Monoterpenoid Glycosides from the Leaves of *Ligustrum robustum* and Their Bioactivities (II)

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Figures S1-S6: ^{1}H NMR, ^{13}C NMR, ^{1}H-^{1}H COSY, HSQC, HMBC, NOEDS, HRESIMS and IR spectra of compounds **1** (Figure S1), **2** (Figure S2), **3** (Figure S3), **4** (Figure S4), **5** (Figure S5) and **6** (Figure S6);

S1: ^{1}H NMR and ^{13}C NMR data of compounds **4a**, **6a, 7**, **8a** and **8b**;

S2: determination of bioactivities.

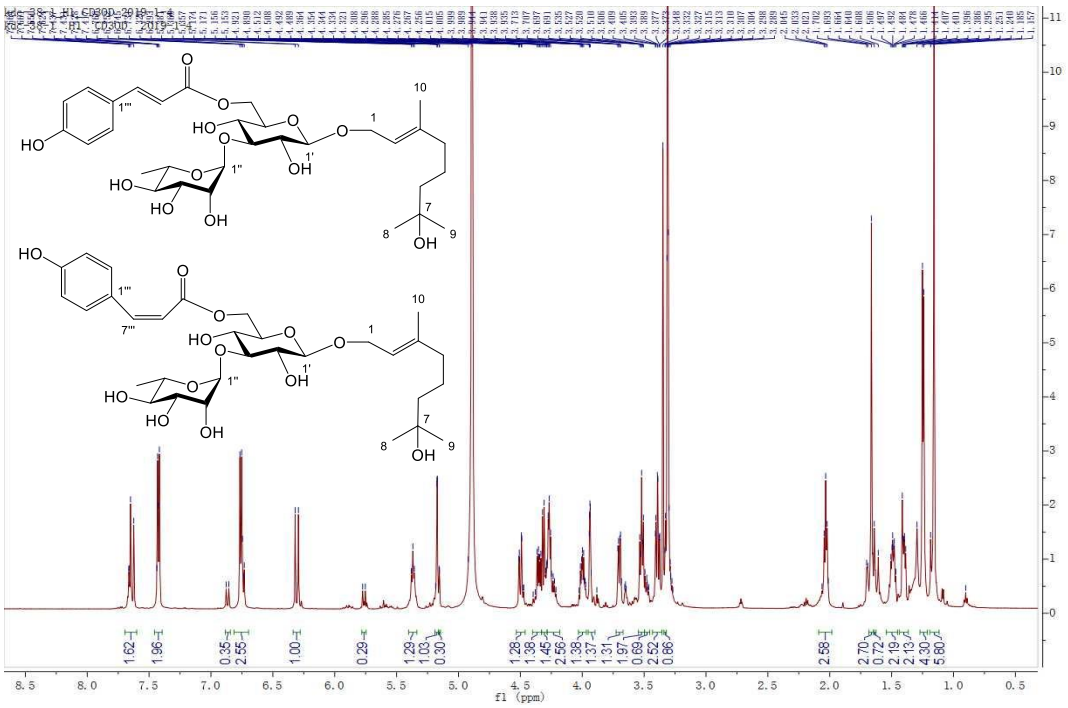

Figure S1-1 ^{1}H NMR spectrum of compound **1** in CD_3OD (600 MHz)

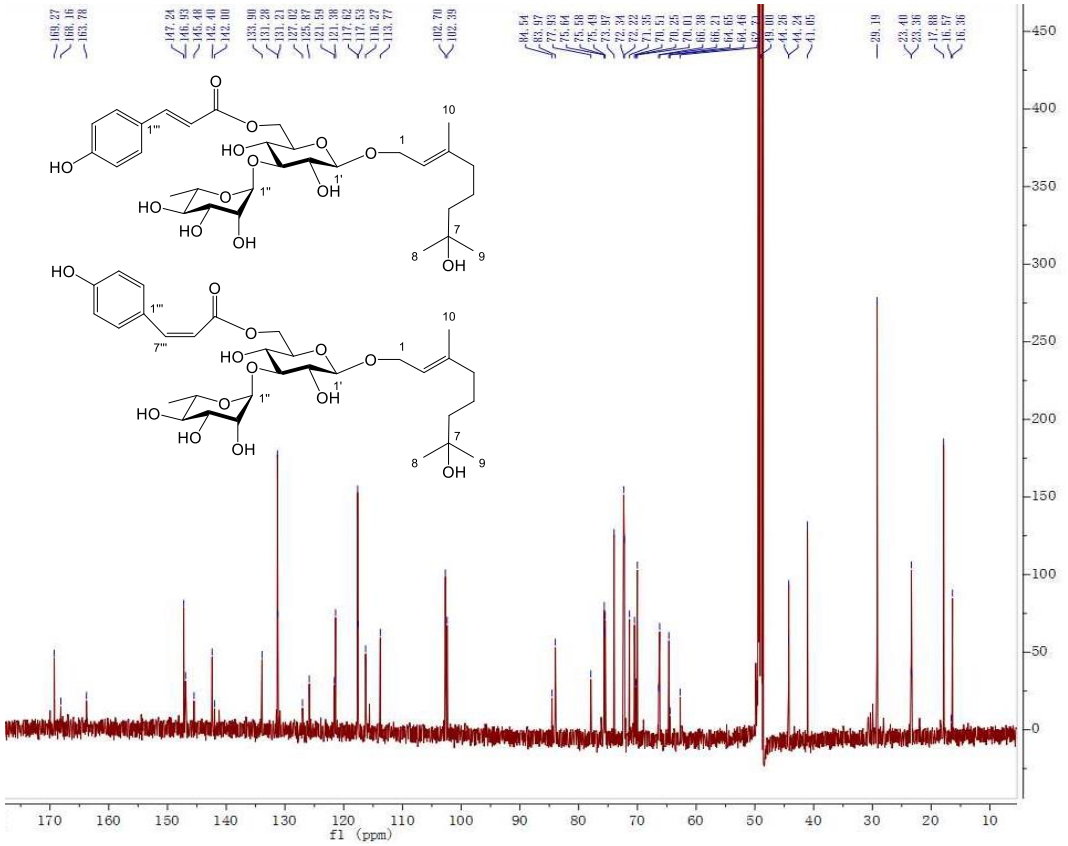

Figure S1-2 ^{13}C NMR spectrum of compound **1** in CD_3OD (150 MHz)

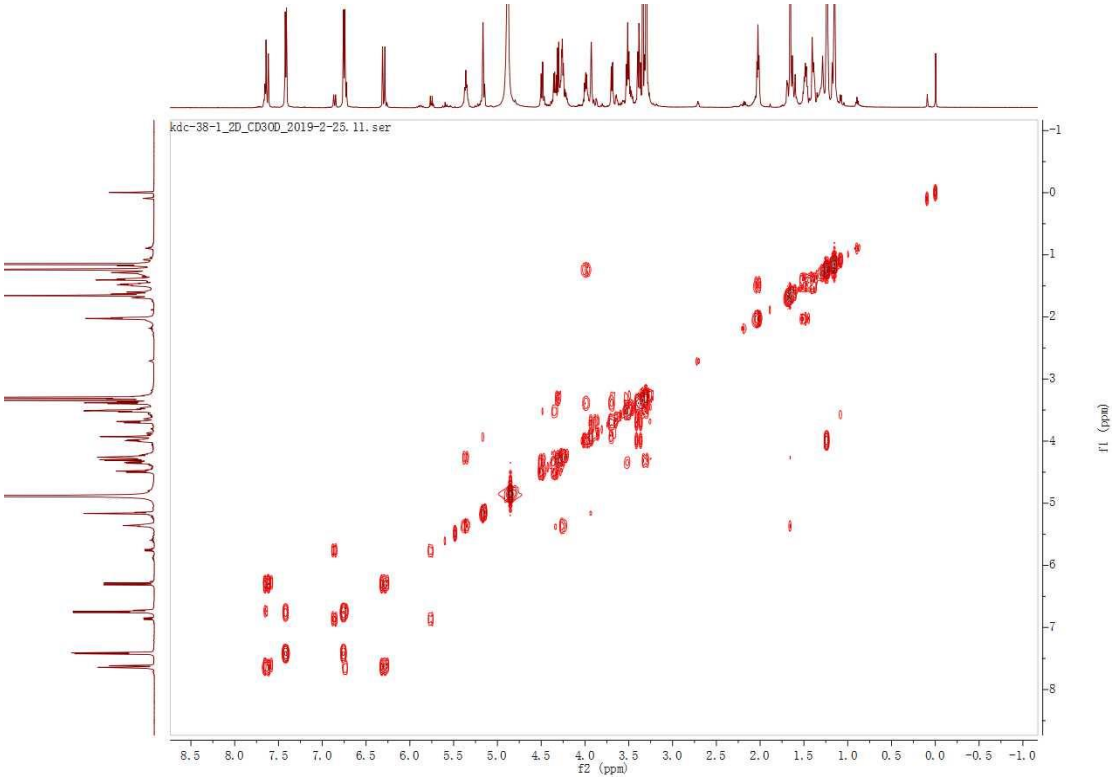

Figure S1-3 ^{1}H-^{1}H COSY spectrum of compound **1** in CD_3OD

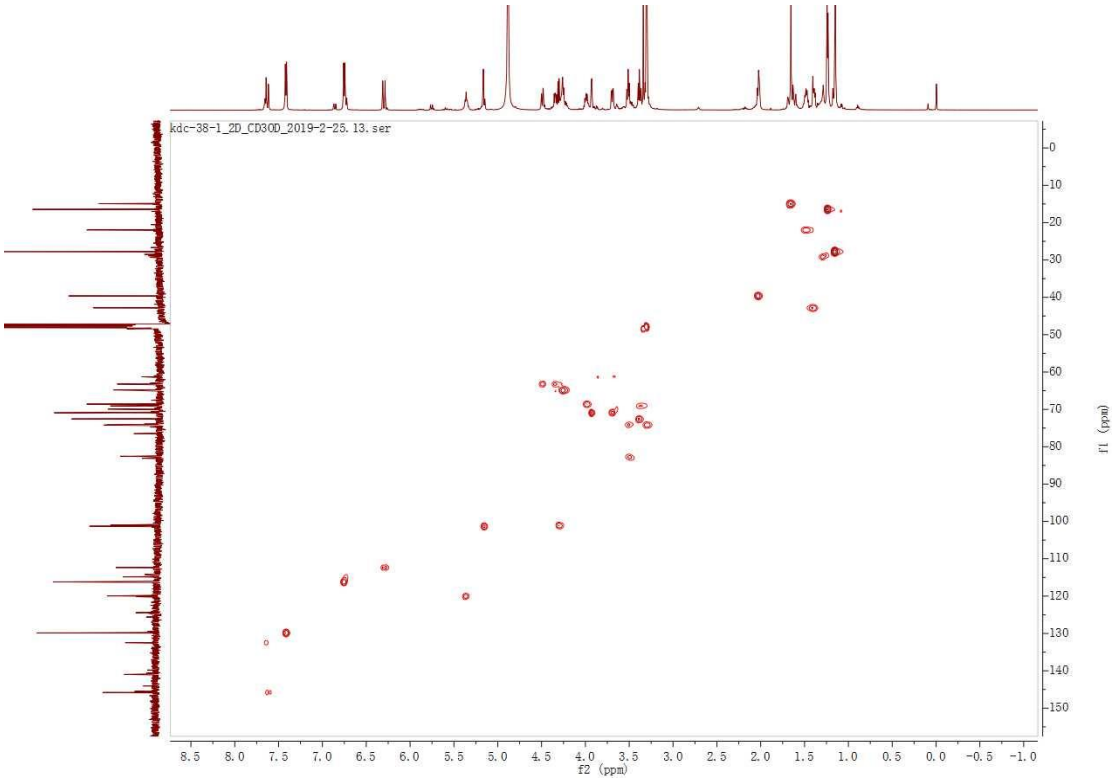

Figure S1-4 HSQC spectrum of compound **1** in CD_3OD

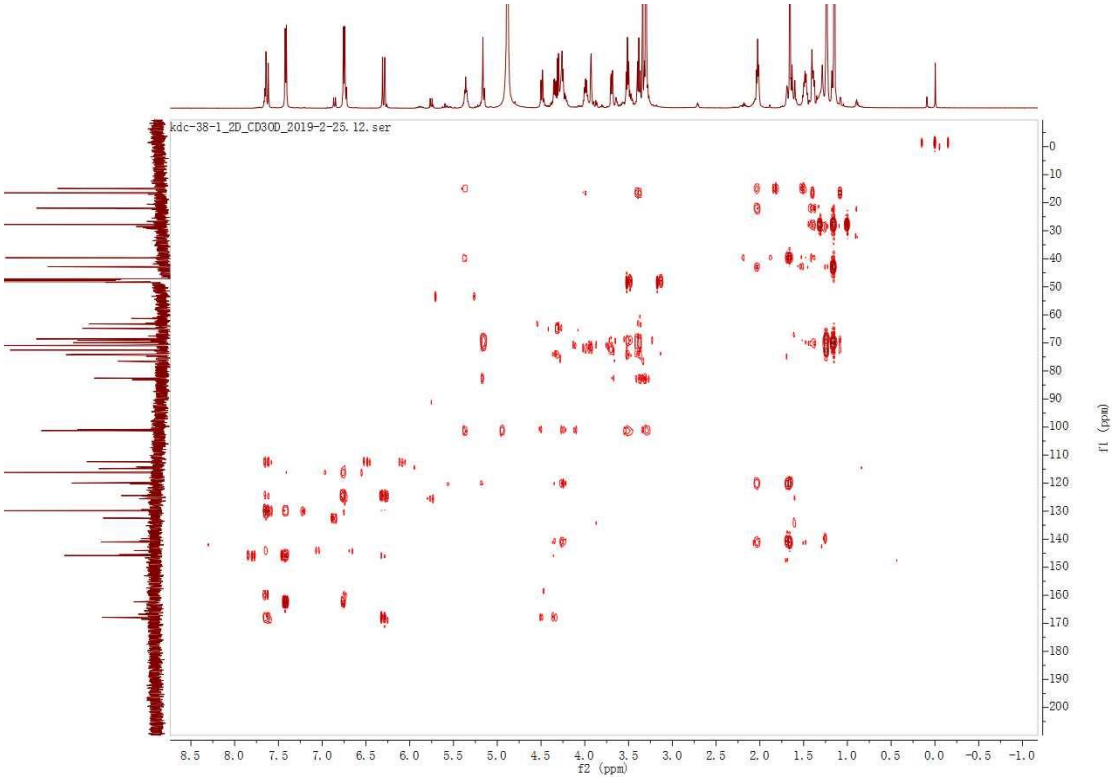

Figure S1-5 HMBC spectrum of compound **1** in CD_3OD

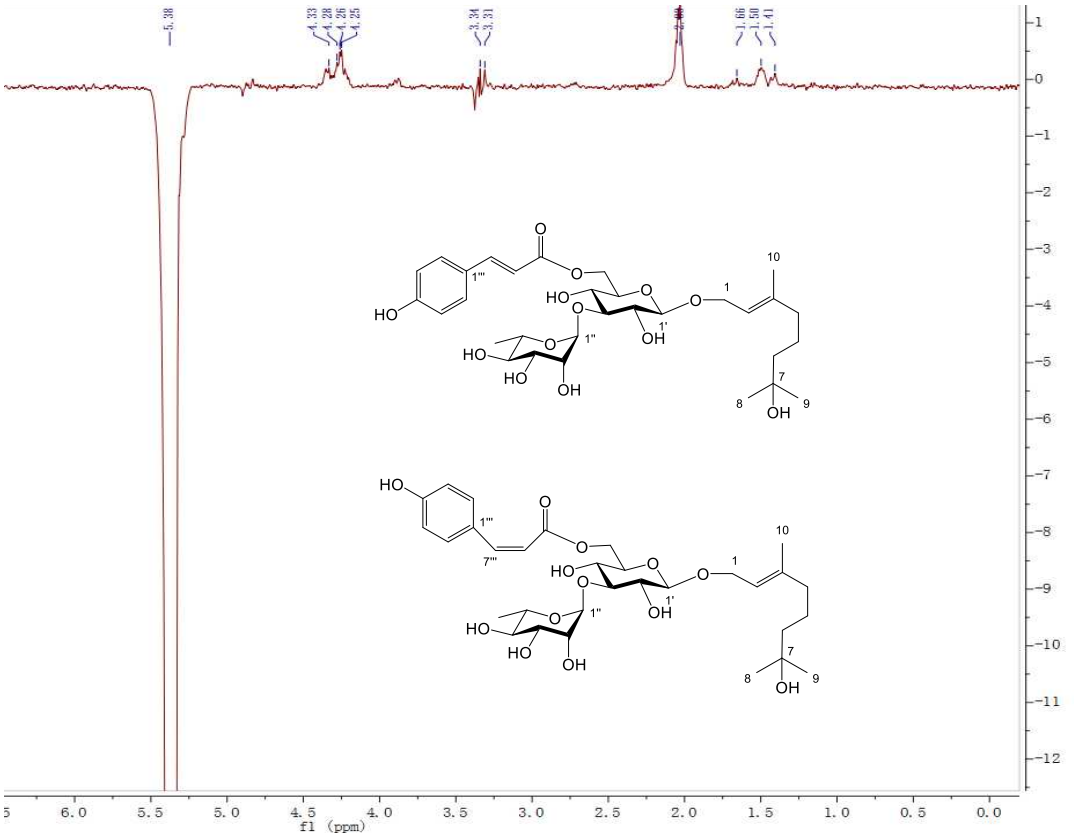

Figure S1-6 NOEDS spectrum of compound **1** in CD_3OD (600 MHz)

