

Preparations of Sulfamates and Sulfamides Using a Selective Sulfamoylation Agent

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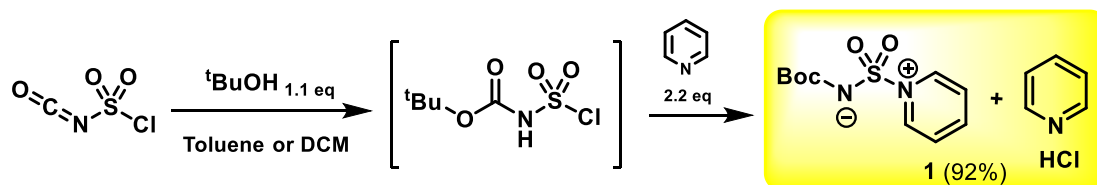
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1. General Methods for Experiments

Solvents and chemical reagents were obtained from commercial sources and used without further purification. ^1H 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).

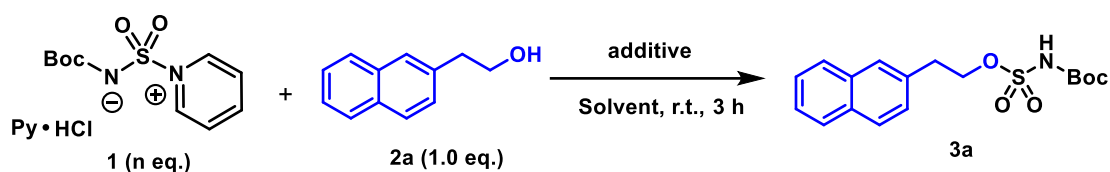
2. Procedure for the Preparation of Sulfamoylation Reagent **1** and Measurement of Saturated Solubility



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 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 ^1H -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.



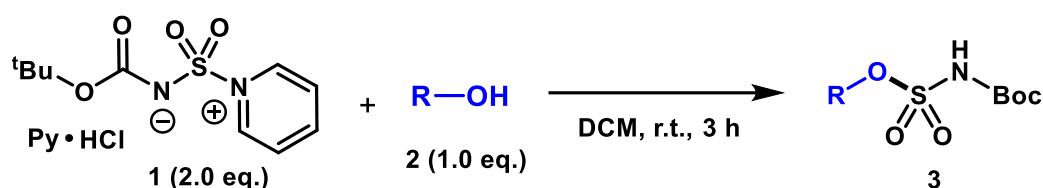
Entry	n	Additive	Solvent	3a yield ^[b]
1	1.5	—	DCM	80%
2	2	—	DCM	82%
3	2.5	—	DCM	79%
4	1.5	—	THF	51%
5	1.5	—	DMF	43%
6	1.5	—	MeCN	79%
7	1.5	—	DCE	71%
8	1.5	Cs ₂ CO ₃	DCM	77%
9	1.5	KO ^t Bu	DCM	61%
10	1.5	DIPEA	DCM	53%
11	1.5	K ₂ CO ₃	DCM	73%
12	1.5	CF ₃ COOH	DCM	34%
13	1.5	AlCl ₃	DCM	32%
14	1.5	CH ₃ COOH	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 ¹H-NMR analysis with mesitylene as an internal standard.

4. General Procedure for the Reactions of Sulfamoylation Reagent **1** with

Alcohols (Phenol)

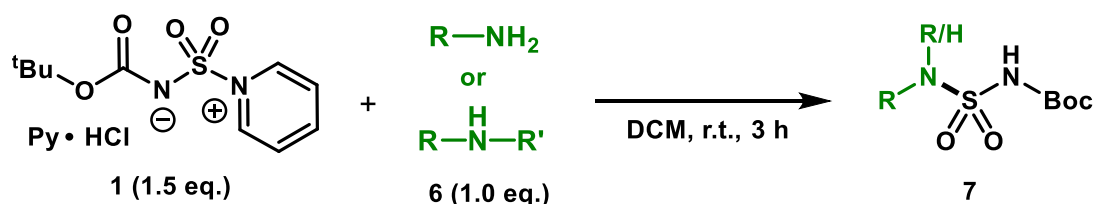


Alcohol (0.2 mmol), **1** (0.3 mmol) and dry dichloromethane (3 mL) were added to a reaction vessel at room temperature and the mixture was stirred for 3 hours. After the completion of the reaction as indicated by TLC, the mixture was concentrated under a reduced pressure. Saturated aqueous Na₂CO₃ (50 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 Na₂SO₄, concentrated under a

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

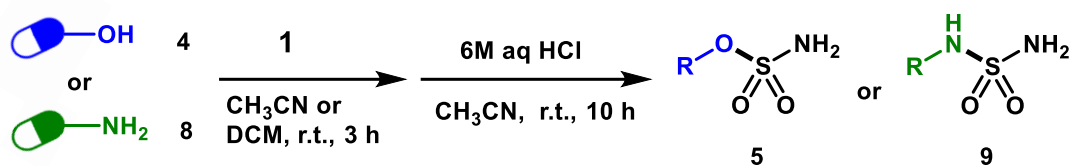
Phenol (0.2 mmol), 1(0.4 mmol) and dry dichloromethane (3 mL) were added to a reaction vessel at room temperature and the mixture was stirred for 3.5 hours. After the completion of the reaction as indicated by TLC, the mixture was concentrated under a reduced pressure. Saturated aqueous Na₂CO₃ (50 mL) 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 Na₂SO₄, 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).



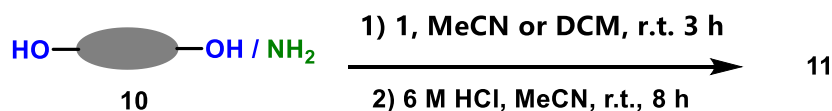
Aniline (0.2 mmol), 1(0.3 mmol) and dry dichloromethane (3 mL) were added to a reaction vessel at room temperature and the mixture was stirred for 3 hours. After the completion of the reaction as indicated by TLC, the mixture was concentrated under a reduced pressure. Saturated aqueous Na₂CO₃ (50 mL) 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 Na₂SO₄, 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 NH₂ Moiety.



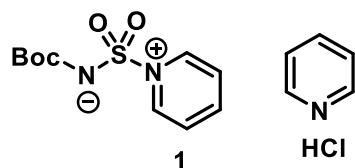
6 or 7 (0.2 mmol), 1 (0.4 mmol) and dry acetonitrile (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3 hours. After the completion of the reaction indicated by TLC, HCl (12M) in water (0.5 mL) was added dropwise, and the mixture was stirred for 8 hours. After the completion of the reaction indicated by TLC, the mixture was concentrated under reduced pressure. Saturated aqueous Na₂CO₃ (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The organic layer was dried over Na₂SO₄ 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 1 with Compounds with Different Nucleophilic Groups.

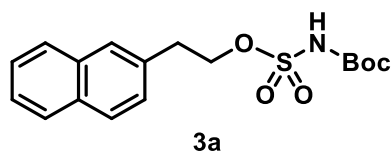


10 (0.2 mmol), 1 (0.3-0.4 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3.3 hours. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na₂CO₃ (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel.

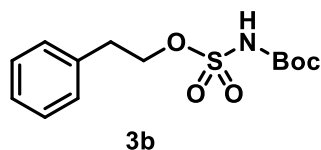
8. Characterization of Products



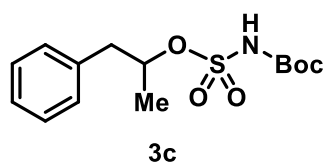
white-solid (6863.2mg, 92% yield). **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.92 (dd, J = 6.5, 1.4 Hz, 4H), 8.54 – 8.47 (m, 2H), 8.03 (dd, J = 7.8, 6.7 Hz, 4H), 7.65 (s, 1H), 1.36 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 152.8, 145.9, 141.4, 127.1, 80.9, 27.9. HRMS (ESI): (tert-butoxycarbonyl) (pyridin-1-ium-1-ylsulfonfyl) amide calc'd for C₁₀H₁₅N₂O₄S⁺ [M+H]⁺: 259.0747, found: 259.0751.



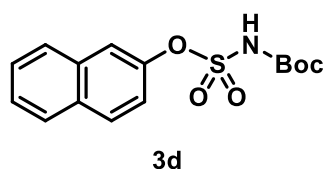
white-solid (57.5 mg, 82% yield). The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.82 – 7.73 (m, 3H), 7.68 – 7.63 (m, 1H), 7.50 – 7.40 (m, 2H), 7.32 (dd, J = 8.5, 1.8 Hz, 1H), 4.57 (t, J = 7.1 Hz, 2H), 3.20 (t, J = 7.1 Hz, 2H), 1.39 (s, 9H). **¹³C 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 C₁₇H₂₅N₂O₅S⁺ [M+ NH₄]⁺: 369.1479, found: 369.1454.



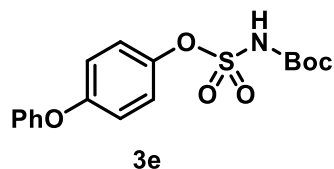
white-solid (50.58 mg, 84% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **¹H NMR** (400 MHz, Acetonitrile-*d*₃) δ 7.38 – 7.24 (m, 5H), 4.51 – 4.46 (m, 2H), 3.05 (t, J = 6.6 Hz, 2H), 1.46 (s, 9H). **¹³C NMR** (101 MHz, Acetonitrile-*d*₃) δ 149.1, 136.9, 128.9, 126.8, 117.3, 83.4, 73.3, 34.6, 27.1. HRMS (ESI): calc'd for C₁₃H₁₉NNaO₅S⁺ [M+ Na]⁺: 324.0876, found: 324.0884.



white-solid (56.72 mg, 90% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **¹H 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). **¹³C 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 C₁₄H₂₅N₂O₅S⁺ [M+ NH₄]⁺: 333.1479, found: 333.1470.

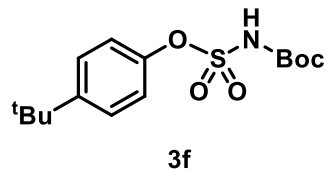


white-solid (48.46 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.89 – 7.72 (m, 4H), 7.54 – 7.38 (m, 3H), 1.43 (s, 9H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 158.5, 149.3, 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 C₁₅H₁₇NNaO₅S⁺ [M+ Na]⁺: 346.0720, found: 346.0719.

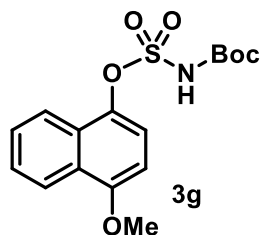


Colorless-oil (61.32 mg, 84% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.33 – 7.17 (m, 4H), 7.11 – 7.04 (m, 1H), 6.97 – 6.85 (m, 4H), 1.40 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*)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

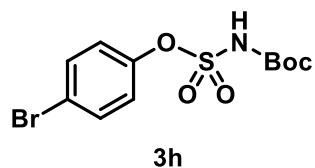
144.9, 130.0, 124.1, 123.2, 119.4, 119.3, 85.1, 27.9. HRMS (ESI): calc'd for $C_{17}H_{23}N_2O_6S^+$ $[M+NH_4]^+$: 383.1271, found: 383.1261.



white-solid (56.59 mg, 86% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) **¹H 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). **¹³C 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.

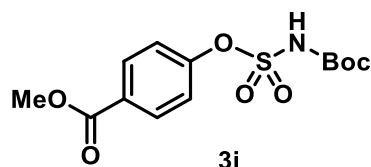


Brown-oil (57.89 mg, 82% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 8.33 – 8.14 (m, 2H), 7.59 – 7.40 (m, 3H), 6.89 – 6.82 (m, 1H), 3.99 (s, 3H), 1.40 (s, 9H). **¹³C NMR** (101 MHz, 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.

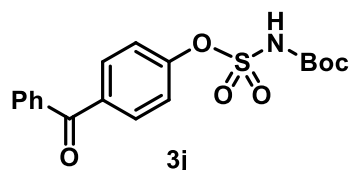


white-solid (49.14 mg, 70% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **¹H**

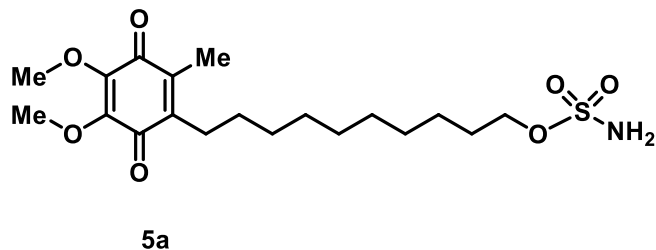
NMR (400 MHz, Methanol-*d*₄) δ 7.54 – 7.50 (m, 2H), 7.24 – 7.20 (m, 2H), 1.45 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 154.5, 136.5, 136.1, 127.6, 122.6, 72.0, 33.7. HRMS (ESI): calc'd for C₁₁H₁₃BrNO₅S⁻ [M-H]⁻: 349.9703, found: 349.9702.



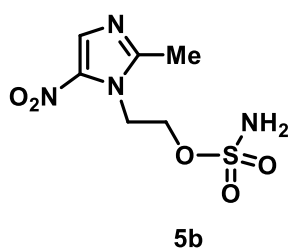
white-solid (50.31 mg, 76% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1). **¹H NMR** (400 MHz, Acetonitrile-*d*₃) δ 8.08 – 7.99 (m, 2H), 7.40 – 7.32 (m, 2H), 3.87 (s, 3H), 1.41 (s, 9H). **¹³C NMR** (101 MHz, Acetonitrile-*d*₃) δ 166.0, 158.9, 130.9, 121.7, 51.8, 27.3. HRMS (ESI): calc'd for C₁₃H₁₆NO₇S⁻ [M-H]⁻: 330.0653, found: 330.0653.



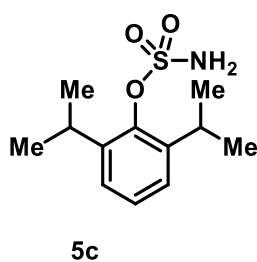
Yellow-oil (49.02 mg, 65% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.85 – 7.64 (m, 4H), 7.58 – 7.51 (m, 1H), 7.49 – 7.33 (m, 4H), 1.41 (s, 9H). **¹³C NMR** (101 MHz, Chloroform-*d*) 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 C₁₈H₂₀NO₆S⁺ [M+H]⁺: 378.1006, found: 378.0478.



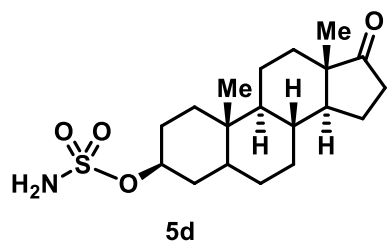
yellow-solid (67.55, 77% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 4.11 (t, *J* = 6.5 Hz, 2H), 3.96 – 3.95 (m, 6H), 2.49 – 2.43 (m, 2H), 1.99 (s, 3H), 1.75 – 1.66 (m, 2H), 1.43 – 1.30 (m, 14H). **¹³C 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 C₁₉H₃₂NO₇S⁺ [M + H]⁺ 418.1894, found 418.1898.



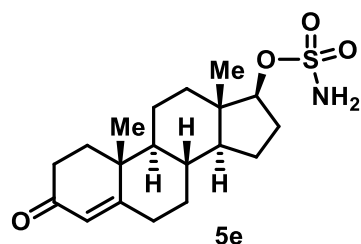
white-solid (40 mg, 80% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.96 (s, 1H), 4.72 – 4.69 (m, 2H), 4.48 – 4.44 (m, 2H), 2.53 (s, 3H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 151.8, 131.4, 67.4, 45.2, 12.8. HRMS calc'd for C₆H₁₁N₄O₅S [M + H]⁺ 251.0445, found 251.0421.



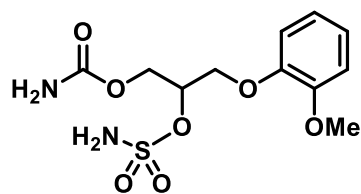
white-solid (38.57 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 9:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.23 – 7.16 (m, 3H), 3.64 – 3.55 (m, 2H), 1.21 (d, 12H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 145.3, 142.6, 126.7, 124.0, 26.9, 22.7. HRMS calc'd for C₁₂H₁₉NO₃S⁺ [M + Na]⁺ 280.0978, found 280.0994.



white-solid (54.64 mg, 74% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H 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). **¹³C 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 C₁₉H₃₂NO₄S [M + H]⁺ 370.2047, found 370.2038.

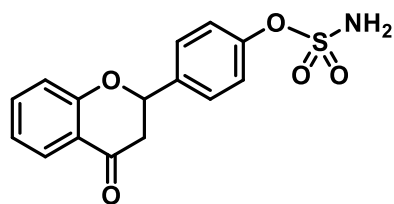


white-solid (59.48 mg, 81% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 5.74 – 5.71 (m, 1H), 4.39 – 4.30 (m, 1H), 2.55 – 2.43 (m, 2H), 2.36 – 2.17 (m, 3H), 2.13 – 2.05 (m, 1H), 2.00 – 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). **¹³C 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 C₁₉H₃₀NO₄S⁺ [M + H]⁺ 368.1890, found 368.1862.



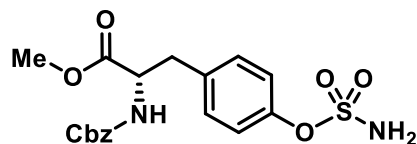
5f

white-solid (47.37 mg, 74% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **¹H 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). **¹³C 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 C₁₁H₁₆N₂NaO₇S⁺ [M + Na]⁺ 343.0570, found 343.0572.



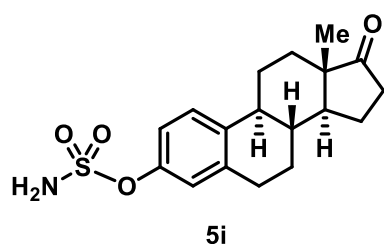
5g

white-solid (48.50 mg, 76% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **¹H 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). **¹³C 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 C₁₅H₁₄NO₅S⁺ [M + H]⁺ 320.0587, found 320.0570.

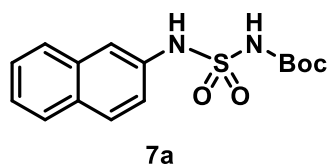


5h

white-solid (57.13 mg, 70% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H 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). **¹³C 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 C₁₈H₂₁N₂O₇S⁺ [M + H]⁺ 409.1064, found 409.1046.

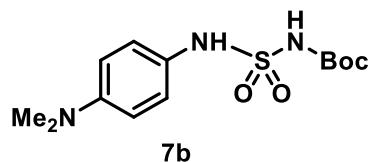


white-solid (56.54 mg, 81% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.37 – 7.29 (m, 1H), 7.10 – 6.99 (m, 2H), 2.98 – 2.86 (m, 2H), 2.55 – 2.39 (m, 2H), 2.35 – 2.24 (m, 1H), 2.21 – 1.99 (m, 3H), 1.93 – 1.83 (m, 1H), 1.68 – 1.41 (m, 6H), 0.91 (s, 3H). **¹³C 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 C₁₈H₂₄NO₄S⁺ [M + H]⁺ 409.1064, found 409.1046.

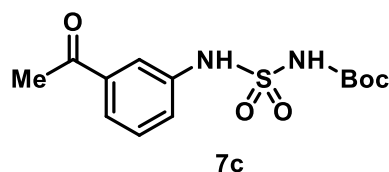


white-solid (54.76 mg, 85% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.84 – 7.74 (m, 3H), 7.71 – 7.67 (m, 1H), 7.50 – 7.35 (m, 3H), 1.34 (s, 9H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 150.7, 135.0, 133.8, 131.0,

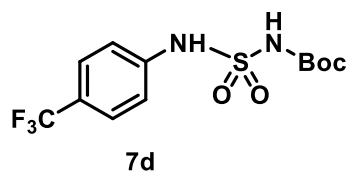
128.6, 127.3, 127.0, 126.3, 124.9, 120.4, 117.1, 82.0, 26.8. HRMS (ESI): calc'd for $C_{15}H_{17}N_2O_4S^-$ $[M-H]^-$ 321.0915, found: 321.0917.



Yellow-solid (51.66 mg, 82% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) 1H 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.

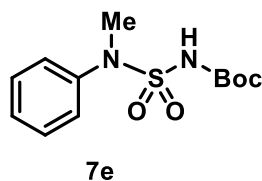


white-solid (47.1 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1). 1H NMR (400 MHz, Methanol- d_4) δ 7.84 (m, 1H), 7.77 (m, 1H), 7.49 – 7.43 (m, 2H), 2.59 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, Methanol- d_4) δ 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.

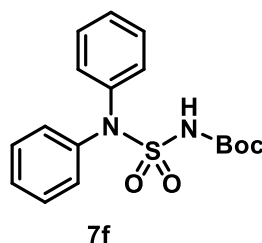


yellow-solid (53.4 mg, 78% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). 1H

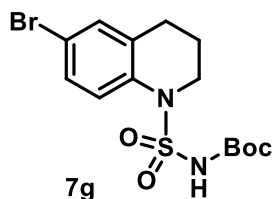
NMR (400 MHz, Methanol-*d*₄) δ 7.62 – 7.58 (m, 2H), 7.38 – 7.34 (m, 2H), 1.36 (s, 9H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 150.4, 141.2, 126.0 (q, *J* = 3.8 Hz), 125.4 (q, *J* = 33.33 Hz), 124.3 (q, *J* = 271.69 Hz), 118.0, 82.2, 26.7. HRMS (ESI): calc'd for C₁₂H₁₄F₃N₂O₄S⁻ [M-H]⁻: 339.0632, found: 339.0627.



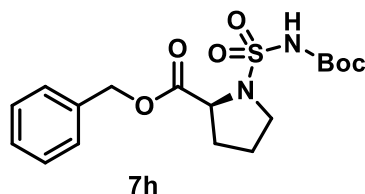
white-solid (50.35 mg, 88% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 7:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.45 – 7.35 (m, 4H), 7.34 – 7.27 (m, 1H), 3.43 (s, 3H), 1.46 (s, 9H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 151.2, 141.4, 128.9, 127.0, 126.0, 82.1, 39.6, 26.9. HRMS (ESI): calc'd for C₁₂H₁₈N₂NaO₄S⁺ [M+Na]⁺: 309.0879, found: 309.0863.



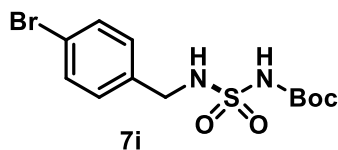
white-solid (63.36 mg, 91% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.56 – 7.49 (m, 4H), 7.40 – 7.32 (m, 4H), 7.30 – 7.23 (m, 2H), 1.44 (s, 9H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 150.7, 141.8, 128.9, 128.0, 127.0, 82.0, 26.9. HRMS (ESI): calc'd for C₁₇H₂₀N₂NaO₄S⁺ [M+Na]⁺: 371.1036, found: 371.1040.



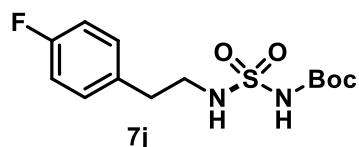
white-solid (62.4 mg, 80% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.56 – 7.47 (m, 1H), 7.29 – 7.22 (m, 2H), 3.91 – 3.77 (m, 2H), 2.77 (t, *J* = 6.5 Hz, 2H), 2.04 – 1.91 (m, 2H), 1.34 (s, 9H). **¹³C 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 C₁₄H₁₈BrN₂O₄S⁻ [M-H]⁻: 389.0176, found: 339.0177.



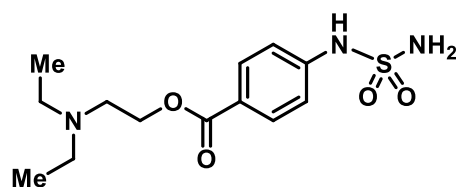
Colorless oil (57.6 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 8:1). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.39 – 7.29 (m, 5H), 5.23 – 5.13 (m, 2H), 4.79 – 4.70 (m, 1H), 3.68 – 3.58 (m, 1H), 3.56 – 3.45 (m, 1H), 2.29 – 2.20 (m, 1H), 2.08 – 1.94 (m, 3H), 1.48 (s, 9H). **¹³C 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 C₁₇H₂₈N₃O₆S⁺ [M+NH₄]⁺: 402.1693, found: 402.1691.



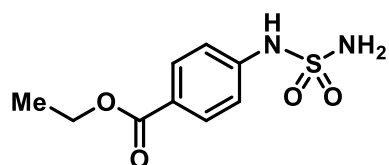
Yellow solid (48.0 mg, 66% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.50 – 7.43 (m, 2H), 7.32 – 7.25 (m, 2H), 4.17 (s, 2H), 1.43 (s, 9H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 151.0, 136.7, 131.2, 129.7, 120.9, 81.8, 46.0, 26.9. HRMS (ESI): calc'd for C₁₂H₁₆BrN₂O₄S⁻ [M-H]⁻: 363.0020, found: 363.0006.



Yellow solid (44.5 mg, 70% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **¹H 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). **¹³C 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 C₁₃H₁₈FN₂O₄S⁻ [M-H]⁻: 317.0977, found: 317.0980.

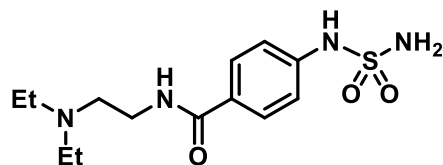


white-solid (42.75 mg, 75% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 6:1). **¹H NMR** (400 MHz, Methanol-*d*₄) δ 8.02 – 7.86 (m, 2H), 7.29 – 7.19 (m, 2H), 4.40 (t, *J* = 5.9 Hz, 2H), 2.90 (t, *J* = 5.9 Hz, 2H), 2.69 (q, *J* = 7.2 Hz, 4H), 1.10 (t, *J* = 7.2 Hz, 6H). **¹³C 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 C₁₃H₂₂N₃O₄S⁺ [M + H]⁺ 316.1326, found 316.1317.



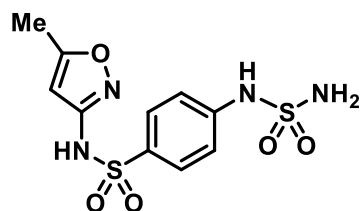
white-solid (40.50 mg, 83% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H**

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). **¹³C 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 C₉H₁₃N₂O₄S⁺ [M + H]⁺ 245.0591, found 245.0581.



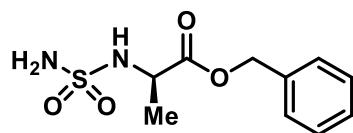
9c

white-solid (50.24 mg, 80% yield). The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 6:1). **¹H 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). **¹³C 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 C₁₃H₂₃N₄O₃S⁺ [M + H]⁺ 315.1485, found 315.1479.



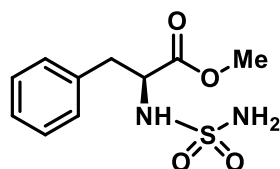
9d

white-solid (42.50 mg, 64% yield). The product was purified by preparative HPLC. **¹H 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). **¹³C 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 C₁₀H₁₃N₄O₅S₂⁺ [M + H]⁺ 333.0322, found 333.0313.



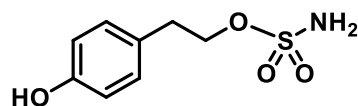
9e

white-solid (32.00 mg, 62% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1). **¹H 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). **¹³C 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 C₁₀H₁₅N₂O₄S⁺ [M + H]⁺ 259.0747, found 259.0737.



9f

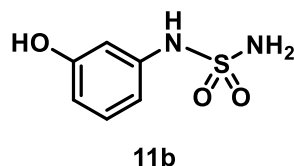
white-solid (35.61 mg, 69% yield) The product was purified by flash column chromatography on silica gel (eluent: dichloromethane/ammonia methanol = 10:1) **¹H NMR** (400 MHz, Methanol-*d*₄) δ 7.35 – 7.17 (m, 5H), 4.23 (t, *J* = 7.0 Hz, 1H), 3.65 (s, 3H), 3.03 (d, *J* = 7.0 Hz, 2H). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 172.8, 136.4, 129.1, 128.1, 126.6, 57.4, 51.3, 38.5. HRMS calc'd for C₁₀H₁₃N₂O₄S⁻ [M - H]⁻ 257.0602, found 257.0602.



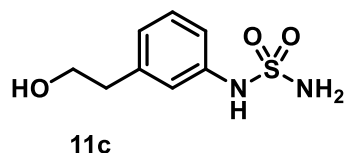
11a

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

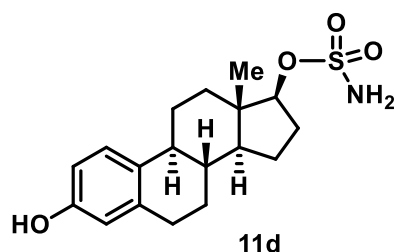
dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na₂CO₃ (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. By comparing with the 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). **¹H 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). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 155.8, 129.6, 127.8, 114.9, 70.3, 34.1 HRMS calc'd for C₈H₁₀NO₄S⁻ [M - H]⁻ 216.0336, found 216.0338.



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 Na₂CO₃ (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na₂SO₄ 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). **¹H 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). **¹³C NMR** (101 MHz, Methanol-*d*₄) δ 157.7, 140.0, 129.4, 110.4, 110.0, 106.3. HRMS calc'd for C₆H₉N₂O₃S⁺ [M + H]⁺ 189.0328, found 189.0328.

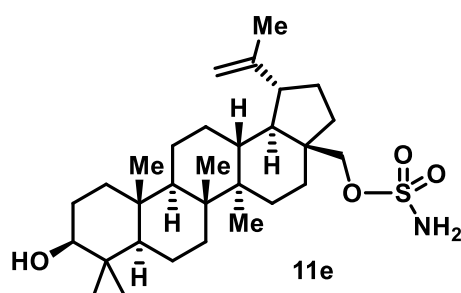


10c (0.2 mmol), 1 (0.2 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 1.5 hours, 1(0.1 mmol) was added. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na₂CO₃ (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na₂SO₄ 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) **¹H 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). **¹³C 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 C₈H₁₆N₃O₃S⁺ [M + NH₄]⁺ 234.0907 , found 234.0908.



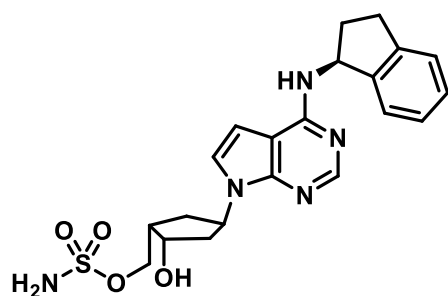
10d (0.2 mmol), 1 (0.3 mmol) and dry dichloromethane (3 mL) were added to the reaction vessel at room temperature, and the mixture was stirred for 3 hours. After the completion of the reaction was indicated by TLC, the solvent was evaporated, anhydrous acetonitrile (3 mL) was added, and HCl (12M) in water (0.5 mL) was added dropwise at room temperature. The mixture was concentrated under reduced pressure. Saturated aqueous Na₂CO₃ (50 mL) was added to the residue, and the resulting mixture

was extracted with EA. The combined organic layer was dried over Na₂SO₄ 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) **¹H 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). **¹³C 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 C₁₈H₂₆NO₄S⁺ [M + H]⁺ 352.1577 , found 352.1572.



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 Na₂CO₃ (50 mL) was added to the residue, and the resulting mixture was extracted with EA. The combined organic layer was dried over Na₂SO₄ 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) **¹H 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 $\text{C}_{30}\text{H}_{51}\text{ClNO}_4\text{S}^- [\text{M} + \text{Cl}]^-$ 556.3233, found 556.3243.



