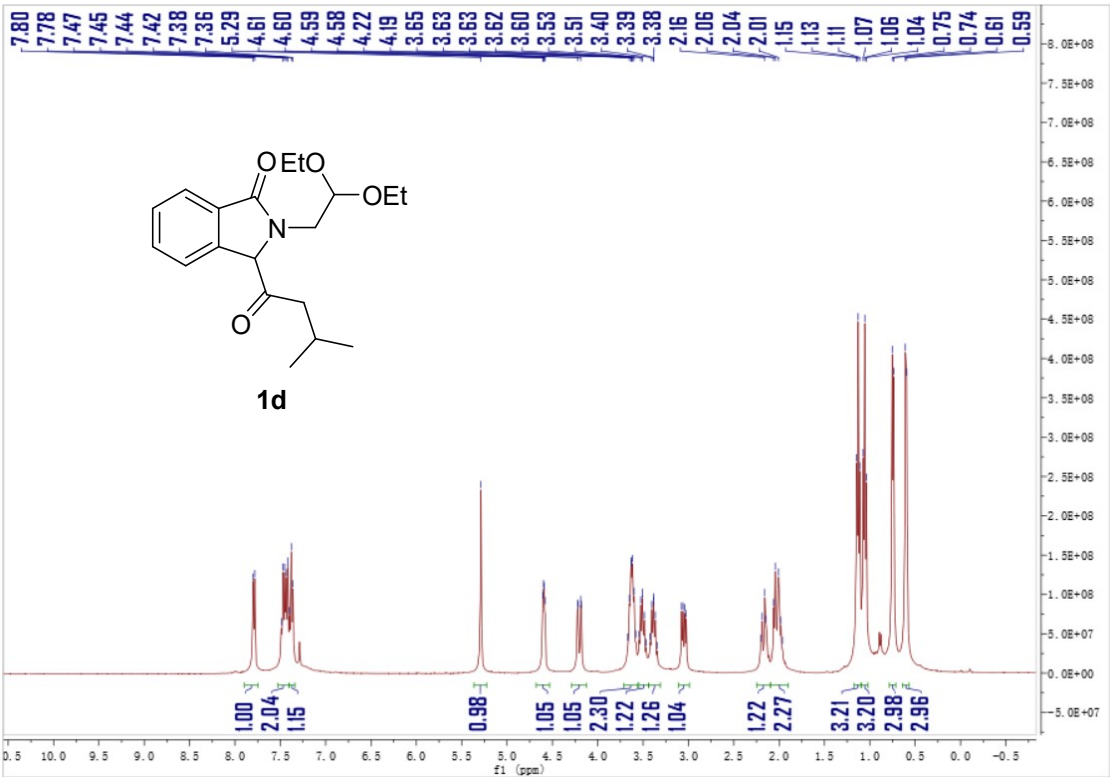

Figure S10. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1d**

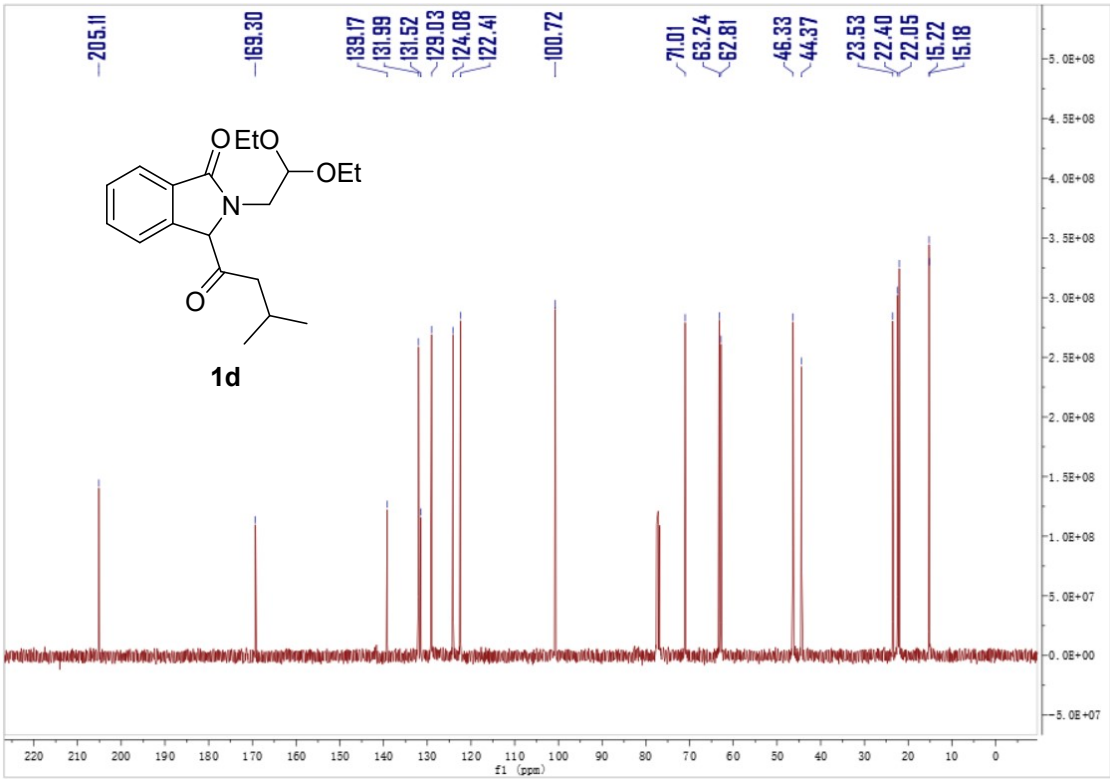

Figure S11. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1d**

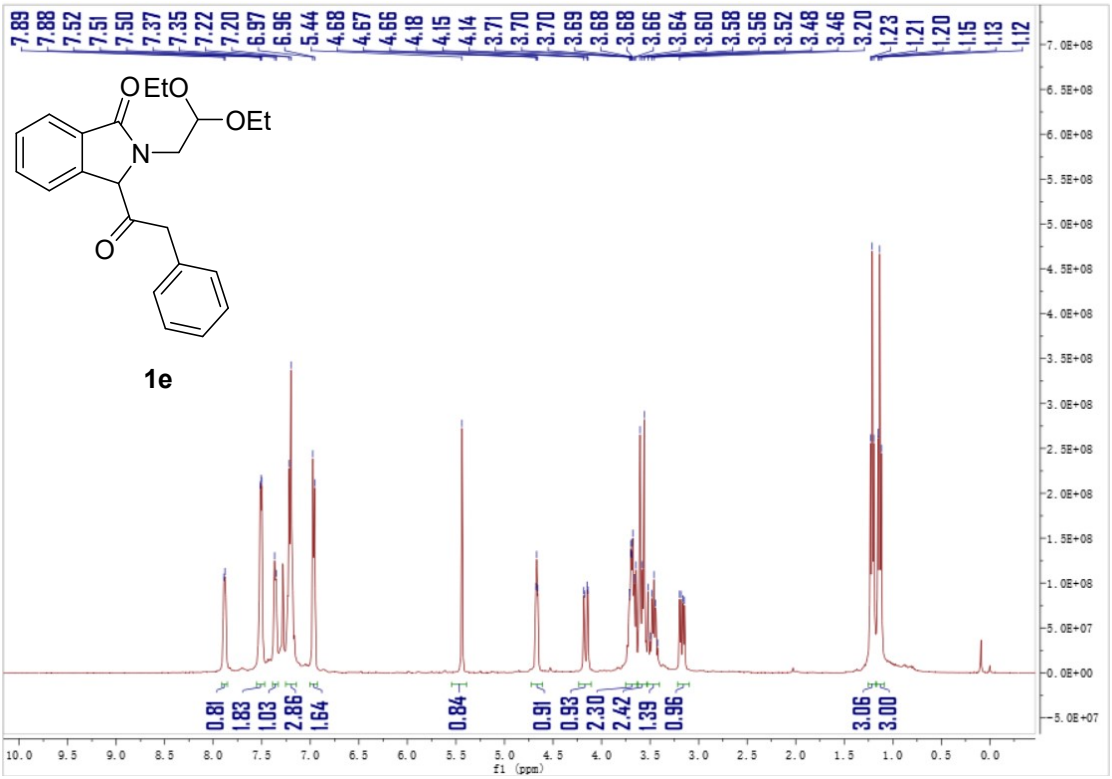

Figure S12. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1e**

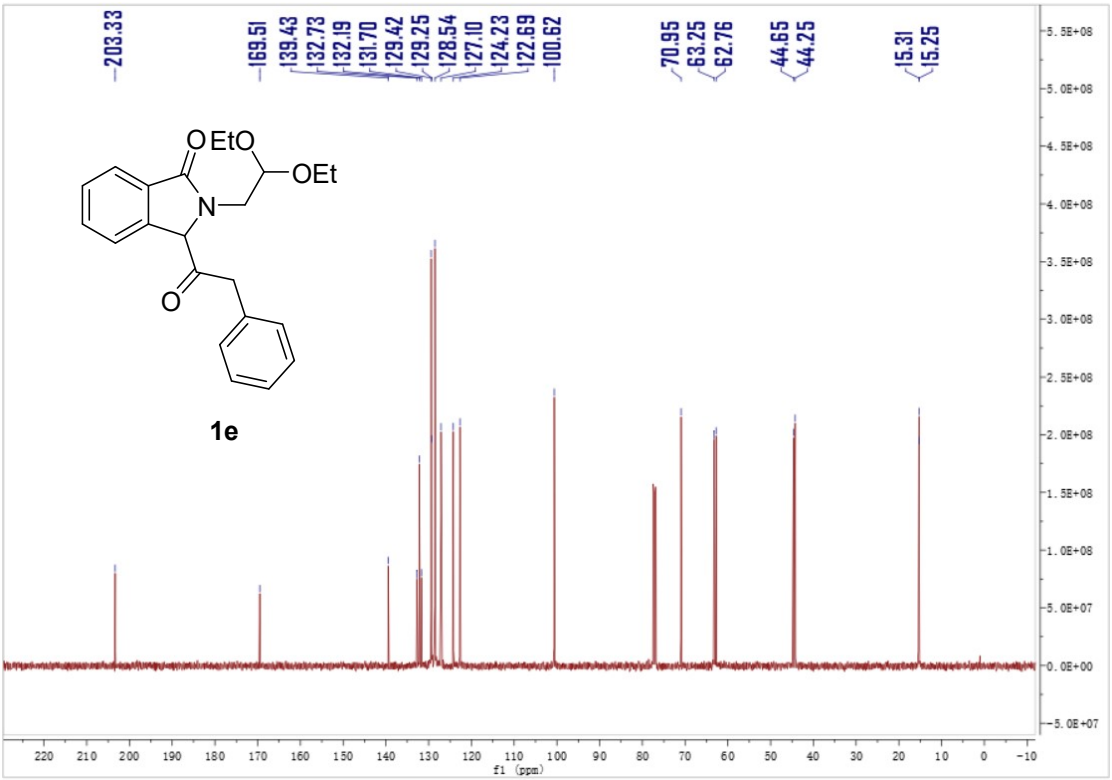

Figure S13. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1e**

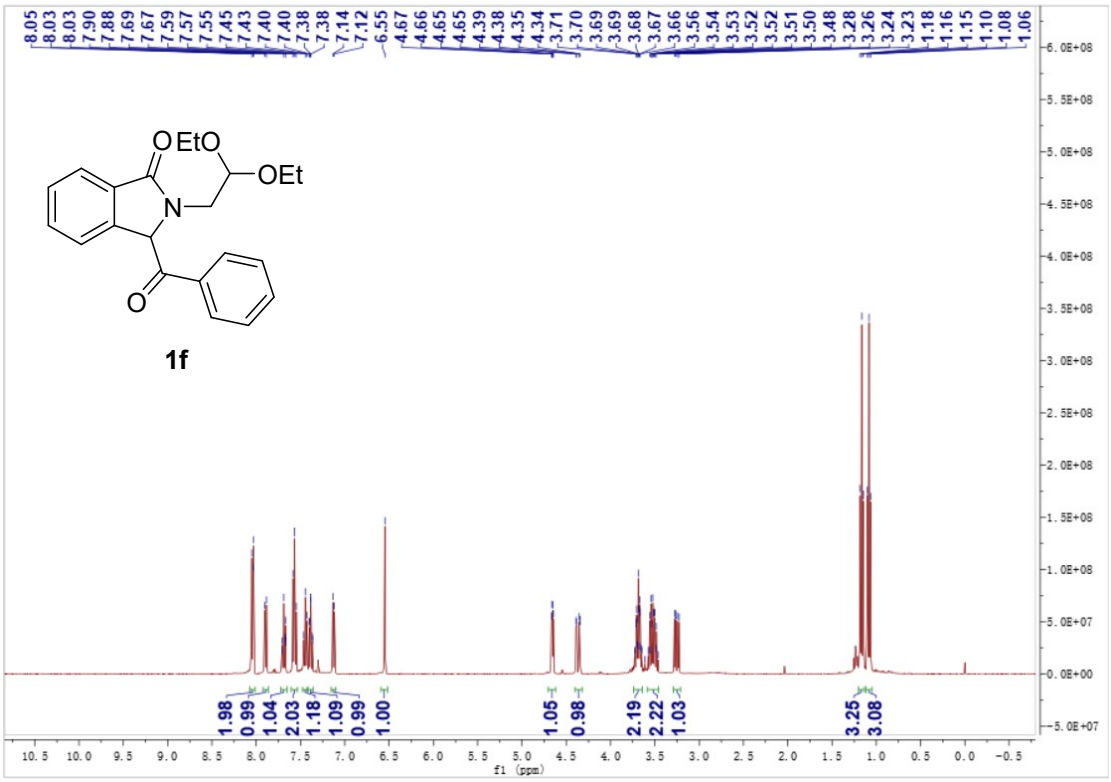

Figure S14. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1f**

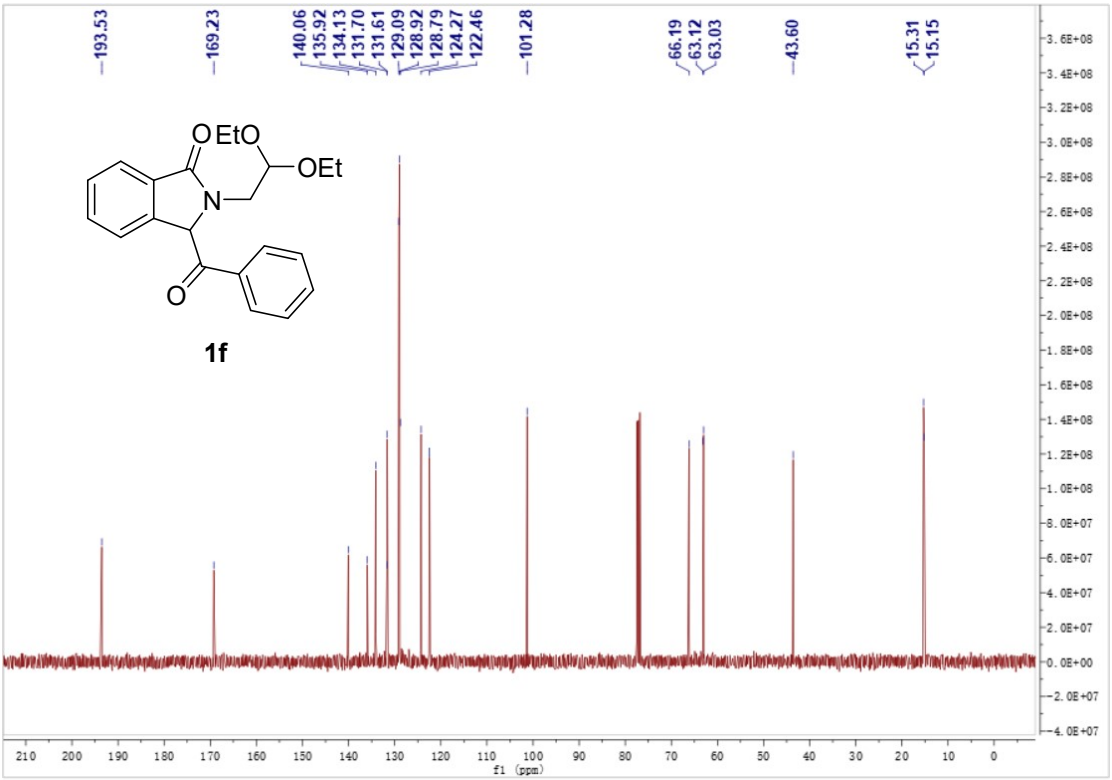

Figure S15. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1f**

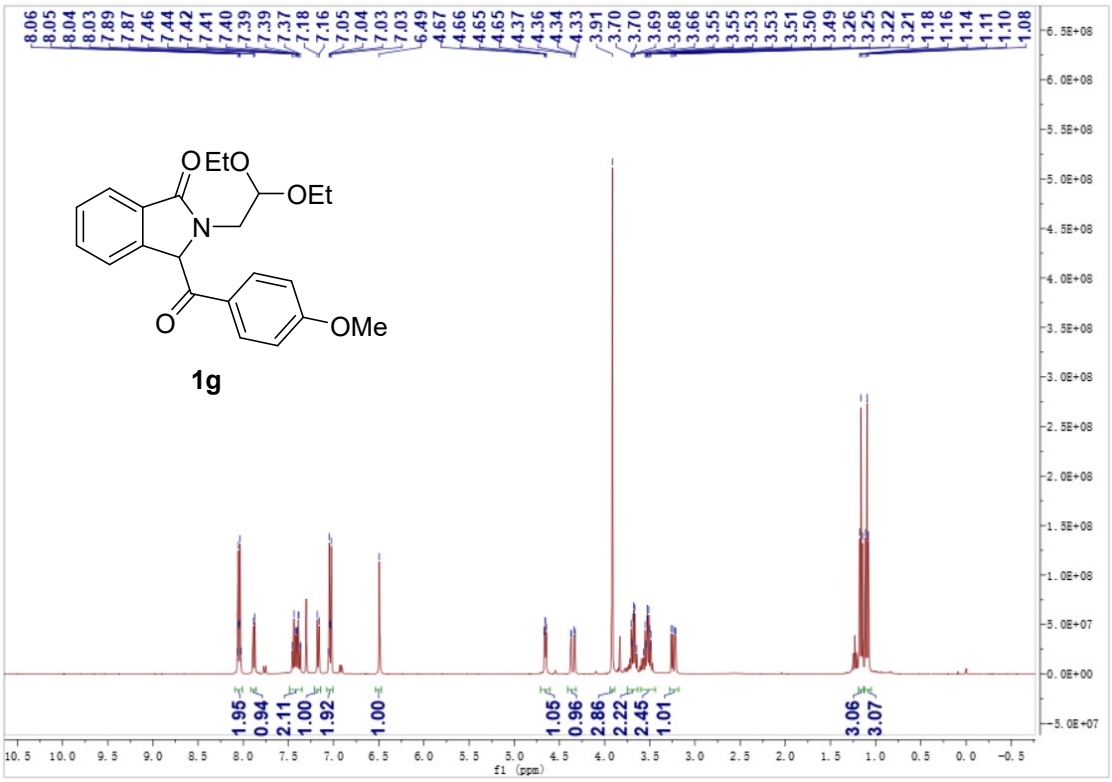

Figure S16. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1g**

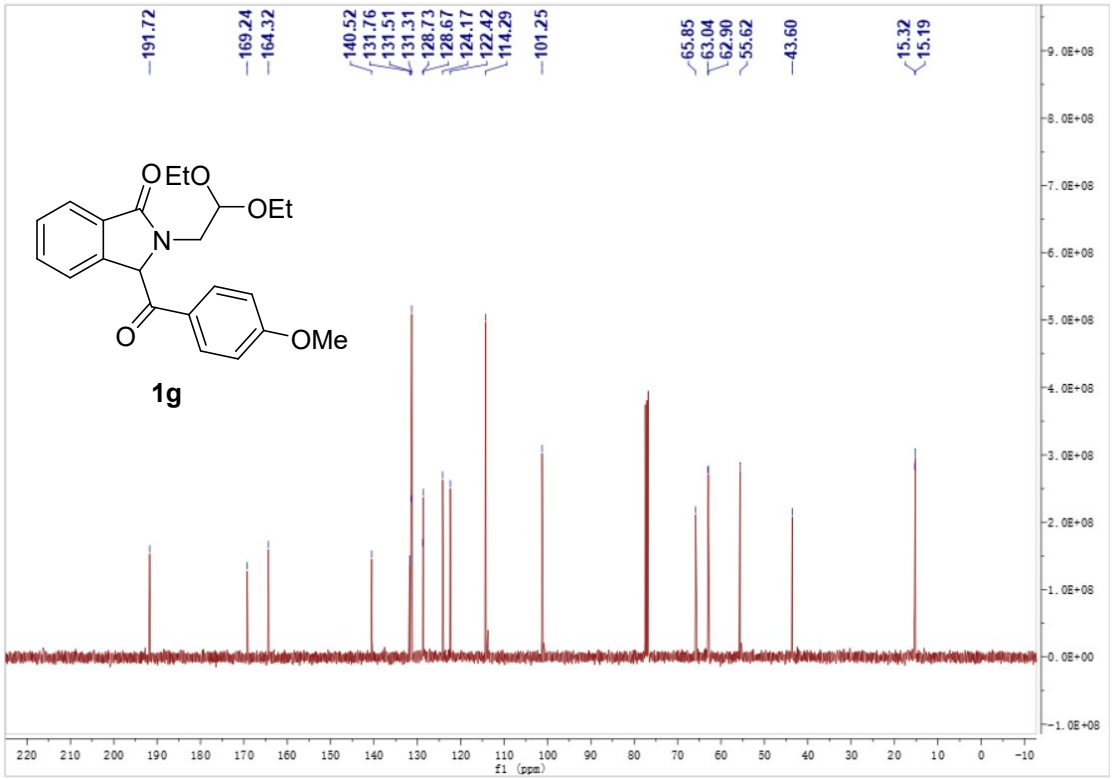

Figure S17. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1g**

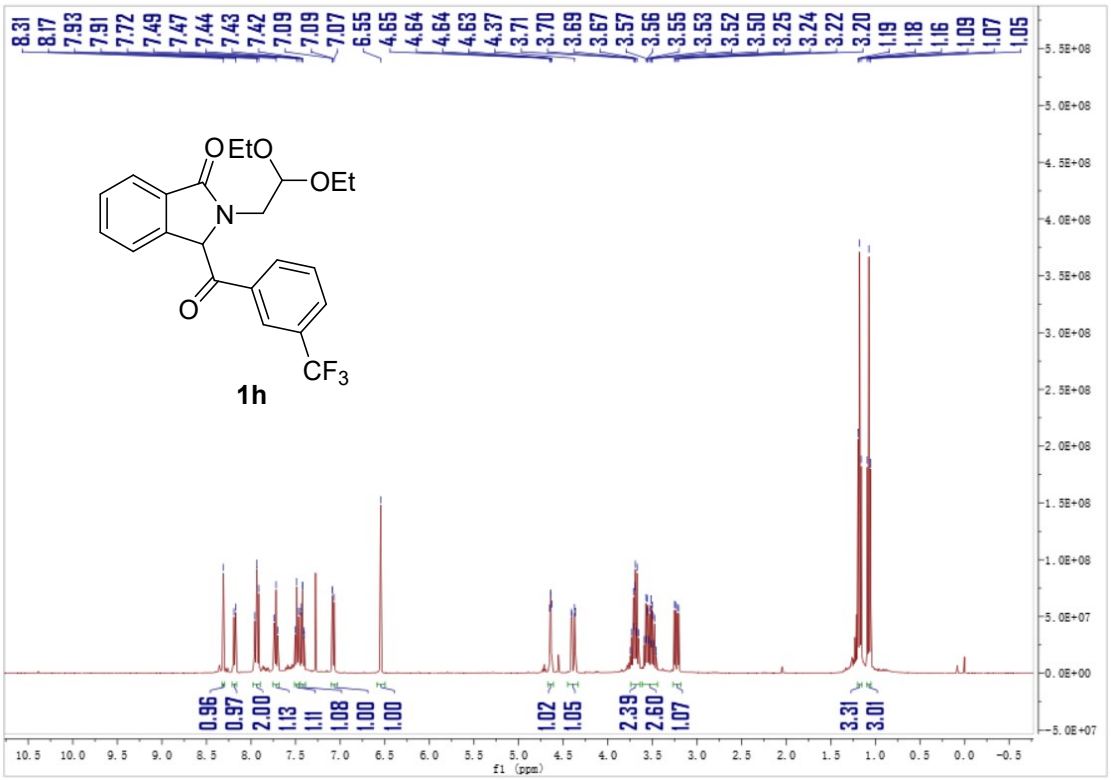

Figure S18. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1h**

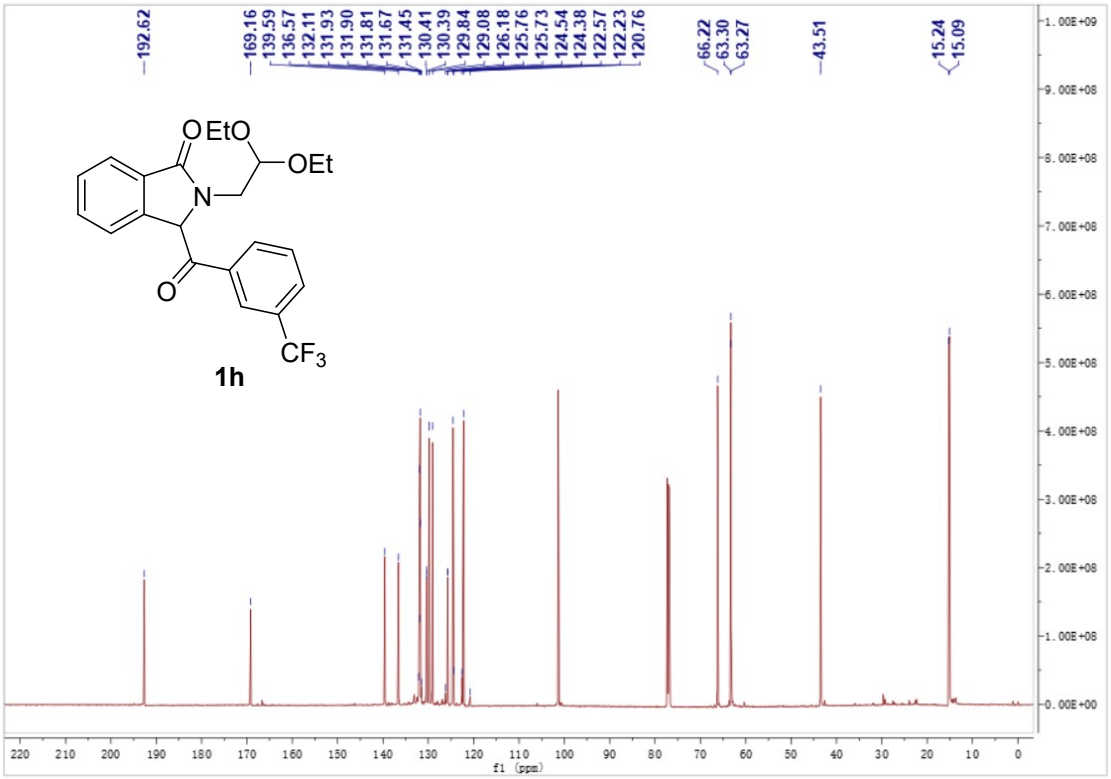

Figure S19. [13]C NMR (151 MHz, Chloroform-*d*) spectrum of compound **1h**

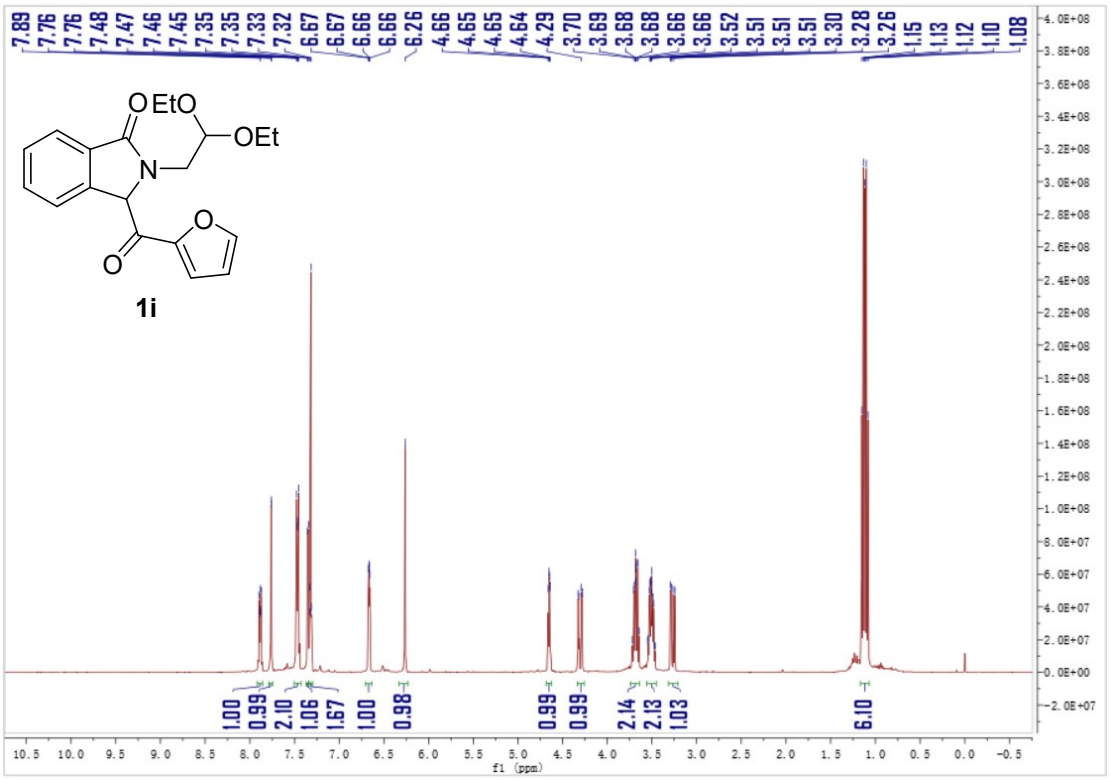

Figure S20. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1i**

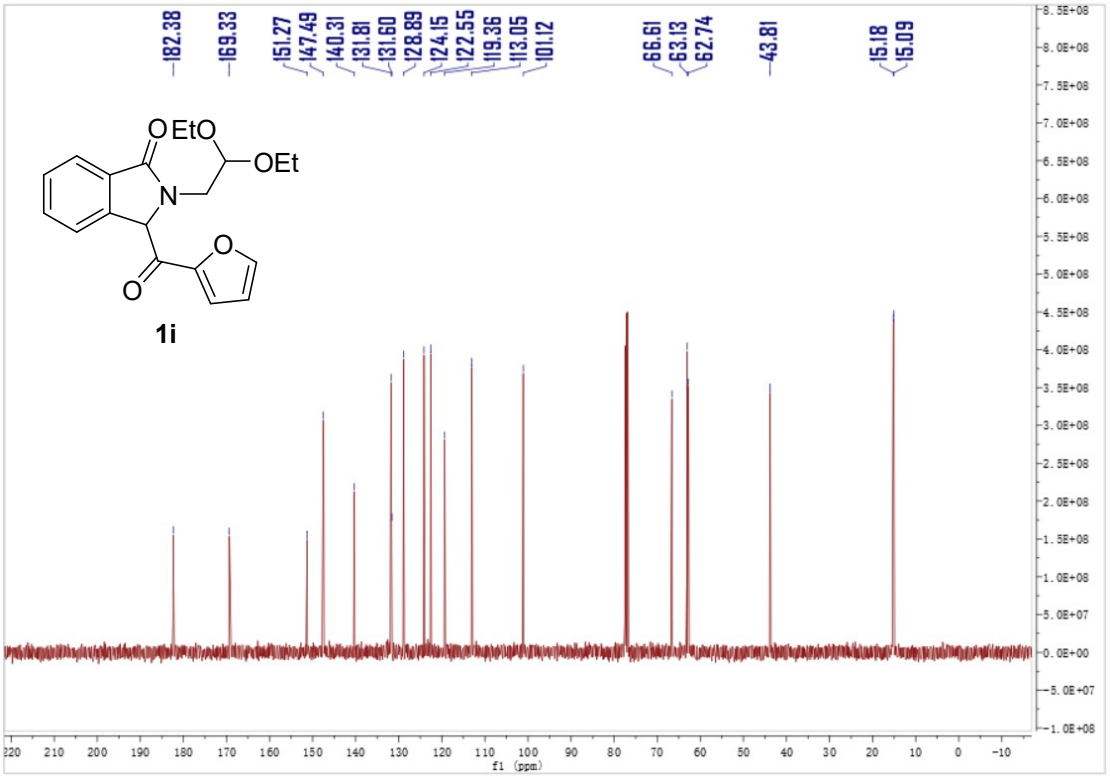

Figure S21. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1i**

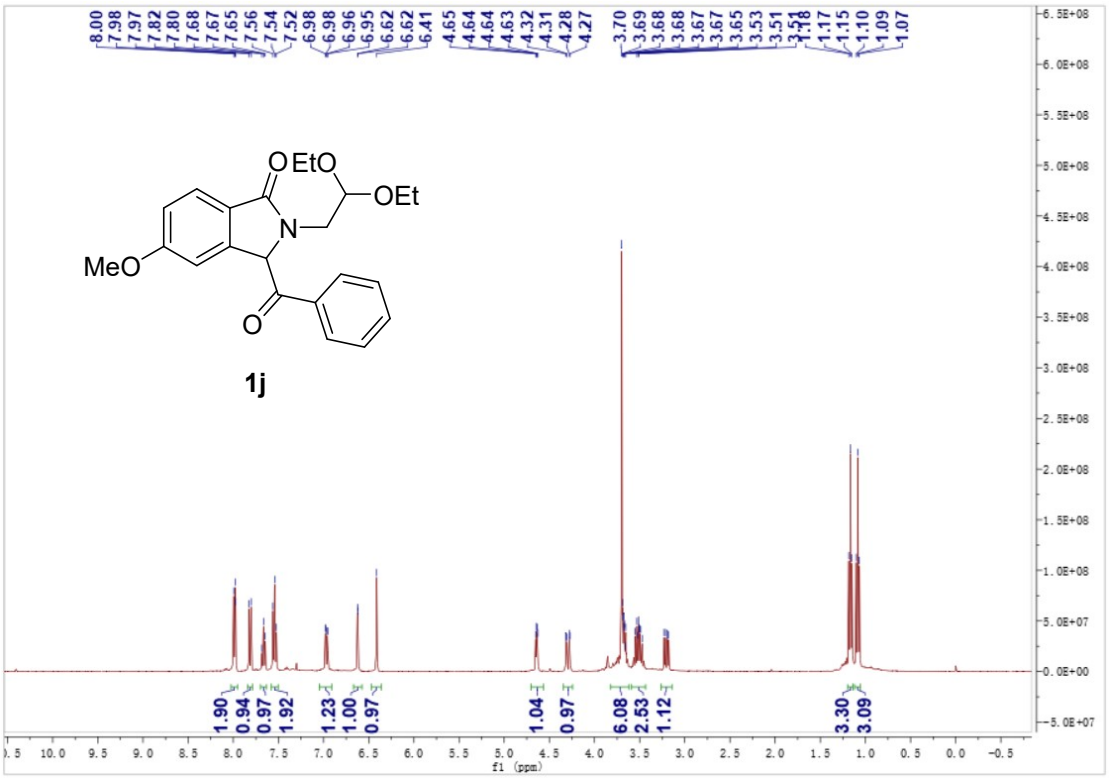

Figure S22. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1j**

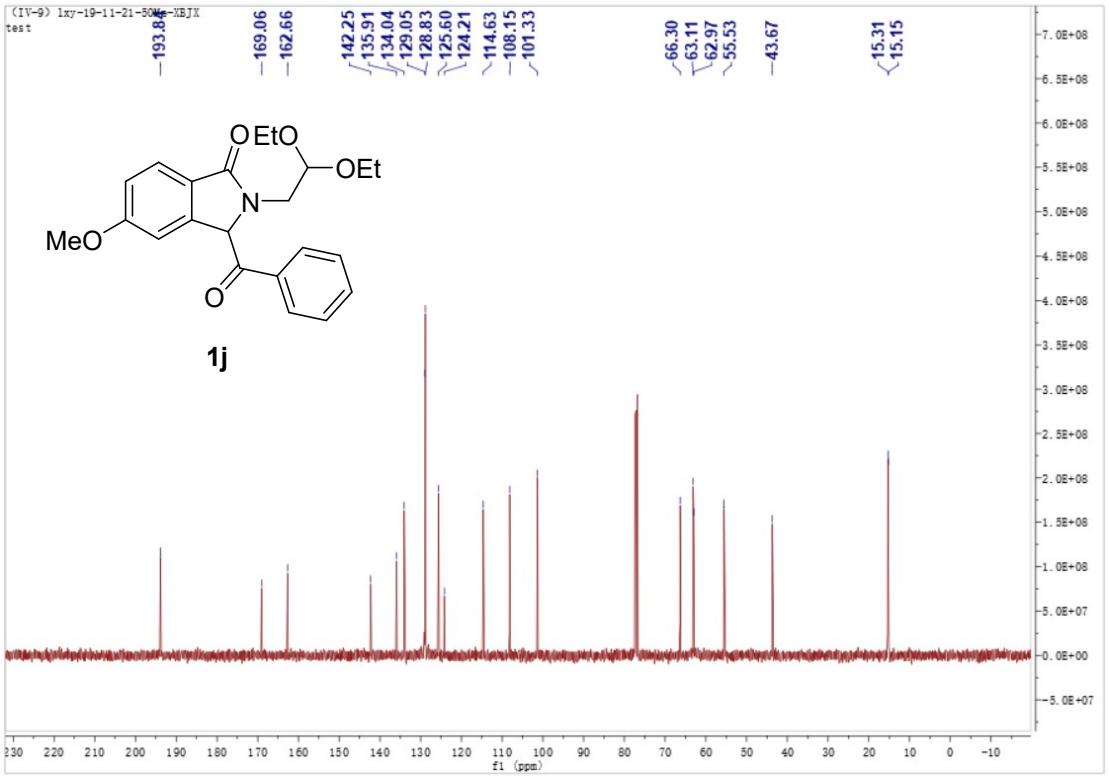

Figure S23. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1j**

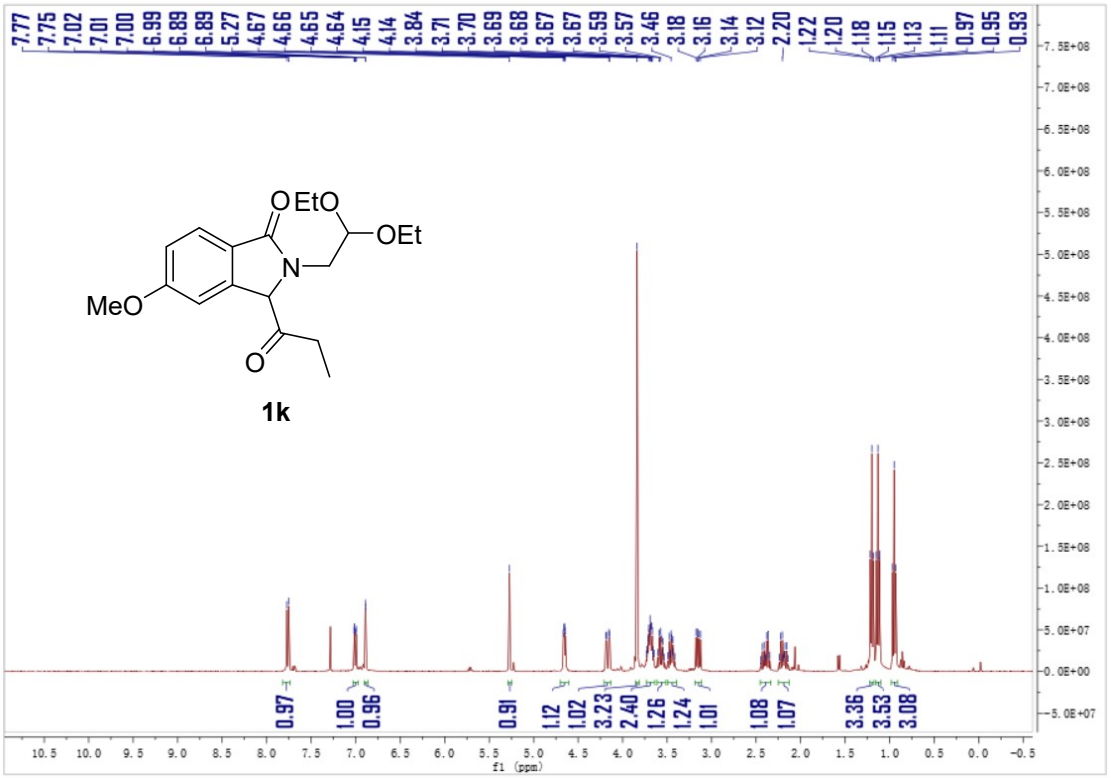

Figure S24. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1k**

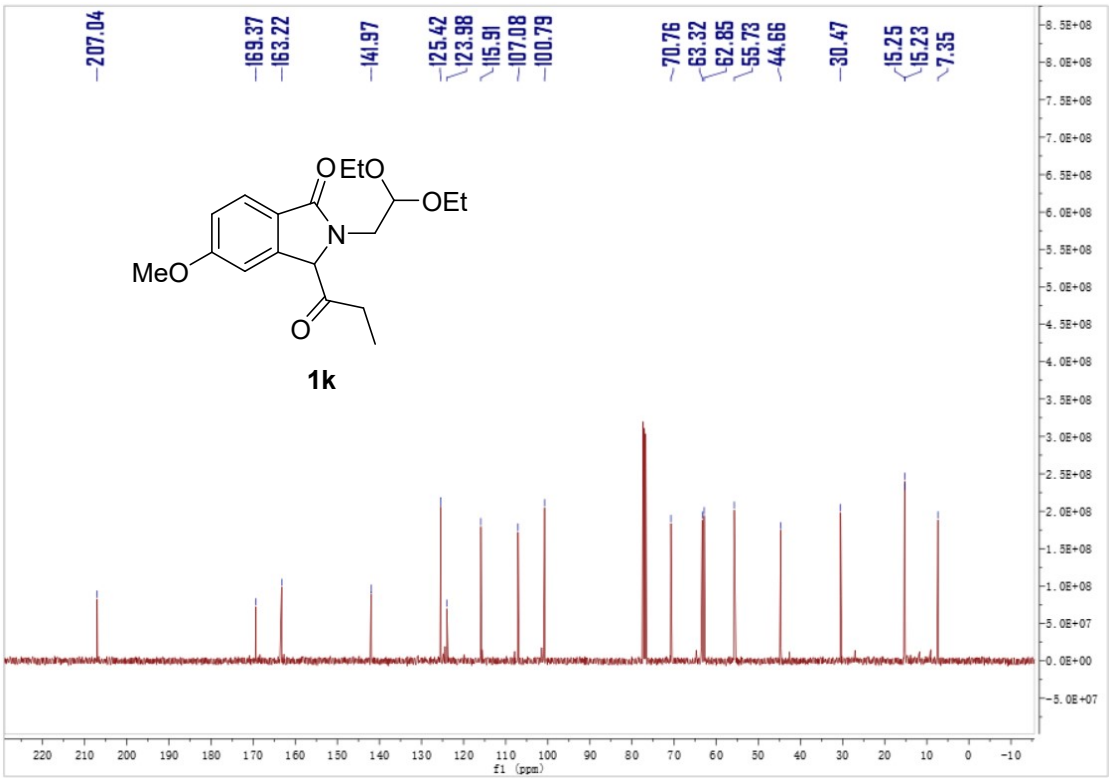

Figure S25. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1k**

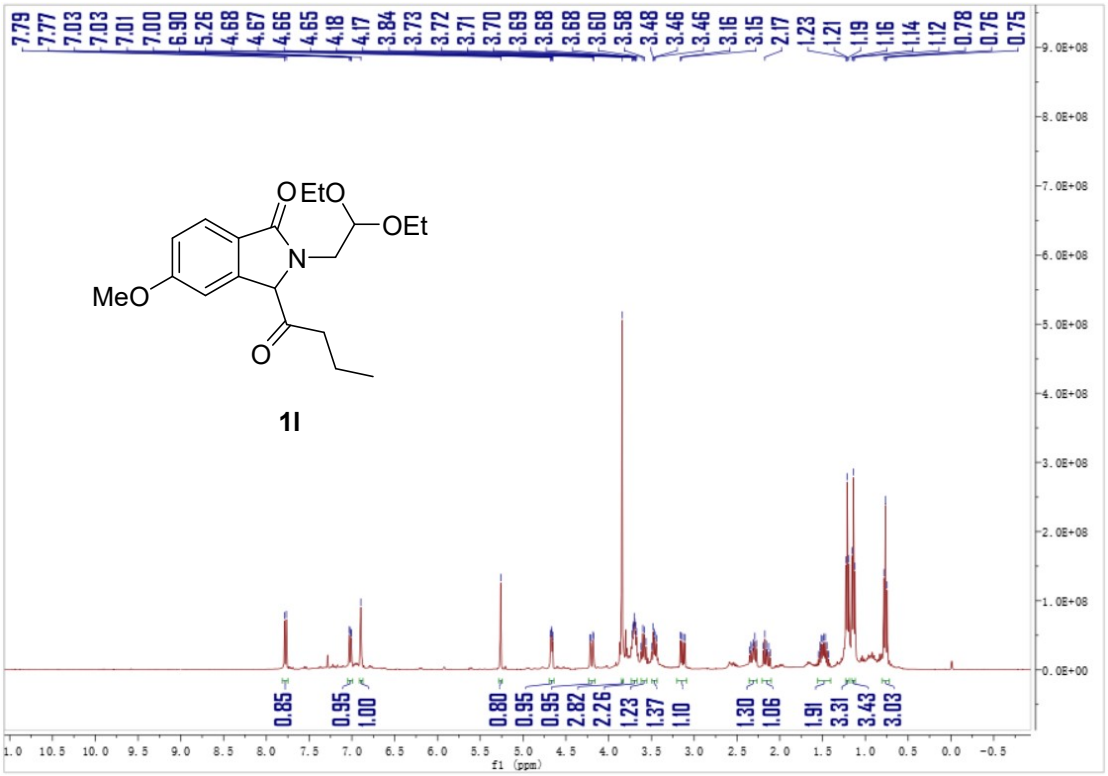

Figure S26. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1l**

