SUPPORTING INFORMATION

Sodium Dithionite as a Bifunctional Reagent for the Cyanoalkylsulfonylation of Morita-Baylis-Hillman Acetates with Cycloketone Oxime Esters

Bathula Maheswari,[ab] C. Bharath kumar, [a] and Srirama Murthy Akondi*[ab]

a. Department of Organic Synthesis and Process Chemistry, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Hyderabad 500007, India; Email: sriramakondi@iict.res.in; sriramiict@gmail.com

b. Academy of scientific and innovative research (AcSIR), Ghaziabad 201002, India

Table of Contents

1. General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All solvents were dried and distilled according to standard procedures. Reactions were monitored by silica gel thin-layer chromatography (TLC). Silica gel (100-200 & 230-400 mesh) packed in glass column was used for the column chromatography. All heating reactions were carried out in an oil bath filled with silicone oil of 330–380 cPs viscosity. ^{1}H NMR spectra were recorded on 300, 400 or 500 MHz spectrophotometer. Chemical shift values are reported in ppm with the solvent resonance referenced to the standard position ($CDCl_3$: ^{1}H NMR: δ = 7.26; ^{13}C NMR: δ = 77.16; DMSO-d_6: ^{1}H NMR: δ = 2.5; ^{13}C NMR: δ = 39.52). Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated s (singlet), d (doublet), t (triplet), p (pentet), dd (doublet of doublets), td (triplet of doublets), m (multiplet); coupling constants (J) are in Hertz (Hz). ^{13}C NMR spectra were recorded on 101 or 75 or 126 MHz with complete proton decoupling spectrophotometer. ^{19}F NMR spectra were recorded on 377 or 471 MHz spectrophotometer. The high-resolution mass spectra (HRMS) were measured by using ESI-TOF techniques. Melting points of solids were recorded using Electrothermal (IA9100) melting point apparatus.

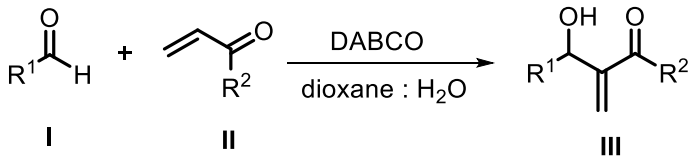
All Baylis-Hillman acetates were prepared according to literature procedures.[1] All cycloketone oxime esters are known compounds and were prepared according to literature procedures.[2]

"Note: $Na_2S_2O_4$ was weighed in the glove box."

2. General experimental procedures

2.1 General procedure for the synthesis of MBH acetates 1

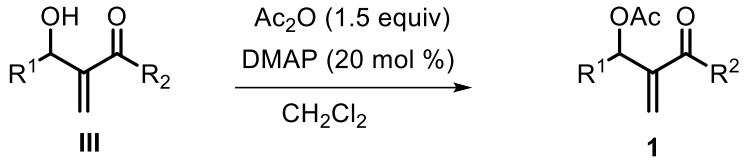
Step-1



To an oven-dried round-bottomed flask equipped with a magnetic stir bar, were added aldehyde **I** (1.0 equiv), 1,4-Diazabicyclo[2.2.2]octane (DABCO) (0.5 equiv), and activated alkene **II** (2.0 equiv), in 1,4-dioxane-H_2O (10 M, 1:1, v/v) as the solvent mixture. The reaction mixture was stirred under air at room temperature for 1-7 days. The completion of the reaction was monitored by using Thin Layer Chromatography (TLC). It was extracted with ethyl acetate (3

× 30 mL). The combined organic layers were dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel, eluting with a mixed solvent of hexane/ethyl acetate to afford MBH alcohol **III**.

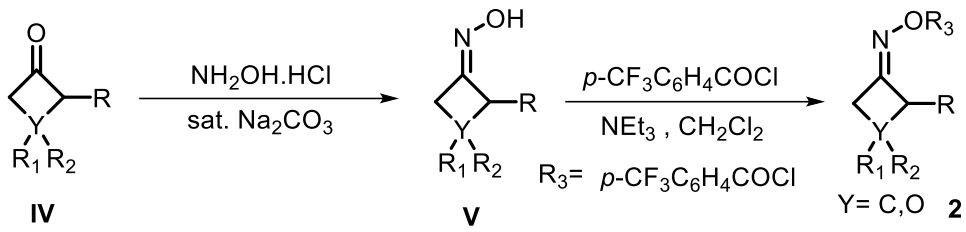
Step-2



To a solution of MBH-alcohol **III** (1.0 equiv) and DMAP (0.2 equiv) in CH_2Cl_2 (0.2 M) was added acetic anhydride (1.5 equiv). The reaction was stirred at room temperature for 1-2 hour. The organic phase was extracted with sodium bicarbonate, dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure and purification was performed using column chromatography to afford the desired MBH acetate **1**.

2.2 General procedure for the synthesis of cyclobutanone oxime esters 2

(i)

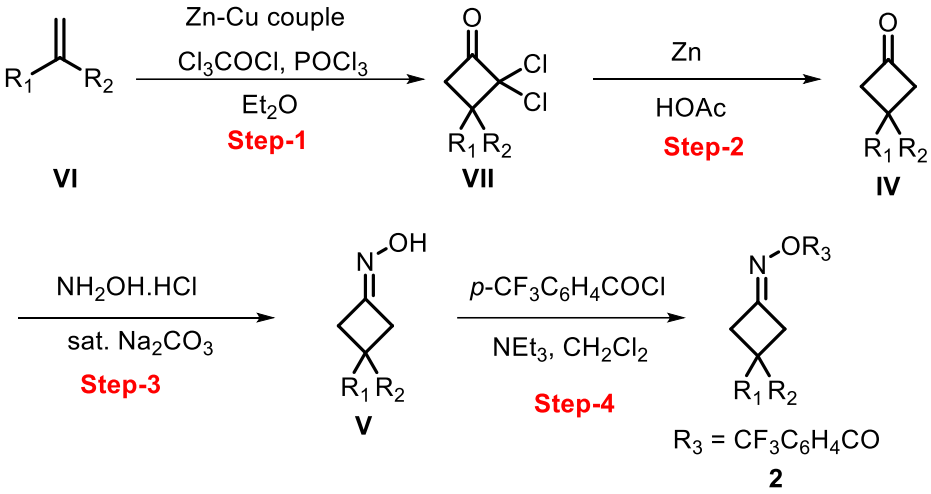


Under air, a 50 mL round-bottom flask equipped with a stir bar was charged with cyclobutanone **IV** (1.0 equiv) and hydroxylamine hydrochloride (1.1 equiv). The pH of the solution was kept at 7–8 by adding saturated aq. sodium carbonate (1.0 M). The resulting solution was stirred at 40 °C in oil bath for about 2 h. After that, the reaction mixture was extracted with EtOAc (3 × 20 mL), the solution was dried over Na_2SO_4 and evaporated to provide crude oxime **V** which was used in the next step without further purification.

In a 50 mL two-necked round-bottom flask, 4-(trifluoromethyl)benzoyl chloride (1.5 equiv) was added into the mixture of the crude cyclobutanone oxime **V**, triethylamine (2 equiv) and 20 mL dichloromethane at 0 °C under N_2 with stirring. After that, the reaction mixture was slowly warmed into room temperature and stirred for about 6 h, subsequently, water (15 mL)

was added into the above solution, and the mixture was diluted with diethyl ether. The organic layer was washed with water and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash column chromatography (eluent: petroleum ether: EtOAc = 5:1, v/v) to give cyclobutanone oxime ester **2**.

(ii) General procedure for the synthesis of cyclobutanone oxime esters from alkenes



Step 1: To a 50 mL two-necked round-bottom flask was added alkene **VI** (1.0 equiv), zinc-copper couple (3.0 equiv), and anhydrous ether (10 mL) under N_2. To this was added a solution of trichloroacetyl chloride (2.0 equiv) and phosphorus oxychloride (1.1 equiv) in ether (15 mL,) over 1 h through an addition funnel. Then, the suspension was stirred overnight at reflux. The resulting mixture was filtered through a pad of Celite and was washed with ether (20 mL). The organic solution was successively washed with water (30 mL), a saturated aqueous solution of $NaHCO_3$ (30 mL) and brine (30 mL), and dried over Na_2SO_4. Then the solution was filtered, concentrated to afford 2,2-dichlorocyclobutanone **VII** which was used in the next step without further purification.

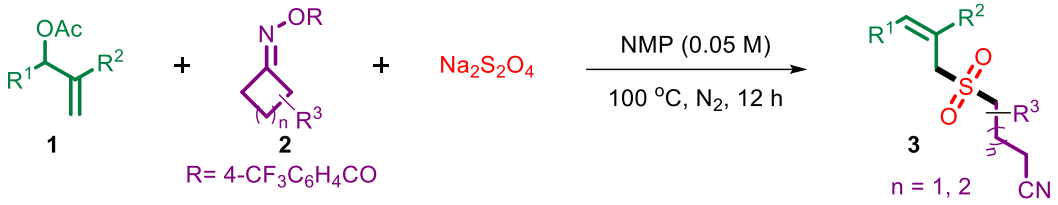
Step 2: A mixture of 2,2-dichlorocyclobutanone **VII** (1.0 equiv) and zinc dust (4.0 equiv) in acetic acid (10 mL) was stirred at room temperature for 2 h and then heated at 80 °C in oil bath for 5 h. The resulting mixture was allowed to cool to room temperature, then, the solution was diluted with water (30 mL) and extracted with ether (3 × 15 mL). The organic phase was washed successively with a saturated solution of aqueous $NaHCO_3$ (3 × 15 mL), water (30 mL) and brine (30 mL), then dried over Na_2SO_4 and concentrated in vacuum. The crude material

was then purified by flash chromatography with a mixture of petroleum ether and ethyl acetate to afford the cyclobutanone **IV**.

Step 3: To a stirred solution of cyclobutanone **IV** (1.0 equiv) in saturated aq. sodium carbonate (1.0 M) was added hydroxylamine hydrochloride (2.0 equiv) at rt. The resulting solution was stirred at 40 °C in oil bath for about 2 h. After that, the reaction mixture was extracted with EtOAc (3 × 20 mL), the solution was dried over Na_2SO_4 and evaporated to provide crude oxime **V** which was used in the next step without further purification.

Step 4: To a mixture of cyclobutanone oxime **V** (1.0 equiv), triethylamine (2.0 equiv) and CH_2Cl_2 (10 mL) in a 50 mL two-necked round-bottom flask was added 4-(trifluoromethyl)benzoyl chloride (1.5 equiv) at 0 °C. After 6 h, water was added to the above solution, and the mixture was diluted with diethyl ether. The organic layer was washed with water and dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash column chromatography (eluent: petroleum ether: EtOAc = 5:1, v/v) to give cyclobutanone oxime ester **2**.

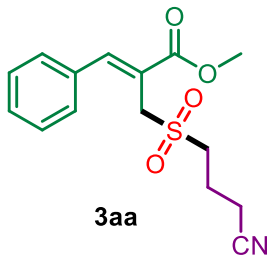
2.3 General procedure for the synthesis of compounds 3



In an oven dried 5.0 mL vial equipped with a magnetic stir bar was charged with Baylis - Hillman Acetate **1** (0.2 mmol, 1.0 equiv.), cycloketone oxime ester **2** (0.3 mmol, 1.5 equiv.) and $Na_2S_2O_4$ (0.6 mmol, 3.0 equiv.) followed by the addition of the solvent N-Methyl-2-pyrrolidone (4.0 mL) under nitrogen atmosphere. The vial was sealed with a septum, evacuated, back filled with nitrogen and stirred at 100 °C for 12 hours. After completion of reaction, the resulting mixture was diluted with ethyl acetate (15 mL) and washed successively with ice cold water (15 mL×2) and $NaHCO_3$ solution (15 mL×2). The organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified via flash chromatography on silica gel to get the desired compounds **3.**

3. Analytical data of the products 3

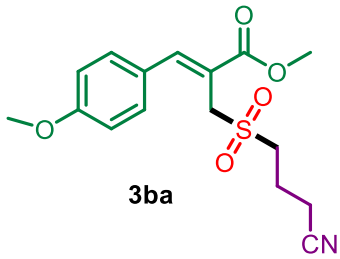
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-phenylacrylate (3aa)



3aa

Colourless oil (49.7 mg, 81% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.50 – 7.40 (m, 2H), 7.50 – 7.39 (m, 3H), 4.34 (s, 2H), 3.90 (s, 3H), 3.22 (t, *J* = 7.3 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.23 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 147.5, 133.6, 130.2, 129.4, 129.1, 120.4, 118.2, 53.2, 52.9, 52.4, 18.5, 16.4; HRMS (ESI) calcd for $C_{15}H_{18}NO_4S^+$ $[M+H]^+$= 308.0952, found = 308.0951.

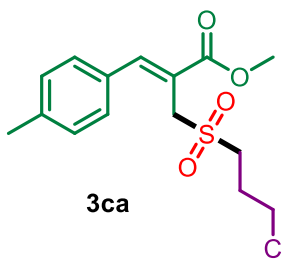
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(4-methoxyphenyl)acrylate (3ba)



3ba

Pale yellow oil (51.2 mg, 76% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.64 – 7.56 (m, 2H), 7.00 – 6.93 (m, 2H), 4.36 (s, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 3.23 (t, *J* = 7.3 Hz, 2H), 2.59 (t, *J* = 7.1 Hz, 2H), 2.24 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 162.9, 148.9, 133.3, 127.5, 119.7, 118.9, 116.0, 56.9, 54.9, 54.3, 53.9, 20.0, 17.9; HRMS (ESI) calcd for $C_{16}H_{19}NO_5SNa^+$ $[M+Na]^+$ = 360.0876, found = 360.0883.

Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(4-(trifluoromethyl)phenyl)acrylate (3ca)

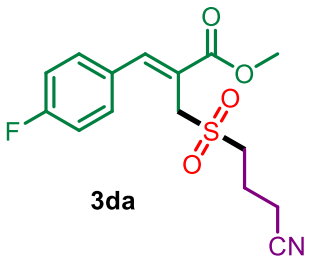


3ca

White solid; mp = 88 – 90 ºC; (36 mg, 57% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.24 (m, 2H), 4.36 (s, 2H), 3.89 (s, 3H), 3.21 (t, *J* = 7.2 Hz, 2H), 2.58 (t, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 2.22 (p, *J* = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, CDCl3) δ 167.5, 147.7, 140.9, 130.8,

129.9, 129.7, 129.2, 129.1, 129.0, 119.4, 118.3, 53.3, 52.9, 52.4, 21.6, 18.6, 16.4; HRMS (ESI) calcd for $C_{16}H_{19}NO_4SNa^+$ $[M+Na]^+$ = 344.0927, found = 344.0931.

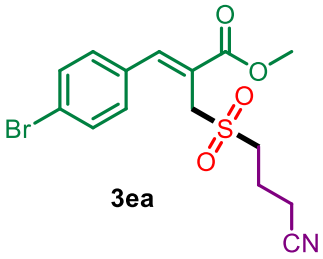
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(4-fluorophenyl)acrylate (3da)



3da

pale yellow oil (30 mg, 45% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.63 – 7.58 (m, 2H), 7.18 – 7.11 (m, 2H), 4.30 (s, 2H), 3.89 (s, 3H), 3.27 (t, *J* = 7.4 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.27 (p, *J* = 7.3 Hz 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 163.9 (d, *J* = 252.2 Hz), 146.6, 131.8 (d, *J* = 8.5 Hz), 129.7 (d, *J* = 2.8 Hz), 120.0, 118.3, 116.48 (d, *J* = 21.9 Hz), 53.4, 53.1, 52.7, 18.6, 16.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.12; HRMS (ESI) calcd for $C_{15}H_{16}FNO_4SNa^+$ $[M+Na]^+$ = 348.0676, found = 348.0678.

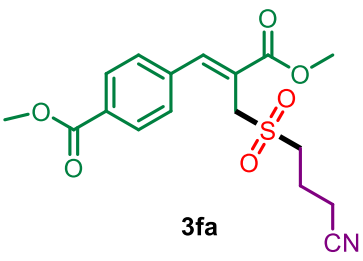
Methyl (*Z*)-3-(4-bromophenyl)-2-(((3-cyanopropyl)sulfonyl)methyl)acrylate (3ea)



3ea

Colourless oil (31.2mg, 41% yield); Flash column eluent: n-Hexane/EtOAc: (70/30) ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.61 – 7.57 (m, 2H), 7.49 – 7.45 (m, 2H), 4.28 (s, 2H), 3.90 (s, 3H), 3.27 (t, *J* = 7.3 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.27 (p, *J* = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 146.5, 132.4, 131.0, 125.0, 120.9, 118.2, 53.4, 53.1, 52.7, 18.6, 16.5; HRMS (ESI) calcd for $C_{15}H_{17}BrNO_4S^+$ $[M+H]^+$ = 386.0056, found = 386.0044.

Methyl (*Z*)-4-(2-(((3-cyanopropyl)sulfonyl)methyl)-3-methoxy-3-oxoprop-1-en-1-yl) benzoate (3fa)

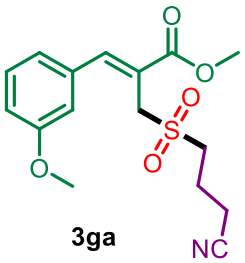


3fa

White solid; mp = 118 – 120 ºC; (27.7 mg, 38% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (s,1H), 8.13 – 8.10 (m, 2H), 7.64 (d, *J* = 8.1 Hz, 2H), 4.29 (s, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.26 (t, *J* = 7.3 Hz,

2H), 2.62 (t, J = 7.1 Hz, 2H), 2.26 (p, J = 7.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 166.4, 146.4, 138.0, 131.5, 131.0, 129.4, 122.2, 118.2, 53.3, 53.2, 52.7, 52.5, 18.6, 16.5; HRMS (ESI) calcd for $C_{17}H_{20}NO_6S^+$ $[M+H]^+$ =366.1006, found = 366.1001.

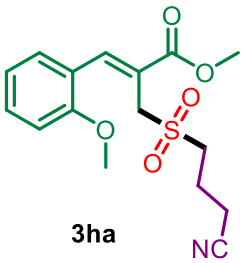
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(3-methoxyphenyl)acrylate (3ga)



3ga

Colourless oil (37 mg, 55% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.18 (s, 1H), 7.09 (d, J = 7.6 Hz, 1H), 6.97 (dd, J = 8.2, 2.0 Hz, 1H), 4.33 (s, 2H), 3.89 (s, 3H), 3.84 (s, 3H), 3.23 (t, J = 7.3 Hz, 2H), 2.59 (t, J = 7.1 Hz, 2H), 2.22 (p, J = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 160.0, 147.5, 134.8, 130.1, 121.8, 120.6, 118.2, 116.6, 113.9, 55.6, 53.3, 52.9, 52.5, 18.5, 16.4; HRMS (ESI) calcd for $C_{16}H_{19}NO_5SNa^+$ $[M+Na]^+$ = 360.0876, found = 360.0881.

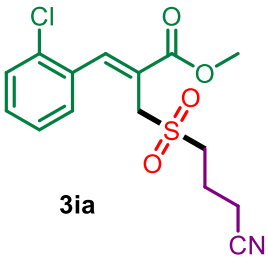
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(2-methoxyphenyl)acrylate (3ha)



3ha

Colourless oil (48.5 mg, 72% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.58 (dd, J = 7.6, 0.9 Hz, 1H), 7.44 – 7.37 (m, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 4.29 (s, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.15 (t, J = 7.1, 2H), 2.54 (t, J = 7.1 Hz, 2H), 2.14 (p, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 157.5, 143.7, 131.7, 129.9, 122.7, 121.0, 120.8, 118.2, 110.9, 55.7, 53.3, 52.8, 52.0, 29.7, 18.5, 16.4; HRMS (ESI) calcd for $C_{16}H_{19}NO_5SNa^+$ $[M+Na]^+$ = 360.0876, found = 360.0881.

Methyl (*Z*)-3-(2-chlorophenyl)-2-(((3-cyanopropyl)sulfonyl)methyl)acrylate (3ia)

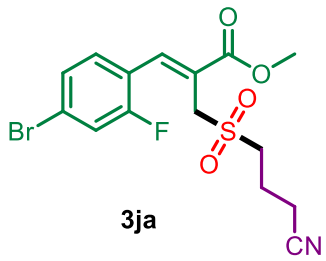


3ia

Colourless oil (30 mg, 45% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.68 – 7.64 (m, 1H), 7.49 – 7.45 (m, 1H), 7.41 – 7.36 (m, 2H), 4.21 (s, 2H), 3.92 (s, 3H), 3.21 (t, J = 7.1 Hz, 2H), 2.59 (t, J = 7.1 Hz, 2H), 2.20

(p, J = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 144.5, 134.0, 132.3, 131.2, 130.4, 130.0, 127.5, 122.9, 118.2, 53.2, 53.2, 52.4, 18.6, 16.4; HRMS (ESI) calcd for $C_{15}H_{16}ClNO_4SNa^+$ $[M+Na]^+$ = 364.0381, found = 364.0376.

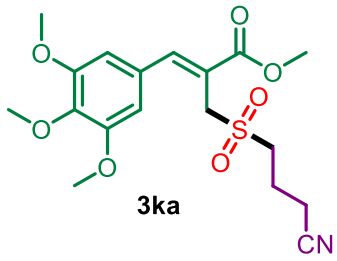
Methyl (Z)-3-(4-bromo-2-fluorophenyl)-2-(((3-cyanopropyl)sulfonyl)methyl)acrylate (3ja)



3ja

Colourless oil (31.5 mg, 39% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.66 (t, J = 8.1 Hz, 1H), 7.41 (dd, J = 8.3, 1.5 Hz, 1H), 7.34 (dd, J = 9.5, 1.8 Hz, 1H), 4.24 (s, 2H), 3.91 (s, 3H), 3.27 (t, J = 7.3 Hz, 2H), 2.63 (t, J = 7.1 Hz, 2H), 2.27 (p, J = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 160.0 (d, J = 255.9 Hz), 139.3 (d, J = 3.5 Hz), 131.2, 128.3 (d, J = 3.3 Hz), 125.1 (d, J = 9.6 Hz), 122.9, 120.7 (d, J = 13.2 Hz), 119.6 (d, J = 24.7 Hz), 118.1, 53.5, 53.1, 52.6, 18.5, 16.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.58; HRMS (ESI) calcd for $C_{15}H_{15}BrFNO_4SNa^+$ $[M+Na]^+$ = 427.9781 found = 427.9748.

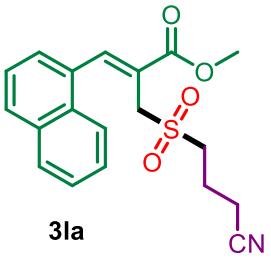
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(3,4,5-trimethoxyphenyl)acrylate (3ka)



3ka

White solid; mp = 98 – 100 ºC; (35 mg, 44% yield); Flash column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 6.89 (s, 2H), 4.34 (s, 2H), 3.88 (s, 12H), 3.32 (t, J = 7.3 Hz, 2H), 2.63 (t, J = 7.1 Hz, 2H), 2.28 (p, J = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 153.4, 148.0, 139.8, 128.8, 119.3, 118.2, 107.0, 61.0, 56.4, 54.1, 52.9, 52.8, 18.5, 16.4; HRMS (ESI) calcd for $C_{18}H_{24}NO_7S^+$ $[M+H]^+$ = 398.1268, found = 398.1258

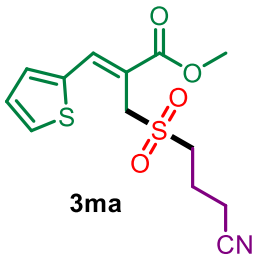
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(naphthalen-1-yl)acrylate (3la)



3la

Colourless oil (48.6 mg, 68% yield); Flash column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.95 – 7.91 (m, 2H), 7.87 – 7.85 (m, 1H), 7.68 (d, *J* = 7.1 Hz, 1H), 7.58 – 7.55 (m, 3H), 4.27 (s, 2H), 3.97 (s, 3H), 3.02 (t, *J* = 7.3 Hz, 2H), 2.30 (t, *J* = 7.2 Hz, 2H), 1.95 (p, *J* = 7.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 147.6, 135.4, 133.0, 132.7, 132.3, 130.9, 129.2, 128.9, 128.7, 127.6, 126.0, 125.4, 120.0, 55.0, 54.8, 54.0, 20.5, 18.0; HRMS (ESI) calcd for $C_{19}H_{19}NO_4SNa^+$ $[M+Na]^+$ = 380.0922, found = 380.0925.

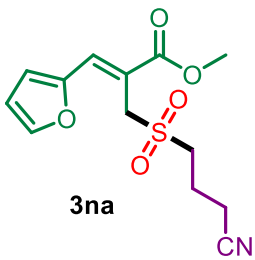
Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(thiophen-2-yl)acrylate (3ma)



3ma

Colourless oil (44.4 mg, 71% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.61 (d, *J* = 5.1 Hz, 1H), 7.55 (d, *J* = 3.7 Hz, 1H), 7.16 (dd, *J* = 5.1, 3.8 Hz, 1H), 4.51 (s, 2H), 3.87 (s, 3H), 3.24 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.27 (p, *J* = 7.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 166.1, 139.3, 136.6, 134.8, 131.6, 128.2, 118.2, 115.4, 53.9, 52.9, 52.2, 18.6, 16.4; HRMS (ESI) calcd for $C_{13}H_{15}NO_4S_2Na^+$ $[M+Na]^+$ = 336.0338, found = 336.0338.

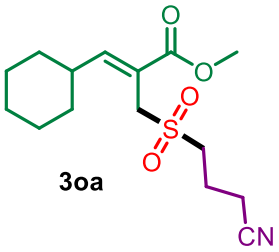
Methyl (Z)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-(furan-2-yl)acrylate (3na)



3na

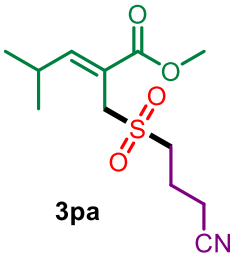
Colourless oil (34.5 mg, 58% yield); Flash column eluent: n-Hexane/EtOAc: (60/40); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.66 (d, *J* = 1.7 Hz, 1H), 6.86 (d, *J* = 3.5 Hz, 1H), 6.56 (dd, *J* = 3.5, 1.8 Hz, 1H), 4.68 (s, 2H), 3.86 (s, 3H), 3.16 (t, *J* = 7.3 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.25 (p, *J* = 7.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 149.9, 146.5, 131.4, 120.1, 118.2, 114.6, 112.8, 53.3, 52.8, 51.4, 18.4, 16.4; HRMS (ESI) calcd for $C_{13}H_{16}NO_5S^+$ $[M+H]^+$ = 298.0744, found = 298.0744.

Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-cyclohexylacrylate (3oa)



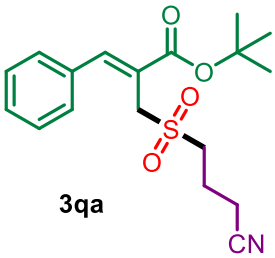
Colourless oil (31.9 mg, 51% yield); Flash column eluent: n-Hexane/EtOAc: (60/40); (*Z* /*E* = 8:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07 (d, *J* = 10.9 Hz, 89/100 ×1H), 6.29 (d, *J* = 9.9 Hz, 11/100 ×1H), 4.13 (s, 89/100 × 2H), 3.96 (s, 11/100 × 2H), 3.82 (s, 11/100 ×3H), 3.80 (s, 89/100 ×3H), 3.13 (t, *J* = 7.2 Hz, 89/100 ×2H), 3.09 (t, *J* = 7.5 Hz, 11/100 ×2H), 2.61 (t, *J* = 7.1 Hz, 2H), 2.55 – 2.44 (m, 1H), 2.25 (p, *J* = 7.2 Hz, 2H), 1.78 – 1.69 (m, 4H), 1.40 – 1.10 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 158.9, 157.4, 117.9, 117.3, 52.3, 51.6, 50.9, 38.8, 31.8, 31.0, 25.4, 25.0, 24.8, 18.2, 16.1; HRMS (ESI) calcd for $C_{15}H_{23}NO_4SNa^+$ $[M+Na]^+$ =336.1240, found = 336.1246.

Methyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-4-methylpent-2-enoate (3pa)



Colourless oil (32.8 mg, 60% yield); Flash column eluent: n-Hexane/EtOAc: (75/25); (*Z* /*E* = 8:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 10.9 Hz, 89/100 × 1H), 6.25 (d, *J* = 10.1 Hz, 11/100 × 1H), 4.11 (s, 89/100 × 2H), 3.95 (s, 11/100 ×2H), 3.81 (s, 11/100 × 3H), 3.79 (s, 89/100 × 3H), 3.16 – 3.06 (m, 2H), 2.86 – 2.76 (m, 1H), 2.60 (t, *J* = 7.0, 11/100 × 2H), 2.61 (t, *J* = 7.0, 89/100 × 2H), 2.28 – 2.20 (m, 2H), 1.08 (d, *J* = 6.5 Hz, 89/100 × 6H), 1.06 (d, *J* = 6.7 Hz, 11/100 × 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 166.4, 160.4, 159.1, 118.3, 117.5, 117.3, 52.6, 51.8, 51.3, 29.7, 29.4, 29.3, 22.1, 21.6, 18.5, 18.3, 16.4; HRMS (ESI) calcd for $C_{12}H_{19}NO_4SNa^+$ $[M+Na]^+$ = 296.0927, found = 296.0924.

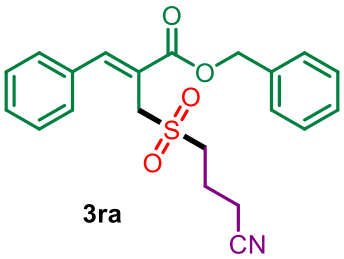
tert-Butyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-phenylacrylate (3qa)



Colourless oil (20.9 mg, 30% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.59 – 7.52 (m, 2H), 7.48–7.39 (m, 3H), 4.30 (s, 2H), 3.16 (t, *J* = 7.1, 2H), 2.56 (t, *J* = 7.1 Hz, 2H), 2.19 (p, *J* = 7.3, 2H), 1.57 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 146.2, 133.9, 129.9, 129.2, 129.0, 122.3, 118.2, 82.6, 53,0

52.3, 28.1, 18.5, 16.5; HRMS (ESI) calcd for $C_{18}H_{24}NO_4S^+$ $[M+H]^+$ = 350.1421, found = 350.1412.

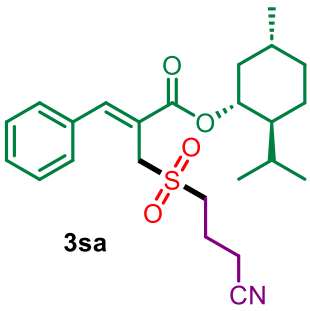
Benzyl (Z)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-phenylacrylate (3ra)



3ra

Colourless oil (38.3 mg, 50% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.62 – 7.54 (m, 2H), 7.50 – 7.33 (m, 8H), 5.31 (s, 2H), 4.34 (s, 2H), 3.12 (t, *J* = 7.3 Hz, 2H), 2.48 (t, *J* = 7.1 Hz, 2H), 2.14 (p, *J* = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 147.8, 135.4, 133.5, 130.3, 129.5, 129.1, 128.8, 128.7, 128.6, 120.4, 118.2, 67.8, 53.2, 52.5, 18.5, 16.3; HRMS (ESI) calcd for $C_{21}H_{22}NO_4S^+$ $[M+H]^+$ = 384.1264, found = 384.1258.

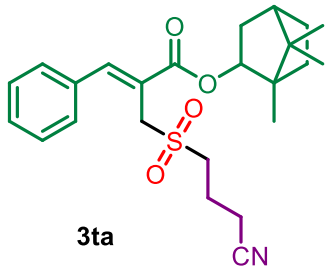
(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-phenylacrylate (3sa)



3sa

Colourless oil (64.7 mg,75% yield); Flash column eluent: n-Hexane/EtOAc: (80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.63 – 7.52 (m, 2H), 7.51 – 7.37 (m, 3H), 4.87 (td, *J* = 10.9, 4.4 Hz, 1H), 4.34 (s, 2H), 3.19 (t, *J* = 7.3 Hz, 2H), 2.57 (t, *J* = 7.2 Hz, 2H), 2.21 (p, *J* = 7.2 Hz, 2H), 2.11 – 2.02 (m, 1H), 1.97–1.89 (m, 1H),1.78 – 1.68 (m, 2H), 1.60 – 1.50 (m, 2H), 1.28 – 1.25 (m, 1H), 1.18 – 1.05 (m, 2H), 0.94 (d, *J* = 6.5 Hz, 3H) 0.93 (d, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 146.6, 133.7, 130.1, 129.4, 129.0, 121.1, 118.2, 76.3, 53.7, 52.9, 47.2, 40.9, 34.2, 31.5, 26.6, 23.6, 22.0, 20.8, 19.1, 17.0, 16.9; HRMS (ESI) calcd for $C_{24}H_{34}NO_4S^+$ $[M+H]^+$ = 432.2203, found = 432.2211.

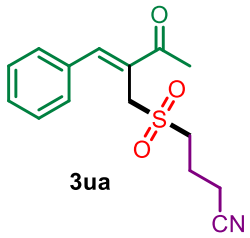
1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl (*Z*)-2-(((3-cyanopropyl)sulfonyl)methyl)-3-phenylacrylate (3ta)



3ta

Colourless oil (51.5 mg, 60% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.56 (dt, *J* = 9.8, 1.7 Hz, 2H), 7.48 – 7.39 (m, 3H), 4.84 (t, *J* = 7.1, 1H), 4.32 (s, 2H), 3.19 (t, *J* = 7.3 Hz, 2H), 2.56 (t, *J* = 7.2 Hz, 2H), 2.20 (p, *J* = 7.2 Hz, 2H), 1.91 – 1.87 (m, 2H), 1.81 (d, *J* = 2.0 Hz, 1H), 1.77 – 1.69 (m, 1H), 1.65 – 1.57 (m, 1H), 1.24 – 1.18 (m, 1H), 1.16 – 1.10 (m, 1H), 1.08 (s, 3H), 0.93 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 146.6, 133.7, 130.1, 129.4, 129.1, 121.2, 118.2, 82.9, 53.1, 52.4, 49.2, 47.1, 45.1, 38.8, 33.7, 27.0, 20.1, 18.6, 16.4, 11.7; HRMS (ESI) calcd for $C_{24}H_{31}NO_4SNa^+$ $[M+Na]^+$ = 452.1866, found = 452.1868.

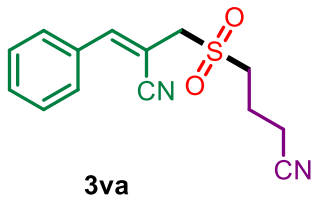
(*Z*)-4-((2-Benzylidene-3-oxobutyl)sulfonyl)butanenitrile (3ua)



3ua

Colourless oil (36.6 mg, 34% yield); Flash column eluent: n-Hexane/EtOAc: (80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.61 (dd, *J* = 7.1, 1.1 Hz, 2H), 7.52 – 7.42 (m, 3H), 4.32 (s, 2H), 3.24 (t, *J* = 7.3 Hz, 2H), 2.61 (t, *J* = 7.2 Hz, 2H), 2.56 (s, 3H), 2.31 – 2.21 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 148.1, 133.5, 130.4, 130.1, 129.5, 129.1, 118.2, 53.1, 52.0, 25.7, 18.7, 16.4; HRMS (ESI) calcd for $C_{15}H_{17}NO_3SNa^+$ $[M+Na]^+$ = 314.0821 found = 314.0824.

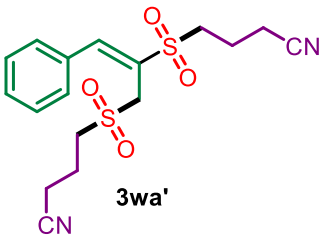
(*Z*)-4-((2-Cyano-3-phenylallyl)sulfonyl)butanenitrile (3va)



3va

Brown solid; mp = 108.0 – 110.0 ºC (26 mg, 48% yield); Flash column eluent: n-Hexane/EtOAc: (60/40); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 – 7.78 (m, 2H), 7.53 – 7.41 (m, 3H), 7.34 (s, 1H), 4.02 (s, 2H), 3.29 (t, *J* = 7.3 Hz, 2H), 2.66 (t, *J* = 7.0 Hz, 2H), 2.31 (p, *J* = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 132.2, 132.1, 129.6, 129.2, 118.0, 117.7, 96.6, 59.0, 50.8, 18.3, 16.4; HRMS (ESI) calcd for $C_{14}H_{13}N_2O_2S$ $[M-H]^-$ = 273.0776, found = 273.0726.

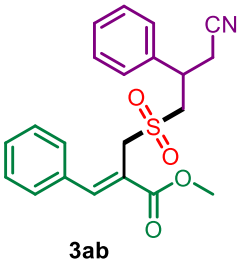
(*E*)-4,4'-(3-Phenylprop-2-ene-1,2-diyldisulfonyl)dibutanenitrile (3wa')



3wa'

Brown syrup (18.5 mg, 23% yield); Flash column eluent: n-Hexane/EtOAc: (60/40); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.65 (dd, *J* = 6.7, 2.7 Hz, 2H), 7.55 – 7.48 (m, 3H), 4.51 (s, 2H), 3.52 (t, *J* = 7.4 Hz, 2H), 3.30 (t, *J* = 7.3 Hz, 2H), 2.64 (t, *J* = 7.0 Hz, 4H), 2.27 (p, *J* = 7.1 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4, 131.8, 131.6, 129.4, 129.1, 118.2, 117.9, 53.3, 52.9, 52.9, 18.9, 18.4, 16.3; HRMS (ESI) calcd for $C_{17}H_{20}N_2O_4S_2Na^+$ $[M+Na]^+$ = 403.0757, found = 403.0760.

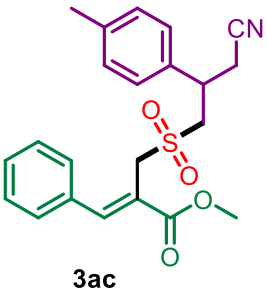
Methyl (*Z*)-2-(((3-cyano-2-phenylpropyl)sulfonyl)methyl)-3-phenylacrylate (3ab)



3ab

Colourless oil (49 mg, 64% yield); Flash column eluent: n-Hexane/EtOAc: (75/25); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.48 – 7.43 (m, 2H), 7.40 – 7.24 (m, 6H), 7.22 – 7.17 (m, 2H), 4.14 (s, 2H), 3.78 (s, 3H), 3.67 (p, *J* = 6.76, Hz, 1H), 3.47 (d, *J* = 6.9 Hz, 2H), 2.92 – 2.85 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 147.3, 139.2, 133.6, 130.2, 129.4, 129.3, 129.1, 128.5, 127.2, 120.4, 117.3, 58.3, 54.7, 53.3, 36.4, 25.0 HRMS (ESI) calcd for $C_{21}H_{22}NO_4S^+$ $[M+H]^+$ = 384.1264, found = 384.1265.

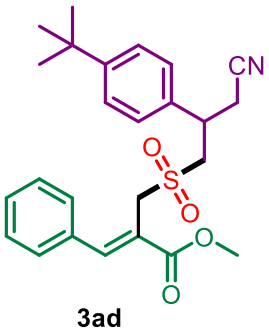
Methyl (*Z*)-2-(((3-cyano-2-(p-tolyl)propyl)sulfonyl)methyl)-3-phenylacrylate (3ac)



3ac

Colourless oil (56.4 mg, 71% yield); Flash column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.53 (dd, *J* = 7.4, 1.9 Hz, 2H), 7.48 – 7.40 (m, 3H), 7.21 – 7.11 (m, 4H), 4.20 (s, 2H), 3.86 (s, 3H), 3.76 – 3.65 (m, 1H), 3.56 – 3.50 (m, 2H), 2.96 – 2.90 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 147.1, 138.1, 135.9, 133.4, 129.9, 129.8, 129.1, 128.8, 126.8, 120.2,117.2, 57.8, 54.1, 52.6, 35.5, 24.5, 20.9; HRMS (ESI) calcd for $C_{22}H_{27}N_2O_4S^+$ $[M+NH_4]^+$ = 415.1686, found = 415.1703.

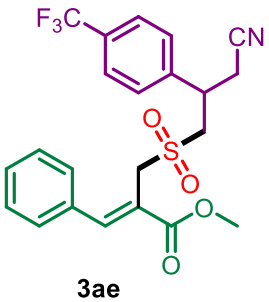
Methyl (*Z*)-2-(((2-(4-(tert-butyl)phenyl)-3-cyanopropyl)sulfonyl)methyl)-phenylacrylate (3ad)



3ad

Colourless oil (50.9 mg, 58% yield); Flash column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.53 (dd, *J* = 7.0, 1.1 Hz, 2H), 7.46 – 7.41 (m, 3H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 4.27 – 4.18 (m, 2H), 3.86 (s, 3H), 3.76 – 3.70 (m, 1H), 3.58 – 3.48 (m, 2H), 3.02 – 2.90 (m, 2H), 1.30 (d, *J* = 7.0 Hz, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 146.2, 133.6,129.9, 129.2, 129.0, 122.3, 118.2, 82.6, 53.0, 52.3, 28.1, 18.5, 16.4; HRMS (ESI) calcd for $C_{25}H_{30}NO_4S^+$ $[M+H]^+$ = 440.1890, found = 440.1893.

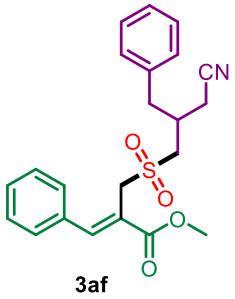
Methyl (*Z*)-2-(((3-cyano-2-(4-(trifluoromethyl)phenyl)propyl)sulfonyl)methyl)-3-phenylacrylate (3ae)



3ae

Colourless oil (44.2 mg, 49% yield); Flash column eluent: n-Hexane/EtOAc: (65/35); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.55 – 7.50 (m, 2H), 7.48 – 7.39 (m, 5H), 4.29 (s, 2H), 3.89 – 3.78 (m, 4H), 3.64 – 3.50 (m, 2H), 3.05 – 2.96 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 147.7, 143.2, 133.6, 131.1 (q, *J* = 32.9 Hz) , 130.4, 129.4, 129.2, 127.9, 126.4 (q, *J* = 3.4 Hz), 122.5 (q, *J* = 272.9 Hz), 120.3, 117.0, 57.5, 54.6, 53.0, 35.8, 24.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.75; HRMS (ESI) calcd for $C_{22}H_{20}F_3NO_4SNa^+$ $[M+Na]^+$ = 474.0963, found = 474.0954.

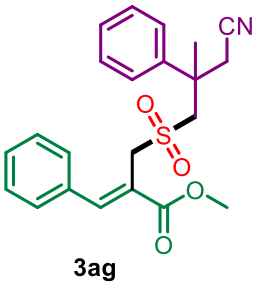
Methyl (*Z*)-2-(((2-benzyl-3-cyanopropyl)sulfonyl)methyl)-3-phenylacrylate (3af)



3af

Colourless oil (42.9 mg, 54% yield); Flash column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.58 – 7.53 (m, 2H), 7.49 – 7.41 (m, 3H), 7.34 (dd, *J* = 9.8, 4.6 Hz, 2H), 7.29 – 7.24 (m, 1H), 7.24 – 7.19 (m, 2H), 4.33 (s, 2H), 3.87 (s, 3H), 3.20 (dd, *J* = 5.5, 2.8 Hz, 2H), 3.02 – 2.90 (m, 1H), 2.81 (dt, *J* = 21.3, 6.4 Hz, 3H), 2.50 (d, *J* = 13.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 147.5, 136.8, 133.6, 130.2, 129.4, 129.2, 129.1, 129.0, 127.3, 120.3, 117.4, 56.1, 54.2, 52.9, 39.5, 31.7, 29.7, 21.1; HRMS (ESI) calcd for $C_{22}H_{23}NO_4SNa^+$ $[M+Na]^+$ = 420.1240, found = 420.1237.