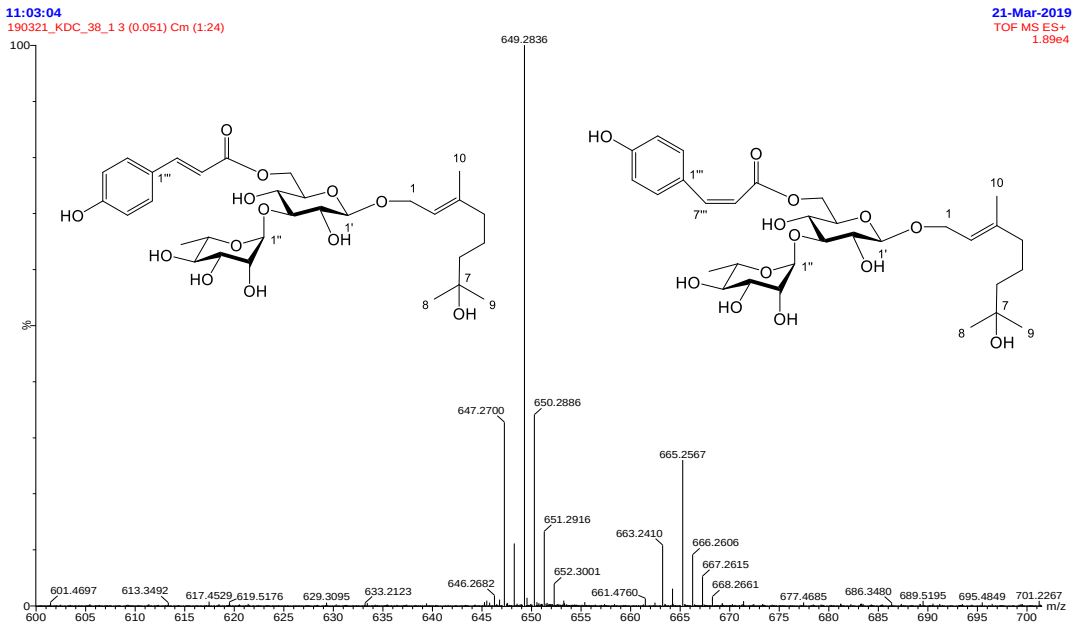

Figure S1-7 HRESIMS spectrum of compound **1**

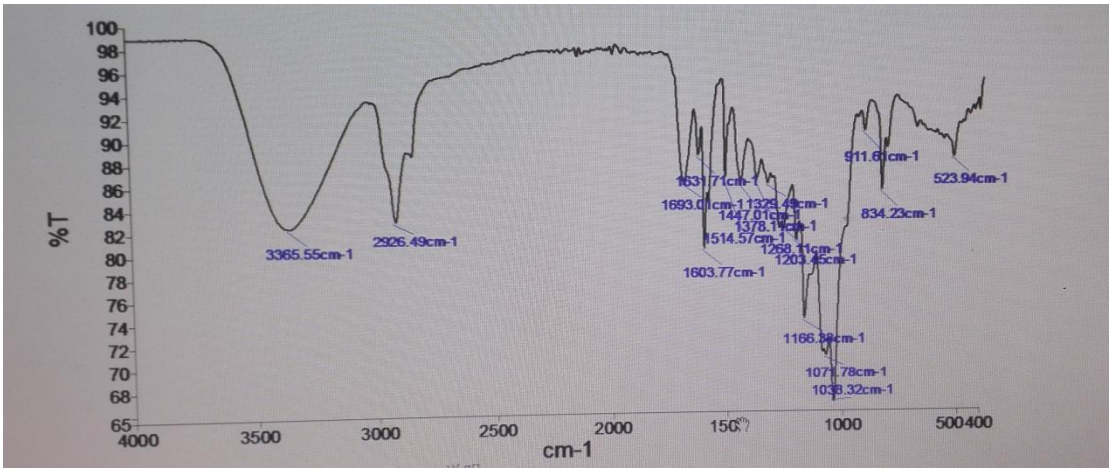

Figure S1-8 IR spectrum of compound **1** (film)

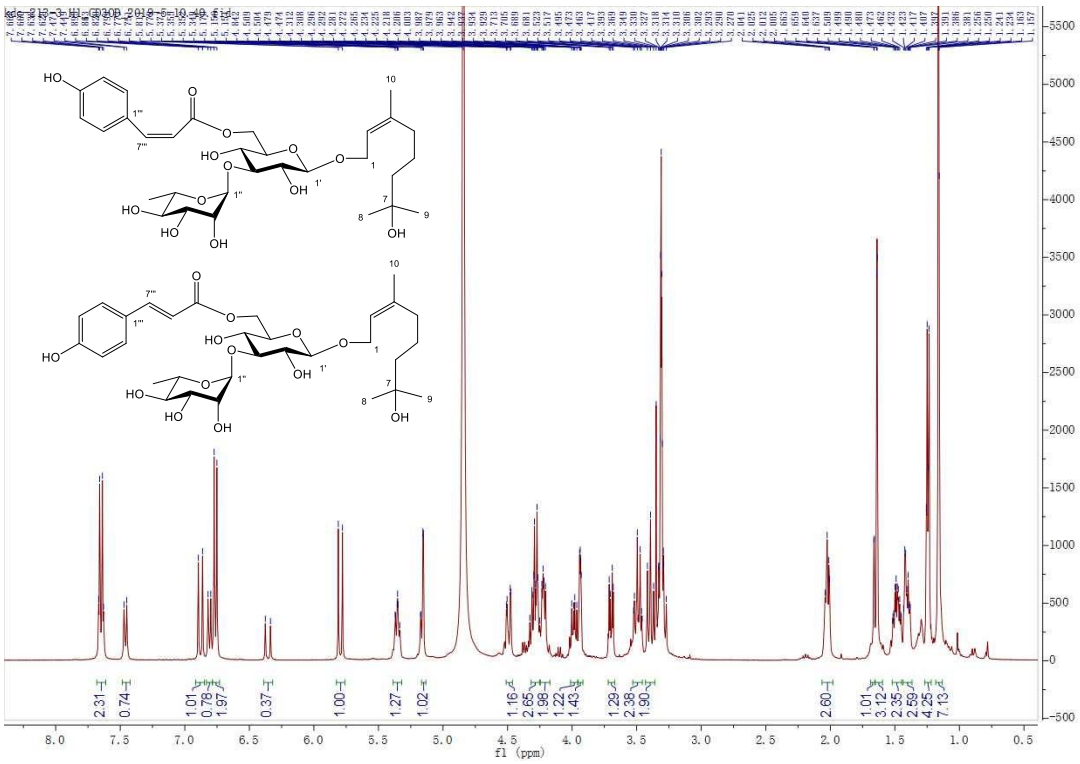

Figure S2-1 ^{1}H NMR spectrum of compound **2** in CD_3OD (400 MHz)

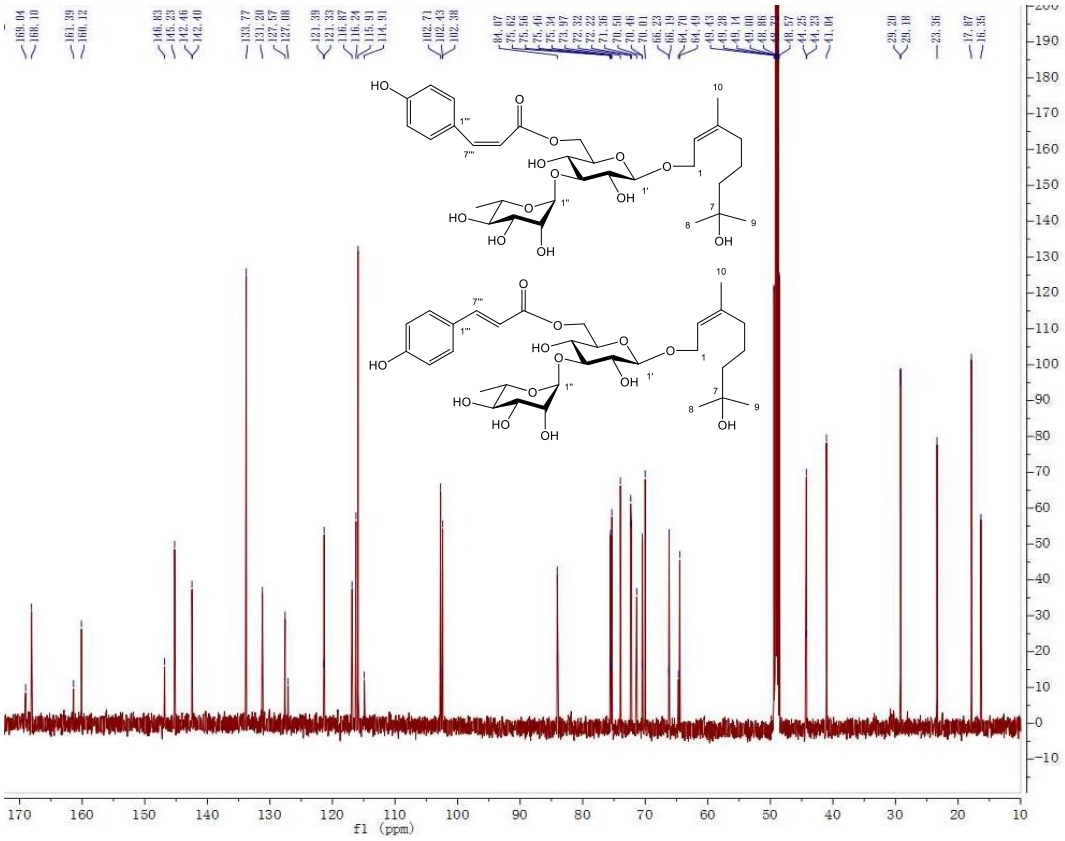

Figure S2-2 ^{13}C NMR spectrum of compound **2** in CD_3OD (150 MHz)

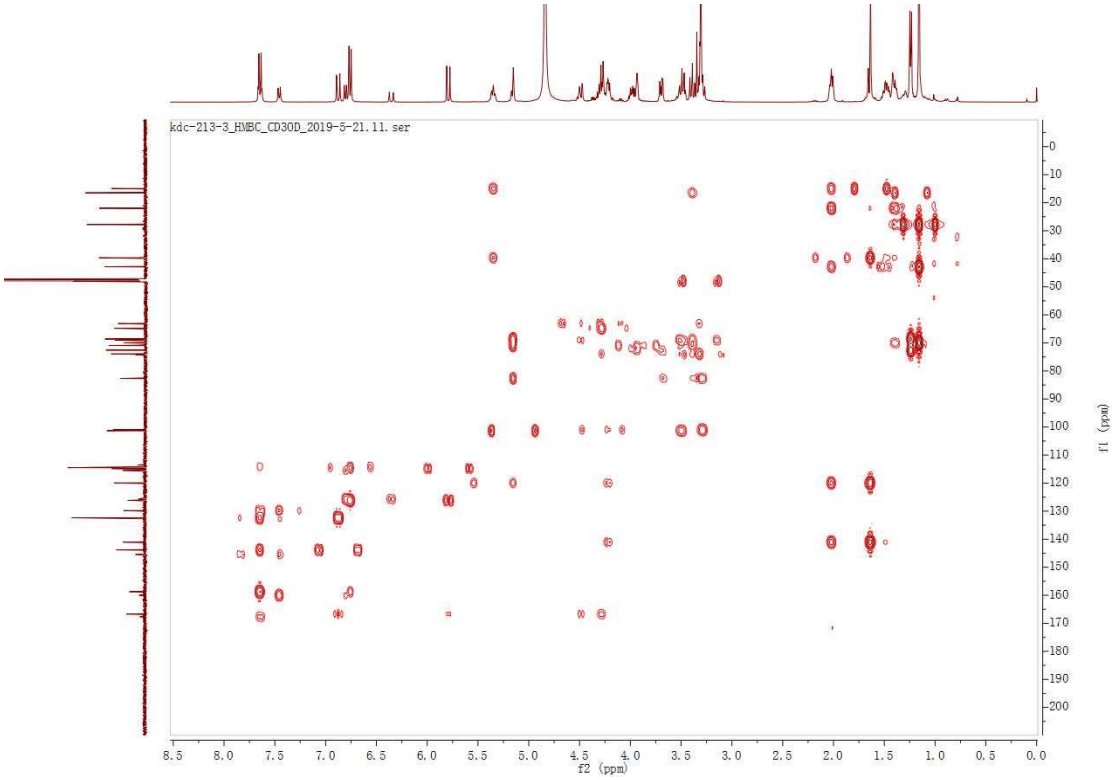

Figure S2-3 HMBC spectrum of compound **2** in CD_3OD

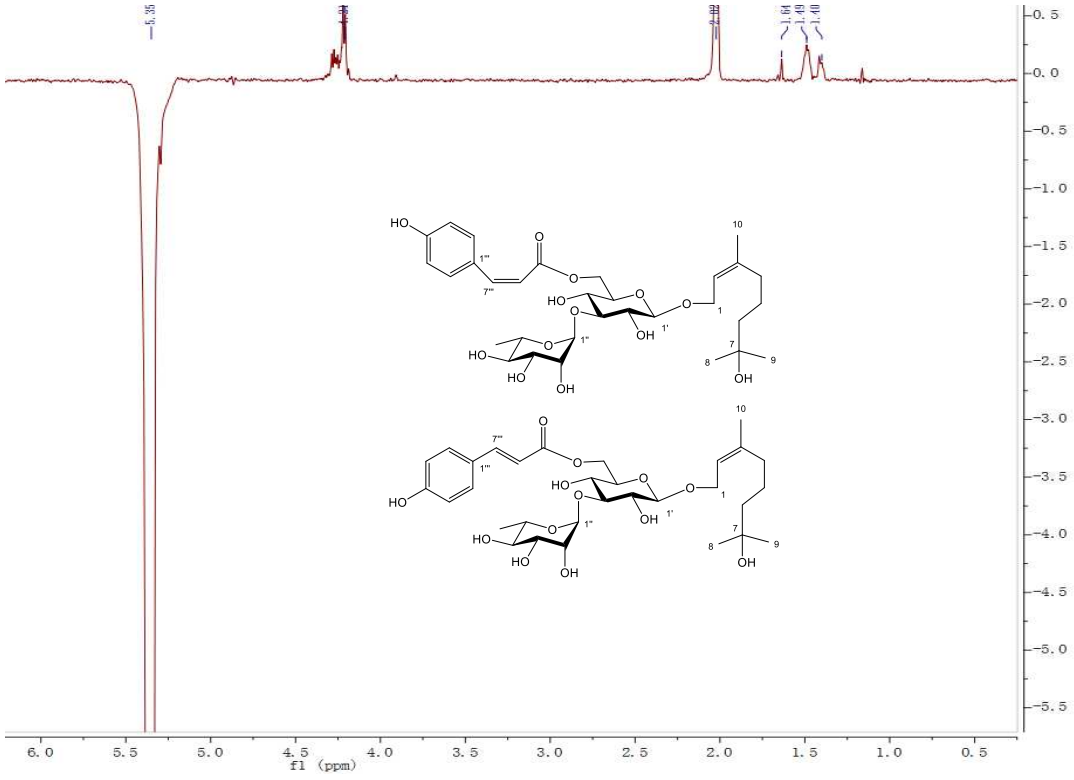

Figure S2-4 NOEDS spectrum of compound **2** in CD_3OD (600 MHz)

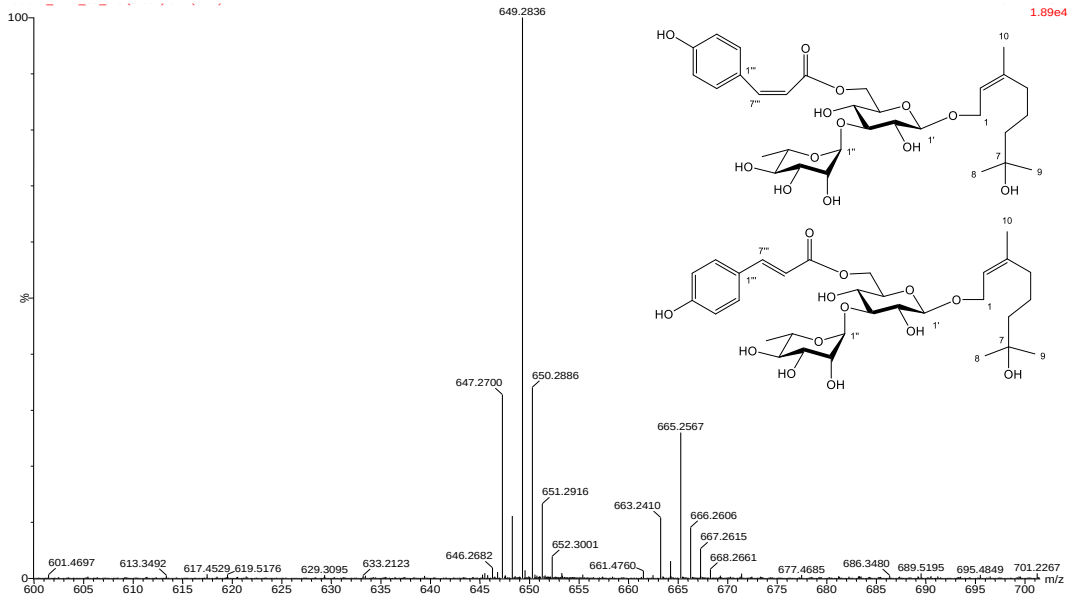

Figure S2-5 HRESIMS spectrum of compound **2**

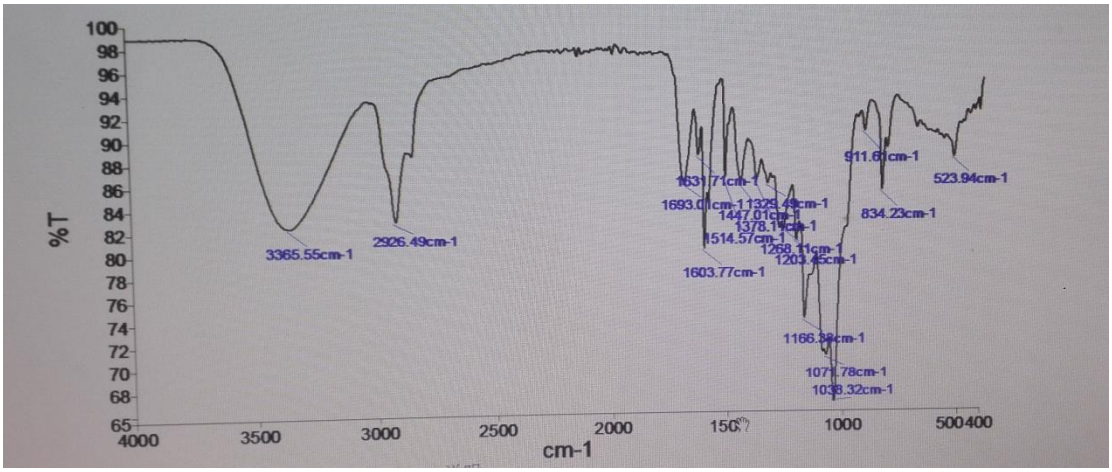

Figure S2-6 IR spectrum of compound **2** (film)

