**Supplementary data**

# Design, Synthesis, Antiviral Bioactivity, and Mechanism of Ferulic Acid Ester Containing Sulfonamide Moiety

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## 1. Materials and methods

The melting points of the products were determined on an XT-4 binocular microscope (Beijing Tech Instrument Co., China) and were not corrected. $^{1}H$ and $^{13}C$ nuclear magnetic resonance (NMR) (solvent DMSO-*d6* or $CDCl_3$) spectra were performed on a JEOL-ECX500 NMR spectrometer at room temperature using tetramethylsilane (TMS) as an internal standard. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. All first-order splitting patterns were assigned based on the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). High resolution mass spectrometer (HRMS) data was conducted using a Thermo Scientific Q Exactive (Thermo, USA). Analytical thin-layer chromatography (TLC) was performed on silica gel GF254 (400 mesh). Thin-layer chromatography purification was carried out using silica gel. All of the reagents and reactants were purchased from commercial suppliers and of analytical reagent grade or chemically pure. All solvents were dried, deoxygenated, and redistilled before use.

## 2. Purification of the viruses

Extraction of TMV. According to the reference method,[1,2] tobacco (*Nicotiana tabacum L.*) the tobacco that has been infected with TMV virus is selected, and the seriously infected leaves are cut and placed in a mortar, added with liquid nitrogen to grind, and then poured into a volume of phosphate (pH 7.20, 0.01 mol/L) buffer that adds twice the weight of the leaves. After sufficient grinding, filter with gauze and centrifuge the filtrate under specific conditions.

The specific steps of the purification steps are as follows:

i. The severely infected leaves are cut and placed in a mortar and treated with liquid nitrogen. Then double the volume of phosphate buffer solution (pH 7.20, 0.01 mol / L) of the blade weight, grind, then add 10% chloroform / n-butanol (1: 1) solution, grind it thoroughly and filter with four layers of gauze.

ii. Centrifuge for 20 minutes (Condition: 8000 g, 4 °C, 260 nm), and add PEG (6%) to the filtered supernatant.

iii. Stir the supernatant with a mixture of PEG (6%) and NaCl (0.1 mol) for 4 h, and

centrifuge for 20 min. The precipitate was completely suspended in PBS (0.02 mol/L). Then repeat the centrifugation twice.

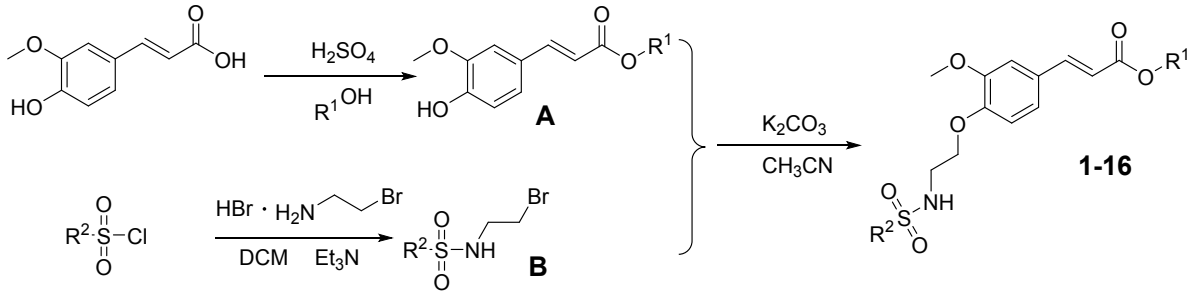
iv. Combine the above supernatant, centrifuge again (78000 g) for 2 hours, and suspend the pellet in PBS (0.02 mol/L). After centrifuging the suspension at low speed, the supernatant was added to the centrifuge tube together with 25% glycerol for 1.5 h (78000 g).

Finally, the purified virus was precipitated and suspended in glycerin.

$$\text{virus concn} = (A_{260} \times \text{dilution ratio}) / E_{1cm}\,0.1\%,260\ \text{nm}.$$

**3 Chemical preparations**

**3.1 General Procedure for the preparation of compounds (1-16)**.




**Scheme S1** Synthetic routes of target compounds **1** to **16**.

Concentrated sulfuric acid (1 mmol) and ferulic acid (1 mmol) was added to the alcohol solution(30 mL), and themixture was heated to reflux for 9 hours, and then cooled to room temperature, intermediate A was obtained.[2] Triethylamine(2 mmol), sulfonyl chloride(1 mmol) and bromoethylamine hydrobromide(1.2 mmol) was added to a dichloromethane solution(30 mL), and the reaction system was placed in an ice water bath for 4-6 hours to obtain Intermediate B.[3] The intermediate A(1 mmol), intermediate B(1.2 mmol) and potassium carbonate(2 mmol) were stirred in 15 mL of acetonitrile at reflux for 6-10 hours. The reaction system was quenched with saturated brine, and then extracted three times with 50 mL of an organic solvent. White or yellow solid with a yield of 21% to 46%. The data of 1 to 16 is as follows.

**3.2 Characterization of intermediates and target compounds**

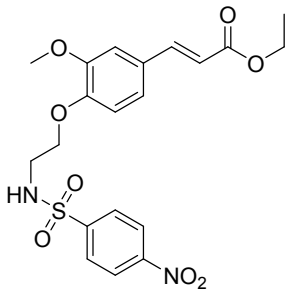


Figure S1

**(E)-3-(3-methoxy-4-(2-((4-nitrophenyl)sulfonamido)ethoxy)phenyl)acrylate ethyl (1) :** Yellow solid; m.p.: 137.4-138.4 °C; Yield: 37%; $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 8.53 – 8.19 (m, 3H), 8.10 – 7.96 (m, 2H), 7.56 (d, *J* = 15.9 Hz, 1H), 7.32 (d, *J* = 1.8 Hz, 1H), 7.17 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.55 (d, *J* = 16.0 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.00 (t, *J* = 5.4 Hz, 2H), 3.79 (s, 3H), 3.23 (t, *J* = 5.2 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 166.98 (s), 149.92 (s), 149.82 (s), 149.46 (s), 146.63 (s), 144.90 (s), 128.45 (s), 128.45 (s), 127.78 (s), 124.93 (s), 124.93 (s), 123.18 (s), 116.32 (s), 113.16 (s), 110.97 (s), 67.42 (s), 60.29 (s), 56.02 (s), 42.38 (s), 14.72 (s). HRMS (ESI) *m/z* for $C_{20}H_{22}N_2O_8KS$ $[M+K]^+$ cacld:489.07284, found. 489.07263.

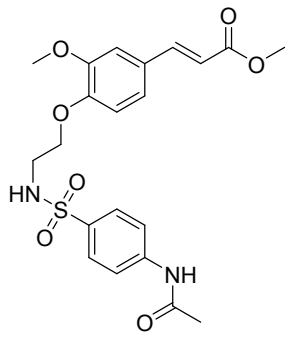


Figure S2

**(E)-3-(4-(2-((4-acetamidophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate methyl. (2)** : White solid; m.p.: 182-184 °C; Yield: 45 %; $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 10.28 (s, 1H), 7.78 (s, 1H), 7.71 (s, 4H), 7.65 (dd, J = 8.7, 6.4 Hz, 1H), 7.57 – 7.53 (m, 1H), 7.30 (dd, J = 12.7, 1.8 Hz, 1H), 7.17 (dd, J = 8.4, 1.8 Hz, 1H), 6.87 (t, J = 8.1 Hz, 1H), 6.53 (d, J = 16.0 Hz, 1H), 3.96 (t, J = 5.7 Hz, 2H), 3.77 (s, 3H), 3.68 (s, 3H), 3.06 (t, J = 5.4 Hz, 2H), 2.04 (s, 3H); 13C NMR (125 MHz, DMSO-*d6*) δ 169.44 (s), 167.44 (s), 150.19 (s), 149.58 (s), 145.12 (s), 143.25 (s), 128.15 (s), 128.15 (s), 127.74 (s), 123.23 (s), 119.03 (s), 119.03 (s), 115.97 (s), 113.33 (s), 111.27 (s), 67.57 (s), 56.10 (s), 51.79 (s), 42.24 (s), 24.60 (s). HRMS (ESI) *m/z* for $C_{21}H_{24}N_2O_7KS$ $[M+K]^+$ cacld:487.09358, found. 487.09216.

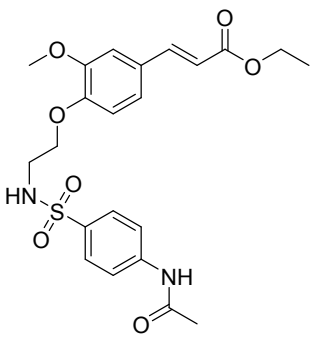


Figure S3

**(E)-3-(4-(2-((4-acetamidophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate ethyl. (3)** : white solid; m.p.:109.6-111.2 ˚C; yield: 38 %; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 16.0 Hz,

1H), 7.21 – 7.16 (m, 2H), 7.08 – 6.84 (m, 2H), 6.69 (d, *J* = 8.8 Hz, 1H), 6.25 (d, *J* = 15.9 Hz, 1H), 5.25 (t, *J* = 6.1 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.96 (t, *J* = 5.1 Hz, 2H), 3.81 (s, 3H), 3.30 (dd, *J* = 10.9, 5.5 Hz, 2H), 2.33 (s, 3H), 1.27 (s, 3H);$^{13}$C NMR (125 MHz, $CDCl_3$) δ 167.12 (s), 149.75 (s), 149.46 (s), 144.18 (s), 144.18 (s), 143.55 (s), 137.02 (s), 129.74 (s), 129.74 (s), 128.75 (s), 127.03 (s), 127.03 (s), 122.23 (s), 116.71 (s), 114.19 (s), 110.18 (s), 68.28 (s), 60.48 (s), 55.79 (s), 42.48 (s), 21.53 (s), 14.36 (s). HRMS (ESI) *m/z* for $C_{22}H_{26}N_2O_7KS$ $[M+K]^+$, cacld:501.10923, found. 501.10791.

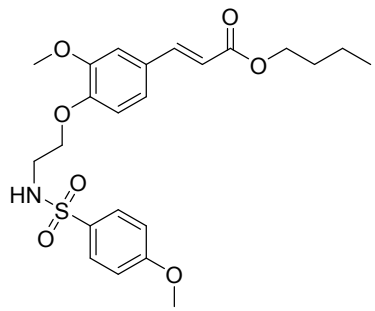


Figure S4

**(E)-3-(3-methoxy-4-(2-((4-methoxyphenyl)sulfonamido)ethoxy)phenyl)acrylate butyl. (4) :** White solid; m.p.: 97.6-99.6 °C; Yield: 39 %; $^1$H NMR (500 MHz, DMSO-*d6*) δ 7.85 – 7.72 (m, 3H), 7.58 (d, *J* = 15.9 Hz, 1H), 7.37 (d, *J* = 1.6 Hz, 1H), 7.24 – 7.16 (m, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 15.9 Hz, 1H), 4.13 (t, *J* = 6.6 Hz, 2H), 4.00 (t, *J* = 5.6 Hz, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 3.07 (d, *J* = 5.7 Hz, 2H), 1.70 – 1.53 (m, 2H), 1.38 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 167.08 (s), 162.60 (s), 150.15 (s), 149.56 (s), 144.98 (s), 132.33 (s), 129.16 (s), 129.16 (s), 127.76 (s), 123.33 (s), 116.27 (s), 115.16 (s), 114.78 (s), 114.78 (s), 113.22 (s), 111.07 (s), 67.57 (s), 63.98 (s), 56.07 (s), 42.23 (s), 30.80 (s), 27.48 (s), 19.17 (s), 14.08 (s). HRMS (ESI) *m/z* for $C_{23}H_{29}NO_7KS$ $[M+K]^+$, cacld:502.12939, found.502.12941.

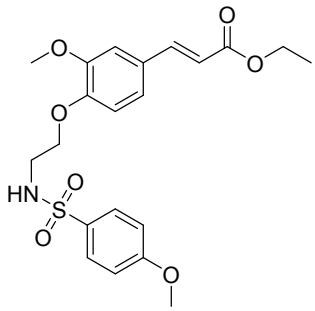


Figure S5

**(E)-3-(3-methoxy-4-(2-((4-methoxyphenyl)sulfonamido)ethoxy)phenyl)acrylate ethyl. (5)** :White solid; m.p.:120.7-121.6 °C; Yield: 42%; $^1$H NMR (500 MHz, DMSO-*d6*) δ 10.34 (s, 1H), 7.74 (s, 4H), 7.57 (d, *J* = 15.9 Hz, 1H), 7.35 (d, *J* = 1.8 Hz, 1H), 7.19 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.00 (t, *J* = 5.6 Hz, 2H), 3.81 (s, 3H), 3.09 (t, *J* = 5.7 Hz, 2H), 2.08 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); $^{13}$C NMR (125

MHz, DMSO-*d6*) δ 169.46 (s), 167.00 (s), 150.14 (s), 149.54 (s), 144.96 (s), 143.20 (s), 134.44 (s), 128.14 (s), 128.14 (s), 127.73 (s), 123.24 (s), 119.01 (s), 119.01 (s), 116.29 (s), 113.22 (s), 111.10 (s), 67.55 (s), 60.29 (s), 56.06 (s), 42.27 (s), 24.60 (s), 14.71 (s). HRMS (ESI) *m/z* for $C_{21}H_{26}NO_7S$ $[M+H]^+$, cacld:436.14172, found. 436.14245.

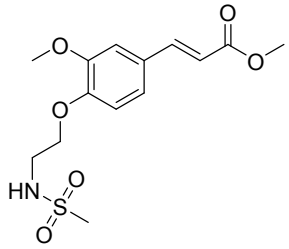


Figure S6

**(E)-3-(3-methoxy-4-(2-(methylsulfonamido)ethoxy)phenyl)acrylate methyl. (6) :** White solid; m.p.: 84-85.6 °C; Yield:42%; $^1$H NMR (500 MHz, DMSO-*d6*) δ 7.60 (d, *J* = 16.0 Hz, 1H), 7.38 (d, *J* = 1.6 Hz, 1H), 7.24 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 4.45 – 4.28 (m, 2H), 3.82 (d, *J* = 3.3 Hz, 3H), 3.81 (dd, *J* = 6.3, 4.4 Hz, 2H), 3.71 (s, 3H), 3.53 (s, 3H); $^{13}$C NMR (125 MHz,DMSO-*d6*) δ 167.49 (s), 150.00 (s), 149.65 (s), 145.14 (s), 128.05 (s), 123.32 (s), 116.17 (s), 113.65 (s), 111.47 (s), 69.01 (s), 56.25 (s), 51.87 (s), 40.34 (s), 31.71 (s). HRMS (ESI) *m/z* for $C_{14}H_{19}NO_6KS$ $[M+K]^+$, cacld:368.05585, found. 368.05647.

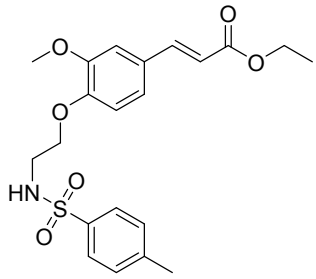


Figure S7

**(E)-3-(3-methoxy-4-(2-((4-methylphenyl)sulfonamido)ethoxy)phenyl)acrylate1 ethyl.(7) :** White solid; m.p.: 91-93 °C; Yield: 48%; $^1$H NMR (400 MHz, DMSO-*d6*) *δ* 7.88 (s, 1H), 7.69 (t, *J* = 10.6 Hz, 2H), 7.64 (dd, *J* = 8.1, 5.5 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.36 (d, *J* = 5.2 Hz, 2H), 7.20 (dd, *J* = 8.3, 1.6 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.61 – 6.55 (m, 1H), 4.17 (dt, *J* = 7.1, 2.7 Hz, 2H), 4.05 – 3.93 (m, 2H), 3.85 – 3.74 (m, 3H), 3.11 (dd, *J* = 17.3, 12.2 Hz, 2H), 2.37 (s, 3H), 1.25 (dd, *J* = 7.1, 2.2 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO-*d6*) *δ* 166.99 (s), 150.15 (s), 149.57 (s), 144.95 (s), 143.15 (s), 137.86 (s), 130.09 (s), 127.78 (s), 127.36 (s), 127.02 (s), 123.25 (s), 116.33 (s), 113.27 (s), 111.13 (s), 67.59 (s), 60.28 (s), 56.08 (s), 42.25 (s), 21.43 (s), 14.71 (s). HRMS (ESI) *m/z* for $C_{21}H_{26}NO_6S$ $[M+H]^+$; cacld:420.14676, found. 420.14753.

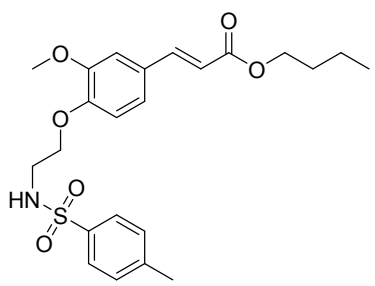


Figure S8

**(E)-3-(3-methoxy-4-(2-((4-methylphenyl)sulfonamido)ethoxy)phenyl)acrylate butyl**. (8): White solid;

m.p.104.4-106.6 °C; Yield: 39%; $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 7.83 (s), 7.66 (d, *J* = 8.5 Hz), 7.53 (d, *J* = 15.9 Hz), 7.33 (dd, *J* = 10.0, 7.5 Hz), 7.16 (d, *J* = 8.7 Hz), 6.86 (d, *J* = 8.5 Hz), 6.53 (d, *J* = 16.0 Hz), 4.09 (dd, *J* = 8.7, 4.9 Hz), 3.96 (dd, *J* = 12.6, 6.6 Hz), 3.76 (s), 3.11 – 2.96 (m), 2.33 (s), 1.65 – 1.53 (m), 1.34 (dt, *J* = 15.2, 7.5 Hz), 0.87 (dd, *J* = 8.6, 6.4 Hz); $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 167.14 (s), 150.20 (s), 149.60 (d, *J* = 3.6 Hz), 145.04 (s), 143.22 (s), 137.90 (s), 130.15 (s), 130.15 (s), 127.82 (s), 127.08 (s), 127.08 (s), 123.38 (s), 116.36 (s), 116.32 (s), 113.29 (s), 111.13 (s), 67.63 (s), 64.04 (s), 56.14 (s), 30.85 (s), 21.50 (s), 19.22 (s), 14.14 (s). HRMS (ESI) *m/z* for $C_{23}H_{30}NO_6S$ $[M+K]^+$, cacld:448.17838, found. 448.17883.

