Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Rapid Synthesis of Spirodienones *via* Electrochemical Dearomative Spirocyclization in Flow

Nan Li,[†a] Zhaojiang Shi,[†a] Yaofeng Yuan,[a] Zhen Li[b] and Ke-Yin Ye*[a]

[a] Institute of Pharmaceutical Science and Technology, College of Chemistry, Fuzhou University, Fuzhou 350108, China.

[b] Institute of Molecular Aggregation Science, Tianjin University, Tianjin 300072, China.

† These authors contributed equally to this work.

Emails: kyye@fzu.edu.cn

Table of Contents

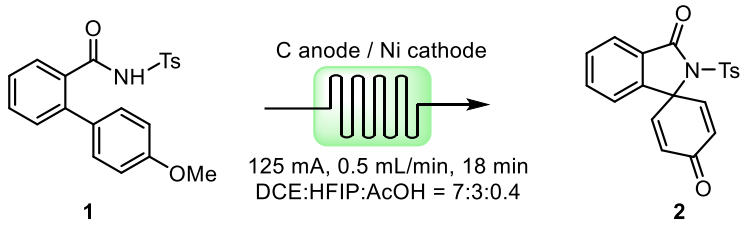
1. General Information

All reactions were performed under an atmosphere of argon using standard Schlenk techniques unless otherwise indicated. All commercial reagents were used without further purification unless otherwise noted. Reactions were monitored by thin-layer chromatography (TLC) analysis. TLC plates were viewed under UV light and stained with potassium permanganate. Yields refer to products isolated after purification by column chromatography unless otherwise stated. Proton nuclear magnetic resonance (^{1}H NMR) spectra, carbon nuclear magnetic resonance (^{13}C NMR) spectra, and fluorine nuclear magnetic resonance (^{19}F NMR) were recorded on Bruker AV-400 (400 MHz), JEOL-500 (500 MHz) spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances IR spectra were obtained from Thermo Scientific NICOLET 380 FT-IR (KCl card). HRMS were obtained on an Exactive Plus LC-MS (ESI) mass spectrometer with the use of a quadrupole analyzer. Cyclic voltammetry data were measured with a CHI 760E potentiostat (Chinstruments). All chemicals were purchased from *Innochem or Energy Chemical* and used as received.

Electrolysis experiments were performed using MESTEK DC power supply. Electrode clips (PT-1 or PT-3) and platinum plate (99.99%, 15*15*0.3 mm or 30*30*0.1 mm) was purchased from Gaoss Union. The carbon cloth (CeTech WOS1002) was cut into 15 x 15 x 0.1 mm pieces before use, and was clamped between electrode clips.

2. Optimization of Reaction Conditions

Table S1. Optimization of conditions



Entry	Deviation from standard conditions	Yield of **2** (%)[b]
1	none	74%/73%[c]
2	115 mA	59%
3	120 mA	65%
4	130 mA	57%
5	0.4 mL/min	71%
6	0.6 mL/min	65%
7	5 mol% $^{n}Bu_4NBF_4$ was added	50%
8	DCE:HFIP:AcOH = 7:3:0.1	47%

[a]Reaction conditions: graphite anode, Ni cathode, fluorinated ethylene propylene (FEP) foil spacer (0.25 mm thickness). **1** (0.04 M), 5.0 mL of the outlet solution was collected and analyzed. [b]Yield determined by ^{1}H-NMR analysis using CH_2Br_2 as the internal standard.[c]Isolated yield

3. Design of the Flow Electrolysis Cell

The design is shown in Figure S1. The flow electrolysis cell is assembled using two aluminum bodies (① and ⑤, 75 mm x 75 mm x 15 mm) with a groove (50 mm x 50 mm x 3.0 mm). The anode (④) , which is made of graphite (C, 49 mm x 49 mm x 5.0 mm), is insulated from the aluminum body by PTFE or silicone film. The cathode (②) is a Ni plate (49 mm x 49 mm x 3.0 mm). The anode and cathode are held apart by a fluorinated ethylene propylene (FEP) foil (③) of 250 μm thickness. A rectangular reaction channel (total length: 313 mm, width: 3.2 mm) is cut in the FEP foil to give an overall channel volume of 250 μL. The whole device is held together by steel screws. The inside view of the device is shown in Figure S1 A. The reaction setups are shown in Figure S1 B.

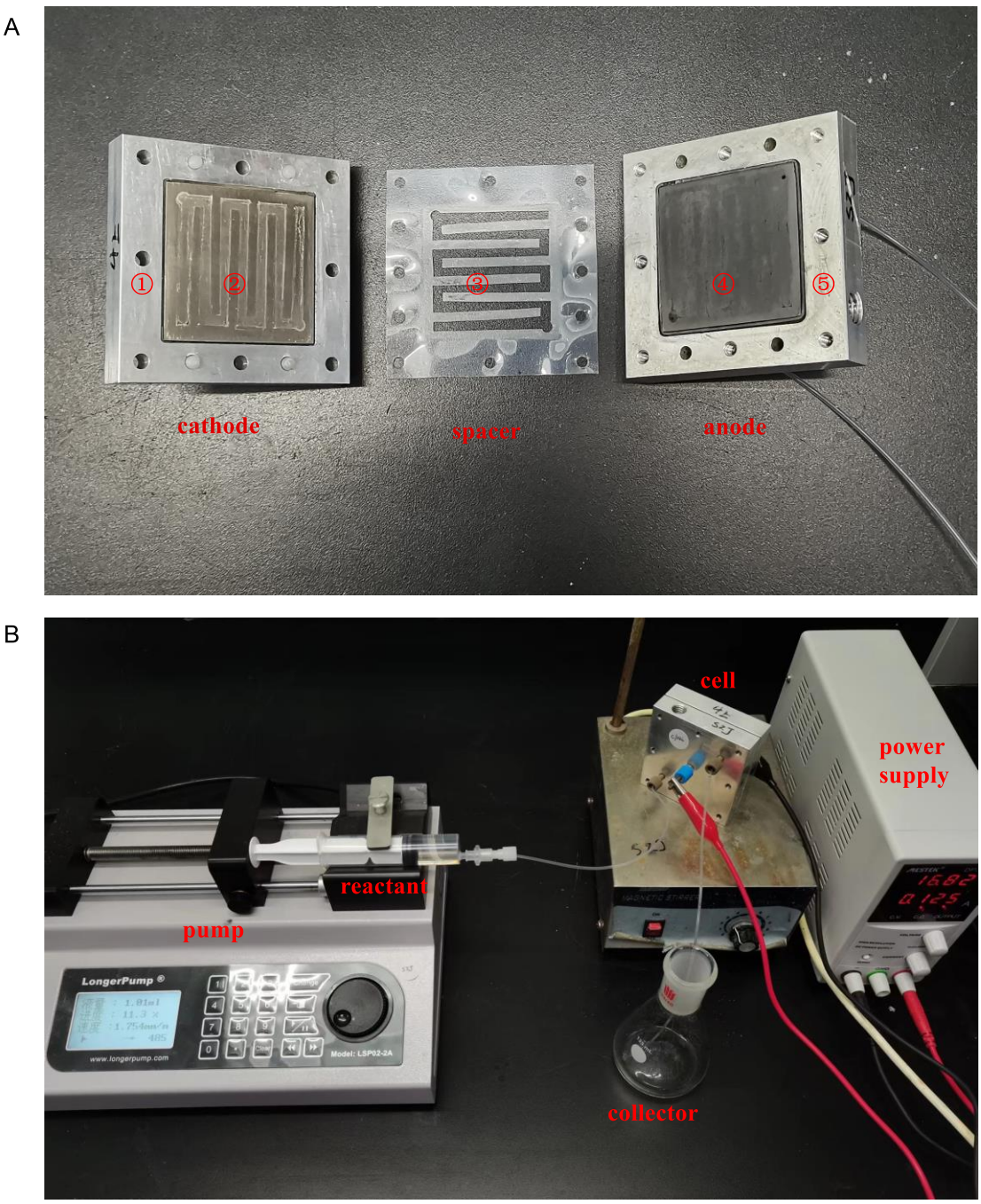


Figure S1. Flow electrolysis setups. Details of the reactor have been reported.[1]

4. General Procedures

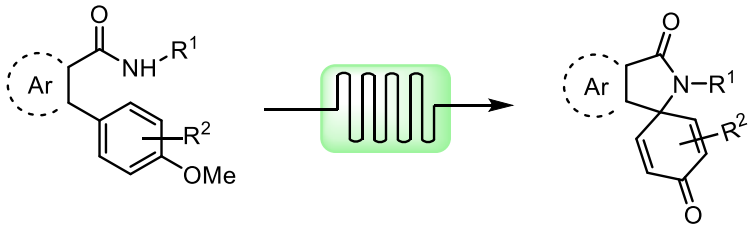
Method A: General procedure for the preparation of substituted 2-(Aryl)-N-tosylbenzamides[2-5]

Step 1: Methyl 2-iodobenzoate (17 mmol) was added to arylboronic acid (22 mmol) and Na_2CO_3 (3.6 g, 34 mmol) dissolved in THF (68 mL) and water (34 mL) mixed solvents. The reaction mixture was degassed three times and charged with N_2, after which $PdCl_2(PPh_3)_2$ (8 mol%, 1 g, 1.4 mmol) was added. The reaction mixture was heated to 60 ℃ overnight. The resulting reaction mixture was cooled to room temperature and added to water, the product was extracted with dichloromethane three times. The combined organic phases were dried with Na_2SO_4 and the solvent was evaporated *in vacuo*. The product was purified by column chromatography to give a colorless liquid.

Step 2: The methyl 2-arylbenzoate was dissolved in a solution of 3.4 g NaOH in 50 mL H_2O and 50 mL MeOH, and then was stirred at 50 ℃ for 6 h. MeOH was removed under vacuum and the reaction mixture was diluted with H_2O, and washed with dichloromethane. The aqueous phase was acidified with 3N HCl, then extracted with dichloromethane three times. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, filtered and the filtration was evaporated under reduced pressure to give the desired product as a solid.

Step 3: An oven-dried round-bottom flask was charged with carboxylic acid (5 mmol), sulfonamide (5 mmol), DMAP (7.5 mmol), and DCM (0.05-0.1 M), EDC (6 mmol) in DCM was added dropwise to the above solution under a nitrogen atmosphere. The reaction mixture was kept stirring at r.t. for 16 h. The reaction was then quenched by HCl (2 M), and extracted with DCM. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo* to obtain a crude residue. The crude residue was further purified by recrystallization from DCM/petroleum (PE).

Method B: General procedure for the flow electrolysis



The electrolysis was conducted with a constant current of 125 mA using a flow electrolytic cell, which was equipped with a graphite anode and a Ni cathode with a surface area of 10 cm^2 and interelectrode distance of 250 μm (Figure S1). The substrate (0.04 M in DCE/HFIP(1,1,1,3,3,3-

hexafluoro-2-propanol)/AcOH (v/v) = 7/3/0.4) was pushed using a syringe pump to pass through the flow electrolytic cell with a flow rate of 0.5 mL min^{-1}. In the beginning the system was stabilized for 2 min. After steady state was reached, the outlet solution was collected for 18 min (9 mL). The formation of bubbles in the tube can be observed during the reaction (Figure S2). The reaction mixture was concentrated *in vacuo*, and the crude residue was subjected to flash column chromatography on silica gel to yield the desired product.

The conditions for the synthesis of compounds **5-6**, **11-14**, **18-19, 26-27** were slight modified with an extra addition of 5 mol% $^{n}Bu_4NOAc$, a constant current electrolysis of 200 mA and a voltage of 31V.

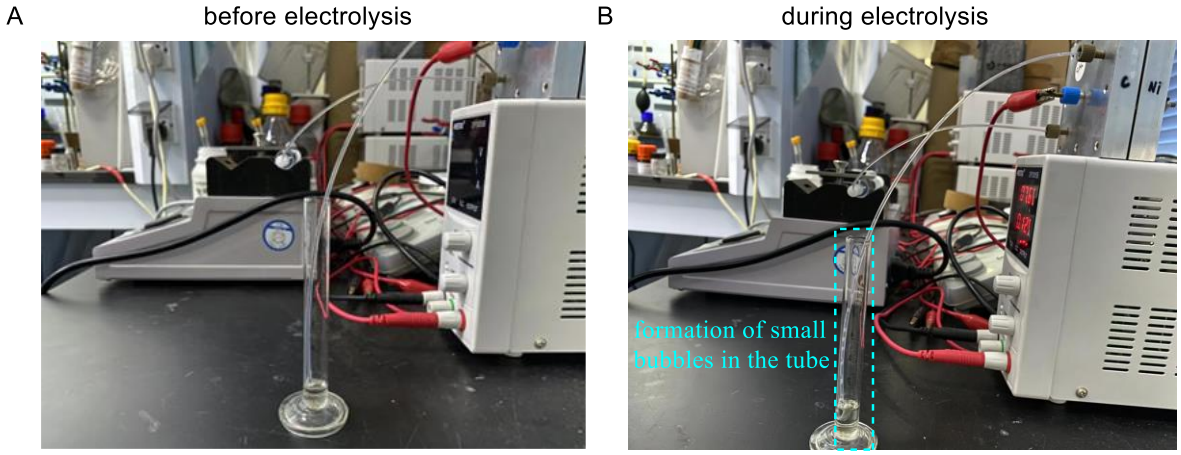
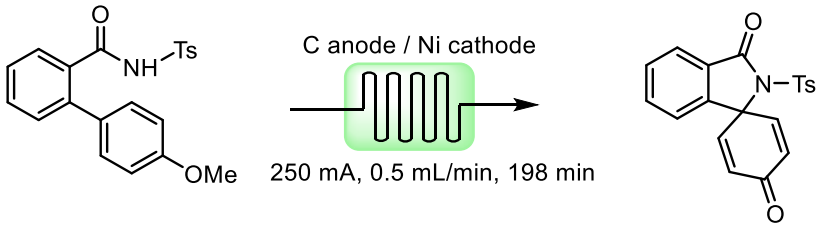


Figure S2. Bubble formation in the tube.

Method C: Gram-scale synthesis



The gram-scale electrolysis was conducted with a constant current of 250 mA using a flow electrolytic cell, which was equipped with a graphite anode and a Ni cathode with a surface area of 10 cm^2 and interelectrode distance of 250 μm (Figure S3). The substrate (0.08 M) and $^{n}Bu_4NOAc$ (10 mol%) were dissolved in DCE/HFIP/AcOH (v/v = 35/14/1), the reactant was pushed using a syringe pump to pass through the flow electrolytic cell with a flow rate of 0.5 mL min^{-1}. In the beginning the system was stabilized for 2 min. After steady state was reached, the outlet solution was collected for 198 min (198 mL). The reaction mixture was concentrated *in vacuo*, and the crude

residue was subjected to flash column chromatography on silica gel to yield the desired product (79%, 4.61g).

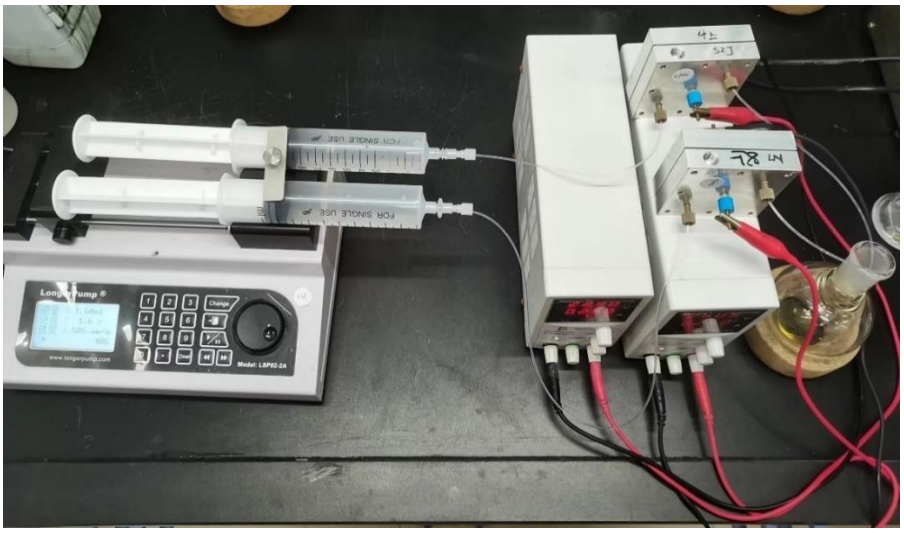
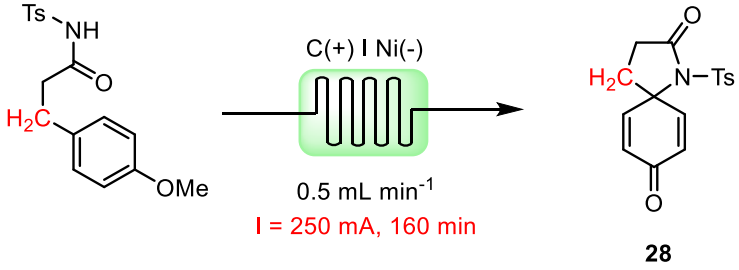
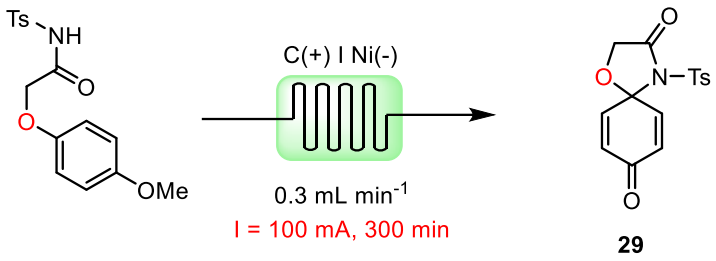


Figure S3. Flow electrolysis setups.

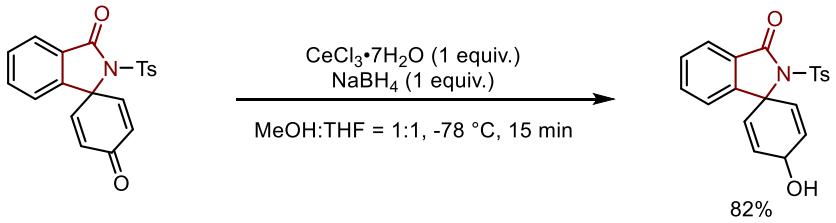


The gram-scale electrolysis was conducted with a constant current of 250 mA using a flow electrolytic cell, which was equipped with a graphite anode and a Ni cathode with a surface area of 10 cm^2 and interelectrode distance of 250 μm (Figure S1). The substrate (0.08 M) and $^nBu_4NOAc$ (5 mol%) were dissolved in DCE/HFIP/AcOH (v/v = 35/14/1), the reactant was pushed using a syringe pump to pass through the flow electrolytic cell with a flow rate of 0.5 mL min^{-1}. In the beginning the system was stabilized for 2 min. After steady state was reached, the outlet solution was collected for 160 min (80 mL). The reaction mixture was concentrated *in vacuo*, and the crude residue was subjected to flash column chromatography on silica gel to yield the desired product (54%, 1.09g).



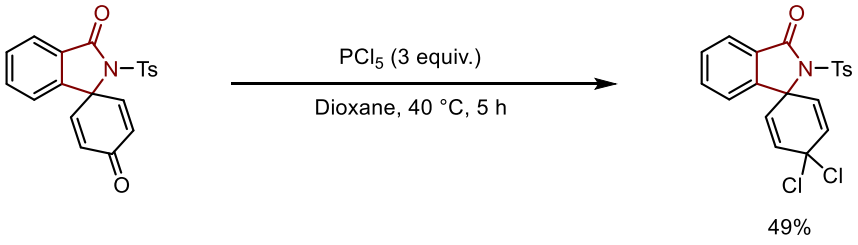
The gram-scale electrolysis was conducted with a constant current of 100 mA using a flow electrolytic cell, which was equipped with a graphite anode and a Ni cathode with a surface area of 10 cm^2 and interelectrode distance of 250 μm (Figure S1). The substrate (0.06 M) and $^nBu_4NOAc$ (5 mol%) were dissolved in DCE/HFIP/AcOH (v/v = 35/14/1), the reactant was pushed using a syringe pump to pass through the flow electrolytic cell with a flow rate of 0.3 mL min^{-1}. In the beginning the system was stabilized for 2 min. After steady state was reached, the outlet solution was collected for 300 min (90 mL). The reaction mixture was concentrated *in vacuo*, and the crude residue was subjected to flash column chromatography on silica gel to yield the desired product (61%, 1.05g).

Method D: Luche reduction of 2 to 24[6]



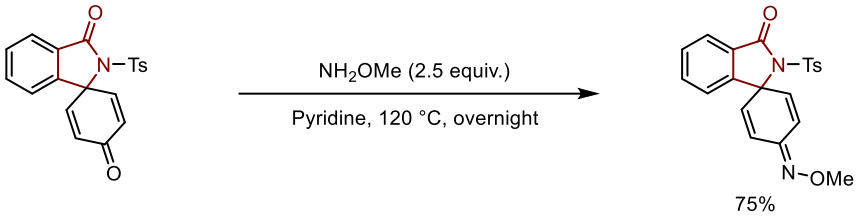
To a solution of **2** (36.5 mg, 0.1 mmol) and $CeCl_3 \cdot 7H_2O$ (37.3 mg, 0.1 mmol) in MeOH (2.5 mL) and THF (2.5 mL) was added $NaBH_4$ (3.8 mg, 0.1 mmol) at −78 °C. After stirring for 15 min, the reaction mixture was diluted with EtOAc and washed with 1 M HCl and brine. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (eluent: petroleum ether/ethyl acetate = 2:1) to give 82% yield of desired product.

Method E: Synthesis of 23[7]



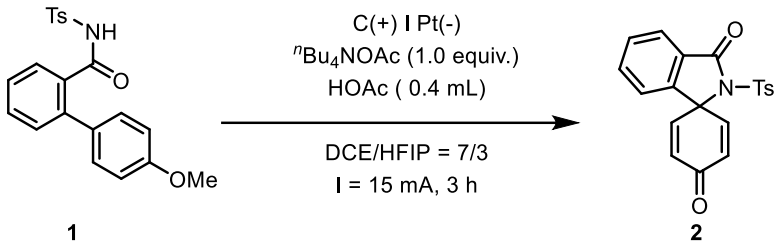
To a solution of **2** (36.5 mg, 0.1 mmol) in dioxane (1 mL) was added PCl_5 (62.4 mg, 0.3 mmol). The reaction mixture was heated to 40 ℃ for 5 h. The reaction mixture was diluted with dichloromethane. Then the reaction solution was slowly added dropwise to the water. The solution was extracted with dichloromethane three times. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (eluent: petroleum ether/ethyl acetate = 10:1 - 5:1) to give 49% yield of desired product.

Method F: Synthesis of the oxime of 22[8]



To a solution of **2** (36.5 mg, 0.1 mmol) in pyridine (2 mL) was added $NH_2OMe \cdot HCl$ (65 mg, 0.25 mmol). The reaction mixture was heated to 120 ℃ overnight. The reaction was then evaporated under reduced pressure and chromatographed (eluent: petroleum ether/ethyl acetate = 5:1 – 2:1) to give 75% yield of the desired product.

Method G: Synthesis of 2 in batch



In an oven-dried undivided three-necked glassware (25 mL) equipped with a stirring bar, **1** (0.4 mmol) and $^{n}Bu_4NOAc$ (0.4 mmol, 1.0 equiv.) were added. The glassware was equipped with carbon cloth (15 mm × 15 mm × 0.1 mm) as the anode and platinum plate (15 mm × 15 mm × 0.3 mm) as the cathode. Under the protection of N_2, CH_3COOH (400 μL) and DCE/HFIP = 7:3 (10 mL) were injected into the glassware *via* syringes. The reaction mixture was stirred and electrolyzed at a constant current of 15 mA at an ambient temperature for 3 h. The reaction mixture was concentrated *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to yield the desired product **2** (111.6 mg, 76%).

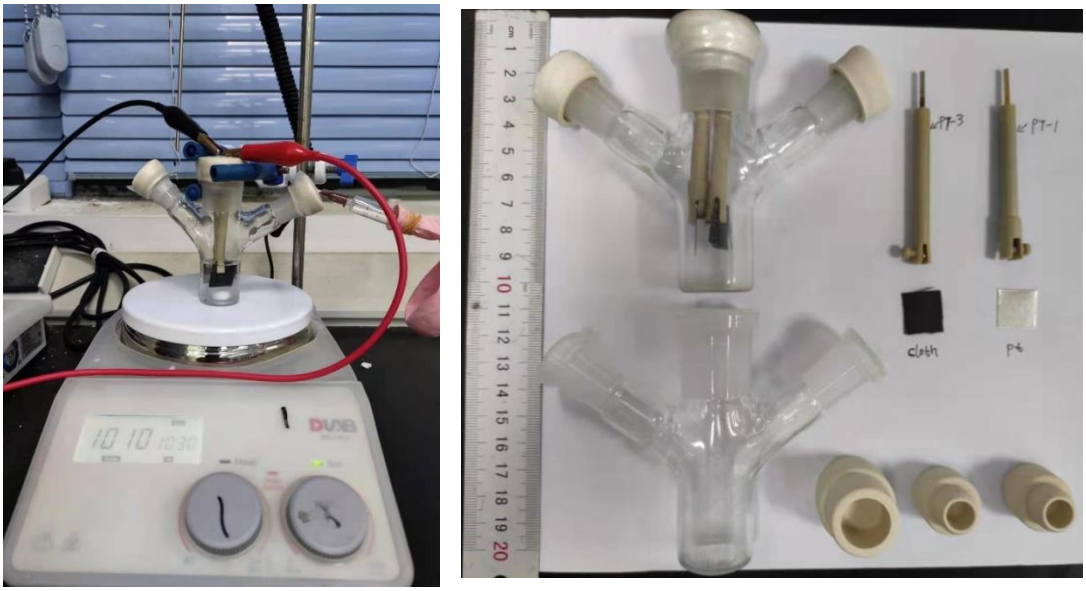


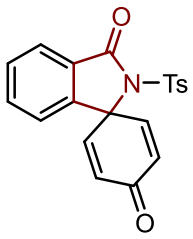
Figure S4. Batch electrolysis setups.

Method H: Synthesis of 2 in IKA ElectraSyn 2.0

In an oven-dried undivided glassware (25 mL) equipped with a stirring bar, **1** (0.4 mmol) and $^{n}Bu_4NOAc$ (0.4 mmol, 1.0 equiv.) were added. The glassware was equipped with carbon block as the anode and platinum plate as the cathode. CH_3COOH (400 μL) and DCE : HFIP = 7:3 (10 mL) were injected into the glassware *via* syringes. The reaction mixture was stirred under the protection of N_2 and electrolyzed at a constant current of 15 mA at an ambient temperature for 3 h. The reaction mixture was concentrated *in vacuo*, the crude residue was subjected to flash column chromatography on silica gel to yield the desired product **2** (79.3 mg, 54%).

Figure S5. Electrolysis using IKA ElectraSyn 2.0.

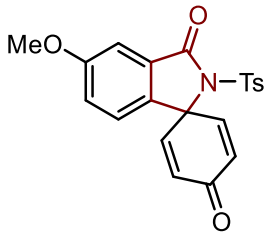
5. Characterization of Products



2: 2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 96.0 mg (73% yield) of **2** as a white solid.

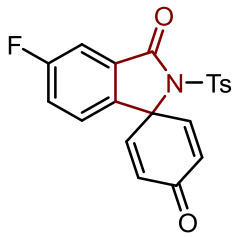
IR (neat, cm^{-1}): 3055 (w), 2924 (w), 1739 (s), 1670 (s), 1466 (m), 1172 (s), 691 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.06 – 7.99 (m, 2H), 7.85 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.64 (td, *J* = 7.6, 1.2 Hz, 1H), 7.53 (td, *J* = 7.5, 1.0 Hz, 1H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.20 (dt, *J* = 7.8, 0.9 Hz, 1H), 6.72 – 6.67 (m, 2H), 6.54 – 6.48 (m, 2H), 2.43 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.5, 165.4, 146.1, 145.8, 141.8, 135.7, 135.1, 130.5, 129.9, 129.8, 129.1, 128.7, 125.8, 123.2, 67.0, 21.8. **HRMS (ESI)** calculated for $C_{20}H_{16}NO_4S^+$ [M+H$^+$]: 366.0795; found: 366.0790.