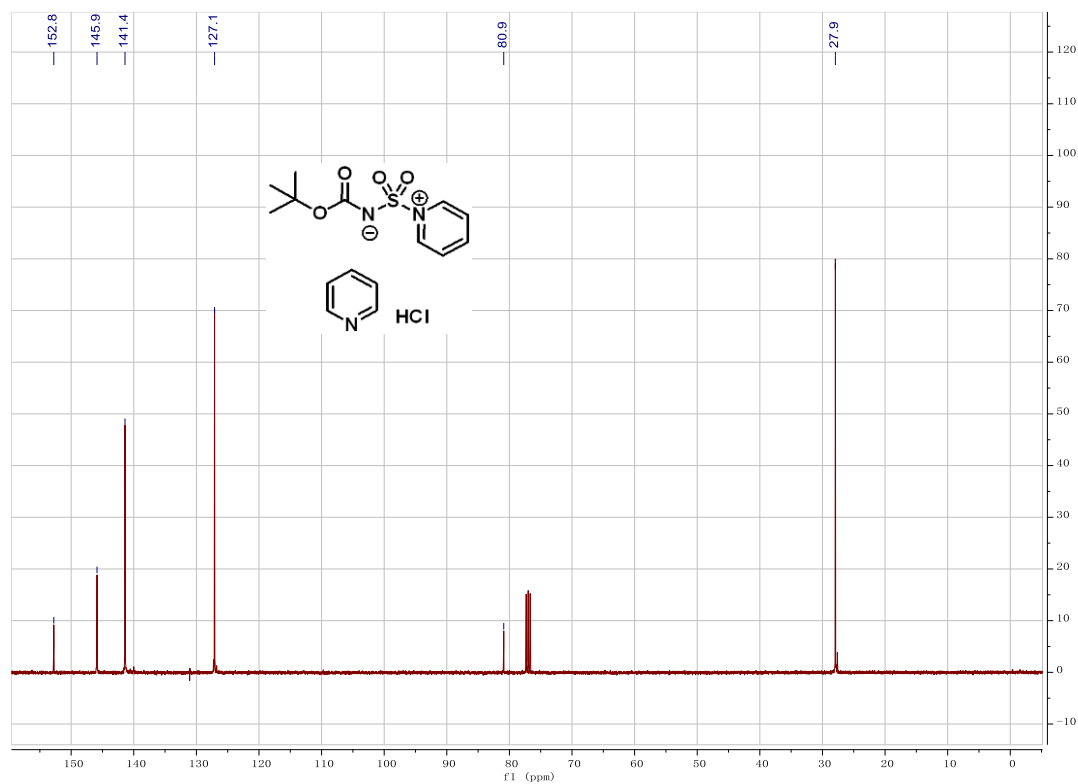
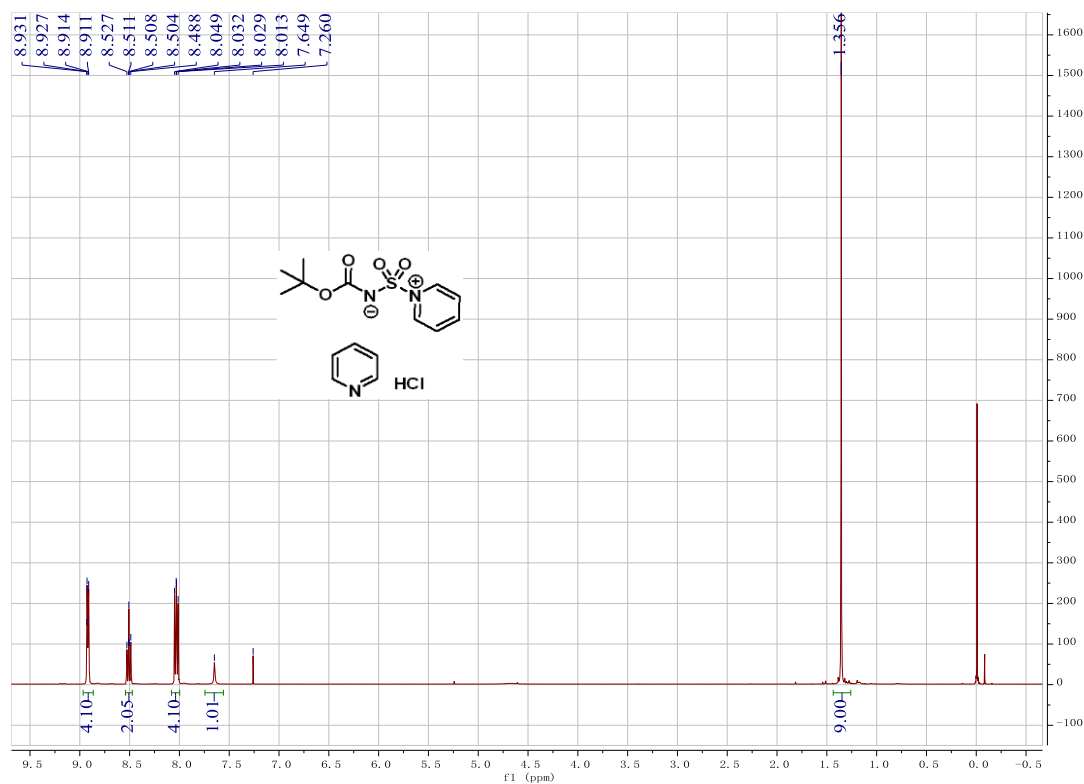
11f

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). **^1H 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,

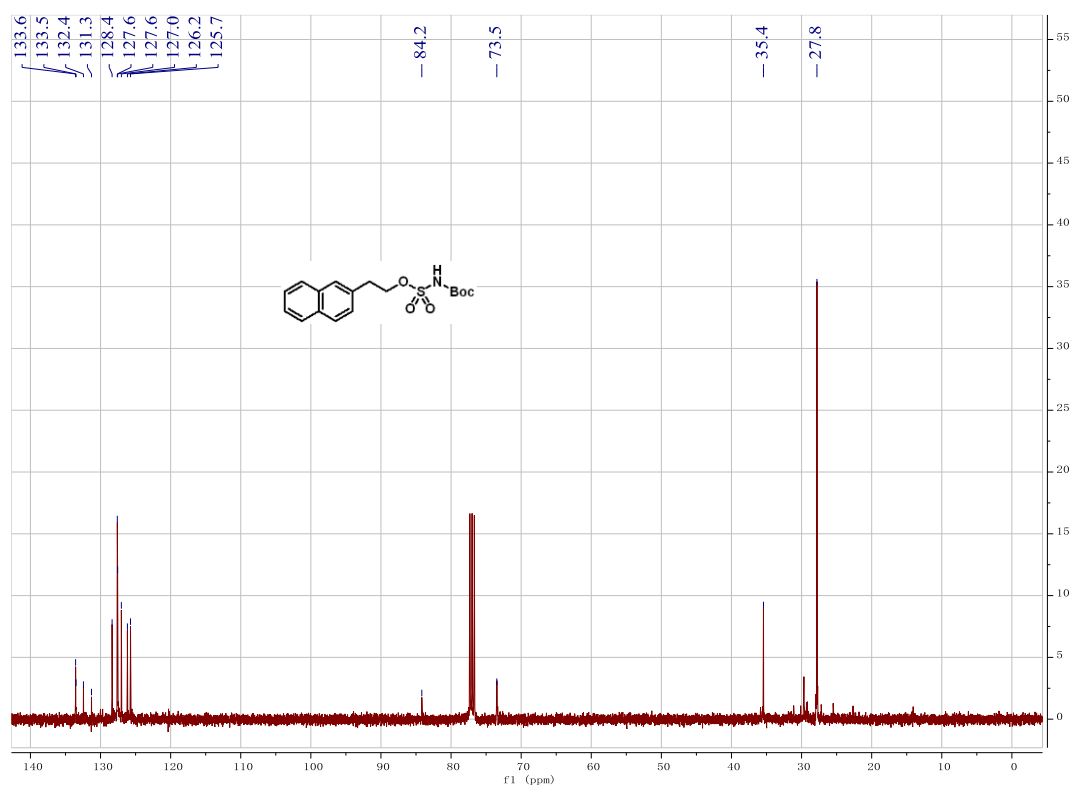
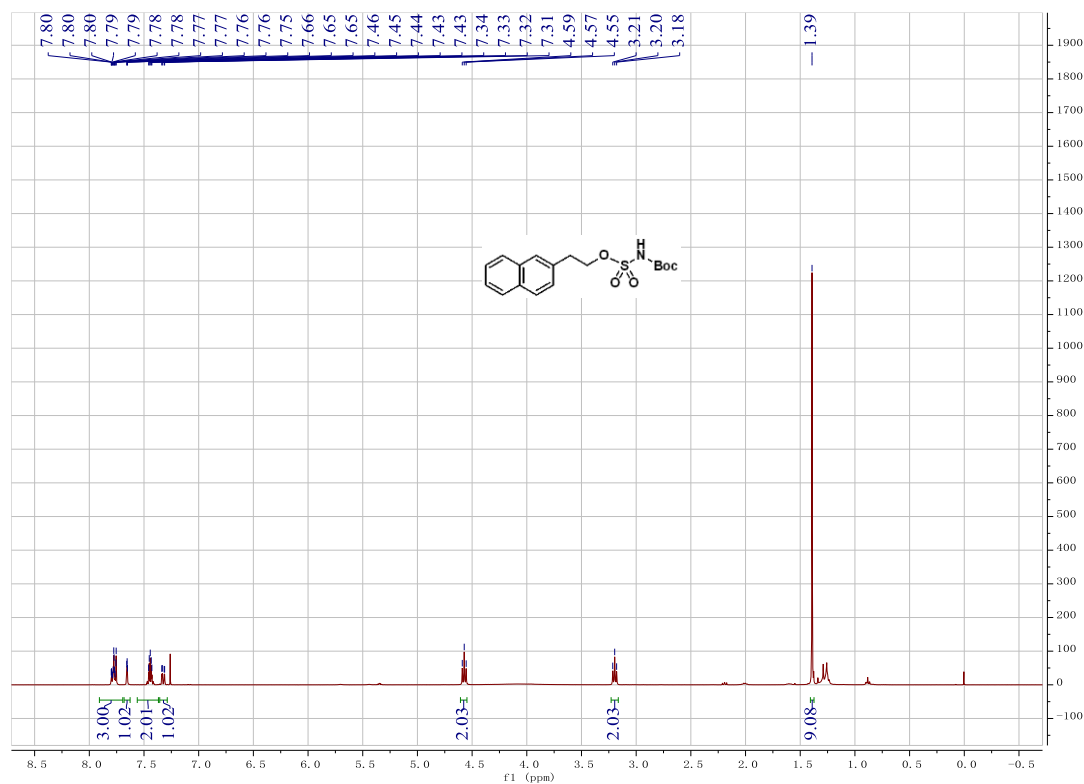
150.6, 148.6, 143.8, 143.2, 127.4, 126.2, 124.3, 123.8, 121.2, 103.4, 99.1, 71.6, 69.4, 55.5, 52.6, 43.3, 42.1, 33.5, 33.2, 29.7. **ESI:** $m/z [M + H]^+$: 444.2 The characterization data were consistent with the literature¹.

9. Copies of NMR spectra data

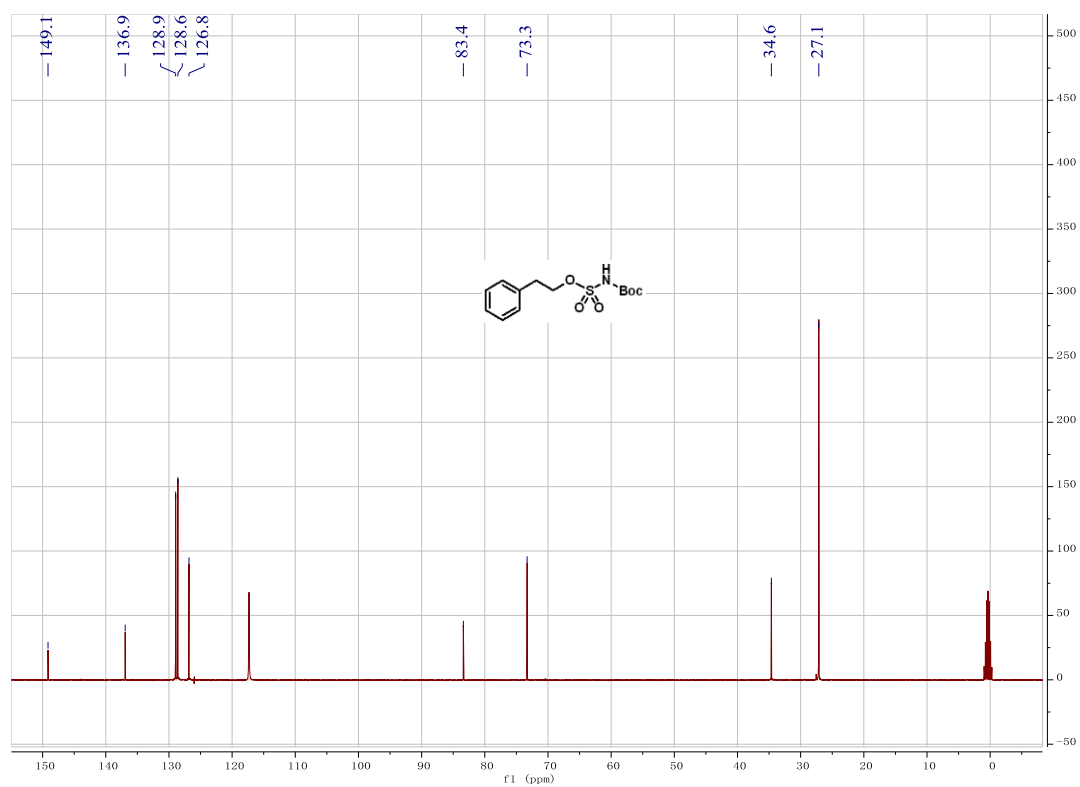
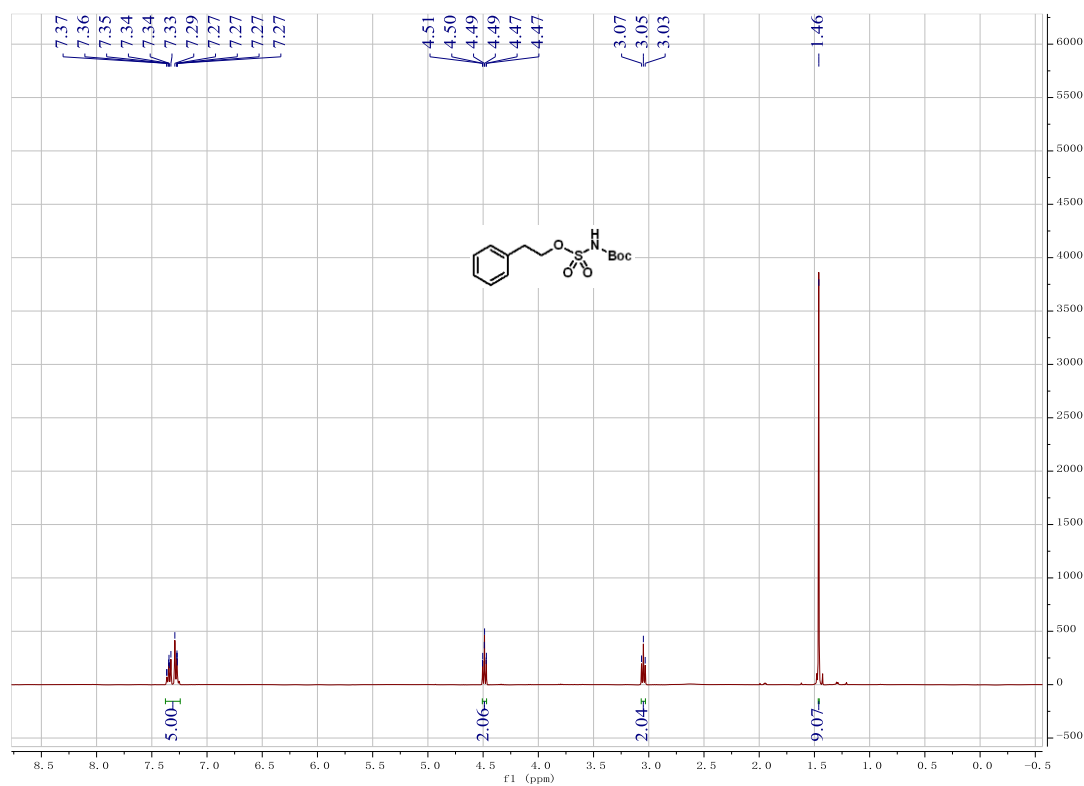
^1H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 1



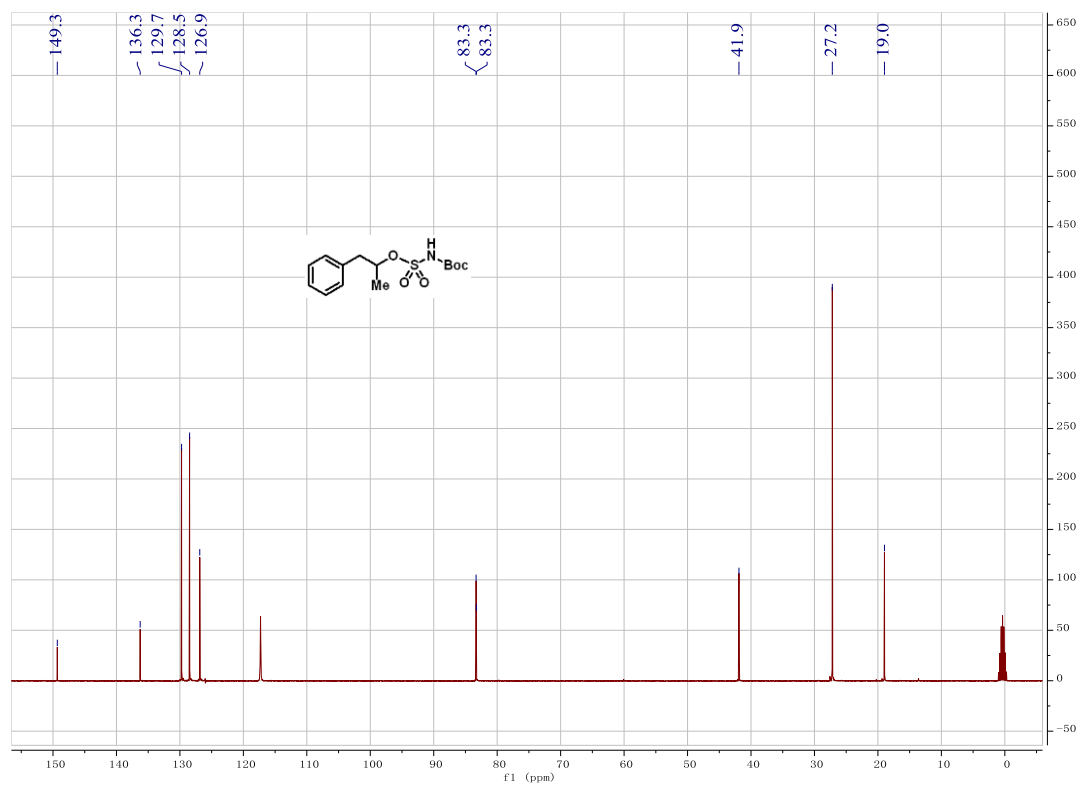
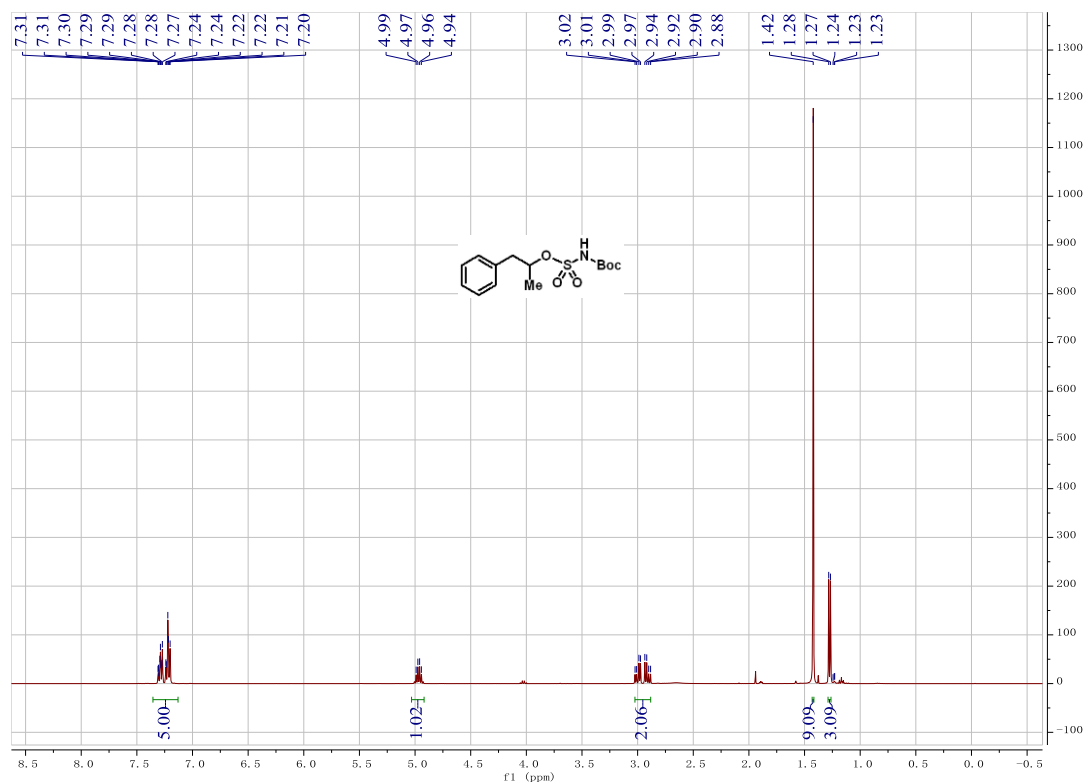
^1H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 3a



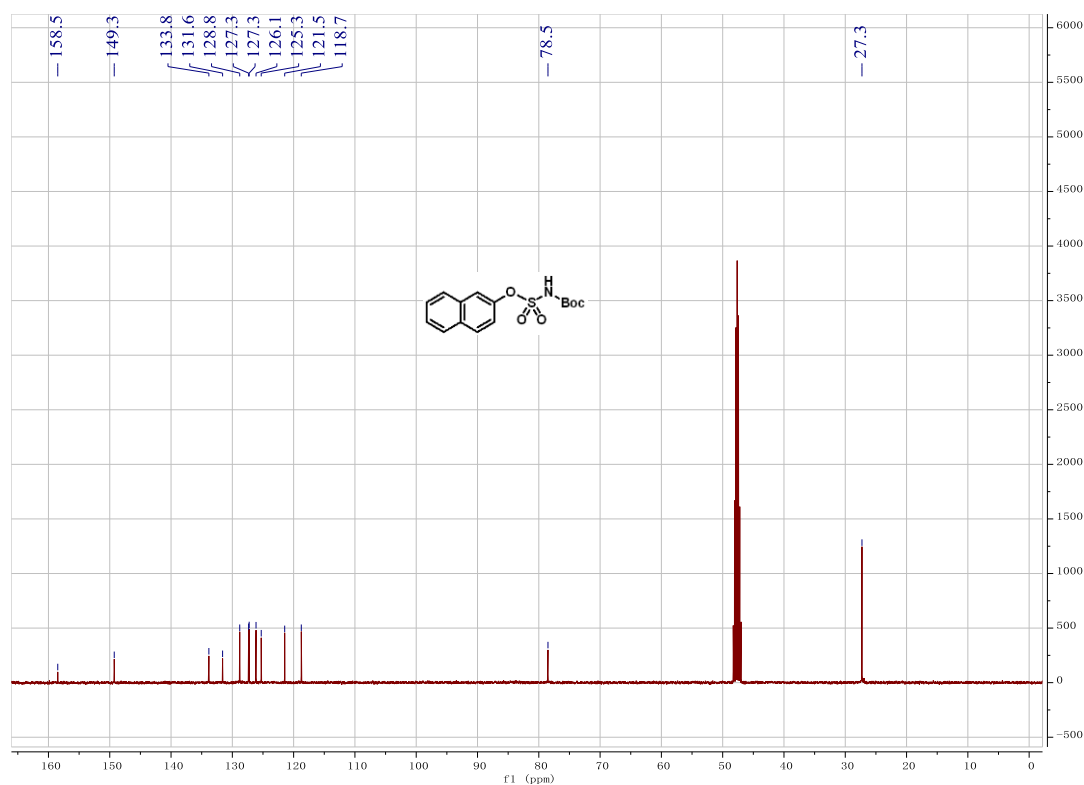
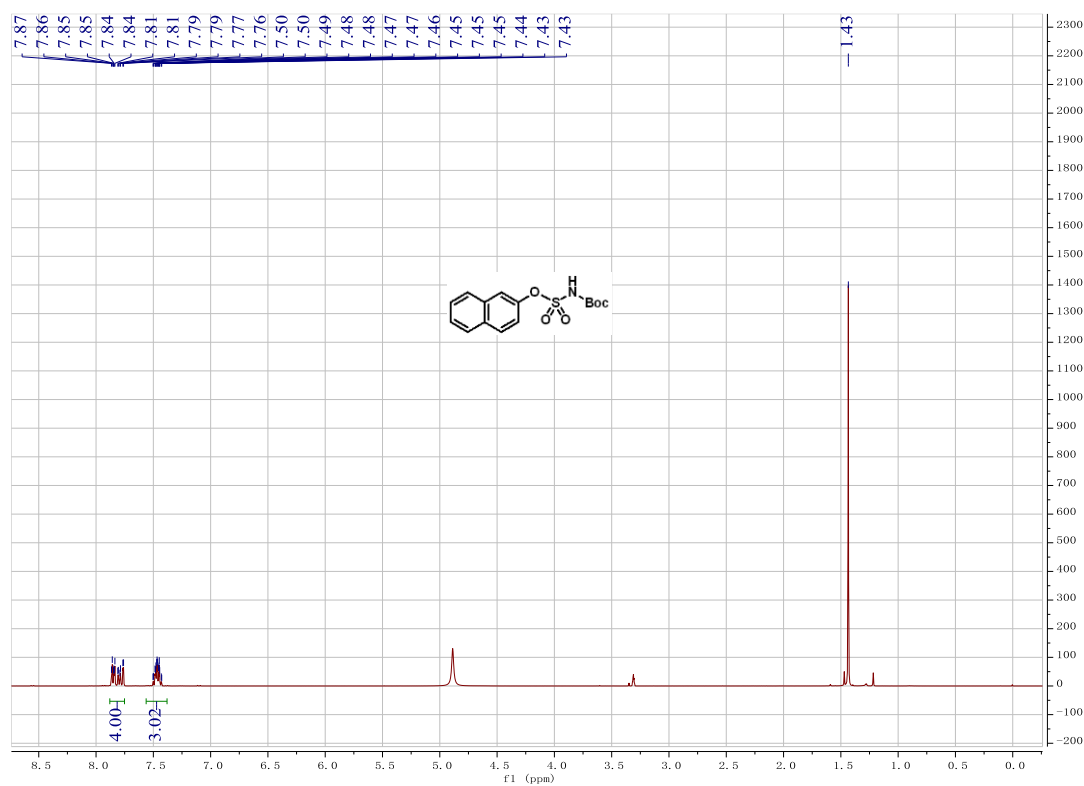
^1H (400 MHz, Acetonitrile- d_3) and ^{13}C (101 MHz, Acetonitrile- d_3) spectra of compound 3b



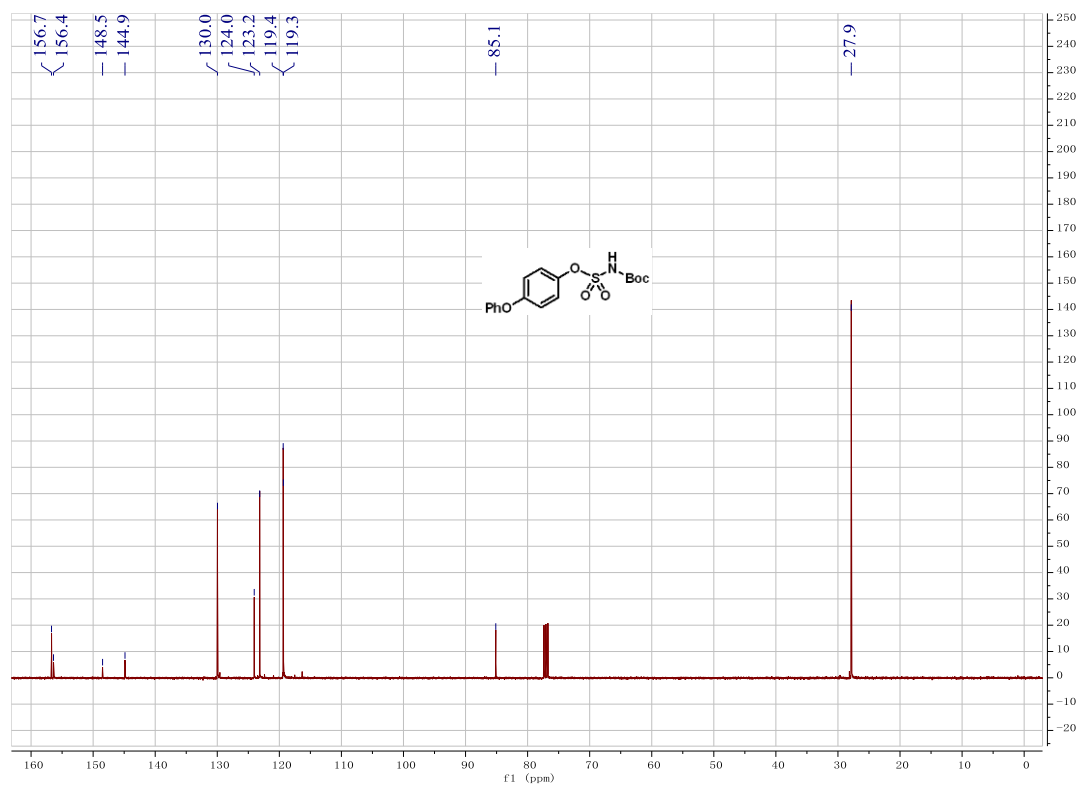
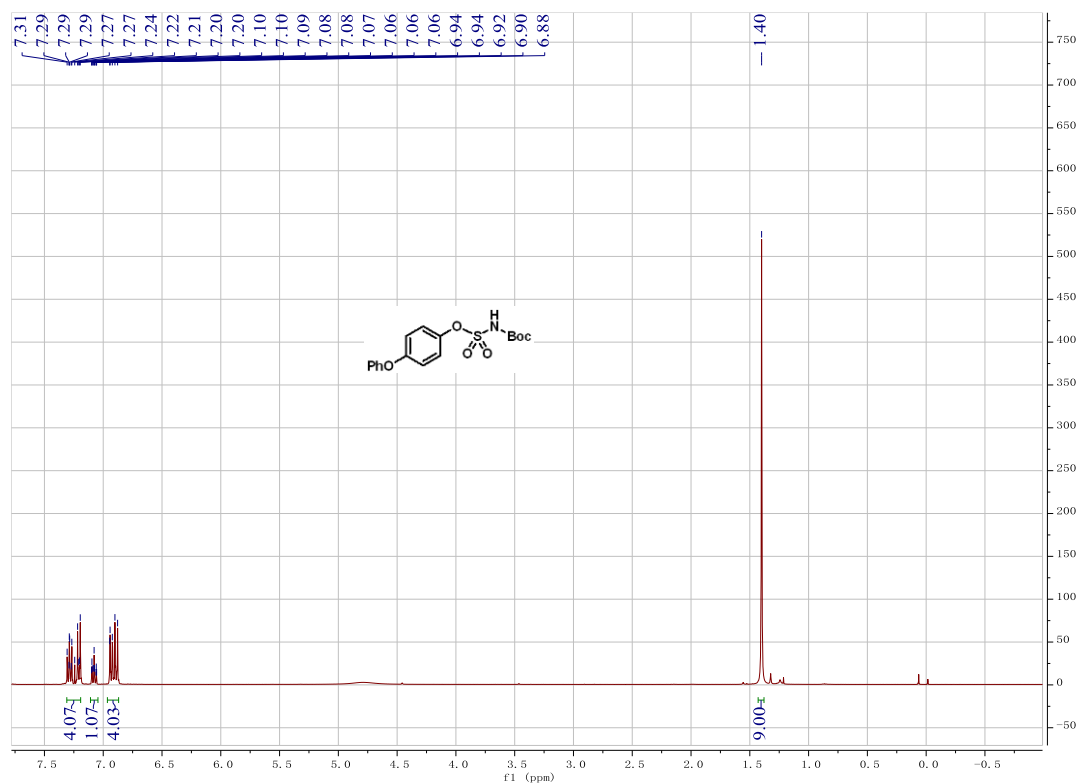
^1H (400 MHz, Acetonitrile- d_3) and ^{13}C (400 MHz, Acetonitrile- d_3) spectra of compound **3c**



