Supporting Information

Late-stage diversification of pharmaceuticals and natural products *via* a direct electrochemical decarboxylative platform

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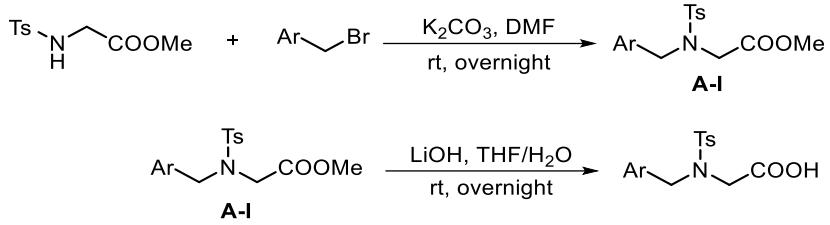
Content

1. General Information

Electrochemical reactions were performed in customized undivided cells. Flash chromatography was performed using silica gel (300-400 mesh) from *Qingdao Ocean Chemical* (China). Commercial reagents were purchased from *Sigma Aldrich*, *J&K Scientific*, *Energy Chemical*, and *Heowns* and used as received. Proton nuclear magnetic resonance (^{1}H-NMR) spectra and carbon nuclear magnetic resonance (^{13}C-NMR) spectra were recorded on a *Bruker-500* (500 MHz) spectrometers. Chemical shifts for protons are reported in parts per million downfield from TMS (tetramethylsilane) and are referenced to residual protium in the NMR solvent ($CDCl_3$ = δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$ = δ 77.2). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz), integration. The mass spectral data were determined with a *Bruker SolariX XR* high-resolution mass spectrometer. Cyclic voltammetry measurements were carried out in a three-electrode cell by using glassy carbon as the working electrode, a Pt wire as auxiliary electrode, and an Ag/AgCl (saturated KCl) as reference electrode on a computer-controlled *CHI600E* instrument at room temperature.

2. General Procedure for Preparation of Substrates

2.1 Preparation of Substrates **1g-1k**

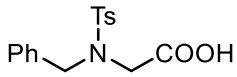


Procedure **A**:

In a 100 mL round bottom flask equipped with a magnetic stirring bar, methyl tosyl-glycinate (15.0 mmol, 1.0 eq.) and anhydrous K_2CO_3 (4.15 g, 30.0 mmol, 2.0 eq.) was added followed by DMF (30 mL, 0.5 M) to form a white suspension. And then corresponding alkyl bromides (18.0 mmol, 1.2 eq.) was added into above system gradually. The mixture would be maintained under room temperature overnight. After that, the mixture could be filtered to acquire yellow solution, which was diluted by H_2O (60 M). The aqueous phase was extracted by EA (30 mL) for three times, the combined organic phase was washed by water, brine, dried over anhydrous Na_2SO_4 and concentrated under vacuum to give a crude product, which was further purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 20:1) to support desired **A-I**.

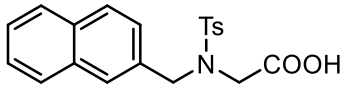
A-I (15 mmol, 1.0 eq.) mentioned above was dissolved with THF (15 mL, 1 M) in a 50 mL round bottom flask, afterwards LiOH aq. (30 mmol, 2.0 eq., 1 M) was added dropwise to obtain white emulsion. The mixture would be maintained under room temperature overnight. Once **A-I** was hydrolyzed completely monitored by TLC, the mixture should be cooled with ice and acidified with HCl (5 M), the precipitated solid could be got by filtration. Final desired acid as substrate was gained by drying under vacuum. And the total yields were given.

Substrates **1g-1k** was prepared directly according to procedure **A**.



***N*-benzyl-*N*-tosylglycine (1g)** [1]

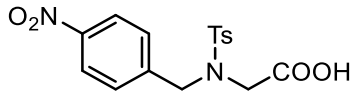
Prepared *via* the general procedure **A**. The product **1g** was furnished as a white solid in 84% yield (2.7 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 2H), 7.34 – 7.29 (m, 5H), 7.24 – 7.19 (m, 2H), 4.47 (s, 2H), 3.93 (s, 2H), 2.44 (s, 3H).



***N*-(naphthalen-2-ylmethyl)-*N*-tosylglycine (1h)**

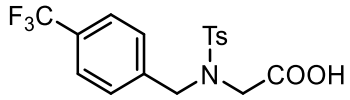
Prepared *via* the general procedure **A**. The product **1h** was furnished as a white solid in 59% yield (2.2 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 4H), 7.76 (dd, J = 6.2, 3.4 Hz, 1H), 7.61 (s, 1H), 7.49 (dt, J = 6.2, 3.4 Hz, 2H), 7.36 (d, J = 8.5 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 4.63 (s, 2H), 3.95 (s, 2H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 143.9, 136.6, 133.12, 133.10, 132.08, 129.7, 128.8, 127.79, 127.76, 127.7,

127.46, 126.44, 126.4, 126.1, 51.6, 46.3, 21.5. Melting point = 164-166 ºC. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{19}NO_4NaS^+$ 392.0932; Found 392.0936.



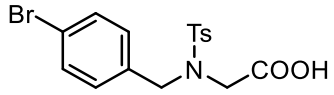
_N_-(4-nitrobenzyl)-_N_-tosylglycine (1i) [2]

Prepared *via* the general procedure **A**. The product **1i** was furnished as a light-yellow solid in 63% yield (2.3 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.7 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 4.56 (s, 2H), 3.96 (s, 2H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 148.0, 144.5 142.7, 136.2, 130.0, 129.3, 127.6, 124.1, 51.3, 47.4, 21.8. Melting point = 138-140 ºC.



_N_-tosyl-_N_-(4-(trifluoromethyl)benzyl)glycine (1j)

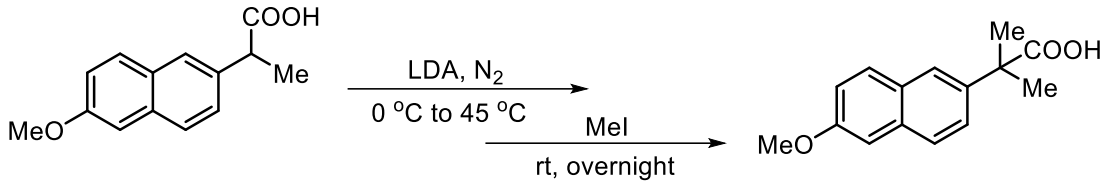
Prepared *via* the general procedure **A**. The product **1j** was furnished as a white solid in 71% yield (2.7 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 2H), 7.52 (d, J = 7.9 Hz, 2H), 7.33 – 7.27 (m, 4H), 4.51 (s, 2H), 3.92 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 144.2, 139.3, 136.4, 130.5 (q, J = 32.4 Hz), 129.9, 128.9, 127.6, 125.8 (q, J = 3.8 Hz), 124.1 (q, J = 272.3 Hz), 51.23, 47.56, 21.68. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.64. Melting point = 143-145 ºC. HRMS (ESI) m/z: $[M - H]^-$ Calcd for $C_{17}H_{15}F_3NO_4S^-$ 386.0679; Found 386.0680.



_N_-(4-bromobenzyl)-_N_-tosylglycine (1k) [3]

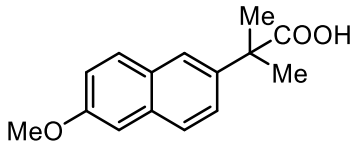
Prepared *via* the general procedure **A**. The product **1k** was furnished as a white solid in 83% yield (3.3 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H), 4.41 (s, 2H), 3.92 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 144.1, 136.5, 134.0, 132.1, 130.4, 130.0, 127.6, 122.5, 51.1, 46.7, 21.7. Melting point = 160-162 ºC.

2.2 Preparation of Methylated Naproxen **1y**



Procedure **B**:

According to Yu's method, a solution of naproxen (10 mmol) in dried THF (10 mL) was added LDA (2.0 M in THF, 20 mL, 40 mmol) under N_2 atmosphere in an ice-bath. The solution was stirred at 45 °C for 1 h. After cooling the reaction mixture again to 0 °C, MeI (3.8 mL, 60 mmol) was added. The reaction was stirred overnight at room temperature, quenched by HCl (2 M) at 0 °C and then diluted with EA. The phases were separated and the aqueous phase was extracted with EA for 3 times. The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4. After filtration and concentration, the crude acid was purified by flash column chromatography to give the desired product **1y** as a white solid.



2-(6-methoxynaphthalen-2-yl)-2-methylpropanoic acid (1y) [4]

Prepared *via* the general procedure **B**. The product **1y** was obtained in 45% yield (0.549 g, 2.3 mmol) as a pale-yellow solid after chromatography on silica gel (petroleum ether : EtOAc = 3 : 1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.72 (m, 3H), 7.55 – 7.51 (m, 1H), 7.19 – 7.12 (m, 2H), 3.93 (s, 3H), 1.72 (s, 6H).

3. Experimental Details for Electrochemical Reactions

3.1 Overview of Materials Involved

As shown in **Figure S1**, our electrochemical reactions were performed using a DC power supply (*MS-305C*, *Mai Sheng* Company) and a magnetic stirrer (*85-2A*, *Heng Yan* Company). The undivided cell (customized from *Rui Jing* Company) was equipped with a magnetic stirring bar (length = 12 mm, Φ = 2 mm). The graphite electrodes of anode and cathode were both consisting of graphite rods (length = 90 mm, Φ = 2 mm) with graphite felts (10 mm x 10 mm x 3 mm). The reaction would be carried out under room temperature in air at a certain voltage for 5 h with the distance of 5 mm between electrodes.

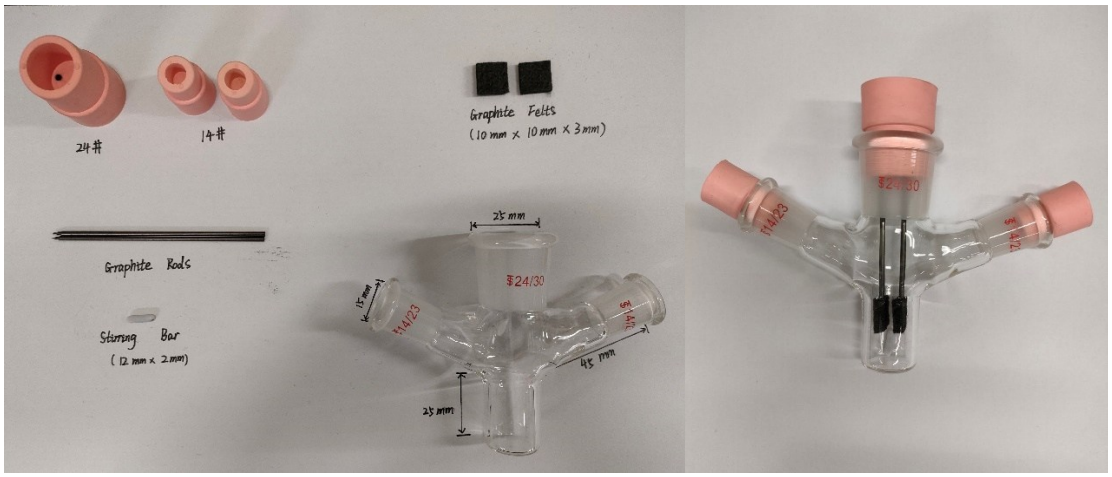
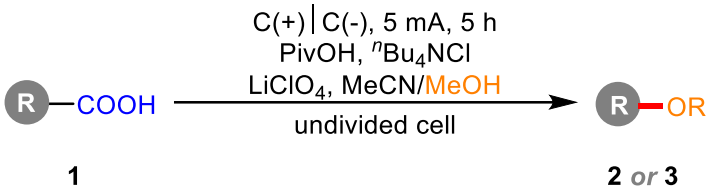


Figure S1. List and Assembly of Electrochemical Experimental Materials

3.2 General Procedure for Electrochemical Reactions



Procedure **C**:

As shown in **Figure S2**, in an undivided cell with graphite electrodes equipped with a magnetic stirring bar, substrate **1** (0.3 mmol, 1.0 eq.), $LiClO_4$ (0.6 mmol, 2.0 eq.), $^{n}Bu_4NCl$ (0.06 mmol, 0.2 eq.), PivOH (0.6 mmol, 2.0 eq.), and acetonitrile/ alcohol (5:1, 6 mL, 0.5 M) were added. After fully stirring for 10 min, electrolysis was initiated under room temperature at a constant current of 5.0 mA for 5 h (unless otherwise noted). Afterward, the solvent was then removed under vacuum, and the residue was purified by flash chromatography on silica gel to afford the desired compound.

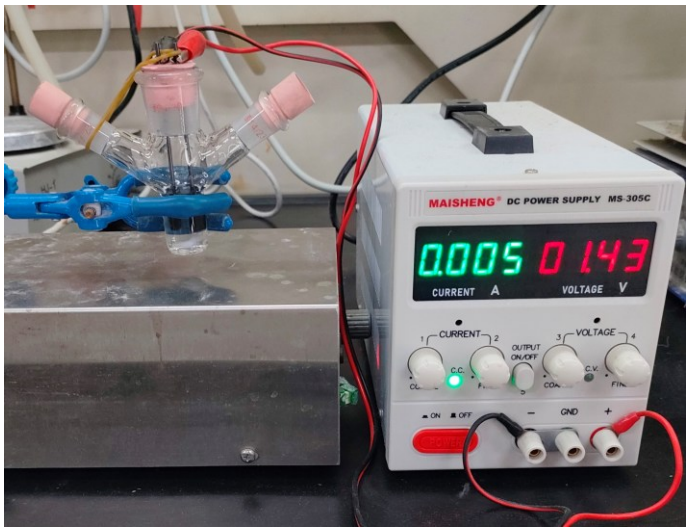
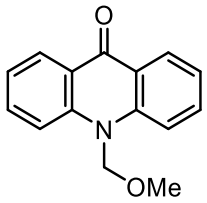
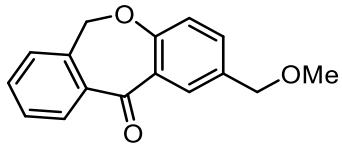


Figure S2. Schematic Diagram of the Experimental Set-up



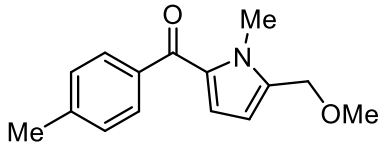
10-(methoxymethyl)acridin-9(10*H*)-one (2a)

Prepared from **1a** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2a** as a yellow oil in 80% yield (57.4 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (dd, *J* = 8.1, 1.7 Hz, 2H), 7.75 – 7.68 (m, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 2H), 5.65 (s, 2H), 3.57 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.4, 142.5, 134.0, 127.6, 122.4, 122.1, 115.1, 77.9, 55.7. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}NO_2^+$ 240.1025; Found 240.1029.



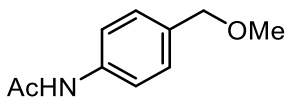
2-(methoxymethyl)dibenzo[*b*,*e*]oxepin-11(6*H*)-one (2b)

Prepared from **1b** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2b** as a yellow oil in 63% yield (48.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, *J* = 2.3 Hz, 1H), 7.90 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.56 (td, *J* = 7.5, 1.4 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 5.20 (s, 2H), 4.46 (s, 2H), 3.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 190.9, 160.9, 140.5, 135.5, 135.0, 132.7, 132.0, 131.3, 129.4, 129.2, 127.8, 124.9, 121.0, 73.8, 73.6, 58.1. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}O_3^+$ 255.1016; Found 255.1017.



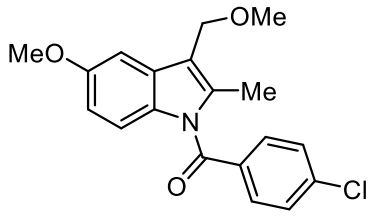
(5-(methoxymethyl)-1-methyl-1H-pyrrol-2-yl)(*p*-tolyl)methanone (2c)

Prepared from **1c** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2c** as a yellow oil in 60% yield (43.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.64 (d, *J* = 4.0 Hz, 1H), 6.17 (d, *J* = 4.0 Hz, 1H), 4.47 (s, 2H), 4.00 (s, 3H), 3.38 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.2, 142.0, 137.4, 137.2, 132.0, 129.5, 128.7, 121.4, 110.1, 65.9, 57.8, 33.2, 21.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}NO_2^+$ 244.1332; Found 244.1342.



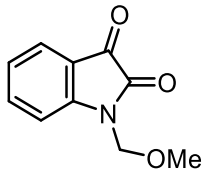
***N*-(4-(methoxymethyl)phenyl)acetamide (2d) [5]**

Prepared from **1d** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 3 : 1) to furnish **2d** as a white solid in 81% yield (43.6 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.1 Hz, 2H), 7.31 – 7.27 (m, 2H), 4.41 (s, 2H), 3.37 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 137.4, 134.1, 128.5, 119.7, 74.2, 58.0, 24.6. Melting point = 164-166 °C



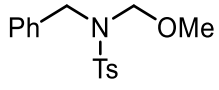
(4-chlorophenyl)(5-methoxy-3-(methoxymethyl)-2-methyl-1H-indol-1-yl)methanone (2e)

Prepared from **1e** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 3 : 1) to furnish **2e** as a yellow oil in 60% yield (61.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 2.6 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 1H), 6.67 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.59 (s, 2H), 3.85 (s, 3H), 3.42 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 156.1, 139.3, 136.9, 133.8, 131.2, 130.9, 130.6, 129.1, 116.0, 114.8, 111.7, 101.6, 64.8, 57.9, 55.7, 13.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{18}ClNNaO_3^+$ 366.0867; Found 366.0877.



1-(methoxymethyl)indoline-2,3-dione (2f) [6]

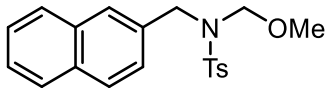
Prepared from **1f** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2f** as a yellow solid in 60% yield (48.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.60 (m, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 5.16 (s, 2H), 3.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.9, 158.4, 150.1, 138.6, 125.5, 124.3, 117.5, 111.6, 71.7, 56.7. Melting point = 74-76 °C.



***N*-benzyl-*N*-(methoxymethyl)-4-methylbenzenesulfonamide (2g)**

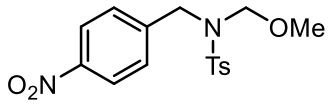
Prepared from **1g** (0.2 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2g** as a yellow oil in 83% yield (50.7 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.32 – 7.20 (m, 7H), 4.59 (s, 2H), 4.33 (s, 2H), 3.19 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.4, 137.3, 135.4, 129.5, 128.6, 128.5, 127.8, 127.4,

78.0, 55.7, 49.1, 21.5. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{19}NO_3SNa^+$ 328.0983; Found 328.0979.



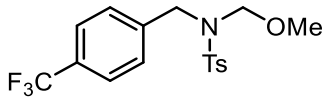
***N*-(methoxymethyl)-4-methyl-*N*-(naphthalen-2-ylmethyl)benzenesulfonamide (2h)**

Prepared from **1h** (0.2 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2h** as a yellow oil in 62% yield (44.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.73 (m, 5H), 7.64 (s, 1H), 7.48 (dd, *J* = 6.3, 3.2 Hz, 2H), 7.37 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 4.63 (s, 2H), 4.51 (s, 2H), 3.22 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 137.4, 133.1, 132.9, 132.8, 129.6, 128.4, 127.74, 127.67, 127.6, 127.5, 126.3, 126.2, 126.1, 78.0, 55.8, 49.3, 21.5. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{21}NO_3NaS^+$ 378.1140; Found 378.1143.



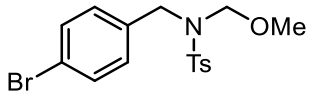
***N*-(methoxymethyl)-4-methyl-*N*-(4-nitrobenzyl)benzenesulfonamide (2i)**

Prepared from **1i** (0.2 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2i** as a yellow oil in 68% yield (47.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.62 (s, 2H), 4.42 (s, 2H), 3.19 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.7, 144.1, 143.6, 137.1, 130.0, 129.3, 127.5, 123.9, 79.3, 56.0, 49.2, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{18}N_2NaO_5S^+$ 373.0829; Found 373.0830.



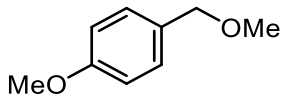
***N*-(methoxymethyl)-4-methyl-*N*-(4-(trifluoromethyl)benzyl)benzenesulfonamide (2j)**

Prepared from **1j** (0.2 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2j** as a yellow oil in 90% yield (67.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 7.9 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.62 (s, 2H), 4.39 (s, 2H), 3.20 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 140.0, 137.3, 130.2 (q, *J* = 32.4 Hz), 129.8, 128.9, 127.6, 125.6 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 272.2 Hz), 78.9, 56.0, 49.1, 21.6. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.57. HRMS (ESI) m/z: $[M + NH_4]^+$ Calcd for $C_{17}H_{22}F_3N_2O_3S^+$ 391.1298; Found 391.1297.



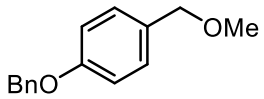
***N*-(4-bromobenzyl)-*N*-(methoxymethyl)-4-methylbenzenesulfonamide (2k)**

Prepared from **1k** (0.2 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2k** as a yellow oil in 99% yield (76.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 4.58 (s, 2H), 4.28 (s, 2H), 3.19 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 137.3, 134.8, 131.8, 130.5, 129.7, 127.6, 122.0, 78.5, 55.9, 48.8, 21.7. HRMS (ESI) m/z: $[M + NH_4]^+$ Calcd for $C_{16}H_{22}BrN_2O_3S^+$ 401.0529; Found 401.0529.



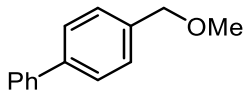
1-methoxy-4-(methoxymethyl)benzene (2l) [7]

Prepared from **1l** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2l** as a yellow oil in 70% yield (32.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 4.39 (s, 2H), 3.81 (s, 3H), 3.36 (s, 3H). ^{13}C NMR (126 MHz, CDCl3) δ 159.2, 131.6, 130.3, 129.3, 113.8, 113.6, 74.3, 57.8, 55.2.



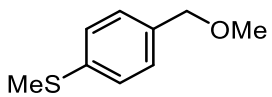
1-(benzyloxy)-4-(methoxymethyl)benzene (2m) [8]

Prepared from **1m** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2m** as a yellow oil in 66% yield (45.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.3 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 5.09 (s, 2H), 4.41 (s, 2H), 3.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.4, 137.0, 130.6, 129.3, 128.5, 127.9, 127.4, 114.7, 74.3, 70.0, 57.8.



4-(methoxymethyl)-1,1'-biphenyl (2n) [9]

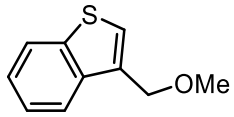
Prepared from **1n** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2n** as a yellow oil in 61% yield (36.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 4H), 7.43 (dd, *J* = 17.2, 7.7 Hz, 4H), 7.35 (t, *J* = 7.4 Hz, 1H), 4.51 (s, 2H), 3.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.9, 140.6, 137.2, 128.7, 128.2, 127.3, 127.2, 127.1, 74.4, 58.2.



(4-(methoxymethyl)phenyl)(methyl)sulfane (2o) [10]

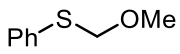
Prepared from **1o** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish

2o as a yellow oil in 46% yield (23.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 4H), 4.42 (s, 2H), 3.37 (s, 3H), 2.48 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 137.7, 135.1, 128.3, 126.7, 74.2, 58.0, 16.0.



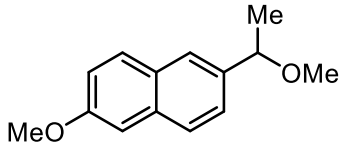
3-(methoxymethyl)benzo[*b*]thiophene (2p) [11]

Prepared from **1p** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2p** as a yellow oil in 68% yield (36.4 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 9.1 Hz, 2H), 7.44 – 7.35 (m, 3H), 4.72 (s, 2H), 3.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.6, 138.1, 133.2, 124.7, 124.5, 124.1, 122.7, 122.1, 68.9, 58.1.



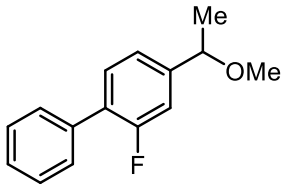
(methoxymethyl)(phenyl)sulfane (2q) [12]

Prepared from **1q** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2q** as a yellow oil in 62% yield (28.7 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 7.0 Hz, 2H), 7.27 (t, J = 7.6 Hz, 2H), 7.20 (t, J = 7.5 Hz, 1H), 4.94 (s, 2H), 3.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0, 130.2, 129.0, 126.8, 77.8, 56.0.



2-methoxy-6-(1-methoxyethyl)naphthalene (2r) [13]

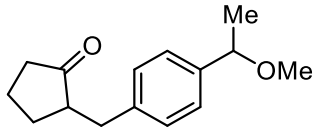
Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2r** as a yellow oil in 86% yield (55.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (t, J = 8.8 Hz, 2H), 7.67 (s, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.16 (d, J = 8.8 Hz, 2H), 4.44 (q, J = 6.5 Hz, 1H), 3.93 (s, 3H), 3.26 (s, 3H), 1.52 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 138.6, 134.1, 129.3, 128.7, 127.2, 125.1, 124.7, 118.8, 105.7, 79.7, 56.4, 55.3, 23.8.



2-fluoro-4-(1-methoxyethyl)-1,1'-biphenyl (2s) [13]

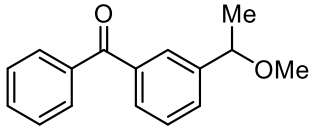
Prepared from **1s** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish **2s** as a yellow oil in 78% yield (53.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 7.9 Hz, 2H), 7.44 (dt, J = 14.8, 7.7 Hz, 3H), 7.37 (t, J = 7.4 Hz, 1H), 7.15 (t, J = 10.6 Hz, 2H), 4.33 (q, J = 6.4 Hz, 1H), 3.29 (s, 3H), 1.47 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126

MHz, $CDCl_3$) δ 159.8 (d, *J* = 248.7 Hz), 145.4, (d, *J* = 6.8 Hz),135.7, 130.7 (d, *J* = 3.8 Hz), 129.0 (d, *J* = 2.9 Hz), 128.4, 128.0 (d, *J* = 13.6 Hz), 127.6, 122.1 (d, *J* = 3.3 Hz), 113.7 (d, *J* = 23.2 Hz), 78.9, 56.6, 23.7. ^{19}F NMR (471 MHz, $CDCl_3$) δ -117.9.



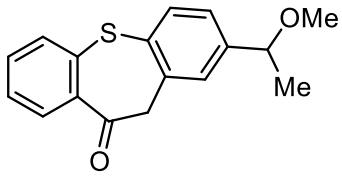
2-(4-(1-methoxyethyl)benzyl)cyclopentan-1-one (2t) [14]

Prepared from **1t** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 10 : 1) to furnish **2t** as a yellow oil in 62% yield (43.3 mg). ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 4.27 (q, *J* = 6.5 Hz, 1H), 3.21 (s, 3H), 3.14 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.52 (dd, *J* = 13.9, 9.5 Hz, 1H), 2.38 – 2.30 (m, 2H), 2.17 – 2.04 (m, 2H), 2.01 – 1.91 (m, 1H), 1.80 – 1.66 (m, 1H), 1.61 – 1.50 (m, 1H), 1.42 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 220.2, 141.3, 139.2, 128.9, 126.3, 79.3, 56.4, 51.0, 38.2, 35.2, 29.2, 23.7, 23.7, 20.5.



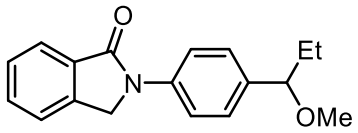
(3-(1-methoxyethyl)phenyl)(phenyl)methanone (2u) [13]

Prepared from **1u** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 10 : 1) to furnish **2u** as a yellow oil in 63% yield (45.5 mg). ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.6 Hz, 2H), 7.76 (s, 1H), 7.70 (d, *J* = 6.9 Hz, 1H), 7.62 – 7.54 (m, 2H), 7.51 – 7.45 (m, 3H), 4.38 (q, *J* = 6.4 Hz, 1H), 3.26 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.7, 144.0, 137.8, 137.6, 132.4, 130.1, 130.0, 129.3, 128.4, 128.3, 127.8, 79.2, 56.6, 23.8.



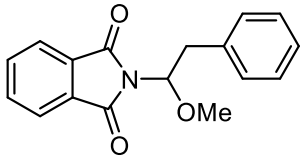
2-(1-methoxyethyl)dibenzo[b,f]thiepin-10(11H)-one (2v)

Prepared from **1v** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 10 : 1) to furnish **2v** as a yellow oil in 55% yield (47.0 mg). ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.39 (s, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 4.38 (s, 2H), 4.29 (q, *J* = 6.4 Hz, 1H), 3.21 (s, 3H), 1.40 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.4, 146.0, 140.3, 137.8, 136.2, 133.3, 132.5, 131.5, 131.4, 130.8, 127.2, 126.8, 124.9, 79.0, 56.6, 51.1, 23.8. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{16}NaO_2S^+$ 307.0763; Found 307.0768.



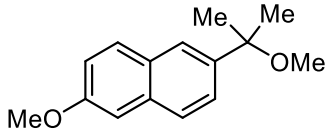
2-(4-(1-methoxypropyl)phenyl)isoindolin-1-one (2w)

Prepared from **1w** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2w** as a white solid in 99% yield (83.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.48 (dd, *J* = 13.9, 7.1 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 2H), 4.83 (s, 2H), 4.02 (t, *J* = 6.6 Hz, 1H), 3.21 (s, 3H), 1.89 – 1.77 (m, 1H), 1.72 – 1.62 (m, 1H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) 167.3, 140.0, 138.6, 138.2, 133.0, 131.9, 128.2, 127.4, 123.9, 122.5, 119.2, 84.9, 56.5, 50.6, 30.7, 10.1. Melting point = 95-98 ºC. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{19}NO_2Na^+$ 304.1313; Found 304.1317.



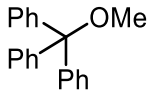
2-(1-methoxy-2-phenylethyl)isoindoline-1,3-dione (2x) [15]

Prepared from **1x** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 5 : 1) to furnish **2x** as a yellow oil in 53% yield (44.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.23 (d, *J* = 4.4 Hz, 4H), 7.17 (h, *J* = 4.2 Hz, 1H), 5.53 (t, *J* = 7.2 Hz, 1H), 3.60 – 3.47 (m, 2H), 3.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 136.3, 134.2, 131.5, 129.2, 128.5, 126.7, 123.5, 84.1, 56.7, 38.6.



2-methoxy-6-(2-methoxypropan-2-yl)naphthalene (2y)

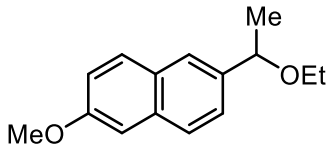
Prepared from **1y** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 10 : 1) to furnish **2y** as a yellow oil in 68% yield (47.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 3H), 7.57 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.15 (d, *J* = 9.0 Hz, 2H), 3.93 (s, 3H), 3.09 (s, 3H), 1.62 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 141.0, 133.6, 129.5, 128.6, 126.8, 125.0, 124.3, 118.7, 105.5, 55.3, 50.7, 27.8. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{18}NaO_2^+$ 253.1199; Found 253.1198.



(methoxymethanetriyl)tribenzene (2z) [16]

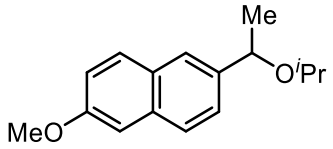
Prepared from **1z** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 15 : 1) to furnish

2z as a yellow oil in 83% yield (68.4 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.6 Hz, 6H), 7.22 (t, *J* = 7.6 Hz, 6H), 7.15 (t, *J* = 7.0 Hz, 3H), 2.98 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 128.7, 127.7, 126.9, 87.0, 52.1.



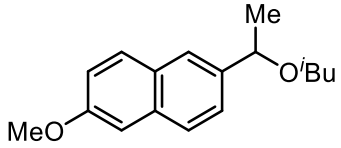
2-(1-ethoxyethyl)-6-methoxynaphthalene (3a) [13]

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3a** as a white solid in 67% yield (46.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (t, 2H), 7.66 (s, 1H), 7.45 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 2H), 4.54 (q, *J* = 6.5 Hz, 1H), 3.92 (s, 3H), 3.38 (q, *J* = 7.0 Hz, 2H), 1.51 (d, *J* = 6.5 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 139.3, 134.1, 129.3, 128.7, 127.1, 124.9, 124.8, 118.8, 105.7, 77.8, 63.9, 55.3, 24.1, 15.4.



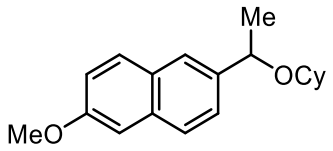
2-(1-isopropoxyethyl)-6-methoxynaphthalene (3b) [13]

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3b** as a white solid in 65% yield (47.7 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.6, 5.1 Hz, 2H), 7.68 (s, 1H), 7.48 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.16 (d, *J* = 8.9 Hz, 2H), 4.68 (q, *J* = 6.5 Hz, 1H), 3.93 (s, 3H), 3.54 (p, *J* = 6.1 Hz, 1H), 1.49 (d, *J* = 6.5 Hz, 3H), 1.20 (d, *J* = 6.1 Hz, 3H), 1.12 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.5, 138.9, 133.0, 128.2, 127.7, 126.0, 123.9, 123.8, 117.8, 104.7, 73.7, 67.4, 54.3, 23.7, 22.3, 20.4.



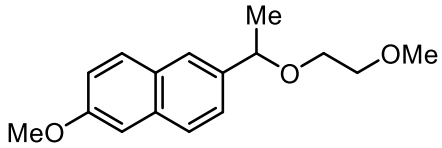
2-(1-isobutoxyethyl)-6-methoxynaphthalene (3c)

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3c** as a white solid in 63% yield (48.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.9, 5.7 Hz, 2H), 7.65 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 2H), 4.50 (q, *J* = 6.5 Hz, 1H), 3.93 (s, 3H), 3.09 (qd, *J* = 9.1, 6.7 Hz, 2H), 1.87 (dp, *J* = 13.3, 6.7 Hz, 1H), 1.51 (d, *J* = 6.5 Hz, 3H), 0.89 (dd, *J* = 6.7, 2.4 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 139.5, 134.0, 129.3, 128.7, 127.0, 124.9, 124.8, 118.8, 105.7, 78.1, 75.6, 55.3, 28.6, 24.1, 19.5, 19.5. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{23}O_2^+$ 259.1693; Found 259.1695.



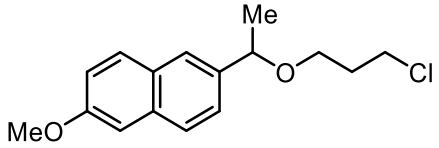
2-(1-(cyclohexyloxy)ethyl)-6-methoxynaphthalene (3d)

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3d** as a white solid in 61% yield (52.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.5 Hz, 2H), 7.67 (s, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 4.73 (q, *J* = 6.5 Hz, 1H), 3.93 (s, 3H), 3.19 (tt, *J* = 9.7, 3.7 Hz, 1H), 2.05 – 1.99 (m, 1H), 1.79 – 1.71 (m, 2H), 1.69 – 1.63 (m, 1H), 1.52 – 1.43 (m, 4H), 1.38 – 1.25 (m, 2H), 1.22 – 1.07 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 140.2, 134.0, 129.3, 128.7, 127.0, 125.0, 124.7, 118.7, 105.7, 74.8, 74.3, 55.3, 33.5, 31.8, 25.8, 24.8, 24.4, 24.2. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{24}NaO_2^+$ 307.1669; Found 307.1674.



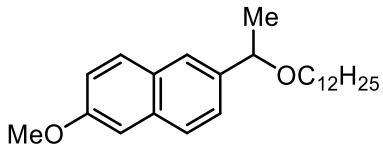
2-methoxy-6-(1-(2-methoxyethoxy)ethyl)naphthalene (3e)

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3e** as a white solid in 75% yield (58.6 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (t, *J* = 8.2 Hz, 2H), 7.67 (s, 1H), 7.46 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.15 (d, *J* = 9.0 Hz, 2H), 4.58 (q, *J* = 6.5 Hz, 1H), 3.92 (s, 3H), 3.55 – 3.45 (m, 4H), 3.38 (s, 3H), 1.54 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 138.8, 134.1, 129.3, 128.7, 127.2, 125.1, 124.8, 118.8, 105.7, 78.5, 72.1, 67.7, 59.0, 55.3, 24.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{20}NaO_3^+$ 283.1305; Found 283.1313.



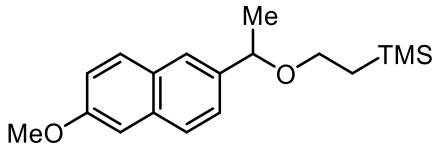
2-(1-(3-chloropropoxy)ethyl)-6-methoxynaphthalene (3f) [13]

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3f** as a white solid in 38% yield (30.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (t, *J* = 8.3 Hz, 2H), 7.65 (s, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.15 (d, *J* = 9.1 Hz, 2H), 4.53 (q, *J* = 6.5 Hz, 1H), 3.93 (s, 3H), 3.74 – 3.60 (m, 2H), 3.52 – 3.40 (m, 2H), 2.08 – 1.95 (m, 2H), 1.51 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 138.8, 134.1, 129.3, 128.7, 127.2, 124.9, 124.6, 118.9, 105.7, 78.3, 65.0, 55.3, 42.1, 33.0, 23.9.



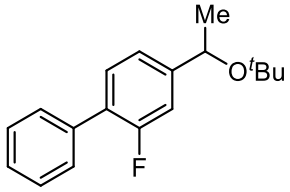
2-(1-(dodecyloxy)ethyl)-6-methoxynaphthalene (3g)

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3g** as a white solid in 41% yield (45.6 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (t, 2H), 7.66 (s, 1H), 7.45 (d, *J* = 9.1 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 4.52 (q, *J* = 6.4 Hz, 1H), 3.93 (s, 3H), 3.32 (t, *J* = 6.6 Hz, 2H), 1.63 – 1.55 (m, 2H), 1.51 (d, *J* = 6.5 Hz, 3H), 1.37 – 1.20 (m, 18H), 0.89 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 139.4, 134.0, 129.3, 128.7, 127.1, 124.9, 124.8, 118.8, 105.7, 77.9, 68.7, 55.3, 31.9, 30.0, 29.7, 29.6, 29.6, 29.6, 29.5, 29.3, 26.2, 24.1, 22.7, 14.1. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{25}H_{38}NaO_2^+$ 393.2764; Found 393.2761.



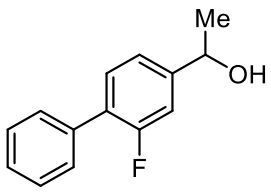
(2-(1-(6-methoxynaphthalen-2-yl)ethoxy)ethyl)trimethylsilane (3h)

Prepared from **1r** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3h** as a white solid in 71% yield (64.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.5, 5.3 Hz, 2H), 7.67 (s, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.16 (d, *J* = 9.0 Hz, 2H), 4.54 (q, *J* = 6.5 Hz, 1H), 3.93 (s, 3H), 3.43 (dtd, *J* = 15.8, 9.4, 6.3 Hz, 2H), 1.51 (d, *J* = 6.5 Hz, 3H), 1.05 – 0.90 (m, 2H), -0.01 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 139.5, 134.0, 129.3, 128.7, 127.0, 124.8, 124.8, 118.7, 105.7, 77.5, 65.6, 55.3, 24.2, 18.4, -1.4. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{26}NaO_2Si^+$ 325.1594; Found 325.1600.



