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Supporting Information

β-Aldehyde ketones as dual inhibitors of aldose reductase and α-glucosidase with antioxidant properties

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1. Experimental section

1.1 Chemistry

All reactions were routinely checked by TLC on silica gel Merck 60F254. Melting points are uncorrected and were recorded on an X-4 microscopic melting point apparatus. NMR spectra were recorded on a Bruker Avance 400 spectrometer (400 MHz for ^{1}H NMR and^{13}C NMR), and chemical shifts are given in δ referenced to the residual solvent peak. HRMS (ESI) was performed using an Agilent 6210 time-of-flight LC/MS. HPLC conditions were the following: Inertsil ODS-2 250 mm × 10 mm, 5 mm column; mobile phase: CH_3CN, for 30 min; room temperature; flow rate: 1 mL min^{-1}; detection at λ 254 nm. All final compounds in biological assays have a purity of ≥ 95%.

*1.2. General procedure for the synthesis of 1-([1,1'-biphenyl]-3-yl) ethan-1-one derivatives (**2**)*

A round-bottomed flask was charged with 3'-bromoacetone **1** (0.398 g, 2 mmol), the corresponding phenylboronic acid (2.2 mmol), K_2CO_3 (0.318 g, 3 mmol), $Pd(dppf)Cl_2$ (0.073 g, 0.1 mmol), then H_2O (2 mL) and 1,4-dioxane (8 mL) were added. The reaction flask was equipped with a reflux condenser and heated to 80 ℃ for 8 h under an atmosphere of nitrogen. Upon cooling to room temperature, the mixture was poured into water (100 mL) and extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated by rotary evaporation under reduced pressure to provide the crude residue which was purified by silica gel chromatography with petroleum ether/ethyl acetate (4:1) to afford desired products **2**.

*1.2.1 1-(4'-hydroxy-[1,1'-biphenyl]-3-yl)ethan-1-one (**2a**)*

Yield: 0.340g (80%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.13 (t, J = 1.8 Hz, 1H), 7.89 (ddd, J = 7.7, 1.8, 1.1 Hz, 1H), 7.74 (ddd, J = 7.7, 1.9, 1.1 Hz, 1H), 7.58 (m, 3H), 6.91 (m, 2H), 5.01 (s, 1H), 2.66 (s, 3H).

*1.2.2 1-(2',4'-dihydroxy-[1,1'-biphenyl]-3-yl)ethan-1-one (**2b**)*

Yield: 0.375g (82%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.95 (m, 2H), 7.60 (m, 2H), 7.14 (d, *J* = 8.1 Hz, 1H), 6.53 (m, 2H), 5.11 (s, 1H), 4.95 (s, 1H), 2.64 (d, *J* = 2.2 Hz, 3H).

*1.2.3 1-(3',4',5'-trimethoxy-[1,1'-biphenyl]-3-yl)ethan-1-one (**2c**)*

Yield: 0.471g (81%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (t, *J* = 1.8 Hz, 1H), 7.90 (m, 1H), 7.75 (ddd, *J* = 7.7, 2.0, 1.1 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 6.79 (s, 2H), 3.92 (d, *J* = 15.8 Hz, 9H), 2.66 (s, 3H).

*1.3. General procedure for the synthesis of (E)-1-([1,1'-biphenyl]-3-yl)-3-hydroxy prop-2-en-1-one derivatives (**3**)*

1-([1,1'-biphenyl]-3-yl) ethan-1-one derivatives (**2**) (1 mmol) was dissolved in dry toluene (10 mL) and the mixture was stirred in the ice bath. CH_3ONa (0.162g, 3 mmol) was added to the solution and the mixture was stirred for 30 min in the ice bath. Ethyl formate (0.148g, 2 mmol) was then added dropwise to the reaction mixture, which was maintained at 0 ℃, after the addition, the reaction mixture was stirred for another 2 h and allowed to warm to room temperature, then stirred overnight (about 15 h). Water (100 mL) was added to the slurry mixture, and the reaction was stirred for an additional 30 min and then partitioned between the organic layer and water. The water layer was extracted with ethyl acetate (2×50 mL). These extracts were discarded and pooled. The aqueous phase was acidified with 5% hydrochloric acid and extracted with ethyl acetate (3×50 mL). This extract was washed with water and brine, dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give yellow solid, and purified further by recrystallization from hexane to afford the products **3**.

*1.3.1 (E)-1-(4'-hydroxy-[1,1'-biphenyl]-3-yl)3-hydroxyprop-2-en-1-one (**3a**)*

Yield: 0.1480g (58%); yellow solid; mp: 120-122 ℃; purity: 99.20%; ^{1}H NMR (400 MHz, Chloroform-d) δ 15.32 (s, 1H), 8.34 (m, 1H), 8.07 (t, J = 1.9 Hz, 1H), 7.82 (dt, J = 7.8, 1.4 Hz, 1H), 7.72 (dt, J = 7.8, 1.4 Hz, 1H), 7.53 (m, 3H), 6.92 (m, 2H), 6.30 (m, 1H), 5.06 (s, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 187.96, 178.87, 155.64, 141.44, 135.42, 132.79, 131.17, 129.13, 128.47, 125.63, 115.86, 98.53; HRMS (ESI) m/z calcd for $[M+H]^+$ 241.0865, found 241.0846.

*1.3.2 (E)-1-(2',4'-dihydroxy-[1,1'-biphenyl]-3-yl)-3-hydroxyprop-2-en-1-one (**3b**)*

Yield: 0.048g (18%); yellow solid; mp: 140-141 ℃; purity: 100%; ^{1}H NMR (400 MHz, DMSO-d6) δ 11.36 (s, 1H), 9.45 (d, J = 37.9 Hz, 2H), 7.73 (m, 5H), 7.12 (dd, J = 8.4, 4.8 Hz, 1H), 6.43 (d, J = 2.4 Hz, 1H), 6.33 (dd, J = 8.4, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 189.90, 179.11, 158.72, 155.74, 139.85, 134.54, 133.93, 132.78, 128.97, 128.81, 128.32, 128.05, 125.31, 107.68, 103.49; HRMS (ESI) m/z calcd for $[M-H]^-$ 255.0657, found 255.0671.

*1.3.3 (E)-1-(3',4',5'-trimethoxy-[1,1'-biphenyl]-3-yl)3-hydroxyprop-2-en-1-one(**3c**)*

Yield: 0.125g (40%); yellow solid; mp: 95-97 ℃; purity: 95.61%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.30 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.08 (t, *J* = 1.8 Hz, 1H), 7.86 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 7.74 (ddd, *J* = 7.7, 1.9, 1.1 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 6.79 (s, 2H), 6.28 (d, *J* = 4.2 Hz, 1H), 3.92 (d, *J* = 15.3 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.93, 178.52, 153.61, 142.08, 138.12, 136.13, 135.58, 131.55, 129.11, 126.19, 125.98, 104.59, 98.53, 60.98, 56.31; HRMS (ESI) m/z calcd for $[M+H]^+$ 315.1232, found 315.1218.

*1.4. General procedure for the synthesis of 1-(3-vinylphenyl)ethan-1-one derivatives (**4**)*

$Pd(OAc)_2$ (0.023 g, 0.10 mmol) and P(o-tolyl)$_3$ (0.043 g, 0.14 mmol)were added to a solution of 3'-bromoacetone (**1**) (0.398 g, 2 mmol) in DMF (8 mL). After being stirred at room temperature under argon for 20 min, the appropriate styrene (1.5 mmol),

Et_3N (2 mL) were added. The reaction mixture was stirred at 100 ℃ for 12 h. After the completion of the reaction, the mixture was poured into water (100 mL) and extracted with ethyl acetate (3×50 mL). The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration and evaporation of ethyl acetate, the residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate (2:1) to give desired products **4**.

*1.4.1 (E)-1-(3-styrylphenyl)ethan-1-one (**4a**)*

Yield: 0.299g (67%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (s, 1H), 7.84 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.71 (dt, *J* = 7.6, 1.4 Hz, 1H), 7.54 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.38 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.29 (m, 1H), 7.23 (m, 2H), 2.65 (s, 3H).

*1.4.2 (E)-1-(3-(4-fluorostyryl)phenyl)ethan-1-one (**4b**)*

Yield: 0.306g (63%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (s, 1H), 7.84 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.69 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.48 (m, 3H), 7.09 (m, 4H), 2.65 (s, 3H).

*1.4.3 (E)-1-(3-(4-chlorostyryl)phenyl)ethan-1-one (**4c**)*

Yield: 0.311g (60%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (t, *J* = 1.8 Hz, 1H), 7.85 (m, 1H), 7.69 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.46 (dd, *J* = 8.2, 6.6 Hz, 3H), 7.34 (m, 2H), 7.12 (d, *J* = 2.3 Hz, 2H), 2.64 (s, 3H).

*1.4.4 (E)-1-(3-(4-(trifluoromethyl)styryl)phenyl)ethan-1-one (**4d**)*

Yield: 0.324g (55%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (t, *J* = 1.7 Hz, 1H), 7.88 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.72 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.62 (s, 4H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.22 (d, *J* = 2.0 Hz, 2H), 2.65 (s, 3H).

*1.4.5 (E)-1-(3-(4-methylstyryl)phenyl)ethan-1-one (**4e**)*

Yield: 0.287g (60%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (t, *J* = 1.8 Hz, 1H), 7.82 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.69 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.44 (m, 3H), 7.16 (m, 4H), 2.64 (s, 3H), 2.37 (s, 3H).

*1.4.6 (E)-1-(3-(4-(tert-butyl)styryl)phenyl)ethan-1-one (**4f**)*

Yield: 0.286g (51%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (t, *J* = 1.8 Hz, 1H), 7.82 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.70 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.43 (m, 5H), 7.14 (q, *J* = 16.3 Hz, 2H), 2.64 (s, 3H), 1.34 (s, 9H).

*1.4.7 (E)-1-(3-(4-methoxystyryl)phenyl)ethan-1-one (**4g**)*

Yield: 0.245g (48%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (t, *J* = 1.8 Hz, 1H), 7.81 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.67 (m, 1H), 7.45 (m, 3H), 7.14 (d, *J* = 16.3 Hz, 1H), 7.00 (d, *J* = 16.4 Hz, 1H), 6.91 (m, 2H), 3.84 (s, 3H), 2.64 (s, 3H).

*1.4.8 (E)-1-(3-(4-hydroxystyryl)phenyl)ethan-1-one (**4h**)*

Yield: 0.238g (49%); yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.62 (s, 1H), 8.10 (t, J = 1.8 Hz, 1H), 7.81 (dt, J = 7.9, 1.2 Hz, 2H), 7.48 (m, 3H), 7.20 (m, 2H), 6.80 (m, 2H), 2.62 (s, 3H).

*1.4.9 (E)-1-(3-(3,4-dimethoxystyryl)phenyl)ethan-1-one (**4i**)*

Yield: 0.322g (56%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (t, J = 1.8 Hz, 1H), 7.82 (m, 1H), 7.69 (dt, J = 7.8, 1.5 Hz, 1H), 7.45 (t, J = 7.7 Hz, 1H), 7.08 (m, 4H), 6.88 (m, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 2.65 (s, 3H).

*1.4.10 (E)-1-(3-(4-hydroxy-3-methoxystyryl)phenyl)ethan-1-one (**4J**)*

Yield: 0.283g (52%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (t, J = 1.8 Hz, 1H), 7.81 (dt, J = 7.8, 1.4 Hz, 1H), 7.68 (dt, J = 7.6, 1.5 Hz, 1H), 7.44 (t, J = 7.7 Hz, 1H), 7.12 (d, J = 16.3 Hz, 1H), 7.05 (m, 2H), 6.99 (d, J = 16.3 Hz, 1H), 6.92 (m, 1H), 5.70 (s, 1H), 3.97 (s, 3H), 2.64 (s, 3H).

*1.4.11 (E)-1-(3-(3-hydroxy-4-methoxystyryl)phenyl)ethan-1-one (**4k**)*

Yield: 0.326g (60%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (s, 1H), 7.81 (dt, J = 7.8, 1.4 Hz, 1H), 7.67 (dt, J = 7.9, 1.5 Hz, 1H), 7.44 (t, J = 7.7 Hz, 1H), 7.07 (m, 4H), 6.85 (d, J = 8.3 Hz, 1H), 5.63 (s, 1H), 3.92 (s, 3H), 2.64 (s, 3H).

*1.4.12 (E)-1-(3-(2,4-dimethoxystyryl)phenyl)ethan-1-one (**4m**)*

Yield: 0.315g (55%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (t, J = 1.8 Hz, 1H), 7.79 (dt, J = 7.7, 1.3 Hz, 1H), 7.70 (dt, J = 7.9, 1.4 Hz, 1H), 7.46 (m, 3H), 7.05 (d, J = 16.5 Hz, 1H), 6.51 (m, 2H), 3.86 (d, J = 17.8 Hz, 6H), 2.64 (s, 3H).

*1.4.13 (E)-1-(3-(4-hydroxy-2-methoxystyryl)phenyl)ethan-1-one (**4n**)*

Yield: 0.278g (51%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (d, J = 1.9 Hz, 1H), 7.67 (dd, J = 36.9, 7.7 Hz, 2H), 7.37 (m, 3H), 6.95 (d, J = 16.5 Hz, 1H), 6.39 (m, 2H), 5.40 (s, 1H), 3.79 (s, 3H), 2.58 (s, 3H).

*1.4.14 (E)-1-(3-(2,4-dihydroxystyryl)phenyl)ethan-1-one (**4o**)*

Yield: 0.243g (47%); yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.69 (s, 1H), 9.46 (s, 1H), 8.02 (t, J = 1.8 Hz, 1H), 7.76 (m, 1H), 7.43 (m, 2H), 7.09 (d, J = 16.5 Hz, 3H), 6.35 (d, J = 2.3 Hz, 1H), 6.27 (dd, J = 8.5, 2.4 Hz, 1H), 2.61 (m, 3H).

*1.4.15 (E)-1-(3-(3,5-dimethoxystyryl)phenyl)ethan-1-one(**4p**)*

Yield: 0.367g (64%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (t, J = 1.8 Hz, 1H), 7.84 (m, 1H), 7.70 (m, 1H), 7.46 (t, J = 7.7 Hz, 1H), 7.12 (s, 2H), 6.69 (d, J = 2.2 Hz, 2H), 6.42 (t, J = 2.3 Hz, 1H), 3.84 (s, 6H), 2.64 (s, 3H).

*1.4.16 (E)-1-(3-(3,4,5-trimethoxystyryl)phenyl)ethan-1-one (**4q**)*

Yield: 0.490g (78%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (s, 1H), 7.84 (dt, J = 7.7, 1.3 Hz, 1H), 7.70 (dt, J = 7.7, 1.5 Hz, 1H), 7.46 (t, J = 7.7 Hz, 1H), 7.09 (q, J = 16.2 Hz, 2H), 6.76 (s, 2H), 3.91 (d, J = 19.6 Hz, 9H), 2.65 (s, 3H).

*1.4.17 (E)-1-(3-(2-(naphthalen-2-yl)vinyl)phenyl)ethan-1-one (**4r**)*

Yield: 0.367g (67%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (s, 1H), 7.85 (m, 5H), 7.75 (m, 2H), 7.48 (m, 3H), 7.34 (m, 2H), 2.66 (s, 3H).

*1.4.18 (E)-1-(3-(2-([1,1'-biphenyl]-4-yl)vinyl)phenyl)ethan-1-one (**4s**)*

Yield: 0.357g (59%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (t, *J* = 1.8 Hz, 1H), 7.84 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.72 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.62 (m, 6H), 7.46 (td, J = 7.8, 5.8 Hz, 3H), 7.36 (m, 1H), 7.21 (m, 2H), 2.65 (s, 3H).

*1.4.19 (E)-1-(3-(2-(6-methoxynaphthalen-2-yl)vinyl)phenyl)ethan-1-one (**4t**)*

Yield: 0.384g (63%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (t, *J* = 1.8 Hz, 1H), 7.83 (m, 2H), 7.73 (ddd, *J* = 6.3, 5.2, 1.8 Hz, 4H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 16.3 Hz, 1H), 7.17 (m, 3H), 3.93 (s, 3H), 2.66 (s, 3H).

*1.4.20 (E)-1-(3-(2-(6-hydroxynaphthalen-2-yl)vinyl)phenyl)ethan-1-one (**4u**)*

Yield: 0.356g (61%); yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.19 (s, 1H), 7.81 (m, 6H), 7.48 (m, 3H), 7.11 (m, 2H), 2.64 (s, 3H).

*1.5. General procedure for the synthesis of (E)-3-hydroxy-1-(3-vinylphenyl)prop-2-en-1-one derivatives (**5**)*

1-(3-vinylphenyl)ethan-1-one derivatives (**4**) (1 mmol) was dissolved in dry toluene (10 mL) and the mixture was stirred in the ice bath. CH_3ONa (0.162g, 3 mmol) was added to the solution and the mixture was stirred for 30 min in the ice bath. Ethyl formate (0.148g, 2 mmol) was then added dropwise to the reaction mixture, which was maintained at 0 ℃, after the addition, the reaction mixture was stirred for another 2 h and allowed to warm to room temperature, then stirred overnight (about 15 h). Water (100 mL) was added to the slurry mixture, and the reaction was stirred for an additional 30 min and then partitioned between the organic layer and water. The water layer was extracted with ethyl acetate (2×50 mL). These extracts were discarded and pooled. The aqueous phase was acidified with 5% hydrochloric acid and extracted with ethyl acetate (3×50mL). This extract was washed with water and brine, dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give yellow solid, and purified further by recrystallization from hexane to afford the products **5**.

*1.5.1 (E)-3-hydroxy-1-(3-((E)-styryl)phenyl)prop-2-en-1-one (**5a**)*

Yield: 0.096g (38%); yellow solid; mp: 81-83 ℃; purity: 98.26%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.32 (s, 1H), 8.31 (d, *J* = 4.2 Hz, 1H), 8.05 (s, 1H), 7.77 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.70 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.53 (m, 2H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.38 (dd, *J* = 8.4, 6.8 Hz, 1H), 7.28 (m, 2H), 7.17 (m, 2H), 6.27 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.82, 178.59, 138.00, 136.83, 135.46, 130.65, 130.11, 129.02, 128.75, 128.03, 127.50, 126.64, 126.35, 125.34, 98.46; HRMS (ESI) m/z calcd for $[M+H]^+$ 251.1072, found 251.1057.

*1.5.2 (E)-1-(3-((E)-4-fluorostyryl)phenyl)-3-hydroxyprop-2-en-1-one (**5b**)*

Yield: 0.127g (47%); yellow solid; mp: 74-76 ℃; purity: 98.66%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.32 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.03 (t, *J* = 1.8 Hz, 1H), 7.76 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.67 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.47 (m, 3H), 7.08 (m, 4H), 6.26 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (101 MHz, CDCl3) δ 187.80, 178.59, 161.32 (d, *J* = 247.8 Hz), 137.85, 135.50, 133.05, 130.59, 129.05, 128.88, 128.13 (d, *J* = 8.1 Hz), 127.31, 127.28, 126.40, 125.26, 115.84 (d, *J* = 22 Hz), 98.46 ; HRMS (ESI) m/z calcd for $[M+H]^+$ 269.0978, found 269.0952.

*1.5.3 (E)-1-(3-((E)-4-chlorostyryl)phenyl)-3-hydroxyprop-2-en-1-one (**5c**)*

Yield: 0.112g (39%); yellow solid; mp: 134-135 ℃; purity: 99.53%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.30 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.04 (t, *J* = 1.8 Hz, 1H), 7.78 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.68 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.46 (m, 3H), 7.34 (m, 2H), 7.12 (d, *J* = 2.2 Hz, 2H), 6.26 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.71, 178.62, 137.65, 135.51, 135.34, 133.62, 130.67, 129.07, 128.97, 128.96, 128.92, 128.75, 128.10, 127.78, 126.57, 125.36, 98.45; HRMS (ESI) m/z calcd for $[M+H]^+$ 285.0682, found 285.0673.

*1.5.4 (E)-3-hydroxy-1-(3-((E)-4-(trifluoromethyl)styryl)phenyl)prop-2-en-1-one (**5d**)*

Yield: 0.098g (30%); yellow solid; mp: 85-88 ℃; purity: 98.91%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.30 (s, 1H), 8.31 (d, *J* = 4.2 Hz, 1H), 8.08 (t, *J* = 1.8 Hz, 1H), 7.81 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.71 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.63 (s, 4H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 2.1 Hz, 2H), 6.27 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.67, 178.64, 140.31, 137.33, 135.63, 130.87, 130.02, 129.51, 129.16, 128.54, 126.98, 126.73, 125.74, 125.59, 122.80 (dd, J =275.4 Hz), 98.47; HRMS (ESI) m/z calcd for $[M+H]^+$ 319.0946, found 319.0927.

*1.5.5 (E)-3-hydroxy-1-(3-((E)-4-methylstyryl)phenyl)prop-2-en-1-one (**5e**)*

Yield: 0.087g (32%); yellow solid; mp: 112-114 ℃; purity: 96.68%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.32 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.03 (s, 1H), 7.75 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.68 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.44 (m, 3H), 7.16 (m, 4H), 6.26 (d, *J* = 4.2 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.88, 178.59, 138.20, 138.01, 135.43, 134.06, 130.55, 130.05, 129.47, 128.99, 126.57, 126.50, 126.15, 125.23, 98.46, 21.28; HRMS (ESI) m/z calcd for $[M+H]^+$ 265.1229, found 265.1218.

*1.5.6 (E)-1-(3-((E)-4-(tert-butyl)styryl)phenyl)-3-hydroxyprop-2-en-1-one (**5f**)*

Yield: 0.101g (33%); yellow solid; mp: 70-72 ℃; purity: 95.72%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.32 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.04 (d, *J* = 1.9 Hz, 1H), 7.72 (m, 2H), 7.44 (m, 5H), 7.12 (m, 2H), 6.27 (d, *J* = 4.2 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.91, 178.56, 151.28, 138.22, 135.45, 134.06, 130.58, 129.92, 128.99, 126.71, 126.40, 126.16, 125.70, 125.24, 98.48, 34.67, 31.27; HRMS (ESI) m/z calcd for $[M+H]^+$ 307.1698, found 307.1686.

*1.5.7 (E)-3-hydroxy-1-(3-((E)-4-methoxystyryl)phenyl)prop-2-en-1-one (**5g**)*

Yield: 0.123g (43%); yellow solid; mp: 85-86 ℃; purity: 99.90%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.32 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.02 (t, *J* = 1.8 Hz, 1H), 7.74 (ddd, *J* = 7.7, 1.8, 1.1 Hz, 1H), 7.66 (dt, *J* = 7.7, 1.5 Hz, 1H), 7.45 (m, 3H), 7.14 (d, *J* = 16.3 Hz, 1H), 7.00 (d, *J* = 16.3 Hz, 1H), 6.92 (m, 2H), 6.26 (d, *J* = 4.2 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.95, 178.57, 159.63, 138.36, 135.44, 130.44, 129.66, 128.99, 127.91, 125.97, 125.39, 125.08, 114.22, 98.47, 55.35; HRMS (ESI) m/z calcd for $[M+H]^+$ 281.1178, found 281.1166.

*1.5.8 (E)-3-hydroxy-1-(3-((E)-4-hydroxystyryl)phenyl)prop-2-en-1-one (**5h**)*

Yield: 0.095g (35%); yellow solid; mp: 151-153 ℃; purity: 96.75%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.31 (s, 1H), 8.31 (d, *J* = 4.2 Hz, 1H), 8.02 (s, 1H), 7.74 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.66 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.43 (m, 2H), 7.26 (s, 1H), 7.13 (d, *J* = 16.3 Hz, 1H), 6.99 (d, *J* = 16.3 Hz, 1H), 6.85 (m, 2H), 6.26 (d, *J* = 4.2 Hz, 1H), 4.95 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 190.10, 179.25, 158.07, 139.66, 138.32, 130.33, 129.74, 129.34, 128.54, 128.36, 125.59, 124.87, 124.52, 116.03, 103.13; HRMS (ESI) m/z calcd for $[M+H]^+$ 267.1021, found 267.1012.

*1.5.9 (E)-1-(3-((E)-3,4-dimethoxystyryl)phenyl)-3-hydroxyprop-2-en-1-one (**5i**)*

Yield: 0.088g (28%); yellow solid; mp: 85-87 ℃; purity: 98.48%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.33 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.04 (s, 1H), 7.71 (dd, *J* = 29.0, 7.8 Hz, 2H), 7.46 (q, *J* = 7.8, 7.0 Hz, 1H), 7.01 (m, 5H), 6.27 (d, *J* = 4.2 Hz, 1H), 3.94 (d, *J* = 17.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.90, 178.63, 149.29, 149.19, 138.24, 135.44, 130.45, 129.96, 129.90, 129.03, 126.05, 125.60, 125.13, 120.18, 111.26, 108.83, 98.48, 55.98, 55.91; HRMS (ESI) m/z calcd for $[M+H]^+$ 311.1283, found 311.1268.

*1.5.10 (E)-3-hydroxy-1-(3-((E)-4-hydroxy-3-methoxystyryl)phenyl)prop-2-en-1-one (**5J**)*

Yield: 0.94g (31%); yellow solid; mp: 124-126 ℃; purity: 96.89%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.32 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.03 (t, *J* = 1.8 Hz, 1H), 7.74 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.67 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 16.3 Hz, 1H), 7.05 (m, 2H), 6.95 (m, 2H), 6.27 (d, *J* = 4.2 Hz, 1H), 5.70 (s, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.91, 178.59, 146.75, 145.96, 138.27, 135.43, 130.40, 130.05, 129.50, 129.00, 125.99, 125.29, 125.08, 120.71, 114.64, 108.36, 98.47, 55.94; HRMS (ESI) m/z calcd for $[M+H]^+$ 297.1127, found 297.1121.

*1.5.11 (E)-3-hydroxy-1-(3-((E)-3-hydroxy-4-methoxystyryl)phenyl)prop-2-en-1-one (**5k**)*

Yield: 0.92g (31%); yellow solid; mp: 103-104 ℃; purity: 95.50%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.31 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.01 (d, *J* = 1.8 Hz, 1H), 7.70 (ddt, *J* = 35.0, 7.8, 1.4 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.13 (m, 2H), 6.99 (m, 2H), 6.85 (d, *J* = 8.3 Hz, 1H), 6.26 (d, *J* = 4.2 Hz, 1H), 5.63 (s, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.92, 178.59, 146.74, 145.84, 138.24, 135.42, 130.63,

130.53, 129.72, 128.99, 126.03, 125.91, 125.12, 119.57, 111.88, 110.67, 98.48, 56.01; HRMS (ESI) m/z calcd for $[M+H]^+$ 297.1127, found 297.1120.

*1.5.12 (E)-1-(3-((E)-2,4-dimethoxystyryl)phenyl)-3-hydroxyprop-2-en-1-one (**5m**)*

Yield: 0.117g (37%); yellow solid; mp: 70-73 ℃; purity: 100%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.33 (s, 1H), 8.30 (dd, *J* = 7.8, 4.2 Hz, 1H), 8.02 (d, *J* = 1.9 Hz, 1H), 7.70 (ddt, *J* = 14.7, 7.8, 1.4 Hz, 2H), 7.46 (m, 3H), 7.04 (d, *J* = 16.4 Hz, 1H), 6.51 (m, 2H), 6.26 (d, *J* = 4.2 Hz, 1H), 3.86 (d, *J* = 17.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.13, 178.51, 160.86, 158.24, 139.03, 135.35, 130.48, 128.90, 127.54, 125.84, 125.74, 125.19, 124.83, 119.05, 105.06, 98.51, 55.52, 55.44; HRMS (ESI) m/z calcd for $[M+H]^+$ 311.1283, found 311.1271.

*1.5.13 (E)-3-hydroxy-1-(3-((E)-4-hydroxy-2-methoxystyryl)phenyl)prop-2-en-1-one (**5n**)*

Yield: 0.86g (29%); yellow solid; mp: 120-122 ℃; purity: 97.75%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.31 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 8.01 (t, *J* = 1.8 Hz, 1H), 7.70 (ddt, *J* = 35.0, 7.8, 1.4 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.06 (m, 4H), 6.85 (d, *J* = 8.3 Hz, 1H), 6.26 (d, *J* = 4.2 Hz, 1H), 5.63 (s, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 183.40, 173.90, 153.66, 152.09, 134.26, 130.55, 125.77, 124.17, 122.94, 121.06, 121.02, 120.46, 120.01, 114.24, 102.83, 94.35, 93.79, 50.80; HRMS (ESI) m/z calcd for $[M+H]^+$ 297.1127, found 297.1120.

*1.5.14 (E)-1-(3-((E)-2,4-dihydroxystyryl)phenyl)-3-hydroxyprop-2-en-1-one (**5o**)*

Yield: 0.054g (19%); yellow solid; mp: 140-141℃; purity: 95.04%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.36 (s, 1H), 9.50 (s, 1H), 9.40 (s, 1H), 7.73 (m, 5H), 7.12 (dd, *J* = 8.4, 4.8 Hz, 1H), 6.38 (m, 4H); ^{13}C NMR (176 MHz, DMSO) 195.92, 170.79, 146.32, 145.89, 138.57, 137.13, 130.46, 129.59, 129.47, 128.90, 126.36, 125.49, 124.60, 124.34, 119.29, 116.17, 113.97; HRMS (ESI) m/z calcd for $[M+H]^+$ 283.0970, found 283.0961.

*1.5.15 (E)-1-(3-((E)-3,5-dimethoxystyryl)phenyl)-3-hydroxyprop-2-en-1-one (**5p**)*

Yield: 0.083g (26%); yellow solid; mp: 65-66 ℃; purity: 99.94%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.31 (s, 1H), 8.31 (d, *J* = 4.2 Hz, 1H), 8.04 (t, *J* = 1.8 Hz, 1H), 7.78 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.69 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.12 (s, 2H), 6.69 (d, *J* = 2.2 Hz, 2H), 6.43 (t, *J* = 2.2 Hz, 1H), 6.27 (d, *J* = 4.2 Hz, 1H), 3.84 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.81, 178.64, 161.04, 138.84, 137.83, 135.49, 130.73, 130.11, 129.06, 128.03, 126.48, 125.42, 104.73, 100.39, 98.48, 55.41; HRMS (ESI) m/z calcd for $[M+H]^+$ 311.1283, found 311.1270.

*1.5.16 (E)-3-hydroxy-1-(3-((E)-3,4,5-trimethoxystyryl)phenyl)prop-2-en-1-one (**5q**)*

Yield: 0.111g (32%); yellow solid; mp: 115-117 ℃; purity: 100%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.30 (s, 1H), 8.31 (d, *J* = 4.3 Hz, 1H), 8.06 (s, 1H), 7.77 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.69 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.09 (q, *J* = 16.3 Hz, 2H), 6.76 (s, 2H), 6.27 (d, *J* = 4.2 Hz, 1H), 3.91 (d, *J* = 19.3 Hz, 9H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 187.80, 178.66, 138.05, 135.51, 134.32, 133.65, 133.21, 130.67, 130.20, 129.08, 128.43, 128.07, 127.81, 127.72, 127.04, 126.40, 126.14, 125.38, 123.38, 98.48; HRMS (ESI) m/z calcd for $[M+H]^+$ 341.1389, found 341.1379.

*1.5.17 (E)-3-hydroxy-1-(3-((E)-2-(naphthalen-2-yl)vinyl)phenyl)prop-2-en-1-one (**5r**)*

Yield: 0.094g (31%); yellow solid; mp: 131-132 ℃; purity: 99.46%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.33 (s, 1H), 8.32 (d, *J* = 4.2 Hz, 1H), 8.10 (s, 1H), 7.81 (m, 7H), 7.48 (m, 3H), 7.36 (d, *J* = 16.3 Hz, 1H), 7.29 (s, 1H), 6.29 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.82, 178.60, 153.46, 138.32, 137.92, 135.49, 132.55, 130.57, 130.06, 129.05, 126.96, 126.31, 125.25, 103.76, 98.46, 60.98, 56.15; HRMS (ESI) m/z calcd for $[M+H]^+$ 301.1229, found 301.1228.

*1.5.18 (E)-1-(3-((E)-2-([1,1'-biphenyl]-4-yl)vinyl)phenyl)-3-hydroxyprop-2-en-1-one (**5s**)*

Yield: 0.077g (23%); yellow solid; mp: 150-152 ℃; purity: 98.96%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.32 (s, 1H), 8.31 (d, *J* = 4.2 Hz, 1H), 8.07 (t, *J* = 1.8 Hz, 1H), 7.78 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.71 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.62 (m, 6H), 7.46 (m, 3H), 7.36 (m, 1H), 7.21 (m, 2H), 6.28 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.83, 178.61, 140.76, 140.53, 138.02, 135.87, 135.51, 130.67, 129.63, 129.06, 128.83, 127.53, 127.43, 127.42, 127.09, 126.92, 126.38, 125.36, 98.48; HRMS (ESI) m/z calcd for $[M+H]^+$ 327.1385, found 327.1385.

*1.5.19 (E)-3-hydroxy-1-(3-((E)-2-(6-methoxynaphthalen-2-yl)vinyl)phenyl)prop-2-en-1-one (**5t**)*

Yield: 0.085g (25%); yellow solid; mp: 145-146 ℃; purity: 99.58%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.33 (s, 1H), 8.31 (d, *J* = 4.2 Hz, 1H), 8.07 (q, *J* = 2.0 Hz, 1H), 7.75 (m, 6H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 16.3 Hz, 1H), 7.16 (m, 3H), 6.27 (d, *J* = 4.2 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.87, 178.68, 158.01, 138.24, 135.48, 134.44, 132.25, 130.59, 130.30, 129.62, 129.06, 127.30, 126.89, 126.77, 126.21, 125.28, 124.01, 119.17, 105.96, 98.50, 55.36; HRMS (ESI) m/z calcd for $[M+H]^+$ 331.1334, found 331.1339.

*1.5.20 (E)-3-hydroxy-1-(3-((E)-2-(6-hydroxynaphthalen-2-yl)vinyl)phenyl)prop-2-en-1-one (**5u**)*

Yield: 0.074g (23%); yellow solid; mp: 185-187 ℃; purity: 99.33%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.13 (s, 1H), 7.79 (m, 7H), 7.46 (m, 3H), 7.11 (m, 2H), 6.53 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 190.10, 179.28, 163.22, 156.22, 134.86, 131.83, 130.06, 129.45, 128.24, 127.28, 127.02, 126.69, 125.93, 124.28, 119.48, 109.41, 103.14, 99.55; HRMS (ESI) m/z calcd for $[M+H]^+$ 317.1178, found 317.1179.

*1.6. General procedure for the synthesis of (E)-1-(3-((E)-3,4-dihydroxystyryl)phenyl)-3-hydroxyprop-2-en-1-one (**5l**)*

(E)-3-hydroxy-1-(3-((E)-3-hydroxy-4-methoxystyryl)phenyl)prop-2-en-1-one

(**5k**) (0.269g, 1 mmol) was dissolved in dry DCM. The resulting solution was cooled by a water-ice bath (0-5 ℃) and treated, under an argon atmosphere, with boron tribromide (1.5 mmol). The reaction mixture was stirred at room temperature overnight. The reaction was quenched with ice-cold water, then the product was extracted with ethyl acetate (3×100 mL). The organic layer was collected and dried over anhydrous Na_2SO_4. The residue was purified by and the solvent was removed under reduced pressure to give yellow solid, and purified further by recrystallization from hexane to afford the product **5l**.

Yield: 0.038g (13%); yellow solid; mp: 125-128 ℃; purity: 99.80%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.02 (m, 2H), 8.08 (m, 2H), 7.79 (m, 2H), 7.49 (dd, J = 7.8, 5.0 Hz, 1H), 7.20 (d, J = 16.5 Hz, 1H), 7.03 (m, 2H), 6.92 (dd, J = 8.2, 2.0 Hz, 1H), 6.76 (d, J = 8.2 Hz, 1H), 6.51 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 186.75, 178.03, 157.50, 155.10, 146.33, 145.89, 138.55, 137.75, 130.52, 129.49, 128.90, 126.35, 125.50, 124.54, 119.30, 116.18, 113.98; HRMS (ESI) m/z calcd for $[M+H]^+$ 283.0970, found 283.0971.

*1.7. General procedure for the synthesis of 1-(3-aminophenyl)ethan-1-one (**6**)*

A 10 mL reaction vessel was charged with Cu_2O (0.143 g, 0.10 mmol), 3'-bromoacetone (**1**) (0.398 g, 2.0 mmol), 1.3 mL of N-methyl pyrrolidinone (NMP), 1.3 mL of ammonium hydroxide solution (29% NH_3, 20.0 mmol) and a magnetic stir bar. The vessel was sealed with a Teflon screw cap, immersed in a preheated oil bath and the reaction mixture was stirred at 80 ℃. Upon completion, the reaction mixture was cooled to 25 ℃, quenched with water, extracted with diethyl ether (3×50 mL). The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration and evaporation of ethyl acetate, the residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1) to give the desired product **6**.

Yield: 0.210g (77%); yellow solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 (m, 3H), 7.64 (m, 1H), 4.56 (s, 2H), 3.32 (d, J = 1.4 Hz, 3H).

1.8. General procedure for the synthesis of (E)-1-(3-(phenyldiazenyl)phenyl)etha n-1-one derivatives (7)

To a solution of 1-(3-aminophenyl)ethan-1-one (**6**) (0.526g, 3.9 mmol) in 6N HCl (5 mL), $NaNO_2$ (0.403 g, 5.85 mmol) was added at 0 ℃; after stirring for 1 h, this mixture was added dropwise to a solution of phenol (0.367 g, 3.9 mmol) in 6N NaOH at 0 ℃. After 1 hour, the obtained red brick solid was collected through filtration, washed with H_2O (100 mL), extracted with diethyl ether (3×50 mL). The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration and evaporation of ethyl acetate, the residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1) to give desired products **7**.

*1.8.1 (E)-1-(3-((4-hydroxyphenyl)diazenyl)phenyl)ethan-1-one (**7a**)*

Yield: 0.735g (78%); Red brick solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.43 (t, J = 1.8 Hz, 1H), 8.07 (m, 2H), 7.91 (m, 2H), 7.61 (t, J = 7.8 Hz, 1H), 6.98 (m, 2H), 5.70 (d, J = 3.2 Hz, 1H), 2.70 (s, 3H).

*1.8.2 (E)-1-(3-((2,4-dihydroxyphenyl)diazenyl)phenyl)ethan-1-one (**7b**)*

Yield: 0.659g (66%); Red brick solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.11 (s, 1H), 10.62 (s, 1H), 8.38 (t, J = 1.8 Hz, 1H), 8.12 (m, 1H), 8.03 (dt, J = 7.7, 1.3 Hz, 1H), 7.70 (m, 2H), 6.51 (dd, J = 8.9, 2.5 Hz, 1H), 6.39 (d, J = 2.5 Hz, 1H), 2.67 (s, 3H).

*1.9. General procedure for the synthesis of (E)-3-hydroxy-1-(3-((E)-phenyldiazen yl)phenyl)prop-2-en-1-one derivatives (**8**)*

(E)-1-(3-(phenyldiazenyl)phenyl)ethan-1-one derivatives (7) (0.224g, 1 mmol) was dissolved in dry toluene (10 mL) and the mixture was stirred in the ice bath. CH_3ONa (0.162g, 3 mmol) was added to the solution and the mixture was stirred for 30 min in the ice bath. Ethyl formate (0.148g, 2 mmol) was then added dropwise to the reaction mixture, which was maintained at 0℃, after the addition, the reaction mixture was stirred for another 2 h and allowed to warm to room temperature, then stirred overnight (about 15 h). Water (100 mL) was added to the slurry mixture, and the reaction was stirred for an additional 30 min and then partitioned between the organic layer and water. The water layer was extracted with ethyl acetate (2×50 mL). These extracts were discarded and pooled. The aqueous phase was acidified with 5% hydrochloric acid and extracted with ethyl acetate (3×50 mL). This extract was washed with water and brine, dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give yellow solid, and purified further by recrystallization from hexane to afford the products **8**.

*1.9.1 (E)-3-hydroxy-1-(3-((E)-(4-hydroxyphenyl)diazenyl)phenyl)prop-2-en-1-one (**8 a**)*

Yield: 0.153g (57%); Red brick solid; mp: 127-129 ℃; purity: 100%; ^{1}H NMR (400 MHz, Chloroform-d) δ 15.29 (s, 1H), 8.36 (m, 2H), 8.06 (ddd, J = 7.9, 2.0, 1.1 Hz, 1H), 8.00 (m, 1H), 7.91 (m, 2H), 7.61 (t, J = 7.9 Hz, 1H), 6.97 (m, 2H), 6.33 (d, J = 4.2 Hz, 1H), 5.41 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 199.28, 189.30, 163.80, 161.80, 152.66, 145.63, 140.17, 130.43, 130.23, 129.68, 126.16, 125.65, 125.59, 122.30, 121.07, 116.47, 102.94; HRMS (ESI) m/z calcd for $[M+H]^+$ 269.0926, found 269.0911.

*1.9.2 (E)-1-(3-((E)-(2,4-dihydroxyphenyl)diazenyl)phenyl)-3-hydroxyprop-2-en-1-one (**8b**)*

Yield: 0.168g (59%); Red brick solid; mp: 183-186 ℃; purity: 99.80%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.17 (s, 1H), 11.54 (s, 1H), 10.61 (s, 1H), 7.95 (m, 5H), 6.52 (dd, J = 8.9, 2.5 Hz, 2H), 6.39 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO) δ 195.56, 189.51, 179.50, 163.85, 157.20, 151.64, 140.27, 137.85, 132.92, 130.40, 125.65, 122.21, 120.94, 109.70, 103.49; HRMS (ESI) m/z calcd for $[M+H]^+$ 285.0875, found 285.0862.

*1.10. General procedure for the synthesis of (E)-1-(3-bromophenyl)-3-hydroxypr op-2-en-1-one (**9**)*

3'-bromoacetone (**1**) (0.198g, 1 mmol) was dissolved in dry toluene (10 mL) and the mixture was stirred in the ice bath. CH_3ONa (0.162g, 3 mmol) was added to the solution and the mixture was stirred for 30 min in the ice bath. Ethyl formate (0.148g, 2 mmol) was then added dropwise to the reaction mixture, which was maintained at 0℃, after the addition, the reaction mixture was stirred for another 2 h and allowed to warm to room temperature, then stirred overnight (about 15 h). Water (100 mL) was added to the slurry mixture, and the reaction was stirred for an additional 30 min and then partitioned between the organic layer and water. The water layer was extracted with ethyl acetate (2×50 mL). These extracts were discarded and pooled. The aqueous phase was acidified with 5% hydrochloric acid and extracted with ethyl acetate (3 × 50mL). This extract was washed with water and brine, dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give yellow solid, and purified further by recrystallization from hexane to afford the product **9**.

Yield: 0.195g (86%); yellow solid; mp: 50-52 ℃; purity: 100%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.12 (s, 1H), 8.28 (d, *J* = 4.2 Hz, 1H), 8.04 (t, *J* = 1.9 Hz, 1H), 7.82 (ddd, *J* = 7.8, 1.7, 1.0 Hz, 1H), 7.68 (m, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 6.19 (d, *J* = 4.2 Hz, 1H)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.36, 178.71, 136.98, 135.64, 130.42, 130.24, 125.88, 122.98, 98.39; HRMS (ESI) m/z calcd for $[M+H]^+$ 226.9708, found 226.9692.

*1.11. General procedure for the synthesis of (E)-1-(4-(4-hydroxy-3-methoxystyryl)phenyl)ethan-1-one (**11**)*

$Pd(OAc)_2$ (0.023 g, 0.10 mmol) and P(o-tolyl)$_3$ (0.043 g, 0.14 mmol)were added to a solution of 4'-bromoacetone (**10**) (0.398 g, 2 mmol) in DMF (8 mL). After being stirred at room temperature under argon for 20 min, the appropriate styrene (1.5 mmol), Et_3N (2 mL) were added. The reaction mixture was stirred at 100 ℃ for 12 h. After the completion of the reaction, the mixture was poured into water (100 mL) and extracted with ethyl acetate (3×50 mL). The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration and evaporation of ethyl acetate, the residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate (2:1) to give the desired product **11**.

Yield: 0.385g (71%); yellow solid; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.94 (m, 2H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 16.3 Hz, 1H), 7.06 (dq, *J* = 3.9, 1.9 Hz, 2H), 6.95 (m, 2H), 5.75 (s, 1H), 3.96 (s, 3H), 2.60 (s, 3H).

*1.12. General procedure for the synthesis of (E)-3-hydroxy-1-(4-((E)-4-hydroxy-3-methoxystyryl)phenyl)prop-2-en-1-one(**12**)*

*(E)-1-(4-(4-hydroxy-3-methoxystyryl)phenyl)ethan-1-one (**11**)* ((0.268g, 1 mmol) was dissolved in dry toluene (10 mL) and the mixture was stirred in the ice bath. CH_3ONa (0.162g, 3 mmol) was added to the solution and the mixture was stirred for 30 min in the ice bath. Ethyl formate (0.148g, 2 mmol) was then added dropwise to the reaction mixture, which was maintained at 0℃, after the addition, the reaction mixture was stirred for another 2 h and allowed to warm to room temperature, then stirred overnight (about 15 h). Water (100 mL) was added to the slurry mixture, and the

reaction was stirred for an additional 30 min and then partitioned between the organic layer and water. The water layer was extracted with ethyl acetate (2×50 mL). These extracts were discarded and pooled. The aqueous phase was acidified with 5% hydrochloric acid and extracted with ethyl acetate (3×50mL). This extract was washed with water and brine, dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give yellow solid, and purified further by recrystallization from hexane to afford the product **12**.