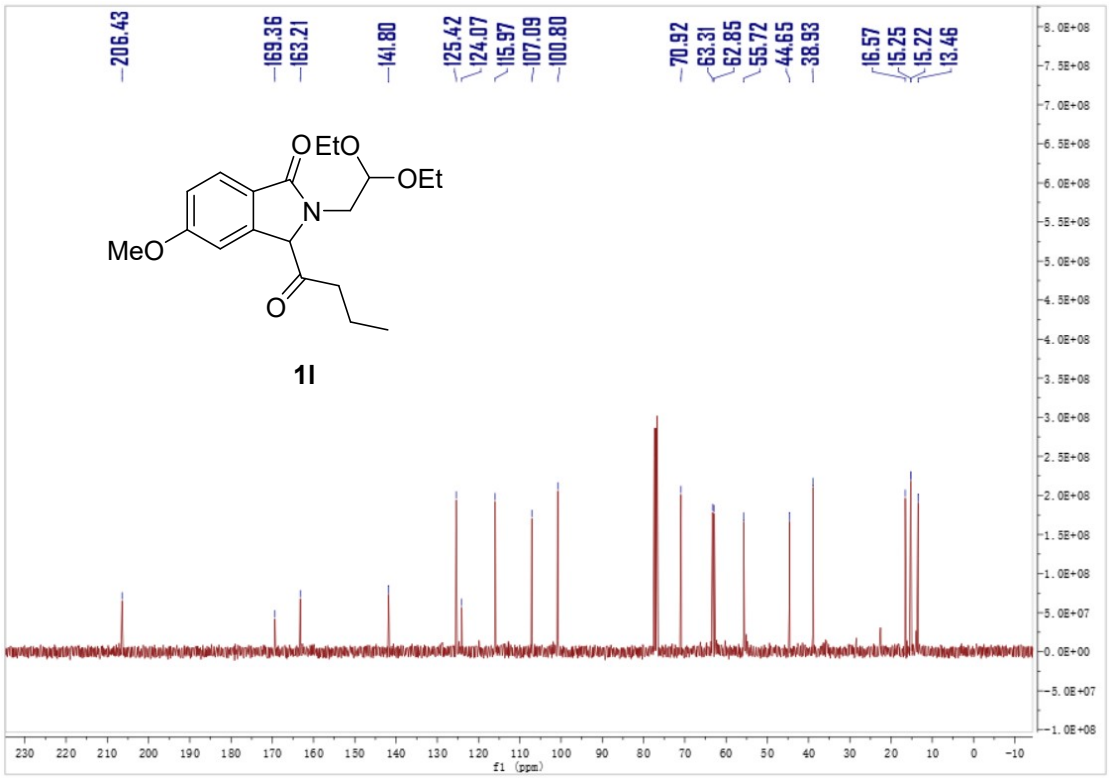

Figure S27. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1l**

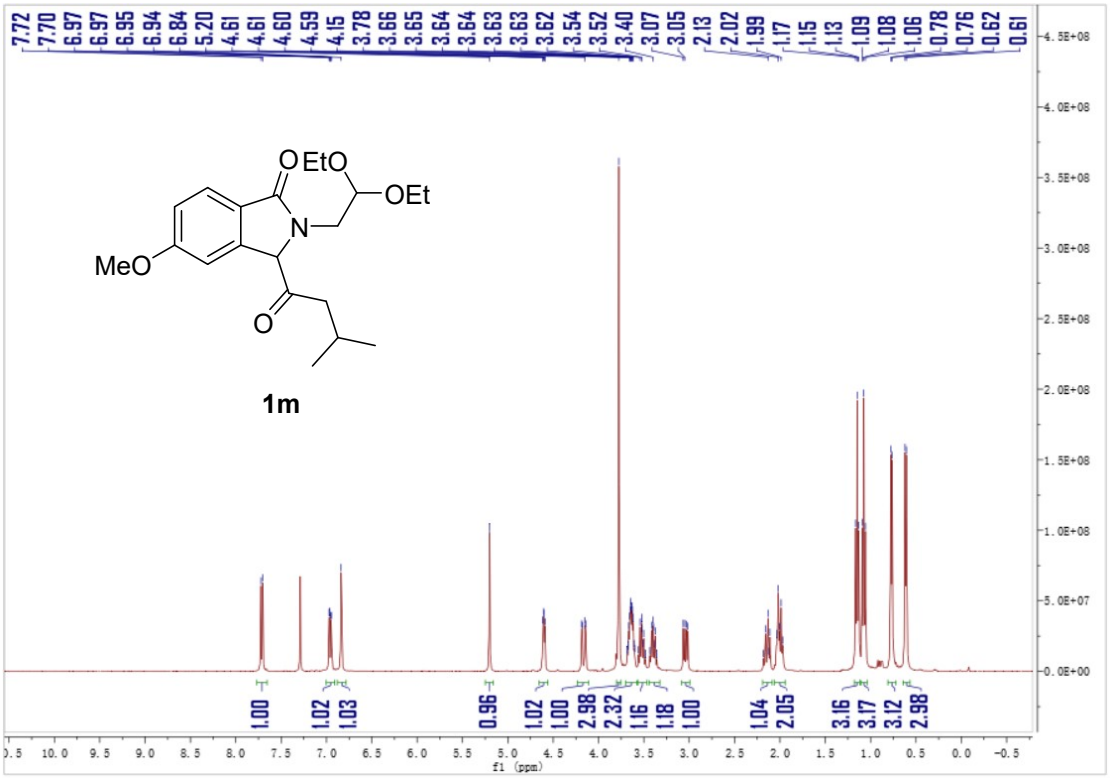

Figure S28. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1m**

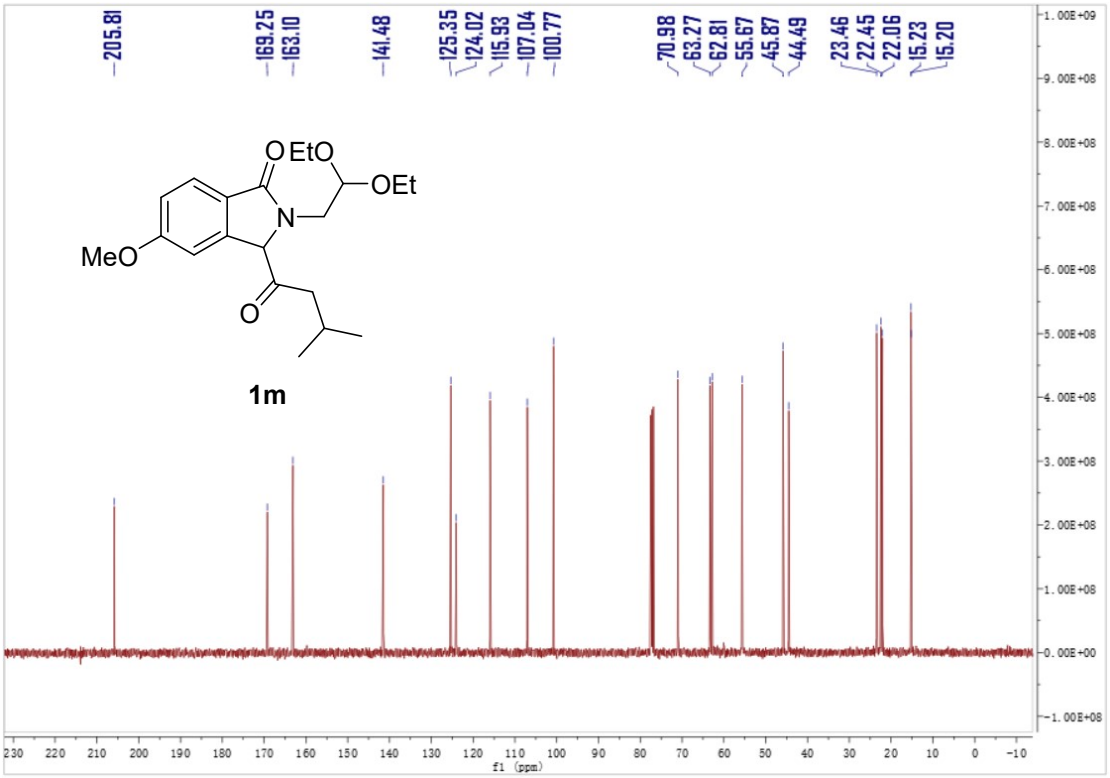

Figure S29. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1m**

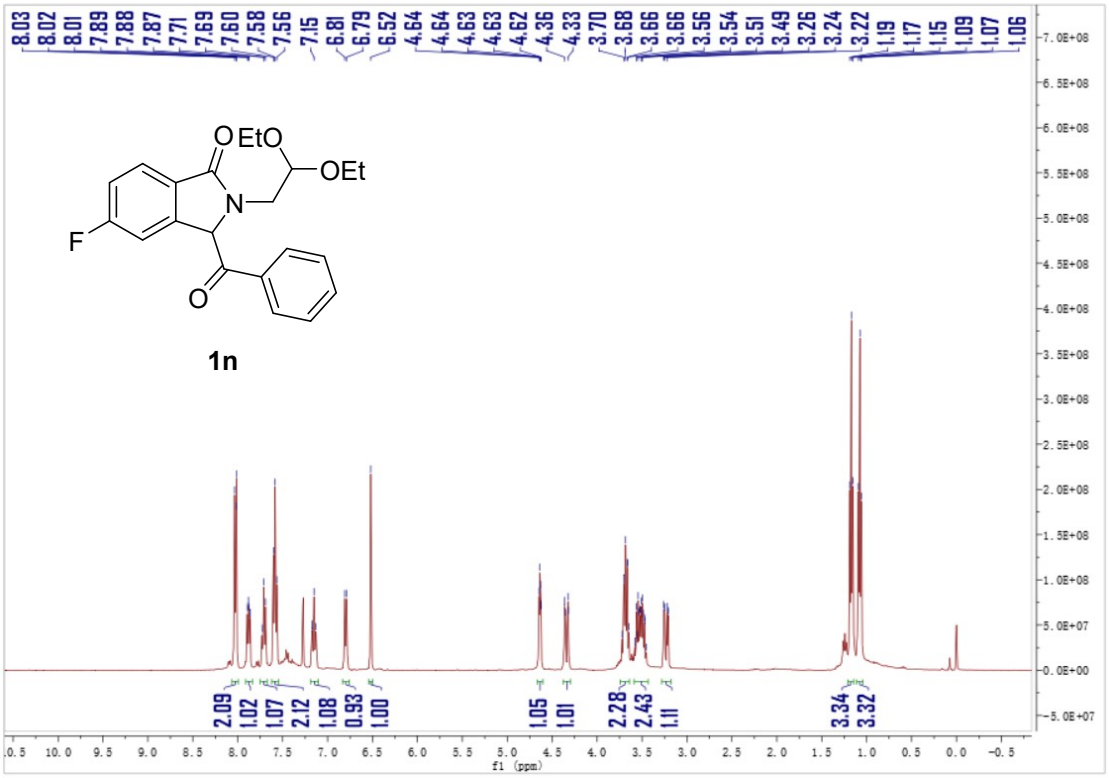

Figure S30. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1n**

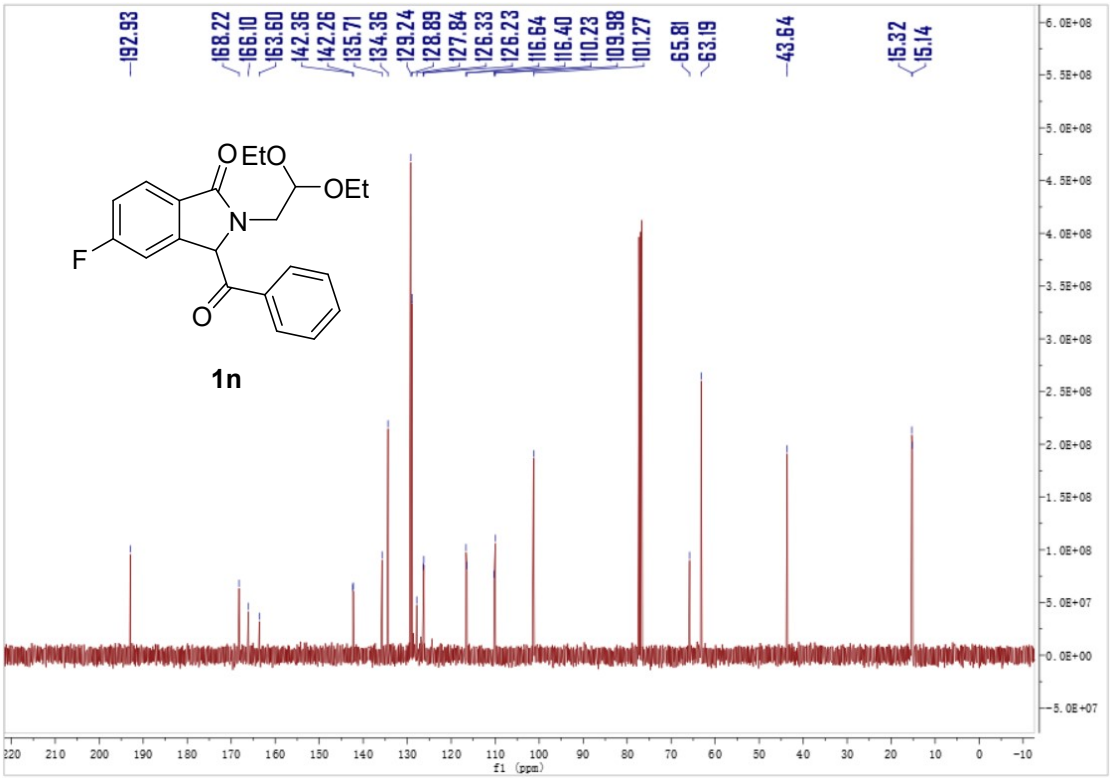

Figure S31. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1n**

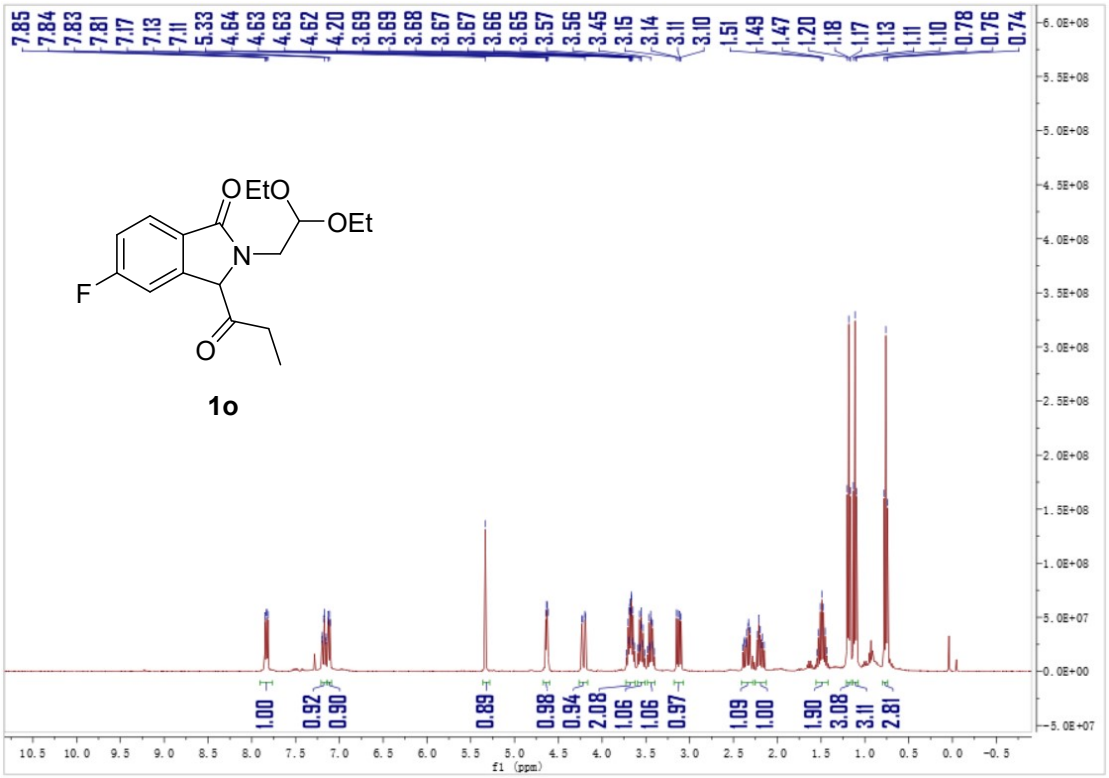

Figure S32. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1o**

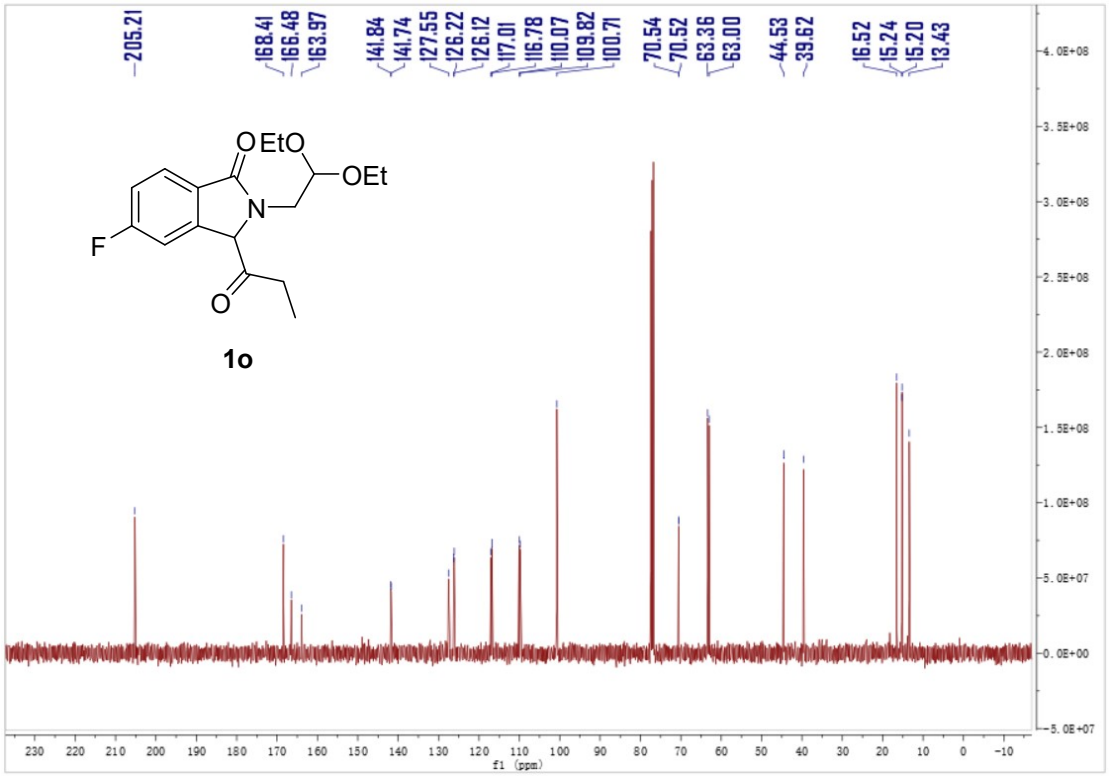

Figure S33. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1o**

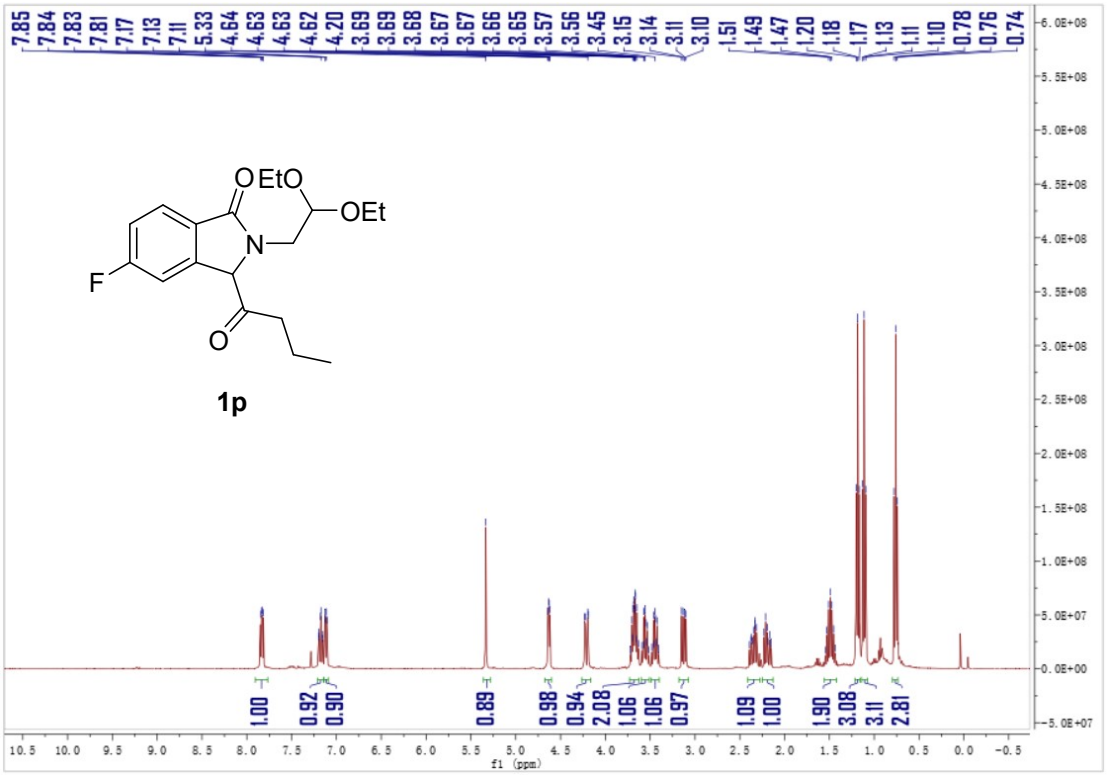

Figure S34. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1p**

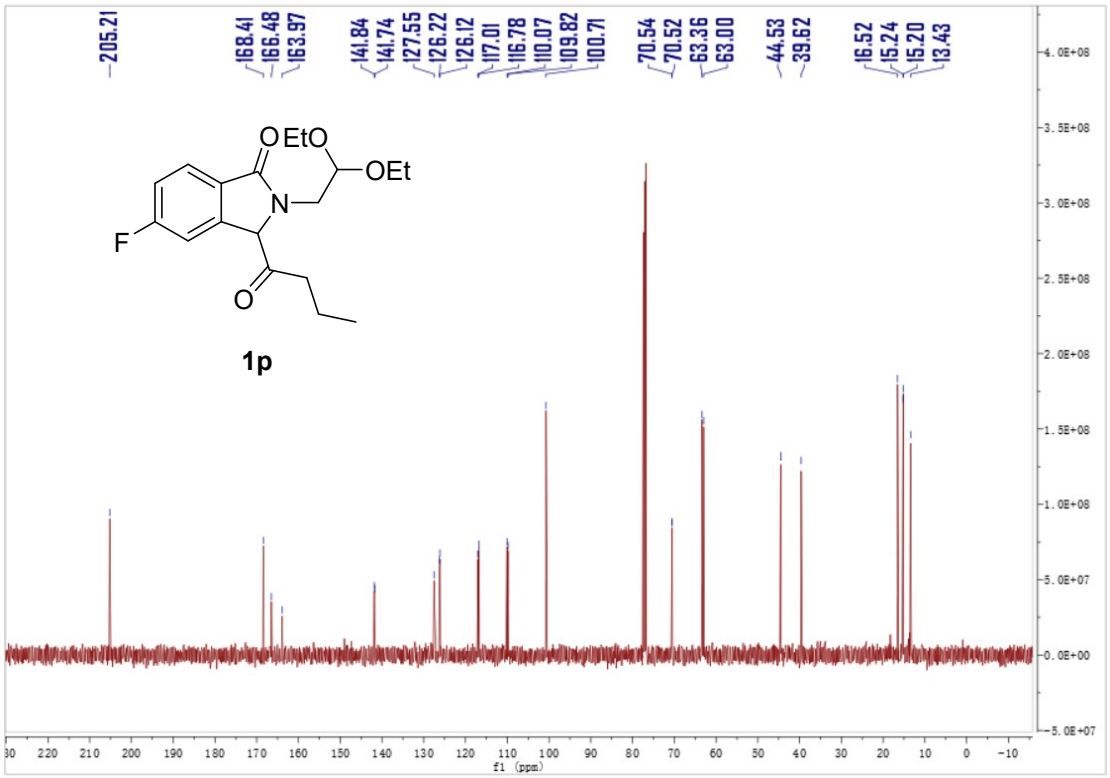

Figure S35. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1p**

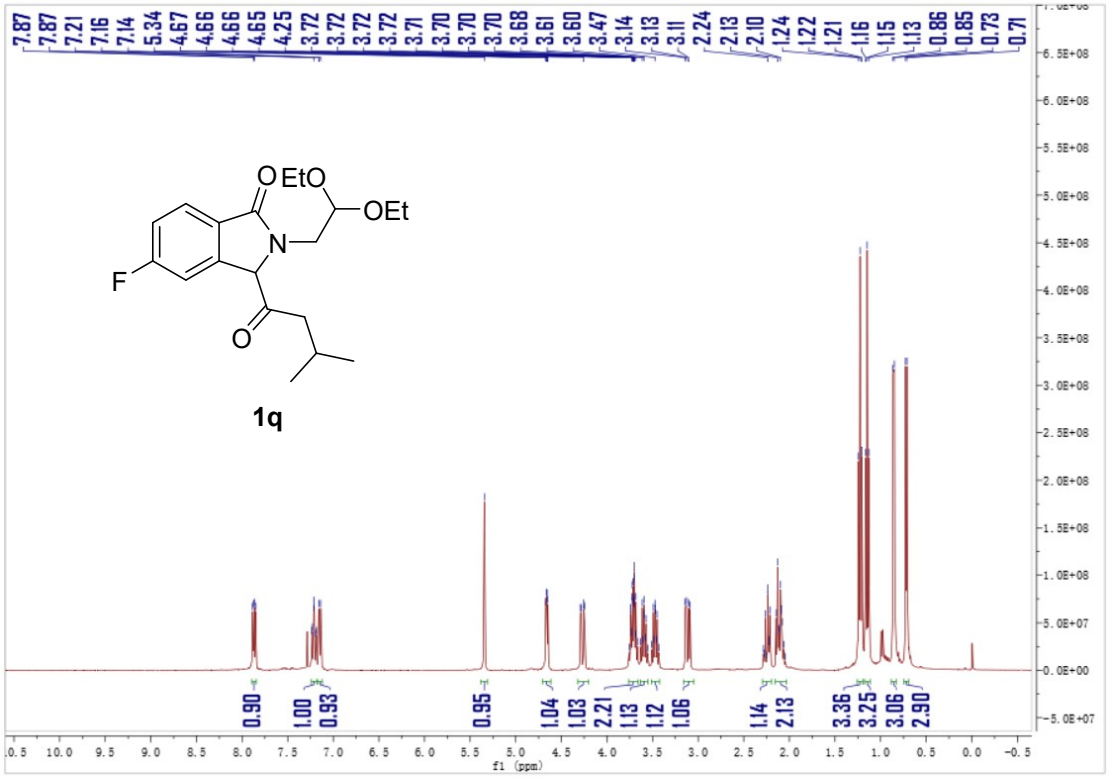

Figure S36. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **1q**

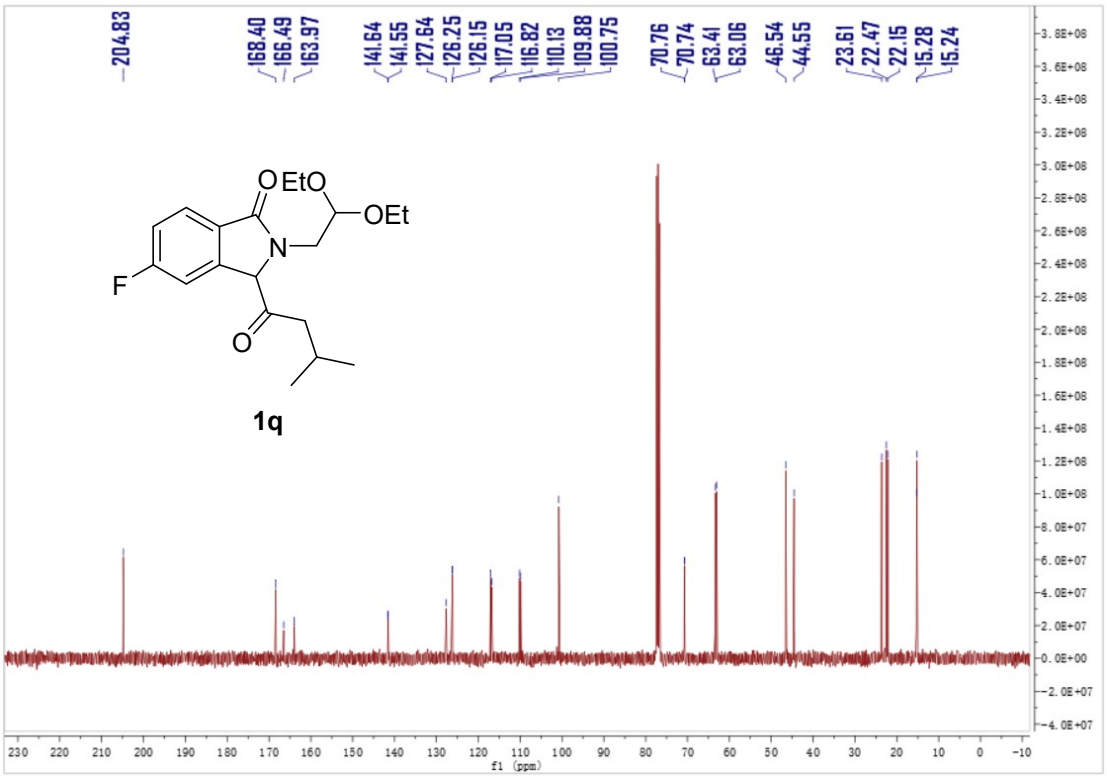

Figure S37. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **1q**

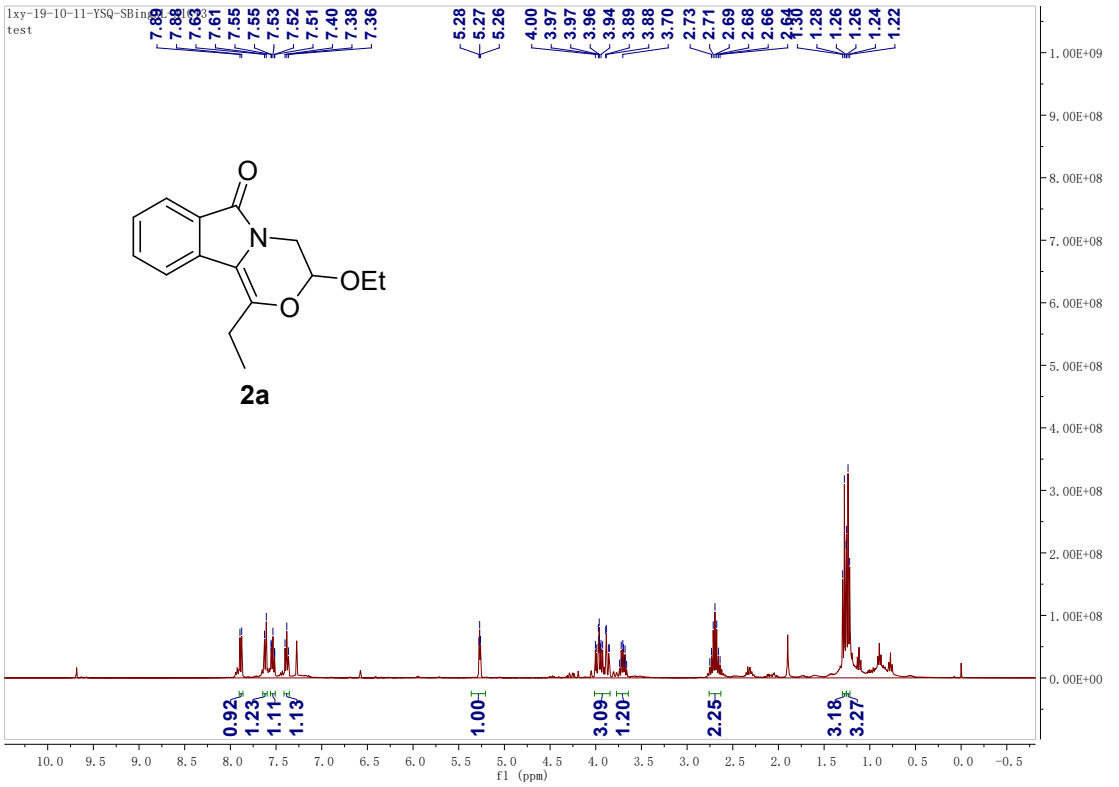

Figure S38. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2a**

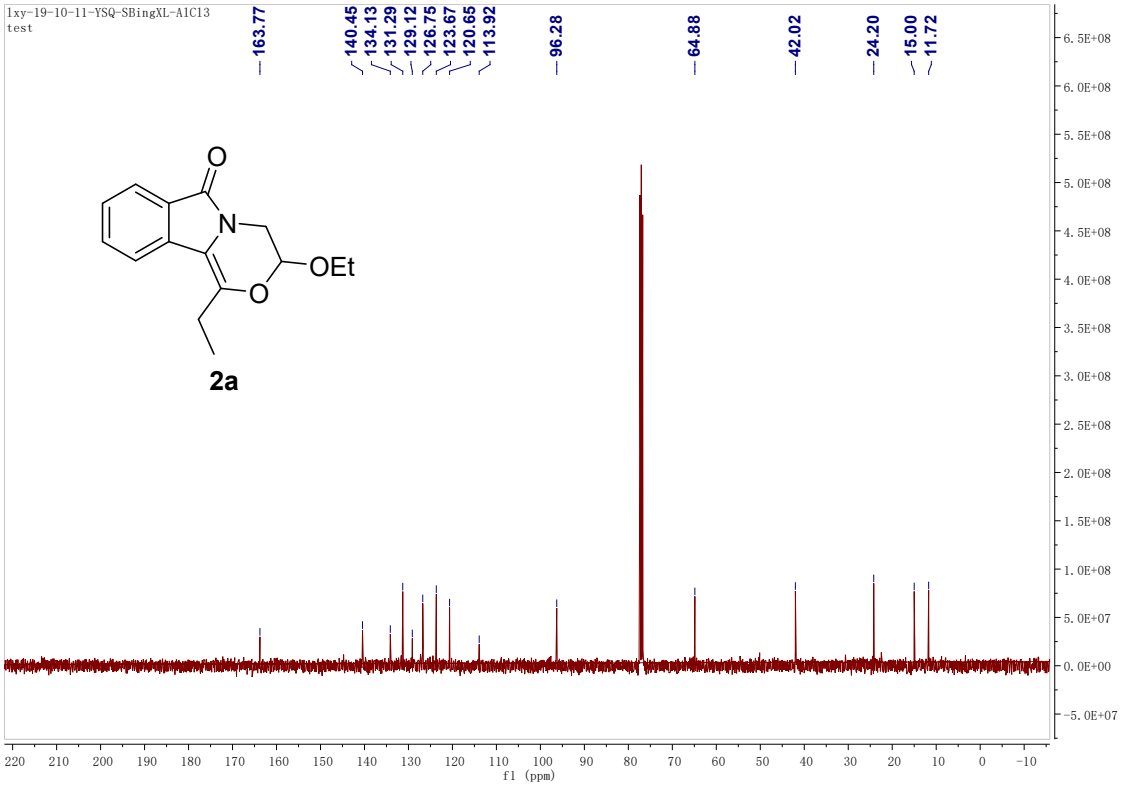

Figure S39. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2a**

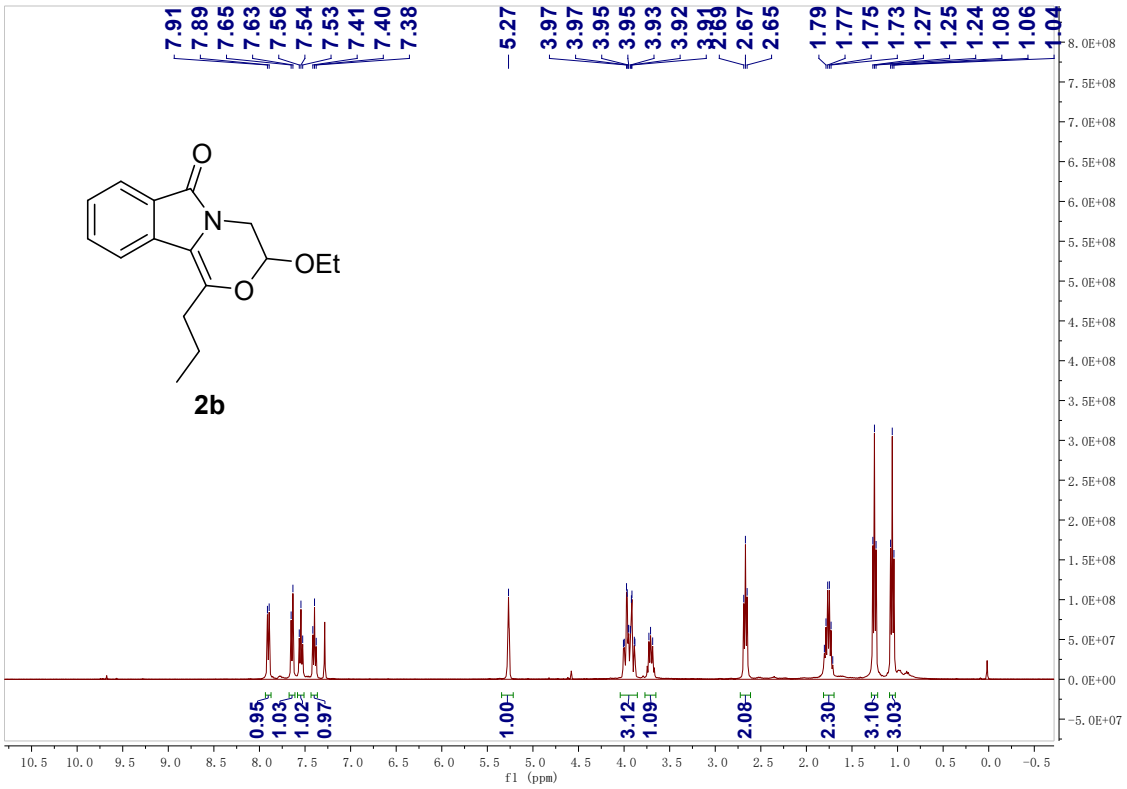

Figure S40. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2b**

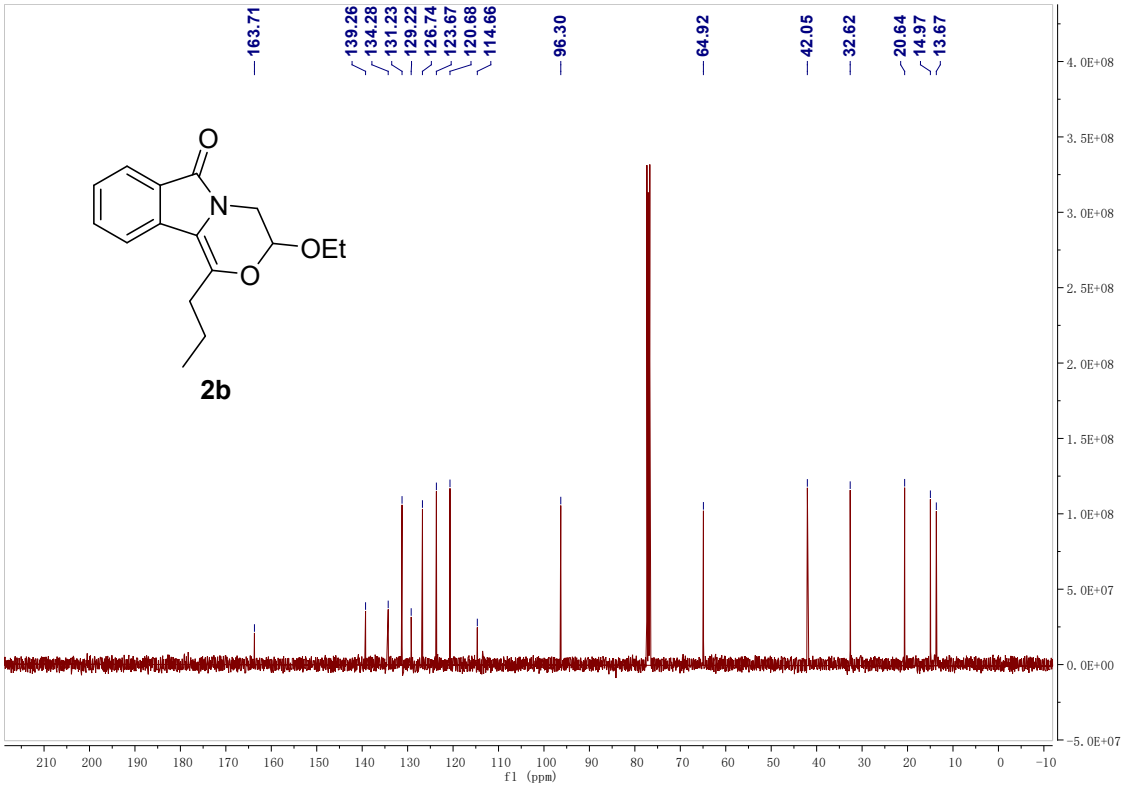

Figure S41. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2b**

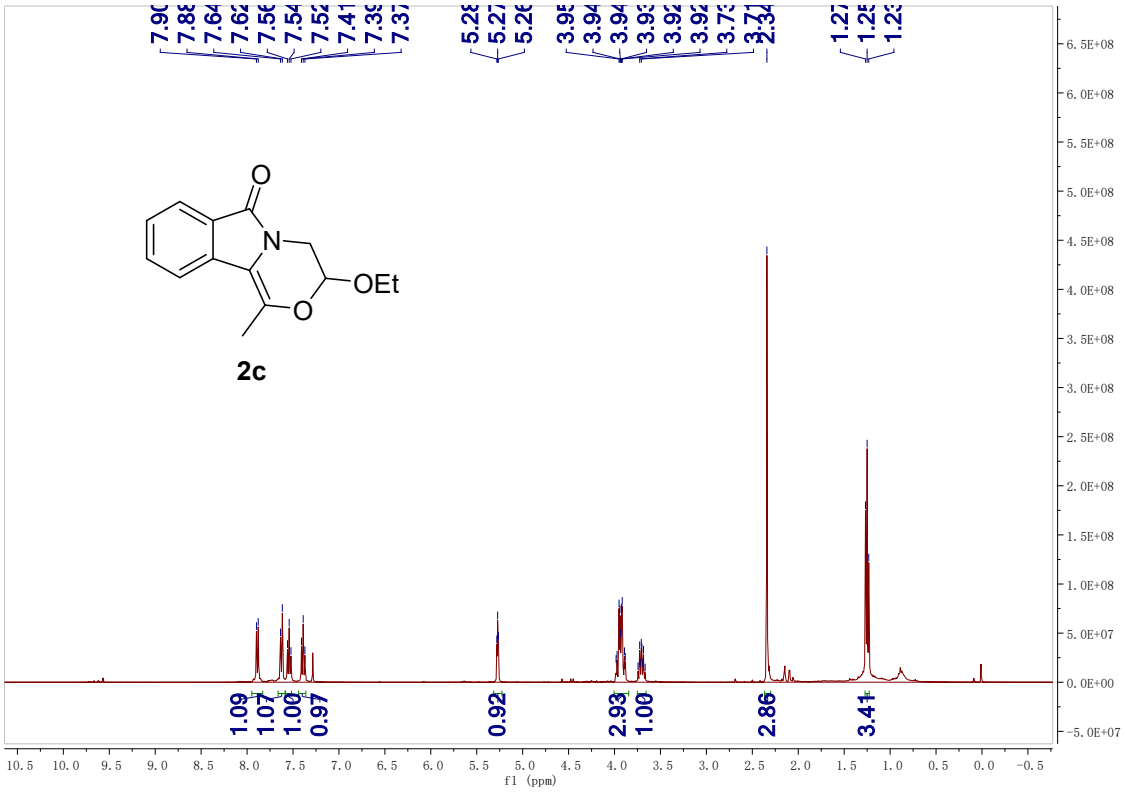

Figure S42. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2c**

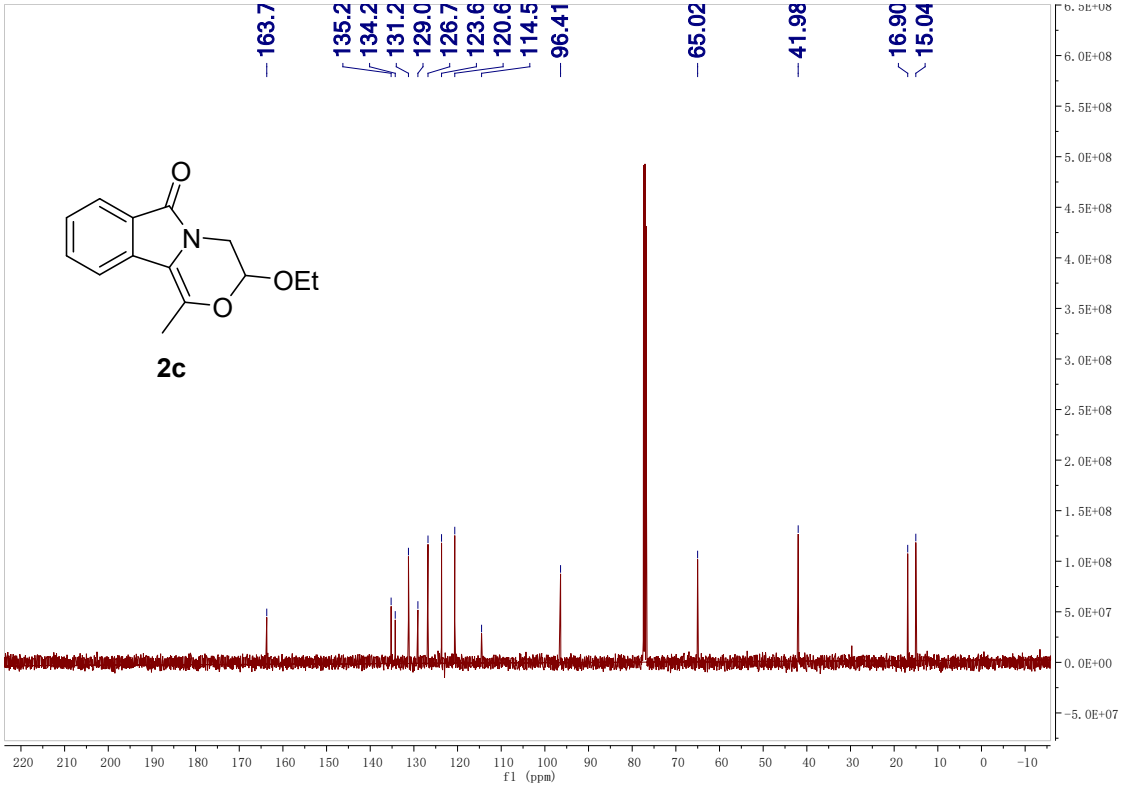