2-fluoro-4-(1-isobutoxyethyl)-1,1'-biphenyl (3i)

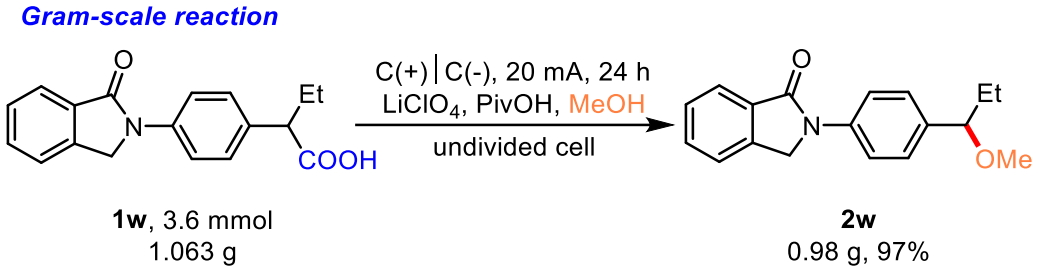
Prepared from **1s** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3i** as a white solid in 51% yield (41.7 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.37 (q, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 8.6 Hz, 2H), 4.70 (q, *J* = 6.6 Hz, 1H), 1.41 (d, *J* = 6.6 Hz, 3H), 1.22 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7 (d, *J* = 248.1 Hz), 149.4 (d, *J* = 6.8 Hz), 135.9, 130.4 (d, *J* = 3.9 Hz), 129.0 (d, *J* = 3.0 Hz), 128.4, 127.4, 127.0 (d, *J* = 13.6 Hz), 121.3 (d, *J* = 3.3 Hz), 113.2 (d, *J* = 23.4 Hz), 74.3, 69.1, 28.5, 26.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ -118.4. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{21}FNaO^+$ 295.1469; Found 295.1471.



1-(2-fluoro-[1,1'-biphenyl]-4-yl)ethan-1-ol (3j) [17]

Prepared from **1s** (0.3 mmol) *via* the general procedure **C**. The crude material was purified by column chromatography (petroleum ether: ethyl acetate = 2 : 1) to furnish **3j** as a white solid in 74% yield (48.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 7.5 Hz, 2H), 7.48 – 7.40 (m, 3H), 7.37 (t, J = 7.4 Hz, 1H), 7.24 – 7.17 (m, 2H), 4.95 (q, J = 6.5 Hz, 1H), 1.89 (s, 1H), 1.54 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8 (d, J = 249.1 Hz), 147.4 (d, J = 6.9 Hz), 135.6, 130.8 (d, J = 3.8 Hz), 129.0 (d, J = 2.9 Hz), 128.4, 128.0 (d, J = 13.6 Hz), 127.6, 121.2 (d, J = 3.2 Hz), 113.1 (d, J = 23.7 Hz), 69.6, 25.2. ^{19}F NMR (471 MHz, $CDCl_3$) δ -117.7.

3.3 Gram Scale-up Reaction



As shown in **Figure S3**, in a 100 mL beaker with graphite electrodes (graphite felts: 50 mm x 25 mm x 3 mm) equipped with a magnetic stirring bar (length = 30 mm, Φ = 10 mm), substrate **1w** (3.6 mmol, 1.063 g, 1.0 eq.), $LiClO_4$ (7.2 mmol, 2.0 eq.), PivOH (7.2 mmol, 2.0 eq.) and MeOH (72 mL, 0.5 M) were added. After fully stirring for 10 min, electrolysis was initiated using a DC power supply (***HSPY-120-01***, *HanSheng PuYuan* Company) under room temperature at a constant current of 20 mA for 24 h. Afterward, the solvent was then removed under vacuum, and the residue was purified by flash chromatography on silica gel to afford the desired compound **2w** (0.98 g, 97%).

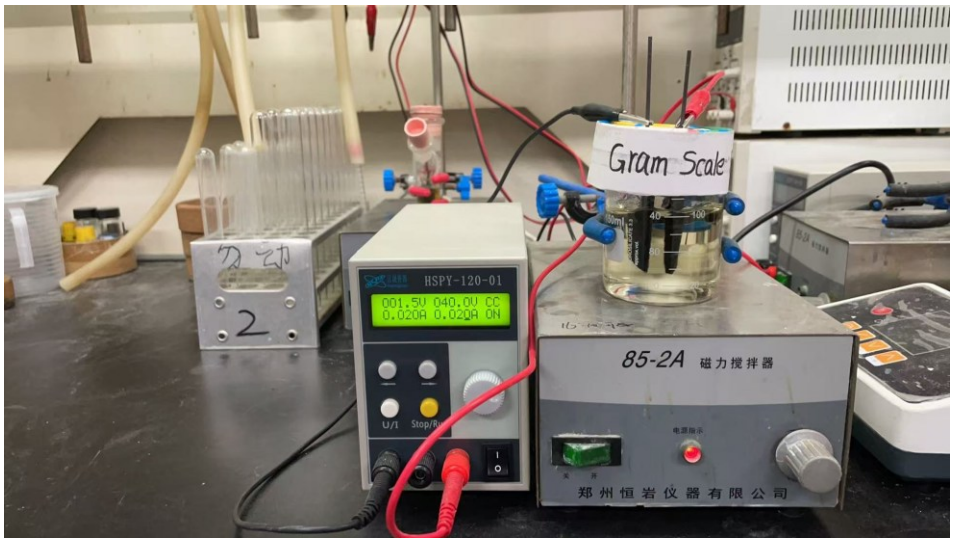
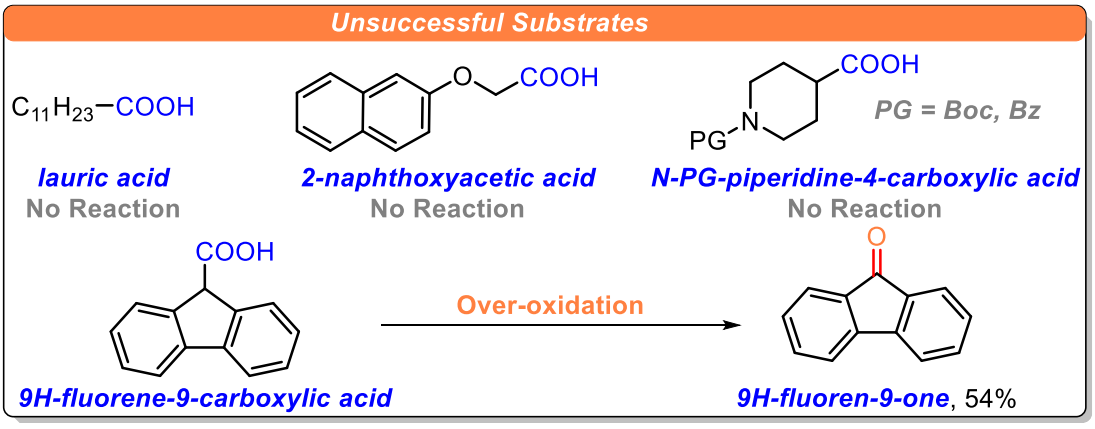


Figure S3. Gram Scaling-up Reaction

3.4 Unsuccessful Substrates



4. Primary Mechanism Explorations

4.1 Chronopotentiometry Experiment

As shown in **Figure S4**, the chronopotentiometry experiment was carried out according to procedure **C**. After fully stirring for 10 min, electrolysis was initiated using Naproxen **1r** under room temperature at a constant current of 5 mA for 5 h. A saturated calomel electrode (SCE: 0.2412 V) was used as a reference electrode to determine the actual potential during the reaction. Measurements were taken every half hour using a multimeter and potential-time curves were plotted as **Figure S5**.

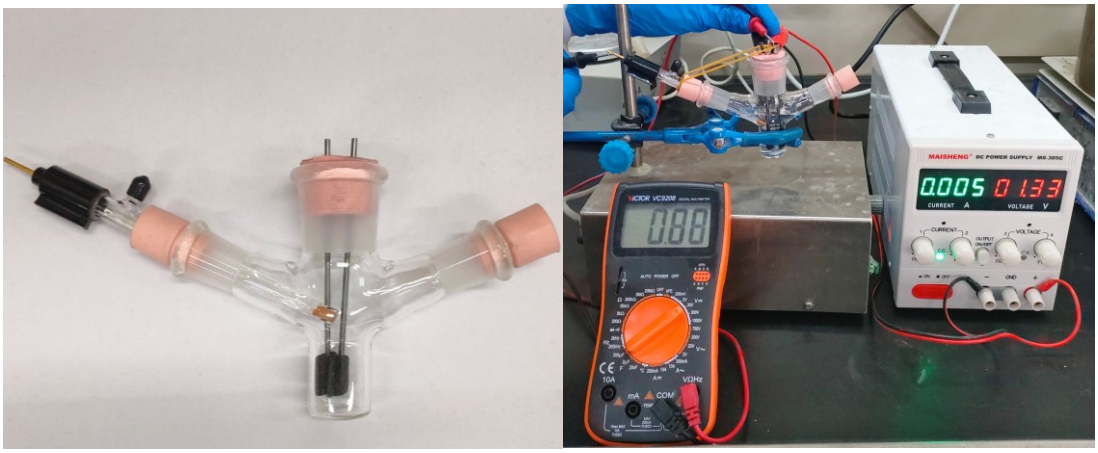


Figure S4. Schematic Diagram of Chronopotentiometry Experiment

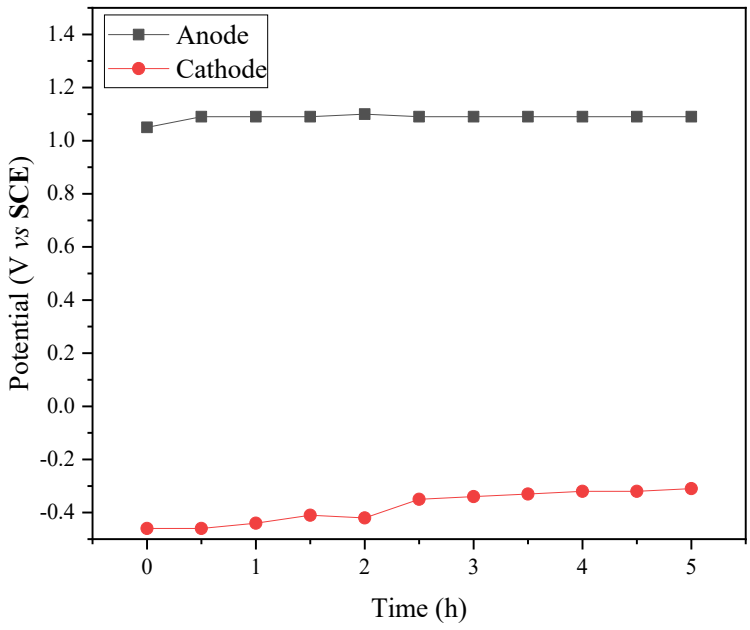
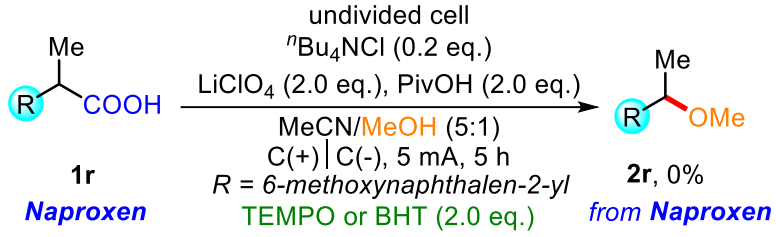


Figure S5. Potential-Time Curves

4.2 Control Experiments



Control experiments were proceeded *via* the procedure **C.** In an undivided cell with graphite electrodes equipped with a magnetic stirring bar, substrate **1r** (0.3 mmol, 1.0 eq.), $LiClO_4$ (0.6 mmol, 2.0 eq.), $^nBu_4NCl$ (0.06 mmol, 0.2 eq.), PivOH (0.6 mmol, 2.0 eq.), radical scavengers (TEMPO or BHT, 0.6 mmol, 2.0 eq.) and acetonitrile/ alcohol (5:1, 6 mL, 0.5 M) were added. After fully stirring for 10 min, electrolysis was initiated under room temperature at a constant current of 5.0 mA for 5 h. No desired products could be obtained.

4.3 CV Experiments

As shown in **Figure S6**, for the cyclic voltametric measurement, IUPAC convention was followed. The CV curves were recorded on a computer-controlled *CHI600E* instrument in an electrolyte of $LiClO_4$ in acetonitrile/MeOH in a three-electrode cell (beaker-type cell) at room temperature (25 ± 2 ºC). For the CV experiments, the initial potential was 0.0 V, switching potential was + 3.0 V and the scan rate was 100 mV/s in the positive direction. All solutions used for the voltametric experiments were deoxygenated by purging with high-purity argon gas up to 5 mins, the measured current had been normalized to mA/ cm^2. All of cyclic voltammograms were obtained using glass carbon as the working electrode, Pt wire and an Ag/AgCl (saturated KCl solution) electrode as the counter and reference electrode, respectively. All the instruments and materials were purchased from *Chen Hua Company* (Shanghai, China).

Working electrode: The working electrode is a glassy carbon electrode (length 60 mm, Φ 3 mm, 0.07 cm^2). Polished with 0.05 μm aluminum oxide and then sonicated in distilled water before drying.

Reference electrode: An Ag/AgCl (saturated KCl solution) electrode (length = 70 mm, Φ = 4 mm) as the reference electrode.

Counter electrode: The counter electrode is a platinum wire (length = 30 mm, Φ = 0.5 mm).

Electrochemical Cell: A beaker-type cell (length = 40 mm, Φ = 25 mm) with a teflon cap was used.

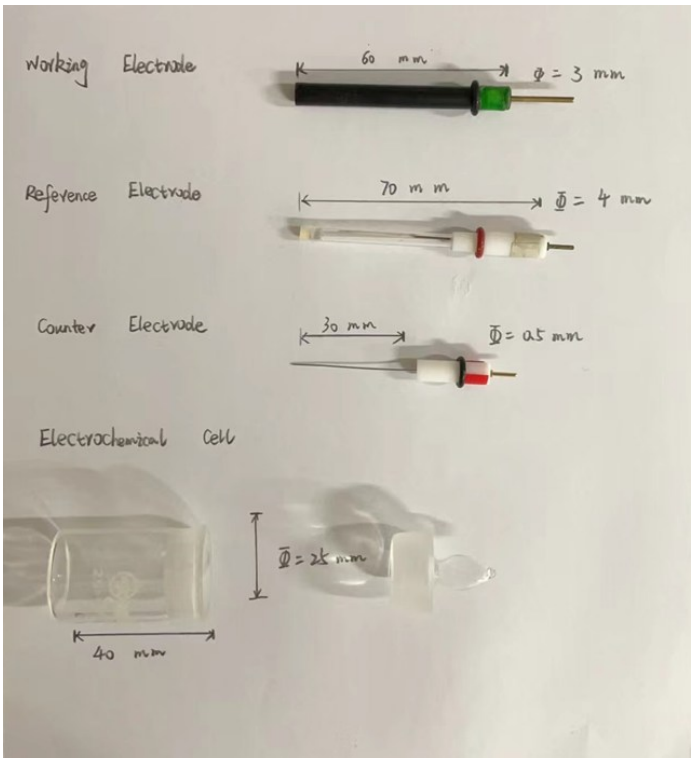


Figure S6. List of Materials for CV Experiments

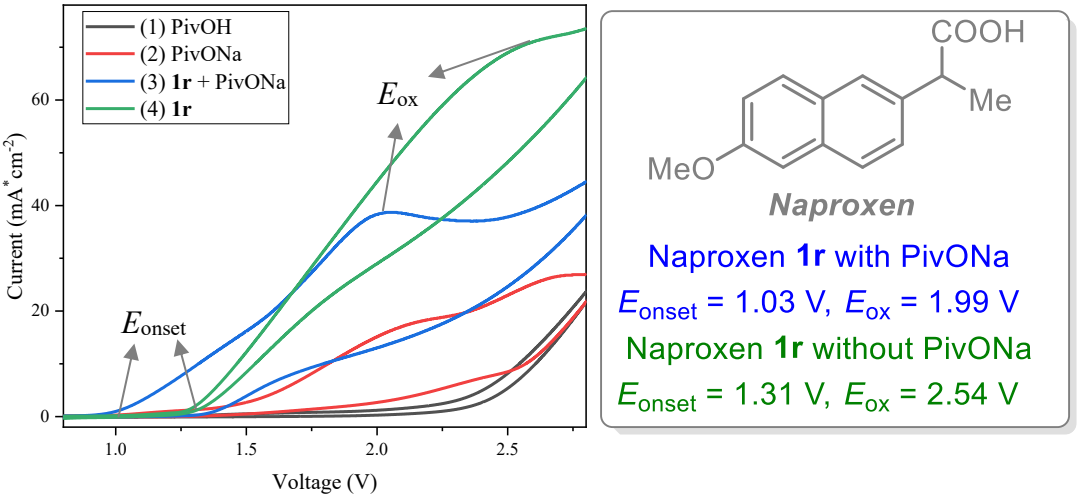
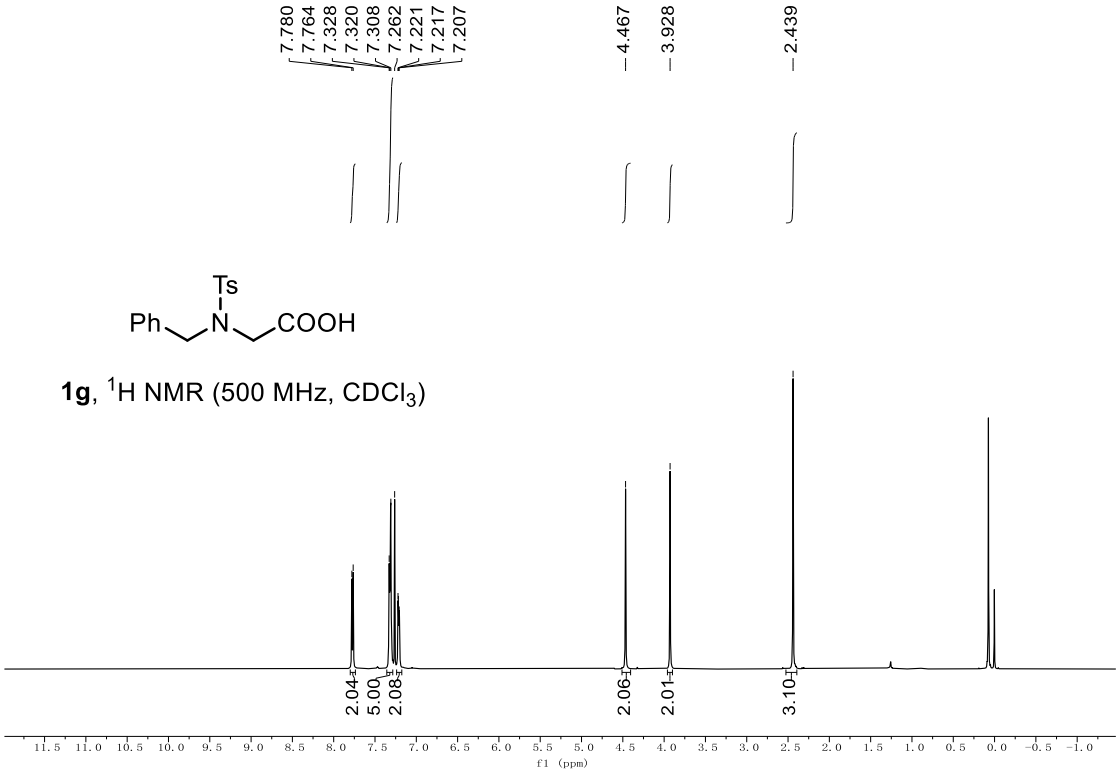


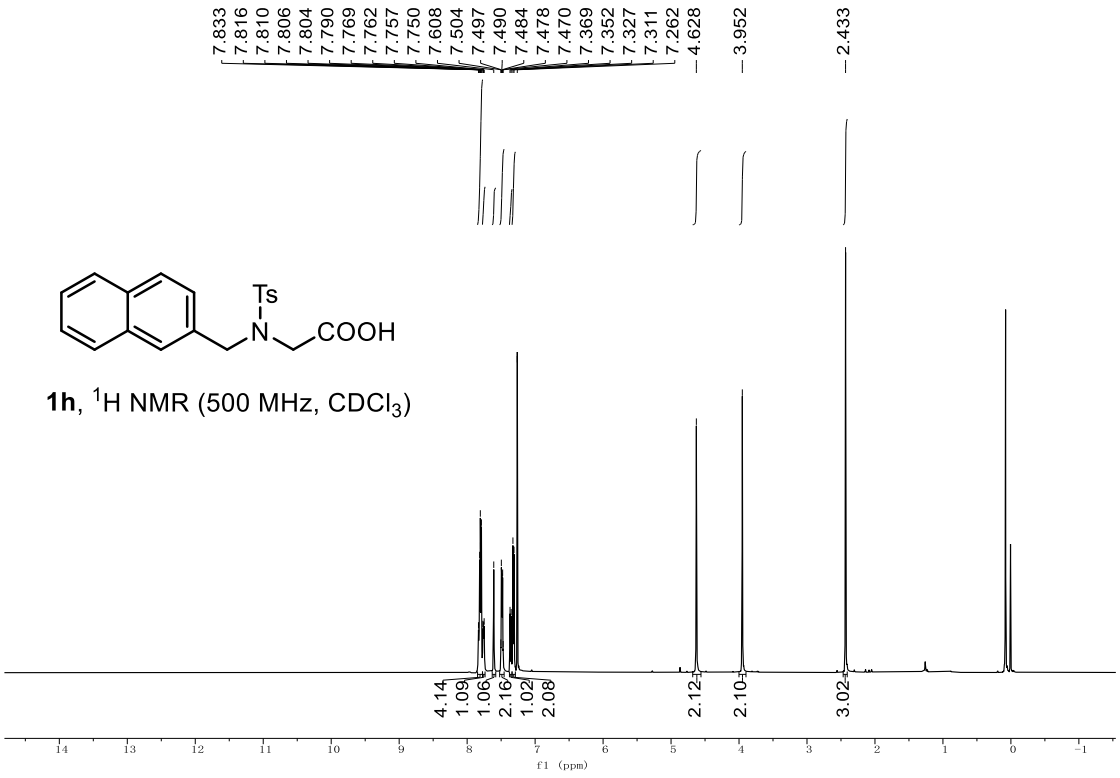
Figure S7. CV Curves of Naproxen **1r**

From top to bottom: (1) MeCN/ MeOH (5:1, 3 mL), $LiClO_4$ (0.3 mmol), PivOH (0.3 mmol); (2) MeCN/ MeOH (5:1, 3 mL), $LiClO_4$ (0.3 mmol), PivONa (0.3 mmol); (3) MeCN/ MeOH (5:1, 3 mL), **1r** (0.15 mmol), $LiClO_4$ (0.3 mmol), PivONa (0.3 mmol); (4) MeCN/ MeOH (5:1, 3 mL), **1r** (0.15 mmol), $LiClO_4$ (0.3 mmol).

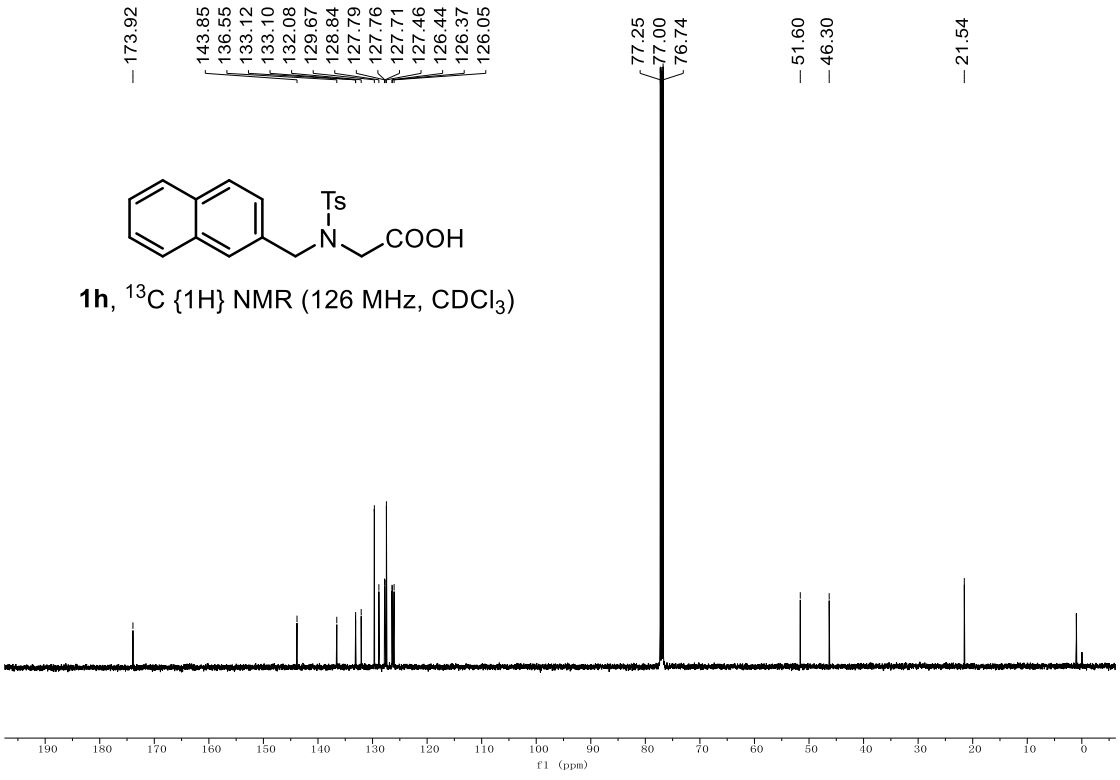
5. NMR Spectra

5.1 NMR Spectra of Substrates

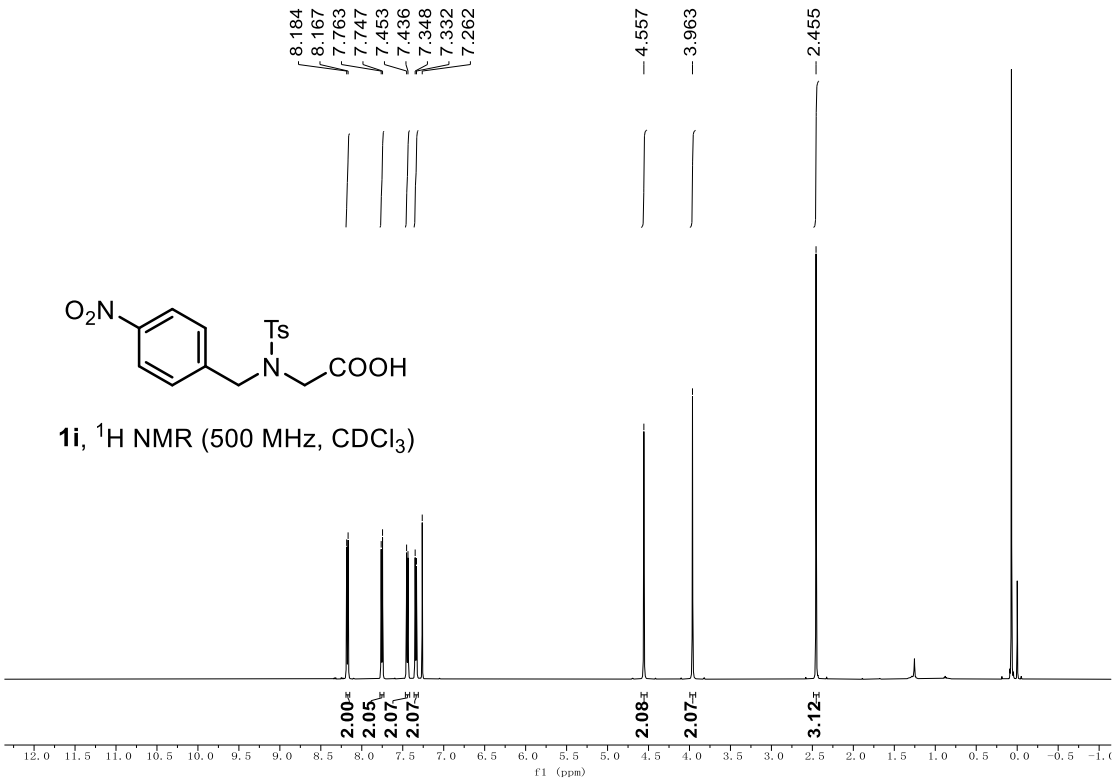




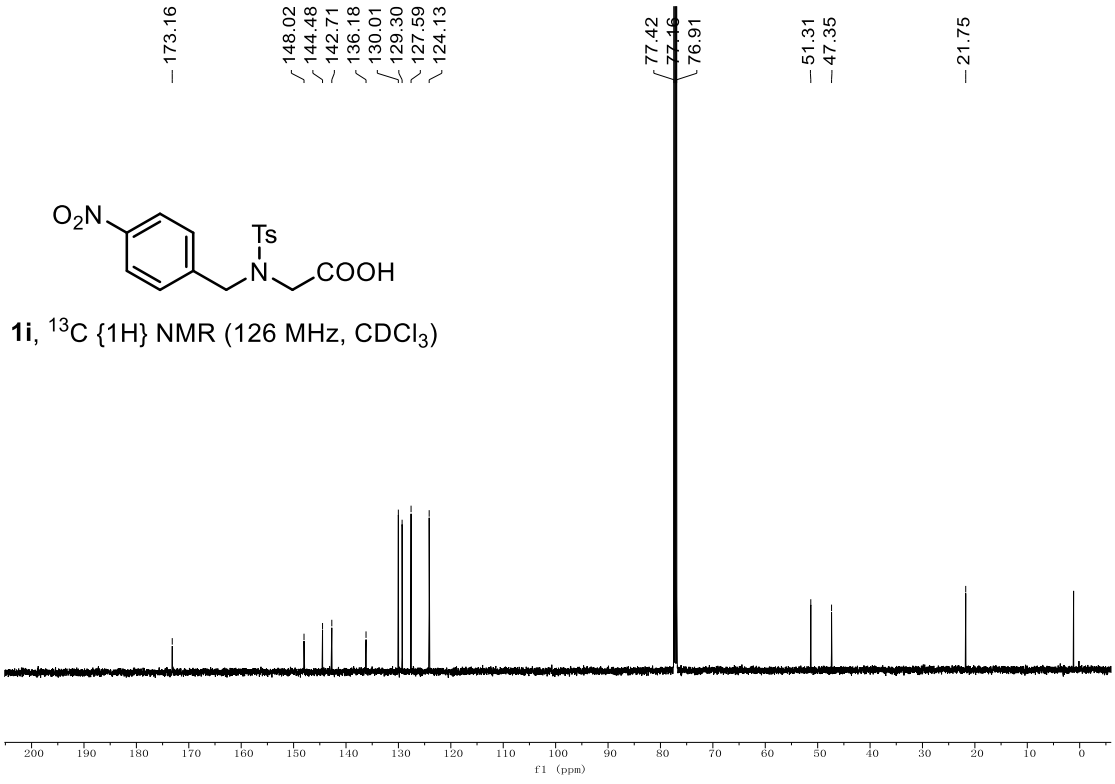
1h, ^{1}H NMR (500 MHz, $CDCl_3$)



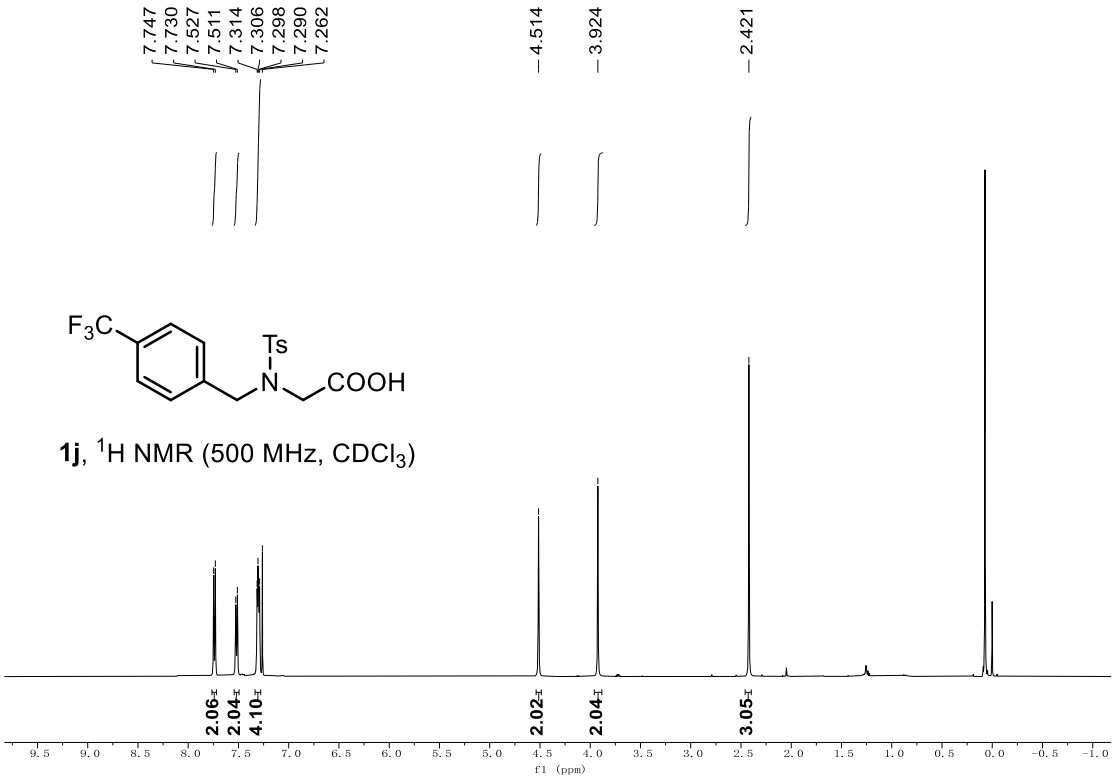
1h, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)

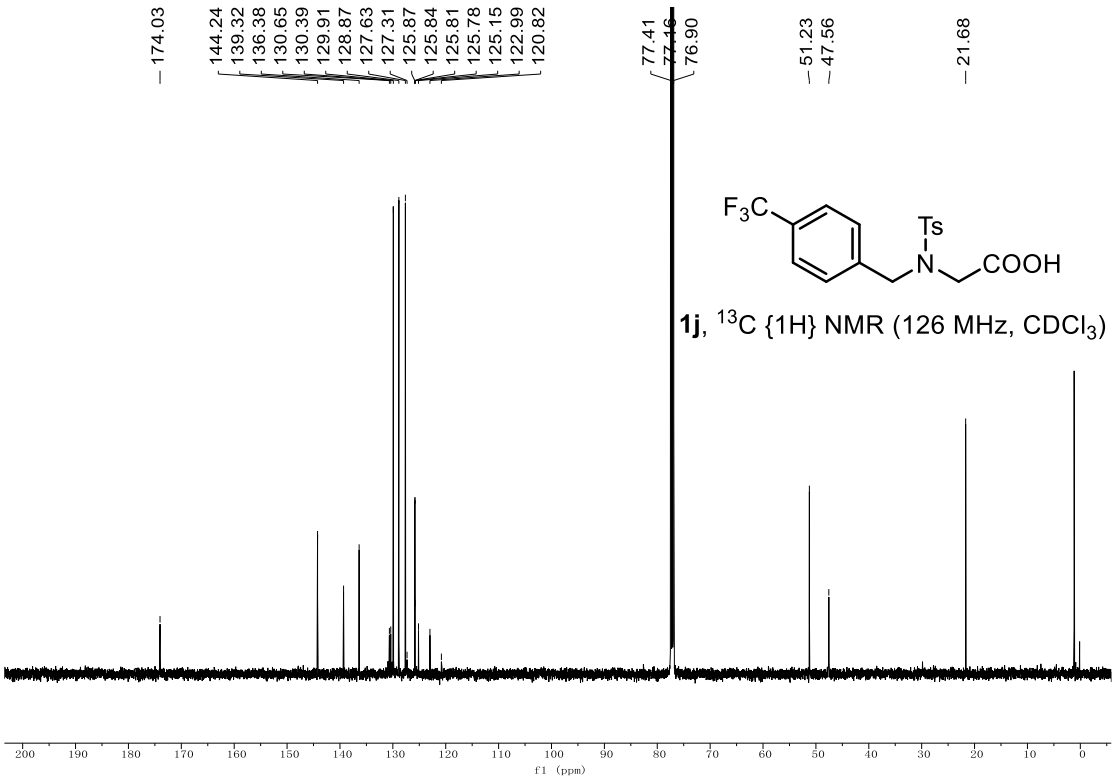


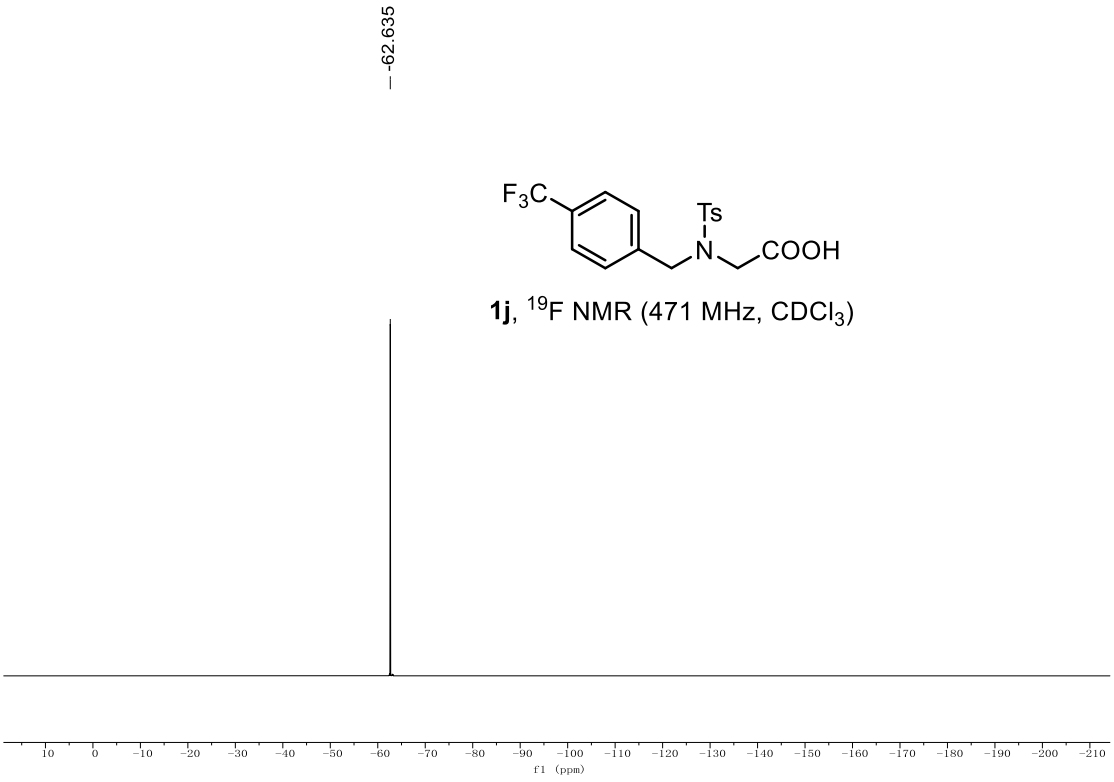
1i, ^{1}H NMR (500 MHz, $CDCl_3$)

