Supplementary Information (SI) for Chemical Science.
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Supporting Information

Electrochemical control enables high-concentration, one-pot macrolactonization

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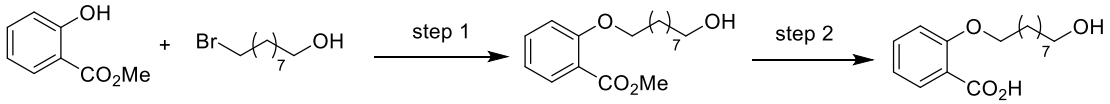
1. General information

Unless otherwise specially indicated, all the reagents were purchased from commercial supplies unless otherwise stated. All solvents used were anhydrous grade, sourced from Energy Chemical, and were used as received. NMR spectra were recorded on a Bruker Avance III spectrometer operating at 600 or 400 MHz for ^{1}H NMR and 150 or 100 MHz for ^{13}C NMR. Chemical shifts were reported in ppm downfield and referenced as follows: ^{1}H: residual internal $CHCl_3$ (δ 7.26 ppm) and DMSO (δ 2.50 ppm); ^{13}C: internal $CDCl_3$ (δ 77.2 ppm) and DMSO (δ 39.5 ppm). Coupling constants were quoted in Hz (*J*). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet).

2. General procedure for the synthesis of starting materials

The hydroxy acids were synthesized according to a previously reported procedure, [1,2,3] which involves two key steps: etherification and ester hydrolysis. This process is illustrated by the synthesis of compound **D** from starting material **A**.

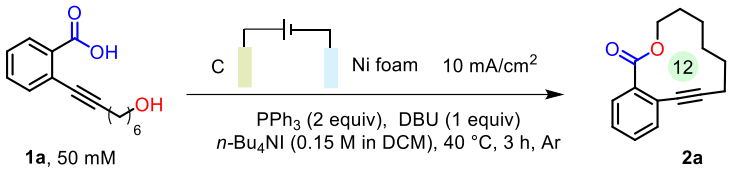


A **B** **C** **D**

Step 1: Methyl salicylate (10 mmol, 1 equiv.) was dissolved in dry DMF (10 mL) in a dry flask under inert atmosphere. K_2CO_3 (15 mmol, 1.5 equiv.) was added in one portion before the addition of **B** (12 mmol, 1.2 equiv.). The reaction was heated to 60 ^{o}C for 5 h. The reaction mixture was diluted with 20 mL water and 50 mL ethyl acetate. The phases were separated, and the aqueous phase was extracted twice with 50 mL of ethyl acetate. The organic phases were combined and washed with brine before drying over anhydrous Na_2SO_4. After filtering to remove solids and concentrating under vacuum, the crude residue was purified via flash chromatography over silica gel (20-40% ethyl acetate in petroleum ether) to afford **C** as a colorless oil (2.6 g, 89%).

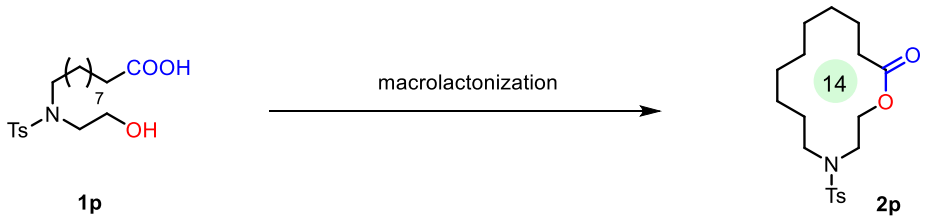
To a flask was added **C** (1.5 g, 5 mmol), then a mixed solution of methanol and water (10 mL, V/V 1:1) and NaOH (25 mmol, 5 equiv.) were added sequentially. The mixture was stirred at room temperature for 12 hours. Then, methanol was removed and the resulting mixture was extracted with ethyl acetate (3 × 30 mL). The combined aqueous layers were then acidized with HCl (4 M) to pH = 2. The crude was extracted with ethyl acetate (3 × 30 mL), dried over anhydrous Na_2SO_4 and filtered. The solvent was removed by rotary evaporation to give **D** as a white solid (1.4 g, 98%).

3. General procedure for the electrochemical synthesis of 2a



An undivided cell was equipped with a graphite plate anode (10 mm × 10 mm × 1 mm) and a Ni foam cathode (10 mm × 10 mm × 1 mm) and connected to a DC regulated power supply. To the cell was added substrate **1a** (1.0 equiv., 0.2 mmol, 50 mg), PPh_3 (2.0 equiv., 0.4 mmol, 105 mg), *n*-Bu_4NI (0.6 mmol, 222 mg) and DBU (1.0 equiv., 0.2 mmol, 31 mg). Then, DCM (4 mL) was added. The mixture was electrolyzed under constant current conditions (10 mA) under Ar at 40 °C for 3 hours. Workup began with the addition of saturated NaCl (15 mL), followed by extraction with DCM (3×10 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated. The crude mixture was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 20:1 to 10:1) to give product **2a** as a light-yellow oil (23 mg, 50%).

4. Comparison studies



4.1 Shiina's method

Due to the difference in substrate concentration from that used in the original

literature, we ensured that the dropping rate of the solution remained as consistent as possible with the reported procedure. The detailed experimental procedure is as follows: To a solution of MNBA (166 mg, 0.48 mmol) and DMAP (118 mg, 0.96 mmol) in DCM (5 mL) at room temperature was slowly added a solution of **1p** (154 mg, 0.4 mmol) in DCM (3 mL) with a mechanically driven syringe over a 0.6 h period. After addition of the solution, the reaction mixture was additionally stirred for 1 h at room temperature. Workup began with the addition of saturated NaCl (15 mL), followed by extraction with DCM (3×10 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated. The crude mixture was purified by flash column chromatography on silica gel to give product **2p** as a light-yellow viscous oil (< 5%).

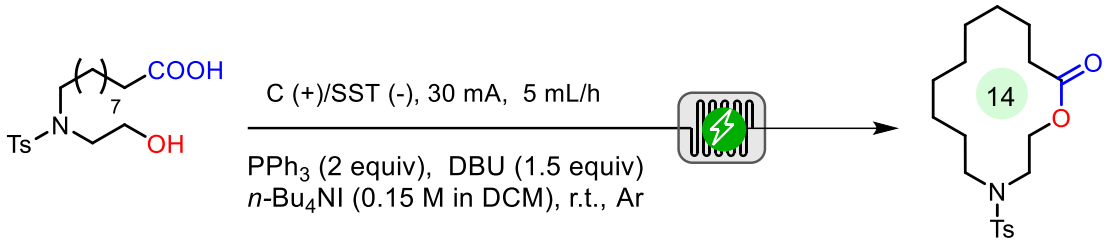
4.2 Zhao's method

To a tube was added **1p** (154 mg, 0.4 mmol), MYTsA (0.44 mmol, 1.1 equiv.), CuCl (0.06 mmol, 0.15 equiv.) and DCM (4.0 mL). Then, the mixture was stirred at room temperature for 24 h. After purification, α-acyloxyenamide (0.2 mmol) was added to a solution of p-toluenesulfonic acid monohydrate (0.03 mmol, 0.15 equiv) in DCM (4.0 mL). The resulting mixture was stirred at room temperature for 4 h. Workup began with the addition of saturated $NaHCO_3$ (15 mL), followed by extraction with DCM (3×10 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated. The crude mixture was purified by flash column chromatography on silica gel to give product **2p** as a light-yellow viscous oil (13 mg, 19%).

4.3 Lebœuf's method

To a sealed tube was added pentafluorobenzoyle chloride (0.24 mmol, 1.2 equiv.) and triethylamine (0.24 mmol, 1.2 equiv.). Then, a solution of **1p** (77 mg, 0.2 mmol) in dry toluene (4 mL) was added to the tube. The reaction mixture was stirred at 110 °C for 24 h. Workup began with the addition of saturated $NaHCO_3$ (15 mL), followed by extraction with DCM (3×10 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated. The crude mixture was purified by flash column chromatography on silica gel to give product **2p** as a light-yellow viscous oil (20 mg, 28%). By capitalizing on non-covalent interactions, this approach suppresses side reactions more effectively than the previous two methods, resulting in a cleaner reaction system.

5. Continuous-flow electrolysis

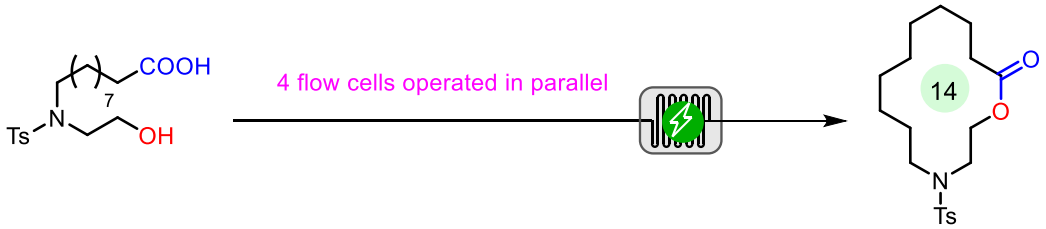


1p **2p**, 49%

The flow electrolytic cell was equipped with a graphite anode and SST cathode, with an exposed electrode surface area of 10 cm^2 and an interelectrode distance of 0.5 mm. The electrolytic solution, containing **1p** (77 mg, 0.2 mmol), PPh_3 (2.0 equiv., 0.4 mmol, 105 mg), *n*-Bu_4NI (0.6 mmol, 222 mg), DBU (1.5 equiv., 0.3 mmol, 47 mg), and DCM (4 mL), was prepared under Ar and delivered through the cell via a syringe pump. The system was operated at a flow rate of 5 mL h^{-1} under a constant current of 30 mA at room temperature. After the electrolysis, the effluent was collected and quenched with saturated aqueous NaCl solution (10 mL). The mixture was extracted with DCM (2 × 15 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude was purified by silica gel column chromatography, eluting with a mixture of ethyl acetate and petroleum ether (1:20 to 1:10 V/V), to afford **2p** as a light-yellow viscous oil (36 mg, 49%).

6. Gram-scale synthesis

6.1 Continuous-flow electrolysis



1p

2 mmol×4

2p

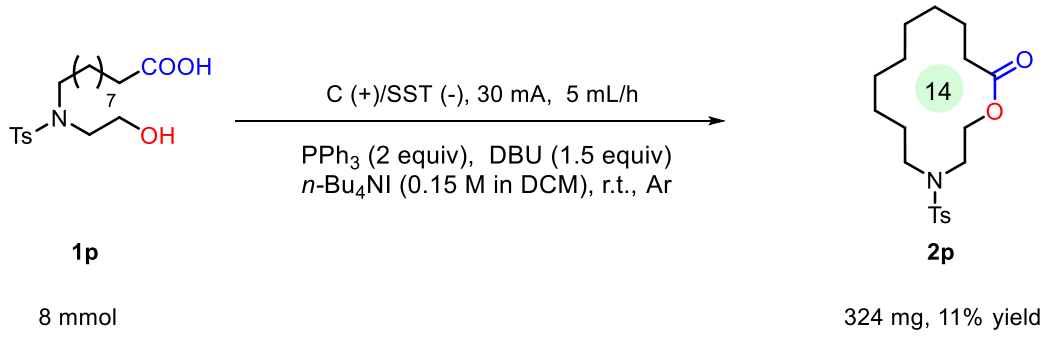
1.17 g, 40% average yield

There are four flow cells operated in parallel for gram-scale synthesis. Each flow electrolytic cell was equipped with a graphite anode and SST cathode, with an exposed

electrode surface area of 10 cm^2 and an interelectrode distance of 0.5 mm. The electrolytic solution, containing **1p** (770 mg, 2 mmol), PPh_3 (2.0 equiv., 4 mmol, 1.05 g), *n*-Bu_4NI (6 mmol, 2.22 g), DBU (1.5 equiv., 3 mmol, 470 mg), and DCM (40 mL), was prepared under Ar and delivered through the cell via a syringe pump. The system was operated at a flow rate of 5 mL h^{-1} under a constant current of 30 mA at room temperature. After the electrolysis, the effluent from the four flow cells was combined and collected and then quenched with saturated aqueous $Na_2S_2O_3$ solution (100 mL). The mixture was extracted with DCM (3 × 50 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude was purified by silica gel column chromatography, eluting with a mixture of ethyl acetate and petroleum ether (1:20 to 1:10 V/V), to afford **2p** as a light-yellow viscous oil (1.17 g, 40% average yield).

Figure S1. Setup for gram-scale synthesis by flow electrolysis

6.2 Batch electrolysis



1p

8 mmol

2p

324 mg, 11% yield

An undivided cell was equipped with a graphite plate anode (30 mm × 10 mm × 1 mm) and a Ni foam cathode (30 mm × 10 mm × 1 mm) and connected to a DC regulated

power supply. To the cell was added substrate **1p** (1.0 equiv., 8 mmol, 3.08 g), PPh_3 (2.0 equiv., 16 mmol, 4.2 g), *n*-Bu_4NI (24 mmol, 8.9 g) and DBU (1.0 equiv., 8 mmol, 1.23 g). Then, DCM (160 mL) was added. The mixture was electrolyzed under constant current conditions (30 mA) under Ar at 40 °C for 40 hours. Workup began with the addition of saturated $Na_2S_2O_3$ (50 mL), followed by extraction with DCM. The organic phase was dried with Na_2SO_4, filtered, and concentrated. The crude mixture was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 20:1 to 10:1) to give product **2p** as a light-yellow oil (324 mg, 11%).

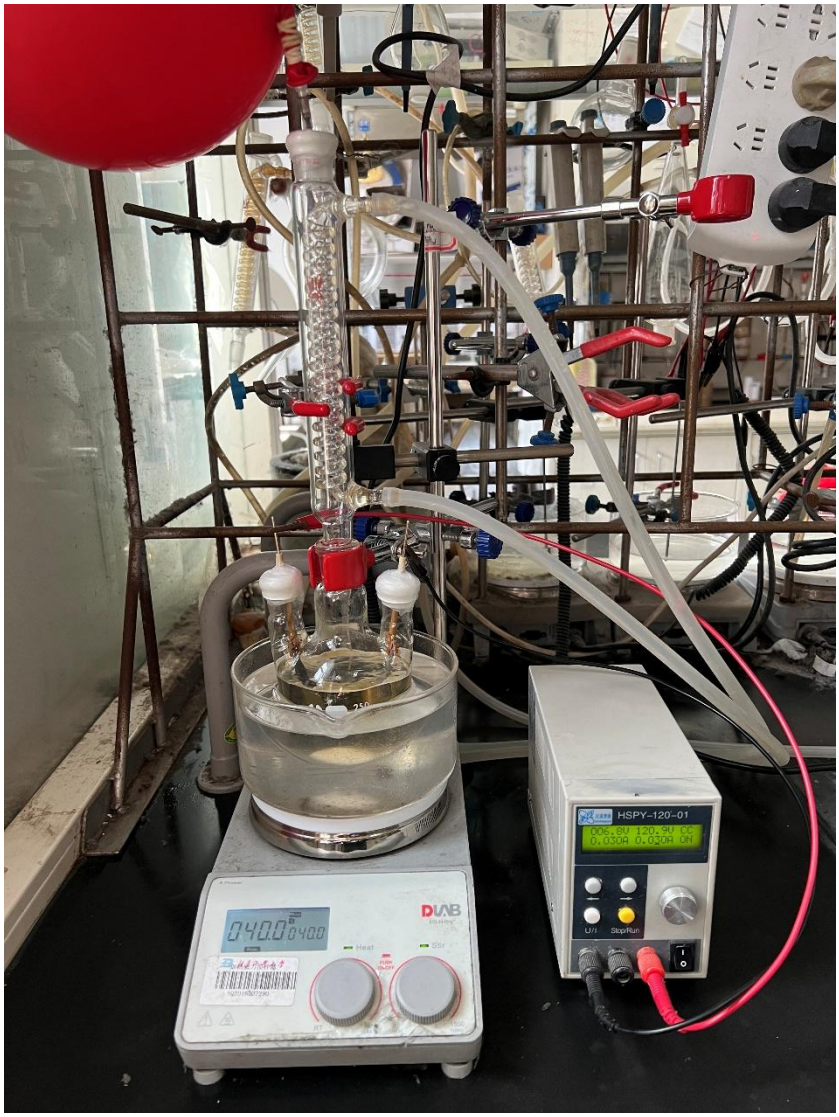


Figure S2. Setup for gram-scale synthesis by batch electrolysis

7. General measurement procedure for cyclic voltammetry (CV)

CV experiments were performed in a three-electrode cell system at room temperature. The working electrode is a steady platinum disk; the counter electrode is a platinum wire. The reference electrode is an $Ag/AgNO_3$ (0.1 M in CH_3CN) electrode. The scan rate is 0.1 V/s. The supporting electrolyte solution is 0.1 M $TBABF_4$ in CH_2Cl_2.

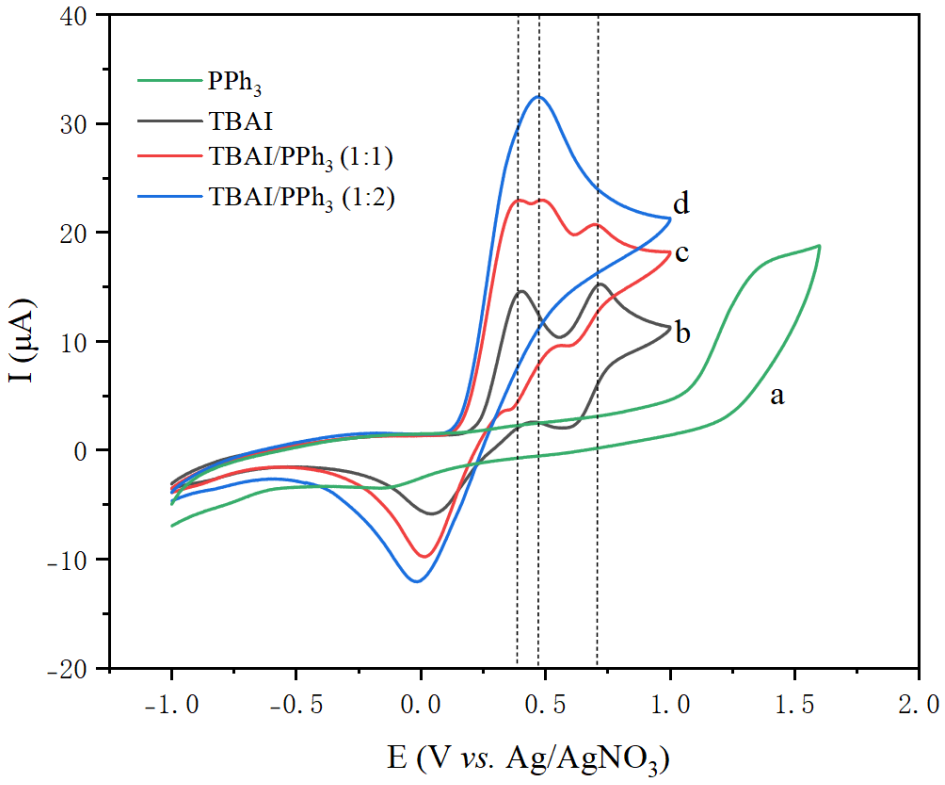


Figure S3. CV of TBAI and PPh_3 in 0.1 M $TBABF_4$ in CH_2Cl_2. PPh_3 (2 mM, curve a), TBAI (2 mM, curve b), TBAI/PPh_3=1:1 (2 mM/2 mM, curve c), TBAI/PPh_3=1:2 (2 mM/4 mM, curve d).

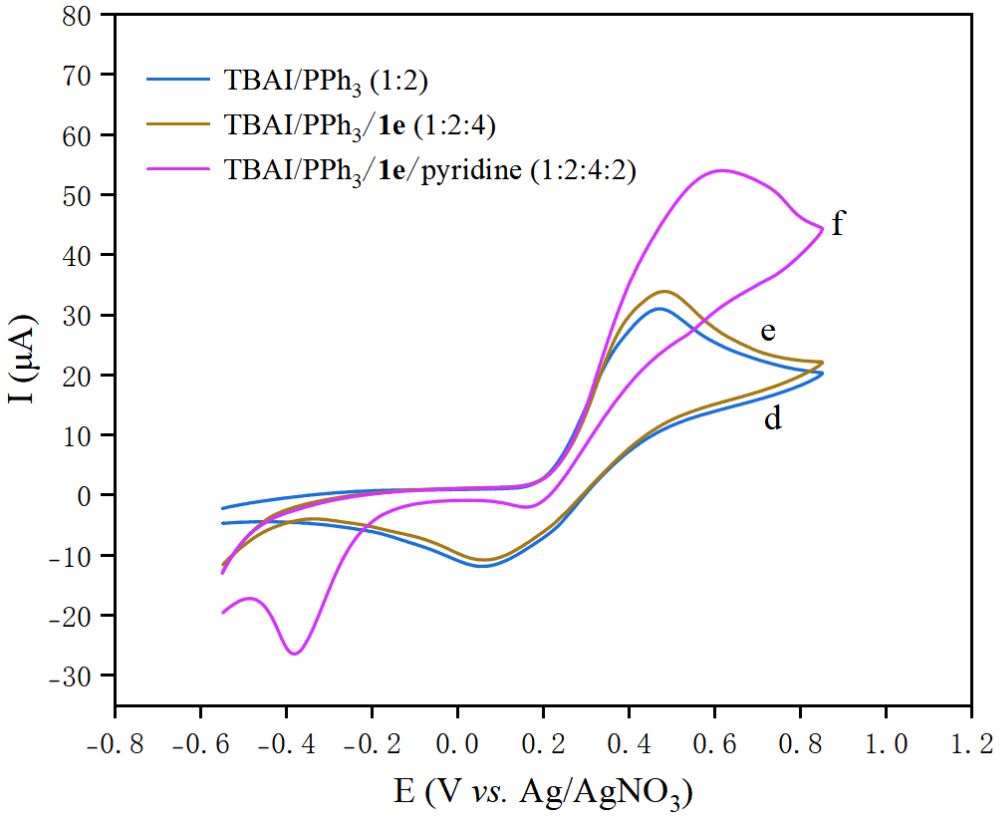
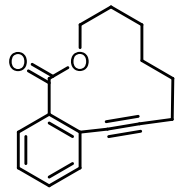


Figure S4. Cyclic Voltammogram of related compound in 0.1 M $TBABF_4$ in CH_2Cl_2. TBAI/PPh_3 = 1:2 (2 mM/4 mM, curve d), TBAI/PPh_3/**1e** = 1:2:4 (2 mM/4 mM/8 mM, curve e), TBAI/PPh_3/**1e**/pyridine = 1:2:4:2 (2 mM/4 mM/8 mM/4 mM, curve f).

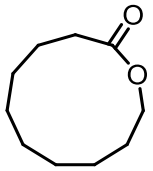
The reason we chose pyridine as the base is that the oxidation peak of DBU interferes with the CV test. This phenomenon has also been observed in a previous report (*Org. Lett.* **2024**, 26, 7347–7351).

8. Characterization data for products 2a-2x



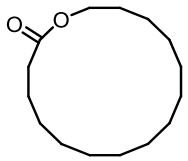
2a

4-Ethynyl-3,4,5,6,7,8,9,10-octahydro-1H-benzo[c][1]oxacyclododecin-1-one ***(2a)***. eluent: petroleum ether/ethyl acetate= 20:1 to 10:1, light yellow oil (23 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.46–7.40 (m, 2H), 7.38–7.30 (m, 1H), 4.46–4.33 (m, 2H), 2.51 (t, *J* = 5.8 Hz, 2H), 1.90-1.74 (m, 4H), 1.73-1.62 (m, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 133.3, 131.2, 130.4, 127.4, 123.5, 95.3, 80.1, 65.7, 26.8, 25.9, 24.2, 24.1, 19.3. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{15}H_{17}O_2^+$ 229.1223, Found 229.1219.



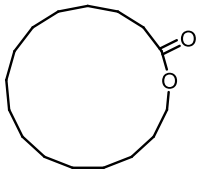
2b

Oxacycloundecan-2-one ***(2b)***.[2] eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow oil (11 mg, 32%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (t, *J* = 5.6 Hz, 2H), 2.31 (t, *J* = 7.2 Hz, 2H), 1.63-1.58 (m, 4H), 1.36-1.30 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 64.0, 34.9, 29.4, 29.1, 29.1, 29.0, 28.7, 26.1, 25.4.