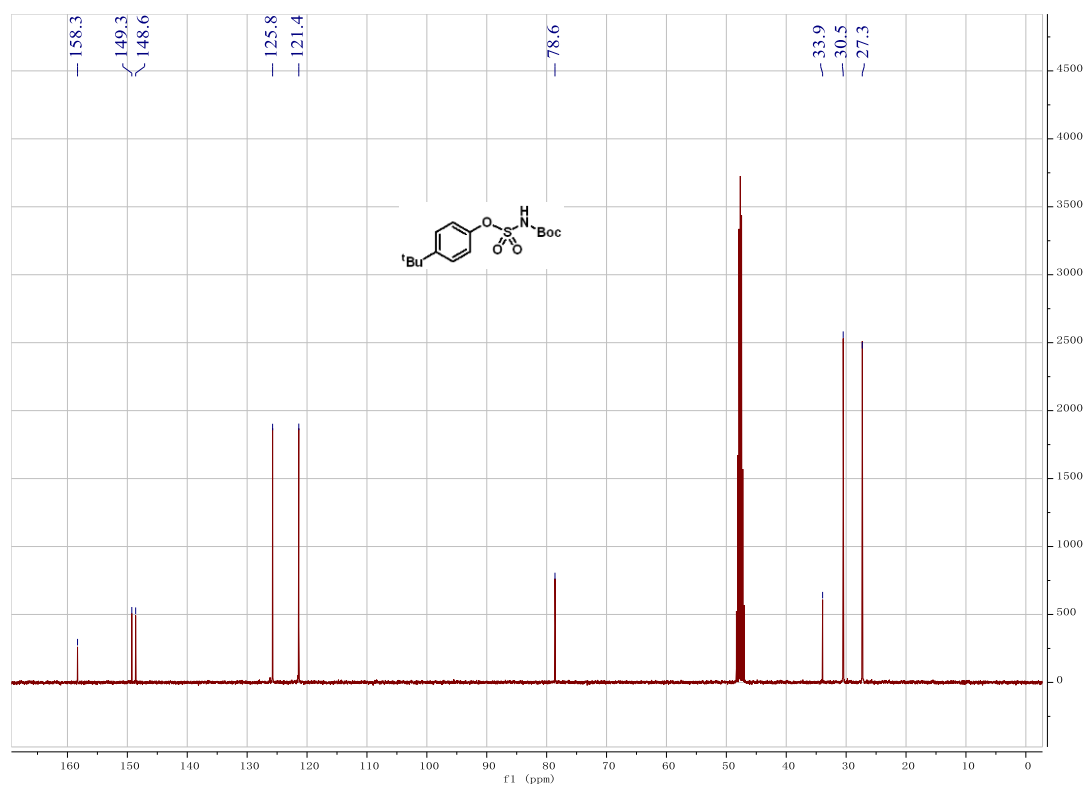
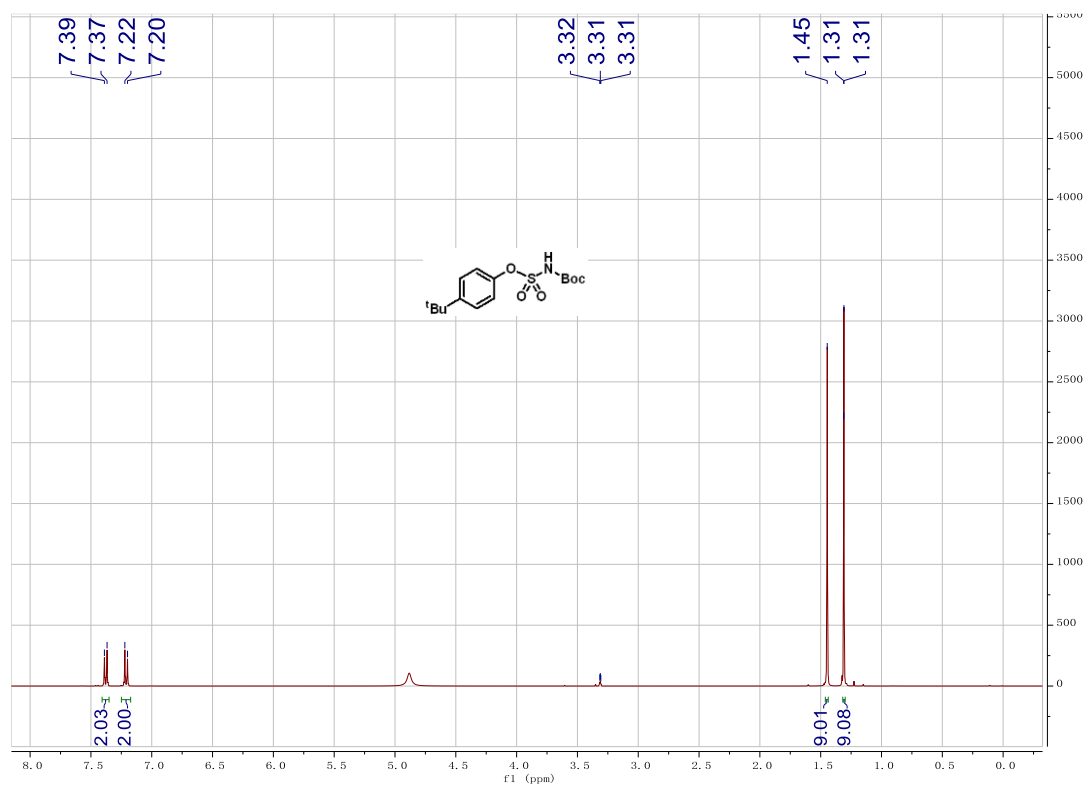
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 3d



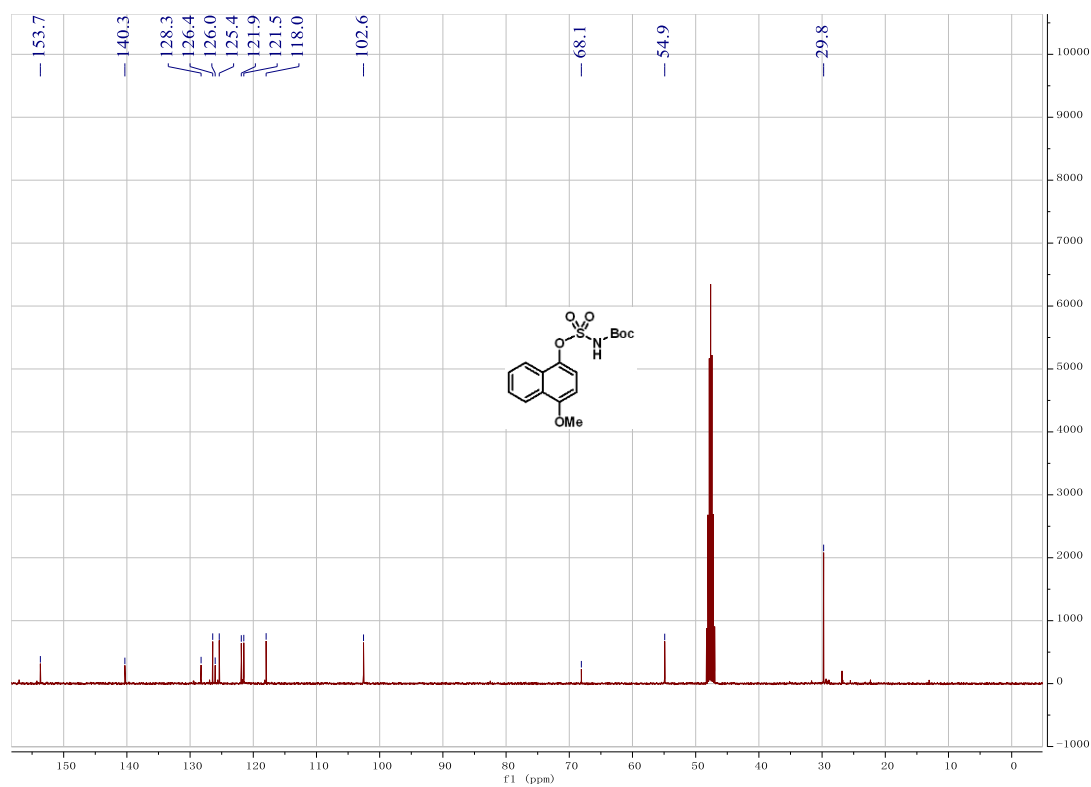
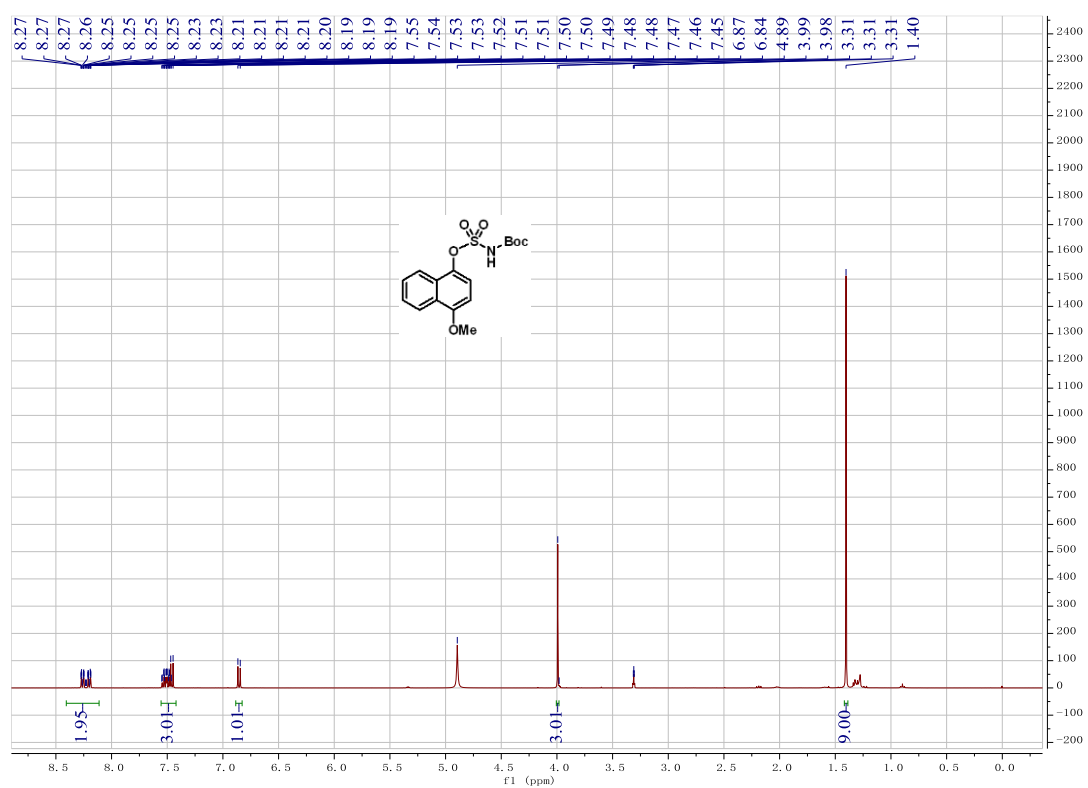
^1H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 3e



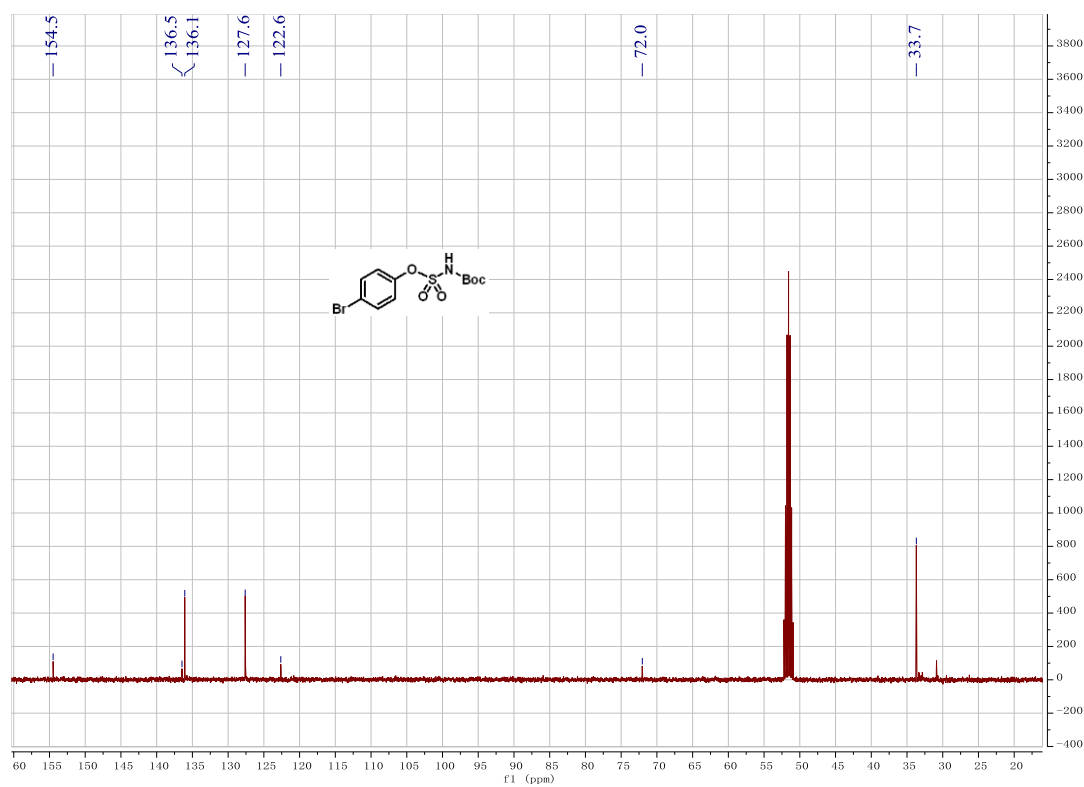
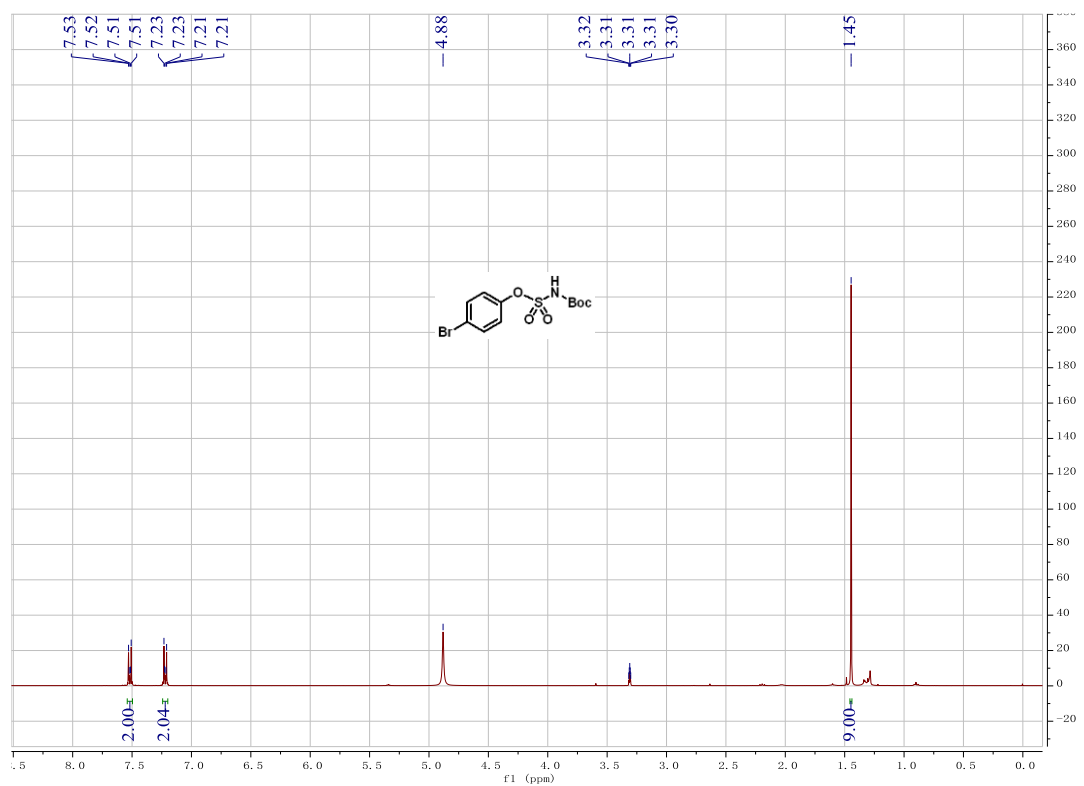
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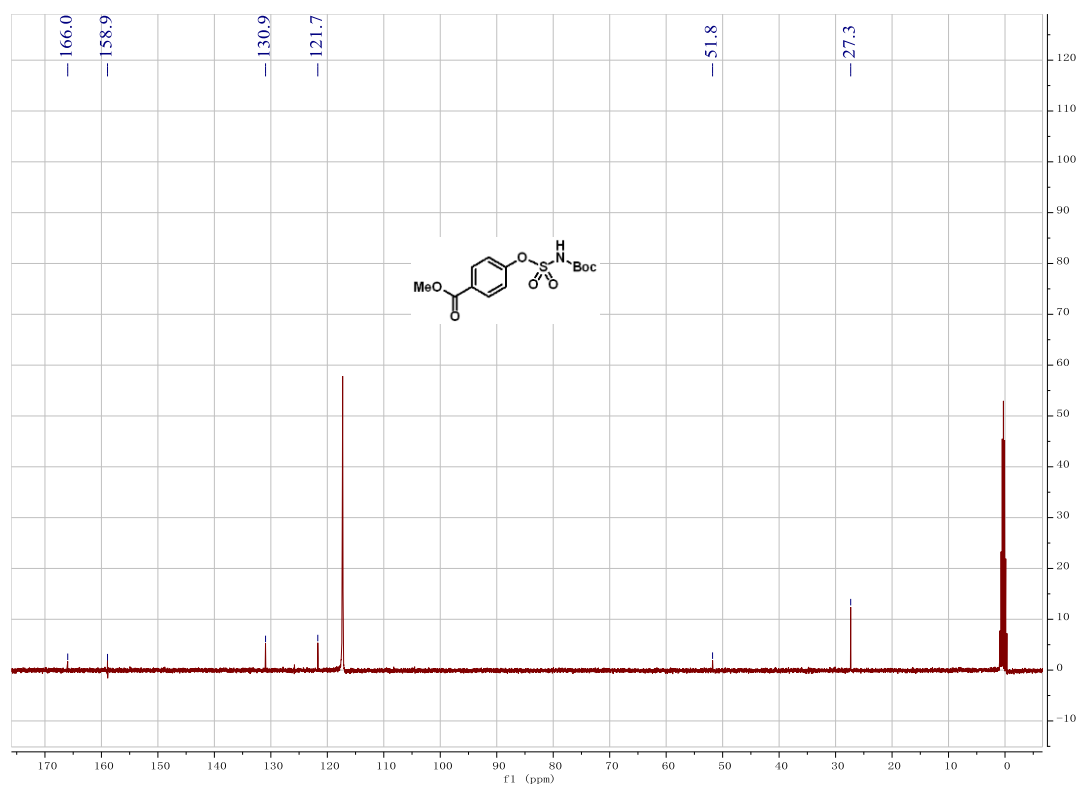
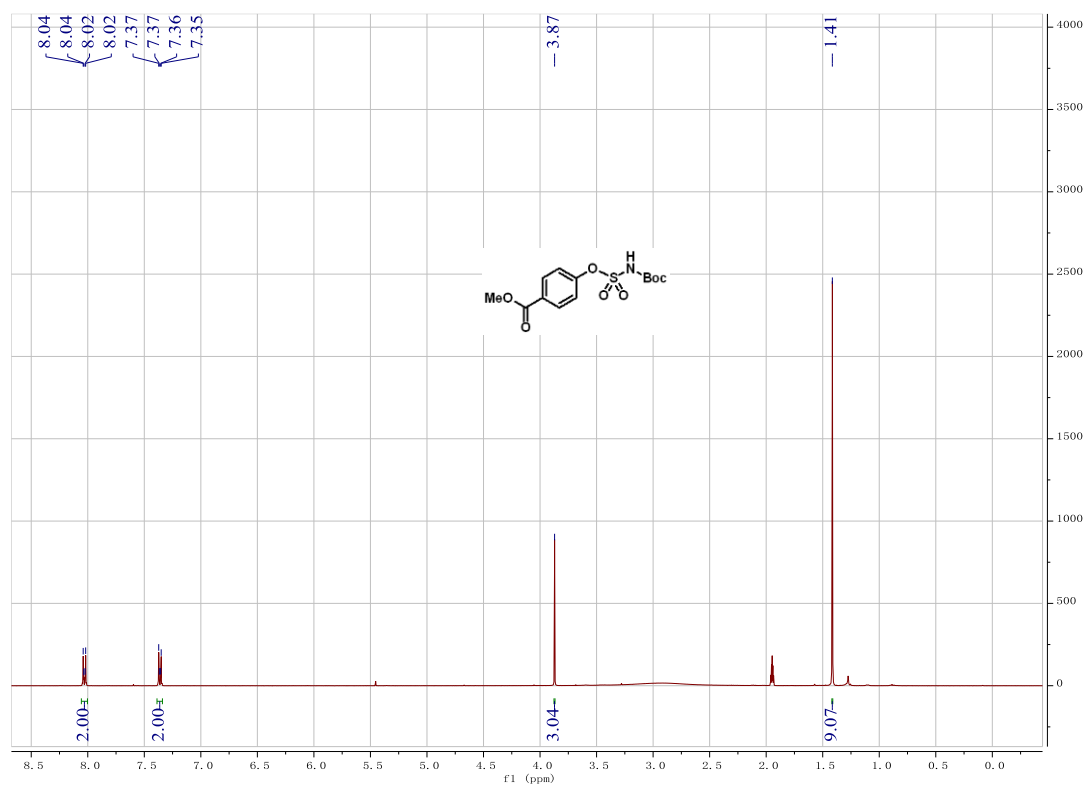
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 3g



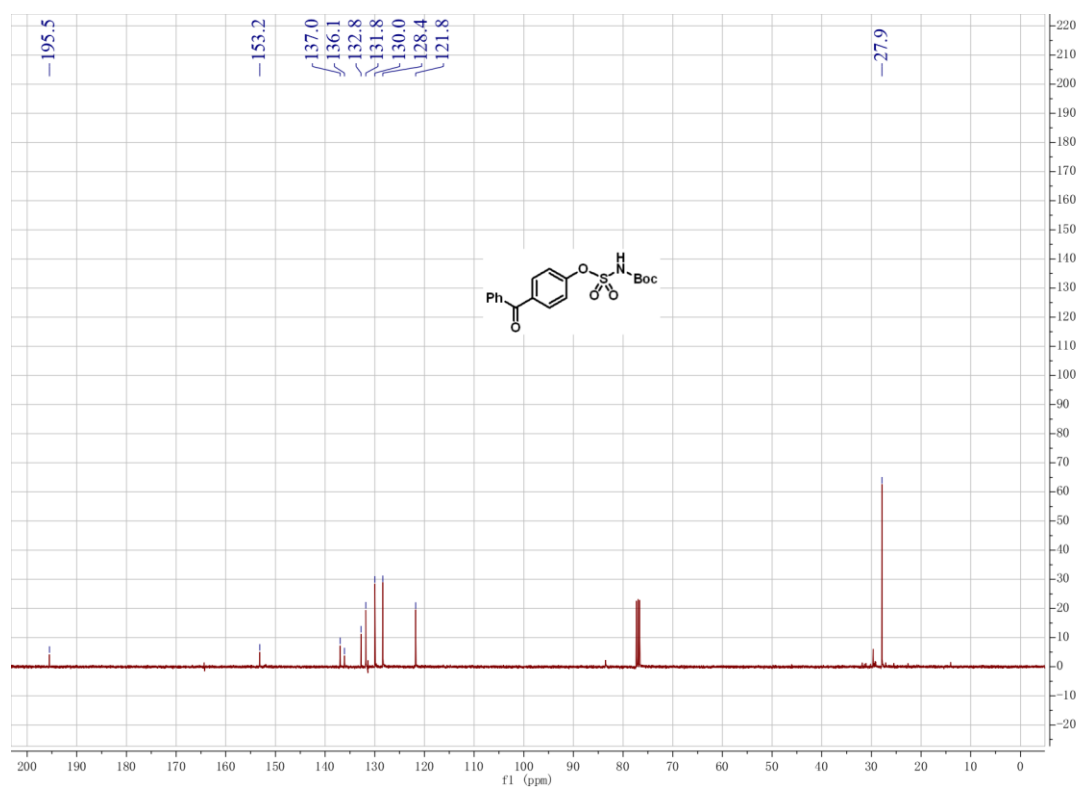
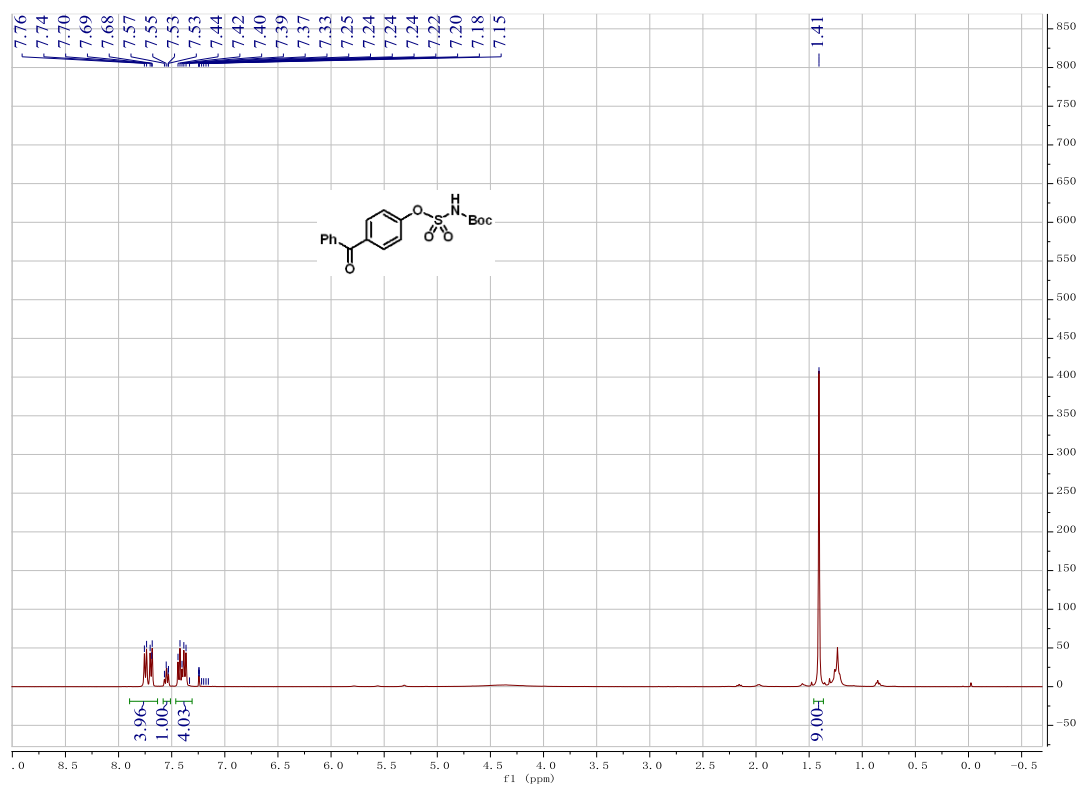
^1H (400 MHz, Methanol- d_4) and ^{13}C (400 MHz, Methanol- d_4) spectra of compound 3h



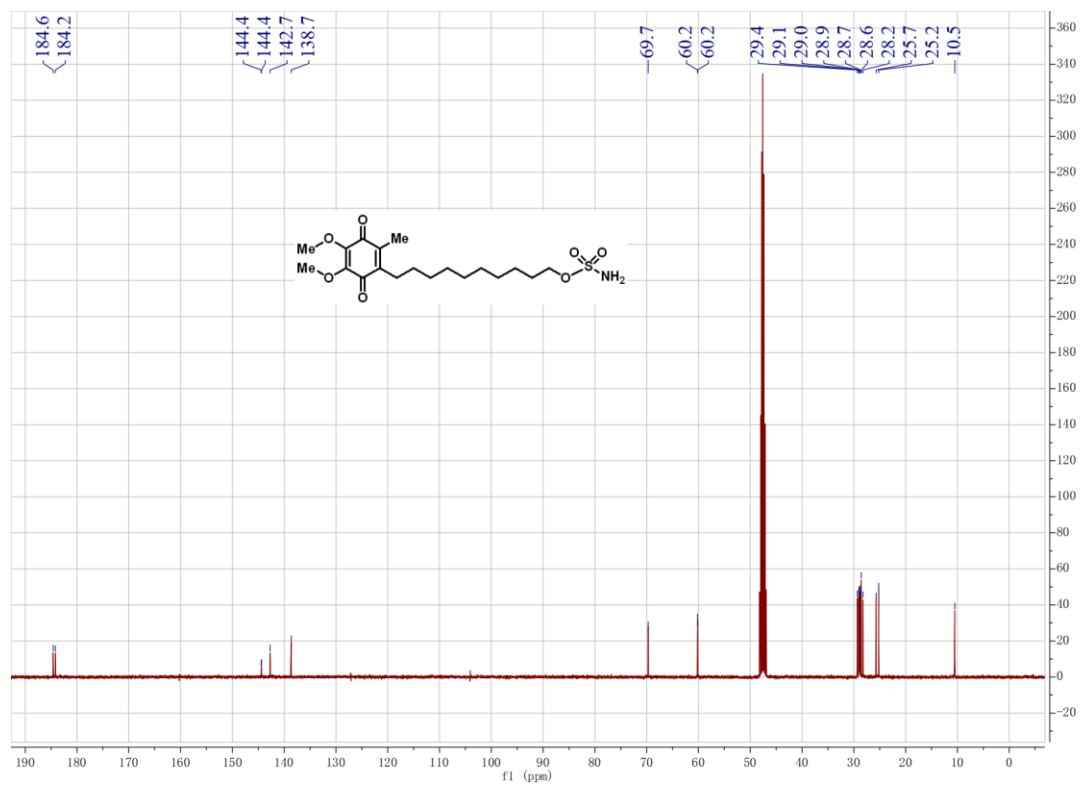
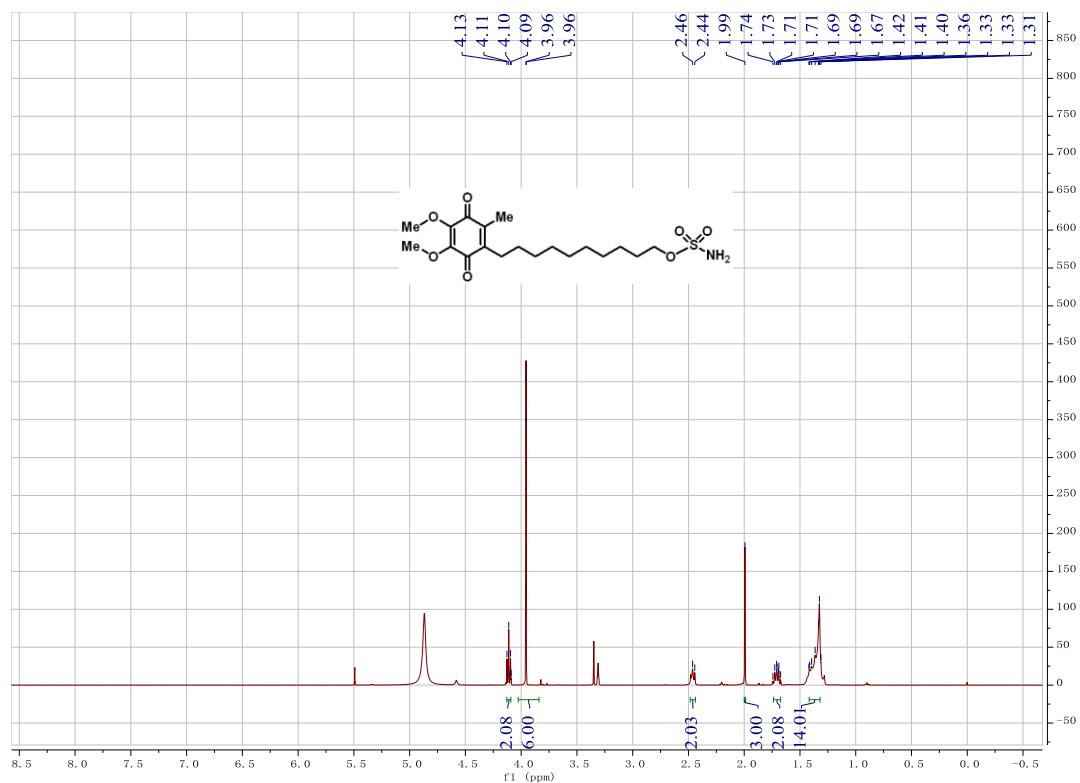
^1H (400 MHz, Acetonitrile- d_3) and ^{13}C (101 MHz, Acetonitrile- d_3) spectra of compound 3i