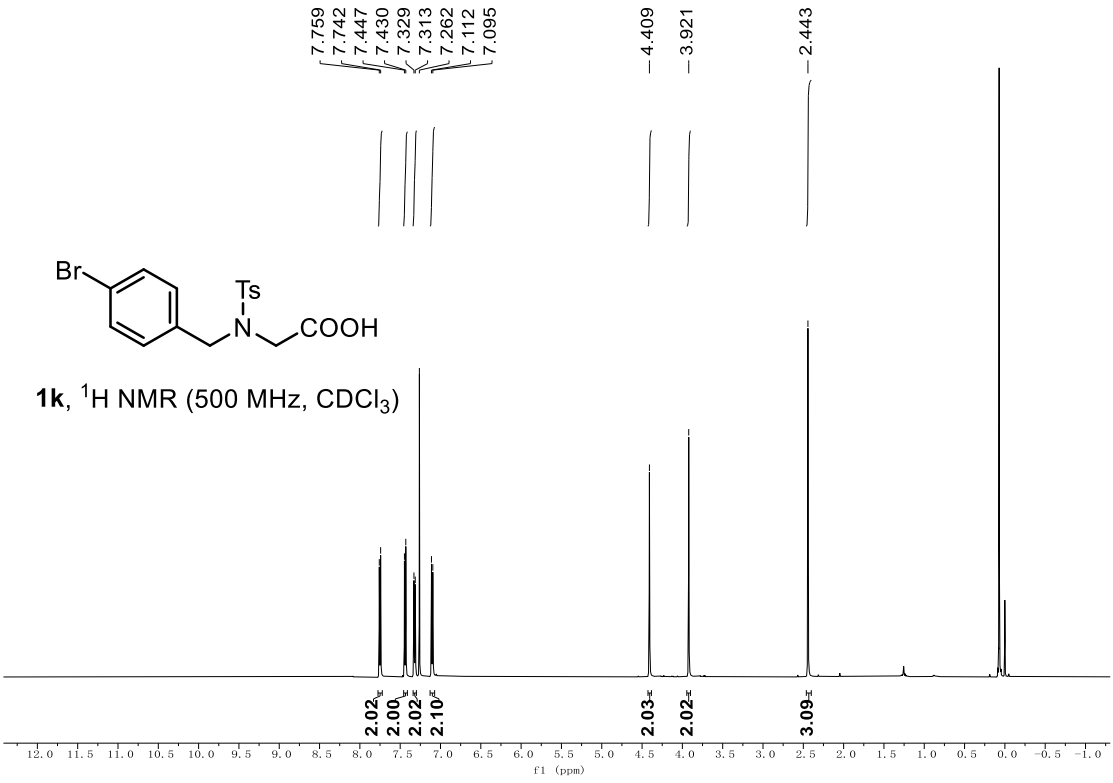


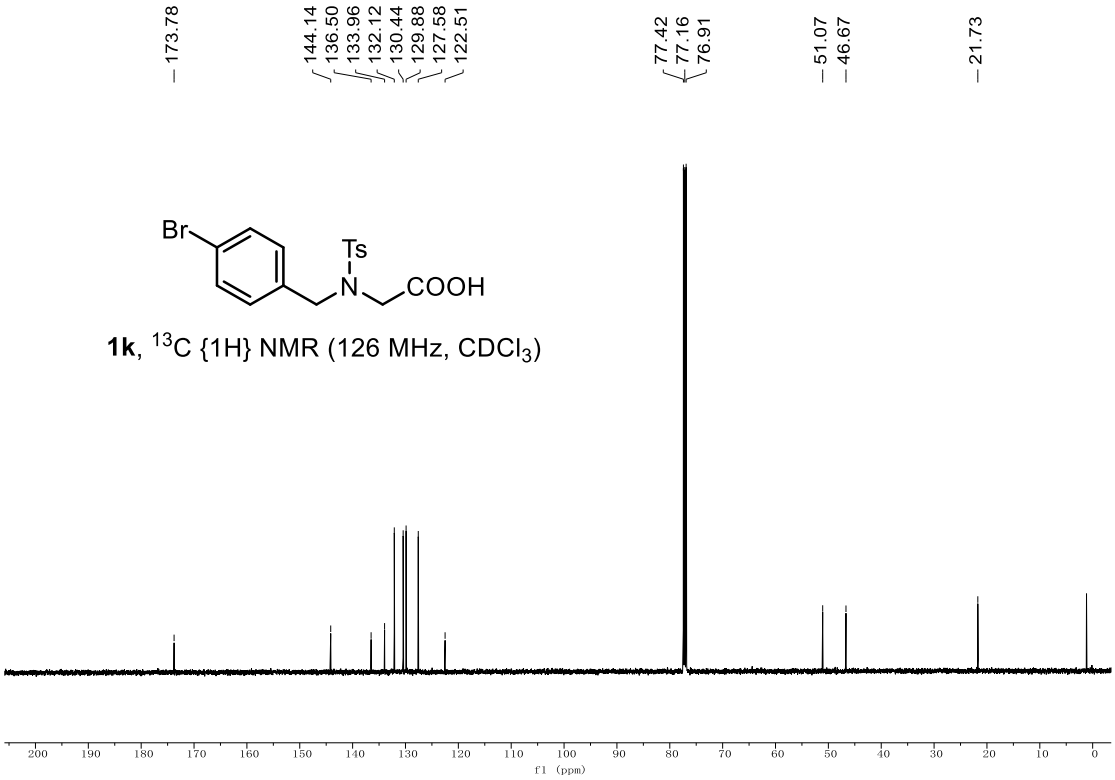
1i, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)


7.747
7.730
7.527
7.511
7.314
7.306
7.298
7.290
7.262
4.514
3.924
2.421
F3C
Ts
N
COOH
1j, 1H NMR (500 MHz, CDCl3)
2.06
2.04
4.10
2.02
2.04
3.05
f1 (ppm)

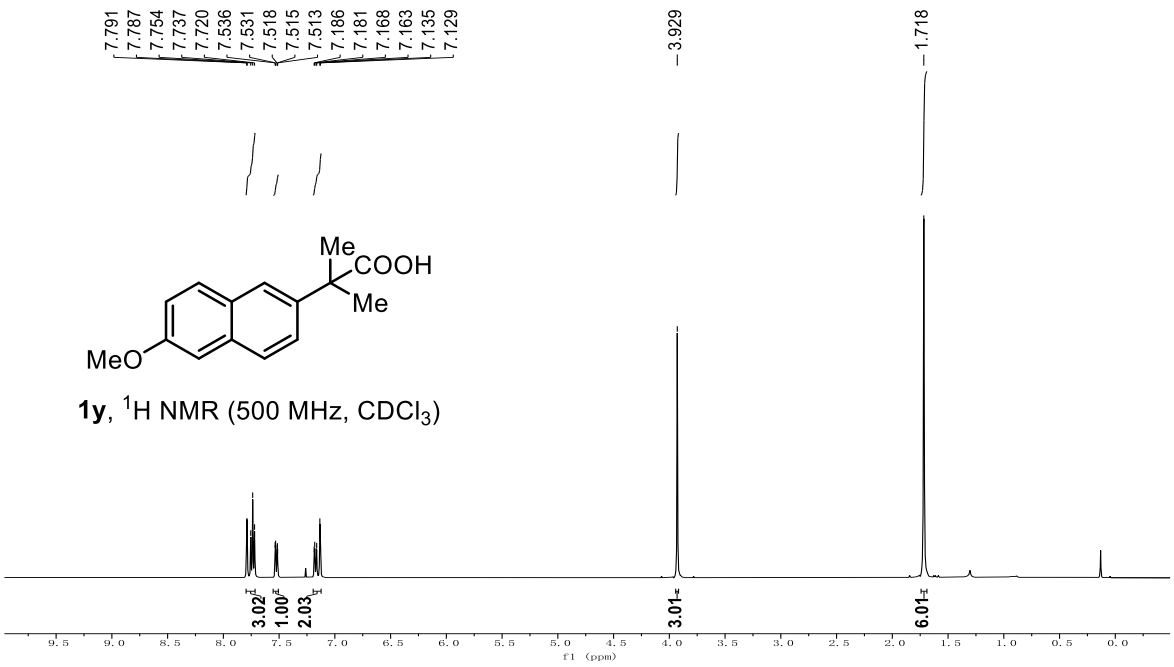

174.03
144.24
139.32
136.38
130.65
130.39
129.91
128.87
127.63
127.31
125.87
125.84
125.81
125.78
125.15
122.99
120.82
77.41
77.16
76.90
51.23
47.56
21.68
F3C
Ts
N
COOH
1j, 13C {1H} NMR (126 MHz, CDCl3)
f1 (ppm)


-62.635
F3C
Ts
N
COOH
1j, 19F NMR (471 MHz, CDCl3)
f1 (ppm)


7.759
7.742
7.447
7.430
7.329
7.313
7.262
7.112
7.095
4.409
3.921
2.443
Br
Ts
N
COOH
1k, 1H NMR (500 MHz, CDCl3)
2.02
2.00
2.02
2.10
2.03
2.02
3.09
f1 (ppm)

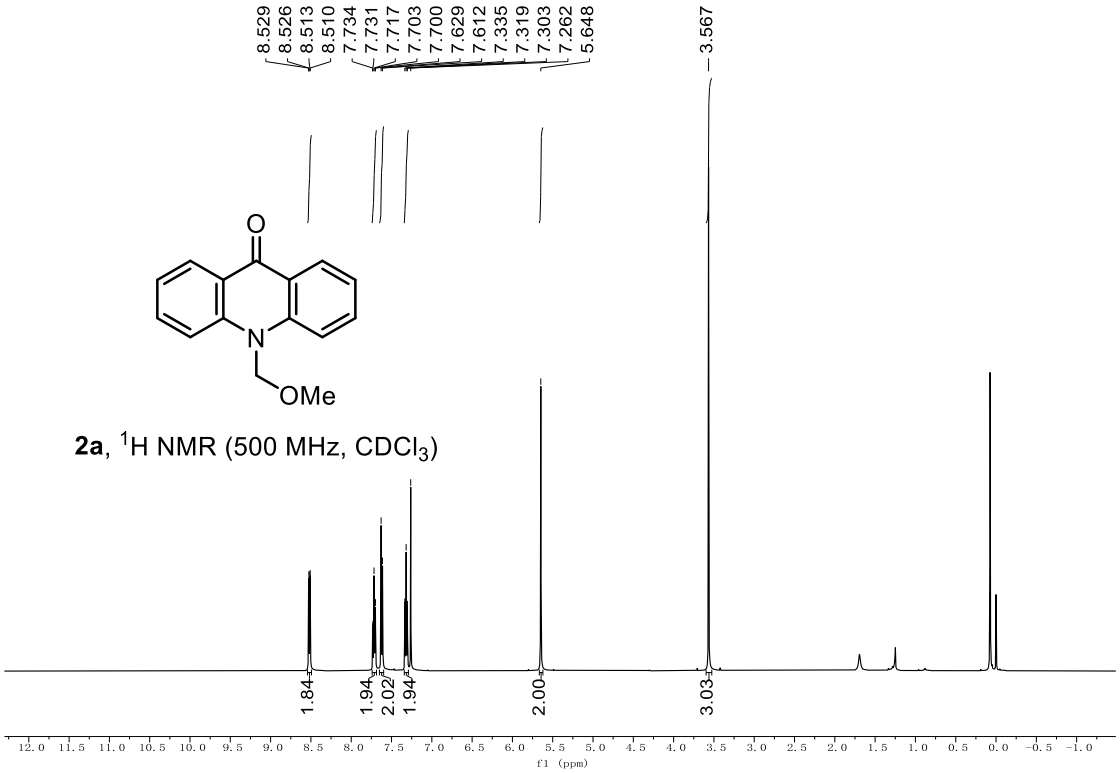


1k, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)

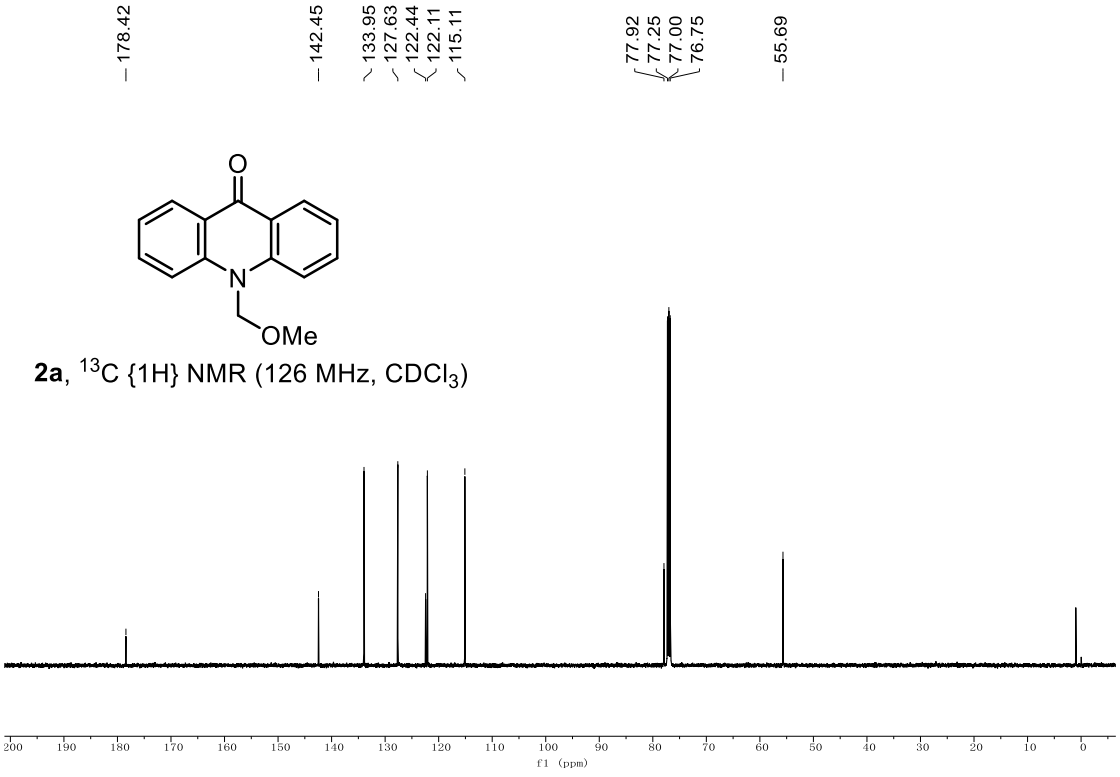


1y, ^{1}H NMR (500 MHz, $CDCl_3$)

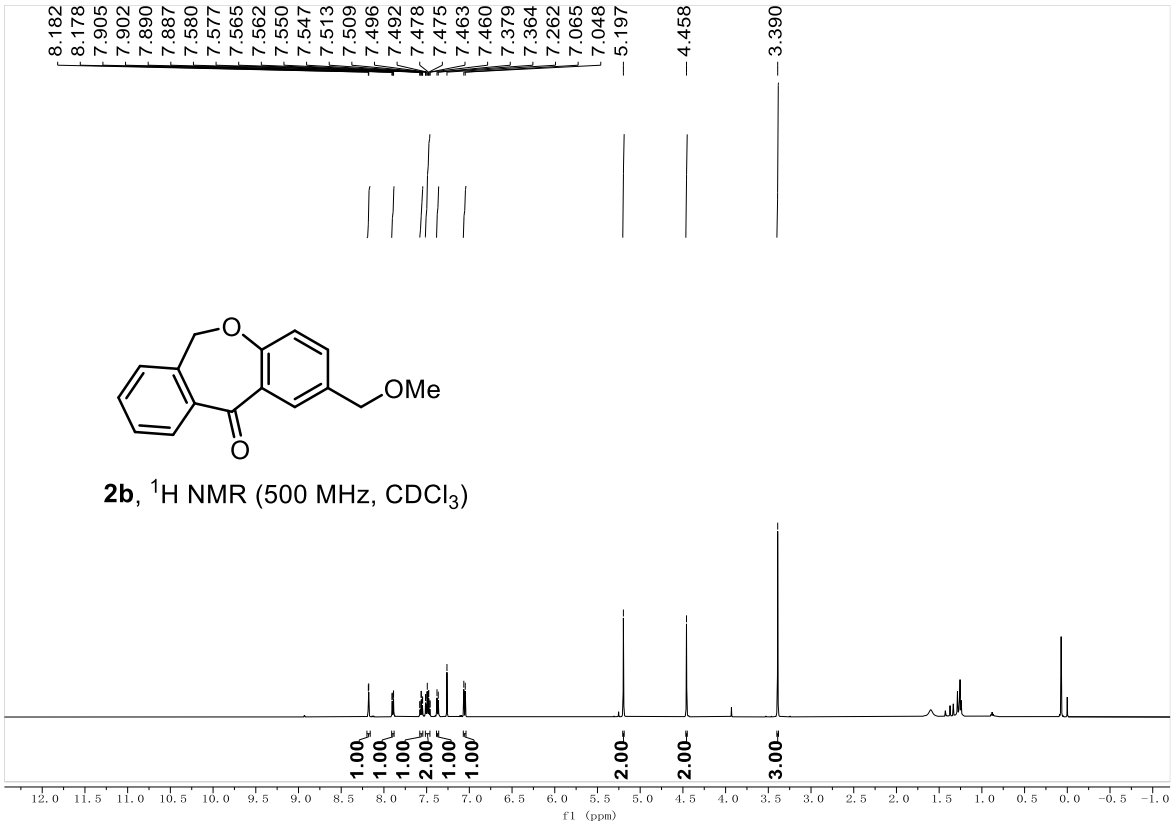
5.2 NMR Spectra of Products



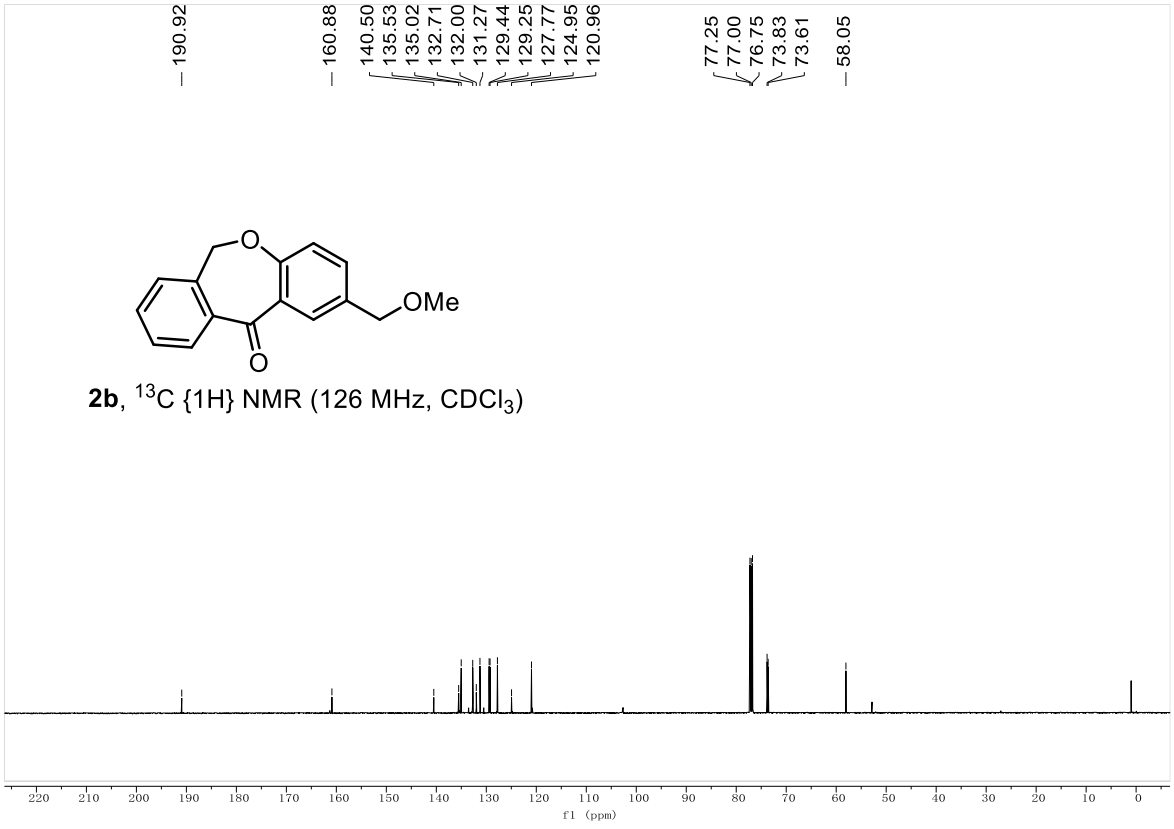
2a, ^{1}H NMR (500 MHz, $CDCl_3$)



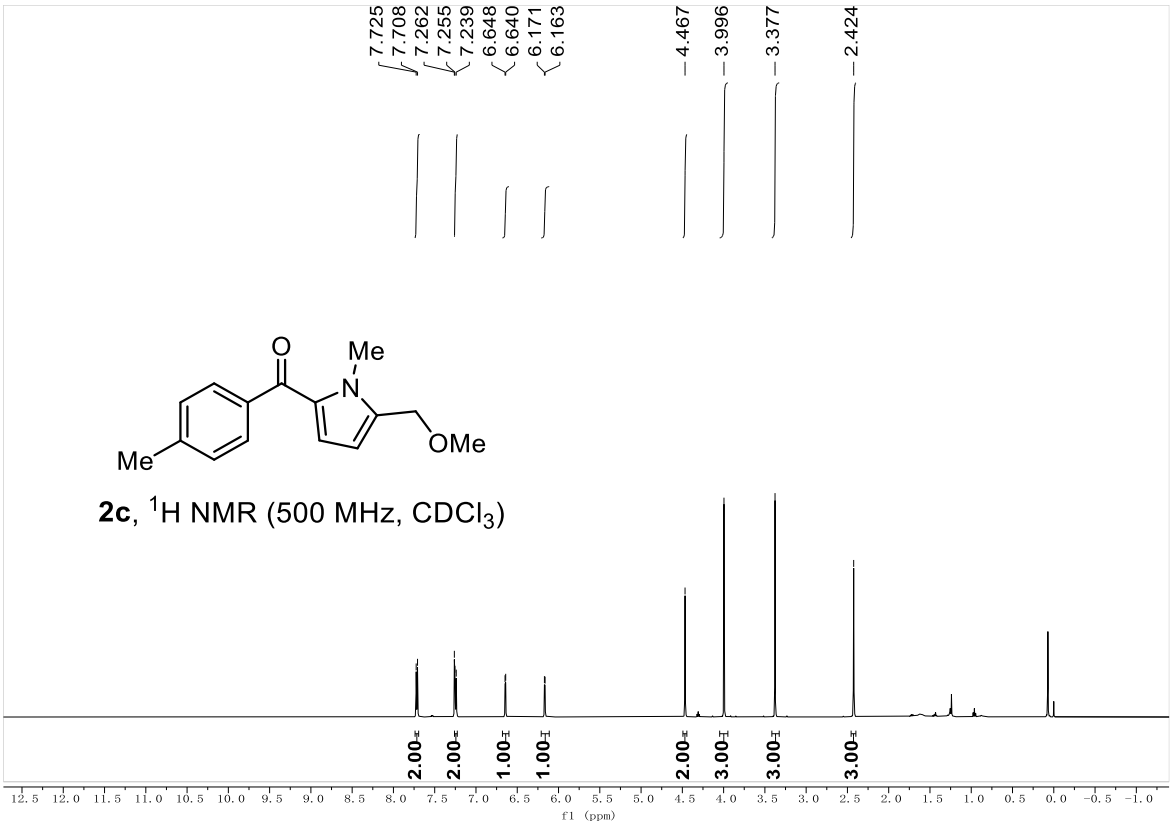
2a, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



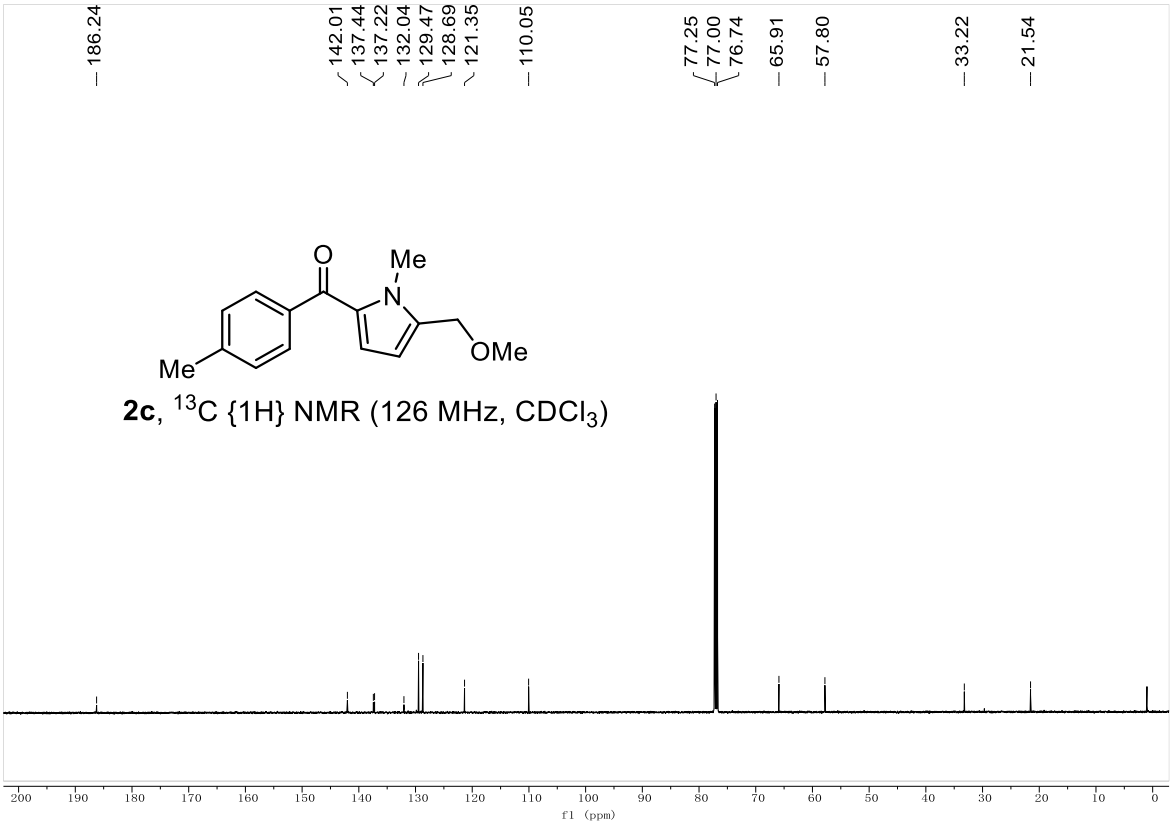
2b, ^{1}H NMR (500 MHz, $CDCl_3$)



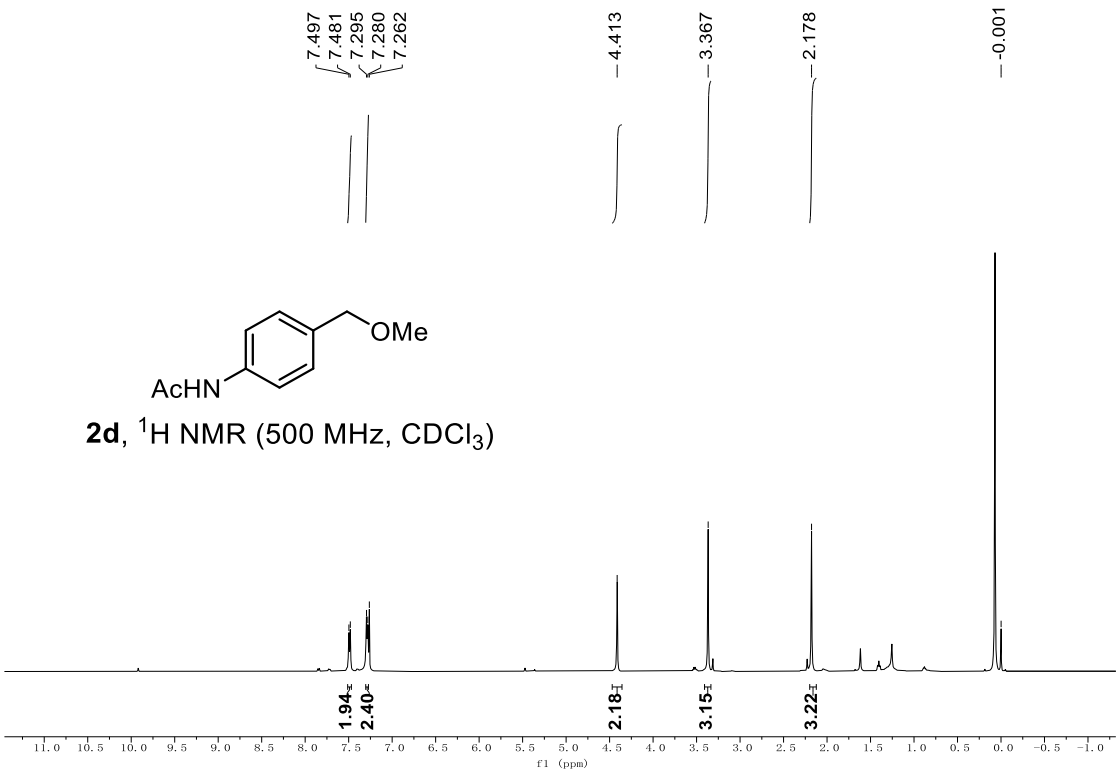
2b, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



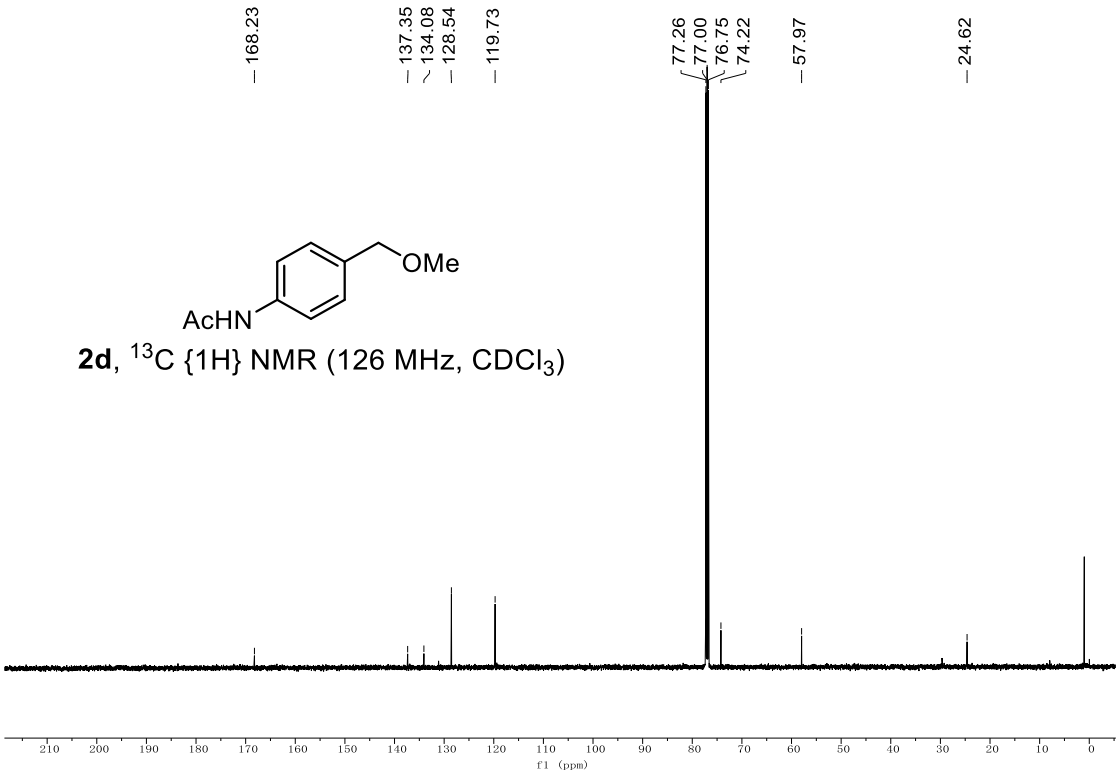
2c, ^{1}H NMR (500 MHz, $CDCl_3$)



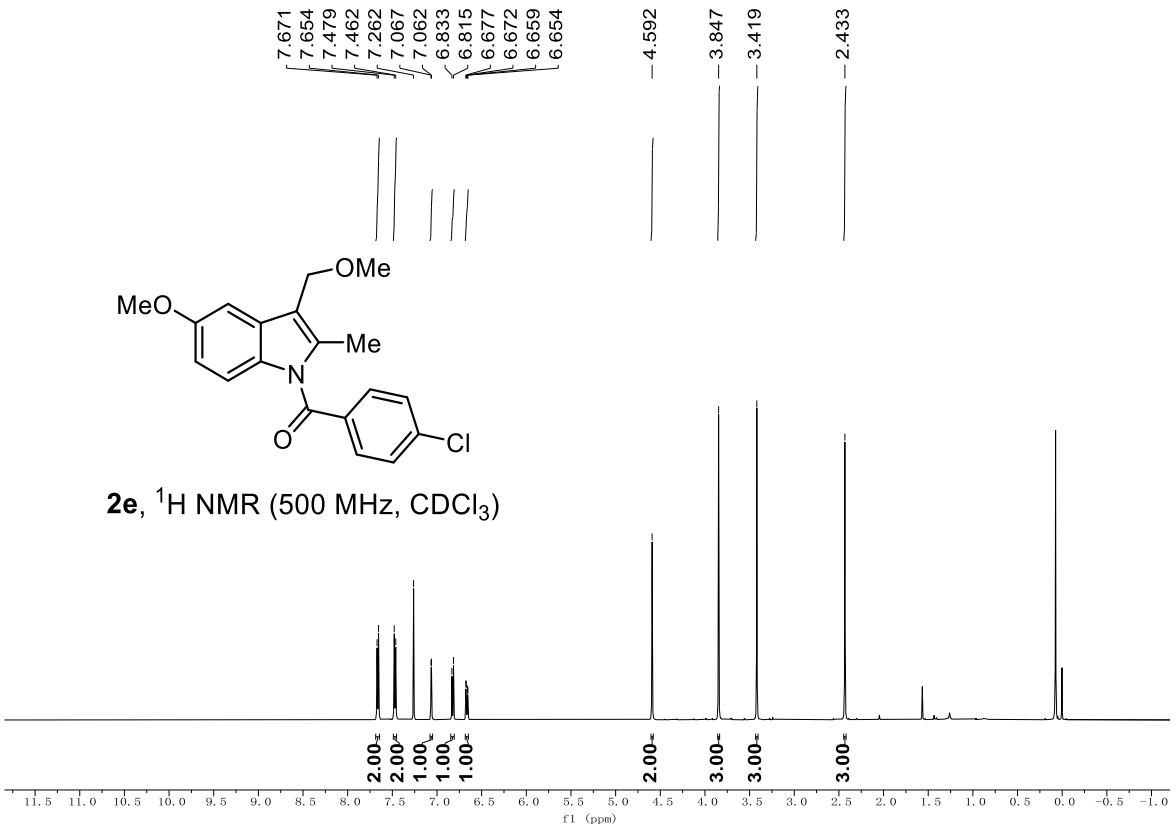
2c, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



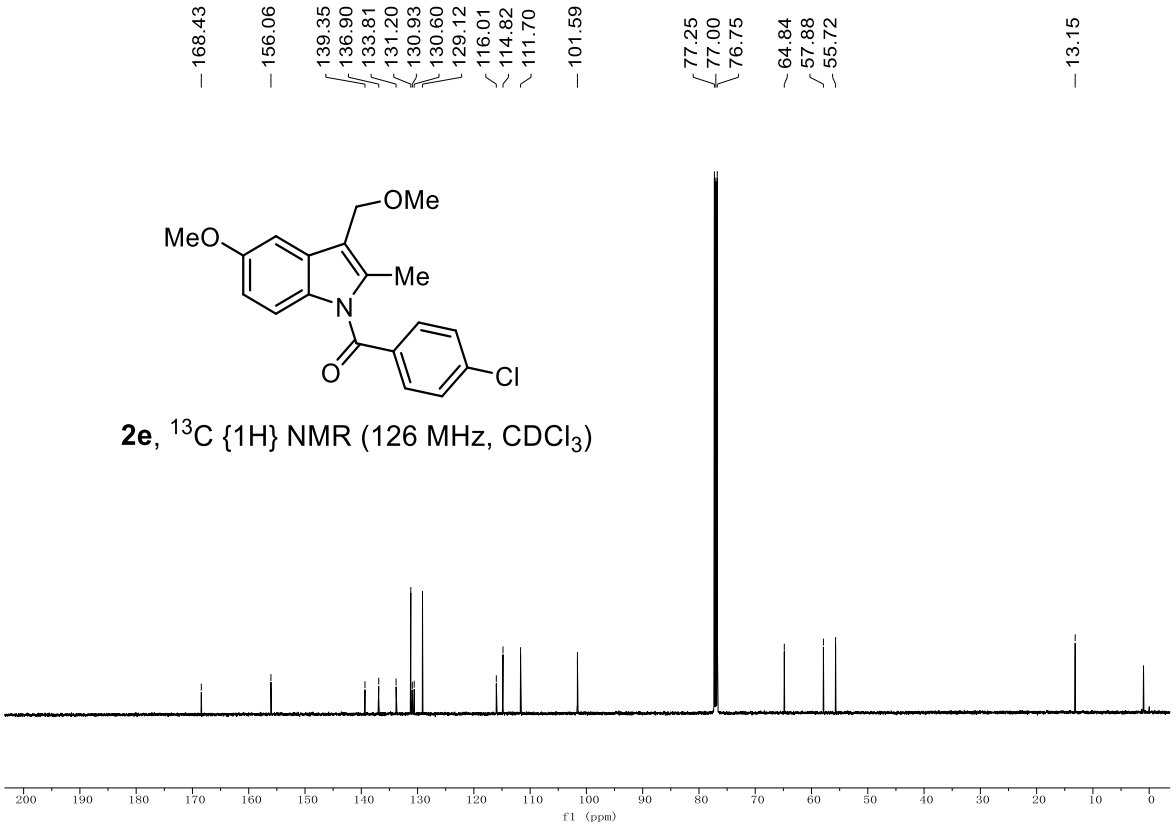
2d, ^{1}H NMR (500 MHz, $CDCl_3$)