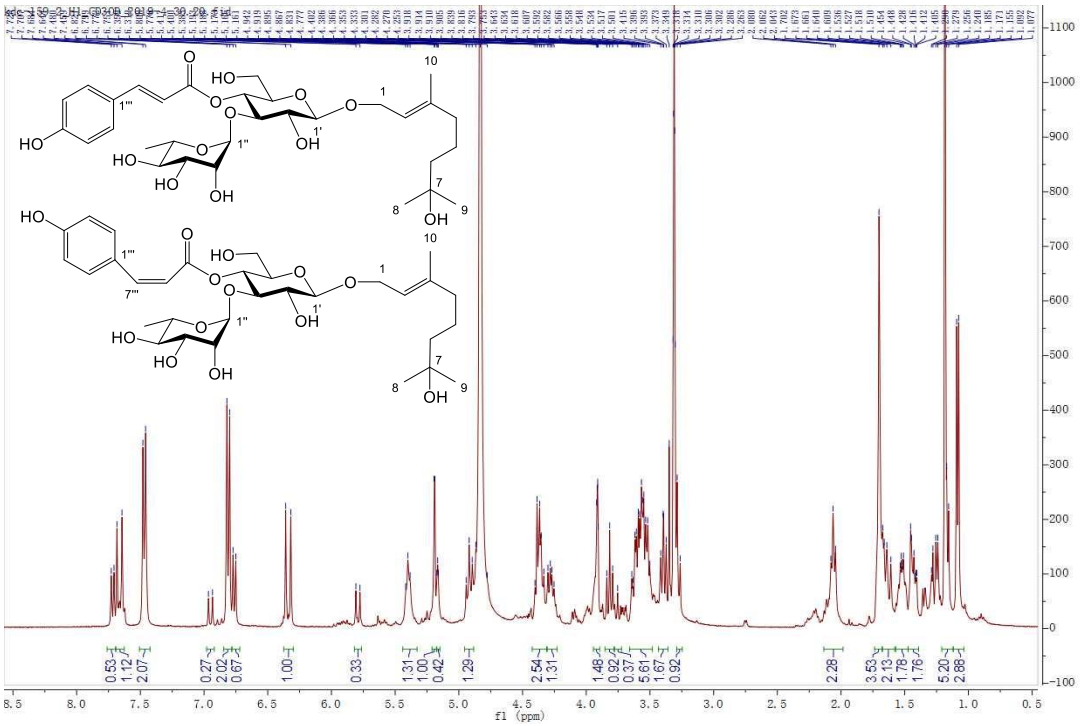

Figure S3-1 ^{1}H NMR spectrum of compound **3** in CD_3OD (400 MHz)

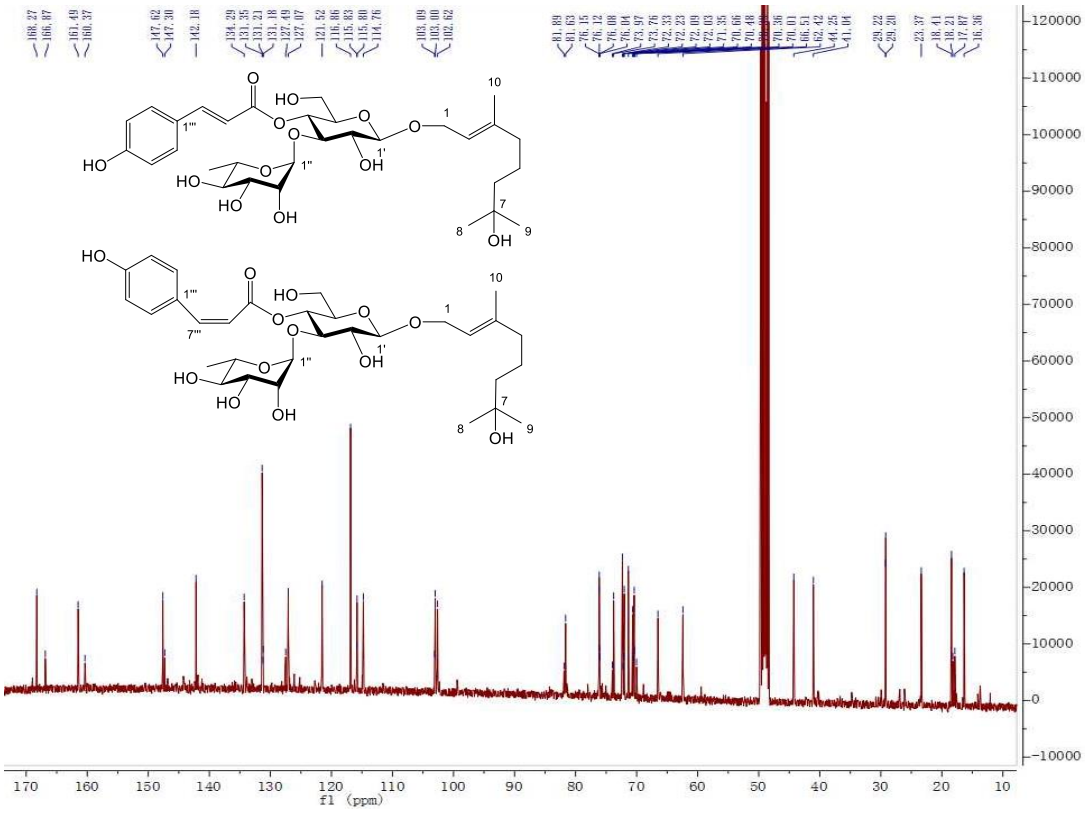

Figure S3-2 ^{13}C NMR spectrum of compound **3** in CD_3OD (100 MHz)

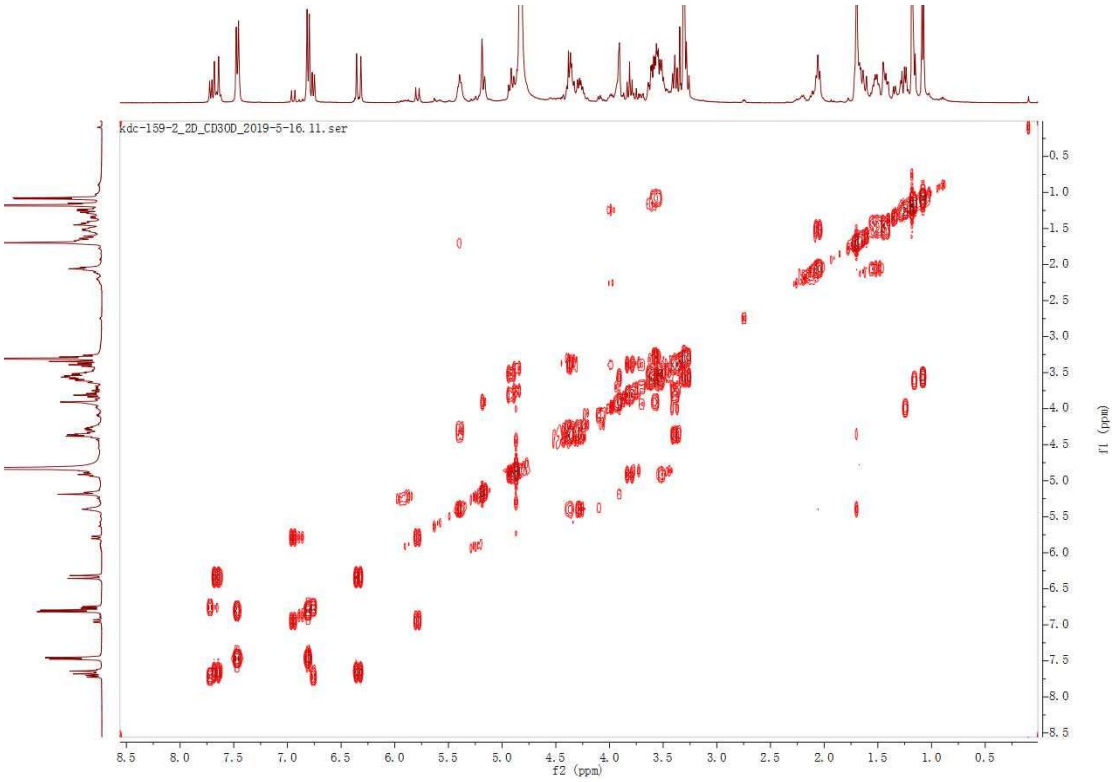

Figure S3-3 ^{1}H-^{1}H COSY spectrum of compound **3** in CD_3OD

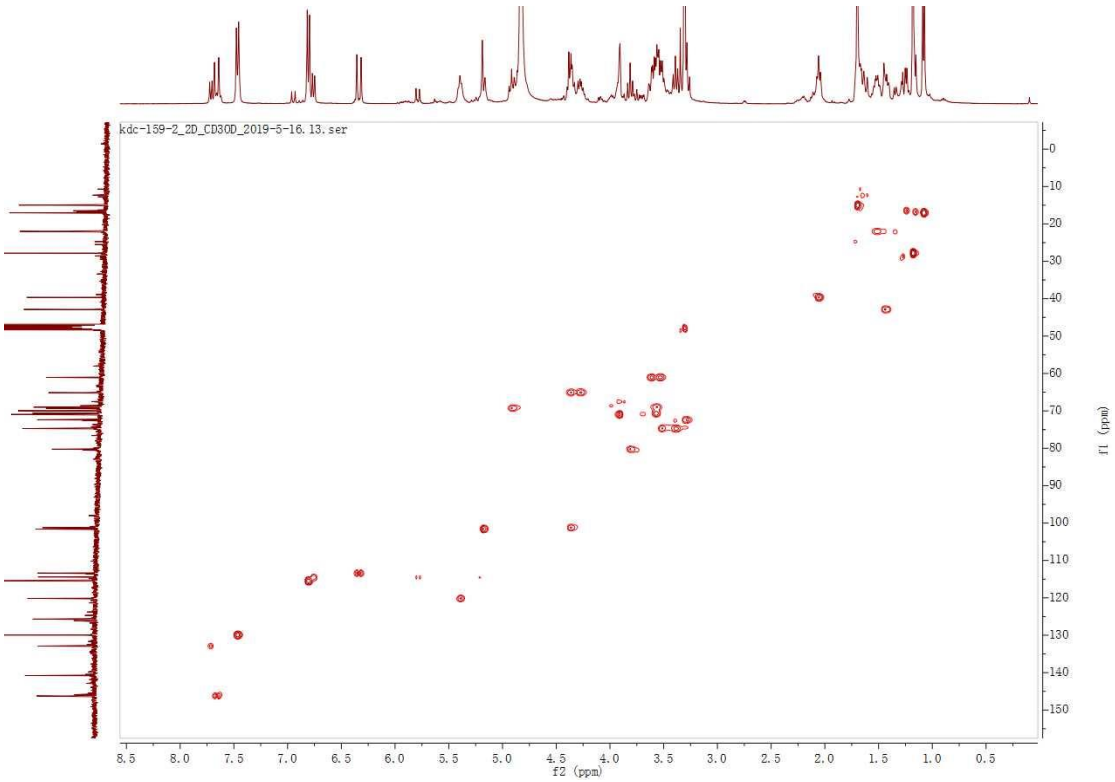

Figure S3-4 HSQC spectrum of compound **3** in CD_3OD

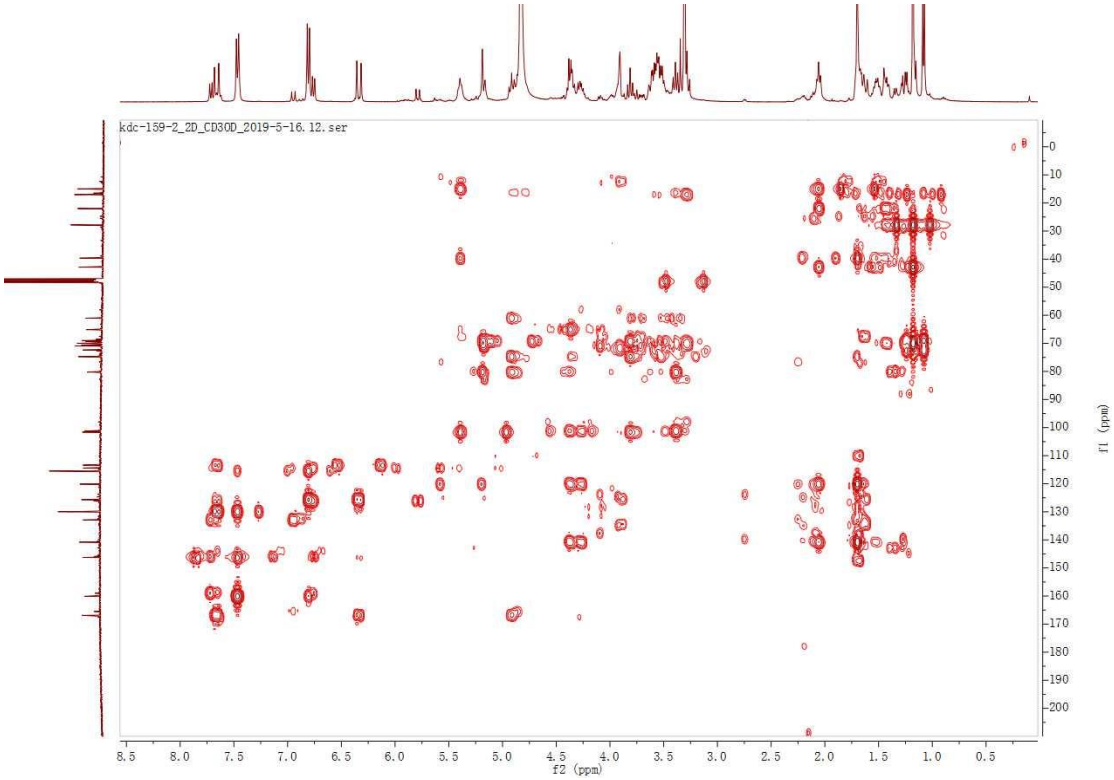

Figure S3-5 HMBC spectrum of compound **3** in CD_3OD

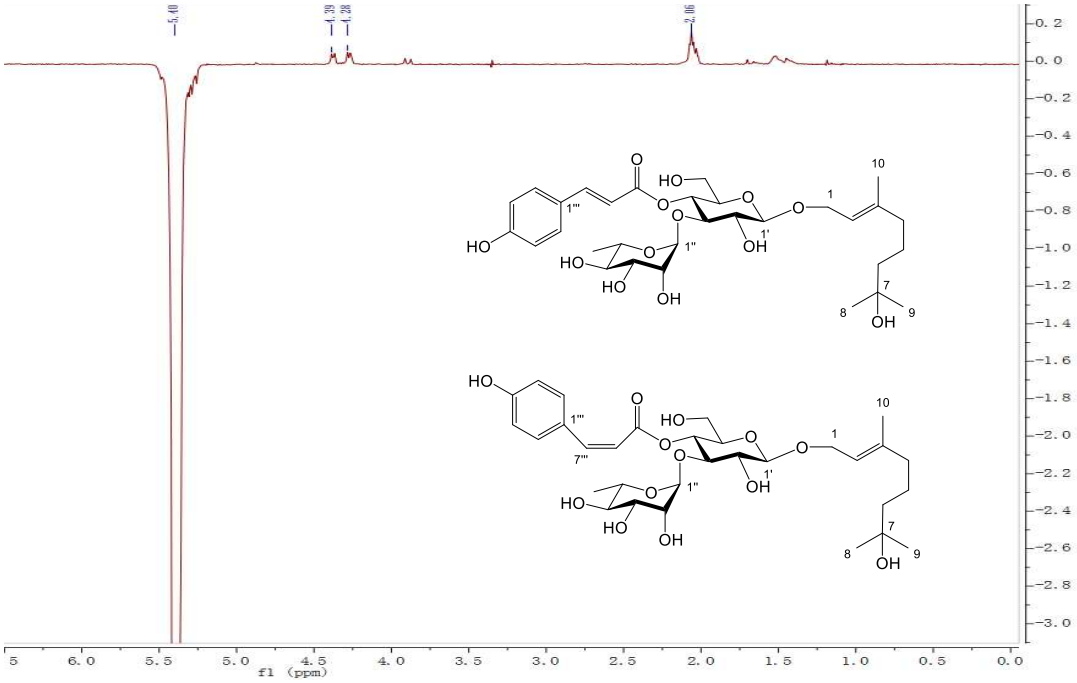

Figure S3-6 NOEDS spectrum of compound **3** in CD_3OD (600 MHz)