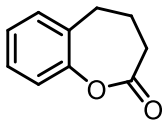
2c

Oxacyclopentadecan-2-one ***(2c)***. [3] eluent: petroleum ether/ethyl acetate = 30:1 to 20:1, light yellow oil (20 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13 (t, *J* = 5.4 Hz, 2H), 2.33 (t, *J* = 6.6 Hz, 2H), 1.71-1.55 (m, 4H), 1.45-1.20 (m, 20H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 64.0, 34.4, 28.4, 27.8, 27.2, 27.1, 26.9, 26.7, 26.4, 26.1, 26.0, 25.9, 25.1, 24.9.



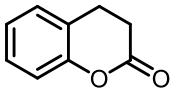
2d

*Oxacyclohexadecan-2-one (**2d**)*.[3] eluent: petroleum ether/ethyl acetate = 30:1 to 20:1, light yellow oil (21 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.11 (t, *J* = 5.6 Hz, 2H), 2.31 (t, *J* = 6.8 Hz, 2H), 1.68-1.59 (m, 4H), 1.40-1.30 (m, 22H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 64.4, 34.7, 28.7, 28.2, 28.0, 27.9, 27.8, 27.7, 27.1, 27.0, 27.0, 26.9, 26.8, 25.6, 25.1.



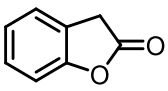
2e

*4,5-Dihydrobenzo[b]oxepin-2(3H)-one (**2e**)*. [4] eluent: petroleum ether/ethyl acetate= 20:1 to 10:1, light yellow oil (25 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 1H), 7.24-7.16 (m, 2H), 7.11 (d, *J* = 7.9 Hz, 1H), 2.85 (t, *J* = 7.3 Hz, 2H), 2.50 (t, *J* = 7.2 Hz, 2H), 2.28-2.25 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 150.9, 130.1, 129.7, 128.3, 125.9, 119.3, 31.1, 28.3, 26.6.



2f

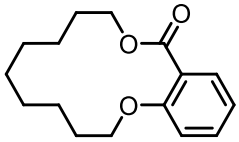
*Chroman-2-one (**2f**)*.[5] eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow oil (22 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.23 (m, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.13-7.11 (m, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 3.06-2.97 (m, 2H), 2.85-2.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 152.0, 128.3, 128.0, 124.4, 122.7, 117.0, 29.3, 23.7.



2g

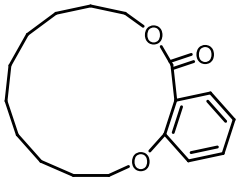
*Benzofuran-2(3H)-one (**2g**)*.[6] eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow oil (20 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.26 (m, 2H), 7.16-7.05

(m, 2H), 3.72 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 154.8, 128.9, 124.6, 124.1, 123.1, 110.8, 33.0.



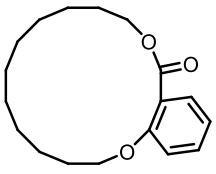
2h

3,4,5,6,7,8,9,10-Octahydro-2H,12H-benzo[b][1,5]dioxacyclotetradecin-12-one (***2h***). eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow viscous oil (28 mg, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.47-7.33 (m, 1H), 7.01-6.86 (m, 2H), 4.43-4.34 (m, 2H), 4.07 (t, *J* = 5.3 Hz, 2H), 1.85-1.77 (m, 2H), 1.77-1.70 (m, 2H), 1.64-1.52 (m, 4H), 1.45 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 157.5, 132.7, 131.4, 121.8, 120.0, 112.5, 67.9, 64.6, 27.9, 27.8, 26.7, 26.1, 25.1, 24.3, 23.8. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{16}H_{23}O_3^+$263.1641, Found 263.1637.



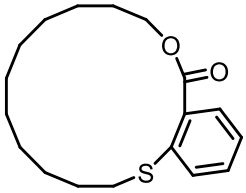
2i

2,3,4,5,6,7,8,9,10,11-decahydro-13H-benzo[b][1,5]dioxacyclopentadecin-13-one (***2i***). eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow viscous oil (23 mg, 42%).^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.43-7.36 (m, 1H), 6.94 (m, 2H), 4.45-4.38 (m, 2H), 4.06 (t, *J* = 5.2 Hz, 2H), 1.85-1.74 (m, 4H), 1.56-1.46 (m, 4H), 1.43-1.41 (m, 8H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.0, 157.7, 132.7, 131.2, 121.7, 119.9, 112.4, 68.8, 64.6, 28.6, 28.4, 27.1, 26.8, 25.9, 25.9, 25.8, 24.9. HRMS (APCI) m/z: $[M + H]^+$ calcd for $C_{17}H_{25}O_3^+$ 277.1798, Found 277.1795.



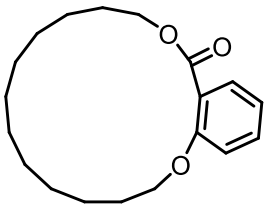
2j

*3,4,5,6,7,8,9,10,11,12-decahydro-2H,14H-benzo[b][1,5]dioxacyclohexadecin-14-one (**2j**).* eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow viscous oil (29 mg, 51%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72-7.70 (m, 1H), 7.42-7.40 (m, 1H), 6.97-6.92 (m, 2H), 4.42-4.34 (m, 2H), 4.05 (t, *J* = 5.2 Hz, 2H), 1.83-1.69 (m, 4H), 1.55-1.45 (m, 4H), 1.42-1.31 (m, 10H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 158.0, 132.8, 131.4, 121.6, 119.9, 112.7, 68.7, 65.2, 28.9, 28.5, 26.9, 26.8, 26.5, 26.1, 25.0, 24.8, 24.4. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{18}H_{27}O_3^+$ 291.1954, Found 291.1949.



2k

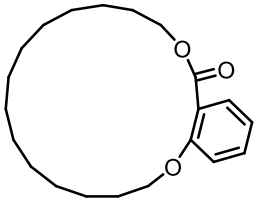
*3,4,5,6,7,8,9,10,11,12-decahydro-2H,14H-benzo[c][1]oxa[5]thiacyclohexadecin-14-one (**2k**).* eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow viscous oil (29 mg, 47%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, J = 7.8, 1.3 Hz, 1H), 7.42-7.37 (m, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.18-7.13 (m, 1H), 4.42 (t, *J* = 6.0 Hz, 2H), 2.98 (t, *J* = 5.4 Hz, 2H), 1.79-1.69 (m, 4H), 1.63-1.53 (m, 4H), 1.37-1.33 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 140.2, 131.9, 131.5, 129.9, 126.4, 124.1, 66.2, 32.8, 28.7, 27.2, 27.1, 26.4, 25.9, 25.8, 25.8, 25.5, 25.4. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{18}H_{27}O_2S^+$ 307.1726, Found 307.1725.



2l

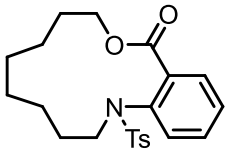
*2,3,4,5,6,7,8,9,10,11,12,13-Dodecahydro-15H-benzo[b][1,5]dioxacycloheptadecin-15-one (**2l**)*. eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow viscous oil (27 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 6.96-6.92 (m, 2H), 4.36 (t, *J* = 6.0 Hz, 2H), 4.05 (t, *J* = 5.6 Hz, 2H), 1.81-1.74 (m, 4H), 1.52-1.32 (m, 16H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.5, 158.0, 132.8, 131.2, 121.5, 119.8, 112.6, 68.6, 64.9, 29.3, 28.8, 27.4, 27.2, 27.2, 26.6, 26.3, 25.8, 25.5,

24.5. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{19}H_{29}O_3^+$ 305.2111, Found 305.2105.



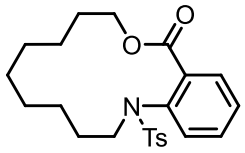
2m

*2,3,4,5,6,7,8,9,10,11,12,13,14,15-tetradecahydro-17H-benzo[b][1,5]dioxacyclononadecin-17-one (**2m**)*. eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow viscous oil (22 mg, 33%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.46-7.39 (m, 1H), 6.99-6.89 (m, 2H), 4.31 (t, *J* = 6.8 Hz, 2H), 4.02 (t, *J* = 6.2 Hz, 2H), 1.83-1.70 (m, 4H), 1.53-1.46 (m, 2H), 1.43-1.27 (m, 18H).^{13}C NMR (150 MHz, $CDCl_3$) δ 167.4, 158.2, 133.0, 131.5, 121.2, 119.9, 112.9, 69.0, 65.2, 29.2, 28.5, 28.0, 27.9, 27.3, 27.0, 26.9, 26.8, 26.5, 25.6, 24.8. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{21}H_{33}O_3^+$ 333.2424, Found 333.2423.



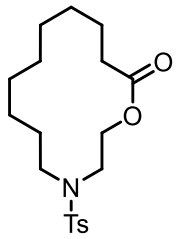
2n

*1-tosyl-2,3,4,5,6,7,8,9-octahydrobenzo[c][1]oxa[5]azacyclotridecin-11(1H)-one (**2n**)*. eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow foam (45 mg, 56%).^{1}H NMR (600 MHz, DMSO) δ 7.86 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.48 (td, *J* = 7.8, 1.2 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 1H), 4.30-4.29 (m, 1H), 4.08-4.04 (m, 1H), 3.88-3.85 (m, 1H), 3.20-3.18 (m, 1H), 2.38 (s, 3H), 1.88-1.02 (m, 12H). ^{13}C NMR (150 MHz, DMSO) δ 167.7, 144.0, 137.3, 133.7, 132.7, 132.4, 132.0, 130.1, 127.9, 127.6, 125.9, 66.8, 46.7, 26.6, 24.7, 23.9, 23.4, 23.0, 22.4, 21.5. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{22}H_{28}NO_4S^+$402.1733, Found 402.1728.



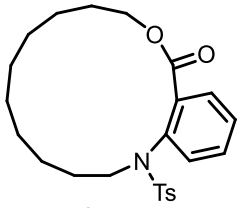
2o

*1-tosyl-1,2,3,4,5,6,7,8,9,10-decahydro-12H-benzo[c][1]oxa[5]azacyclotetradecin-12-one (**2o**)*. eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow foam (41 mg, 49%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06-7.90 (m, 1H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.39-7.32 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.78-6.59 (m, 1H), 4.53-4.50 (m, 2H), 3.91 (br s, 1H), 3.16 (br s, 1H), 2.41 (s, 3H), 1.88-1.71 (m, 2H), 1.59 (s, 2H), 1.45-1.17 (m, 10H).^{13}C NMR (150 MHz, $CDCl_3$) δ 167.3, 143.4, 137.8, 134.3, 133.7, 132.3, 131.5, 129.3, 128.1, 127.3, 125.8, 64.5, 49.1, 27.1, 26.5, 25.5, 25.0, 24.8, 24.2, 22.0, 21.5. HRMS(APCI) m/z: $[M+H]^+$ calcd for $C_{23}H_{30}NO_4S^+$ 416.1890, Found 416.1889.



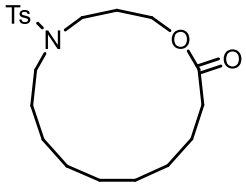
2p

*4-tosyl-1-oxa-4-azacyclotetradecan-14-one (**2p**)*. eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow viscous oil (33 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.28-4.25 (m, 2H), 3.49-3.34 (m, 2H), 3.19-3.01 (m, 2H), 2.42 (s, 3H), 2.39-2.33 (m, 2H), 1.74-1.66 (m, 2H), 1.63-1.52 (m, 2H), 1.40-1.29 (m, 10H).^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 143.4, 136.1, 129.7, 127.3, 64.6, 50.3, 48.6, 33.0, 28.0, 26.4, 25.7, 25.7, 24.5, 24.0, 23.6, 21.5. HRMS(APCI) m/z: $[M+H]^+$ calcd for $C_{19}H_{29}NO_4S^+$ 368.1890, Found 368.1884.



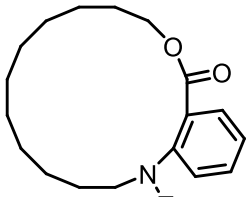
2q

*1-tosyl-2,3,4,5,6,7,8,9,10,11-decahydrobenzo[c][1]oxa[5]azacyclopentadecin-13(1H)-one (**2q**)*. eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow foam (35 mg, 41%).^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00-7.85 (m, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.40-7.31 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.80-6.61 (m, 1H), 4.41-4.33 (m, 2H), 3.83 (br s, 1H), 3.21 (br s, 1H), 2.41 (s, 3H), 1.89 (s, 1H), 1.70 (s, 1H), 1.59 (s, 2H), 1.42-1.26 (m, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.7, 143.2, 137.6, 135.2, 133.8, 131.8, 131.5, 129.4, 127.7, 127.6, 127.4, 65.9, 49.6, 27.1, 26.0, 25.9, 25.3, 24.4, 24.2, 24.0, 23.4, 21.5. HRMS (APCI) m/z: $[M + H]^+$ calcd for $C_{24}H_{32}NO_4S^+$ 430.2046, Found 430.2044.



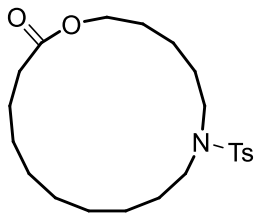
2r

*5-tosyl-1-oxa-5-azacyclopentadecan-15-one(**2r**)*. eluent: petroleum ether/ethyl aceta te = 20:1 to 4:1, light yellow foam (32 mg, 42%). ^{1}H NMR (600 MHz, CDCl $_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.19-4.11 (t, *J* = 5. 4 Hz, 2H), 3.24-3.16 (m, 2H), 3.15-3.06 (m, 2H), 2.43 (s, 3H), 2.36-2.29 (m, 2H), 2.00-1.91 (m, 2H), 1.69-1.63 (m, 2H), 1.57-1.51 (m, 2H), 1.36-1.29 (m, 1 0H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.7, 143.2, 136.8, 129.7, 127.2, 61.4, 4 8.7, 45.8, 34.0, 29.3, 27.5, 27.2, 26.7, 26.4, 25.8, 24.7, 24.3, 21.5. HRMS (AP CI) m/z: $[M+H]^+$ calcd for $C_{20}H_{32}NO_4S^+$382.2047, Found 382.2043.



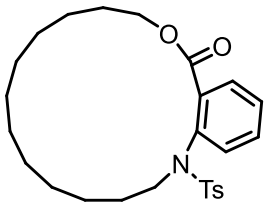
2s

*1-Tosyl-1,2,3,4,5,6,7,8,9,10,11,12-dodecahydro-14H-benzo[c][1]oxa[5]azacyclohexadecin-14-one (**2s**).* eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow foam (43 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00–7.91 (m, 1H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.42–7.30 (m, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 6.76–6.68 (m, 1H), 4.50–4.30 (m, 2H), 3.91–3.73 (m, 1H), 3.26-3.07 (m, 1H), 2.41 (s, 3H), 1.85 (s, 1H), 1.71 (s, 2H), 1.53-1.25 (m, 15H).^{13}C NMR (150 MHz, DMSO) δ 167.1, 143.8, 138.0, 135.3, 133.3, 132.8, 131.8, 130.2, 128.3, 127.9, 127.8, 65.1, 50.3, 28.2, 26.7, 26.0, 26.0, 25.9, 25.1, 25.0, 24.4, 24.2, 21.5. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{25}H_{34}NO_4S^+$ 444.2203, Found 444.2195.



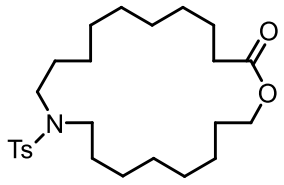
2t

*7-Tosyl-1-oxa-7-azacycloheptadecan-17-one (**2t**).* eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow viscous oil (35 mg, 43%).^{1}H NMR (600 MHz, $CDCl_3$) δ ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.10 (t, *J* = 5.4 Hz, 2H), 3.12-2.96 (m, 4H), 2.42 (s, 3H), 2.35-2.29 (m, 2H), 1.67-1.61 (m, 6H), 1.56-1.44 (m, 4H), 1.37-1.28 (m, 10H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.1, 143.0, 136.3, 129.6, 127.3, 64.1, 49.6, 49.5, 34.3, 29.3, 28.6, 28.2, 27.8, 27.4, 27.3, 27.2, 25.4, 24.8, 24.2, 21.5. HRMS (APCI) m/z: $[M + H]^+$ calcd for $C_{22}H_{35}NO_4S^+$ 410.2359, Found 410.2354.



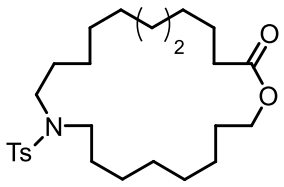
2u

1-tosyl-2,3,4,5,6,7,8,9,10,11,12,13-dodecahydrobenzo[c][1]oxa[5]azacycloheptadecin-15(1H)-one ***(2u)***. eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow foam (42 mg, 46%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97-7.89 (m, 1H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.42-7.35 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.86-6.79 (m, 1H), 4.31 (br s, 2H), 3.74 (br s, 1H), 3.34 (br s, 1H), 2.41 (s, 3H), 1.78 (s, 2H), 1.46-1.13 (m, 18H).^{13}C NMR (150 MHz, $CDCl_3$) δ 167.2, 143.2, 138.1, 135.9, 133.4, 131.9, 131.8, 129.4, 128.7, 127.8, 127.6, 65.7, 51.2, 43.3, 30.5, 28.6, 27.6, 26.8, 26.6, 26.6, 25.7, 25.3, 24.9, 21.5. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{26}H_{36}NO_4S^+$ 458.2360, Found 458.2356.



2v

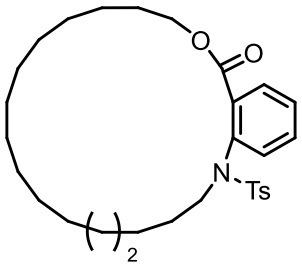
10-tosyl-1-oxa-10-azacycloicosan-20-one ***(2v)***. eluent: petroleum ether/ethyl acetate = 20:1 to 10:1, light yellow viscous oil (31 mg, 35%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 4.11 (t, *J* = 5.9 Hz, 2H), 3.04-3.01 (m, 4H), 2.42 (s, 3H), 2.31 (t, *J* = 6.7 Hz, 2H), 1.65-1.59 (m, 4H), 1.58-1.49 (m, 4H), 1.41-1.26 (m, 18H)..^{13}C NMR (150 MHz, $CDCl_3$) δ 173.9, 142.9, 136.4, 129.6, 127.2, 64.0, 60.4, 49.1, 48.9, 34.8, 29.2, 29.0, 28.8, 28.8, 28.7, 28.6, 28.6, 26.1, 26.0, 25.3, 21.5, 14.2. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{25}H_{42}NO_4S^+$ 452.2829, Found 452.2826.



2w

11-tosyl-1-oxa-11-azacyclohenicosan-21-one ***(2w)***. eluent: petroleum ether/ethyl

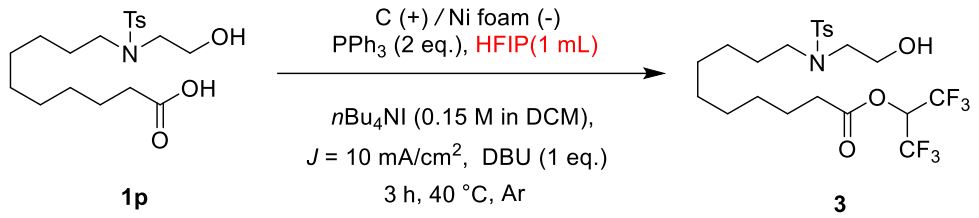
acetate = 20:1 to 4:1, light yellow viscous oil (24 mg, 26%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 4.10 (t, *J* = 6.0 Hz, 2H), 3.04-3.00 (m, 4H), 2.41 (s, 3H), 2.34-2.26 (m, 2H), 1.65-1.59 (m, 4H), 1.58-1.49 (m, 4H), 1.37-1.24 (m, 20H).^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 142.9, 136.4, 129.6, 127.2, 64.0, 49.5, 34.6, 29.3, 29.1, 29.1, 28.9, 28.8, 28.8, 28.7, 28.6, 28.6, 26.3, 26.2, 25.9, 25.2, 21.5. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{26}H_{44}NO_4S^+$ 466.2986 Found 466.2987.



2x

1-tosyl-2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17-hexadecahydrobenzo[c][1]oxa[5]azacyclohenicosin-19(1H)-one (***2x***). eluent: petroleum ether/ethyl acetate = 20:1 to 4:1, light yellow foam (30 mg, 29%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97-7.86 (m, 1H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.41-7.33 (m, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 6.88-6.79 (m, 1H), 4.26 (br s, 2H), 3.72 (br s, 1H), 3.37 (br s, 1H), 2.41 (s, 3H), 1.78 (d, *J* = 4.4 Hz, 2H), 1.46-1.39 (m, 2H), 1.39-0.94 (m, 24H).^{13}C NMR (150 MHz, $CDCl_3$) δ 167.1, 143.1, 138.1, 136.0, 133.5, 131.8, 131.7, 129.4, 128.9, 127.9, 127.6, 65.8, 51.5, 28.8, 28.6, 28.5, 28.4, 28.00, 27.5, 27.4, 27.3, 26.8, 26.7, 25.7, 21.5. HRMS (APCI) m/z: $[M+H]^+$ calcd for $C_{30}H_{44}NO_4S^+$ 514.2986, Found 514.2990.

9. Control Experiments



1,1,1,3,3,3-hexafluoropropan-2-yl10-((N-(2-hydroxyethyl)-4-methylphenyl)sulfonamido)decanoate (**3**) An undivided cell was equipped with a graphite plate anode (10 mm × 10 mm × 1 mm) and a Ni foam cathode (10 mm × 10 mm × 1 mm) which were connected to a DC regulated power supply. To the cell was added substrate **1p** (1.0 equiv., 0.2 mmol), PPh_3 (2.0 equiv., 0.4 mmol), *n*-Bu_4NI (0.6 mmol), HFIP (1 mL) and DBU (1.0 equiv., 0.2 mmol). Then, DCM (4 mL) was added. The mixture was electrolyzed under constant current conditions (10 mA) under Ar at 40 °C for 3 hours. After the reaction was completed, the organic layers were combined and concentrated under vacuum. The crude mixture was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate 20:1 to 10:1) to give product **3** as a light-yellow oil (39 mg, 37%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 5.81-5.77 (m, 1H), 3.78 (t, *J* = 4.8 Hz, 2H), 3.24 (t, *J* = 5.4 Hz, 2H), 3.18-3.15 (m, 2H), 2.53 (t, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 1.73-1.68 (m, 2H), 1.57-1.56 (m, 2H), 1.35-1.28 (m, 10H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.4, 143.5, 136.1, 129.8, 127.3, 120.5 (q, *J* = 280.7 Hz), 66.3 (quintet, *J* = 34.3 Hz), 61.5, 50.9, 50.2, 33.3, 29.2, 29.1, 29.0, 28.8, 28.7, 26.6, 24.5, 21.5. **^{13}F NMR** (565 MHz, $CDCl_3$) δ -73.36, -73.37. **HRMS (APCI)** m/z: $[M+H]^+$ calcd for $C_{22}H_{32}F_6NO_5^+$ 536.1900, Found 536.1899.

10. Reference

[1] Wender Paul A, et al. Computer-guided design, synthesis, and protein kinase C affinity of a new salicylate-based class of bryostatin analogs. *Org. Lett.*, 2014, **16**, 5136-9.

[2] M. Yang, X. Wang, J. Zhao, Ynamide-Mediated Macrolactonization, *ACS Catal.*, 2020, **10**, 5230-5235.

[3] G. Force, A. Perfetto, R. J. Mayer, I. Ciofini, D. Lebœuf, Macrolactonization Reactions Driven by a Pentafluorobenzoyl Group, *Angew. Chem. Int. Ed.*, 2021, **60**, 19843-19851.

