Supporting Information

Prenylated Coumarins from the Fruits of *Manilkara zapota* with Potential Anti-inflammatory Effects and Anti-HIV Activities

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List of Supporting Information

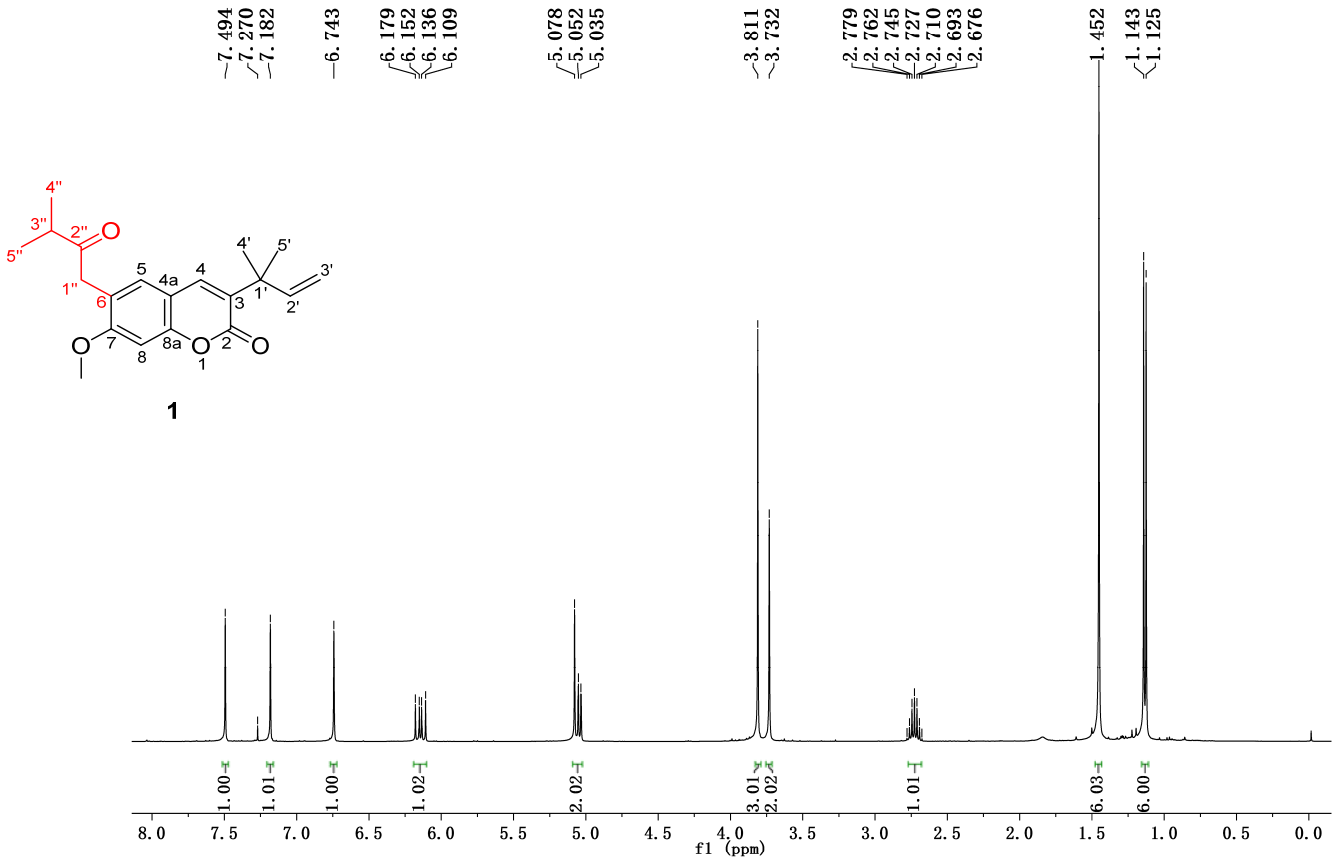

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Figure S1. ^{1}H-NMR spectrum of manizapotin A (**1**) in $CDCl_3$.

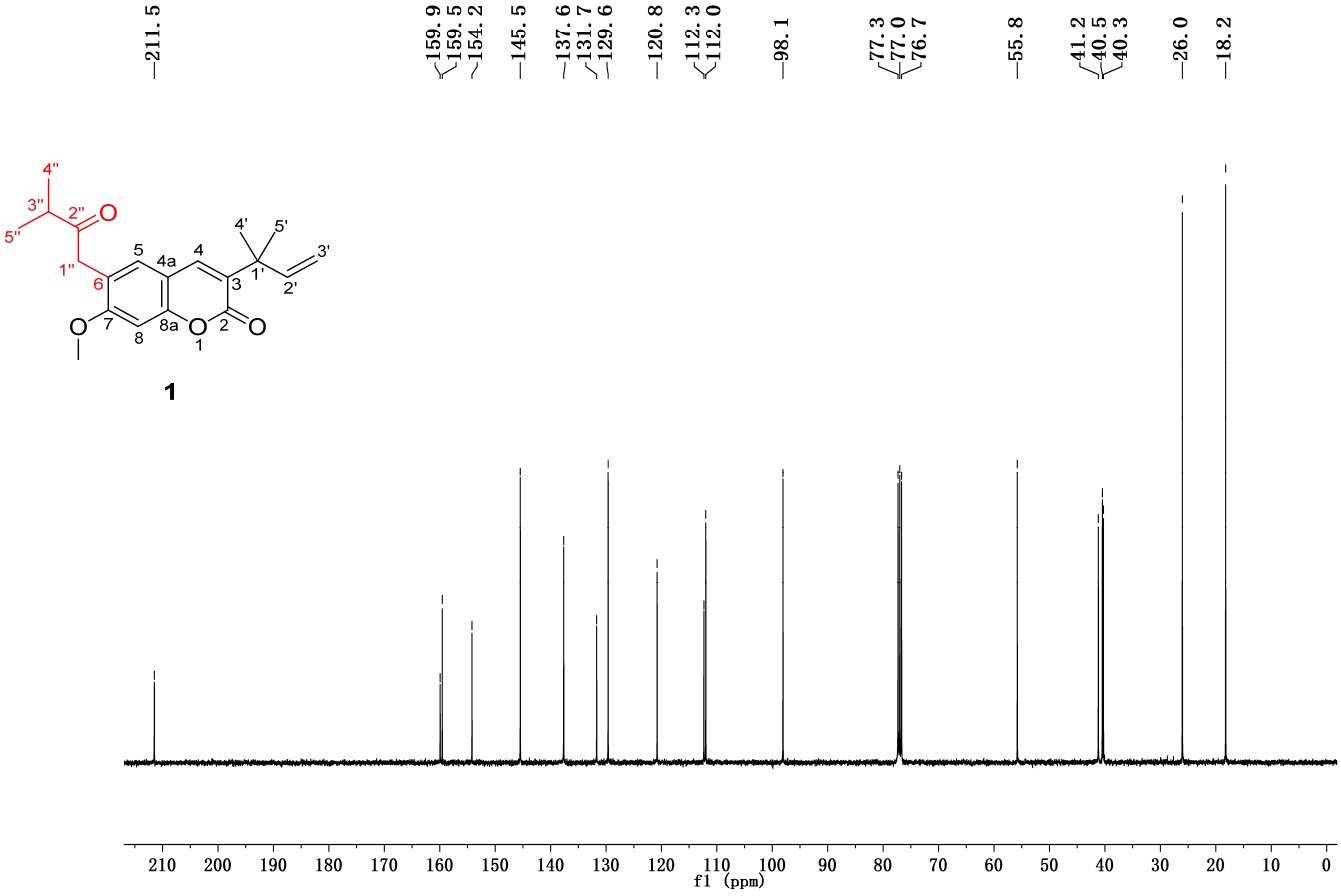

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Figure S2. ^{13}C-NMR spectrum of manizapotin A (**1**) in $CDCl_3$.

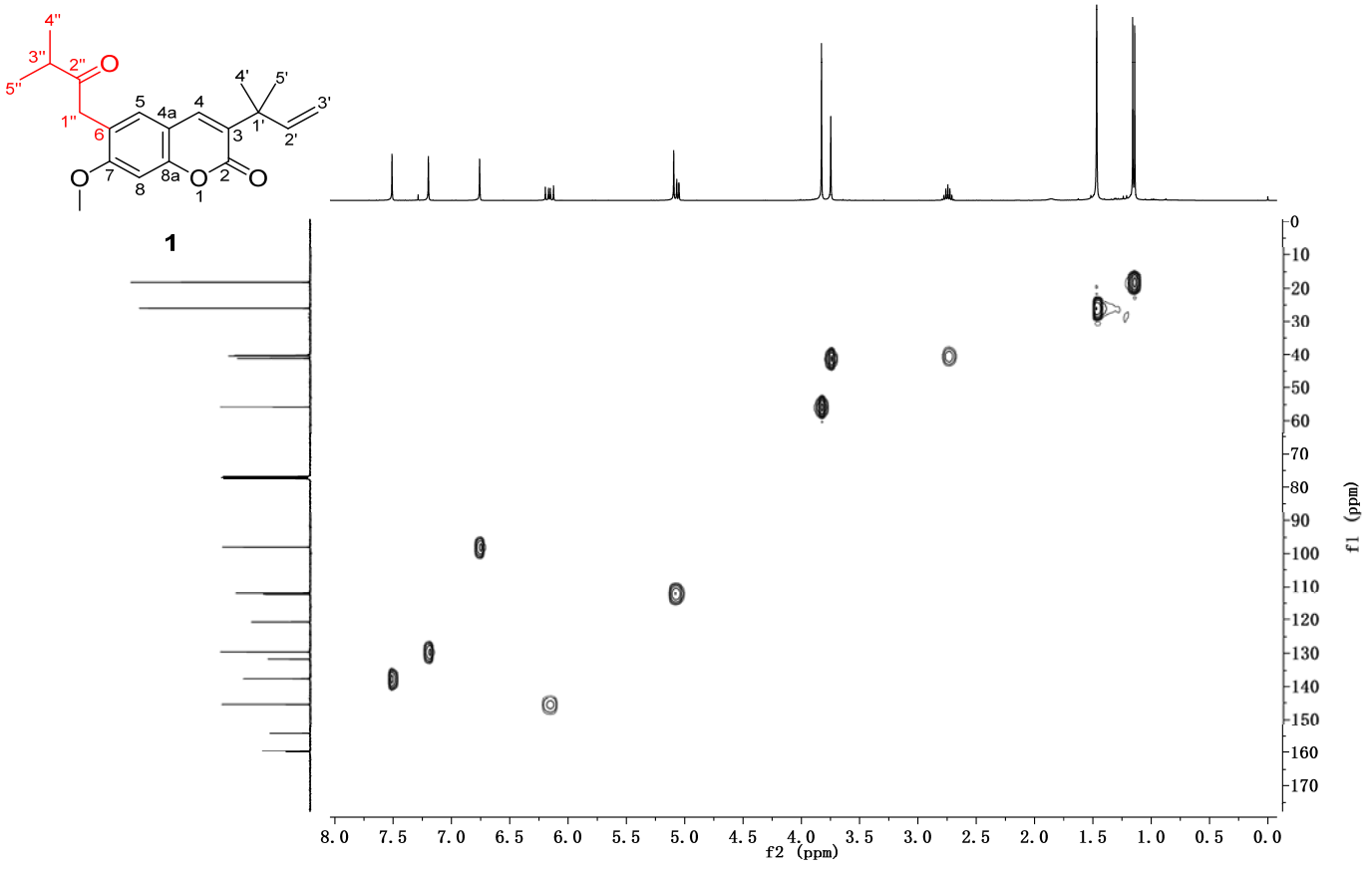


Figure S3. HSQC spectrum of manizapotin A (**1**) in $CDCl_3$.