Figure S43. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2c**

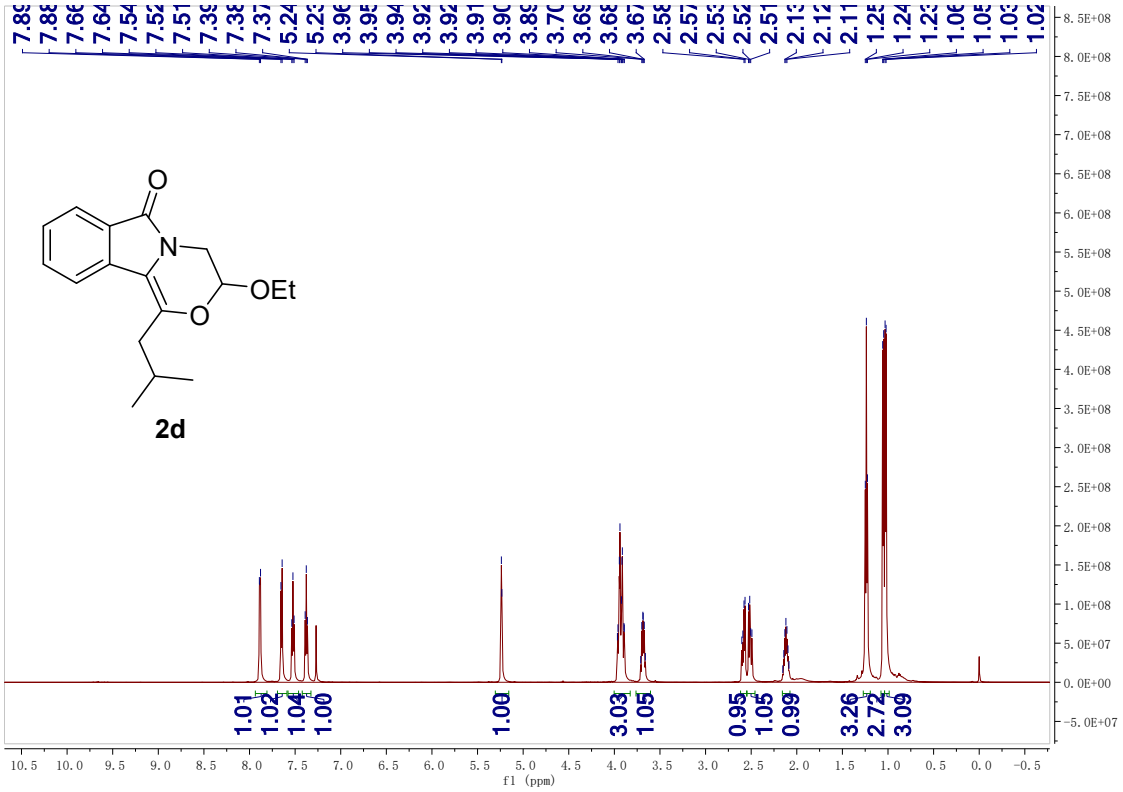

Figure S44. ^{1}H NMR (600 MHz, Chloroform-*d*) spectrum of compound **2d**

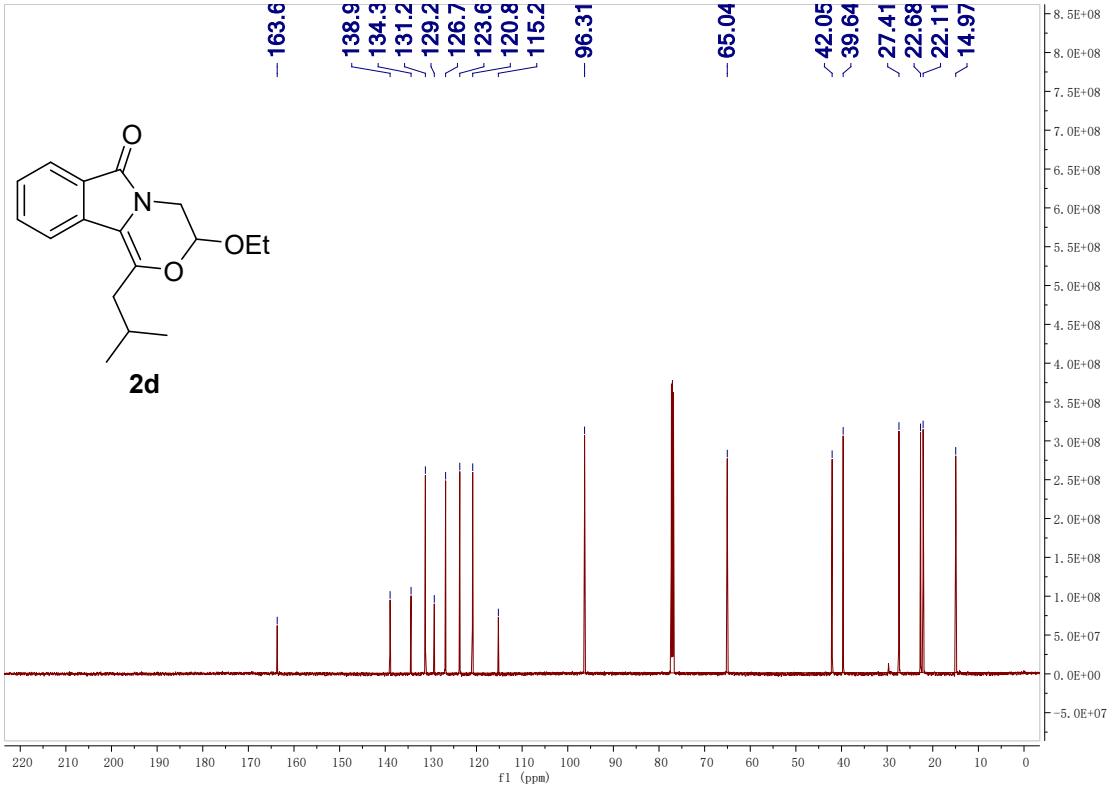

Figure S45. ^{13}C NMR (151 MHz, Chloroform-*d*) spectrum of compound **2d**

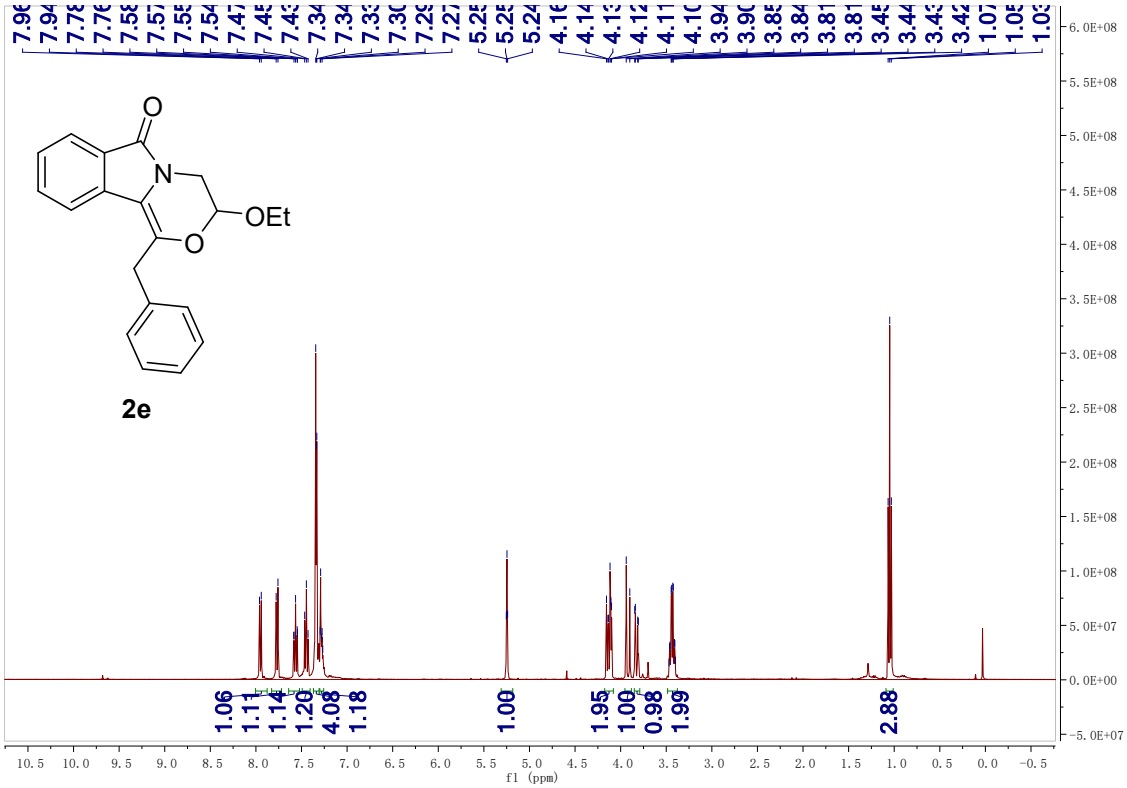

Figure S46. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2e**

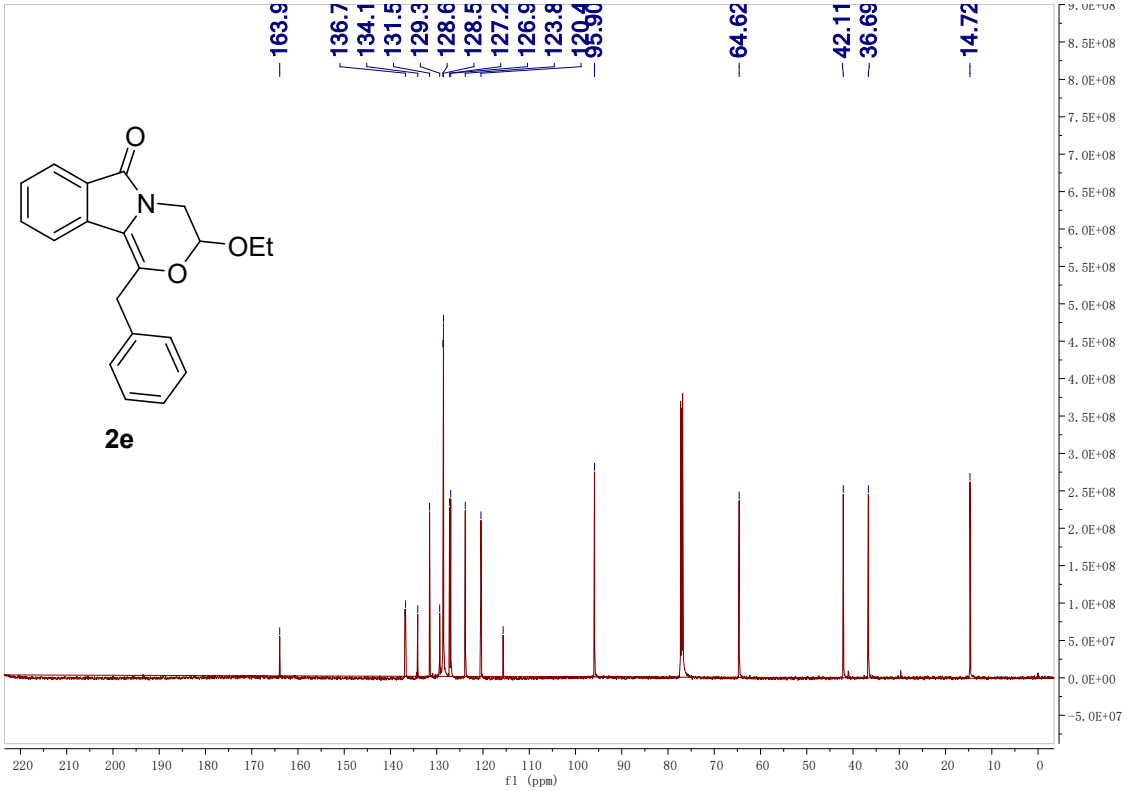

Figure S47. ^{13}C NMR (151 MHz, Chloroform-*d*) spectrum of compound **2e**

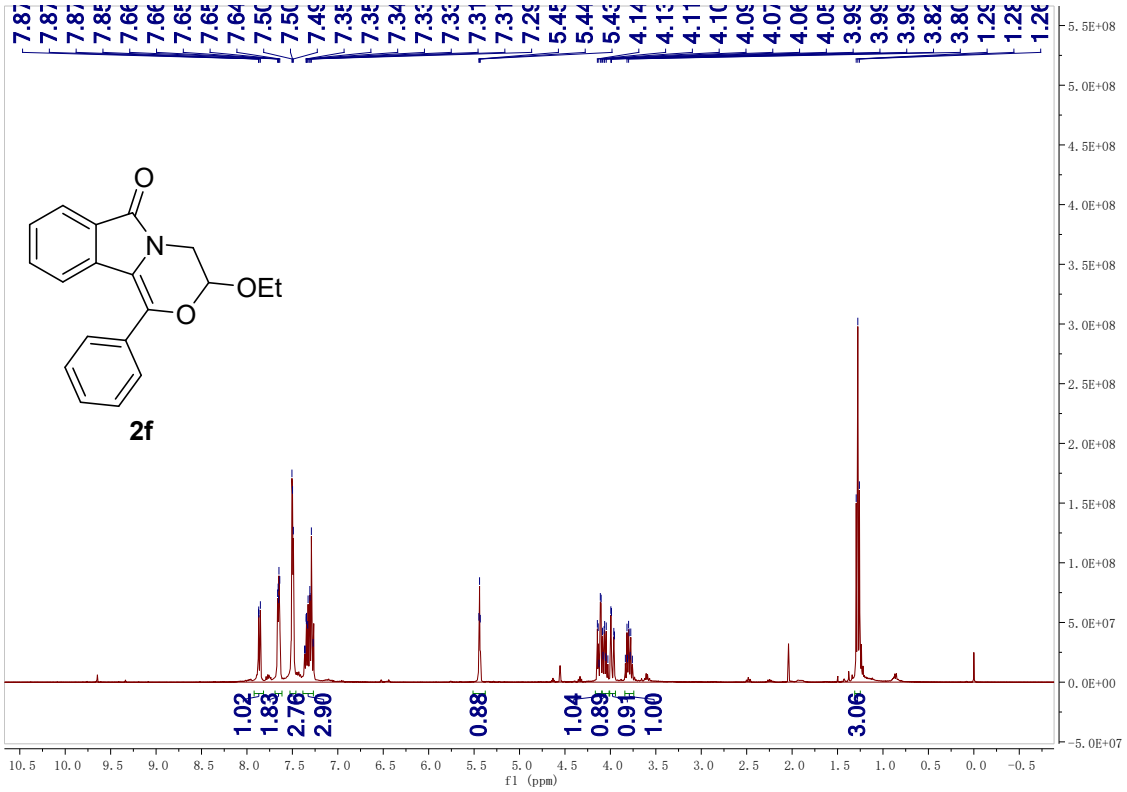

Figure S48. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2f**

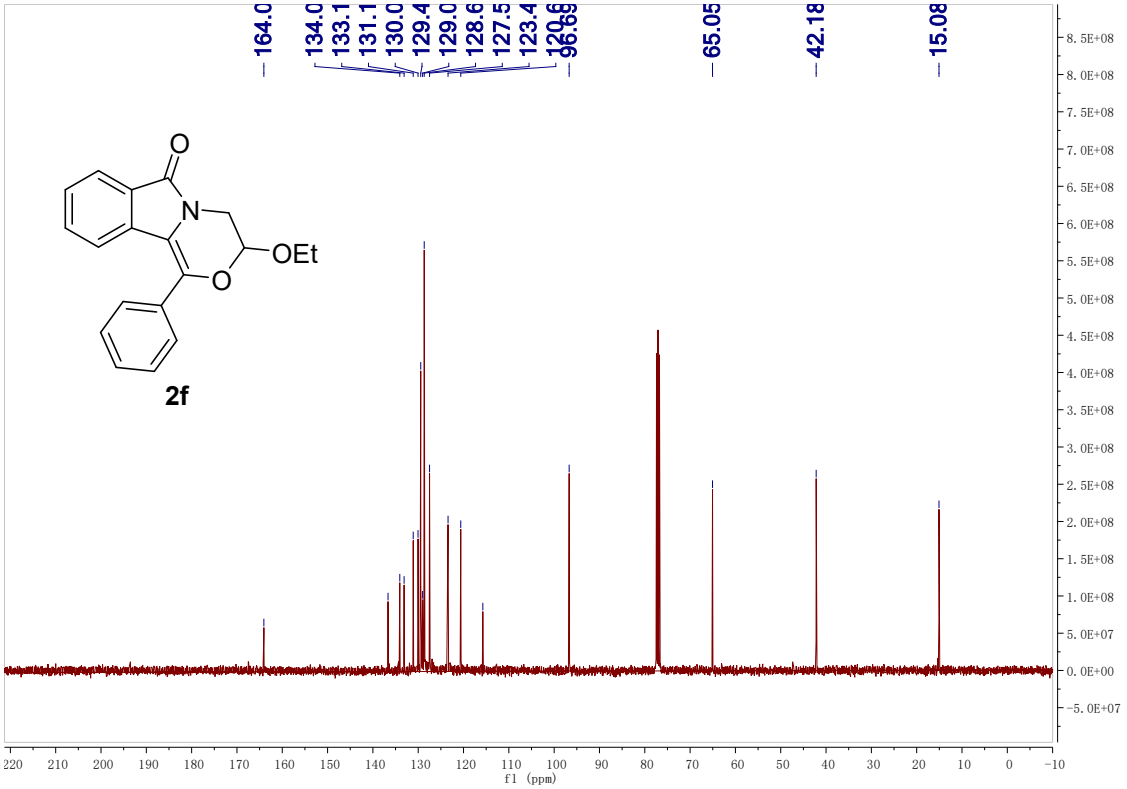

Figure S49. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2f**

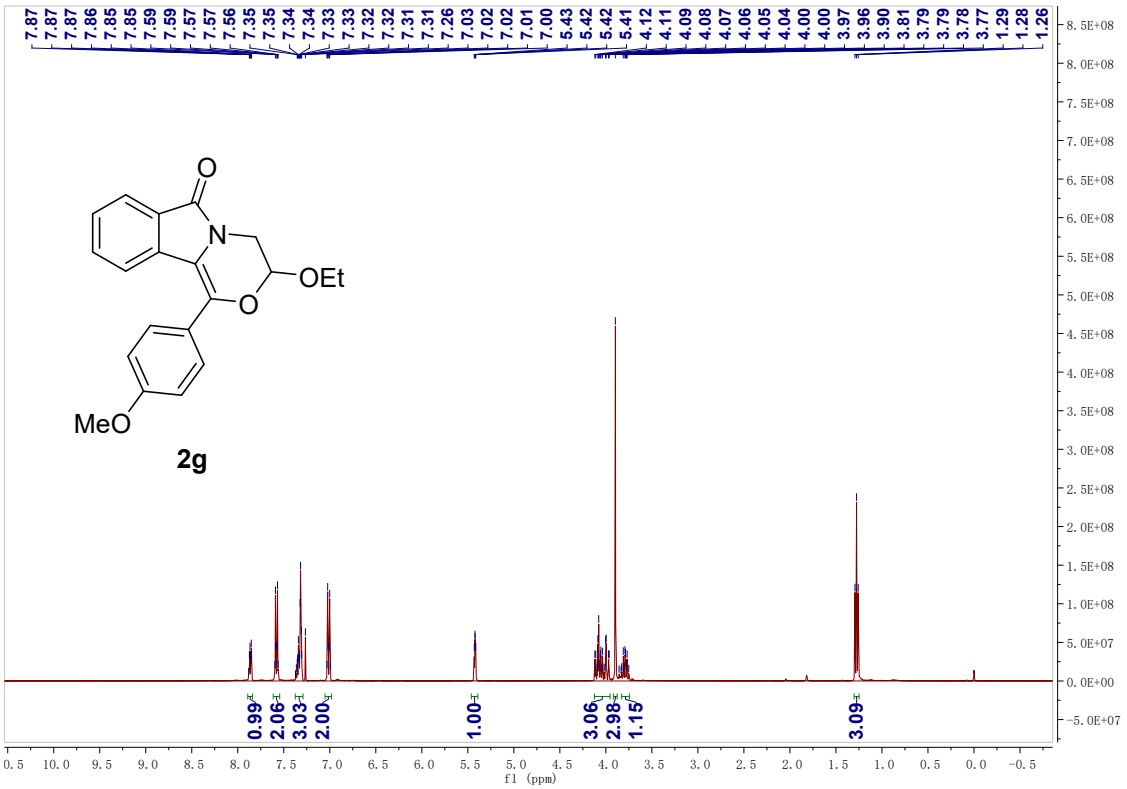

Figure S50. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2g**

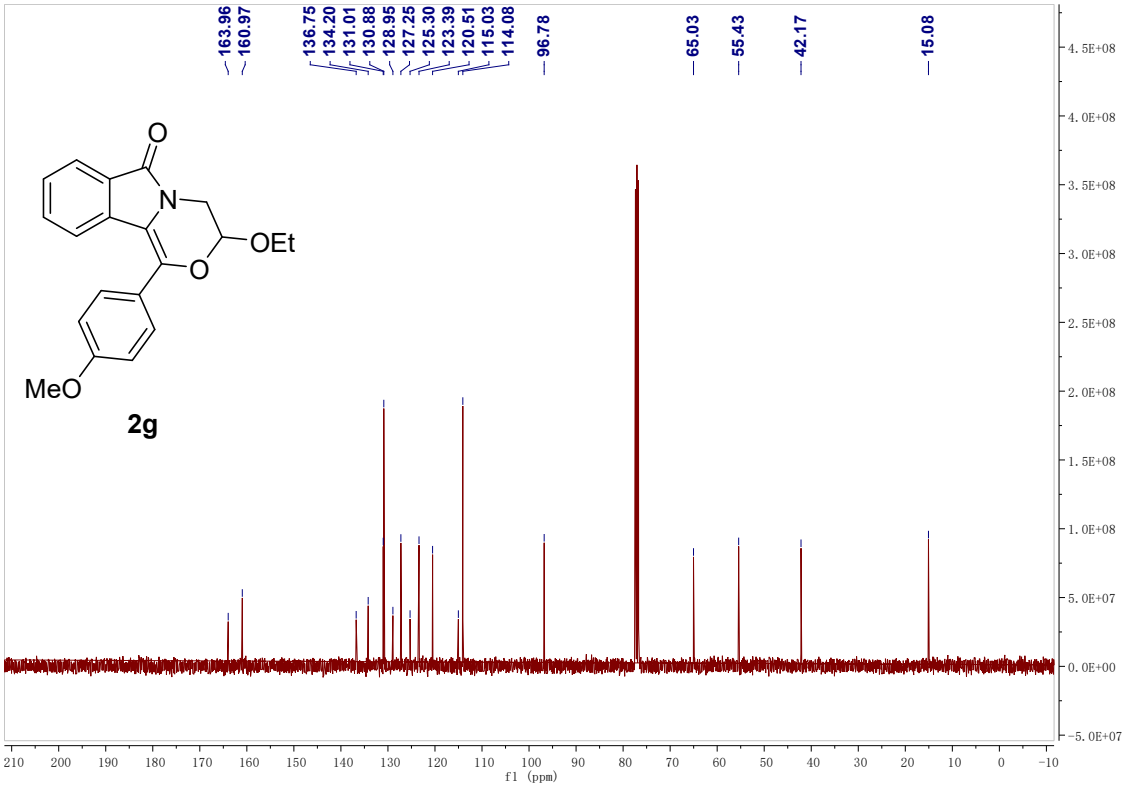

Figure S51. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2g**

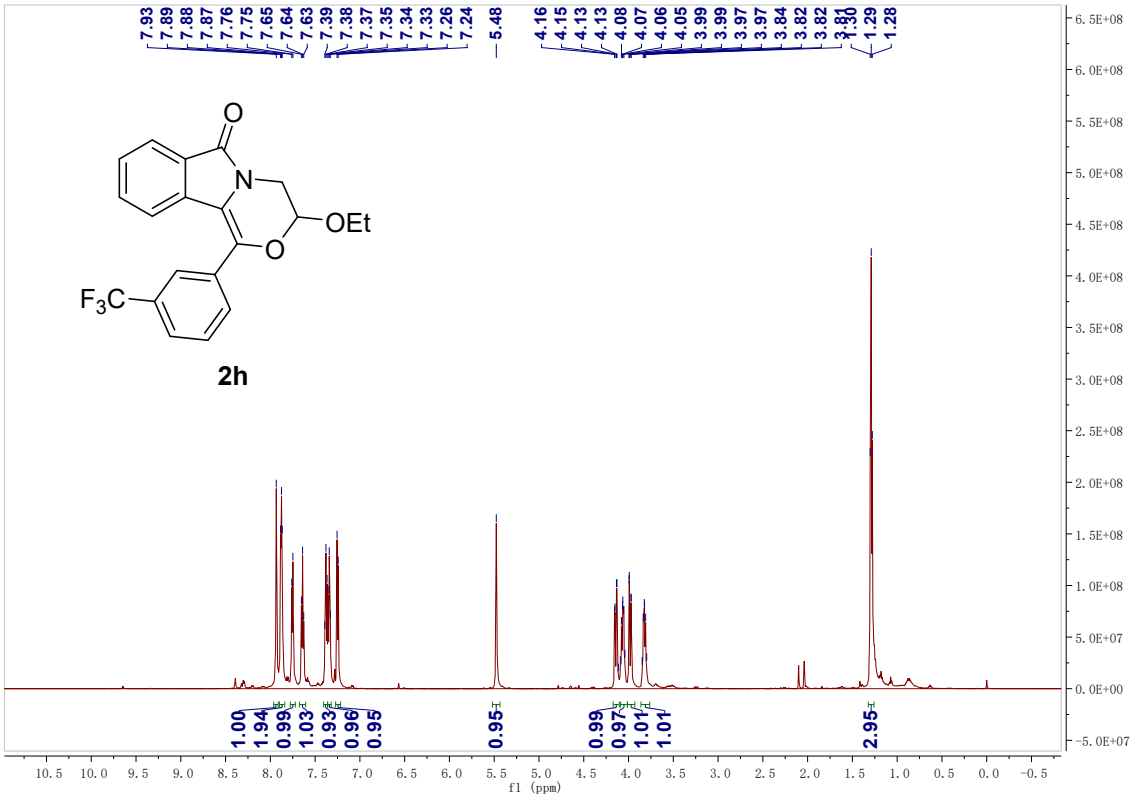

Figure S52. [1]H NMR (600 MHz, Chloroform-*d*) spectrum of compound **2h**

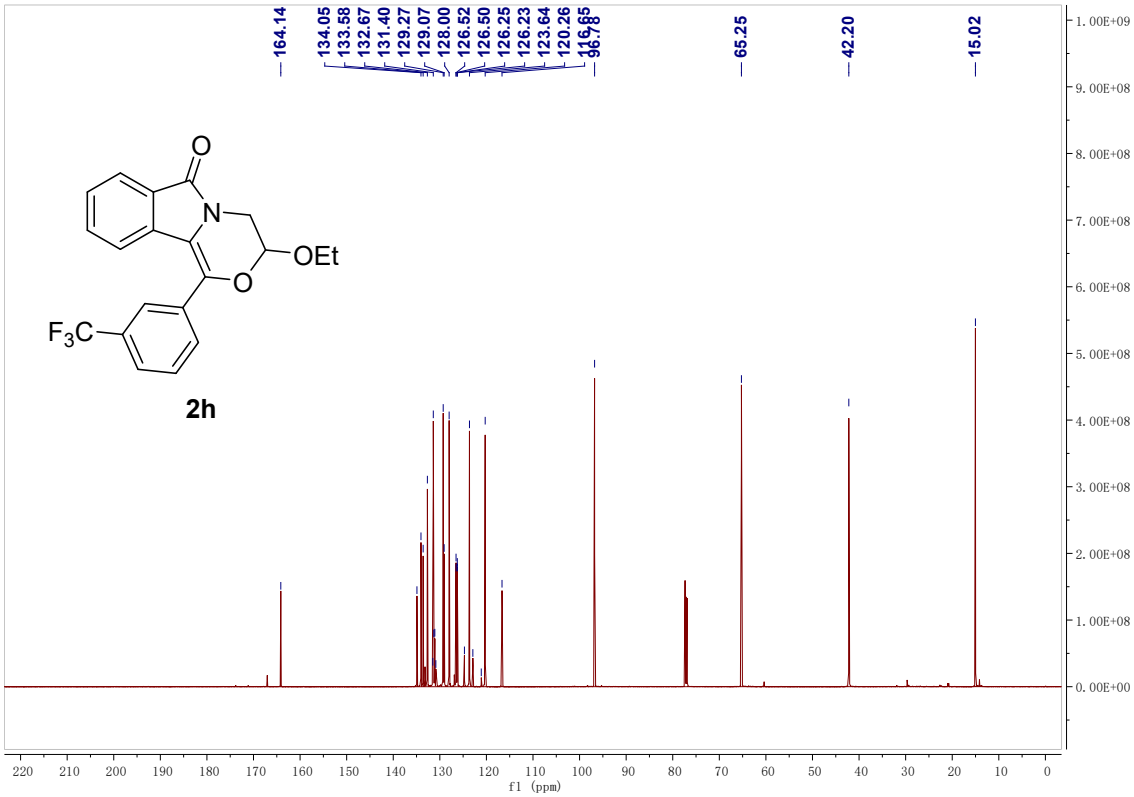

Figure S53. [13]C NMR (151 MHz, Chloroform-*d*) spectrum of compound **2h**

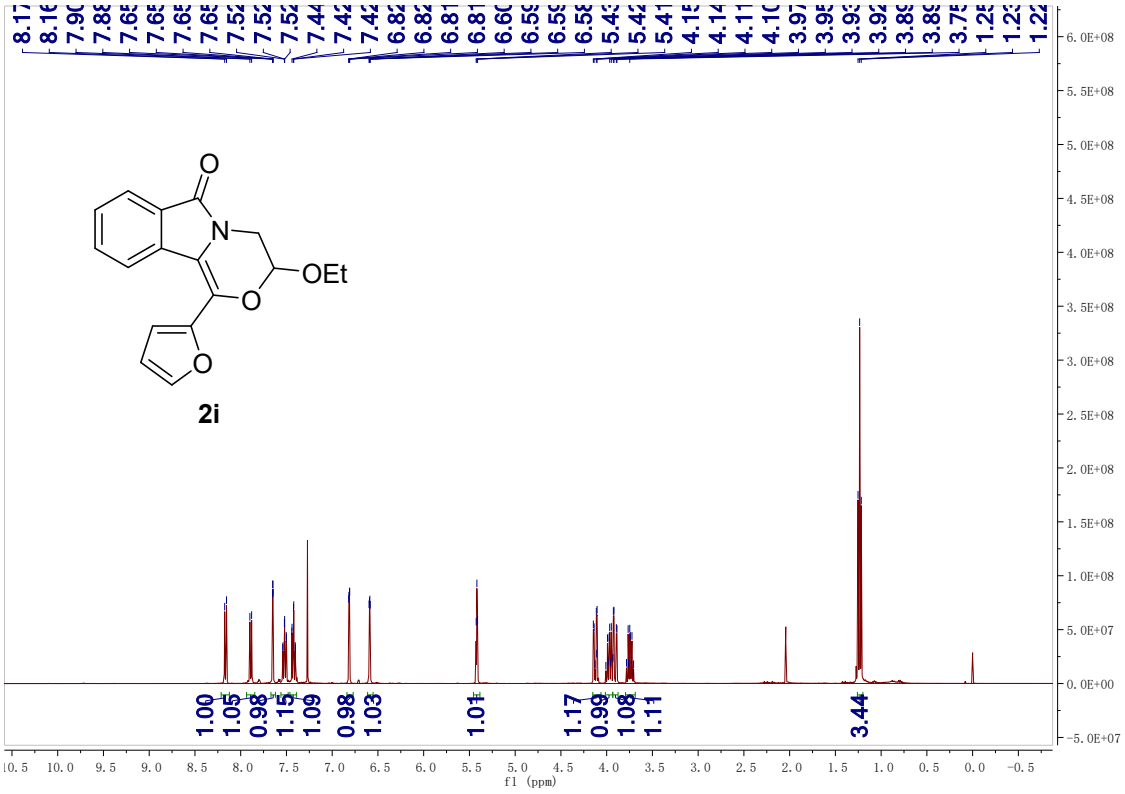

Figure S54. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2i**

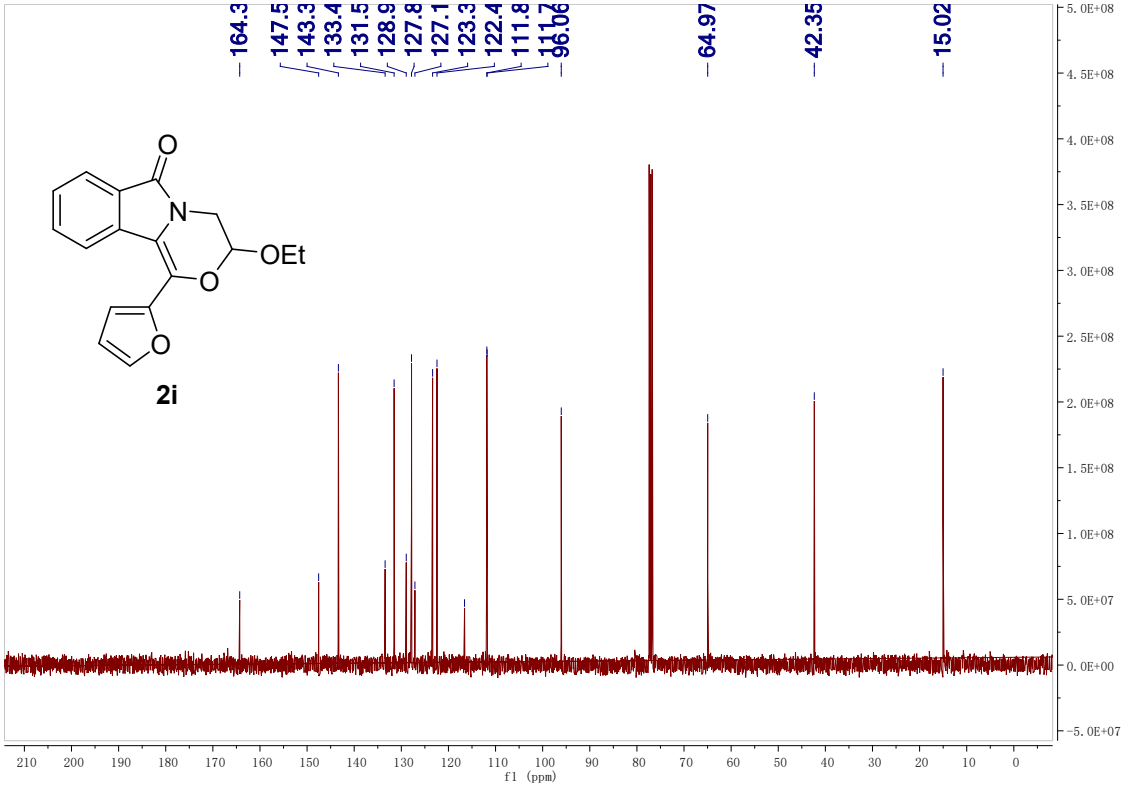

Figure S55. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2i**

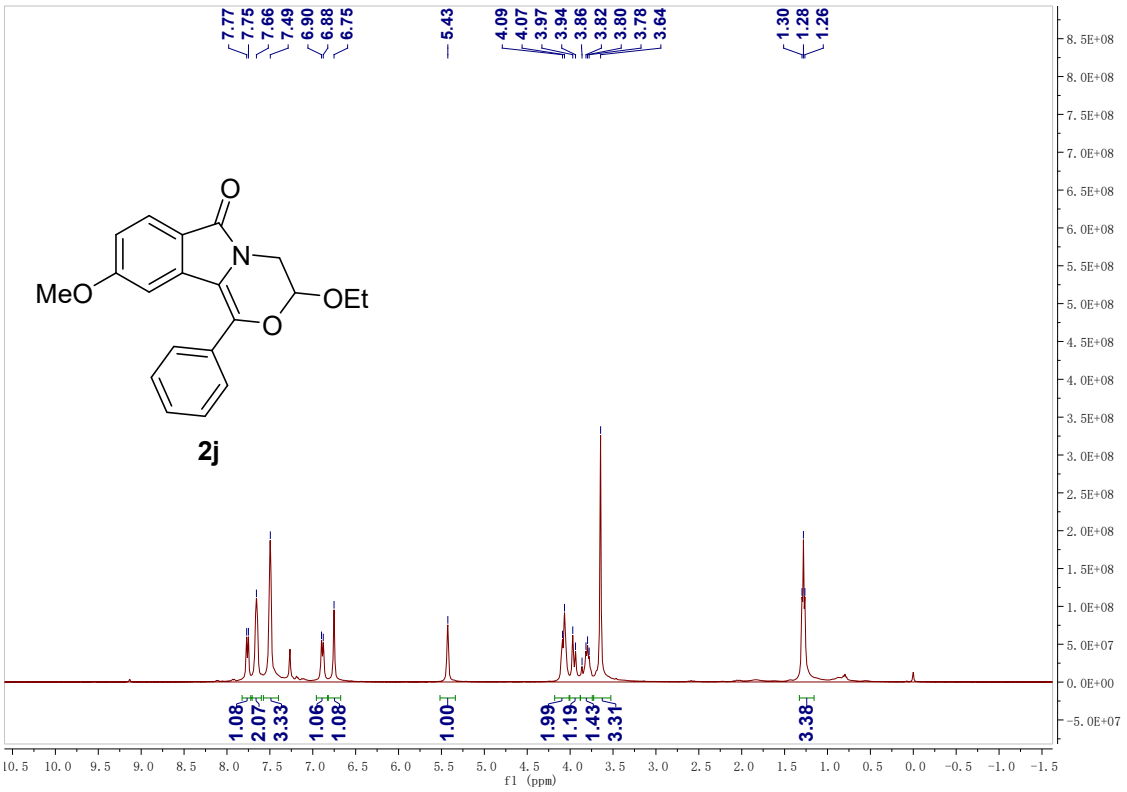

Figure S56. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2j**

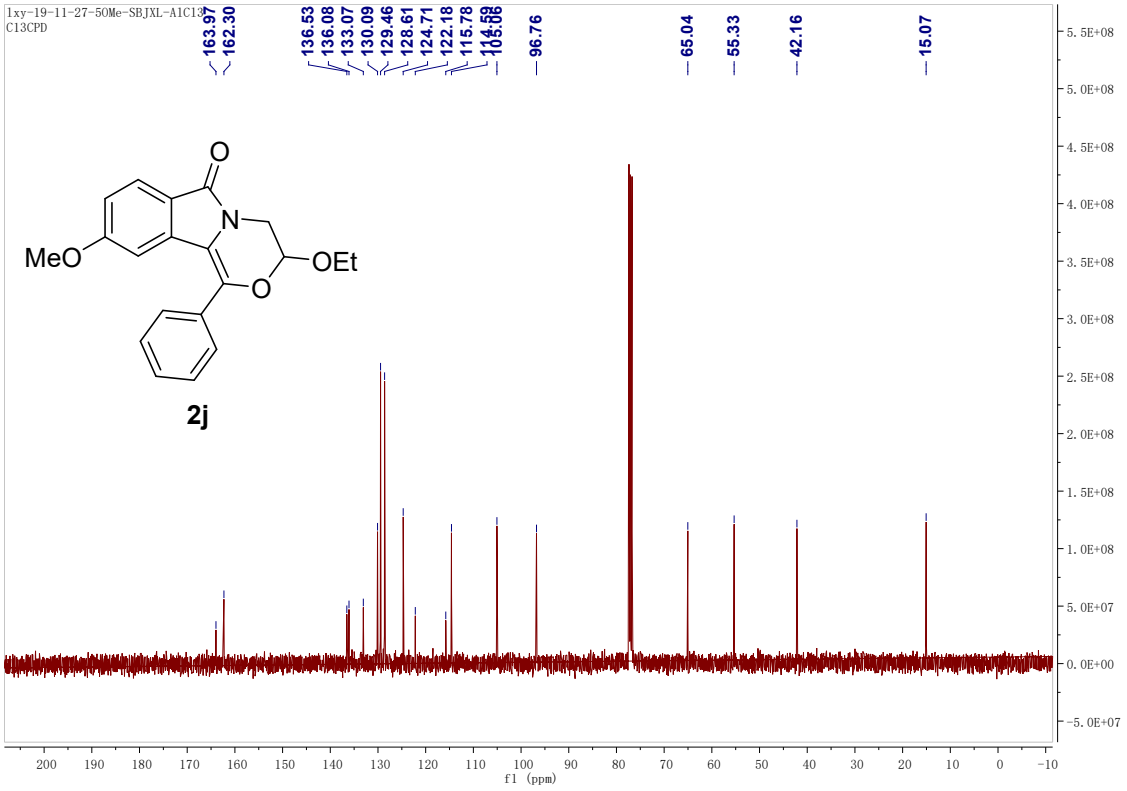

Figure S57. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2j**

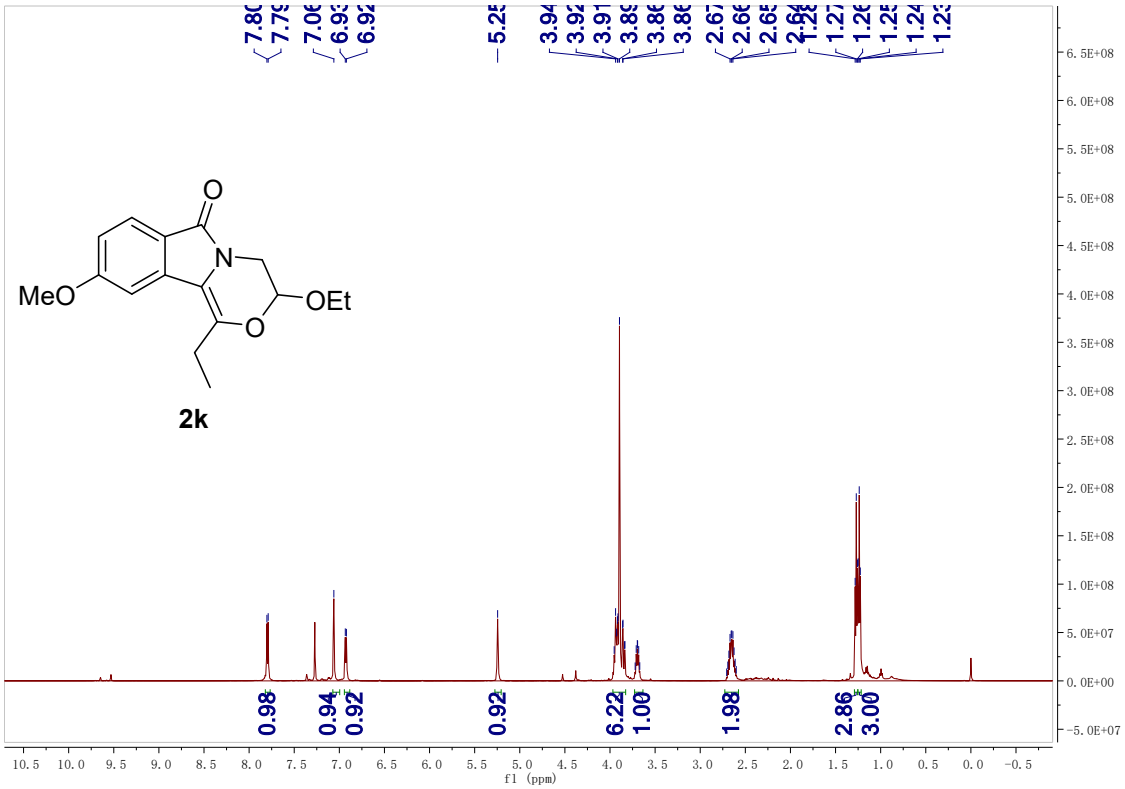

Figure S58. ^{1}H NMR (600 MHz, Chloroform-*d*) spectrum of compound **2k**

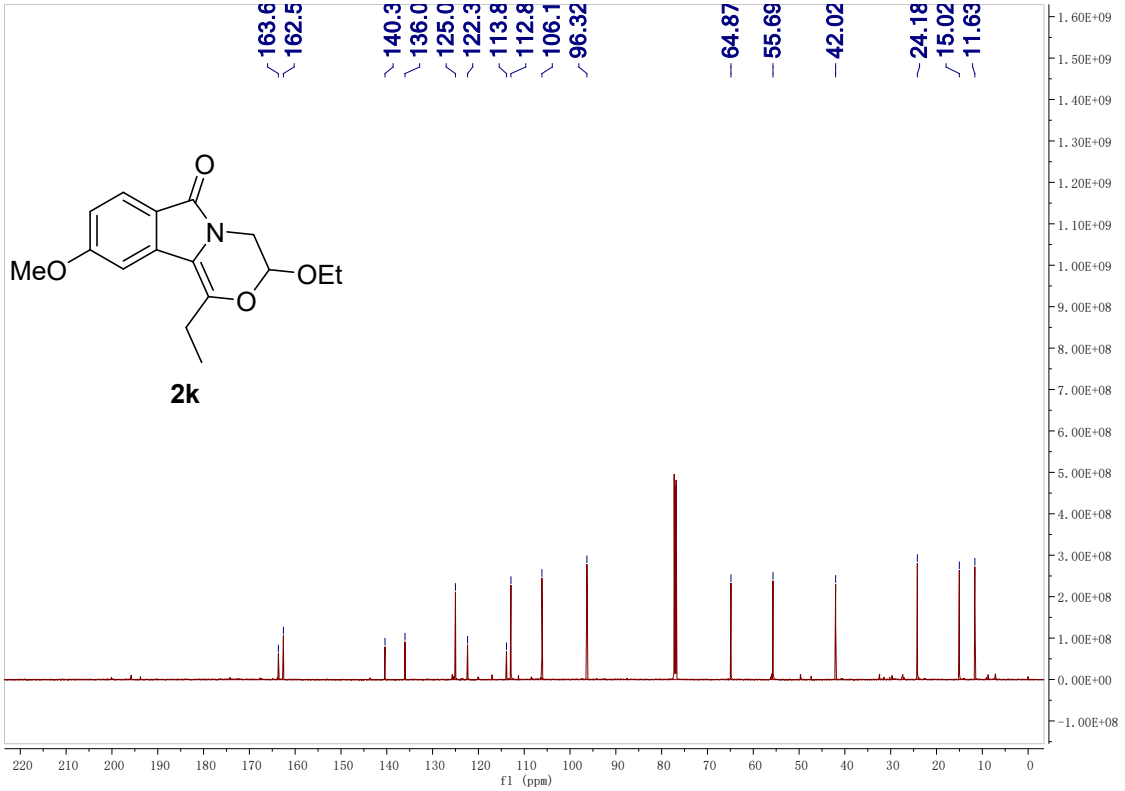

Figure S59. ^{13}C NMR (151 MHz, Chloroform-*d*) spectrum of compound **2k**

