Supporting Information for

Genome Mining for Fungal Polyketide-Diterpenoid Hybrids: Discovery of Key Terpene Cyclases and Multifunctional P450s for Structural Diversification

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Supplementary Methods

Isolation and Purification of Each Metabolite

Purification conditions for chevalone E (**1**):
The extract from *A. oryzae* NSAR1 with *cle1, cle3, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **1** were further purified by reverse-phase preparative HPLC (55% aqueous acetonitrile, 3.0 mL/min) to yield 10.0 mg of a white solid: $[\alpha]^{25}_{D}$ -81.1 (*c* 0.1, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S4 and Figures S3-S8; HRMS found *m/z* 415.2852 $[M + H]^+$ (calcd 415.2852 for $C_{26}H_{39}O_4$).

Purification conditions for 20-hydroxychevalone E (**2**):
The extract from *A. oryzae* NSAR1 with *cle1, cle2, cle3, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **2** were further purified by reverse-phase preparative HPLC (35% aqueous acetonitrile, 3.0 mL/min) to yield 15.0 mg of a white solid: $[\alpha]^{25}_{D}$ -110.6 (*c* 0.1, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S5 and Figures S9-S14; HRMS found *m/z* 431.2801 $[M + H]^+$ (calcd 431.2792 for $C_{26}H_{39}O_5$).

Purification conditions for 20-carboxychevalone E (**3**):
The extract from *A. oryzae* NSAR1 with *cle1, cle2, cle3, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **3** were further purified by reverse-phase preparative HPLC (35% aqueous acetonitrile, 3.0 mL/min) to yield 14.0 mg of a white solid: $[\alpha]^{25}_{D}$ -87.0 (*c* 0.1, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S6 and Figures S15-S20; HRMS found *m/z* 445.2593 $[M + H]^+$ (calcd 445.2585 for $C_{26}H_{37}O_6$).

Purification conditions for 11-hydroxychevalone E (**4**):
The extract from *A. oryzae* NSAR1 with *cle1, cle2, cle3, cle4, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **4** were further purified by reverse-phase preparative HPLC (35% aqueous acetonitrile, 3.0 mL/min) to yield 2.0 mg of a white solid: $[\alpha]^{25}_{D}$ -87.5 (*c* 0.1, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S7 and Figures S21-S26; HRMS found *m/z* 431.2798 $[M + H]^+$ (calcd 431.2792 for $C_{26}H_{39}O_5$).

Purification conditions for 11,12-dihydroxychevalone E (**5**):
The extract from *A. oryzae* NSAR1 with *cle1, cle3, cle4, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **5** were further purified by reverse-phase preparative HPLC (40% aqueous acetonitrile, 3.0 mL/min) to yield 14.0 mg of a white solid: $[\alpha]^{25}_{D}$ -102.2 (*c* 0.05, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S8 and Figures S27-S32; HRMS found *m/z* 447.2752 $[M + H]^+$ (calcd 447.2741 for $C_{26}H_{39}O_6$).

Purification conditions for 11,20-dihydroxychevalone E (**6**):

The extract from *A. oryzae* NSAR1 with *cle1, cle2, cle3, cle4, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **6** were further purified by reverse-phase preparative HPLC (20% aqueous acetonitrile, 3.0 mL/min) to yield 5.0 mg of a white solid: $[\alpha]^{25}_{D}$ -65.2 (*c* 0.05, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S9 and Figures S33-S38; HRMS found *m/z* 447.2749 $[M + H]^+$ (calcd 447.2741 for $C_{26}H_{39}O_6$).

Purification conditions for 20,11-olide-chevalone E (**7**):

The extract from *A. oryzae* NSAR1 with *cle1, cle2, cle3, cle4, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **7** were further purified by reverse-phase preparative HPLC (30% aqueous acetonitrile, 3.0 mL/min) to yield 6.0 mg of a white solid: $[\alpha]^{25}_{D}$ -86.0 (*c* 0.1, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S10 and Figures S39-S44; HRMS found *m/z* 443.2431 $[M + H]^+$ (calcd 443.2428 for $C_{26}H_{35}O_6$).

Purification conditions for 12-hydroxy-20,11-olide-chevalone E (**8**):

The extract from *A. oryzae* NSAR1 with *cle1, cle2, cle3, cle4, cle5, cle6,* and *cle7* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **8** were further purified by reverse-phase preparative HPLC (20% aqueous acetonitrile, 3.0 mL/min) to yield 6.0 mg of a white solid: $[\alpha]^{25}_{D}$ -88.0 (*c* 0.1, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S11 and Figures S45-S50; HRMS found *m/z* 459.2368 $[M + H]^+$ (calcd 459.2383 for $C_{26}H_{35}O_7$).

Purification conditions for geranylgeranyl-triacetate lactone (**9**):

The extract from *A. oryzae* NSAR1 with *cle1, cle5,* and *cle6* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **9** were further purified by reverse-phase preparative HPLC (80% aqueous acetonitrile, 3.0 mL/min) to yield 100.0 mg of a white solid: for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S12 and Figures S51-S55; HRMS found *m/z* 421.2715 $[M + Na]^+$ (calcd 421.2713 for $C_{26}H_{38}O_3Na$).

Purification conditions for dihydroxygeranylgeranyl-triacetate lactone (**10**):

The extract from *A. oryzae* NSAR1 with *cle1, cle3, cle5,* and *cle6* was subjected to silica-gel column chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **10** were further purified by reverse-phase preparative HPLC (45% aqueous acetonitrile, 3.0 mL/min) to yield 20.0 mg of a white solid: $[\alpha]^{25}_{D}$ -76.0 (*c* 0.1, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Table S13 and Figures S56-S60; HRMS found *m/z* 455.2779 $[M + Na]^+$ (calcd 455.2768 for $C_{26}H_{40}O_5Na$).

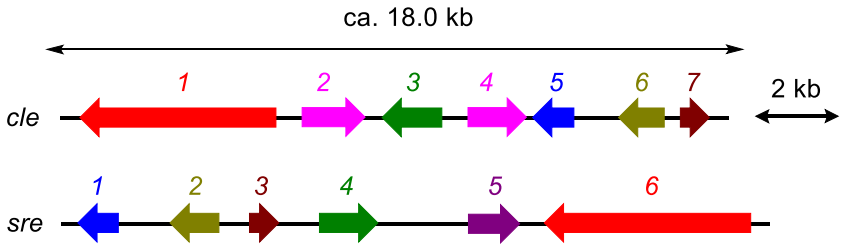
Purification conditions for sartorypyrone D (**11**):

The extract from *A. oryzae* NSAR1 with *cle1, cle3, cle5, cle6,* and *sre3* was subjected to silica-gel column

chromatography and eluted stepwise using a chloroform:methanol gradient (100:0 to 90:10). Fractions that contained **11** were further purified by reverse-phase preparative HPLC (40% aqueous acetonitrile, 3.0 mL/min) to yield 3.0 mg of a white solid: $[\alpha]^{25}_{D}$ -18.0 (*c* 0.5, CH_3OH); for UV spectrum see Figure S1; for ^{1}H and ^{13}C NMR data see Figures S61 and S62; HRMS found *m/z* 415.2826 $[M + H]^+$ (calcd 415.2843 for $C_{26}H_{39}O_4$).

Table S1. Annotation of each protein encoded by the *cle* and *sre* cluster.

The *cle* cluster from *Aspergillus versicolor* 0312 and *sre* cluster from *Aspergullus felis* 0260



Gene	Amino acids (base pairs)	Protein homologue, origin	Similarity/identity (%)	Proposed function
cle1	1807 (5488)	MPAS, *Cladonia uncialis*	50/33	polyketide synthase
cle2	544 (1824)	PrhD, *Penicillium brasilianum*	61/41	cytochrome P450 monooxygenase
cle3	491 (1636)	AtmM, *Aspergillus flavus*	66/50	FAD-dependent monooxygenase
cle4	496 (1711)	RoqO, *Penicillium rubens*	61/41	cytochrome P450 monooxygenase
cle5	321 (1090)	Pyr6, *Aspergillus fumigatus*	64/47	UbiA-like prenyltransferase
cle6	380 (1323)	AtmG, *Aspergillus flavus*	69/56	geranylgeranyl pyrophosphate synthase
cle7	242 (783)	AtmB, *Aspergillus flavus*	58/36	terpene cyclase
sre1	342 (1134)	Pyr6, *Aspergillus fumigatus*	63/46	UbiA-like prenyltransferase
sre2	364 (1257)	AtmG, *Aspergillus flavus*	79/64	geranylgeranyl pyrophosphate synthase
sre3	239 (804)	AtmB, *Aspergillus flavus*	56/38	terpene cyclase
sre4	476 (1612)	AtmM, *Aspergillus flavus*	65/50	FAD-dependent monooxygenase
sre5	434 (1361)	Pyr8, *Aspergillus fumigatus*	53/38	acetyltransferase
sre6	1840 (5584)	MPAS, *Cladonia uncialis*	53/36	polyketide synthase