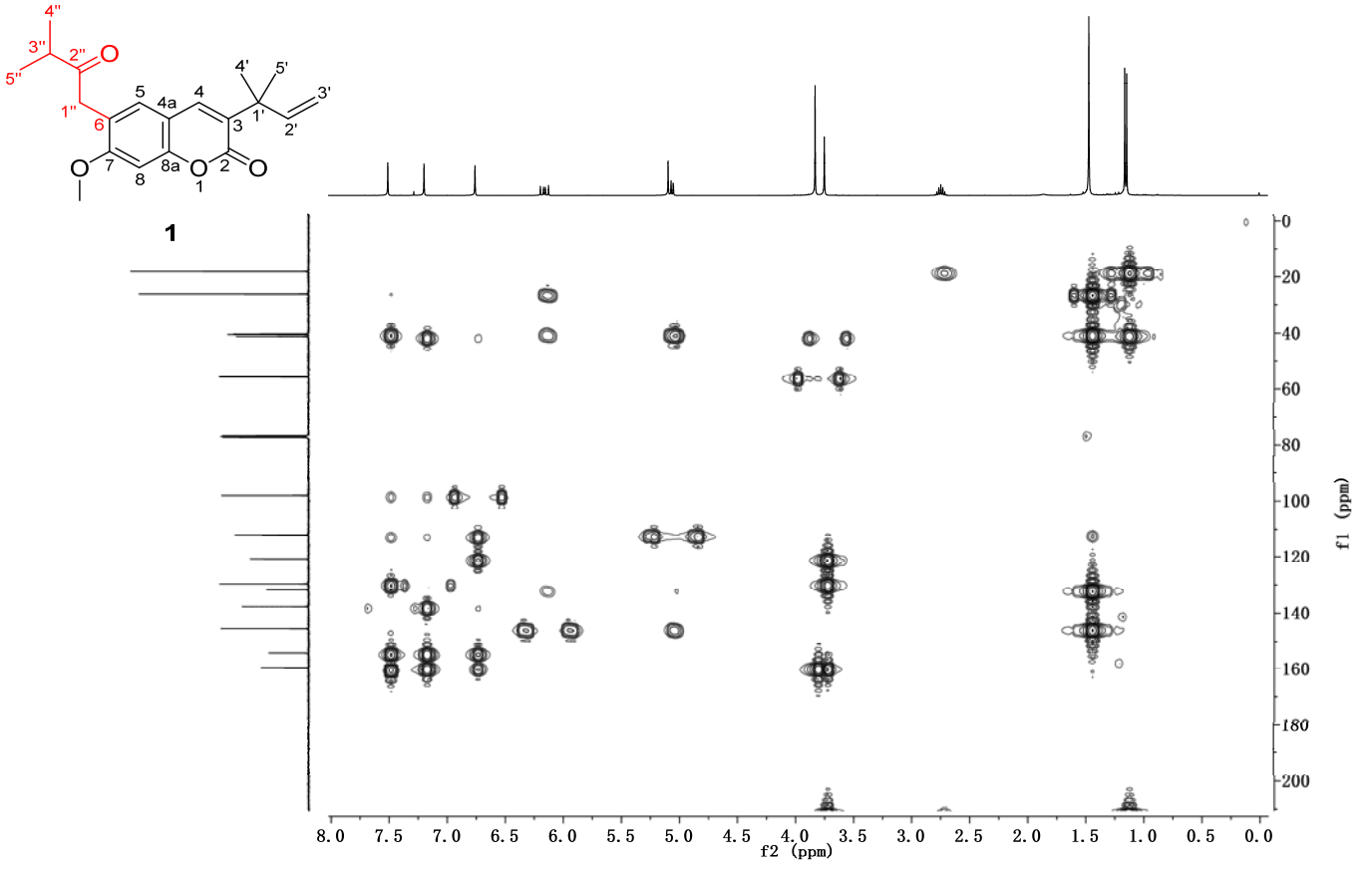


Figure S4. HMBC spectrum of manizapotin A (**1**)in $CDCl_3$.

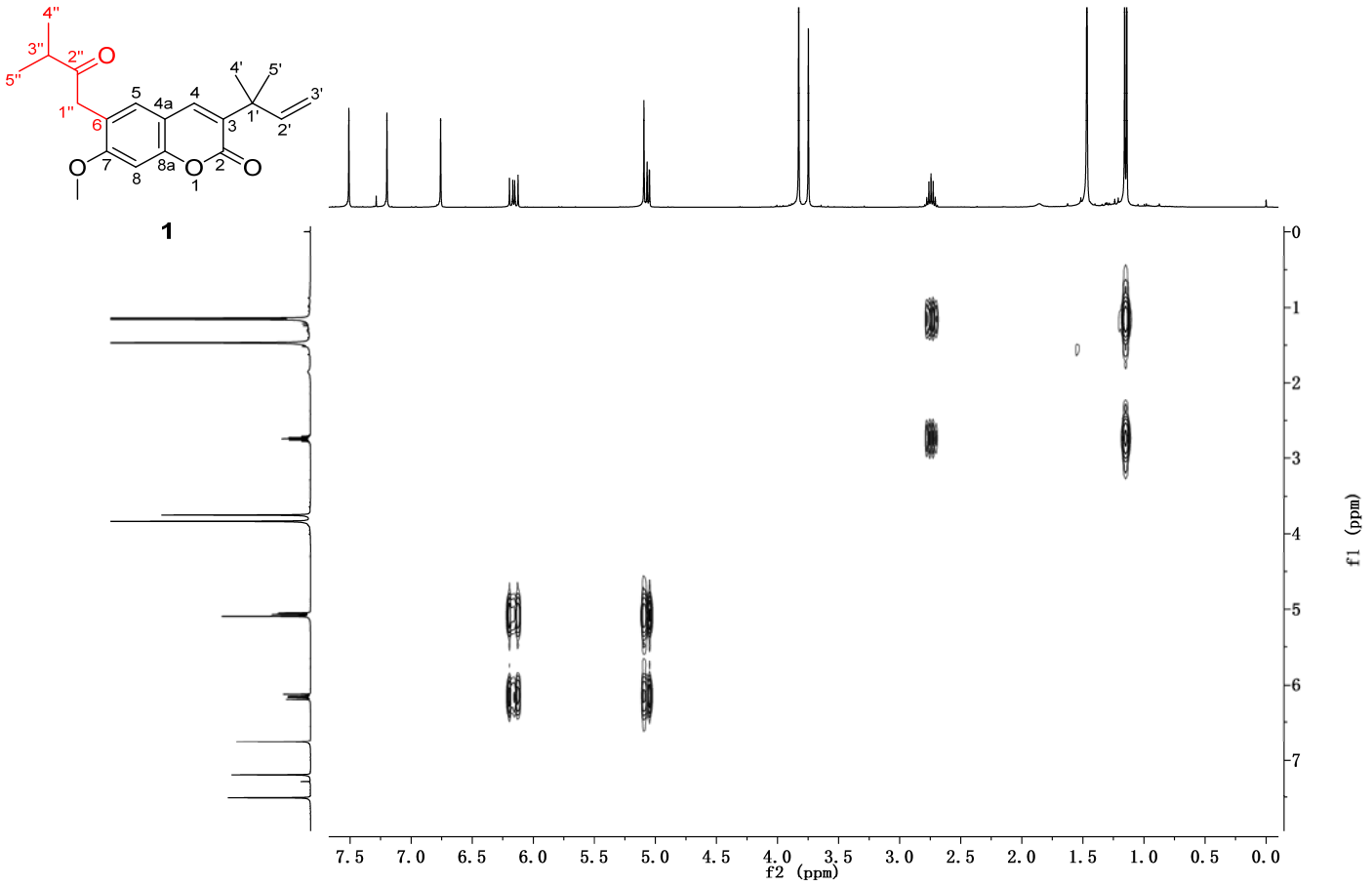


Figure S5. ^{1}H-^{1}H COSY spectrum of manizapotin A (**1**) in $CDCl_3$.

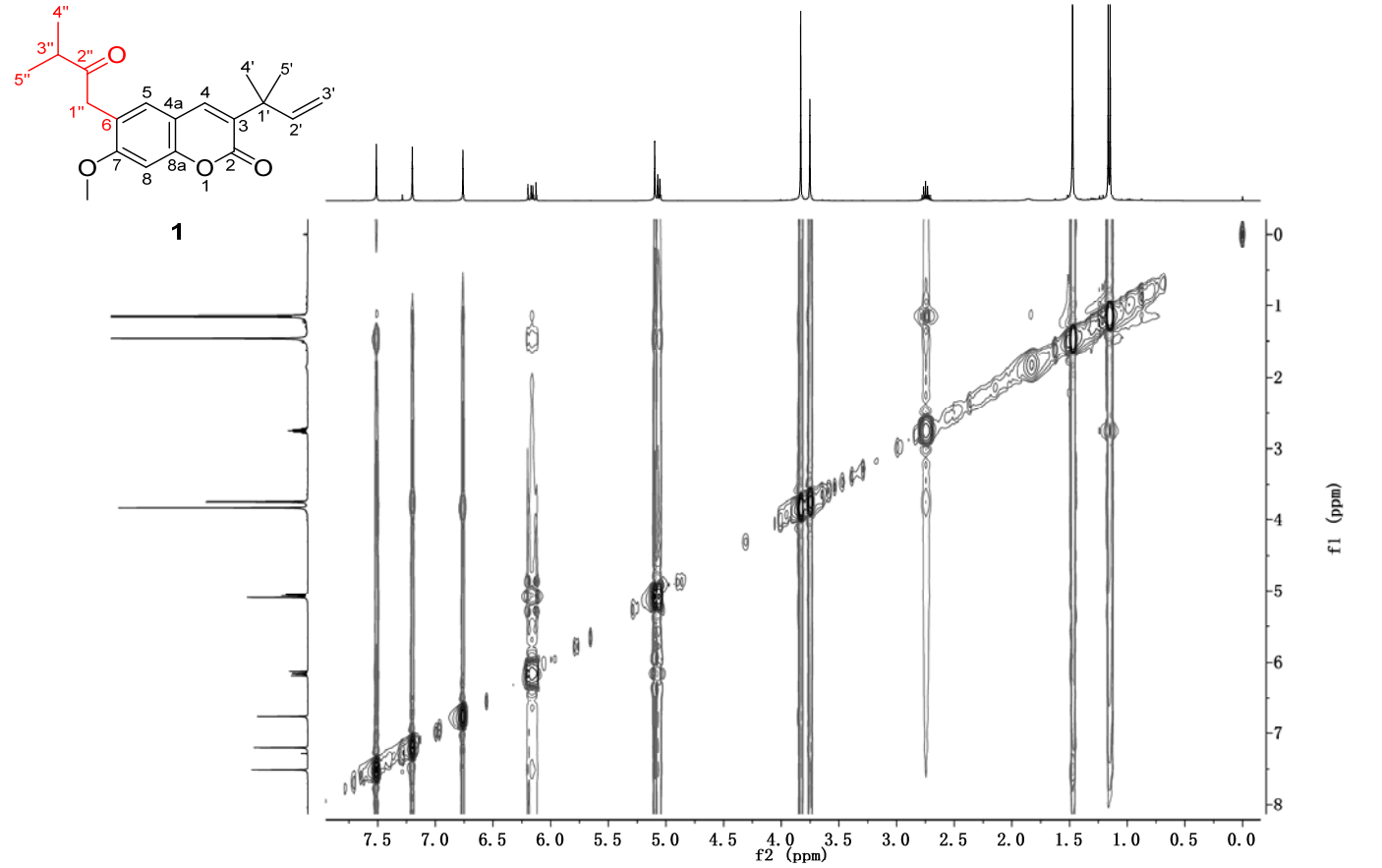


Figure S6. ROESY spectrum of manizapotin A (**1**) in $CDCl_3$.

