Supplementary material for

Efficient discovery of potent *α*-glucosidase inhibitors from *Paeoniae lactiflora* by enzyme-MOFs nanocomposite and competitive indicator

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Support information list

Characterization of UiO-66-NH$_2$. The synthesized UiO-66-NH$_2$ exhibited a representative XRD pattern in consistent with the reported UiO-66 topology (Fig. S1B). Besides, observing from the figure S1A, the UiO-66-NH$_2$ powder had regular structure, smooth surface, and high crystallinity. All the above-mentioned results revealed that the UiO-66-NH$_2$ was successfully synthesized and could be the vehicle for immobilizing enzyme.

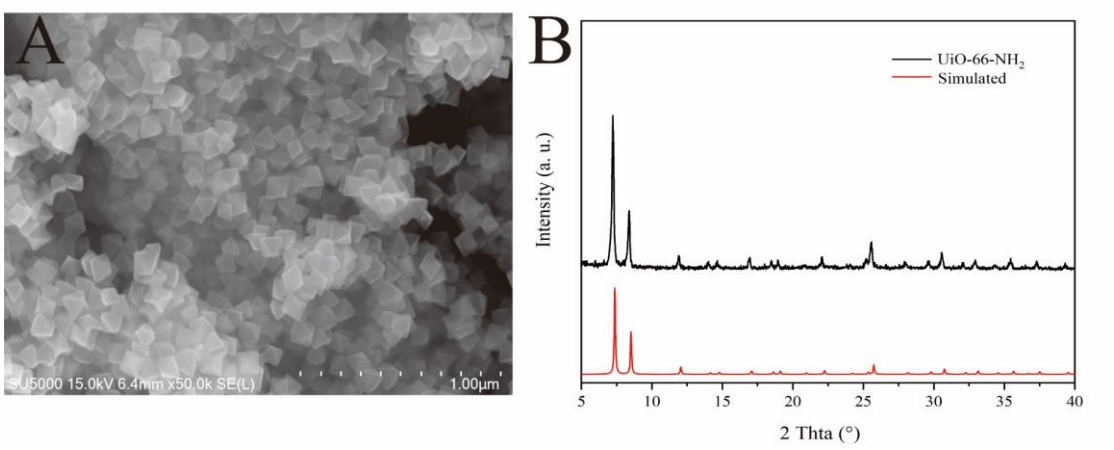


Fig. S1. SEM image (A) and XRD spectrum (B) of UiO-66-NH$_2$.

Performance testing of GAA@UiO-66-NH$_2$. Briefly, 1 μL of GAA@UiO-66-NH$_2$ (5 mg/ml) and free GAA (1 mg/ml) were diluted with 59 μL PBS, respectively, and then was incubated with 40 μL *p*NPG at different temperatures ranging from 20 °C to 45 °C for 10 min. The activity of GAA@UiO-66-NH$_2$ was determined as above-mentioned. Besides, GAA@UiO-66-NH$_2$ and free GAA were incubated with *p*NPB in 50 mM PBS at different pH values (6.0-10.0) for 10 min at 37 °C, respectively, and the activity was then measured accordingly.

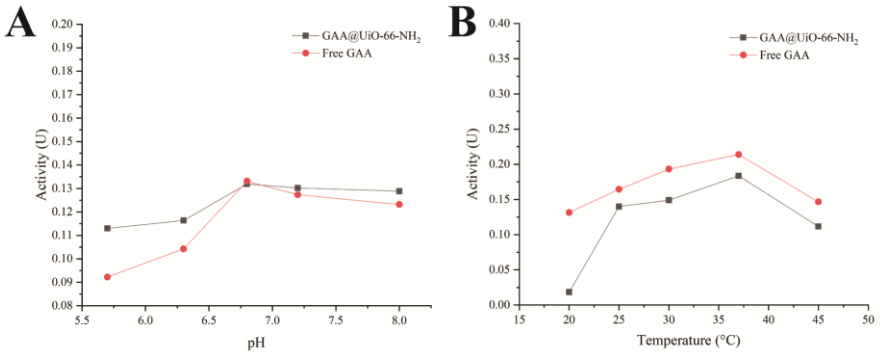


Figure S2. (A) Effects of pH and (B) temperature on the activity of free GAA and GAA@UiO-66-NH$_2$.

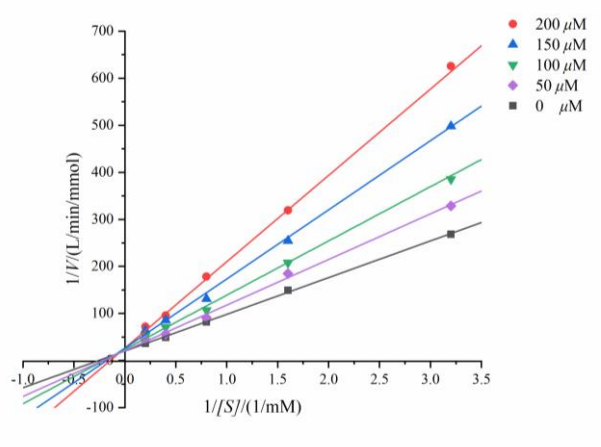


Figure S3. Lineweaver-Burk double reciprocal plots of NG, c(GAA) = 0.5 U mL^{-1}, c(*p*NPG)= 0.3125, 0.625. 1.25, 2.5, 5 mM.

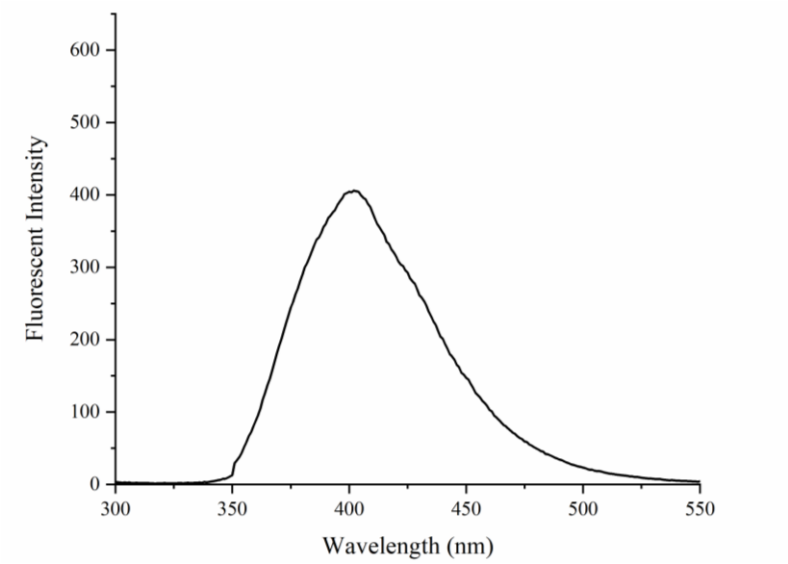


Figure S4. The fluorescence spectra of compound **5** in PBS (50 mM, pH 6.8).

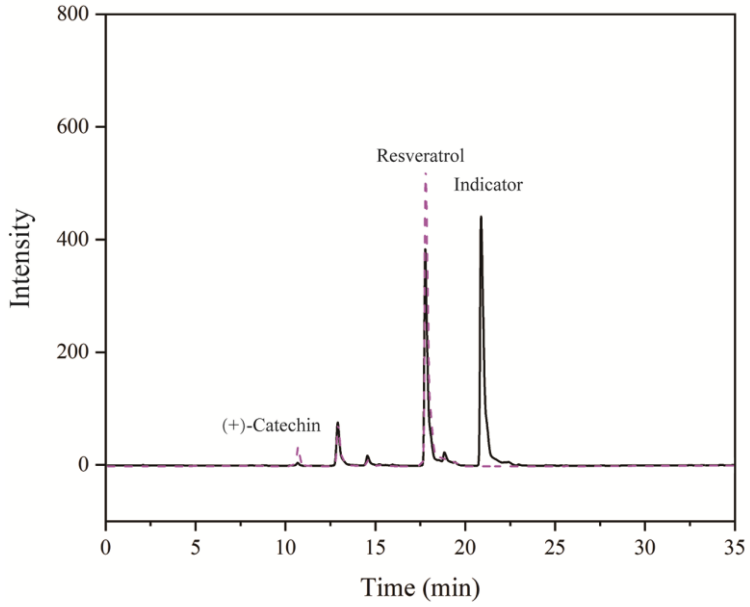


Figure S5. HPLC chromatograms obtained from the samples that using NG as indicator. E2A′ was sample acquired from GAA@UiO-66-NH_2 incubation with indicator and mixed sample (contained resveratrol and (+)-catechin). E2B′ was sample acquired from GAA@UiO-66-NH_2 only incubation with mixed sample (contained resveratrol and (+)-catechin).

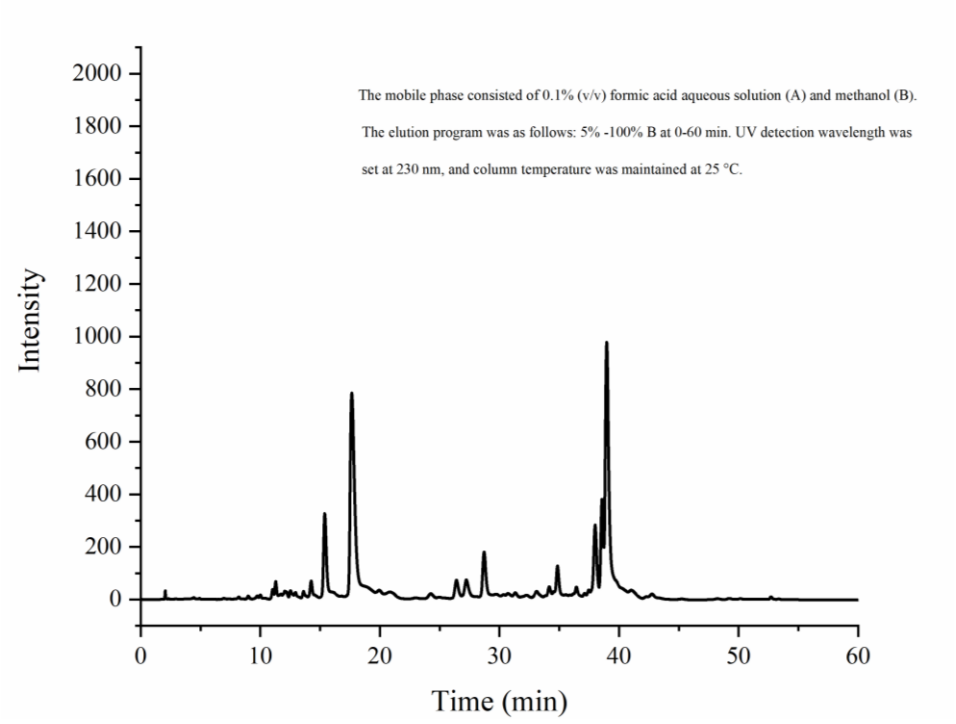


Figure S6. HPLC chromatogram of PS extract

Table S1. Experimental data for the relative activity recovery.

	Free GAA	GAA@UiO-66-NH_2
Activity (U)	0.30	0.14

Table S2. Experimental data for the protein loading capacity.

Washing time	0	1	2	3
Protein amount of supernatant (μg)	555.68	171.32	15.52	8.50

Table S3. Retention time and MS data of compounds in eluent of *Paeoniae lactiflora* seeds sample (PS-E) by HPLC-Q-TOF-MS/MS.

Peak	t_R(min)	Ions (*m/z*)	MS/MS fragment mass (*m/z*)	Elemental composition	Molecular formula
1	12.077	687.2163 $[M+COOH]^-$	641.2090, 519.1720, 323.0989,	$C_{29}H_{38}O_{16}$	Isomaltopaeoniflorin
2	13.048	525.1628 $[M-H]^-$	525.1624	$C_{24}H_{30}O_{13}$	Mudanpioside E
3	16.596	687.2125 $[M+COOH]^-$	593.1884, 489.1620, 323.0991, 165.0557	$C_{29}H_{38}O_{16}$	6′-O-β-D-glucopyranosylalbiflorin
4	18.280	525.1641 $[M+COOH]^-$	449.1459, 327.1089, 165.0557	$C_{23}H_{28}O_{11}$	Paeoniflorin
5	25.218	725.2036 $[M+COOH]^-$	679.1981, 585.1562, 479.1129	$C_{42}H_{32}O_9$	Suffruticosol A
6	30.478	725.2041 $[M+COOH]^-$	679.1986, 585.1573	$C_{42}H_{32}O_9$	Suffruticosol B
7	37.631	227.0727 $[M-H]^-$	227.0727	$C_{14}H_{12}O_3$	Resveratrol
8	40.583	723.1890	583.1403	-	-
9	53.254	499.1423 $[M+COOH]^-$	453.1353, 347.0925, 225.0559	$C_{28}H_{22}O_6$	Trans-ε-viniferin
10	55.702	679.1983 $[M-H]^-$	679.2001	$C_{42}H_{32}O_9$	Vitisin E
11	56.497	285.0422 $[M-H]^-$	285.0441, 133.0295	$C_{15}H_{10}O_6$	Luteolin
12	58.012	725.2069 $[M+COOH]^-$	679.1993, 585.1565	$C_{42}H_{32}O_9$	-
13	58.413	725.2039 $[M+COOH]^-$	679.1988, 585.1562	$C_{42}H_{32}O_9$	Ampelopsin E
14	60.480	499.1404	453.1360	-	-
15	62.007	329.0671	329.0671	-	-

Procedures of synthesizing the indicator.

4-Pentyn-1-tosylate: It was obtained from the reaction of pent-4-yn-1-ol (11.87 mmol, 1 g), triethylamine (11.87 mmol, 1.65 mL) and tosyl chloride (15.45 mmol, 2.94 g) which were dissolve in dichloromethane (DCM) at 0 ℃ to room temperature. The crude product was purified by column chromatography using 200-300 mesh silica gel with ethylacetate: *n*-hexane as eluent and 4-pentyn-1-tosylate was obtained as viscous transparent liquid. Yield 1.8 g, 63%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (2H, J = 8.3 Hz, d), 7.33 (2H, J = 8.0 Hz, d), 4.12 (2H, m), 2.42 (3H, s), 2.23 (2H, J = 6.9, 2.6 Hz, td), 1.87 (1H, J = 3.6, 1.6 Hz, dd), 1.83 (2H, m).

Compound 2: Potassium carbonate (2.46 mmol, 338 mg) was added to a solution of deoxynojirimycin (1.23 mmol, 200 mg) and 4-pentyn-1-tosylate (1.47 mmol, 350 mg) in DMF. The reaction mixture was heated to 80 ℃ for 24 h under argon. The DMF was evaporated under reduced pressure. The crude product was purified by column chromatography using 200-300 mesh silica gel with dichloromethane: methanol as eluent and compound 2 was obtained as transparent crystals. Yield 123.9 mg, 44 %. ^{1}H NMR (500 MHz, CD_3OD): δ 3.86 (1H, J = 11.8, 2.4 Hz, dd), 3.80 (1H, J = 11.9, 2.9 Hz, dd), 3.55 (1H, J = 12.2, 7.5, 4.5 Hz, ddd), 3.42 (1H, m), 3.27 (1H, m), 3.09 (1H, J = 9.1 Hz, t), 2.94 (1H, J = 11.2, 4.9 Hz, dd), 2.87 (1H, m), 2.63 (1H, J = 19.8, 6.9 Hz, dt), 2.15 (3H, J = 20.2, 9.0 Hz, dt), 2.07 (1H, J = 9.5, 2.7 Hz, dt), 1.65 (2H, m). ^{13}C NMR (125 MHz, CD_3OD): δ 80.53, 78.88, 75.85, 72.05, 70.75, 67.36, 59.51, 57.79, 52.52, 24.52, 16.89. ESI-HRMS *m/z* 230.1386 $[M + H]^+$ (calcd for $C_{11}H_{20}NO_4$, 230.1387).