Table S2. Primers used in this study

Primer Sequence	(5' to 3')
0312-19-1F	agcaagctccgaattATGTCCTCCTCAATCCCTTCT
0312-19-1R	taccgagctcgaattCTAGACAGCCCCGTTATATATAT
0312-19-2F	agcaagctccgaattATGCTGCAAACCCAACTCCA
0132-19-2R	taccgagctcgaattTTACACAGTAGCCATTGGACAAG
0312-19-3F	agcaagctccgaattATGTATAGGGTACGCAGCAT
0312-19-3R	taccgagctcgaattTCAGAACGAGGAGAATCTAGC
0312-19-4F	agcaagctccgaattATGACAGTATTTGACATTTTCACC
0312-19-4R	taccgagctcgaattCTAGAACTCTAGCCCTATATCGT
0312-19-5F	agcaagctccgaattATGACATACAAGCAGAGGAAC
0312-19-5R	taccgagctcgaattCTAACAGCCATTTCCCCCAATAA
0312-19-6F	agcaagctccgaattATGCACTCTGTCCGTACTTC
0312-19-6R	taccgagctcgaattTCACTCCTTCAACTCCAGAAAAT
0312-19-7F	agcaagctccgaattATGGAAGAAGGCTGGGACTT
0312-19-7R	taccgagctcgaattTTAGGCCACCTTGTCTCTCT
PTA-0260-18-TC.F	agcaagctccgaattatggacgcatttgaccttTC
PTA-0260-18-TC.R	taccgagctcgaatttcacgccttctgtactttgg
pUSA-0260-18-TC.R	ACGAGCTACTACAGATCCCCtcacgccttctgtactttgG
Inf-PamyB-F	TGCCTGCAGGTCGACTCTAGACGACTCCAATCTTCAAGAGC
Inf-TamyB-R	ATGACTAGTAGATCCTCTAGGTAAGATACATGAGCTTCGGTG
Inf-link-F1	TTGCTCGCGAGCGCGTTCCACTGCATCATCAGTCTAGA
Inf-link-R1	TGGAACGCGCTCGCGAGCAAGTACCATACAGTACCGCG
Inf-0312-19-3F	TGAATTCGAGCTCGGTACCCATGTATAGGGTACGCAGCAT
Inf-0312-19-7R	ACGAGCTACTACAGATCCCCTTAGGCCACCTTGTCTCTCT
InF-pPTRI-F	TGATTACGCCAAGCTTCGACTCCAATCTTCAAGAGC
InF-pBARI-R	GCAGGCATGCAAGCTTGTAAGATACATGAGCTTCG

Table S3. Plasmids constructed in this study and PCR conditions

Plasmid	Vector	Insert	Primer 1	Primer 2	PCR Template
pTAex3-*cle1*	pTAex3 digested with *Eco*RI	*cle1*	0312-19-1F	0312-19-1R	gDNA
pTAex3-*cle*2	pTAex3 digested with *Eco*RI	*cle2*	0312-19-2F	0312-19-2R	gDNA
pTAex3-*cle*3	pTAex3 digested with *Eco*RI	*cle3*	0312-19-3F	0312-19-3R	gDNA
pTAex3-*cle*4	pTAex3 digested with *Eco*RI	*cle4*	0312-19-4F	0312-19-4R	gDNA
pTAex3-*cle*5	pTAex3 digested with *Eco*RI	*cle5*	0312-19-5F	0312-19-5R	gDNA
pTAex3-*cle*6	pTAex3 digested with *Eco*RI	*cle6*	0312-19-6F	0312-19-6R	gDNA
pTAex3-*cle*7	pTAex3 digested with *Eco*RI	*cle7*	0312-19-7F	0312-19-7R	gDNA
pTAex3-*sre*3	pTAex3 digested with *Eco*RI	*sre3*	PTA-0260-18-TC.F	PTA-0260-18-TC.R	gDNA
pBarI-*cle2*	pBARI digested with *Hin*dIII	*PamyB-cle2-TamyB*	InF-pPTRI-F	InF-pBARI-R	pTAex3-*cle2*
pBarI-*cle*3	pBARI digested with *Hin*dIII	*PamyB-cle3-TamyB*	InF-pPTRI-F	InF-pBARI-R	pTAex3-*cle3*
pBarI-*cle*4	pBARI digested with *Hin*dIII	*PamyB-cle4-TamyB*	InF-pPTRI-F	InF-pBARI-R	pTAex3-*cle4*
pBarI-*cle2+4*	pBARI digested with *Hin*dIII	*PamyB-cle2-TamyB*	InF-pPTRI-F	Inf-link-R1	pTAex3-*cle2*
		PamyB-cle4-TamyB	Inf-link-F1	InF-pBARI-R	pTAex3-*cle4*
pAdeA-*cle5+6*	pAdeA digested with *Xba*I	*PamyB-cle5-TamyB*	Inf-PamyB-F	Inf-link-R1	pTAex3-*cle5*
		PamyB-cle6-TamyB	Inf-link-F1	Inf-TamyB-R	pTAex3-*cle6*
pUSA-*cle3+7*	pUSA digested with S*ma*I	*cle3-TamyB*	Inf-0312-19-3F	Inf-link-R1	pTAex3-*cle3*
		PamyB-cle7	Inf-link-F1	Inf-0312-19-7R	pTAex3-*cle7*
pUSA-*cle3+sre3*	pUSA digested with S*ma*I	*cle3-TamyB*	Inf-0312-19-3F	Inf-link-R1	pTAex3-*cle3*
		PamyB-sre5	Inf-link-F1	pUSA-0260-18-TC.R	pTAex3-*sre3*

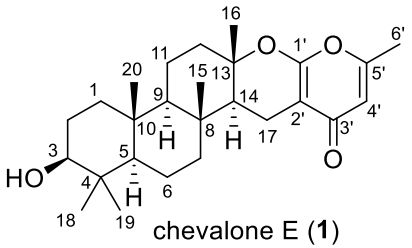
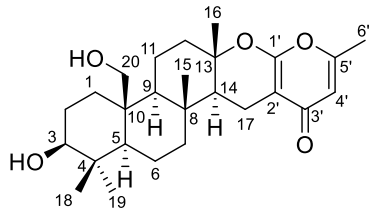


Table S4. **NMR data for chevalone E (1)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in $CDCl_3$)

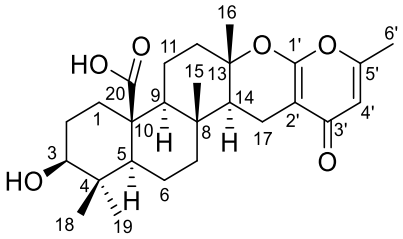
	^{13}C	^{1}H					
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	38.2 t	0.93α	overlap	1H	2, 3, 5, 9, 10, 20	H-1β, H-2α	H-1β, H-2α, H-3α, H-9α
		1.68β	overlap	1H	2, 3, 5, 9, 10	H-1α	H-1α, H-2β, H_3-20β
2	27.0 t	1.56α	overlap	1H	1, 3, 4, 10	H-1α, H-3α	H-1α, H-3α
		1.61β	overlap	1H	1, 3, 4, 10	H-3α	H-1β, H-3α
3	78.4 d	3.15α	d (*J* = 11.1 Hz)	1H	1, 2, 4, 5, 18, 19	H-2α, H-2β	H-1α, H-2α, H-5α, H_3-19α
4	38.7 s						
5	55.2 d	0.73α	overlap	1H	1, 3, 4, 6, 7, 9, 10, 18, 19, 20	H-6α, H-6β	H-3α, H-6α, H-7α, H-9α, H_3-19α
6	17.8 t	1.40α	m	1H	4, 5, 7, 8, 10	H-5α, H-6β, H-7α, H-7β	H-5α, H-6β, H-7β
		1.55β	overlap	1H	4, 5, 7, 10	H-5α, H-6α, H-7α, H-7β	H-6α, H-7α, H_3-15β
7	40.9 t	0.98α	overlap	1H	5, 6, 8, 14, 15	H-6α, H-6β, H-7β	H-5α, H-6α, H-7β, H-9α, H-14α
		1.92β	dd (*J* = 12.8, 2.5 Hz)	1H	5, 6, 8, 9, 15	H-6α, H-6β, H-7α	H-6α, H-7α, H_3-15β
8	37.0 s						
9	60.1 d	0.88α	d (*J* = 12.1 Hz)	1H	1, 5, 8, 10, 11, 12, 14, 15, 20	H-11β	H-1α, H-5α, H-7α, H-11α, H-12α, H-14α
10	37.1 s						
11	18.5 t	1.30β	q (*J* = 13.1 Hz)	1H	8, 9, 12, 13	H-9α, H-11α, H-12α, H-12β	H-11α, H_3-15β, H_3-20β
		1.68α	overlap	1H	8, 9, 10, 12, 13	H-11β, H-12β	H-9α, H-11β, H-12α
12	39.9 t	1.64α	overlap	1H	9, 11, 13, 14, 16	H-11β, H-12β	H-9α, H-11α, H-14α
		2.05β	m	1H	9, 11, 13, 14, 16	H-11α, H-11β, H-12α	H-11β, H_3-16β
13	84.2 s						
14	52.2 d	1.45α	d (*J* = 12.9 Hz)	1H	7, 8, 9, 12, 13, 15, 16, 17, 2’	H-17α, H-17β	H-9α, H-12α, H-17α
15	15.9 q	0.83β	s	3H	7, 8, 9, 14		H-6β, H-7β, H_3-16β, H-17β
16	20.4 q	1.23β	s	3H	12, 13, 14		H-11β, H-12β, H_3-15β, H-17β
17	15.2 t	2.09β	dd (*J* = 16.2, 2.7 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17α	H-7β, H_3-15β, H_3-16β, H-17α
		2.49α	ddd (*J* = 16.2, 3.8, 2.7 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17β	H-14α, H-17β
18	15.1 q	0.73β	s	3H	3, 4, 5, 19		H-2β, H-6β, H_3-19α
19	27.8 q	0.92α	s	3H	3, 4, 5, 18		H-3α, H-5α, H-6α, H_3-18β
20	16.3 q	0.79	s	3H	1, 5, 9, 10		H-1β, H-11β
1’	162.5 s						
2’	98.4 s						
3’	180.5 s						
4’	111.7 d	5.94	s	1H	2’, 3’, 5’, 6’		H_3-6’
5’	160.4 s						
6’	19.1 q	2.15	d (*J* = 1.5 Hz)	3H	4’, 5’		H-4’