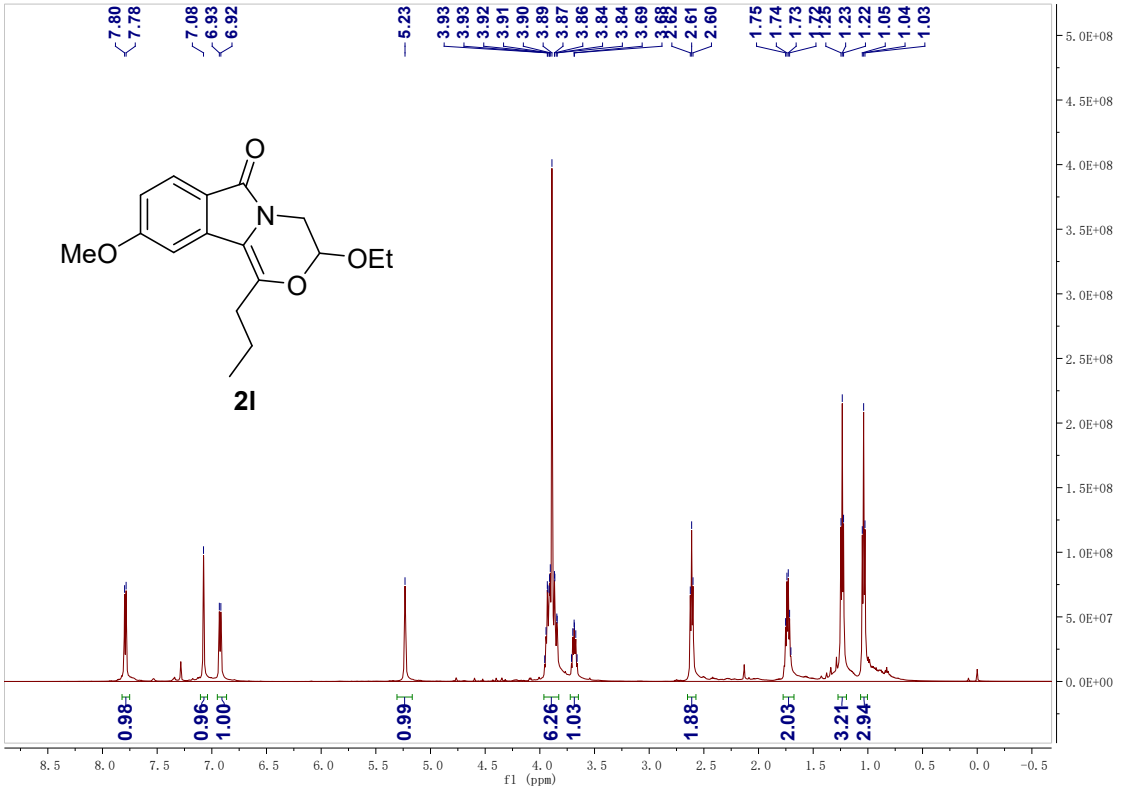

Figure S60. ^{1}H NMR (600 MHz, Chloroform-*d*) spectrum of compound **2l**

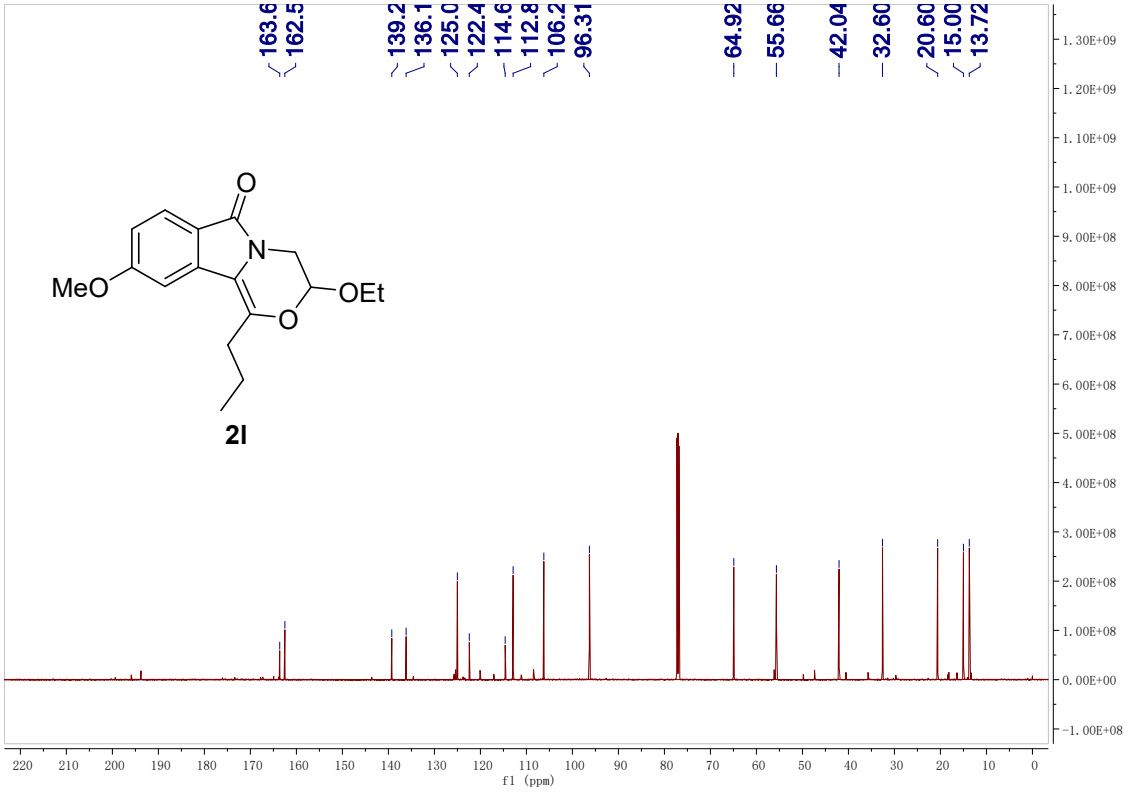

Figure S61. ^{13}C NMR (151 MHz, Chloroform-*d*) spectrum of compound **2l**

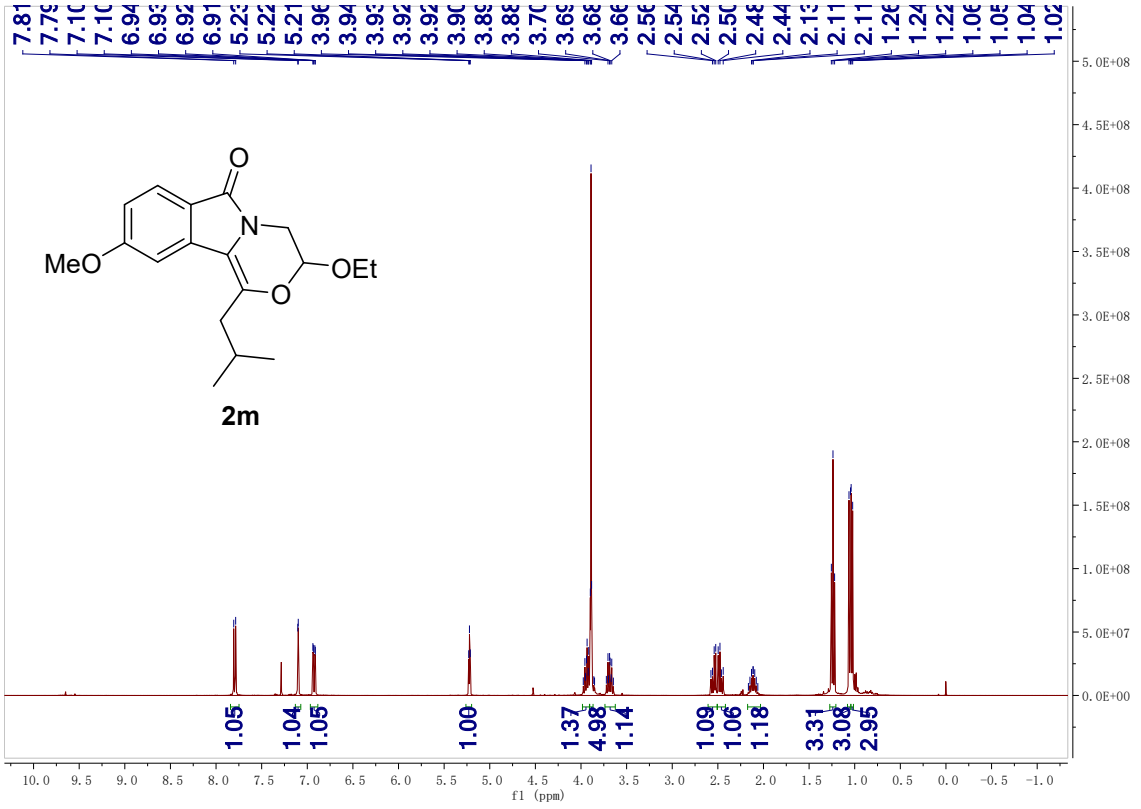

Figure S62. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2m**

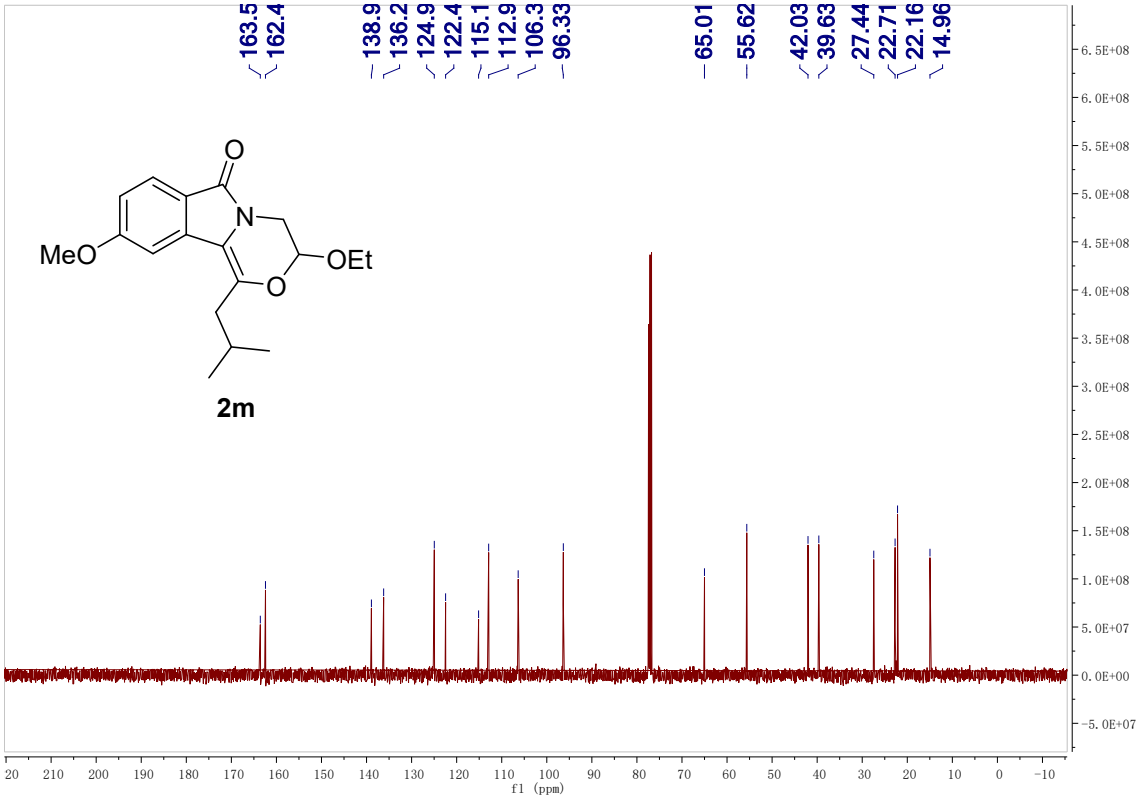

Figure S63. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2m**

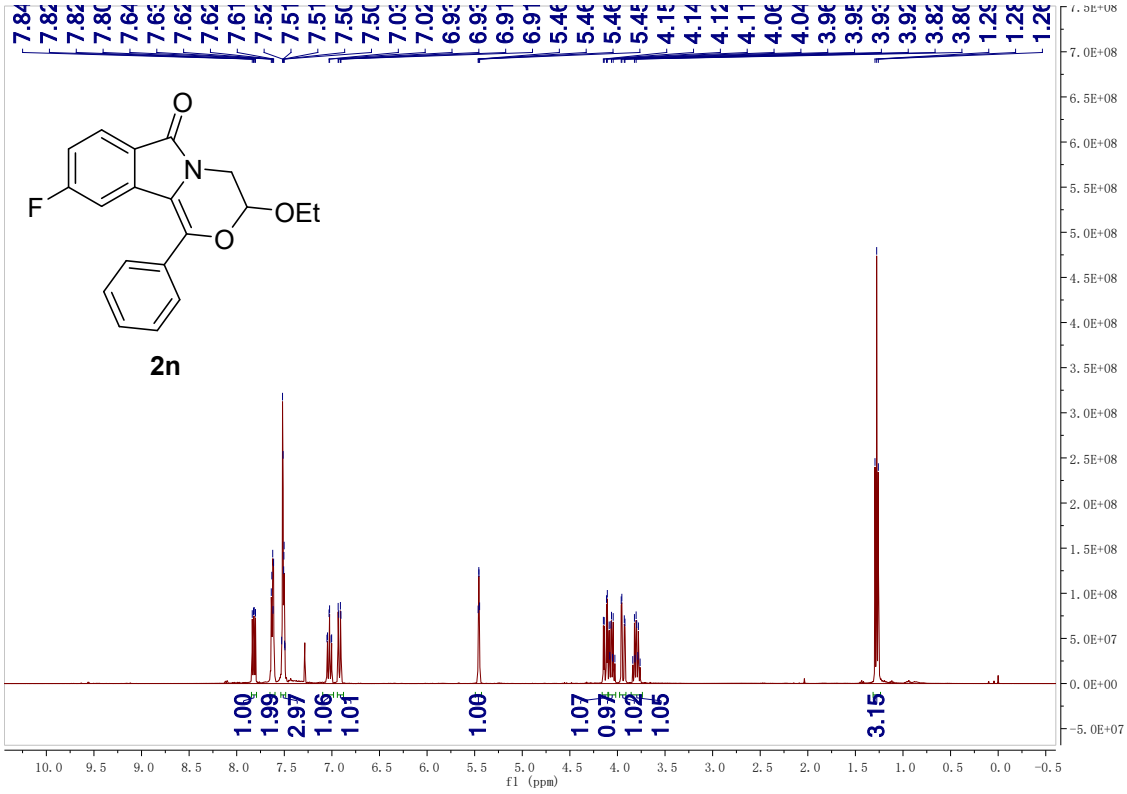

Figure S64. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2n**

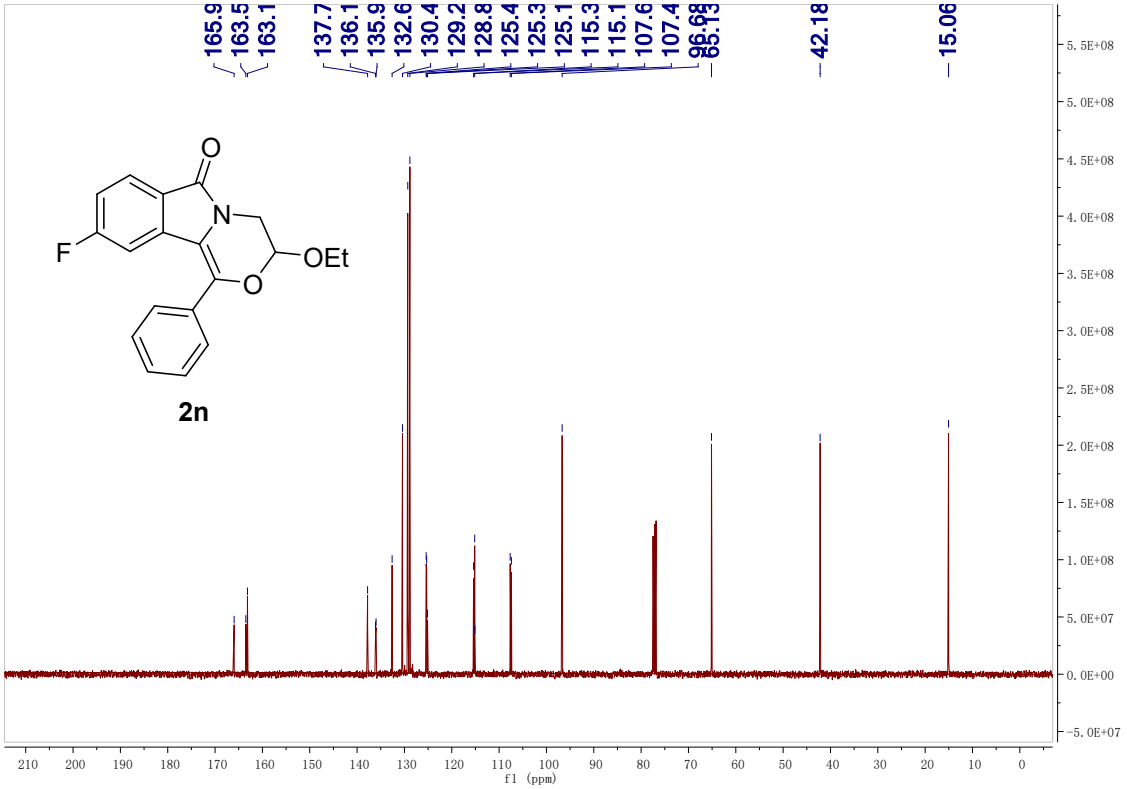

Figure S65. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2n**

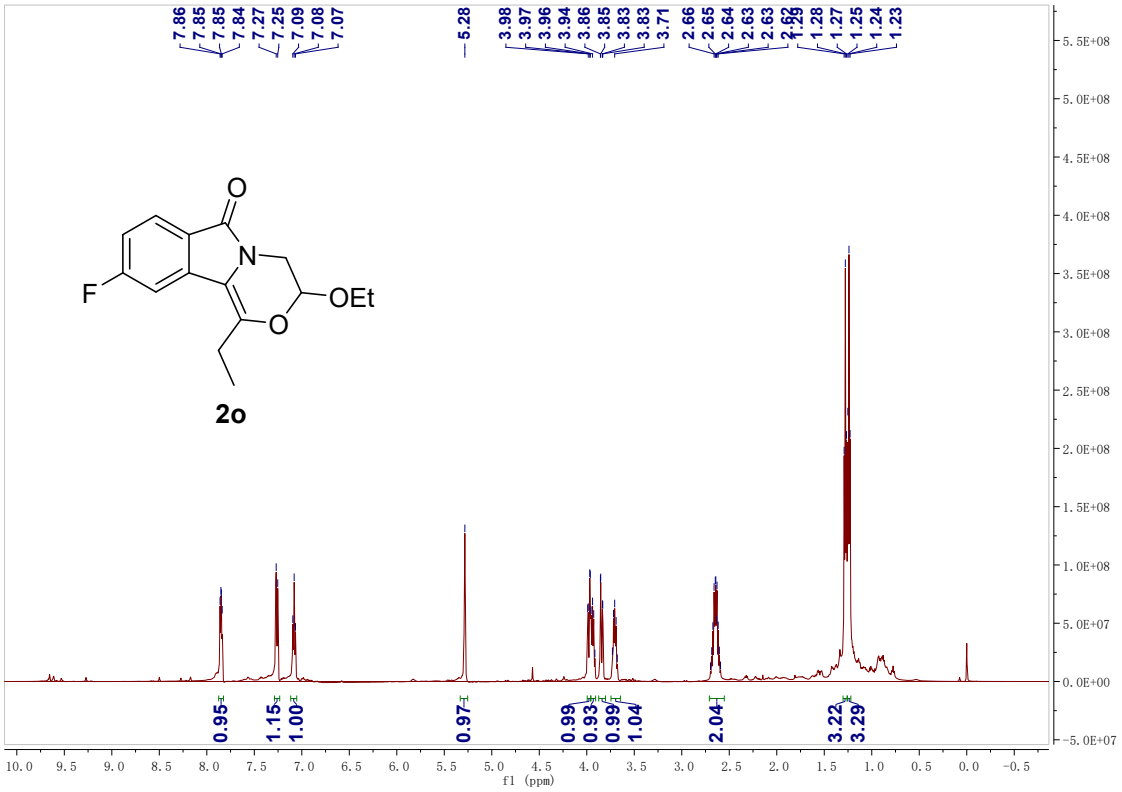

Figure S66. ^{1}H NMR (600 MHz, Chloroform-*d*) spectrum of compound **2o**

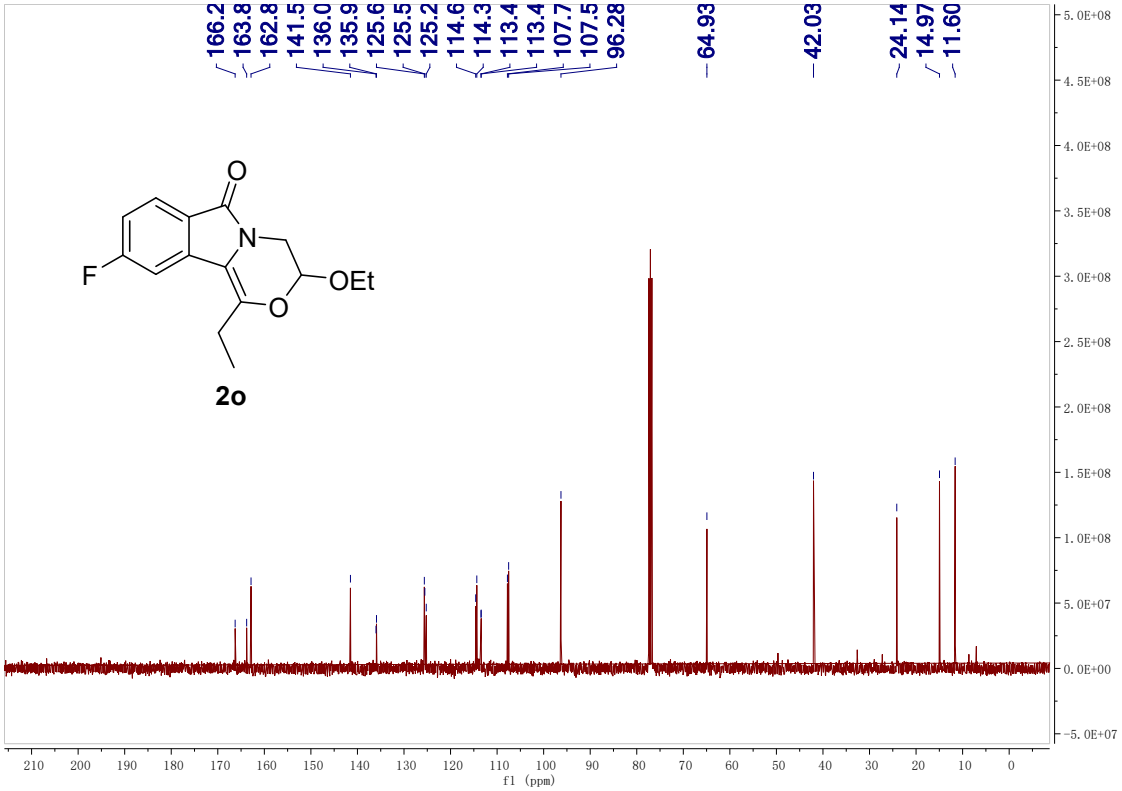

Figure S67. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2o**

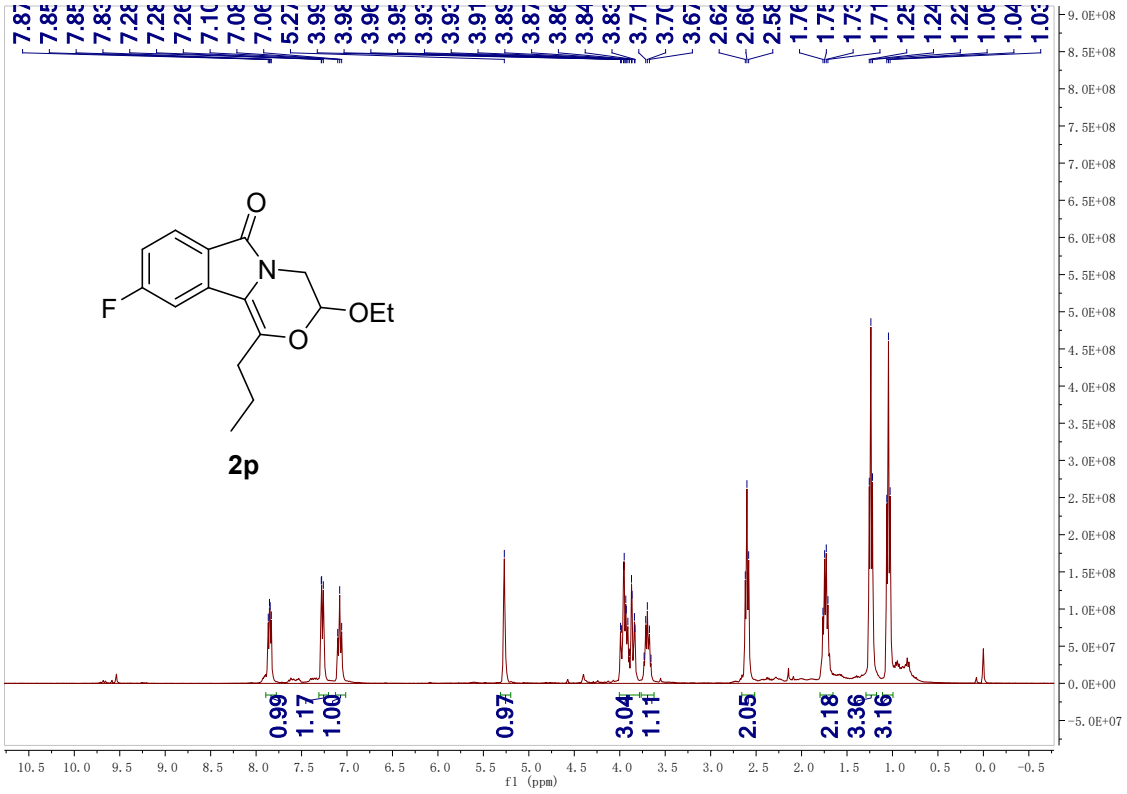

Figure S68. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2p**

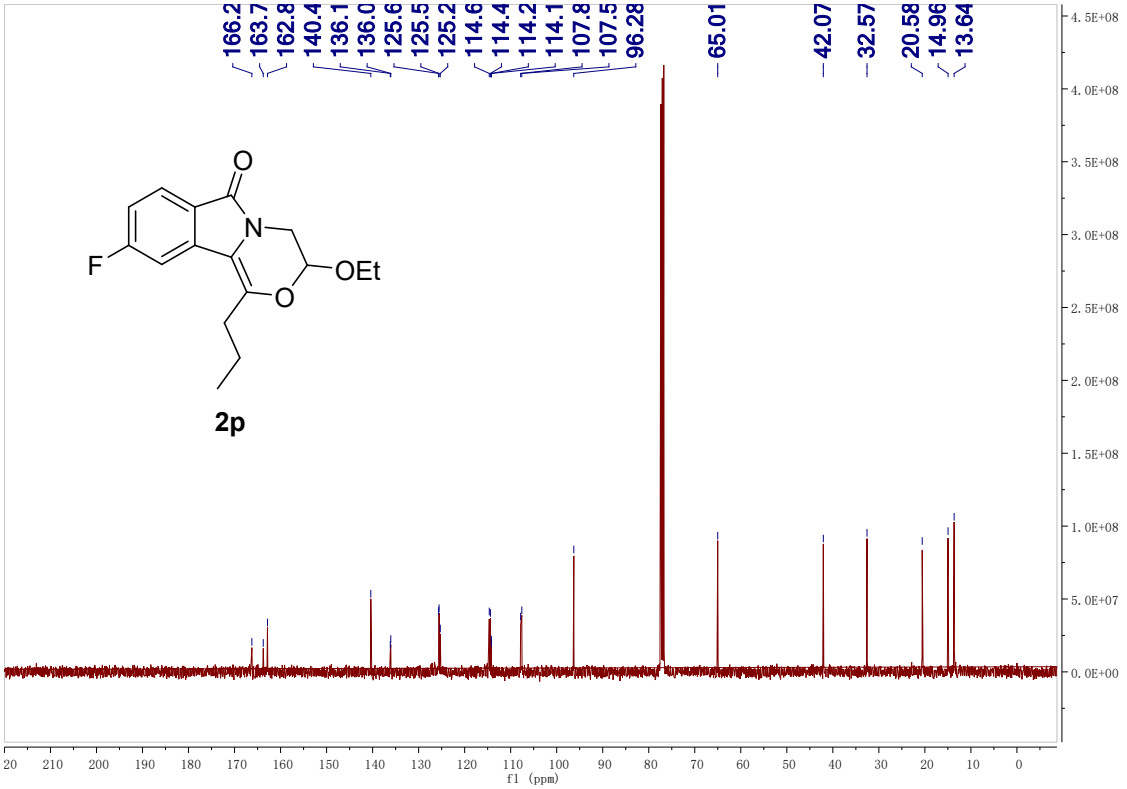

Figure S69. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2p**

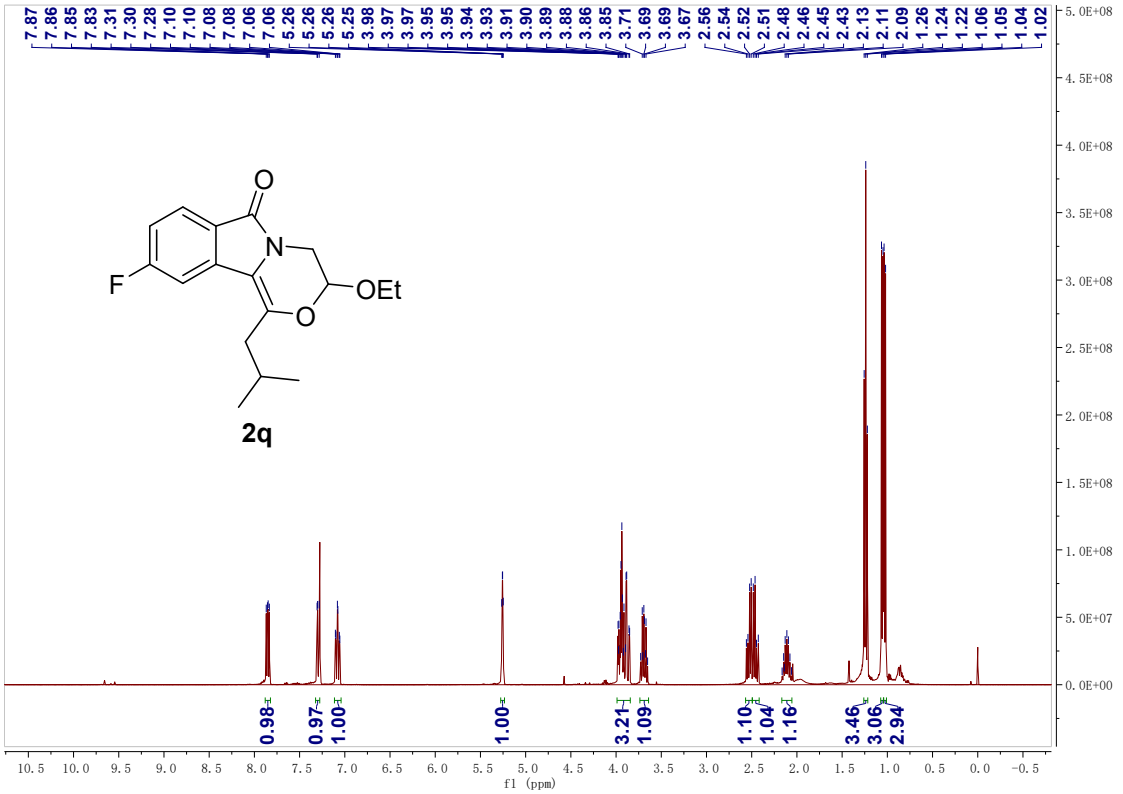

Figure S70. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **2q**

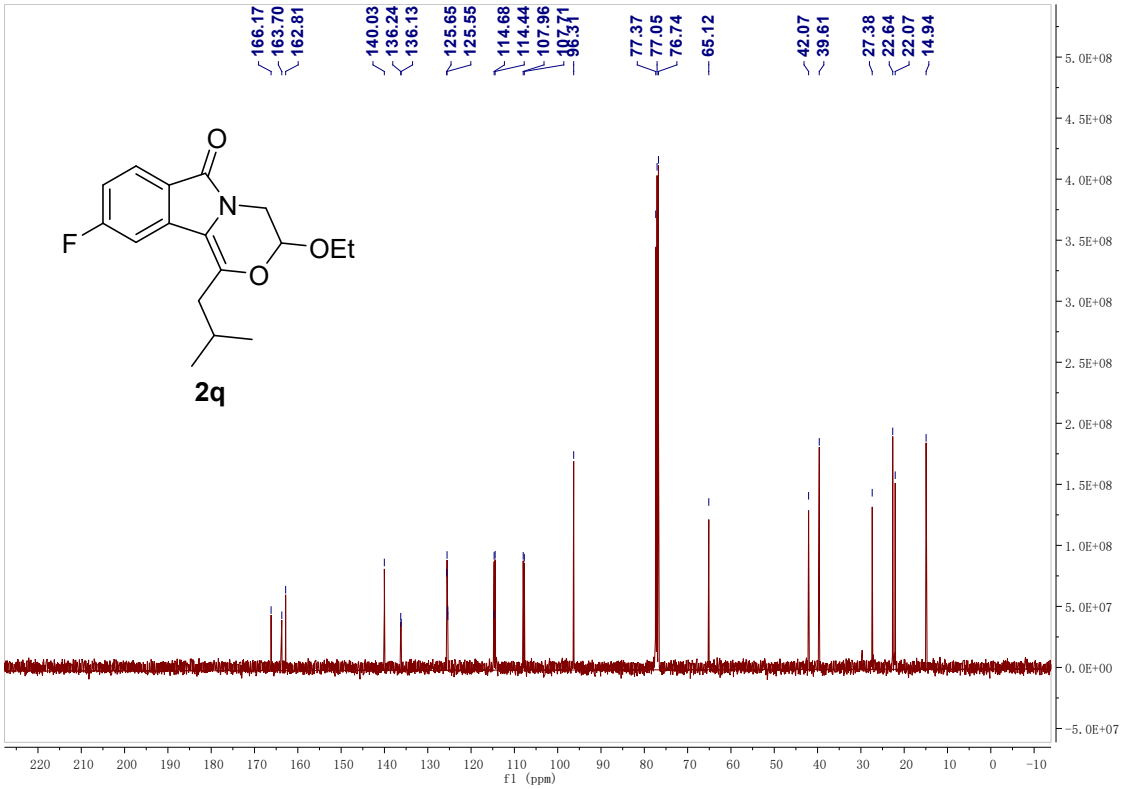

Figure S71. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **2q**

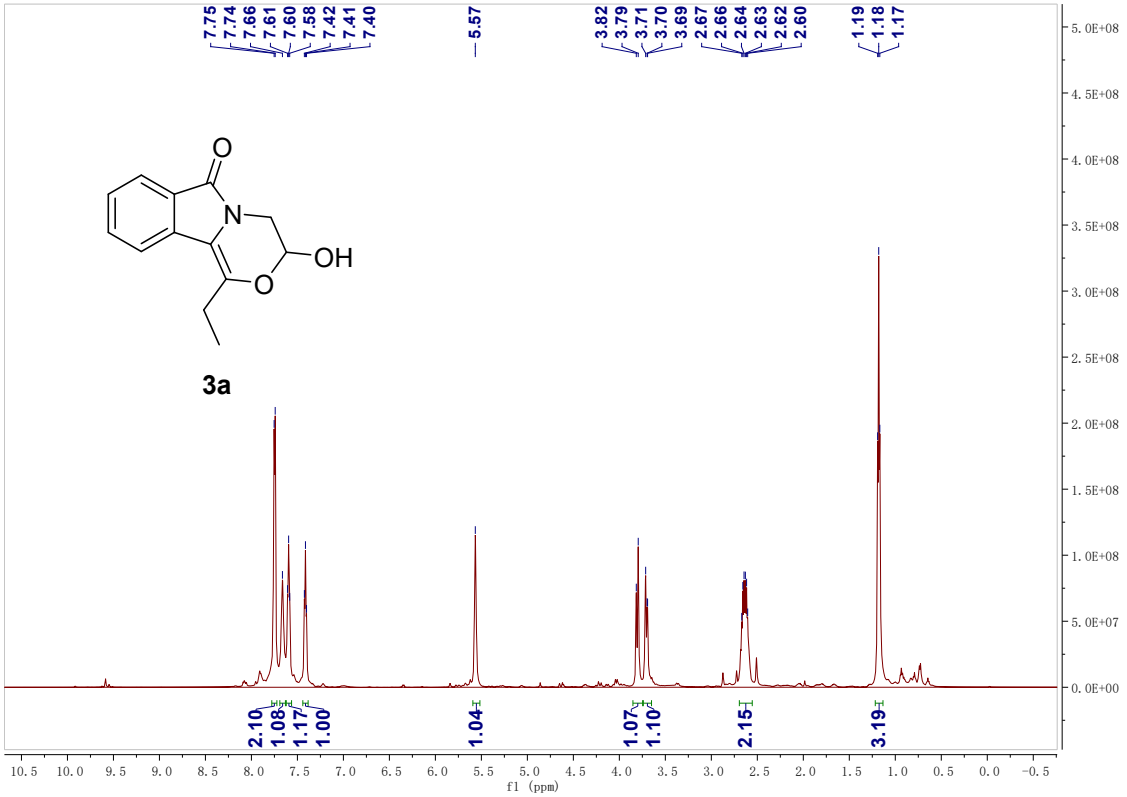

Figure S72. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **3a**

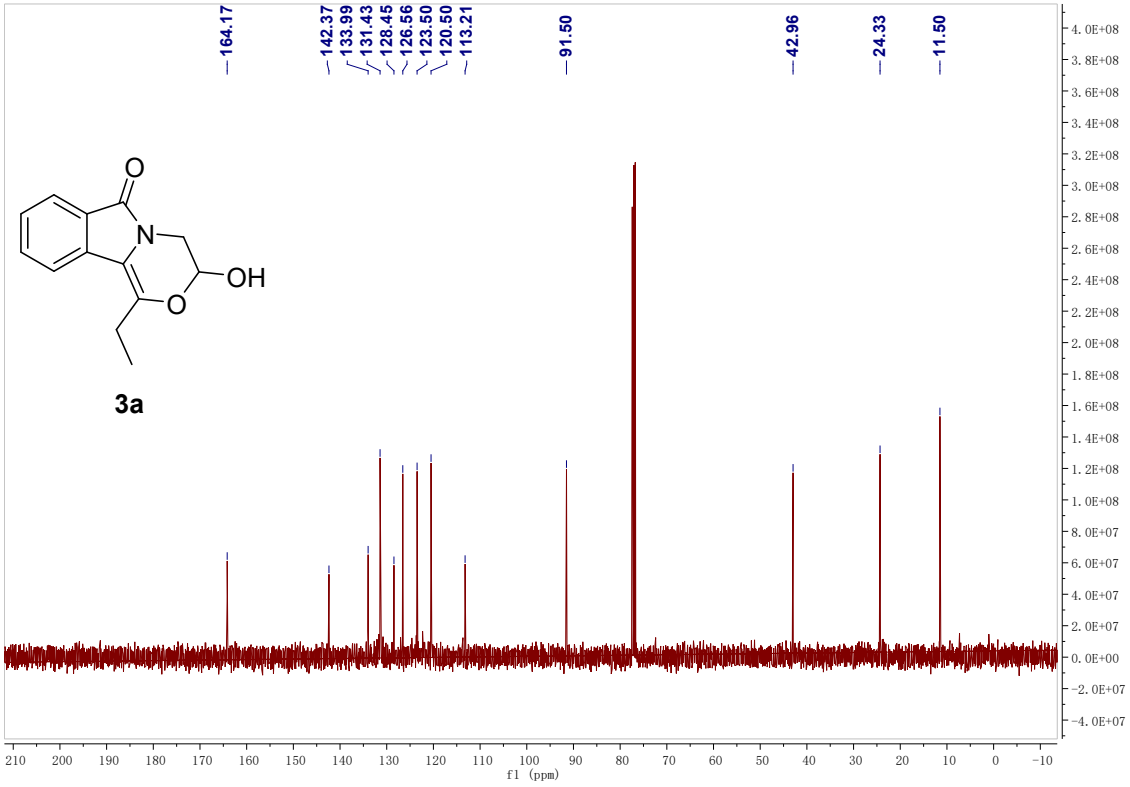

Figure S73. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **3a**

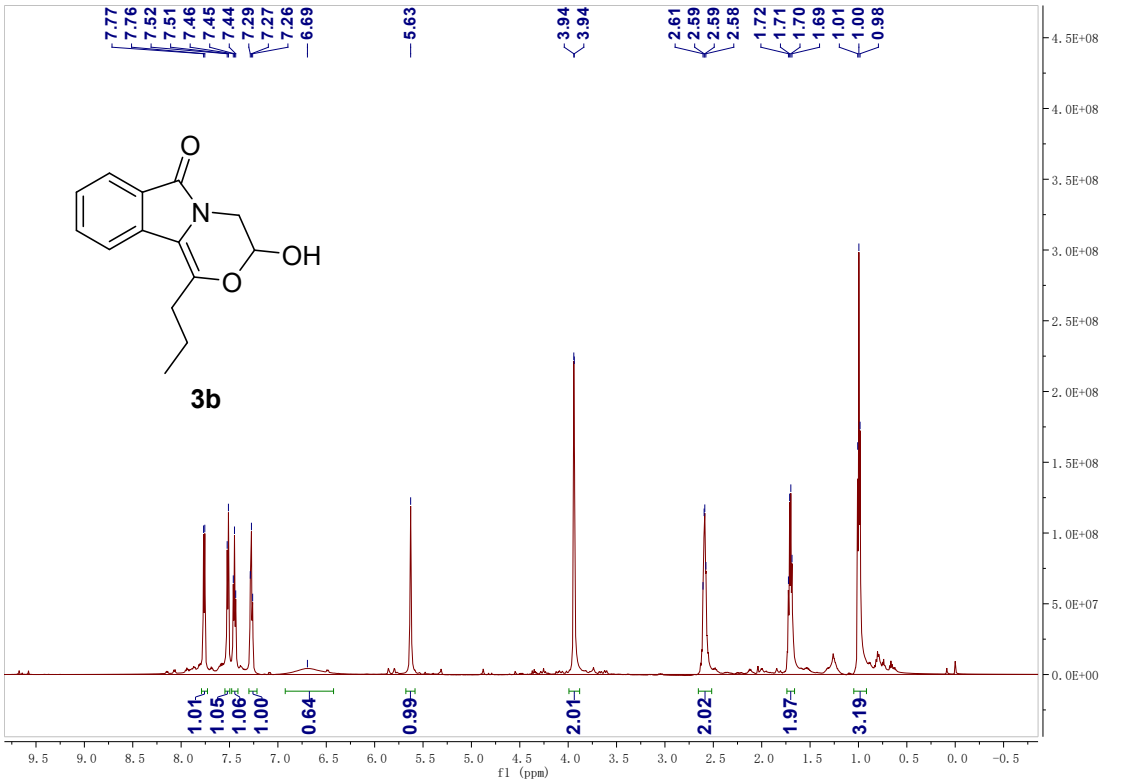

Figure S74. ^{1}H NMR (600 MHz, Chloroform-*d*) spectrum of compound **3b**

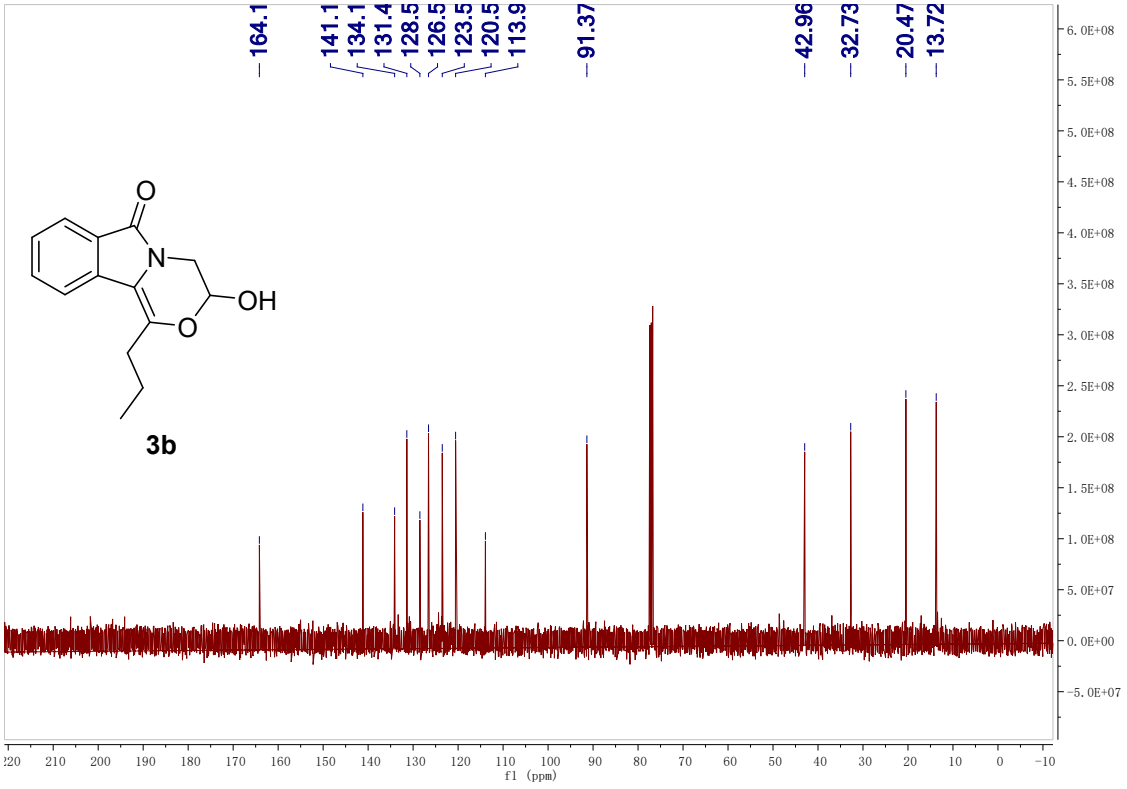

Figure S75. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **3b**

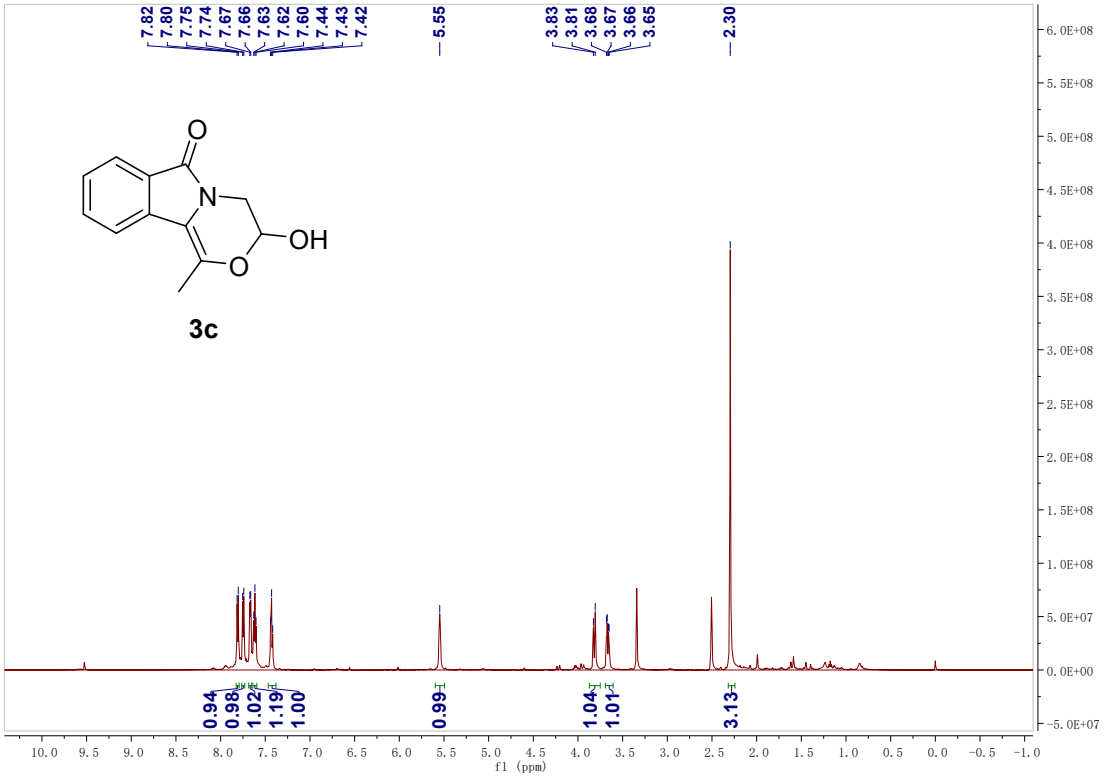