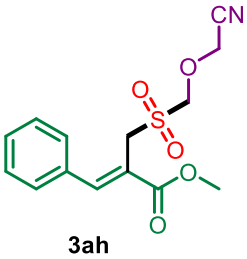
Methyl (*Z*)-2-(((3-cyano-2-methyl-2-phenylpropyl)sulfonyl)methyl)-3-phenylacrylate (3ag)



3ag

Colourless oil (36.5 mg, 46% yield); Flash column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.52 – 7.36 (m, 9H), 7.34 – 7.27 (m, 1H), 3.99 (s, 2H), 3.87 (s, 3H), 3.68 (t, *J* = 12.3 Hz, 1H), 3.55 (s, 1H), 3.50 (s, 1H), 3.22 (t, *J* = 3.9 Hz, 2H), 1.81 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 147.1, 141.8, 133.6, 130.0, 129.3, 129.1, 129.0, 128.0, 125.6, 120.7, 117.5, 63.5, 55.5, 52.8, 40.2, 29.2, 26.0; HRMS (ESI) calcd for $C_{22}H_{24}NO_4S^+$ $[M+H]^+$ = 398.1421, found = 398.1420.

Methyl (*Z*)-2-((((cyanomethoxy)methyl)sulfonyl)methyl)-3-phenylacrylate (3ah)

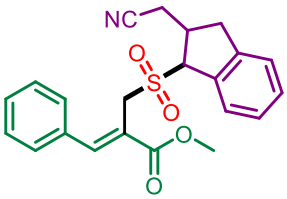


3ah

Colourless oil (25.9 mg, 42% yield); Flash column eluent: n-Hexane/EtOAc: (75/25); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.55 – 7.51 (m, 2H), 7.45 (dd, *J* = 5.6, 3.8 Hz, 3H), 4.67 (d, *J* = 0.6 Hz, 4H), 4.38 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 147.3,

133.3, 130.0, 129.1, 128.9, 119.8, 114.3, 82.8, 56.9, 52.7, 50.6, 29.5; HRMS (ESI) calcd for $C_{14}H_{16}NO_5S^+$ $[M+H]^+$ = 310.0744, found = 310.0739.

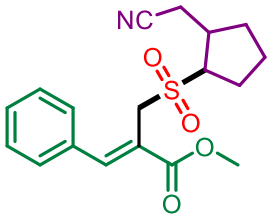
Methyl (*Z*)-2-((((1S)-2-(cyanomethyl)-2,3-dihydro-1H-inden-1-yl)sulfonyl)methyl)-3-phenylacrylate (3ai)



3ai

Colourless oil (32.4 mg, 41% yield); Flash column eluent: n-Hexane/EtOAc: (60/40); dr ratio: 1.4:1.0 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.59 (dt, *J* = 3.7, 2.4 Hz, 2H), 7.51 – 7.41 (m, 3H), 7.33 – 7.24 (m, 3H), 7.25 – 7.19 (m, 1H), 4.48 – 4.27 (m, 2H), 4.20 – 4.07 (m, 1H), 3.96 – 3.85 (m, 4H), 3.43 (dd, *J* = 16.3, 7.7 Hz, 1H), 3.34 – 3.26 (m, 1H), 3.06 (dd, *J* = 5.0, 2.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 147.3, 139.5, 139.2, 133.7, 130.1, 129.3, 129.1, 128.8, 128.0, 124.9, 123.5, 120.4, 117.4, 65.9, 53.0, 51.7, 41.2, 33.6, 22.9; HRMS (ESI) calcd for $C_{22}H_{25}N_2O_4S^+$ $[M+NH_4]^+$ = 413.1530, found = 413.1544.

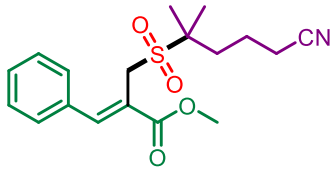
Methyl (*Z*)-2-((((1R)-2-(cyanomethyl)cyclopentyl)sulfonyl)methyl)-3-phenylacrylate (3aj)



3aj

Colourless oil (32.6 mg, 47% yield); Flash column eluent: n-Hexane/EtOAc: (75/25); dr ratio: 1.5:1.0 ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.64 – 7.53 (m, 2H), 7.50 – 7.39 (m, 3H), 4.29 (d, *J* = 3.5 Hz, 2H), 3.88 (d, *J* = 1.5 Hz, 3H), 3.67 (dt, *J* = 14.6, 6.9 Hz, 1H), 2.49 – 2.39 (m, 3H), 2.37 – 2.22 (m, 2H), 2.19 – 2.07 (m, 1H), 2.04 – 1.92 (m, 1H), 1.89 – 1.78 (m, 1H), 1.75 – 1.60 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 146.9, 133.8, 130.1, 129.3, 129.0, 120.8, 118.5, 118.1, 62.0, 61.6, 52.8, 51.4, 51.2, 36.9, 35.7, 32.5, 32.1, 31.8, 31.7, 26.0, 25.9, 21.9, 21.7; HRMS (ESI) calcd for $C_{18}H_{22}NO_4S^+$ $[M+H]^+$ = 348.1264, found = 348.1270.

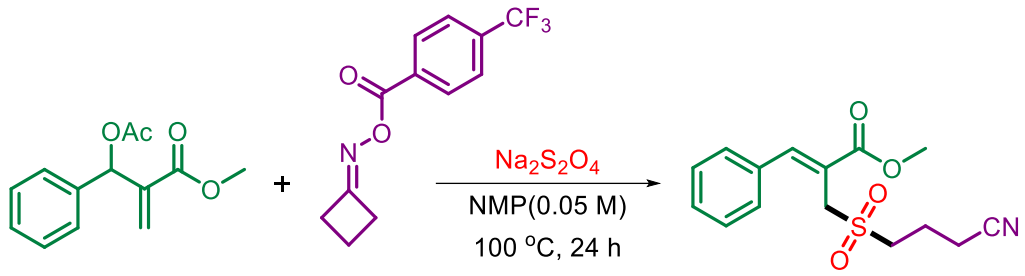
Methyl (*Z*)-2-(((5-cyano-2-methylpentan-2-yl)sulfonyl)methyl)-3-phenylacrylate (3ak)



3ak

Colourless oil (27.9 mg, 40% yield); Flash column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.74 – 7.63 (m, 2H), 7.47 – 7.39 (m, 3H), 4.31 (s, 2H), 3.88 (s, 3H), 2.39 (t, *J* = 6.7 Hz, 2H), 1.98 – 1.79 (m, 4H), 1.44 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 146.6, 133.9, 129.9, 129.2, 128.9, 119.9, 119.0, 62.9, 52.7, 46.1, 35.0, 21.1, 20.5, 17.6; HRMS (ESI) calcd for $C_{18}H_{24}NO_4S^+$ $[M+H]^+$ = 350.1421, found = 350.1421.

4. Gram scale reaction



1a 1.0 mmol

2a 1.5 mmol

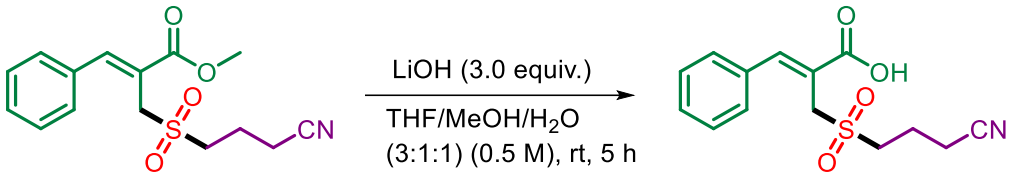
3aa

In an oven dried 5.0 mL vial equipped with a magnetic stir bar was charged with MBH acetate **1a** (234 mg, 1.0 mmol, 1.0 equiv.), cycloketone oxime ester **2a** (385.5 mg, 1.5 mmol, 1.5 equiv.) and $Na_2S_2O_4$ (522 mg, 3.0 mmol, 3.0 equiv.) followed by the addition of N-Methyl-2-pyrrolidone (20 mL) under nitrogen atmosphere, and stirred at 100 ^{0}C for 24 hours.

After completion of reaction, the resulting mixture was diluted with ethyl acetate (15 mL) and washed successively with ice cold water (15 mL×2) and $NaHCO_3$ solution (15 mL×2). The organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified via flash chromatography on silica gel to get the desired product **3aa** (190.3 mg, 62%).

5. Derivatization of product 3aa

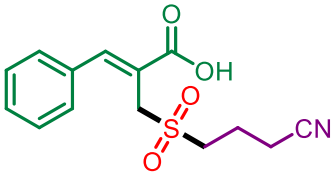
5.1 Synthesis of the Compound (4)



3aa **4**, 67%

An oven dried 5.0 mL vial equipped with a magnetic stir bar was charged with **3aa** (0.16 mmol, 1.0 equiv.), anhydrous LiOH (0.48 mmol, 3.0 equiv.), followed by THF/MeOH/H_2O (0.32 mL) [3:1:1]. The vial was sealed with a septum and stirred for 5 hours. After completion of reaction, the resulting mixture was evaporated to dryness then diluted with 50 mL of ethyl acetate, the solution is quenched with 1M HCl until the pH reaches 1 and washed successively with water (50 mL×2) and brine solution (50 mL×2). The organic layer was concentrated to get the desired compound (**4**).

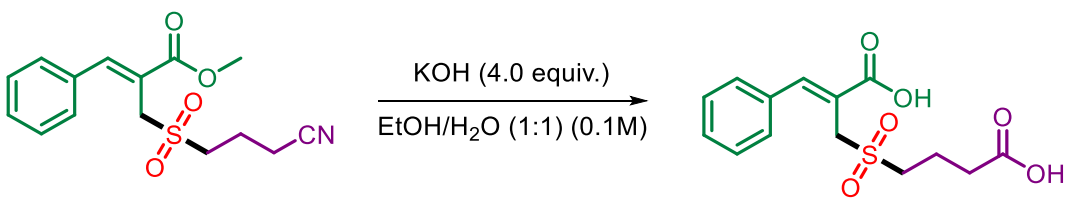
(*Z*)-2-(((3-Cyanopropyl)sulfonyl)methyl)-3-phenylacrylic acid 4



4

Colourless oil (31.4 mg, 67% yield); column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.67 – 7.60 (m, 2H), 7.52 – 7.43 (m, 3H), 4.37 (s, 2H), 3.27 (t, J = 7.1, 2H), 2.61 (t, J = 7.0 Hz, 2H), 2.24 (p, J = 7.4, 2H); ^{13}C NMR (126 MHz, CDCl3) δ 169.7, 149.4, 133.1, 130.4, 129.4, 128.9, 119.1, 118.0, 52.7, 52.3, 29.5, 18.3, 16.2; HRMS(ESI) calcd for $C_{14}H_{14}NO_4S^-$ $[M-H]^-$ = 292.0649, found = 292.0650

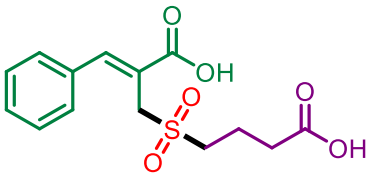
5.2 Synthesis of the Compound (5)



3aa **5**, 46%

To a 50 mL round bottom flask equipped with a magnetic stir bar was added **3aa** (0.2 mmol, 60.0 mg), KOH (0.8 mmol, 44.8 mg, 4.0 equiv), EtOH/H_2O (2 mL, v/v = 1/1). Then, the reaction mixture was stirred at reflux in oil bath. Upon completion (16 h), it was cooled to room temperature, ethanol was removed by evaporation, and the resulting aqueous layer was extracted with EtOAc and the organic layers were discarded. The aqueous layer was acidified with 2 N HCl to pH = 2 - 3 and extracted with EtOAc. After that, the combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum to give the pure desired product light yellow oil (20 mg, 46% yield).

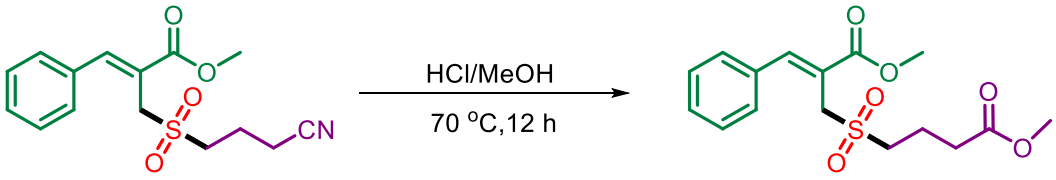
(*Z*)-4-((2-Carboxy-3-phenylallyl)sulfonyl)butanoic acid (5)



5

White solid; mp = 118 – 120 °C; (28.8 mg, 46% yield); column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (400 MHz, DMSO-d_6) δ ^{1}H NMR (400 MHz, DMSO) δ 12.63 (s, 2H), 7.97 (s, 1H), 7.67 (d, *J* = 6.7 Hz, 2H), 7.46 (d, *J* = 6.7 Hz, 3H), 4.35 (s, 2H), 3.16 (t, *J* = 7.4 Hz, 2H), 2.34 (t, *J* = 7.2 Hz, 2H), 1.89 (p , *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 173.5, 168.0, 144.5, 133.9, 129.7, 129.4, 128.8, 121.6, 52.8, 52.0, 39.5, 31.8, 17.4; HRMS(ESI) calcd for $C_{14}H_{16}O_6NaS^+$ $[M+Na]^+$ = 335.0565, found = 335.0601.

5.3 Synthesis of the Compound (6)

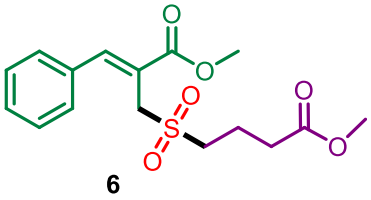


3aa **6**, 52%

To a solution of **3aa** (30.7 mg, 0.1 mmol) in MeOH (1 mL), conc. HCl (1 mL) was added and heated to 70 °C under reflux conditions for 12 h. After cooling to room temperature, the reaction mixture was quenched with 10 mL of H_2O, and extracted with EtOAc (10 mL×3). The

combined organic layer was washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuum. The residue was purified by flash chromatography to afford the desired product **6** in 52% yield.

Methyl (*Z*)-4-((2-(methoxycarbonyl)-3-phenylallyl)sulfonyl)butanoate (6)

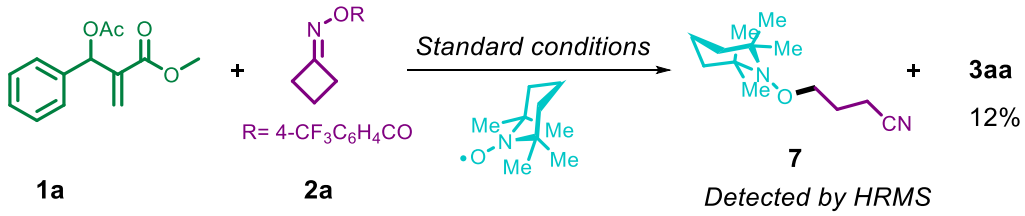


6

Colourless oil (17.6 mg, 52% yield); column eluent: n-Hexane/EtOAc: (70/30); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.60 – 7.55 (m, 2H), 7.47 – 7.37 (m, 3H), 4.31 (s, 2H), 3.87 (s, 3H), 3.67 (s, 3H), 3.19 – 3.09 (m, 2H), 2.48 (t, J = 7.2 Hz, 2H), 2.18 – 2.08 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 167.4, 147.1, 133.8, 130.1, 129.5, 129.1, 120.8, 53.5, 52.9, 52.6, 51.9, 32.3, 17.8; HRMS(ESI) calcd for $C_{16}H_{24}O_6SN^+$ $[M+NH_4]^+$ = 358.1319, found = 358.1335.

6. Mechanistic Studies

6.1. Radical inhibition and trapping experiments:



In an oven dried 5.0 mL vial equipped with a magnetic stir bar was charged with MBH acetate **1a** (46.8 mg, 0.2 mmol, 1.0 equiv.), cycloketone oxime ester **2a** (77.1 mg, 0.3 mmol, 1.5 equiv.) and $Na_2S_2O_4$ (104.4 mg, 0.6 mmol, 3.0 equiv.) and TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv.) followed by the addition of N-Methyl-2-pyrrolidone (4 mL) under nitrogen atmosphere, and stirred at 100 ºC for 12 hours. After completion of reaction, the resulting mixture was diluted with ethyl acetate (15 mL) and washed successively with ice cold water (15 mL×2) and $NaHCO_3$ solution (15 mL×2). The organic layer was dried over anhydrous Na_2SO_4,

concentrated, and in this reaction, the formation of product **3aa** was decreased to 12% and the TEMPO cyano alkyl adduct **7** was characterized by HRMS (Figure S1); HRMS(ESI) calcd for $C_{13}H_{24}N_2O$ $[M+H]^+$ = 225.1961 found = 225.1957.

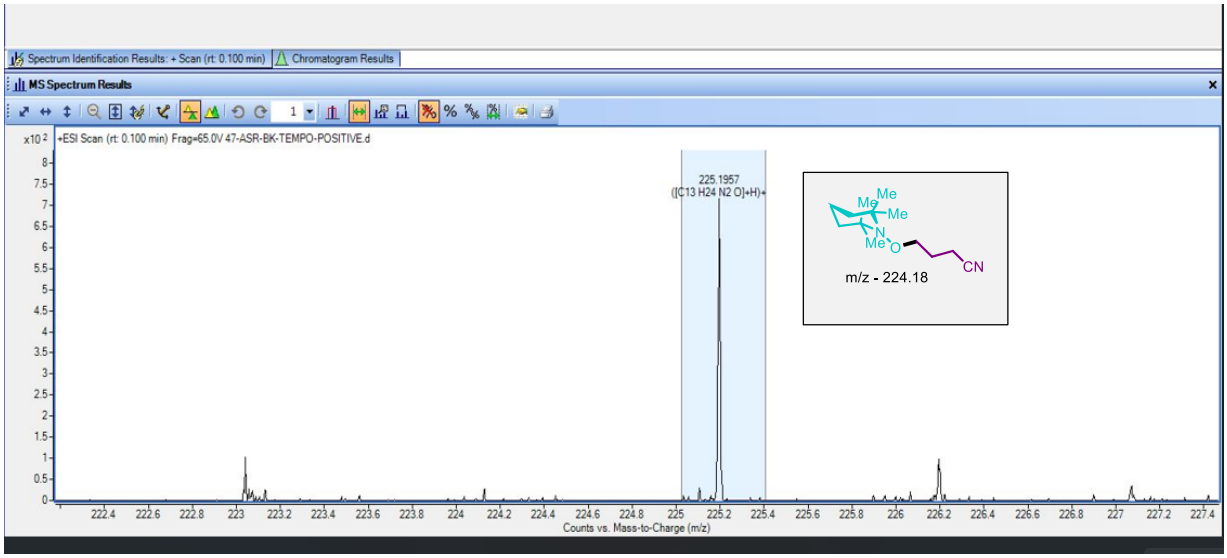
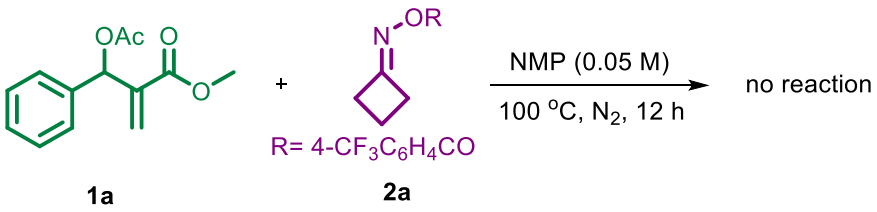


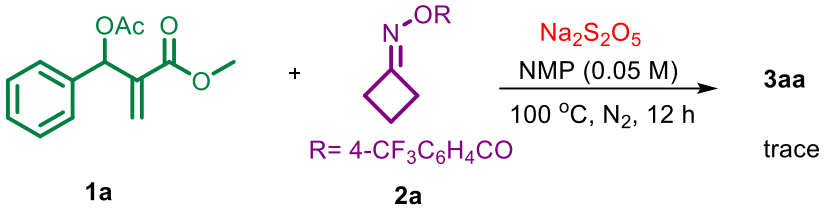
Figure S1. HRMS (ESI) Spectrum of compound **7**

6.2. Heating in the absence of $Na_2S_2O_4$:



In an oven dried 5.0 mL vial equipped with a magnetic stir bar was charged with MBH acetate **1a** (46.8 mg, 0.2 mmol, 1.0 equiv.), cycloketone oxime ester **2a** (77.1 mg, 0.3 mmol, 1.5 equiv.) and N-Methyl-2-pyrrolidone (4 mL) under nitrogen atmosphere, and stirred at 100 °C for 12 hours. No desired product was detected under this condition.

6.3. Using $Na_2S_2O_5$ instead of $Na_2S_2O_4$:

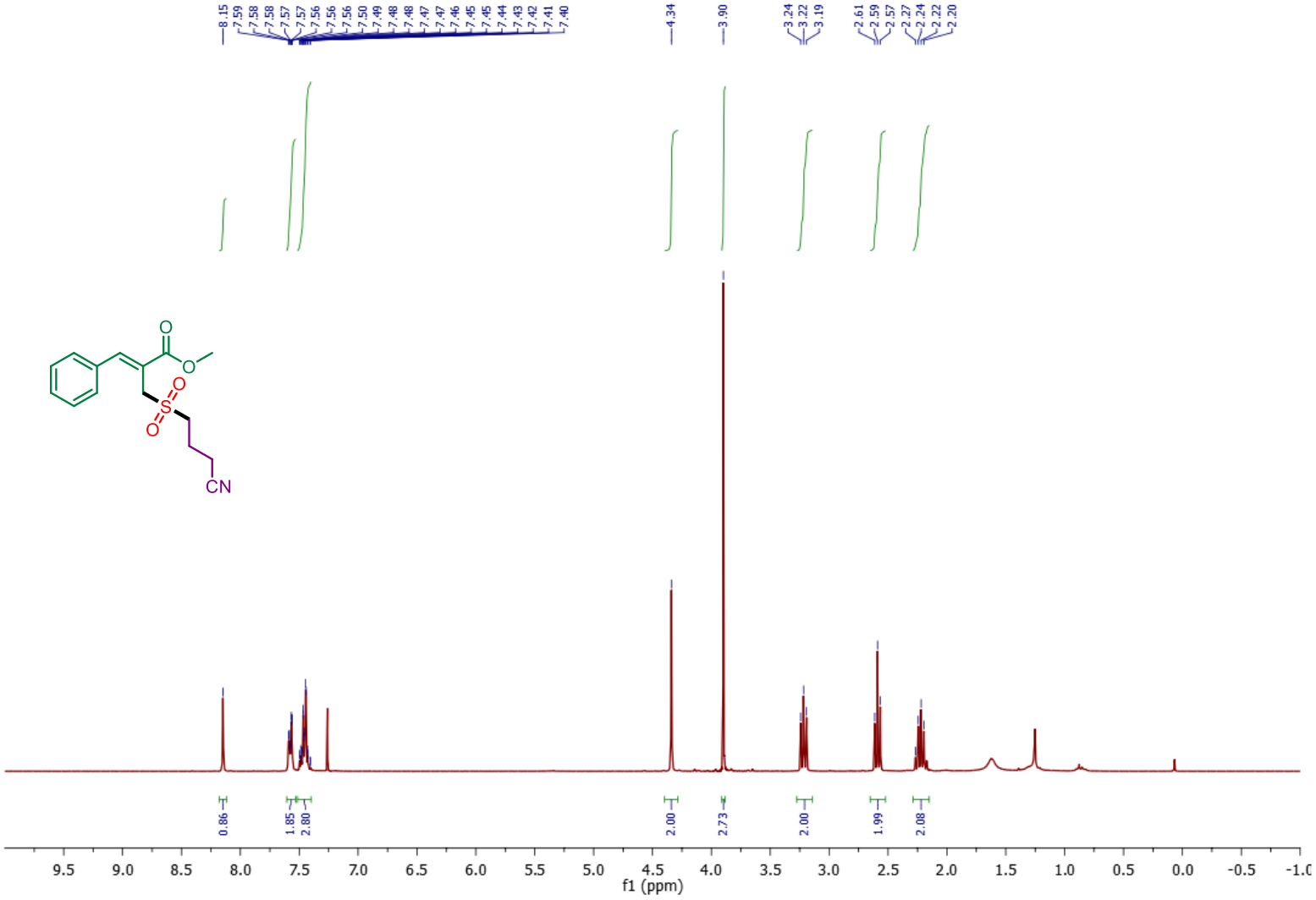


In an oven dried 5.0 mL vial equipped with a magnetic stir bar was charged with MBH acetate **1a** (46.8 mg, 0.2 mmol, 1.0 equiv.), cycloketone oxime ester **2a** (77.1 mg, 0.3 mmol, 1.5 equiv.) and $Na_2S_2O_5$ (114 mg, 0.6 mmol, 3.0 equiv.) followed by the addition of N-Methyl-2-pyrrolidone (4 mL) under nitrogen atmosphere, and stirred at 100 °C for 12 hours. Only a trace amount of desired compound **3aa** was detected under this condition.

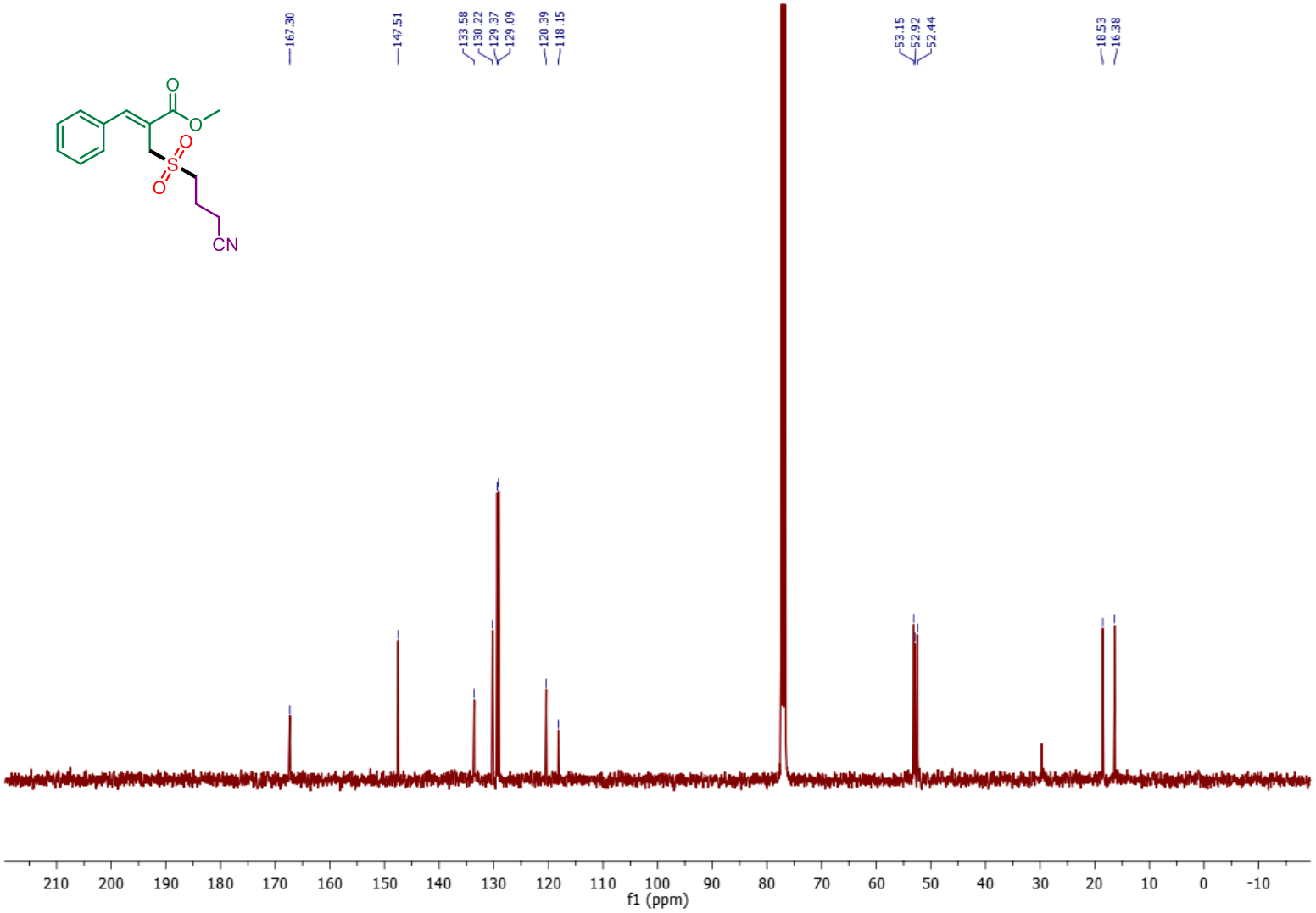
7. References:

1. (a) A. Latorre, J. A. Sáez, S. Rodríguez and F. V. González, *Tetrahedron*, 2014, **70**, 97–102; (b) I. D. G. Watson and A. K. Yudin, *J. Am. Chem. Soc.*, 2005, **127**, 17516–17529; (c) N. S. Camilo, H. Santos, L. A. Zeoly, F. S. Fernandes, M. T. Rodrigues Jr, T. S. Silva, S. R. Lima, J. C. Serafim, A. S. B. de Oliveira, A. G. Carpanez, G. W. Amarante and F. Coelho, *European J. Org. Chem.*, DOI:10.1002/ejoc.202101448; (d) X. Zhang, Y. Zhang, X. Li, B. Li, S. Xiao, Y. Tang, P. Xie and T.-P. Loh, *Org. Lett.*, 2023, **25**, 6863–6868.
2. (a) J. Bai, M. Li, C. Zhou, Y. Sha, J. Cheng, J. Sun and S. Sun, *Org. Lett.*, 2021, **23**, 9654–9658; (b) E. Lee-Ruff and G. Mladenova, *Chem. Rev.*, 2003, **103**, 1449–1483; (c) L. Li, H. Chen, M. Mei and L. Zhou, *Chem. Commun.*, 2017, **53**, 11544–11547; (d) Y.-R. Gu, X.-H. Duan, L. Yang and L.-N. Guo, *Org. Lett.*, 2017, **19**, 5908–5911; (d) X.-Y. Lu, J.-C. Wang, X.-M. Sun, M.-T. Gao, W.-J. Ying, M.-Y. Ge, Z.-H. Wei, Z. Liu and X.-K. Chen, *J. Org. Chem.*, 2023, **88**, 513–524.

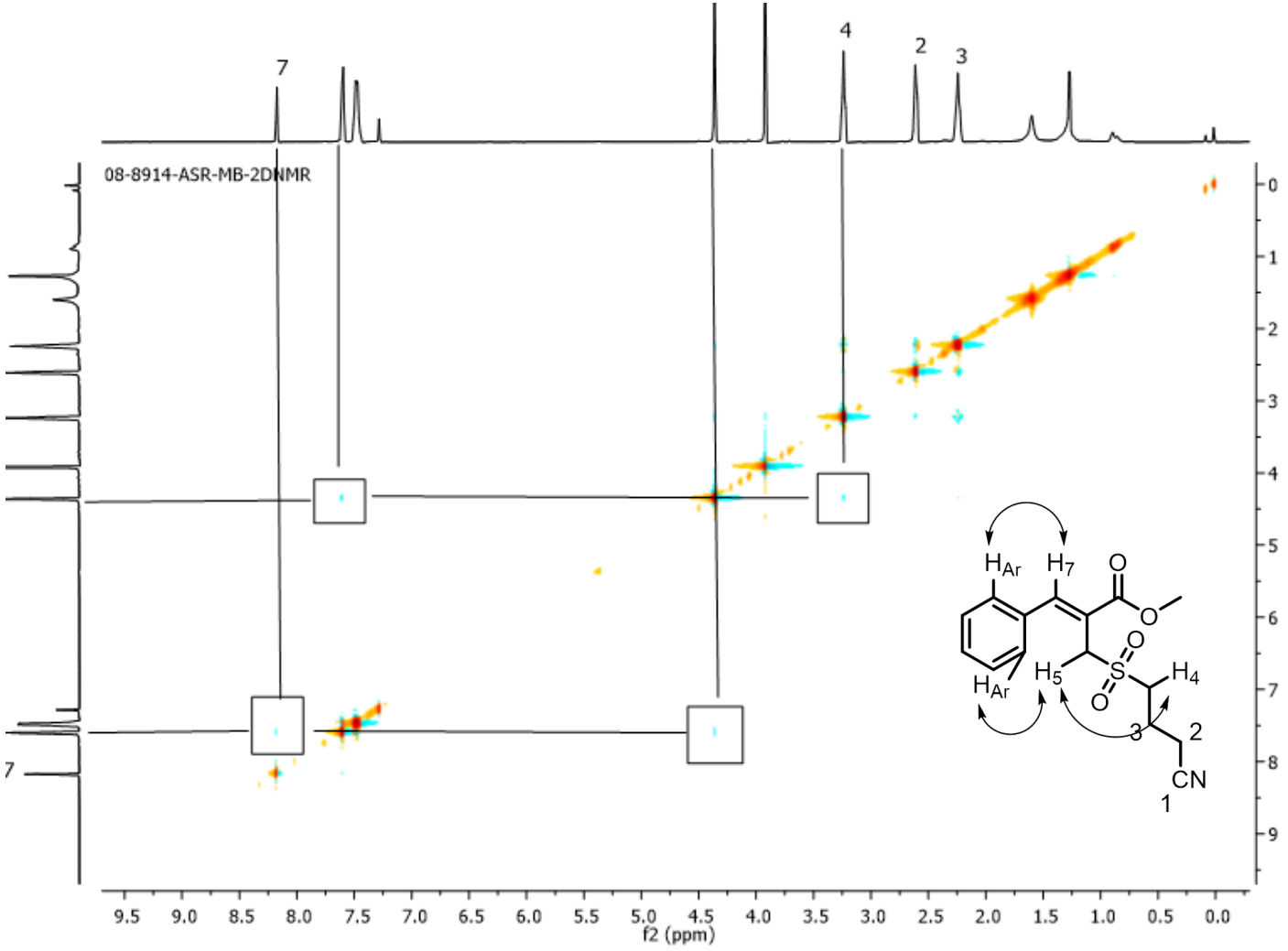
[1]H NMR (400 MHz, CDCl3) Spectrum of Compound **(3aa)**



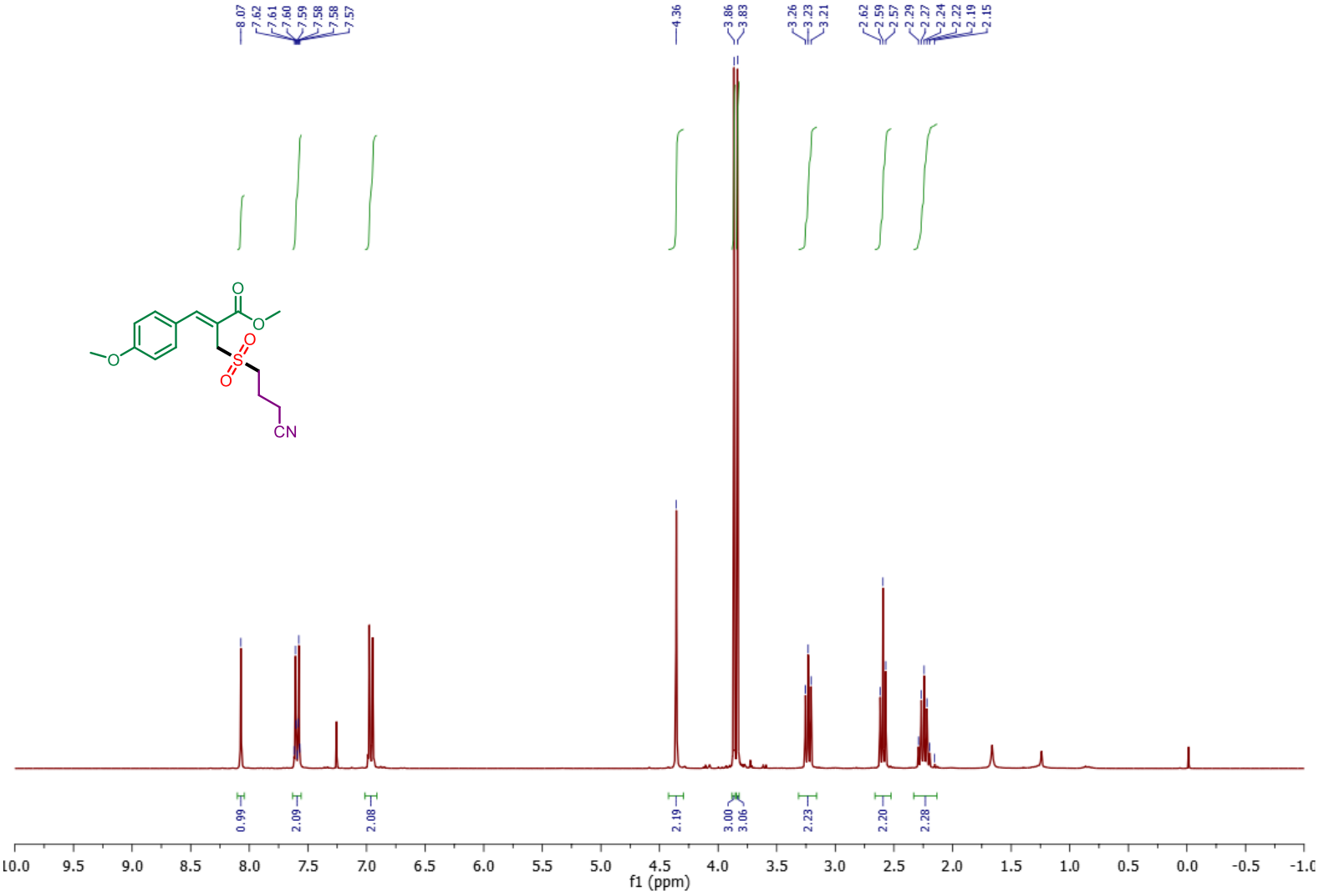
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3aa)**



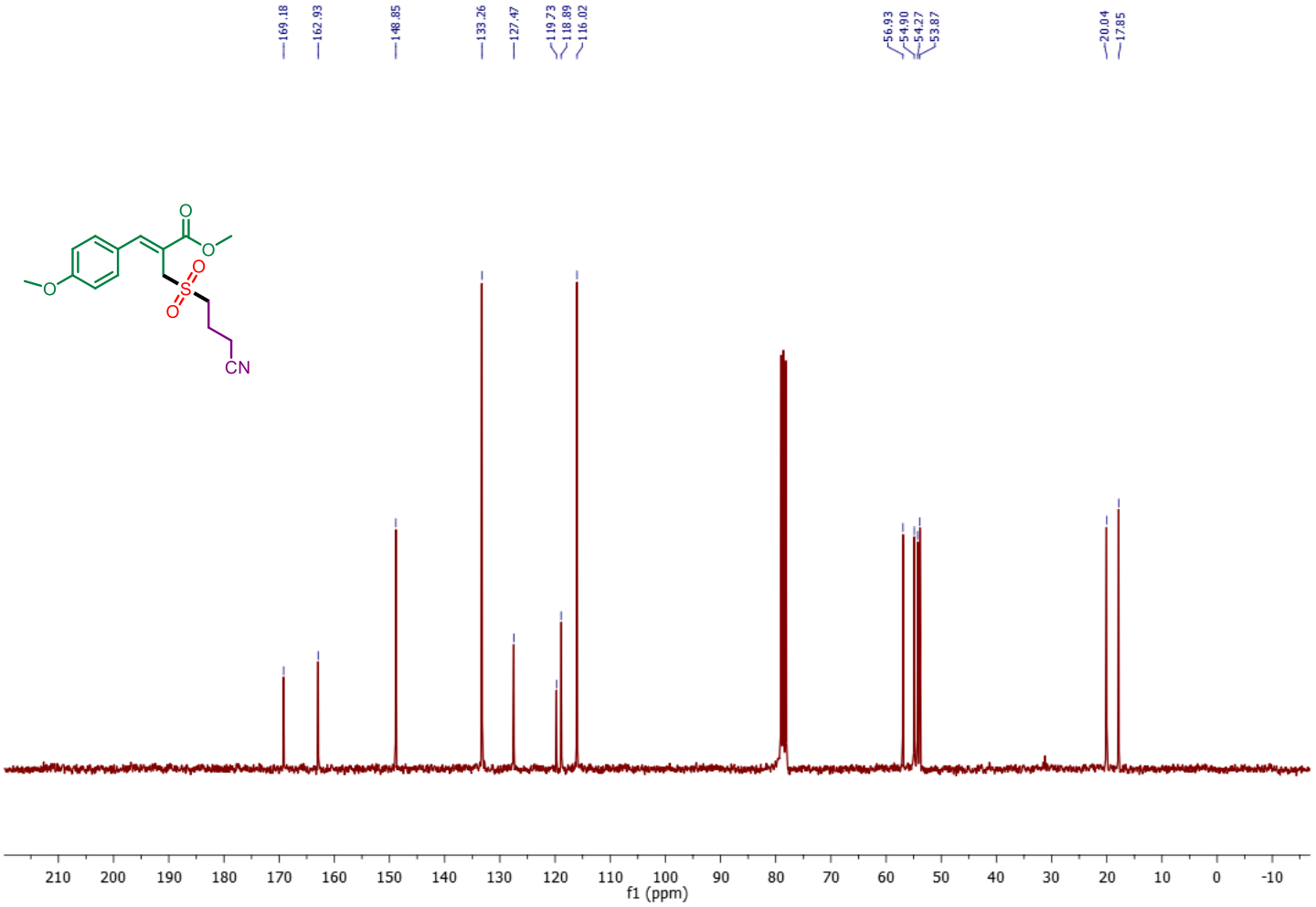
^{1}H-^{1}H 2D-NOESY spectrum of **(3aa)**



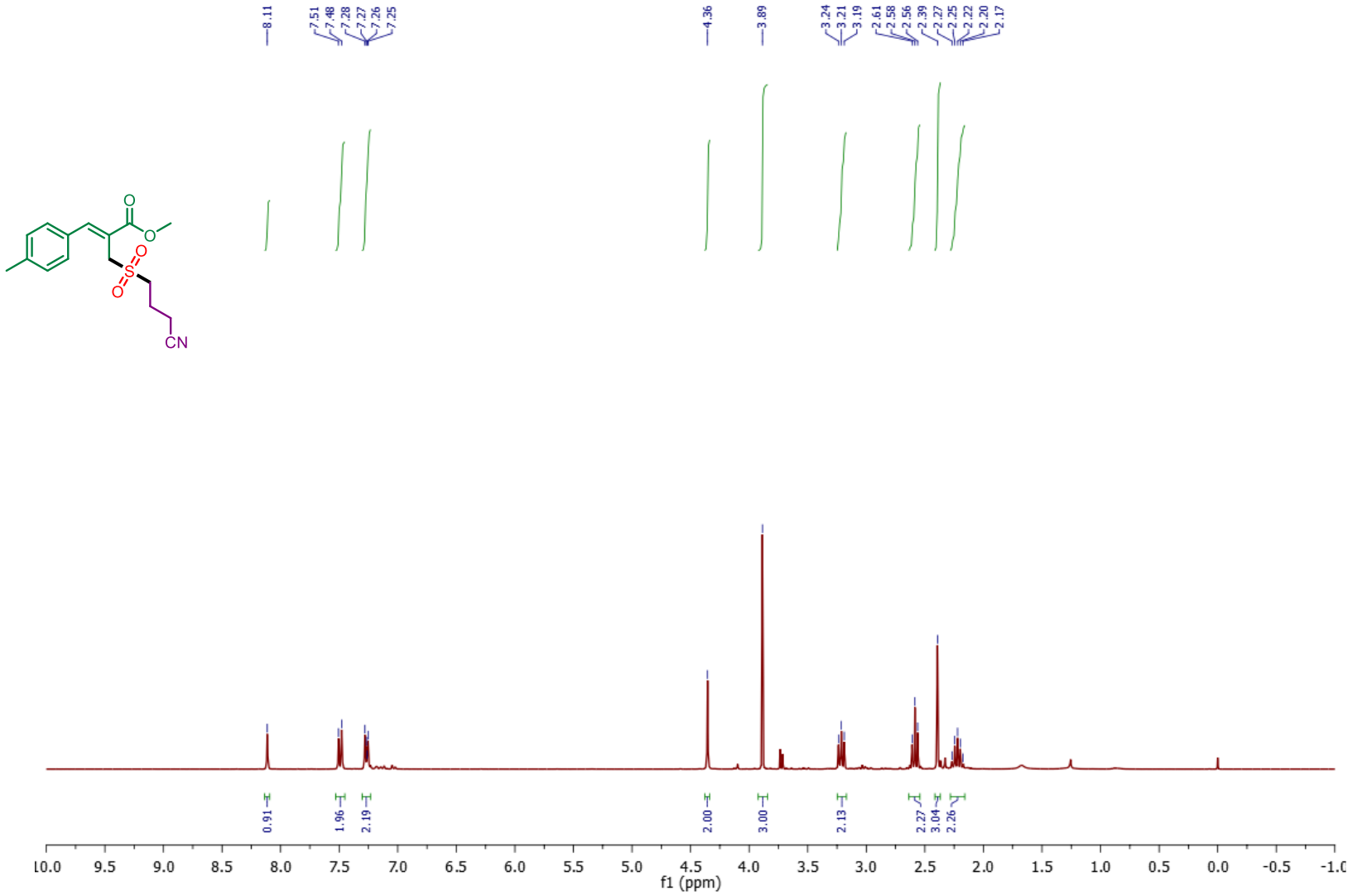
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum of Compound **(3ba)**