3: 5'-methoxy-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 89.7 mg (63% yield) of **3** as a white solid.

IR (neat, cm^{-1}): 3058 (w), 2924 (w), 2842 (w), 1734 (s), 1669 (s), 1489 (m), 1168 (s), 660 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.07 – 7.98 (m, 2H), 7.35 (dd, *J* = 8.0, 0.7 Hz, 2H), 7.26 (d, *J* = 2.0 Hz, 1H), 7.17 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.07 (d, *J* = 8.6 Hz, 1H), δ 6.69 – 6.60 (m, 2H), 6.50 – 6.43 (m, 2H), 3.82 (s, 3H), 2.43 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.7, 165.5, 161.6, 146.4, 145.9, 135.8, 133.5, 130.6, 129.8, 129.7, 128.7, 124.2, 123.8, 107.9, 66.7, 56.0, 21.8. **HRMS (ESI)** calculated for $C_{21}H_{18}NO_5S^+$ [M+H$^+$]: 396.0900; found:396.0901.

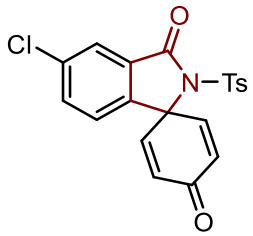


4: 5'-fluoro-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 110.3 mg (80% yield) of **4** as a white solid.

IR (neat, cm^{-1}): 3068 (w), 2925 (w), 1735 (s), 1669 (s), 1482(m), 1271 (s), 1192 (s), 663 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.03 – 7.98 (m, 2H), 7.49 (dd, *J* = 7.0, 2.5 Hz, 1H), 7.38 – 7.27 (m, 3H), 7.19 (dd, *J* = 8.5, 4.1 Hz, 1H), 6.70 – 6.63 (m, 2H), 6.53 – 6.46 (m, 2H), 2.43 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.4, 164.3 (d, *J* = 3.5 Hz), 163.8 (d, *J* = 252.8 Hz), 146.1, 145.7, 137.3, 135.4, 131.3 (d, *J* = 9.1 Hz), 130.1, 129.9, 128.7, 125.3 (d, *J* = 8.6 Hz), 123.0 (d, *J* = 24.1 Hz), 112.3 (d, *J* = 24.0 Hz), 66.6, 21.8. **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -108.2 (m).

HRMS (ESI) calculated for $C_{20}H_{15}FNO_4S^+$ [M+H$^+$]: 384.0700; found: 384.0700.

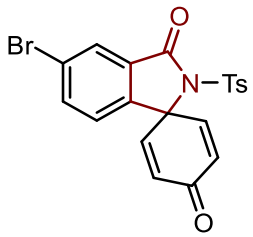


5: 5'-chloro-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (5 mol% ^{n}Bu$_4$NOAc was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 128.1 mg (89% yield) of **5** as a white solid.

IR (neat, cm^{-1}): 3058 (w), 2925 (w), 1742 (s), 1672 (s), 1467 (m), 1172 (s), 735 (m), 697 (s); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.00 (d, *J* = 8.1 Hz, 2H), 7.78 (d, *J* = 2.0 Hz, 1H), 7.59 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.3 Hz, 1H), 6.66 (d, *J* = 9.7 Hz, 2H), 6.50 (d, *J* = 9.7 Hz, 2H), 2.43 (s, 3H)；**^{13}C NMR (101 MHz, Chloroform-*d*)** δ 184.3, 164.1, 146.1, 145.4, 140.0, 137.0, 135.4, 135.3, 130.8, 130.2, 129.9, 128.7, 125.7, 124.6, 66.7, 21.8.

HRMS (ESI) calculated for $C_{20}H_{15}ClNO_4S^+$ [M+H$^+$]: 400.0405; found: 400.0406.

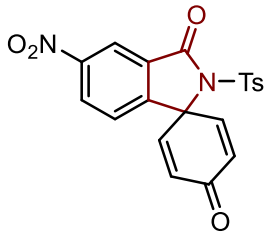


6: 5'-bromo-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (5 mol% $^{n}Bu_4NOAc$ was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 140.8 mg (88% yield) of **6** as a white solid.

IR (neat, cm^{-1}): 3058 (w), 2924 (w), 1739 (s), 1671 (s), 1463 (m), 1171 (s), 662 (s), 579 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.05 – 7.99 (m, 2H), 7.97 (d, *J* = 1.8 Hz, 1H), 7.75 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 1H), 6.70 – 6.63 (m, 2H), 6.55 – 6.48 (m, 2H), 2.44 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.3, 164.1, 146.2, 145.4, 140.6, 138.2, 135.5, 131.1, 130.3, 129.9, 128.82, 128.79, 124.81, 124.79, 66.8, 21.9.

HRMS (ESI) calculated for $C_{20}H_{15}BrNO_4S^+$ [M+H$^+$]: 443.9900; found: 443.9904.

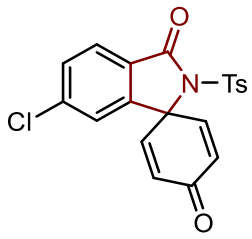


7: 5'-nitro-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 28.1 mg (19% yield) of **7** as a white solid.

IR (neat, cm^{-1}): 3269(w), 3099 (w), 2925 (w), 1744 (s), 1670 (s), 1466 (m), 1163 (s), 662 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.67 (dd, *J* = 2.2, 0.6 Hz, 1H), 8.48 (dd, *J* = 8.5, 2.1 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.41 (dd, *J* = 8.6, 0.6 Hz, 1H), 7.40 – 7.37 (m, 2H), 6.73 – 6.65 (m, 2H), 6.63 – 6.56 (m, 2H), 2.45 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 183.9, 163.3, 149.7, 147.4, 146.5, 144.4, 135.2, 131.1, 131.0, 130.1, 129.7, 128.9, 124.9, 121.4, 66.9, 21.9.

HRMS (ESI) calculated for $C_{20}H_{15}N_2O_6S^+$ [M+H$^+$]: 411.0645; found: 411.0647.

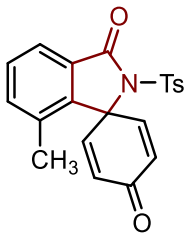


8: 6'-chloro-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 138.2 mg (96% yield) of **8** as a white solid.

IR (neat, cm^{-1}): 3064 (w), 2926 (w), 2853 (w), 1743 (s), 1673 (s), 1369 (m), 1173 (s), 664 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.05 – 7.99 (m, 2H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.50 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 1.7 Hz, 1H), 6.71 – 6.64 (m, 2H), 6.57 – 6.50 (m, 2H), 2.44 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.3, 164.5, 146.1, 145.4, 143.6, 141.8, 135.6, 131.4, 130.5, 130.0, 128.8, 127.6, 127.1, 123.6, 66.5, 21.9.

HRMS (ESI) calculated for $C_{20}H_{15}ClNO_4S^+$ [M+H$^+$]: 400.0405; found: 400.0407.

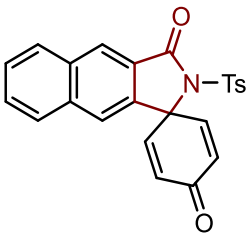


9: 7'-methyl-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 102.4 mg (75% yield) of **9** as a white solid.

IR (neat, cm^{-1}): 3046 (w), 2928 (w), 1738 (s), 1669 (s), 1484 (m), 1174 (s), 666 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.04 – 7.99 (m, 2H), 7.73 (d, *J* = 6.9 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 6.65 – 6.61 (m, 2H), 6.61 – 6.55 (m, 2H), 2.42 (s, 3H), 2.18 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.7, 165.8, 145.8, 143.3, 138.5, 137.6, 136.0, 135.0, 131.9, 130.6, 129.7, 129.6, 128.8, 123.7, 66.6, 21.8, 16.8.

HRMS (ESI) calculated for $C_{21}H_{18}NO_4S^+$ [M+H$^+$]: 380.0951; found: 380.0951.

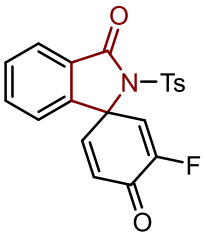


10: 2-tosylspiro[benzo[f]isoindole-1,1'-cyclohexane]-2',5'-diene-3,4'(2H)-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 71.8 mg (48% yield) of **10** as a white solid.

IR (neat, cm^{-1}): 3269 (w), 3099 (w), 2925 (w), 1744 (s), 1670 (s), 1348 (s), 1163 (s), 662 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.08 – 8.04 (m, 2H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.69 – 7.62 (m, 1H), 7.59 – 7.52 (m, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 6.76 – 6.71 (m, 4H), 2.43 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.9, 166.0, 145.8, 145.3, 139.2, 136.9, 136.1, 132.4, 132.0, 129.9, 129.8, 129.2, 128.8, 128.5, 127.6, 126.9, 122.8, 120.2, 66.7, 21.8.

HRMS (ESI) calculated for $C_{24}H_{18}NO_4S^+$ [M+H$^+$]: 416.0951; found: 416.0960.

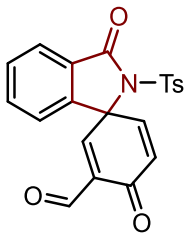


11: 3-fluoro-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (5 mol% ^{n}Bu$_4$NOAc was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 106.3 mg (77% yield) of **11** as a white solid.

IR (neat, cm^{-1}): 3066 (w), 2925 (w), 1740 (s), 1686 (s), 1664 (s), 1363 (m), 1169 (s), 665 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.03 – 7.97 (m, 2H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.68 (td, *J* = 7.6, 1.2 Hz, 1H), 7.56 (td, *J* = 7.6, 0.9 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 1H), 6.72 (dd, *J* = 9.9, 2.8 Hz, 1H), 6.52 (dd, *J* = 9.9, 6.9 Hz, 1H), 6.23 (dd, *J* = 11.0, 2.8 Hz, 1H), 2.43 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 177.6 (d, *J* = 22.0 Hz), 165.0, 154.2 (d, *J* = 270.5 Hz), 147.1, 146.1, 141.3, 135.6, 135.3, 130.9, 130.0, 129.03, 128.99, 128.7, 126.1, 123.1, 122.6 (d, *J* = 16.3 Hz), 67.8 (d, *J* = 9.0 Hz), 21.8; **^{19}F NMR (471 MHz, Chloroform-*d*)** δ -125.3 (m).

HRMS (ESI) calculated for $C_{20}H_{15}FNO_4S^+$ [M+H$^+$]: 384.0700; found: 384.0700.

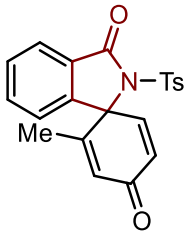


12: 3',4-dioxo-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3-carbaldehyde

Followed **Method B** (5 mol% $^{n}Bu_4NOAc$ was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 53.8 mg (38% yield) of **12** as a white solid.

IR (neat, cm^{-1}): 3265 (w), 3066 (w), 2925 (w), 1743 (s), 1672 (s), 1597 (s), 1335 (m), 1164 (s), 664 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 10.31 (s, 1H), 8.01 – 7.95 (m, 2H), 7.90 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.66 (td, *J* = 7.6, 1.3 Hz, 1H), 7.58 (td, *J* = 7.5, 1.0 Hz, 1H), 7.39 – 7.36 (m, 2H), 7.34 (d, *J* = 3.2 Hz, 1H), 7.14 (dt, *J* = 7.8, 0.9 Hz, 1H), 6.82 (dd, *J* = 9.9, 3.2 Hz, 1H), 6.60 (d, *J* = 10.0 Hz, 1H), 2.45 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 188.3, 183.4, 165.0, 150.2, 146.5, 146.3, 140.2, 135.3, 133.0, 131.2, 130.1, 129.9, 129.5, 128.8, 126.4, 123.4, 66.7, 21.9.

HRMS (ESI) calculated for $C_{21}H_{16}NO_5S^+$ [M+H$^+$]: 394.0744; found: 394.07645.

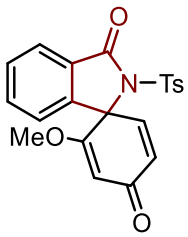


13: 2-methyl-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (5 mol% $^{n}Bu_4NOAc$ was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 91.5 mg (67% yield) of **13** as a white solid.

IR (neat, cm^{-1}): 3056 (w), 2923 (w), 1737 (s), 1669 (s), 1466 (m), 1170 (s), 691 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.04 (d, *J* = 8.4 Hz, 2H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.63 (td, *J* = 7.6, 1.2 Hz, 1H), 7.53 (td, *J* = 7.5, 1.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.53 – 6.44 (m, 2H), 6.38 (t, *J* = 1.5 Hz, 1H), 2.43 (s, 3H), 1.70 (d, *J* = 1.4 Hz, 3H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 185.3, 165.8, 155.8, 145.9, 145.7, 143.0, 135.7, 135.2, 130.5, 129.9, 129.8, 129.4, 128.81, 128.79, 125.7, 122.4, 69.7, 21.8, 18.3.

HRMS (ESI) calculated for $C_{21}H_{18}NO_4S^+$ [M+H$^+$]: 380.0951; found: 380.0951.

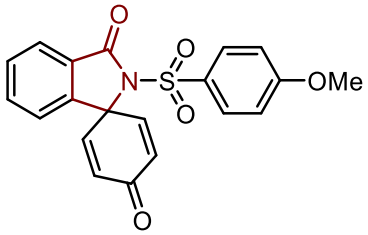


14: 2-methoxy-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Current = 200 mA, Q = 6.22 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 28.5 mg (20% yield) of **14** as a white solid.

IR (neat, cm^{-1}): 3068 (w), 2925 (w), 2850 (w), 1740 (s), 1661 (s), 1600 (s), 1352 (m), 1172 (s), 729 (s); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.00 (d, *J* = 7.4 Hz, 2H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.46 (q, *J* = 9.8 Hz, 2H), 5.80 (s, 1H), 3.55 (s, 3H), 2.43 (s, 3H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 186.7, 170.4, 166.0, 145.7, 142.8, 142.2, 136.0, 134.9, 130.4, 129.6, 129.5, 129.4, 128.8, 125.6, 122.1, 103.5, 67.8, 56.3, 21.8.

HRMS (ESI) calculated for $C_{21}H_{18}NO_5S^+$ [M+H$^+$]: 396.0900; found: 396.0900.

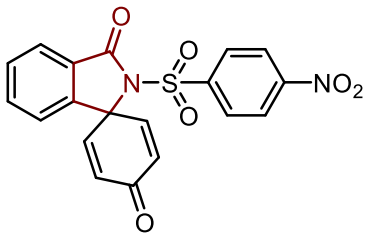


15: 2'-((4-methoxyphenyl)sulfonyl)spiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 105.7 mg (77% yield) of **15** as a white solid.

IR (neat, cm^{-1}): 3057 (w), 2948 (w), 1737 (s), 1670 (s), 1465 (m), 1165 (s), 692 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.10 – 8.03 (m, 2H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.02 – 6.96 (m, 2H), 6.72 – 6.66 (m, 2H), 6.53 – 6.46 (m, 2H), 3.86 (s, 3H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 184.6, 165.5, 164.4, 146.2, 141.7, 135.0, 131.1, 130.5, 130.01, 129.96, 129.3, 125.8, 123.2, 114.4, 67.0, 55.9.

HRMS (ESI) calculated for $C_{20}H_{16}NO_5S^+$ [M+H$^+$]: 382.0744; found: 382.0738.

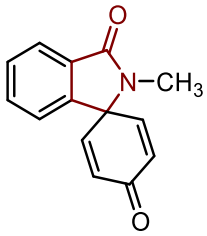


16: 2'-((4-nitrophenyl)sulfonyl)spiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 64.2 mg (45% yield) of **16** as a white solid.

IR (neat, cm^{-1}): 3108 (w), 3067 (w), 1744 (s), 1671 (s), 1466 (m), 1177 (s), 619 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.44 – 8.35 (m, 4H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.70 (td, *J* = 7.7, 1.3 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 6.69 (dd, *J* = 10.4, 2.3 Hz, 2H), 6.59 – 6.53 (m, 2H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.3, 165.5, 151.2, 145.2, 144.0, 142.1, 135.7, 130.9, 130.5, 130.3, 128.5, 126.2, 124.5, 123.4, 67.2.

HRMS (ESI) calculated for $C_{19}H_{13}N_2O_6S^+$ [M+H$^+$]: 397.0489; found: 397.0484.

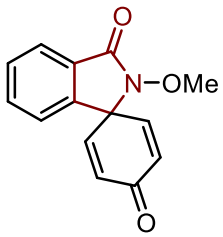


17: 2'-methylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 30.8 mg (38% yield) of **17** as a white solid.

IR (neat, cm^{-1}): 3053 (w), 2925 (w), 1699 (s), 1671 (s), 1467 (m), 1264 (m), 729 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.93 – 7.88 (m, 1H), 7.61 – 7.49 (m, 2H), 7.27 – 7.22 (m, 1H), 6.59 – 6.50 (m, 2H), 6.50 – 6.41 (m, 2H), 3.01 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.6, 168.1, 146.9, 141.4, 132.7, 132.2, 132.0, 130.0, 124.7, 122.8, 64.9, 26.2.

HRMS (ESI) calculated for $C_{14}H_{12}NO_2^+$ [M+H$^+$]: 226.0863; found:226.0872.

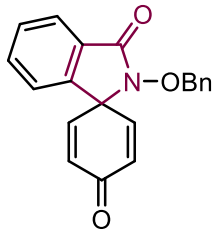


18: 2'-methoxyspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (E_{cell} = 31 V), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 67.7 mg (78% yield) of **18** as a white solid.

IR (neat, cm^{-1}): 3050 (w), 2924 (w), 2853 (w), 1718 (s), 1669 (s), 1466 (m), 1007 (m), 686 (s); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.91 (d, *J* = 7.4 Hz, 1H), 7.64 – 7.51 (m, 2H), 7.19 (d, *J* = 7.5 Hz, 1H), 6.64 (d, *J* = 9.0 Hz, 2H), 6.51 (d, *J* = 8.9 Hz, 2H), 3.95 (s, 3H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 184.7, 165.5, 145.8, 139.5, 133.6, 131.7, 130.3, 129.4, 125.1, 122.9, 66.2, 65.3.

HRMS (ESI) calculated for $C_{14}H_{12}NO_3^+$ [M+H$^+$]: 242.0812; found:242.0807.



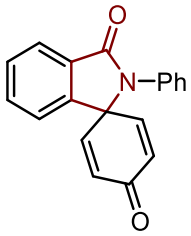
19: 2'-(benzyloxy)spiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (5 mol% $^{n}Bu_4NOAc$ was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 84.5 mg (74% yield) of **19** as a white solid.

IR (neat, cm^{-1}): 3051 (w), 2926 (w), 1723 (s), 1670 (s), 1466 (m), 995 (m), 750 (s), 691 (s);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (dd, *J* = 7.0, 1.7 Hz, 1H), 7.55 (pd, *J* = 7.4, 1.4 Hz, 2H), 7.39 – 7.27 (m, 5H), 7.11 (dd, *J* = 6.8, 1.6 Hz, 1H), 6.38 – 6.25 (m, 4H), 5.12 (s, 2H); **^{13}C NMR (101 MHz, Chloroform-*d*))** δ 184.8, 166.6, 145.7, 139.9, 134.8, 133.6, 131.0, 130.17, 130.15, 129.4, 129.3, 128.7, 125.0, 122.9, 79.8, 65.4.

HRMS (ESI) calculated for $C_{20}H_{16}NO_3^+$ [M+H$^+$]: 318.1125; found: 318.1130.

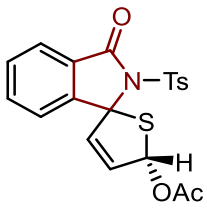


20: 2'-phenylspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 85.9 mg (83% yield) of **20** as a white solid.

IR (neat, cm^{-1}): 3077 (w), 3041 (w), 1702 (s), 1669 (s), 1465 (m), 1348 (s), 690 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.92 (dt, *J* = 7.3, 1.0 Hz, 1H), 7.56 (td, *J* = 7.5, 1.4 Hz, 1H), 7.52 (td, *J* = 7.4, 1.1 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.34 – 7.28 (m, 2H), 7.25 – 7.18 (m, 2H), 6.73 – 6.64 (m, 2H), 6.39 – 6.31 (m, 2H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.6, 167.6, 148.0, 141.0, 136.4, 133.3, 131.8, 130.7, 130.1, 129.3, 127.7, 125.8, 125.2, 122.8, 66.9.

HRMS (ESI) calculated for $C_{19}H_{14}NO_2^+$ [M+H$^+$]: 288.1019; found: 288.1013.

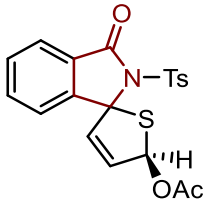


22a: (5'S)-3-oxo-2-tosyl-5'H-spiro[isoindoline-1,2'-thiophen]-5'-yl acetate

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 71.8mg (48% yield) of **22a** as a white solid.

IR (neat, cm^{-1}): 3066 (w), 2924 (w), 2854 (w), 1736 (s), 1367 (m), 1172 (s), 665 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.23 – 8.03 (m, 2H), 7.72 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.68 (td, *J* = 7.6, 1.1 Hz, 1H), 7.51 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.47 (td, *J* = 7.5, 1.0 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 2H), 7.08 (dd, *J* = 2.5, 1.3 Hz, 1H), 6.30 (dd, *J* = 6.0, 2.4 Hz, 1H), 6.06 (dd, *J* = 6.0, 1.3 Hz, 1H), 2.42 (s, 3H), 2.20 (s, 3H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.7, 165.2, 147.8, 145.4, 136.4, 136.0, 134.9, 131.8, 130.1, 129.4, 129.3, 126.9, 124.31, 124.29, 87.0, 86.9, 21.8, 21.0.

HRMS (ESI) calculated for $C_{20}H_{18}NO_5S_2^+$ [M+H$^+$]: 416.0621; found: 416.0619.

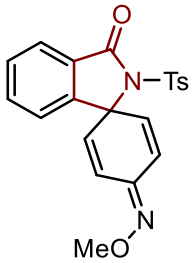


22b: (5'R)-3-oxo-2-tosyl-5'H-spiro[isoindoline-1,2'-thiophen]-5'-yl acetate

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 41.9mg (28% yield) of **22b** as a white solid.

IR (neat, cm^{-1}): 3064 (w), 2924 (w), 2855 (w), 1737 (s), 1370 (m), 1174 (s), 665 (s); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.10 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 2.8 Hz, 1H), 6.36 (dd, *J* = 6.0, 2.8 Hz, 1H), 6.13 (d, *J* = 6.0 Hz, 1H), 2.41 (s, 3H), 2.24 (s, 3H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 171.1, 165.3, 147.2, 145.3, 136.9, 136.1, 134.9, 130.7, 130.0, 129.4, 129.2, 127.5, 124.5, 123.8, 86.3, 85.3, 21.8, 21.1.

HRMS (ESI) calculated for $C_{20}H_{18}NO_5S_2^+$ [M+H$^+$]: 416.0621; found: 416.0619.

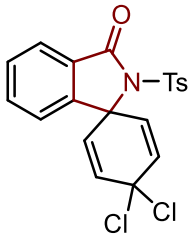


23: 4-(methoxyimino)-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-dien-3'-one

Followed **Method F**, the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 29.6 mg (75% yield) of **23** as a white solid.

IR (neat, cm^{-1}): 2924 (w), 2854 (w), 1738 (s), 1670 (s), 1466 (m), 1171 (s), 691 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.06 – 8.01 (m, 2H), 7.79 (d, *J* = 7.7 Hz, 1H), 7.60 (td, *J* = 7.6, 1.2 Hz, 1H), 7.47 (td, *J* = 7.5, 1.0 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.22 – 7.16 (m, 2H), 6.59 (dd, *J* = 9.9, 1.8 Hz, 1H), 6.04 (dd, *J* = 10.1, 2.4 Hz, 1H), 5.89 (dd, *J* = 10.0, 2.4 Hz, 1H), 4.04 (s, 3H), 2.41 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 165.9, 146.6, 145.8, 145.4, 136.4, 135.5, 134.8, 131.7, 129.9, 129.6, 128.8, 128.1, 125.8, 125.1, 123.7, 117.6, 68.7, 62.7, 21.8.

HRMS (ESI) calculated for $C_{21}H_{19}N_2O_4S^+$ [M+H$^+$]: 395.1060; found: 395.1065.

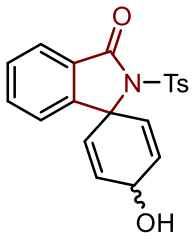


24: 4,4-dichloro-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-dien-3'-one

Followed **Method E**, the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 10:1 - 5:1) to give 20.2 mg (48% yield) of **24** as a white solid.

IR (neat, cm^{-1}): 2934 (w), 1734 (s), 1465 (m), 1172 (s), 734 (m), 692 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.10 – 8.04 (m, 2H), 7.76 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.73 (dt, *J* = 7.9, 0.9 Hz, 1H), 7.62 (td, *J* = 7.6, 1.3 Hz, 1H), 7.51 (td, *J* = 7.5, 1.0 Hz, 1H), 7.40 – 7.31 (m, 2H), 6.43 (dd, *J* = 2.7, 1.2 Hz, 1H), 6.22 – 6.19 (m, 1H), 6.09 (ddd, *J* = 10.0, 2.0, 0.6 Hz, 1H), 6.03 (ddd, *J* = 2.7, 1.9, 0.6 Hz, 1H), 2.44 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 166.1, 145.7, 143.2, 136.0, 134.6, 133.3, 130.6, 129.7, 129.5, 128.9, 128.6, 126.4, 125.5, 124.9, 123.1, 73.5, 60.7, 21.9.

HRMS (ESI) calculated for $C_{20}H_{16}Cl_2NO_3S^+$ [M+H$^+$]: 420.0222; found: 420.0226.

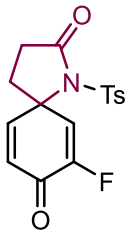


25: 4-hydroxy-2'-tosylspiro[cyclohexane-1,1'-isoindoline]-2,5-dien-3'-one

Followed **Method D**, the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 2:1) to give 30.1 mg (82% yield) of **25** as a white solid.

IR (neat, cm^{-1}): 3524(w), 3038 (w), 2924 (w), 1735 (s), 1466 (m), 1172 (s), 692 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.03 (d, *J* = 8.4 Hz, 2H), 7.77 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.60 (td, *J* = 7.6, 1.2 Hz, 1H), 7.45 (td, *J* = 7.5, 1.0 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 1H), 6.41 (dd, *J* = 10.0, 4.0 Hz, 2H), 5.70 (dd, *J* = 10.0, 1.1 Hz, 2H), 4.65 (s, 1H), 2.70 (s, 1H), 2.41 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 166.2, 147.9, 145.4, 136.3, 134.7, 131.7, 129.6, 129.6, 128.8, 128.0, 127.6, 124.9, 123.5, 66.5, 60.9, 21.8.

HRMS (ESI) calculated for $C_{20}H_{18}NO_4S^+$ [M+H$^+$]: 368.0951; found: 368.0945.



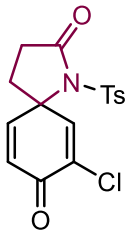
26: 7-fluoro-1-tosyl-1-azaspiro[4.5]deca-6,9-diene-2,8-dione

Followed **Method B** (5 mol% ^{n}Bu$_4$NOAc was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 78.5 mg (65% yield) of **26** as a white solid.