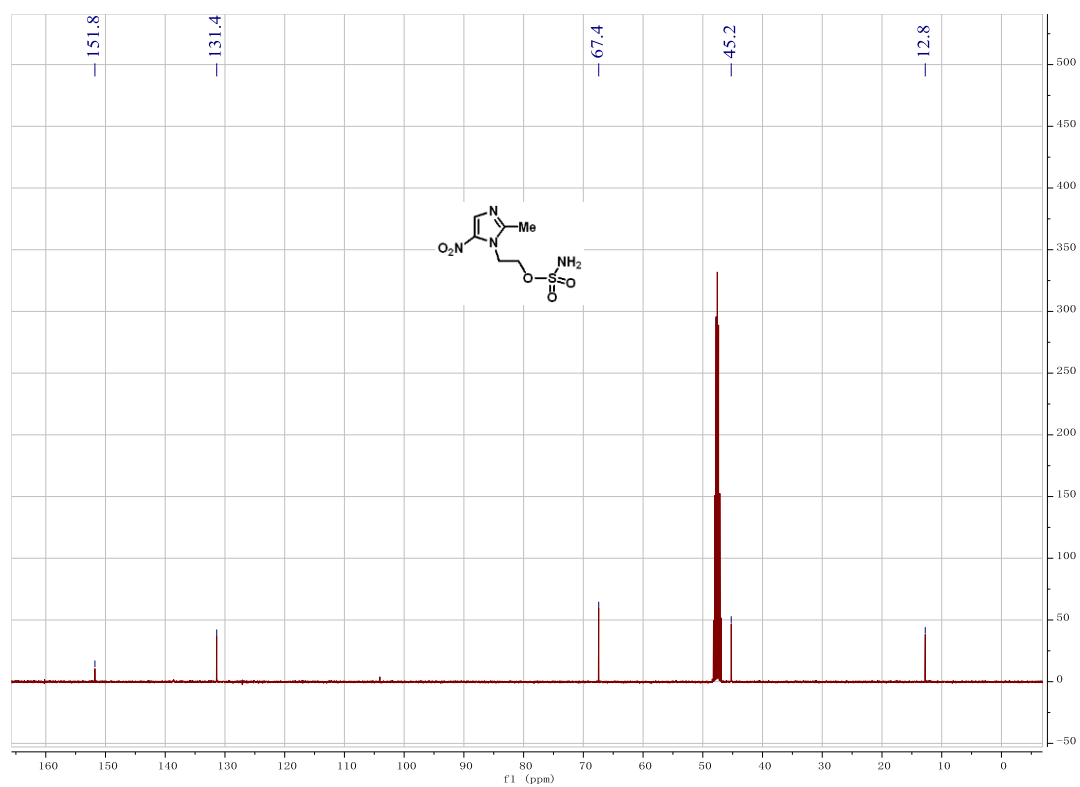
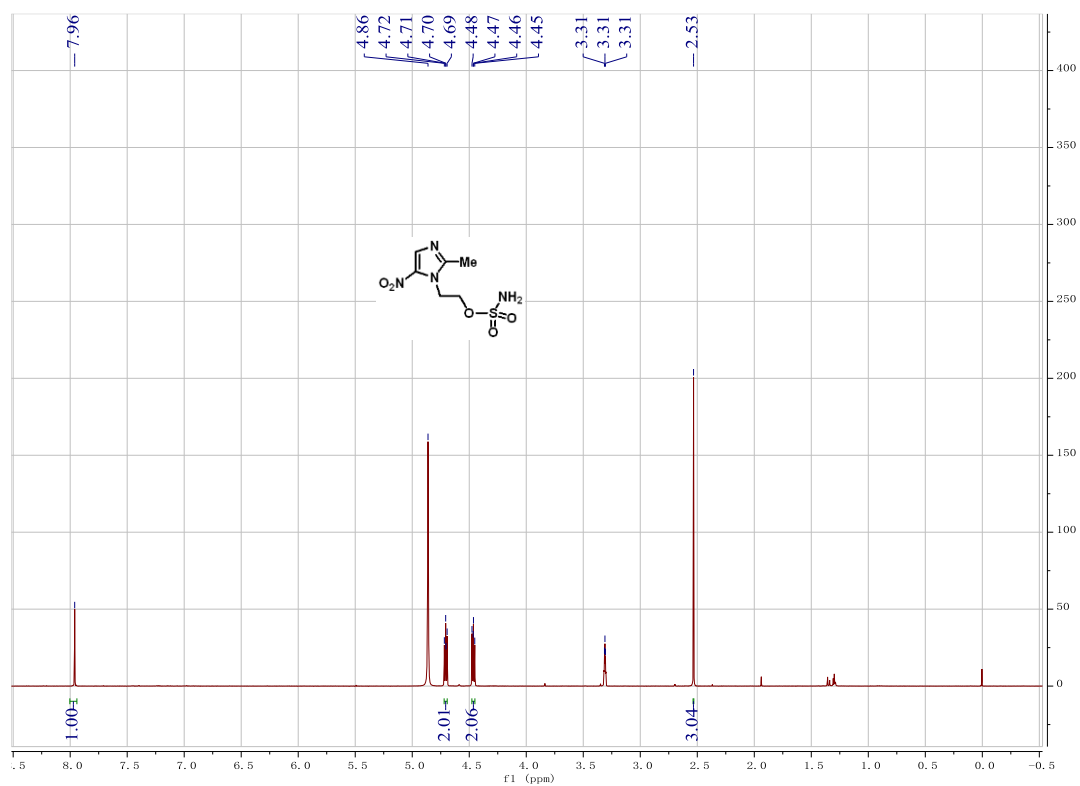
^1H (400 MHz, Chloroform-*d*) and ^{13}C (101 MHz, Chloroform-*d*) spectra of compound 3j



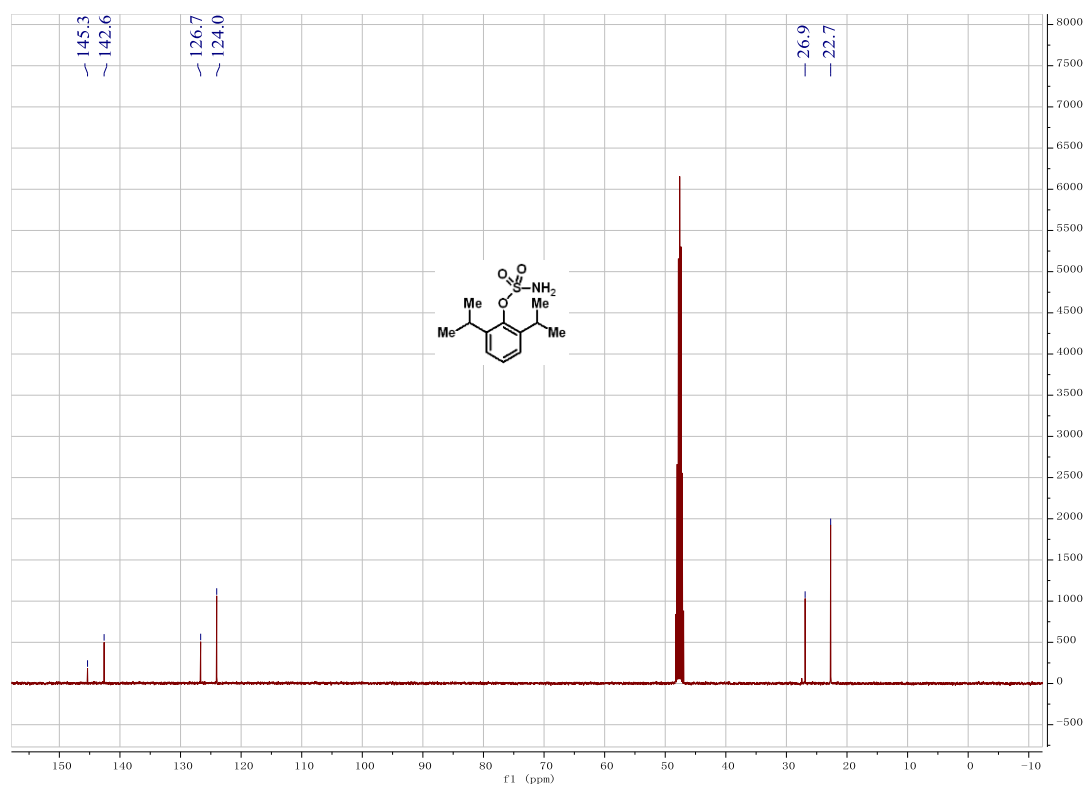
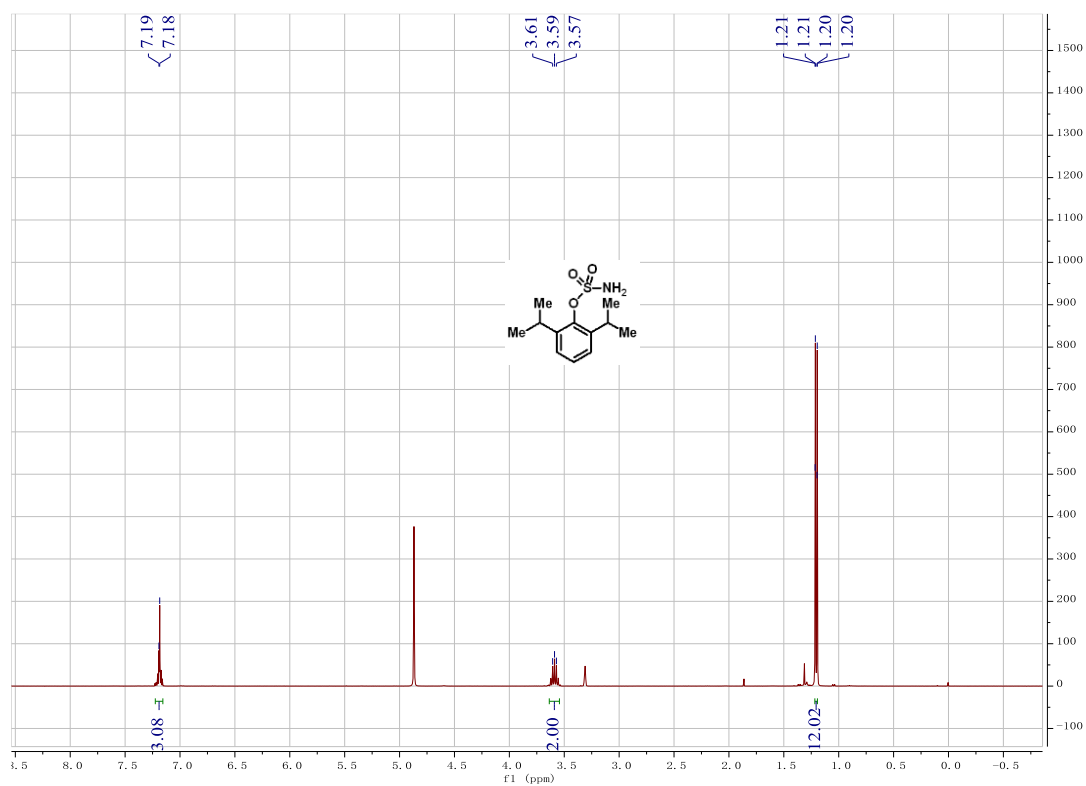
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 5a



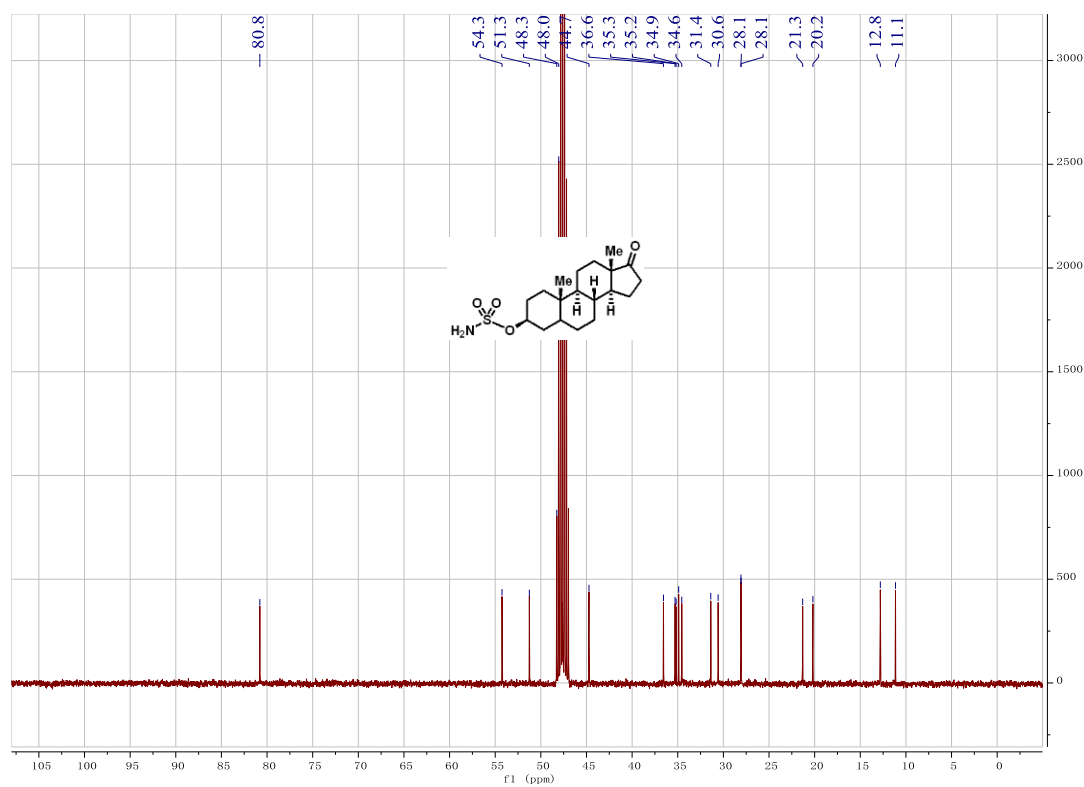
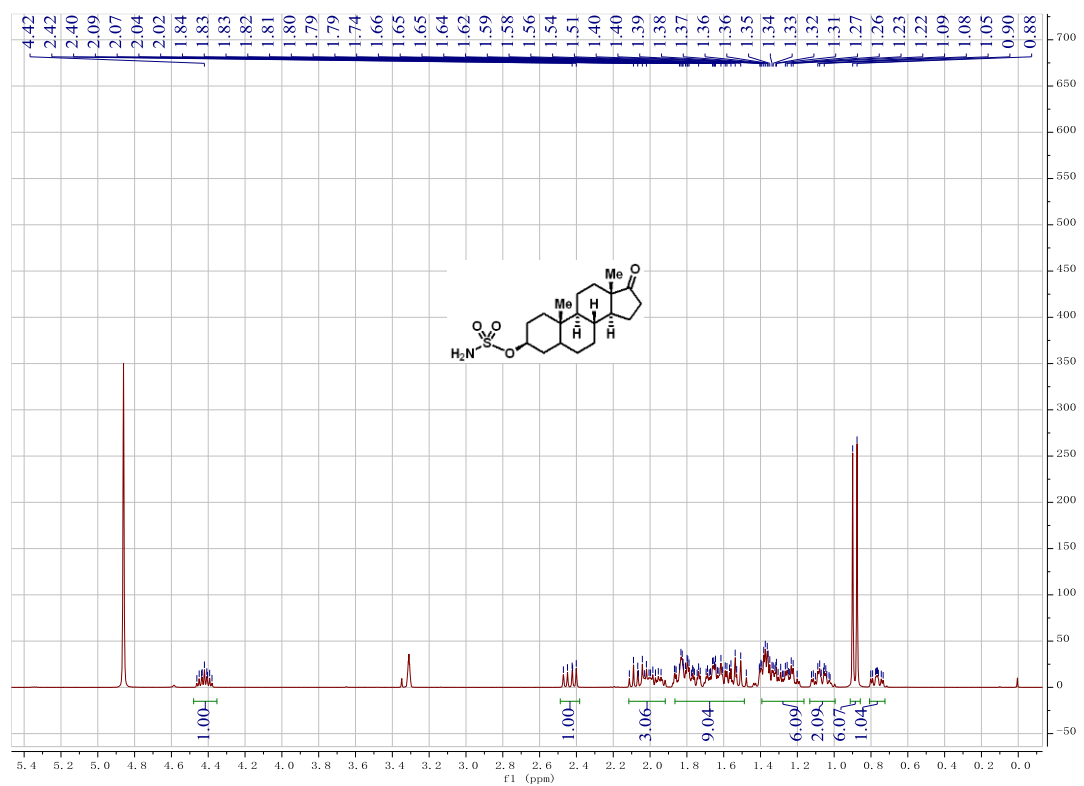
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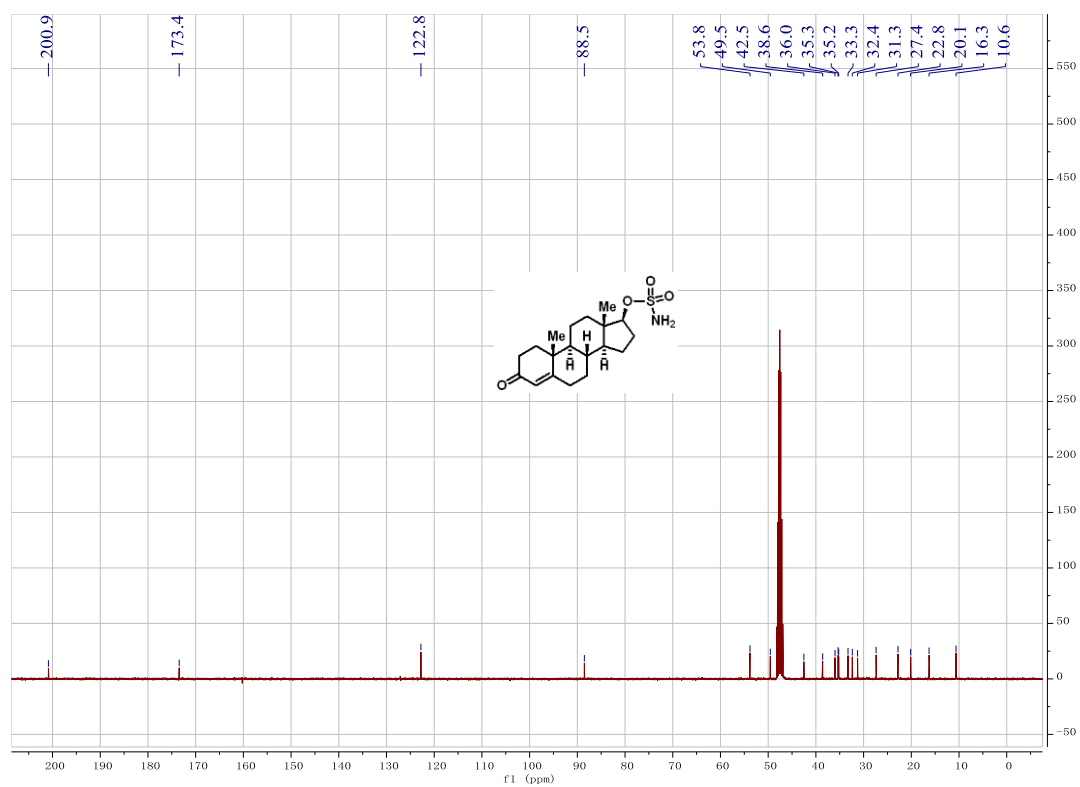


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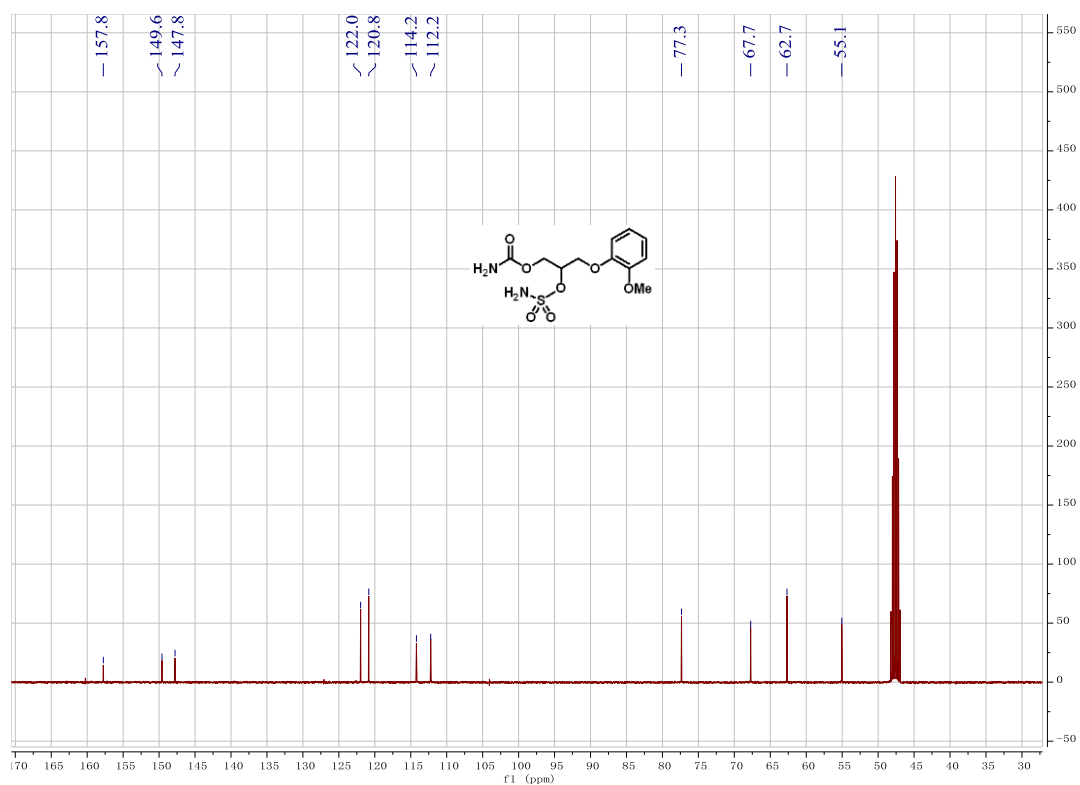
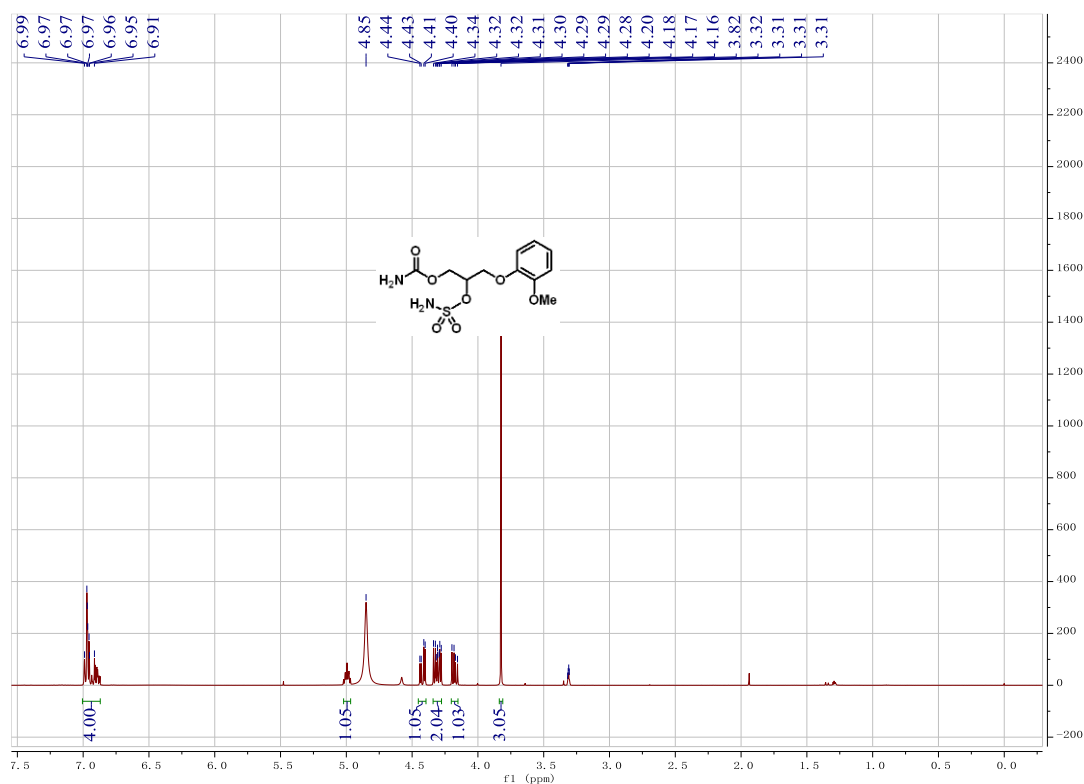


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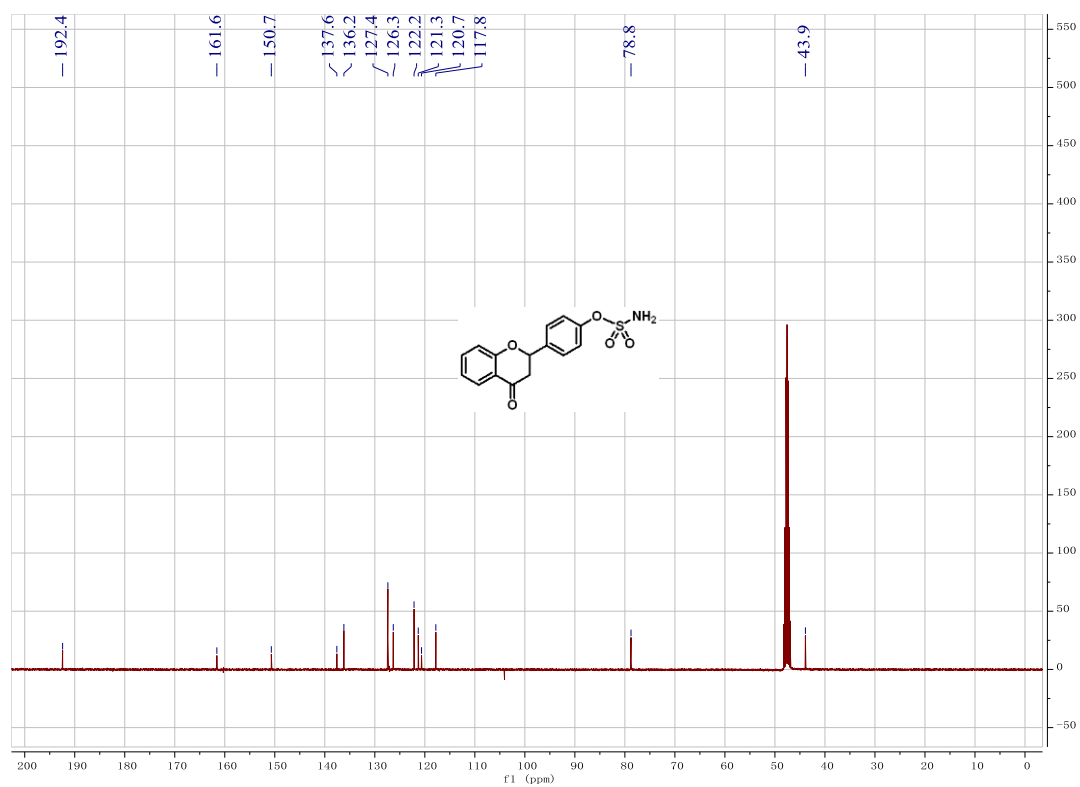
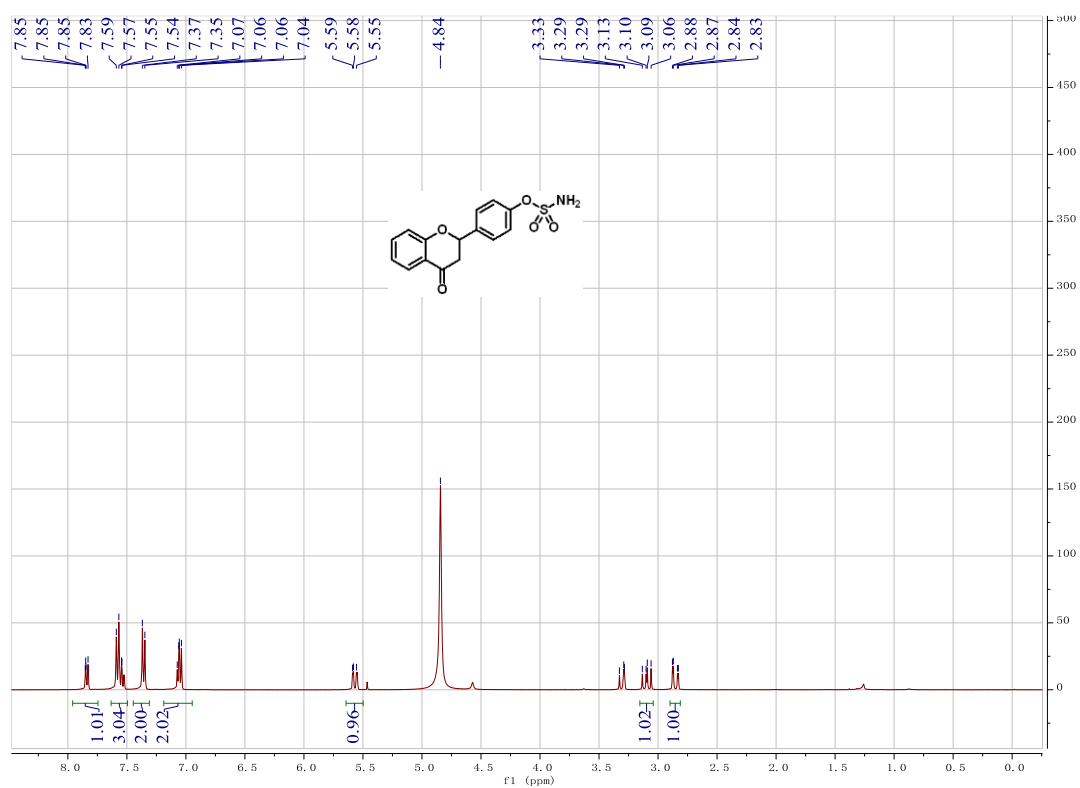