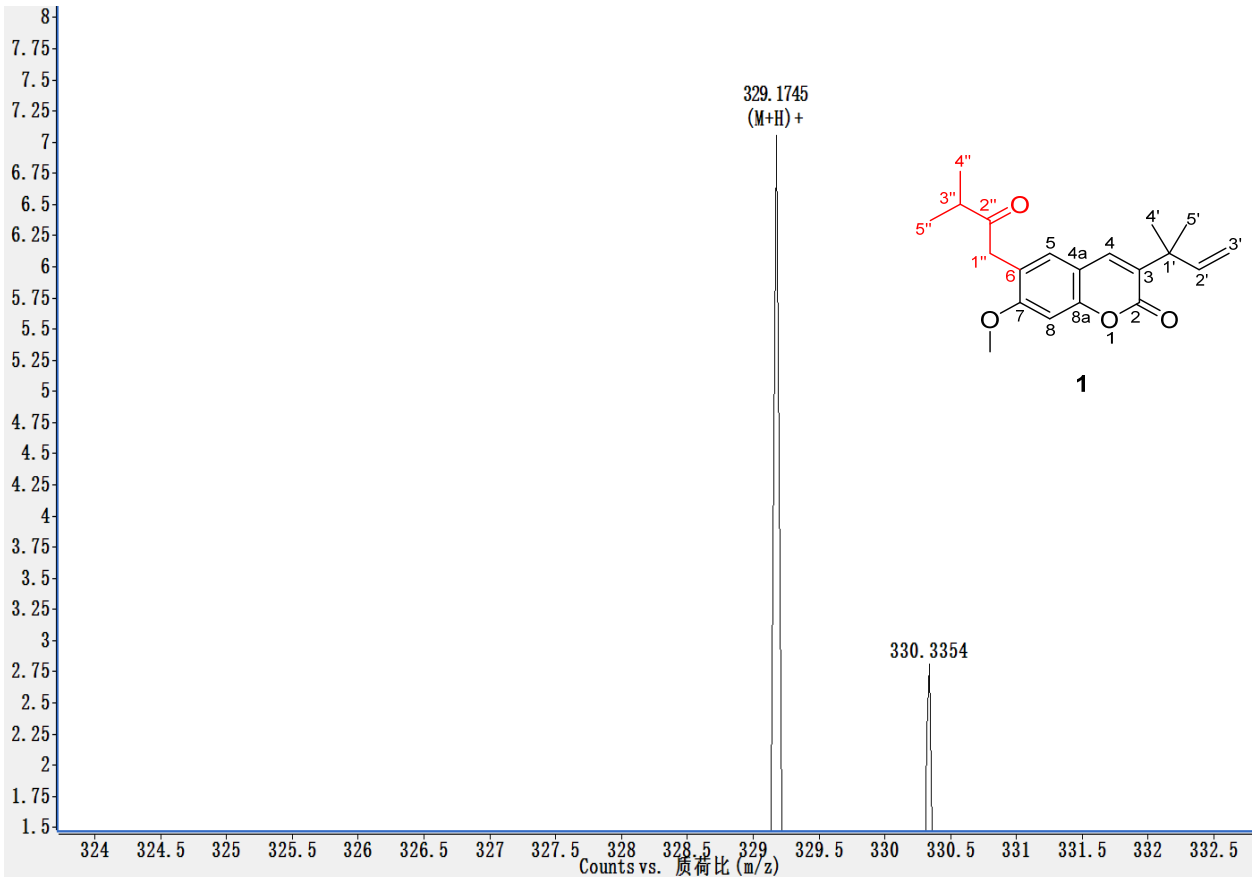


Figure S7. HRESIMS spectrum of manizapotin A (**1**).

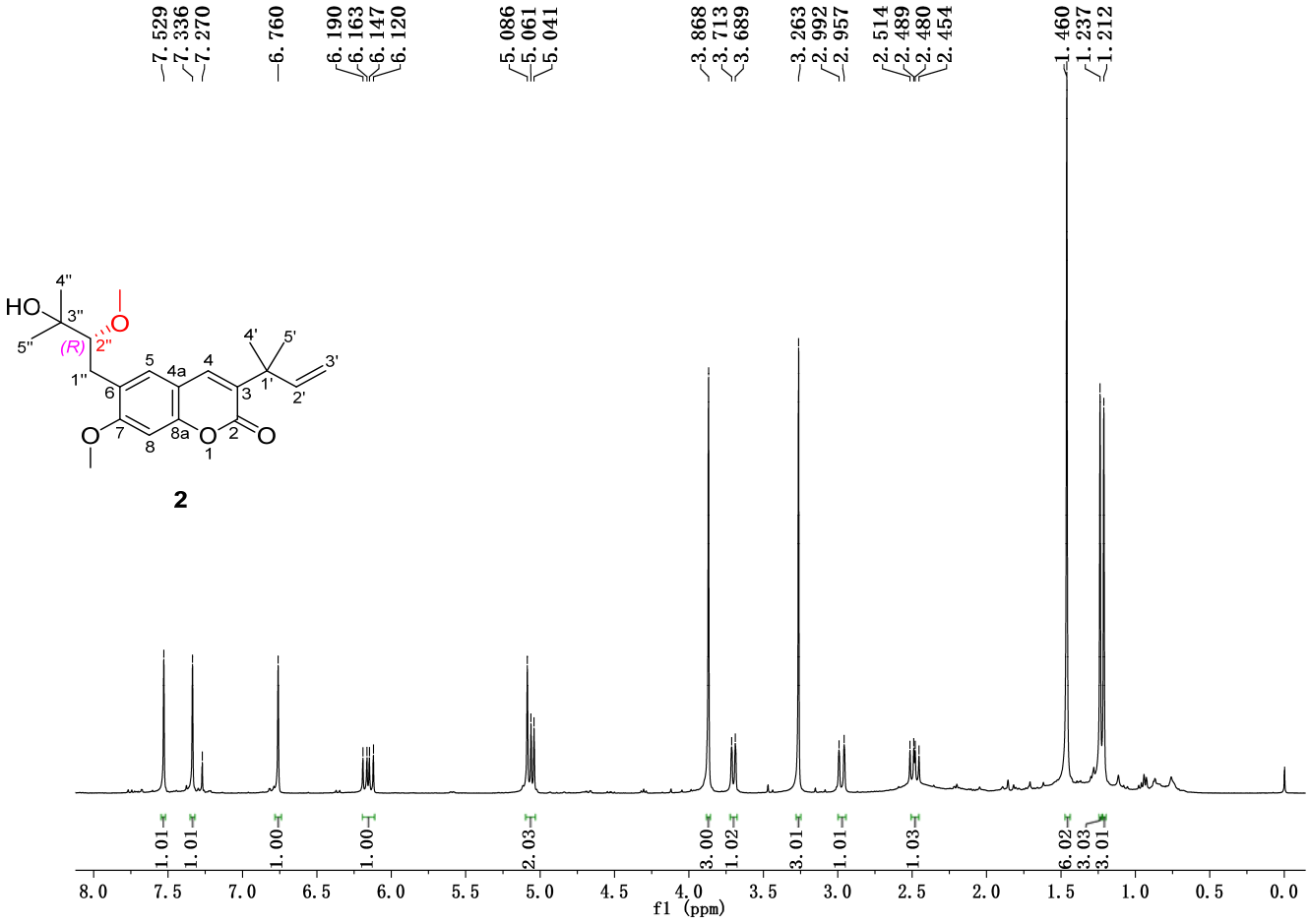


Figure S8. ^{1}H-NMR spectrum of manizapotin B (**2**) in $CDCl_3$.

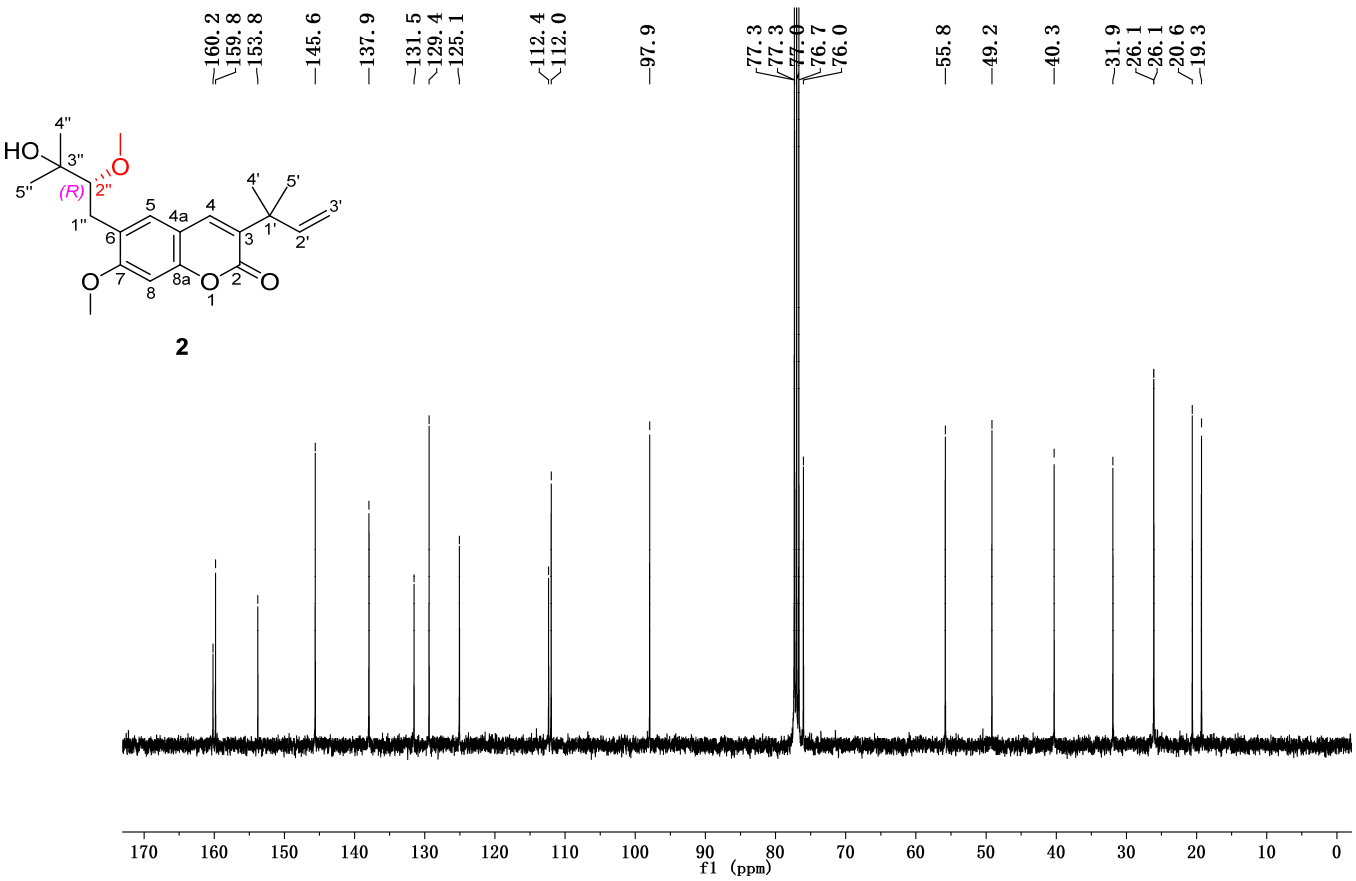


Figure S9. ^{13}C-NMR spectrum of manizapotin B (**2**) in $CDCl_3$.