Yield: 0.128g (43%); yellow solid; mp: 155-158 ℃; purity: 100%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 15.38 (s, 1H), 8.30 (d, *J* = 4.2 Hz, 1H), 7.89 (m, 2H), 7.56 (m, 2H), 7.16 (d, *J* = 16.3 Hz, 1H), 7.06 (m, 2H), 6.95 (m, 2H), 6.22 (d, *J* = 4.2 Hz, 1H), 5.74 (s, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.06, 178.59, 146.79, 146.26, 142.27, 133.30, 131.44, 129.35, 127.91, 126.33, 125.19, 121.08, 114.69, 108.44, 98.16, 55.96; HRMS (ESI) m/z calcd for $[M+H]^+$ 297.1127, found 297.1110.

1.13. Biology, Materials, and methods

ALR2 and ALR1 were obtained from Wistar rats, body weight 200-250 g, supplied by SPF (Beijing) Biotechnology Co.Ltd. (certificate: 110229013482187, Beijing, China). DL-glyceraldehyde, sodium D-glucuronate, and NADPH were purchased from Sigma-Aldrich. All other chemicals were of reagent grade. ALR2 and ALR1 were prepared according to the reported procedure of Kinoshita J and La Motta C[1-3]. Enzyme activity was assayed spectrophotometrically on a Unico 4802S UV/vis double beam spectrophotometer by measuring the decrease in absorption of NADPH at 340 nm, which accompanies the oxidation of NADPH catalyzed by ALR2 and ALR1. α-glycosidase and p-nitrophenyl-α-d-glucopyranoside were purchased from Sigma-Aldrich, α-glycosidase activity was assayed spectrophotometrically on a Unico 4802S UV/vis double beam spectrophotometer. Malondialdehyde (MDA) assay kit (TBA method) and Total protein quantitative assay kit (Coomassie Brilliant Blue) were purchased from Nanjing Jiancheng Bioengineering Institute (Nanjing, China).

1.14. Enzyme assays

The ALR2 inhibition activity was tested in a reaction mixture containing 0.25 mL NADPH (0.10 mM), 0.25 mL sodium phosphate buffer (pH = 6.2, 0.1 M), 0.1 mL enzyme extract, 0.15 mL deionized water, and 0.25 mL DL-glyceraldehyde (10 mM) as substrate in a final volume of 1 mL. At the same time, set up blank control (containing 0.25 mL NADPH (0.10 mM), 0.5 mL sodium phosphate buffer (pH = 6.2, 0.1 M), 0.1 mL enzyme extract, 0.15 mL deionized water). Before adding to DL-glyceraldehyde, the reaction mixture was incubated at 30 ℃ for 10 min, then the substrate was added to start the reaction, which was monitored for 5 min. Change in the absorbance at 340 nm due to NADPH oxidation was measured by a double beam spectrophotometer.

The ALR1 inhibition activity was performed at 36 ℃ in a reaction mixture containing 0.25 mL NADPH (0.12 mM), 0.1 mL enzyme extract, 0.25 mL sodium phosphate buffer (pH = 7.2, 0.1 M), 0.15 mL deionized water, and 0.25 mL sodium D-glucuronate (20 mM) as substrate in a final volume of 1 mL. Before adding to sodium

D-glucuronate, the reaction mixture was incubated at 37 ℃ for 10 min, then the substrate was added to start the reaction, which was monitored for 5 min. Change in the absorbance at 340 nm due to NADPH oxidation was measured by a double beam spectrophotometer.

The inhibitory activity of the newly synthesized compounds against ALR2 and ALR1 was assayed by adding 5 mL of the inhibitor solution to the reaction mixture described above. All compounds were dissolved in dimethyl sulfoxide (DMSO), and the concentration of DMSO in the final mixture was 0.5%. To correct for the nonenzymatic oxidation of NADPH, the rate of NADPH oxidation in the presence of all of the reaction mixture components except the substrate was subtracted from each experimental rate. The inhibitory effect of the synthetic compounds was routinely estimated at 10^{-4} M (the concentration is referenced to that of the compound in the reaction mixture). The compounds found to be active were tested at additional concentrations between 10^{-4} and 10^{-8} M, the log(dose)-response curves were then constructed from the inhibitory data, and the IC_{50} values were calculated by least-square analysis of the linear portion of the log(dose) versus response curves ($0.912 < r^2 < 0.996$).

1.15 Assessment of α-glucosidase Inhibitory Activity in Vitro

The inhibitory effect on α-glycosidase activity was evaluated according to the method reported in the previous literature[4] using p-nitrophenyl-α-d-glucopyranoside as a substrate, and acarbose as a clinically used α-glycosidase inhibitor, was employed as a reference drug. The specific steps are as follows: adding 40 μL α-glycosidase solution (0.2 U / ml) into the reaction system, then adding 40 μl sample, reacting in 37 ℃ constant temperature water bath incubation for 5 min, then adding 40 μ L PNPG solution (8 mM), reacting in 37 ℃ constant temperature water bath for 30 min. The reaction was stopped by adding 0.25 M Na_2CO_3 (0.25 ml). The increase in absorbance at 405 nm was measured. Each experiment was conducted in triplicate. The IC_{50} values of compounds were calculated by the nonlinear regression analysis and expressed as the mean ± SD of three distinct experiments.

The calculation formula is as follows:

Inhibition rate (%) = [1 - (sample OD-sample blank OD) / (control OD- control blank OD)] × 100%

1.16. DPPH radical scavenging activity

To investigate the antioxidant activity of the given compounds in a homogeneous system, an experiment based on the stable free radical DPPH scavenging rate was conducted. Briefly, 100 μL methanolic solution of the title compounds and the reference compound Trolox with different concentrations was added to 1 mL of DPPH methanolic solution (0.025 mg/mL) and 1.9 mL of methanol solution respectively to give final concentrations of 100, 50, 10, 5 and 1 μM for the tested compounds. The mixture was shaken vigorously and allowed to stand at room temperature for 40 min. The absorbance was measured at 517 nm with UV-Vis spectrophotometer. The lower absorbance of the reaction mixture indicated higher free radicals scavenging activity. Methanol was used as the solvent and Trolox as the standard.

The radical scavenging activity was calculated using the following equation:

Scavenging effect% = [(control OD-sample OD)/control OD] ×100%.

1.17. Lipid peroxidation inhibition

Used rats as our experimental model as it is extensively used for studies in published Letters. The central nervous system in the rat brain is especially more sensitive to increased ROS due to its high content of unsaturated lipids and the comparatively low activity of the antioxidative enzyme system. Male Wistar rats were anesthetized and perfused through the heart with 0.9% NaCl (4 ℃). Freshly isolated rat brains were crushed with ice-cold normal saline to prepare a homogenate. The homogenate was centrifuged for 10 min at a speed of 3000 rpm, and the supernatant was used for biochemical analyses. The reaction mixture containing the title compounds (100 μM), $FeCl_3$ (0.02 μM), ascorbic acid (0.1 μM) and brain homogenate supernatant was incubated at 37 ℃ for 30 min, then the brain homogenates were mixed with the solutions in the MDA kit and all the subsequent steps were followed according to the instruction of manufacturer. All of the experiments were performed in triplicates. MDA levels in the brain homogenates were determined at 532 nm using UV-Vis spectrophotometer. Protein concentrations were determined using a kit. The data were analyzed using a one-way analysis of variance (ANOVA).

1.18. Docking studies

The molecular interaction behind the inhibition mechanism of compound **5l** and molecular docking studies were carried out using Autodock VINA.

1.19 MTT cytotoxicity assay

The toxicity of compound **5l** to 293T cells was determined by 24 h continuous MTT assay. After the cells were incubated in a 96-well plate overnight, then 100 μl of compound were added. After 24 hours, an appropriate amount of MTT (5 mg / ml) solution was added and incubation was continued for 4 h (37 °C). The MTT solution was removed and then DMSO was added. After adding DMSO for 10 min, then their absorbance was determined at 570 nm. Tested compound was dissolved in DMSO, and the final DMSO concentration in assay was 0.1% (v/v). The amount of formed formazan was calculated as a percentage of the control cells, which were treated only with DMSO and were assigned as 100%.