1-Azidopropyl-3-tosylate (Compound 3): Triethylamine (4.02 mmol, 0.56 mL) was added in the mixture solution of 3-Azido-1-propanol (3.96 mmol, 400 mg) and tosyl chloride (4.28 mmol, 816 mg) dissolved in DCM. The reaction was stirred at 0 - room temperature until completion. After completion (TLC), the reaction mixture was partitioned between dichloromethane and water. Organic layer was separated and dried over anhydrous sodium sulphate (Na_2SO_4) and evaporated under reduced pressure. The obtained crude derivative was purified by column chromatography using 200-300 mesh silica gel with ethyl acetate: *n*-hexane as eluent to afford product. Yield, 543

mg, 54%.^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (2H, J = 8.2 Hz, d), 7.36 (2H, J = 8.0 Hz, d), 4.11 (2H, J = 5.9 Hz, t), 3.38 (2H, J = 6.5 Hz, t), 2.46 (3H, s), 1.89 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.63, 133.43, 130.54, 128.52, 67.58, 47.91, 29.09, 22.26. ESI-HRMS *m/z* 278.0569 $[M + Na]^+$ (calcd for $C_{10}H_{13}N_3O_3SNa$, 278.0570).

Compound 4: Potassium carbonated (1.5 mmol, 208 mg) was added to a solution of 7-hydroxy-4-(trifluoromethyl) coumarin (0.75 mmol, 174 mg) and 1-azidopropyl-3-tosylate (0.81 mmol, 205 mg) in 5 mL DMF. The mixture was reacted at room temperature for 12 h under argon. Most of the DMF was evaporated under reduced pressure. The residue was dissolved in ethyl acetate, washed twice with water, and then dried over anhydrous Na_2SO_4. After filtration, the solvent was removed. The crude product was purified via silica gel column chromatography using petroleum ether: ethyl acetate and afford **4** as colorless prisms. Yield 198 mg, 84%.^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (1H, J = 9.0, 1.7 Hz, dd), 6.90 (1H, J = 9.0, 2.5 Hz, dd), 6.85 (1H, J = 2.5 Hz, d), 6.60 (1H, s), 4.12 (2H, J = 5.9 Hz, t), 3.53 (2H, J = 6.5 Hz, t), 2.08 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.10, 159.92, 156.85, 142.11 (q, J = 32.8 Hz), 128.48, 126.99, 114.11, 112.98 (q, J = 5.7 Hz), 107.80, 102.54, 65.87, 48.50, 29.04. ESI-HRMS *m/z* 336.0564 $[M + Na]^+$ (calcd for $C_{13}H_{10}F_3N_3O_3Na$, 336.0566).

Compound 5: Copper (II) sulfate (0.025 mmol, 4 mg) and L-ascorbic acid (0.076 mmol, 13 mg) were added to a solution of compound **4** (0.54 mmol, 169 mg) and compound **5** (0.54 mmol, 124 mg) in 4.5 mL of H_2O/DMF (1:2). The reaction mixture was stirred at room temperature for 12 h under argon. Most of the DMF and H_2O were purified via silica gel column chromatography using dichloromethane: methanol to afford transparent crystals. Yield 92.7 mg, 32%. ^{1}H NMR (500 MHz, CD_3OD): δ 7.80 (1H, s), 7.65 (1H, m), 6.99 (1H, J = 9.1, 2.1 Hz, dq), 6.96 (1H, J = 2.5 Hz, t), 6.72-6.66 (1H, m), 4.59 (2H, J = 6.8 Hz, t), 4.11 (2H, J = 5.8 Hz, t), 3.79 (2H, m), 3.44 (1H, J = 10.5, 9.1, 4.8 Hz, ddd), 3.33 (1H, m), 3.11 (1H, J = 9.0 Hz, t), 2.98 (1H, J = 11.1, 4.9 Hz, dd), 2.86 (1H, J = 13.4, 9.8, 6.5 Hz, ddd), 2.68 (2H, J = 7.5 Hz, t), 2.53 (1H, J = 13.7, 9.4, 4.8 Hz, ddd), 2.41 (2H, J = 6.4 Hz, p), 2.11 (1H, J = 10.9 Hz, t), 2.06 (1H, J = 9.5, 2.8 Hz, dt), 1.84 (2H, m). ^{13}C NMR (125 MHz, CD_3OD): δ 164.13, 160.86, 157.65, 148.84, 127.39, 127.38, 123.60, 114.65, 113.75, 113.73, 108.25, 103.19, 80.58, 71.98, 70.77, 67.62, 66.68, 59.34, 57.65, 52.65, 48.12, 30.71, 25.52, 23.87.

ESI-HRMS *m/z* 543.2064 $[M + H]^+$ (calcd for $C_{24}H_{30}F_3N_4O_7$, 543.2061).

Extraction and isolation

0.1% formic acid was added to all solvents unless otherwise indicated. The air-dried and powdered aerial parts of *Paeoniae lactiflora* seeds (500 g) were extracted by ultrasonic extraction with 80% (v/v) aqueous EtOH (2L×3). After filtration, the EtOH extract was evaporated under reduced pressure to yield a crude extract (22 g), which was subjected to ODS column chromatography (CC) and eluted with a gradient solvent system of MeOH-H_2O (10:90, 20:80, 30:70, 40:60, 50:50, 60:40, 70:30, 100:0, v/v) to obtain twelve subfractions (Fr. PS1-12). Fr. PS3 was applied to ODS CC eluted with gradient MeOH-H_2O (15:85-19:81, v/v) to afford subfractions (Fr. PS3-21) and acquired paeoniflorin (6 mg). Fr. PS4 was applied to ODS CC eluted with isocratic MeOH-H_2O (20:80, v/v) to afford subfractions (Fr. PS4-1……Fr. PS4-58) and yield suffruticosol A (280 mg). Then, Fr. PS4-58 was further purified by preparative HPLC (MeOH-H_2O, 30:70. v/v) to yield suffruticosol B (17 mg). Fr. PS6 was separated on preparative HPLC (MeOH-H_2O, 40:60, v/v) to yield resveratrol. Fr. PS9 and Fr. PS11 were separated together on silica gel CC eluting with PE-EtOAc solvent system (10:7, 1:1, 0:1, v/v) to give forty-four fractions and yield luteolin (95 mg). Fr. PS9-41 was further purified by preparative HPLC (MeOH-H_2O, 43:57, v/v) to yield Vitisin E (33 mg) and Ampelopsin E (89 mg).

Structural identification of *α*-glucosidase inhibitors in extract of PS by NMR data.

Suffruticosol A: light yellow powder; negative HRESIMS *m/z* 725.2031 $[M+COOH]^-$ (calcd. for $C_{43}H_{33}O_{11}$, 725.2028); ^{1}H-NMR (500 MHz, CD_3OD) δ 7.12 (2H, d, J = 1.7 Hz, H-2", 6"), 6.97 (2H, d, J = 8.1 Hz, H-2, 6), 6.70 (2H, d, J = 8.3 Hz, H-3", 5"), 6.50 (2H, d, J = 8.2 Hz, H-2', 6'), 6.39 (2H, d, J = 8.1 Hz, H-3, 5), 6.27 (1H, d, J = 2.2 Hz, H-12"), 6.22 (1H, s, H-12'), 6.14 (2H, d, J = 8.1 Hz, H-3', 5'), 6.08 (1H, t, J = 2.3 Hz, H-12), 6.01 (2H, d, J = 2.3 Hz, H=10, 14), 5.95 (1H, d, J = 2.3, H-14"), 5.70 (1H, d, J = 11.7 Hz, H-7"), 5.45 (1H, d, J = 3.3 Hz, H-7'), 4.76 (1H, s, H-8), 4.37 (1H, d, J = 11.7 Hz, H-8"), 3.96 (1H, dt, J = 6.3, 2.2 Hz, H-8'), 3.71 (1H, d, J = 7.7 Hz, H-7). ^{13}C NMR (151 MHz, CD_3OD) δ 160.16 (C-11'), 159.26 (C-11, 13), 158.92 (C-4"), 156.66 (C-13"), 156.48 (C-4), 155.12 (C-13'), 154.94 (C-11"), 154.48 (C-4'), 148.39 (C-9), 144.65 (C-9'), 141.78 (C-9"), 135.53 (C-1), 133.92 (C-1'), 130.84 (C-1"), 130.74 (C-2', 6'), 130.72 (C-2, 6), 130.45 (C-2", 6"), 126.94 (C-

10"), 123.01 (C-14'), 117.26 (C-10'), 116.24 (C-3", 5"), 115.44 (C-3, 5), 114.16 (C-3', 5'), 106.84 (C-10, 14), 105.94 (C-14"), 101.93 (C-12"), 101.37 (C-12), 96.22 (C-12'), 91.48 (C-7"), 61.04 (C-7), 54.55 (C-8), 48.78 (C-8"), 48.58(C-8'), 39.75 (C-7'). According to the reported research[1], Fr. PS4-46 was identified as suffruticosol A.

Suffruticosol B: yellow powder; negative HRESIMS *m/z* 725.2030 $[M+COOH]^-$ (calcd. for $C_{43}H_{33}O_{11}$, 725.2028); ^{1}H-NMR(600 MHz, CD_3OD) δ 7.58 (2H, d, J = 12 Hz, H-2", 6"), 6.92 (2H, brs, H-2', 6'), 6.91 (2H, d, J = 12 Hz, H-3", 5"), 6.51 (2H, d, J = 6 Hz, H-3', 5'), 6.29 (2H, d, J = 12 Hz, H-3, 5), 6.25 (2H, d, J = 6 Hz, H-2, 6), 6.23 (1H, s, H-10), 6.22 (1H, s, H-14), 6.19 (1H, s, H-12'), 6.18 (1H, d, J = 6 Hz, H-12"), 5.95 (1H, t, H-12), 5.95 (1H,d, J = 2.4 Hz, H-14"), 5.87 (1H, d, J = 12 Hz, H-7"), 5.08 (1H, d, J = 12 Hz, H-8"), 4.22 (1H, d, J = 12 Hz, H-7'), 4.11 (1H, m, H-8'), 4.09 (1H, s, H-8), 3.81 (1H, d, J = 6 Hz, H-7). ^{13}C NMR (151 MHz, CD_3OD) δ 160.18 (C-11'), 159.36 (C-11, 13), 159.10 (C-4"), 158.38 (C-13"), 157.15 (C-11"), 156.13 (C-4'), 156.03 (C-4), 155.72 (C-13'), 147.47 (C-9'), 147.46 (C-9), 142.38 (C-9"), 135.52 (C-1), 133.80 (C-1'), 133.04 (C-2', 6'), 130.92 (C-1"), 130.51 (C-2", 6"), 129.47 (C-2, 6), 123.57 (C-14'), 122.86 (C-10"), 118.49 (C-10'), 116.52 (C-3", 5"), 115.17 (C-3, 5), 114.72 (C-3', 5'), 107.36 (C-10, 14), 104.98 (C-12"), 103.72 (C -14"), 101.48 (C-12), 96.26 (C-12'), 91.10 (C-7"), 63.07 (C-7), 56.87 (C-8), 49.10 (C-8"), 47.81 (C-8'), 46.46 (C-7'). According to the reported research[1], Fr. PS4-58-2 was identified as suffruticosol B.

Resveratrol: white powder; ^{1}H NMR (600 MHz, CD_3OD) δ 7.37 (2H, d, J = 8.3Hz, H-2', 6'), 6.96 (1H, d, J = 16.2 Hz, H-β), 6.81 (1H, d, J = 16.2 Hz, H-α), 6.77 (2H, d, J = 8.3 Hz, H-3', 5'), 6.46 (2H, d, J = 2.2 Hz, H-2, 6), 6.17 (1H, t, J = 2.2 Hz, H-4). ^{13}C NMR (151 MHz, CD_3OD) δ 159.64(C-3), 158.36(C-4'), 141.30(C-1), 130.41(C-1′), 129.38(C-2'), 128.78(C-β), 127.00(C-α), 116.48(C-3'), 105.75(C-2), 102.63(C-4). According to the reported research[2], Fr. PS6-3 was identified as resveratrol.

Vitisin E: colorless crystalline powder; negative HRESIMS *m/z* 725.2036 $[M+COOH]^-$ (calcd. for $C_{43}H_{33}O_{11}$, 725.2028); ^{1}H NMR (600 MHz, CD_3COCD_3) δ 7.17 (2H, d, J = 8.2 Hz, H-2", 6"), 7.11 (2H, d, J = 8.2 Hz, H-2, 6), 6.80 (4H, m, H-3, 5, 3", 5"), 6.60 (4H, m, H-2', 3', 5', 6'), 6.41 (1H, s,

H-12), 6.36 (2H, s, H-10", 14"), 6.34 (1H, s, H-12"), 6.25 (1H, s, H-14), 6.18 (1H, s, H-12'), 5.81 (1H, d, *J* = 11.4 Hz, H-7), 5.45 (1H, d, *J* = 4.0 Hz, H-7"), 5.01 (1H, s, H-7'), 4.29 (1H, d, *J* = 4.0 Hz, H-8"), 4.25 (1H, d, *J* = 11.5 Hz, H-8), 3.28 (1H, m, H-8'α), 2.82 (1H, d, *J* = 18.0 Hz, H-8'β). ^{13}C NMR (151 MHz, CD_3COCD_3) δ 160.93 (C-13′), 160.35 (C-11′), 160.03 (C-11", 13"), 158.46 (C-4), 158.06 (C-4"), 157.18 (C-11), 156.60 (C-13), 155.88 (C-4'), 147.29 (C-9"), 142.41 (C-9), 134.78 (C-9'), 134.50 (C-1"), 134.26 (C-1'), 130.94 (C-1), 129.97 (C-2, 6), 128.30 (C-2', 6'), 127.62 (C-2", 6"), 122.43 (C-10), 121.27 (C-10'), 120.08 (C-14'), 116.10 (C-3", 5"), 115.98 (C-3, 5), 115.66 (C-3', 5'), 107.10 (C-10", 14"), 105.37 (C-14), 102.16 (C-12"), 101.36 (C-12), 93.81 (C-7"), 90.42 (C-12'), 88.57 (C-7), 57.08 (C-8"), 49.25(C-8), 35.63 (C-7'), 30.47 (C-8'). According to the reported research[3], Fr. PS8-2 was identified as vitisin E.

Luteolin: yellow powder; negative HRESIMS *m/z* 285.0414 $[M-H]^-$ (calcd. for $C_{15}H_9O_6$, 285.0405); ^{1}H NMR (500 MHz, CD_3SOCD_3) δ 7.42 (1H, d, *J* = 2.3 Hz, H-6'), 7.40 (1H, s, H-2'), 6.90 (1H, d, *J* = 8.4 Hz, H-5'), 6.67 (1H, s, H-3), 6.46 (1H, d, *J* = 2.1 Hz, H-8), 6.20 (1H, d, *J* = 2.1 Hz, H-6). ^{13}C NMR (126 MHz, CD_3SOCD_3) δ 181.64 (C-4), 164.15 (C-2), 163.88 (C-7), 161.44 (C-9), 157.26 (C-5), 149.69 (C-4'), 145.73 (C-3'), 121.47 (C-1'), 118.95 (C-6'), 116.04 (C-5'), 113.37 (C-2'), 103.67 (C-10), 102.84 (C-3), 98.83 (C-6), 93.85 (C-8). According to the reported research[4], Fr. PS9-25 was identified as luteolin.