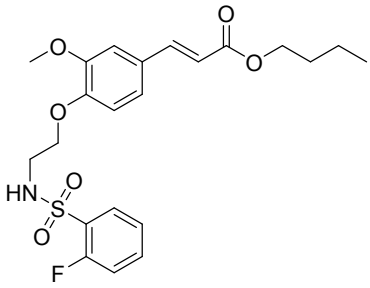


Figure S9

**(E)-3-(4-(2-((2-fluorophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate butyl.(9) :** White solid; m.p.: 71.5-73.4 °C; Yield: 35%; $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 8.29 (s, 1H), 7.88 (td, *J* = 7.6, 1.7 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.63 (d, *J* = 15.9 Hz, 1H), 7.52 – 7.37 (m, 3H), 7.25 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.63 (d, *J* = 16.0 Hz, 1H), 4.19 (t, *J* = 6.6 Hz, 2H), 4.08 (t, *J* = 5.7 Hz, 2H), 3.85 (s, 3H), 3.32 (t, *J* = 5.2 Hz, 2H), 1.73 – 1.59 (m, 2H), 1.43 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 167.07 (s), 159.93 (s), 157.42 (s), 150.11 (s), 149.60 (s), 144.97 (s), 135.62 (d, *J* = 8.4 Hz), 129.99 (s), 128.84 (d, *J* = 14.2 Hz), 127.82 (s), 125.28 (d, *J* = 3.7 Hz), 123.28 (s), 117.81 (s), 117.60 (s), 116.31 (s), 113.31 (s), 111.14 (s), 67.48 (s), 63.98 (s), 56.10 (s), 42.22 (s), 30.80 (s), 19.16 (s), 14.07 (s). HRMS (ESI) *m/z* for $C_{22}H27FNO6S$ $[M+H]^+$, cacld:452.15295, found. 452.15376.

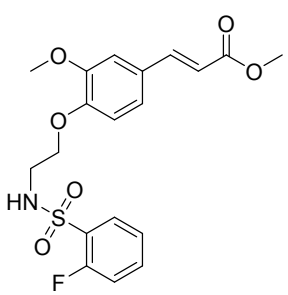


Figure S10

**(E)-3-(4-(2-((2-fluorophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate methyl.(10):** white solid; m.p.: 145-148 °C; Yield: 31% $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 8.37 (s, 1H), 7.91 – 7.85 (m, 1H), 7.70 – 7.56 (m, 3H), 7.32 (d, *J* = 1.7 Hz, 1H), 7.18 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.88 (d, *J*

= 8.4 Hz, 1H), 6.57 (d, *J* = 16.0 Hz, 1H), 4.00 (t, *J* = 5.7 Hz, 2H), 3.78 (s, 3H), 3.71 (s, 3H), 3.32 (d, *J* = 4.6 Hz, 2H); $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 167.44 (s), 150.02 (s), 149.55 (s), 145.14 (s), 140.11 (s), 133.88 (s), 132.44 (s), 129.92 (s), 129.89 (s), 127.75 (s), 123.12 (s), 115.95 (s), 113.21 (s), 111.12 (s), 67.40 (s), 56.03 (s), 51.79 (s), 42.40 (s).

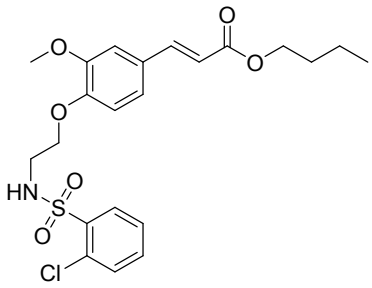


Figure S11

**(E)-3-(4-(2-((2-chlorophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate butyl.(11) :** White solid; m.p.: 78-80 °C; Yield: 39%; $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 8.01 – 7.85 (m, 3H), 7.65 (d, *J* = 4.0 Hz, 3H), 7.53 – 7.47 (m, 2H), 7.36 (d, *J* = 1.5 Hz, 1H), 7.24 – 7.15 (m, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.59 (d, *J* = 16.0 Hz, 1H), 4.14 (t, *J* = 6.6 Hz, 2H), 4.07 (t, *J* = 5.4 Hz, 2H), 3.75 (s, 3H), 3.67 (t, *J* = 5.3 Hz, 2H), 1.72 – 1.54 (m, 2H), 1.44 – 1.32 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 149.92 (s), 149.58 (s), 144.96 (s), 137.99 (s), 137.11 (s), 134.89 (s), 134.53 (s), 132.66 (s), 132.24 (s), 131.14 (s), 128.04 (s), 123.25 (s), 116.38 (s), 113.24 (s), 111.09 (s), 67.49 (s), 63.99 (s), 56.12 (s), 41.51 (s), 30.80 (s), 19.17 (s), 14.08 (s). HRMS (ESI) *m/z* for C22H27ClNO6S $[M+H]^+$, cacld:468.12268, found. 422.12421.

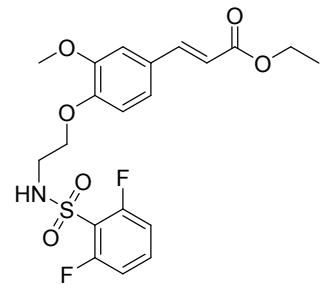


Figure S12

**(E)-3-(4-(2-((2,6-difluorophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate ethyl.(12):** White solid; m.p.: 79-81°C;Yield: 40%; $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 7.97 – 7.73 (m, 3H), 7.69 (t, *J* = 8.3 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.37 (s, 1H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.16 – 7.05 (m, 3H), 6.92 (d, *J* = 8.3 Hz, 1H), 6.58 (dd, *J* = 15.9, 6.7 Hz, 1H), 4.18 (q, *J* = 7.0 Hz, 2H), 4.00 (t, *J* = 5.6 Hz, 2H), 3.82 (d, *J* = 6.7 Hz, 5H), 1.26 (t, *J* = 7.1 Hz, 3H); $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 166.99 (s), 162.60 (s), 150.15 (s), 149.56 (s), 144.95 (s), 132.33 (s), 129.16 (s), 29.16 (s), 123.26 (s), 116.31 (s), 114.78 (s), 114.78 (s), 113.24 (s), 111.10 (s), 67.57 (s), 60.28 (s), 56.07 (s), 42.23 (s), 14.71 (s). HRMS (ESI) *m/z* for $C_{20}H_{22}F_2NO_6S$ $[M+H]^+$, cacld:442.11209, found. 442.11304.

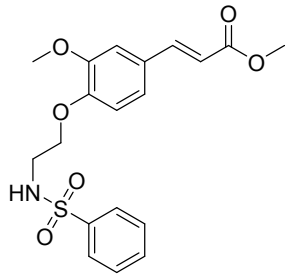


Figure S13

**(E)-3-(3-methoxy-4-(2-(phenylsulfonamido)ethoxy)phenyl)acrylate methyl.(13):** white solid; m.p.:99-101 °C; Yield: 26%; $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.79 (dd, J = 16.7, 15.2 Hz, 2H), 7.57 – 7.39 (m, 4H), 7.07 – 6.86 (m, 2H), 6.75 – 6.66 (m, 1H), 6.30 – 6.15 (m, 1H), 5.21 (dd, J = 22.4, 8.4 Hz, 1H), 4.10 – 3.93 (m, 2H), 3.89 – 3.78 (m, 3H), 3.74 (d, J = 5.7 Hz, 3H), 3.29 (d, J = 24.6 Hz, 2H). $^{13}$C NMR (125 MHz, $CDCl_3$) *δ* 149.77 (s), 144.45 (s), 132.76 (s), 129.18 (s), 126.99 (s), 122.28 (s), 116.28 (s), 114.29 (s), 110.23 (s), 77.35 (s), 77.04 (s), 76.72 (s), 68.37 (s), 55.81 (s), 51.73 (s), 42.52 (s). HRMS (ESI) *m/z* for $C_{19}H_{20}NO_6S$ $[M-H]^+$cacld. 390.10058, found. 390.10223. HRMS (ESI) *m/z* for $C_{19}H_{22}NO_6S$ $[M+H]^+$, cacld:392.11533, found. 392.11623.

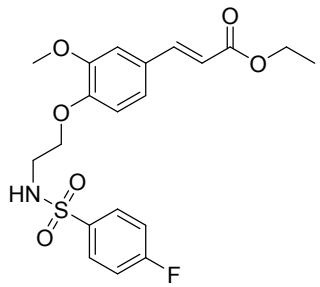


Figure S14

**(E)-3-(4-(2-((4-fluorophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate ethyl. (14):** White solid; m.p.: 118-120 °C; Yield:31%; 1H NMR (500 MHz, DMSO-*d6*) δ 7.75 – 7.70 (m, 2H), 7.69 – 7.60 (m, 1H), 7.56 – 7.52 (m, 1H), 7.33 (s, 1H), 7.17 (d, J = 10.1 Hz, 1H), 7.06 (d, J = 8.9 Hz, 2H), 6.88 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 15.9 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.96 (t, J = 5.7 Hz, 2H), 3.79 (s, 3H), 3.10 – 2.97 (m, 2H), 1.22 (t, J = 7.1 Hz, 3H). 13C NMR (125 MHz, DMSO-*d6*) δ 167.06 (s), 162.67 (s), 150.22 (s), 149.64 (s), 145.02 (s), 132.40 (s), 129.23 (s), 127.84 (s), 123.32 (s), 116.39 (s), 115.07 (d, J = 10.3 Hz), 114.85 (s), 113.33 (s), 111.19 (s), 67.64 (s), 60.35 (s), 56.14 (s), 42.30 (s), 14.77 (s). HRMS (ESI) *m/z* for $C_{20}H_{23}FNO_6S$ $[M+H]^+$, cacld:424.12173, found. 424.12246.

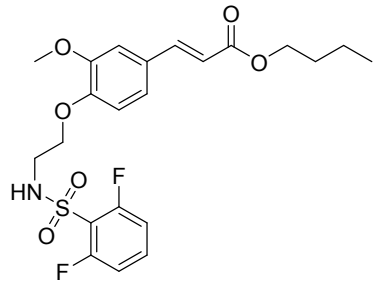


Figure S15

**(E)-3-(4-(2-((2,6-difluorophenyl)sulfonamido)ethoxy)-3-methoxyphenyl)acrylate butyl.(15):** White solid; m.p.:90-92 °C; Yield:21%; 1H NMR (500 MHz, DMSO-*d6*) δ 7.61 (ddd, J = 8.5, 6.1, 2.4 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.30 (d, J = 1.9 Hz, 1H), 7.22 (s, 1H), 7.19 (d, J = 8.9 Hz, 2H), 7.15 (s, 1H), 6.88 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 15.9 Hz, 1H), 4.09 (d, J = 6.6 Hz, 2H), 4.01 (t, J = 5.6 Hz, 2H),

3.74 (s, 3H), 3.66 (d, J = 16.2 Hz, 2H), 1.60 – 1.56 (m, 2H), 1.34 (d, J = 7.5 Hz, 2H), 0.88 (t, J = 7.4 Hz, 3H). 13C NMR (125 MHz, DMSO-*d6*) δ 167.13 (s), 160.07 (s), 158.18 – 157.91 (m), 150.15 (s), 149.94 (s), 149.67 (t, J = 2.1 Hz), 145.02 (s), 135.43 (s), 127.97 (d, J = 18.9 Hz), 123.26 (d, J = 4.0 Hz), 116.41 (d, J = 9.9 Hz), 113.93 (s), 113.73 (d, J = 3.3 Hz), 113.39 (s), 111.17 (s), 67.59 (s), 64.05 (s), 56.10 (d, J = 3.0 Hz), 42.36 (s), 30.86 (s), 19.22 (s), 14.12 (s).

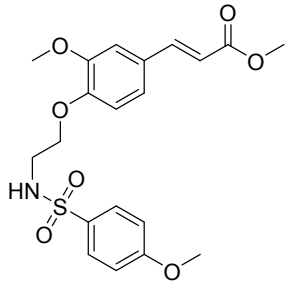


Figure S16

**(E)-3-(3-methoxy-4-(2-((4-methoxyphenyl)sulfonamido)ethoxy)phenyl)acrylate methyl.(16):** White solid; m.p.: 111-113°C; Yield: 37%; $^{1}$H NMR (500 MHz, DMSO-*d6*) δ 7.75 (t, J = 5.8 Hz), 7.71 (s), 7.55 (d, J = 15.9 Hz), 7.32 (d, J = 2.0 Hz), 7.17 (d, *J* = 8.4 Hz), 7.05 (d, *J* = 8.9 Hz), 6.87 (d, *J* = 8.4 Hz), 6.53 (d, *J* = 16.0 Hz), 3.95 (t, *J* = 5.7 Hz), 3.78 (s), 3.76 (s), 3.67 (s), 3.04 – 3.01 (m). $^{13}$C NMR (125 MHz, DMSO-*d6*) δ 167.51 (s), 162.66 (s), 150.25 (s), 149.61 (s), 145.18 (s), 132.38 (s), 129.22 (s), 127.78 (s), 123.32 (s), 116.02 (s), 114.84 (s), 113.32 (s), 111.25 (s), 100.00 (s), 67.63 (s), 56.14 (s), 51.87 (s), 42.30 (s). HRMS (ESI) *m/z* for $C_{20}H_{24}NO_7S$ $[M+H]^+$, cacld:422.12598, found. 422.12680.