IR (neat, cm^{-1}): 2922 (w), 2852 (w), 1743 (s), 1686 (s), 1365 (m), 1167 (s), 671 (s), 568 (s);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.98 (dd, *J* = 10.0, 2.8 Hz, 1H), 6.40 (ddd, *J* = 17.1, 10.7, 5.0 Hz, 2H), 2.61 (td, *J* = 7.9, 1.8 Hz, 2H), 2.45 (s, 3H), 2.38 – 2.18 (m, 2H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 177.4 (d, *J* = 22.1 Hz), 172.1, 153.7 (d, *J* = 269.5 Hz), 149.2 (d, *J* = 2.3 Hz), 146.1, 134.9, 129.9, 129.0, 127.8 (d, *J* = 4.3 Hz), 124.0 (d, *J* = 14.8 Hz), 65.6 (d, *J* = 8.6 Hz), 32.1 (d, *J* = 2.6 Hz), 29.9, 21.9; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -127.61 (s).

HRMS (ESI) calculated for $C_{16}H_{15}FNO_4S^+$ [M+H$^+$]: 336.0700; found: 336.0706.



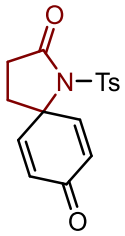
27: 7-chloro-1-tosyl-1-azaspiro[4.5]deca-6,9-diene-2,8-dione

Followed **Method B** (5 mol% ^{n}Bu$_4$NOAc was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 111.5 mg (88% yield) of **27** as a white solid.

IR (neat, cm^{-1}): 3051 (w), 2925 (w), 1742 (s), 1675 (s), 1364 (m), 1170 (s), 665 (s), 563 (s);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.02 – 6.94 (m, 2H), 6.46 – 6.38 (m, 1H), 2.61 (ddd, *J* = 9.4, 5.8, 1.9 Hz, 2H), 2.44 (s, 3H), 2.36 – 2.17 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*)) δ 177.5, 172.1, 148.8, 146.1, 143.6, 134.8, 133.5, 129.9, 128.9, 127.6, 65.6, 31.5, 29.9, 21.8.

HRMS (ESI) calculated for $C_{16}H_{15}ClNO_4S^+$ [M+H$^+$]: 352.0405; found: 352.0412.



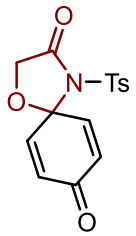
28: 1-tosyl-1-azaspiro [4.5] deca-6,9-diene-2,8-dione

Followed **Method C** (Q = 7.19 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 1.09 g (54% yield) of **28** as a white solid.

IR (neat, cm^{-1}): 3053 (w), 2925 (w), 1739 (s), 1670 (s), 1361 (m), 1168 (s), 671 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 7.91 – 7.85 (m, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 6.95 – 6.88 (m, 2H), 6.36 –

6.29 (m, 2H), 2.59 (t, *J* = 8.1 Hz, 2H), 2.43 (s, 3H), 2.19 (t, *J* = 8.2 Hz, 2H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 184.3, 172.5, 148.1, 145.9, 135.1, 129.7, 129.0, 64.3, 32.0, 30.0, 21.8.

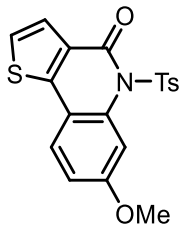
HRMS (ESI) calculated for $C_{16}H_{16}NO_4S^+$ [M+H$^+$]: 318.0795; found: 318.0796.



29: 4-tosyl-1-oxa-4-azaspiro[4.5]deca-6,9-diene-3,8-dione[9]

Followed **Method C** (Q = 5.65 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 2:1) to give 1.05 g (61% yield) of **29** as a white solid.

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.95 – 7.89 (m, 2H), 7.42 – 7.34 (m, 2H), 6.75 – 6.68 (m, 2H), 6.41 – 6.34 (m, 2H), 4.36 (s, 2H), 2.46 (s, 3H).

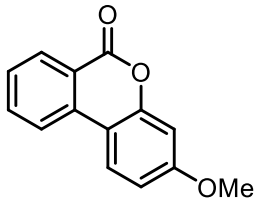


31: 7-methoxy-5-tosylthieno[3,2-c]quinolin-4(5H)-one

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1) to give 115.2 mg (83% yield) of **31** as a white solid.

IR (neat, cm^{-1}): 3013 (w), 2926 (w), 2851 (w), 1674 (s), 1610 (s), 1245 (m), 1176 (s), 666 (s); **^{1}H NMR (500 MHz, Chloroform-*d*)** δ 8.03 (d, *J* = 2.4 Hz, 1H), 8.02 – 7.98 (m, 2H), 7.79 (d, *J* = 8.7 Hz, 1H), 7.75 (d, *J* = 5.2 Hz, 1H), 7.52 (d, *J* = 5.2 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 2H), 6.96 (dd, *J* = 8.7, 2.4 Hz, 1H), 3.93 (s, 3H), 2.42 (s, 3H); **^{13}C NMR (126 MHz, Chloroform-*d*)** δ 159.8, 158.4, 145.3, 144.1, 137.8, 137.1, 136.0, 129.6, 128.6, 127.6, 125.6, 122.3, 113.7, 112.2, 105.7, 55.8, 21.8.

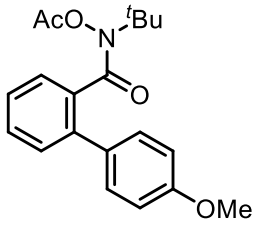
HRMS (ESI) calculated for $C_{19}H_{16}NO_4S_2^+$ [M+H$^+$]: 386.0515; found:386.0508.



33: 3-methoxy-6H-benzo[c]chromen-6-one[3]

Followed **Method B** (Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 50.5 mg (62% yield) of **33** as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 8.8 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 6.87 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.80 (d, *J* = 2.6 Hz, 1H), 3.85 (s, 3H).



U1: N-acetoxy-N-(tert-butyl)-4'-methoxy-[1,1'-biphenyl]-2-carboxamide

Followed **Method B** (5 mol% ^{n}Bu$_4$NOAc was added, Q = 3.89 F/mol), the desired product was purified using silica gel chromatography (petroleum ether/ethyl acetate = 5:1 - 2:1) to give 47.9 mg (39% yield) of **U1** as a white solid.

IR (neat, cm^{-1}): 3364 (w), 2965 (w), 2917 (w), 1755 (s), 1657 (s), 1619 (s), 1365 (m), 1214 (s), 727 (s); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.73 – 7.67 (m, 1H), 7.40 – 7.33 (m, 2H), 7.27 (d, *J* = 7.0 Hz, 1H), 7.24 (dd, *J* = 5.7, 3.4 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.70 (d, *J* = 2.6 Hz, 1H), 6.37 (s, 1H), 3.85 (s, 3H), 1.99 (s, 3H), 1.12 (s, 9H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.2, 168.5, 160.4, 148.7, 138.1, 133.9, 132.7, 129.8, 129.7, 129.0, 128.0, 126.0, 112.3, 107.9, 55.8, 51.4, 28.3, 20.8.

HRMS (ESI) calculated for $C_{20}H_{24}NO_4^+$ [M+H$^+$]: 342.1700; found: 342.1706.

6. Comparison of the Batch and Flow Electrolysis

We selected several substrates for the comparison of both the batch and flow electrolysis. For compound **8**, flow electrolysis afforded a higher yield while batch electrolysis gave a much higher yield for compound **14**. However, in most cases, the batch and flow electrolysis afforded similar results. In our opinion, the direct comparison between these protocols might be difficult as a customer-made modification of reaction conditions might need for each individual substrate both in the batch and flow electrolysis.

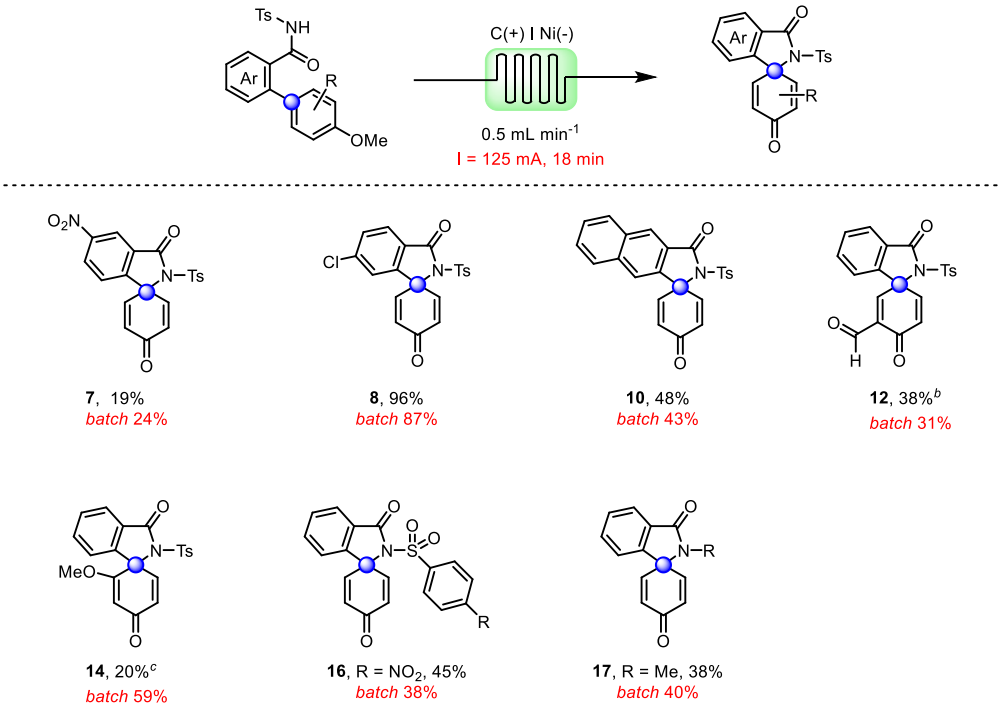
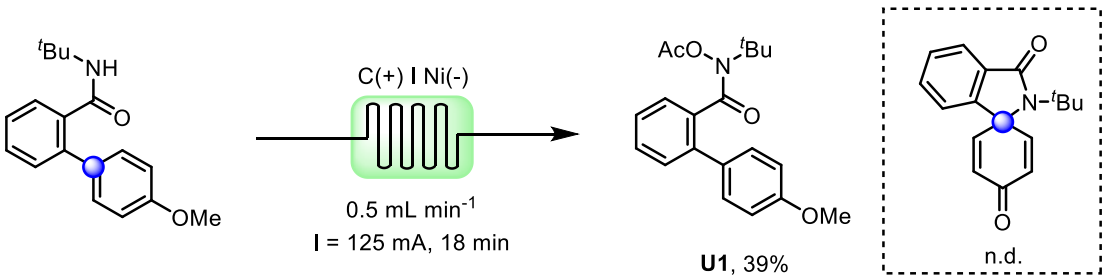


Figure S6. Comparison of both the batch and flow electrolysis

7. Unsuccessful Substrate

Unfortunately, the N-*tert*-butyl derivative only afforded the N-acetoxy derivative (**U1**). The steric hindrance of the *tert*-butyl group might prohibit the addition of the generated amidyl radical to the congested *ipso* position.



8. Cyclic Voltammetry Studies

General information: Cyclic voltammetry (CV) experiments were conducted in a 10 mL glass vial fitted with a glassy carbon working electrode (3 mm in diameter), a platinum wire auxiliary electrode, and an SCE reference electrode. The current was reported in mA, while all potentials were reported in V. The scan rate was 0.1 V/s.

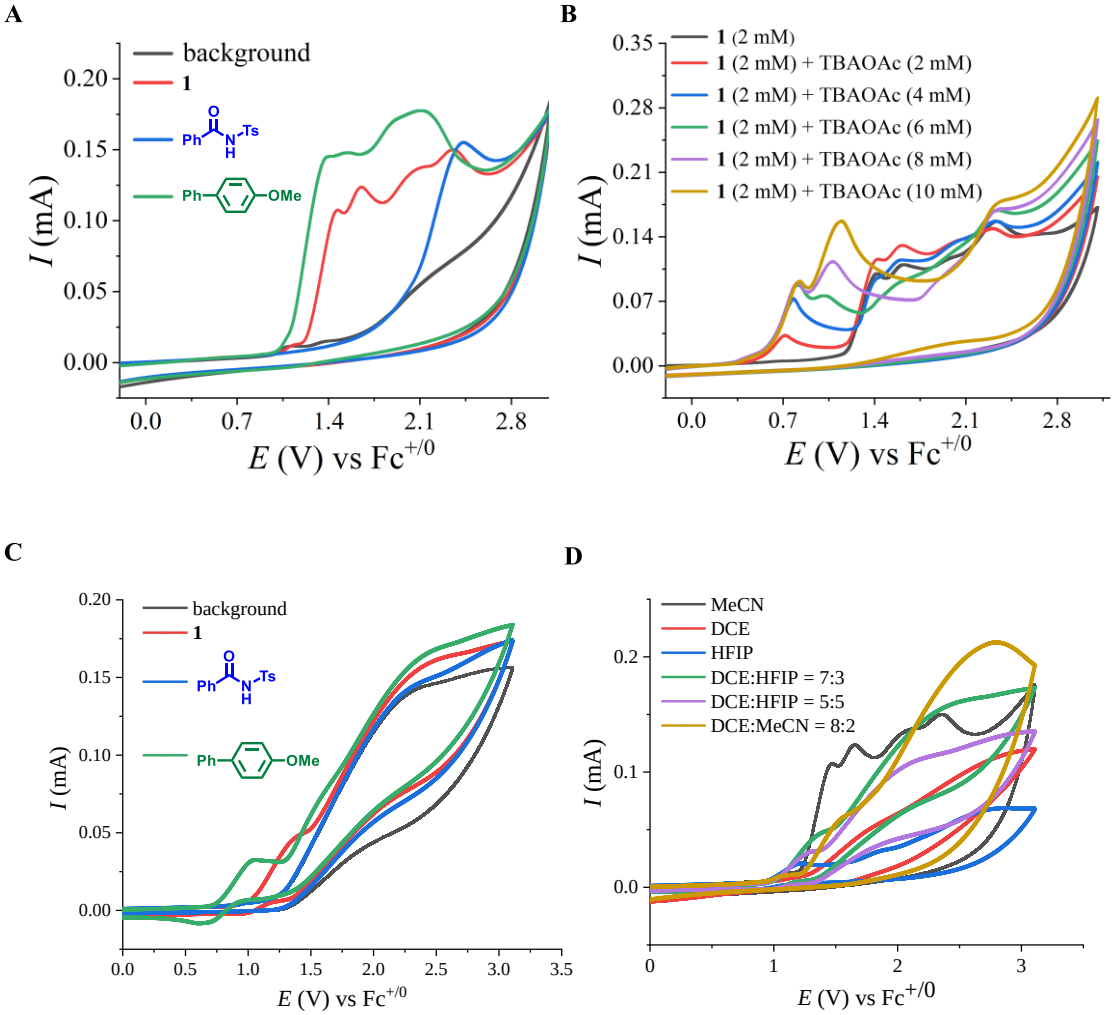


Figure S7. Cyclic voltammograms.

A: Cyclic voltammograms of **1** (2 mM), N-tosylbenzamide (2 mM), and 4-methoxy-1,1'-biphenyl (2 mM) in acetonitrile (MeCN) containing 10 mM $^{n}Bu_4NPF_6$.

B: Cyclic voltammograms of **1** (2 mM) in acetonitrile (MeCN) containing 10 mM $^{n}Bu_4NPF_6$ and varying concentrations of $^{n}Bu_4NOAc$.

C: Cyclic voltammograms of **1** (2 mM), N-tosylbenzamide (2 mM), and 4-methoxy-1,1'-biphenyl (2 mM) in solvent (DCE : HFIP = 7:3) containing 10 mM $^{n}Bu_4NPF_6$.

D: Cyclic voltammograms of **1** (2 mM) in different solvents.

9. NMR Studies

In the nuclear magnetic tube containing 0.02 M **1** dissolved in chloroform-*d*, respectively added: no, HFIP (1 μL), $^{n}Bu_4NOAc$ (1.0 equiv.), HFIP (1 μL) and $^{n}Bu_4NOAc$ (1.0 equiv.)

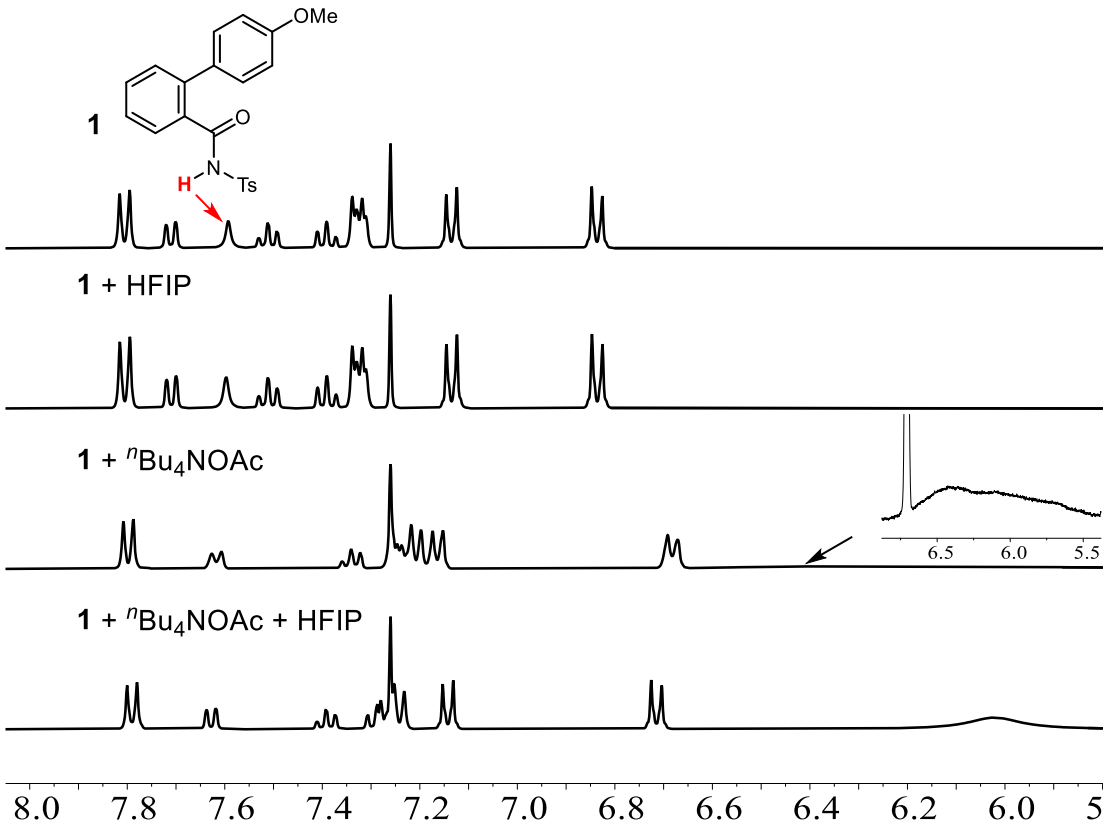
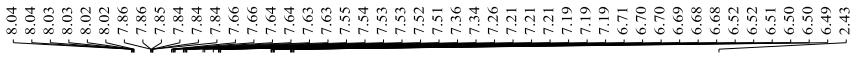
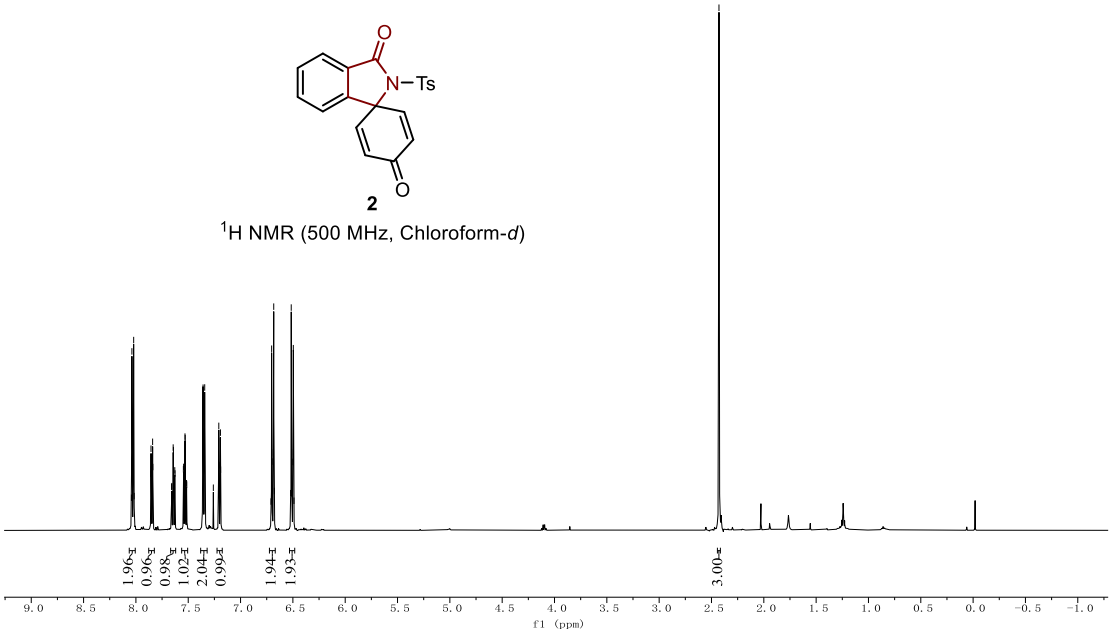
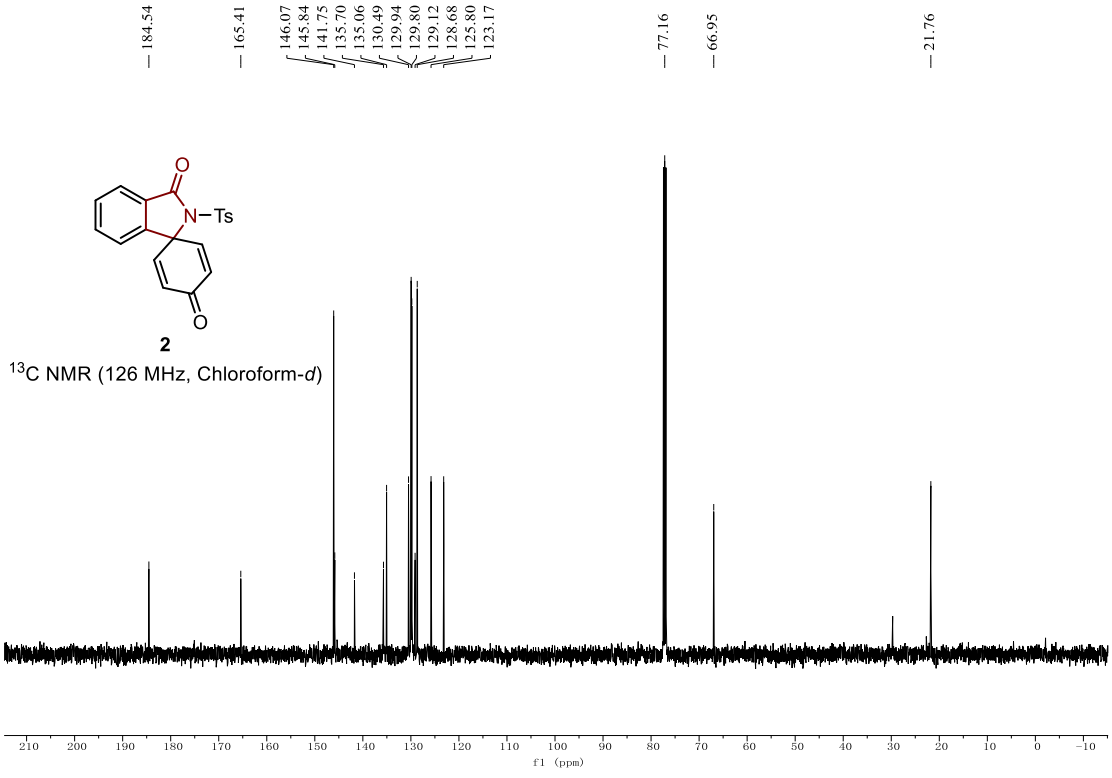


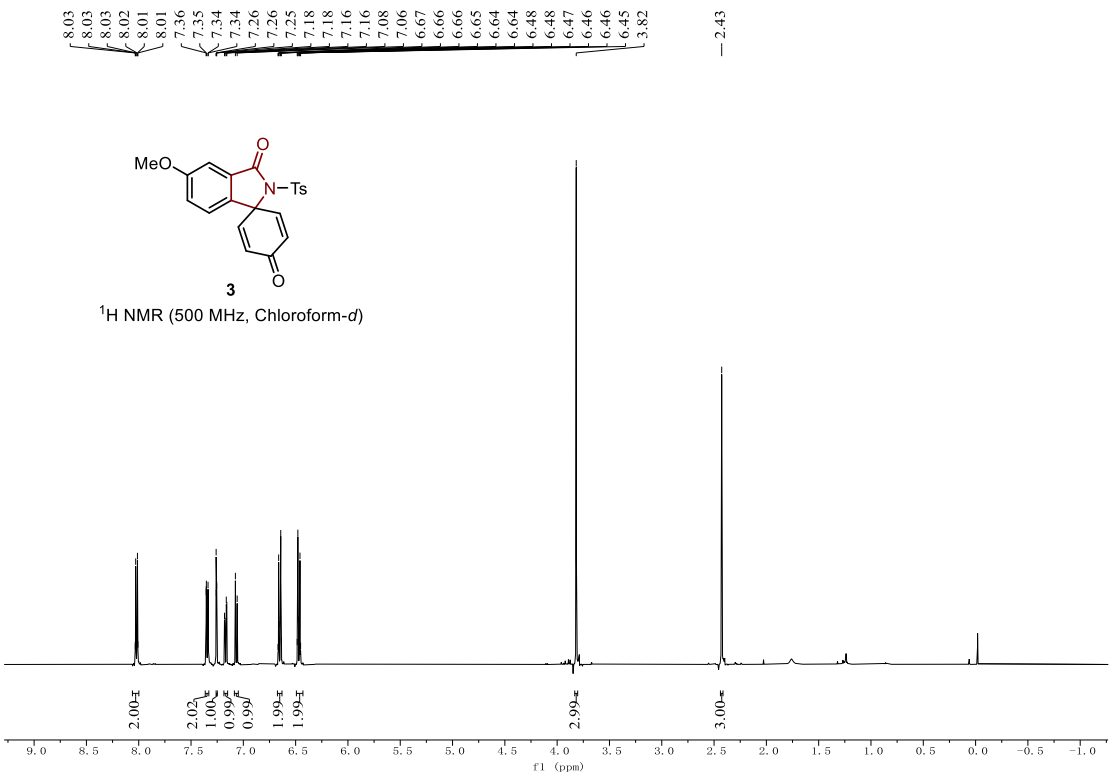
Figure S8. NMR studies.