Ampelopsin E: colorless crystalline powder; negative HRESIMS *m/z* 679.1965 $[M-H]^-$ (calcd. for $C_{43}H_{31}O_9$, 679.1974); ^{1}H NMR (600 MHz, CD_3COCD_3) δ 7.27 (4H, d, *J* = 8.5 Hz, H-2, 6, 2", 6"), 6.88 (4H, d, *J* = 8.5 Hz, H-3, 5, 3", 5"), 6.86 (2H, d, *J* = 8.5 Hz, H-2', 6'), 6.62 (1H, d, *J* = 16 Hz, H-7'), 6.60 (1H, d, *J* = 16 Hz, H-8'), 6.57 (2H, d, *J* = 8.5 Hz, H-3', 5'), 6.47 (1H, s, H-12'),6.25 (4H, d, *J* = 2.2 Hz, H-10, 14, 10", 14"), 6.22 (2H, t, *J* = 2.2 Hz, H-12, 12"), 5.48 (2H, d, *J* = 5.1 Hz, H-7, 7"), 4.56 (2H, d, *J* = 5.1 Hz, H-8, 8"). ^{13}C NMR (151 MHz, CD_3COCD_3) δ 162.54(C-11', 13'), 159.85(C-11, 13, 11", 13"), 158.15(C-4, 4"), 158.06(C-4'), 147.35(C-9, 9"), 133.97(C-8'), 133.83(C-1, 1"), 133.09(C-1'), 130.15(C-9'), 128.56(C-2', 6'), 127.92(C-2, 6, 2", 6"), 122.24(C-7'), 119.99(C-10', 14'), 116.13(C-3, 5, 3", 5"), 116.04(C-3', 5'), 106.94(C-10, 14, 10", 14"), 101.98(C-12, 12"), 94.02(C-7, 7"), 91.30(C-12'), 57.94(C-8, 8"). According to the reported research[5], Fr. PS91-4-2 was identified as ampelopsin E.

Paeoniflorin: colorless crystalline powder; ^{1}H NMR (600 MHz, CD_3OD) δ 8.06 (1H, d, J = 7.7 Hz, H-6''), 7.62 (1H, t, J = 7.3 Hz, H-4''), 7.50 (1H, t, J = 7.6 Hz, H-5''), 5.43 (1H, s, H-9), 4.75 (2H, t, J = 8.6 Hz, H-8), 4.54 (1H, d, J = 7.6 Hz, H-1'), 3.86 (1H, d, J = 12.0 Hz, H-6'α), 3.62 (1H, dd, J = 12.0, 4.6 Hz, H-6'β), 3.36-3.20 (4H, m), 2.60 (1H, d, J = 6.7 Hz, H-5), 2.50 (1H, dd, J = 11.1, 6.7 Hz, H-7α), 2.20 (1H, d, J = 12.6 Hz, H-3α), 1.97 (1H, d, J = 11.0 Hz, H-7β), 1.82 (1H, d, J = 12.6 Hz, H-3β), 1.38 (3H, s). ^{13}C NMR (151 MHz, CD_3OD) δ 168.00 (C-7''), 134.44 (C-4''), 131.18 (C-1''), 130.73 (C-6''), 130.67 (C-2''), 129.64 (C-3''), 129.60 (C-5''), 106.40 (C-4), 102.28 (C-9), 100.17 (C-1'), 89.33 (C-1), 87.25 (C-2), 78.03 (C-3'), 77.93 (C-5'), 75.00 (C-2'), 72.22 (C-6), 71.73 (C-4'), 62.86 (C-6'), 61.71 (C-8), 44.53 (C-3), 43.95 (C-5), 23.41 (C-7), 19.61 (C-2-CH_3). According to the reported research[6], Fr. PS3-19 was identified as Paeoniflorin.

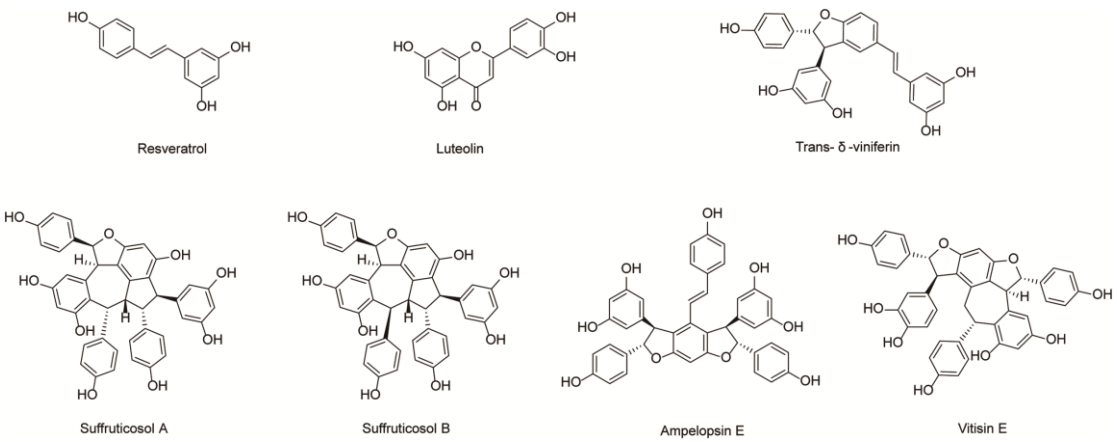


Figure S7. The structure of potent inhibitors screened from *Paeoniae lactiflora* seeds by ligand fishing based on competitive indicator and GAA@UiO-66-NH_2.

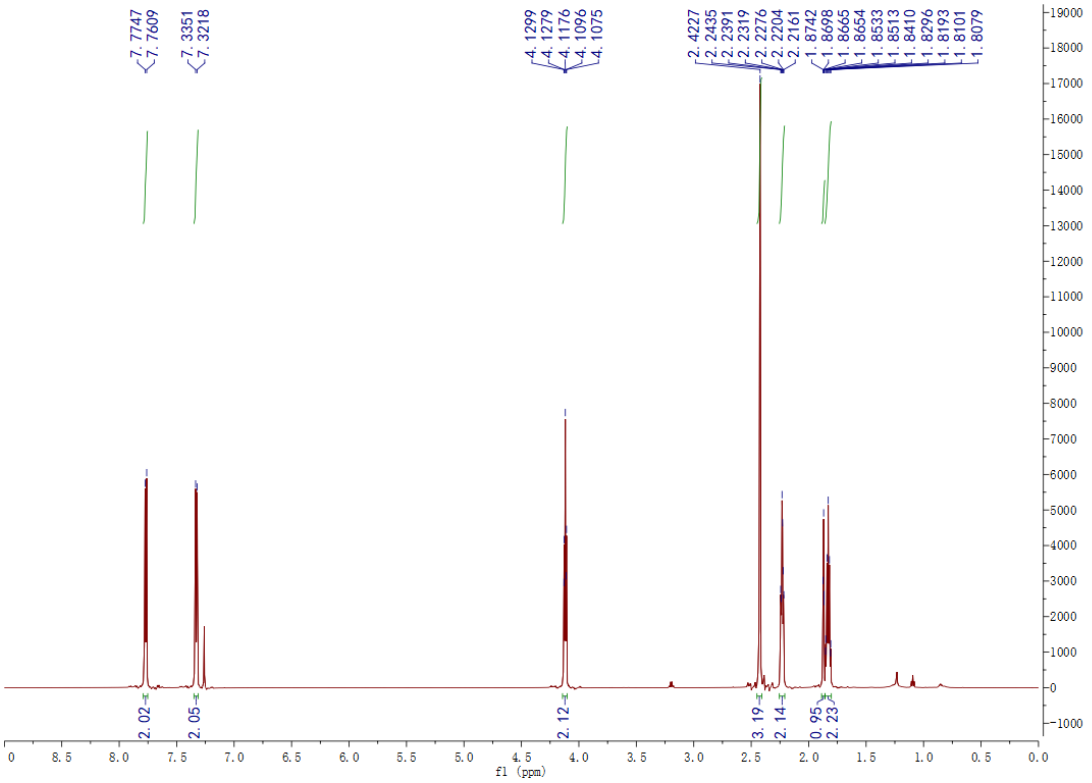


Figure S8. ^{1}H NMR spectrum of 4-pentyn-1-tosylate (500 MHz, $CDCl_3$).

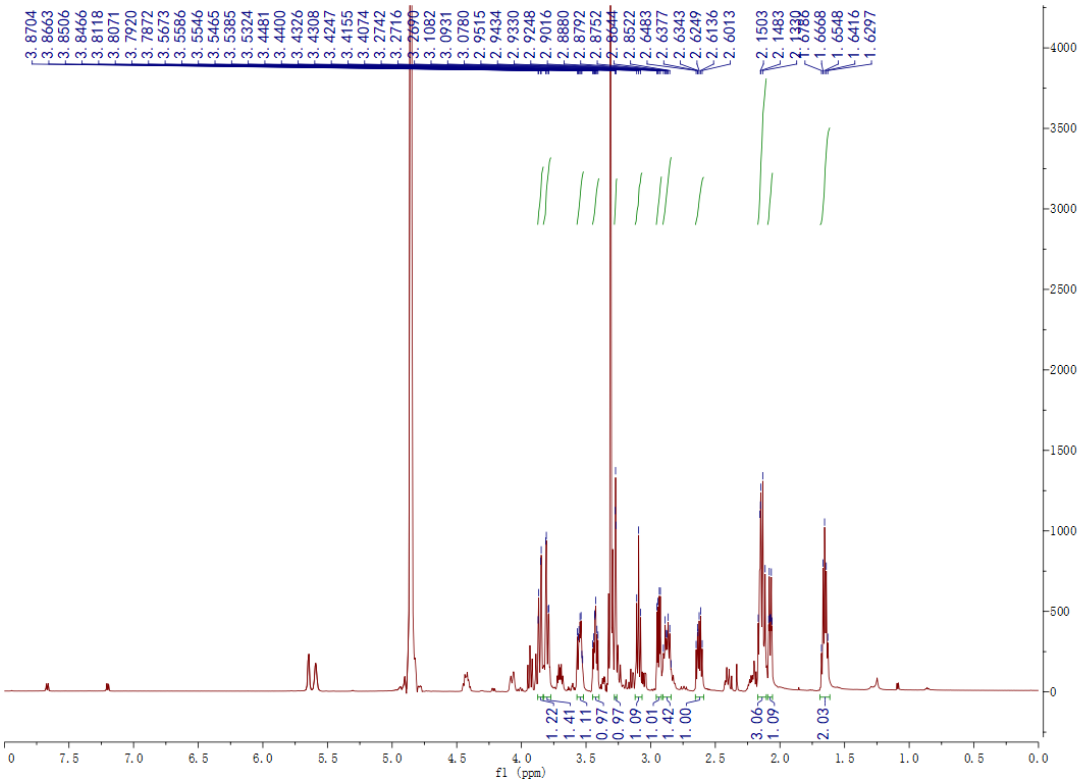


Figure S9. ^{1}H NMR spectrum of compound **2** (500 MHz, CD_3OD).

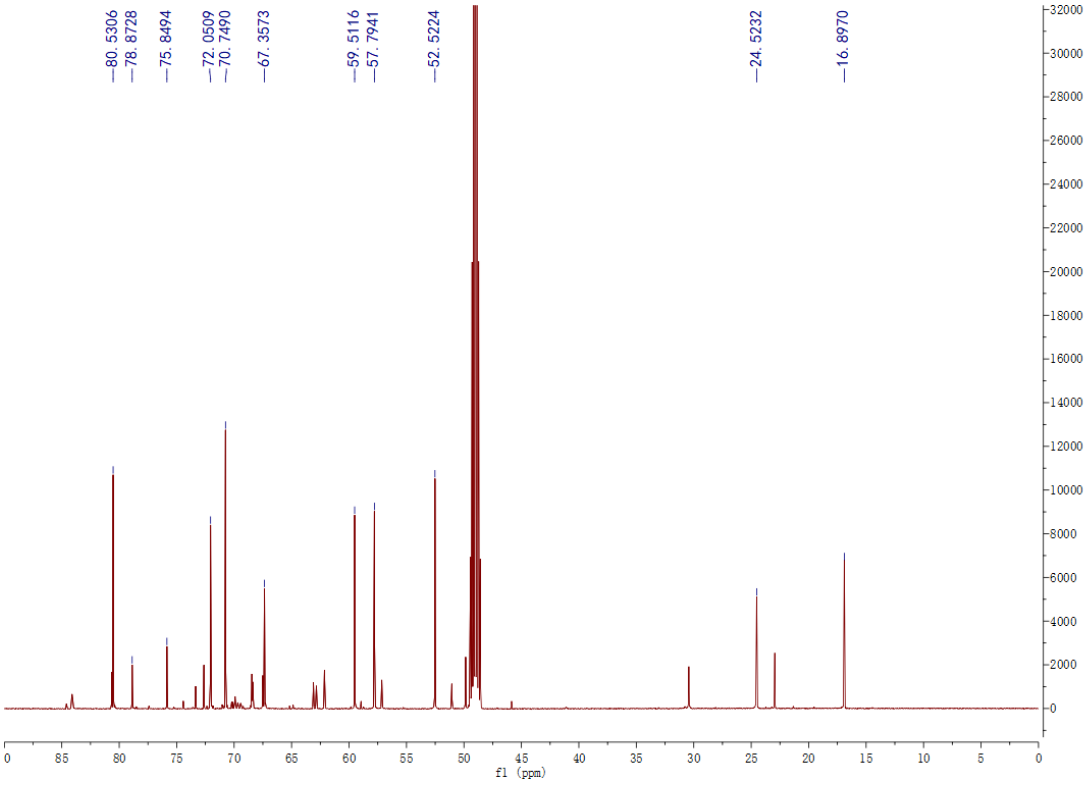
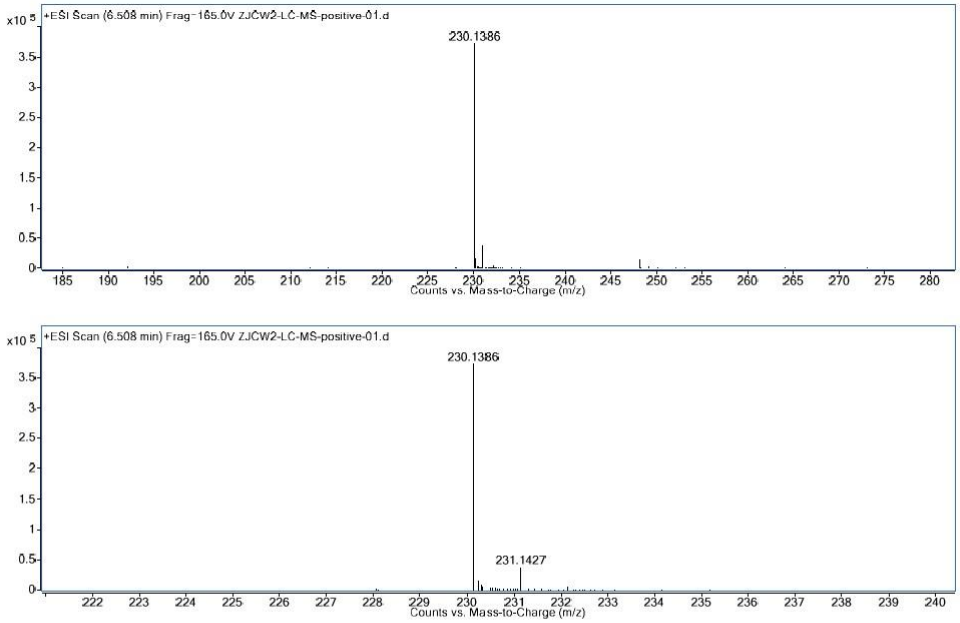


Figure S10. ^{13}C NMR spectrum of compound **2** (125 MHz, CD_3OD).



Elemental Composition Calculator

Target m/z:	230.1386	**Result type:**	Positive ions	**Species:**	$[M+H]^+$
Elements:		C (0-80); H (0-120); O (0-30) ; N(0-5)			
Ion Formula		**Calcalated m/z**		**PPM Error**	
C11H20NO4		230.1387		0.54	

Figure S11. HRESIMS spectrum of compound **2**.