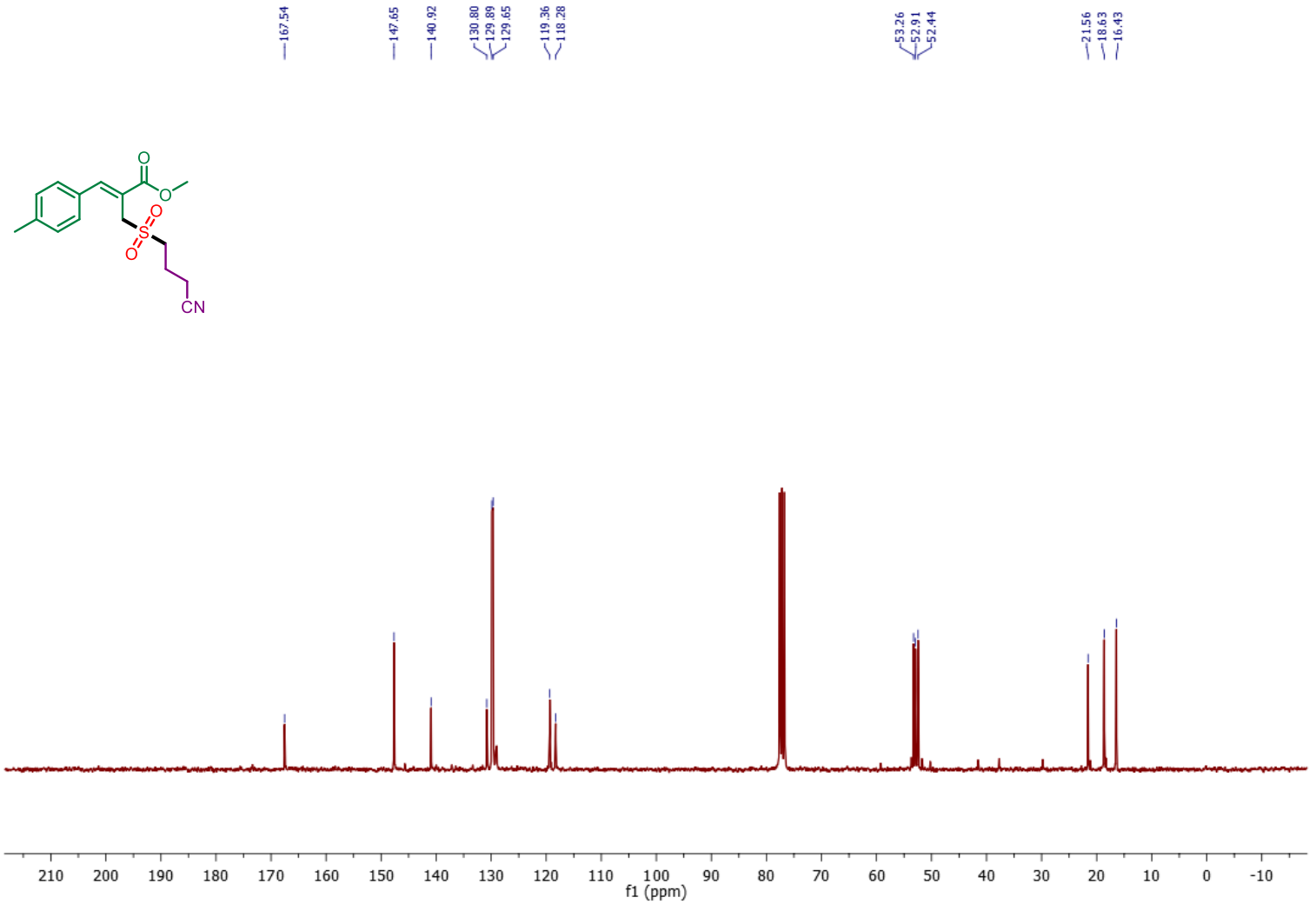
^{13}C NMR (75 MHz, CDCl3) Spectrum of Compound **(3ba)**



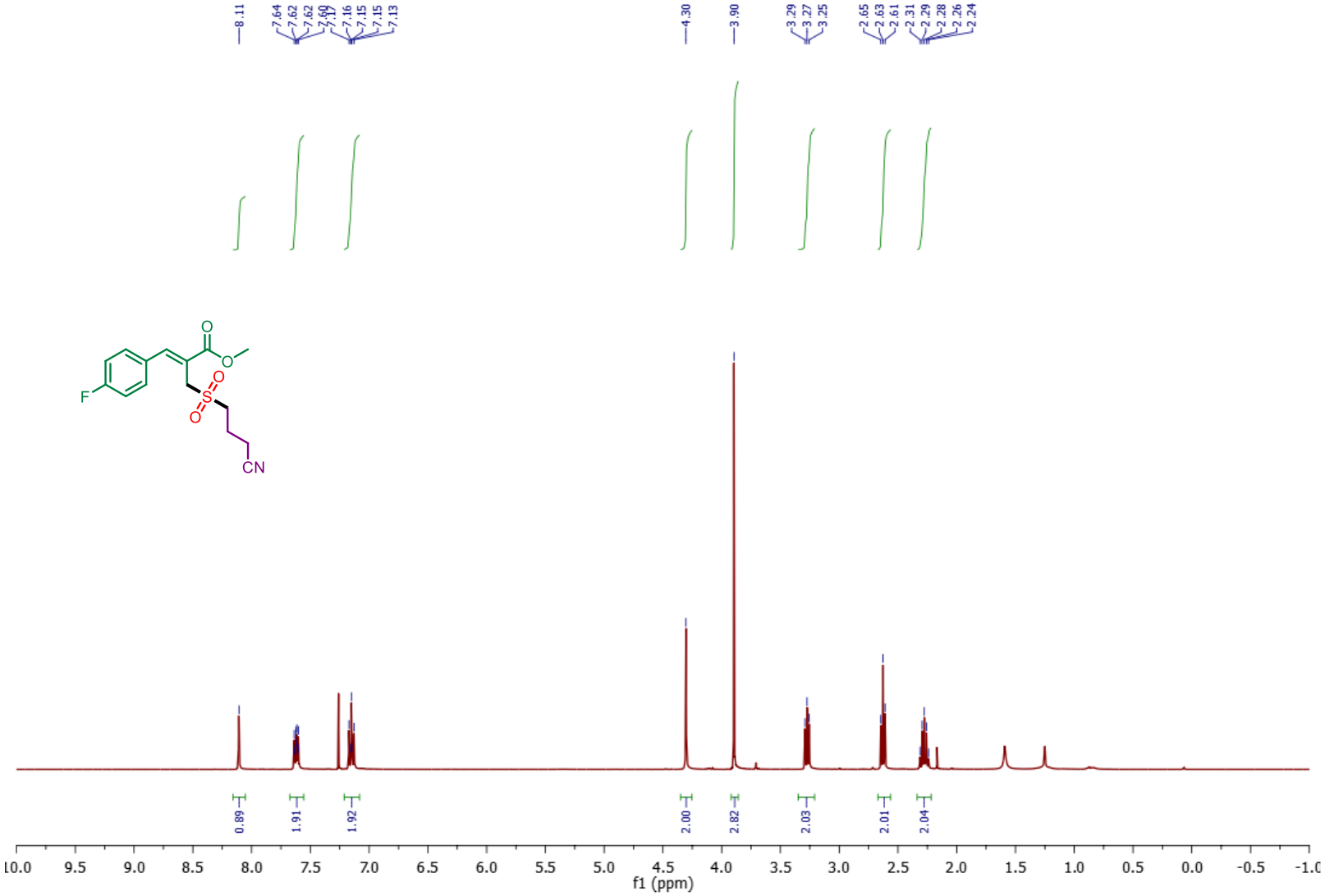
[1]H NMR (300 MHz, CDCl3) Spectrum of Compound (**3ca**)



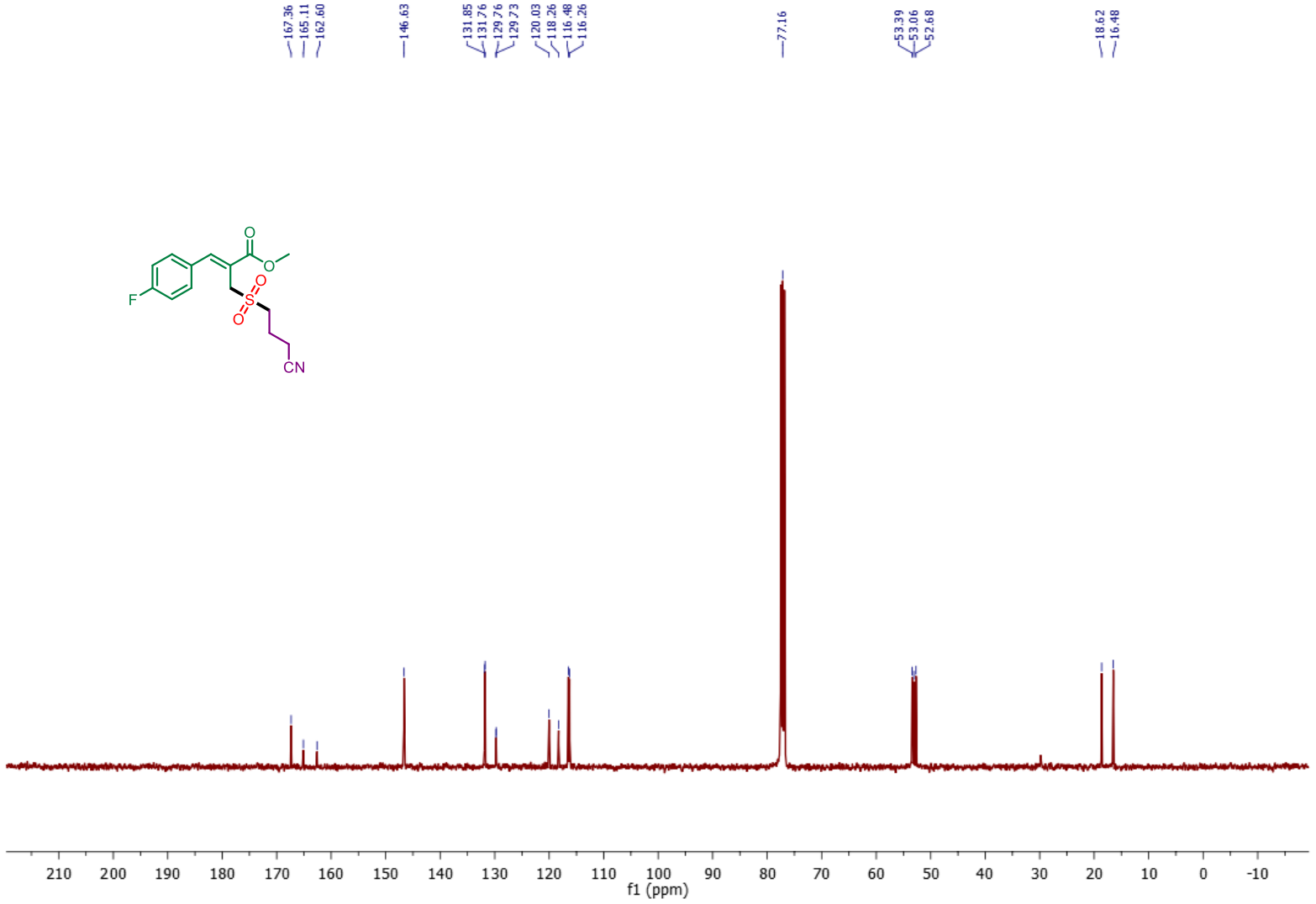
^{13}C NMR (75 MHz, $CDCl_3$) Spectrum of Compound (**3ca**)



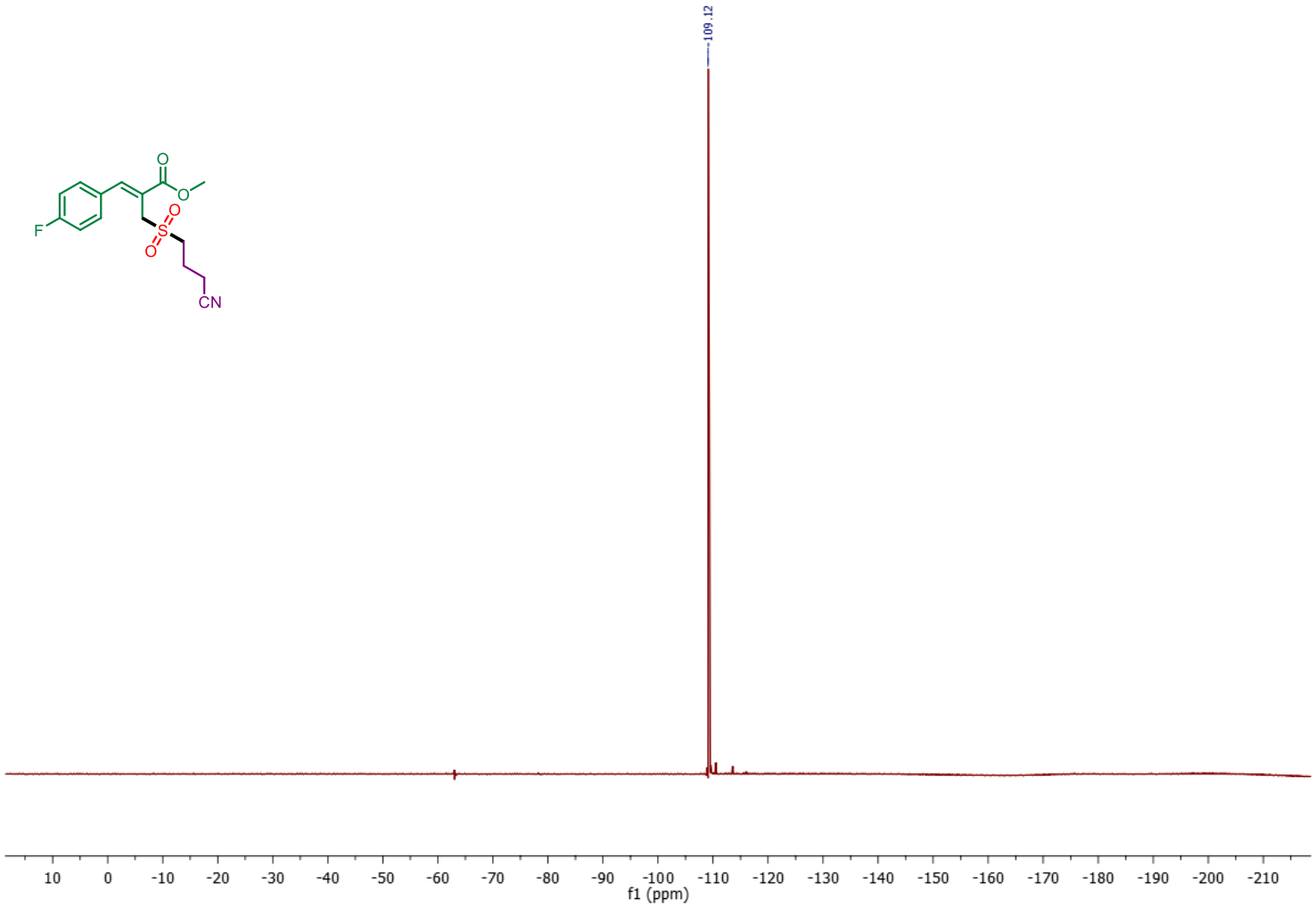
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound (**3da**)



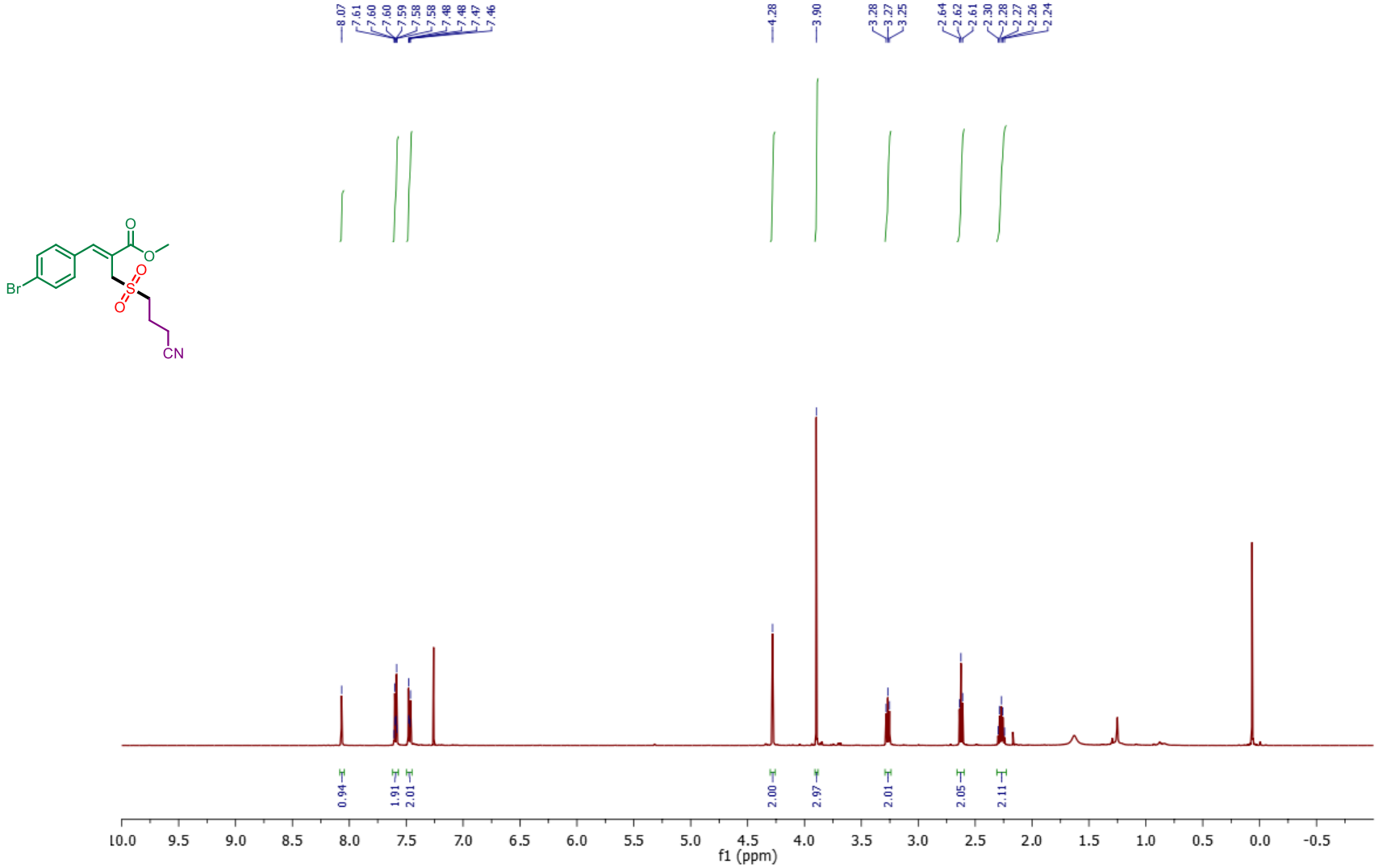
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound (**3da**)



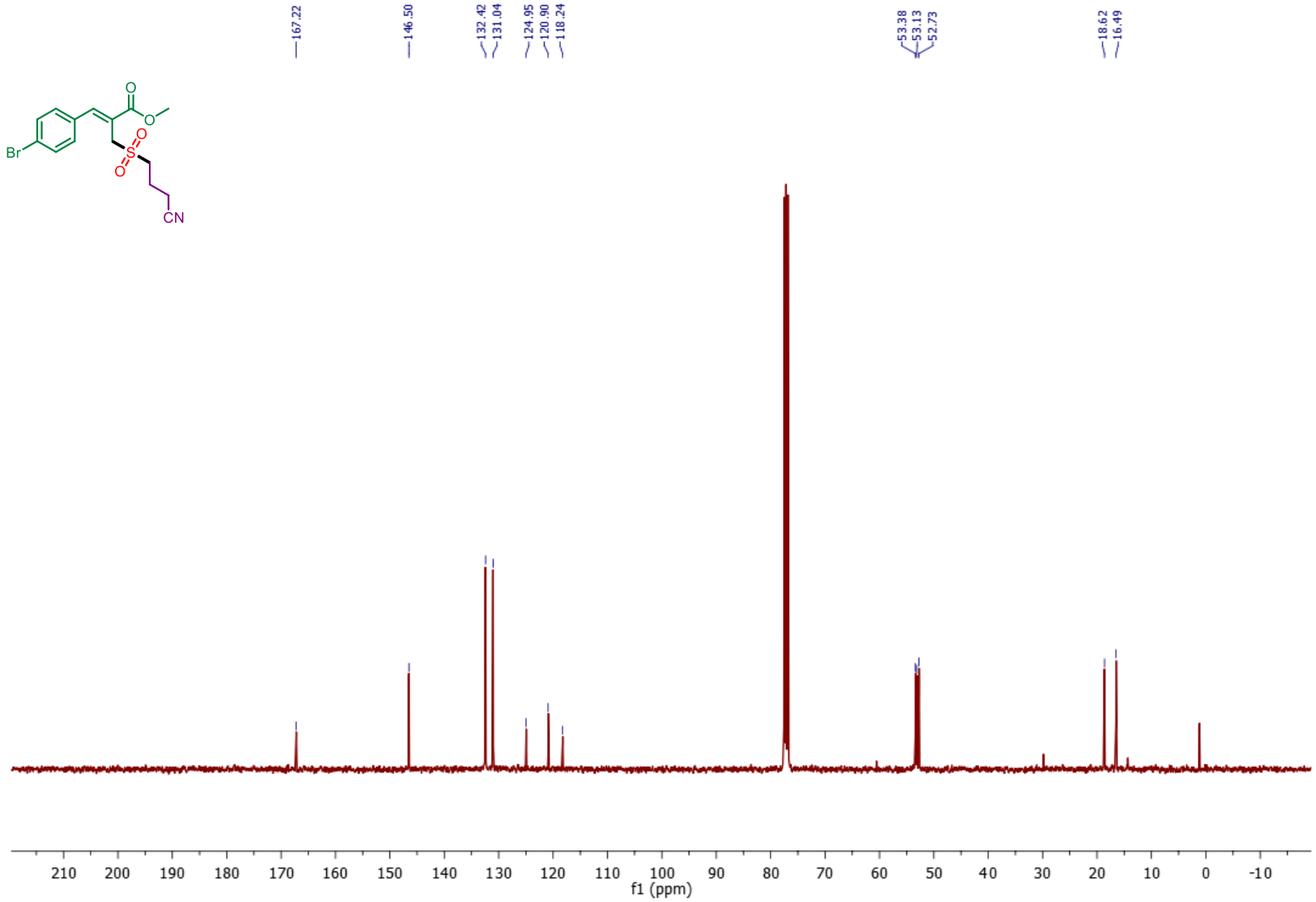
^{19}F NMR (376 MHz, $CDCl_3$) Spectrum of Compound **(3da)**



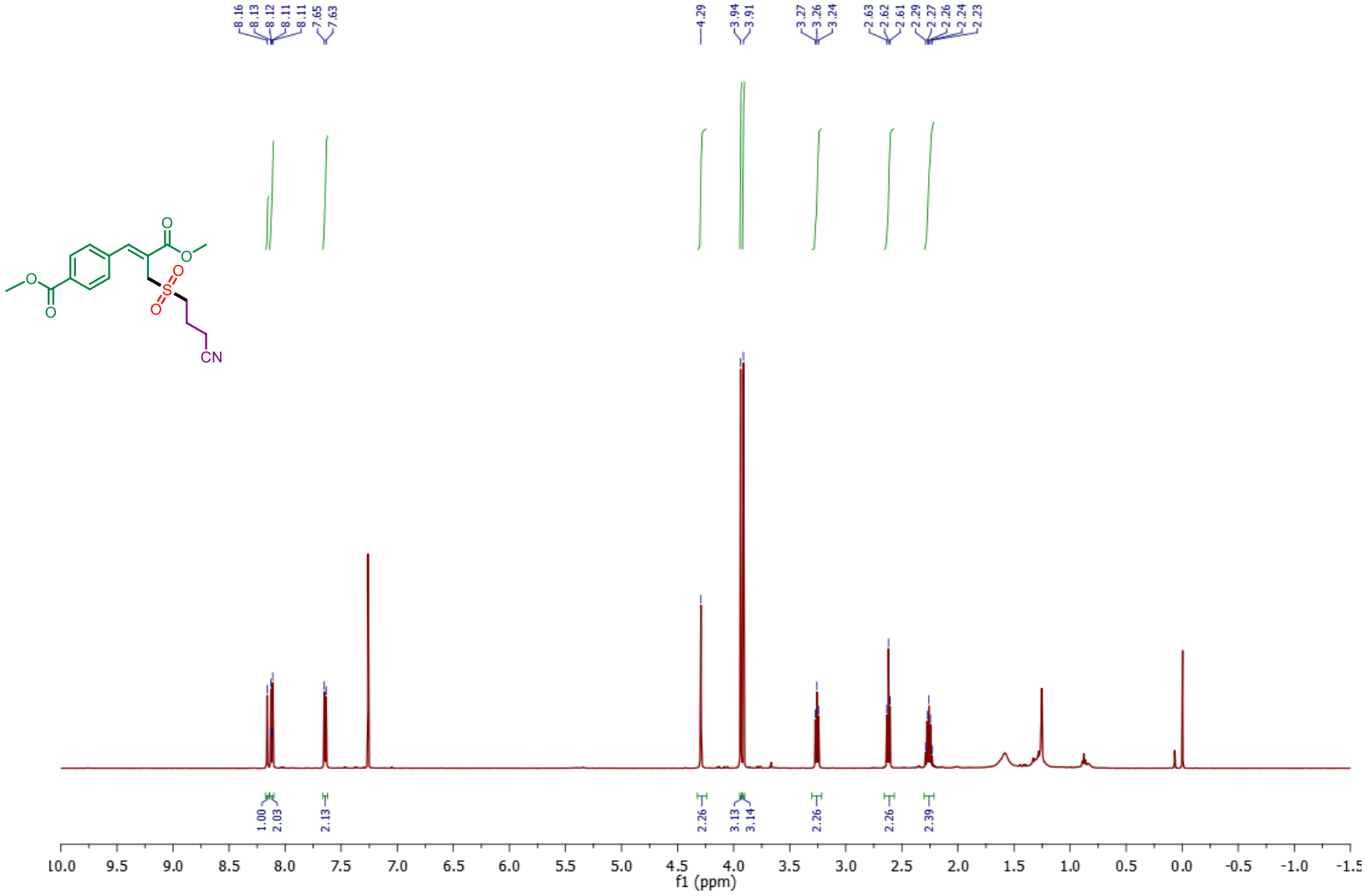
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3ea)**



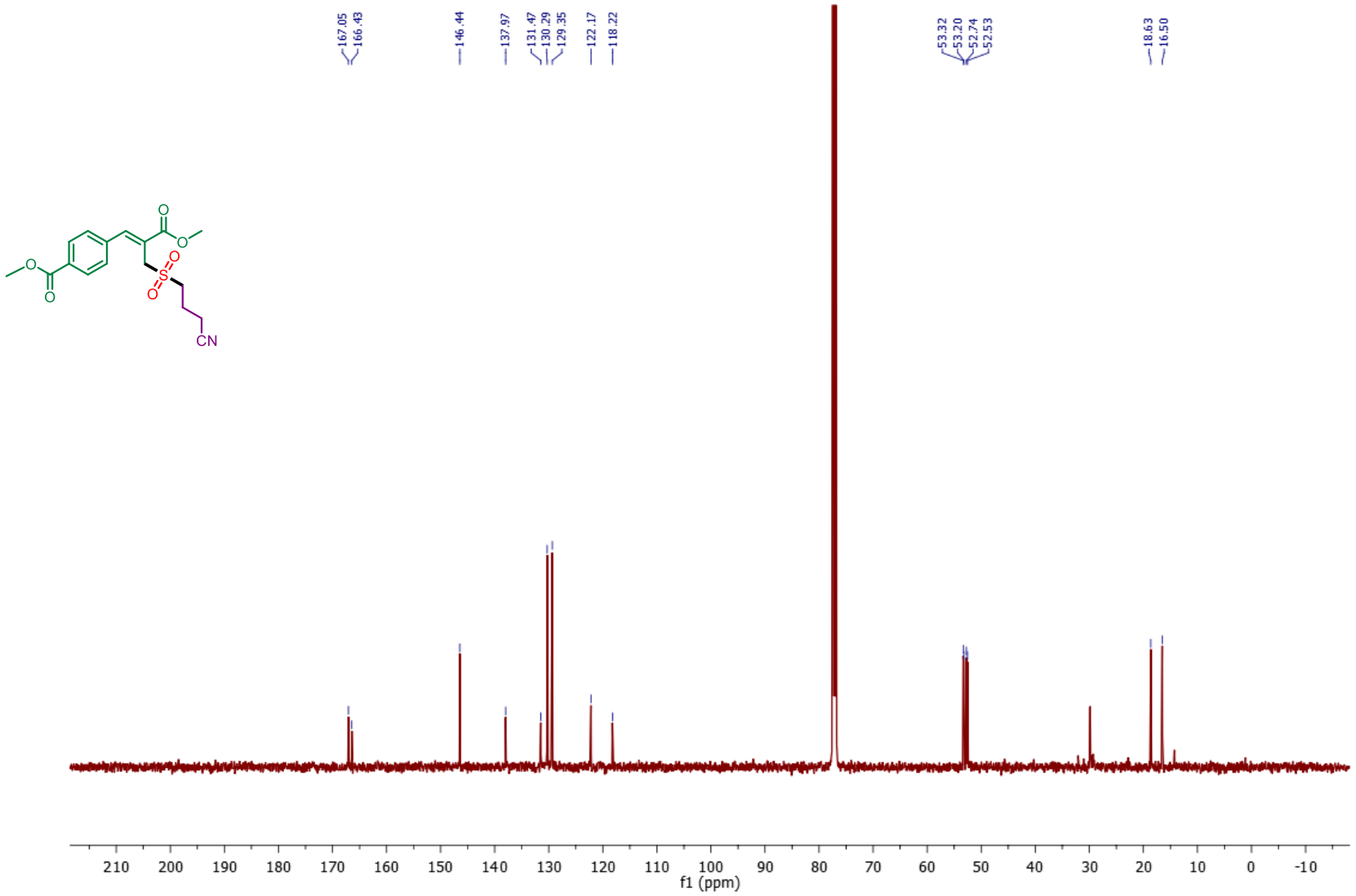
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ea)**



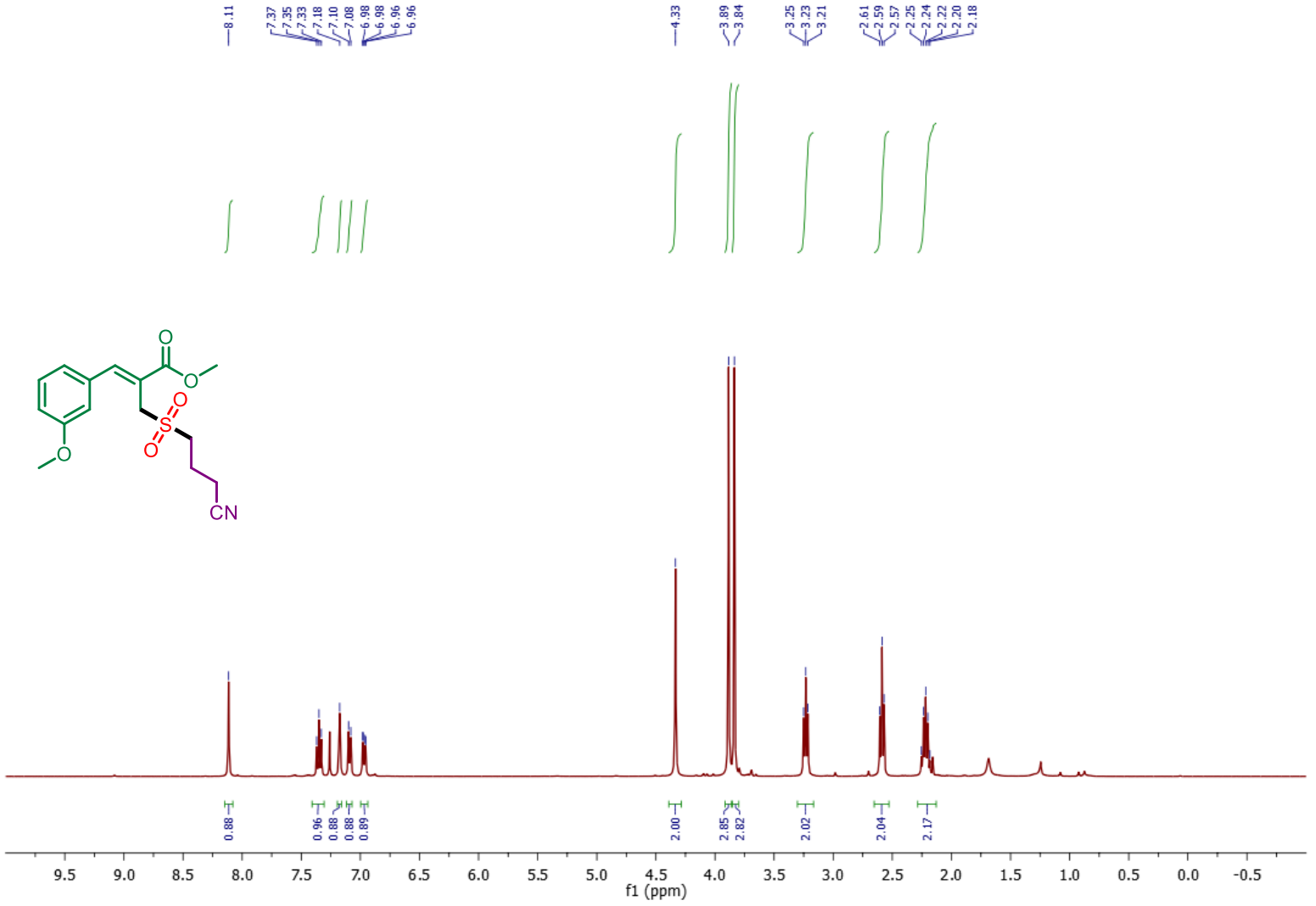
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3fa)**



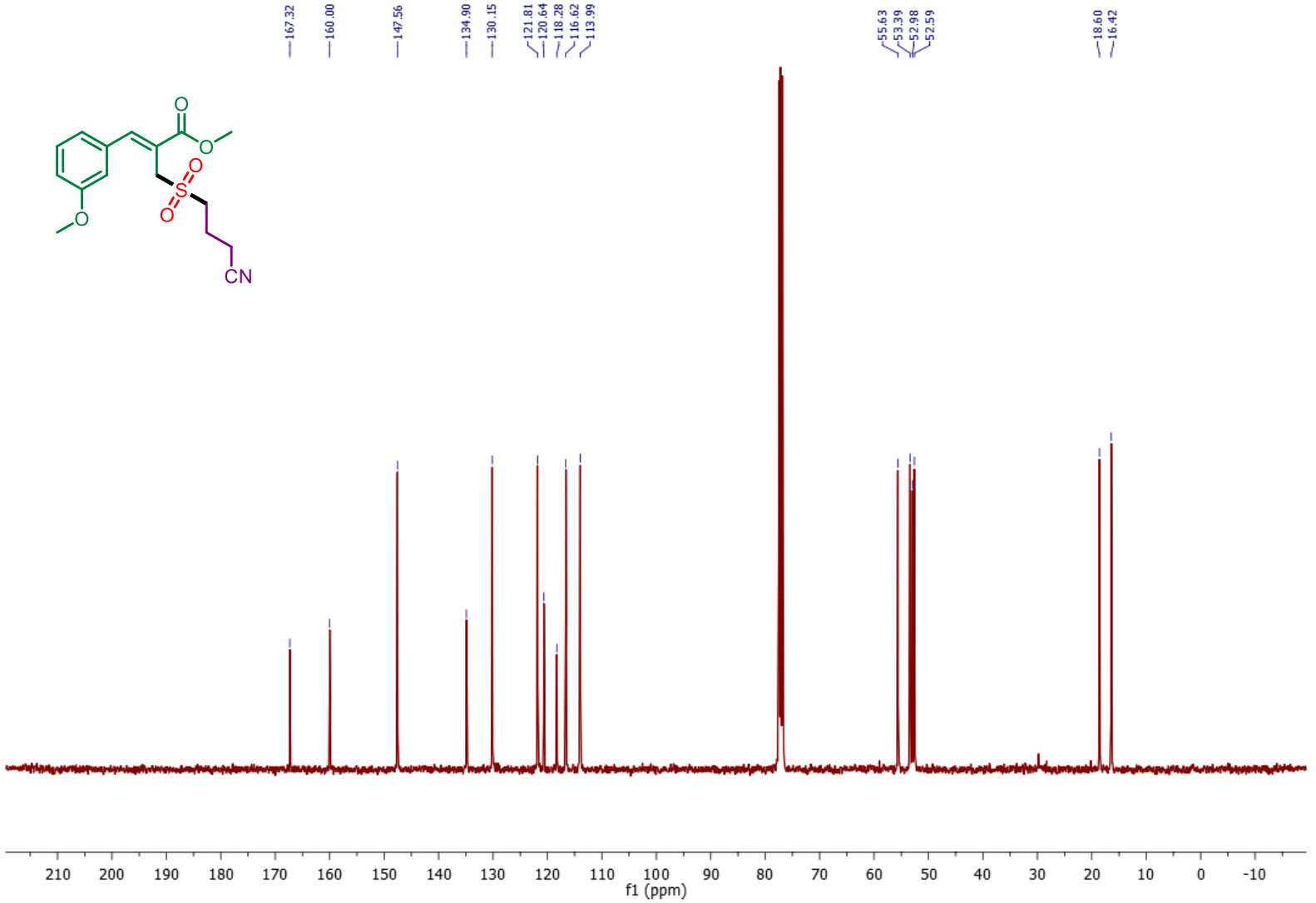
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3fa)**



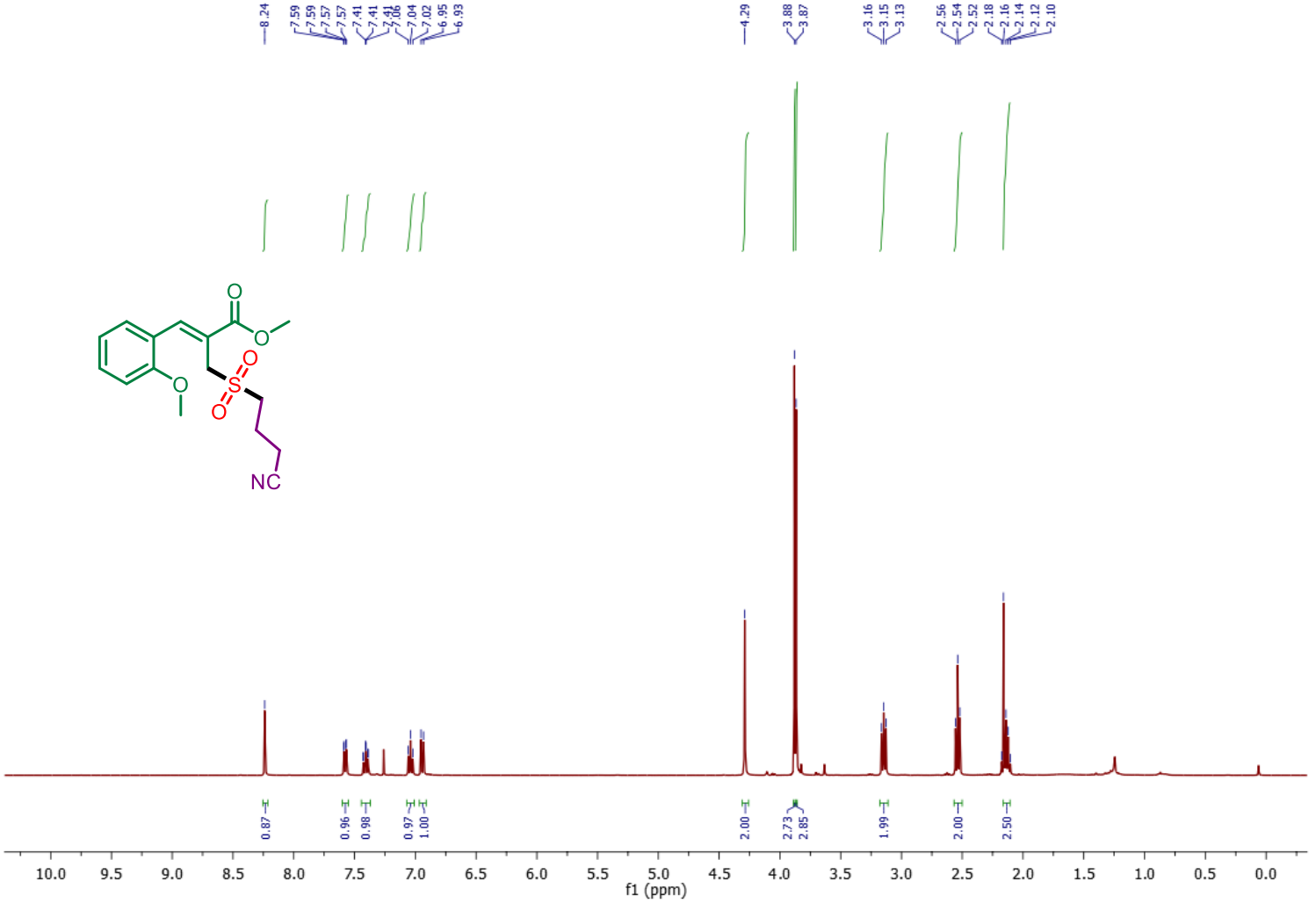
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound (**3ga**)