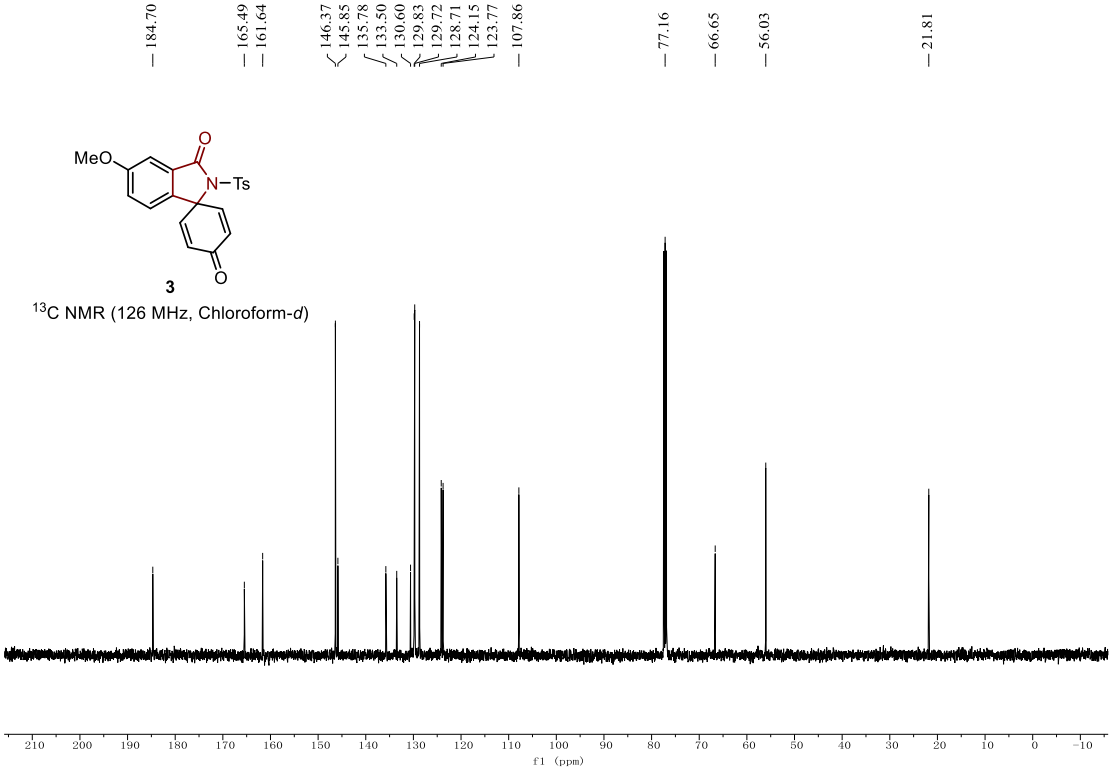
10. Spectral Data (^{1}H, ^{13}C, ^{19}F)

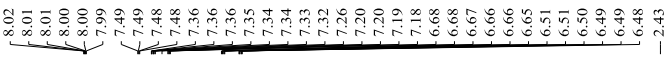


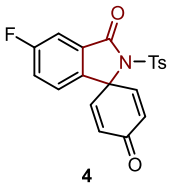





8.03
8.03
8.03
8.02
8.01
8.01
7.36
7.35
7.34
7.34
7.26
7.26
7.25
7.18
7.18
7.16
7.16
7.08
7.06
6.67
6.66
6.66
6.65
6.64
6.64
6.48
6.48
6.47
6.46
6.46
6.45
3.82
2.43
MeO
N–Ts
O
O
3
1H NMR (500 MHz, Chloroform-d)
2.00
2.02
1.00
0.99
0.99
1.99
1.99
2.99
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)

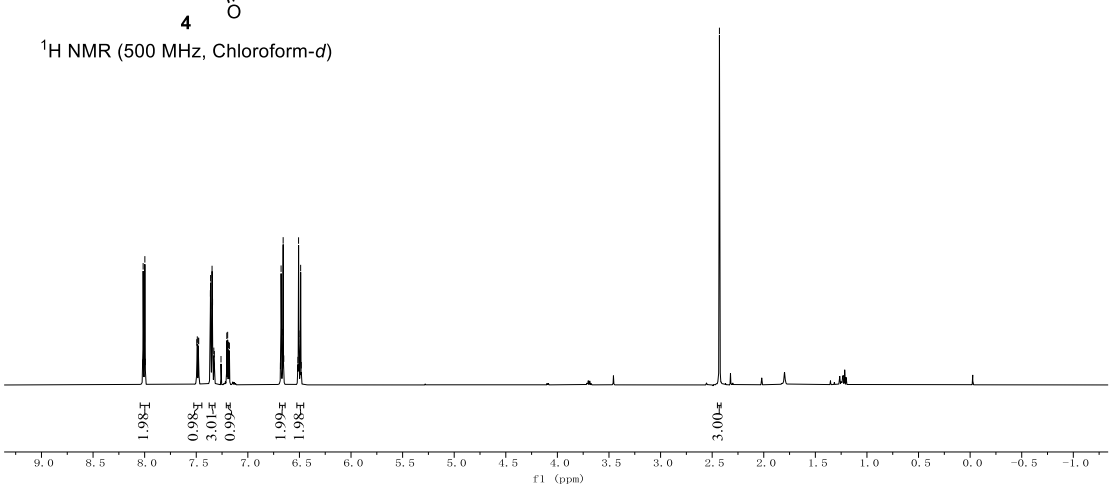

184.70
165.49
161.64
146.37
145.85
135.78
133.50
130.60
129.83
129.72
128.71
124.15
123.77
107.86
77.16
66.65
56.03
21.81
MeO
N–Ts
O
O
3
13C NMR (126 MHz, Chloroform-d)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

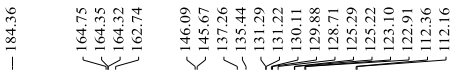


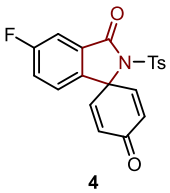


4

^{1}H NMR (500 MHz, Chloroform-*d*)

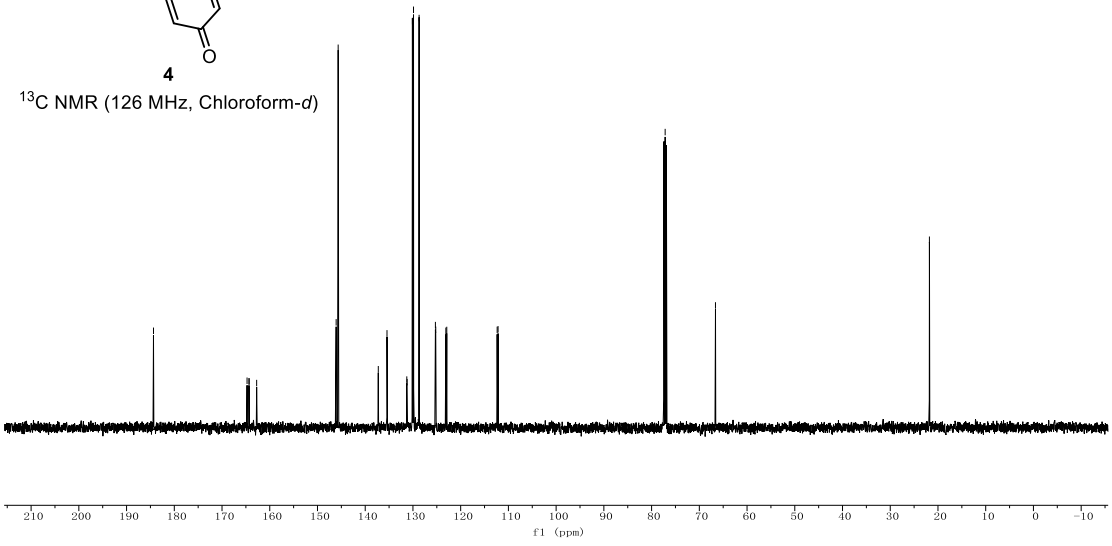


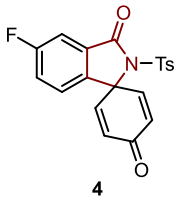




4

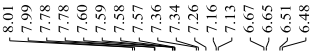
^{13}C NMR (126 MHz, Chloroform-*d*)

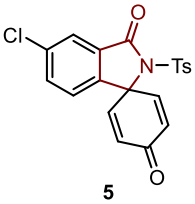




4

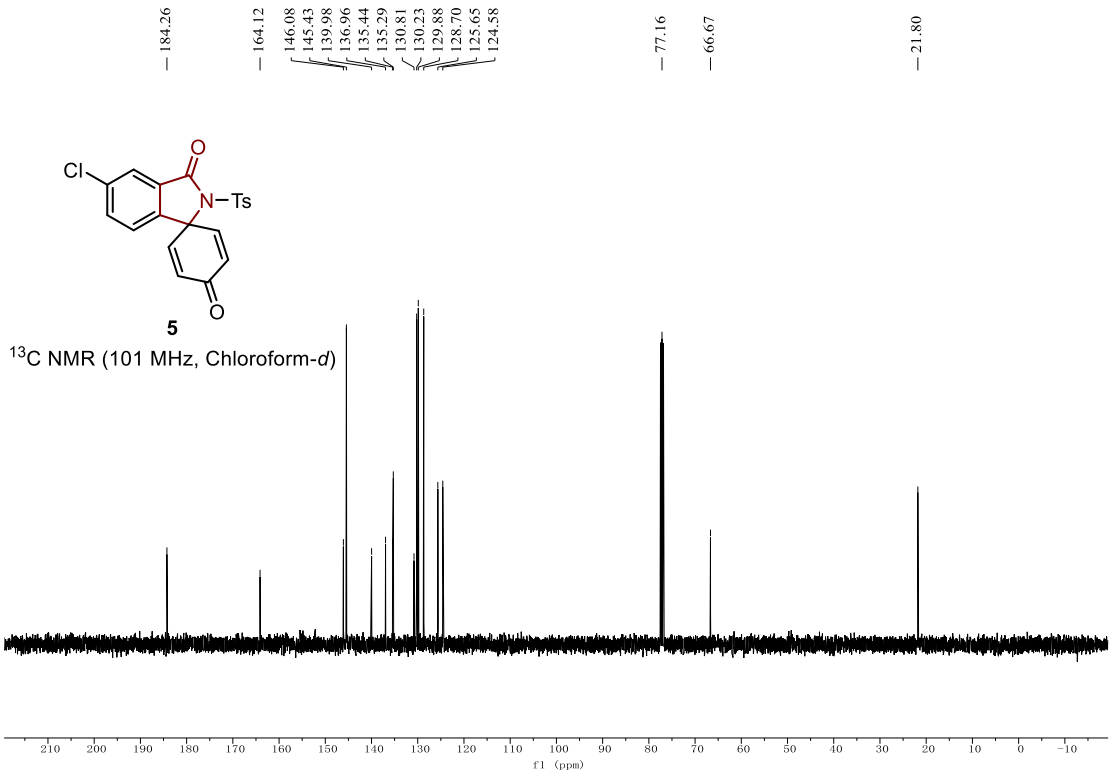
^{19}F NMR (471 MHz, Chloroform-*d*)

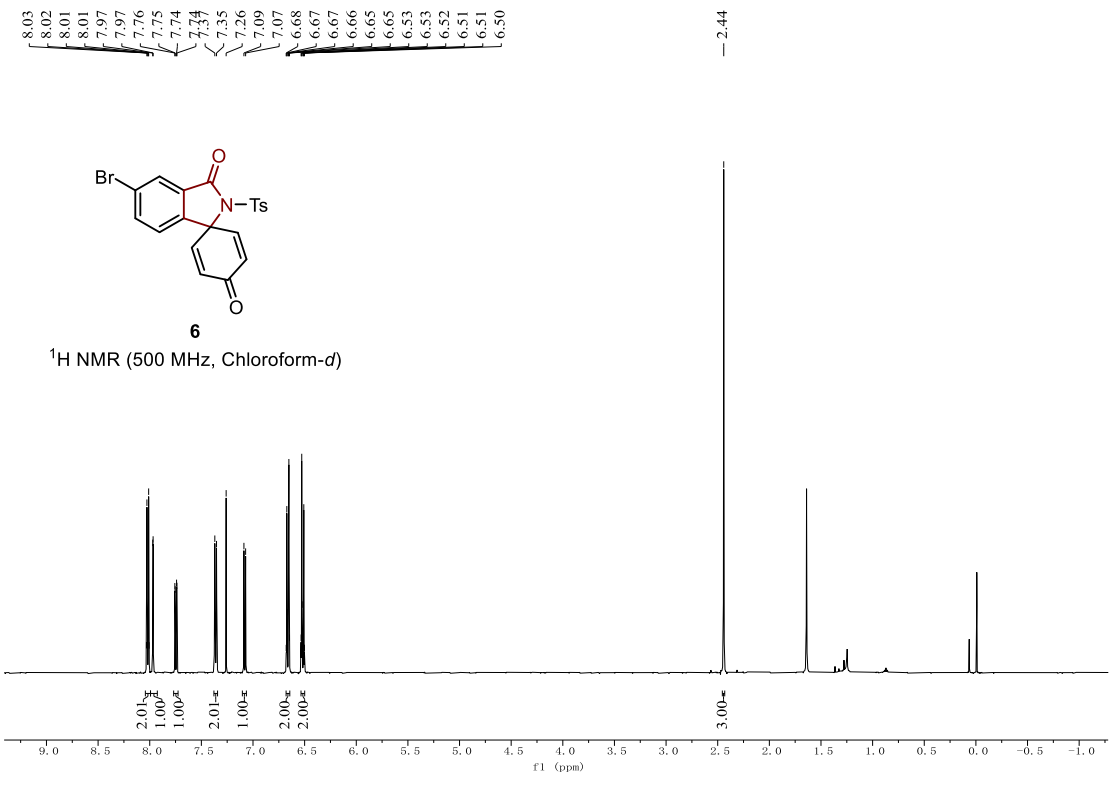


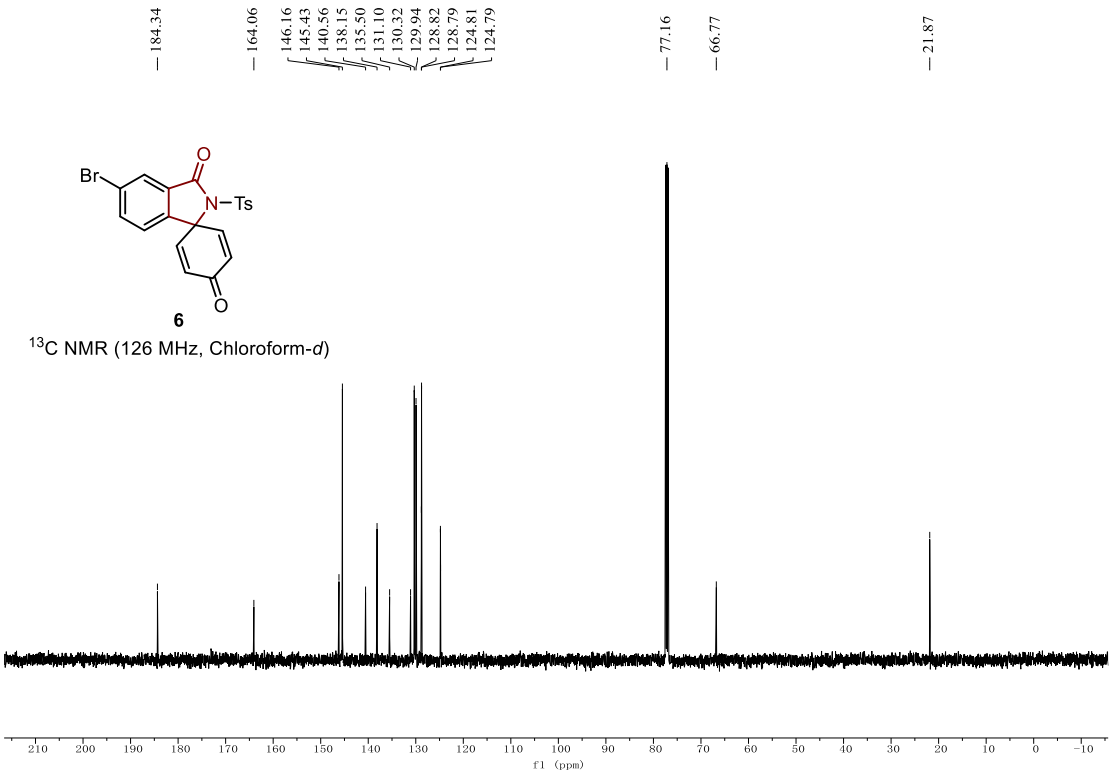


5

^{1}H NMR (400 MHz, Chloroform-*d*)

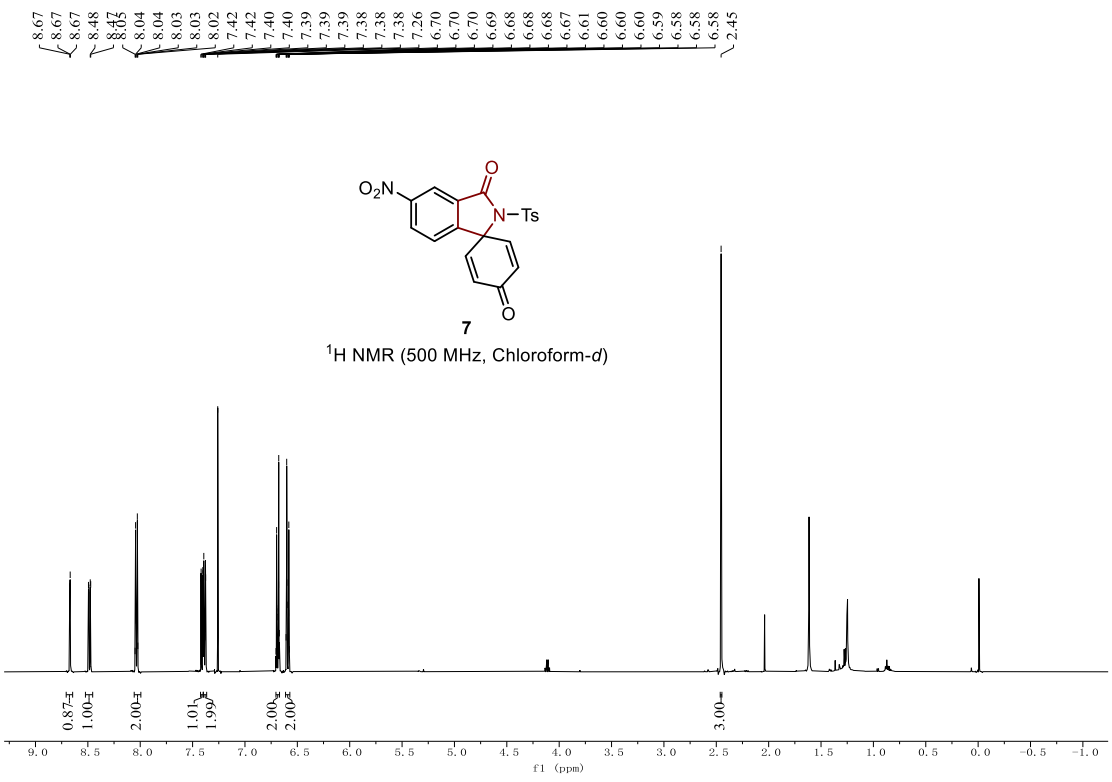

184.26
164.12
146.08
145.43
139.98
136.96
135.44
135.29
130.81
130.23
129.88
128.70
125.65
124.58
77.16
66.67
21.80
Cl
N—Ts
O
O
5
13C NMR (101 MHz, Chloroform-d)
f1 (ppm)


8.03
8.02
8.01
8.01
7.97
7.97
7.76
7.75
7.74
7.74
7.33
7.35
7.26
7.09
7.07
6.68
6.67
6.67
6.66
6.65
6.65
6.53
6.53
6.52
6.51
6.51
6.50
2.44
Br
N—Ts
O
O
6
1H NMR (500 MHz, Chloroform-d)
2.01
1.00
1.00
2.01
1.00
2.00
2.00
3.00
f1 (ppm)



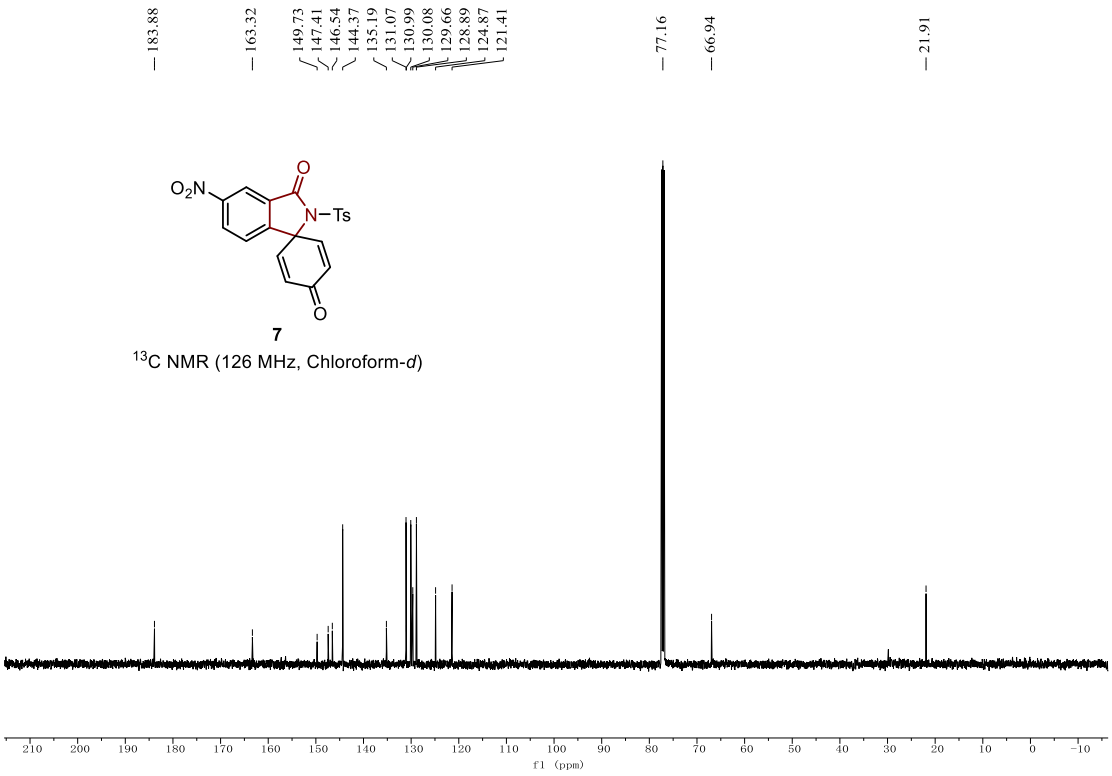
6

^{13}C NMR (126 MHz, Chloroform-*d*)



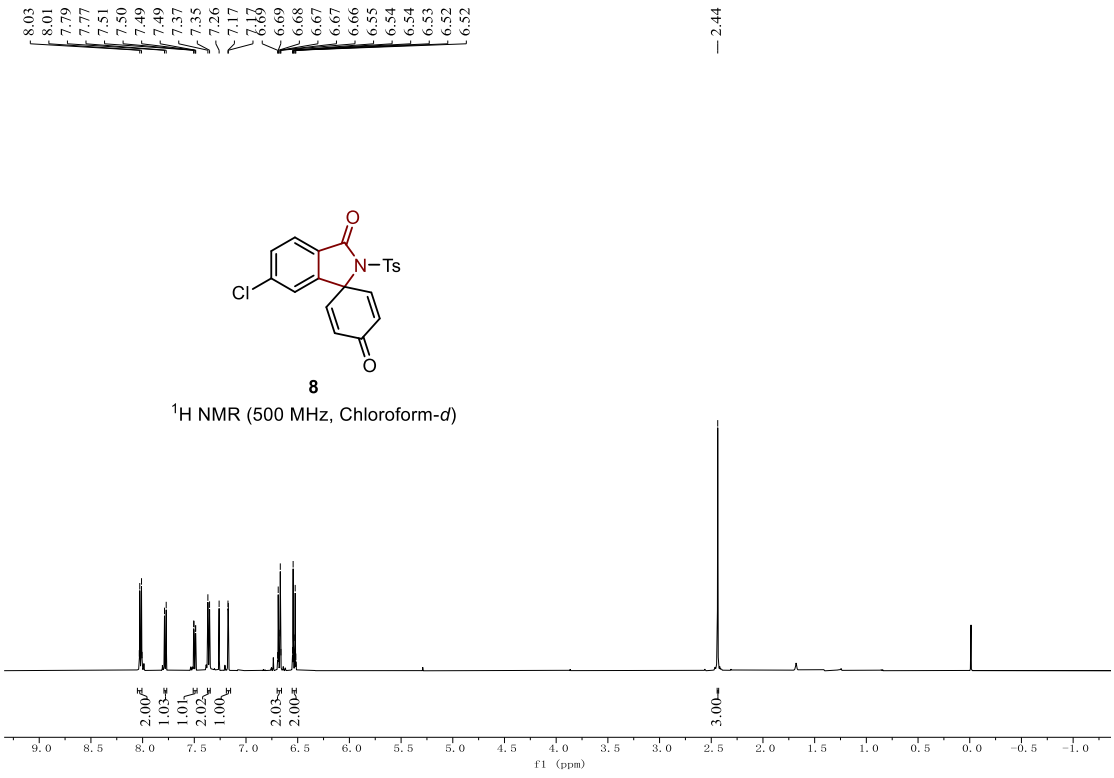
7

^{1}H NMR (500 MHz, Chloroform-*d*)



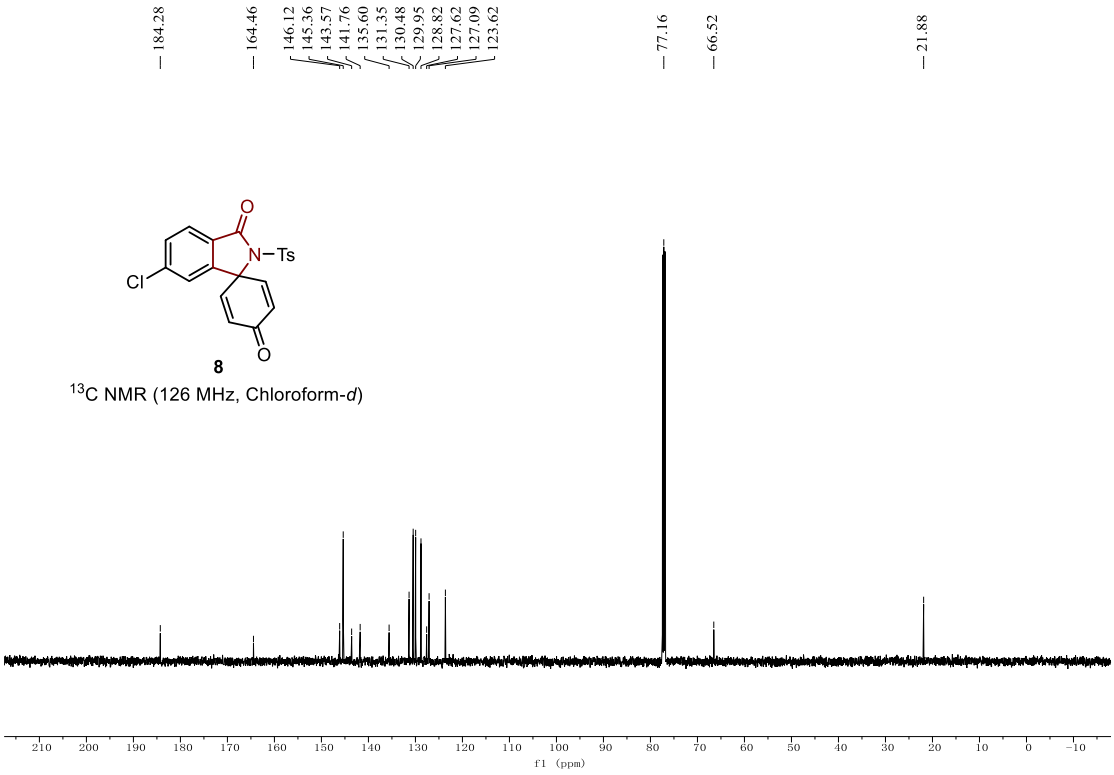
7

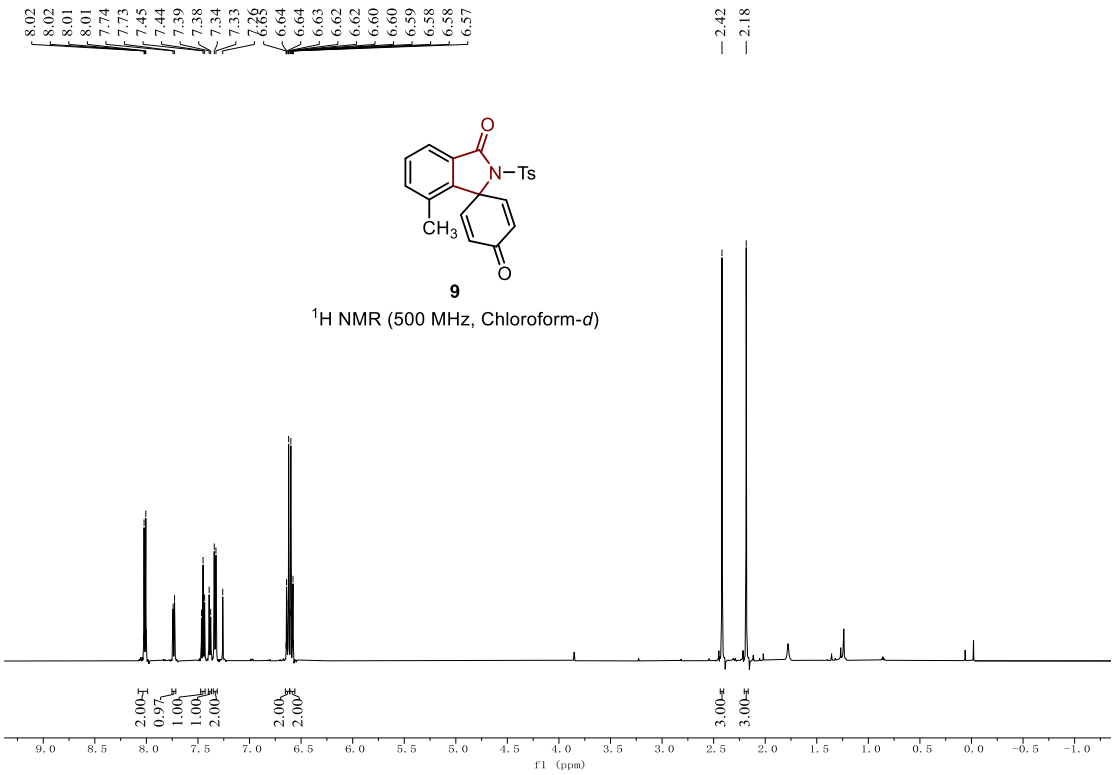
^{13}C NMR (126 MHz, Chloroform-*d*)