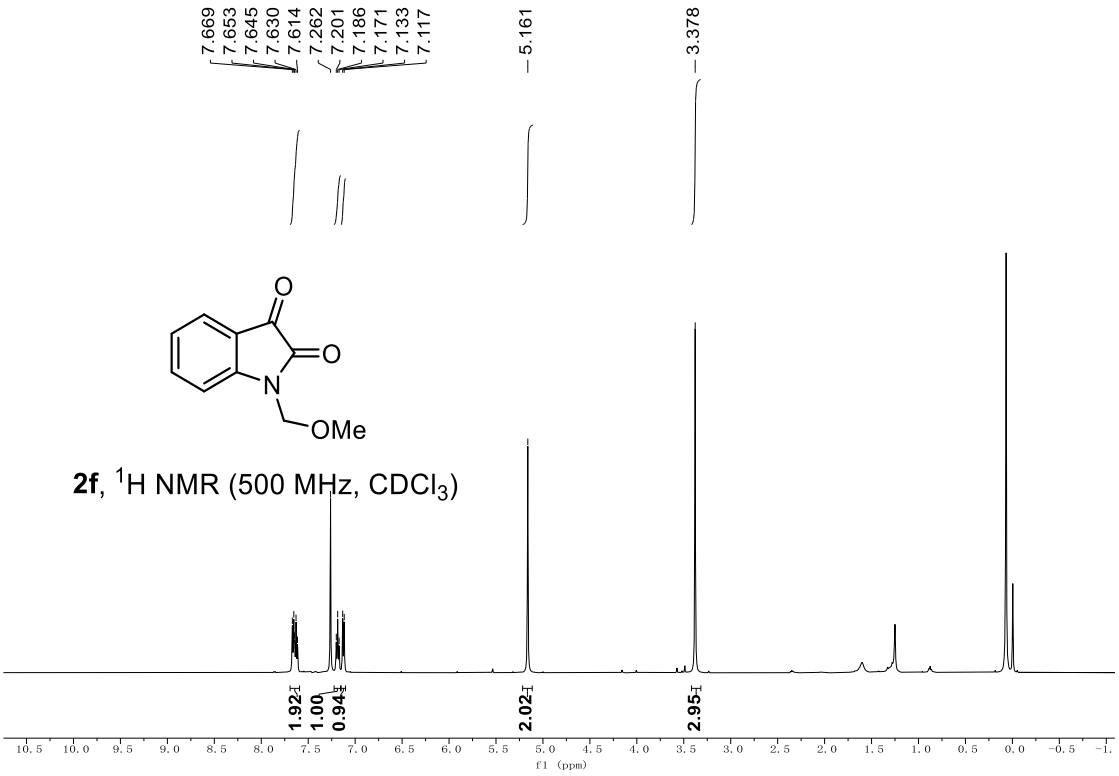
2d, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



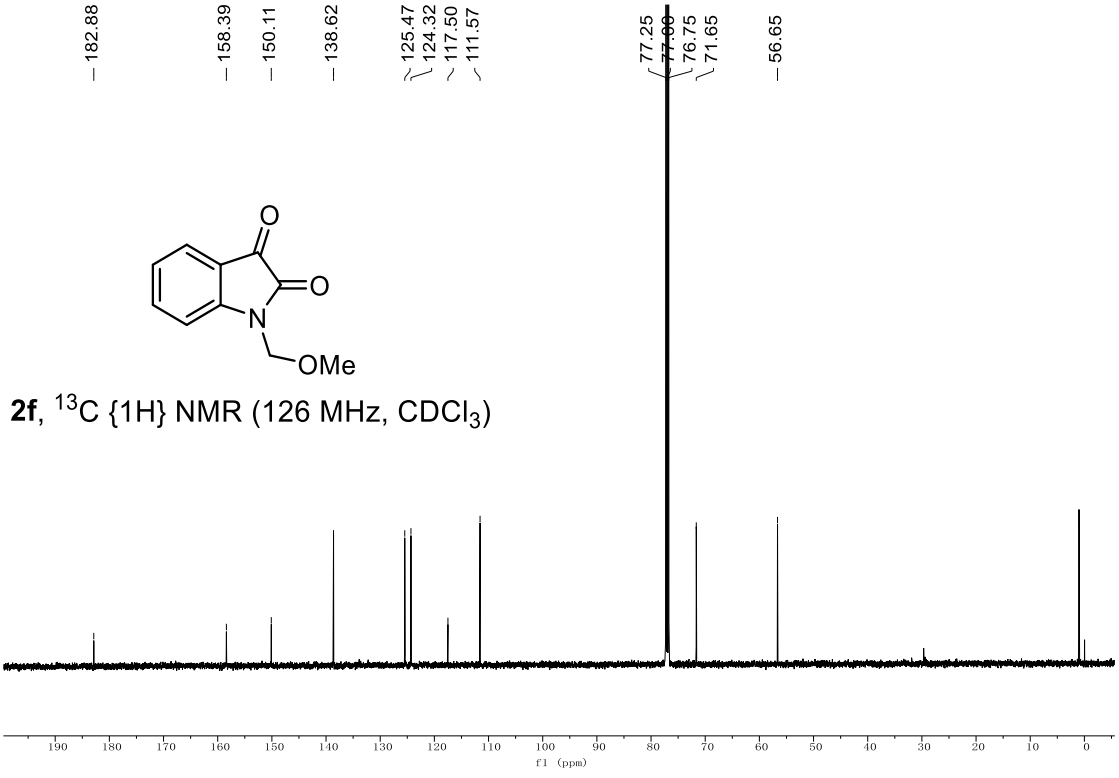
2e, ^{1}H NMR (500 MHz, $CDCl_3$)



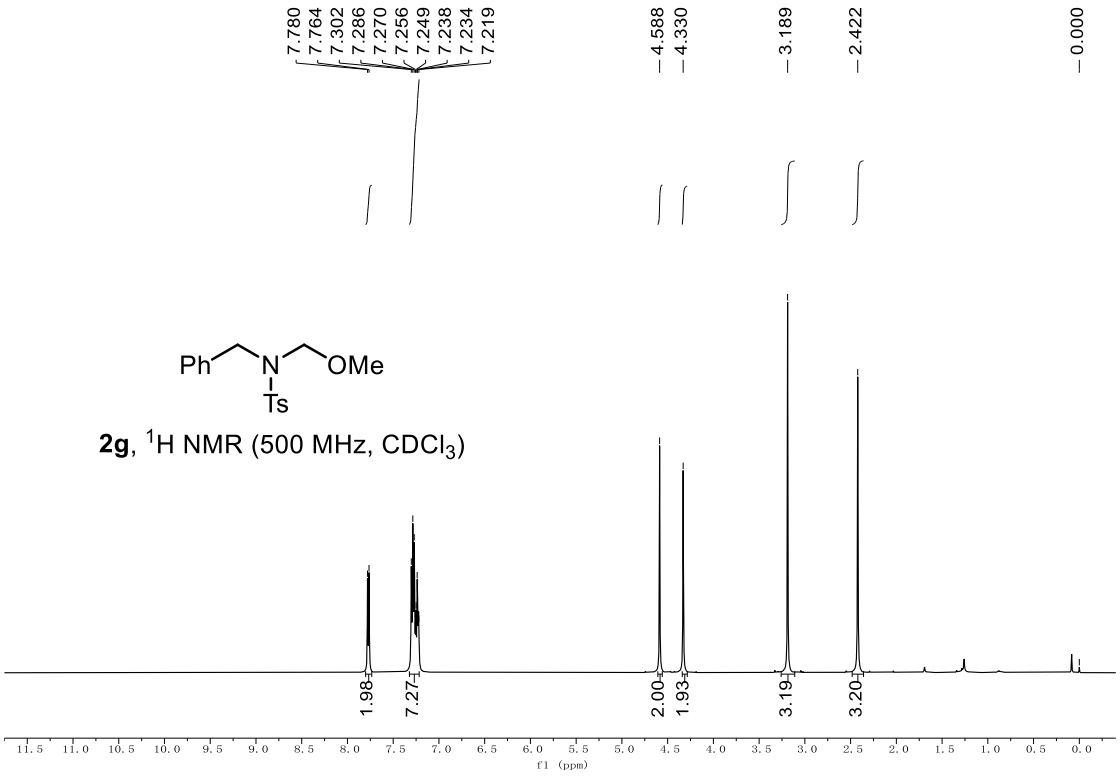
2e, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



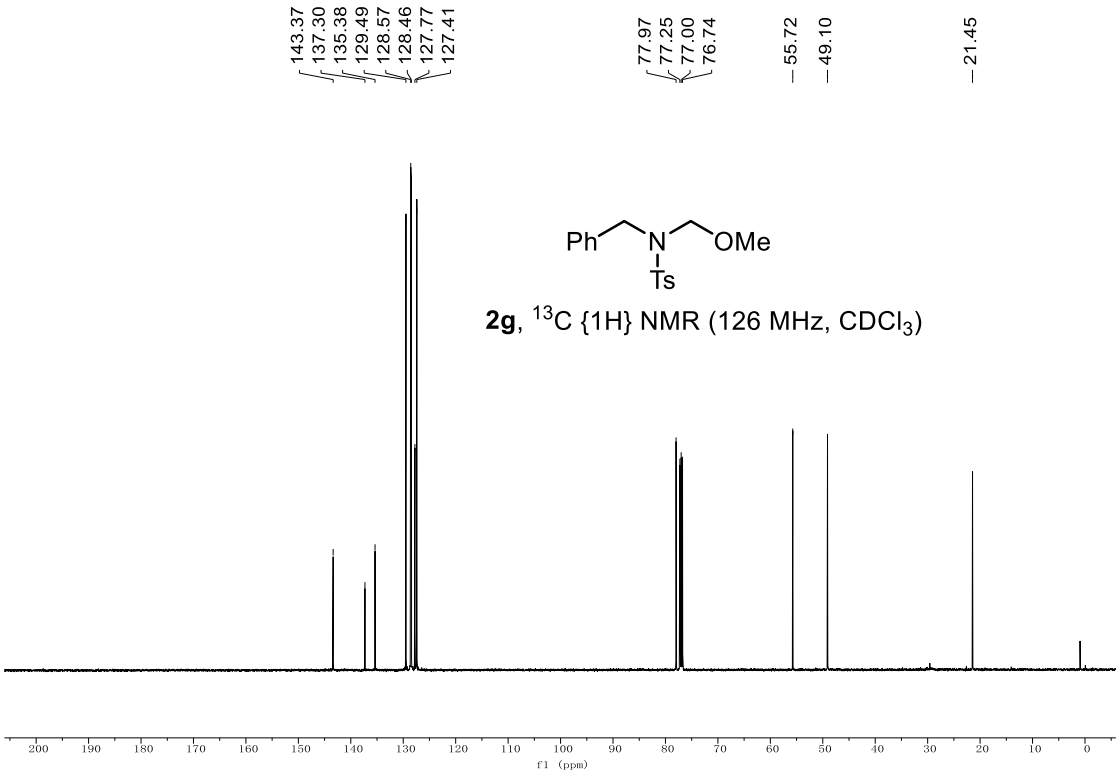
2f, ^{1}H NMR (500 MHz, $CDCl_3$)



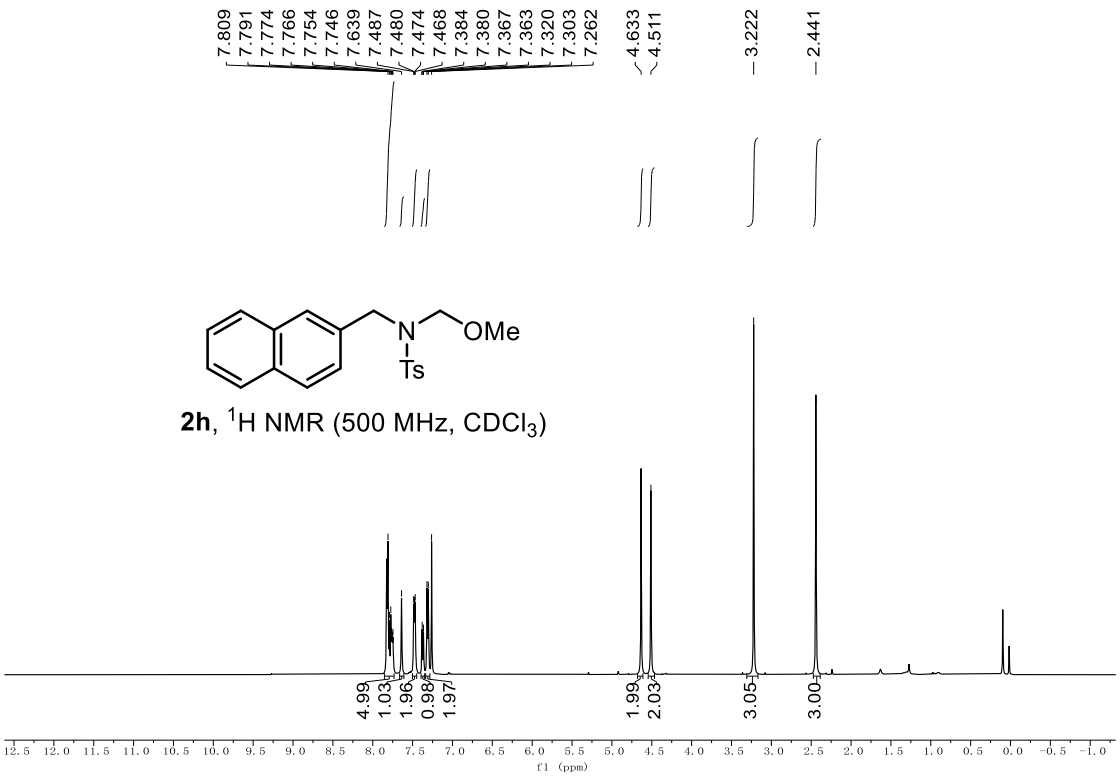
2f, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



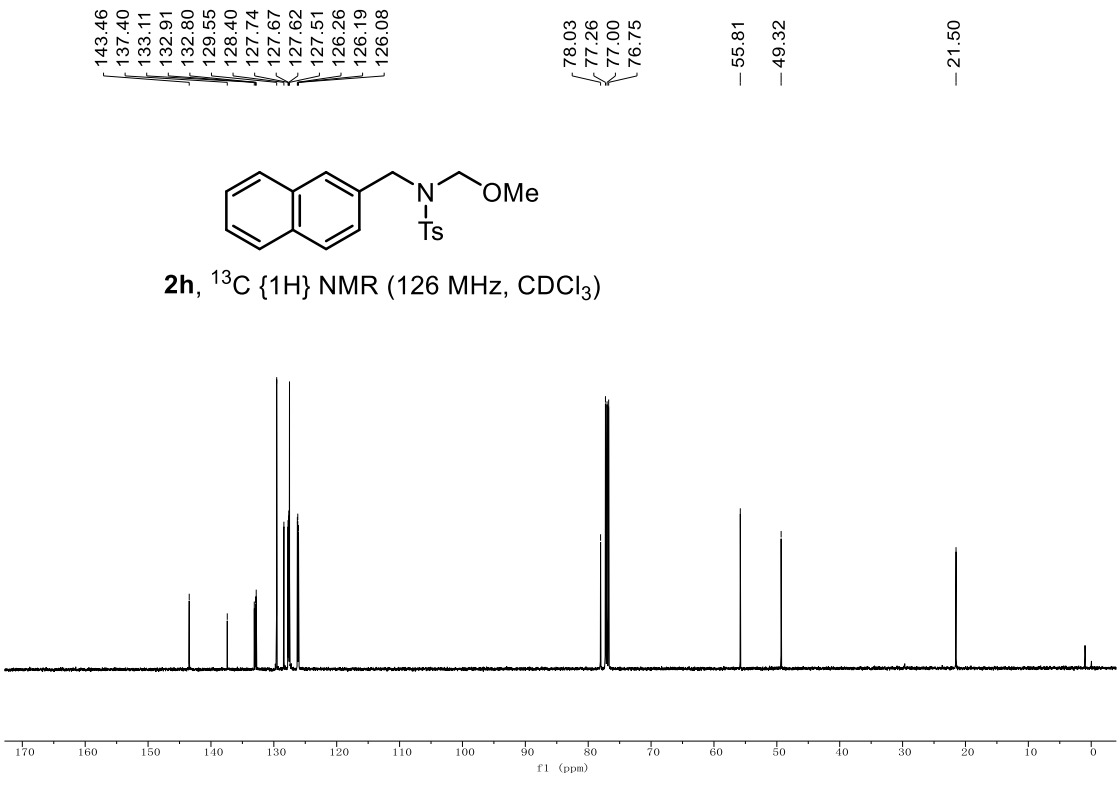
2g, ^{1}H NMR (500 MHz, $CDCl_3$)



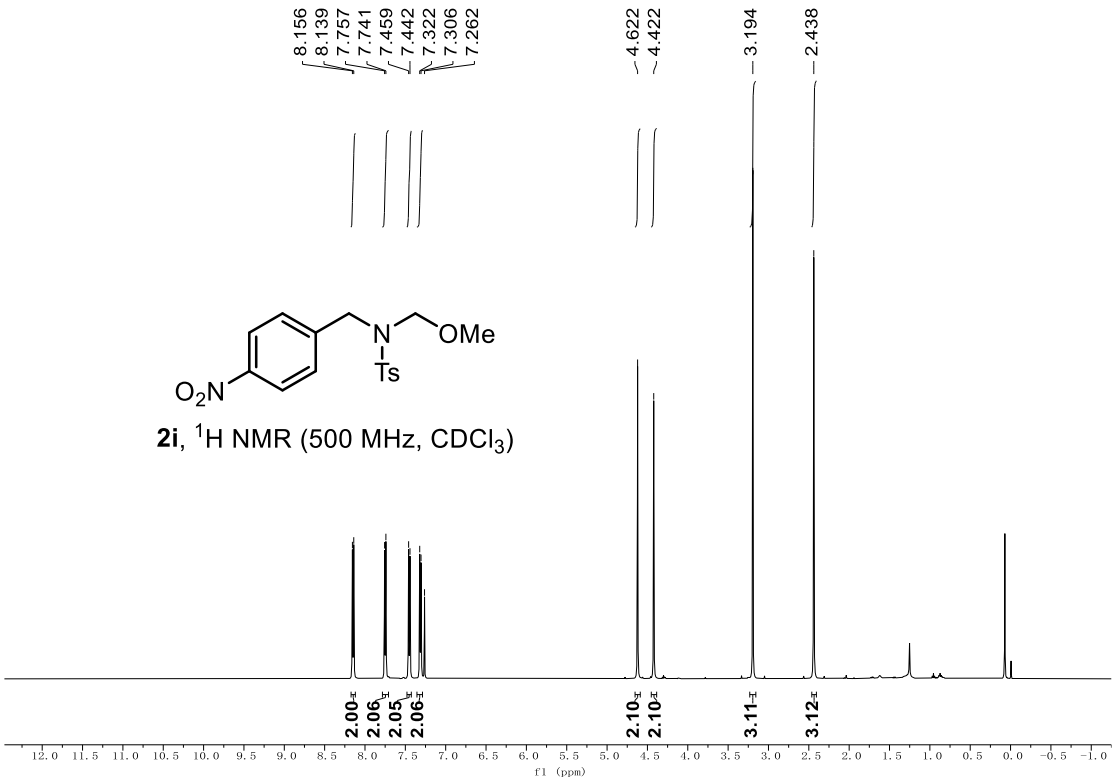
2g, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



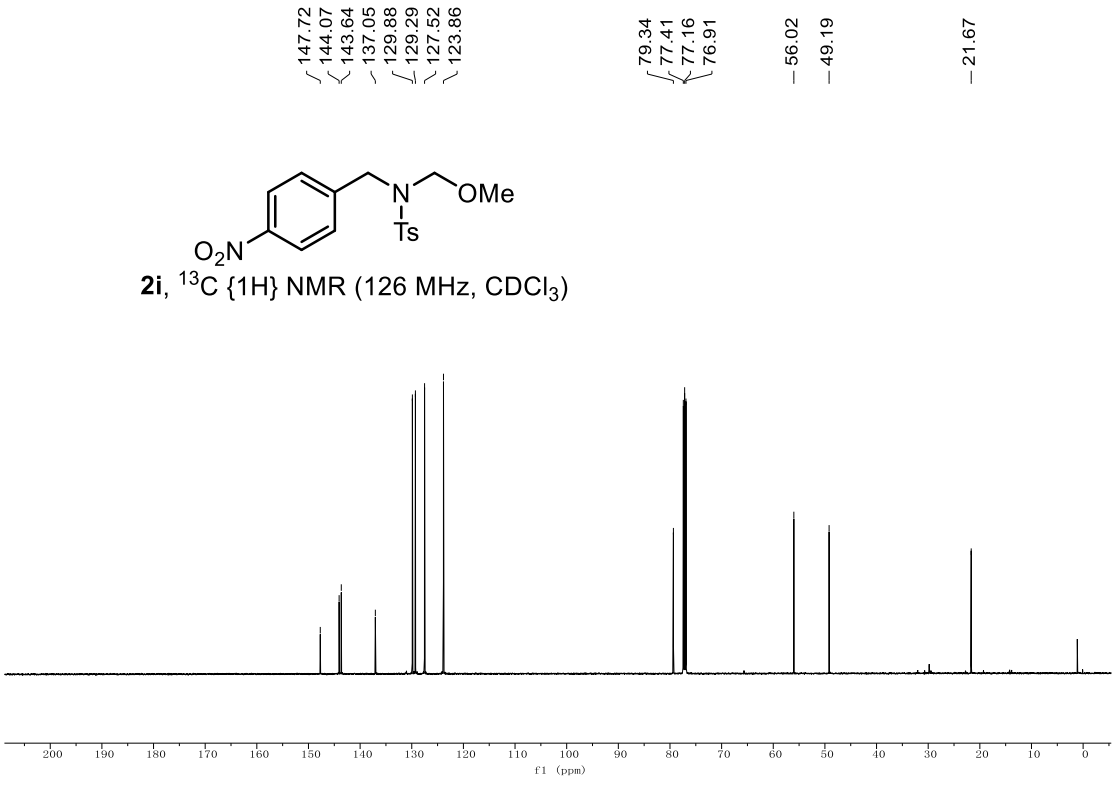
2h, ^{1}H NMR (500 MHz, $CDCl_3$)



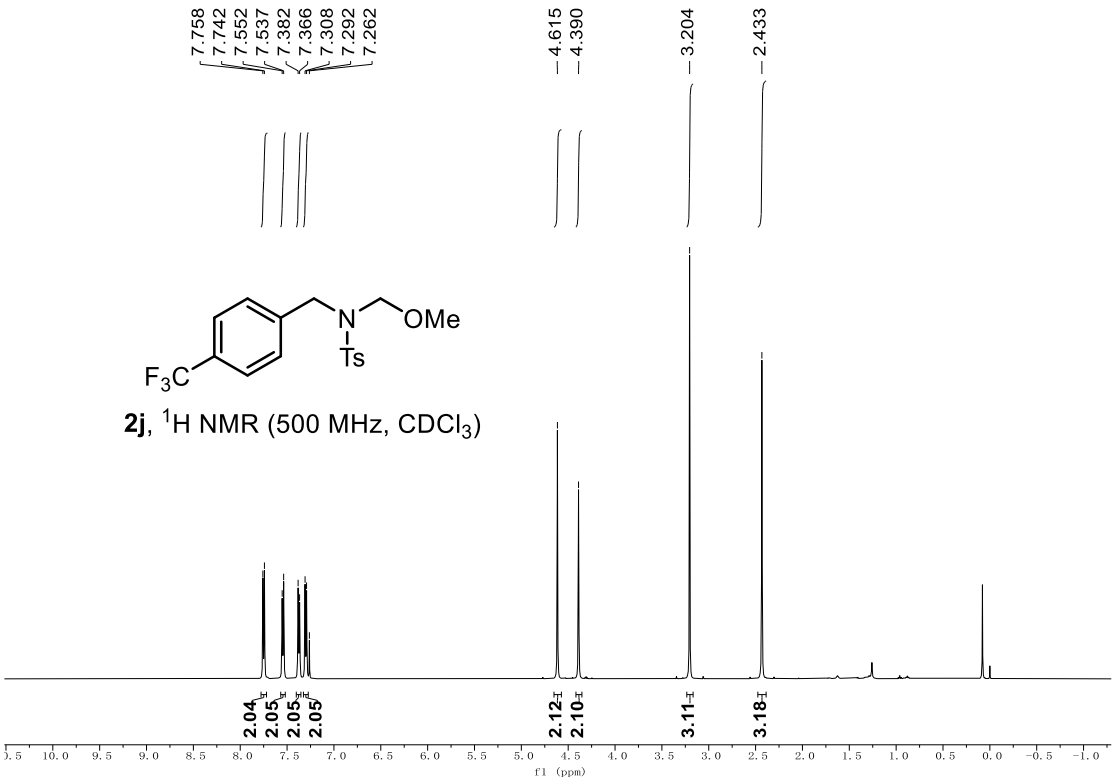
2h, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



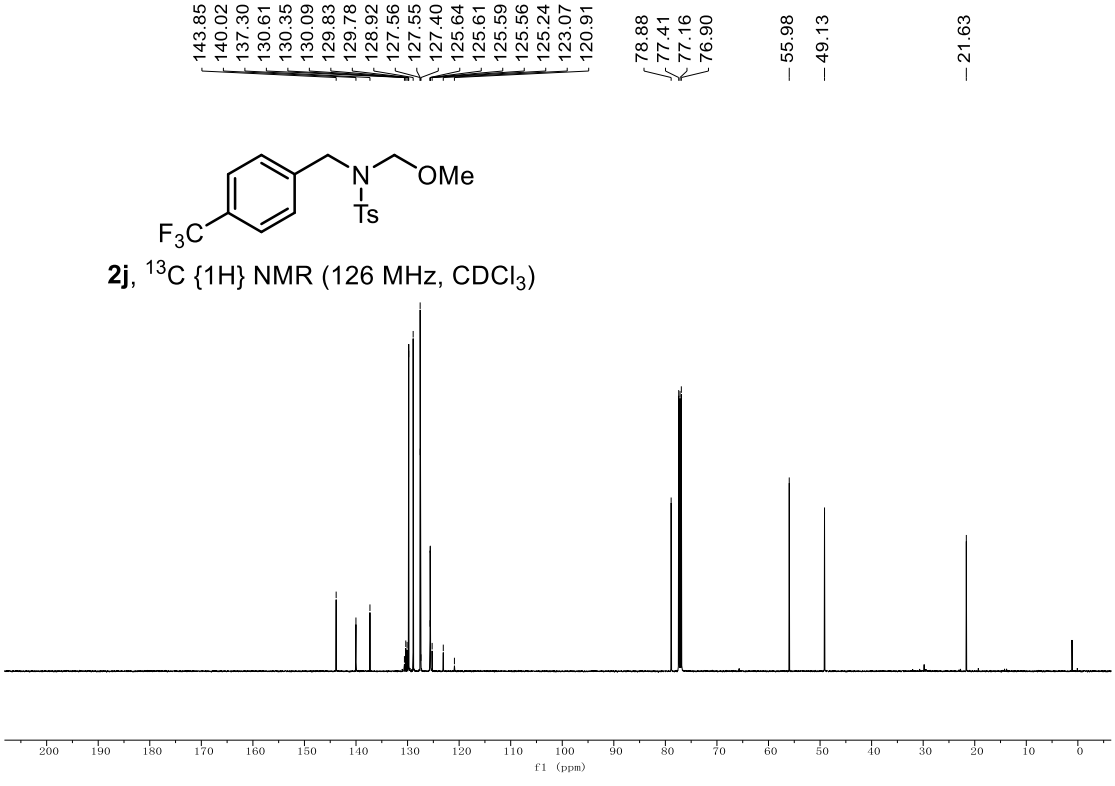
2i, ^{1}H NMR (500 MHz, $CDCl_3$)



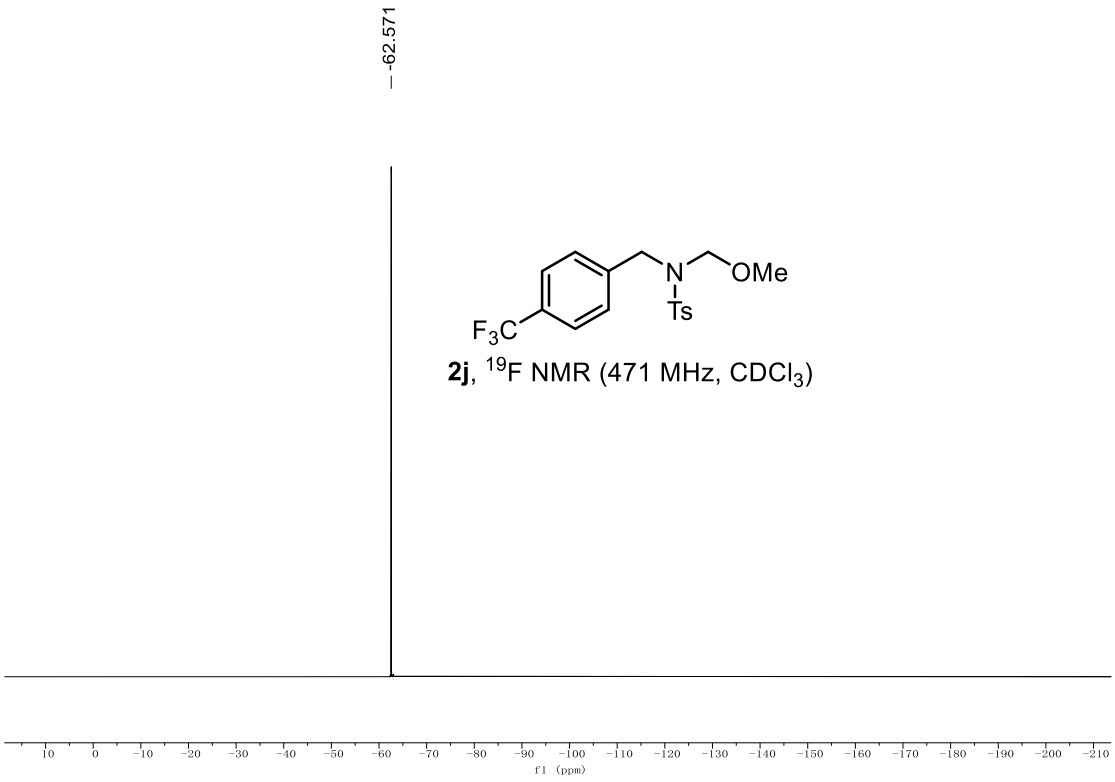
2i, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



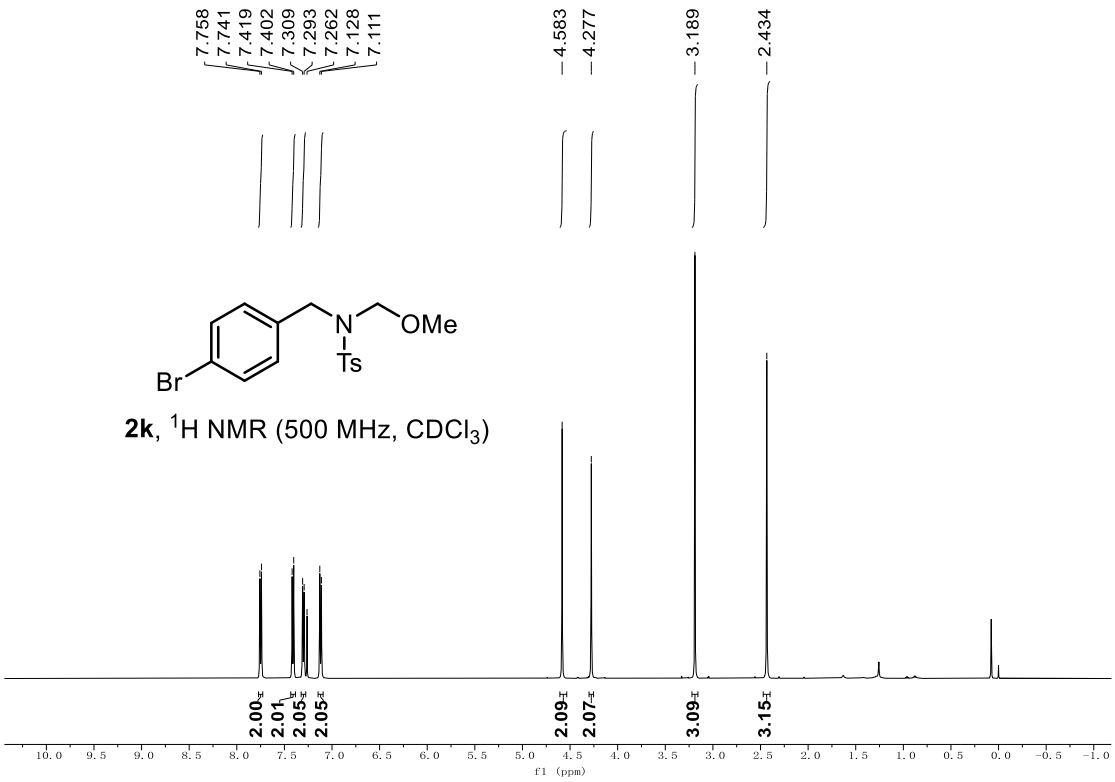
2j, ^{1}H NMR (500 MHz, $CDCl_3$)



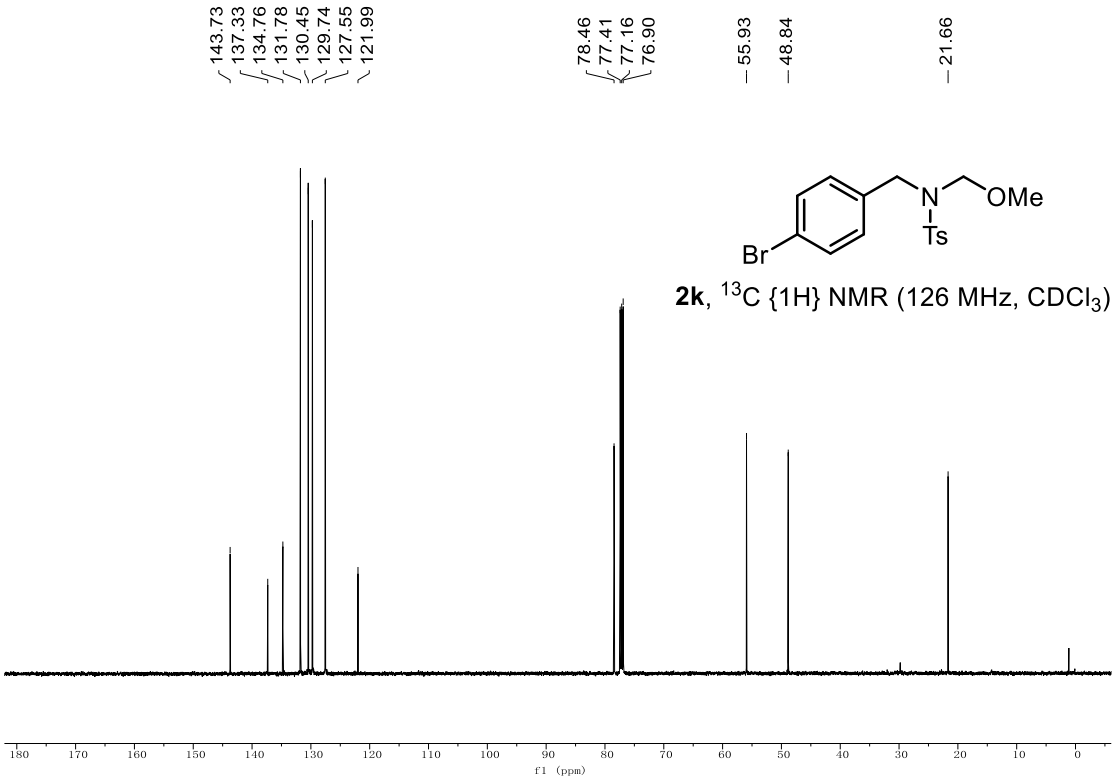
2j, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



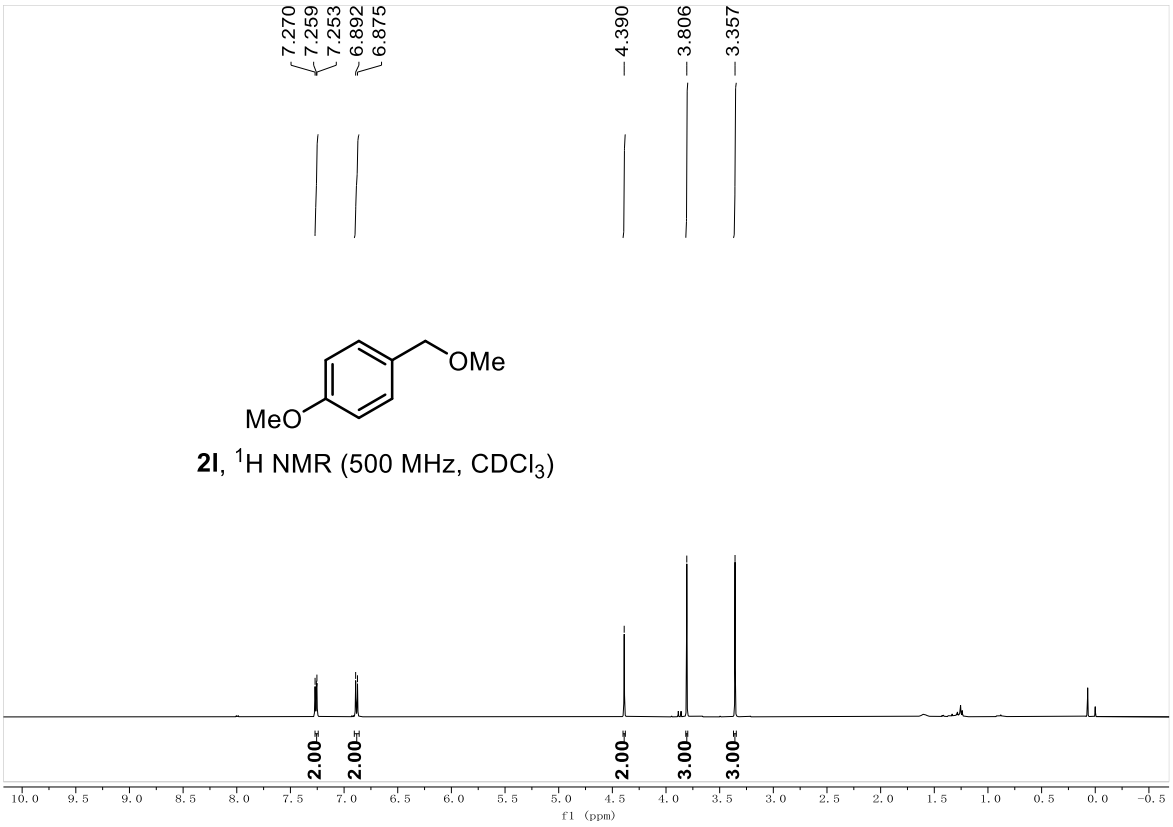
2j, ^{19}F NMR (471 MHz, $CDCl_3$)