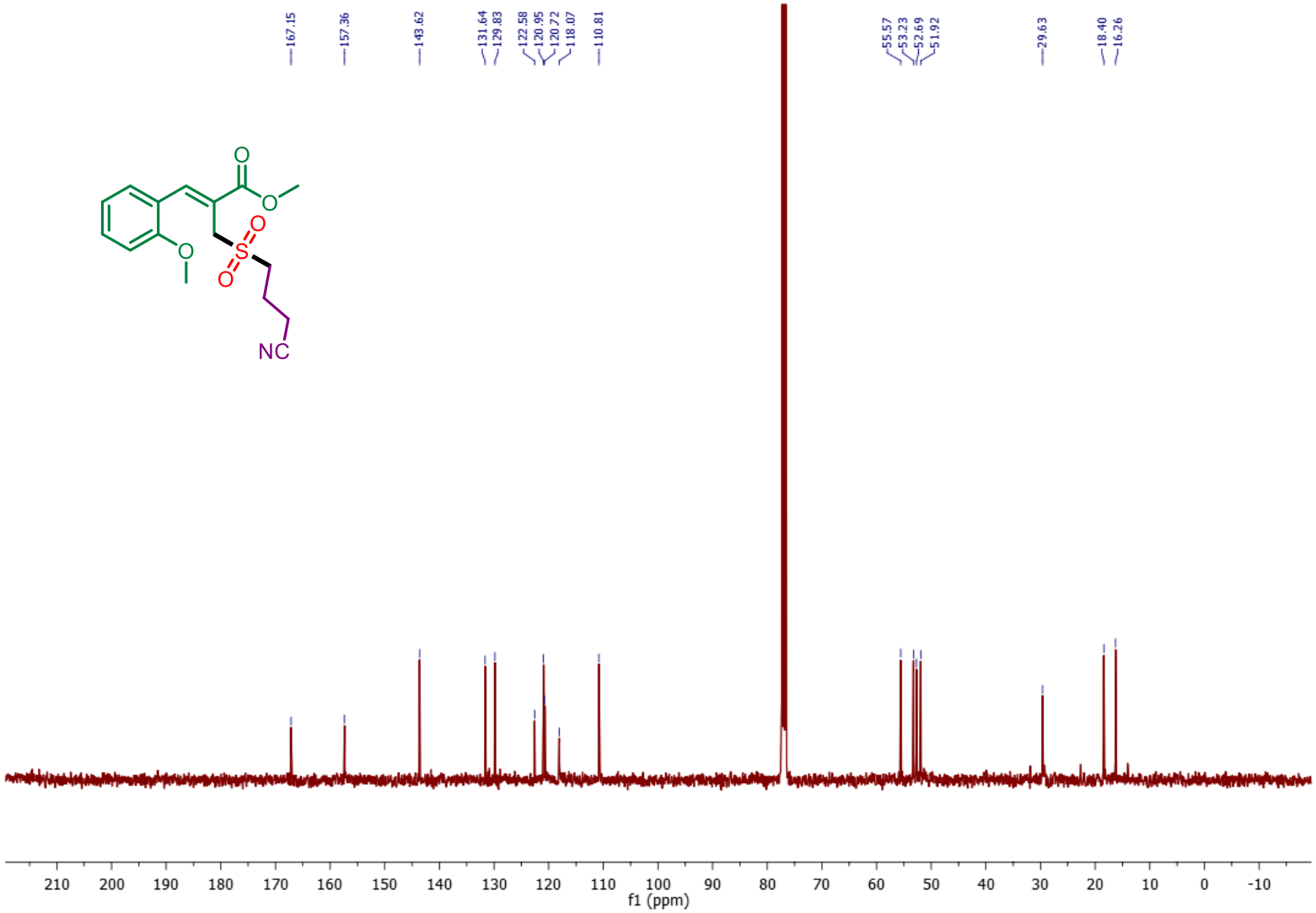
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound (**3ga**)



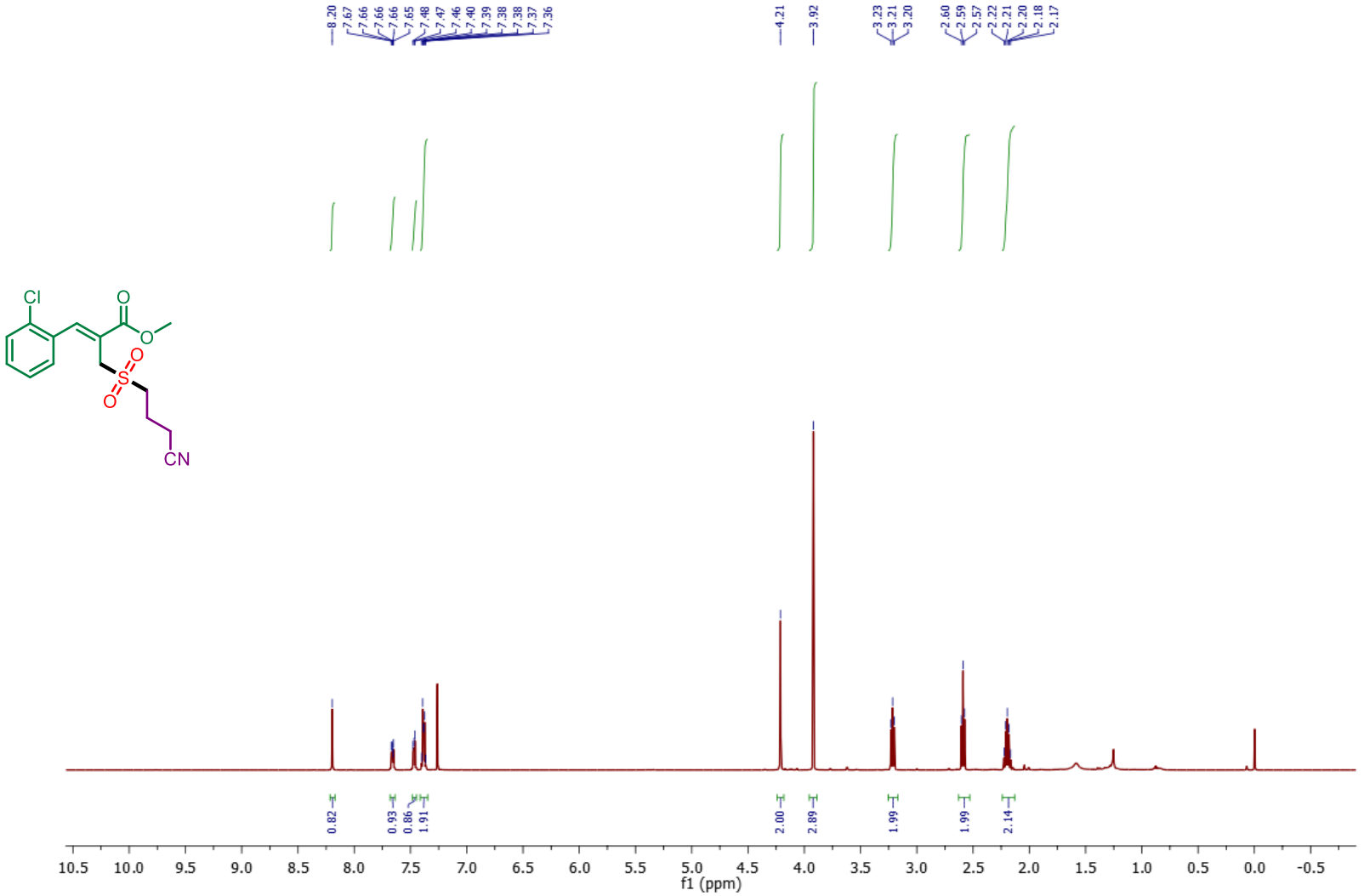
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound (**3ha**)



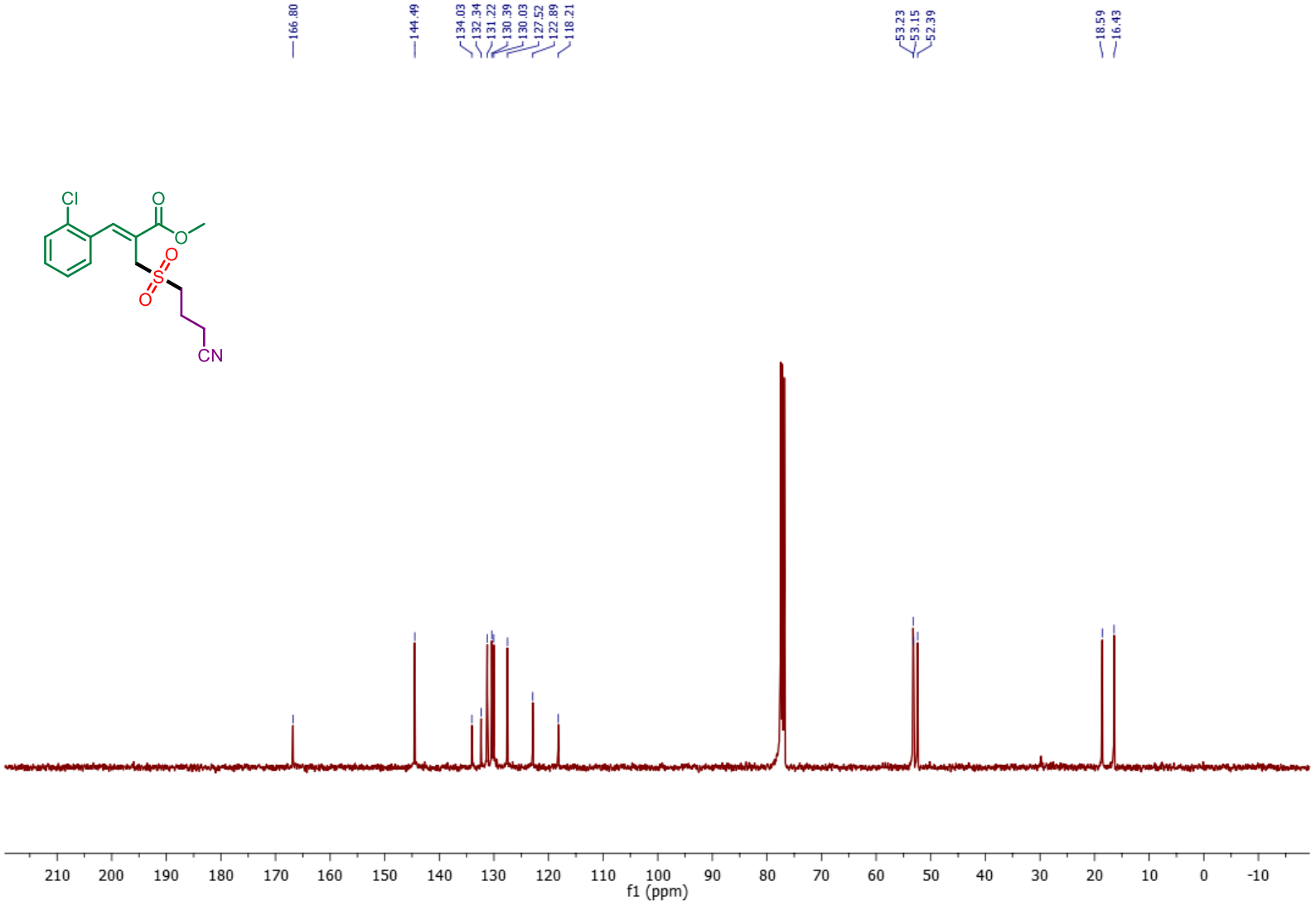
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound (**3ha**)



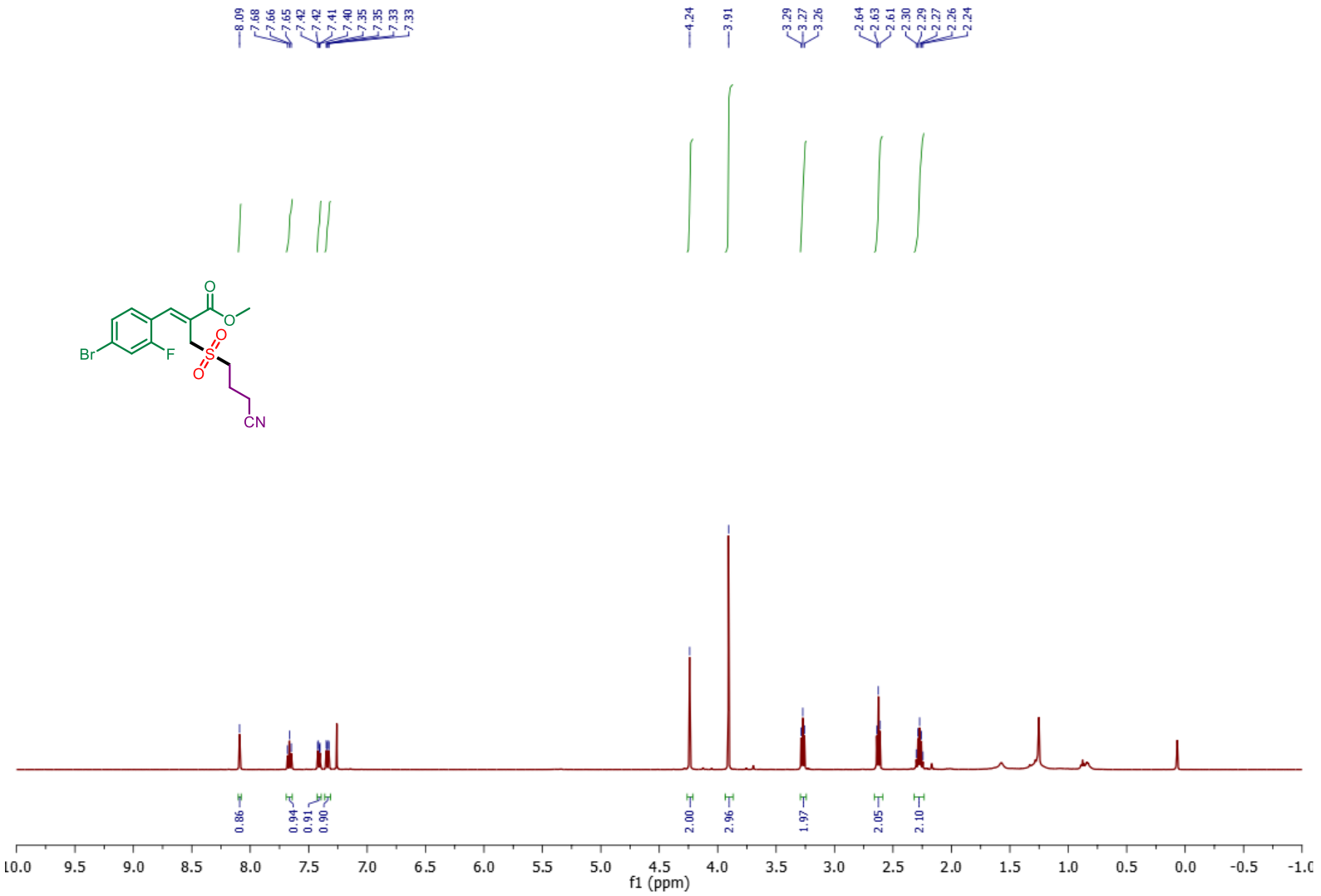
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound (**3ia)**



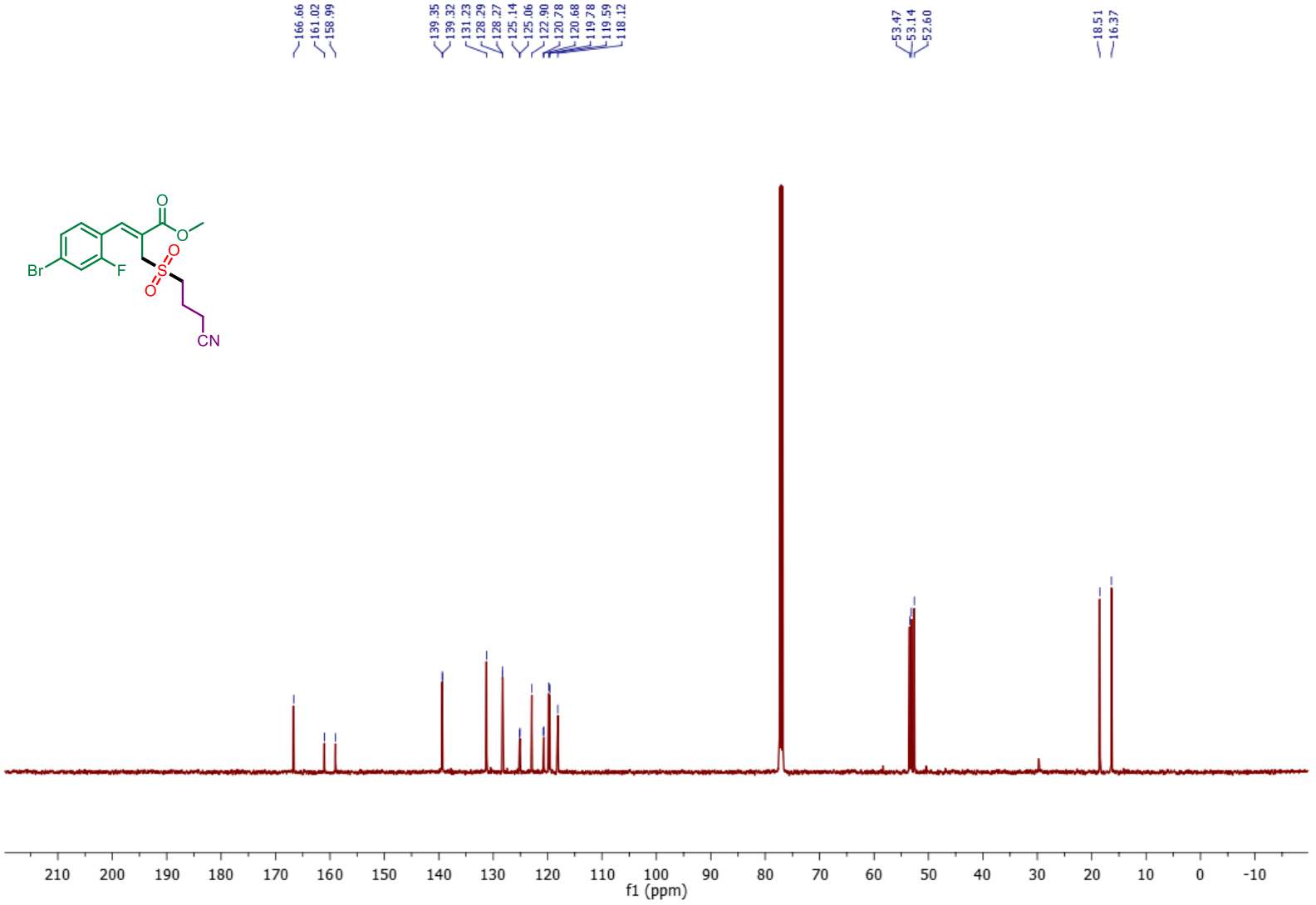
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound (**3ia**)



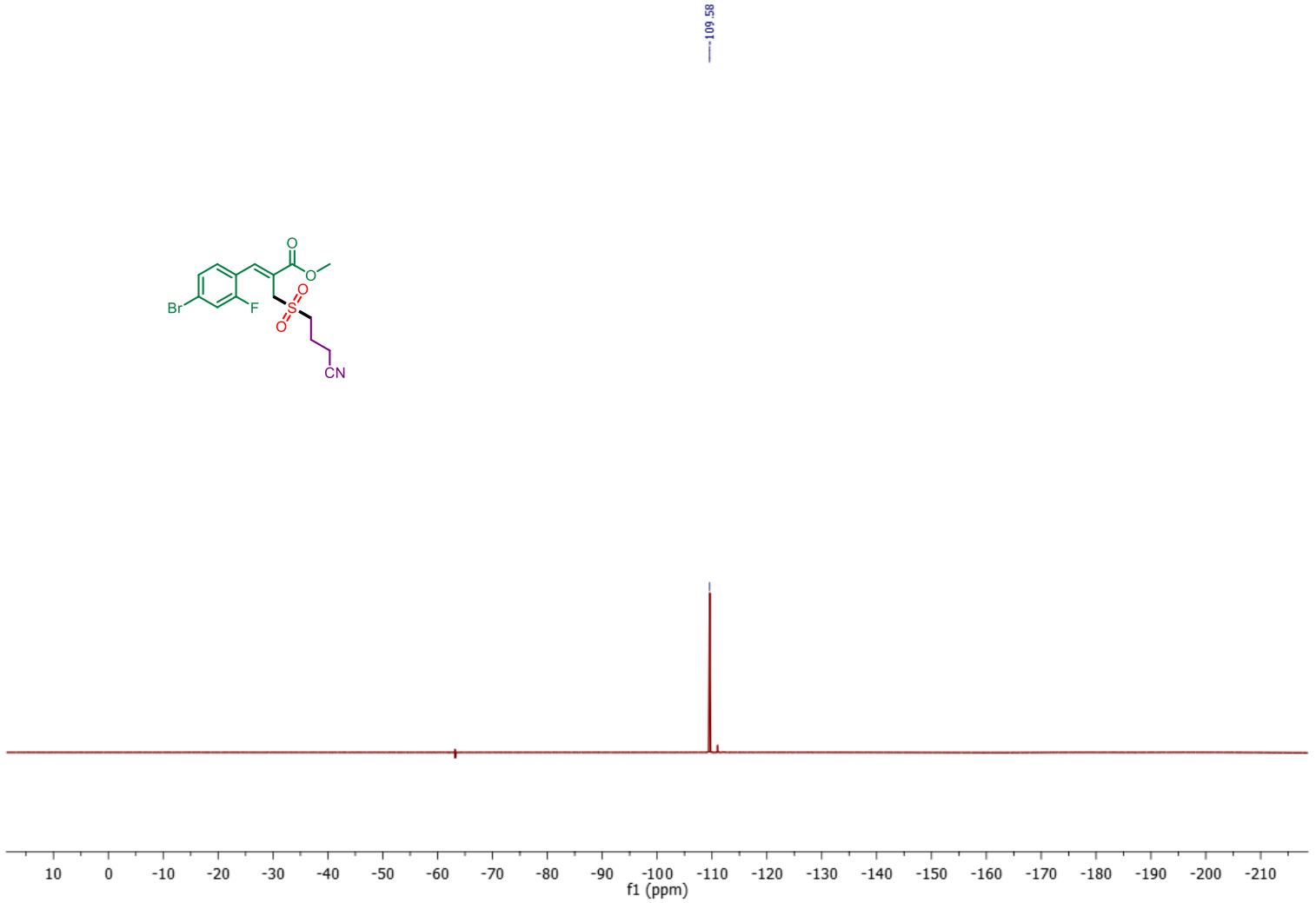
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3ja)**



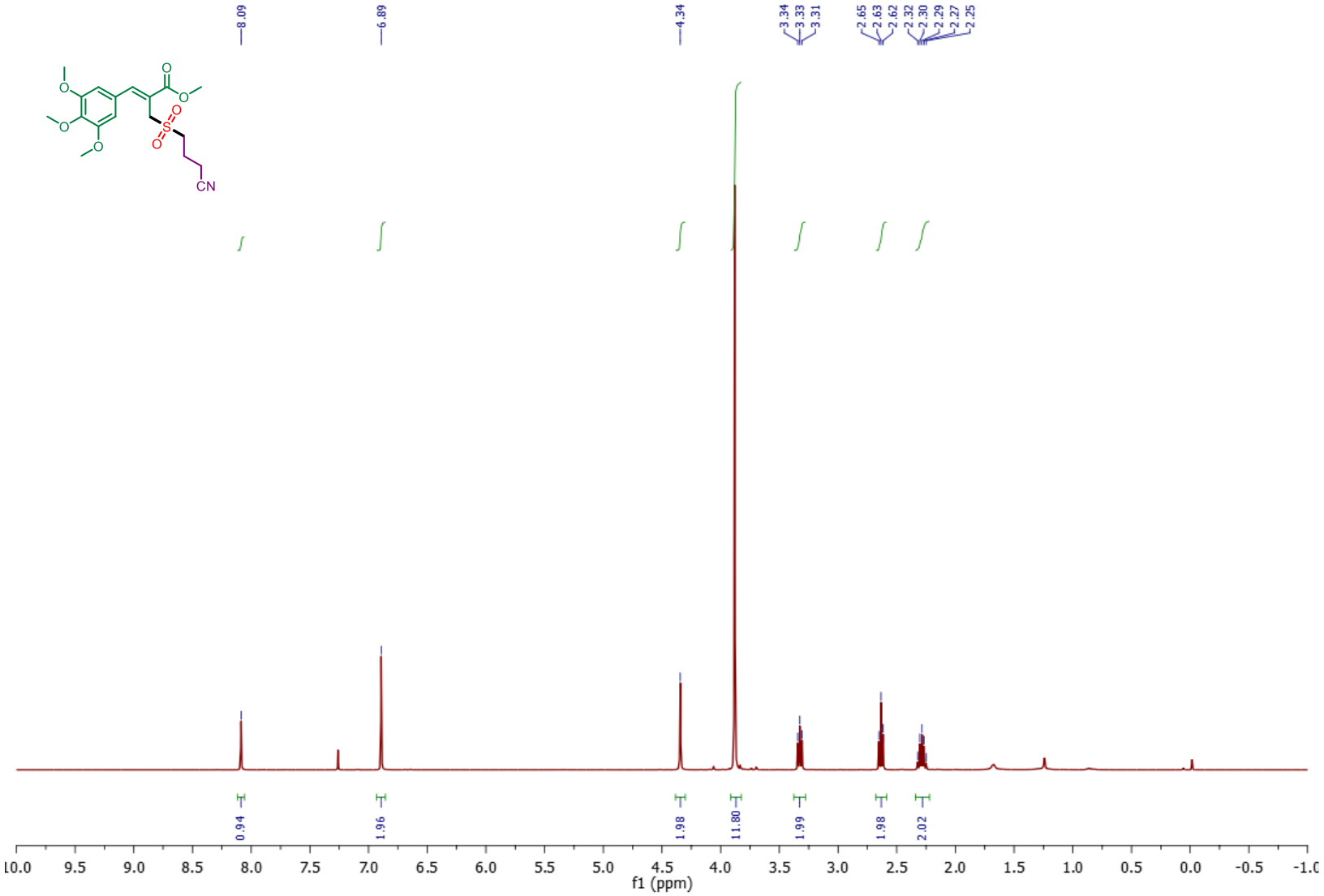
^{13}CNMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3ja)**



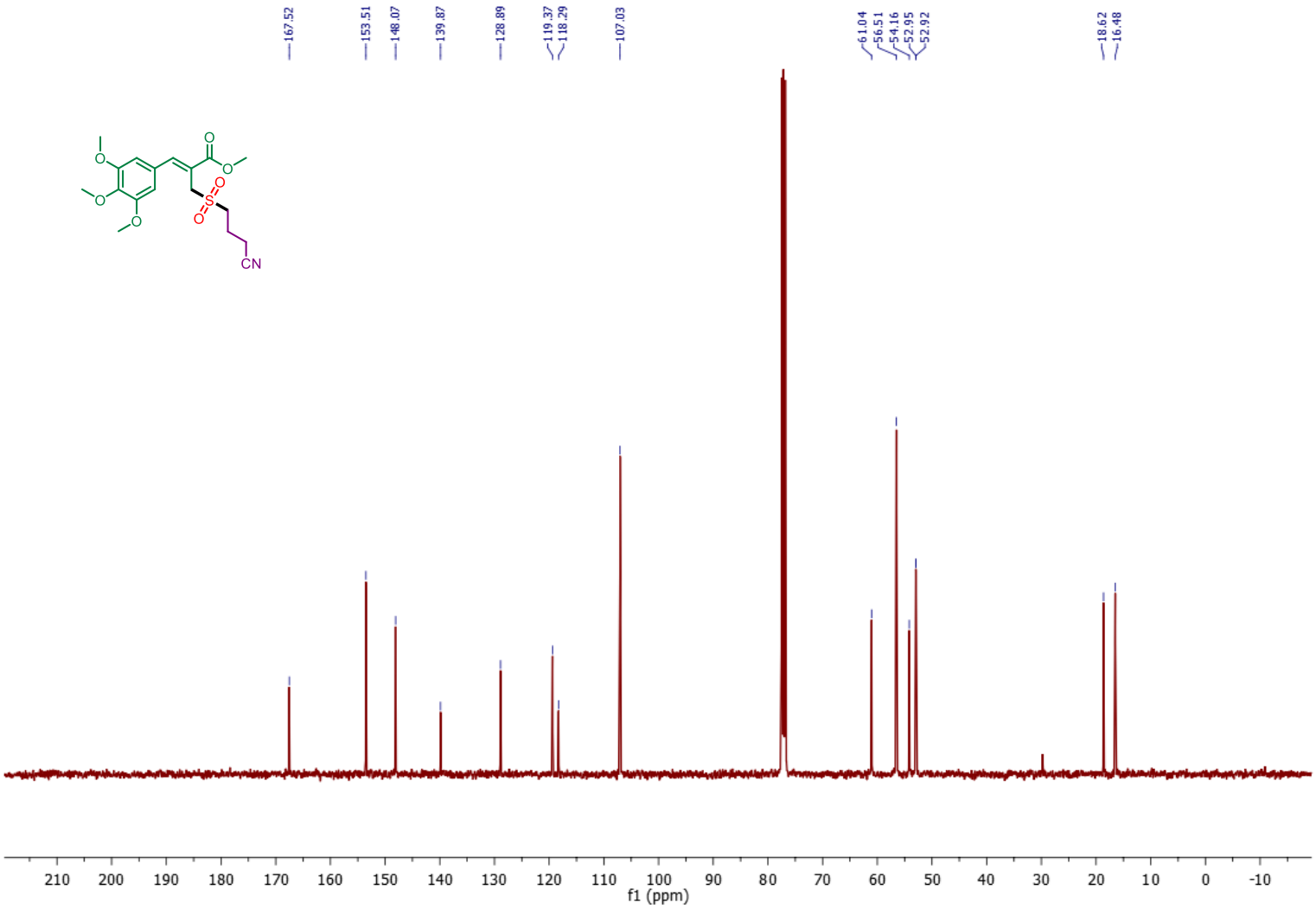
^{19}F NMR (376 MHz, $CDCl_3$) Spectrum of Compound **(3ja)**



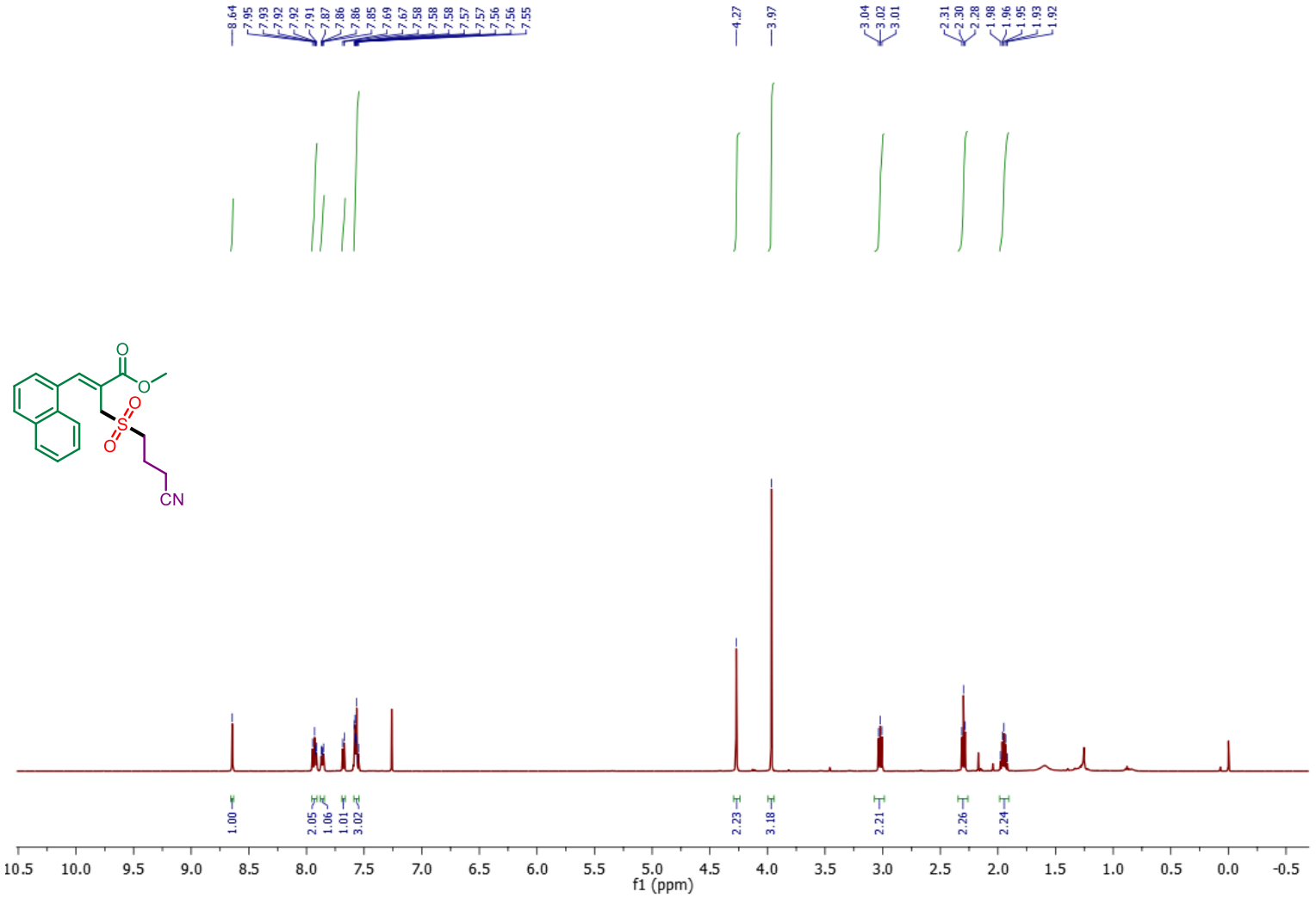
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3ka)**



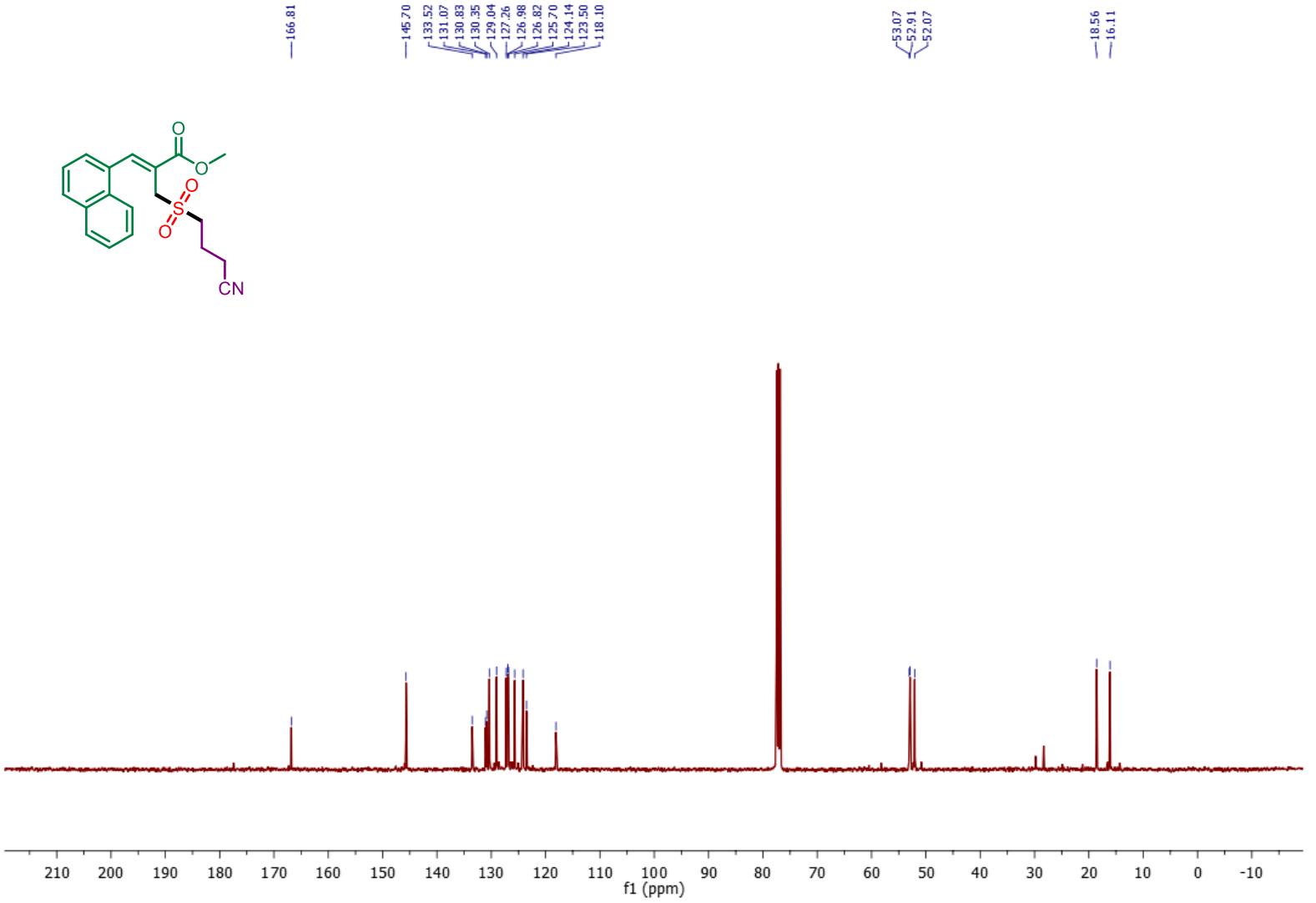
^{13}CNMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ka)**



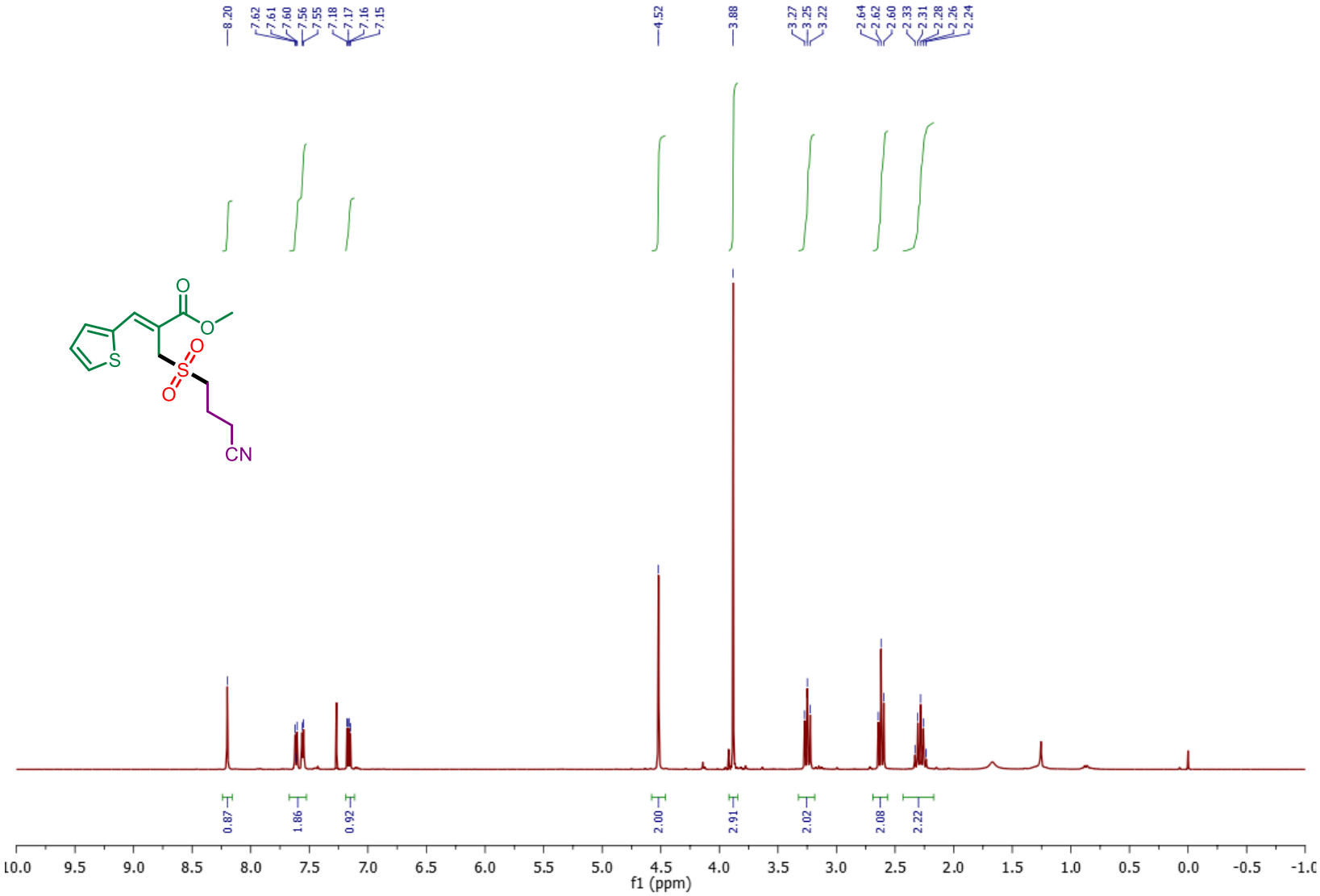
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3la)**



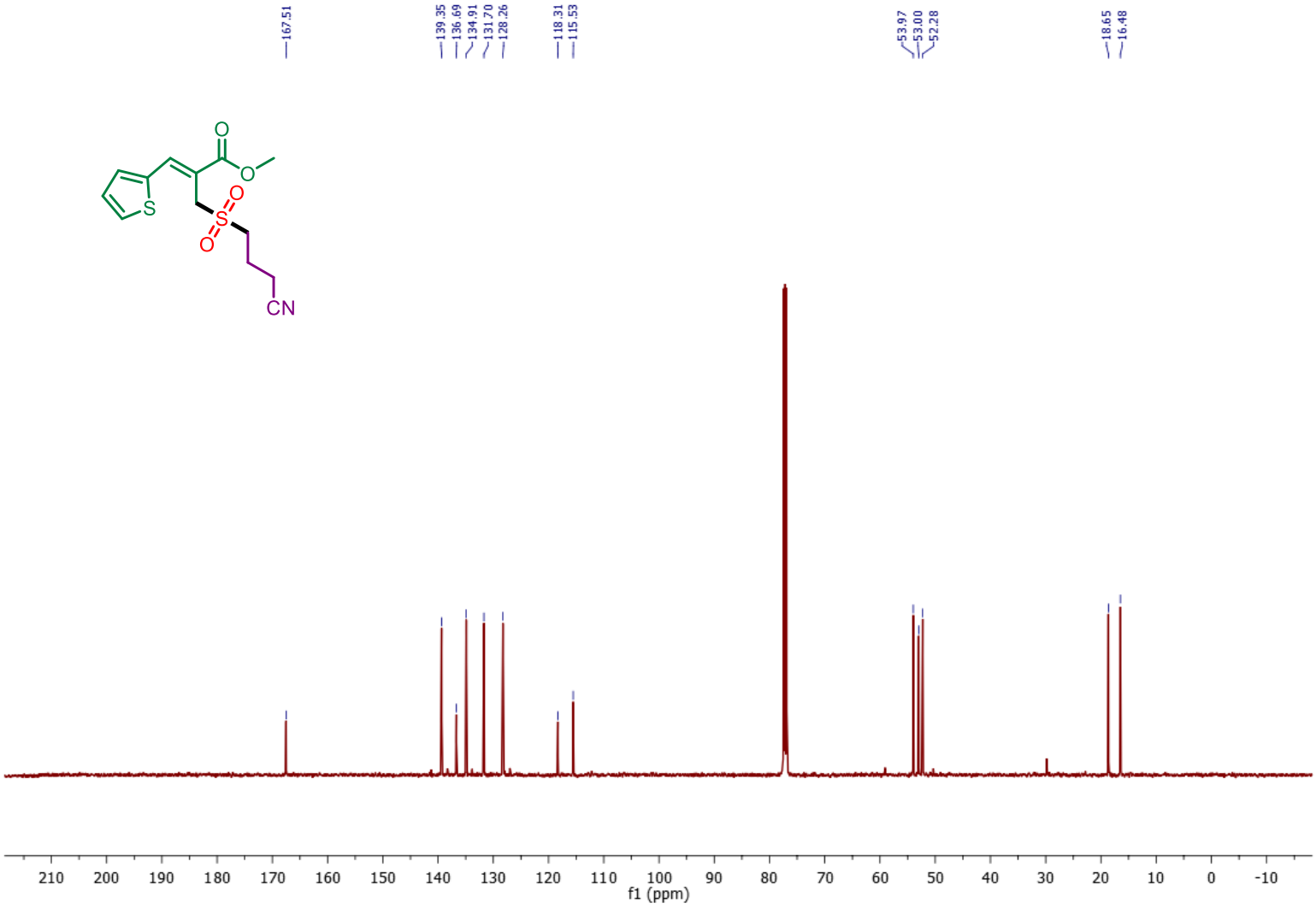
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3la)**