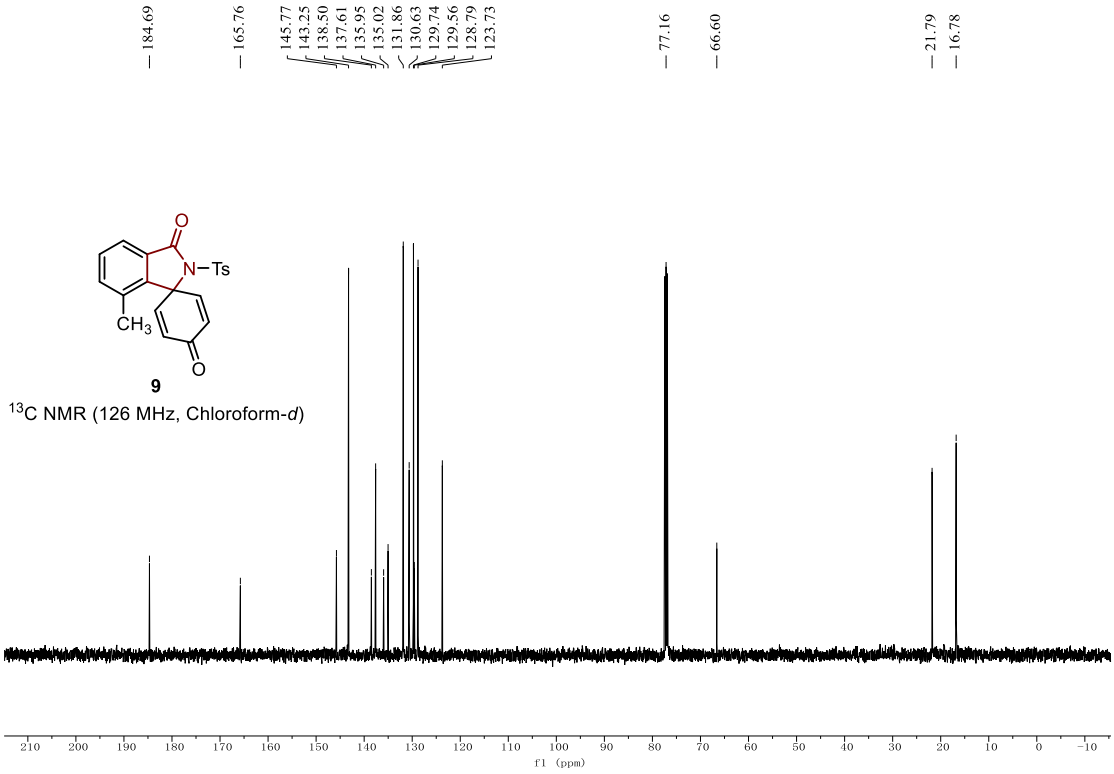


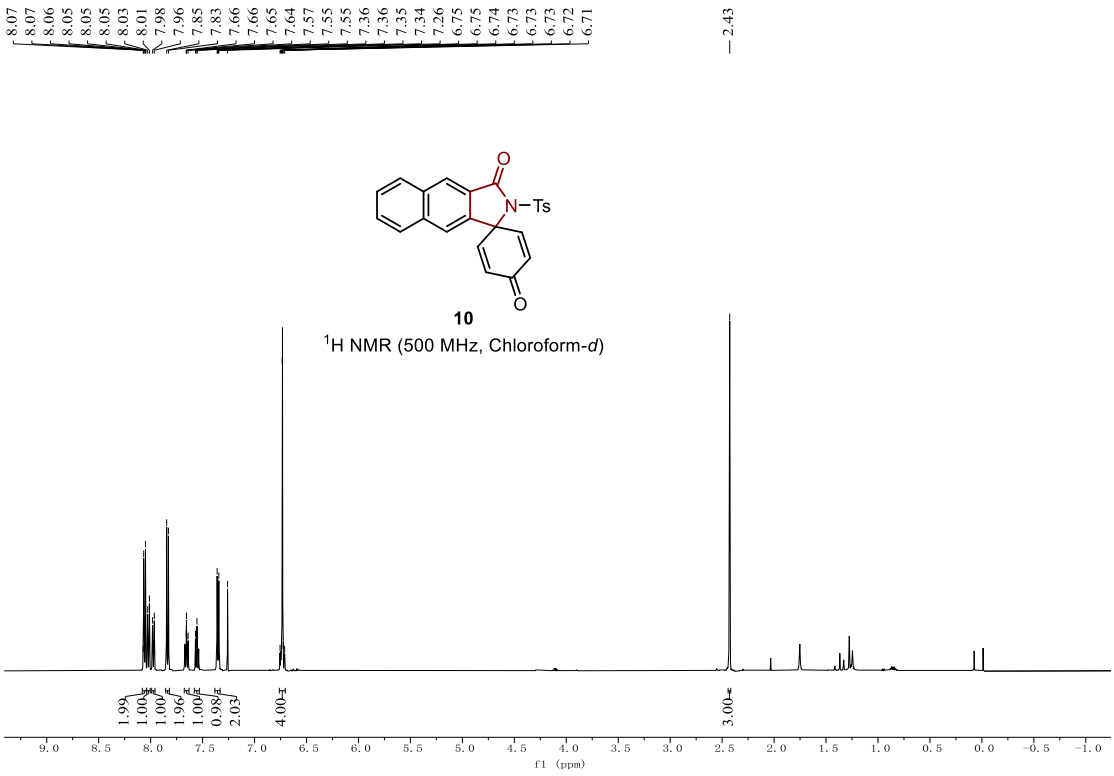
8

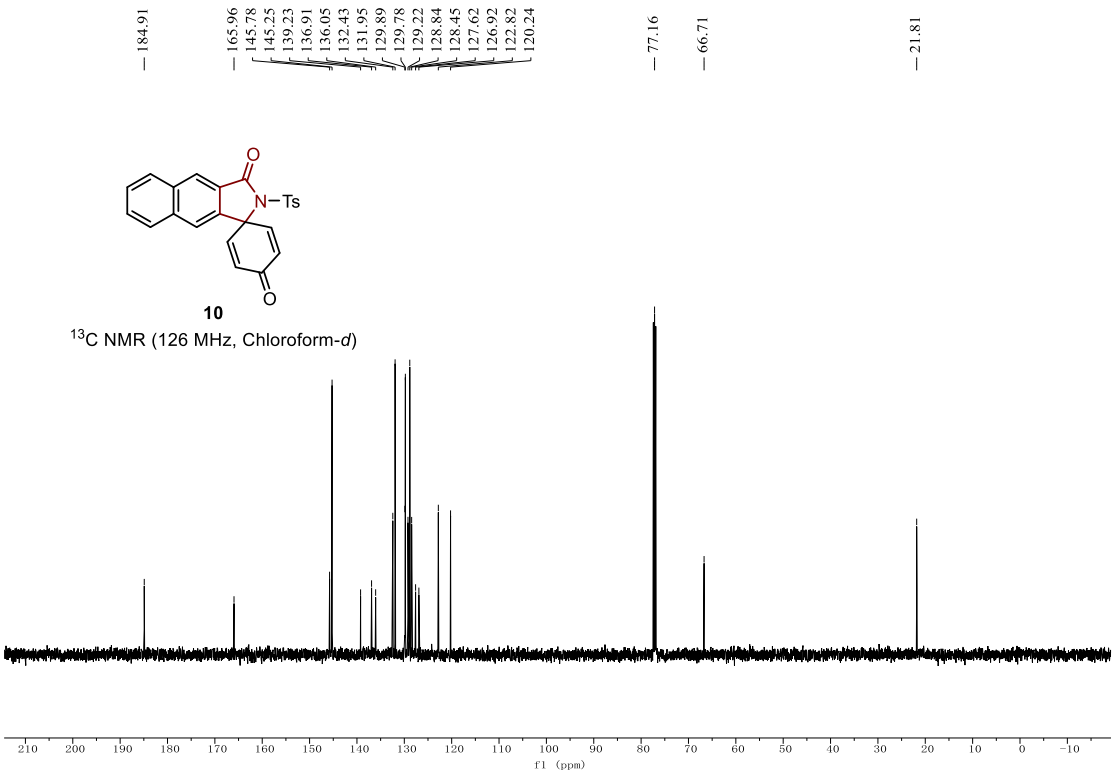
^{1}H NMR (500 MHz, Chloroform-*d*)


184.28
164.46
146.12
145.36
143.57
141.76
135.60
131.35
130.48
129.95
128.82
127.62
127.09
123.62
77.16
66.52
21.88
O
N–Ts
Cl
O
8
13C NMR (126 MHz, Chloroform-d)
f1 (ppm)


8.02
8.02
8.01
8.01
7.74
7.73
7.45
7.44
7.39
7.38
7.34
7.33
7.26
6.65
6.64
6.64
6.63
6.62
6.62
6.60
6.60
6.60
6.59
6.58
6.58
6.57
2.42
2.18
O
N–Ts
CH3
O
9
1H NMR (500 MHz, Chloroform-d)
2.00
0.97
1.00
1.00
2.00
2.00
2.00
3.00
3.00
f1 (ppm)

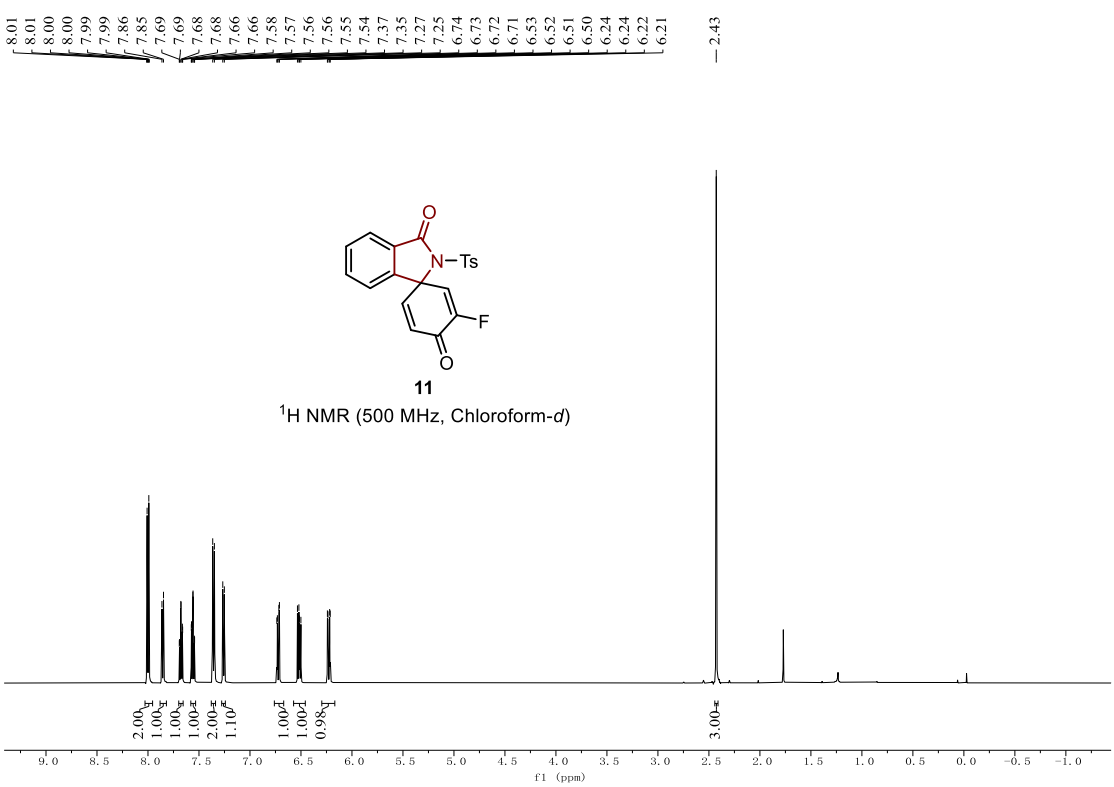

184.69
165.76
145.77
143.25
138.50
137.61
135.95
135.02
131.86
130.63
129.74
129.56
128.79
123.73
77.16
66.60
21.79
16.78
O
N–Ts
CH3
O
9
13C NMR (126 MHz, Chloroform-d)
f1 (ppm)


8.07
8.07
8.06
8.05
8.05
8.05
8.03
8.01
7.98
7.96
7.85
7.83
7.66
7.66
7.65
7.64
7.57
7.55
7.55
7.36
7.36
7.35
7.34
7.26
6.75
6.75
6.74
6.73
6.73
6.73
6.72
6.71
2.43
O
N–Ts
O
10
1H NMR (500 MHz, Chloroform-d)
1.99
1.00
1.00
1.96
1.00
0.98
2.03
4.00
3.00
f1 (ppm)



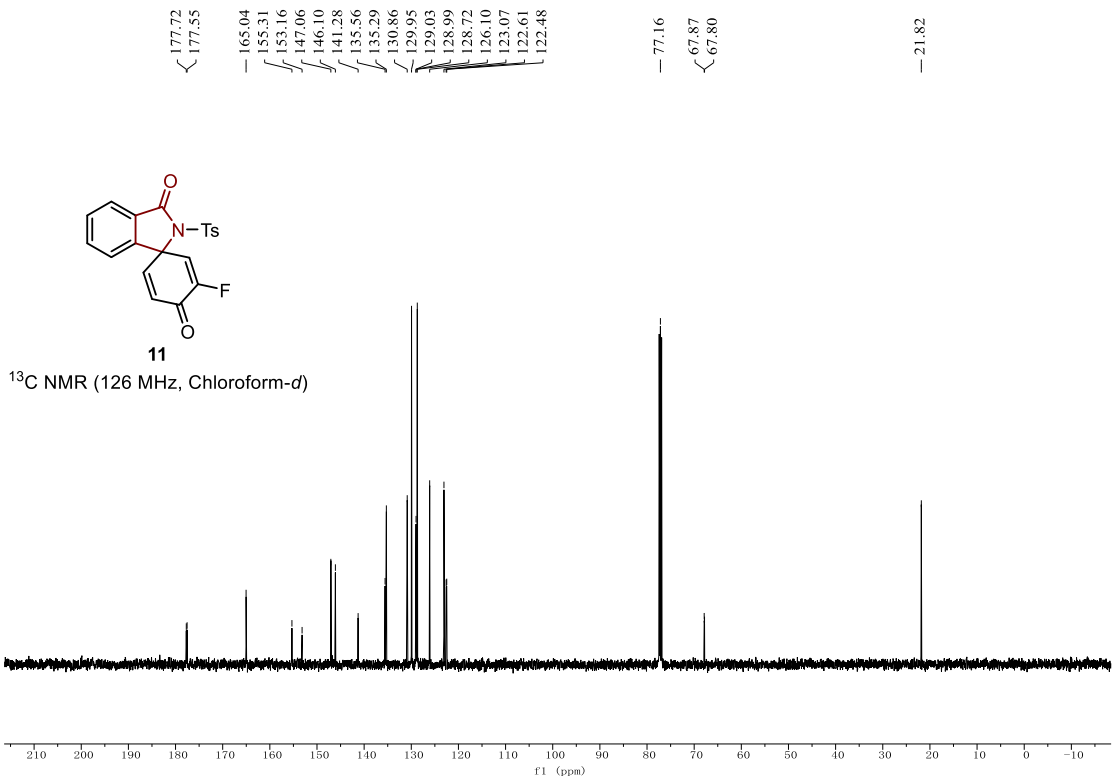
10

^{13}C NMR (126 MHz, Chloroform-*d*)



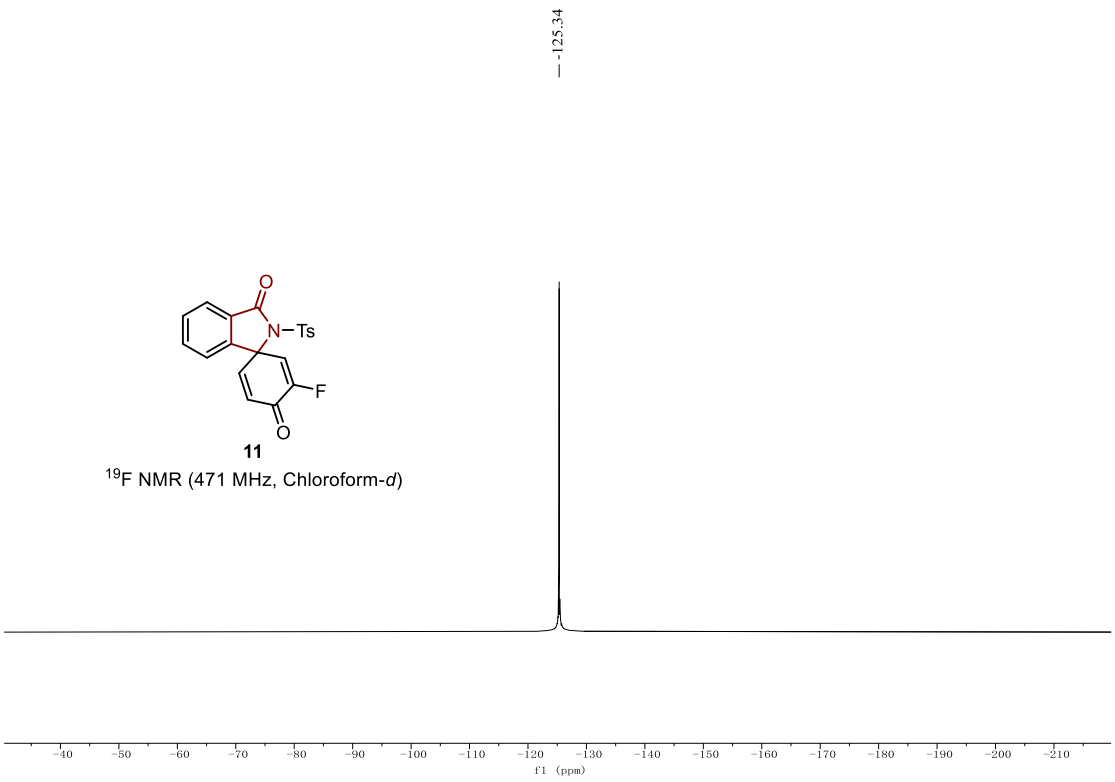
11

^{1}H NMR (500 MHz, Chloroform-*d*)



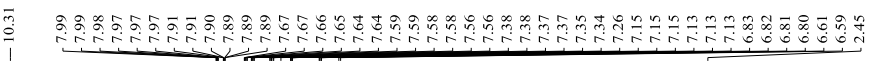
11

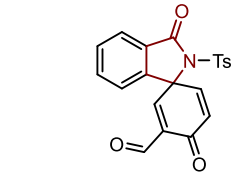
^{13}C NMR (126 MHz, Chloroform-*d*)



11

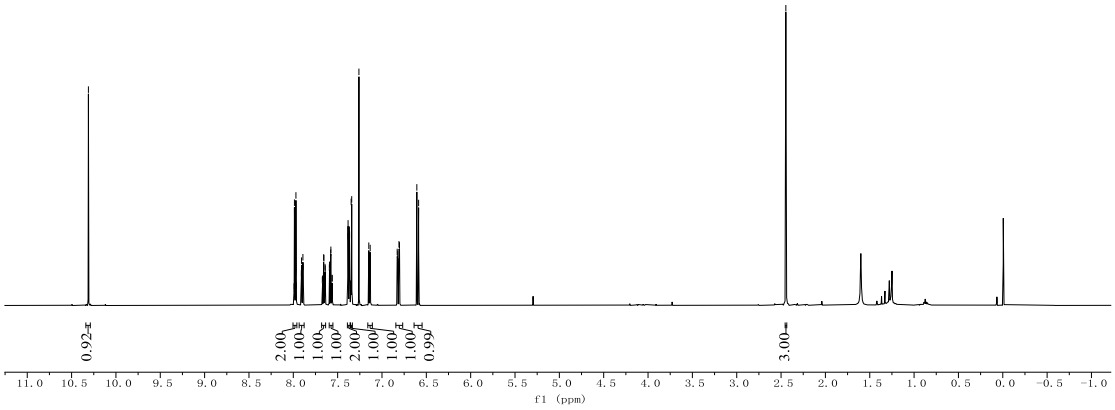
^{19}F NMR (471 MHz, Chloroform-*d*)

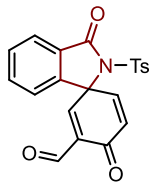




12

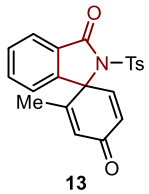
^{1}H NMR (500 MHz, Chloroform-*d*)





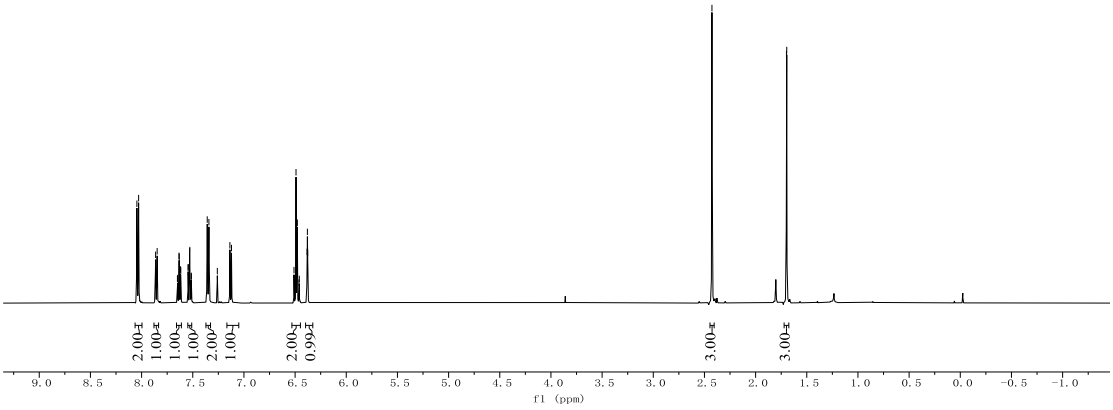
12

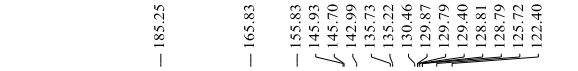
^{13}C NMR (126 MHz, Chloroform-*d*)

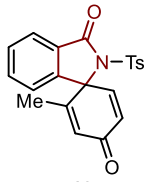


13

^{1}H NMR (500 MHz, Chloroform-*d*)

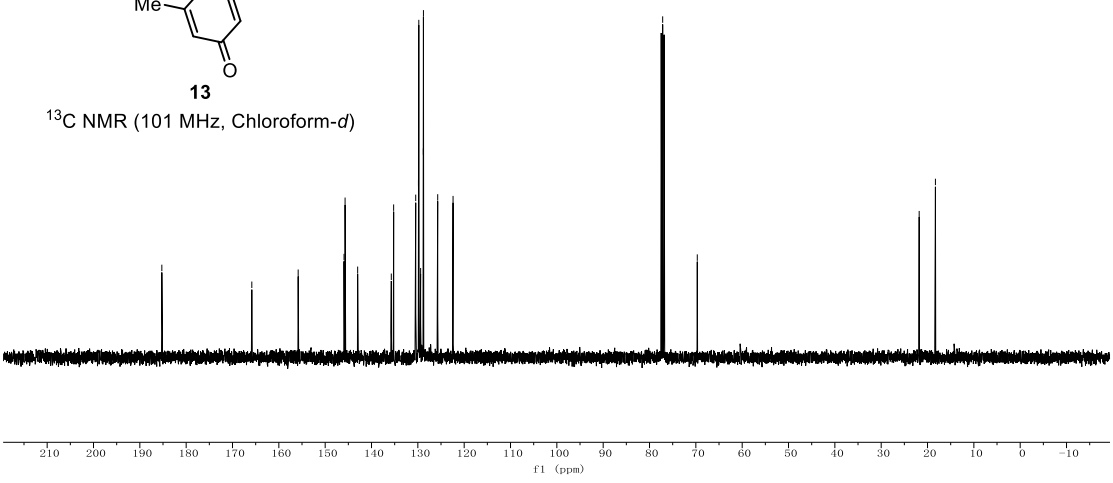


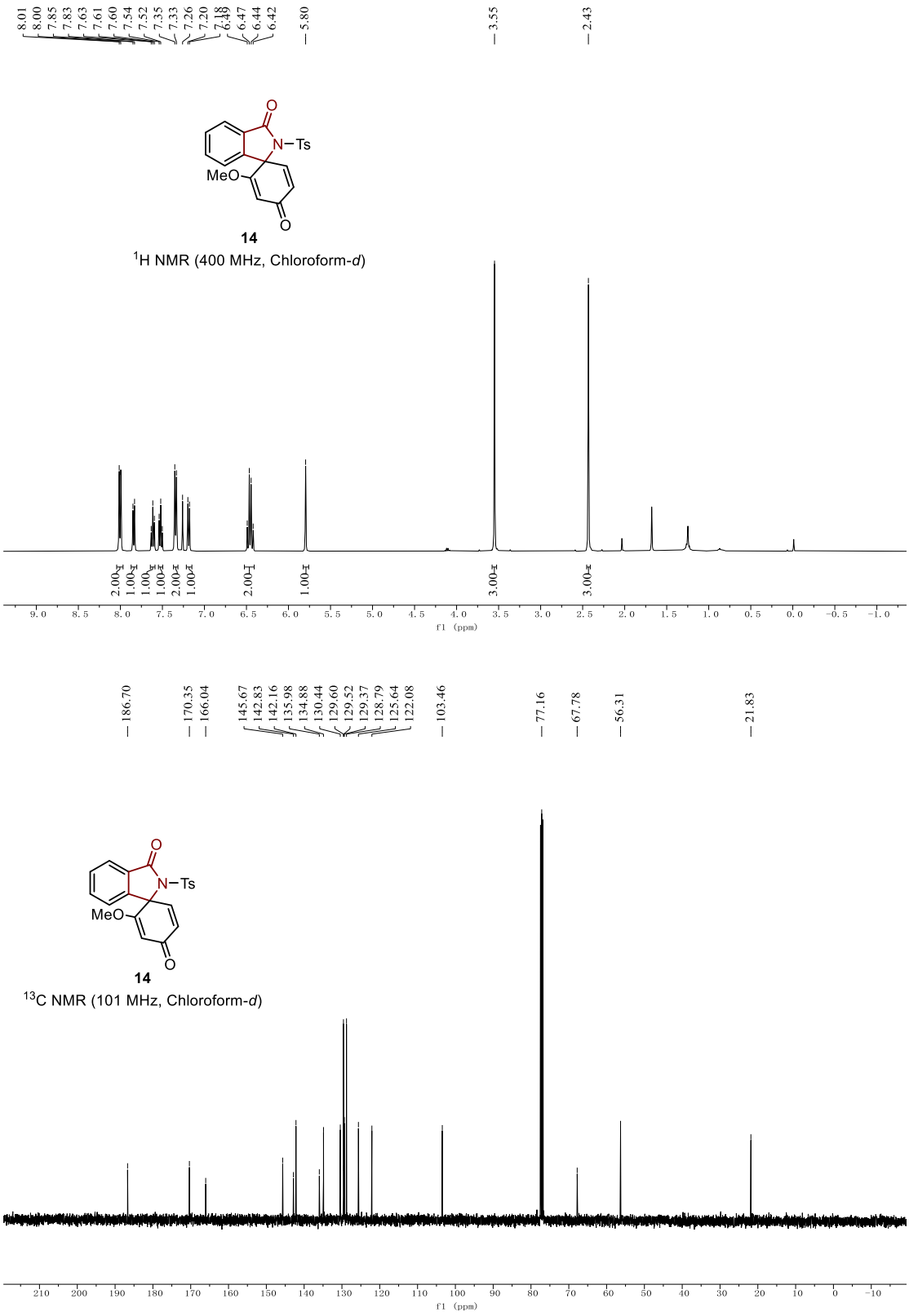


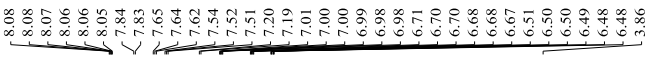


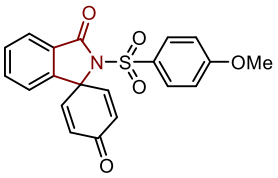
13

^{13}C NMR (101 MHz, Chloroform-*d*)