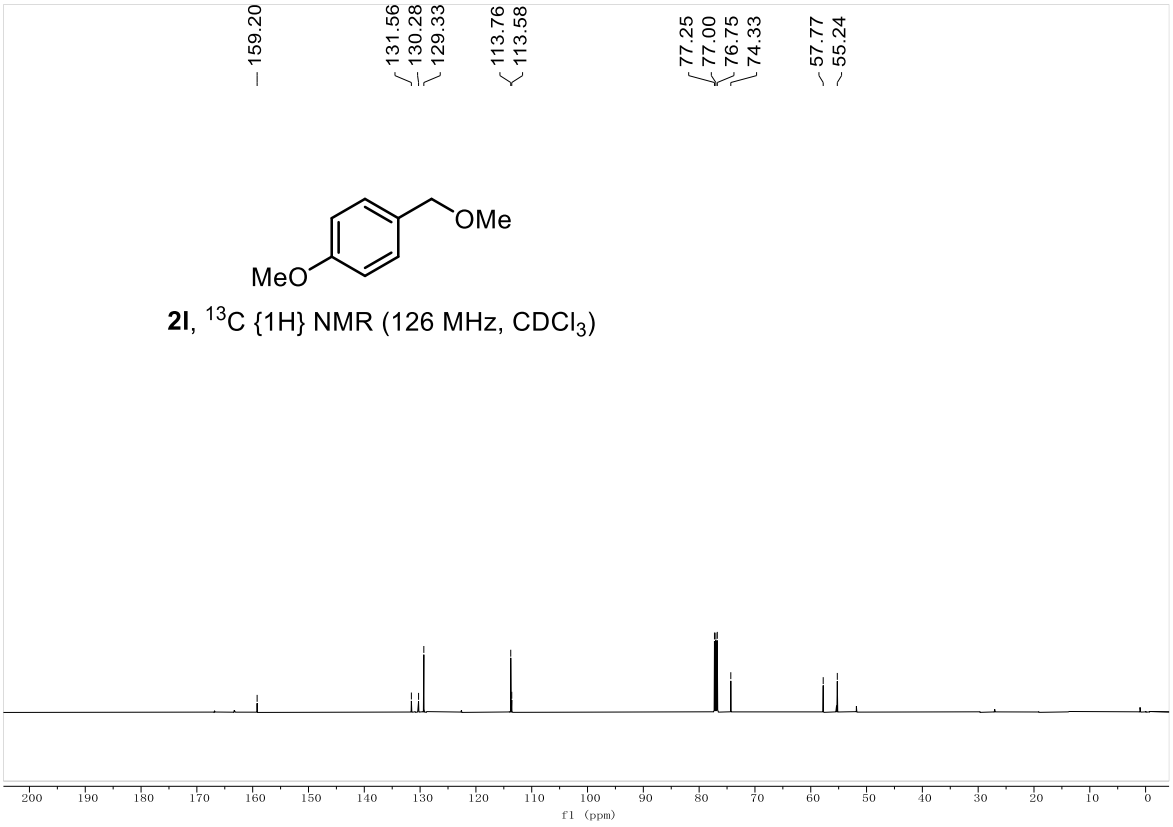
2k, ^{1}H NMR (500 MHz, $CDCl_3$)



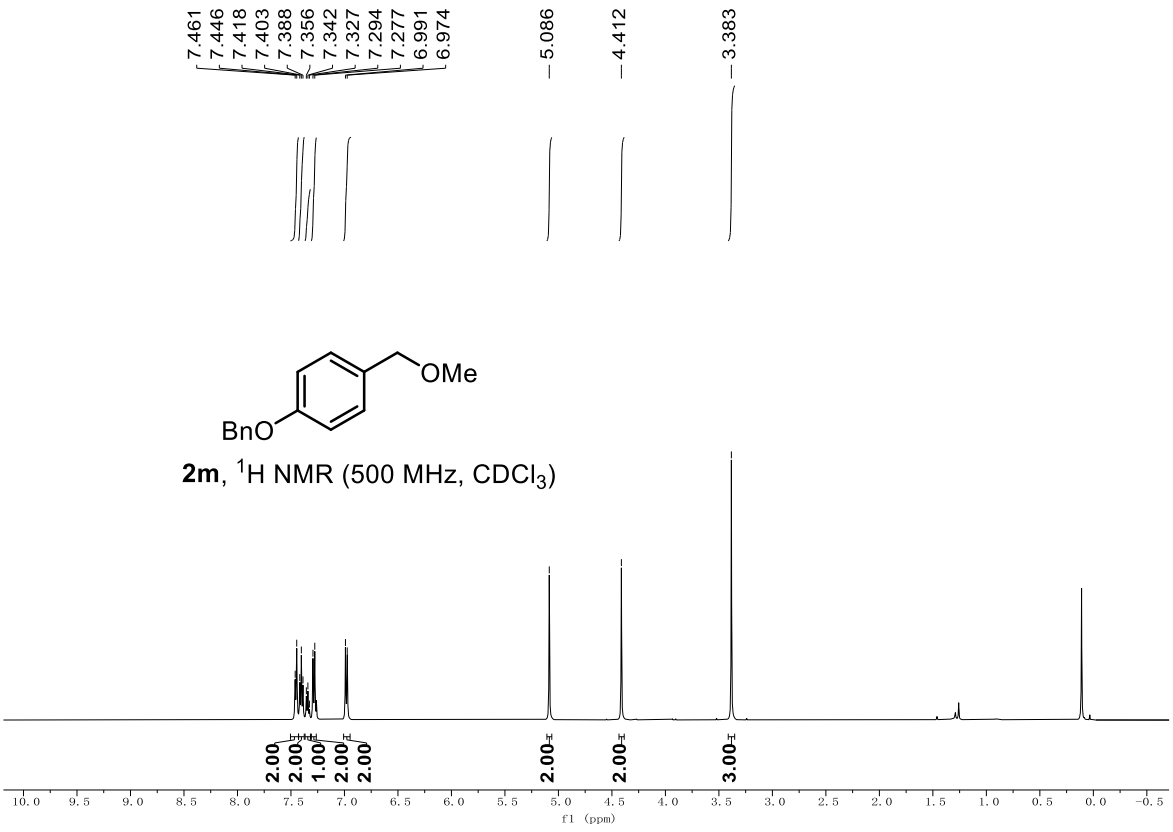
2k, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



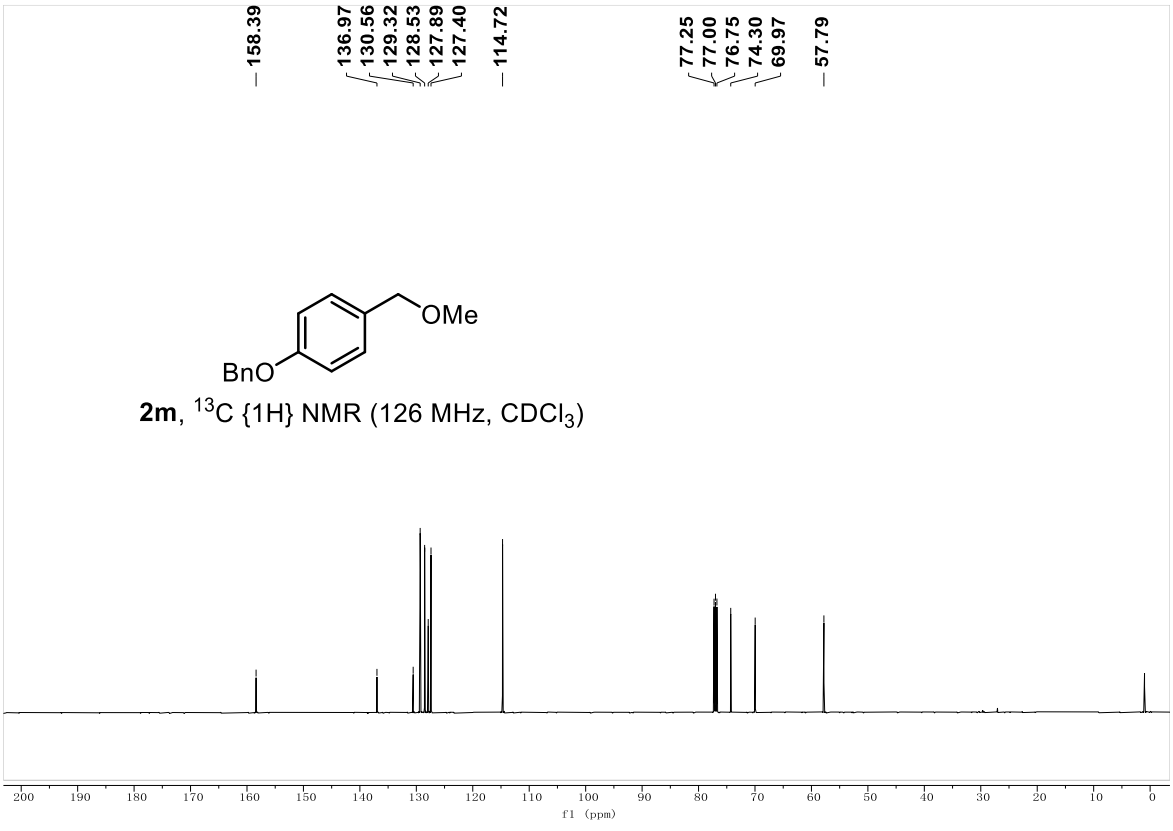
2l, ^{1}H NMR (500 MHz, $CDCl_3$)



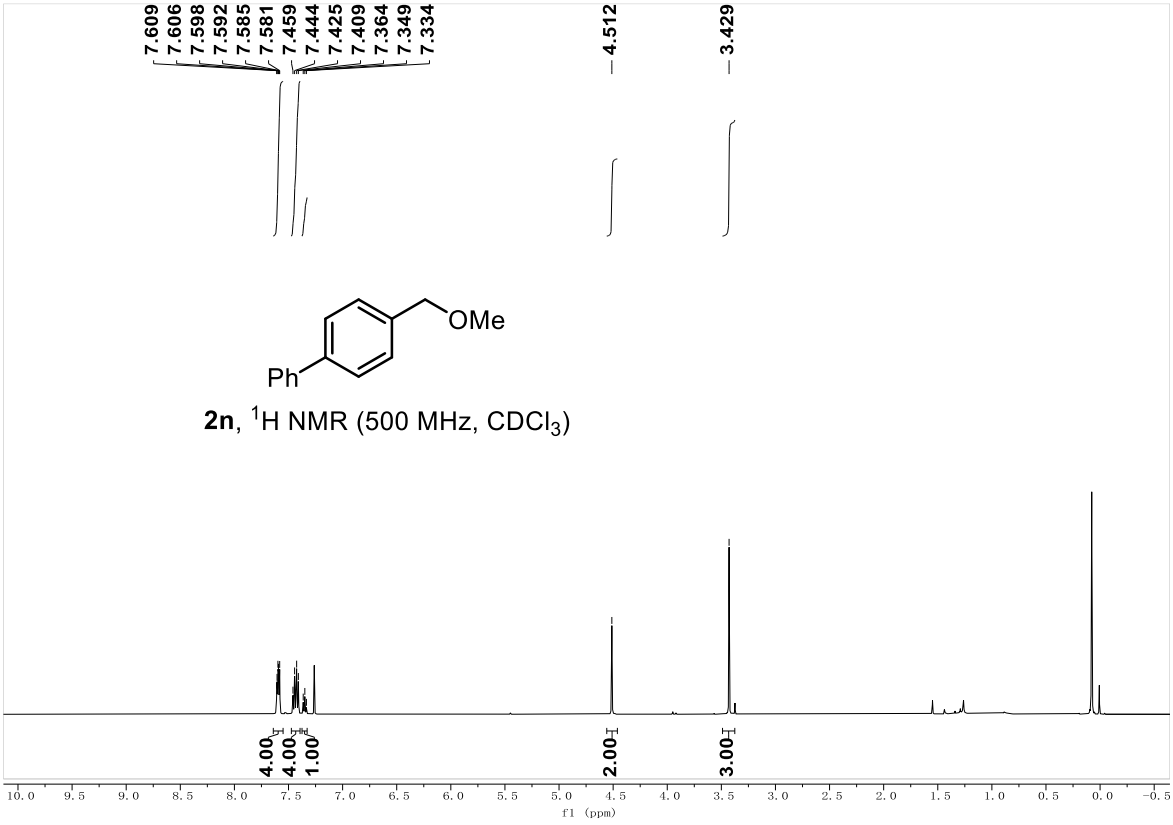
2l, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



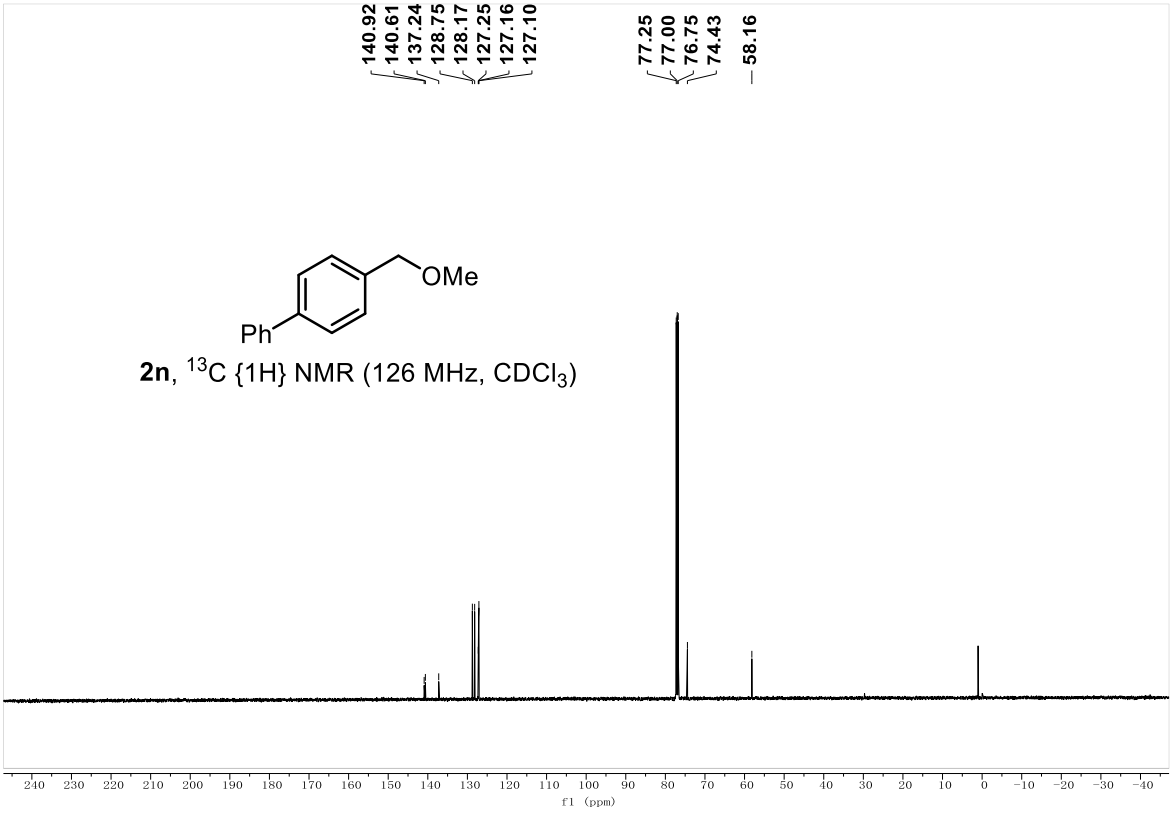
2m, ^{1}H NMR (500 MHz, $CDCl_3$)



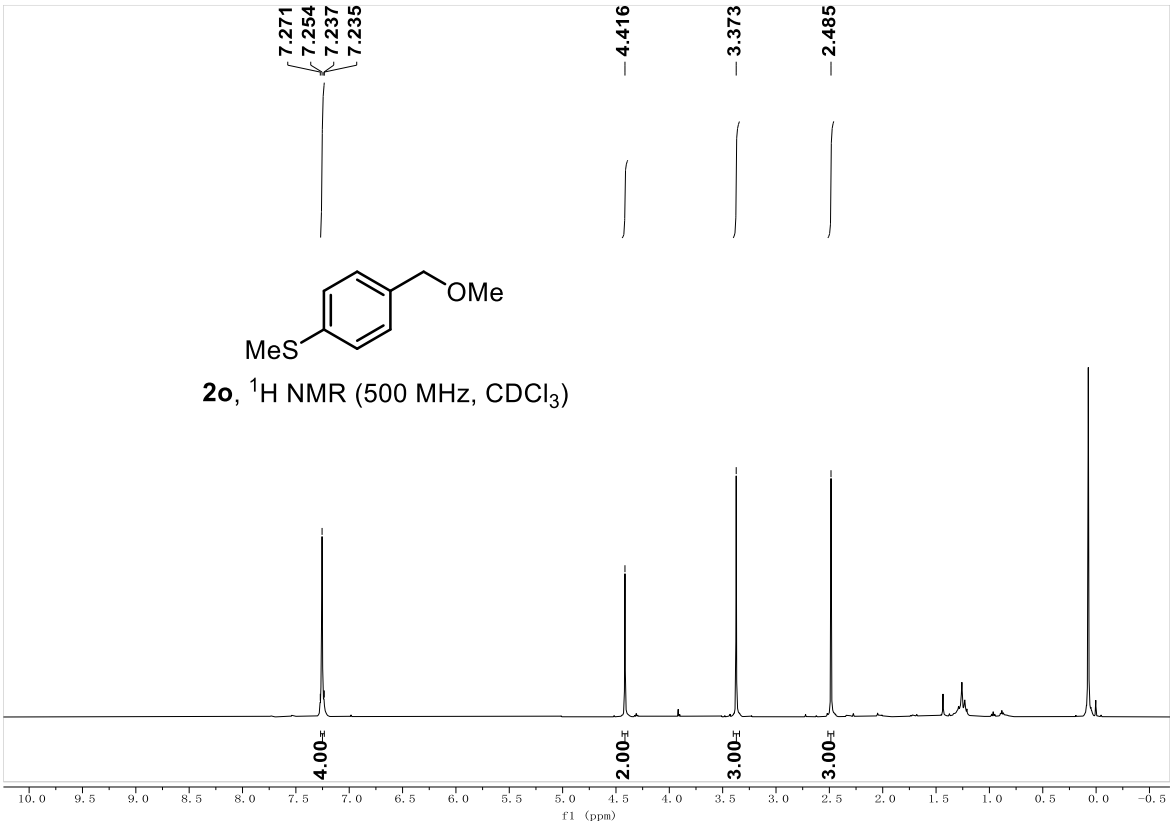
2m, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



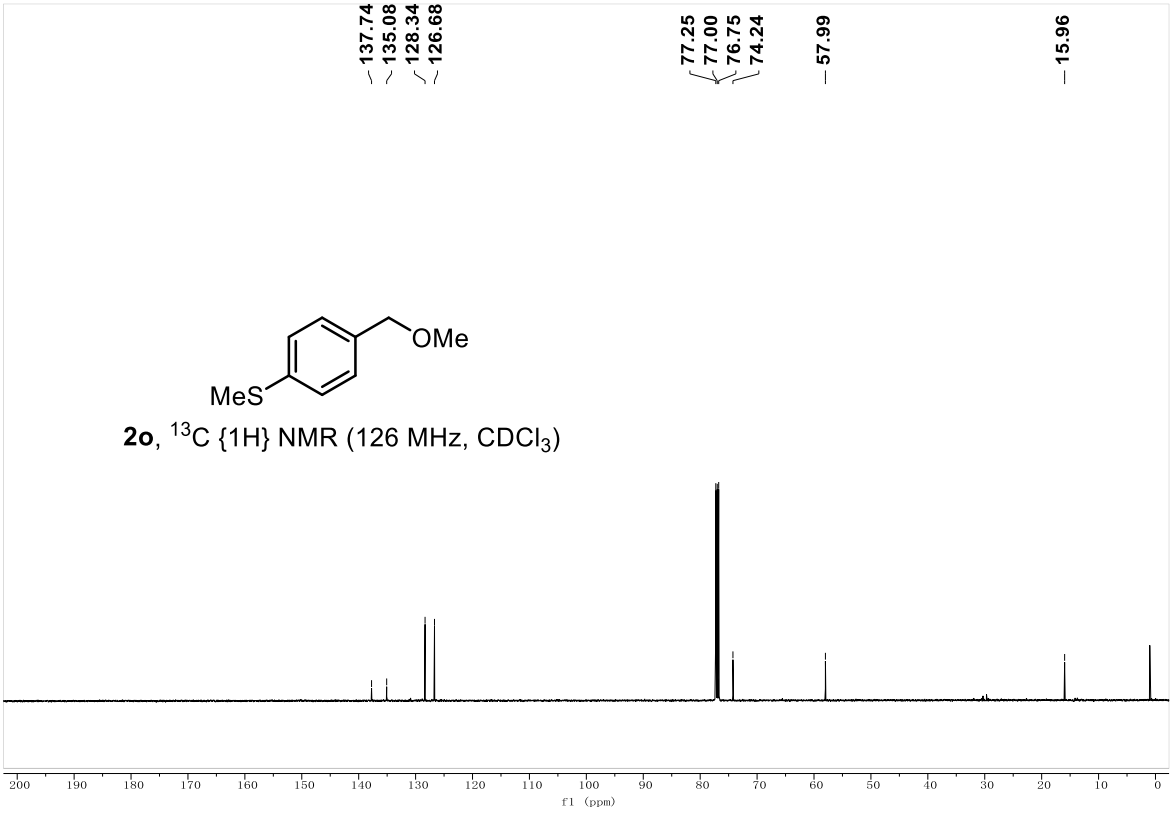
2n, ^{1}H NMR (500 MHz, $CDCl_3$)



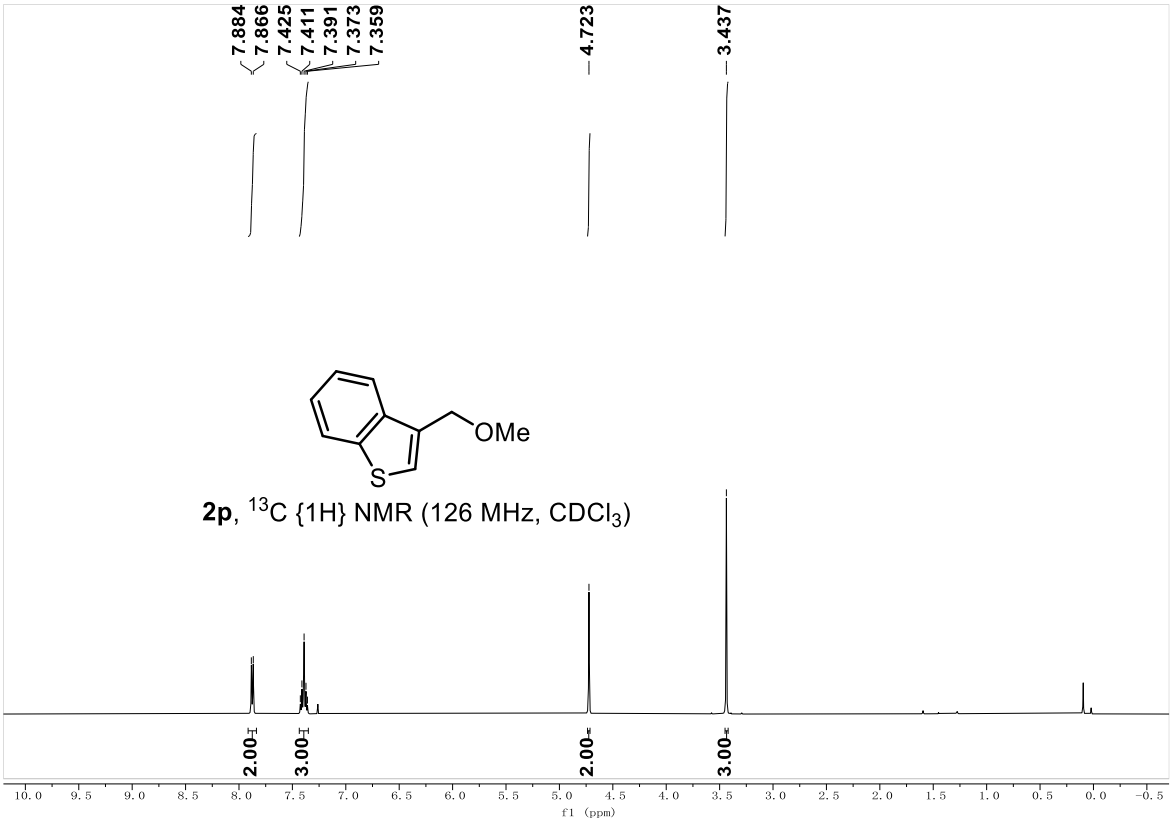
2n, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



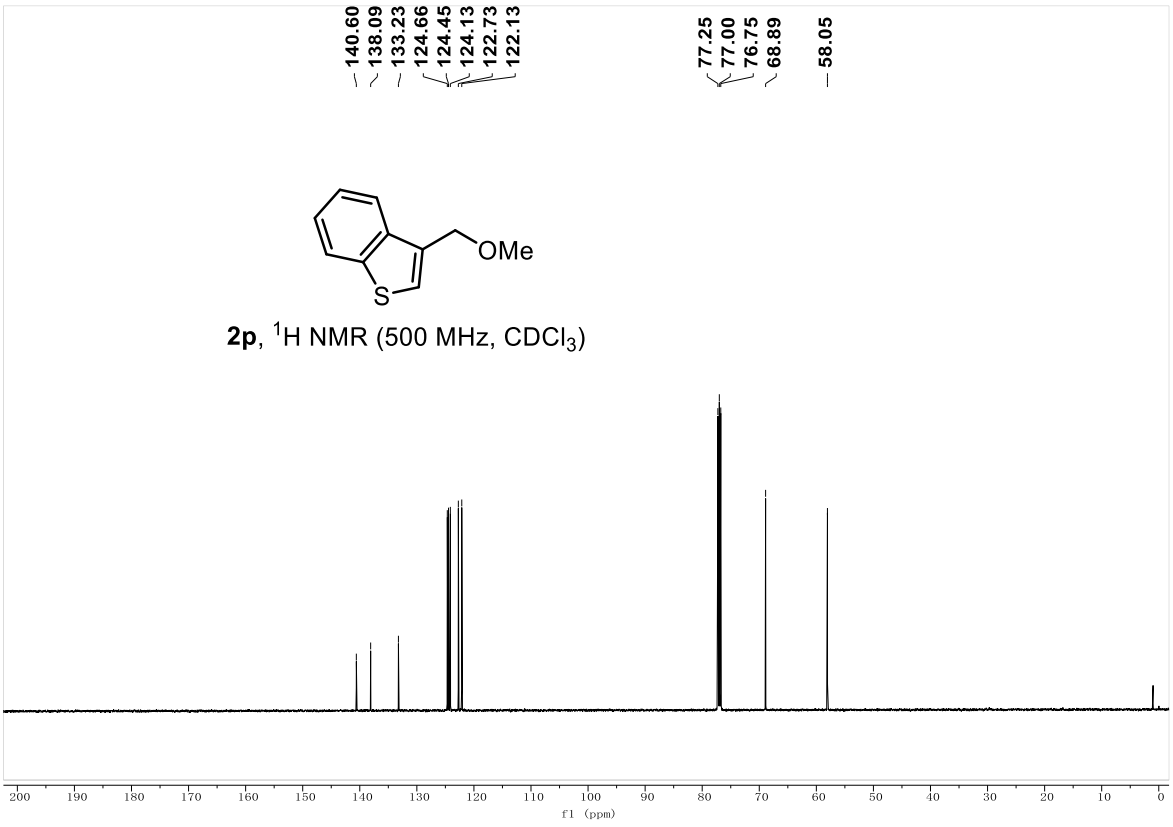
2o, ^{1}H NMR (500 MHz, $CDCl_3$)



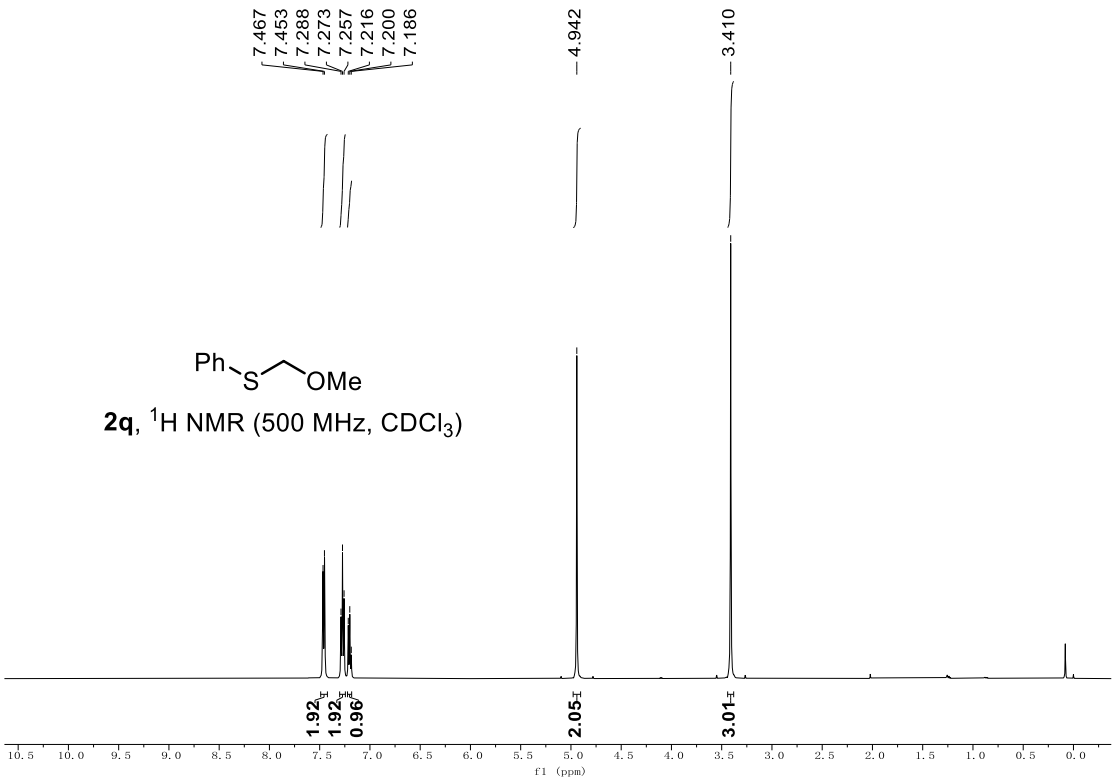
2o, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



2p, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)

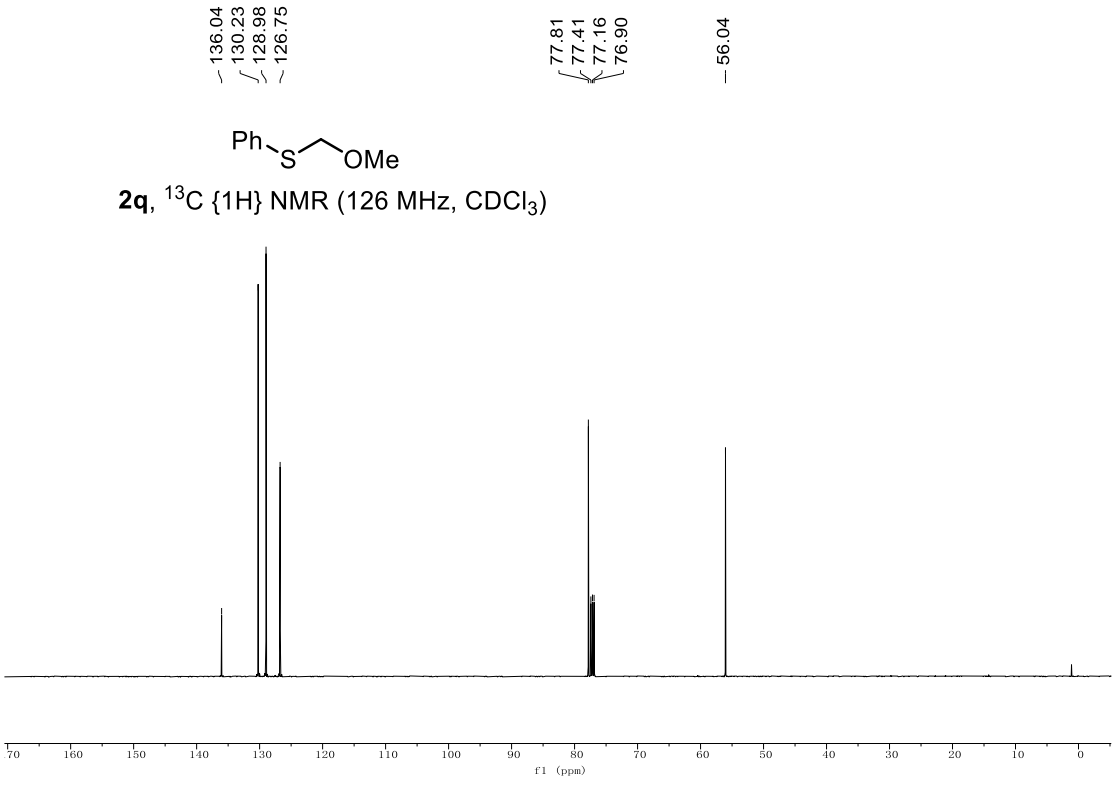


2p, ^{1}H NMR (500 MHz, $CDCl_3$)



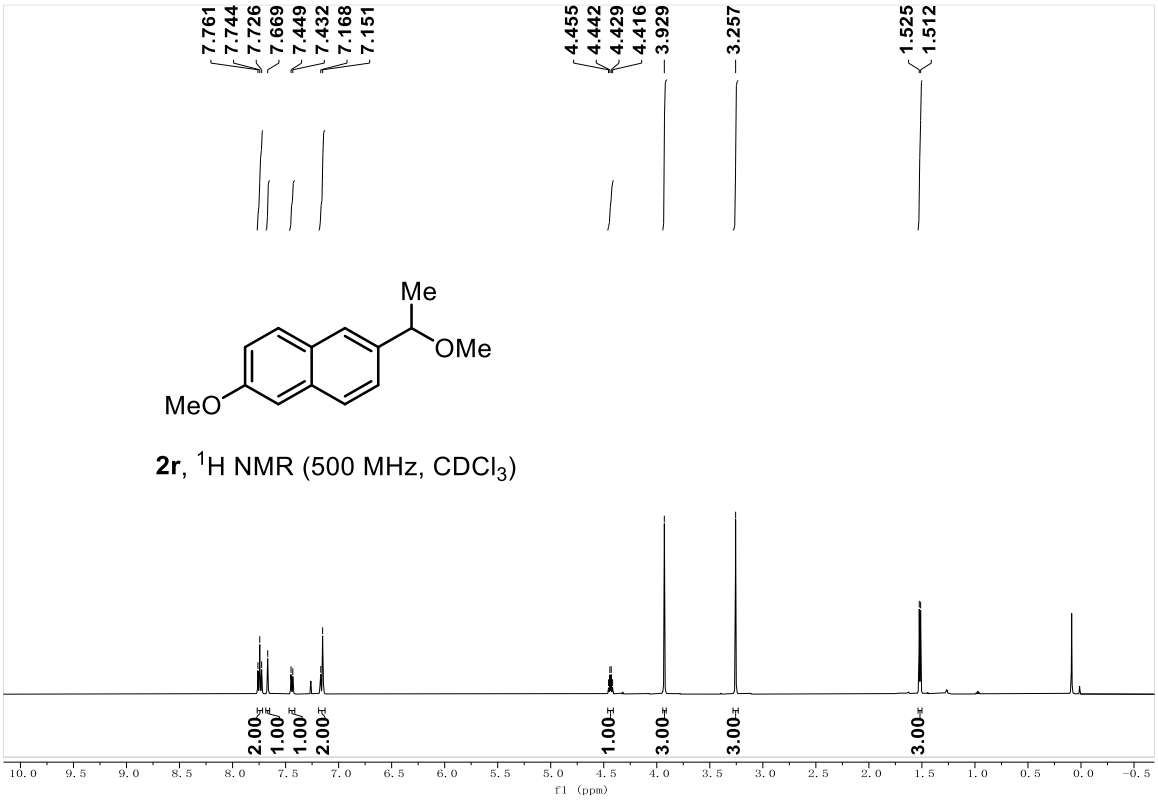
Ph–S–OMe

2q, ^{1}H NMR (500 MHz, $CDCl_3$)

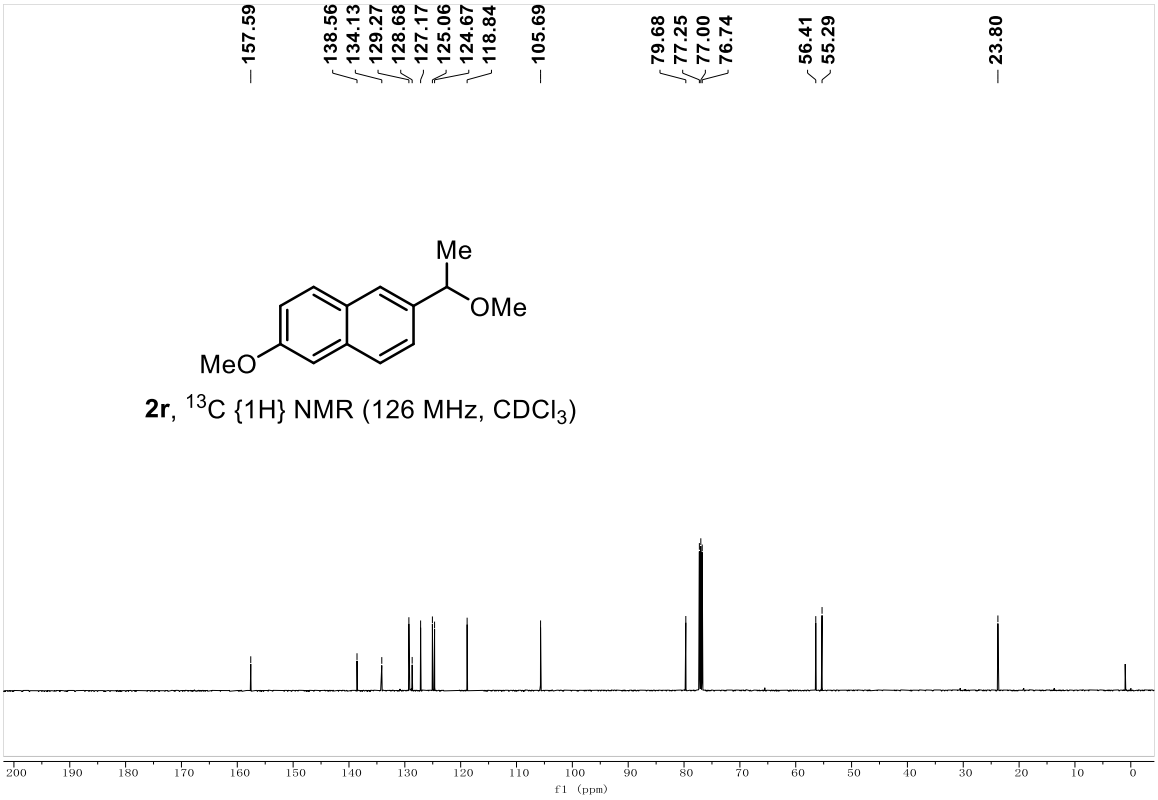


Ph–S–OMe

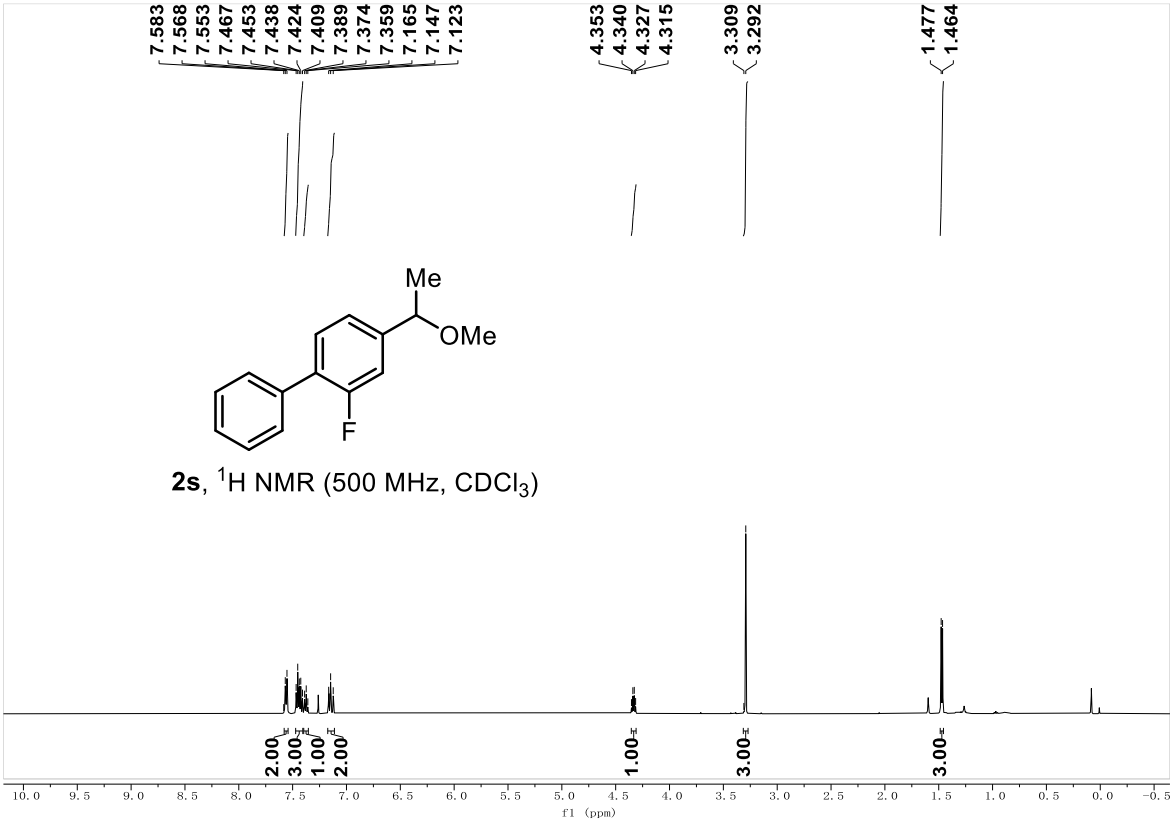
2q, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