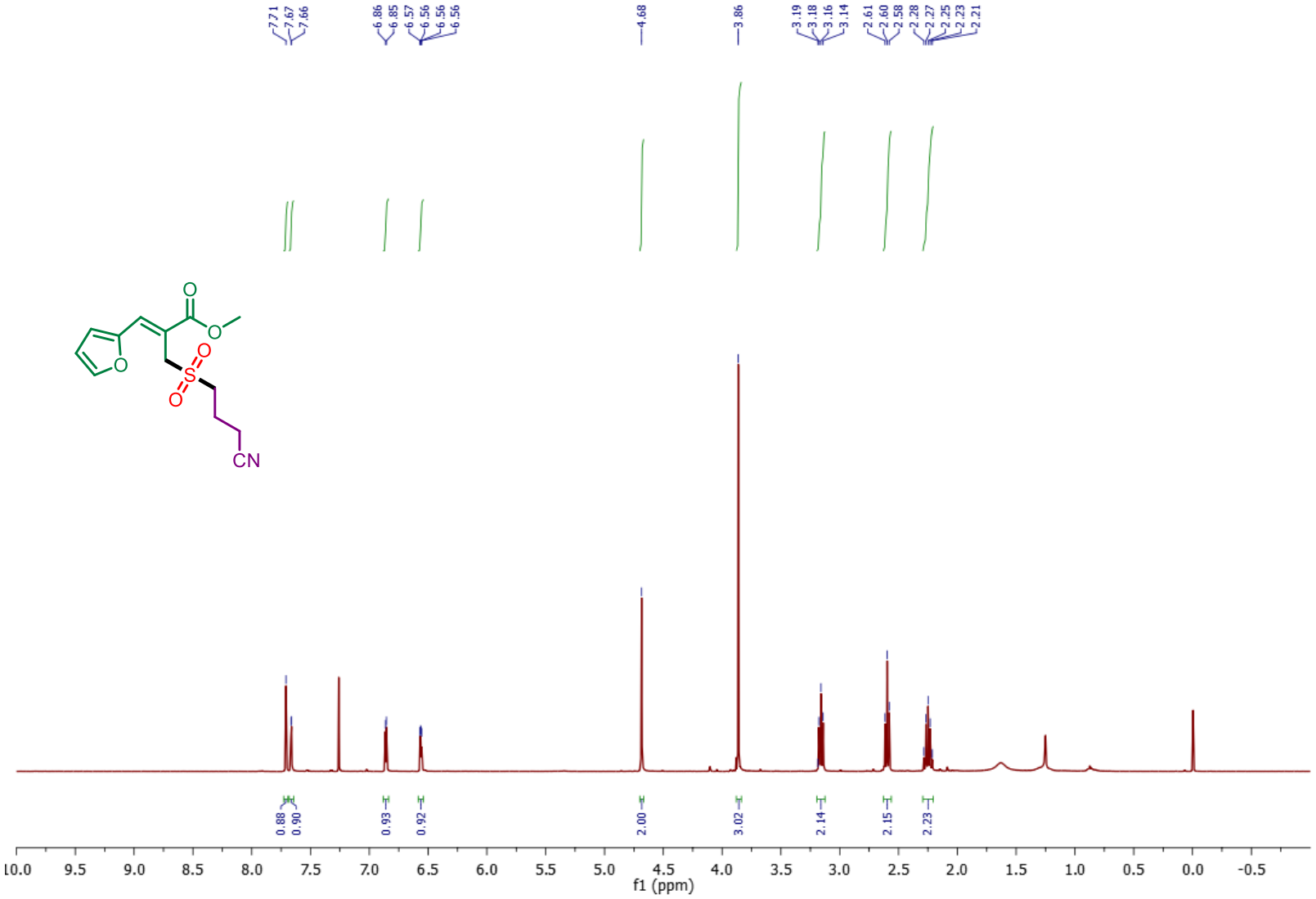
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum of Compound **(3ma)**



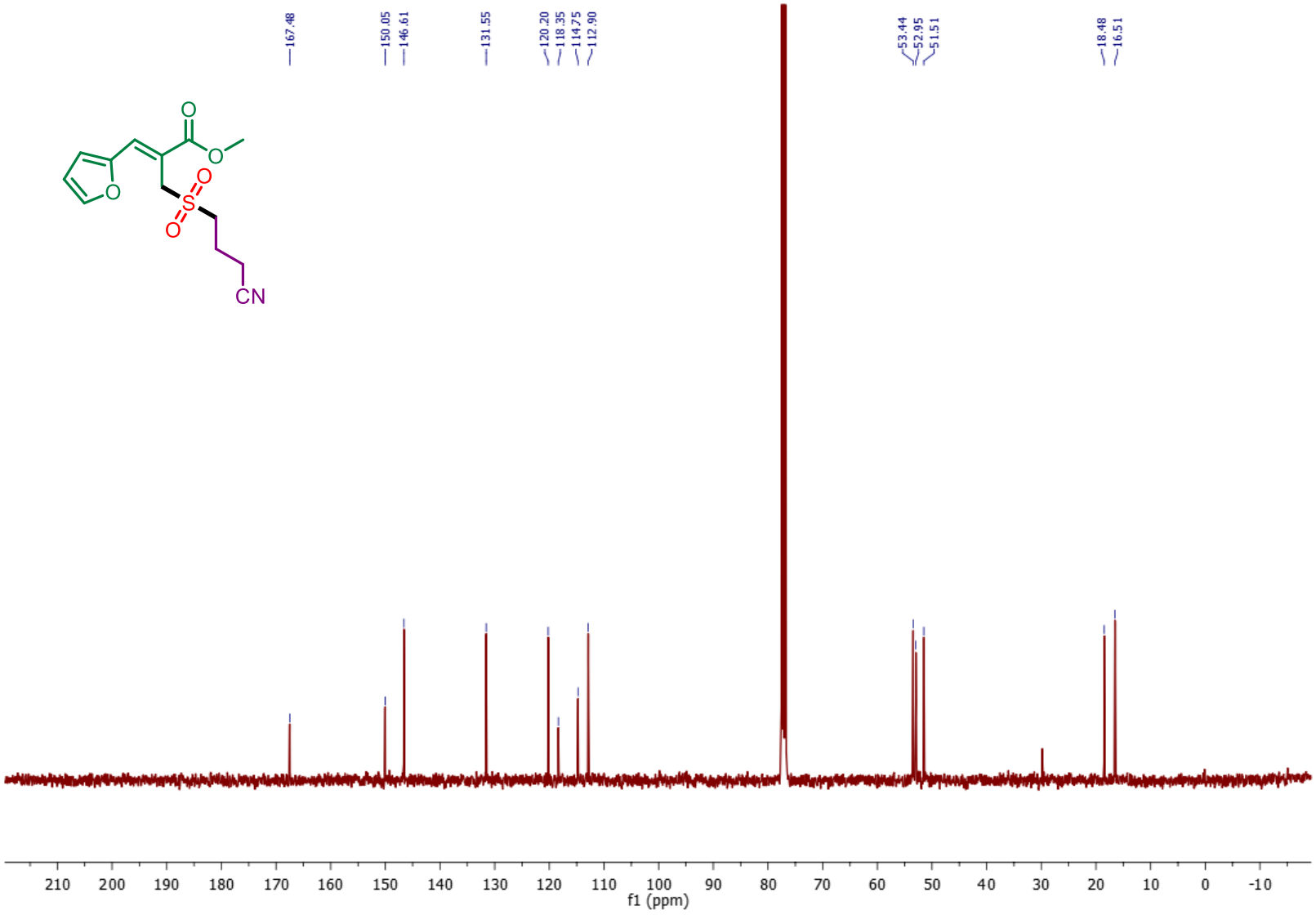
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3ma)**



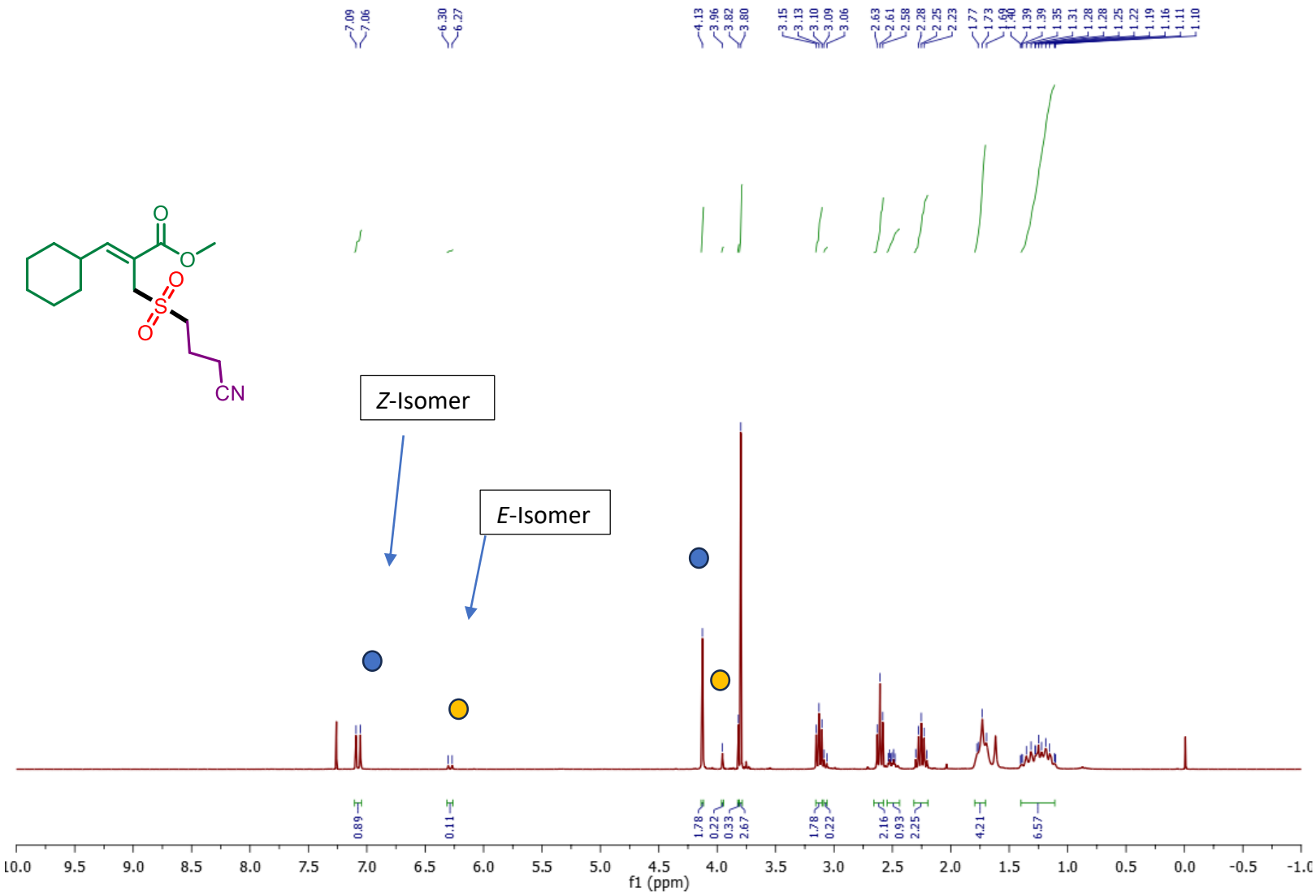
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3na)**



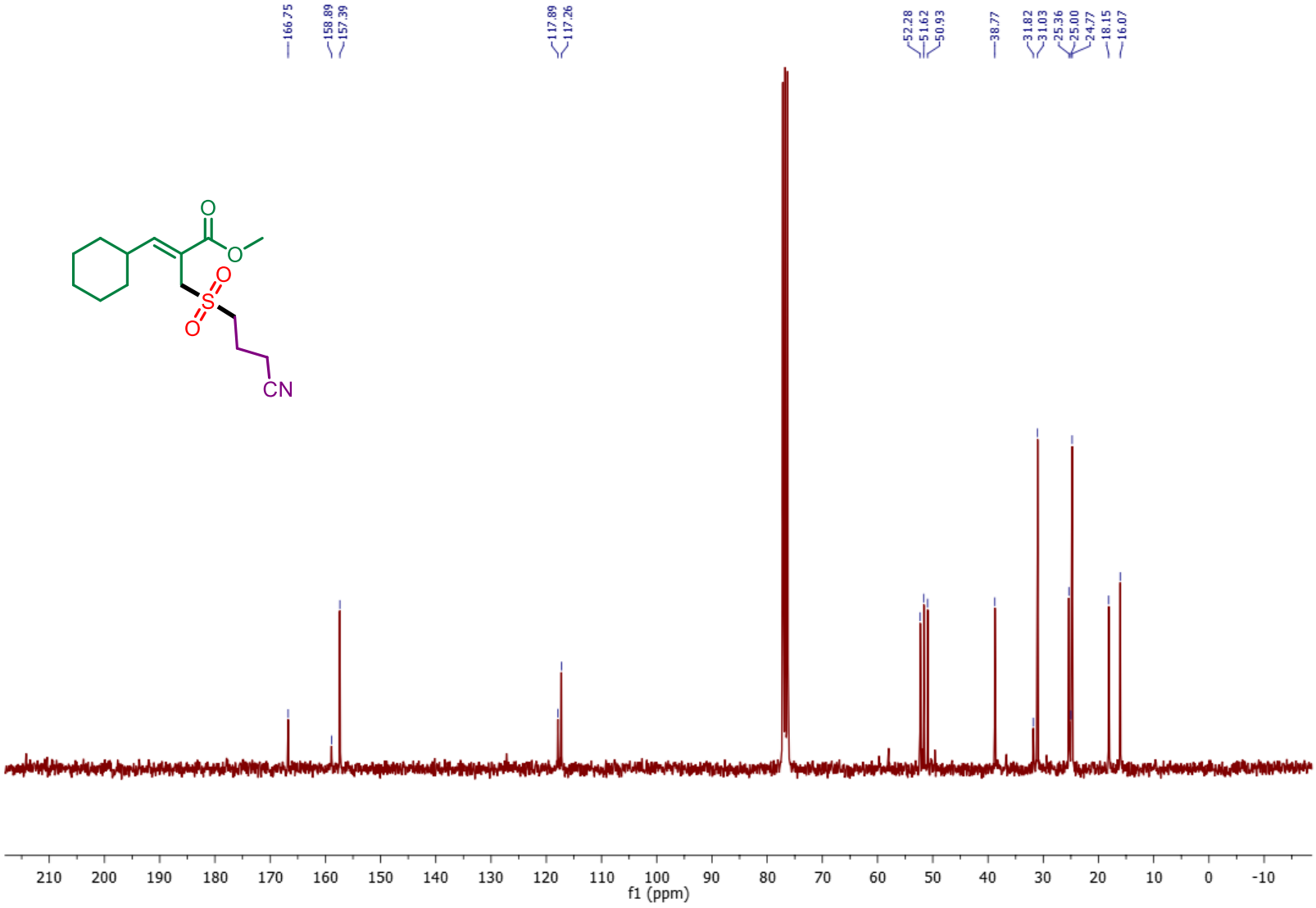
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3na)**



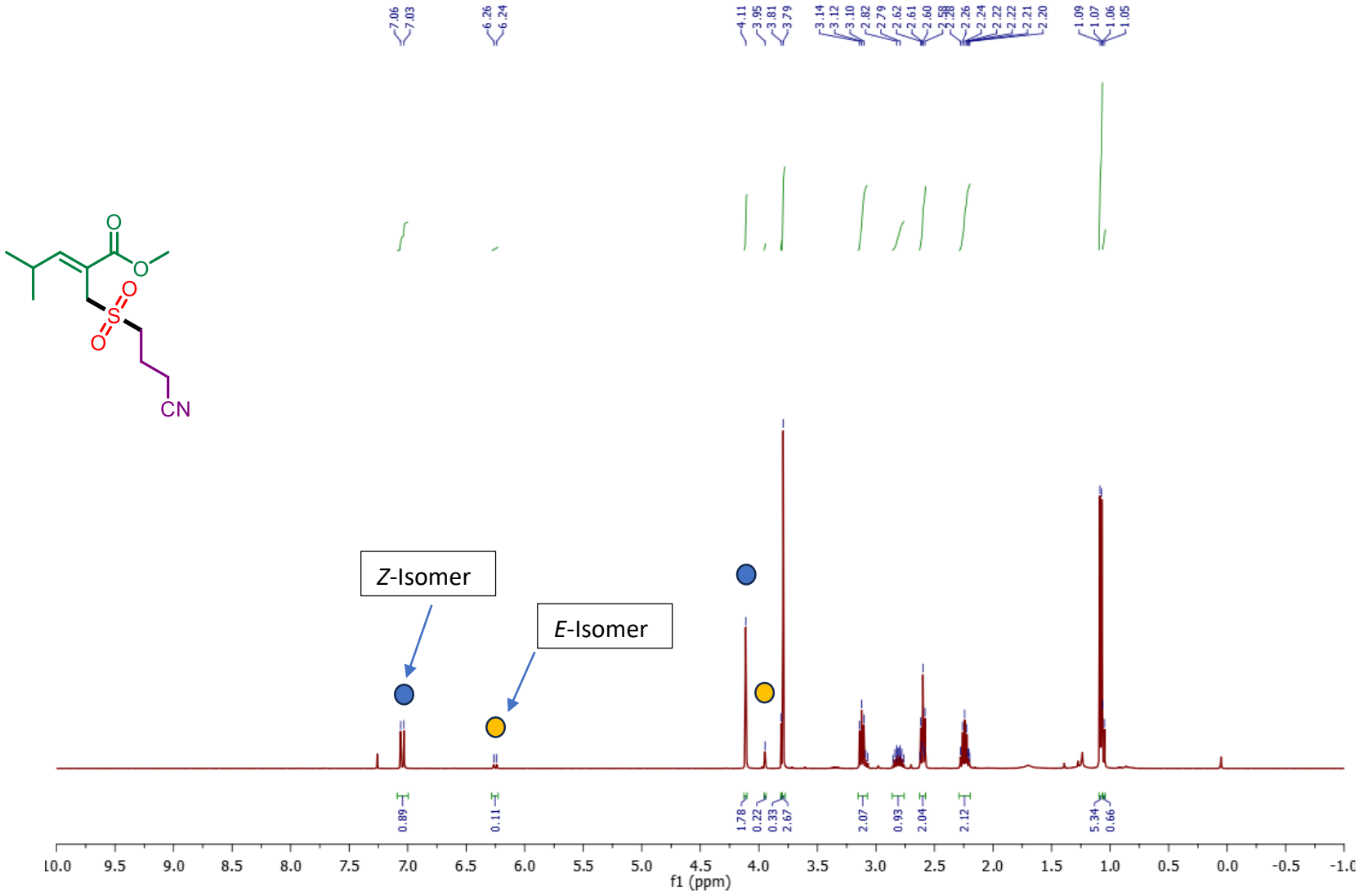
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum of Compound **(3oa)**



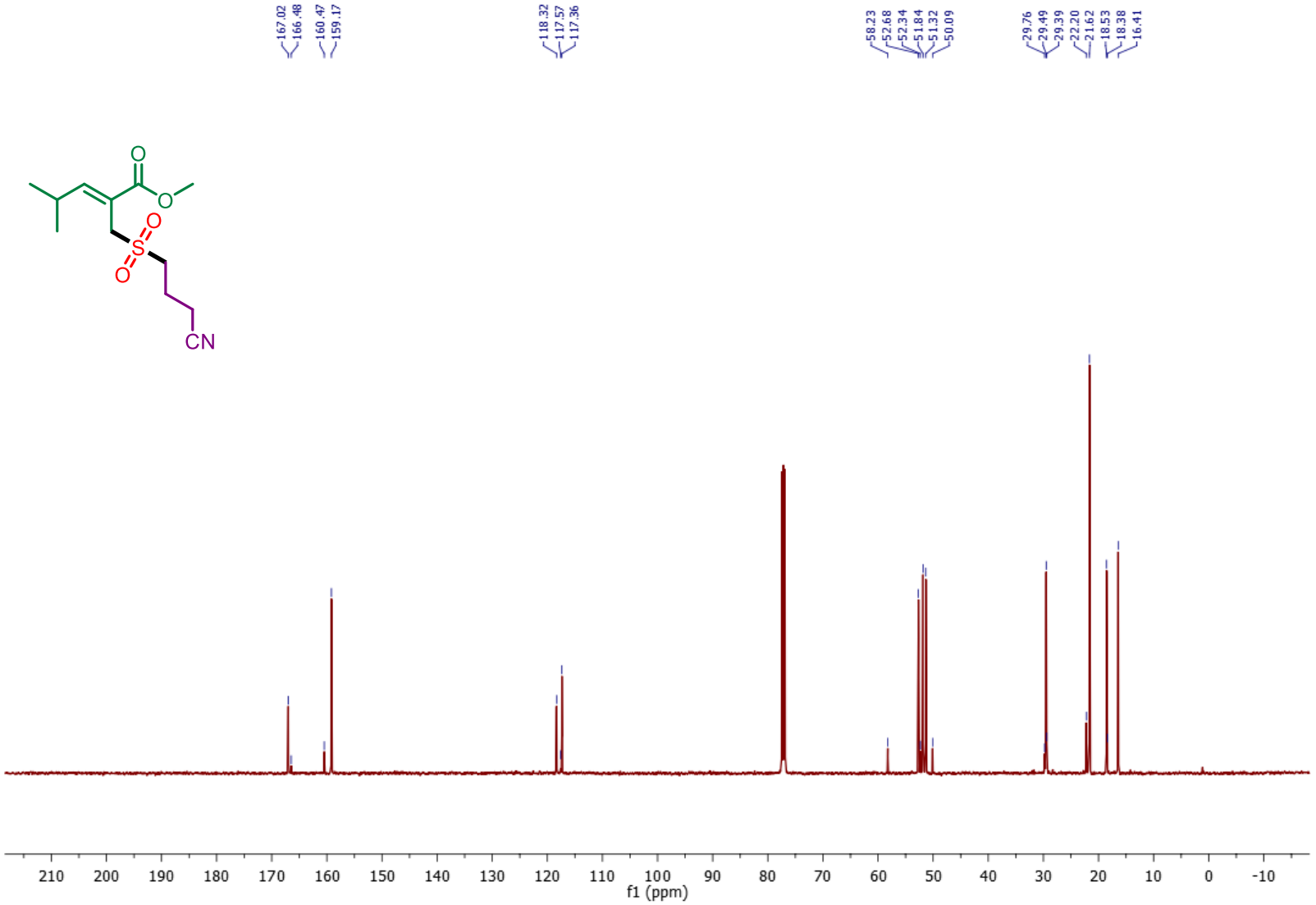
^{13}C NMR (75 MHz, $CDCl_3$) Spectrum of Compound **(3oa)**



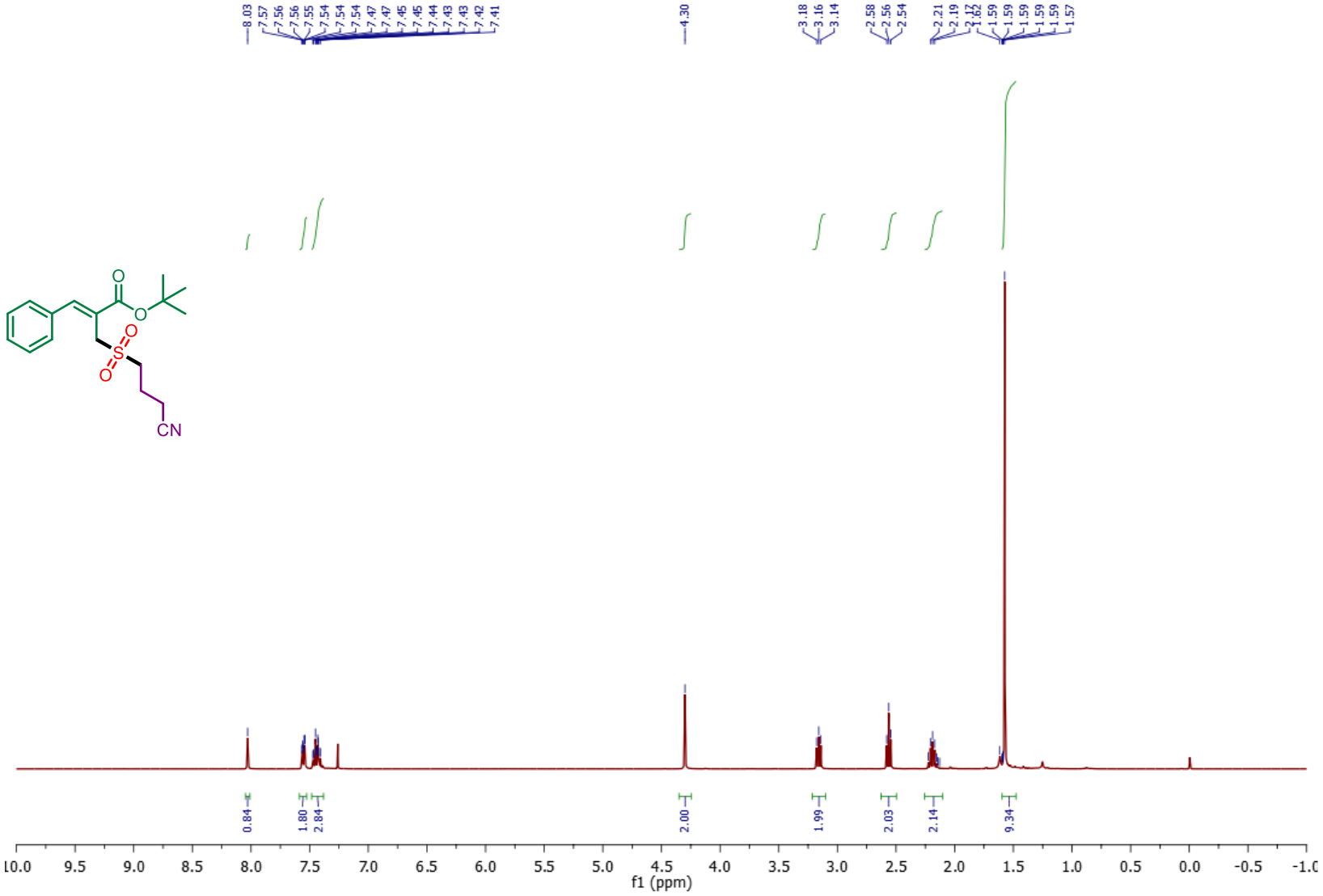
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3pa)**



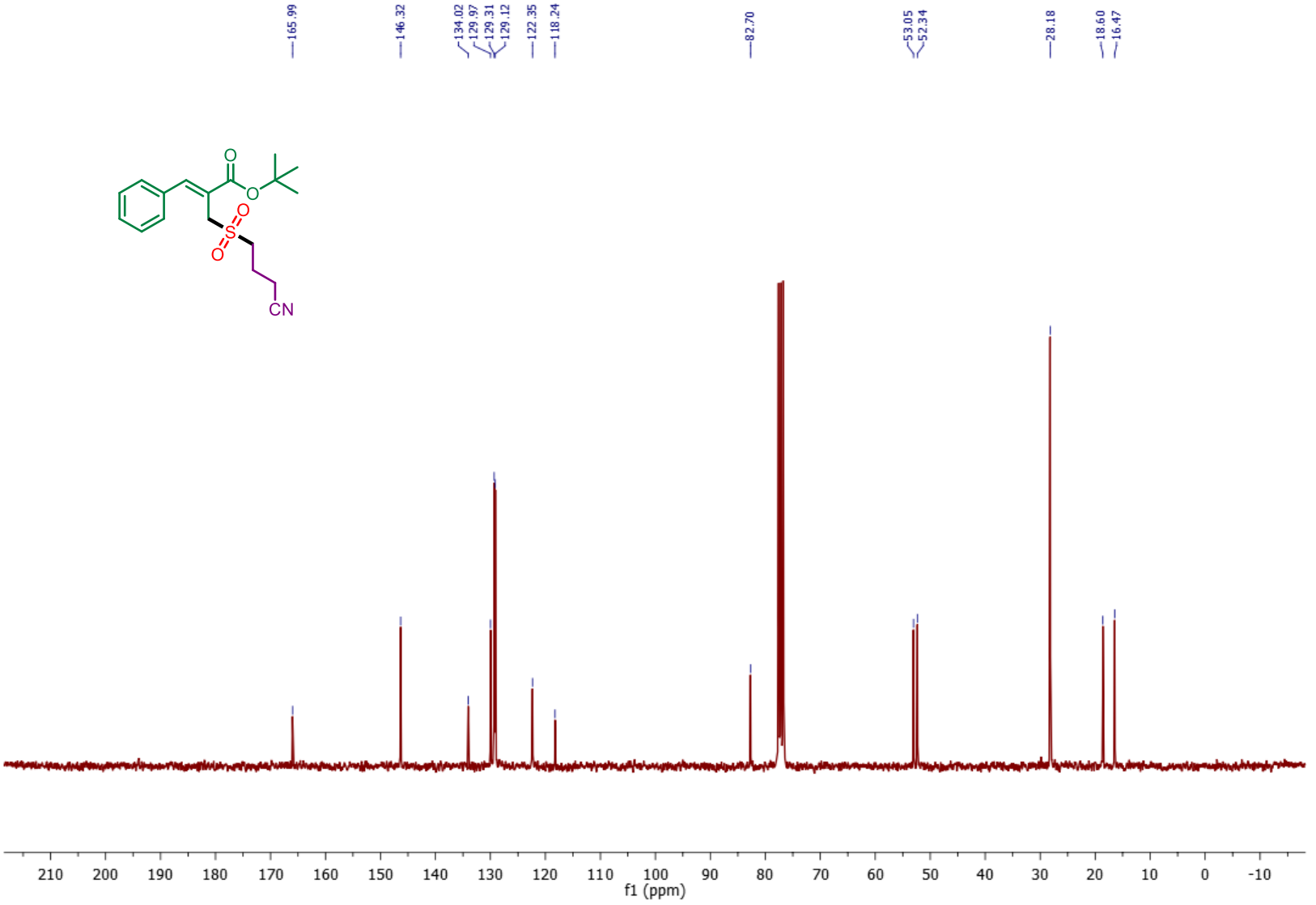
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3pa)**



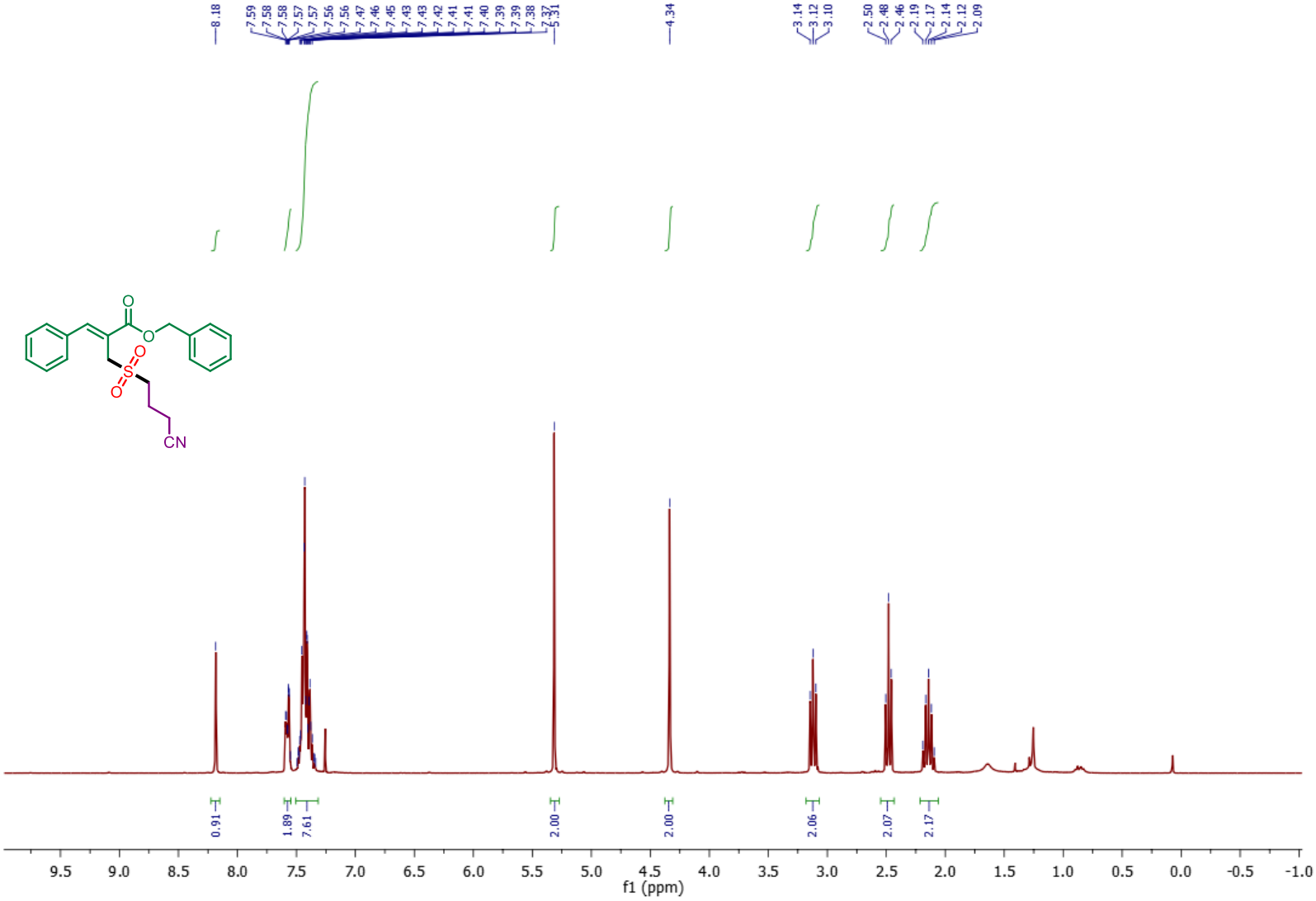
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3qa)**



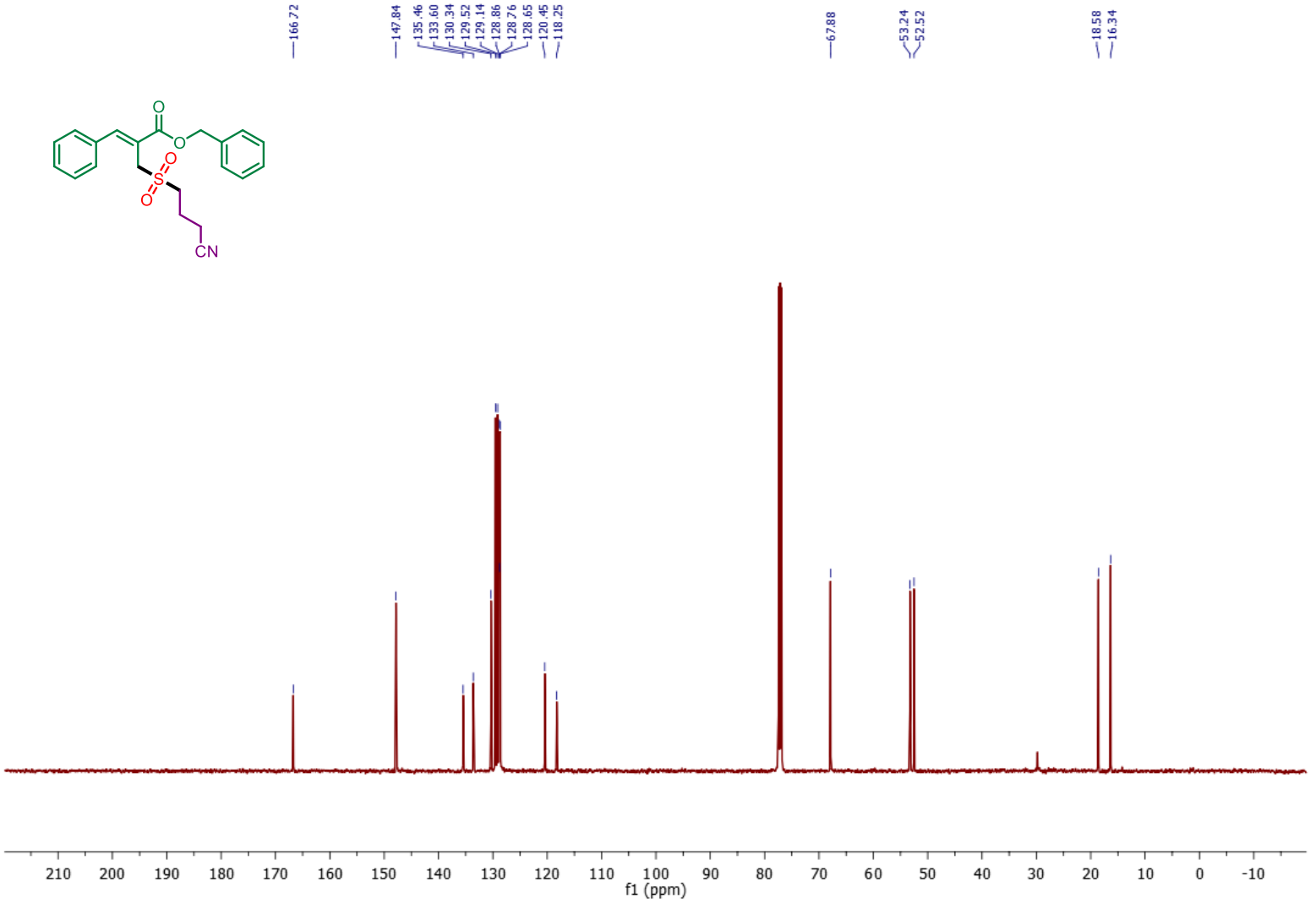
^{13}C NMR (75 MHz, $CDCl_3$) Spectrum of Compound **(3qa)**



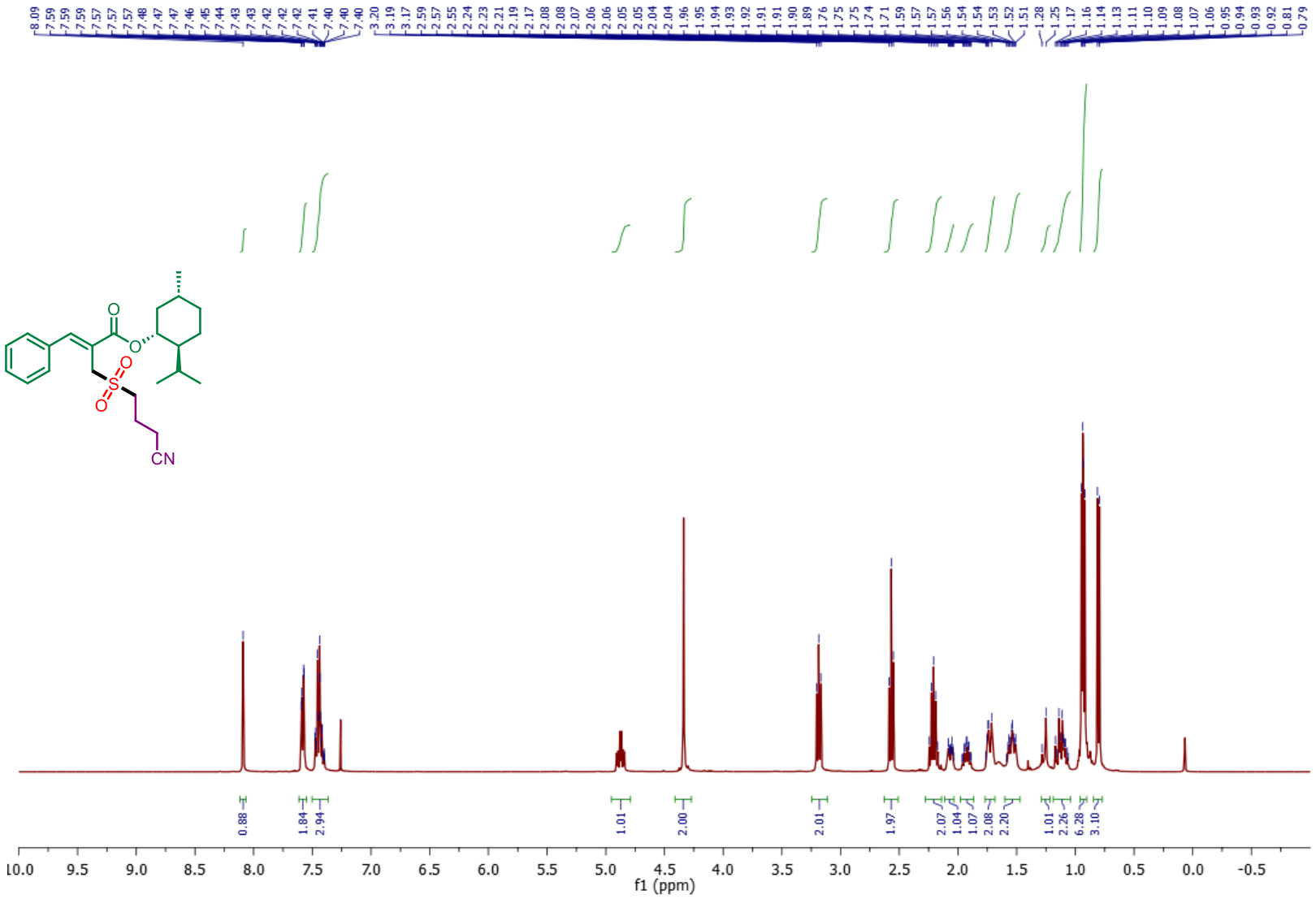
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum of Compound **(3ra)**



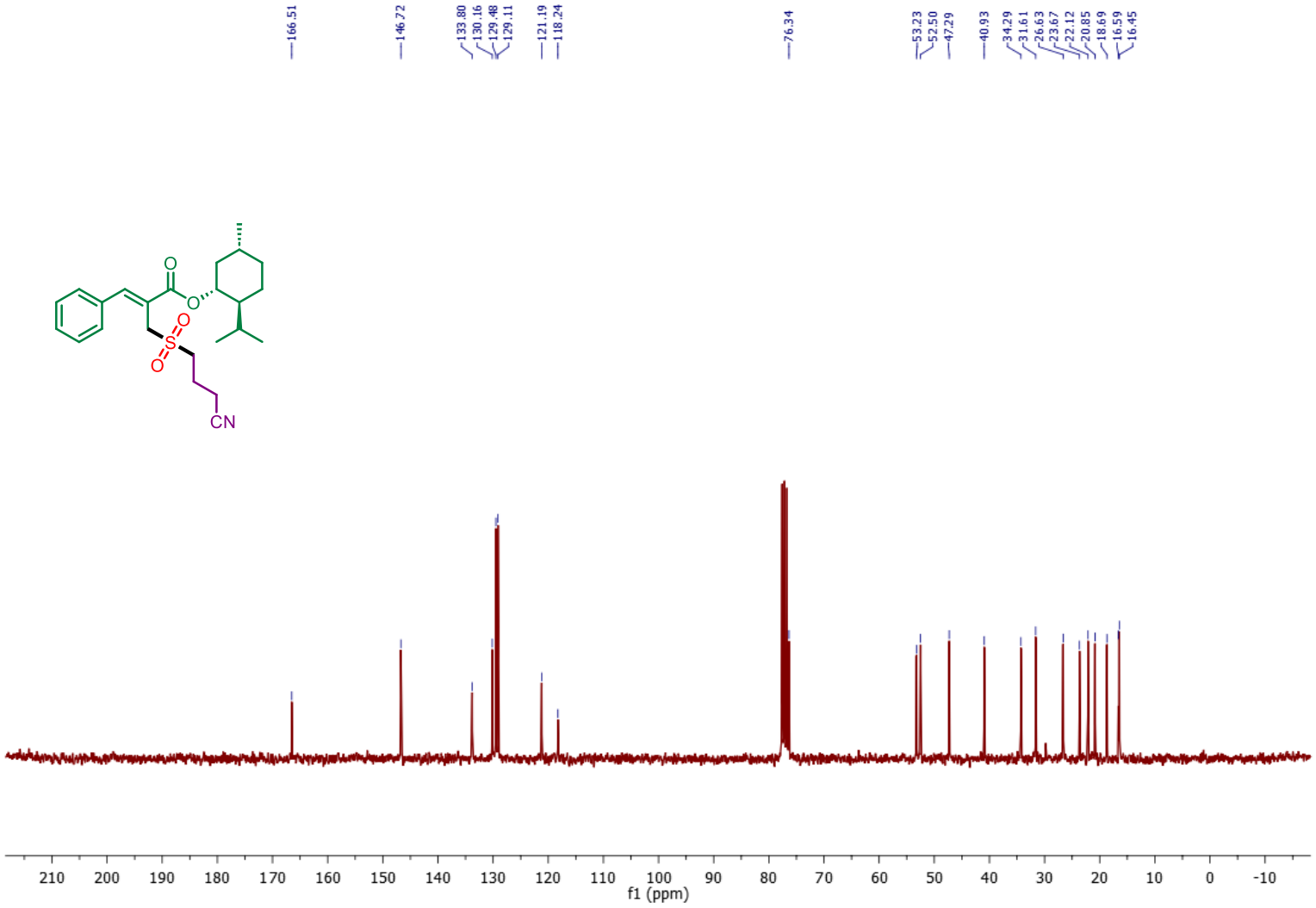
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3ra)**