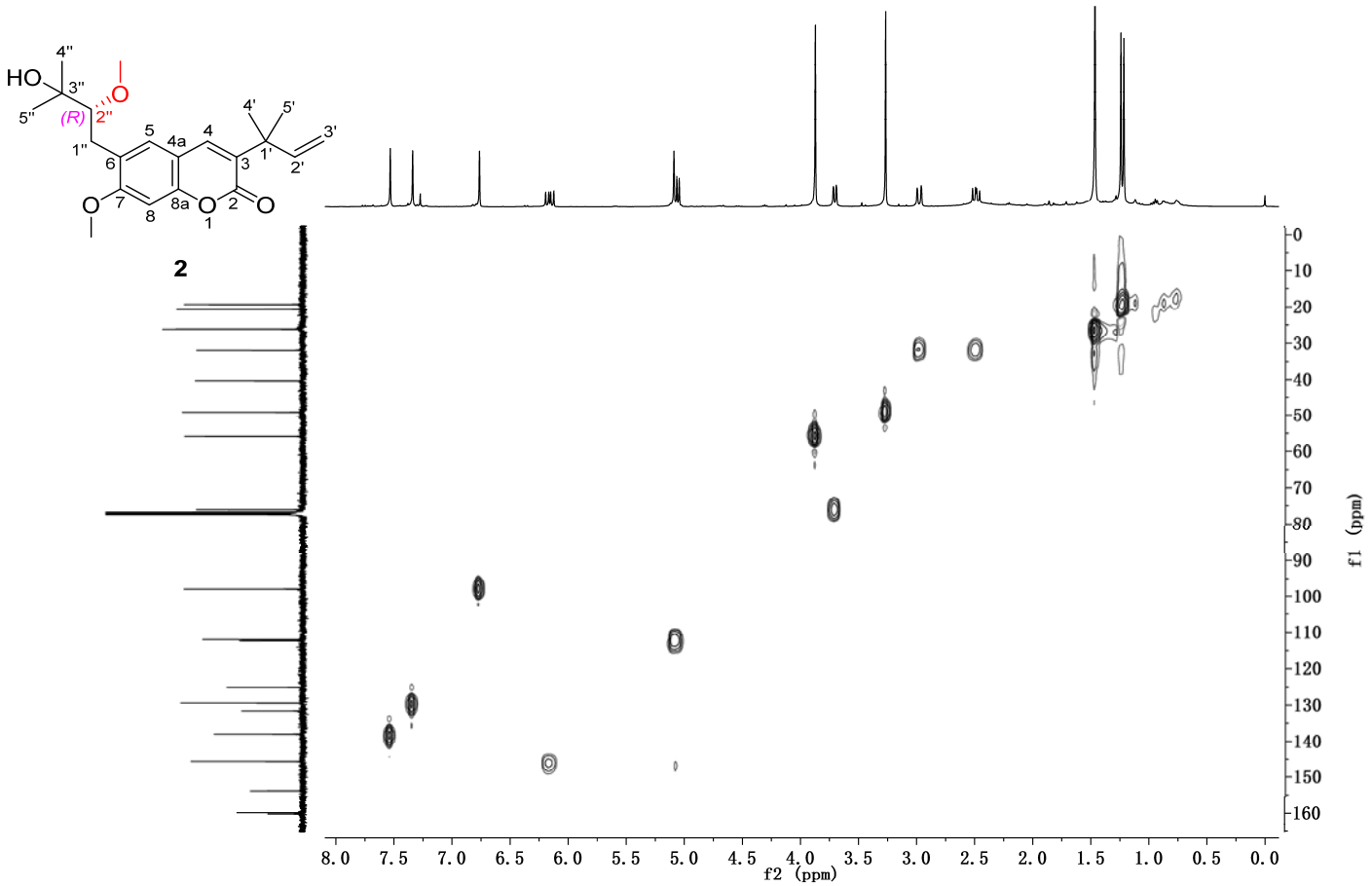
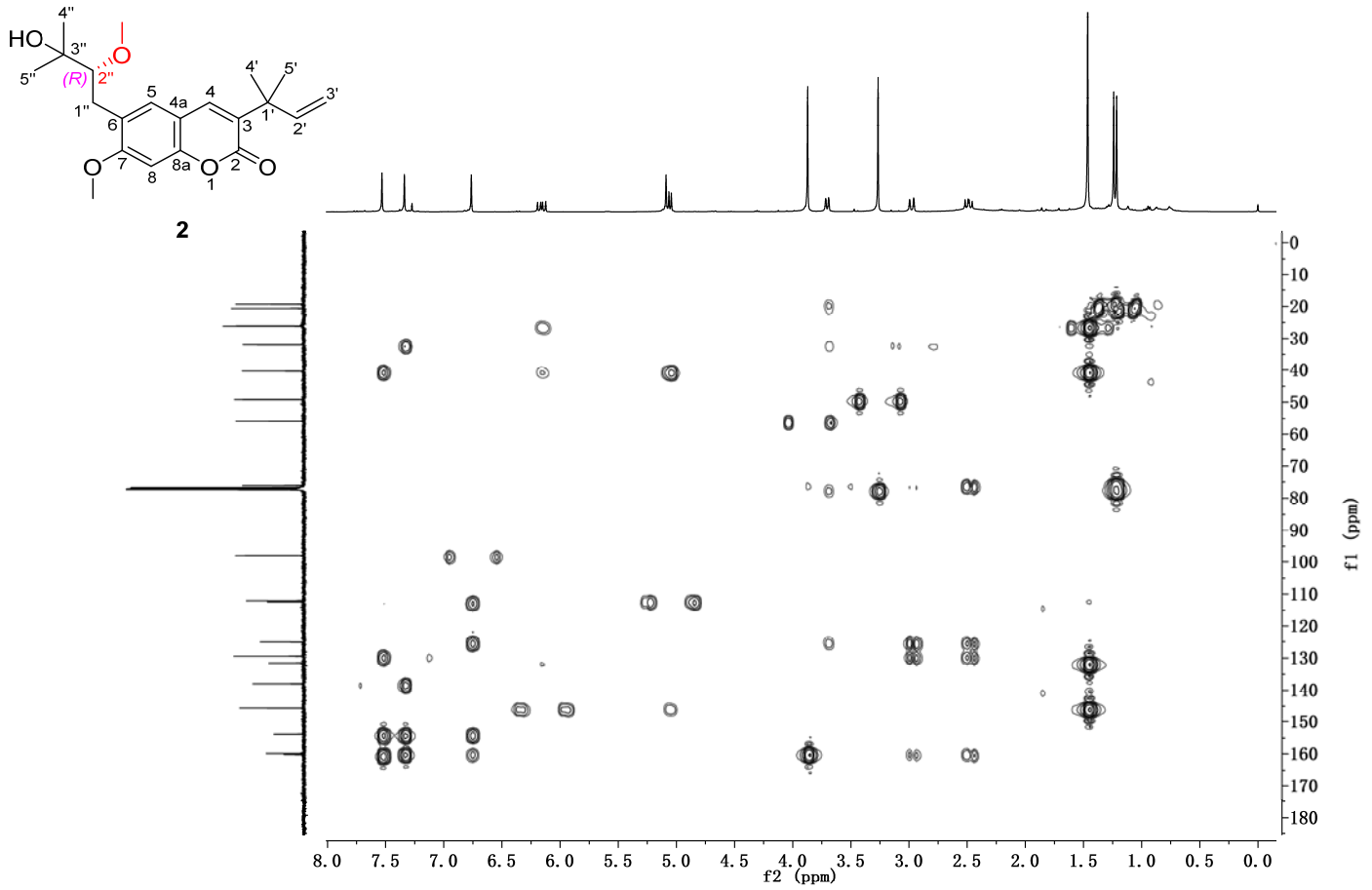


Figure S10. HSQC spectrum of manizapotin B (**2**) in $CDCl_3$.



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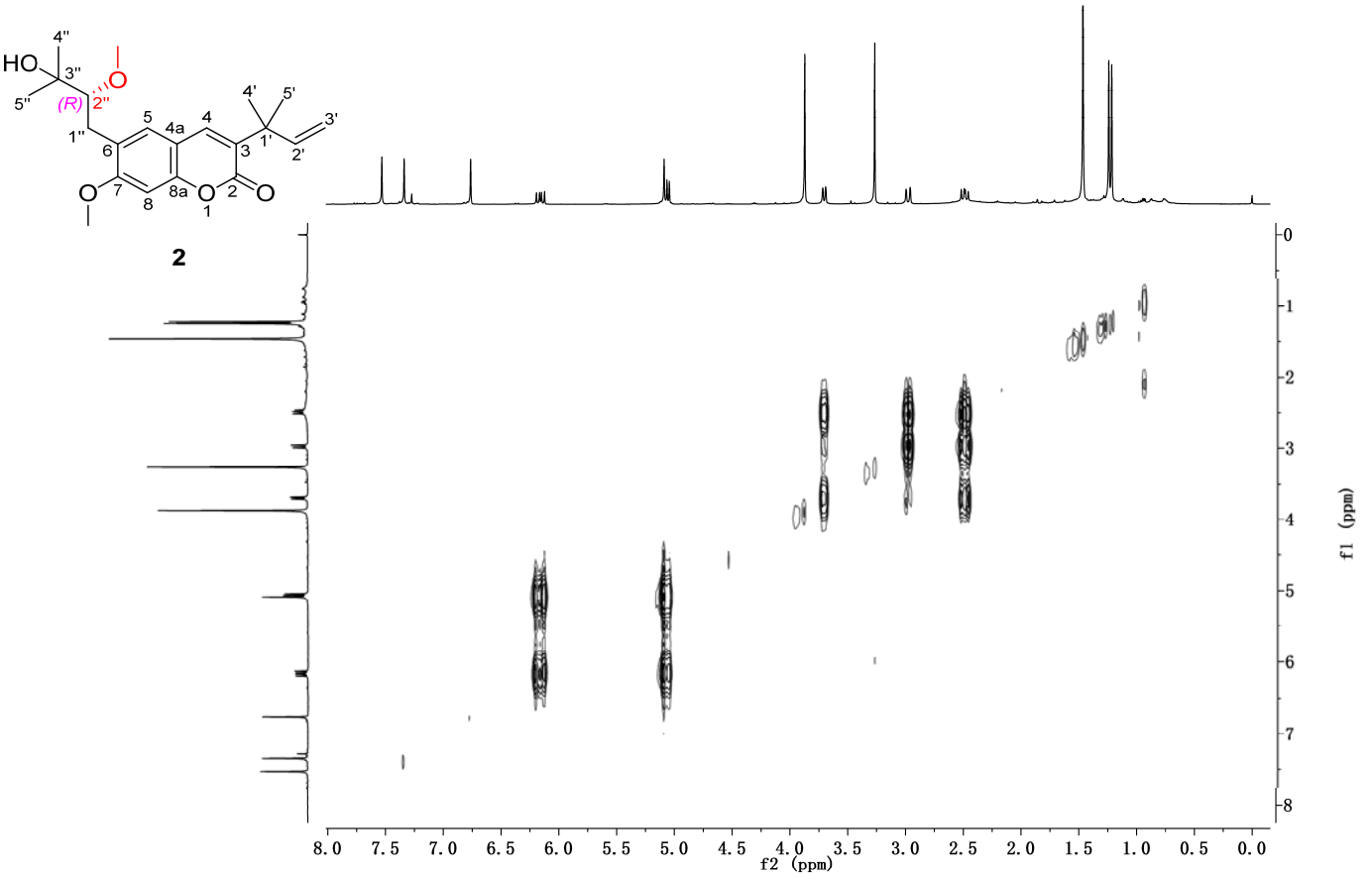

Figure S12. ^{1}H-^{1}H COSY spectrum of manizapotin B (**2**) in $CDCl_3$.

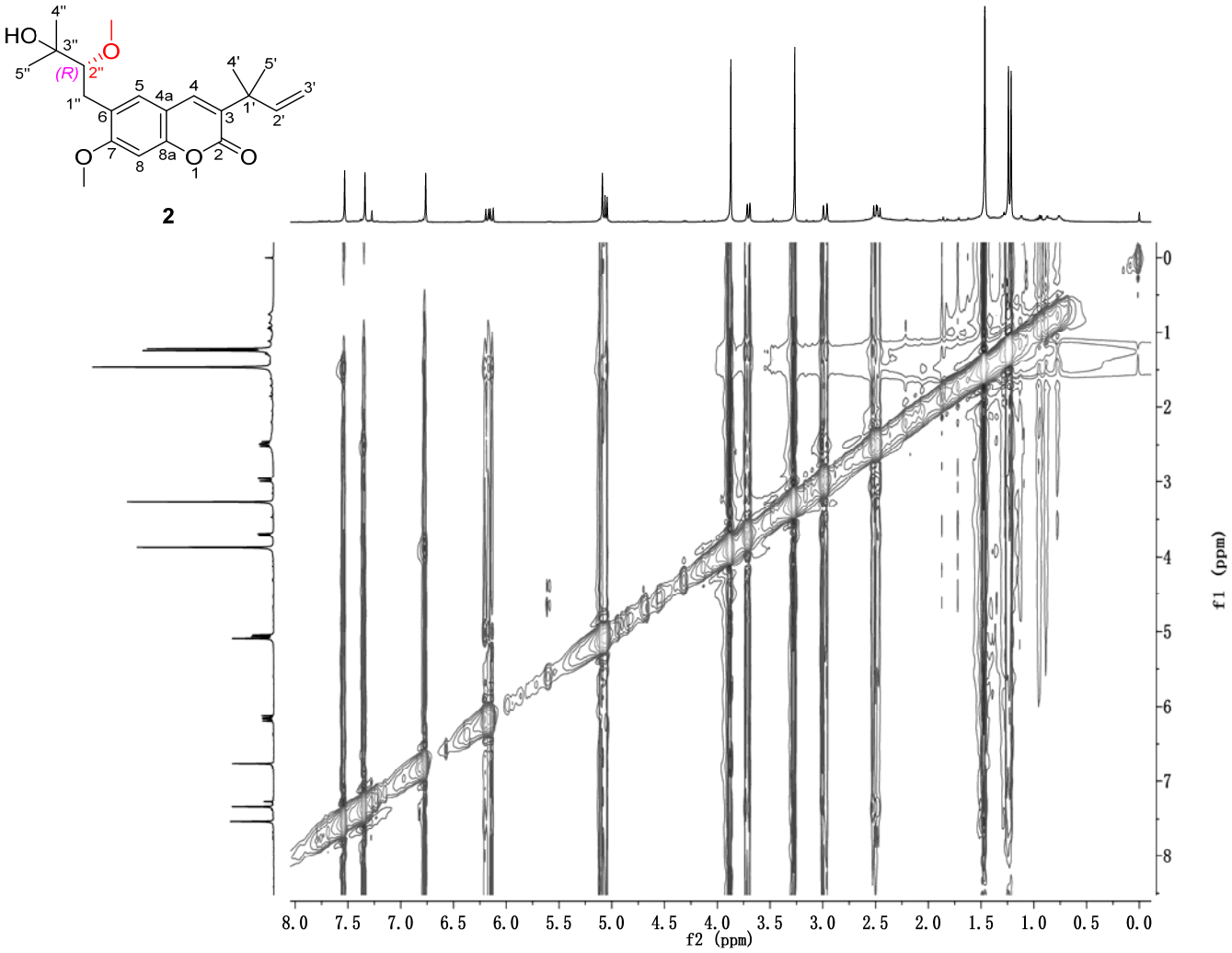

Figure S13. ROESY spectrum of manizapotin B (**2**) in $CDCl_3$.

