

# **Discovery of a 4-Hydroxy-3'-Trifluoromethoxy-Substituted Resveratrol Derivative as an Anti-Aging Agent**

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## **Supporting Information**

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### 1. Effects of resveratrol derivatives on *t*-BHP-induced oxidative stress in Raw264.7 cells

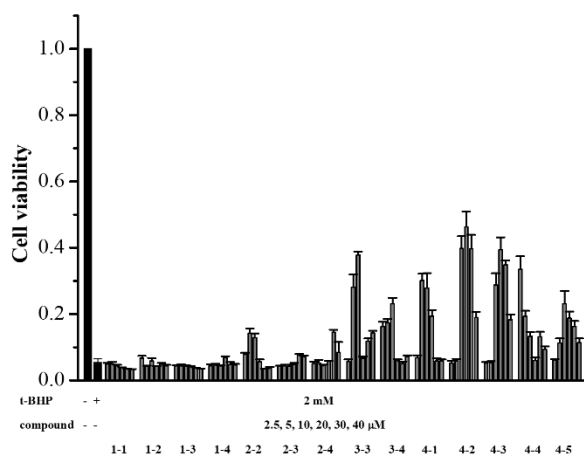


Figure S1. Effects of resveratrol derivatives on *t*-BHP-induced oxidative stress in Raw264.7 cells. Raw264.7 cells were treated with the compound for 24 h, and then induced with 2 mM *t*-BHP for 3 h. Measurement of cytotoxicity using the MTT assay. Data were expressed as means  $\pm$  SD ( $n = 3$ ) from independent experiments.

### 2. Cell viability of resveratrol derivatives in Raw264.7 cells

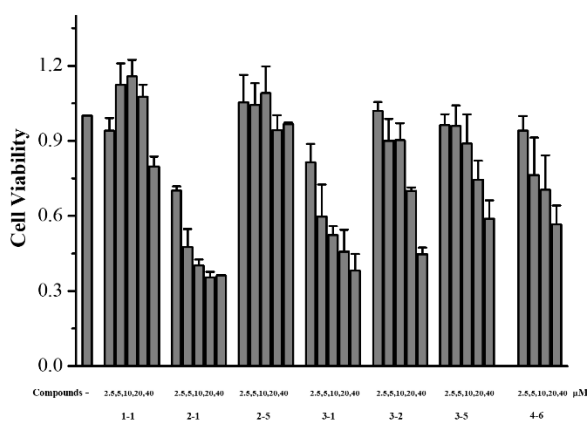


Figure S2. Cell viability of resveratrol derivatives in Raw264.7 cells. Raw264.7 cells were treated with the compound for 24 h. Measurement of cytotoxicity using the MTT assay. Data were expressed as means  $\pm$  SD ( $n = 3$ ) from independent experiments.

### 3. General procedure for the synthesis of resveratrol derivatives

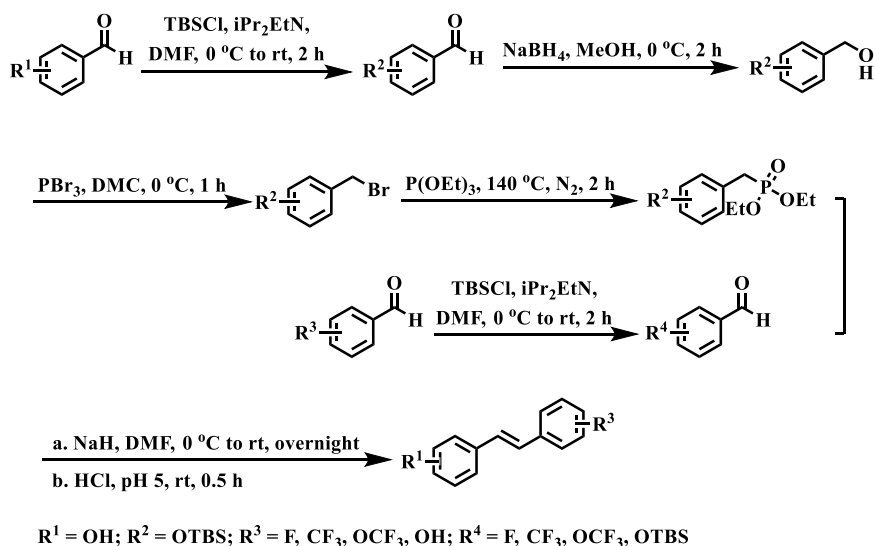


Figure S3. Synthetics routs of resveratrol derivatives.

All chemicals were obtained from Energy Chemical, Tan sole and sigma-aldrich.

Resveratrol derivatives were synthesized from corresponding aldehyde and benzyl phosphonate by the Witting-Horner reaction according to our previously published paper<sup>[1,2]</sup>, and their <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy witnessed previously published work.

Diethyl-(*tert*-butyldimethylsilyloxy)benzyl phosphonates were prepared according to the published procedure<sup>[3,4]</sup>. Briefly, NaH (10 mmol) was added in portions to a solution of diethyl- (*tert*-butyldimethylsilyloxy)benzyl phosphonate (2.6 mmol) in DMF at 0 °C. After 15 min stirring, fluorine-substituted aldehyde (2.0 mmol) in DMF (10 mL) was added dropwise and the reaction mixture was stirred overnight at room temperature under N<sub>2</sub> atmosphere. Then, the reaction was quenched by addition of H<sub>2</sub>O at 0 °C and dilute HCl solution was added to the aqueous solution to adjust the pH to 5. The solution was extracted with ethyl acetate and the organic phase was washed with H<sub>2</sub>O, dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The crude products were purification by column chromatography to afford the pure resveratrol derivatives.

## 2. <sup>1</sup>H NMR, <sup>13</sup>C NMR and <sup>19</sup>F NMR spectra

### 3,5-dihydroxy-4'-fluoro-*trans*-stilbene (**1-2**)<sup>[5]</sup>

<sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta_H$  (ppm): 9.25(s, 2OH), 7.64-7.61 (m, 2H), 7.21 (t,  $J = 8.8$  Hz, 2H), 7.07 (d,  $J = 16.4$  Hz, 1H), 7.02 (d,  $J = 16.4$  Hz, 1H), 6.44 (d,  $J = 2.0$  Hz, 2H), 6.17(t,  $J = 2.0$  Hz, 1H); <sup>13</sup>C-NMR(101 MHz, DMSO-*d*<sub>6</sub>),  $\delta_C$ (ppm): 163.18 (d,  $J_{C-F} = 245.43$  Hz), 158.93, 139.07, 134.04 (d,  $J_{C-F} = 3.03$  Hz), 129.27 (d,  $J_{C-F} = 2.02$  Hz), 128.76 (d,  $J_{C-F} = 8.08$  Hz), 127.05, 116.00 (d,  $J_{C-F} = 22.22$  Hz), 105.06, 102.73; <sup>19</sup>F-NMR(DMSO-*d*<sub>6</sub>),  $\delta_F$ (ppm): -114.51.

3,5-dihydroxy-4'-trifluoromethyl-*trans*-stilbene (**1-3**)<sup>[6]</sup>

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta_H$  (ppm): 7.62 (d,  $J = 8.8$  Hz, 2H), 7.58 (d,  $J = 8.8$  Hz, 2H), 7.05 (s, 2H), 6.60 (d,  $J = 2.0$  Hz, 2H), 6.32 (t,  $J = 2.0$  Hz, 1H); <sup>13</sup>C-NMR (101 MHz, DMSO-*d*<sub>6</sub>),  $\delta_C$  (ppm): 158.53, 141.17 (d,  $J = 1.31$  Hz), 138.12, 131.85, 126.91, 126.25, 125.42 (d,  $J = 3.54$  Hz), 105.01, 102.90; <sup>19</sup>F-NMR (DMSO-*d*<sub>6</sub>),  $\delta_F$  (ppm): -60.84.

3,5-dihydroxy-4'-trifluoromethoxy-*trans*-stilbene (**1-4**)<sup>[7]</sup>

<sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta_H$  (ppm): 9.29 (s, 2OH), 7.71 (d,  $J = 8.8$  Hz, 2H), 7.35 (d,  $J = 8.00$  Hz, 2H), 7.09 (s, 2H), 6.46 (d,  $J = 2.0$  Hz, 2H), 6.19 (t,  $J = 2.0$  Hz, 1H); <sup>13</sup>C-NMR (101 MHz, DMSO-*d*<sub>6</sub>),  $\delta_C$  (ppm): 158.97, 147.84 (d,  $J_{C-F} = 1.72$  Hz), 138.84, 136.93, 130.67, 128.51, 126.69, 121.64, 119.23, 105.24, 103.00; <sup>19</sup>F-NMR (DMSO-*d*<sub>6</sub>),  $\delta_F$  (ppm): -56.83.

4,4'-dihydroxy-*trans*-stilbene (**2-1**)<sup>[8]</sup>

<sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta_H$  (ppm): 9.47 (s, 2OH), 7.37 (d,  $J = 8.0$  Hz, 4H), 6.90 (s, 2H), 6.77 (d,  $J = 8.4$  Hz, 4H); <sup>13</sup>C-NMR (101 MHz, DMSO-*d*<sub>6</sub>),  $\delta_C$  (ppm): 157.20, 129.03, 127.78, 125.64, 115.94.

4-hydroxy-4'-fluoro-*trans*-stilbene (**2-2**)<sup>[9]</sup>

<sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta_H$  (ppm): 9.59 (s, 1OH), 7.59 (dd,  $J = 5.6$  and  $8.8$  Hz, 2H), 7.42 (d,  $J = 8.8$  Hz, 2H), 7.19 (t,  $J = 8.8$  Hz, 2H), 7.11 (d,  $J = 16.4$  Hz, 1H), 7.03 (d,  $J = 16.8$  Hz, 1H), 6.79 (d,  $J = 8.8$  Hz, 2H); <sup>13</sup>C-NMR (101 MHz, DMSO-*d*<sub>6</sub>),  $\delta_C$  (ppm): 162.86 (d,  $J = 244.82$  Hz), 157.70, 134.55 (d,  $J = 3.13$  Hz), 128.77 (d,  $J = 2.32$  Hz), 128.40, 128.22, 128.14, 124.30, 115.96 (d,  $J = 21.51$  Hz), 115.75; <sup>19</sup>F-NMR (DMSO-*d*<sub>6</sub>),  $\delta_F$  (ppm): -115.29.

4-hydroxy-4'-trifluoromethyl-*trans*-stilbene (**2-3**)<sup>[8]</sup>

<sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta_H$  (ppm): 9.66 (s, 1OH), 7.74 (d,  $J = 8.4$  Hz, 2H), 7.67 (d,  $J = 8.4$  Hz, 2H), 7.47 (d,  $J = 8.4$  Hz, 2H), 7.32 (d,  $J = 16.4$  Hz, 1H), 7.11 (d,  $J = 16.4$  Hz, 1H), 6.79 (d,  $J = 8.4$  Hz, 2H); <sup>13</sup>C-NMR (101 MHz, DMSO-*d*<sub>6</sub>),  $\delta_C$  (ppm): 158.29, 142.14, 131.78, 128.77, 127.92, 126.85, 125.92 (q,  $J = 3.84$  Hz), 123.85, 116.02; <sup>19</sup>F-NMR (DMSO-*d*<sub>6</sub>),  $\delta_F$  (ppm): -60.76.

4-hydroxy-4'-trifluoromethoxy-*trans*-stilbene (**2-4**)<sup>[7]</sup>

<sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>),  $\delta_H$  (ppm): 9.65 (s, 1OH), 7.64 (d,  $J = 8.8$  Hz, 2H), 7.43 (d,  $J = 8.4$  Hz, 2H), 7.31 (d,  $J = 8.0$  Hz, 2H), 7.18 (d,  $J = 16.4$  Hz, 1H), 7.05 (d,  $J = 16.4$  Hz, 1H), 6.78 (d,  $J = 8.4$  Hz, 2H); <sup>13</sup>C-NMR (101 MHz, DMSO-*d*<sub>6</sub>),  $\delta_C$  (ppm):

158.02, 147.46(d,  $J = 1.72$  Hz), 137.48, 130.18, 128.51, 128.19, 128.00, 123.89, 121.71, 119.28, 116.01;  $^{19}\text{F}$ -NMR(DMSO- $d_6$ ),  $\delta_F$ (ppm): -56.89.

4-hydroxy-*trans*-stilbene (**2-5**)<sup>[8]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.60(s, 1OH), 7.55(d,  $J = 7.2$  Hz, 2H), 7.45(d,  $J = 8.8$  Hz, 2H), 7.37(t,  $J = 7.6$  Hz, 2H), 7.24(t,  $J = 7.2$  Hz, 1H), 7.17(d,  $J = 16.8$  Hz, 1H), 7.04(d,  $J = 16.4$  Hz, 1H), 6.80(d,  $J = 8.4$  Hz, 2H);  $^{13}\text{C}$ -NMR (101 MHz, DMSO- $d_6$ ),  $\delta_C$  (ppm): 157.77, 137.97, 129.06, 128.88, 128.50, 128.32, 127.39, 126.46, 125.51, 116.00.

3,4,4'-trihydroxy-*trans*-stilbene (**3-1**)<sup>[10]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.43(s, 1OH), 8.92(s, 2OH), 7.36(d,  $J = 8.4$  Hz, 2H), 6.93(s, 1H), 6.81-6.79(m, 3H), 6.75-6.70(m, 3H);  $^{13}\text{C}$ -NMR (101 MHz, DMSO- $d_6$ ),  $\delta_C$  (ppm): 157.15, 145.80, 145.44, 129.60, 129.02, 127.77, 126.00, 125.51, 118.45, 116.14, 115.90, 113.39.

3,4-dihydroxy-4'-fluoro-*trans*-stilbene (**3-2**)<sup>[11]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.048(s, 2OH), 7.59(dd,  $J = 5.6$  and  $8.4$  Hz, 2H), 7.18(t,  $J = 8.8$  Hz, 2H), 7.04-6.99(m, 2H), 6.93(d,  $J = 16.4$  Hz, 1H), 6.87(dd,  $J = 1.6$  and  $8.4$  Hz, 1H), 6.74(d,  $J = 8.0$  Hz, 1H);  $^{13}\text{C}$ -NMR(101 MHz, DMSO- $d_6$ ),  $\delta_C$ (ppm): 162.82(d,  $J = 244.72$  Hz), 145.99, 145.80, 134.54(d,  $J = 3.13$  Hz), 129.14(d,  $J = 2.32$  Hz), 128.95, 128.22(d,  $J = 7.88$  Hz), 124.17, 118.92, 116.08, 115.92(d,  $J = 21.41$  Hz), 113.71;  $^{19}\text{F}$ -NMR(DMSO- $d_6$ ),  $\delta_F$ (ppm): -110.62.

3,4-dihydroxy-4'-trifluoromethyl-*trans*-stilbene (**3-3**)<sup>[11]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.21(s, 1OH), 8.99(s, 1OH), 7.76(d,  $J = 8.0$  Hz, 2H), 7.68(d,  $J = 8.4$  Hz, 2H), 7.26(d,  $J = 16.4$  Hz, 1H), 7.04(d,  $J = 2.0$  Hz, 1H), 7.03(d,  $J = 16.4$  Hz, 1H), 6.94(dd,  $J = 2.0$  and  $8.0$  Hz, 1H), 6.76(d,  $J = 8.4$  Hz, 1H);  $^{13}\text{C}$ -NMR(101 MHz, DMSO- $d_6$ ),  $\delta_C$ (ppm): 146.20, 145.43, 141.72(d,  $J = 1.21$  Hz), 131.75, 128.04, 126.42, 125.40(d,  $J = 3.64$  Hz), 123.29, 119.12, 115.68, 113.65;  $^{19}\text{F}$ -NMR(DMSO- $d_6$ ),  $\delta_F$ (ppm): -60.76.

3,4-dihydroxy-4'-trifluoromethoxy-*trans*-stilbene (**3-4**)<sup>[7]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.18(s, 1OH), 8.98(s, 1OH), 7.66(d,  $J = 8.8$ Hz, 2H), 7.33(d,  $J = 8.4$  Hz, 2H), 7.12(d,  $J = 16.4$  Hz, 1H), 7.01(d,  $J = 2.0$  Hz, 1H), 6.97(d,  $J = 16.4$  Hz, 1H), 6.89(dd,  $J = 2.0$  and  $8.0$  Hz, 1H), 6.75(d,  $J = 8.0$  Hz, 1H);  $^{13}\text{C}$ -NMR(101 MHz, DMSO- $d_6$ ),  $\delta_C$ (ppm): 147.38(d,  $J = 1.62$  Hz), 146.27, 145.82,

137.44, 130.54, 128.71, 127.97, 123.74, 121.60, 119.19, 116.09, 113.87;  $^{19}\text{F}$ -NMR(DMSO- $d_6$ ),  $\delta_F$ (ppm): -56.84.

3,4-dihydroxy-*trans*-stilbene (**3-5**)<sup>[8]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.06(s, 2OH), 7.54(d,  $J = 7.6$  Hz, 2H), 7.35(t,  $J = 7.6$  Hz, 2H), 7.23(t,  $J = 7.2$  Hz, 1H), 7.09(d,  $J = 16.4$  Hz, 1H), 7.01(d,  $J = 2.4$  Hz, 1H), 6.94(d,  $J = 16.4$  Hz, 1H), 6.89(dd,  $J = 2.0$  and 8.1 Hz, 1H), 6.75(d,  $J = 8.4$  Hz, 1H);  $^{13}\text{C}$ -NMR (101 MHz, DMSO- $d_6$ ),  $\delta_C$  (ppm): 146.01, 145.81, 137.90, 129.19, 128.99, 127.29, 126.41, 125.33, 118.99, 116.10, 113.73.

4-hydroxy-2'-fluoro-*trans*-stilbene (**4-1**)<sup>[9]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.66(s, 1OH), 7.75(t,  $J = 8.0$  Hz, 1H), 7.46(d,  $J = 8.8$  Hz, 2H), 7.28-7.17(m, 4H), 7.08(d,  $J = 16.8$  Hz, 1H), 6.80(d,  $J = 8.8$  Hz, 2H);  $^{13}\text{C}$ -NMR (101 MHz, DMSO- $d_6$ ),  $\delta_C$  (ppm): 161.07(d,  $J = 247.85$  Hz), 158.08, 131.59(d,  $J = 4.55$  Hz), 128.93(d,  $J = 8.38$  Hz), 128.50, 128.19, 127.36(d,  $J = 3.64$  Hz), 125.51(d,  $J = 11.82$  Hz), 125.01(d,  $J = 3.33$  Hz), 117.07(d,  $J = 3.54$  Hz), 116.15(d,  $J = 22.02$  Hz), 115.99;  $^{19}\text{F}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_F$  (ppm): -118.80.

4-hydroxy-2'-trifluoromethyl-*trans*-stilbene (**4-2**)<sup>[1]</sup>

$^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta_H$  (ppm): 7.77(d,  $J = 8.0$  Hz, 1H), 7.67(d,  $J = 7.6$  Hz, 1H), 7.54(t,  $J = 7.2$  Hz, 1H), 7.45(d,  $J = 8.8$  Hz, 2H), 7.36-7.31(m, 2H), 7.05(d,  $J = 16$  Hz, 1H), 6.87(d,  $J = 8.4$  Hz, 2H);  $^{13}\text{C}$ -NMR(101 MHz,  $\text{CDCl}_3$ ),  $\delta_C$ (ppm): 155.66, 136.65, 132.00, 131.81, 129.96, 128.40, 127.41(d,  $J = 29.80$  Hz), 126.82, 126.72, 125.97(q,  $J = 5.76$  Hz), 123.12, 122.31(d,  $J = 1.82$  Hz), 115.675;  $^{19}\text{F}$ -NMR( $\text{CDCl}_3$ ),  $\delta_F$ (ppm): -59.39.

4-hydroxy-2'-trifluoromethoxy-*trans*-stilbene (**4-3**)<sup>[1]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.72(s, 1OH), 7.94(d,  $J = 8.0$  Hz, 1H), 7.70(d,  $J = 8.0$  Hz, 1H), 7.66(t,  $J = 7.6$  Hz, 1H), 7.43-7.40(m, 3H), 7.25(d,  $J = 16$  Hz, 1H), 7.15(dd,  $J = 16.0$  and 2.0 Hz, 1H), 6.81(d,  $J = 8.4$  Hz, 2H);  $^{13}\text{C}$ -NMR(101 MHz, DMSO- $d_6$ ),  $\delta_C$ (ppm): 158.49, 136.59, 133.57, 133.09, 128.76, 127.88, 127.59, 127.27, 126.24(q,  $J = 5.86$  Hz), 125.99(d,  $J = 26.36$  Hz), 123.65, 119.98(d,  $J = 1.72$  Hz), 116.19;  $^{19}\text{F}$ -NMR(DMSO- $d_6$ ),  $\delta_F$ (ppm): -58.09.

4-hydroxy-3'-fluoro-*trans*-stilbene (**4-4**)<sup>[12]</sup>

$^1\text{H}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_H$  (ppm): 9.65(s, 1OH), 7.44(d,  $J = 8.4$  Hz, 2H), 7.41-7.35(m, 3H), 7.25(d,  $J = 16.4$  Hz, 1H), 7.05-7.00(m, 2H), 6.80(d,  $J = 8.4$  Hz, 2H);  $^{13}\text{C}$ -NMR (101 MHz, DMSO- $d_6$ ),  $\delta_C$  (ppm): 164.23(d,  $J = 243.41$  Hz), 158.00, 140.76(d,  $J$

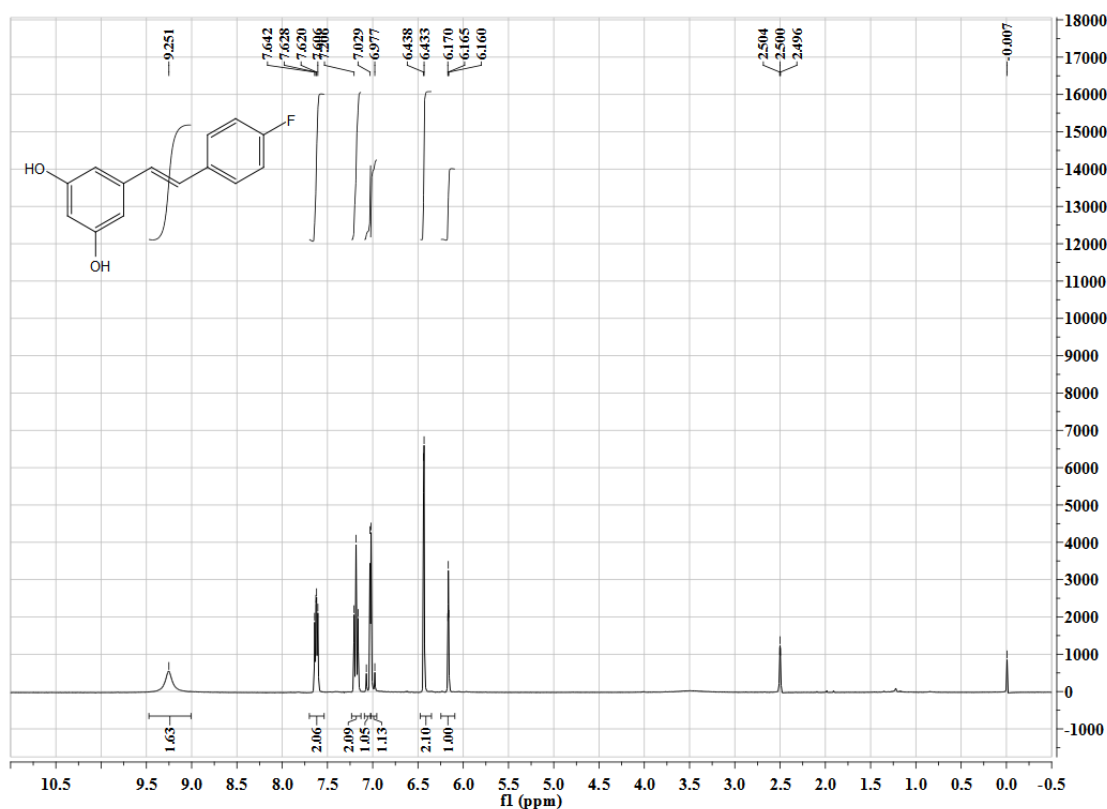
= 8.08 Hz), 130.86(d,  $J = 8.08$  Hz), 130.43, 128.49, 128.08, 124.23(d,  $J = 3.03$ ), 122.79(d,  $J = 2.02$  Hz), 115.97, 113.98(d,  $J = 21.21$  Hz), 112.50(d,  $J = 22.22$  Hz);  $^{19}\text{F}$ -NMR (400 MHz, DMSO- $d_6$ ),  $\delta_F$  (ppm): -113.53.

