Preparations of Sulfamates and Sulfamides Using a Selective Sulfamoylation Agent

Hai-Ming Wang,[a] Chao-Dong Xiong,[c,d] Xiao-Qu Chen,[b] Chun Hu*[a] and Dong-Yu Wang*[b]

[a] Key Laboratory of Structure-based Drug Design & Discovery, Ministry of Education; School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang 110016, China.

[b] School of Pharmacy, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, China.

[c] CAS Key Laboratory of Receptor Research, Shanghai Institute of *Materia Medica* (SIMM), Chinese Academy of Sciences, Shanghai 201203, China.

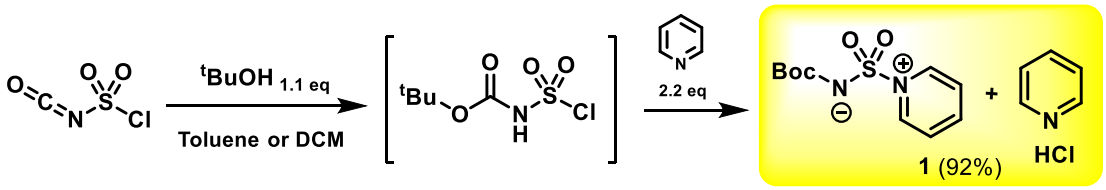
[d] University of Chinese Academy of Sciences, Beijing 100049, China.

Table of Contents

1. General Methods for Experiments

Solvents and chemical reagents were obtained from commercial sources and used without further purification. ^{1}H NMR spectral data were recorded in chloroform-d, DMSO-d6, or Methanol-d4 on Varian Mercury 400, 500 or 600 NMR spectrometer, and ^{13}C NMR was recorded in chloroform-d, DMSO-d6 or methanol-d4 on Varian Mercury 500, 600 NMR spectrometer. Low-resolution mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a Thermo Fisher Finnigan LTQ or Agilent G6520 Q-TOF spectrometer. Column chromatography was carried out on silica gel (200−300 mesh). All reactions were monitored using thin layer chromatography (TLC) on silica gel plates (15 mm × 50mm).

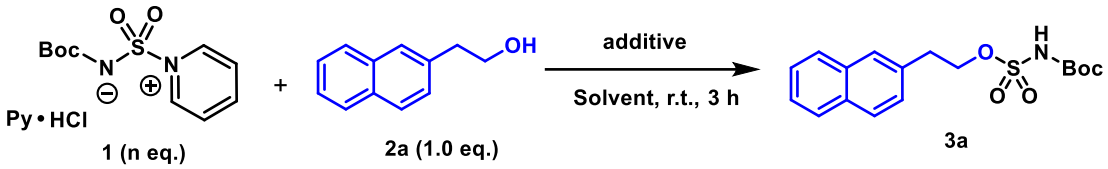
2. Procedure for the Preparation of Sulfamoylation Reagent 1 and Measurement of Saturated Solubility



In order to prepare 1, Tert-butyl alcohol (1630 mg, 22 mmol, 1.1 equiv) and anhydrous toluene (400.0 mL, 3.76 mol, 16.3 equiv) were added to a reaction vessel under nitrogen and the mixture was cooled to 0°C. chlorosulfonyl isocyanate (2830 mg, 20 mmol, 1.0 equiv) was added at a rate that kept the temperature below 0 °C and the mixture was stirred for 1 hour. Pyridine (3480 mg, 44 mmol, 2.2 equiv) was added while keeping the temperature below 0 °C and the mixture was then stirred for 4 hours at at room temperature. Sulfamoylating reagent 1 was collected by filtration and dried under vacuum giving a white solid (6863 mg, 18.4 mmol, 92% yield).

To Measure the saturated solubility of sulfamoylation reagent **1**, acetonitrile-d3 (1.0 ml), **1** (1.0 mmol) were added to a vial at room temperature and the mixture was stirred for 5 min. After a filtration, the concentration of **1** was calculated based on ^{1}H-NMR analysis with mesitylene as an internal standard. The saturated solubility of Burgess-type reagent (**C**) was measured with the same procedure.

3. Optimization for Reaction Conditions.

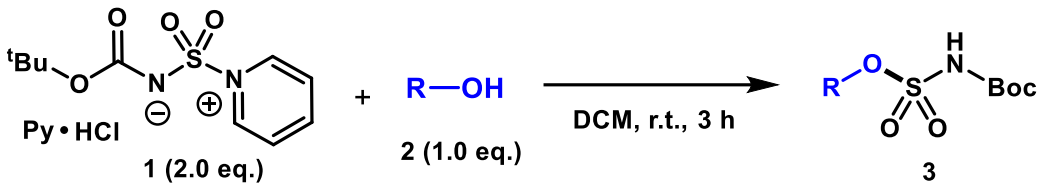


Entry	n	Additive	Solvent	**3a** yield[b]
1	1.5	–	DCM	80%
2	2	–	DCM	82%
3	2.5	–	DCM	79%
4	1.5	–	THF	51%
5	1.5	–	DMF	43%
6	1.5	–	MeCN	79%
7	1.5		DCE	71%
8	1.5	Cs_2CO_3	DCM	77%
9	1.5	KO^{t}Bu	DCM	61%
10	1.5	DIPEA	DCM	53%
11	1.5	K_2CO_3	DCM	73%
12	1.5	CF_3COOH	DCM	34%
13	1.5	$AlCl_3$	DCM	32%
14	1.5	CH_3COOH	DCM	43%

[a] Reaction conditions: 2-(naphthalen-2-yl)ethan-1-ol (**2a**, 0.2 mmol), **1** (n eq.), additive (0.4 mmol), Ligand (0.024 mmol), Solvent (1 ml), room temperature, 3 h.

[b] Yields were calculated based on ^{1}H-NMR analysis with mesitylene as an internal standard.

4. General Procedure for the Reactions of Sulfamoylation Reagent 1 with Alcohols (Phenol)

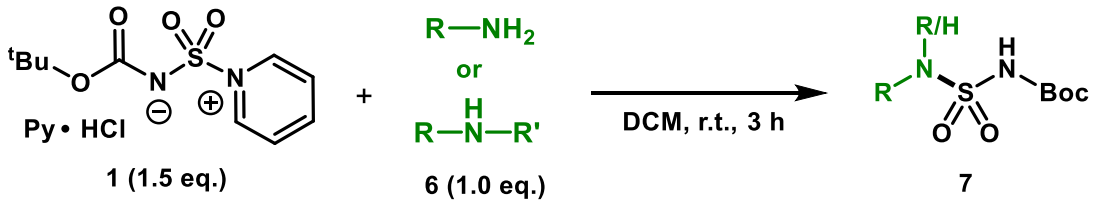


Alcohol (0.2 mmol), 1(0.3 mmol) and dry dichloromethane (3 mL) were added to a reaction vessel at room temperature and the mixture was stirred for 3 hours. After the completion of the reaction as indicated by TLC, the mixture was concentrated under a reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue and the resulting mixture was extracted with EA. The organic layers were washed with HCl (0.5M) in water. The organic layer was dried over Na_2SO_4, concentrated under a

reduced pressure. The residue was purified by flash column chromatography on silica gel

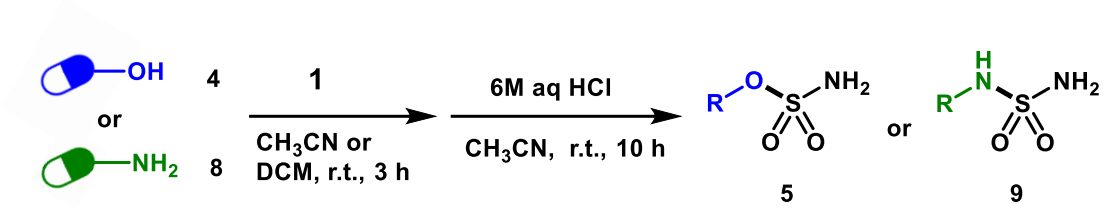
Phenol (0.2 mmol), 1(0.4 mmol) and dry dichloromethane (3 mL) were added to a reaction vessel at room temperature and the mixture was stirred for 3.5 hours. After the completion of the reaction as indicated by TLC, the mixture was concentrated under a reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue and the resulting mixture was extracted with EA. The organic layers were washed with HCl (0.5M) in water. The organic layer was dried over Na_2SO_4, concentrated under a reduced pressure. The residue was purified by flash column chromatography on silica gel.

5. General Procedure for the Reactions of Sulfamoylation Reagent 1 with RNHR'(H).



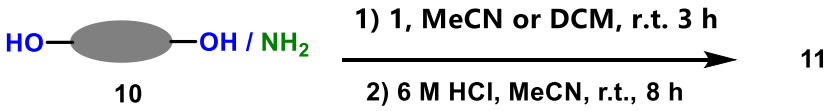
Aniline (0.2 mmol), 1(0.3 mmol) and dry dichloromethane (3 mL) were added to a reaction vessel at room temperature and the mixture was stirred for 3 hours. After the completion of the reaction as indicated by TLC, the mixture was concentrated under a reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue and the resulting mixture was extracted with EA. The organic layers were washed with HCl (0.5M) in water. The organic layer was dried over Na_2SO_4, concentrated under a reduced pressure. The residue was purified by flash column chromatography on silica gel

6. General Procedure for the Reactions of Sulfamoylation Reagent 1 with Various Pharmaceuticals and Bioactive Molecules, or Their Derivatives Containing an OH or NH_2 Moiety.



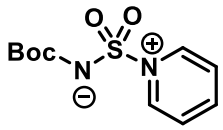
6 or 7 (0.2 mmol), 1 (0.4 mmol) and dry acetonitrile (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3 hours. After the completion of the reaction indicated by TLC, HCl (12M) in water (0.5 mL) was added dropwise. and the mixture was stirred for 8 hours. After the completion of the reaction indicated by TLC, the mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel

7. General Procedure for the Reactions of Sulfamoylation Reagent 1with Compounds with Different Nucleophilic Groups.



10 (0.2 mmol), 1 (0.3-0.4 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3.3 hours. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel.

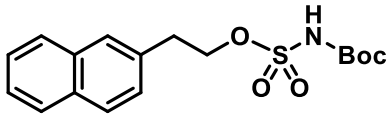
8. Characterization of Products



1

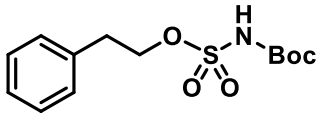
HCl

white-solid (6863.2mg, 92% yield).**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.92 (dd, *J* = 6.5, 1.4 Hz, 4H), 8.54 – 8.47 (m, 2H), 8.03 (dd, *J* = 7.8, 6.7 Hz, 4H), 7.65 (s, 1H), 1.36 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 152.8, 145.9, 141.4, 127.1, 80.9, 27.9. HRMS (ESI): (tert-butoxycarbonyl) (pyridin-1-ium-1-ylsulfonyl) amide calc'd for $C_{10}H_{15}N_2O_4S^+$ $[M+H]^+$: 259.0747, found: 259.0751.



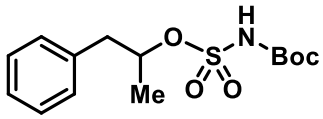
3a

white-solid (57.5 mg, 82% yield). The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.82 – 7.73 (m, 3H), 7.68 – 7.63 (m, 1H), 7.50 – 7.40 (m, 2H), 7.32 (dd, *J* = 8.5, 1.8 Hz, 1H), 4.57 (t, *J* = 7.1 Hz, 2H), 3.20 (t, *J* = 7.1 Hz, 2H), 1.39 (s, 9H).**^{13}C NMR** (101 MHz, Chloroform-*d*) δ 133.6, 133.5, 132.4, 131.3, 128.4, 127.6, 127.6, 127.0, 126.2, 125.7, 84.2, 73.5, 35.4, 27.8. HRMS (ESI): calc'd for $C_{17}H_{25}N_2O_5S^+$ $[M+ NH^4]^+$: 369.1479, found: 369.1454.



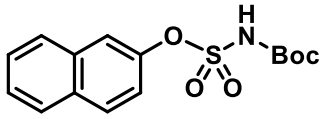
3b

white-solid (50.58 mg, 84% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **^{1}H NMR** (400 MHz, Acetonitrile-d_3) δ 7.38 – 7.24 (m, 5H), 4.51 – 4.46 (m, 2H), 3.05 (t, *J* = 6.6 Hz, 2H), 1.46 (s, 9H).**^{13}C NMR** (101 MHz, Acetonitrile-d_3) δ 149.1, 136.9, 128.9, 126.8, 117.3, 83.4, 73.3, 34.6, 27.1. HRMS (ESI): calc'd for $C_{13}H_{19}NNaO_5S^+$ $[M+ Na]^+$: 324.0876, found: 324.0884.



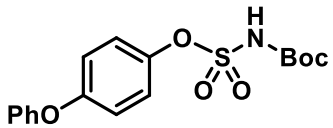
3c

white-solid (56.72 mg, 90% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **^{1}H NMR** (400 MHz, Acetonitrile-d_3) δ 7.39 – 7.01 (m, 5H), 4.97 (m, 1H), 3.04 – 2.86 (m, 2H), 1.42 (s, 9H), 1.27 (d, J = 6.3 Hz, 3H).**^{13}C NMR** (101 MHz, Acetonitrile-d_3) δ 149.3, 136.3, 129.7, 126.9, 117.3, 83.3, 83.3, 41.9, 27.2, 19.0 HRMS (ESI): calc'd for $C_{14}H_{25}N_2O_5S^+$ $[M+ NH^4]^+$: 333.1479, found: 333.1470.



3d

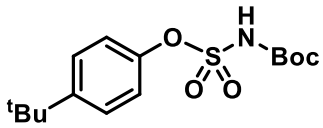
white-solid (48.46 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.89 – 7.72 (m, 4H), 7.54 – 7.38 (m, 3H), 1.43 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 158.5, 149.3, 133.8, 131.6, 128.8, 127.3, 127.3, 126.1, 125.3, 121.5, 118.7, 78.5, 27.3. HRMS (ESI): calc'd for $C_{15}H_{17}NNaO_5S^+$ $[M+ Na]^+$: 346.0720, found: 346.0719.



3e

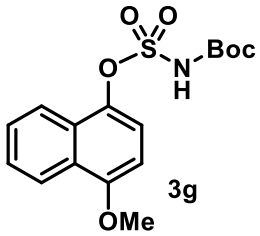
Colorless-oil (61.32 mg, 84% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.33 – 7.17 (m, 4H), 7.11 – 7.04 (m, 1H), 6.97 – 6.85 (m, 4H), 1.40 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-d) δ 156.7, 156.4, 148.5,

144.9, 130.0, 124.1, 123.2, 119.4, 119.3, 85.1, 27.9. HRMS (ESI): calc'd for $C_{17}H_{23}N_2O_6S^+$ [M+ NH^4]$^+$: 383.1271, found: 383.1261.



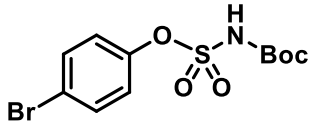
3f

white-solid (56.59 mg, 86% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.38 (d, J = 8.8 Hz, 2H), 7.21 (d, J = 8.8 Hz, 2H), 1.45 (s, 9H), 1.31 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 158.3, 149.3, 148.6, 125.8, 121.4, 78.6, 33.9, 30.5, 27.3. HRMS (ESI): calc'd for $C_{15}H_{23}NNaO_5S^+$ [M+ Na]$^+$: 352.1189, found: 352.1192.



3g

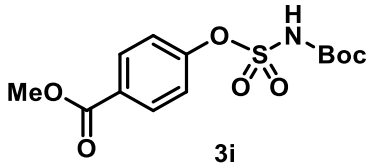
Brown-oil (57.89 mg, 82% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 8.33 – 8.14 (m, 2H), 7.59 – 7.40 (m, 3H), 6.89 – 6.82 (m, 1H), 3.99 (s, 3H), 1.40 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 153.7, 140.3, 128.3, 126.4, 126.0, 125.4, 121.9, 121.5, 118.0, 102.6, 68.1, 54.9, 29.8. HRMS (ESI): calc'd for $C_{16}H_{23}N_2O_6S^+$ [M+NH^4]$^+$: 371.1271, found: 371.1253.



3h

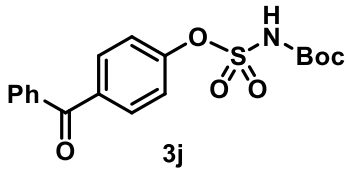
white-solid (49.14 mg, 70% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **^{1}H**

NMR (400 MHz, Methanol-d_4) δ 7.54 – 7.50 (m, 2H), 7.24 – 7.20 (m, 2H), 1.45 (s, 9H).**^{13}C NMR** (101 MHz, Chloroform-*d*) δ 154.5, 136.5, 136.1, 127.6, 122.6, 72.0, 33.7. HRMS (ESI): calc'd for $C_{11}H_{13}BrNO_5S^-$ [M-H]$^-$: 349.9703, found: 349.9702.



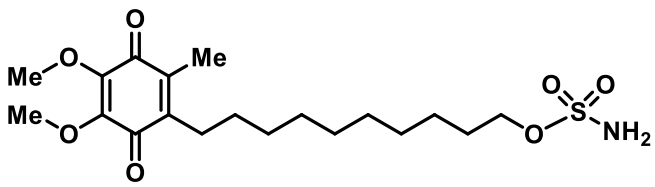
3i

white-solid (50.31 mg, 76% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) **^{1}H NMR** (400 MHz, Acetonitrile-d_3) δ 8.08 – 7.99 (m, 2H), 7.40 – 7.32 (m, 2H), 3.87 (s, 3H), 1.41 (s, 9H).**^{13}C NMR** (101 MHz, Acetonitrile-d_3) δ 166.0, 158.9, 130.9, 121.7, 51.8, 27.3. HRMS (ESI): calc'd for $C_{13}H_{16}NO_7S^-$ [M-H]$^-$: 330.0653, found: 330.0653.



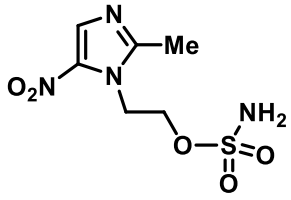
3j

Yellow-oil (49.02 mg, 65% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.85 – 7.64 (m, 4H), 7.58 – 7.51 (m, 1H), 7.49 – 7.33 (m, 4H), 1.41 (s, 9H).**^{13}C NMR** (101 MHz, Chloroform-*d*) δ 195.5, 153.2, 137.0, 136.1, 132.8, 131.8, 130.0, 128.4, 121.8, 27.9. HRMS (ESI): calc'd for $C_{18}H_{20}NO_6S^+$ [M+H]$^+$: 378.1006, found: 378.0478.



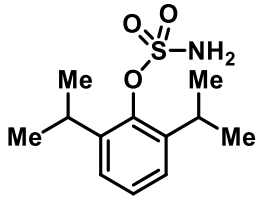
5a

yellow-solid (67.55, 77% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 4.11 (t, J = 6.5 Hz, 2H), 3.96 – 3.95 (m, 6H), 2.49 – 2.43 (m, 2H), 1.99 (s, 3H), 1.75 – 1.66 (m, 2H), 1.43 – 1.30 (m, 14H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 184.6, 184.2, 144.4, 144.4, 142.7, 138.7, 69.7, 60.2, 60.2, 29.4, 29.1, 29.0, 28.9, 28.7, 28.6, 28.2, 25.7, 25.2, 10.5. HRMS calc'd for $C_{19}H_{32}NO_7S^+$ [M + H]$^+$ 418.1894, found 418.1898.



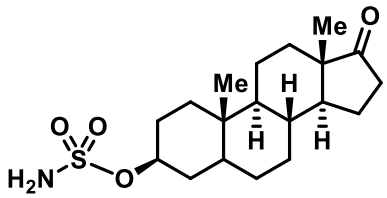
5b

white-solid (40 mg, 80% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.96 (s, 1H), 4.72 – 4.69 (m, 2H), 4.48 – 4.44 (m, 2H), 2.53 (s, 3H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 151.8, 131.4, 67.4, 45.2, 12.8. HRMS calc'd for $C_6H_{11}N_4O_5S$ [M + H]$^+$251.0445, found 251.0421.



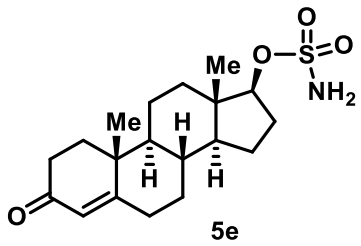
5c

white-solid (38.57 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 9:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.23 – 7.16 (m, 3H), 3.64 – 3.55 (m, 2H), 1.21 (d, 12H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 145.3, 142.6, 126.7, 124.0, 26.9, 22.7. HRMS calc'd for $C_{12}H_{19}NO_3S^+$ [M + Na]$^+$ 280.0978, found 280.0994.



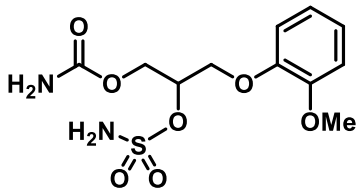
5d

white-solid (54.64 mg, 74% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 4.47 – 4.37 (m, 1H), 2.49 – 2.38 (m, 1H), 2.11 – 1.91 (m, 3H), 1.86 – 1.49 (m, 9H), 1.39 – 1.17 (m, 6H), 1.13 – 0.99 (m, 2H), 0.89 (d, *J* = 9.5 Hz, 6H), 0.81 – 0.72 (m, 1H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 80.8, 54.3, 51.3, 44.7, 36.6, 35.3, 35.2, 34.9, 34.6, 31.4, 30.6, 28.1, 28.1, 21.3, 20.2, 12.8, 11.1. HRMS calc'd for $C_{19}H_{32}NO_4S$ $[M + H]^+$ 370.2047, found 370.2038.



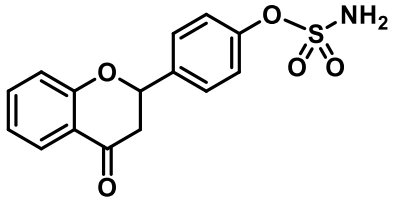
5e

white-solid (59.48 mg, 81% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 5.74 – 5.71 (m, 1H), 4.39 – 4.30 (m, 1H), 2.55 – 2.43 (m, 2H), 2.36 – 2.17 (m, 3H), 2.13 – 2.05 (m, 1H), 2.00 – 1.62 (m, 7H), 1.56 – 1.37 (m, 2H), 1.36 – 1.26 (m, 2H), 1.25 (s, 3H), 1.13 – 0.96 (m, 3H), 0.89 (s, 3H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 200.9, 173.4, 122.8, 88.5, 53.8, 49.6, 42.5, 38.6, 36.0, 35.3, 35.2, 33.3, 32.4, 31.3, 27.4, 22.8, 20.1, 16.3, 10.6. HRMS calc'd for $C_{19}H_{30}NO_4S^+$ $[M + H]^+$ 368.1890, found 368.1862.



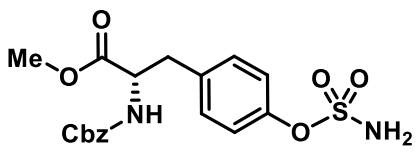
5f

white-solid (47.37 mg, 74% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.03 – 6.84 (m, 4H), 5.06 – 4.94 (m, 1H), 4.42 (dd, *J* = 12.0, 4.0 Hz, 1H), 4.35 – 4.26 (m, 2H), 4.18 (dd, *J* = 10.6, 6.3 Hz, 1H), 3.82 (s, 3H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 157.8, 149.6, 147.8, 122.0, 120.8, 114.2, 112.2, 77.4, 67.7, 62.7, 55.1. HRMS calc'd for $C_{11}H_{16}N_2NaO_7S^+$ $[M + Na]^+$ 343.0570, found 343.0572.



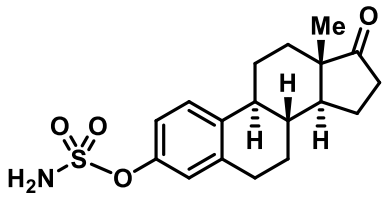
5g

white-solid (48.50 mg, 76% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.92 – 7.80 (m, 1H), 7.67 – 7.52 (m, 3H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.15 – 7.02 (m, 2H), 5.63 – 5.55 (m, 1H), 3.18 – 3.05 (m, 1H), 2.87 (dd, *J* = 16.9, 3.1 Hz, 1H). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 192.4, 161.6, 150.7, 137.6, 136.2, 127.4, 126.3, 122.2, 121.3, 120.7, 117.8, 78.8, 43.9. HRMS calc'd for $C_{15}H_{14}NO_5S^+$ $[M + H]^+$ 320.0587, found 320.0570.



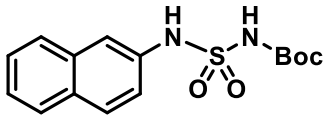
5h

white-solid (57.13 mg, 70% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.55 – 7.07 (m, 9H), 5.03 (s, 2H), 4.48 – 4.39 (m, 1H), 3.71 (s, 3H), 3.24 – 3.12 (m, 1H), 3.01 – 2.88(m,1H). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 172.3, 157.0, 149.6, 136.7, 135.7, 130.1, 128.1, 127.6, 127.3, 121.9, 66.2, 55.5, 51.4, 36.5. HRMS calc'd for $C_{18}H_{21}N_2O_7S^+$ $[M + H]^+$ 409.1064, found 409.1046.



5i

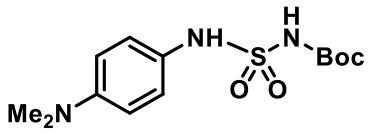
white-solid (56.54 mg, 81% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.37 – 7.29 (m, 1H), 7.10 – 6.99 (m, 2H), 2.98 – 2.86 (m, 2H), 2.55 – 2.39 (m, 2H), 2.35 – 2.24 (m, 1H), 2.21 – 1.99 (m, 3H), 1.93 – 1.83 (m, 1H), 1.68 – 1.41 (m, 6H), 0.91 (s, 3H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 222.1, 148.6, 138.2, 138.2, 126.1, 121.8, 119.0, 50.2, 44.0, 38.1, 35.3, 31.3, 28.9, 26.0, 25.5, 21.1, 12.8. HRMS calc'd for $C_{18}H_{24}NO_4S^+$ $[M + H]^+$ 409.1064, found 409.1046.



7a

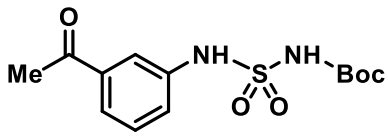
white-solid (54.76 mg, 85% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.84 – 7.74 (m, 3H), 7.71 – 7.67 (m, 1H), 7.50 – 7.35 (m, 3H), 1.34 (s, 9H)**.^{13}C NMR** (101 MHz, Methanol-d_4) δ 150.7, 135.0, 133.8, 131.0,

128.6, 127.3, 127.0, 126.3, 124.9, 120.4, 117.1, 82.0, 26.8.HRMS (ESI): calc'd for $C_{15}H_{17}N_2O_4S^-$ $[M-H]^-$ 321.0915, found: 321.0917.



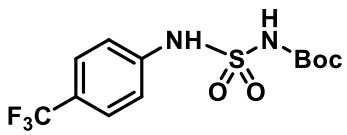
7b

Yellow-solid (51.66 mg, 82% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.10 (d, J = 9.0 Hz, 2H), 6.73 (d, J = 9.0 Hz, 2H), 2.90 (s, 6H), 1.45 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 151.1, 149.3, 126.3, 124.4, 113.0, 81.8, 39.8, 26.9. HRMS (ESI): calc'd for $C_{13}H_{22}N_3O_4S^+$ $[M+H]^+$: 316.1326, found: 316.1303.



7c

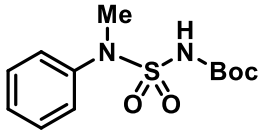
white-solid (47.1 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.84 (m, 1H), 7.77 (m, 1H), 7.49 – 7.43 (m, 2H), 2.59 (s, 3H), 1.38 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 198.4, 138.2, 137.9, 129.2, 124.9, 124.2, 119.7, 81.9, 26.8, 25.4. HRMS (ESI): calc'd for $C_{13}H_{22}N_3O_5S^+$ $[M+HH^4]^+$: 332.1275, found: 332.1260.



7d

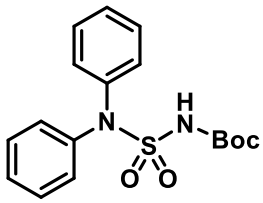
yellow-solid (53.4 mg, 78% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1)).**^{1}H**

NMR (400 MHz, Methanol-d_4) δ 7.62 – 7.58 (m, 2H), 7.38 – 7.34 (m, 2H), 1.36 (s, 9H). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 150.4, 141.2, 126.0 (q, J = 3.8 Hz), 125.4 (q, J = 33.33 Hz), 124.3 (q, J = 271.69 Hz), 118.0, 82.2, 26.7. HRMS (ESI): calc'd for $C_{12}H_{14}F_3N_2O_4S^-$ $[M-H]^-$: 339.0632, found: 339.0627.



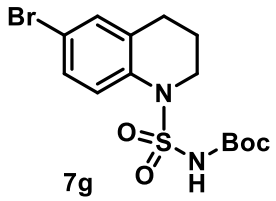
7e

white-solid (50.35 mg, 88% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.45 – 7.35 (m, 4H), 7.34 – 7.27 (m, 1H), 3.43 (s, 3H), 1.46 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 151.2, 141.4, 128.9, 127.0, 126.0, 82.1, 39.6, 26.9. HRMS (ESI): calc'd for $C_{12}H_{18}N_2NaO_4S^+$ $[M+Na]^+$: 309.0879, found: 309.0863.



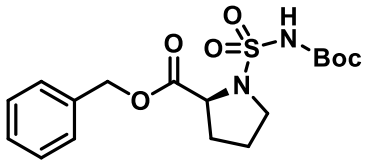
7f

white-solid (63.36 mg, 91% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.56 – 7.49 (m, 4H), 7.40 – 7.32 (m, 4H), 7.30 – 7.23 (m, 2H), 1.44 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 150.7, 141.8, 128.9, 128.0, 127.0, 82.0, 26.9. HRMS (ESI): calc'd for $C_{17}H_{20}N_2NaO_4S^+$ $[M+Na]^+$: 371.1036, found: 371.1040.



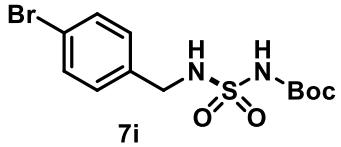
7g

white-solid (62.4 mg, 80% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.56 – 7.47 (m, 1H), 7.29 – 7.22 (m, 2H), 3.91 – 3.77 (m, 2H), 2.77 (t, J = 6.5 Hz, 2H), 2.04 – 1.91 (m, 2H), 1.34 (s, 9H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 136.2, 131.6, 131.4, 128.9, 122.9, 116.0, 82.1, 26.7,26.7 21.9. HRMS (ESI): calc'd for $C_{14}H_{18}BrN_2O_4S^-$ [M-H]$^-$: 389.0176, found: 339.0177.



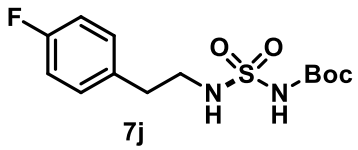
7h

Colorless oil (57.6 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.39 – 7.29 (m, 5H), 5.23 – 5.13 (m, 2H), 4.79 – 4.70 (m, 1H), 3.68 – 3.58 (m, 1H), 3.56 – 3.45 (m, 1H), 2.29 – 2.20 (m, 1H), 2.08 – 1.94 (m, 3H), 1.48 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 172.0, 150.1, 135.5, 128.6, 128.4, 128.1, 83.5, 67.1, 61.9, 49.0, 30.8, 28.0, 24.7. HRMS (ESI): calc'd for $C_{17}H_{28}N_3O_6S^+$ [M+NH_4]$^+$: 402.1693, found: 402.1691.



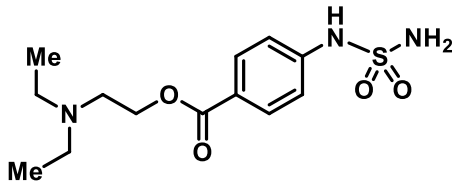
7i

Yellow solid (48.0 mg, 66% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.50 – 7.43 (m, 2H), 7.32 – 7.25 (m, 2H), 4.17 (s, 2H), 1.43 (s, 9H). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 151.0, 136.7, 131.2, 129.7, 120.9, 81.8, 46.0, 26.9. HRMS (ESI): calc'd for $C_{12}H_{16}BrN_2O_4S^-$ [M-H]$^-$: 363.0020, found: 363.0006.



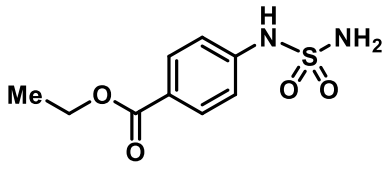
7j

Yellow solid (44.5 mg, 70% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.29 – 7.18 (m, 2H), 7.07 – 6.95 (m, 2H), 3.21 (t, J = 7.5 Hz, 2H), 2.83 (t, J = 7.5 Hz, 2H), 1.48 (s, 9H). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 161.7 (d, J = 243.1 Hz), 151.3, 134.6 (d, J = 3.2 Hz), 130.1 (d, J = 8.0 Hz), 114.8 (d, J = 21.5 Hz), 81.9, 44.6, 34.5, 27.0. HRMS (ESI): calc'd for $C_{13}H_{18}FN_2O_4S^-$ [M-H]$^-$: 317.0977, found: 317.0980.