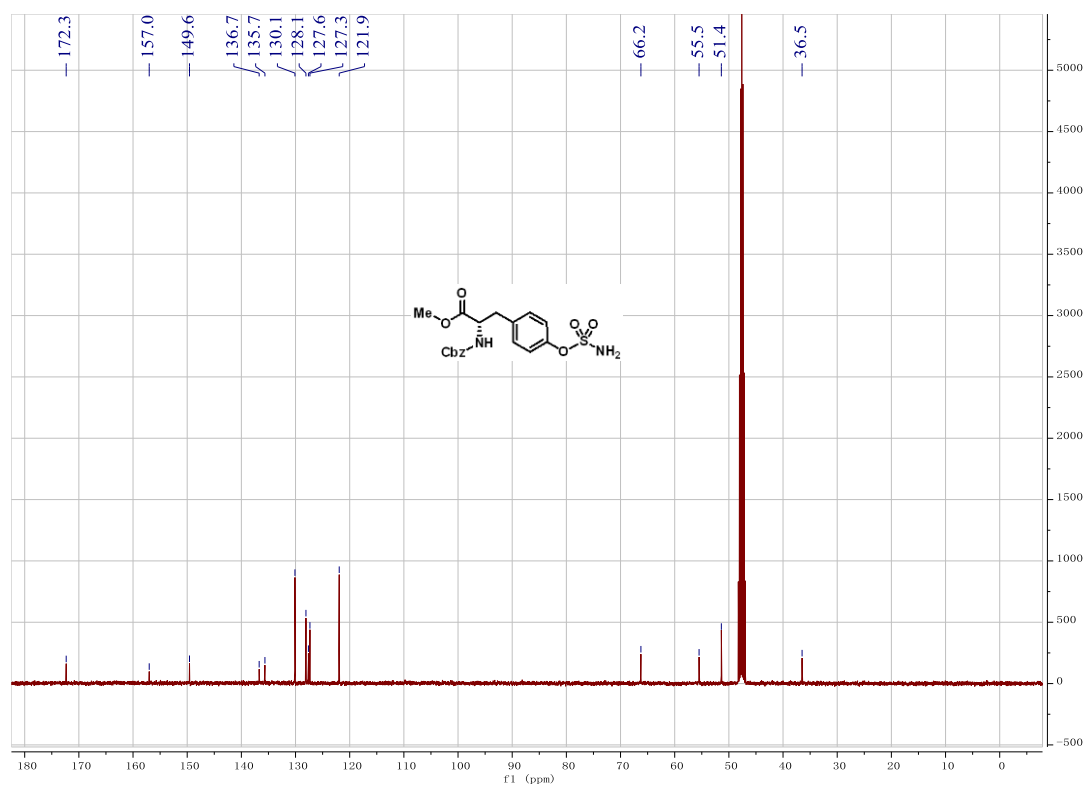
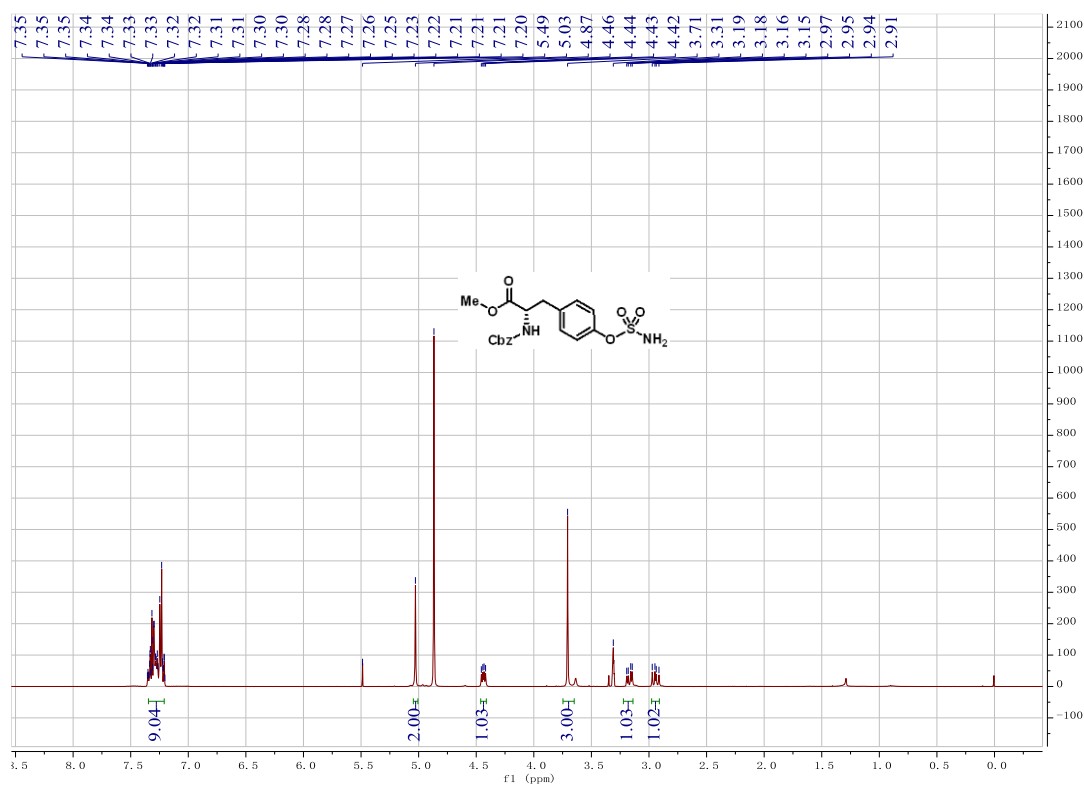
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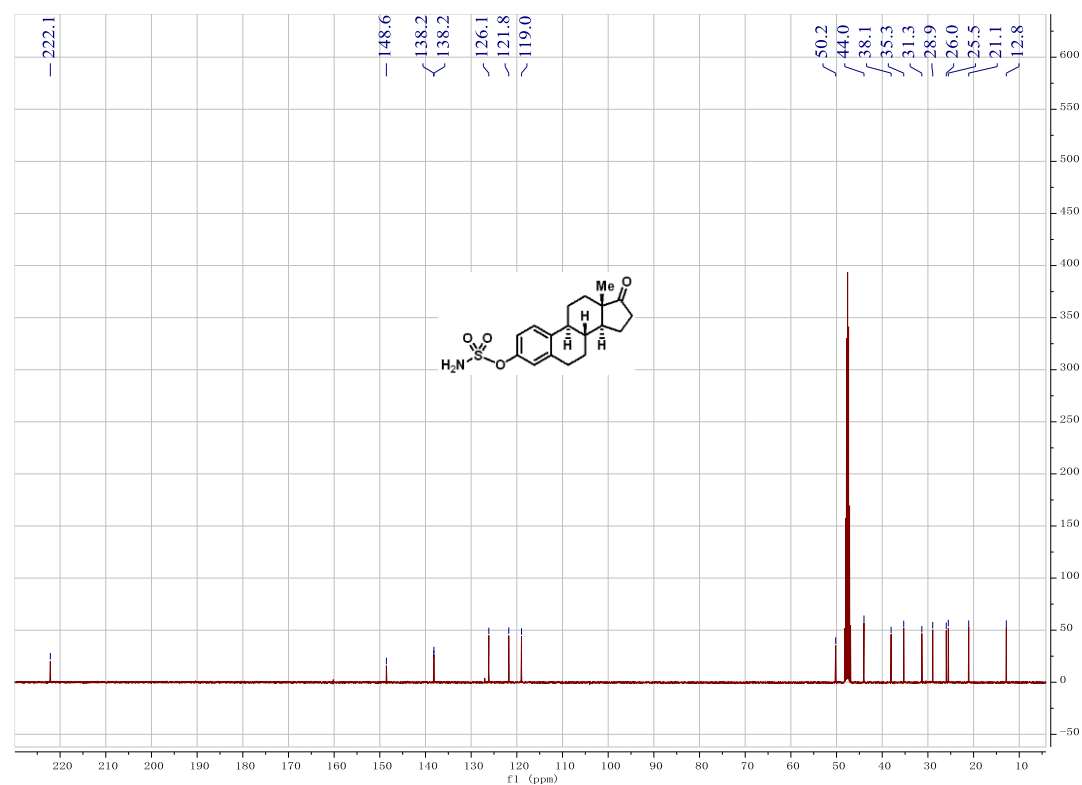
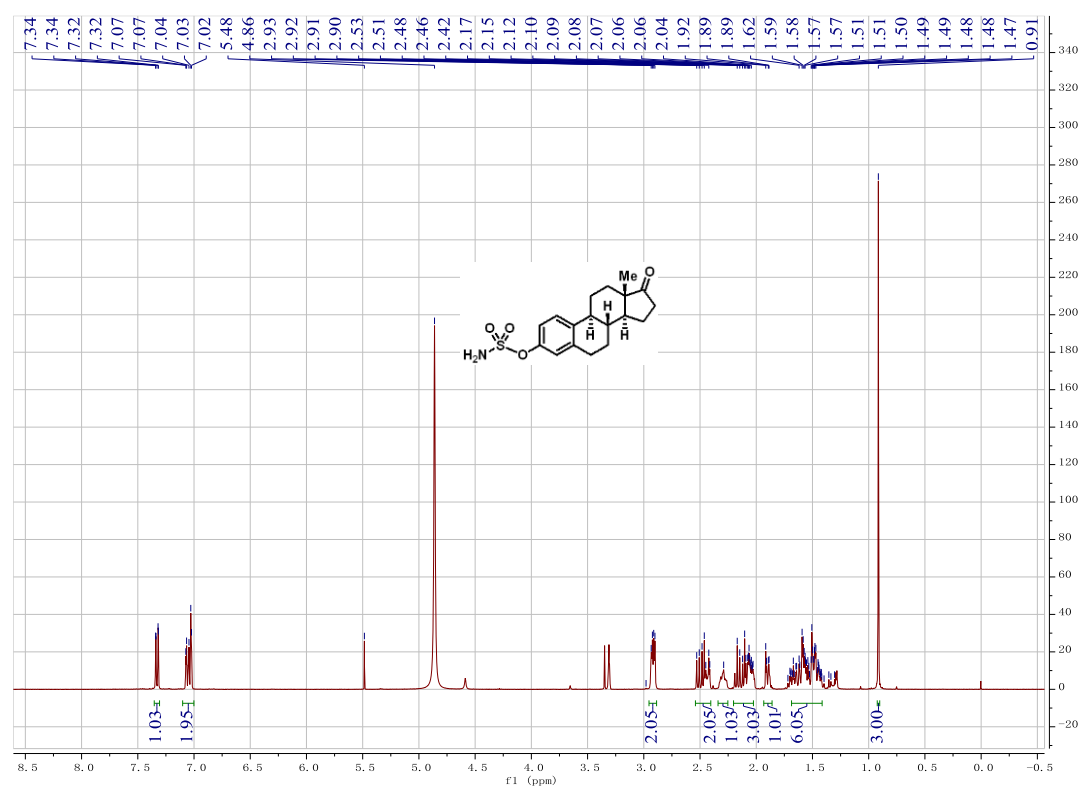
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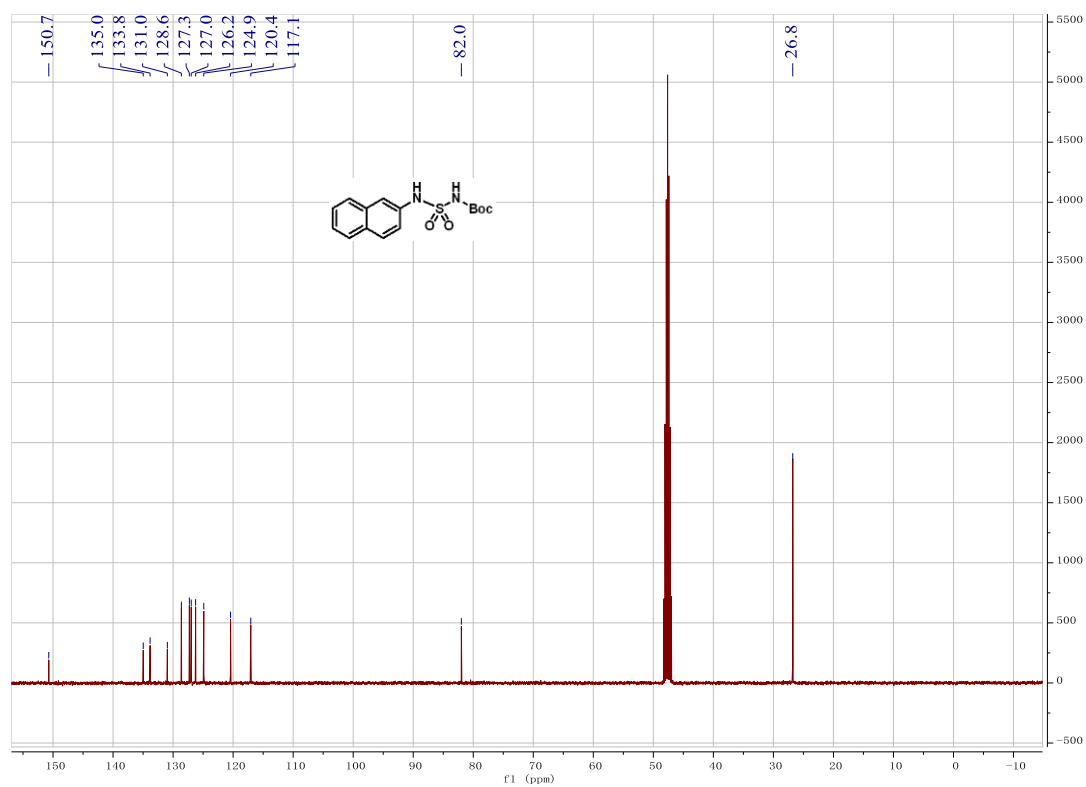
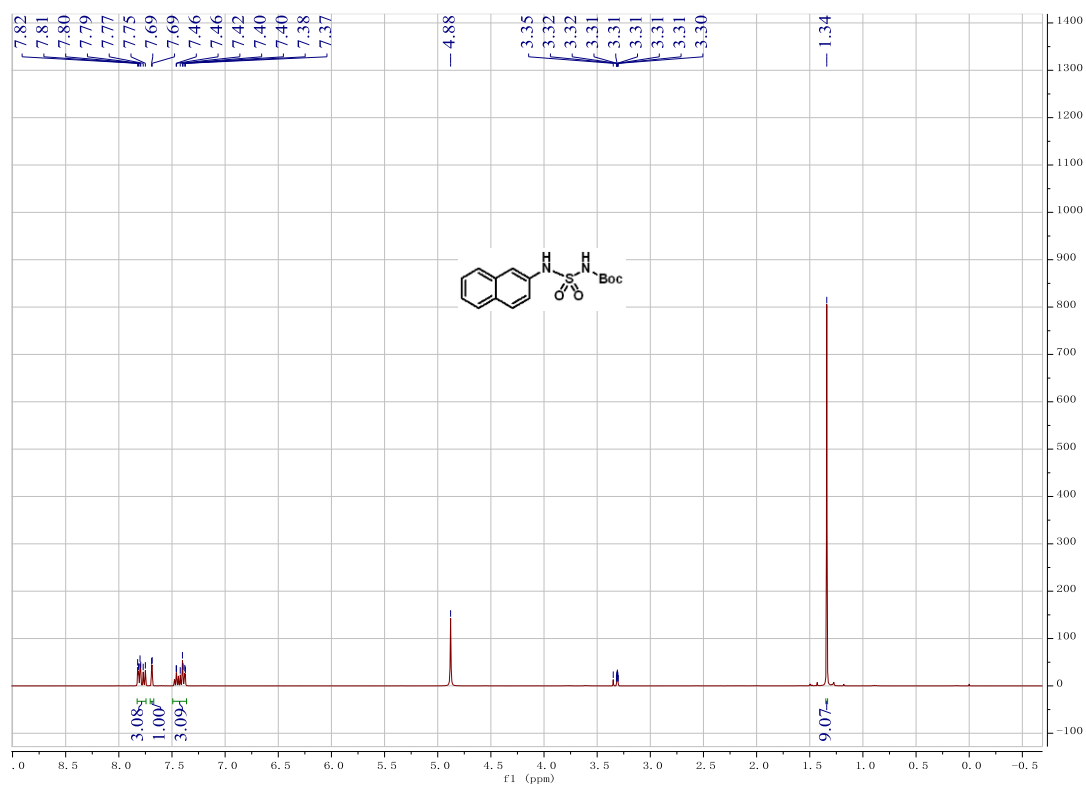
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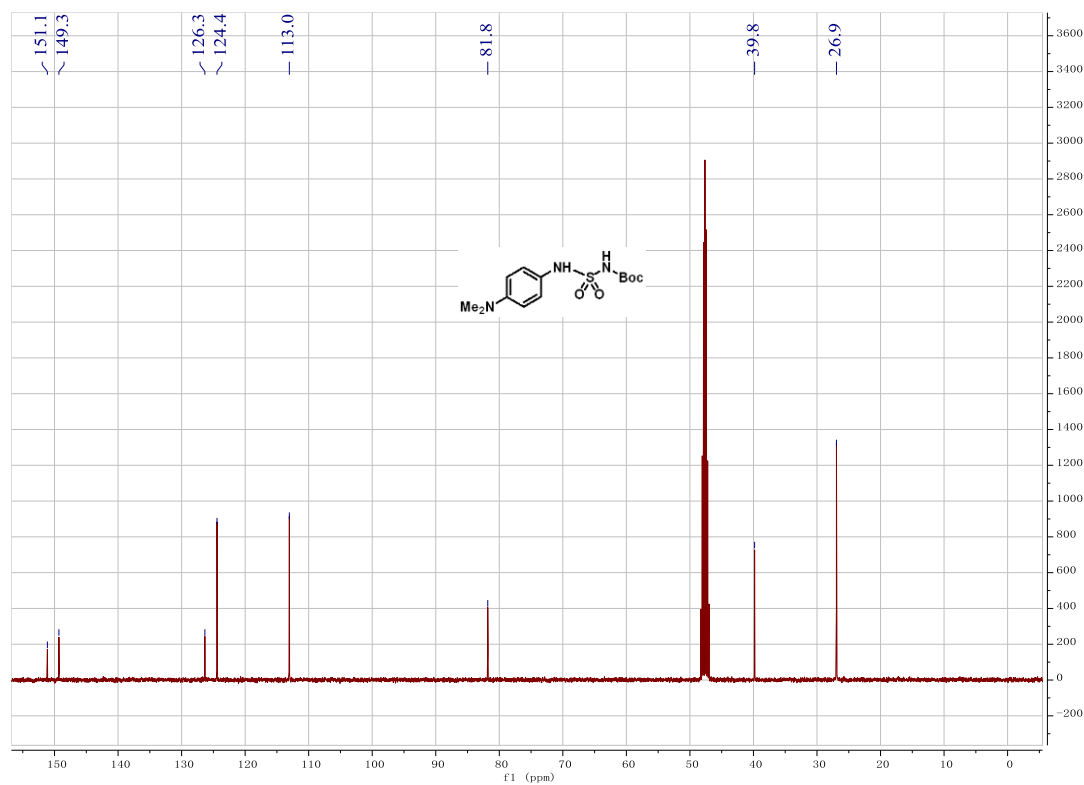
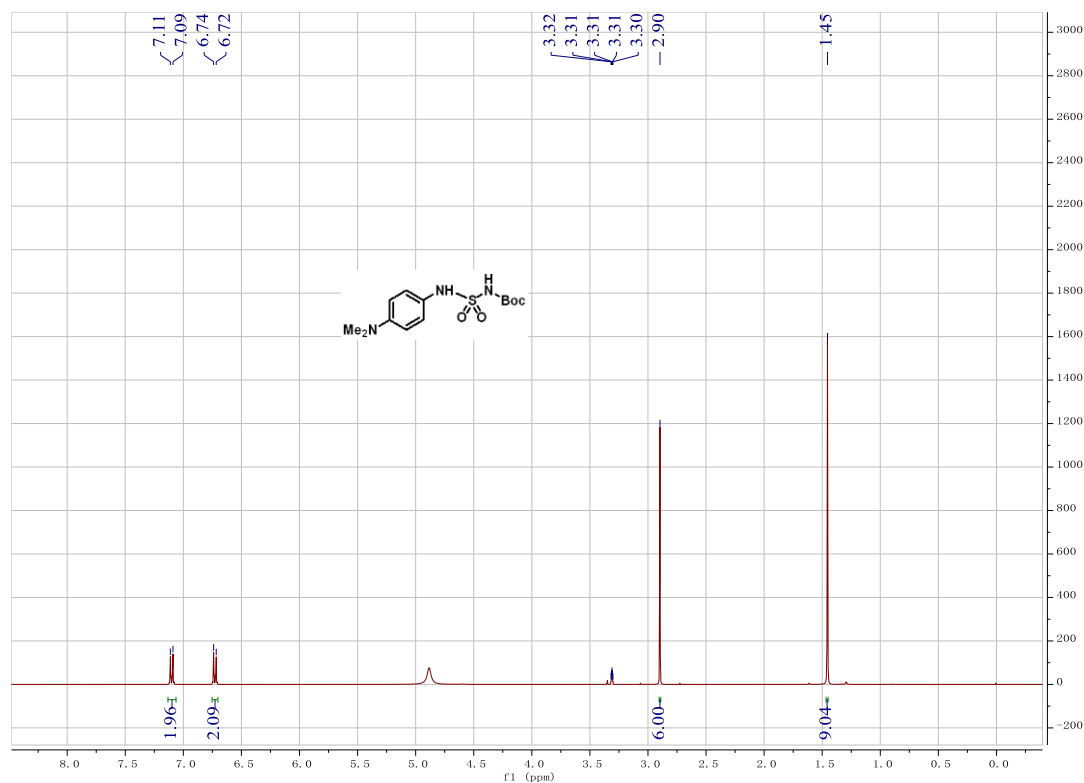
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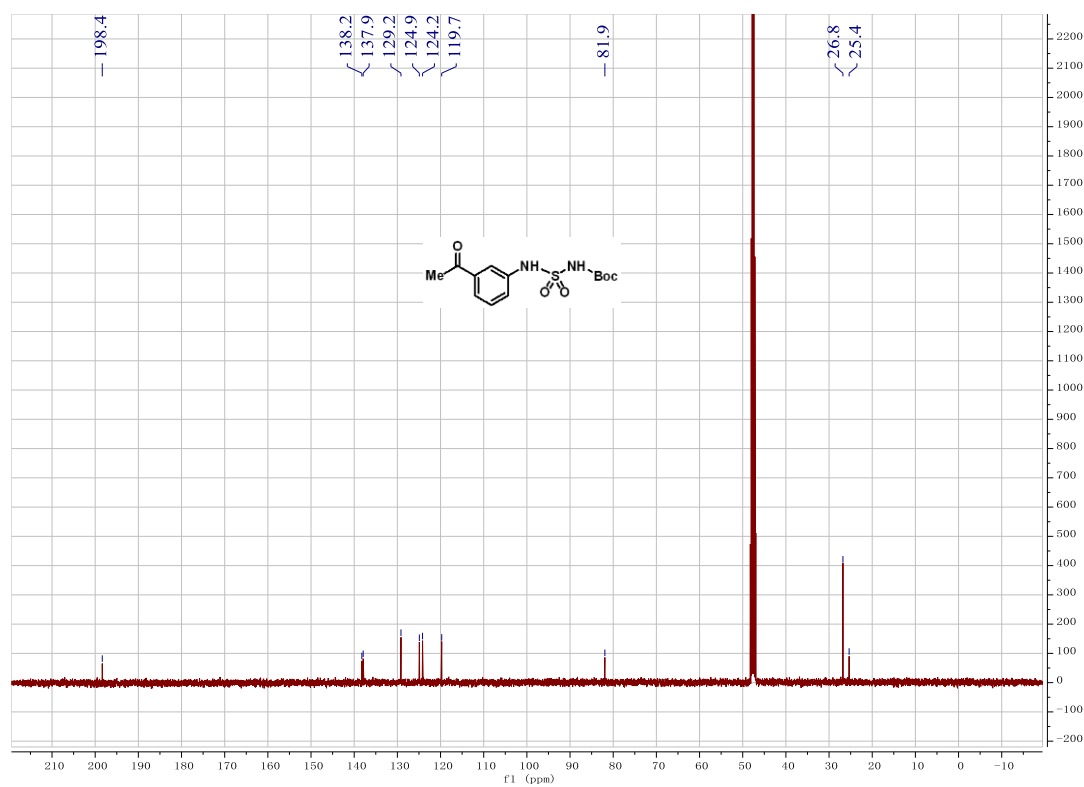
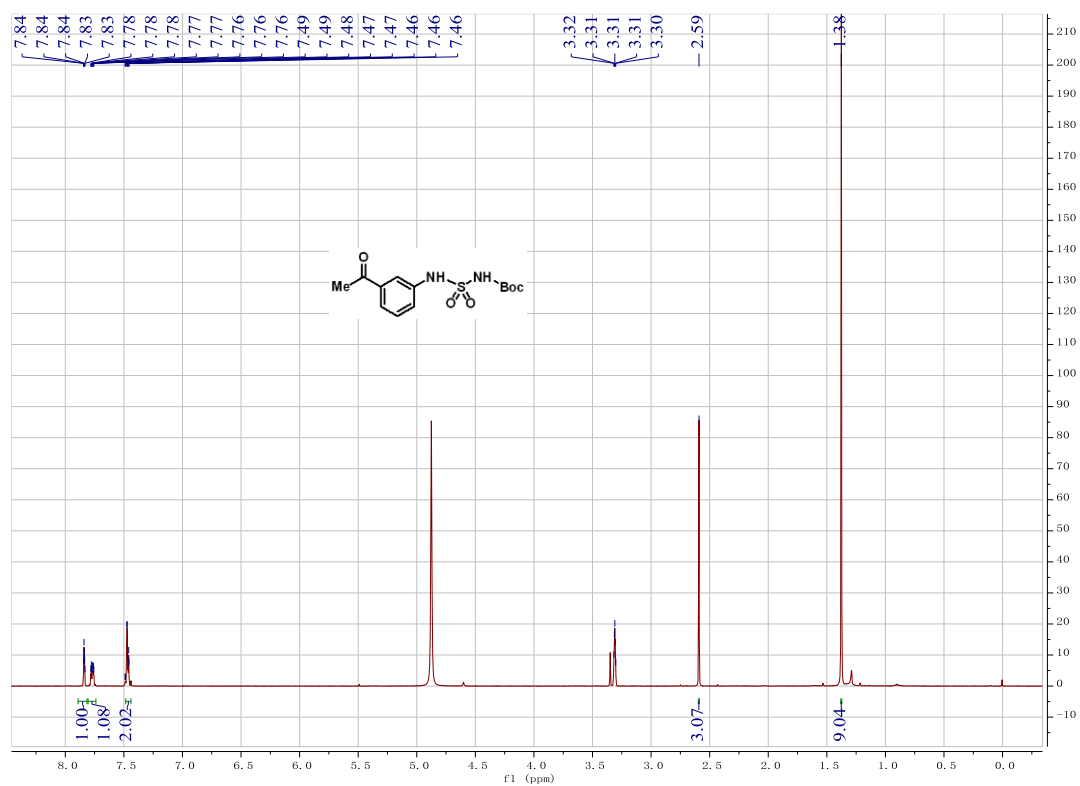
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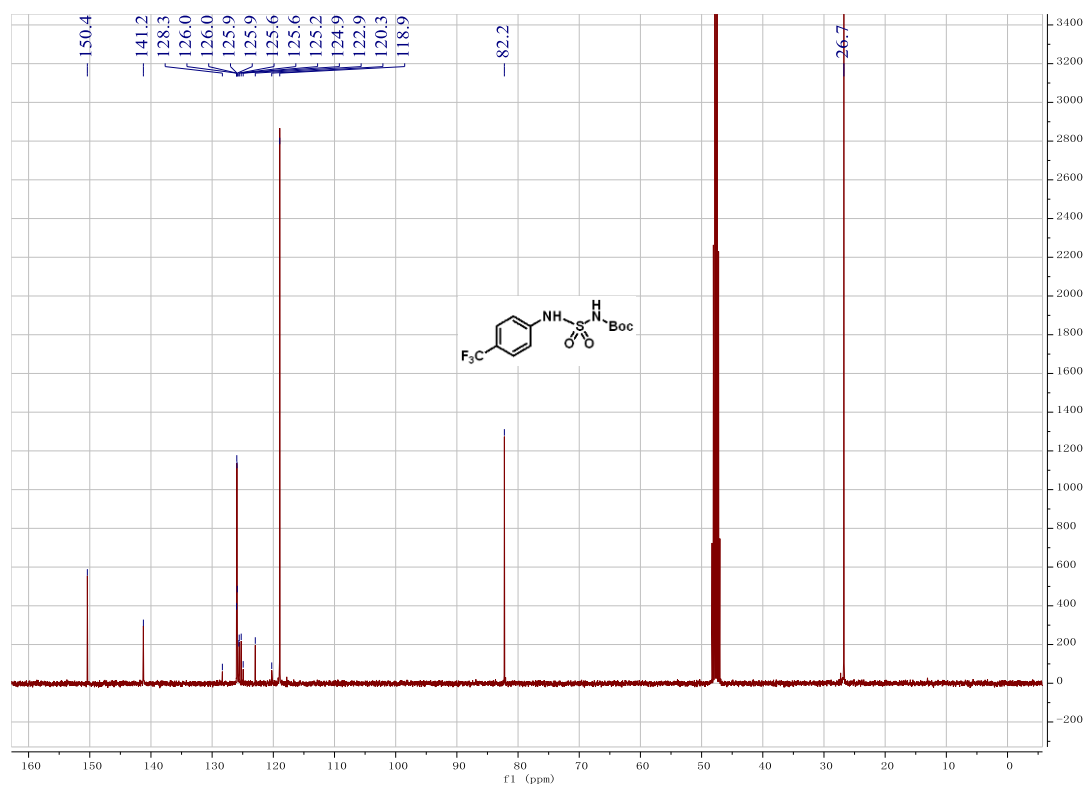
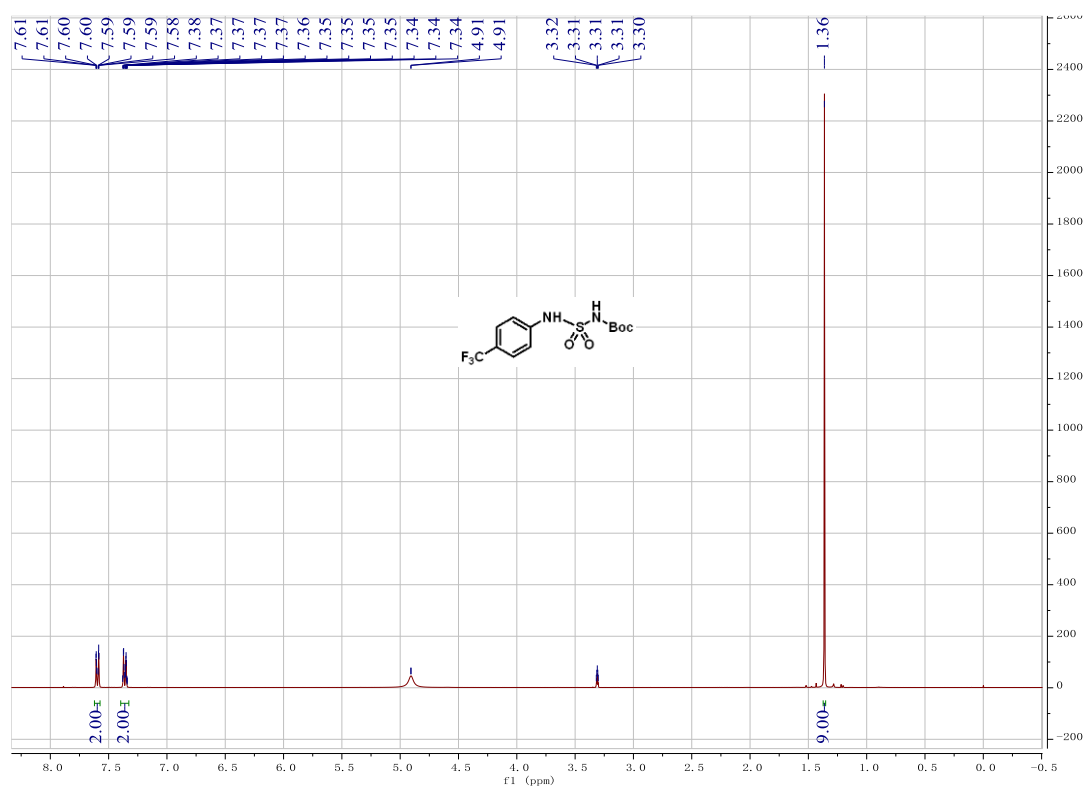
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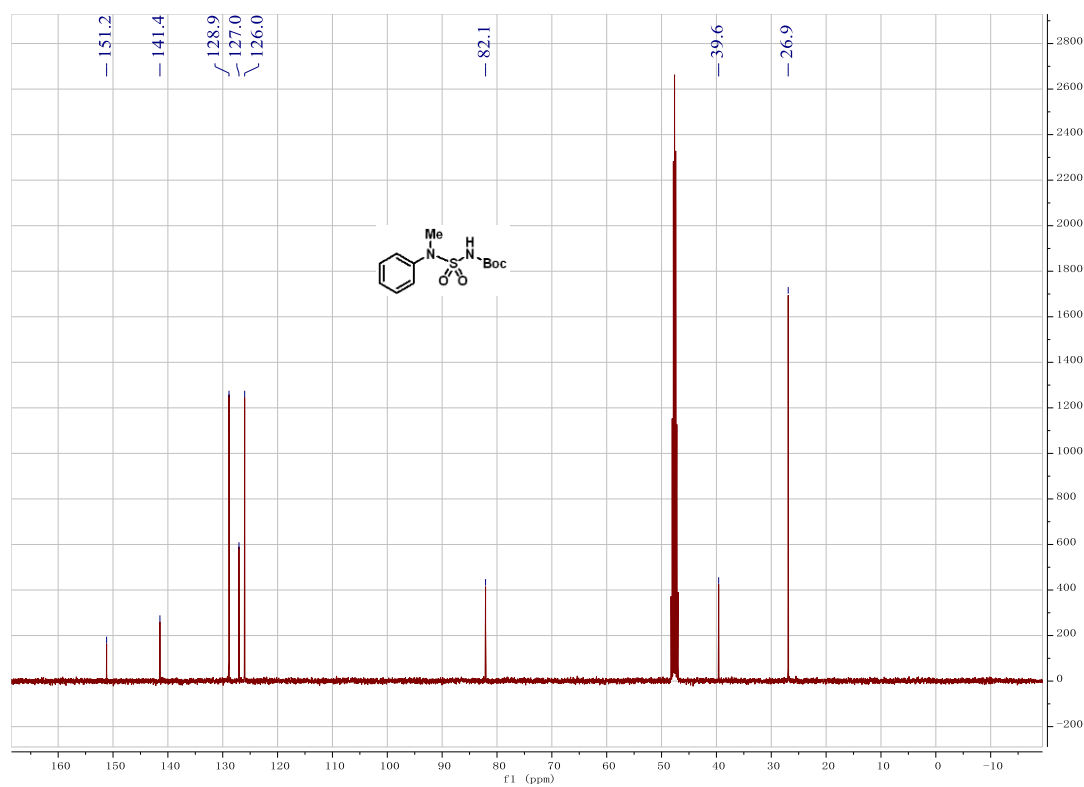
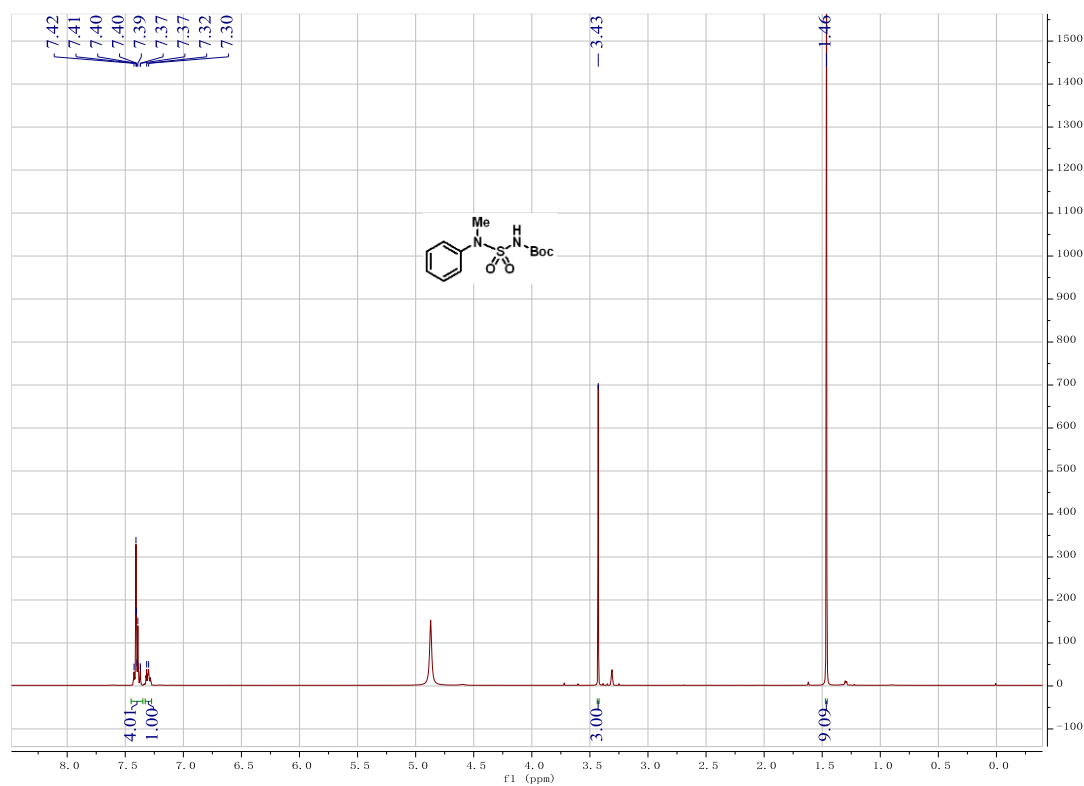
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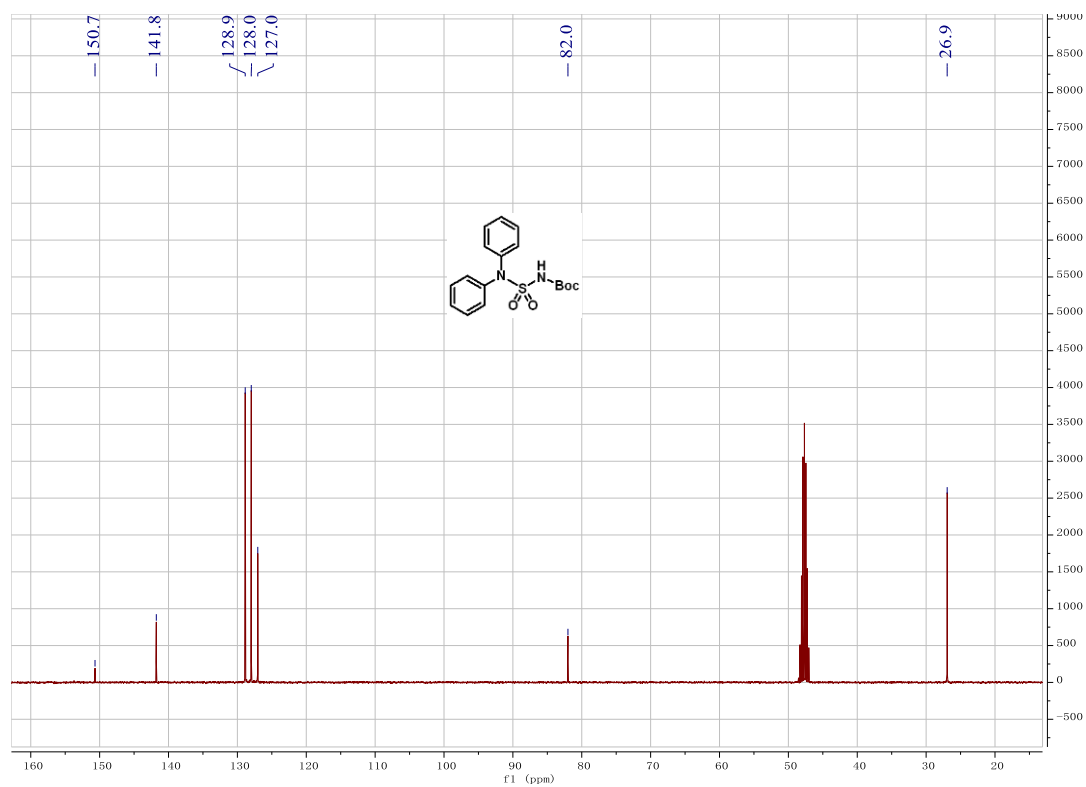
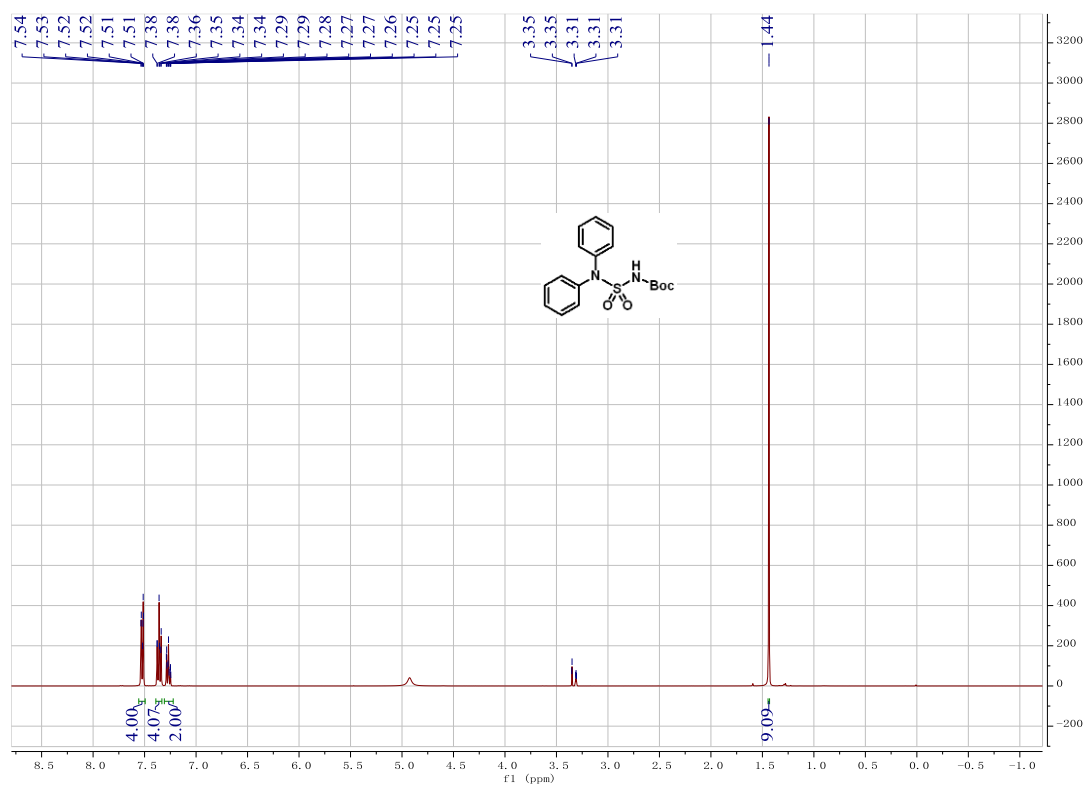
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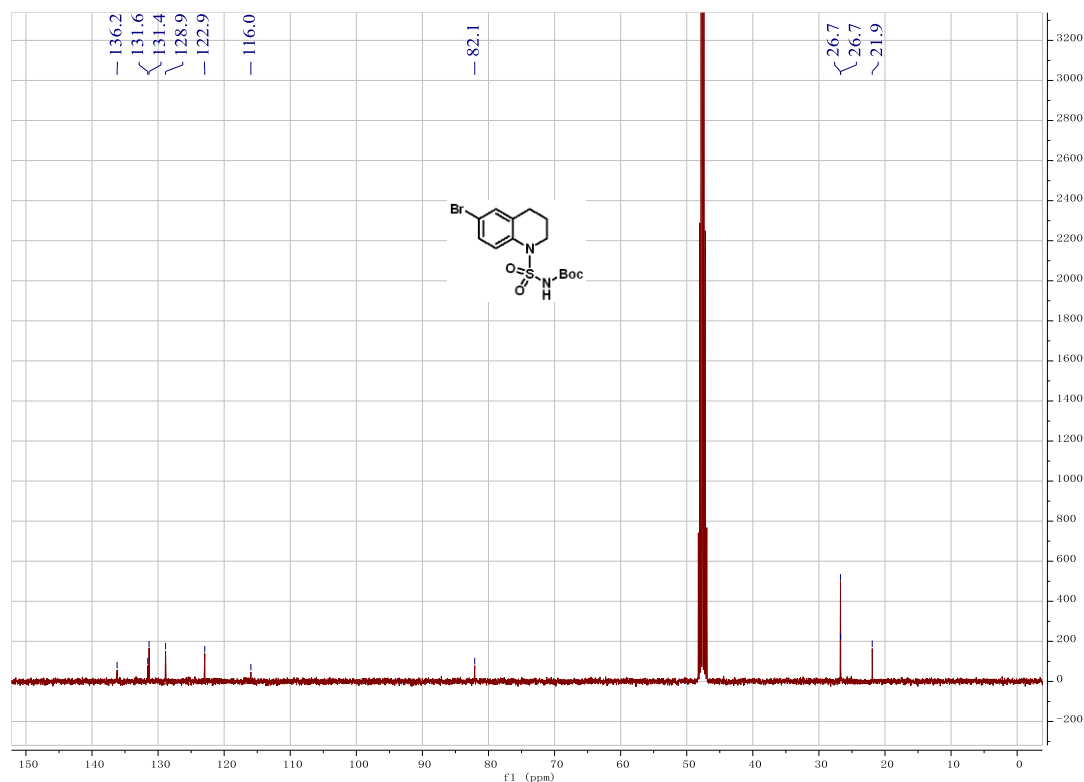
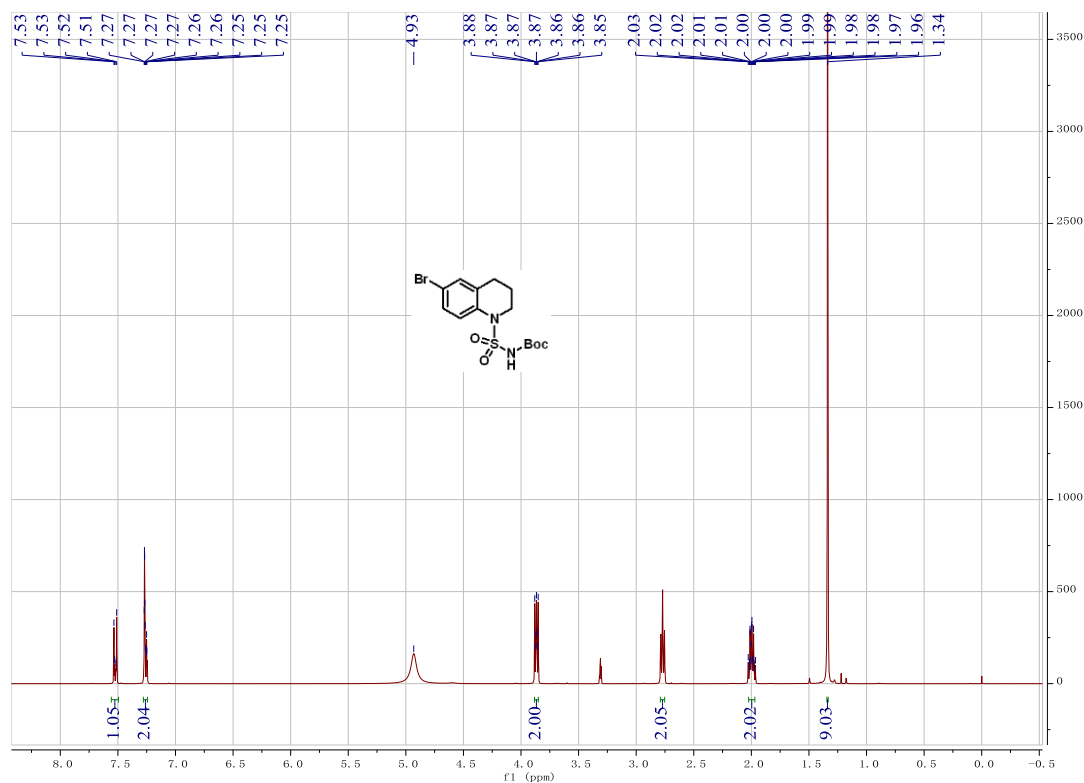
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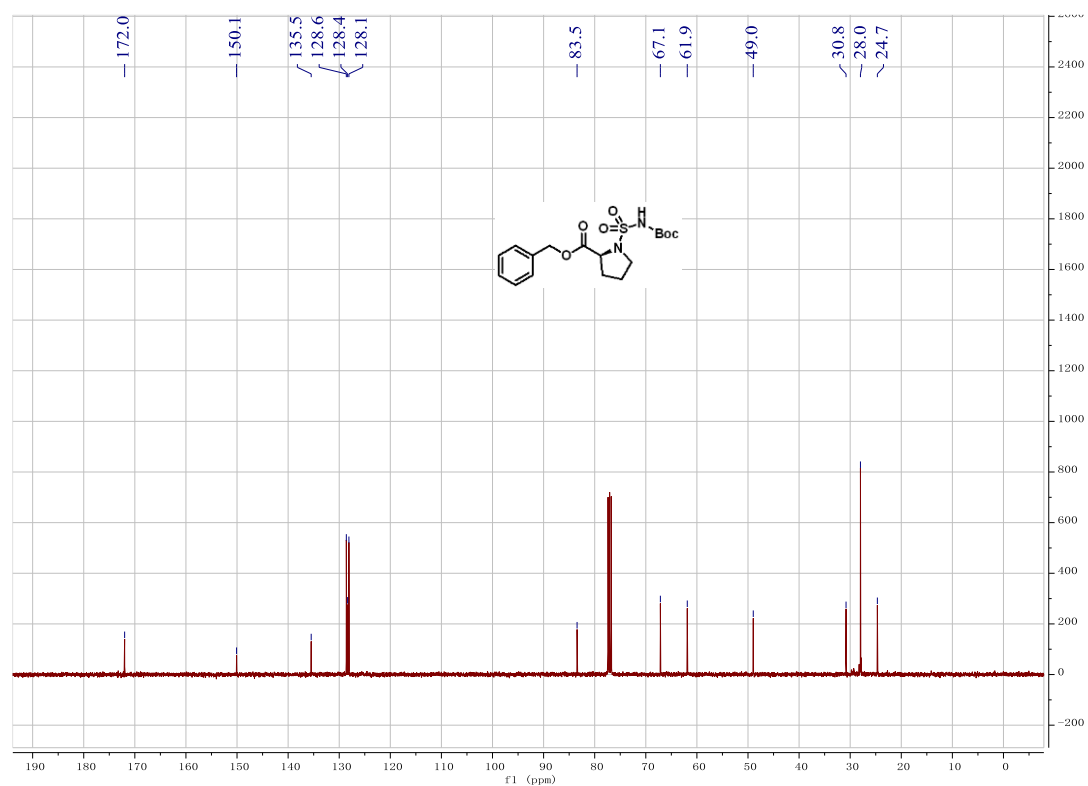
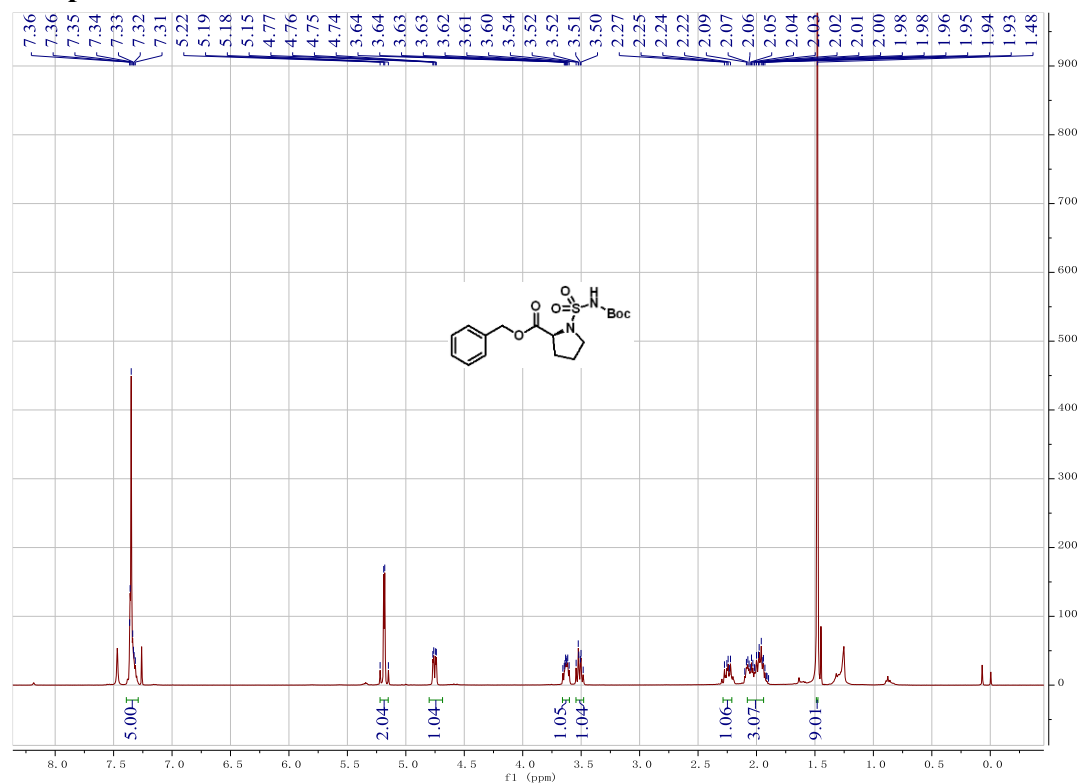
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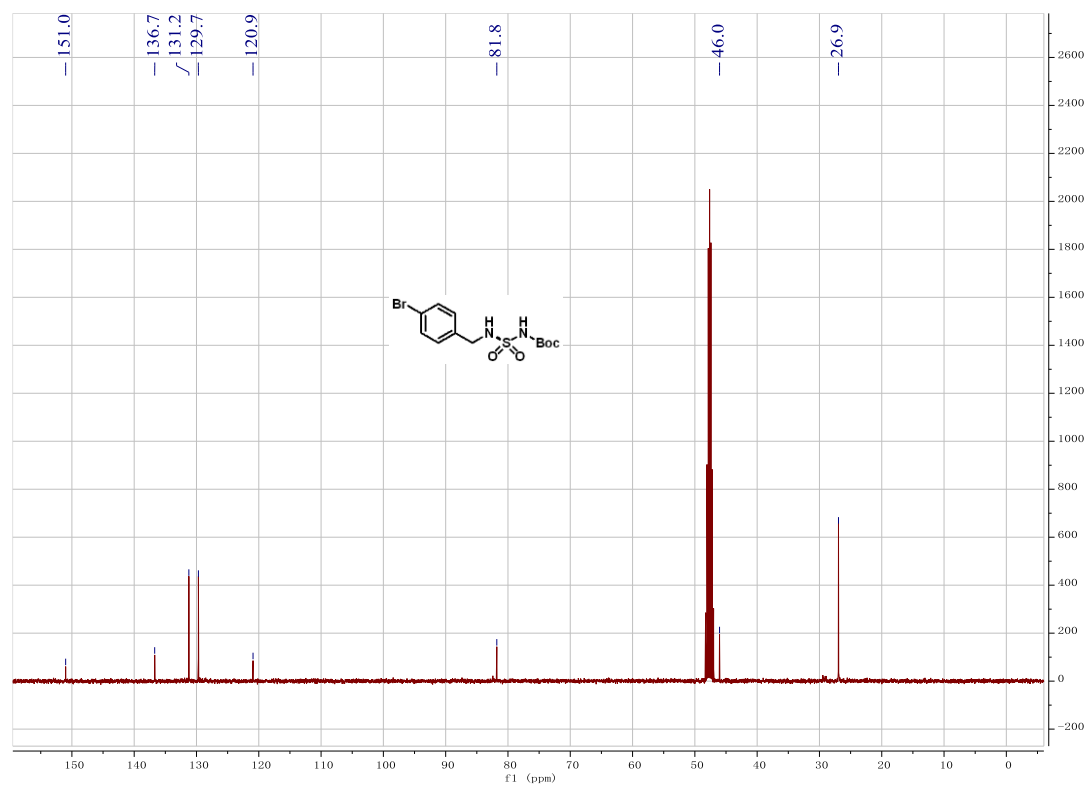
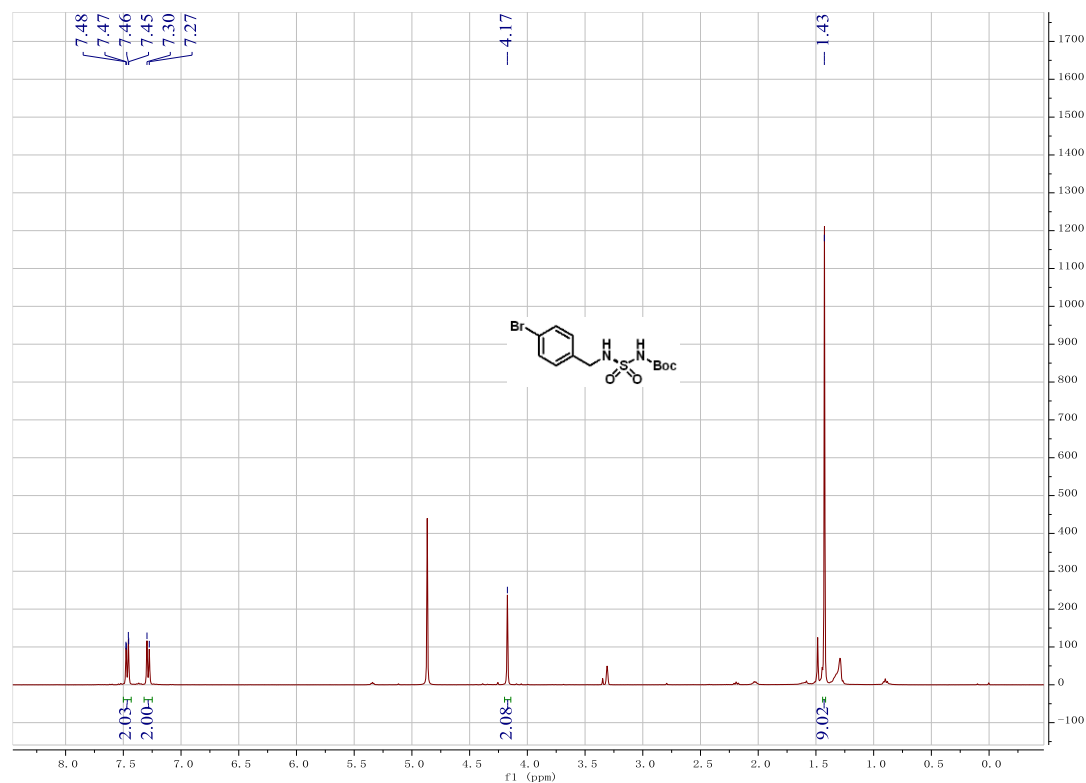
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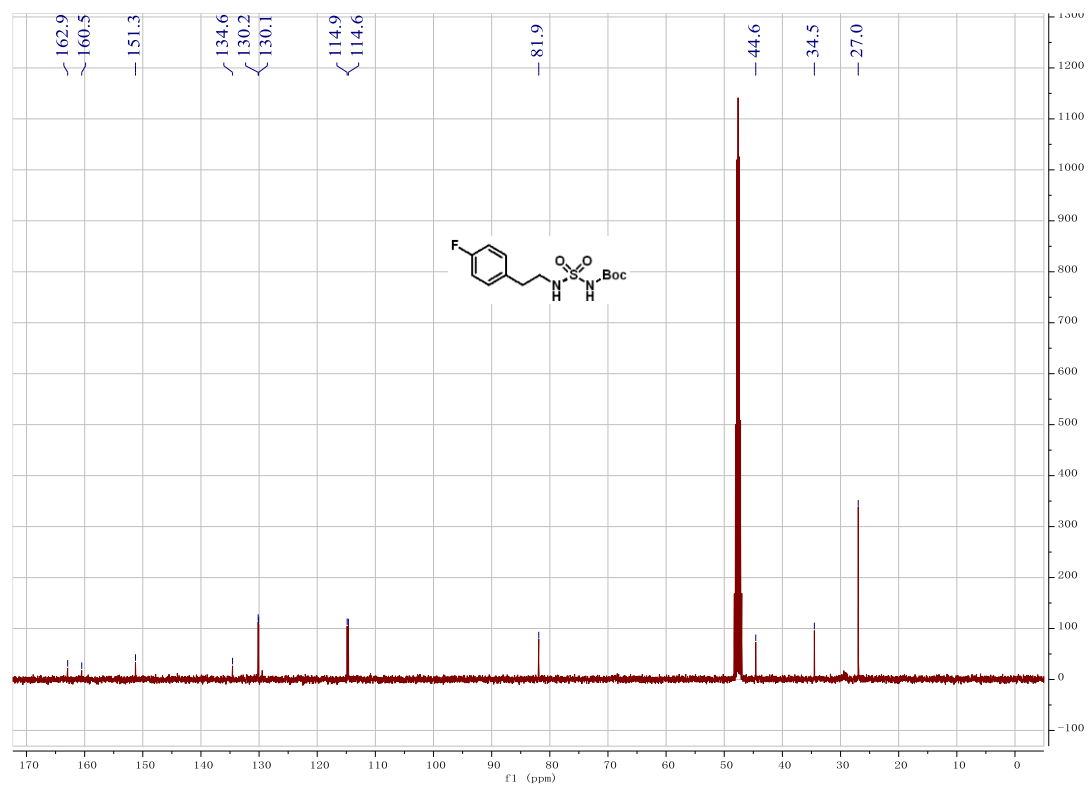
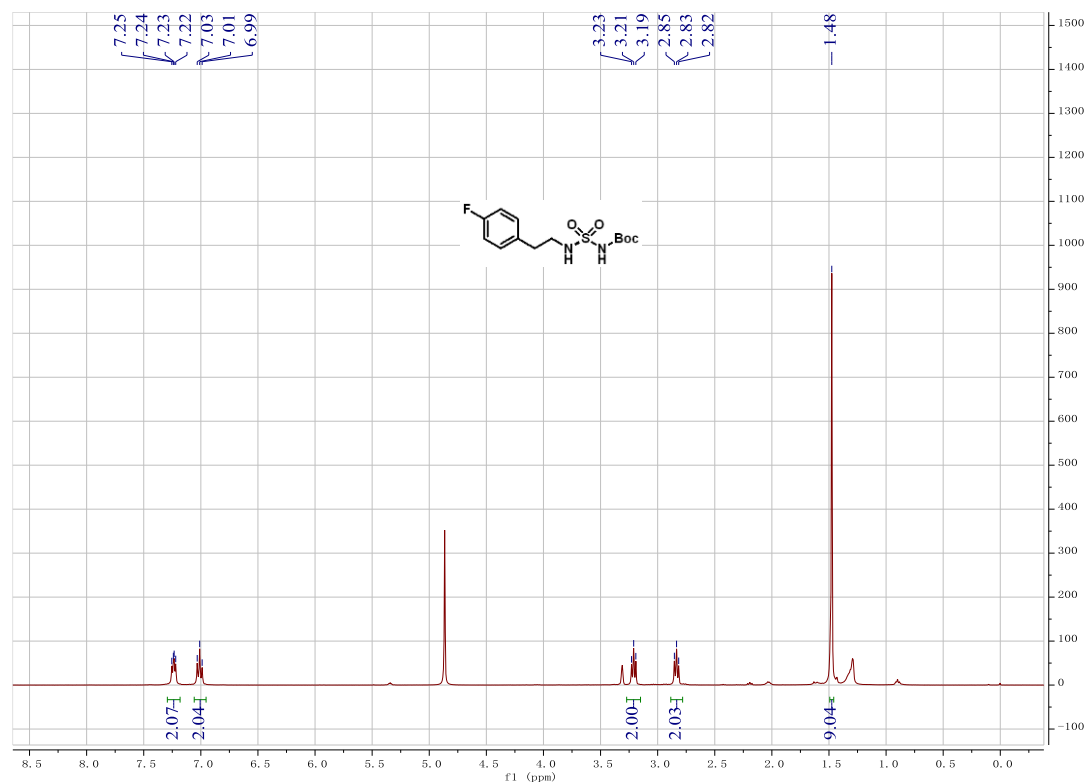
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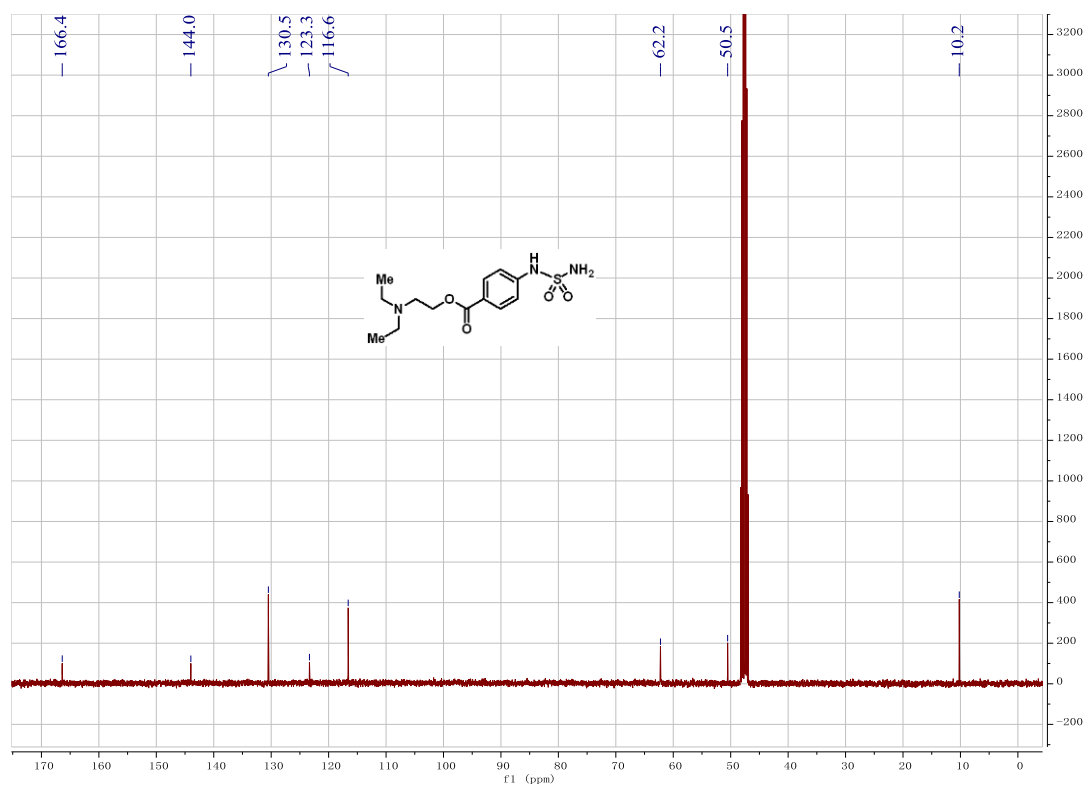
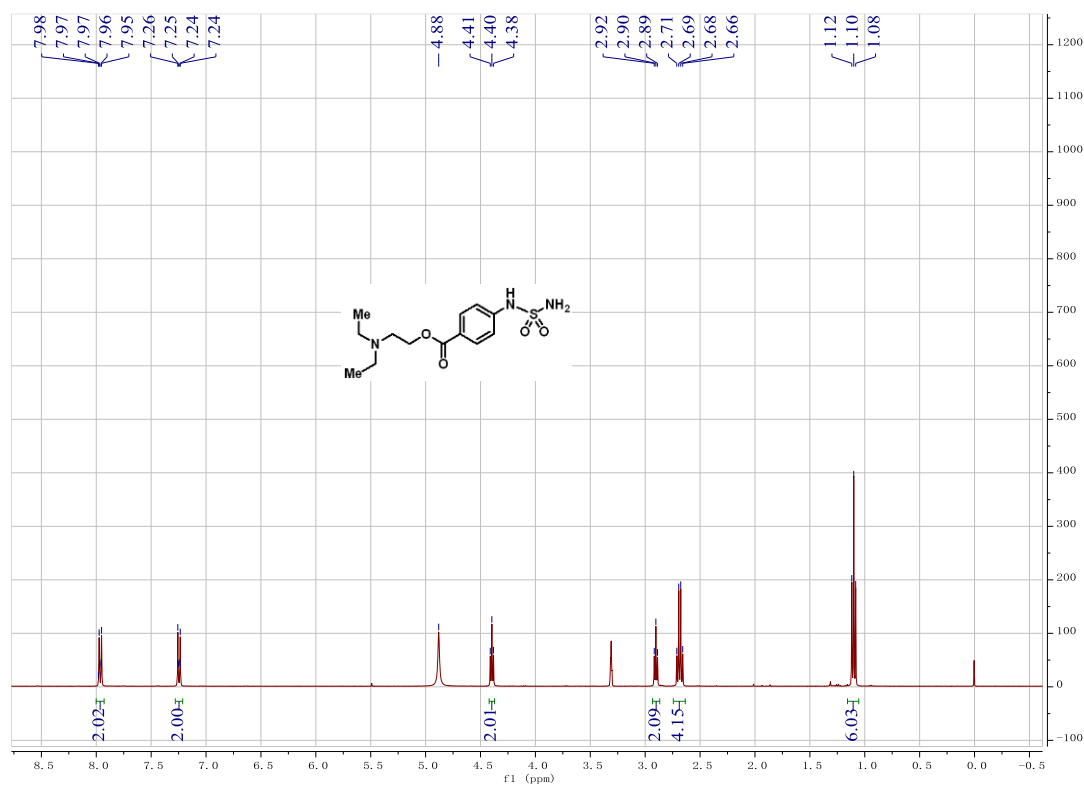
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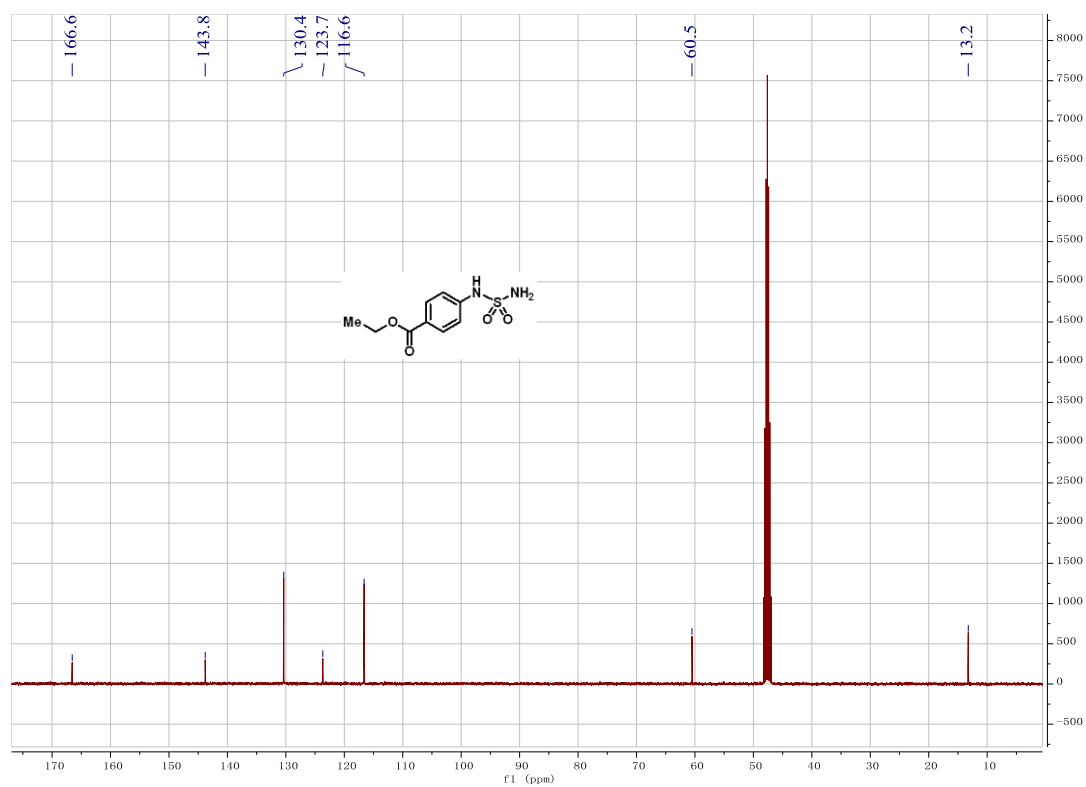
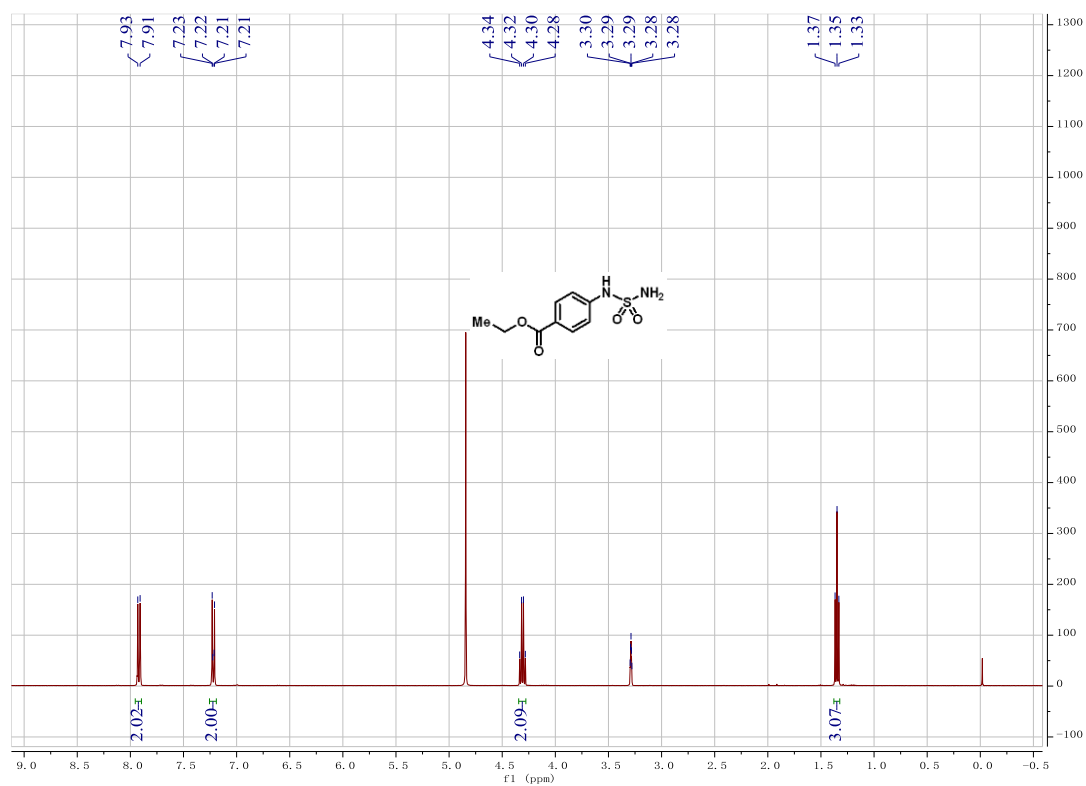
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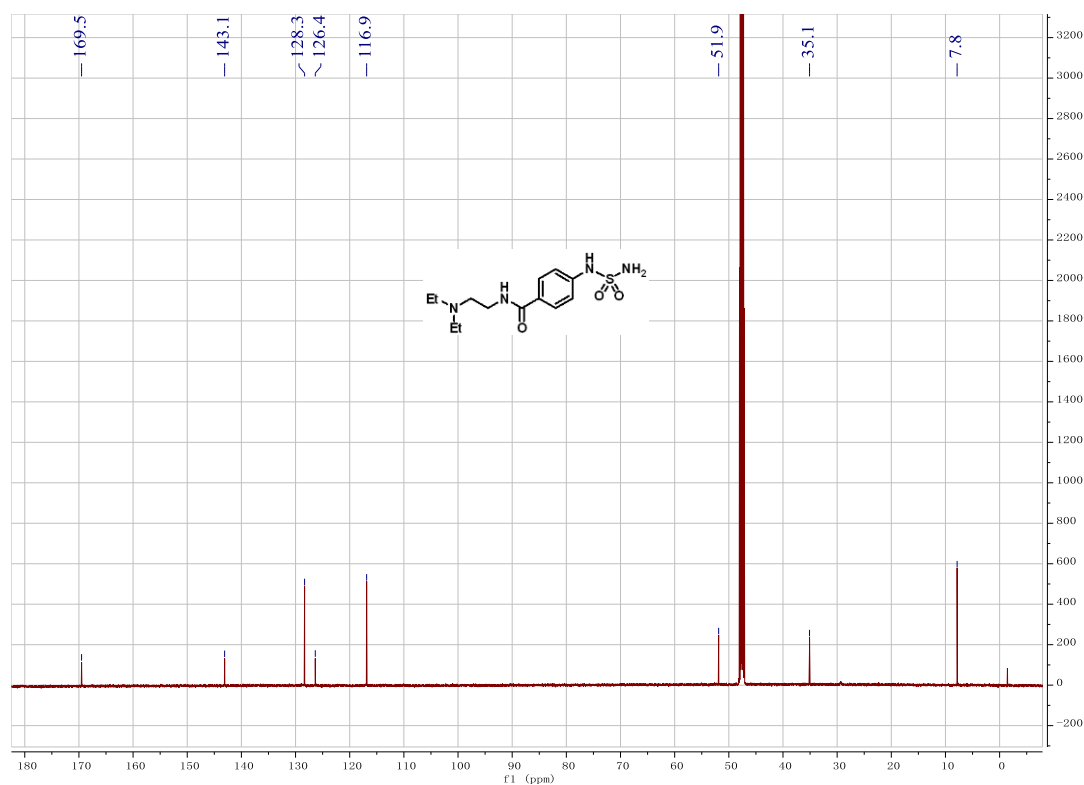
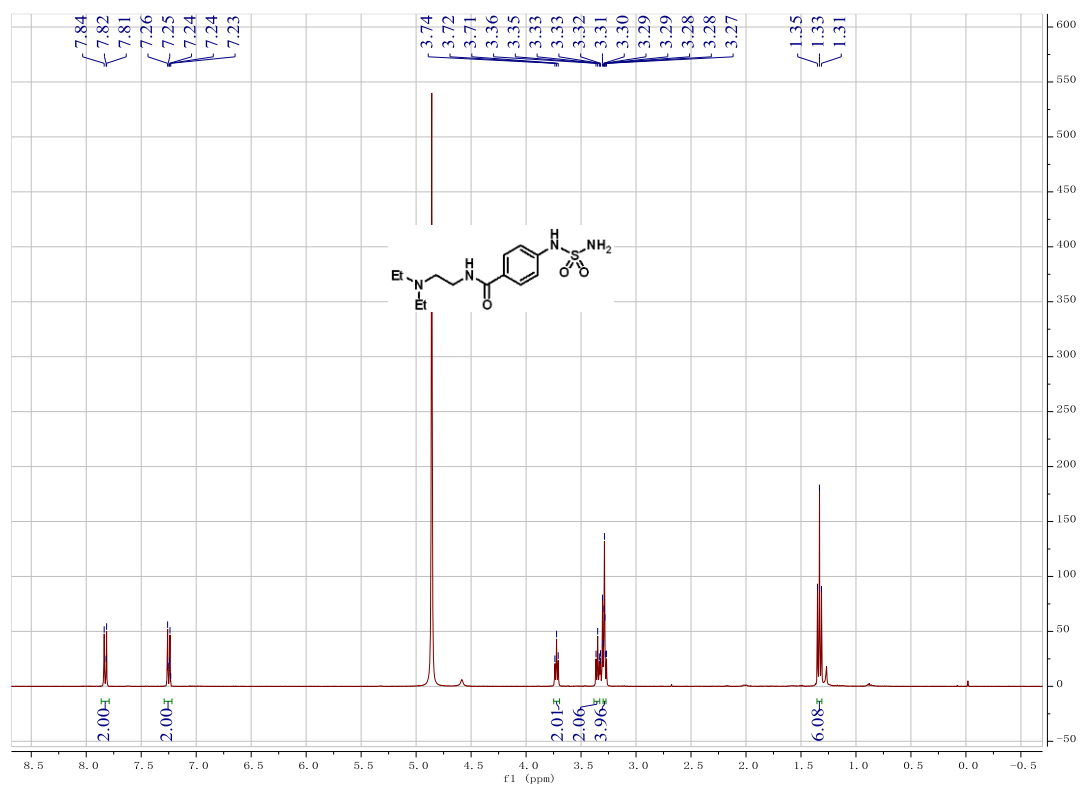
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 9a