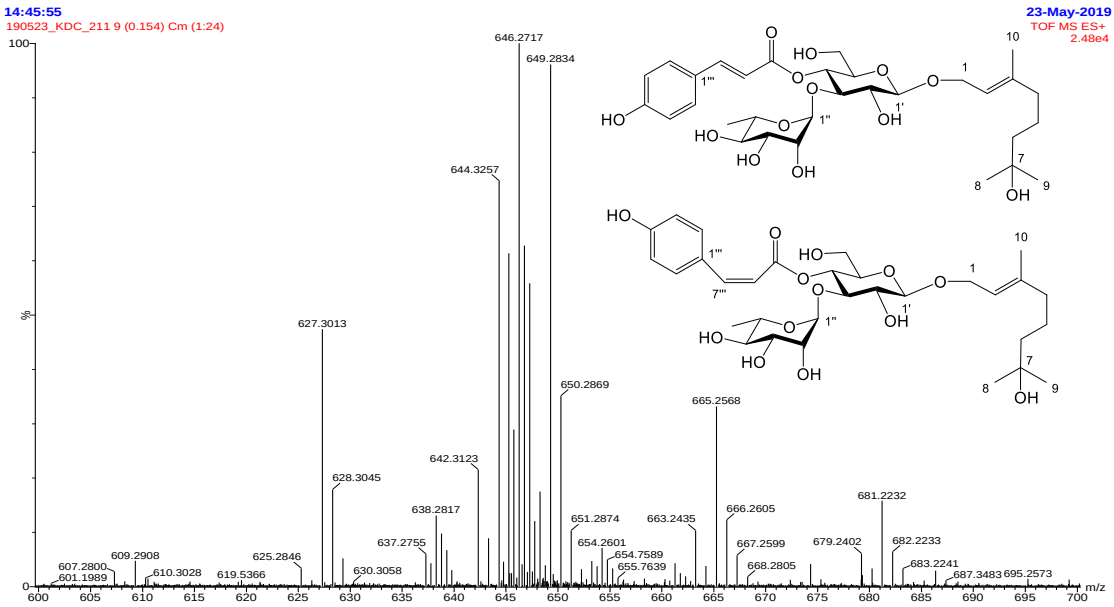

Figure S3-7 HRESIMS spectrum of compound **3**

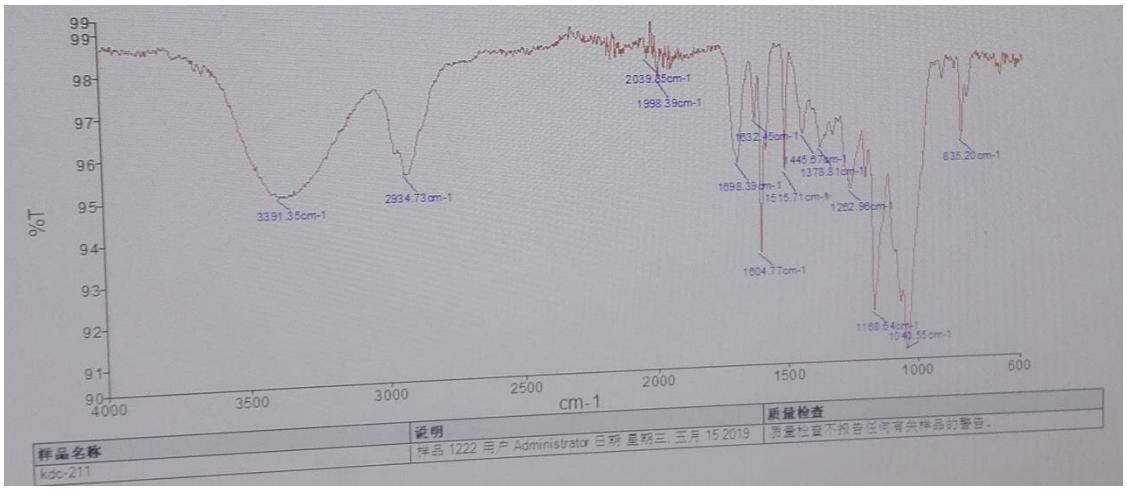

Figure S3-8 IR spectrum of compound **3** (film)

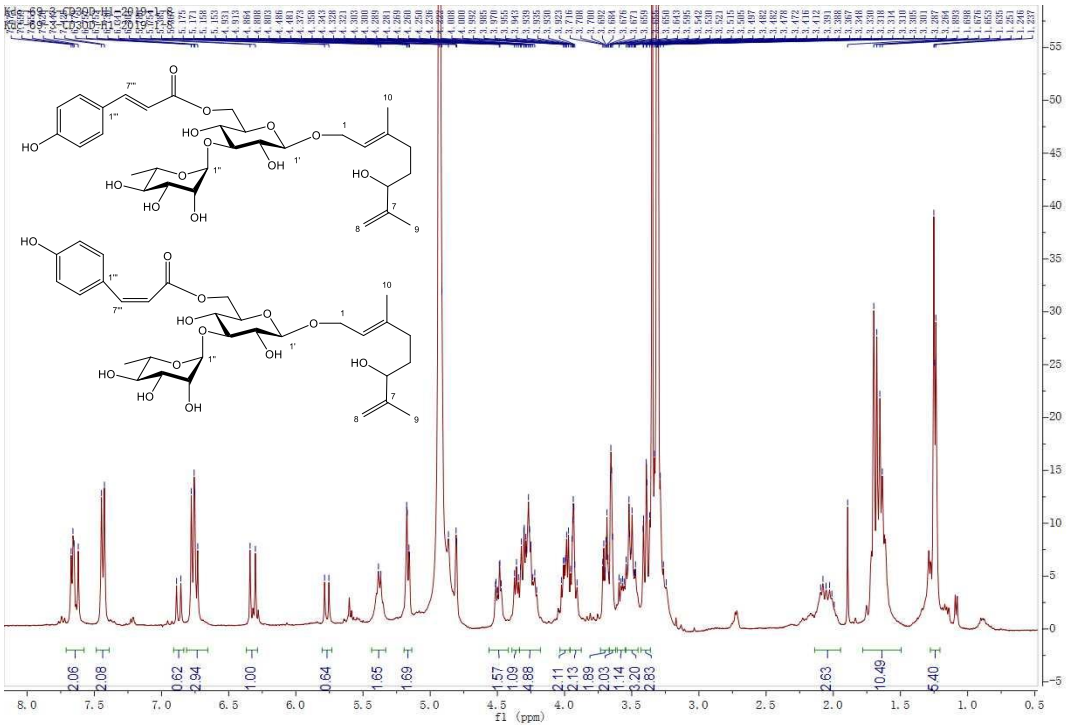

Figure S4-1 ^{1}H NMR spectrum of compound **4** in CD_3OD (400 MHz)

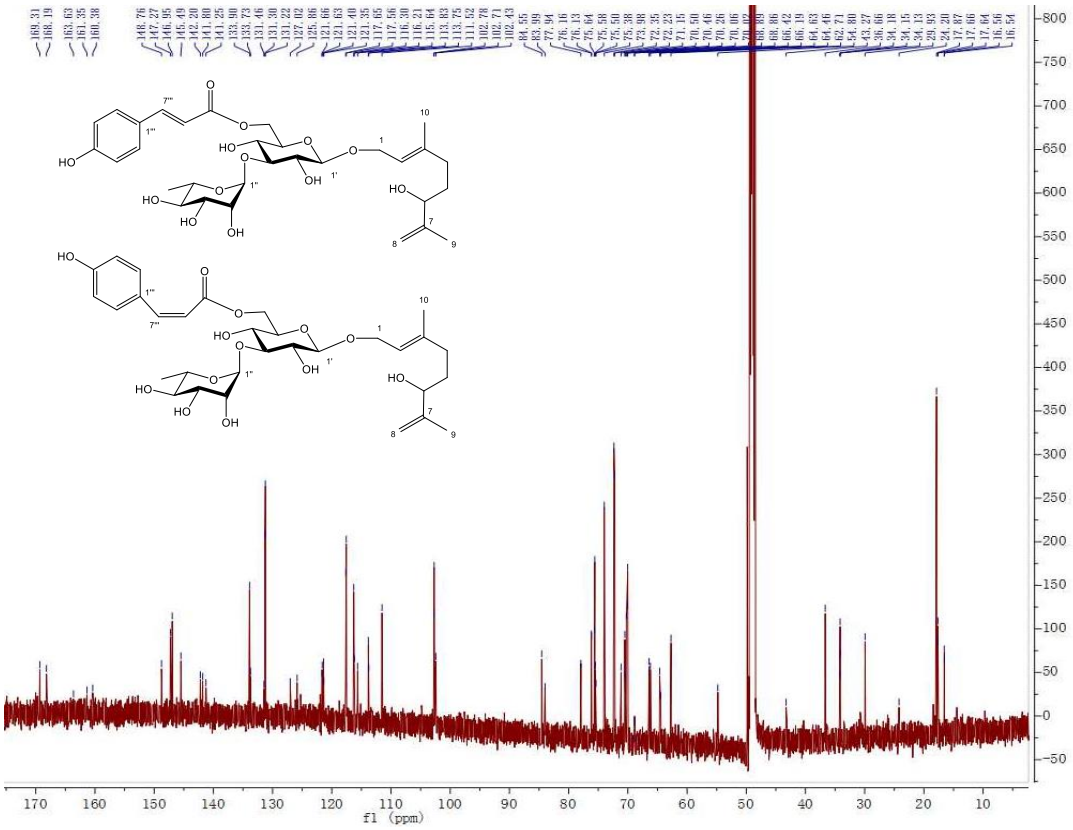

Figure S4-2 ^{13}C NMR spectrum of compound **4** in CD_3OD (150 MHz)