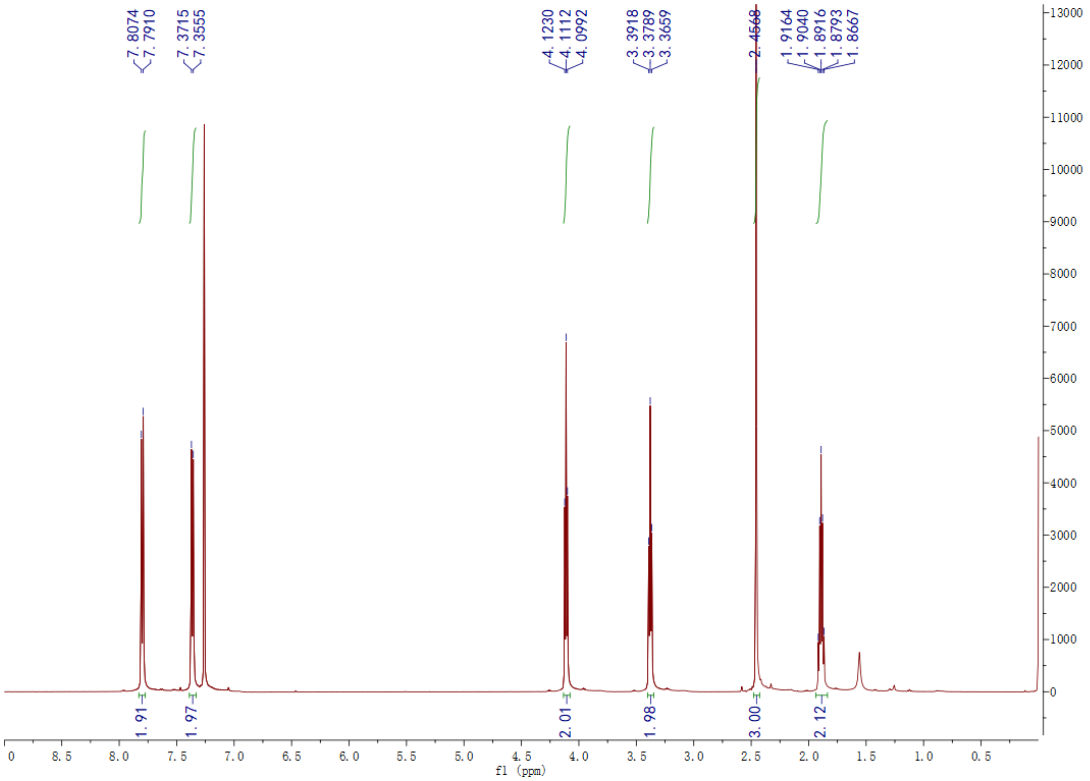


Figure S12. ^{1}H NMR spectrum of 1-azidopropyl-3-tosylate (500 MHz, $CDCl_3$).

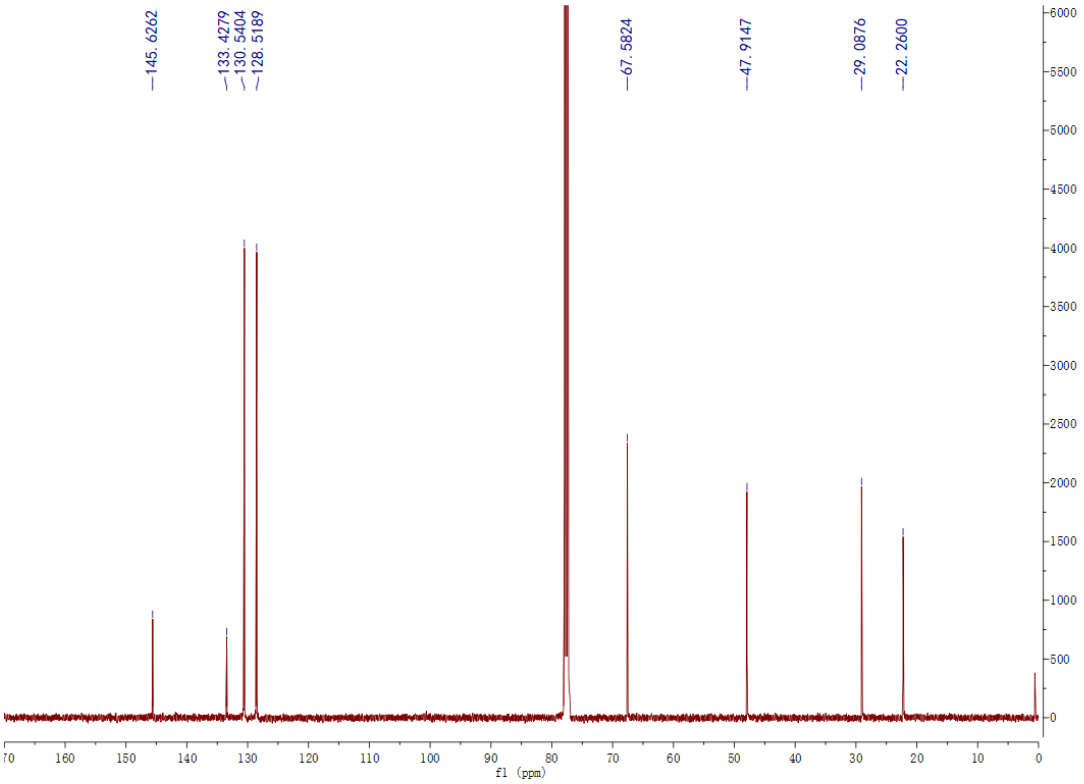
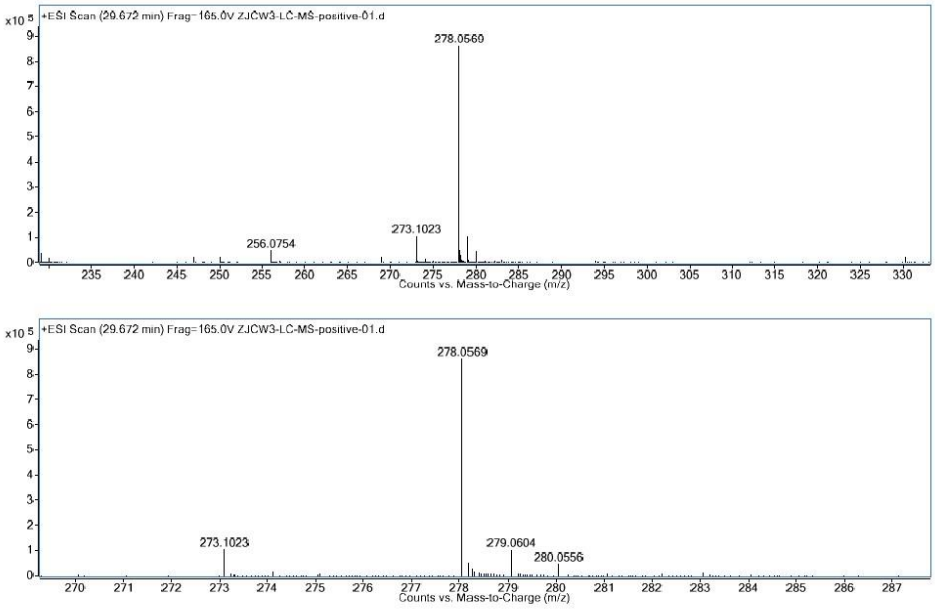


Figure S13. ^{13}C NMR spectrum of 1-azidopropyl-3-tosylate (125 MHz, $CDCl_3$).



Elemental Composition Calculator

Target m/z:	278.0569	**Result type:**	Positive ions	**Species:**	$[M+Na]^+$
Elements:		C (0-80); H (0-120); O (0-30); Na (0-5)); N (0-5)); S (0-5)			
Ion Formula		**Calculated m/z**		**PPM Error**	
C10H13N3NaO3S		278.0570		0.45	

Figure S14. HRESIMS spectrum of 1-azidopropyl-3-tosylate.

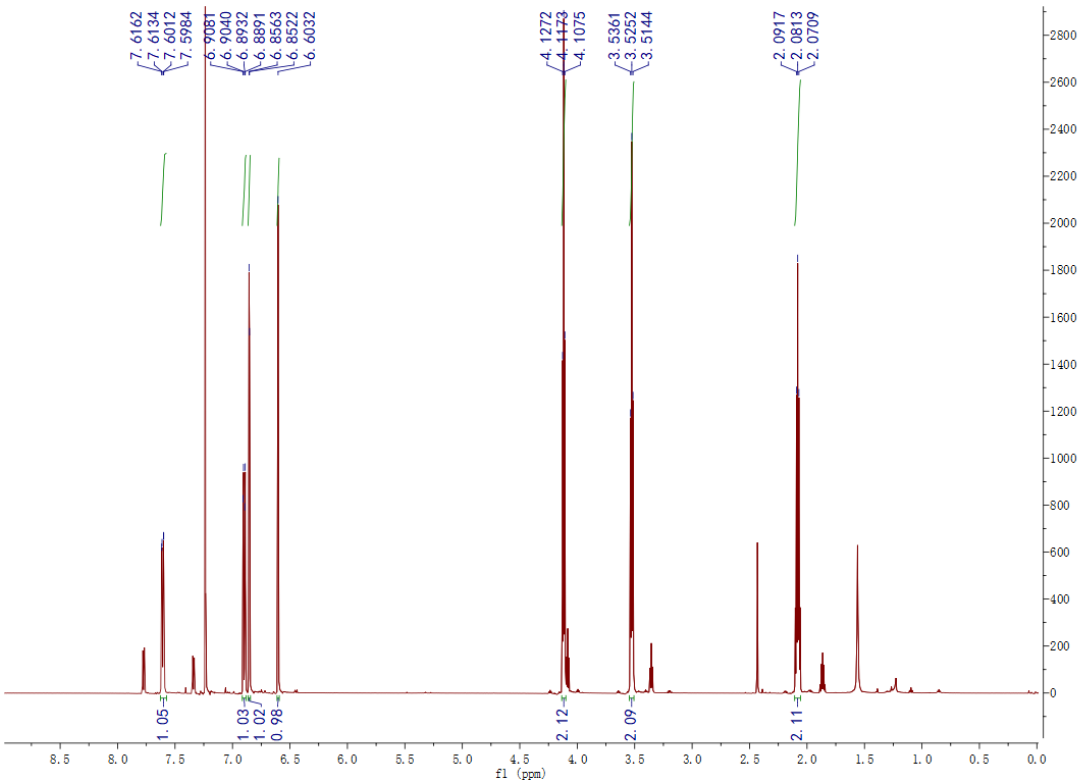


Figure S15. ^{1}H NMR spectrum of compound **4** (500 MHz, $CDCl_3$).

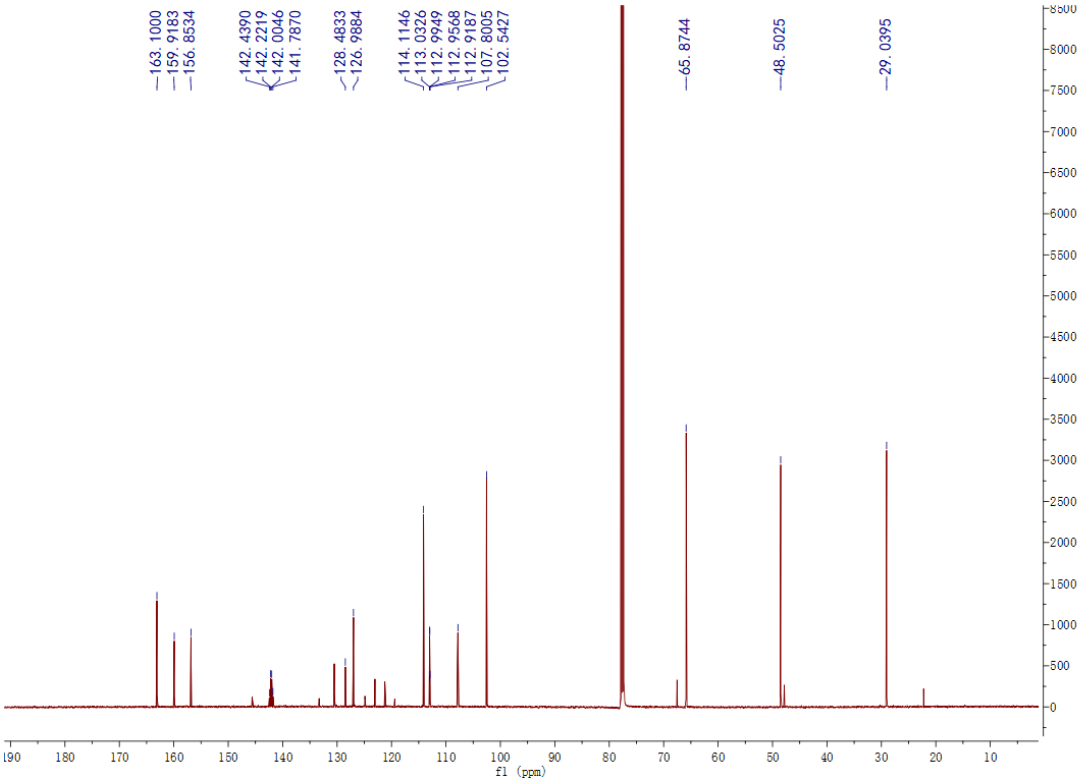
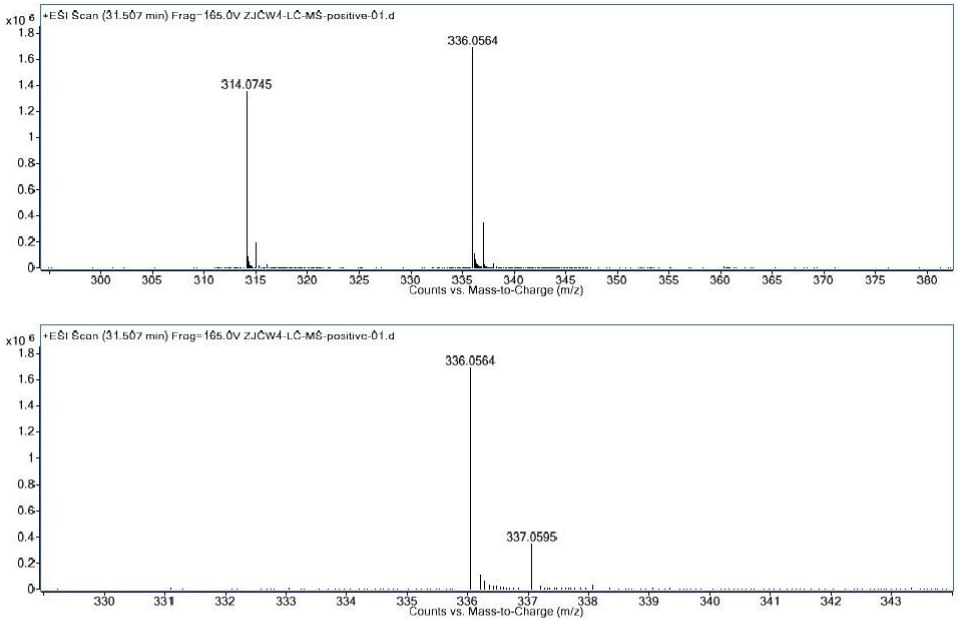


Figure S16. ^{13}C NMR spectrum of compound **4** (125 MHz, $CDCl_3$).



Elemental Composition Calculator

Target m/z:	336.0564	**Result type:**	Positive ions	**Species:**	$[M+Na]^+$
Elements:		C (0-80); H (0-120); O (0-30); Na (0-5)); N (0-5)); F (0-5)			
Ion Formula		**Calculated m/z**		**PPM Error**	
C13H10F3N3NaO3		336.0566		0.69	

Figure S17. HRESIMS spectrum of compound **4**.