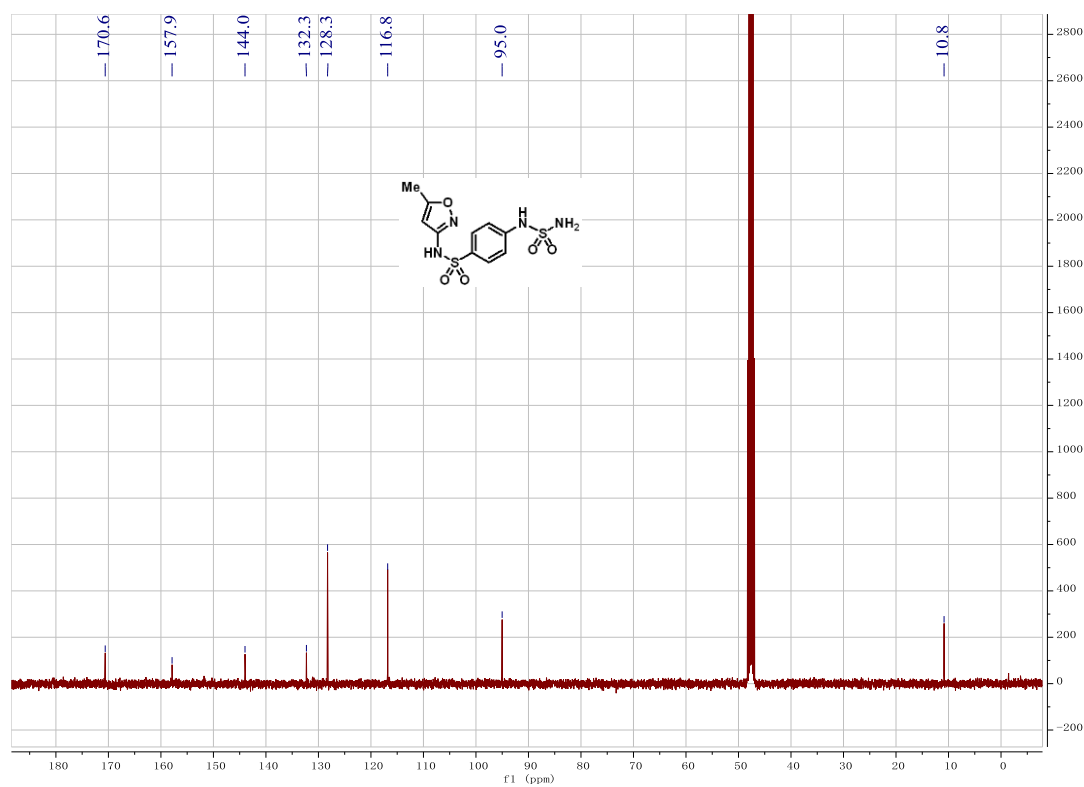
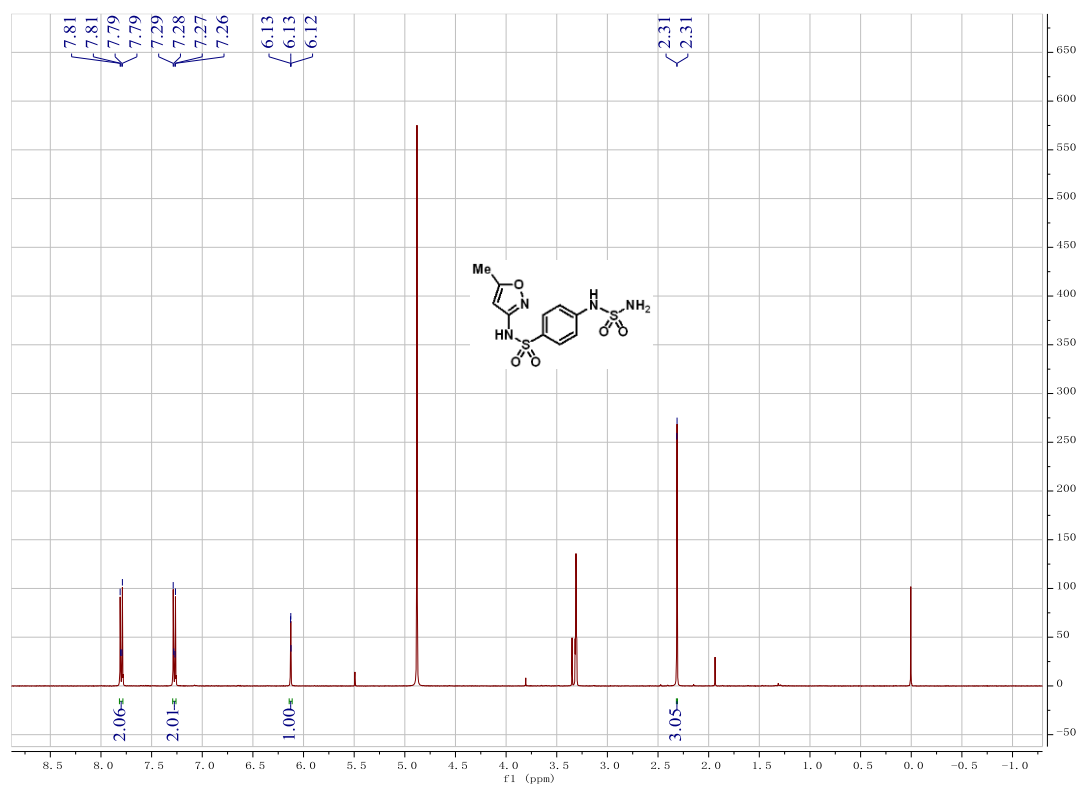
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 9b