2. Table S1. The lipid-water partition coefficients

Compound	$logD_{7.4}$
5l	0.26
Epalrestat	0.14

3. NMR spectra, HRMS and HPLC

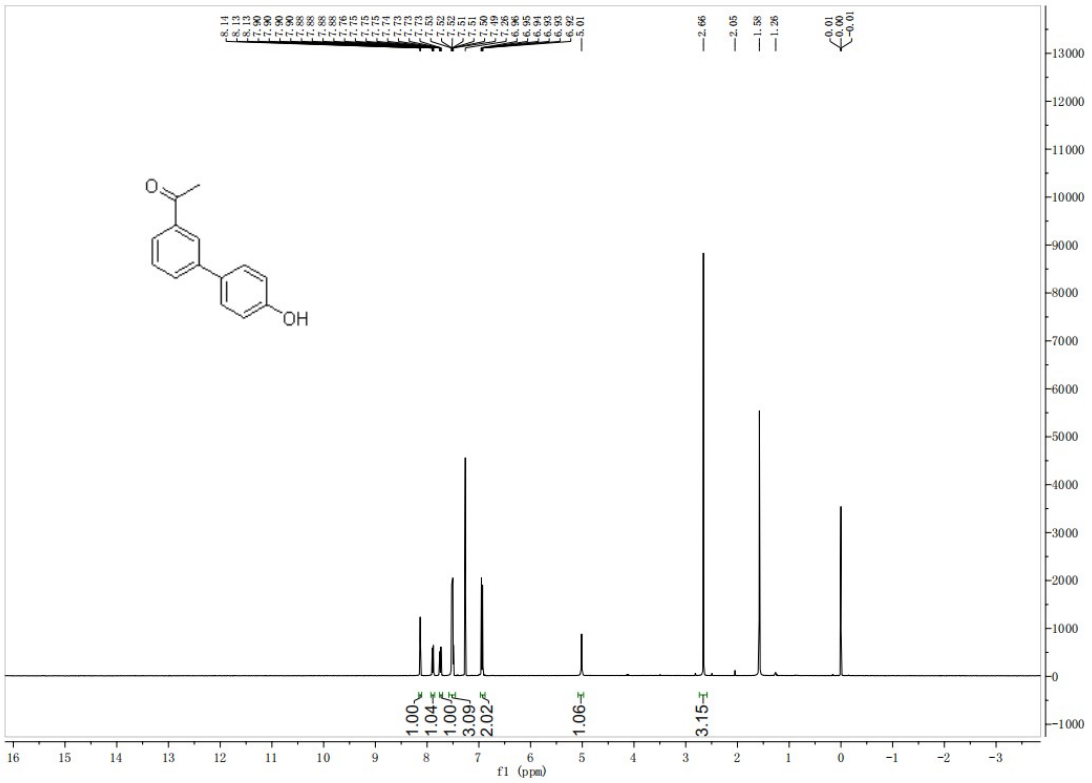

Figure S1.[1]H-NMR (400 MHz, Chloroform-d) of **2a**

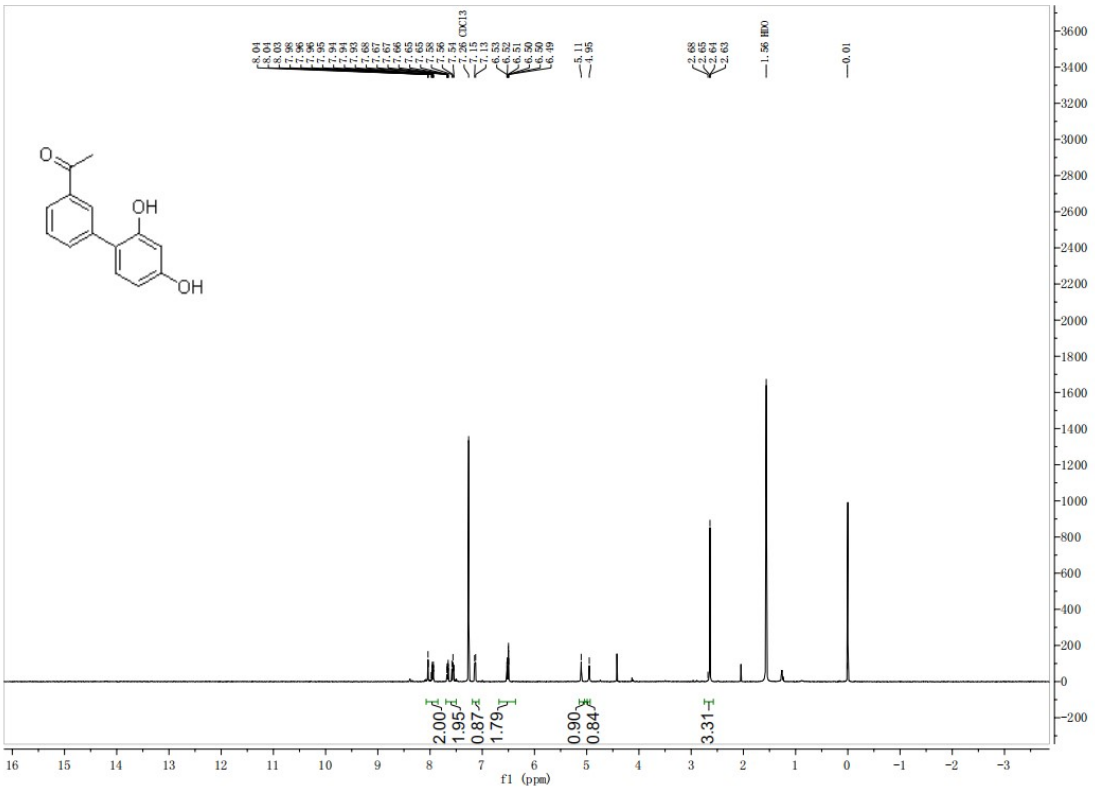

Figure S2.[1]H-NMR (400 MHz, Chloroform-d) of **2b**

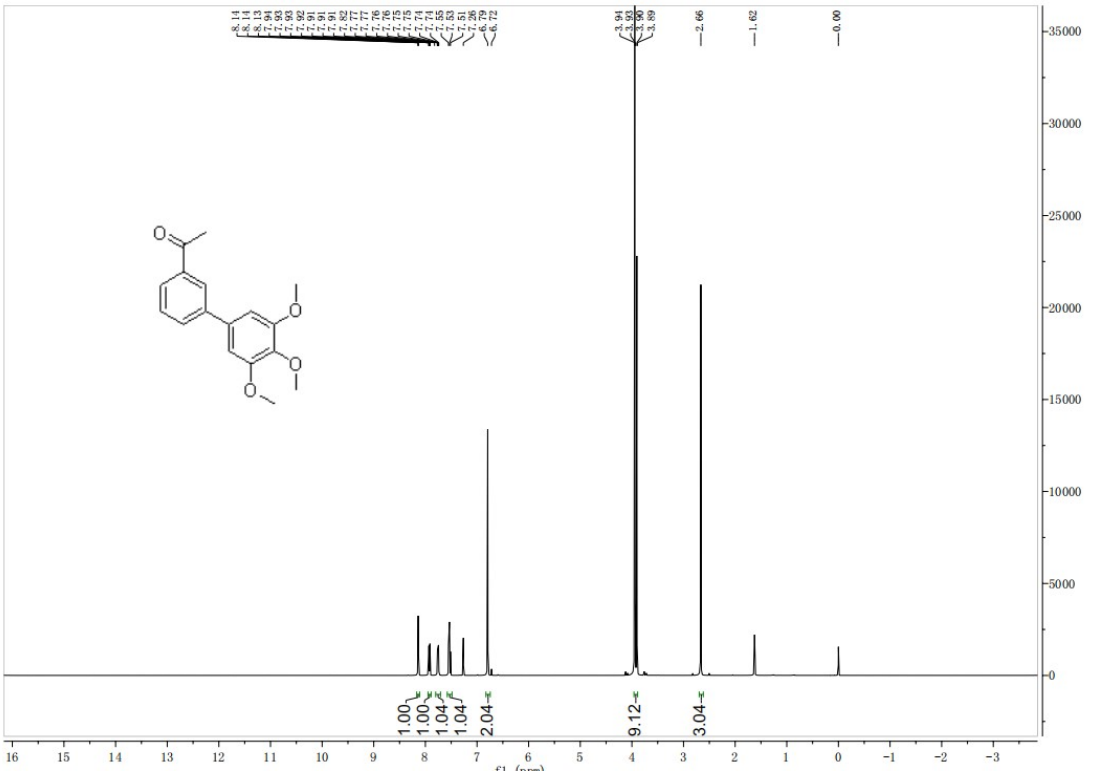

Figure S3.[1]H-NMR (400 MHz, Chloroform-d) of **2c**

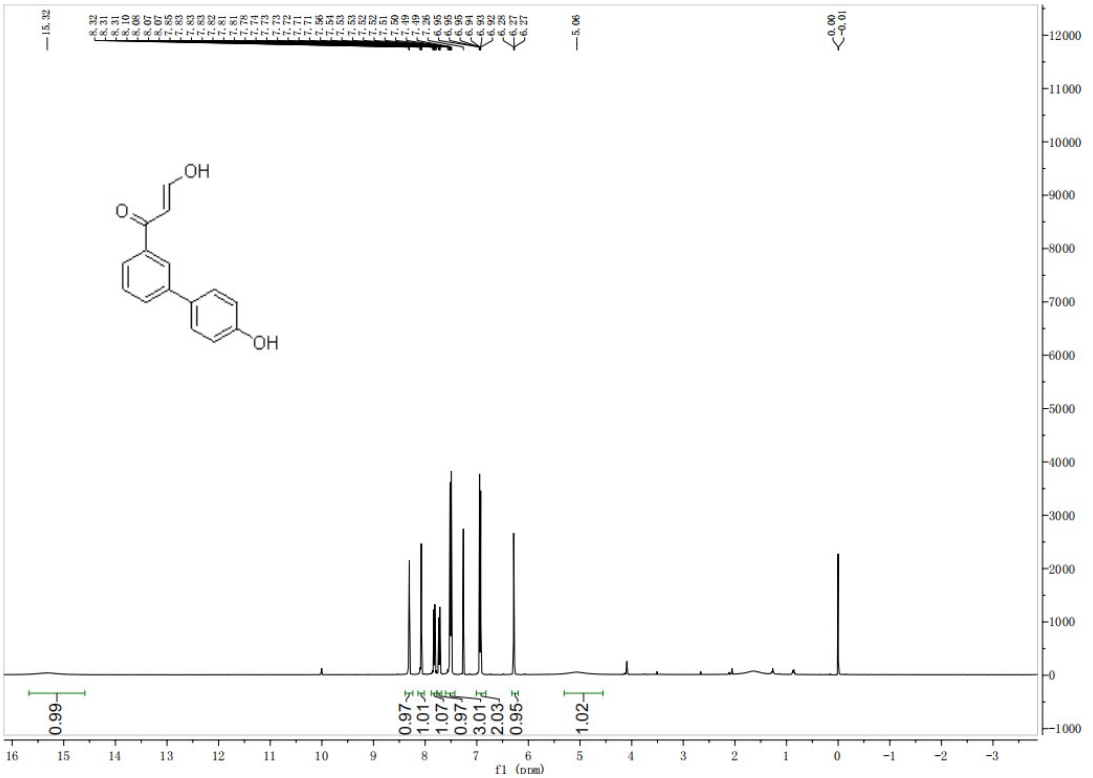

Figure S4.[1]H-NMR (400 MHz, Chloroform-d) of **3a**

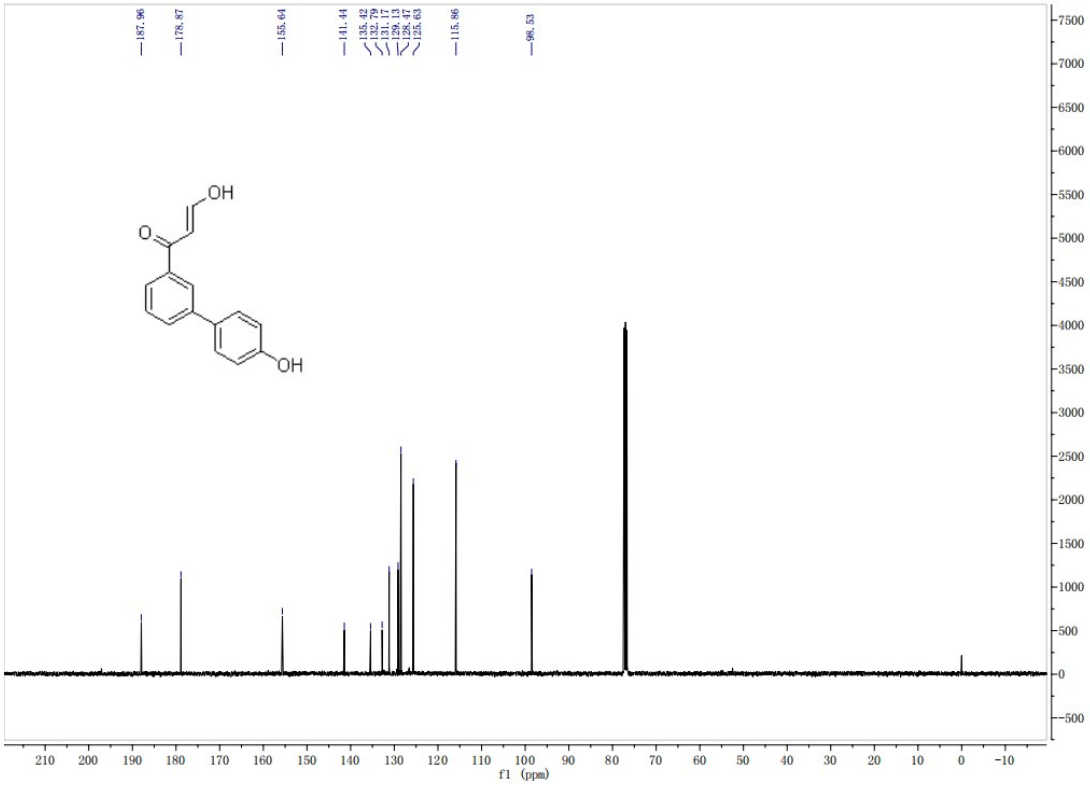

Figure S5.[13]C-NMR (100 MHz, Chloroform-d) of **3a**

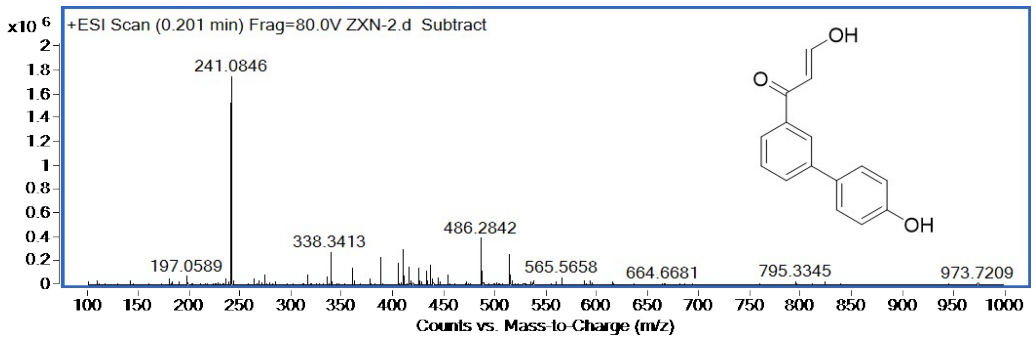

Figure S6. HRMS of **3a**

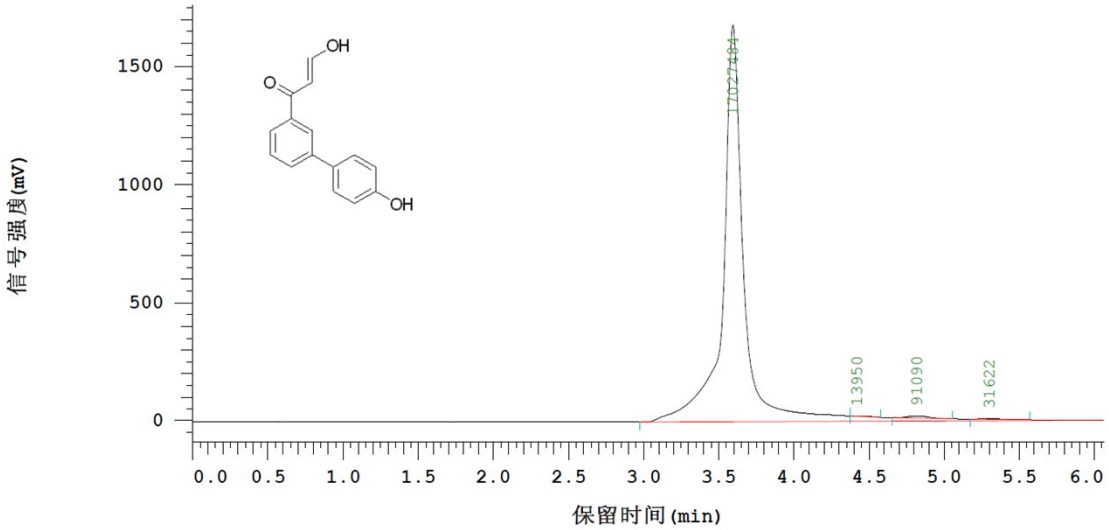

Figure S7. HPLC of **3a**

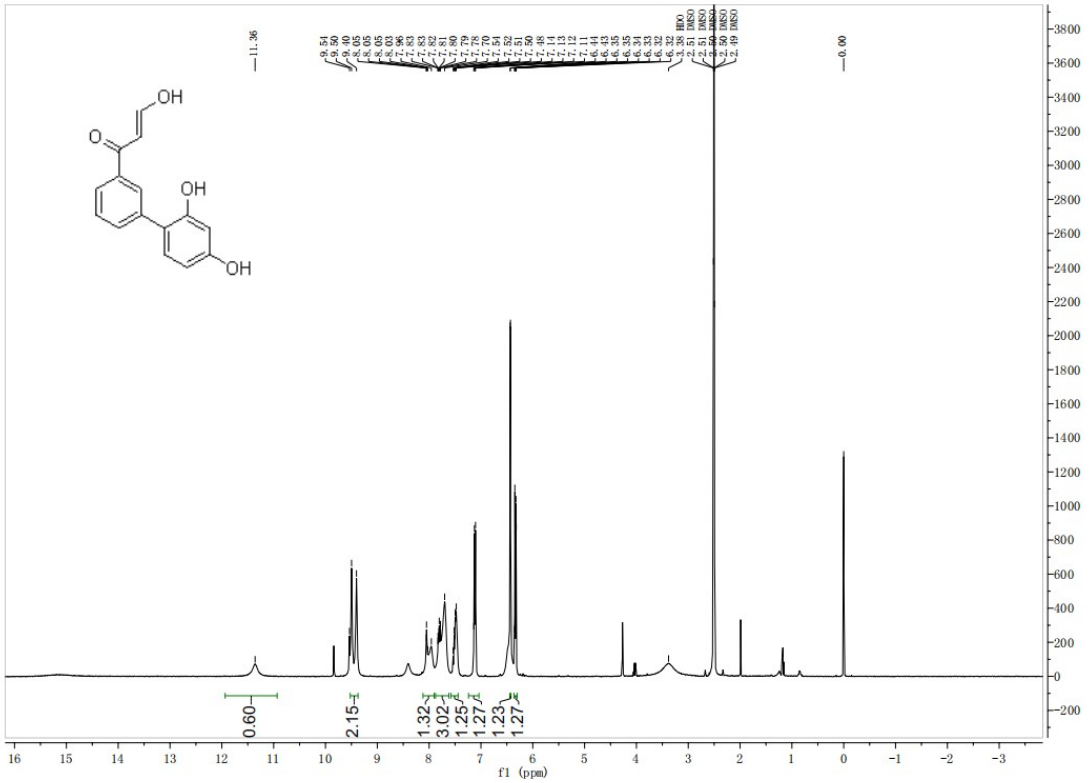

Figure S8.[1]H-NMR (400 MHz, DMSO-d6) of **3b**

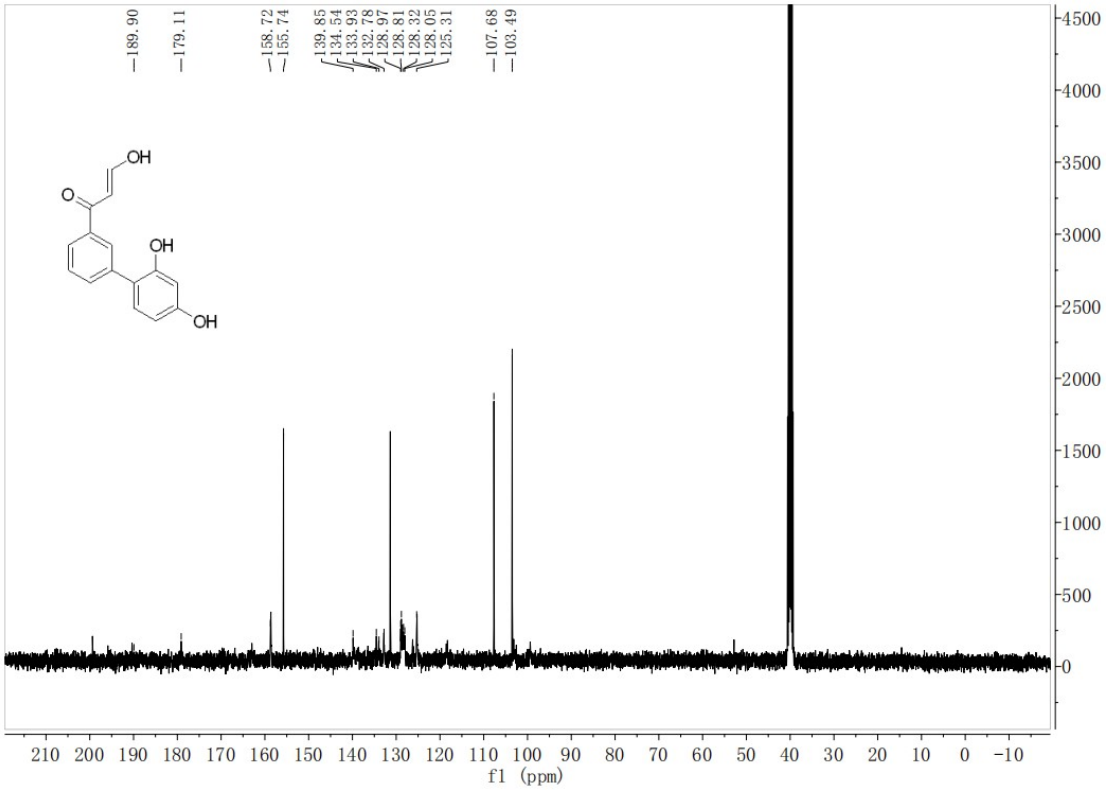

Figure S9.[13]C-NMR (100 MHz, DMSO-d6) of **3b**

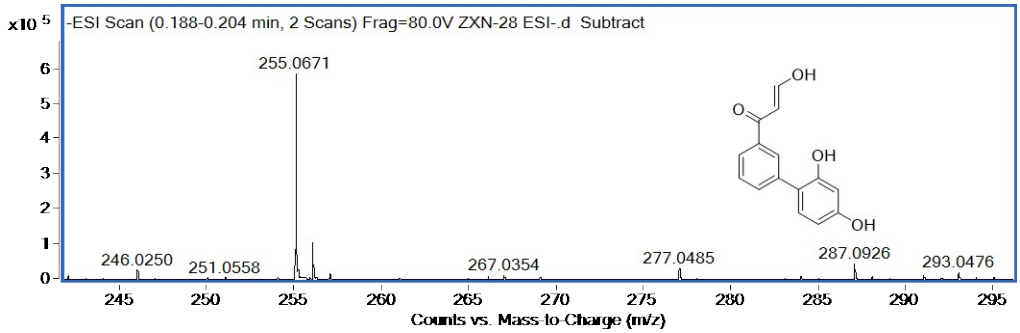

Figure S10. HRMS of **3b**

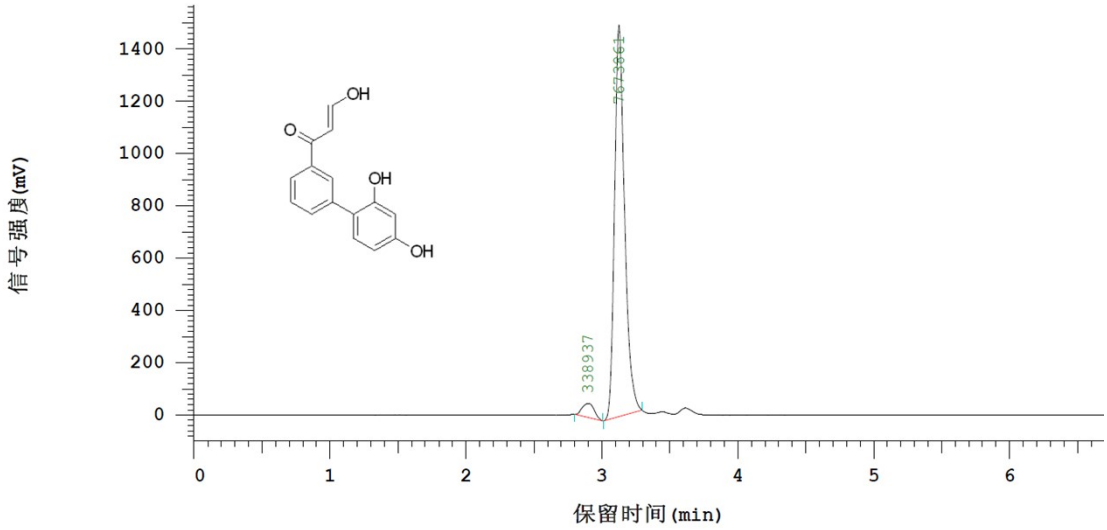

Figure S11. HPLC of **3b**

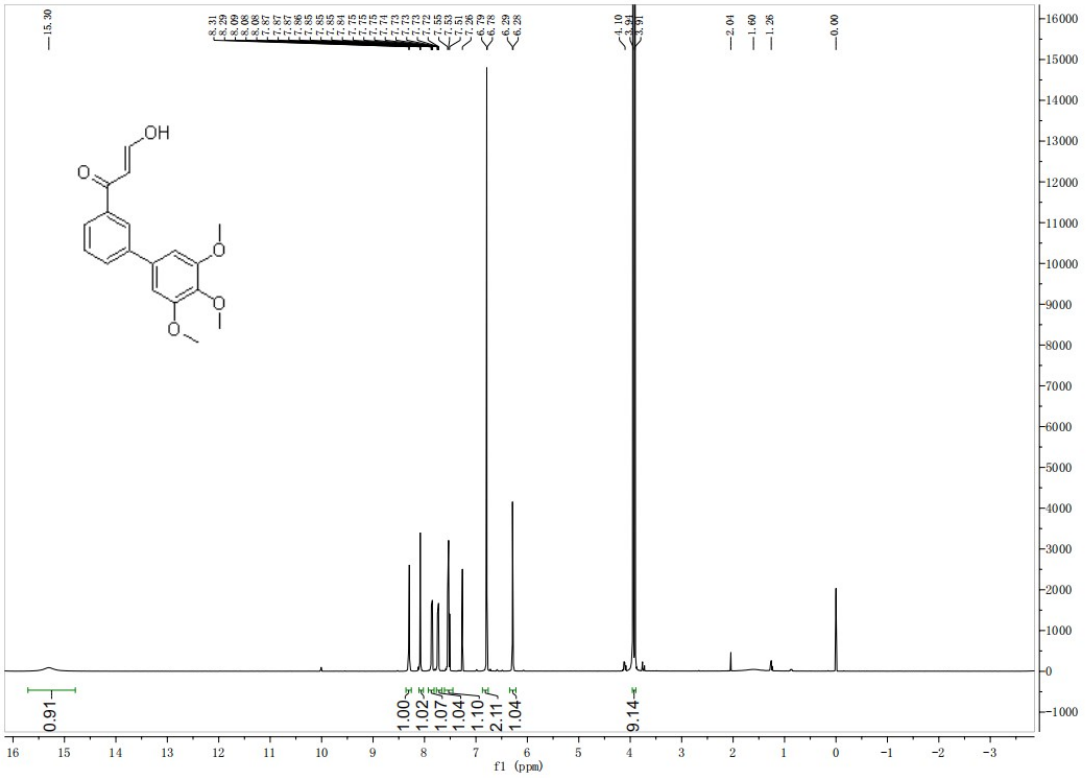

Figure S12.[1]H-NMR (400 MHz, Chloroform-d) of **3c**

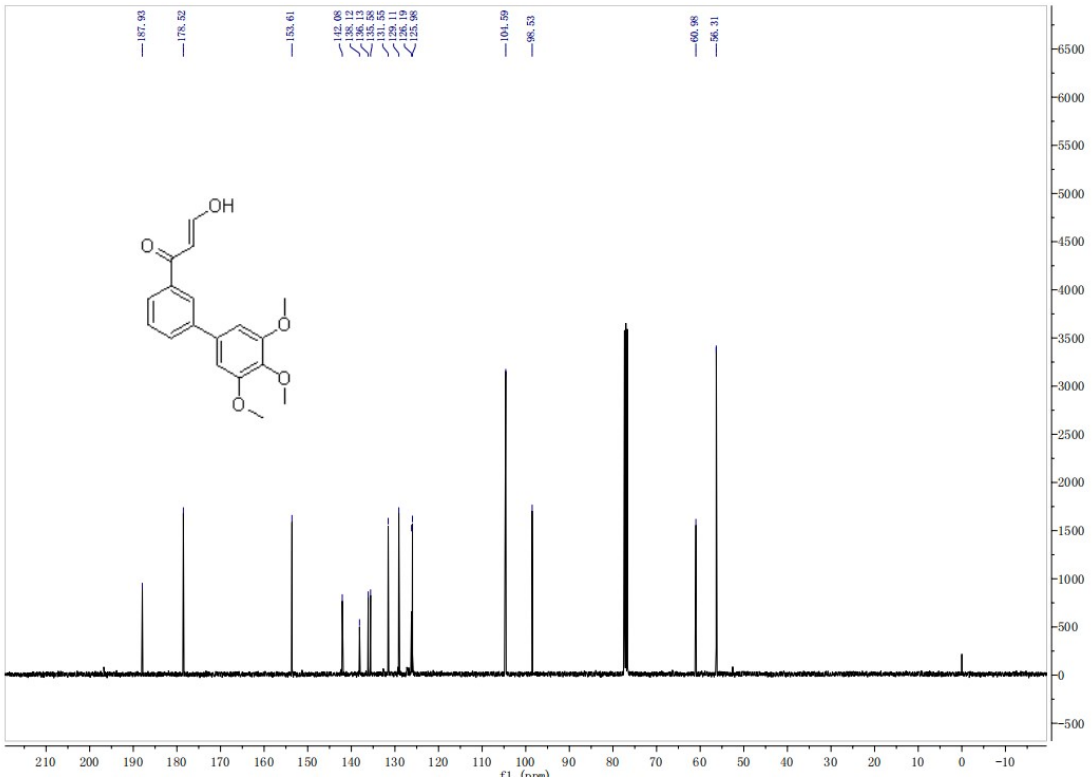

Figure S13.[13]C-NMR (100 MHz, Chloroform-d) of **3c**

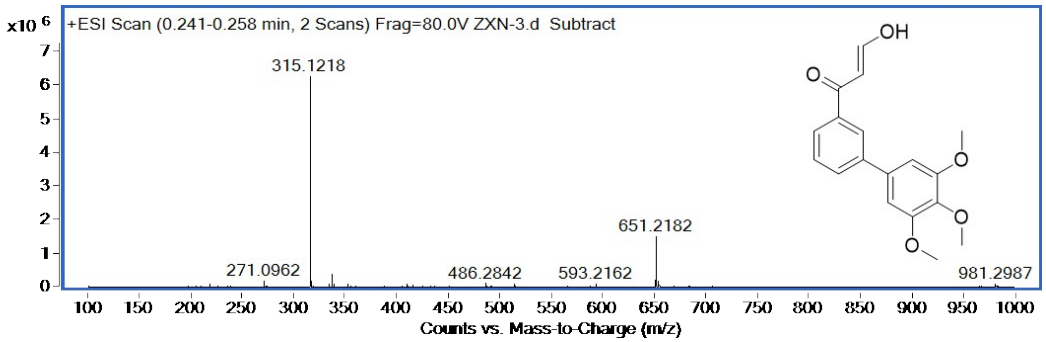

Figure S14. HRMS of **3c**

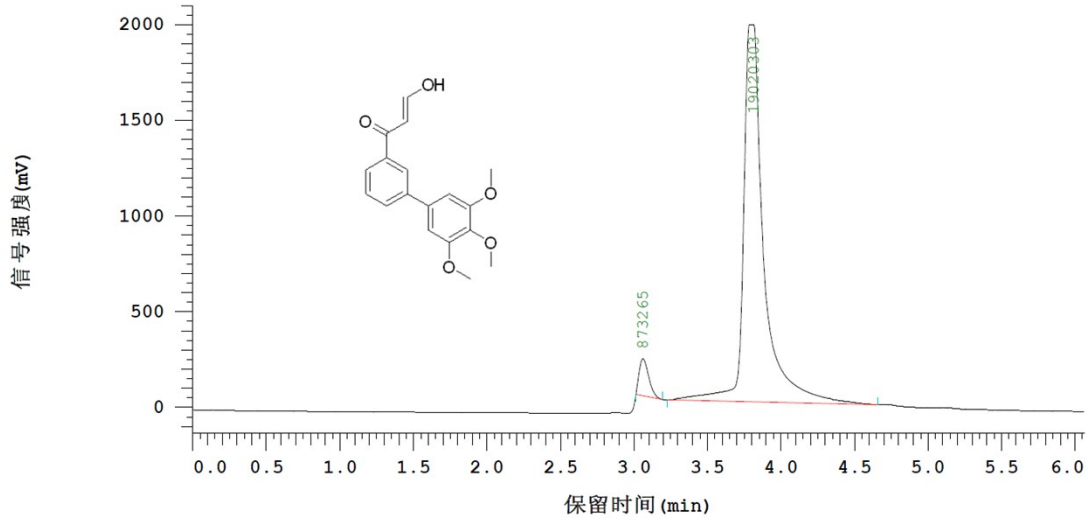

Figure S15. HPLC of **3c**

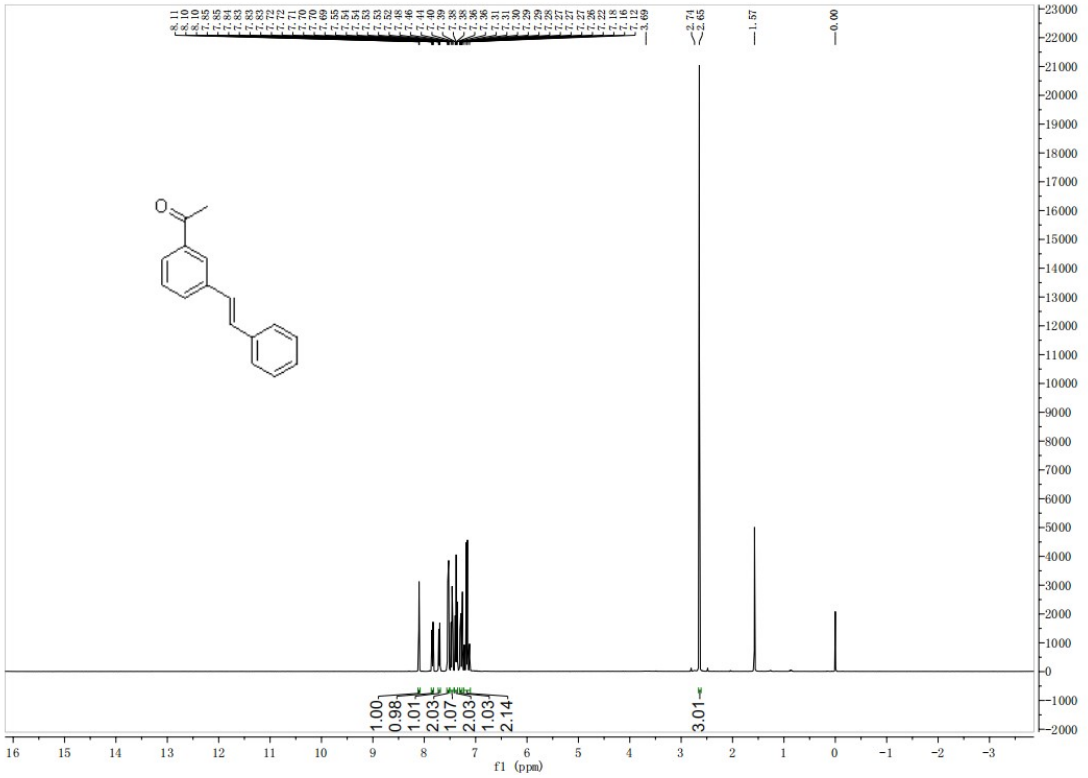

Figure S16.[1]H-NMR (400 MHz, Chloroform-d) of **4a**

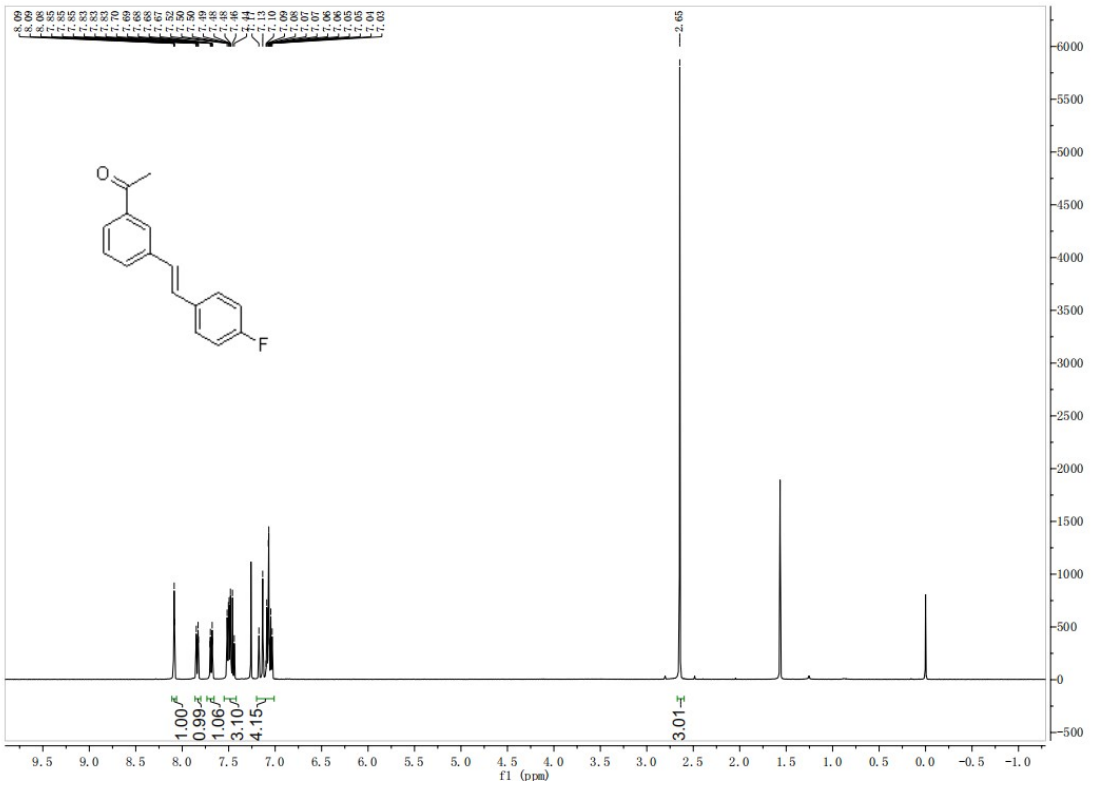

Figure S17.[1]H-NMR (400 MHz, Chloroform-d) of **4b**

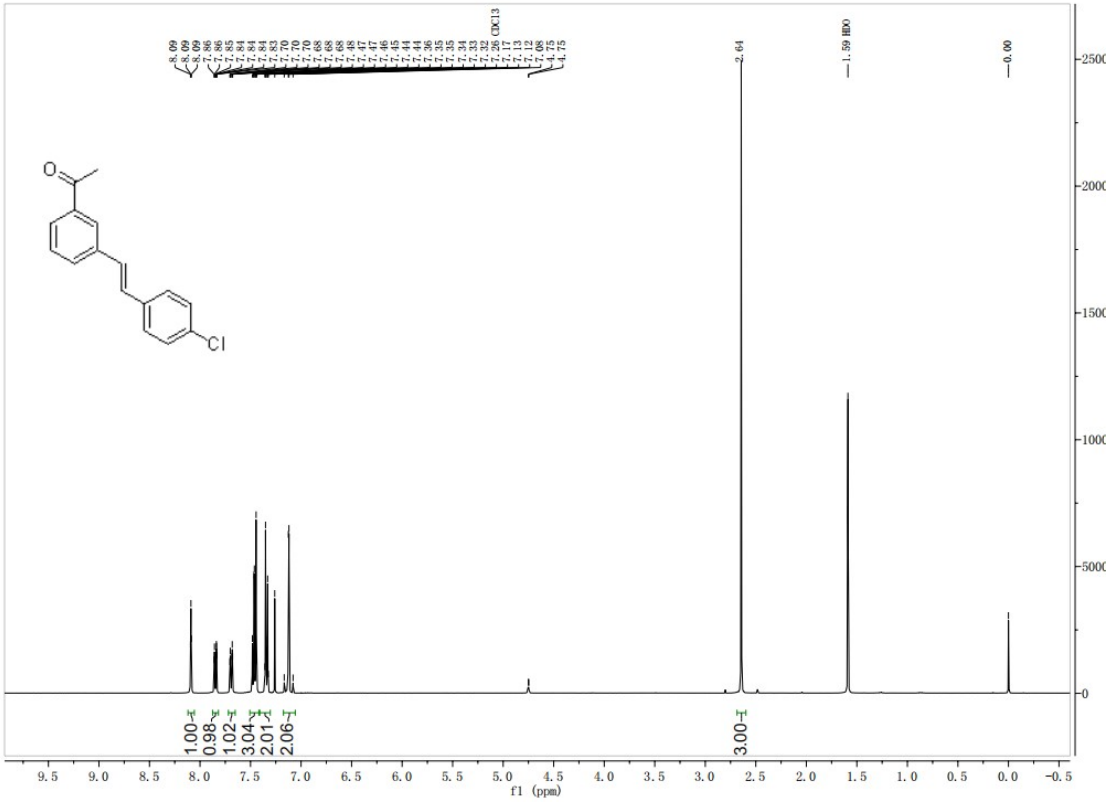

Figure S18.[1]H-NMR (400 MHz, Chloroform-d) of **4c**

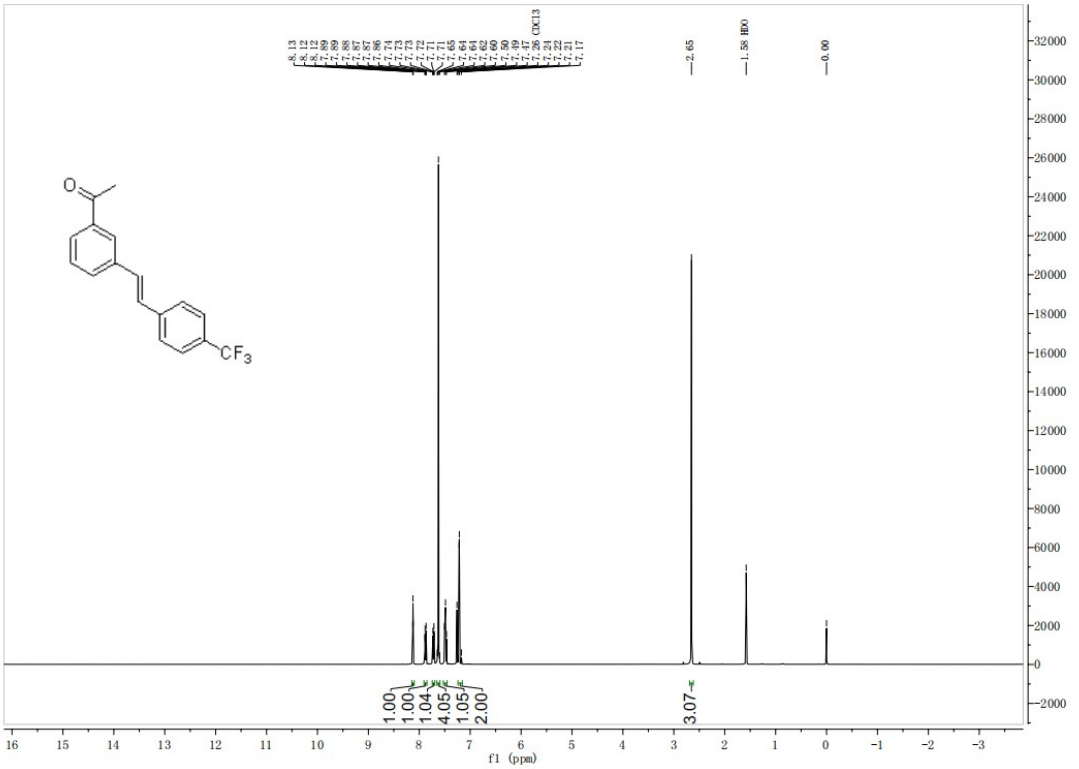

Figure S19.[1]H-NMR (400 MHz, Chloroform-d) of **4d**

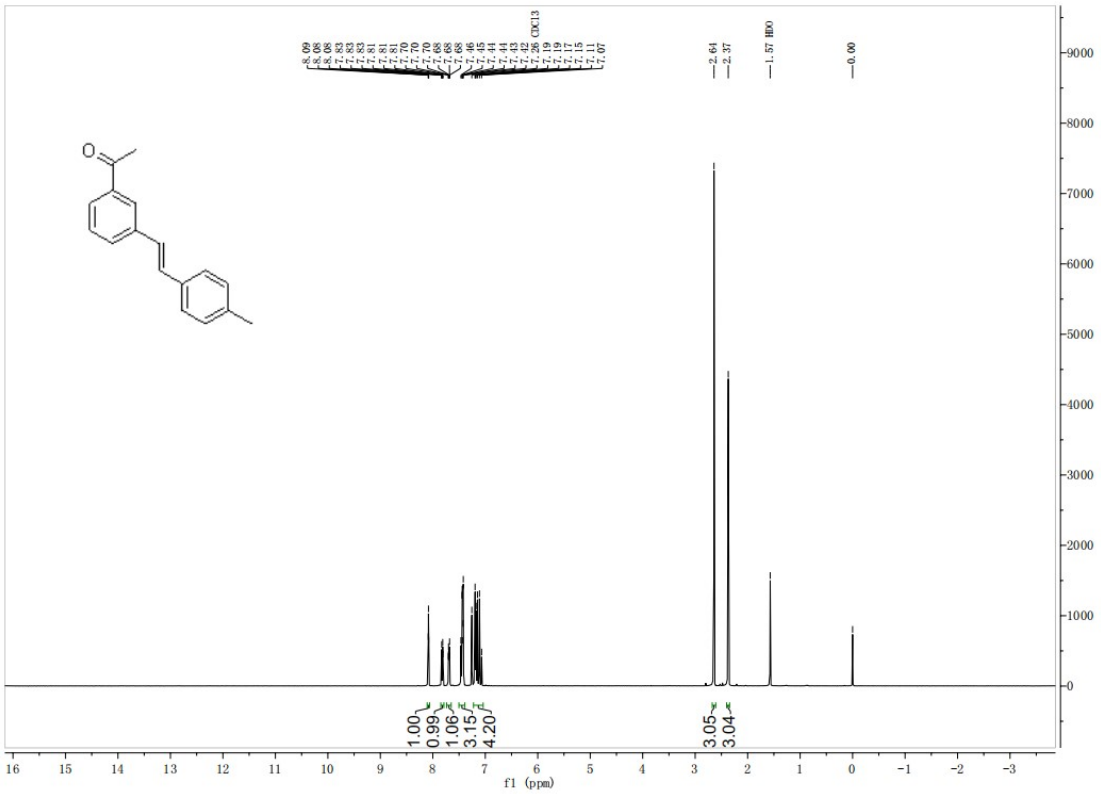

Figure S20.[1]H-NMR (400 MHz, Chloroform-d) of **4e**

Figure S21.[1]H-NMR (400 MHz, Chloroform-d) of **4f**

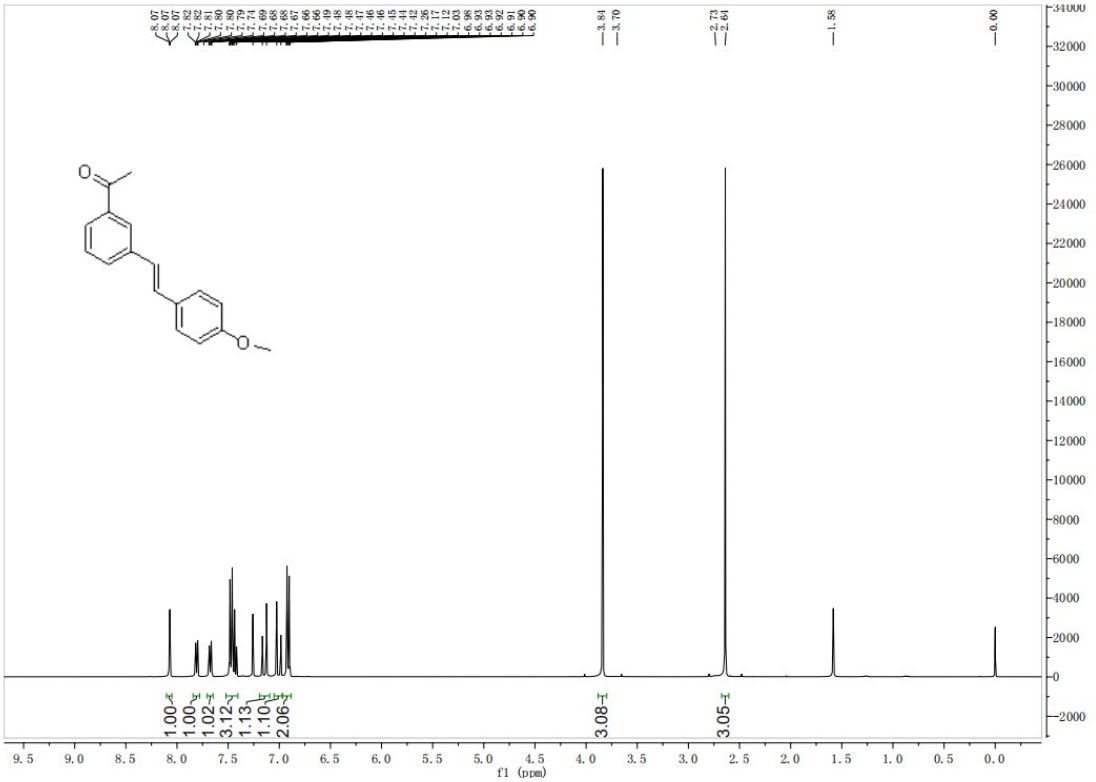