4-hydroxy-3'-trifluoromethyl-*trans*-stilbene (**4-5**)<sup>[13]</sup>

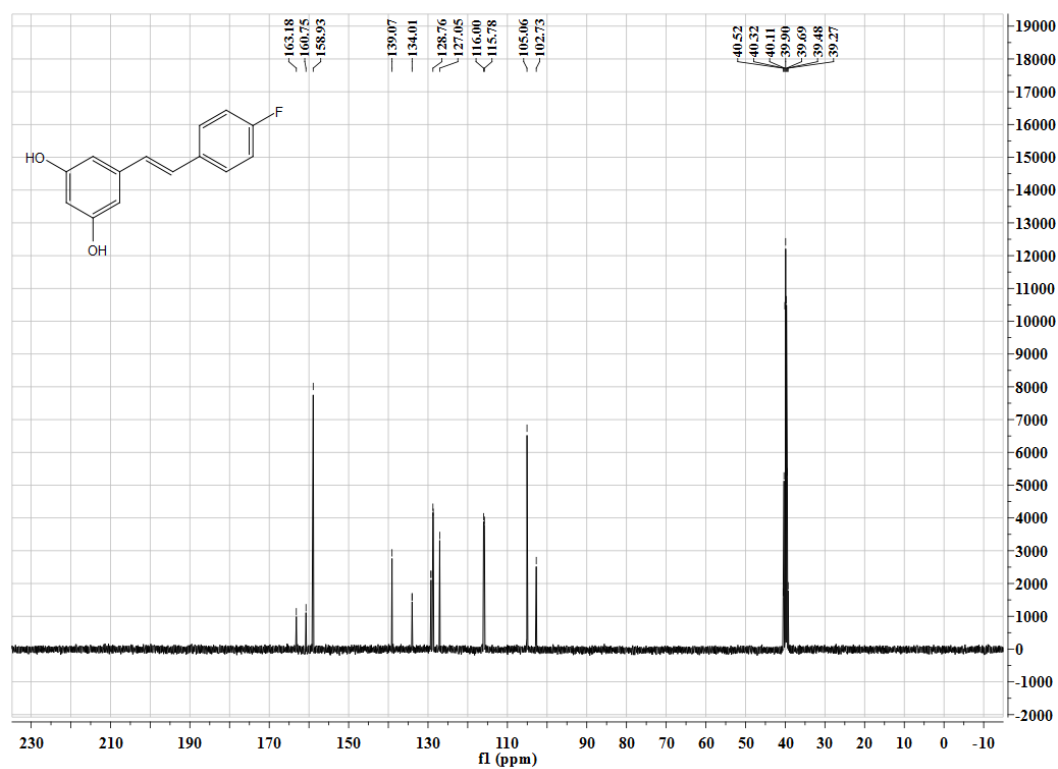
$^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta_H$  (ppm): 7.71(s, 1H), 7.63(d,  $J = 7.2$  Hz, 1H), 7.48-7.41(m, 4H), 7.12(d,  $J = 16.4$  Hz, 1H), 6.98(d,  $J = 16.0$  Hz, 1H), 6.85(d,  $J = 8.8$  Hz, 2H);  $^{13}\text{C}$ -NMR(101 MHz,  $\text{CDCl}_3$ ),  $\delta_C$ (ppm): 155.57, 138.37, 131.52(q,  $J = 32.02$ ), 129.91, 129.77, 129.29, 129.04, 128.17, 125.52, 125.12, 123.70(q,  $J = 3.74$ ), 122.85(q,  $J = 3.74$ ), 115.71;  $^{19}\text{F}$ -NMR( $\text{CDCl}_3$ ),  $\delta_F$ (ppm): -62.78.

4-hydroxy-3'-trifluoromethoxy-*trans*-stilbene (**4-6**)<sup>[14]</sup>

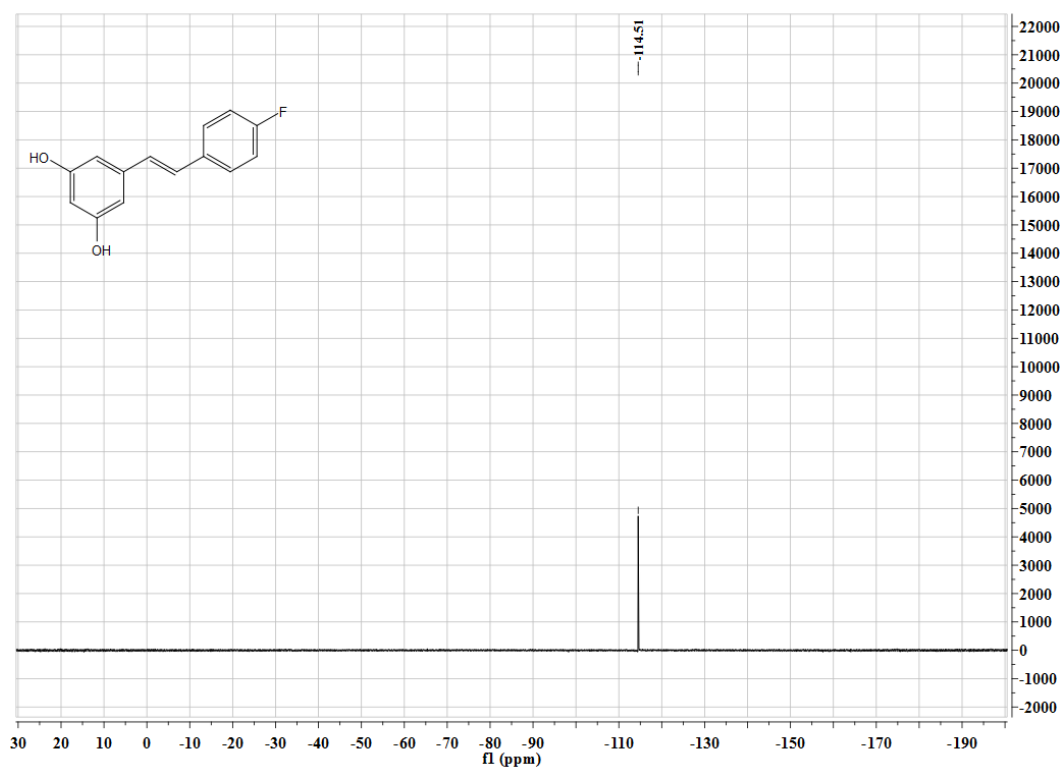
$^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta_H$  (ppm): 7.42-7.37(m, 3H), 7.35-7.32(m, 2H), 7.08-7.04(m, 2H), 6.95(d,  $J = 16.0$  Hz, 1H), 6.85(d,  $J = 8.8$  Hz, 2H);  $^{13}\text{C}$ -NMR(101 MHz,  $\text{CDCl}_3$ ),  $\delta_C$ (ppm): 155.66, 149.68, 139.80, 129.86(d,  $J = 2.22$  Hz), 129.68, 128.15, 125.08, 124.61, 121.78, 119.34, 118.38, 115.70;  $^{19}\text{F}$ -NMR( $\text{CDCl}_3$ ),  $\delta_F$ (ppm): 57.68.



(up)  $^1\text{H}$  NMR spectrum of compound **1-2** (400 MHz, DMSO- $d_6$ )

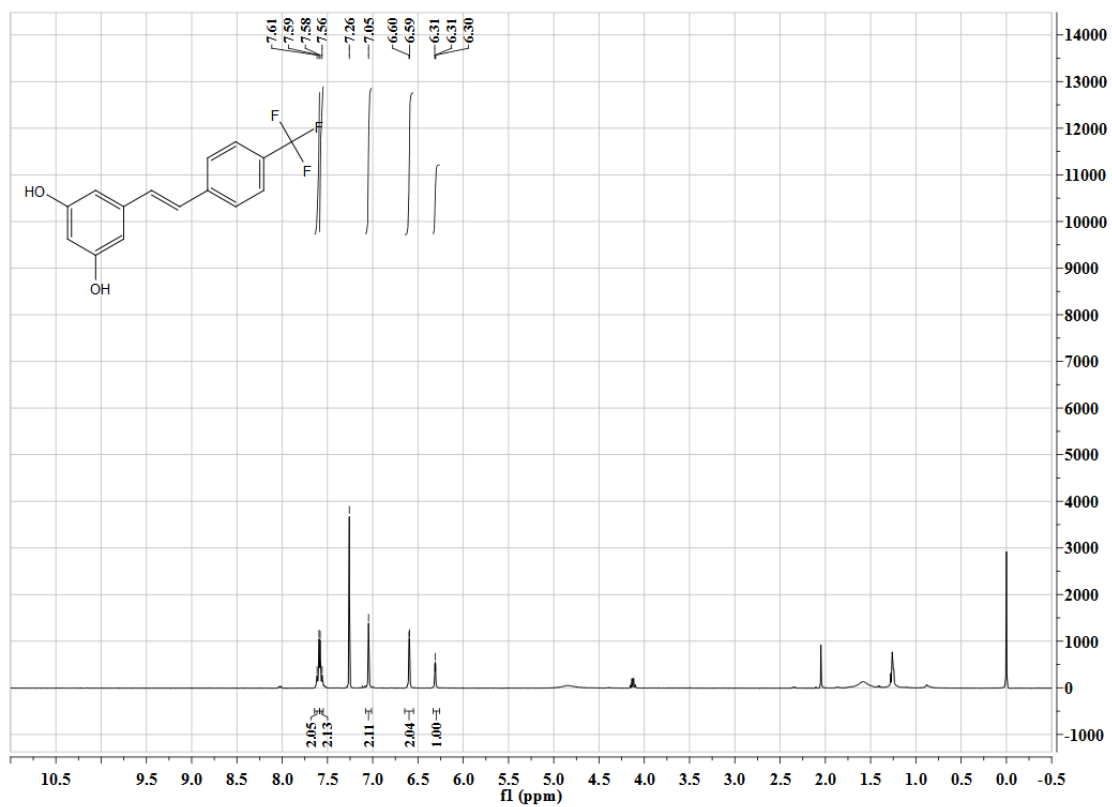


(up) <sup>13</sup>C NMR spectrum of compound **1-2** (101 MHz, DMSO-*d*<sub>6</sub>)

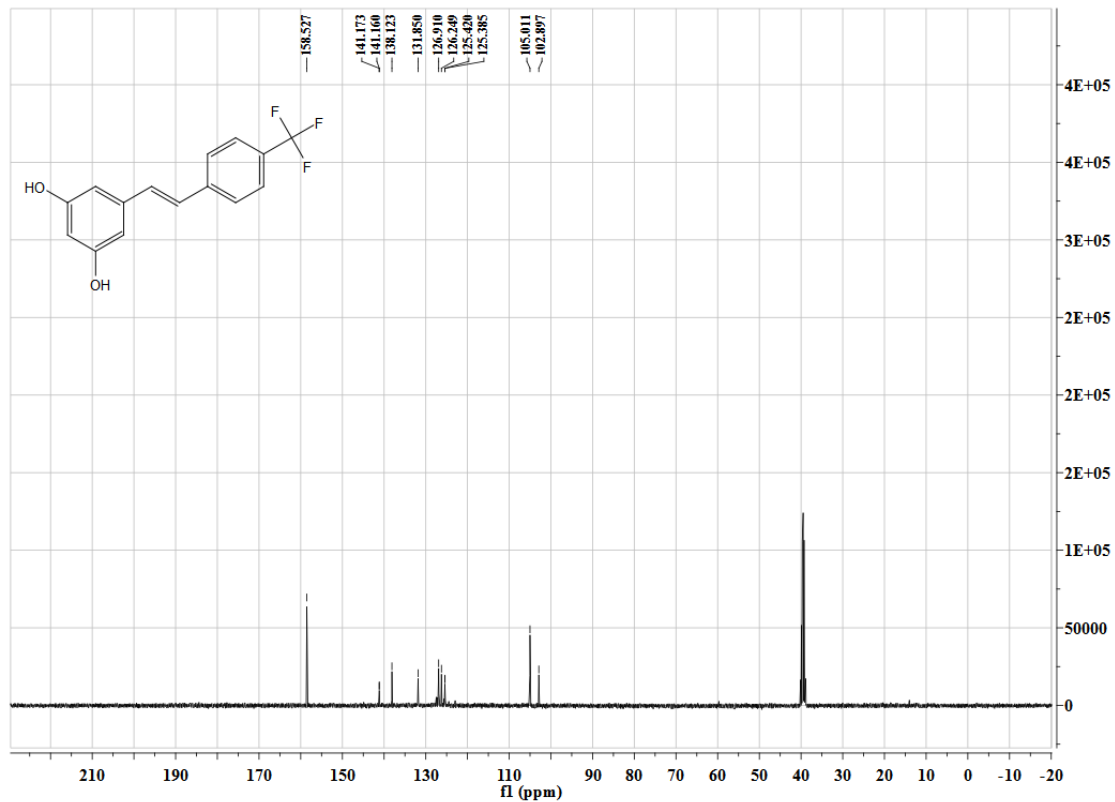


(up) <sup>19</sup>F NMR spectrum of compound **1-2** (400 MHz, DMSO-*d*<sub>6</sub>)

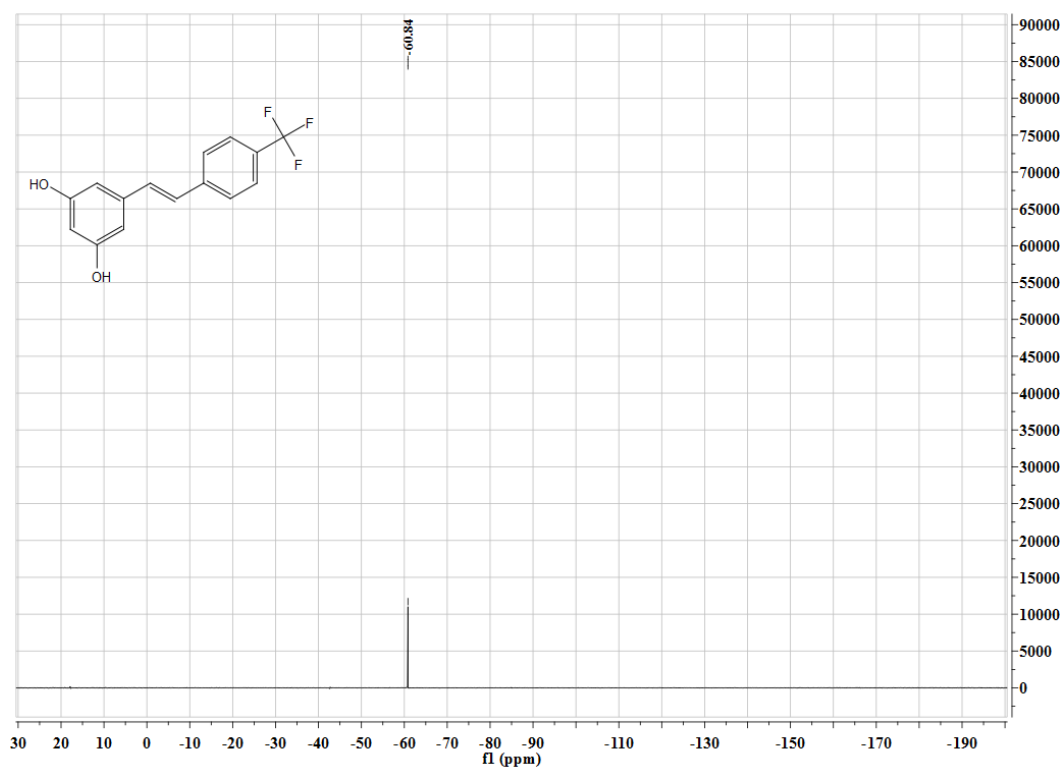




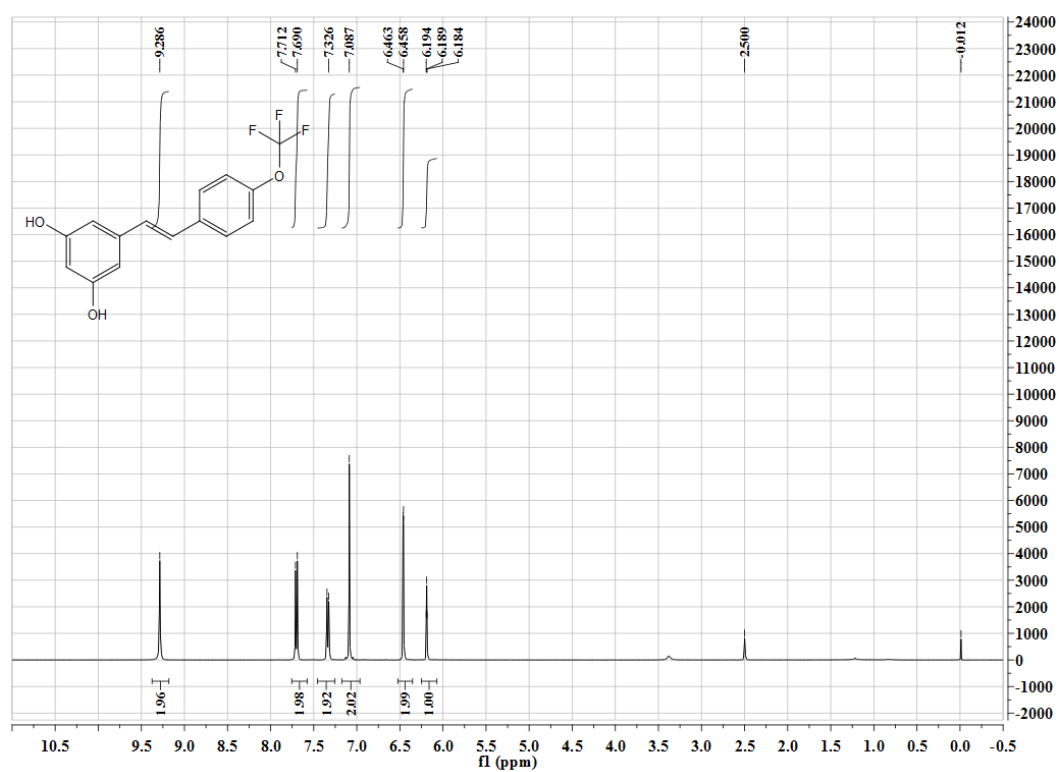
(up) <sup>1</sup>H NMR spectrum of compound **1-3** (400 MHz, CDCl<sub>3</sub>)



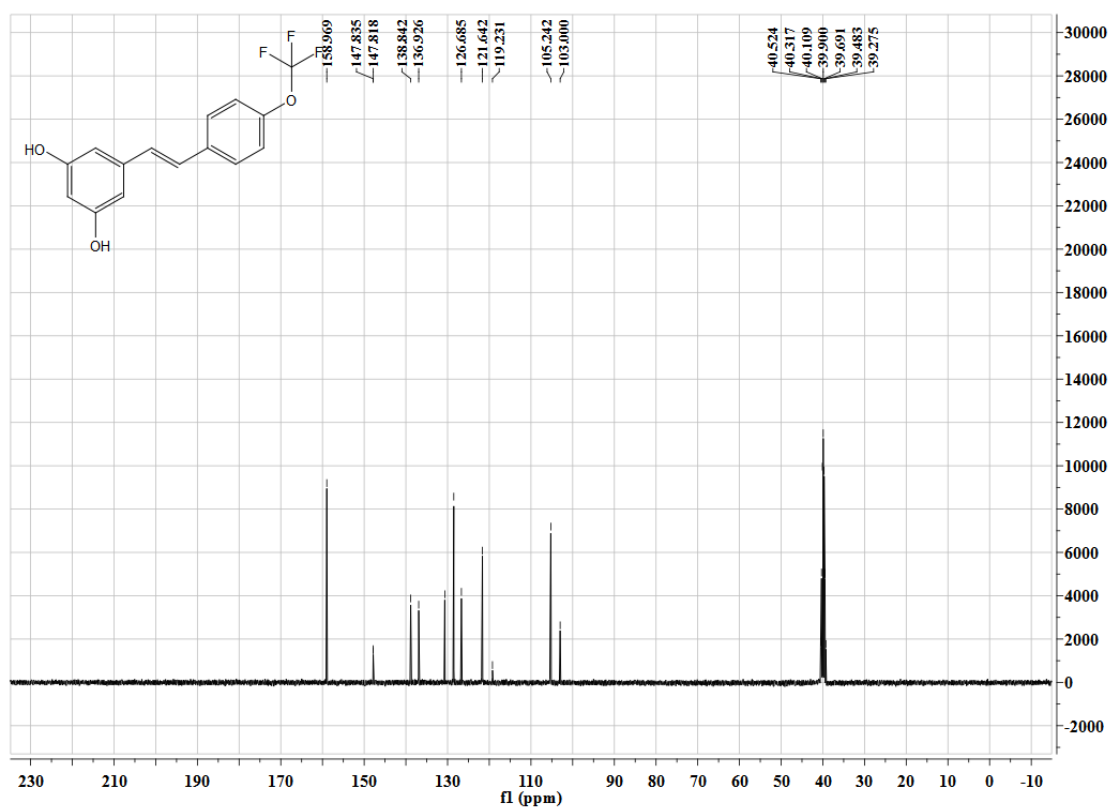
(up) <sup>13</sup>C NMR spectrum of compound **1-3** (101 MHz, DMSO-*d*<sub>6</sub>)



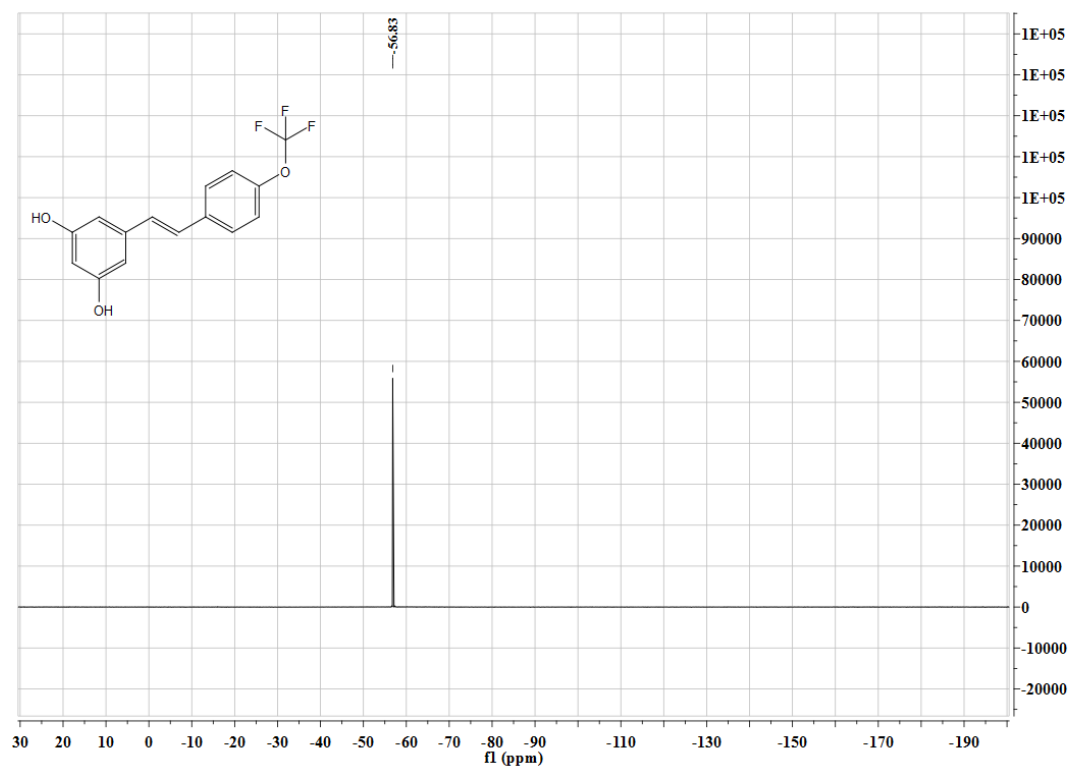
(up)  $^{19}\text{F}$  NMR spectrum of compound **1-3** (400 MHz,  $\text{DMSO}-d_6$ )



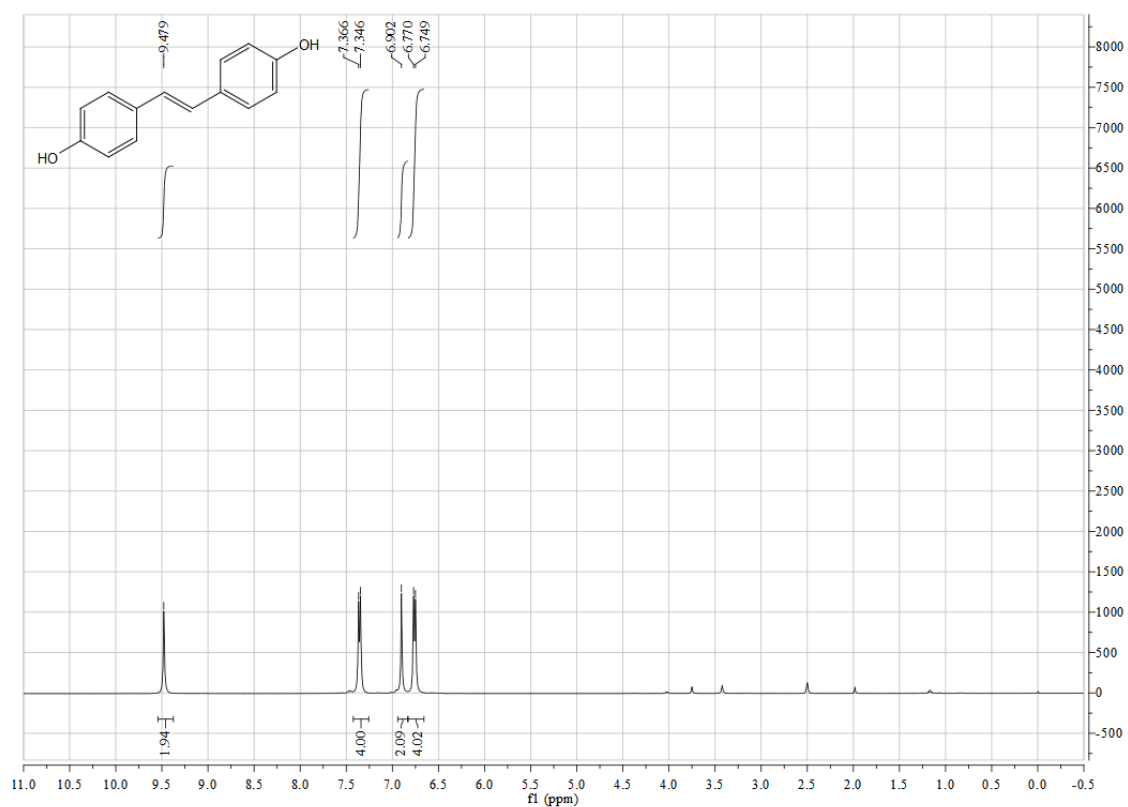
(up)  $^1\text{H}$  NMR spectrum of compound **1-4** (400 MHz,  $\text{DMSO}-d_6$ )