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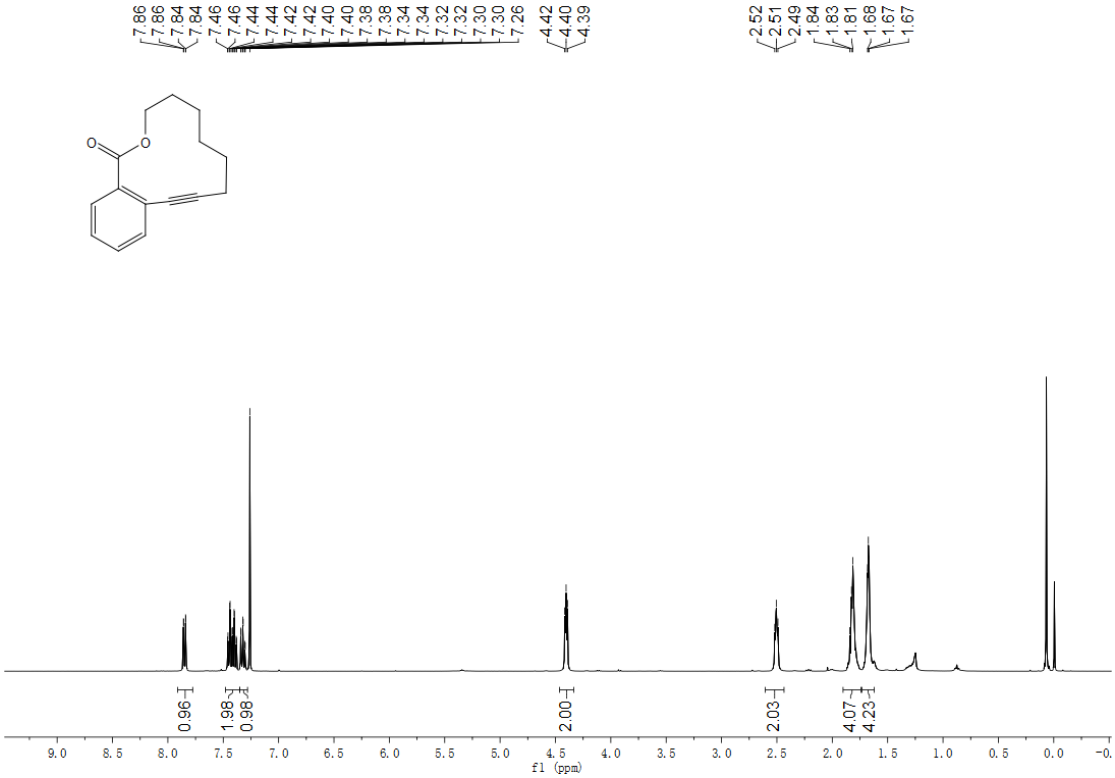
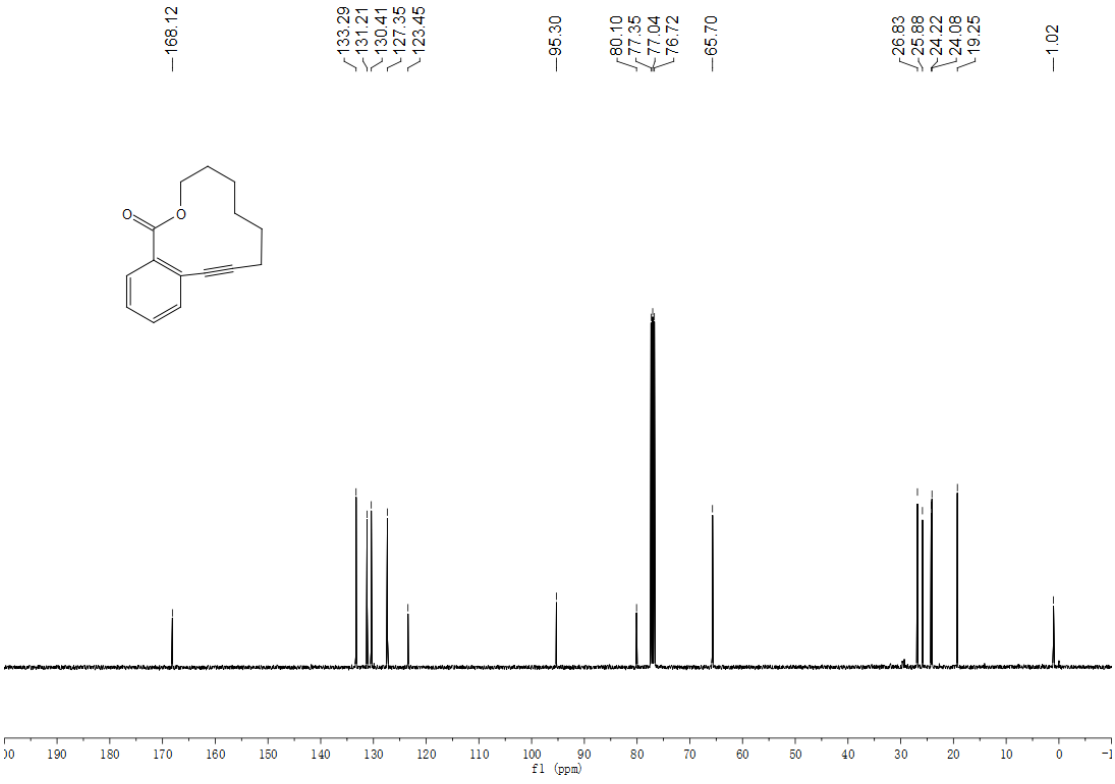
[5] J. L. Tu, H. Gao, M. Luo, L. Zhao, et al. Iron-catalyzed ring-opening of cyclic carboxylic acids enabled by photoinduced ligand-to-metal charge transfer. *Green Chem.*, 2022, **24**, 5553-5558.

[6] X. Zhang, C. M. Beaudry, Regioselective Synthesis of Benzofuranones and Benzofurans. *J. Org. Chem.*, 2021, **86**, 6931-6936.

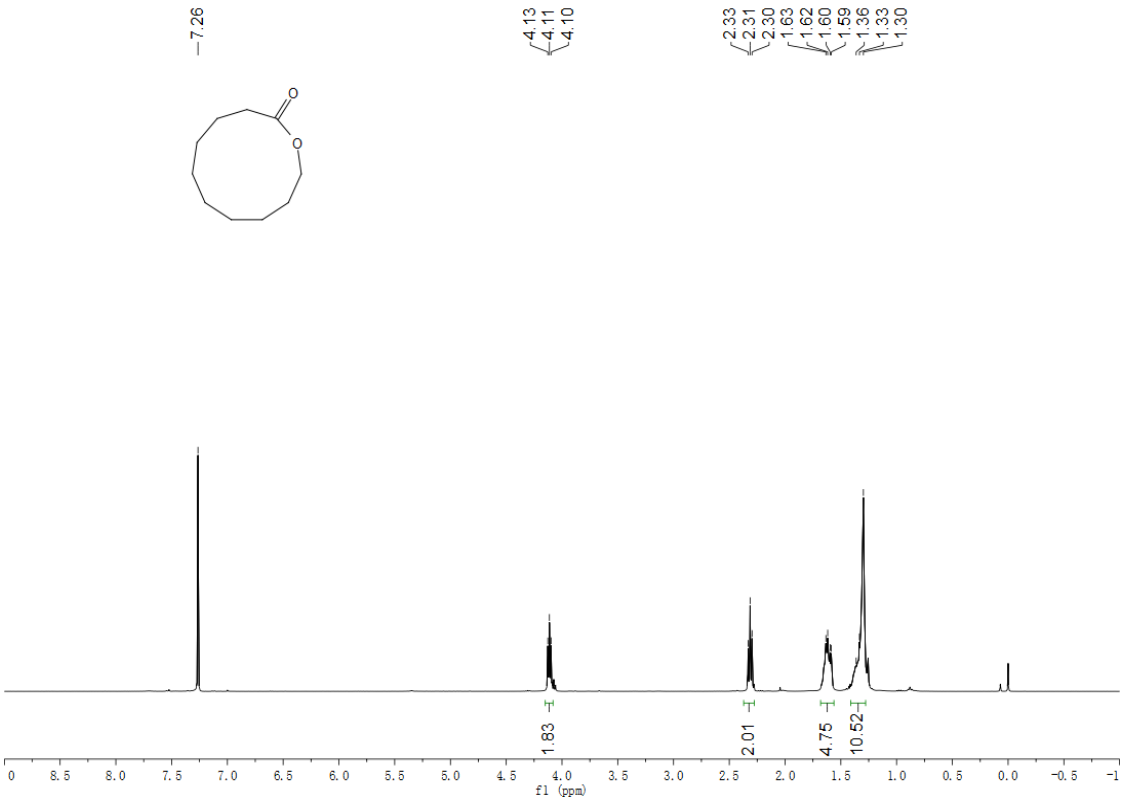
11. Copies of NMR spectra



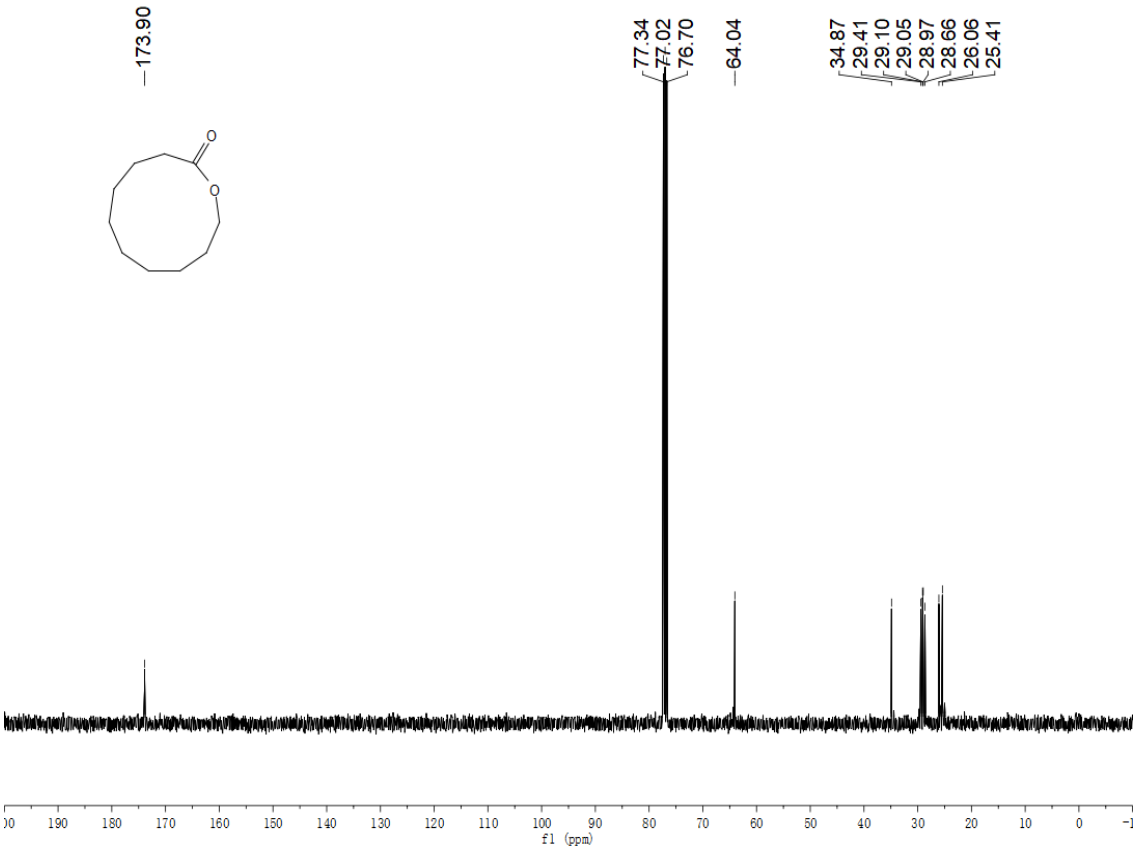
^{1}H NMR of **2a** ($CDCl_3$, 400 MHz)



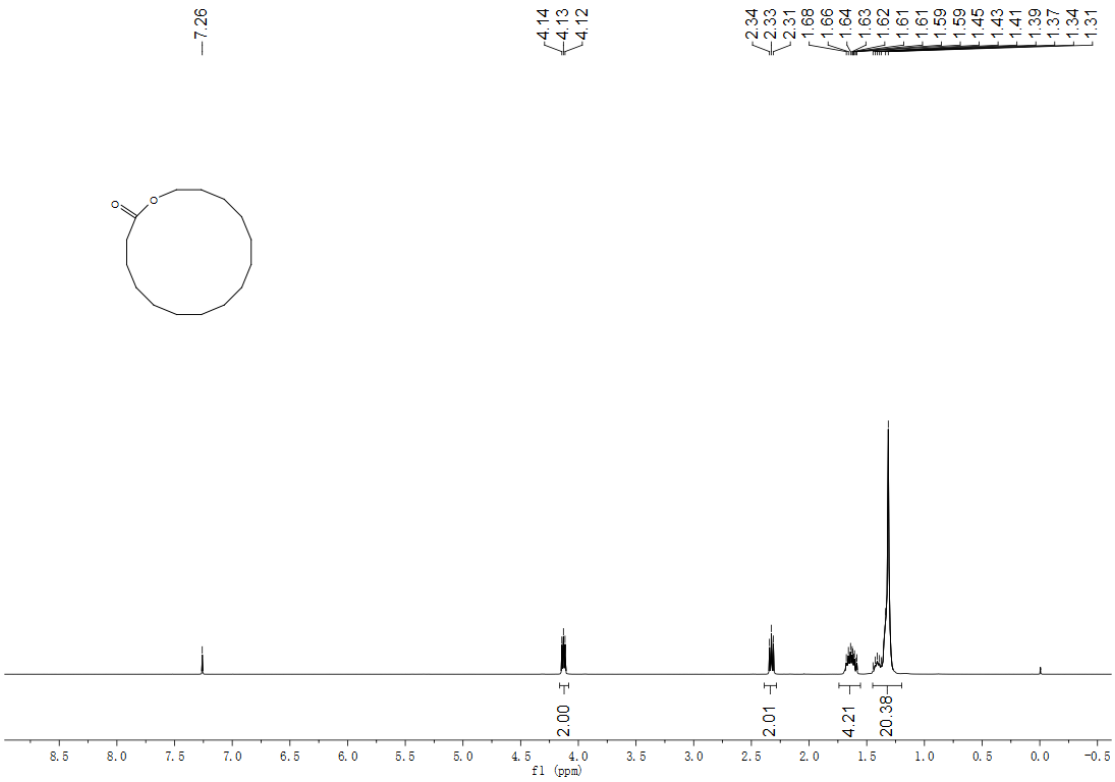
^{13}C NMR of **2a** ($CDCl_3$, 100 MHz)



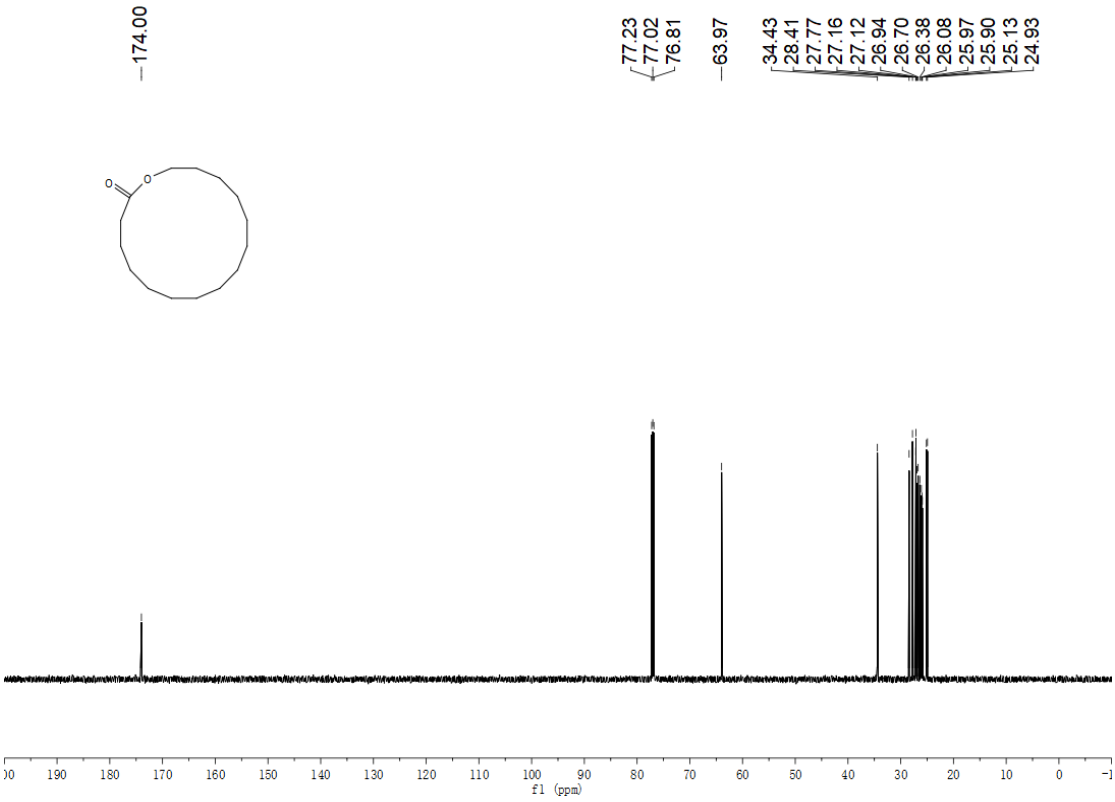
^{1}H NMR of **2b** ($CDCl_3$, 400 MHz)



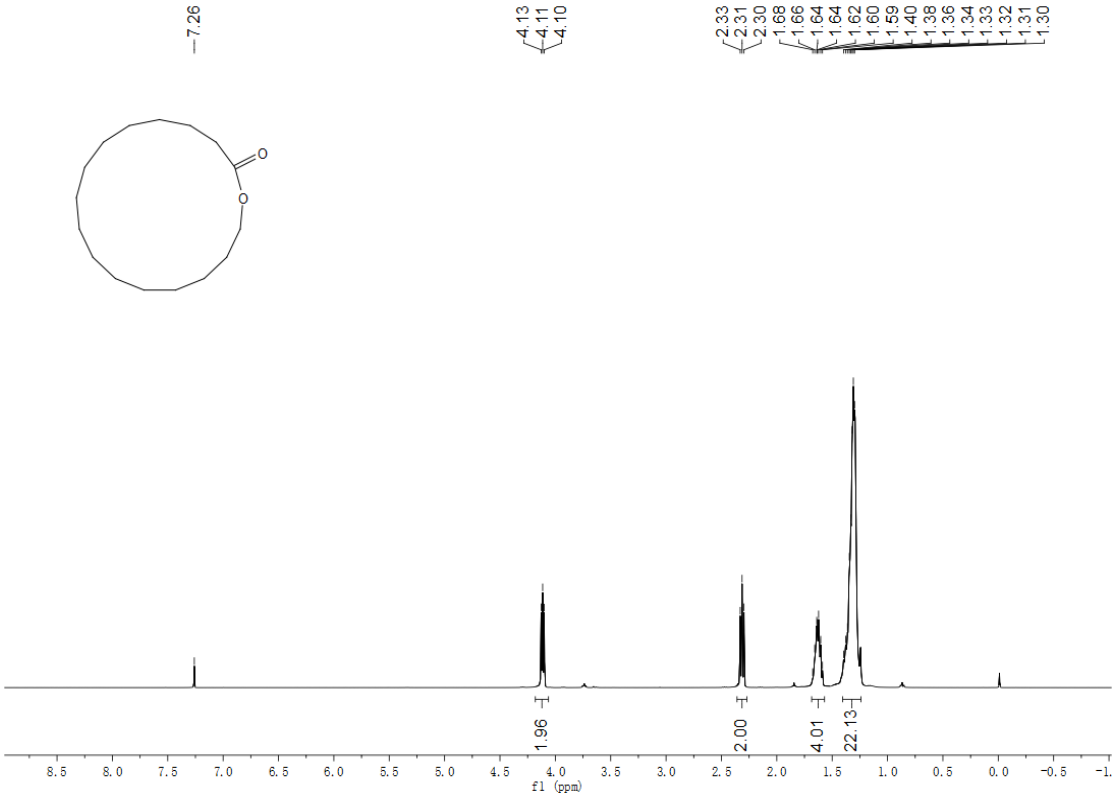
^{13}C NMR of **2b** ($CDCl_3$, 100 MHz)



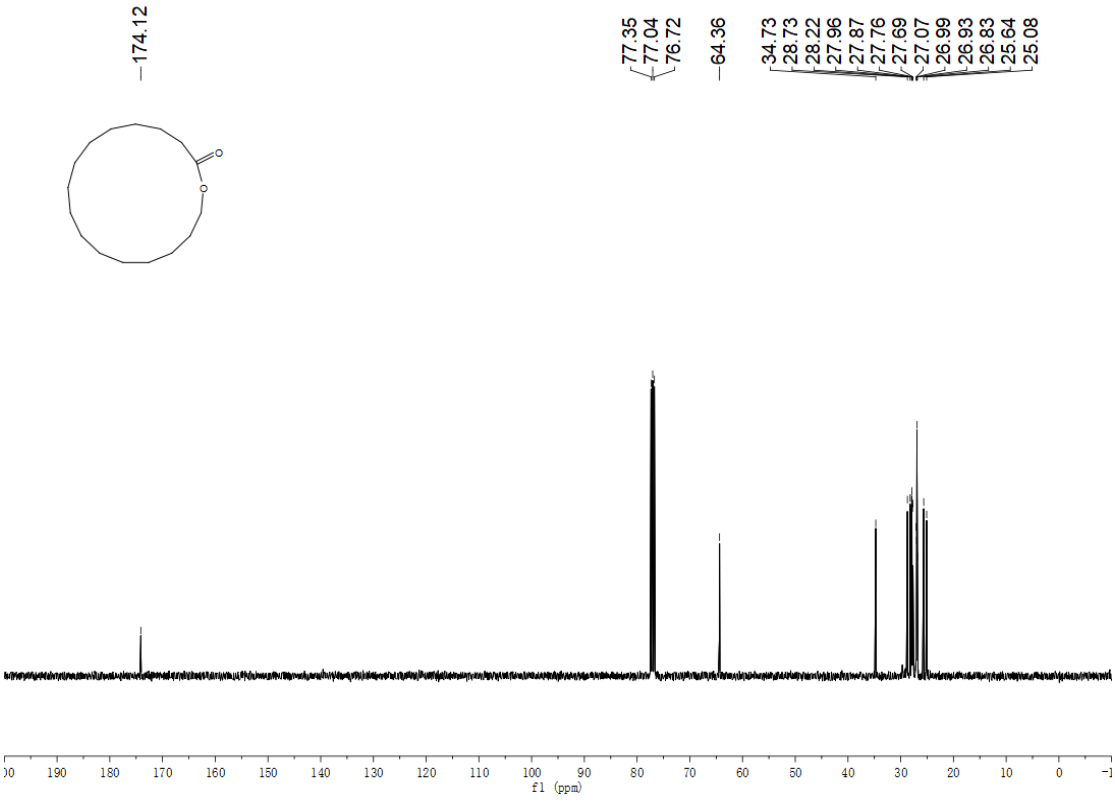
^{1}H NMR of **2c** ($CDCl_3$, 400 MHz)