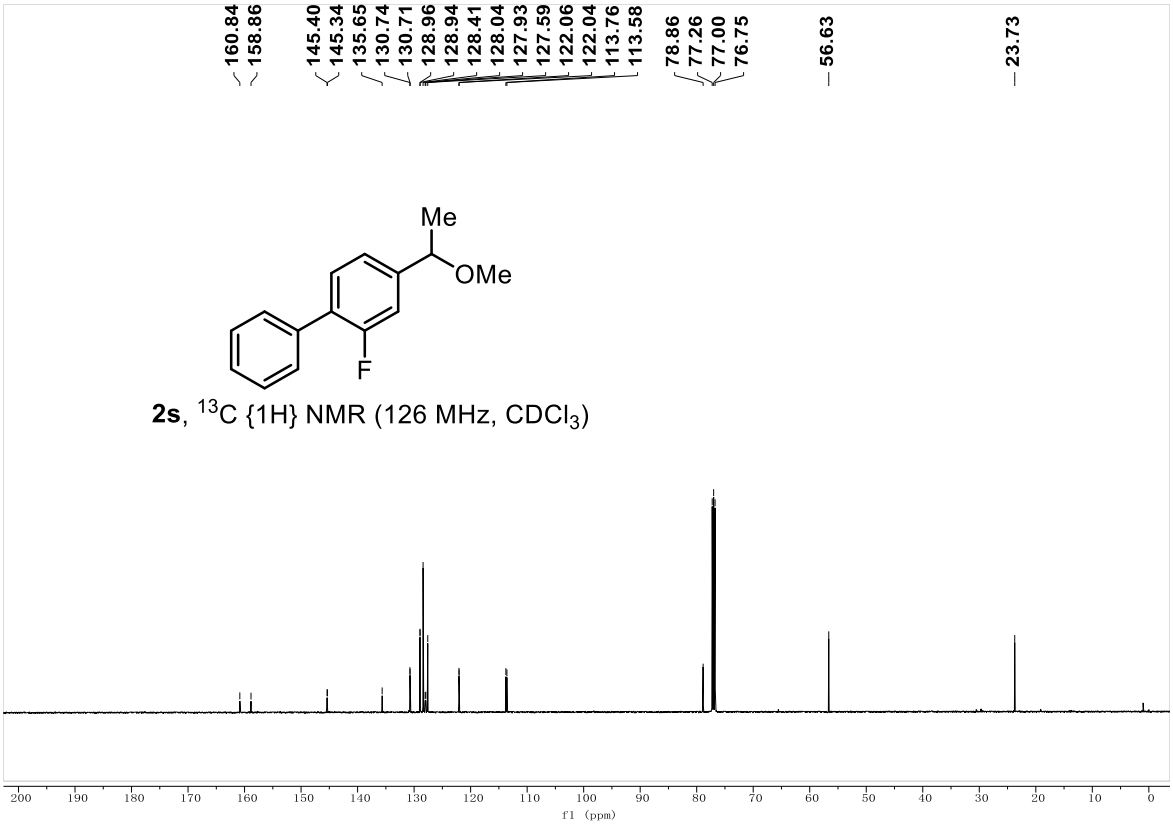
2r, ^{1}H NMR (500 MHz, $CDCl_3$)



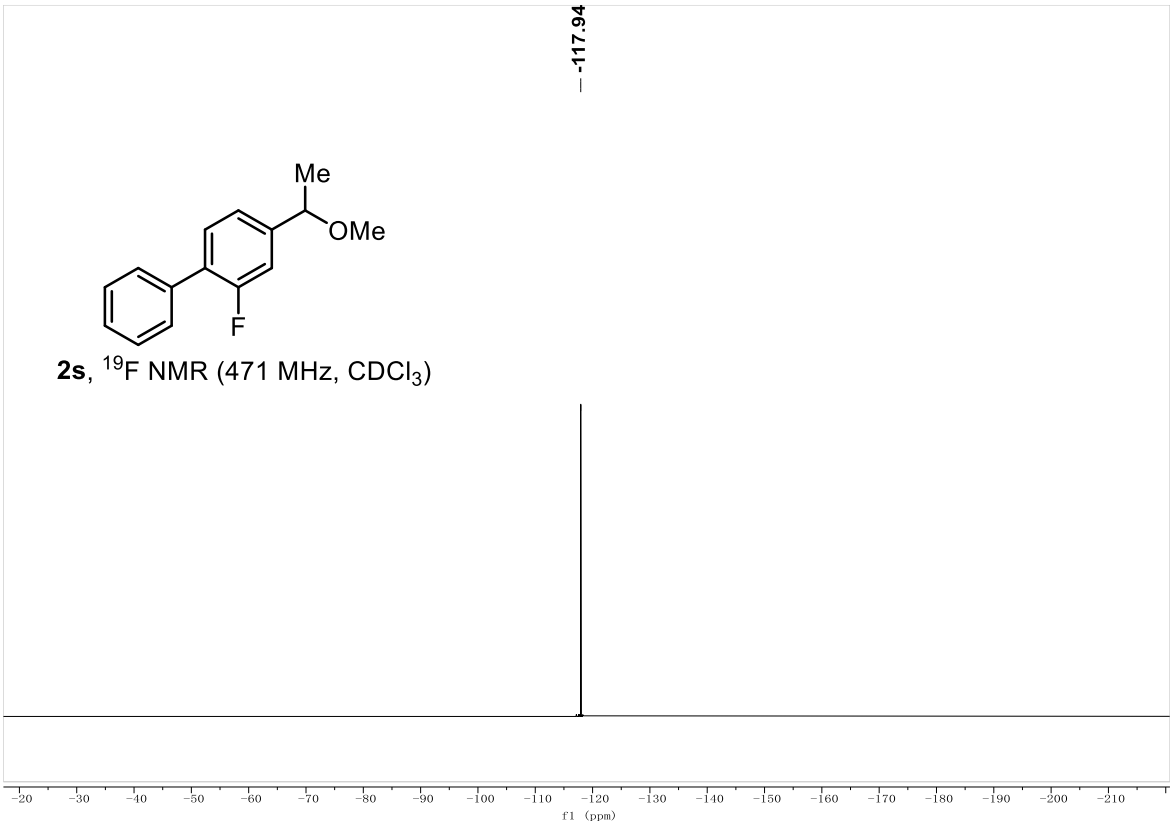
2r, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



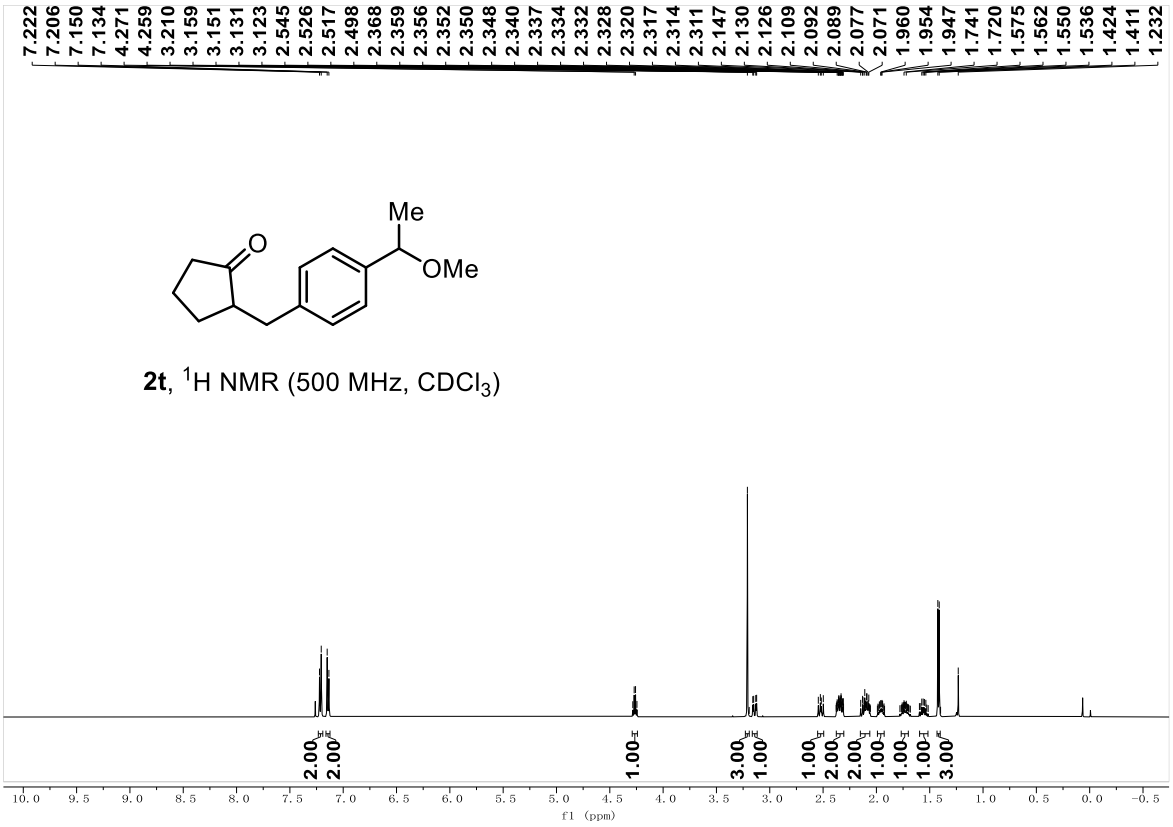
2s, ^{1}H NMR (500 MHz, $CDCl_3$)



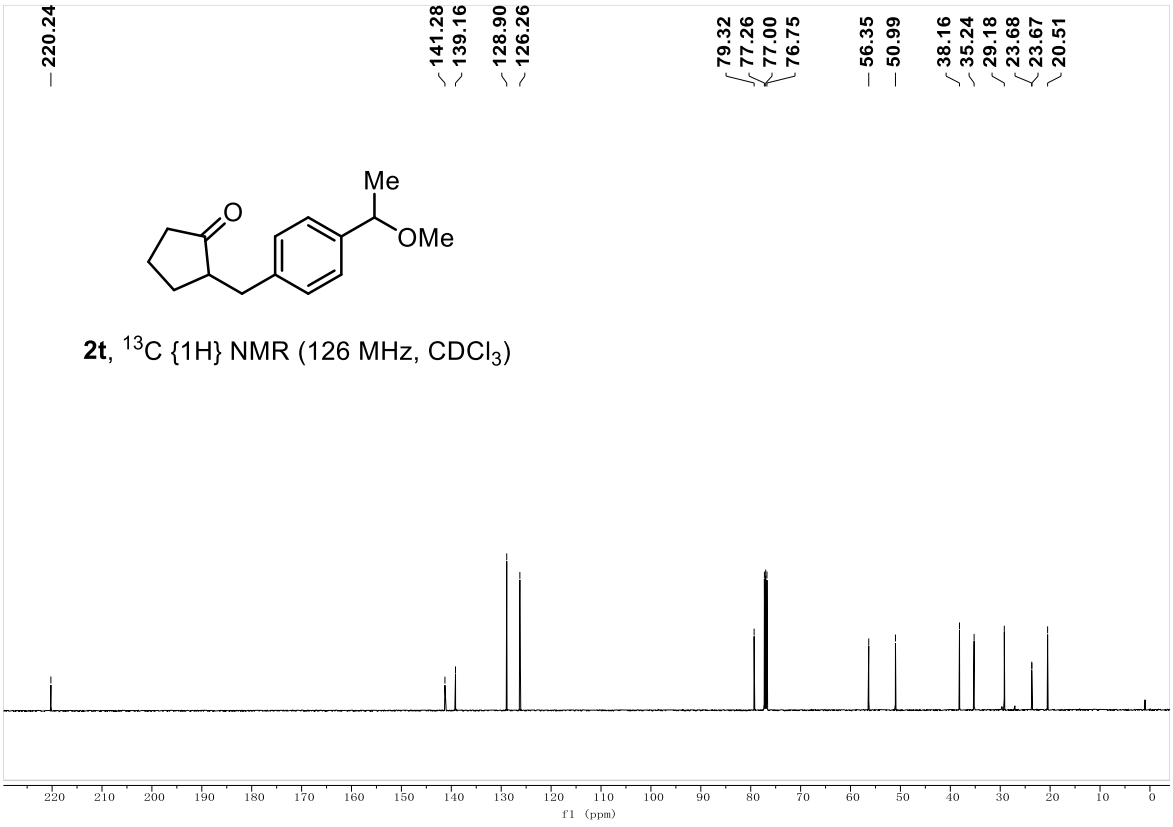
2s, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



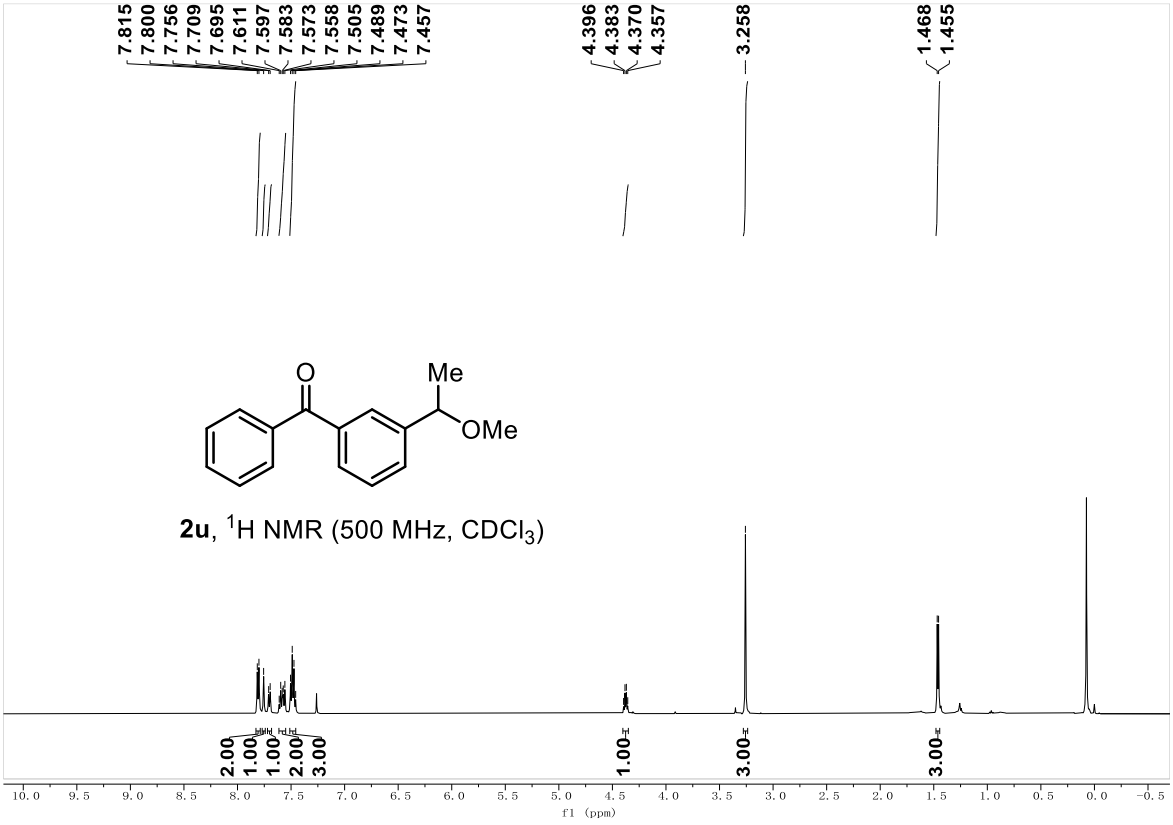
2s, ^{19}F NMR (471 MHz, $CDCl_3$)



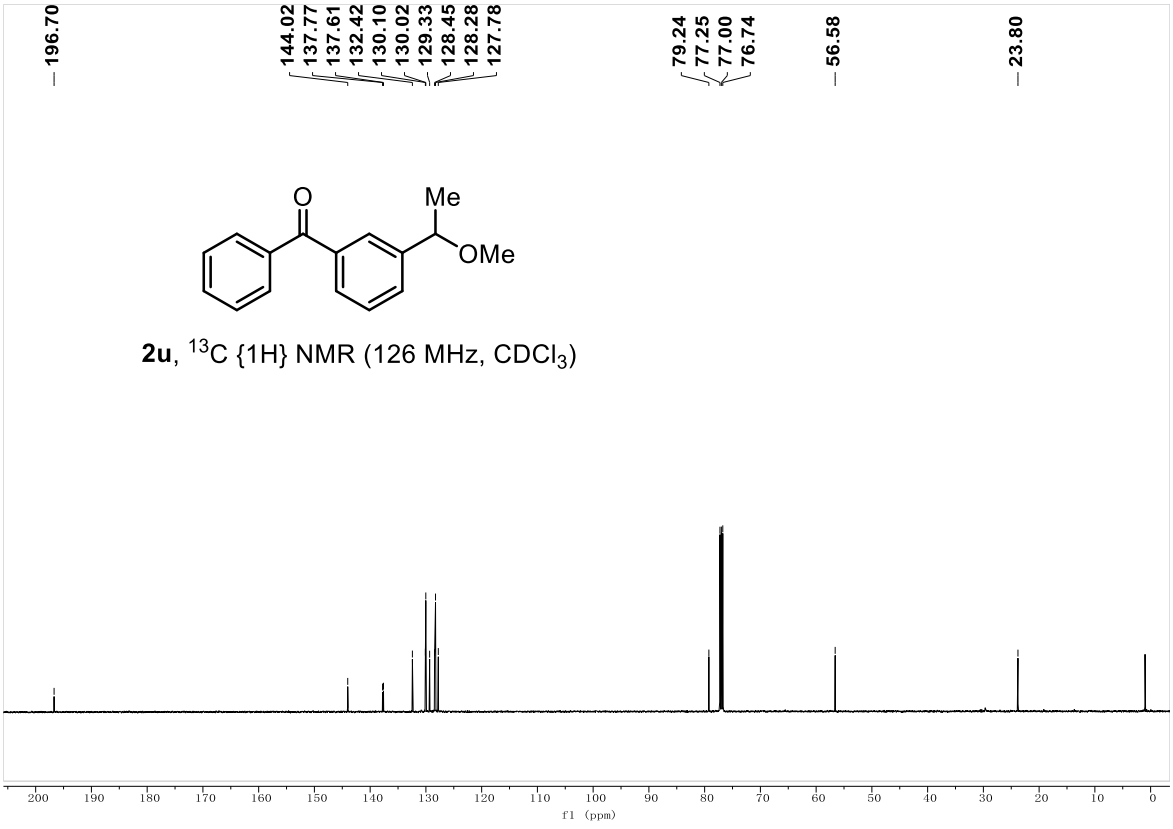
2t, ^{1}H NMR (500 MHz, $CDCl_3$)



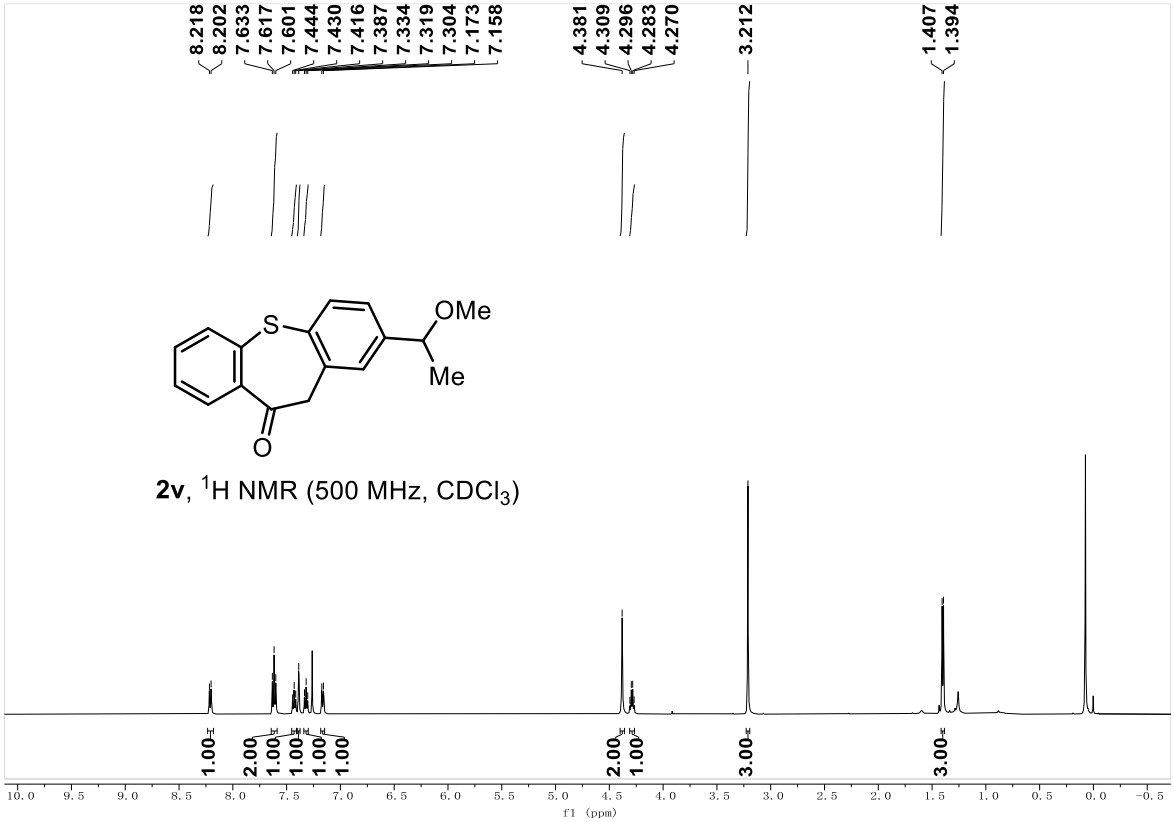
2t, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



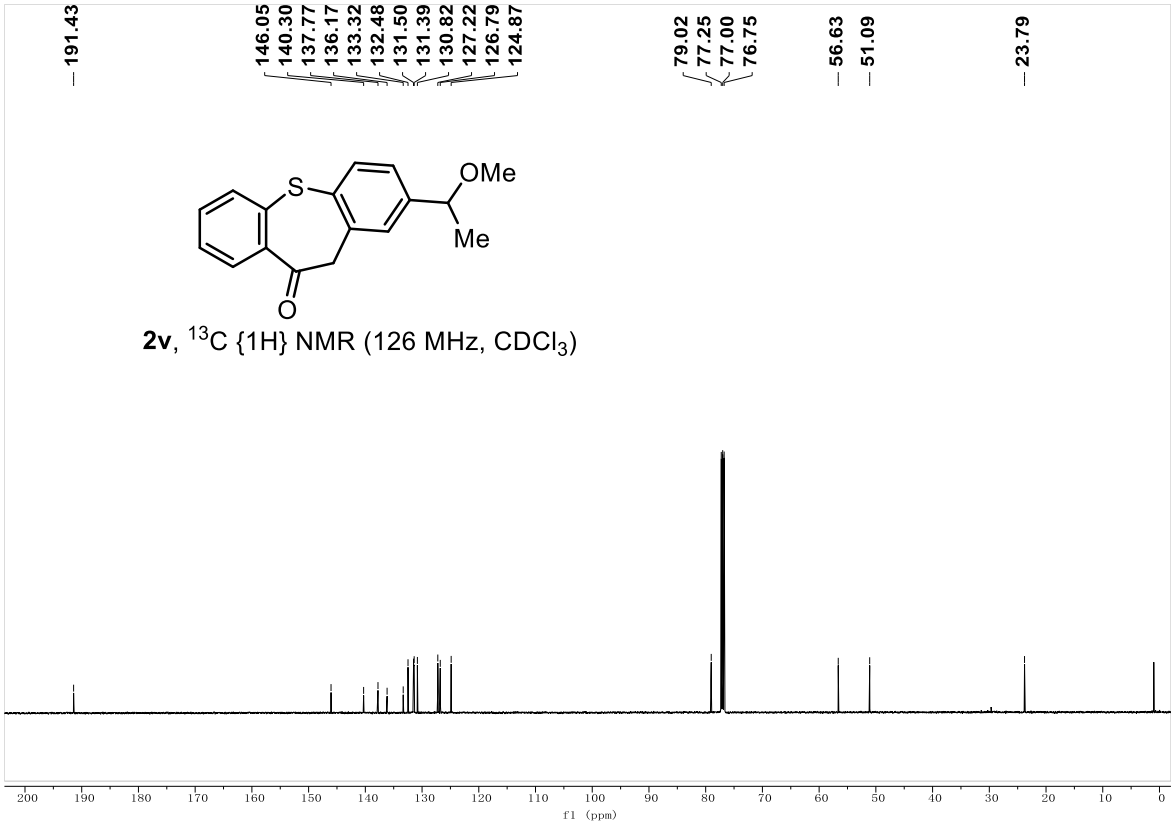
2u, ^{1}H NMR (500 MHz, $CDCl_3$)



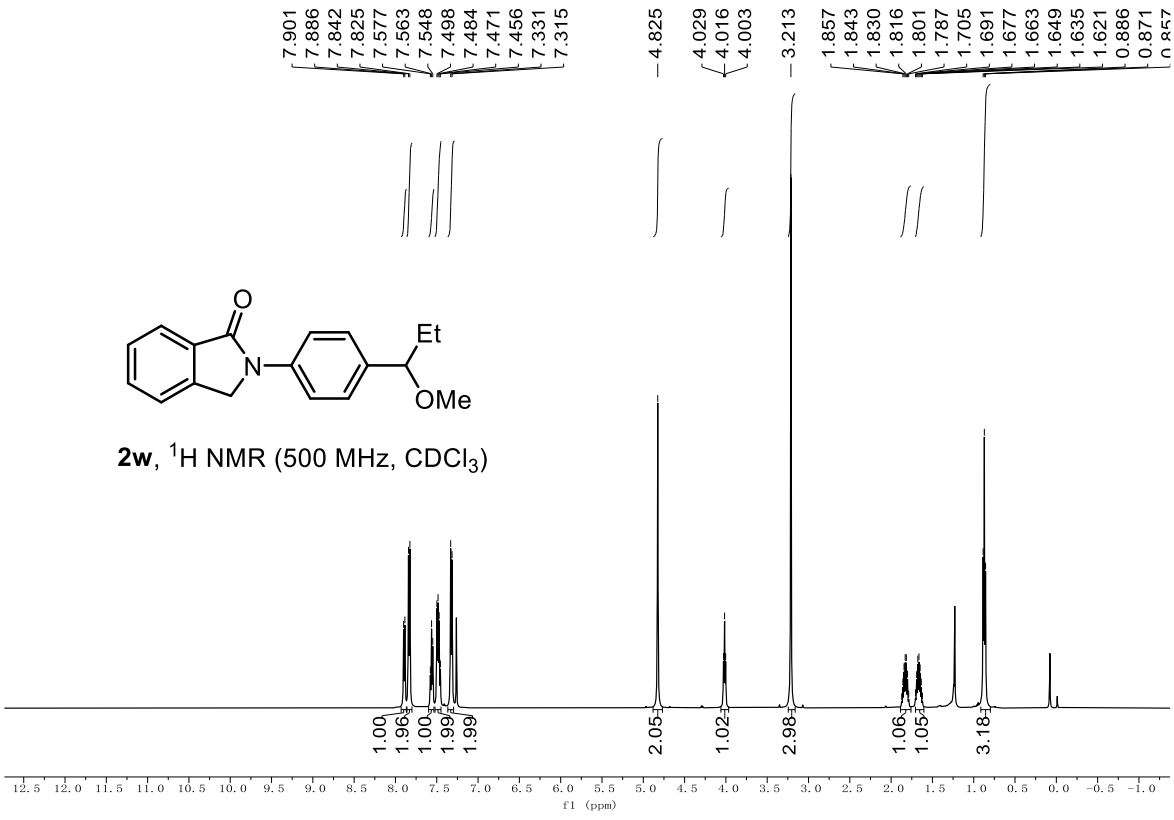
2u, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



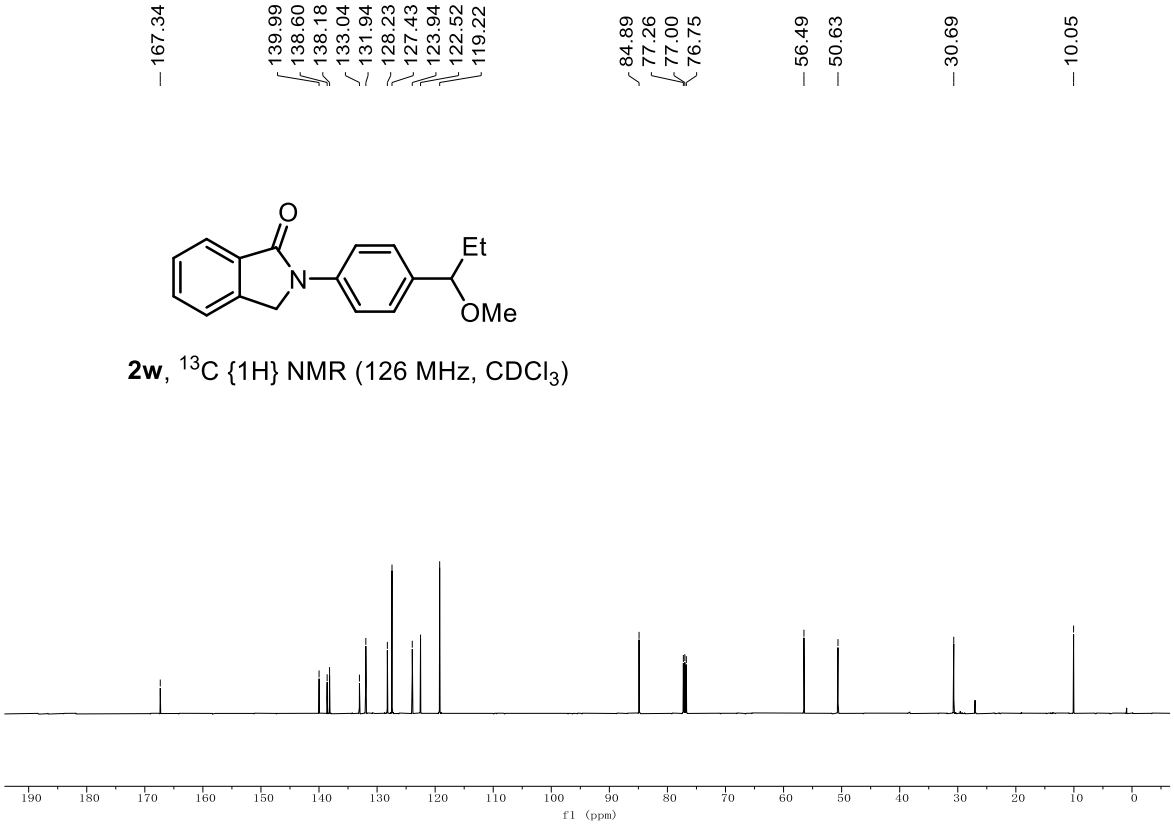
2v, ^{1}H NMR (500 MHz, $CDCl_3$)



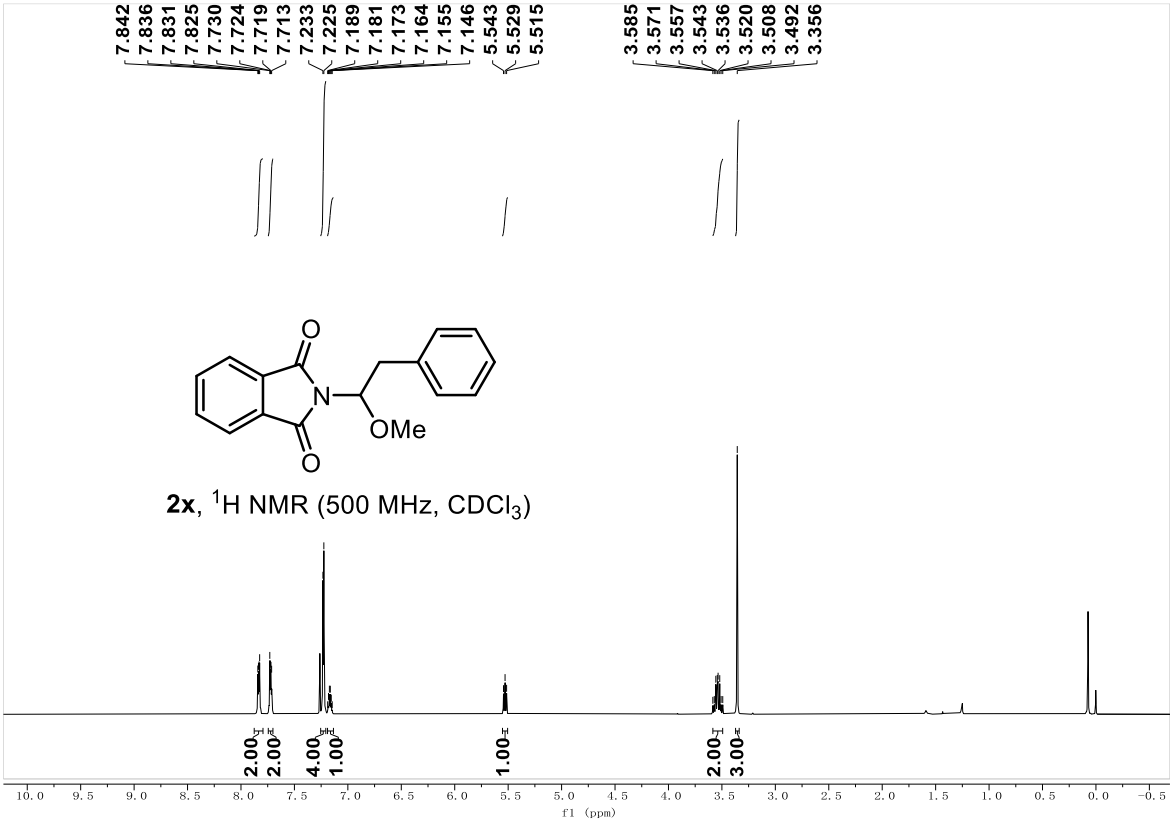
2v, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



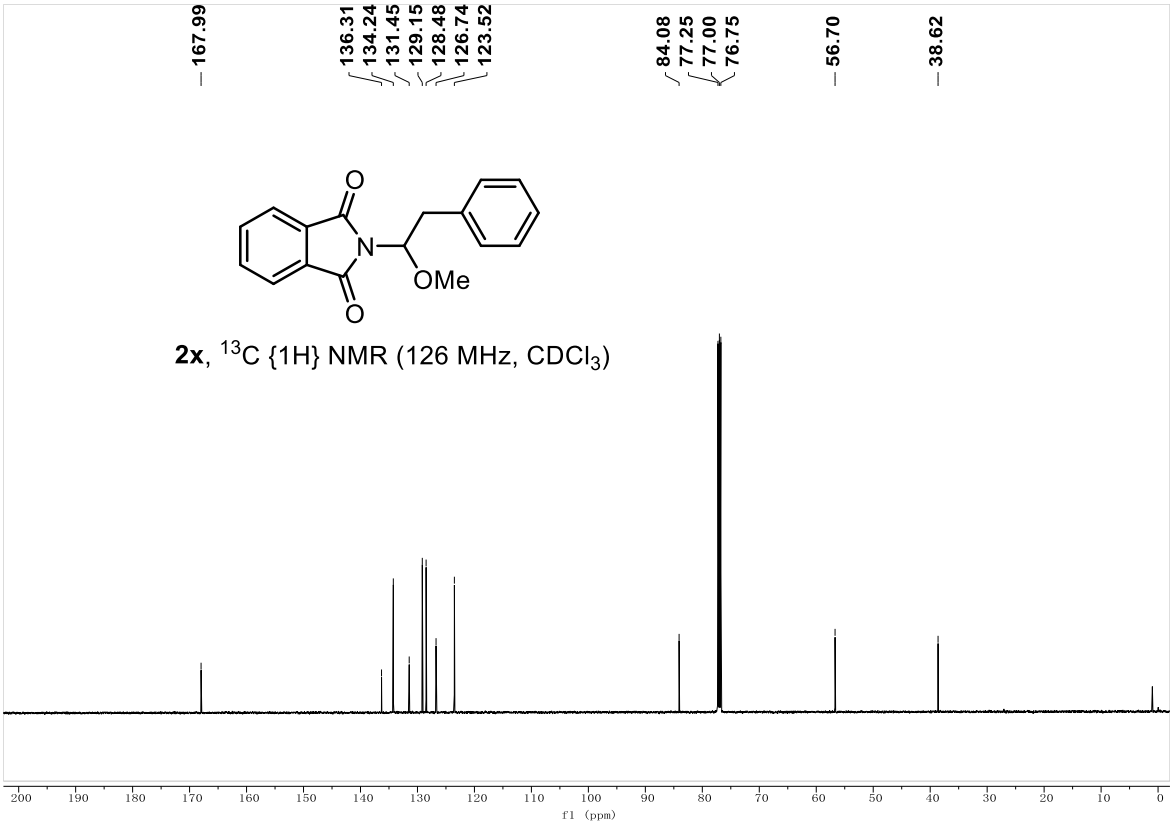
2w, ^{1}H NMR (500 MHz, $CDCl_3$)