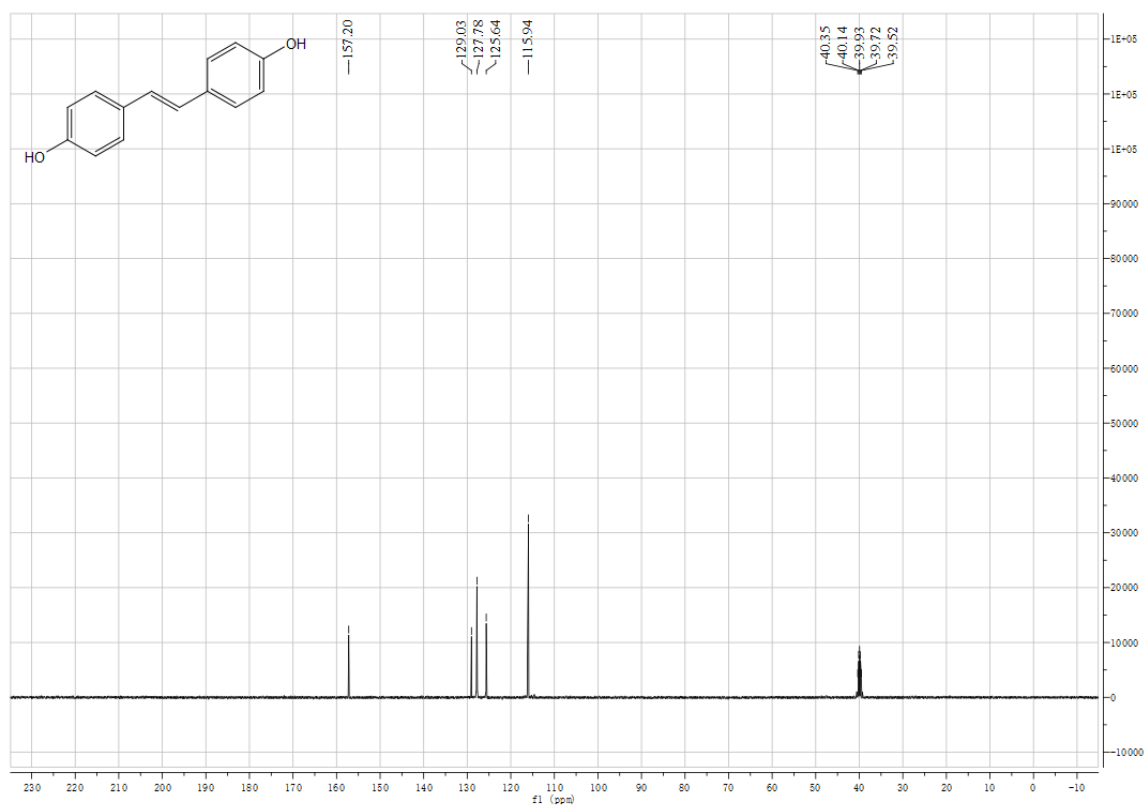
(up) <sup>13</sup>C NMR spectrum of compound **1-4** (101 MHz, DMSO-*d*<sub>6</sub>)



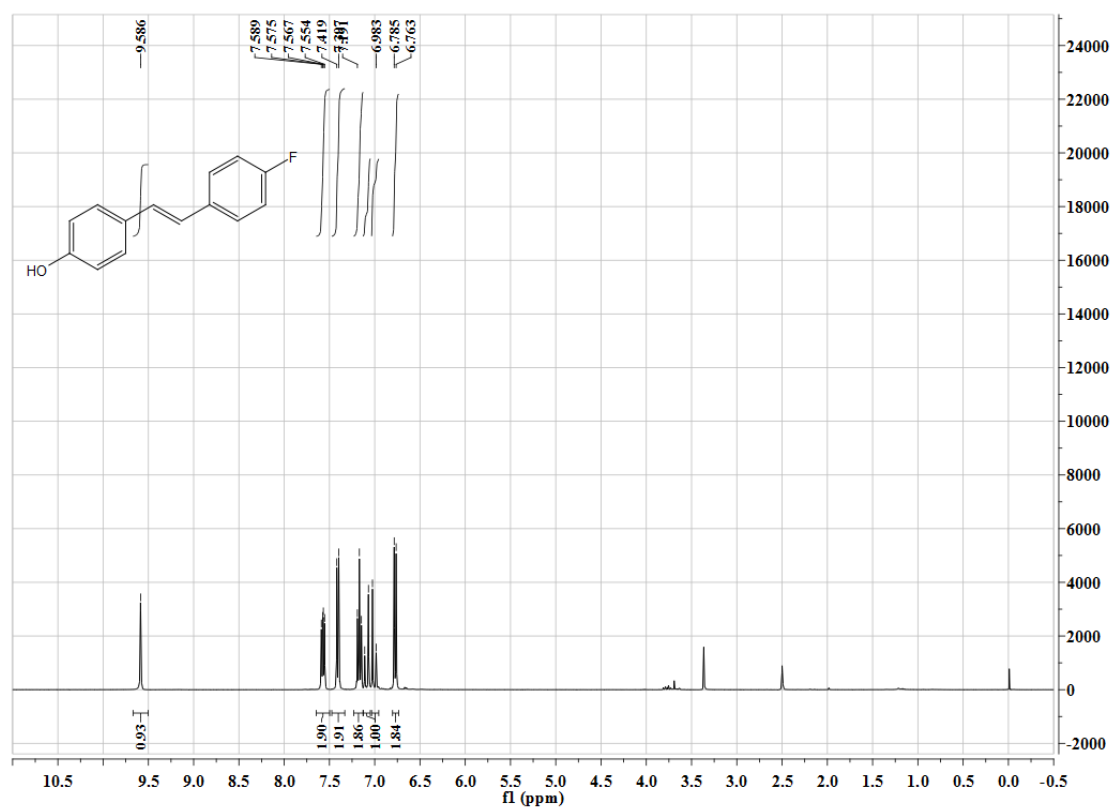
(up) <sup>19</sup>F NMR spectrum of compound **1-4** (400 MHz, DMSO-*d*<sub>6</sub>)



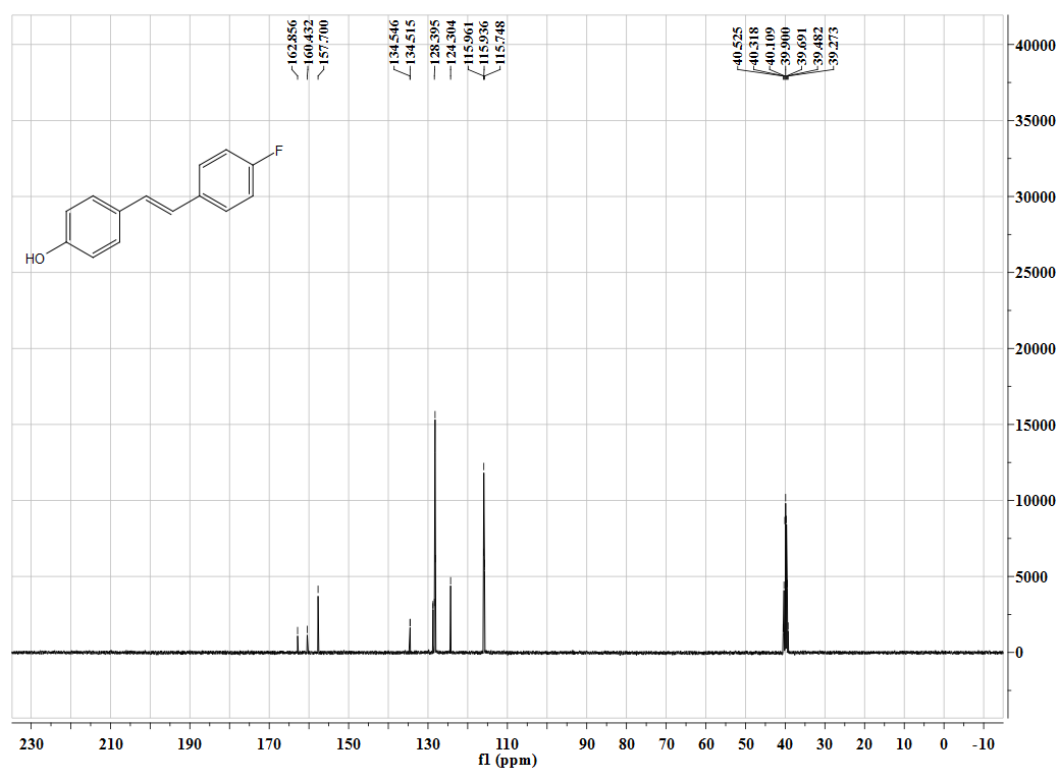
(up) <sup>1</sup>H NMR spectrum of compound **2-1** (400 MHz, DMSO-*d*<sub>6</sub>)



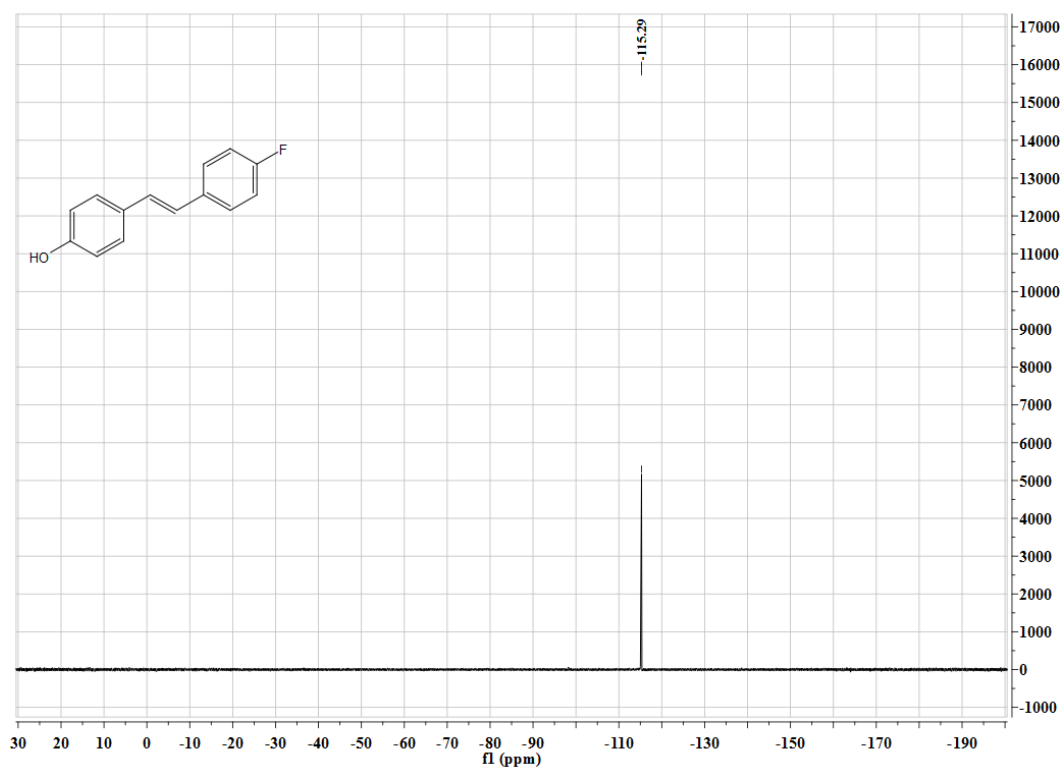
(up) <sup>13</sup>C NMR spectrum of compound **2-1** (101 MHz, DMSO-*d*<sub>6</sub>)



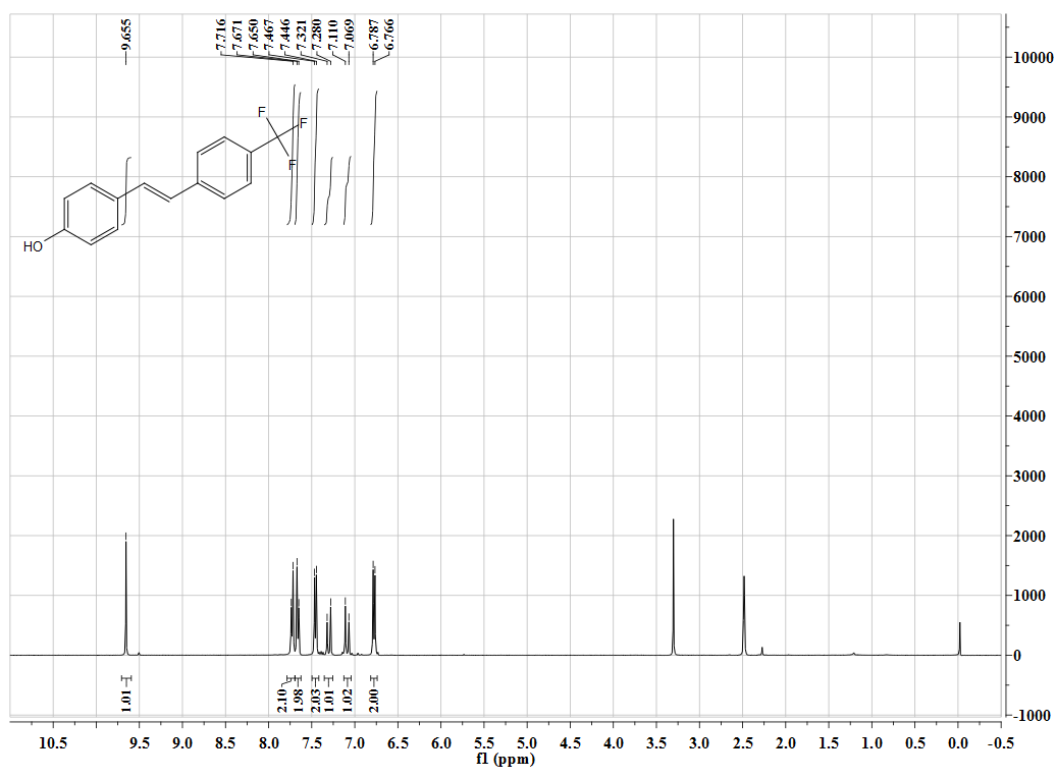
(up) <sup>1</sup>H NMR spectrum of compound **2-2** (400 MHz, DMSO-*d*<sub>6</sub>)



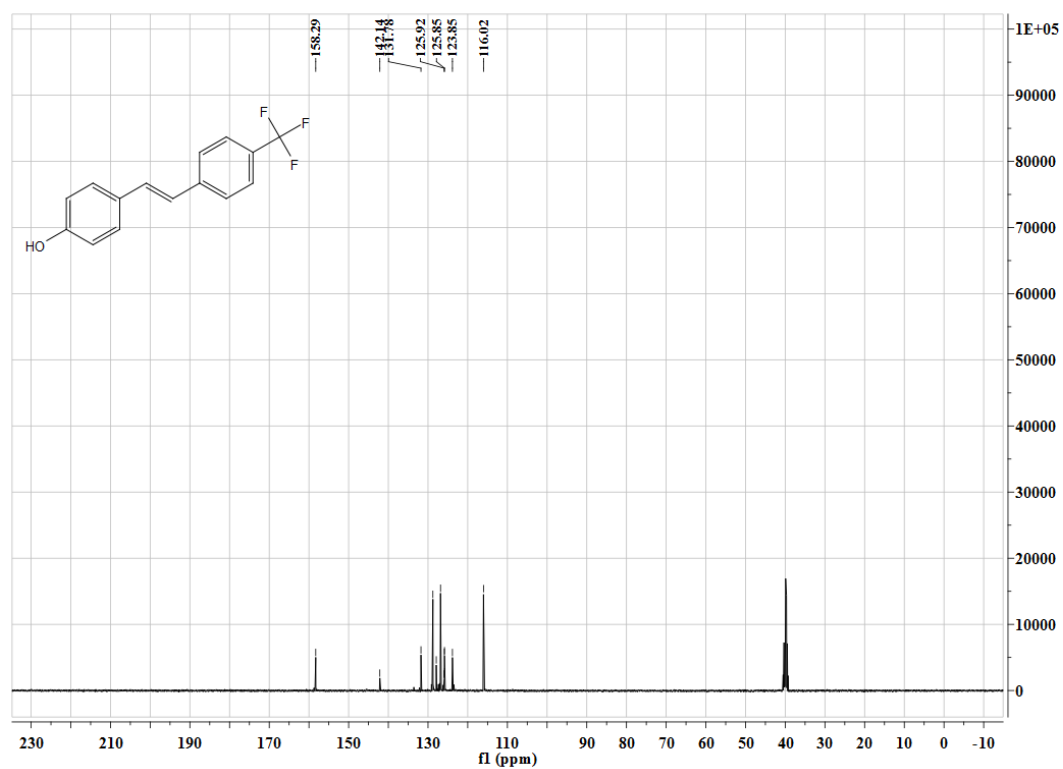
(up) <sup>13</sup>C NMR spectrum of compound **2-2** (101 MHz, DMSO-*d*<sub>6</sub>)



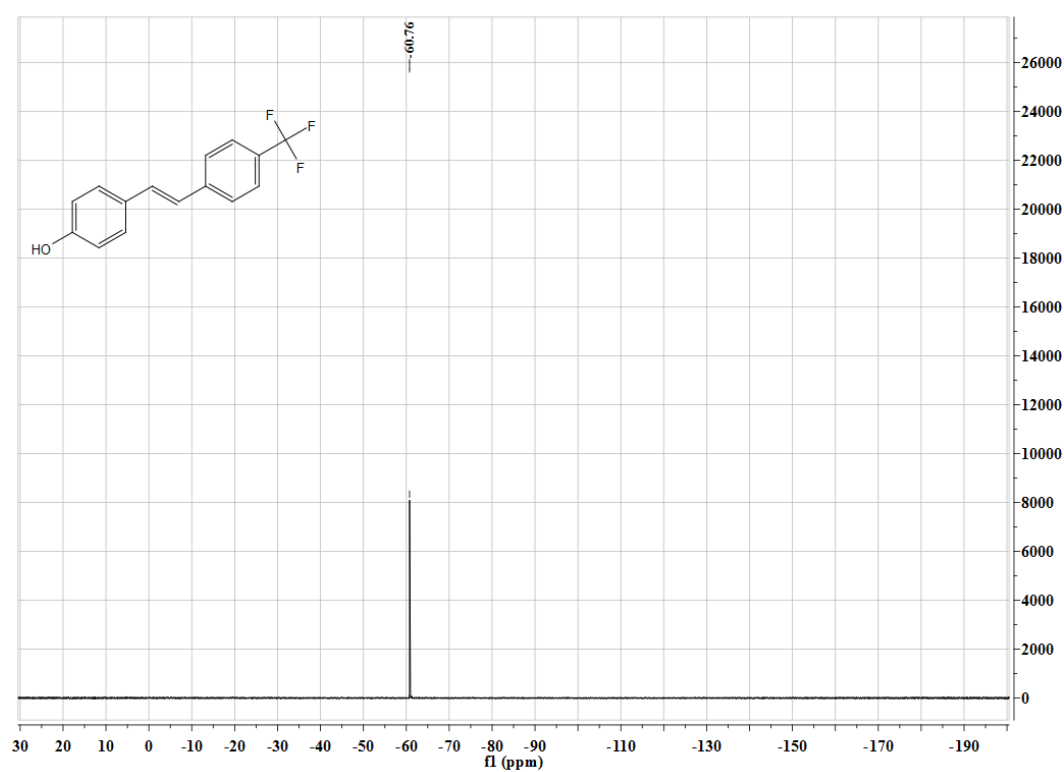
(up)  $^{19}\text{F}$  NMR spectrum of compound **2-2** (400 MHz,  $\text{DMSO-}d_6$ )



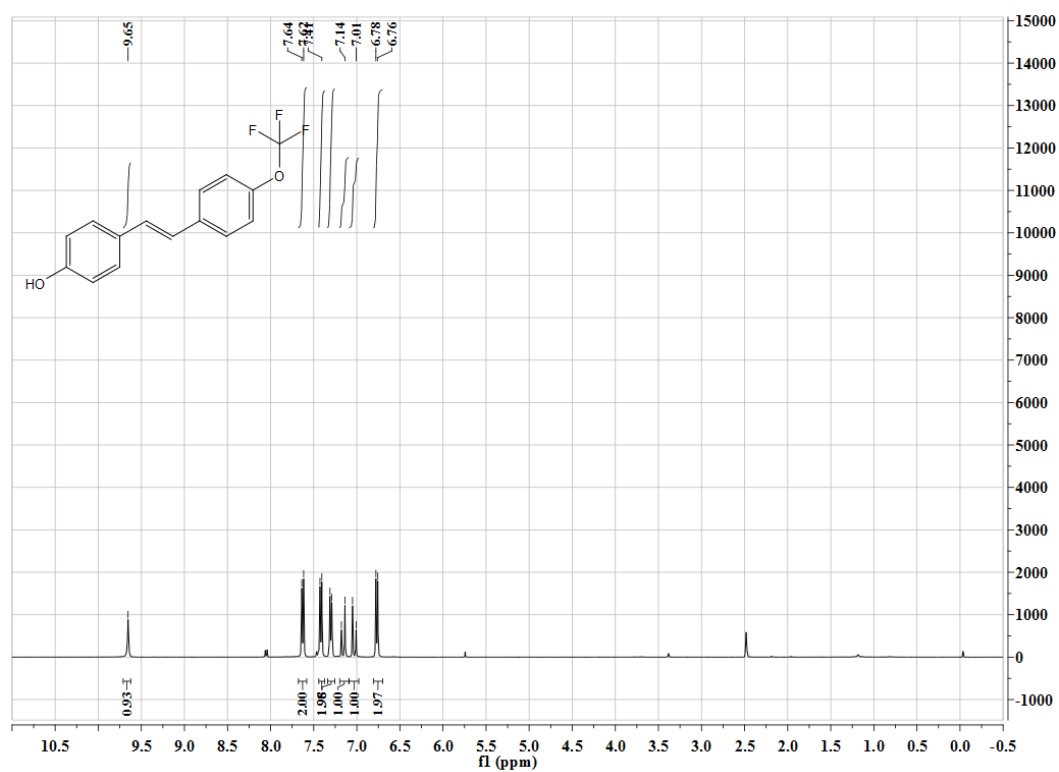
(up)  $^1\text{H}$  NMR spectrum of compound **2-3** (400 MHz,  $\text{DMSO-}d_6$ )



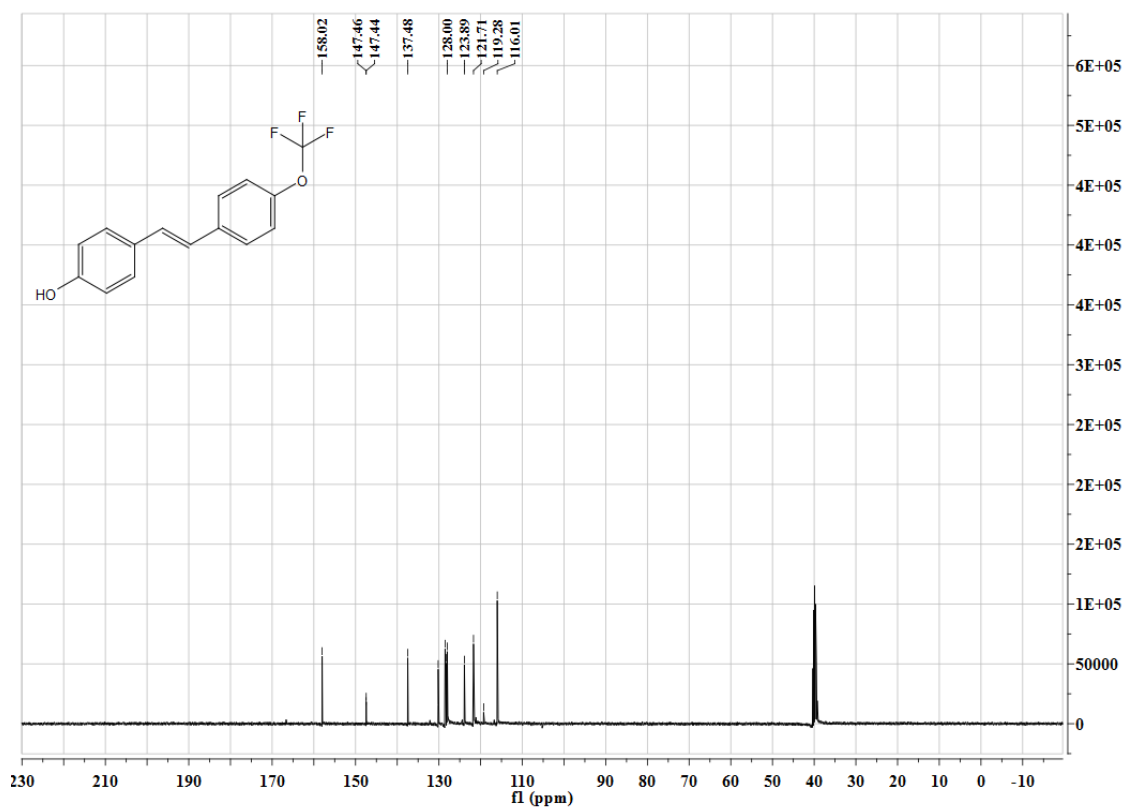
(up)  $^{13}\text{C}$  NMR spectrum of compound **2-3** (101 MHz,  $\text{DMSO-}d_6$ )



(up)  $^{19}\text{F}$  NMR spectrum of compound **2-3** (400 MHz,  $\text{DMSO-}d_6$ )

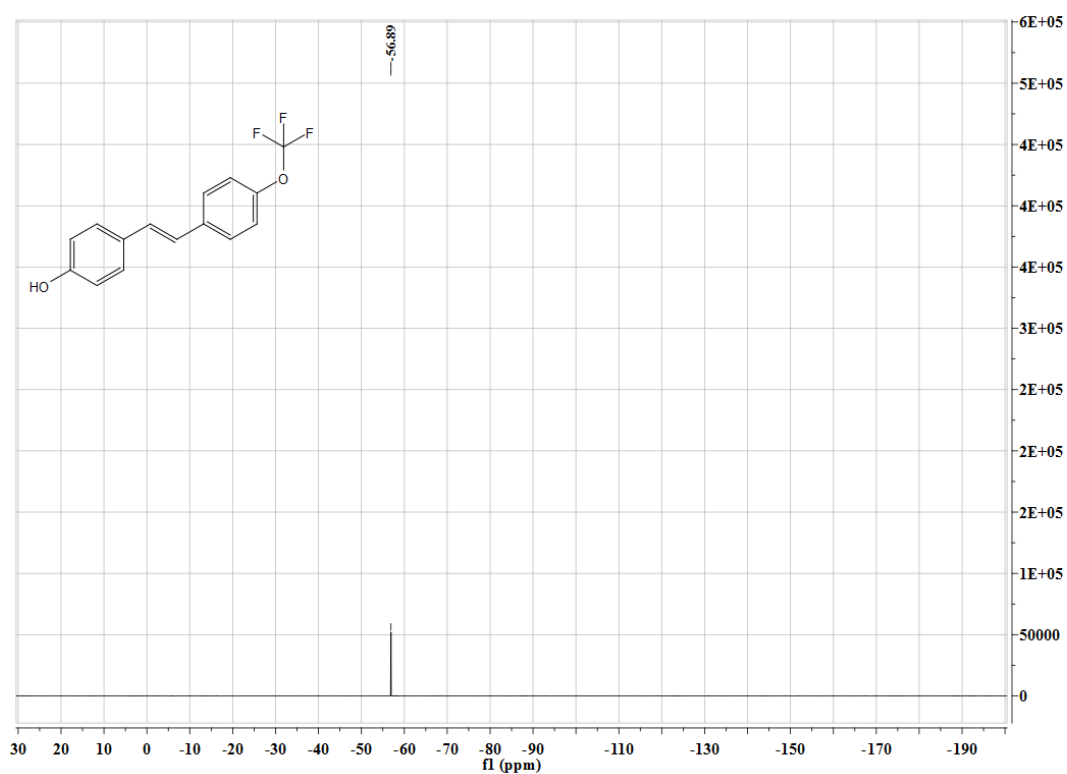


(up) <sup>1</sup>H NMR spectrum of compound **2-4** (400 MHz, DMSO-*d*<sub>6</sub>)