9a

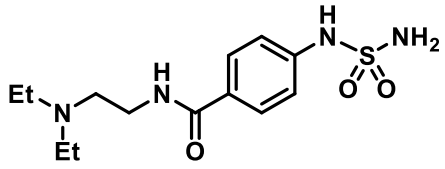
white-solid (42.75 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 6:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 8.02 – 7.86 (m, 2H), 7.29 – 7.19 (m, 2H), 4.40 (t, J = 5.9 Hz, 2H), 2.90 (t, J = 5.9 Hz, 2H), 2.69 (q, J = 7.2 Hz, 4H), 1.10 (t, J = 7.2 Hz, 6H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 166.4, 144.0, 130.5, 123.3, 116.6, 62.2, 50.5, 10.2. HRMS calc'd for $C_{13}H_{22}N_3O_4S^+$ [M + H]$^+$ 316.1326, found 316.1317.



9b

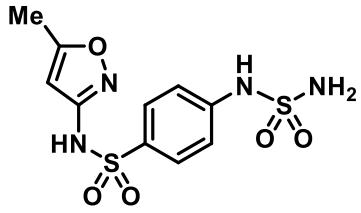
white-solid (40.50 mg, 83% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H**

NMR (400 MHz, Methanol-d_4) δ 7.96 – 7.87 (m, 2H), 7.27 – 7.17 (m, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 166.6, 143.8, 130.4, 123.7, 116.6, 60.5, 13.2. HRMS calc'd for $C_9H_{13}N_2O_4S^+$ $[M + H]^+$ 245.0591, found 245.0581.



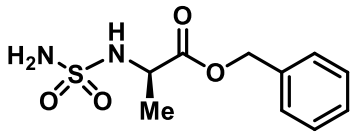
9c

white-solid (50.24 mg, 80% yield). The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 6:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.90 – 7.74 (m, 2H), 7.42 – 7.07 (m, 2H), 3.72 (t, *J* = 6.1 Hz, 2H), 3.39 – 3.31 (m, 2H), 3.29 (q, *J* = 1.8 Hz, 4H), 1.33 (t, *J* = 7.3 Hz, 6H).**^{13}C NMR** (151 MHz, Methanol-d_4) δ 169.5, 143.1, 128.3, 126.4, 116.9, 51.9, 35.1, 7.8. HRMS calc'd for $C_{13}H_{23}N_4O_3S^+$ $[M + H]^+$ 315.1485 , found 315.1479.



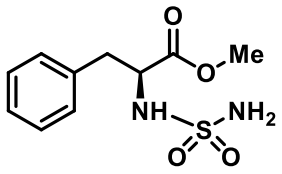
9d

white-solid (42.50 mg, 64% yield). The product was purified by preparative HPLC. **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.83 – 7.77 (m, 2H), 7.30 – 7.25 (m, 2H), 6.14 – 6.12 (m, 1H), 2.32 – 2.31 (m, 3H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 170.6, 157.9, 144.0, 132.3, 128.3, 116.8, 95.0, 10.9. HRMS calc'd for $C_{10}H_{13}N_4O_5S_2^+$ $[M + H]^+$ 333.0322 , found 333.0313.



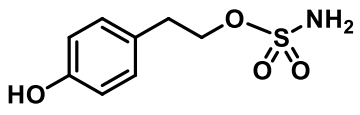
9e

white-solid (32.00 mg, 62% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.54 – 7.17 (m, 5H), 5.22 – 5.15 (m, 2H), 4.10 (q, J = 7.2 Hz, 1H), 1.39 (d, J = 7.2 Hz, 3H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 173.4, 135.9, 128.2, 127.9, 127.9, 66.6, 51.7, 17.7. HRMS calc'd for $C_{10}H_{15}N_2O_4S^+$ $[M + H]^+$ 259.0747 , found 259.0737.



9f

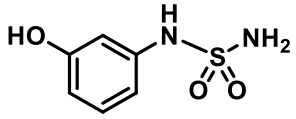
white-solid (35.61 mg, 69% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.35 – 7.17 (m, 5H), 4.23 (t, J = 7.0 Hz, 1H), 3.65 (s, 3H), 3.03 (d, J = 7.0 Hz, 2H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 172.8, 136.4, 129.1, 128.1, 126.6, 57.4, 51.3, 38.5. HRMS calc'd for $C_{10}H_{13}N_2O_4S^-$ $[M - H]^-$ 257.0602, found 257.0602.



11a

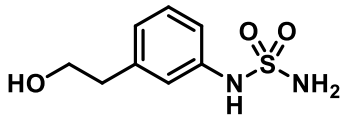
10a (0.2 mmol), 1 (0.4 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3.2 hours. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added

dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. By comparing with the raw material NMR data and mass spectrum data, the correctness of the structure is proved. white-solid (34.72 mg, 80% yield). The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 6:1)**.** **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.11 – 7.02 (m, 2H), 6.75 – 6.70 (m, 2H), 4.24 (t, J = 7.1 Hz, 2H), 2.91 (t, J = 7.1 Hz, 2H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 155.8, 129.6, 127.8, 114.9, 70.3, 34.1 HRMS calc'd for $C_8H_{10}NO_4S^-$ $[M - H]^-$ 216.0336, found 216.0338.



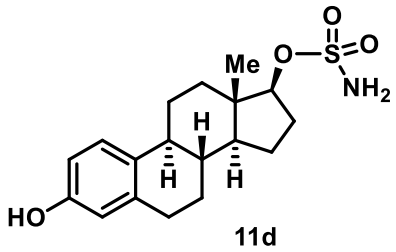
11b

10b (0.2 mmol), 1 (0.3 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3.4 hours. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. By comparing with the raw material NMR data and mass spectrum data, the correctness of the structure is proved white-solid (28.20 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.08 (t, J = 8.1 Hz, 1H), 6.75 – 6.72 (m, 1H), 6.70 – 6.65 (m, 1H), 6.53 – 6.44 (m, 1H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 157.7, 140.0, 129.4, 110.4, 110.0, 106.3. HRMS calc'd for $C_6H_9N_2O_3S^+$ $[M + H]^+$ 189.0328 , found 189.0328.



11c

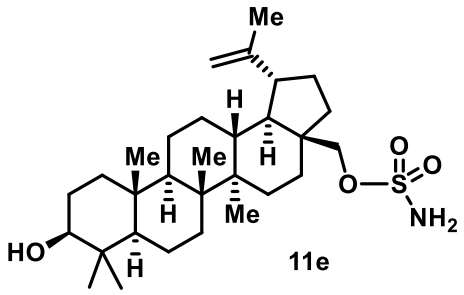
10c (0.2 mmol), 1 (0.2 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 1.5 hours, 1(0.1 mmol) was added. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. By comparing with the raw material NMR data and mass spectrum data, the correctness of the structure is proved .white-solid (33.70 mg, 78% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.25 – 7.18 (m, 1H), 7.13 – 7.04 (m, 2H), 6.97 – 6.91 (m, 1H), 3.76 (t, J = 7.0 Hz, 2H), 2.80 (t, J = 7.0 Hz, 2H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 140.1, 138.9, 128.6, 123.7, 119.9, 117.2, 62.7, 38.8. HRMS calc'd for $C_8H_{16}N_3O_3S^+$ $[M + NH^4]^+$ 234.0907 , found 234.0908.



11d

10d (0.2 mmol), 1 (0.3 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3 hours. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture

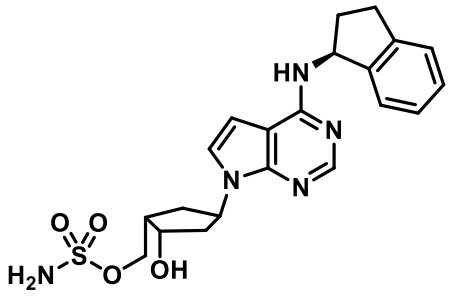
was extracted with EA. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. By comparing with the raw material NMR data and mass spectrum data, the correctness of the structure is proved .white-solid (49.16 mg, 70% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, Methanol-d_4) δ 7.06 (d, *J* = 8.5 Hz, 1H), 6.54 (dd, *J* = 8.4, 2.7 Hz, 1H), 6.47 (d, *J* = 2.7 Hz, 1H), 4.44 – 4.38 (m, 1H), 2.83 – 2.70 (m, 2H), 2.32 – 2.20 (m, 2H), 2.16 – 2.00 (m, 2H), 1.88 – 1.71 (m, 3H), 1.46 – 1.24 (m, 6H), 0.84 (s, 3H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 154.6, 137.4, 130.9, 125.9, 114.7, 112.4, 88.8, 49.1, 43.7, 43.0, 38.8, 36.3, 29.2, 27.5, 27.0, 26.0, 22.6, 10.8. HRMS calc'd for $C_{18}H_{26}NO_4S^+$ $[M + H]^+$ 352.1577 , found 352.1572.



11e

10e (0.2 mmol), 1 (0.4 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3 hours. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. By comparing with the raw material NMR data and mass spectrum data, the correctness of the structure is proved . white-solid (64.60 mg, 62% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **^{1}H NMR** (400 MHz, DMSO-d_6)

δ 7.43 (s, 2H), 4.73 – 4.68 (m, 1H), 4.60 – 4.55 (m, 1H), 4.28 (d, *J* = 5.1 Hz, 1H), 4.12 (d, *J* = 9.6 Hz, 1H), 3.75 (d, *J* = 9.6 Hz, 1H), 3.02 – 2.89 (m, 1H), 2.45 – 2.37 (m, 1H), 2.03 – 1.85 (m, 1H), 1.84 – 1.53 (m, 10H), 1.48 – 1.22 (m, 10H), 1.19 – 0.94 (m, 10H), 0.88 – 0.75 (m, 7H), 0.70 – 0.60 (m, 4H).**^{13}C NMR** (151 MHz, DMSO-d_6) δ 149.1, 109.5, 76.2, 66.7, 54.2, 49.1, 47.5, 46.6, 45.4, 41.6, 39.8, 37.9, 37.6, 36.6, 36.1, 33.1, 33.0, 28.2, 28.2, 27.5, 26.6, 25.8, 24.1, 19.7, 18.1, 17.3, 15.3, 15.2, 15.1, 13.9. HRMS calc'd for $C_{30}H_{51}ClNO_4S^-$ [M + Cl]$^-$ 556.3233 , found 556.3243.



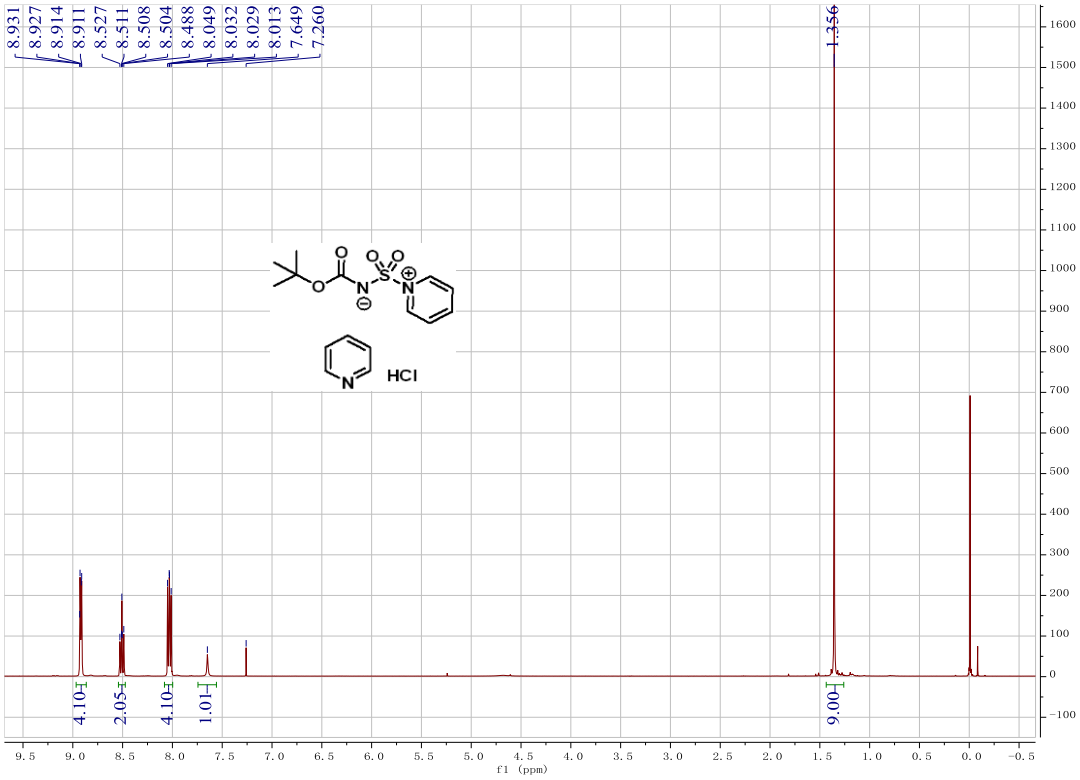
11f

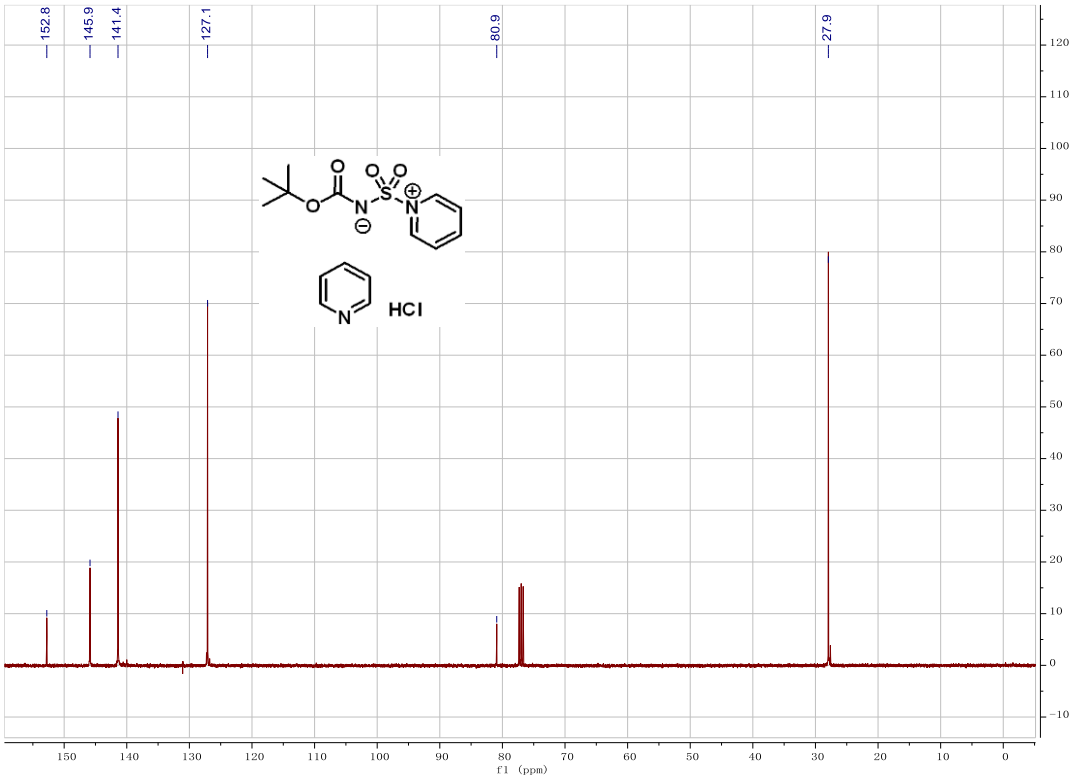
10f (0.2 mmol), 1 (0.4 mmol) and dry acetonitrile (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3 hours. After the completion of the reaction indicated by TLC, HCl (12M) in water (0.5 mL) was added dropwise and the mixture was stirred for 8 hours. After the completion of the reaction indicated by TLC, the mixture was concentrated under reduced pressure. Saturated aqueous Na_2CO_3 (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel. By comparing with the raw material NMR data and mass spectrum data, the correctness of the structure is proved. white-solid (34.72 mg, 80% yield). The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). colorless-solid (80% yield). **^{1}H NMR** (400 MHz, Methanol-d_4) δ 8.18 (s, 1H), 7.29 – 7.01 (m, 5H), 6.64 (d, *J* = 3.6 Hz, 1H), 5.85 (t, *J* = 7.7 Hz, 1H), 5.53 – 5.35 (m, 1H), 4.54 – 4.45 (m, 1H), 4.43 – 4.33 (m, 1H), 4.29 – 4.15 (m, 1H), 3.10 – 2.97 (m, 1H), 2.96 – 2.73 (m, 2H), 2.68 – 2.57 (m, 1H), 2.42 – 2.14 (m, 3H), 2.09 – 1.92 (m, 2H).**^{13}C NMR** (101 MHz, Methanol-d_4) δ 156.4,

150.6, 148.6, 143.8, 143.2, 127.4, 126.2, 124.3, 123.8, 121.2, 103.4, 99.1, 71.6, 69.4, 55.5, 52.6, 43.3, 42.1, 33.5, 33.2, 29.7. **ESI**: m/z $[M + H]^+$: 444.2 The characterization data were consistent with the literature[1].

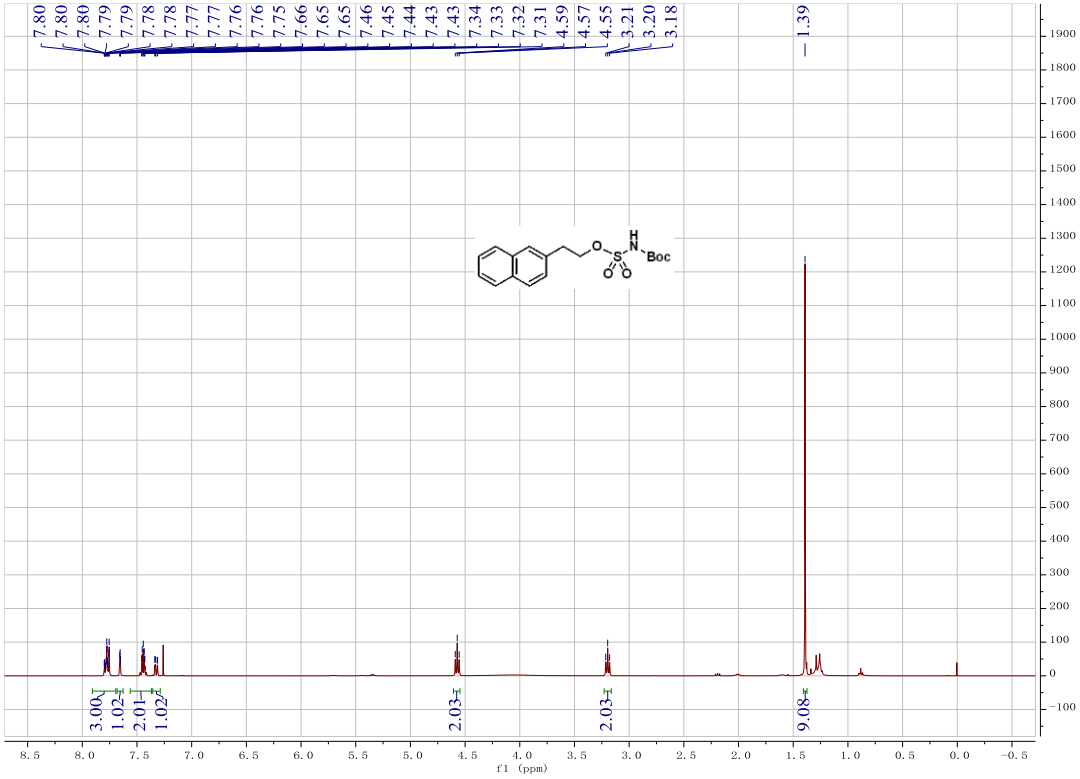
9. Copies of NMR spectra data

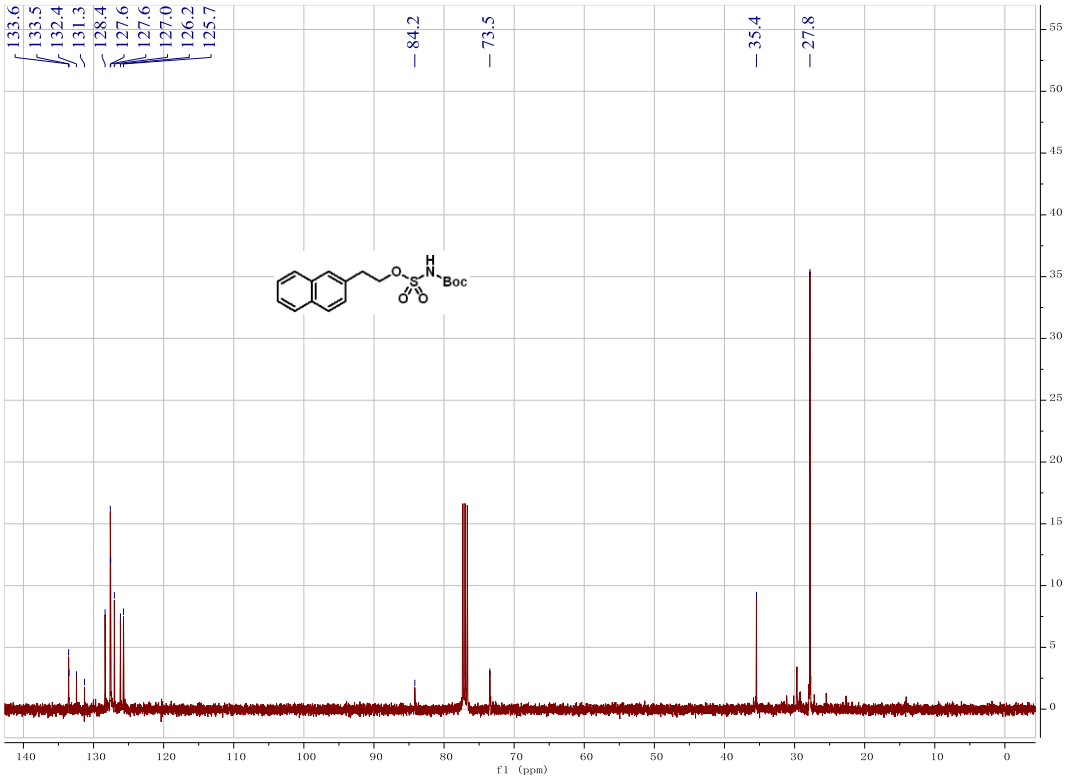
^{1}H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 1



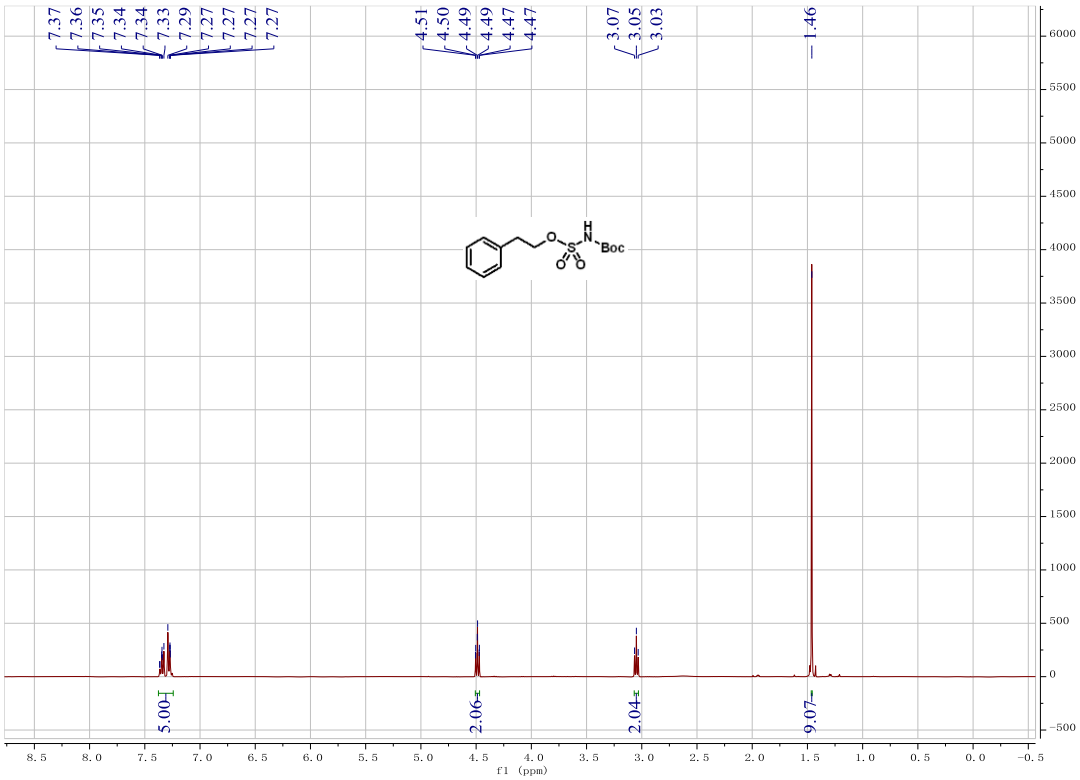


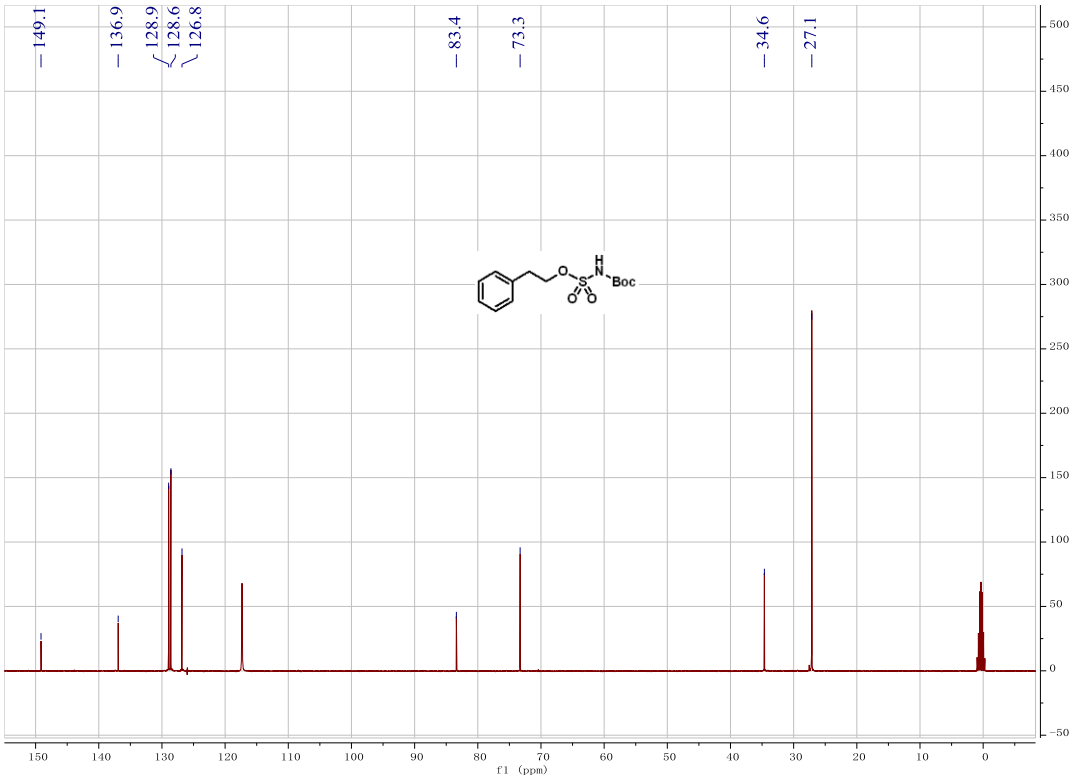
^{1}H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 3a



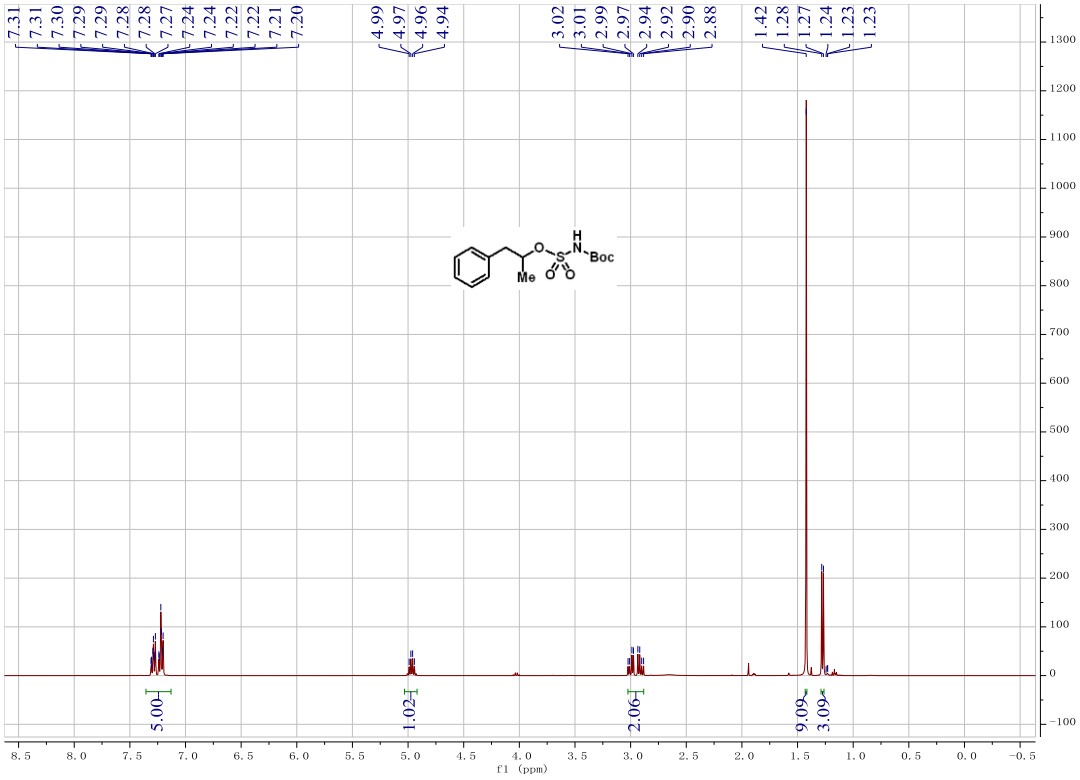


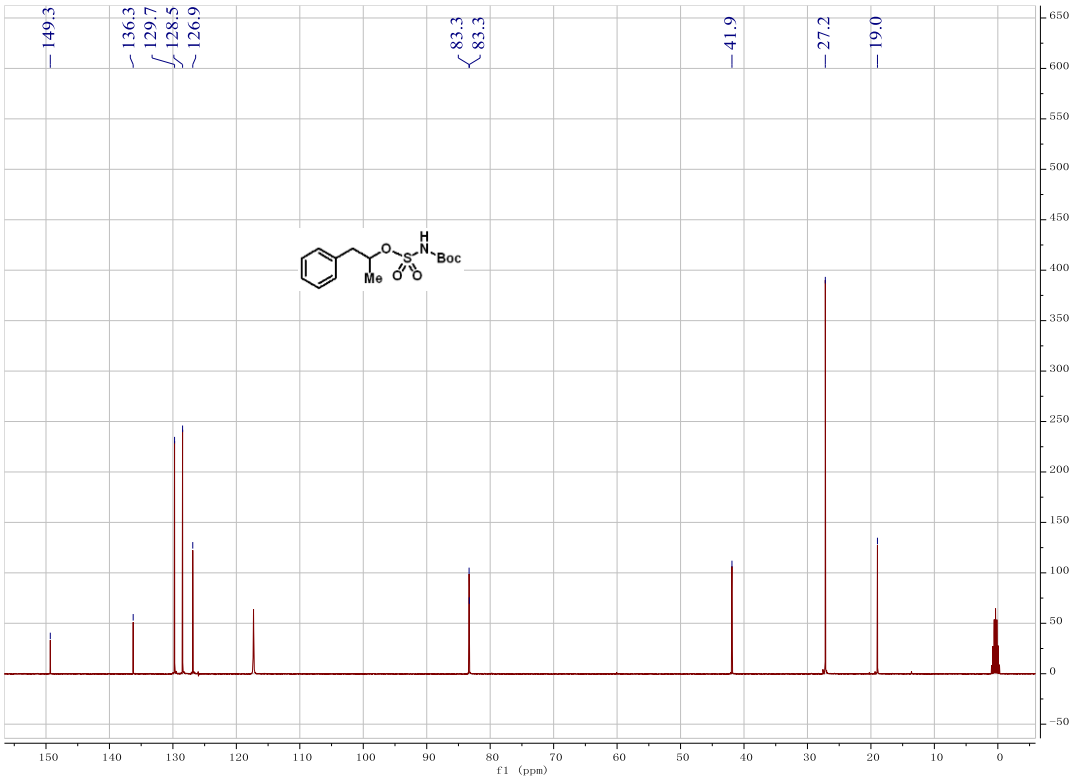
^{1}H (400 MHz, Acetonitrile-d_3) and ^{13}C (101 MHz, Acetonitrile-d_3) spectra of compound 3b