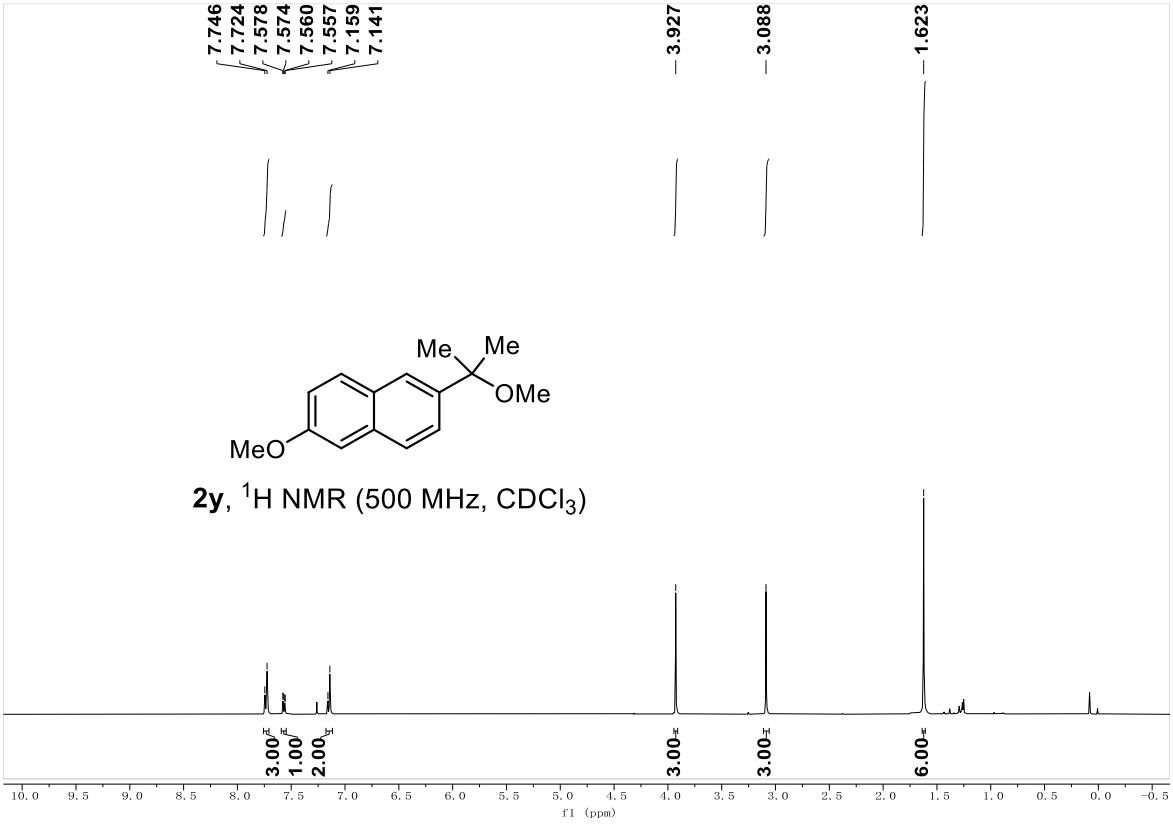
2w, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



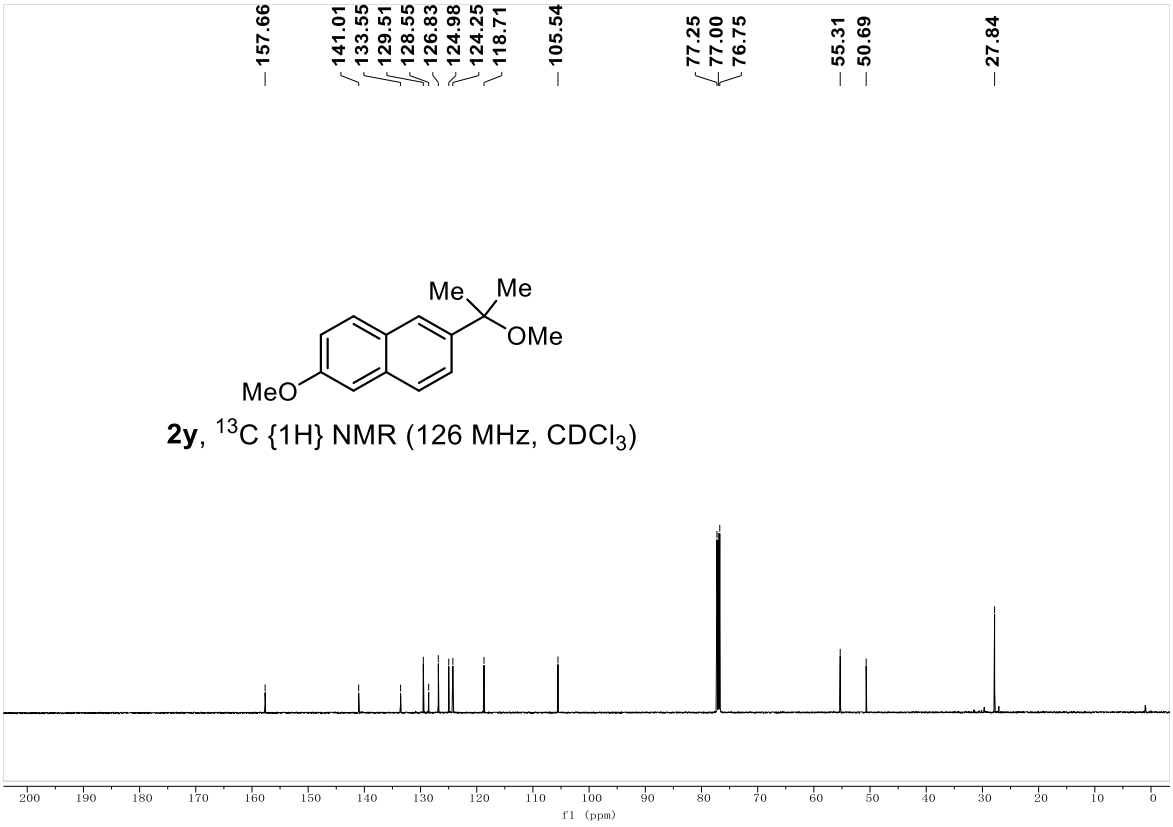
2x, ^{1}H NMR (500 MHz, $CDCl_3$)



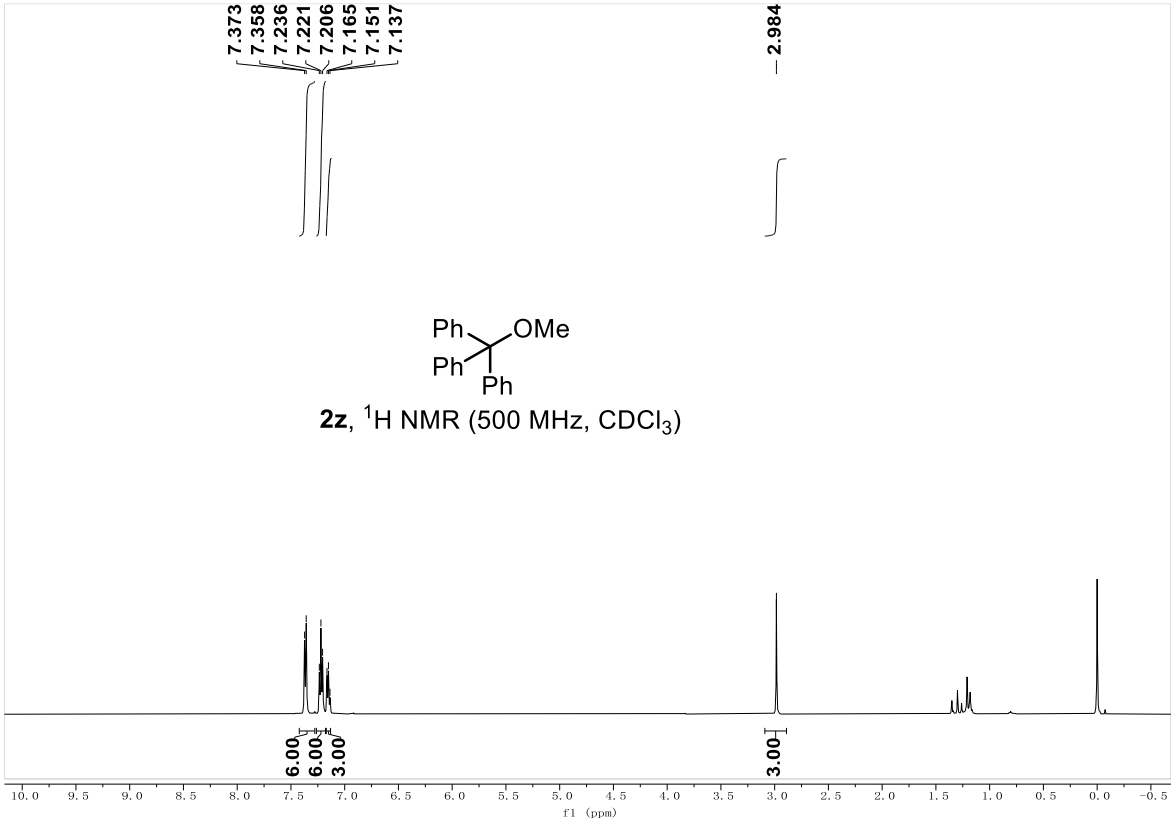
2x, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



2y, ^{1}H NMR (500 MHz, $CDCl_3$)

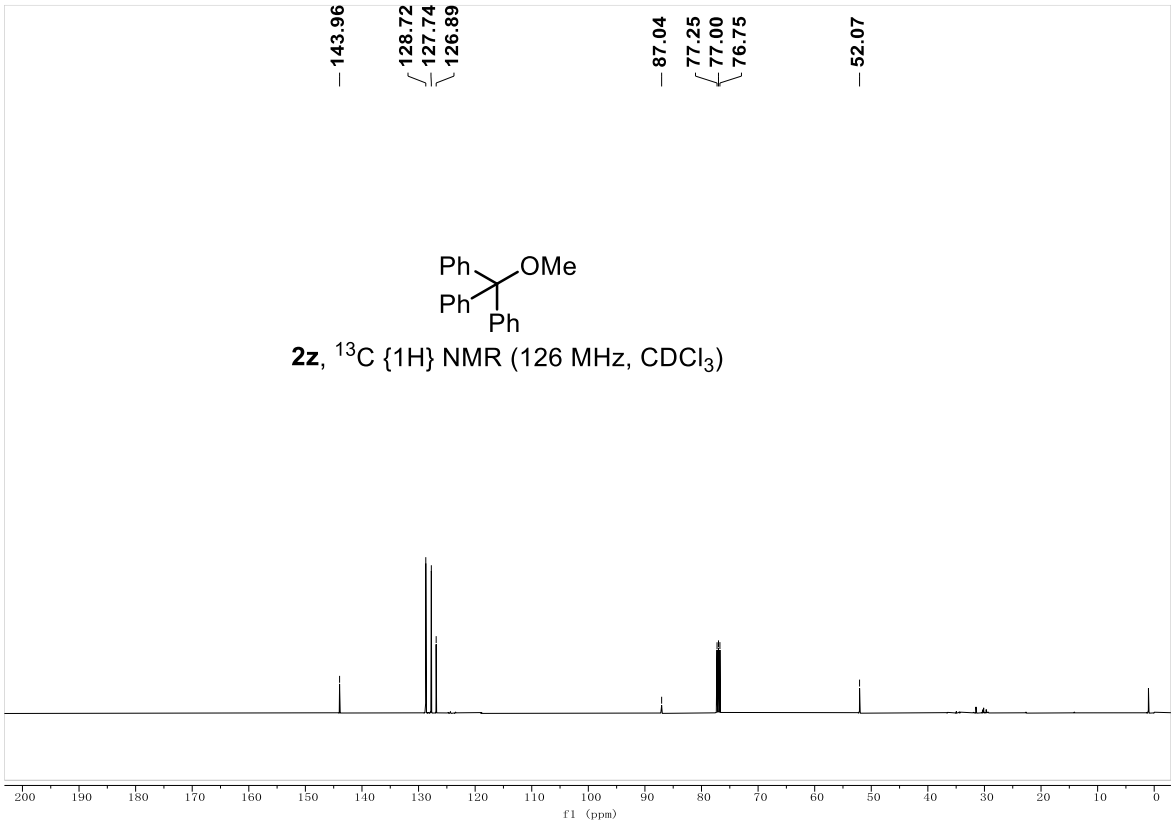


2y, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



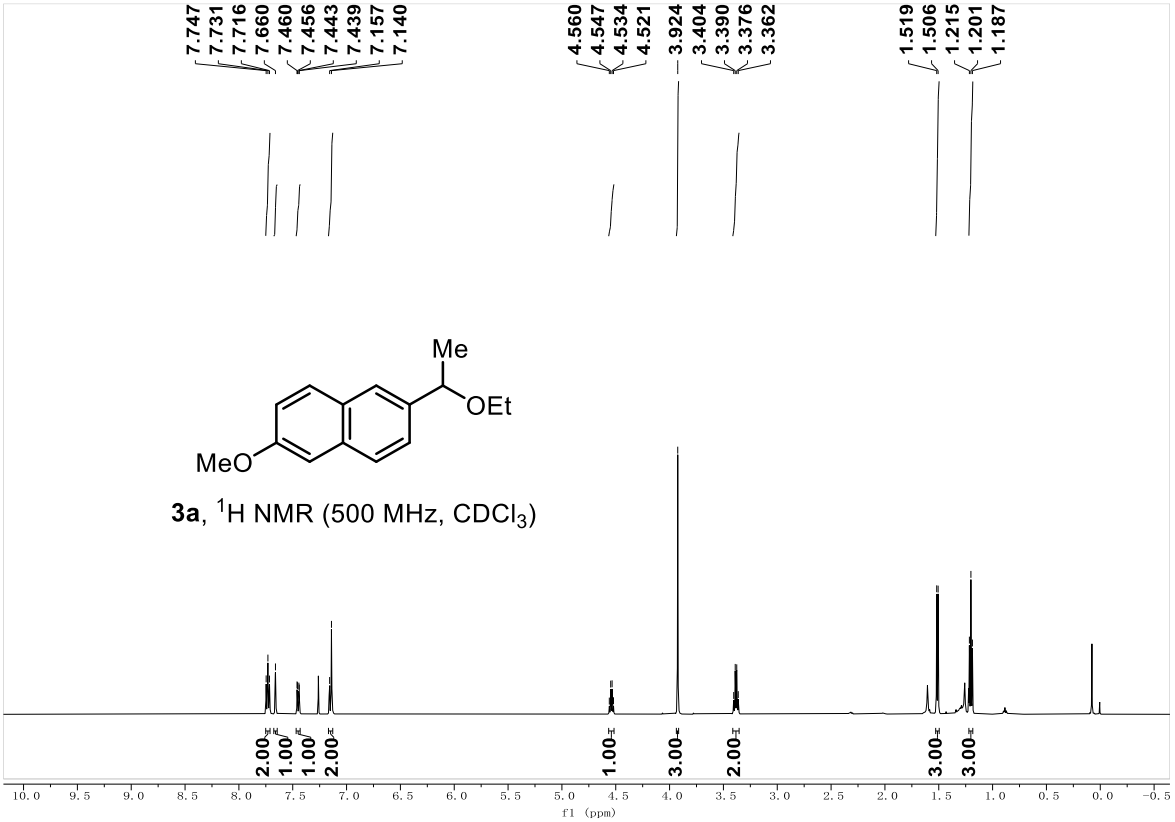
Ph, OMe, Ph, Ph

2z, ^{1}H NMR (500 MHz, $CDCl_3$)

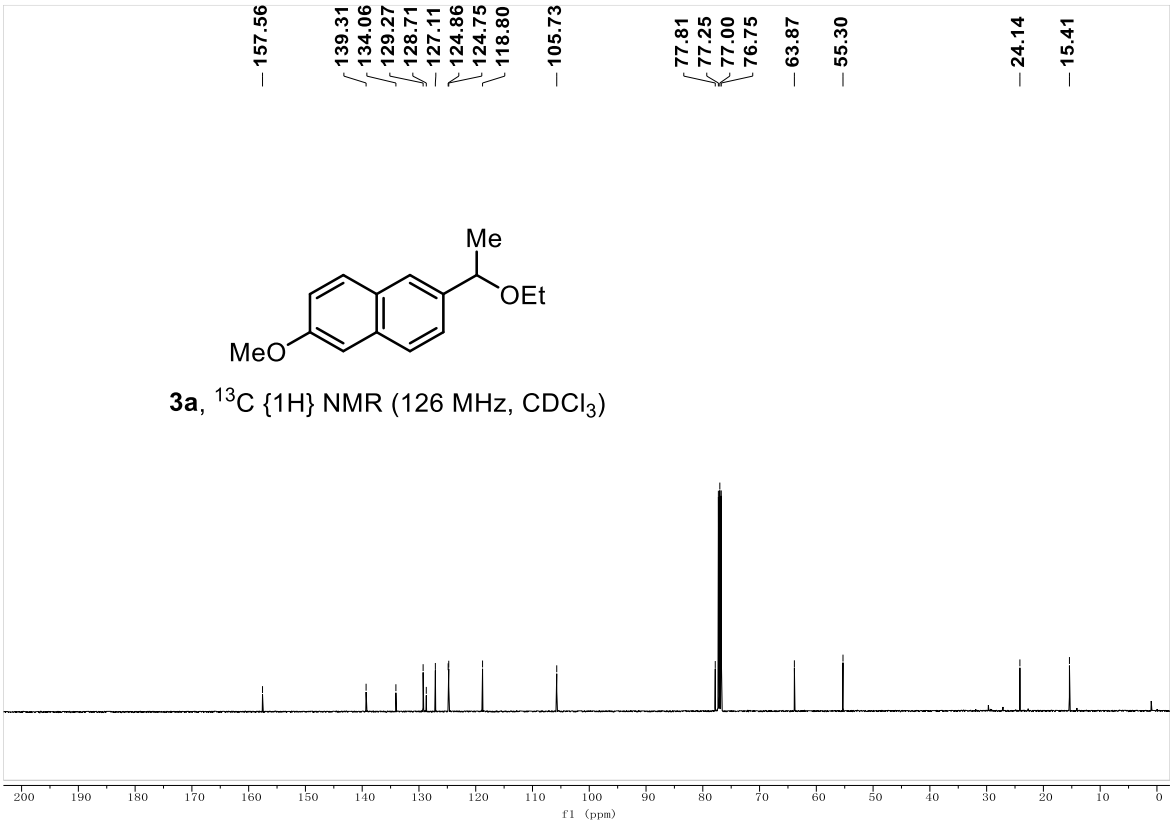


Ph, OMe, Ph, Ph

2z, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



3a, ^{1}H NMR (500 MHz, $CDCl_3$)



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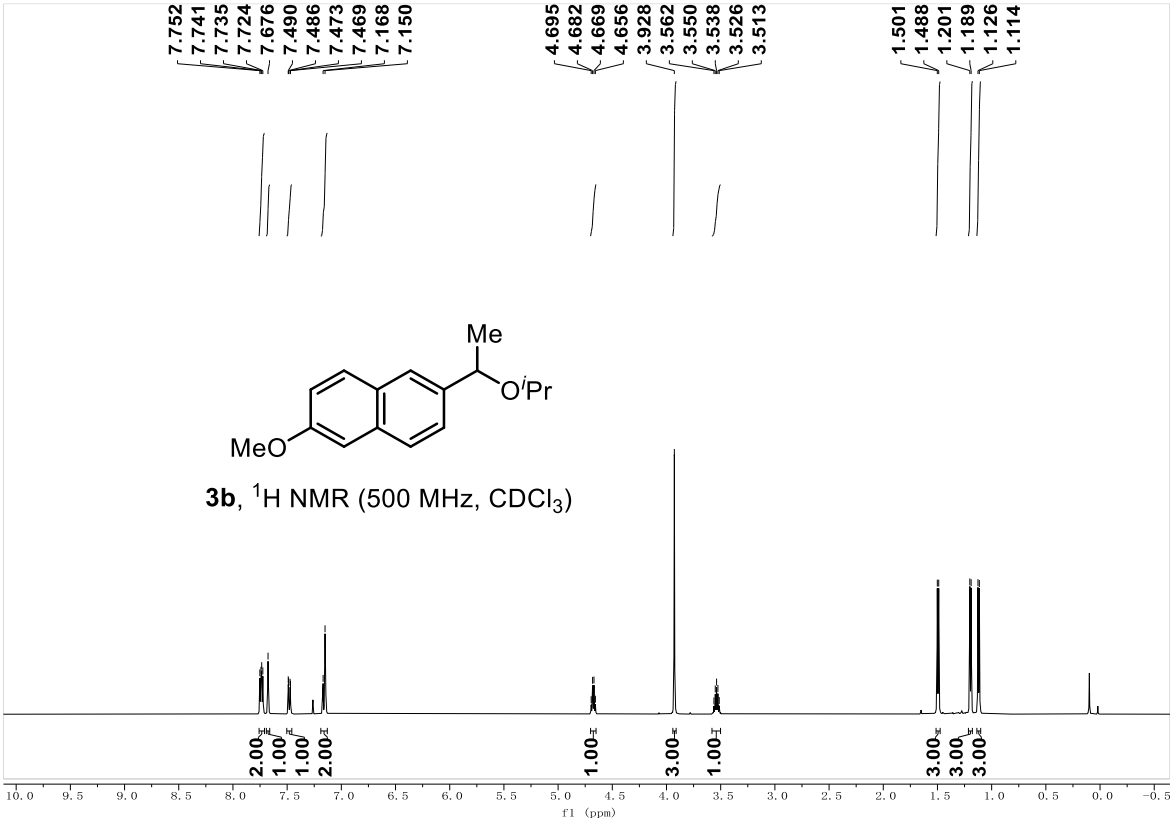

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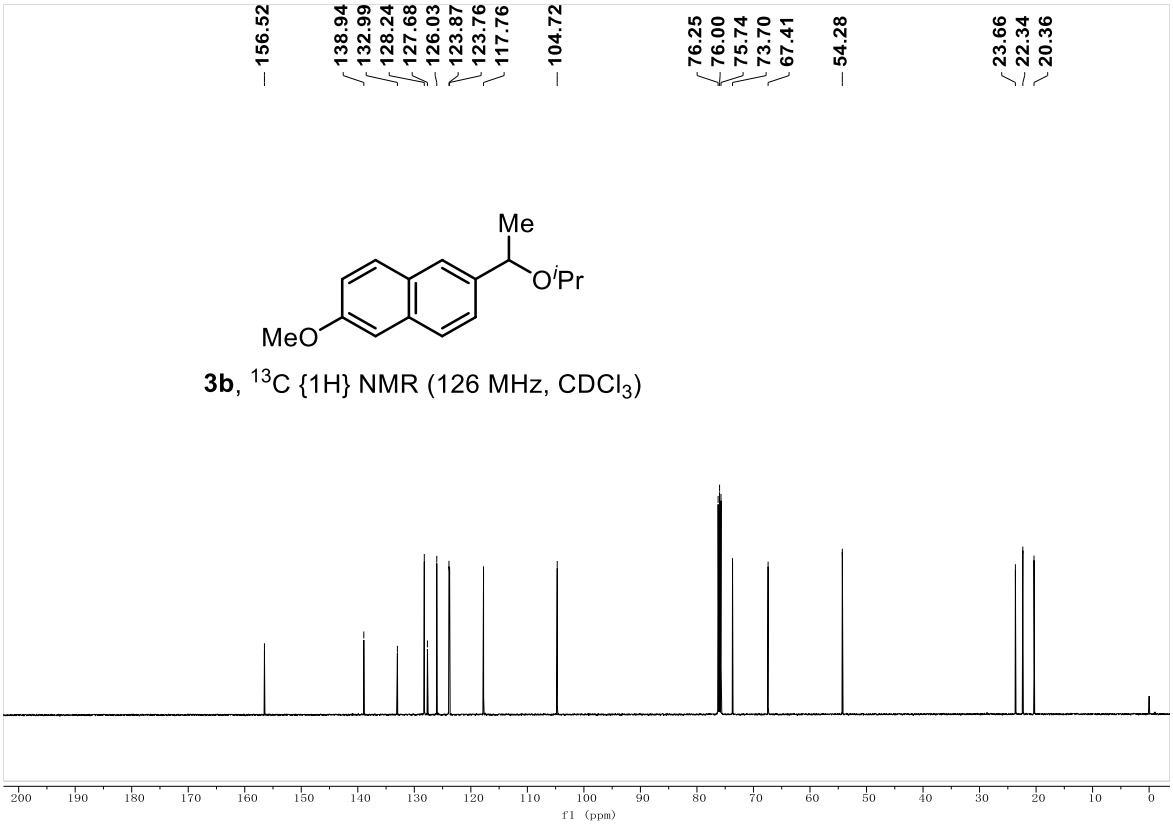

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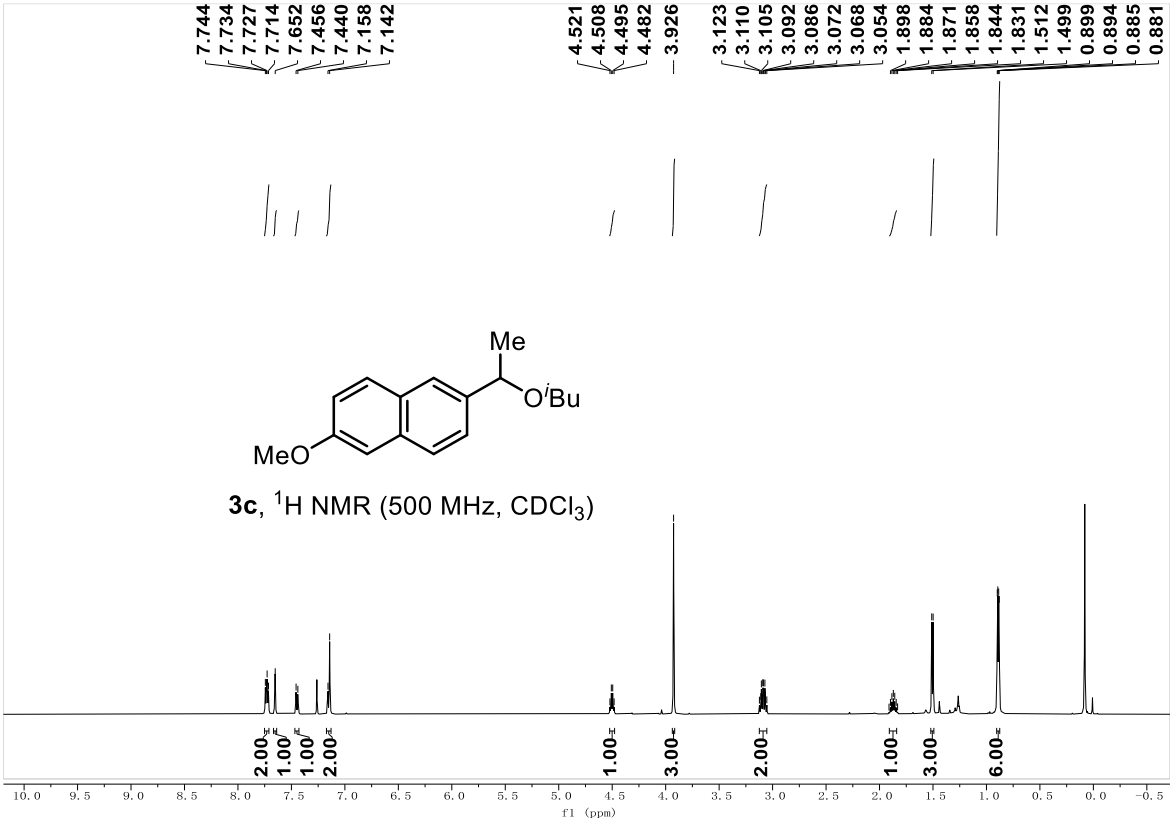

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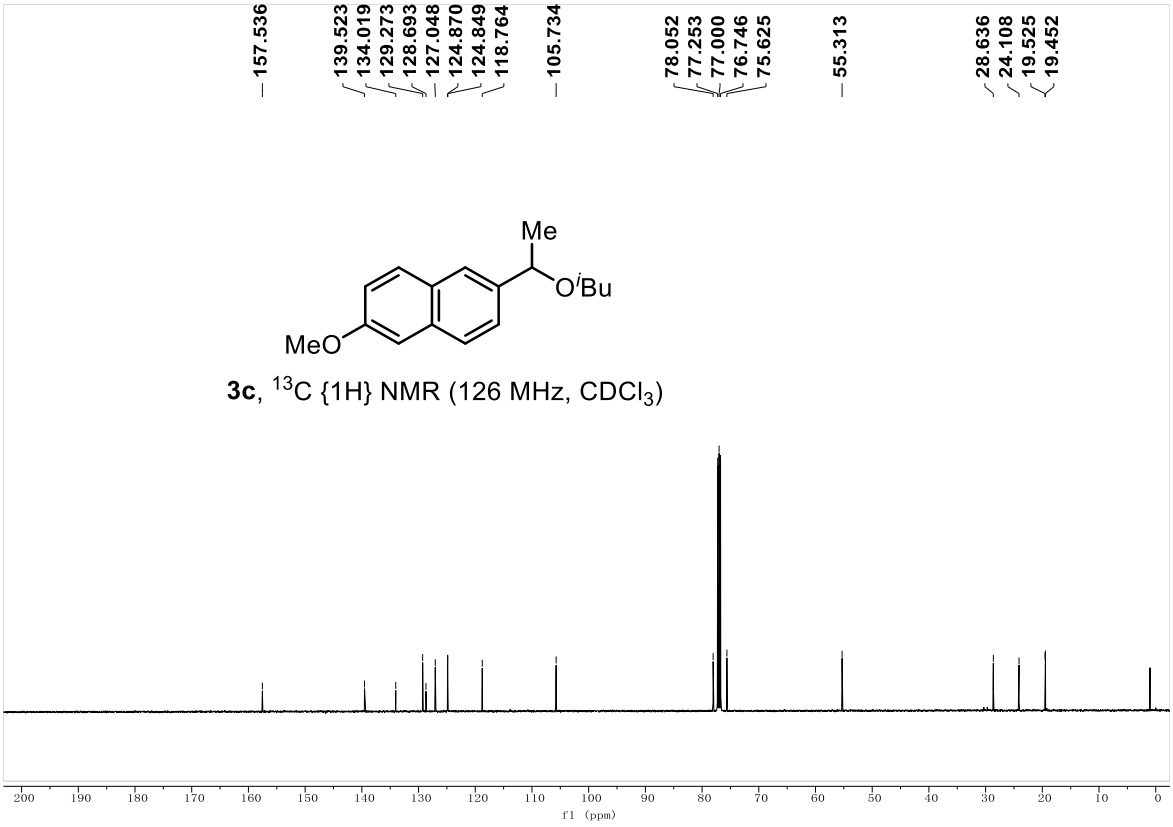

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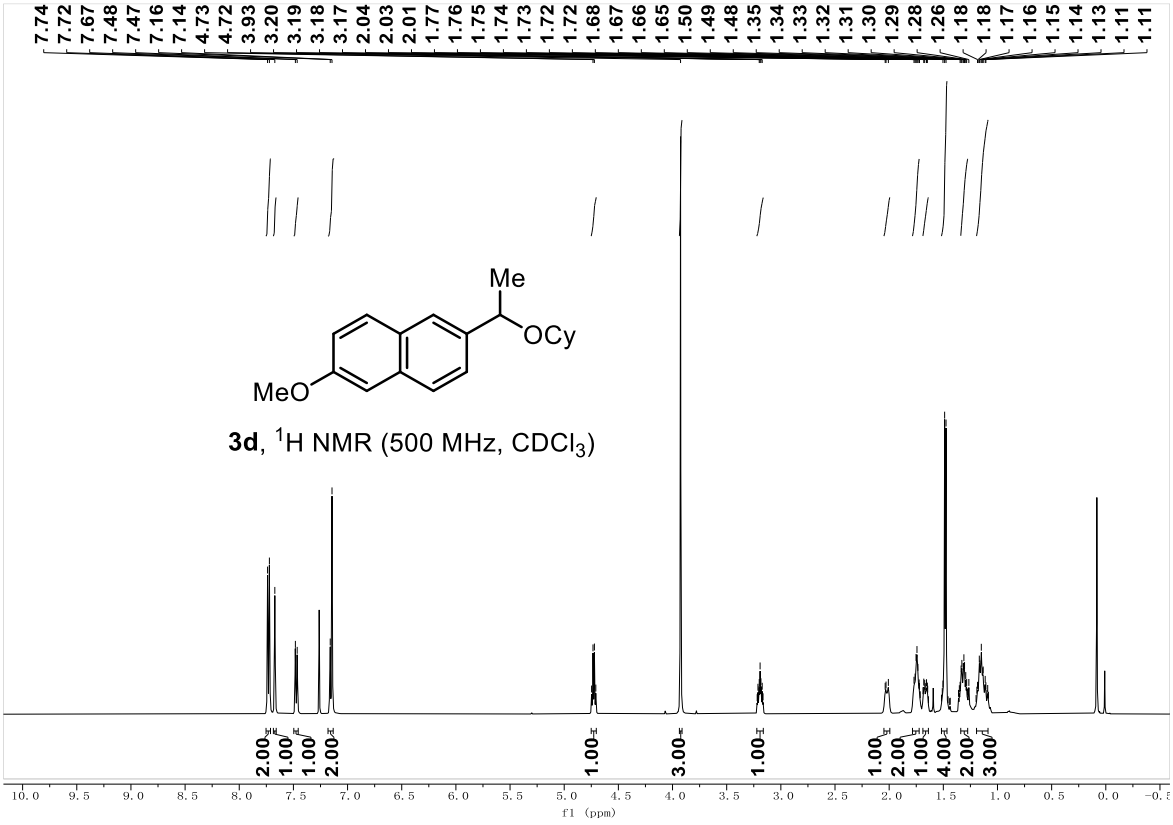

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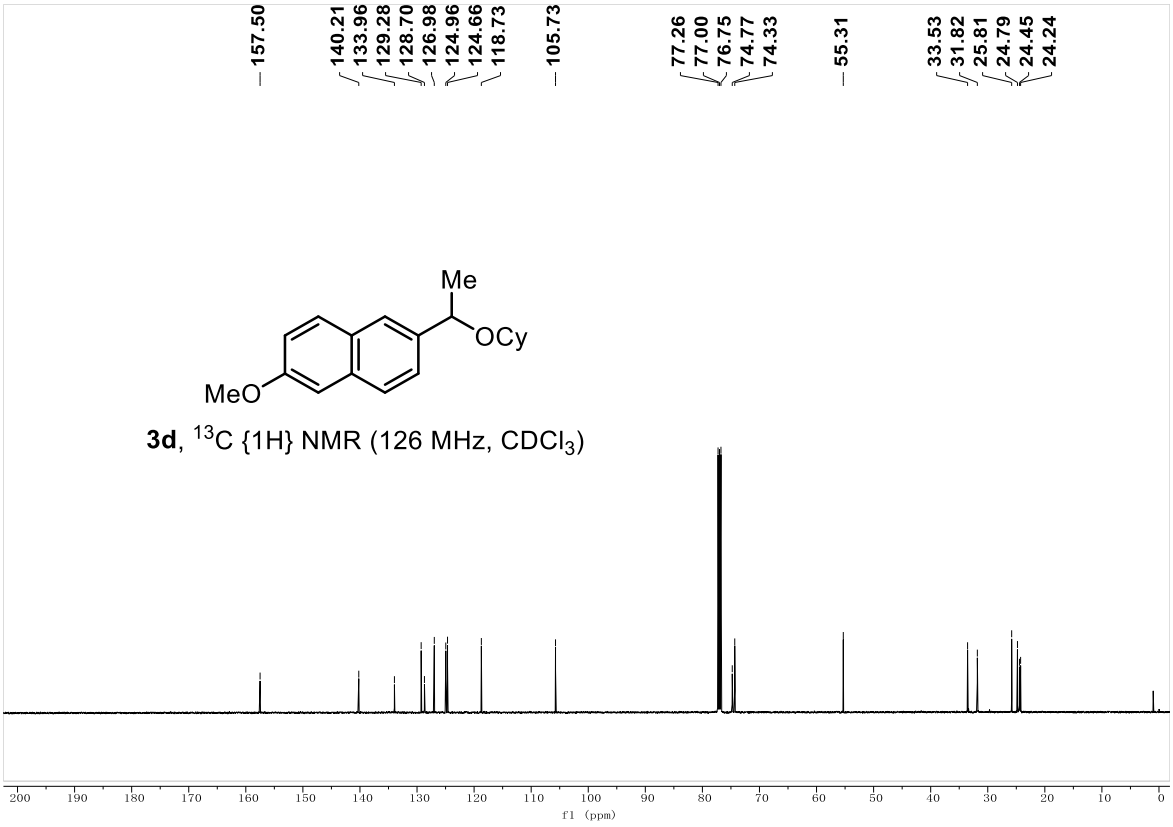

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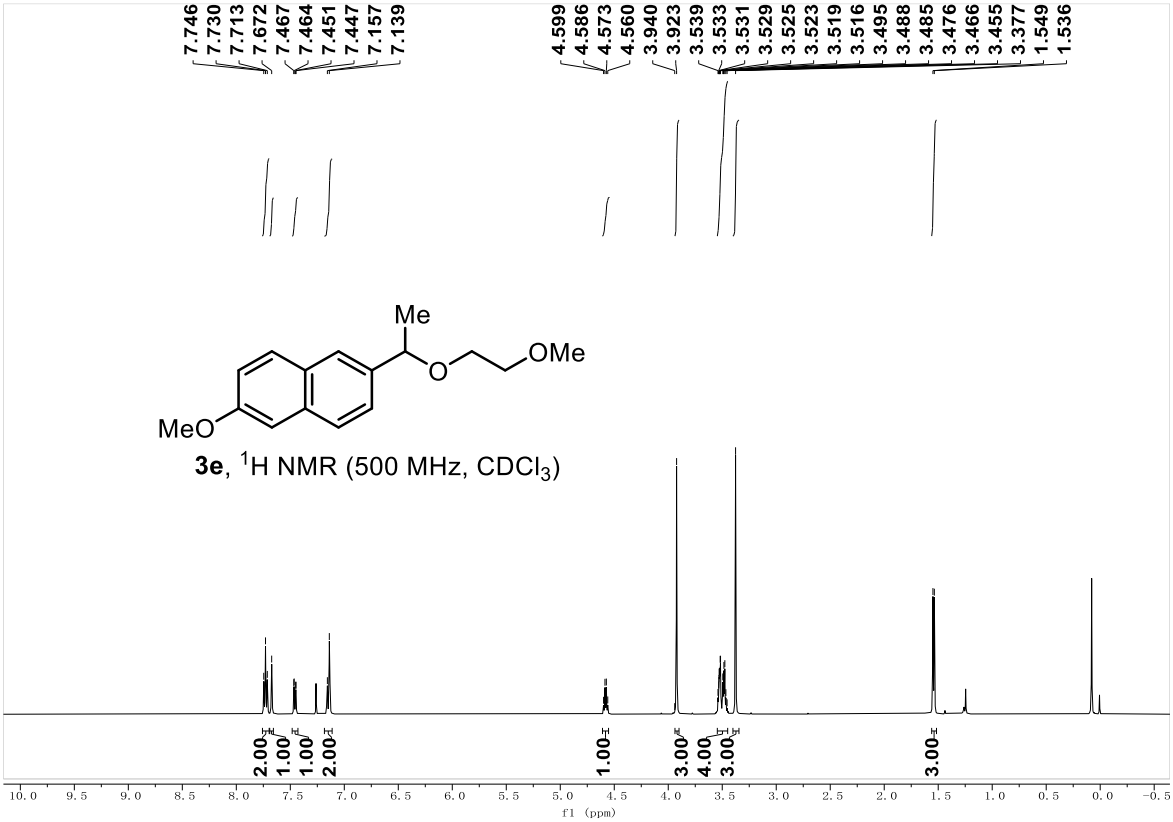