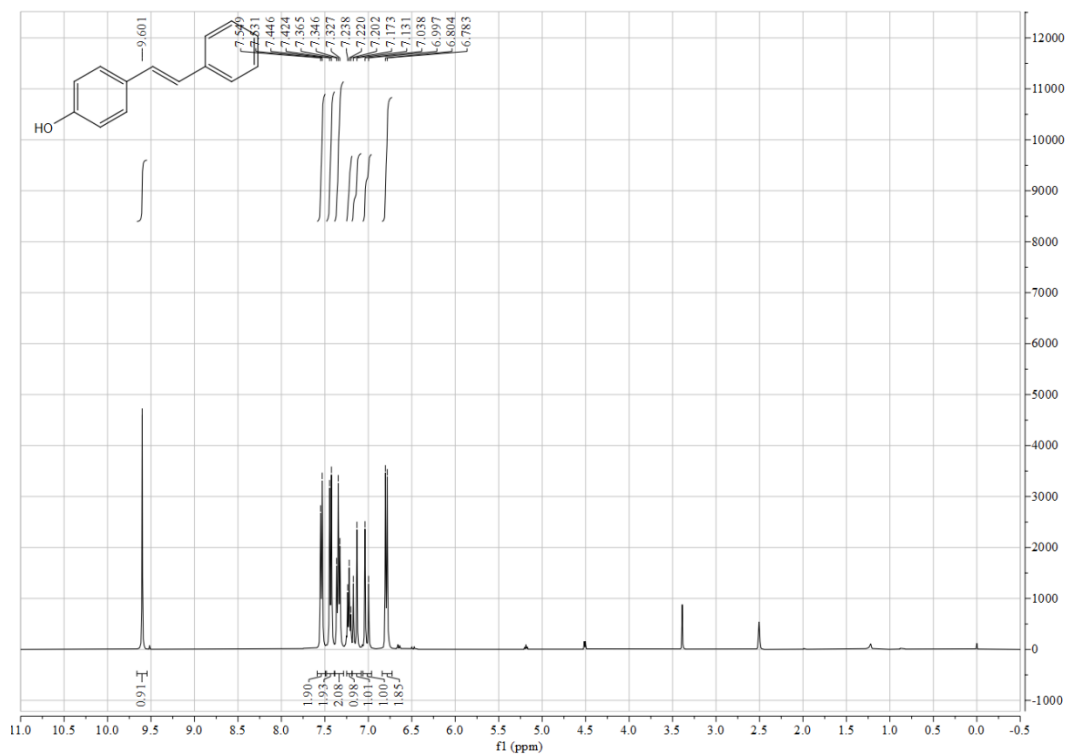


(up) <sup>13</sup>C NMR spectrum of compound **2-4** (101 MHz, DMSO-*d*<sub>6</sub>)

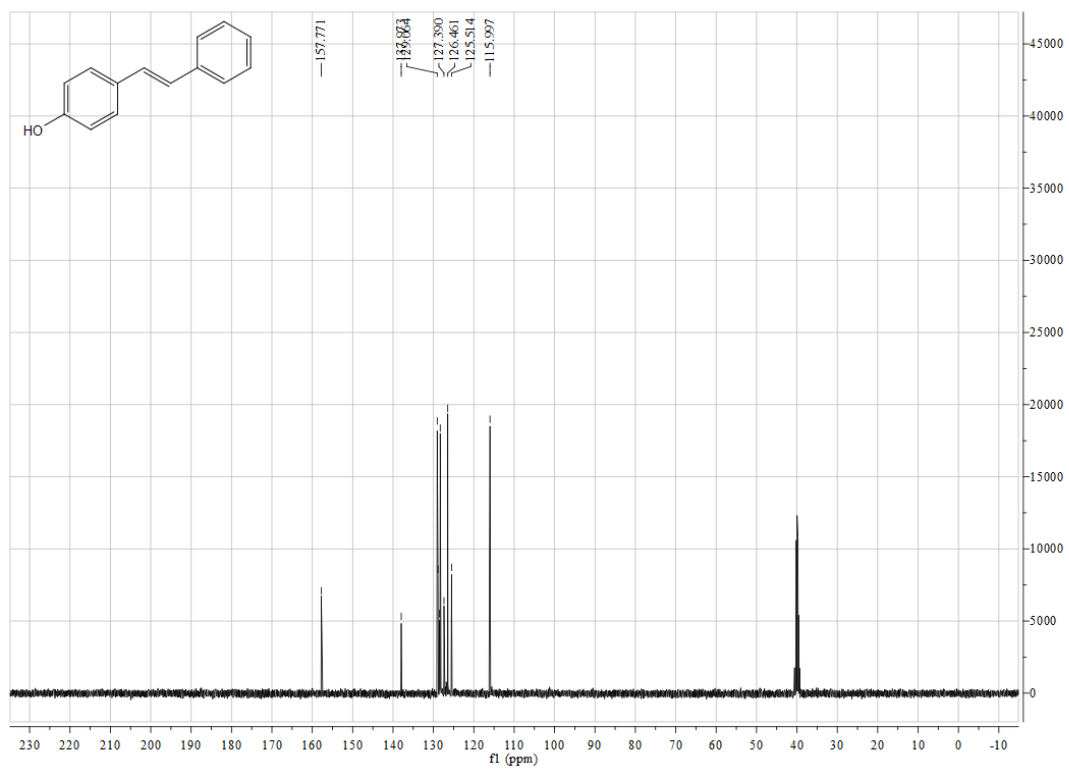




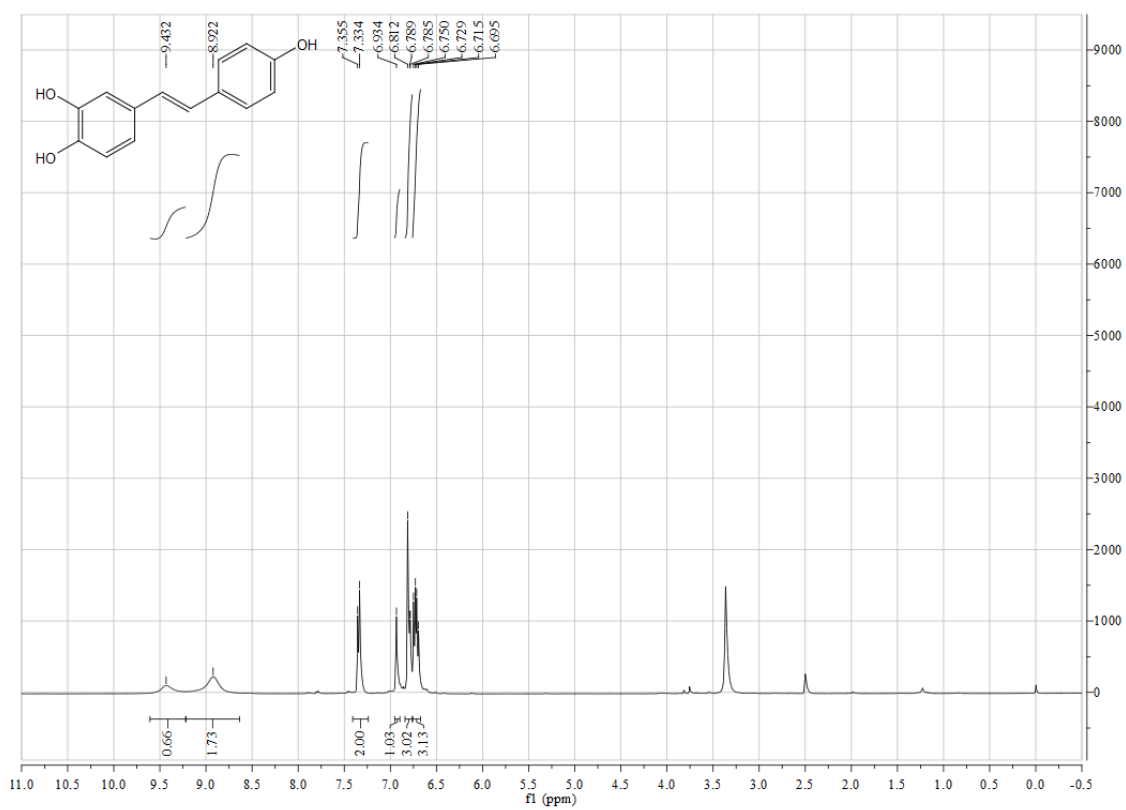
(up)  $^{19}\text{F}$  NMR spectrum of compound 2-4 (400 MHz,  $\text{DMSO}-d_6$ )



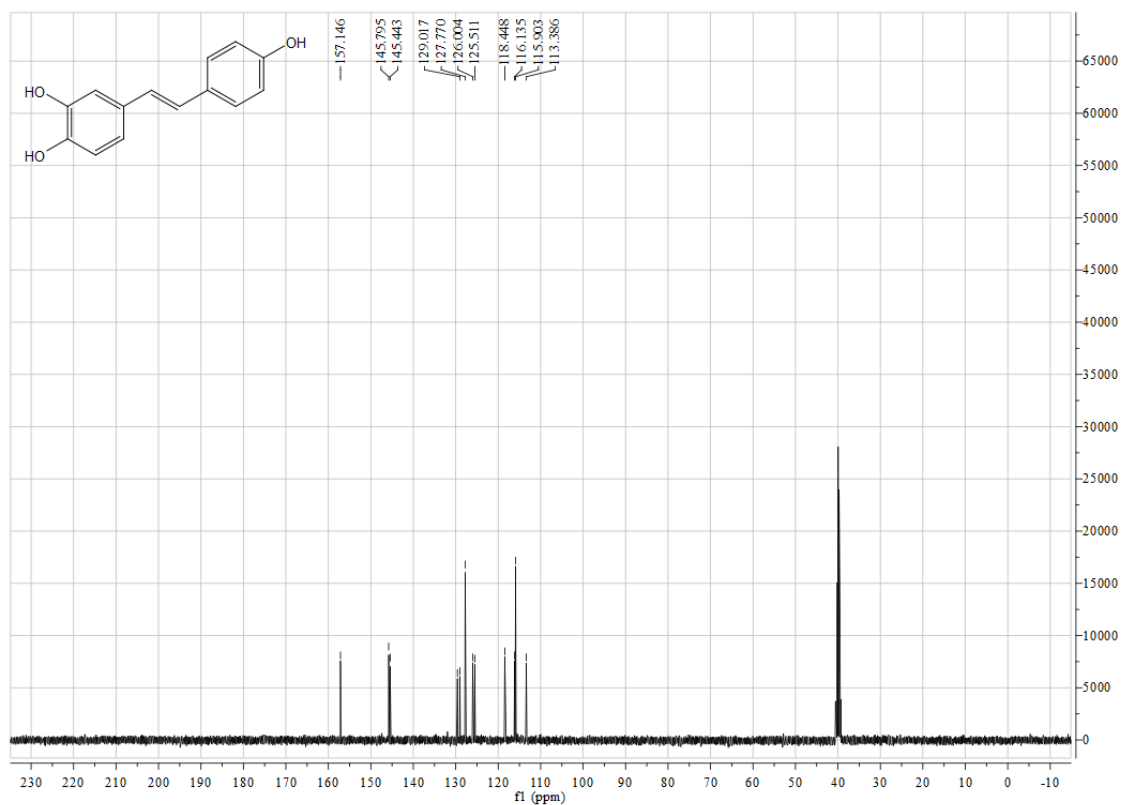
(up)  $^1\text{H}$  NMR spectrum of compound 2-5 (400 MHz,  $\text{DMSO}-d_6$ )



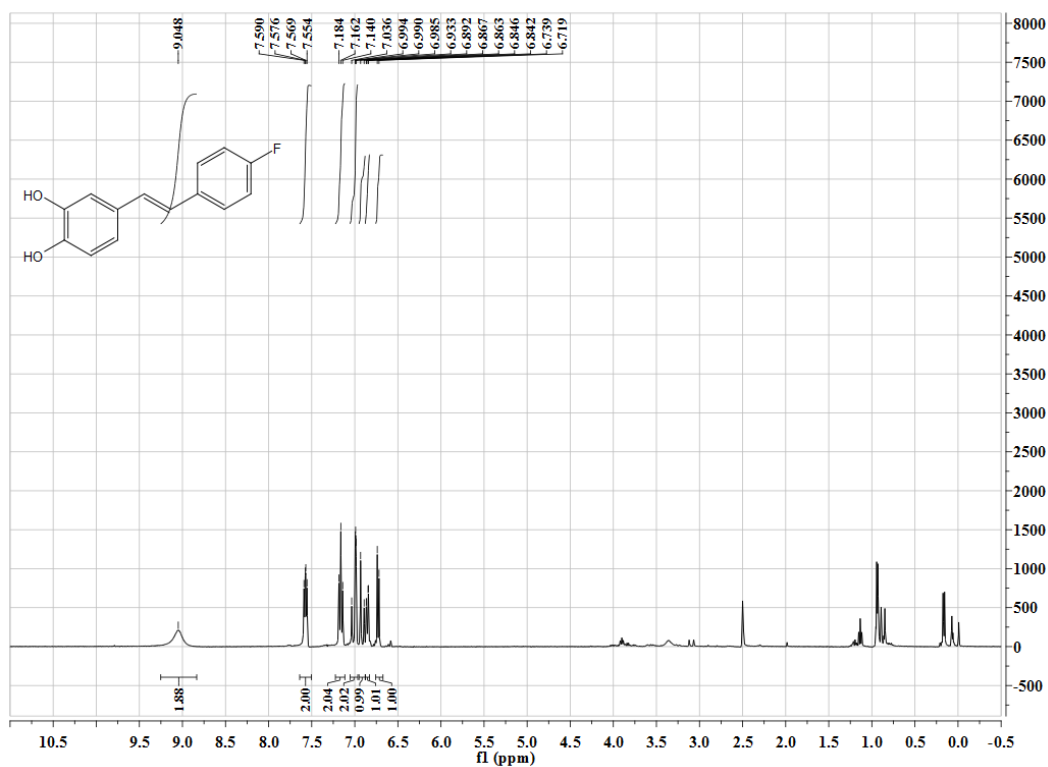
(up) <sup>13</sup>CNMR spectrum of compound **2-5** (101 MHz, DMSO-*d*<sub>6</sub>)



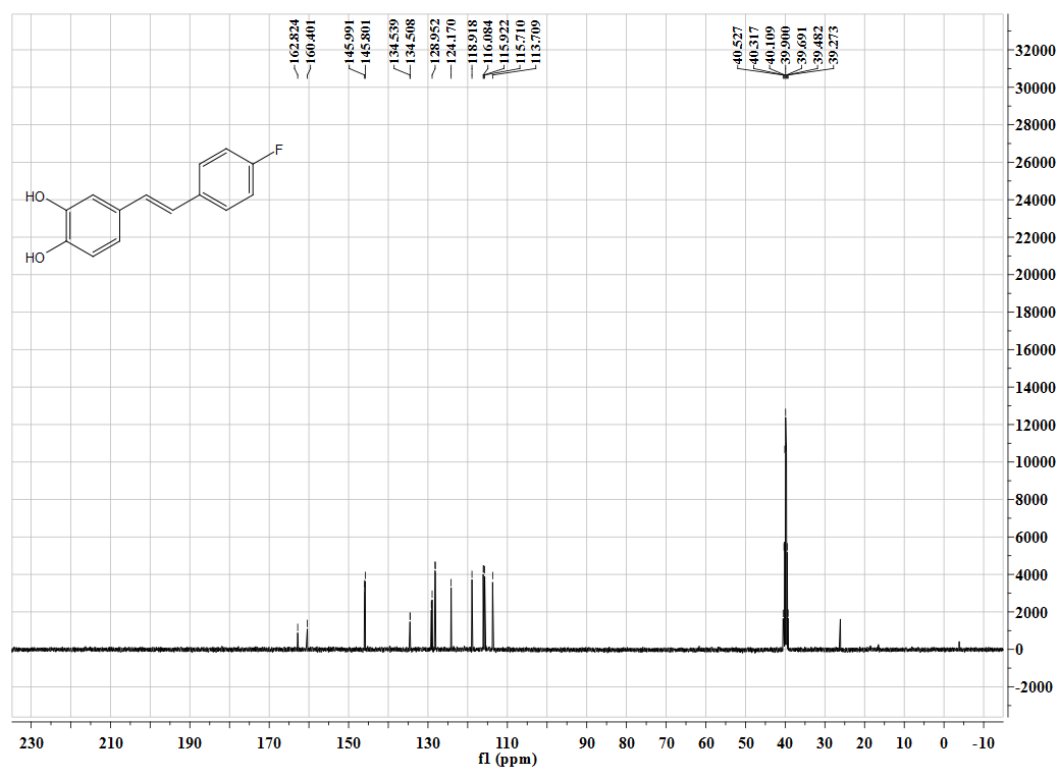
(up) <sup>1</sup>H NMR spectrum of compound **3-1** (400 MHz, DMSO-*d*<sub>6</sub>)



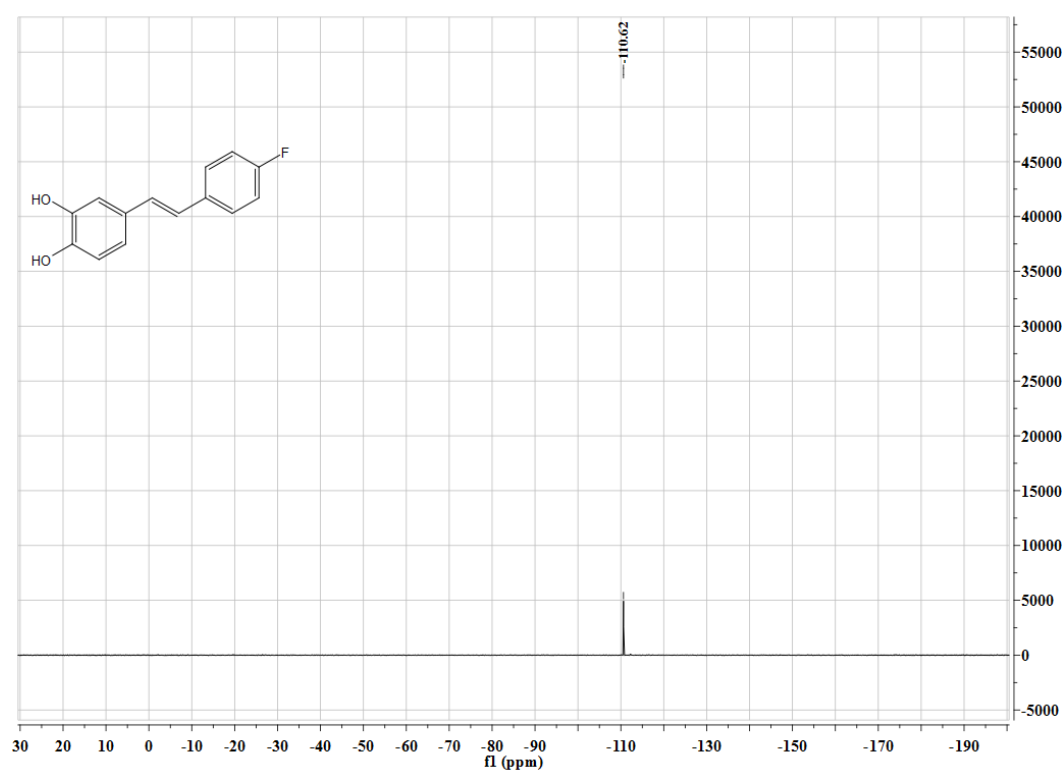
(up)  $^{13}\text{C}$  NMR spectrum of compound **3-1** (101 MHz,  $\text{DMSO}-d_6$ )



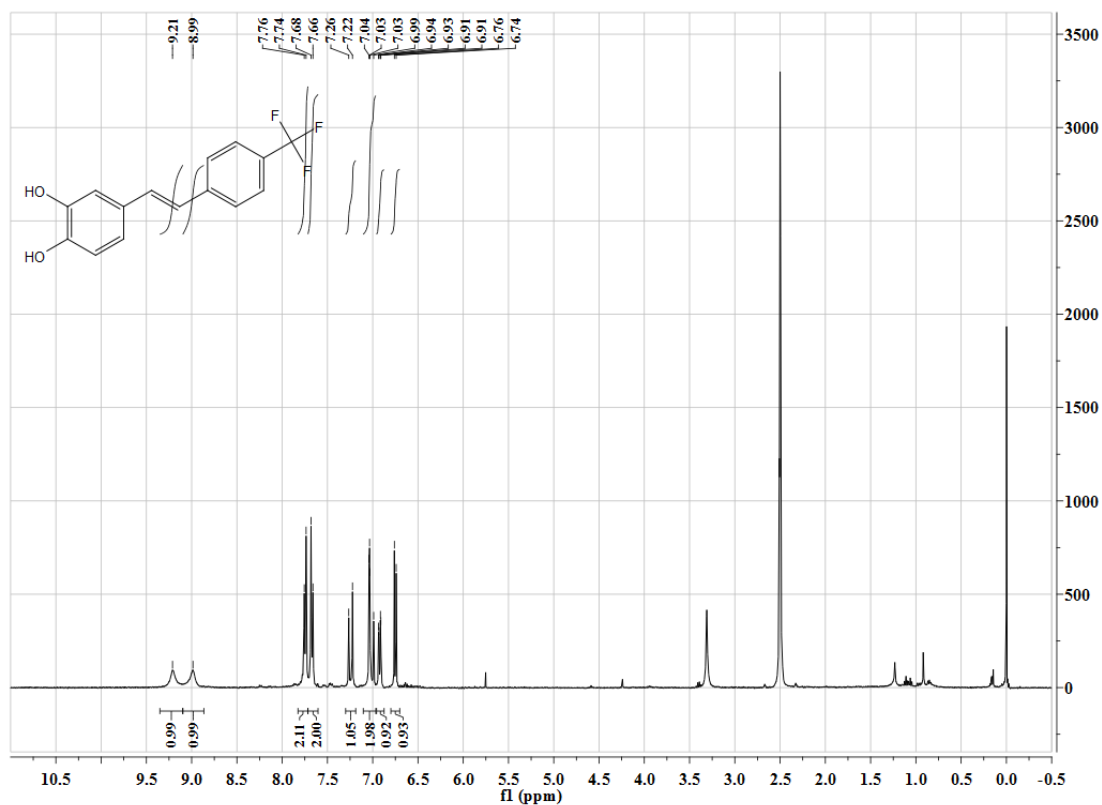
(up)  $^1\text{H}$  NMR spectrum of compound **3-2** (400 MHz,  $\text{DMSO}-d_6$ )



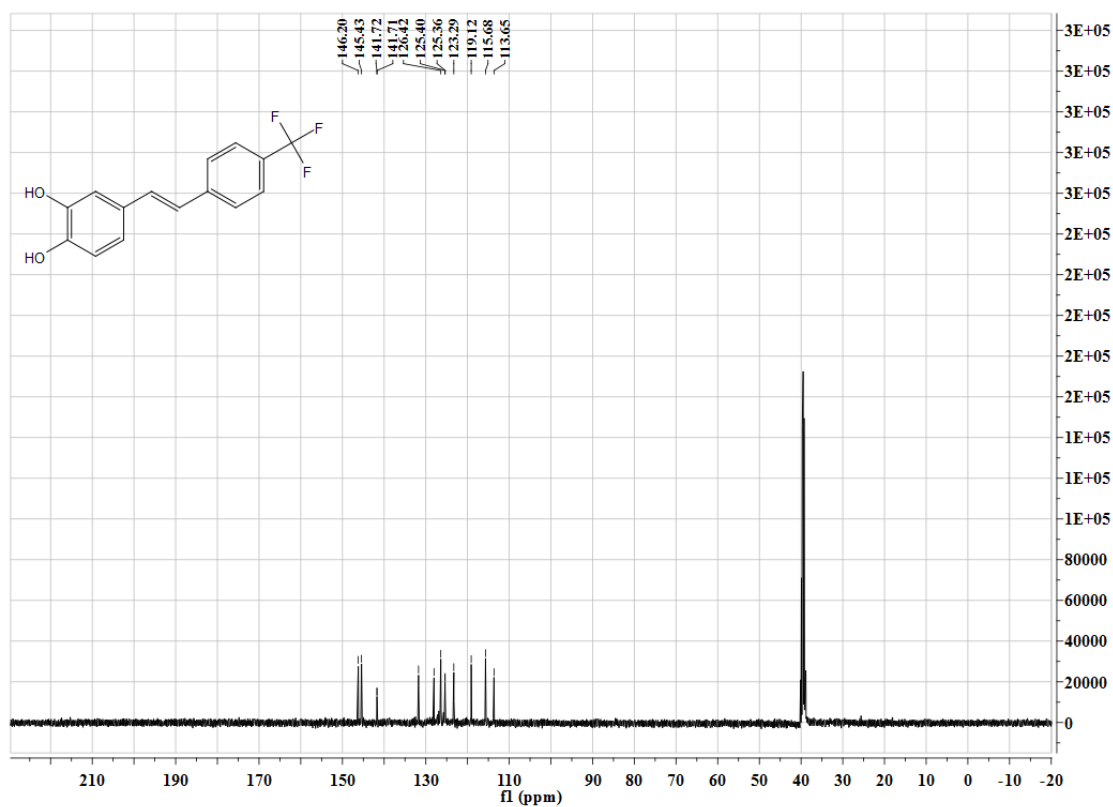
(up) <sup>13</sup>C NMR spectrum of compound **3-2** (101 MHz, DMSO-*d*<sub>6</sub>)