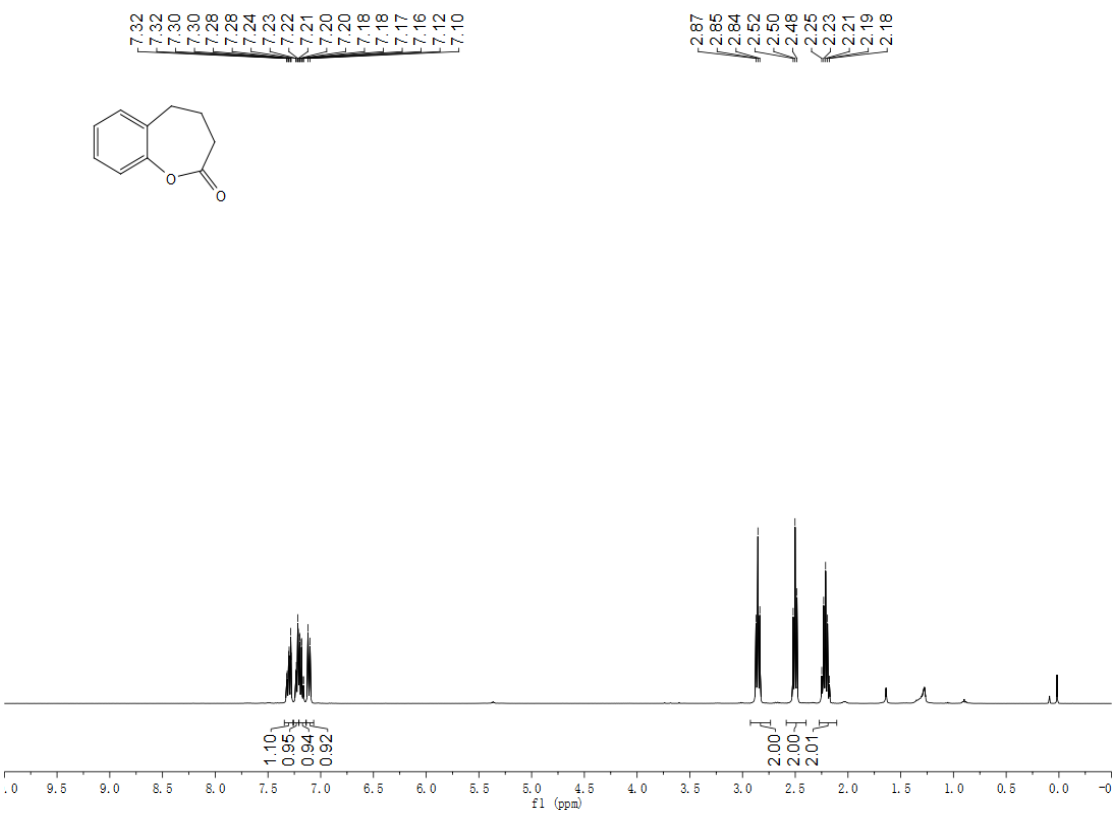
^{13}C NMR of **2c** ($CDCl_3$, 150 MHz)



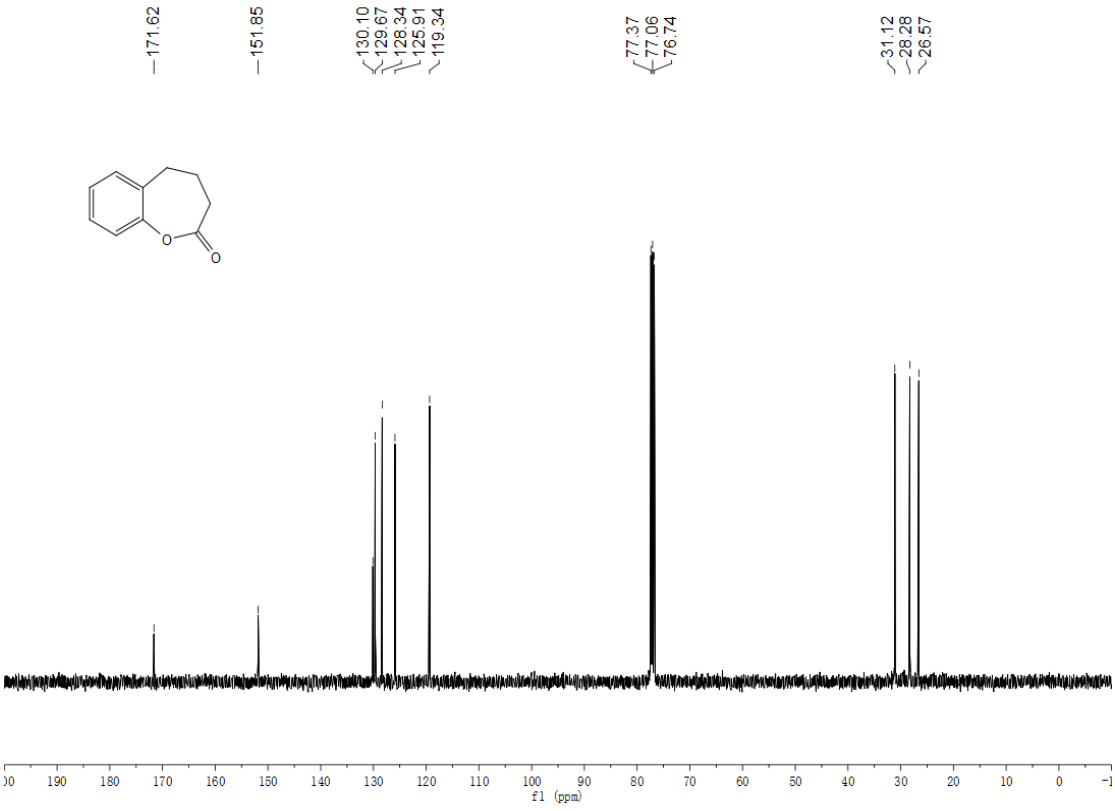
^{1}H NMR of **2d** ($CDCl_3$, 400 MHz)



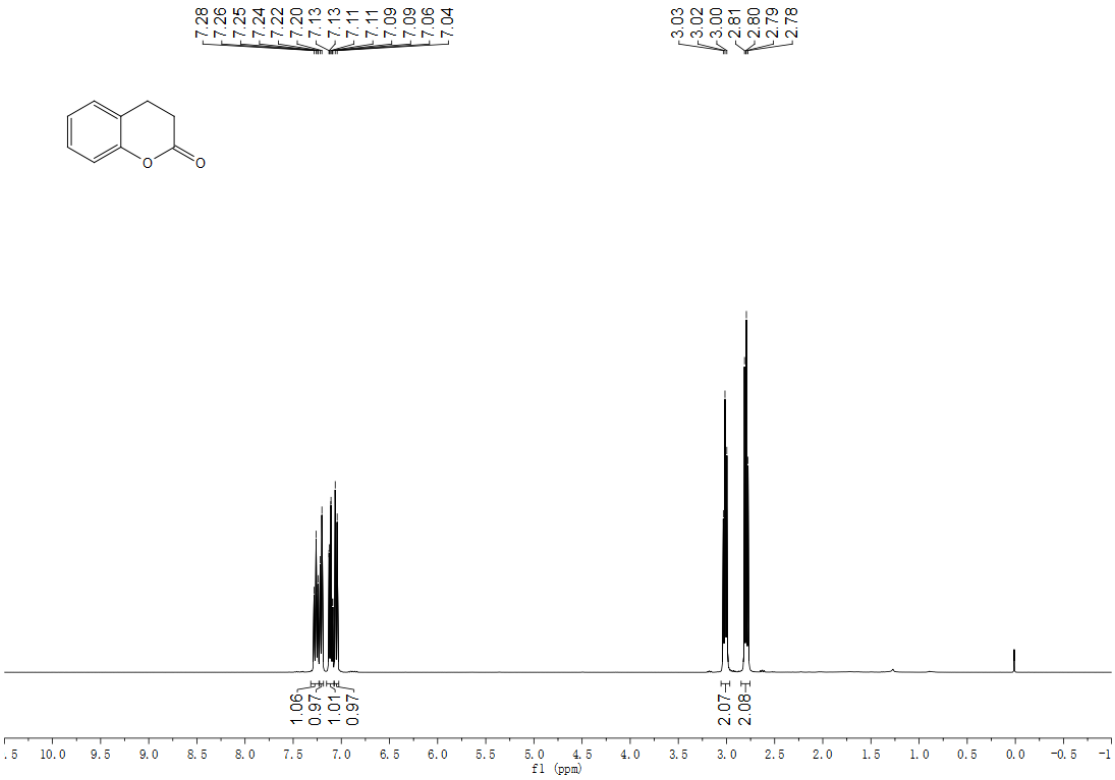
^{13}C NMR of **2d** ($CDCl_3$, 100 MHz)



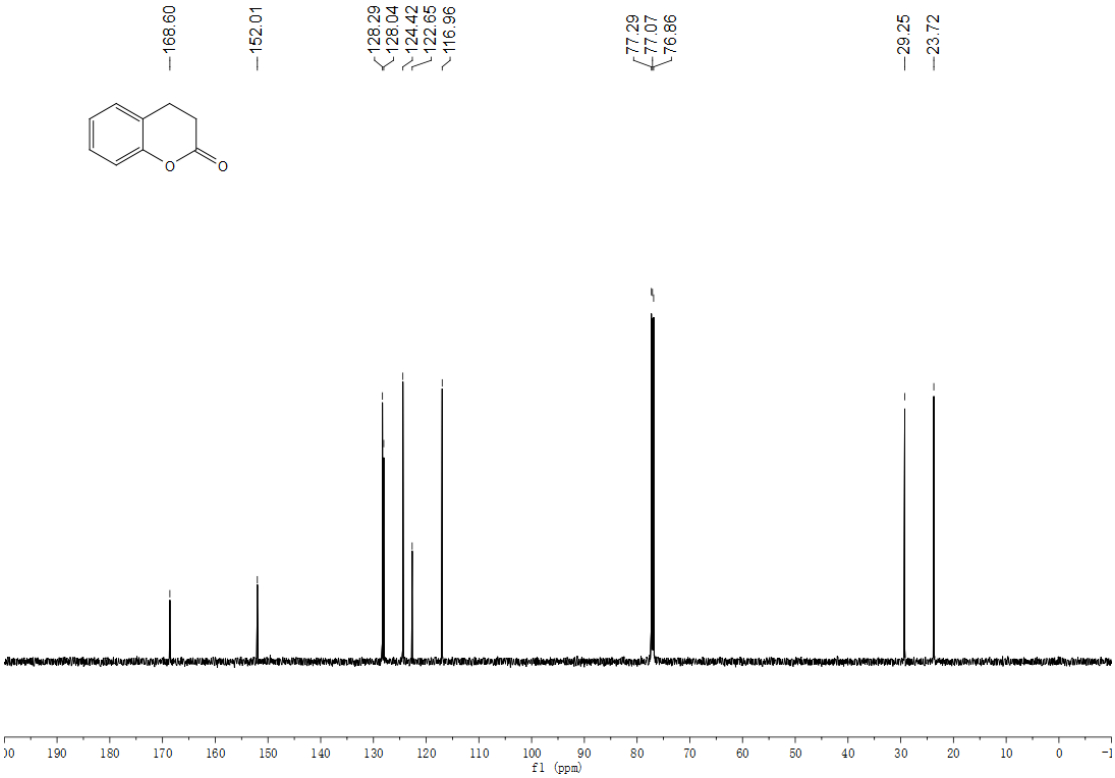
^{1}H NMR of **2e** ($CDCl_3$, 400 MHz)



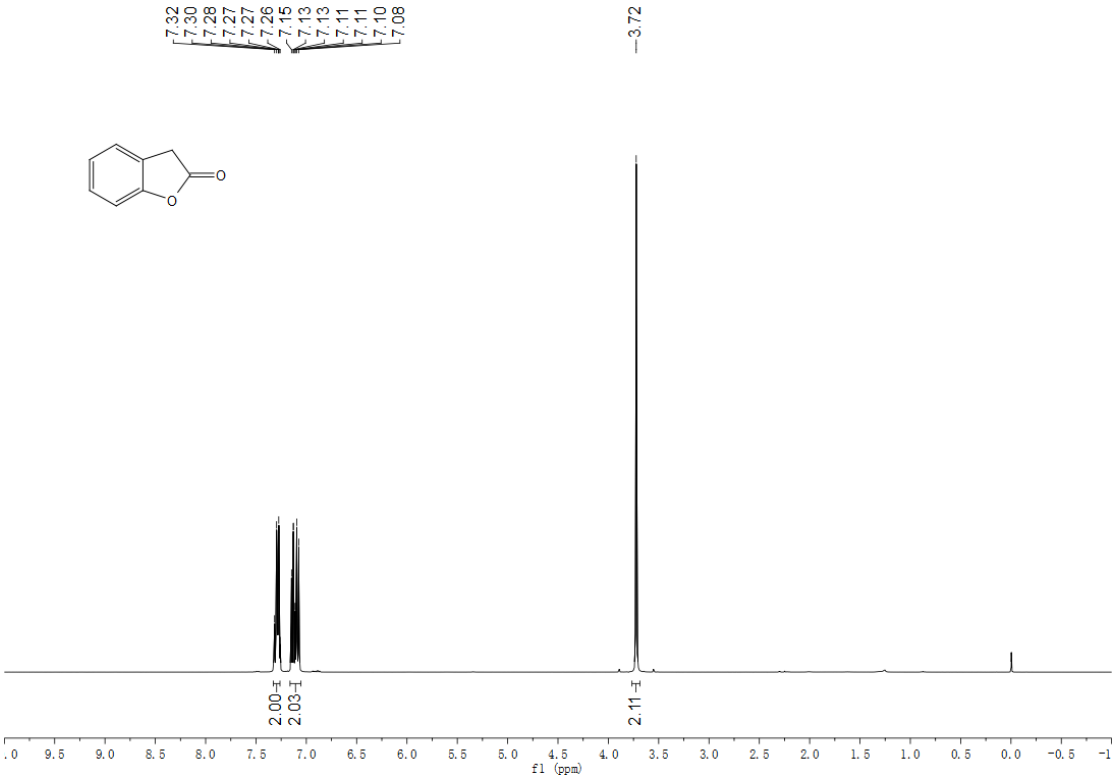
^{13}C NMR of **2e** ($CDCl_3$, 100 MHz)



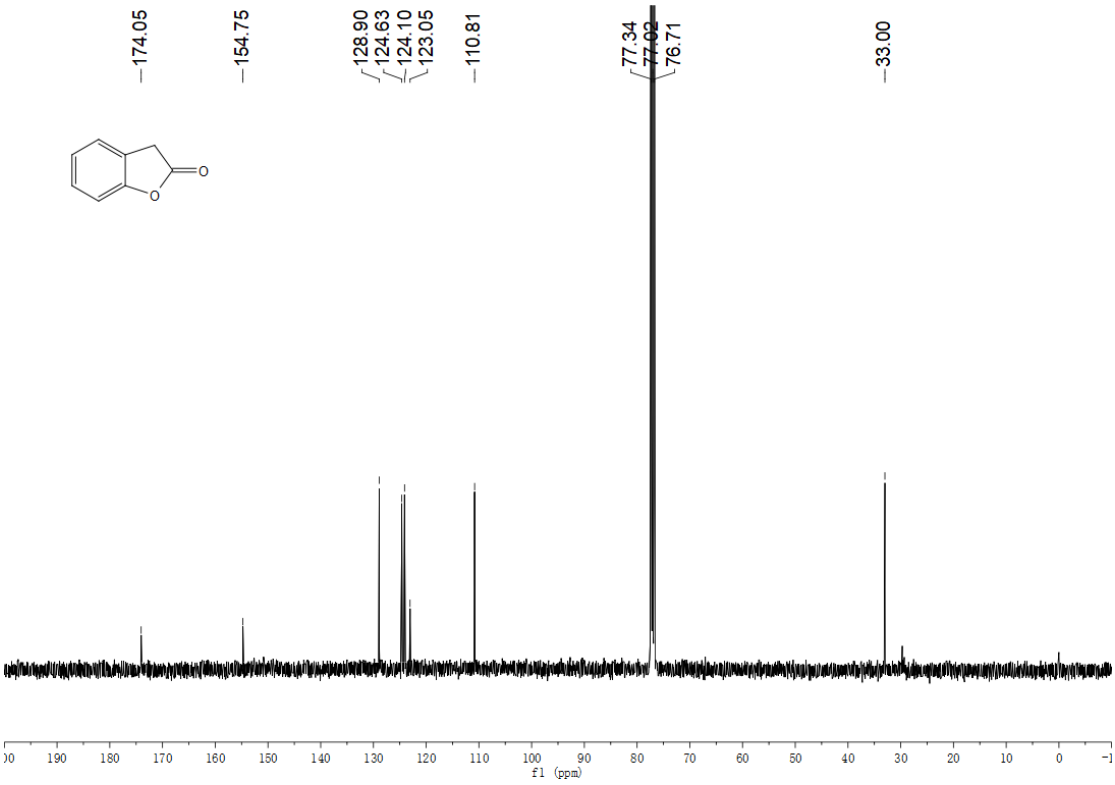
^{1}H NMR of **2f** ($CDCl_3$, 400 MHz)



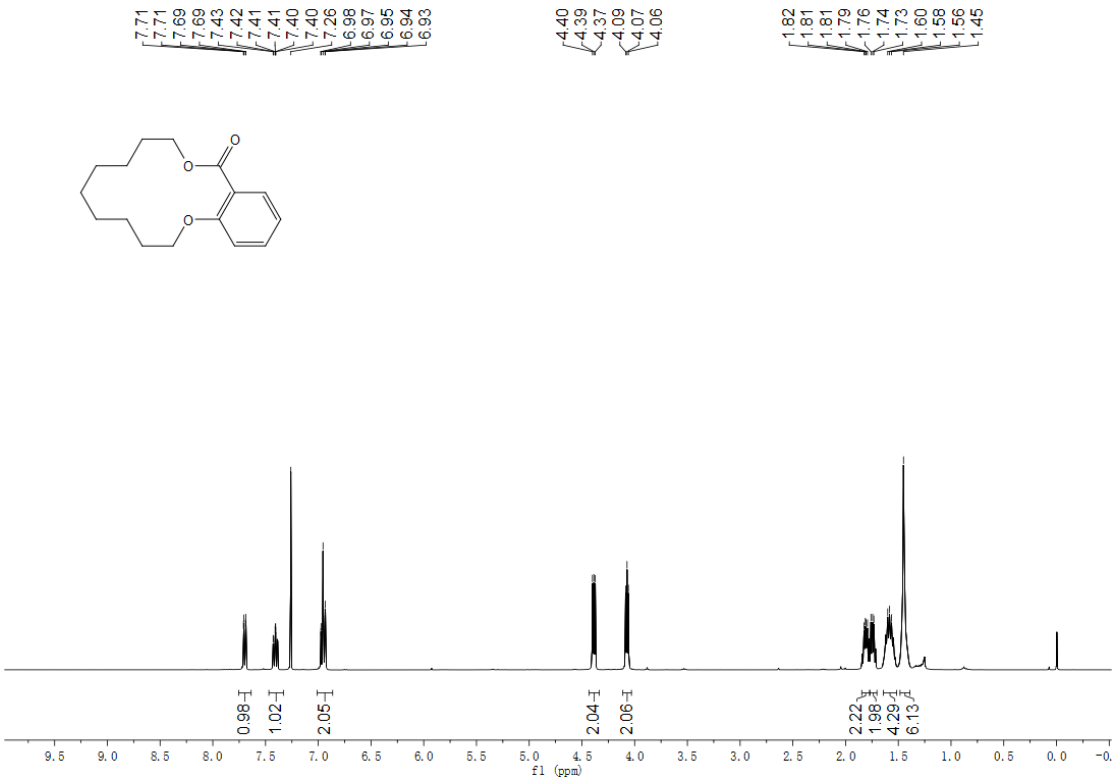
^{13}C NMR of **2f** ($CDCl_3$, 100 MHz)



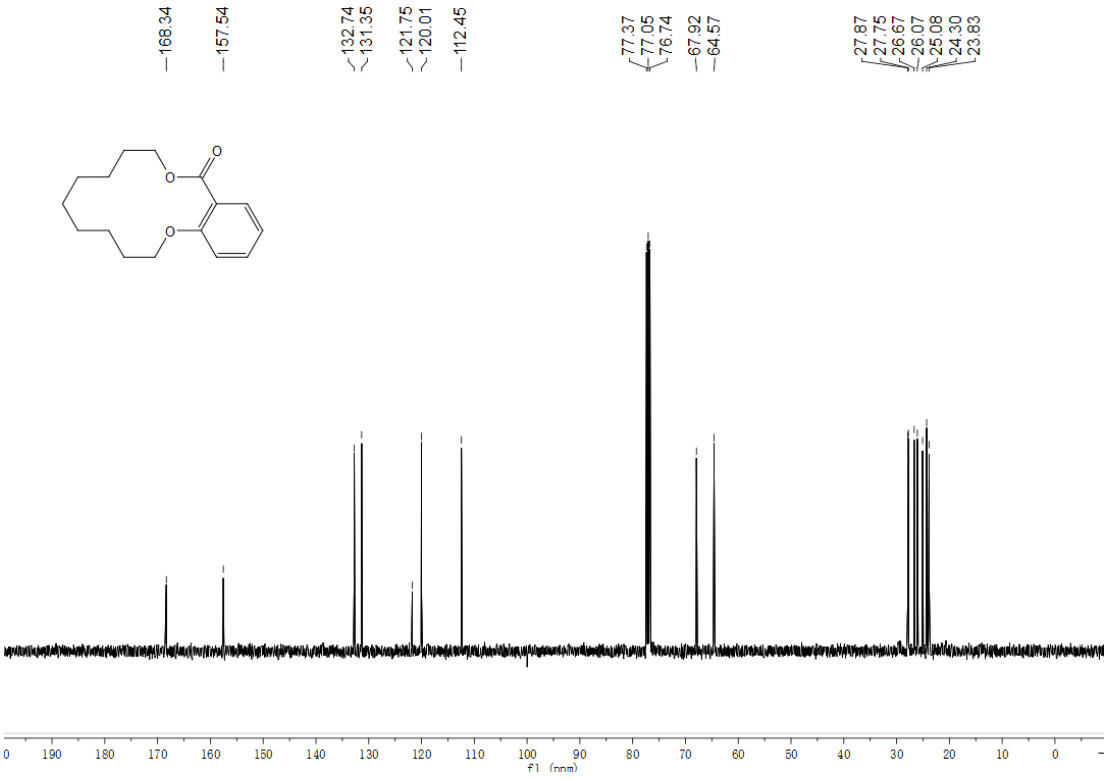
^{1}H NMR of **2g** ($CDCl_3$, 400 MHz)



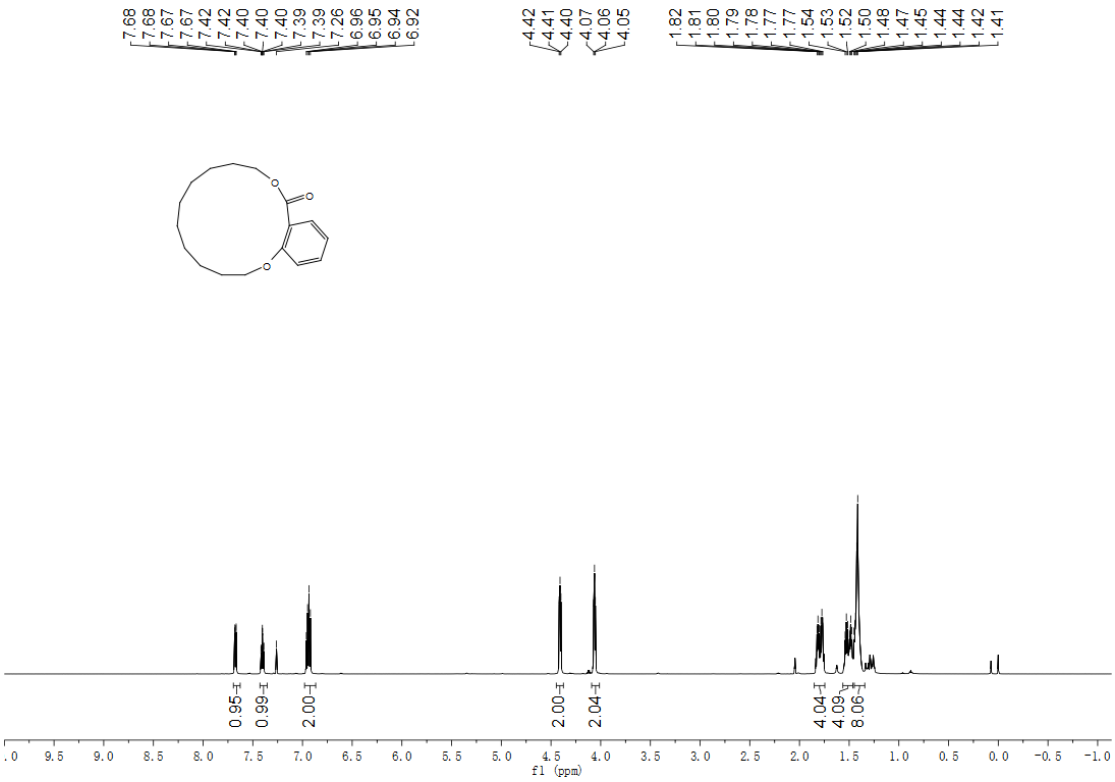
^{13}C NMR of **2g** ($CDCl_3$, 100 MHz)



