Supporting Information

Organocatalytic Asymmetric [3+2] Annulation of 1, 4-Dithiane-2, 5-diol with Azlactones: Access to Chiral Dihydrothiophen-2(*3H*)-one Derivatives

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Table of Contents

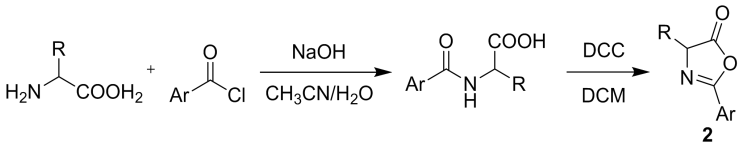
1. General Information

All reactions were performed under oxygen atmosphere using glassware unless otherwise noted, and all reagents were commercially available and used without further purification unless specified otherwise. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Reactions were monitored by thin layer chromatography (TLC), which carried out on GF254 plates. Visualization was performed by fluorescence quenching with UV light at 254 nm, phosphormolybdic acid or $KMnO_4$ straining solution followed by heating. Flash chromatography was performed with 200-300 mesh silica gels. ^1H NMR spectra were measured on a Bruker 400 (400 MHz) spectrometer and Bruker 500 (500 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from the residual solvent as an internal standard (δ 7.26 for $CDCl_3$, δ 2.50 for DMSO and δ 0.00 for TMS), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, AB q = AB quartet, m = multiplet, br = broad, and app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were measured on a Bruker 400 and 500 (101 and 126 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard (δ 77.16 for $CDCl_3$ and δ 2.50 for DMSO). HRMS were recorded on a LCMS-IT-TOF. Mass spectra were obtained using electrospray ionization (ESI) mass spectrometer. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiralcel OD-H column.

2. Synthesis and Characterization of Compounds

2.1 General Procedure for Synthesis of azlactones

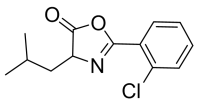
The azlactones **2a**[1], **2d**[2], **2h**[3], **2j**[4], **2l**, **2m**, **2n**, **2p**[5] were prepared according to known procedures. **2b**, **2c**, **2e-2g**, **2i**, **2k**, **2o**, **2q-2t** were afforded as follow procedures.



Step 1: The corresponding racemic amino acid (1 equiv.) and NaOH (2 equiv.) were dissolved in H_2O/CH_3CN (v/v = 3/1). After cooling to 0 °C, the corresponding benzoyl chloride (1.2 equiv.) was added dropwise at this temperature. After the addition was complete, the mixture was allowed to warm to room temperature and was stirred for 3 h. 2M HCl was added to cause precipitation under stirring. The mixture was extracted with ethyl acetate, the organic phase was dried with anhydrous Na_2SO_4 and concentrated in vacuo to get the *N*-substituted amino acid.

Step 2: The corresponding *N*-substituted amino acid (1 equiv.) was suspended in CH_2Cl_2 (10 mmol/mL), the mixture was cooled to 0 ºC and DCC (1.1 equiv.) was added portionwise. After complete addition, the mixture was allowed to warm to room temperature and stirred overnight. After completed, a precipitate was filtered off and the filtrate was concentrated in vacuo. The product was purified by silica gel column chromatography using PE/EA.

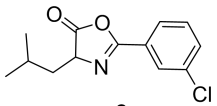
2-(2-Chlorophenyl)-4-isobutyloxazol-5(4*H*)-one (2b)



2b

Compound **2b** was prepared according to **step 1**, **step 2** with 2-chlorobenzoyl chloride as starting material, white solid, 71% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.48 – 7.43 (m, 1H), 7.37 (td, *J* = 7.6, 1.4 Hz, 1H), 4.46 (dd, *J* = 8.7, 5.8 Hz, 1H), 2.13 – 2.01 (m, 1H), 1.88 (ddd, *J* = 13.4, 7.4, 5.8 Hz, 1H), 1.72 (ddd, *J* = 13.8, 8.7, 6.6 Hz, 1H), 1.03 (dd, *J* = 7.8, 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.49, 159.97, 133.80, 132.75, 131.34, 131.27, 126.86, 125.40, 64.12, 40.61, 25.26, 22.63, 22.20; **HRMS** (ESI) calcd. for $C_{13}H_{15}NO_2Cl^+$ $[M+H]^+$ 252.0786, found 252.0780.

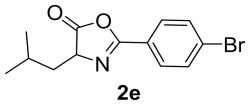
2-(3-Chlorophenyl)-4-isobutyloxazol-5(4*H*)-one (2c)



2c

Compound **2c** was prepared according to **step 1**, **step 2** with 3-chlorobenzoyl chloride as starting material, white solid, 70% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.87 (d, *J* = 7.7 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 4.42 (dd, *J* = 9.0, 5.6 Hz, 1H), 2.06 (dp, *J* = 13.6, 6.7 Hz, 1H), 1.89 – 1.80 (m, 1H), 1.72 – 1.62 (m, 1H), 1.03 (dd, *J* = 9.3, 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.46, 160.38, 135.04, 132.71, 130.12, 127.90, 127.78, 125.98, 64.01, 40.74, 25.26, 22.73, 22.01; **HRMS** (ESI) calcd. for $C_{13}H_{15}NO_2Cl^+$ $[M+H]^+$ 252.0786, found 252.0774.

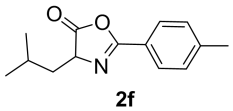
2-(4-Bromophenyl)-4-isobutyloxazol-5(4*H*)-one (2e)



2e

Compound **2e** was prepared according to **step 1**, **step 2** with 4- methylbenzoyl chloride as starting material, white solid, 77% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 4.41 (dd, *J* = 9.0, 5.6 Hz, 1H), 2.14 – 2.01 (m, 1H), 1.86 (ddd, *J* = 13.5, 7.8, 5.6 Hz, 1H), 1.69 (ddd, *J* = 13.8, 9.0, 6.3 Hz, 1H), 1.04 (dd, *J* = 8.5, 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.59, 160.72, 132.15, 129.29, 127.57, 125.01, 64.04, 40.74, 25.26, 22.72, 22.02; **HRMS** (ESI) calcd. for $C_{13}H_{15}NO_2Br^+$ $[M+H]^+$ 296.0281, found 296.0286.

3-(4-Isobutyl-2-(p-tolyl)oxazol-5(4*H*)-one (2f)

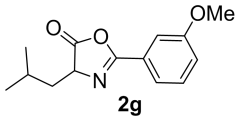


2f

Compound **2f** was prepared according to **step 1**, **step 2** with 4-bromobenzoyl chloride as starting material, white solid, 62% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.41 (dd, *J* = 8.8, 5.7 Hz, 1H), 2.45 (s, 3H), 2.16 – 2.01 (m, 1H), 1.86

(ddd, *J* = 13.5, 7.7, 5.7 Hz, 1H), 1.70 (ddd, *J* = 13.7, 8.8, 6.3 Hz, 1H), 1.04 (dd, *J* = 8.8, 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.15, 161.46, 143.32, 129.48, 127.84, 123.30, 63.90, 40.84, 25.22, 22.72, 22.08, 21.66; **HRMS** (ESI) calcd. for $C_{14}H_{18}NO_2^+$ $[M+H]^+$ 232.1332, found 232.1326.

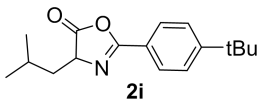
4-Isobutyl-2-(3-methoxyphenyl)oxazol-5(4*H*)-one (2g)



2g

Compound **2g** was prepared according to **step 1**, **step 2** with 3-methoxybenzoyl chloride as starting material, white solid, 74% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.51 (d, *J* = 1.3 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.11 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.41 (dd, *J* = 8.8, 5.8 Hz, 1H), 3.86 (s, 3H), 2.07 (dp, *J* = 13.5, 6.7 Hz, 1H), 1.90 – 1.78 (m, 1H), 1.75 – 1.63 (m, 1H), 1.02 (dd, *J* = 9.1, 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.98, 161.32, 159.81, 129.88, 127.25, 120.39, 119.39, 112.09, 64.00, 55.50, 40.79, 25.19, 22.72, 22.10; **HRMS** (ESI) calcd. for $C_{14}H_{18}NO_3^+$ $[M+H]^+$ 248.1281, found 248.1272.

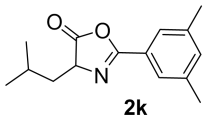
2-(4-(Tert-butyl)phenyl)-4-isobutyloxazol-5(4*H*)-one (2i)



2i

Compound **2i** was prepared according to **step 1**, **step 2** with 4-(tert-butyl)benzoyl chloride as starting material, white solid, 76% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.3 Hz, 2H), 4.40 (dd, *J* = 8.7, 5.8 Hz, 1H), 2.05 (dp, *J* = 13.4, 6.7 Hz, 1H), 1.88 – 1.79 (m, 1H), 1.73 – 1.63 (m, 1H), 1.35 (s, 9H), 1.02 (dd, *J* = 10.4, 6.7 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.19, 161.43, 156.40, 127.74, 125.79, 123.18, 63.87, 40.84, 35.14, 31.11, 25.18, 22.76, 22.16; **HRMS** (ESI) calcd. for $C_{17}H_{24}NO_2^+$ $[M+H]^+$ 274.1802, found 274.1792.

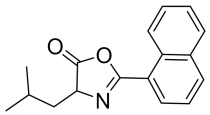
2-(3,5-Dimethylphenyl)-4-isobutyloxazol-5(4*H*)-one (2k)



2k

Compound **2k** was prepared according to **step 1**, **step 2** with 3,5-dimethylbenzoyl chloride as starting material, white solid, 77% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (s, 2H), 7.21 (s, 1H), 4.41 (dd, *J* = 8.8, 5.7 Hz, 1H), 2.39 (s, 6H), 2.14 – 2.02 (m, 1H), 1.90 – 1.81 (m, 1H), 1.74 – 1.65 (m, 1H), 1.04 (dd, *J* = 10.5, 6.7 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.17, 161.77, 138.57, 134.43, 128.31, 125.58, 63.89, 40.83, 25.19, 22.77, 22.08, 21.18; **HRMS** (ESI) calcd. for $C_{15}H_{20}NO_2^+$ $[M+H]^+$ 246.1489, found 246.1487.

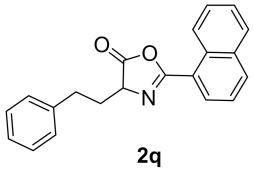
4-Isobutyl-2-(naphthalen-1-yl)oxazol-5(4*H*)-one (2o)



2o

Compound **2o** was prepared according to **step 1**, **step 2** with 1-naphthoyl chloride as starting material, white solid, 84% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.27 (d, *J* = 8.7 Hz, 1H), 8.13 (d, *J* = 7.2 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.64 (ddd, *J* = 8.5, 6.9, 1.3 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 4.53 (dd, *J* = 9.0, 5.6 Hz, 1H), 2.20 – 2.08 (m, 1H), 1.92 (ddd, *J* = 13.4, 7.6, 5.7 Hz, 1H), 1.75 (ddd, *J* = 13.8, 9.0, 6.5 Hz, 1H), 1.06 (dd, *J* = 9.2, 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.69, 161.19, 133.88, 133.50, 130.84, 130.12, 128.80, 128.16, 126.54, 126.02, 124.67, 121.82, 64.53, 40.95, 25.48, 22.77, 22.19; **HRMS** (ESI) calcd. for $C_{17}H_{18}NO_2^+$ $[M+H]^+$ 268.1332, found 268.1321.

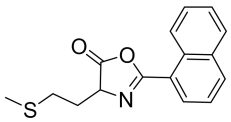
2-(Naphthalen-1-yl)-4-phenethyloxazol-5(4*H*)-one (2q)



2q

Compound **2q** was prepared according to **step 1**, **step 2** with 2-amino-4-phenylbutanoic acid and 1-naphthoyl chloride as starting material, white solid, 82% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.27 (d, *J* = 8.7 Hz, 1H), 8.14 (dd, *J* = 7.3, 1.1 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.66 (ddd, *J* = 8.5, 6.9, 1.3 Hz, 1H), 7.59 – 7.54 (m, 1H), 7.51 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.32 – 7.24 (m, 4H), 7.23 – 7.18 (m, 1H), 4.51 (dd, *J* = 7.6, 5.9 Hz, 1H), 2.93 (t, *J* = 7.7 Hz, 2H), 2.44 – 2.34 (m, 1H), 2.31 – 2.18 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.07, 161.60, 140.27, 133.89, 133.64, 130.84, 130.23, 128.85, 128.71, 128.61, 128.24, 126.60, 126.42, 126.00, 124.69, 121.70, 65.06, 33.36, 31.67; **HRMS** (ESI) calcd. for $C_{21}H_{18}NO_2^+$ $[M+H]^+$ 316.1332, found 316.1330.

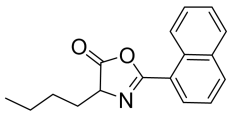
4-(2-(Methylthio)ethyl)-2-(naphthalen-1-yl)oxazol-5(4*H*)-one (2r)



2r

Compound **2r** was prepared according to **step 1**, **step 2** with 2-amino-4-(methylthio)butanoic acid and 1-naphthoyl chloride as starting material, white solid, 69% yield in total; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.25 (d, *J* = 8.7 Hz, 1H), 8.16 (d, *J* = 7.3 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 4.76 (t, *J* = 6.5 Hz, 1H), 2.81 (t, *J* = 7.0 Hz, 2H), 2.40 (dq, *J* = 13.3, 6.6 Hz, 1H), 2.24 (dq, *J* = 14.3, 7.2 Hz, 1H), 2.14 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.17, 161.89, 133.85, 133.68, 130.79, 130.26, 128.86, 128.24, 126.60, 125.95, 124.70, 121.67, 64.29, 30.54, 30.26, 15.22; **HRMS** (ESI) calcd. for $C_{16}H_{16}NO_2S^+$ $[M+H]^+$ 286.0896, found 286.0898.

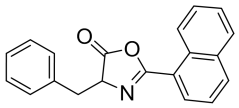
4-Butyl-2-(naphthalen-1-yl)oxazol-5(4H)-one (2s)



2s

Compound **2s** was prepared according to **step 1**, **step 2** with 2-aminohexanoic acid and 1-naphthoyl chloride as starting material, white solid, 71% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.26 (d, *J* = 8.7 Hz, 1H), 8.15 (dd, *J* = 7.3, 1.1 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.66 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.60 – 7.50 (m, 2H), 4.56 (dd, *J* = 7.1, 5.6 Hz, 1H), 2.17 – 2.06 (m, 1H), 2.01 – 1.90 (m, 1H), 1.61 – 1.50 (m, 2H), 1.48 – 1.38 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.30, 161.38, 133.88, 133.50, 130.84, 130.11, 128.80, 128.16, 126.55, 125.99, 124.67, 121.84, 65.98, 31.44, 27.52, 22.35, 13.82; **HRMS** (ESI) calcd. for $C_{17}H_{18}NO_2^+$ $[M+H]^+$ 268.1332, found 268.1333.

4-Benzyl-2-(naphthalen-1-yl)oxazol-5(4H)-one (2t)

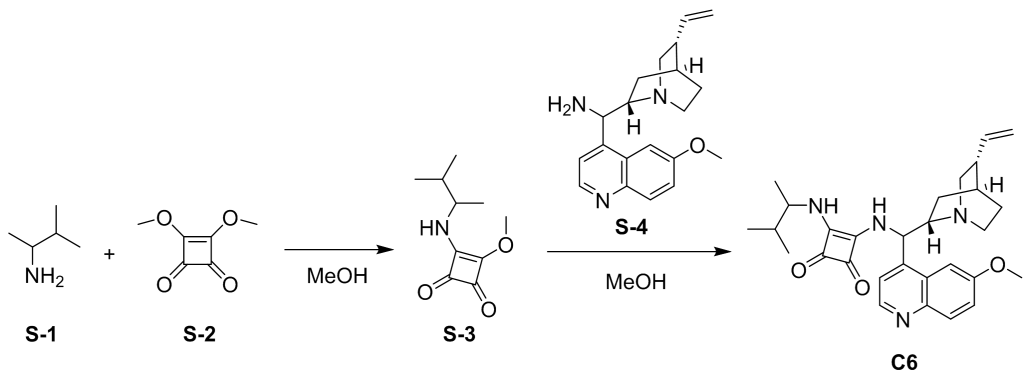


2t

Compound **2t** was prepared according to **step 1**, **step 2** with 2-amino-3-phenylpropanoic acid and 1-naphthoyl chloride as starting material, white solid, 83% yield in total; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.01 (d, *J* = 8.5 Hz, 1H), 7.99 (t, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.2 Hz, 2H), 7.25 (dt, *J* = 16.4, 7.1 Hz, 3H), 4.85 (t, *J* = 5.6 Hz, 1H), 3.47 (dd, *J* = 13.9, 5.0 Hz, 1H), 3.31 (dd, *J* = 13.9, 6.3 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.38, 161.63, 135.30, 133.75, 133.45, 130.74, 129.97, 129.71, 128.73, 128.50, 128.05, 127.28, 126.54, 125.90, 124.63, 121.82, 67.15, 37.37; **HRMS** (ESI) calcd. for $C_{20}H_{16}NO_2^+$ $[M+H]^+$ 302.1176, found 302.1174.

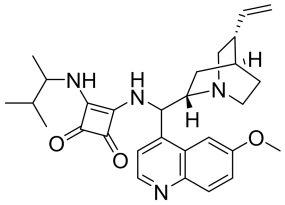
2.2 General procedure for the synthesis of cinchona alkaloid-derived squaramide catalyst[6]

The Catalysts **C1-C5** and **C9** were commercial available, the **C6-C8，C10，C11** were afforded as follow procedures.



An oven-dried 10 mL of Schlenk tube was charged with 1,2-dimethylpropylamine **S-1** (0.3 mmol) and 3,4-dimethoxycyclobut-3-ene-1,2-dione **S-2** (0.3 mmol), dissolved in 5 mL of MeOH. After stirred for 24 h, the organic solvent was removed under reduced pressure. The obtained residue was purified by flash column chromatography (DCM/MeOH = 30/1) to afford the intermediate **S-3**. Then， the intermediate (0.3 mmol) was dissolved in 5 mL of MeOH with 9-Amino-(9-deoxy)epidihydroquinine **S-4** (0.3 mmol), After stirred for 48 h, the organic solvent was removed under reduced pressure. The obtained residue was purified by flash column chromatography (DCM/MeOH = 30/1) to afford the Cinchona Alkaloid Squaramide catalyst.

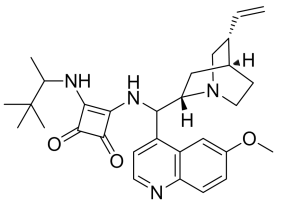
3-(((6-methoxyquinolin-4-yl)((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)amino)-4-((3-methylbutan-2-yl)amino)cyclobut-3-ene-1,2-dione (C6)



C6

Afforded according to the general procedure as a white solid in 85% yield; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.65 (d, *J* = 3.9 Hz, 1H), 8.04 (d, *J* = 9.2 Hz, 1H), 7.84 (d, *J* = 21.8 Hz, 1H), 7.57 (dd, *J* = 25.8, 4.2 Hz, 1H), 7.42 (dd, *J* = 9.2, 2.2 Hz, 1H), 6.16 (s, 1H), 5.79 (td, *J* = 17.1, 7.6 Hz, 1H), 4.98 (t, *J* = 14.3 Hz, 2H), 4.79 (s, 1H), 3.96 (s, 4H), 3.49 (d, *J* = 51.5 Hz, 2H), 3.26 – 3.10 (m, 1H), 2.97 (s, 2H), 2.83 – 2.66 (m, 2H), 2.29 (s, 1H), 1.72 – 1.39 (m, 5H), 1.01 (s, 3H), 0.75 (d, *J* = 6.3 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 182.68, 167.34, 158.67, 147.66, 144.69, 141.23, 141.09, 131.72, 122.40, 114.82, 114.77, 101.46, 55.97, 55.95, 55.79, 40.68, 39.40, 39.30, 33.98, 27.71, 27.65, 27.53, 27.48, 26.02, 18.71, 18.57, 18.35, 18.27, 18.14; **HRMS** (ESI) calcd. for $C_{29}H_{37}N_4O_3^+$ $[M+H]^+$ 489.2860, found 489.2838.

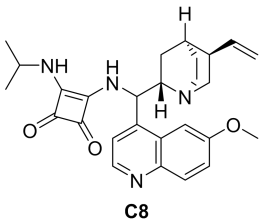
3-((3,3-dimethylbutan-2-yl)amino)-4-(((6-methoxyquinolin-4-yl)((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione (C7)



C7

Afforded according to the general procedure as a white solid in 77% yield; **^{1}H NMR** (400 MHz, DMSO) δ 8.80 (d, *J* = 4.5 Hz, 1H), 7.97 (d, *J* = 9.2 Hz, 1H), 7.80 (d, *J* = 15.4 Hz, 2H), 7.61 (d, *J* = 4.2 Hz, 1H), 7.44 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.22 (s, 1H), 6.03 – 5.89 (m, 2H), 5.00 (dd, *J* = 21.3, 13.8 Hz, 2H), 3.94 (s, 3H), 3.88 – 3.81 (m, 1H), 3.24 – 3.15 (m, 1H), 2.75 – 2.61 (m, 2H), 2.27 (s, 1H), 1.53 (d, *J* = 21.9 Hz, 4H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9H), 0.59 (s, 1H); **^{13}C NMR** (101 MHz, DMSO) δ 182.58, 182.13, 168.04, 166.89, 158.33, 148.25, 144.78, 142.62, 131.94, 127.96, 122.41, 120.05, 114.78, 102.04, 59.23, 58.25, 56.17, 34.84, 31.41, 27.79, 26.70, 26.15, 17.15; **HRMS** (ESI) calcd. for $C_{30}H_{38}N_4O_3^+$ $[M+H]^+$ 503.3017, found 503.3005.

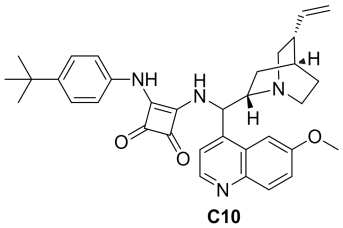
3-(isopropylamino)-4-(((6-methoxyquinolin-4-yl)((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione (C8)



C8

Afforded according to the general procedure as a white solid in 84% yield; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.6 Hz, 1H), 8.03 (d, *J* = 9.2 Hz, 1H), 7.88 (s, 1H), 7.70 (d, *J* = 4.3 Hz, 1H), 7.42 (dd, *J* = 9.2, 2.4 Hz, 1H), 6.30 (s, 1H), 5.85 (ddd, *J* = 17.4, 10.1, 7.5 Hz, 1H), 5.18 – 4.91 (m, 2H), 4.11 (dd, *J* = 13.0, 6.4 Hz, 1H), 3.99 (s, 3H), 3.91 (s, 1H), 3.71 (dt, *J* = 21.8, 10.9 Hz, 2H), 3.39 – 3.27 (m, 1H), 3.00 (d, *J* = 10.4 Hz, 1H), 2.88 (s, 1H), 2.42 (s, 1H), 1.74 (d, *J* = 12.8 Hz, 3H), 1.59 (s, 1H), 1.06 (dd, *J* = 24.6, 5.8 Hz, 5H), 0.84 (d, *J* = 7.3 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.51, 181.57, 167.16, 167.00, 158.75, 147.74, 144.65, 140.27, 131.66, 122.35, 115.47, 101.50, 58.28, 56.07, 55.57, 46.63, 40.95, 38.89, 27.39, 27.07, 25.76, 23.88, 23.65, 20.06, 18.43; **HRMS** (ESI) calcd. for $C_{27}H_{32}N_4O_3^+$ $[M+H]^+$ 461.2547, found 461.2539.

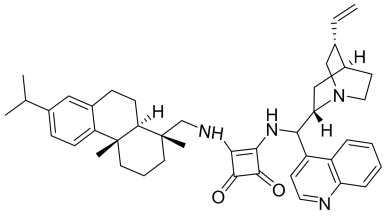
3-((4-(tert-butyl)phenyl)amino)-4-(((6-methoxyquinolin-4-yl)((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione (C10)



C10

Afforded according to the general procedure as a white solid in 73% yield; **^{1}H NMR** (400 MHz, DMSO) δ 8.83 (d, *J* = 4.4 Hz, 1H), 8.00 (d, *J* = 9.2 Hz, 1H), 7.78 (s, 1H), 7.69 (d, *J* = 4.5 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.31 (s, 4H), 6.10 – 5.92 (m, 2H), 5.04 (dd, *J* = 22.3, 13.8 Hz, 2H), 3.95 (s, 3H), 2.75 (s, 2H), 2.34 (s, 1H), 1.60 (d, *J* = 20.1 Hz, 7H), 1.27 (s, 7H), 1.23 (s, 9H); **^{13}C NMR** (101 MHz, DMSO) δ 184.07, 181.81, 180.23, 168.20, 165.91, 158.41, 148.28, 146.15, 145.76, 144.80, 136.57, 132.04, 127.86, 126.50, 126.44, 122.48, 118.71, 118.40, 101.89, 59.36, 56.18, 34.51, 34.44, 31.63, 31.60, 27.67; **HRMS** (ESI) calcd. for $C_{34}H_{38}N_4O_3^+$ $[M+H]^+$ 551.3017, found 551.3002.

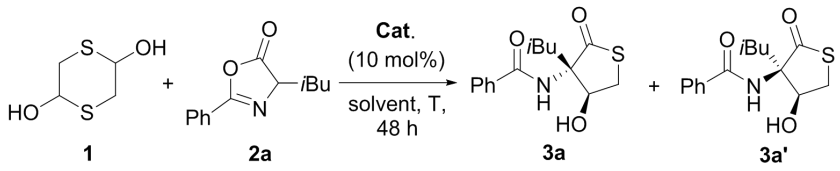
3-((((1R,4aS,10aR)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-4-((quinolin-4-yl((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione (C11)

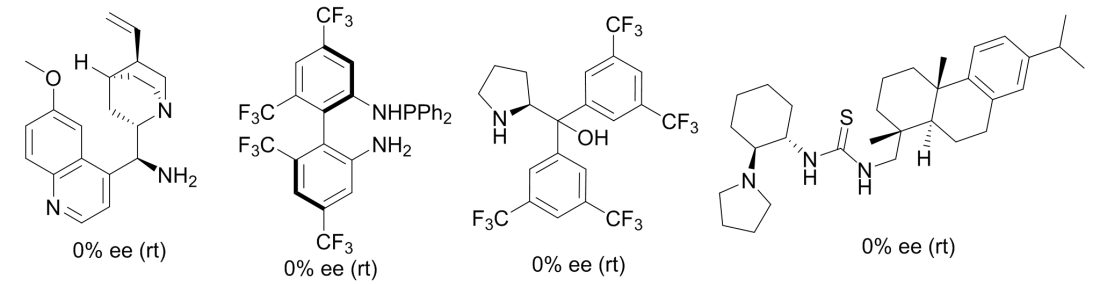


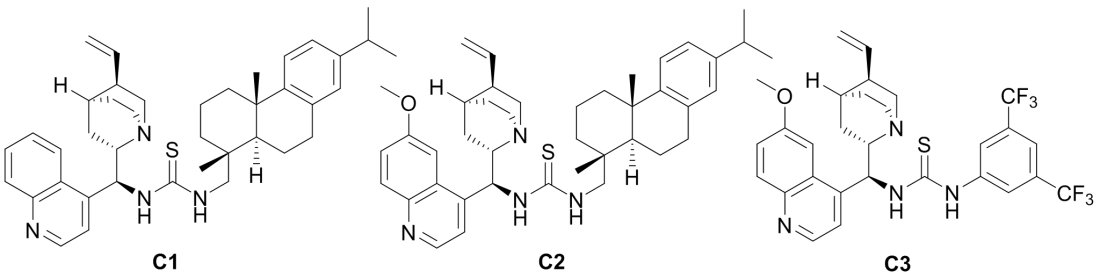
C11

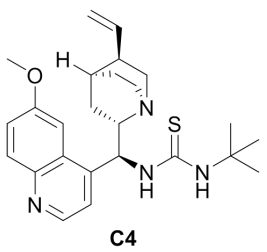
Afforded according to the general procedure as a white solid in 84% yield; **^{1}H NMR** (400 MHz, DMSO) δ 8.93 (dd, *J* = 21.1, 3.7 Hz, 1H), 8.42 (t, *J* = 8.0 Hz, 1H), 8.06 (t, *J* = 8.1 Hz, 1H), 8.01 – 7.74 (m, 3H), 7.66 (dd, *J* = 21.3, 14.3 Hz, 2H), 7.45 – 7.32 (m, 1H), 7.09 (d, *J* = 7.7 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 6.72 (s, 1H), 6.06 (s, 1H), 5.90 – 5.77 (m, 1H), 5.17 (d, *J* = 17.1 Hz, 1H), 5.08 (d, *J* = 10.0 Hz, 1H), 3.54 (s, 1H), 3.15 (s, 1H), 2.89 (s, 3H), 2.72 (dd, *J* = 15.0, 5.8 Hz, 2H), 2.22 (d, *J* = 11.0 Hz, 1H), 1.75 (s, 1H), 1.56 (s, 6H), 1.33 – 1.20 (m, 4H), 1.12 (d, *J* = 7.0 Hz, 9H), 0.91 (s, 2H), 0.83 (d, *J* = 8.6 Hz, 5H), 0.77 (s, 1H); **^{13}C NMR** (101 MHz, DMSO) δ 182.80, 182.48, 168.54, 167.44, 150.82, 148.59, 147.16, 145.36, 140.94, 137.91, 134.60, 130.41, 129.87, 127.52, 126.83, 125.60, 124.53, 124.00, 123.72, 119.68, 115.09, 59.65, 56.10, 54.33, 49.43, 46.31, 45.01, 39.08, 38.32, 37.62, 37.41, 35.50, 33.33, 30.12, 27.73, 26.41, 25.56, 24.35, 20.14, 19.81, 18.47, 12.27; **HRMS** (ESI) calcd. for $C_{43}H_{52}N_4O_2^+$ $[M+H]^+$ 657.4163, found 657.4162.

3. Table of the Optimization of Reaction Conditions[a]

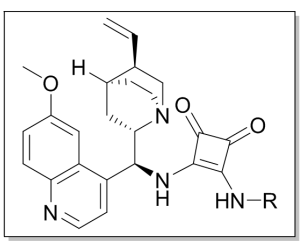




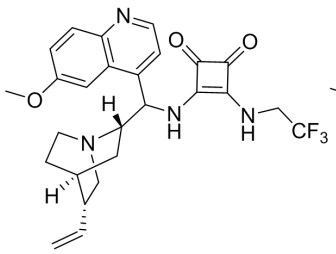




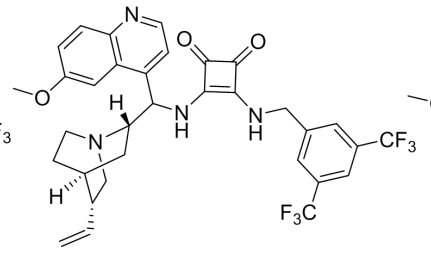
C4



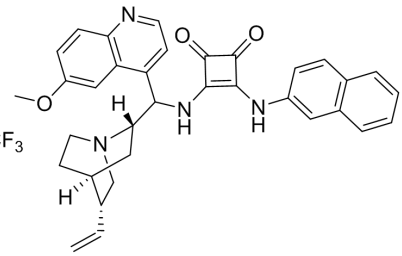
C5: R = 3,5-di-CF_3-C_6H_3
C6: R = -CH(*i*-Pr)CH_3
C7: R = -CH(*t*-Bu)CH_3
C8: R = isopropyl
C9: R = *tert*-butyl
C10: R = 4-(*t*-Bu)C_6H_4
C11: R = (+)-Dehydroabietyl



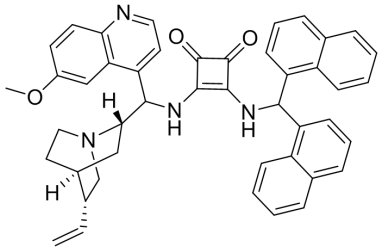
56% ee



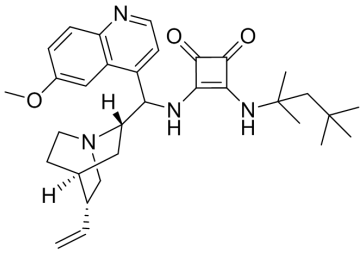
56% ee



40% ee



34% ee

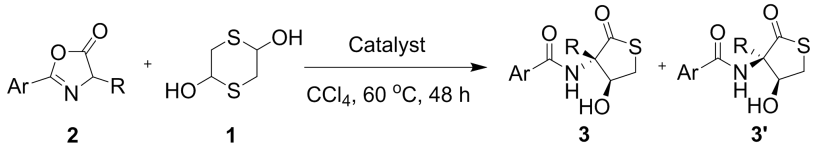


68% ee

entry	Cat.	solvent	Temp.(°C)	Conv.(%)[b]	ee(%)[c]
1[d]	Et_3N	MTBE	rt	99	0
2	**C1**	MTBE	rt	20	25
3	**C1**	MTBE	60	73	34
4	**C2**	MTBE	60	80	52
5	**C3**	MTBE	60	91	23
6	**C4**	MTBE	60	98	56
7	**C5**	MTBE	60	90	50
8	**C6**	MTBE	60	91	63
9	**C7**	MTBE	60	90	62
10	**C8**	MTBE	60	89	64
11	**C9**	MTBE	60	94	66
12	**C10**	MTBE	60	90	40
13	**C11**	MTBE	60	89	58
14	**C9**	THF	60	98	30
15	**C9**	EA	60	67	55
16	**C9**	Toluene	60	86	66
17	**C9**	DCM	60	89	69
18	**C9**	**CCl_4**	**60**	**90**	**73**
19	**C9**	CCl_4	rt	trace	69
20	**C9**	CCl_4	80	76	64
21	**C9**	CCl_4	60	89	67

[a]Unless otherwise stated, all reactions were conducted on a 0.2 mmol scale with **1** (1.1 equiv), **2a** (1.0 eqiuv), and catalyst (0.1 equiv) in solvent (2.0 mL) at tested temperature for 48 h, and 3:1 dr values were detected by ^{1}H NMR. [b]Determined by ^{1}H NMR (400 MHZ) analysis of the crude reaction mixture based on **2a**. [c]the ee values were determined by HPLC. [d]2 h was detected.

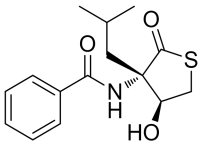
4. General Procedure for Asymmetric [3+2] Annulation Reaction



2 1 3 3'

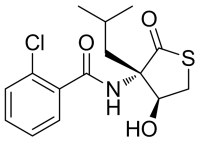
An oven-dried 10 mL of Schlenk tube was charged with Azlactone **2** (0.2 mmol), 1, 4-dithiane-2, 5-diol **1** (0.2 mmol) and cinchona alkaloid-derived catalyst, dissolved in CCl_4 (2 mL), After stirred at 60 °C for 48 h, the organic solvent was removed under reduced pressure, The obtained residue was purified by flash column chromatography to afford the product **3** (PE/EA = 8/1) and **3**' (PE/EA = 2/1).

***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)benzamide (3a)**



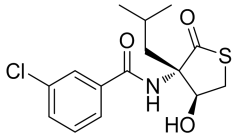
Afforded according to the general procedure as a white solid in 90% yield; m.p. = 94.6-96.0 °C; $[\alpha]^{20}_D$ = -10.22 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 5.2, 3.4 Hz, 2H), 7.60 – 7.54 (m, 1H), 7.48 (dd, *J* = 10.4, 4.7 Hz, 2H), 7.17 (s, 1H), 6.58 (s, 1H), 4.55 (dd, *J* = 9.9, 7.2 Hz, 1H), 3.45 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.25 (dd, *J* = 11.1, 10.0 Hz, 1H), 2.31 (dd, *J* = 14.9, 6.4 Hz, 1H), 1.82 – 1.72 (m, 1H), 1.68 (dd, *J* = 14.9, 5.4 Hz, 1H), 0.93 (d, *J* = 2.4 Hz, 3H), 0.91 (d, *J* = 2.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.05, 168.64, 133.09, 132.48, 128.92, 127.08, 77.27, 71.67, 35.58, 32.18, 24.48, 24.25, 23.20; **HRMS** (ESI) calcd. for $C_{15}H_{19}NO_3S^+$ $[M+H]^+$ 294.1158, found 294.1145; **HPLC**: The ee value was 71%, t_R (minor) = 8.093 min, t_R (major) = 5.510 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

2-Chloro-*N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)benzamide (3b)



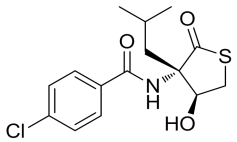
Afforded according to the general procedure as a white solid in 78% yield; m.p. = 94.2-95.6 °C; $[\alpha]^{20}_D$ = -8.31 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.40 – 7.34 (m, 2H), 6.28 (s, 1H), 4.61 (dd, *J* = 9.7, 7.3 Hz, 1H), 3.47 (dd, *J* = 11.3, 7.1 Hz, 1H), 3.33 – 3.24 (m, 1H), 2.35 (dd, *J* = 15.1, 5.4 Hz, 1H), 1.89 – 1.78 (m, 1H), 1.69 (dd, *J* = 15.0, 6.1 Hz, 1H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.46, 167.86, 133.65, 132.08, 130.94, 130.62, 129.88, 127.25, 77.11, 72.30, 36.00, 32.17, 24.59, 24.33, 22.97; **HRMS** (ESI) calcd. for $C_{15}H_{19}NO_3SCl^+$ $[M+H]^+$ 328.0769, found 328.0792; **HPLC**: The ee value was 76%, t_R (minor) = 9.747 min, t_R (major) = 6.650 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

3-Chloro-*N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)benzamide (3c)



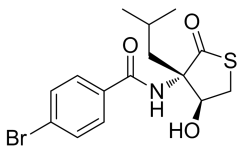
Afforded according to the general procedure as a white solid in 81% yield; m.p. = 95.0-95.7 °C; $[\alpha]^{20}_D$ = -14.22 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, CDCl3) δ 7.80 (s, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.56–7.49 (m, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.15 (s, 1H), 6.35 (s, 1H), 4.54 (dd, *J* = 9.8, 7.3 Hz, 1H), 3.44 (dd, J = 11.2, 7.1 Hz, 1H), 3.25 (t, *J* = 10.6 Hz, 1H), 2.28 (dd, *J* = 14.9, 6.2 Hz, 1H), 1.81 – 1.68 (m, 1H), 1.68 (dd, *J* = 14.9, 5.3 Hz, 1H), 0.92 (dd, *J* = 6.5, 3.0 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.90, 167.25, 135.24, 134.89, 132.50, 130.18, 127.57, 124.96, 77.18, 71.78, 35.65, 32.16, 24.44, 24.26, 23.16; **HRMS** (ESI) calcd. for $C_{15}H_{19}NO_3SCl^+$ $[M+H]^+$ 328.0769, found 328.0754; **HPLC**: The ee value was 61%, t_R (minor) = 6.737 min, t_R (major) =5.930 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

4-Chloro-*N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)benzamide (3d)



Afforded according to the general procedure as a white solid in 87% yield; m.p. = 90.5-91.5 °C; $[\alpha]^{20}_D$ = -2.62 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.13 (s, 1H), 6.45 (s, 1H), 4.55 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.46 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.27 (t, *J* = 10.6 Hz, 1H), 2.30 (dd, *J* = 14.9, 6.4 Hz, 1H), 1.80–1.72 (m, 1H), 1.69 (dd, *J* = 15.1, 5.4 Hz, 1H), 0.93 (dd, *J* = 8.5, 6.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.95, 167.50, 138.88, 131.47, 129.19, 128.52, 77.19, 71.73, 35.60, 32.16, 24.45, 24.21, 23.18; **HRMS** (ESI) calcd. for $C_{15}H_{19}NO_3SCl^+$ $[M+H]^+$ 328.0769, found 328.0758; **HPLC**: The ee value was 56%, t_R (minor) = 8.523 min, t_R (major) = 7.823 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

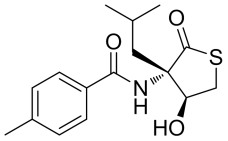
4-Bromo-*N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)benzamide (3e)



Afforded according to the general procedure as a white solid in 83% yield; m.p. = 108.0-109.8 °C; $[\alpha]^{20}_D$ = -7.20 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.6 Hz, 2H), 7.11 (s, 1H), 6.41 (s, 1H), 4.53 (dd, *J* = 9.7, 7.3 Hz, 1H), 3.45 (dd, *J* = 11.2, 7.2 Hz, 1H), 3.25 (t, *J* = 10.6 Hz, 1H), 2.28 (dd, *J* = 14.8, 6.2 Hz, 1H), 1.79 – 1.71 (m, 1H), 1.67 (dd, *J* = 15.0, 5.3 Hz, 1H), 0.91 (t, *J* = 6.9 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.97, 167.61, 132.19, 131.91, 128.66, 127.39, 77.18, 71.74, 35.57, 32.18, 24.48, 24.22, 23.19; **HRMS** (ESI) calcd. for $C_{15}H_{18}NO_3SBrNa^+$ $[M+Na]^+$ 394.0083, found 394.0075; **HPLC**: The ee value was 70%,

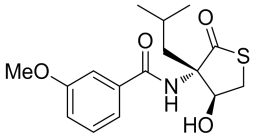
t_R (minor) = 22.117 min, t_R (major) = 20.850 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 95:5, flow rate = 0.5 mL/min, UV = 254 nm).