### 3.3 $^{1}H$, $^{13}C$ NMR, HRMS data of title compounds (1−16)

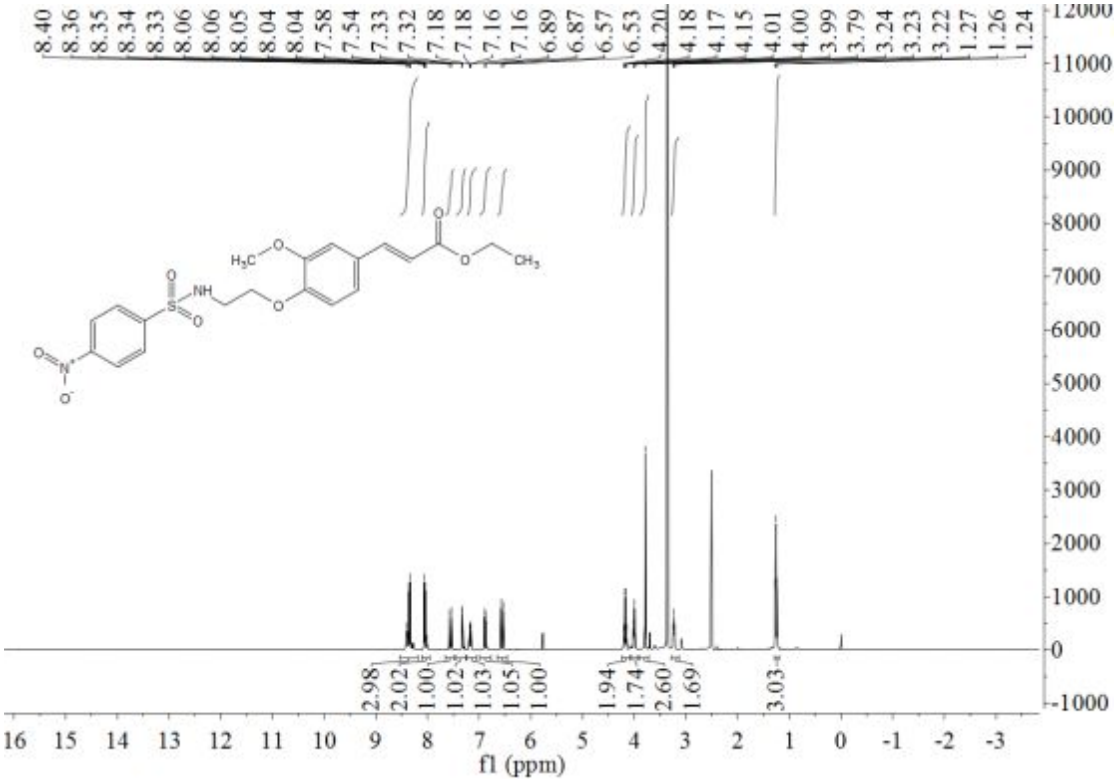



Figure S17 $^{1}H$ NMR of compound **1**

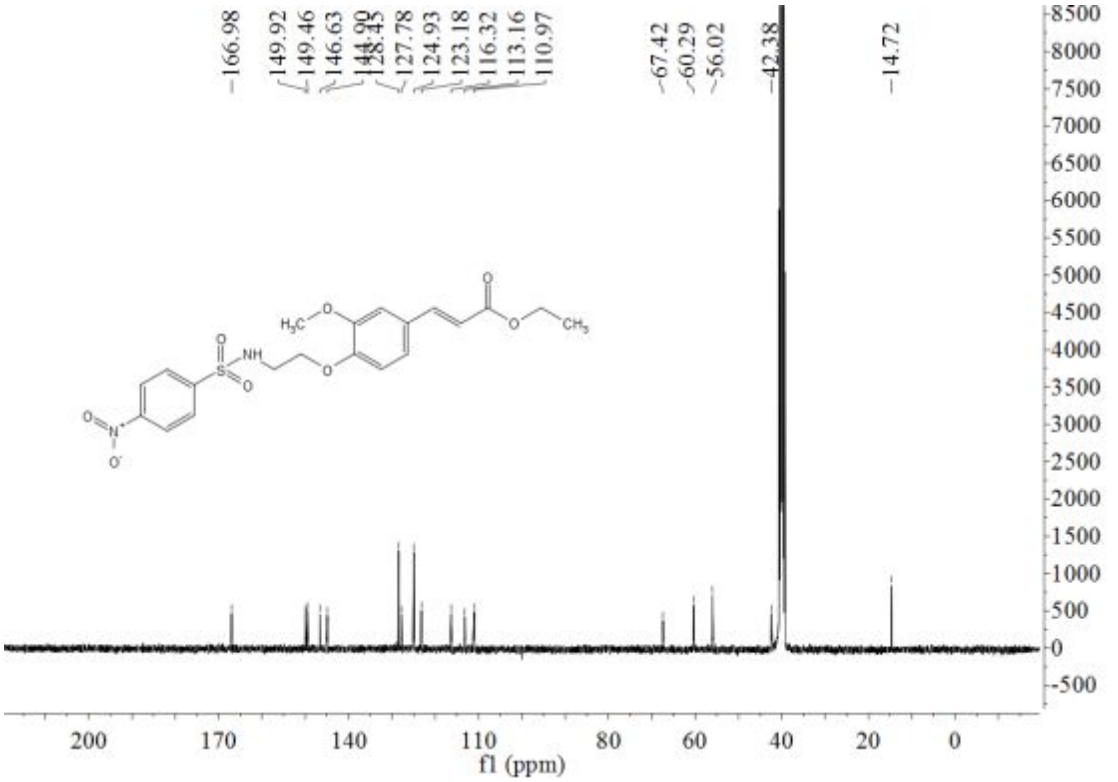



Figure S18 $^{13}C$ NMR of compound **1**

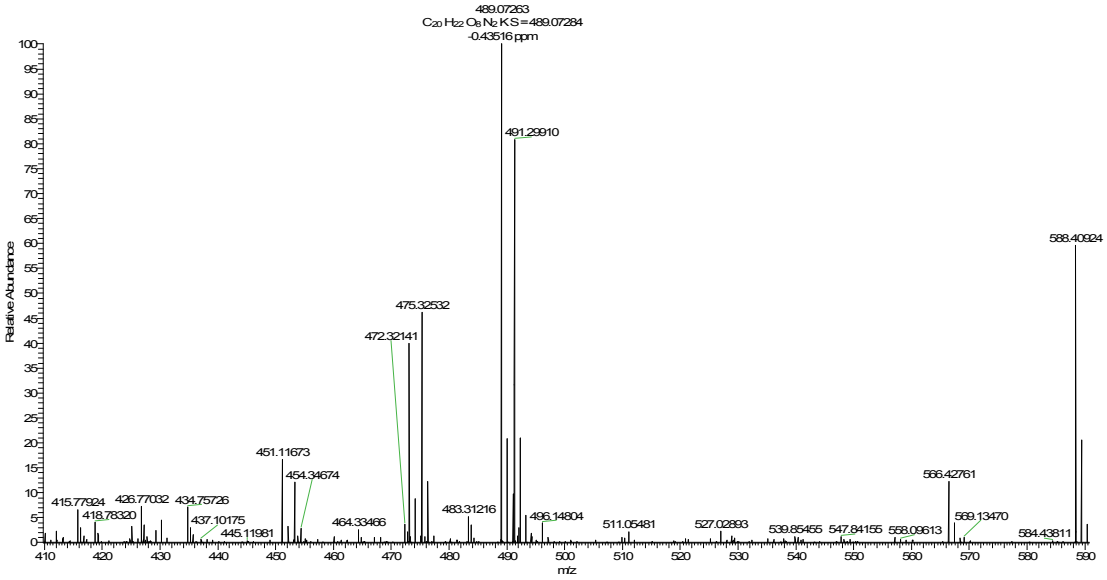



Figure S19 HRMS of compound **1**

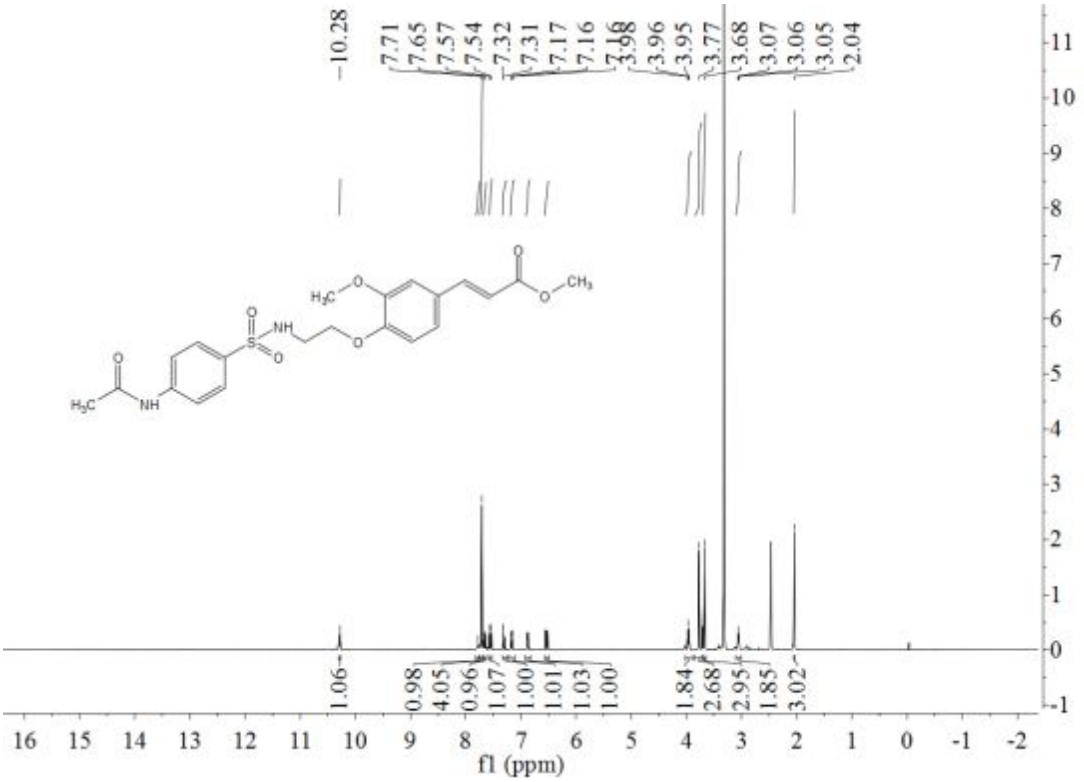



Figure S20 $^{1}$H NMR of compound **2**

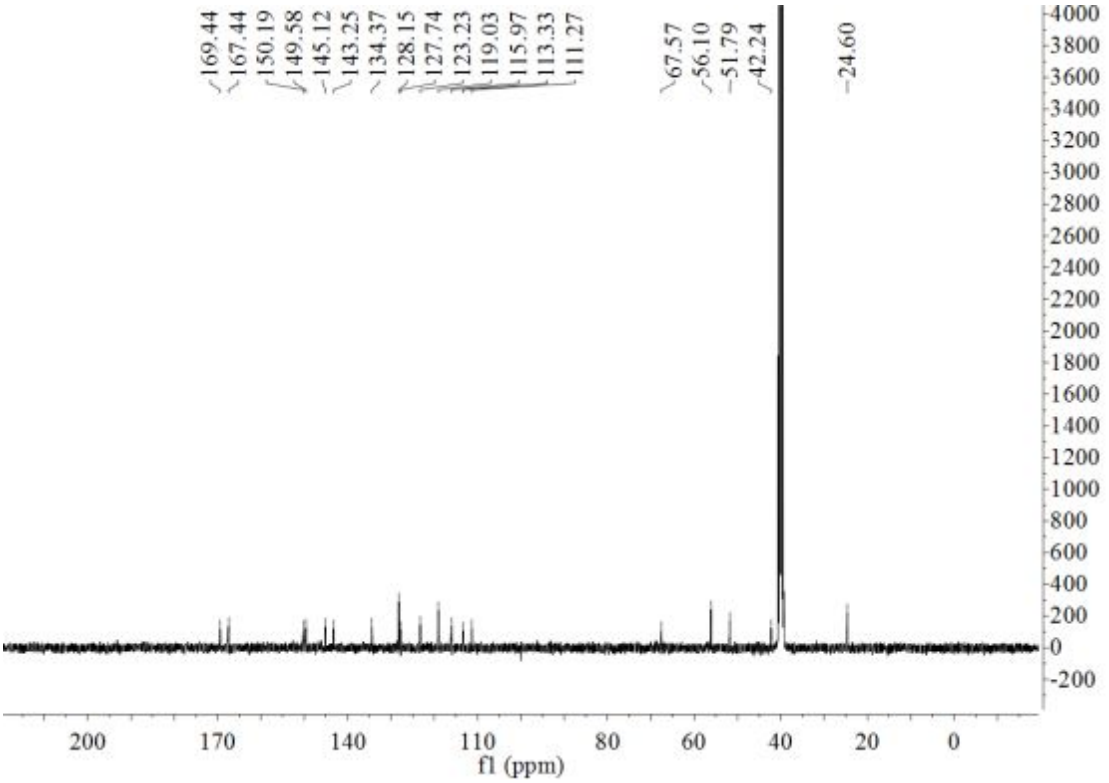



Figure S21 $^{13}$C NMR of compound **2**

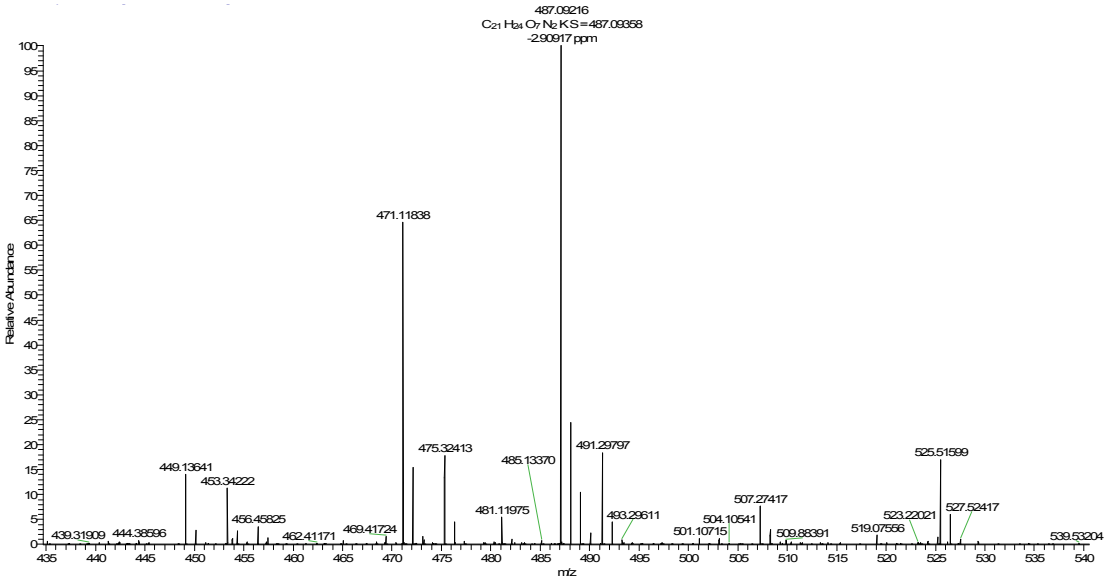



Figure S22 HRMS of compound **2**

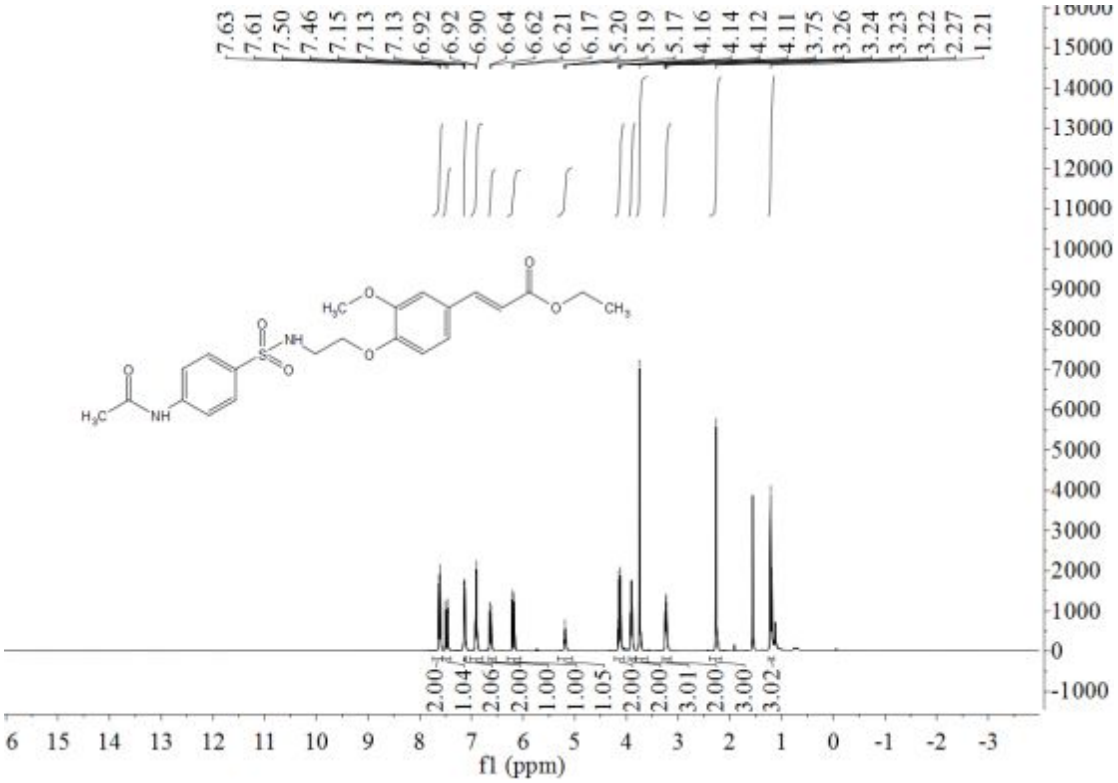



Figure S23 $^{1}$H NMR of compound **3**

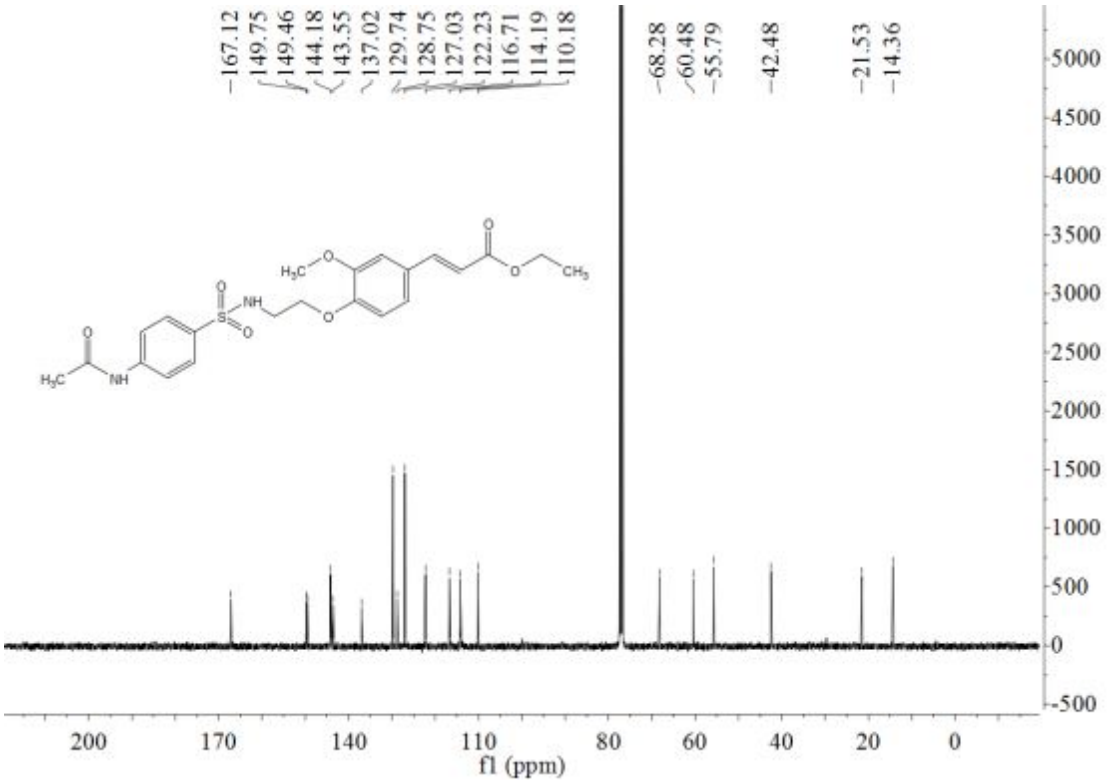



Figure S24 $^{13}$C NMR of compound **3**

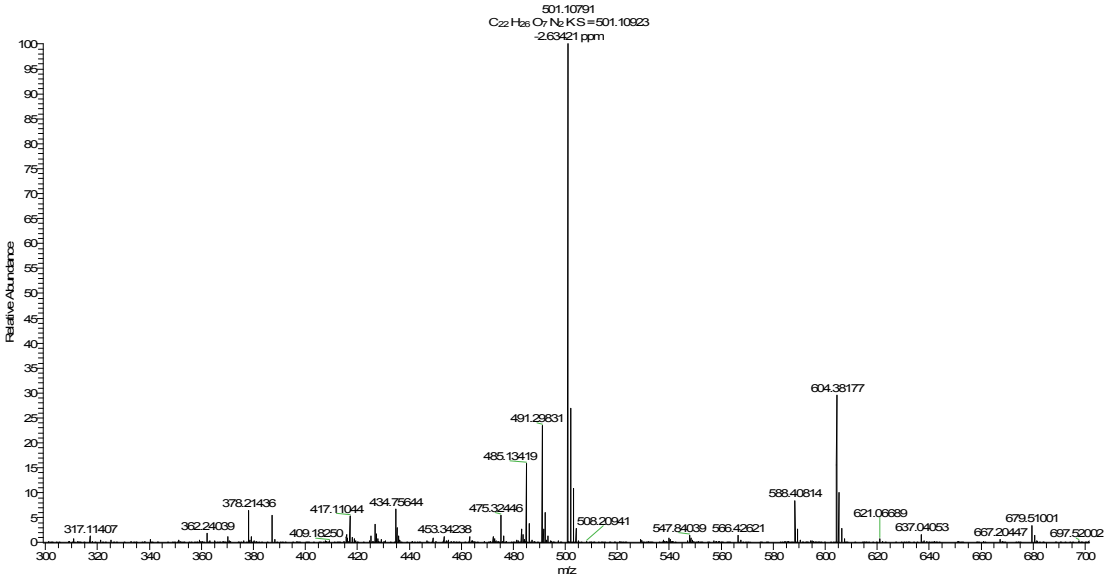



Figure S25 HRMS of compound **3**