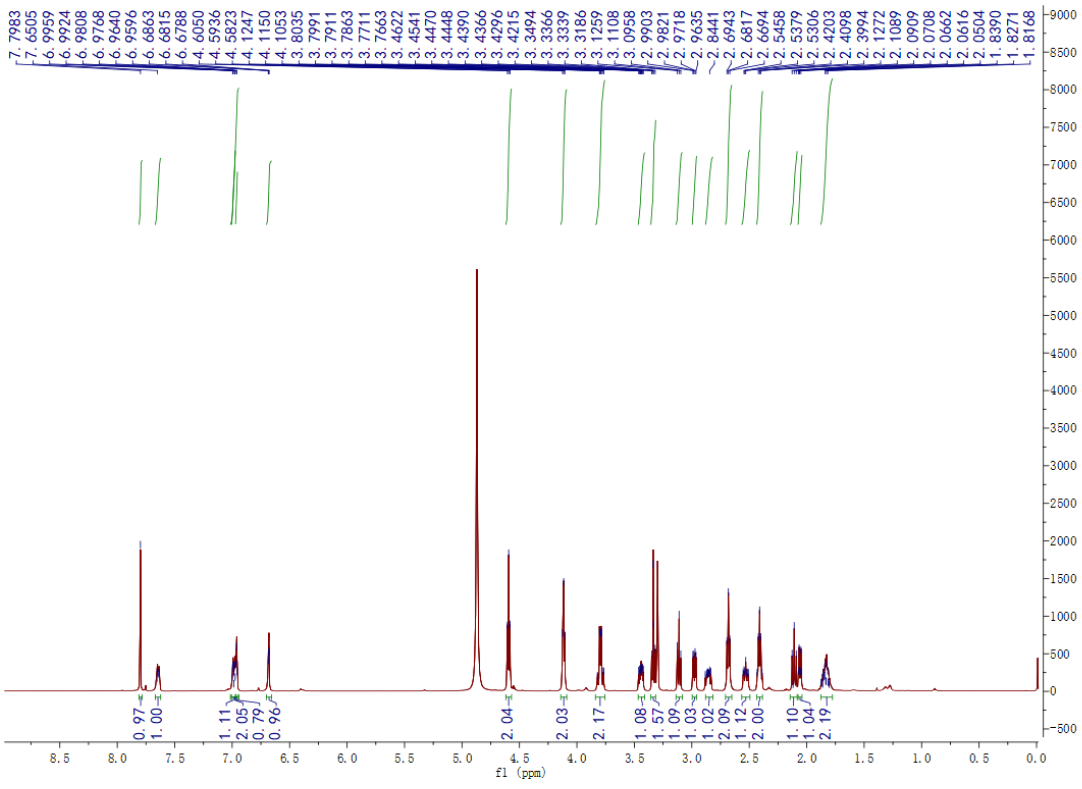


Figure S18. ^{1}H NMR spectrum of compound **5** (500 MHz, CD_3OD).

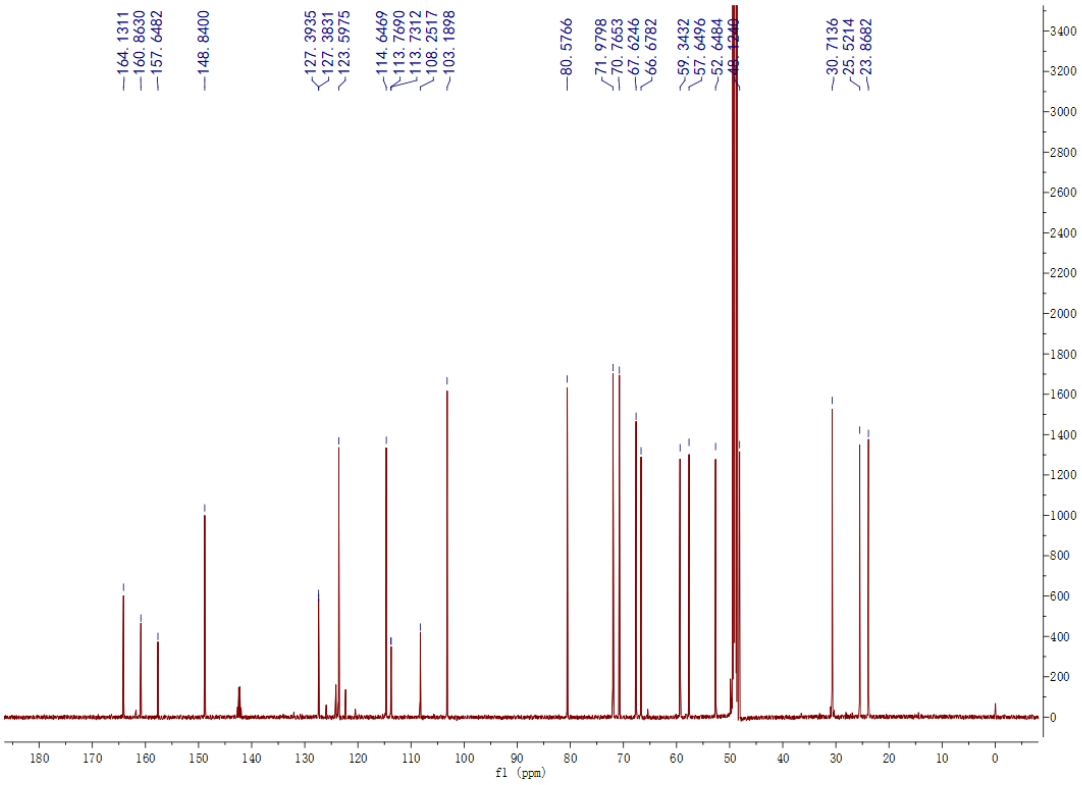
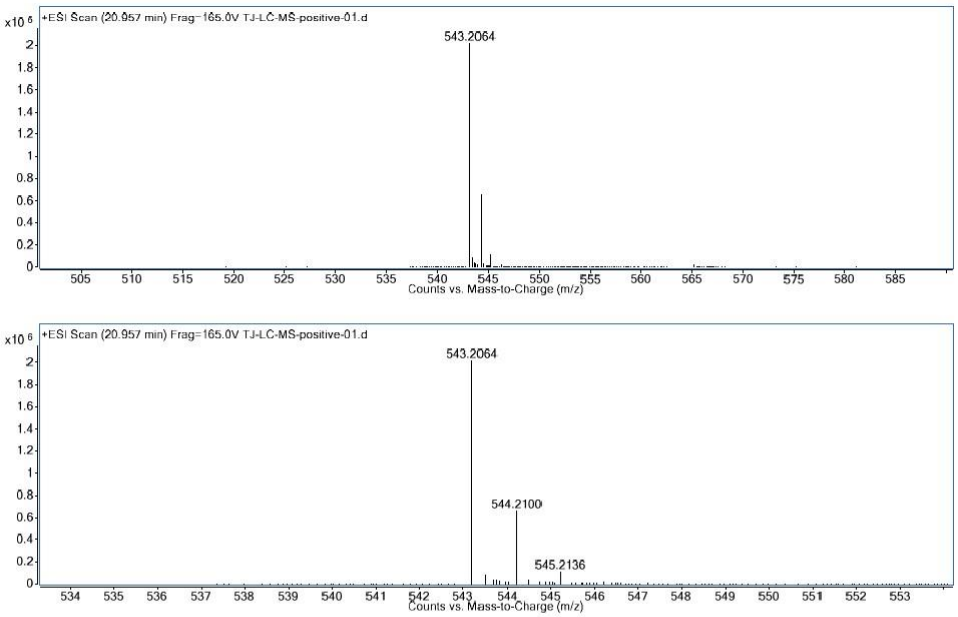


Figure S19. ^{13}C NMR spectrum of compound **5** (125 MHz, CD_3OD).



Elemental Composition Calculator

Target m/z:	543.2064	**Result type:**	Positive ions	**Species:**	$[M+H]^+$
Elements:		C (0-80); H (0-120); O (0-30) ; N(0-5); F(0-5)			
Ion Formula		**Calcalated m/z**		**PPM Error**	
C24H30F3N4O7		543.2061		-0.56	

Figure S20. HRESIMS spectrum of compound **5**.

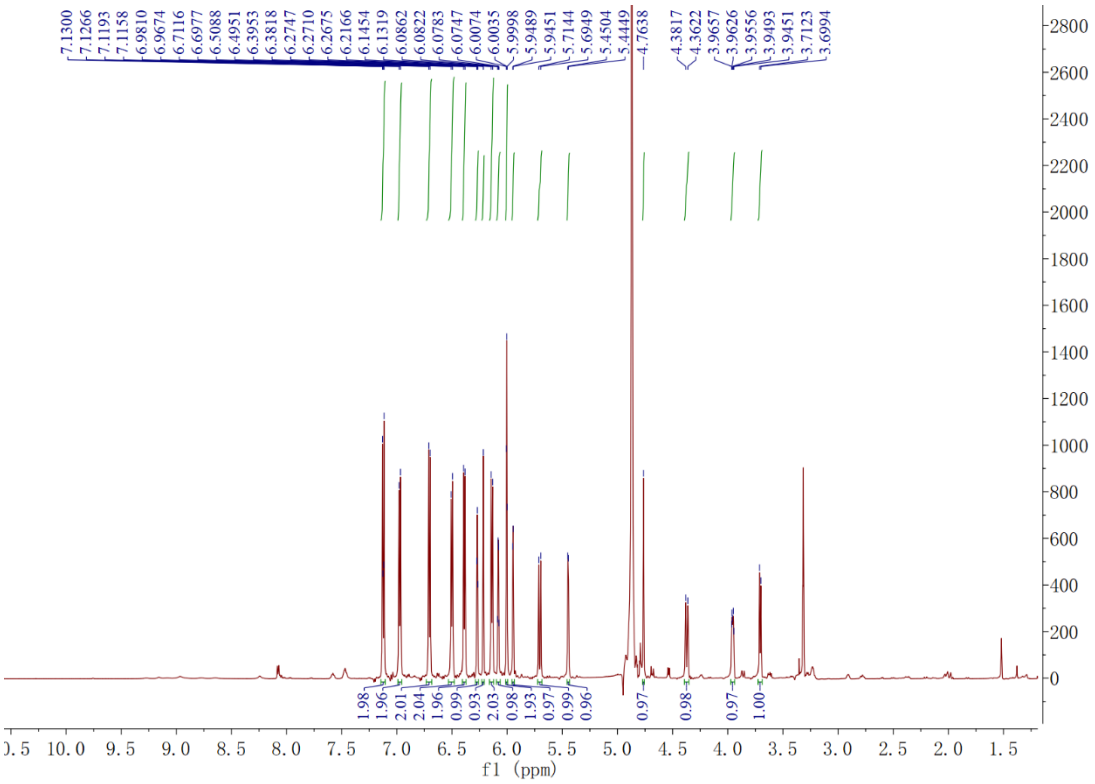


Figure S21. ^{1}H NMR spectrum of Suffruticosol A (600 MHz, CD_3OD).

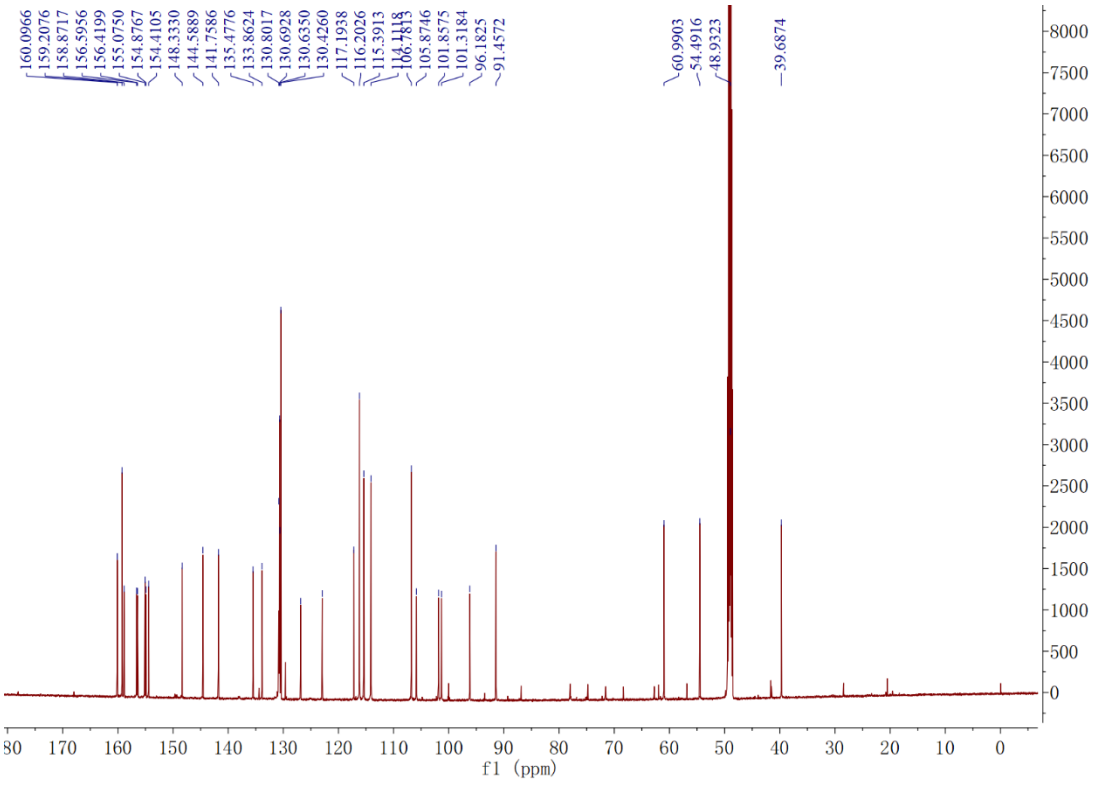
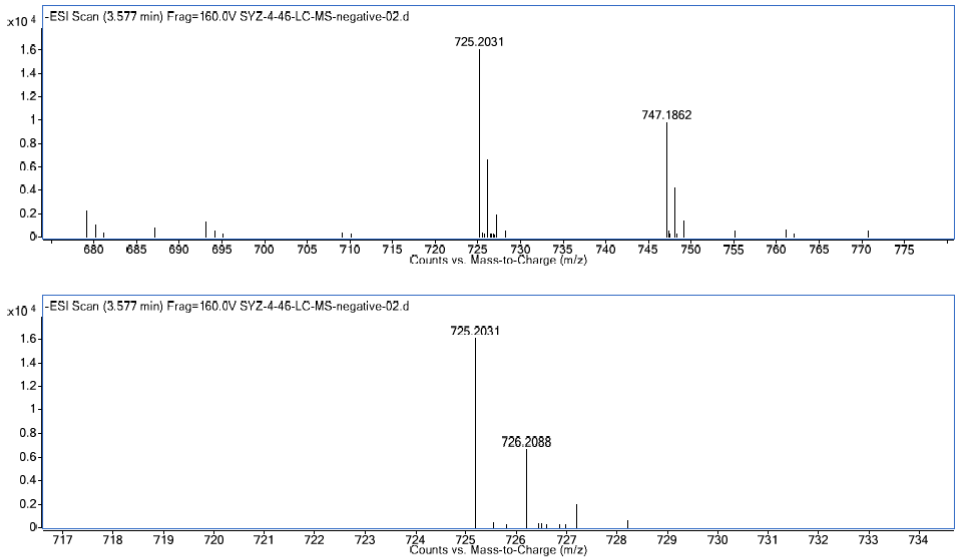


Figure S22. ^{13}C NMR spectrum of Suffruticosol A (150 MHz, CD_3OD).



Elemental Composition Calculator

Target m/z:	725.2031	**Result type:**	Negative ions	**Species:**	[M+COOH]⁻
Elements:		C (0-80); H (0-120); O (0-30); N(0-5)			
Ion Formula		**Calculated m/z**		**PPM Error**	
C43H33O11		725.2028		-0.39	

Figure S23. HRESIMS spectrum of Suffruticosol A.