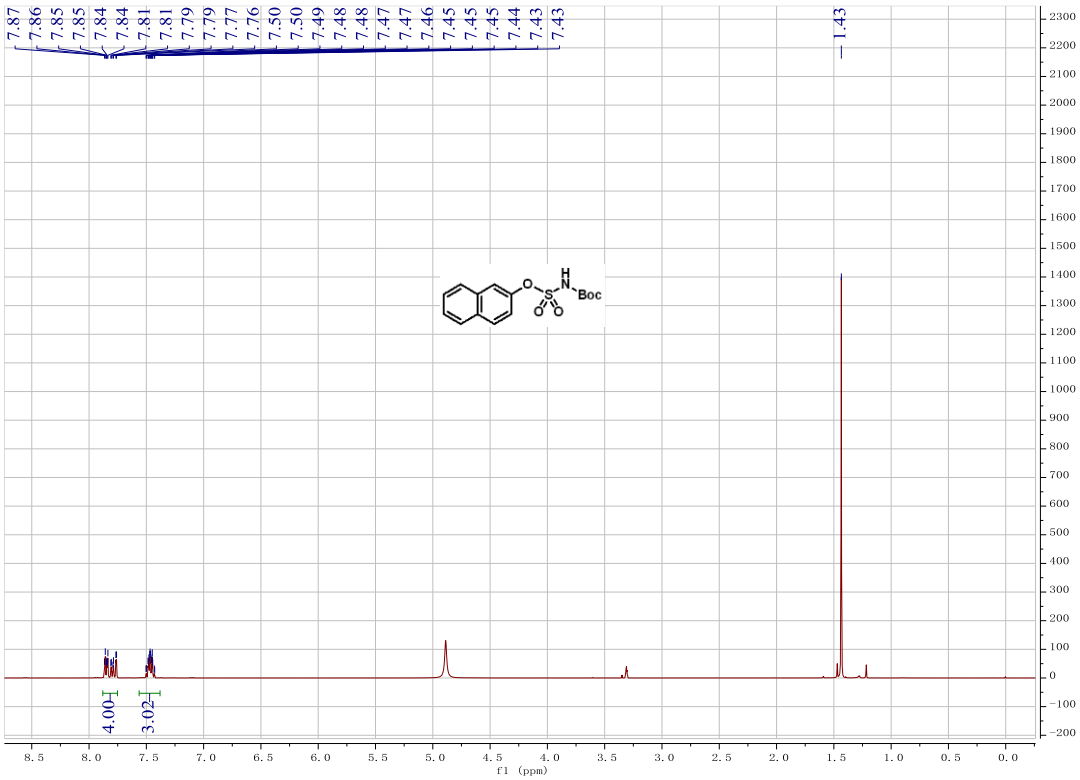


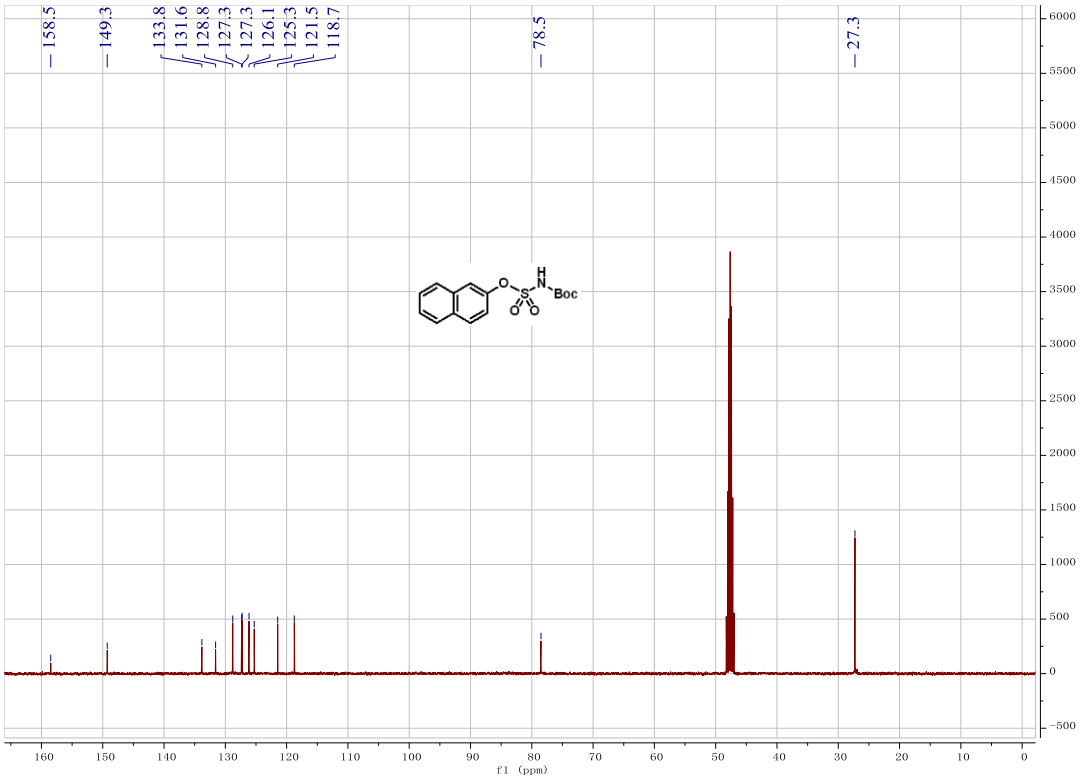
^{1}H (400 MHz, Acetonitrile-d_3) and ^{13}C (400 MHz, Acetonitrile-d_3) spectra of compound 3c



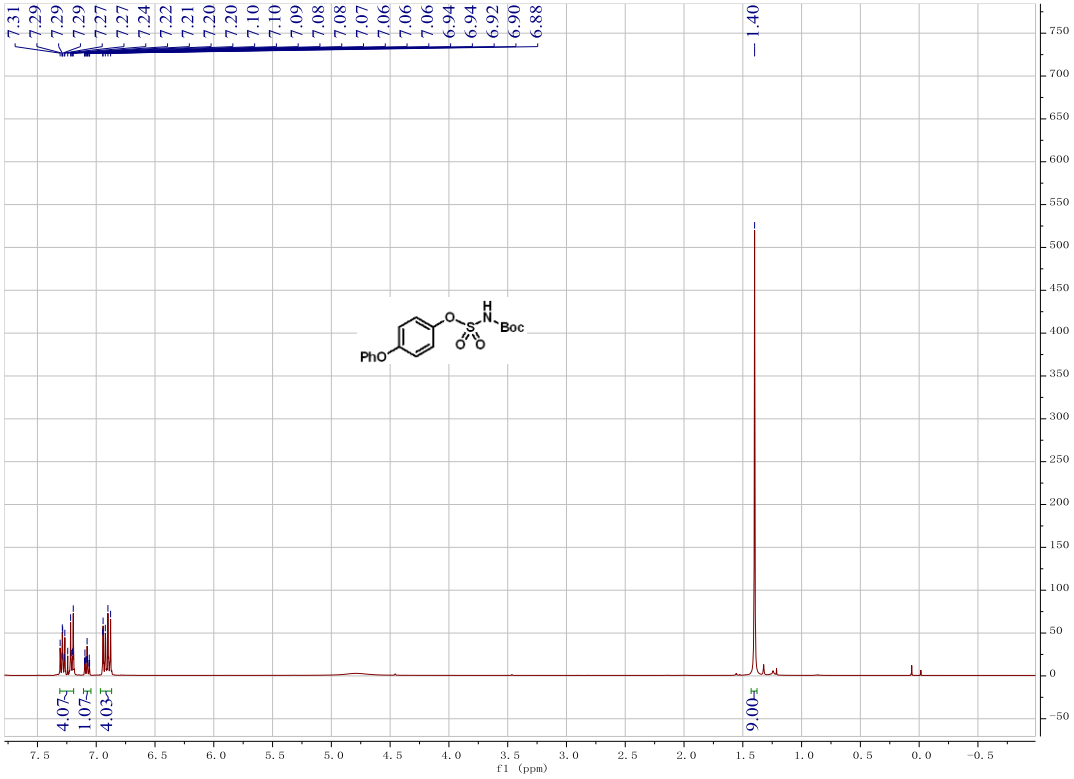


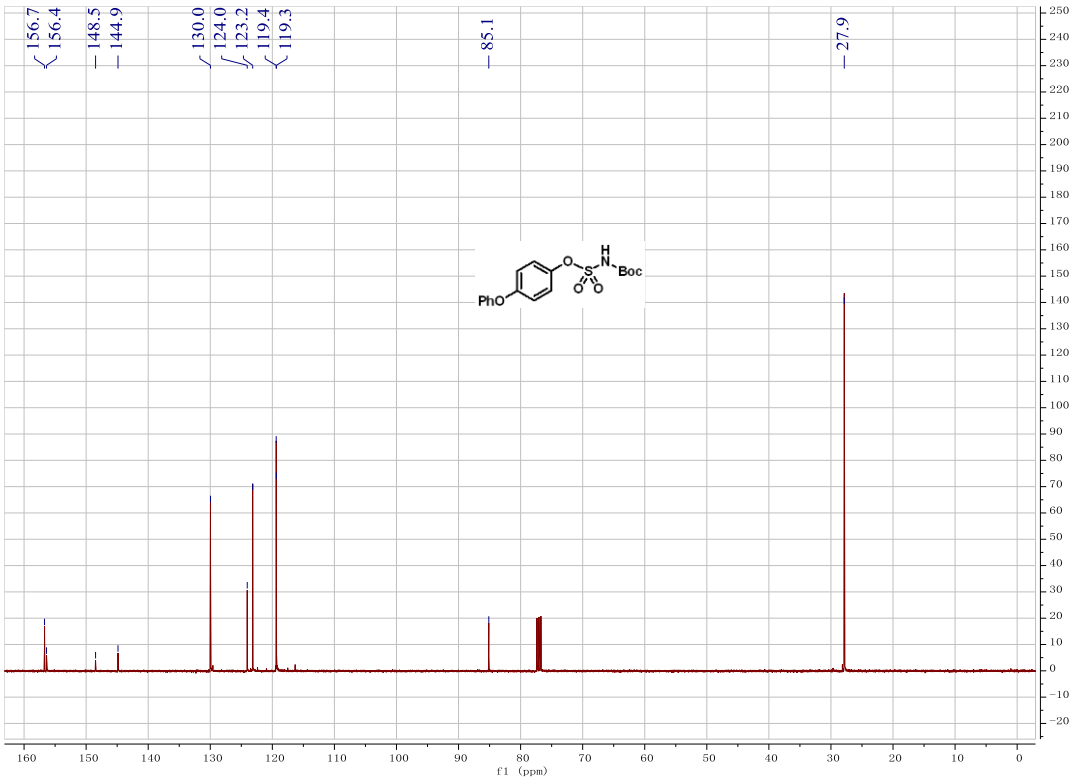
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 3d



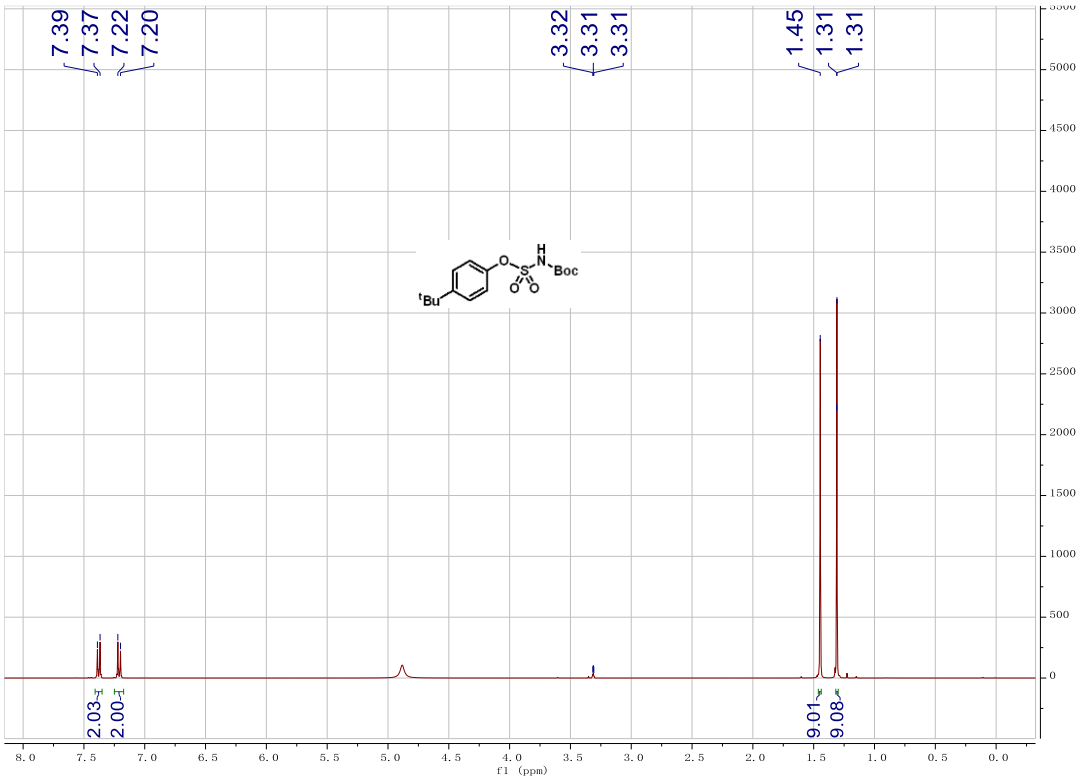


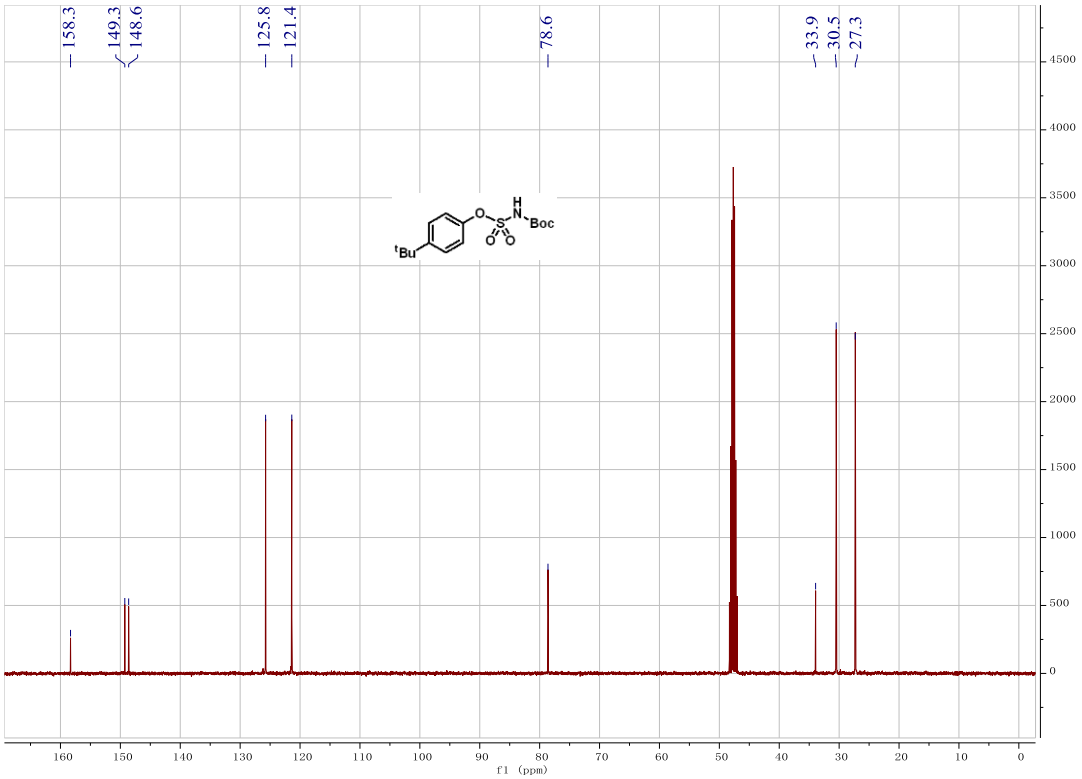
^{1}H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 3e



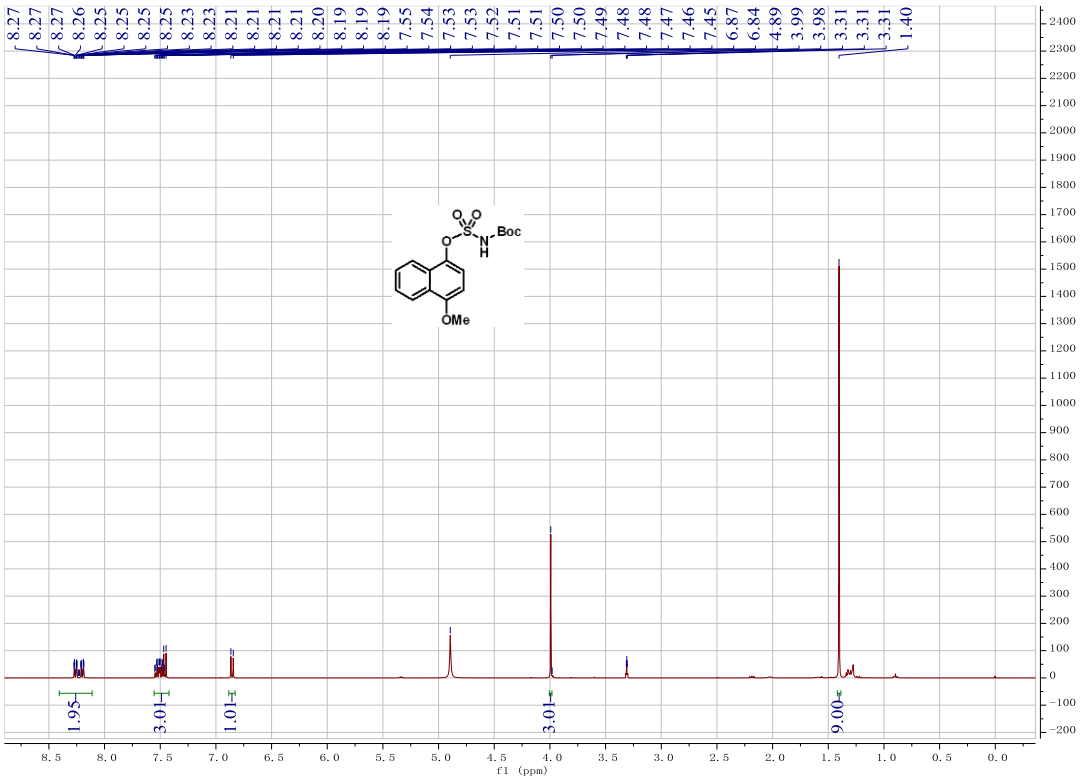


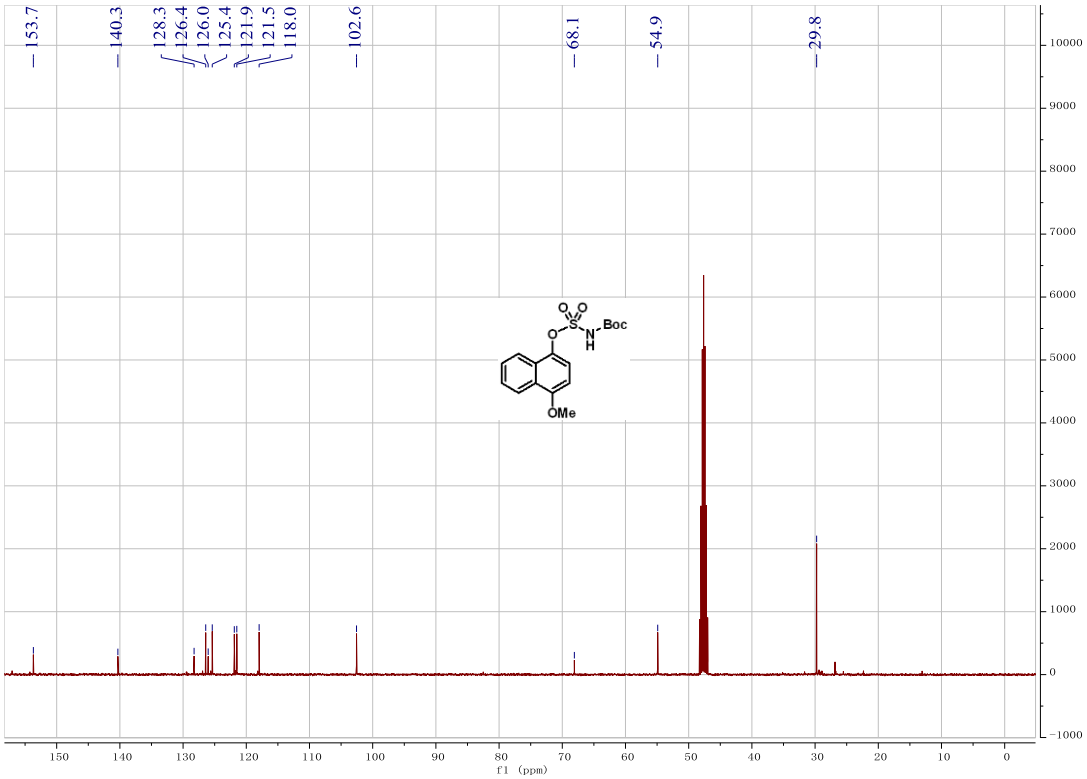
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 3f



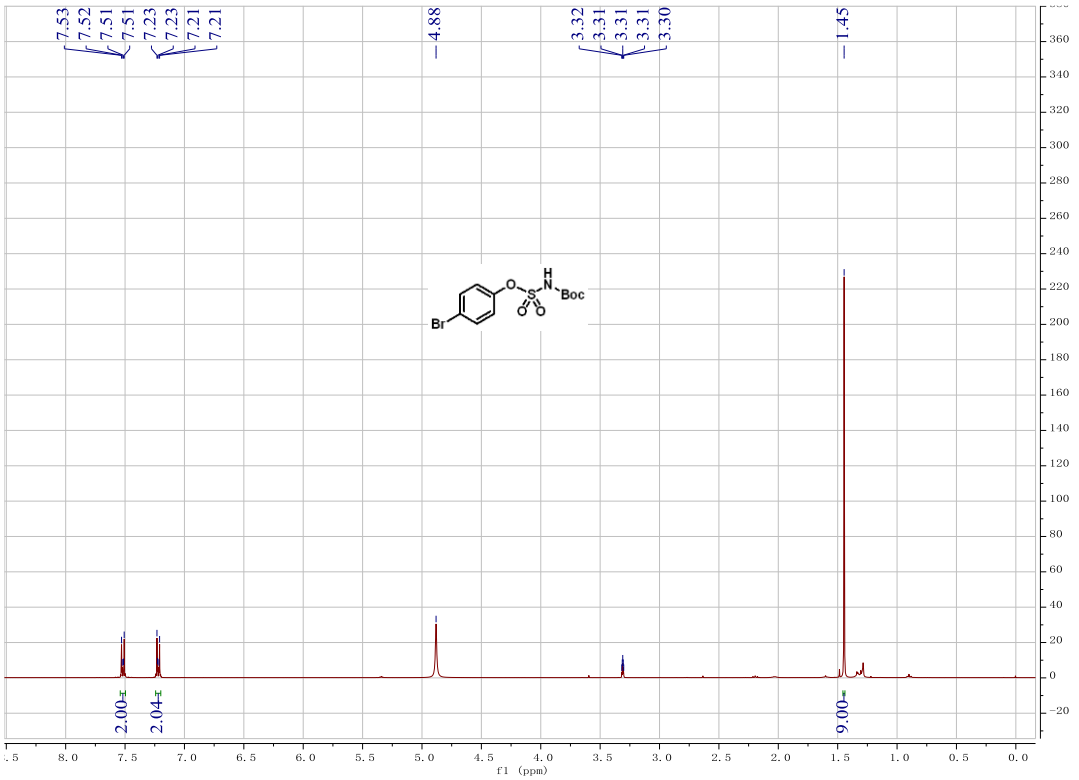


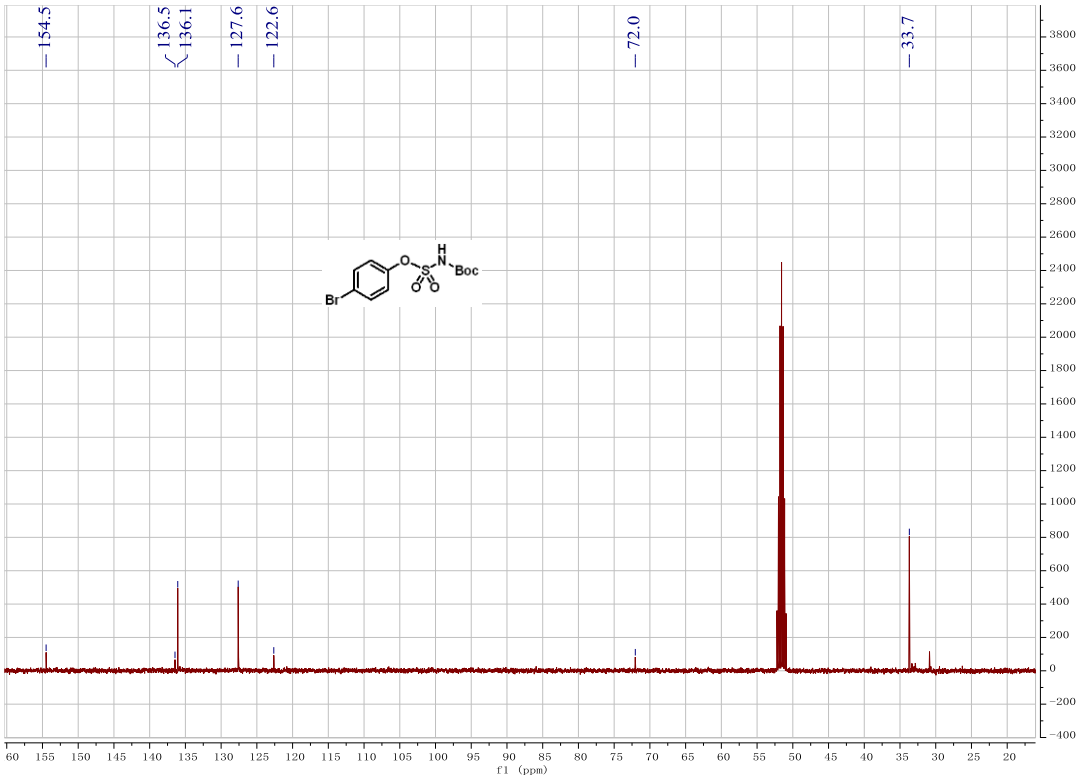
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 3g



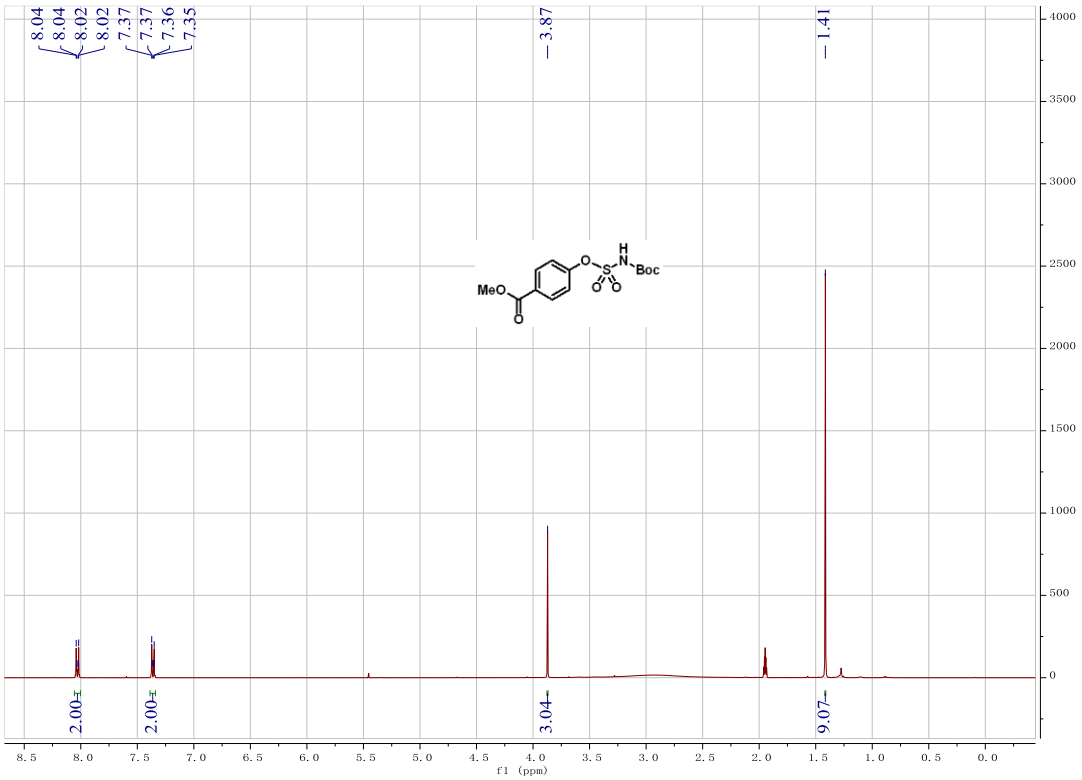


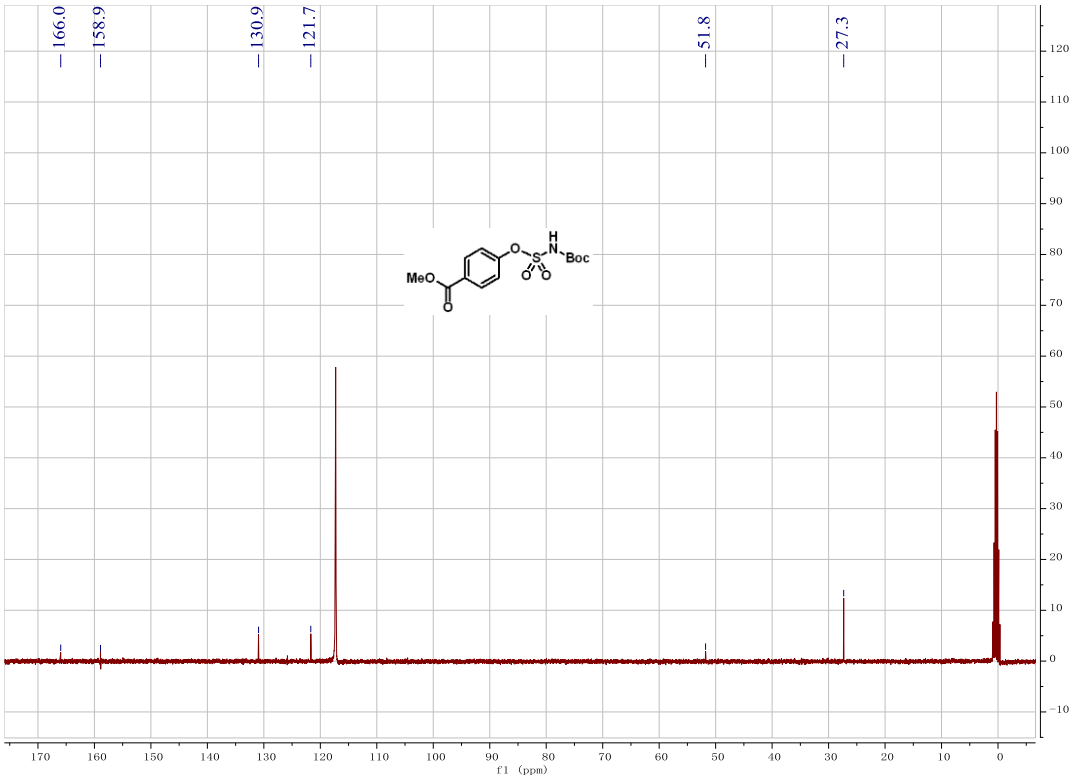
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (400 MHz, Methanol-d_4) spectra of compound 3h