***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)-4-methylbenzamide (3f)**



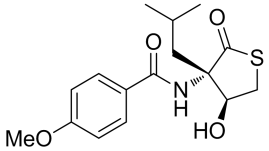
Afforded according to the general procedure as a white solid in 94% yield; m.p. = 102.0-103.5 °C; $[\alpha]^{20}_D$ = -15.76 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 7.13 (s, 1H), 6.65 (s, 1H), 4.54 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.44 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.25 (t, *J* = 10.6 Hz, 1H), 2.42 (s, 3H), 2.31 (dd, *J* = 14.9, 6.4 Hz, 1H), 1.80 – 1.70 (m, 1H), 1.66 (dd, *J* = 14.9, 5.3 Hz, 1H), 0.97 – 0.85 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.13, 168.58, 143.15, 130.20, 129.56, 127.10, 77.29, 71.60, 35.53, 32.18, 24.49, 24.22, 23.18, 21.53; **HRMS** (ESI) calcd. for $C_{16}H_{22}NO_3S^+$ $[M+H]^+$ 308.1315, found 308.1319; **HPLC**: The ee value was 68%, t_R (minor) = 9.443 min, t_R (major) = 7.393 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)-3-methoxybenzamide (3g)**



Afforded according to the general procedure as a white oil in 92% yield; $[\alpha]^{20}_D$ = -19.58 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 10.8, 4.8 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.15 (s, 1H), 7.09 (dd, *J* = 8.1, 2.4 Hz, 1H), 6.53 (s, 1H), 4.54 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.86 (s, 3H), 3.44 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.25 (t, *J* = 10.6 Hz, 1H), 2.30 (dd, *J* = 14.9, 6.3 Hz, 1H), 1.81–1.71 (m, 1H), 1.67 (dd, *J* = 14.9, 5.3 Hz, 1H), 0.92 (d, *J* = 6.5 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.92, 168.49, 160.04, 134.55, 129.91, 118.80, 118.57, 112.49, 77.23, 71.66, 55.49, 35.60, 32.15, 24.46, 24.24, 23.18; **HRMS** (ESI) calcd. for $C_{16}H_{22}NO_4S^+$ $[M+H]^+$ 324.1264, found 324.1258; **HPLC**: The ee value was 72%, t_R (minor) = 7.590 min, t_R (major) = 6.540 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

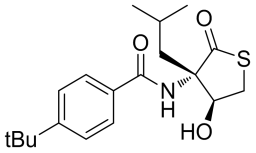
***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)-4-methoxybenzamide (3h)**



Afforded according to the general procedure as a white solid in 91% yield; m.p. = 118.2-119.5 °C; $[\alpha]^{20}_D$ = -12.71 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.7 Hz, 2H), 7.08 (s, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.69 (s, 1H), 4.54 (dd, *J* = 9.7, 7.3 Hz, 1H), 3.88 (s, 3H), 3.45 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.25 (t, *J* = 10.6 Hz, 1H), 2.32 (dd, *J* = 14.9, 6.4 Hz, 1H), 1.83 – 1.62 (m, 2H), 0.96 – 0.89 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.18, 168.10, 162.97, 129.01, 125.22,

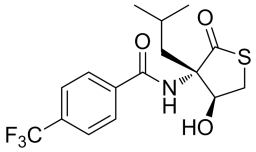
114.09, 71.56, 55.49, 35.55, 32.17, 24.47, 24.20, 23.19; **HRMS** (ESI) calcd. for $C_{16}H_{22}NO_4S^+$ $[M+H]^+$ 324.1264, found 324.1267; **HPLC**: The ee value was 72%, t_R (minor) = 9.590 min, t_R (major) = 7.957 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

4-(Tert-butyl)-*N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)benzamide (3i)



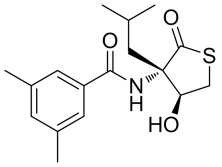
Afforded according to the general procedure as a white solid in 85% yield; m.p. = 84.5-85.0 °C; $[\alpha]^{20}_D$ = -13.12 (c = 1.0, CH2Cl2); 1H NMR (400 MHz, CDCl3) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 6.65 (s, 1H), 4.53 (dd, *J* = 9.7, 7.3 Hz, 1H), 3.44 (dd, *J* = 11.1, 7.1 Hz, 1H), 3.26 (d, *J* = 10.3 Hz, 1H), 2.32 (dd, *J* = 14.9, 6.3 Hz, 1H), 1.80 – 1.71 (m, 1H), 1.66 (dd, *J* = 15.9, 6.3 Hz, 2H), 1.34 (s, 9H), 0.92 (d, *J* = 6.6 Hz, 6H); 13C NMR (101 MHz, CDCl3) δ 205.12, 168.58, 156.19, 130.17, 126.97, 125.86, 71.60, 35.57, 35.06, 32.17, 31.11, 24.46, 24.28, 23.20; HRMS (ESI) calcd. for C19H27NO3SNa+ [M+Na]+ 372.1604, found 372.1594; HPLC: The ee value was 75%, t_R (minor) = 15.347 min, t_R (major) = 14.200 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 95:5, flow rate = 1 mL/min, UV = 254 nm).

***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)-4-(trifluoromethyl)benzamide (3j)**



Afforded according to the general procedure as a white solid in 88% yield; m.p. = 76.0-78.0 °C; $[\alpha]^{20}_D$ = -5.25 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.21 (s, 1H), 6.33 (s, 1H), 4.57 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.47 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.28 (t, *J* = 10.6 Hz, 1H), 2.31 (dd, *J* = 14.7, 6.1 Hz, 1H), 1.83 – 1.67 (m, 2H), 0.94 (t, *J* = 6.1 Hz, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.12; ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.84, 167.27, 136.37, 134.12 (J_{C-F} = 198.0 Hz), 127.60, 125.98 (J_{C-F} = 21.0 Hz,), 77.11, 71.85, 35.61, 32.15, 24.45, 24.22, 23.19. **HRMS** (ESI) calcd. for $C_{16}H_{18}NO_3F_3SNa^+$ $[M+Na]^+$ 384.0852, found 384.0843; **HPLC**: The ee value was 68%, t_R (minor) = 6.827 min, t_R (major) = 7.997 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

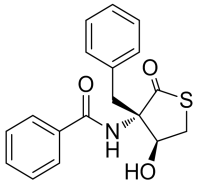
***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)-3,5-dimethylbenzamide (3k)**



Afforded according to the general procedure as a white solid in 71% yield; m.p. = 125.5-127.0 °C; $[\alpha]^{20}_D$ = -13.14 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 (s, 2H), 7.19 (s, 1H), 7.13 (s, 1H), 6.63 (s, 1H), 4.53 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.44 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.25 (dd, *J* = 11.1,

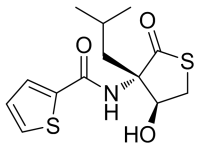
10.0 Hz, 1H), 2.37 (s, 6H), 2.32 (dd, *J* = 15.0, 6.3 Hz, 1H), 1..82 – 1.70 (m, 1H), 1.66 (dd, *J* = 15.0, 5.4 Hz, 1H), 0.92 (dd, *J* = 6.6, 3.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.21, 169.07, 138.71, 134.12, 133.02, 124.79, 77.35, 71.64, 35.56, 32.19, 24.47, 24.30, 23.13, 21.24; **HRMS** (ESI) calcd. for $C_{17}H_{24}NO_3S^+$ $[M+H]^+$ 322.1471, found 322.1478; **HPLC**: The ee value was 62%, t_R (minor) = 9.997 min, t_R (major) = 9.160 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 95:5, flow rate = 1 mL/min, UV = 254 nm).

***N*-(3-benzyl-4-hydroxy-2-oxotetrahydrothiophen-3-yl)benzamide (3l)**



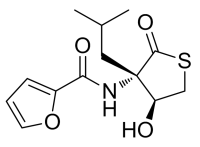
Afforded according to the general procedure as a white solid in 91% yield; m.p. = 105.9-106.4 °C; $[\alpha]^{20}_D$ = +8.74 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.30 – 7.23 (m, 3H), 7.08 (dd, *J* = 7.6, 1.6 Hz, 2H), 6.80 (s, 1H), 6.74 (s, 1H), 4.73 (dd, *J* = 9.9, 7.3 Hz, 1H), 3.67 (d, *J* = 14.2 Hz, 1H), 3.56 (dd, *J* = 11.2, 7.2 Hz, 1H), 3.37 (dd, *J* = 11.1, 10.1 Hz, 1H), 3.09 (d, *J* = 14.2 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.27, 169.19, 133.71, 133.02, 132.51, 130.65, 128.83, 128.25, 127.40, 127.17, 76.46, 72.25, 33.86, 32.17; **HRMS** (ESI) calcd. for $C_{18}H_{17}NO_3SNa^+$ $[M+Na]^+$ 350.0821, found 350.0805; **HPLC**: The ee value was 71%, t_R (minor) = 8.09 min, t_R (major) = 5.51 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)thiophene-2-carboxamide (3m)**



Afforded according to the general procedure as a light yellow solid in 98% yield; m.p. = 95.0-96.0 °C; $[\alpha]^{20}_D$ = -22.45 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 3.7 Hz, 2H), 7.12 (t, *J* = 4.2 Hz, 1H), 6.98 (s, 1H), 6.33 (s, 1H), 4.54 (t, *J* = 8.4 Hz, 1H), 3.44 (dd, *J* = 10.9, 7.3 Hz, 1H), 3.24 (t, *J* = 10.6 Hz, 1H), 2.26 (dd, *J* = 14.8, 6.5 Hz, 1H), 1.81 – 1.61 (m, 2H), 0.93 (d, *J* = 6.4 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.75, 163.15, 137.46, 131.67, 129.20, 128.09, 77.17, 71.83, 35.69, 32.15, 24.50, 24.15, 23.22; **HRMS** (ESI) calcd. for $C_{13}H_{18}NO_3S_2^+$ $[M+H]^+$ 300.0723, found 300.0714; **HPLC**: The ee value was 66%, t_R (minor) = 11.627 min, t_R (major) = 7.260 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

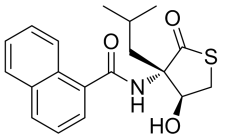
***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)furan-2-carboxamide (3n)**



Afforded according to the general procedure as a lightyellow oil in 98% yield; $[\alpha]^{20}_D$ = -19.35 (*c* =

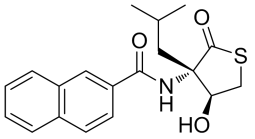
1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.34 (s, 1H), 7.16 (d, *J* = 3.5 Hz, 1H), 6.55 (dd, *J* = 3.4, 1.7 Hz, 1H), 6.36 (s, 1H), 4.53 (dd, *J* = 9.8, 7.2 Hz, 1H), 3.43 (dd, *J* = 11.2, 7.1 Hz, 1H), 3.29 – 3.18 (m, 1H), 2.23 (dd, *J* = 14.9, 6.6 Hz, 1H), 1.81 – 1.70 (m, 1H), 1.67 (dd, *J* = 15.0, 5.3 Hz, 1H), 0.91 (dd, *J* = 6.6, 2.8 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.30, 159.37, 146.71, 145.18, 115.81, 112.51, 71.51, 35.84, 32.07, 24.47, 24.07, 23.14; **HRMS** (ESI) calcd. for $C_{13}H_{18}NO_4S^+$ $[M+H]^+$ 284.0951, found 284.0958; **HPLC**: The ee value was 77%, t_R (minor) = 12.220 min, t_R (major) = 6.477 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)-1-naphthamide (3o)**



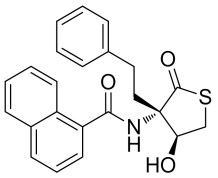
Afforded according to the general procedure as a colourless solid in 96% yield; m.p. = 149.5-151.0 ºC; $[\alpha]^{20}_D$ = -14.78 = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.3 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.64 (dd, *J* = 7.1, 1.1 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.48 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.05 (s, 1H), 6.55 (s, 1H), 4.71 (dd, *J* = 9.6, 7.4 Hz, 1H), 3.49 (dd, *J* = 11.3, 7.1 Hz, 1H), 3.30 (dd, *J* = 11.2, 9.9 Hz, 1H), 2.44 (dd, *J* = 15.0, 5.6 Hz, 1H), 1.89 – 1.78 (m, 1H), 1.75 (dd, *J* = 15.0, 5.8 Hz, 1H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.68, 171.27, 133.80, 132.62, 131.73, 129.95, 128.57, 127.59, 126.75, 125.24, 124.92, 124.63, 77.41, 72.14, 36.02, 32.22, 24.69, 24.44, 23.17; **HRMS** (ESI) calcd. for $C_{19}H_{22}NO_3S^+$ $[M+H]^+$ 344.1315, found 344.1309; **HPLC**: The ee value was 83%, t_R (minor) = 13.280 min, t_R (major) = 16.510 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, UV = 254 nm).

***N*-(4-hydroxy-3-isobutyl-2-oxotetrahydrothiophen-3-yl)-2-naphthamide (3p)**



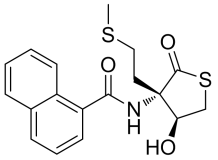
Afforded according to the general procedure as a colourless solid in 83% yield; m.p. = 146.0-146.6 ºC; $[\alpha]^{20}_D$ = -9.70 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.99 – 7.87 (m, 3H), 7.83 (d, *J* = 8.6 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.32 (s, 1H), 6.64 (s, 1H), 4.60 (dd, *J* = 9.6, 7.3 Hz, 1H), 3.47 (dd, *J* = 11.1, 7.1 Hz, 1H), 3.28 (t, *J* = 10.5 Hz, 1H), 2.37 (dd, *J* = 15.0, 6.4 Hz, 1H), 1.86 – 1.75 (m, 1H), 1.71 (dd, *J* = 15.1, 5.3 Hz, 1H), 0.94 (dd, *J* = 6.4, 3.7 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.18, 168.69, 135.12, 132.54, 130.19, 129.14, 128.93, 128.28, 128.03, 127.82, 127.15, 123.14, 77.33, 71.80, 35.62, 32.23, 24.53, 24.28, 23.22; **HRMS** (ESI) calcd. for $C_{19}H_{21}NO_3SNa^+$ $[M+Na]^+$ 366.1134, found 366.1123; **HPLC**: The ee value was 79%, t_R (minor) = 7.280 min, t_R (major) = 6.407 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, UV = 254 nm).

***N*-(4-hydroxy-2-oxo-3-phenethyltetrahydrothiophen-3-yl)-1-naphthamide (3q)**



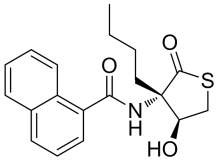
Afforded according to the general procedure as a colourless oil in 94% yield; $[\alpha]^{20}_{D}$ = -18.33 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.92 – 7.88 (m, 1H), 7.64 – 7.54 (m, 3H), 7.47 (dd, *J* = 8.1, 7.2 Hz, 1H), 7.30 – 7.16 (m, 5H), 7.00 (s, 1H), 6.51 (s, 1H), 4.81 (dd, *J* = 9.6, 7.6 Hz, 1H), 3.54 (dd, *J* = 11.3, 7.2 Hz, 1H), 3.32 (dd, *J* = 11.2, 10.0 Hz, 1H), 2.86 (ddd, *J* = 14.4, 12.2, 5.4 Hz, 1H), 2.80 – 2.62 (m, 2H), 2.07 (ddd, *J* = 14.5, 11.5, 5.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.12, 171.43, 140.59, 133.80, 132.40, 131.79, 129.98, 128.68, 128.65, 128.60, 128.38, 127.65, 126.77, 126.34, 125.39, 124.91, 124.61, 72.13, 60.41, 32.33, 29.62, 29.16, 21.07, 14.23; **HRMS** (ESI) calcd. for $C_{23}H_{21}NO_3SNa^+$ $[M+Na]^+$ 414.1134, found 414.1135; **HPLC**: The ee value was 70%, t_R (minor) = 9.320 min, t_R (major) = 15.423 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 75:25, flow rate = 1 mL/min, UV = 254 nm).

***N*-(4-hydroxy-3-(2-(methylthio)ethyl)-2-oxotetrahydrothiophen-3-yl)-1-naphthamide (3r)**



Afforded according to the general procedure as a light yellow solid in 93% yield; m.p. = 136.5-137.6 °C; $[\alpha]^{20}_{D}$ = -11.82 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 7.0 Hz, 1H), 7.63 – 7.52 (m, 2H), 7.49 (t, *J* = 7.6 Hz, 1H), 6.98 (s, 1H), 6.43 (s, 1H), 4.85 – 4.70 (m, 1H), 3.54 (dd, *J* = 11.3, 7.2 Hz, 1H), 3.31 (t, *J* = 10.6 Hz, 1H), 2.90 – 2.77 (m, 1H), 2.65 – 2.46 (m, 2H), 2.12 (s, 3H), 2.11 – 2.02 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.84, 171.42, 133.80, 132.28, 131.90, 129.94, 128.62, 127.69, 126.81, 125.44, 124.84, 124.61, 76.92, 71.86, 32.30, 27.96, 27.67, 15.72; **HRMS** (ESI) calcd. for $C_{18}H_{19}NO_3S_2Na^+$ $[M+Na]^+$ 384.0699, found 384.0680; **HPLC**: The ee value was 66%, t_R (minor) = 10.943 min, t_R (major) = 18.093 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, UV = 254 nm).

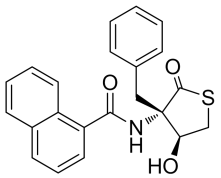
***N*-(3-butyl-4-hydroxy-2-oxotetrahydrothiophen-3-yl)-1-naphthamide (3s)**



Afforded according to the general procedure as a colourless solid in 92% yield; m.p. = 91.5-93.0 °C; $[\alpha]^{20}_{D}$ = 3.50 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 7.0 Hz, 1H), 7.61 – 7.50 (m, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 6.96 (s, 1H), 6.52 (s, 1H), 4.81 – 4.72 (m, 1H), 3.49 (dd, *J* = 11.1, 7.2 Hz, 1H),

3.29 (t, *J* = 10.6 Hz, 1H), 2.51 (dd, *J* = 18.4, 8.1 Hz, 1H), 1.82 – 1.70 (m, 1H), 1.45 – 1.27 (m, 4H), 0.92 (t, *J* = 6.6 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 204.17, 171.34, 133.80, 132.65, 131.67, 129.98, 128.55, 127.56, 126.73, 125.31, 124.90, 124.62, 76.83, 72.24, 32.26, 27.49, 24.73, 22.80, 13.90; **HRMS** (ESI) calcd. for $C_{19}H_{21}NO_3SNa^+$ $[M+Na]^+$ 366.1134, found 366.1121; **HPLC**: The ee value was 84%, t_R (minor) = 8.533 min, t_R (major) = 10.427 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, UV = 254 nm).

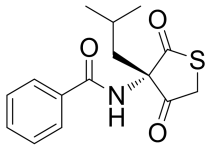
***N*-(3-benzyl-4-hydroxy-2-oxotetrahydrothiophen-3-yl)-1-naphthamide (3t)**



Afforded according to the general procedure as a colourless solid in 91% yield; m.p. = 101.7-102.5 °C; $[\alpha]^{20}_D$ = 10.91 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.54 –7.44 (m, 2H), 7.34 – 7.24 (m, 2H), 7.23 – 7.16 (m, 3H), 7.12 (d, *J* = 4.9 Hz, 2H), 6.71 (s, 1H), 6.59 (s, 1H), 4.81 – 4.73 (m, 1H), 3.72 (d, *J* = 14.2 Hz, 1H), 3.49 (dd, *J* = 11.2, 7.2 Hz, 1H), 3.29 (t, *J* = 10.6 Hz, 1H), 3.08 (d, *J* = 14.2 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.29, 171.42, 133.80, 133.77, 132.04, 131.89, 130.86, 130.05, 128.55, 128.36, 127.58, 127.49, 126.66, 125.70, 124.95, 124.50, 76.86, 72.60, 34.05, 32.21; **HRMS** (ESI) calcd. for $C_{22}H_{19}NO_3SNa^+$ $[M+Na]^+$ 400.0978, found 400.0967; **HPLC**: The ee value was 72%, t_R (minor) = 11.260 min, t_R (major) = 12.947 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 80:20, flow rate = 1 mL/min, UV = 254 nm).

General Procedure for the Synthesis of compound 4.[7]

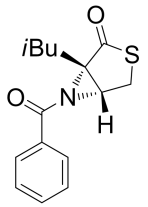
To a stirred solution of pyridinium dichromate (PDC, 1.0 mmol) in dichloromethane (2.5 mL), **3a** (0.5 mmol) was added. After reflux at 40 °C for about 12 h , the mixture was concentrated in vacuo and purified by flash column chromatography (PE/EA = 10 /1) to afford the product **4**.



As a white solid in 98% yield; m.p. = 151.0-152.4 °C; $[\alpha]^{20}_D$ = +6.84 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 6.85 (s, 1H), 4.23 (d, *J* = 17.4 Hz, 1H), 4.05 (d, *J* = 17.4 Hz, 1H), 1.97 – 1.75 (m, 3H), 1.02 (dd, *J* = 6.4, 2.5 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.53, 200.65, 166.71, 132.63, 131.25, 128.75, 127.40, 65.66, 43.05, 38.96, 24.13, 24.09, 24.04; **HRMS** (ESI) calcd for $C_{15}H_{18}NO_3S^+$ $[M+H]^+$ 292.1002, found 292.0995; **HPLC**: The ee value was 63%, t_R (minor) = 16.307 min, t_R (major) = 11.083 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

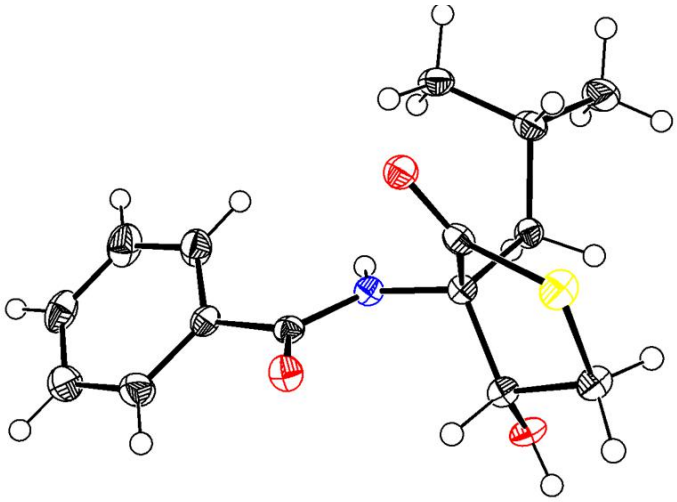
General Procedure for the Synthesis of compound 5.

To a flame-dried 50 mL round bottom flask, containing a stir bar, was added **3a** (0.2 mmol), anhydrous CH_2Cl_2 (2 mL), and pyridine (0.2 mmol) under an atmosphere of N_2. After cooling in an ice bath, trifluoromethyanesulfonic anhydride (0.24 mmol) was added dropwise. The reaction was then allowed to warm to room temperature with stirring. After 3 h, the reaction was diluted with H_2O and extracted into CH_2Cl_2. The organic layers were combined, dried over $NaSO_4$, and filtered. The filtrate was concentrated in vacuo and purified by flash column chromatography (PE/EA = 10 /1) to afforded the product **5**.



As a white oil in 96% yield; $[\alpha]^{20}_D$ = -5.20 (*c* = 1.0, CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 – 7.93 (m, 2H), 7.55 – 7.46 (m, 1H), 7.40 (dd, *J* = 10.5, 4.6 Hz, 2H), 5.29 (dd, *J* = 5.9, 1.4 Hz, 1H), 3.75 (dd, *J* = 13.2, 5.9 Hz, 1H), 3.65 (dd, *J* = 13.2, 1.5 Hz, 1H), 1.98 (qd, *J* = 14.3, 6.5 Hz, 2H), 1.77 (tt, *J* = 13.3, 6.7 Hz, 1H), 0.98 (dd, *J* = 9.1, 6.6 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 205.04, 164.01, 132.08, 128.70, 128.43, 126.47, 87.59, 83.80, 43.24, 34.62, 24.73, 24.16, 23.72; **HRMS** (ESI) calcd for $C_{15}H_{18}NO_2S^+$ $[M+H]^+$ 276.1053, found 276.1044; **HPLC**: The ee value was 68%, t_R (minor) = 7.803 min, t_R (major) = 6.400 min (Chiralcel OD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate = 1 mL/min, UV = 254 nm).

5. 1) X-Ray Crystallographic Data of 3a (CCDC number: 1817567)



Bond precision:	C-C = 0.0019 A		Wavelength = 1.54184
Cell:	a = 10.0093 (2)	b = 14.3918 (3)	c = 10. 7208 (2)
	alpha = 90	beta = 104.176 (2)	gamma = 90
Temperature:	100 K		
	Calculated		Reported
Volume	1497.32 (5)		1497.33(6)
Space group	P 21/c		P 1 21/c 1
Hall group	-P 2ybc		-P 2ybc
Moiety formula	C15 H19 N O3 S		C15 H19 N O3 S
Sum formula	C15 H19 N O3 S		C15 H19 N O3 S
Mr	293.37		293.37
Dx,g cm-3	1.354		1.354
Z	4		4
Mu (mm-1)	2.060		2.060
F000	624.0		624.0
F000'	627.06		
h,k,lmax	7, 26, 11		7, 26, 11
Nref	2554		2540
Tmin,Tmax	0.781, 0.814		0.757, 1.000
Tmin'	0.539		

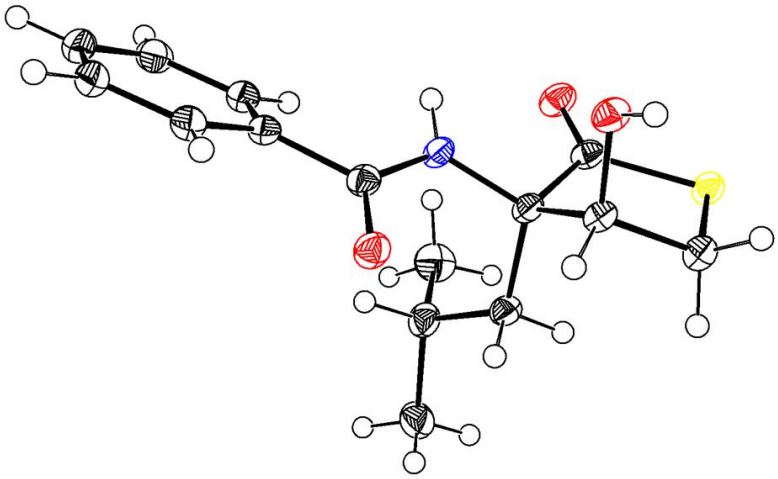
Correction method= # Reported T Limits: Tmin = 0.006 Tmax = 1.000
AbsCorr = MULTI-SCAN

Data completeness = 0.995 Theta(max) = 67.080

R(reflections) = 0.0348(2441) wR2(reflections) = 0.0940 (2540)

S = 1.057 Npar = 184

2) X-Ray Crystallographic Data of 3a' (CCDC number: 1817568)



Bond precision:	C-C = 0.0020 A		Wavelength = 1.54184
Cell:	a = 6.54242 (11)	b = 22.4359 (3)	c = 10. 03319 (17)
	alpha = 90	beta = 102.1649 (17)	gamma = 90
Temperature:	100 K		
	Calculated		Reported
Volume	1439.65 (4)		1439.65(4)
Space group	P 21/c		P 1 21/c 1
Hall group	-P 2ybc		-P 2ybc
Moiety formula	C15 H19 N O3 S		C15 H19 N O3 S
Sum formula	C15 H19 N O3 S		C15 H19 N O3 S
Mr	293.37		293.37
Dx,g cm-3	1.301		1.301
Z	4		4
Mu (mm-1)	1.981		1.981
F000	624.0		624.0
F000'	627.06		
h,k,lmax	11, 17, 12		11, 17, 12
Nref	2667 [5038]		2663
Tmin,Tmax	0.653, 0.820		0.515, 1.000
Tmin'	0.431		

Correction method= # Reported T Limits: Tmin = 0.006 Tmax = 1.000
AbsCorr = MULTI-SCAN

Data completeness = 0.999 Theta(max) = 67.079

R(reflections) = 0.0297(2520) wR2(reflections) = 0.0756 (2663)

S = 1.037 Npar = 184

6. References

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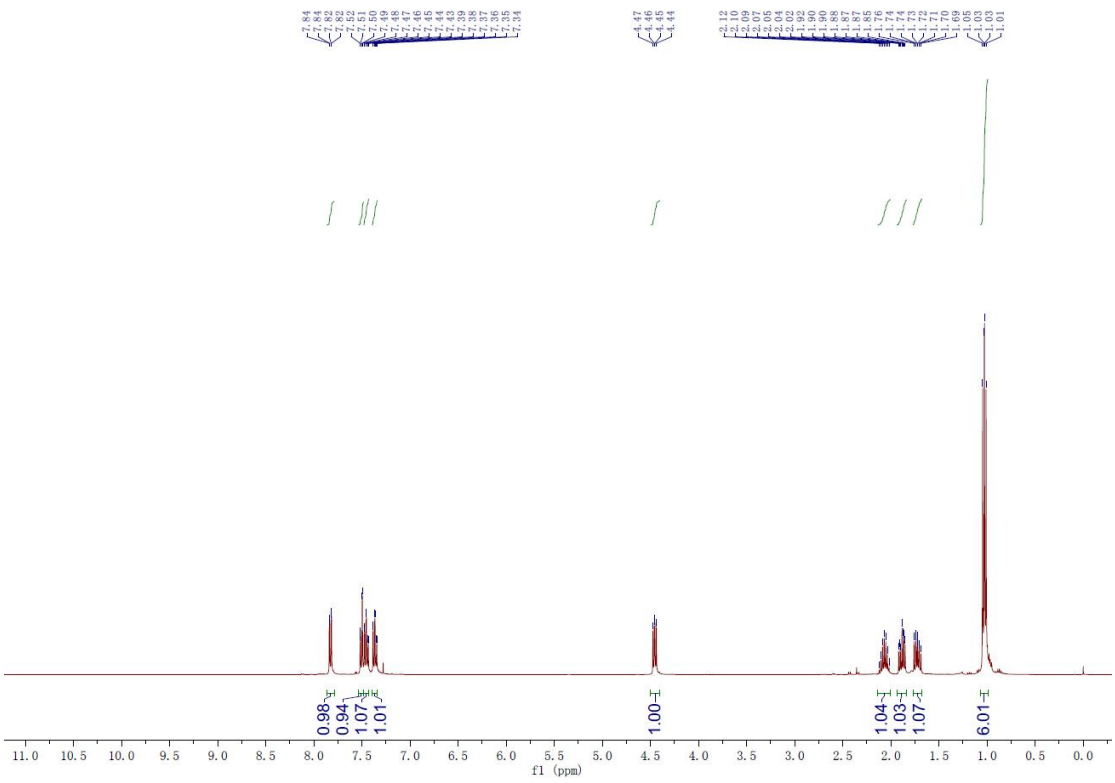
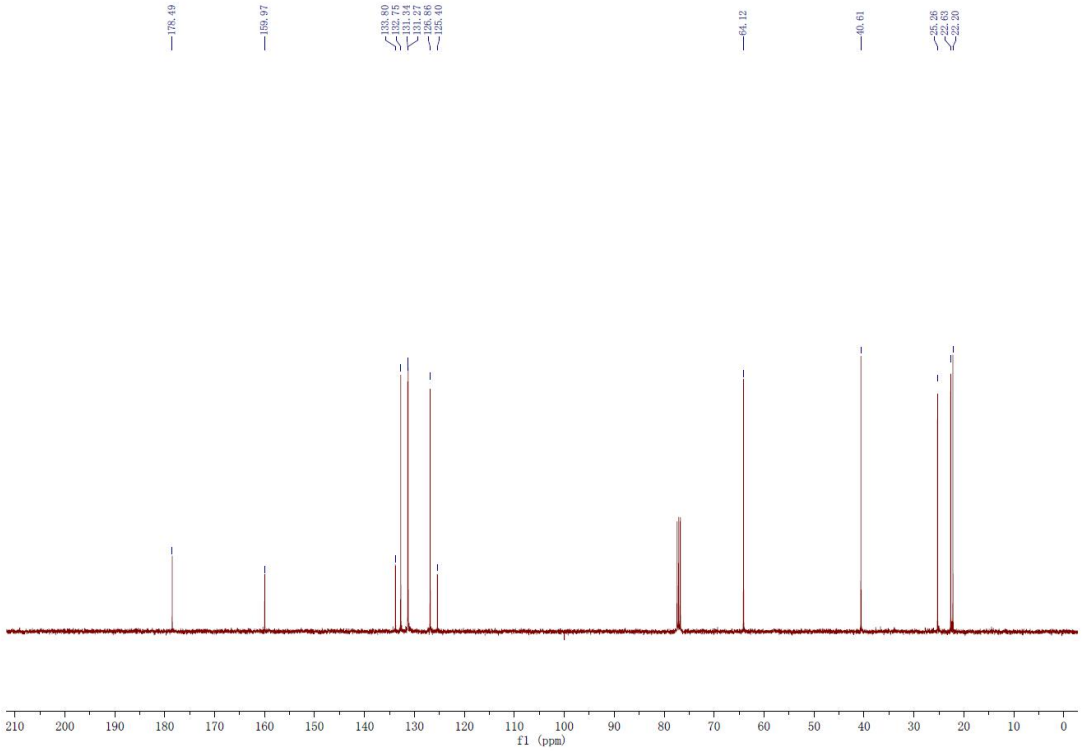
7. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR, HPLC Spectra of All Products