20-hydroxychevalone E (**2**)

Table S5. **NMR data for 20-hydroxychevalone E (2)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in methanol-d_4)

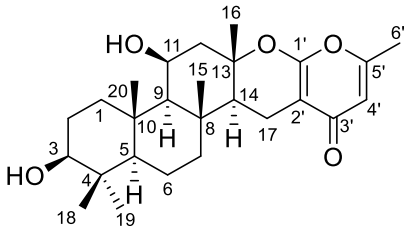
	^{13}C	^{1}H					
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	34.1 t	0.88α	td (*J* = 13.4, 3.0 Hz)	1H	3, 5, 9, 10, 20	H-2β	H-1β, H-2α, H-3α, H-9α
		2.32β	dt (*J* = 13.4, 3.4 Hz)	1H	2, 3, 5, 9, 10, 20	H-1α	H-1α, H-2α, H-2β, H$_2$-11, H-20b
2	28.0 t	1.61α	m	1H	1, 3, 4, 10	H-2β	H-1α, H-1β, H-3α
		1.68β	m	1H	1, 3, 4	H-1α, H-3α	H-1β, H-3α, H$_3$-18β, H-20b
3	79.5 d	3.17α	dd (*J* = 11.9, 4.6 Hz)	1H	1, 4, 5, 18, 19	H-2β	H-1α, H-2α, H$_3$-19α
4	39.8 s						
5	57.4 d	0.90α	overlap	1H	1, 7, 9, 10, 18, 19, 20	H$_2$-6	H-3α, H$_2$-6, H$_3$-19α
6	18.8 t	1.55	overlap	2H	4, 7, 8, 10	H-5α, H-7α	H-5α, H-7α, H-7β, H$_3$-15β, H-20a
7	42.9 t	1.14α	td (*J* = 12.7, 4.2 Hz)	1H	5, 6, 8, 9, 14, 15	H-7β	H-5α, H$_2$-6, H-7β, H-14α
		1.91β	overlap	1H	5, 6, 8, 9, 14, 15	H-6, H-7α	H-6, H-7α, H$_3$-15β
8	38.6 s						
9	62.6 d	1.04α	dd (*J* = 11.5, 2.5 Hz)	1H	1, 5, 7, 8, 10, 11, 12, 14, 15, 20	H$_2$-11	H-1α, H-5α, H-7α, H$_2$-11, H-14α
10	43.4 s						
11	22.9 t	1.89	overlap	2H	8, 9, 12, 13	H-9α, H-12α	H-1α, H-9α, H-12α, H$_3$-16β
12	42.4 t	1.52α	overlap	1H	9, 11, 13, 16	H$_2$-11, H-12β	H$_2$-11, H$_3$-16β
		2.04β	dt (*J* = 12.2, 3.1 Hz)	1H	9, 11, 13, 14, 16	H$_2$-11	H$_2$-11
13	86.3 s						
14	53.8 d	1.56α	overlap	1H	7, 8, 9, 12, 15, 16, 17, 2’	H-17α, H-17β	H-7α, H-9α, H-12α, H-17α, H-17β
15	16.1 q	1.09β	s	3H	7, 8, 9, 14		H-7β, H$_3$-16β, H-17β
16	20.5 q	1.29β	s	3H	12, 13, 14		H-12β, H$_3$-15β, H-17β
17	16.4 t	2.50α	dd (*J* = 16.3, 4.8 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17β	H-7α, H-7β, H-14α, H-17β
		2.16β	dd (*J* = 16.3, 12.8 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17α	H$_3$-15β, H$_3$-16β, H-17α
18	16.5 q	0.74β	s	3H	3, 4, 5, 19		H-2β, H$_2$-6, H$_3$-19α, H-20a
19	29.3 q	0.97α	s	3H	3, 4, 5, 18		H-2α, H-3α, H$_3$-18β
20	62.3 t	3.94a	d (*J* = 11.9 Hz)	1H	1, 5, 9, 10	H-20b	H-1β, H-2β, H$_3$-18β
		3.81b	d (*J* = 11.9 Hz)	1H	1, 5, 9, 10	H-20a	H$_2$-6, H$_3$-19α
1’	165.1 s						
2’	99.6 s						
3’	182.9 s						
4’	111.8 d	6.03	d (*J* = 0.7 Hz)	1H	2’, 3’, 5’, 6’		H$_3$-6’
5’	163.7 s						
6’	19.1 q	2.24	br s	3H	4’, 5’		H-4’



20-carboxychevalone E (**3**)

Table S6. **NMR data for 20-carboxychevalone E (3)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in methanol-d_4)

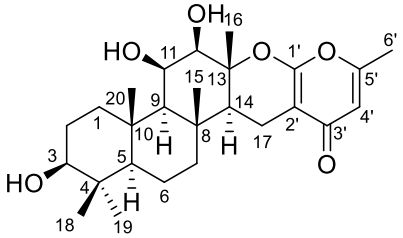
	^{13}C	^{1}H					
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	38.7 t	0.91α	br dd (*J* = 13.0, 2.5 Hz)	1H	2, 3, 5, 10	H-1β, H-2α	H-1β, H-2α, H-3α, H-9α
		2.62β	dt (*J* = 13.0, 3.1 Hz)	1H	2, 3, 5, 9, 10, 20	H-1α, H-2β	H-1α, H-2β, H-11β
2	29.9 t	1.53α	overlap	1H	1, 3, 4, 10	H-1α, H-3α	H-1α, H-1β, H-3α
		1.58β	overlap	1H	1, 3, 4, 10	H-1β	H-1β, H-3α
3	80.1 d	3.15α	dd (*J* = 11.8, 4.1 Hz)	1H	1, 4, 18, 19	H-2α	H-2α, H_3-19α
4	40.6 s						
5	57.2 d	0.97α	overlap	1H	1, 6, 9, 10, 18, 19, 20	H-6β	H-3α, H-6α, H_3-19α
6	19.9 t	1.58α	overlap	1H	4, 5, 7, 8, 10	H-6β	H-5α, H-6α, H-7β
		2.57β	m	1H	4, 5, 7, 10	H-5α, H-6α, H-7α	H-6α, H-6β, H-7α, H_3-15β
7	42.8 t	1.11α	td (*J* = 12.9, 3.4 Hz)	1H	5, 6, 8, 14, 15	H-6β, H-7β	H-5α, H_2-6, H-7β, H-14α
		1.92β	dt (*J* = 12.9, 3.3 Hz)	1H	5, 6, 8, 9, 15	H-6α, H-7α	H_2-6, H-7α, H_3-15β
8	38.7 s						
9	60.7 d	1.15α	br d (*J* = 10.9 Hz)	1H	1, 5, 8, 10, 11, 12, 14, 15, 20	H-11α	H-1α, H-5α, H-7α, H-11α, H-14α
10	49.8 s						
11	22.0 t	1.58β	overlap	1H	8, 9, 12, 13	H-9α, H-11β	H-11α, H_3-15β, H_3-16β
		2.04α	dd (*J* = 14.1, 1.7 Hz)	1H	8, 9, 10, 12, 13	H-12α	H-9α, H-11α, H-12β
12	41.5 t	1.68α	m	1H	9, 13, 16	H-12β	H-9α, H-14α, H-17α
		2.12β	overlap	1H	9, 13, 14, 16	H-11β	H-11β, H_3-16β
13	86.2 s						
14	53.6 d	1.50α	dd (*J* = 12.7, 4.9 Hz)	1H	7, 8, 9, 12, 15, 16, 17, 2’	H-17α, H-17β	H-9α, H-12α, H-17α
15	14.6 q	0.96β	s	3H	7, 8, 9, 14		H-7β, H_3-16β, H-17β
16	20.8 q	1.28β	s	3H	12, 13, 14		H-12β, H_3-15β, H-17β
17	16.4 t	2.10β	overlap	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17α	H-7α, H-7β, H-14α, H-17α
		2.51α	dd (*J* = 16.3, 4.8 Hz)	1H	13, 14, 1’, 2’, 3’	H-14α, H-17β	H_3-15β, H_3-16β, H-17β
18	17.1 q	0.86β	s	3H	3, 4, 5, 19		H-2β, H-6β, H_3-19α
19	28.9 q	0.98α	s	3H	3, 4, 5, 18		H-3α, H-6α, H_3-18β
20	180.3 s						
1’	165.2 s						
2’	99.7 s						
3’	183.0 s						
4’	111.8 d	6.03	d (*J* = 0.4 Hz)	1H	2’, 3’, 5’, 6’		H_3-6’
5’	163.7 s						
6’	19.1 q	3.03	dt (*J* = 3.2, 0.4 Hz)	3H	4’, 5’		H-4’



11-hydroxychevalone E (4)

Table S7. **NMR data for 11-hydroxychevalone E (4)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in pyridine-d_5)