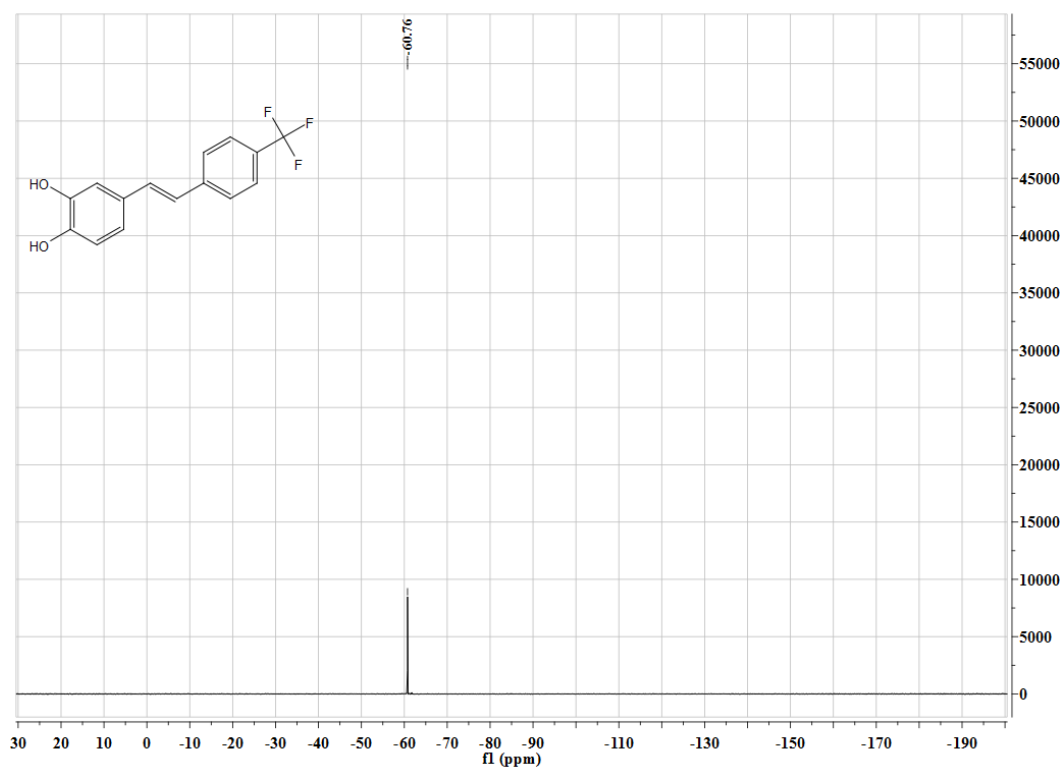
(up) <sup>19</sup>F NMR spectrum of compound **3-2** (400 MHz, DMSO-*d*<sub>6</sub>)



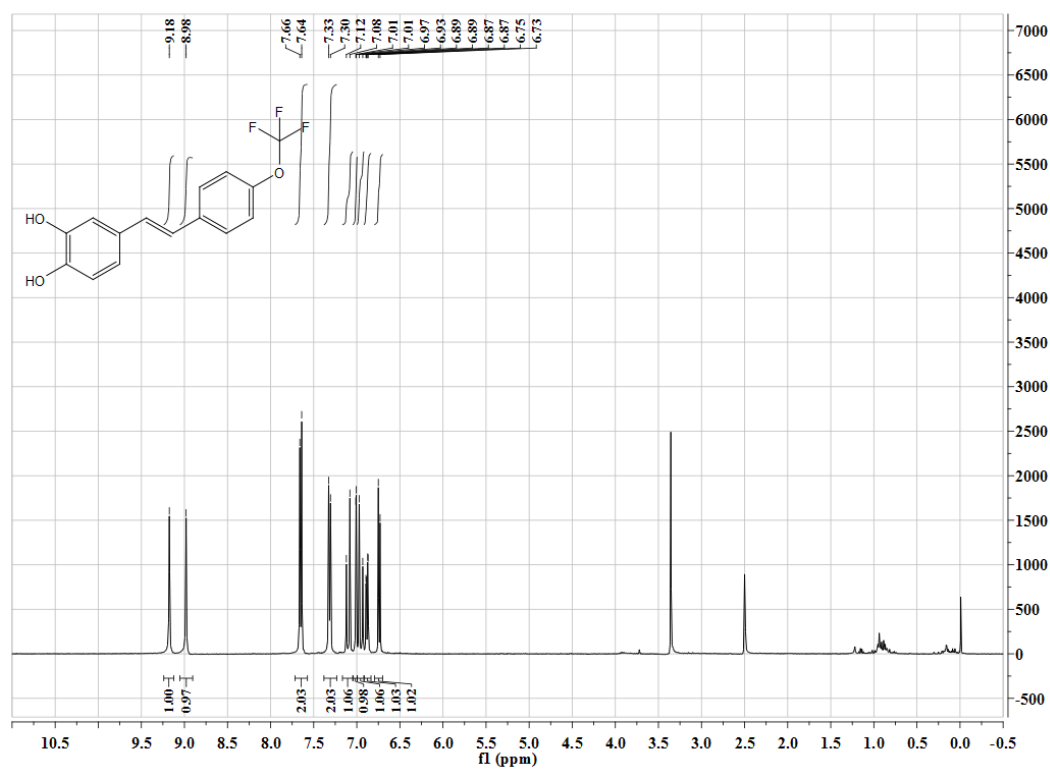
(up) <sup>1</sup>H NMR spectrum of compound **3-3** (400 MHz, DMSO-*d*<sub>6</sub>)



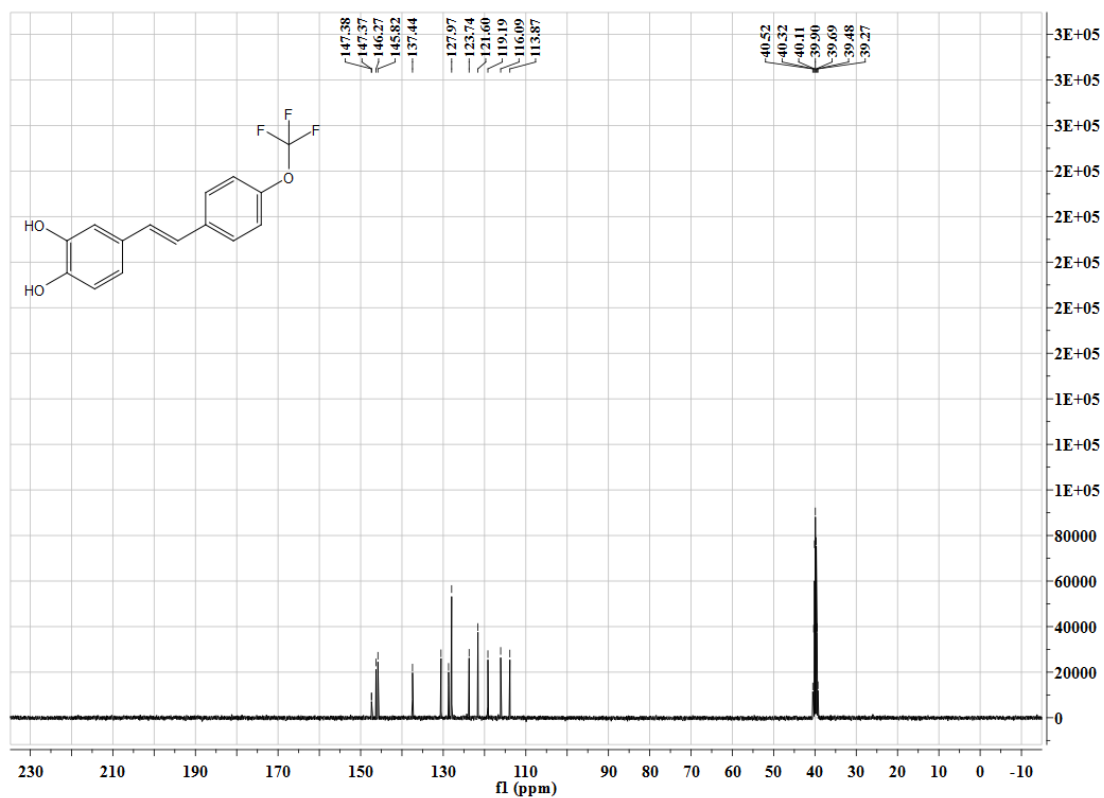
(up) <sup>13</sup>C NMR spectrum of compound **3-3** (101 MHz, DMSO-*d*<sub>6</sub>)



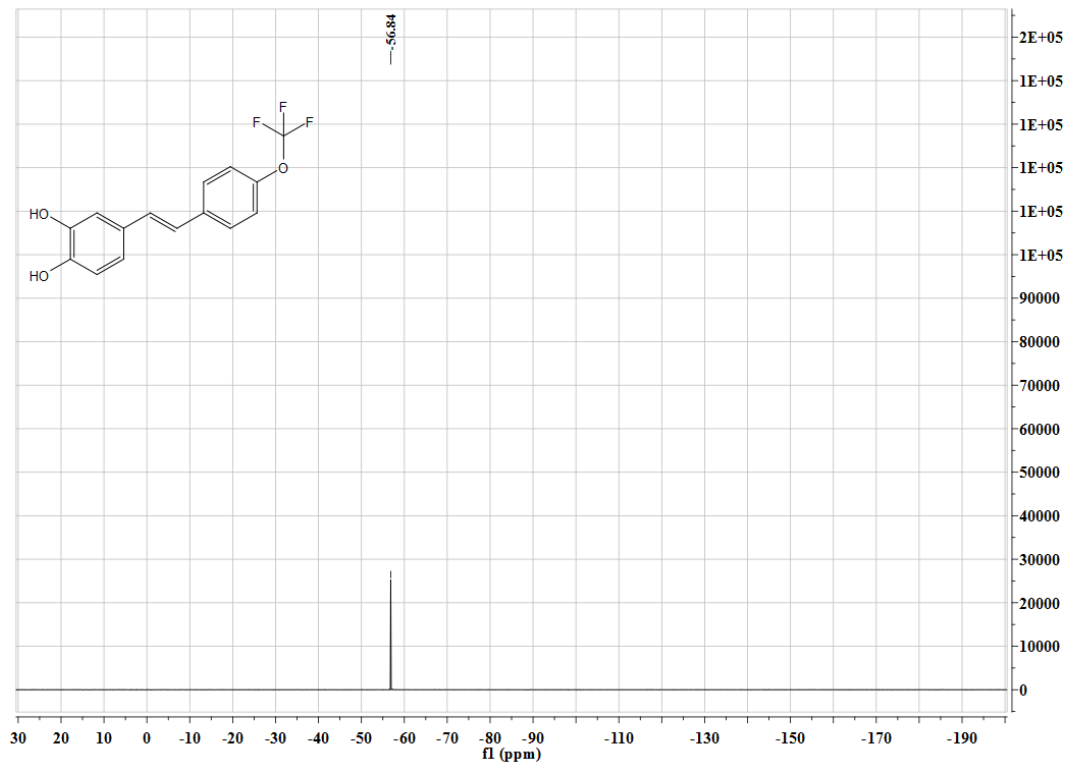
(up)  $^{19}\text{F}$  NMR spectrum of compound **3-3** (400 MHz,  $\text{DMSO}-d_6$ )



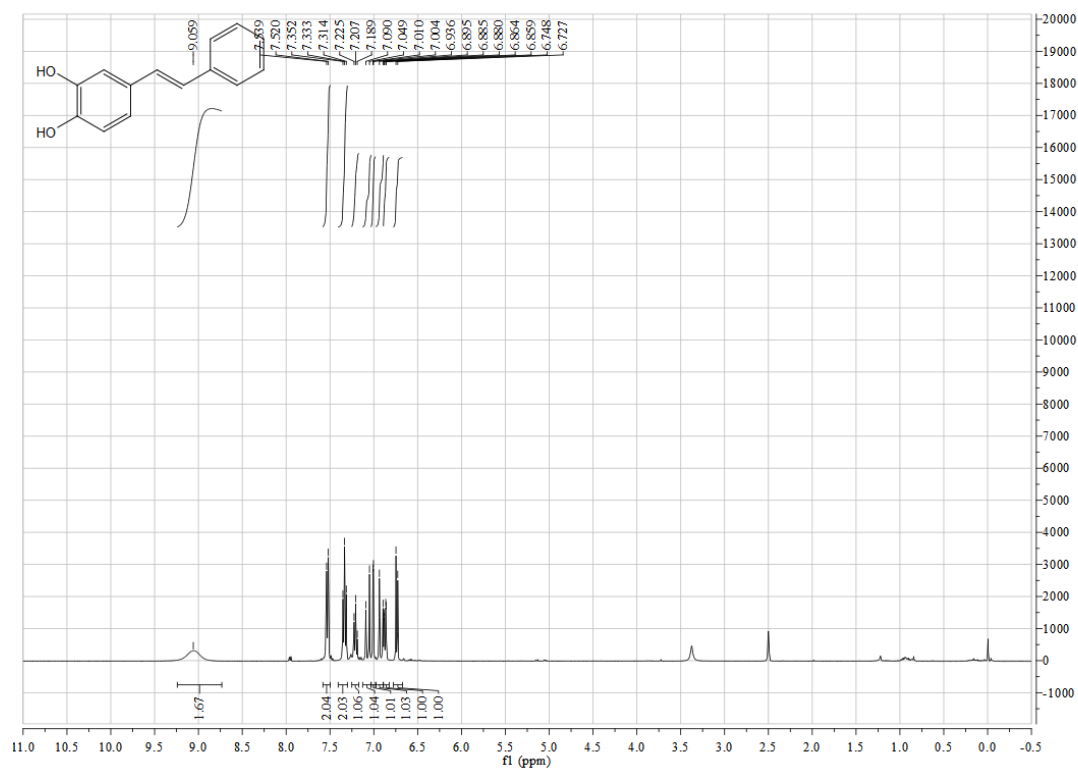
(up)  $^1\text{H}$  NMR spectrum of compound **3-4** (400 MHz,  $\text{DMSO}-d_6$ )



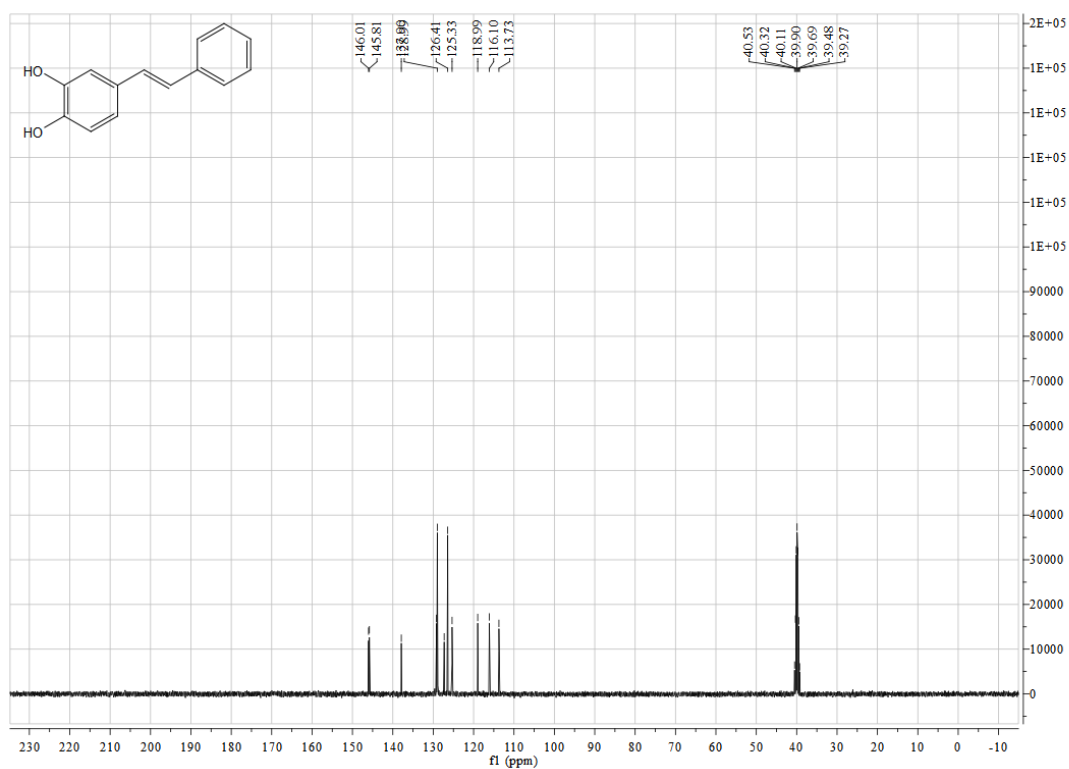
(up) <sup>13</sup>C NMR spectrum of compound **3-4** (101 MHz, DMSO-*d*<sub>6</sub>)



(up) <sup>19</sup>F NMR spectrum of compound **3-4** (400 MHz, DMSO-*d*<sub>6</sub>)

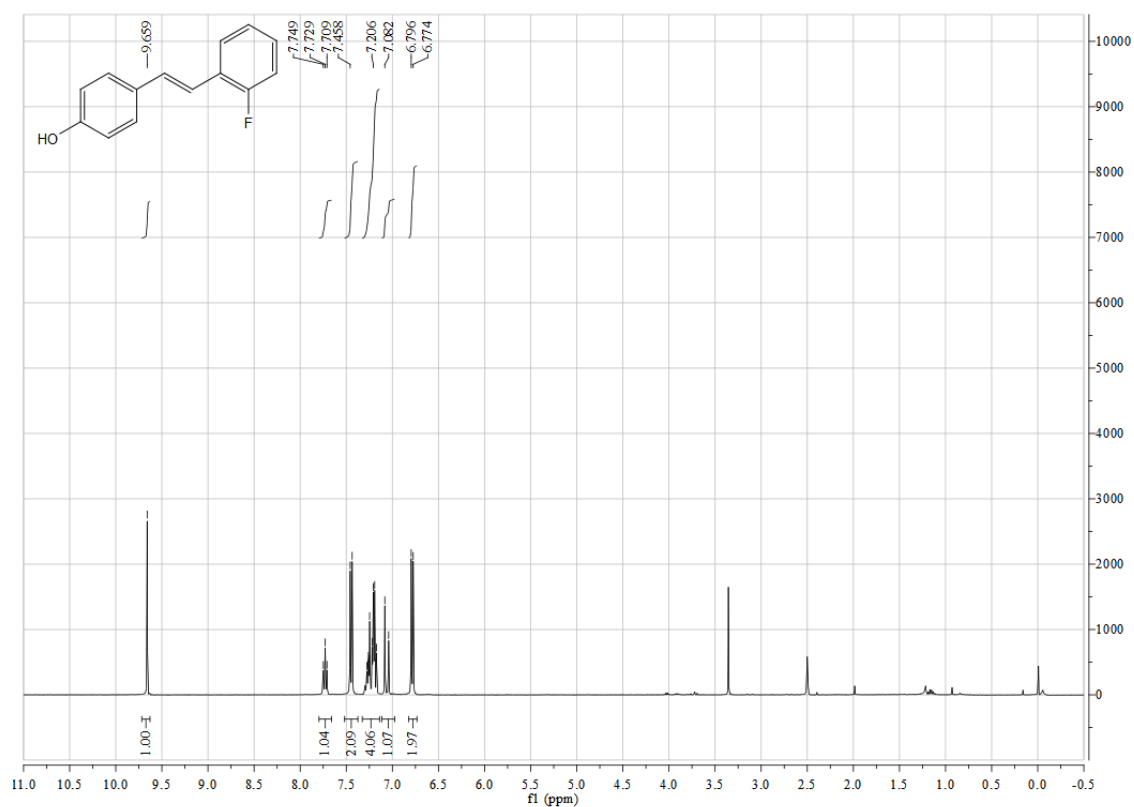


(up) <sup>1</sup>H NMR spectrum of compound **3-5** (400 MHz, DMSO-*d*<sub>6</sub>)

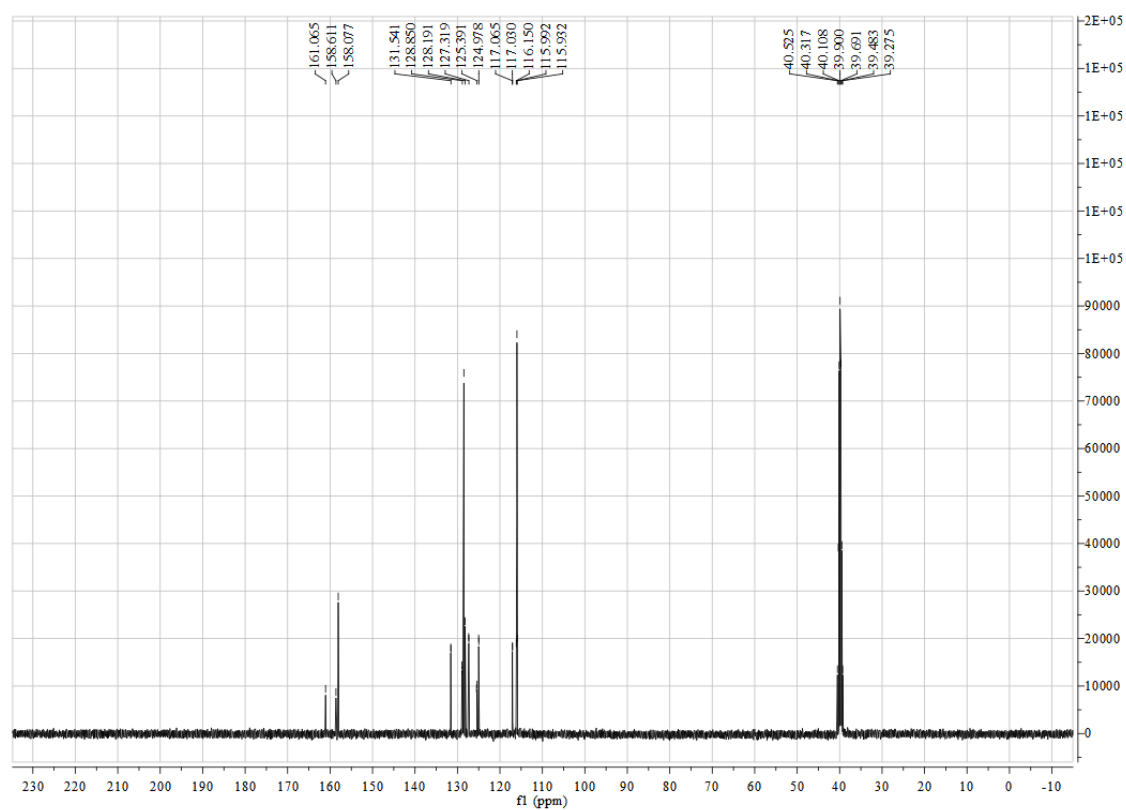


(up) <sup>13</sup>C NMR spectrum of compound **3-5** (101 MHz, DMSO-*d*<sub>6</sub>)

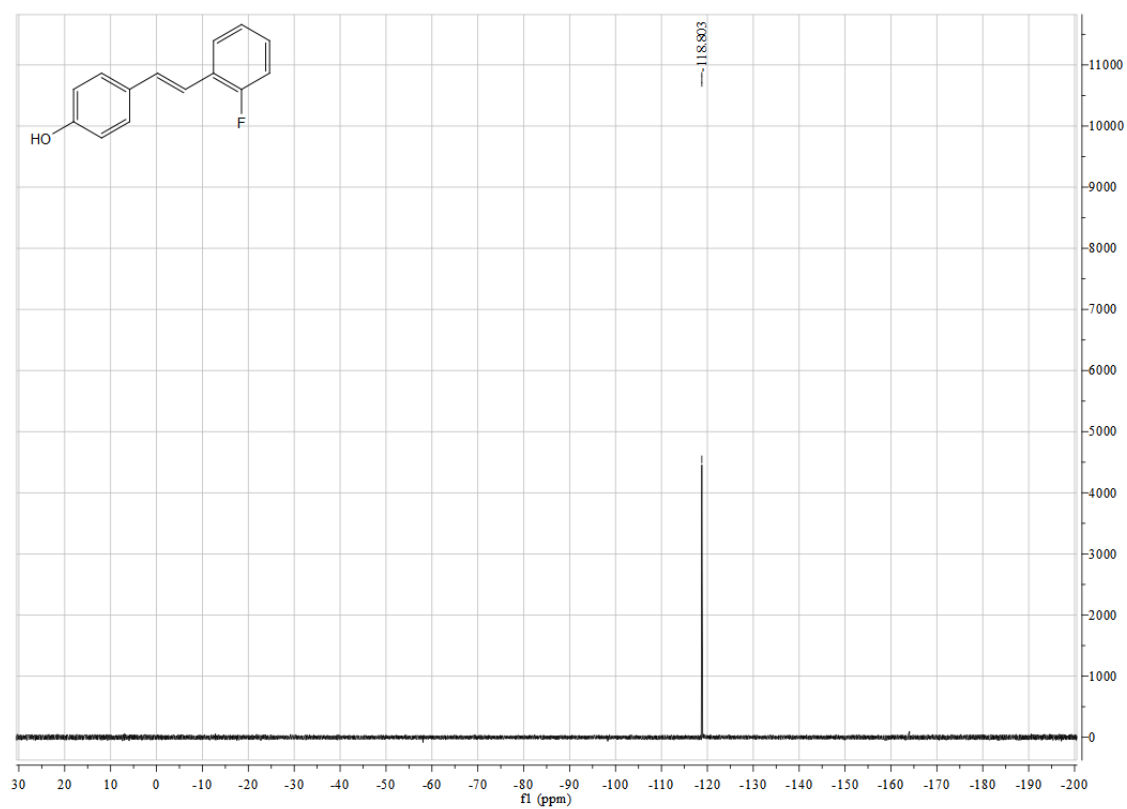




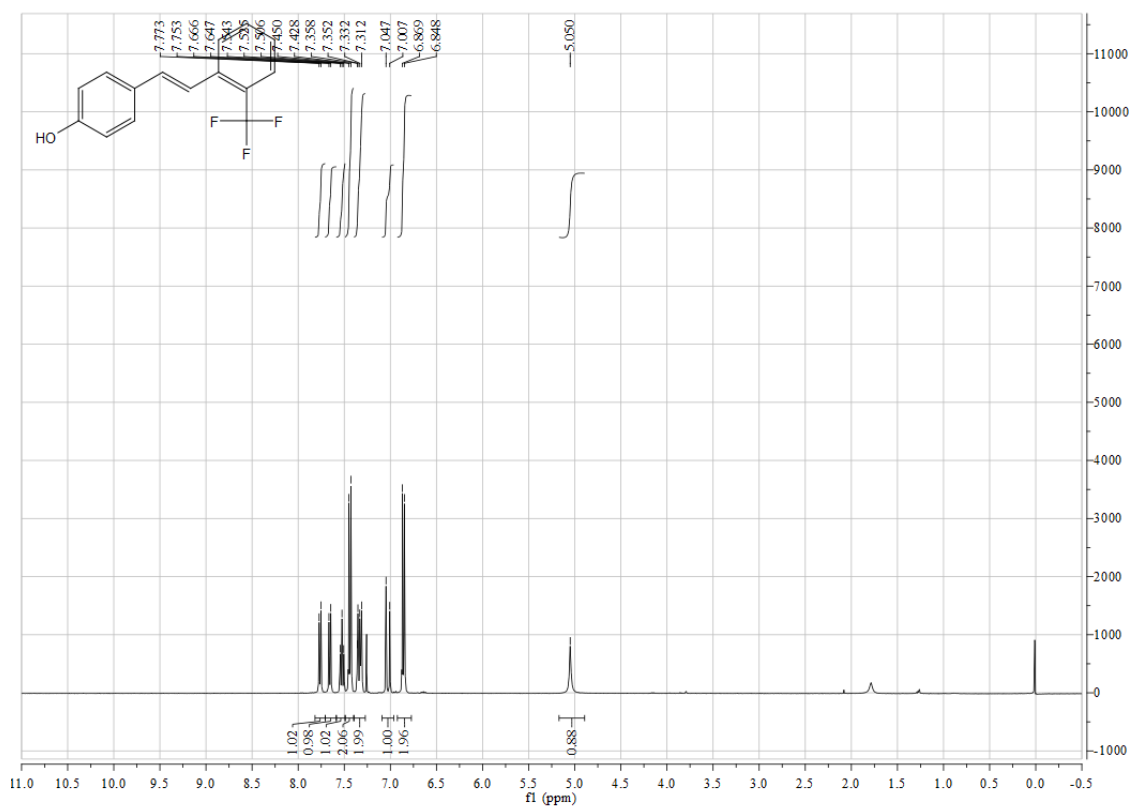
(up) <sup>1</sup>H NMR spectrum of compound **4-1** (400 MHz, DMSO-*d*<sub>6</sub>)