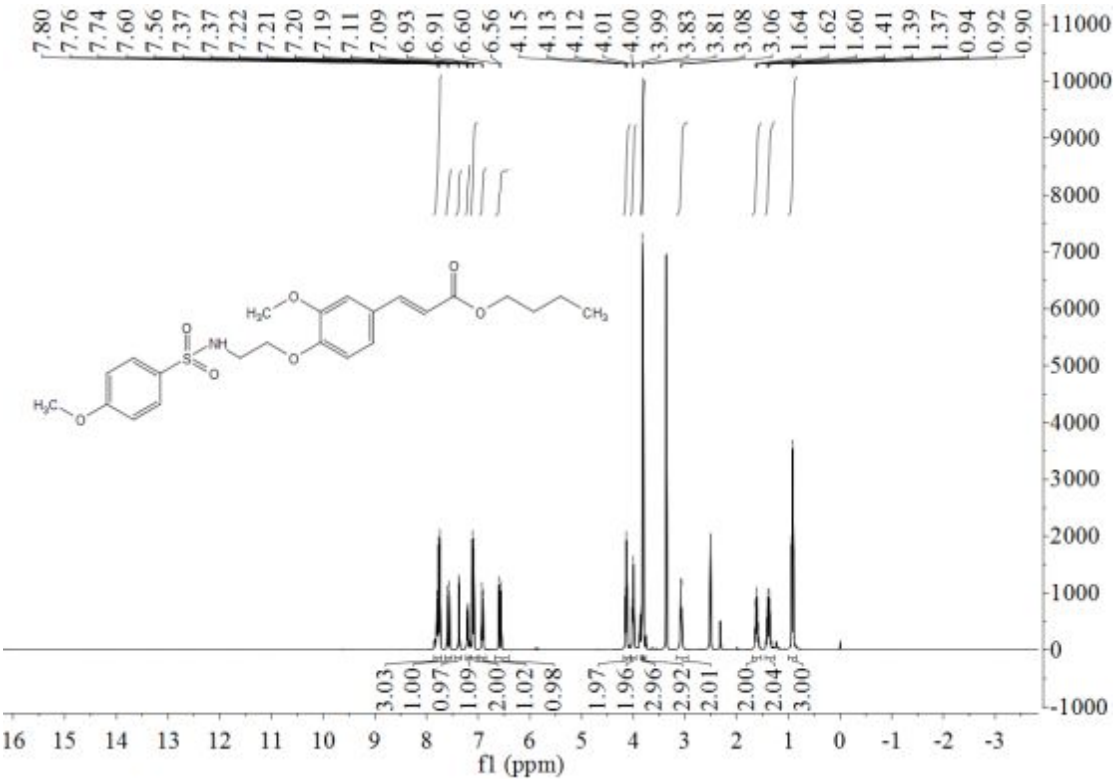



Figure S26 $^{1}$H NMR of compound **4**

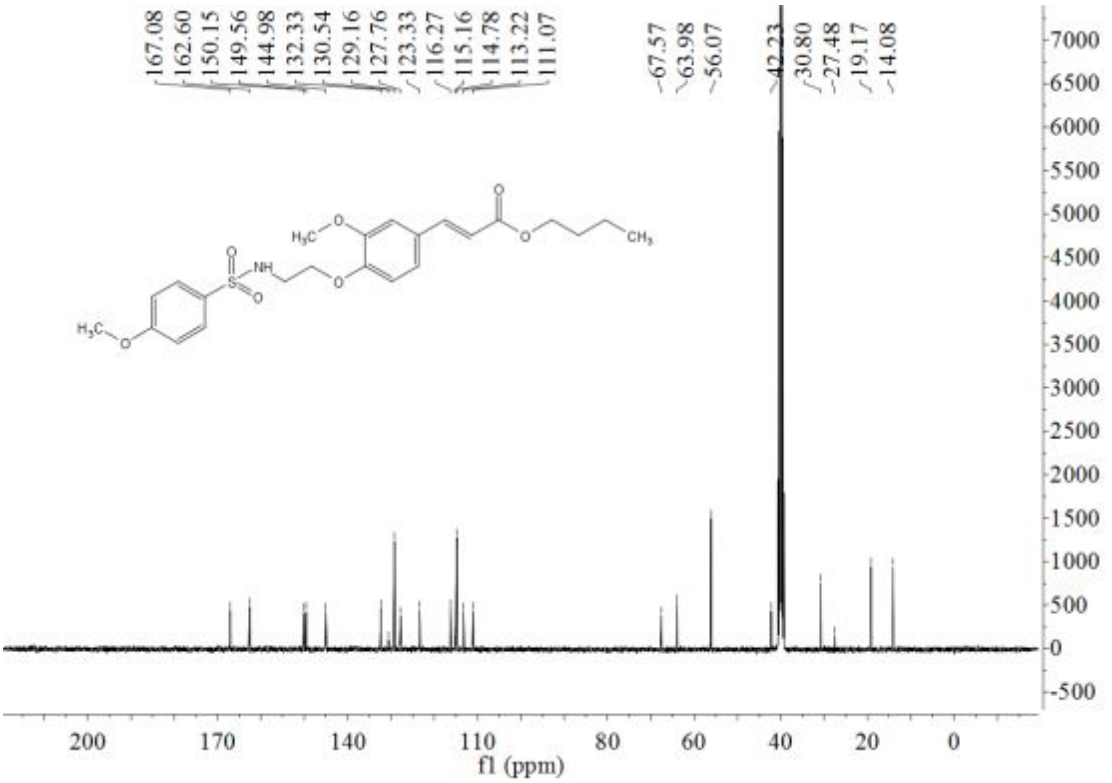



Figure S27 $^{13}C$ NMR of compound **4**

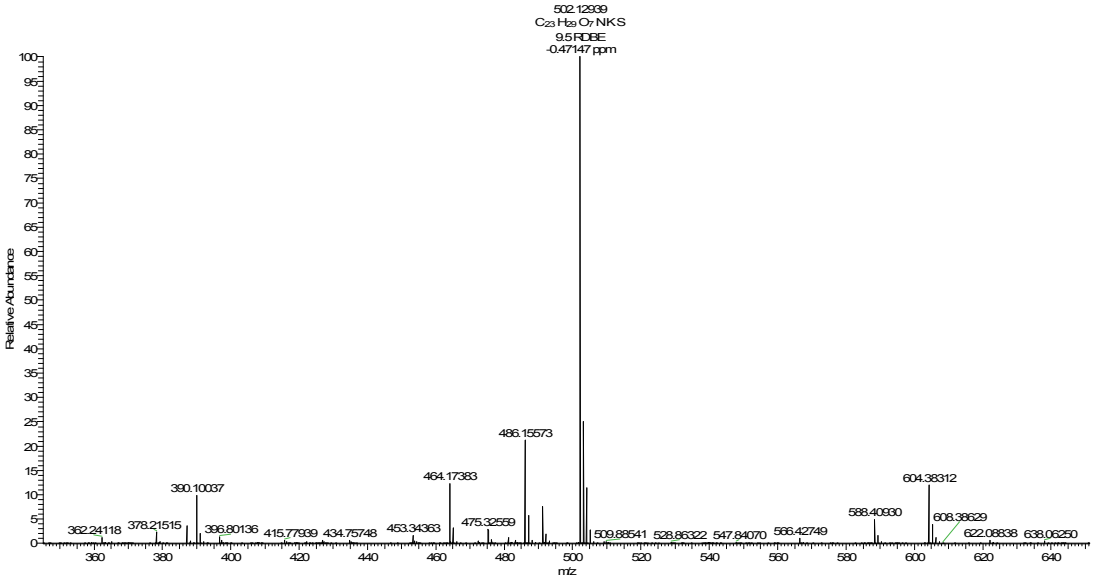



Figure S28 HRMS of compound **4**

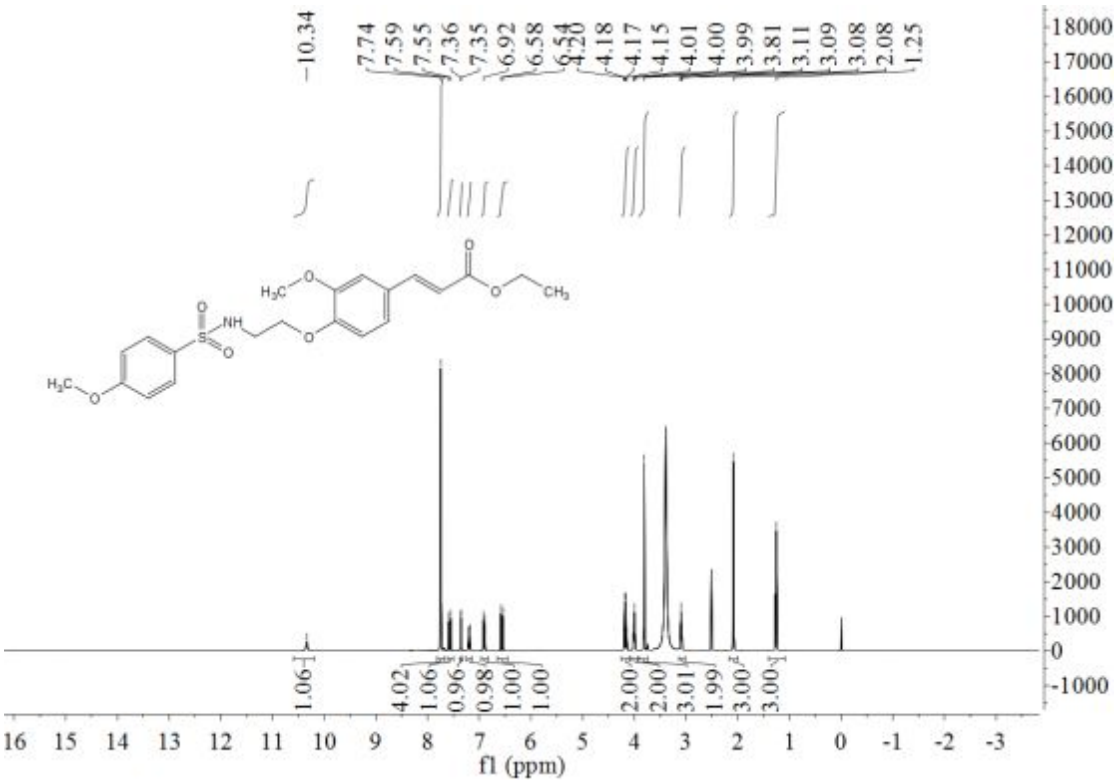



Figure S29 $^{1}$H NMR of compound **5**

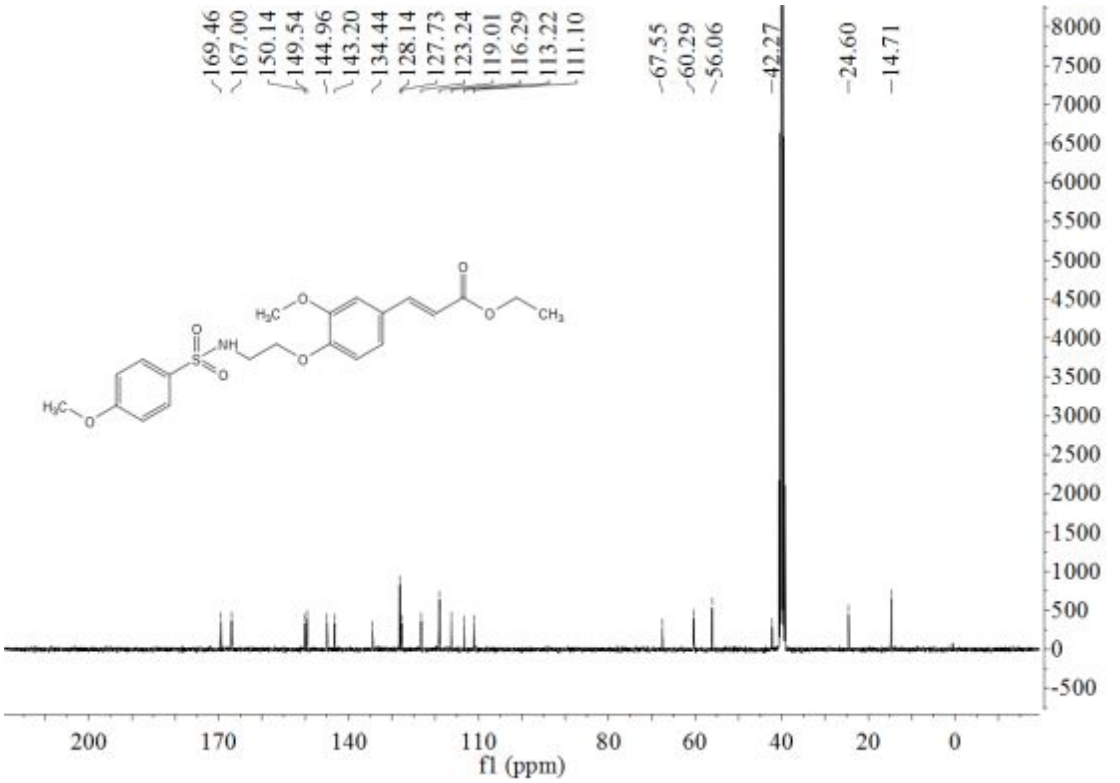



Figure S30 $^{13}$C NMR of compound **5**

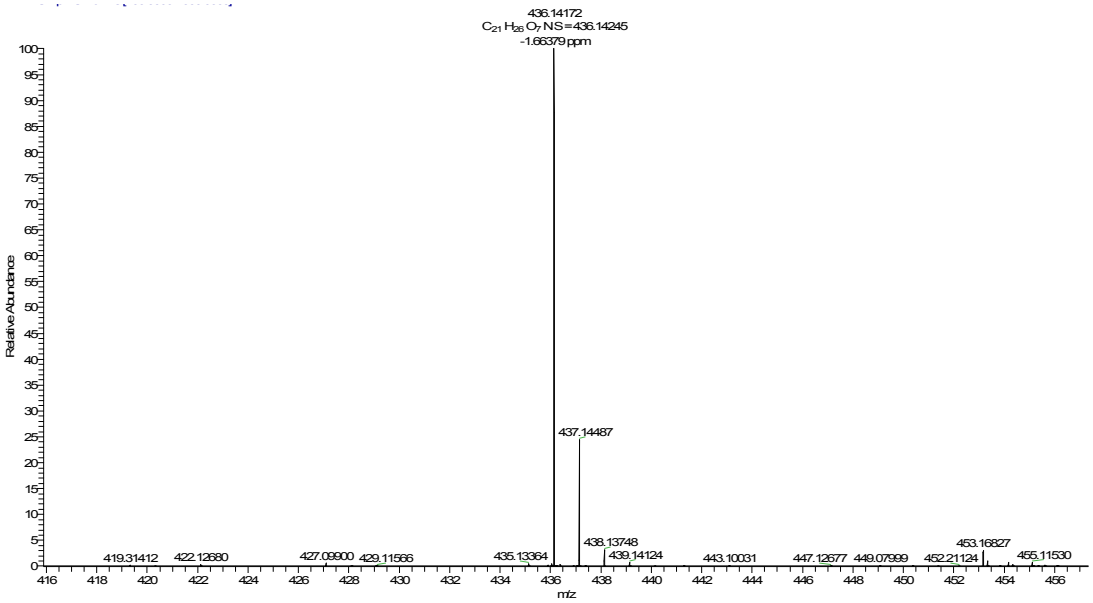



Figure S31 HRMS of compound **5**

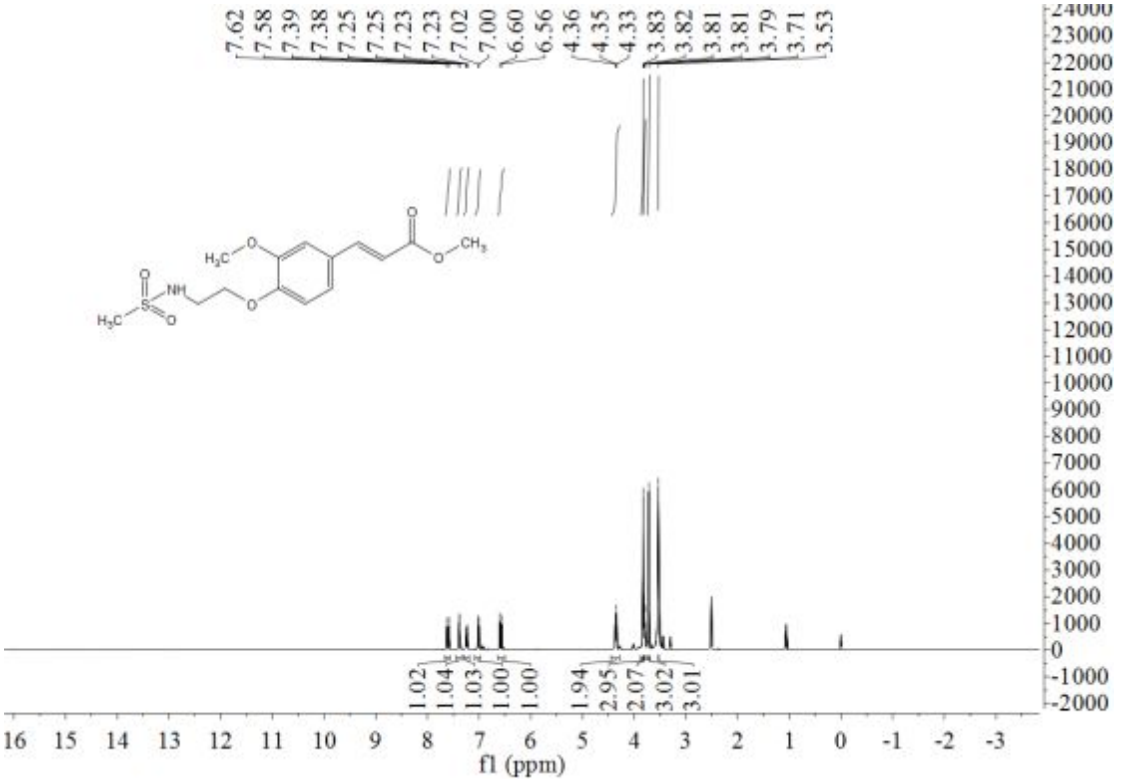



Figure S32 $^{1}$H NMR of compound **6**

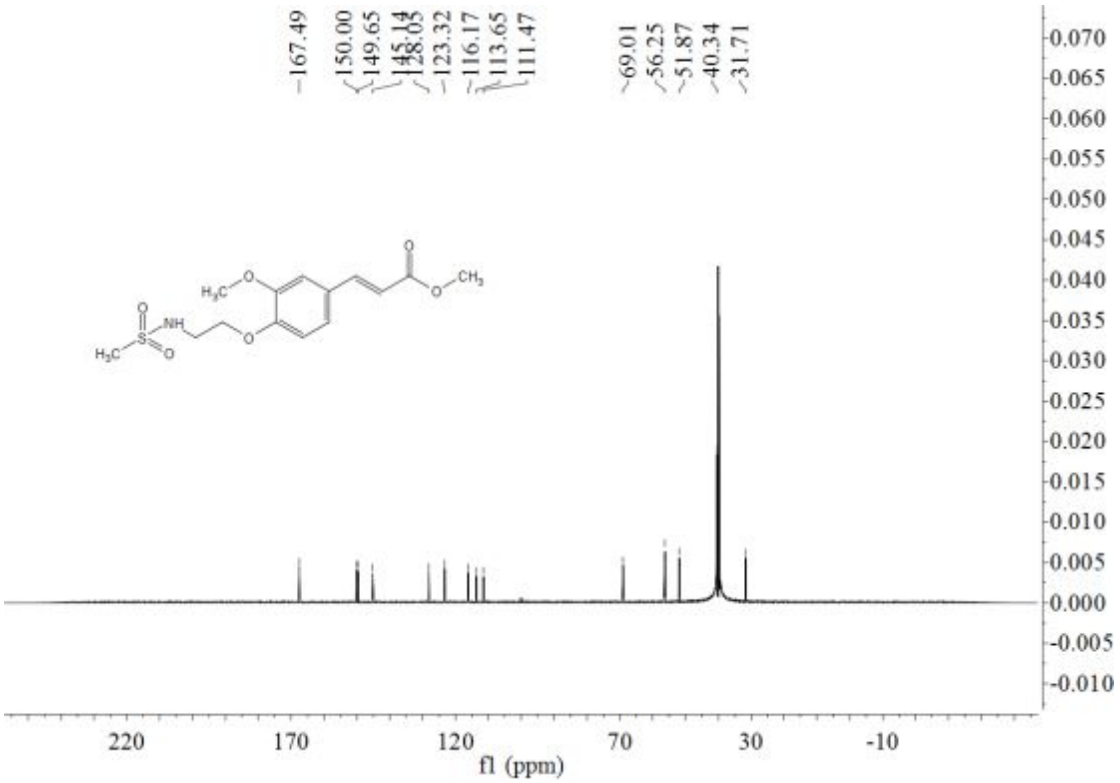



Figure S33 $^{13}C$ NMR of compound **6**

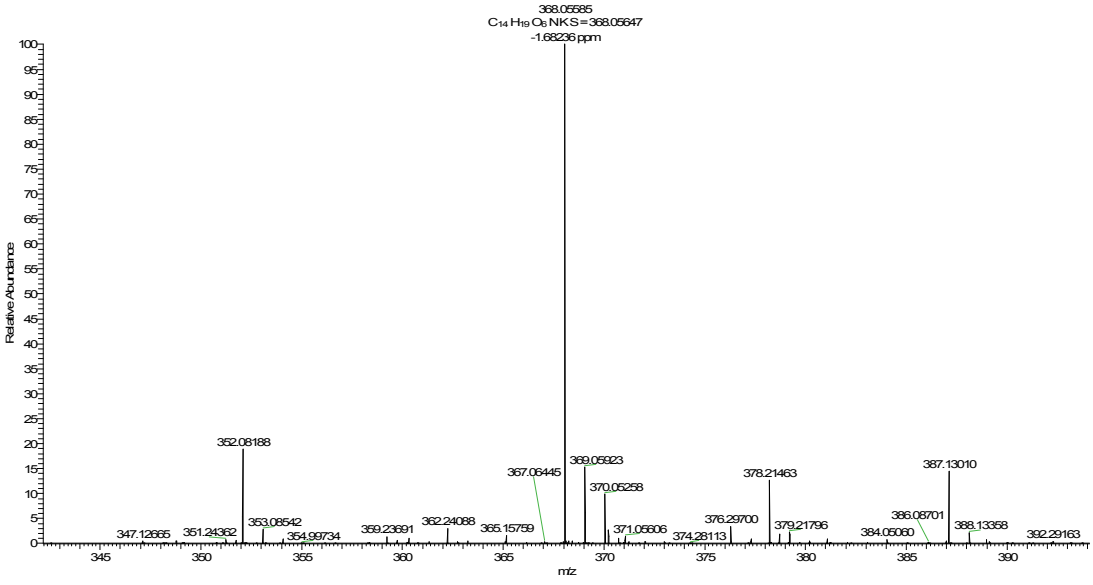



Figure S34 HRMS of compound **6**

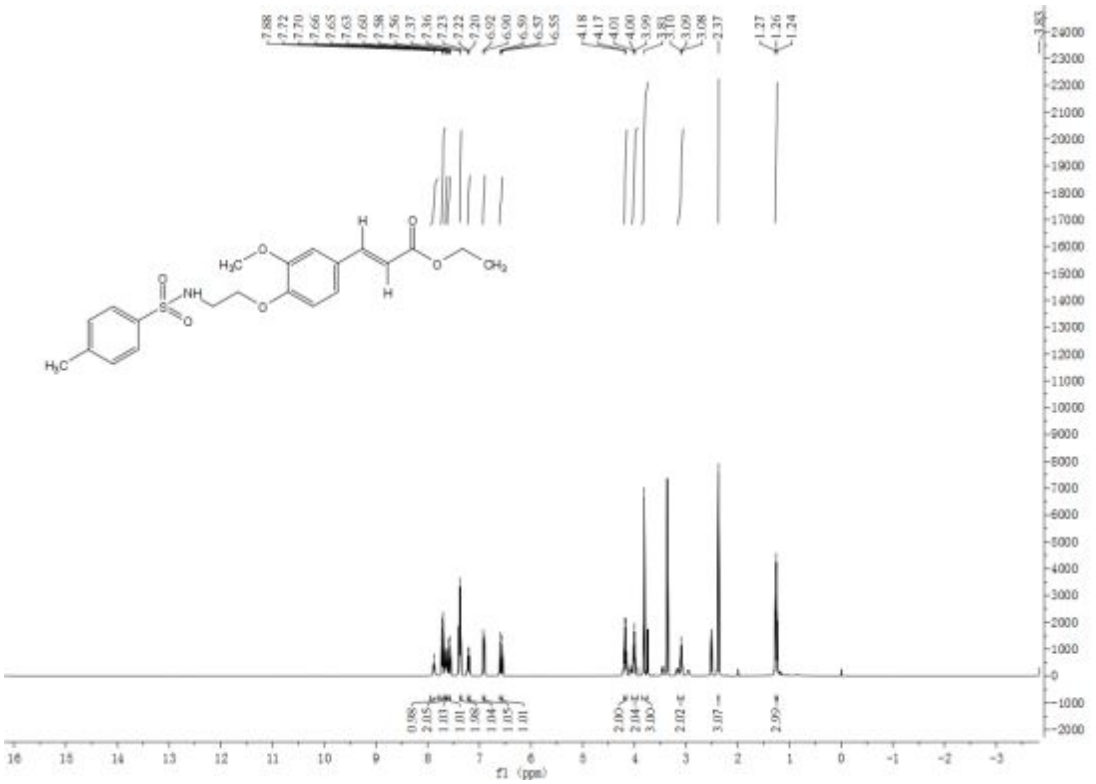