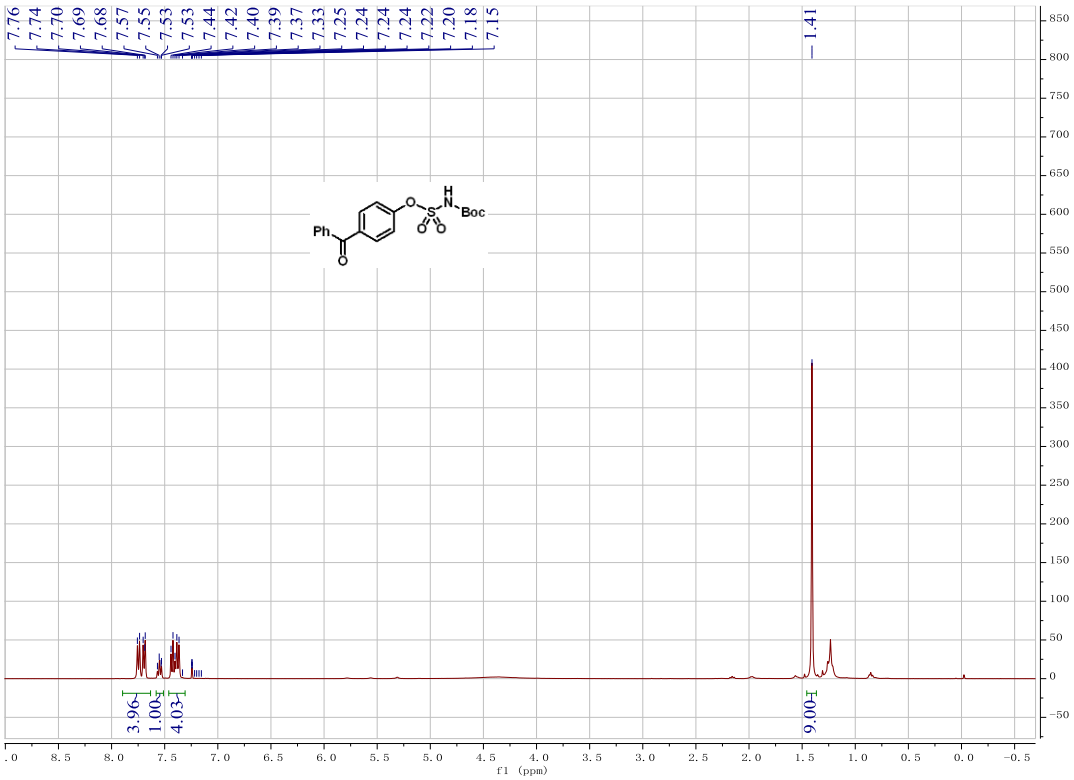


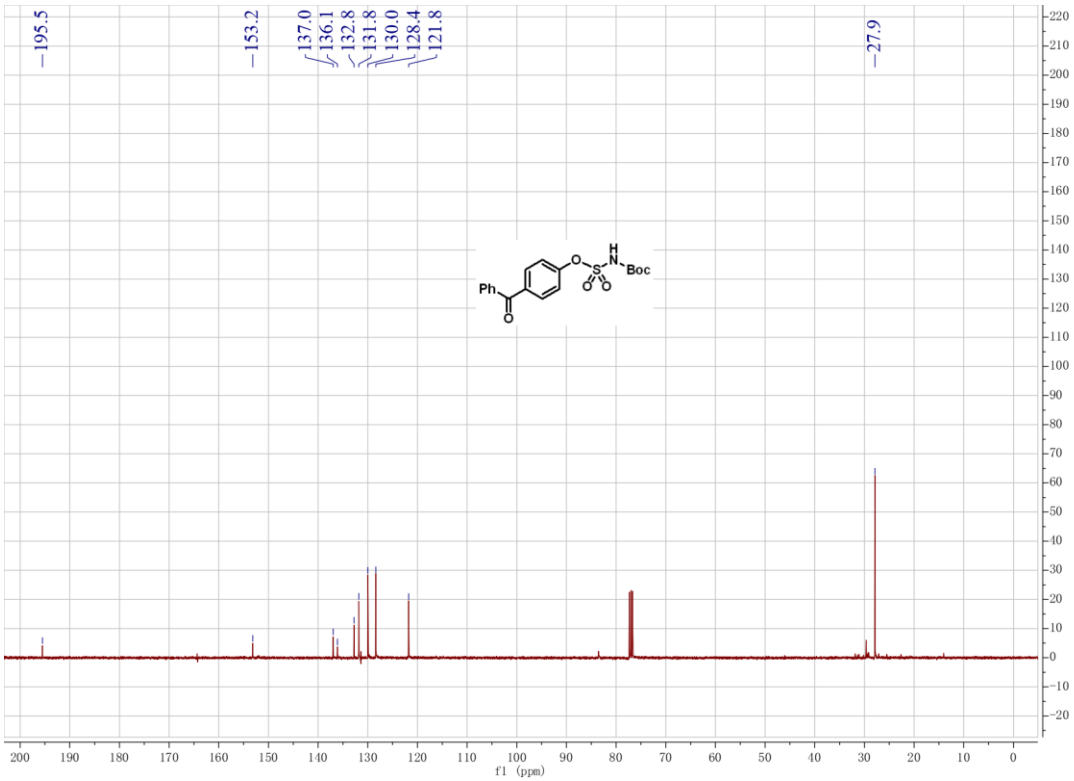
^{1}H (400 MHz, Acetonitrile-d_3) and ^{13}C (101 MHz, Acetonitrile-d_3) spectra of compound 3i



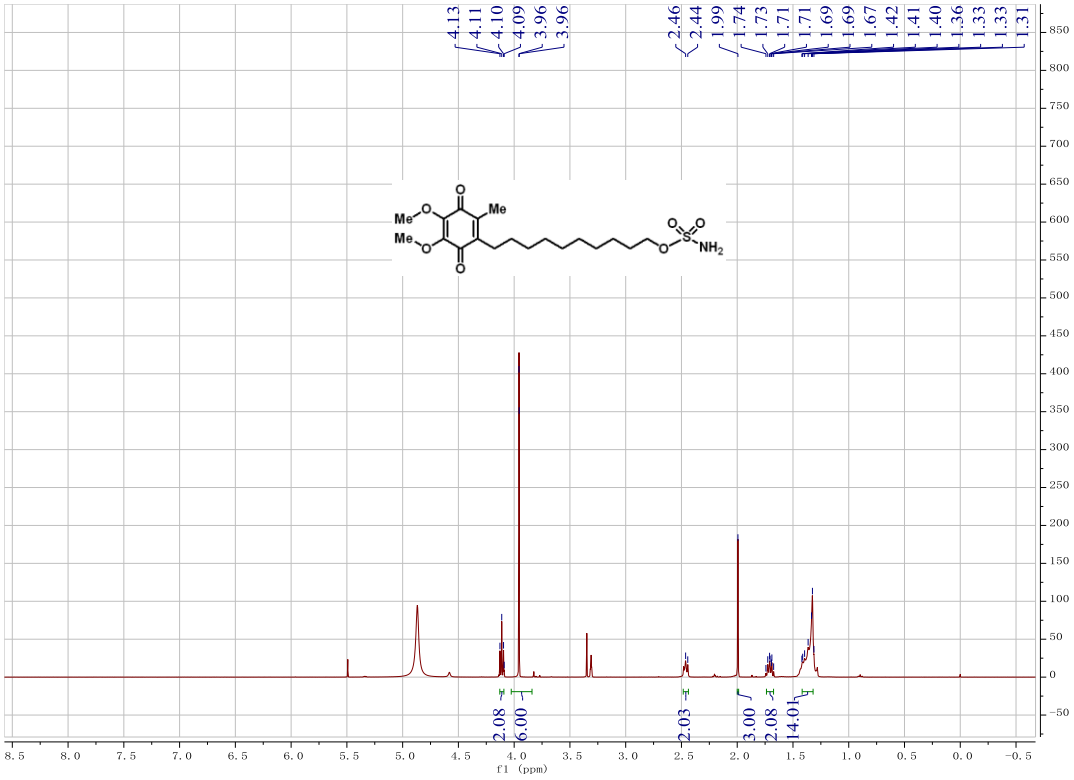


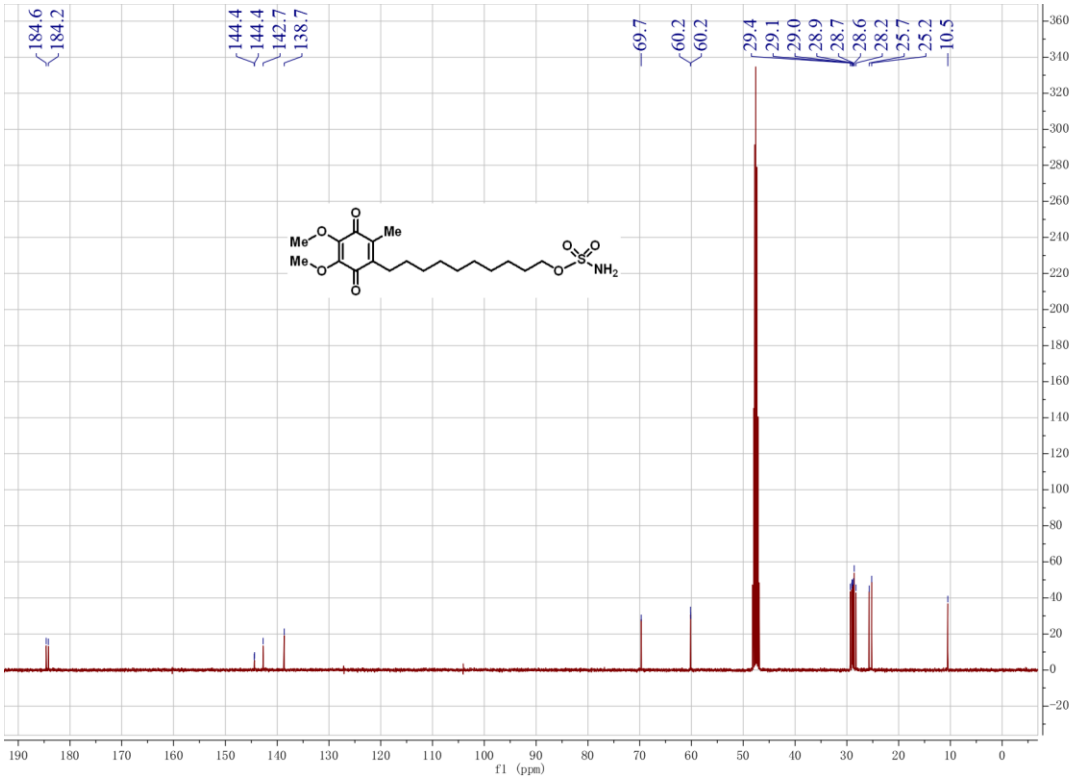
^{1}H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 3j



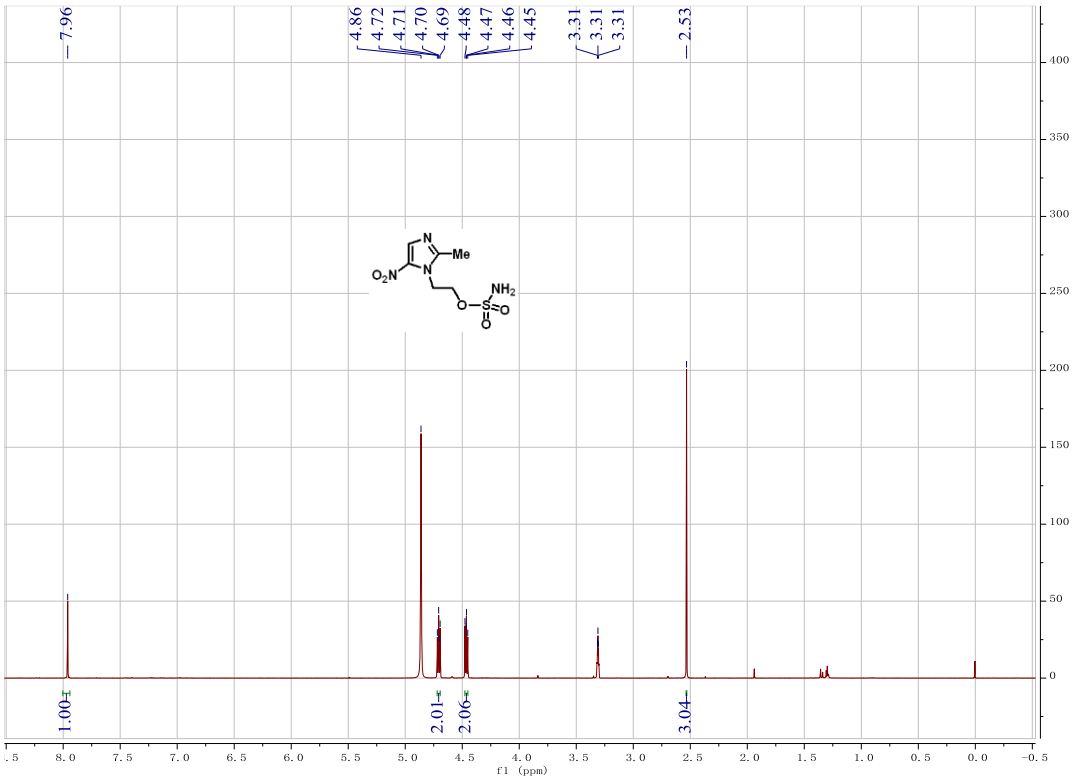


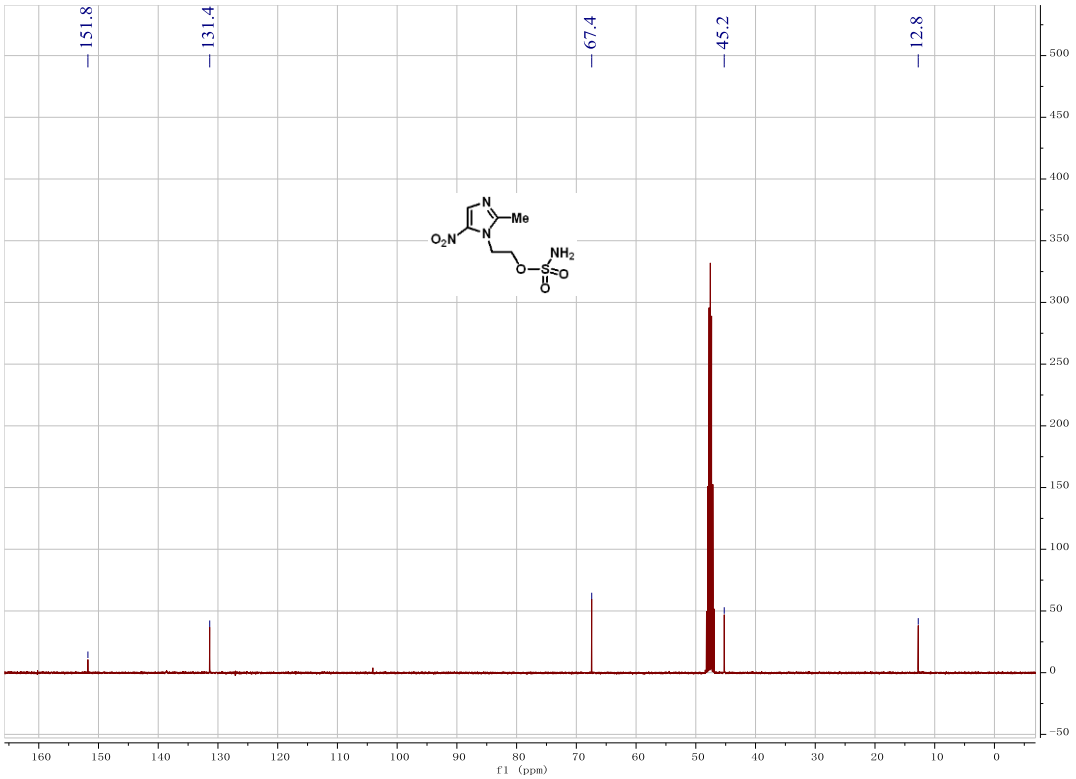
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 5a



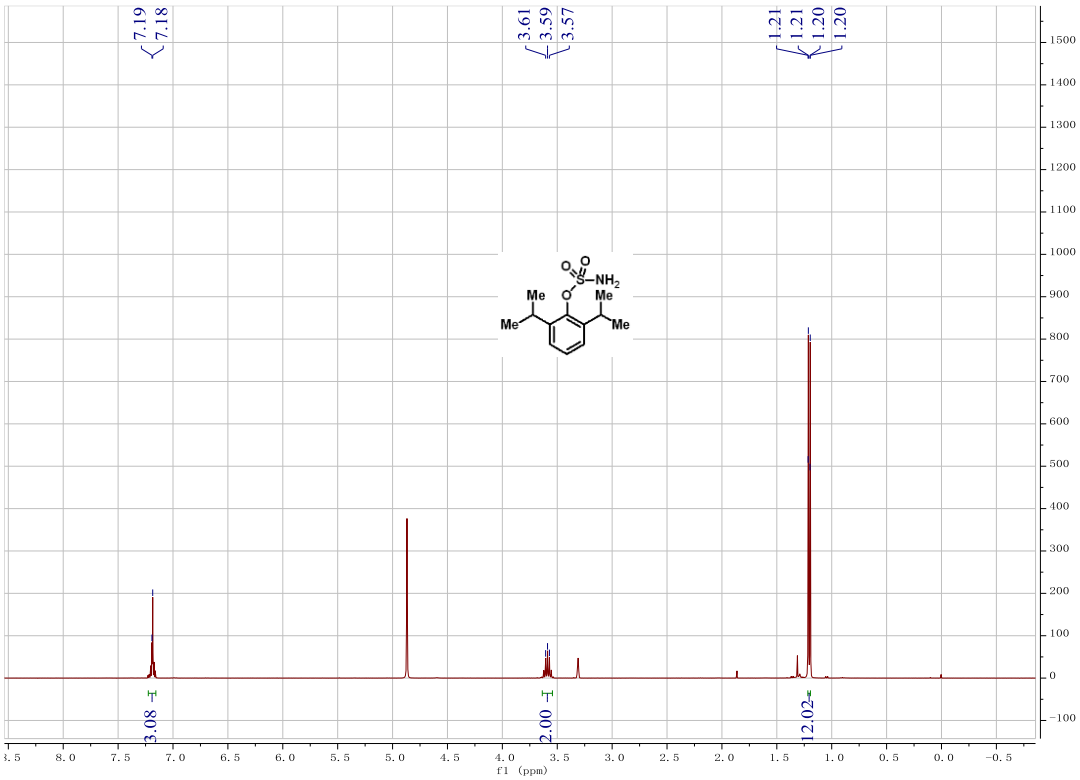


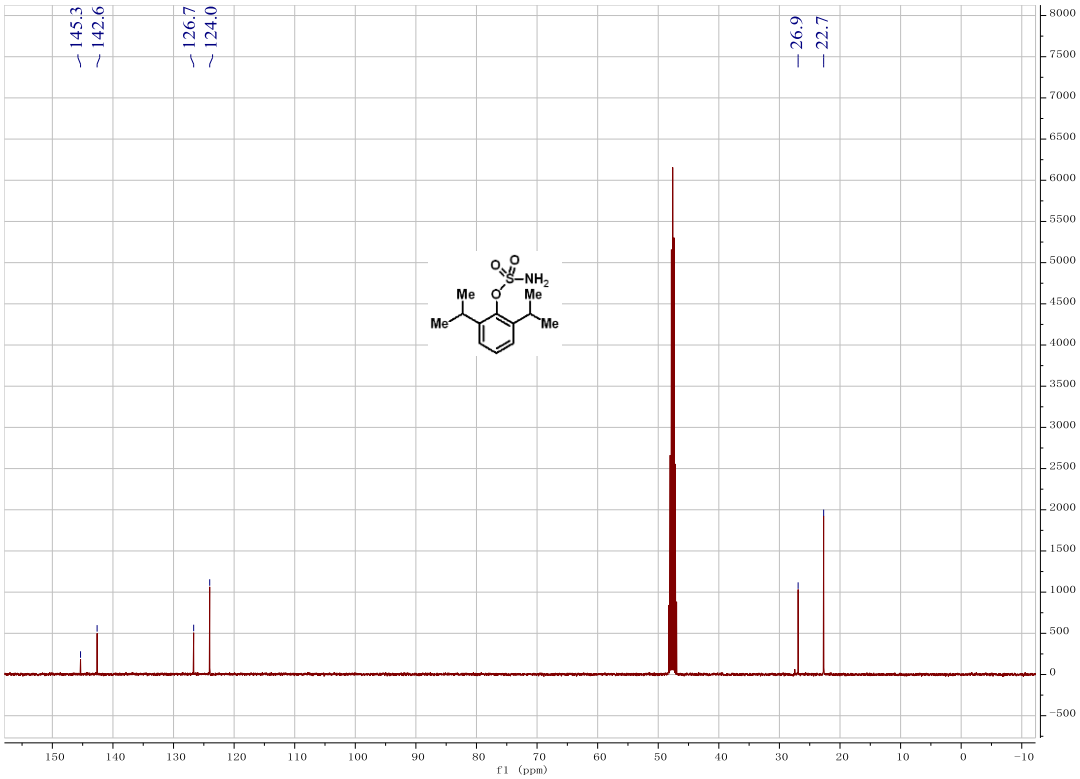
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 5b



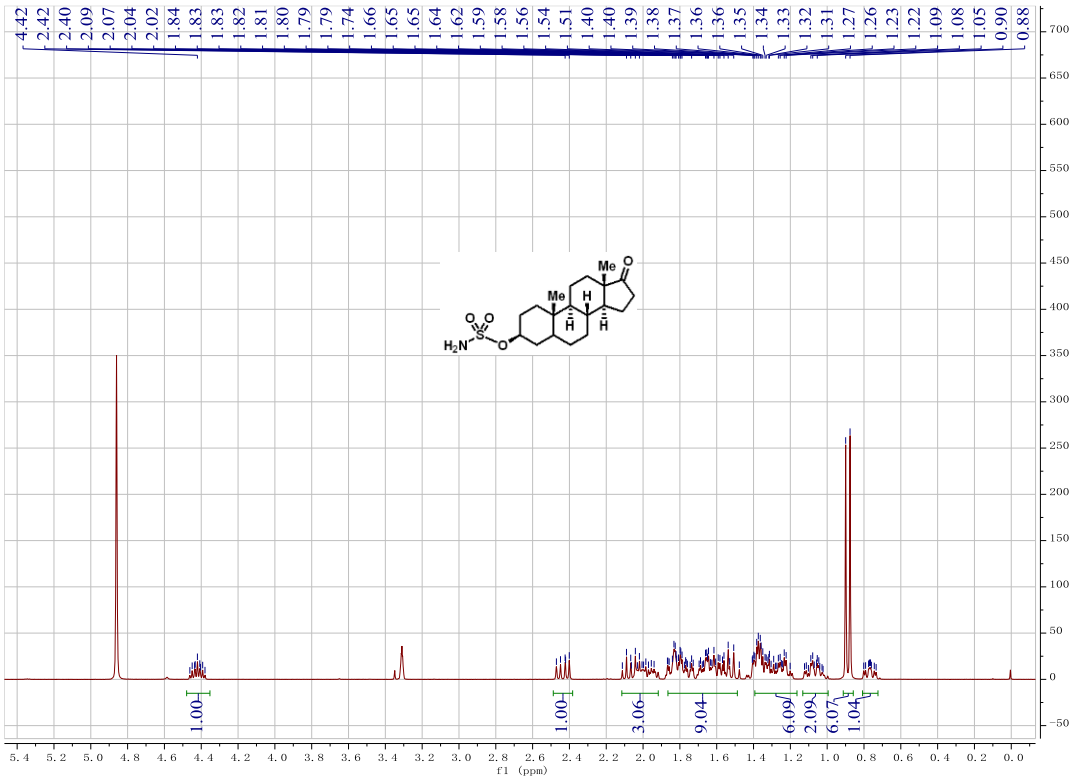


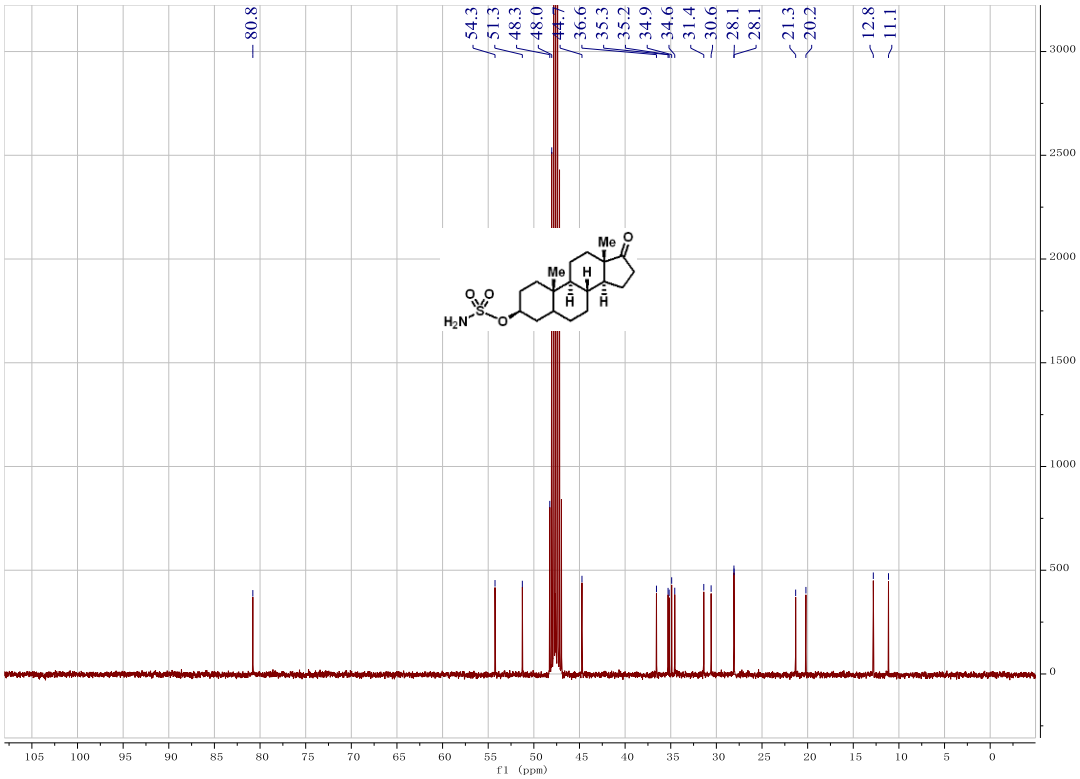
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 5c



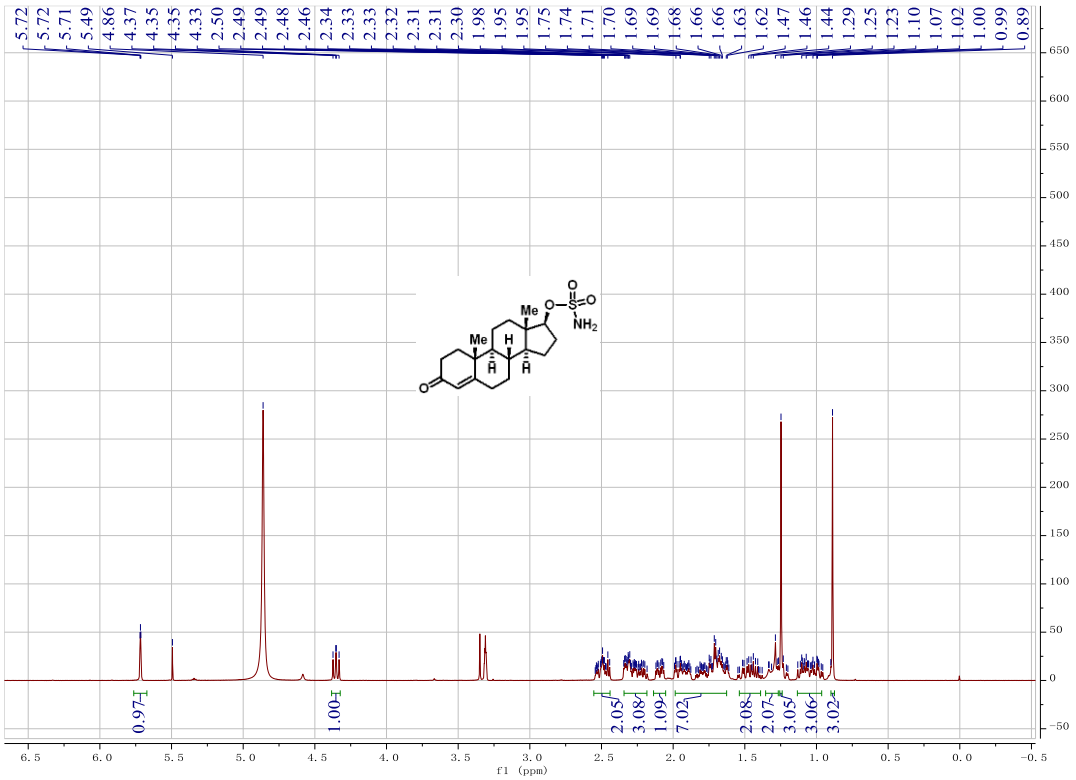


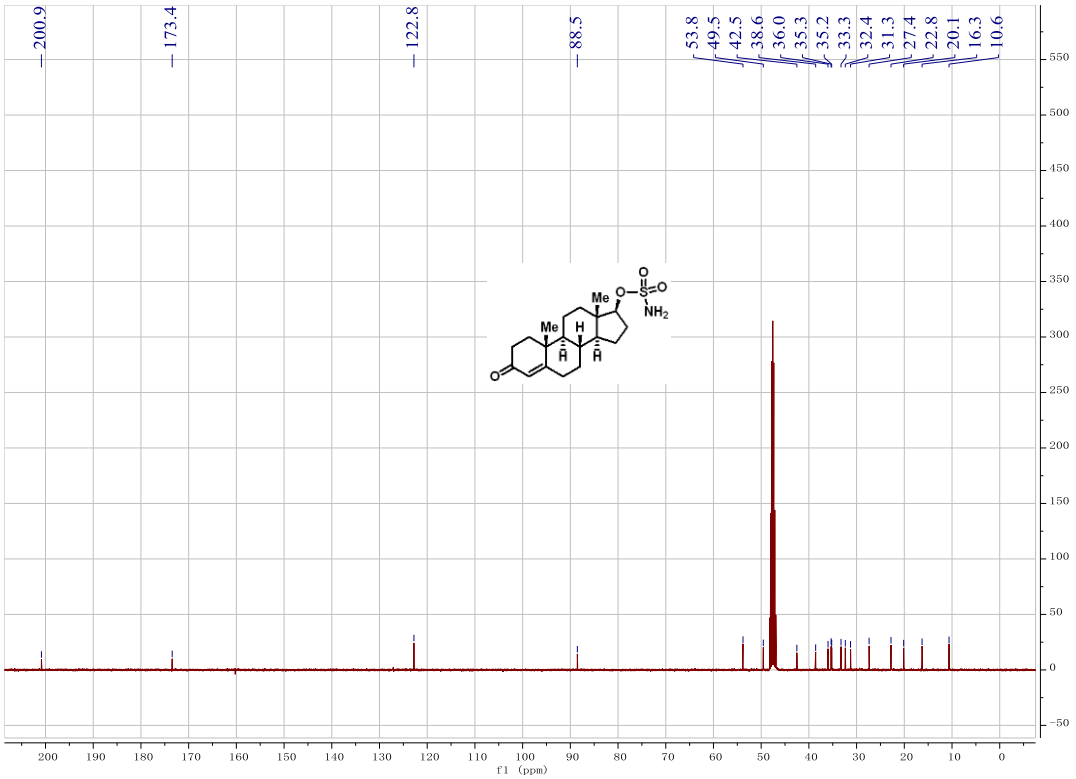
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 5d



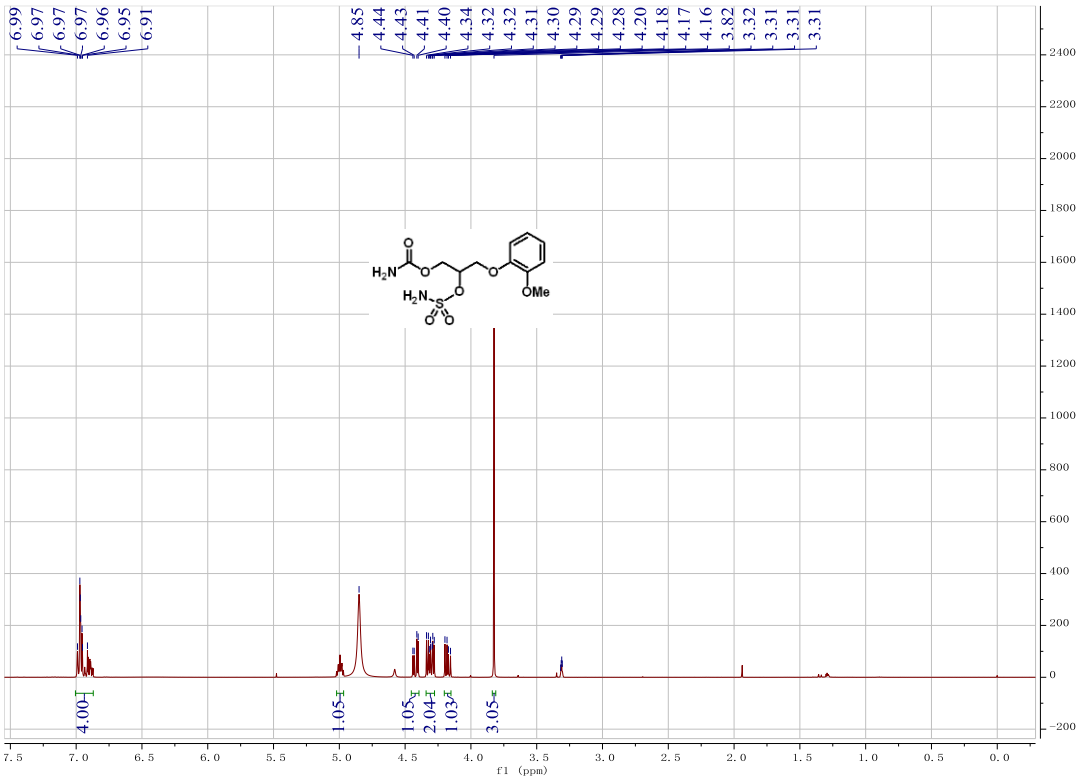


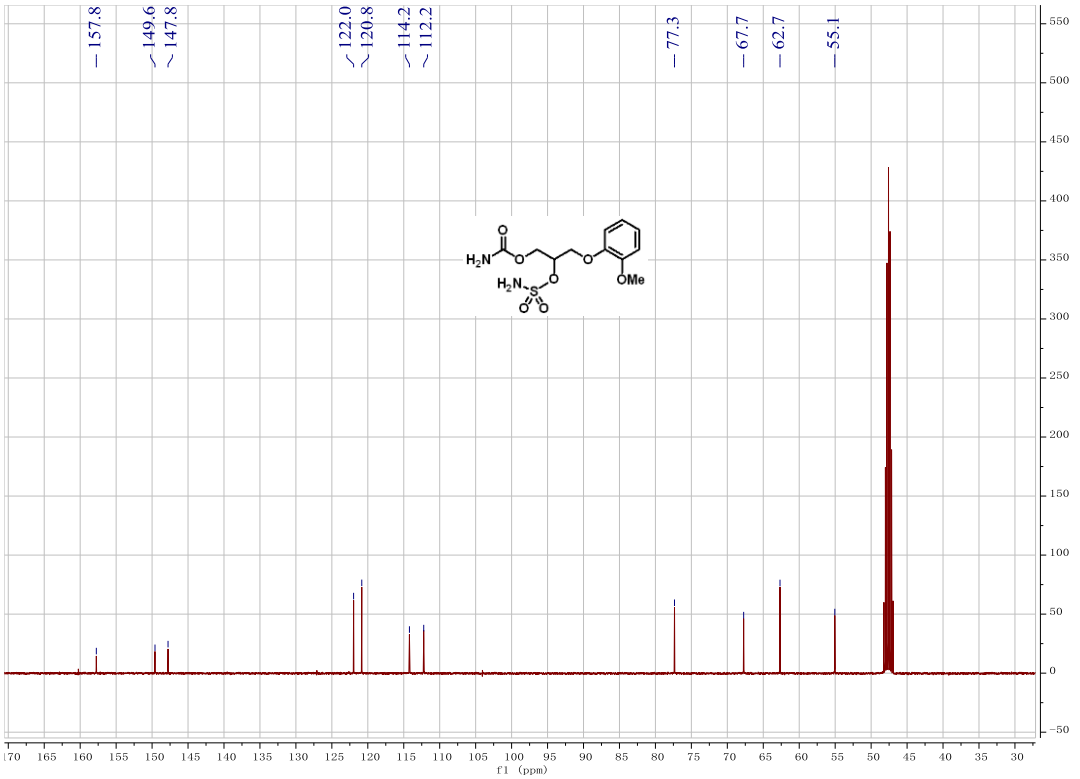
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 5e