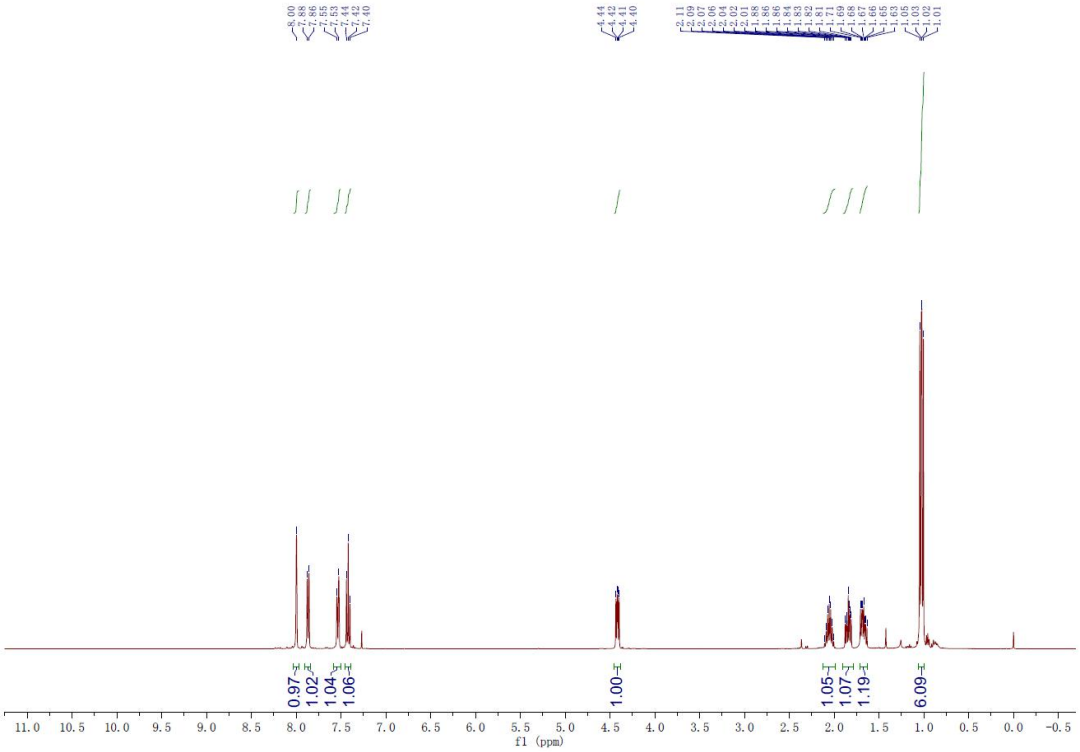
^{1}H NMR of **2b**



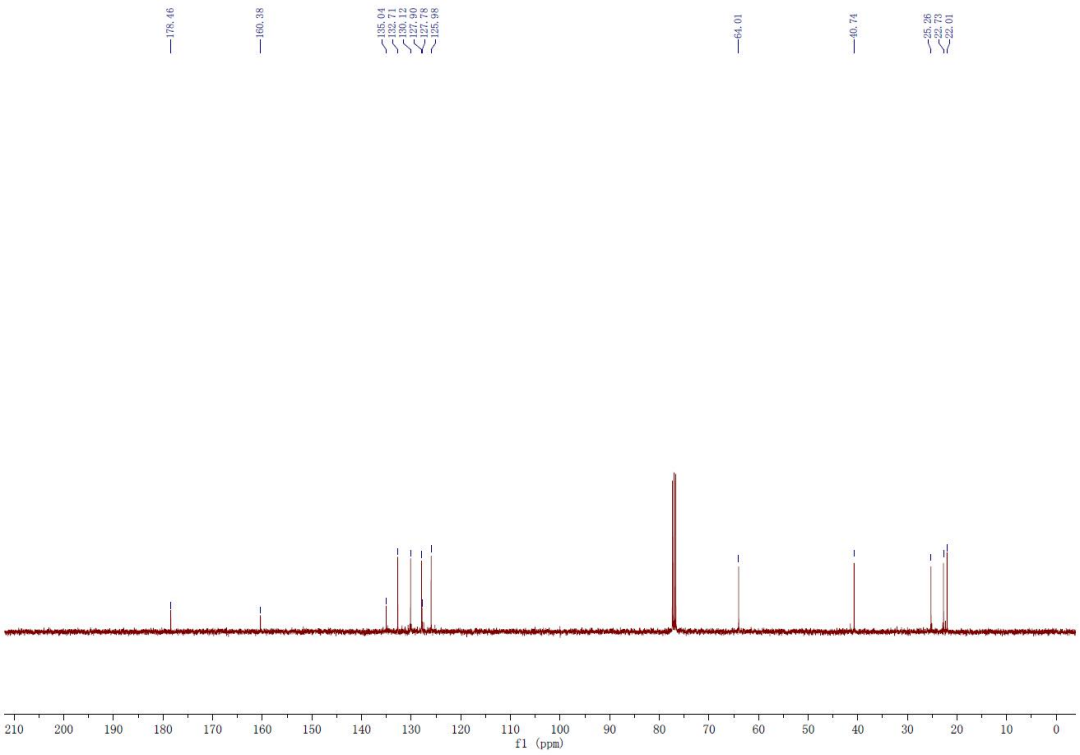
^{13}C NMR of **2b**



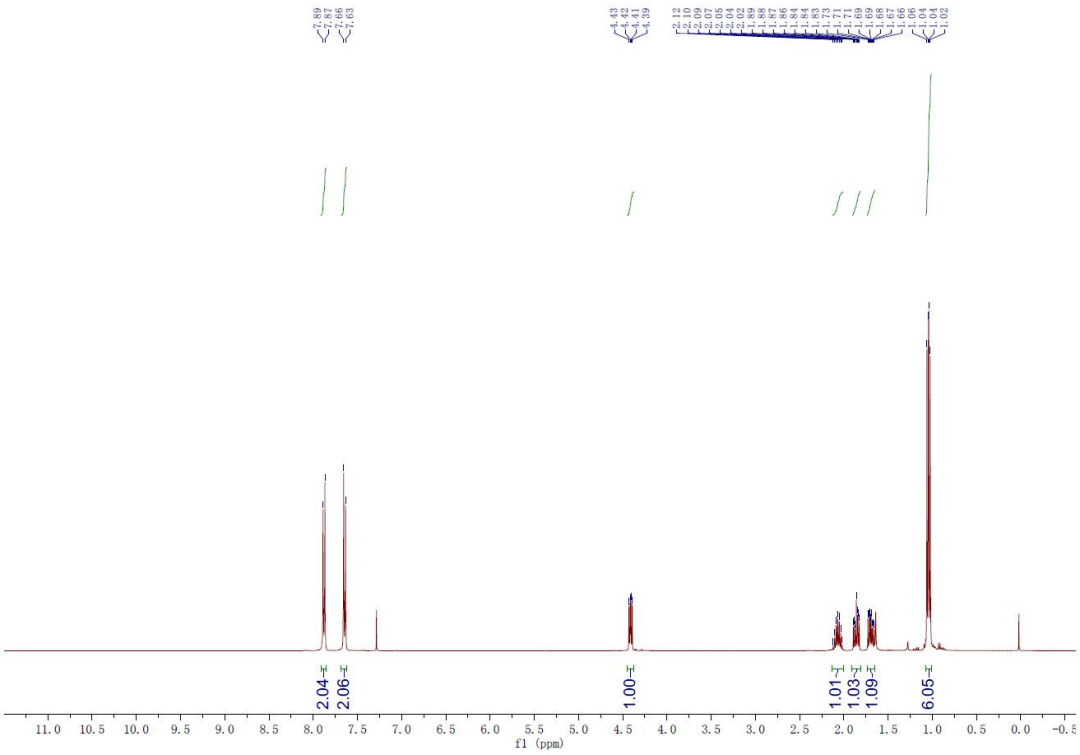
^{1}H NMR of **2c**



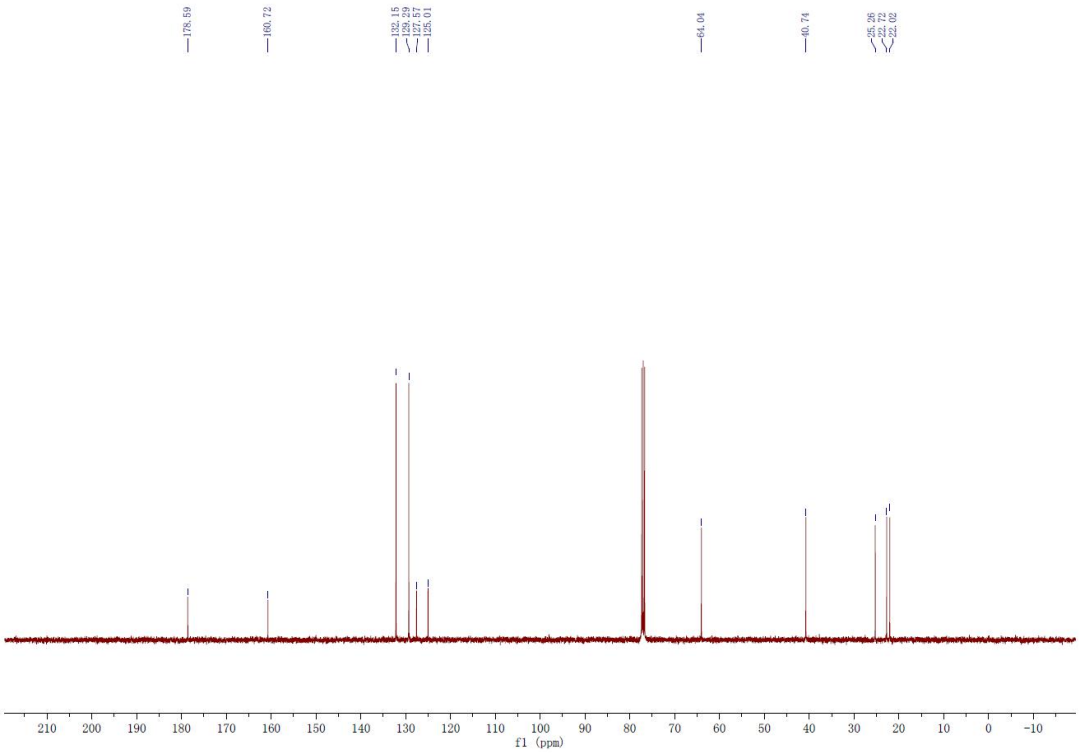
^{13}C NMR of **2c**



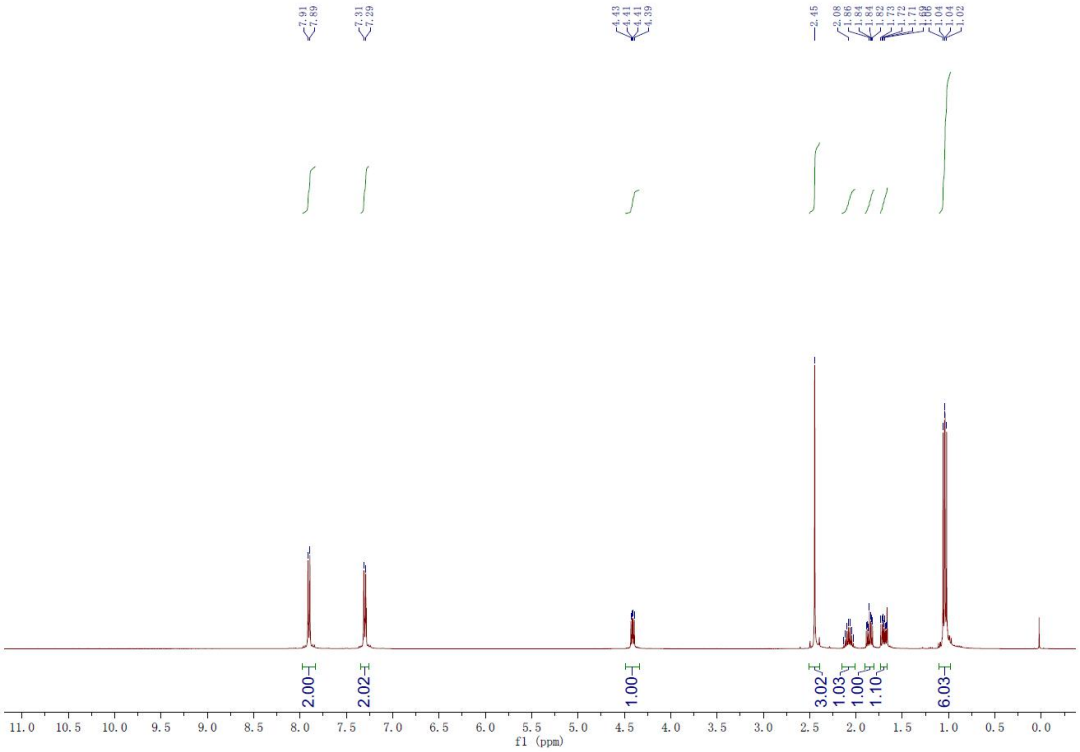
^{1}H NMR of **2e**



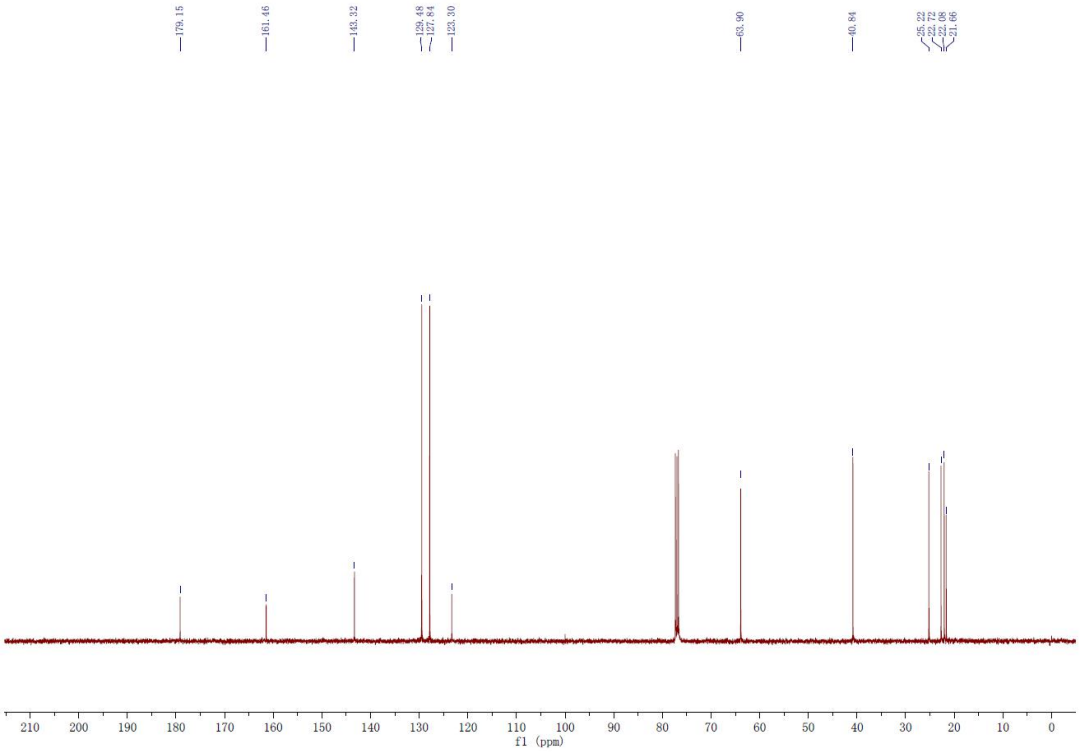
^{13}C NMR of **2e**



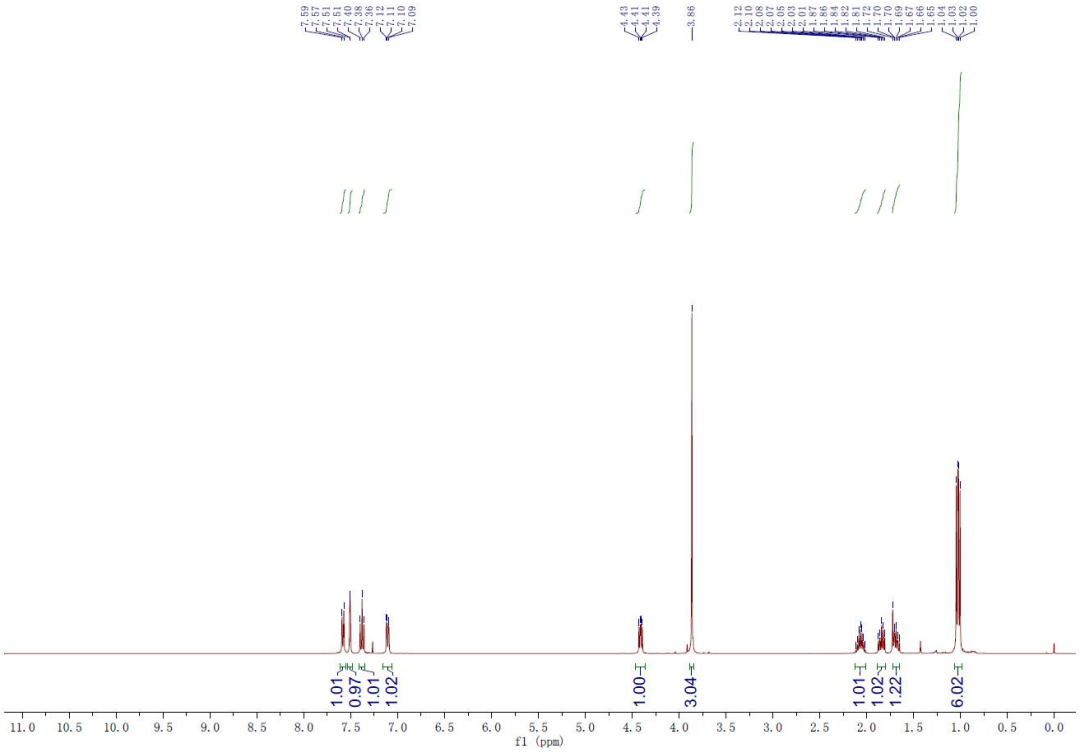
^{1}H NMR of **2f**



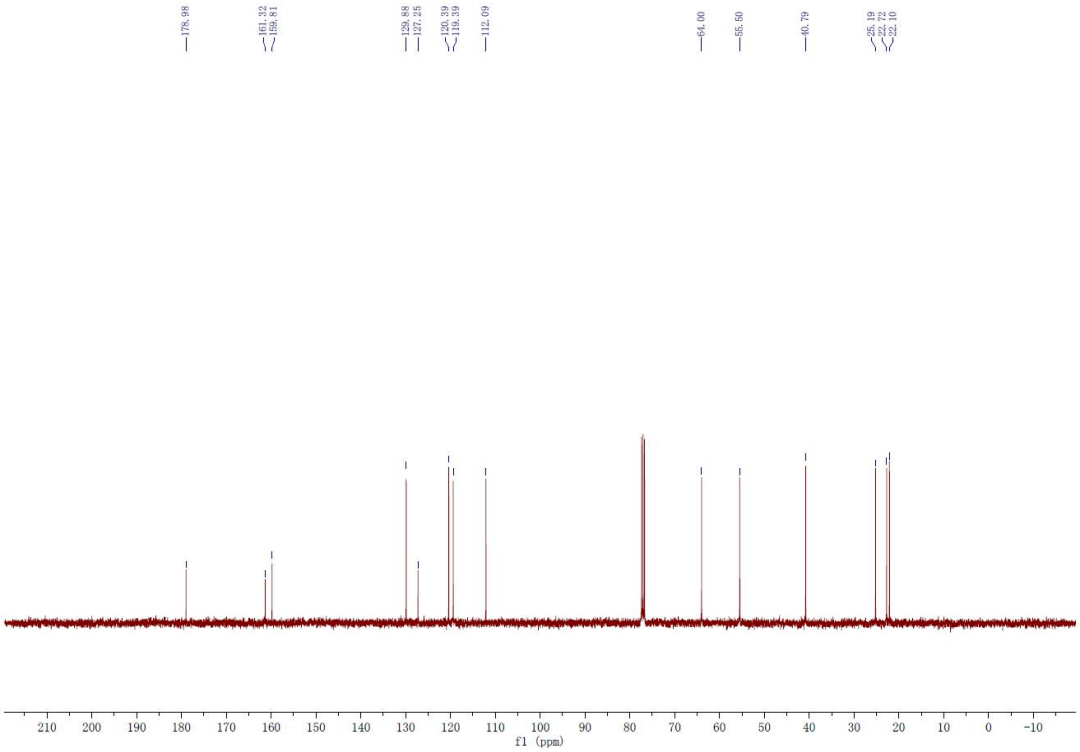
^{13}C NMR of **2f**



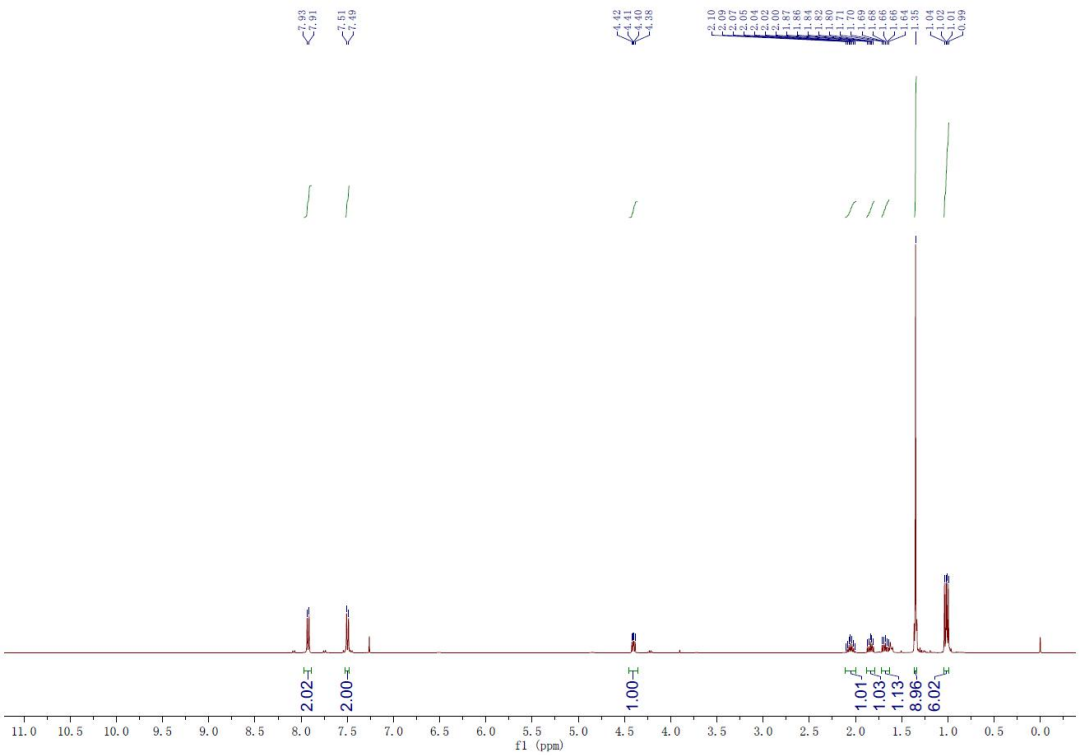
^{1}H NMR of **2g**



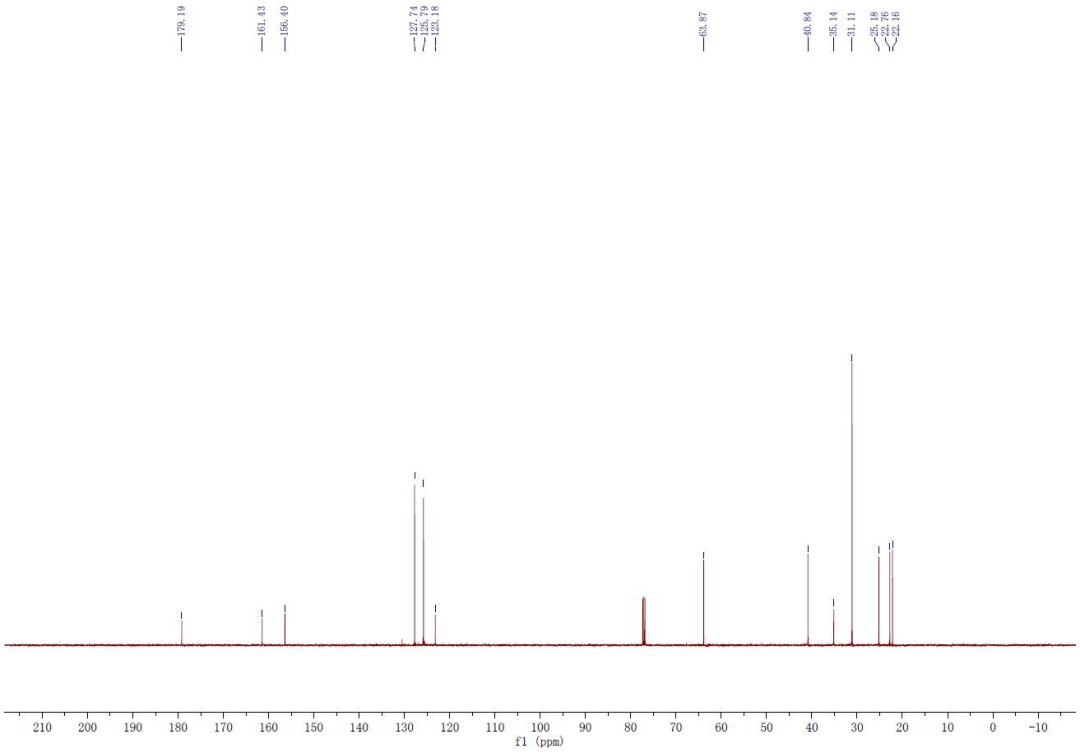
^{13}C NMR of **2g**



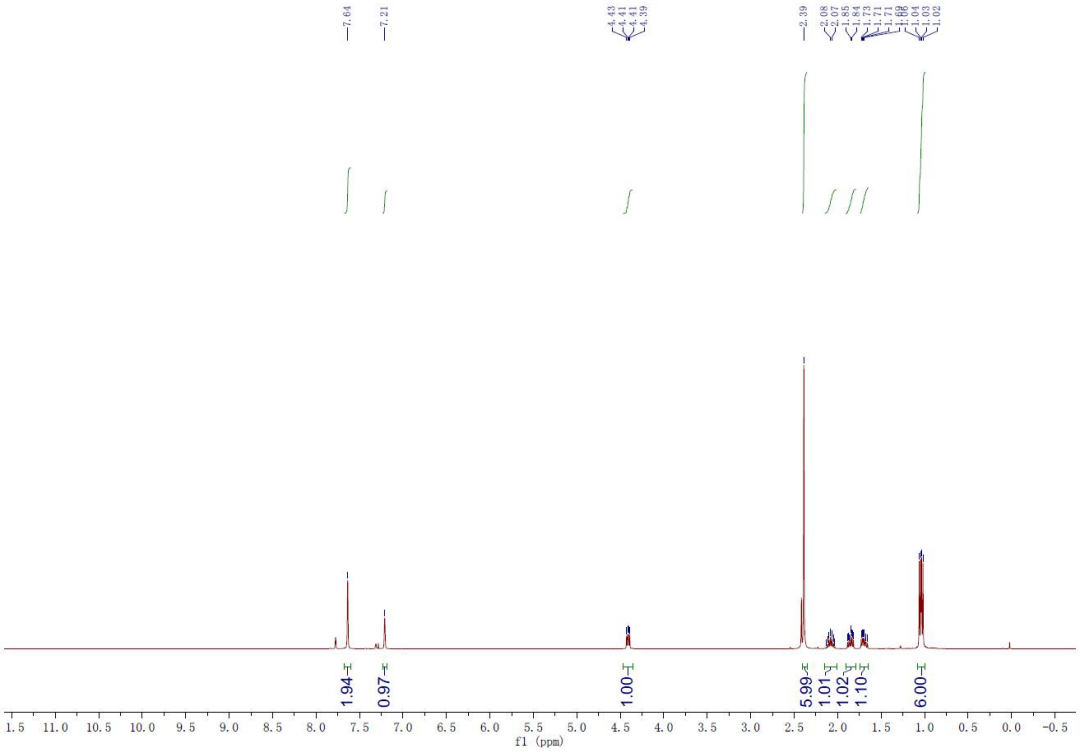
^{1}H NMR of **2i**



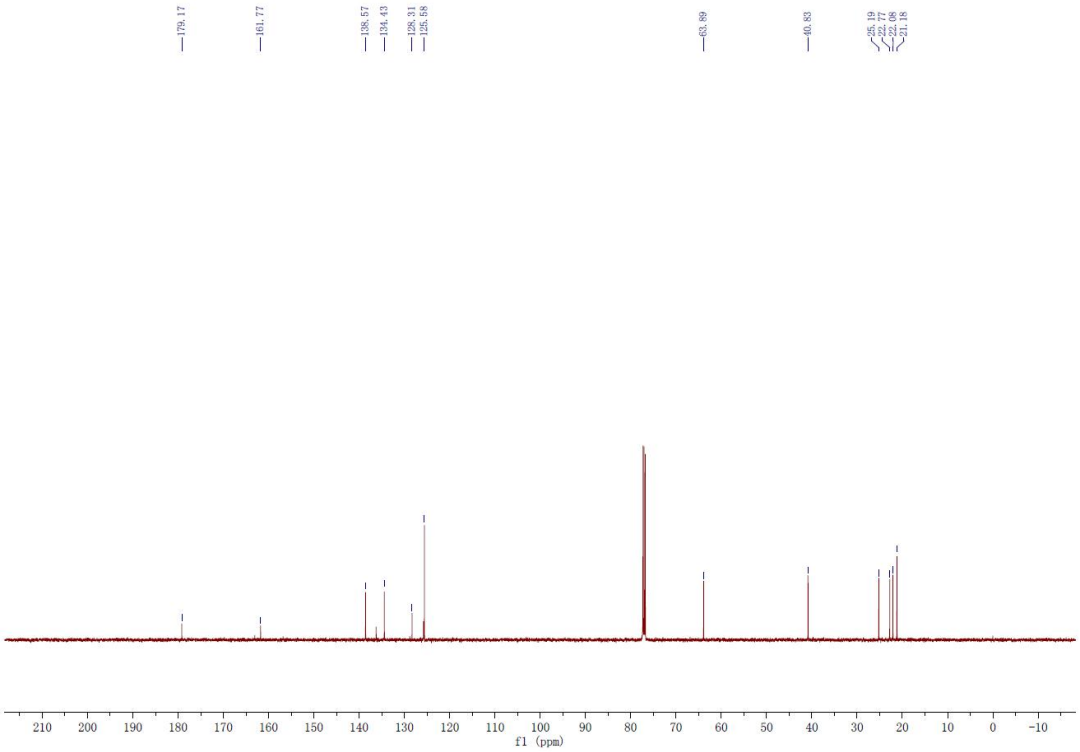
^{13}C NMR of **2i**



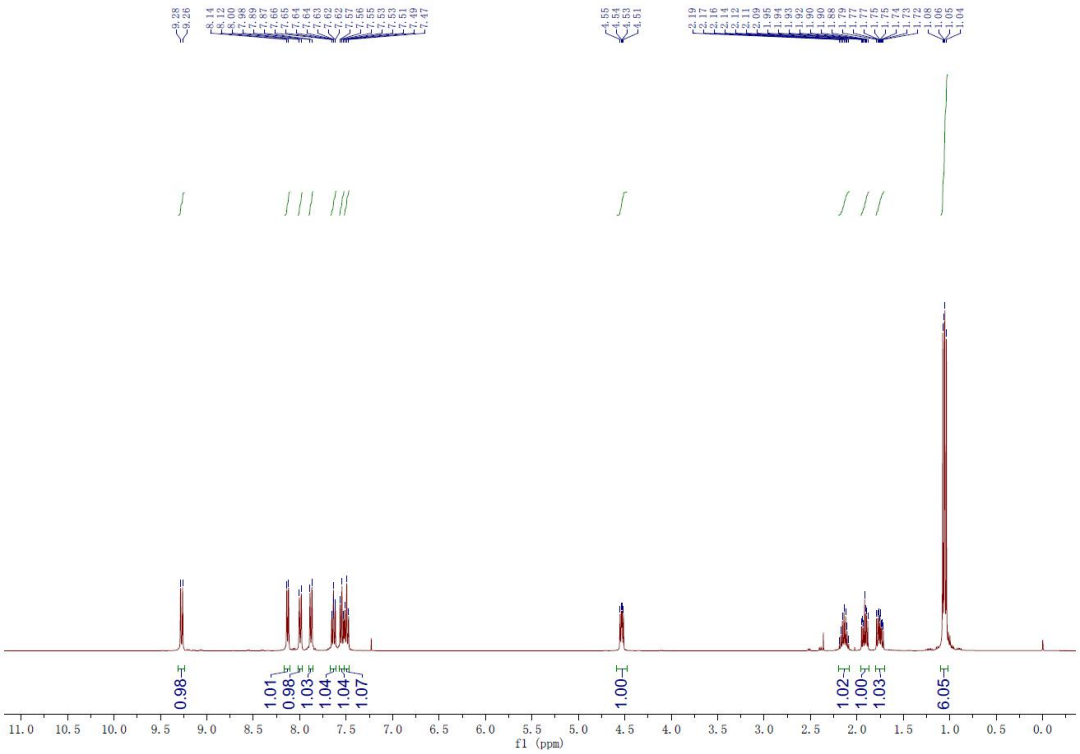
^{1}H NMR of **2k**



^{13}C NMR of **2k**



^{1}H NMR of **2o**



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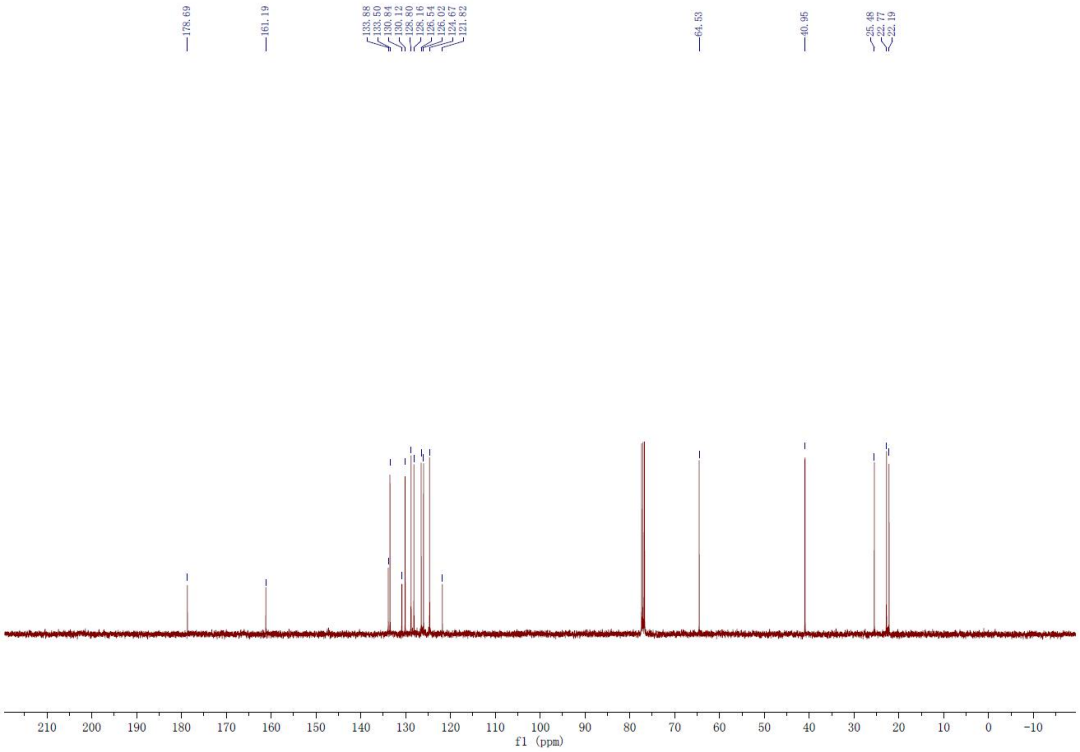

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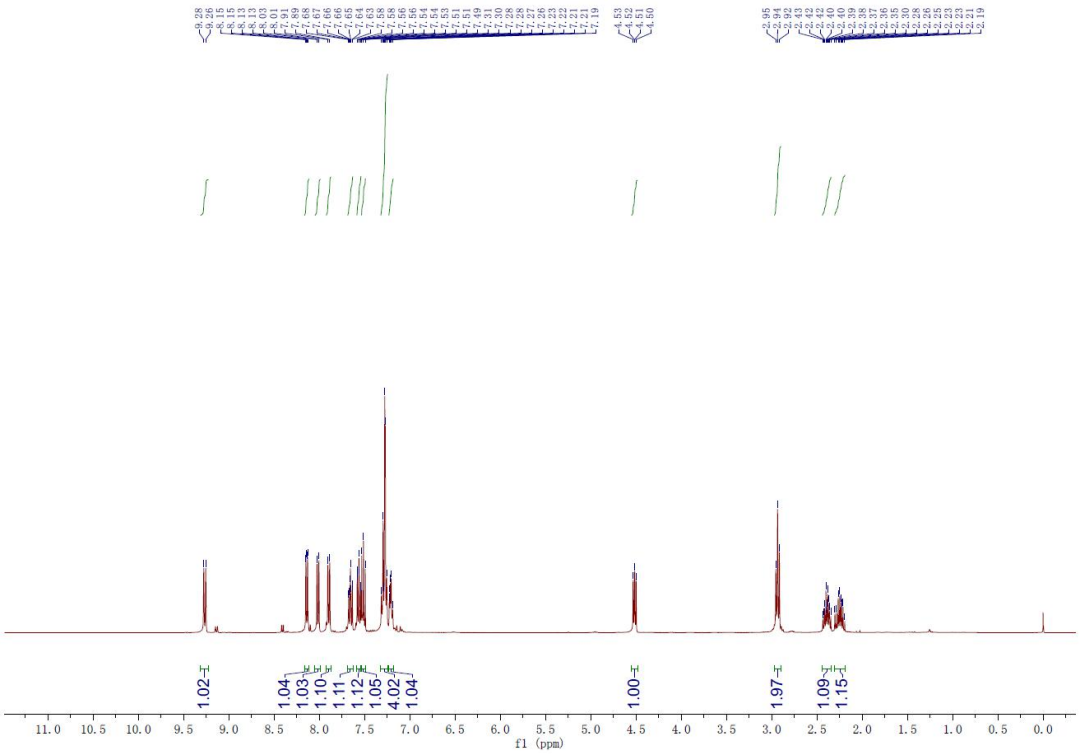
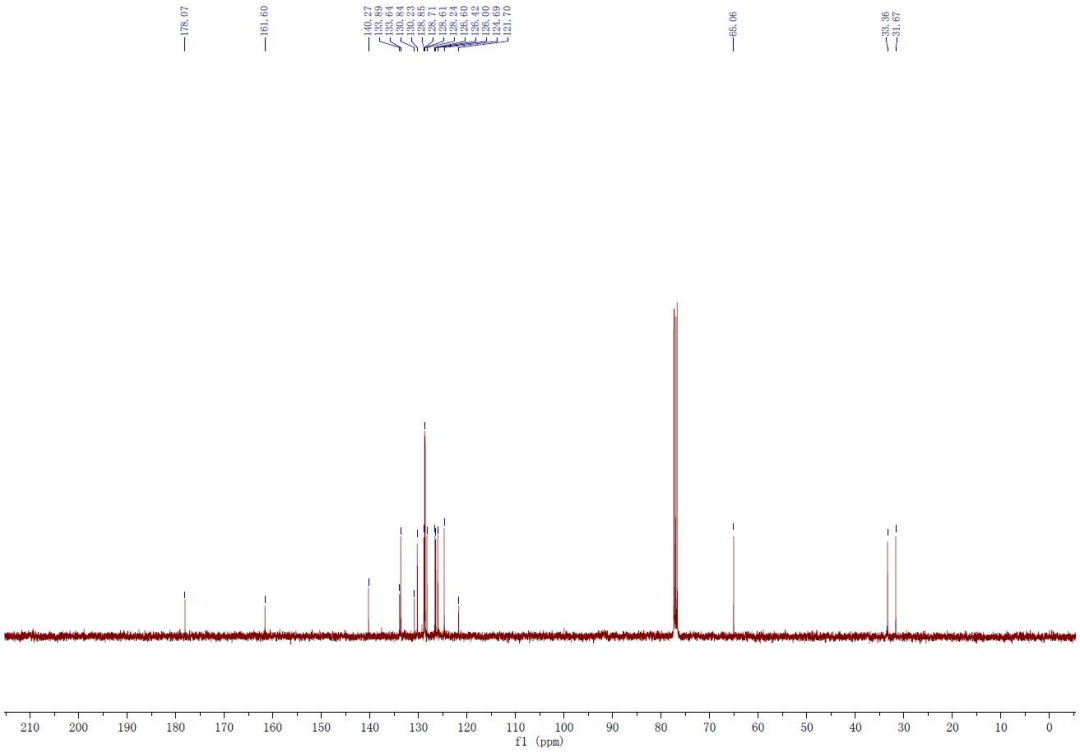


^{13}C NMR of **2q**



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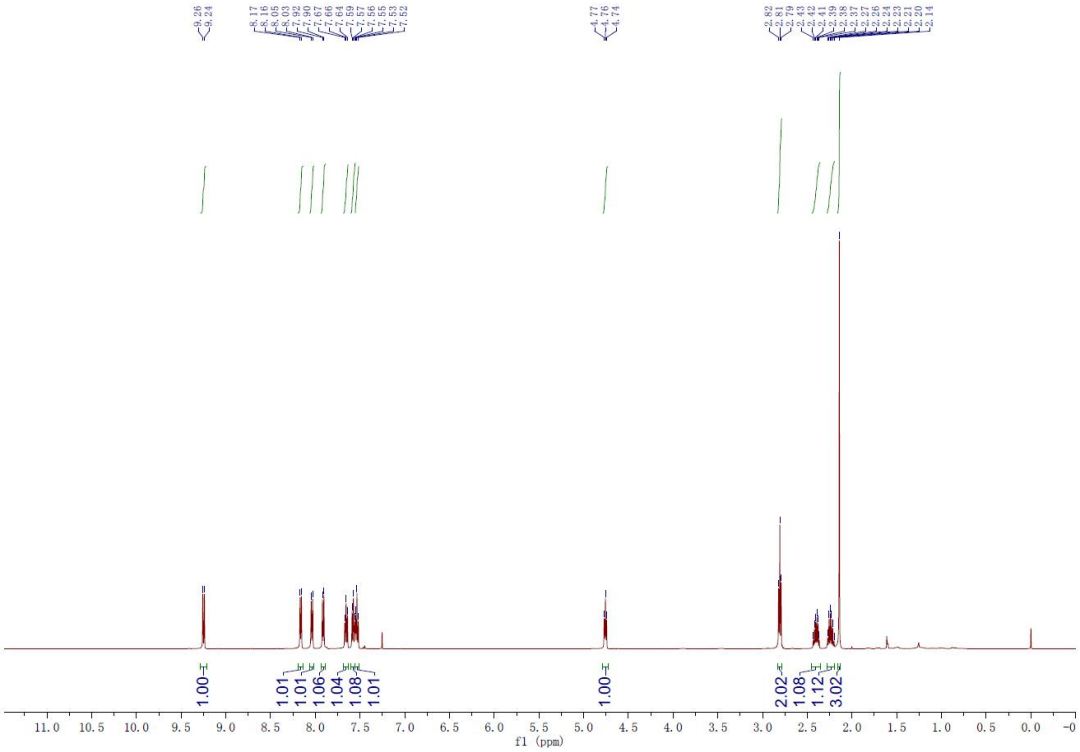
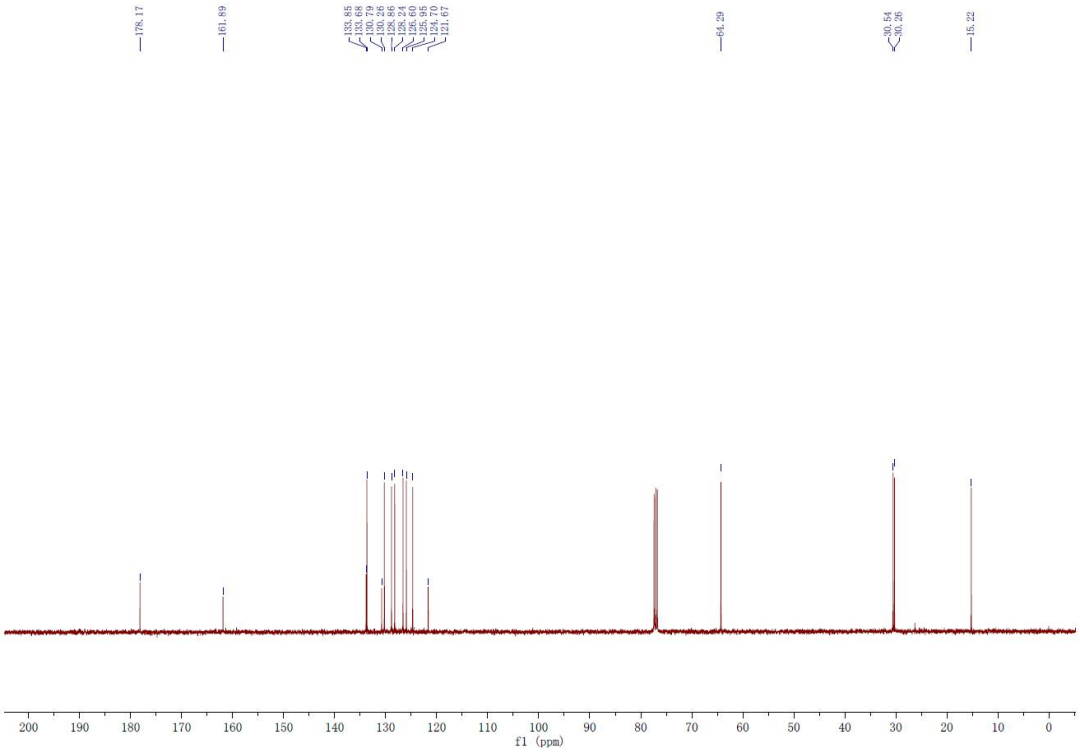