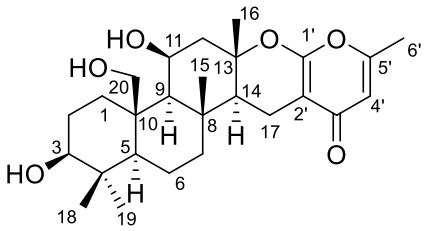
	^{13}C	^{1}H					
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	38.7 t	1.06α	overlap	1H	9, 20	H-1β, H-2β	H-1β, H-2α, H-3α, H-9α
		1.98β	overlap	1H	2, 3, 5, 10, 20	H-1α	H-1α, H-11β, H_3-20β
2	28.2 t	1.99β	overlap	1H	1, 3, 10	H-1α, H-3α	H-1α, H-1β, H-3α
		0.89α	m	1H	3, 10	H-3α	H-1β
3	78.0 d	3.44α	br d (*J* = 11.6 Hz)	1H	2, 4, 18, 19	H-2α, H-2β	H-2α, H-5α, H_3-18β, H_3-19α
4	39.6 s						
5	56.4 d	0.78α	dd (*J* = 9.5, 5.0 Hz)	1H	4, 7, 9, 10, 18, 19, 20	H_2-6	H-1α, H-3α, H-9α, H_3-19α
6	18.8 t	1.58	m	2H	4, 5, 7, 8	H-5α, H-7α	H-5α, H-6α, H-7β, H_3-15β, H_3-18β, H_3-19α
7	43.4 t	0.97α	m	1H	5, 8, 9, 14, 15	H_2-6, H-7β	H-5α, H_2-6, H-7β, H-14α
		1.71β	overlap	1H	5, 8, 9, 14, 15	H-7α	H_2-6, H-7α, H_3-15β, H-17β
8	37.9 s						
9	60.9 d	0.89α	dd (*J* = 6.6, 4.5 Hz)	1H	1, 5, 7, 8, 10, 11, 12, 14, 15, 20	H-11α	H-1α, H-5α, H-11α, H-12α, H-14α
10	38.5 s						
11	66.5 d	4.78α	br s	1H	8, 9, 13	H-9α, H-12α, H-12β	H-1α, H-9α, H-12α
12	48.9 t	2.05α	dd (*J* = 13.2, 3.1 Hz)	1H	11, 13, 16	H-11α, H-12β	H-9α, H-11α, H-12β, H-14α
		2.48β	overlap	1H	9, 11, 13, 14, 16	H-11α, H-12α	H-11α, H-12α, H_3-15β, H_3-16β
13	84.7 s						
14	53.2 d	1.63α	dd (*J* = 12.7, 4.8 Hz, 1H)	1H	8, 9, 12, 13, 15, 16, 17, 2’	H-17α, H-17β	H-7α, H-9α, H-12α, H-17α
15	17.5 q	1.41β	s	3H	7, 8, 9, 14		H_2-6, H_3-16β, H-17β
16	22.0 q	1.52β	s	3H	12, 13, 14		H_3-15β, H-17β
17	16.1 t	2.49β	overlap	1H	13, 14, 1’, 2’, 3’	H-14α, H-17α	H-7α, H-7β, H-14α, H-17α
		2.88α	dd (J = 16.2, 4.8 Hz, 1H)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17β	H_3-15β, H_3-16β, H-17β
18	16.2 q	1.08β	s	3H	3, 4, 5, 19		H_2-6, H_3-19α, H_3-20β
19	28.7 q	1.22α	s	3H	3, 4, 5, 18		H-5α, H_3-18β
20	17.8 q	1.52β	s	3H	1, 5, 9, 10		H-1β, H_3-15β, H_3-18β
1’	162.6 s						
2’	98.9 s						
3’	179.9 s						
4’	112.3 d	6.19	d (*J* = 0.4 Hz)	1H	2’, 3’, 5’, 6’		H_3-6’
5’	160.7 s						
6’	18.8 q	2.01	s	3H	4’, 5’		H-4’



11,12-dihydroxychevalone E (5)

Table S8. **NMR data for 11,12-dihydroxychevalone E (5)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in pyridine-d_5)

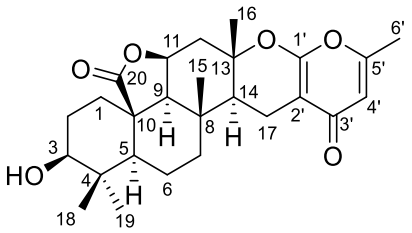
	^{13}C	^{1}H					
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	38.6 t	1.02α	td (*J* = 12.4, 2.9 Hz)	1H	2, 3, 5, 9, 10, 20	H-1β, H-2β	H-1β, H-3α, H-5α, H-9α, H-11α
		1.93β	dt (*J* = 12.4, 3.3 Hz)	1H	2, 3, 5, 10, 20	H-1α	H-1α, H-2α, H-11α, H$_3$-20β
2	28.1 t	1.97β	m	1H	3, 10	H-1α, H-3α, 3-OHβ	H-1α, H-1β, H-2β, H-3α
		1.83α	m	1H	3, 10	H-1β, H-3α	H-1α, H-2α, H$_3$-20β
3	78.0 d	3.41α	m	1H	4, 18, 19	H-2α, H-2β	H-1α, H-2α, H-5α, H$_3$-19α
4	39.5 s						
5	56.5 d	0.78α	dd (*J* = 10.3, 4.2 Hz)	1H	1, 3, 4, 6, 7, 9, 10, 18, 19, 20	H$_2$-6	H-3α, H$_2$-6, H-9α, H$_3$-19α
6	18.8 t	1.59	overlap	2H	4, 5, 7, 8, 10	H-5α, H-7α	H-5α, H-7α, H$_3$-15β, H$_3$-18β, H$_3$-19α
7	43.3 t	0.94α	overlap	1H	5, 8, 14, 15	H$_2$-6, H-7β	H-5α, H$_2$-6, H-7β, H-14α
		1.70β	dt (*J* = 12.3, 3.0 Hz)	1H	5, 8, 9, 15	H-7α	H$_2$-6, H-7α, H$_3$-15β, H-17β
8	37.9 s						
9	59.8 d	0.95α	overlap	1H	1, 5, 7, 8, 10, 11, 12, 14, 15, 20	H-11α	H-1α, H-5α, H-11α, H-12α, H-14α
10	38.4 s						
11	71.5 d	4.77α	br s	1H	8, 9, 10, 12, 13	H-9α, 11-OHβ, H-12α	H-1α, H-9α, 11-OHβ, H-12α
12	78.0 d	4.04α	br s	1H	13, 16	H-11α	H-9α, H-11α, 12-OHβ, H-14α, H$_3$-16β
13	88.8 s						
14	51.7 d	1.60α	overlap	1H	7, 8, 9, 12, 13, 15, 16, 17, 2’	H-17α, H-17β	H-7α, H-9α, H-12α, H-17α
15	17.5 q	1.42β	s	3H	7, 8, 9, 14		11-OHβ, H$_3$-16β, H-17β, H$_3$-20β
16	16.0 q	1.77β	s	3H	12, 13, 14		11-OHβ, H-12α, H$_3$-15β, H-17β
17	15.9 t	2.56β	dd (*J* = 16.0, 12.7 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17α	H$_3$-15β, H$_3$-16β, H-17α
		2.89α	dd (*J* = 16.0, 4.8 Hz)	1H	12, 13, 14, 1’, 2’, 3’	H-14α, H-17β	H-7α, H-7β, H-14α, H-17β
18	16.1 q	1.08β	s	3H	3, 4, 5, 19		H-2β, H$_2$-6, H$_3$-19α, H$_3$-20β
19	28.7 q	1.21α	s	3H	3, 4, 5, 18		H-3α, H-5α, H$_3$-18β
20	18.8 q	1.56β	s	3H	1, 5, 9, 10		H-1β, H$_3$-15β, H$_3$-18β
1’	162.8 s						
2’	98.7 s						
3’	179.8 s						
4’	112.3 d	6.18	d (*J* = 0.4 Hz)	1H	2’, 3’, 5’, 6’		H$_3$-6’
5’	160.6 s						
6’	18.3 q	2.00	s	3H	4’, 5’		H-4’
3-OH		5.75β	d (*J* = 5.3 Hz)	1H	2, 3, 4	H-3α	H-2α, H-2β, H-3α, H$_3$-18β, H$_3$-19α
11-OH		5.92β	br s	1H	9, 11	H-11α	H$_3$-15β, H$_3$-16β, H$_3$-20β
12-OH		7.19β	br s	1H	11, 12, 13	H-12α	11-OHβ, H-12α, H$_3$β



11,20-dihydroxychevalone E (6)

Table S9. **NMR data for 11,20-dihydroxychevalone E (6)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in pyridine-d_5)