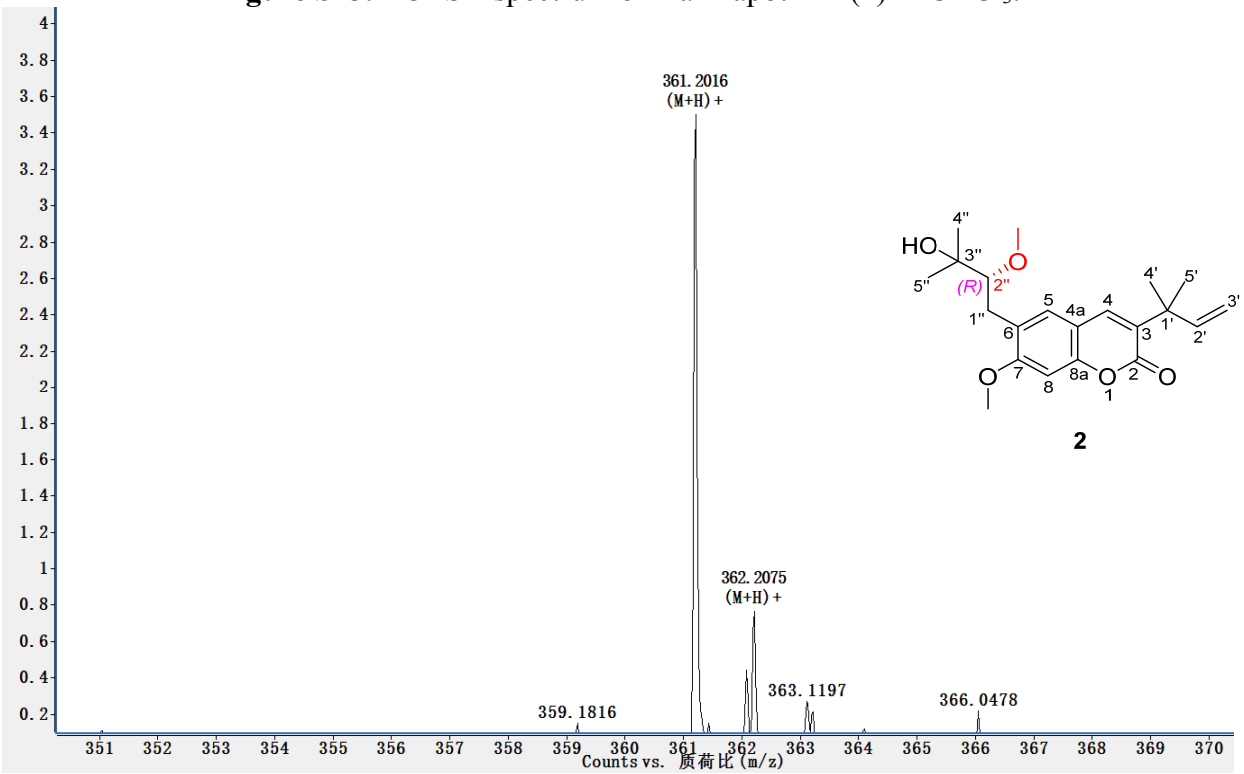

Figure S14. HRESIMS spectrum of manizapotin B (**2**).

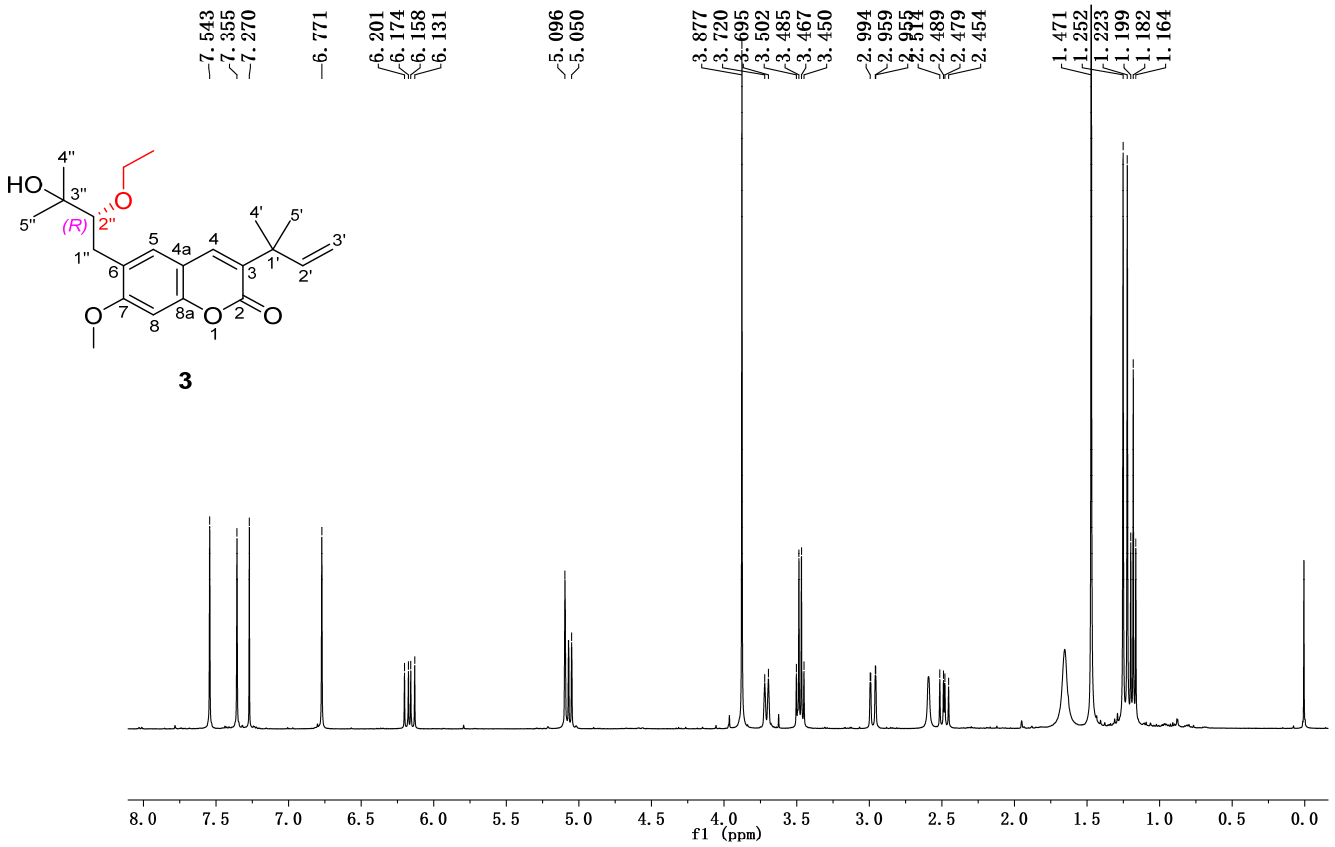

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Figure S15. ^{1}H-NMR spectrum of manizapotin C (**3**) in $CDCl_3$.

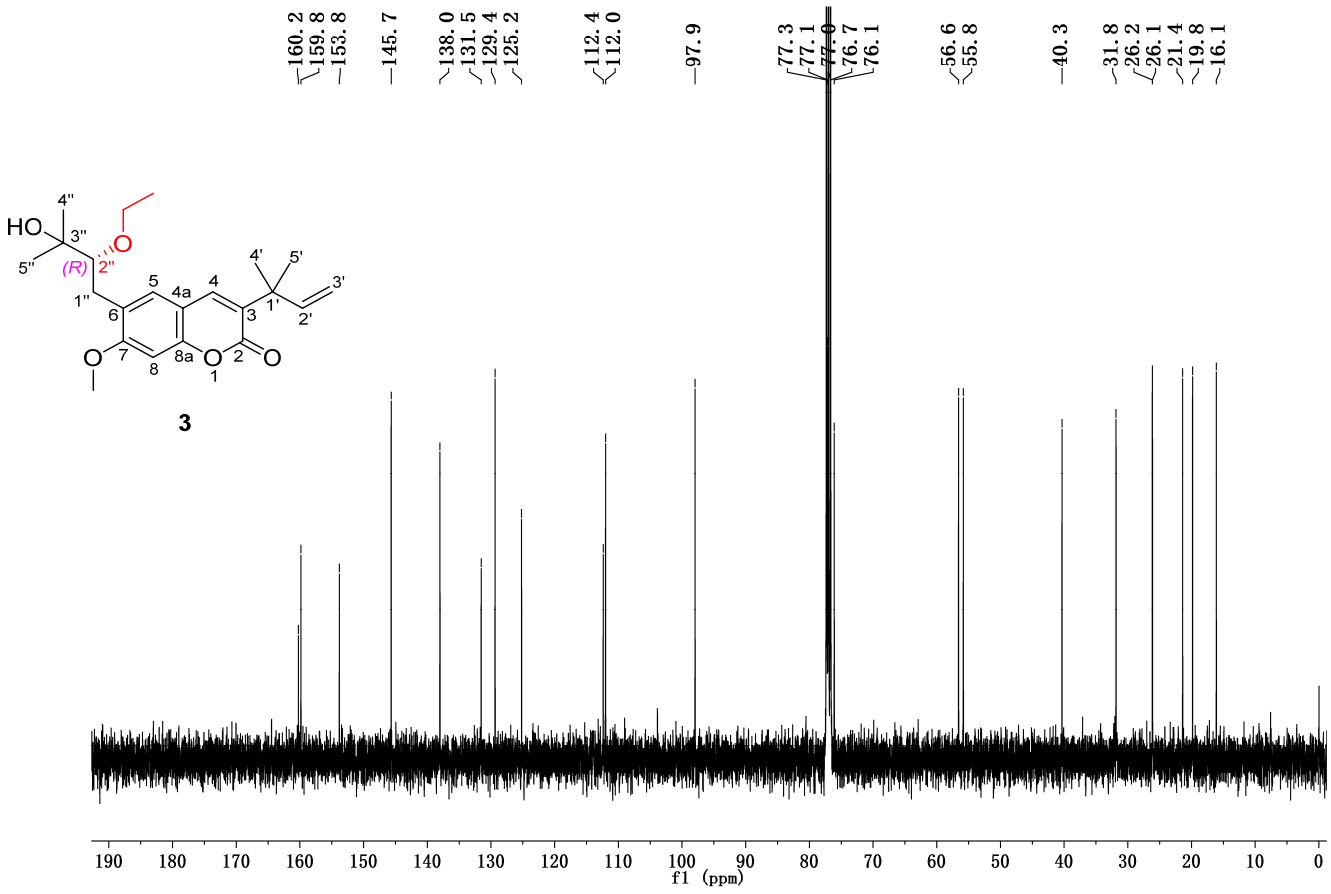

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Figure S16. ^{13}C-NMR spectrum of manizapotin C (**3**) in $CDCl_3$.