Figure S35 $^{1}$H NMR of compound **7**

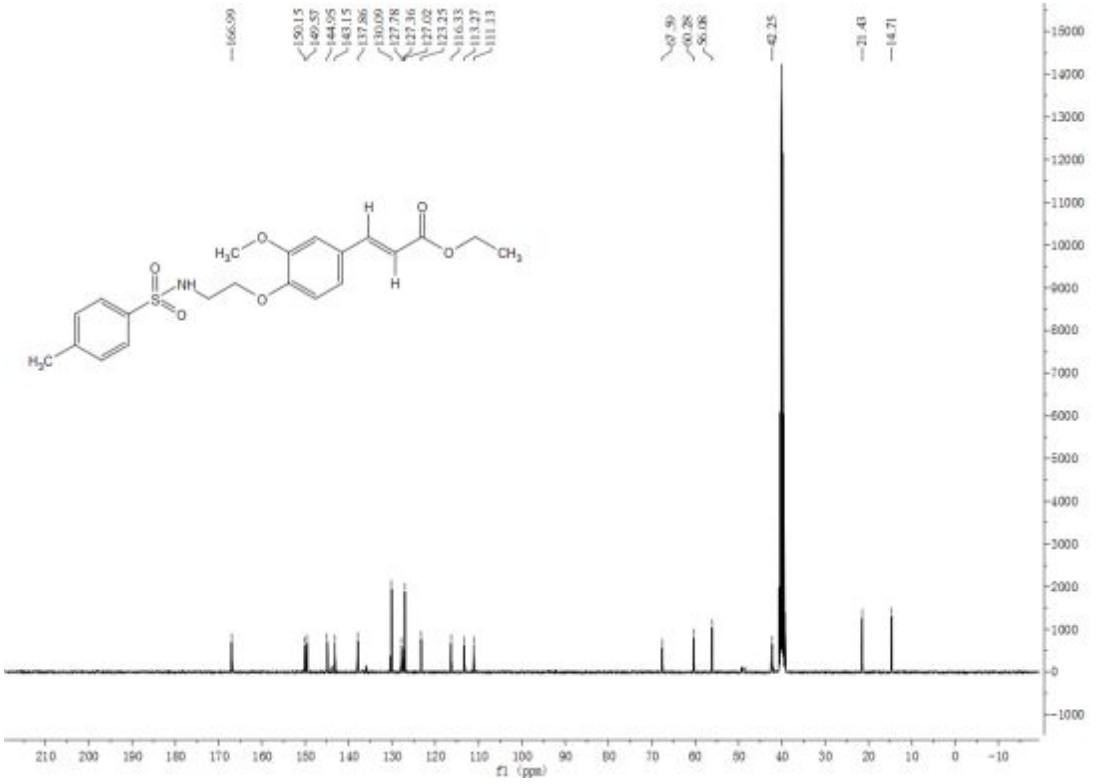


Figure S36 $^{13}$C NMR of compound **7**

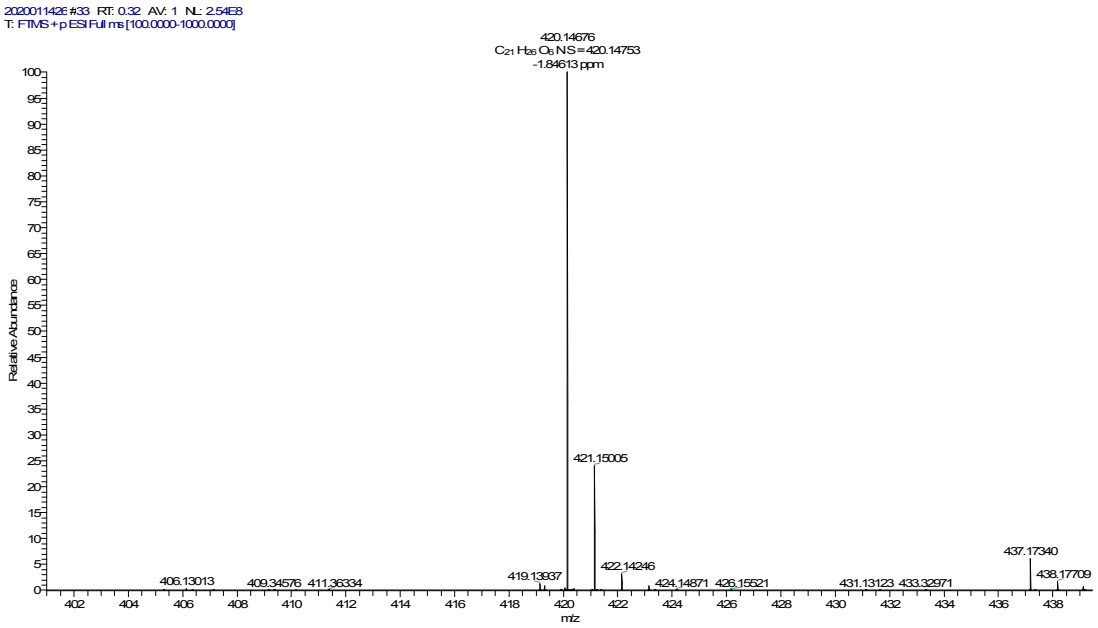



Figure S37 HRMS of compound **7**

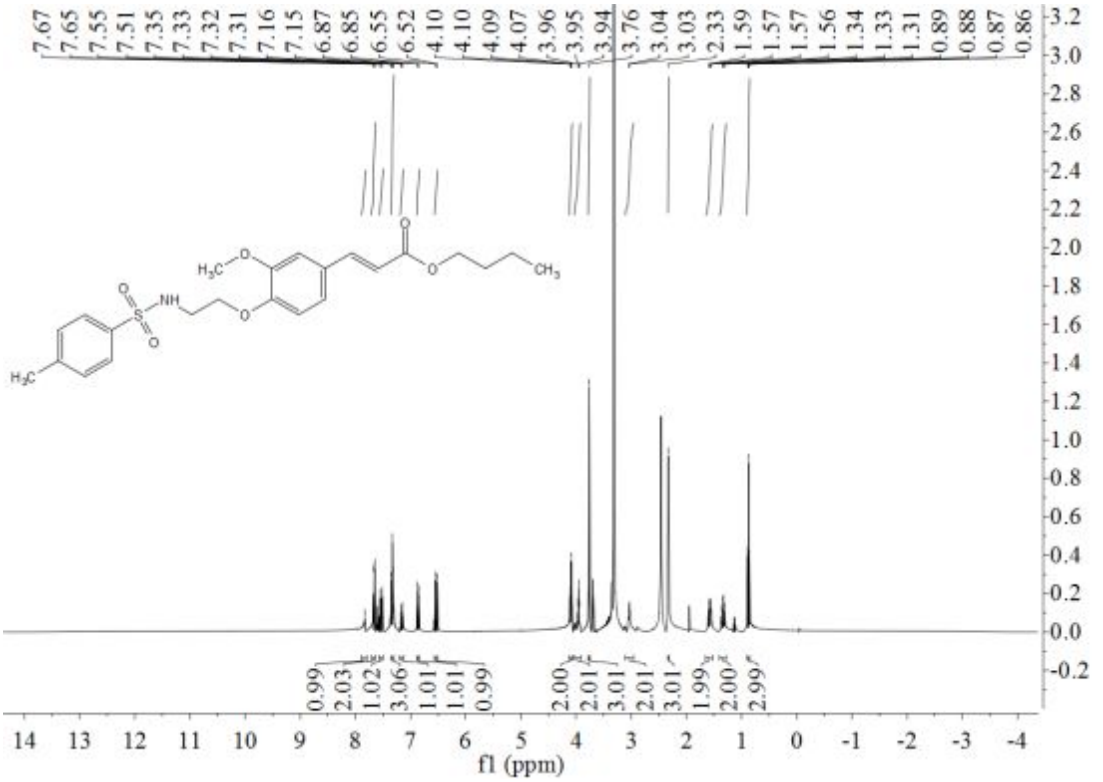



Figure S38 $^{1}$H NMR of compound **8**

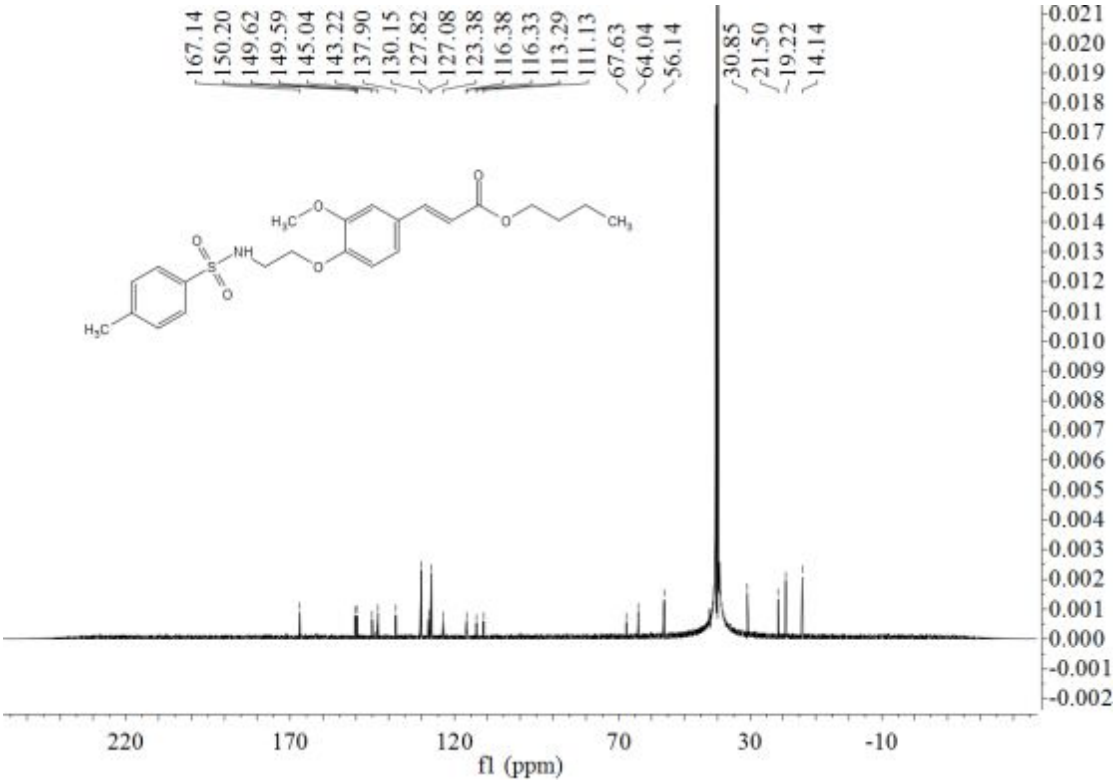



Figure S39 $^{13}C$ NMR of compound **8**

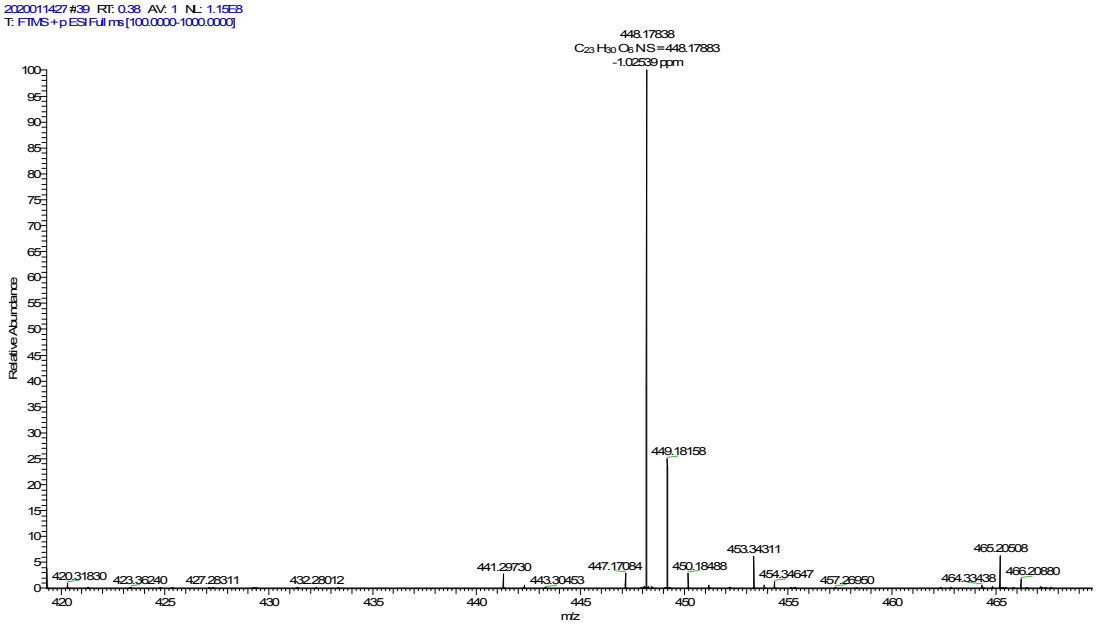



Figure S40 HRMS of compound **8**

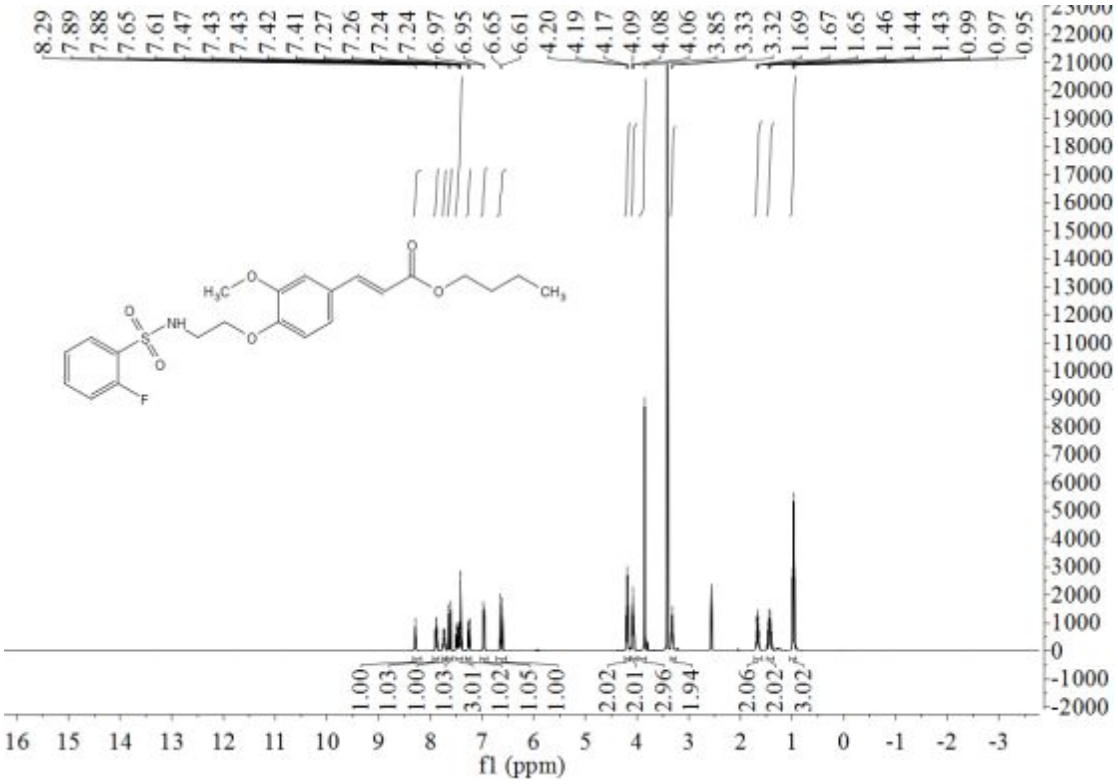



Figure S41 $^{1}$H NMR of compound **9**

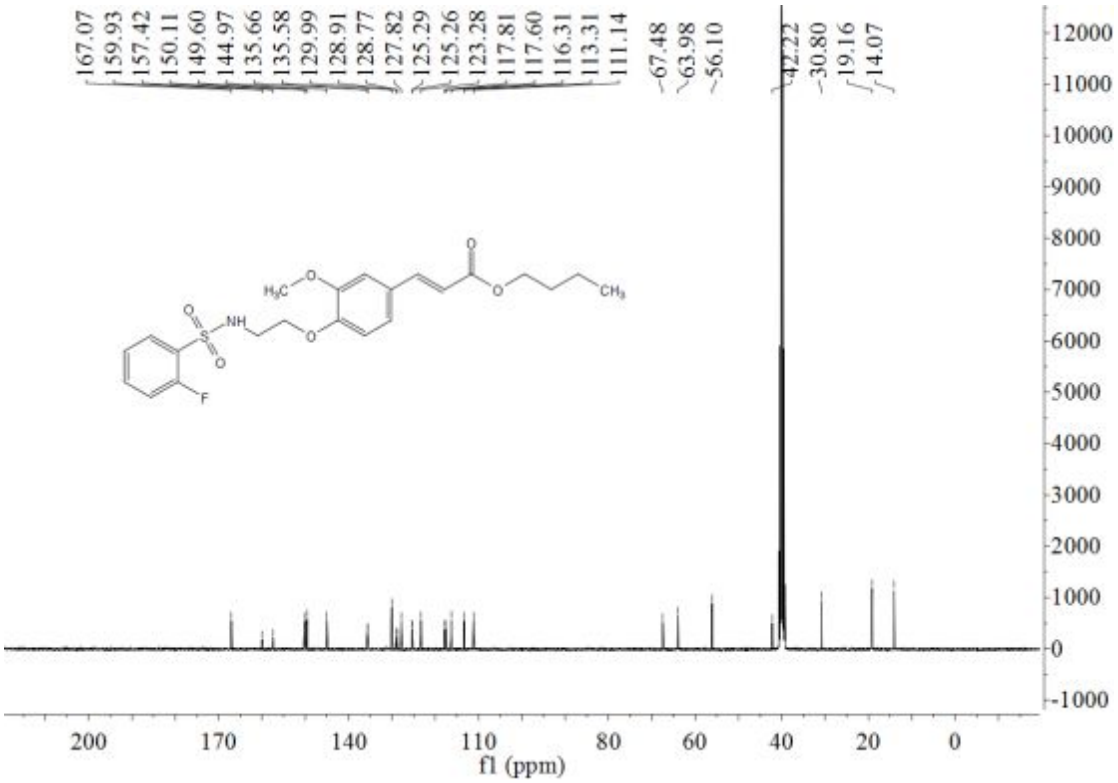



Figure S42 $^{13}$C NMR of compound **9**

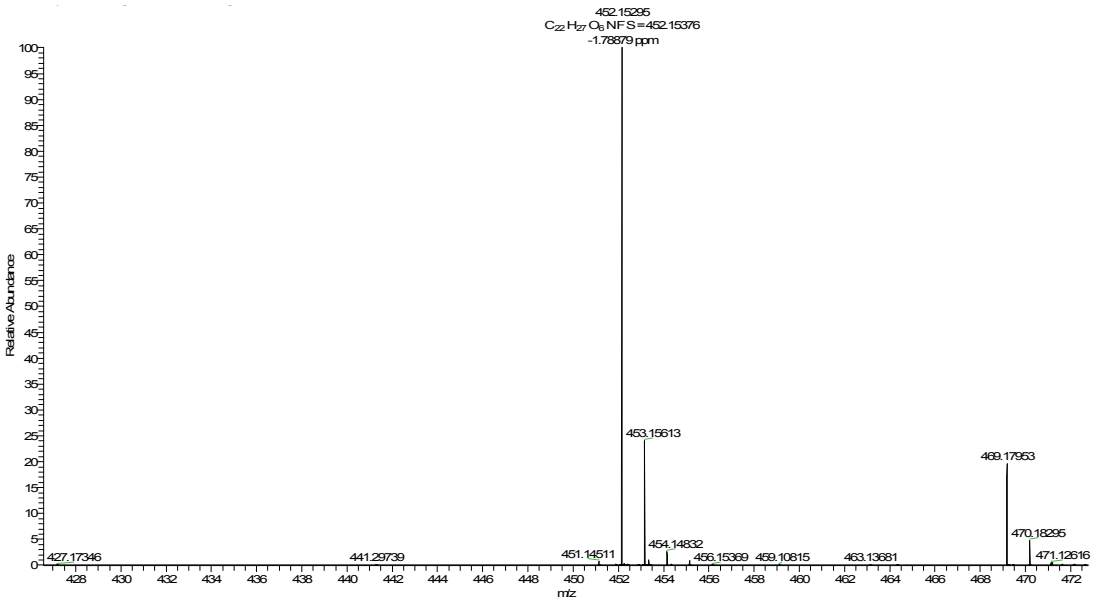



Figure S43 HRMS of compound **9**

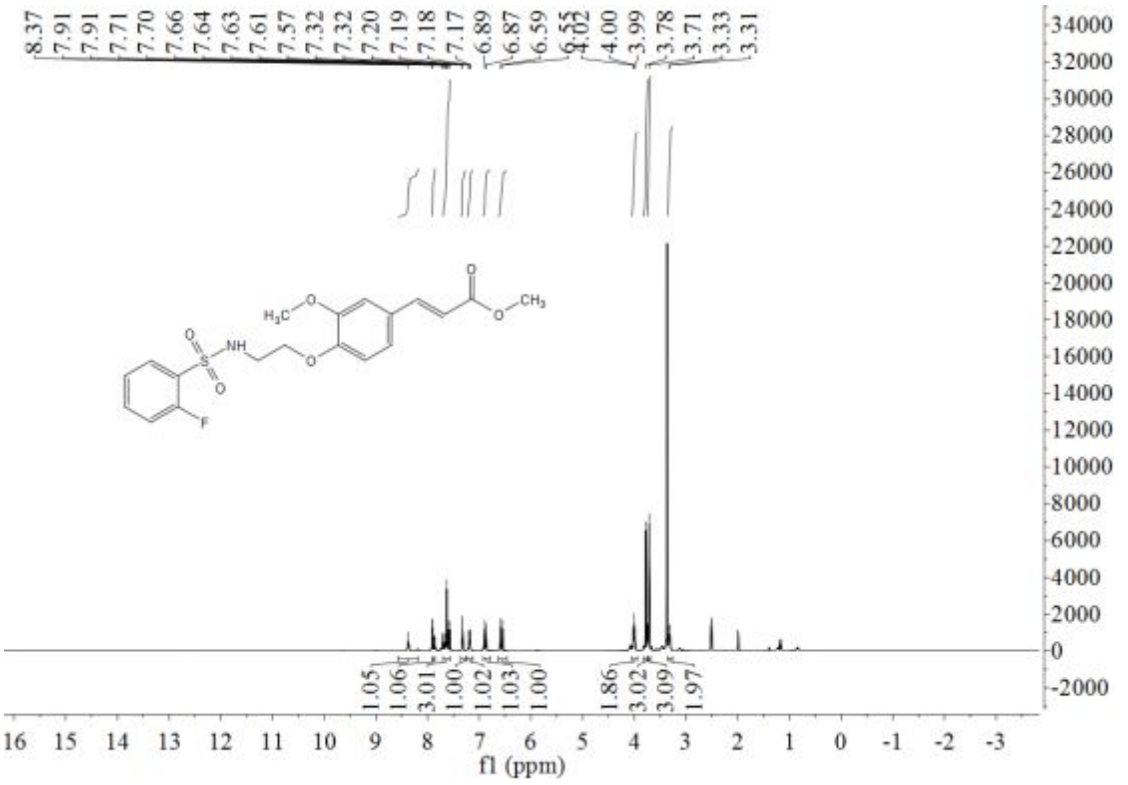



Figure S44 $^{1}$H NMR of compound **10**