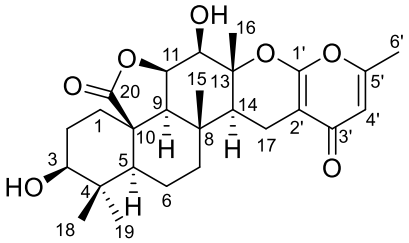
	^{13}C	^{1}H					
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	32.7 t	0.93α	td (*J* = 13.0, 2.6 Hz)	1H	2, 3, 9, 10, 20	H-1β, H-2α, H-2β	H-1β, H-2α, H-3α, H-9α, H-11α
		2.61β	dt (*J* = 13.0, 3.2 Hz)	1H	2, 3, 5, 10	H-1α, H-2α	H-1α, H-2α, H-2β, H-20a
2	27.8 t	1.91α	m	1H	1, 3, 4, 10	H-1α, H-1β, H-3α	H-1α, H-1β, H-3α
		1.99β	s	1H	1, 3, 4, 10	H-1α, H-3α	H-1β, H-3α, H-18β, H-20a
3	78.0 d	3.51α	d (*J* = 10.2 Hz)	1H	4, 18, 19	H-2α, H-2β	H-1α, H-2α, H-2β, H-5α, H_3-18β, H_3-19α
4	39.5 s						
5	57.4 d	1.03α	overlap	1H	1, 3, 4, 6, 9, 10, 18, 19, 20	H_2-6	H-3α, H_2-6, H-9α, H_3-19α
6	18.3 t	1.51	m	2H	5, 7, 8, 9, 10	H-5α, H-7α	H-5α, H-7α, H-7β, H-17α, H_3-19α
7	44.0 t	1.01α	overlap	1H	6, 8, 9, 14	H_2-6, H-7β	H_2-6, H-7β, H-9α, H-14α
		1.73β	overlap	1H	5, 6, 8, 9, 14, 15	H-7α	H_2-6, H-7α, H_3-15β
8	37.7 s						
9	62.9 d	1.15α	s	1H	1, 5, 8, 10, 11, 12, 14, 15, 20	H-11α	H-1α, H-7α, H-11α, H-12α, H-14α
10	44.0 s						
11	65.3 d	4.62α	br s	1H	8, 9, 10, 12, 13	H-9α, H-12α, H-12β	H-1α, H-9α, H-12α, H-12β, H_3-15β, H_3-16β
12	46.6 t	2.07α	dd (*J* = 13.0, 3.2 Hz)	1H	11, 13, 14, 16	H-11α, H-12β	H-9α, H-11α, H-12β, H-14α, H_3-16β
		2.65β	dd (*J* = 13.0, 2.9 Hz)	1H	9, 11, 13, 14, 16	H-11α, H-12α	H-11α, H-12α, H_3-16β
13	84.7 s						
14	53.7 d	1.66α	dd (*J* = 12.7, 4.8 Hz)	1H	7, 8, 9, 12, 13, 15, 16, 17, 2’	H-17α, H-17β	H-7α, H-9α, H-12α, H-17α, H-17β
15	17.5 q	1.49β	s	3H	7, 8, 9, 14		H-7β, H_3-16β, H-17β, H-20b
16	22.0 q	1.73β	s	3H	12, 13, 14		H-12α, H-12β, H_3-15β, H-17β
17	16.2 t	2.48β	dd (*J* = 16.2, 12.7 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17α	H-15β, H_3-16β, H-17α
		2.88α	dd (*J* = 16.2,4.8 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17β	H-7α, H-14α, H-17β
18	17.4 q	1.06β	s	3H	3, 4, 5, 19		H-2β, H-3α, H_3-19α, H-20a
19	29.8 q	1.25α	s	3H	3, 4, 5, 18		H-3α, H_2-6, H_3-18β
20	59.6 t	4.18b	d (*J* = 11.8 Hz)	1H	1, 5, 9, 10	H-20a	H_3-15β, H-20a
		4.38a	d (*J* = 11.8 Hz)	1H	1, 5, 9, 10	H-20b	H-1β, H-2β, H-7β, H_3-18β, H-20b
1’	162.7 s						
2’	98.8 s						
3’	197.9 s						
4’	112.3 d	6.20	d (*J* = 0.7 Hz)	1H	2’, 3’, 5’, 6’		H-6’
5’	160.7 s						
6’	18.9 q	2.02	s	3H	4’, 5’		H-4’



20,11-olide-chevalone E (7)

Table S10. **NMR data for 20,11-olide-chevalone E (7)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in pyridine-d_5)

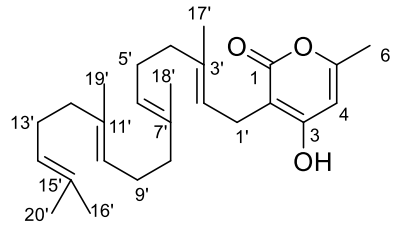
	^{13}C	^{1}H					
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	34.4 t	1.42α	overlap	1H	2, 3, 5, 10	H-1β, H-2β	H-1β, H-2α, H-3α, H-5α, H-9α
		2.17β	dt (*J* = 13.5, 3.5 Hz)	1H	2, 3, 5, 9, 10, 20	H-1α	H-1α, H-2α, H-11α
2	28.1 t	1.93α	ddd (*J* = 12.7, 7.1, 3.5 Hz)	1H	1, 3, 4, 10	H-2β, H-3α	H-1α, H-1β, H-2β, H-3α
		2.21β	m	1H	1, 3, 4, 10	H-1α, H-2α, H-3α	H-1α, H-2α, H_3-19α
3	77.8 d	3.50α	dd (*J* = 7.1, 4.3 Hz)	1H	2, 4, 5, 10, 18, 19	H-2α, H-2β, 3-OH	H-1α, H-2α, 3-OH, H-5α, H_3-18β, H_3-19α
4	39.9 s						
5	51.0 d	1.40α	dd (*J* = 9.1, 3.7 Hz)	1H	1, 3, 4, 6, 9, 10, 18, 19, 20	H_2-6	H-1α, H-3α, H-7α, H-9α, H_3-19α
6	19.5 t	1.66	overlap	2H	4, 5, 7, 8, 10	H-5α, H-7α	H-5α, H-7α, H-7β
7	35.4 t	1.09α	td (*J* = 12.3, 4.7 Hz)	1H	5, 6, 8, 9, 14, 15	H_2-6, H-7β	H-5α, H_2-6, H-7β, H-9α, H-14α, H-17α
		1.55β	m	1H	5, 6, 8, 9, 14, 15	H-7α	H_2-6, H-7α, H-14α, H-17α, H-17β
8	33.8 s						
9	57.7 d	1.61α	d (*J* = 3.4 Hz)	1H	1, 7, 8, 10, 12, 14, 15, 20	H-11α	H-1α, H-5α, H-7α, H-11α, H-12α
10	48.9 s						
11	73.8 d	4.96α	overlap	1H	8, 9, 10, 12, 13	H-9α, H-12α	H-1β, H-9α, H-12α, H-12β
12	39.3 t	2.32α	overlap	1H	9, 11, 13, 14, 16	H-11α, H-12β	H-11α, H-12β, H-14α
		2.62β	d (*J* = 16.4 Hz)	1H	9, 11, 13, 14, 16,	H-12α	H-12α, H_3-15β, H_3-16β
13	83.0 s						
14	48.3 d	1.65α	overlap	1H	7, 8, 9, 12, 13, 15, 16, 17, 2’	H-17α, H-17β	H-7α, H_3-16β, H-17α
15	16.6 q	1.03β	s	3H	7, 8, 9, 14		H-7β, H-14α, H_3-16β, H-17β
16	24.8 q	1.36β	s	3H	12, 13, 14		H-12β, H_3-15β
17	16.0 t	2.29β	overlap	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17α	H-7β, H_3-15β, H_3-16β, H-17α
		2.73α	dd (*J* = 16.1, 4.7 Hz)	1H	13, 14, 1’, 2’, 3’	H-14α, H-17β	H-7α, H-7β, H-14α, H-17β
18	15.9 q	1.64β	s	3H	3, 4, 5, 19		H-3α, H-5α, H_3-19α
19	28.3 q	1.21α	s	3H	3, 4, 5, 18		H-3α, H_3-18β
20	176.9 s						
1’	162.8 s						
2’	99.7 s						
3’	179.7 s						
4’	112.4 d	6.18	d (*J* = 0.8 Hz)	1H	2’, 3’, 5’, 6’		H_3-6’
5’	161.0 s						
6’	18.8 q	2.03	d (*J* = 0.6 Hz)	3H	4’, 5’		H-4’
3-OH		6.11	s	1H	2, 3, 4	H-3α	H-3α



12-hydroxy-20,11-olide-chevalone E (8)

Table S11. **NMR data for 12-hydroxy-20,11-olide-chevalone E (8)** (^{1}H NMR:800 MHz, ^{13}C NMR: 200 MHz, δ in ppm, recorded in pyridine-d_5)

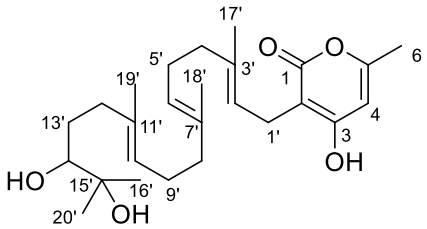
	^{13}C				^{1}H		
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation	NOESY correlation
1	34.0 t	1.41α	td (*J* = 13.5, 2.7 Hz)	1H	2, 3, 5, 9, 10, 20	H-1β, H-2β	H-1β, H-2α, H-3α, H-9α
		2.17β	dt (*J* = 13.5, 3.4 Hz)	1H	2, 3, 5	H-1α, H-2α	H-1α, H-2α, H-11α
2	28.0 t	1.91α	m	1H	1, 3, 4, 10	H-2β, H-3α	H-1α, H-2β, H-3α
		2.23β	m	1H	1, 3, 4, 10	H-1α, H-2α, H-3α	H-1α, H-2α, H_3-18β
3	77.8 d	3.50α	d (*J* = 10.6 Hz)	1H	2, 4, 18, 19	H-2α, H-2β, 3-OH	H-2α, H-5α, H_3-19α
4	39.9 s						
5	51.1 d	1.45α	dd (*J*= 13.2, 5.4 Hz)	1H	1, 3, 4, 6, 7, 9, 10, 18, 19, 20	H_2-6	H-3α, H_2-6, H-9α, H_3-19α
6	19.8 t	1.71	m	2H	4, 5, 8, 10	H-5α, H-7α	H-5α, H-7α
7	35.7 t	1.15α	overlap	1H	5, 6, 8, 9, 14, 15	H_2-6, H-7β,	H-7β, H-17α
		1.60β	m	1H	5, 6, 8, 9	H-7α	H_2-6, H-7α
8	34.8 s						
9	57.1 d	1.75α	overlap	1H	1, 5, 7, 8, 10, 11, 12, 14, 15, 20	H-11α	H-1α, H-5α, H-11α, H-12α, H-14α
10	49.0 s						
11	77.5 d	5.25α	dd (*J* =5.7, 2.9 Hz)	1H	8, 9, 10, 12, 13	H-9α, H-12α	H-9α, H-12α
12	75.9 d	4.44α	d (*J* =5.1 Hz)	1H	13, 16	H-11α, 12-OHβ	H-9α, H-11α
13	88.4 s						
14	47.1 d	1.75α	overlap	1H	7, 8, 9, 12, 13, 15, 16, 17, 2’	H-17α, H-17β	H-9α, H-12α, H-17α
15	16.6 q	1.17α	s	3H	7, 8, 9, 14		H-7β, H_3-16β, H-17β
16	19.4 q	1.67α	m	3H	12, 13, 14		H-12α, H_3-15β, H-17β
17	15.9 t	2.50β	dd (*J* = 16.2, 12.8 Hz)	1H	8, 13, 14, 1’, 2’, 3’	H-14α, H-17α	H_3-15β, H_3-16β, H-17α
		2.80α	dd (*J* = 16.2, 4.9 Hz)	1H	8, 12, 13, 14, 1’, 2’, 3’	H-14α, H-17β	H-7β, H-14α, H-17β
18	15.7 q	1.65β	s	3H	3, 4, 5, 19		H-2β, H_3-19α
19	28.2 q	1.20α	s	3H	3, 4, 5, 18		H-3α, H-5α, H_3-18β
20	177.2 s						
1’	162.8 s						
2’	98.9 s						
3’	179.7 s						
4’	112.4 d	6.19	d (*J* = 0.7 Hz)	1H	2’, 3’, 5’, 6’		H_3-6’
5’	160.9 s						
6’	18.8 q	2.04	d (*J* = 0.7 Hz)	3H	4', 5'		H-4’
3-OH		6.09β	s	1H		H-3α	
12-OH		8.08β	s	1H		H-12α	