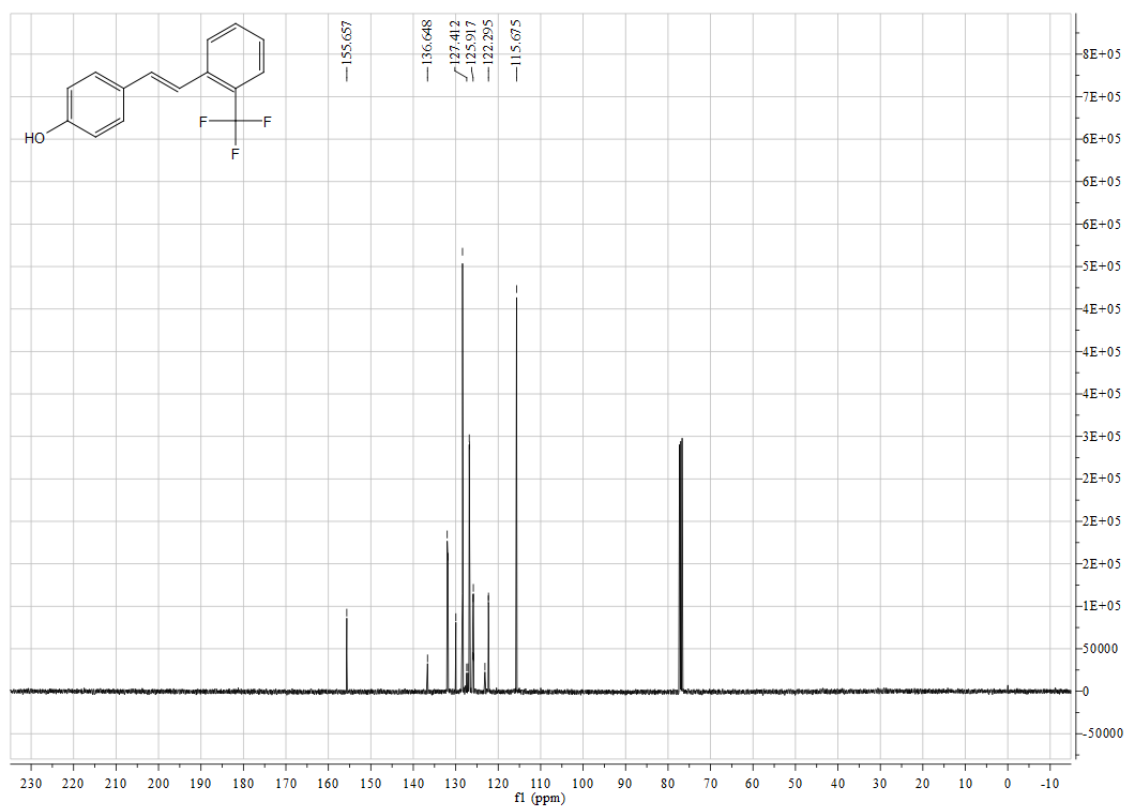
(up) <sup>13</sup>C NMR spectrum of compound **4-1** (101 MHz, DMSO-*d*<sub>6</sub>)



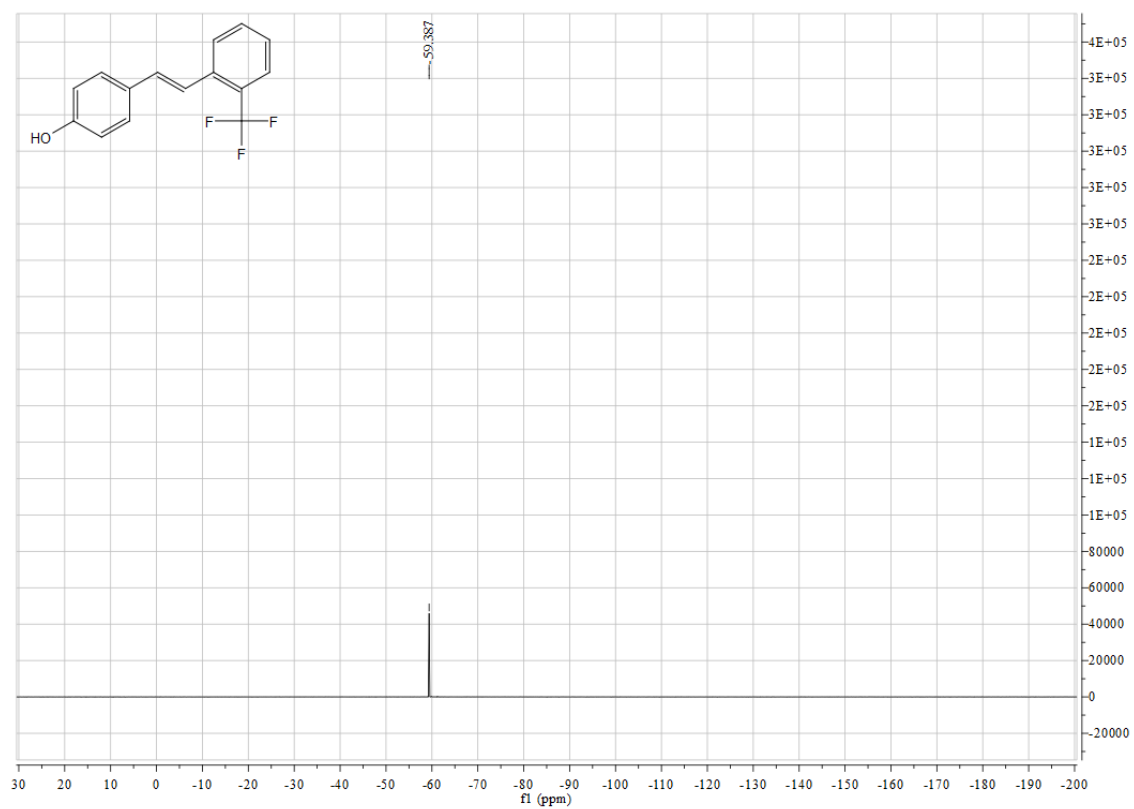
(up)  $^{19}\text{F}$  NMR spectrum of compound **4-1** (400 MHz,  $\text{DMSO}-d_6$ )



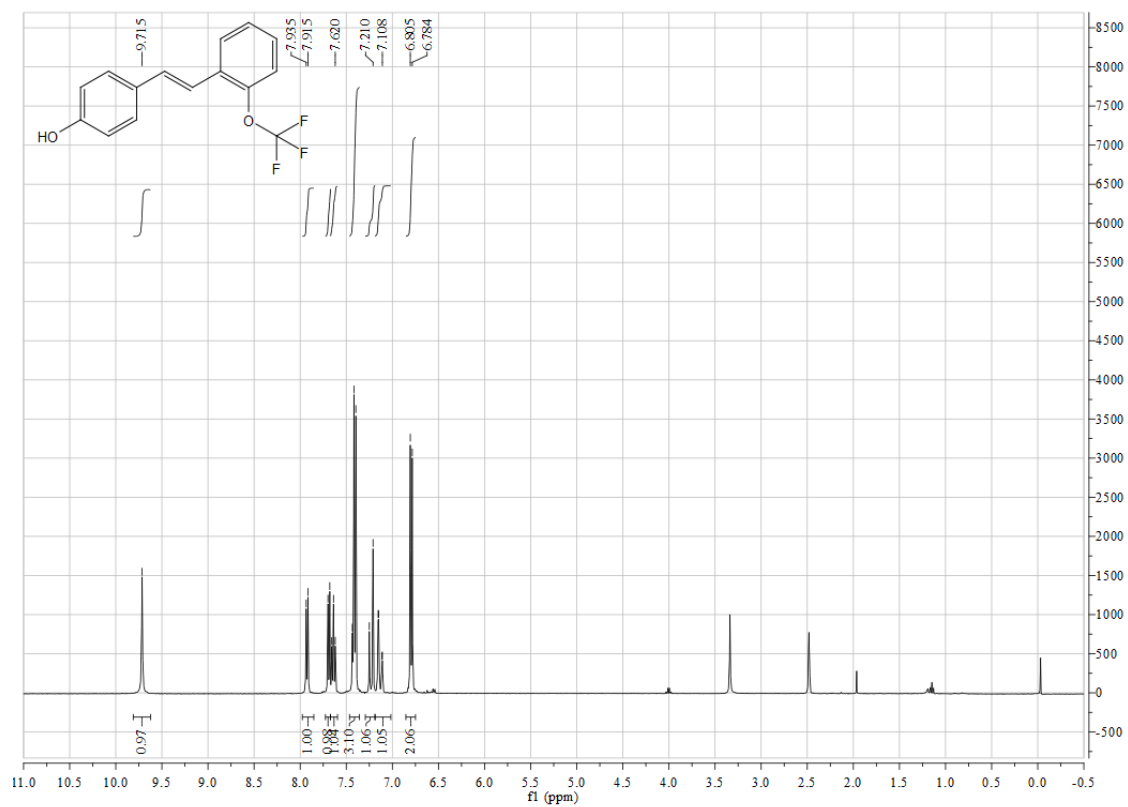
(up)  $^1\text{H}$  NMR spectrum of compound **4-2** (400 MHz,  $\text{CDCl}_3$ )



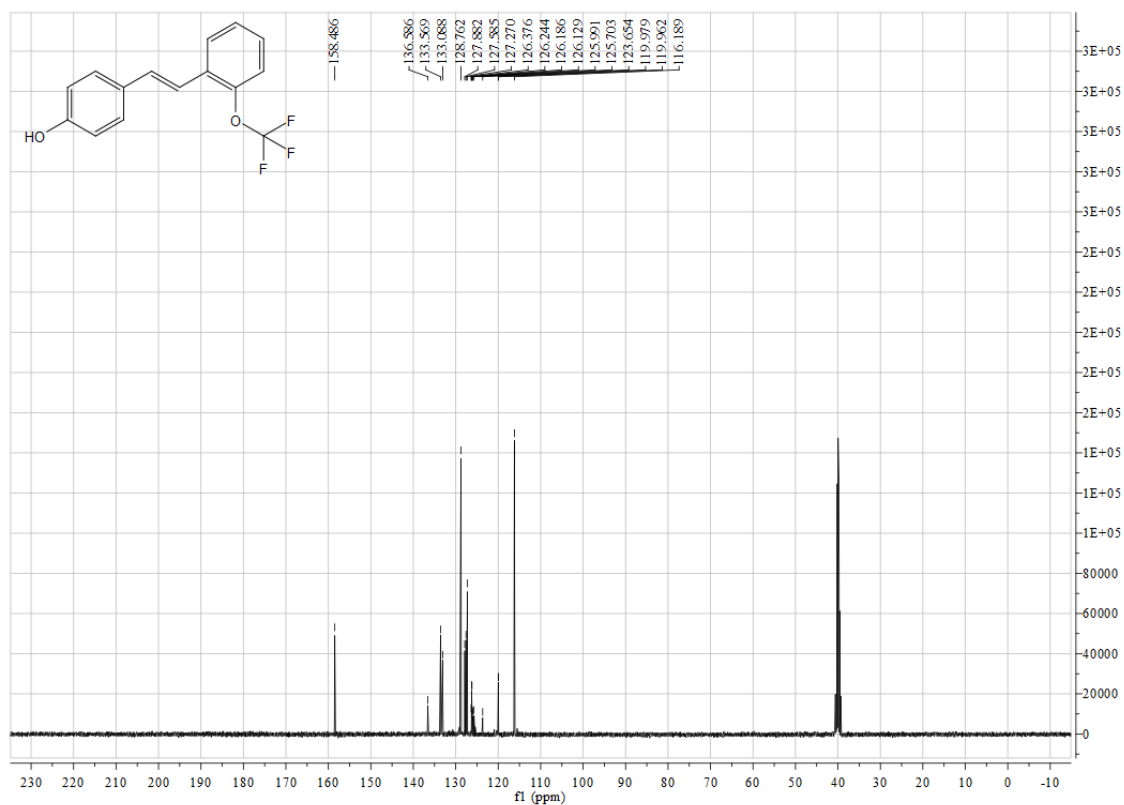
(up) <sup>13</sup>C NMR spectrum of compound **4-2** (101 MHz, CDCl<sub>3</sub>)



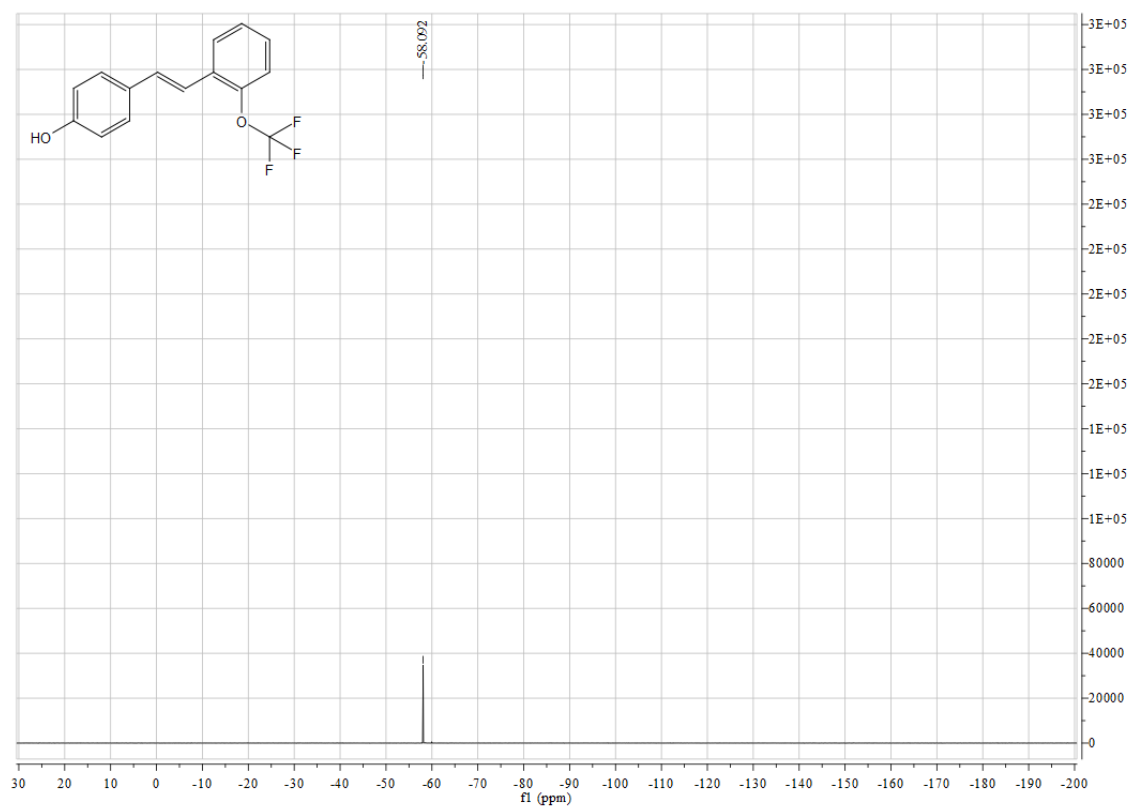
(up)  $^{19}\text{F}$  NMR spectrum of compound **4-2** (400 MHz,  $\text{CDCl}_3$ )



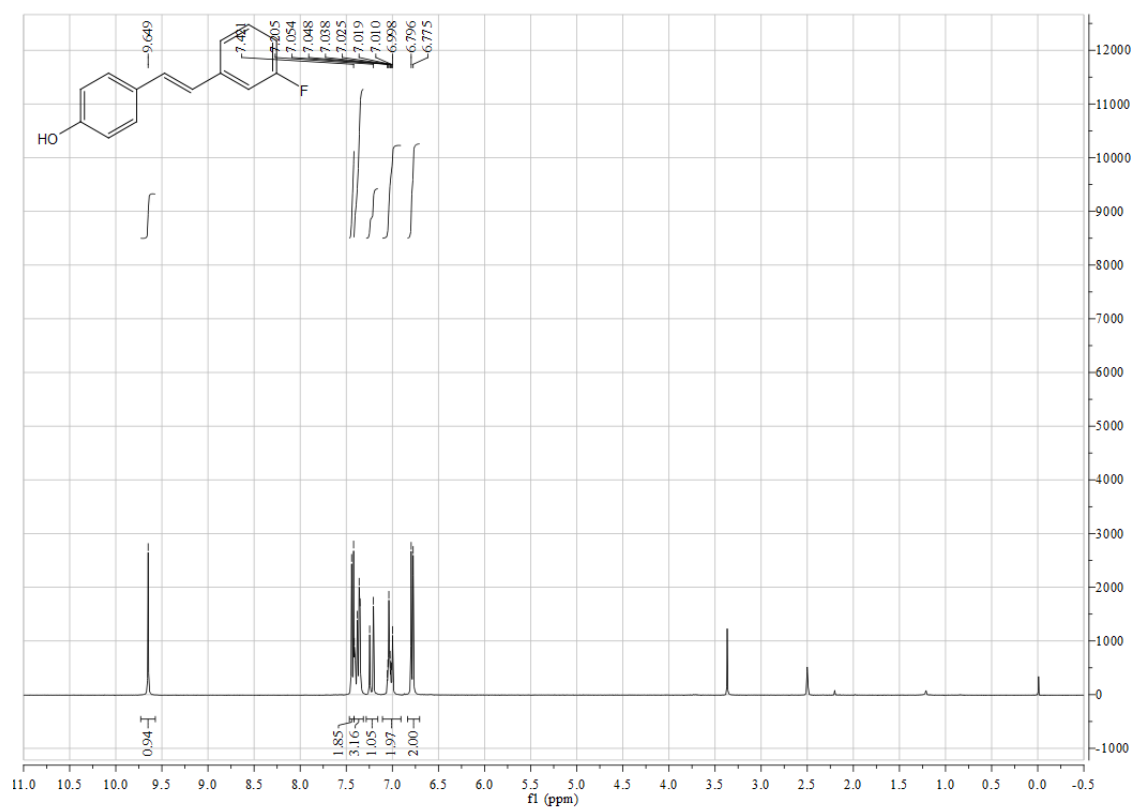
(up)  $^1\text{H}$  NMR spectrum of compound **4-3** (400 MHz,  $\text{DMSO}-d_6$ )



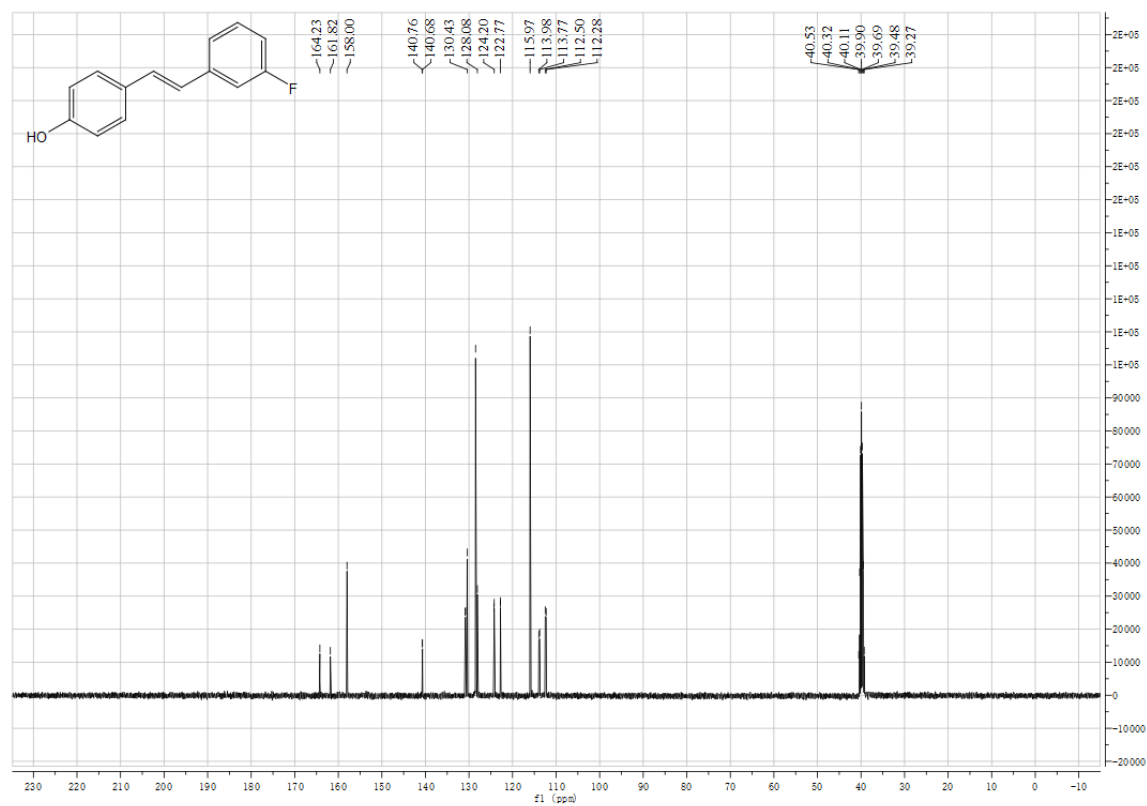
(up)  $^{13}\text{C}$  NMR spectrum of compound **4-3** (101 MHz,  $\text{DMSO-d}_6$ )



(up)  $^{19}\text{F}$  NMR spectrum of compound **4-3** (400 MHz,  $\text{DMSO-d}_6$ )



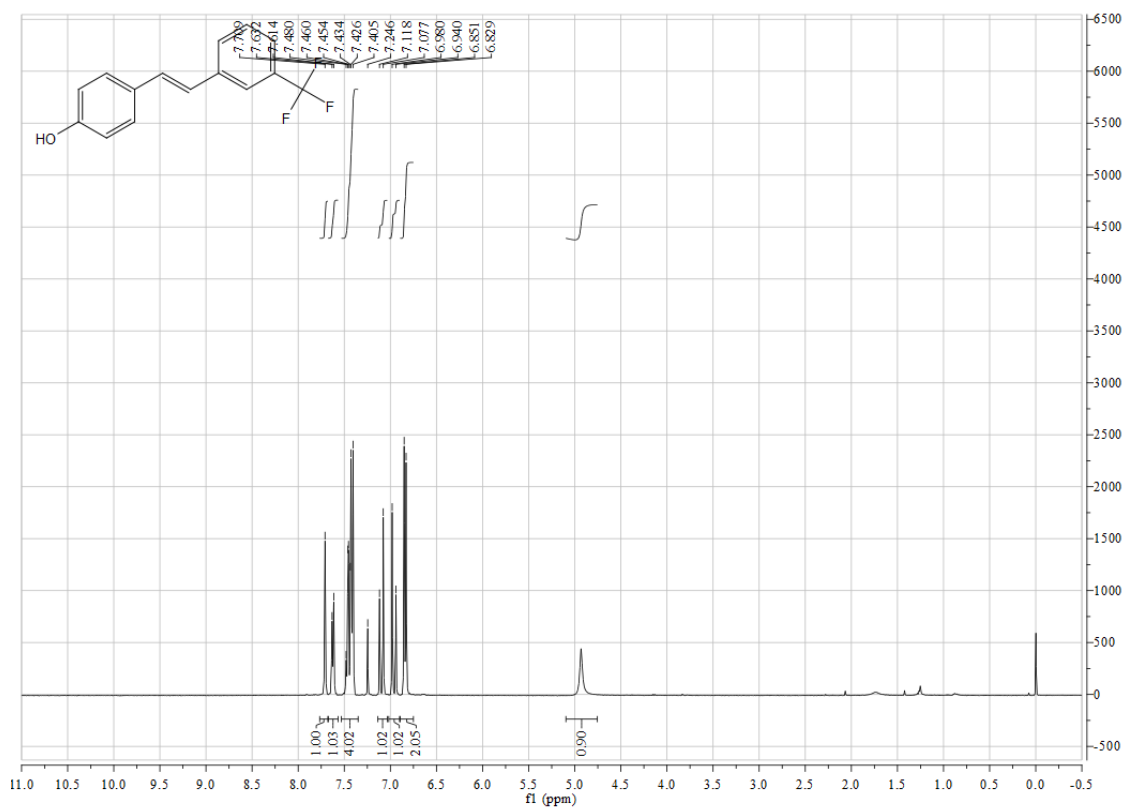
(up) <sup>1</sup>H NMR spectrum of compound **4-4** (400 MHz, DMSO-*d*<sub>6</sub>)