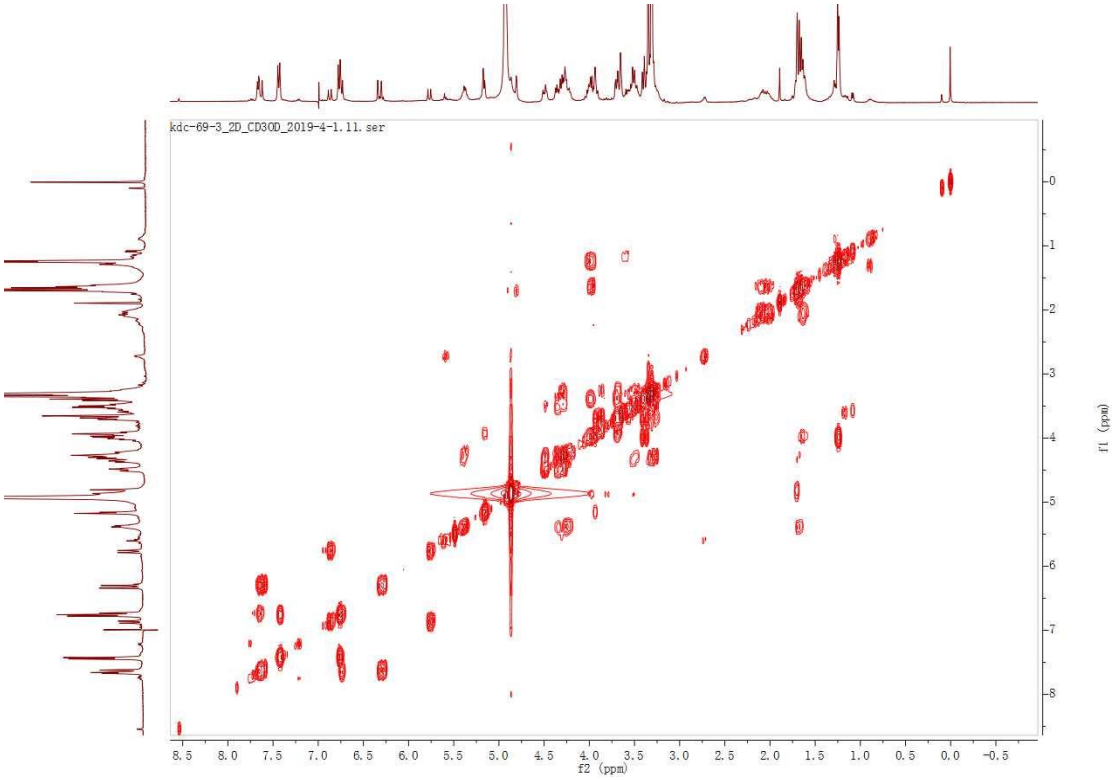

Figure S4-3 ^{1}H-^{1}H COSY spectrum of compound **4** in CD_3OD

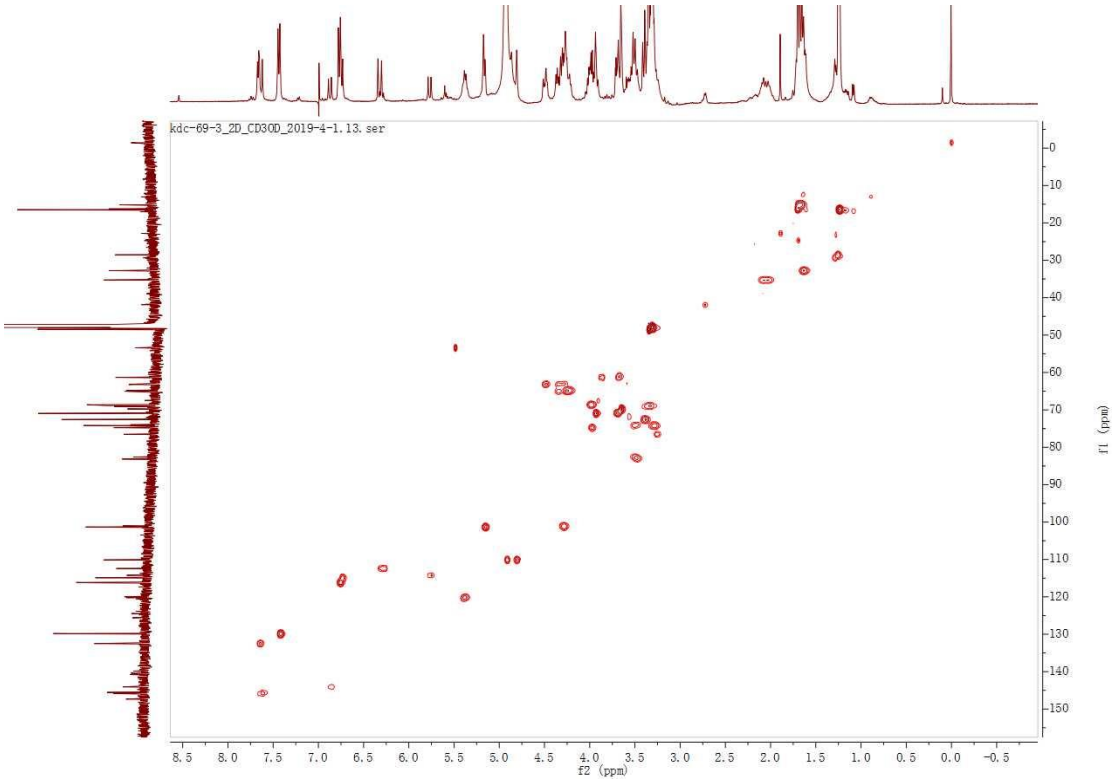

Figure S4-4 HSQC spectrum of compound **4** in CD_3OD

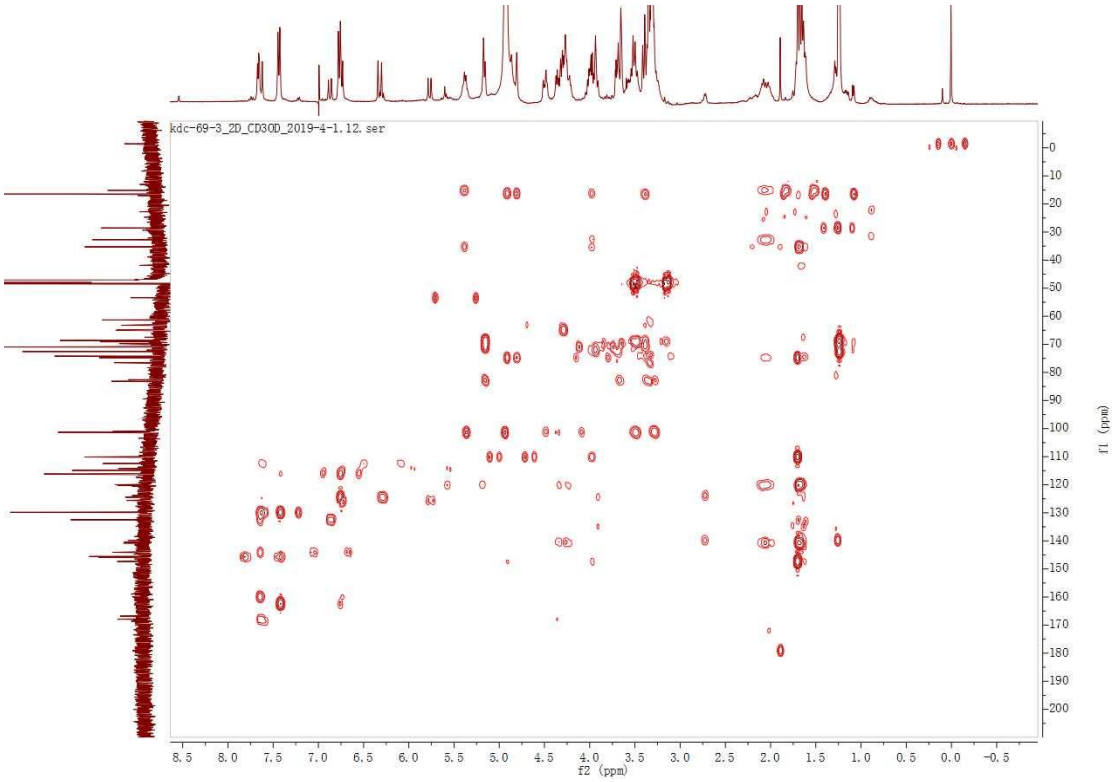

Figure S4-5 HMBC spectrum of compound **4** in CD_3OD

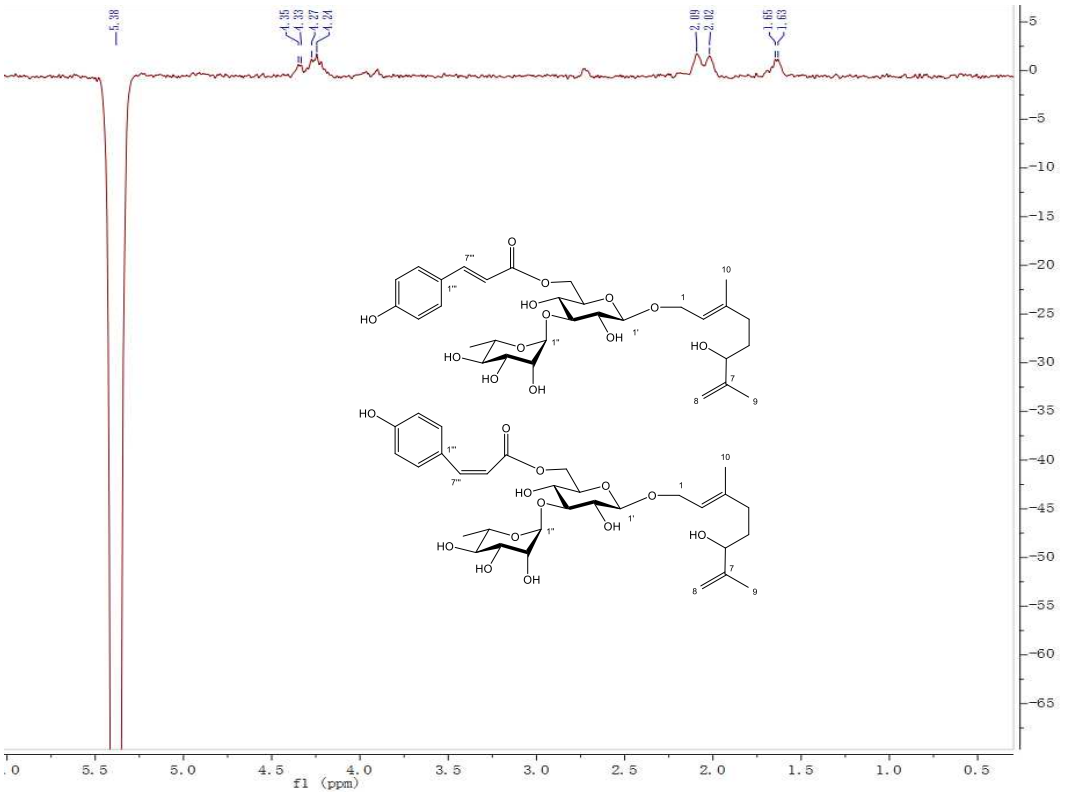

Figure S4-6 NOEDS spectrum of compound **4** in CD_3OD (600 MHz)

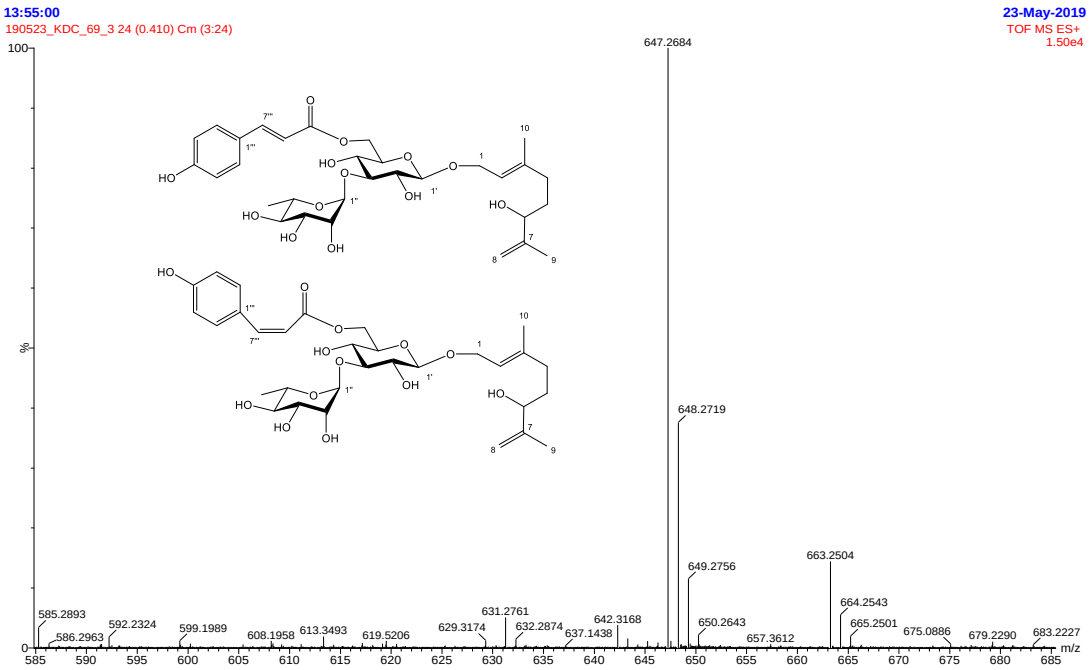

Figure S4-7 HRESIMS spectrum of compound **4**

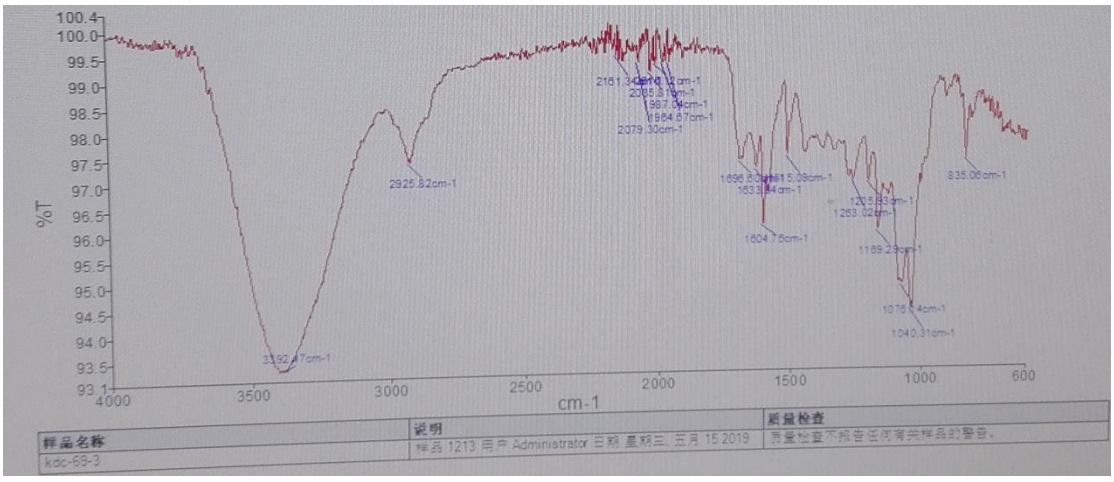

Figure S4-8 IR spectrum of compound **4** (film)

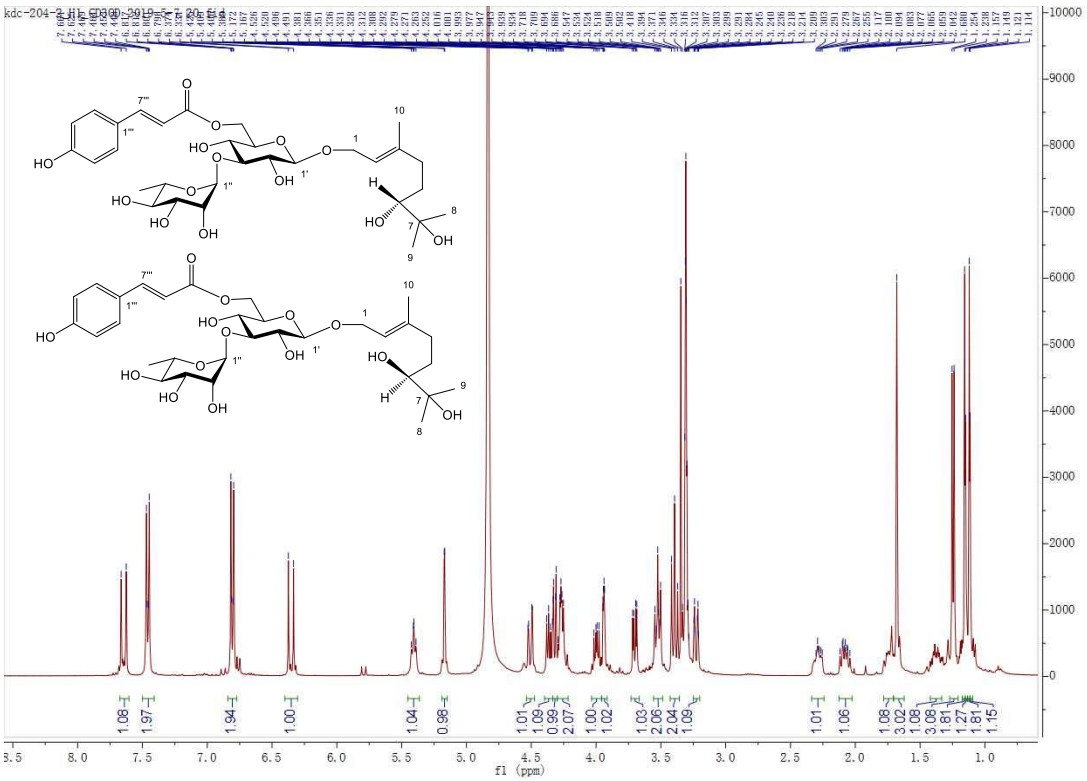

Figure S5-1 ^{1}H NMR spectrum of compound **5** in CD_3OD (400 MHz)

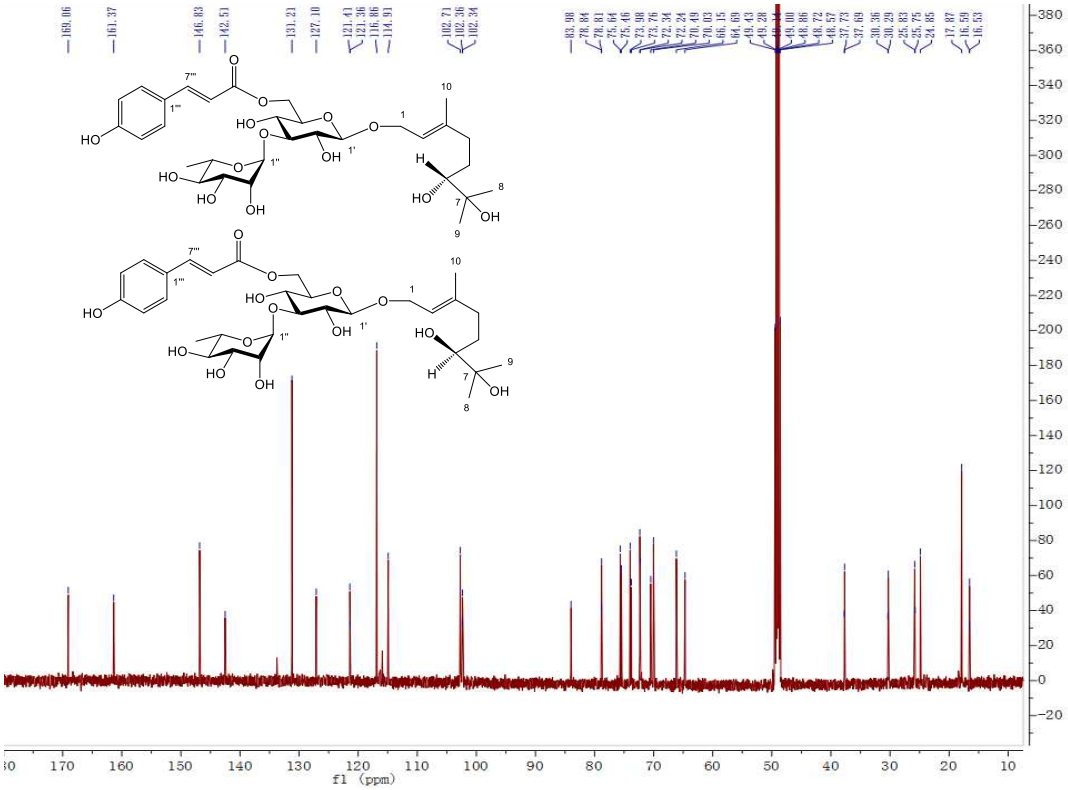

Figure S5-2 ^{13}C NMR spectrum of compound **5** in CD_3OD (150 MHz)