geranylgeranyl-triacetate lactone (**9**)

Table S12. **NMR data for geranylgeranyl-triacetate lactone (9)** (^{1}H NMR:600 MHz, ^{13}C NMR: 150 MHz, δ in ppm, recorded in acetone-d_6)

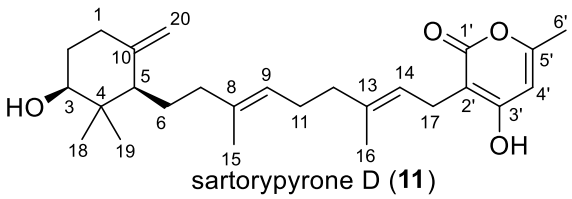
	^{13}C				^{1}H	
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation
1	165.7 s					
2	102.4 s					
3	165.4 s					
4	100.8 d	5.98	s	1H	2, 3, 5, 6	
5	160.7 s					
6	19.6 q	2.04	s	3H	4, 5	
1’	22.7 t	3.09	d (J = 7.0 Hz)	2H	1, 2, 3, 2’, 3’	H-2’
2’	122.6 d	5.23	t (J = 7.0 Hz)	1H	1’, 4’, 17’	H_2-1’
3’	135.3 s					
4’	40.4 t	1.93	overlap	2H	2’, 3’, 5’, 6’, 17’	H_2-5’
5’	27.2 t	2.05	overlap	2H	3’, 4’, 6’, 7’	H_2-4’, H-6’
6’	125.1 d	5.12	overlap	1H	4’, 5’, 8’, 18’	H_2-5’
7’	135.6 s					
8’	40.4 t	2.04	overlap	2H	6’, 7’, 9’, 10’	H_2-9’
9’	27.2 t	1.93	overlap	2H	7’, 8’, 10’, 11’	H_2-8’, H-10’
10’	125.1 d	5.12	overlap	1H	8’, 9’, 12’, 19’	H_2-9’
11’	135.4 s					
12’	40.5 t	2.04a	overlap	1H	10’, 11’, 13’, 14’	H-12’b, H-13’a, H-13’b
		1.93b	overlap	1H	10’, 11’, 13’, 14’, 19’	H-12’a, H-13’a, H-13’b
13’	27.4 t	2.04a	overlap	1H	11’, 12’, 14’	H-12’a, H-13’b, H-14’
		1.93b	overlap	1H	11’, 12’, 15	H-12’b, H-13’a
14’	125.0 d	5.12	overlap	1H	12’, 16’, 20’	H-13’a
15’	131.5 s					
16’	17.7 q	1.74	s	3H	20’	
17’	16.1 q	1.59	s	3H	2’, 3’, 4’	
18’	16.1 q	1.59	s	3H	6’, 7’, 8’	
19’	16.3 q	1.59	s	3H	10’, 11’, 12’	
20’	25.8 q	1.65	s	3H	16’	



dihydroxygeranylgeranyl-triacetate lactone (**10**)

Table S13. **NMR data for dihydroxygeranylgeranyl-triacetate lactone (10)** (^{1}H NMR:600 MHz, ^{13}C NMR: 150 MHz, δ in ppm, recorded in acetone-d_6)

	^{13}C				^{1}H	
position	δ (ppm)	δ (ppm)	Multiplicity	intensity	HMBC correlation	COSY correlation
1	171.0 s					
2	100.5 s					
3	167.0 s					
4	103.6 d	5.98	s	1H	2, 5, 6	
5	159.0 s					
6	19.7 q	2.04	s	3H	4, 5	
1’	23.0 t	3.06	d (J = 7.0 Hz)	2H	1, 2, 3, 2’, 3’	H-2’
2’	124.4 d	5.28	t (J = 7.0 Hz)	1H	1’, 4’, 17’	H_2-1’
3’	134.0 s					
4’	40.4 t	2.06	overlap	2H	2’, 3’, 5’, 6’	H_2-5’
5’	27.2 t	2.07	overlap	2H	3’, 4’, 6’, 7’	H_2-4’, H-6’
6’	125.2 d	5.12	overlap	1H	4’, 5’, 8’, 18’	H_2-5’
7’	135.1 s					
8’	40.6 t	1.93	overlap	2H	6’, 7’, 9’, 10’	H_2-9’
9’	27.3 t	1.93	overlap	2H	7’, 10’, 11’	H_2-8’, H-10’ (weak)
10’	124.9 d	5.12	overlap	1H	9’, 12’, 19’	H_2-9’ (weak)
11’	135.8 s					
12’	37.6 t	2.24a	m	1H	10’, 11’, 13’, 14’, 19’	H-12’b, H-13’a
		1.99b	overlap	1H	10’, 11’, 13’, 19’	H-12’a, H-13’a
13’	30.8 t	1.64a	overlap	1H		H-12’a, H-13’b
		1.33b	overlap	1H	14’	H-12’b, H-13’a, H-14’
14’	78.5 d	3.25	d (J = 10.4 Hz)	1H	12’, 13’, 15’, 16’, 20’	H-13’a
15’	72.8 s					
16’	25.0 q	1.10	s	3H	14’, 15’, 20’	
17’	16.1 q	1.73	s	3H	2’, 3’, 4’	
18’	16.4 q	1.57	s	3H	6’, 7’, 8’	
19’	16.2 q	1.58	s	3H	10’, 11’, 12’	
20’	26.0 q	1.11	s	3H	14’, 15’, 16’	



sartorypyrone D (**11**)

Table S14. **^{13}C NMR data for sartorypyrone D (11)**

position	200 MHz CD_3OD	100 MHz[a] CD_3Cl
1	34.8 t	32.4 t
2	33.2 t	32.0 t
3	78.0 d	77.3 d
4	41.6 s	40.4 s
5	52.0 d	51.2 d
6	24.6 t	23.9 t
7	40.9 t	38.6 t
8	136.3 s	136.3 s
9	125.4 d	123.2 d
10	149.0 s	147.3 s
11	27.5 t	26.0 t
12	39.6 t	39.6 t
13	136.5 s	140.6 s
14	122.5 d	120.4 d
15	16.1 q	16.2 q
16	16.3 q	16.3 q
17	22.8 t	22.9 t
18	15.7 q	16.2 q
19	26.4 q	26.1 q
20	108.5 t	108.5 t
1’	168.6 s	165.9 s
2’	103.1 s	100.7 s
3’	167.5 s	165.8 s
4’	101.6 d	100.7 d
5’	161.6 s	160.3 s
6’	19.6 q	19.7 q

([a] δ in ppm, data reported in *The Journal of Antibiotics*, *68*, 403–405 (2015))

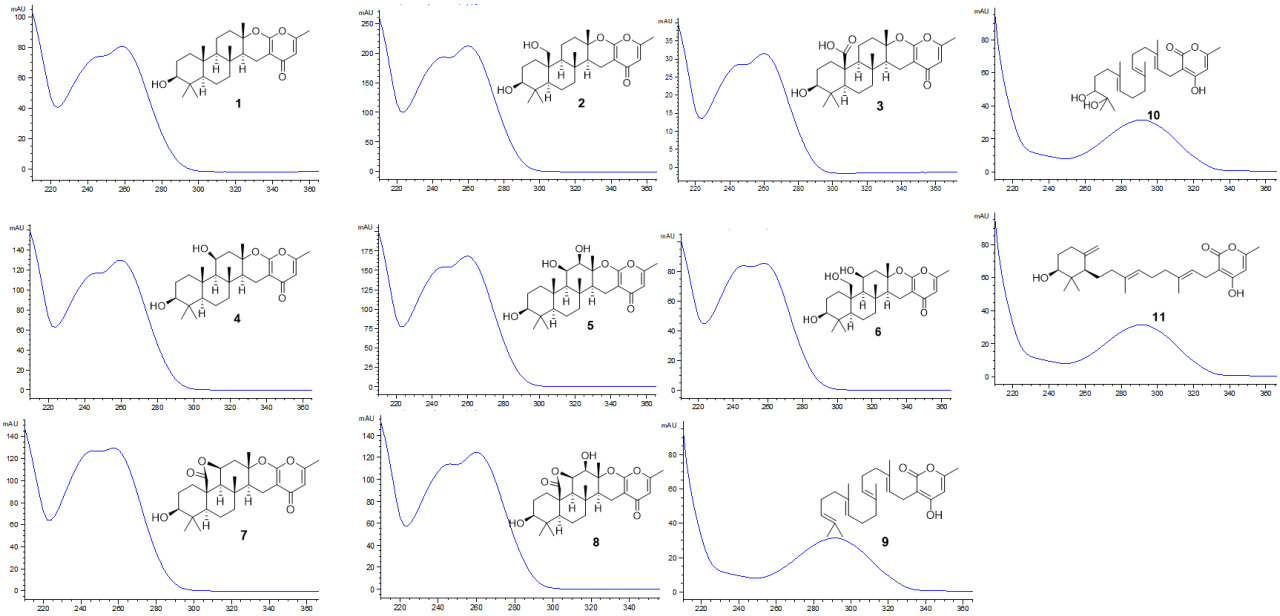


Figure S1. UV spectra of secondary metabolites isolated in this study.