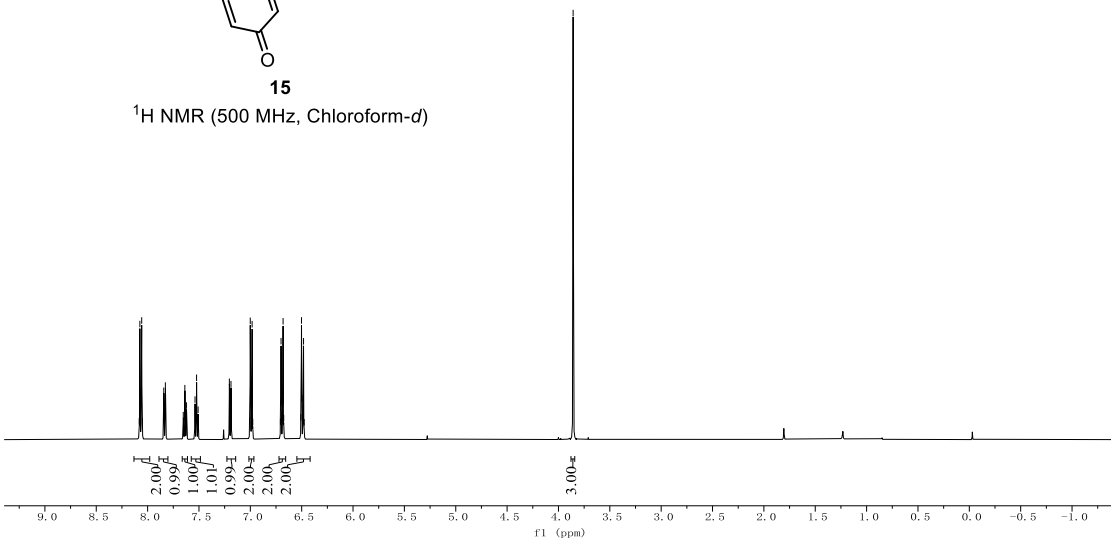

8.01
8.00
7.85
7.83
7.63
7.61
7.60
7.54
7.52
7.35
7.33
7.26
7.20
7.18
6.48
6.47
6.44
6.42
5.80
3.55
2.43
O
N−Ts
MeO
O
14
1H NMR (400 MHz, Chloroform-d)
2.00
1.00
1.00
1.00
2.00
1.00
2.00
1.00
3.00
3.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)
186.70
170.35
166.04
145.67
142.83
142.16
135.98
134.88
130.44
129.60
129.52
129.37
128.79
125.64
122.08
103.46
77.16
67.78
56.31
21.83
O
N−Ts
MeO
O
14
13C NMR (101 MHz, Chloroform-d)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

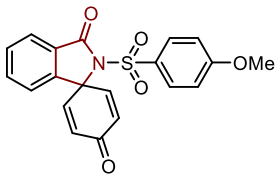




15

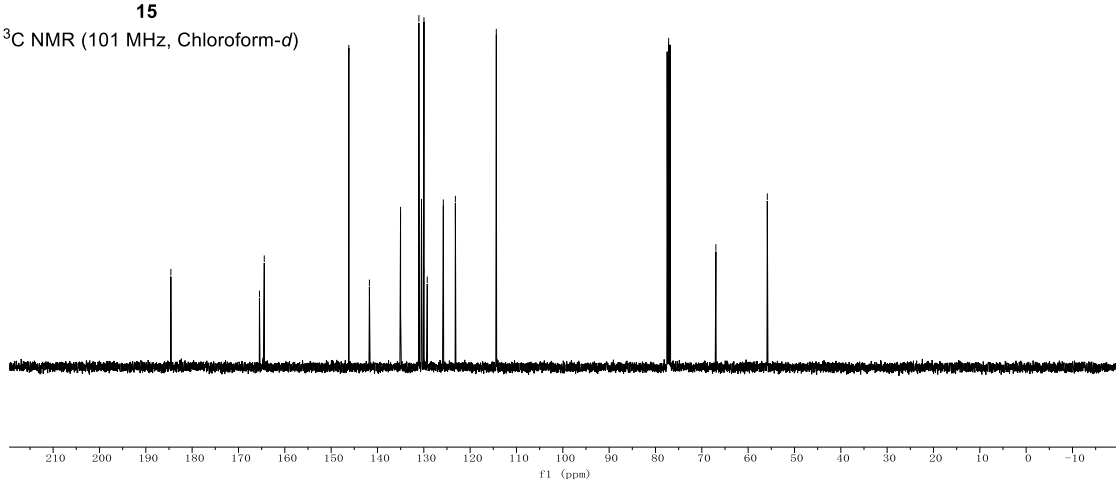
^{1}H NMR (500 MHz, Chloroform-*d*)

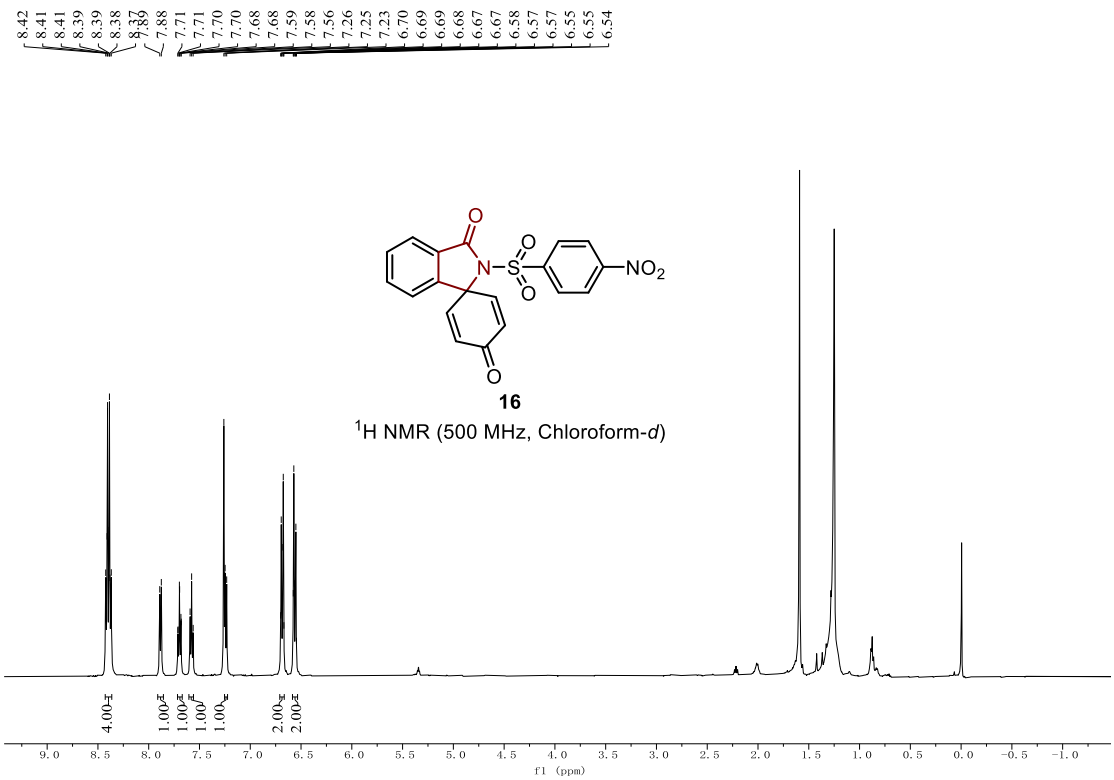


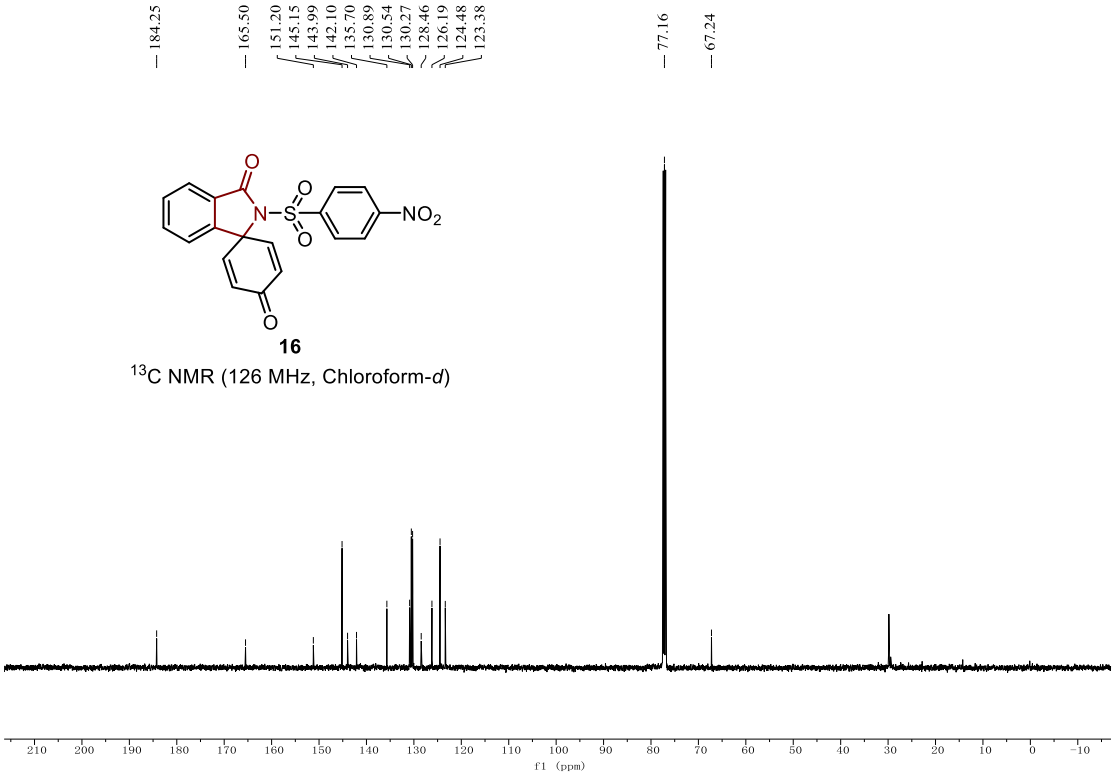


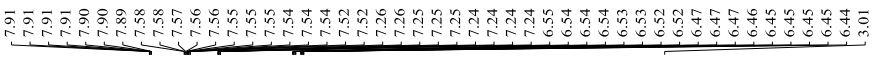
15

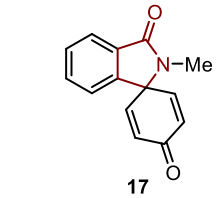
^{13}C NMR (101 MHz, Chloroform-*d*)




8.42
8.41
8.41
8.39
8.39
8.38
8.37
7.89
7.88
7.71
7.71
7.70
7.70
7.68
7.68
7.59
7.58
7.56
7.26
7.25
7.23
6.70
6.69
6.69
6.68
6.67
6.67
6.58
6.57
6.57
6.55
6.55
6.54
O
O
N
S
O
O
NO2
O
16
1H NMR (500 MHz, Chloroform-d)
4.00
1.00
1.00
1.00
1.00
2.00
2.00
f1 (ppm)

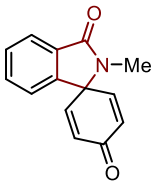

184.25
165.50
151.20
145.15
143.99
142.10
135.70
130.89
130.54
130.27
128.46
126.19
124.48
123.38
77.16
67.24
O
O
N
S
O
O
NO2
O
16
13C NMR (126 MHz, Chloroform-d)
f1 (ppm)





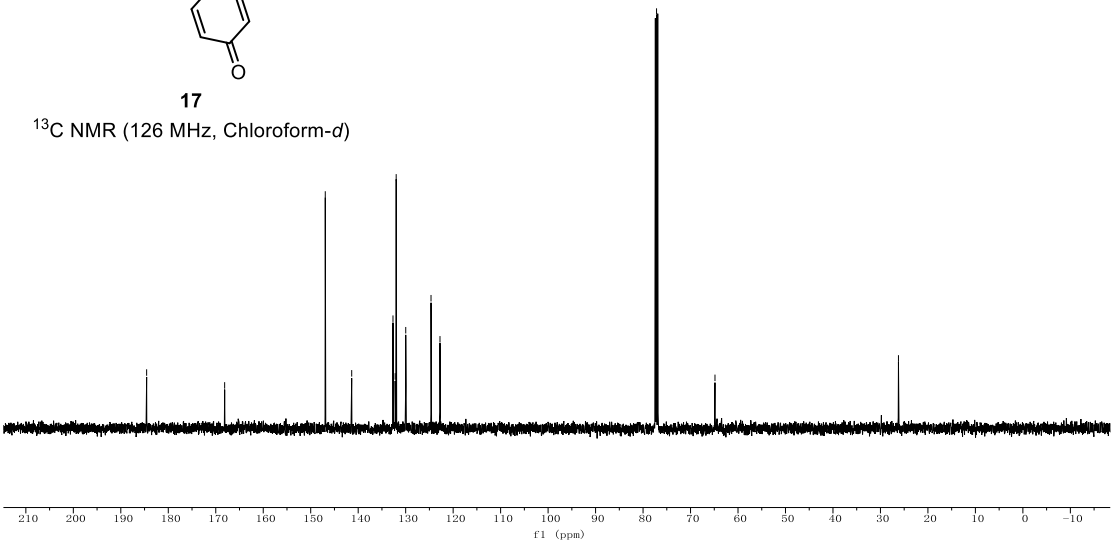
17

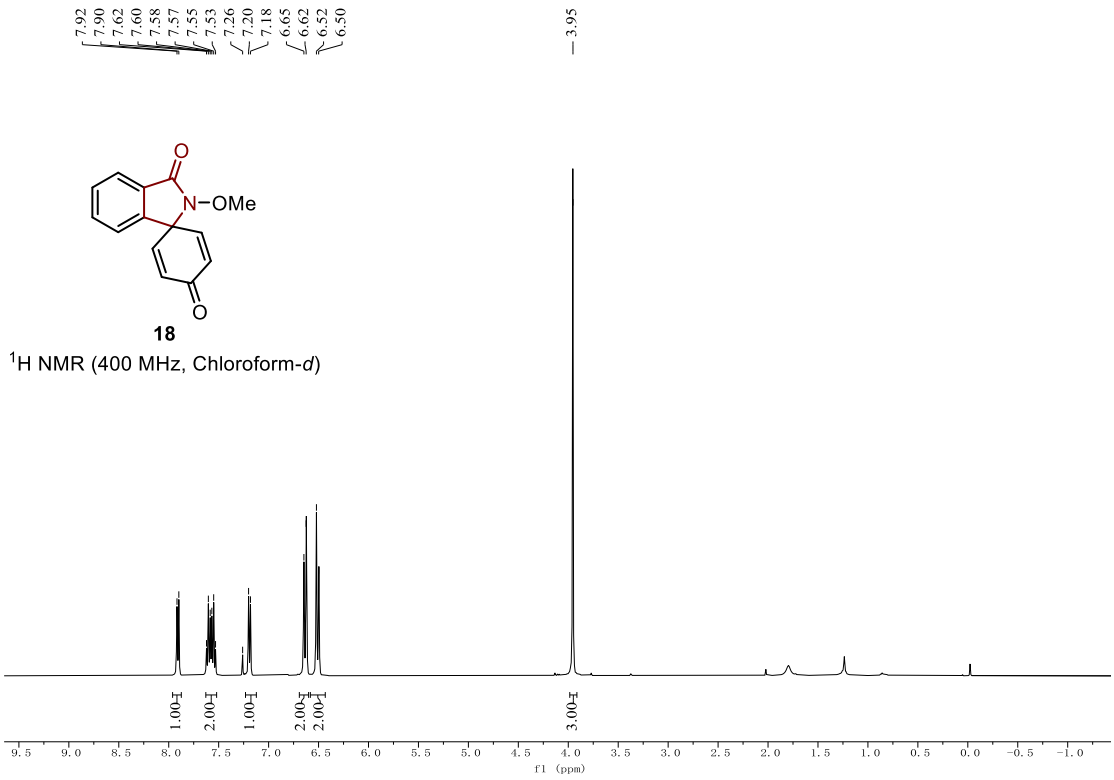
^{1}H NMR (500 MHz, Chloroform-*d*)



17

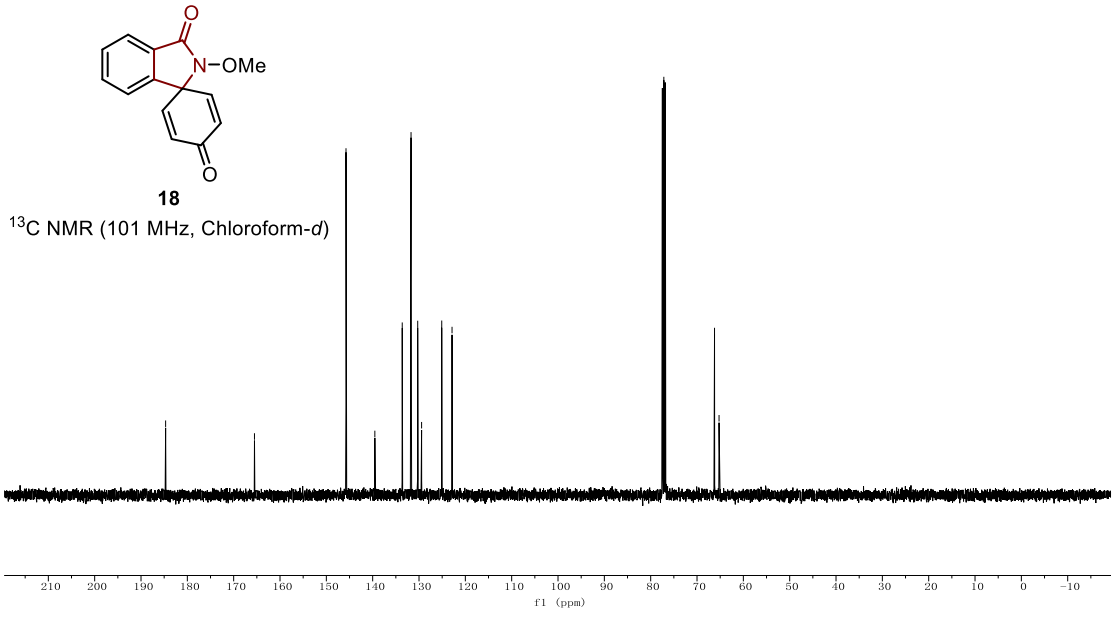
^{13}C NMR (126 MHz, Chloroform-*d*)





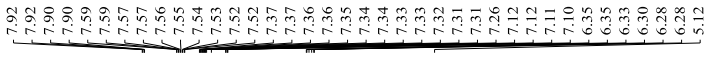
18

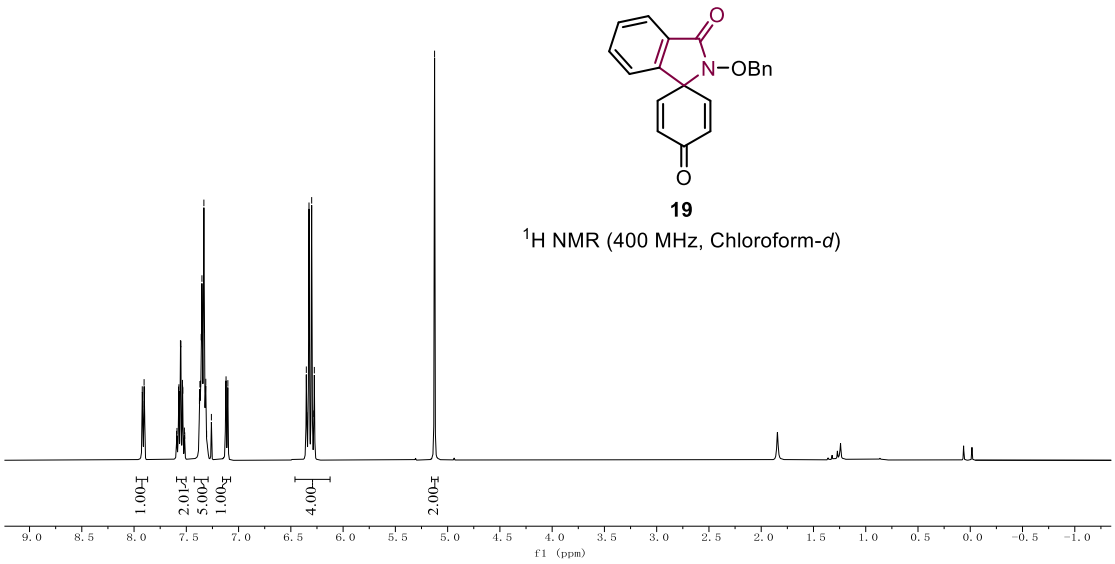
^{1}H NMR (400 MHz, Chloroform-*d*)



18

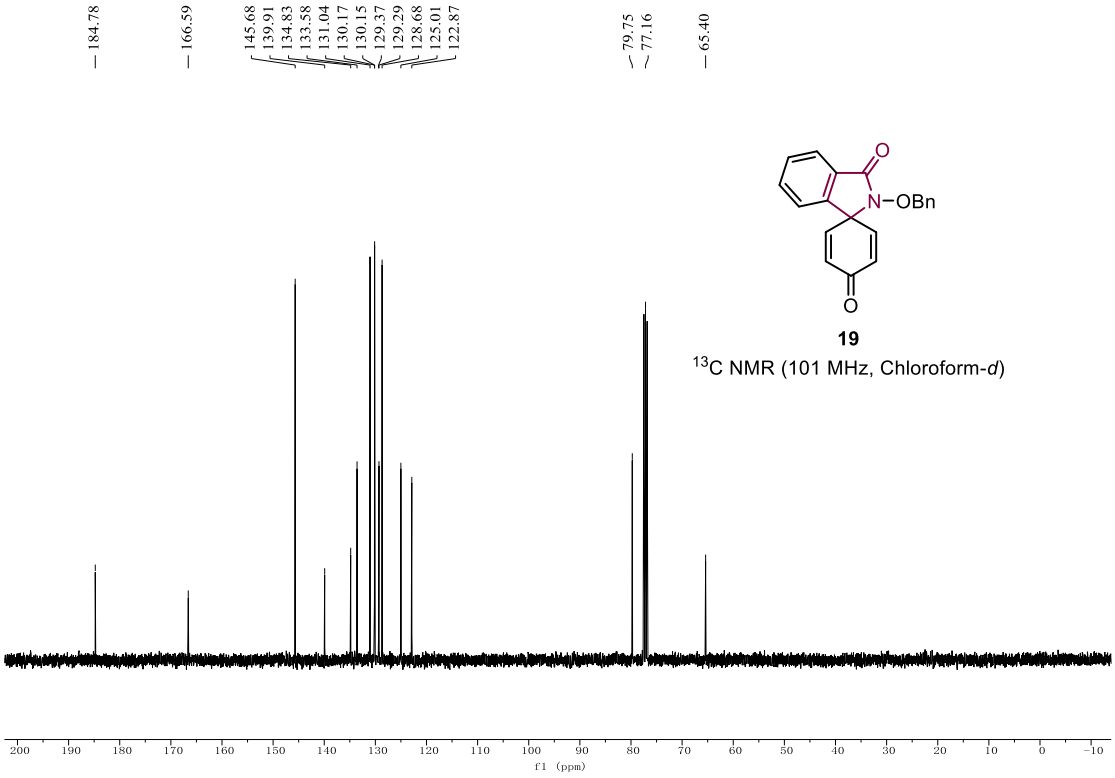
^{13}C NMR (101 MHz, Chloroform-*d*)





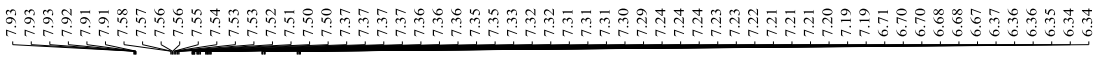
19

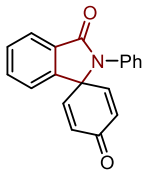
^{1}H NMR (400 MHz, Chloroform-*d*)



19

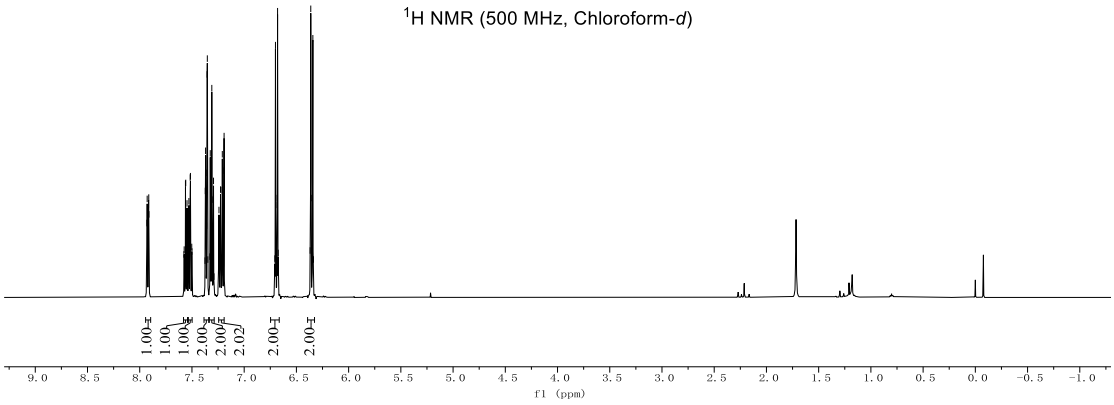
^{13}C NMR (101 MHz, Chloroform-*d*)

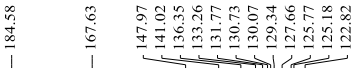


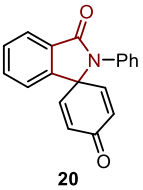


20

^{1}H NMR (500 MHz, Chloroform-*d*)