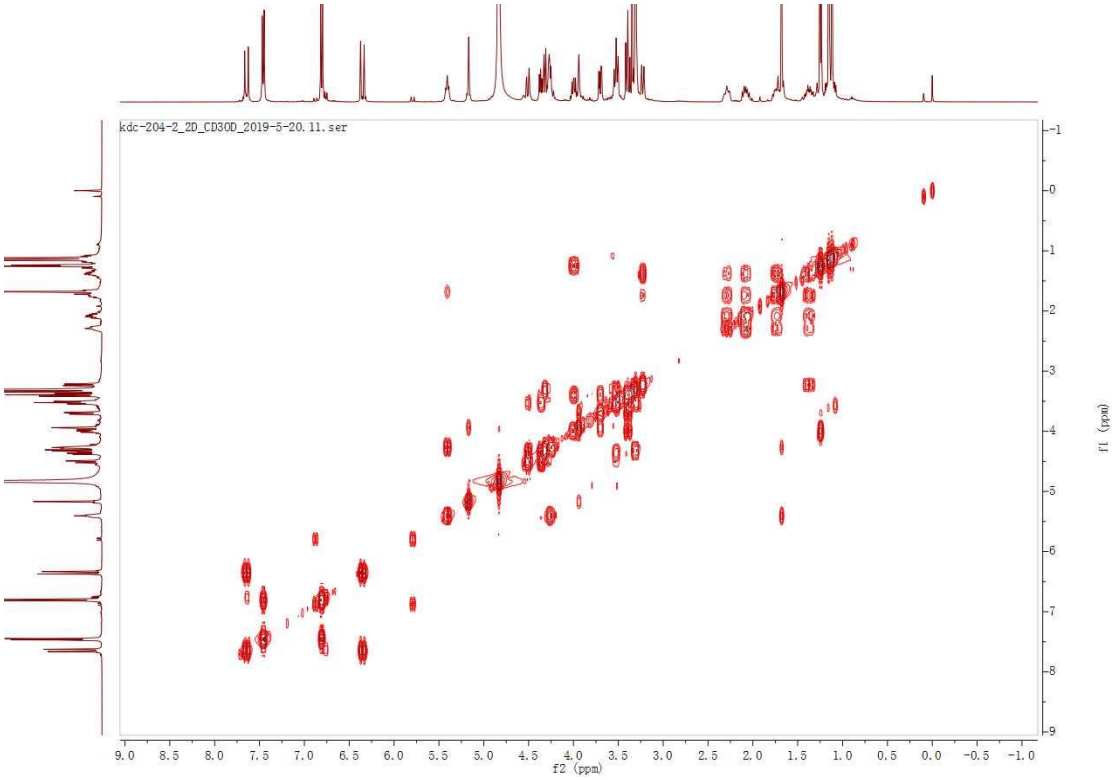

Figure S5-3 ^{1}H-^{1}H COSY spectrum of compound **5** in CD_3OD

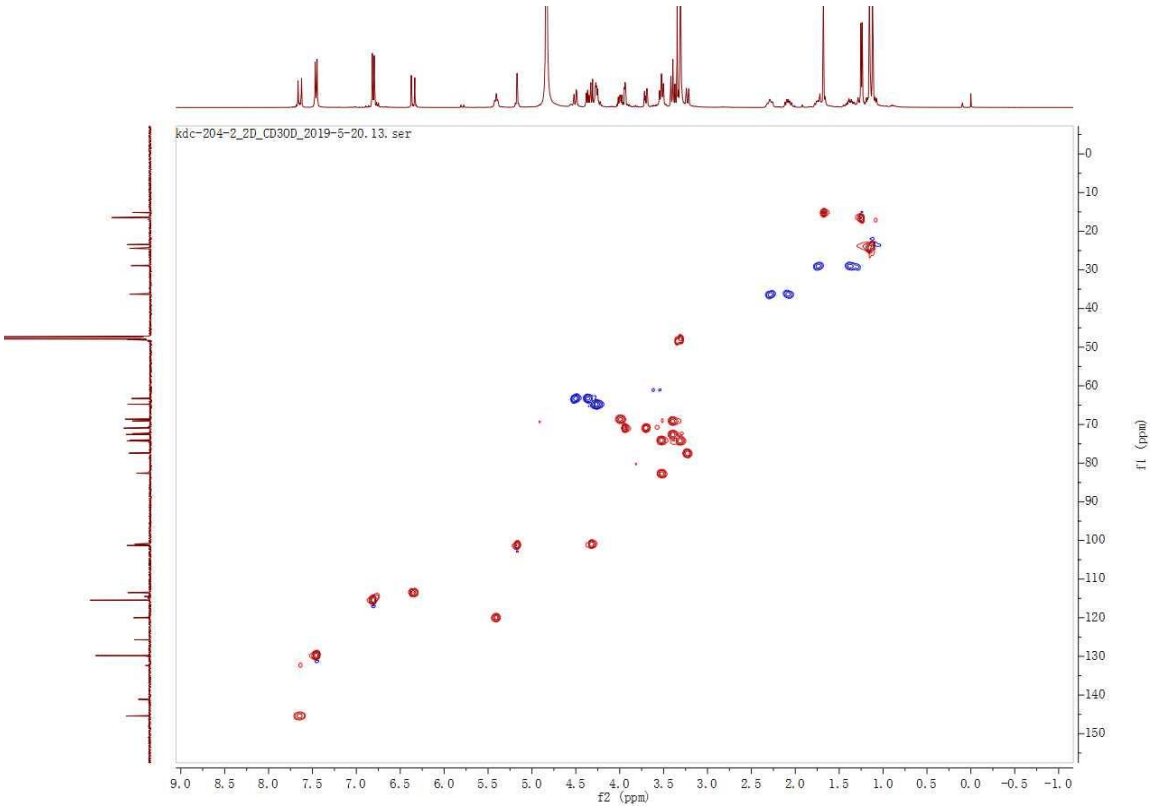

Figure S5-4 HSQC spectrum of compound **5** in CD_3OD

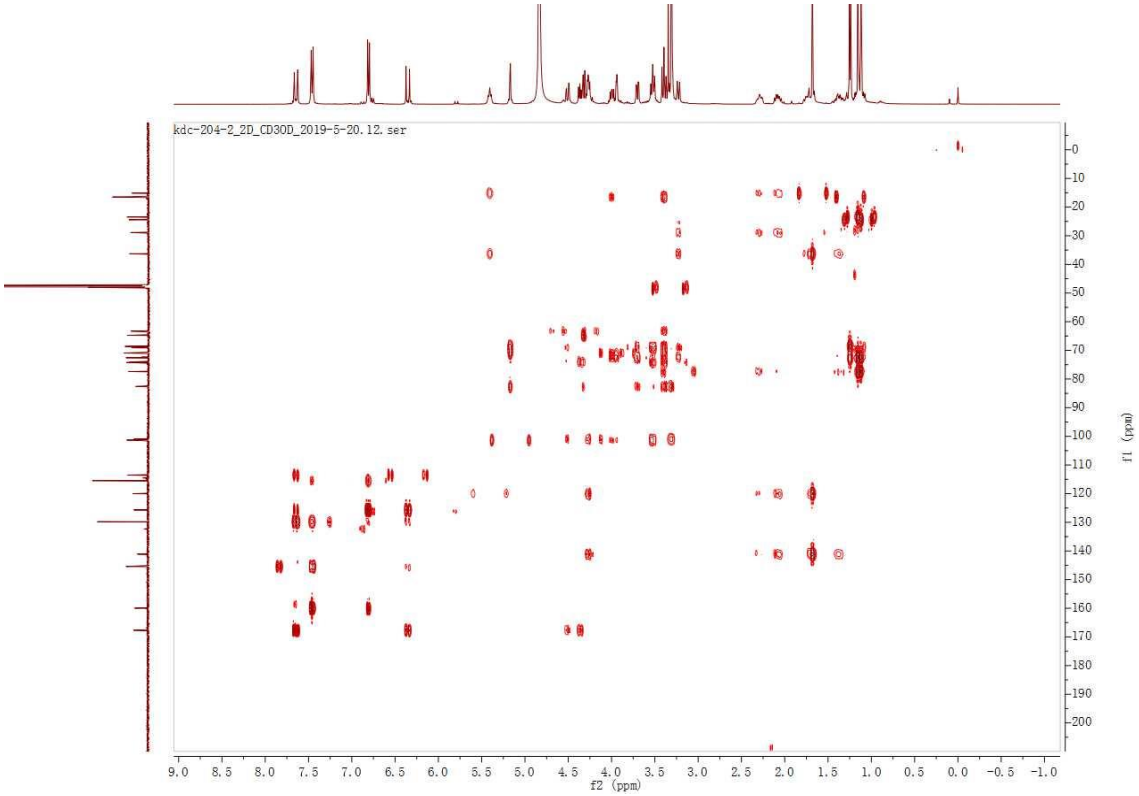

Figure S5-5 HMBC spectrum of compound **5** in CD_3OD

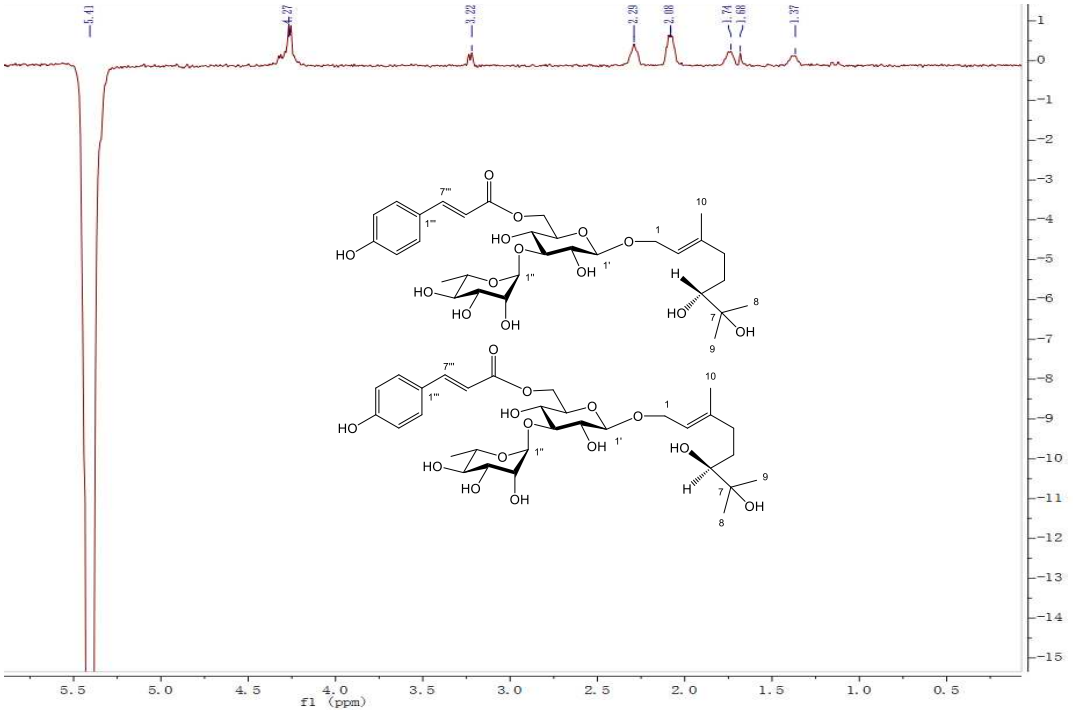

Figure S5-6 NOEDS spectrum of compound **5** in CD_3OD (600 MHz)

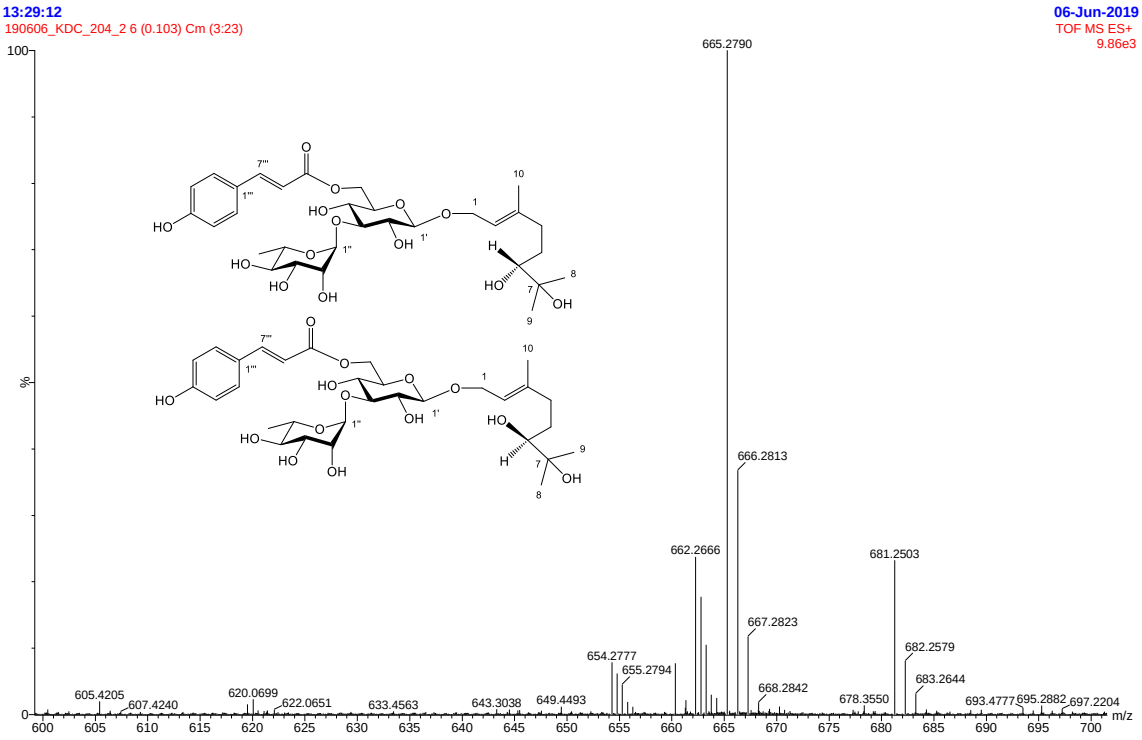

Figure S5-7 HRESIMS spectrum of compound **5**

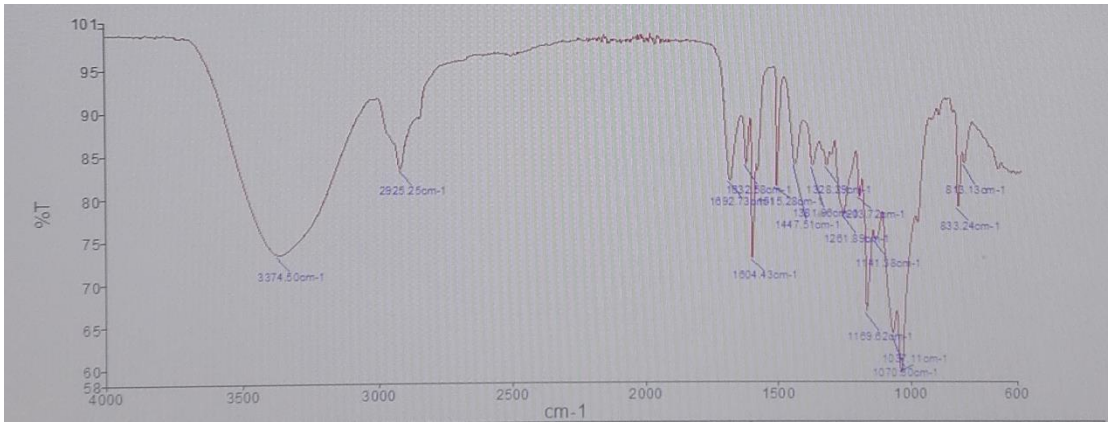

Figure S5-8 IR spectrum of compound **5** (film)

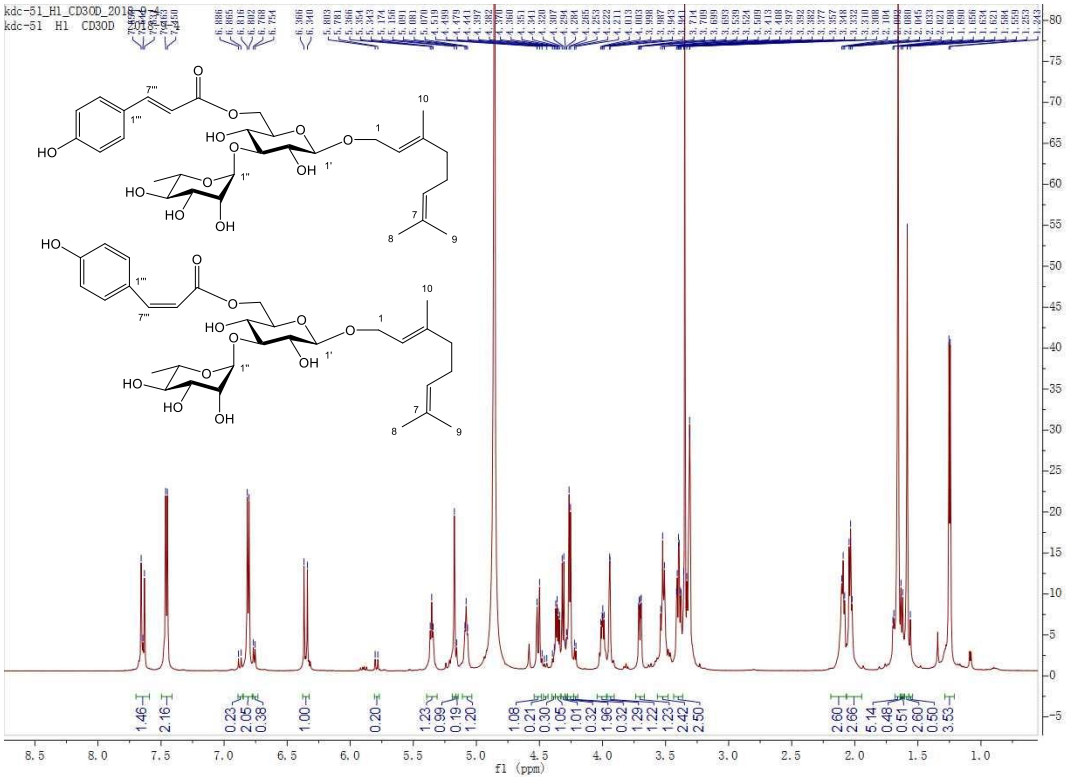

Figure S6-1 ^{1}H NMR spectrum of compound **6** in CD_3OD (600 MHz)

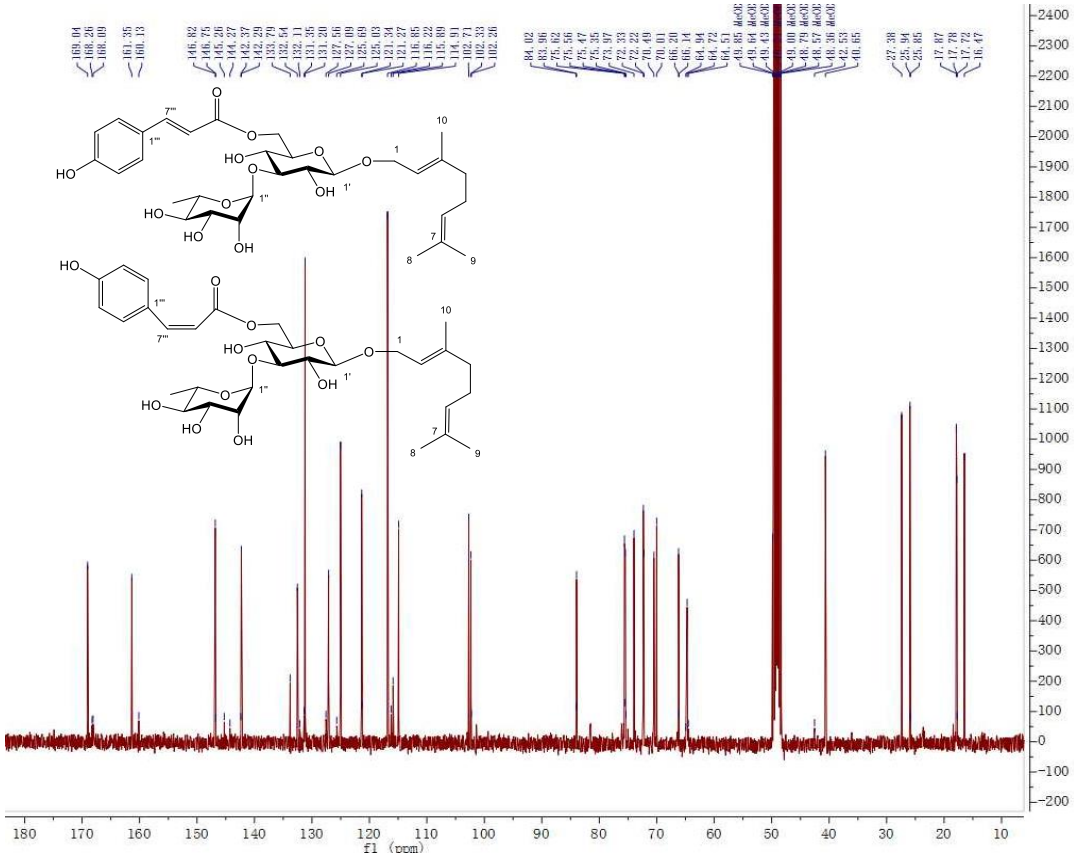

Figure S6-2 ^{13}C NMR spectrum of compound **6** in CD_3OD (100 MHz)