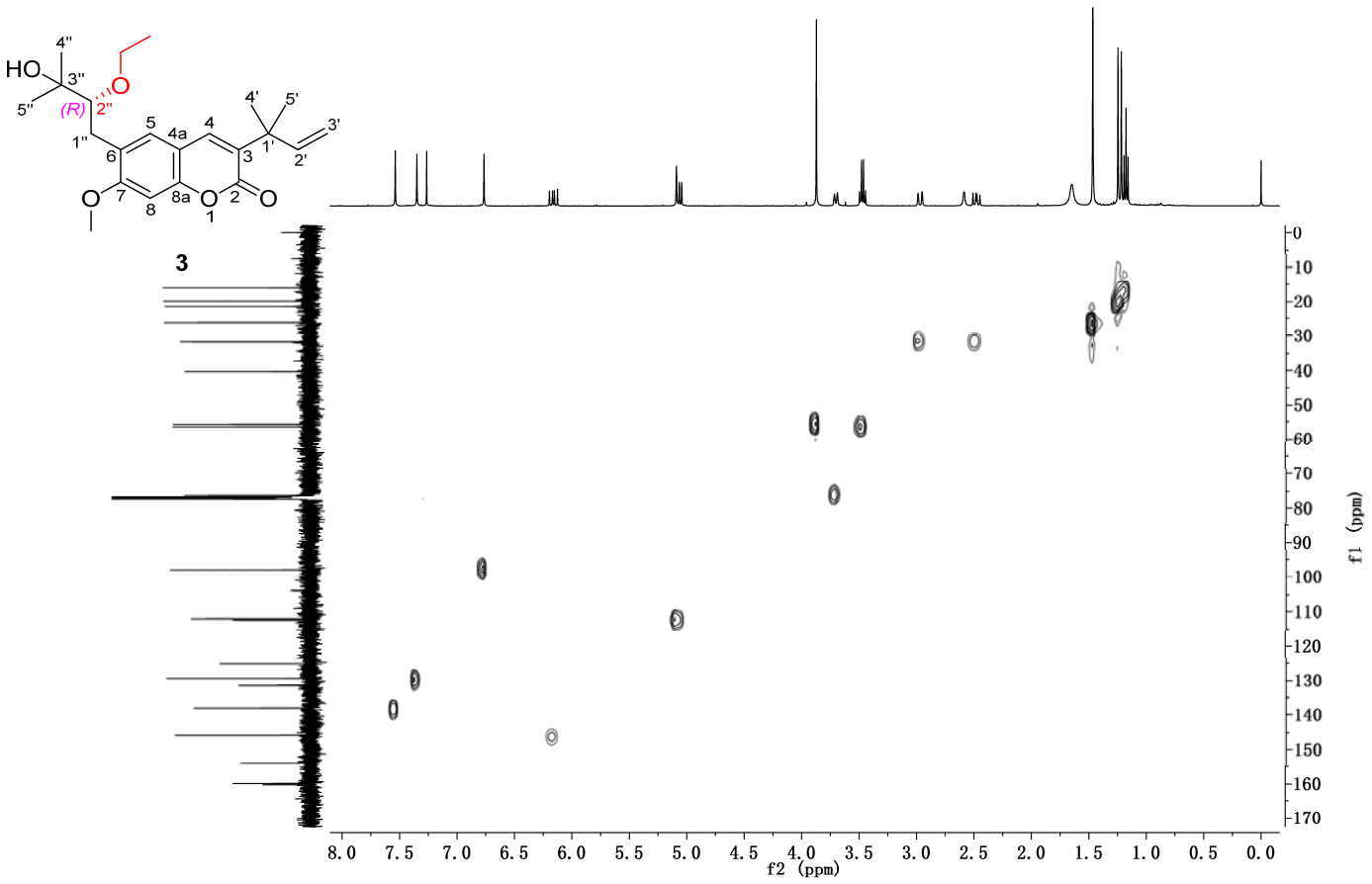

Figure S17. HSQC spectrum of manizapotin C (**3**) in $CDCl_3$.

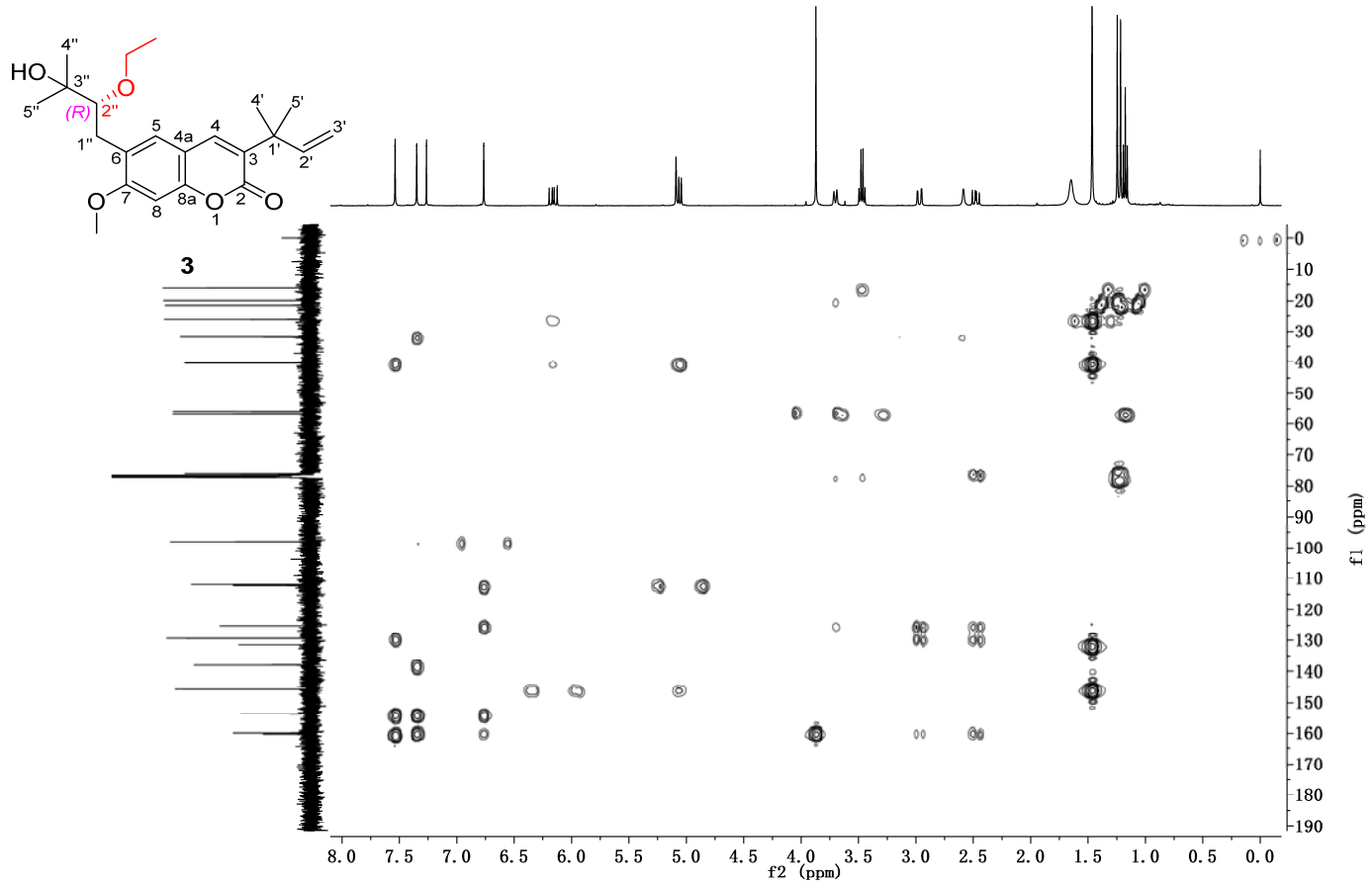

Figure S18. HMBC spectrum of manizapotin C (**3**) in $CDCl_3$.

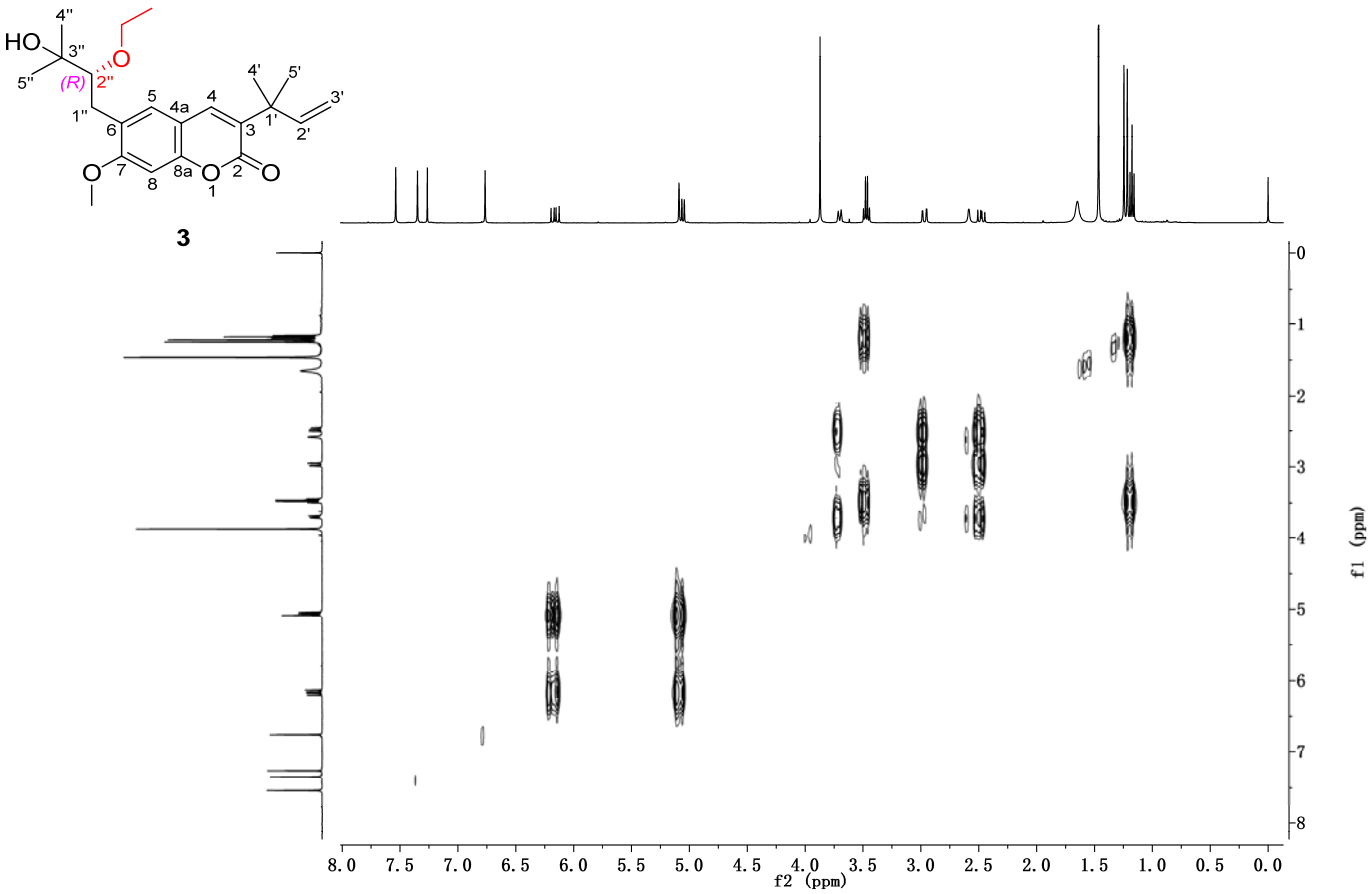

Figure S19. ^{1}H-^{1}H COSY spectrum of manizapotin C (**3**) in $CDCl_3$.

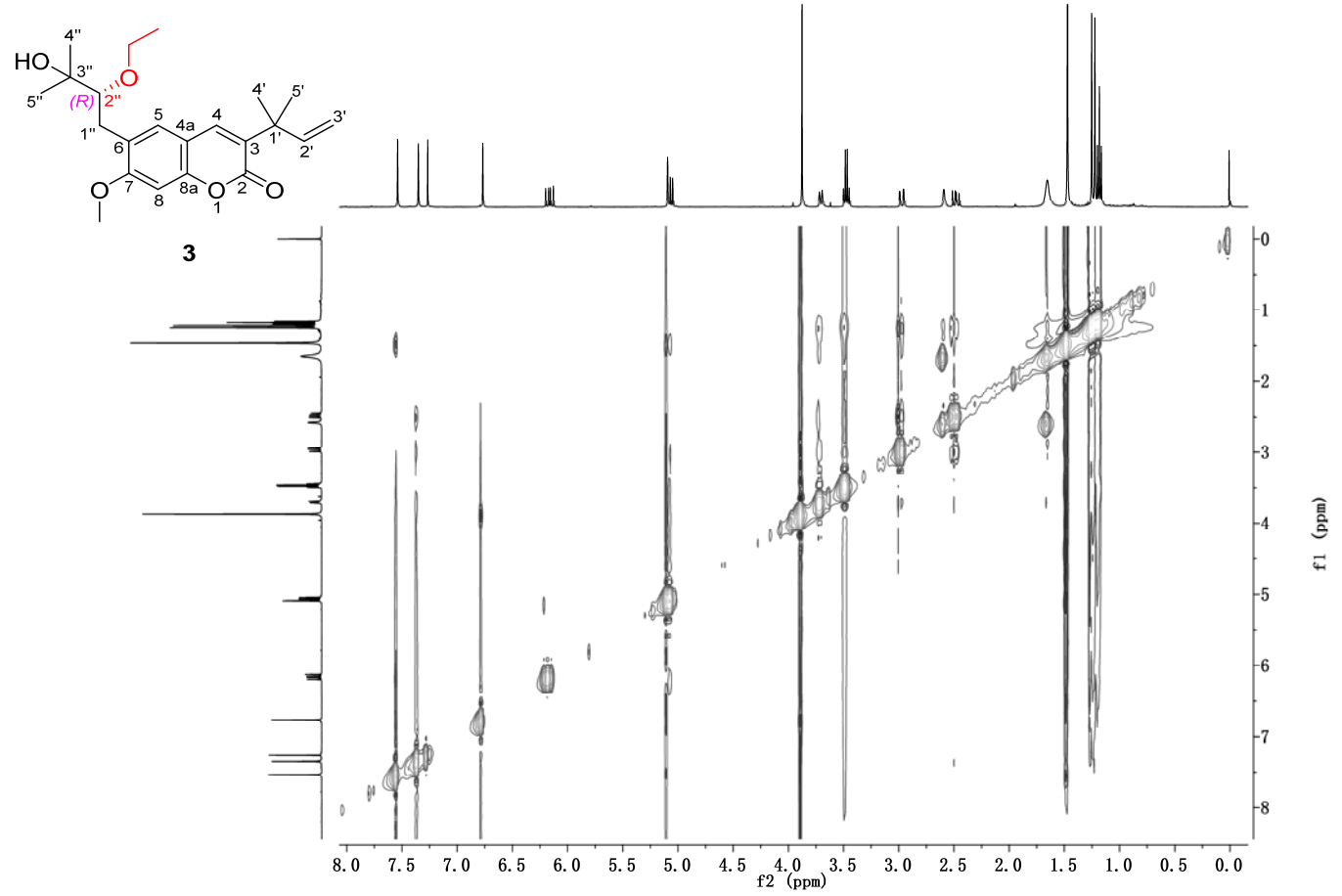

Figure S20. ROESY spectrum of manizapotin C (**3**) in $CDCl_3$.