Figure S76. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **3c**

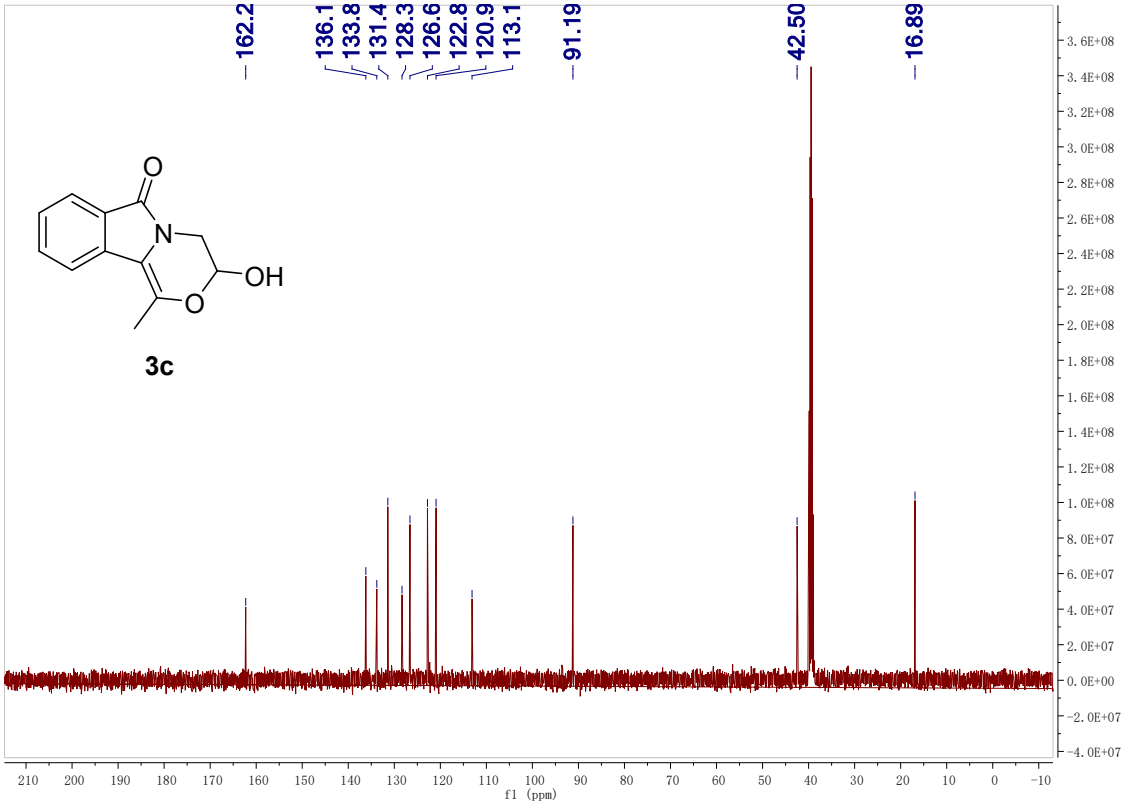

Figure S77. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3c**

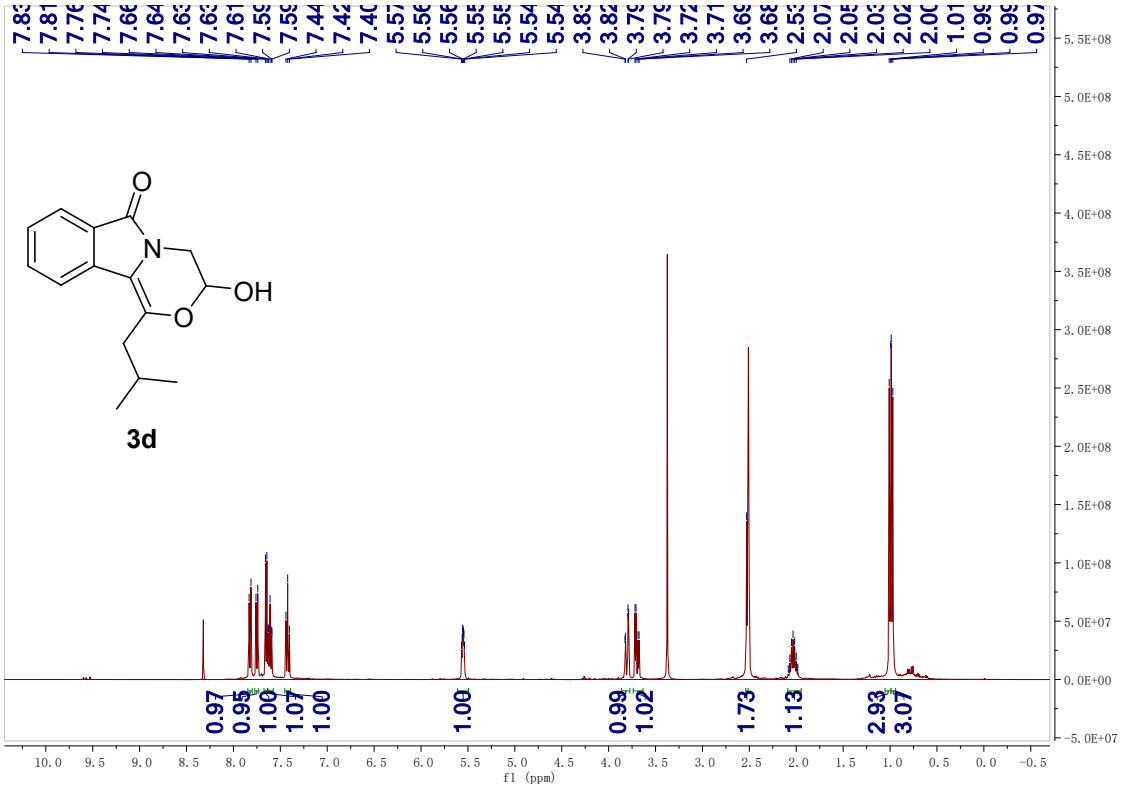

Figure S78. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **3d**

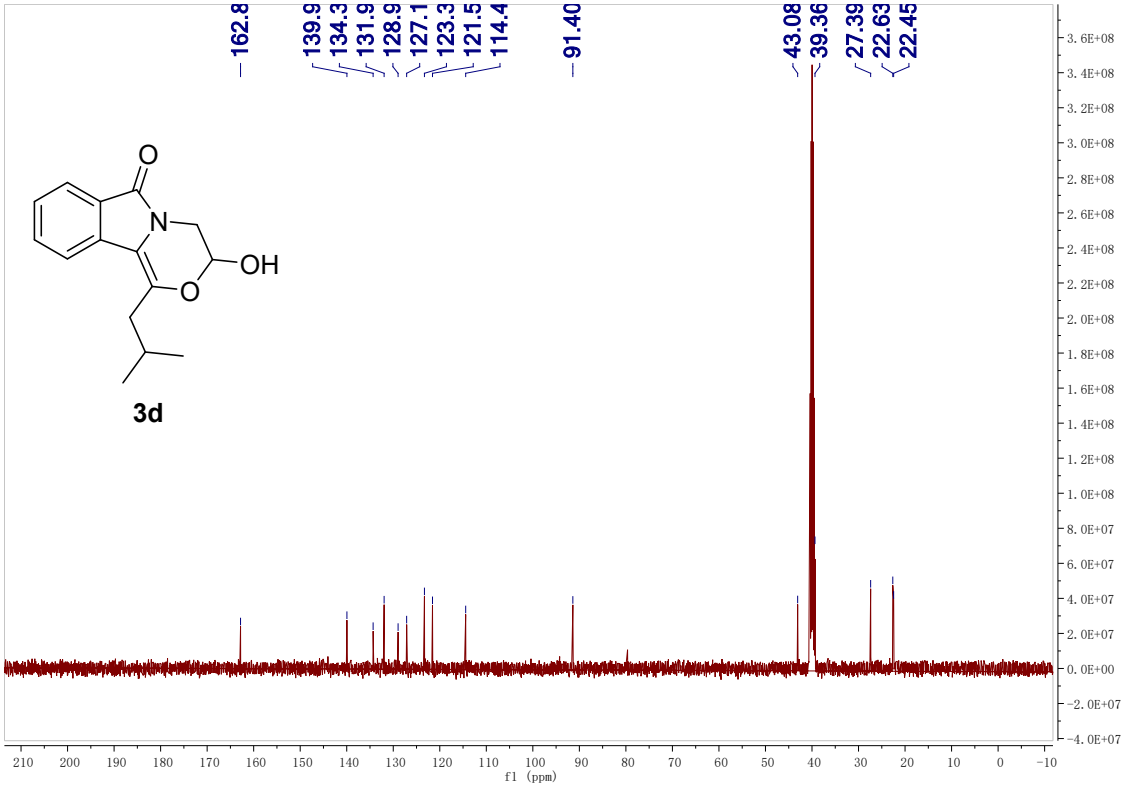

Figure S79. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3d**

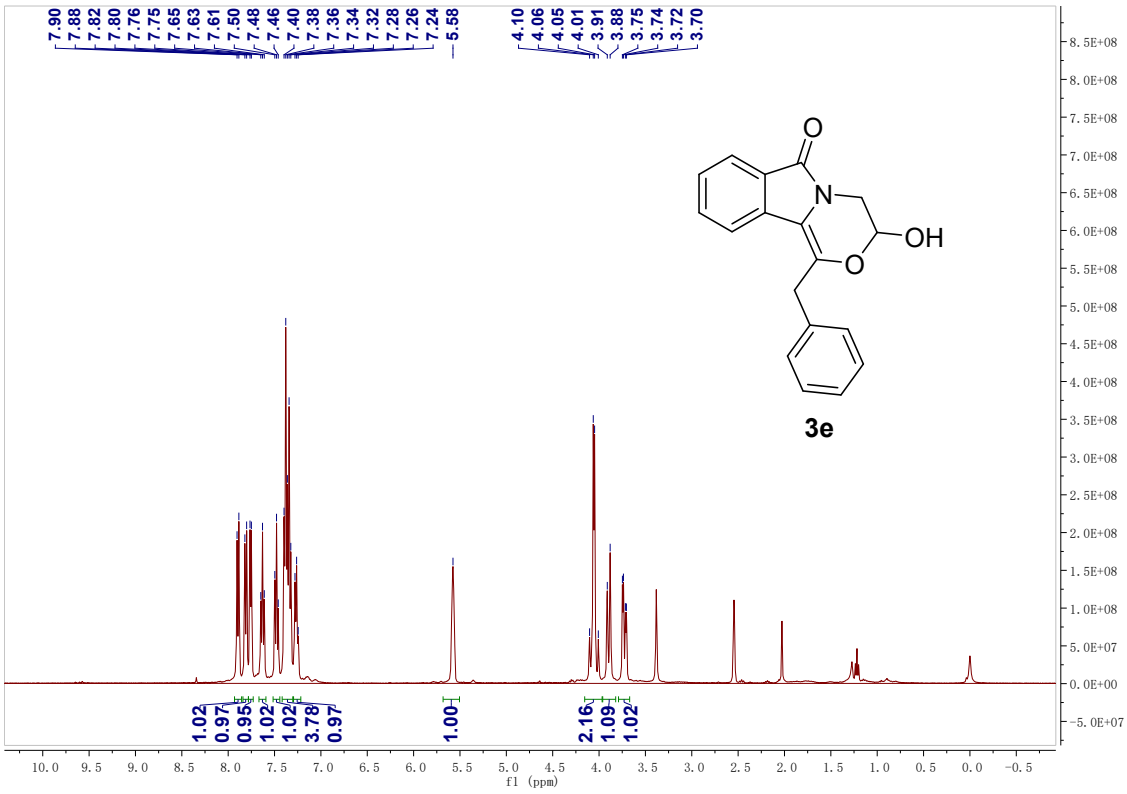

Figure S80. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **3e**

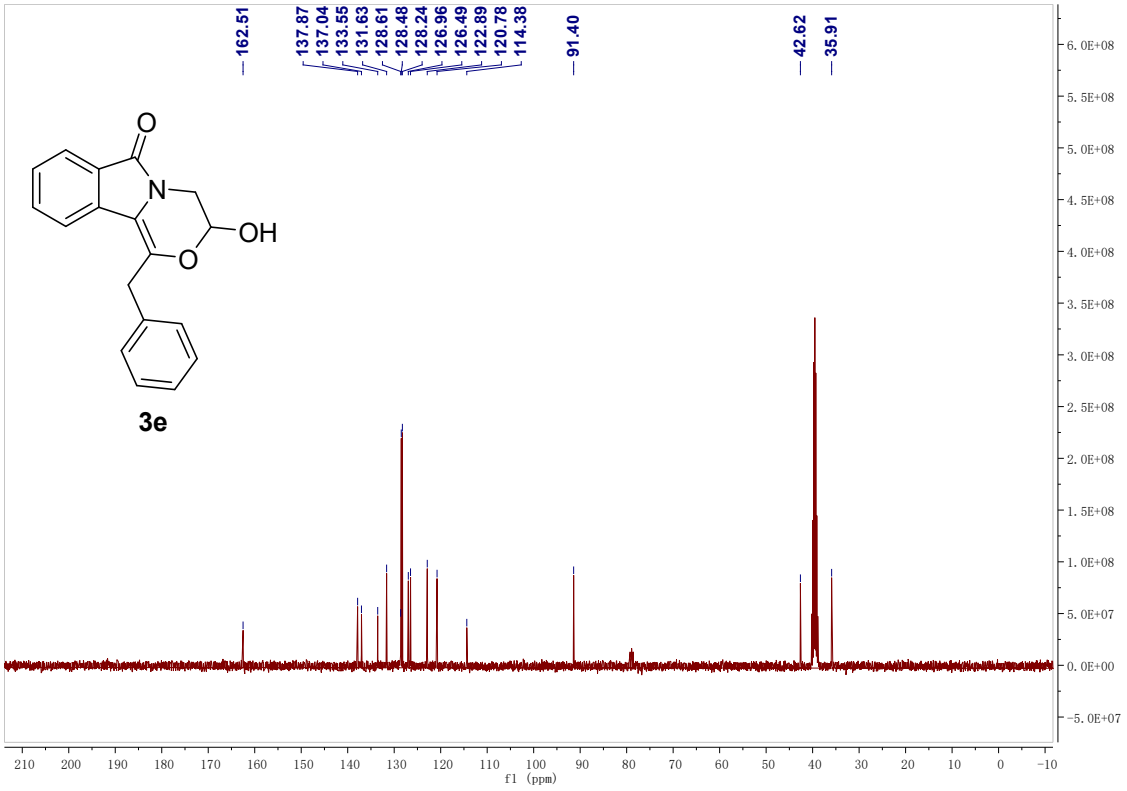

Figure S81. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3e**

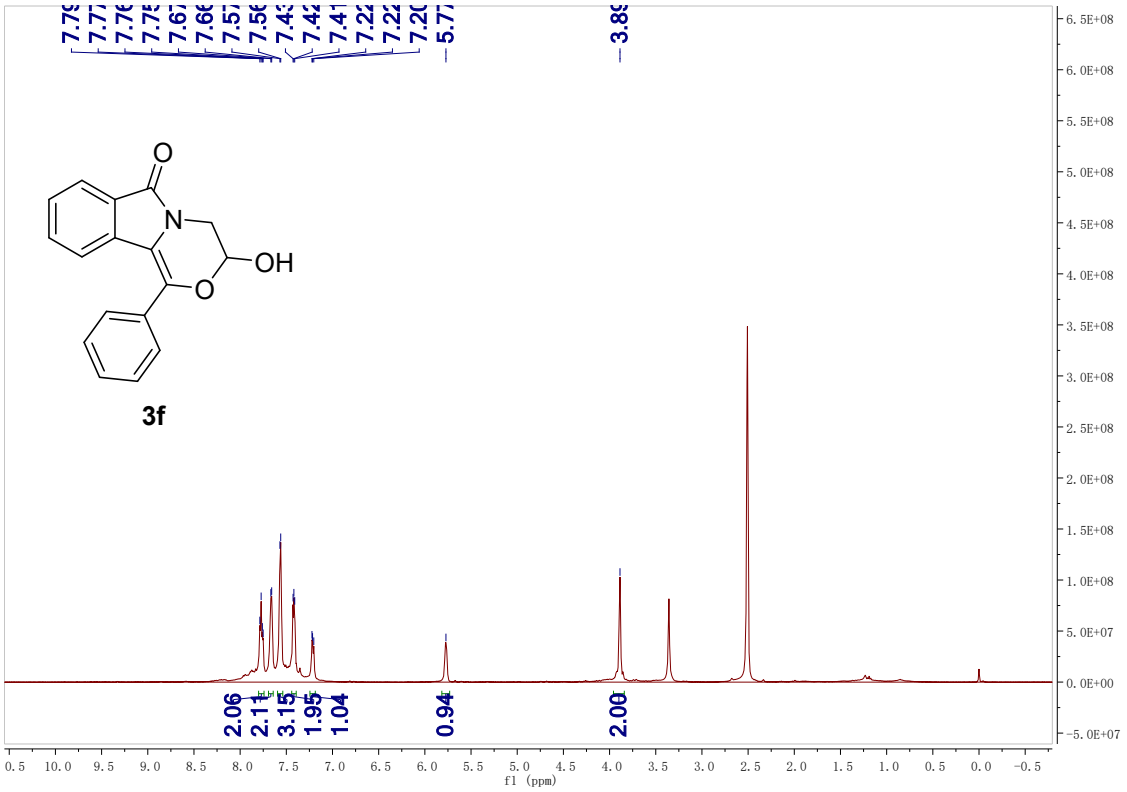

Figure S82. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **3f**

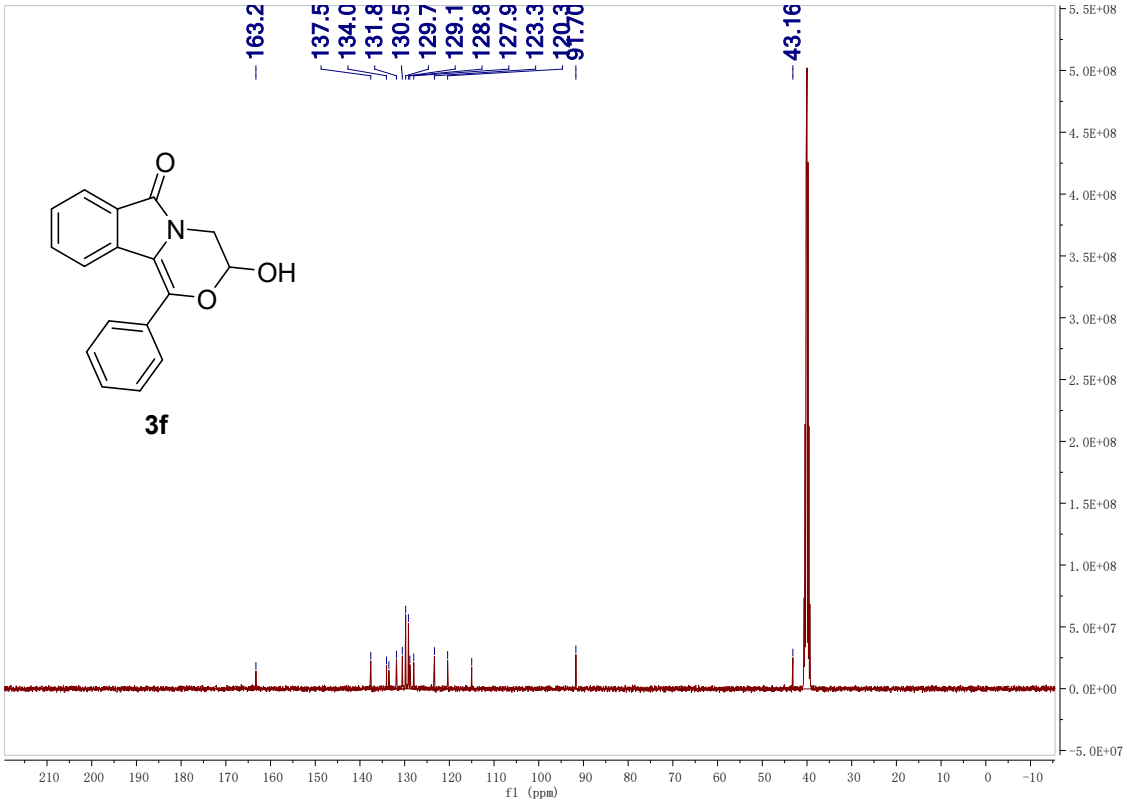

Figure S83. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3f**

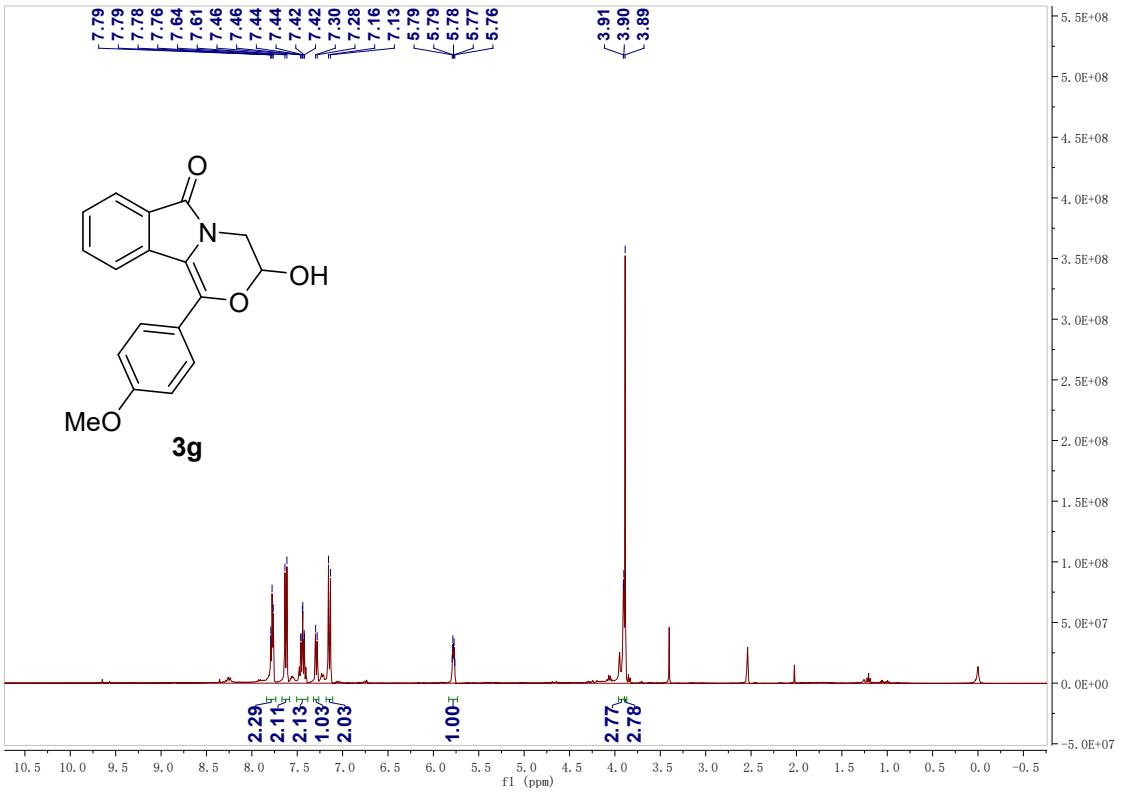

Figure S84. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **3g**

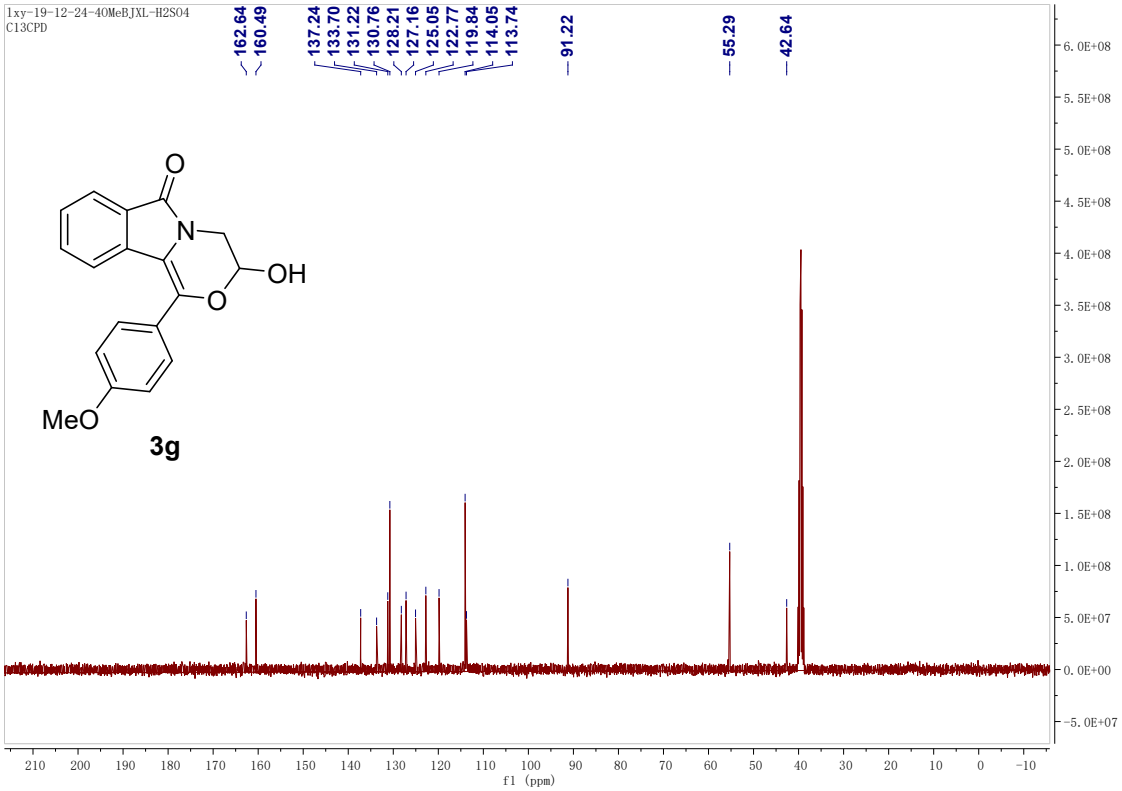

Figure S85. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3g**

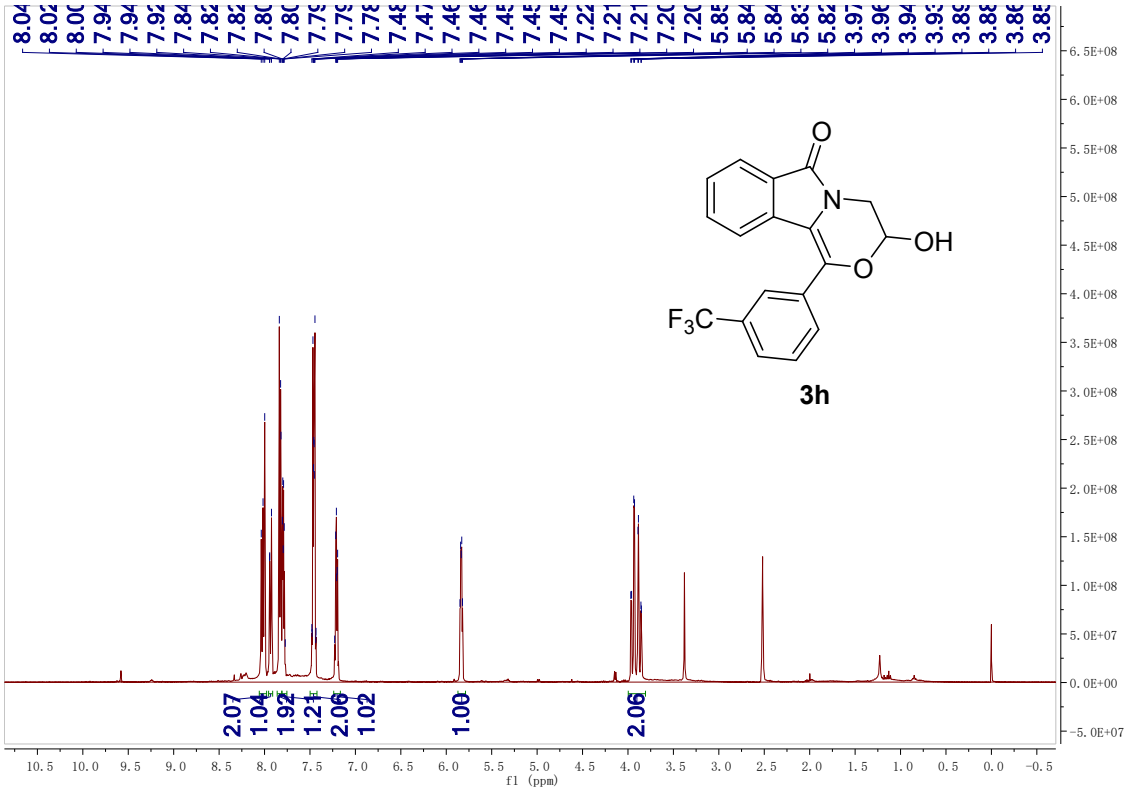

Figure S86. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **3h**

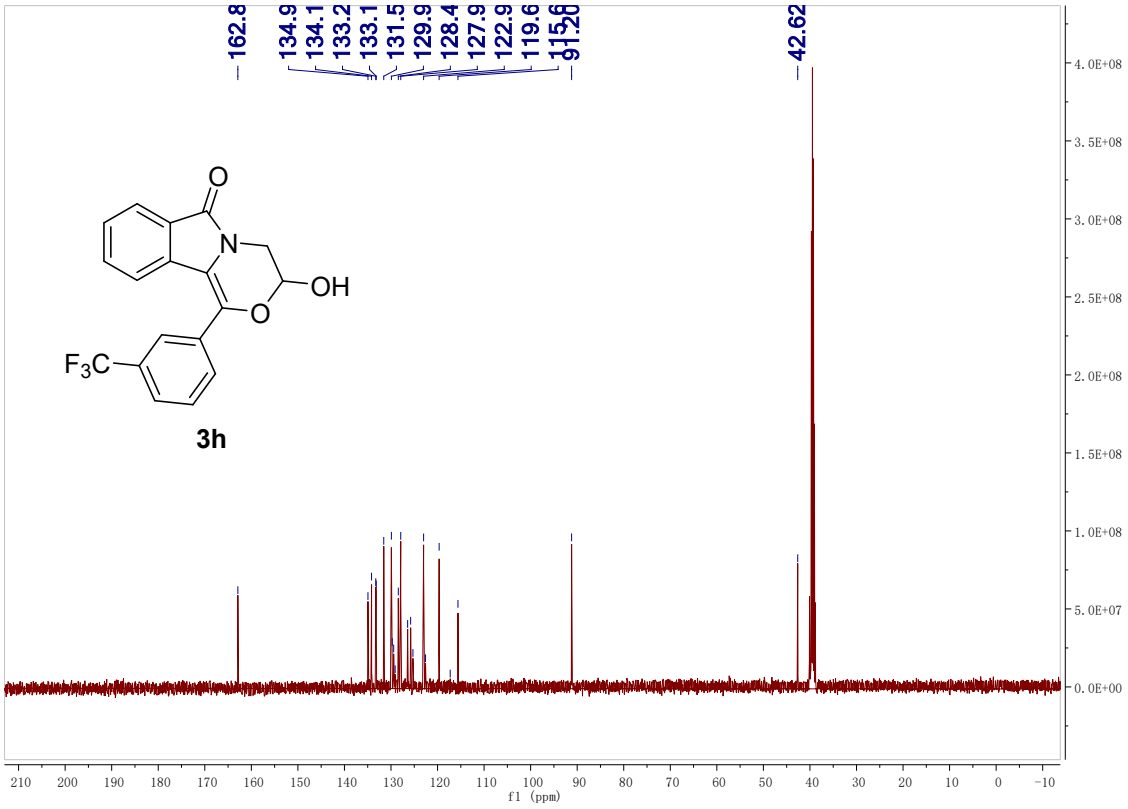

Figure S87. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3h**

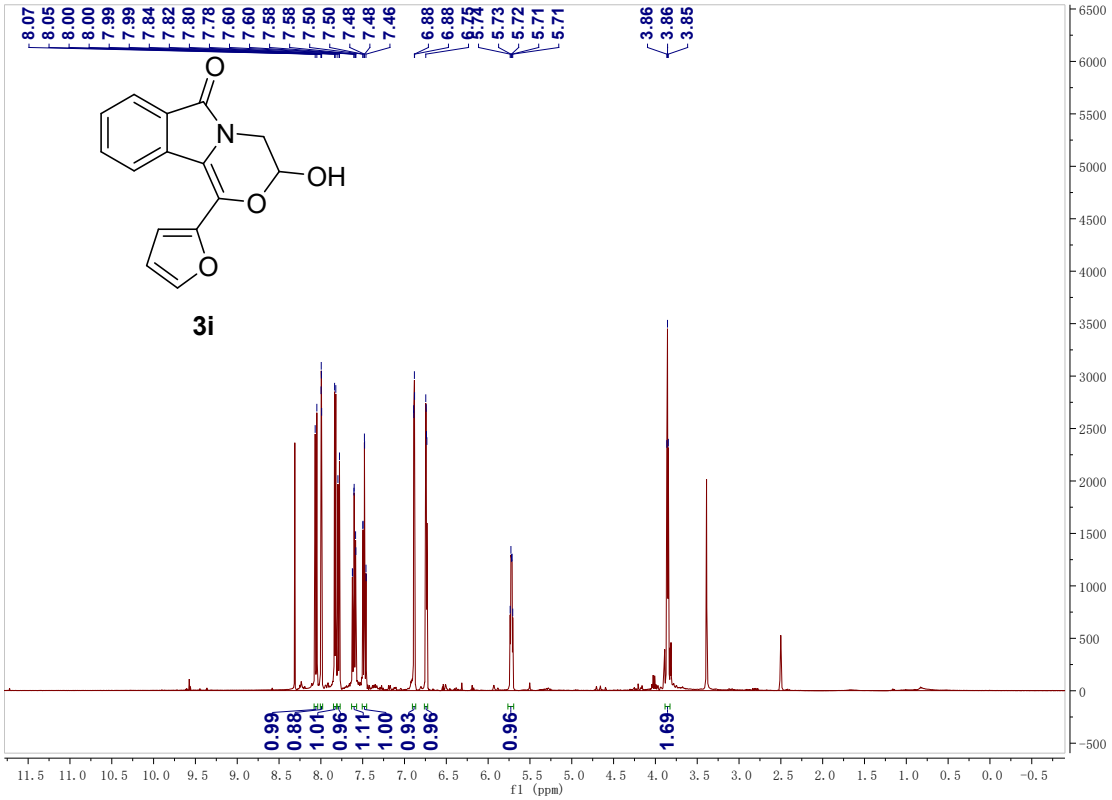

Figure S88. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **3i**

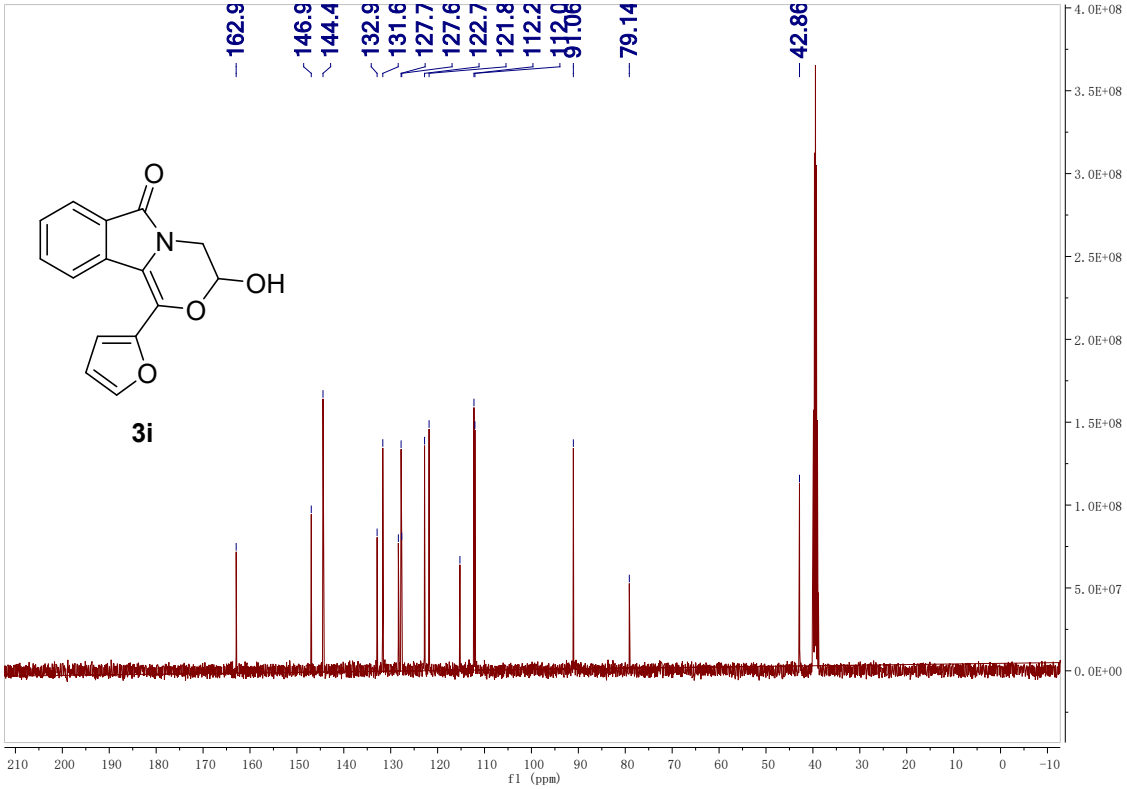

Figure S89. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3i**

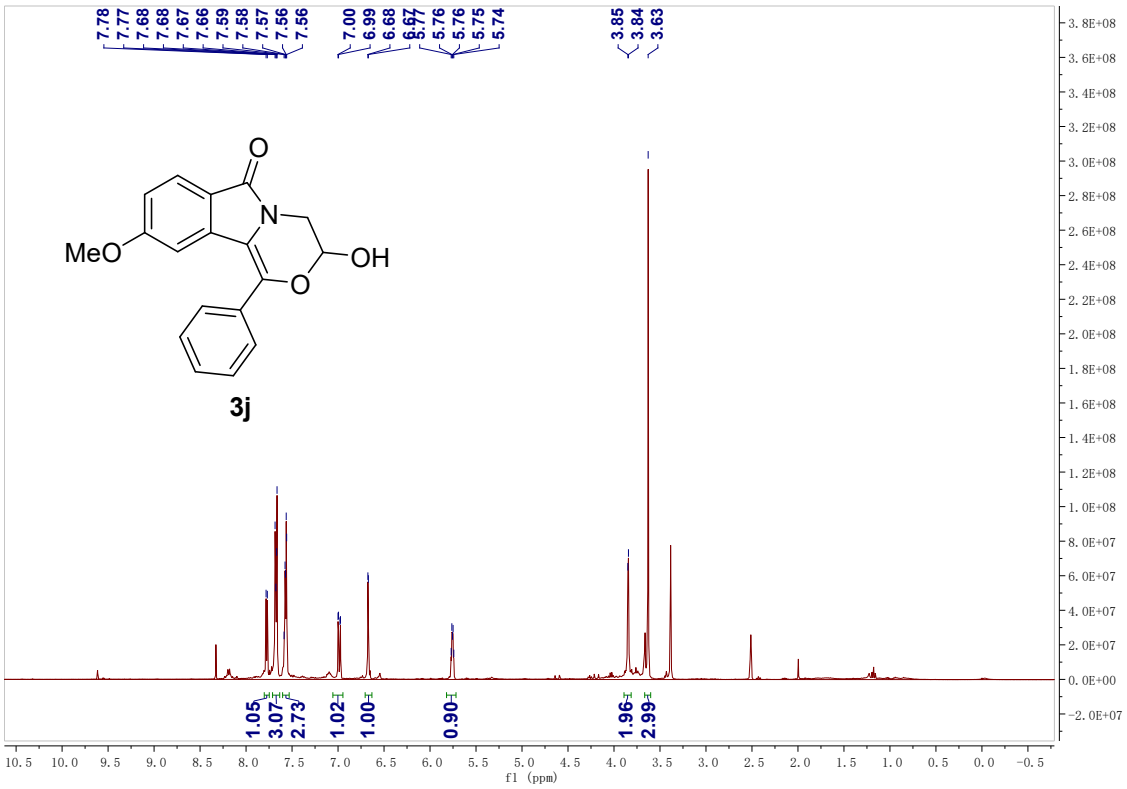

Figure S90. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of compound **3j**

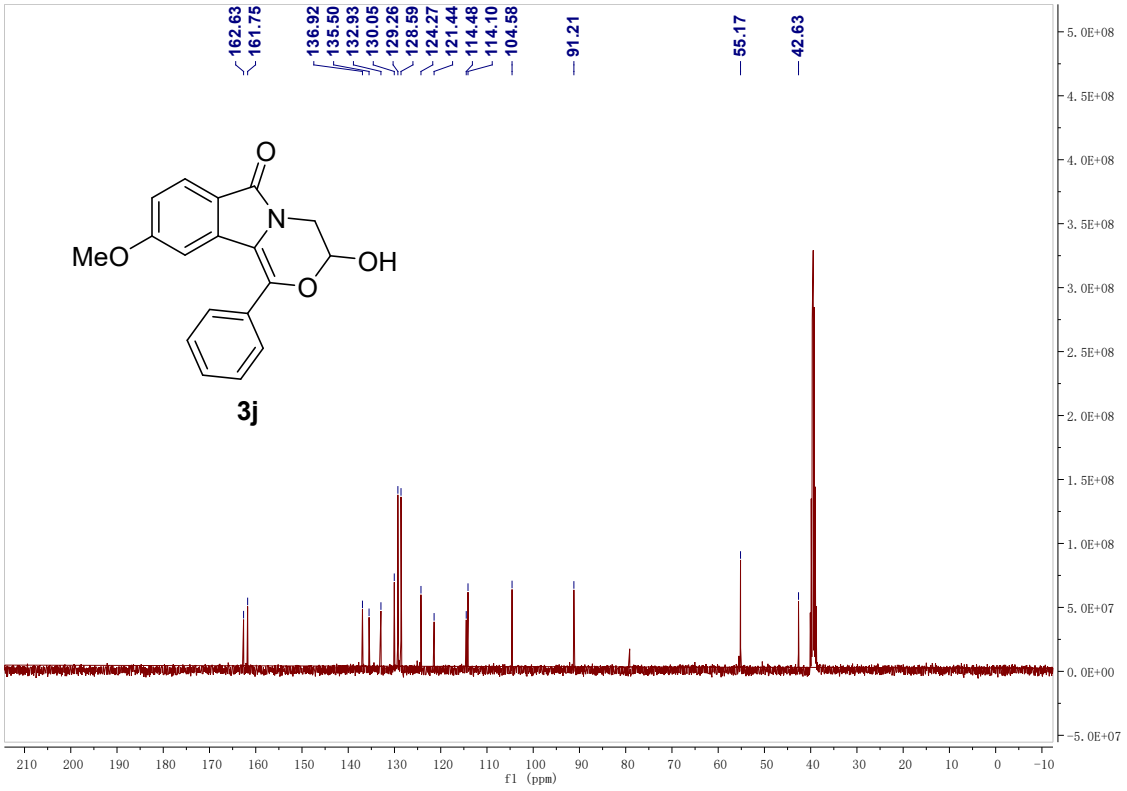

Figure S91. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3j**

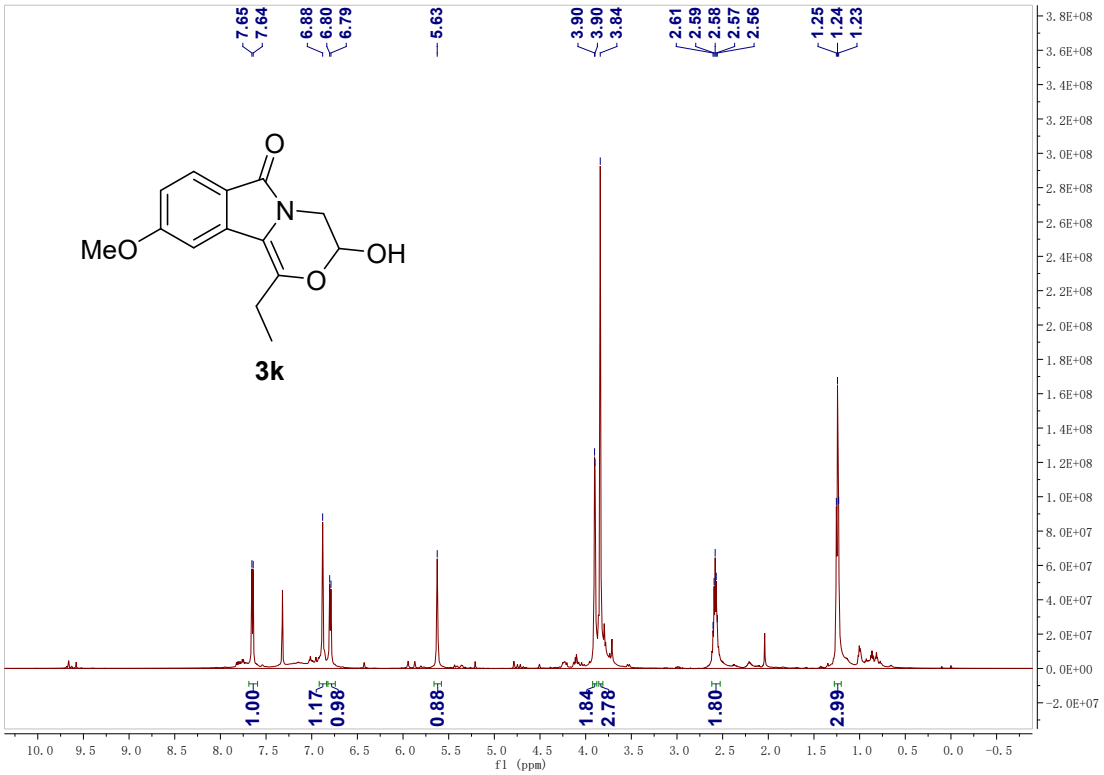

Figure S92. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of compound **3k**