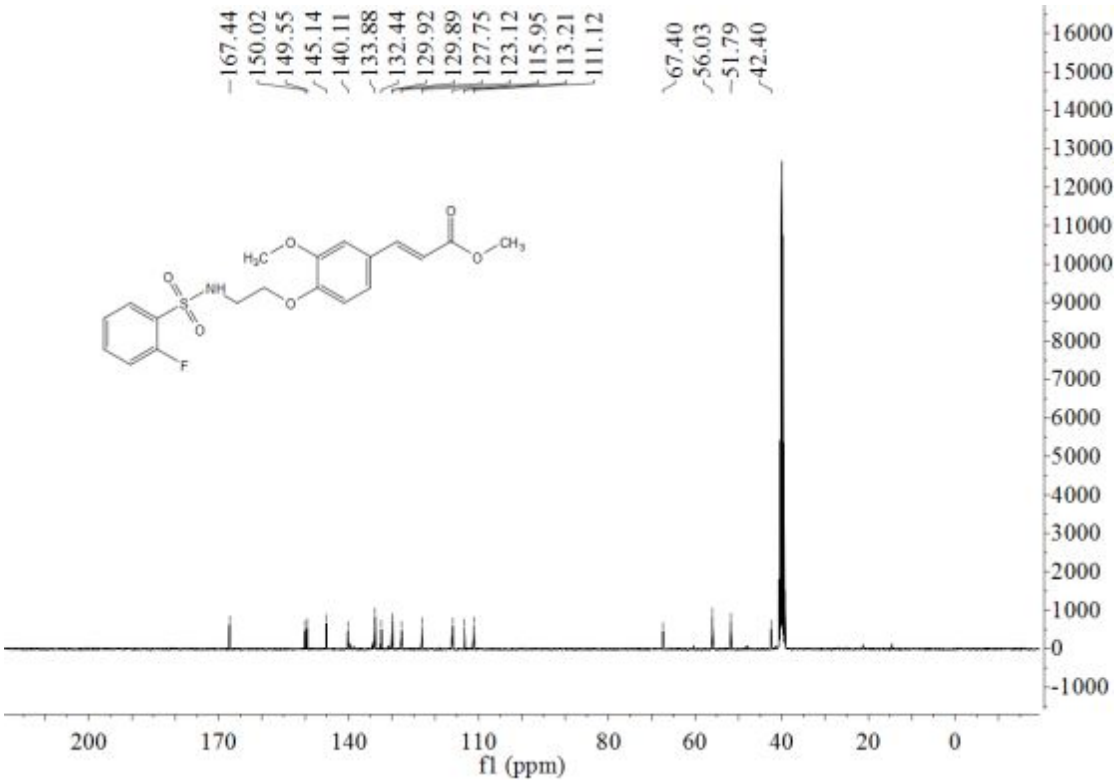



Figure S45 $^{13}$C NMR of compound **10**

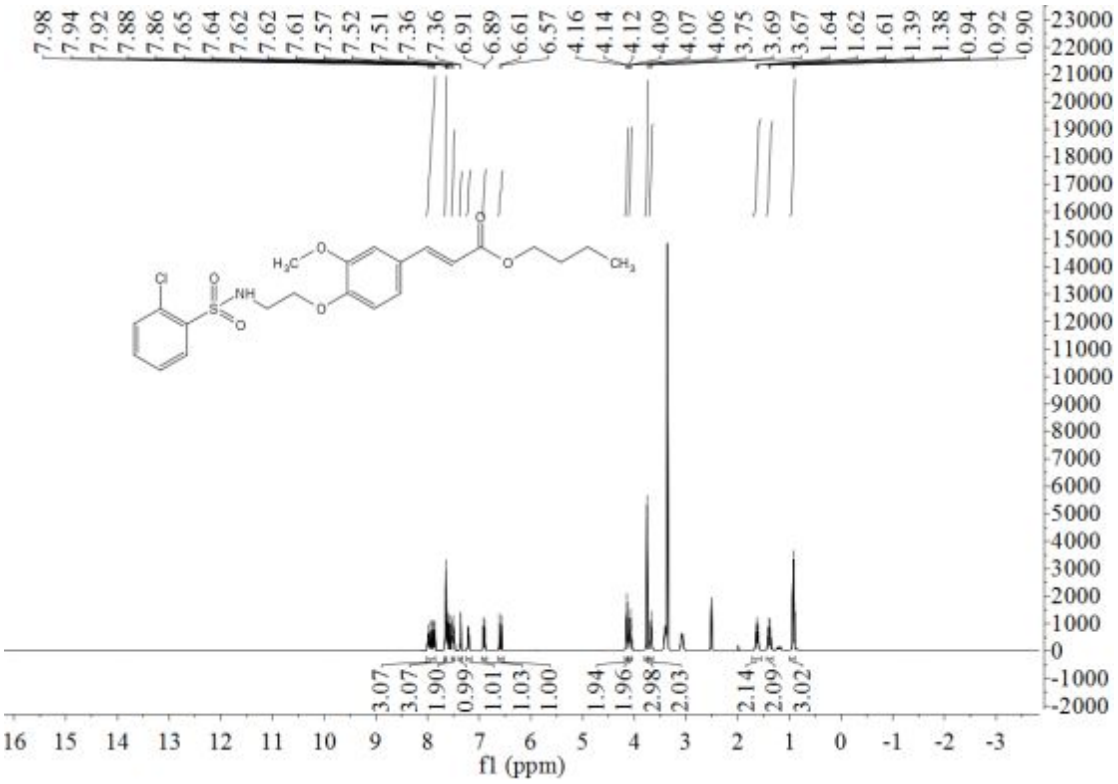



Figure S46 $^{1}$H NMR of compound **11**

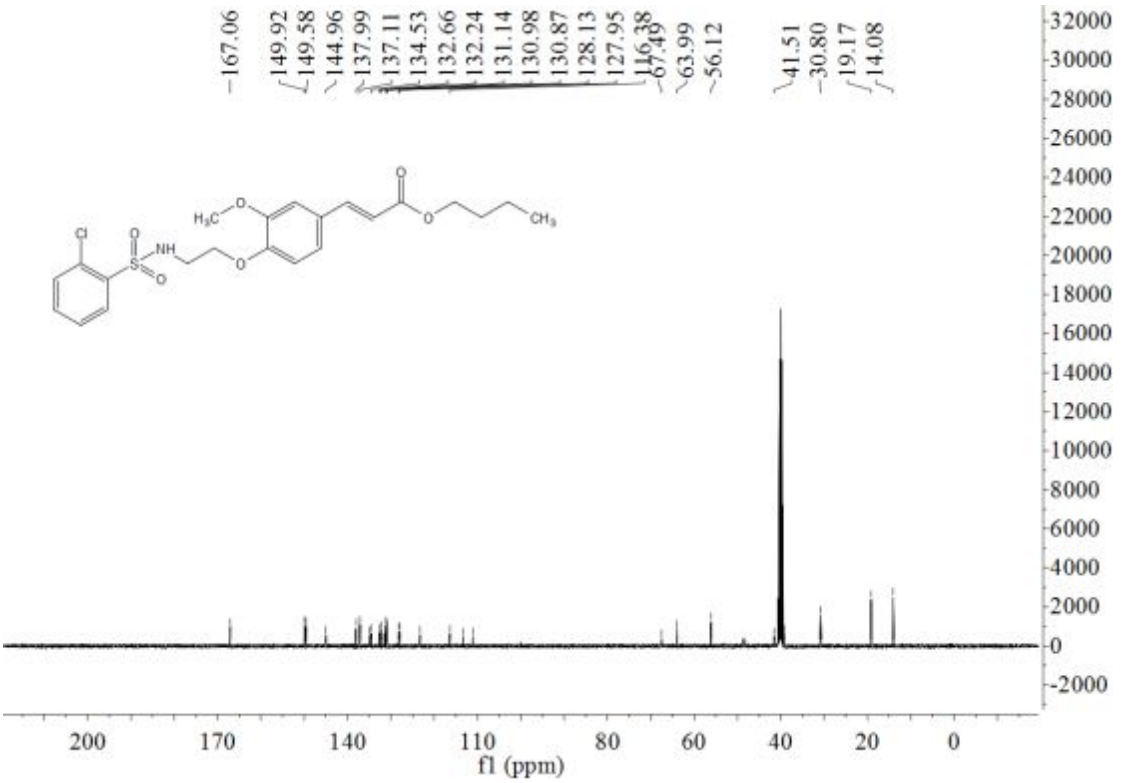



Figure S47 $^{13}C$ NMR of compound **11**

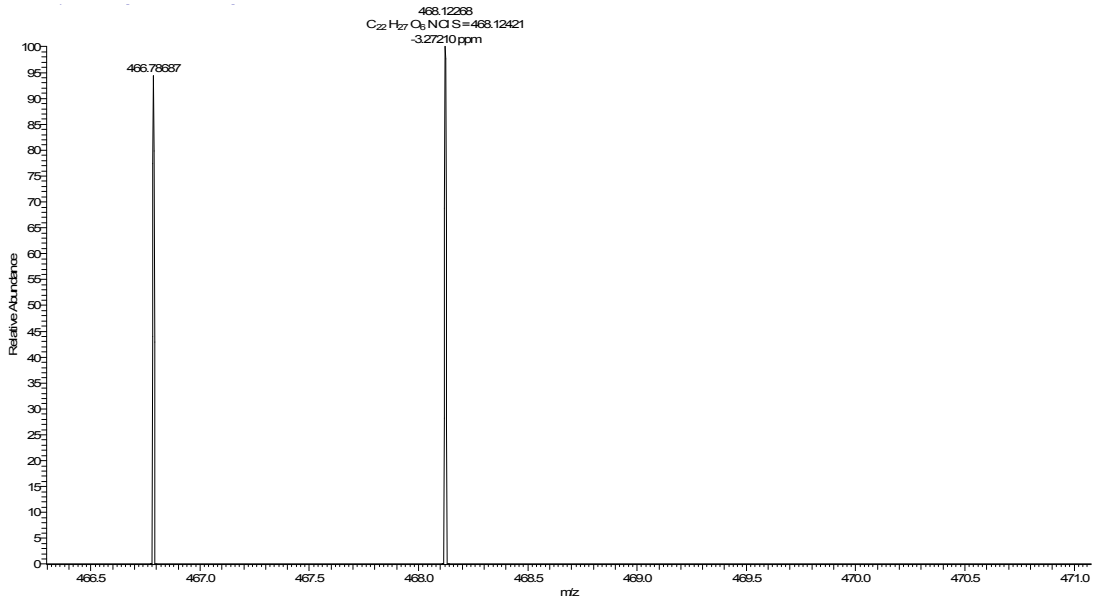



Figure S48 HRMS of compound **11**

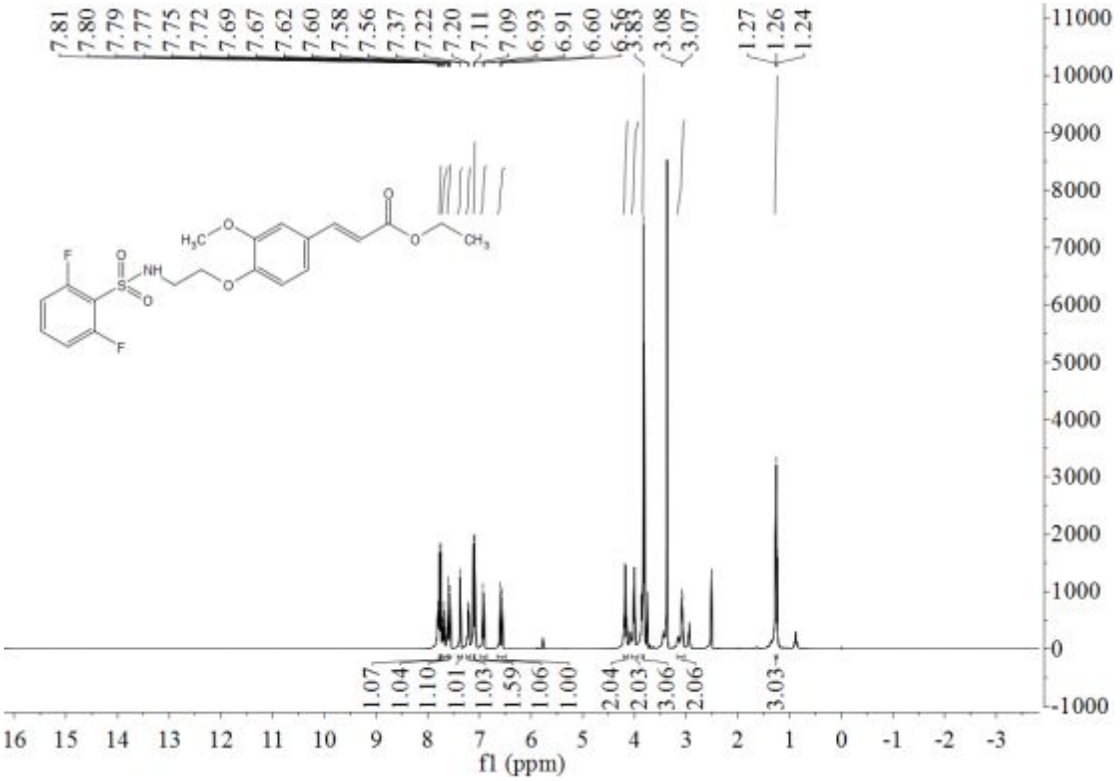



Figure S49 $^{1}$H NMR of compound **12**

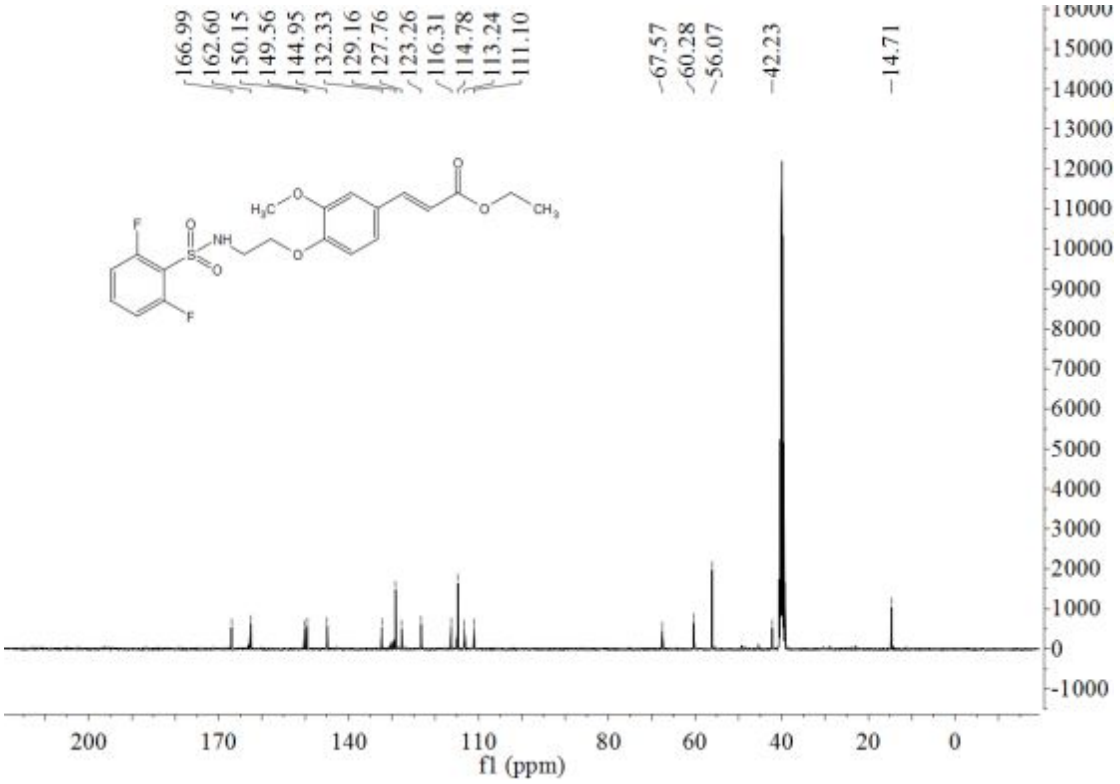



Figure S50 $^{13}$C NMR of compound **12**

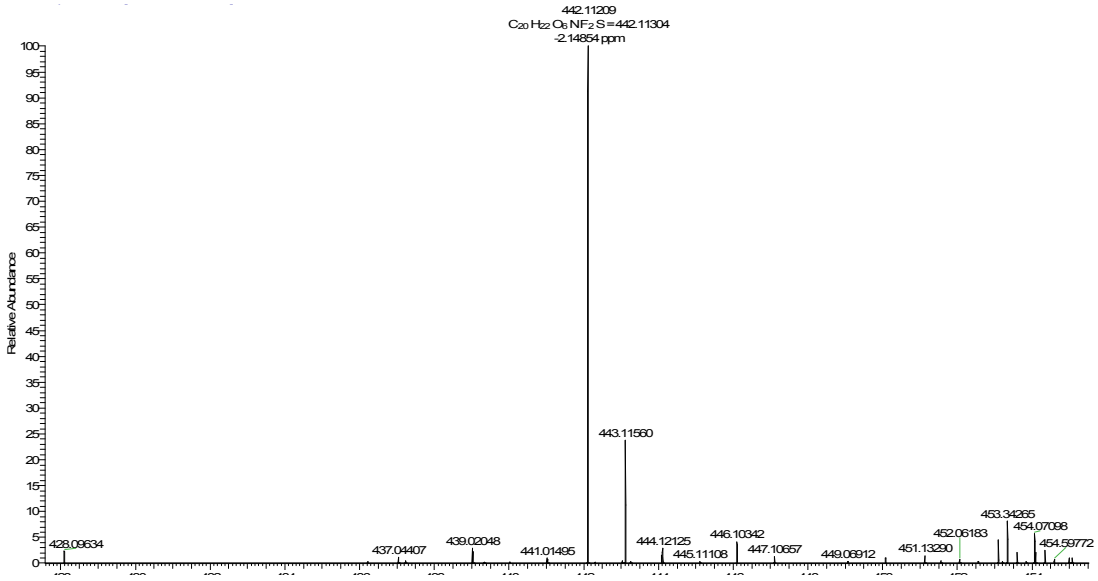



Figure S51 HRMS of compound **12**

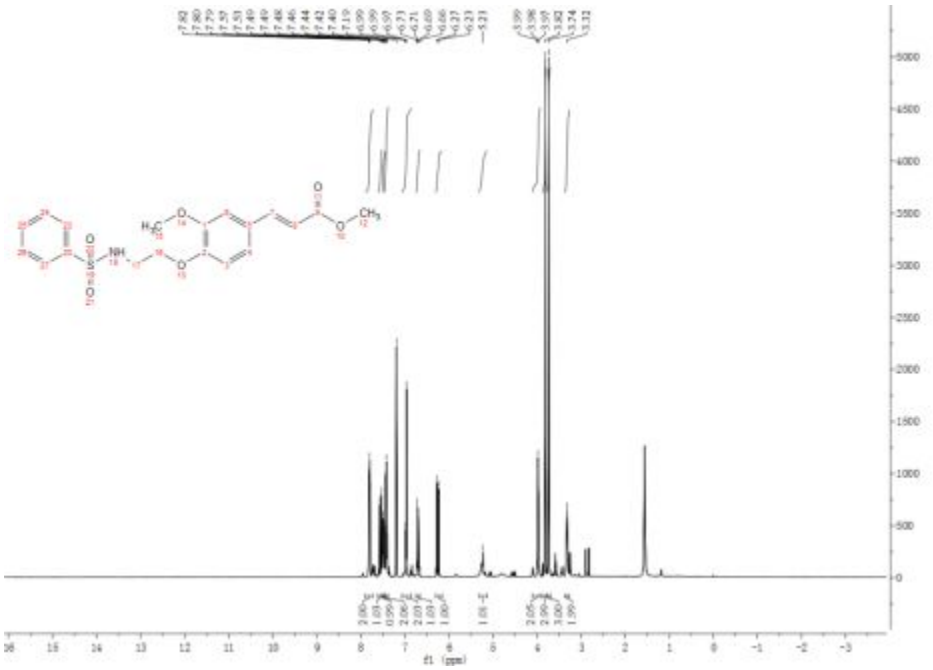


Figure S52 $^{1}$H NMR of compound **13**

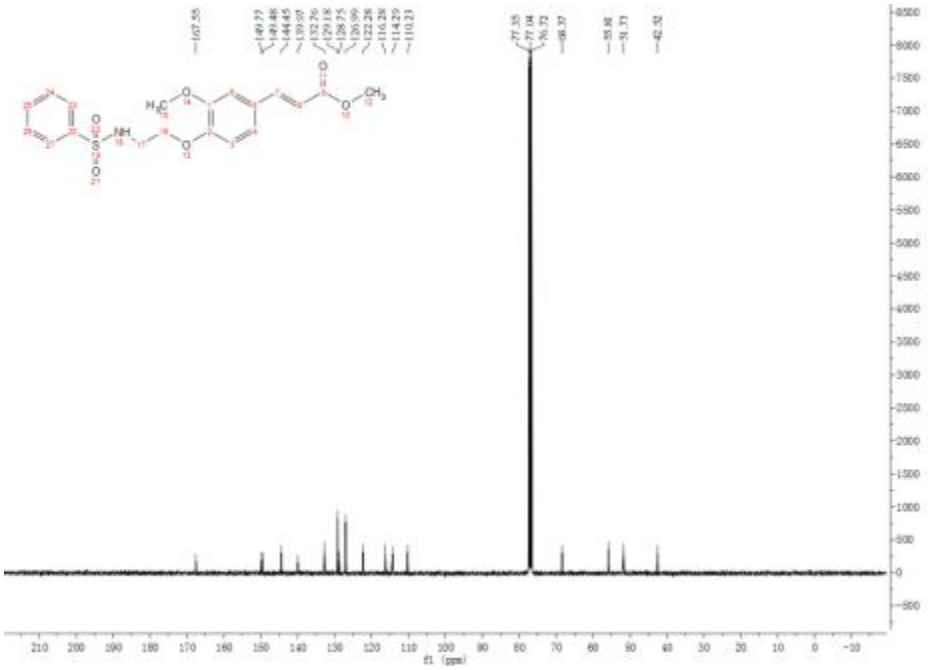


Figure S53 $^{13}C$ NMR of compound **13**

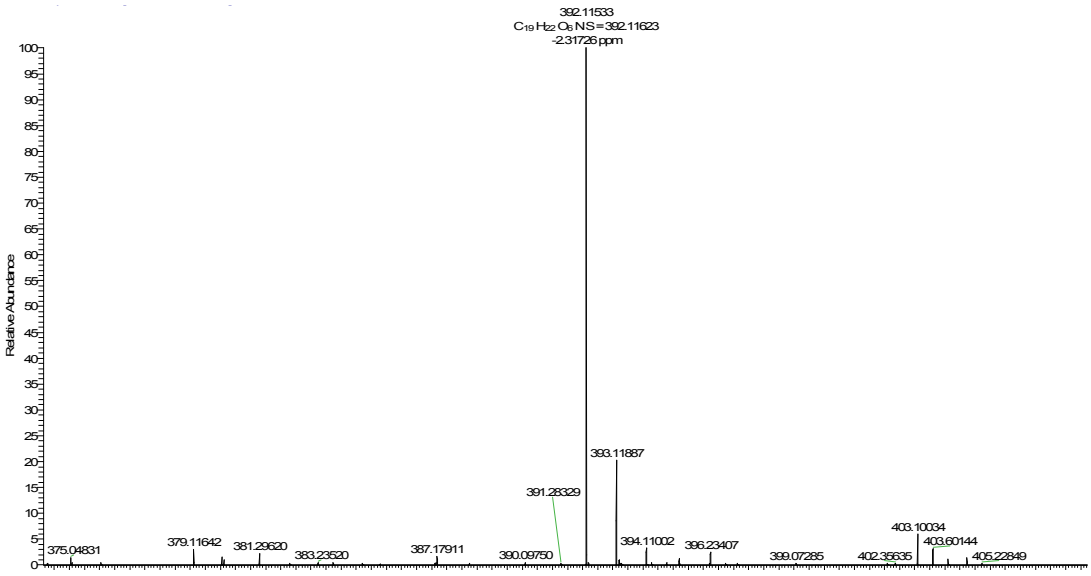