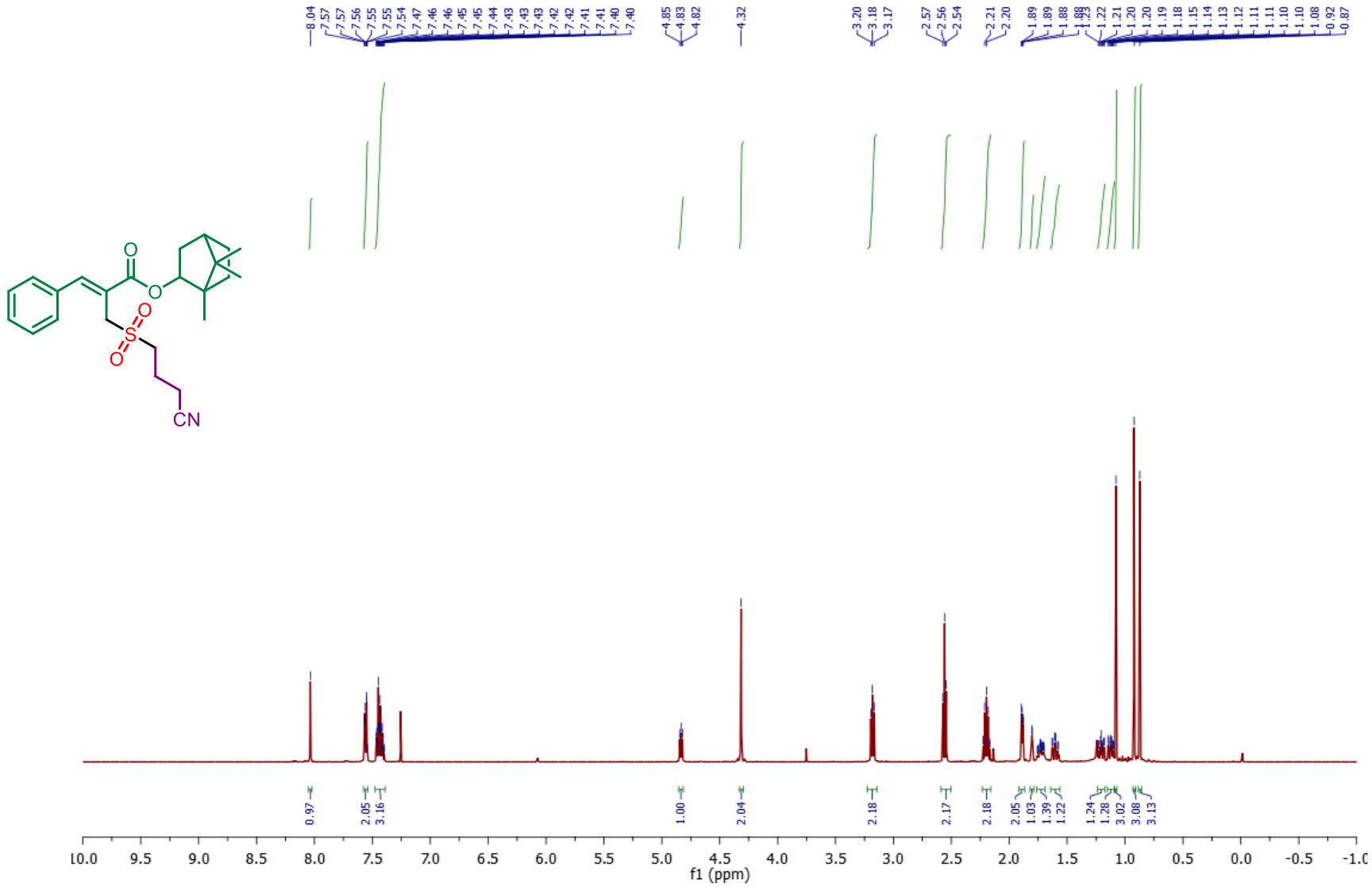
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3sa)**



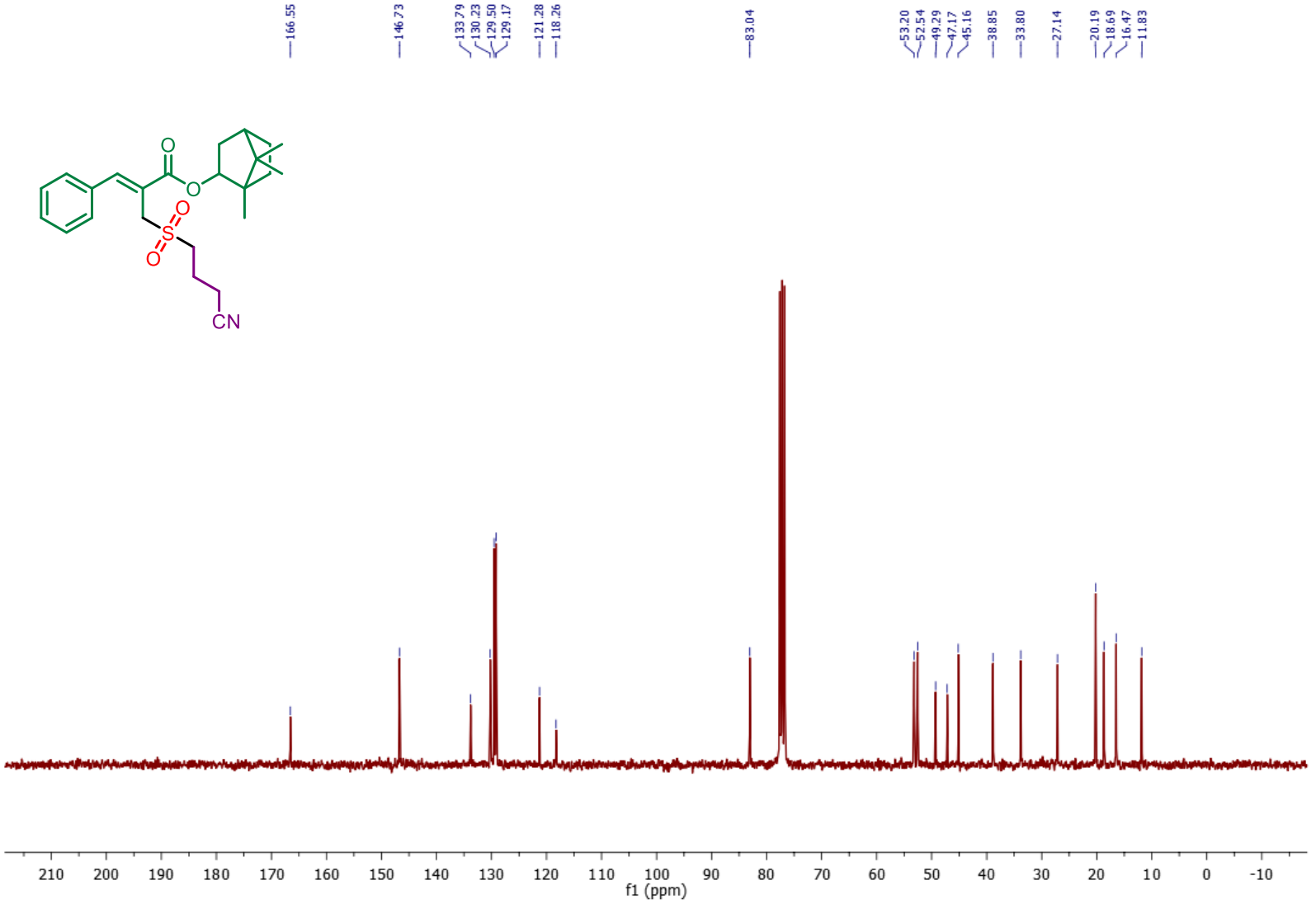
^{13}C NMR (75 MHz, $CDCl_3$) Spectrum of Compound **(3sa)**



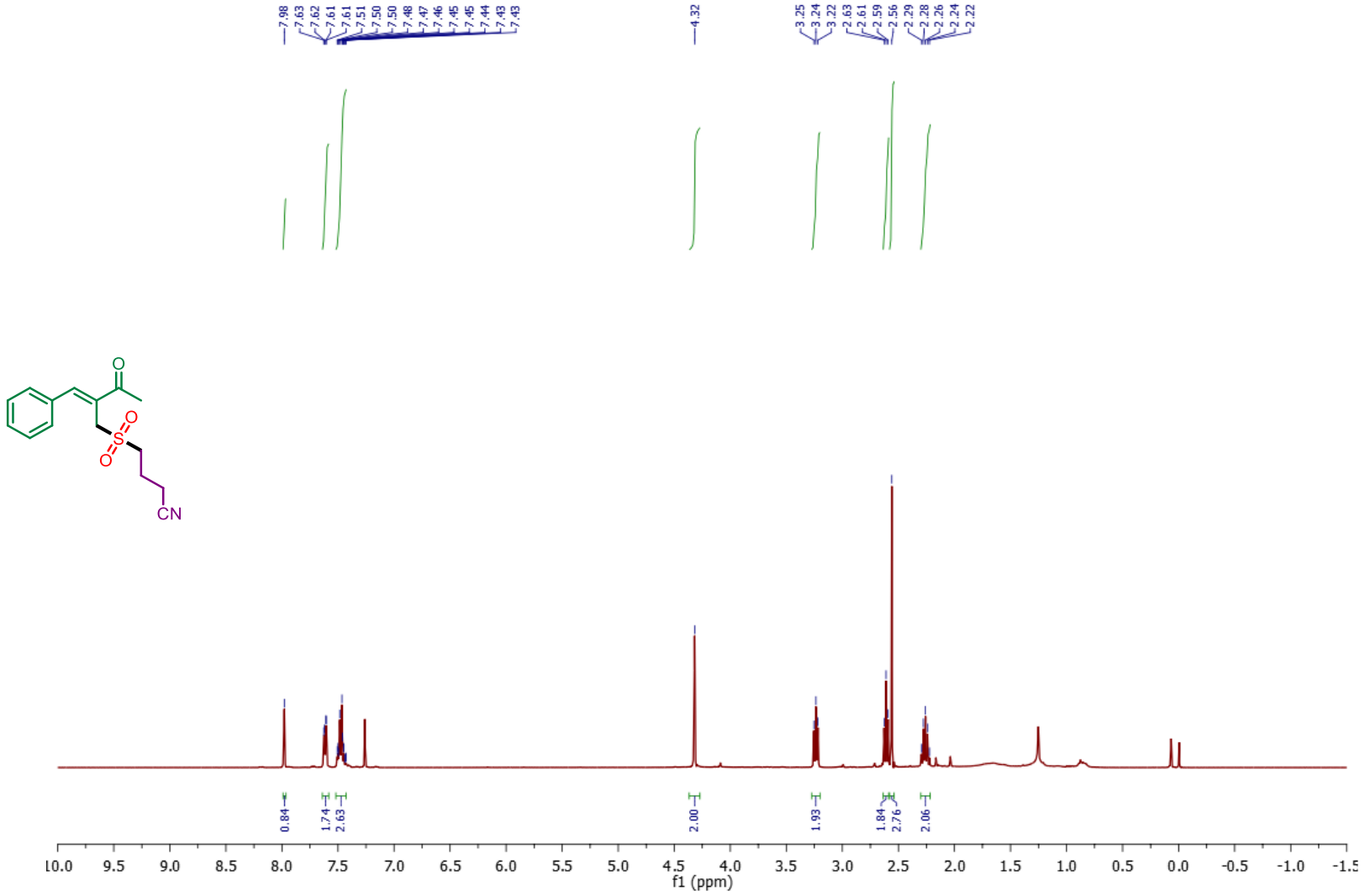
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3ta)**



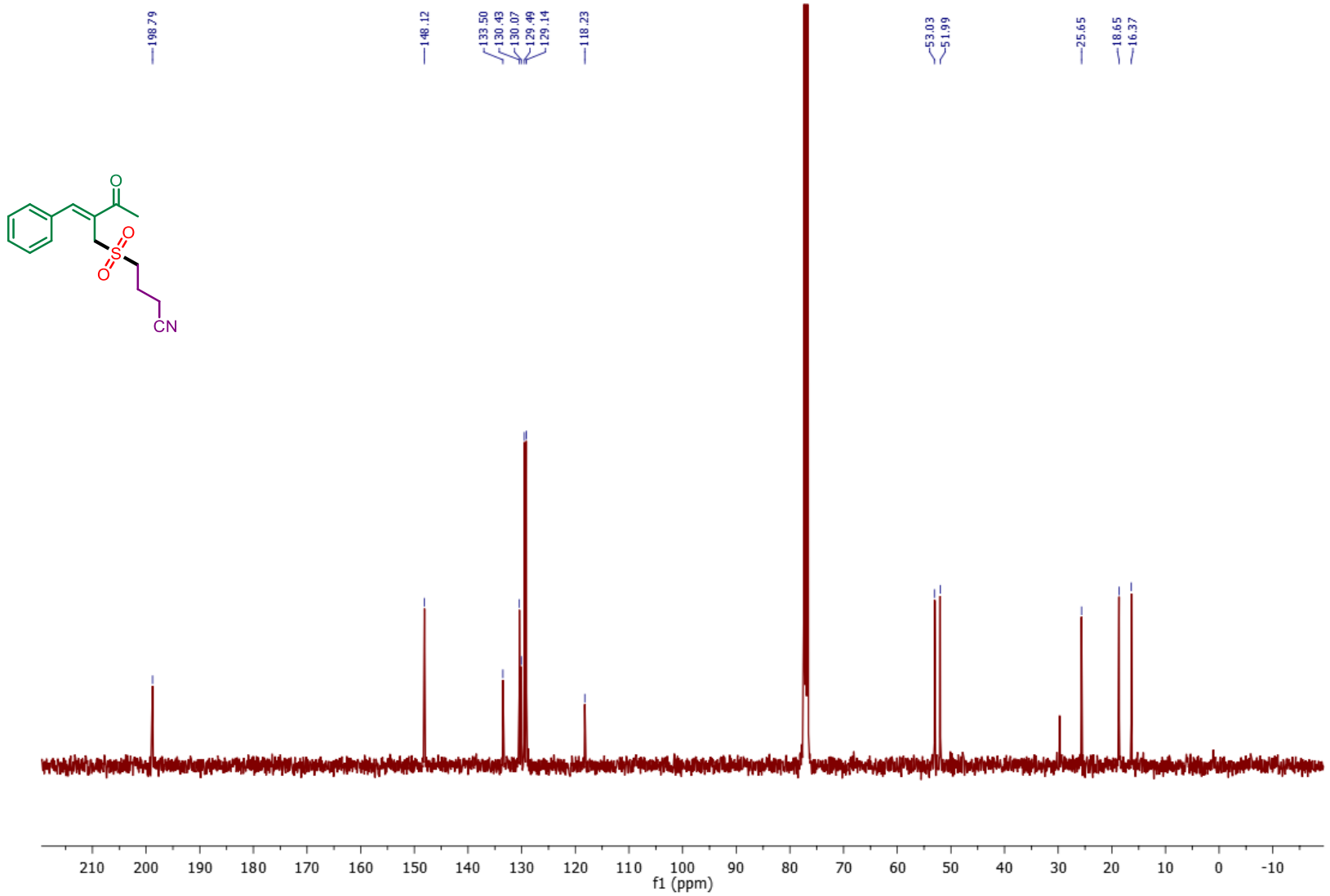
^{13}C NMR (75 MHz, $CDCl_3$) Spectrum of Compound **(3ta)**



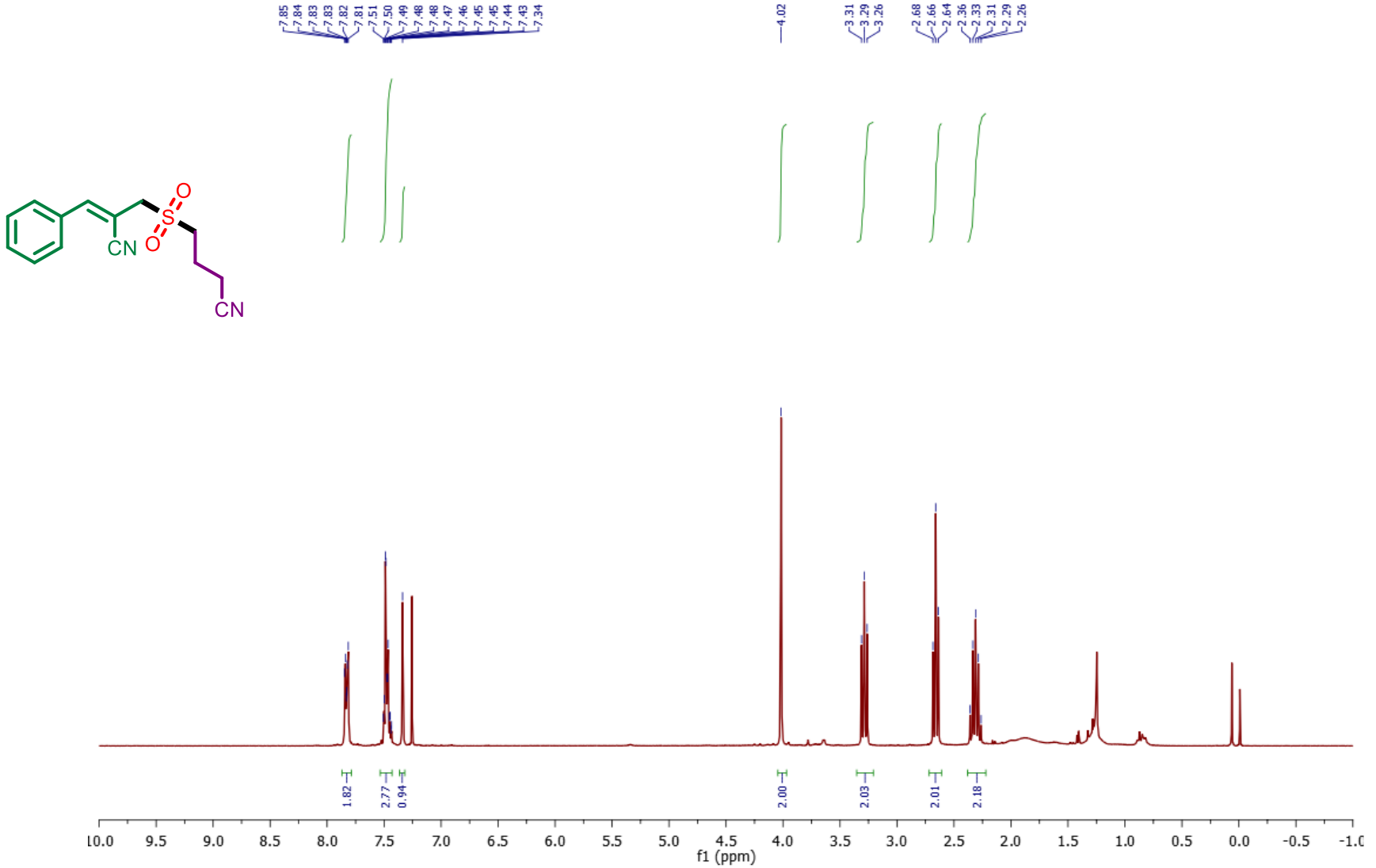
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3ua)**



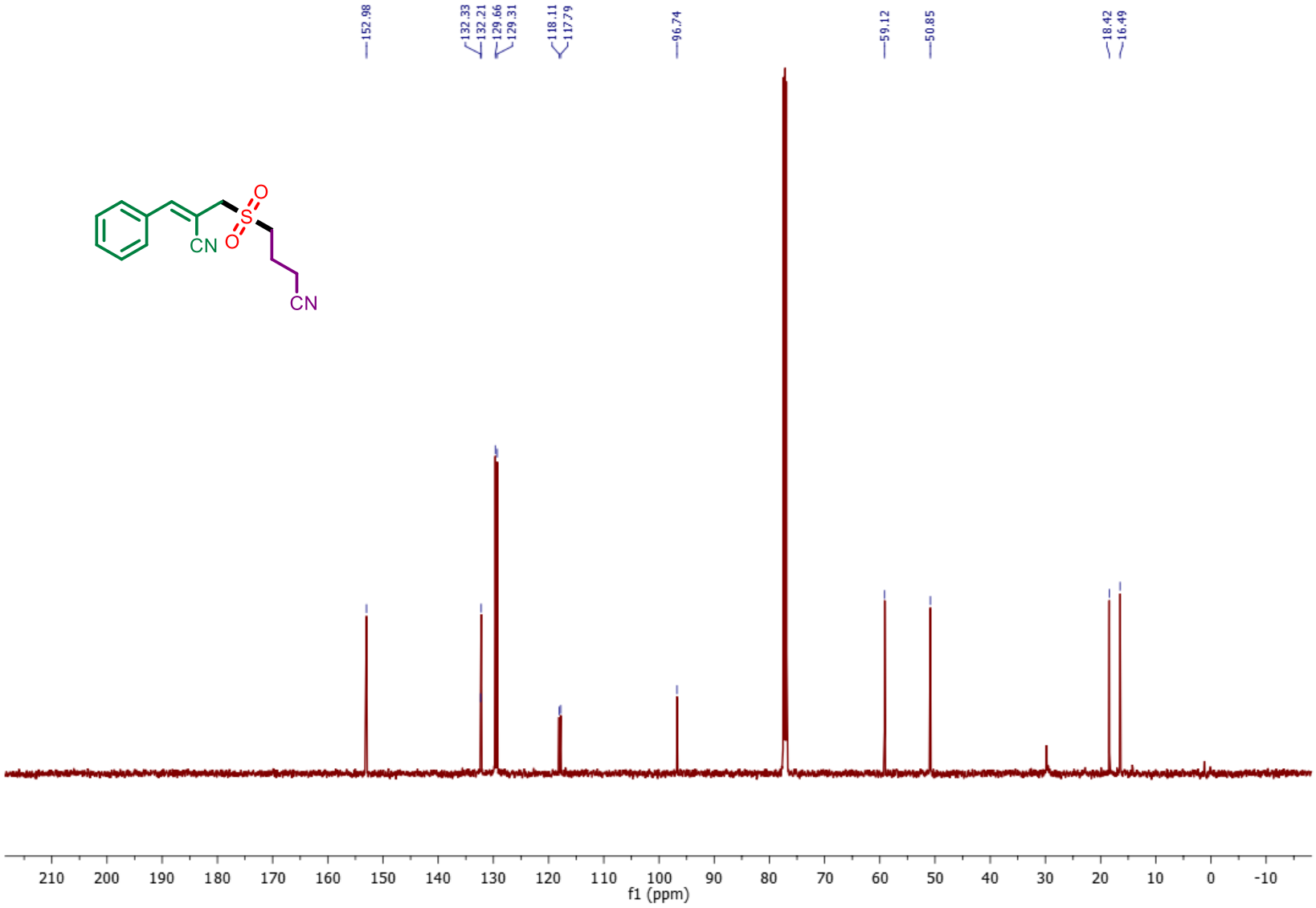
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ua)**



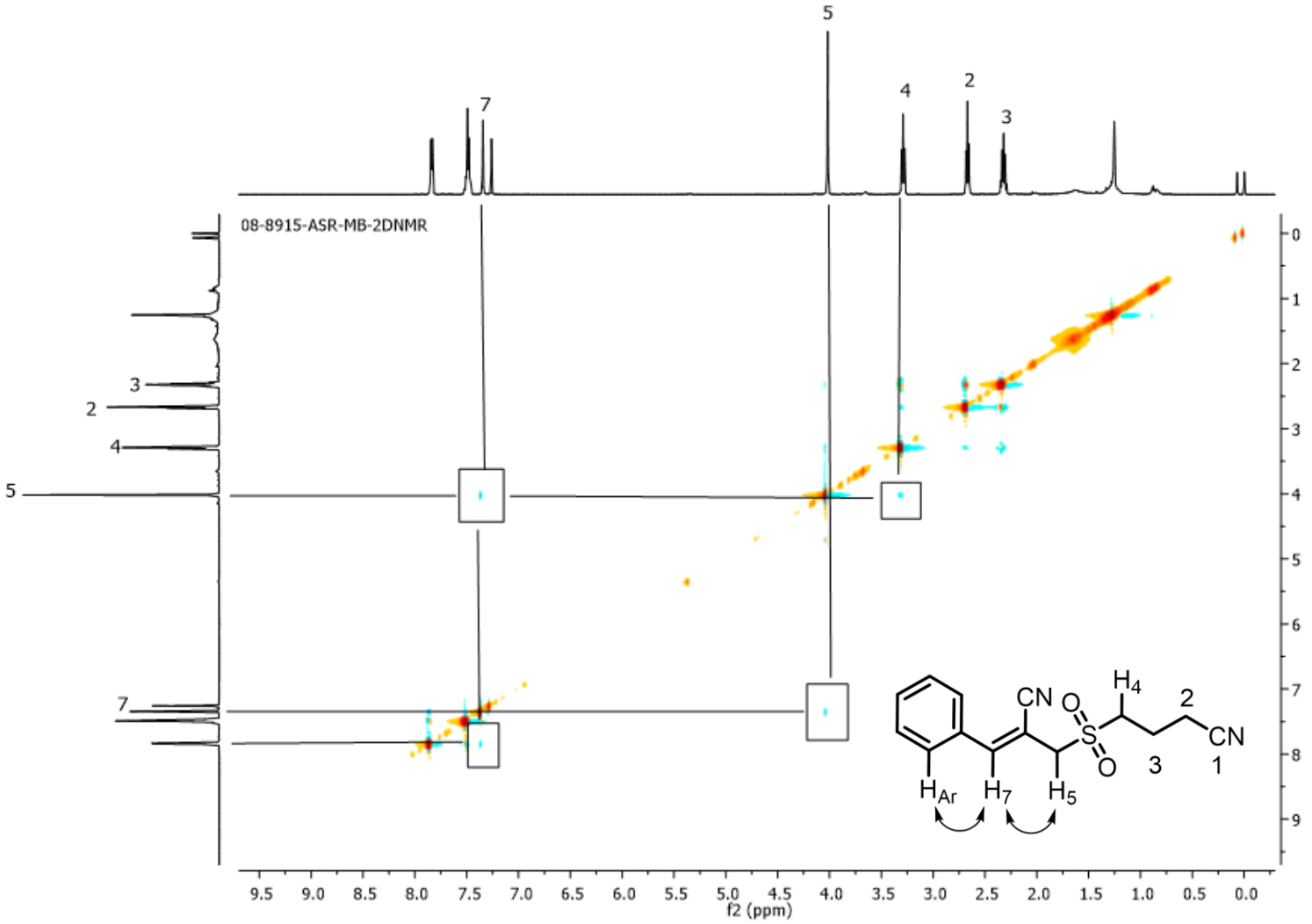
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum of Compound **(3va)**



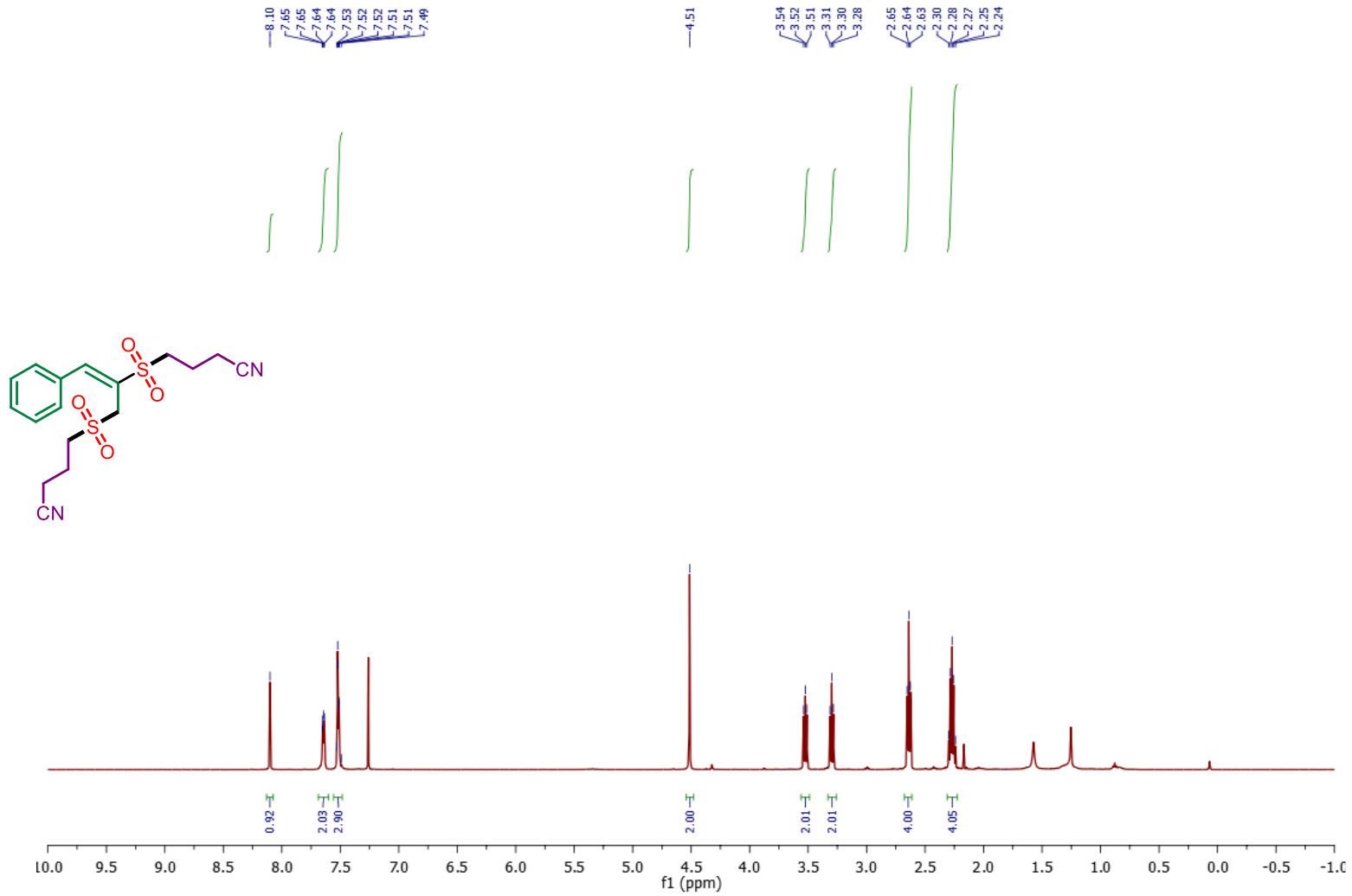
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3va)**



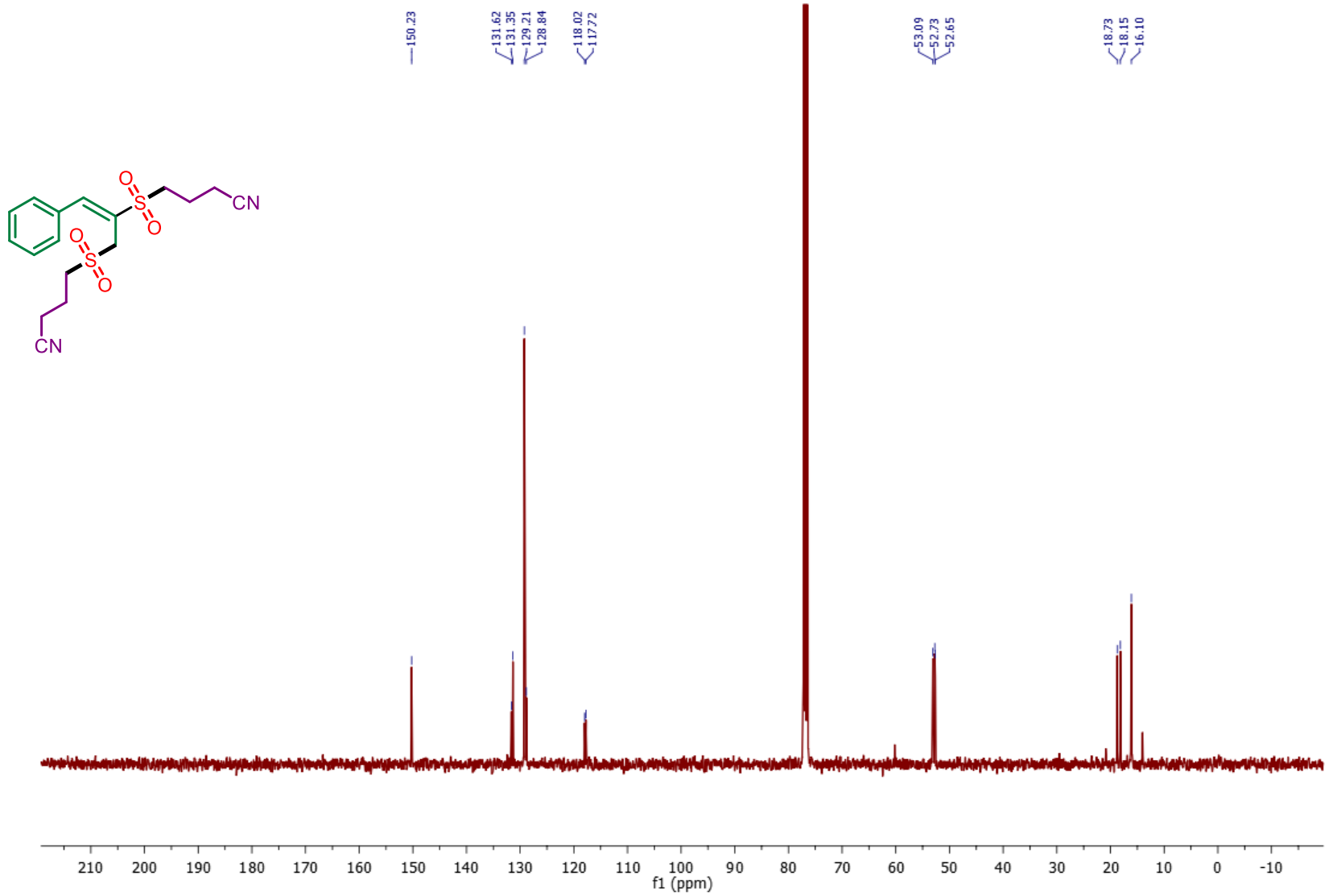
^{1}H-^{1}H 2D-NOESY spectrum of **(3va)**



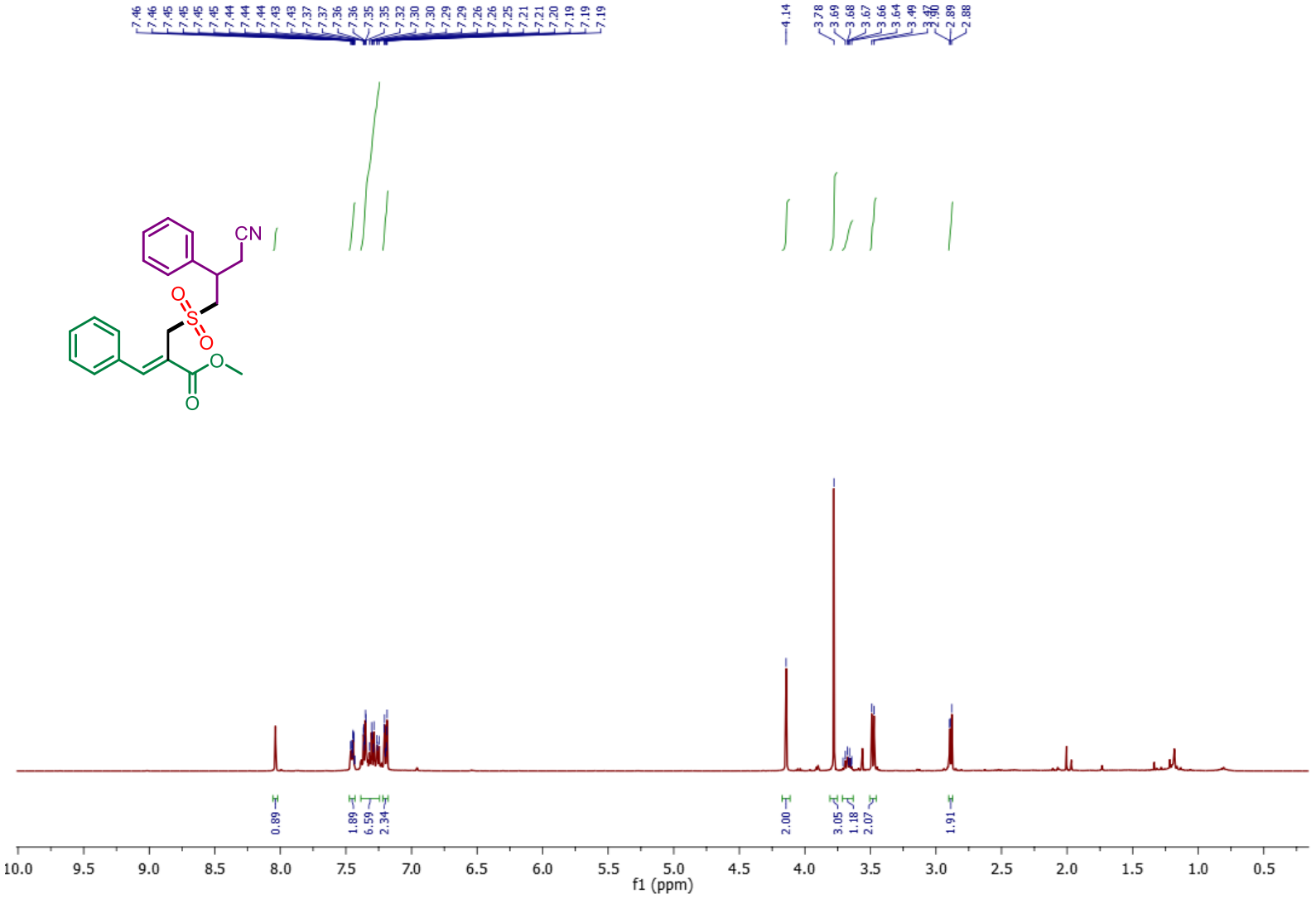
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3wa')**



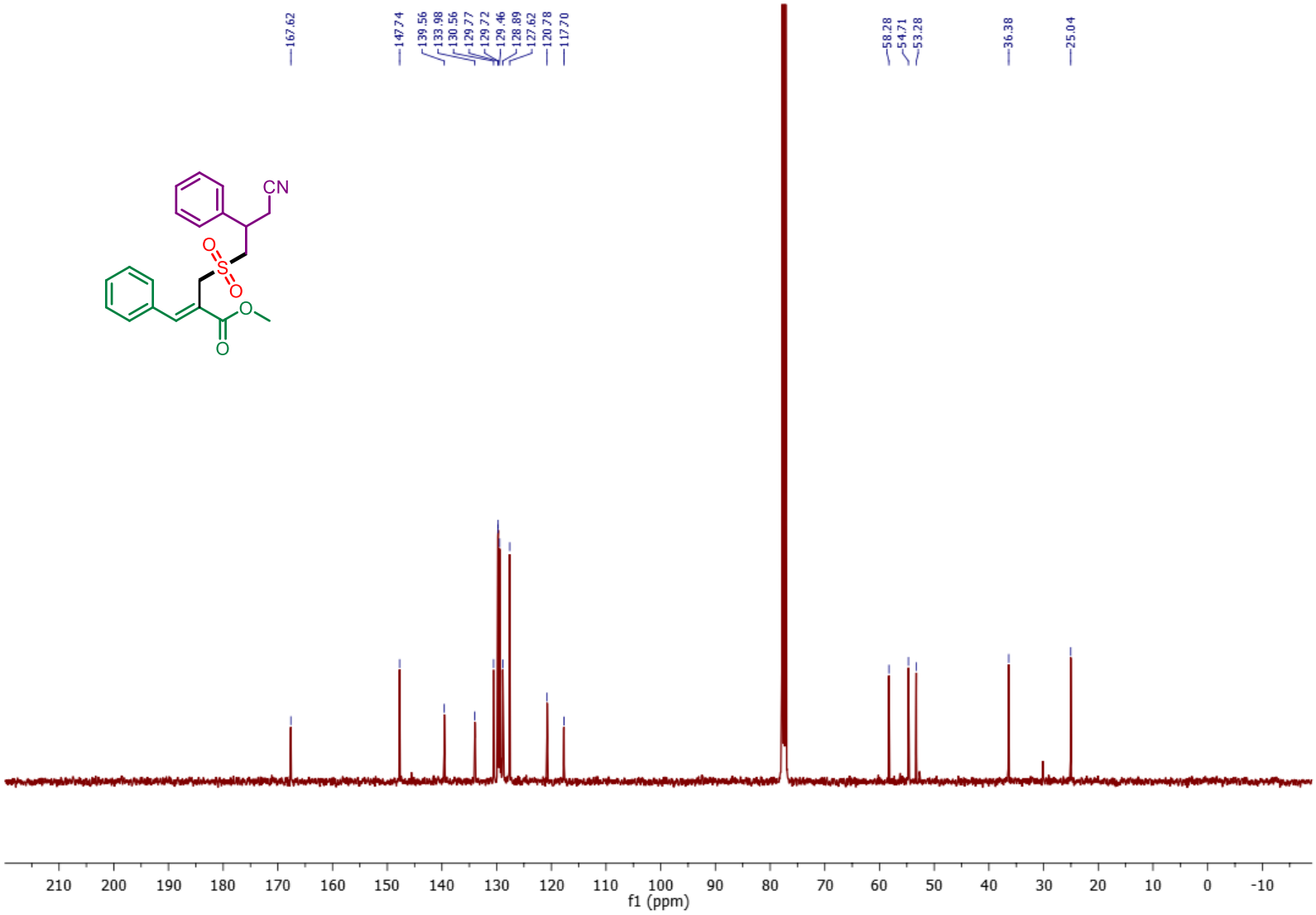
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3wa')**



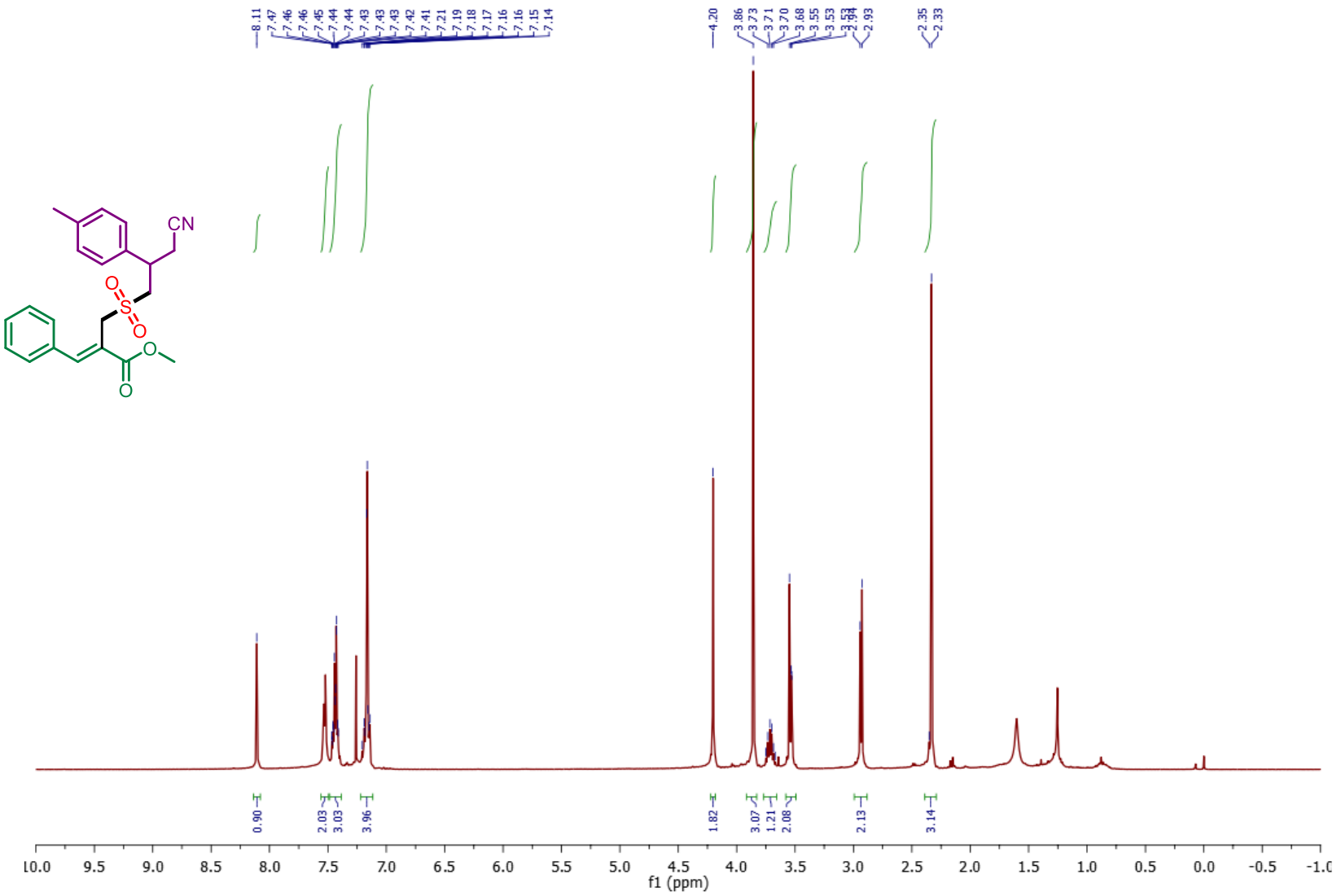
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3ab)**