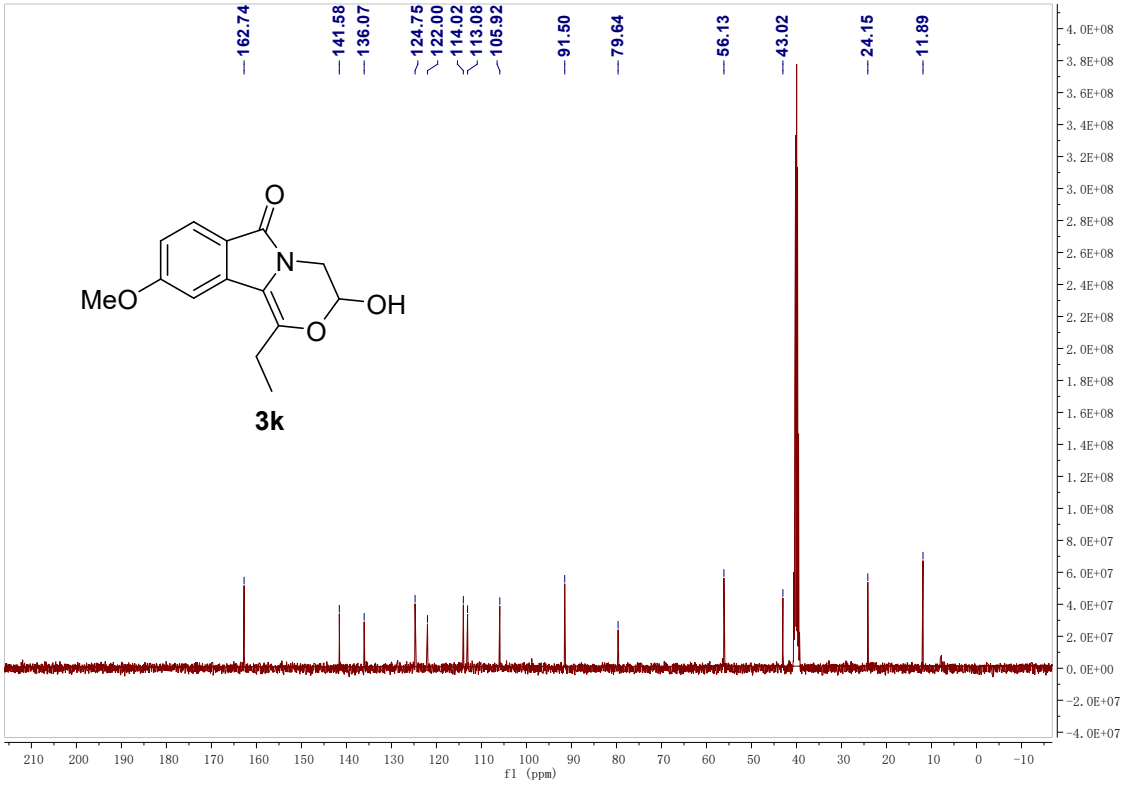

Figure S93. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3k**

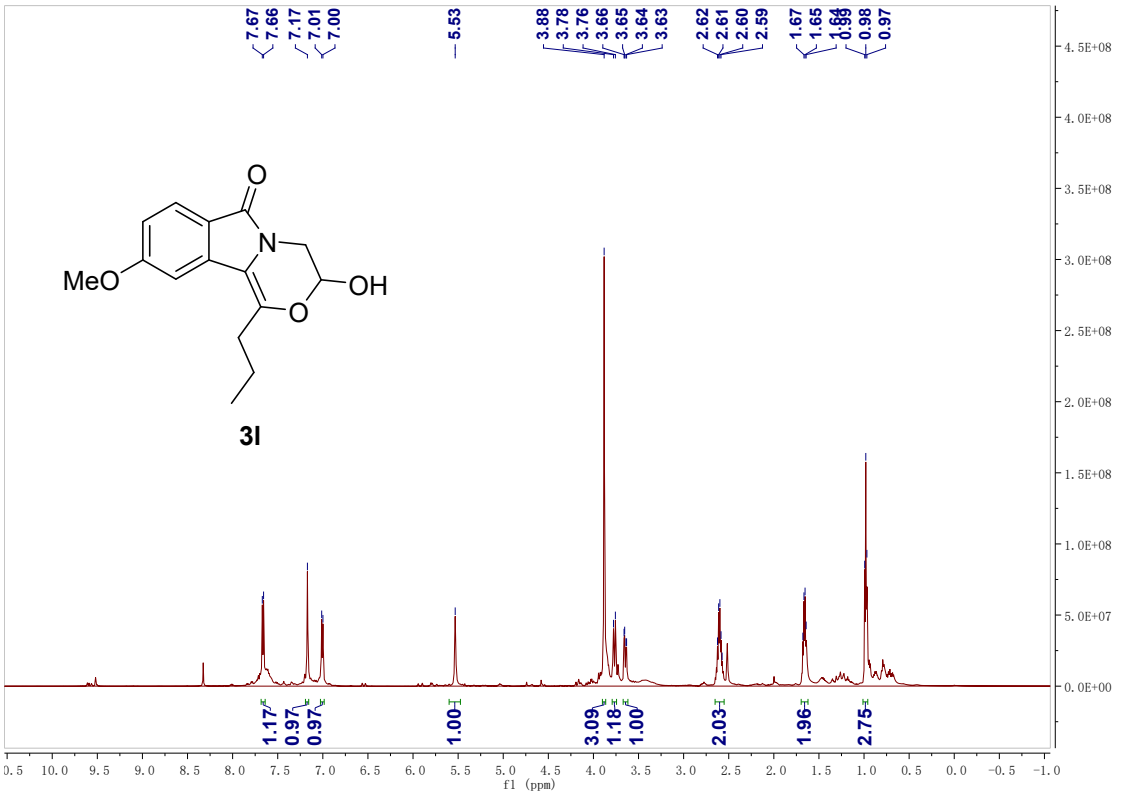

Figure S94. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **3l**

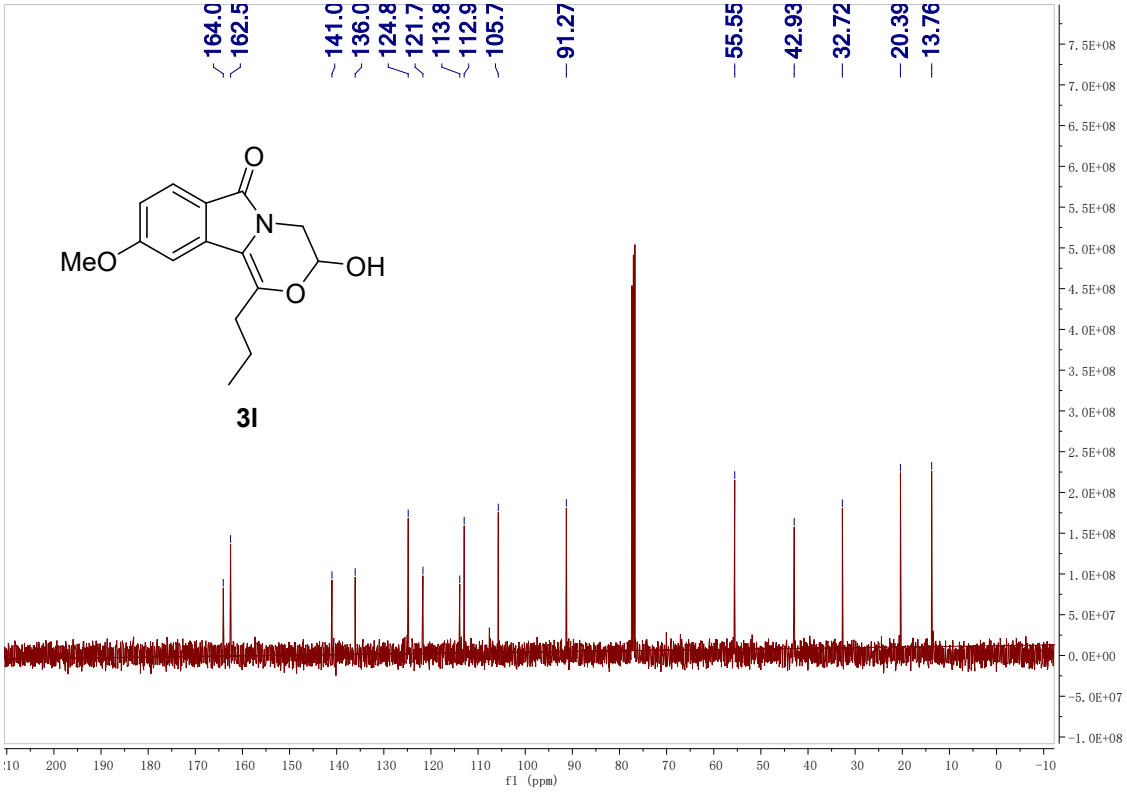

Figure S95. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **3l**

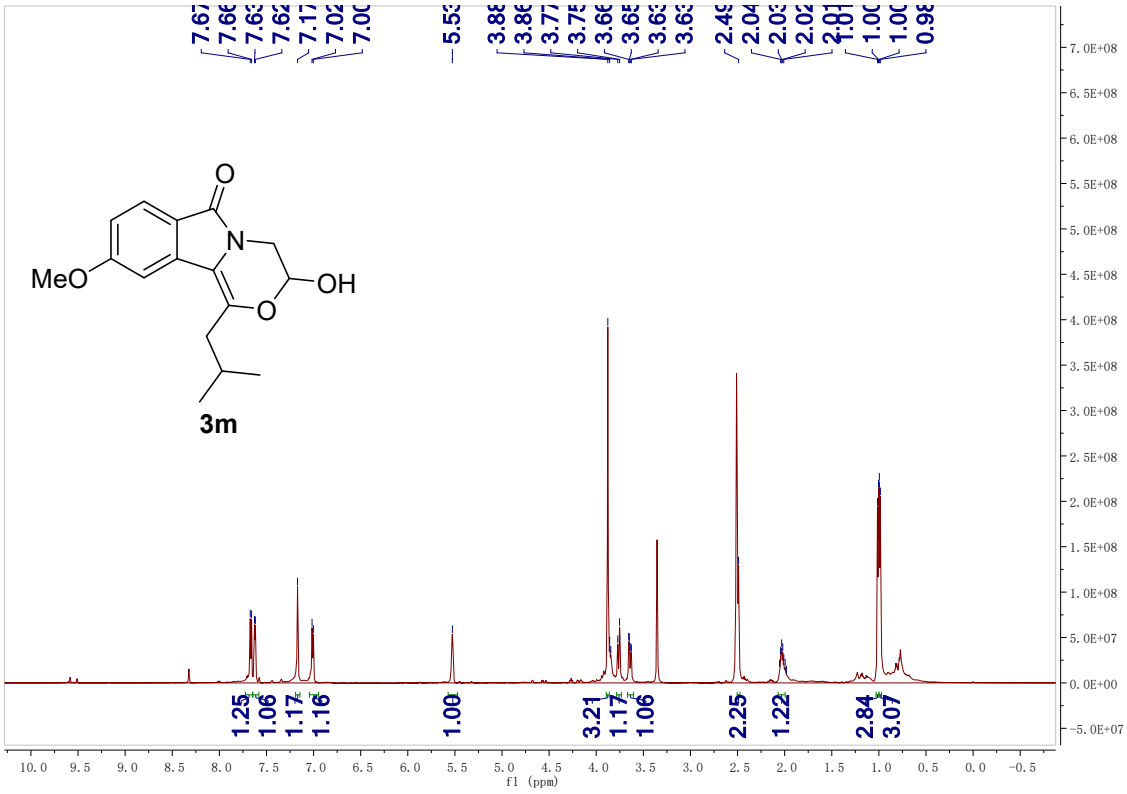

Figure S96. ^{1}H NMR (600 MHz, Chloroform-*d*) spectrum of compound **3m**

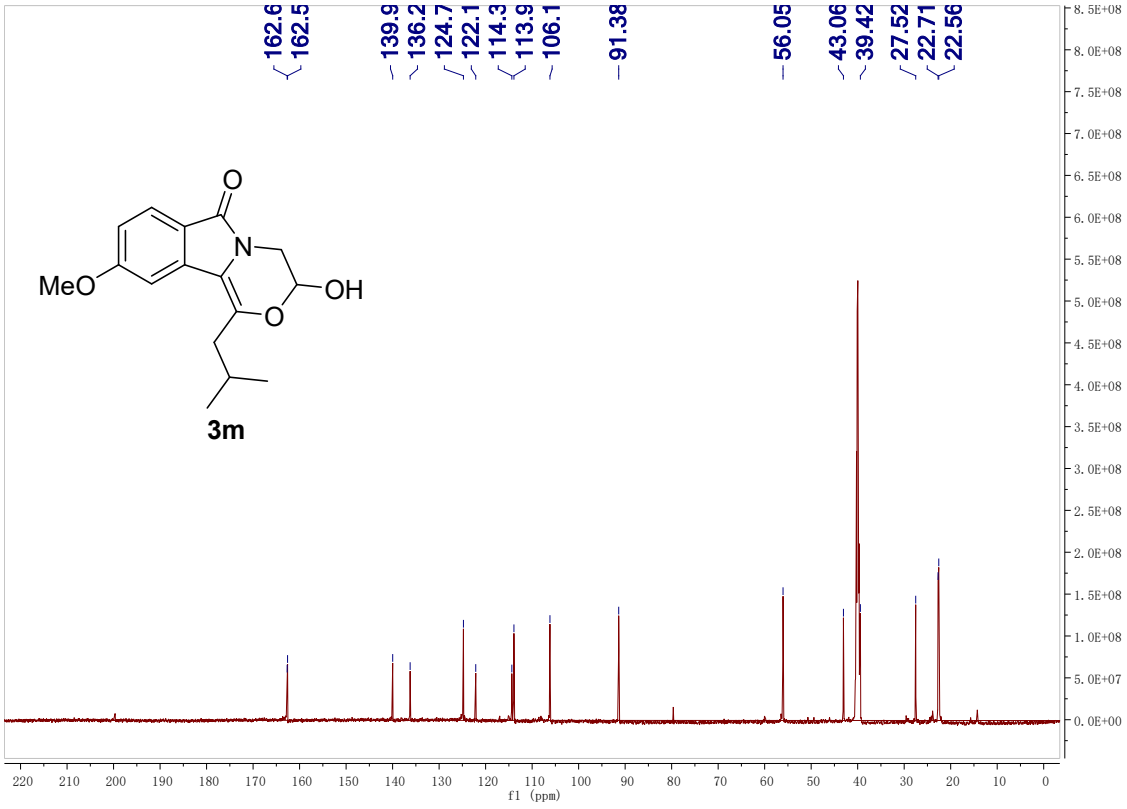

Figure S97. ^{13}C NMR (151 MHz, Chloroform-*d*) spectrum of compound **3m**

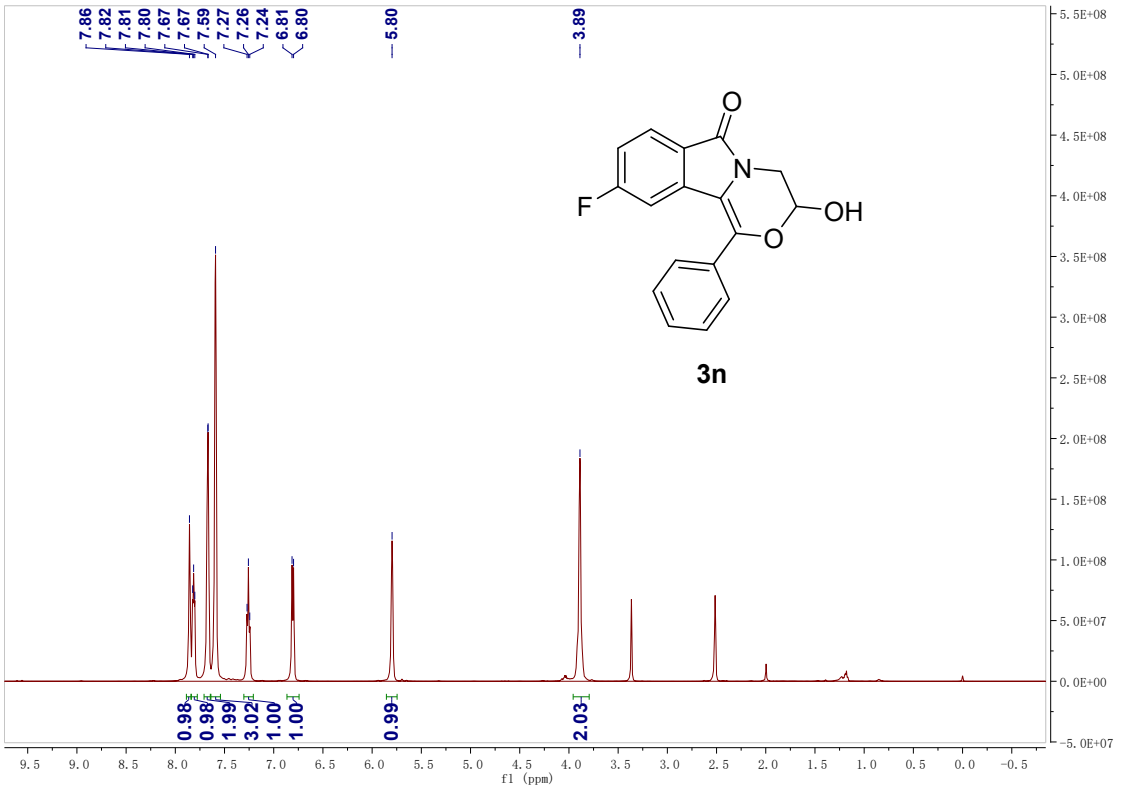

Figure S98. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **3n**

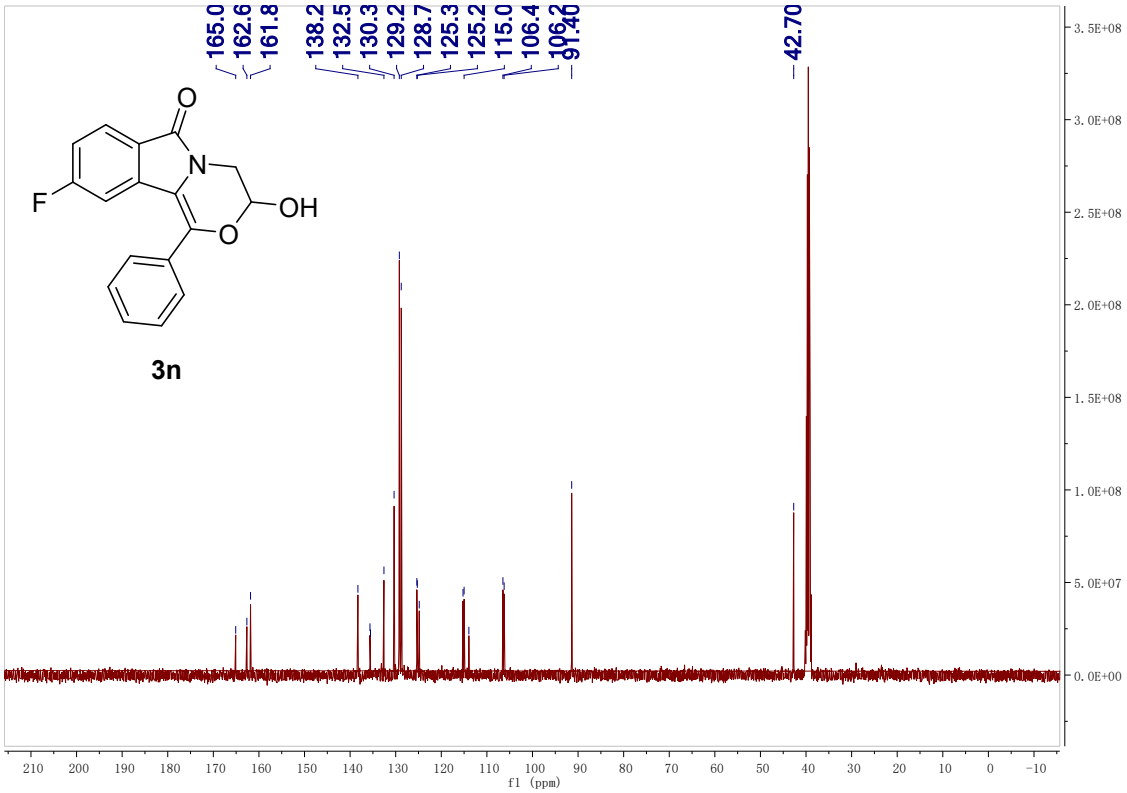

Figure S99. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3n**

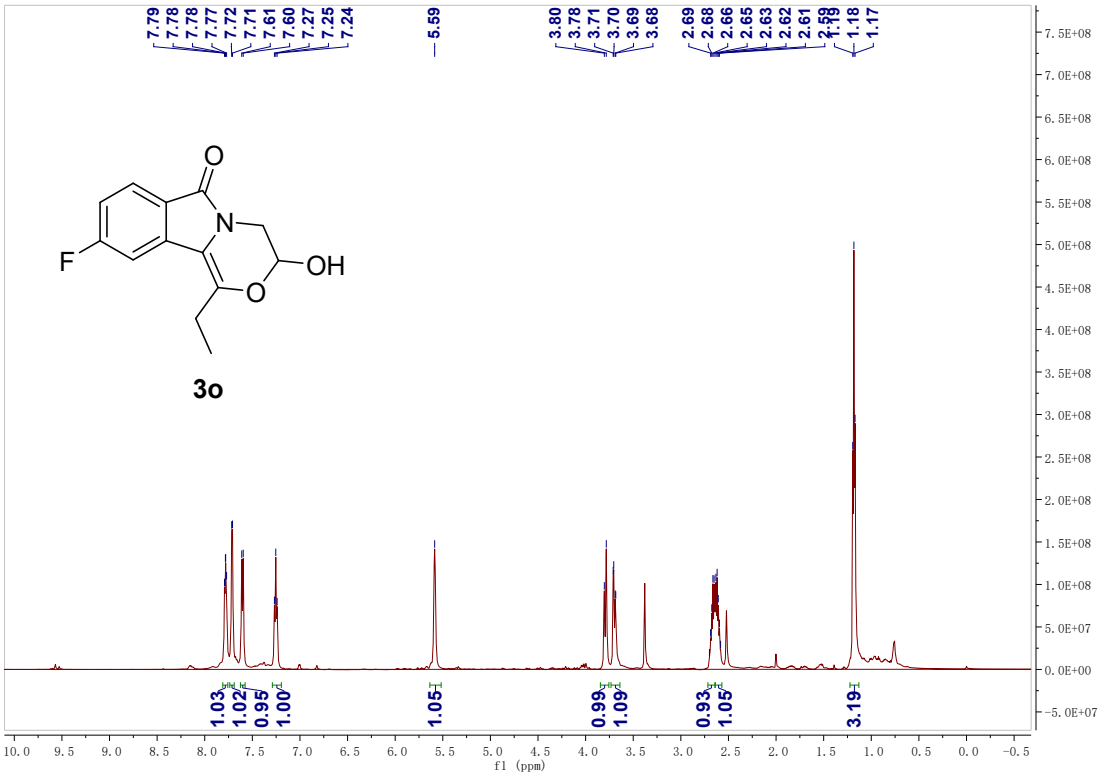

Figure S100. ^{1}H NMR (600 MHz, DMSO-d_6) spectrum of compound **3o**

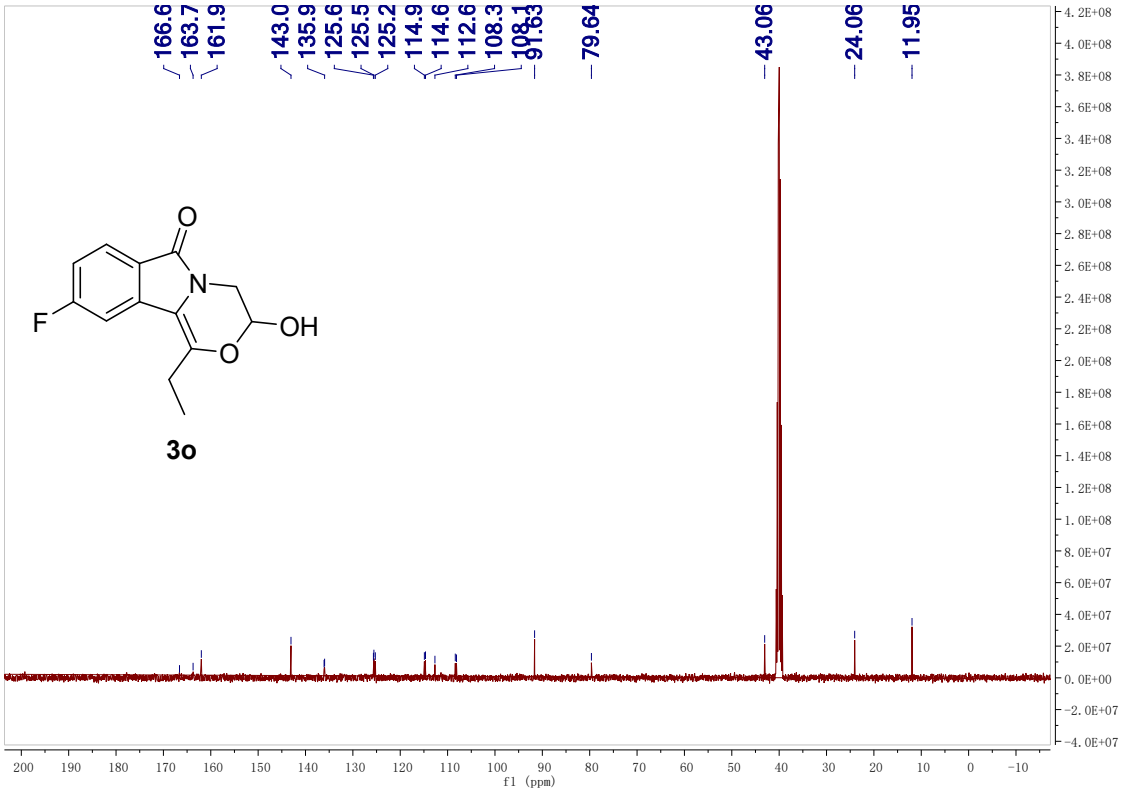

Figure S101. ^{13}C NMR (100 MHz, DMSO-d_6) spectrum of compound **3o**

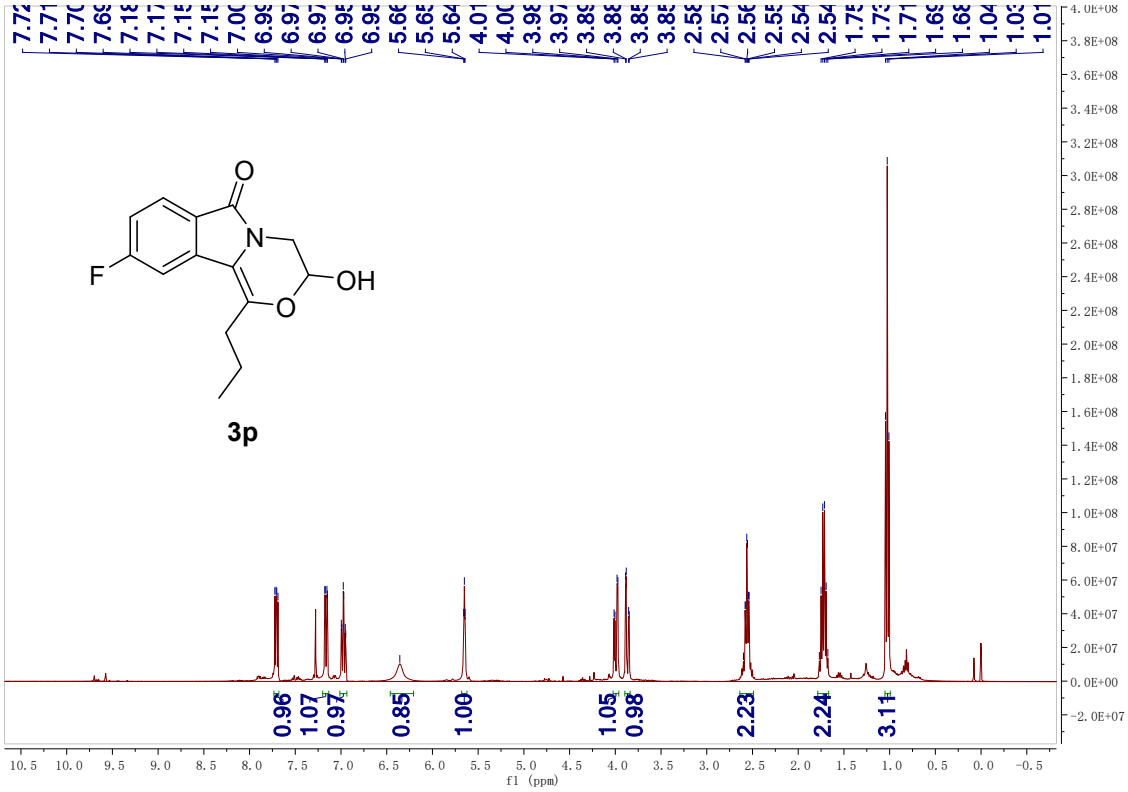

Figure S102. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **3p**

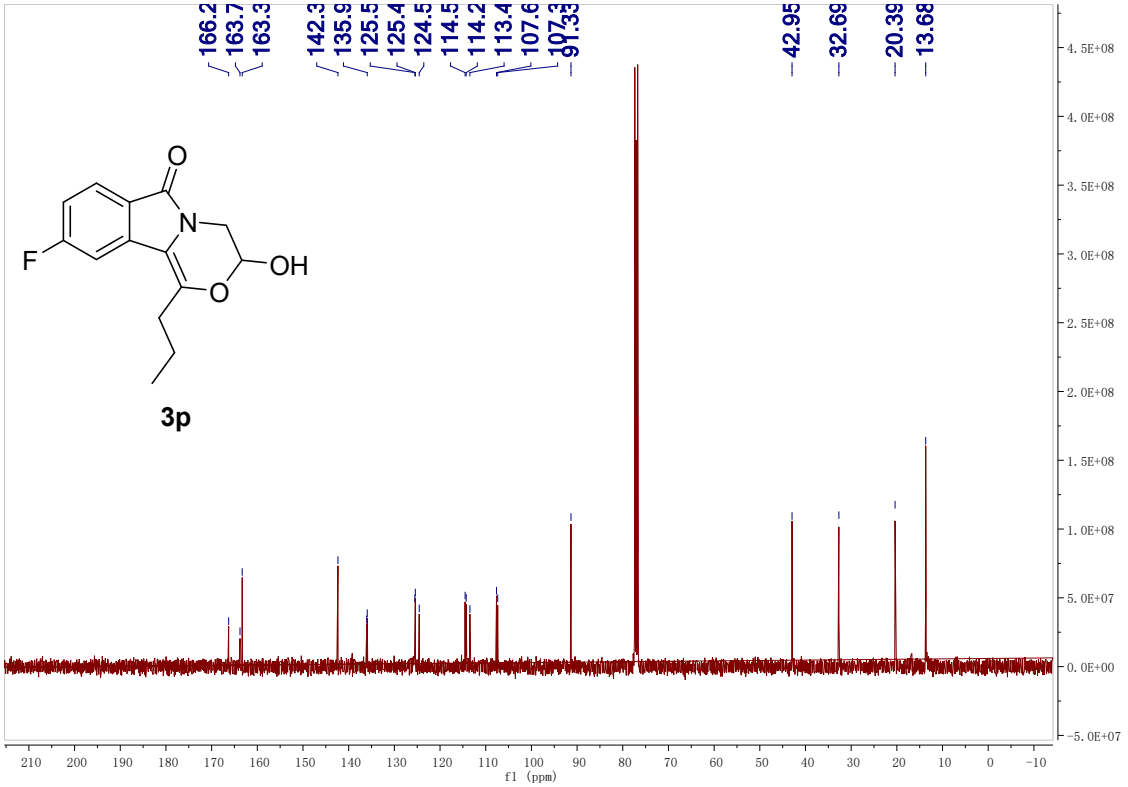

Figure S103. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **3p**

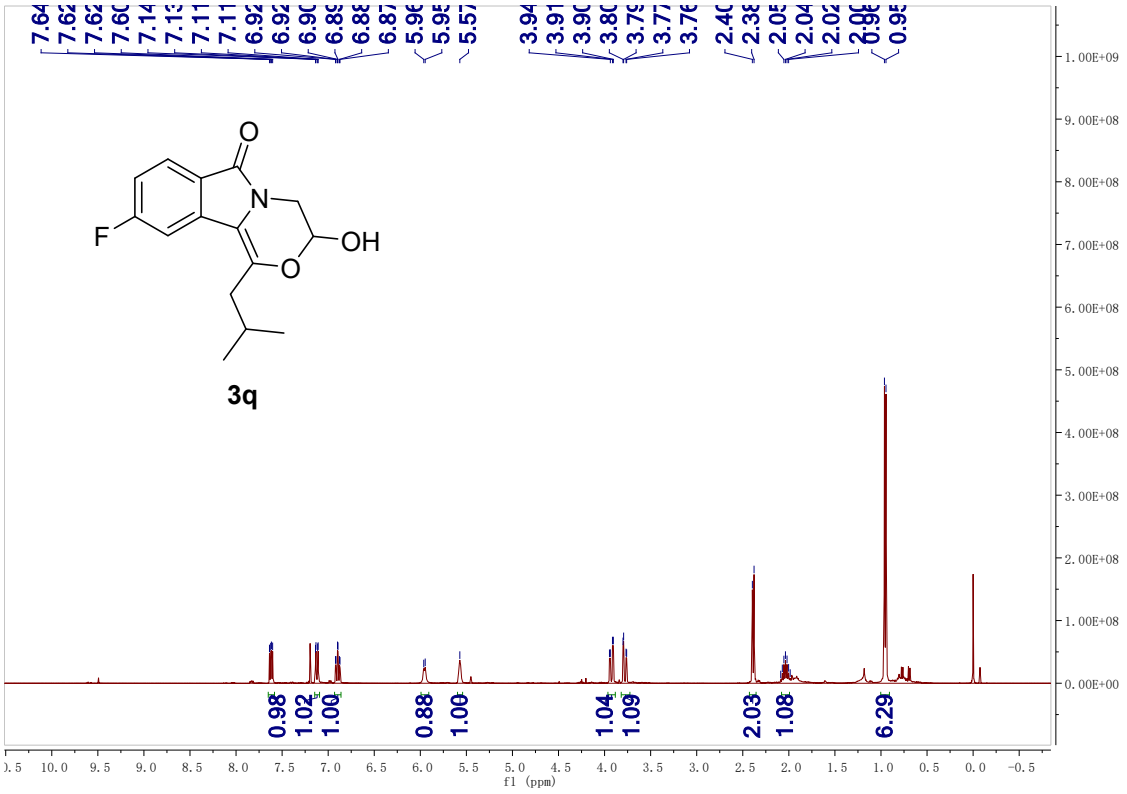

Figure S104. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **3q**

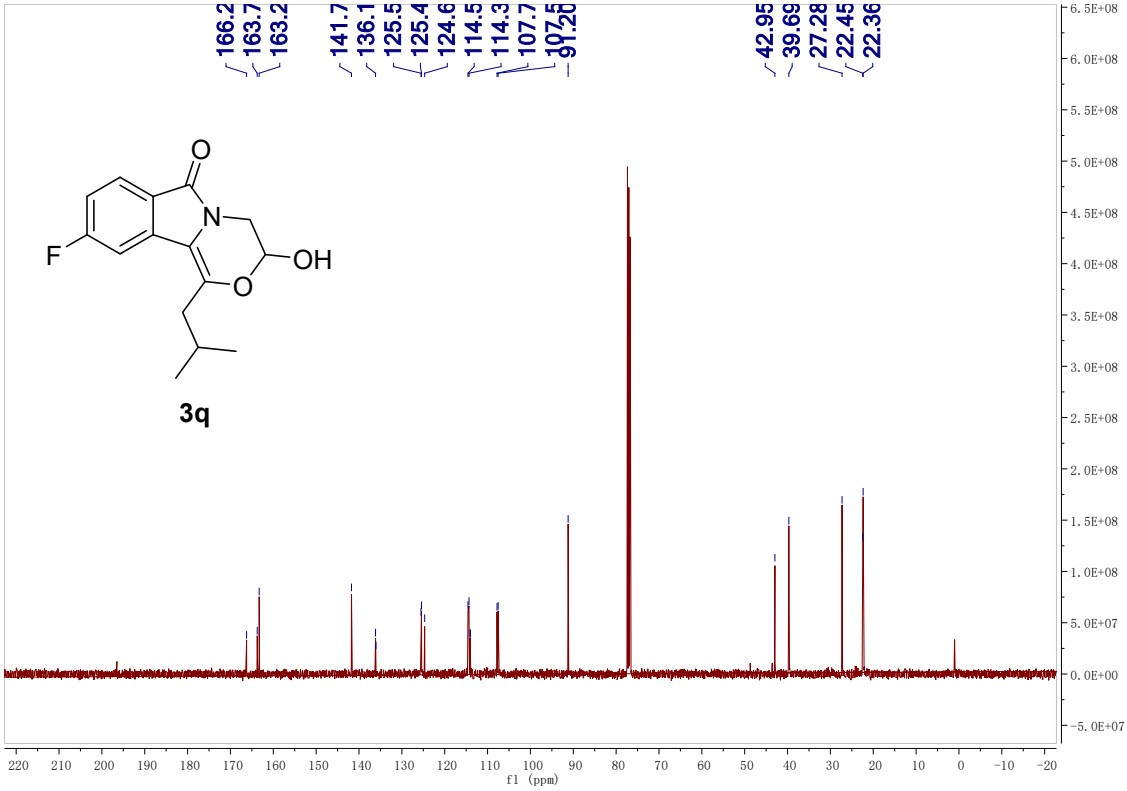

Figure S105. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **3q**

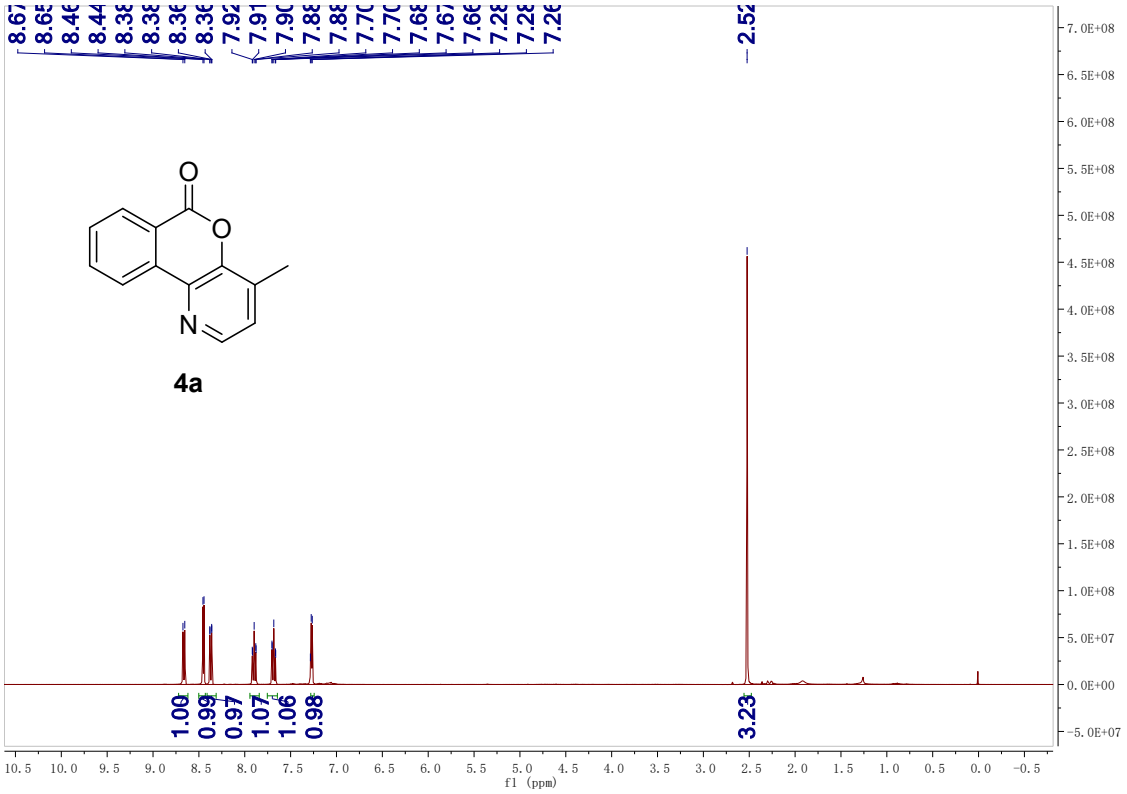

Figure S106. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4a**

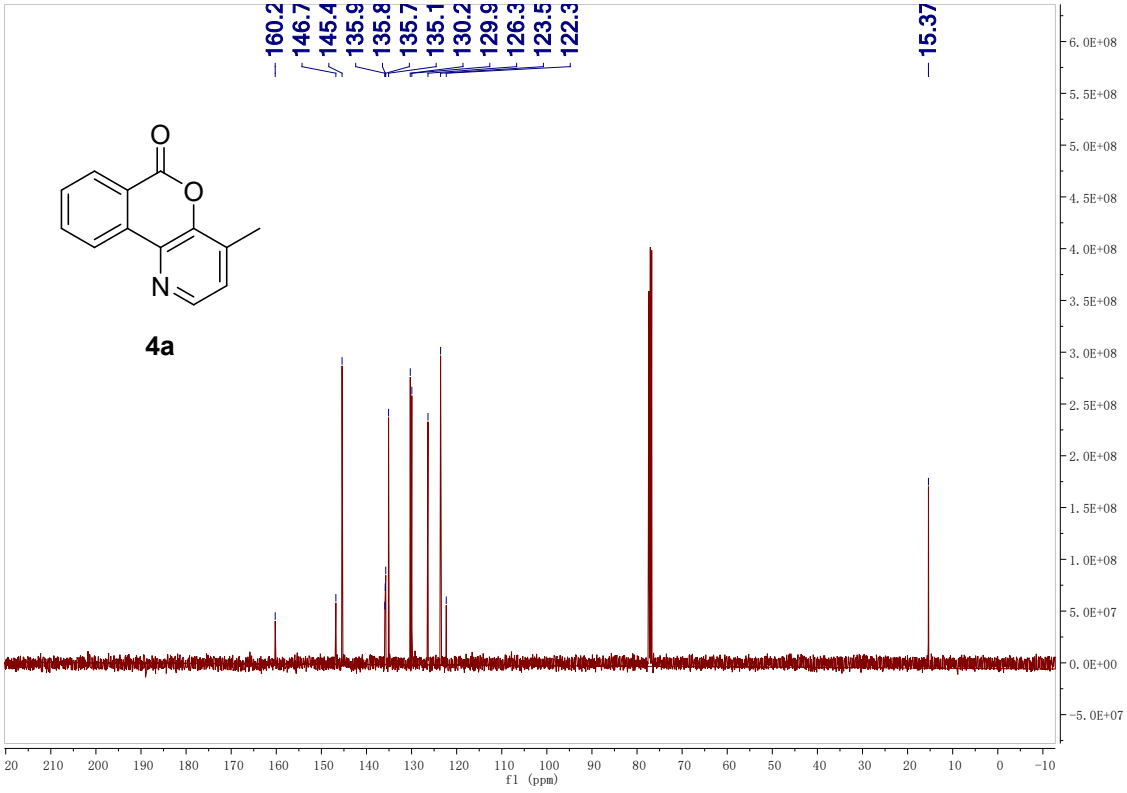

Figure S107. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4a**

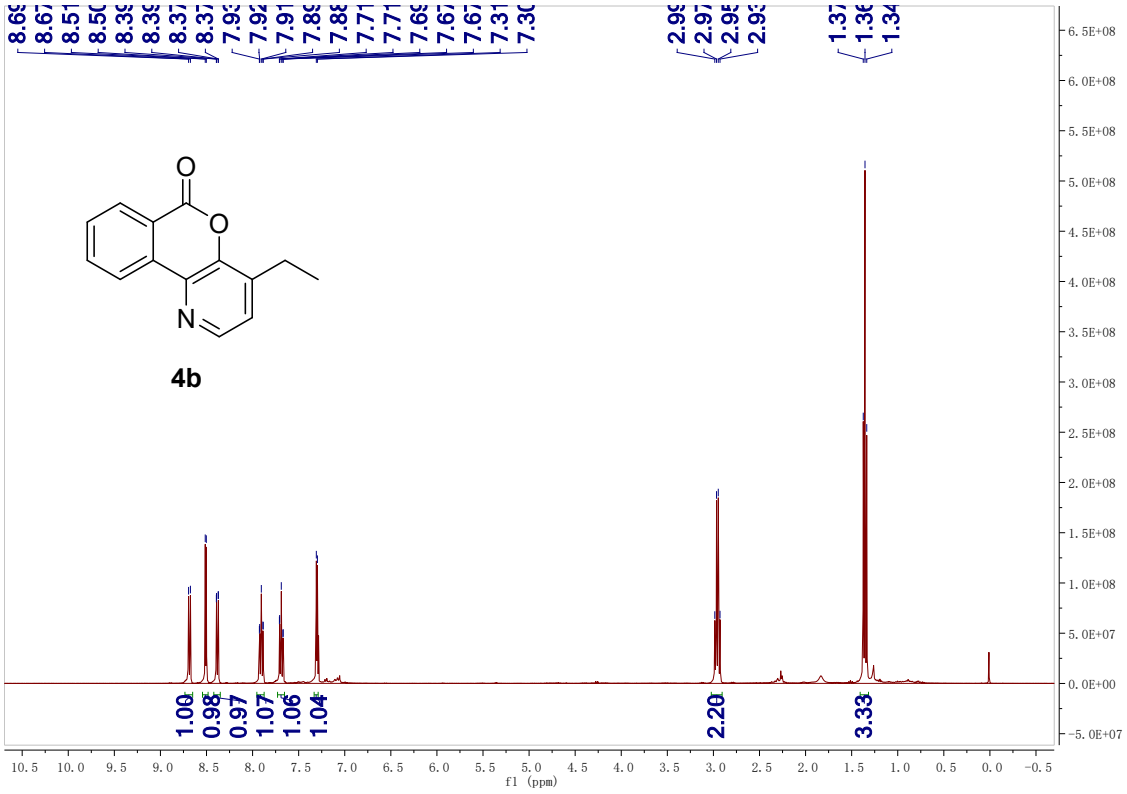

Figure S108. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4b**

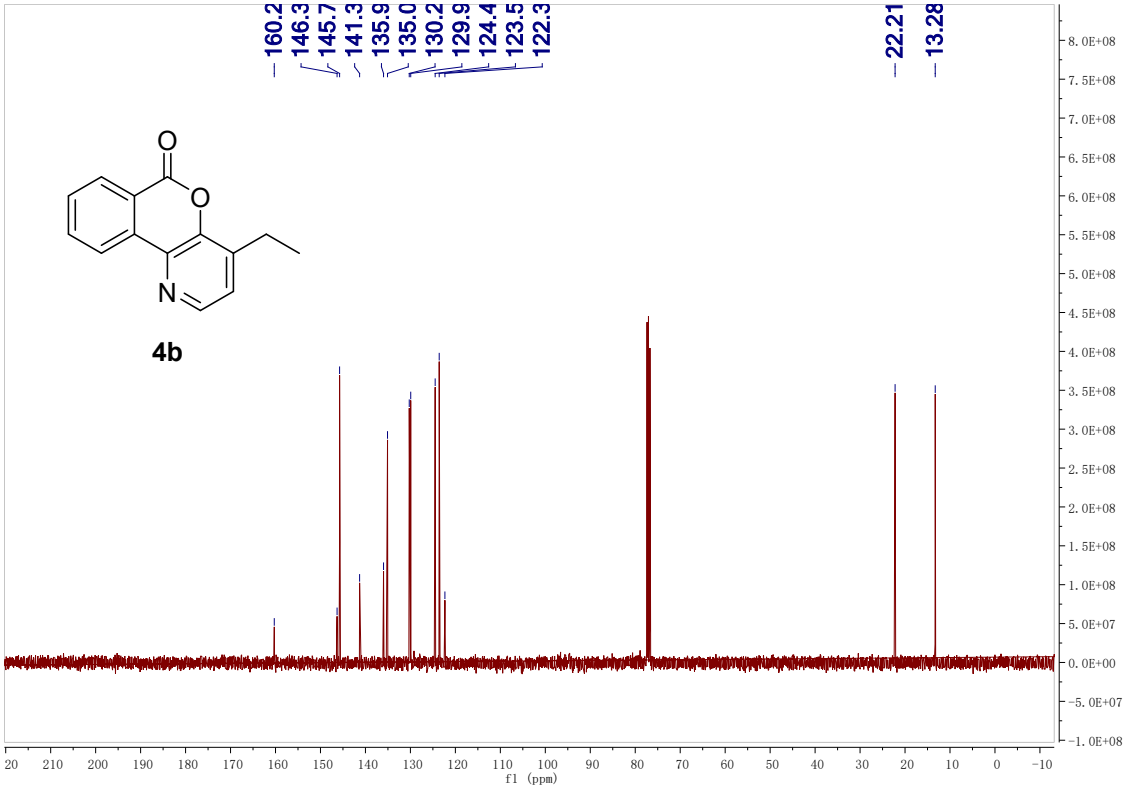

Figure S109. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4b**

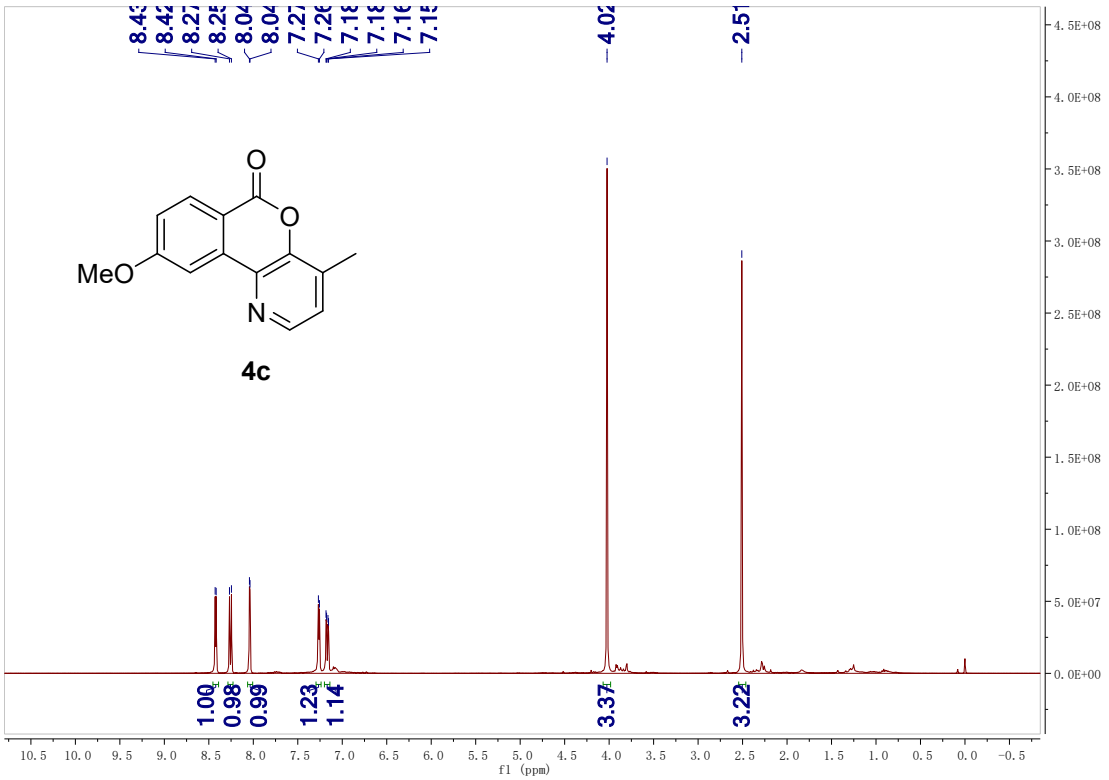