^{13}C NMR of **2r**



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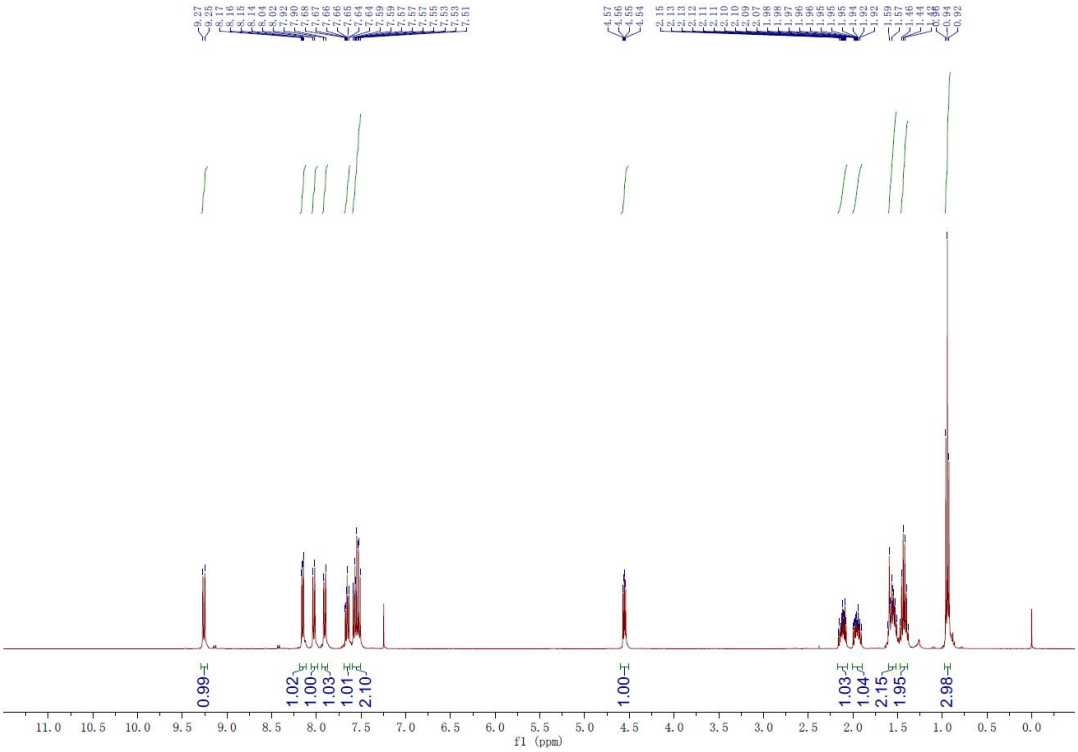

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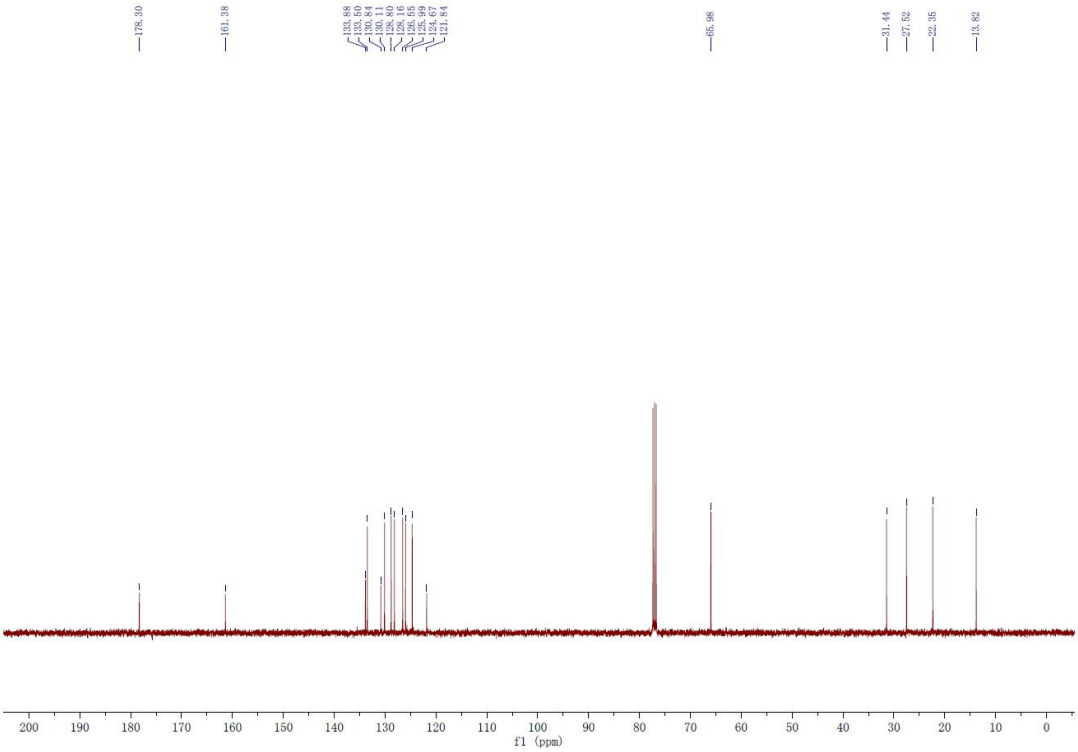
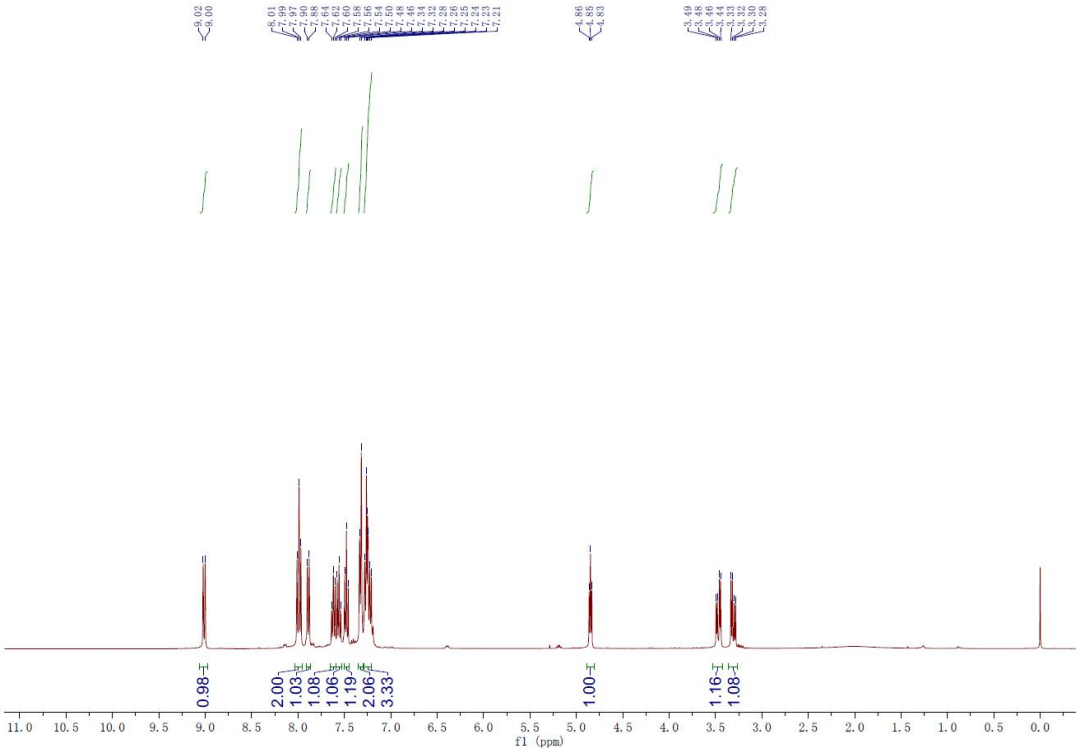


^{1}H NMR of **2t**



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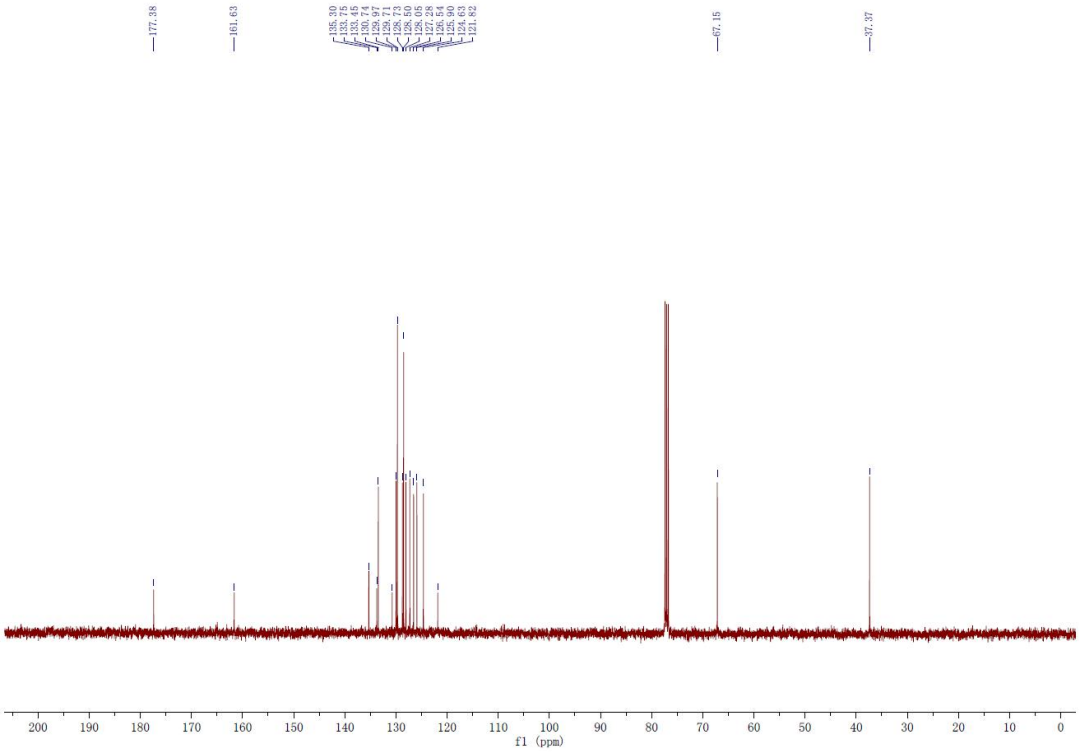
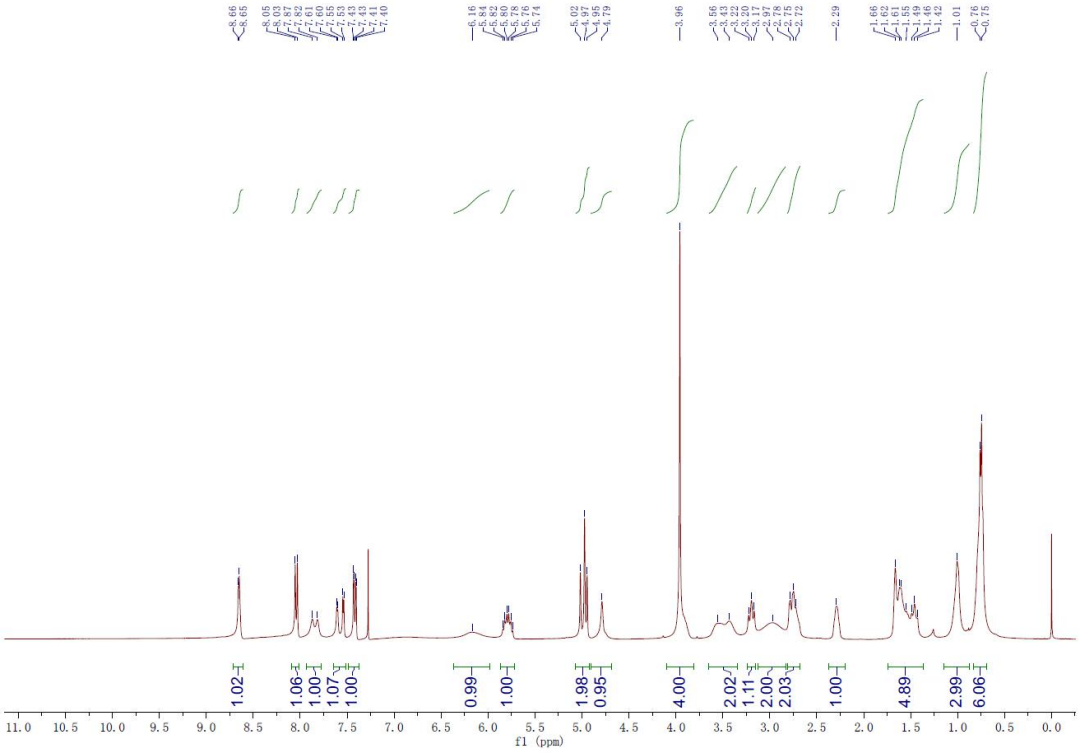
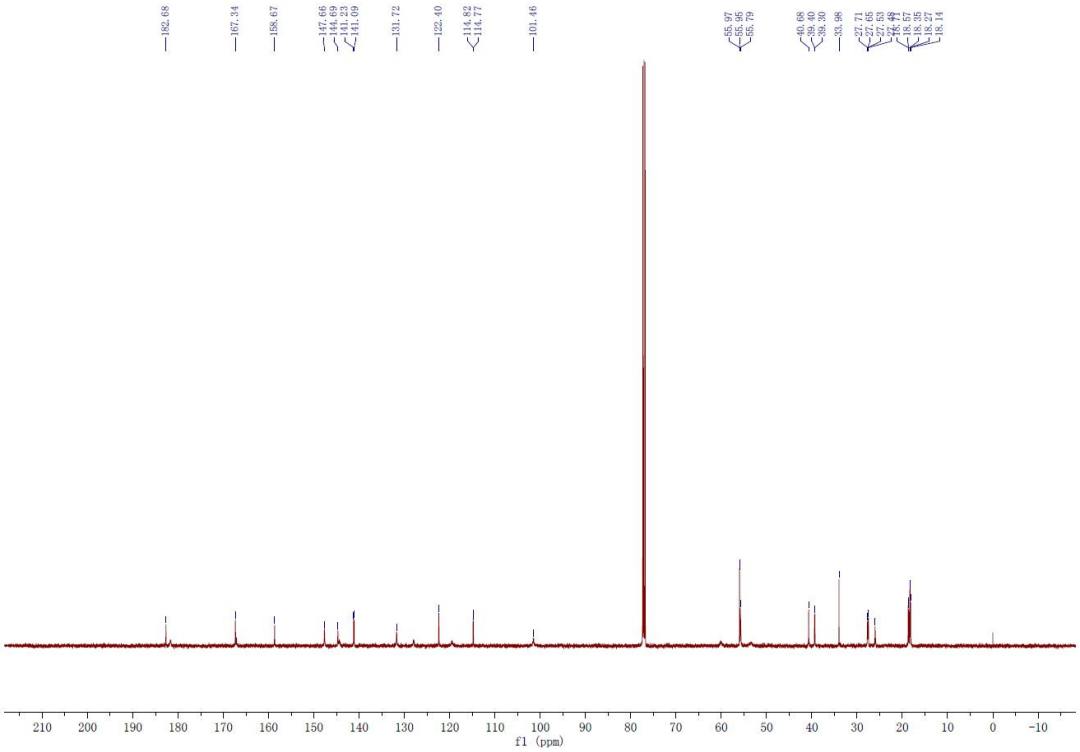


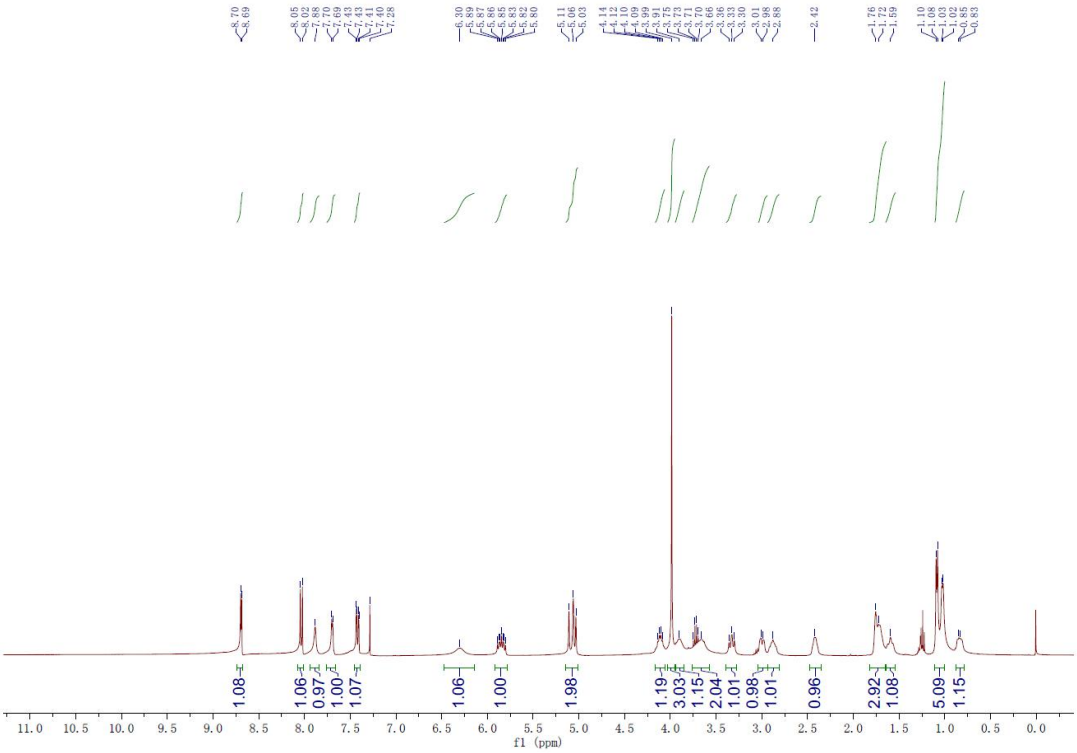
^{1}H NMR of **C6**



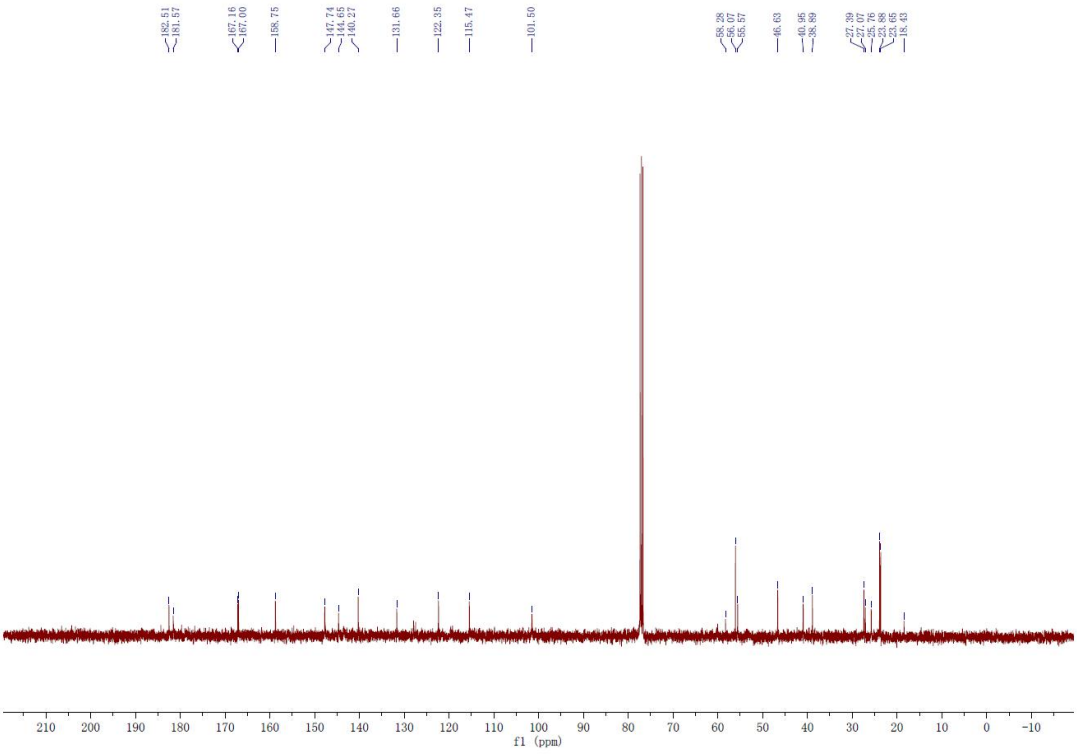
^{13}C NMR of **C6**



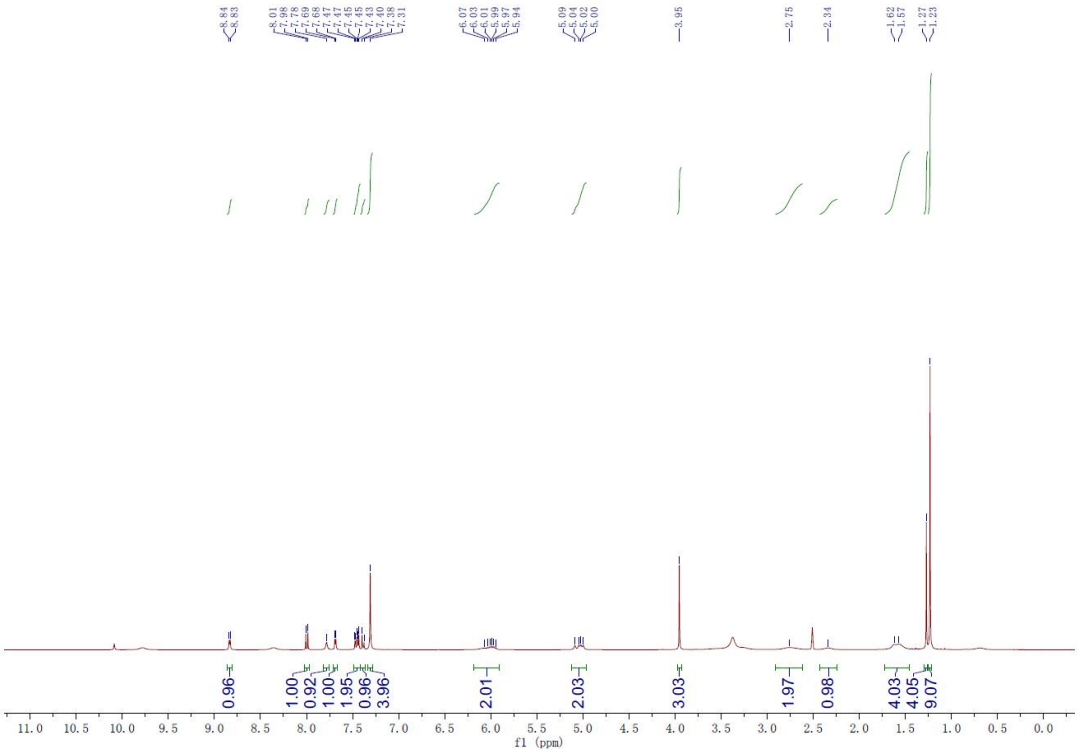
^{1}H NMR of **C8**



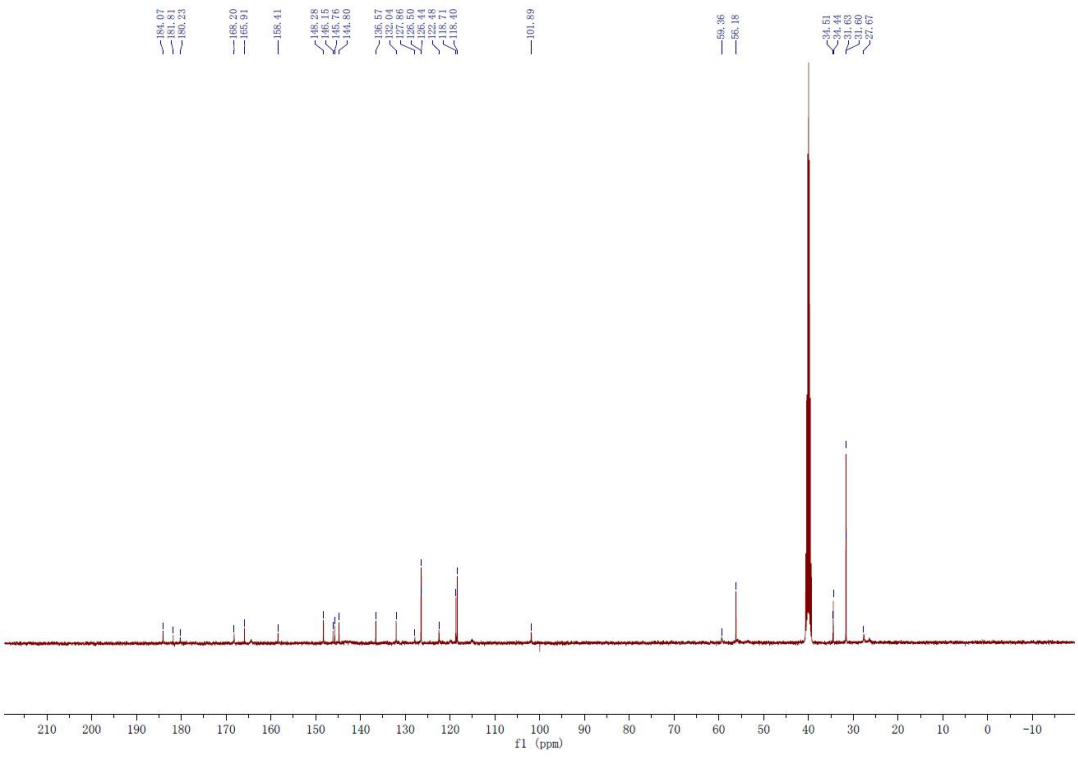
^{13}C NMR of **C8**



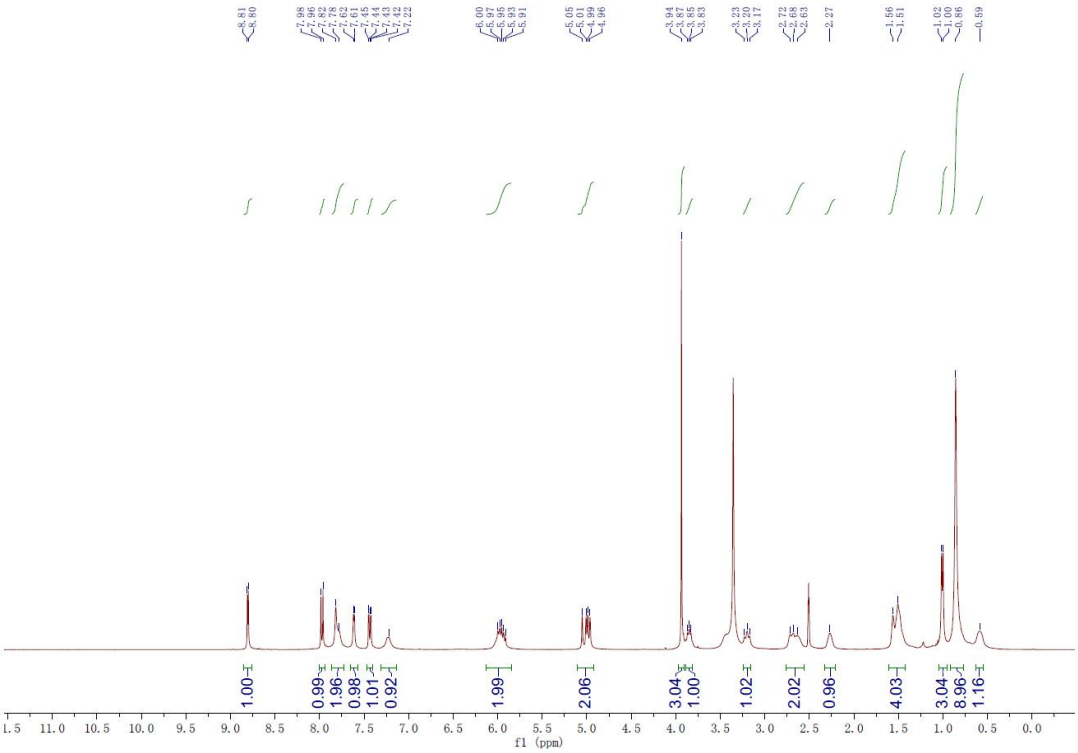
^{1}H NMR of **C9**



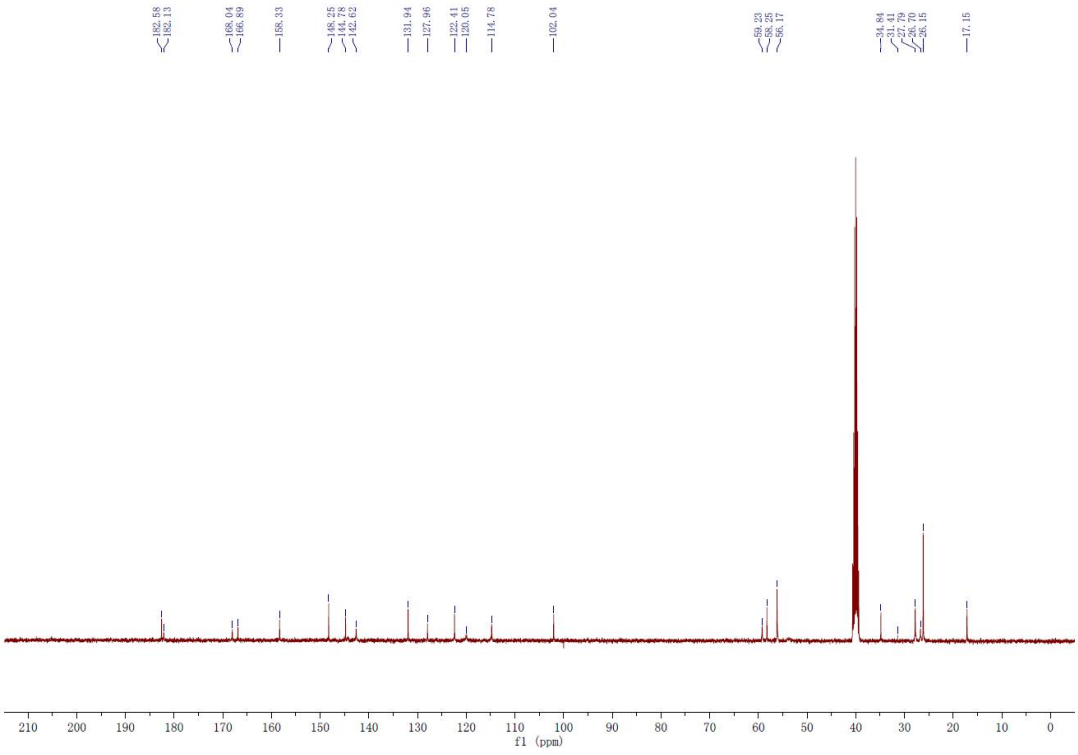
^{13}C NMR of **C9**



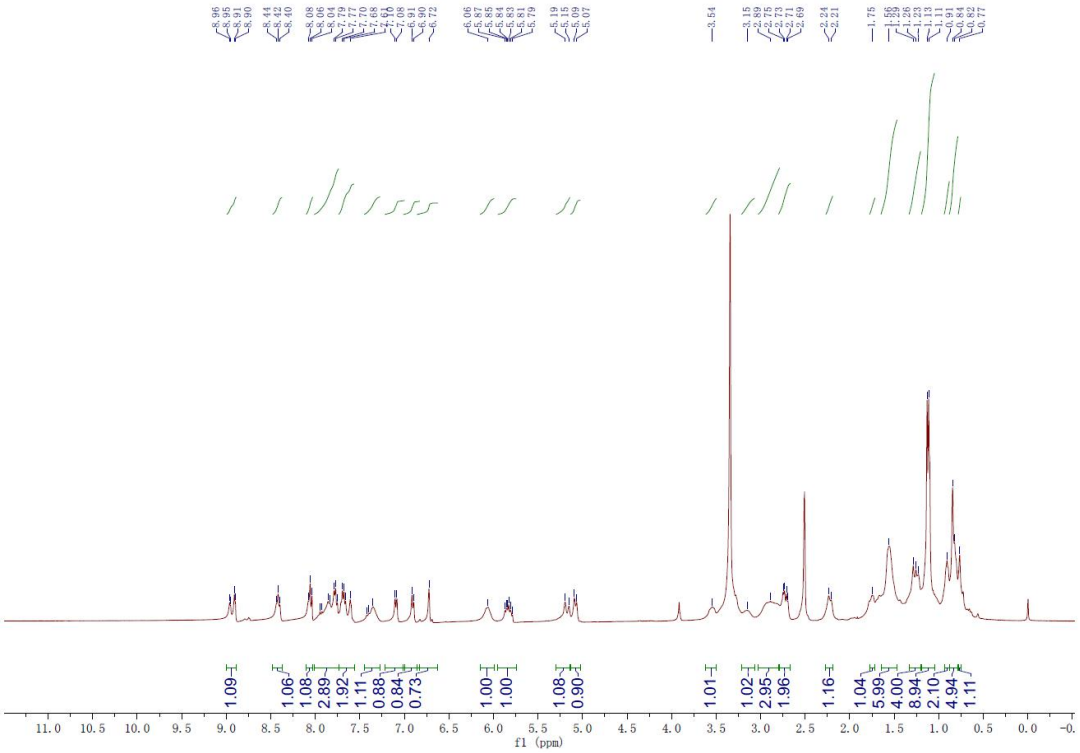
^{1}H NMR of **C10**



^{13}C NMR of **C10**



^{1}H NMR of **C11**



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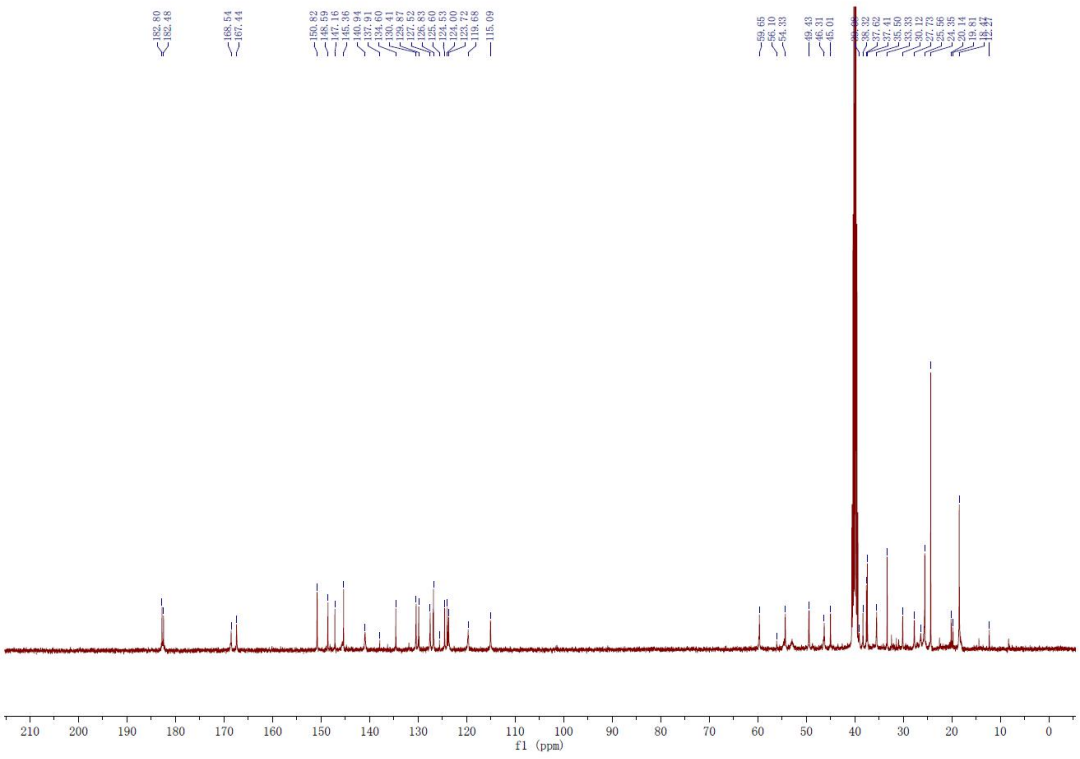
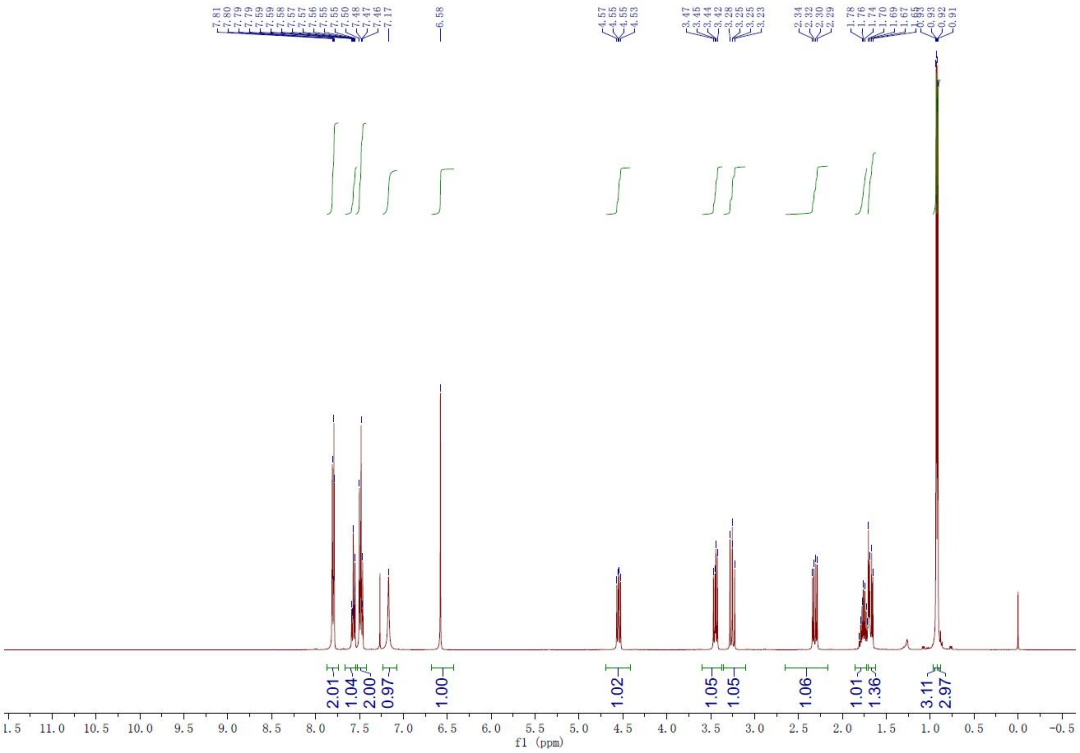
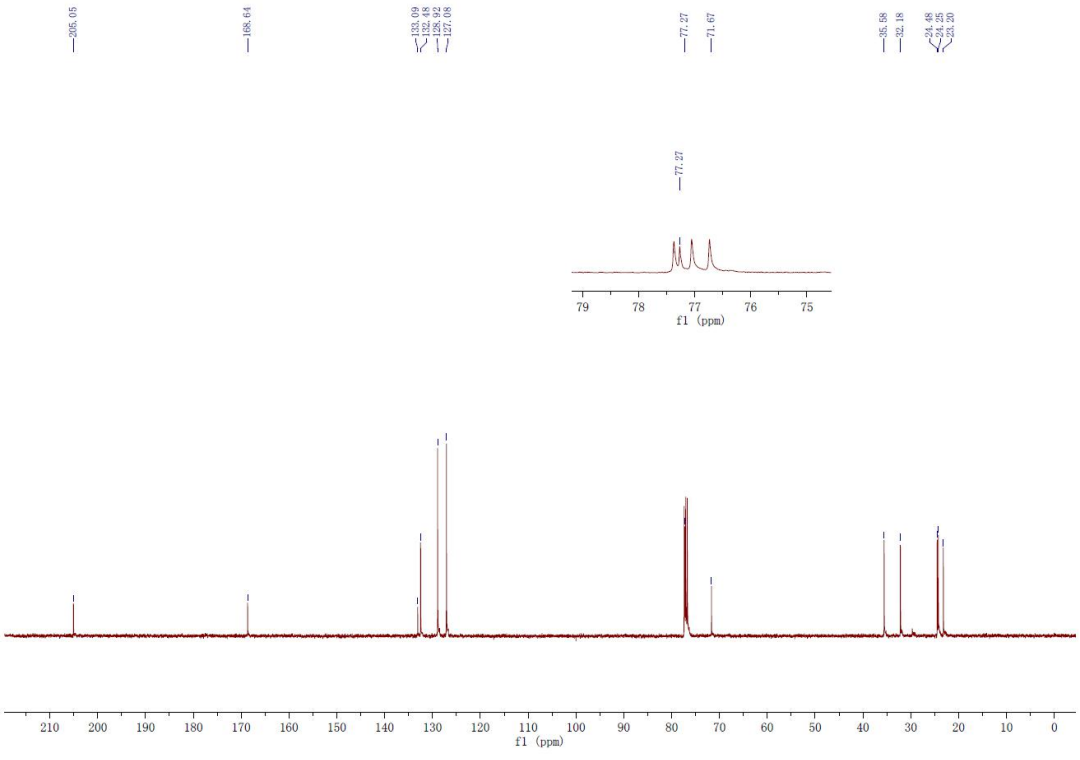