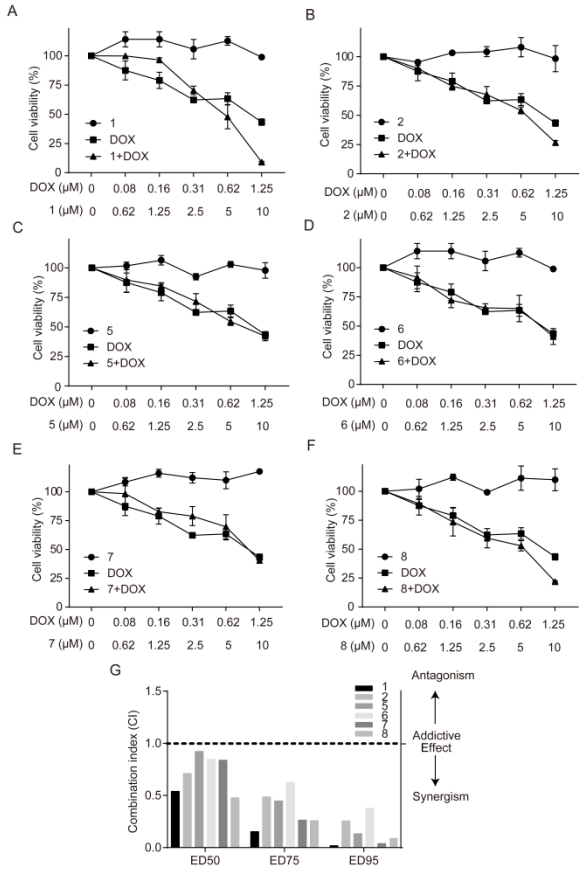


Figure S2. Compounds **1**, **2**, **5-8** synergistically enhances cytotoxicity of DOX in MCF-7 breast cancer cells. (A–F) MCF-7 cells were treated with DOX, compounds 1, 2, 5-8, or the combination of both agents at a 1 : 8 M ratio. After 48 h, cell viability was determined using the colorimetric MTT assay. (G) Combination index values were calculated using CompuSyn software to determine drug interaction. A CI < 1 indicates synergism, CI = 1 indicates additive effects, and CI > 1 indicates antagonism. The data are presented as mean ± standard deviation of three independent experiments.

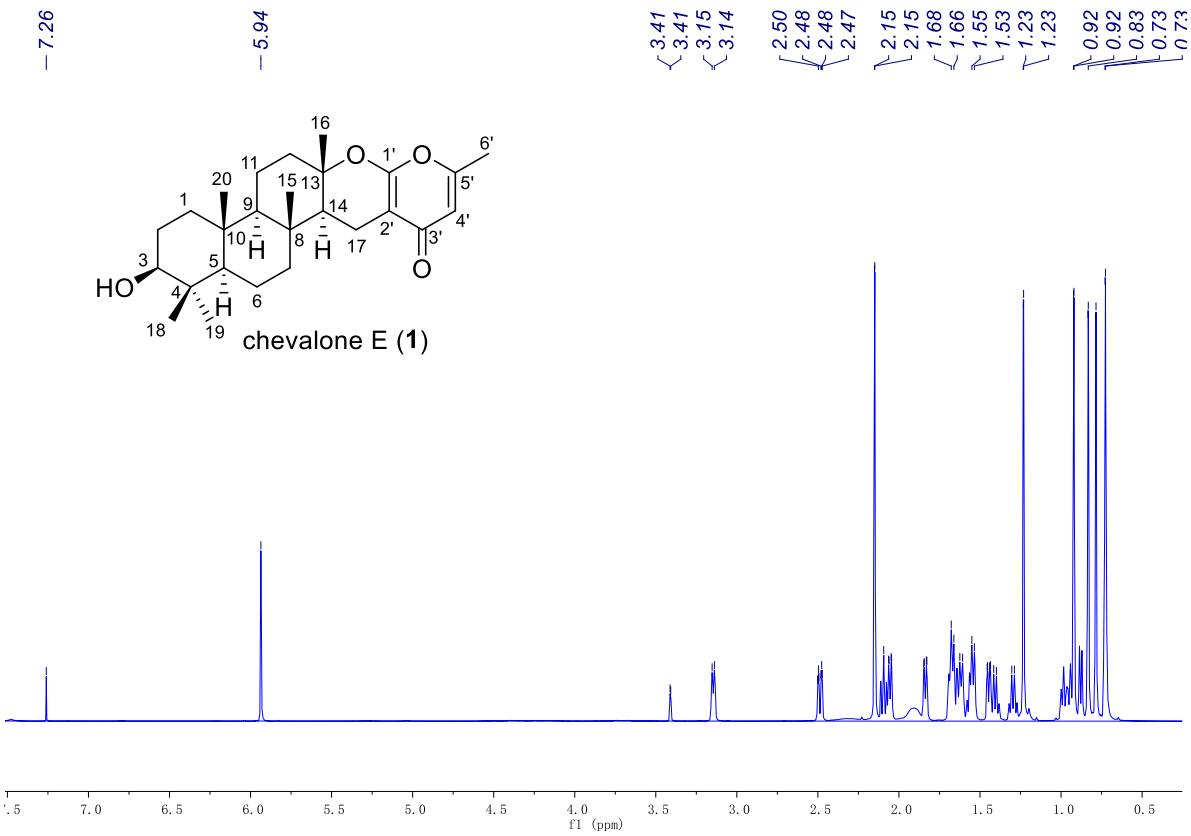


Figure S3. ^{1}H NMR spectrum of chevalone E (**1**)

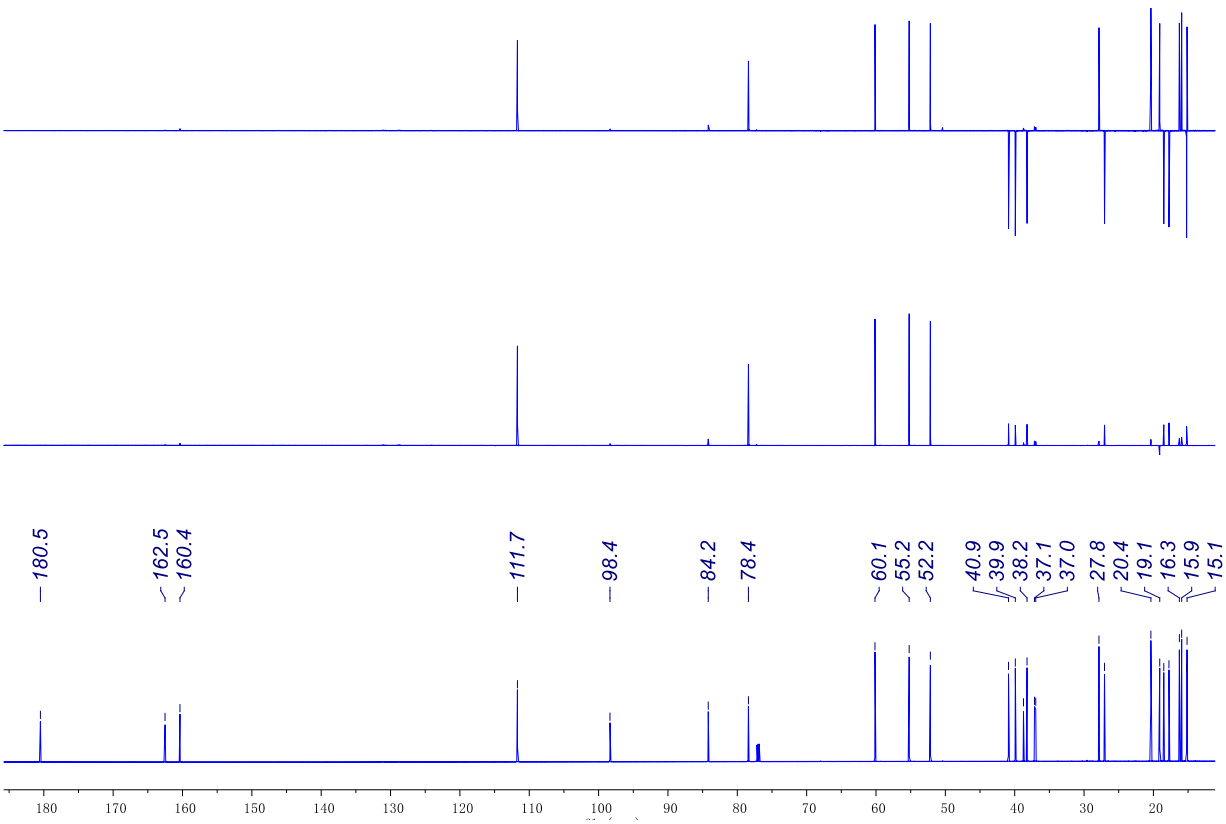


Figure S4. ^{13}C NMR spectrum of chevalone E (**1**)