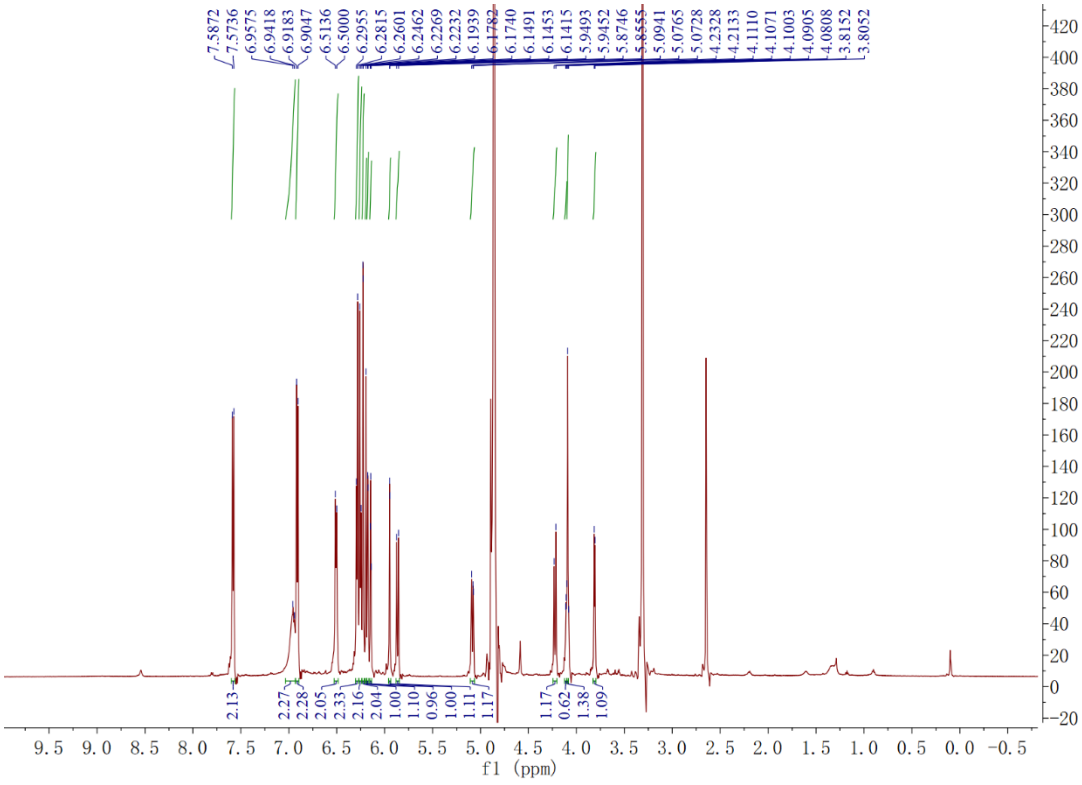


Figure S24. ^{1}H NMR spectrum of Suffruticosol B (600 MHz, CD_3OD).

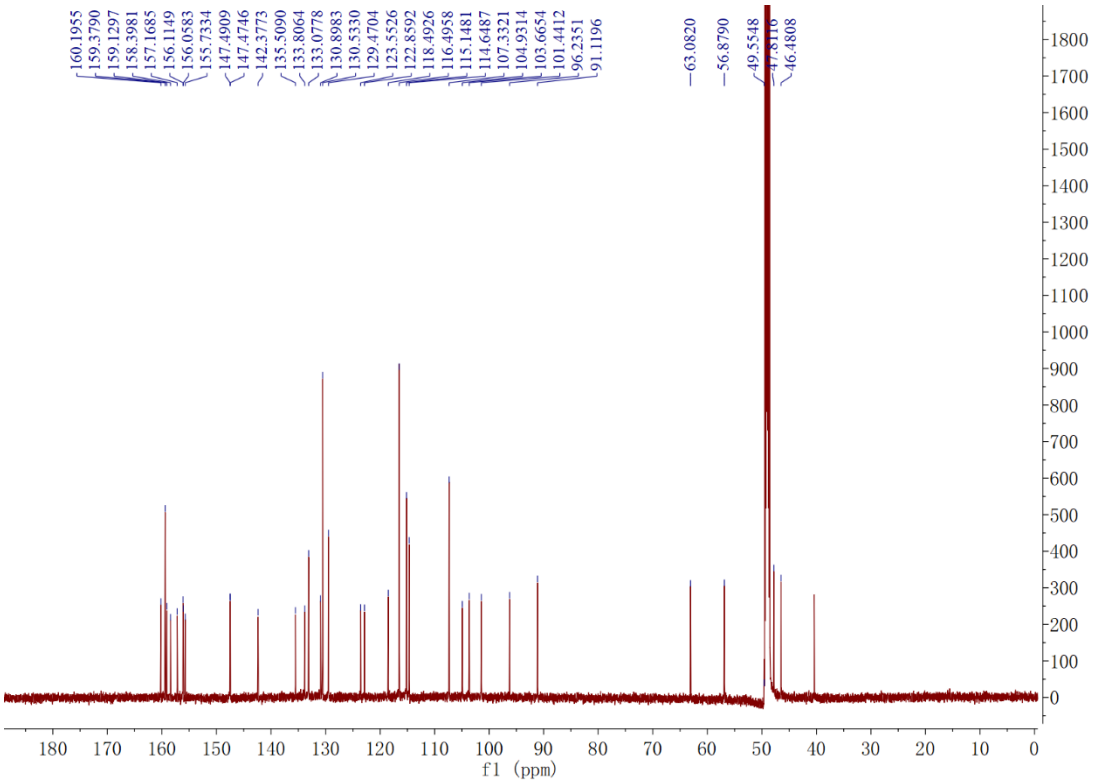
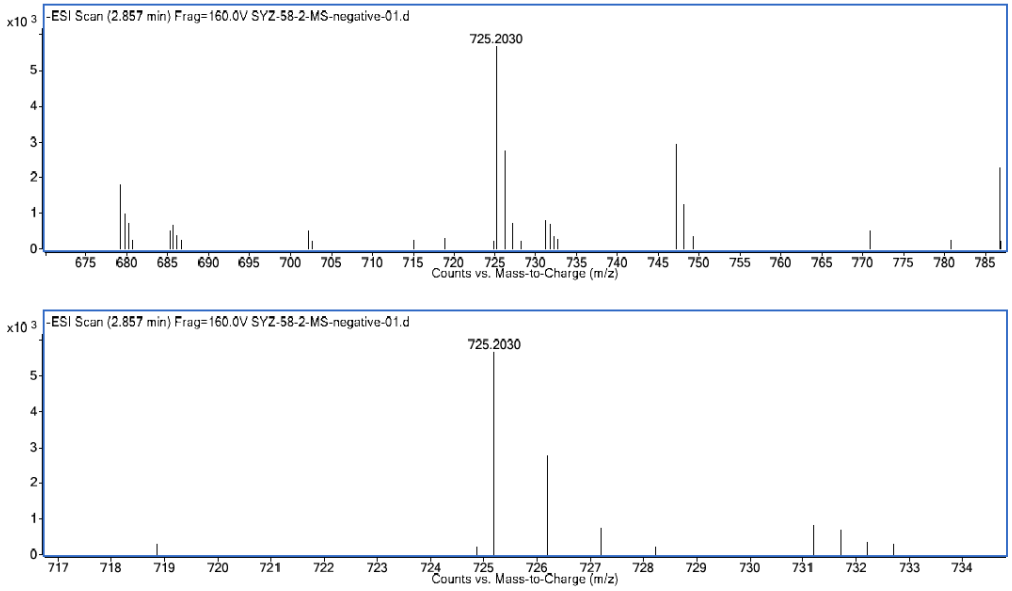


Figure S25. ^{13}C NMR spectrum of Suffruticosol B (150 MHz, CD_3OD).



Elemental Composition Calculator

Target m/z:	725.2030	**Result type:**	Negative ions	**Species:**	[M+COOH]$^-$
Elements:		C (0-80); H (0-120); O (0-30); N(0-5)			
Ion Formula		**Calculated m/z**		**PPM Error**	
C43H33O11		725.2028		-0.26	

Figure S26. HRESIMS spectrum of Suffruticosol B.

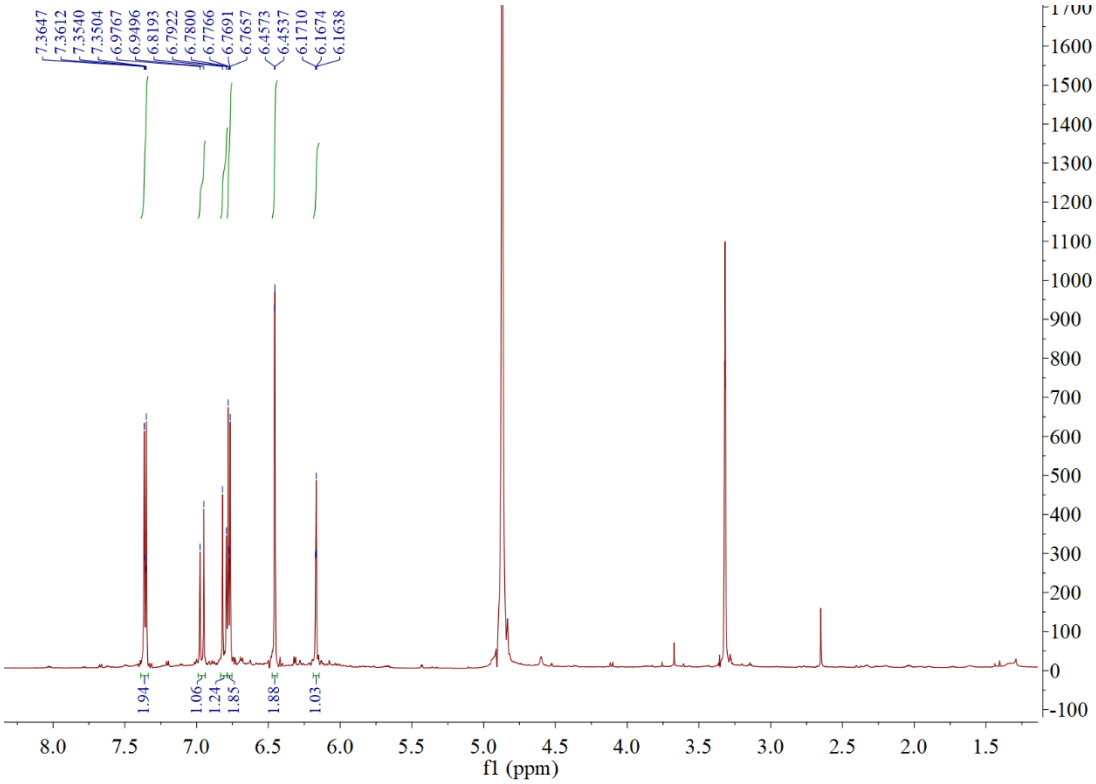


Figure S27. ^{1}H NMR spectrum of Resveratrol (600 MHz, CD_3OD).

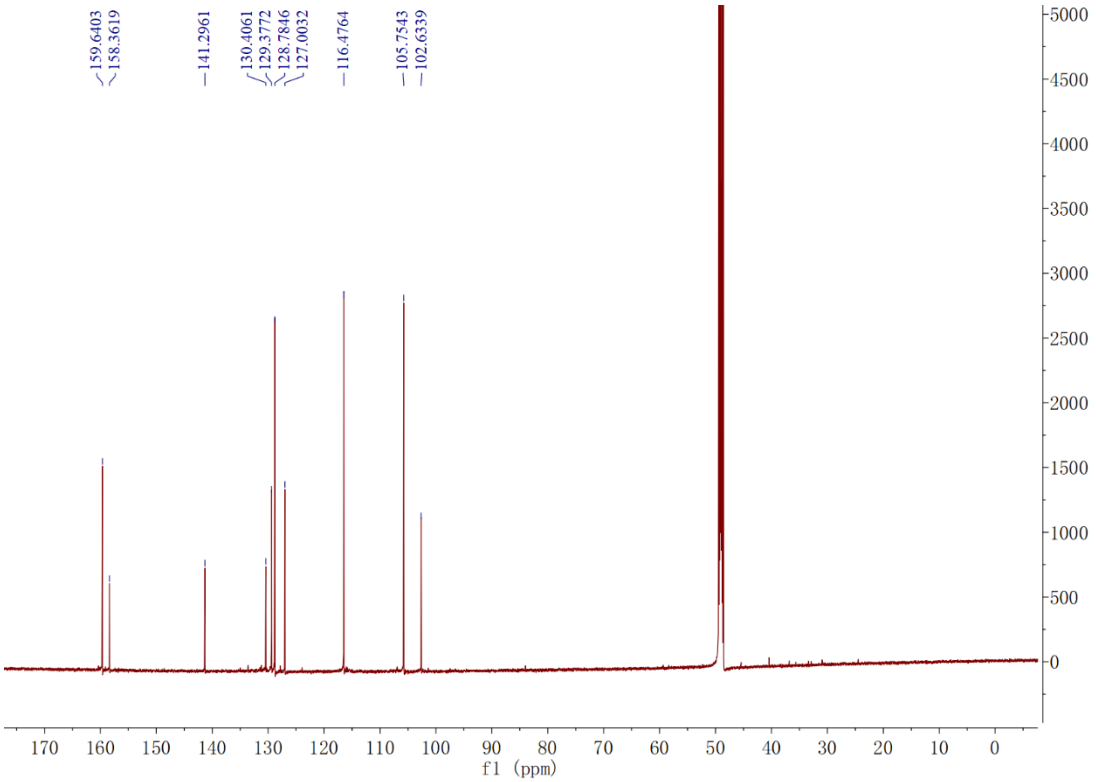


Figure S28. ^{13}C NMR spectrum of Resveratrol (150 MHz, CD_3OD).

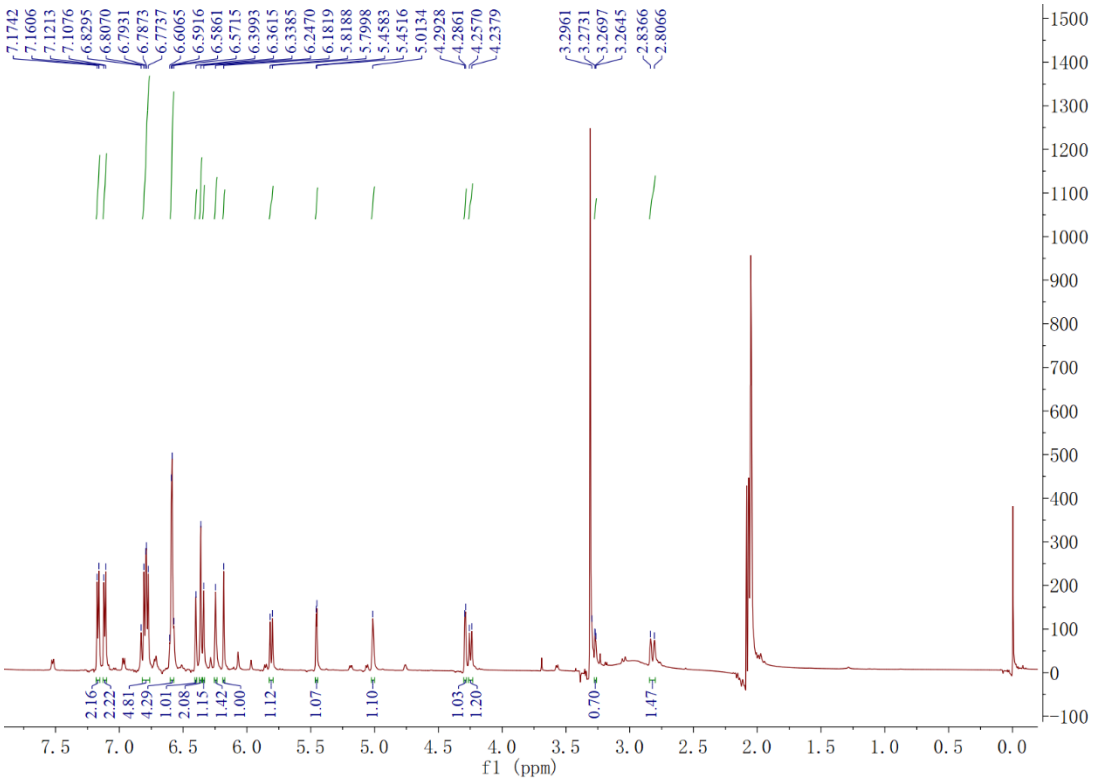


Figure S29. ^{1}H NMR spectrum of Vitisin E (600 MHz, CD_3COCD_3).