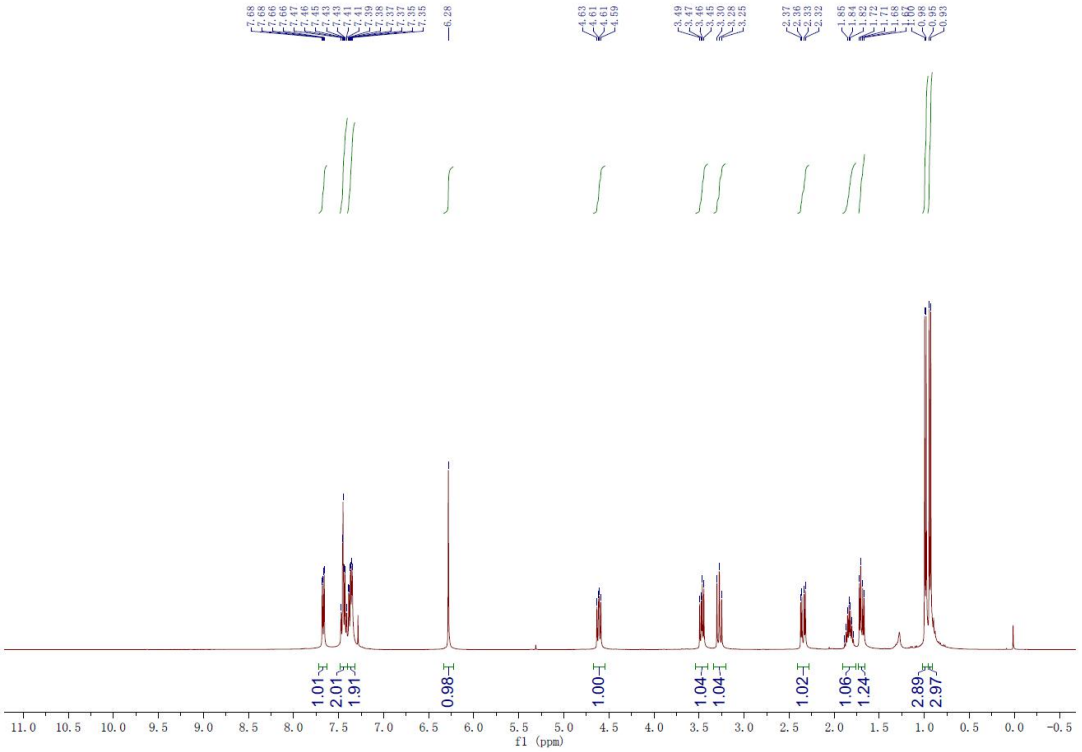
^{1}H NMR of **3a**



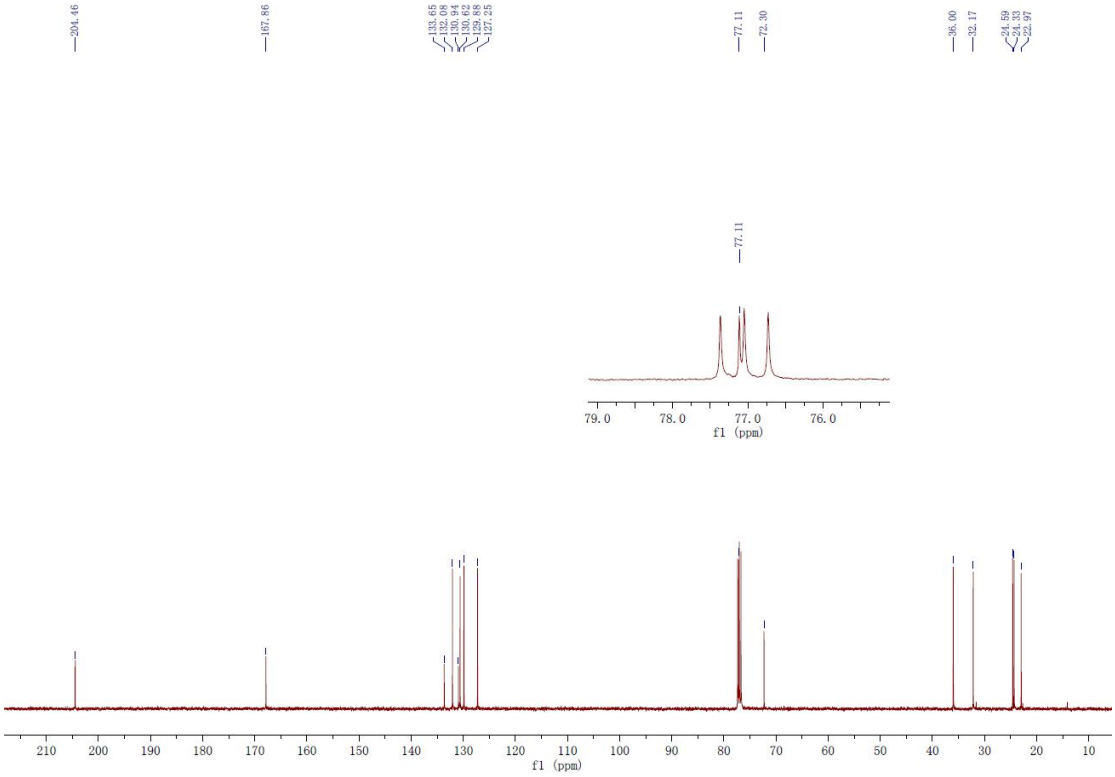
^{13}C NMR of **3a**



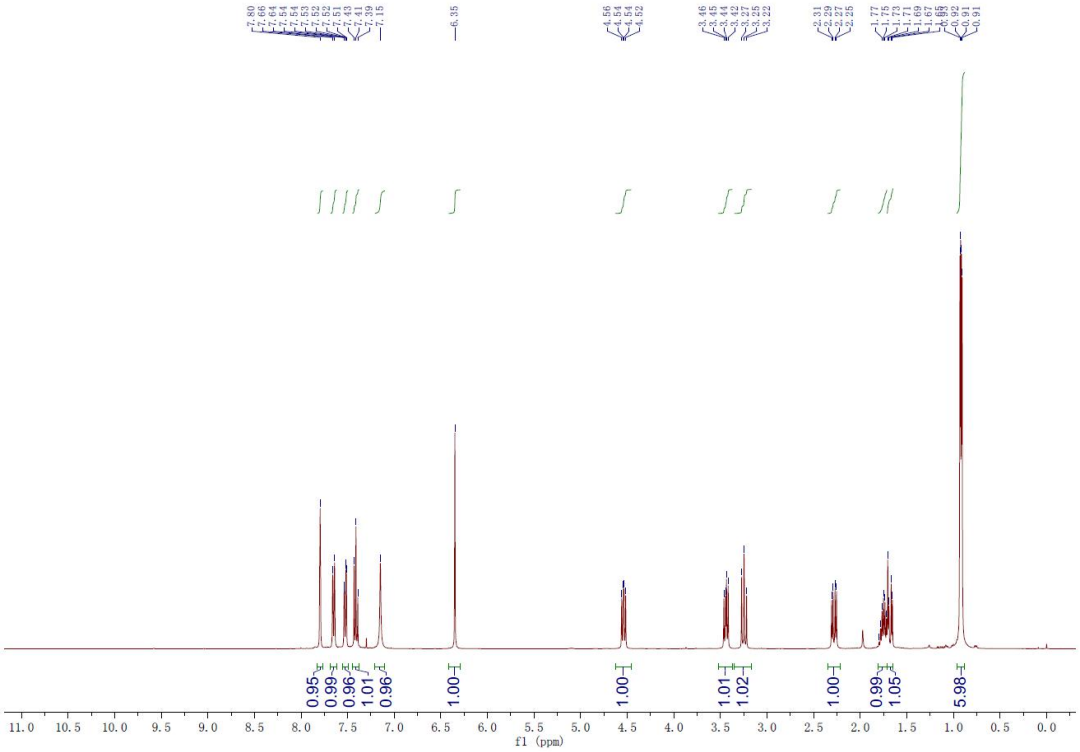
^{1}H NMR of **3b**



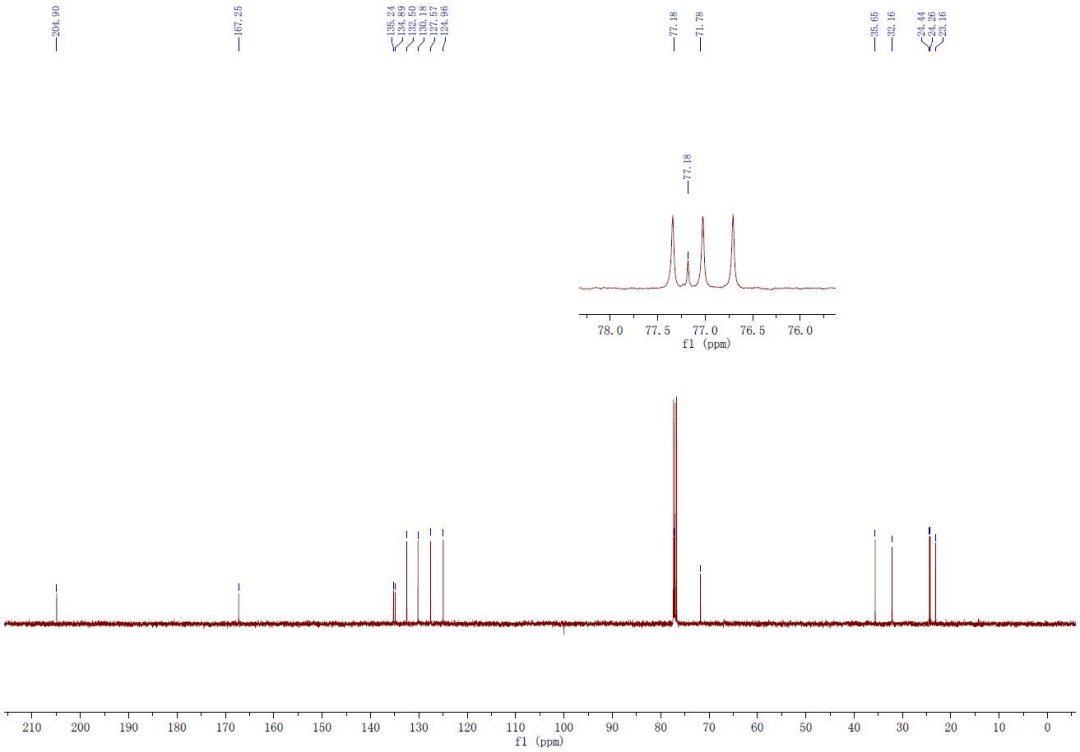
^{13}C NMR of **3b**



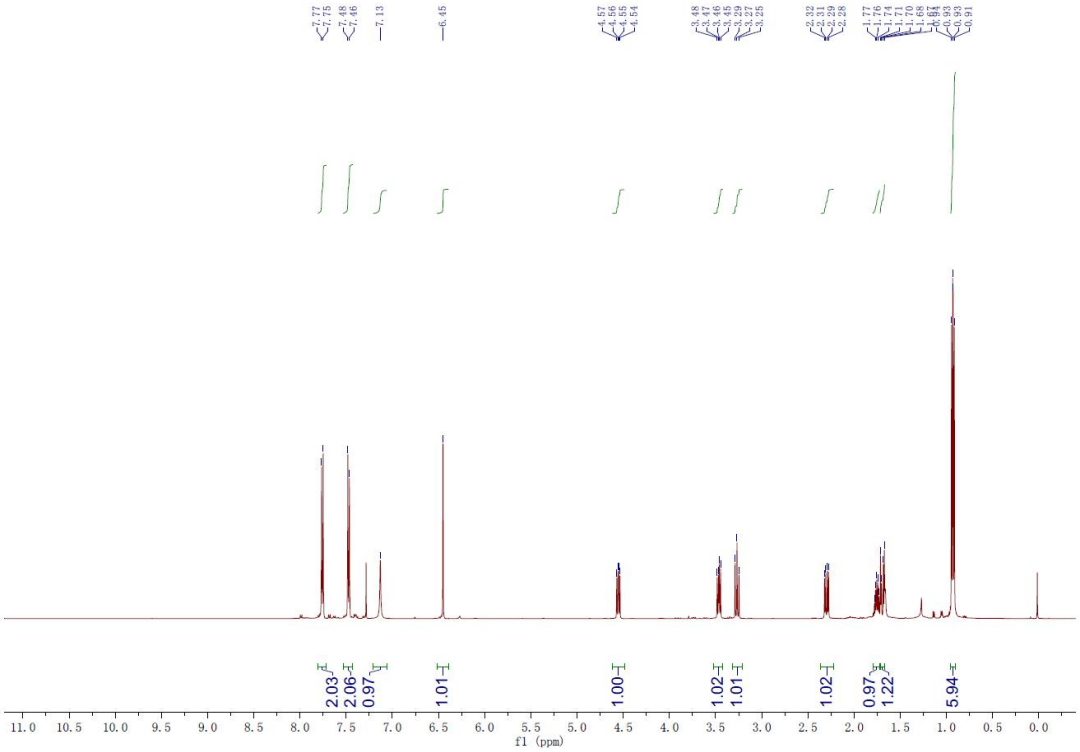
^{1}H NMR of **3c**



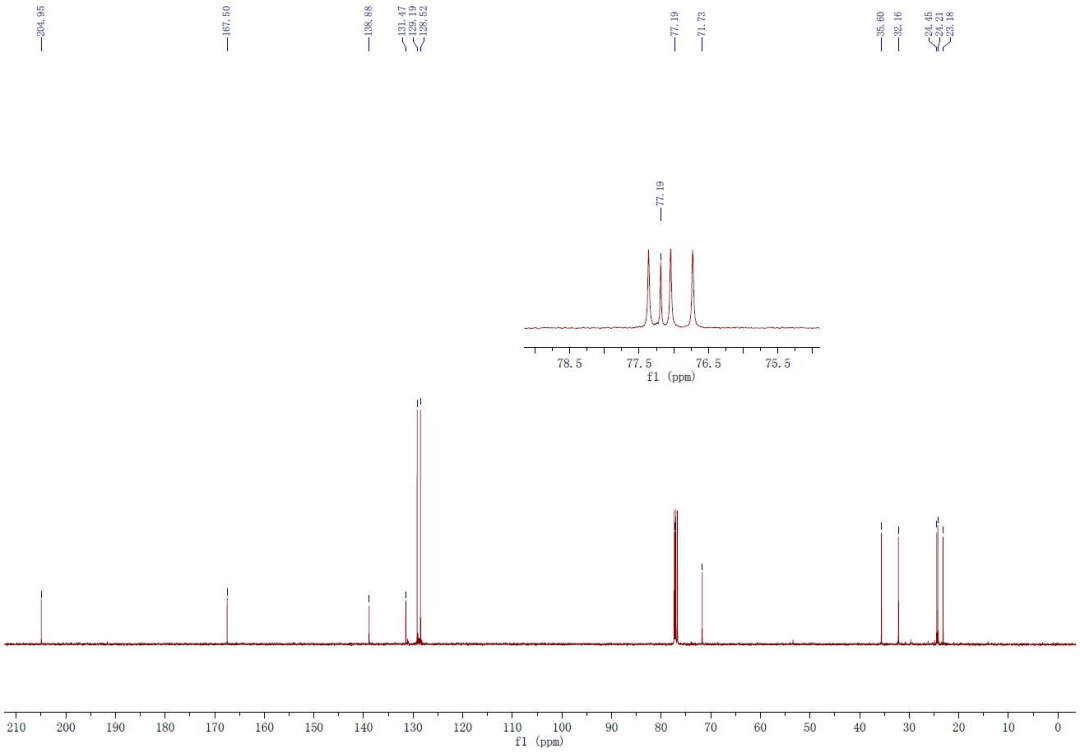
^{13}C NMR of **3c**



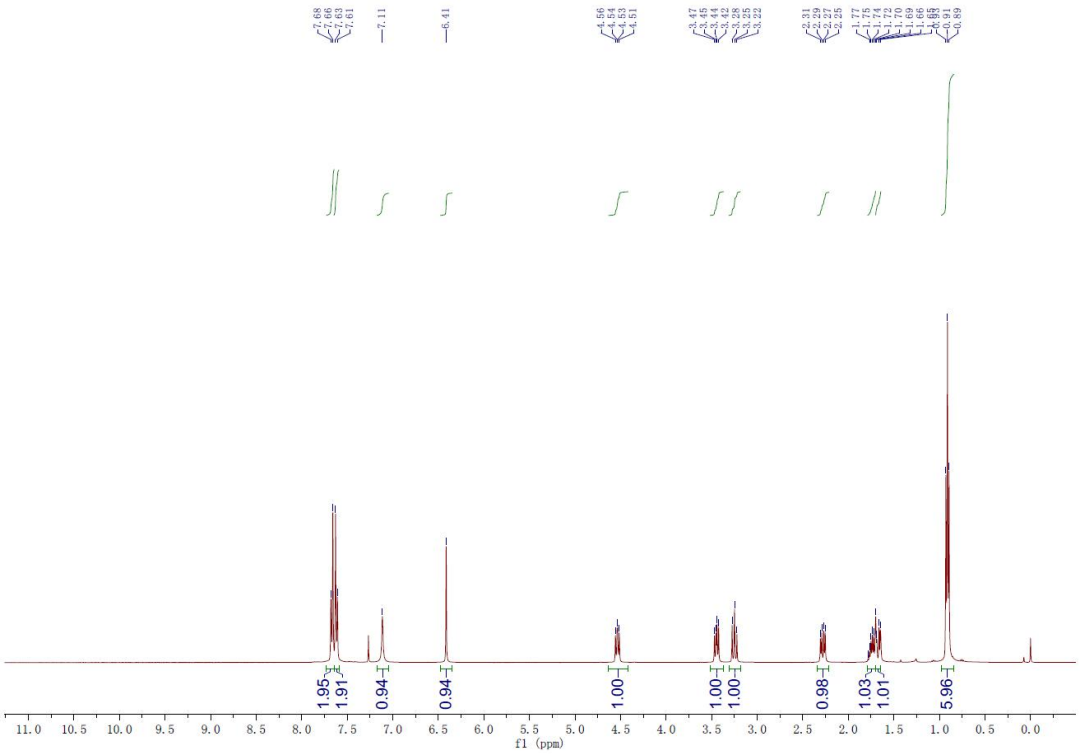
^{1}H NMR of **3d**



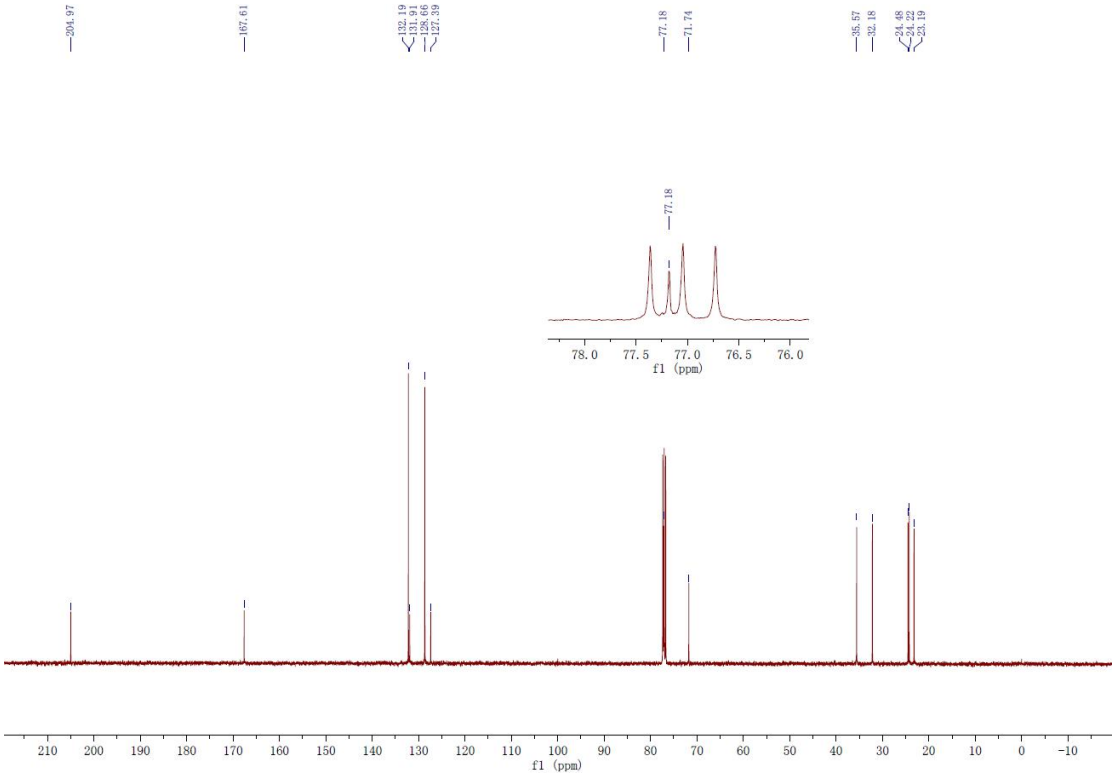
^{13}C NMR of **3d**



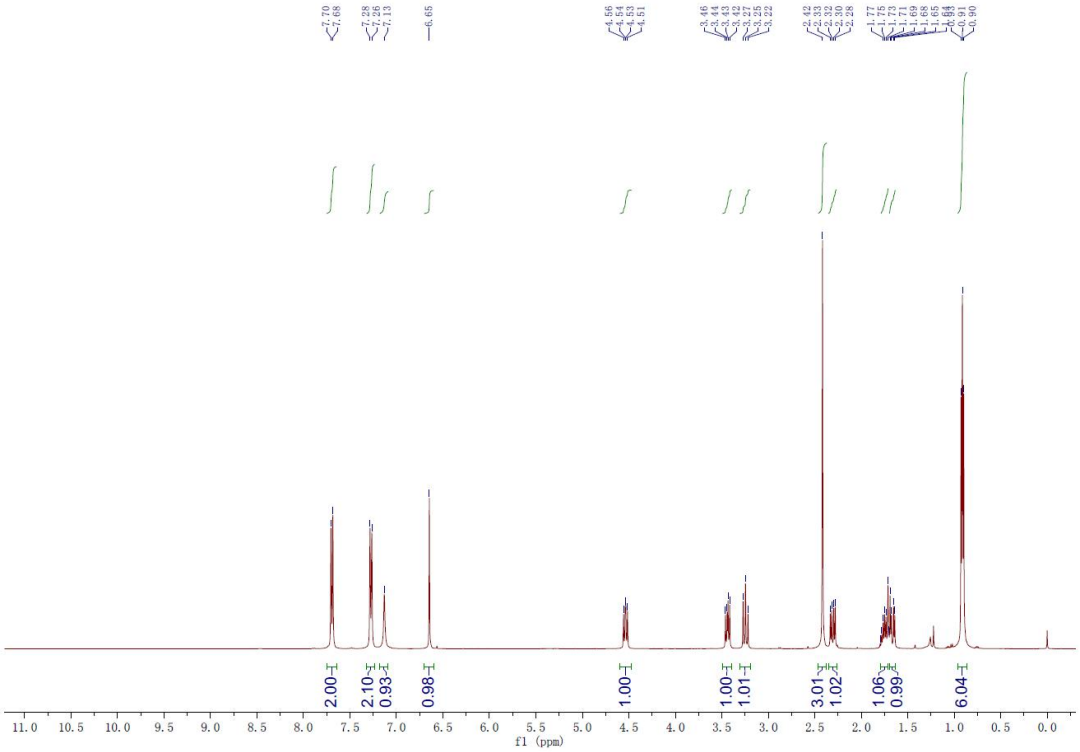
^{1}H NMR of **3e**



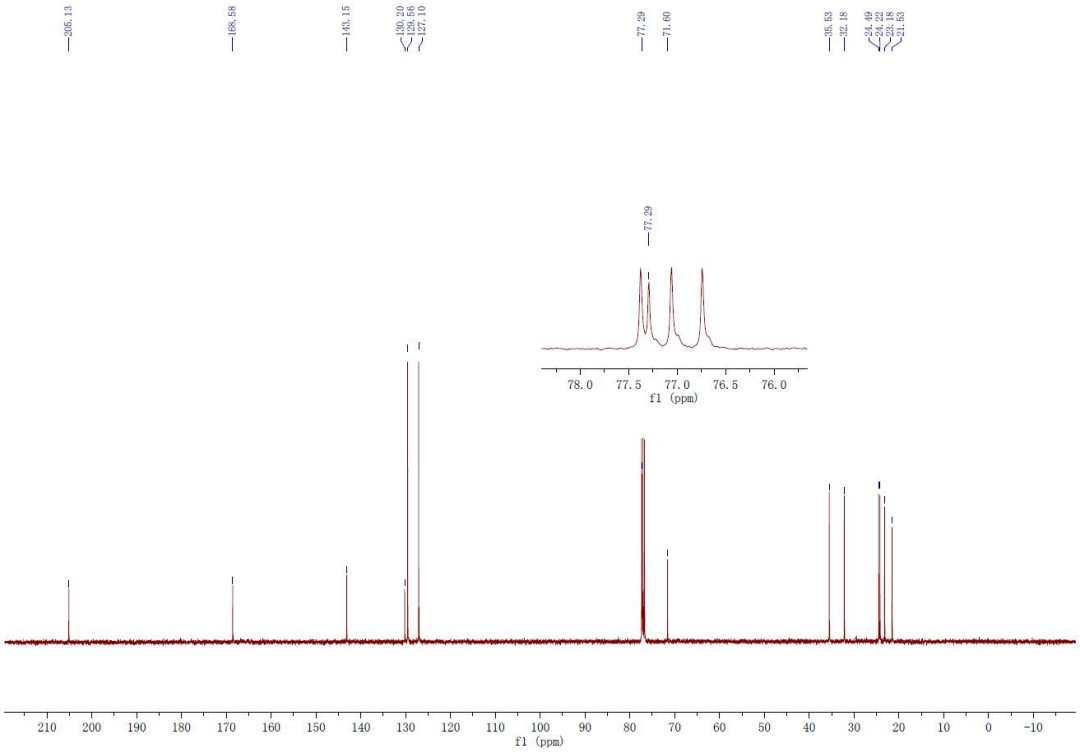
^{13}C NMR of **3e**



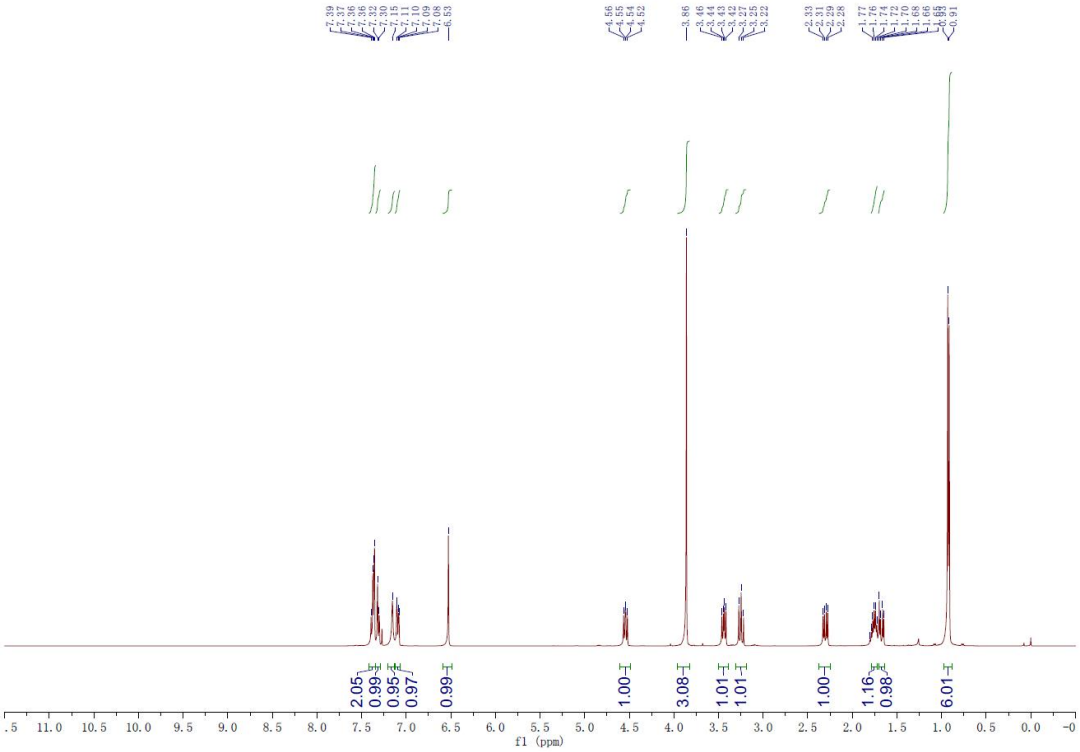
^{1}H NMR of **3f**



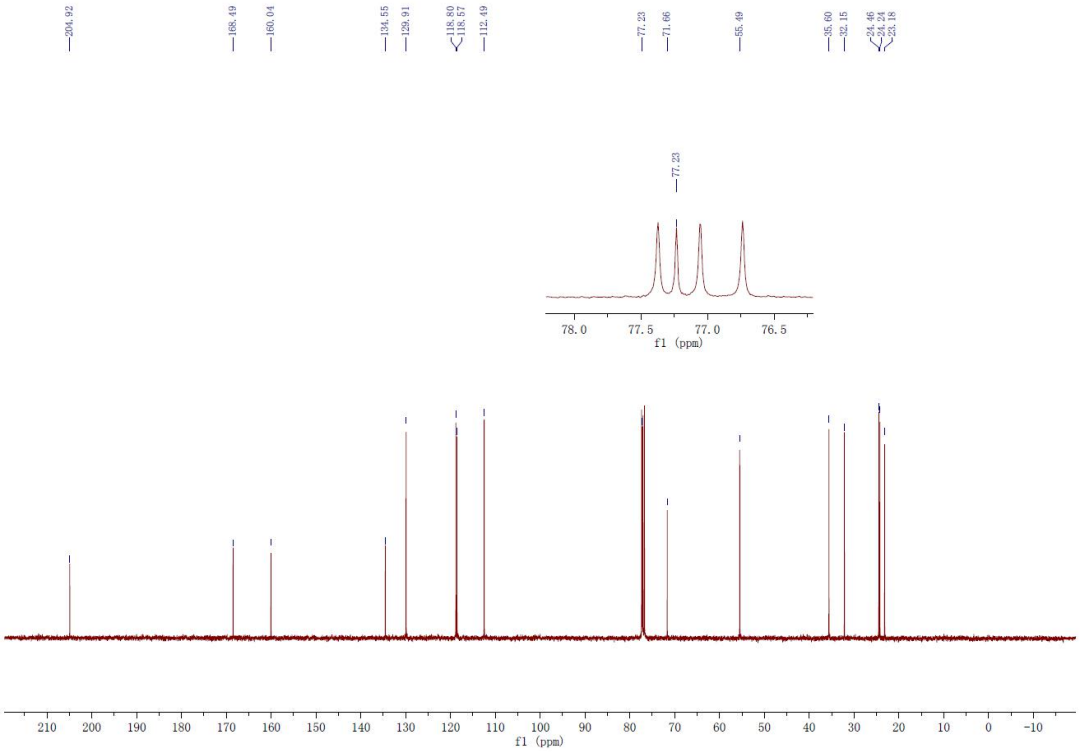
^{13}C NMR of **3f**



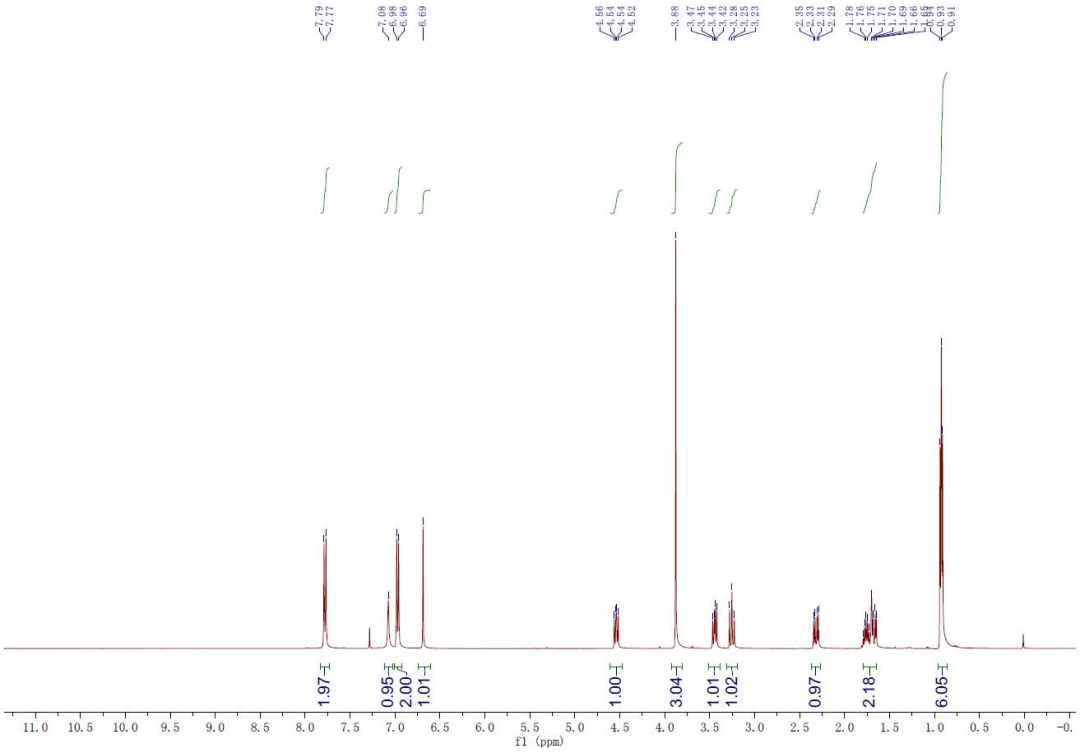
^{1}H NMR of **3g**



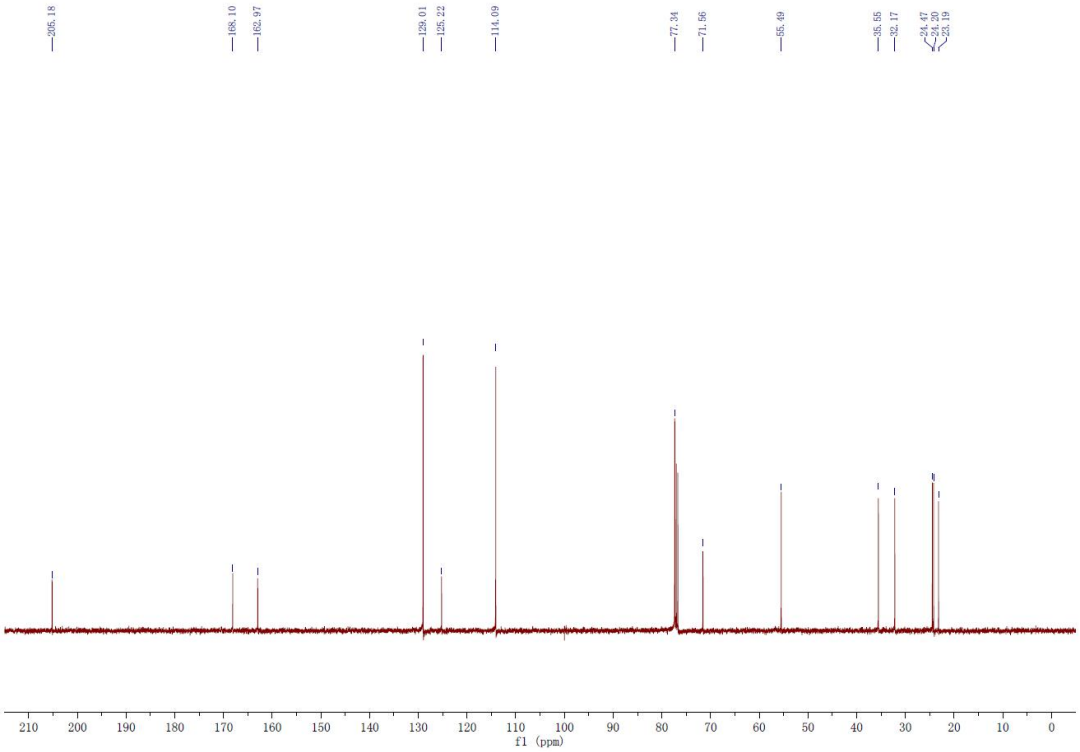
^{13}C NMR of **3g**



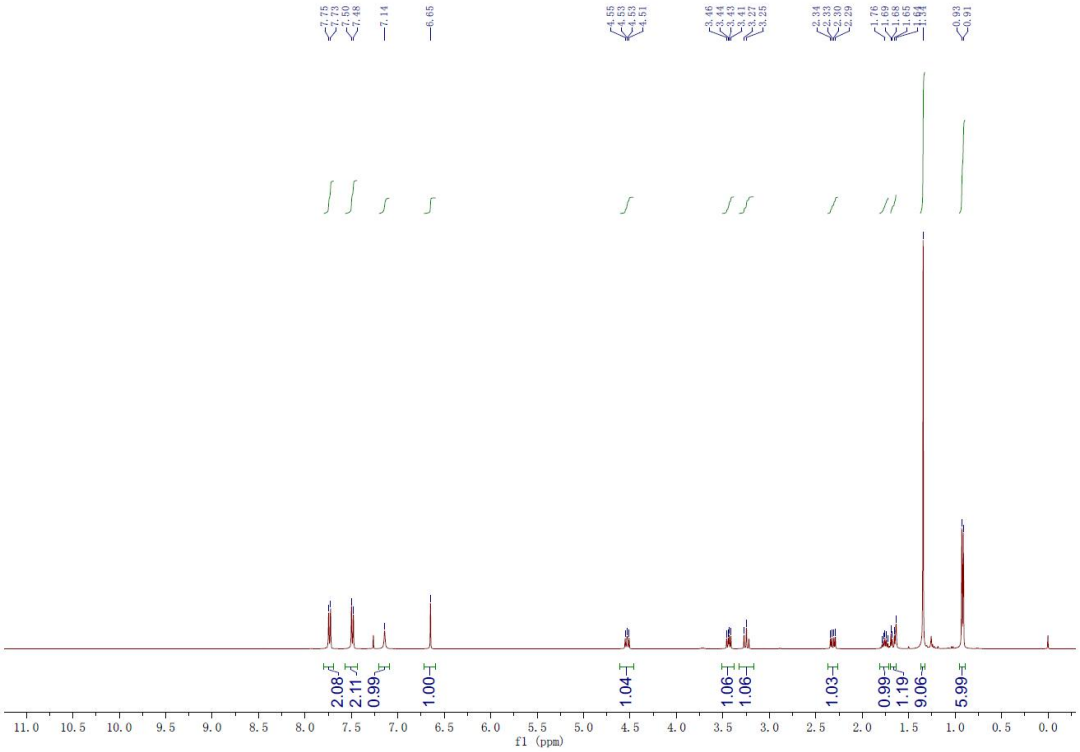
^{1}H NMR of **3h**



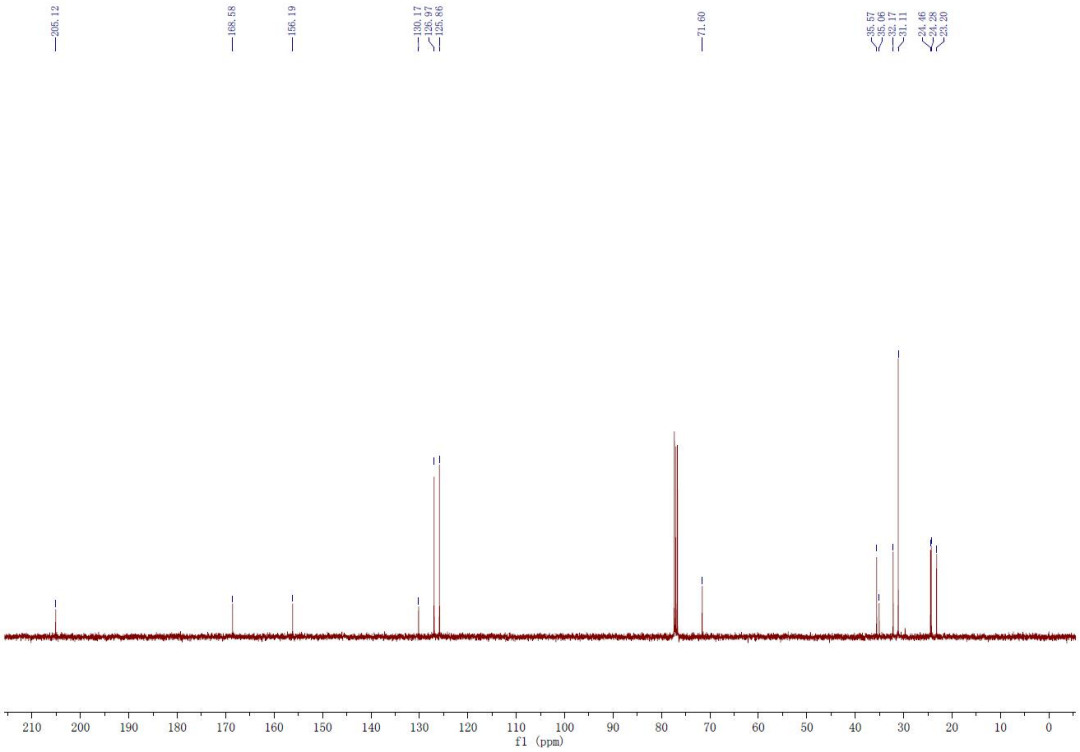
^{13}C NMR of **3h**



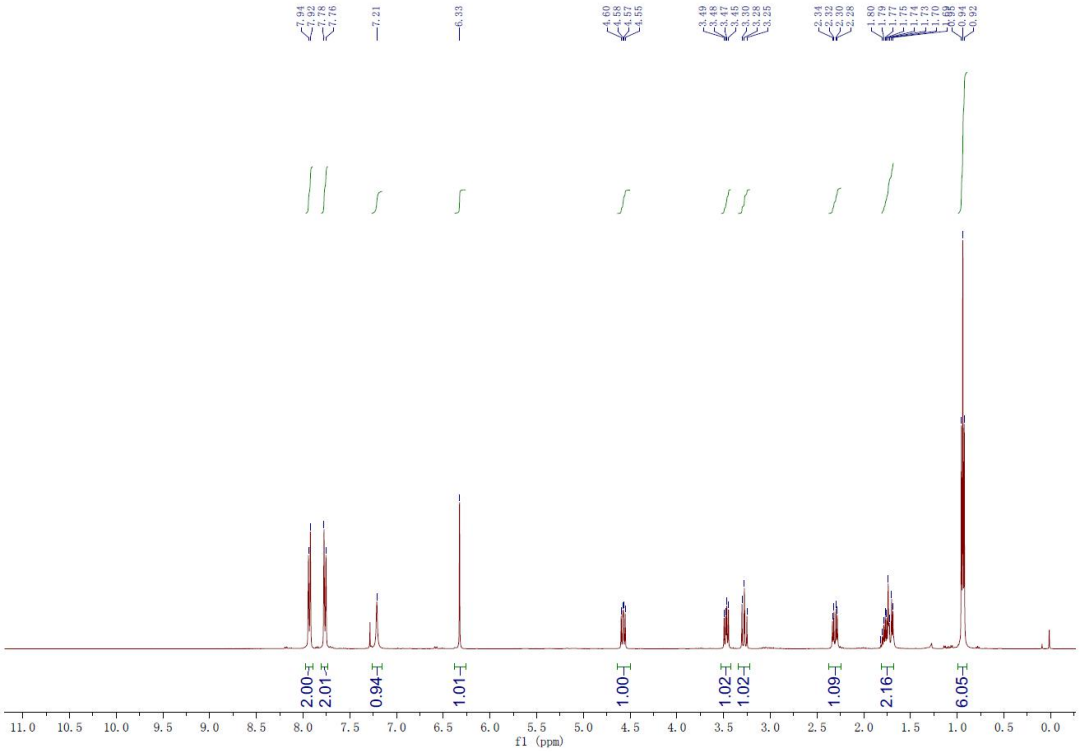
^{1}H NMR of **3i**



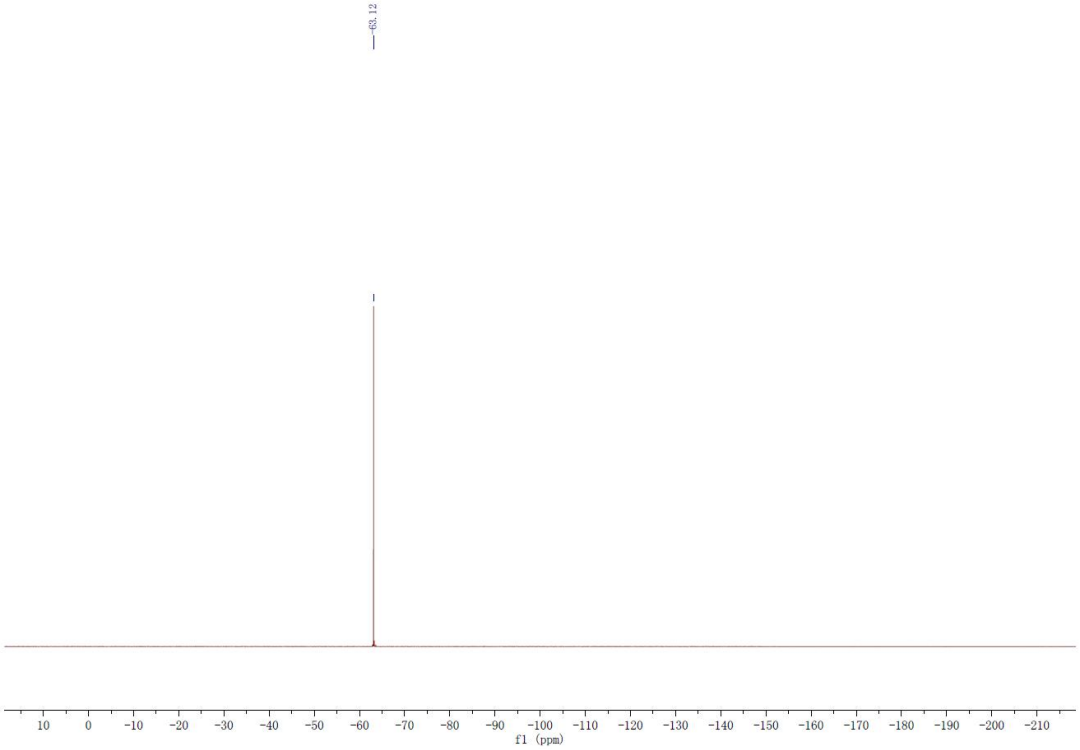
^{13}C NMR of **3i**



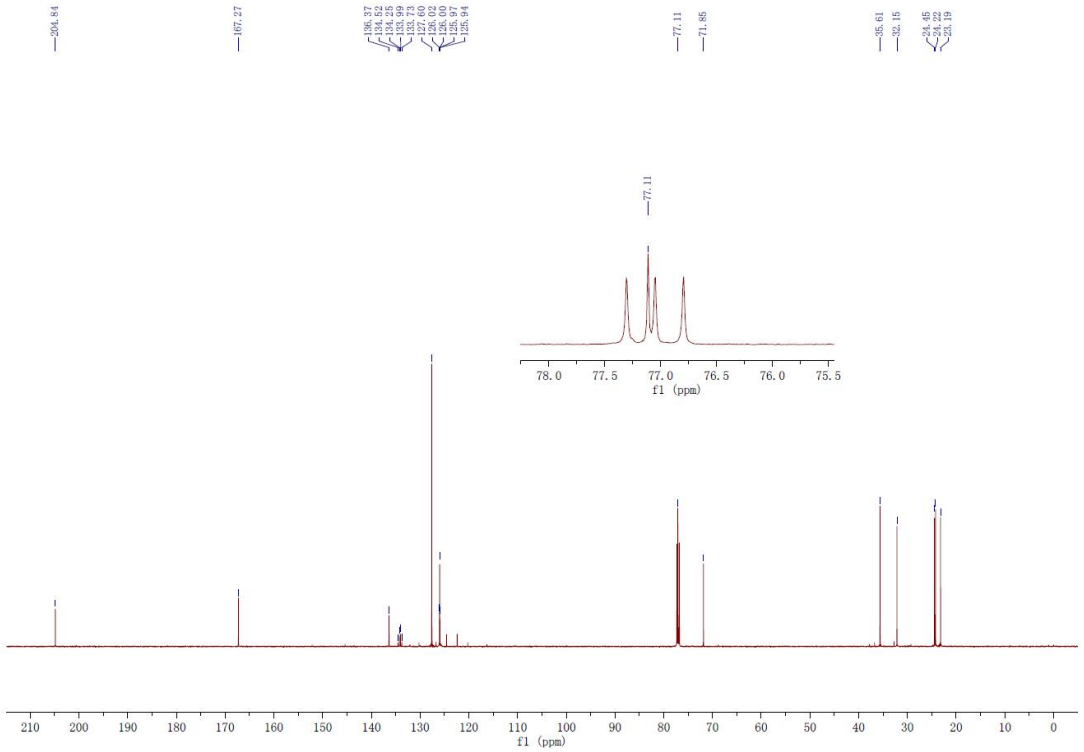
^{1}H NMR of **3j**



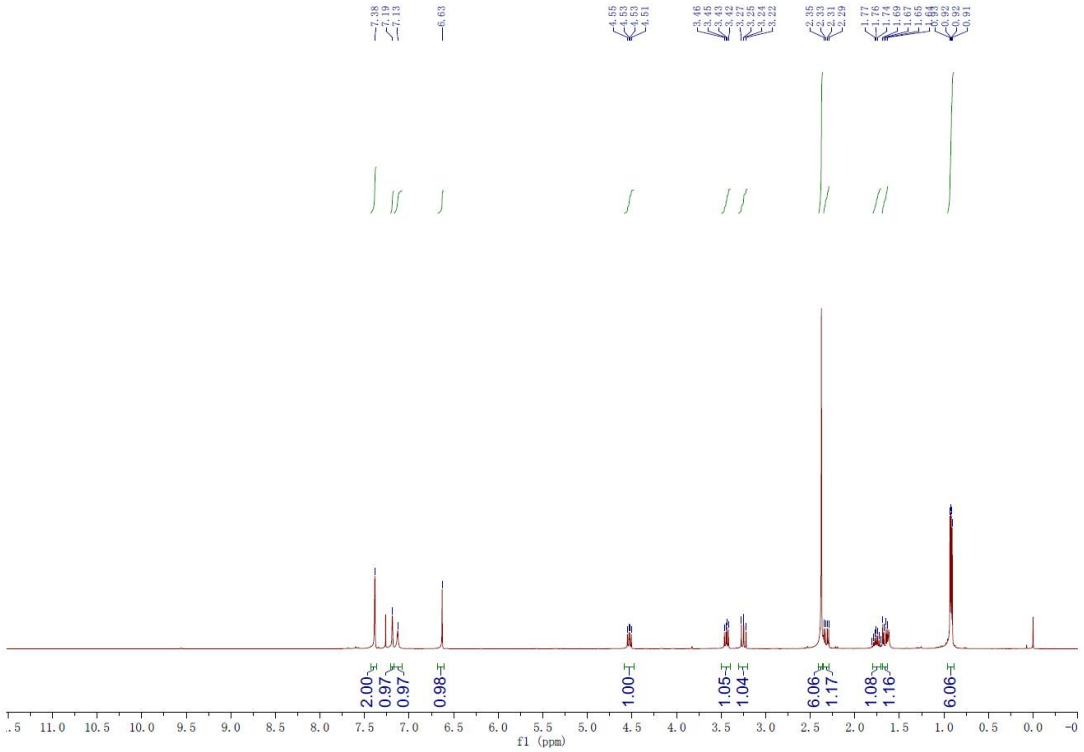
^{19}F NMR of **3j**



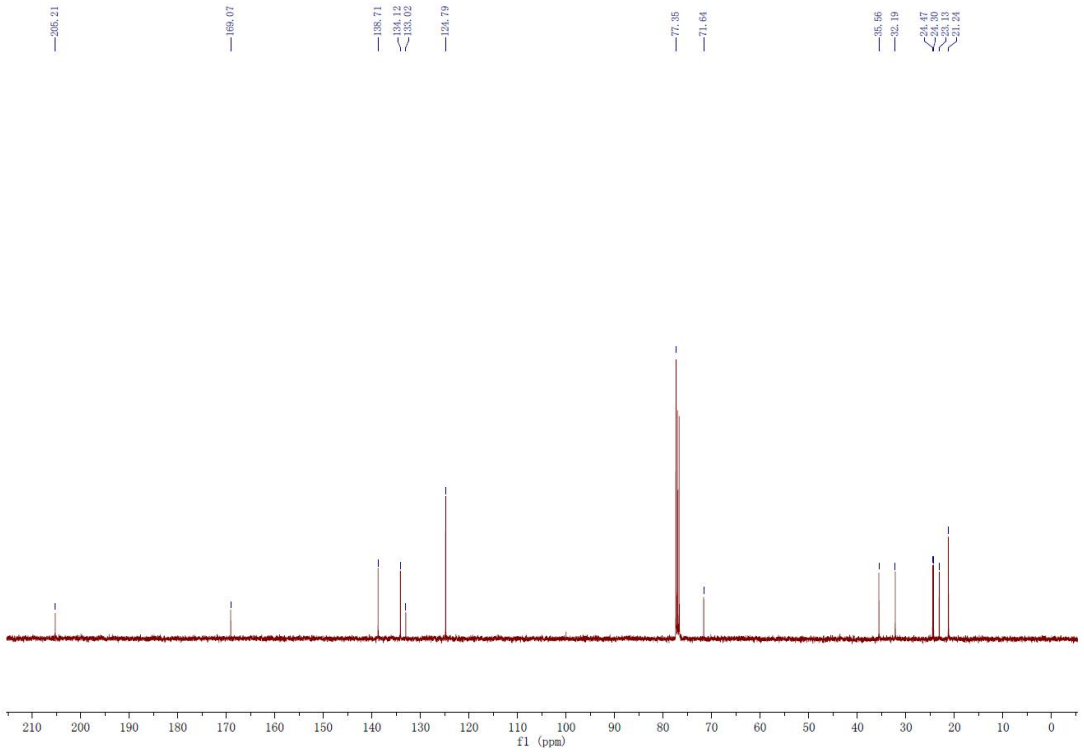
^{13}C NMR of **3j**



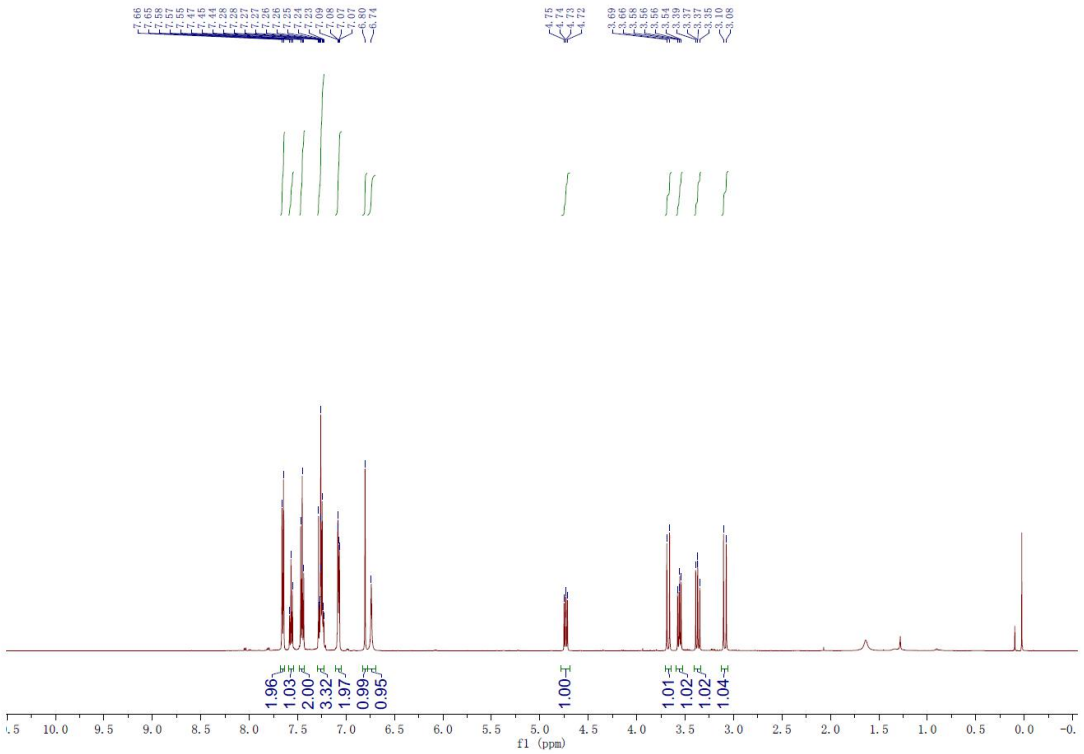
^{1}H NMR of **3k**



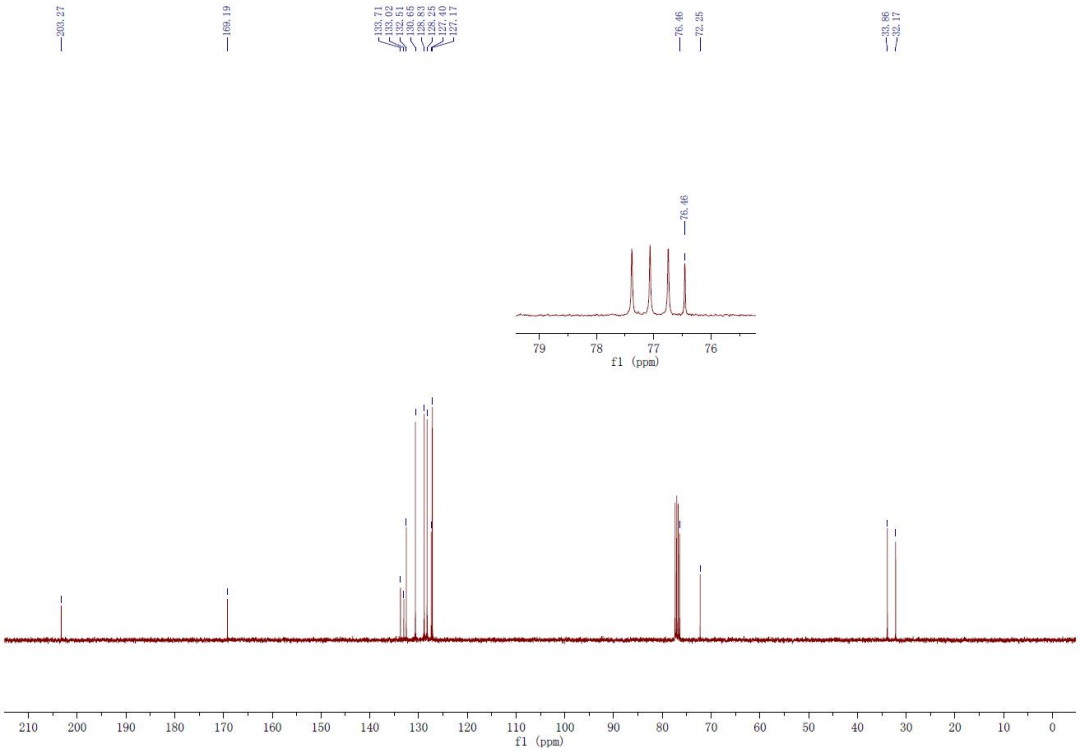
^{13}C NMR of **3k**



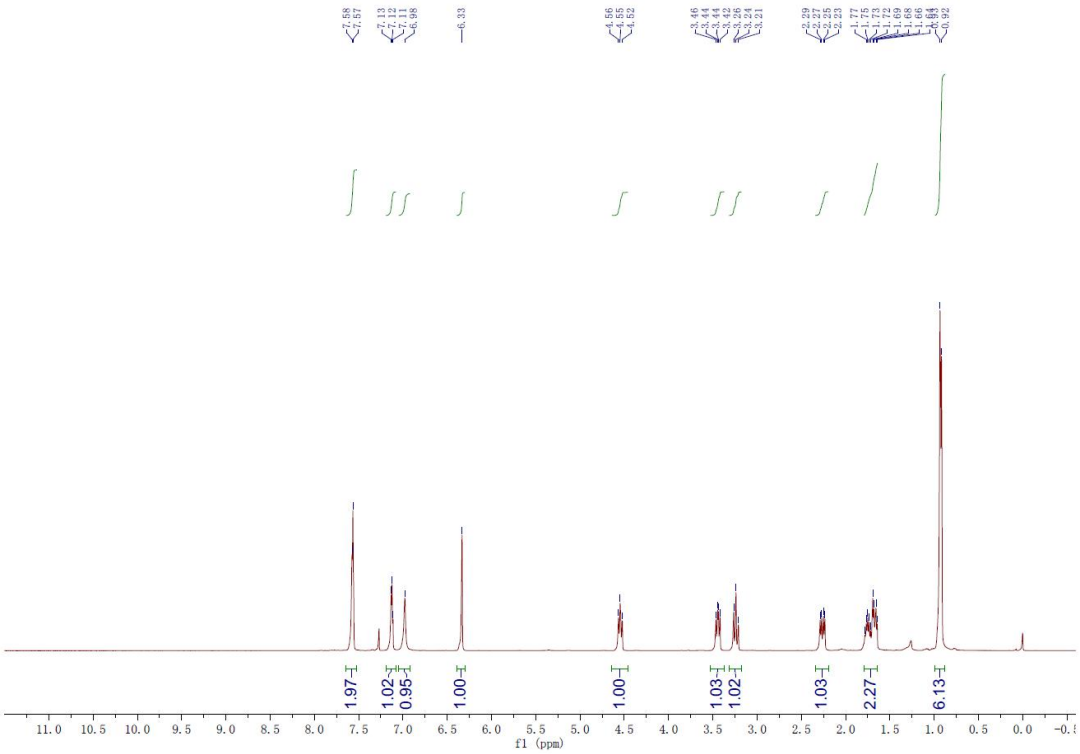