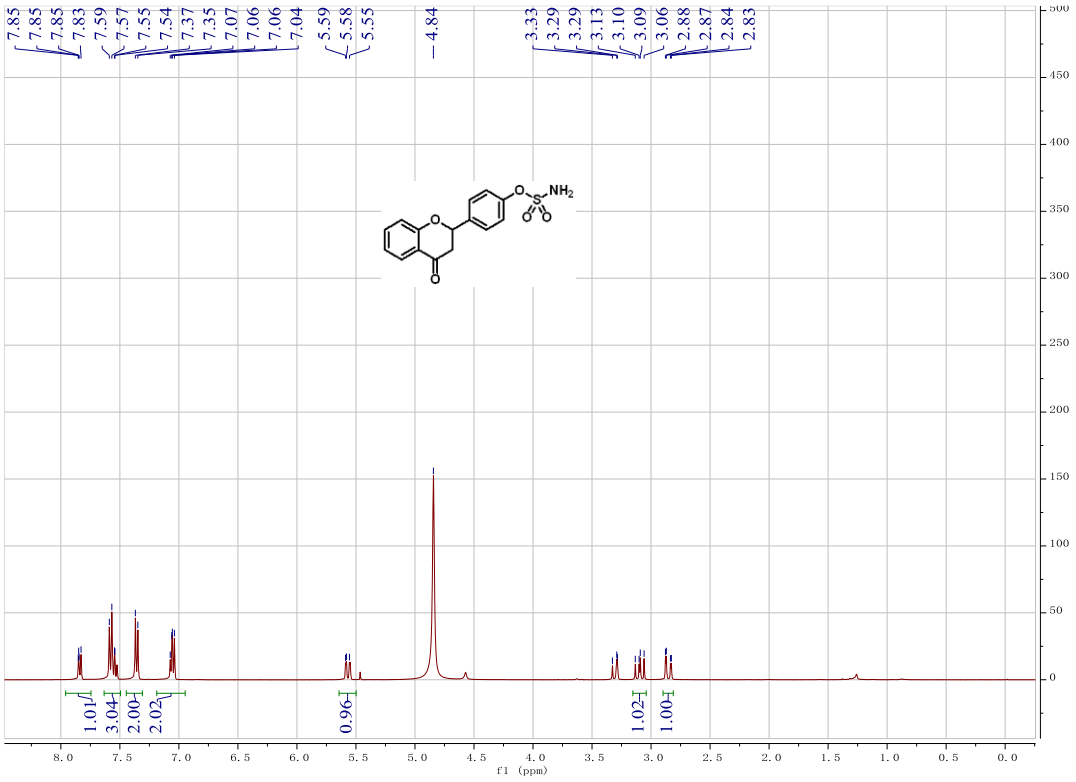


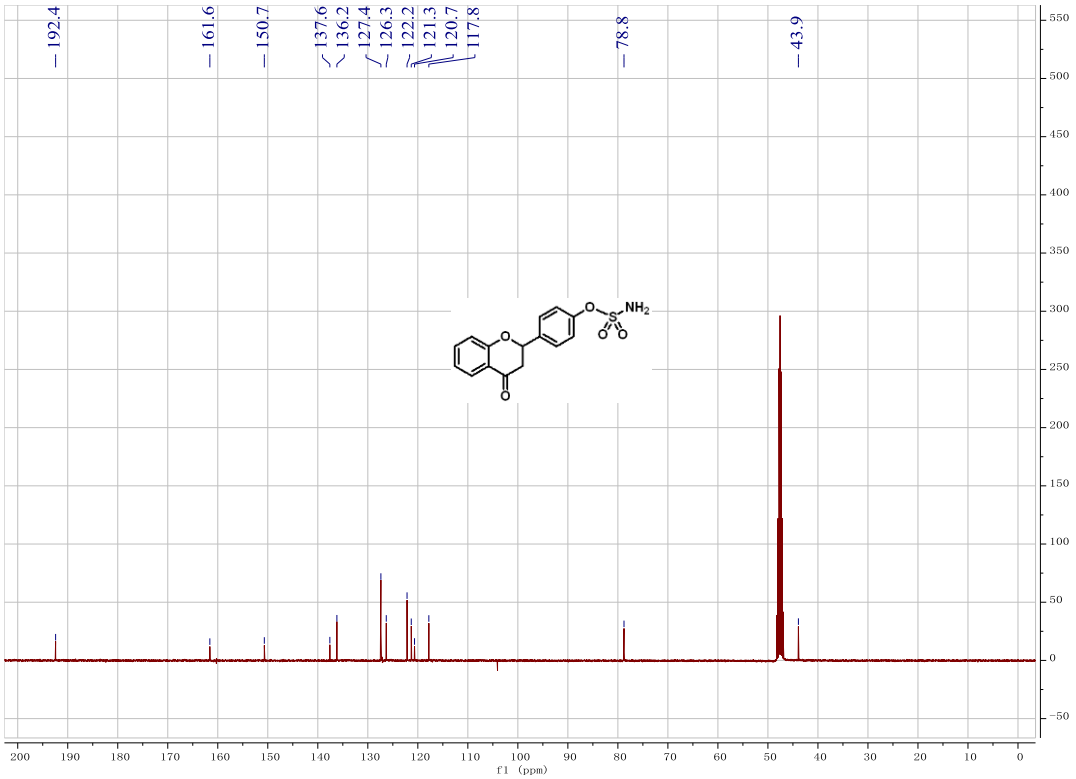
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 5f



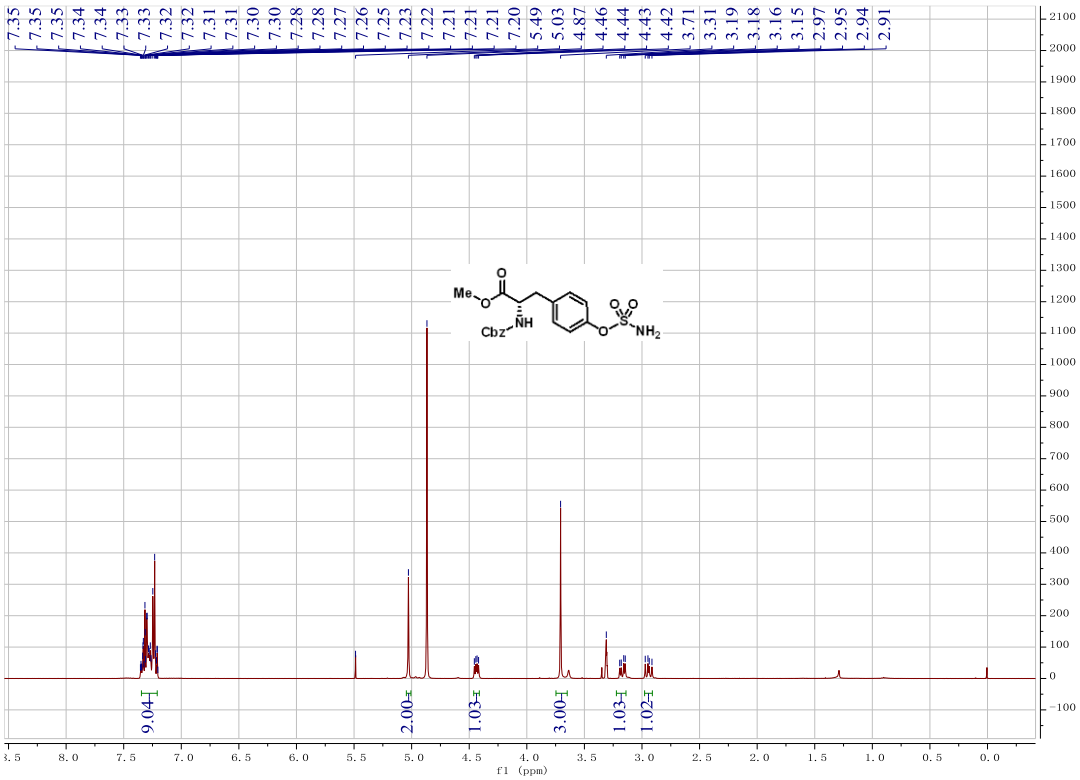


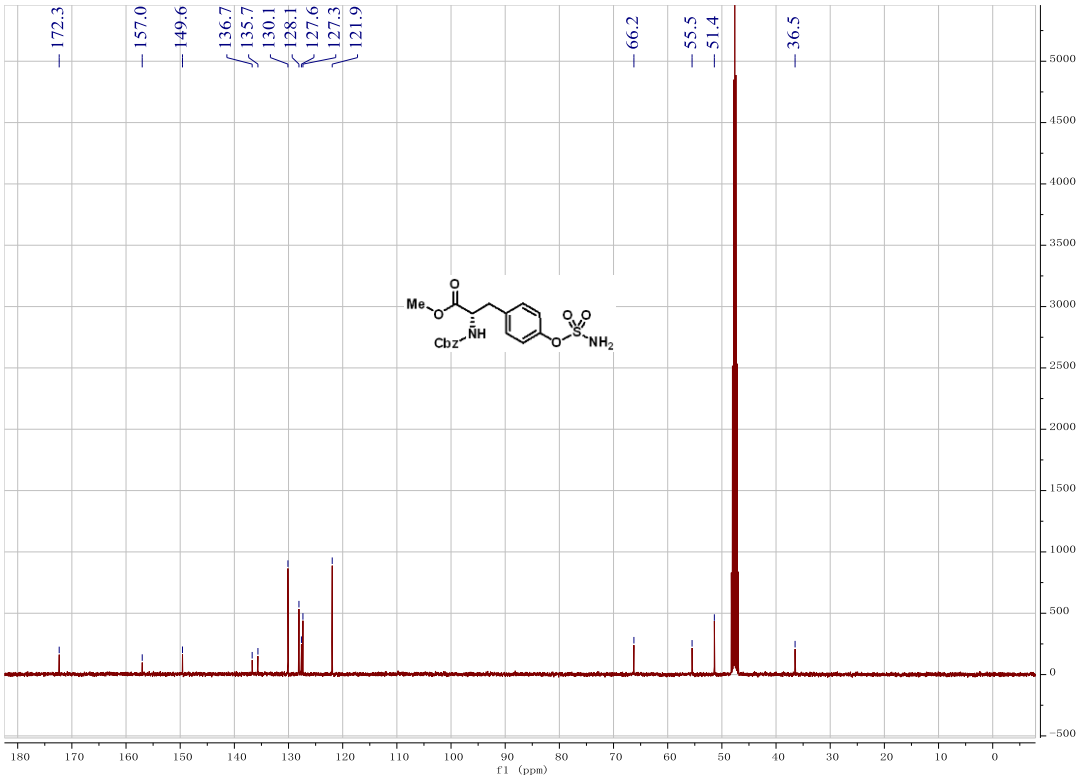
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 5g



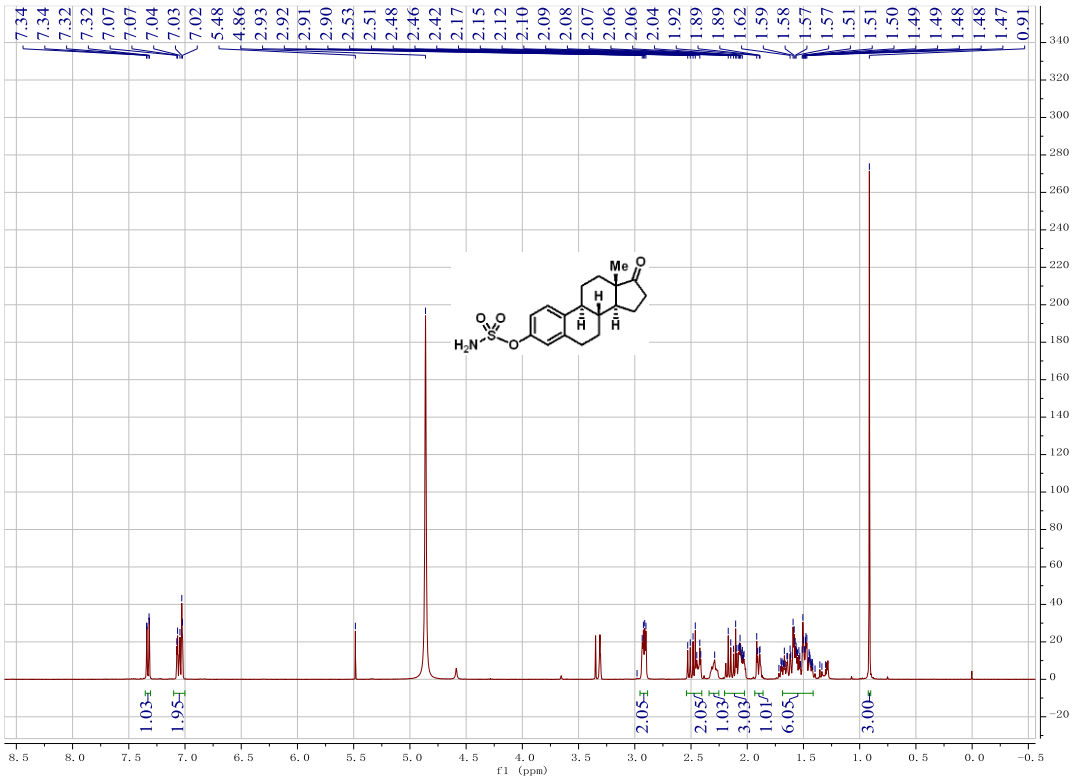


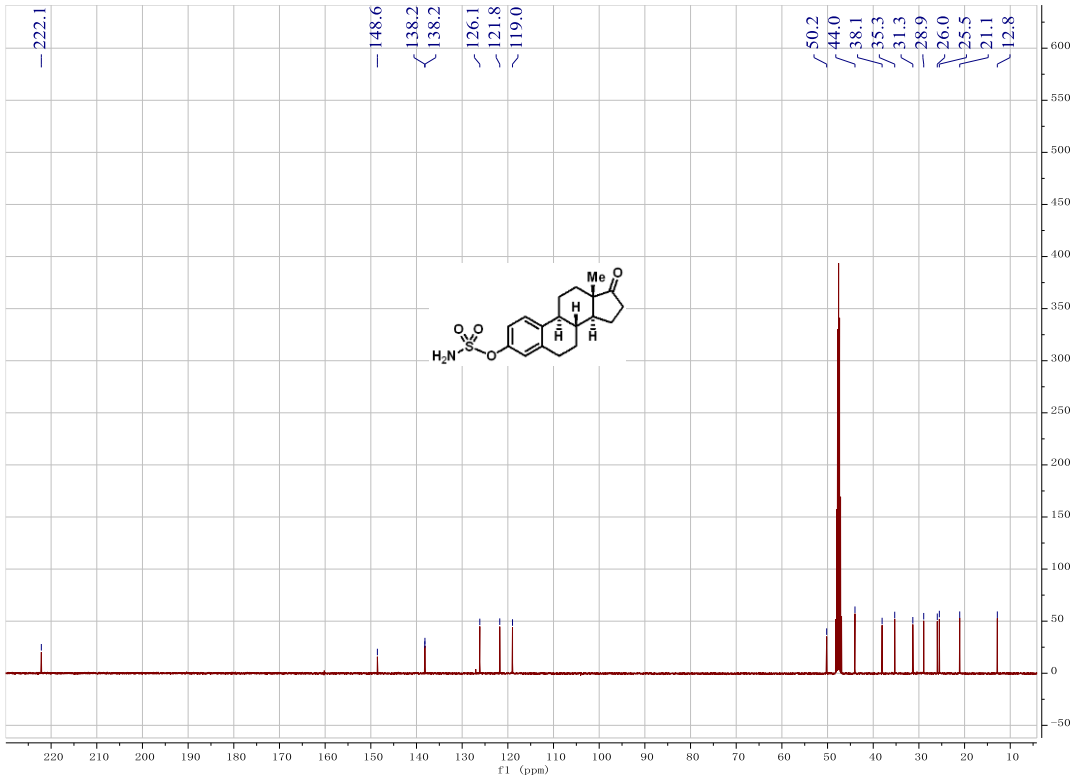
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 5h



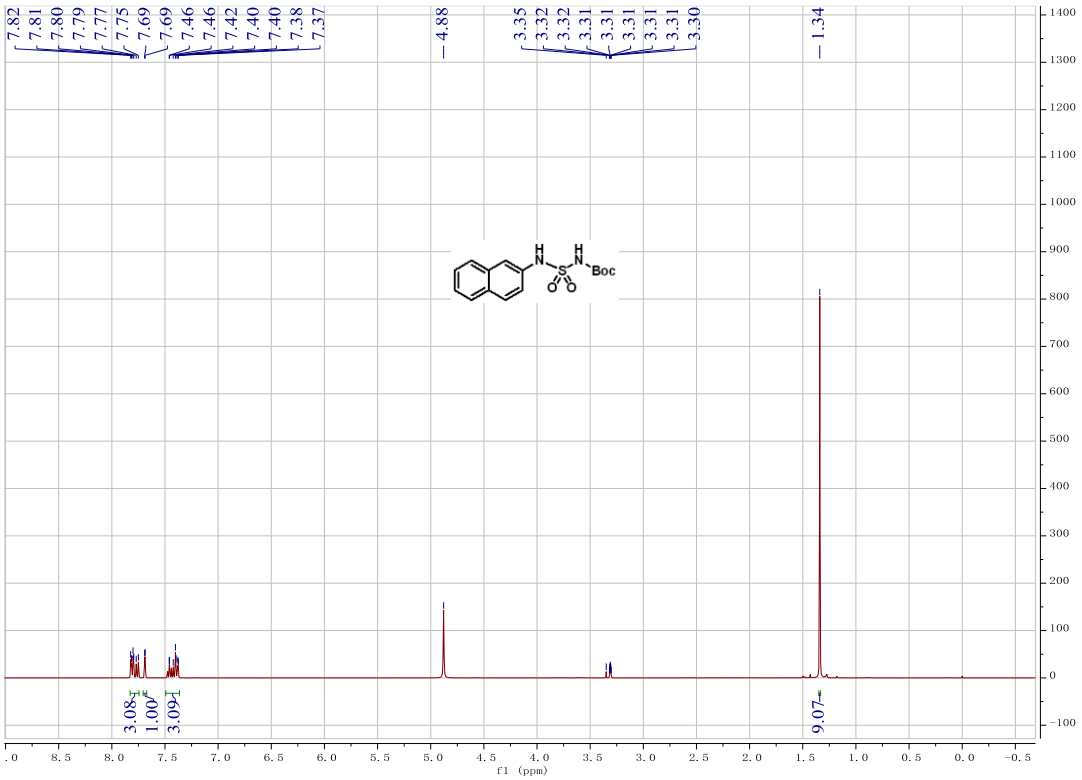


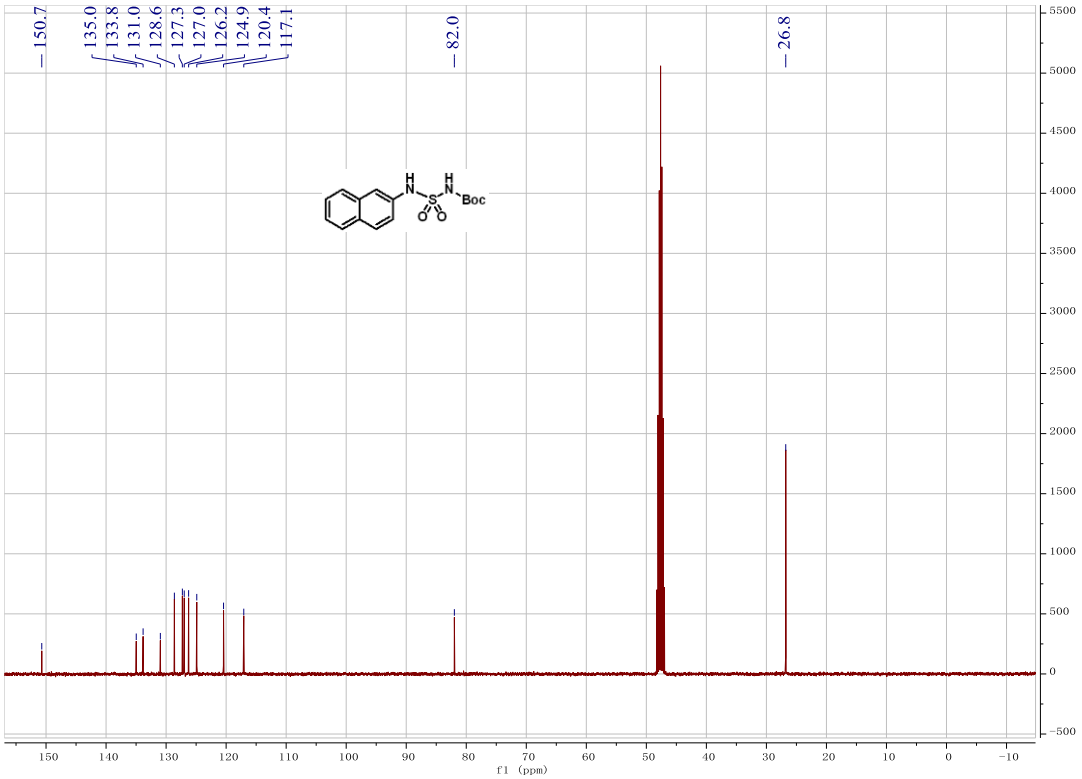
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 5i



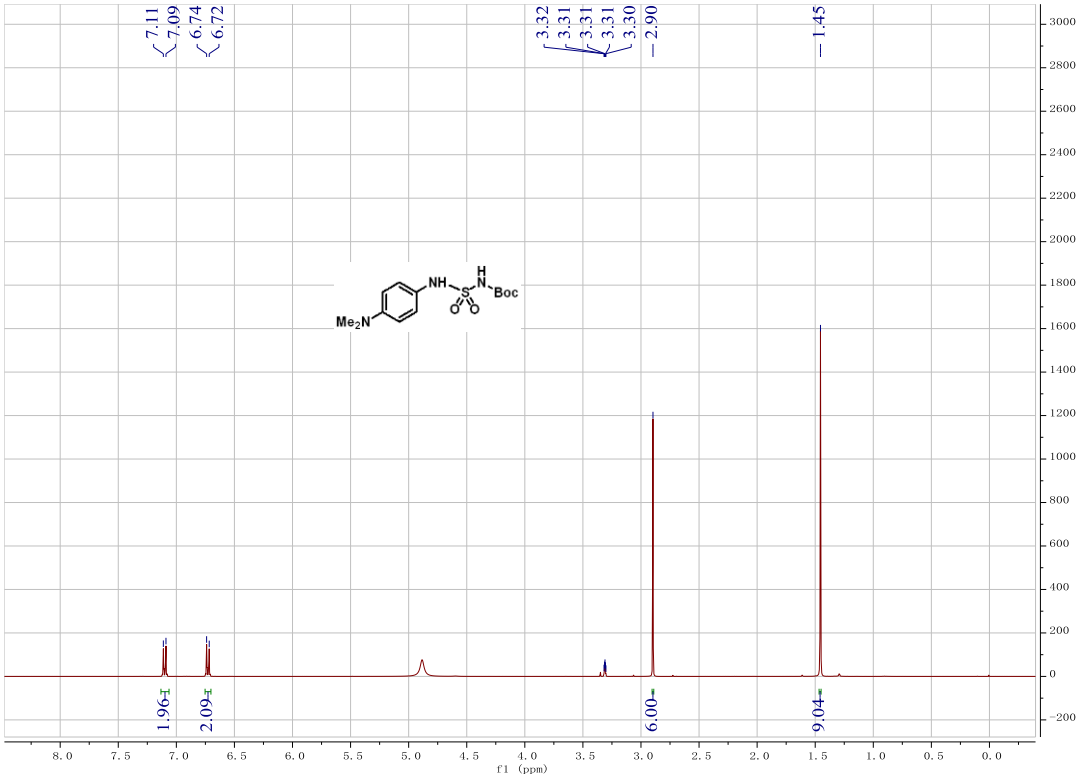


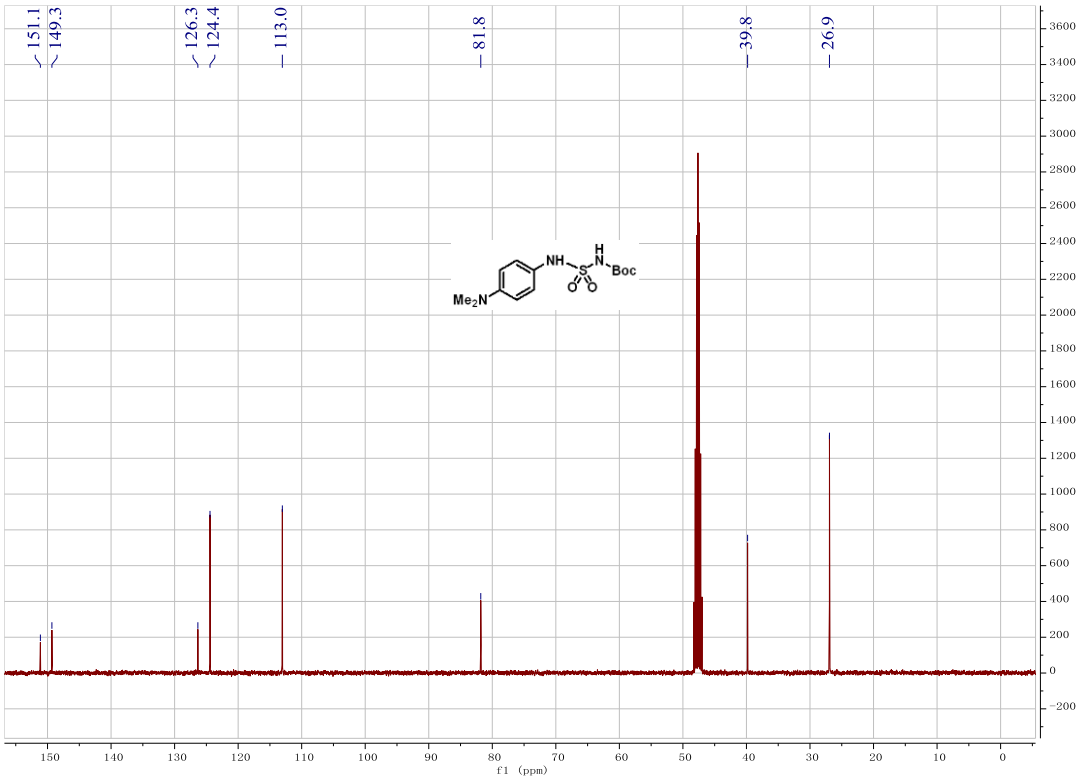
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 7a



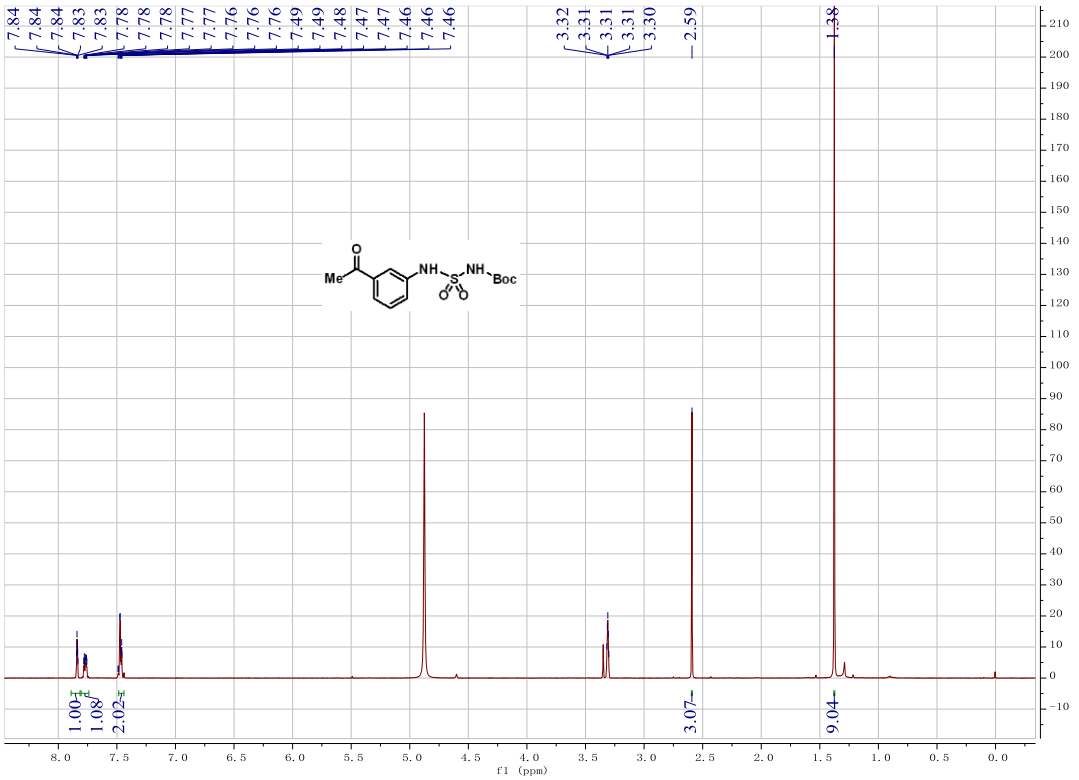


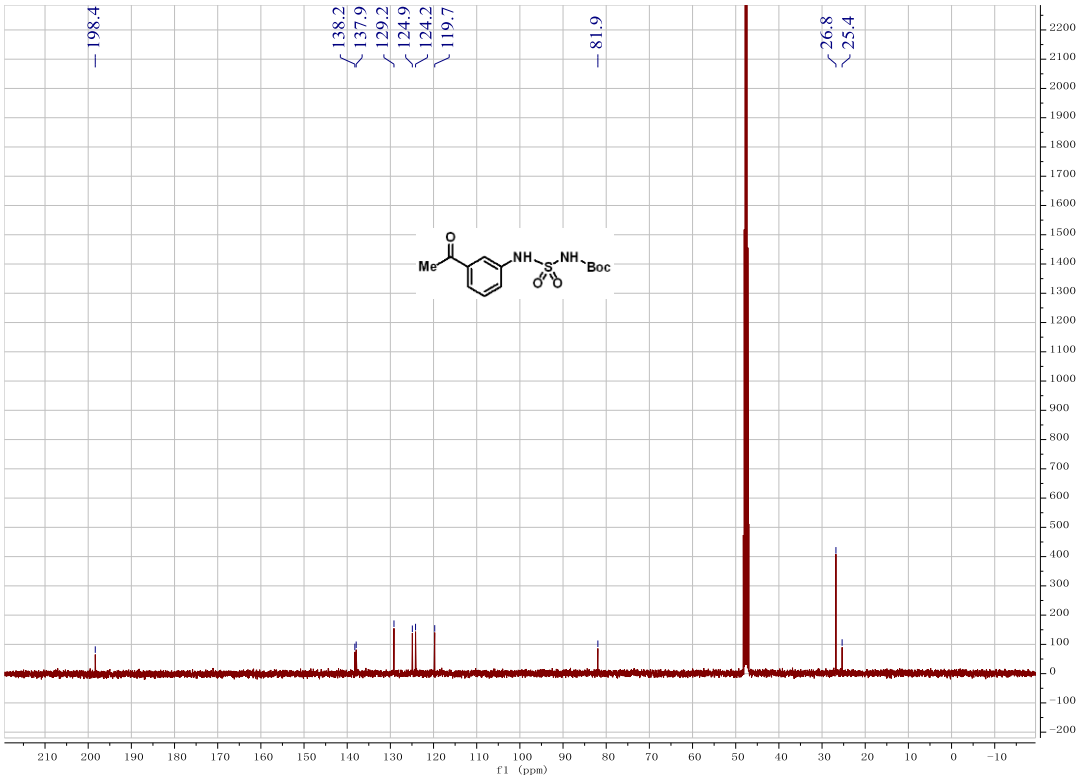
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 7b