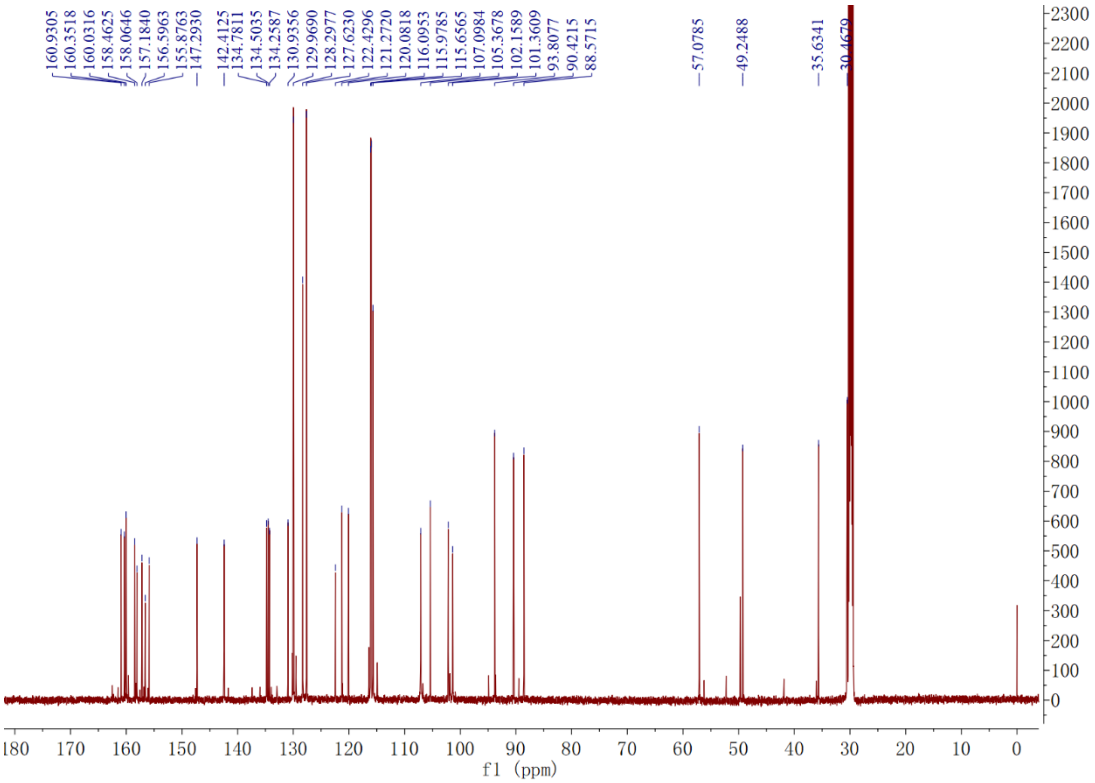
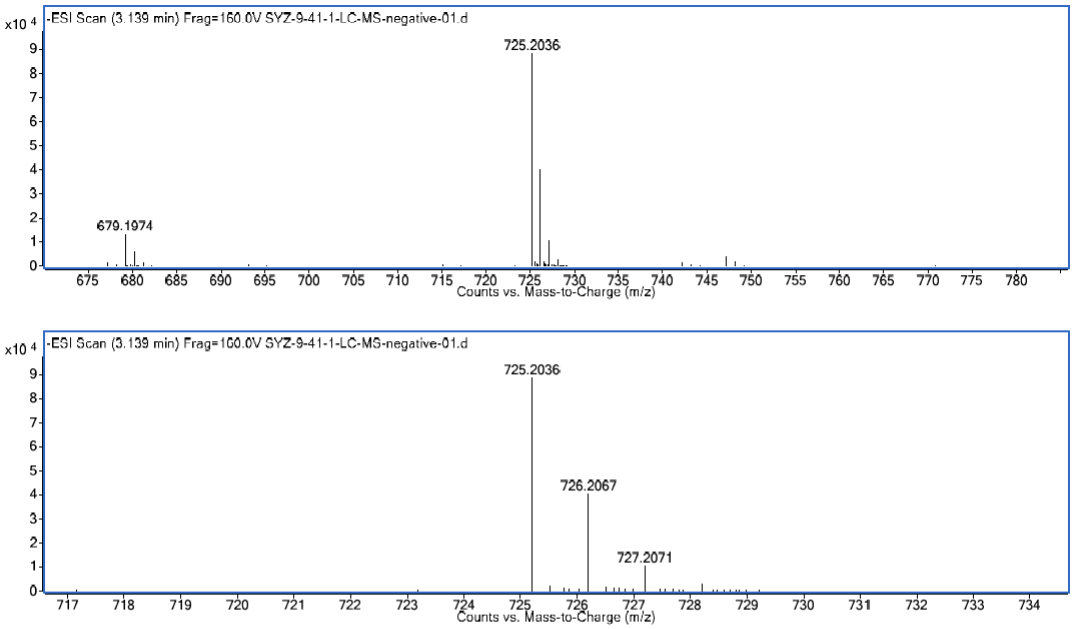


Figure S30. ^{13}C NMR spectrum of Vitisin E (150 MHz, CD_3COCD_3).



Elemental Composition Calculator

Target m/z:	725.2036	**Result type:**	Negative ions	**Species:**	$[M+COOH]^-$
Elements:		C (0-80); H (0-120); O (0-30); N(0-5)			
Ion Formula		**Calculated m/z**		**PPM Error**	
C43H33O11		725.2028		-1.04	

Figure S31. HRESIMS spectrum of Vitisin E.

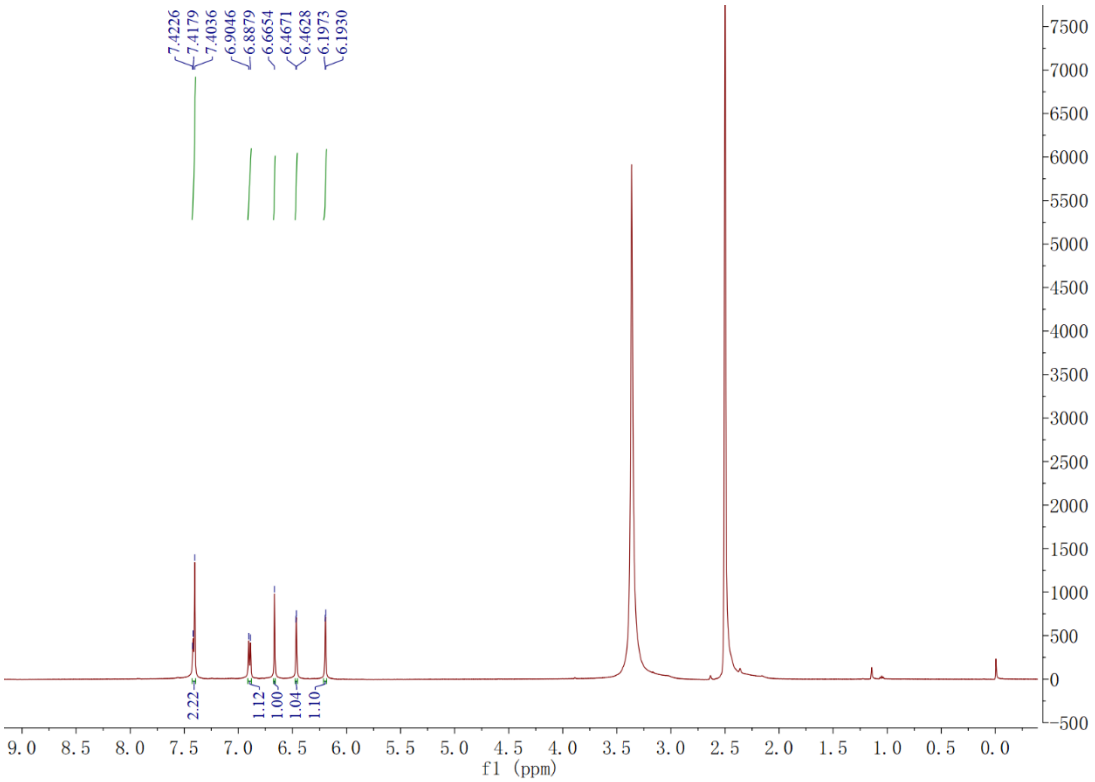


Figure S32. ^{1}H NMR spectrum of Luteolin (500 MHz, CD_3OD).

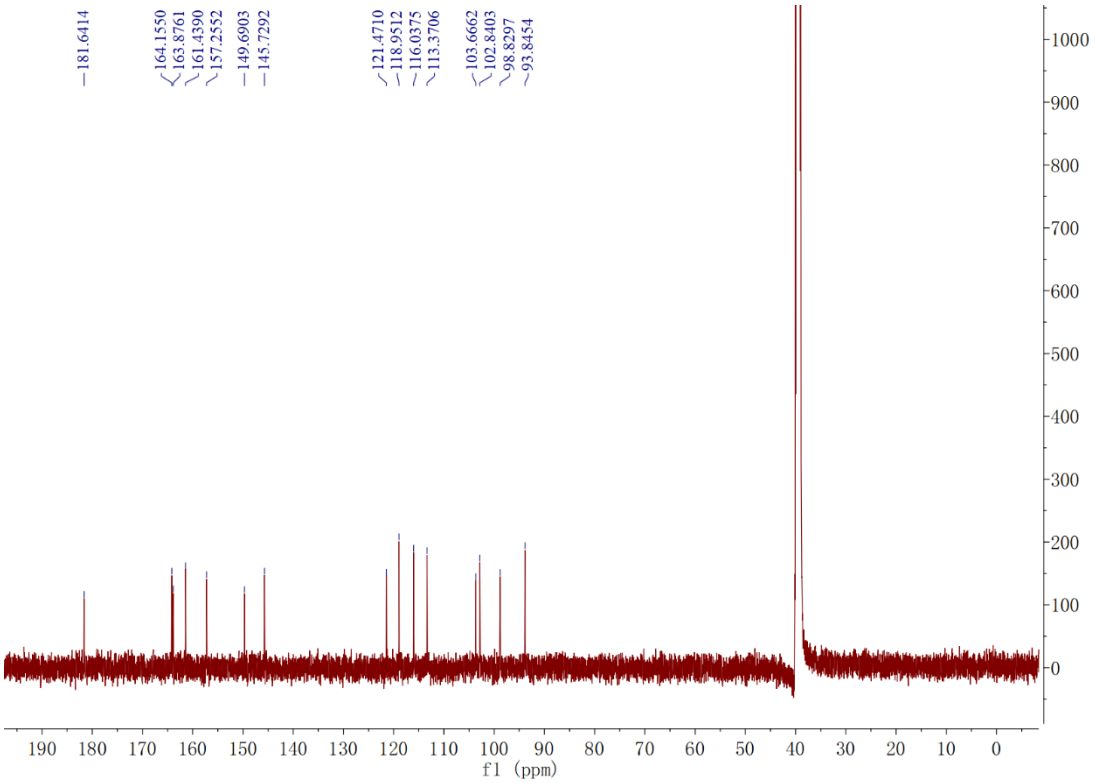
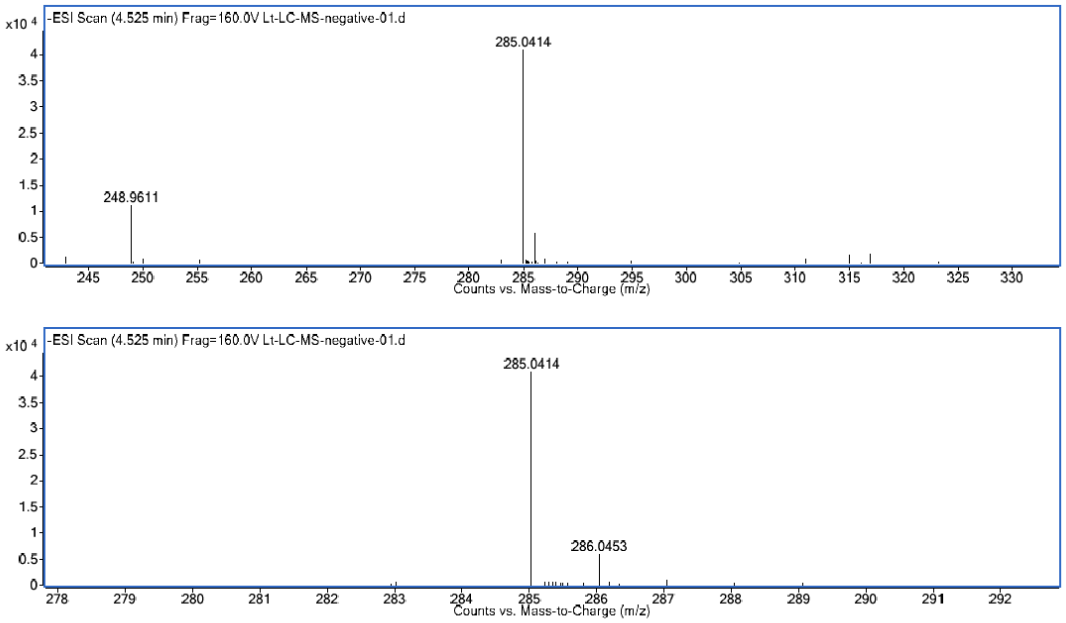


Figure S33. ^{13}C NMR spectrum of Luteolin (125 MHz, CD_3OD).



Elemental Composition Calculator

Target m/z:	285.0414	**Result type:**	Negative ions	**Species:**	$[M-H]^-$
Elements:		C (0-80); H (0-120); O (0-30); N(0-5)			
Ion Formula		**Calculated m/z**		**PPM Error**	
C15H9O6		285.0405		-3.39	

Figure S34. HRESIMS spectrum of Luteolin.

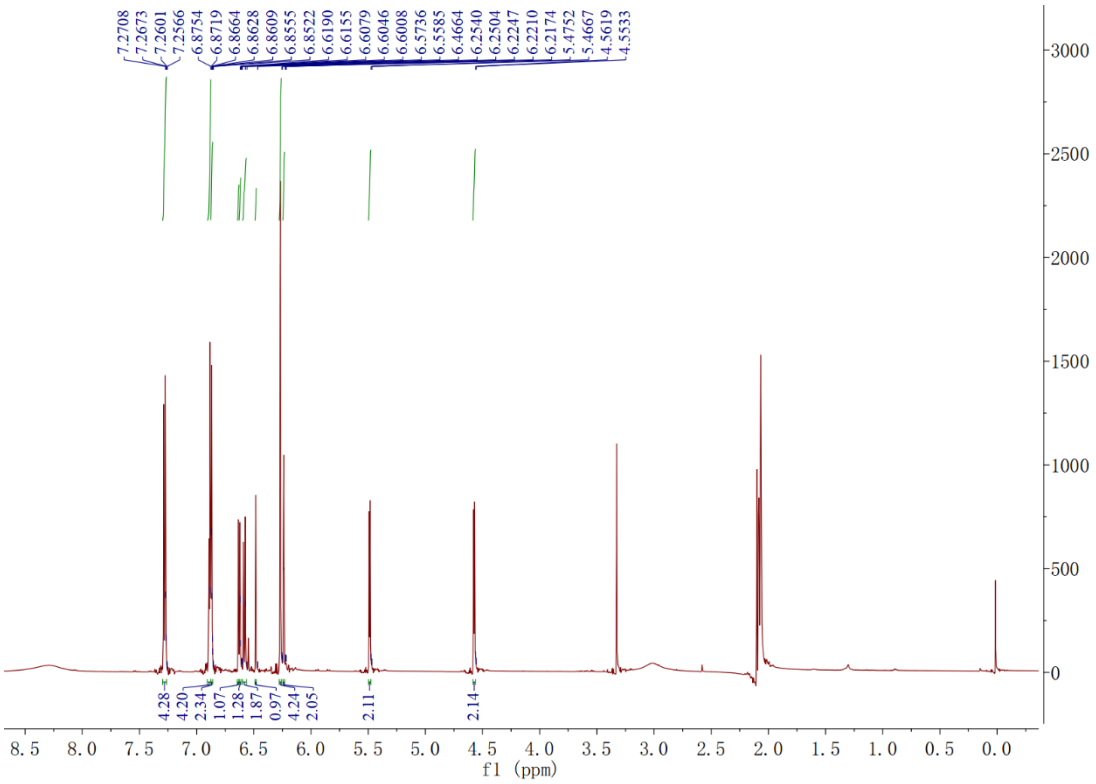


Figure S35. ^{1}H NMR spectrum of Ampelopsin E (600 MHz, CD_3COCD_3).