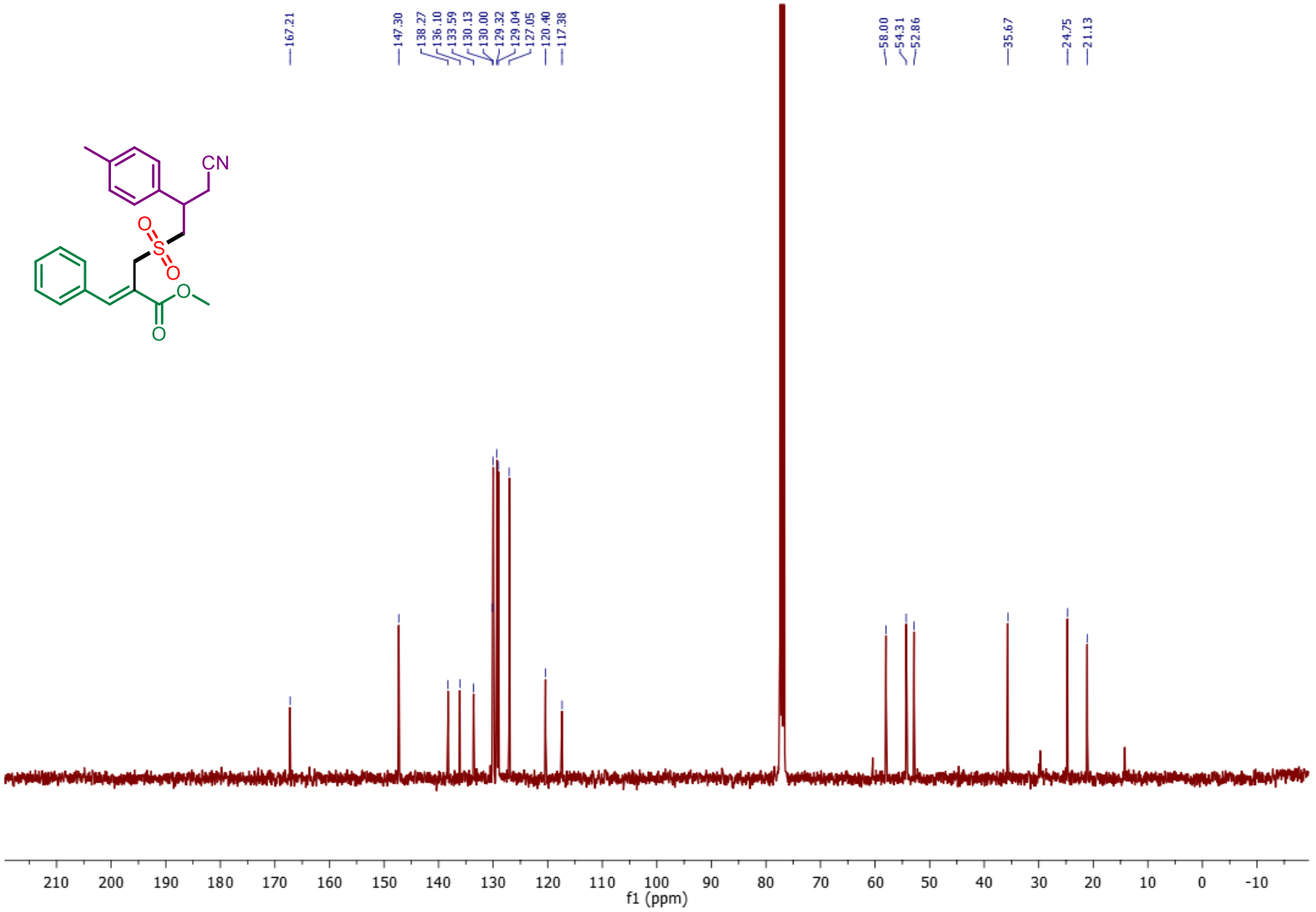
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ab)**



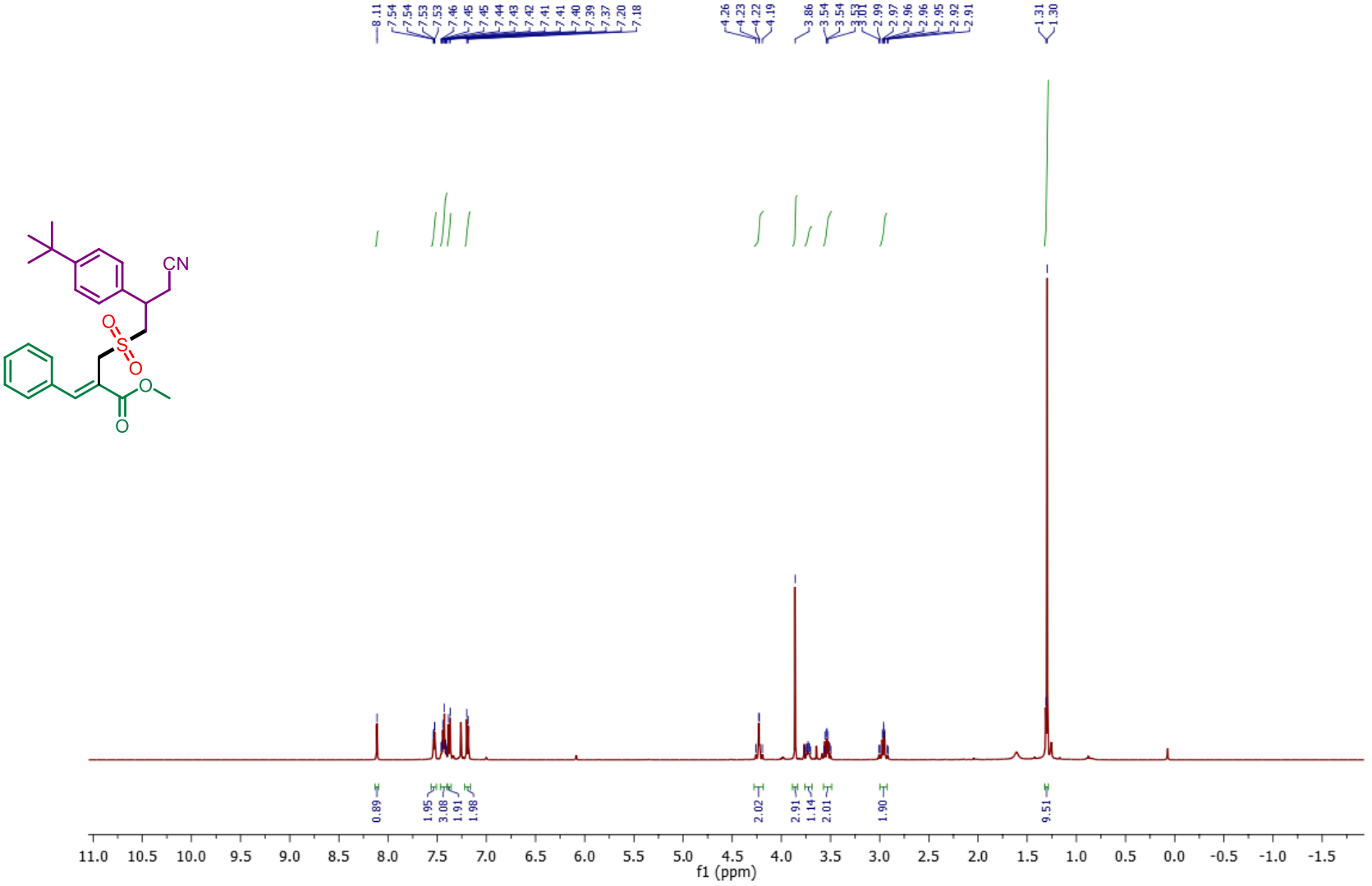
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3ac)**



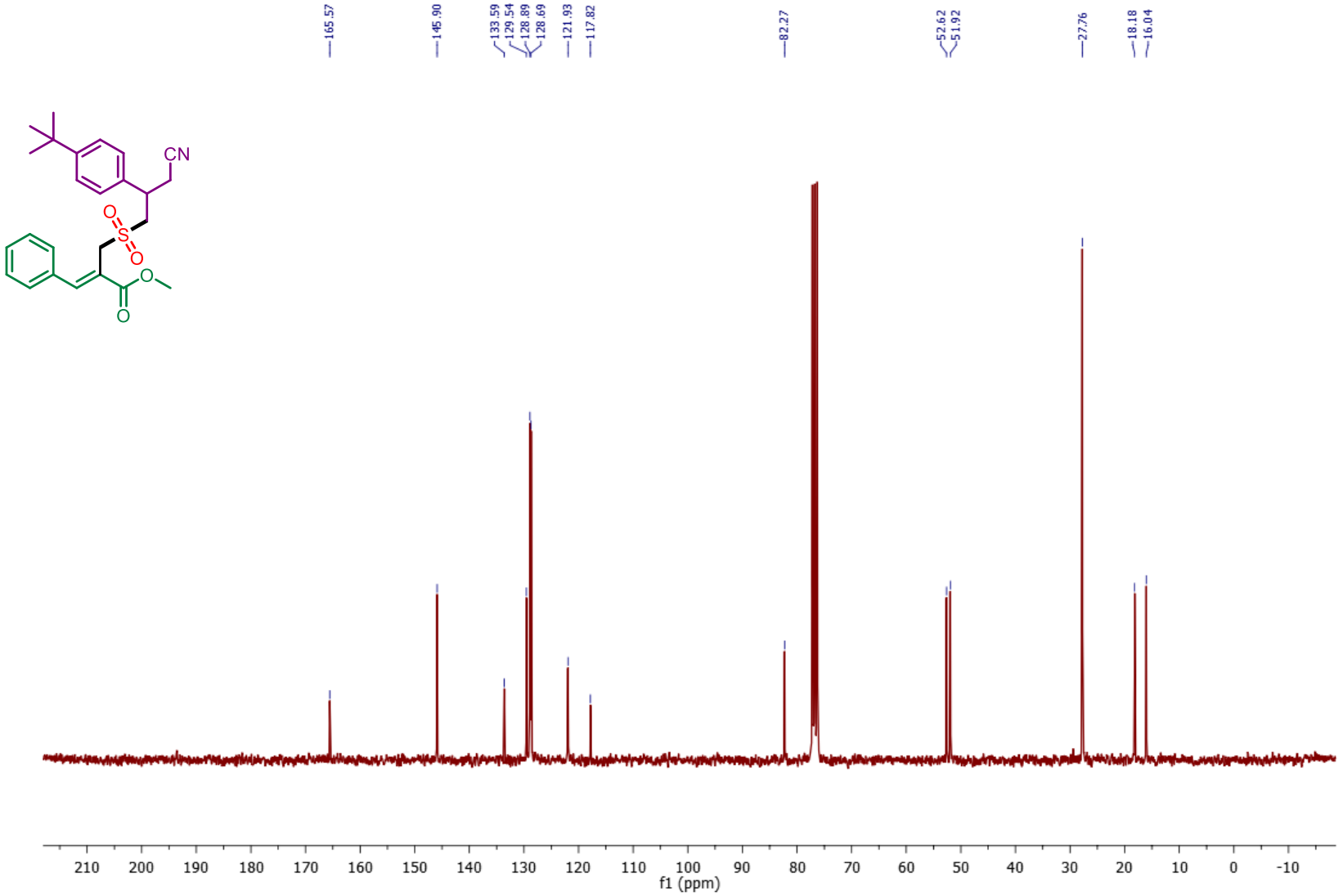
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ac)**



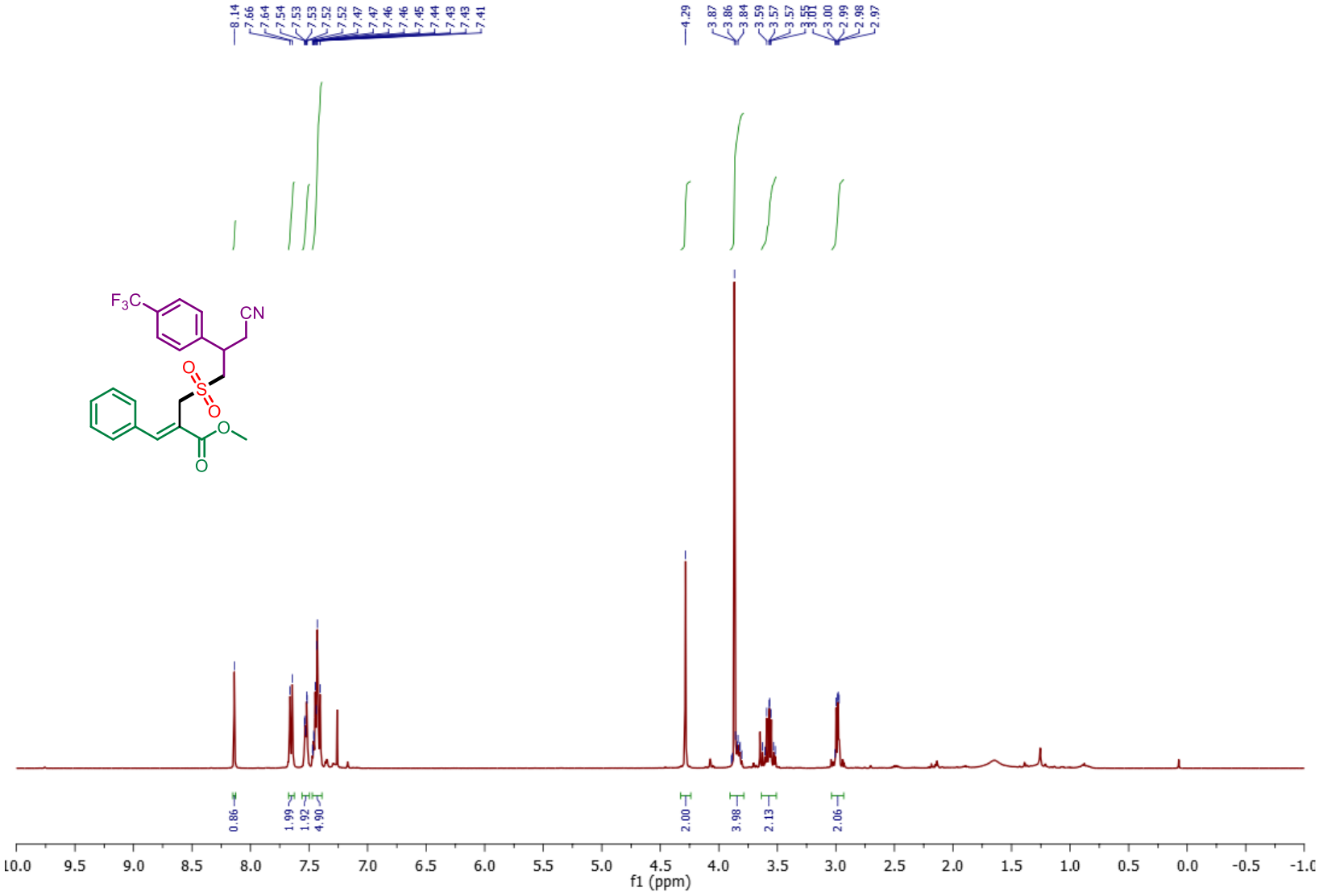
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3ad)**



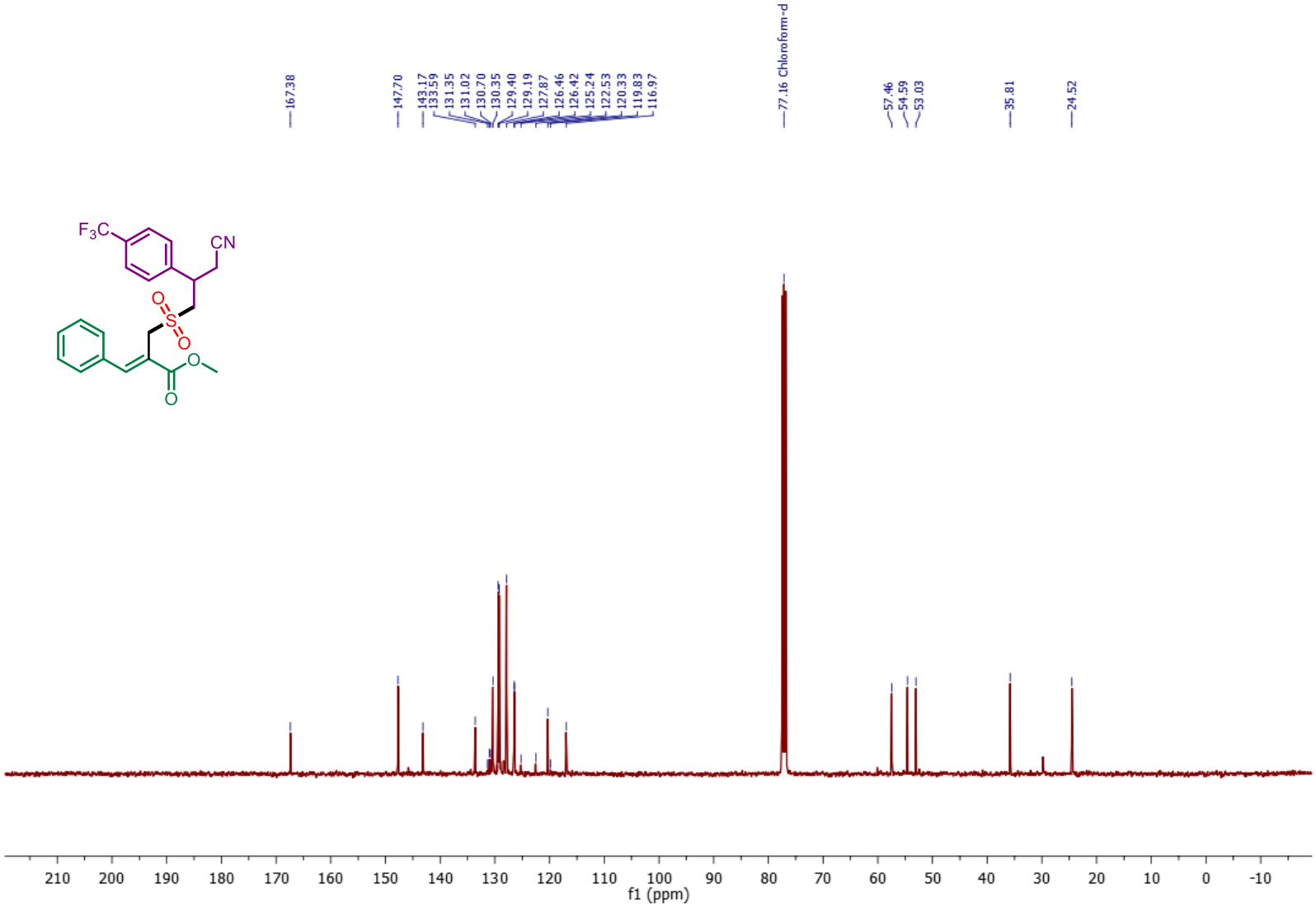
^{13}C NMR (75 MHz, $CDCl_3$) Spectrum of Compound **(3ad)**



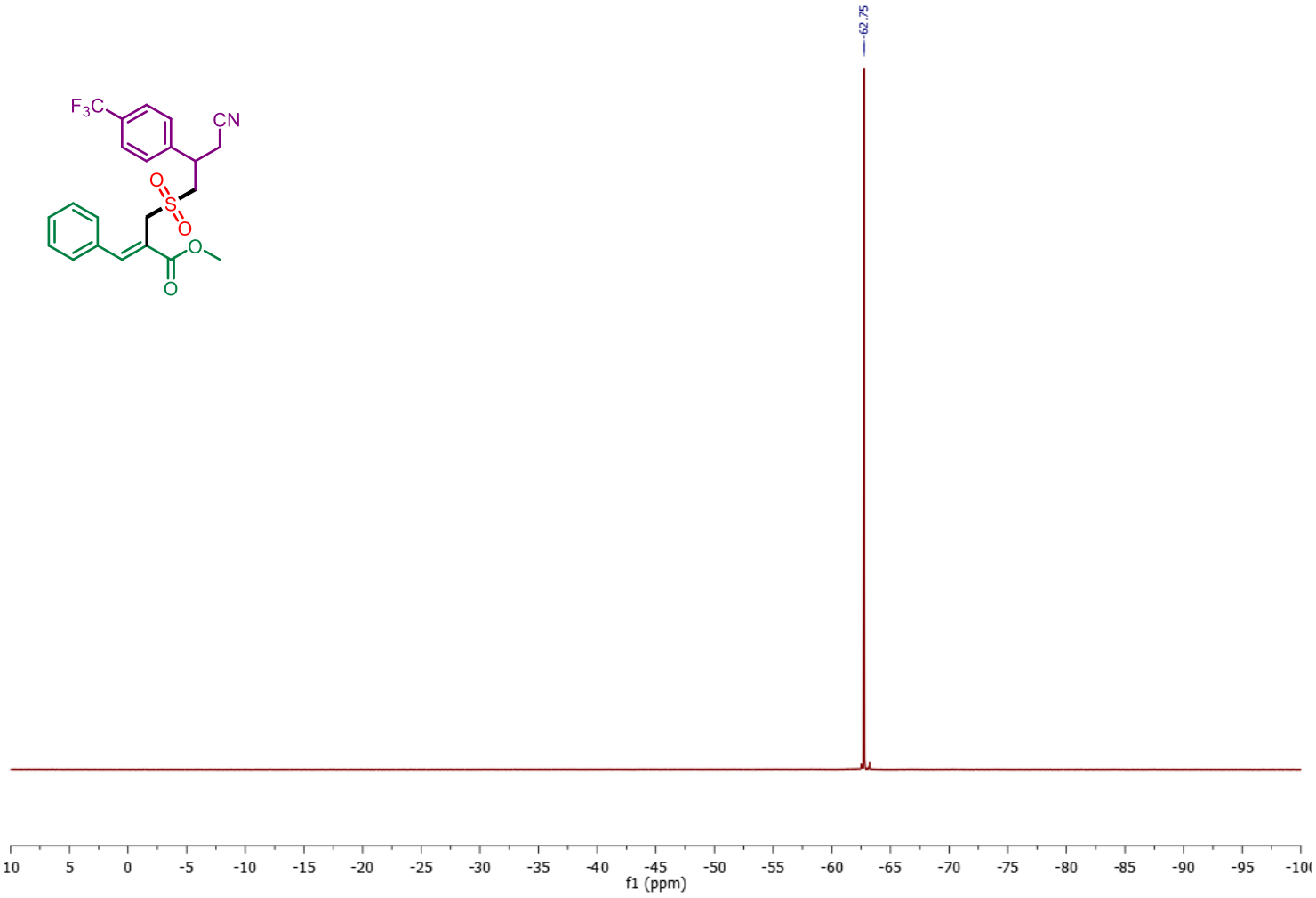
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3ae)**



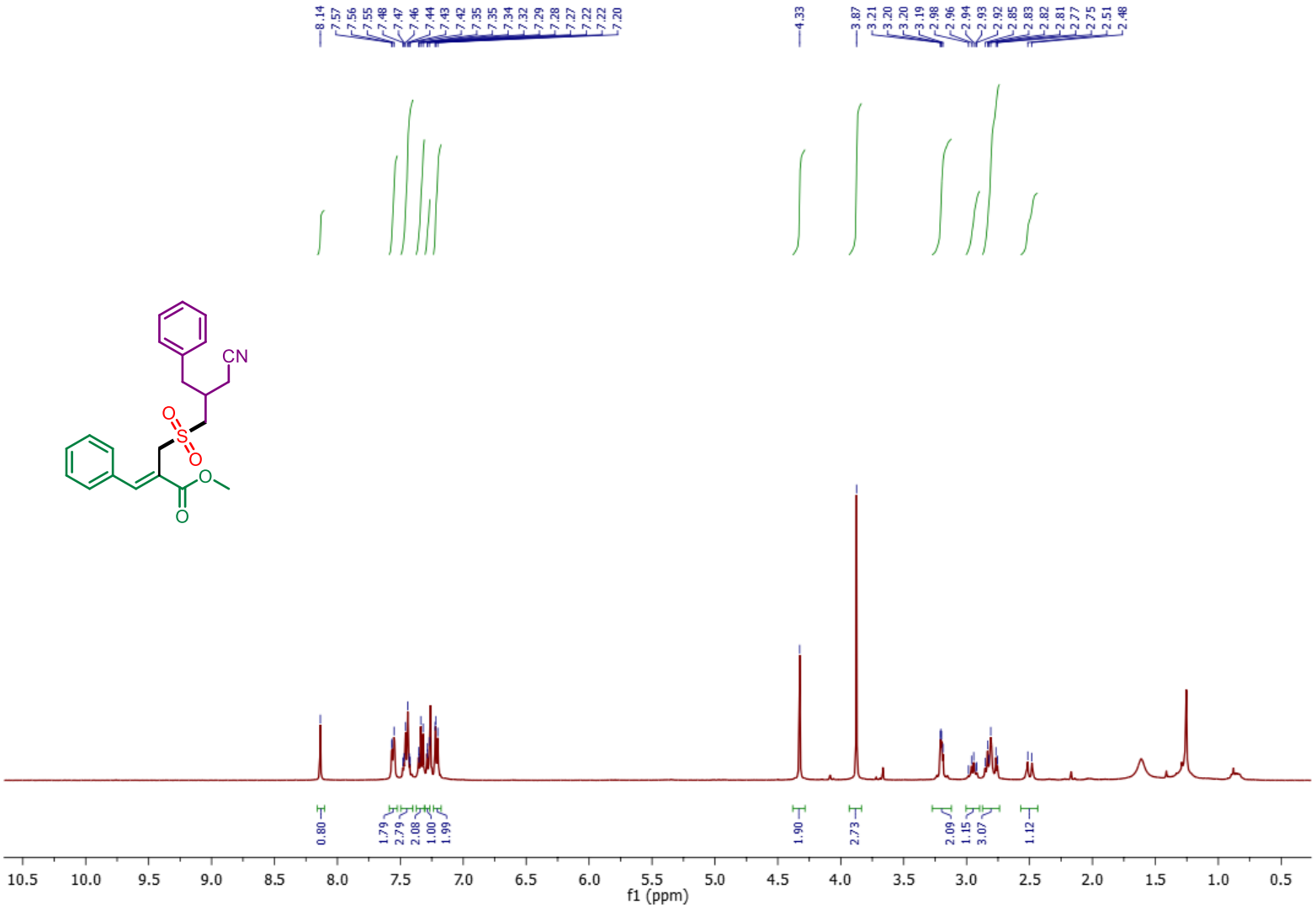
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ae)**



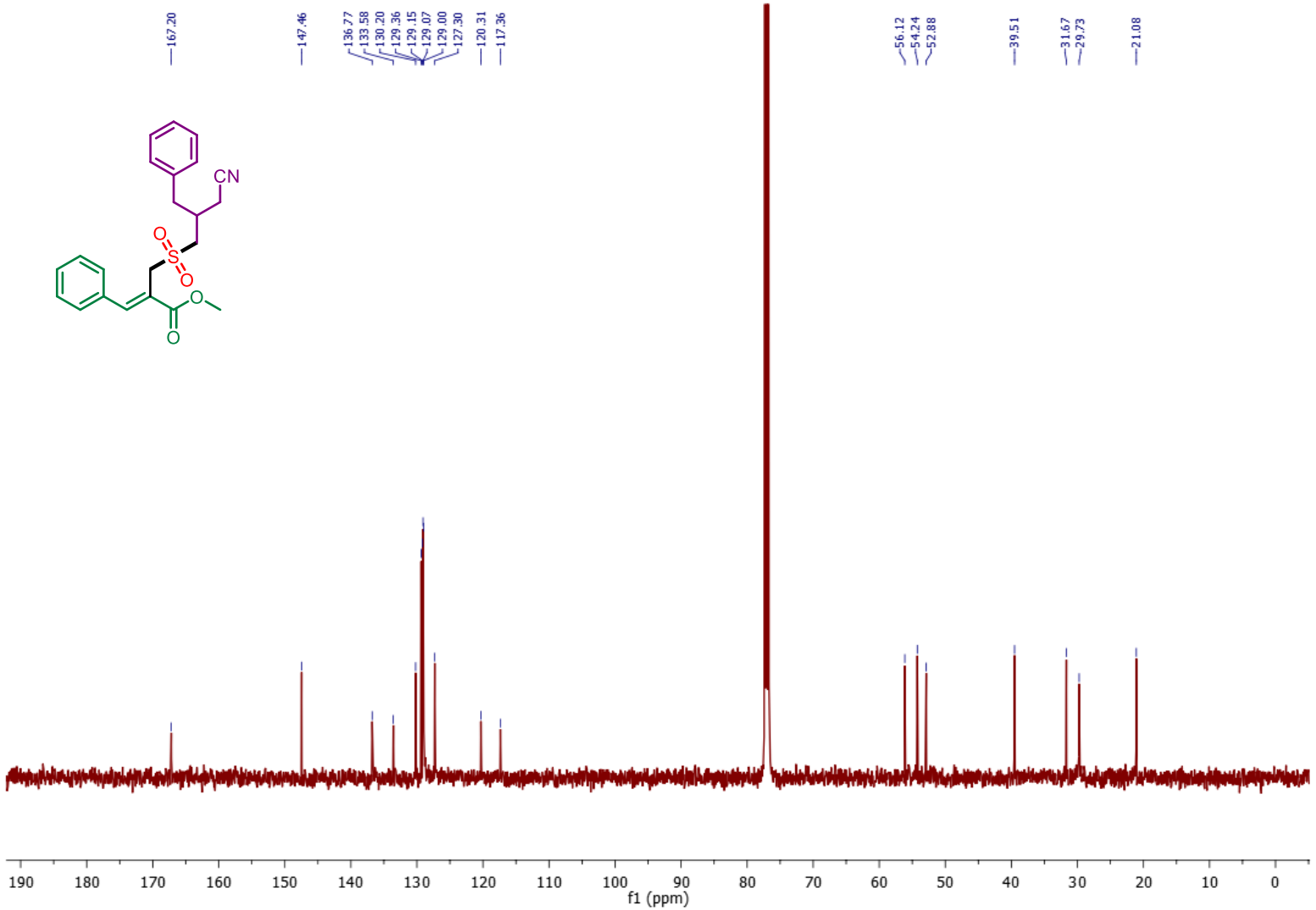
^{19} F NMR (376 MHz, $CDCl_3$) Spectrum of Compound **(3ae)**



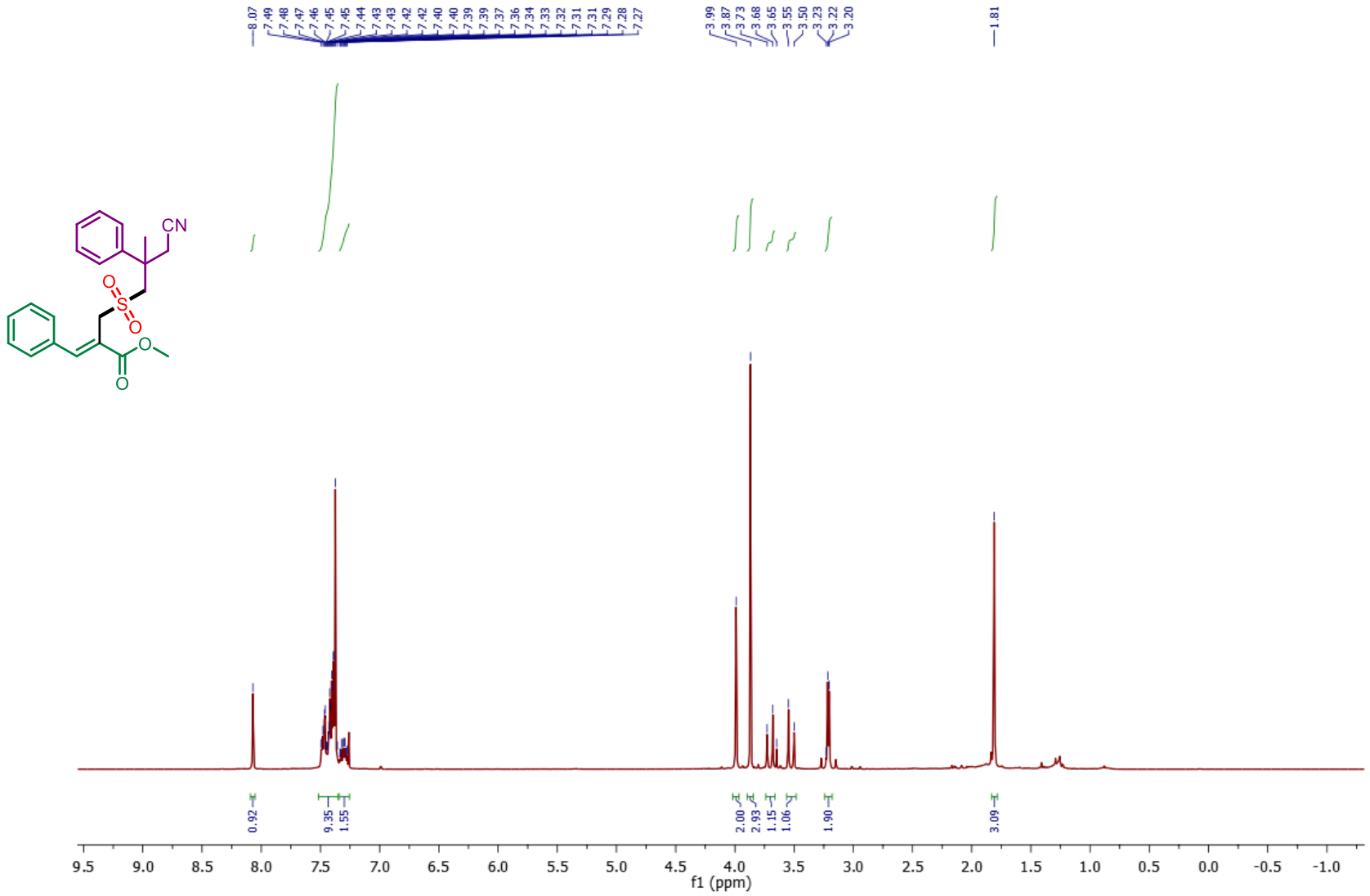
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3af)**



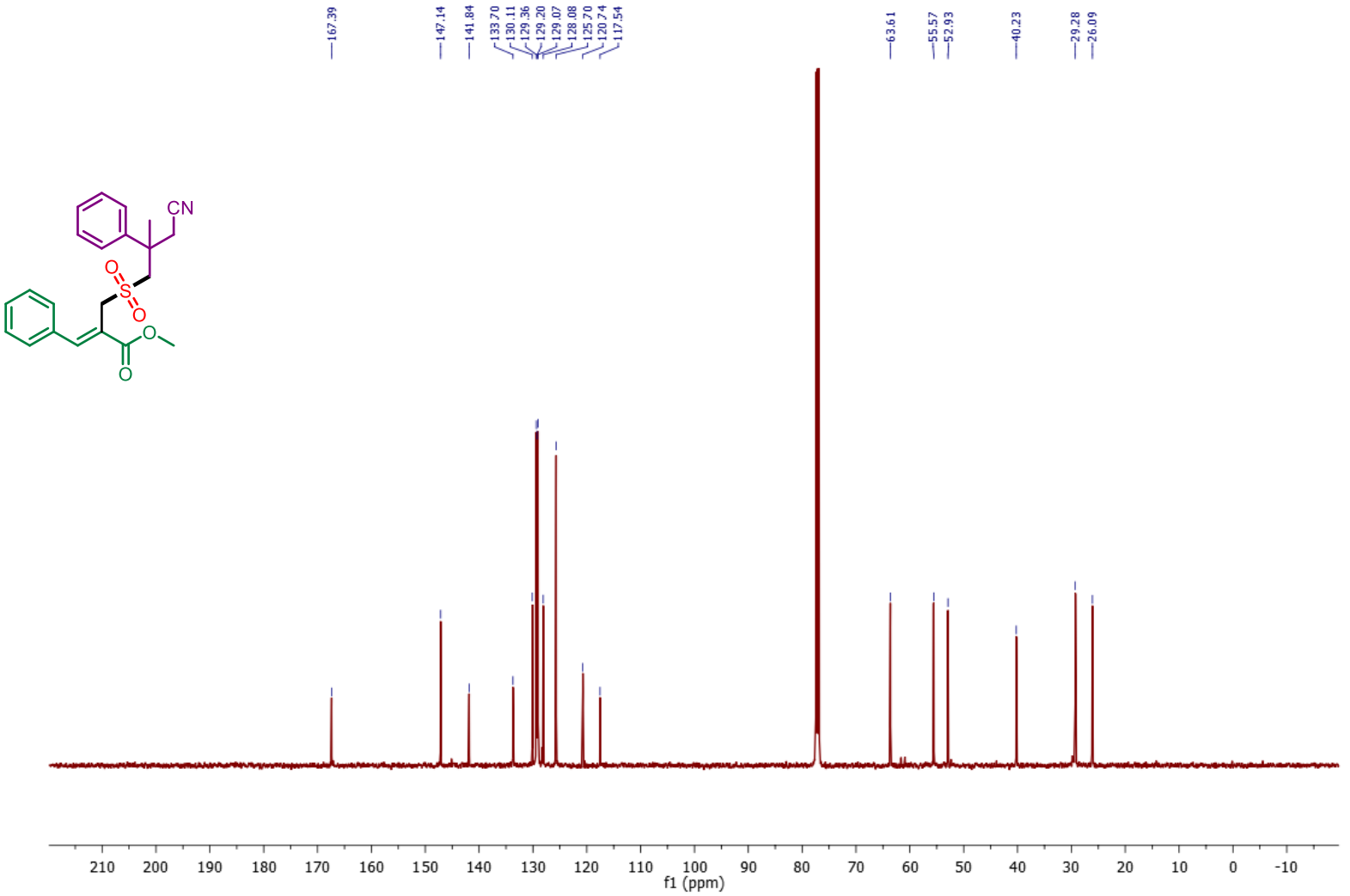
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3af)**



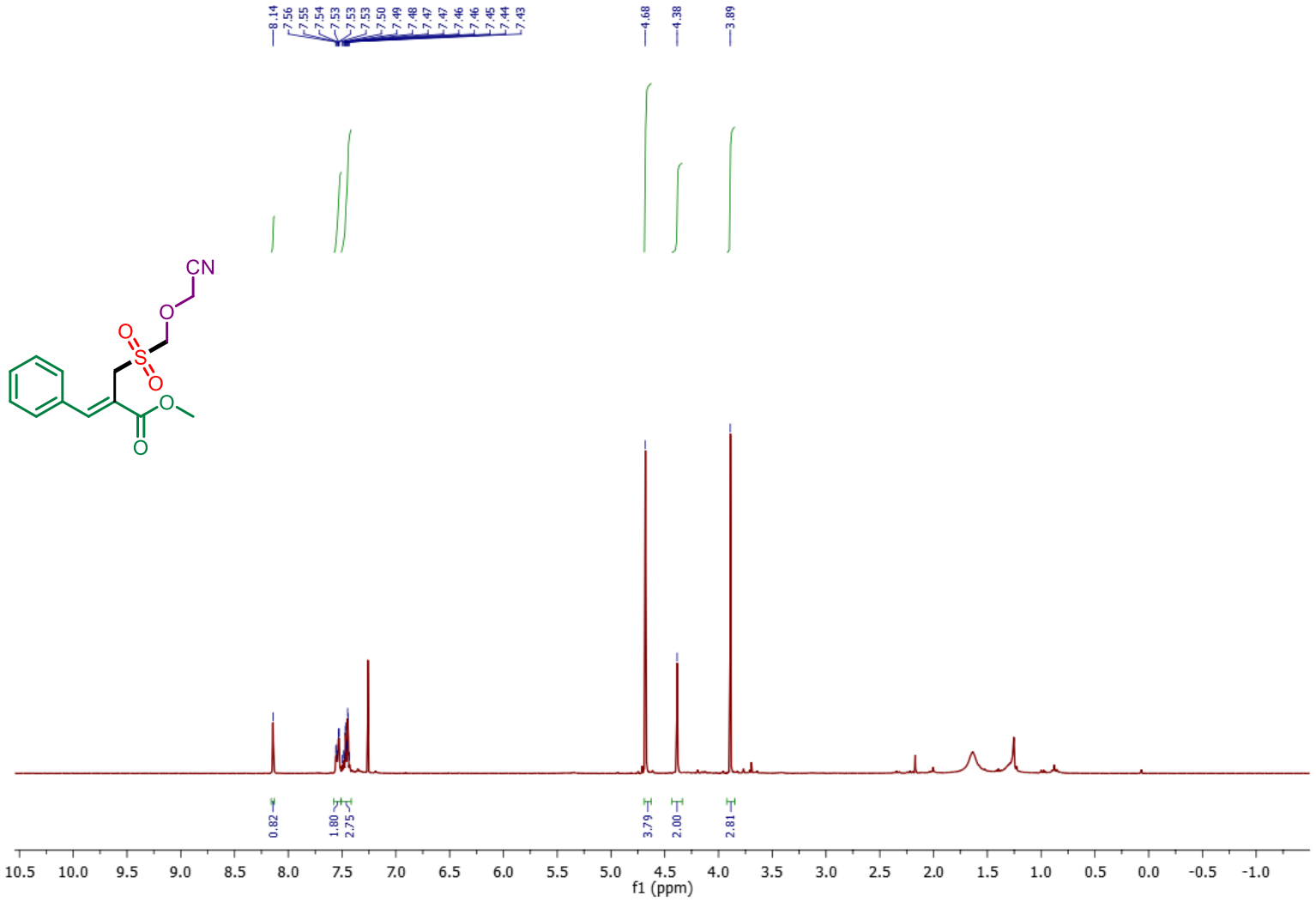
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum of Compound **(3ag)**