Figure S22.[1]H-NMR (400 MHz, Chloroform-d) of **4g**

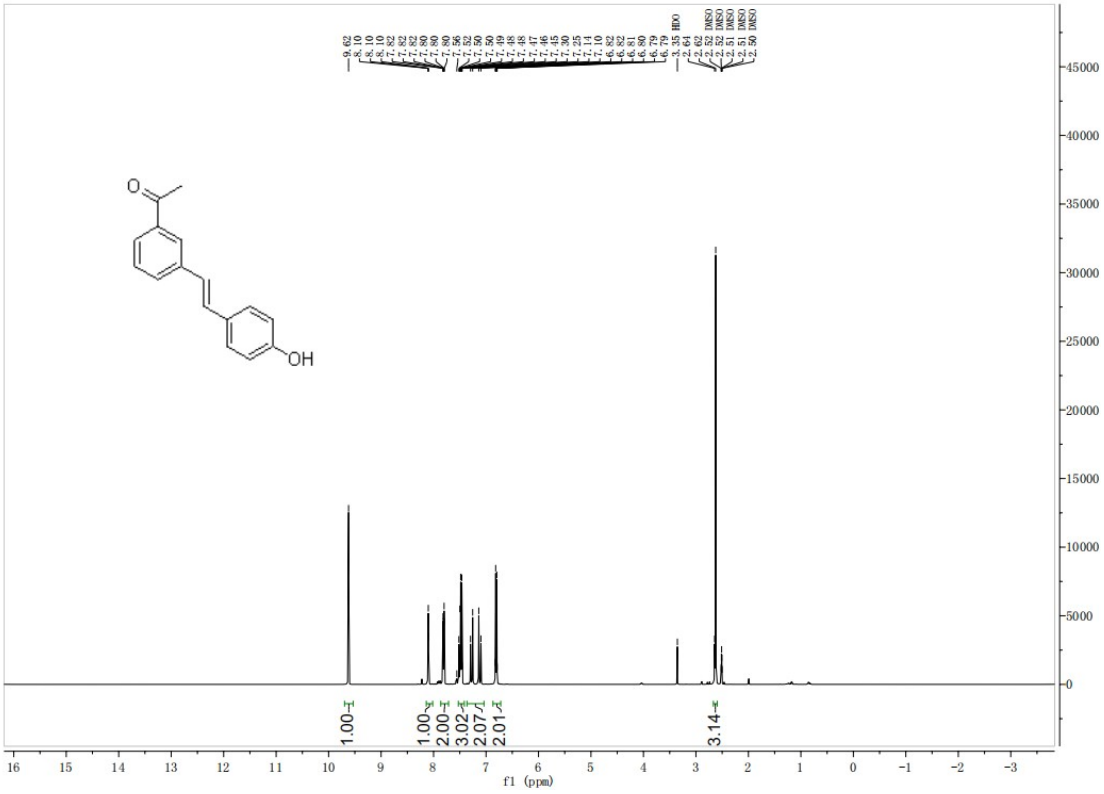

Figure S23.[1]H-NMR (400 MHz, DMSO-*d6*) of **4h**

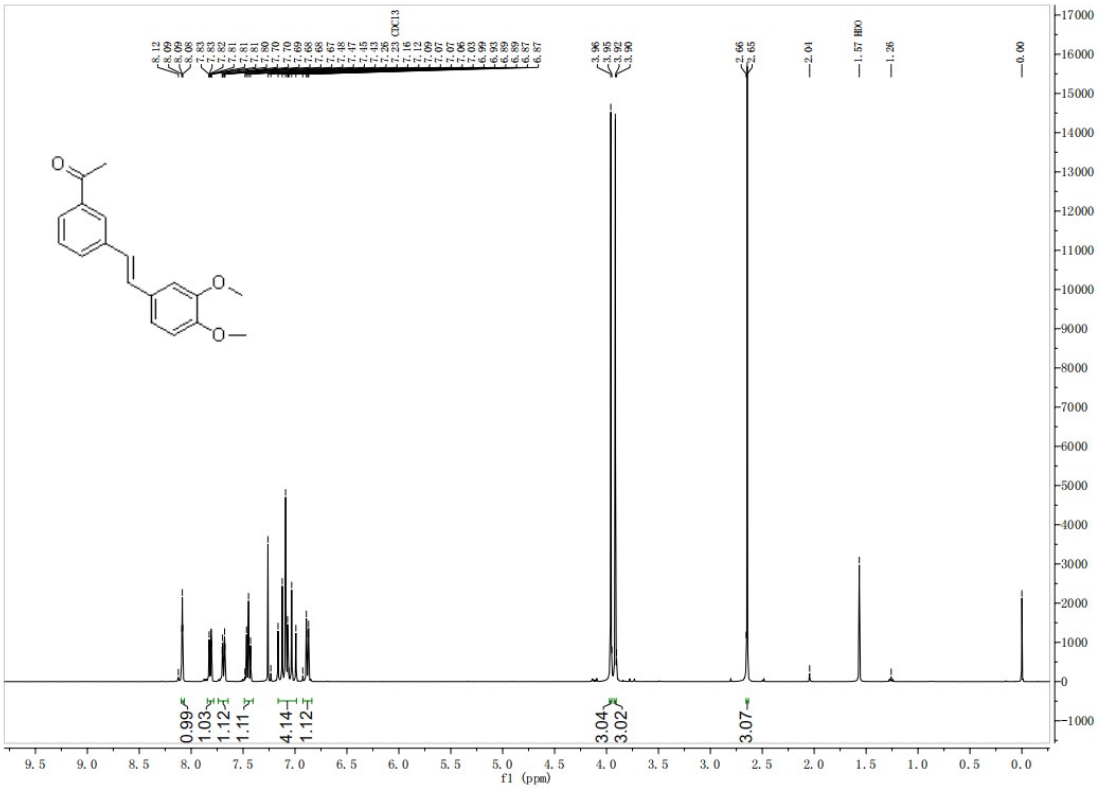

Figure S24.[1]H-NMR (400 MHz, Chloroform-d) of **4i**

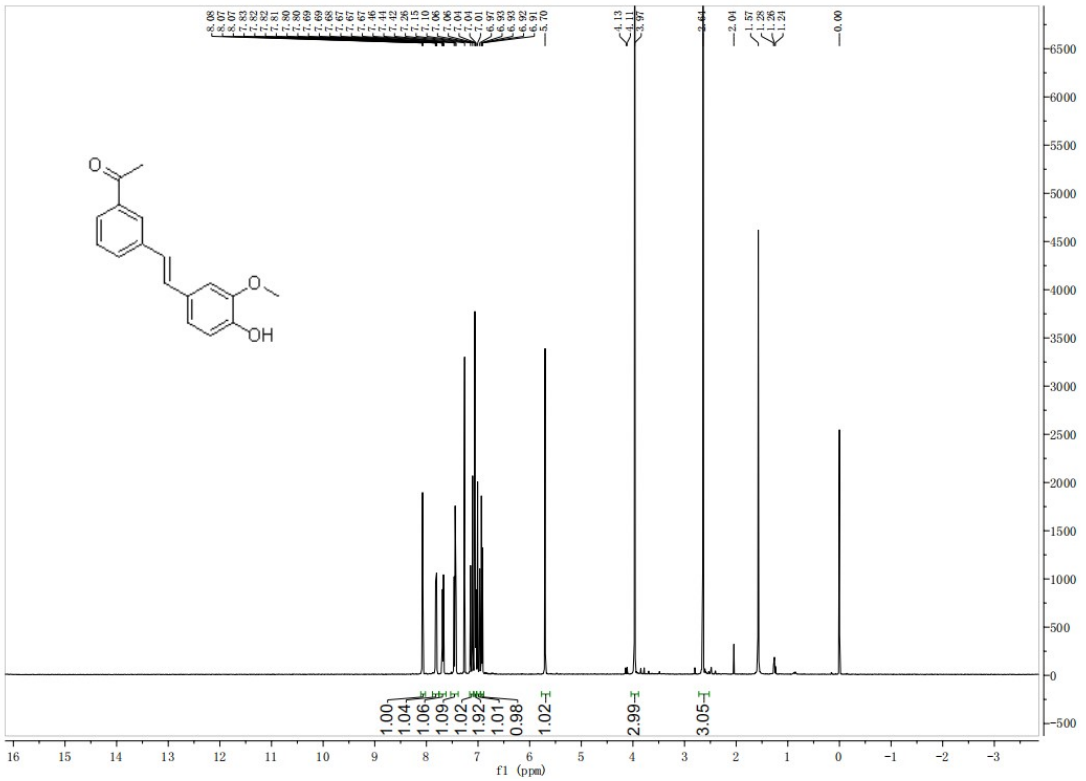

Figure S25.[1]H-NMR (400 MHz, Chloroform-d) of **4j**

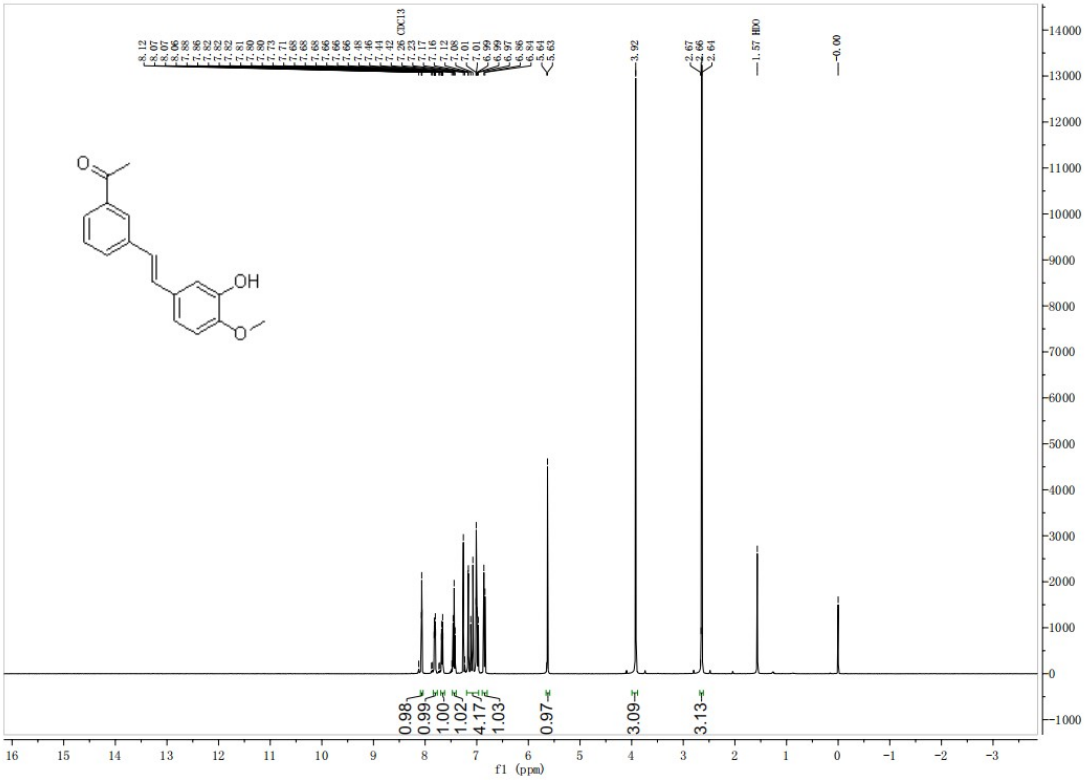

Figure S26.[1]H-NMR (400 MHz, Chloroform-d) of **4k**

Figure S27.[1]H-NMR (400 MHz, Chloroform-d) of **4m**

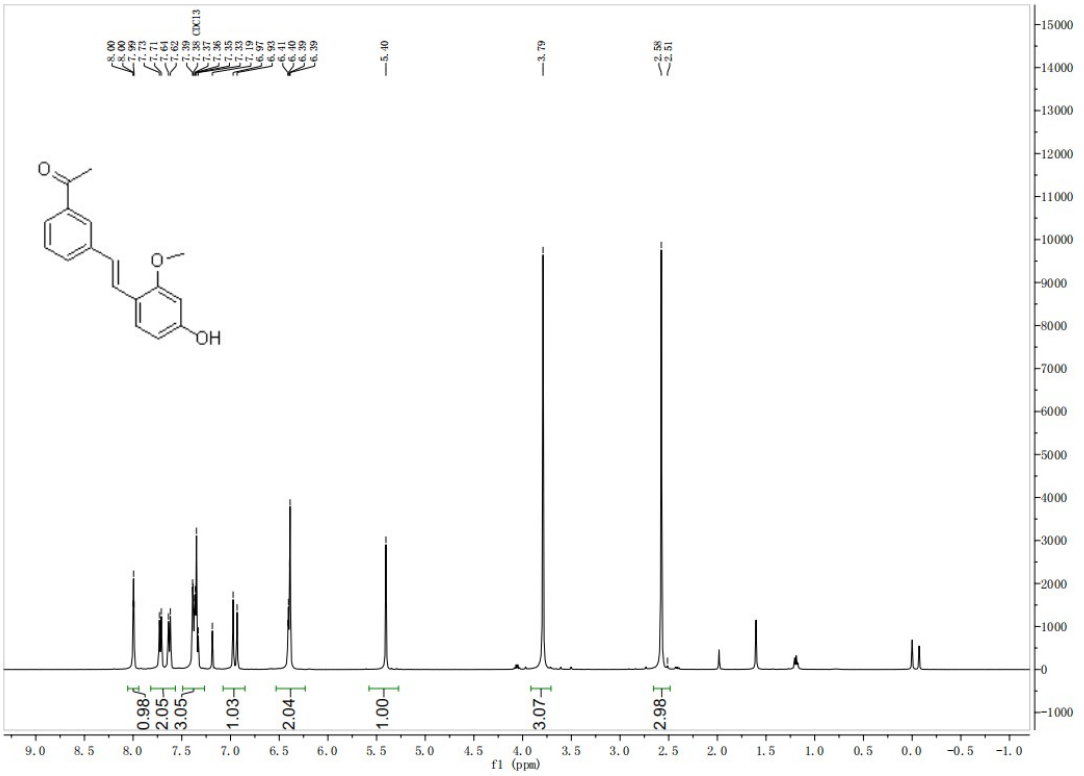

Figure S28.[1]H-NMR (400 MHz, Chloroform-d) of **4n**

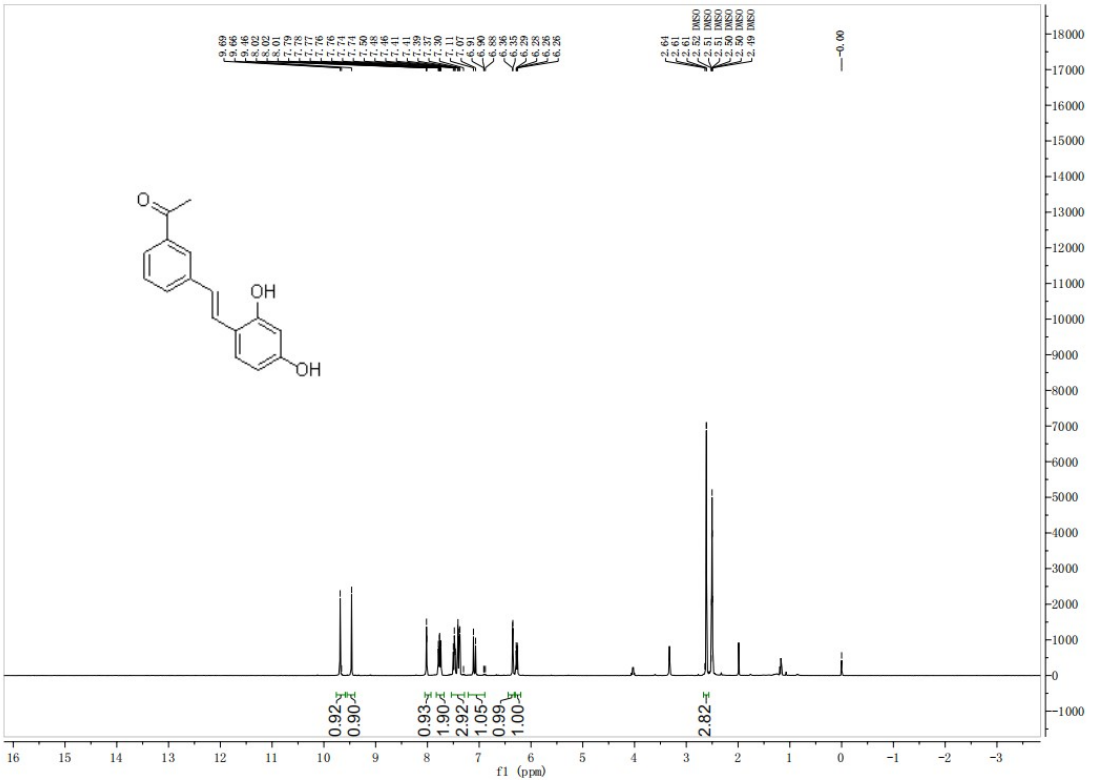

Figure S29.[1]H-NMR (400 MHz, DMSO-*d6*) of **4o**

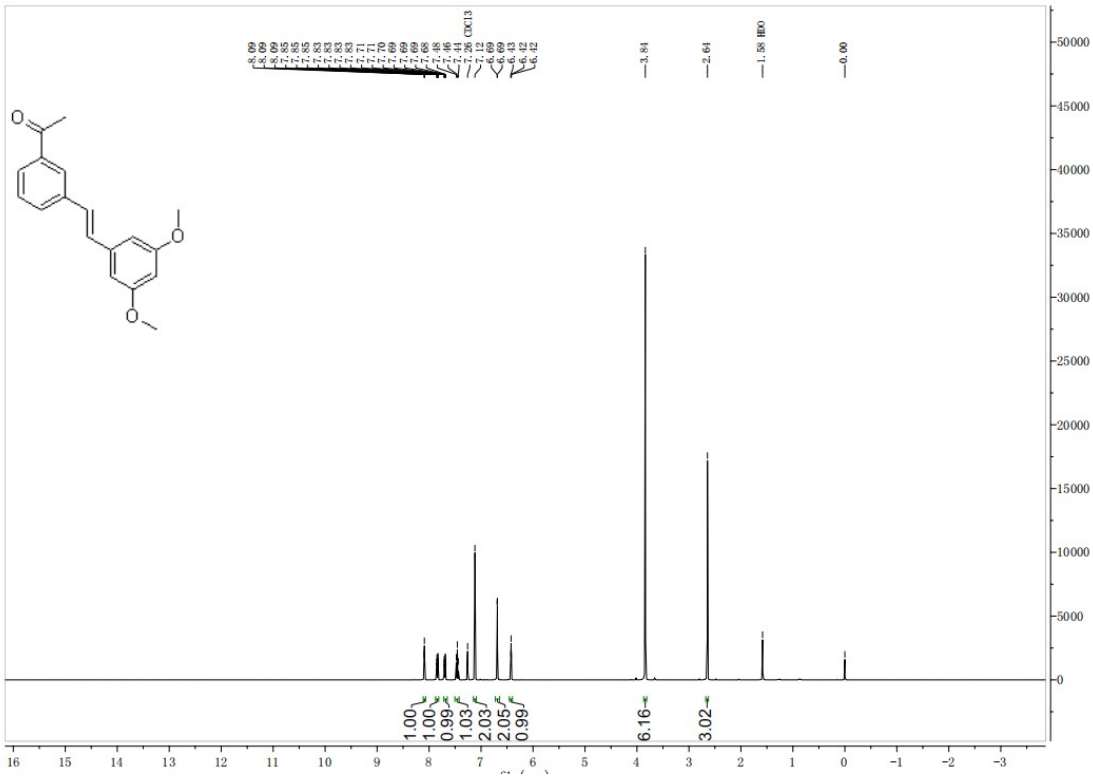

Figure S30.[1]H-NMR (400 MHz, Chloroform-d) of **4p**

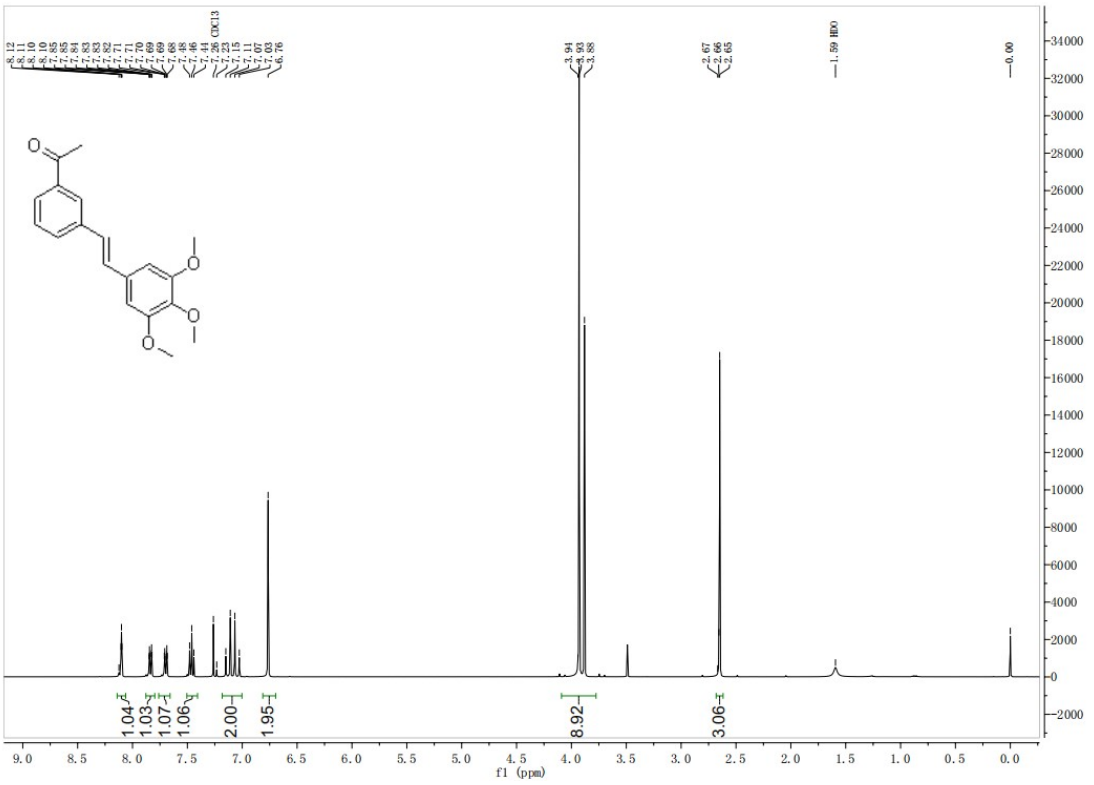

Figure S31.[1]H-NMR (400 MHz, Chloroform-d) of **4q**

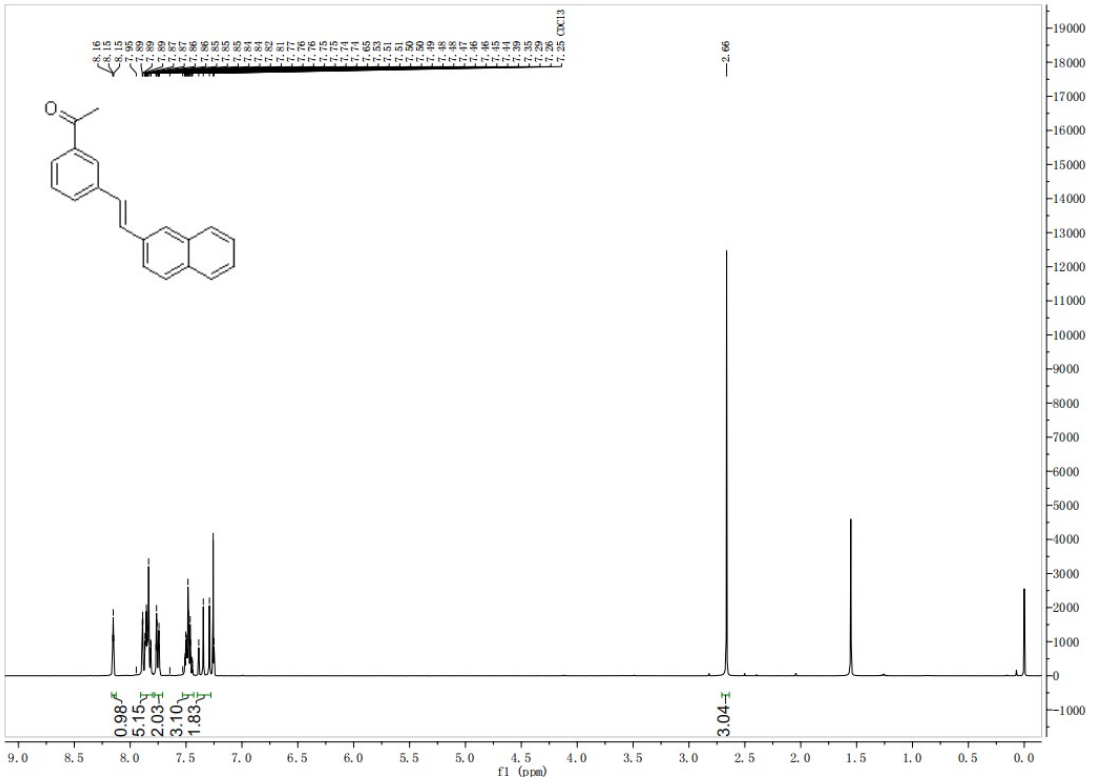

Figure S32.[1]H-NMR (400 MHz, Chloroform-d) of **4r**

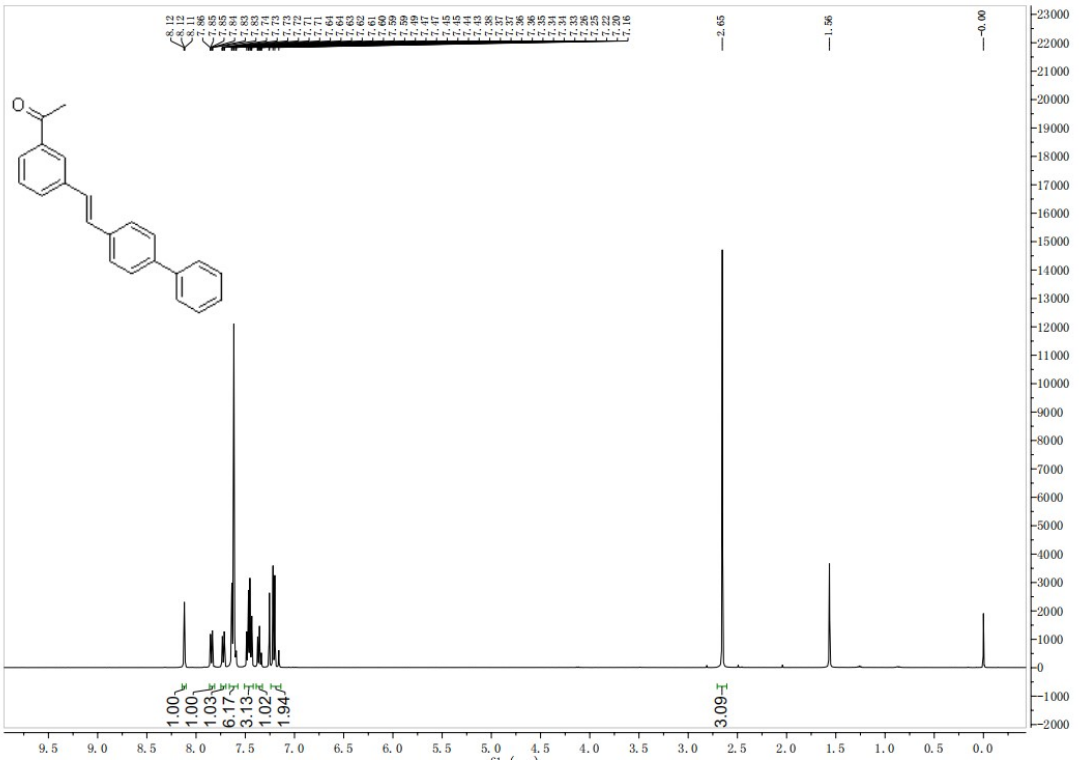

Figure S33.[1]H-NMR (400 MHz, Chloroform-d) of **4s**

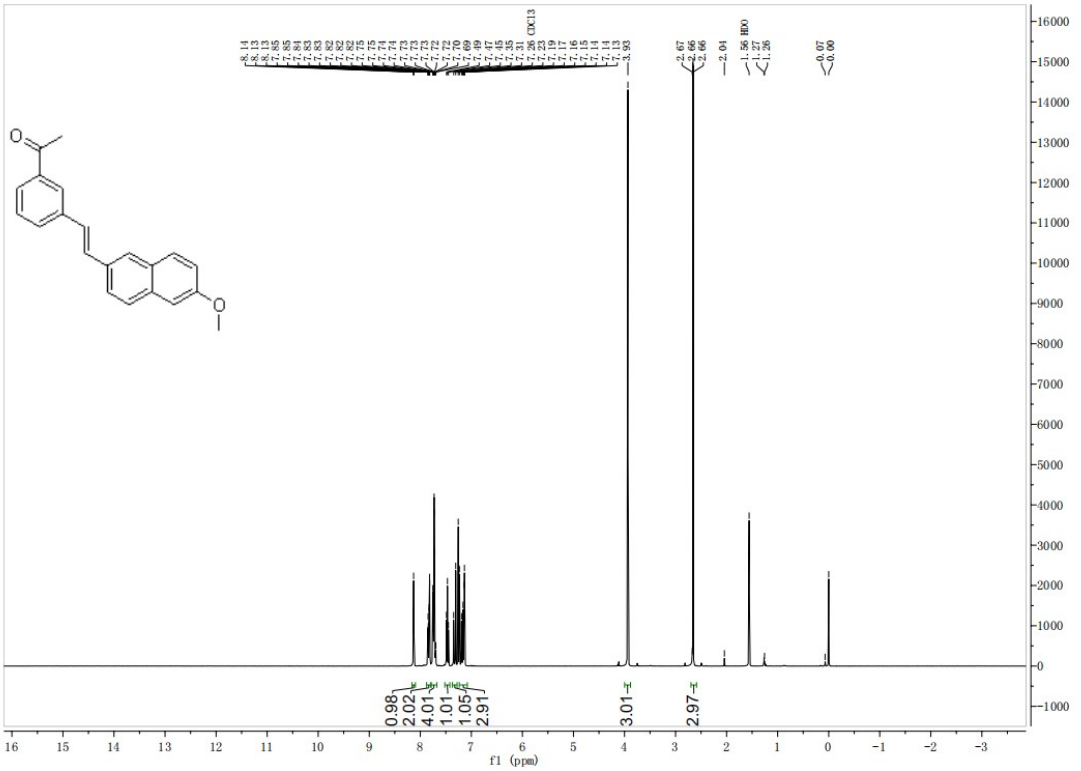

Figure S34.[1]H-NMR (400 MHz, Chloroform-d) of **4t**

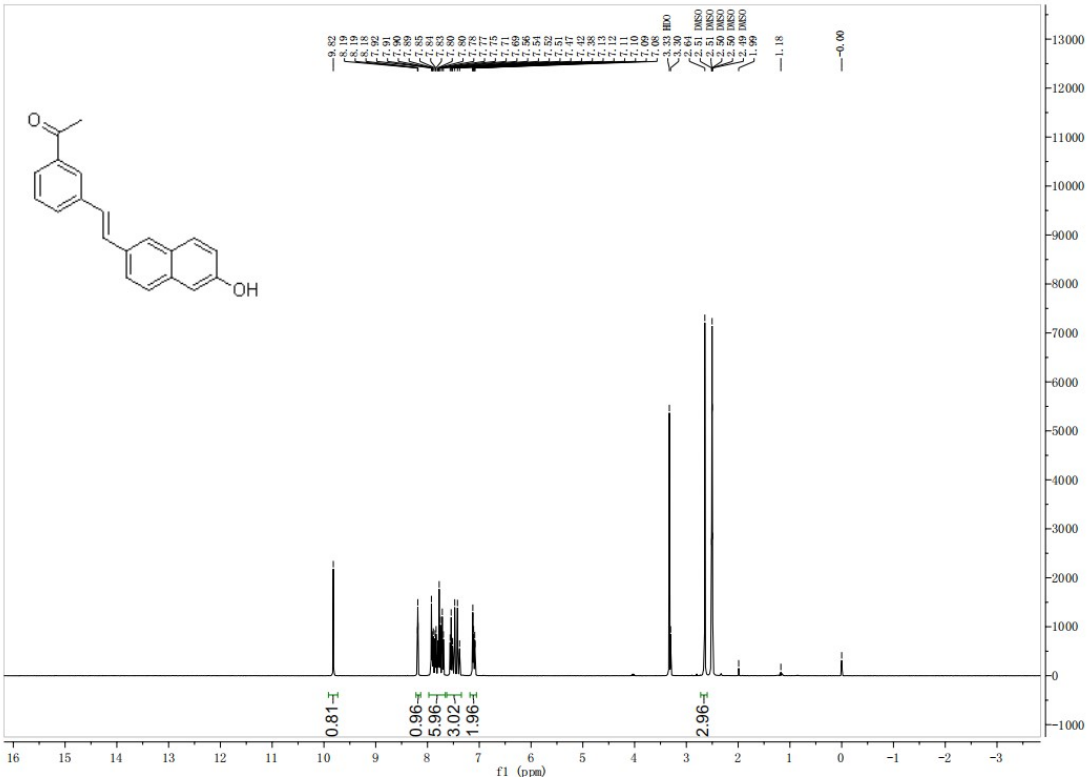

Figure S35.[1]H-NMR (400 MHz, DMSO-*d6*) of **4u**

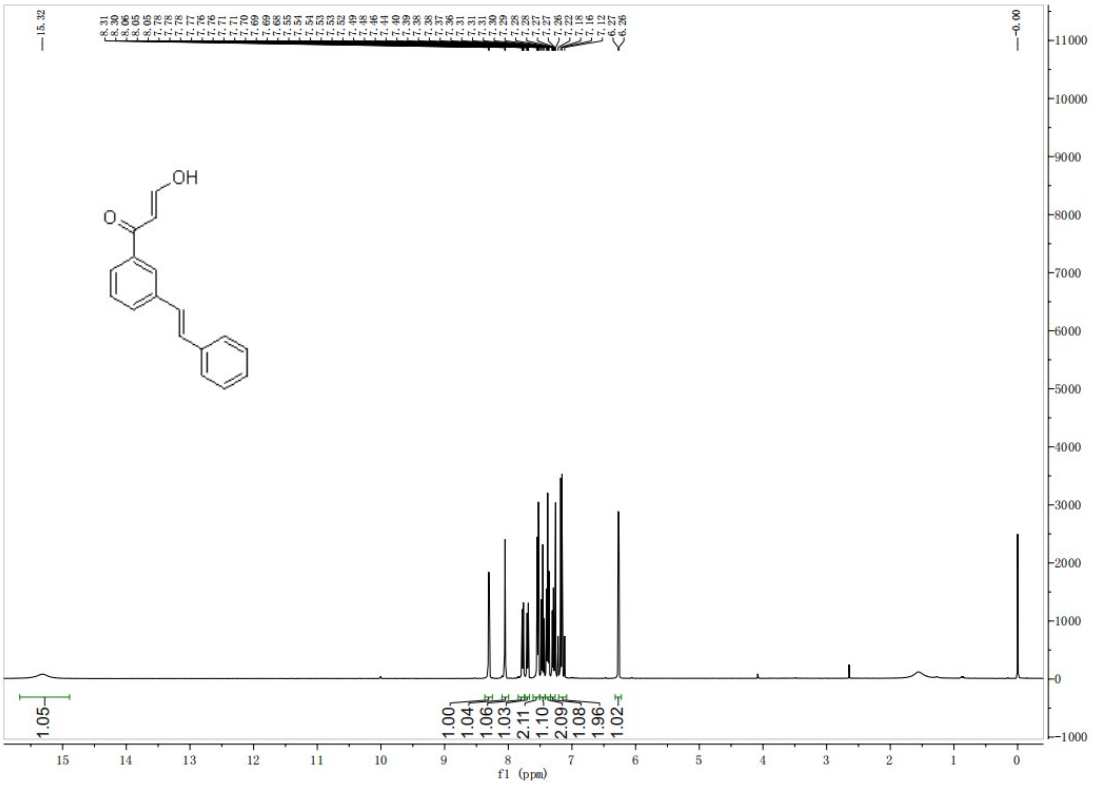

Figure S36.[1]H-NMR (400 MHz, Chloroform-d) of **5a**

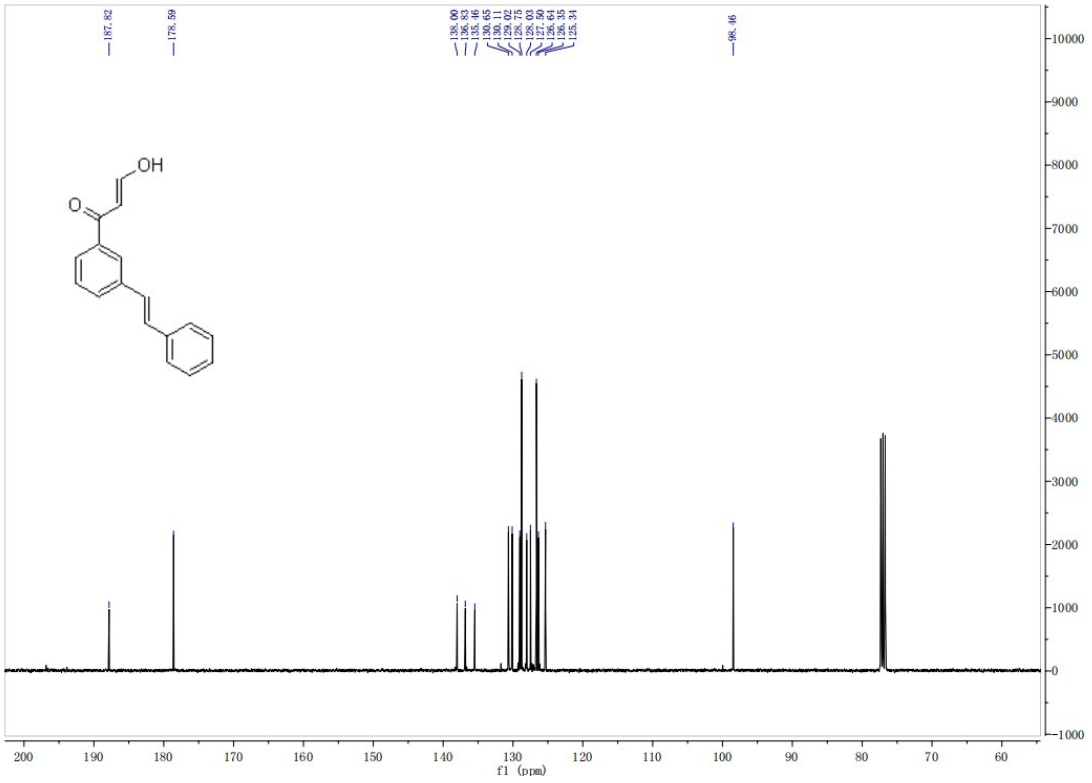

Figure S37.^{13}C-NMR (100 MHz, Chloroform-d) of **5a**

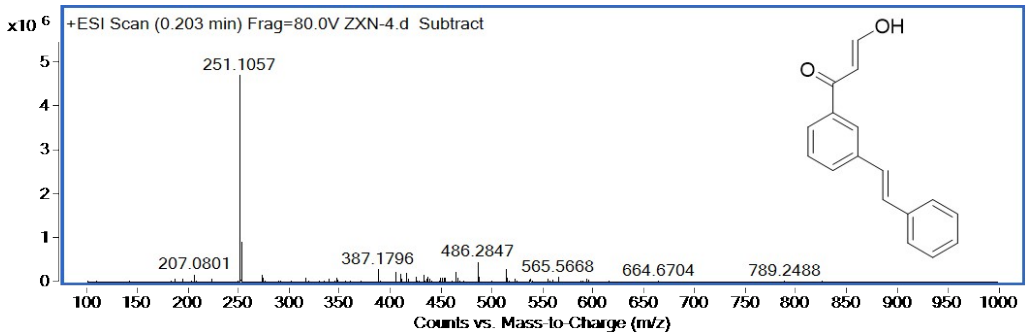

Figure S38. HRMS of **5a**

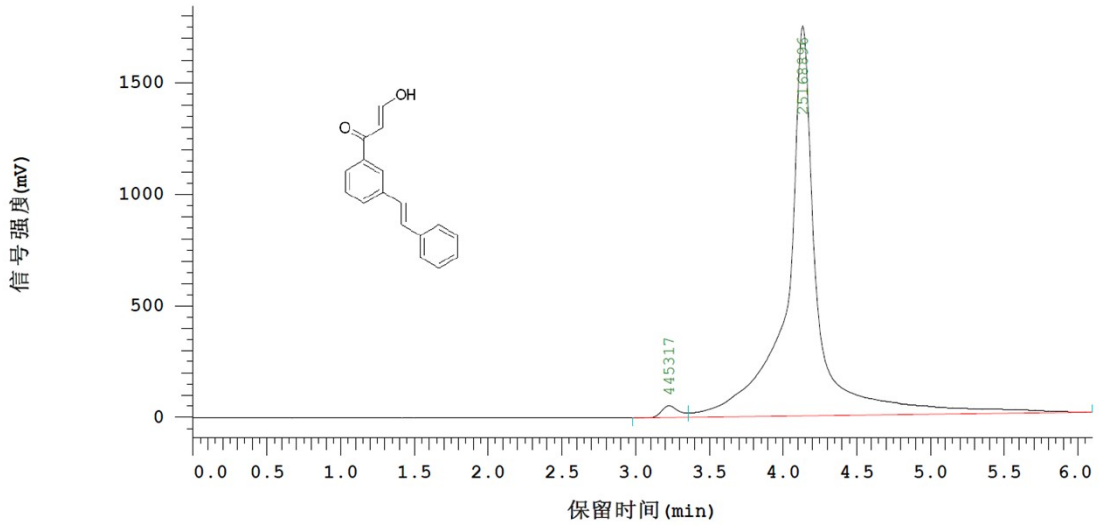

Figure S39. HPLC of **5a**

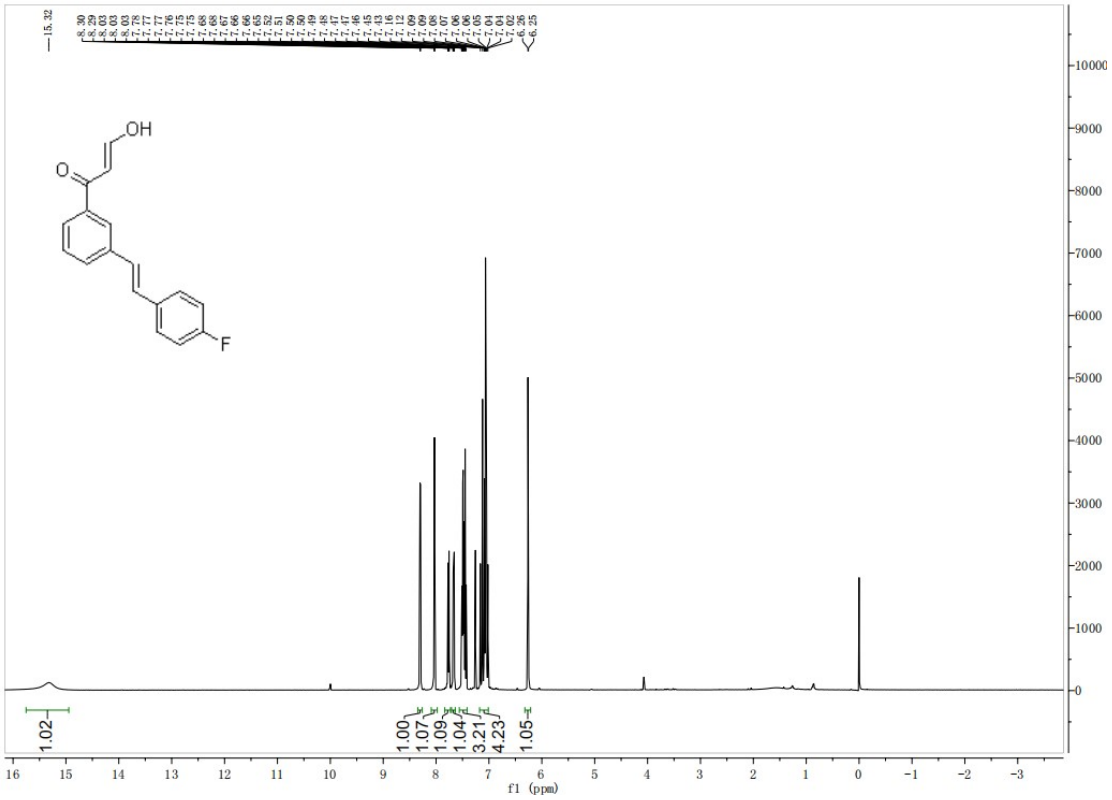

Figure S40.[1]H-NMR (400 MHz, Chloroform-d) of **5b**

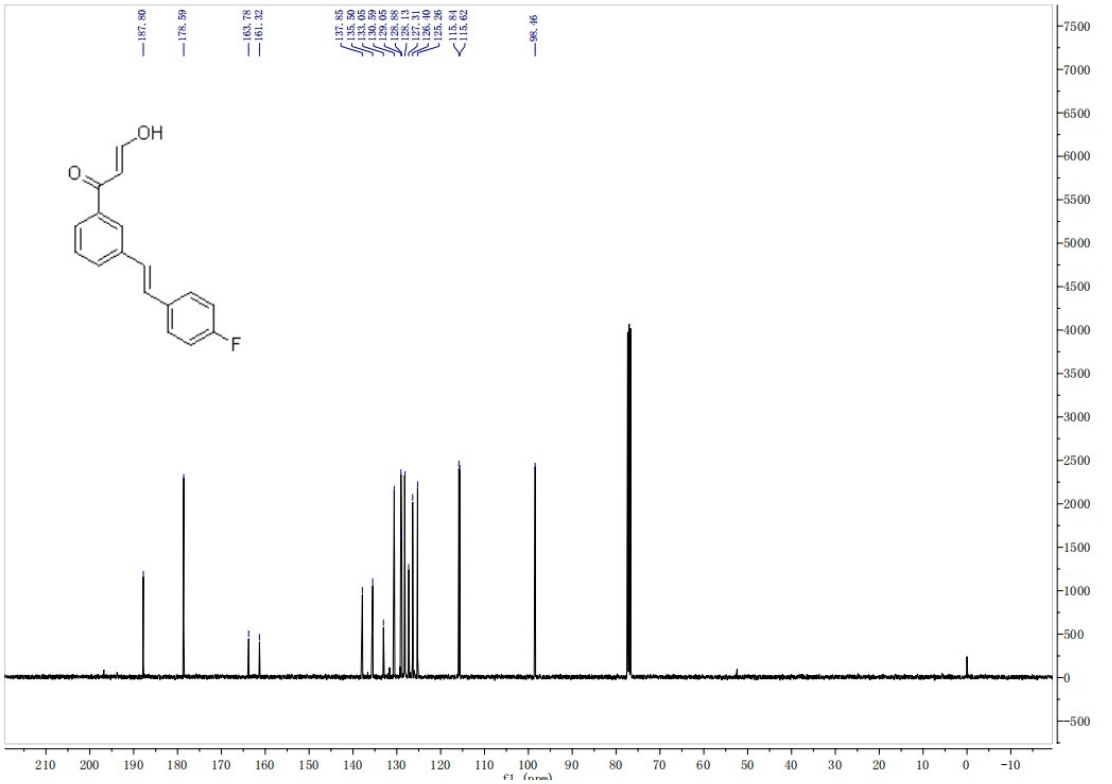

Figure S41.[13]C-NMR (100 MHz, Chloroform-d) of **5b**

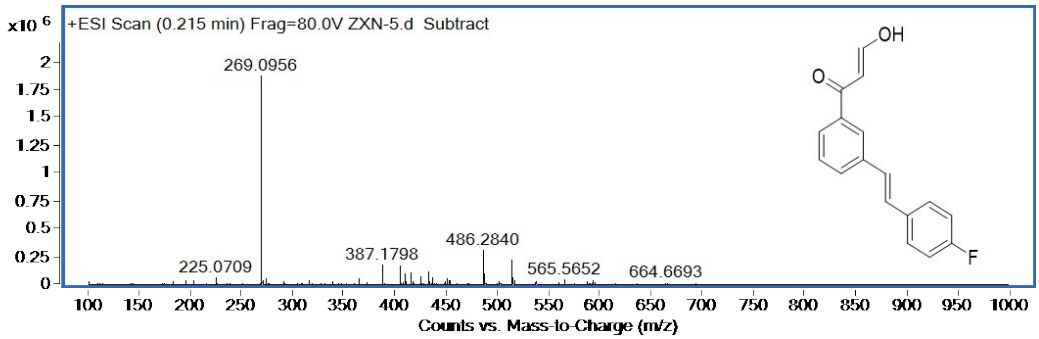

Figure S42. HRMS of **5b**

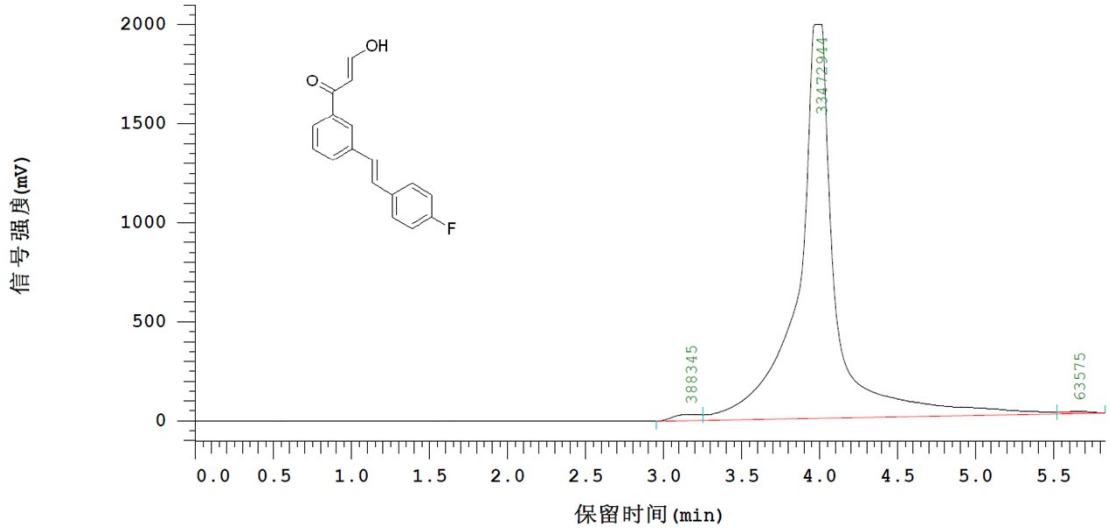

Figure S43. HPLC of **5b**

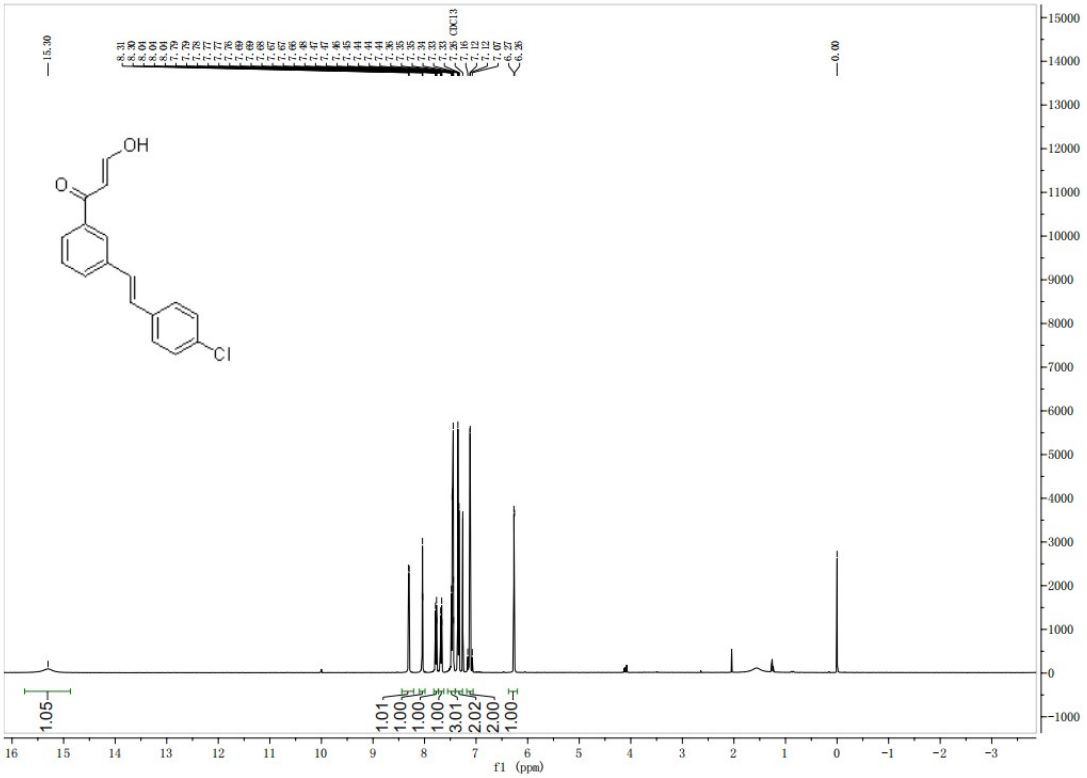

Figure S44.[1]H-NMR (400 MHz, Chloroform-d) of **5c**