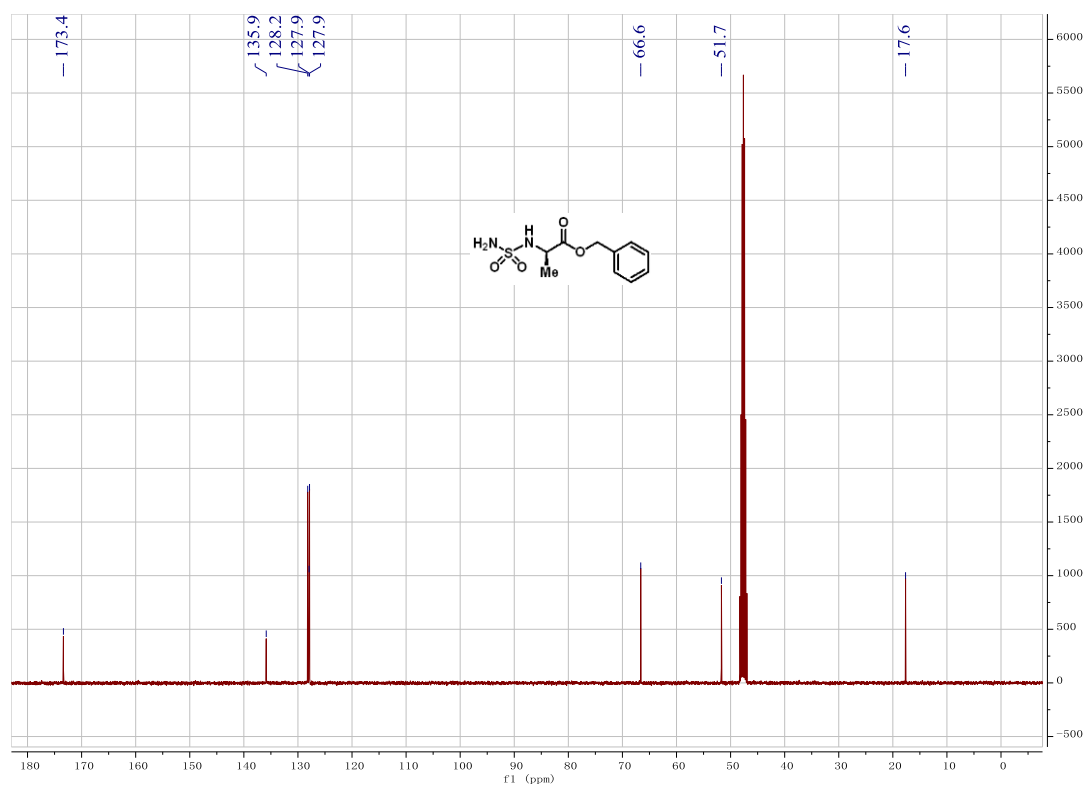
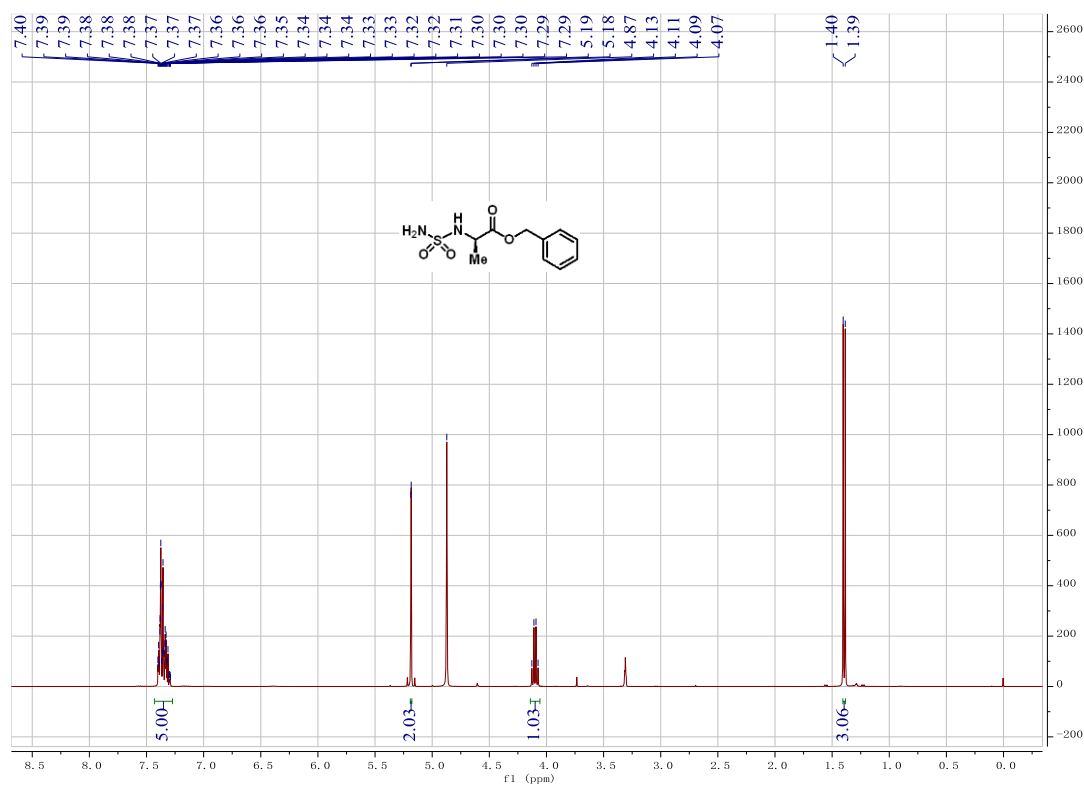
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 9c



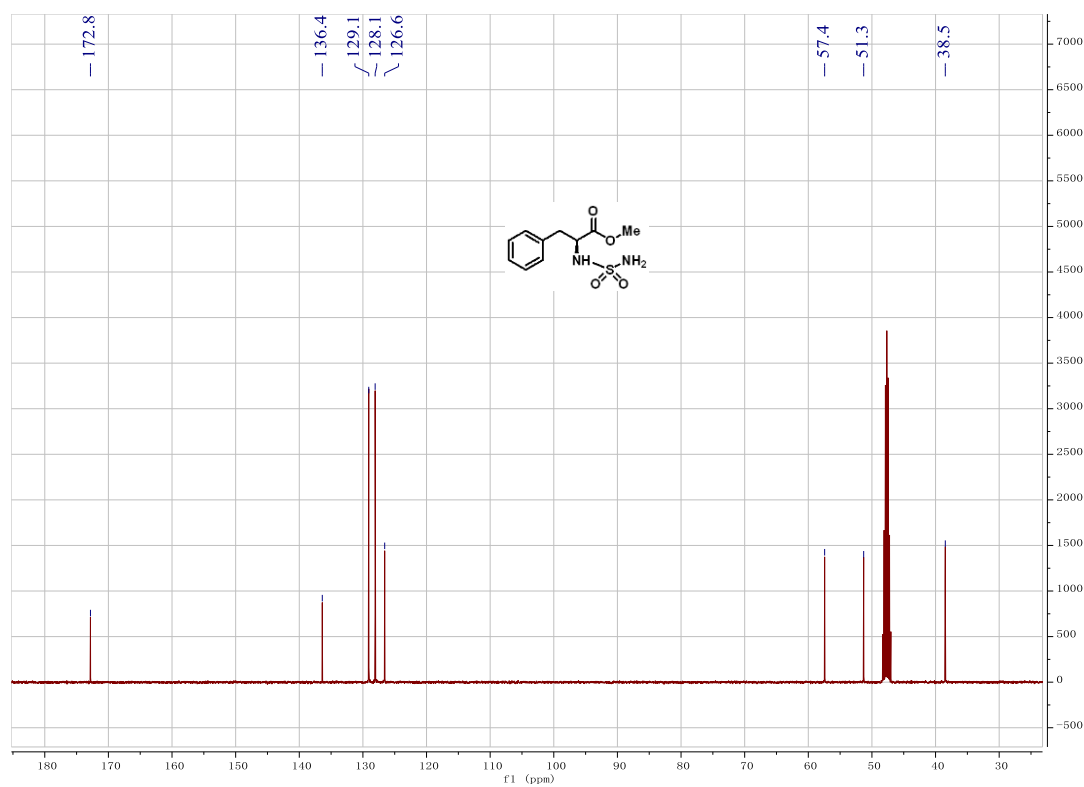
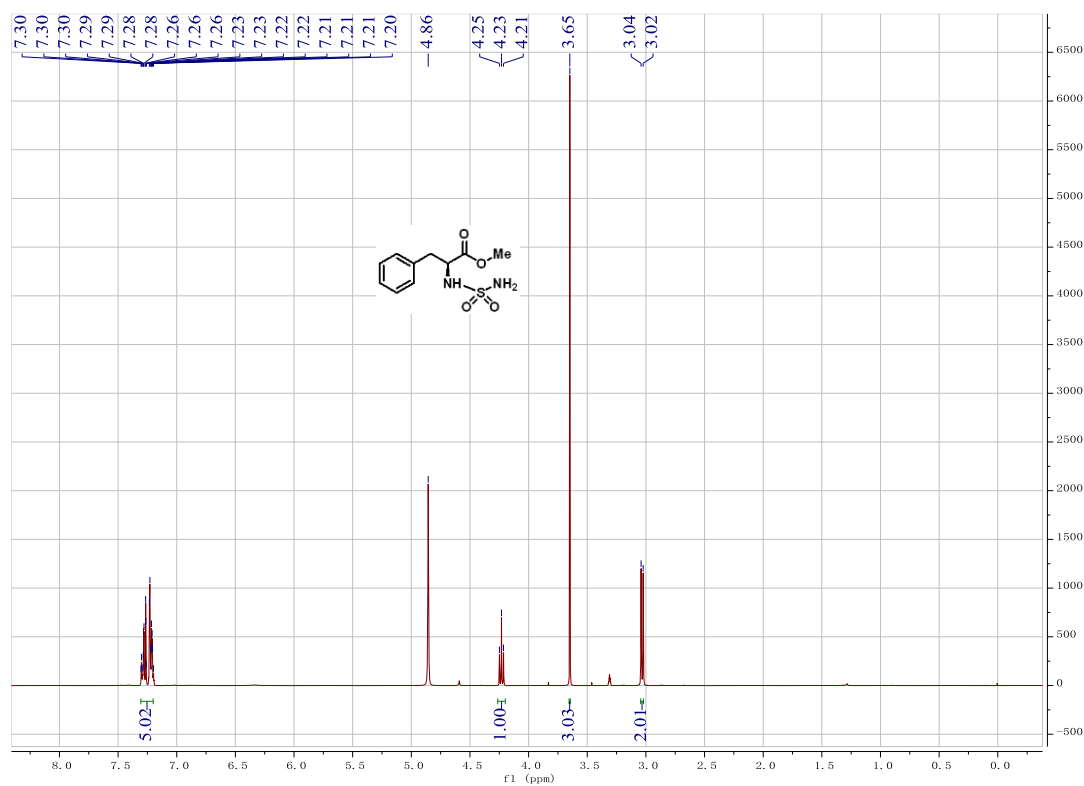
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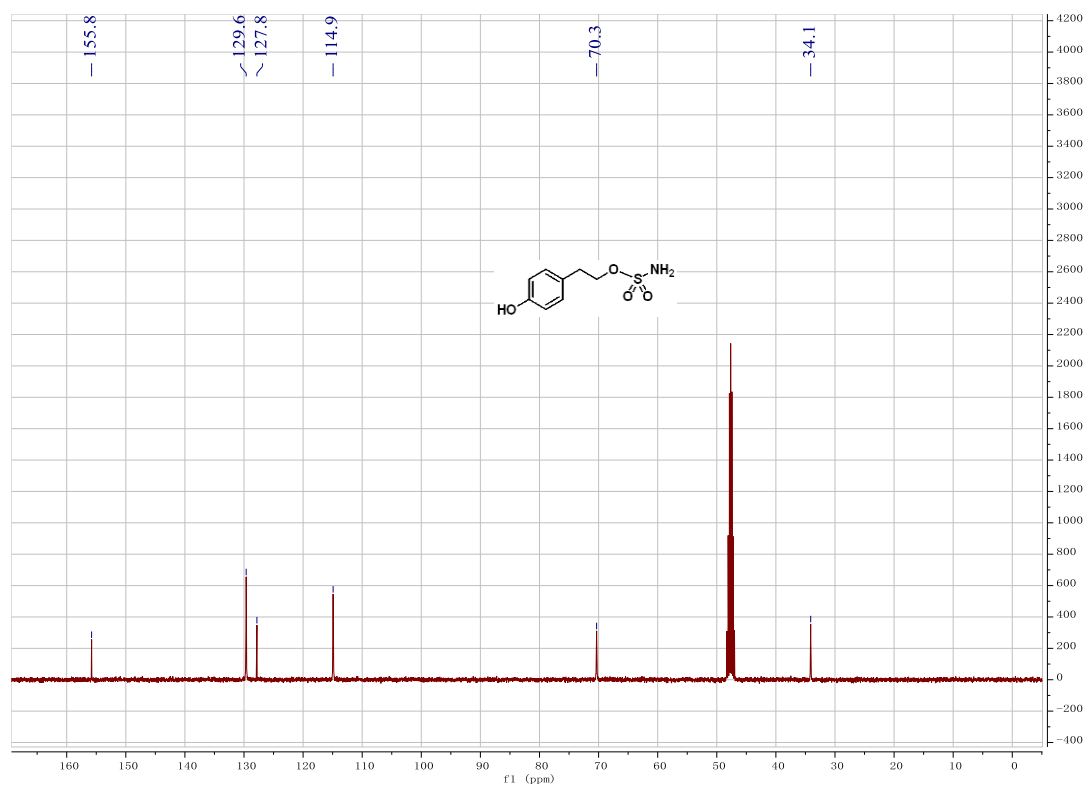
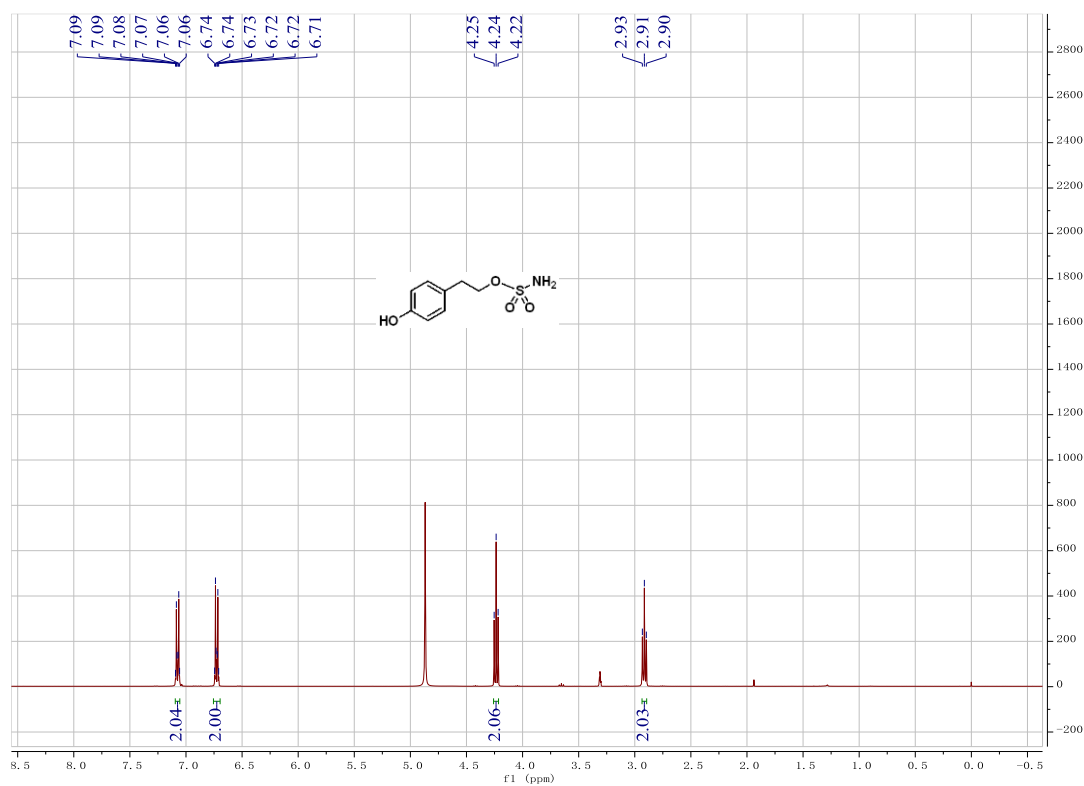
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 9e