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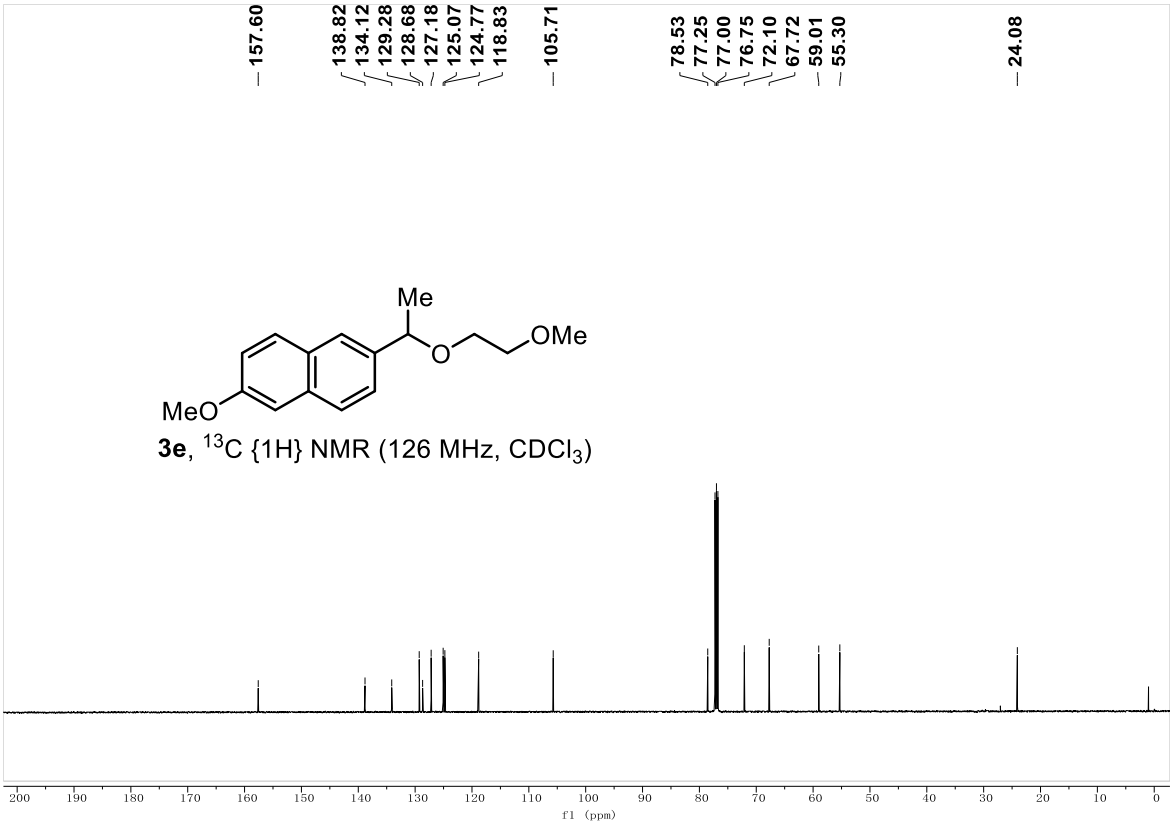

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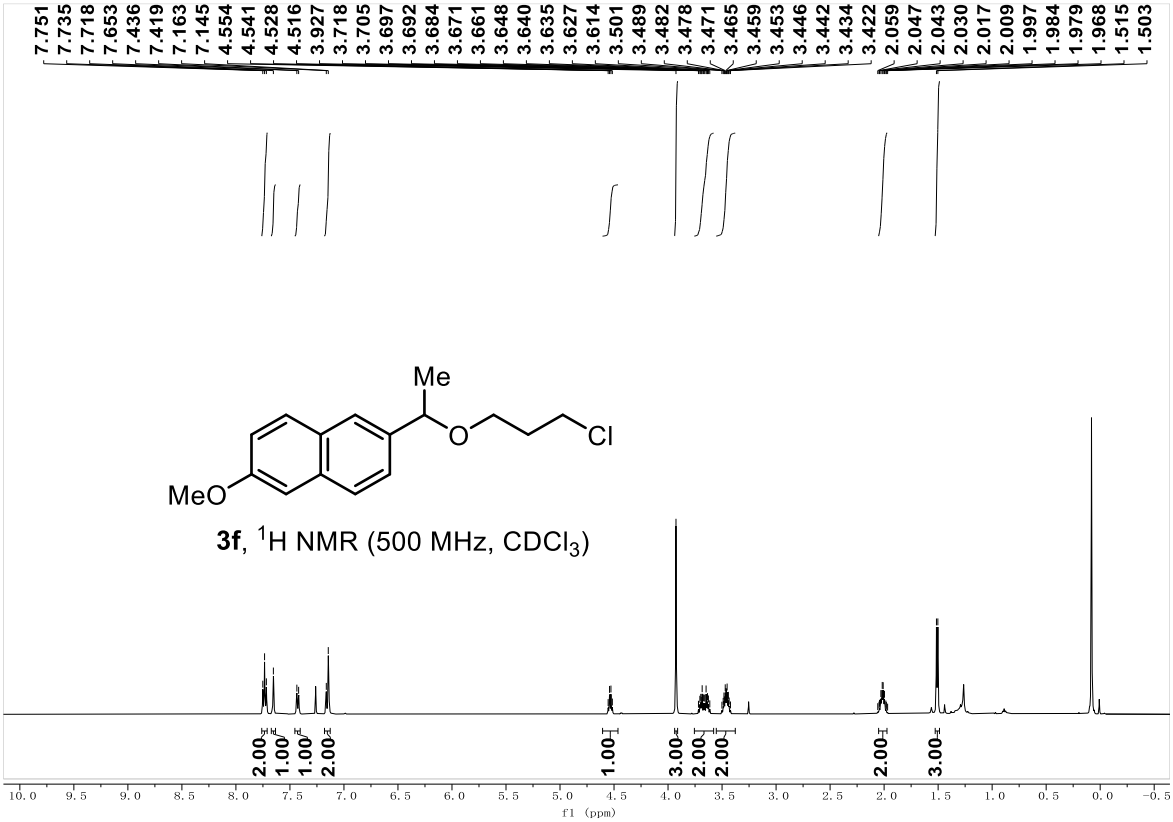

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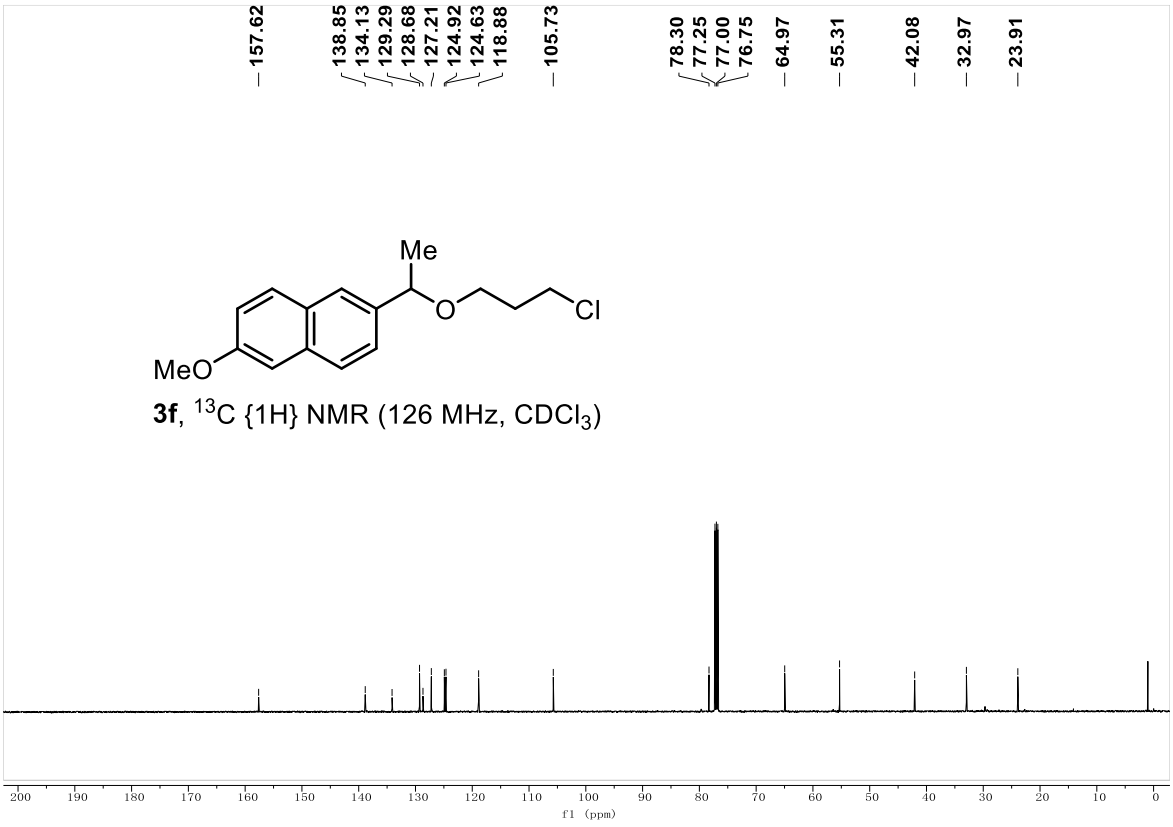

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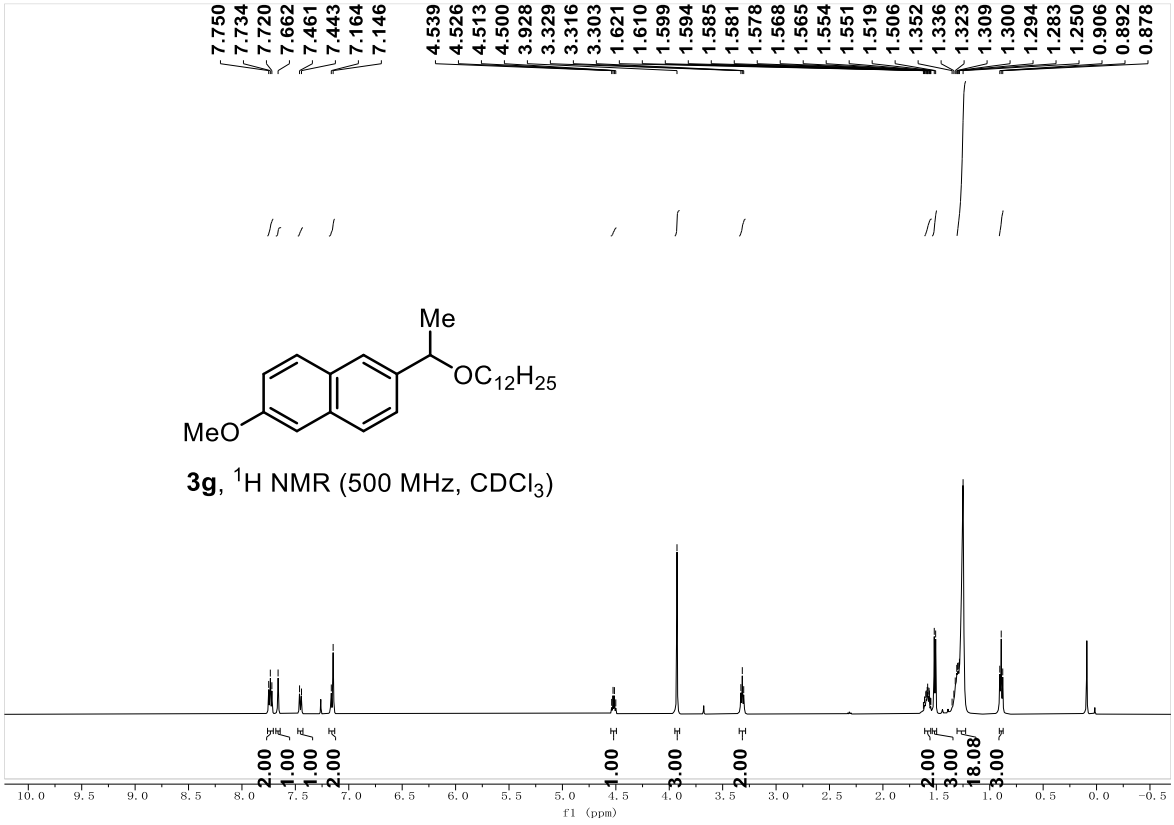

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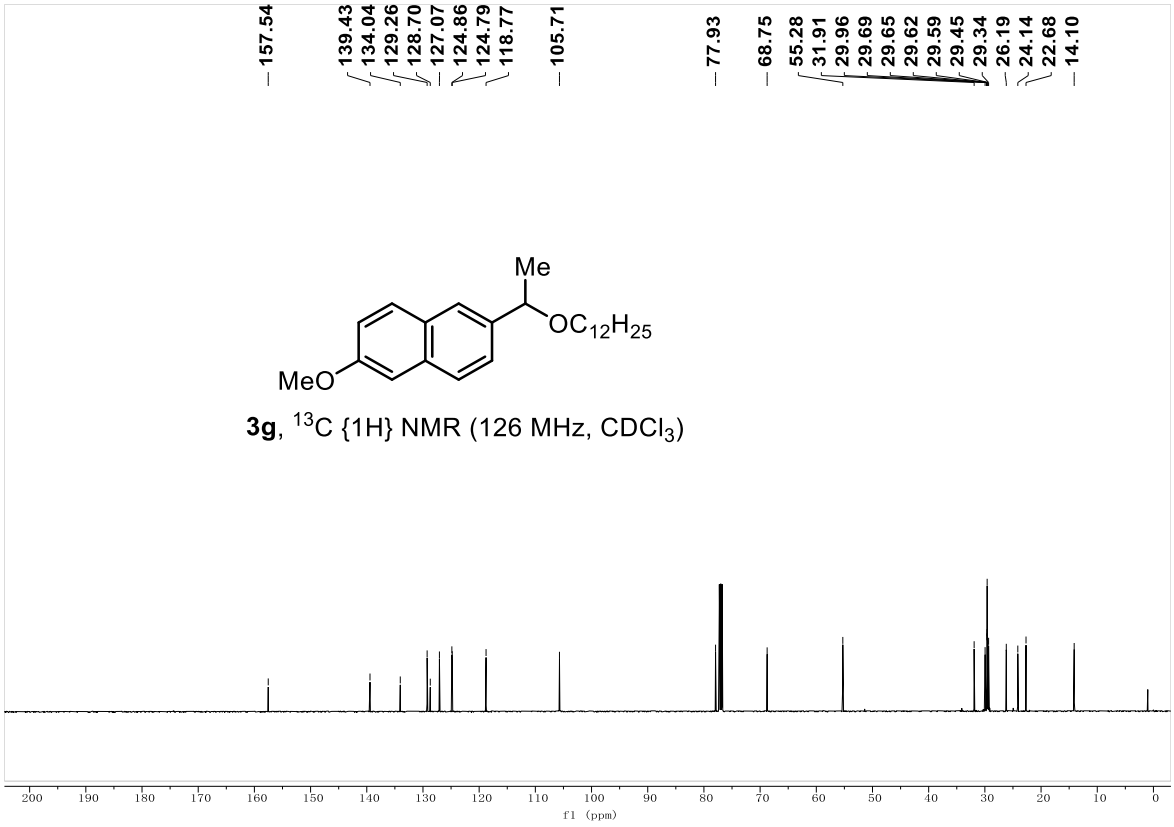

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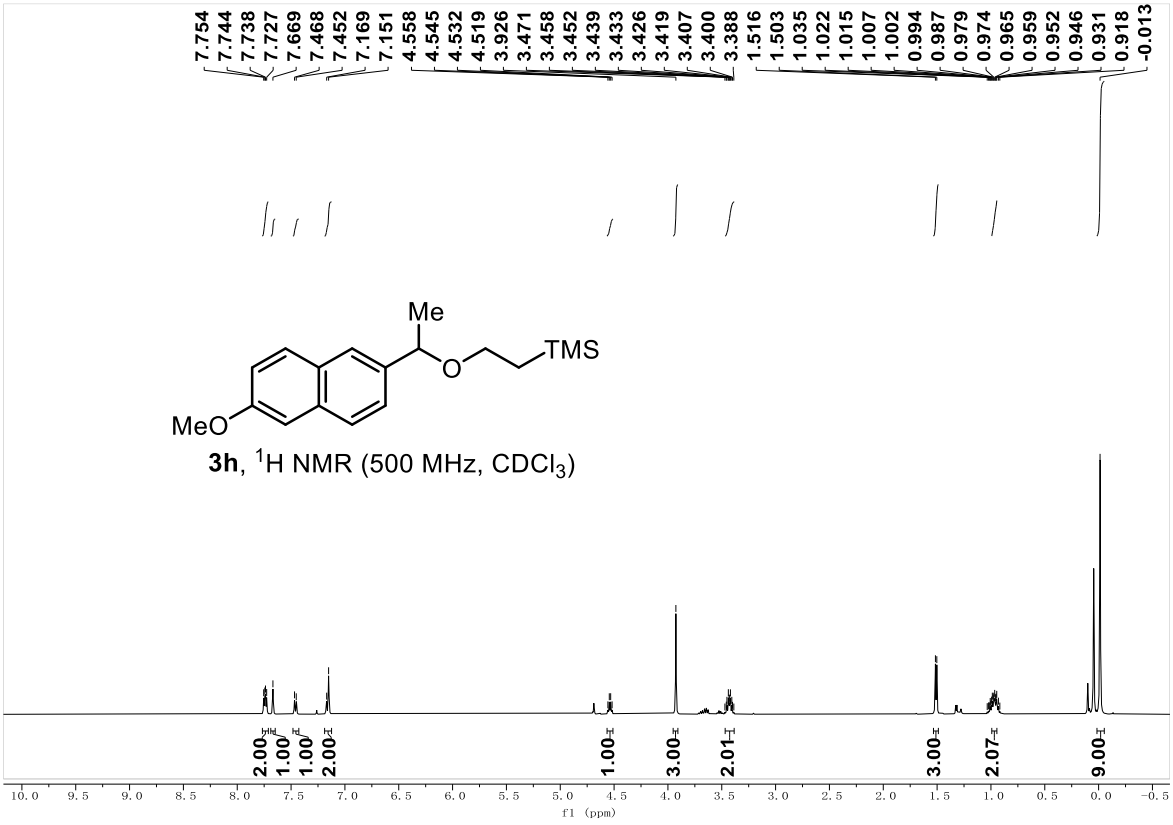

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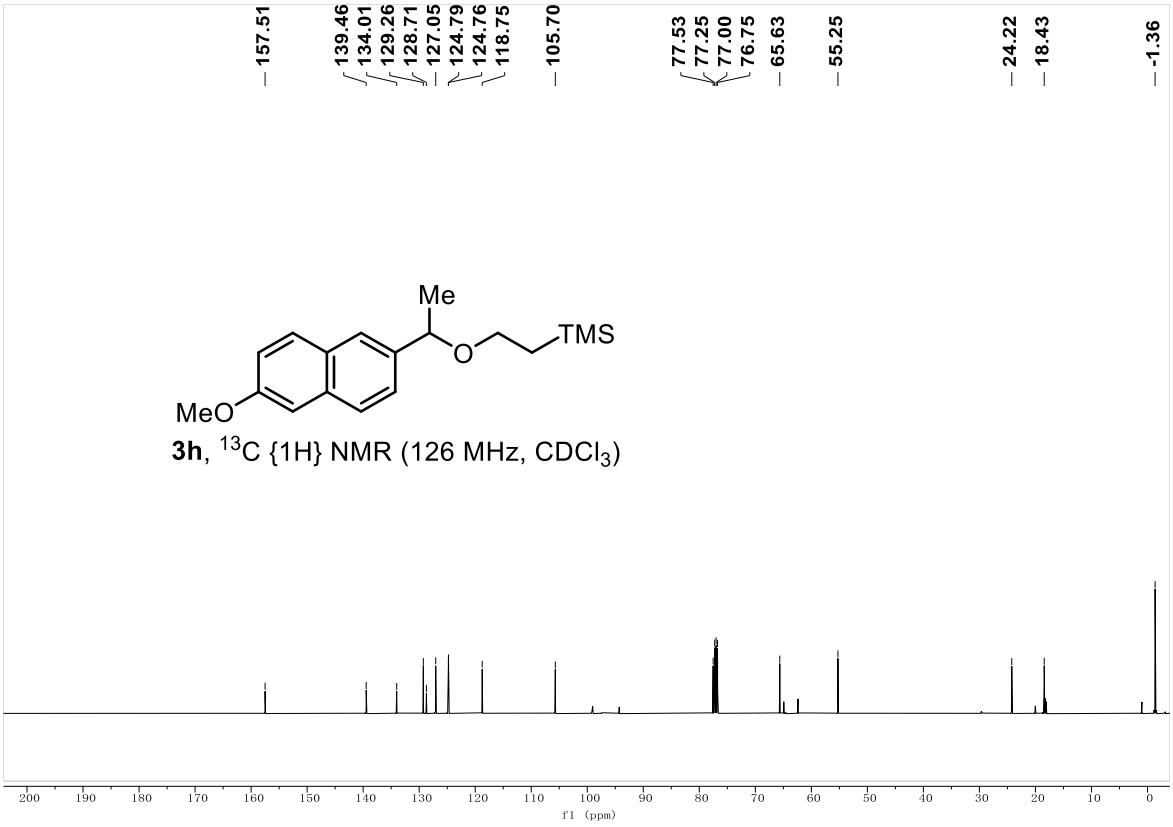

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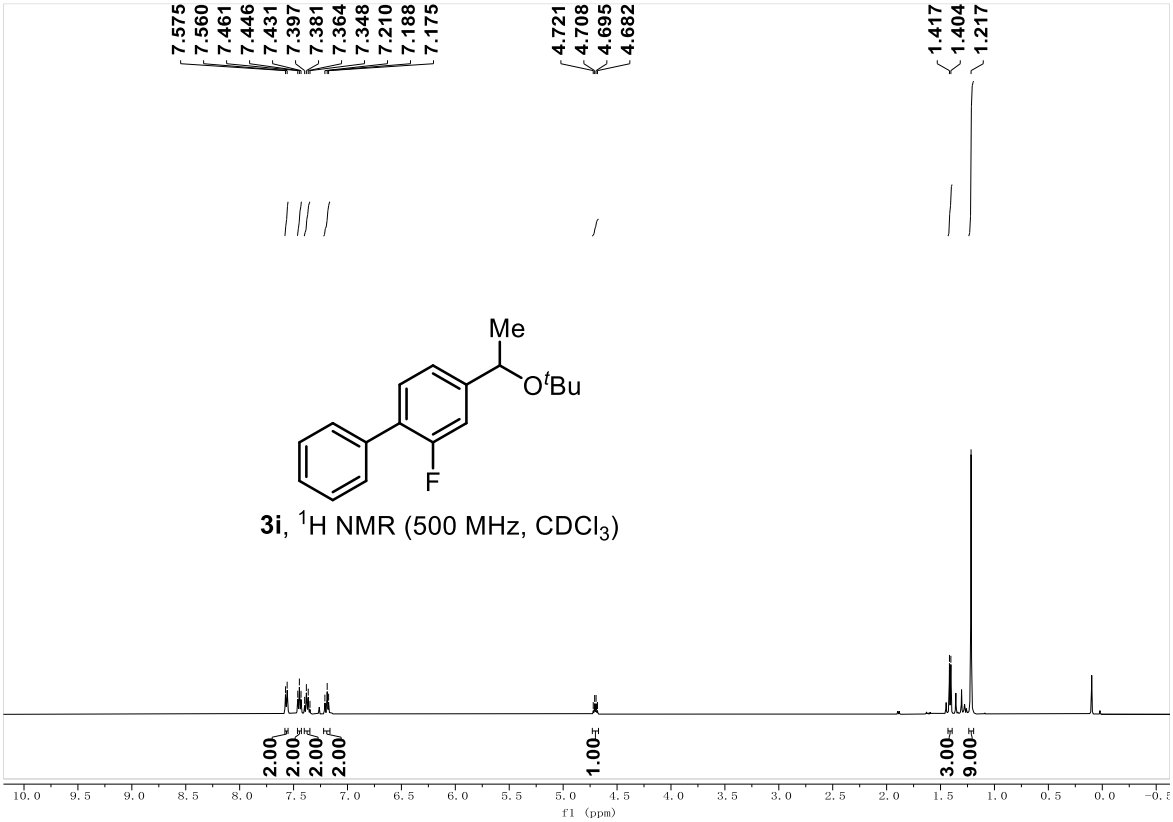

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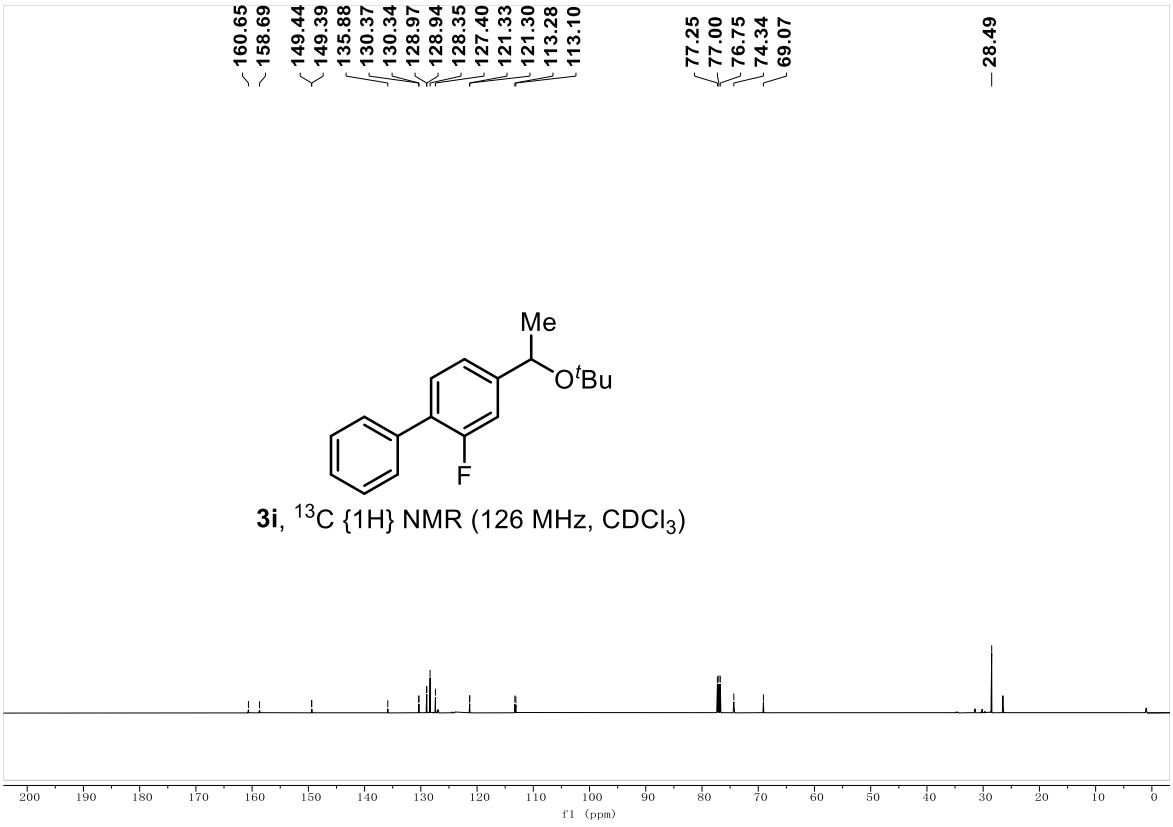
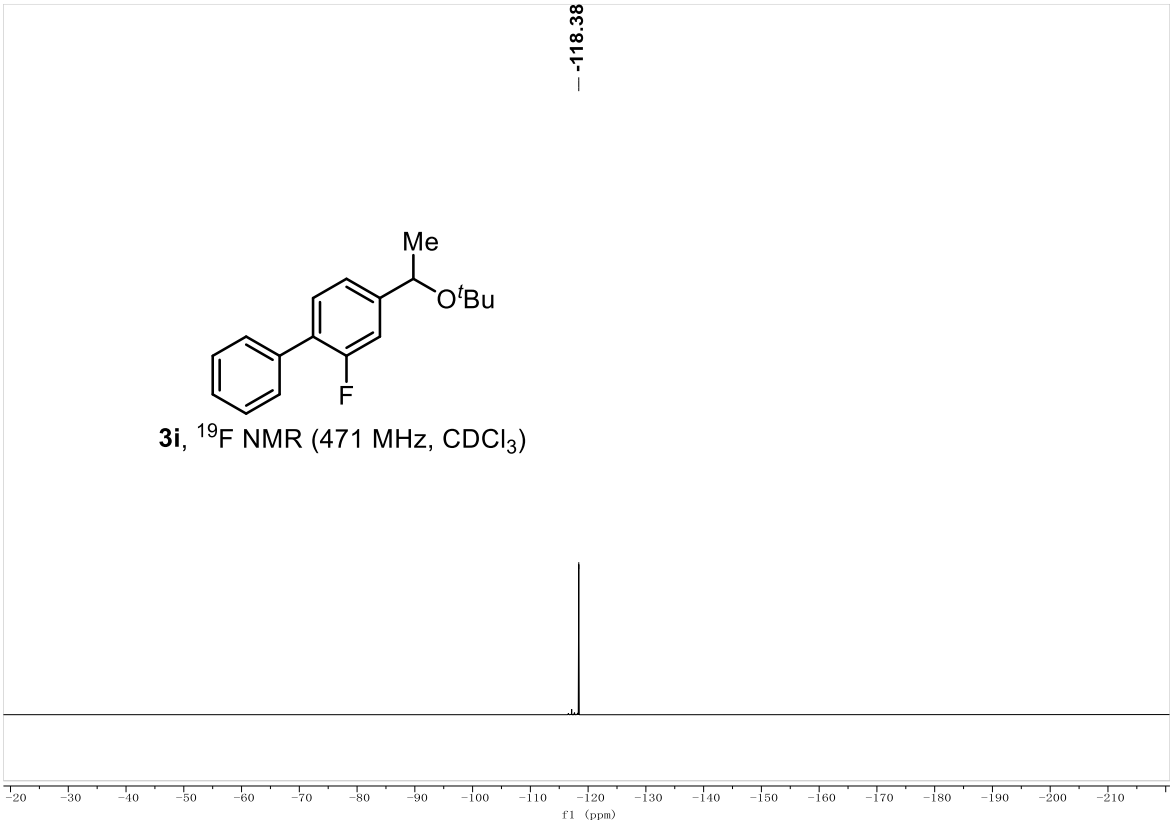
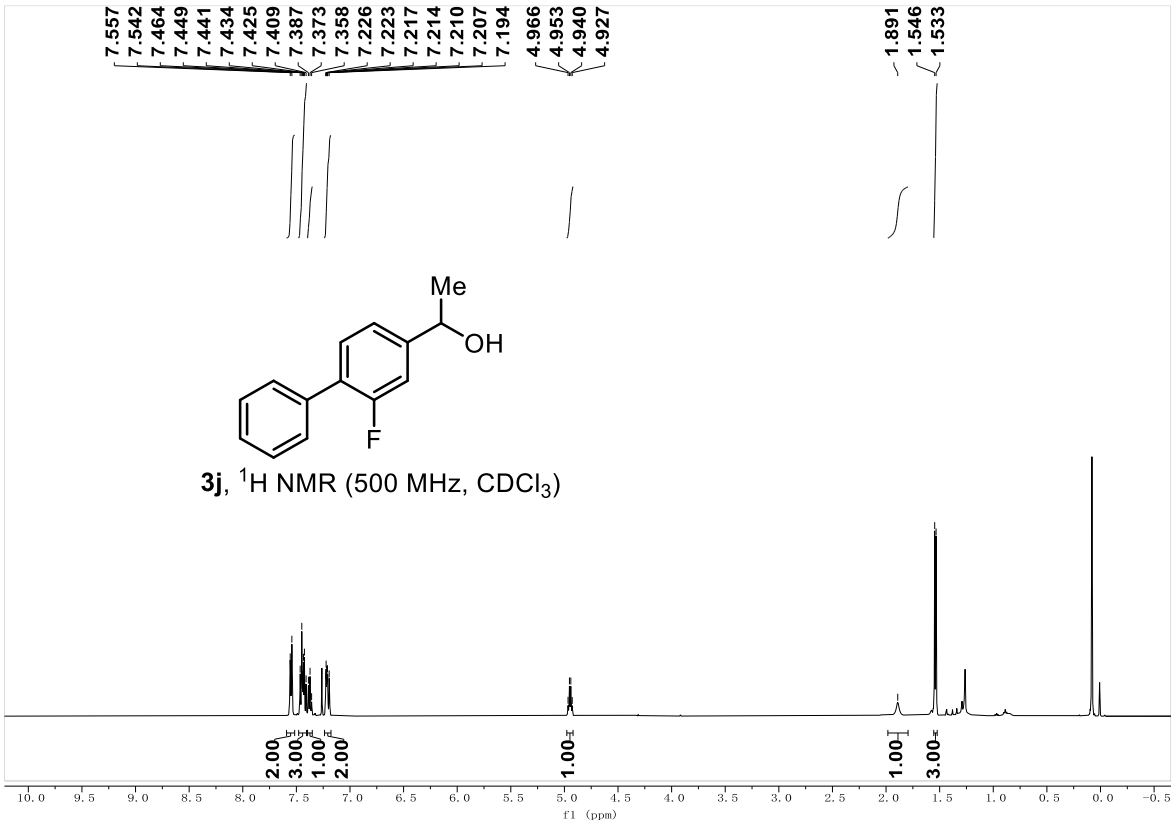


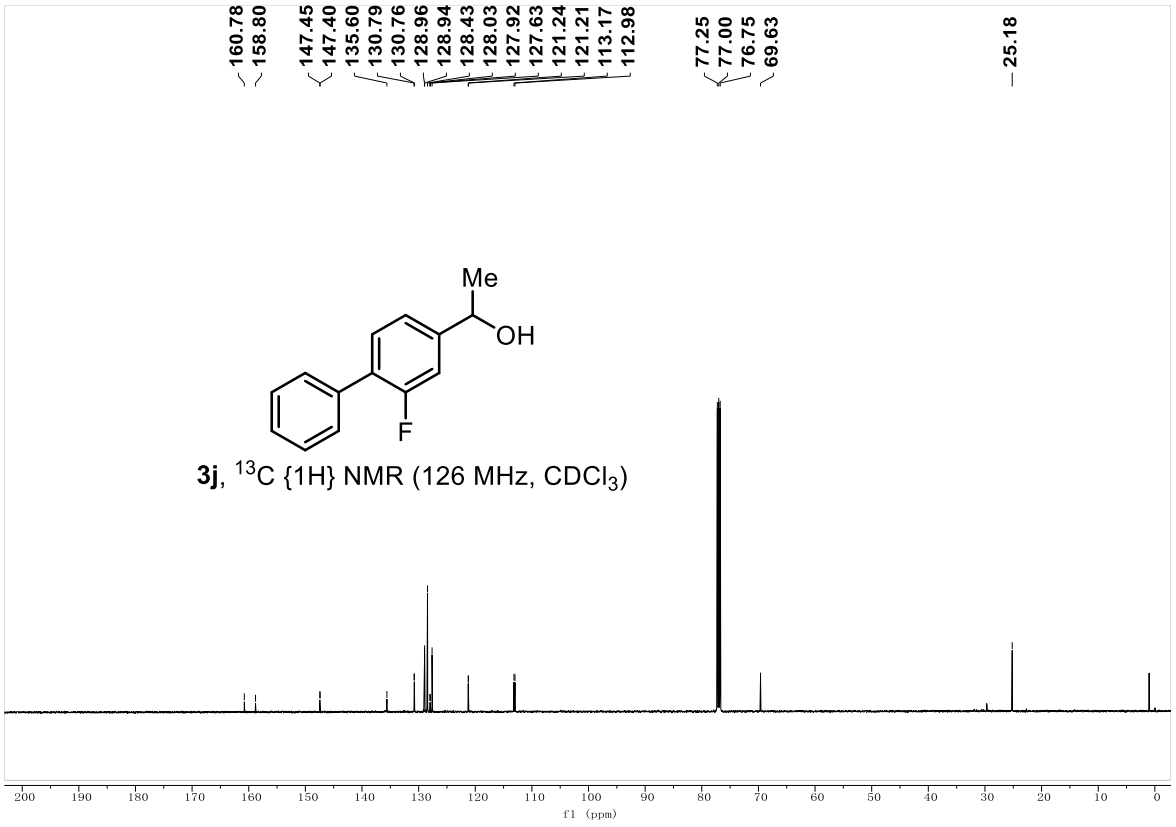
3i, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



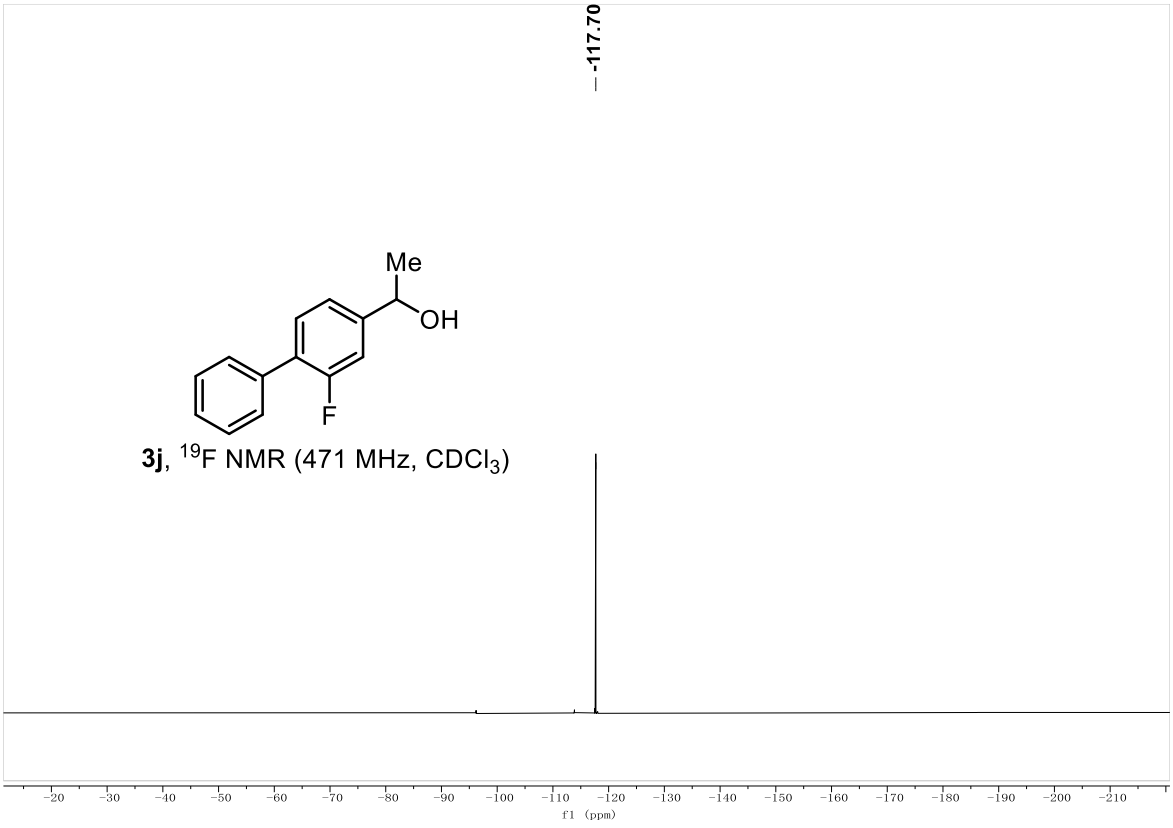
3i, ^{19}F NMR (471 MHz, $CDCl_3$)



3j, ^{1}H NMR (500 MHz, $CDCl_3$)



3j, ^{13}C {1H} NMR (126 MHz, $CDCl_3$)



3j, ^{19}F NMR (471 MHz, $CDCl_3$)

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