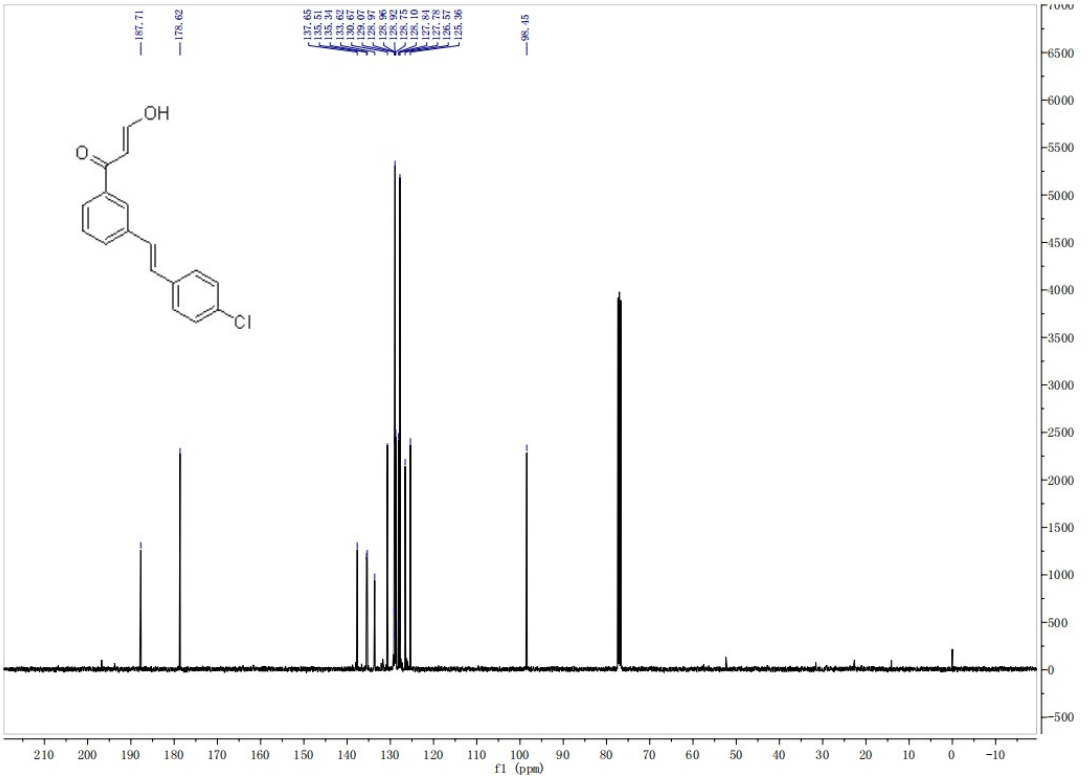

Figure S45.[13]C-NMR (100 MHz, Chloroform-d) of **5c**

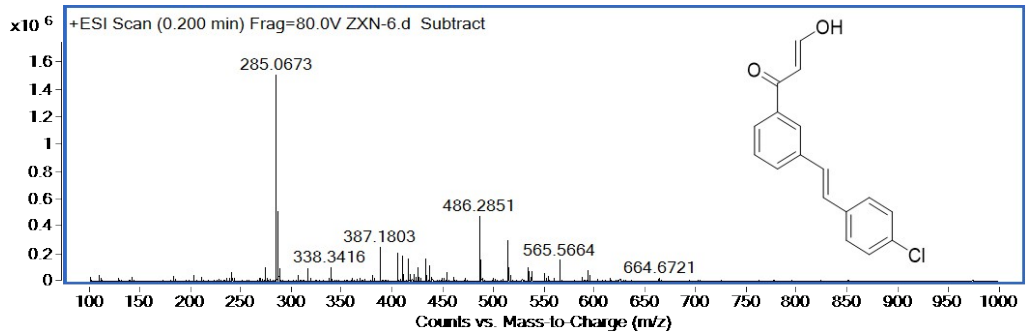

Figure S46. HRMS of **5c**

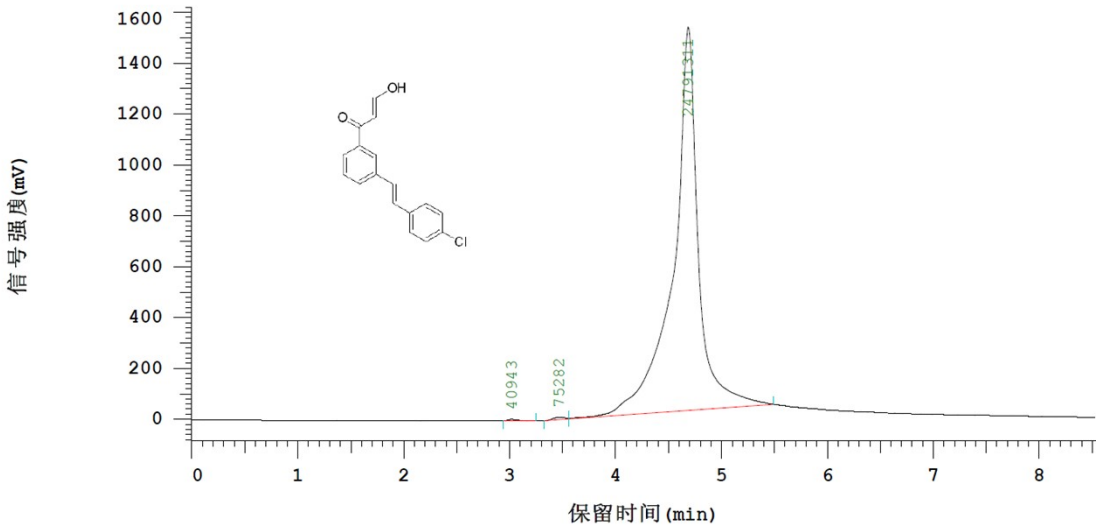

Figure S47. HPLC of **5c**

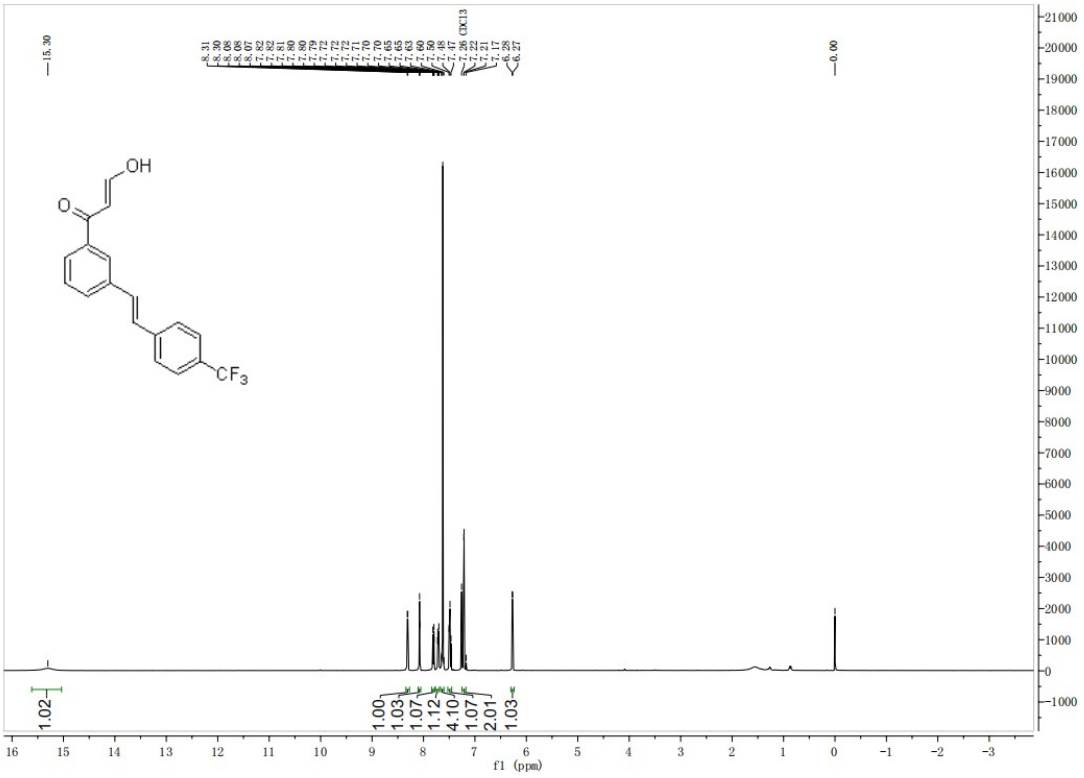

Figure S48.[1]H-NMR (400 MHz, Chloroform-d) of **5d**

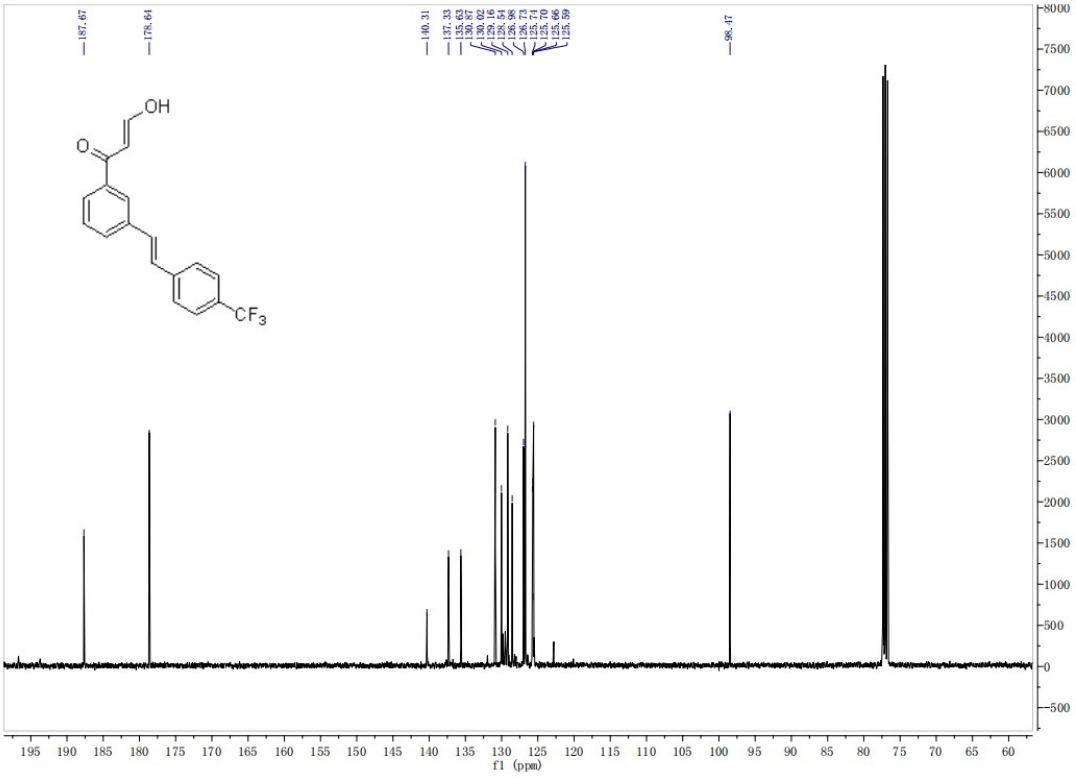

Figure S49.[13]C-NMR (100 MHz, Chloroform-d) of **5d**

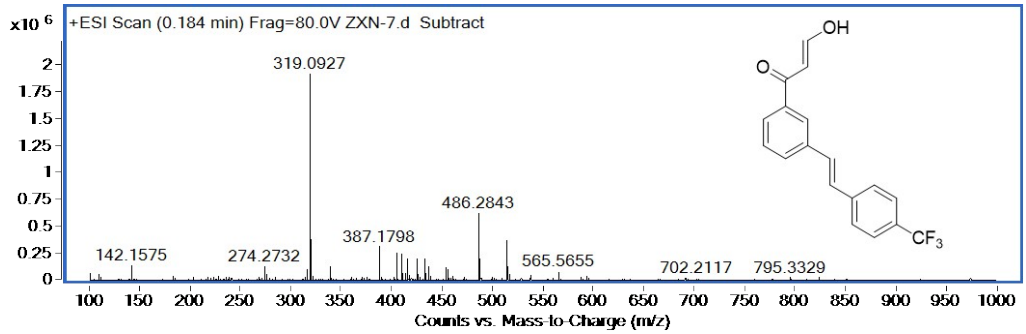

Figure S50. HRMS of **5d**

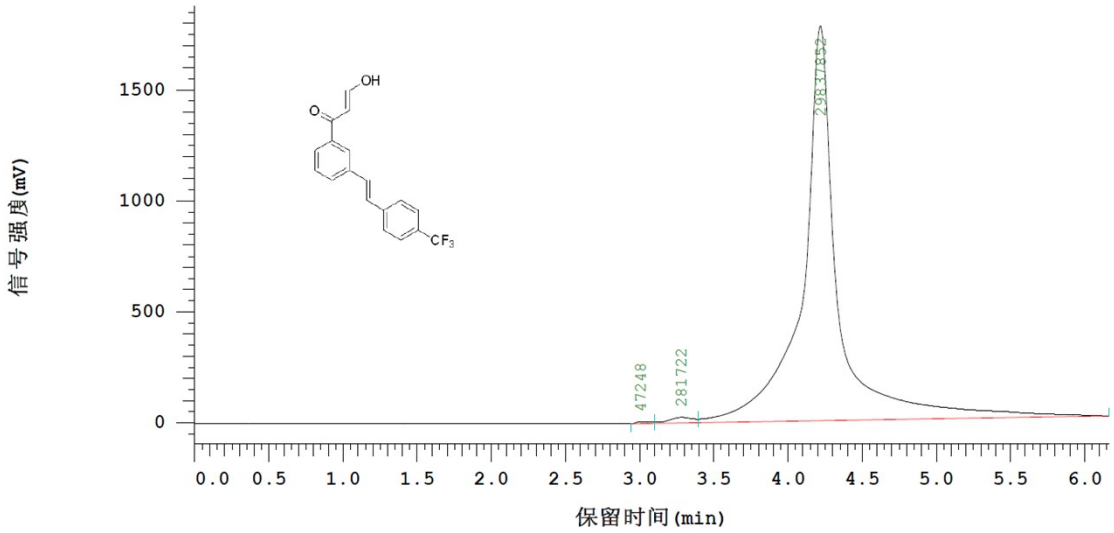

Figure S51. HPLC of **5c**

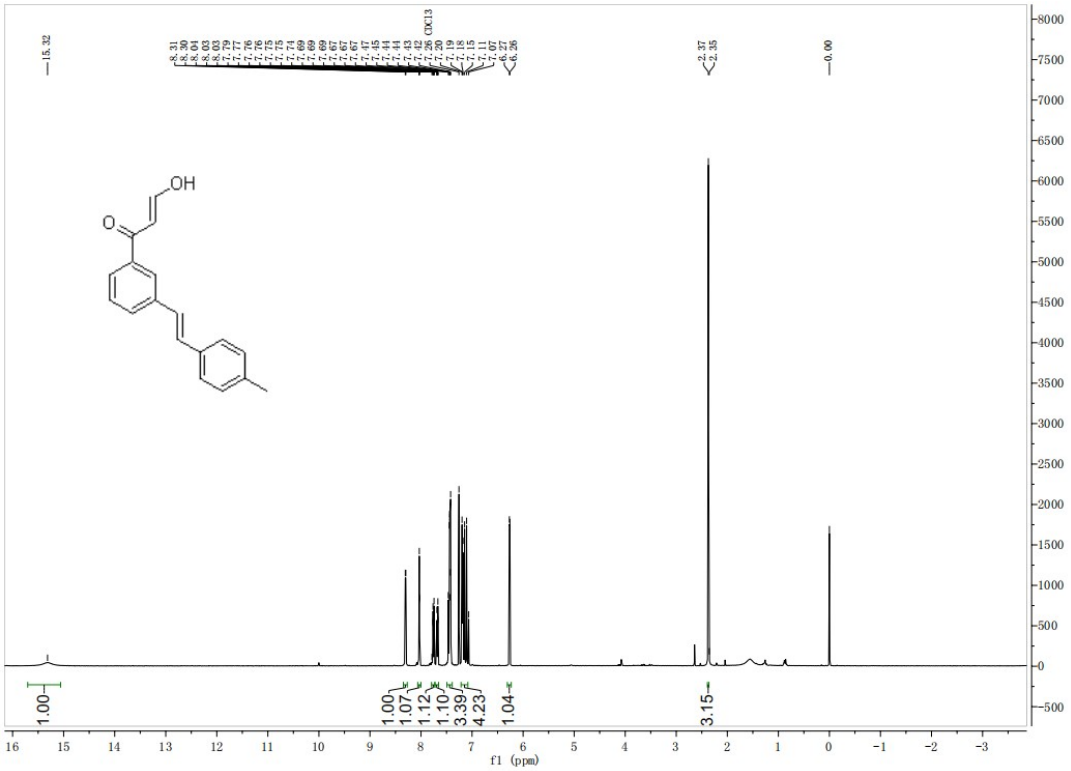

Figure S52.[1]H-NMR (400 MHz, Chloroform-d) of **5e**

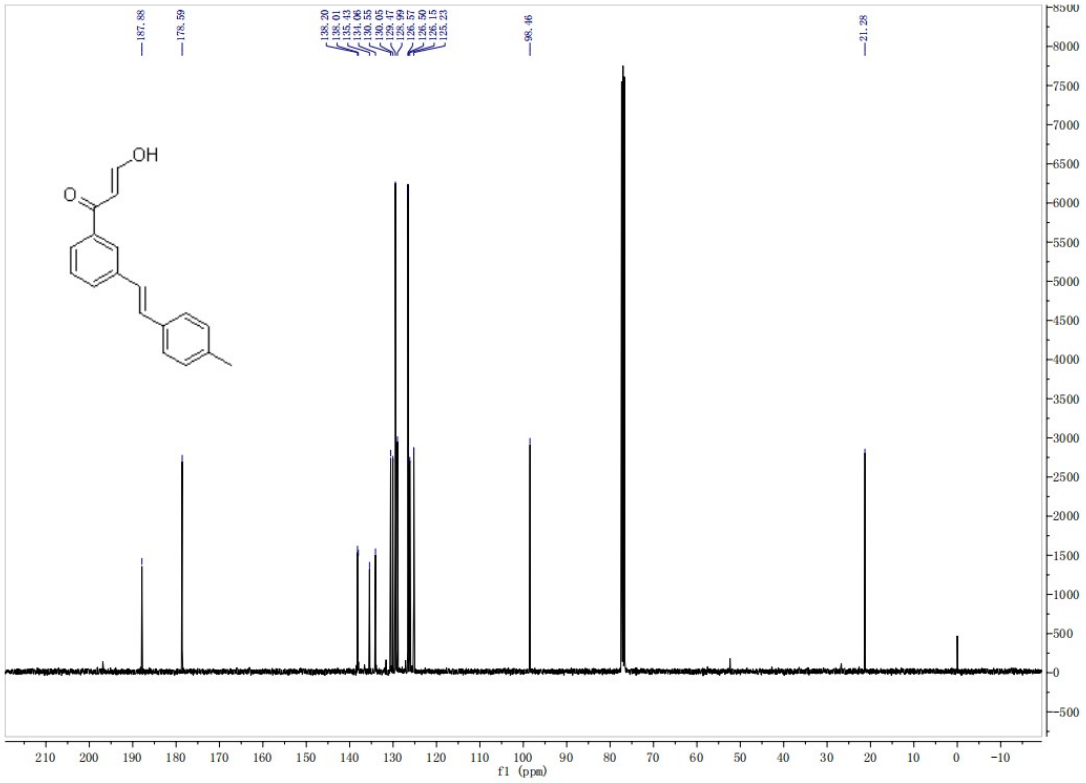

Figure S53.^{13}C-NMR (100 MHz, Chloroform-d) of **5e**

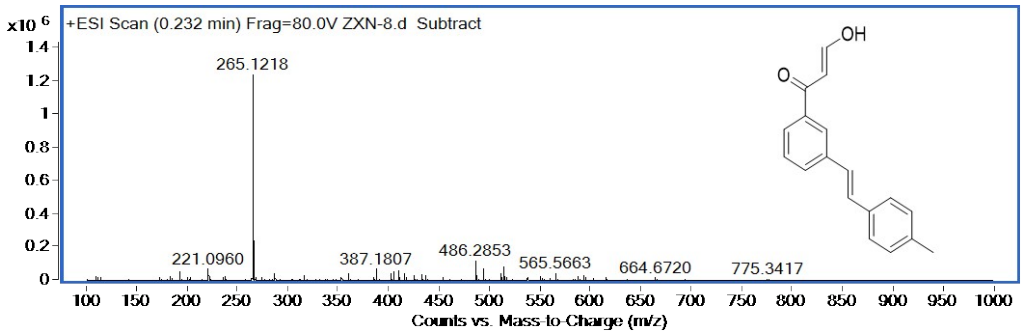

Figure S54. HRMS of **5e**

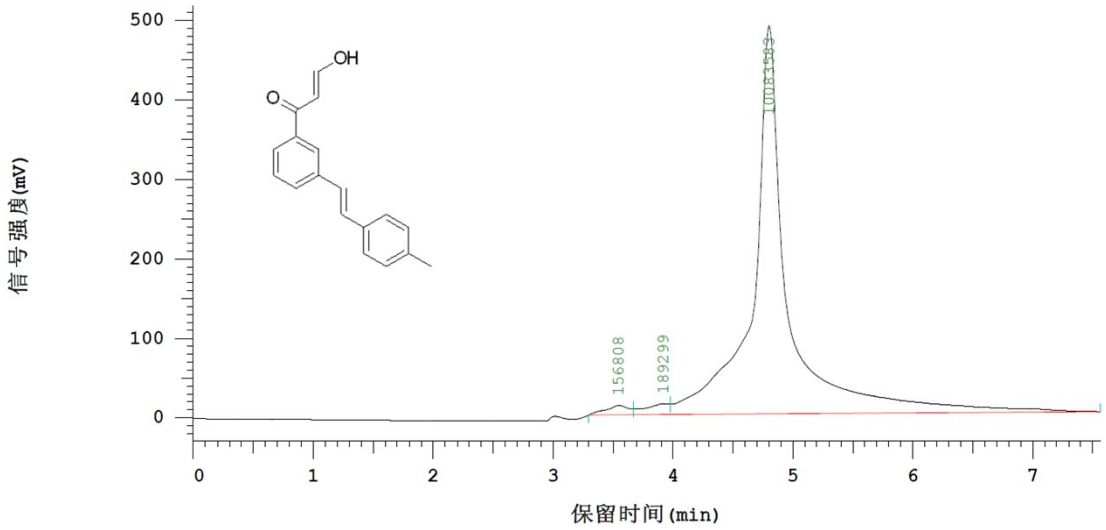

Figure S55. HPLC of **5e**

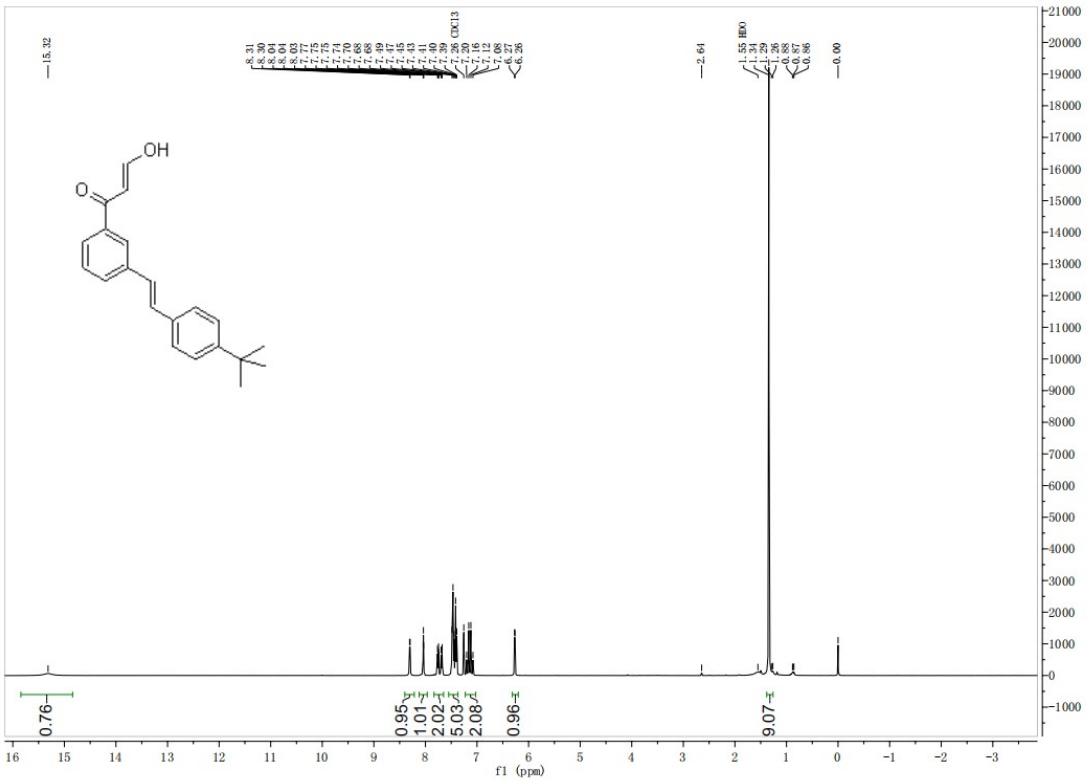

Figure S56.[1]H-NMR (400 MHz, Chloroform-d) of **5f**

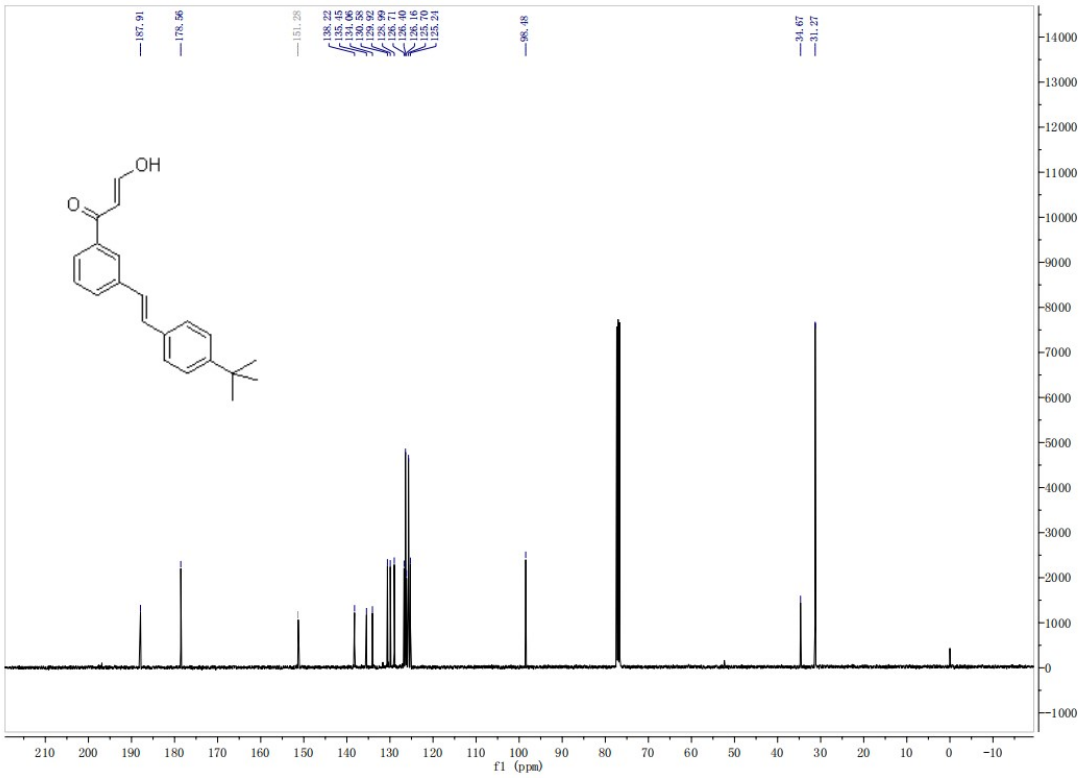

Figure S57.^{13}C-NMR (100 MHz, Chloroform-d) of **5f**

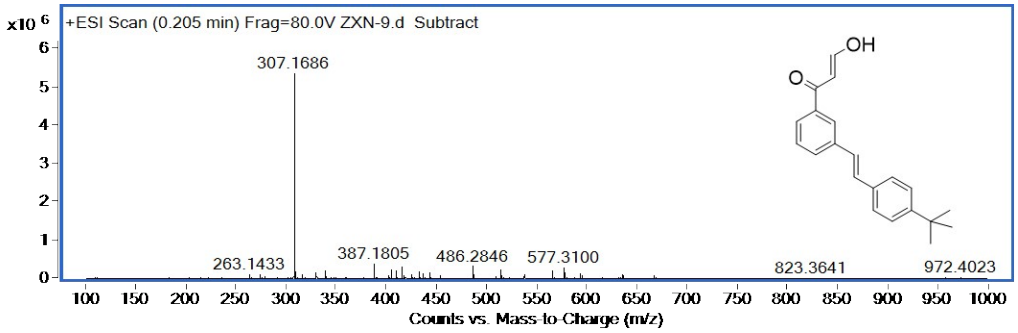

Figure S58. HRMS of **5f**

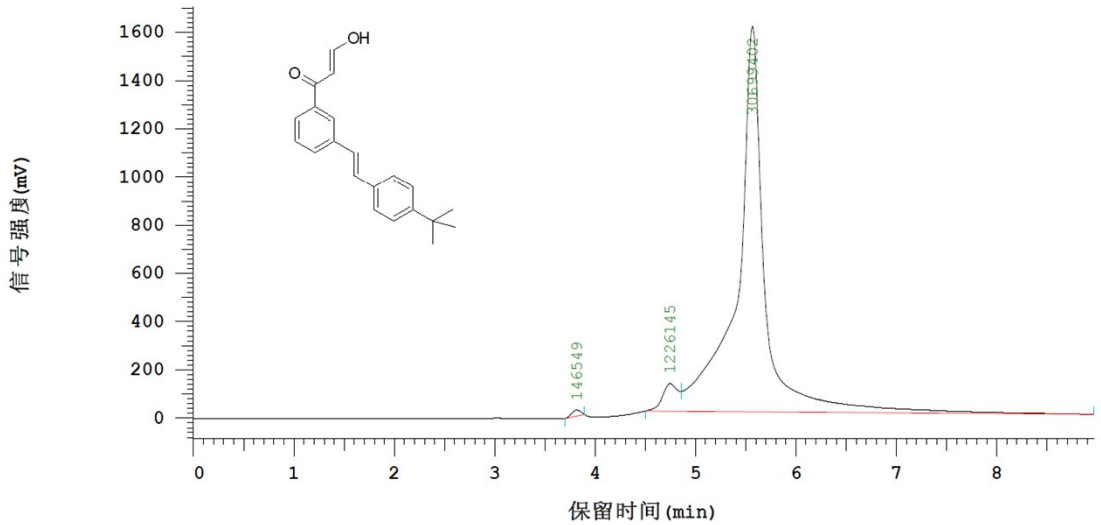

Figure S59. HPLC of **5f**

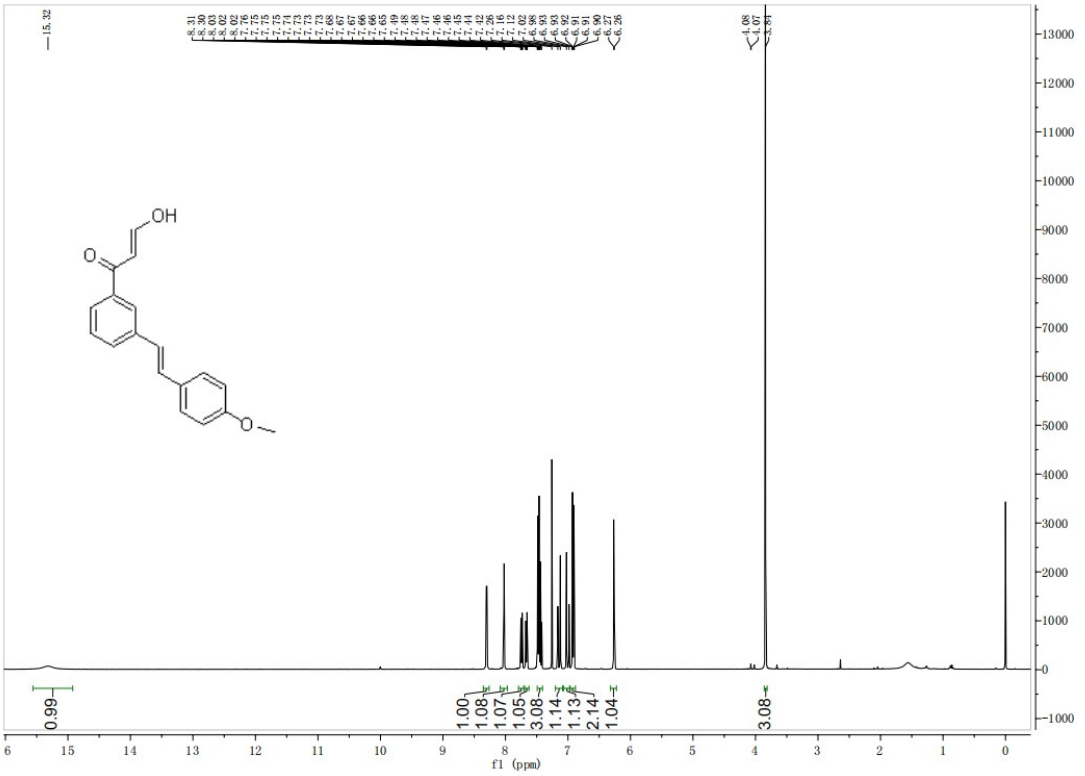

Figure S60.[1]H-NMR (400 MHz, Chloroform-d) of **5g**

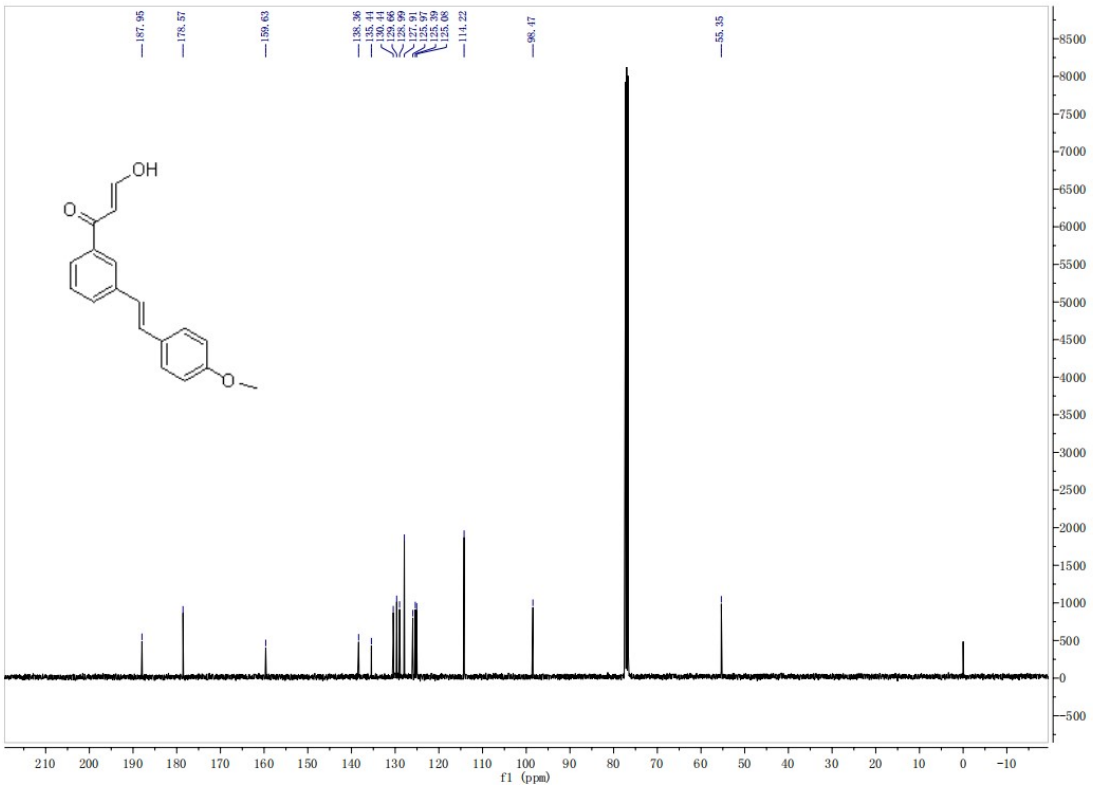

Figure S61.[13]C-NMR (100 MHz, Chloroform-d) of **5g**

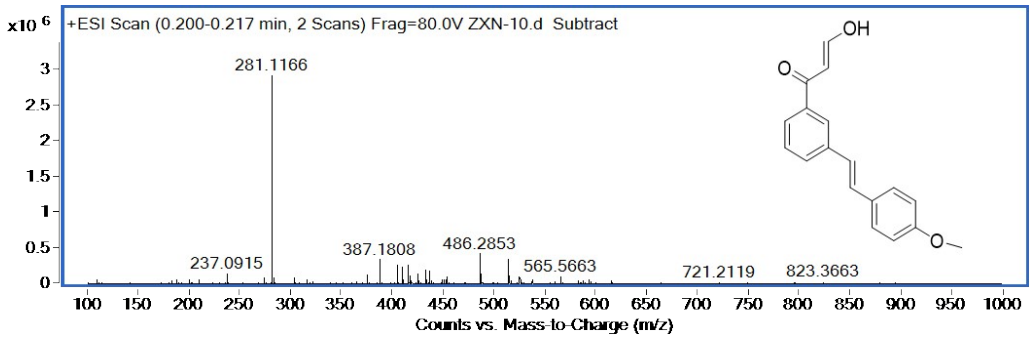

Figure S62. HRMS of **5g**

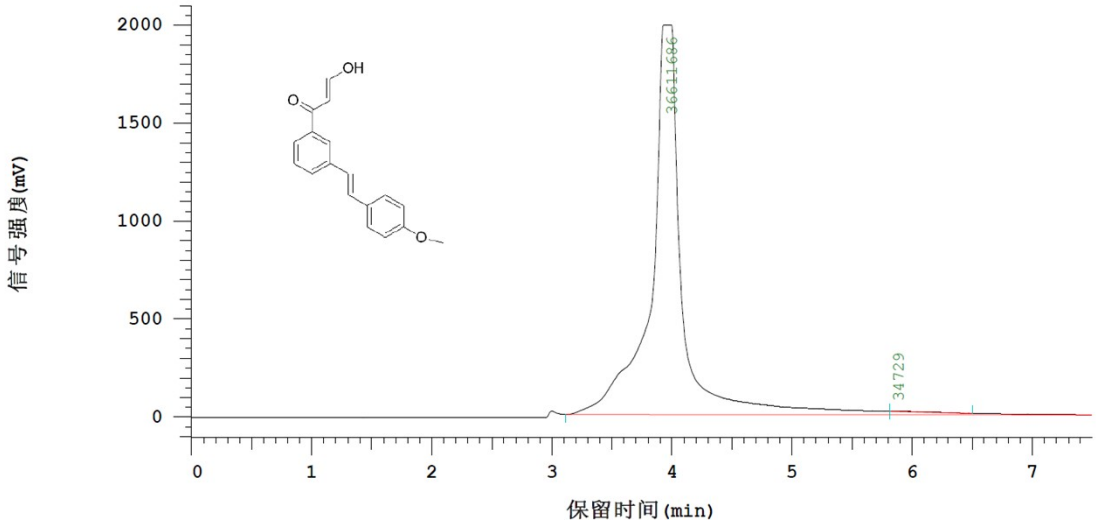

Figure S63. HPLC of **5g**

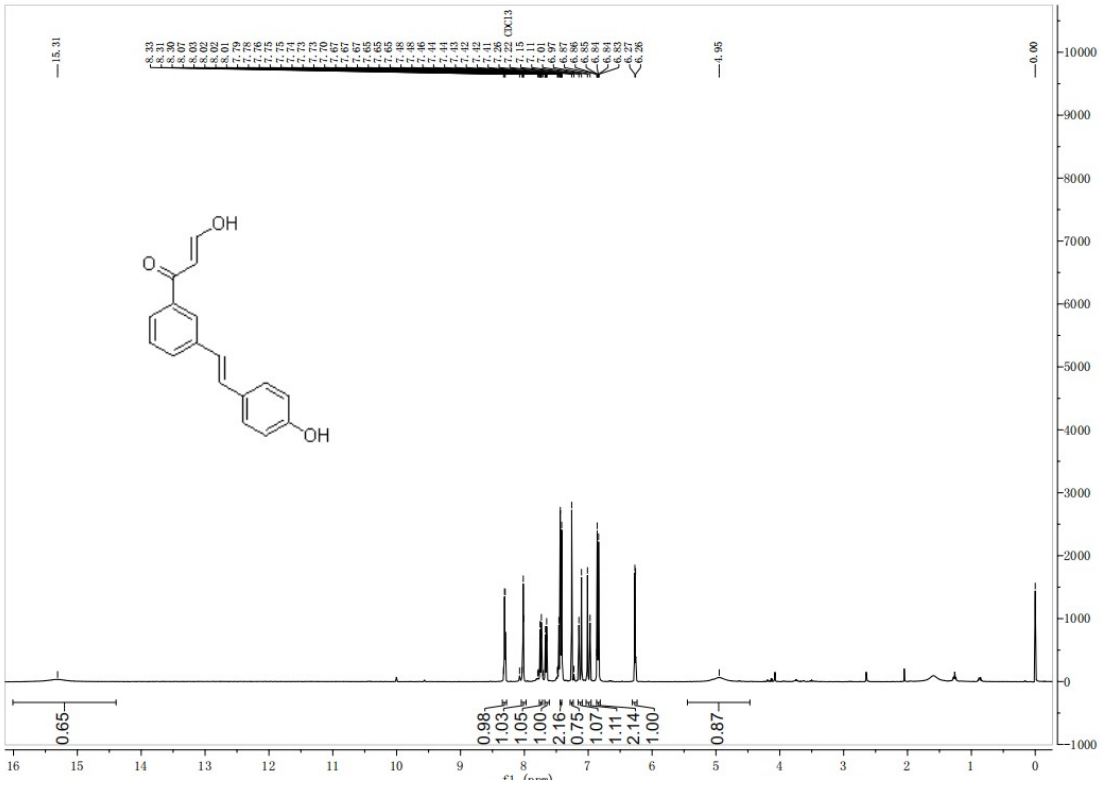

Figure S64.[1]H-NMR (400 MHz, Chloroform-d) of **5h**

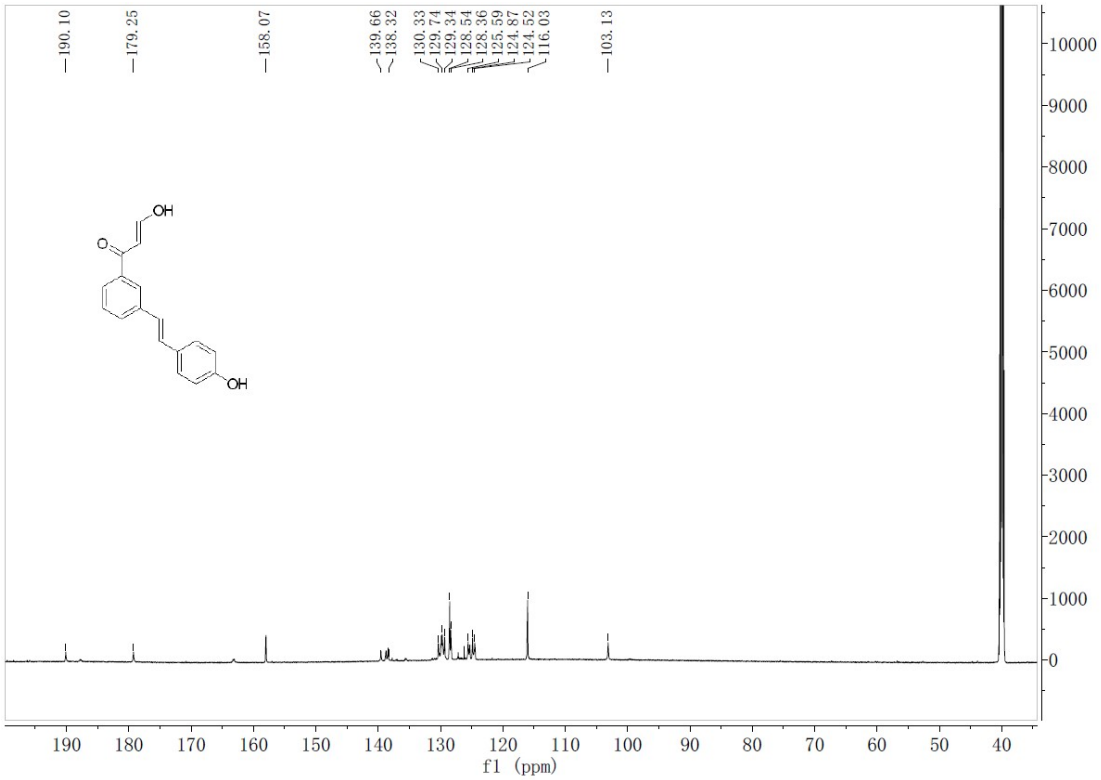

Figure S65.[13]C-NMR (100 MHz, Chloroform-d) of **5h**

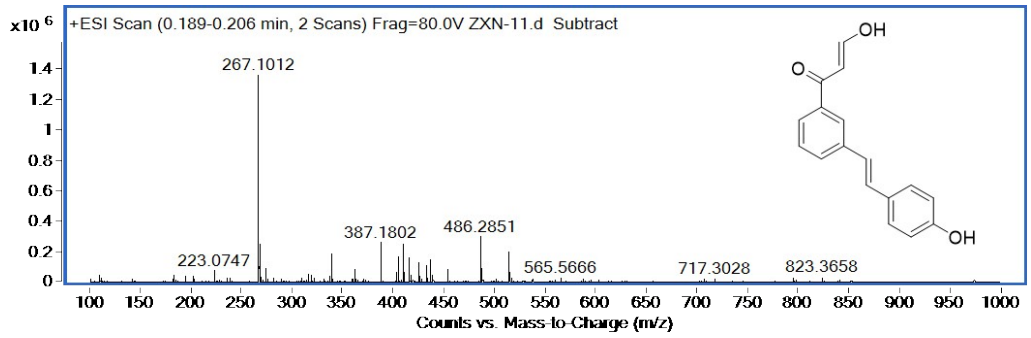

Figure S66. HRMS of **5h**

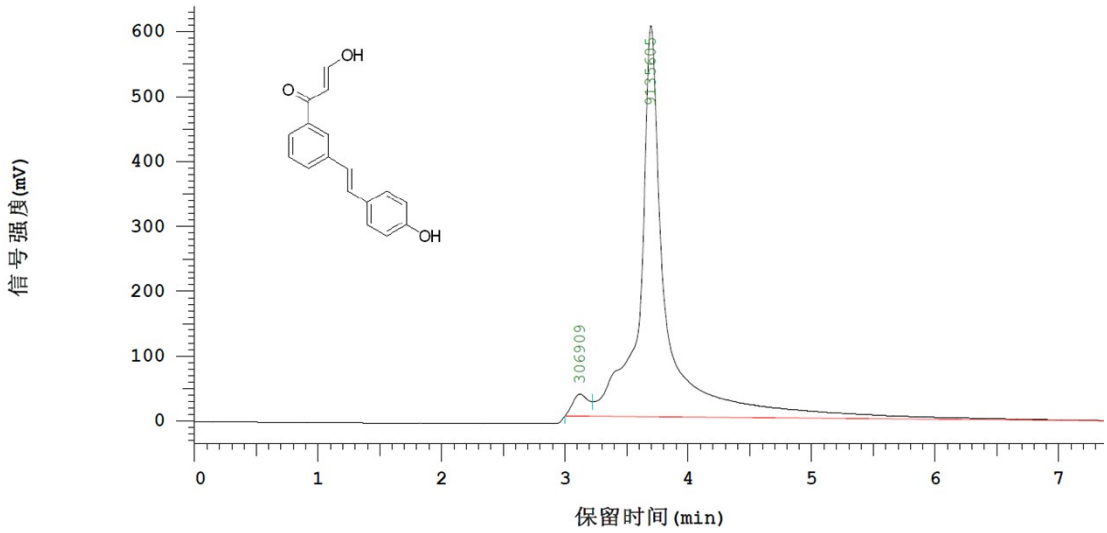

Figure S67. HPLC of **5h**

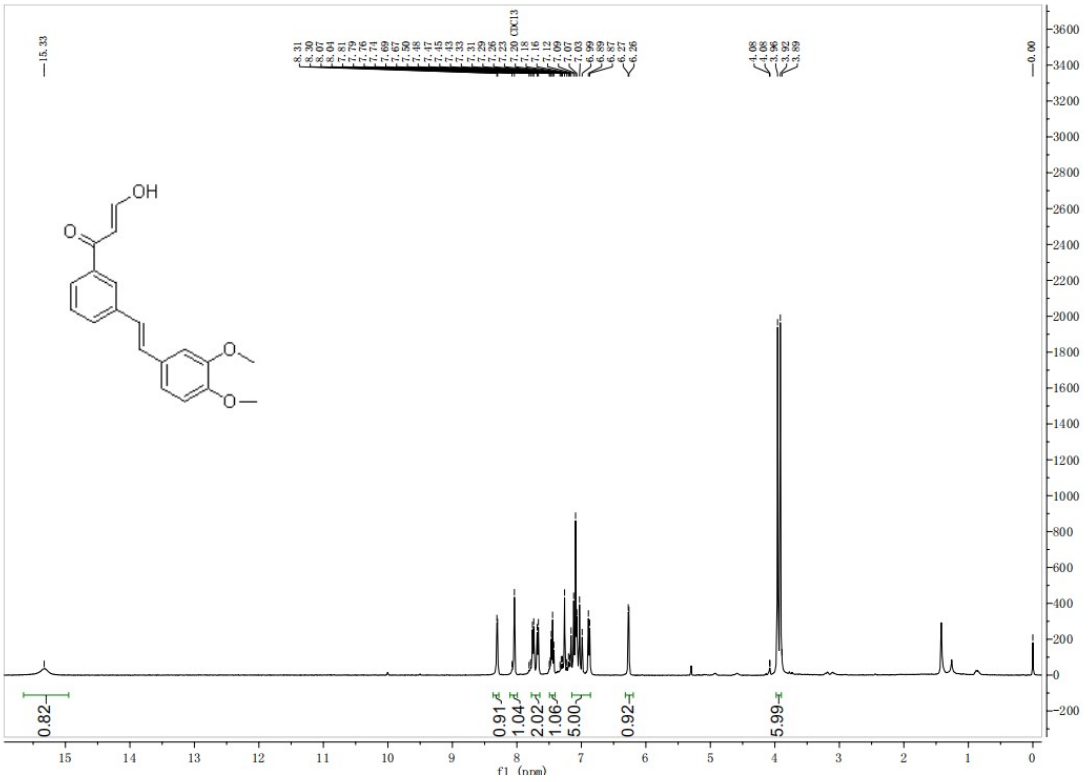

Figure S68.[1]H-NMR (400 MHz, Chloroform-d) of **5i**