Figure S54 HRMS of compound **13**

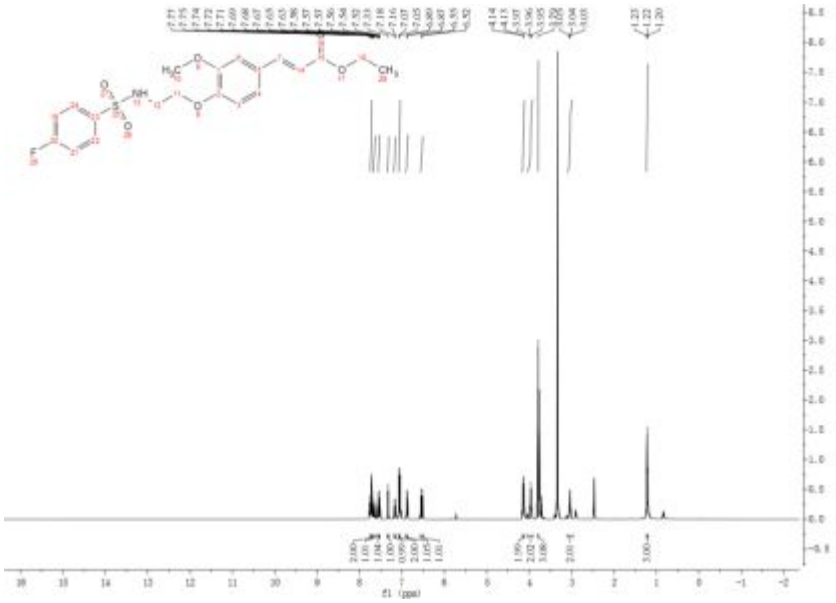


Figure S55 $^{1}$H NMR of compound **14**

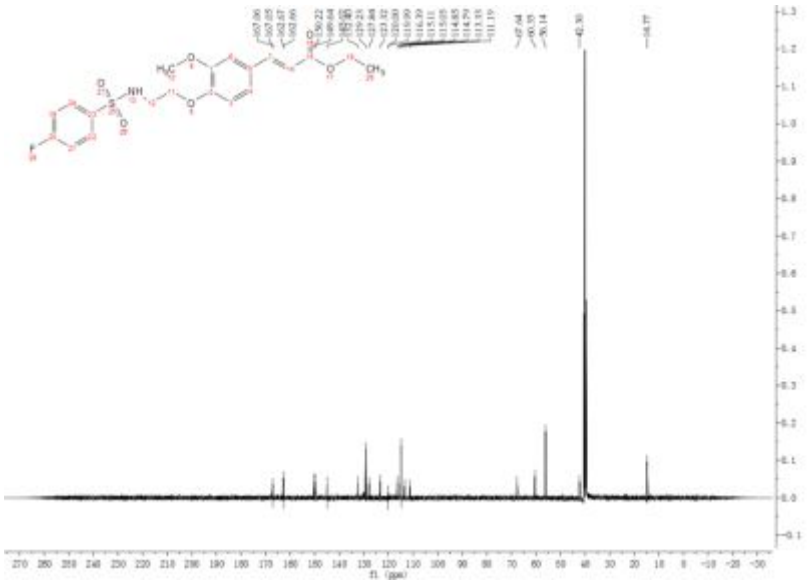


Figure S56 $^{13}$C NMR of compound **14**

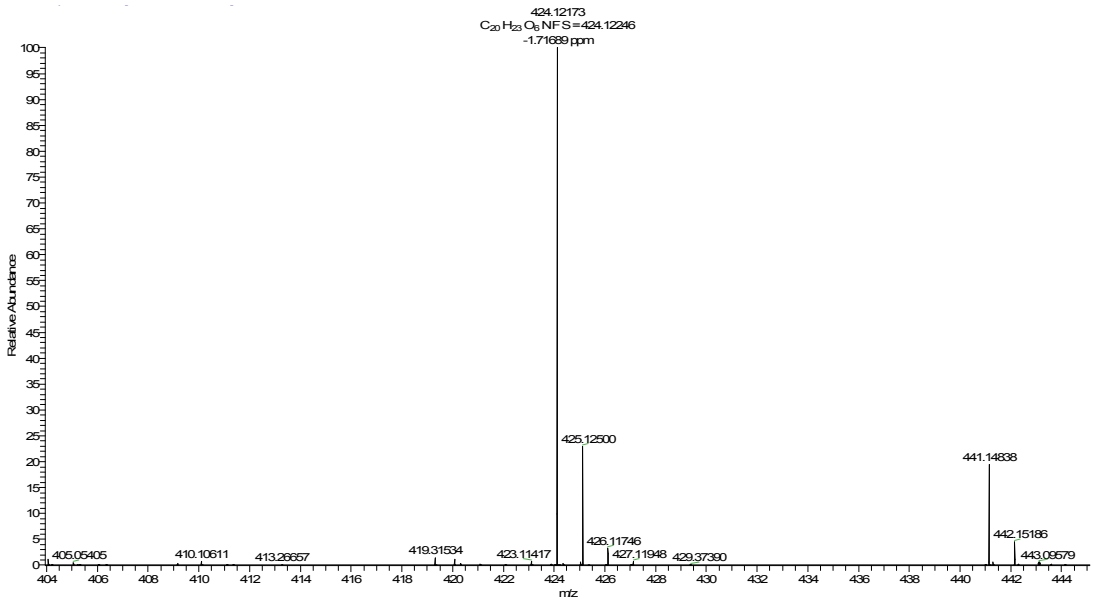



Figure S57 HRMS of compound **14**

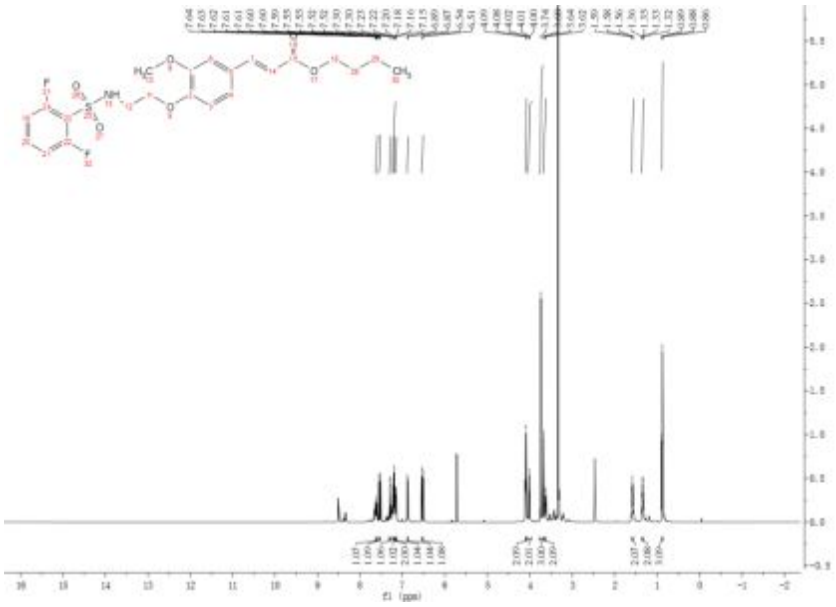


Figure S58 $^{1}$H NMR of compound **15**

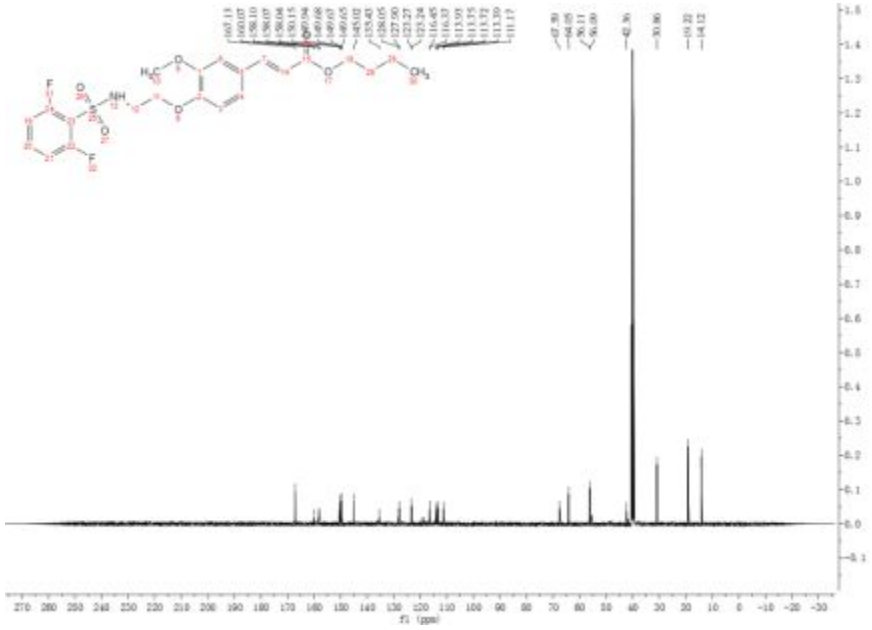


Figure S59 $^{13}$C NMR of compound **15**

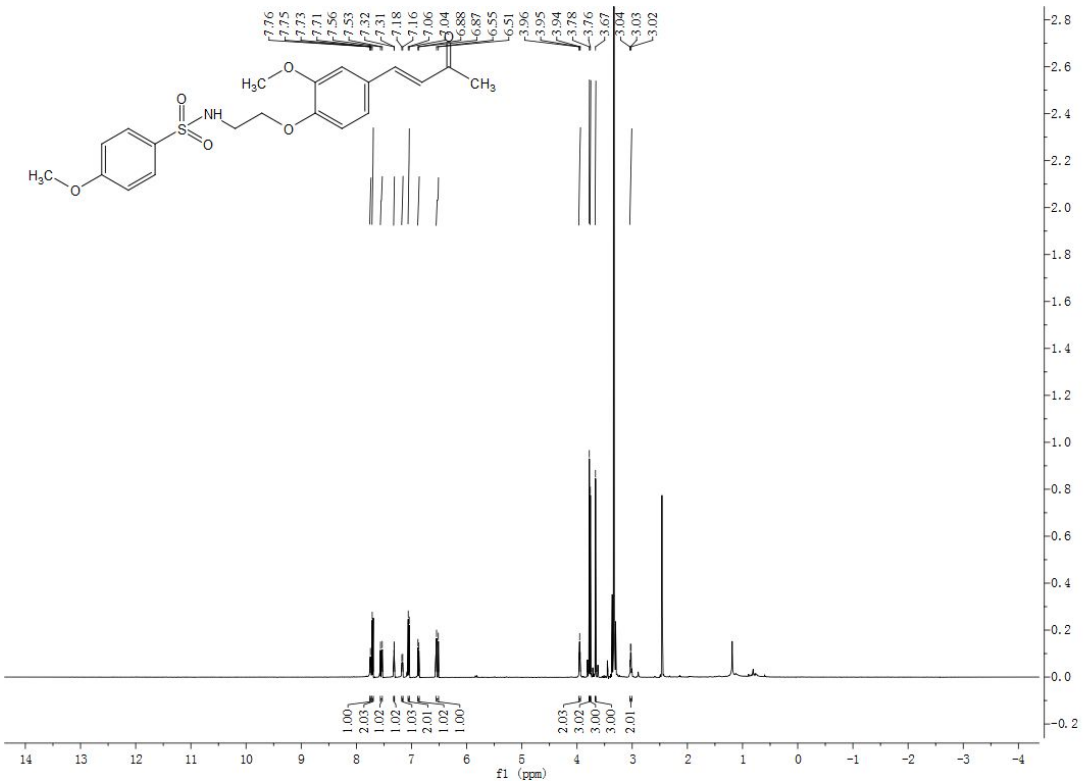


Figure S60 $^{1}$H NMR of compound **16**

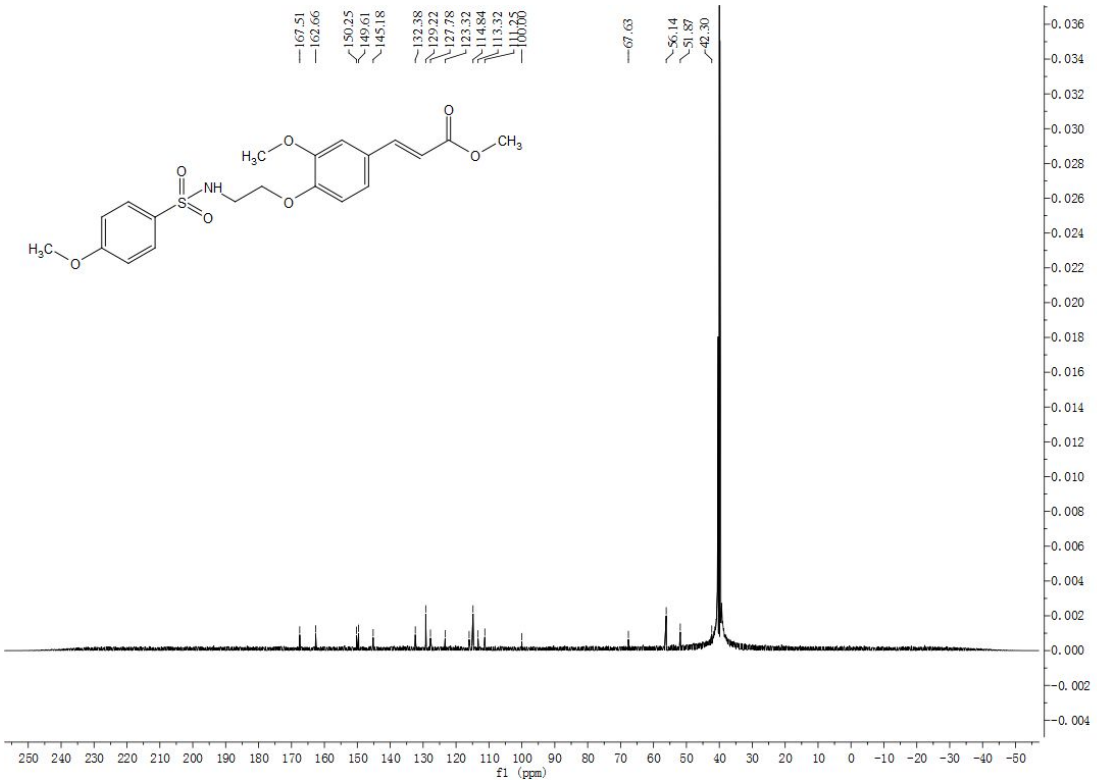



Figure S61 $^{13}C$ NMR of compound **16**

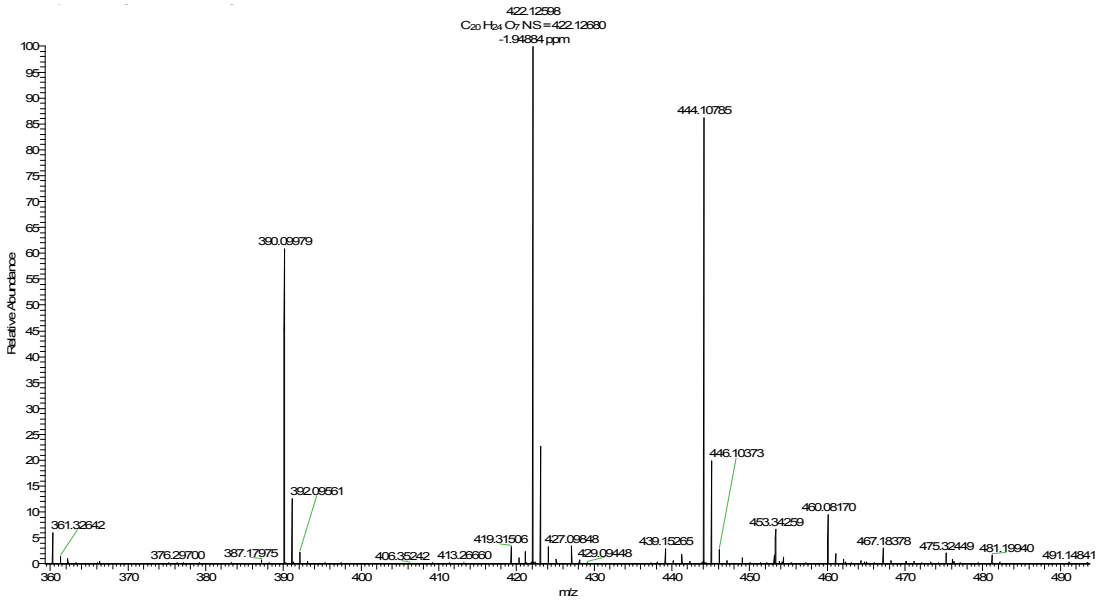



Figure S62 HRMS of compound **16**

## 4. Reference

(1) Wang YY, Xu FZ, Luo DX, Guo, SX, He F, Dai AL, Song BA, Wu J. Synthesis of anthranilic diamide derivatives containing moieties of trifluoromethylpyridine and hydrazone as potential anti-viral agents for plants. *J. Agric. Food Chem.* **2019**, *67*, 13344−13352.

(2) Gooding, GV.; Hebert, TT. Effect of nitrogen and chloride nutrition on susceptibility and effect of fungicide applications on control of fusicoccum canker of peach. *Phytopathology*. **1967**, *57*, 1285−1285.

(3) Khatkar A, Nanda A, Kumar Pand Narasimhan B. Synthesis and antimi-crobial evaluation of ferulic acid derivatives. *Res Chem Intermed*. **2015**, *41*, 299–309.

(4) Bassetto M, Leyssen P, Neyts J, Yerukhimovich MM, Frick DN, Smith MC, Brancale A. In silico identification, design and synthesis of novel piperazine-based anti-HCV agents. *Eur. J. Med. Chem*. **2017**, *125*, 1115-1131.