^{1}H NMR of **3l**



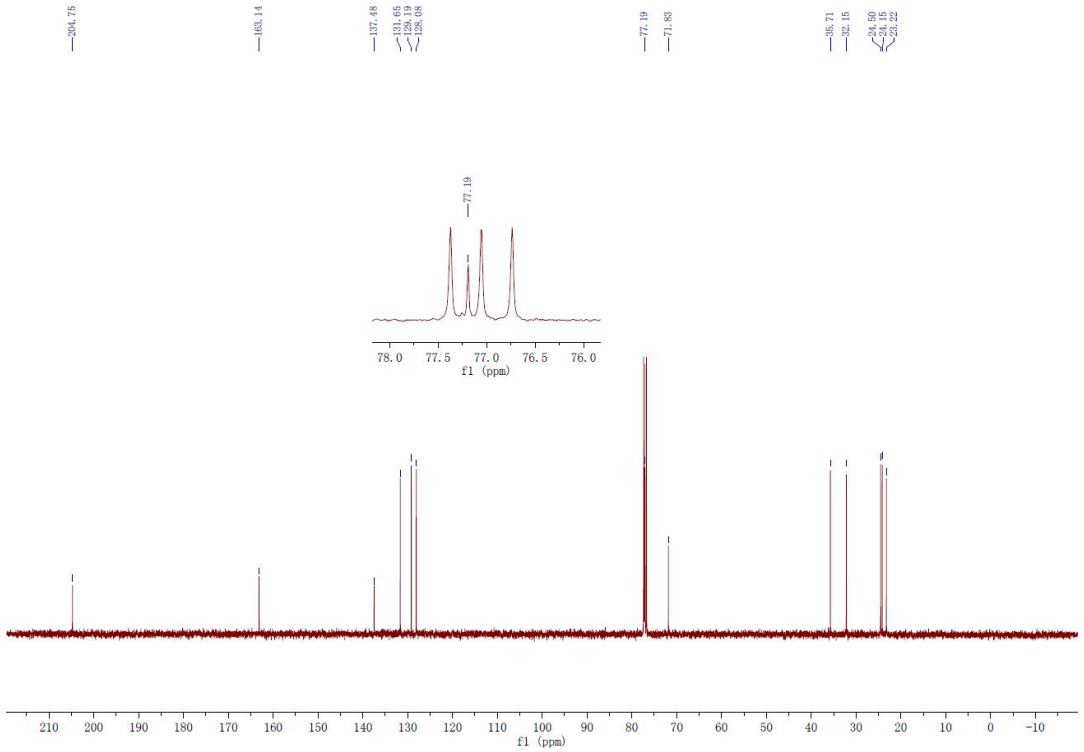
^{13}C NMR of **3l**



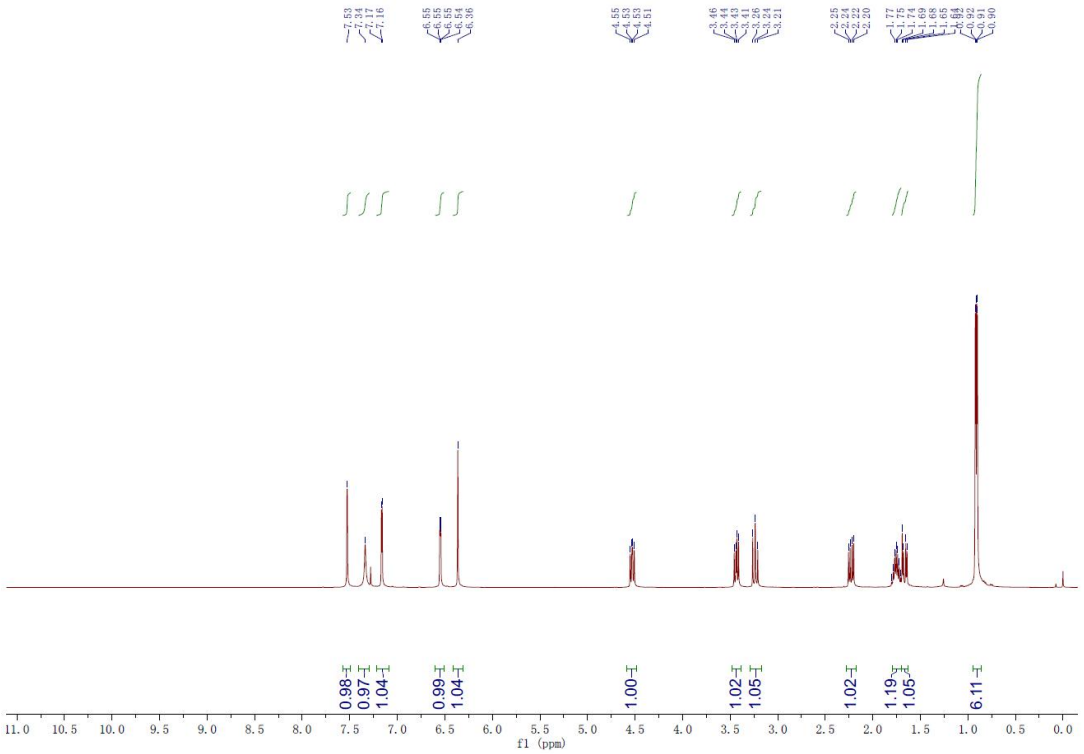
^{1}H NMR of **3m**



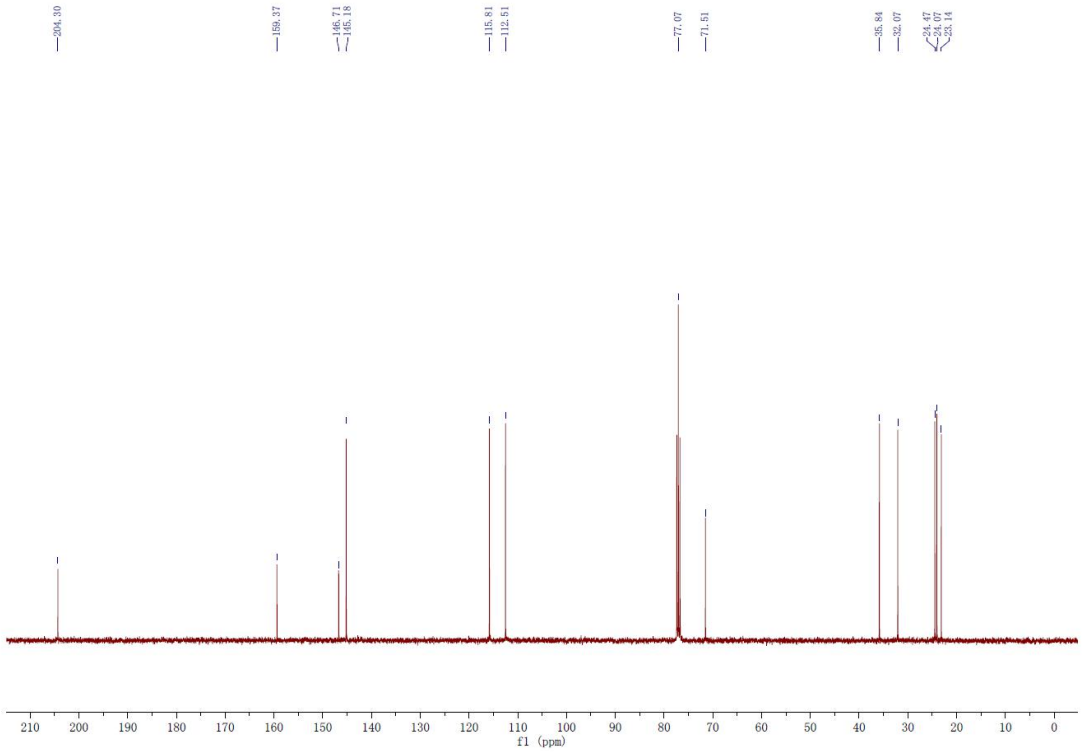
^{13}C NMR of **3m**



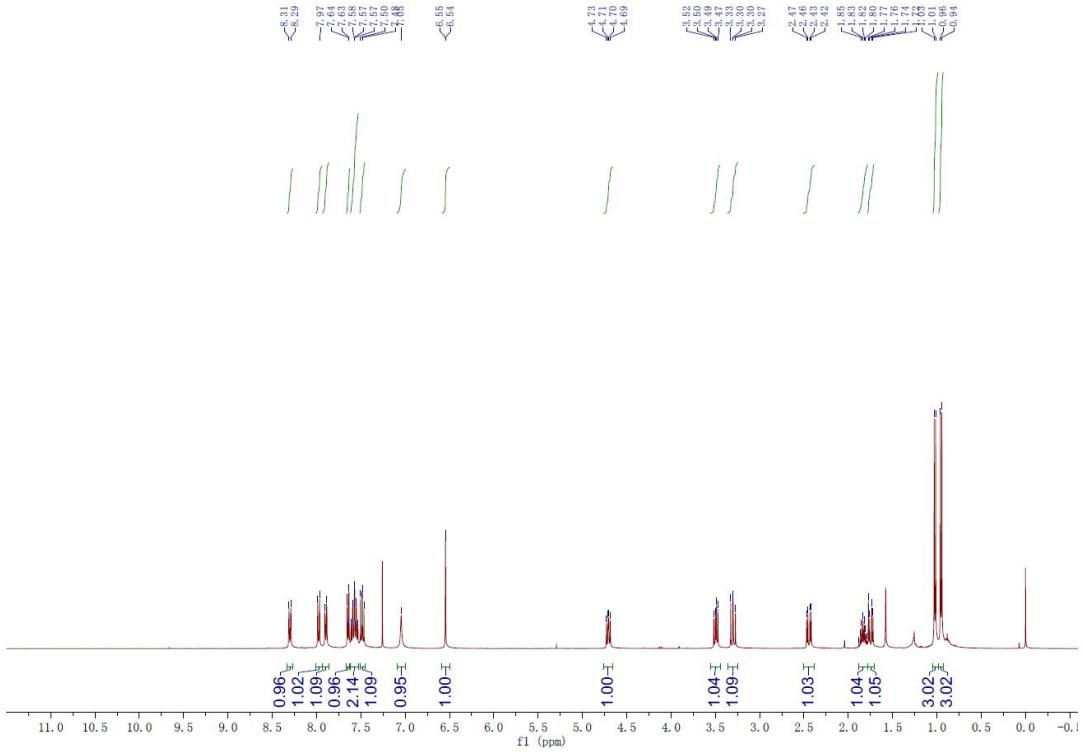
^{1}H NMR of **3n**



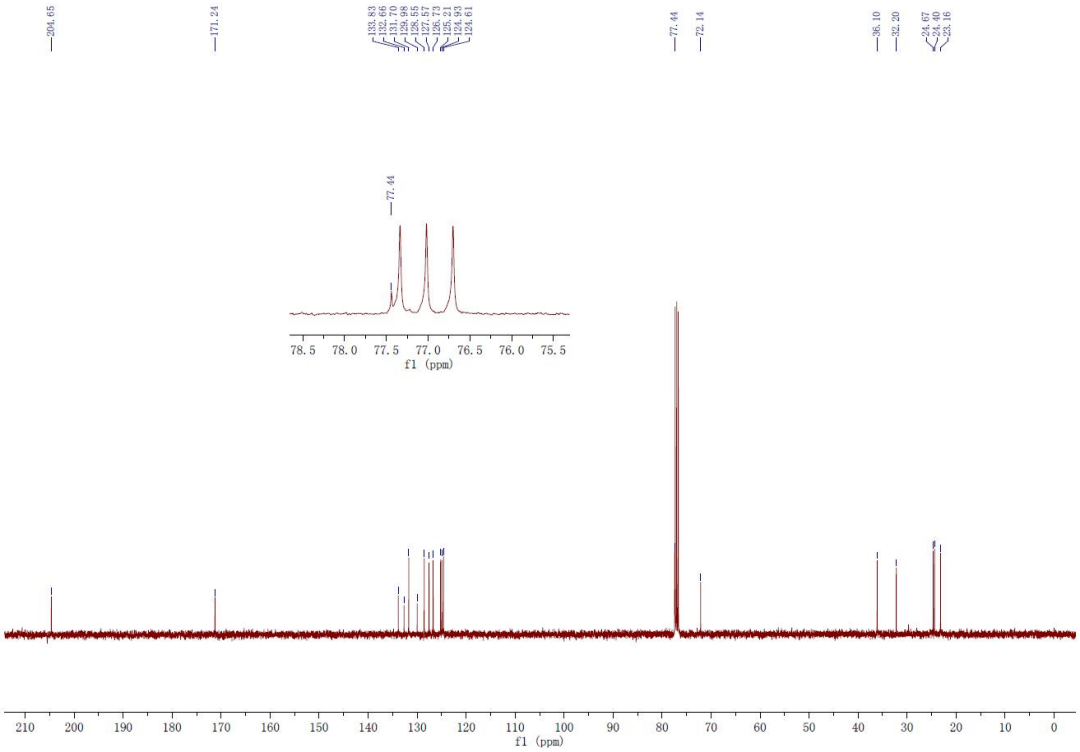
^{13}C NMR of **3n**



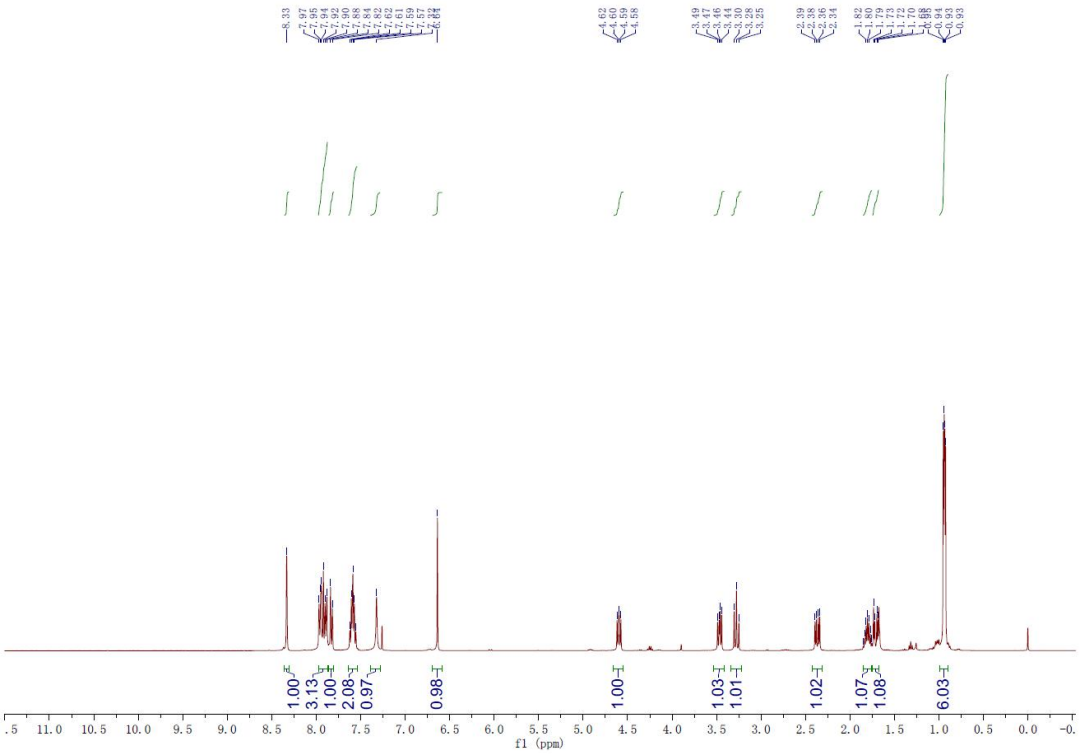
^{1}H NMR of **3o**



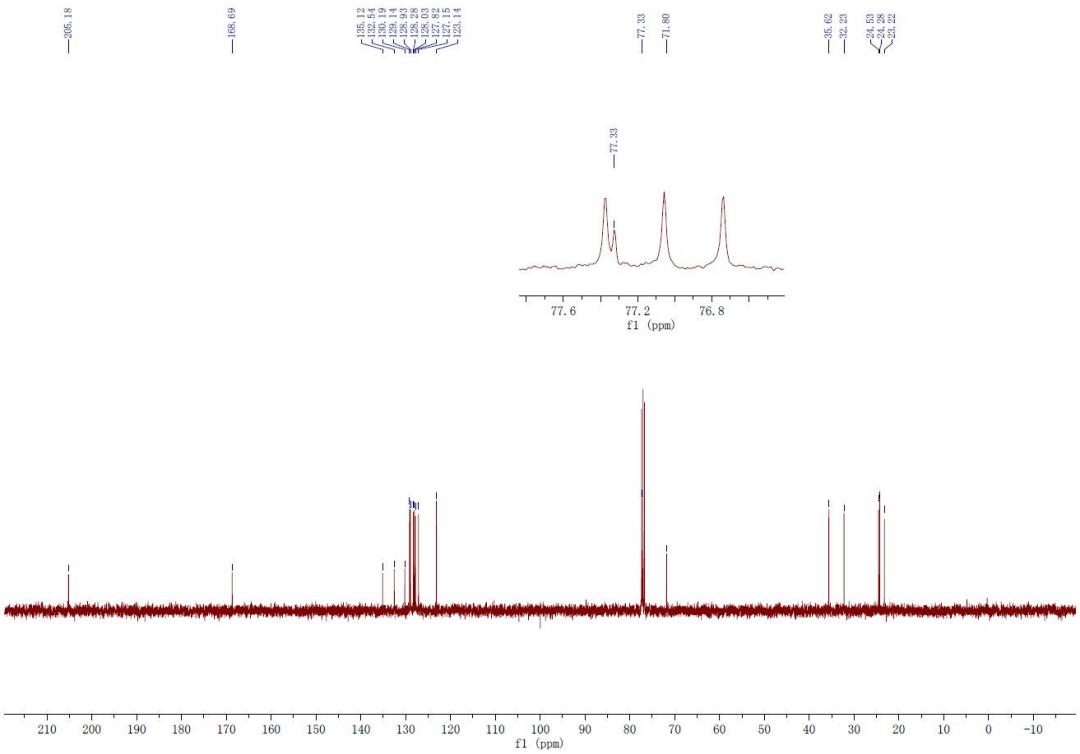
^{13}C NMR of **3o**



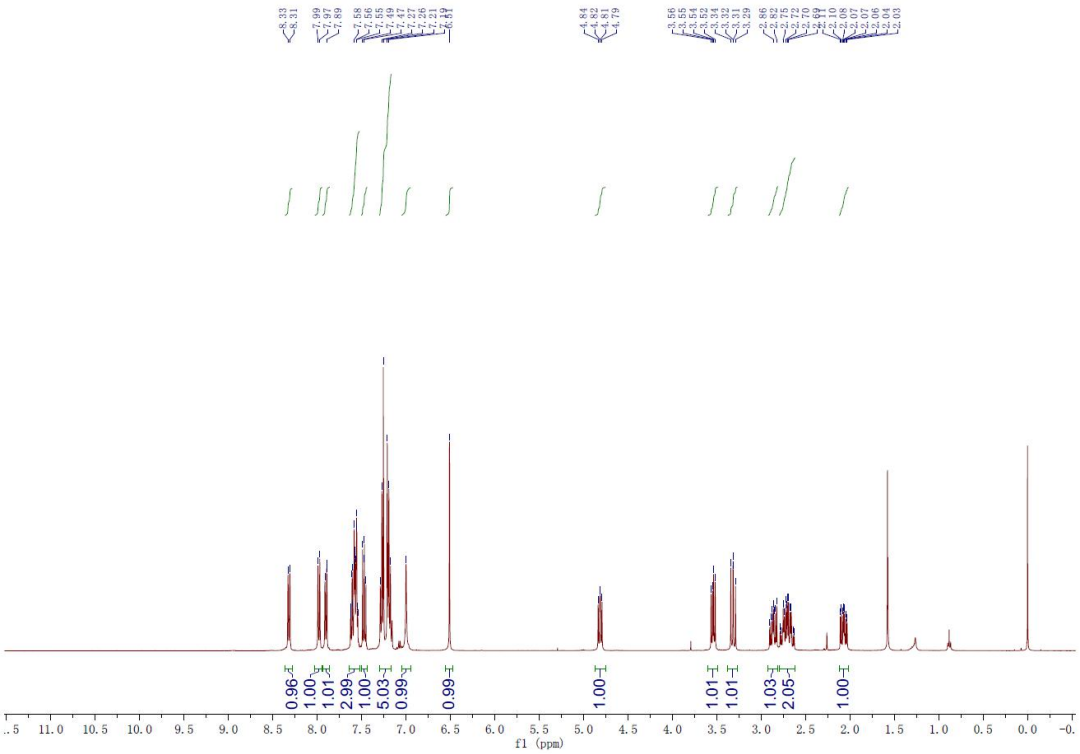
^{1}H NMR of **3p**



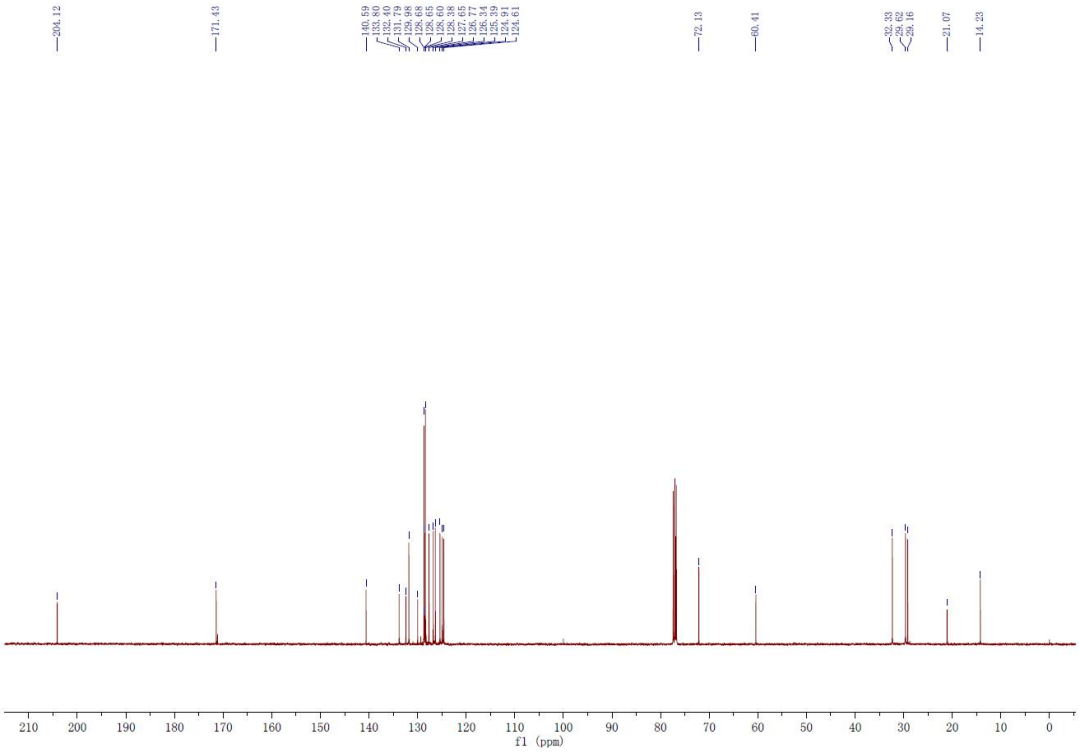
^{13}C NMR of **3p**



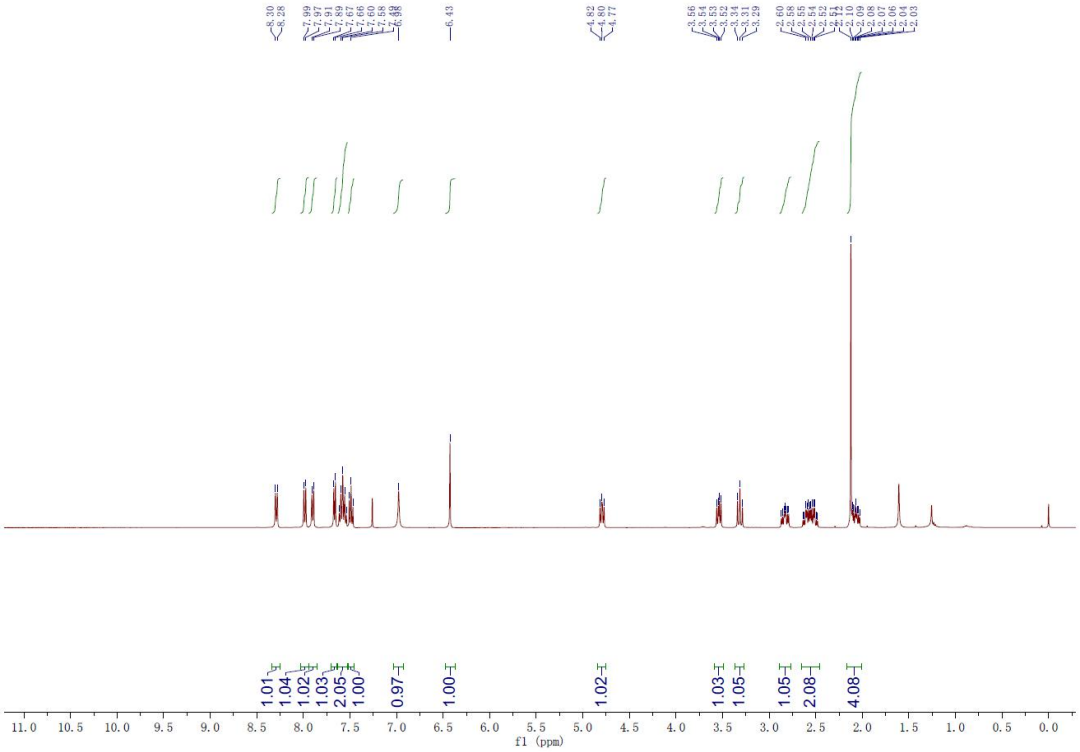
^{1}H NMR of **3q**



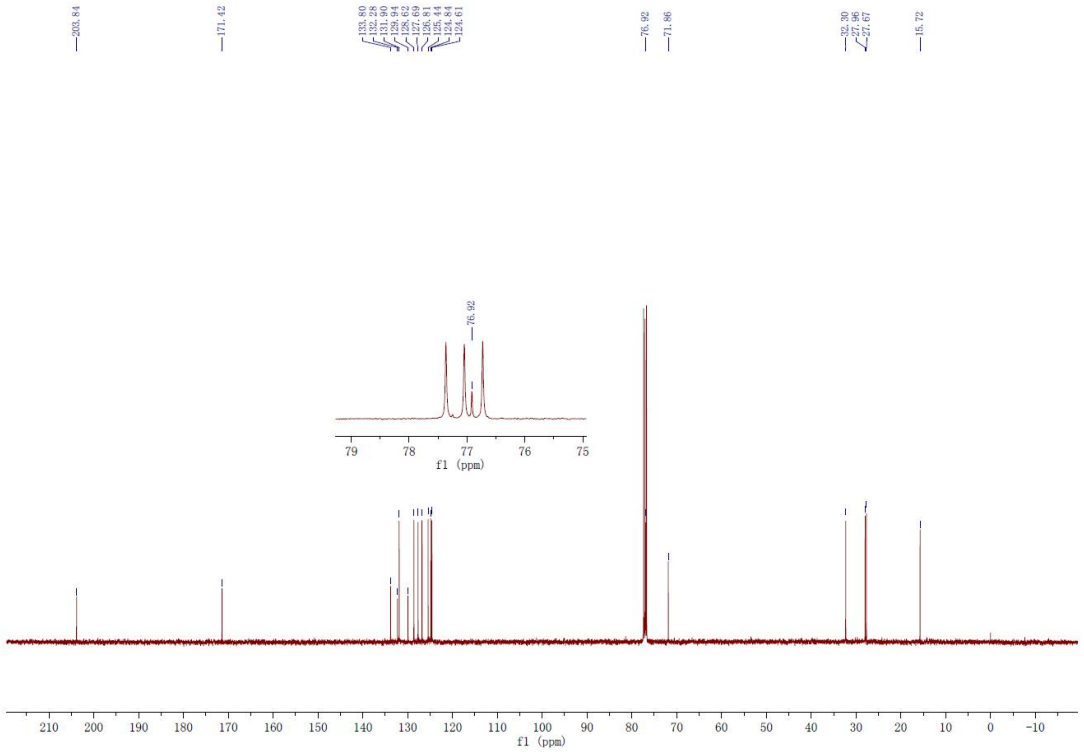
^{13}C NMR of **3q**



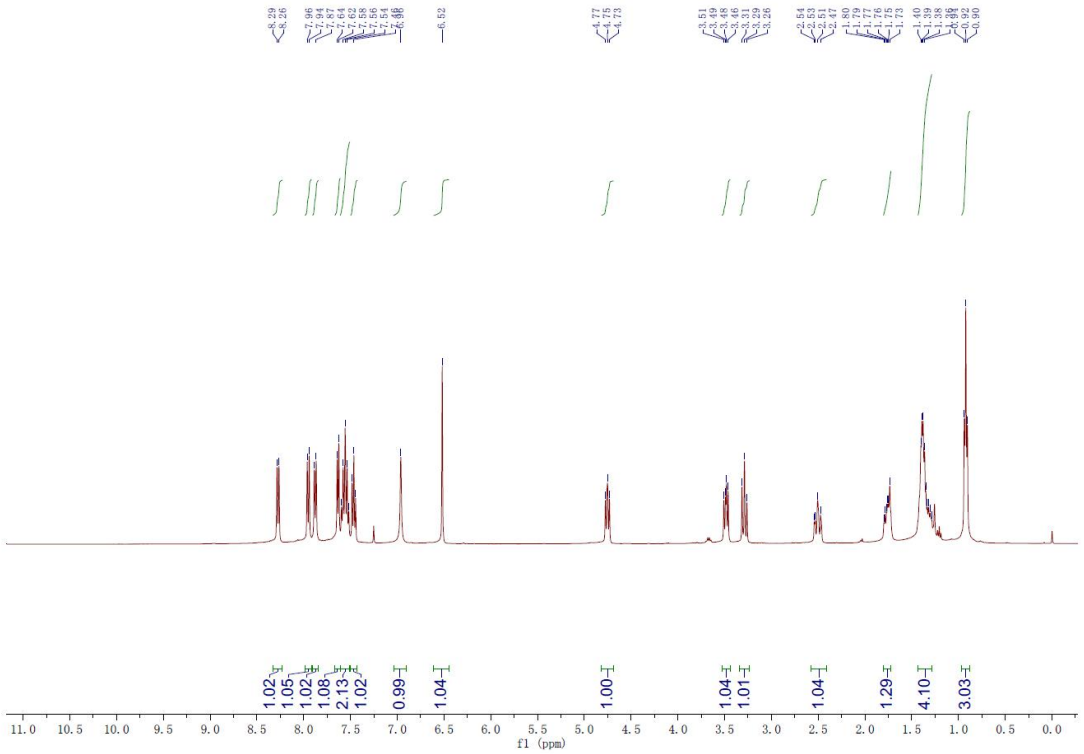
^{1}H NMR of **3r**



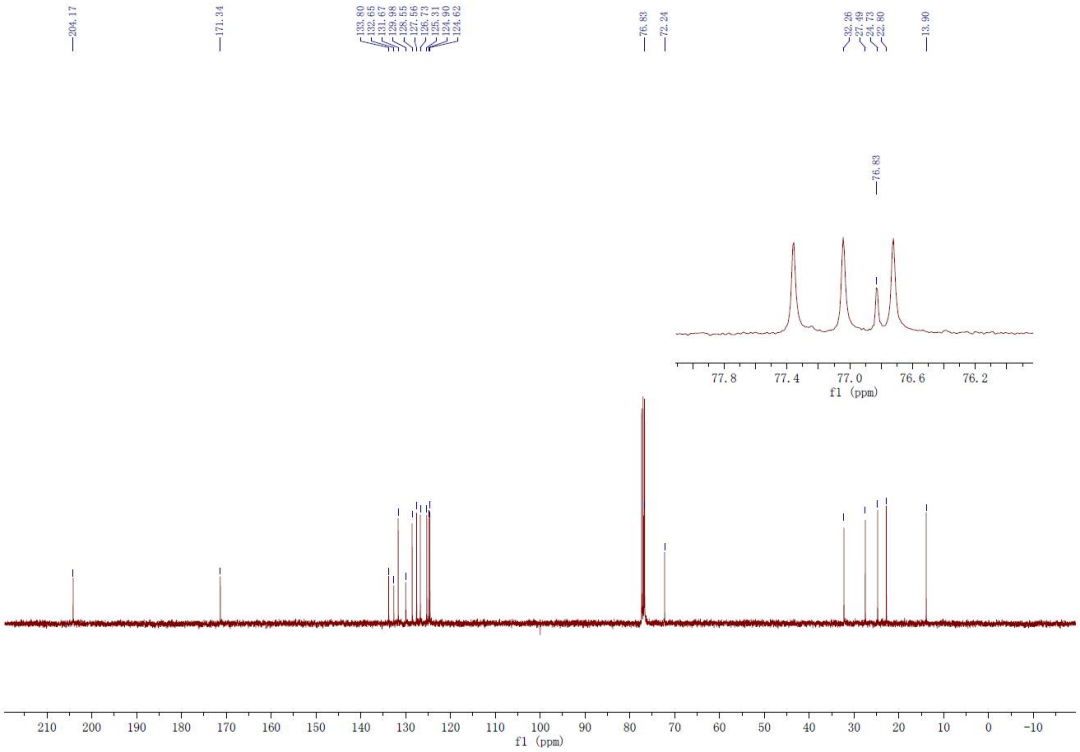
^{13}C NMR of **3r**



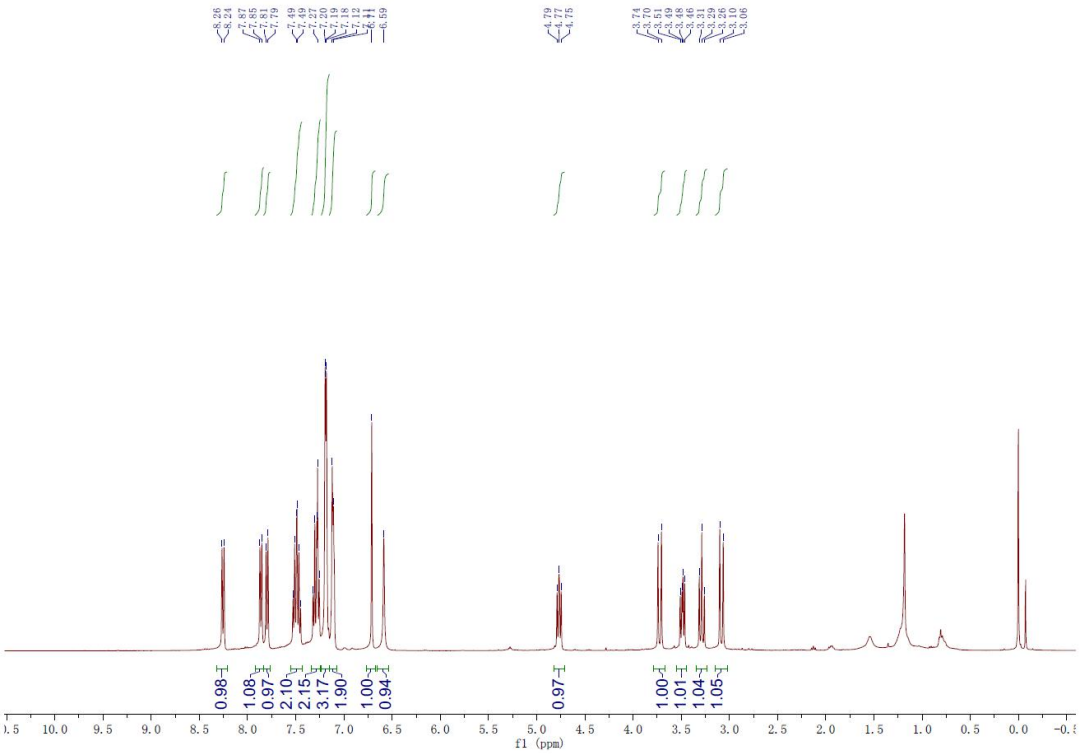
^{1}H NMR of **3s**



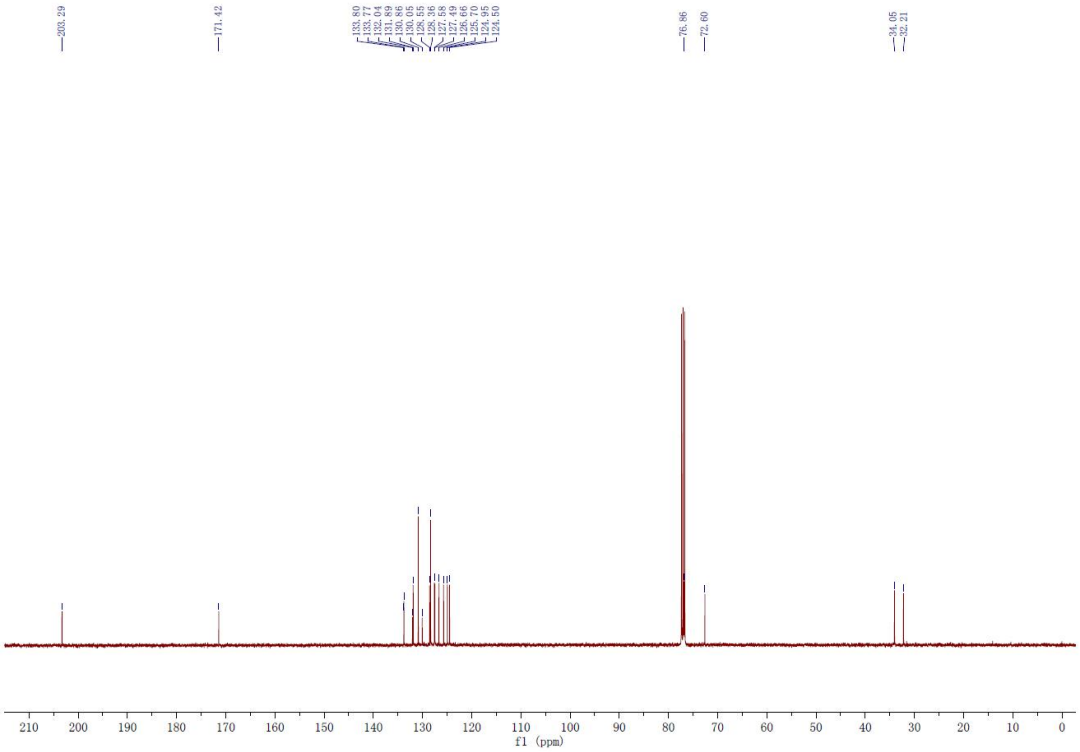
^{13}C NMR of **3s**



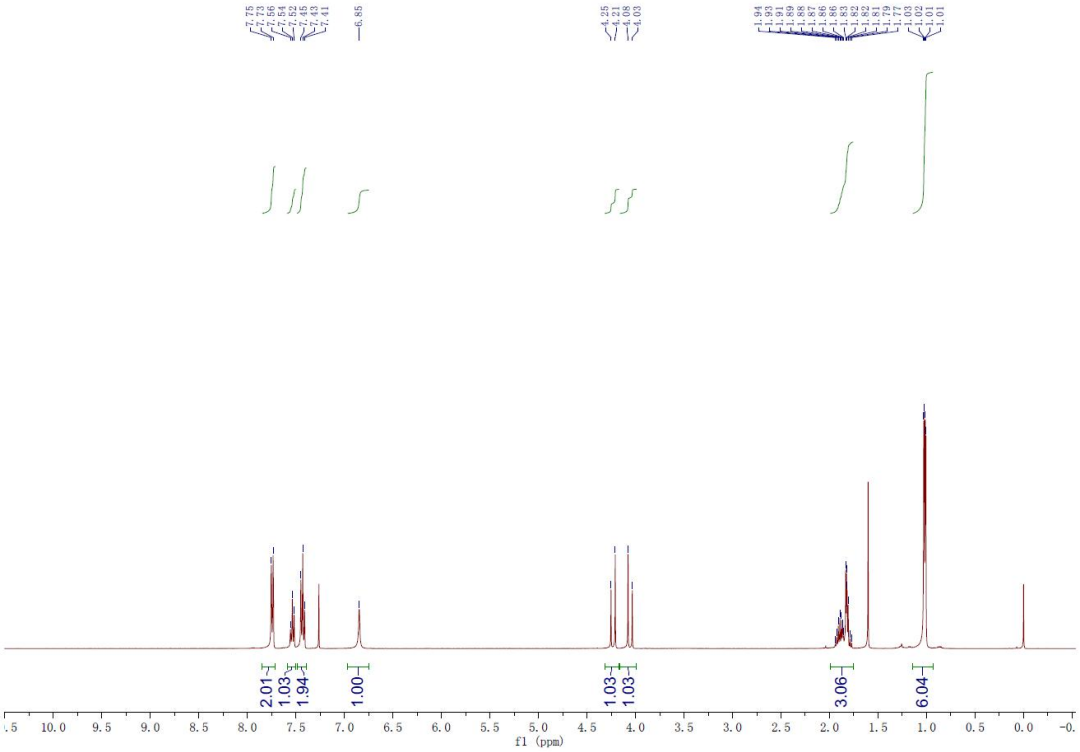
^{1}H NMR of **3t**



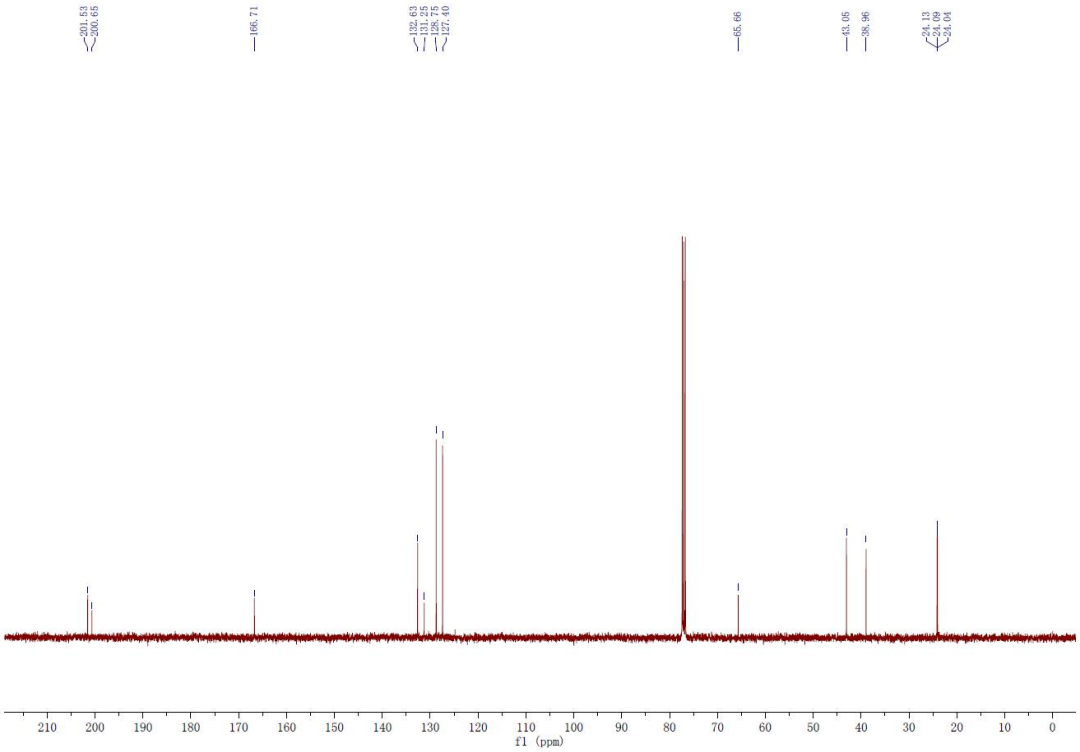
^{13}C NMR of **3t**



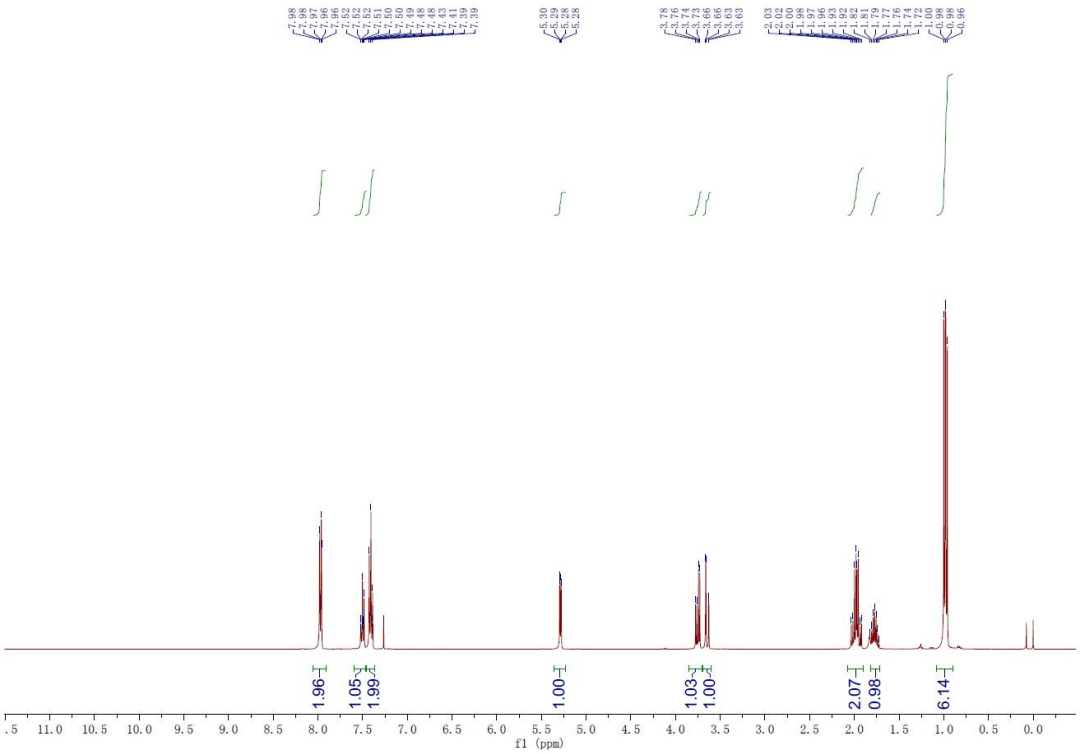
^{1}H NMR of **4**



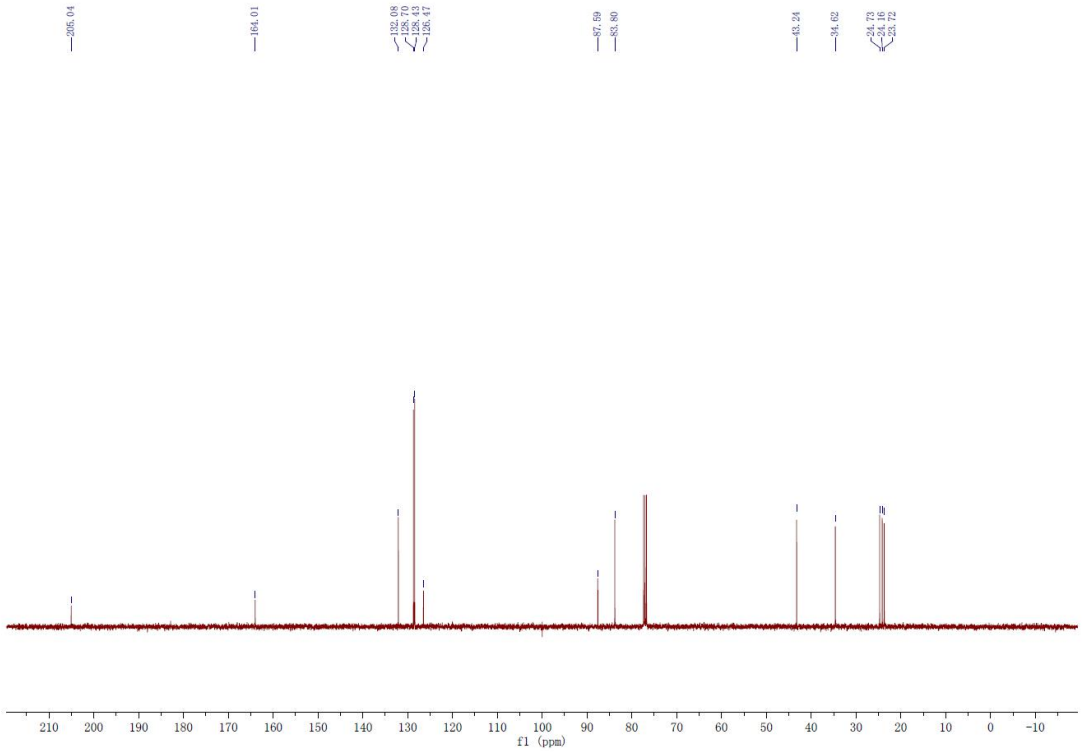
^{13}C NMR of **4**



^{1}H NMR of **5**

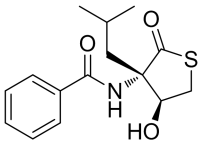


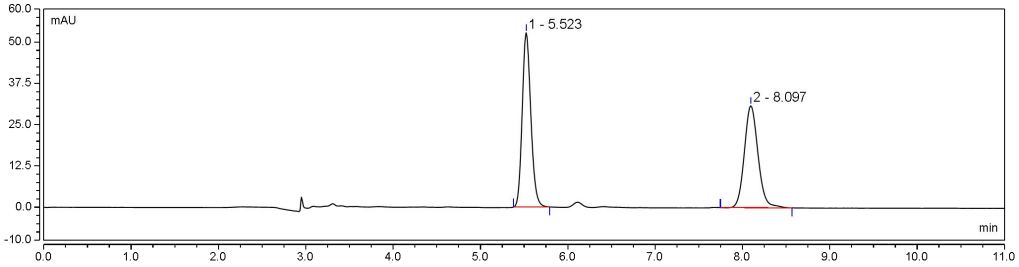
^{13}C NMR of **5**


205.04
164.01
130.08
129.10
128.43
126.47
87.59
83.80
63.24
54.62
34.73
34.15
25.72
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