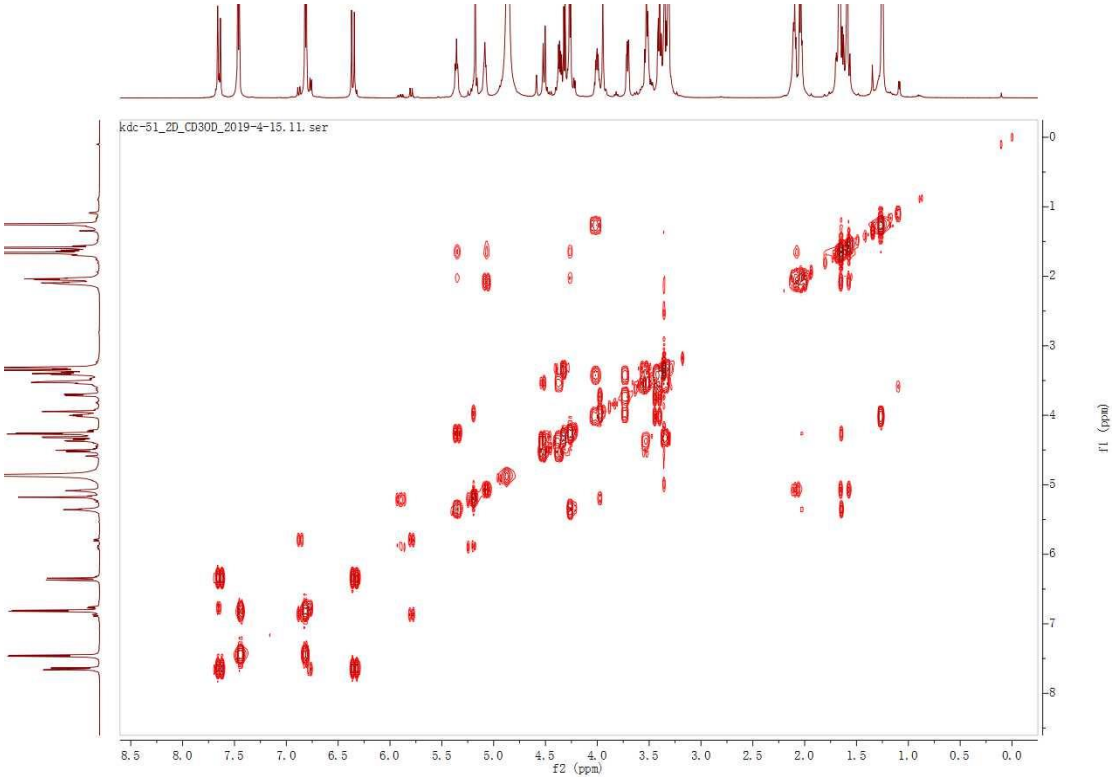

Figure S6-3 ^{1}H-^{1}H COSY spectrum of compound **6** in CD_3OD

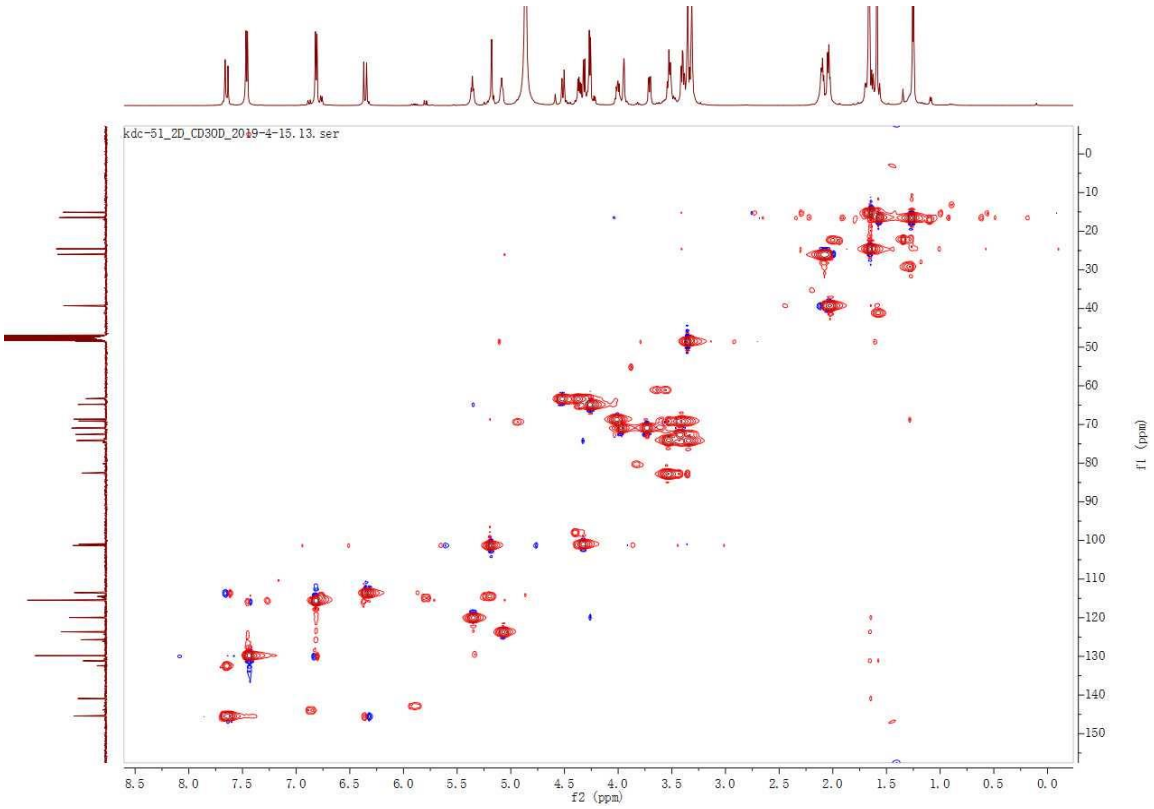

Figure S6-4 HSQC spectrum of compound **6** in CD_3OD

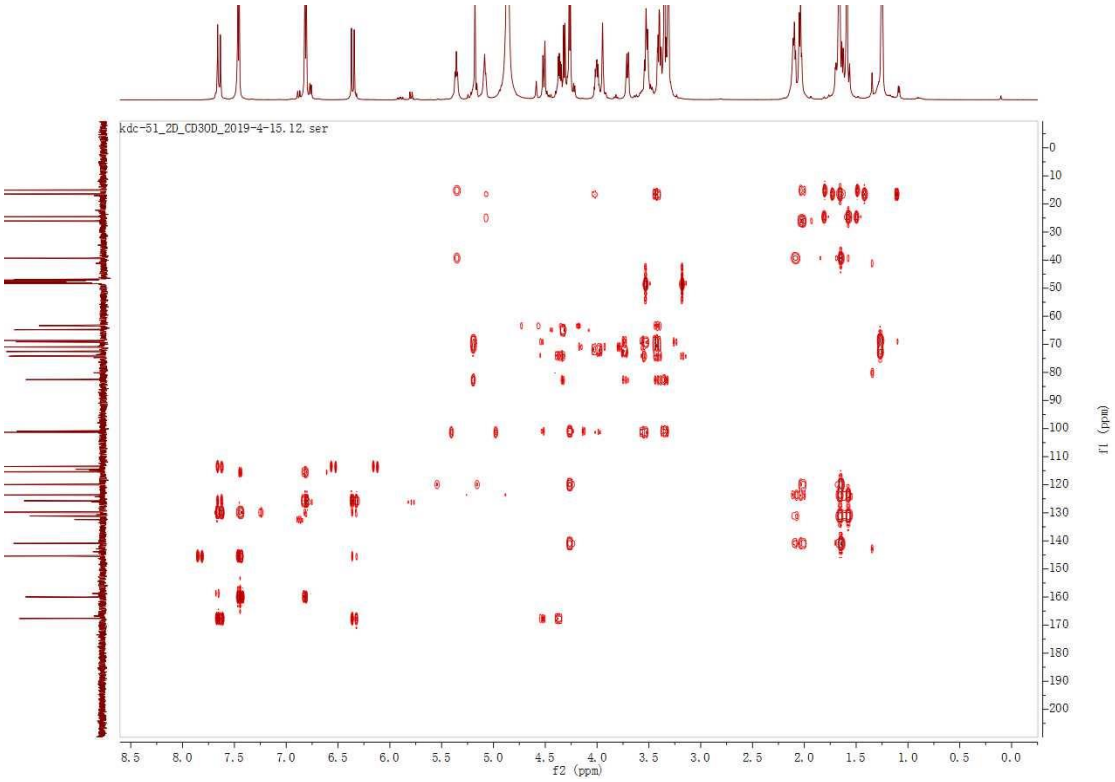

Figure S6-5 HMBC spectrum of compound **6** in CD_3OD

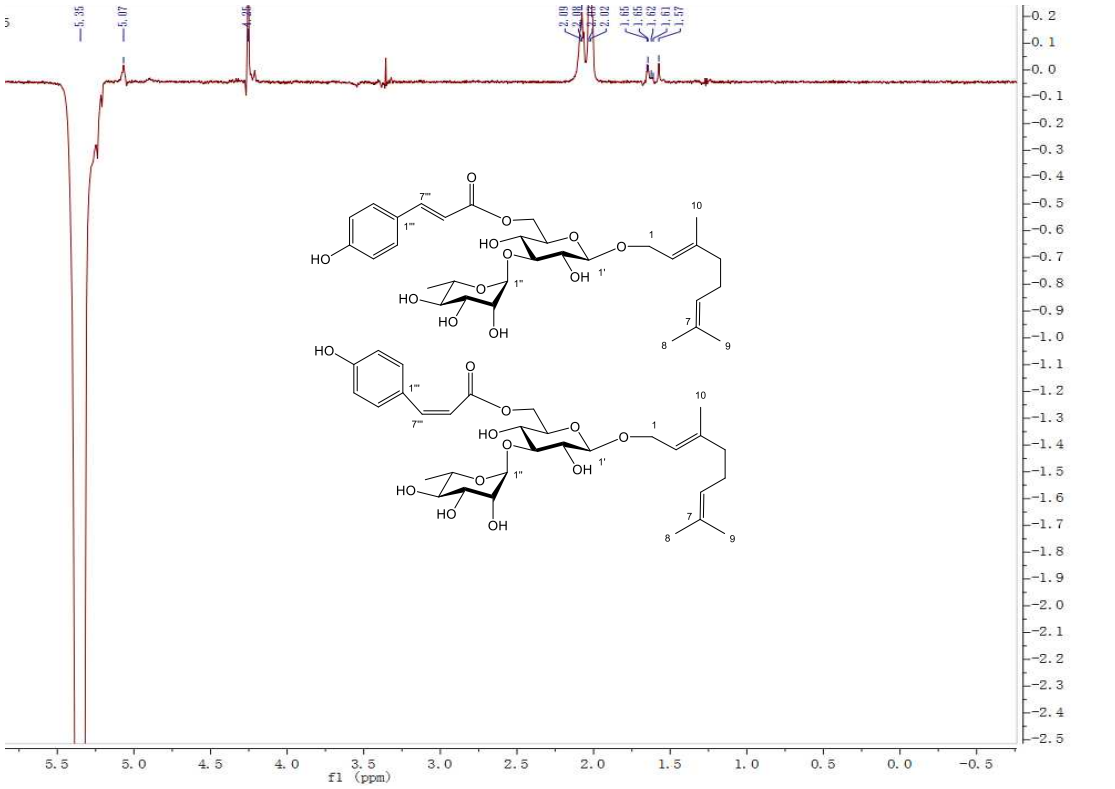

Figure S6-6 NOEDS spectrum of compound **6** in CD_3OD (600 MHz)

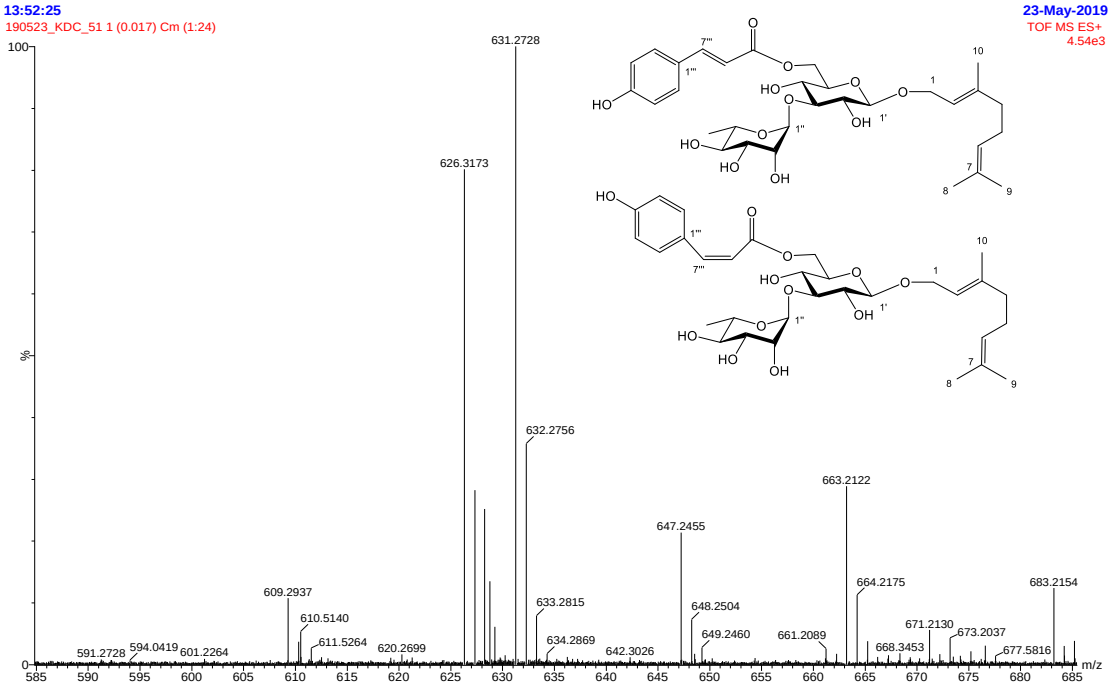

Figure S6-7 HRESIMS spectrum of compound **6**

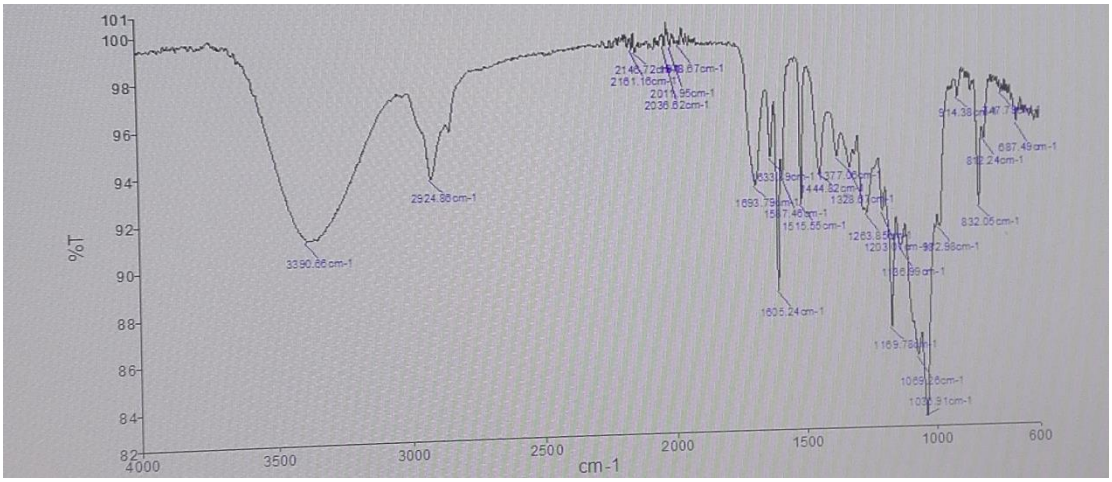

Figure S6-8 IR spectrum of compound **6** (film)

*S1. ^{1}H, ^{13}C NMR data of Compounds **4a**, **6a**, **7**, **8a** and **8b***

Compound **4a** (ligurobustoside F): white amorphous powder. ^{1}H NMR (400 MHz, CD_3OD) δ: aglycone 4.25 (1H, dd, *J* = 6.4, 6.0 Hz, H-1a), 4.34 (1H, dd, *J* = 12.0, 6.0 Hz, H-1b), 5.38 (1H, dd, *J* = 12.0, 6.4 Hz, H-2), 2.07 (2H, m, H-4), 1.63 (2H, m, H-5), 3.97 (1H, t, *J* = 6.0 Hz, H-6), 4.81 (1H, d, *J* = 2.0 Hz, H-8a), 4.91 (1H, d, *J* = 2.0 Hz, H-8b), 1.70 (3H, s, H-9), 1.68 (3H, s, H-10); Glc 4.31 (1H, d, *J* = 8.0 Hz, H-1'), 3.29 (1H, m, H-2'), 3.50 (1H, m, H-3'), 3.37 (1H, m, H-4'), 3.51 (1H, m, H-5'), 4.35 (1H, dd, *J* = 12.0, 6.0 Hz, H-6a'), 4.50 (1H, dd, *J* = 12.0, 2.0 Hz, H-6b'); Rha 5.17 (1H, d, *J* = 1.6 Hz, H-1''), 3.93 (1H, m, H-2''), 3.70 (1H, dd, *J* = 9.6, 3.2 Hz, H-3''), 3.39 (1H, m, H-4''), 4.00 (1H, dd, *J* = 9.6, 6.4 Hz, H-5''), 1.25 (3H, d, *J* = 6.4 Hz, H-6''); Cou 7.44 (2H, d, *J* = 8.8 Hz, H-2''', 6'''), 6.77 (2H, d, *J* = 8.8 Hz, H-3''', 5'''), 7.64 (1H, d, *J* = 16.0 Hz, H-7'''), 6.32 (1H, d, *J* = 16.0 Hz, H-8'''). ^{13}C NMR (150 MHz, CD_3OD) δ: aglycone 66.4 (C-1), 121.7 (C-2), 144.2 (C-3), 36.7 (C-4), 34.2 (C-5), 76.2 (C-6), 148.8 (C-7), 111.5 (C-8), 17.6 (C-9), 16.6 (C-10); Glc 102.4 (C-1'), 75.6 (C-2'), 84.6 (C-3'), 70.5 (C-4'), 75.5 (C-5'), 64.6 (C-6'); Rha 102.7 (C-1''), 72.4 (C-2''), 72.3 (C-3''), 74.0 (C-4''), 70.1 (C-5''), 17.9 (C-6''); Cou 125.9 (C-1'''), 131.2 (C-2''', 6'''), 117.6 (C-3''', 5'''), 163.6 (C-4'''), 147.3 (C-7'''), 113.8 (C-8'''), 169.3 (CO).