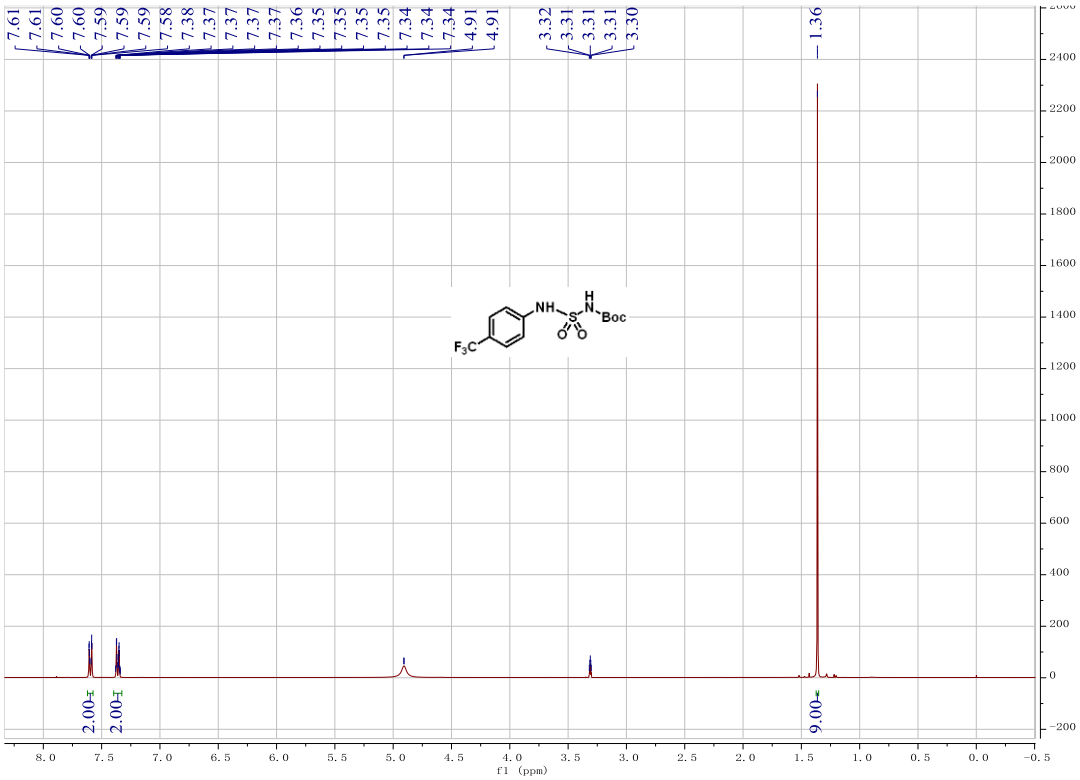


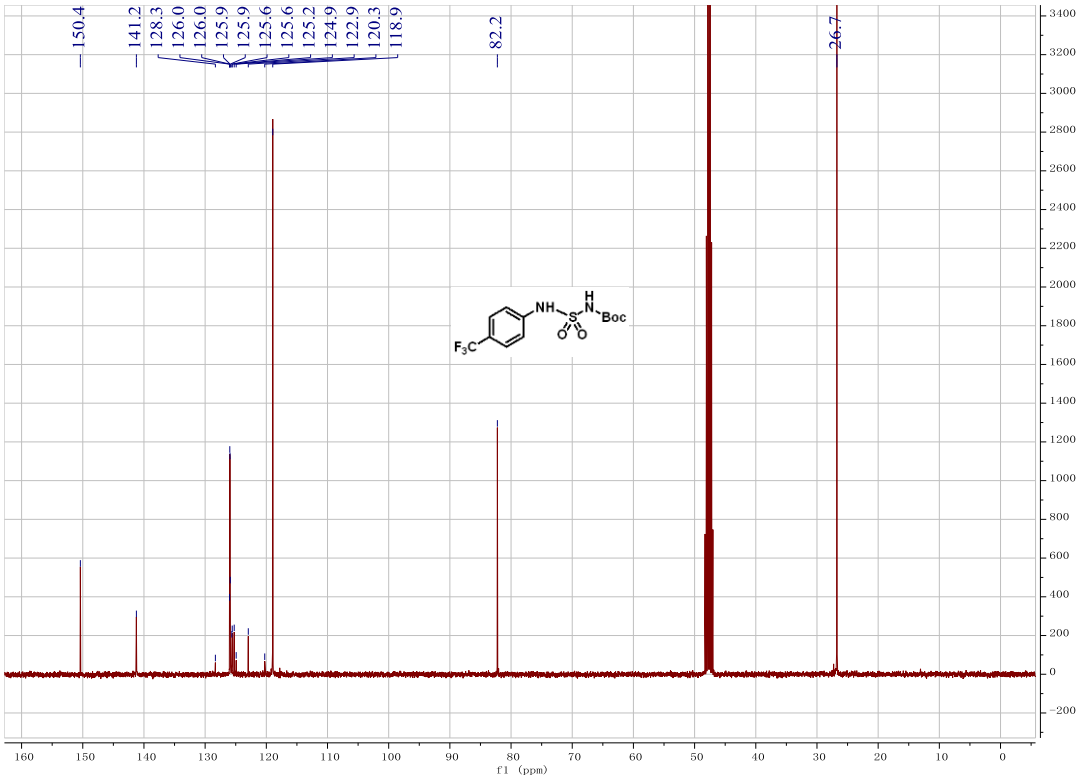
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 7c



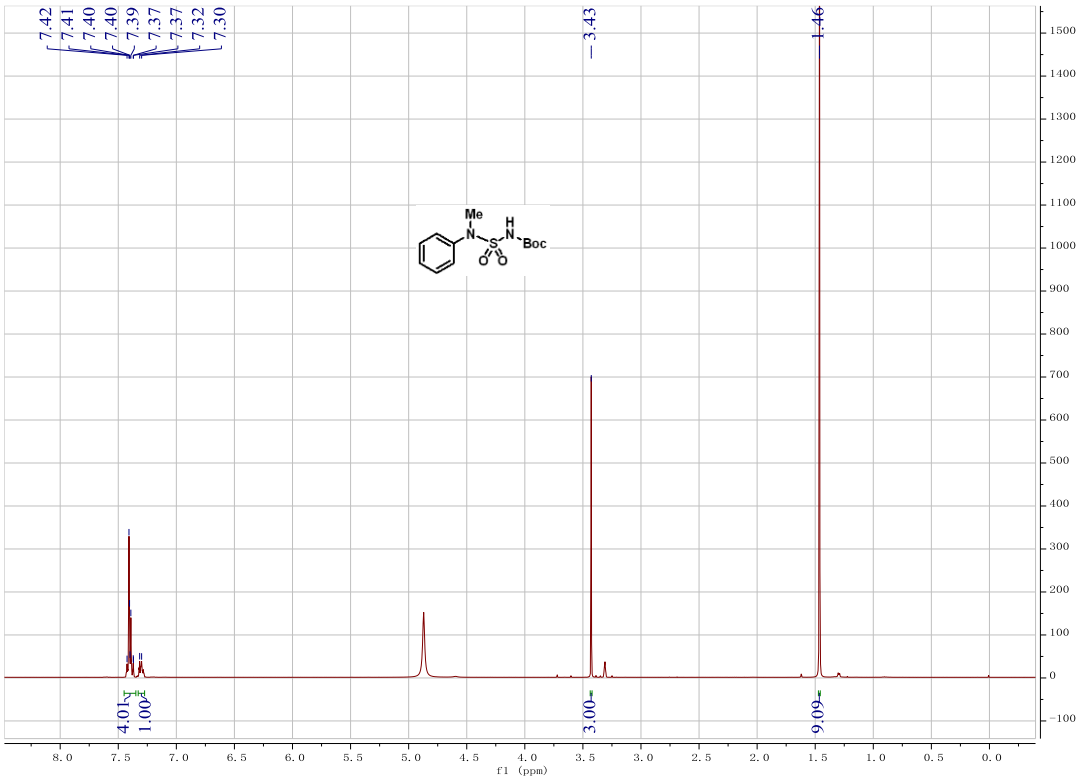


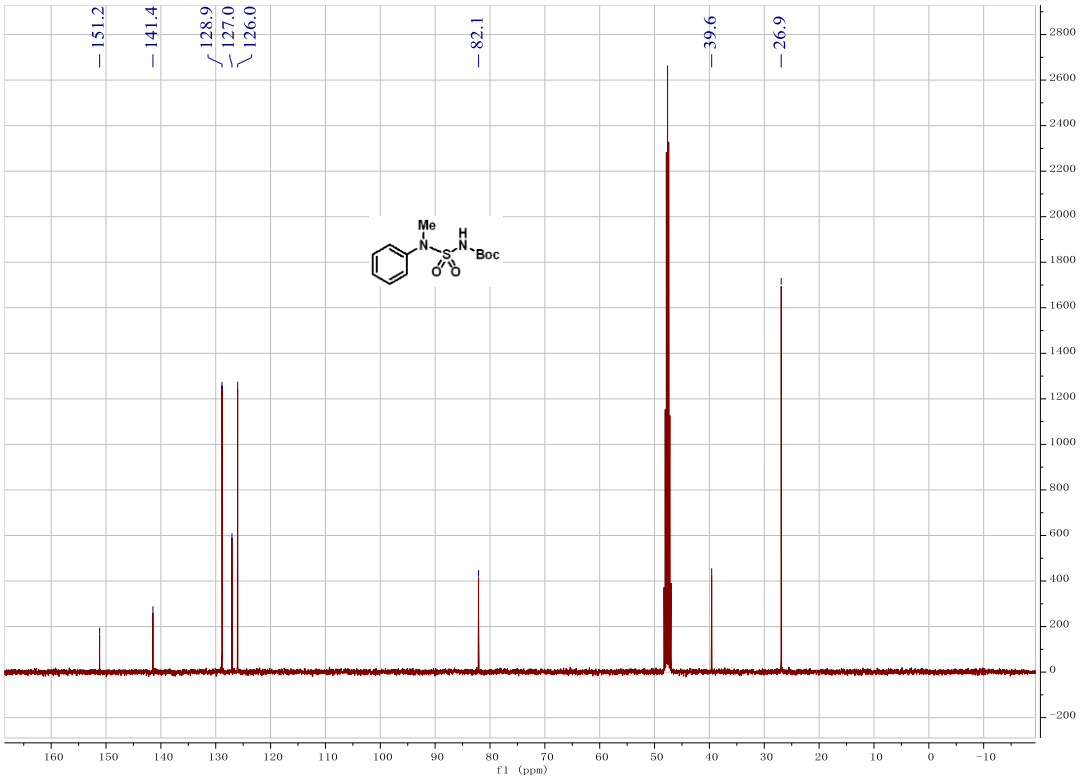
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 7d



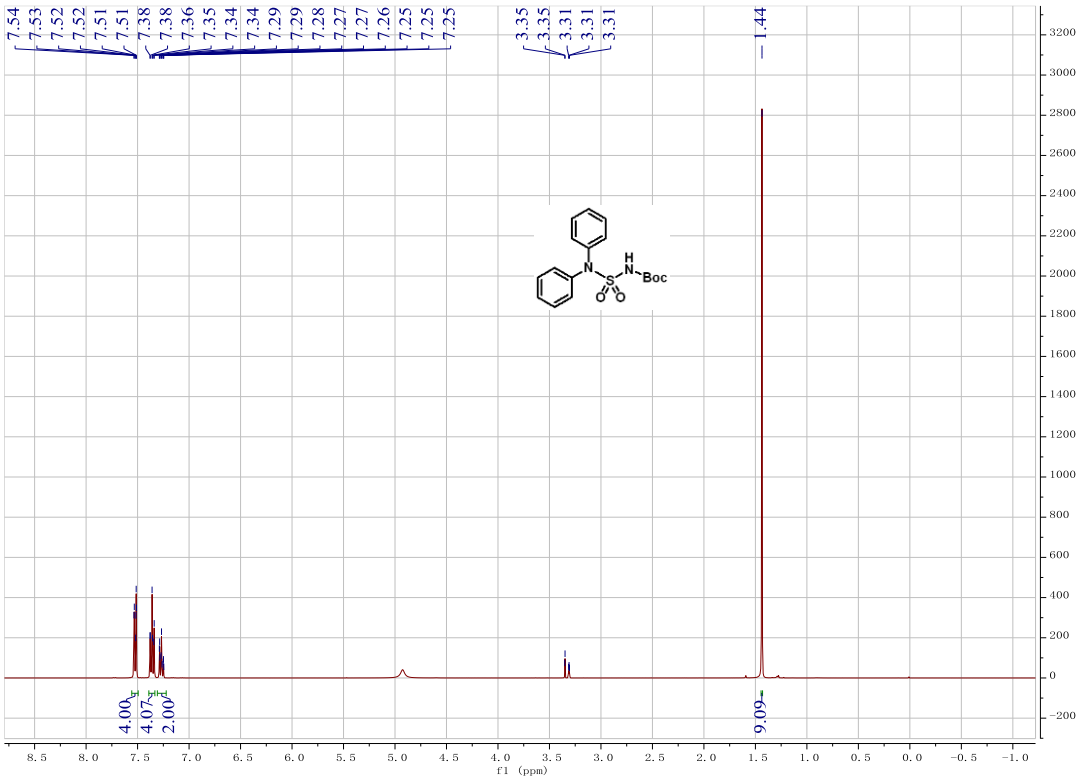


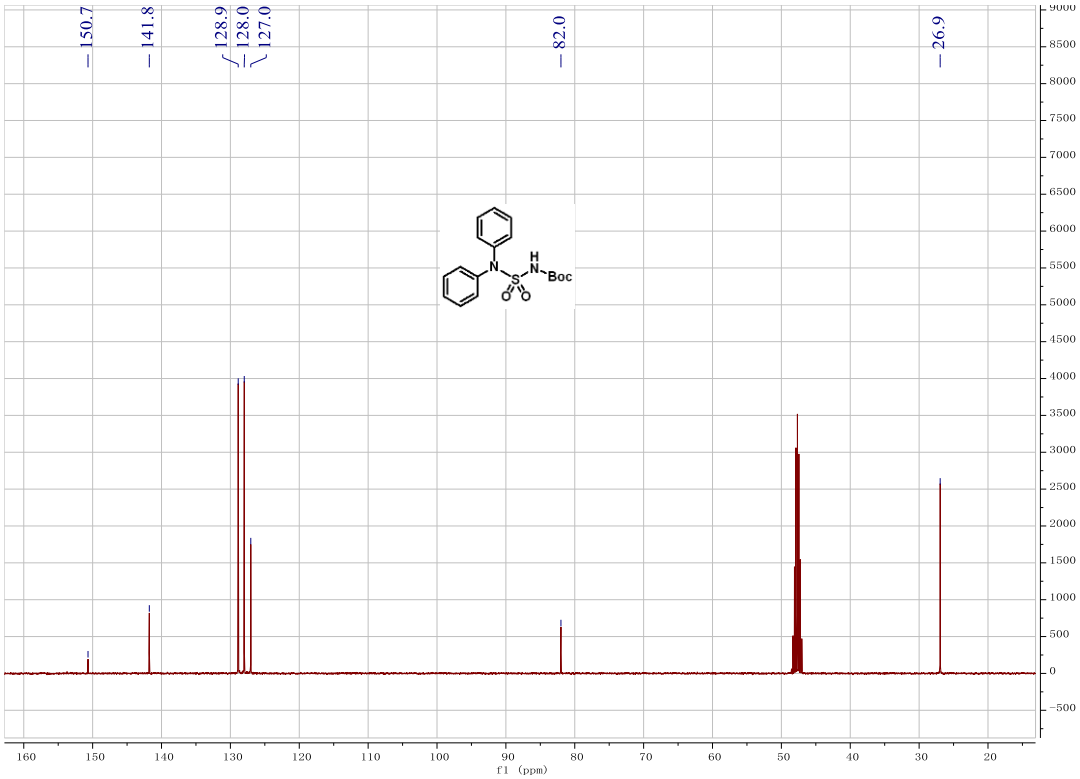
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 7e



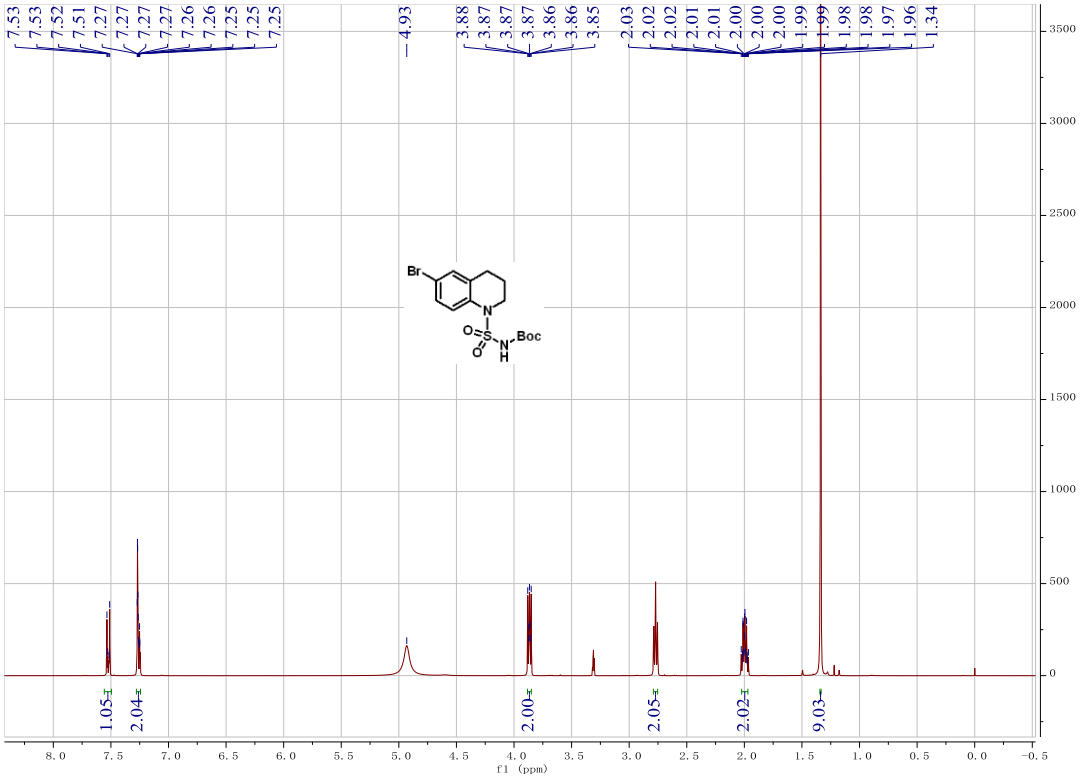


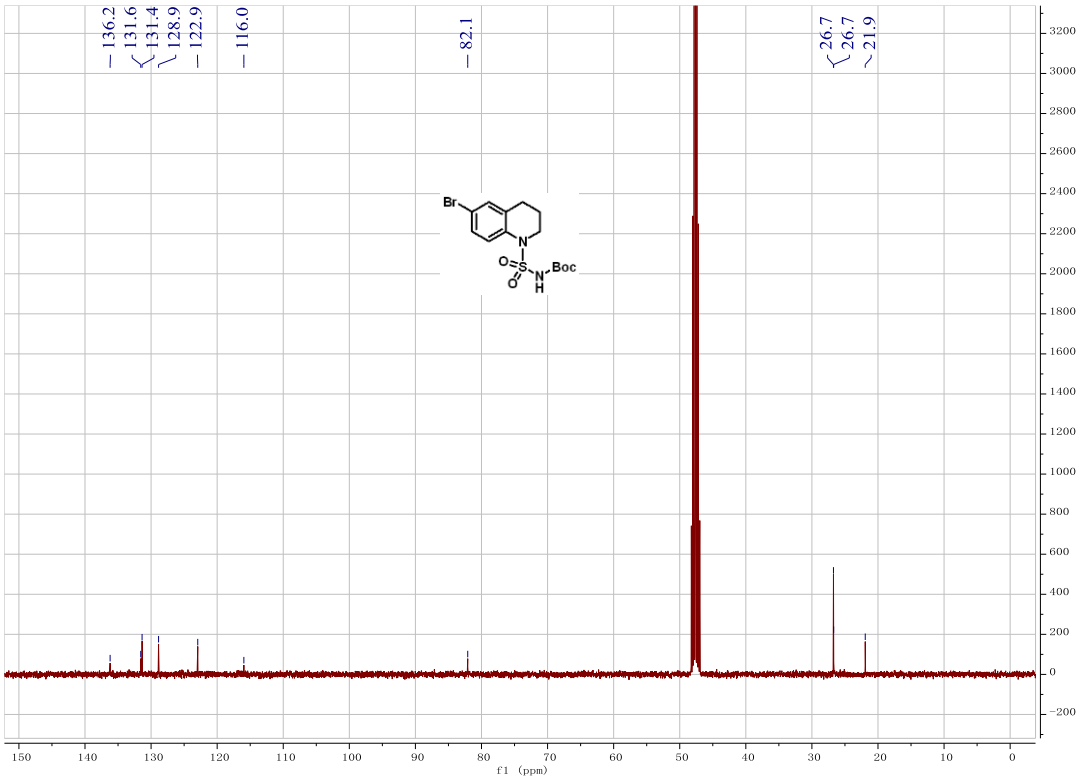
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 7f



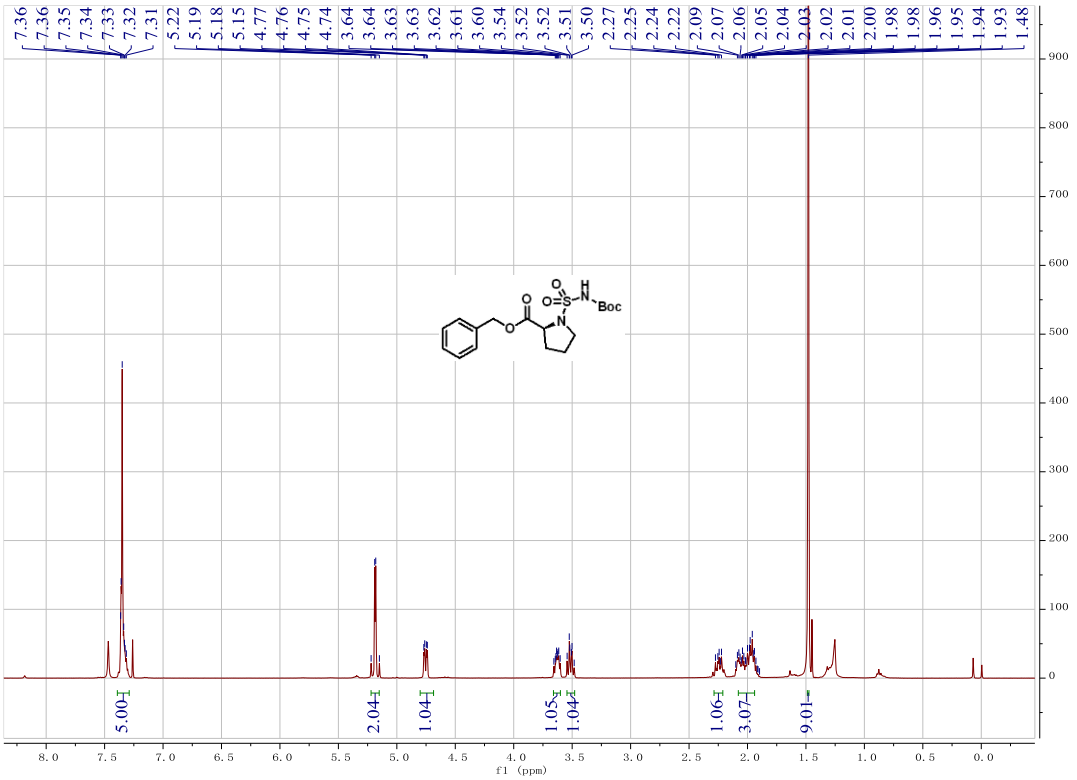


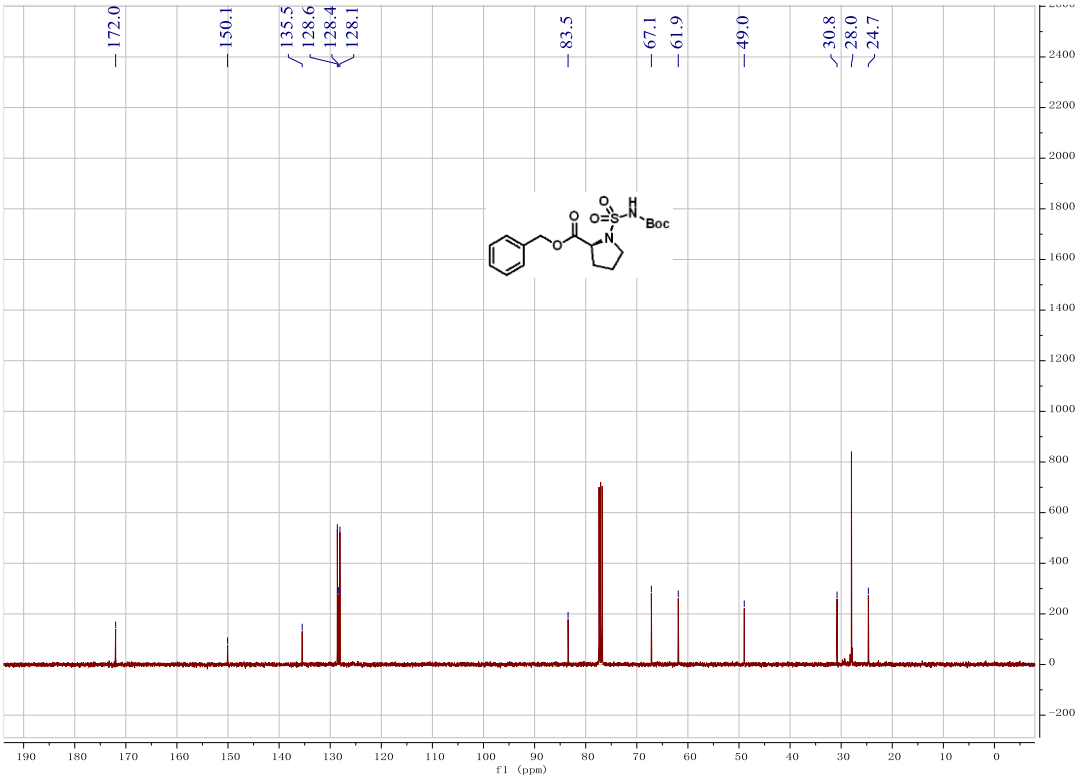
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 7g



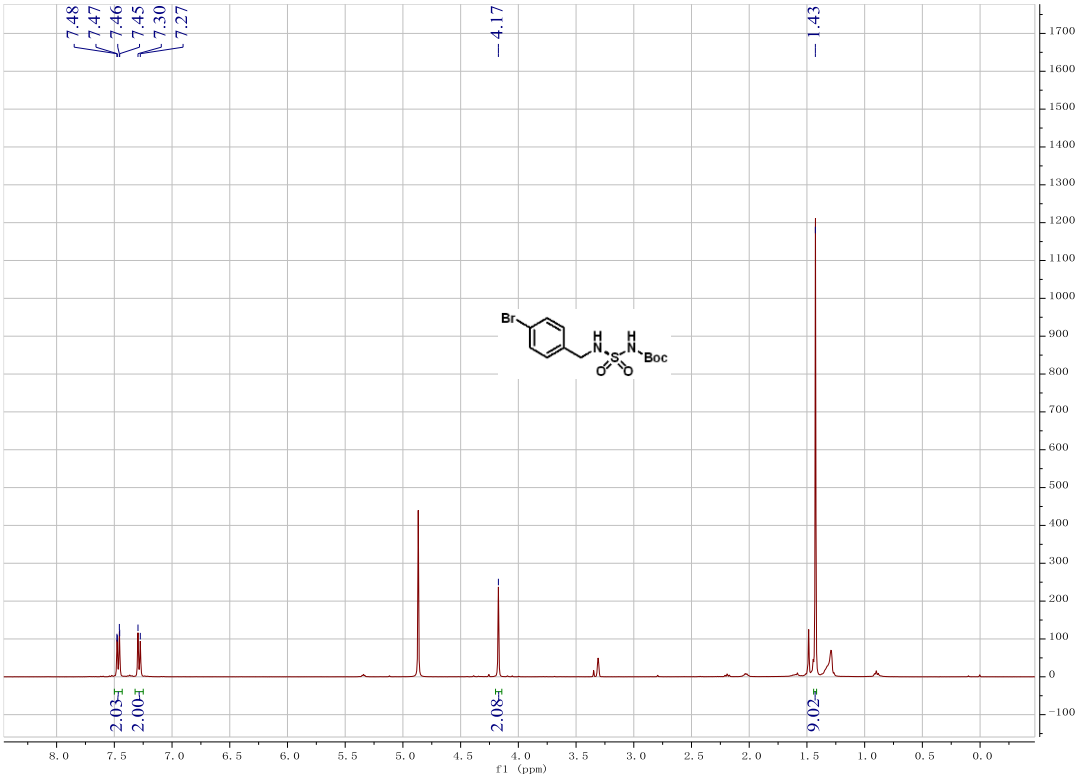


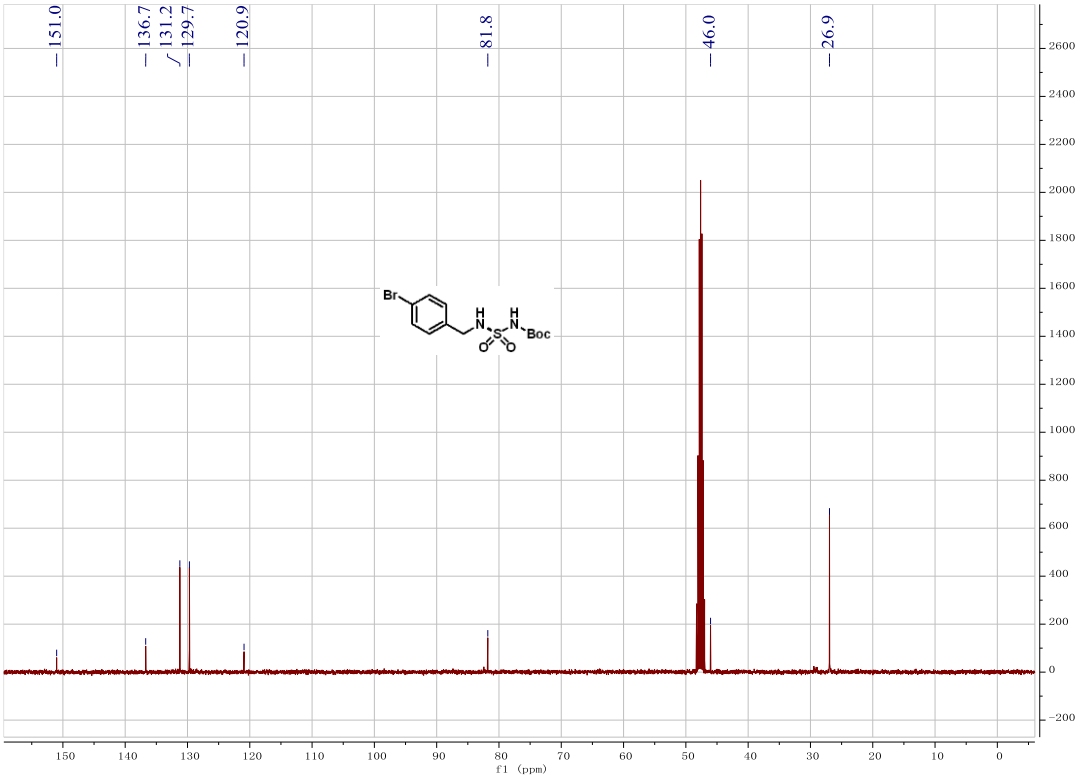
^{1}H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 7h



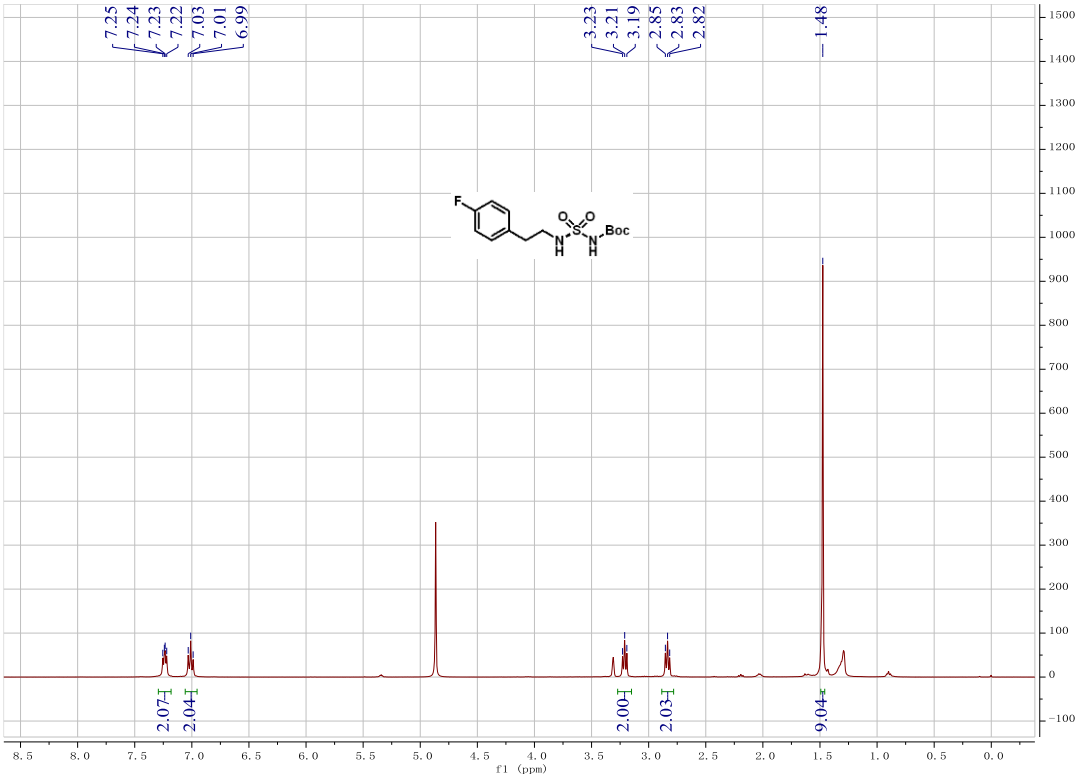


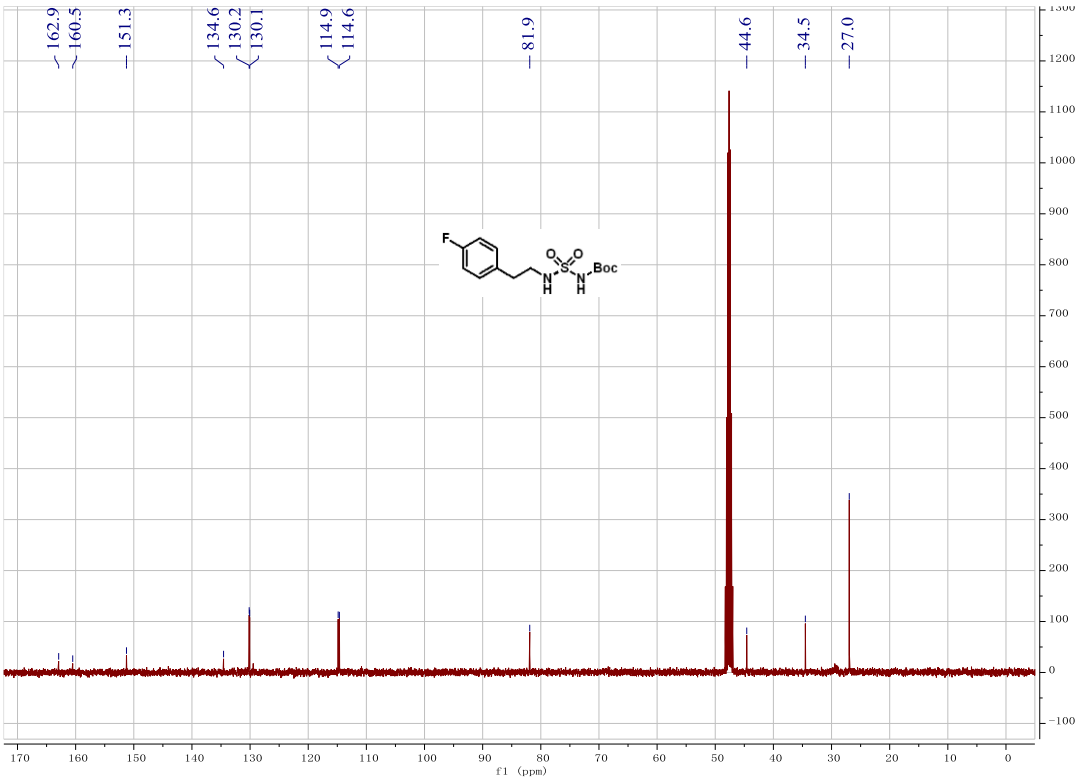
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 7i