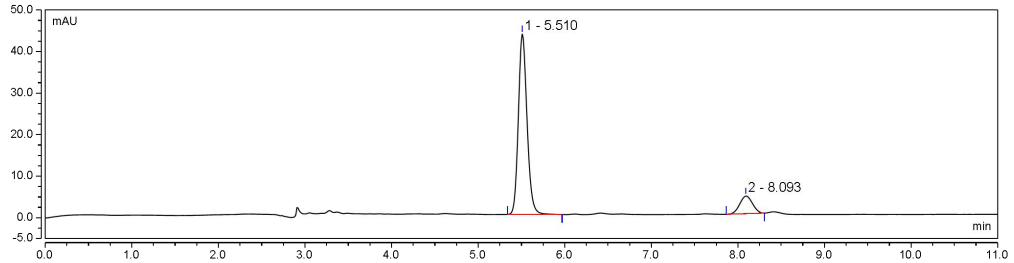
HPLC Chromatograms

HPLC Chromatogram of **3a**



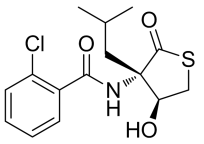


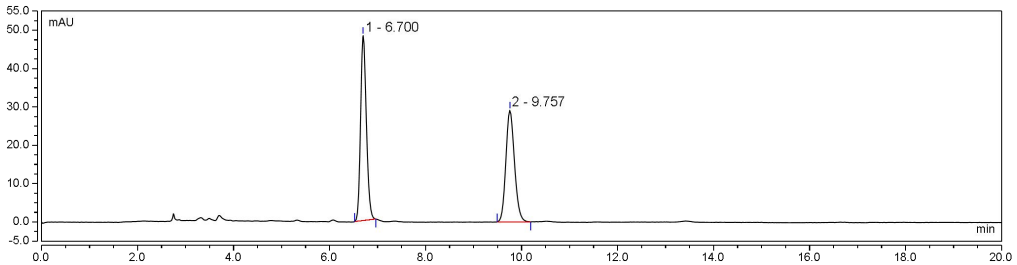
Entry	Retention Time	Area	Area(%)	Height
1	5.523	6.0432	51.96	52.76
2	8.097	5.5877	48.04	30.88



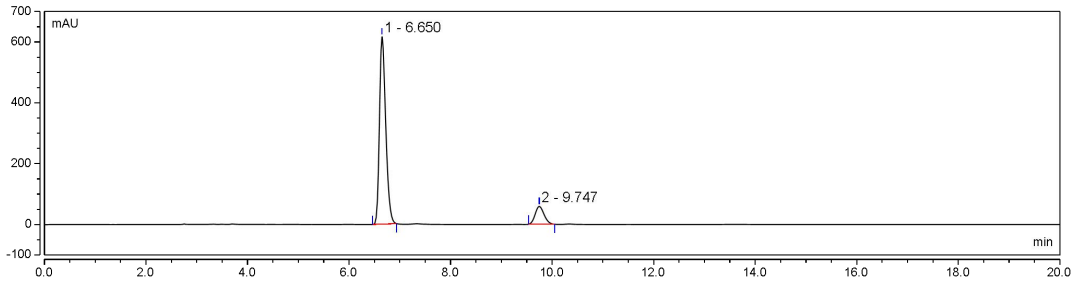
Entry	Retention Time	Area	Area(%)	Height
1	5.510	4.9882	86.72	43.43
2	8.093	0.7638	13.28	4.25

HPLC Chromatogram of **3b**



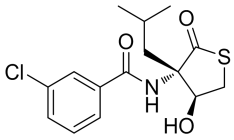


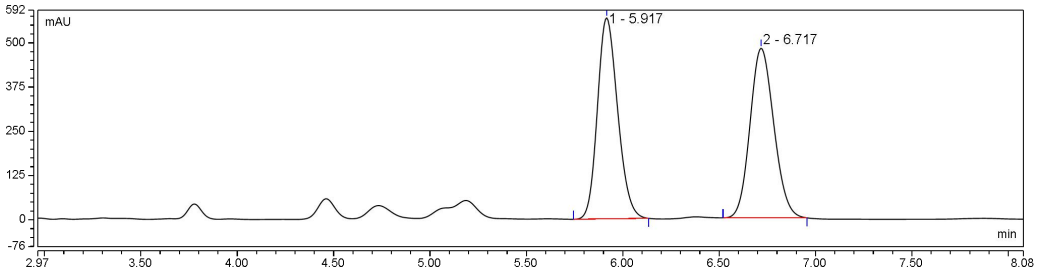
Entry	Retention Time	Area	Area(%)	Height
1	6.700	6.7059	52.51	48.23
2	9.757	6.0644	47.49	29.13



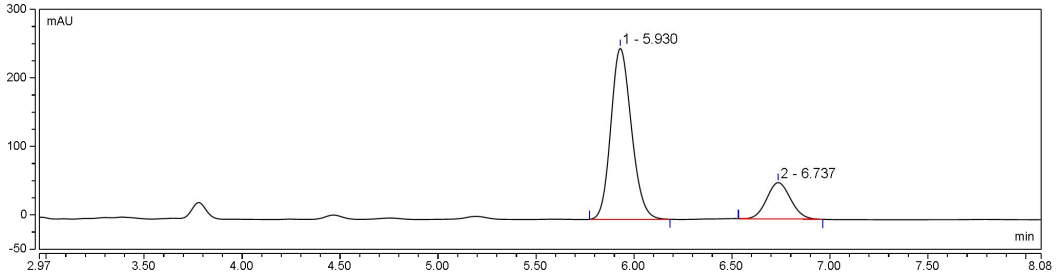
Entry	Retention Time	Area	Area(%)	Height
1	6.650	88.1409	88.08	615.87
2	9.747	11.9282	11.92	58.87

HPLC Chromatogram of **3c**



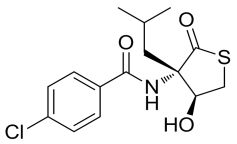


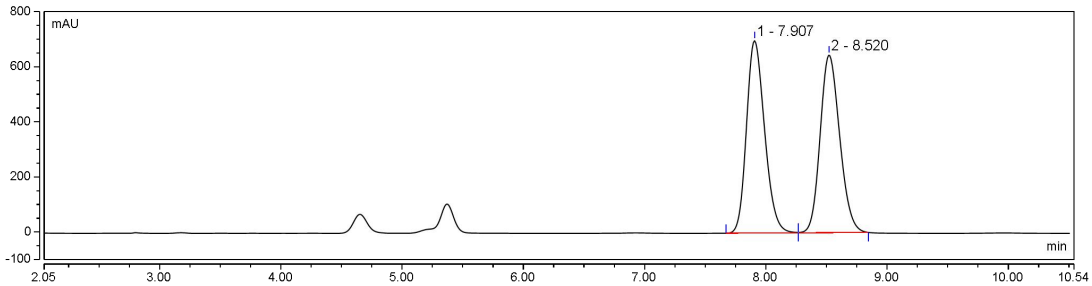
Entry	Retention Time	Area	Area(%)	Height
1	5.917	69.0503	50.11	567.86
2	6.717	68.7444	49.89	479.15



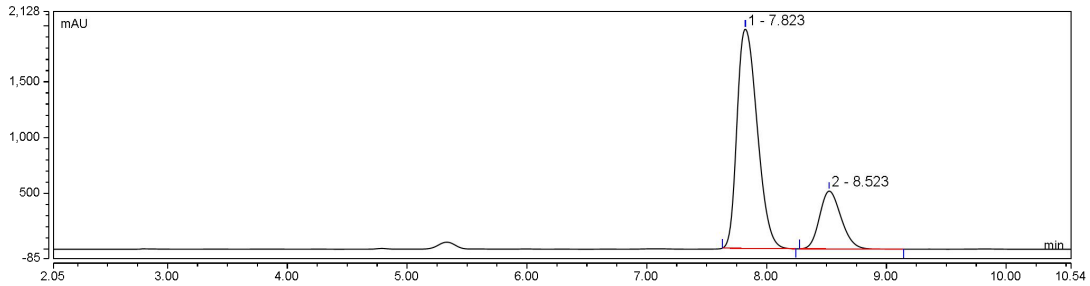
Entry	Retention Time	Area	Area(%)	Height
1	5.930	30.5365	80.61	249.67
2	6.737	7.3421	19.39	53.13

HPLC Chromatogram of **3d**



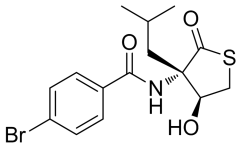


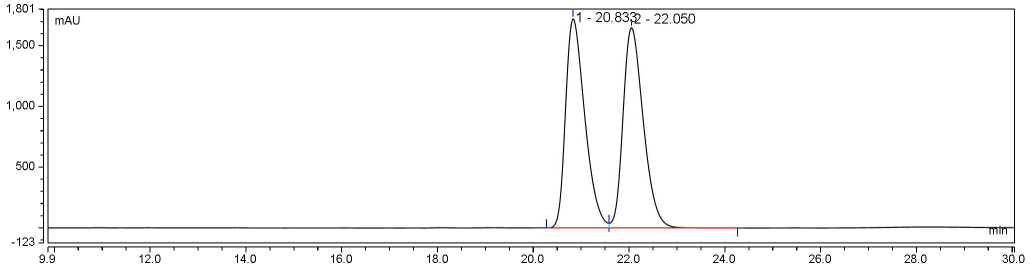
Entry	Retention Time	Area	Area(%)	Height
1	7.907	120.8816	50.11	698.72
2	8.520	120.3506	49.89	645.07



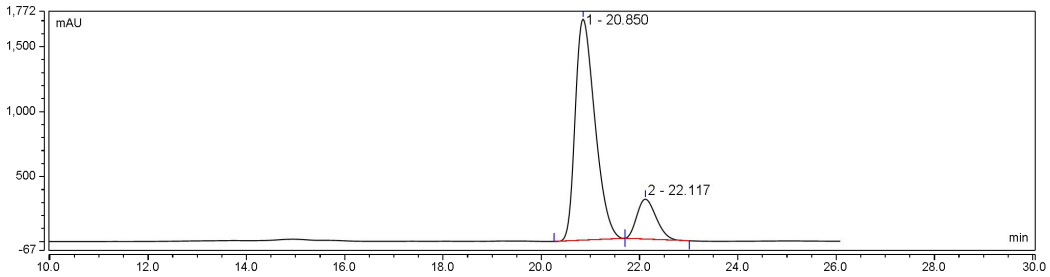
Entry	Retention Time	Area	Area(%)	Height
1	7.823	384.0387	78.09	1965.60
2	8.523	107.7582	21.91	518.43