Figure S110. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4c**

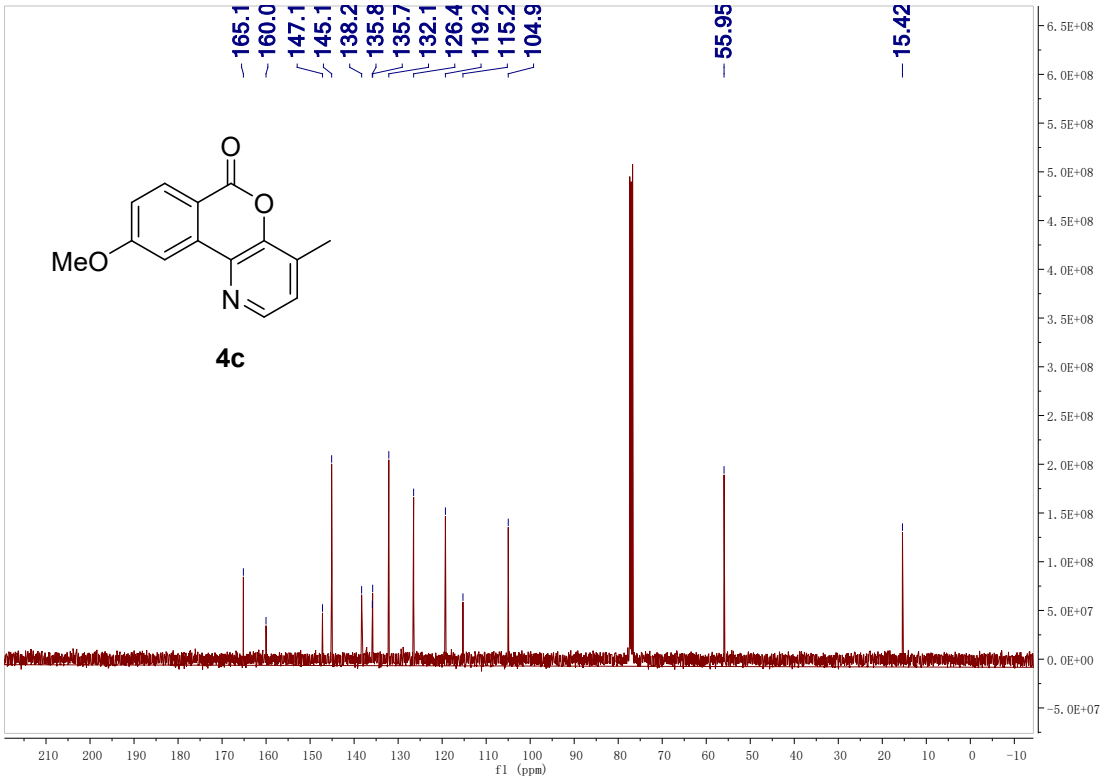

Figure S111. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4c**

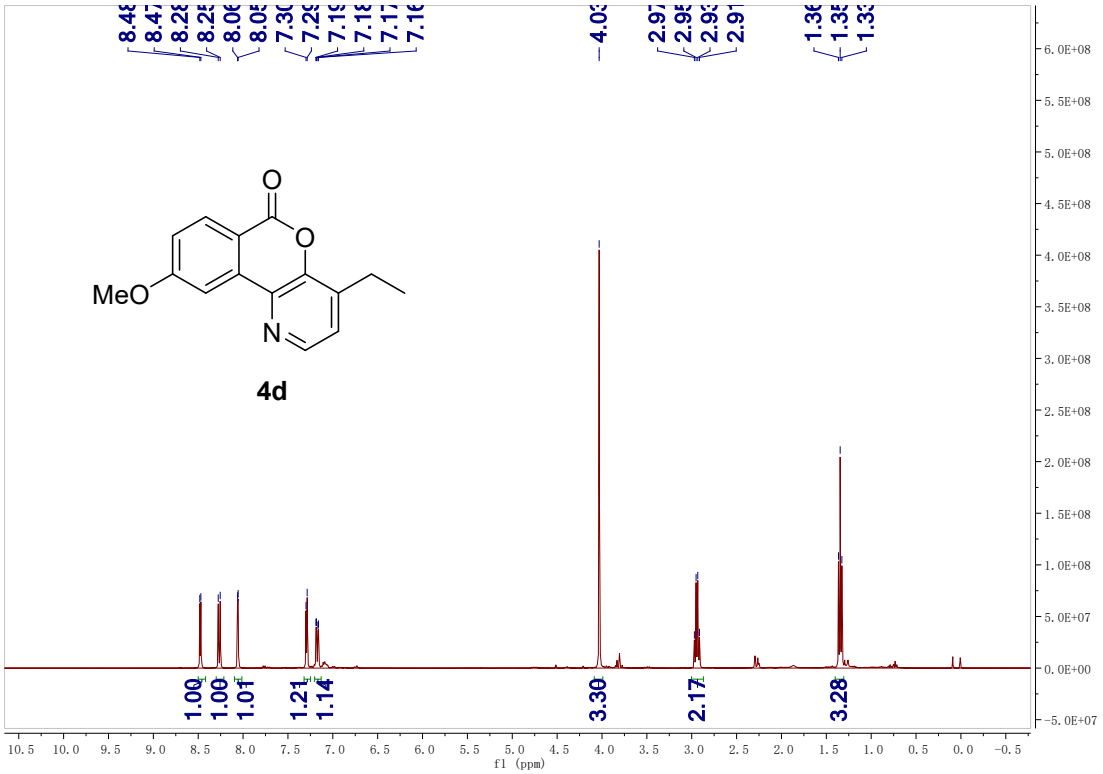

Figure S112. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4d**

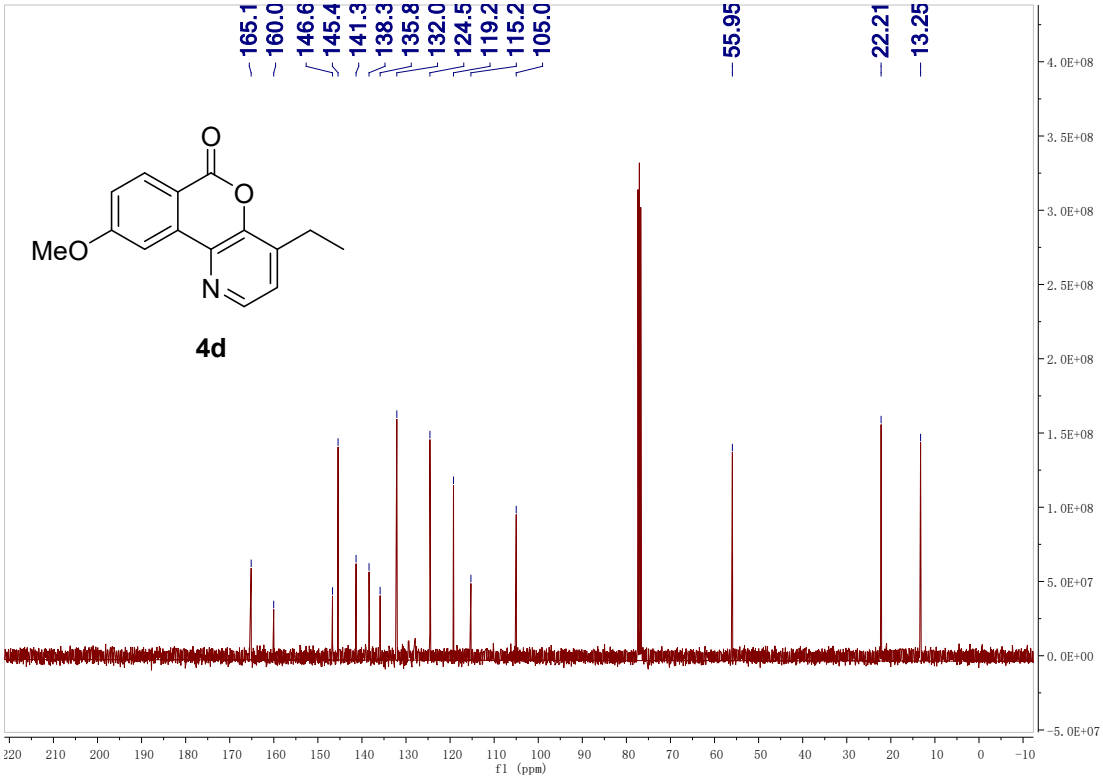

Figure S113. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4d**

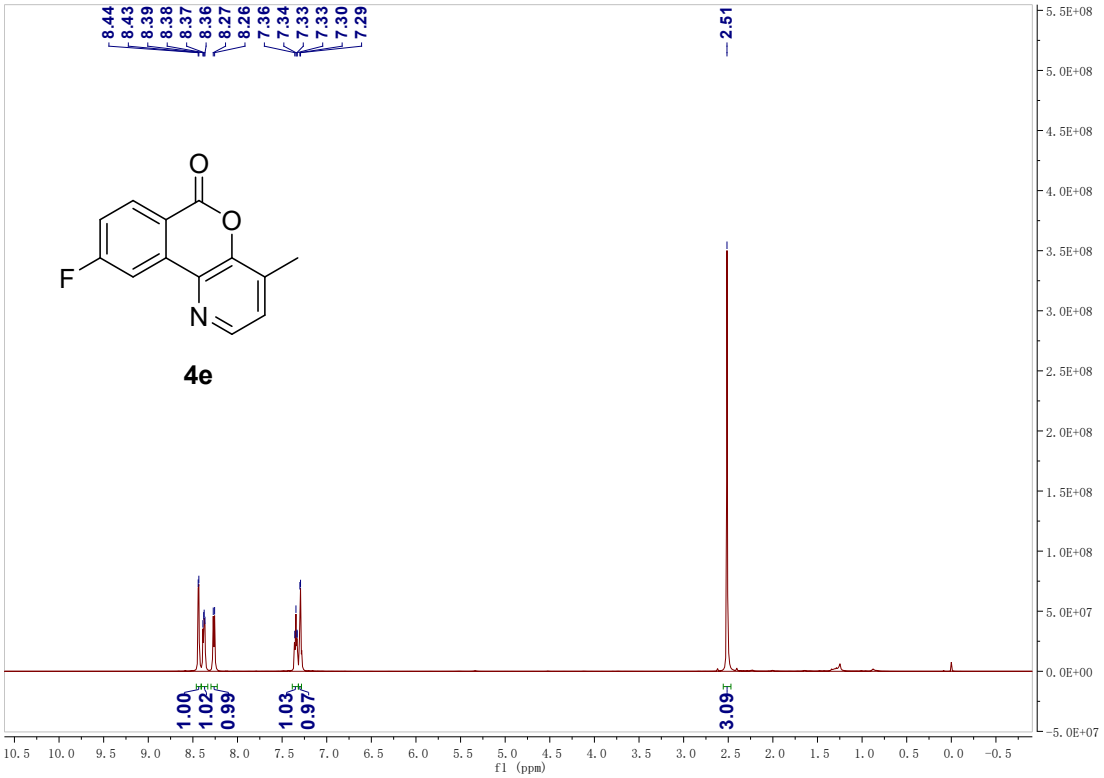

Figure S114. ^{1}H NMR (600 MHz, Chloroform-*d*) spectrum of compound **4e**

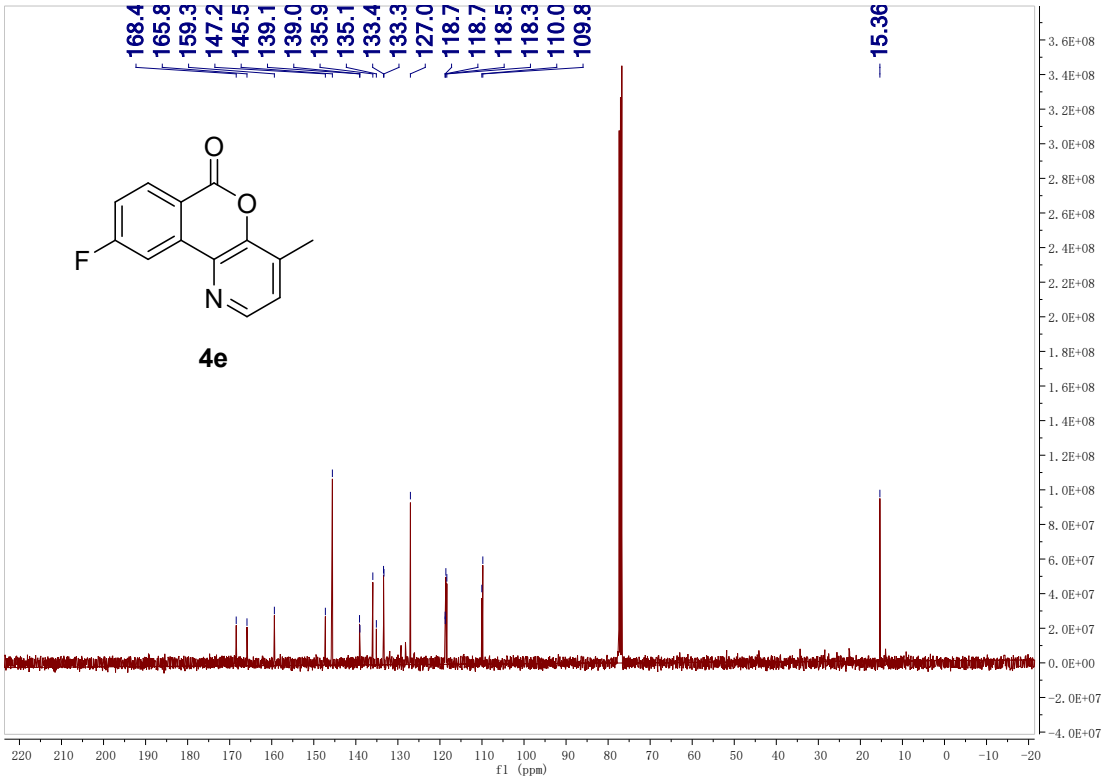

Figure S115. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4e**

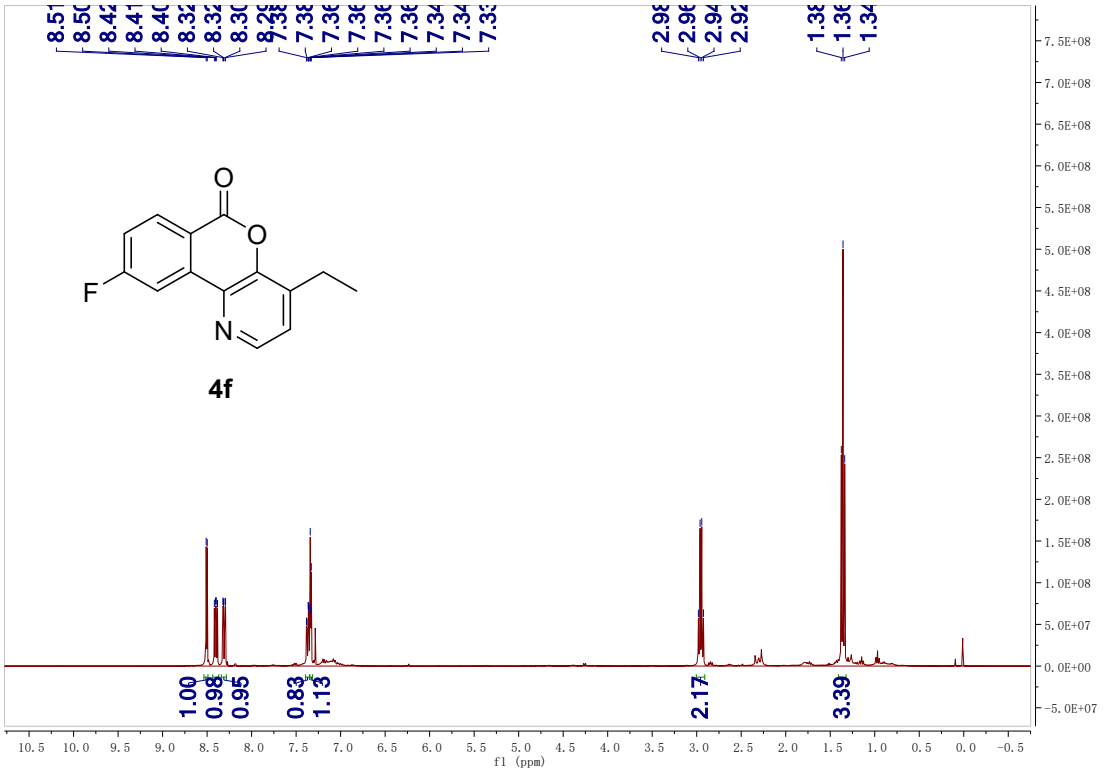

Figure S116. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4f**

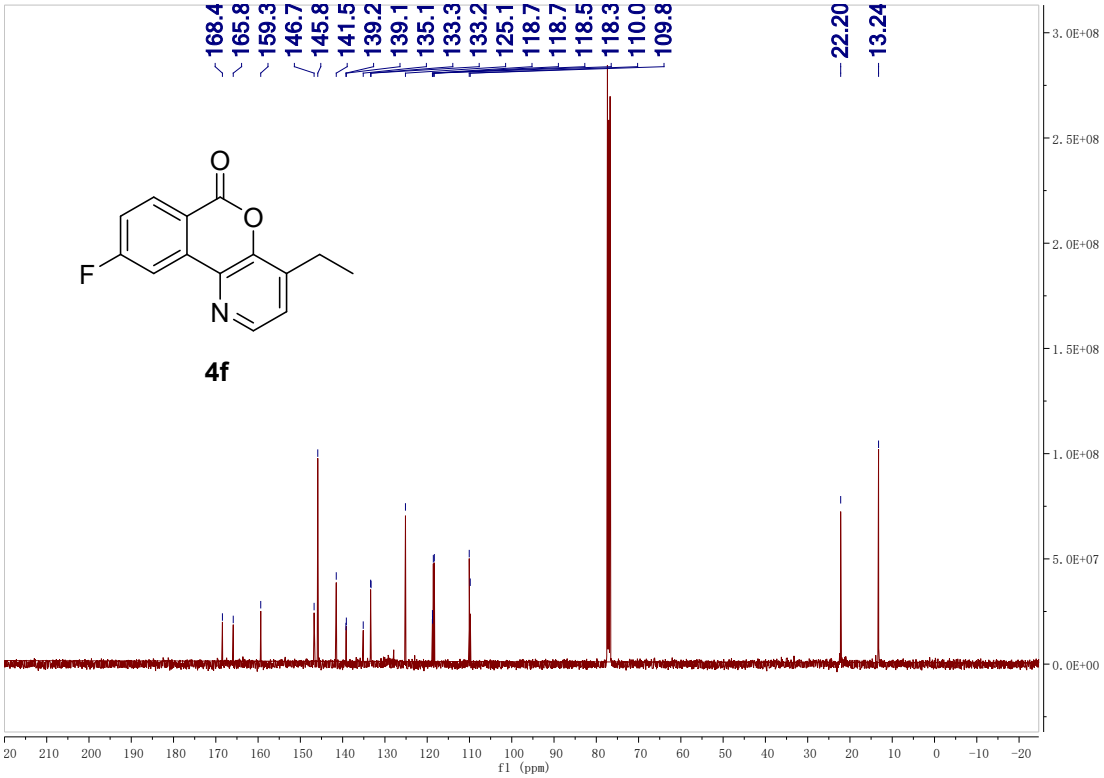

Figure S117. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4f**

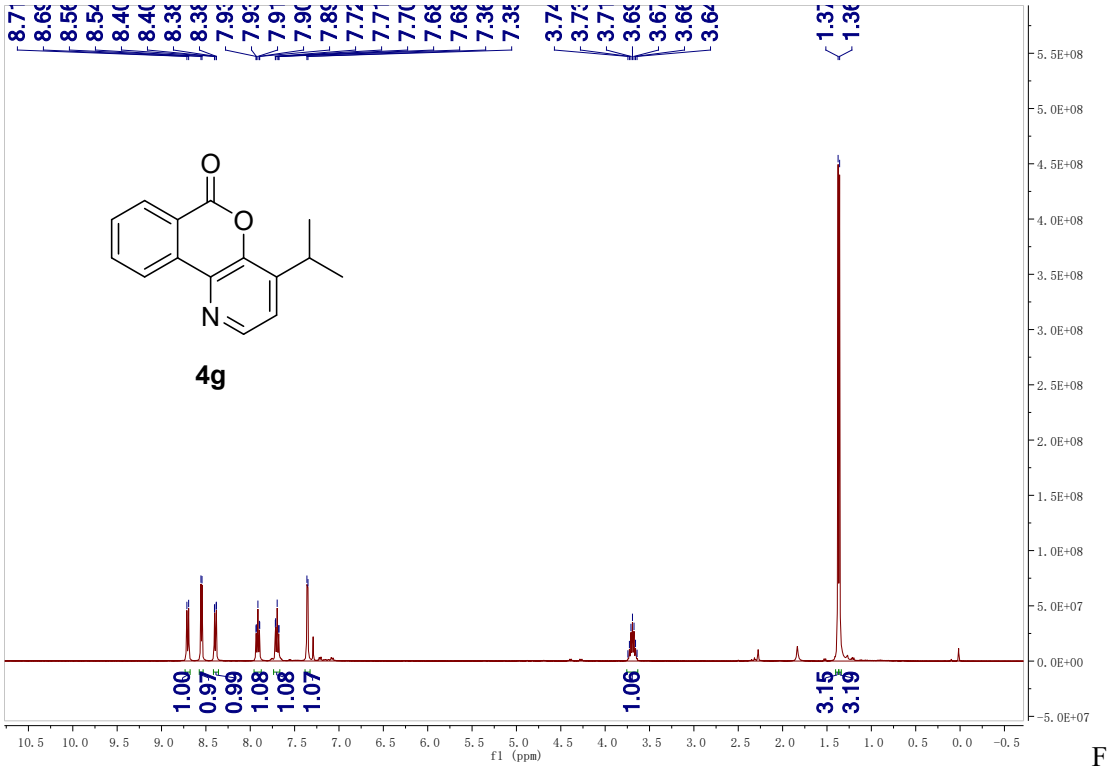

Figure S118. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4g**

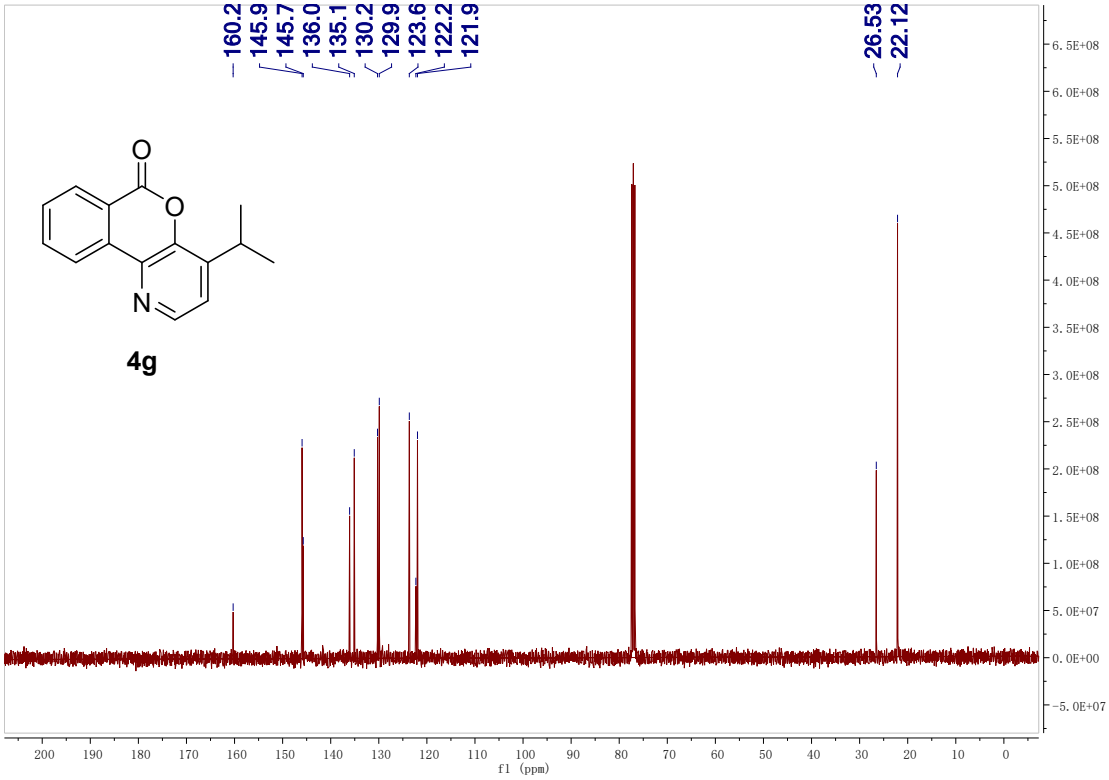

Figure S119. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4g**

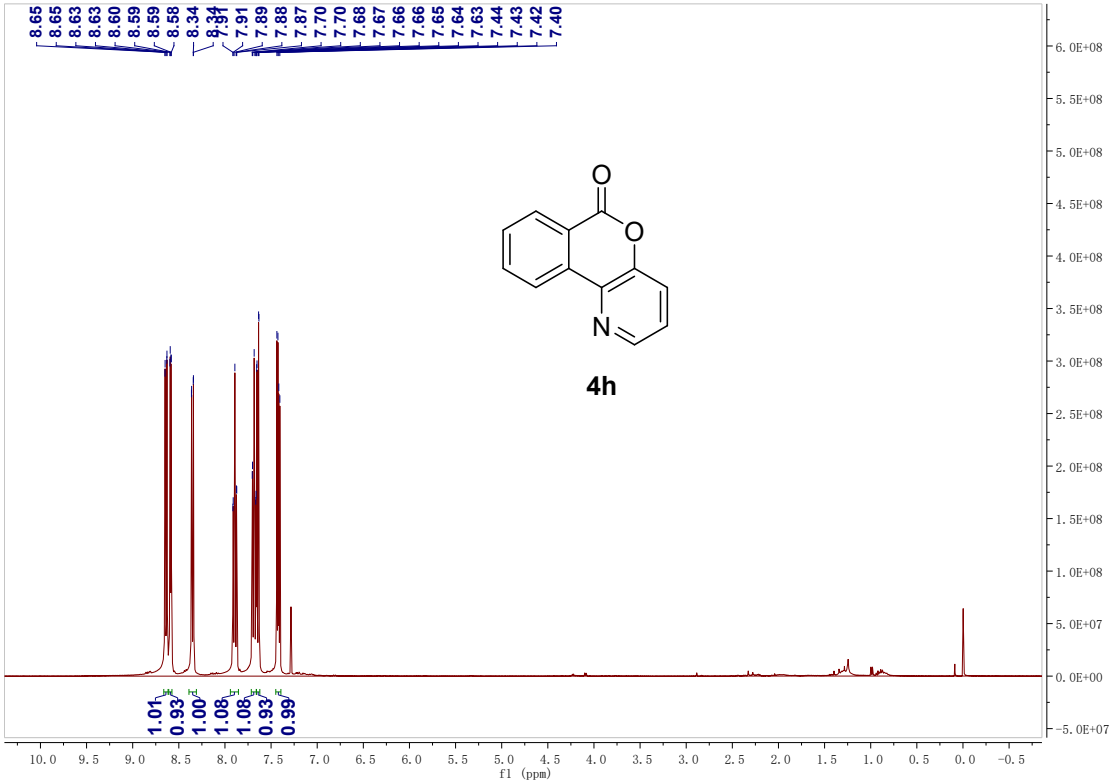

Figure S120. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4h**

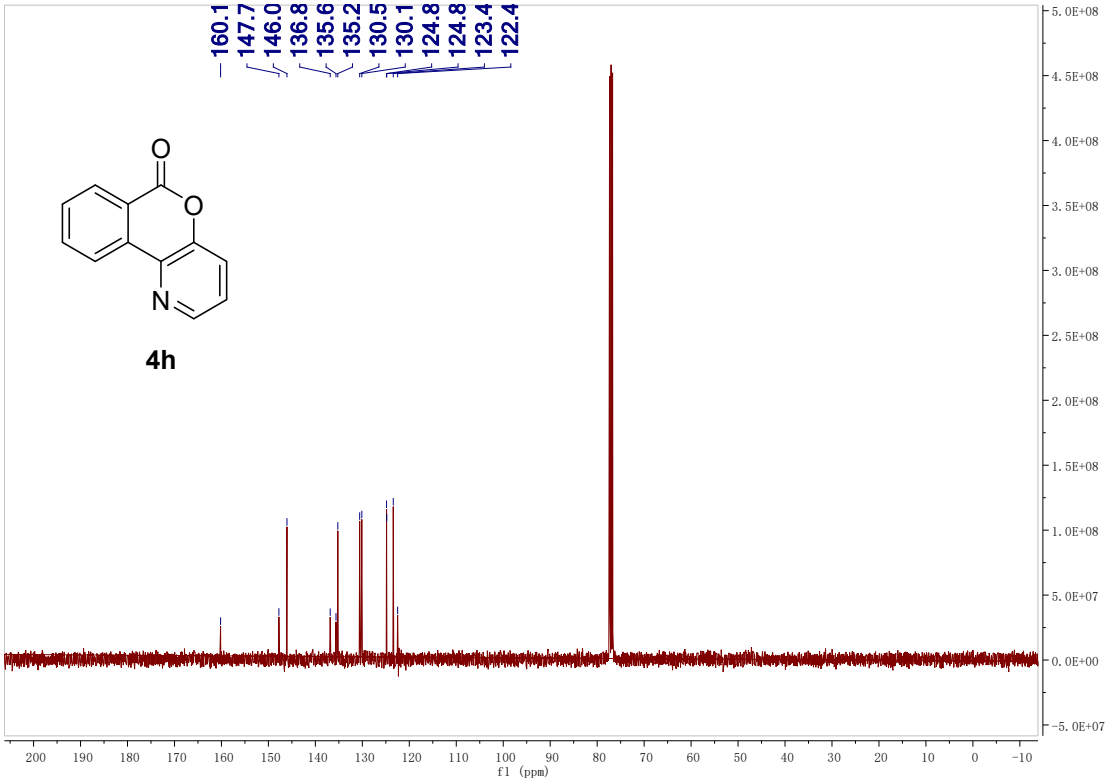

Figure S121. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4h**

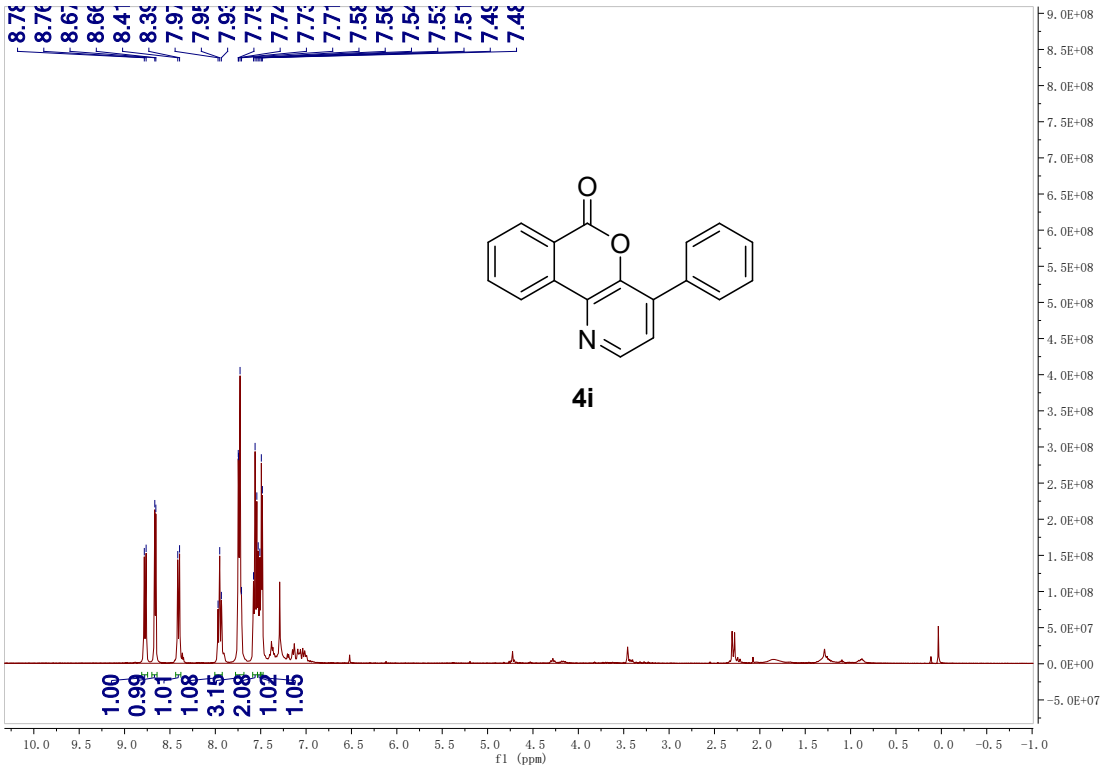

Figure S122. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4i**

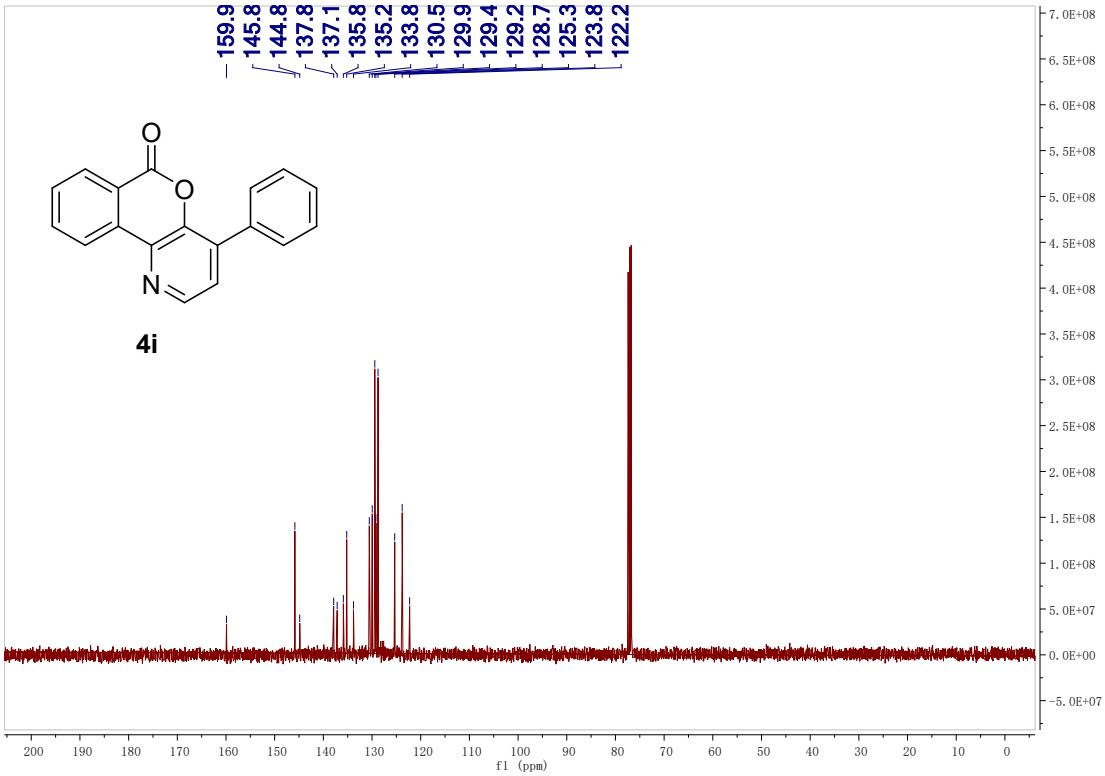

Figure S123. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4i**

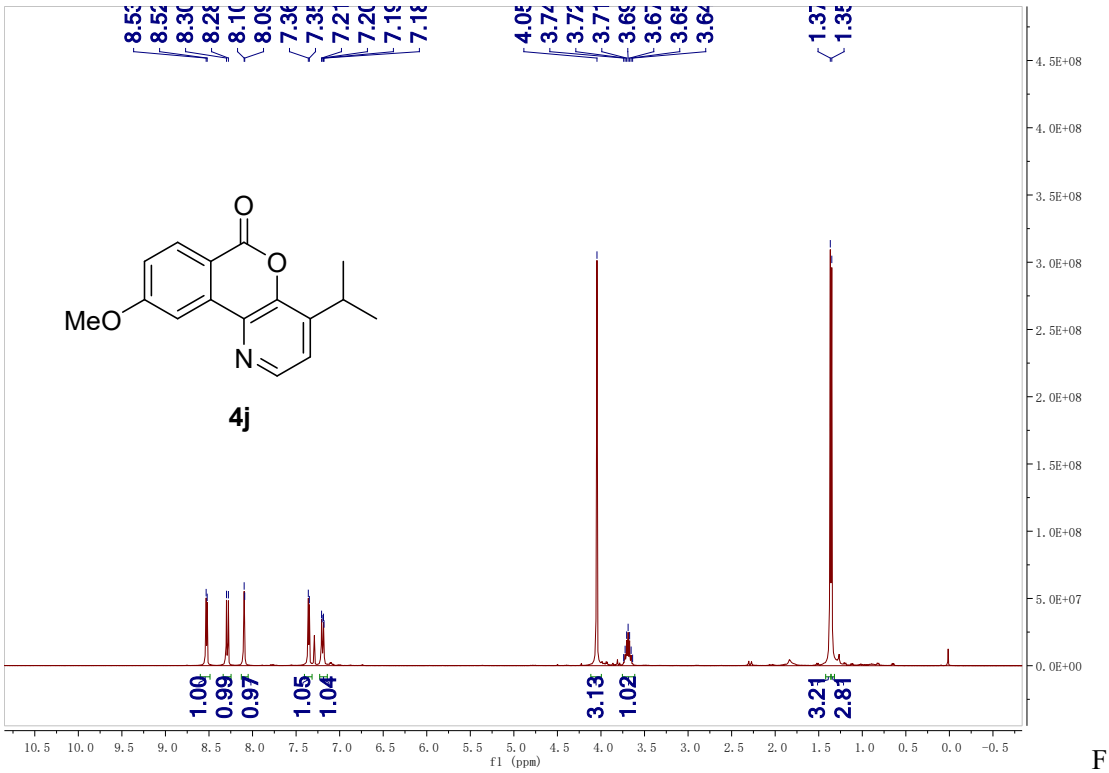

Figure S124. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4j**

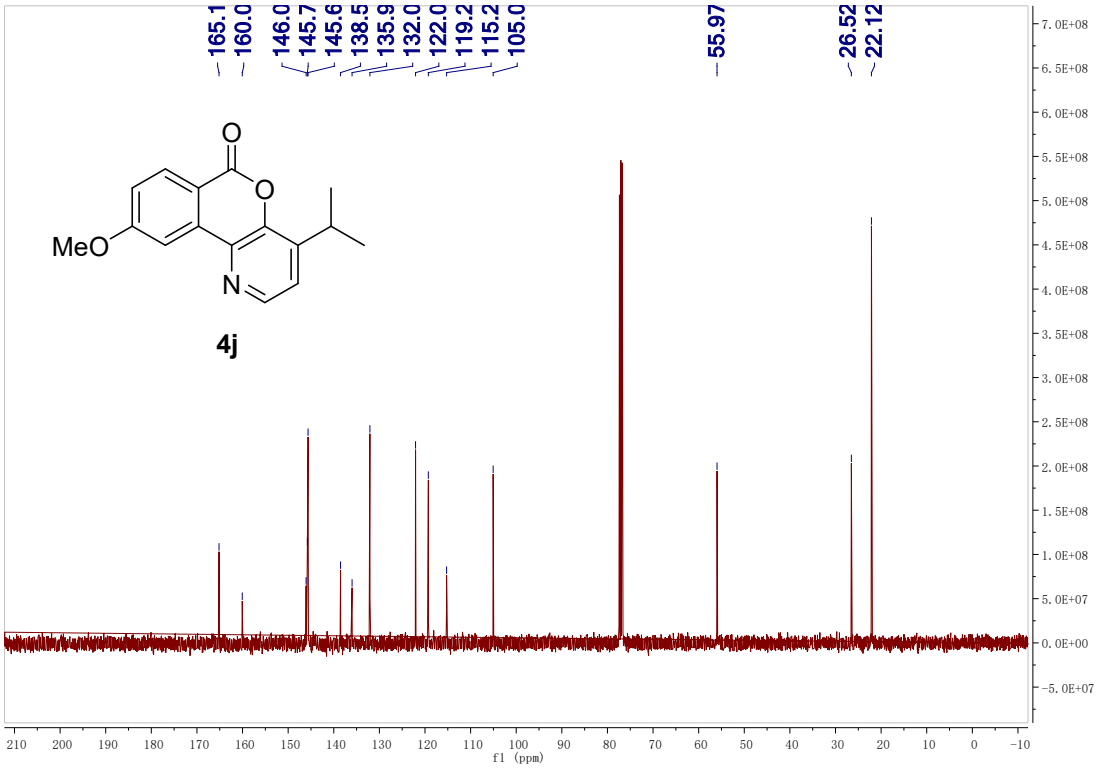

Figure S125. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4j**

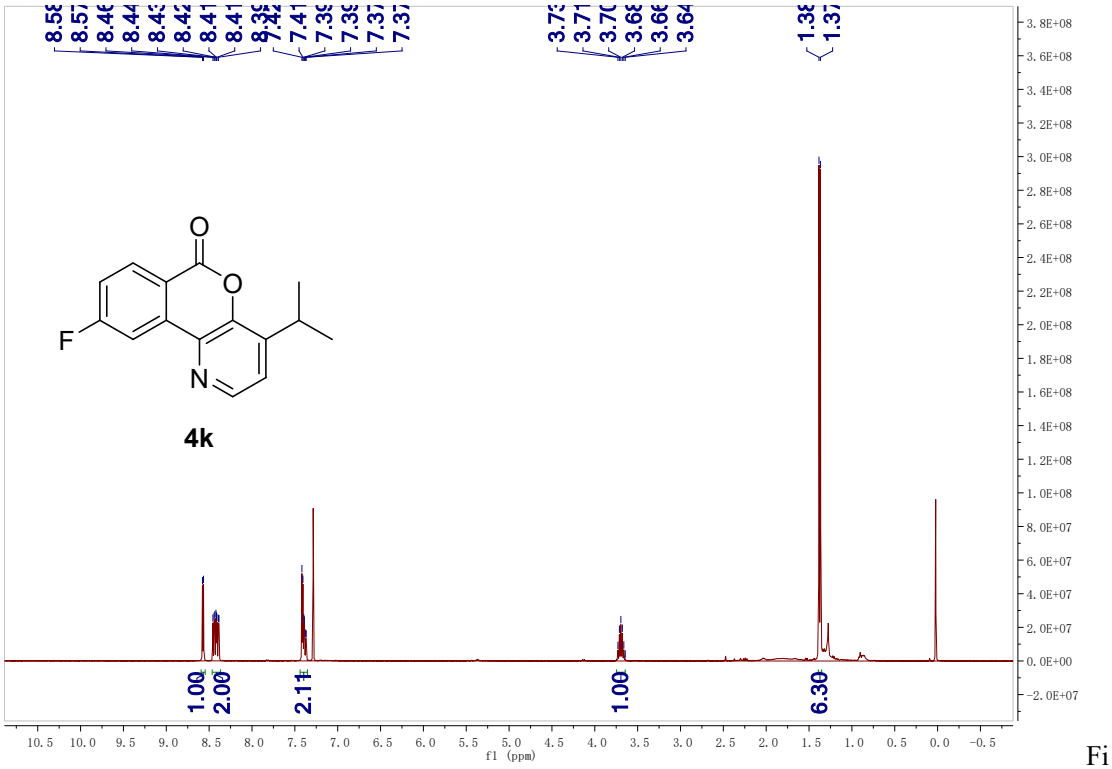

Figure S126. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **4k**

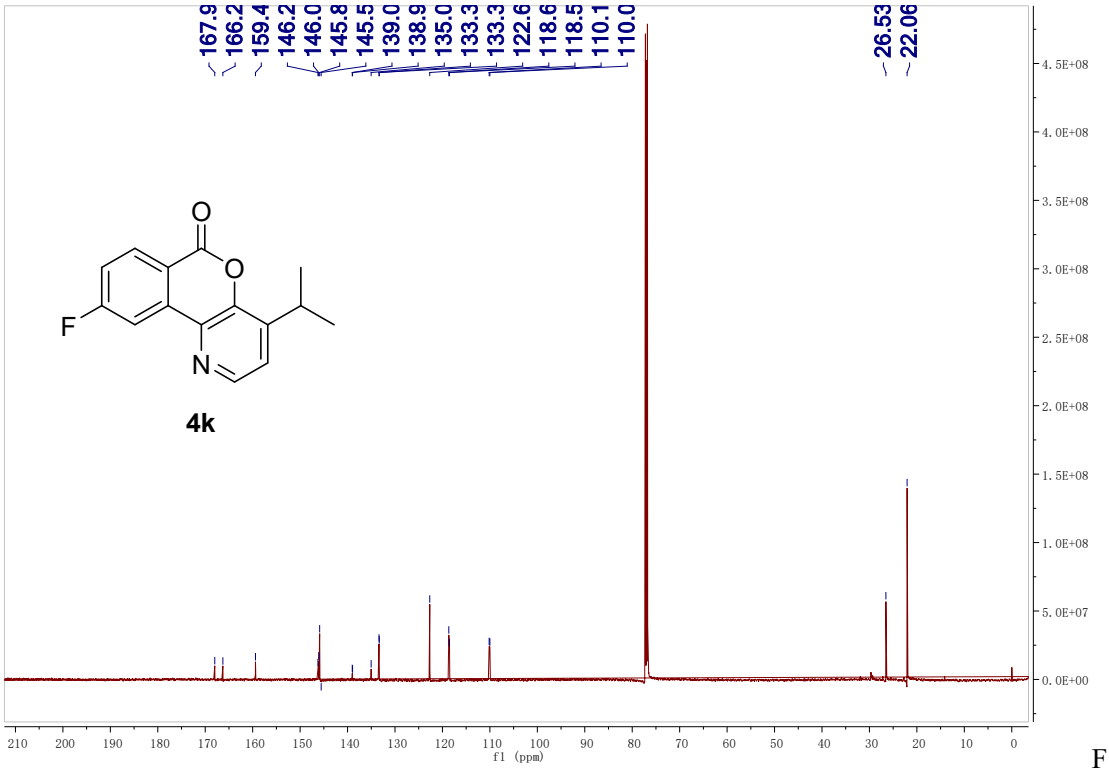