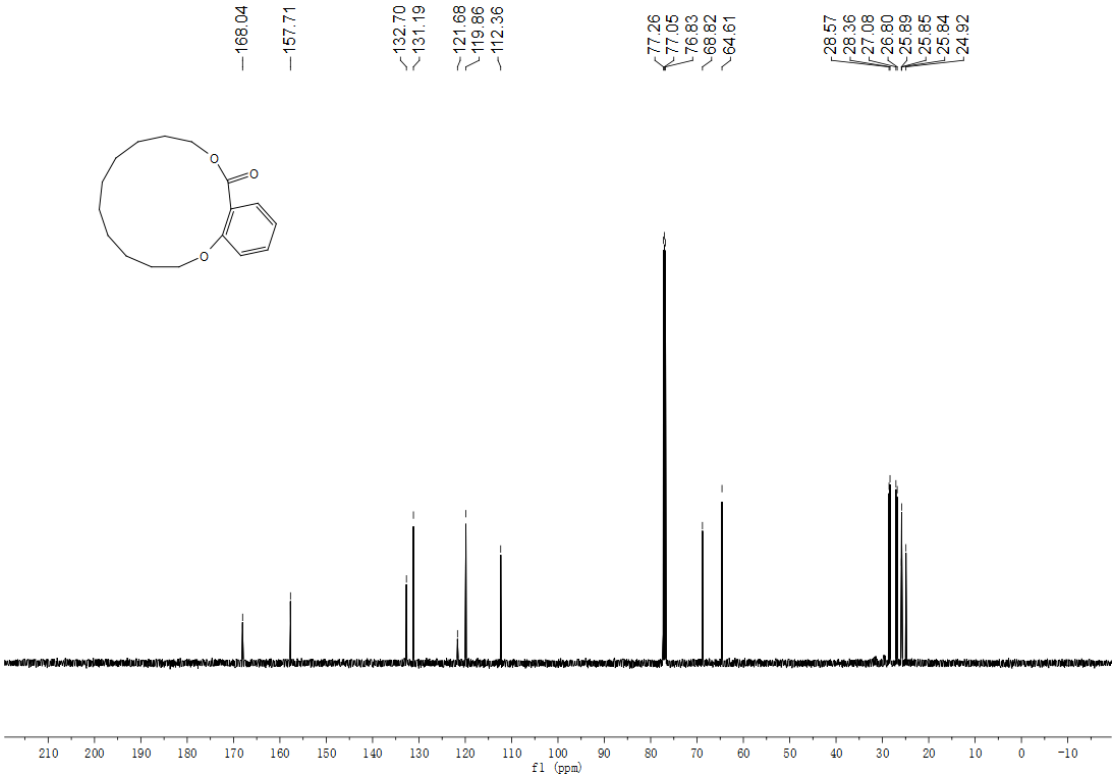
^{1}H NMR of **2h** ($CDCl_3$, 400 MHz)



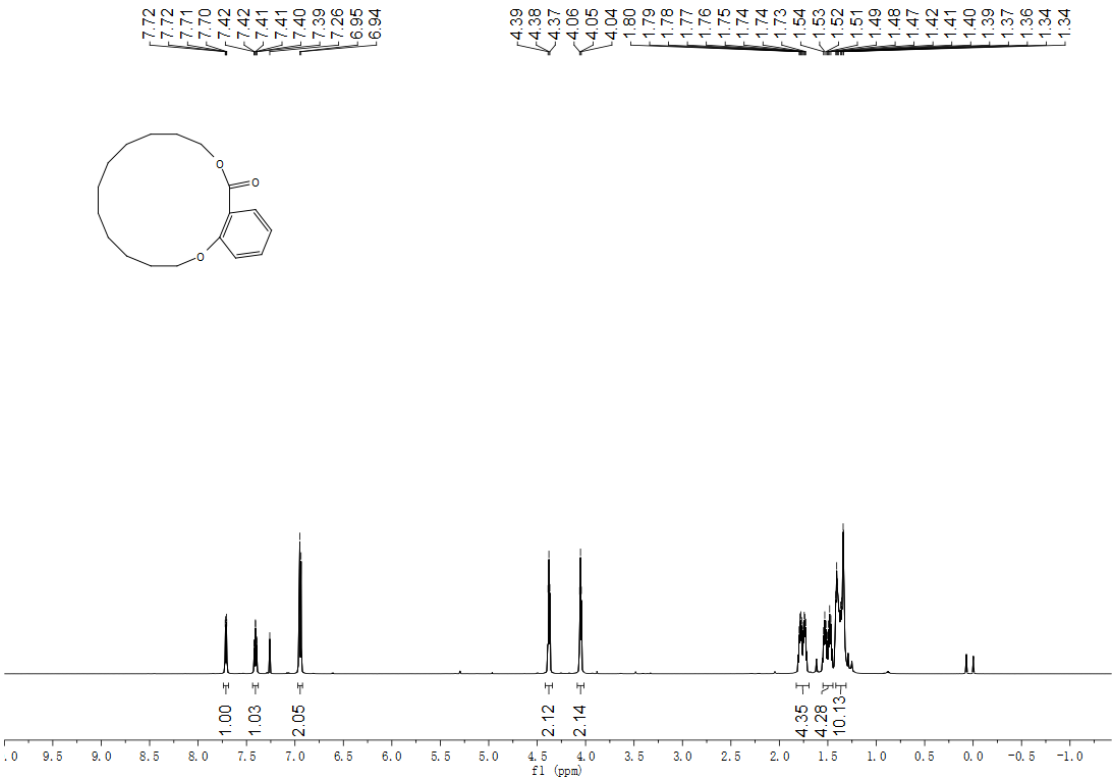
^{13}C NMR of **2h** ($CDCl_3$, 100 MHz)



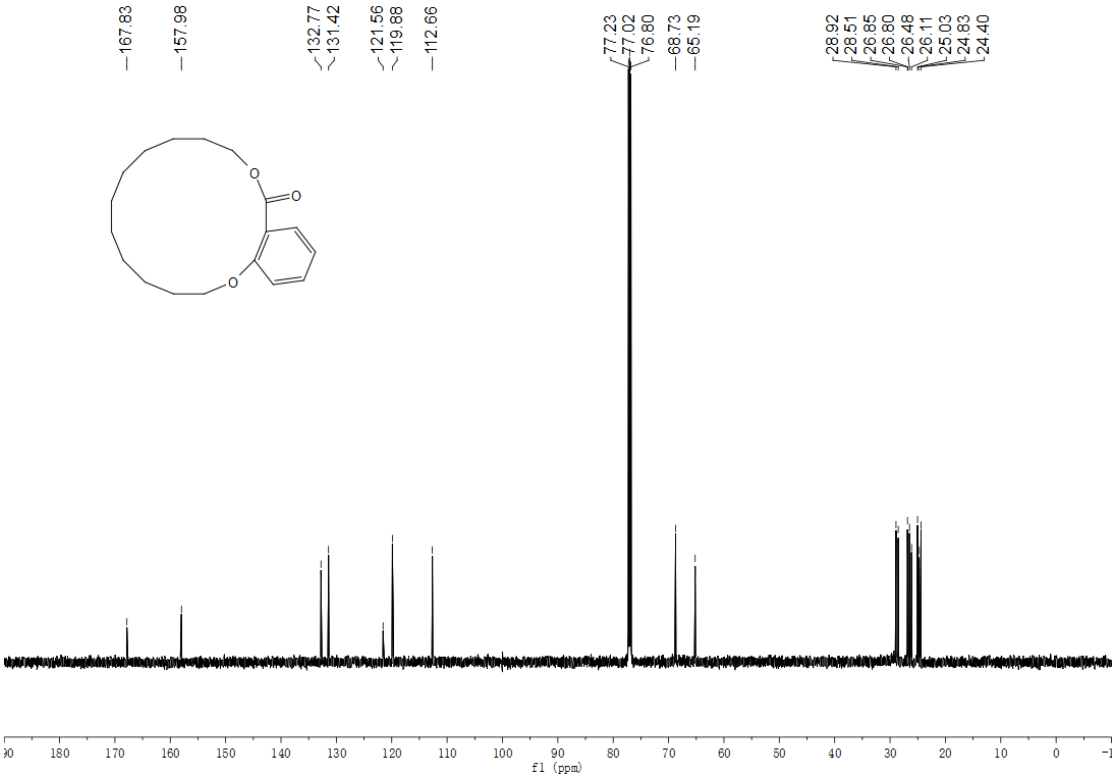
^{1}H NMR of **2i** ($CDCl_3$, 600 MHz)



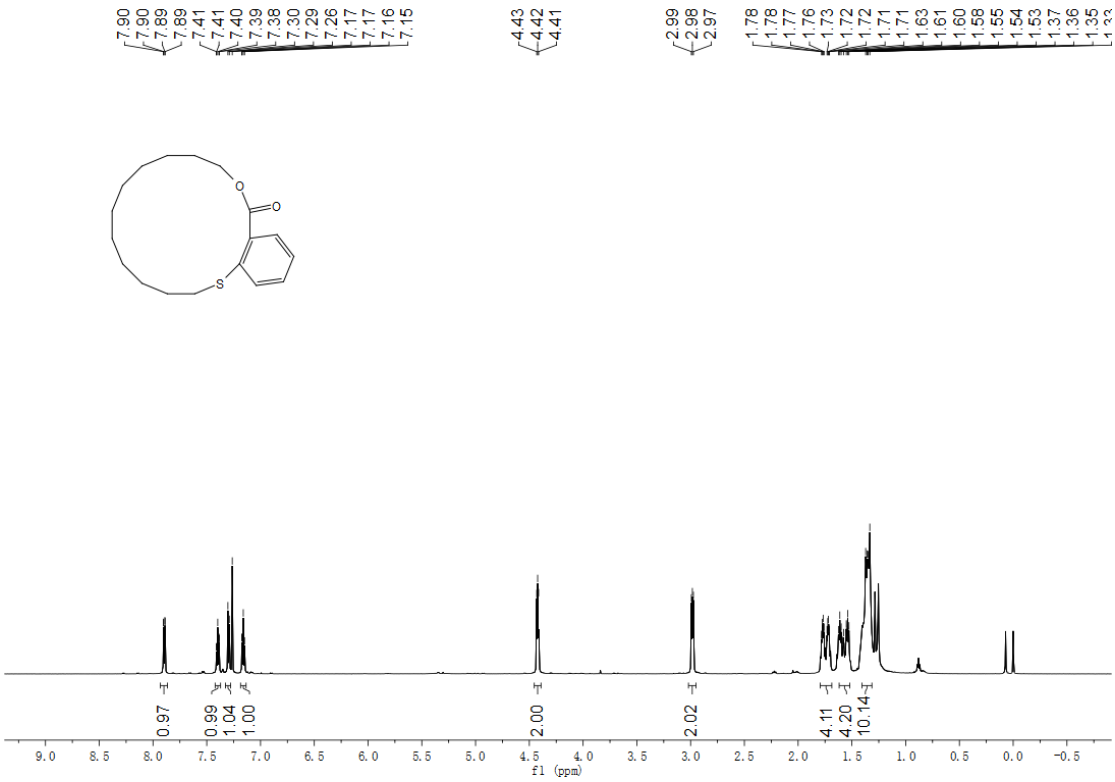
^{13}C NMR of **2i** ($CDCl_3$, 150 MHz)



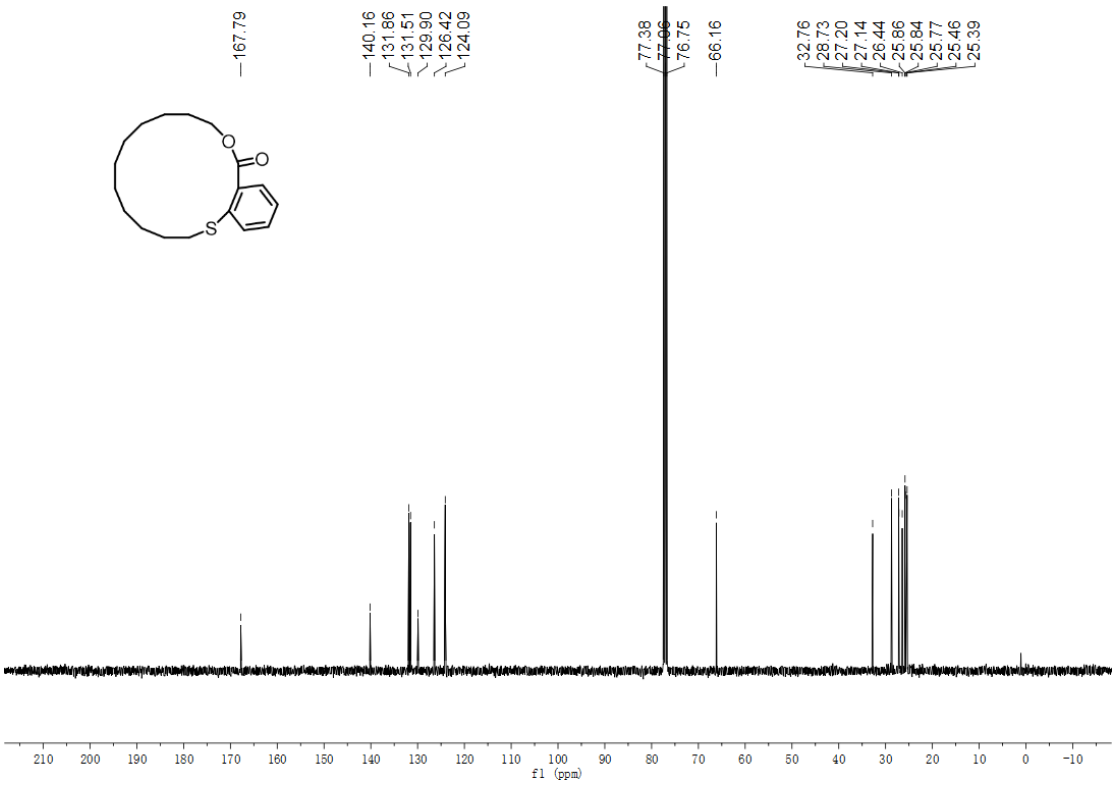
^{1}H NMR of **2j** ($CDCl_3$, 600 MHz)



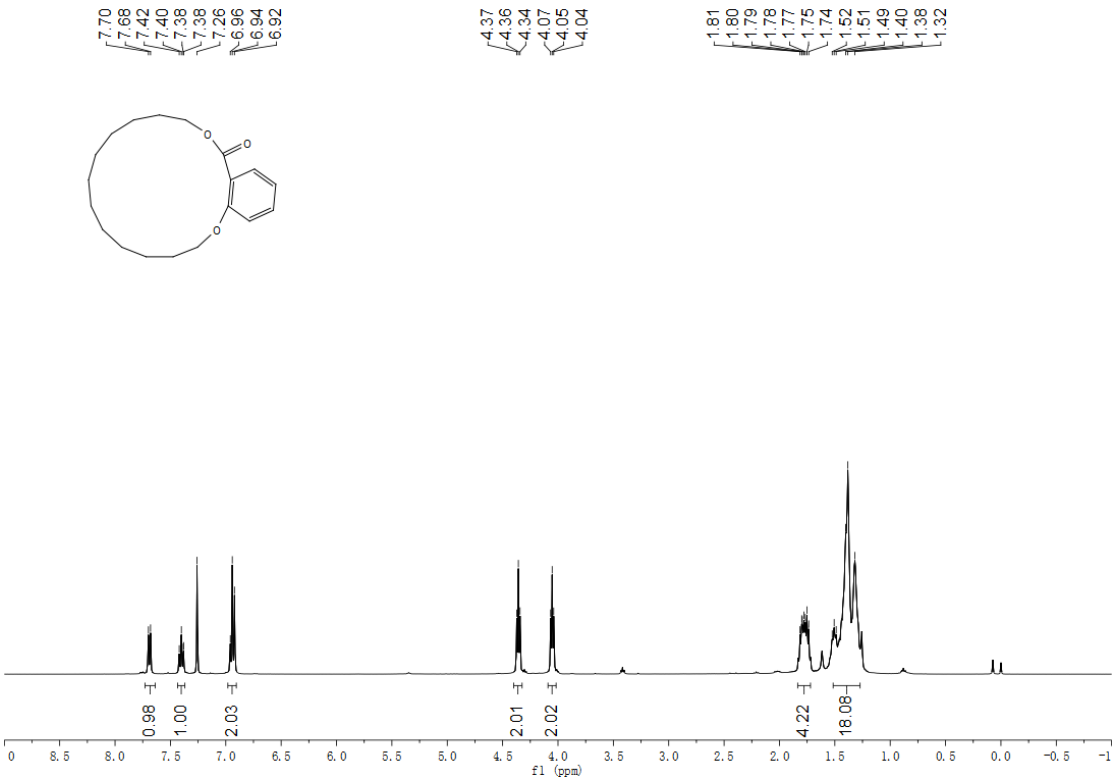
^{13}C NMR of **2j** ($CDCl_3$, 150 MHz)



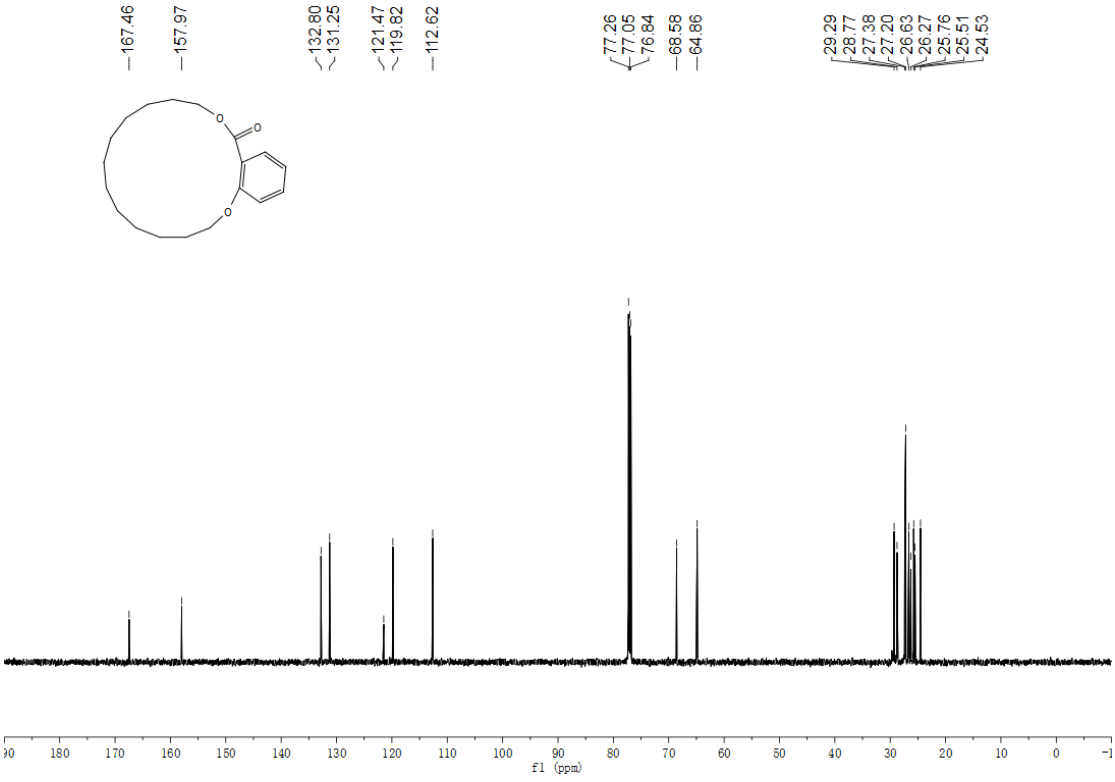
^{1}H NMR of **2k** ($CDCl_3$, 600 MHz)



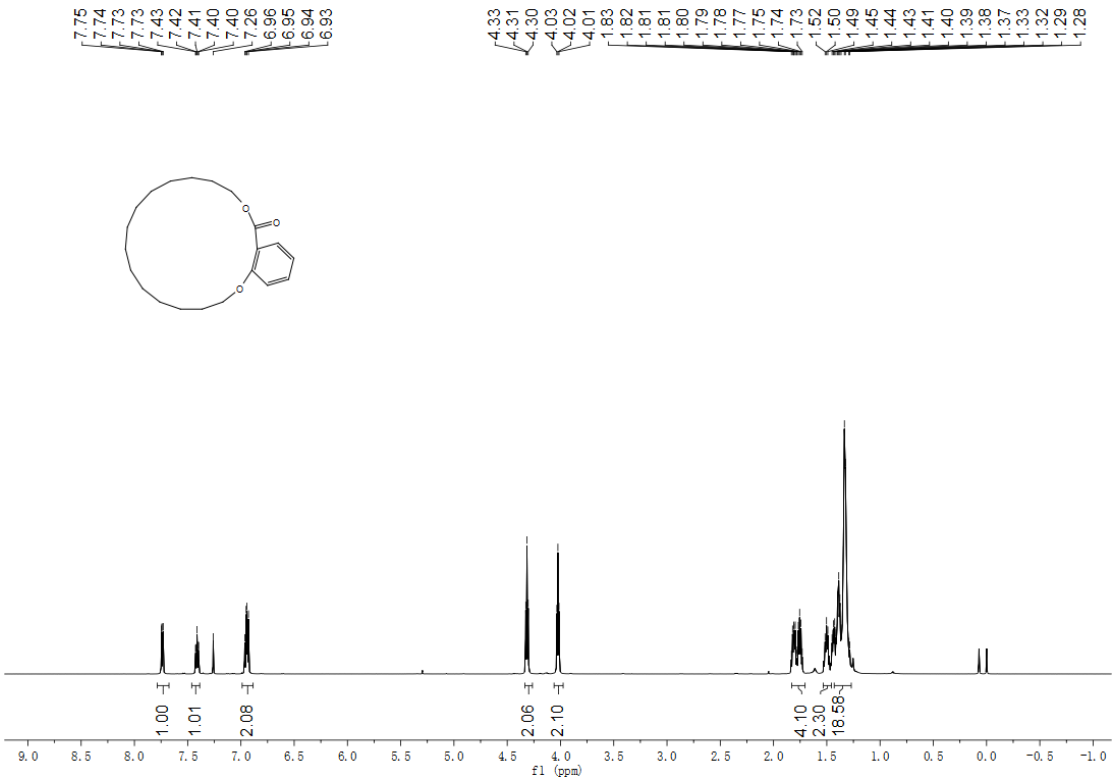
^{13}C NMR of **2k** ($CDCl_3$, 100 MHz)