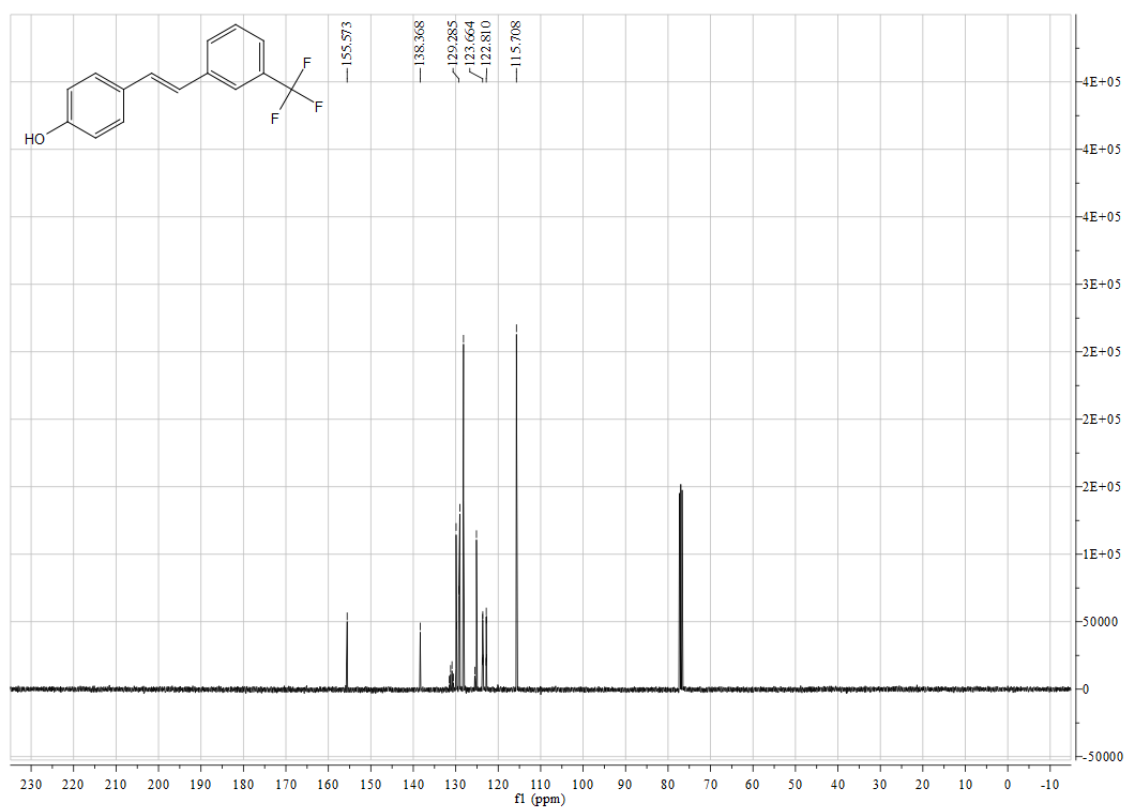
(up) <sup>13</sup>C NMR spectrum of compound **4-4** (101 MHz, DMSO-*d*<sub>6</sub>)



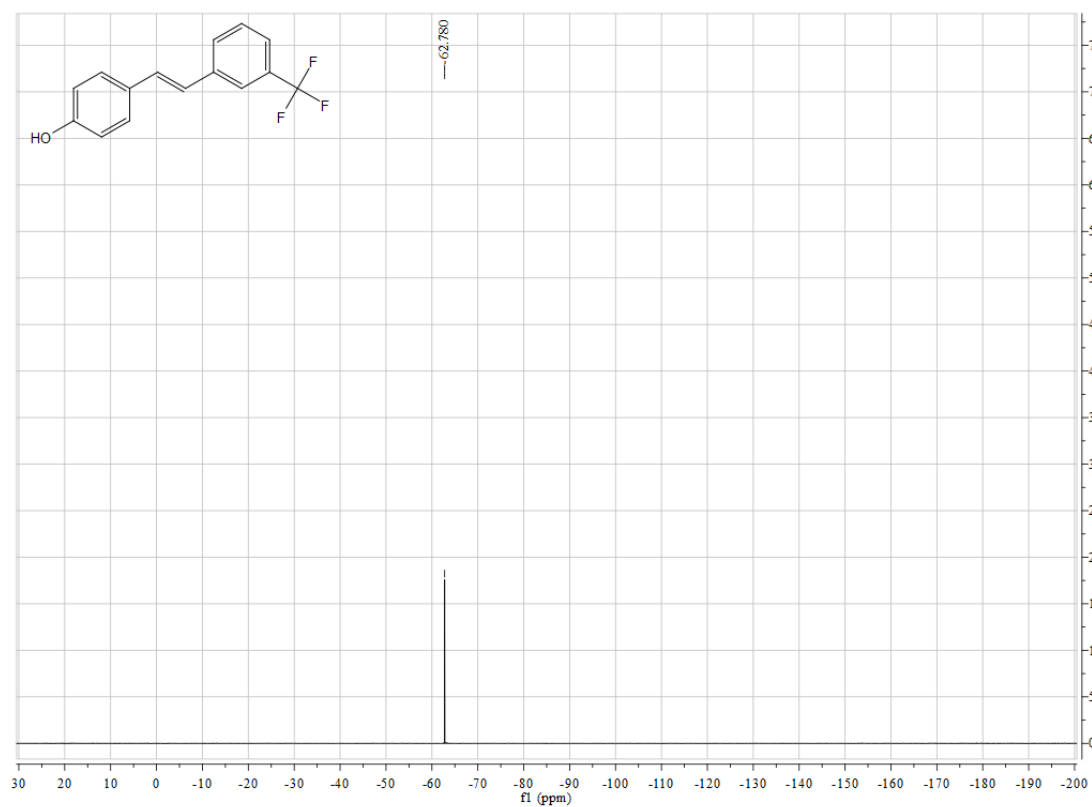
(up)  $^{19}\text{F}$  NMR spectrum of compound 4-4 (400 MHz,  $\text{DMSO}-d_6$ )



(up)  $^1\text{H}$  NMR spectrum of compound 4-5 (400 MHz,  $\text{CDCl}_3$ )

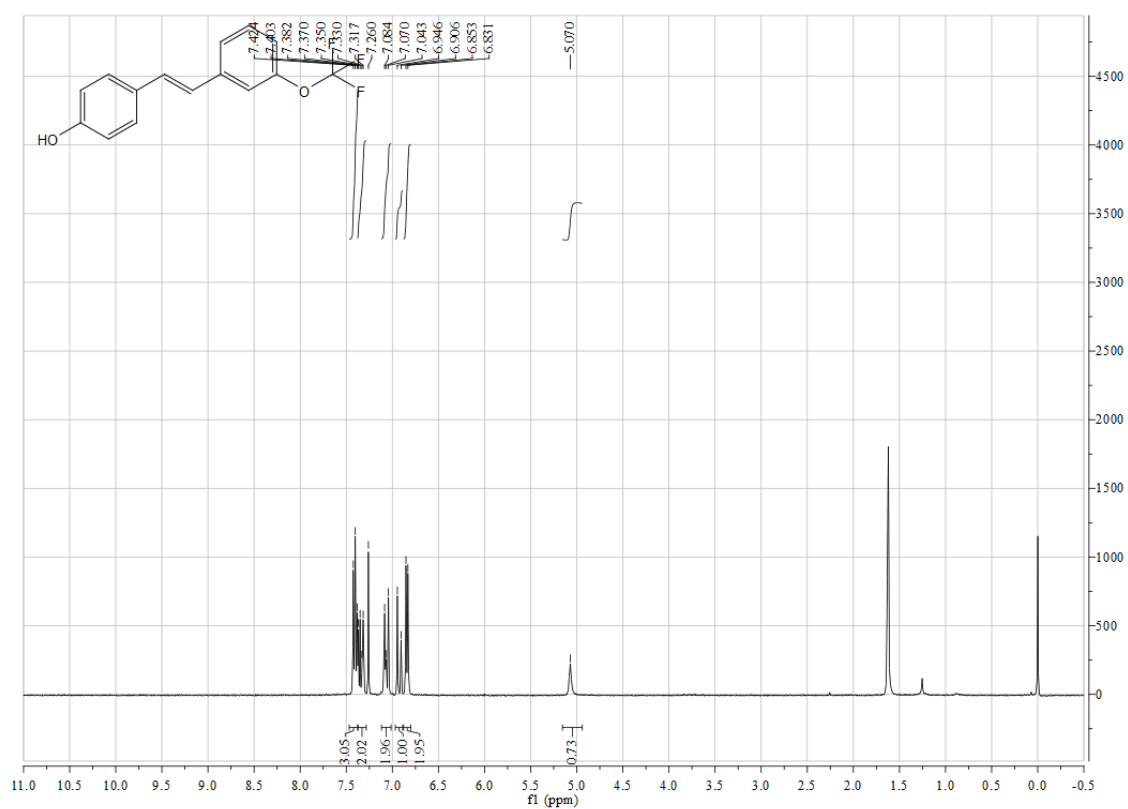


(up)  $^{13}\text{C}$  NMR spectrum of compound **4-5** (101 MHz,  $\text{CDCl}_3$ )

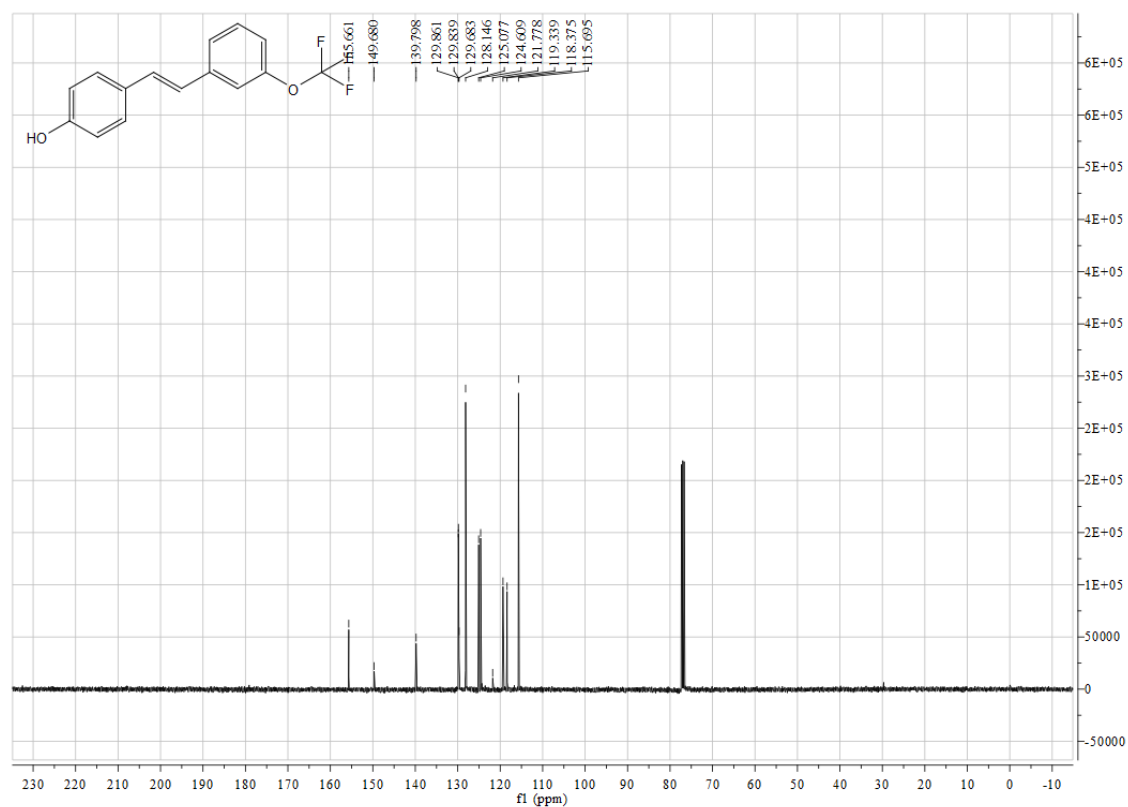


(up)  $^{19}\text{F}$  NMR spectrum of compound **4-5** (400 MHz,  $\text{CDCl}_3$ )

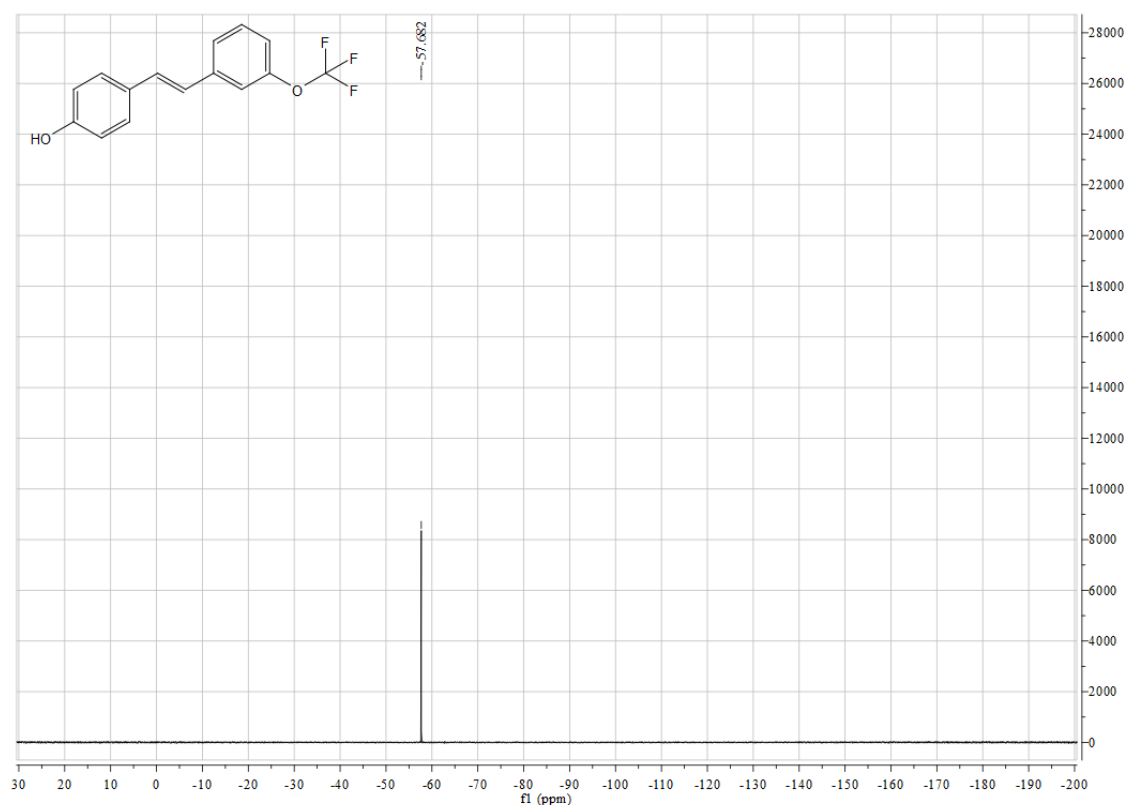




(up) <sup>1</sup>H NMR spectrum of compound 4-6 (400 MHz, CDCl<sub>3</sub>)



(up)  $^{13}\text{C}$  NMR spectrum of compound **4-6** (101 MHz,  $\text{CDCl}_3$ )



(up)  $^{19}\text{F}$  NMR spectrum of compound **4-6** (400 MHz,  $\text{CDCl}_3$ )

#### 4. HPLC spectra resveratrol derivatives

The purity of compounds was checked by HPLC and listed in Table 1 (see below).

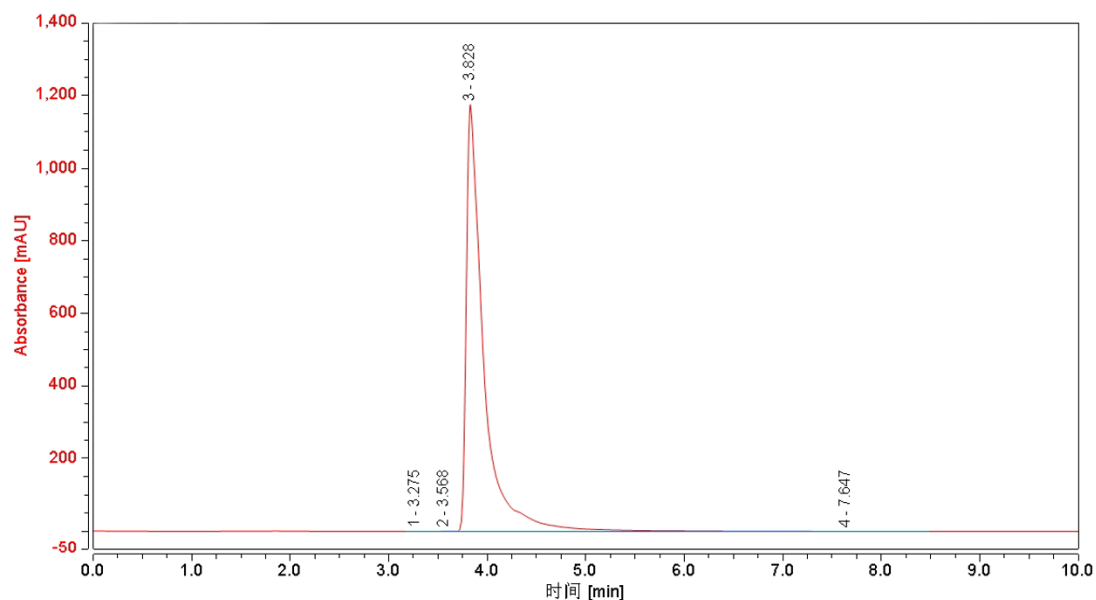
Table S1. HPLC analysis data for the tested compounds<sup>[a]</sup>

Compound	Eluent	Retention time	Purity
	(water/acetonitrile, v/v)	(min)	(%)
<b>1-2</b> <sup>[b]</sup>	20:80	3.828	97.66
<b>1-3</b> <sup>[a]</sup>	20:80	4.877	99.82
<b>1-4</b> <sup>[a]</sup>	20:80	3.283	98.78
<b>2-1</b> <sup>[b]</sup>	20:80	2.392	99.25
<b>2-2</b> <sup>[a]</sup>	20:80	3.917	97.58
<b>2-3</b> <sup>[a]</sup>	20:80	4.850	98.90
<b>2-4</b> <sup>[a]</sup>	20:80	5.117	97.02
<b>2-5</b> <sup>[b]</sup>	20:80	3.558	97.66
<b>3-1</b> <sup>[b]</sup>	20:80	2.423	96.85
<b>3-2</b> <sup>[a]</sup>	20:80	3.233	99.29
<b>3-3</b> <sup>[a]</sup>	20:80	3.700	98.73

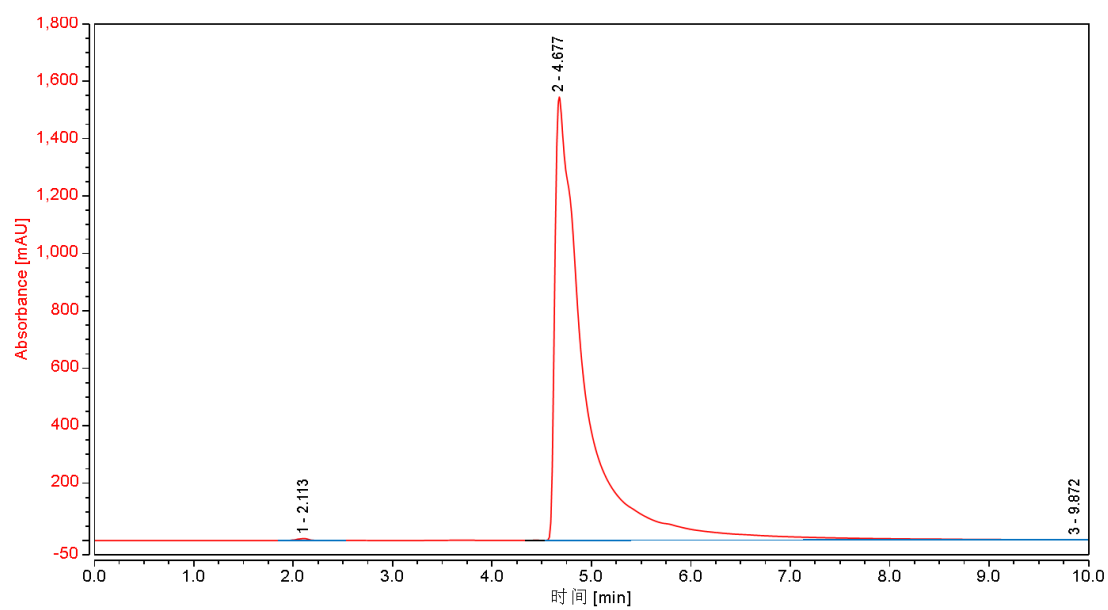
<b>3-4</b> <sup>[a]</sup>	20:80	3.883	98.99
<b>3-5</b> <sup>[b]</sup>	20:80	2.935	99.96
<b>6-1</b> <sup>[a]</sup>	20:80	4.050	97.03
<b>6-2</b> <sup>[a]</sup>	20:80	4.683	99.68
<b>6-3</b> <sup>[a]</sup>	20:80	4.717	99.43
<b>6-4</b> <sup>[b]</sup>	20:80	3.568	99.83
<b>6-5</b> <sup>[a]</sup>	20:80	4.733	99.61
<b>6-6</b> <sup>[b]</sup>	20:80	4.523	99.98

[<sup>a</sup>] HPLC analysis was performed using a Persee L600 instrument, with photodiode array detector and a Pgrandsil-STC-C18 (4.6x250 mm, 5  $\mu$ m particle size, 100 Å). The flow rate was set at 1 mL/min.

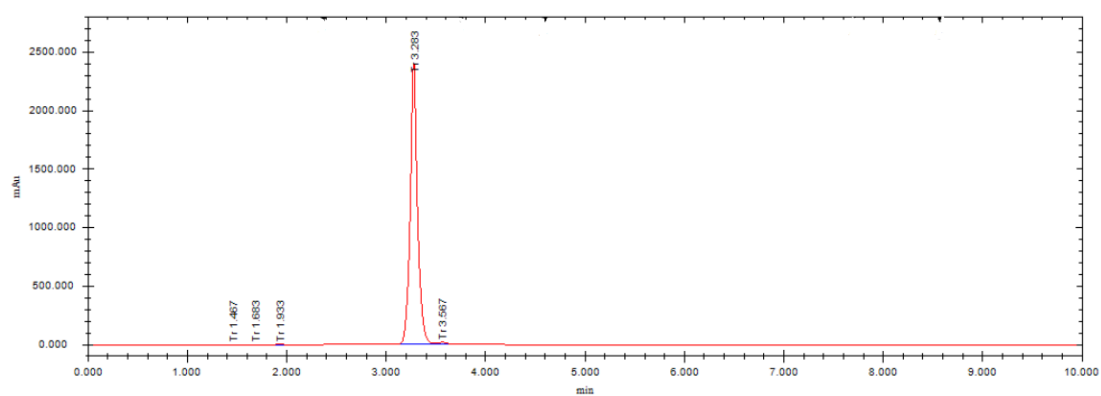
[<sup>b</sup>] HPLC analysis was performed using a UltiMate 3000 instrument, with photodiode array detector and a Eclipse-XDB-C18 (4.6x250 mm, 5  $\mu$ m particle size, 100 Å). The flow rate was set at 1 mL/min.