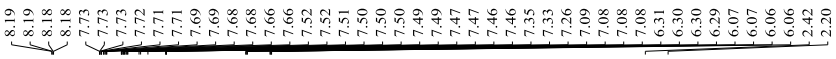


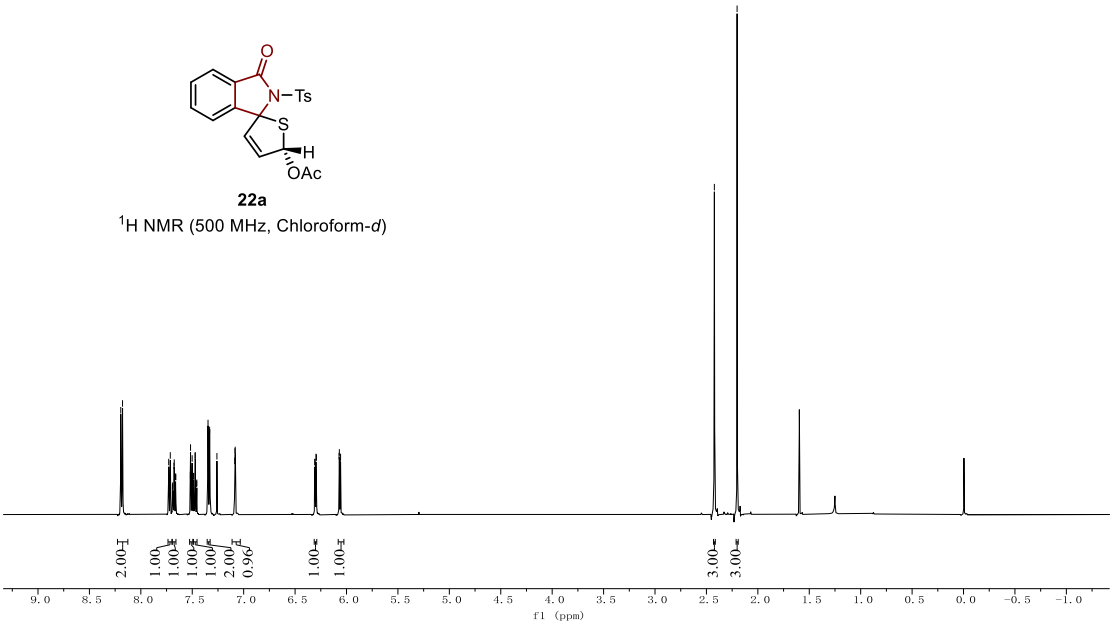




20

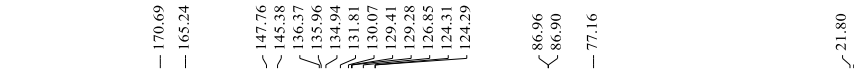
^{13}C NMR (126 MHz, Chloroform-*d*)

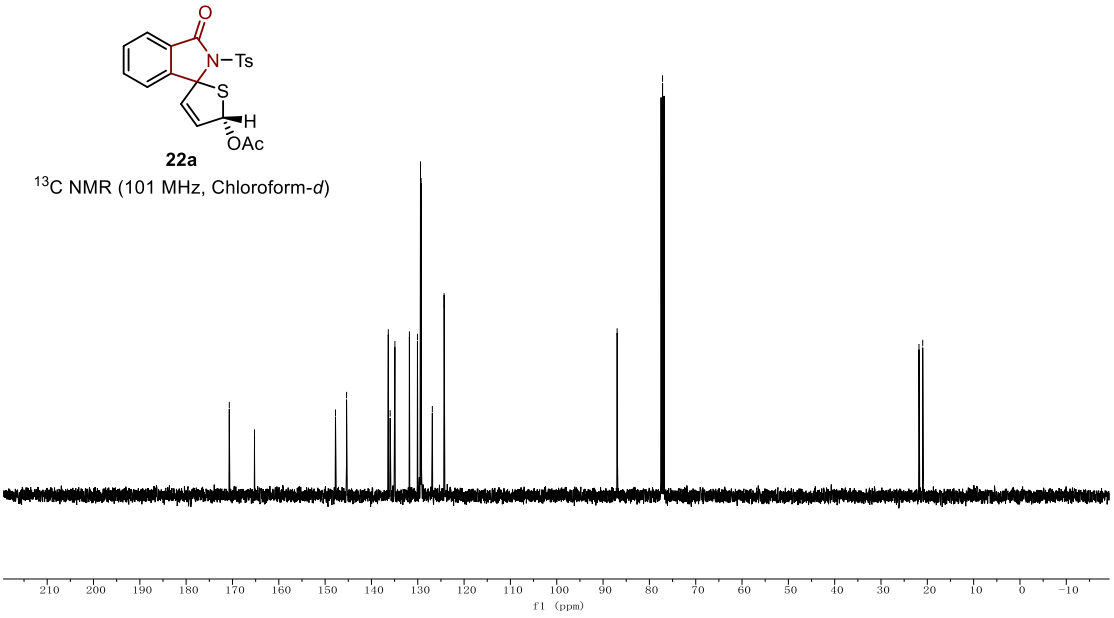




22a

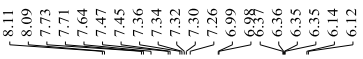
^{1}H NMR (500 MHz, Chloroform-*d*)

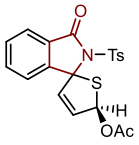




22a

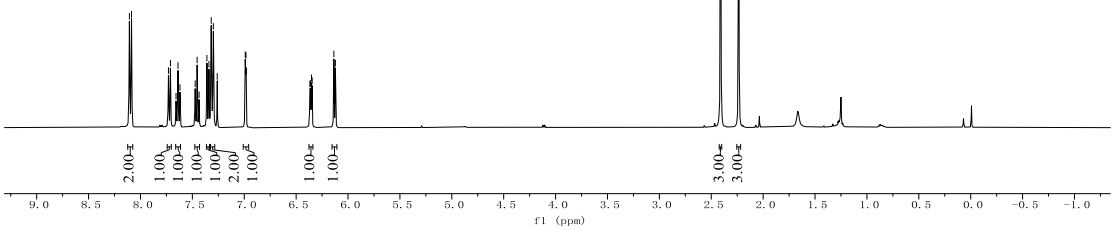
^{13}C NMR (101 MHz, Chloroform-*d*)

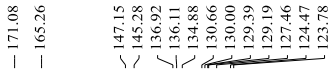


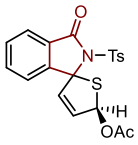


22b

^{1}H NMR (400 MHz, Chloroform-*d*)

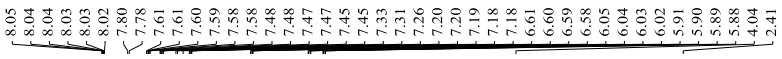


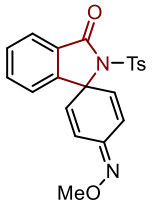




22b

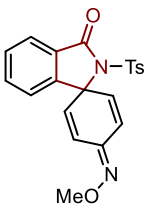
^{13}C NMR (101 MHz, Chloroform-*d*)





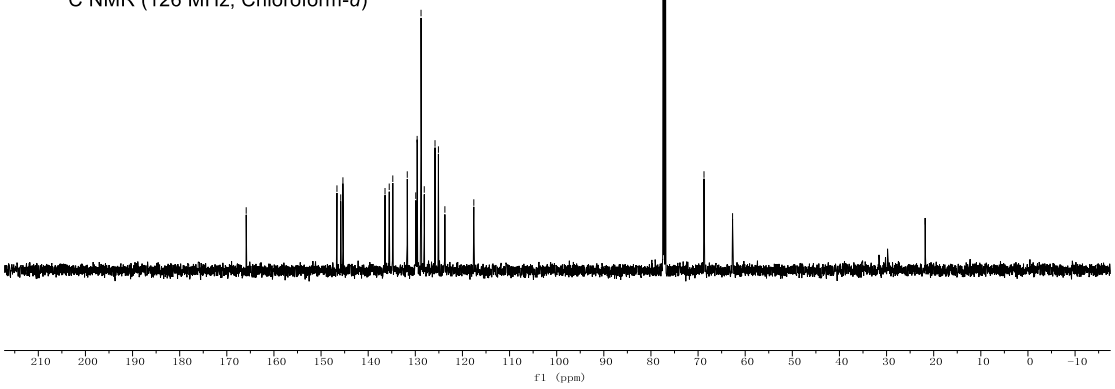
23

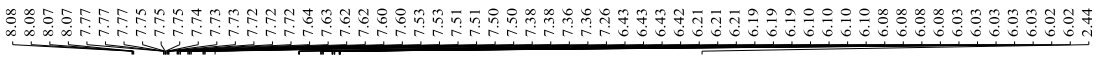
^{1}H NMR (500 MHz, Chloroform-*d*)

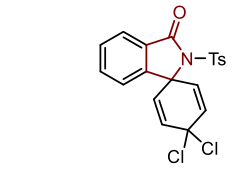


23

^{13}C NMR (126 MHz, Chloroform-*d*)

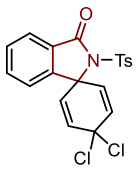






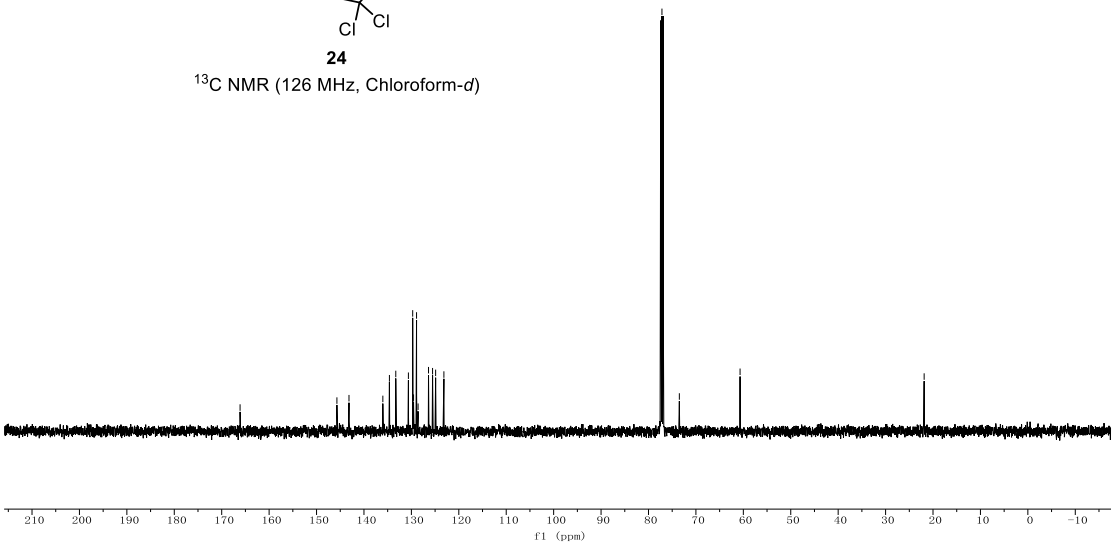
24

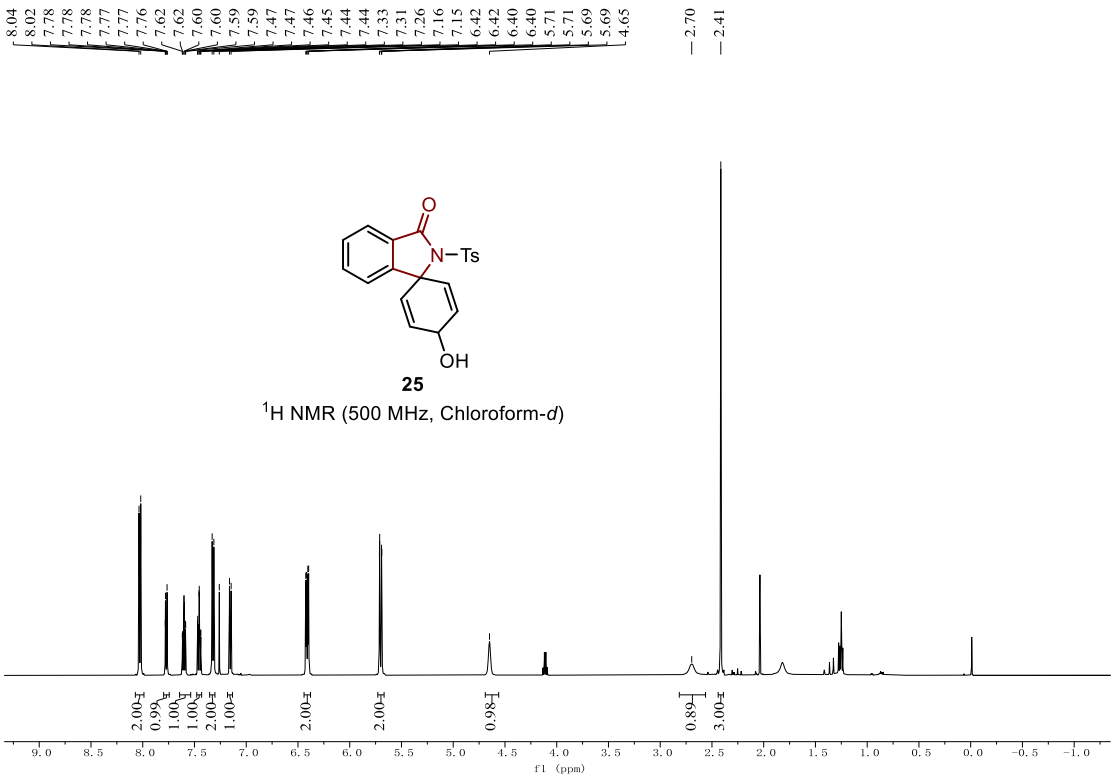
^{1}H NMR (500 MHz, Chloroform-*d*)



24

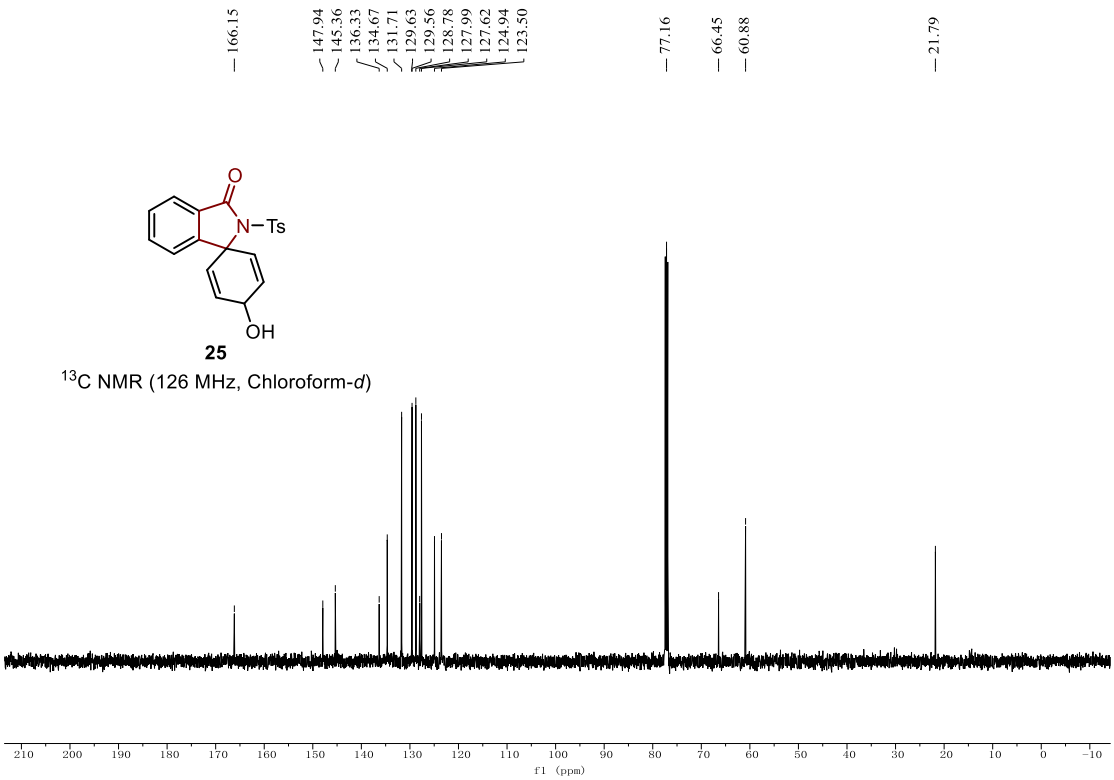
^{13}C NMR (126 MHz, Chloroform-*d*)





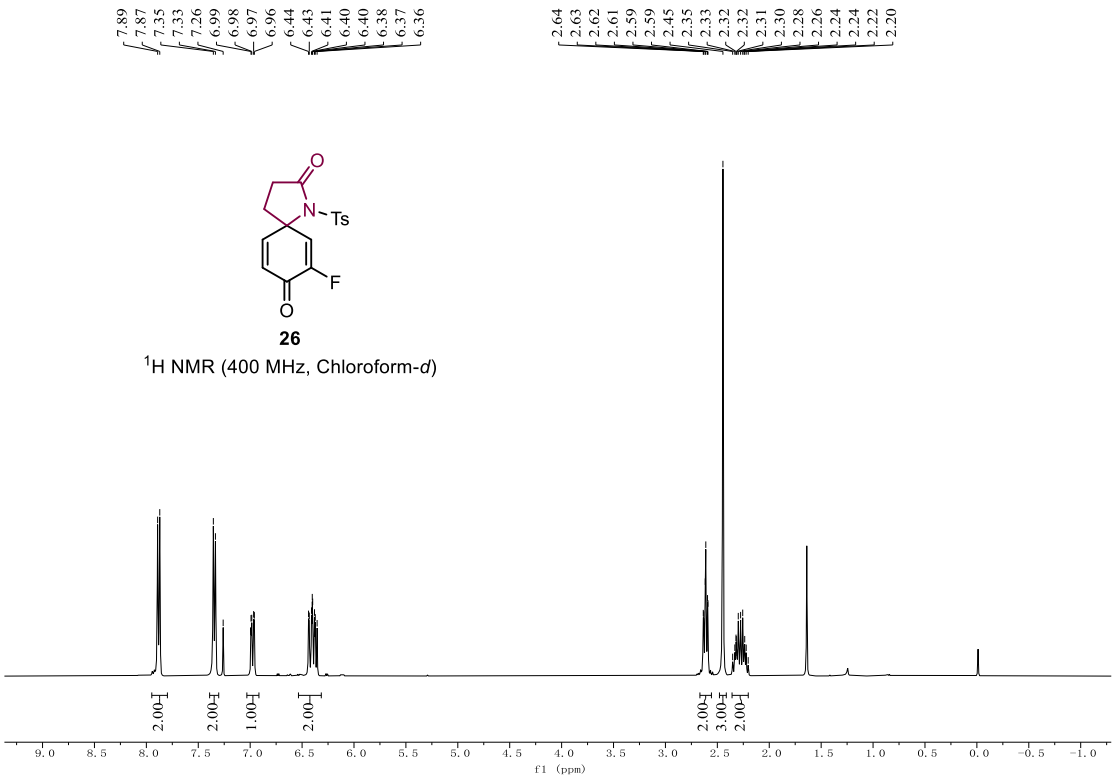
25

^{1}H NMR (500 MHz, Chloroform-*d*)



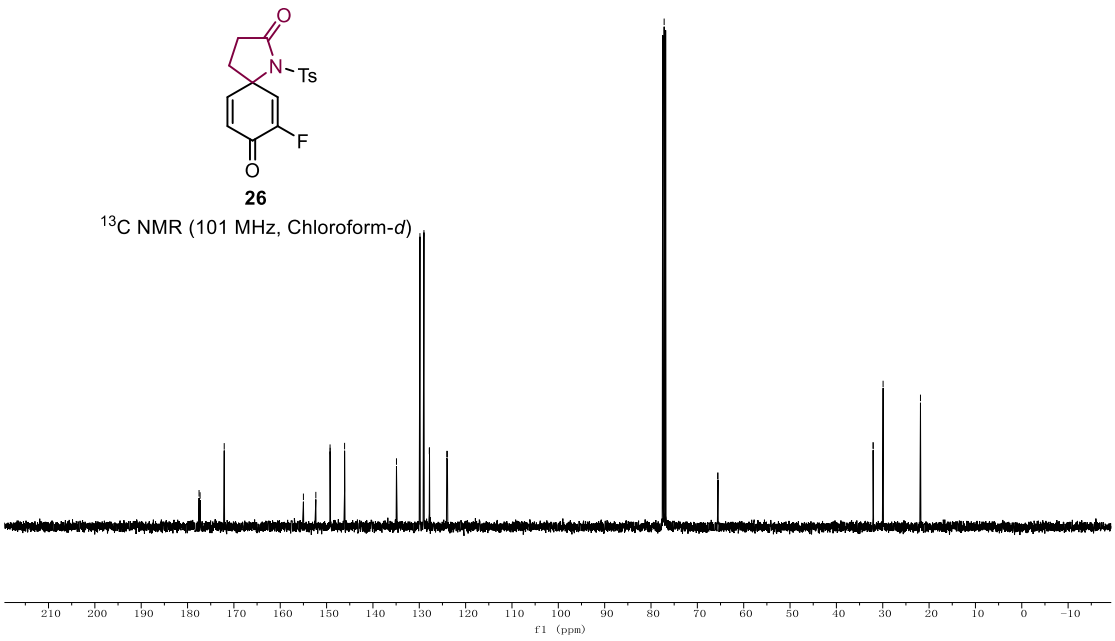
25

^{13}C NMR (126 MHz, Chloroform-*d*)



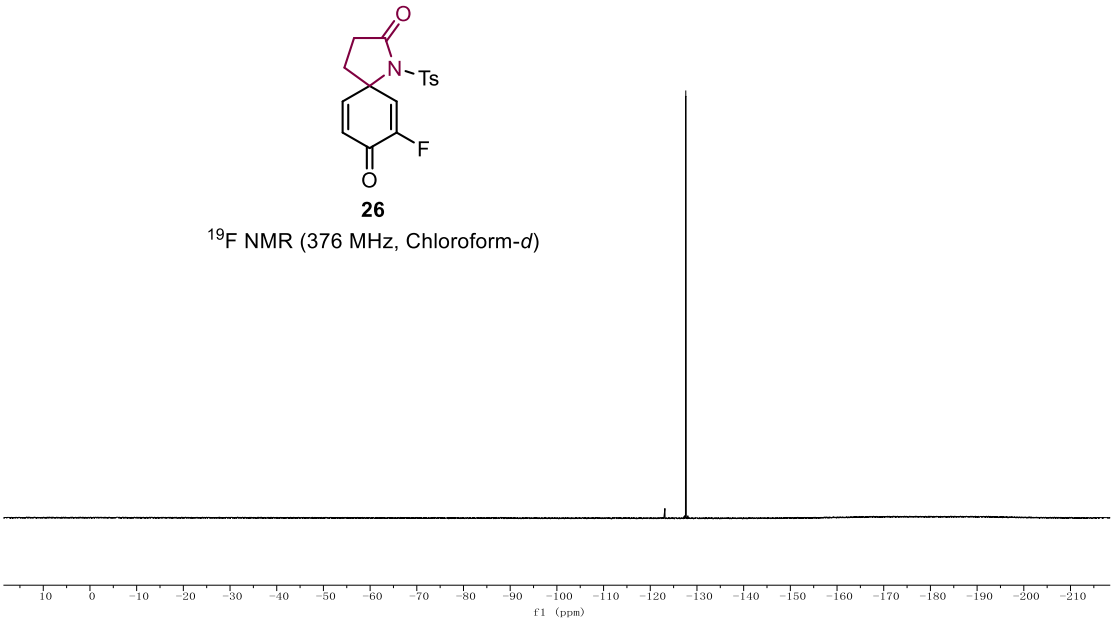
26

^{1}H NMR (400 MHz, Chloroform-*d*)



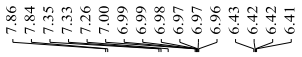
26

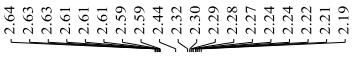
^{13}C NMR (101 MHz, Chloroform-*d*)



26

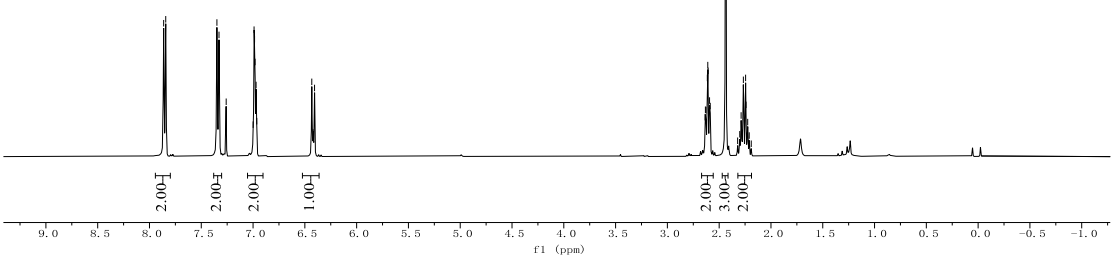
^{19}F NMR (376 MHz, Chloroform-*d*)

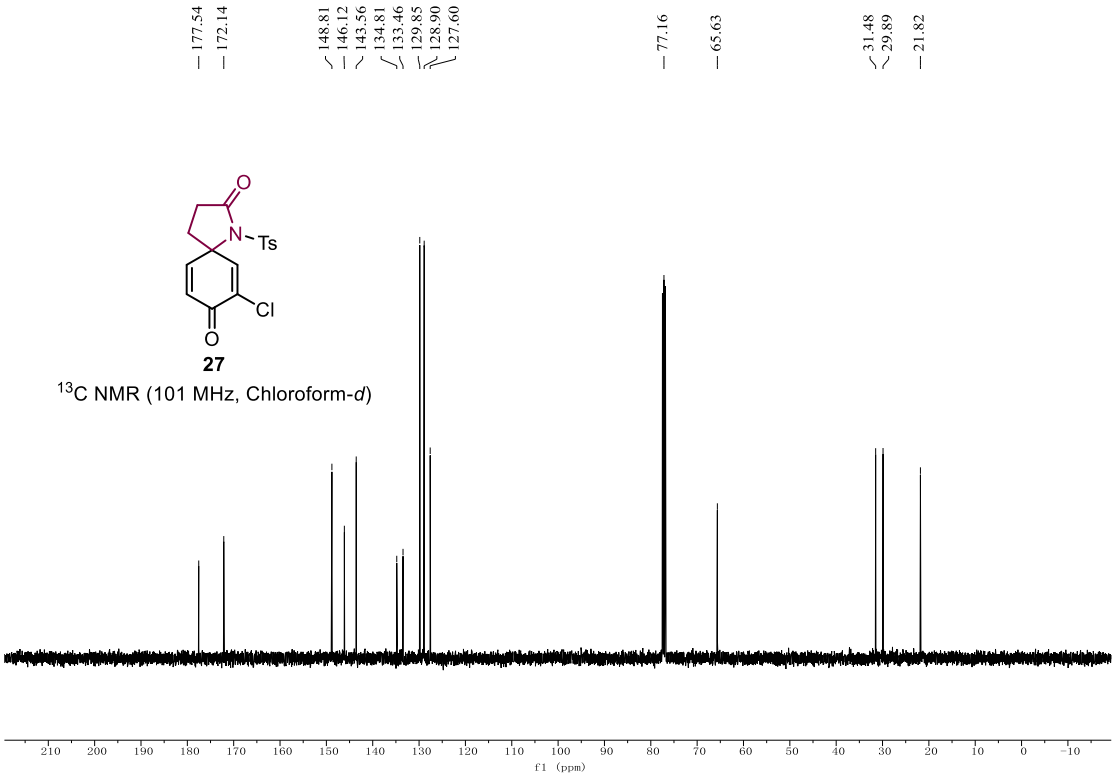




27

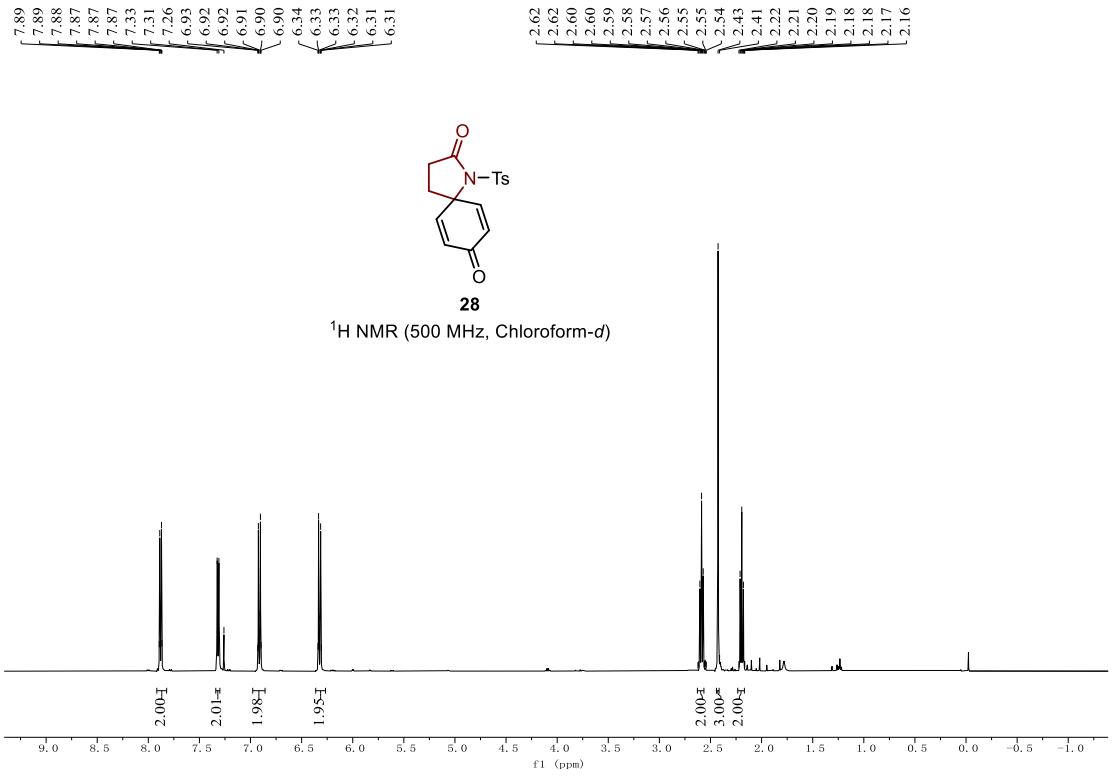
^{1}H NMR (400 MHz, Chloroform-*d*)