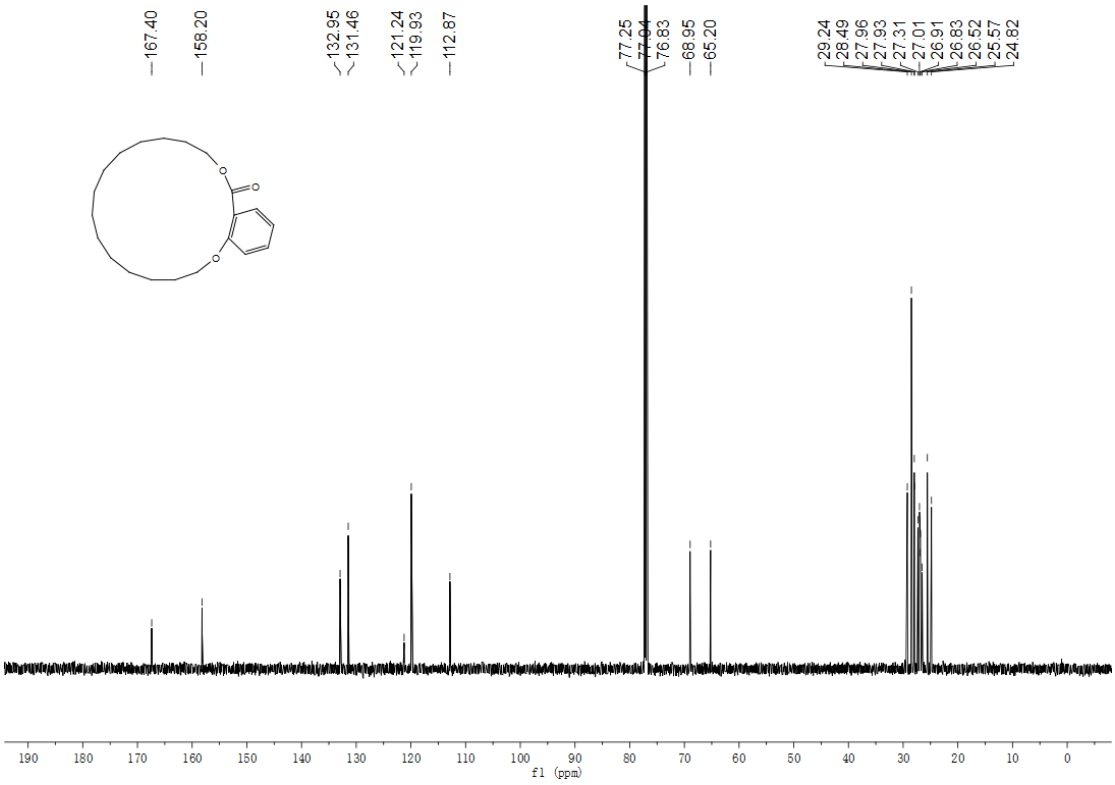
^{1}H NMR of **2l** ($CDCl_3$, 400 MHz)



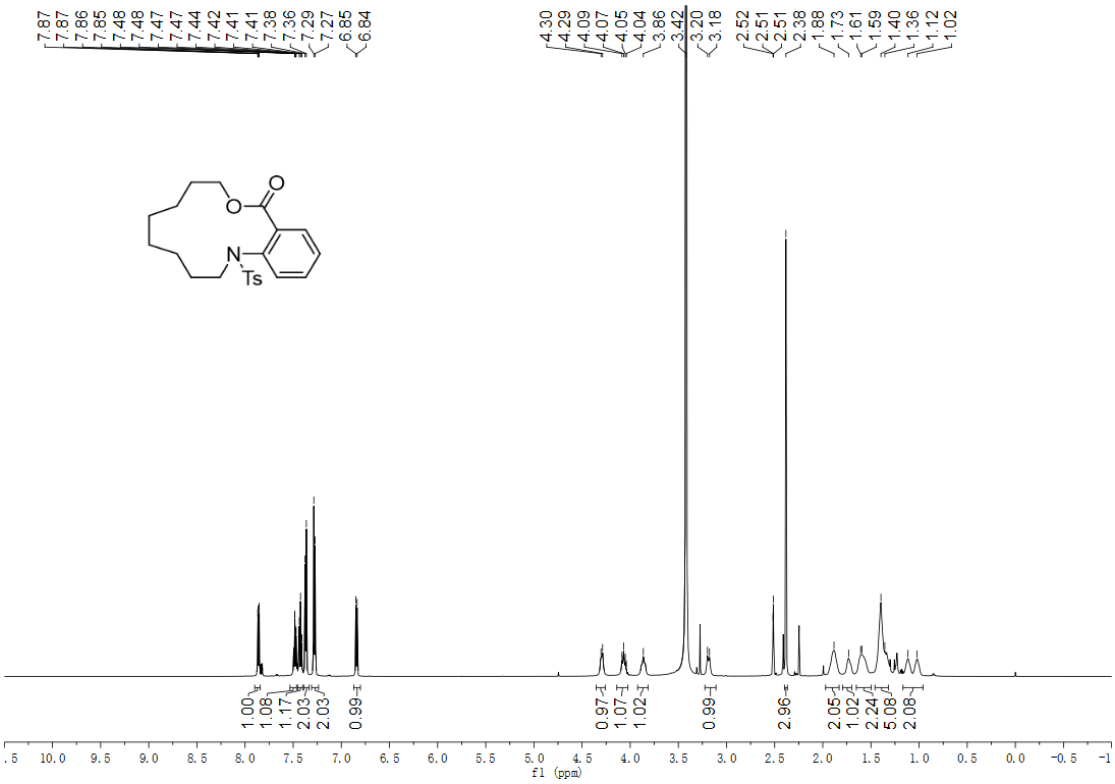
^{13}C NMR of **2l** ($CDCl_3$, 150 MHz)



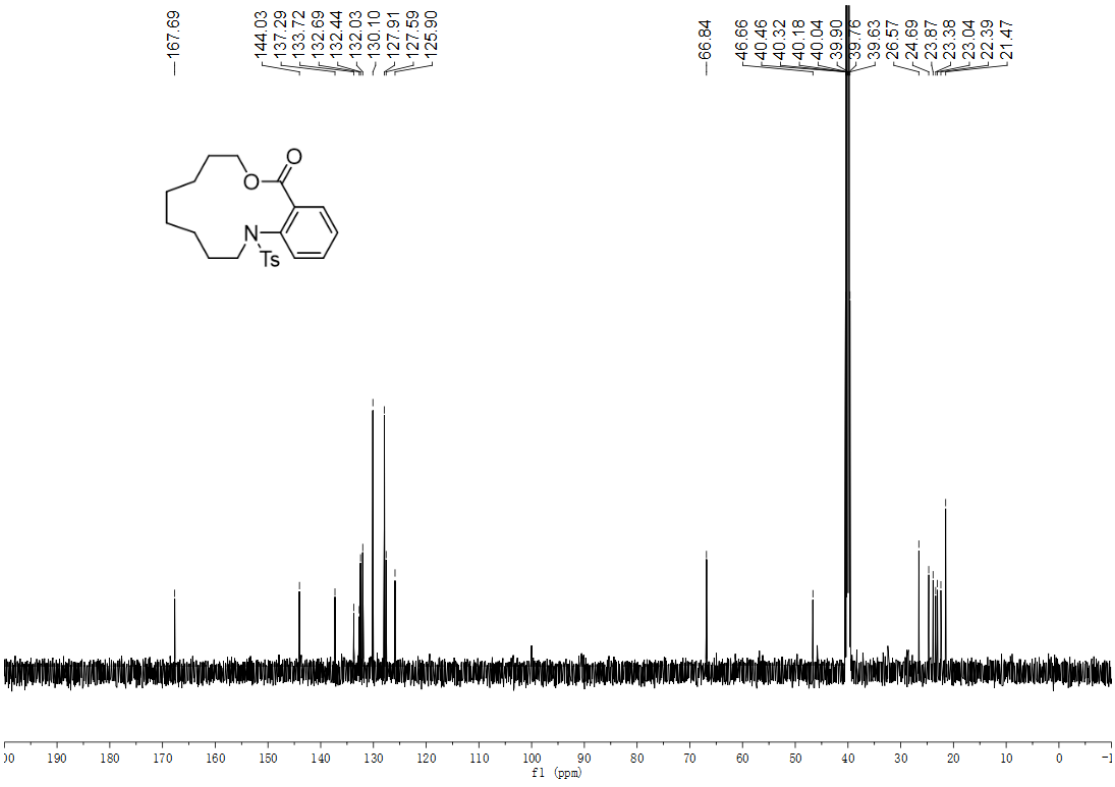
^{1}H NMR of **2m** ($CDCl_3$, 600 MHz)



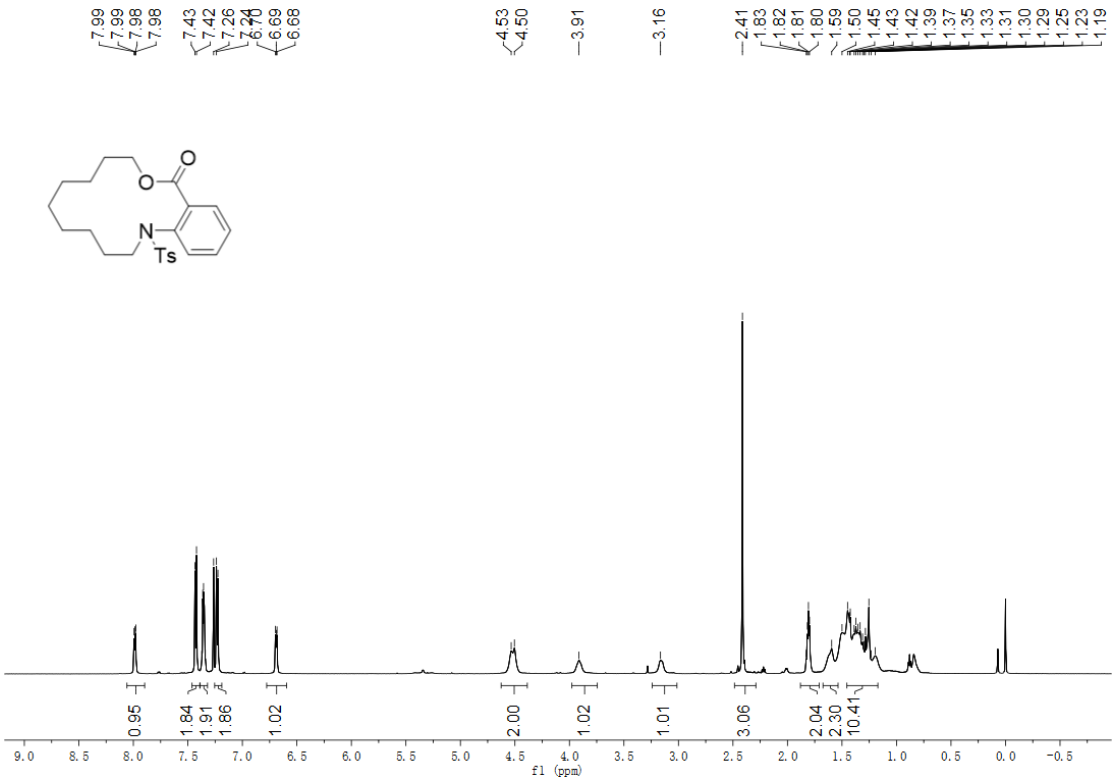
^{13}C NMR of **2m** ($CDCl_3$, 150 MHz)



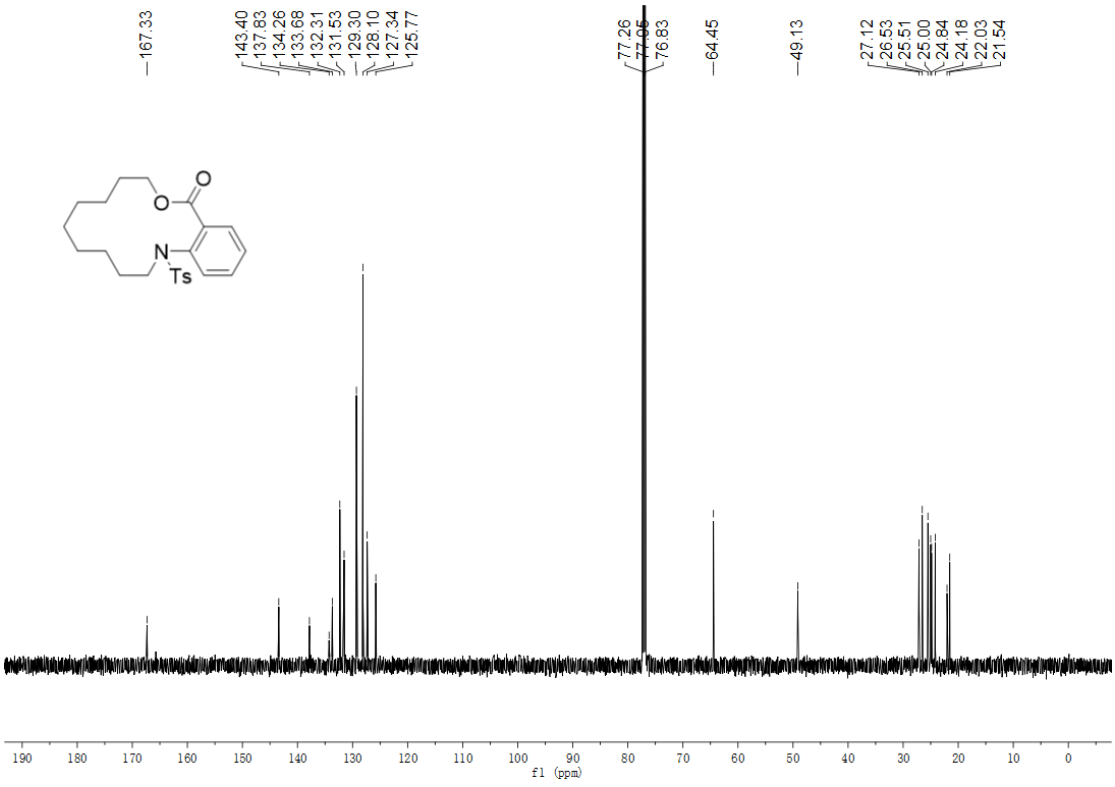
^{1}H NMR of **2n** (DMSO-d_6, 600 MHz)



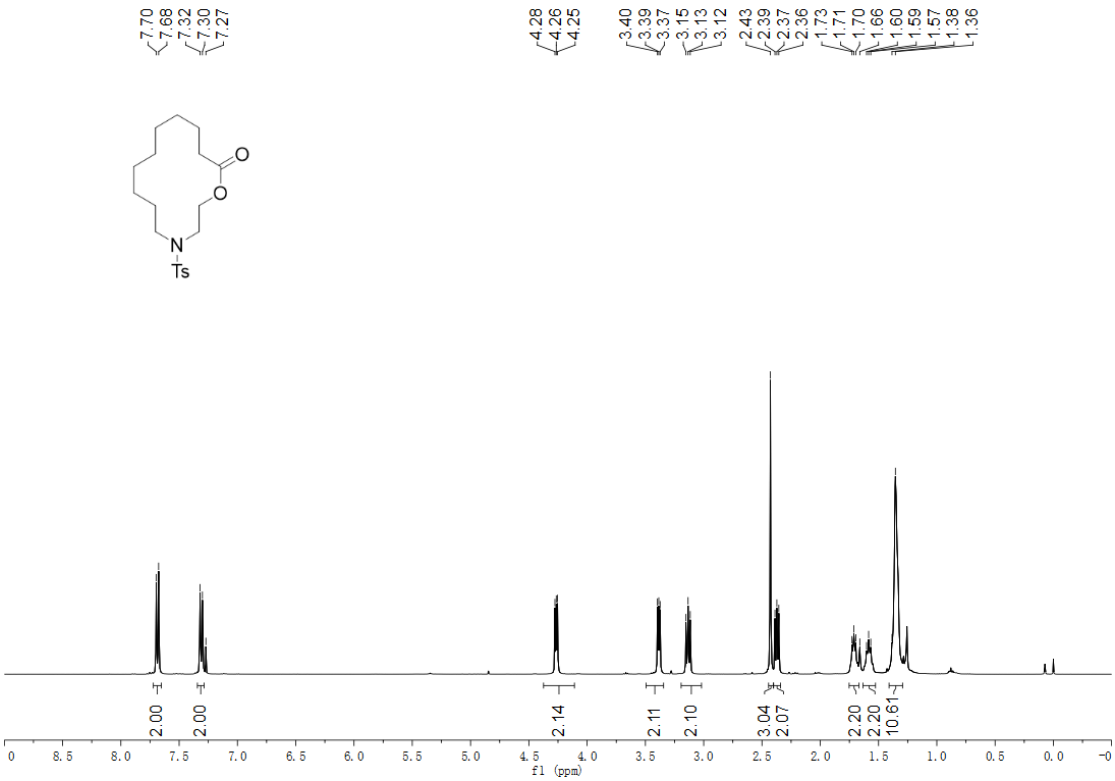
^{13}C NMR of **2n** (DMSO-d_6, 150 MHz)



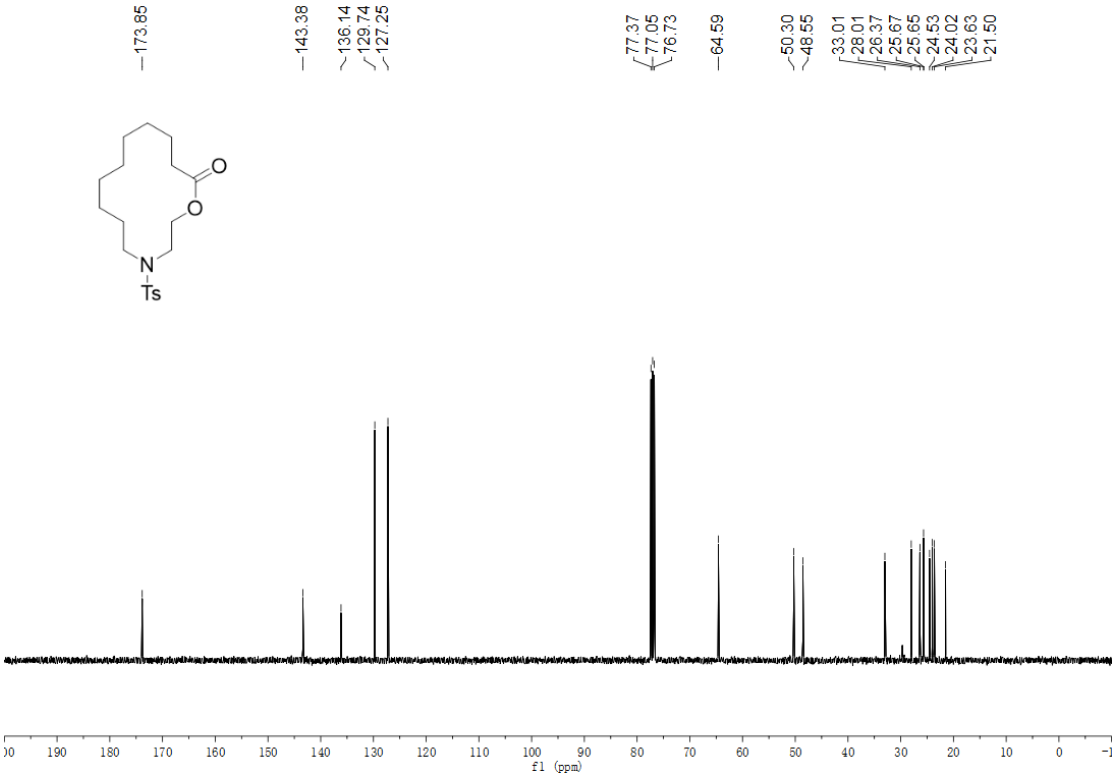
^{1}H NMR of **2o** ($CDCl_3$, 600 MHz)



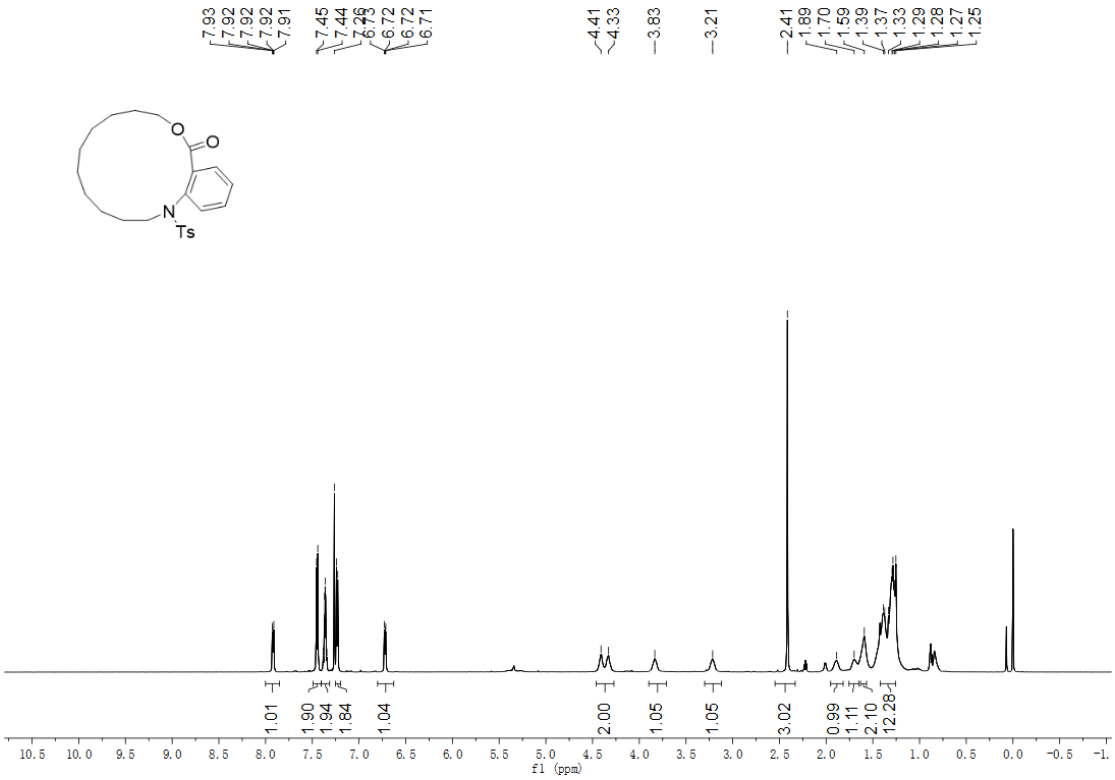
^{13}C NMR of **2o** ($CDCl_3$, 150 MHz)



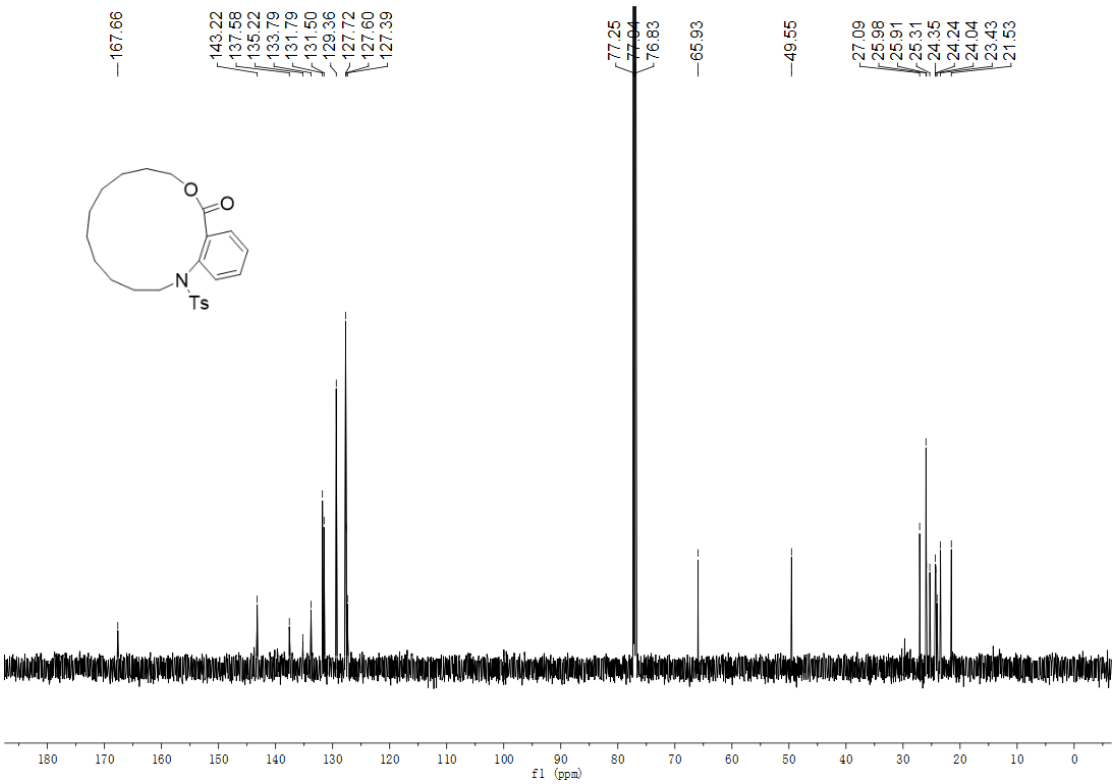
^{1}H NMR of **2p** ($CDCl_3$, 400 MHz)