Compound **6a** (ligurobustoside E): yellow oil. ^{1}H NMR (600 MHz, CD_3OD) δ: aglycone 4.26 (2H, d, *J* = 7.2 Hz, H-1a), 5.35 (1H, t, *J* = 7.2 Hz, H-2), 2.03 (2H, t, *J* = 7.2 Hz, H-4), 2.09 (2H, m, H-5), 5.08 (1H, t, *J* = 6.6 Hz, H-6), 1.66 (3H, s, H-8), 1.58 (3H, s, H-9), 1.66 (3H, s, H-10); Glc 4.31 (1H, d, *J* = 7.8 Hz, H-1'), 3.34 (1H, m, H-2'), 3.52 (1H, m, H-3'), 3.40 (1H, t, *J* = 9.6 Hz, H-4'), 3.52 (1H, m, H-5'), 4.35 (1H, dd, *J* = 12.0, 6.0 Hz, H-6a'), 4.50 (1H, br. d, *J* = 12.0 Hz, H-6b'); Rha 5.17 (1H, br. s, H-1''), 3.94 (1H, m, H-2''), 3.70 (1H, dd, *J* = 9.6, 3.6 Hz, H-3''), 3.40 (1H, t, *J* = 9.6 Hz, H-4''), 4.00 (1H, dd, *J* = 9.6, 6.0 Hz, H-5''), 1.25 (3H, d, *J* = 6.0 Hz, H-6''); Cou 7.46 (2H, d, *J* = 8.4 Hz, H-2''', 6'''), 6.81 (2H, d, *J* = 8.4 Hz, H-3''', 5'''), 7.64 (1H, d, *J* = 16.2 Hz, H-7'''), 6.35 (1H, d, *J* = 16.2 Hz, H-8'''). ^{13}C NMR (100 MHz, CD_3OD) δ: aglycone 66.2 (C-1), 121.3 (C-2), 142.3 (C-3), 40.7 (C-4), 27.4 (C-5), 125.0 (C-6), 132.5 (C-7), 25.9 (C-8), 17.8 (C-9), 16.5 (C-10); Glc 102.3 (C-1'), 75.6 (C-2'), 84.0 (C-3'), 70.5 (C-4'), 75.5 (C-5'), 64.7 (C-6'); Rha 102.7 (C-1''), 72.3 (C-2''), 72.2 (C-3''), 74.0 (C-4''), 70.0 (C-5''), 17.9 (C-6''); Cou 127.1 (C-1'''), 131.2 (C-2''', 6'''), 116.9 (C-3''', 5'''), 161.3 (C-4'''), 146.8 (C-7'''), 114.9 (C-8'''), 169.0 (CO).

Compound **7** (ligurobustoside J): white amorphous powder. ^{1}H NMR (400 MHz, CD_3OD) δ: aglycone 4.28 (1H, dd, *J* = 12.8, 7.2 Hz, H-1a), 4.34 (1H, dd, *J* = 12.8, 6.4

Hz, H-1b), 5.38 (1H, t, *J* = 6.4 Hz, H-2), 2.07 (2H, t, *J* = 6.8 Hz, H-4), 2.13 (2H, t, *J* = 6.8 Hz, H-5), 5.12 (1H, m, H-6), 1.68 (3H, s, H-8), 1.61 (3H, s, H-9), 1.68 (3H, s, H-10); Glc 4.37 (1H, d, *J* = 8.0 Hz, H-1'), 3.51 (1H, m, H-2'), 3.81 (1H, t, *J* = 9.2 Hz, H-3'), 4.94 (1H, t, *J* = 9.2 Hz, H-4'), 3.56 (1H, m, H-5'), 3.54 (1H, m, H-6a'), 3.62 (1H, m, H-6b'); inner Rha 5.19 (1H, d, *J* = 1.6 Hz, H-1''), 3.86 (1H, dd, *J* = 3.2, 1.6 Hz, H-2''), 3.67 (1H, dd, *J* = 9.2, 3.2 Hz, H-3''), 3.39 (1H, t, *J* = 9.2 Hz, H-4''), 3.60 (1H, m, H-5''), 1.09 (3H, d, *J* = 6.0 Hz, H-6''); outer Rha 5.04 (1H, d, *J* = 1.6 Hz, H-1'''), 3.88 (1H, dd, *J* = 3.2, 1.6 Hz, H-2'''), 3.51 (1H, m, H-3'''), 3.32 (1H, m, H-4'''), 3.46 (1H, dd, *J* = 9.6, 6.0 Hz, H-5'''), 1.06 (3H, d, *J* = 6.0 Hz, H-6'''); Cou 7.48 (2H, d, *J* = 8.4 Hz, H-2'''', 6''''), 6.83 (2H, d, *J* = 8.4 Hz, H-3'''', 5''''), 7.66 (1H, d, *J* = 16.0 Hz, H-7''''), 6.33 (1H, d, *J* = 16.0 Hz, H-8''''). ^{13}C NMR (150 MHz, CD_3OD) *δ*: aglycone 66.5 (C-1), 121.5 (C-2), 142.1 (C-3), 40.7 (C-4), 27.4 (C-5), 125.1 (C-6), 132.5 (C-7), 25.9 (C-8), 17.7 (C-9), 16.5 (C-10); Glc 102.5 (C-1'), 76.1 (C-2'), 81.6 (C-3'), 70.5 (C-4'), 76.1 (C-5'), 62.4 (C-6'); inner Rha 102.7 (C-1''), 72.8 (C-2''), 72.6 (C-3''), 81.7 (C-4''), 68.9 (C-5''), 19.2 (C-6''); outer Rha 103.5 (C-1'''), 72.3 (C-2'''), 72.3 (C-3'''), 73.8 (C-4'''), 70.3 (C-5'''), 17.8 (C-6'''); Cou 127.0 (C-1''''), 131.4 (C-2'''', 6''''), 117.1 (C-3'''', 5''''), 161.5 (C-4''''), 147.6 (C-7''''), 114.7 (C-8''''), 168.1 (CO).

Compound **8a** (lipedoside B-II): white amorphous powder. ^{1}H NMR (600 MHz, CD_3OD) *δ*: aglycone 5.22 (1H, dd, *J* = 10.8, 1.2 Hz, H-1a), 5.25 (1H, dd, *J* = 17.4, 1.2 Hz, H-1b), 5.93 (1H, dd, *J* = 17.4, 10.8 Hz, H-2), 1.59 (1H, m, H-4a), 1.62 (1H, m, H-4b), 2.05 (2H, m, H-5), 5.10 (1H, t, *J* = 7.2 Hz, H-6), 1.67 (3H, s, H-8), 1.60 (3H, s, H-9), 1.39 (3H, s, H-10); Glc 4.40 (1H, d, *J* = 7.8 Hz, H-1'), 3.37 (1H, m, H-2'), 3.72 (1H, t, *J* = 9.6 Hz, H-3'), 4.89 (1H, t, *J* = 9.6 Hz, H-4'), 3.46 (1H, m, H-5'), 3.50 (1H, m, H-6a'), 3.57 (1H, m, H-6b'); Rha 5.16 (1H, d, *J* = 1.2 Hz, H-1''), 3.91 (1H, m, H-2''), 3.59 (1H, m, H-3''), 3.29 (1H, m, H-4''), 3.57 (1H, m, H-5''), 1.16 (3H, d, *J* = 6.6 Hz, H-6''); Cou 7.72 (2H, d, *J* = 8.4 Hz, H-2''', 6'''), 6.76 (2H, d, *J* = 8.4 Hz, H-3''', 5'''), 6.94 (1H, d, *J* = 12.6 Hz, H-7'''), 5.79 (1H, d, *J* = 12.6 Hz, H-8'''). ^{13}C NMR (100 MHz, CD_3OD) *δ*: aglycone 115.9 (C-1), 144.3 (C-2), 81.6 (C-3), 42.6 (C-4), 23.6 (C-5), 125.6 (C-6), 132.2 (C-7), 25.8 (C-8), 17.7 (C-9), 23.1 (C-10); Glc 99.4 (C-1'), 76.1 (C-2'), 82.2 (C-3'), 70.6 (C-4'), 75.7 (C-5'), 62.5 (C-6'); Rha 103.0 (C-1''), 72.3 (C-2''), 72.1 (C-3''), 73.7 (C-4''), 70.3 (C-5''), 18.2 (C-6''); Cou 127.5 (C-1'''), 134.3 (C-2''', 6'''), 115.8 (C-3''', 5'''), 160.4 (C-4'''), 147.2 (C-7'''), 115.9 (C-8'''), 166.9 (CO).

Compound **8b** (lipedoside B-III): white amorphous powder. ^{1}H NMR (600 MHz, CD_3OD) *δ*: aglycone 5.22 (1H, dd, *J* = 10.8, 1.2 Hz, H-1a), 5.25 (1H, dd, *J* = 17.4, 1.2

Hz, H-1b), 5.93 (1H, dd, *J* = 17.4, 10.8 Hz, H-2), 1.59 (1H, m, H-4a), 1.62 (1H, m, H-4b), 2.05 (2H, m, H-5), 5.10 (1H, t, *J* = 7.2 Hz, H-6), 1.67 (3H, s, H-8), 1.60 (3H, s, H-9), 1.39 (3H, s, H-10); Glc 4.43 (1H, d, *J* = 7.8 Hz, H-1'), 3.37 (1H, m, H-2'), 3.77 (1H, t, *J* = 9.6 Hz, H-3'), 4.89 (1H, t, *J* = 9.6 Hz, H-4'), 3.46 (1H, m, H-5'), 3.50 (1H, m, H-6a'), 3.57 (1H, m, H-6b'); Rha 5.18 (1H, d, *J* = 1.2 Hz, H-1''), 3.91 (1H, m, H-2''), 3.59 (1H, m, H-3''), 3.29 (1H, m, H-4''), 3.57 (1H, m, H-5''), 1.08 (3H, d, *J* = 6.0 Hz, H-6''); Cou 7.47 (2H, d, *J* = 8.4 Hz, H-2''', 6'''), 6.81 (2H, d, *J* = 8.4 Hz, H-3''', 5'''), 7.65 (1H, d, *J* = 16.2 Hz, H-7'''), 6.33 (1H, d, *J* = 16.2 Hz, H-8'''). ^{13}C NMR (100 MHz, CD_3OD) *δ*: aglycone 115.9 (C-1), 144.3 (C-2), 81.6 (C-3), 42.6 (C-4), 23.6 (C-5), 125.6 (C-6), 132.2 (C-7), 25.8 (C-8), 17.7 (C-9), 23.1 (C-10); Glc 99.4 (C-1'), 76.2 (C-2'), 81.9 (C-3'), 70.7 (C-4'), 75.7 (C-5'), 62.5 (C-6'); Rha 103.0 (C-1''), 72.3 (C-2''), 72.0 (C-3''), 73.7 (C-4''), 70.3 (C-5''), 18.4 (C-6''); Cou 127.1 (C-1'''), 131.3 (C-2''', 6'''), 116.8 (C-3''', 5'''), 161.4 (C-4'''), 147.5 (C-7'''), 114.8 (C-8'''), 168.3 (CO).

S2. Determination of bioactivities

S2.1. Determination of FAS inhibitory activity

Compounds **1**-**8** (1.0-1.7 mg) were dissolved in DMSO (100 μL) and then diluted with potassium phosphate buffer (0.1 M, pH 7.0). Sample solution (100 μL, 20-2000 μM, 37 °C) and FAS substrates (1.8 mL, 37 °C) were mixed in a cuvette, and then FAS solution (100 μL, 37 °C, isolated from chicken liver and kept in ice-bath before use) was added. The absorbance of reaction compound was monitored by a UV-vis spectrophotometer at 340 nm in 1 min. The inhibitory effect was calculated by the following equation: FAS inhibition (%) = ($A_{control}$ - A_{sample})/$A_{control}$ × 100%, where $A_{control}$ represented the FAS activity in the control group (phosphate buffer instead of sample solution), A_{sample} represented the FAS activity in the sample groups. The FAS activity was calculated as (A_0 - A_1)/1 min, in which A_0 was the absorbance of the reaction compound when the FAS was added, and A_1 was the absorbance of the reaction compound after reaction 1 min. Orlistat was used as the positive control.

FAS substrates: 0.1 M potassium phosphate buffer (pH 7.0), 1 mM ethylene-diaminetetraacetic acid (EDTA), 1 mM dithiothreitol, 3 μM acetyl-coenzyme A, 10 μM methylmalonyl coenzyme A, 35 μM NADPH.

S2.2. Determination of *α*-glucosidase inhibitory activity

Compounds **1**-**8** (1.0-1.7 mg) were dissolved in DMSO (100 μL) and then diluted with phosphate buffer (0.1 M, pH 6.8). Sample solution (50 μL, 0.078-78 nM) and

4-nitrophenyl α-D-glucopyranoside (pNPG) solution (50 μL, 5 mM) were mixed and incubated in a 96-well microplate at 37 °C for 5 min. α-Glucosidase from yeast (50 μL, 0.2 U/mL) was added and incubated at 37 °C for another 30 min. Finally, 50 μL of Na_2CO_3 (1M) was added to terminate the reaction. The absorbance of compound was measured using a microplate reader at a wavelength 405 nm. The background absorbance (phosphate buffer instead of substrate pNPG) of all samples in no more than 20 μM at 405 nm was little, therefore the inhibitory effect was calculated by the following equation: α-glucosidase inhibition (%) = $(A_{control} - A_{sample})/A_{control} \times 100\%$, where $A_{control}$ represented the absorbance of phosphate buffer control without test samples, A_{sample} represented the absorbance of test samples. Acarbose was used as the positive control.

S2.3. Determination of α-amylase inhibitory activity

Phosphate buffer (20 mM, pH 6.9, containing 6 mM NaCl) was used as the solvent in this assay. Sample solution (50 μL, 50-1500 μM) and starch solution (50 μL, 1%, w/v) were mixed and incubated in a 96-well microplate at 37 °C for 10 min. Then, α-amylase solution (50 μL, 0.2 U/mL) was added and the compound was incubated at 37 °C for an additional 10 min. The reaction was stopped by addition of 3, 5-dinitrosalicylic acid colour reagent (100 μL, 27.6 mM) and the 96-well microplate was immediately heated in 95 °C water bath for 10 min. When the reaction solution cooled to room temperature, all samples were diluted by adding distilled water (50 μL), and then their absorbance was measured using a microplate reader at 540 nm. All samples had little background absorbance (phosphate buffer instead of starch solution) at 540 nm, thus the inhibitory activity was calculated as $(A_{control} - A_{sample})/A_{control} \times 100\%$, in which A_{sample} was the absorbance of the sample and $A_{control}$ was the absorbance of the phosphate buffer control without test samples. Acarbose was used as the positive control.

S2.4. DPPH radical scavenging assay

The DPPH radical scavenging assay was used to evaluate the antioxidant activity of compounds **1**-**8**. In a 96-well microplate, 100 μL of DPPH solution (200 μM in ethanol) was added to 100 μL sample in ethanol at graded concentrations ranging

from 7 to 500 μM. The compound was incubated in the dark at room temperature for 30 min. The absorbance of the reaction compound was measured at 517 nm using a microplate reader. The DPPH scavenging activity was calculated by the following formula: DPPH scavenging activity (%) = ($A_{control}$ - A_{sample})/$A_{control}$ × 100%, where $A_{control}$ was the absorbance of ethanol control without samples, A_{sample} was the absorbance of sample. Ascorbic acid was used as the positive control in the experiment.

S2.5. ABTS radical scavenging assay

The ABTS radical scavenging assay was used also to evaluate the antioxidant activity of compounds **1**-**8**. The ABTS free radical cation ($ABTS^{\bullet+}$) was manufactured by reacting ABTS stock solution (7 mM) with potassium persulphate (2.45 mM) in the dark at room temperature for 12-16 h. The $ABTS^{\bullet+}$ solution was diluted with ethanol to an absorbance of 0.7 at 734 nm. Sample solution (100 μL, 2-100 μM in ethanol) was mixed with 150 μL diluted $ABTS^{\bullet+}$ solution. After reaction in the dark at room temperature for 20 min, the absorbance of the reaction compound at 734 nm was recorded. The $ABTS^{\bullet+}$ scavenging capability was calculated as ($A_{control}$ - A_{sample})/$A_{control}$ × 100%, in which $A_{control}$ was the absorbance of ethanol control without samples, A_{sample} was the absorbance of sample. Ascorbic acid was used as the positive control.