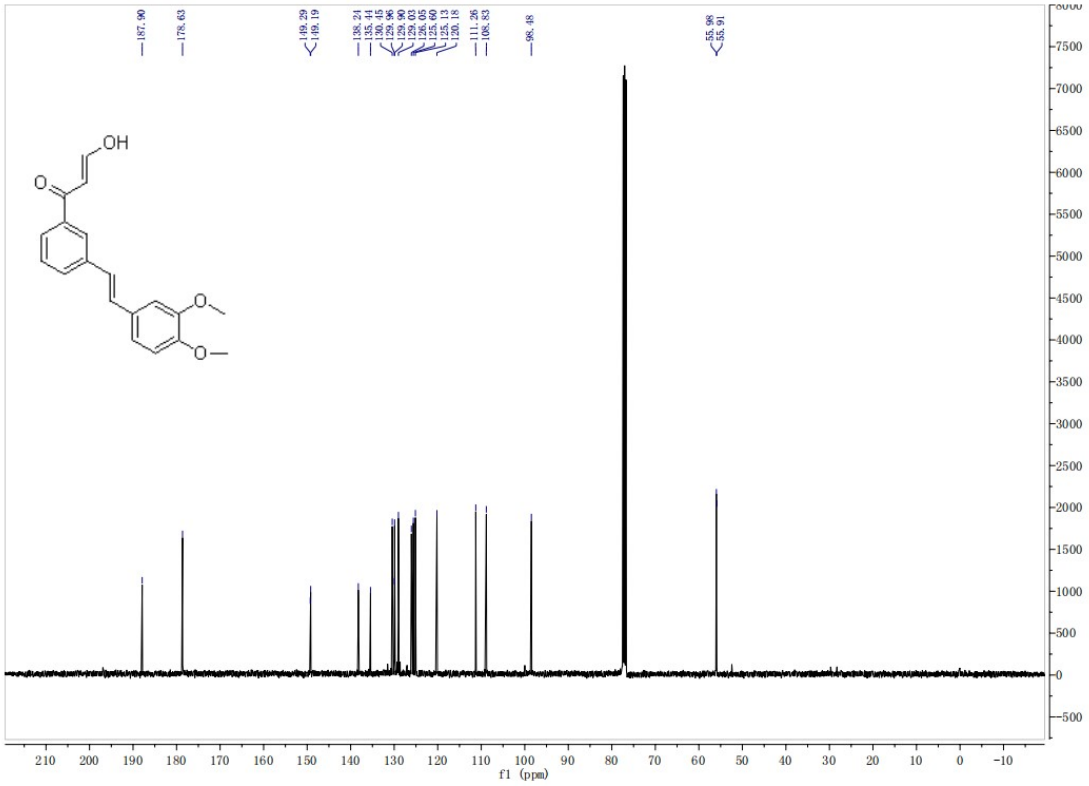

Figure S69.[13]C-NMR (100 MHz, Chloroform-d) of **5i**

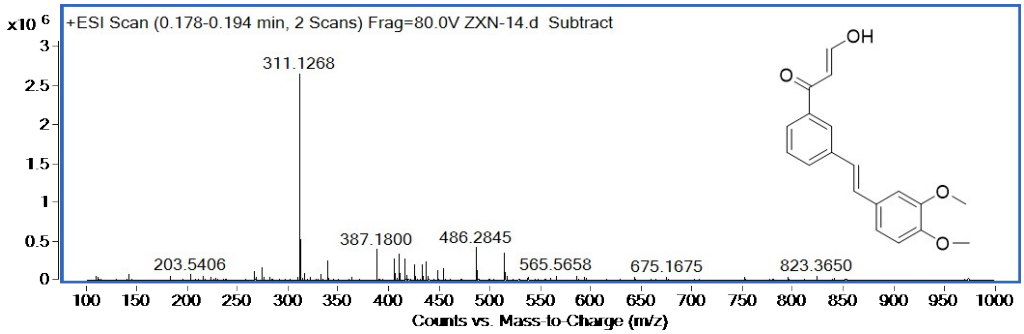

Figure S70. HRMS of **5i**

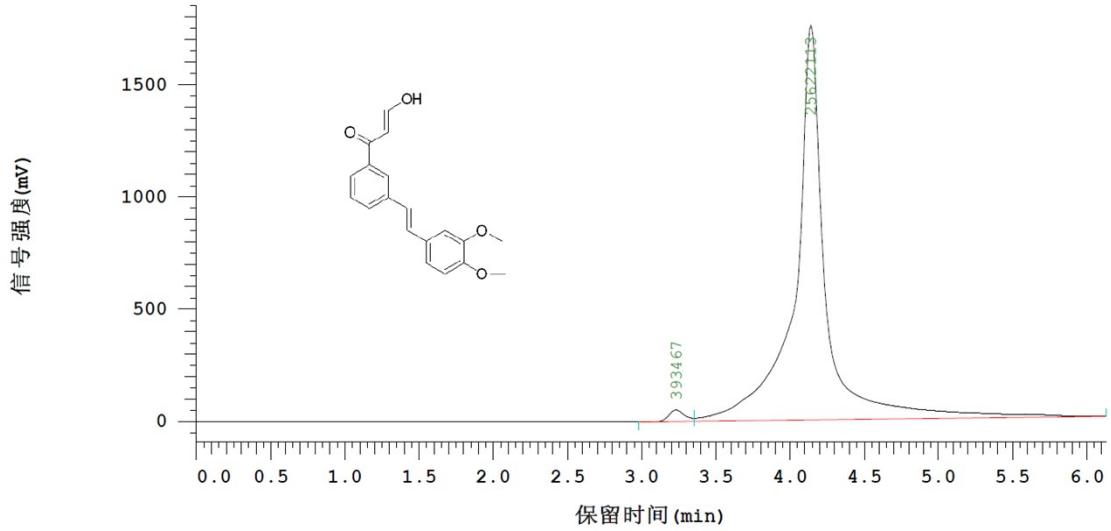

Figure S71. HPLC of **5i**

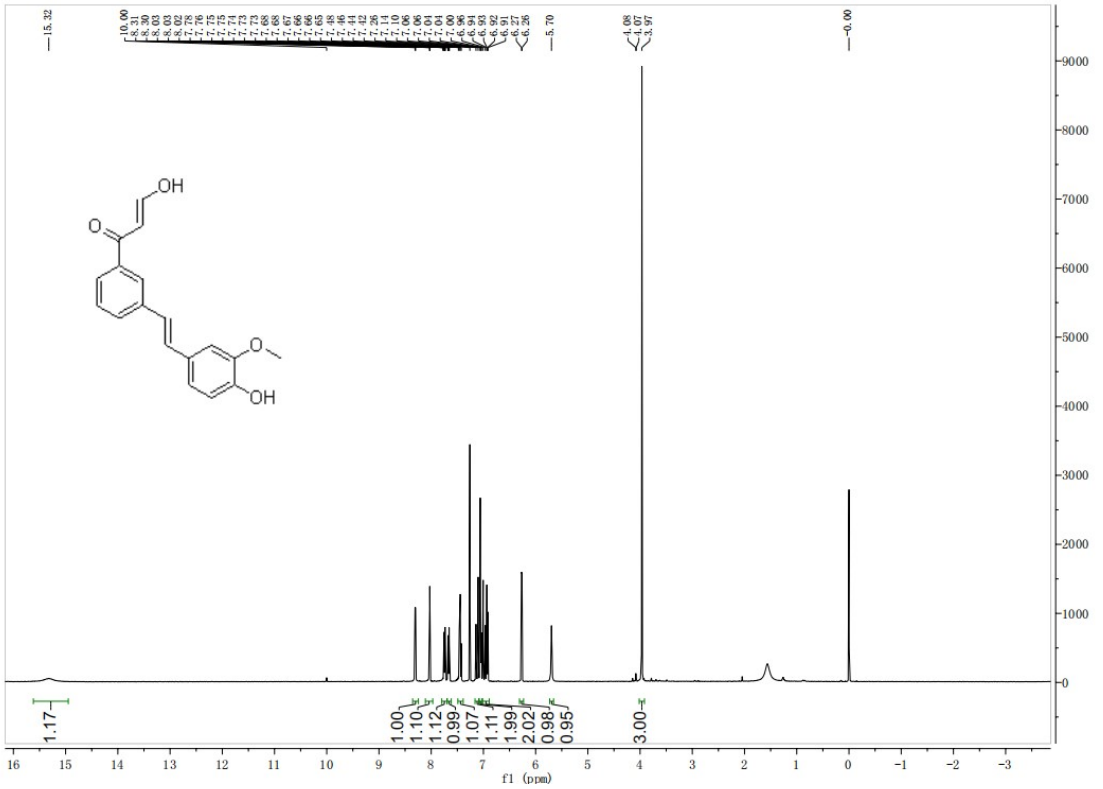

Figure S72.[1]H-NMR (400 MHz, Chloroform-d) of **5j**

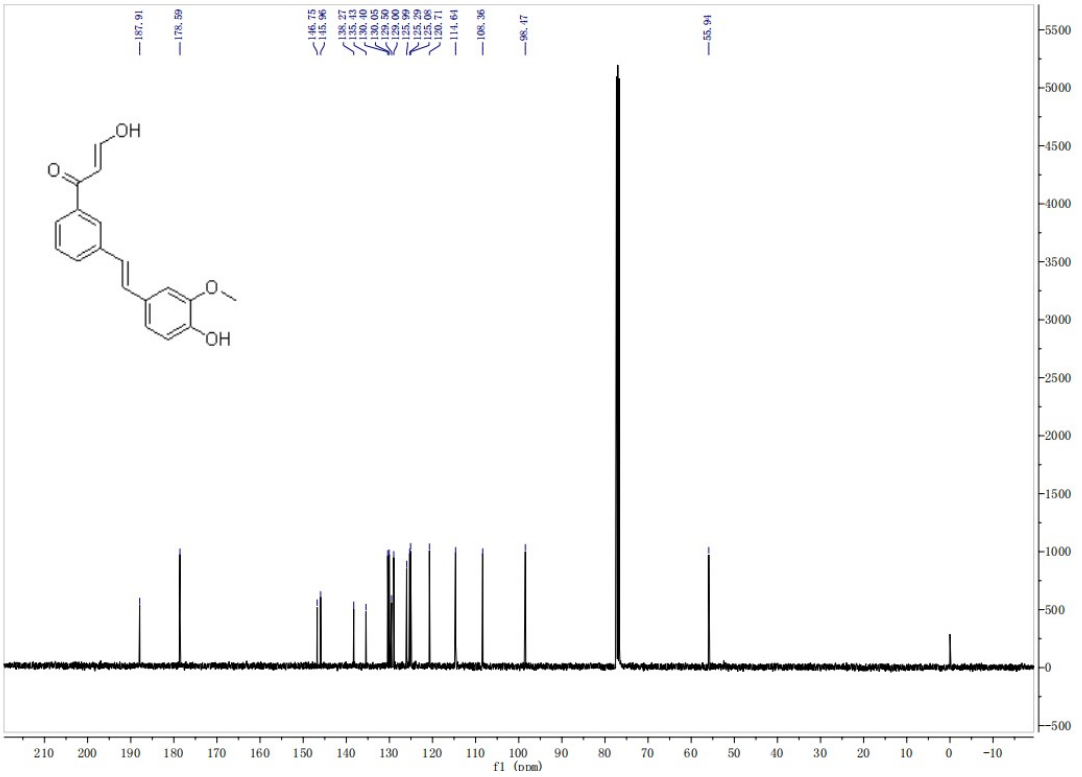

Figure S73.[13]C-NMR (100 MHz, Chloroform-d) of **5j**

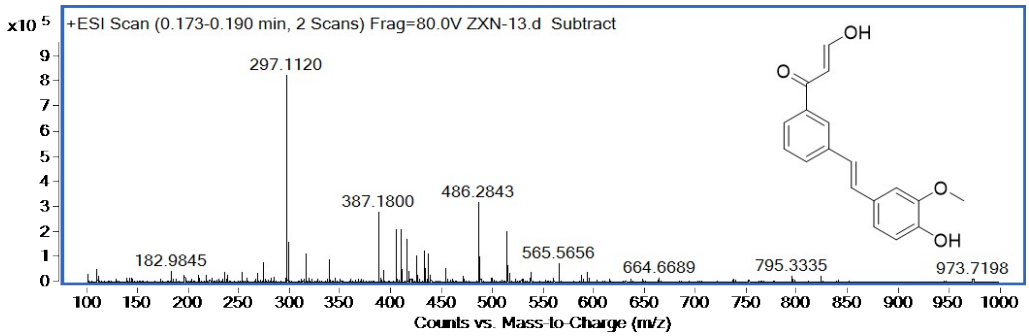

Figure S74. HRMS of **5j**

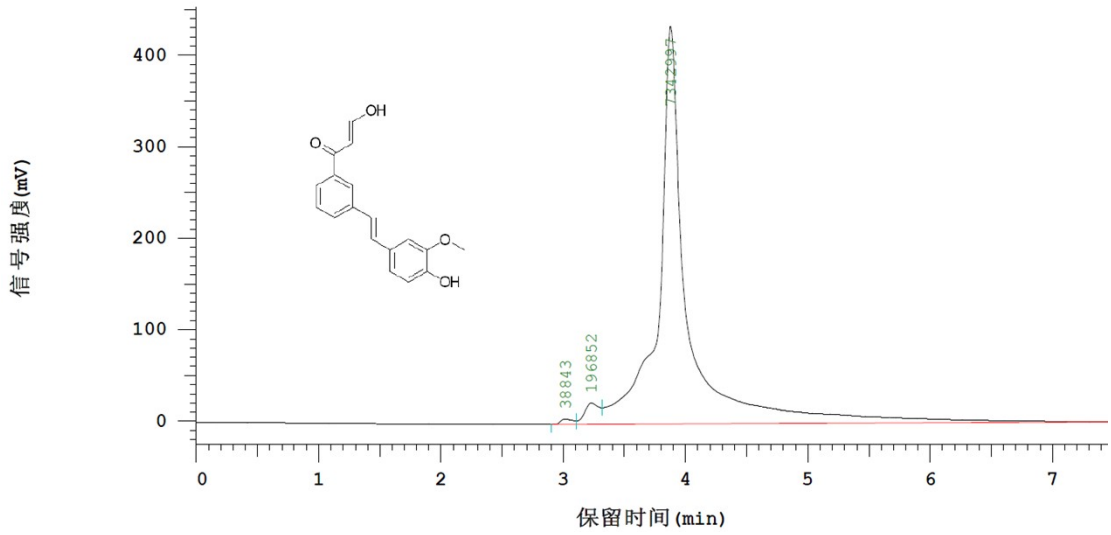

Figure S75. HPLC of **5j**

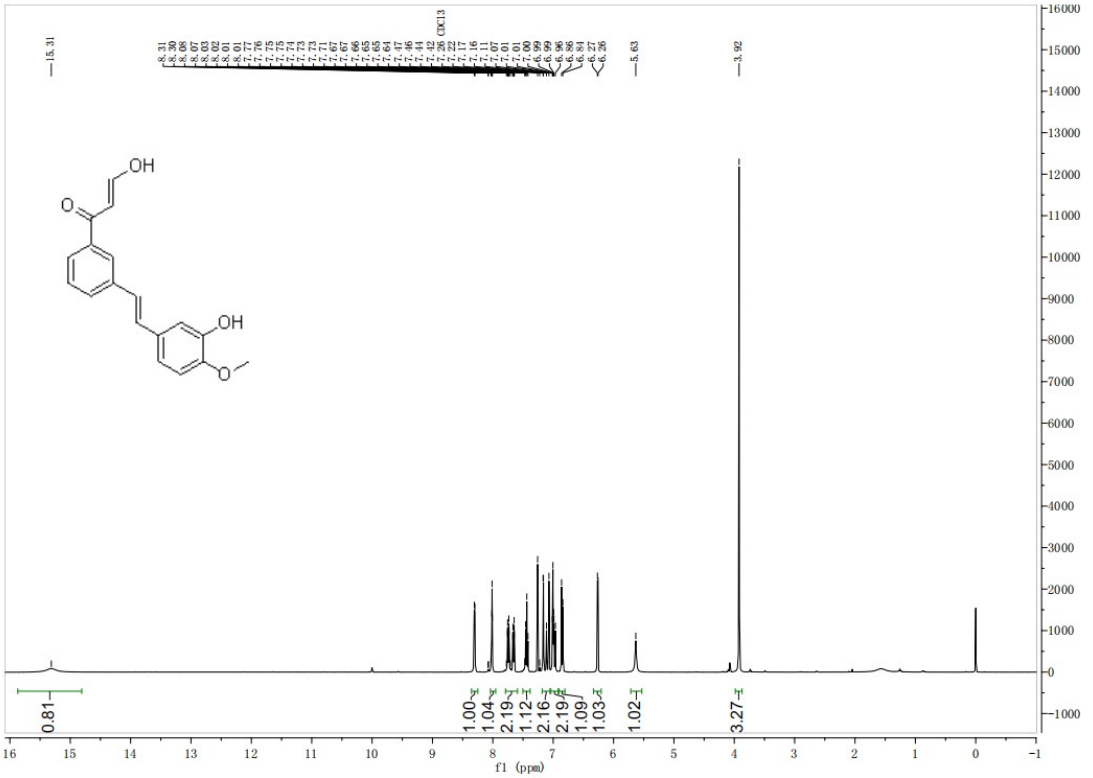

Figure S76.[1]H-NMR (400 MHz, Chloroform-d) of **5k**

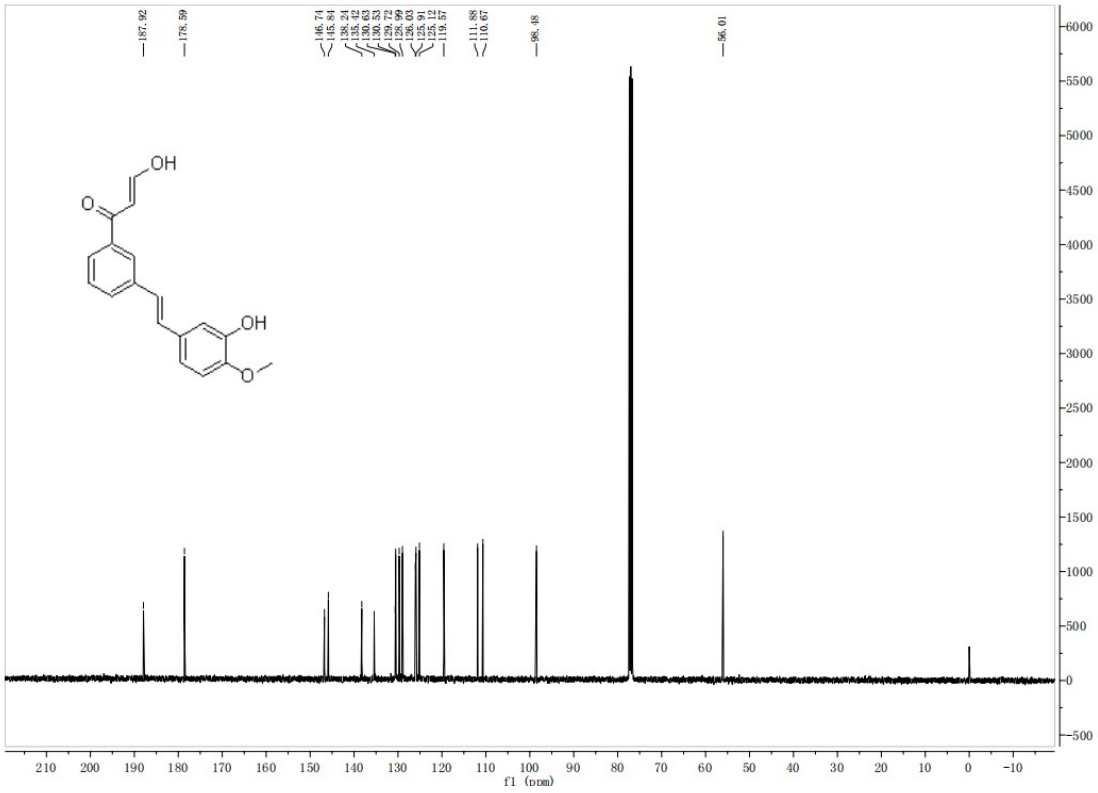

Figure S77.[13]C-NMR (100 MHz, Chloroform-d) of **5k**

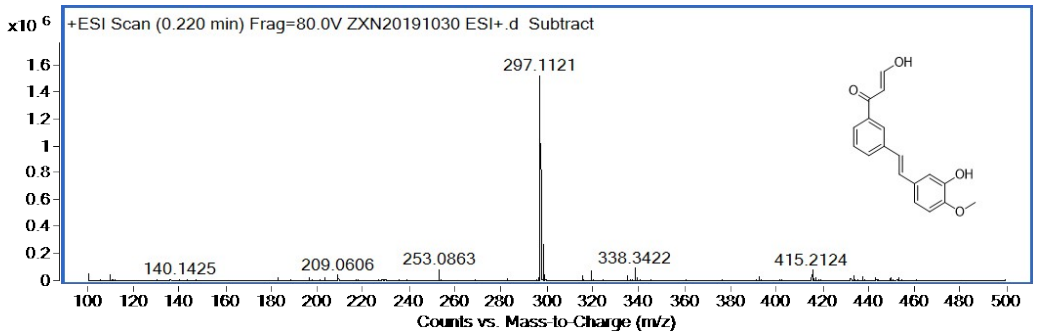

Figure S78. HRMS of **5k**

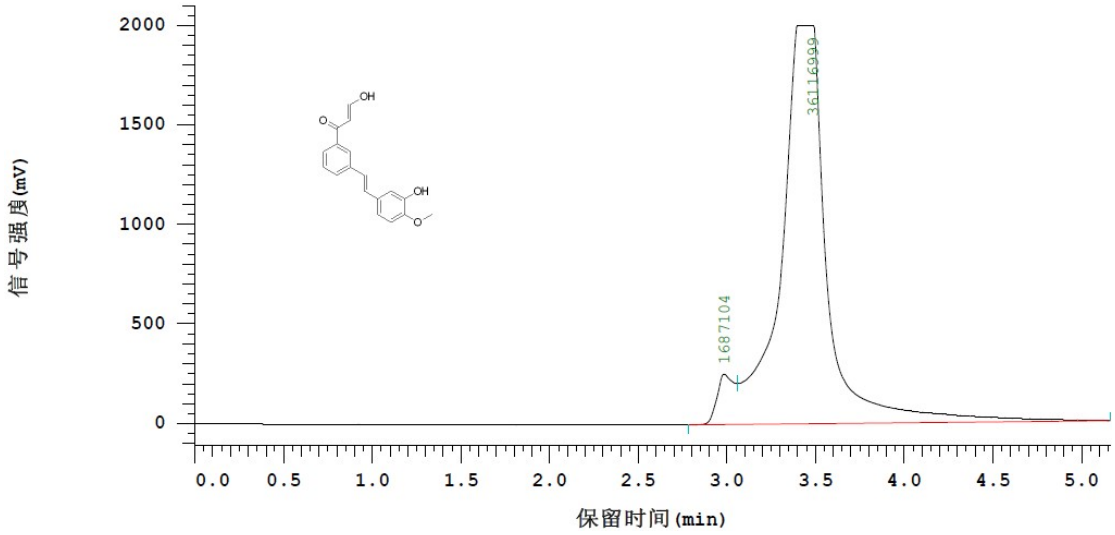

Figure S79. HPLC of **5k**

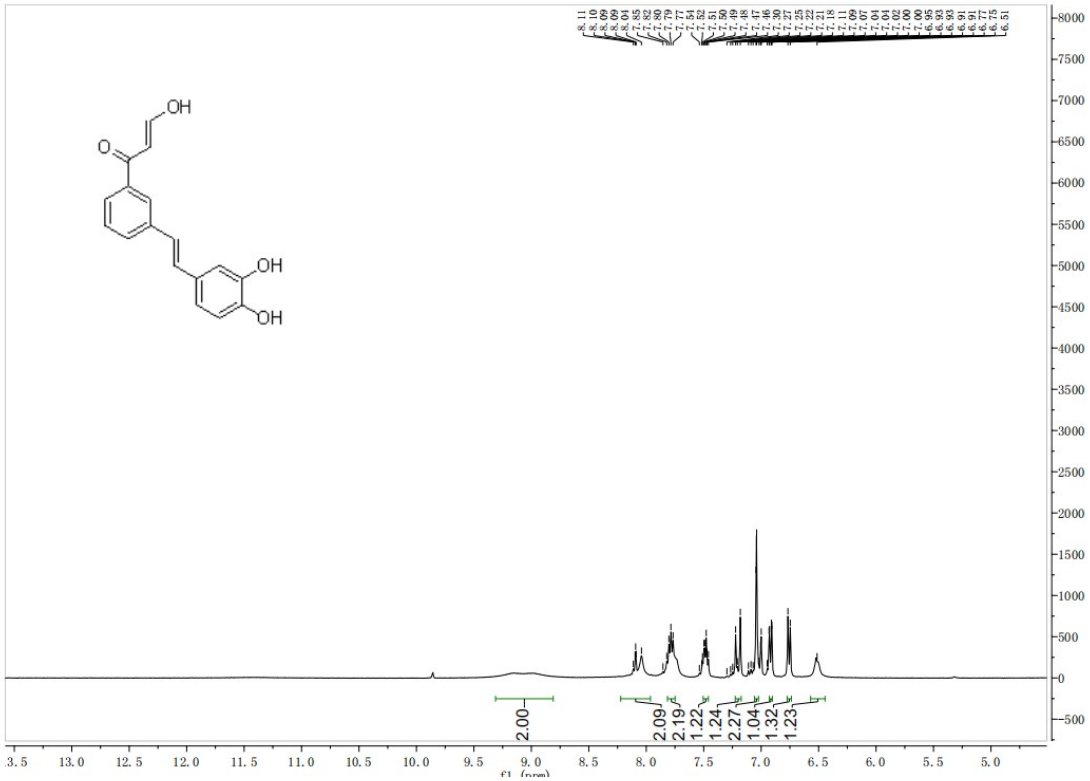

Figure S80.[1]H-NMR (400 MHz, DMSO-*d6*) of **5l**

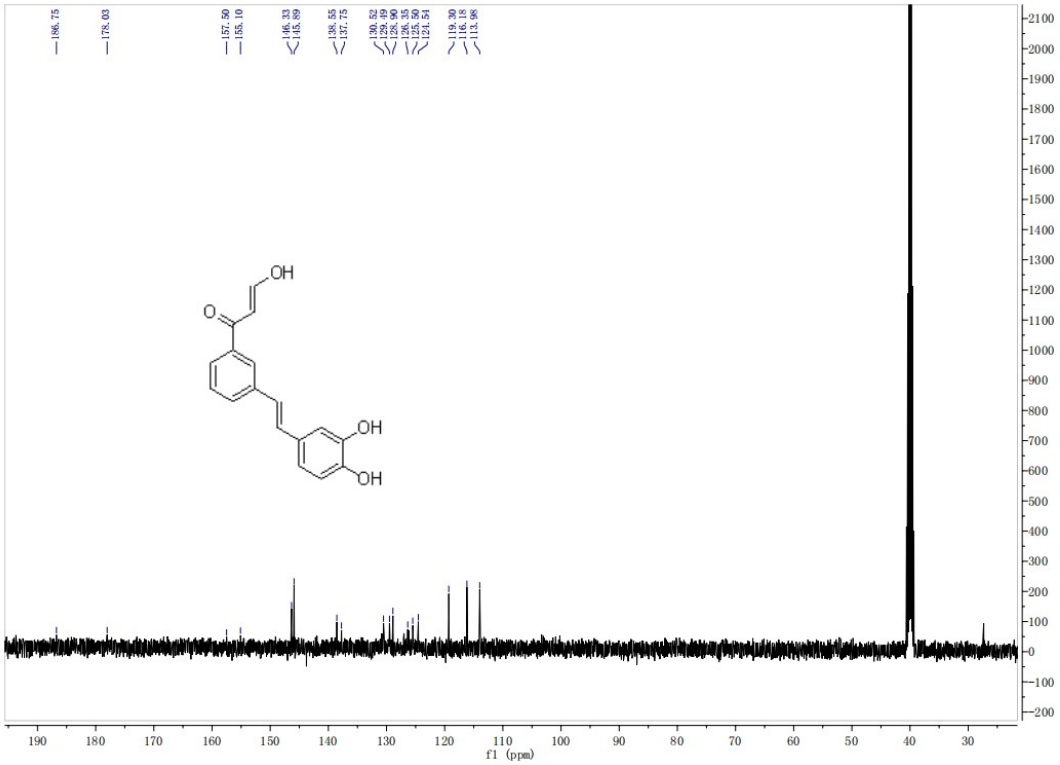

Figure S81.[13]C-NMR (100 MHz, DMSO-*d6*) of **5l**

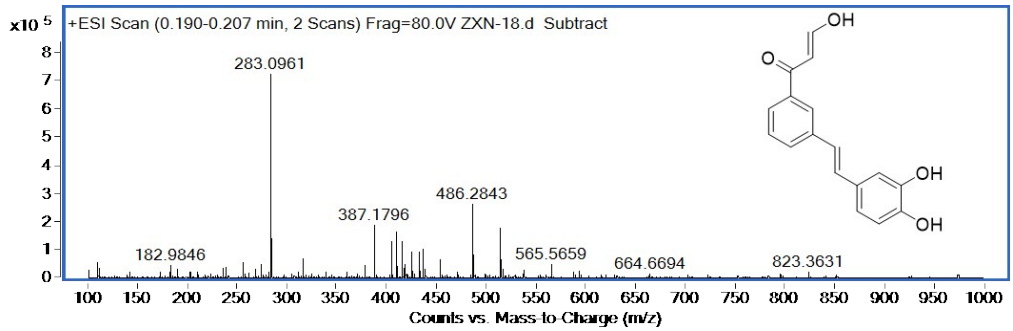

Figure S82. HRMS of **5l**

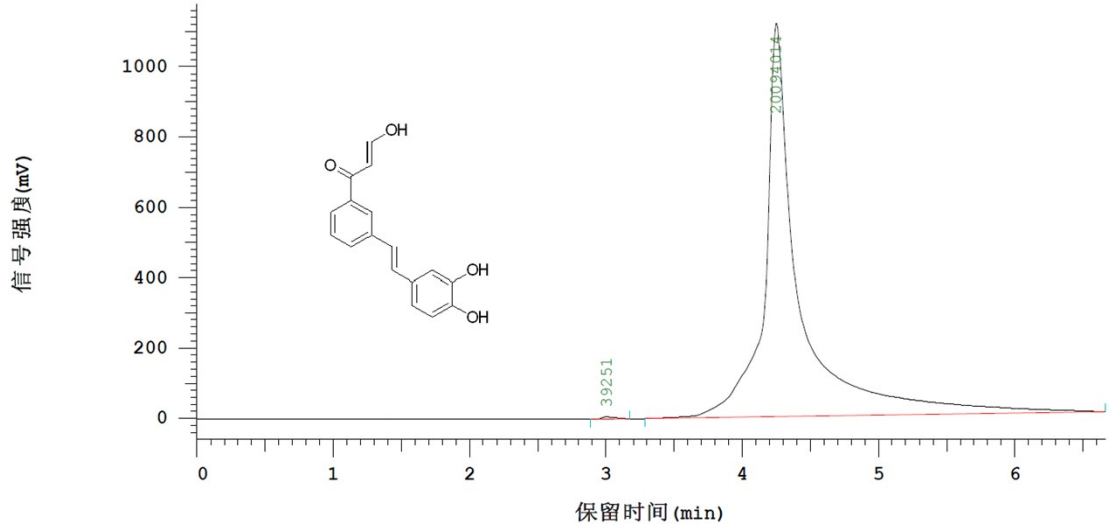

Figure S83. HPLC of **5l**

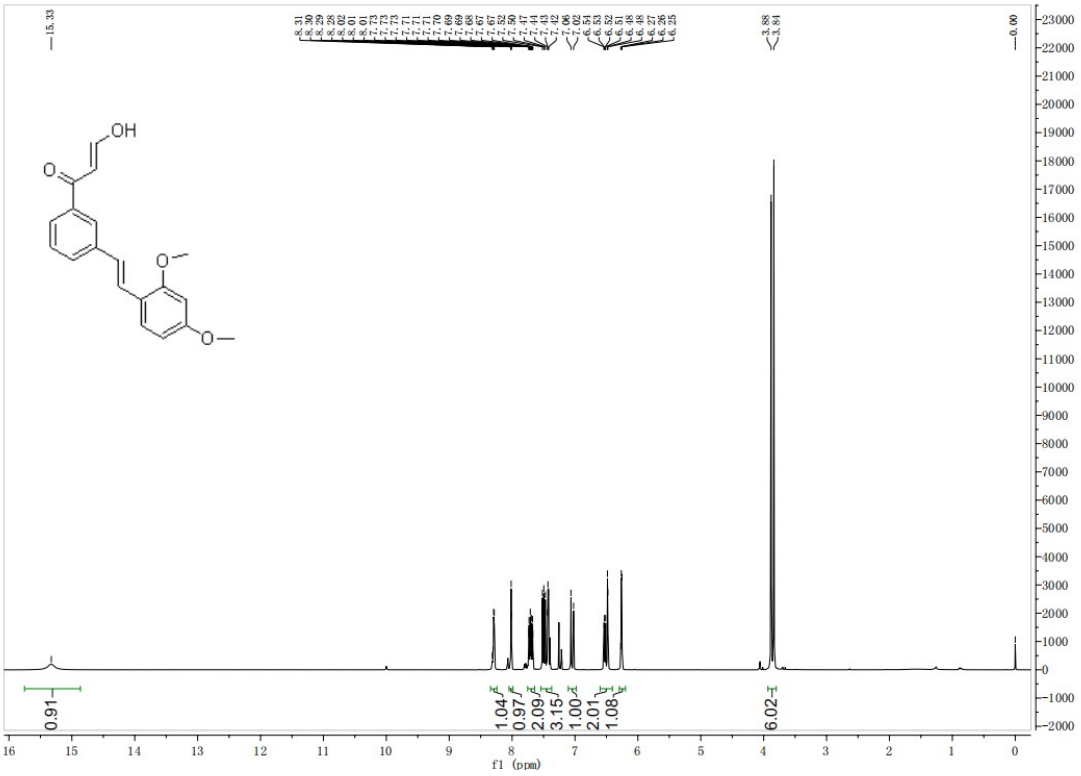

Figure S84.[1]H-NMR (400 MHz, Chloroform-d) of **5m**

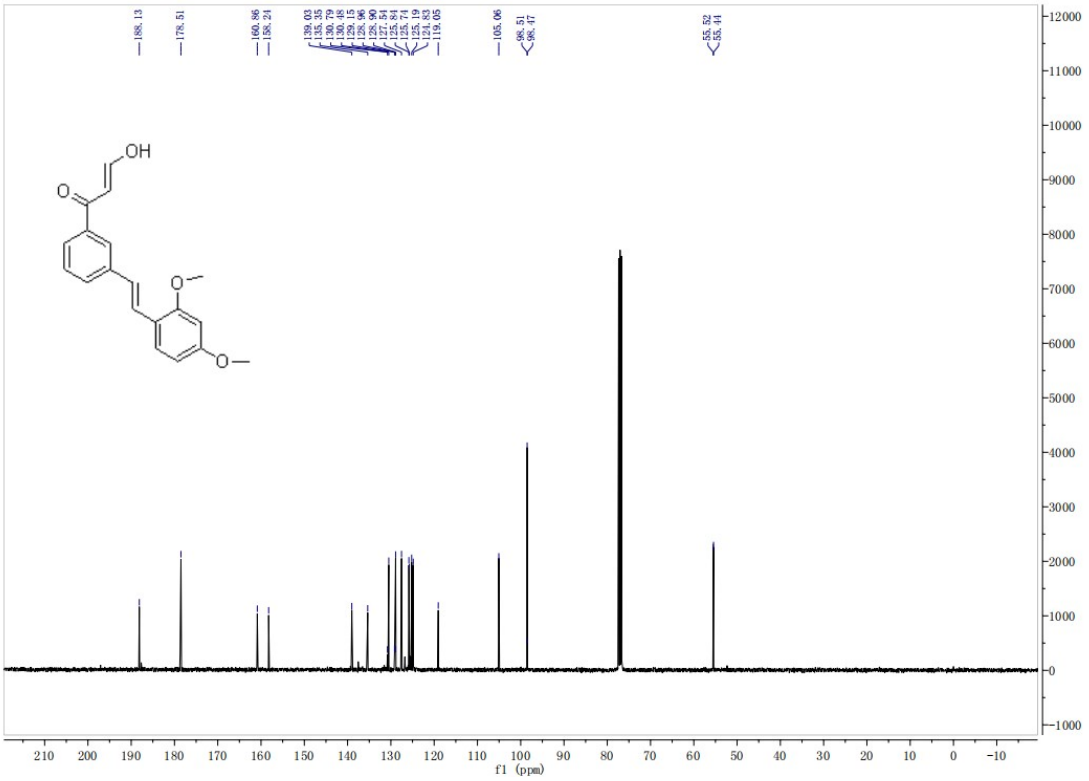

Figure S85.[13]C-NMR (100 MHz, Chloroform-d) of **5m**

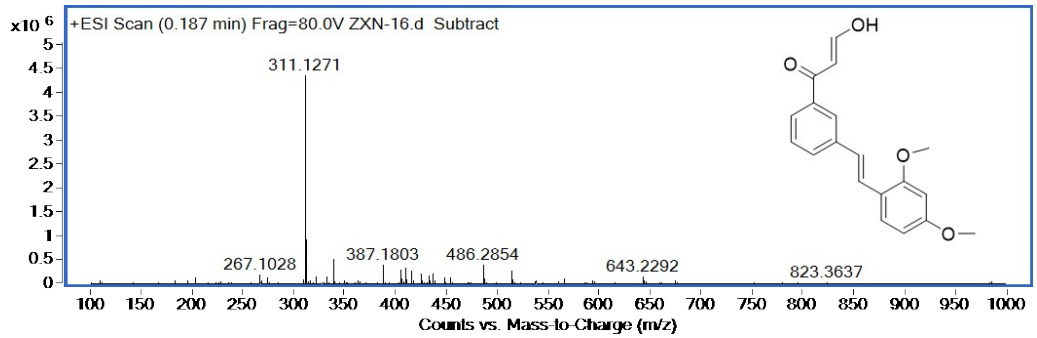

Figure S86. HRMS of **5m**

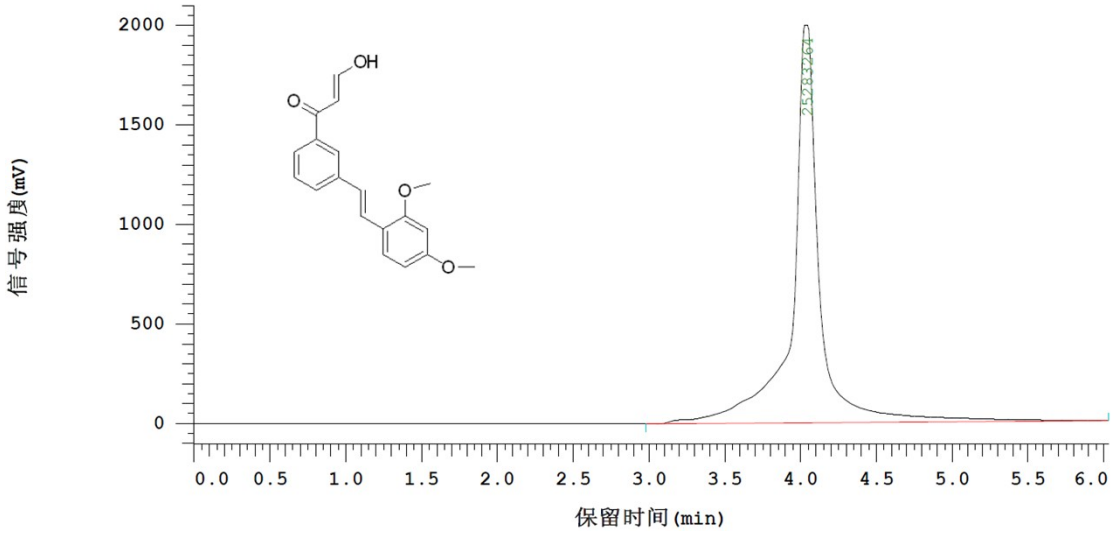

Figure S87. HPLC of **5m**

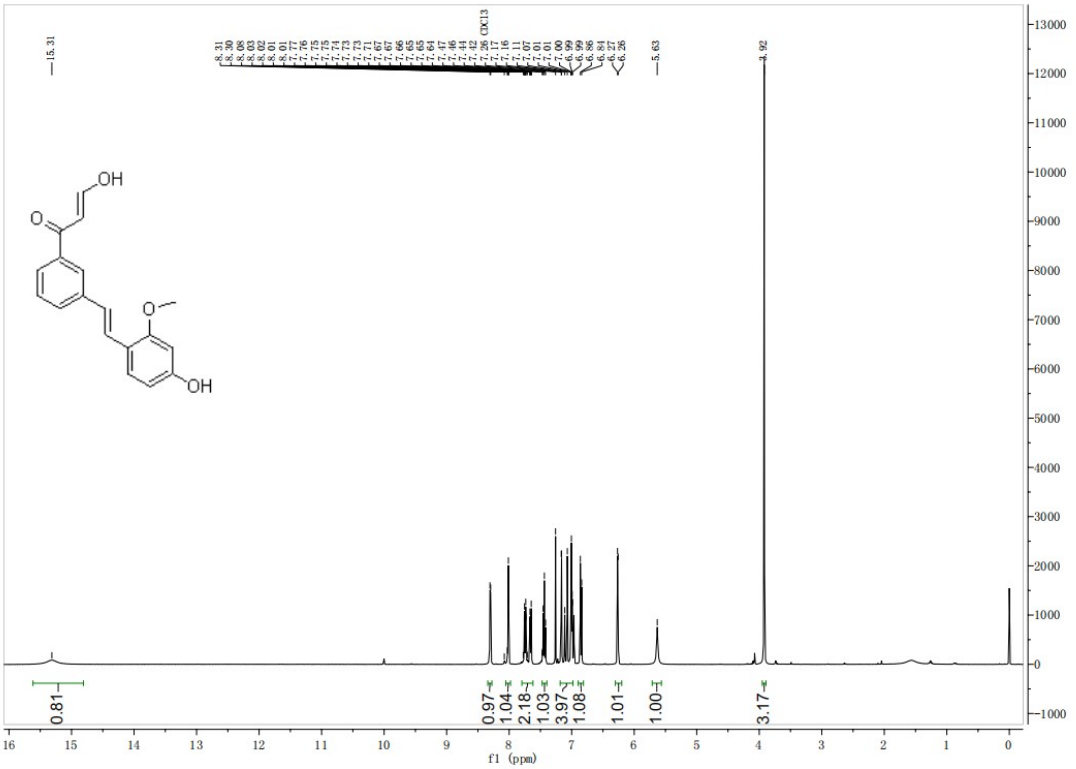

Figure S88.[1]H-NMR (400 MHz, Chloroform-d) of **5n**

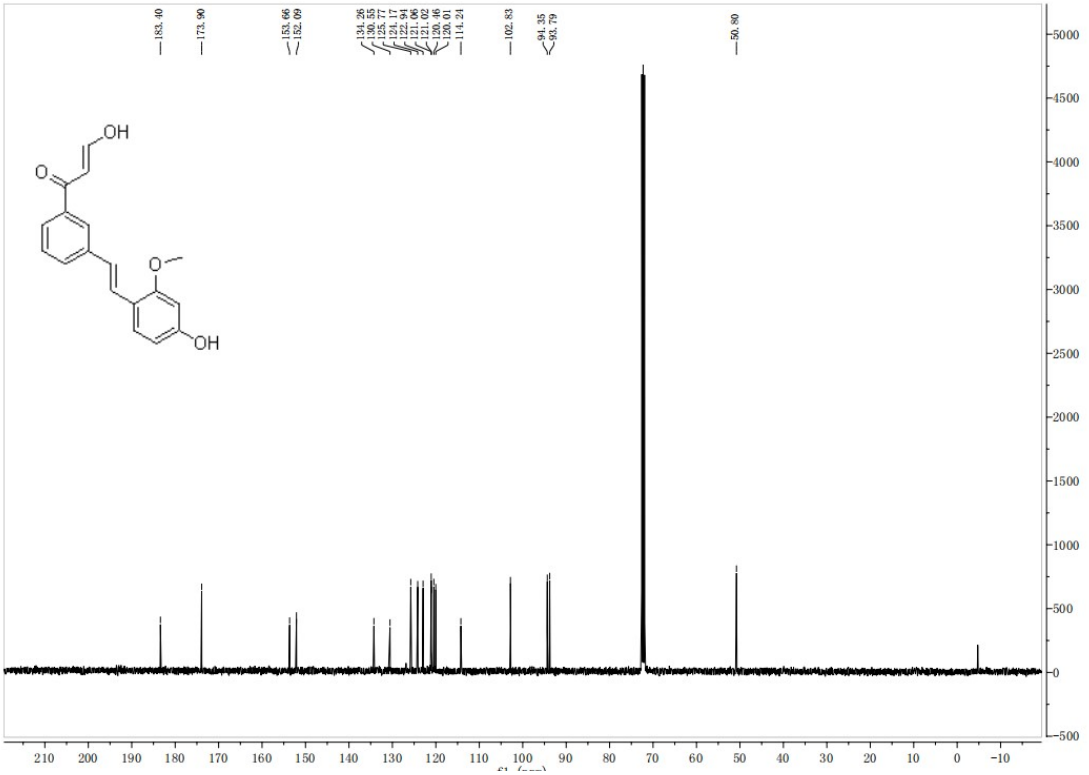

Figure S89.[13]C-NMR (100 MHz, Chloroform-d) of **5n**

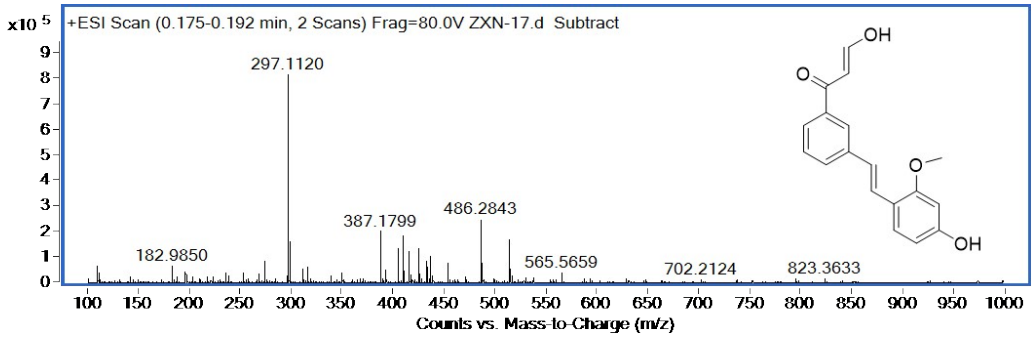

Figure S90. HRMS of **5n**

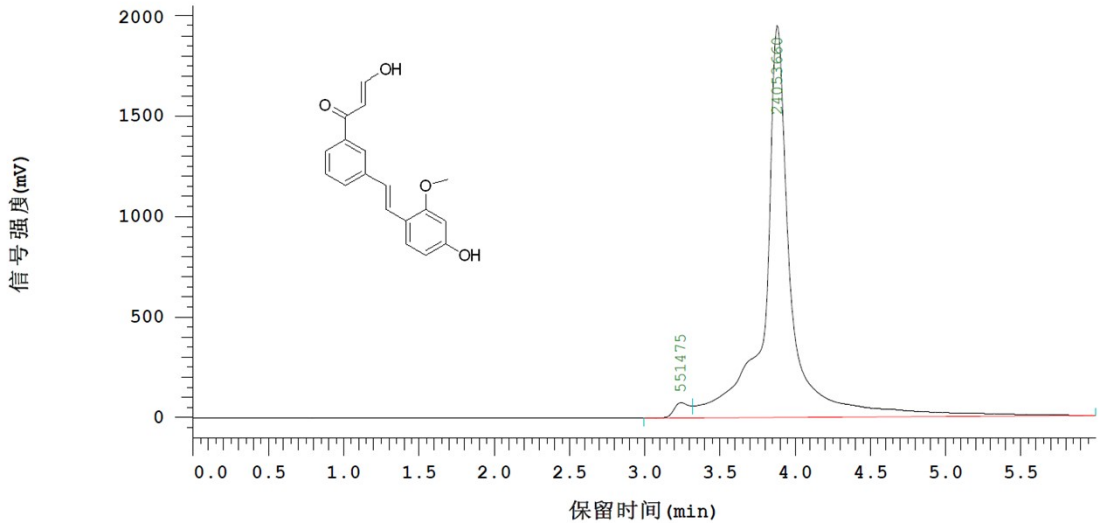

Figure S91. HPLC of **5n**

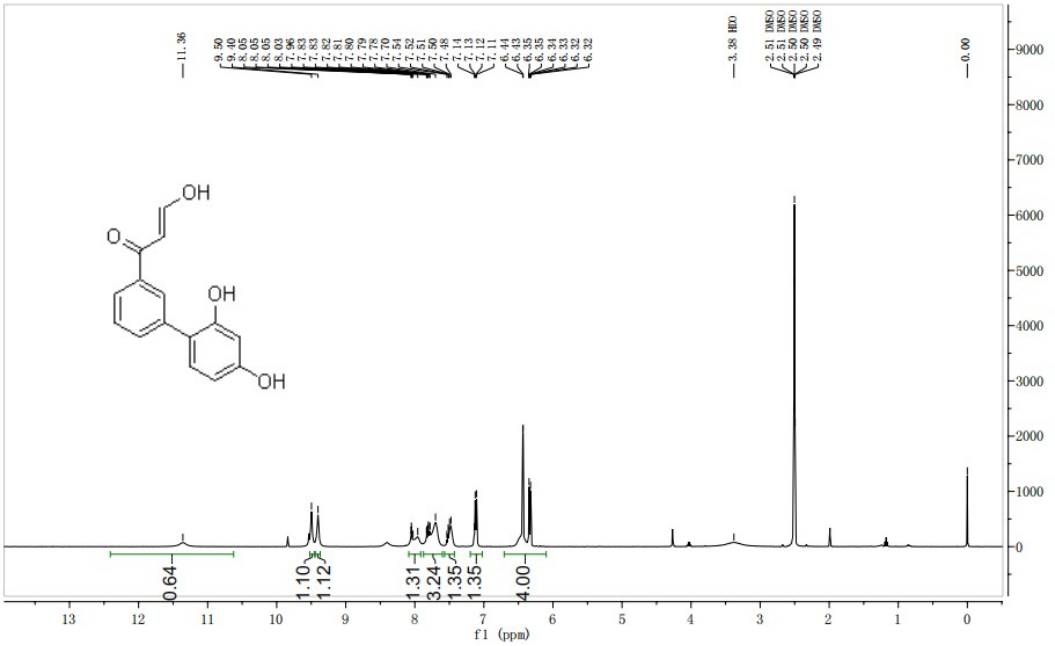

Figure S92.[1]H-NMR (400 MHz, DMSO-*d6*) of **5o**