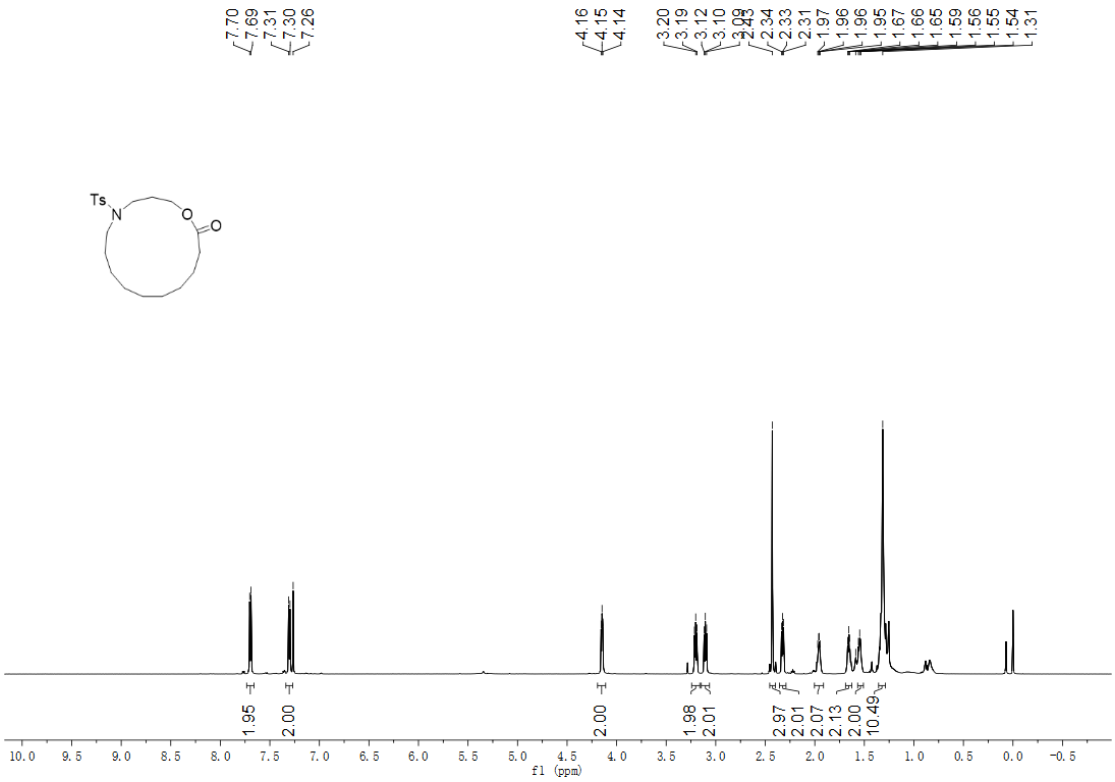
^{13}C NMR of **2p** ($CDCl_3$, 100 MHz)



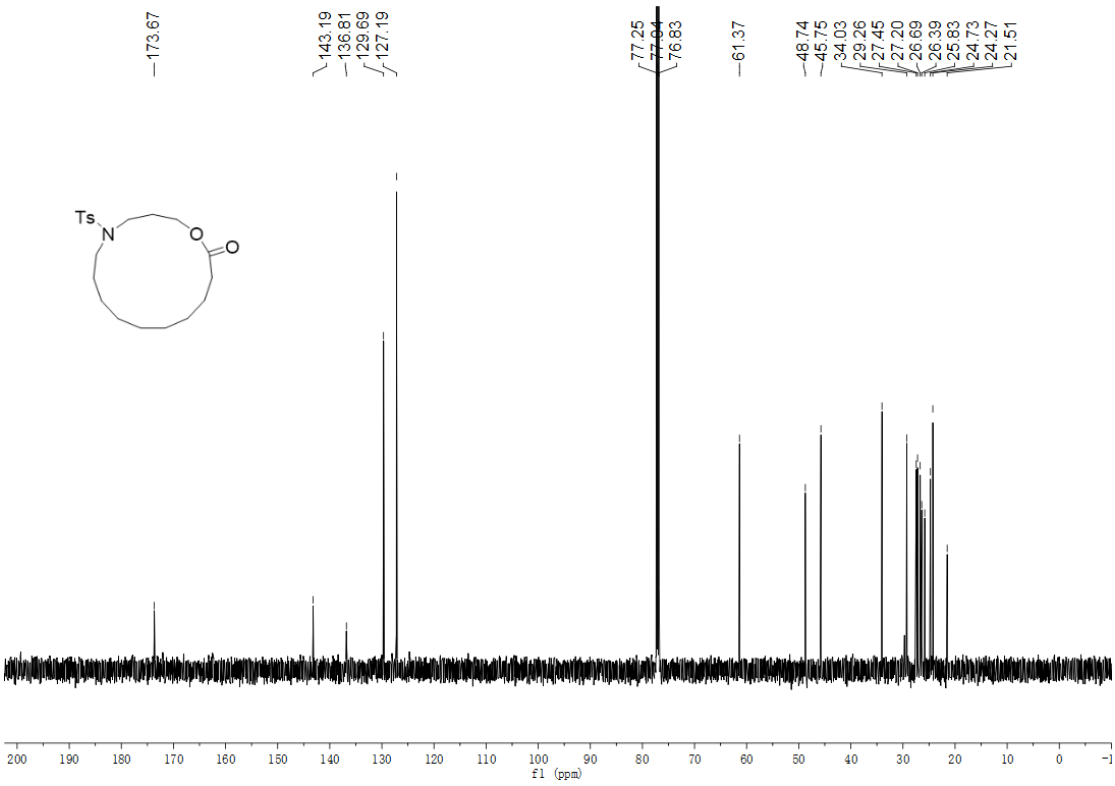
^{1}H NMR of **2q** ($CDCl_3$, 600 MHz)



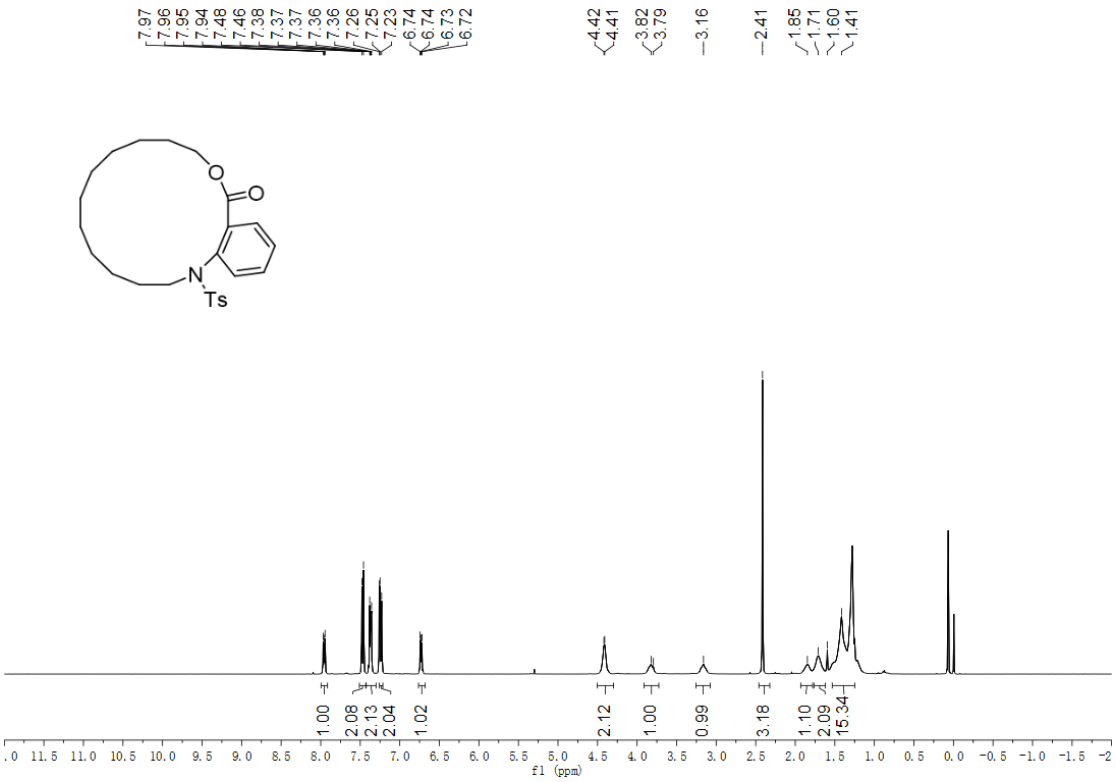
^{13}C NMR of **2q** ($CDCl_3$, 150 MHz)



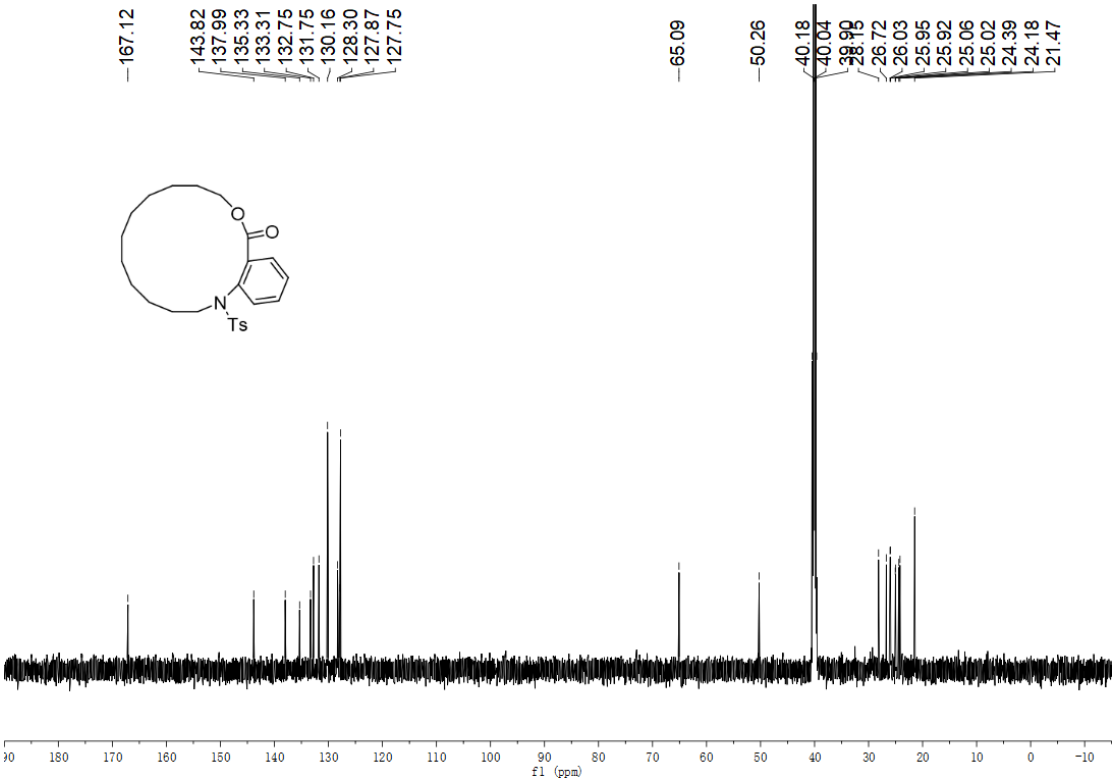
^{1}H NMR of **2r** ($CDCl_3$, 600 MHz)



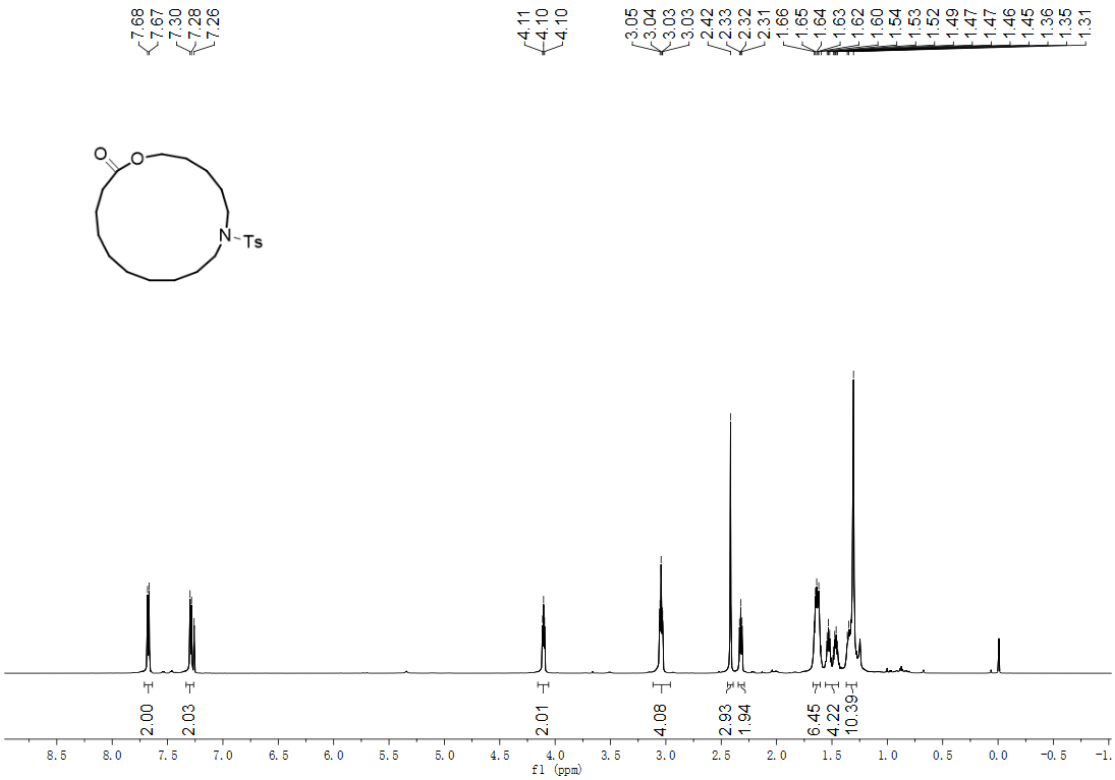
^{13}C NMR of **2r** ($CDCl_3$, 150 MHz)



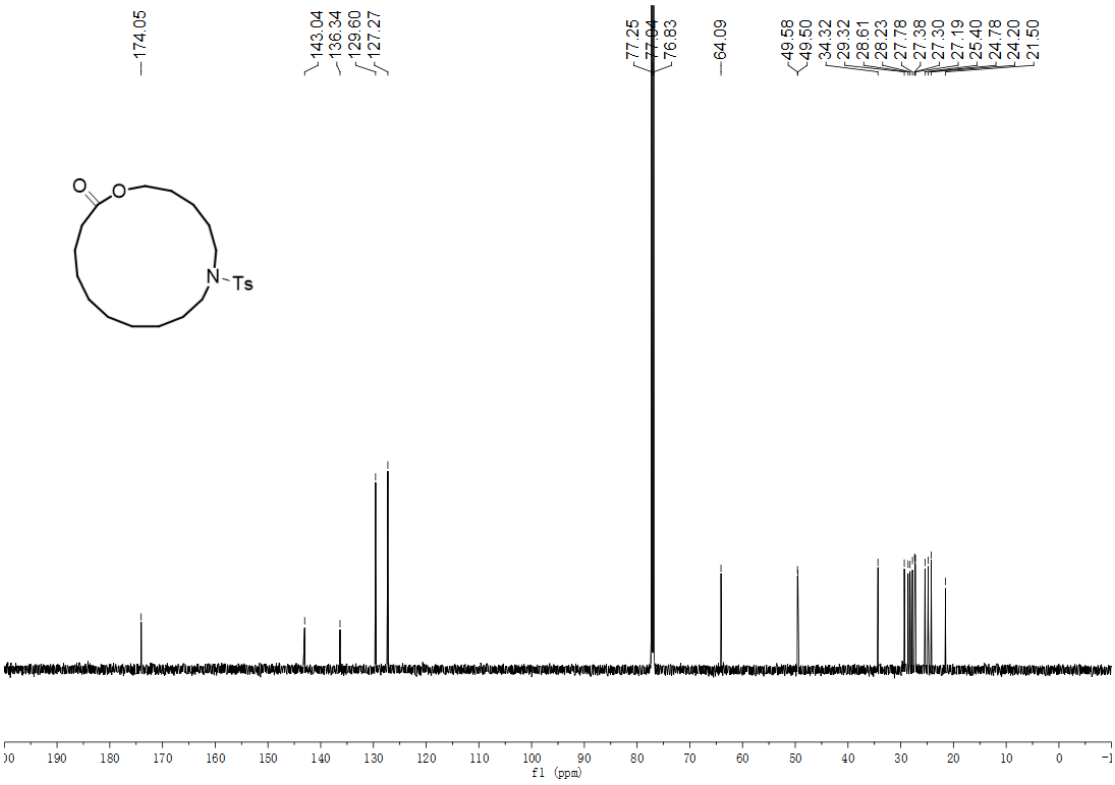
^{1}H NMR of **2s** ($CDCl_3$, 400 MHz)



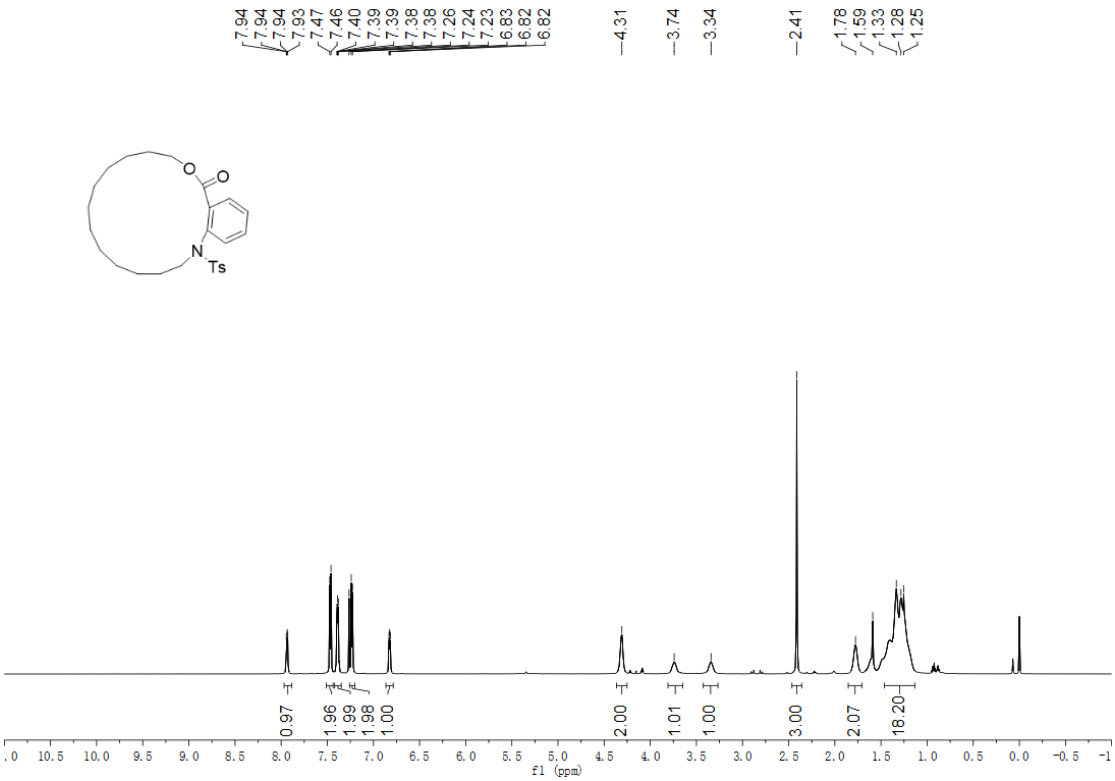
^{13}C NMR of **2s** (DMSO-d_6, 150 MHz)



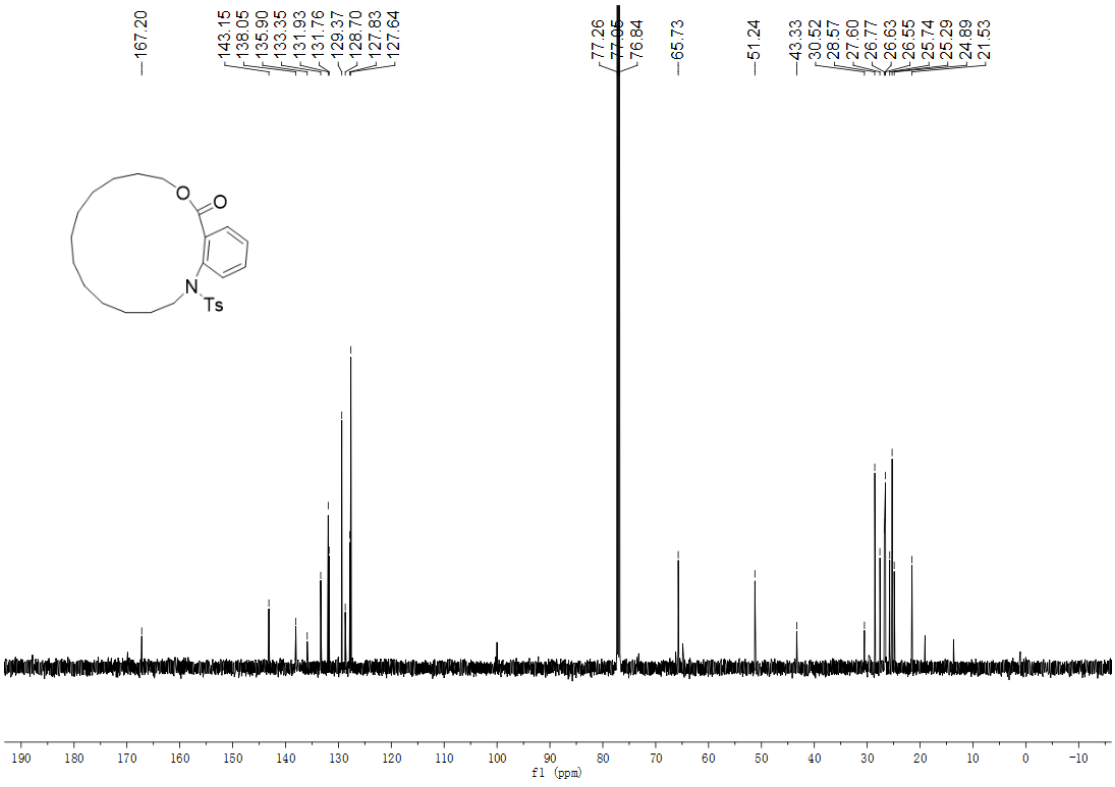
^{1}H NMR of **2t** ($CDCl_3$, 600 MHz)



^{13}C NMR of **2t** ($CDCl_3$, 150 MHz)



^{1}H NMR of **2u** ($CDCl_3$, 600 MHz)