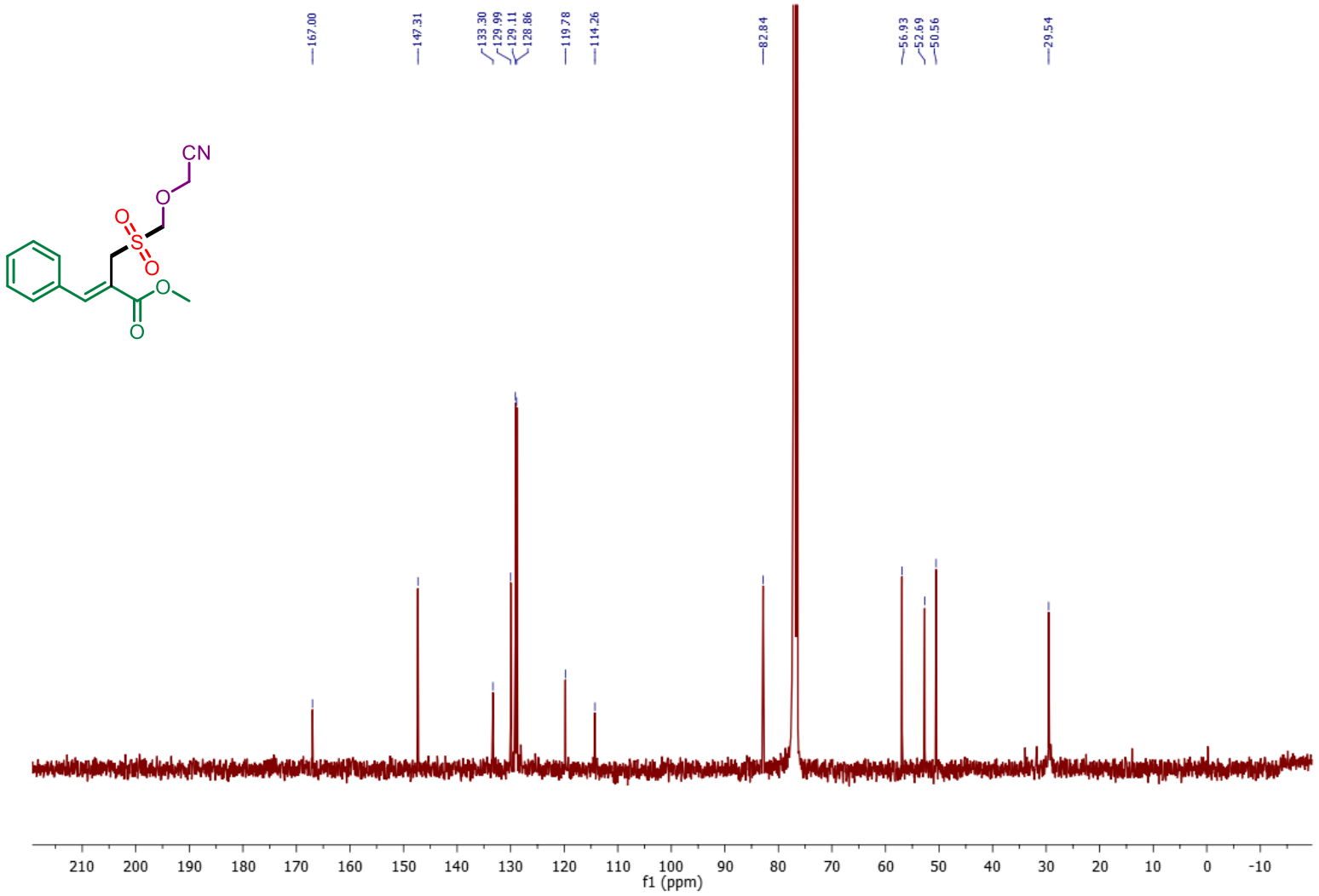
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(3ag)**



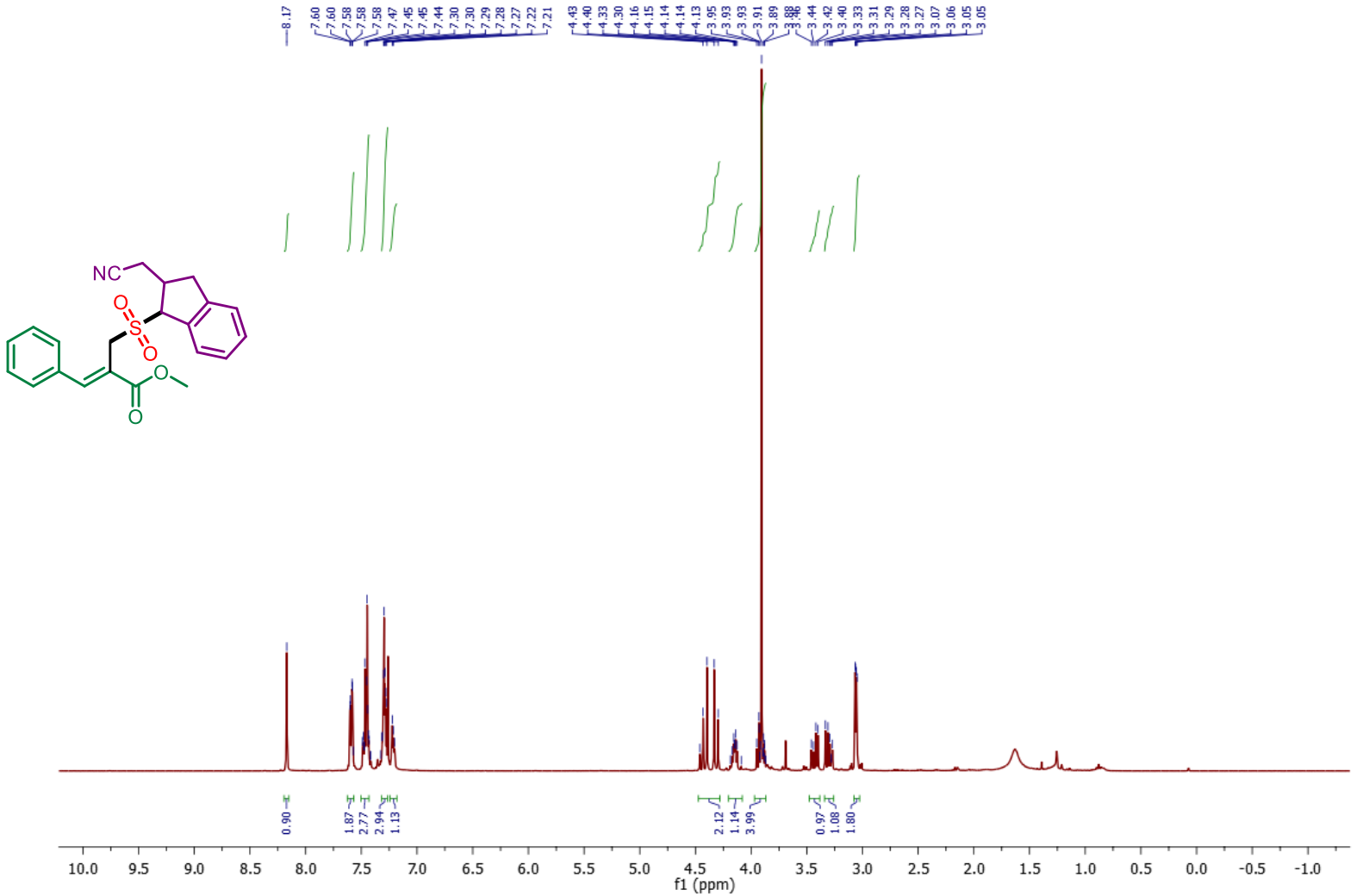
^{1}H NMR (500 MHz, $CDCl_3$) Spectrum of Compound **(3ah)**



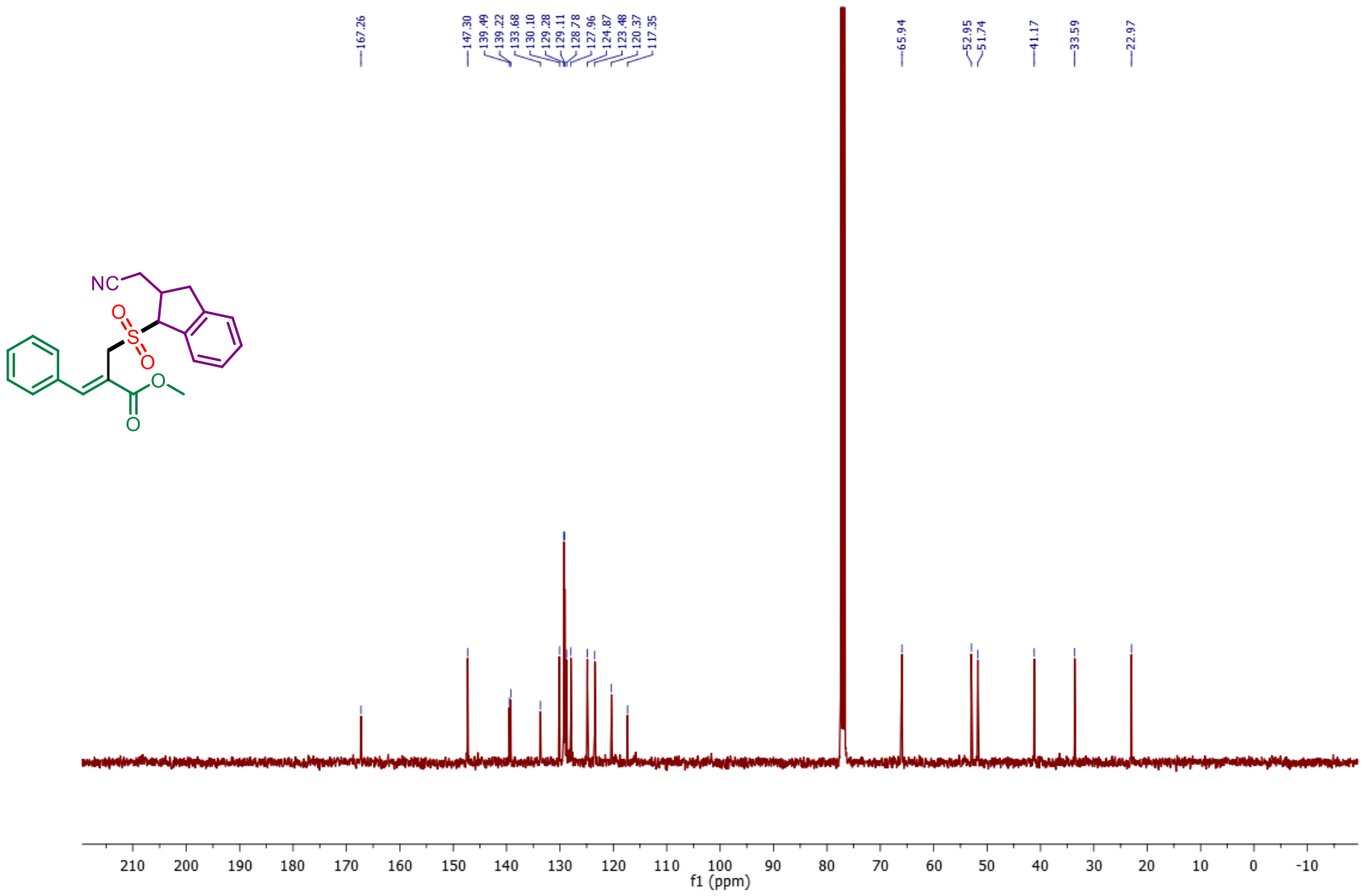
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ah)**



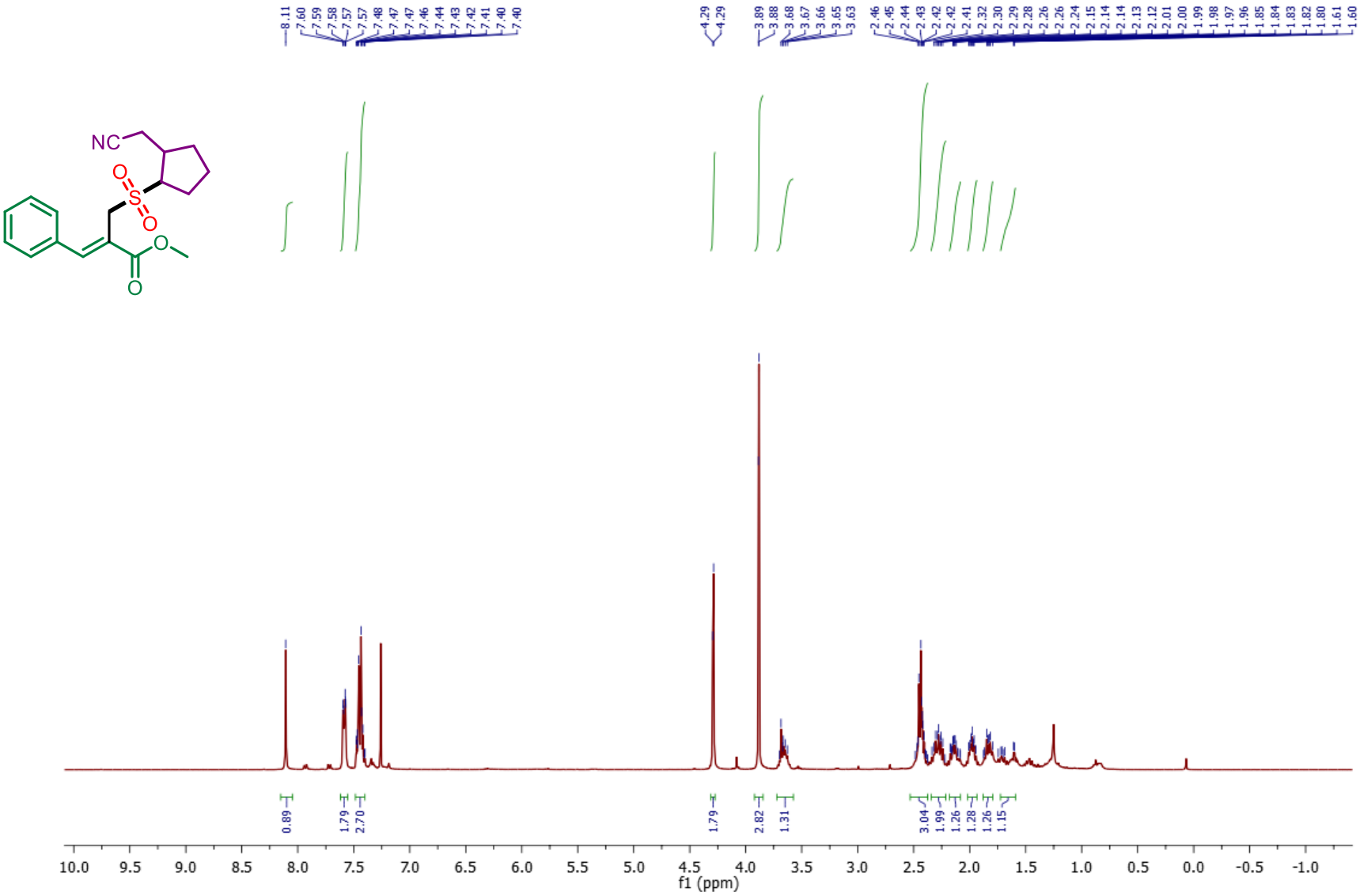
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3ai)**



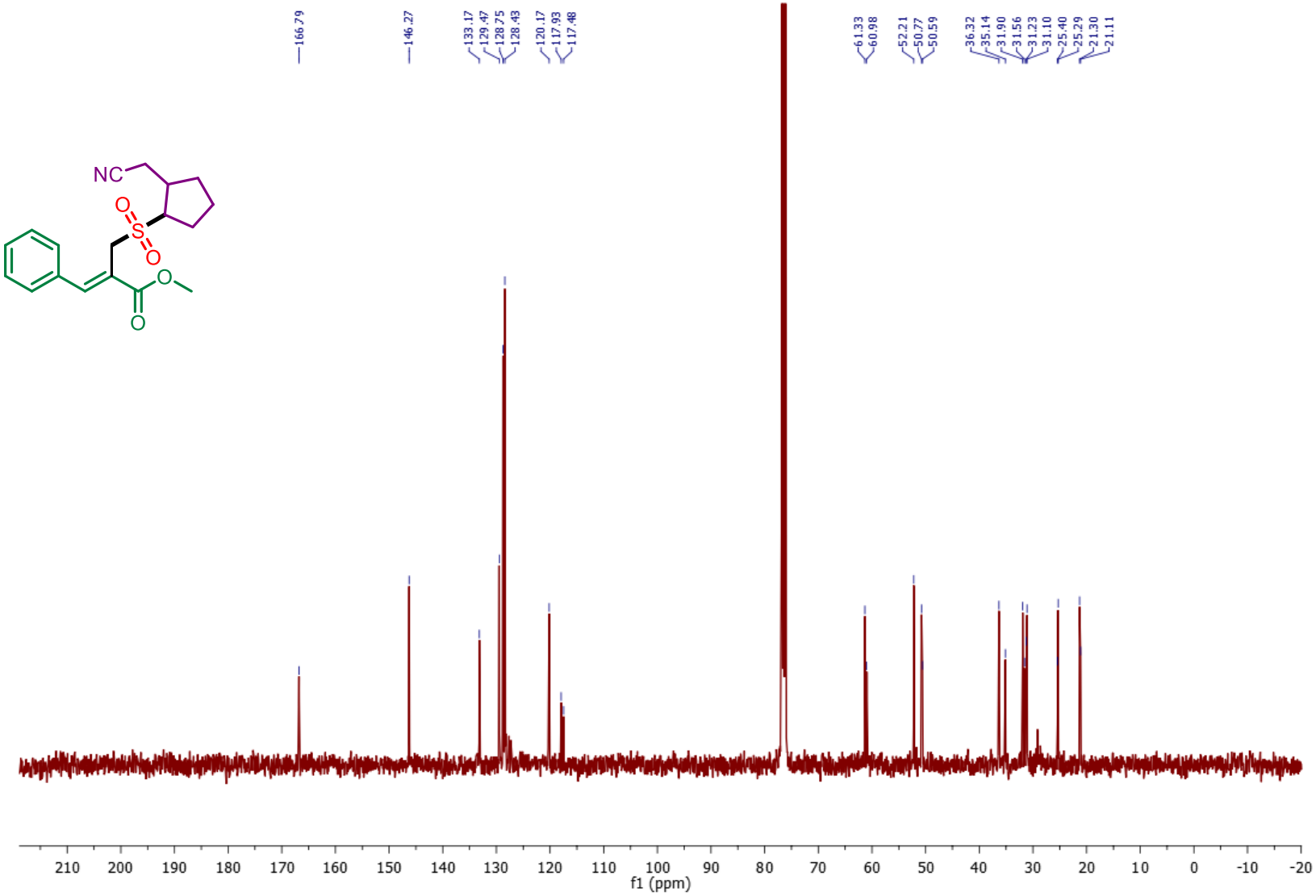
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3ai)**



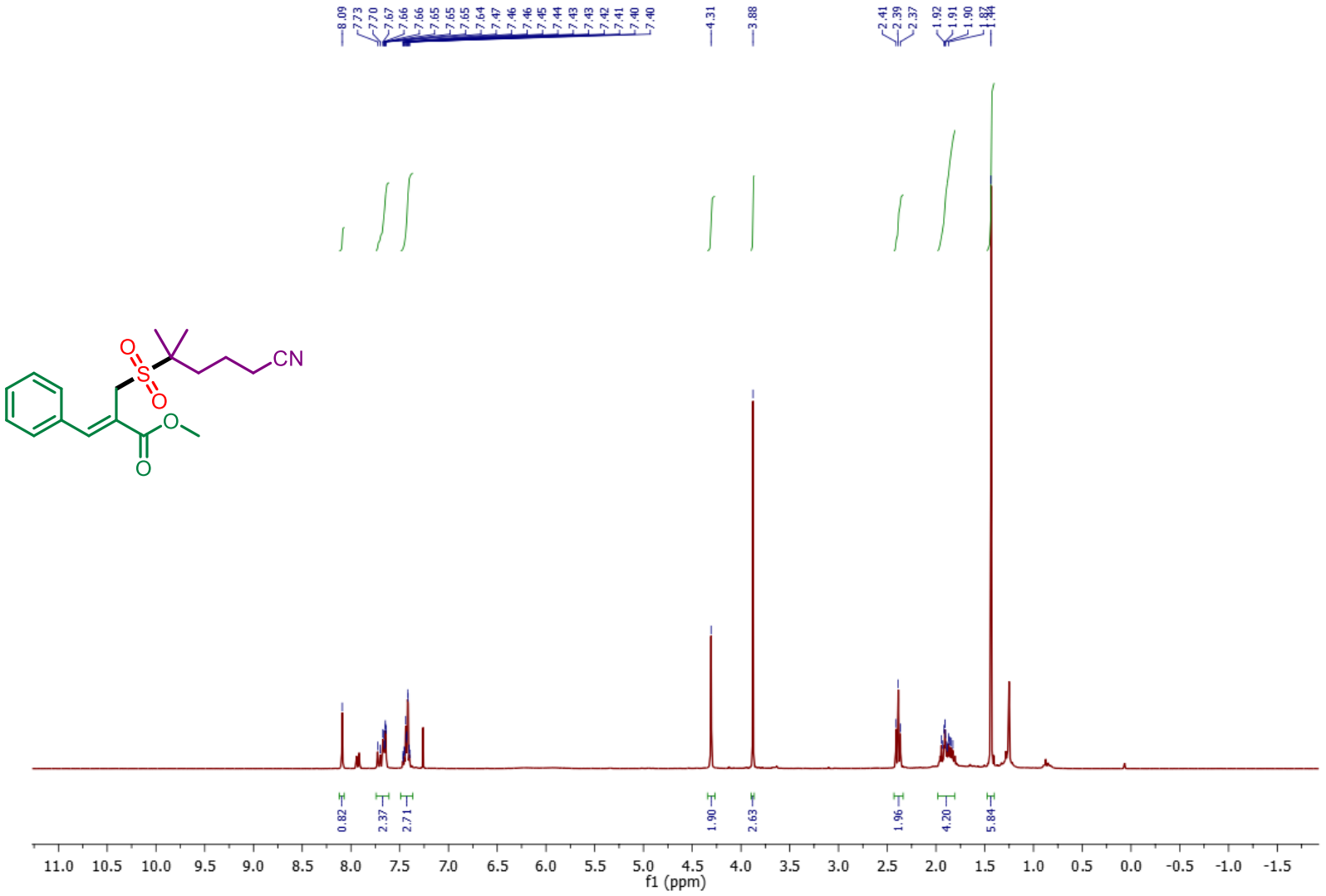
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(3aj)**



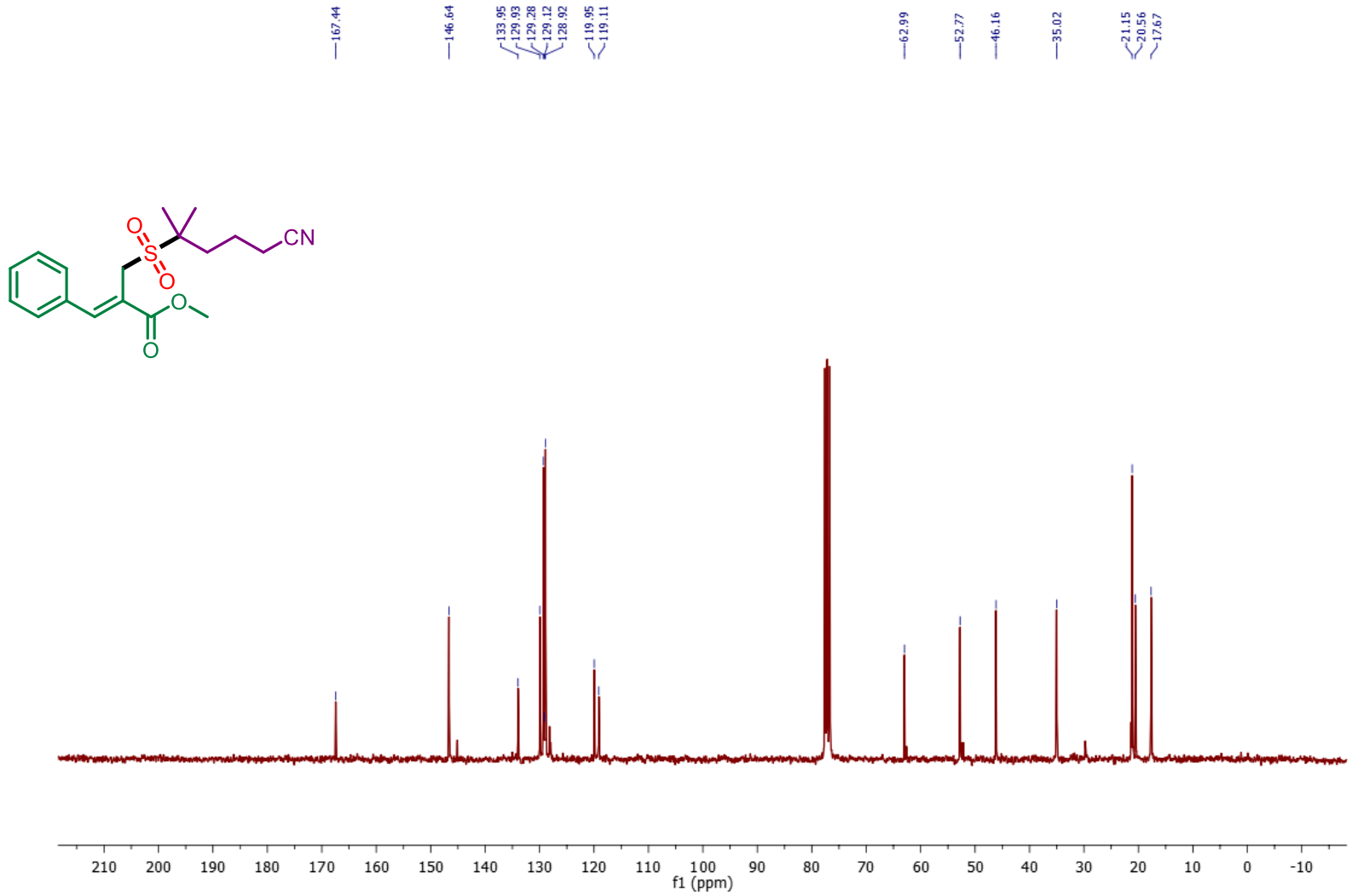
^{13}C NMR (101 MHz, $CDCl_3$) Spectrum of Compound **(3aj)**



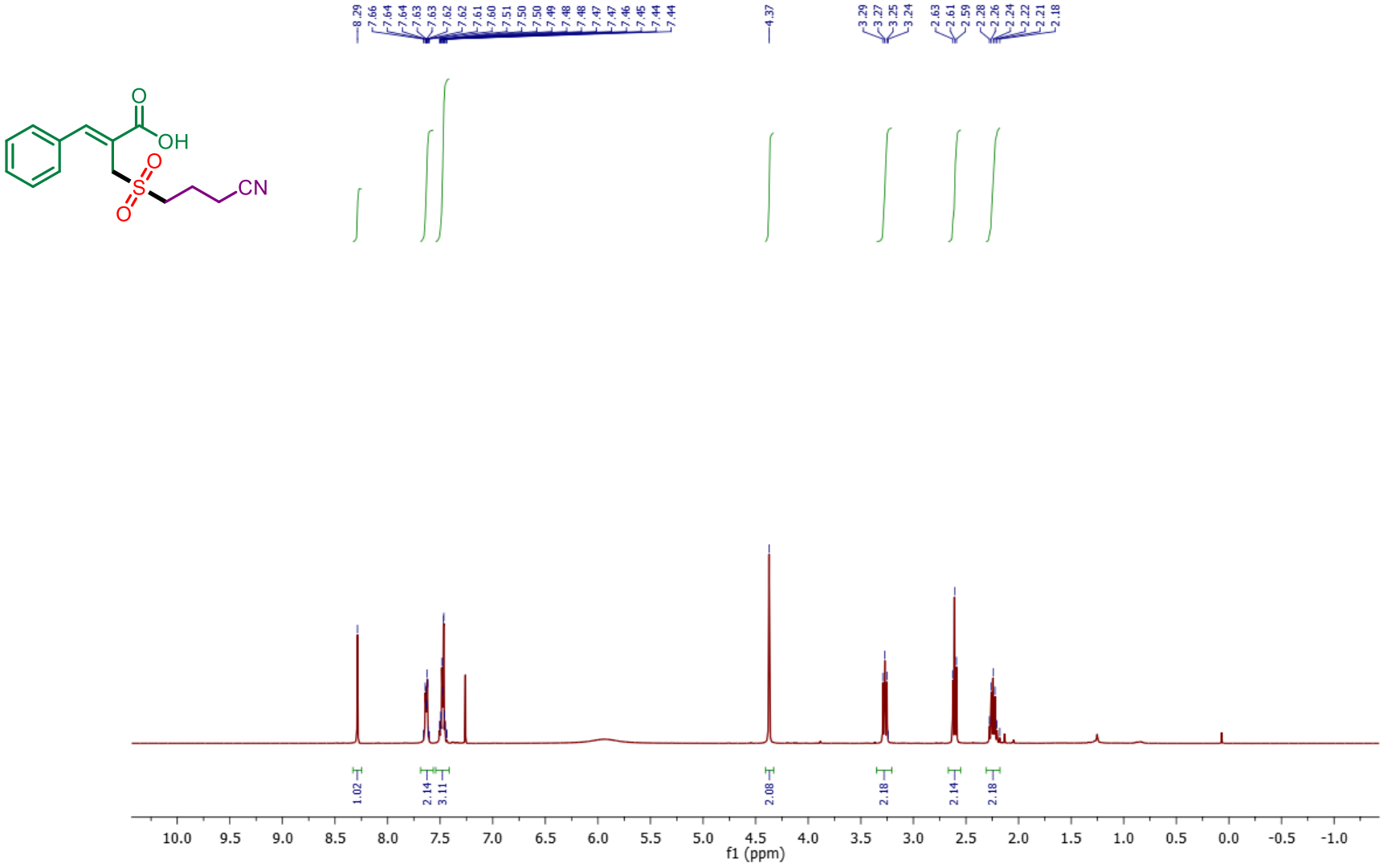
^{1}H NMR (300 MHz, $CDCl_3$) Spectrum of Compound **(3ak)**



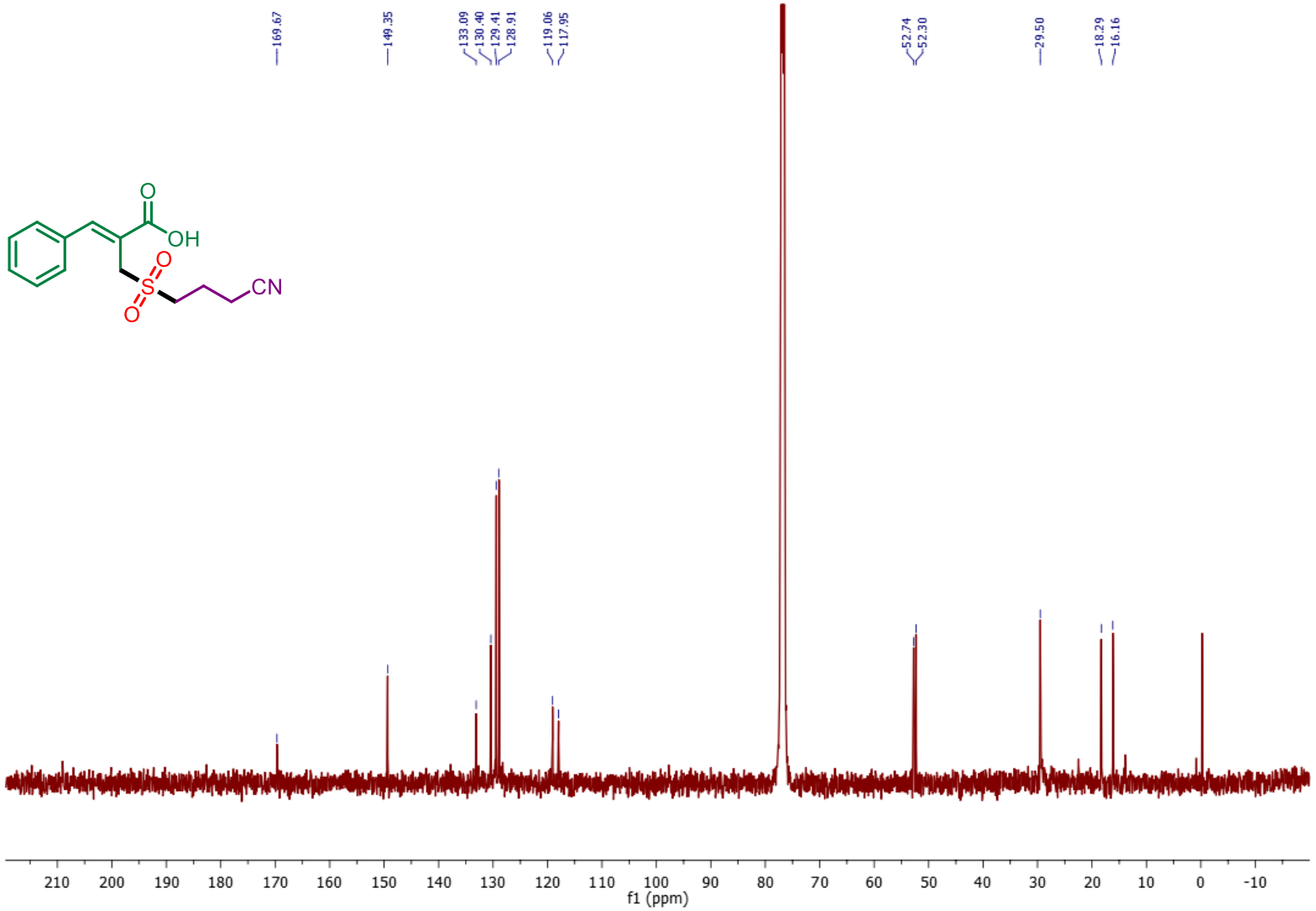
^{13}C NMR (75MHz, $CDCl_3$) Spectrum of Compound **(3ak)**



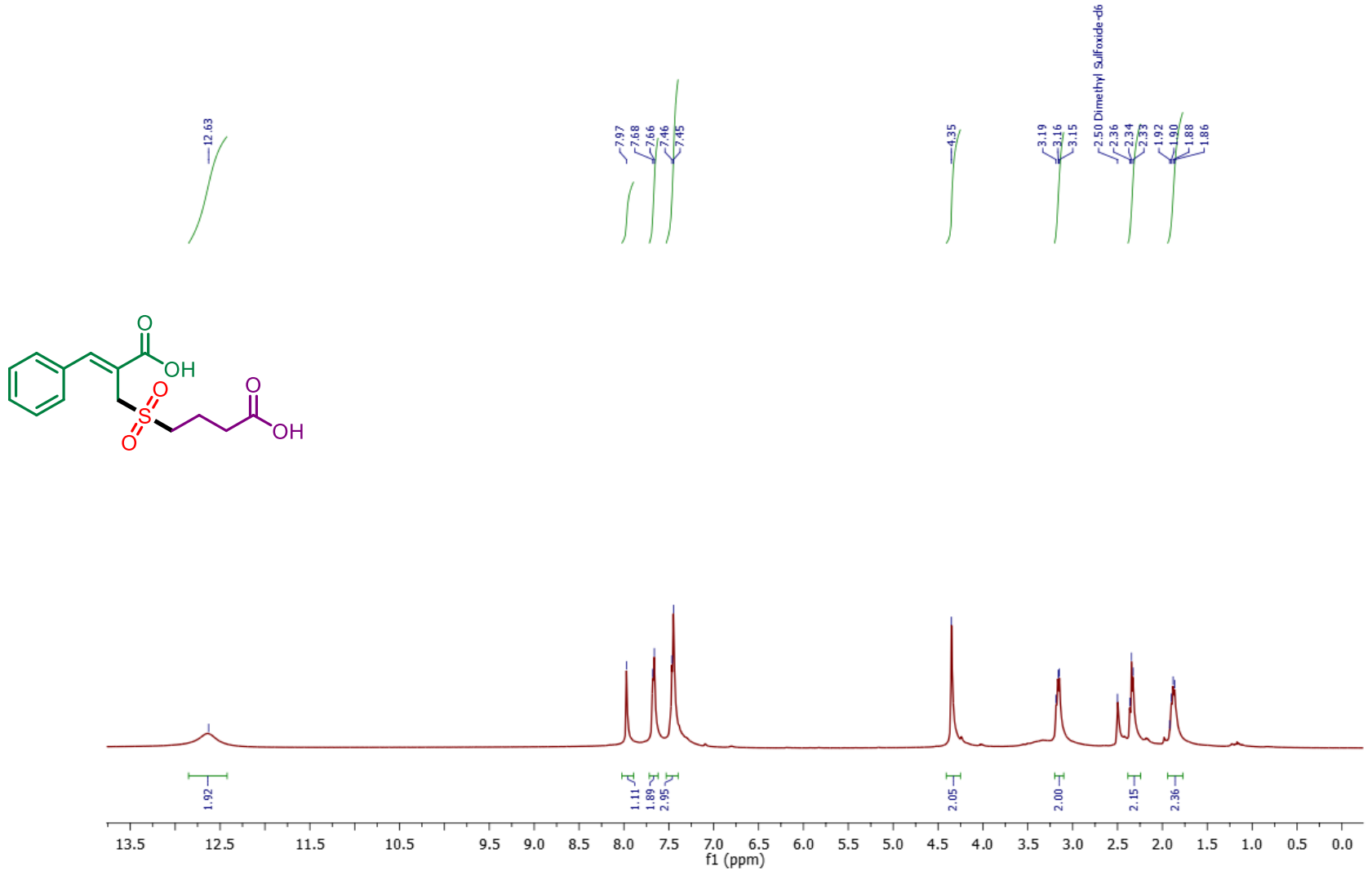
^{1}H NMR (400 MHz, $CDCl_3$) Spectrum of Compound **(4)**



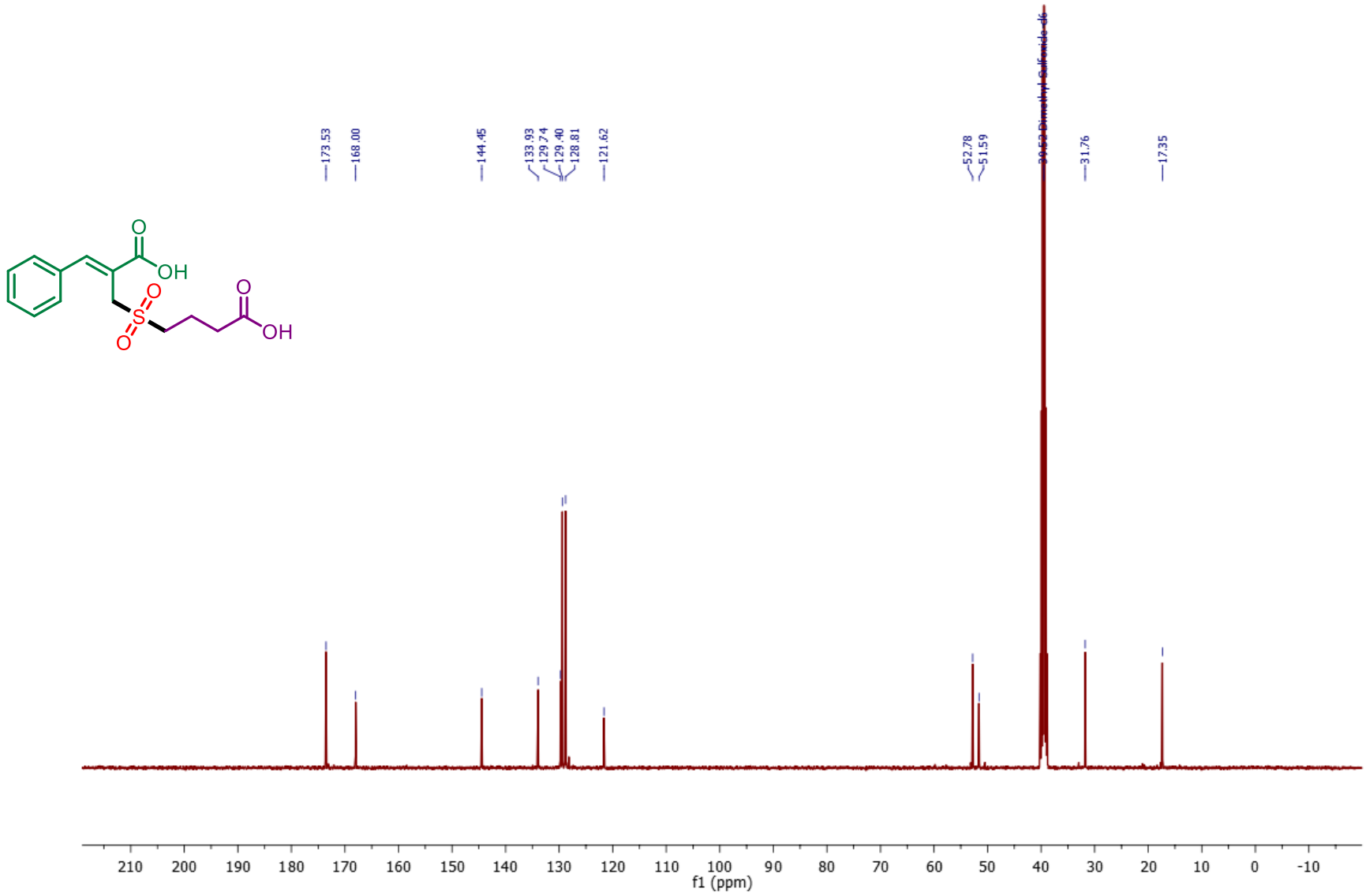
^{13}C NMR (126 MHz, $CDCl_3$) Spectrum of Compound **(4)**



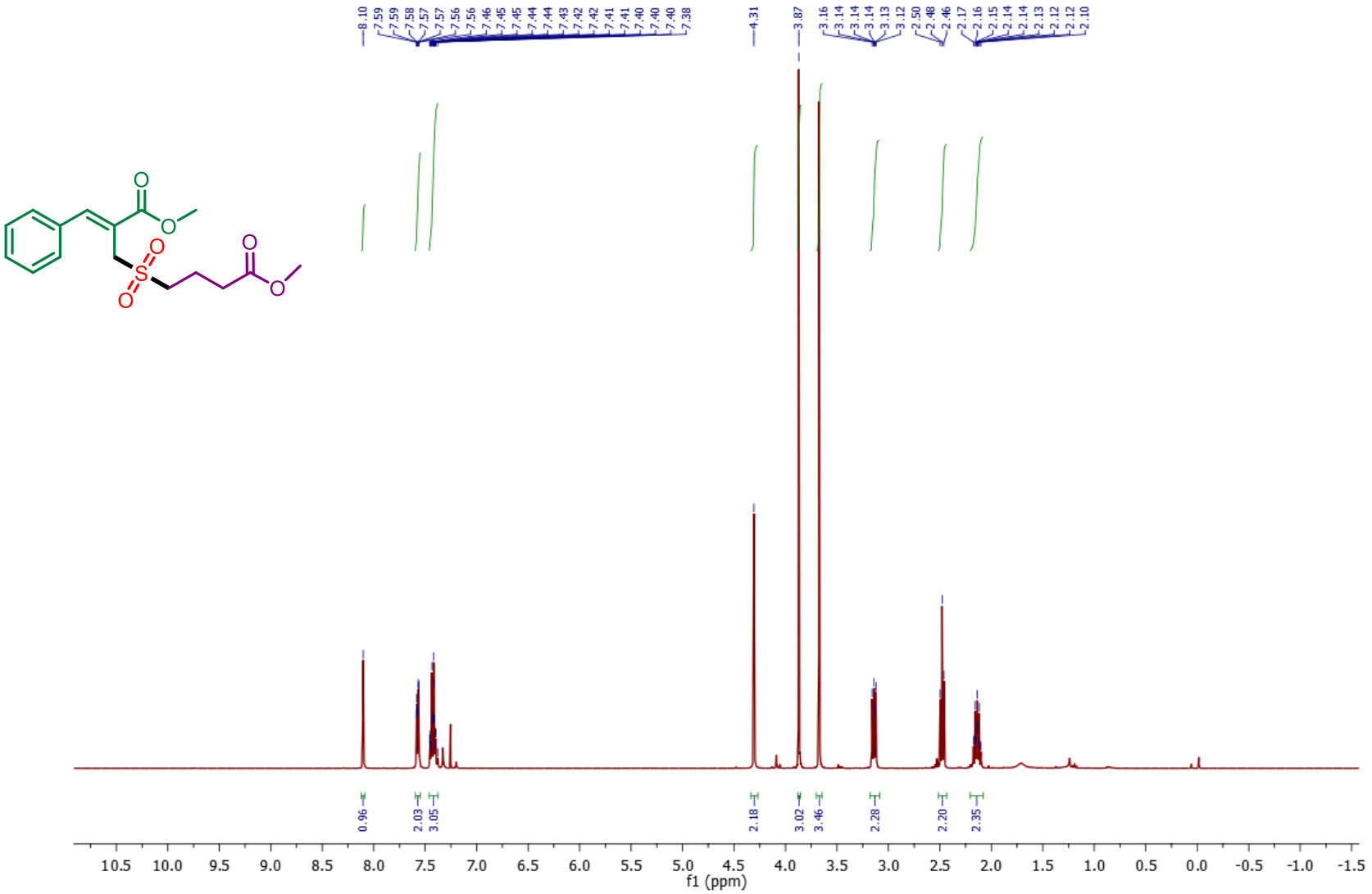
^{1}H NMR (400 MHz,DMSO) Spectrum of Compound **(5)**



^{13}C NMR (101 MHz, DMSO) Spectrum of Compound **(5)**



[1]H NMR (400 MHz, CDCl3) Spectrum of Compound **(6)**



^{13}C NMR (101 MHz, CDCl3) Spectrum of Compound **(6)**