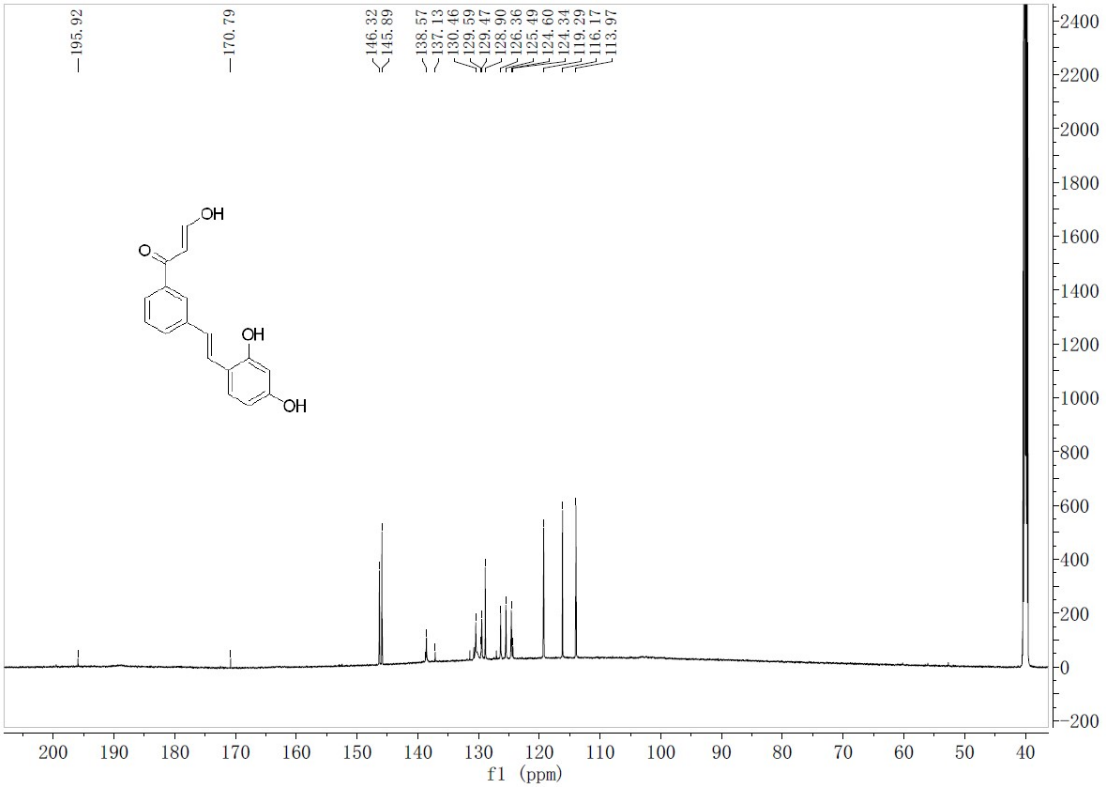

Figure S93.^{13}C-NMR (100 MHz, DMSO-*d6*) of **5o**

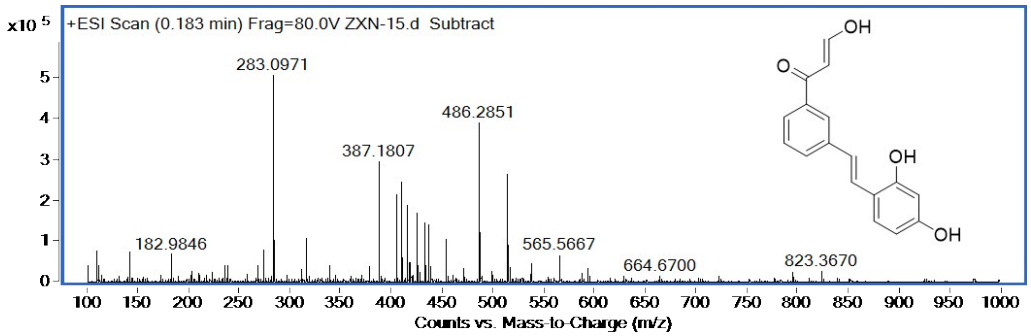

Figure S94. HRMS of **5o**

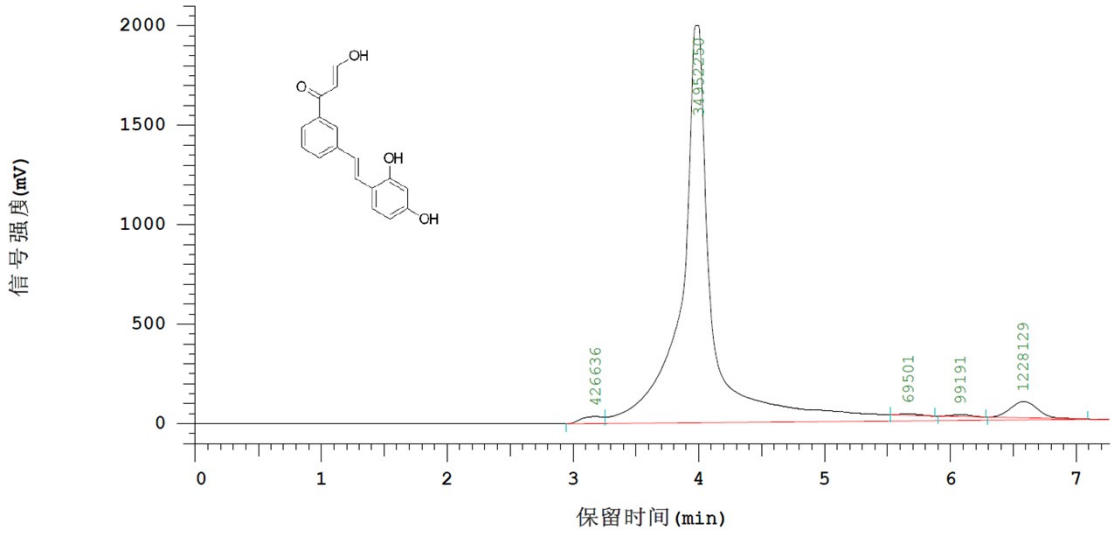

Figure S95. HPLC of **5o**

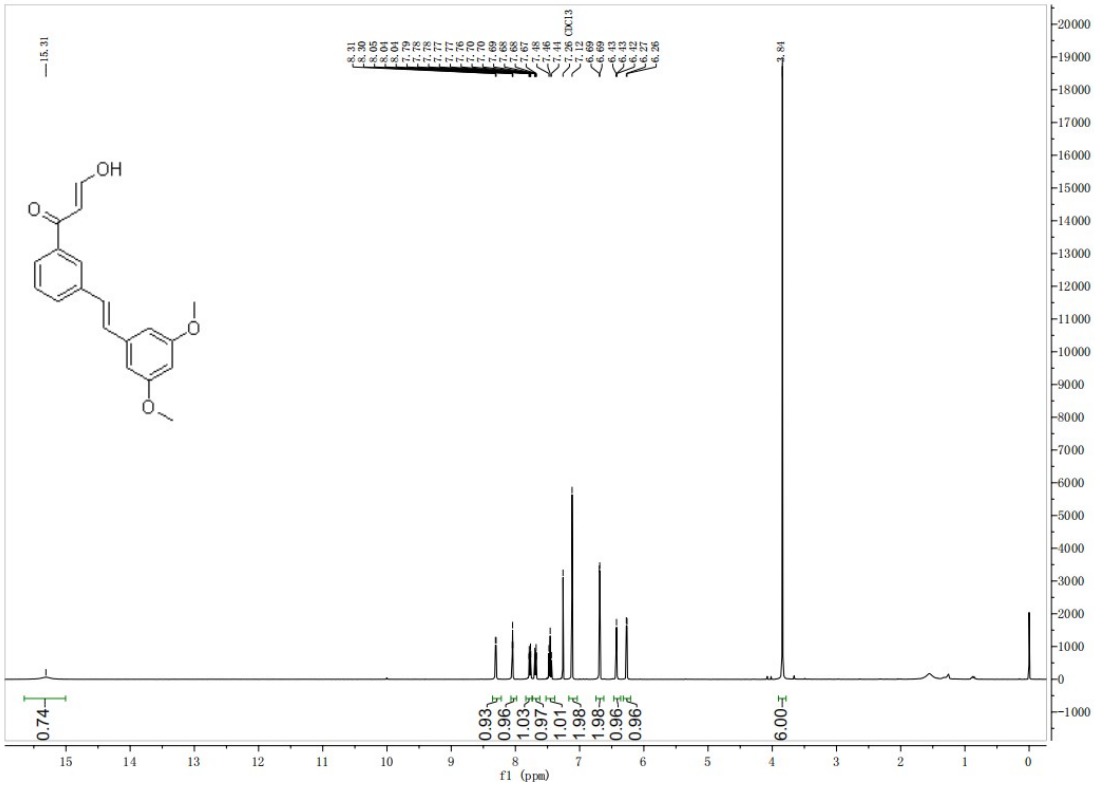

Figure S96.[1]H-NMR (400 MHz, Chloroform-d) of **5p**

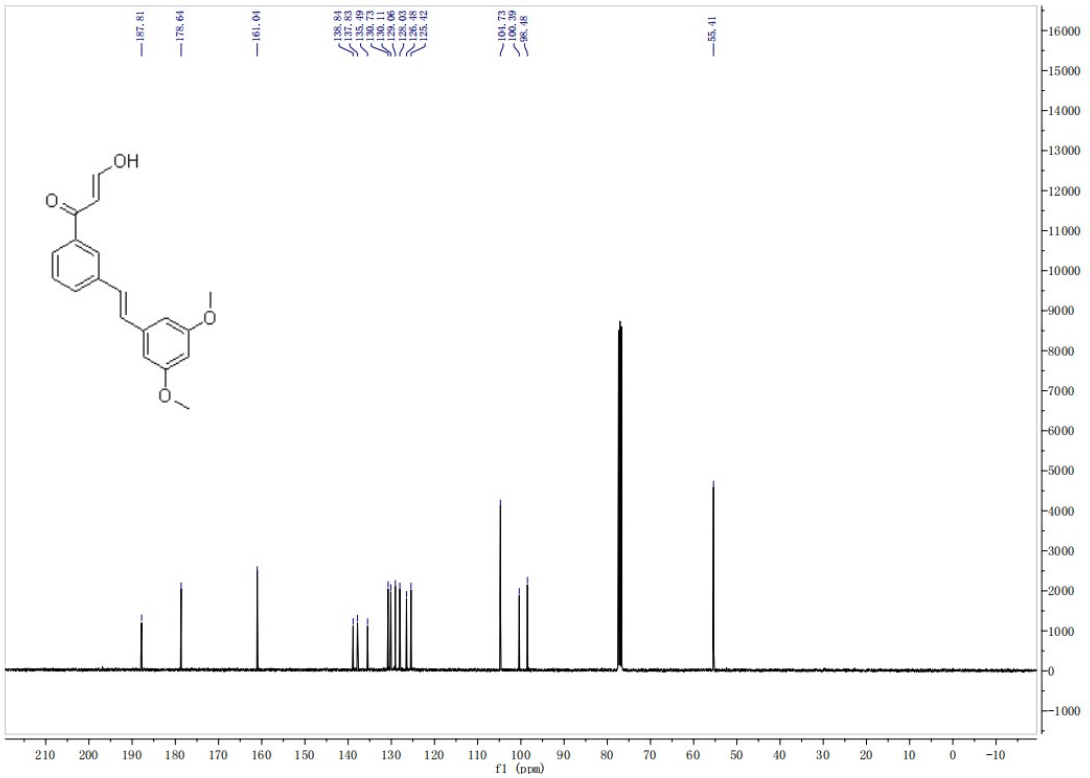

Figure S97.[13]C-NMR (100 MHz, Chloroform-d) of **5p**

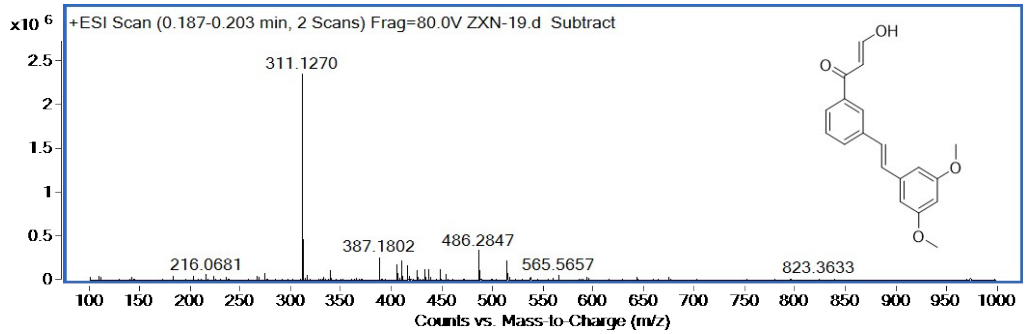

Figure S98. HRMS of **5p**

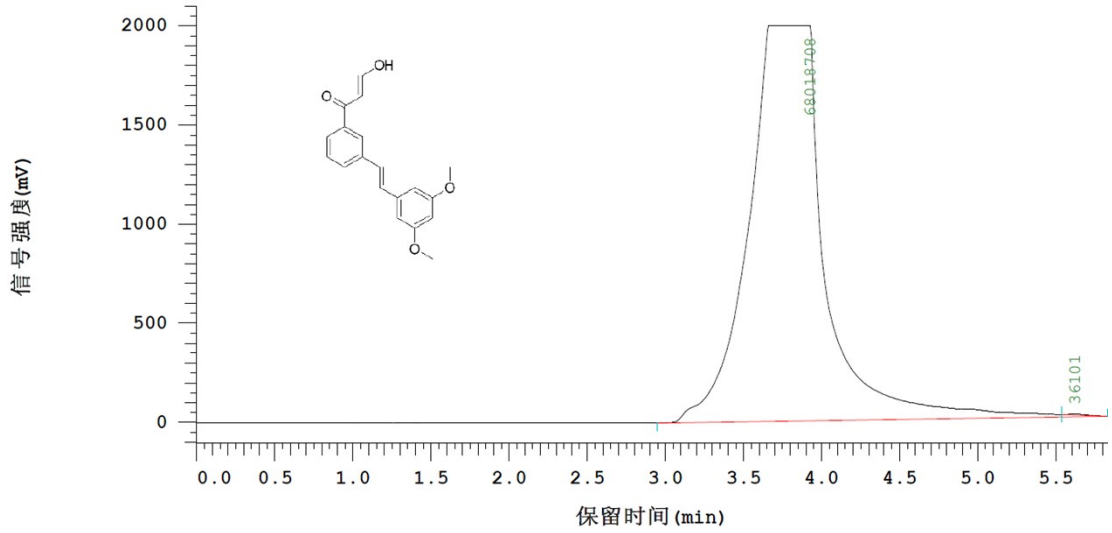

Figure S99. HPLC of **5p**

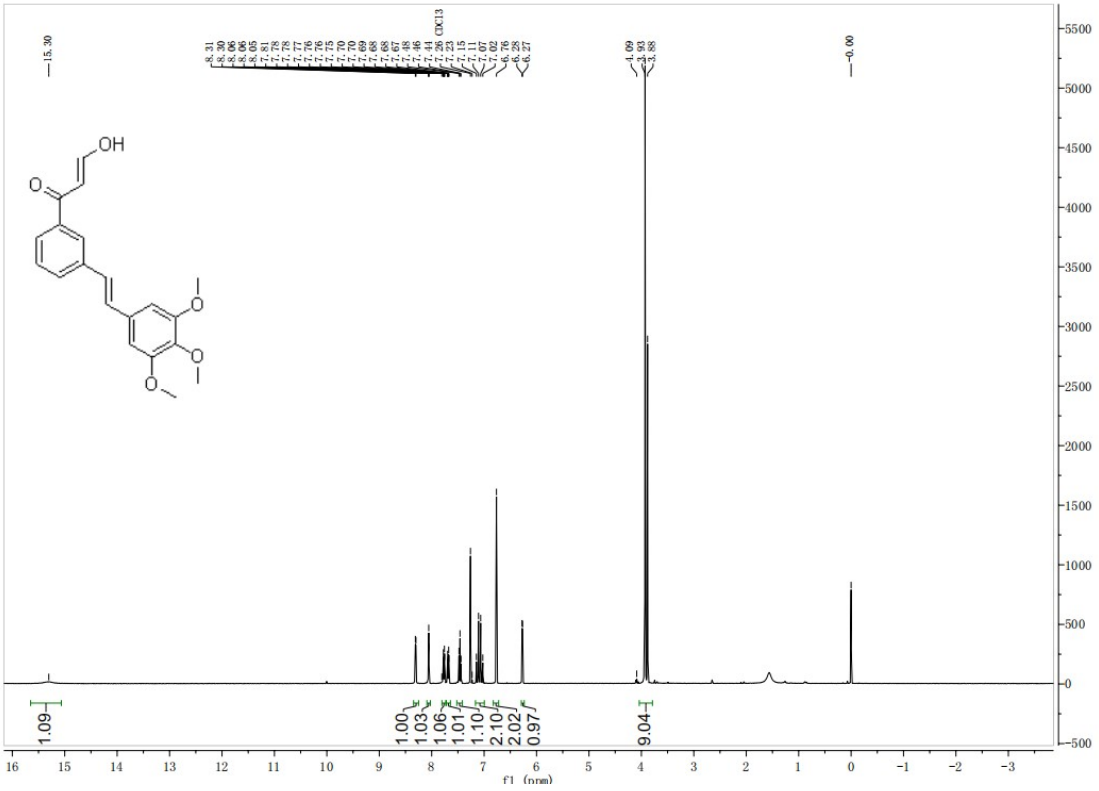

Figure S100.[1]H-NMR (400 MHz, Chloroform-d) of **5q**

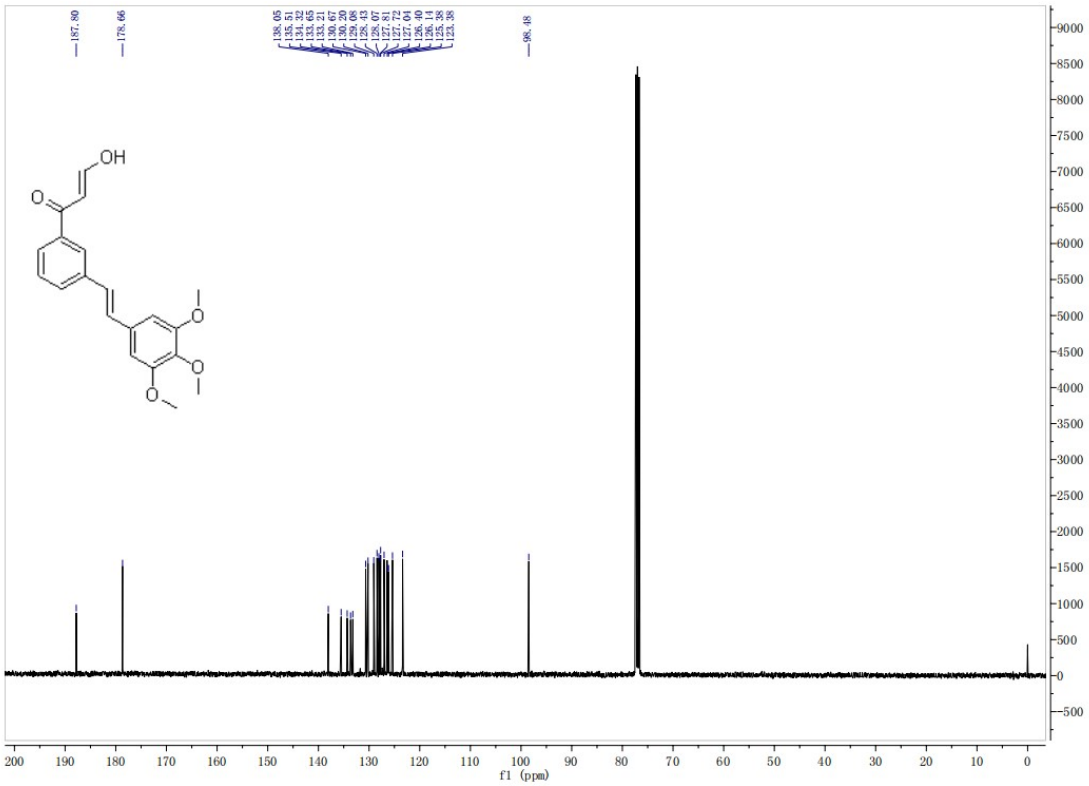

Figure S101.[13]C-NMR (100 MHz, Chloroform-d) of **5q**

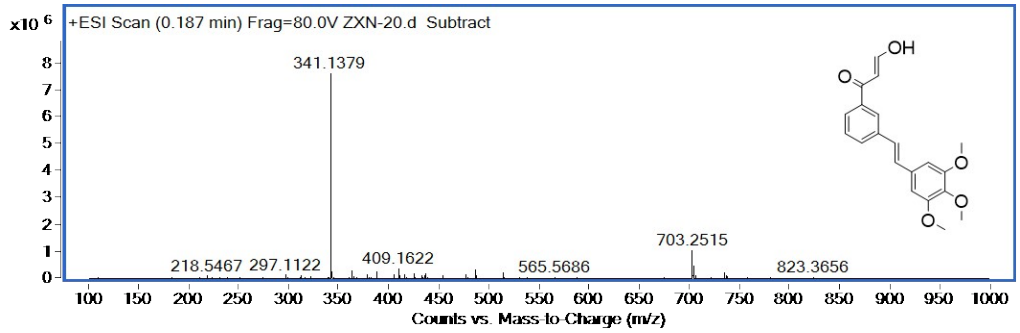

Figure S102. HRMS of **5q**

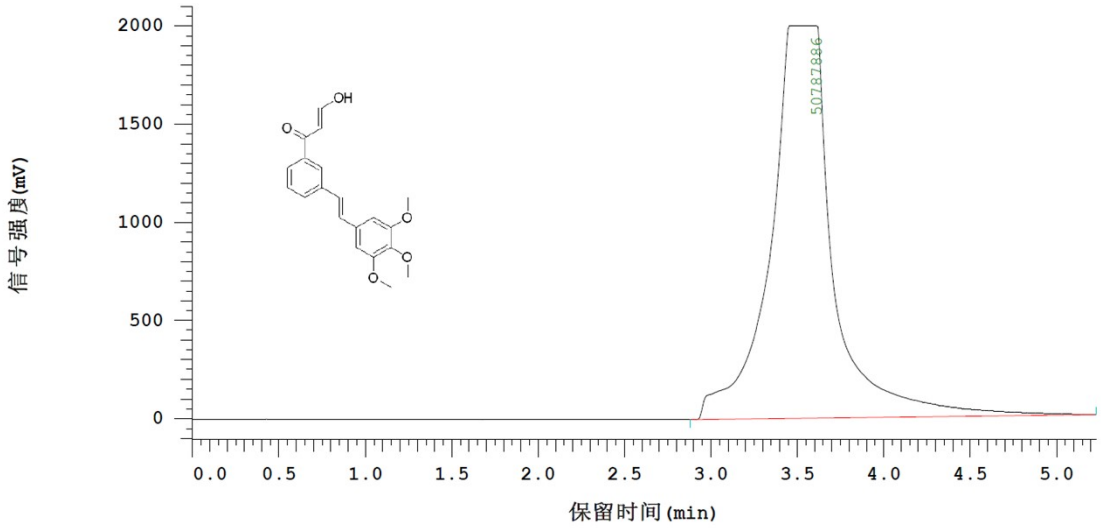

Figure S103. HPLC of **5q**

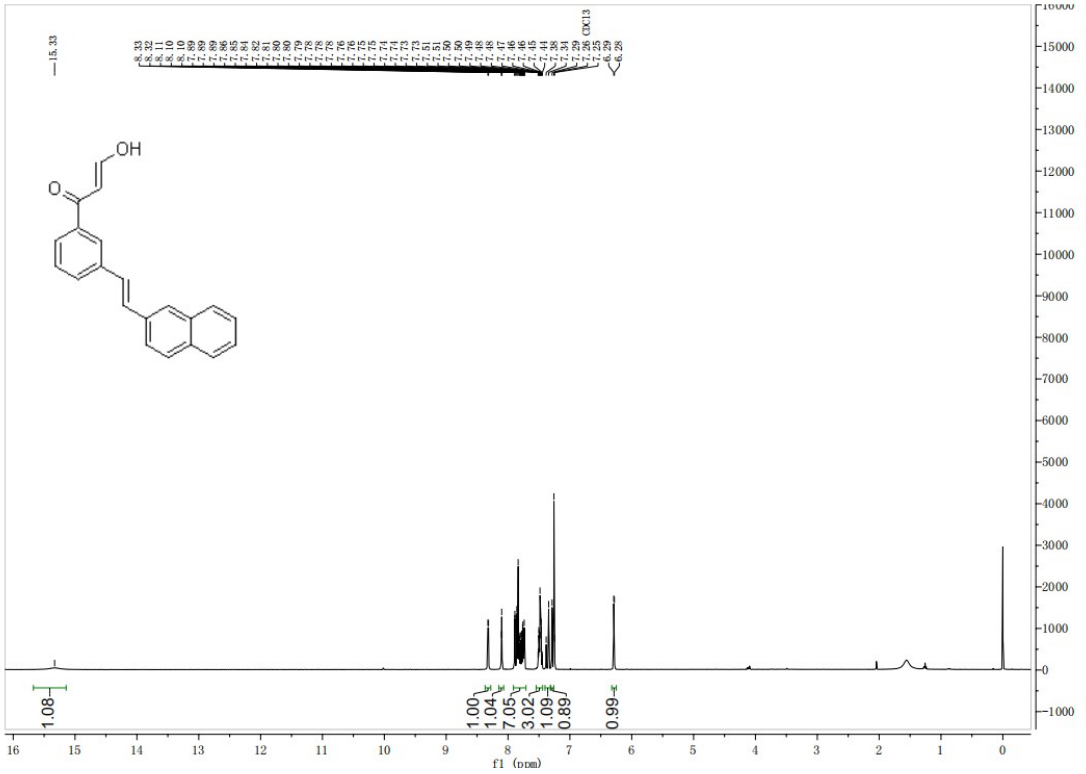

Figure S104.[1]H-NMR (400 MHz, Chloroform-d) of **5r**

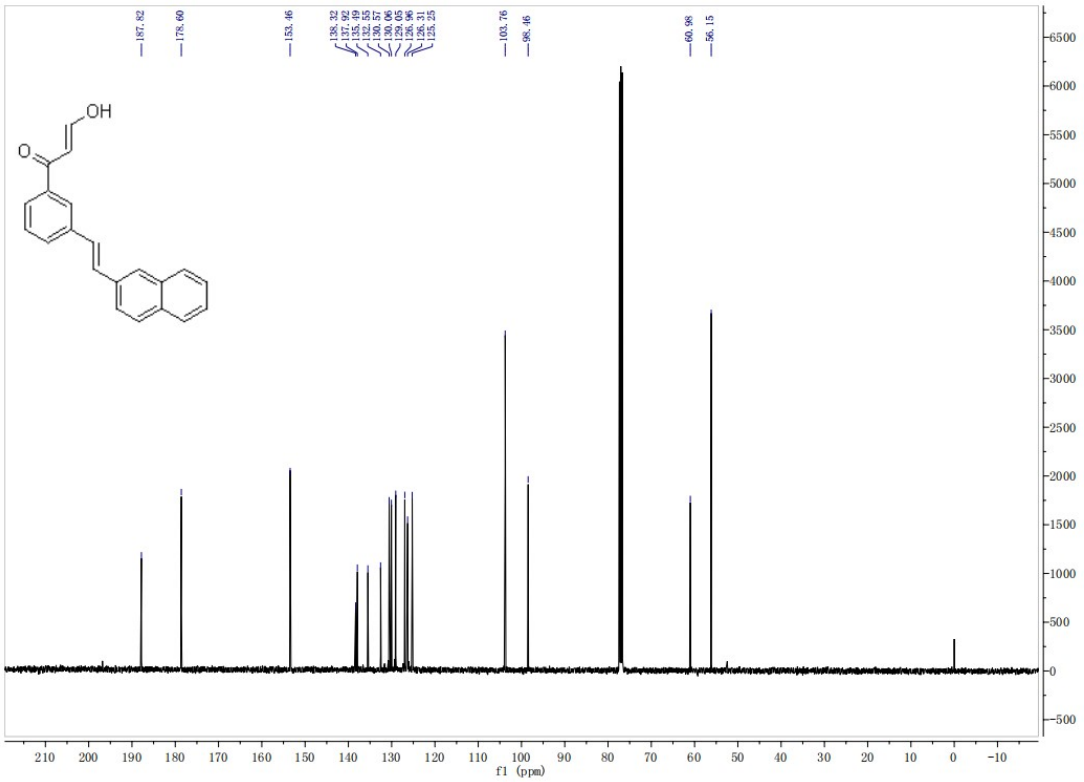

Figure S105.^{13}C-NMR (100 MHz, Chloroform-d) of **5r**

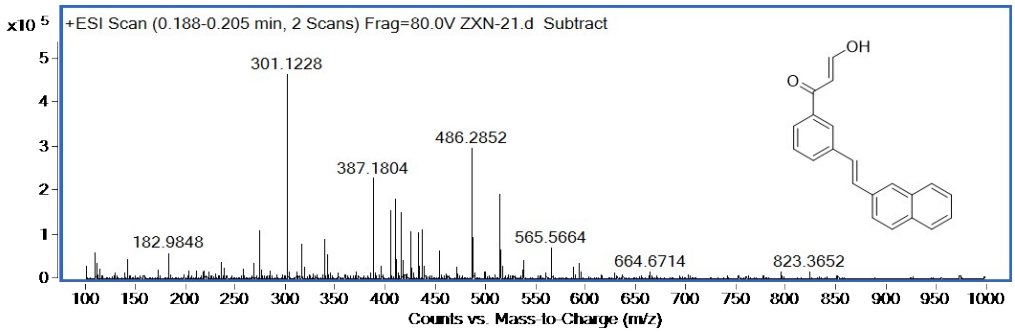

Figure S106. HRMS of **5r**

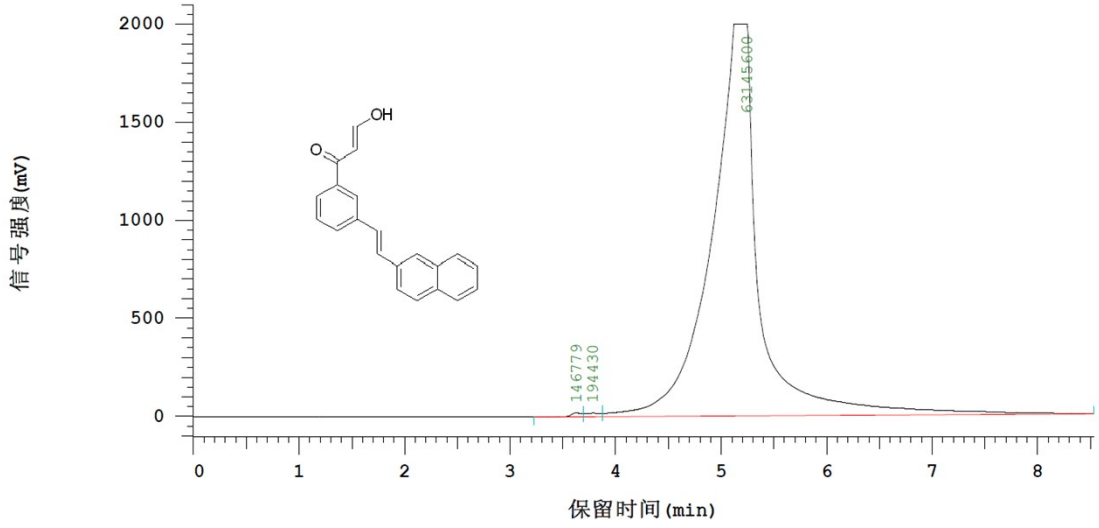

Figure S107. HPLC of **5r**

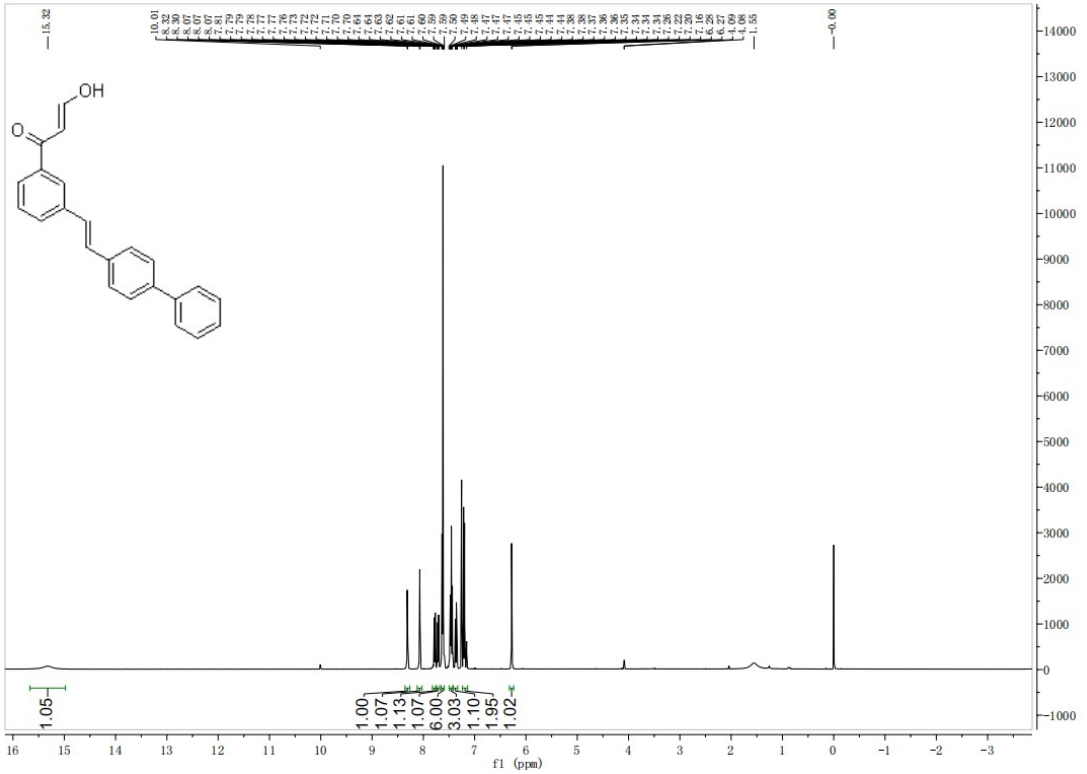

Figure S108.[1]H-NMR (400 MHz, Chloroform-d) of **5s**

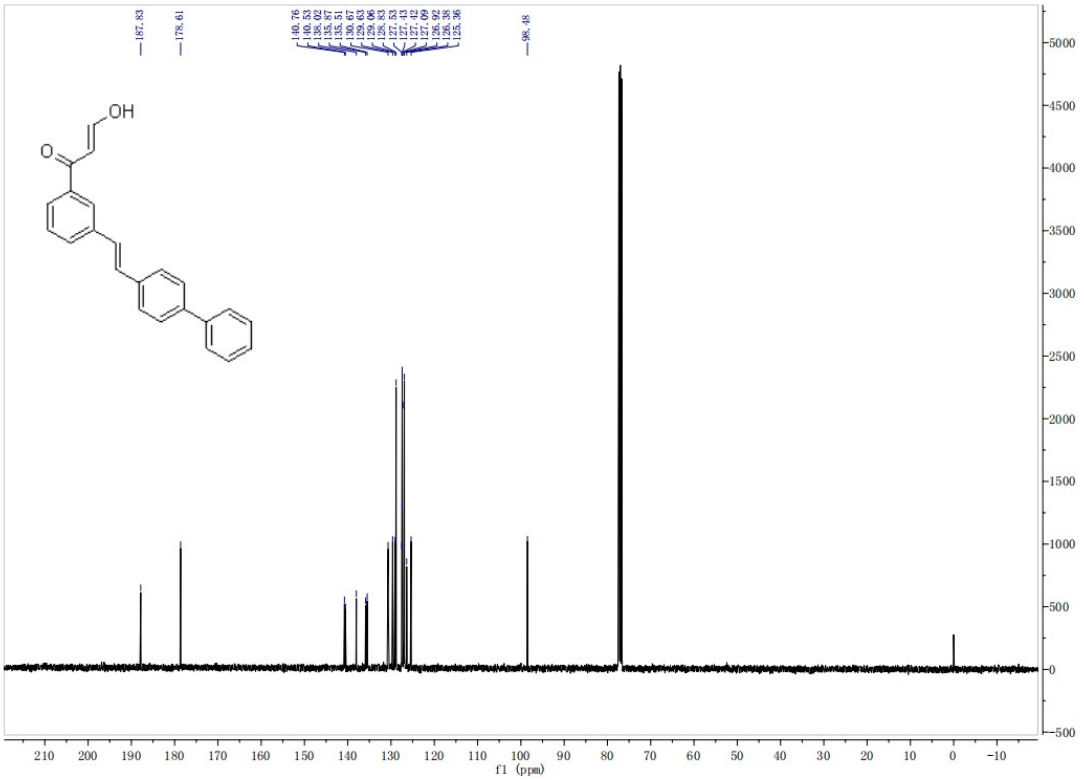

Figure S109.[13]C-NMR (100 MHz, Chloroform-d) of **5s**

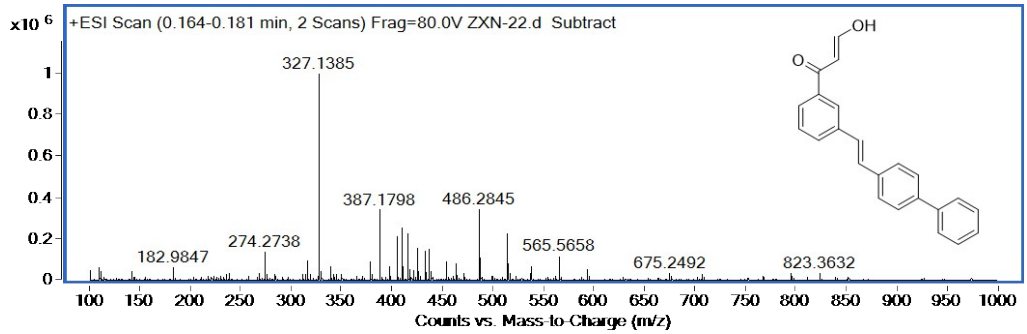

Figure S110. HRMS of **5s**

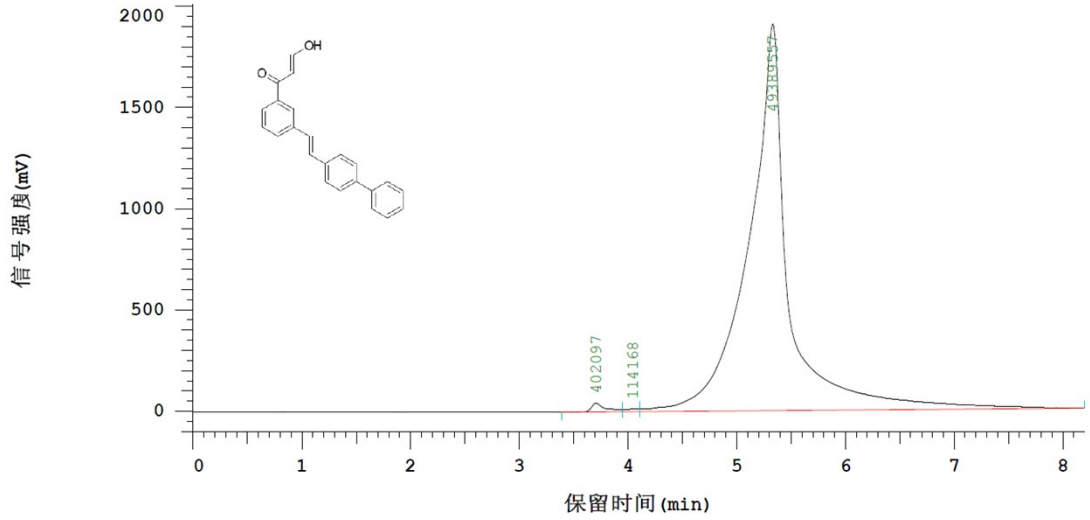

Figure S111. HPLC of **5s**

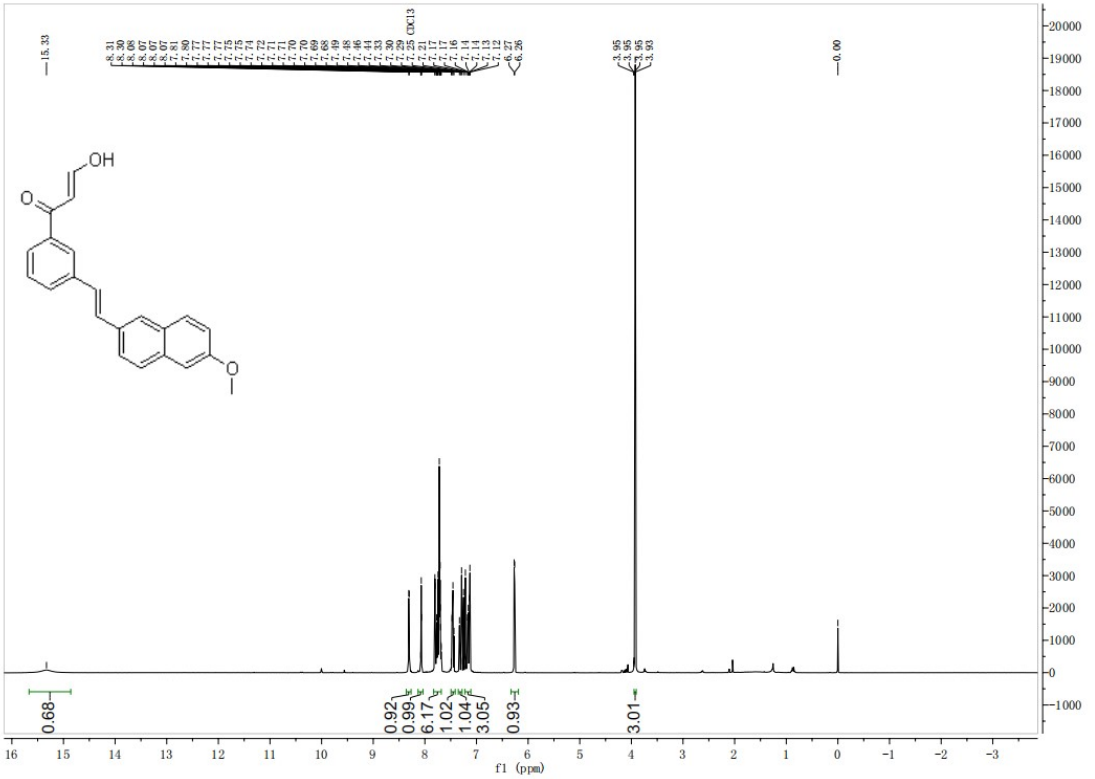

Figure S112.[1]H-NMR (400 MHz, Chloroform-d) of **5t**

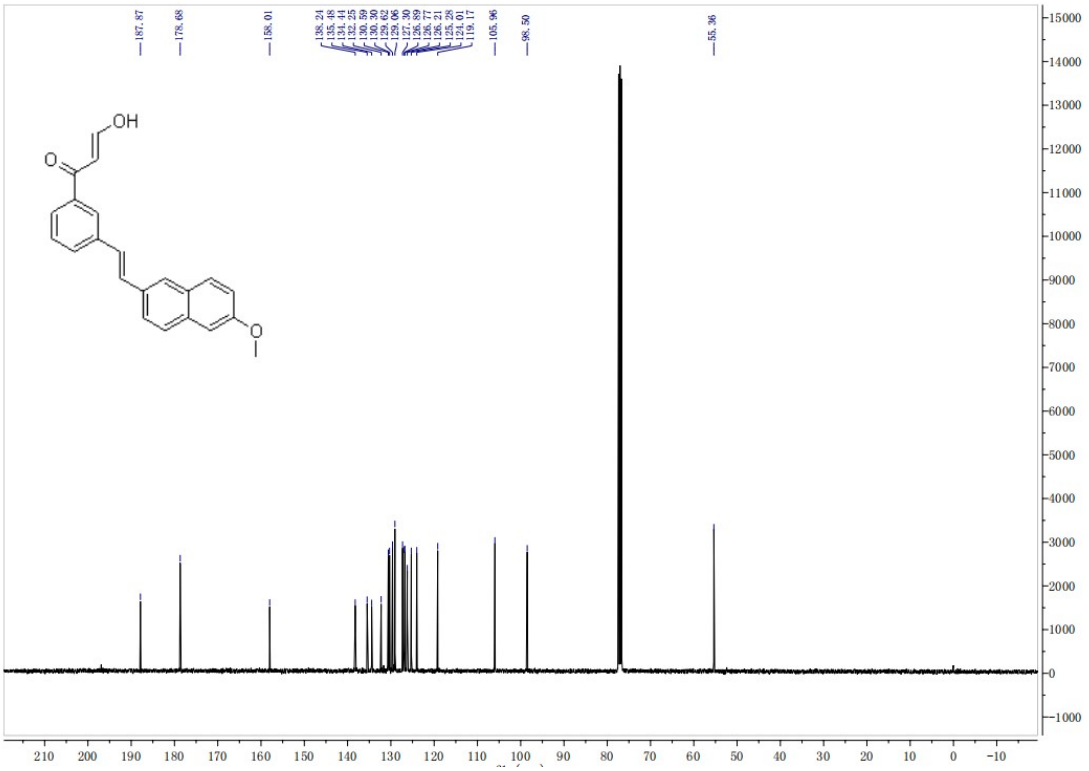

Figure S113.[13]C-NMR (100 MHz, Chloroform-d) of **5t**

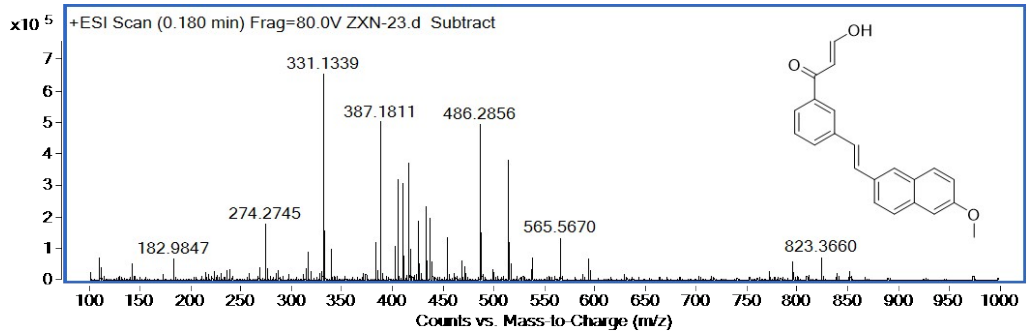

Figure S114. HRMS of **5t**

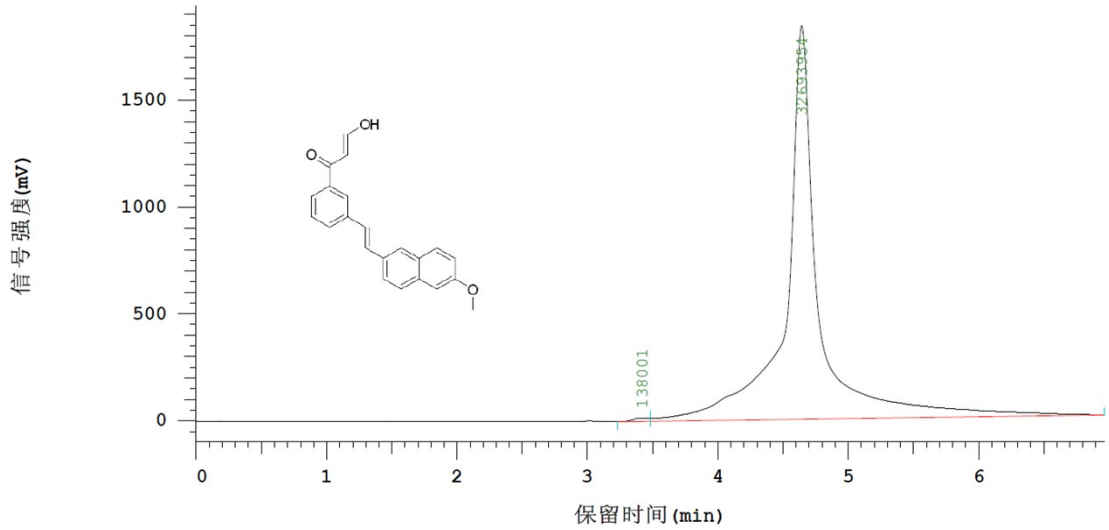

Figure S115. HPLC of **5t**

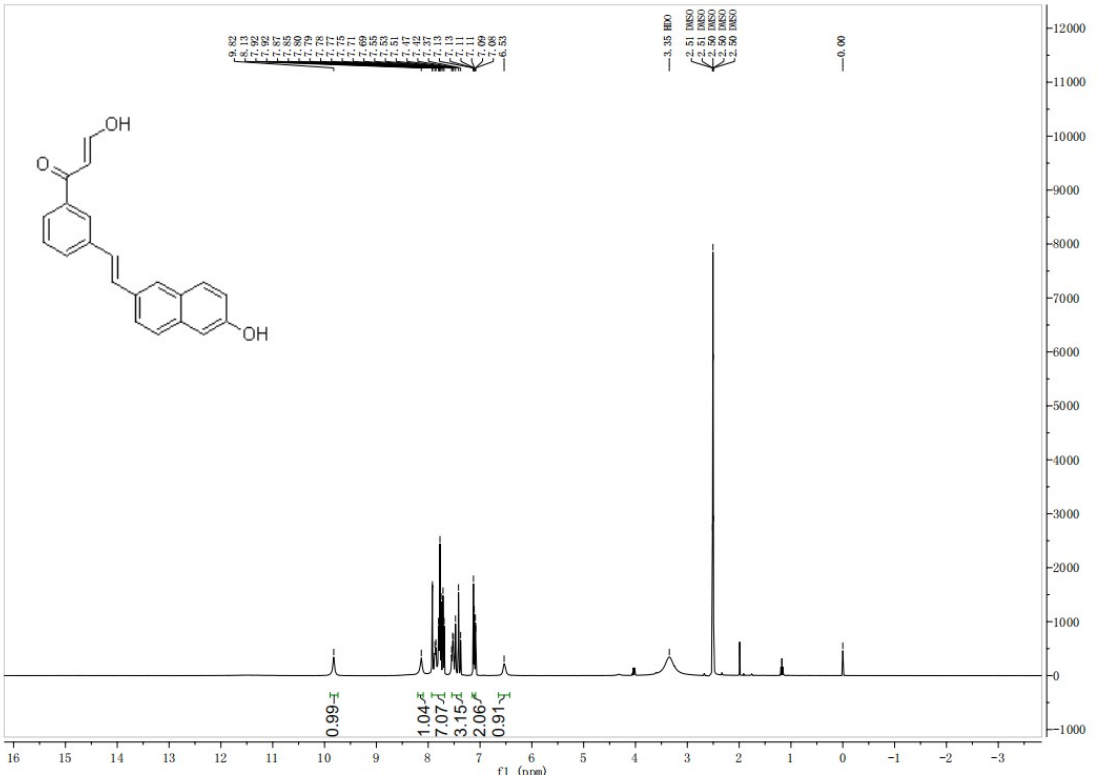

Figure S116.[1]H-NMR (400 MHz, DMSO-*d6*) of **5u**