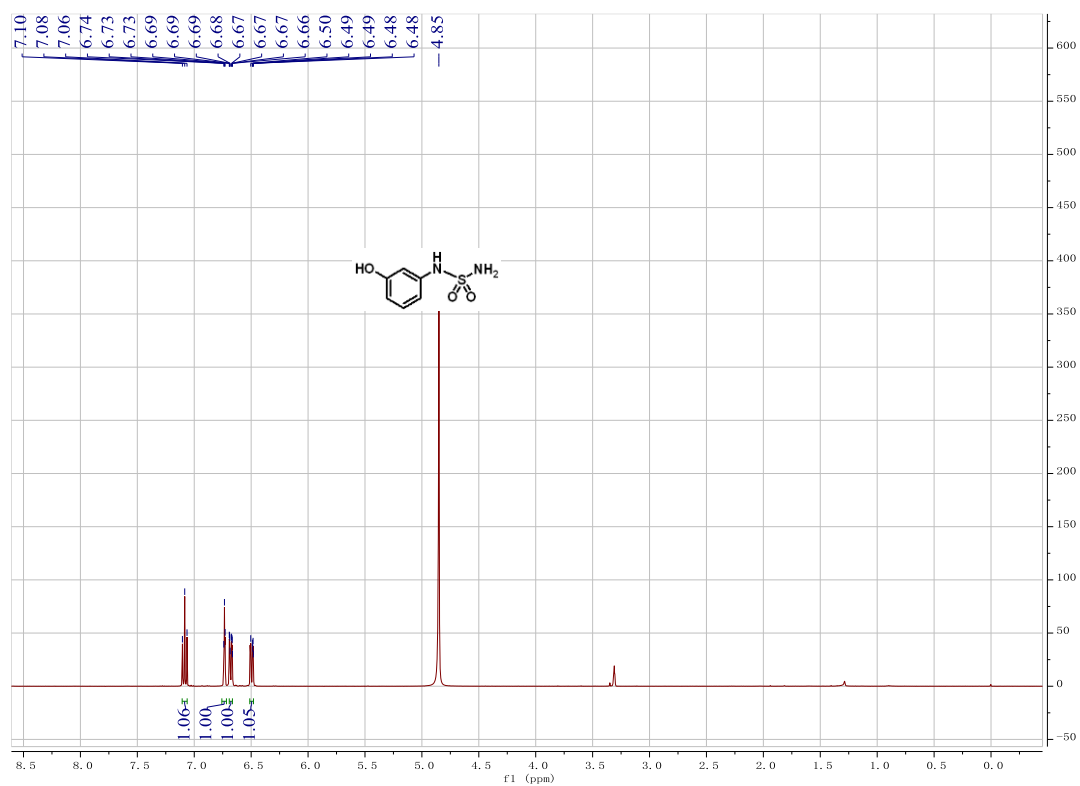
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 9f



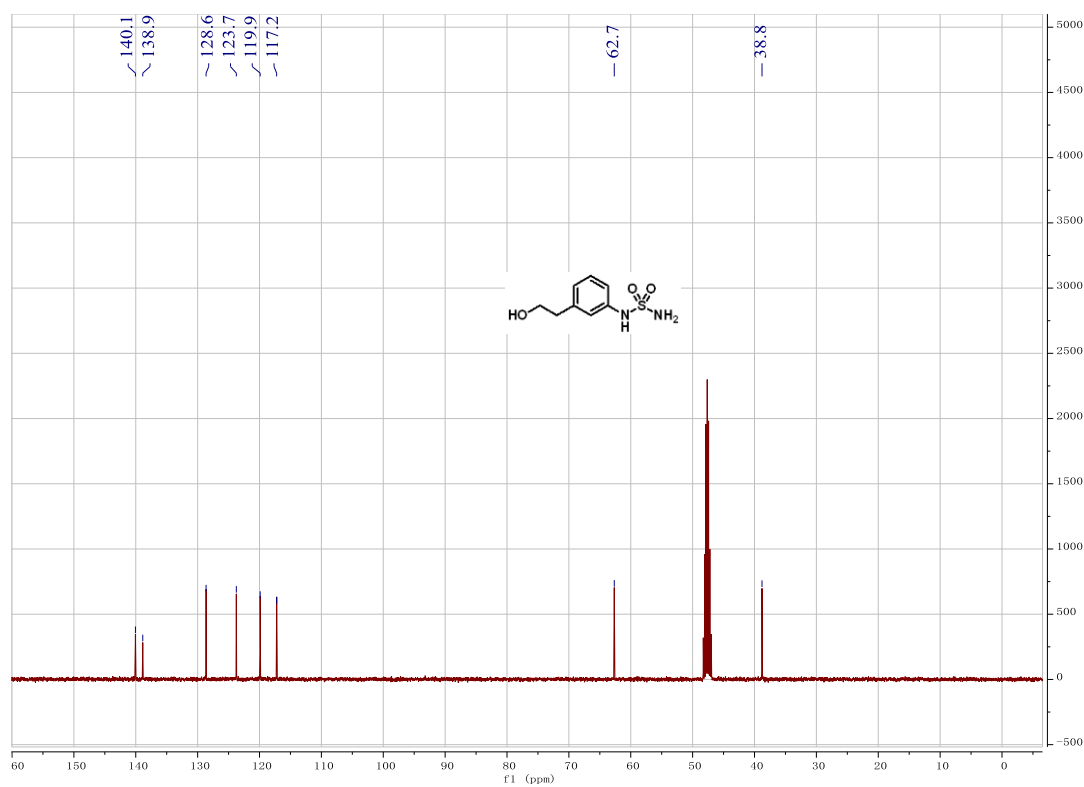
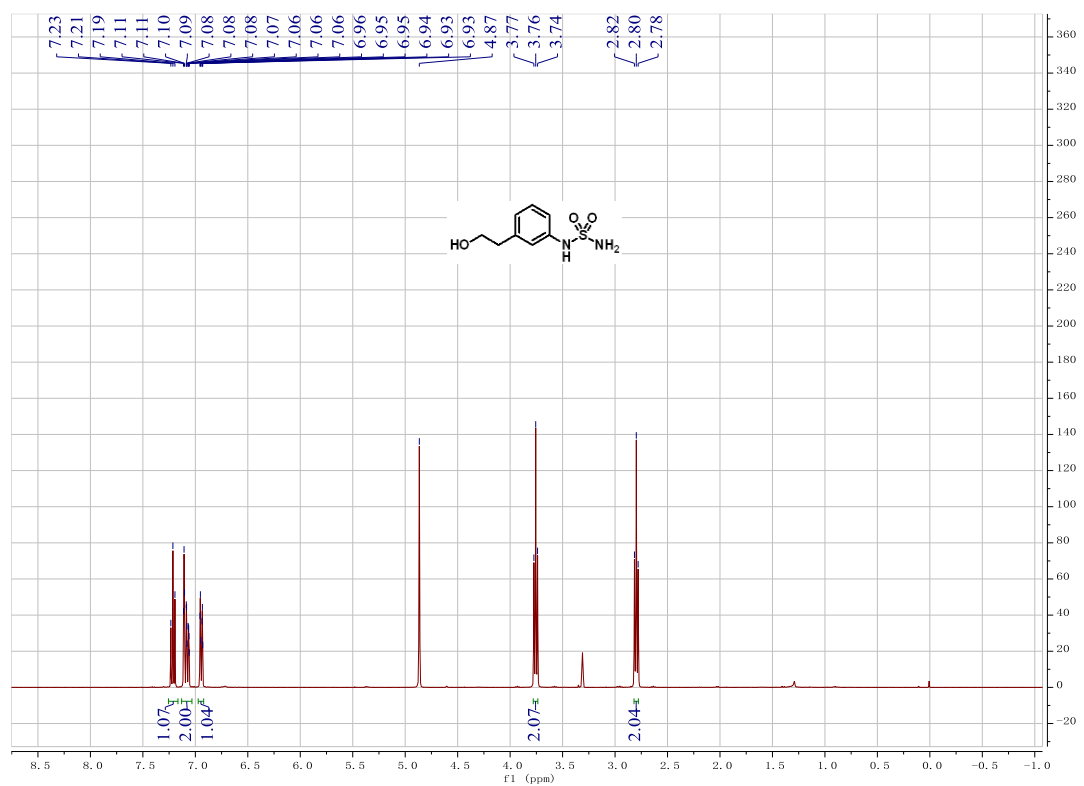
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 11a



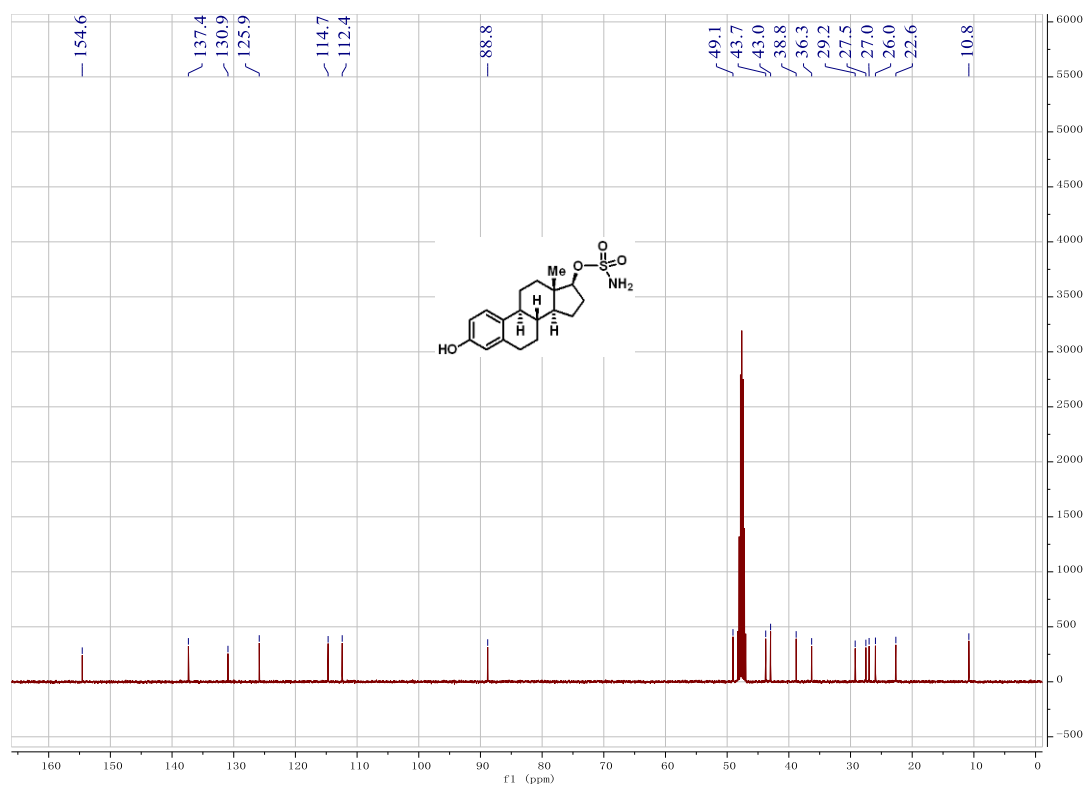
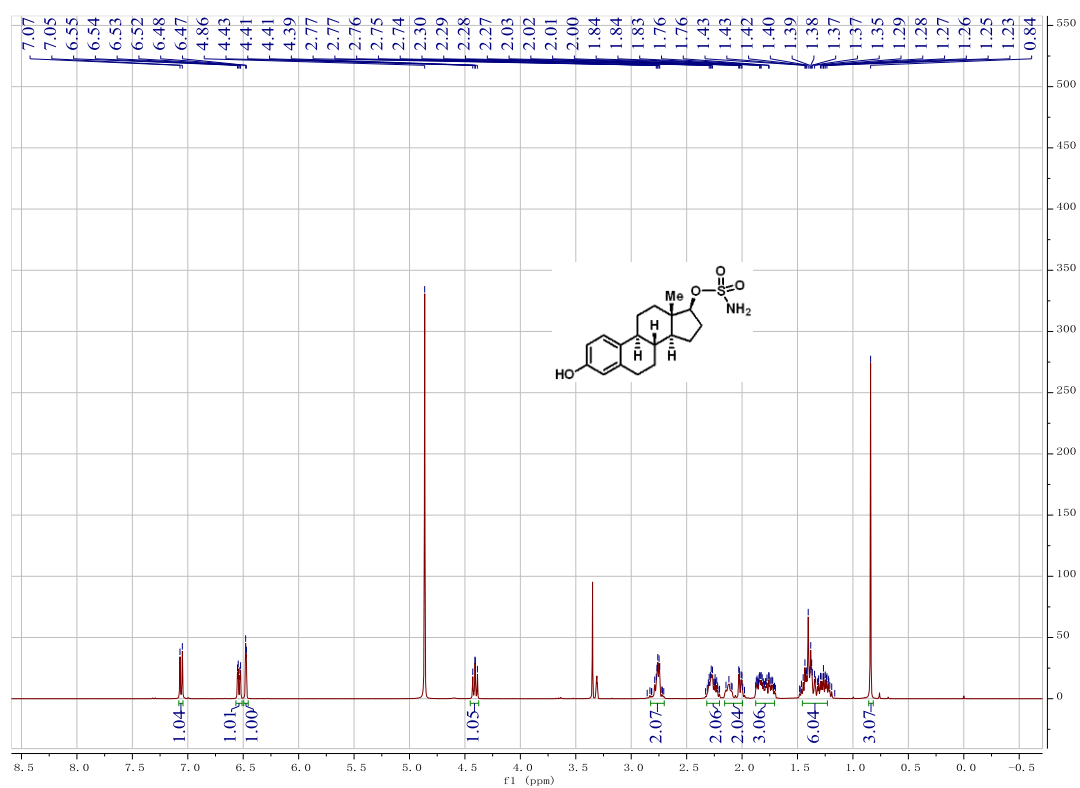
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 11b



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



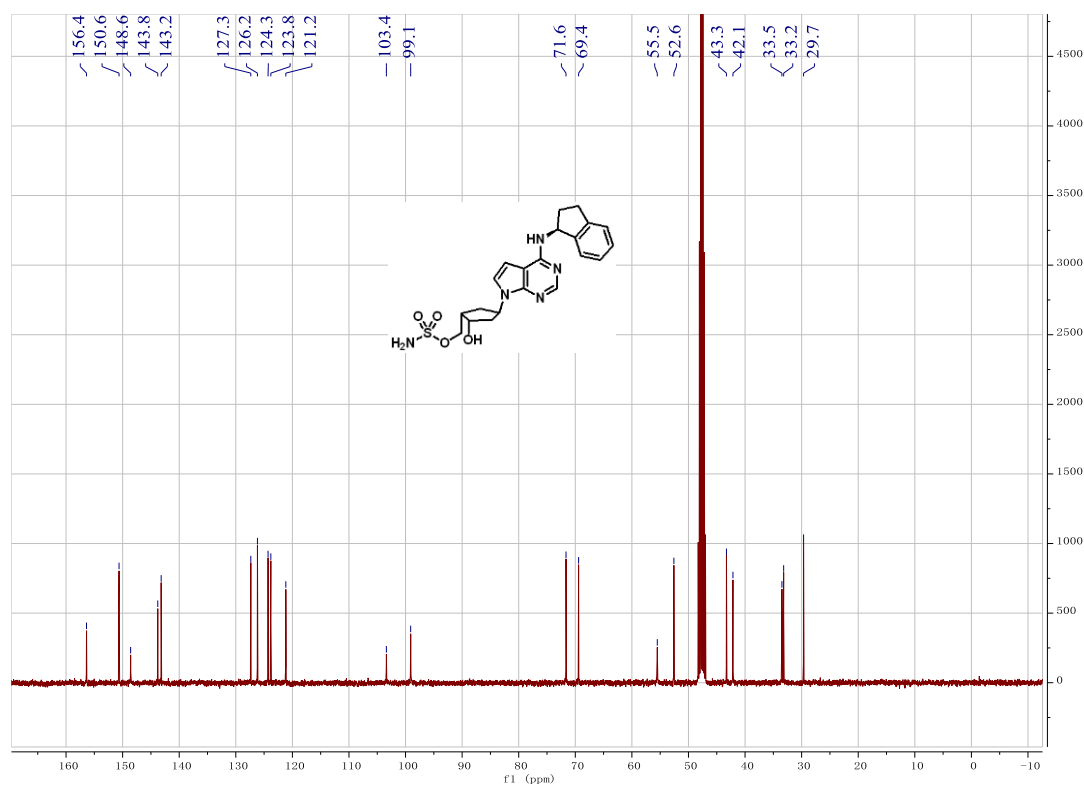
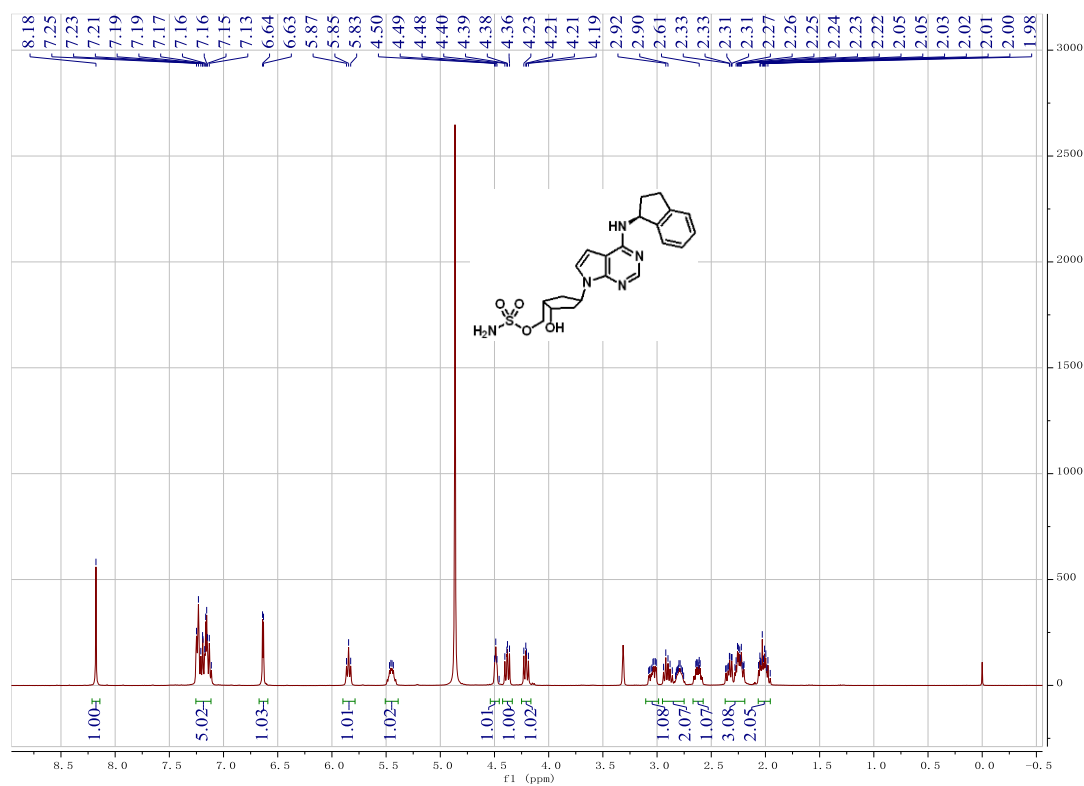
^1H (400 MHz, Methanol- d_4) and ^{13}C (101 MHz, Methanol- d_4) spectra of compound 11d



Chemical structure of compound 10:

CC1(C)CC2(C)C(C1)C(C(C2)C)C(C(C3C(C4C(C3)C(C4)C)C)C)C(C(C5C(C4)C(C5)C)C)C(C(C6C(C5)C(C6)C)C)C(C(C7C(C6)C(C7)C)C)C(C(C8C(C7)C(C8)C)C)C(C(C9C(C8)C(C9)C)C)C(C(C10C(C9)C(C10)C)C)C(C(C11C(C10)C(C11)C)C)C(C(C12C(C11)C(C12)C)C)C(C(C13C(C12)C(C13)C)C)C(C(C14C(C13)C(C14)C)C)C(C(C15C(C14)C(C15)C)C)C(C(C16C(C15)C(C16)C)C)C(C(C17C(C16)C(C17)C)C)C(C(C18C(C17)C(C18)C)C)C(C(C19C(C18)C(C19)C)C)C(C(C20C(C19)C(C20)C)C)C(C(C21C(C20)C(C21)C)C)C(C(C22C(C21)C(C22)C)C)C(C(C23C(C22)C(C23)C)C)C(C(C24C(C23)C(C24)C)C)C(C(C25C(C24)C(C25)C)C)C(C(C26C(C25)C(C26)C)C)C(C(C27C(C26)C(C27)C)C)C(C(C28C(C27)C(C28)C)C)C(C(C29C(C28)C(C29)C)C)C(C(C30C(C29)C(C30)C)C)C(C(C31C(C30)C(C31)C)C)C(C(C32C(C31)C(C32)C)C)C(C(C33C(C32)C(C33)C)C)C(C(C34C(C33)C(C34)C)C)C(C(C35C(C34)C(C35)C)C)C(C(C36C(C35)C(C36)C)C)C(C(C37C(C36)C(C37)C)C)C(C(C38C(C37)C(C38)C)C)C(C(C39C(C38)C(C39)C)C)C(C(C40C(C39)C(C40)C)C)C(C(C41C(C40)C(C41)C)C)C(C(C42C(C41)C(C42)C)C)C(C(C43C(C42)C(C43)C)C)C(C(C44C(C43)C(C44)C)C)C(C(C45C(C44)C(C45)C)C)C(C(C46C(C45)C(C46)C)C)C(C(C47C(C46)C(C47)C)C)C(C(C48C(C47)C(C48)C)C)C(C(C49C(C48)C(C49)C)C)C(C(C50C(C49)C(C50)C)C)C(C(C51C(C50)C(C51)C)C)C(C(C52C(C51)C(C52)C)C)C(C(C53C(C52)C(C53)C)C)C(C(C54C(C53)C(C54)C)C)C(C(C55C(C54)C(C55)C)C)C(C(C56C(C55)C(C56)C)C)C(C(C57C(C56)C(C57)C)C)C(C(C58C(C57)C(C58)C)C)C(C(C59C(C58)C(C59)C)C)C(C(C60C(C59)C(C60)C)C)C(C(C61C(C60)C(C61)C)C)C(C(C62C(C61)C(C62)C)C)C(C(C63C(C62)C(C63)C)C)C(C(C64C(C63)C(C64)C)C)C(C(C65C(C64)C(C65)C)C)C(C(C66C(C65)C(C66)C)C)C(C(C67C(C66)C(C67)C)C)C(C(C68C(C67)C(C68)C)C)C(C(C69C(C68)C(C69)C)C)C(C(C70C(C69)C(C70)C)C)C(C(C71C(C70)C(C71)C)C)C(C(C72C(C71)C(C72)C)C)C(C(C73C(C72)C(C73)C)C)C(C(C74C(C73)C(C74)C)C)C(C(C75C(C74)C(C75)C)C)C(C(C76C(C75)C(C76)C)C)C(C(C77C(C76)C(C77)C)C)C(C(C78C(C77)C(C78)C)C)C(C(C79C(C78)C(C79)C)C)C(C(C80C(C79)C(C80)C)C)C(C(C81C(C80)C(C81)C)C)C(C(C82C(C81)C(C82)C)C)C(C(C83C(C82)C(C83)C)C)C(C(C84C(C83)C(C84)C)C)C(C(C85C(C84)C(C85)C)C)C(C(C86C(C85)C(C86)C)C)C(C(C87C(C86)C(C87)C)C)C(C(C88C(C87)C(C88)C)C)C(C(C89C(C88)C(C89)C)C)C(C(C90C(C89)C(C90)C)C)C(C(C91C(C90)C(C91)C)C)C(C(C92C(C91)C(C92)C)C)C(C(C93C(C92)C(C93)C)C)C(C(C94C(C93)C(C94)C)C)C(C(C95C(C94)C(C95)C)C)C(C(C96C(C95)C(C96)C)C)C(C(C97C(C96)C(C97)C)C)C(C(C98C(C97)C(C98)C)C)C(C(C99C(C98)C(C99)C)C)C(C(C100C(C99)C(C100)C)C)C(C(C101C(C100)C(C101)C)C)C(C(C102C(C101)C(C102)C)C)C(C(C103C(C102)C(C103)C)C)C(C(C104C(C103)C(C104)C)C)C(C(C105C(C104)C(C105)C)C)C(C(C106C(C105)C(C106)C)C)C(C(C107C(C106)C(C107)C)C)C(C(C108C(C107)C(C108)C)C)C(C(C109C(C108)C(C109)C)C)C(C(C110C(C109)C(C110)C)C)C(C(C111C(C110)C(C111)C)C)C(C(C112C(C111)C(C112)C)C)C(C(C113C(C112)C(C113)C)C)C(C(C114C(C113)C(C114)C)C)C(C(C115C(C114)C(C115)C)C)C(C(C116C(C115)C(C116)C)C)C(C(C117C(C116)C(C117)C)C)C(C(C118C(C117)C(C118)C)C)C(C(C119C(C118)C(C119)C)C)C(C(C120C(C119)C(C120)C)C)C(C(C121C(C120)C(C121)C)C)C(C(C122C(C121)C(C122)C)C)C(C(C123C(C122)C(C123)C)C)C(C(C124C(C123)C(C124)C)C)C(C(C125C(C124)C(C125)C)C)C(C(C126C(C125)C(C126)C)C)C(C(C127C(C126)C(C127)C)C)C(C(C128C(C127)C(C128)C)C)C(C(C129C(C128)C(C129)C)C)C(C(C130C(C129)C(C130)C)C)C(C(C131C(C130)C(C131)C)C)C(C(C132C(C131)C(C132)C)C)C(C(C133C(C132)C(C133)C)C)C(C(C134C(C133)C(C134)C)C)C(C(C135C(C134)C(C135)C)C)C(C(C136C(C135)C(C136)C)C)C(C(C137C(C136)C(C137)C)C)C(C(C138C(C137)C(C138)C)C)C(C(C139C(C138)C(C139)C)C)C(C(C140C(C139)C(C140)C)C)C(C(C141C(C140)C(C141)C)C)C(C(C142C(C141)C(C142)C)C)C(C(C143C(C142)C(C143)C)C)C(C(C144C(C143)C(C144)C)C)C(C(C145C(C144)C(C145)C)C)C(C(C146C(C145)C(C146)C)C)C(C(C147C(C146)C(C147)C)C)C(C(C148C(C147)C(C148)C)C)C(C(C149C(C148)C(C149)C)C)C(C(C150C(C149)C(C150)C)C)C(C(C151C(C150)C(C151)C)C)C(C(C152C(C151)C(C152)C)C)C(C(C153C(C152)C(C153)C)C)C(C(C154C(C153)C(C154)C)C)C(C(C155C(C154)C(C155)C)C)C(C(C156C(C155)C(C156)C)C)C(C(C157C(C156)C(C157)C)C)C(C(C158C(C157)C(C158)C)C)C(C(C159C(C158)C(C159)C)C)C(C(C160C(C159)C(C160)C)C)C(C(C161C(C160)C(C161)C)C)C(C(C162C(C161)C(C162)C)C)C(C(C163C(C162)C(C163)C)C)C(C(C164C(C163)C(C164)C)C)C(C(C165C(C164)C(C165)C)C)C(C(C166C(C165)C(C166)C)C)C(C(C167C(C166)C(C167)C)C)C(C(C168C(C167)C(C168)C)C)C(C(C169C(C168)C(C169)C)C)C(C(C170C(C169)C(C170)C)C)C(C(C171C(C170)C(C171)C)C)C(C(C172C(C171)C(C172)C)C)C(C(C173C(C172)C(C173)C)C)C(C(C174C(C173)C(C174)C)C)C(C(C175C(C174)C(C175)C)C)C(C(C176C(C175)C(C176)C)C)C(C(C177C(C176)C(C177)C)C)C(C(C178C(C177)C(C178)C)C)C(C(C179C(C178)C(C179)C)C)C(C(C180C(C179)C(C180)C)C)C(C(C181C(C180)C(C181)C)C)C(C(C182C(C181)C(C182)C)C)C(C(C183C(C182)C(C183)C)C)C(C(C184C(C183)C(C184)C)C)C(C(C185C(C184)C(C185)C)C)C(C(C186C(C185)C(C186)C)C)C(C(C187C(C186)C(C187)C)C)C(C(C188C(C187)C(C188)C)C)C(C(C189C(C188)C(C189)C)C)C(C(C190C(C189)C(C190)C)C)C(C(C191C(C190)C(C191)C)C)C(C(C192C(C191)C(C192)C)C)C(C(C193C(C192)C(C193)C)C)C(C(C194C(C193)C(C194)C)C)C(C(C195C(C194)C(C195)C)C)C(C(C196C(C195)C(C196)C)C)C(C(C197C(C196)C(C197)C)C)

^1H (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.