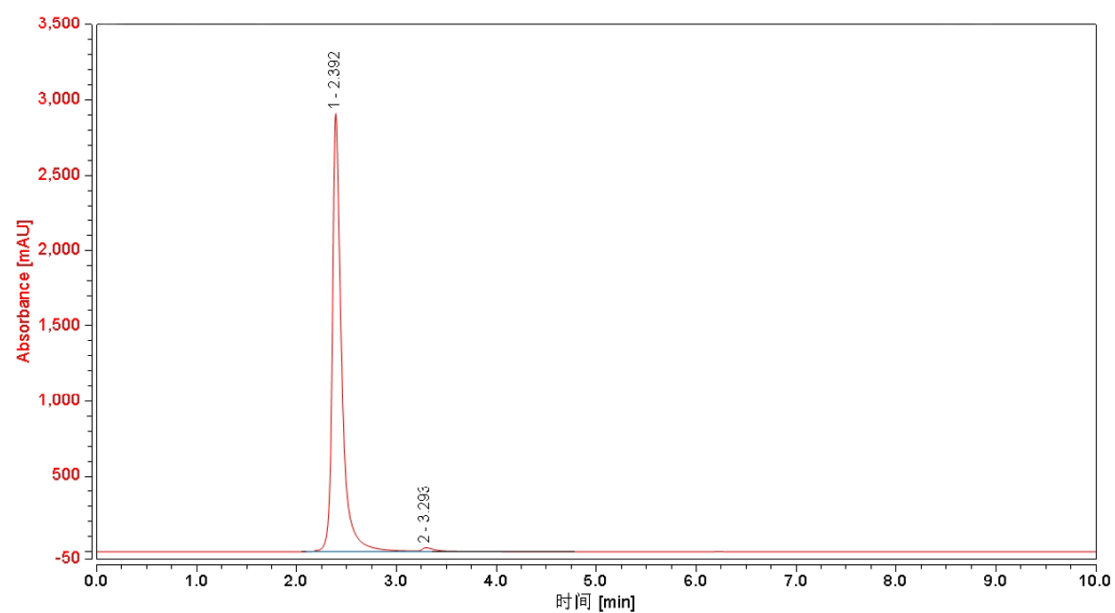
(up) HPLC spectrum of compound **1-2**



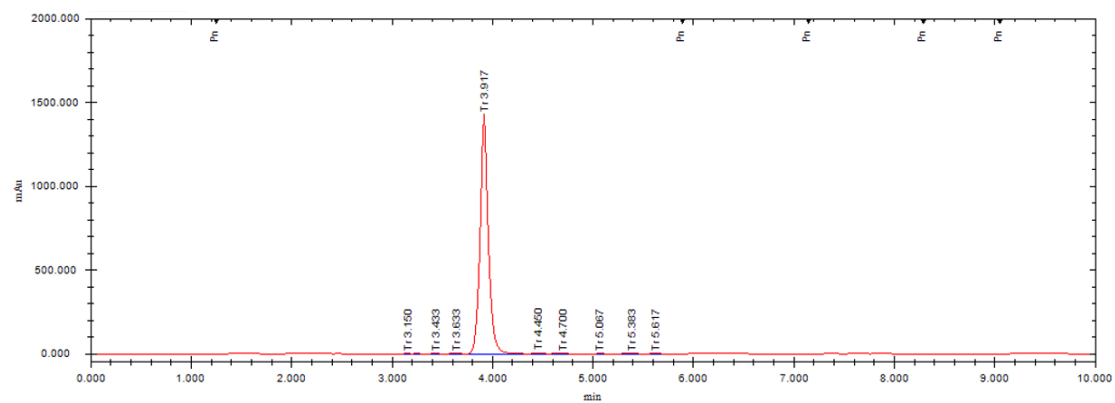
(up) HPLC spectrum of compound 1-3



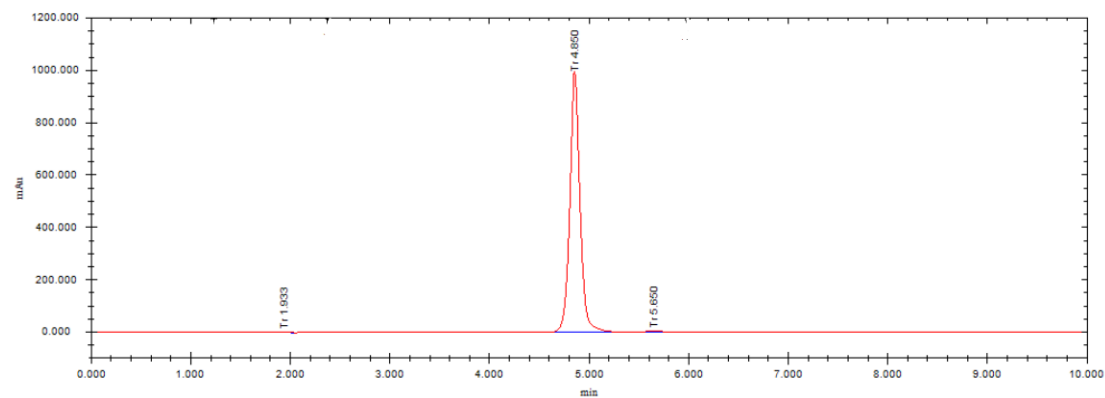
(up) HPLC spectrum of compound 1-4



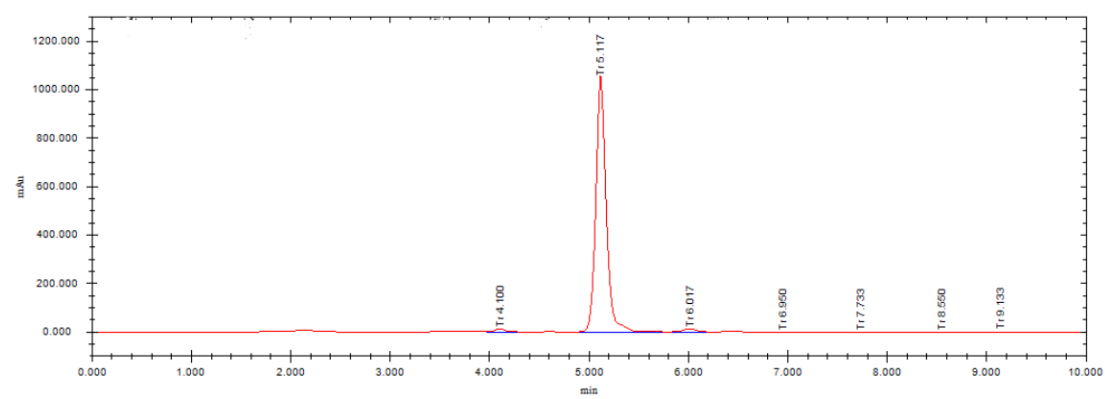
(up) HPLC spectrum of compound **2-1**



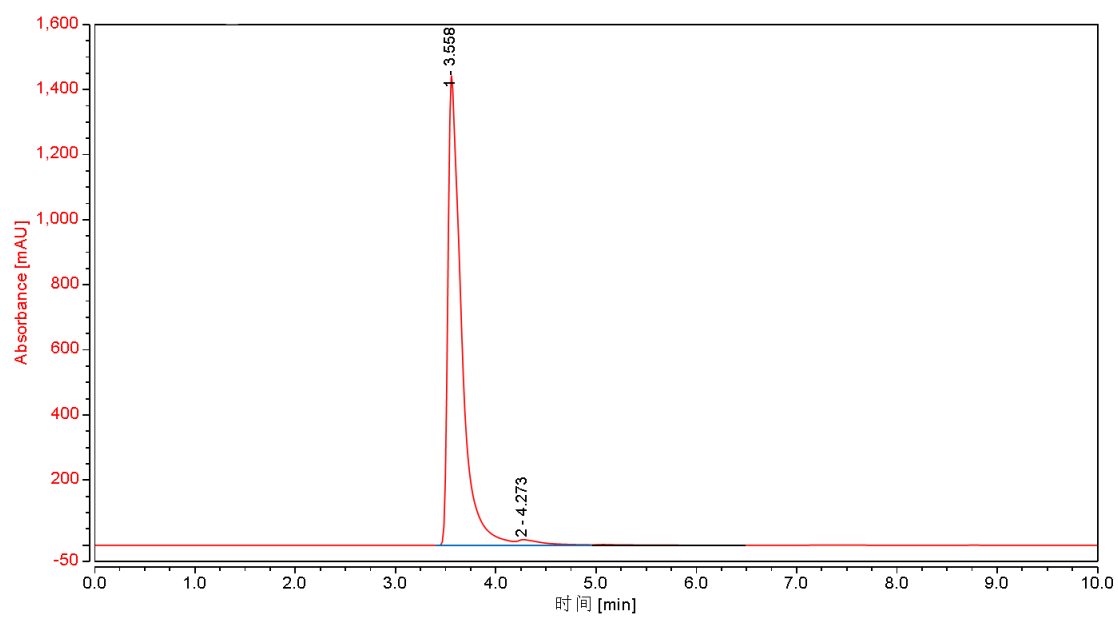
(up) HPLC spectrum of compound **2-2**



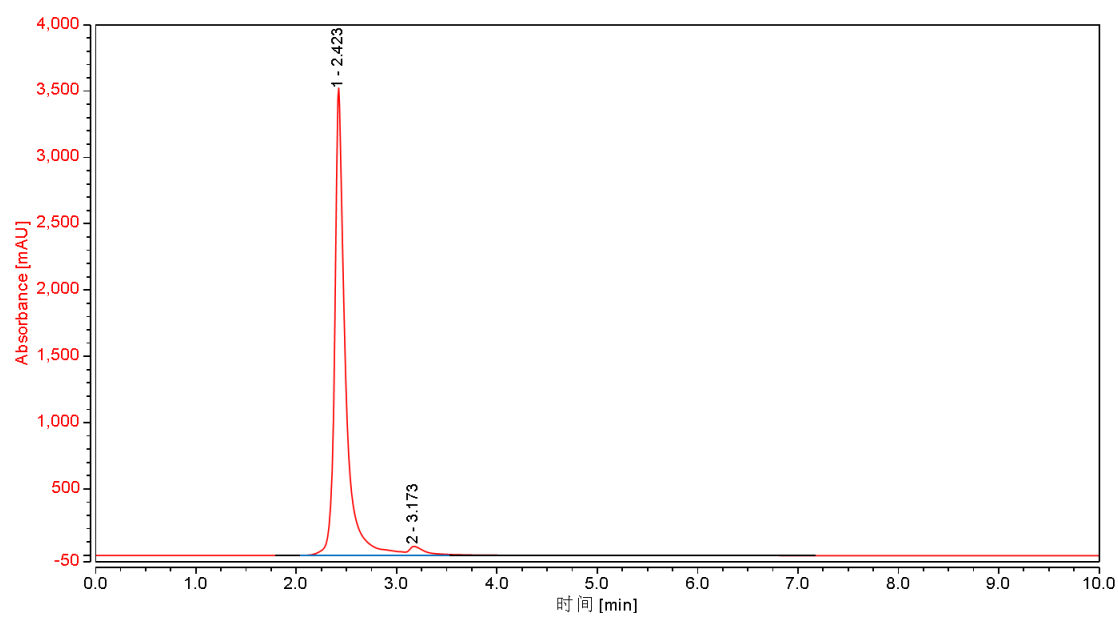
(up) HPLC spectrum of compound **2-3**



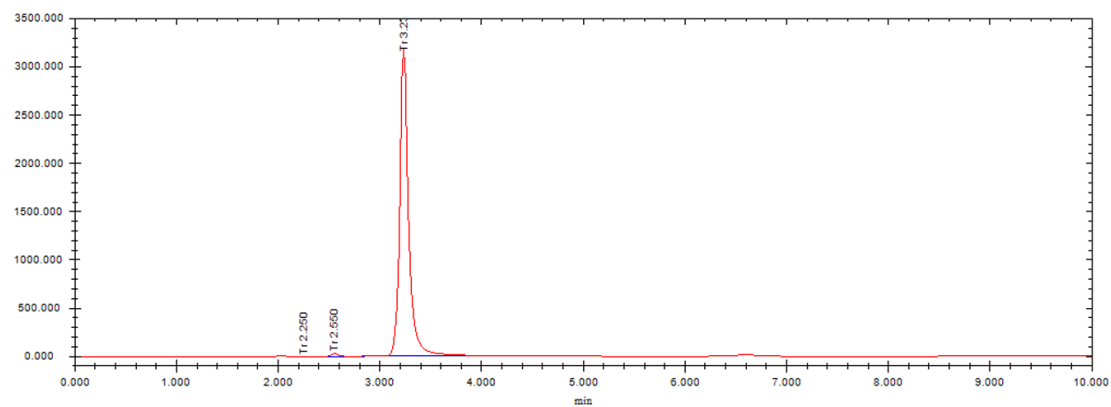
(up) HPLC spectrum of compound **2-4**



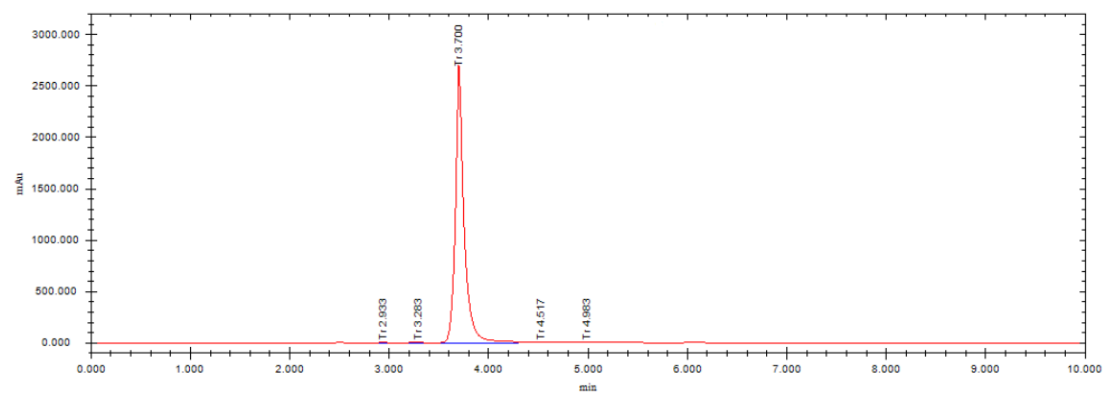
(up) HPLC spectrum of compound 2-5



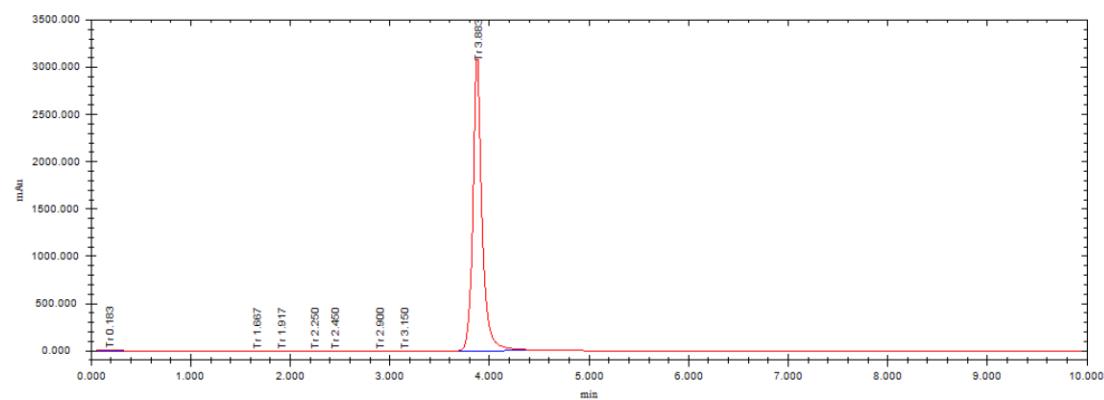
(up) HPLC spectrum of compound 3-1



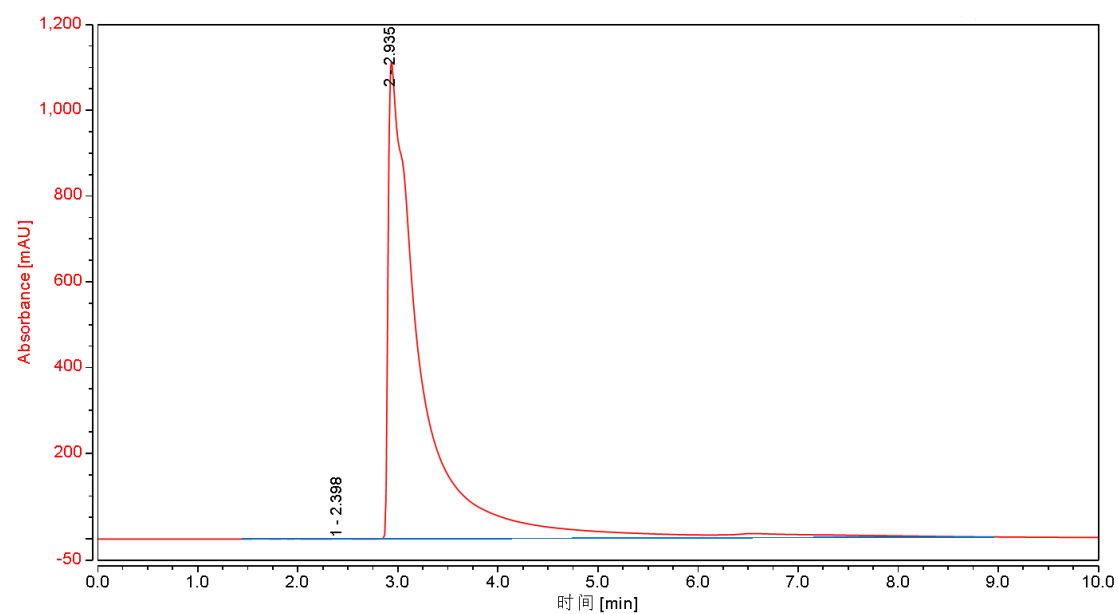
(up) HPLC spectrum of compound **3-2**



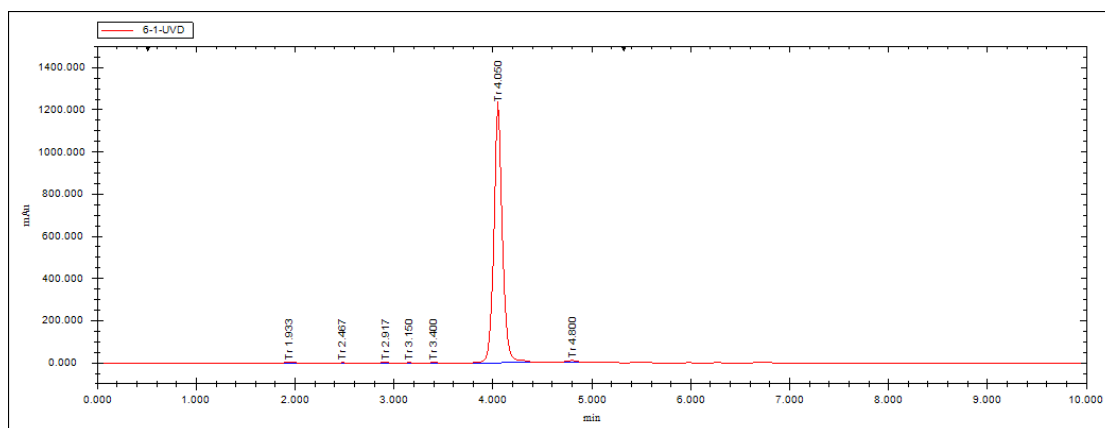
(up) HPLC spectrum of compound **3-3**



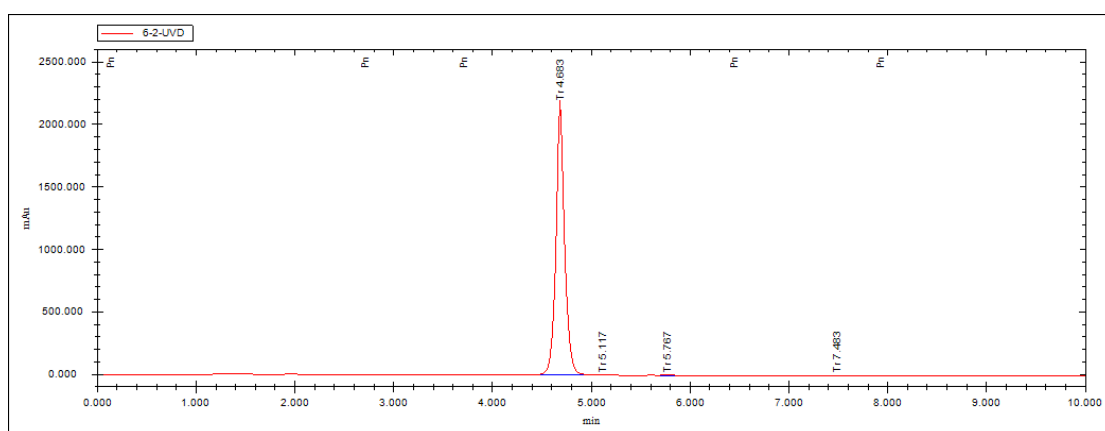
(up) HPLC spectrum of compound **3-4**



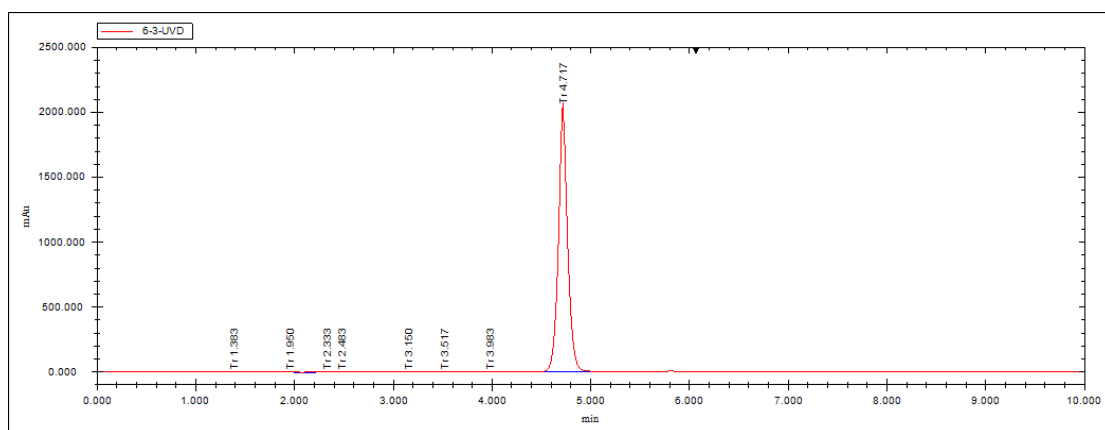
(up) HPLC spectrum of compound **3-5**



(up) HPLC spectrum of compound 4-1

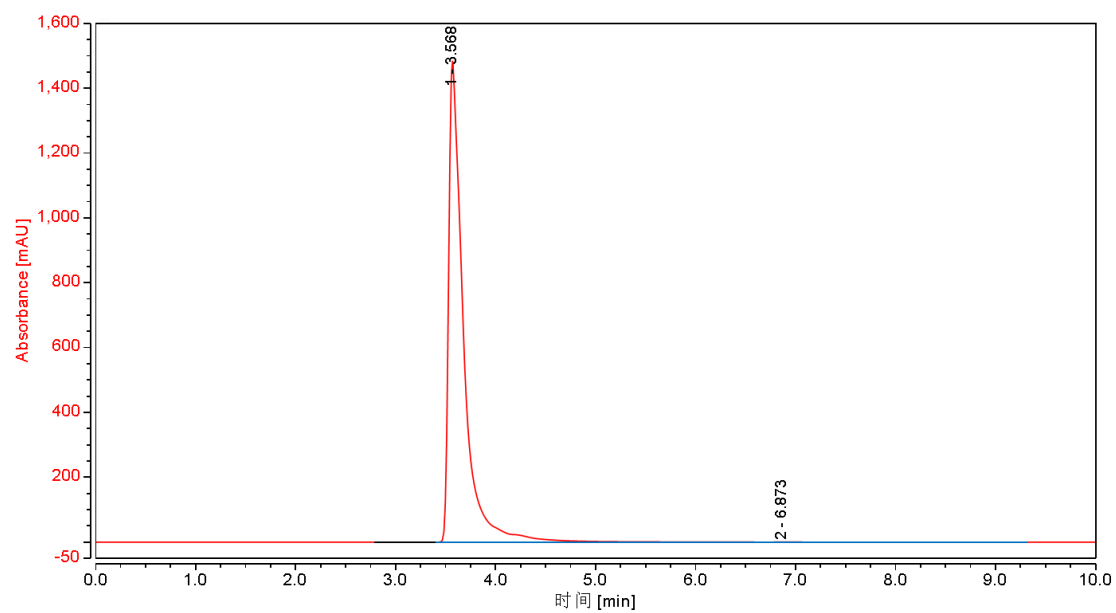


(up) HPLC spectrum of compound 4-2

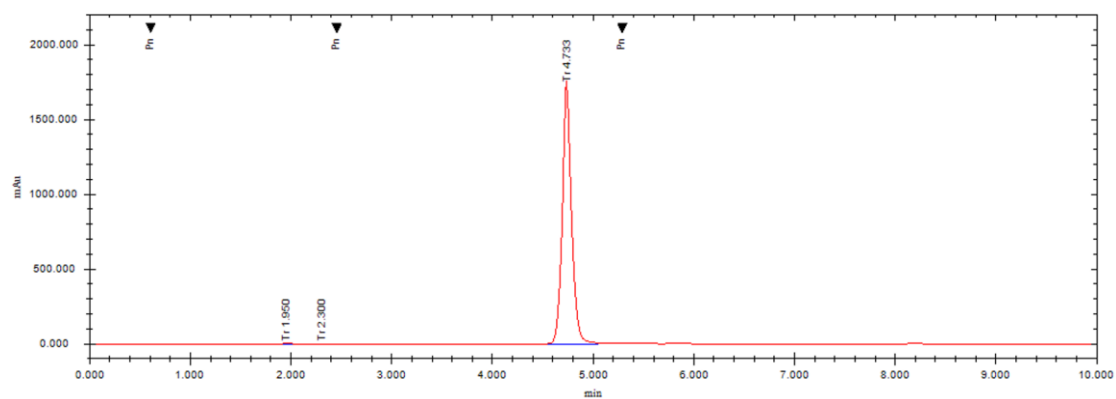


(up) HPLC spectrum of compound 4-3

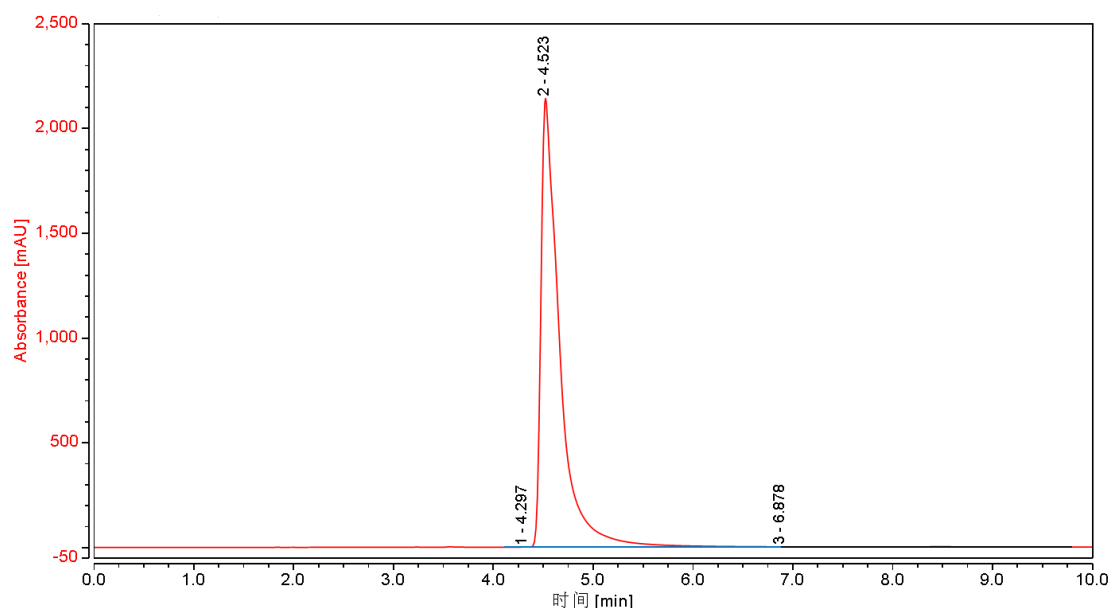




(up) HPLC spectrum of compound **4-4**



(up) HPLC spectrum of compound **4-5**



(up) HPLC spectrum of compound **4-6**

## References

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