HPLC Chromatogram of **3e**



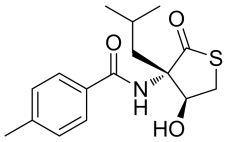


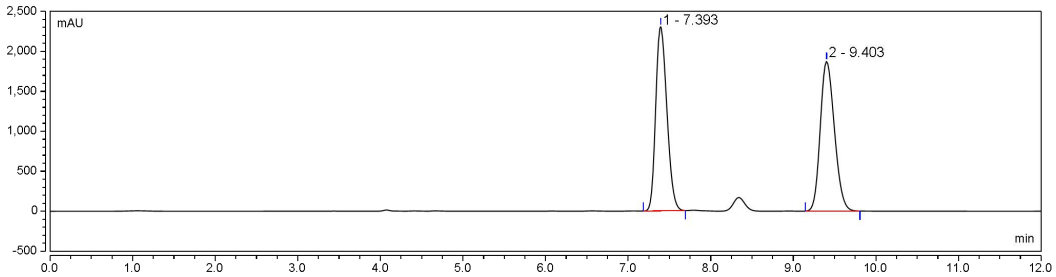
Entry	Retention Time	Area	Area(%)	Height
1	20.833	800.6653	49.77	1722.87
2	22.050	807.9279	50.23	1649.46



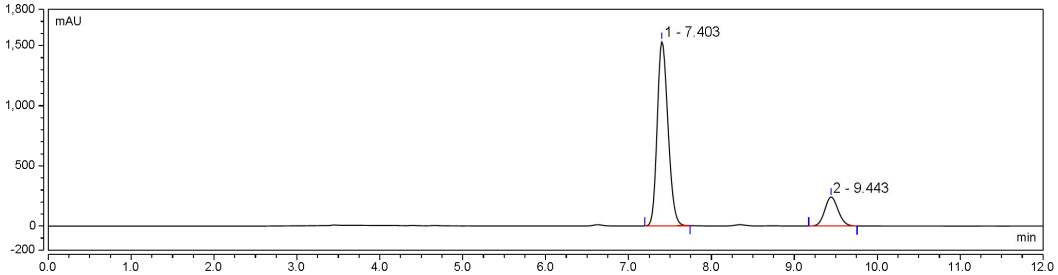
Entry	Retention Time	Area	Area(%)	Height
1	20.850	790.4015	84.99	1702.23
2	22.117	139.6236	15.01	307.40

HPLC Chromatogram of **3f**



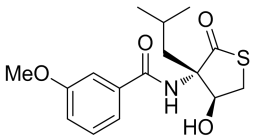


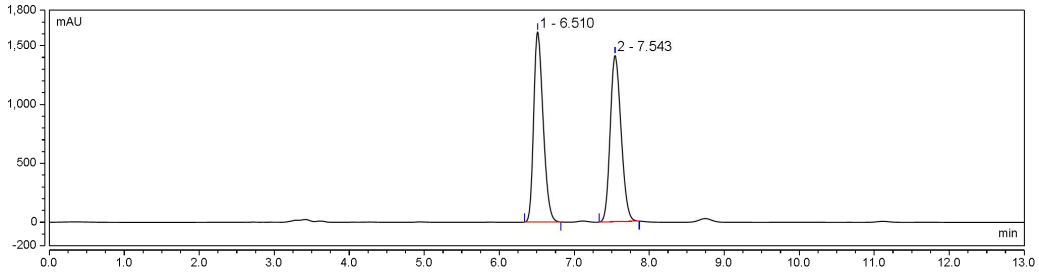
Entry	Retention Time	Area	Area(%)	Height
1	7.393	361.0165	49.23	2304.33
2	9.403	372.3746	50.77	1873.15



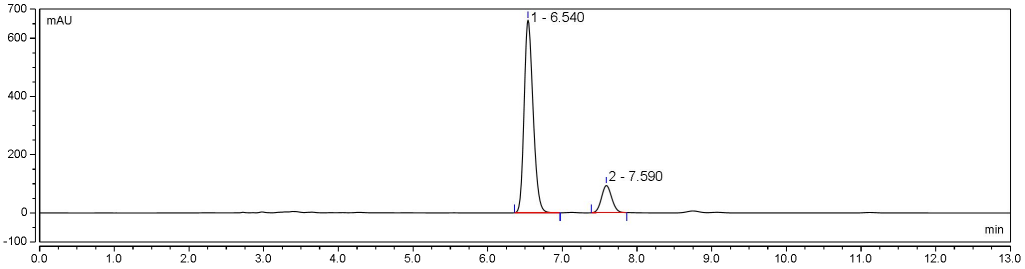
Entry	Retention Time	Area	Area(%)	Height
1	7.403	231.8409	83.99	1534.50
2	9.443	44.1852	16.01	241.08

HPLC Chromatogram of **3g**



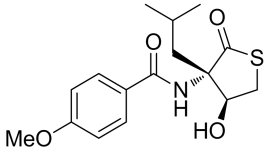


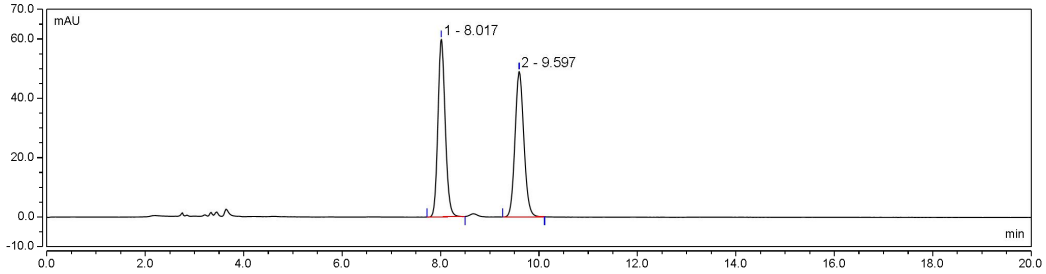
Entry	Retention Time	Area	Area(%)	Height
1	6.510	235.7324	49.87	1615.16
2	7.543	236.9663	50.13	1411.28



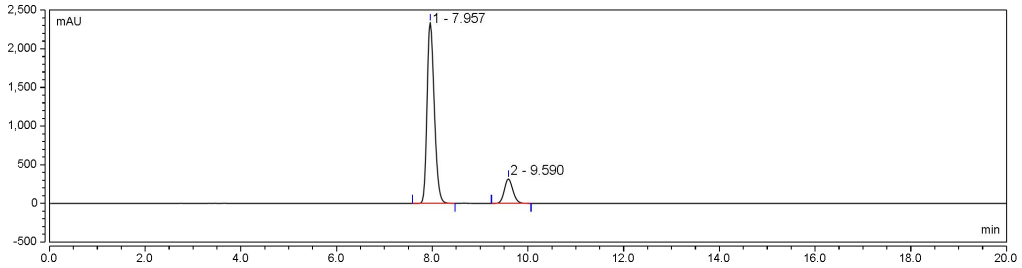
Entry	Retention Time	Area	Area(%)	Height
1	6.540	92.3115	86.17	662.12
2	7.590	14.8179	13.83	93.68

HPLC Chromatogram of **3h**



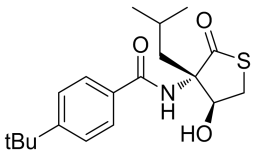


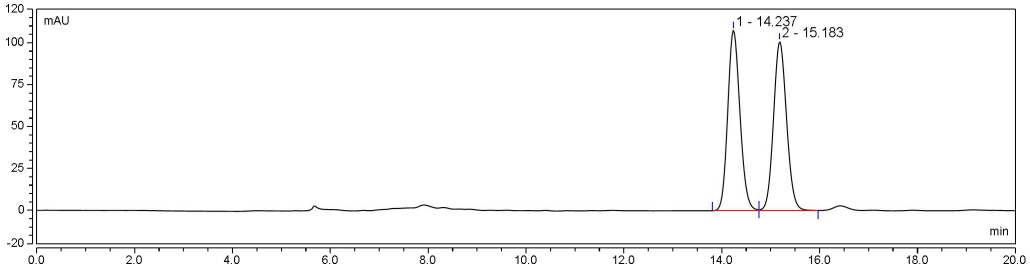
Entry	Retention Time	Area	Area(%)	Height
1	8.017	10.2658	50.08	59.86
2	9.597	10.2311	49.92	49.03



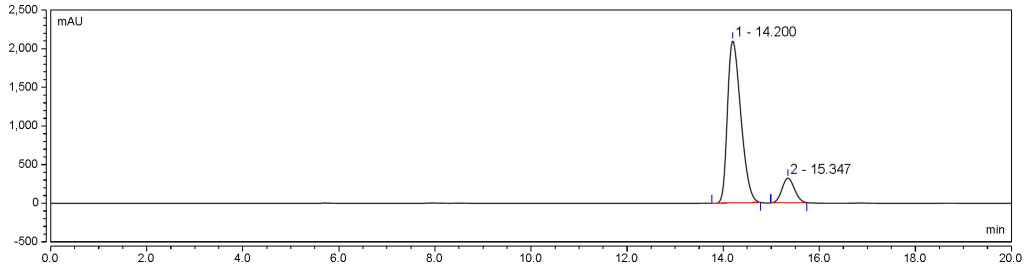
Entry	Retention Time	Area	Area(%)	Height
1	7.957	409.7811	86.18	2340.10
2	9.590	65.6988	13.82	317.07

HPLC Chromatogram of **3i**



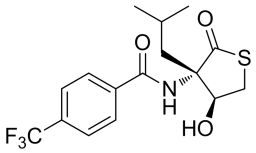


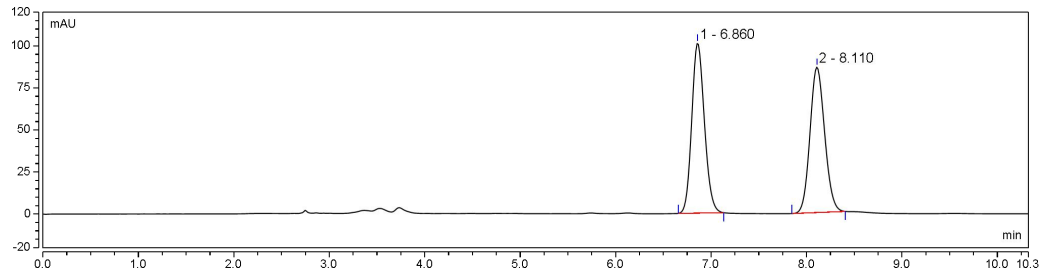
Entry	Retention Time	Area	Area(%)	Height
1	14.237	31.2486	50.00	107.74
2	15.183	31.2450	50.00	100.85



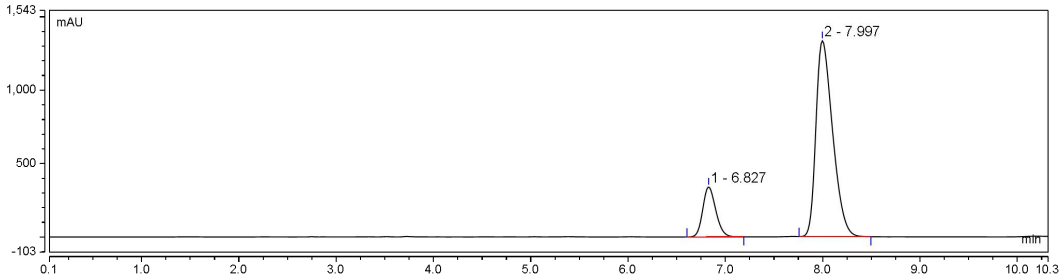
Entry	Retention Time	Area	Area(%)	Height
1	14.200	674.4919	87.54	2099.93
2	15.347	96.0209	12.46	319.80

HPLC Chromatogram of **3j**



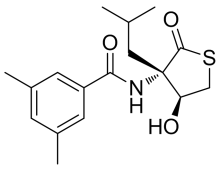


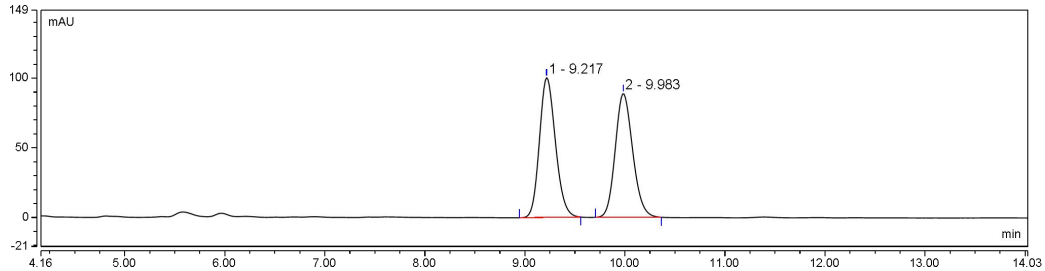
Entry	Retention Time	Area	Area(%)	Height
1	6.860	15.5458	50.24	101.25
2	8.110	15.5458	49.76	86.51



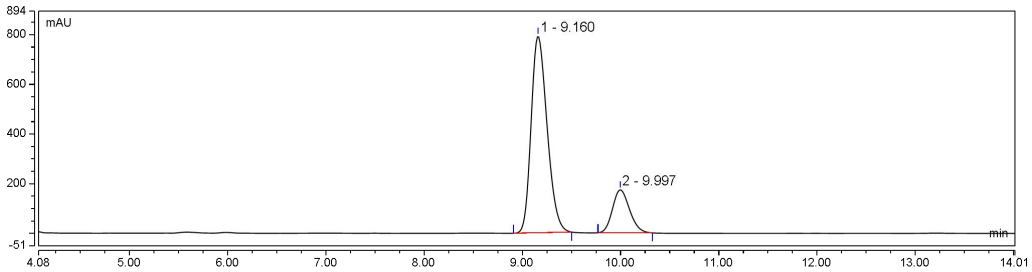
Entry	Retention Time	Area	Area(%)	Height
1	6.827	51.7131	16.27	340.52
2	7.997	266.1935	83.73	1335.20

HPLC Chromatogram of **3k**



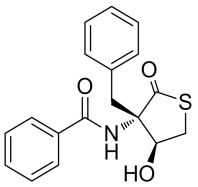


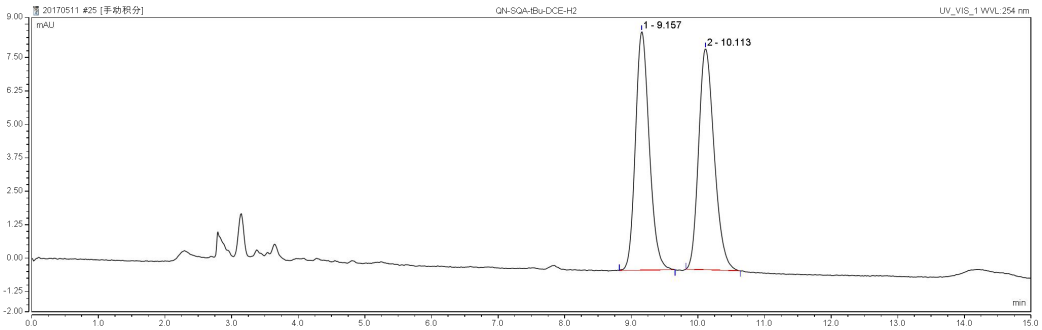
Entry	Retention Time	Area	Area(%)	Height
1	9.217	18.5936	50.87	100.33
2	9.983	17.9588	49.13	88.83



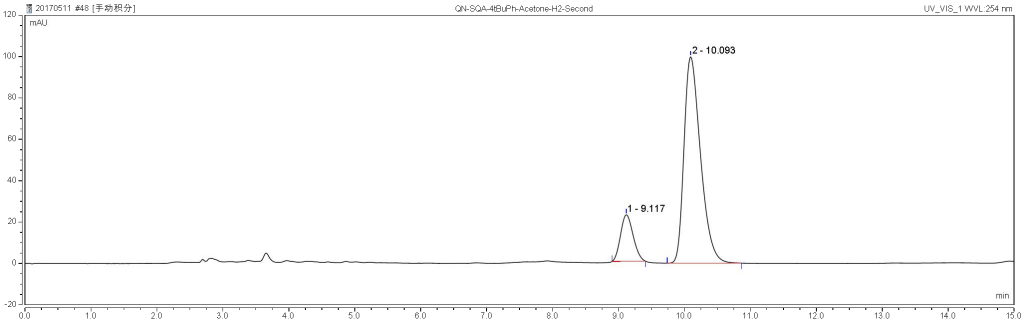
Entry	Retention Time	Area	Area(%)	Height
1	9.160	149.2685	81.12	791.88
2	9.997	34.7476	18.88	173.00

HPLC Chromatogram of **3l**



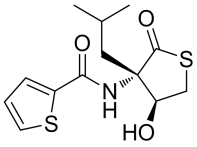


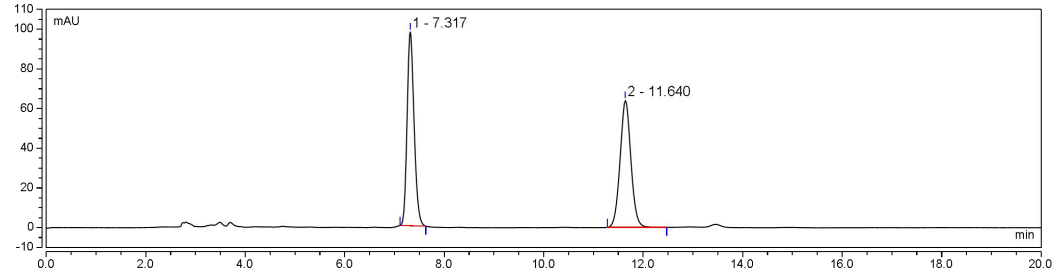
Entry	Retention Time	Area	Area(%)	Height
1	9.157	2.1476	48.94	8.92
2	10.113	2.2408	51.06	8.26



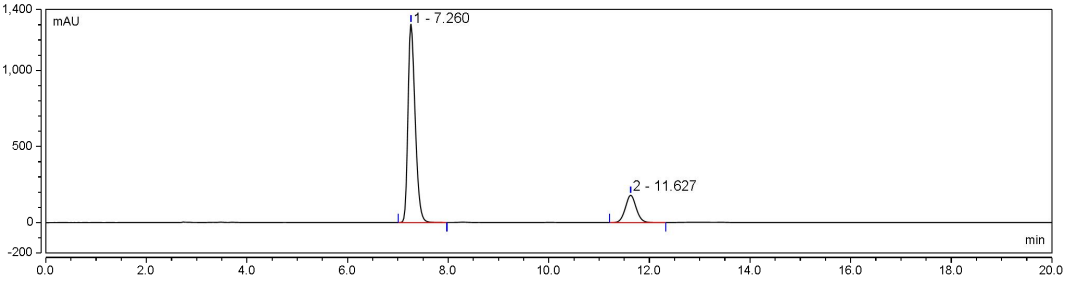
Entry	Retention Time	Area	Area(%)	Height
1	9.117	4.9687	14.67	22.49
2	10.093	28.9008	85.33	99.77

HPLC Chromatogram of **3m**



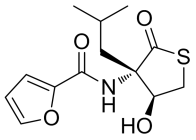


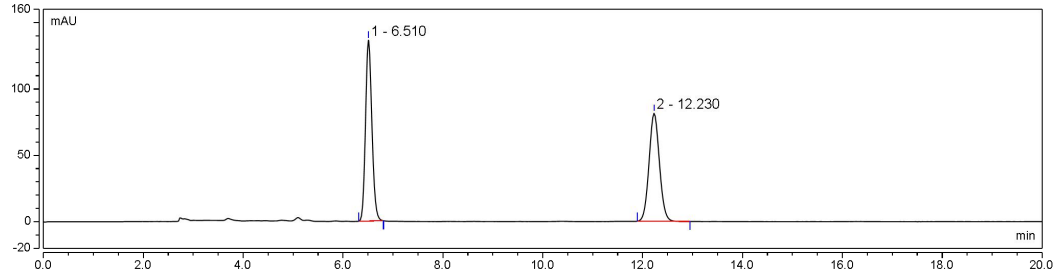
Entry	Retention Time	Area	Area(%)	Height
1	7.317	15.8622	49.59	97.72
2	11.640	16.1267	50.41	64.03



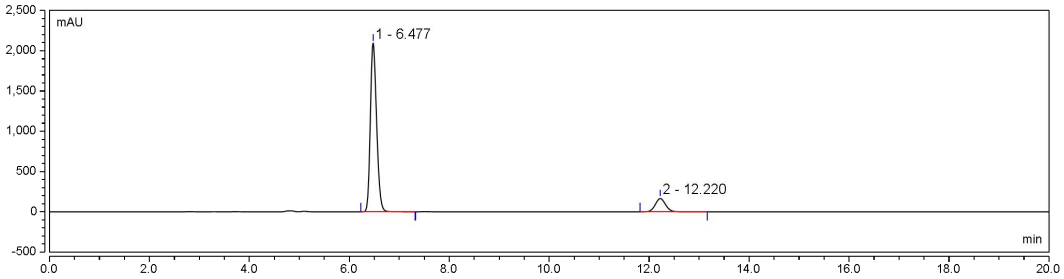
Entry	Retention Time	Area	Area(%)	Height
1	7.260	215.6287	82.86	1303.69
2	11.627	44.6118	17.14	179.77

HPLC Chromatogram of **3n**



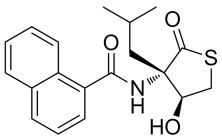


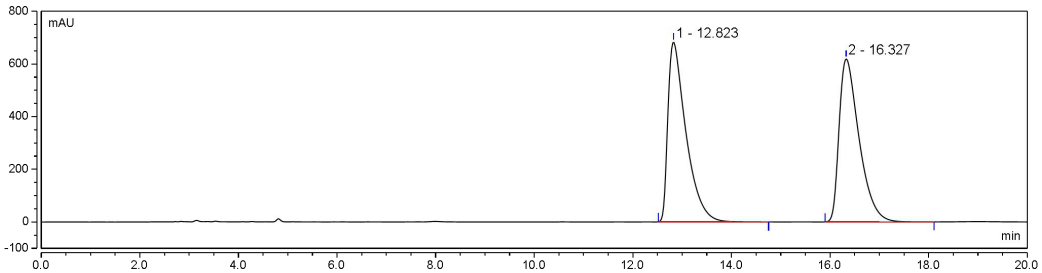
Entry	Retention Time	Area	Area(%)	Height
1	6.510	20.1978	50.75	136.29
2	12.230	19.6034	49.25	81.40



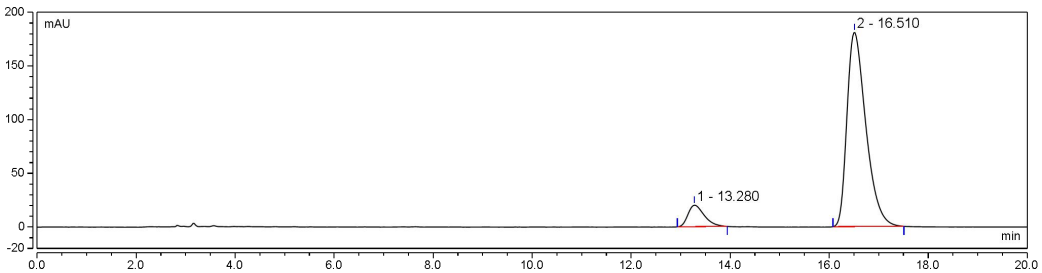
Entry	Retention Time	Area	Area(%)	Height
1	6.477	302.6774	88.42	2097.20
2	12.220	39.6523	11.58	165.74

HPLC Chromatogram of **3o**



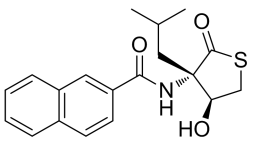


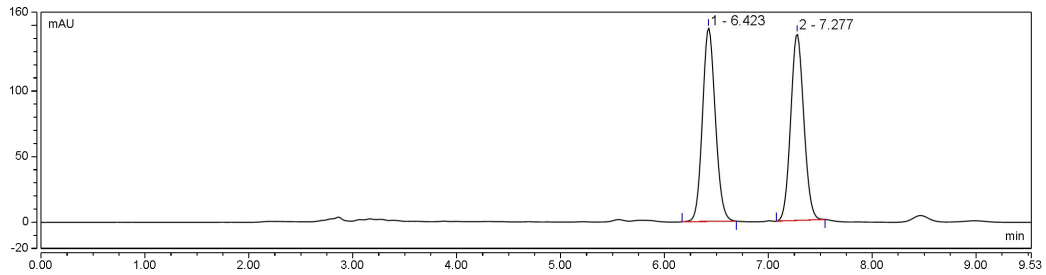
Entry	Retention Time	Area	Area(%)	Height
1	12.823	289.7467	49.96	683.17
2	16.327	290.2084	50.04	619.21



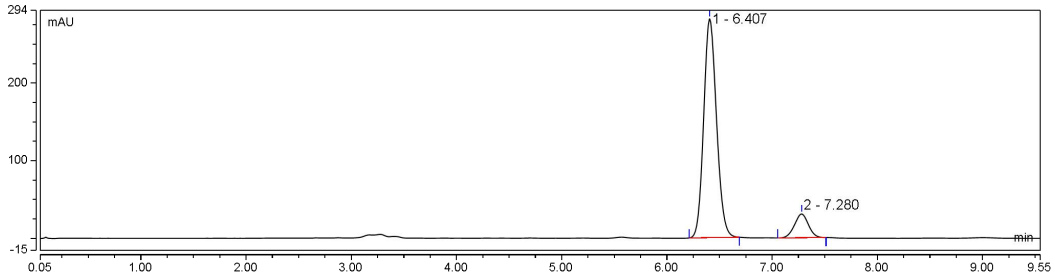
Entry	Retention Time	Area	Area(%)	Height
1	13.280	7.6112	8.69	19.99
2	16.510	79.9397	91.31	181.08

HPLC Chromatogram of **3p**



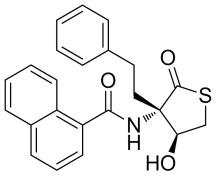


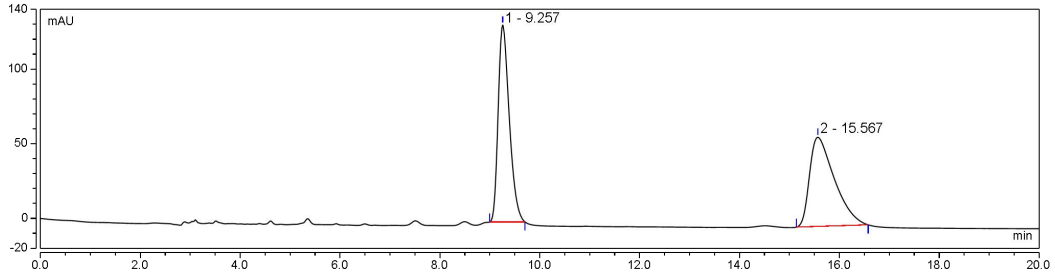
Entry	Retention Time	Area	Area(%)	Height
1	6.423	21.2229	50.51	147.61
2	7.277	20.7957	49.49	142.25



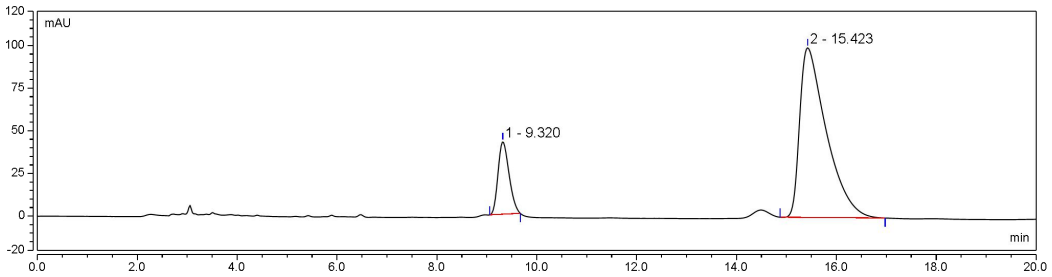
Entry	Retention Time	Area	Area(%)	Height
1	6.407	39.8315	89.50	281.94
2	7.280	4.6729	10.50	30.66

HPLC Chromatogram of **3q**



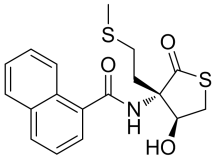


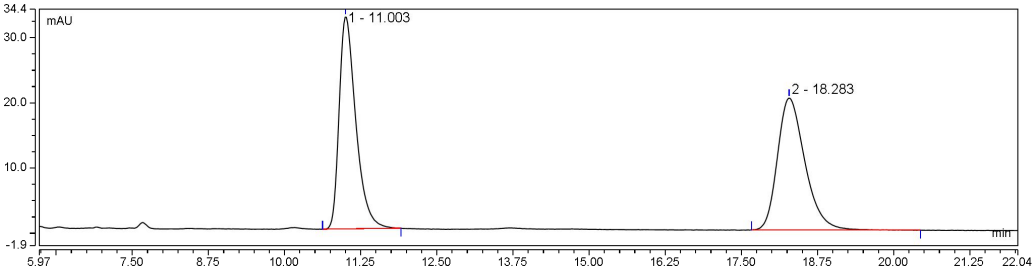
Entry	Retention Time	Area	Area(%)	Height
1	9.257	34.0551	49.77	132.00
2	15.567	34.3711	50.23	59.77



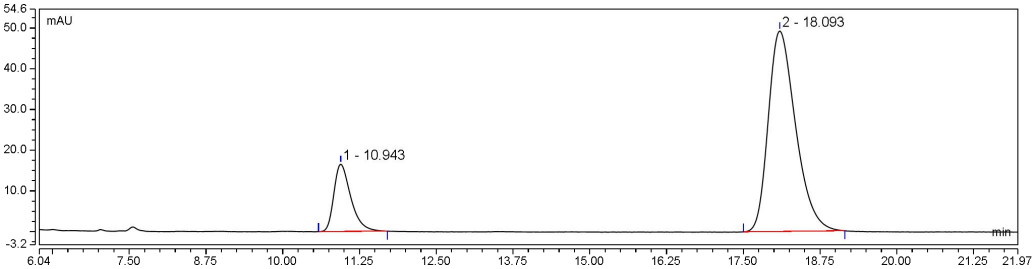
Entry	Retention Time	Area	Area(%)	Height
1	9.320	10.8697	15.06	42.49
2	15.423	61.3264	84.94	99.45

HPLC Chromatogram of **3r**



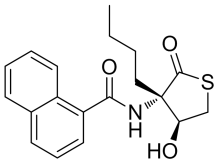


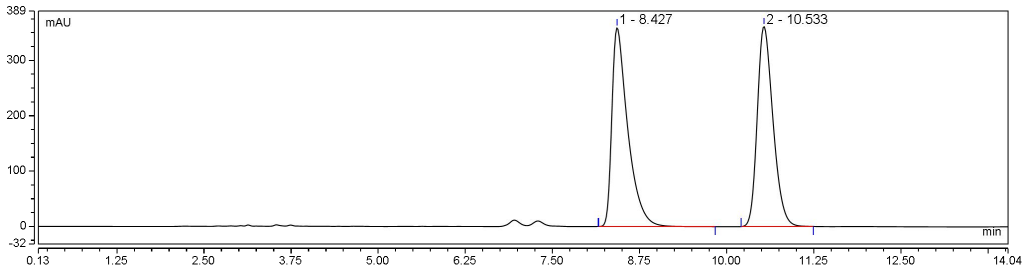
Entry	Retention Time	Area	Area(%)	Height
1	11.003	10.3501	49.48	32.59
2	18.283	10.5682	50.52	20.23



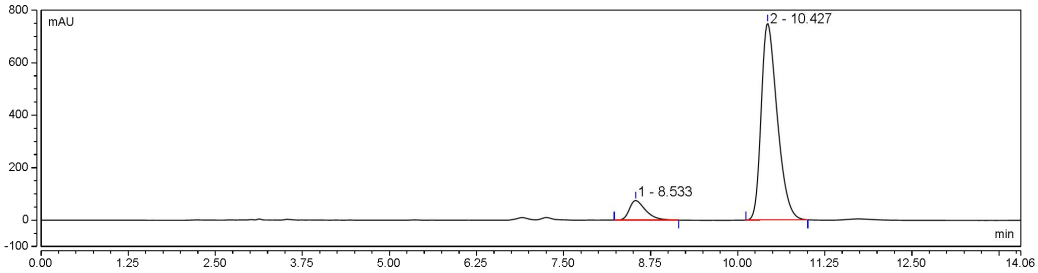
Entry	Retention Time	Area	Area(%)	Height
1	10.943	5.1849	16.91	16.54
2	18.093	25.4752	83.09	49.26

HPLC Chromatogram of **3s**



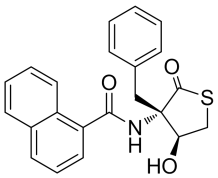


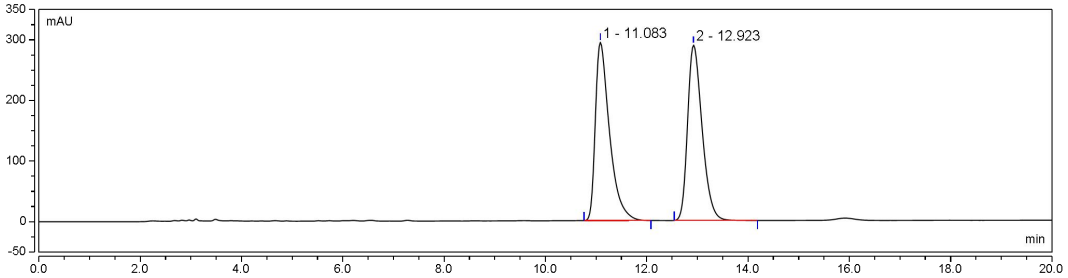
Entry	Retention Time	Area	Area(%)	Height
1	8.427	95.1339	50.11	359.35
2	10.533	94.7156	49.89	361.73



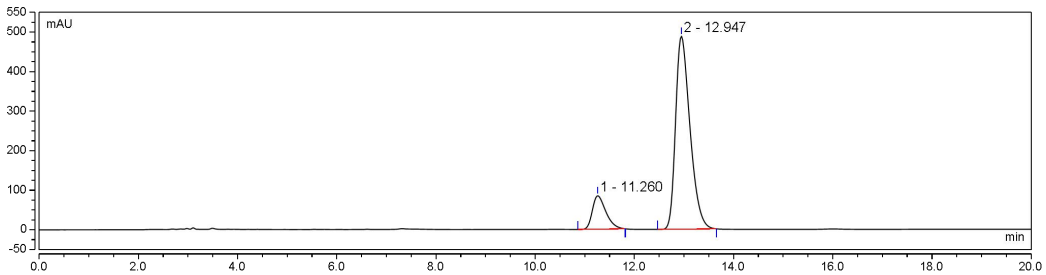
Entry	Retention Time	Area	Area(%)	Height
1	8.533	17.6167	8.00	74.44
2	10.427	202.7059	92.00	749.73

HPLC Chromatogram of **3t**



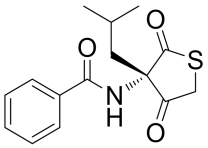


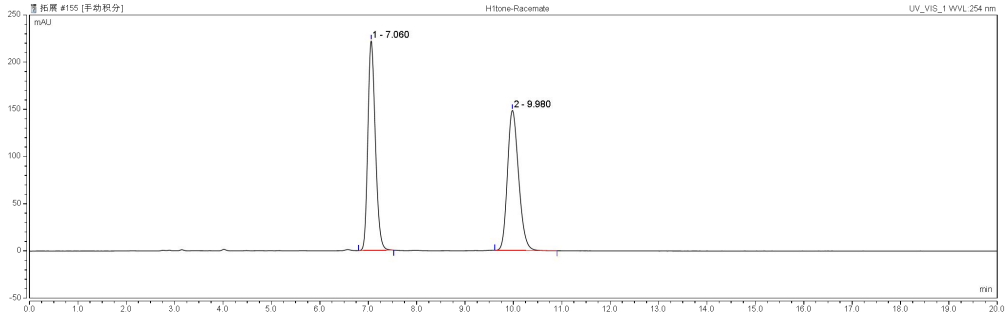
Entry	Retention Time	Area	Area(%)	Height
1	11.083	95.3211	49.80	294.15
2	12.923	96.1028	50.20	289.36



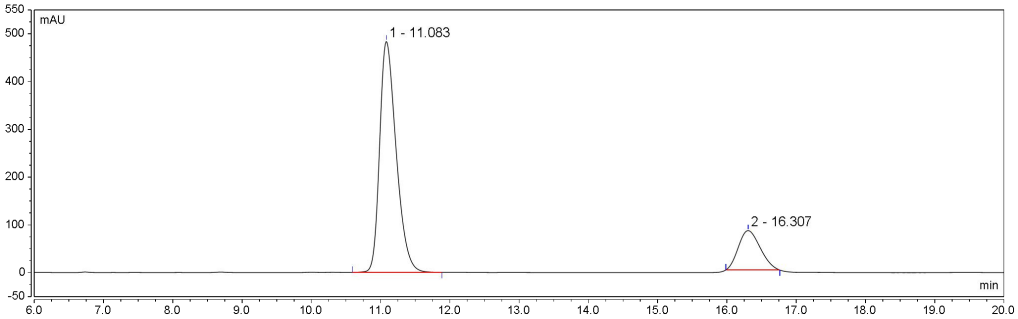
Entry	Retention Time	Area	Area(%)	Height
1	11.260	26.6148	13.95	84.63
2	12.947	164.2381	86.05	488.49

HPLC Chromatogram of **4**



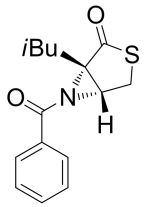


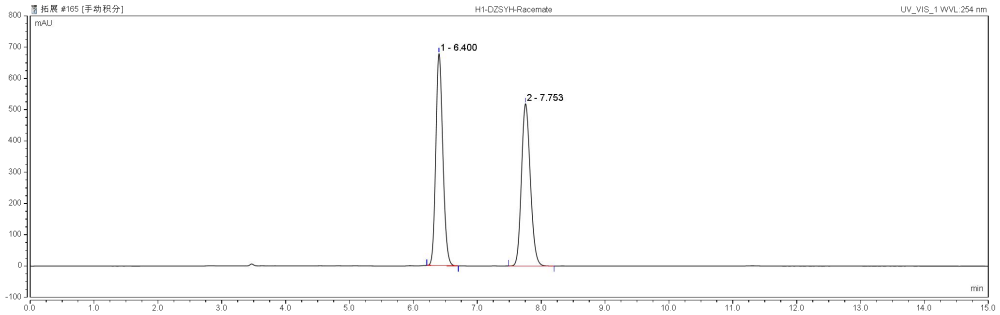
Entry	Retention Time	Area	Area(%)	Height
1	7.060	39.5803	50.02	221.93
2	9.980	39.5474	86.05	148.58



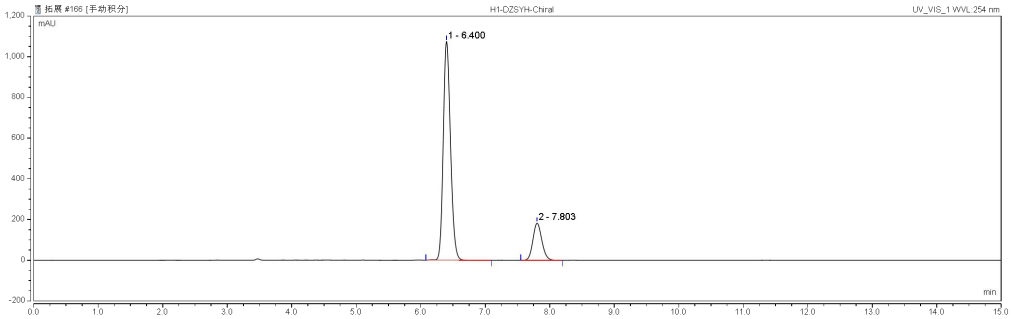
Entry	Retention Time	Area	Area(%)	Height
1	11.083	133.6949	81.61	483.78
2	16.307	30.1229	18.39	82.43

HPLC Chromatogram of **5**





Entry	Retention Time	Area	Area(%)	Height
1	6.400	86.7477	50.97	678.17
2	7.753	83.4363	49.03	519.11



Entry	Retention Time	Area	Area(%)	Height
1	6.400	139.7047	83.97	1075.26
2	7.803	29.2788	16.03	182.75