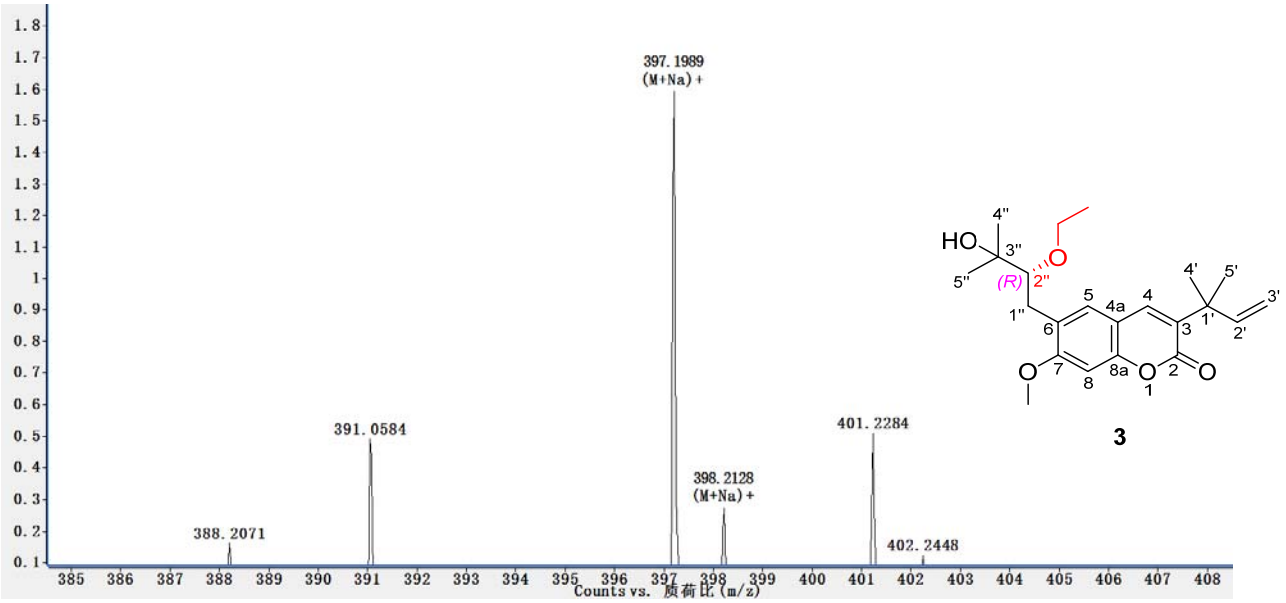

Figure S21. HRESIMS spectrum of manizapotin C (**3**).

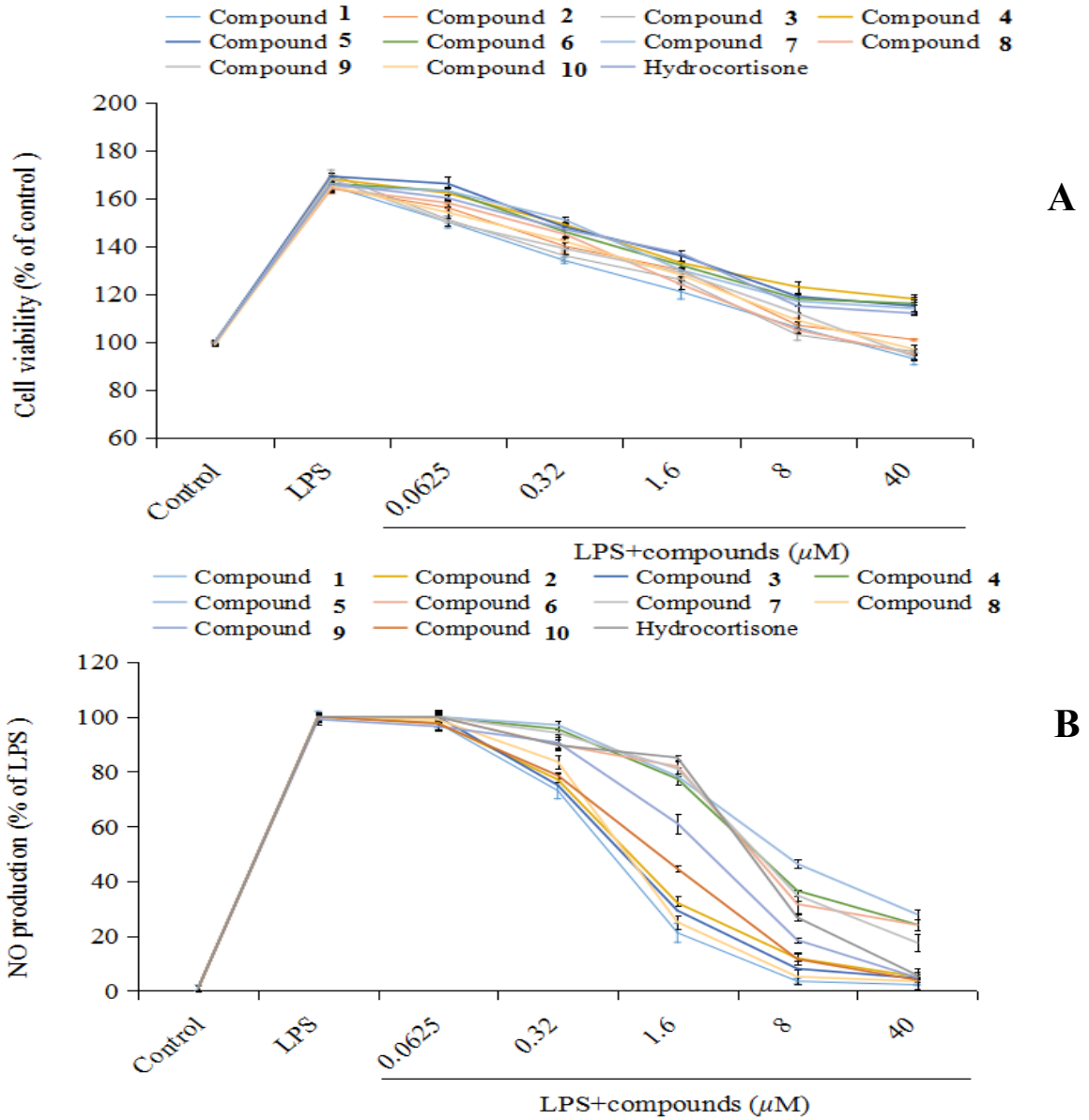

Figure S22. Cell viability (**A**) and inhibitory activities on LPS-stimulated NO production (**B**) in RAW 264.7 cells of compounds **1**–**10**.

Table S1. Anti-inflammatory Effects of 10 Fractions (Fr.1–Fr.10) from the Fruits of *M. zapota*.

Fraction	IC_{50} (μM)[a]	Fraction	IC_{50} (μM)[a]
Fr. 1	39.58 ± 0.12	Fr. 6	> 40.00
Fr. 2	5.83 ± 0.09	Fr. 7	> 40.00
Fr. 3	38.63 ± 0.17	Fr. 8	> 40.00
Fr. 4	> 40.00	Fr. 9	> 40.00
Fr. 5	> 40.00	Fr. 10	> 40.00
hydrocortisone[b]	3.95 ± 0.12		

[a]IC_{50} value was defined as 50% inhibitory concentration on NO production induced by lipopolysaccharide in mouse macrophage RAW 264.7 cells *in vitro* and expressed as the mean ± SD of triplicate determinations. [b]Positive control.

Table S2. Anti-HIV Activities of 10 Fractions (Fr.1–Fr.10) from the Fruits of *M. zapota*.

Fraction	CC_{50} (μM)[a]	EC_{50} (μM)[b]	TI[c]
Fr. 1	> 200.00	193.29	> 1.03
Fr. 2	> 200.00	0.98	> 204.01
Fr. 3	> 200.00	187.68	> 1.07
Fr. 4	> 200.00	> 200.00	Negative
Fr. 5	> 200.00	> 200.00	Negative
Fr. 6	> 200.00	> 200.00	Negative
Fr. 7	> 200.00	> 200.00	Negative
Fr. 8	> 200.00	> 200.00	Negative
Fr. 9	> 200.00	> 200.00	Negative
Fr. 10	> 200.00	> 200.00	Negative
AZT[d]	3927.52	0.01968	199569.11

[a]CC_{50}: 50% Cytotoxic concentration. [b]EC_{50}: 50% Effective concentration. [c]TI (therapeutic index) = CC_{50}/EC_{50}. [d]AZT (3'-azido-3'-deoxythymidine) was used as a positive control.

Extraction, Isolation and Identification of Compounds 11–40 from Fractions 1, 3–10.

The fresh ripe fruits of *M. zapota* (36.2 kg) were shredded by means of a multi-function food processor which were further soaked and extracted using 48 L of 90% ethanol at 26–36℃ for six times, each time for nine days. The ethanol extraction solvent was coalesced and then condensed under reduced pressure to afford a crude extract (5634.2 g). The crude extract (5632.0 g) was

separated over a silica gel CC, using chloroform/methanol (98:2 to 30:70, *v*/*v*) as the eluent to yield 10 fractions (Fr.1–Fr.10). Fr.1 (68.7 g) was further separated over a silica gel CC, using petroleum ether/ethyl acetate (95:5 to 40:60, *v*/*v*) as the eluent to produce eight fractions (Fr.1A–Fr.1H). Compounds **11** (32.7 mg), **14** (52.9 mg), **17** (28.3 mg) and **22** (17.3 mg) were separated from Fr.1D (7.6 g), purified *via* a Sephadex LH-20 gel CC (CH_3OH/H_2O, 50:50, *v*/*v*) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 90% CH_3OH, 3.5 mL/min, t_R 28.7, 34.5, 41.6 and 48.9 min), respectively. Compounds **12** (19.3 mg), **18** (34.7 mg), **20** (76.2 mg), **21** (102.5 mg) and **24** (21.6 mg),were isolated from Fr.1E (6.3 g), purified by a Sephadex LH-20 gel CC (CH_3OH/H_2O, 50:50, *v*/*v*) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 82% CH_3CN, 2.8 mL/min, t_R 27.8, 33.6 38.3, 45.7 and 50.6 min), respectively. Compounds **13** (43.9 mg), **15** (28.5 mg), **16** (33.9 mg) and **19** (203.8 mg) and **23** (43.2 mg) were obtained from Fr.1F (8.9 g), purified by a Sephadex LH-20 gel CC (CH_3OH/H_2O, 50:50, *v*/*v*) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 85% CH_3OH, 2.8 mL/min, t_R 32.9, 37.2, 40.8, 46.3 and 53.2 min), respectively. Fr. 3 (28.9 g) was further separated over an ODS gel medium-pressure CC (CH_3OH/H_2O, 45:55 to 100:0, *v*/*v*) to yield seven fractions (Fr.3A–Fr.3G). Compounds **25** (7.8 mg) and **32** (63.6 mg) were isolated from Fr.3B (4.1 g), purified *via* a Sephadex LH-20 gel CC (CH_3OH) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 48% CH_3CN, 3.6 mL/min, t_R 28.4 and 35.9 min), respectively. Compounds **26** (28.3 mg), **27** (48.2 mg) and **35** (37.7 mg) were separated from Fr.3C (3.8 g), purified by a Sephadex LH-20 gel CC (CH_3OH) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 53% CH_3CN, 3.8 mL/min, t_R 32.8, 37.6 and 43.5 min), respectively. Fr.4 (45.7 g) was further separated over an ODS gel medium-pressure CC (CH_3OH/H_2O, 35:65 to 85:15, *v*/*v*) to yield nine fractions (Fr.4A–Fr.4I). Compounds **28** (53.7 mg) and **38** (28.5 mg) were separated from Fr.4C (6.1 g), purified *via* a Sephadex LH-20 gel CC (CH_3OH) and then prepared