Figure S127. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **4k**

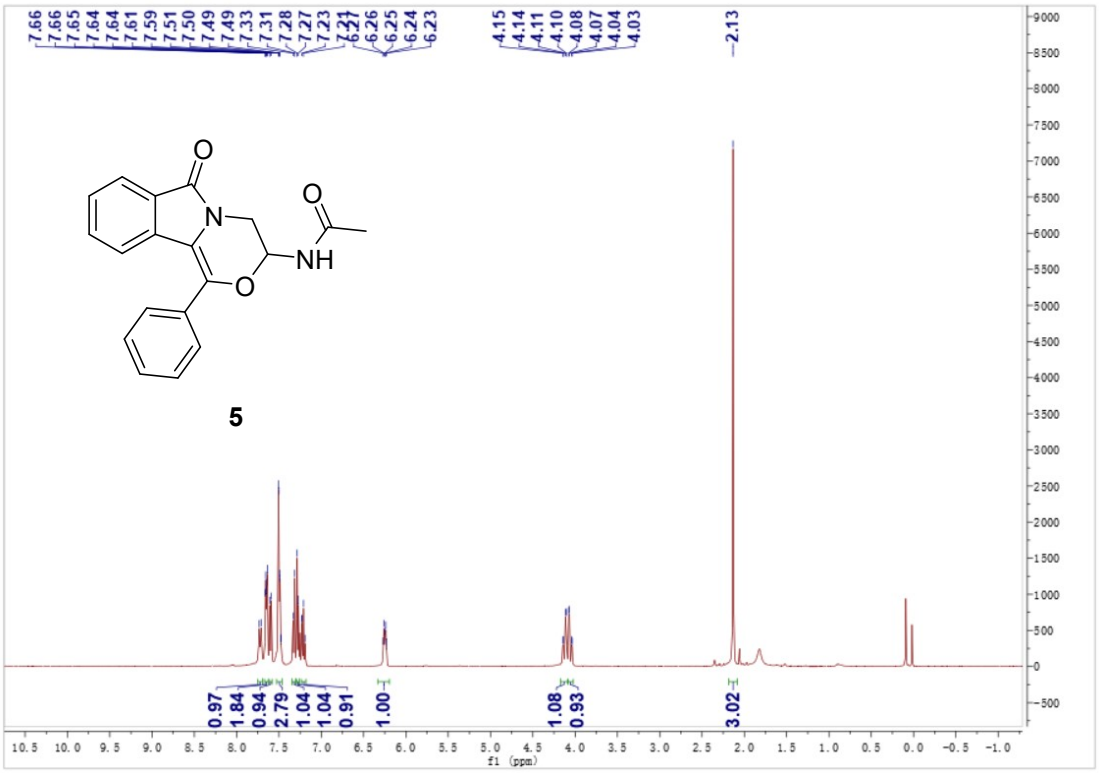

Figure S128. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **5**

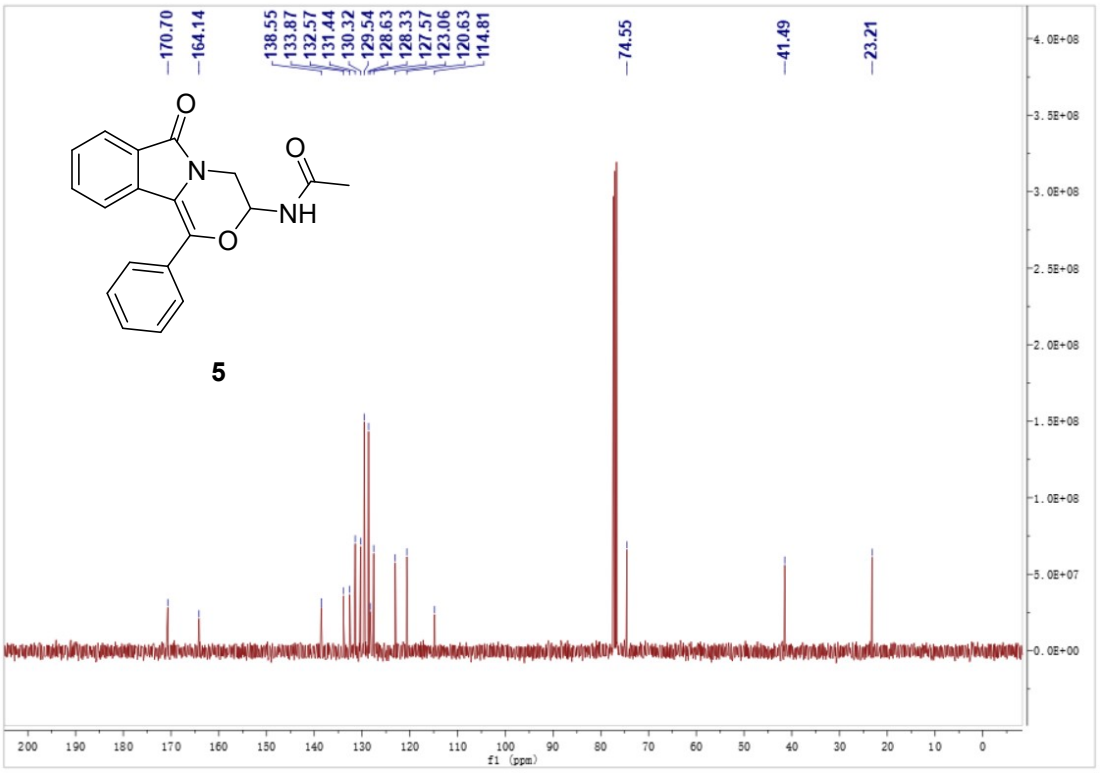

Figure S129. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **5**

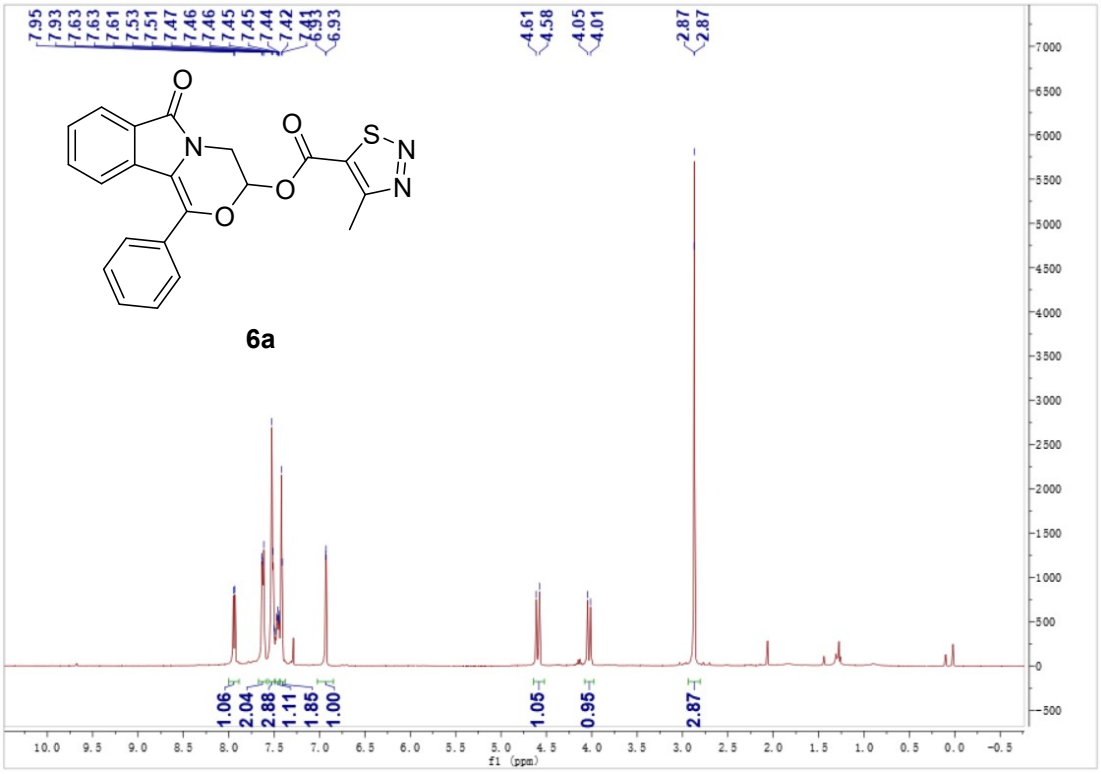

Figure S130. ^{1}H NMR (400 MHz, Chloroform-*d*) spectrum of compound **6a**

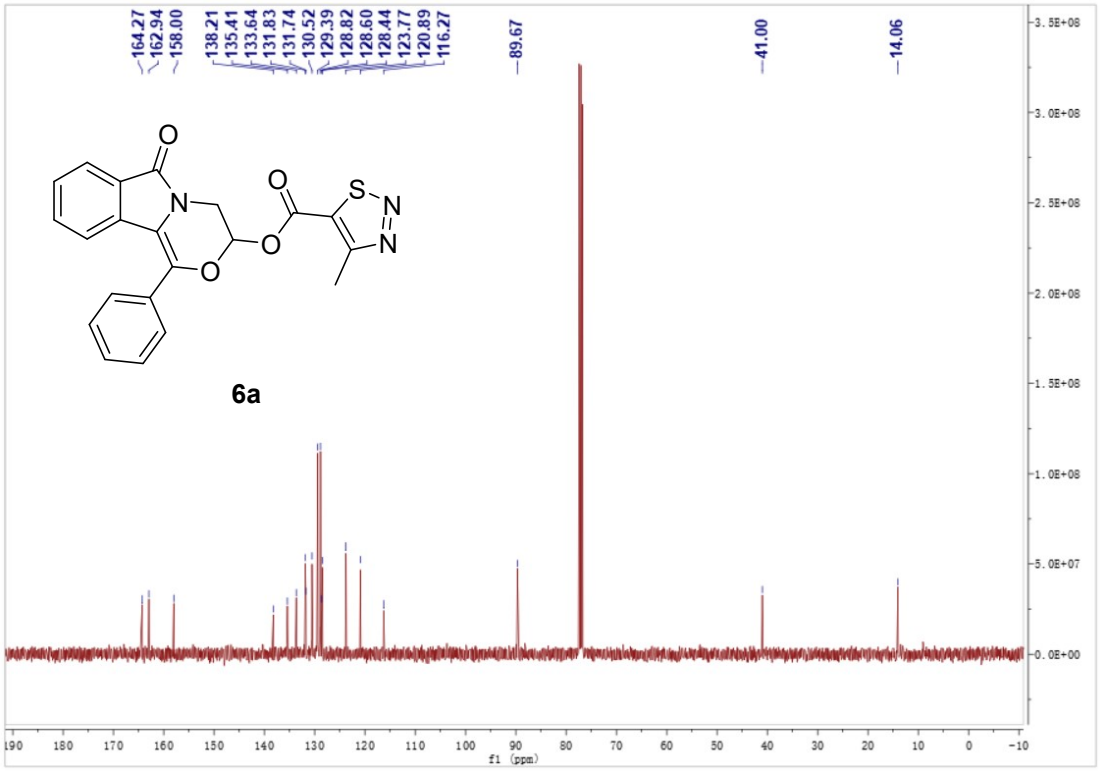

Figure S131. ^{13}C NMR (100 MHz, Chloroform-*d*) spectrum of compound **6a**

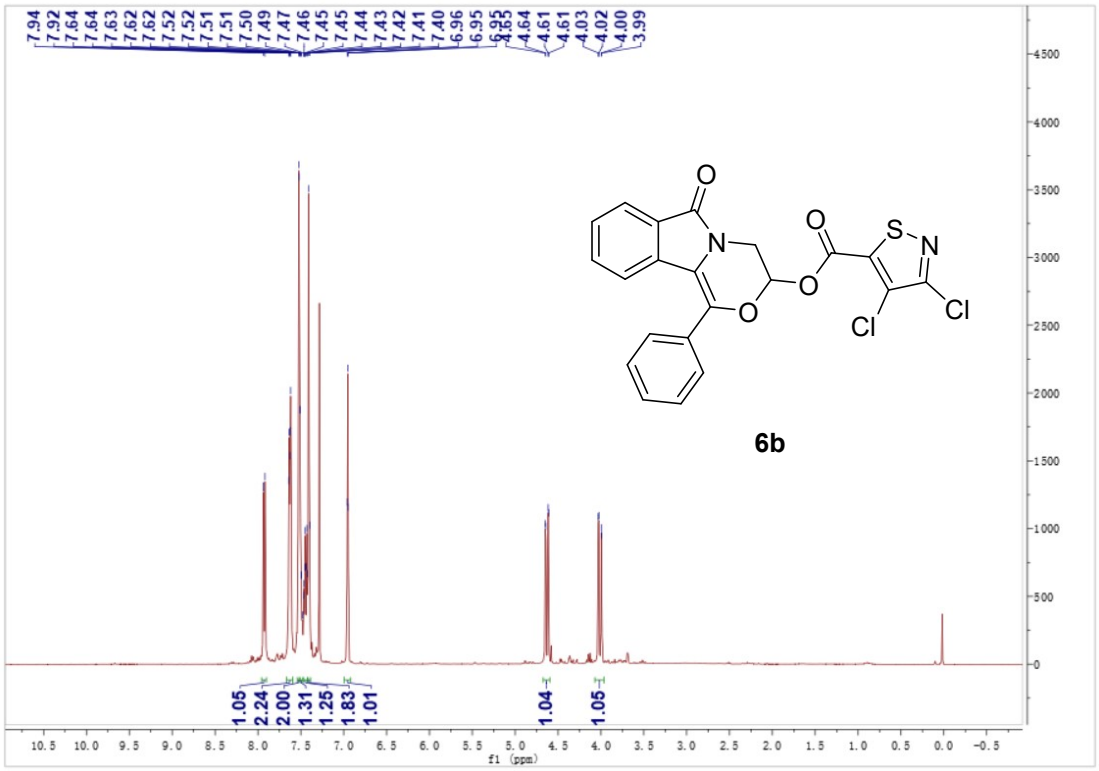

Figure S132. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **6b**

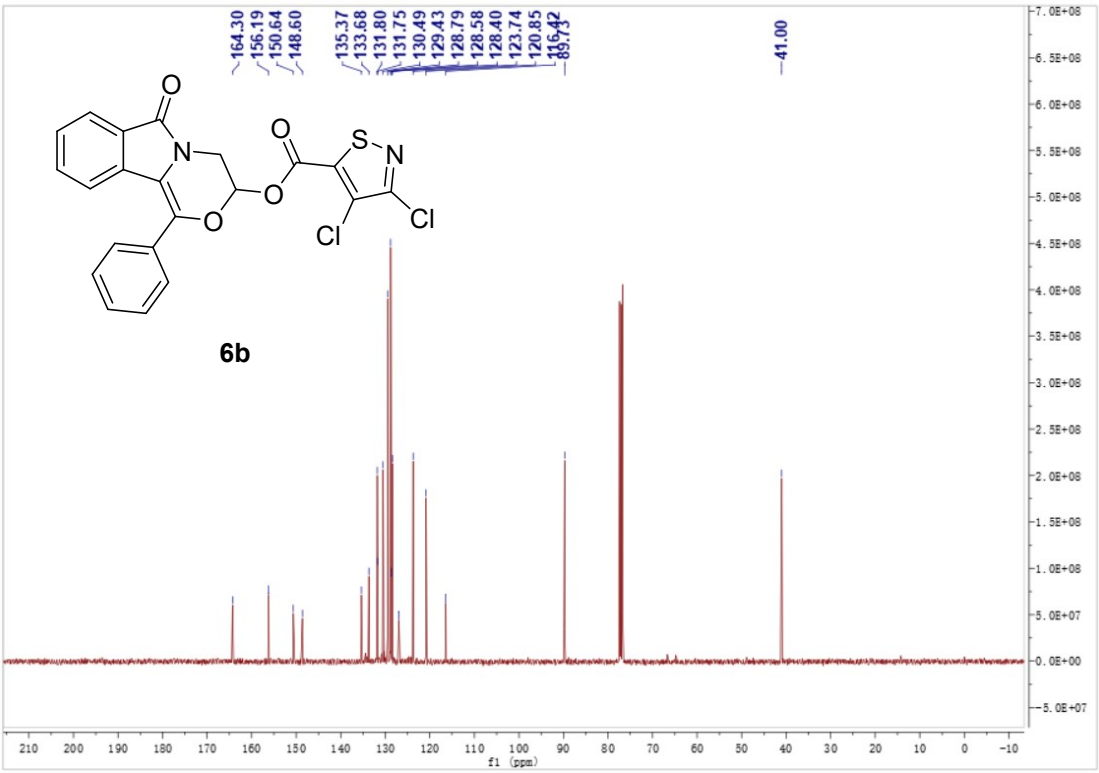

Figure S133. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **6b**

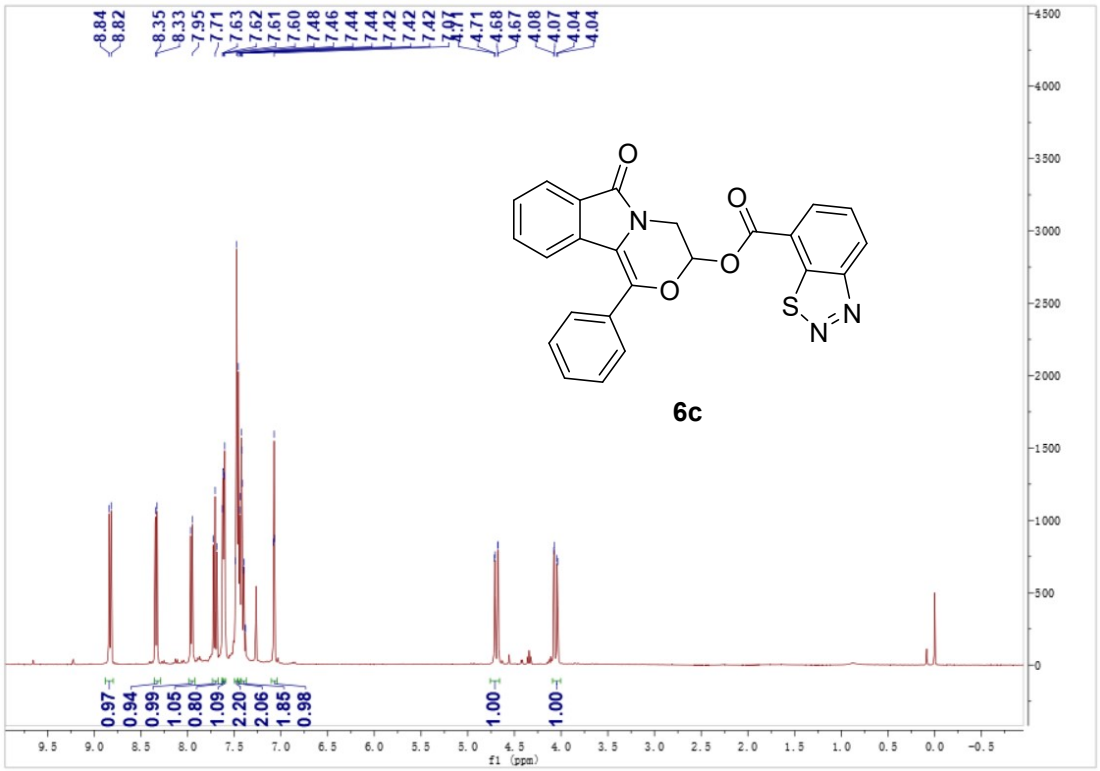

Figure S134. [1]H NMR (400 MHz, Chloroform-*d*) spectrum of compound **6c**

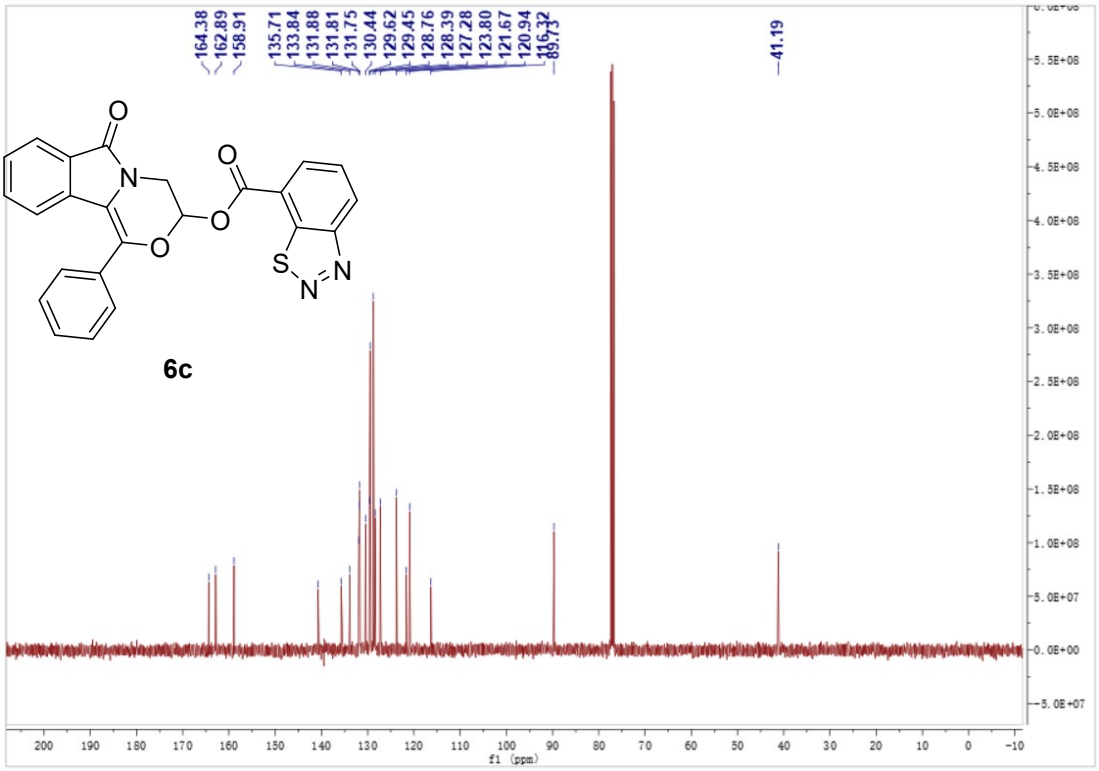

Figure S135. [13]C NMR (100 MHz, Chloroform-*d*) spectrum of compound **6c**

13. Copies of IR Spectra for Compounds 4

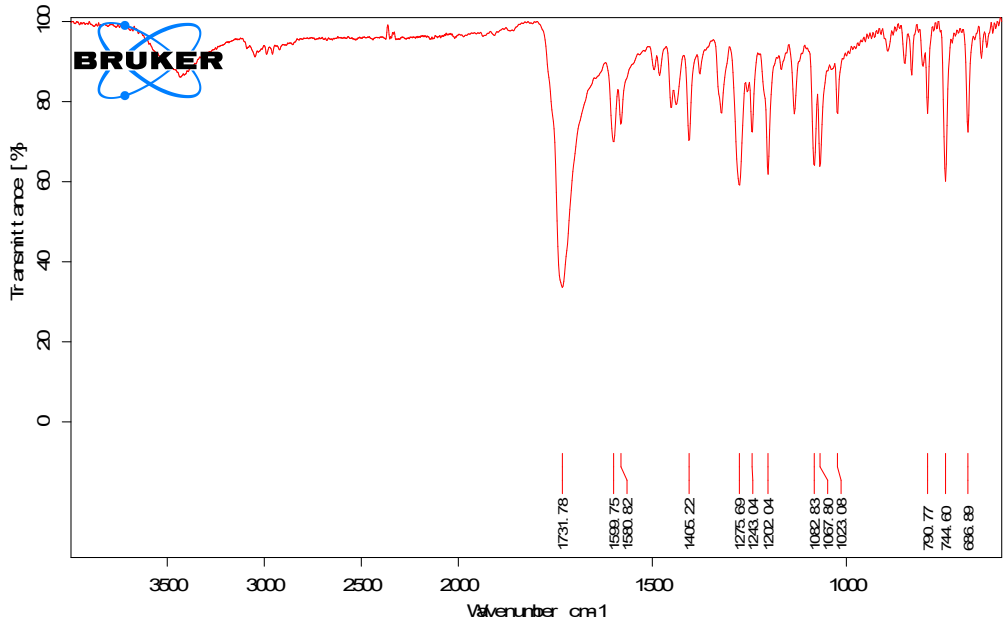

Figure S136. IR spectrum of compound **4a**

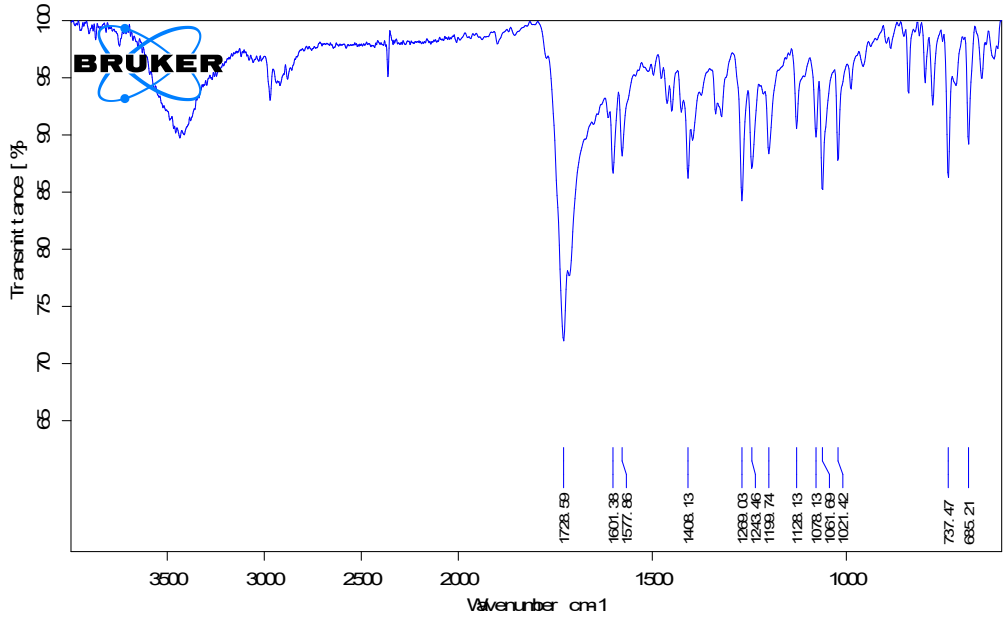

Figure S137. IR spectrum of compound **4b**

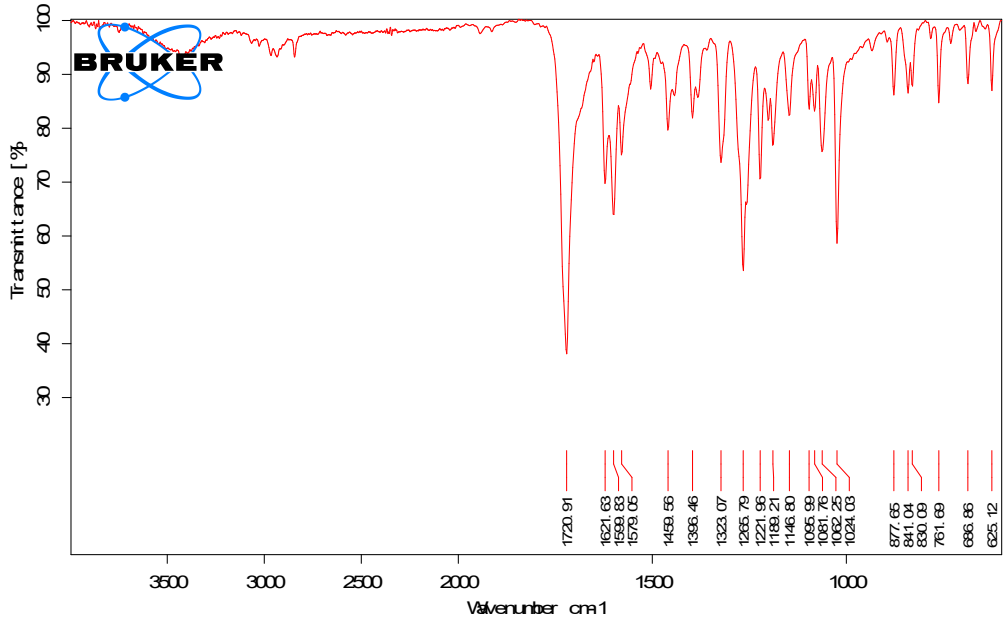

Figure S138. IR spectrum of compound **4c**

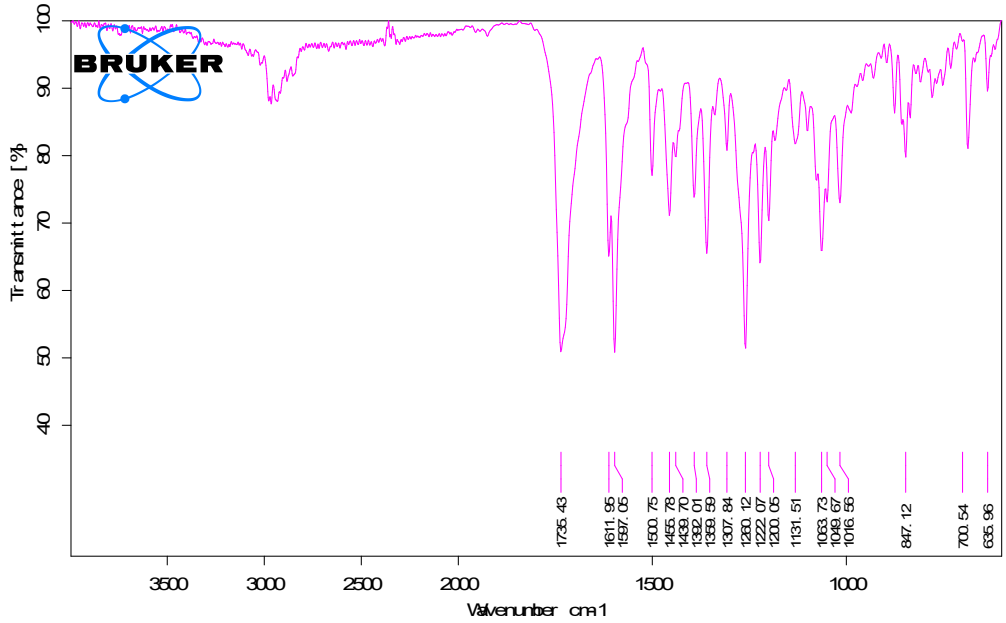

Figure S139. IR spectrum of compound **4d**

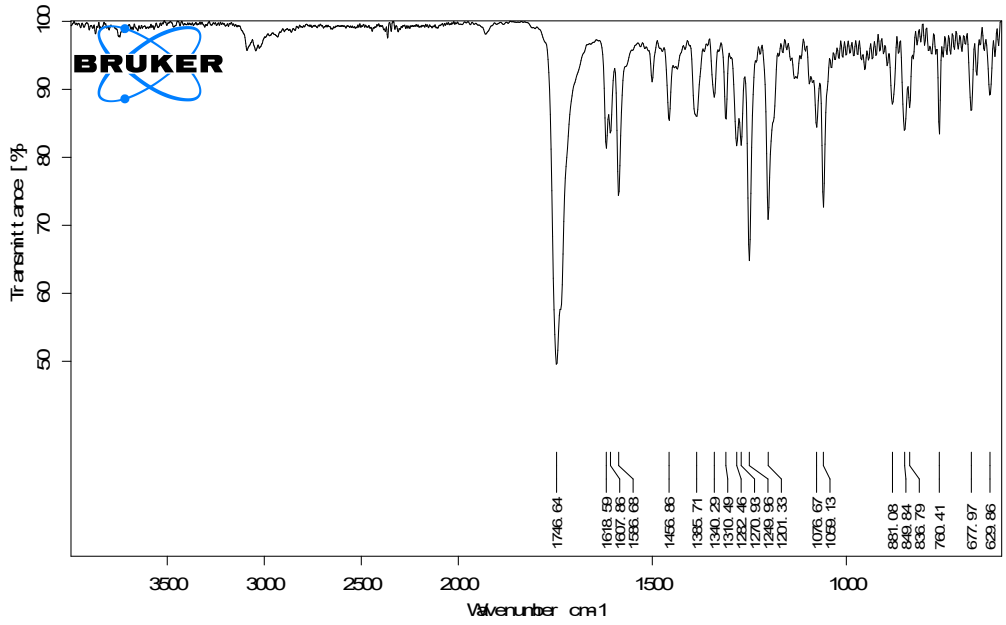

Figure S140. IR spectrum of compound **4e**

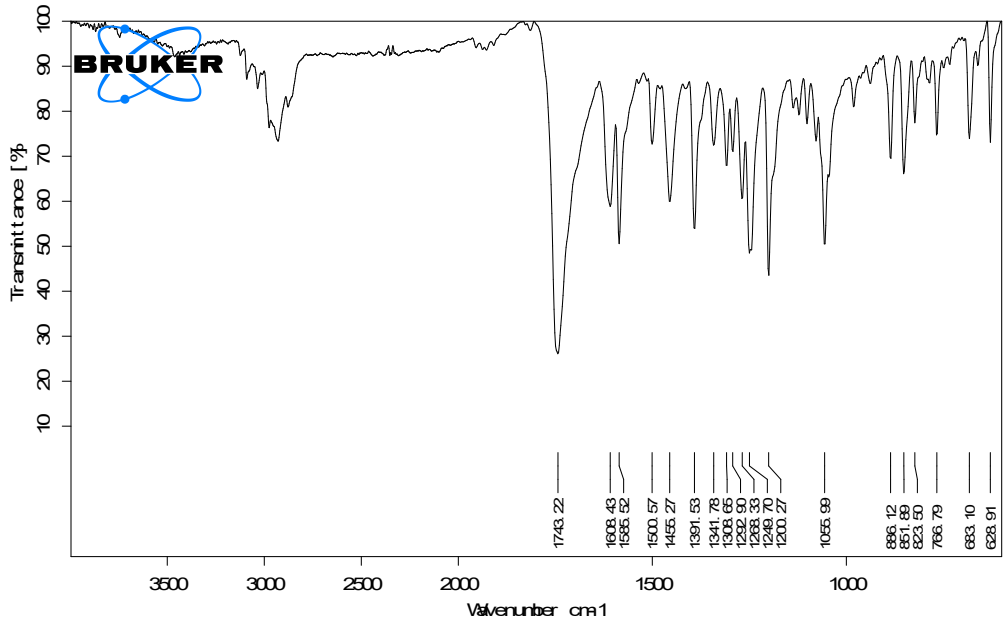

Figure S141. IR spectrum of compound **4f**

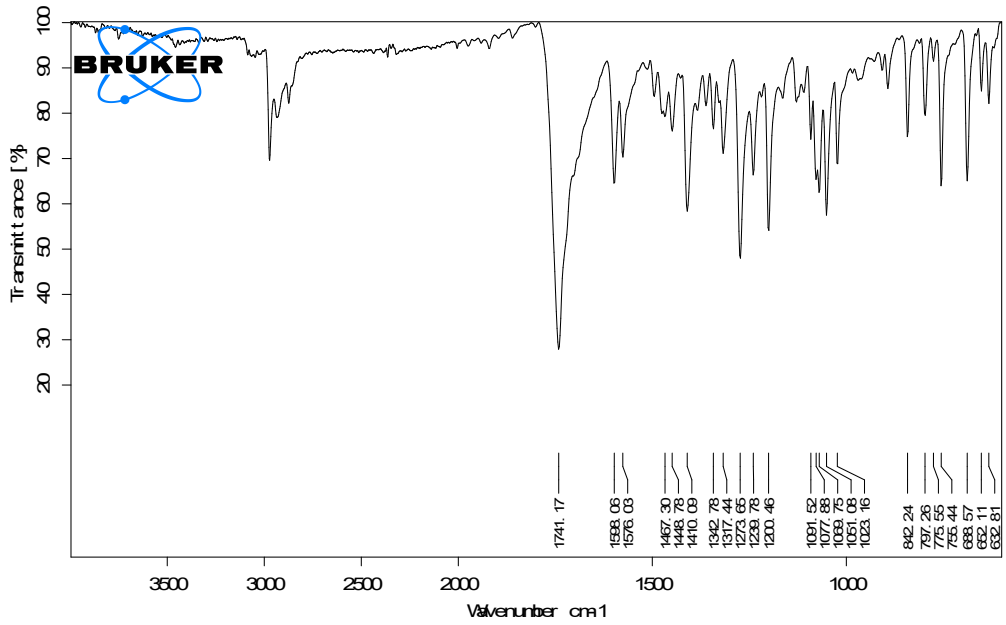

Figure S142. IR spectrum of compound **4g**

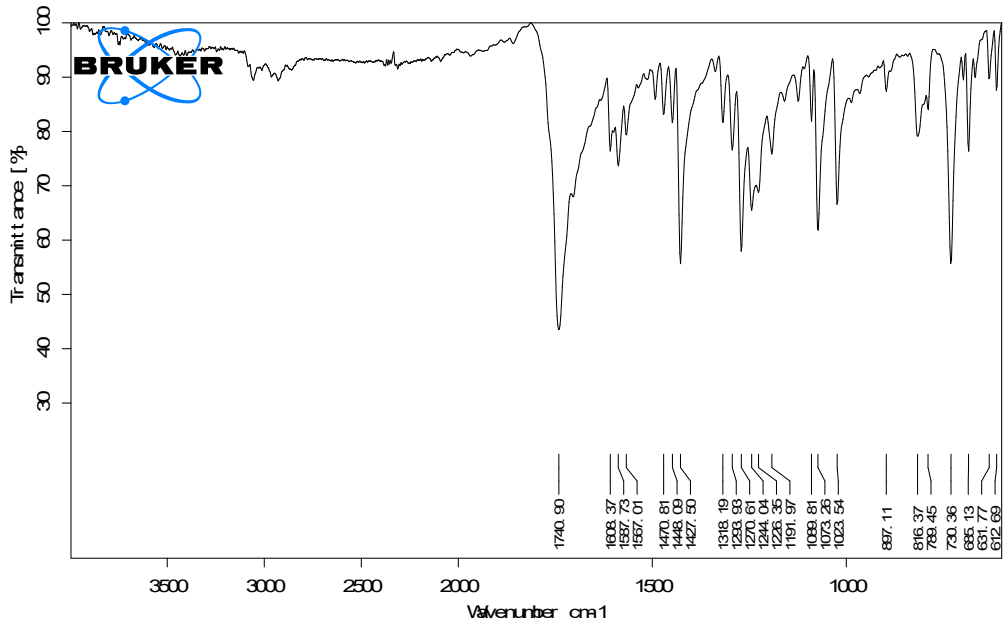

Figure S143. IR spectrum of compound **4h**

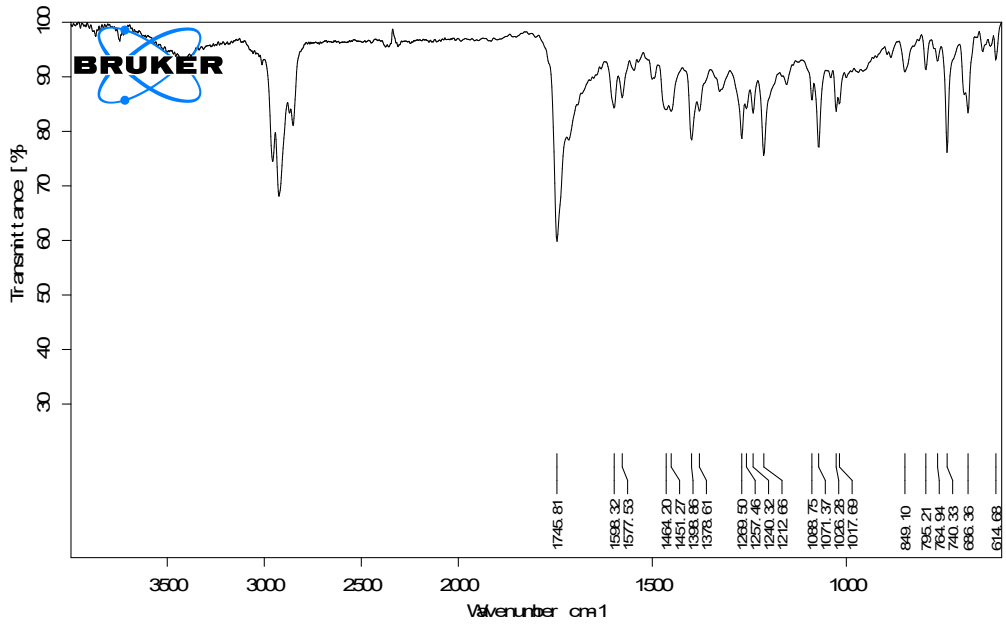

Figure S144. IR spectrum of compound **4i**

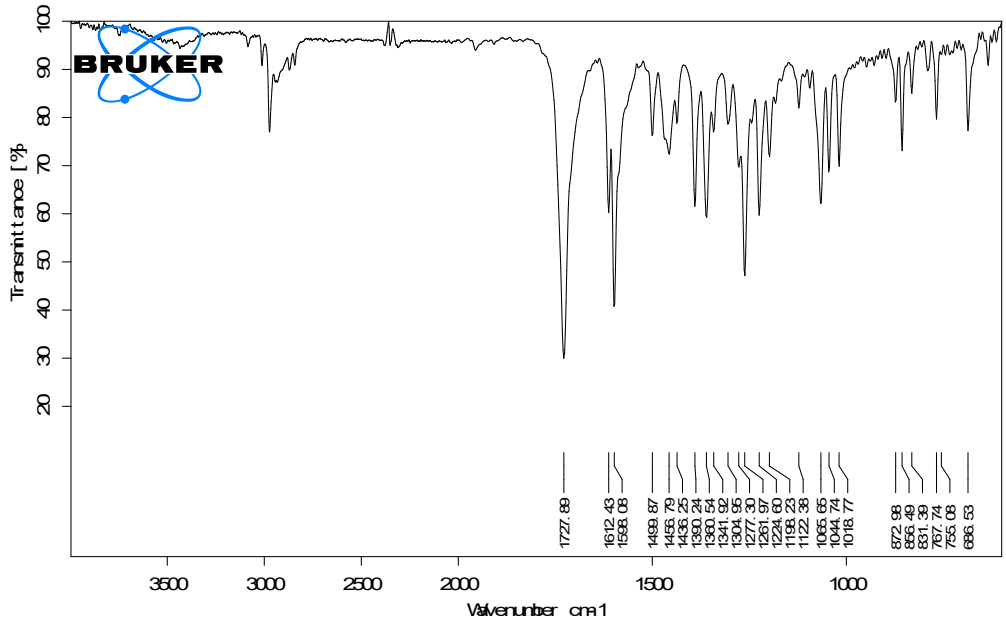

Figure S145. IR spectrum of compound **4j**

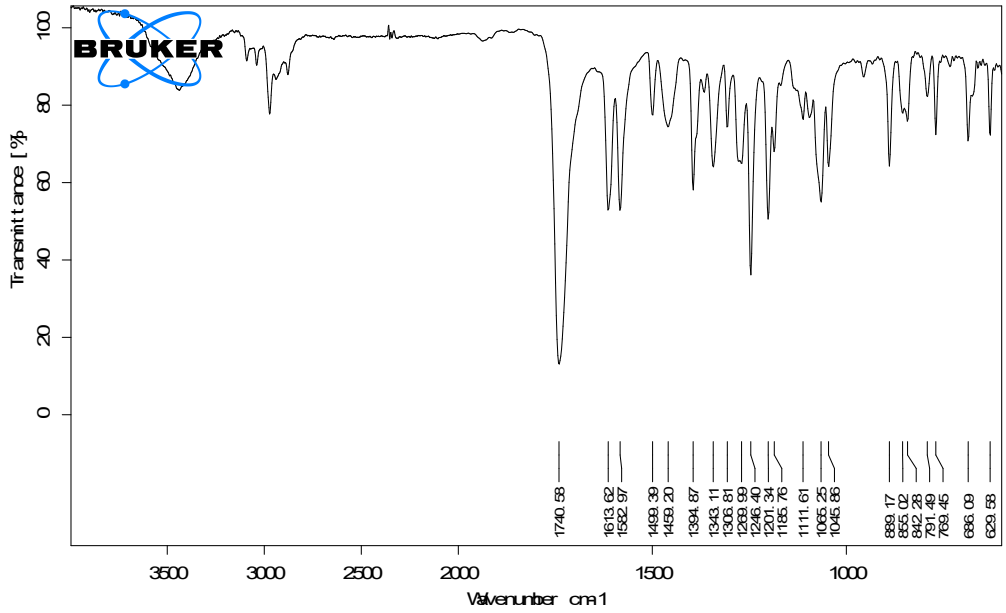

Figure S146. IR spectrum of compound **4k**