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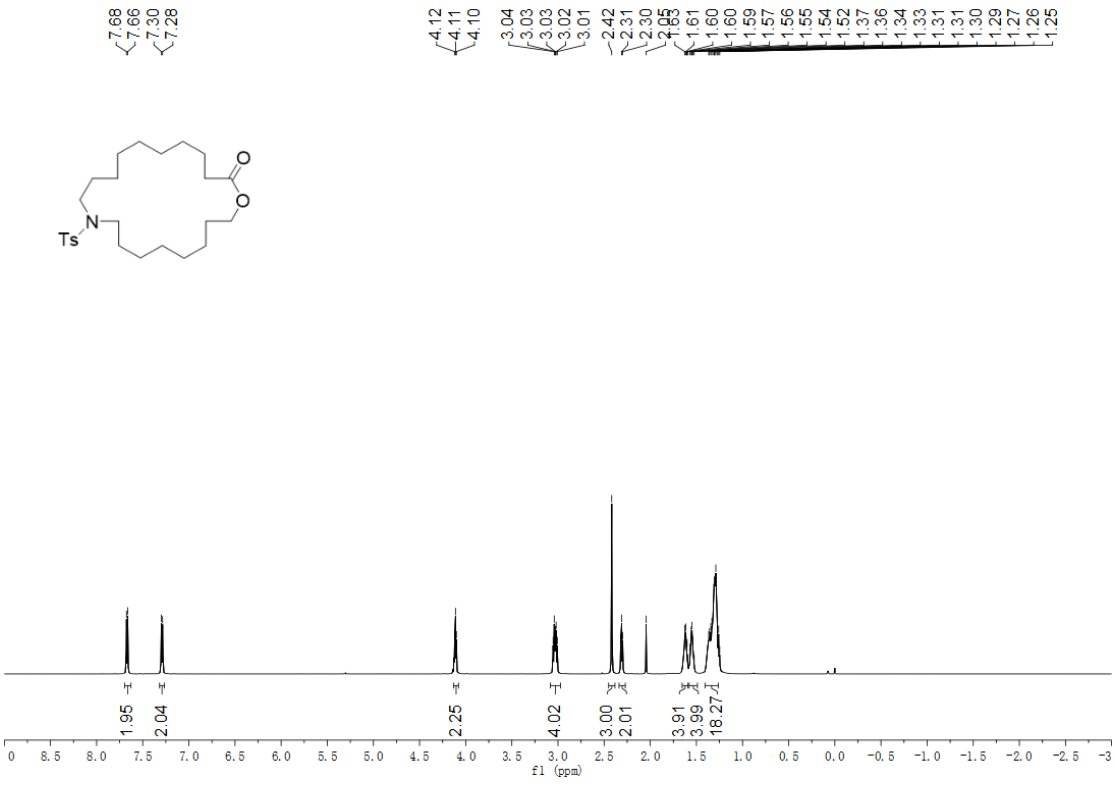
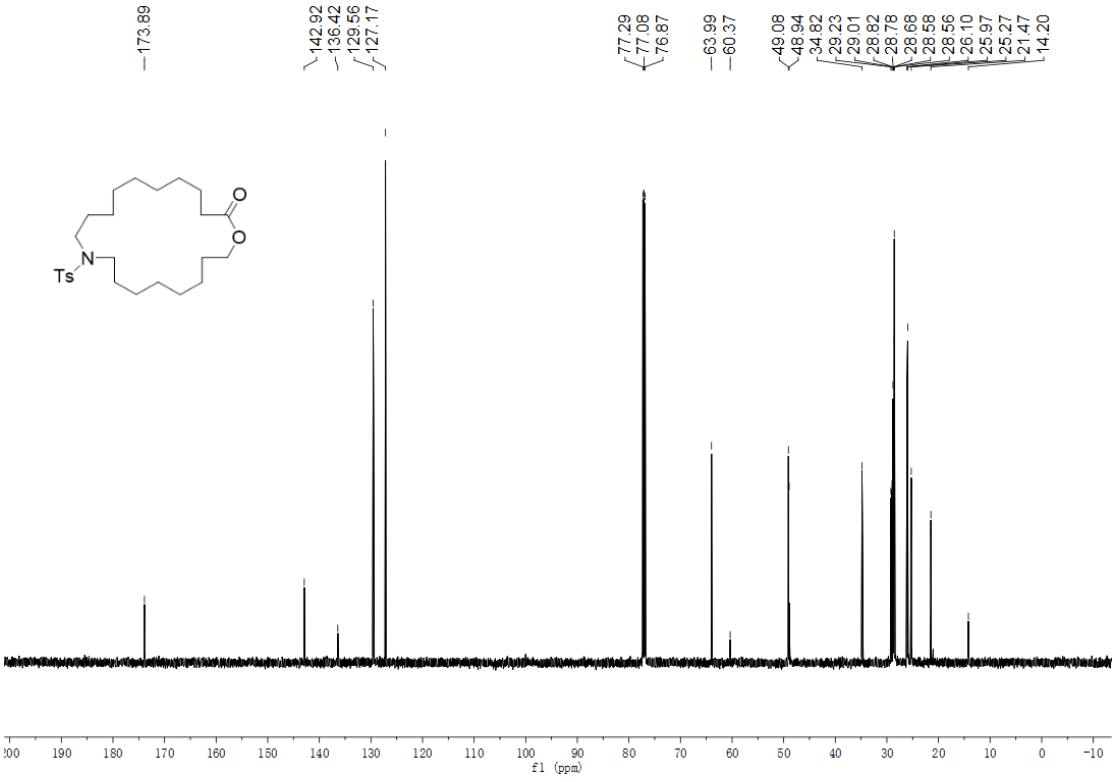
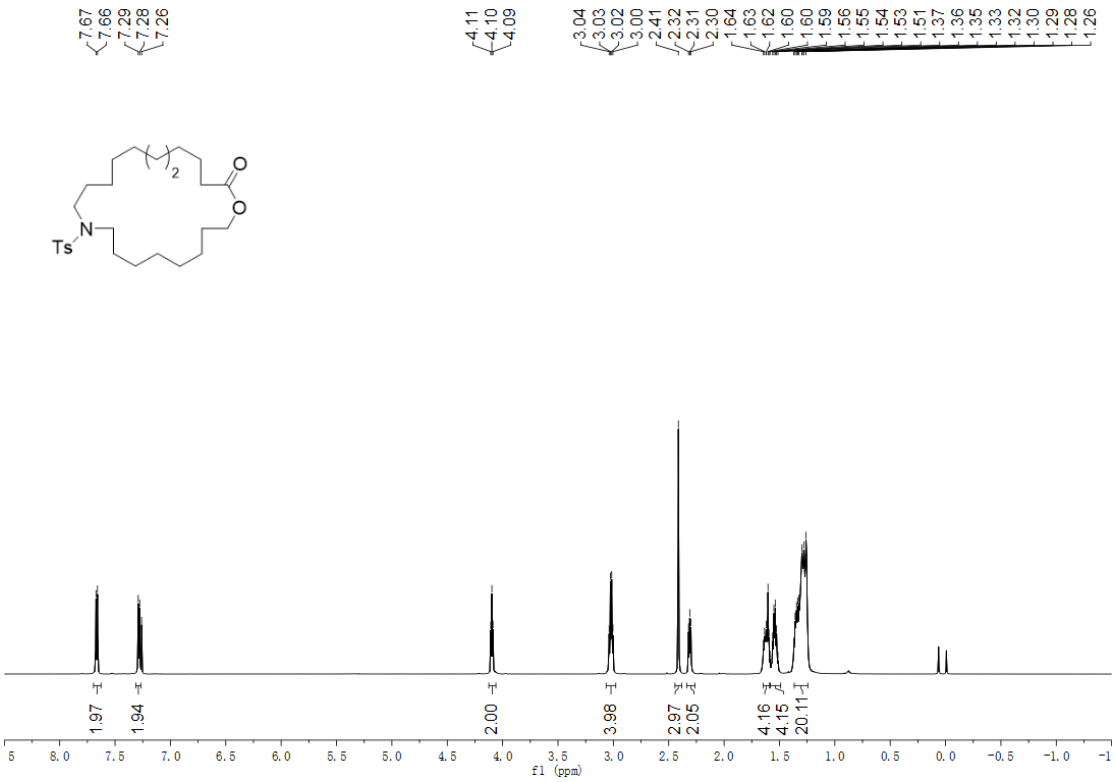


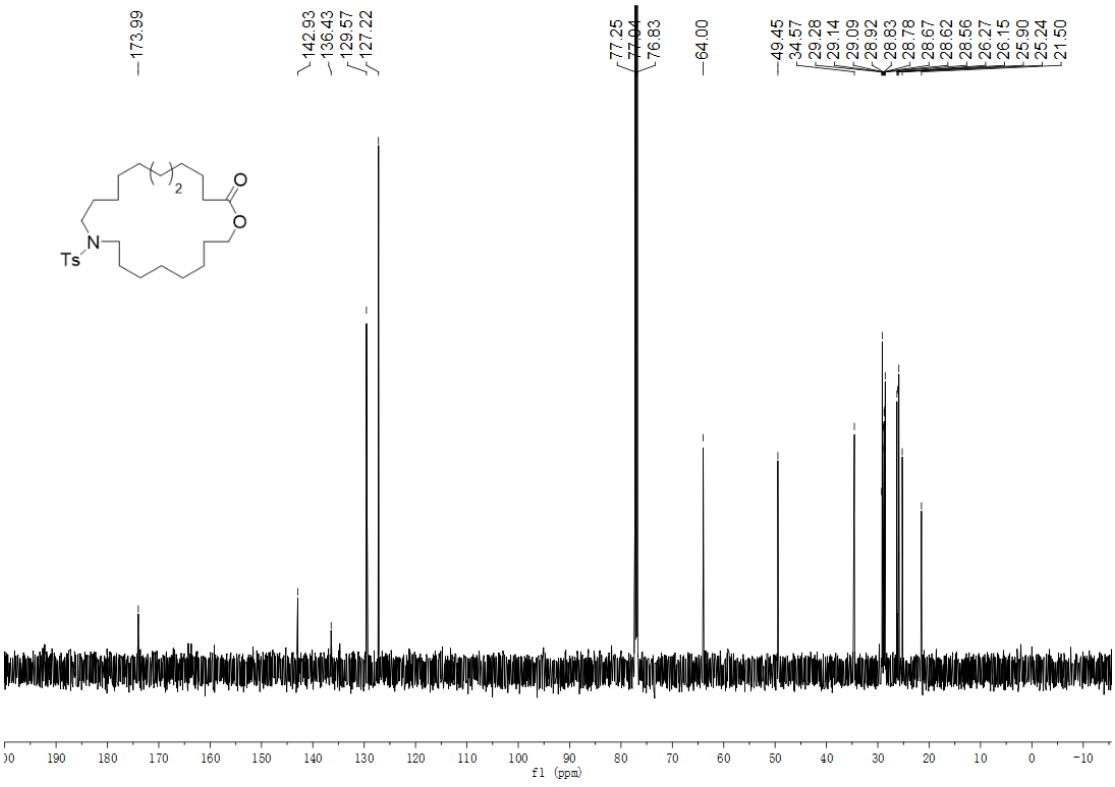
^{1}H NMR of **2v** ($CDCl_3$, 600 MHz)



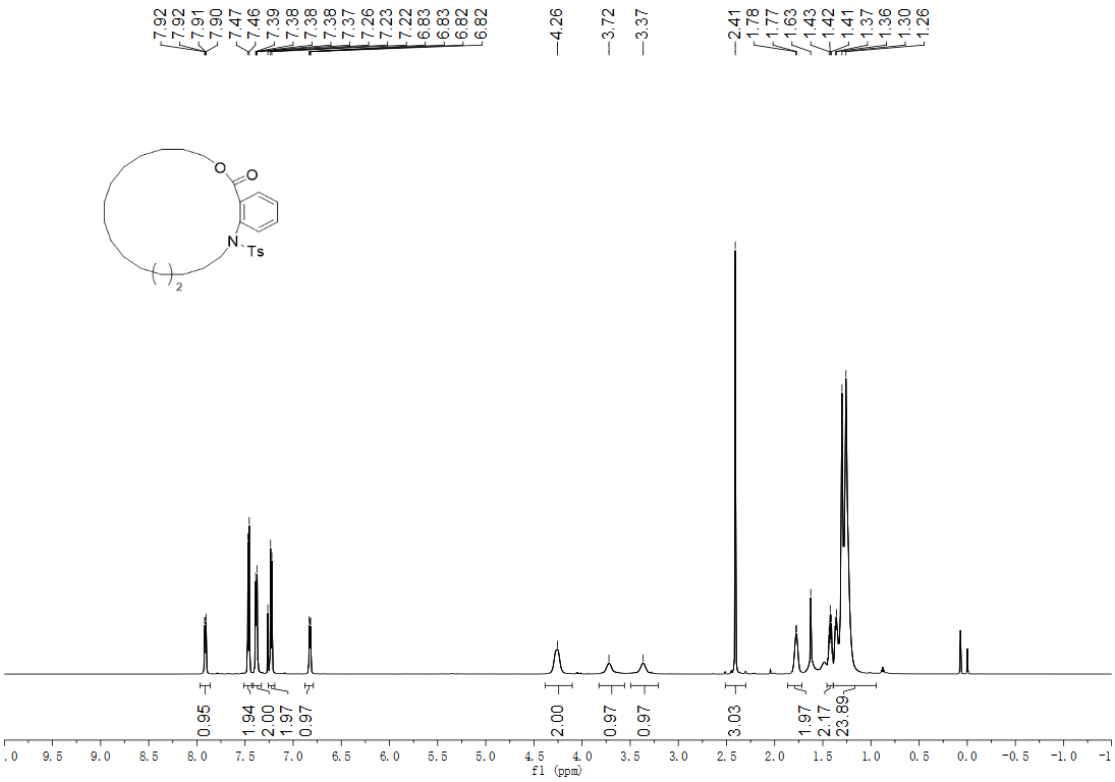
^{13}C NMR of **2v** ($CDCl_3$, 150 MHz)



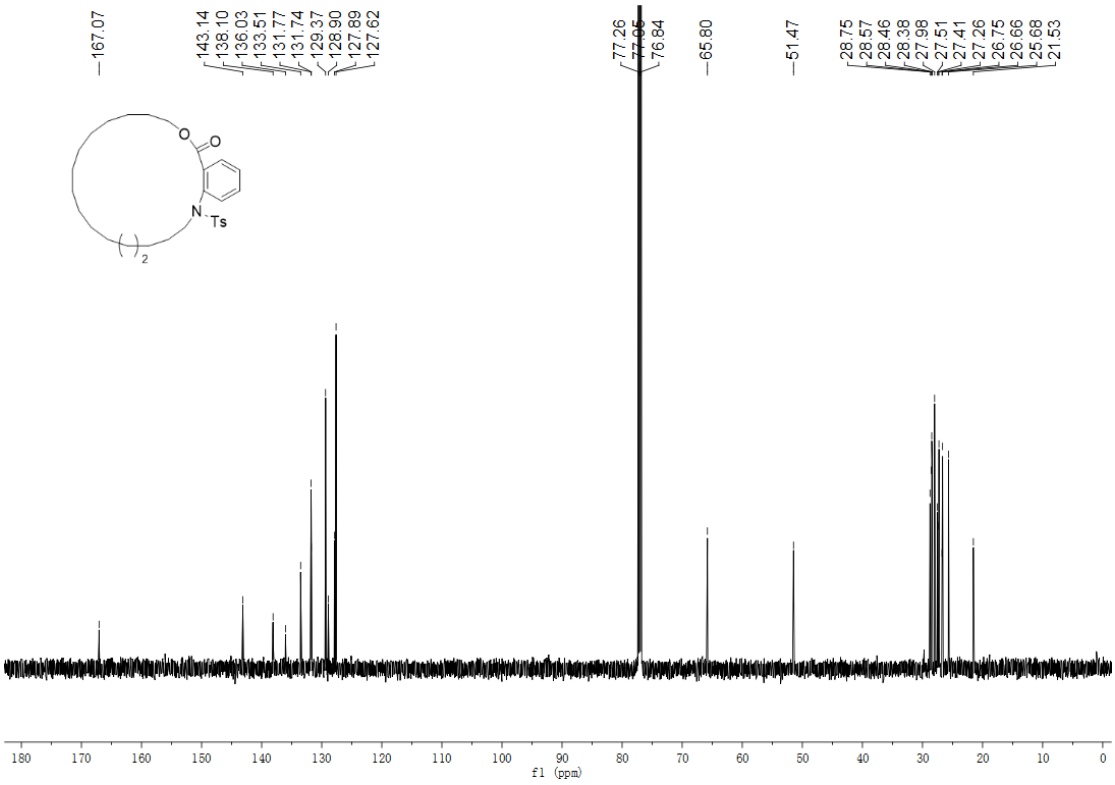
^{1}H NMR of **2w** ($CDCl_3$, 600 MHz)



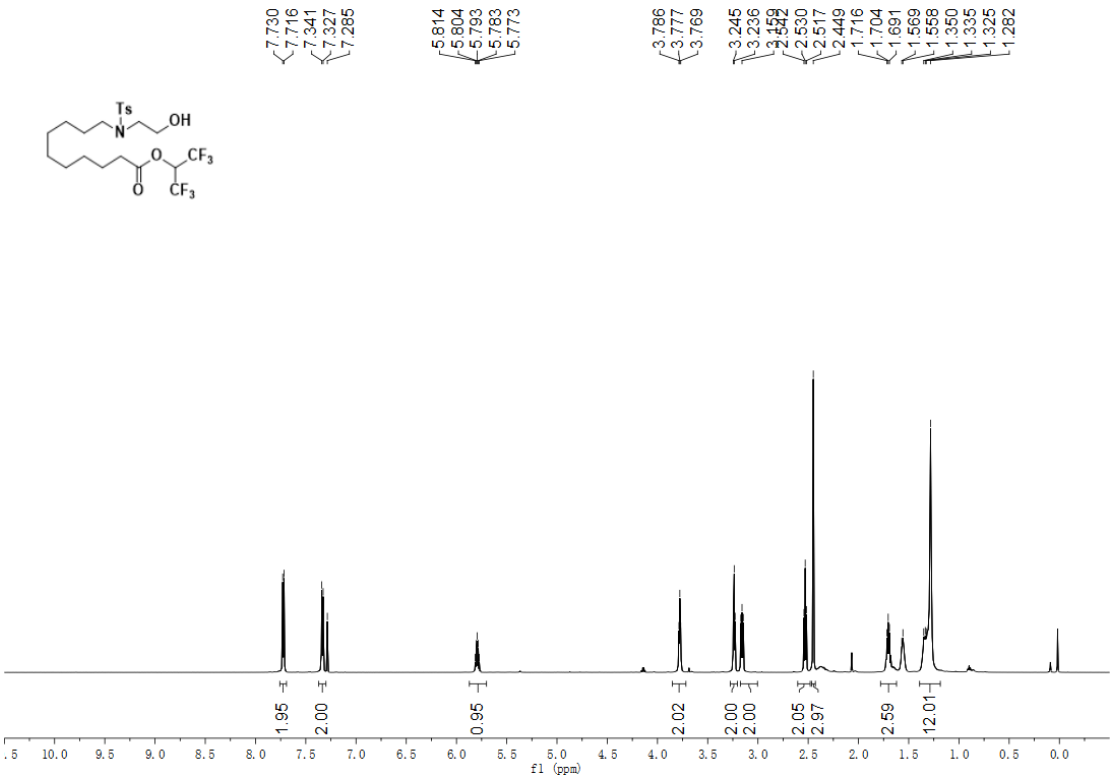
^{13}C NMR of **2w** ($CDCl_3$, 150 MHz)



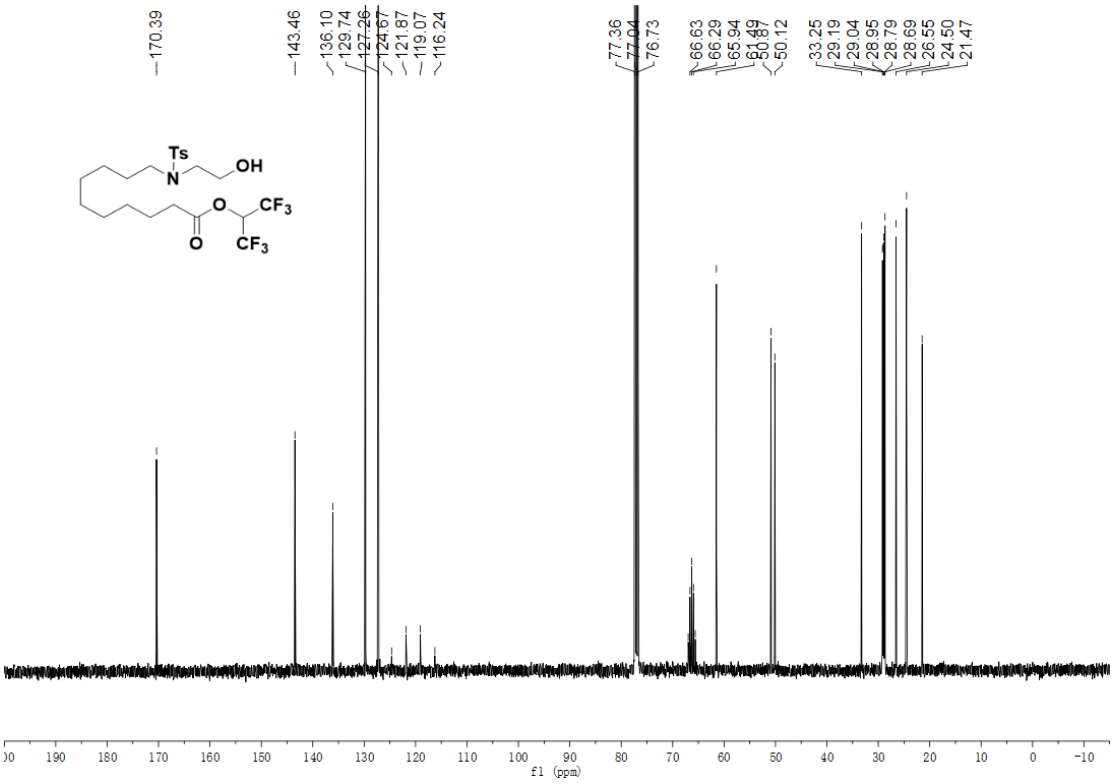
^{1}H NMR of **2x** ($CDCl_3$, 600 MHz)



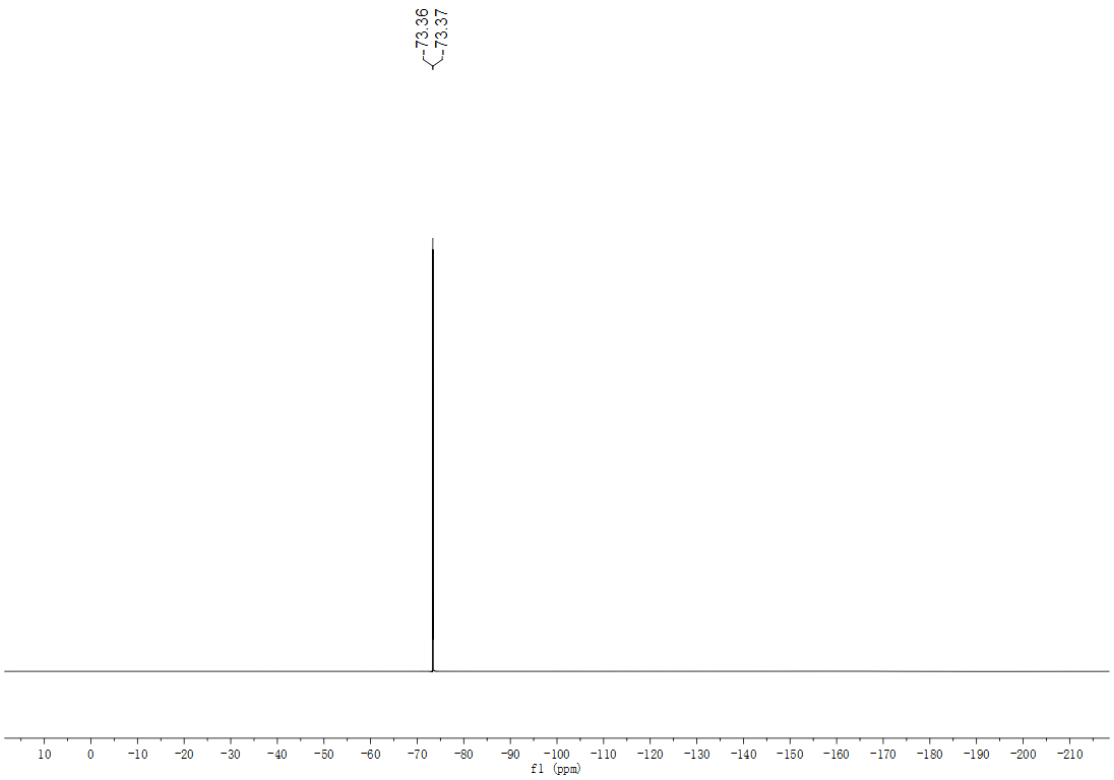
^{13}C NMR of **2x** ($CDCl_3$, 150 MHz)



^{1}H NMR of **3** ($CDCl_3$, 400 MHz)



^{13}C NMR of **3** ($CDCl_3$, 100 MHz)



^{19}F NMR of **3** ($CDCl_3$, 565 MHz)