using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 20% CH_3CN, 3.5 mL/min, t_R 29.3 and 36.9 min), respectively. Compounds **29** (35.8 mg), **36** (35.8 mg) and **40** (52.2 mg) were isolated from Fr.4D (4.2 g), purified by a Sephadex LH-20 gel CC (CH_3OH) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 37% CH_3OH, 3.4 mL/min, t_R 29.2, 36.8 and 45.8 min), respectively. Fr.5 (78.9 g) was further separated over an ODS gel medium-pressure CC (CH_3OH/H_2O, 20:80 to 70:30, *v*/*v*) to afford eight fractions (Fr.5A–Fr.5H). Compounds **30** (43.6 mg), **33** (12.8 mg) and **39** (86.4 mg) were separated from Fr.5B (6.2 g), purified *via* a Sephadex LH-20 gel CC (CH_3OH) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 18% CH_3CN, 3.7 mL/min, t_R 29.2, 37.3 and 44.8 min), respectively. Compounds **31** (21.5 mg), **34** (32.1 mg) and **37** (63.7 mg) were isolated from Fr.5C (5.9 g), purified by a Sephadex LH-20 gel CC (CH_3OH) and then prepared using semi-preparative HPLC (Agilent Eclipse XDB-C_{18} column, i.d. 250×9.4 mm, 5 μm, 26% CH_3OH, 2.8 mL/min, t_R 20.7, 39.8 and 45.2 min), respectively. Due to the large polarity and severe pigment of Fr.6–Fr.10, the separation and purification of the chemical components of Fr.6–Fr.10 was not carried out.

Compounds **11**–**40** were identified as glycerol monolinoleate (**11**),[1] 1-*O*-(9*Z*,12*Z*,15*Z*-octadeca trienoate)glycerol (**12**),[2] rabdosia acid A (**13**),[3] rabdosia acid B (**14**),[3] (+)-(3*R*,4*E*,6*E*,15*E*)-3-meth oxyoctadecatrienoic acid (**15**),[4] (+)-(9*R*,10*E*,12*E*)-9-methoxyoctadecadienoic acid (**16**),[4] ent-4(15)-eudesmene-1β,6α-diol (**17**),[5] 5-*epi*-eudesma-4(15)-ene-1β,6β-diol (**18**),[6] eudesma-4(15)-ene-1β,5α-diol (**19**),[7] 4-hydroxy-4,7-dimethyl-1-tetralone (**20**),[5] canangaterpene III (**21**),[8] 10α-hydroxy-cadin-4-en-15-al (**22**),[9] 10β-hydroxyisodauc-6-en-14-al (**23**),[10] aphanamol I (**24**),[11] (2*S*)-4′,5,7- trihydroxy flavan-(4β→8)-afzelechin (**25**),[12] (2*S*)-4′,5,7-trihydroxyflavan-(4β→8)-*epi*-afzelechin (**26**),[12] (2*S*)-3',4',7-trihydroxyflavan-(4β→8)-catechin (**27**),[13] (2*S*)-3',4',7-trihydroxyflavan-(4α→8)-catechin (**28**),[13] (-)-fisetinidol-(4α→8)-catechin (**29**),[13] (+)-fisetinidol-(4β→8)-catechin (**30**),[13] catechin-(4α→8)-ent-epicatechin (**31**),[14] avaraol I (**32**),[15] catechin-(4α→8)-gallocatechin (**33**),[16] epirobinetinidol-

(4β→8)-catechin (**34**),[17] balanophotannin E (**35**),[18] jamutannin A (**36**),[19] foegraecumoside E (**37**),[20] foegraecumoside K (**38**),[20] 3-*O*-α-L-rhamnopyranosyl-(1/2)-β-D-glucopyranosyl-(1/4)-α-L-arabino pyranosyl-cyclamiretin A (**39**),[21] and ardisimamilloside H (**40**)[22] by comparing their experimental physical data with these reported data in the literatures.

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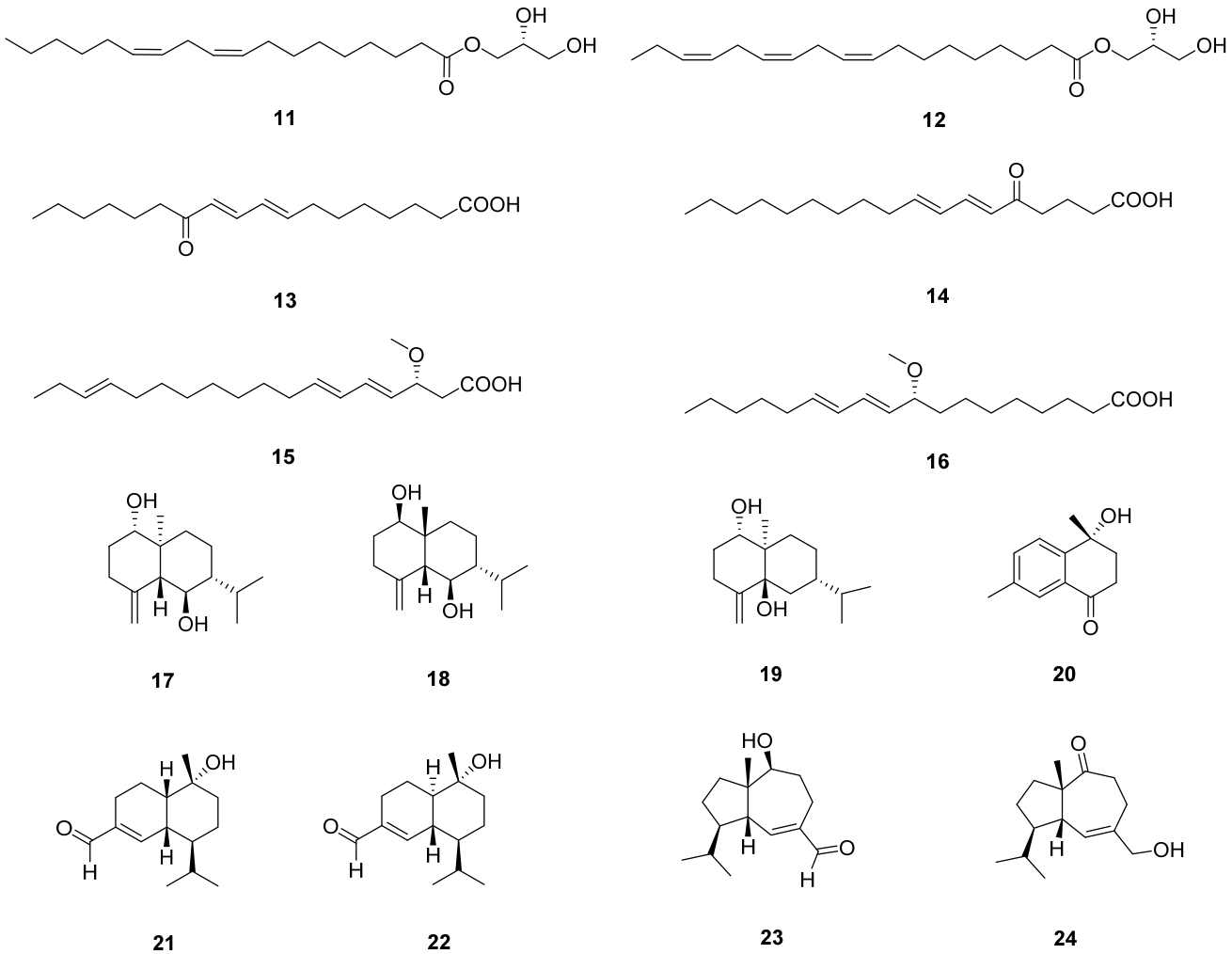

Figure S23. Chemical structures of compounds **11**–**24** isolated from the fruits of *M. zapota.*

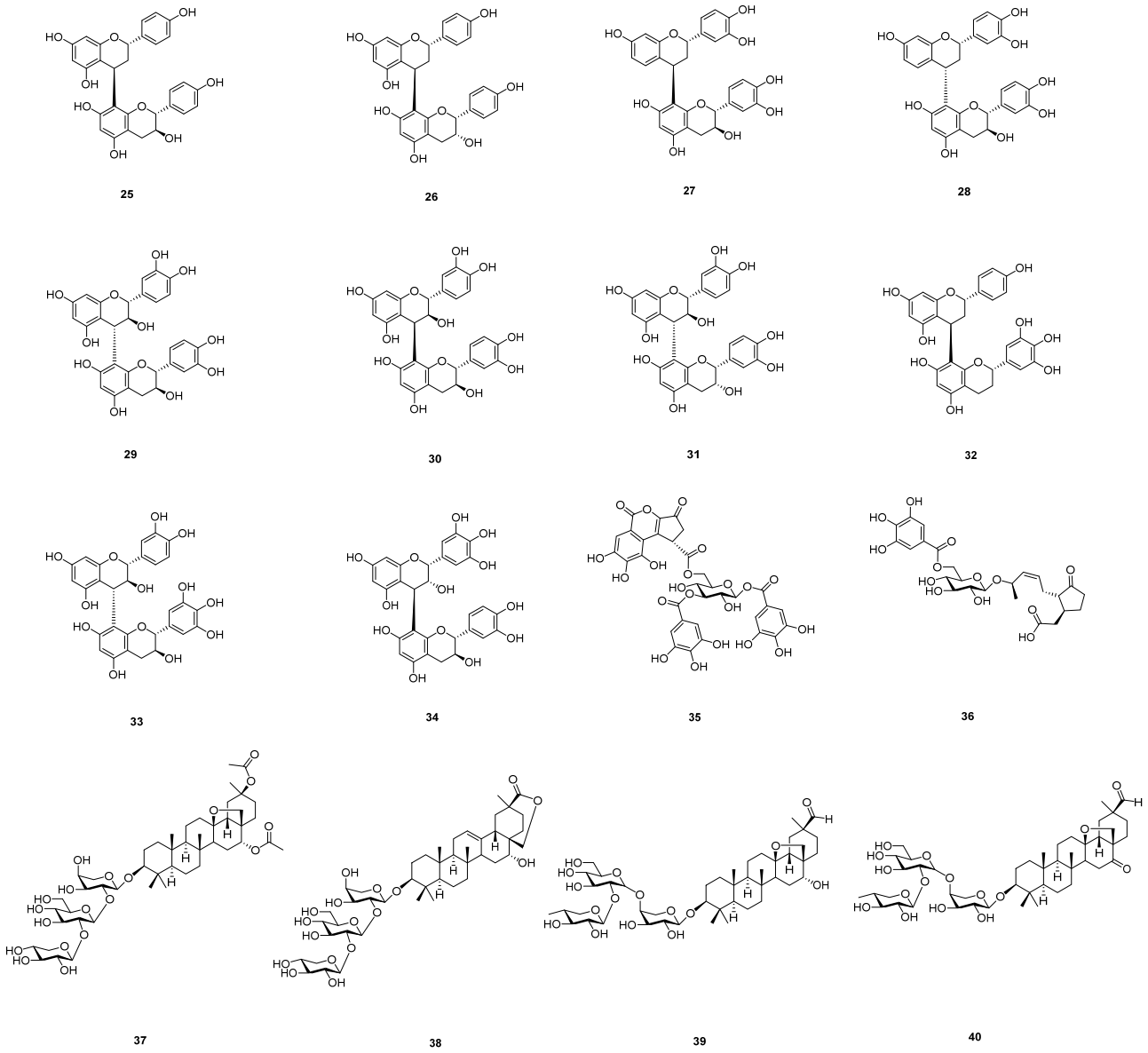

Figure S24. Chemical structures of compounds **25**–**40** isolated from the fruits of *M. zapota.*