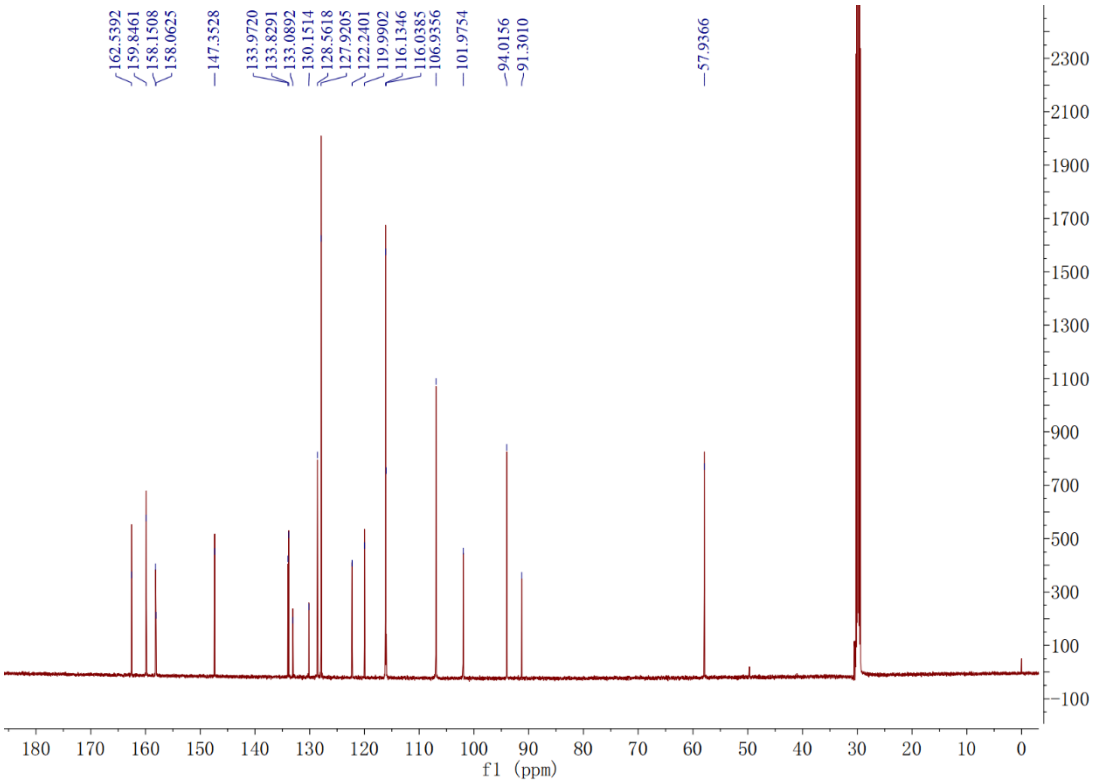
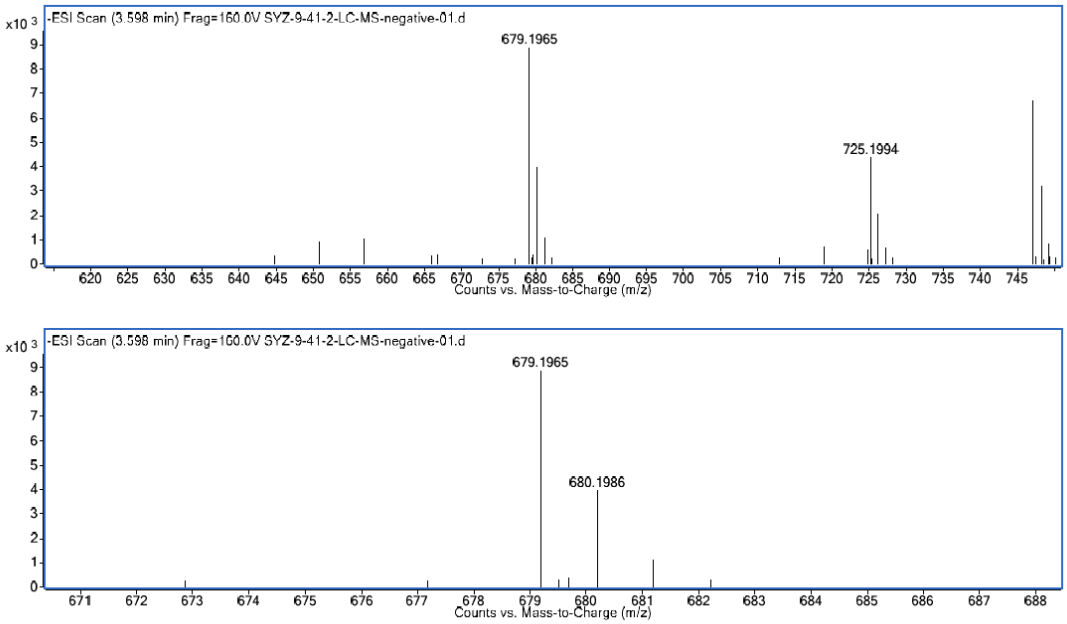


Figure S36. ^{13}C NMR spectrum of Ampelopsin E (150 MHz, CD_3COCD_3).



Elemental Composition Calculator

Target m/z:	679.1965	**Result type:**	Negative ions	**Species:**	$[M-H]^-$
Elements:		C (0-80); H (0-120); O (0-30); N(0-5)			
Ion Formula		**Calculated m/z**		**PPM Error**	
$C_{43}H_{31}O_9$		679.1974		1.19	

Figure S37. HRESIMS spectrum of Ampelopsin E.

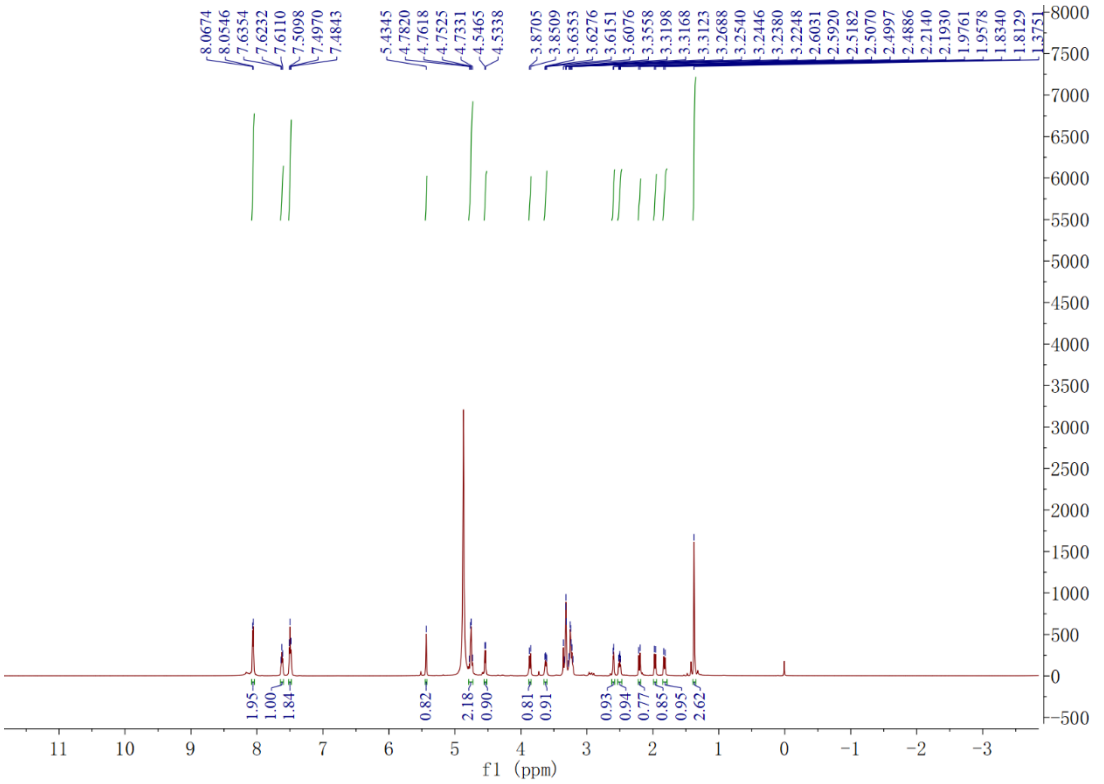


Figure S38. ^{1}H NMR spectrum of Paeoniflorin (600 MHz, CD_3OD).

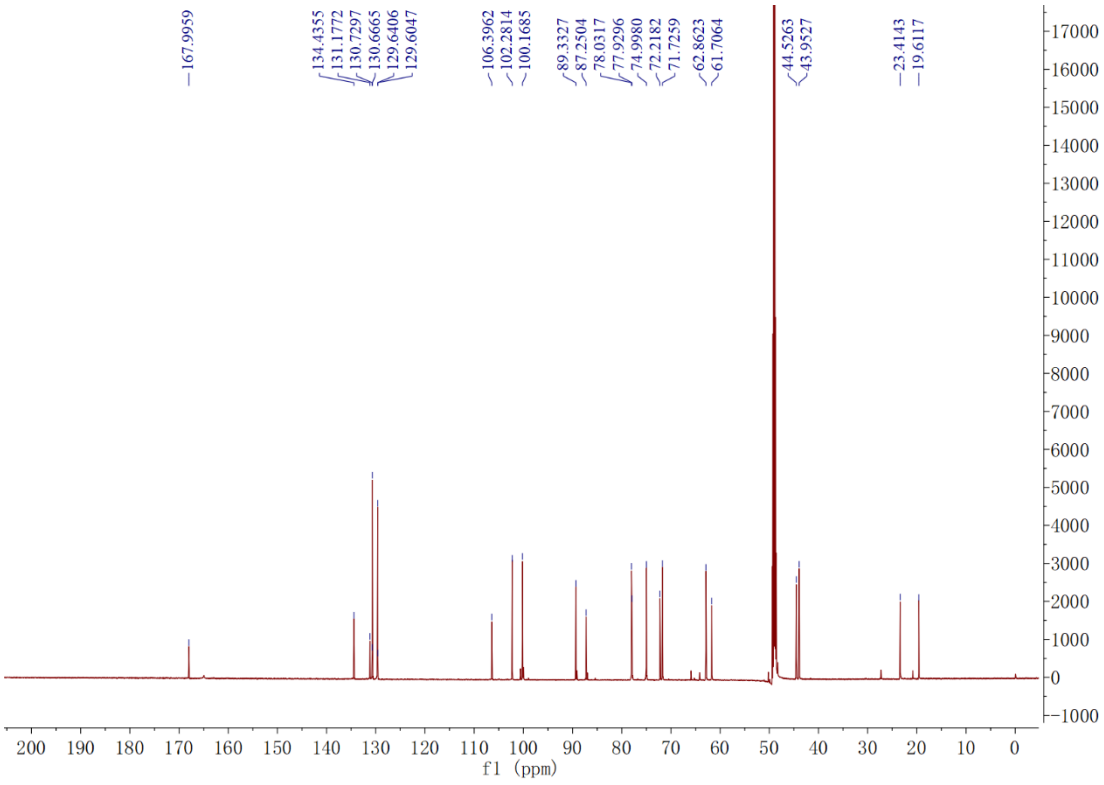
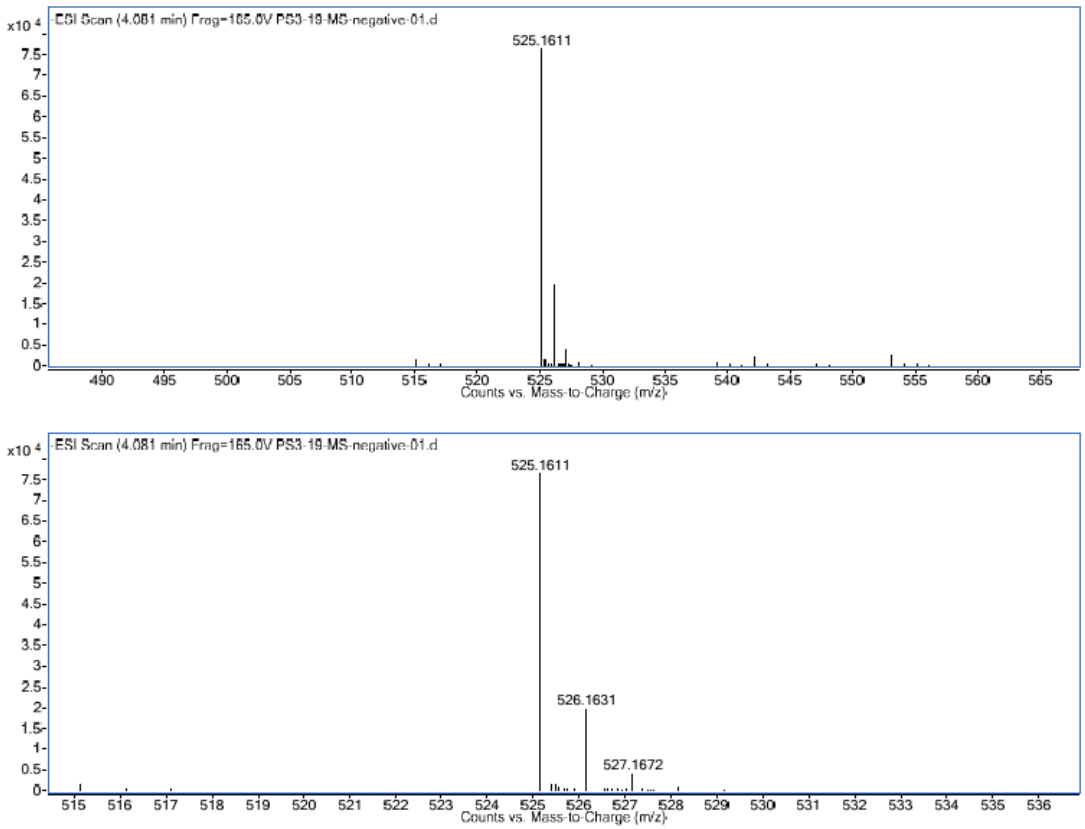


Figure S39. ^{13}C NMR spectrum of Paeoniflorin (150 MHz, CD_3OD).



Elemental Composition Calculator

Target m/z:	525.1611	**Result type:**	Negative ions	**Species:**	$[M+COOH]^-$
Elements:		C (0-80); H (0-120); O (0-30)			
Ion Formula		**Calculated m/z**		**PPM Error**	
C24H29O13		525.1614		0.43	

Figure S40. HRESIMS spectrum of Paeoniflorin.

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