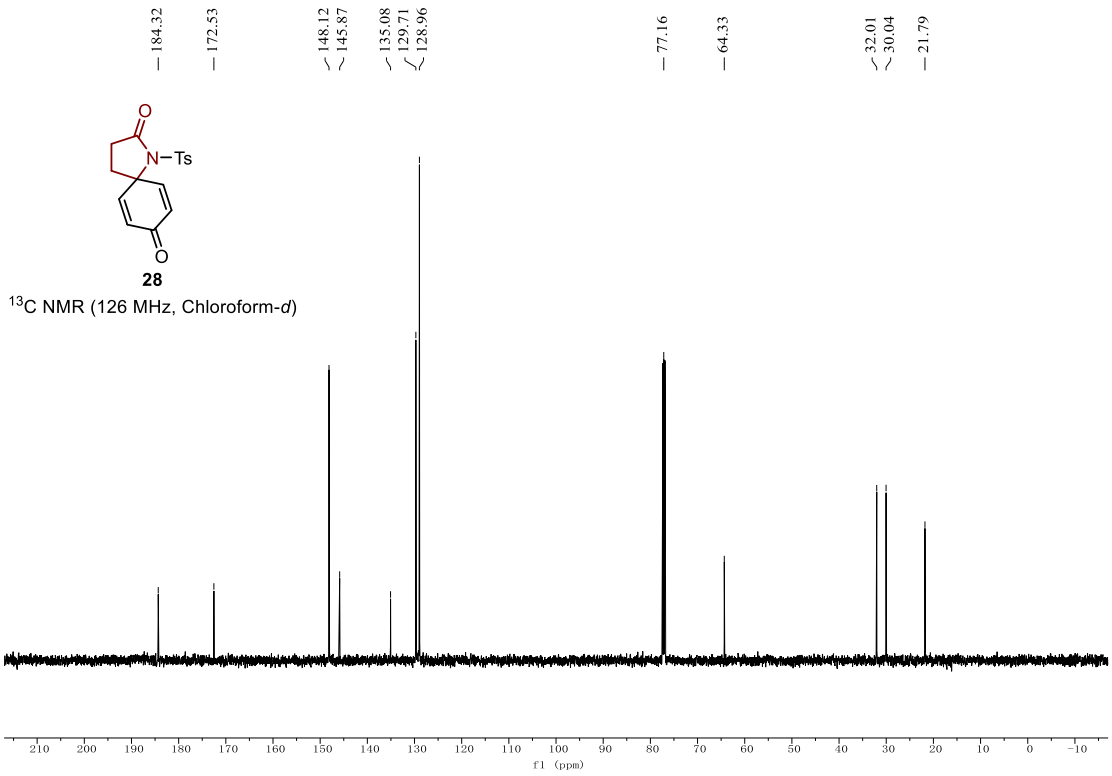
27

^{13}C NMR (101 MHz, Chloroform-*d*)



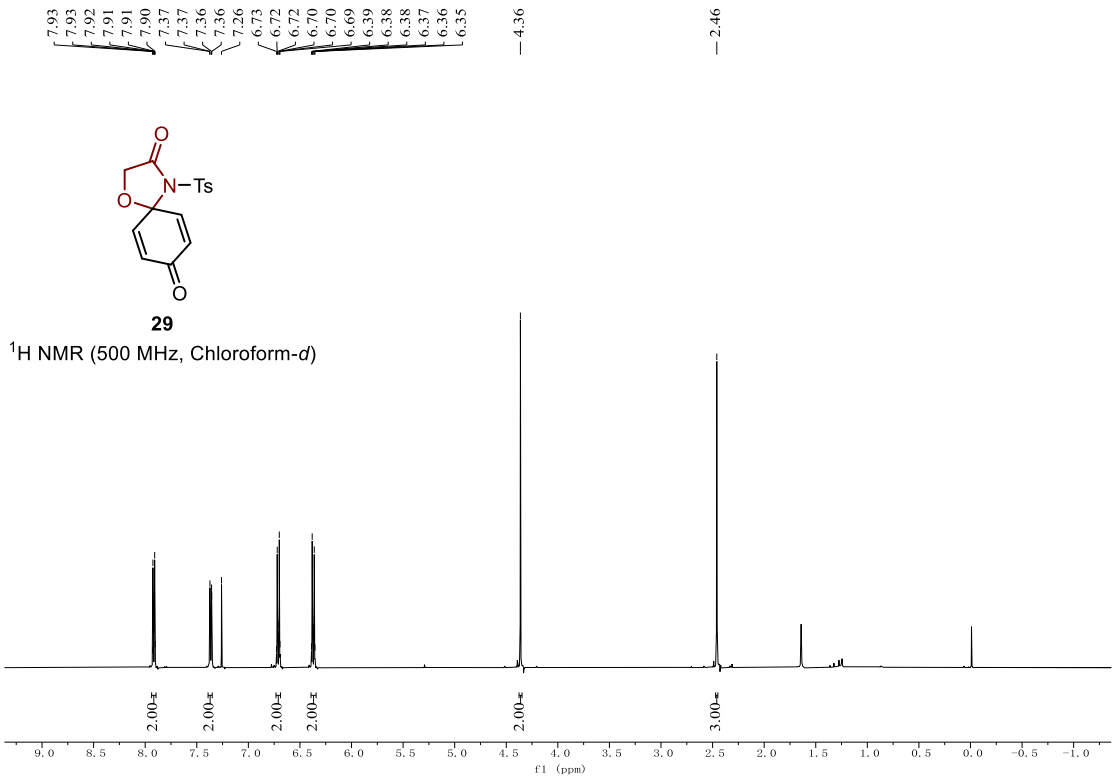
28

^{1}H NMR (500 MHz, Chloroform-*d*)



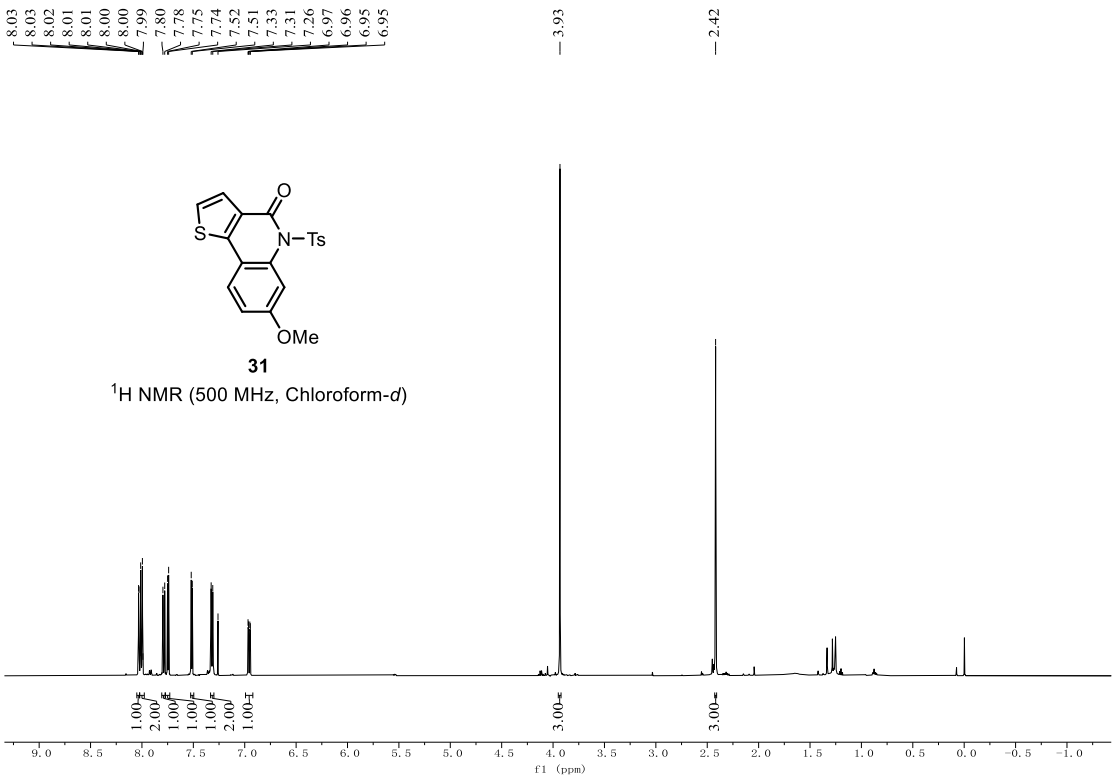
28

^{13}C NMR (126 MHz, Chloroform-*d*)



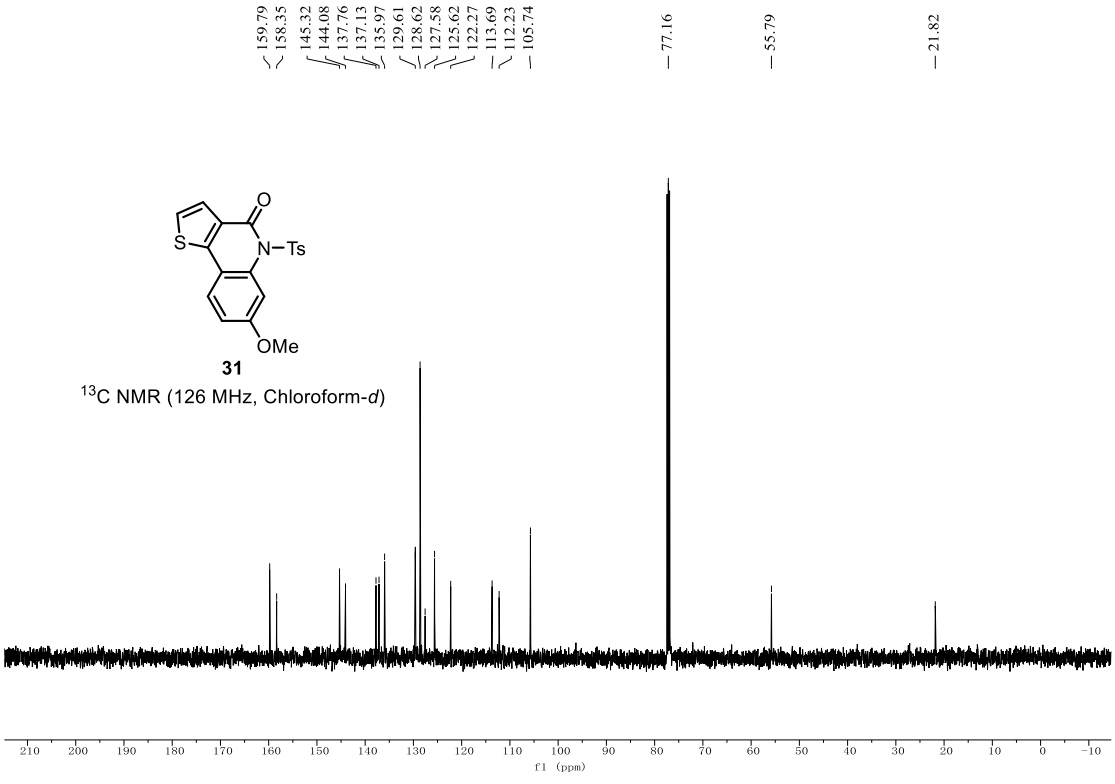
29

^{1}H NMR (500 MHz, Chloroform-*d*)



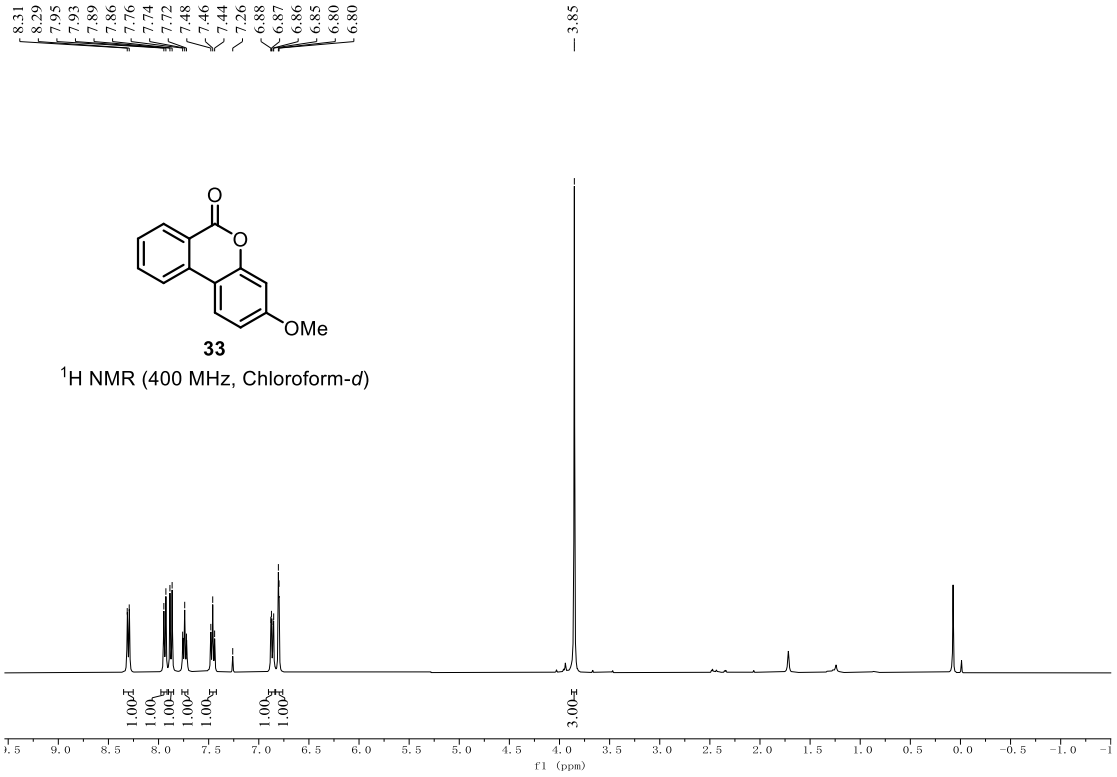
31

^{1}H NMR (500 MHz, Chloroform-*d*)



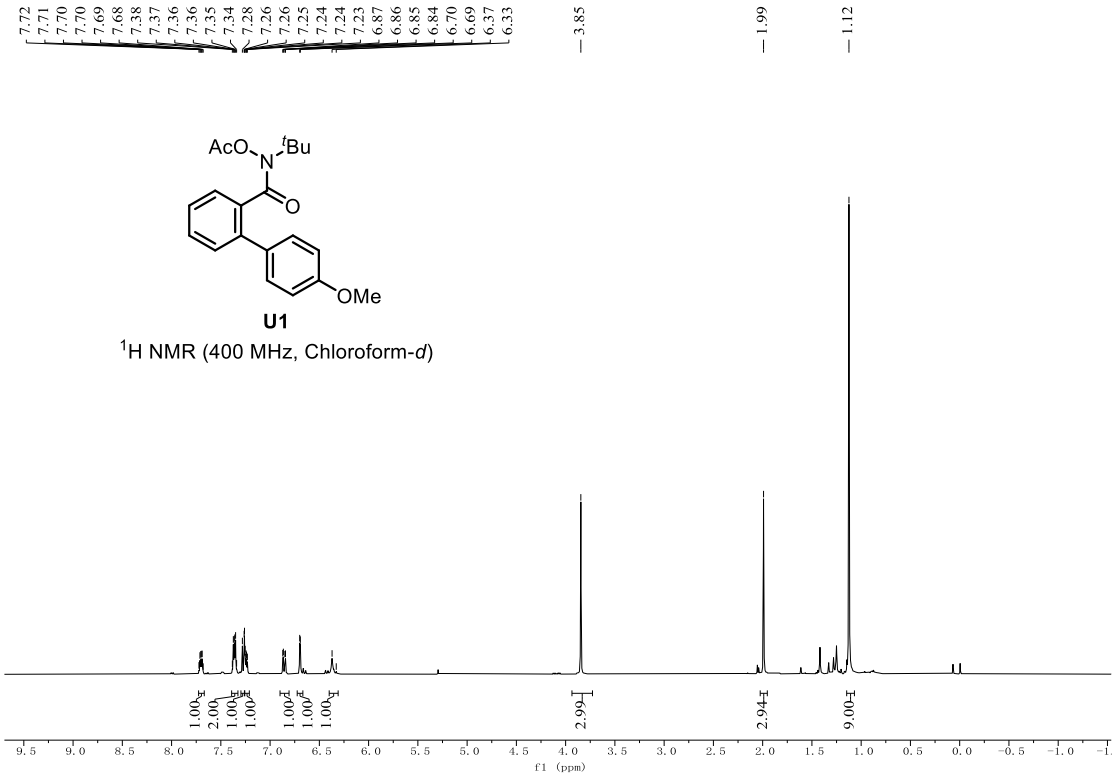
31

^{13}C NMR (126 MHz, Chloroform-*d*)



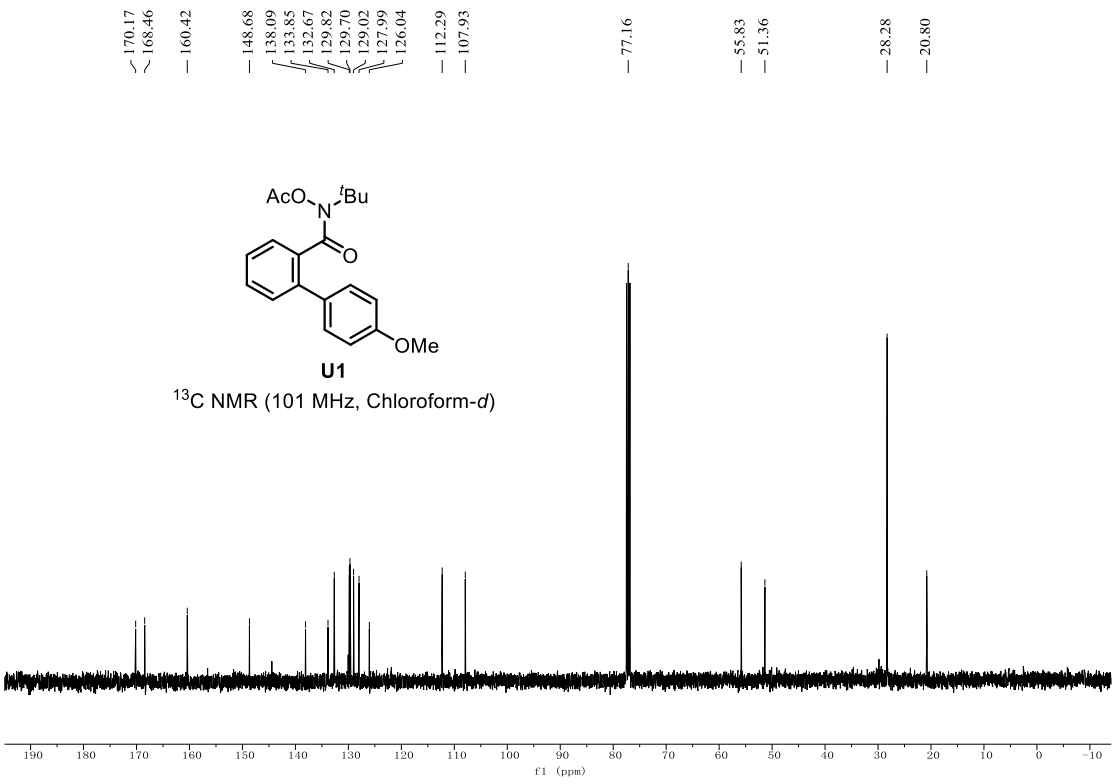
33

^{1}H NMR (400 MHz, Chloroform-*d*)



U1

^{1}H NMR (400 MHz, Chloroform-*d*)



U1

^{13}C NMR (101 MHz, Chloroform-*d*)

11. References

(1) Huang, C.; Qian, X. Y.; Xu, H. C., Continuous-Flow Electrosynthesis of Benzofused S-Heterocycles by Dehydrogenative C-S Cross-Coupling. *Angew .Chem. Int .Ed.* **2019,** *58*, 6650-6653.

(2) James, S. N.; Coster, M. J., Synthesis of N-alkylsulfonamides by borane–dimethyl sulfide reduction of N-acylsulfonamides. *Tetrahedron Lett.* **2015,** *56*, 2059-2061.

(3) Li, Y.; Ding, Y.-J.; Wang, J.-Y.; Su, Y.-M.; Wang, X.-S., Pd-Catalyzed C–H Lactonization for Expedient Synthesis of Biaryl Lactones and Total Synthesis of Cannabinol. *Org. Lett.* **2013,** *15*, 2574-2577.

(4) Mizuno, C. S.; Chittiboyina, A. G.; Patny, A.; Kurtz, T. W.; Pershadsingh, H. A.; Speth, R. C.; Karamyan, V. T.; Avery, M. A., Design, synthesis, and docking studies of telmisartan analogs for the treatment of metabolic syndrome. *Med. Chem. Res.* **2009,** *18*, 611.

(5) Pi, J. J.; Lu, X. Y.; Liu, J. H.; Lu, X.; Xiao, B.; Fu, Y.; Guimond, N., Exploration of Biaryl Carboxylic Acids as Proton Shuttles for the Selective Functionalization of Indole C-H Bonds. *J. Org. Chem.* **2018,** *83*, 5791-5800.

(6) Lee, E.; Hwang, Y.; Kim, Y. B.; Kim, D.; Chang, S., Enantioselective Access to Spirolactams via Nitrenoid Transfer Enabled by Enhanced Noncovalent Interactions. *J. Am. Chem. Soc.* **2021,** *143*, 6363-6369.

(7) Kutyrev, A. A.; Biryukov, V. V.; Litvinov, I. A.; Katayeva, O. N.; Musin, R. Z.; Enikeyev, K. M.; Naumov, V. A.; Ilyasov, A. V.; Moskva, V. V., Intramolecular cyclization of 9,10-anthraquinones promoted by reaction with halogenophosphoranes. *Tetrahedron* **1990,** *46*, 4333-4352.

(8) Nair, A. M.; Halder, I.; Khan, S.; Volla, C. M. R., Metal Free Sulfonylative Spirocyclization of Alkenyl and Alkynyl Amides via Insertion of Sulfur Dioxide. *Adv. Synth. Catal.* **2019,** *362*, 224-229.

(9) Chen, C.; Luo, Y.; Yin, H.; Zhong, Q.; Zheng, S.; Liu, R.; Zhao, C.; Wang, G.; He, L., Design, synthesis, and antitumor activity evaluation of novel acyl sulfonamide spirodienones. *Bioorg. Med. Chem.* **2022,** *60*.

12. X-ray Crystallographic Data

12.1 The structure of **2** was determined by the X-ray diffraction. Recrystallized from DCM and n-hexane. Further information can be found in the CIF file (Deposition number: CCDC 2182957)

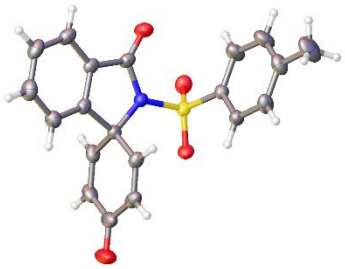


Figure S9 X-ray structure of 2

Bond precision: C-C = 0.0031 A Wavelength=0.71073

Cell: a=9.9923(7) b=16.2483(13) c=23.5565(18)
alpha=90 beta=93.807(3) gamma=90
Temperature: 296 K

	Calculated	Reported
Volume	3816.1(5)	3816.1(5)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C20 H15 N O4 S [+ solvent]	C20 H15 N O4 S, 1.15[H2O], 1.15[H2O]
Sum formula	C20 H15 N O4 S [+ solvent]	C20 H15 N O4 S
Mr	365.39	365.39
Dx,g cm-3	1.272	1.272
Z	8	8
Mu (mm-1)	0.193	0.193
F000	1520.0	1520.0
F000'	1521.72	
h,k,lmax	11,19,28	11,19,28
Nref	6739	6738
Tmin,Tmax	0.981,0.981	0.657,0.746
Tmin'	0.981	

Correction method= # Reported T Limits: Tmin=0.657 Tmax=0.746
AbsCorr = ?

Data completeness= 1.000 Theta(max)= 25.027

R(reflections)= 0.0395(5336) wR2(reflections)= 0.1149(6738)

S = 1.036 Npar= 471

12.2 The structure of **22a** was determined by the X-ray diffraction. Recrystallized from DCM and n-hexane. Further information can be found in the CIF file (Deposition number: CCDC 2182958)

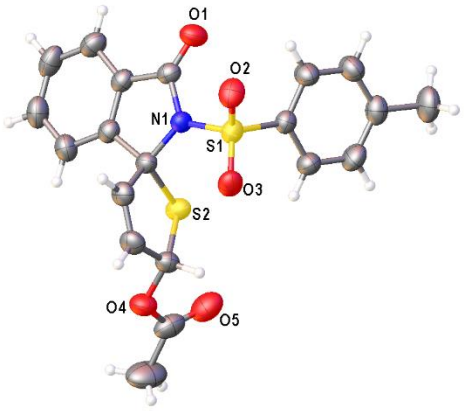


Figure S10 X-ray structure of 22a

Bond precision: C-C = 0.0027 A Wavelength=0.71073

Cell: a=7.8826(5) b=10.1995(6) c=12.8076(7)
alpha=98.238(2) beta=102.254(2) gamma=96.272(2)
Temperature: 296 K

	Calculated	Reported
Volume	985.43(10)	985.43(10)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C20 H17 N O5 S2	C20 H17 N O5 S2
Sum formula	C20 H17 N O5 S2	C20 H17 N O5 S2
Mr	415.47	415.46
Dx,g cm-3	1.400	1.400
Z	2	2
Mu (mm-1)	0.302	0.302
F000	432.0	432.0
F000'	432.70	
h,k,lmax	9,12,15	9,12,15
Nref	3506	3500
Tmin,Tmax	0.970,0.970	0.675,0.745
Tmin'	0.970	

Correction method= # Reported T Limits: Tmin=0.675 Tmax=0.745
AbsCorr = NONE

Data completeness= 0.998 Theta(max)= 25.049

R(reflections)= 0.0321(3026) wR2(reflections)= 0.0845(3500)

S = 1.062 Npar= 256