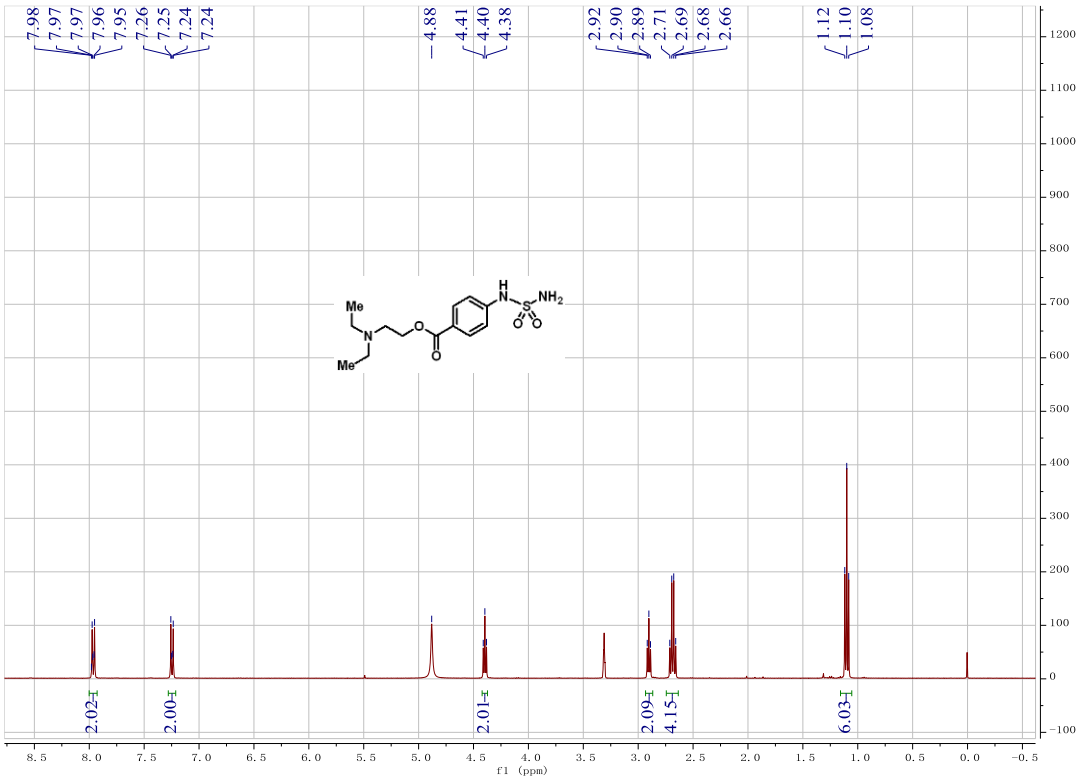


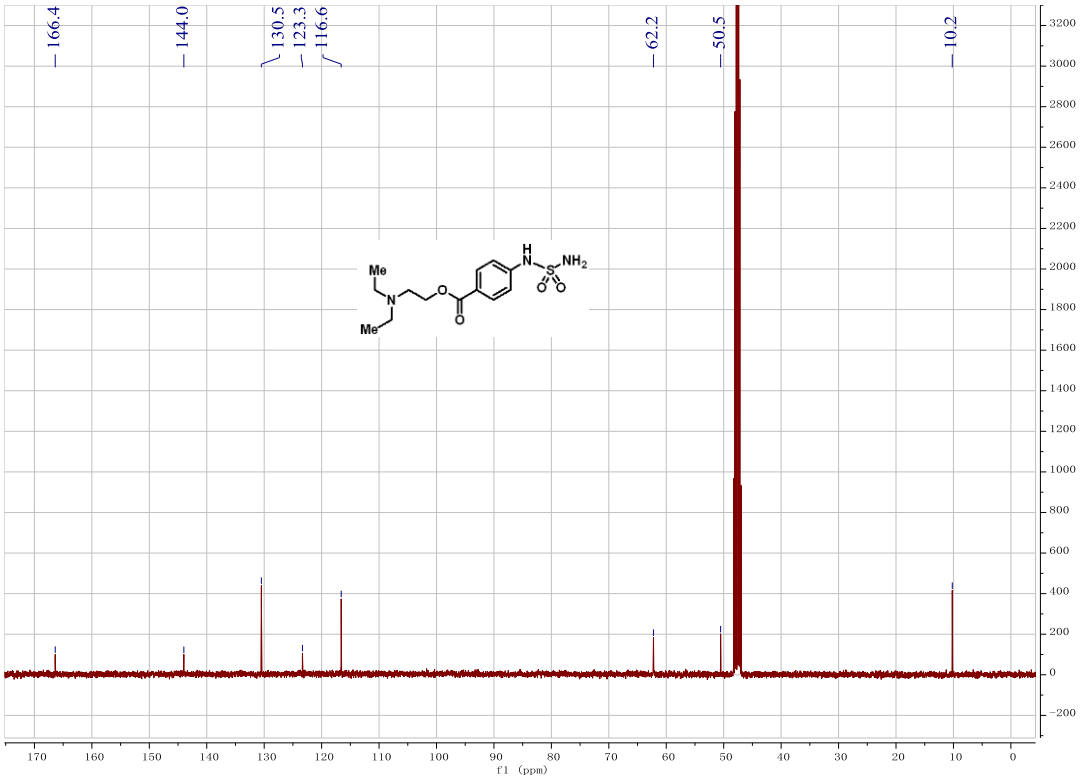
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 7j



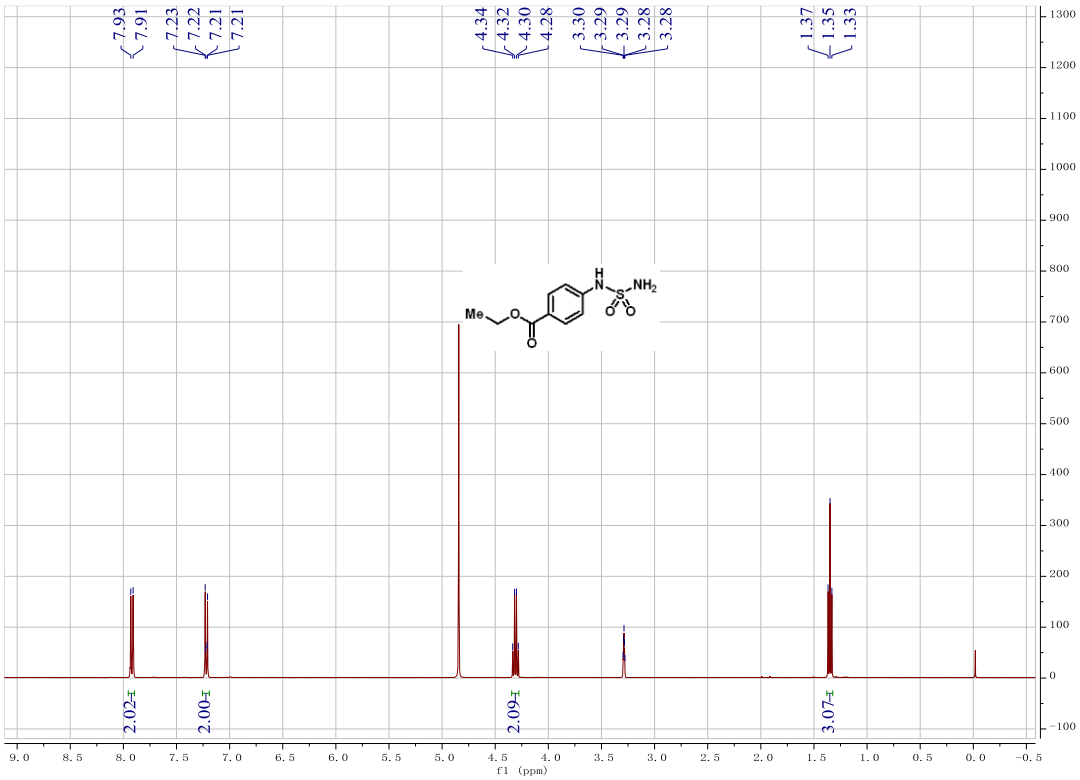


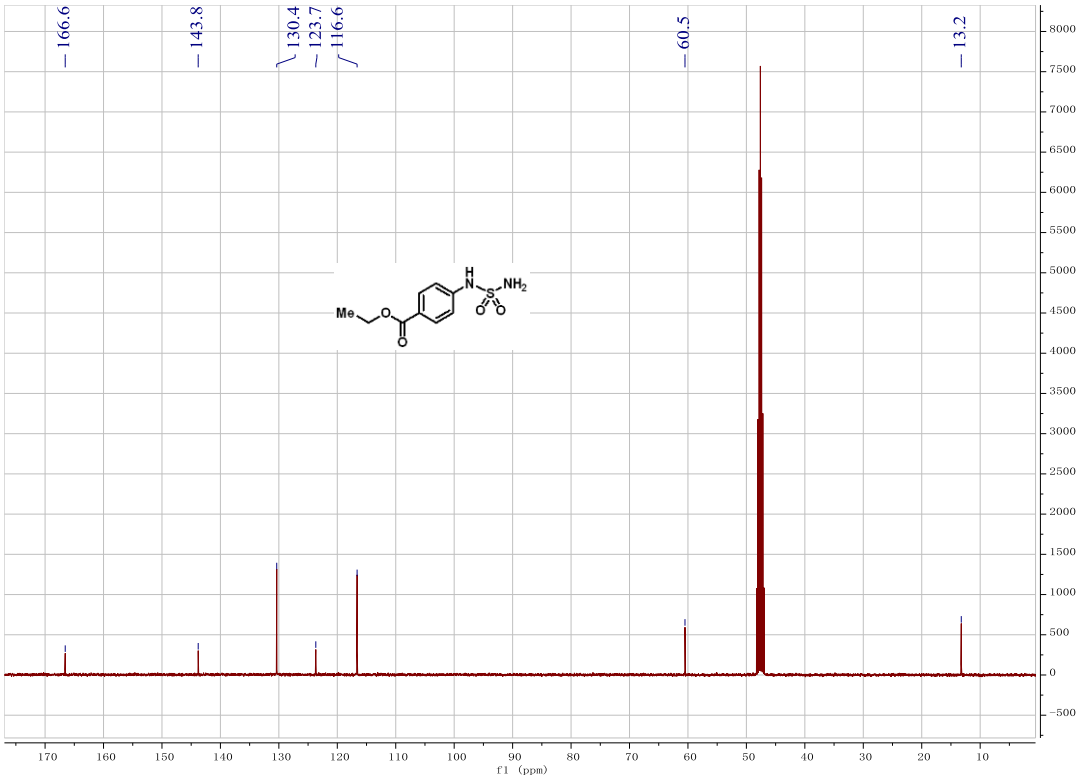
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 9a



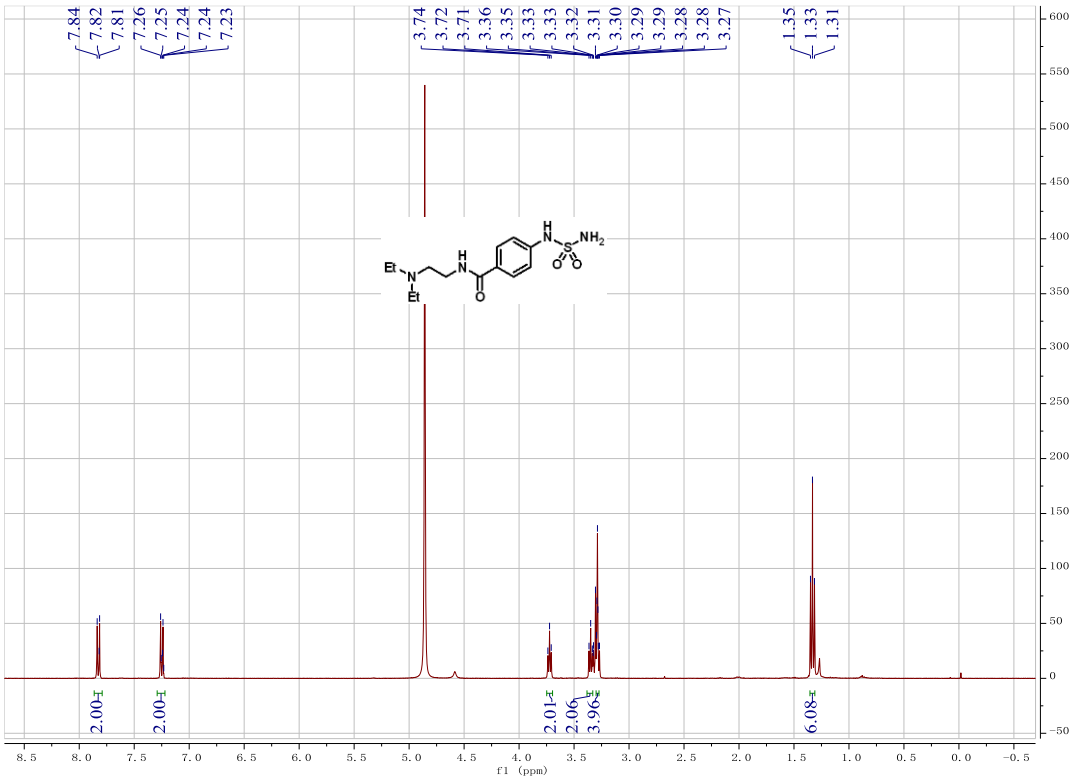


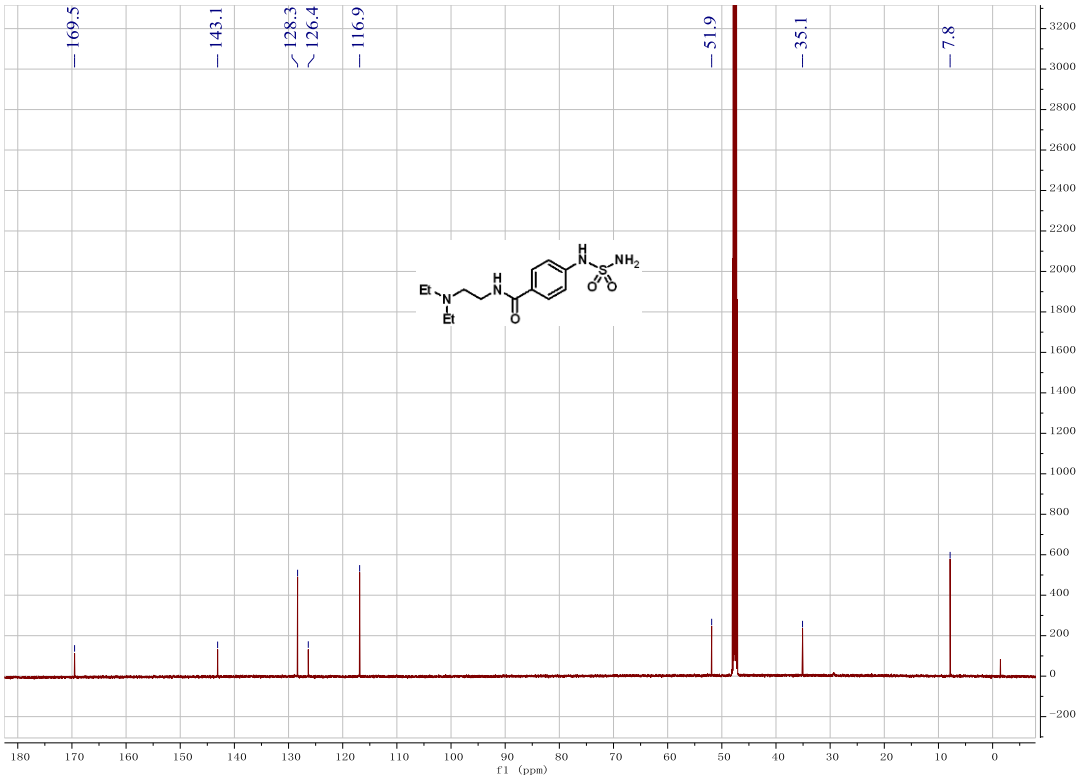
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 9b



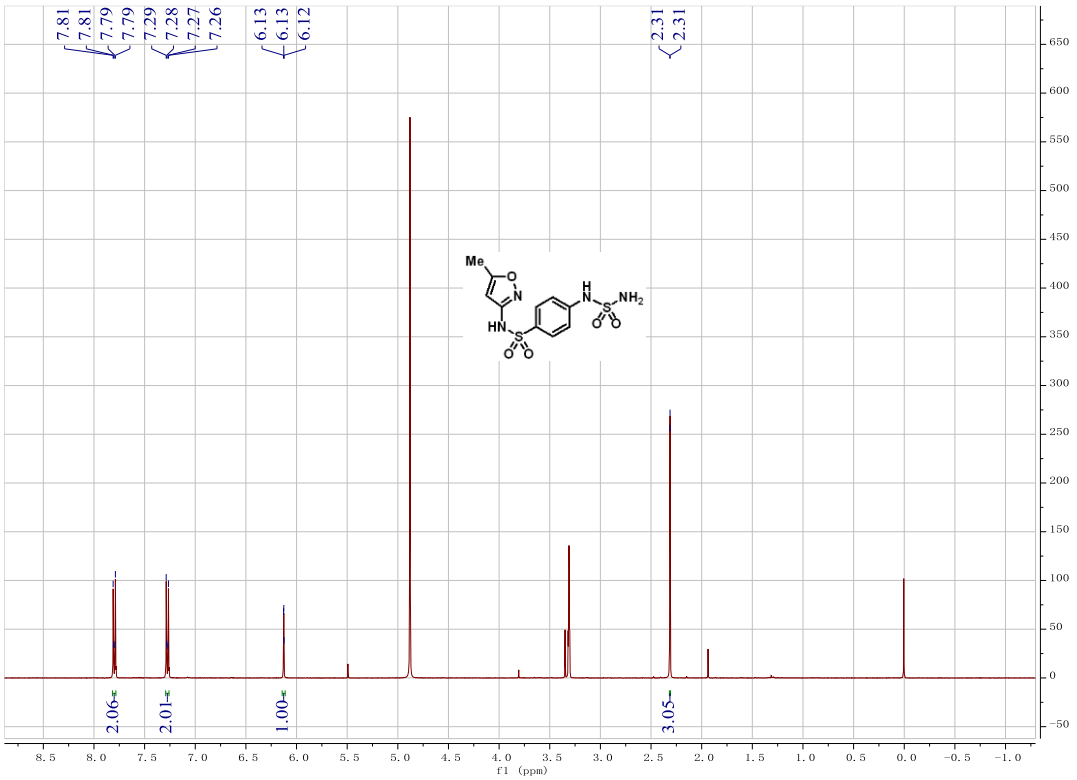


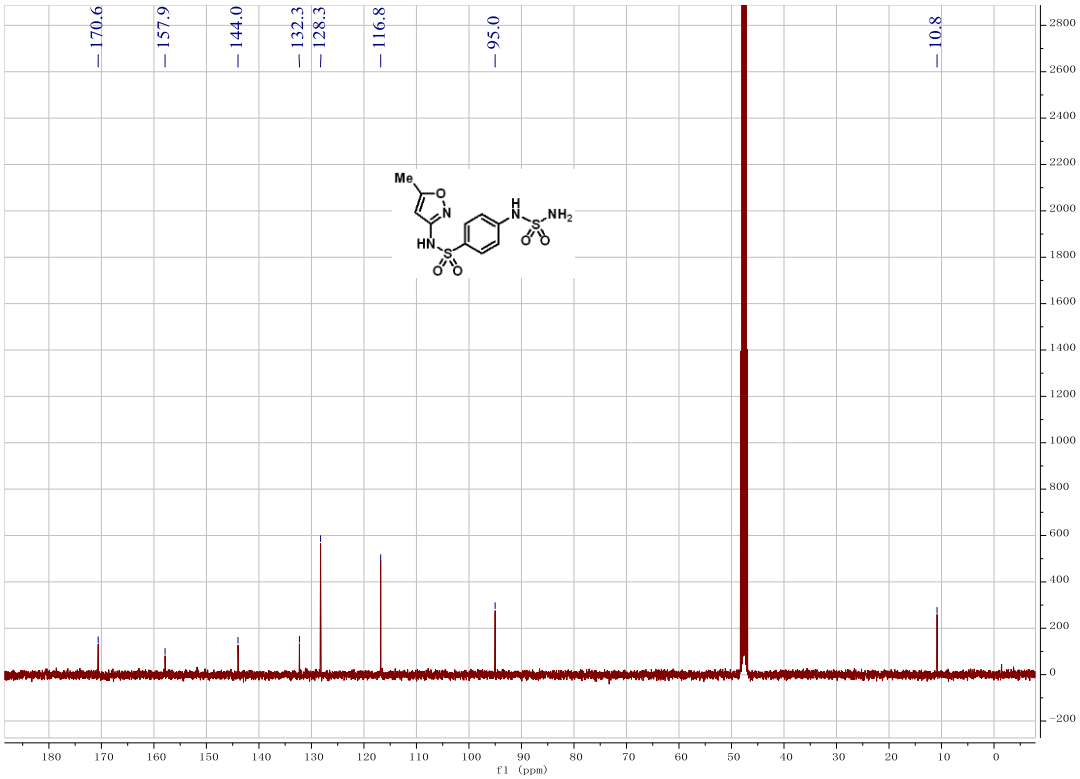
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 9c



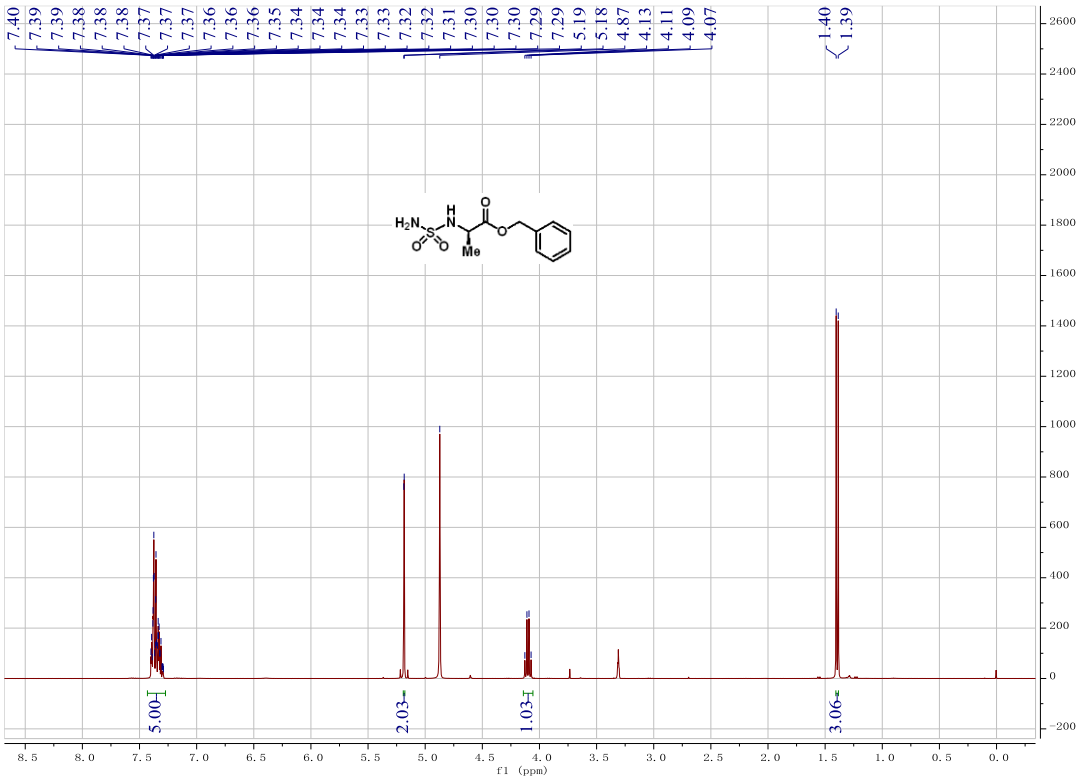


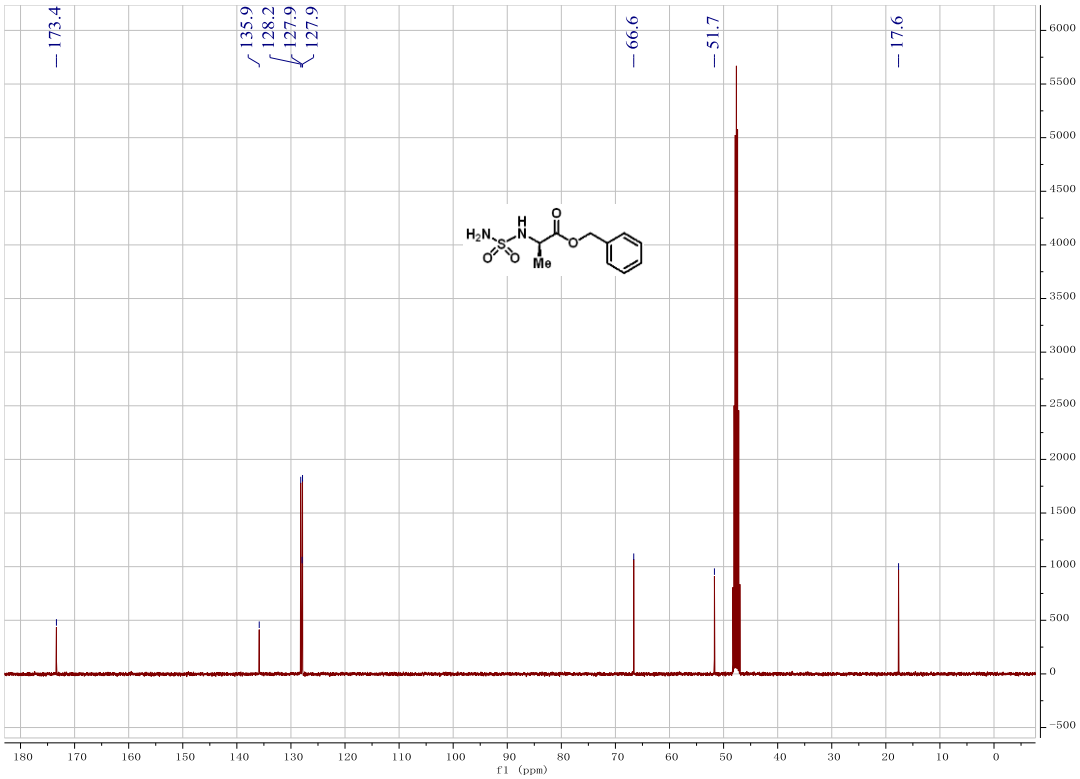
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 9d



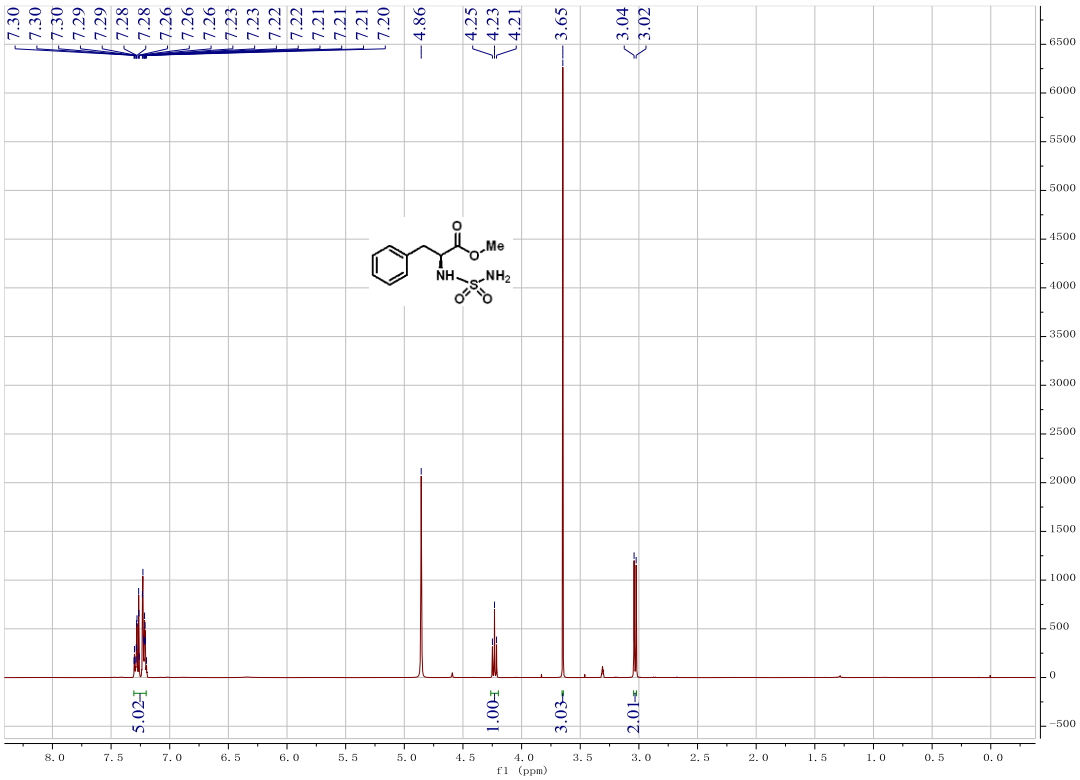


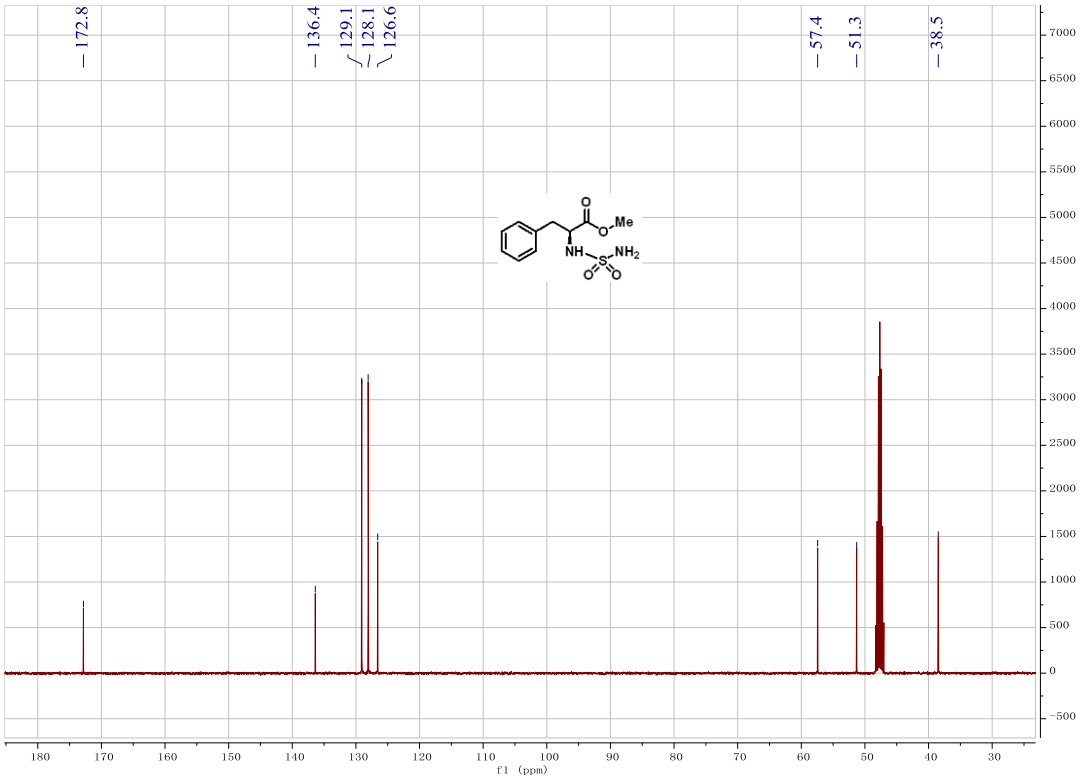
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 9e