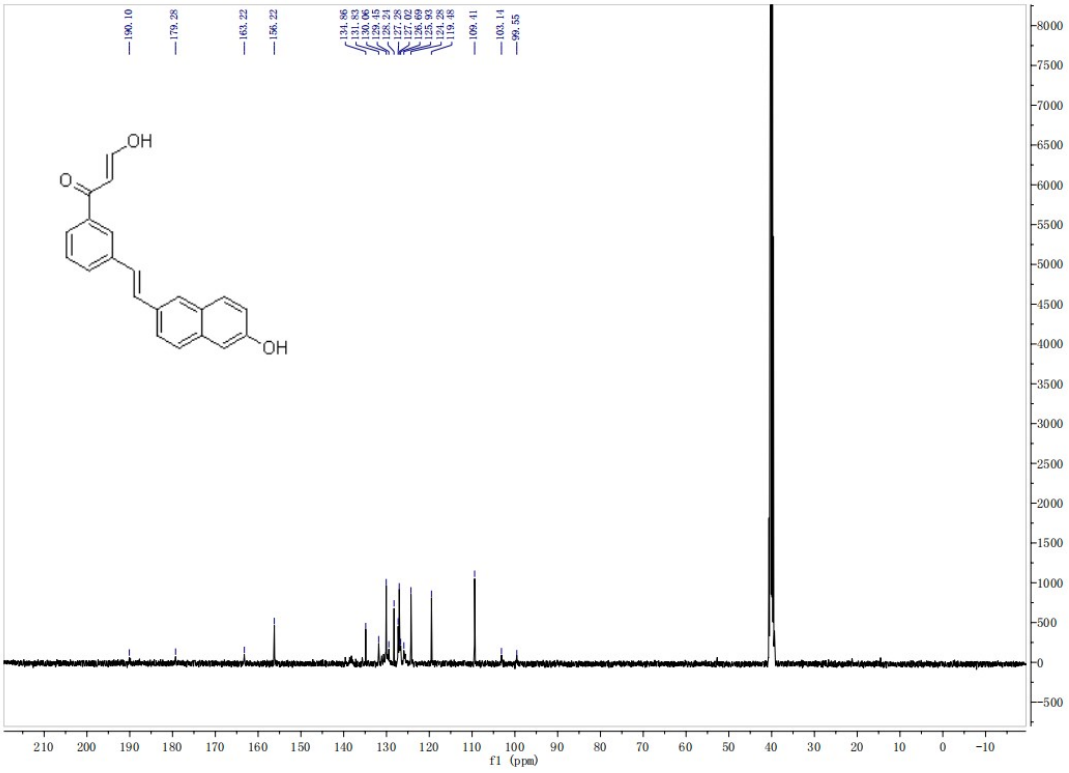

Figure S117.[13]C-NMR (100 MHz, DMSO-*d6*) of **5u**

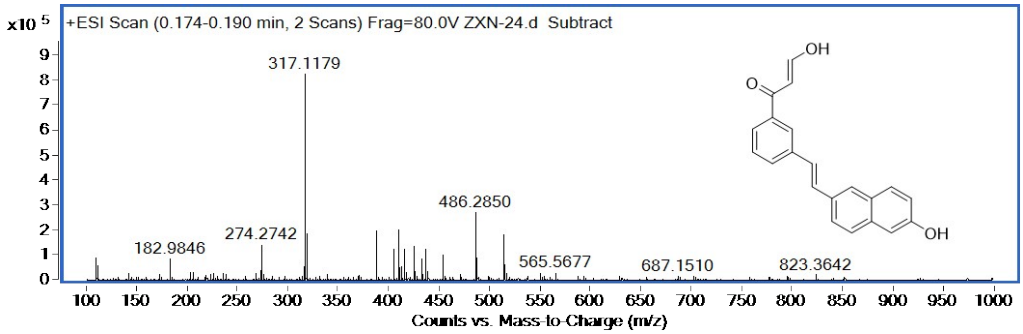

Figure S118. HRMS of **5u**

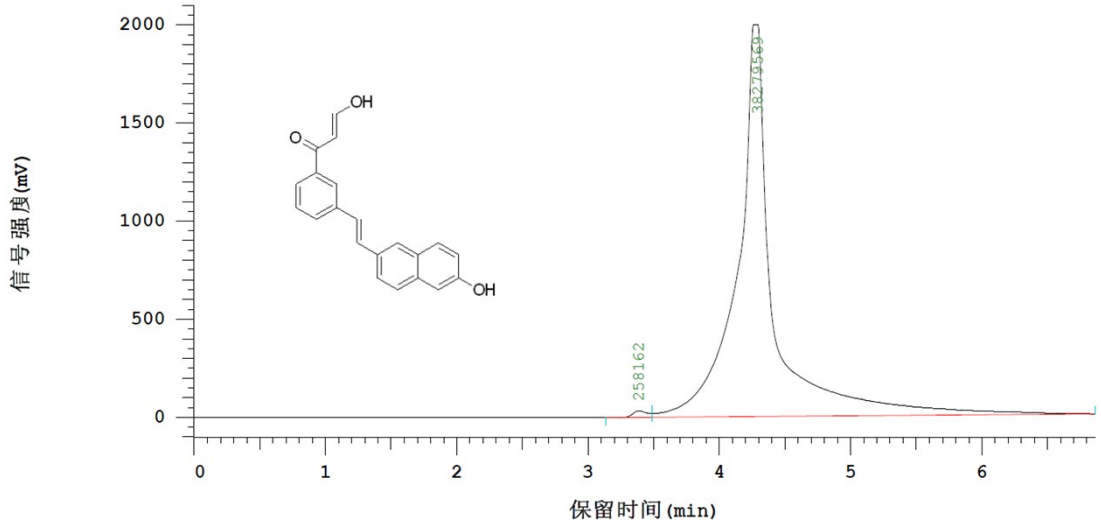

Figure S119. HPLC of **5u**

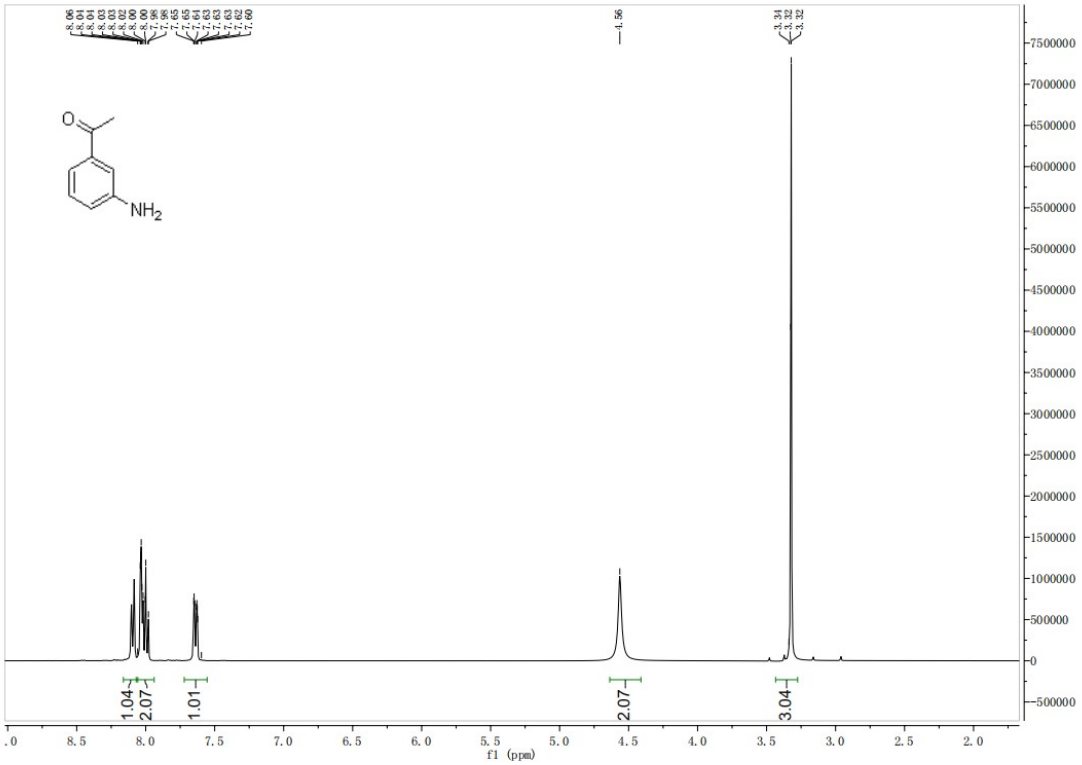

Figure S120.[1]H-NMR (400 MHz, DMSO-*d6*) of **6**

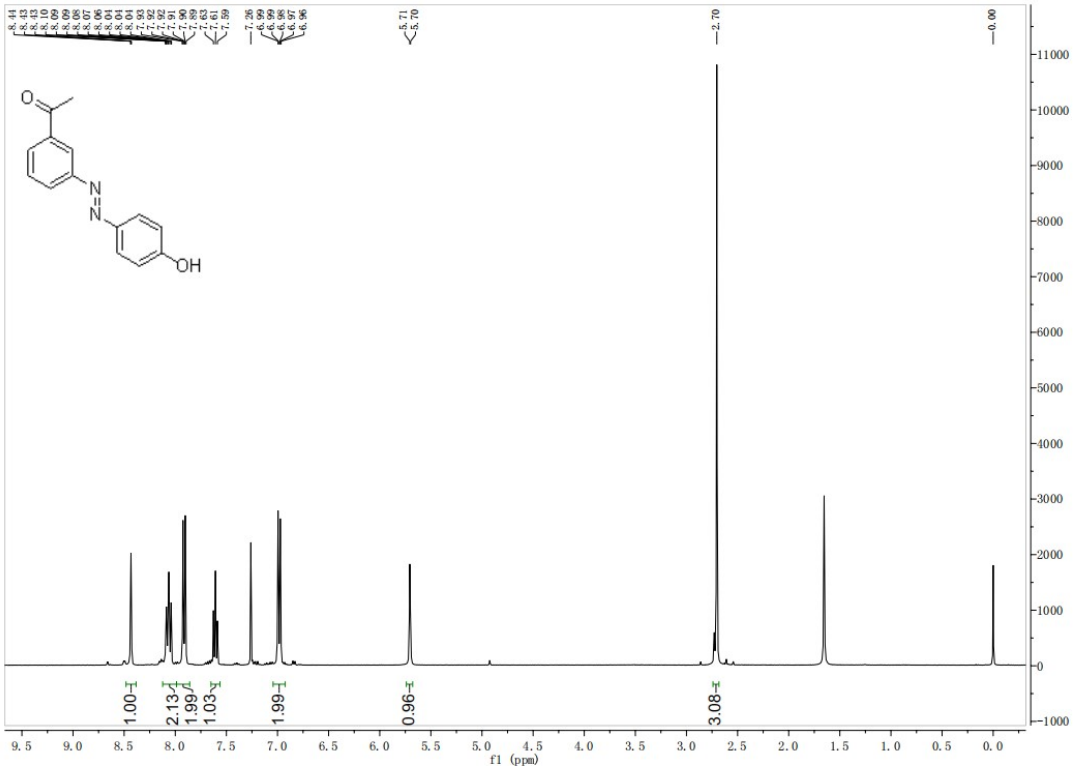

Figure S121.[1]H-NMR (400 MHz, Chloroform-d) of **7a**

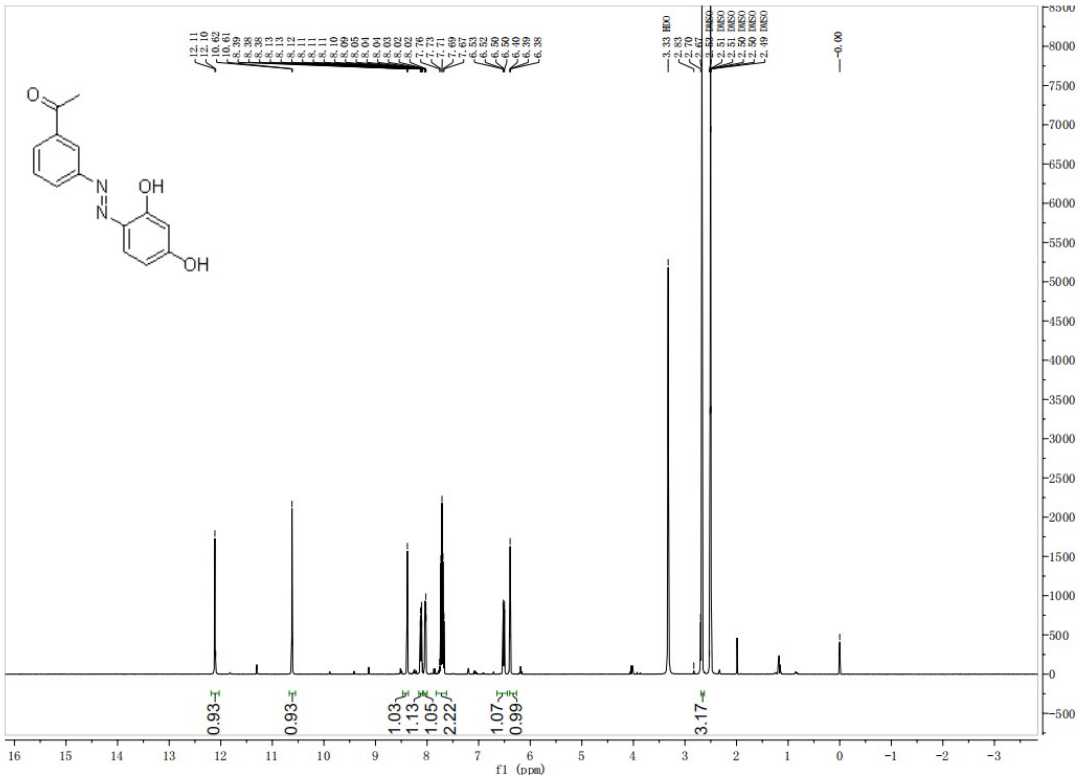

Figure S122.[1]H-NMR (400 MHz, DMSO-*d6*) of **7b**

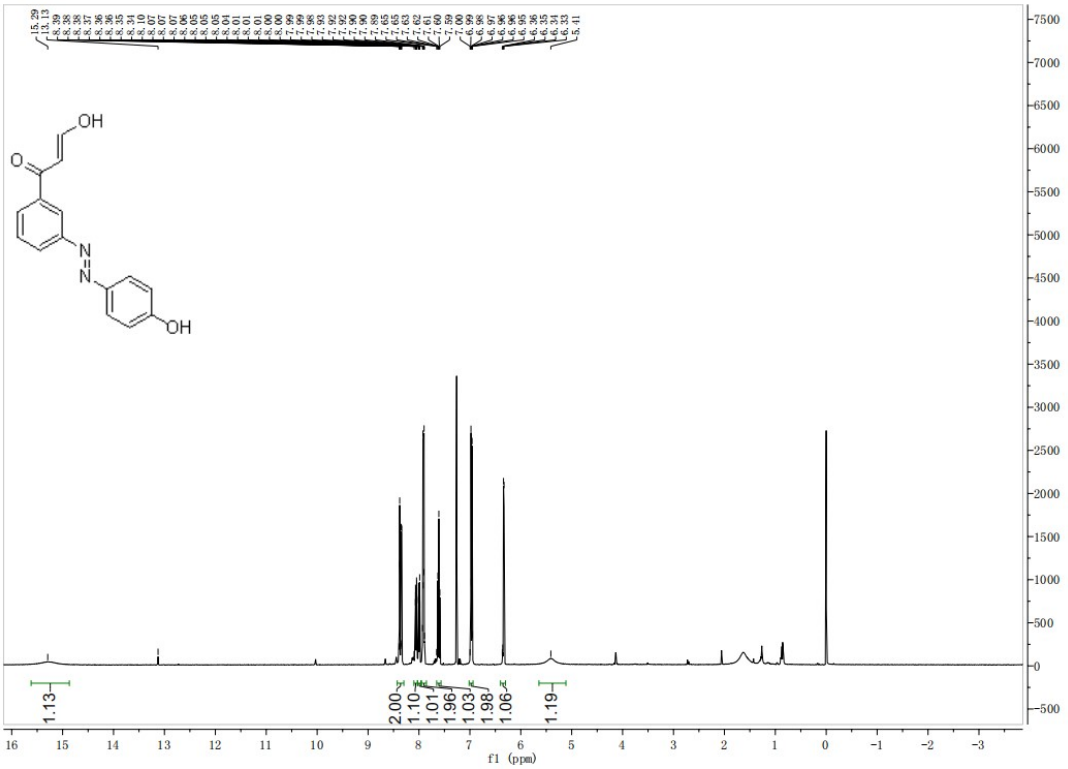

Figure S123.[1]H-NMR (400 MHz, Chloroform-d) of **8a**

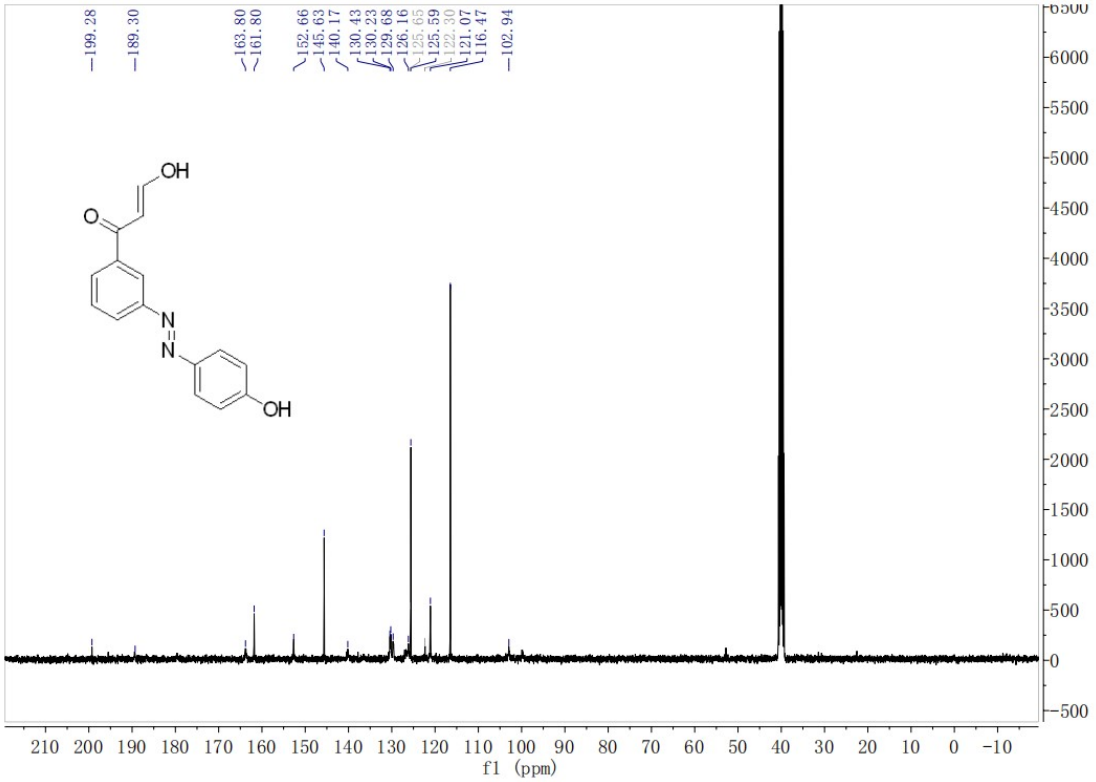

Figure S124.[13]C-NMR (100 MHz, Chloroform-d) of **8a**

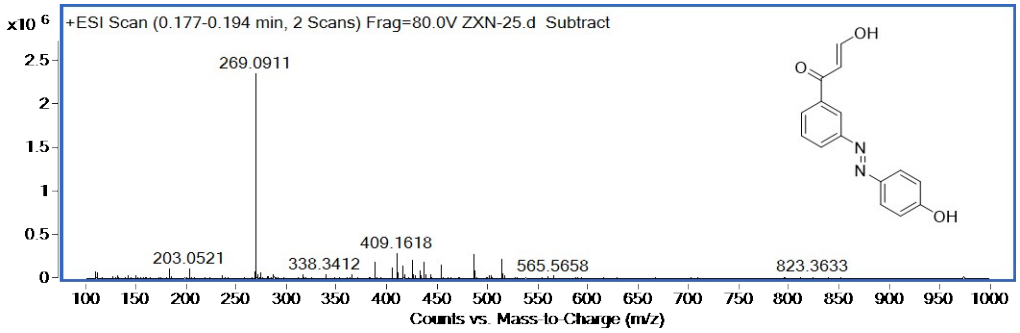

Figure S125. HRMS of **8a**

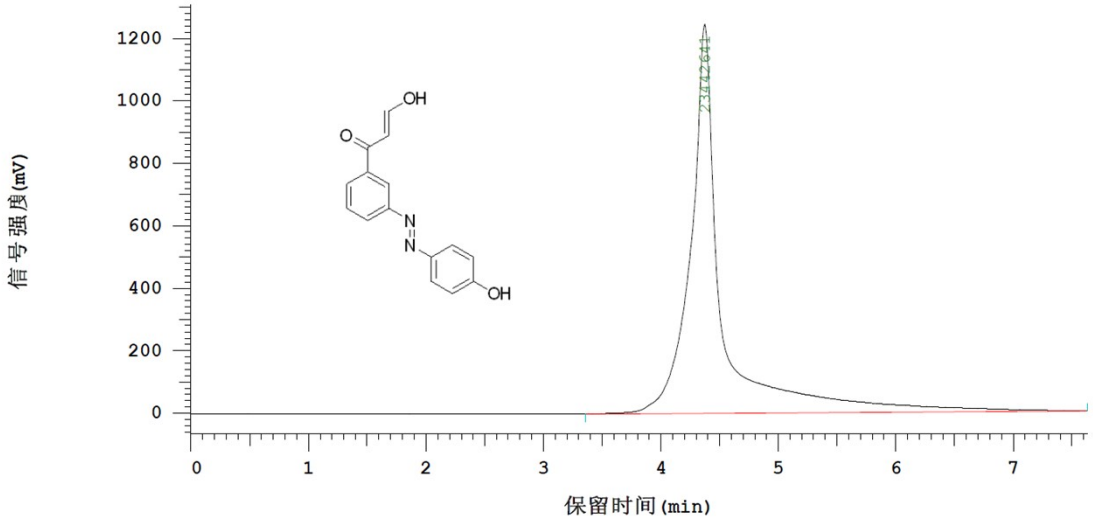

Figure S126. HPLC of **8a**

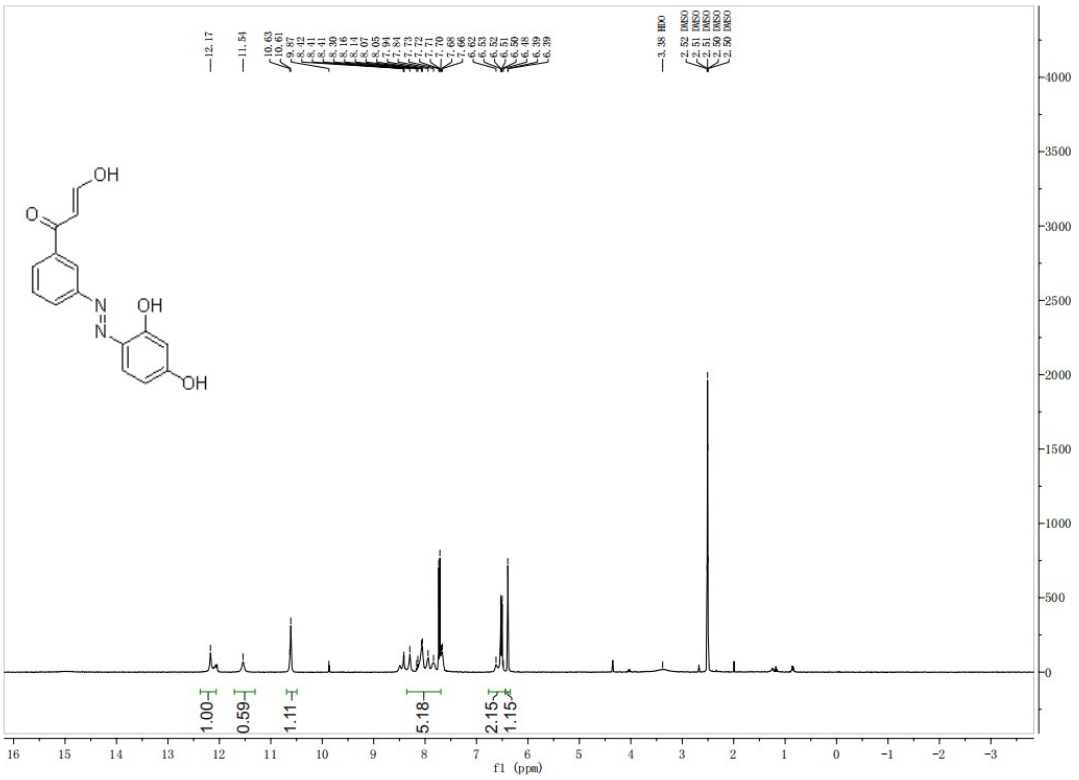

Figure S127.[1]H-NMR (400 MHz, DMSO-*d6*) of **8b**

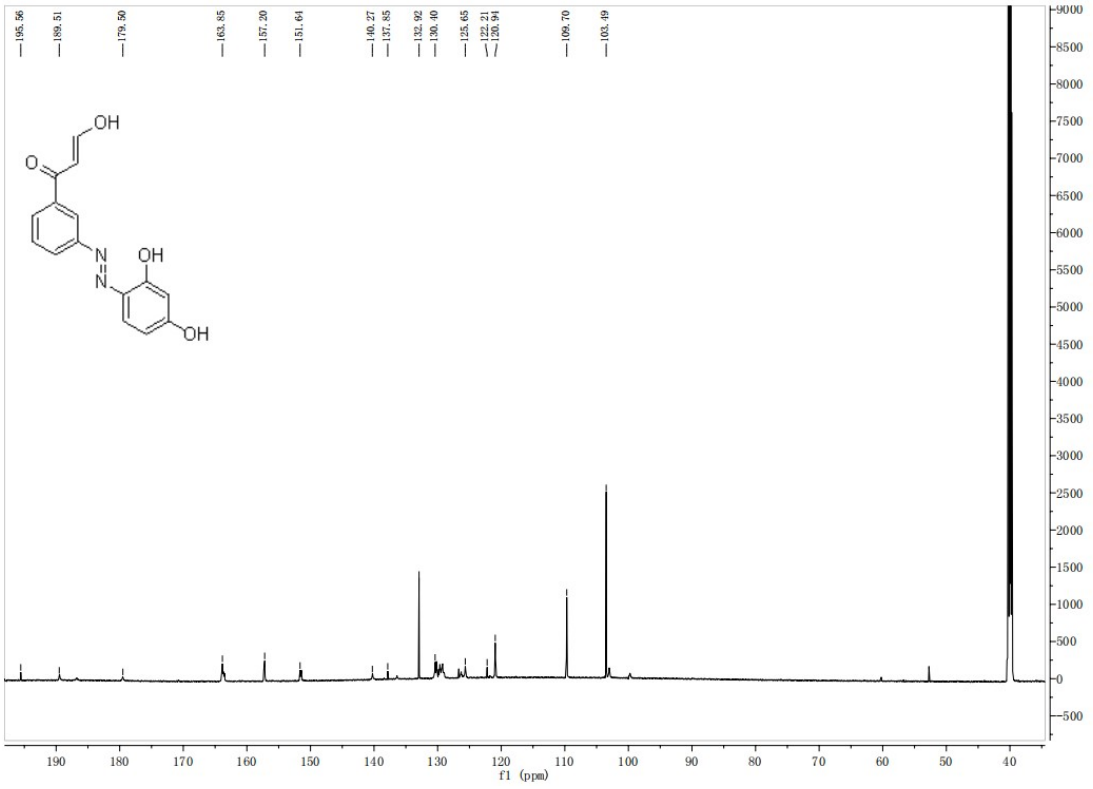

Figure S128.[13]C-NMR (100 MHz, DMSO-*d6*) of **8b**

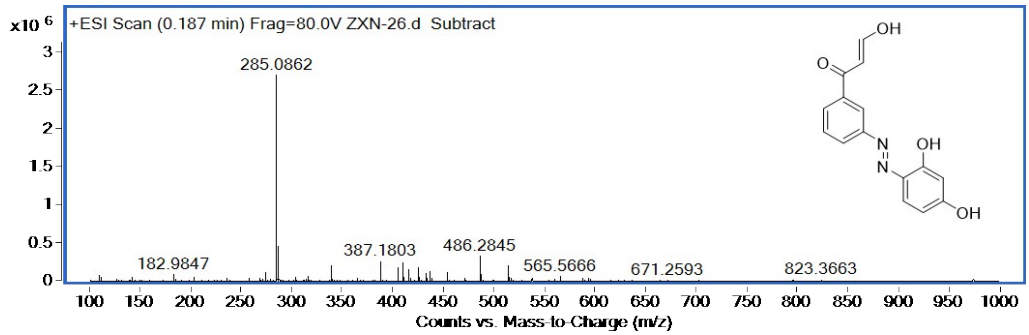

Figure S129. HRMS of **8b**

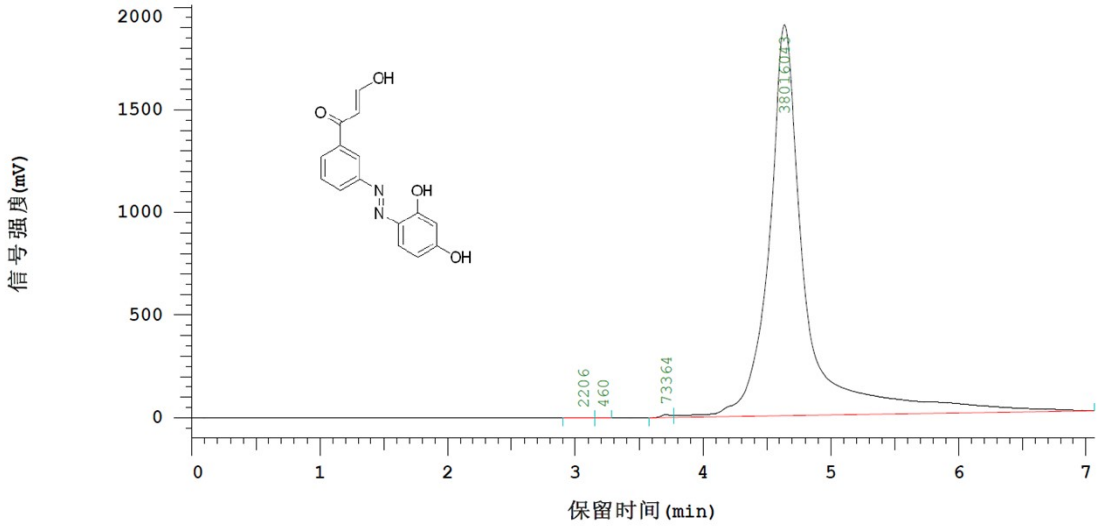

Figure S130. HPLC of **8b**

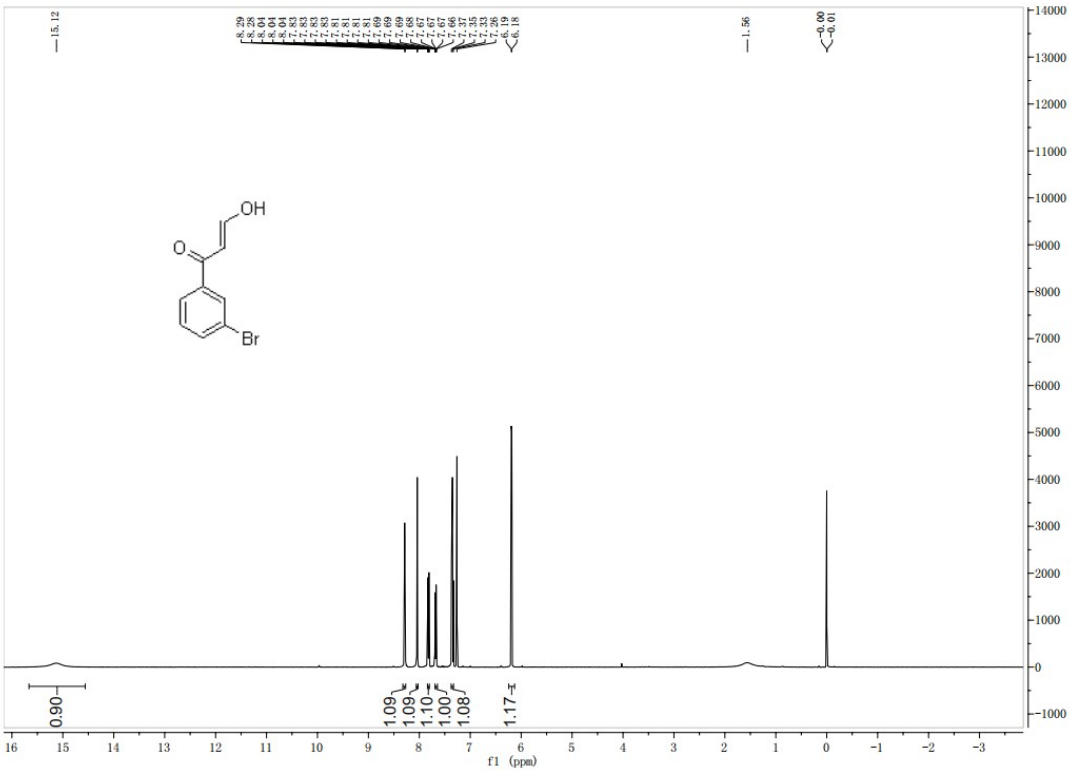

Figure S131.[1]H-NMR (400 MHz, Chloroform-d) of **9**

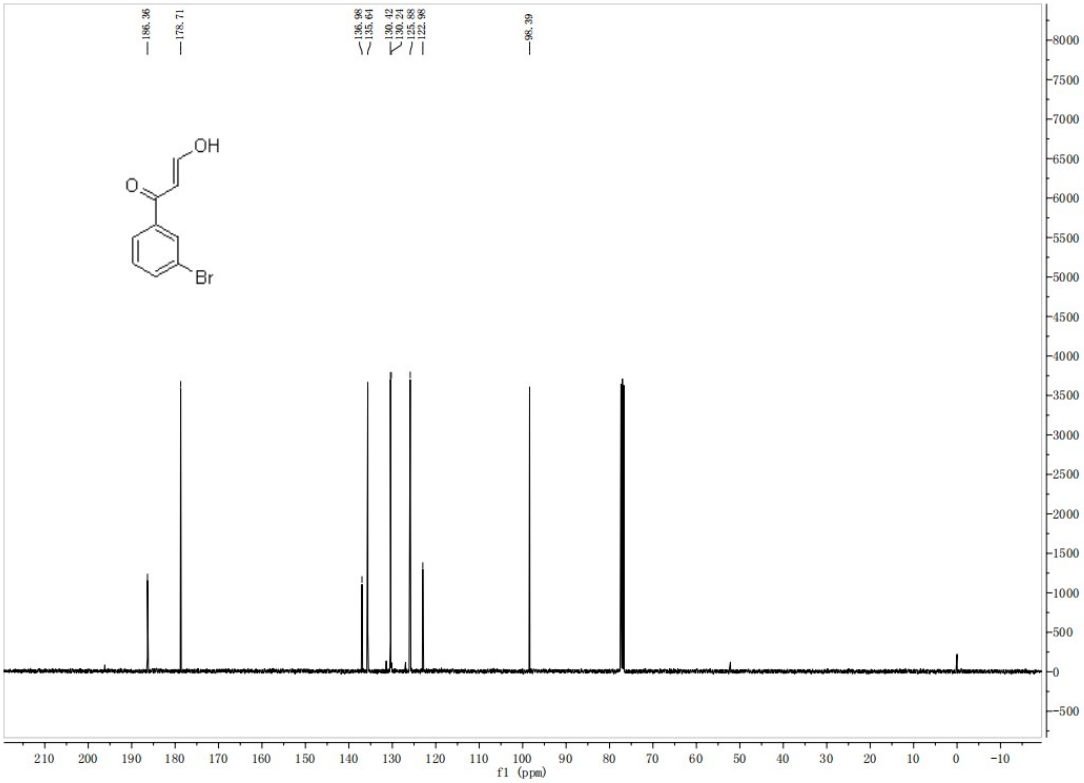

Figure S132.[13]C-NMR (100 MHz, Chloroform-d) of **9**

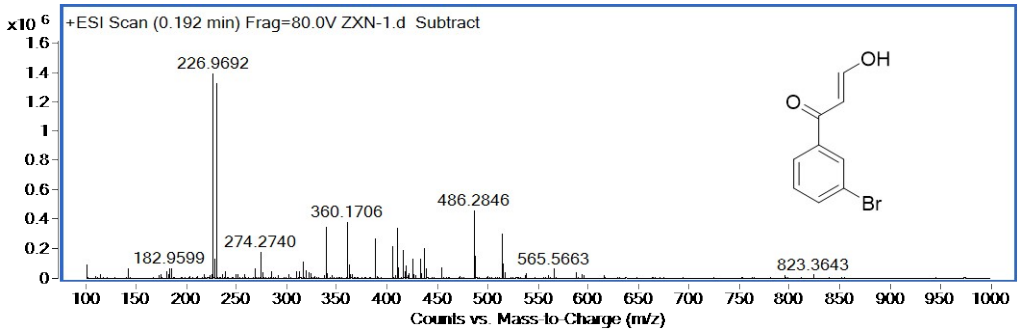

Figure S133. HRMS of **9**

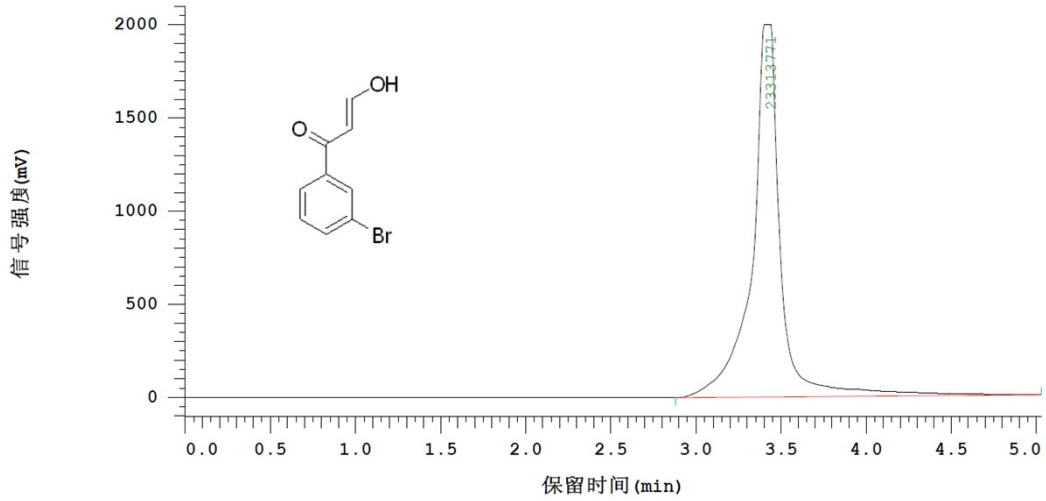

Figure S134. HPLC of **9**

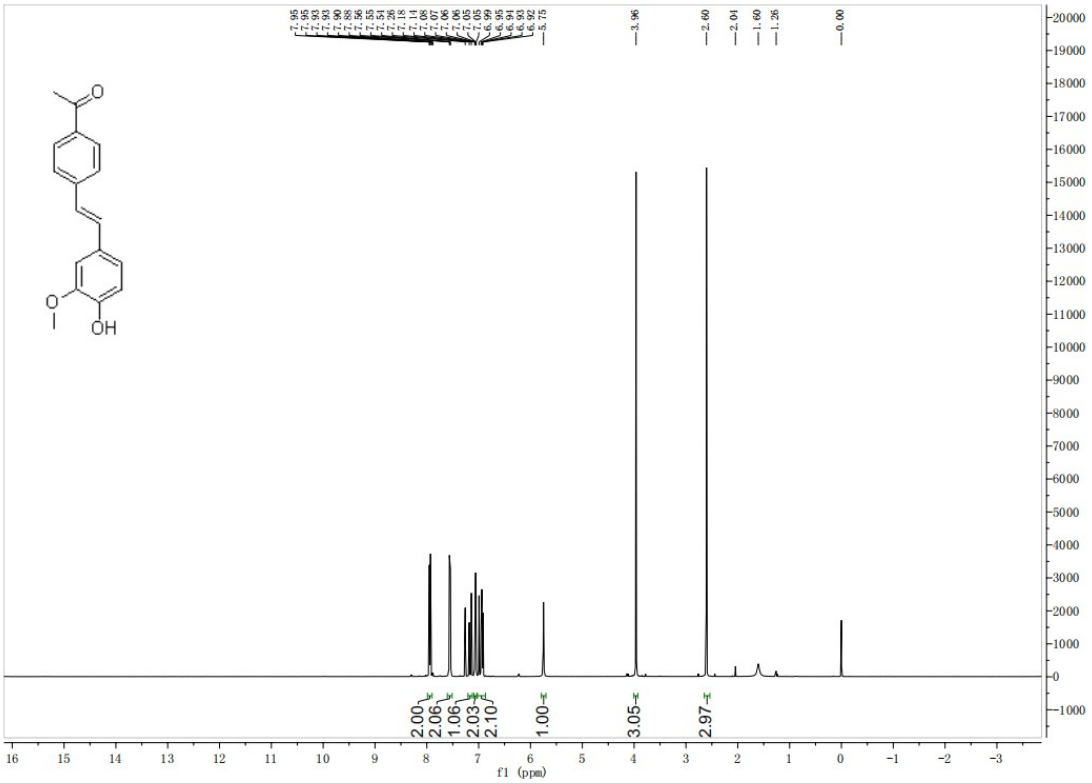

Figure S135.[1]H-NMR (400 MHz, Chloroform-d) of **11**

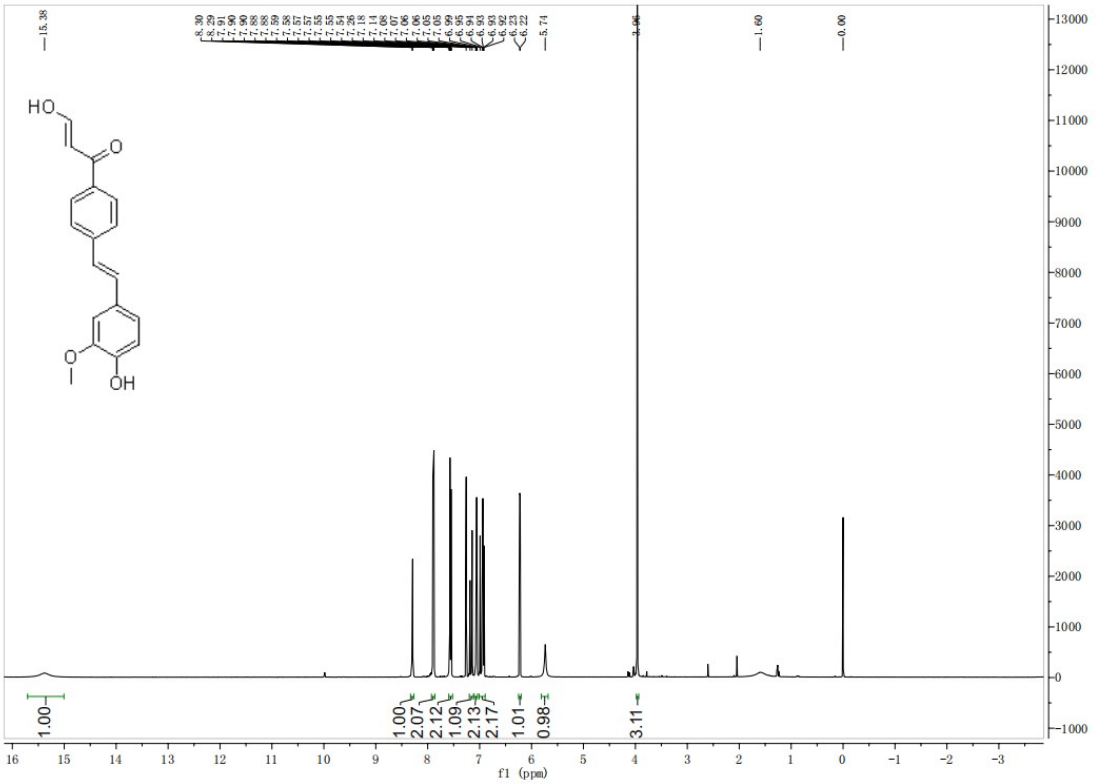

Figure S136.[1]H-NMR (400 MHz, Chloroform-d) of **12**

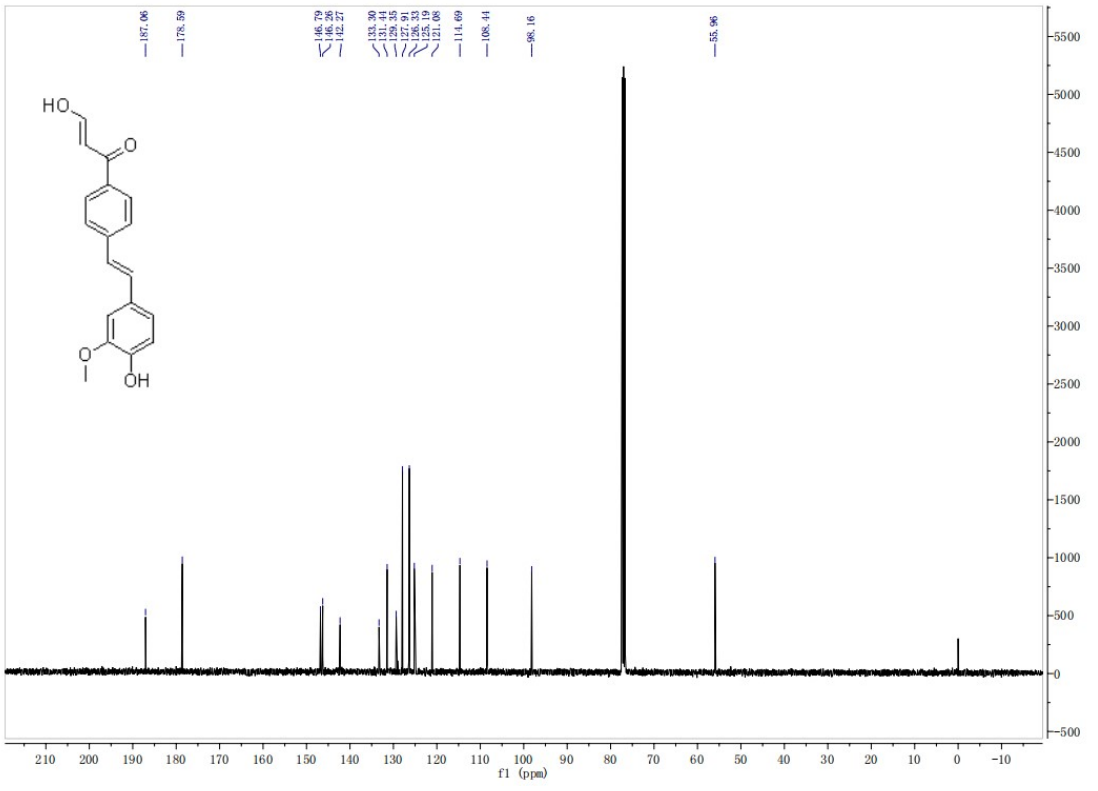

Figure S137.[13]C-NMR (100 MHz, Chloroform-d) of **12**

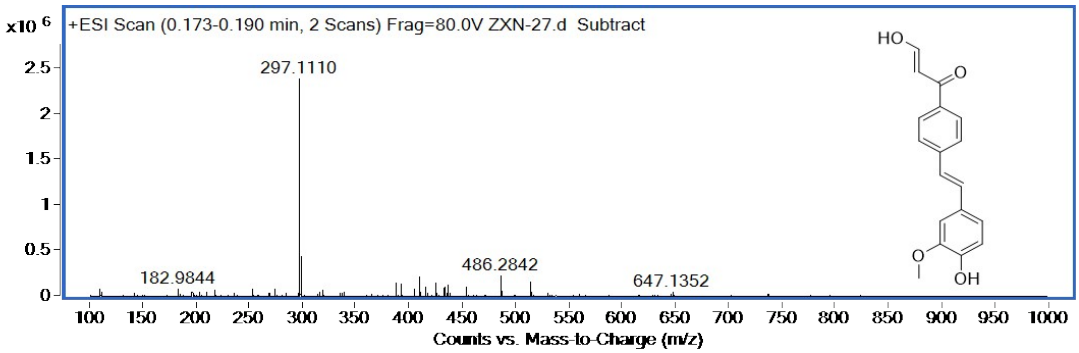

Figure S138. HRMS of **12**

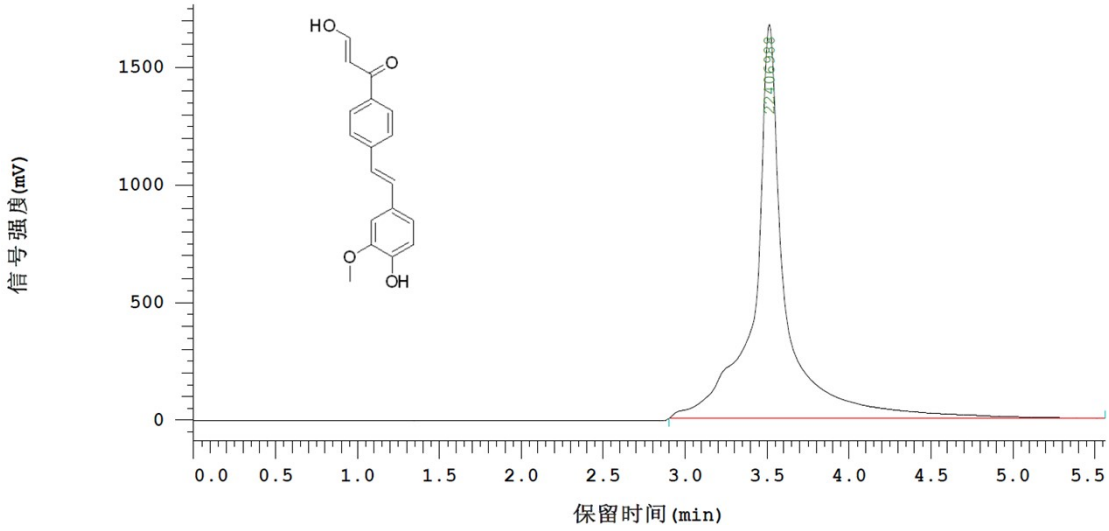

Figure S139. HPLC of **12**

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