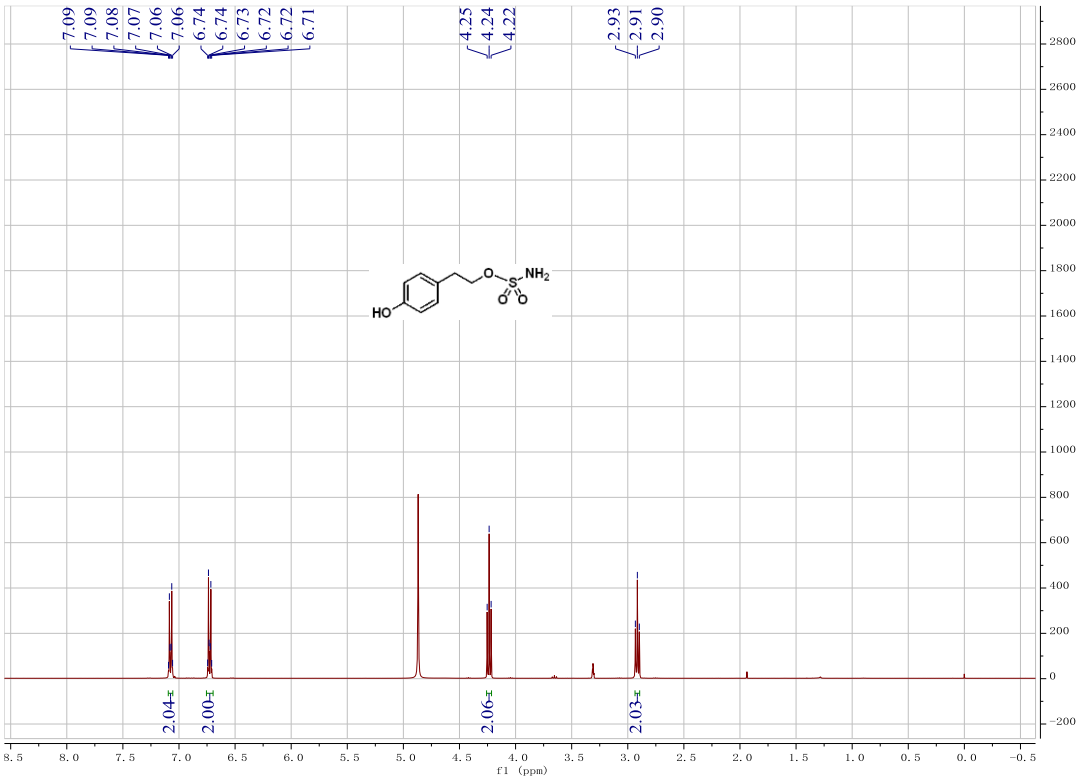


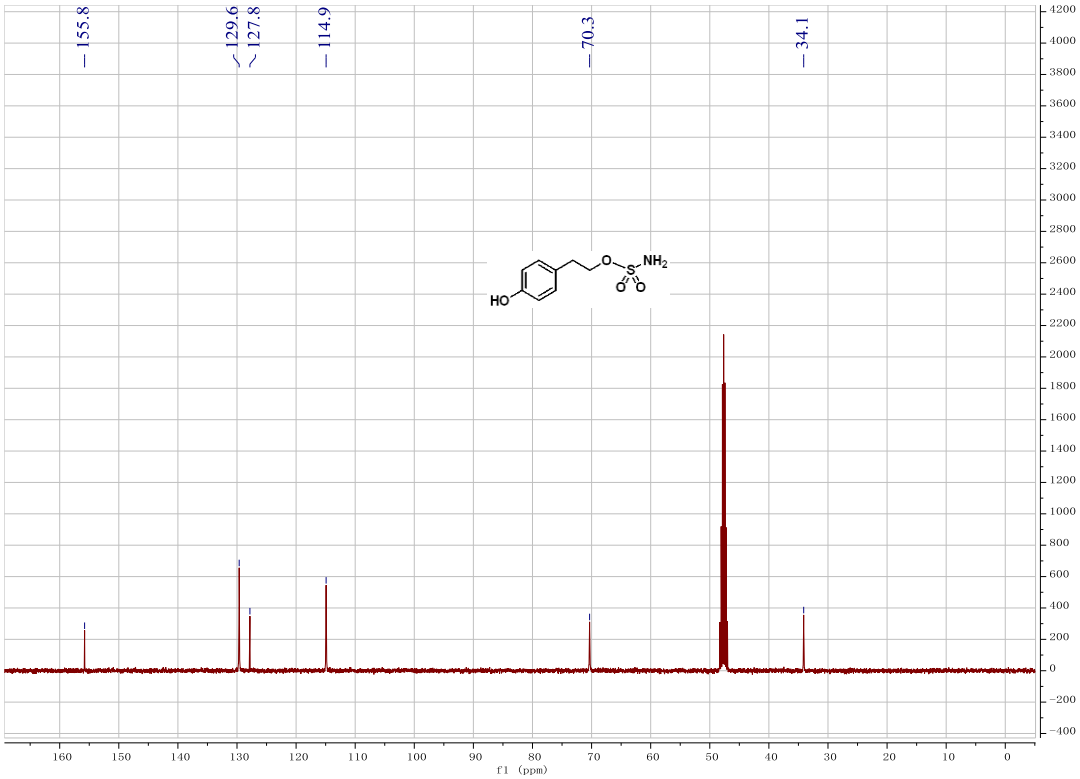
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 9f



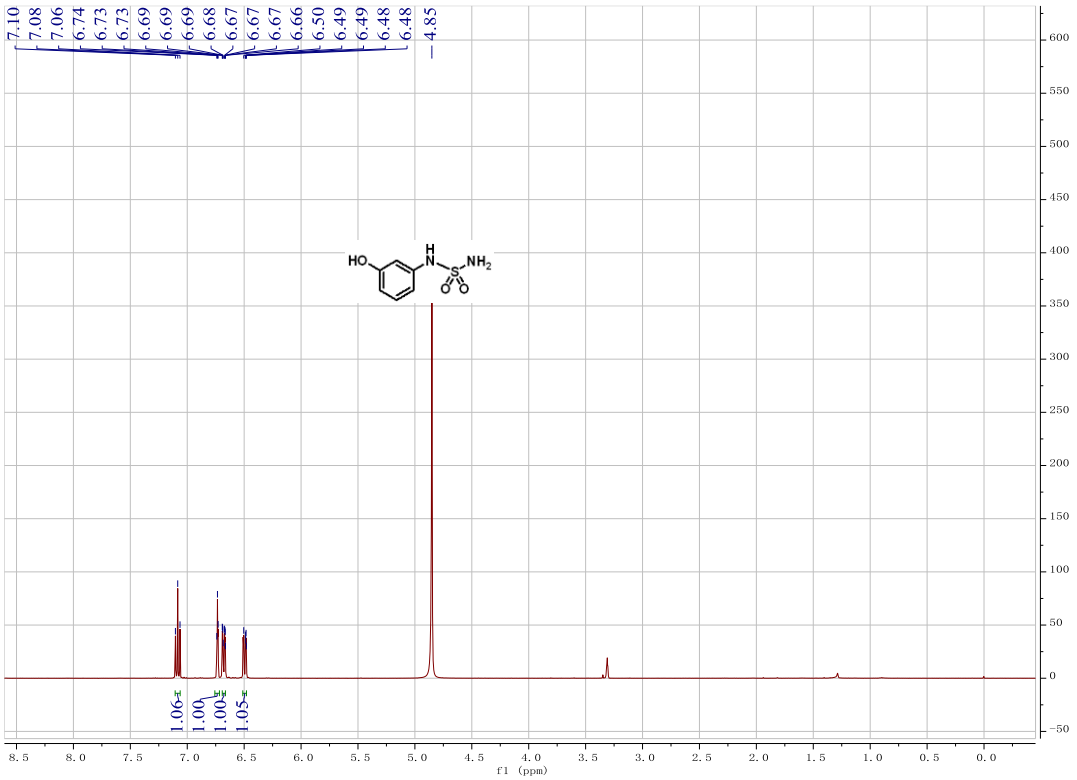


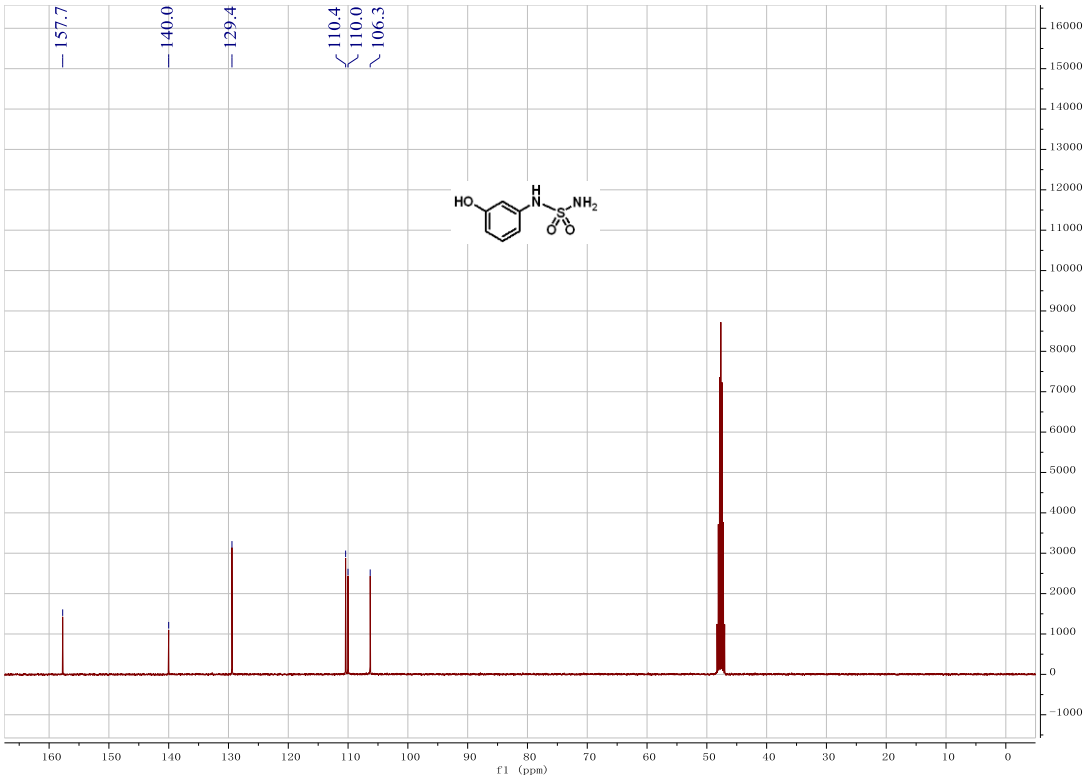
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 11a



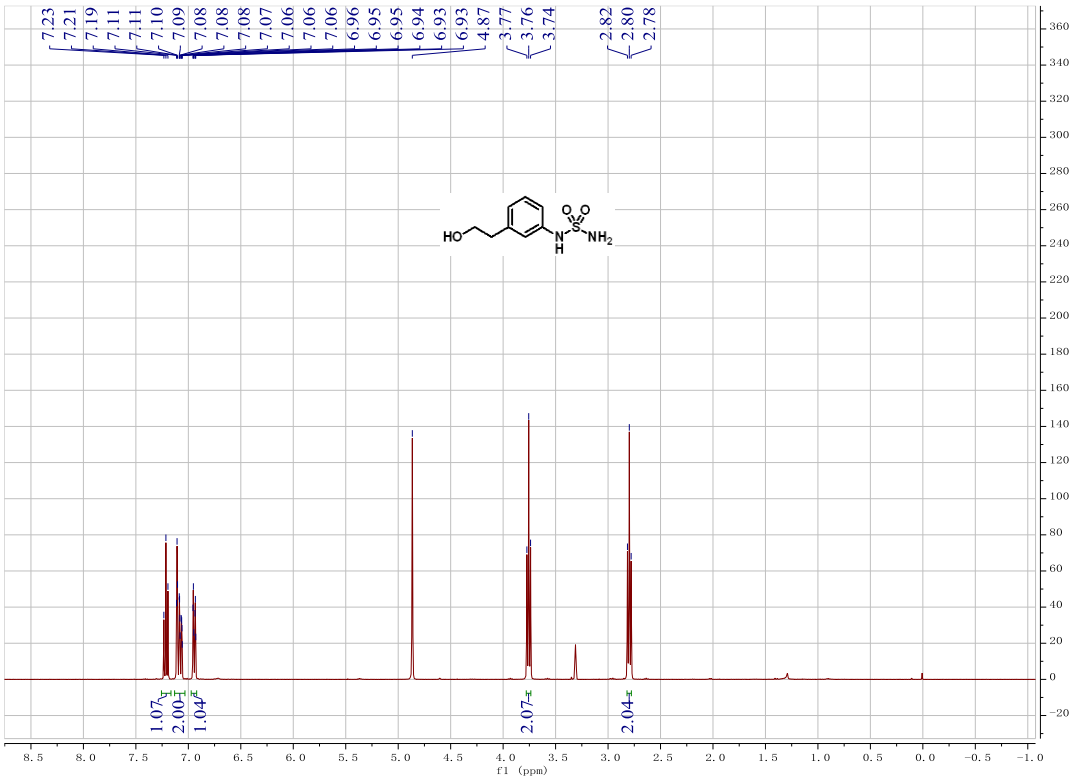


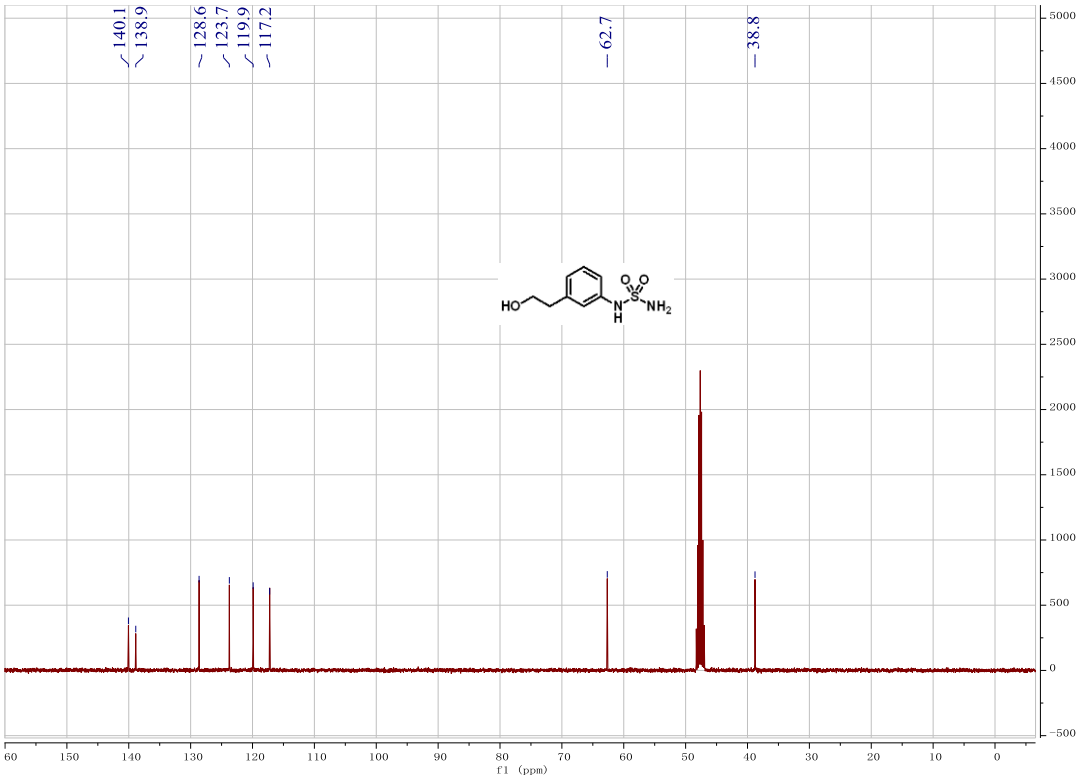
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 11b



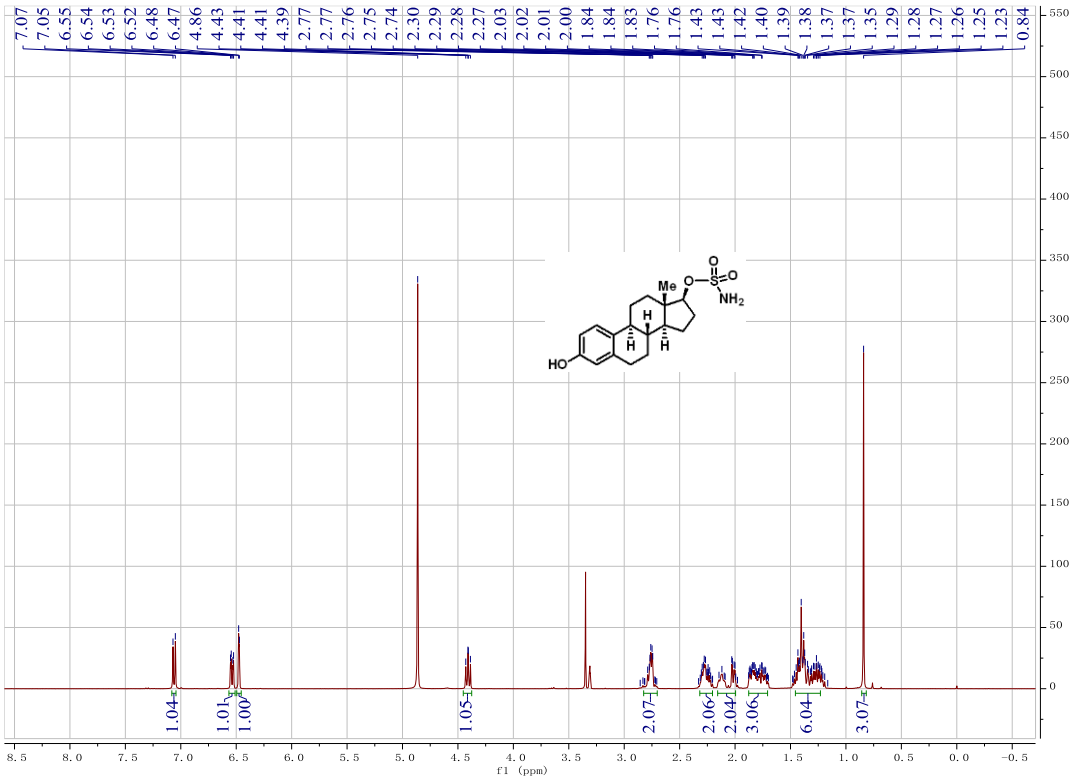


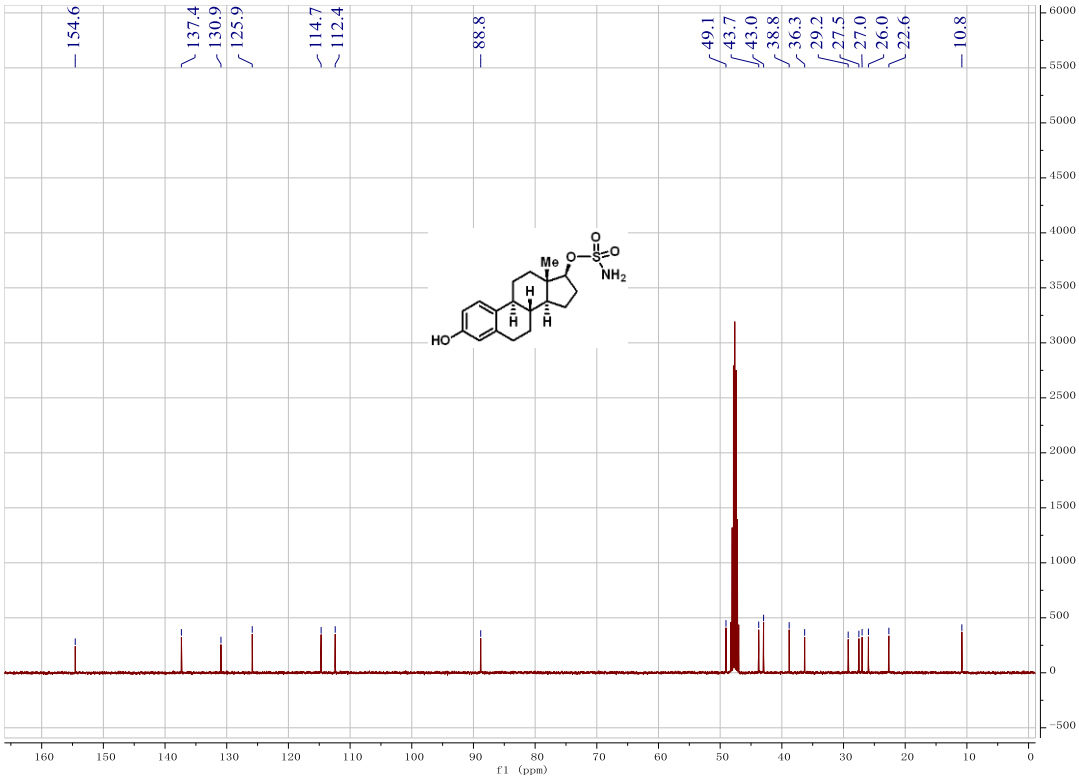
^{1}H (400 MHz, Methanol-*d*$_4$) and ^{13}C (101 MHz, Methanol-*d*$_4$) spectra of compound 11c



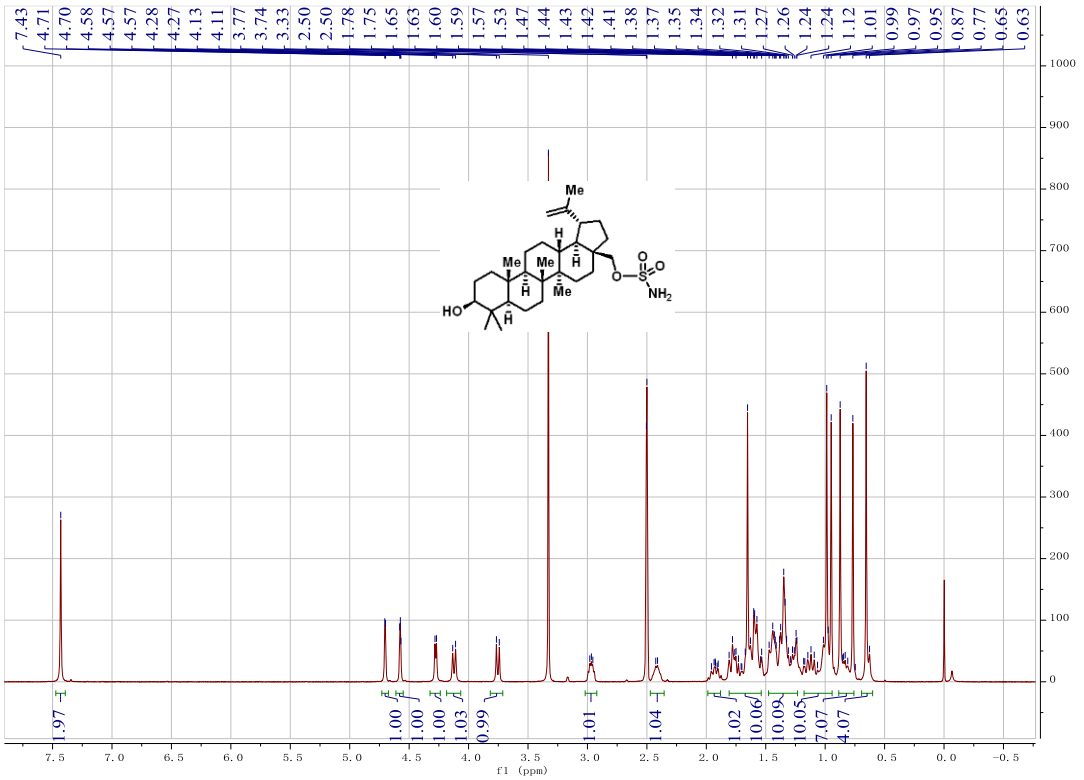


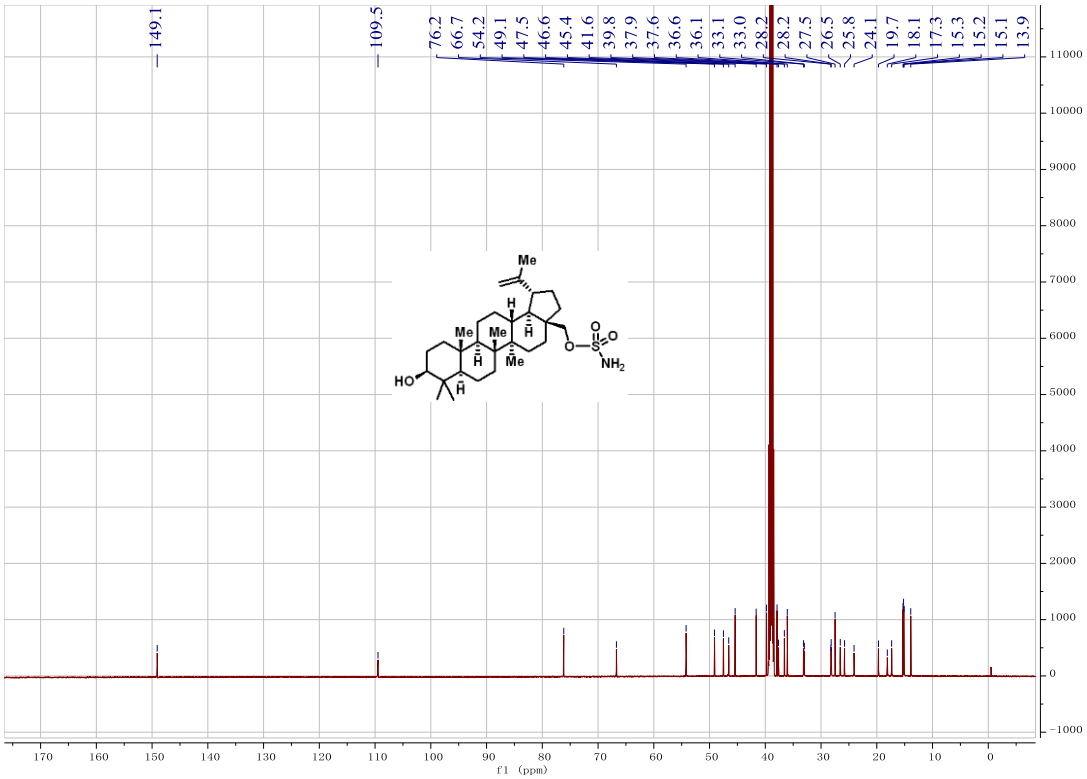
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 11d



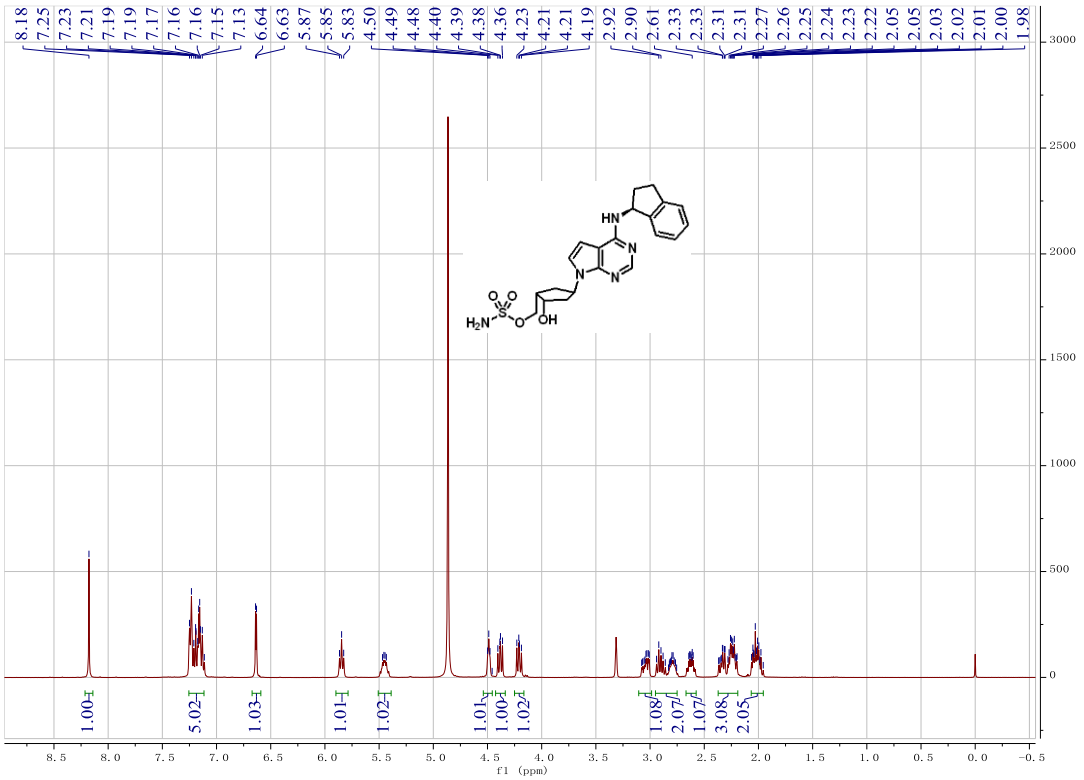


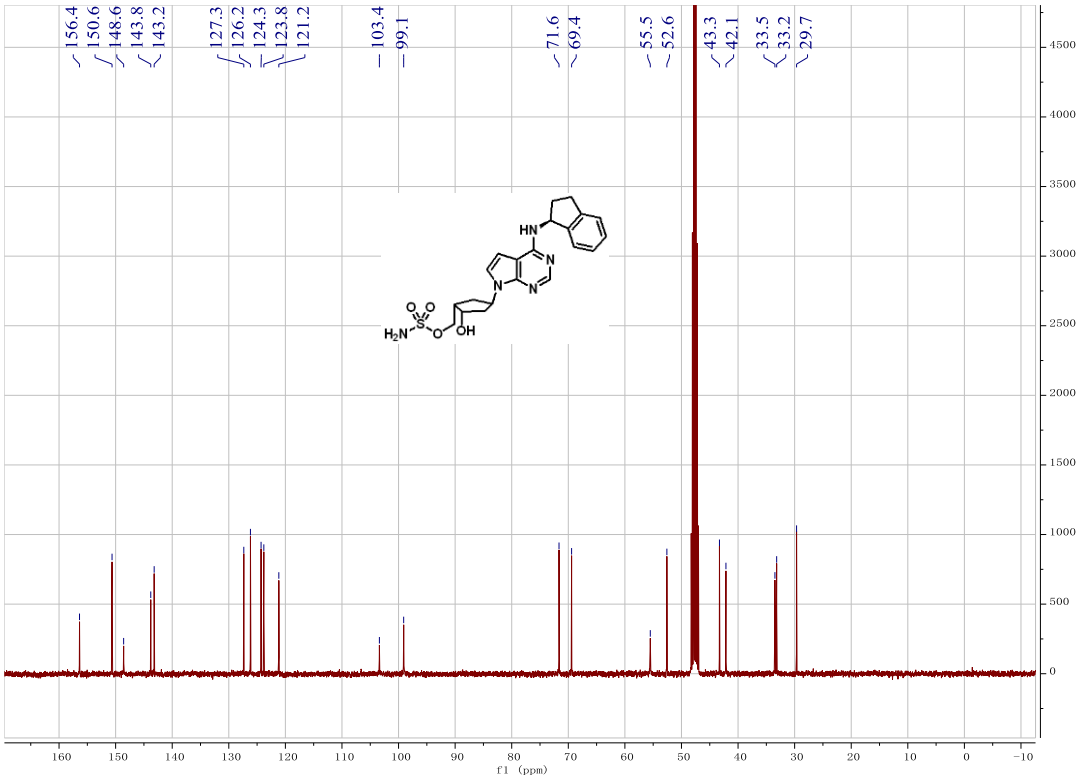
^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 11e





^{1}H (400 MHz, Methanol-d_4) and ^{13}C (101 MHz, Methanol-d_4) spectra of compound 11f





References

(1) Soucy, T. A.; Smith, P. G.; Milhollen, M. A.; Berger, A J.; Gavin, J. M.; Adhikari, S.; Brownell, J. E.; Burke, K E.; Cardin, D. P.; Critchley, S.; Cullis, C. A.; Doucette, A.; Garnsey, J. J. Gaulin, J. L.; Gershman, R. E.; Lublinsky, A. R.; McDonald, A.; Mizutani, H.; Narayanan, U.; Olhava, E. J.; Peluso, S.; Rezaei, M.; Sintchak, M. D.; Talreja, T.; Thomas, M. P.; Traore, T.; Vyskocil, S.; Weatherhead, G. S.; Yu, J.; Zhang, J.; Dick, L. R.; Claiborne, C. F.; Rolfe, M.; Bolen, J. B.; Langston, S. P. An inhibitor of NEDD8-activating enzyme as a new approach to treat cancer. *Nature.* **2009**, *458*, 732-736.