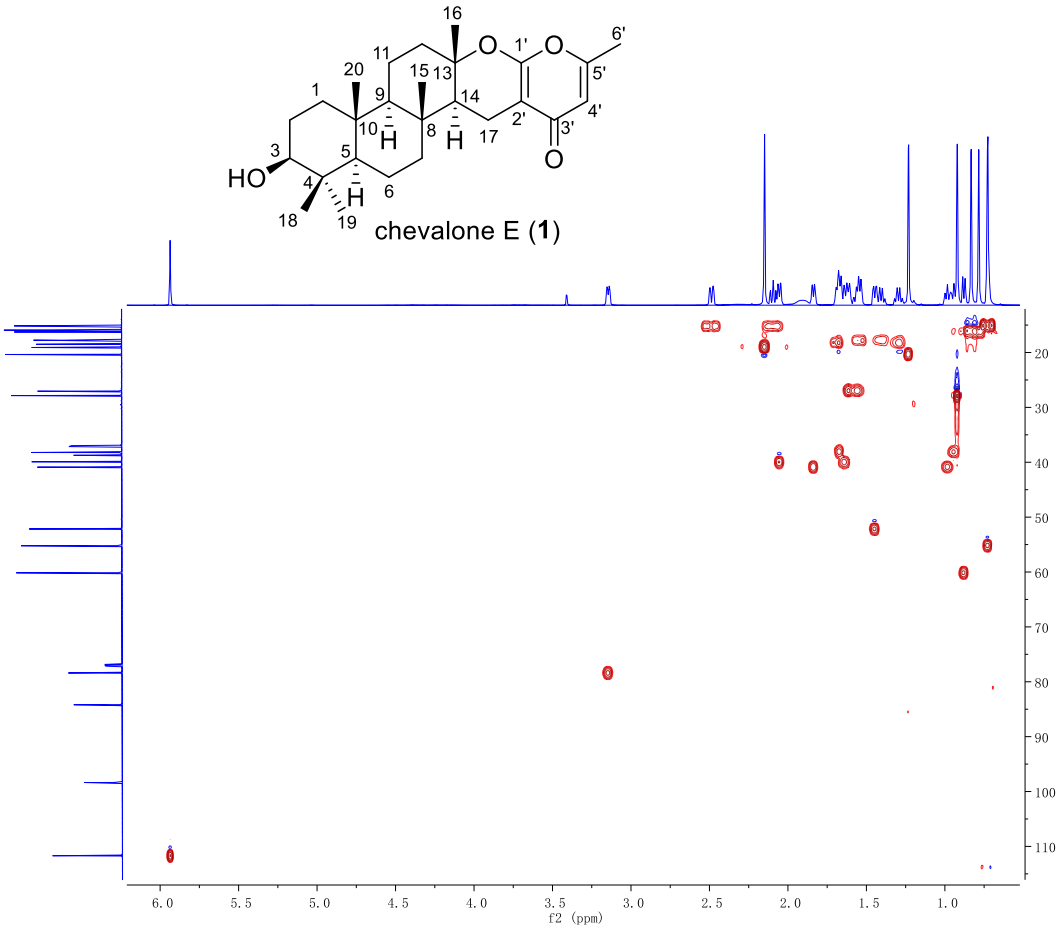


Figure S5. HSQC spectrum of chevalone E (**1**)

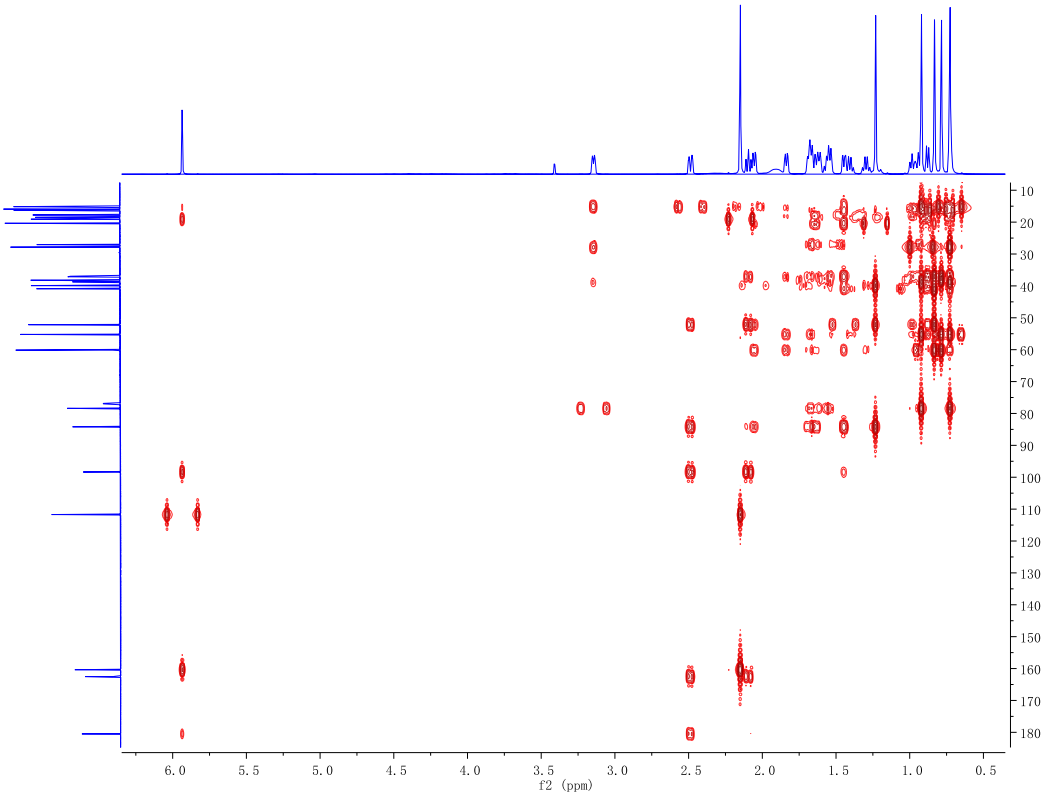


Figure S6. HMBC spectrum of chevalone E (**1**)

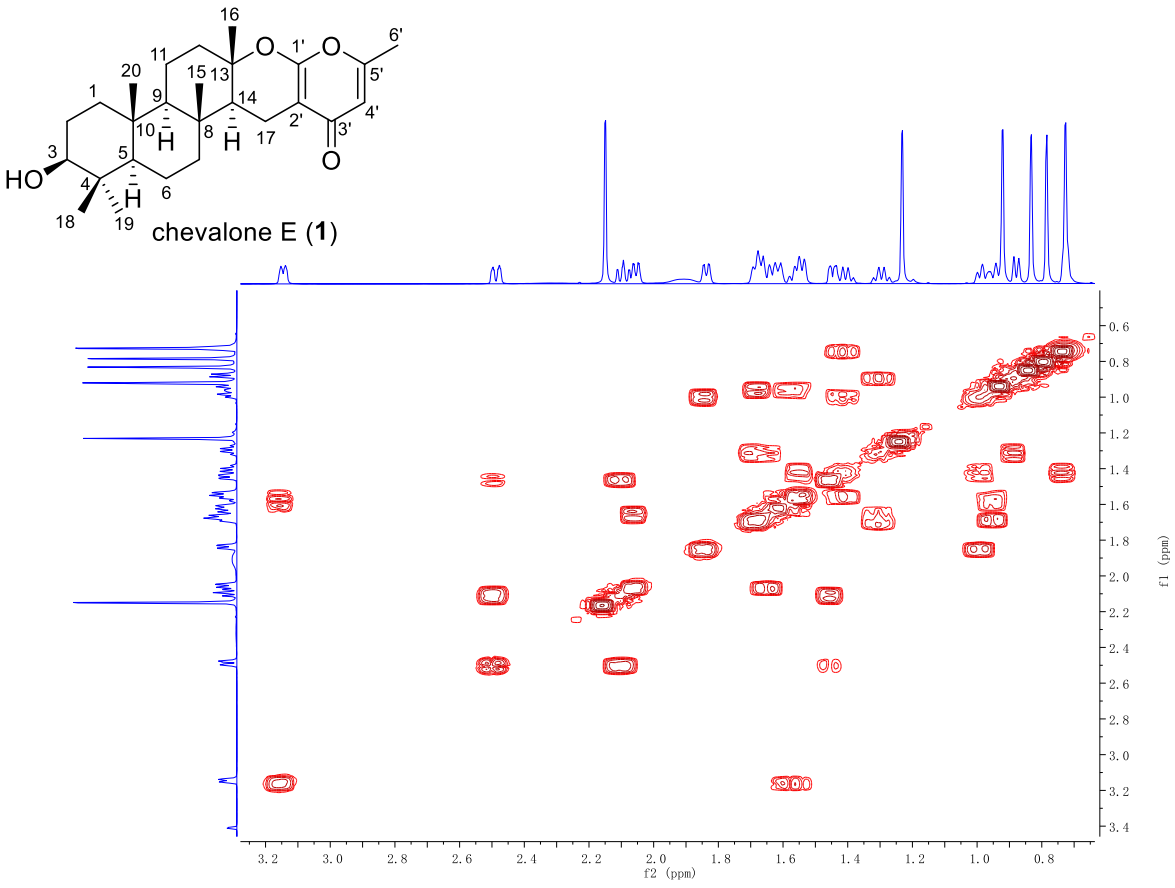


Figure S7. ^{1}H-^{1}H COSY spectrum of chevalone E (**1**)

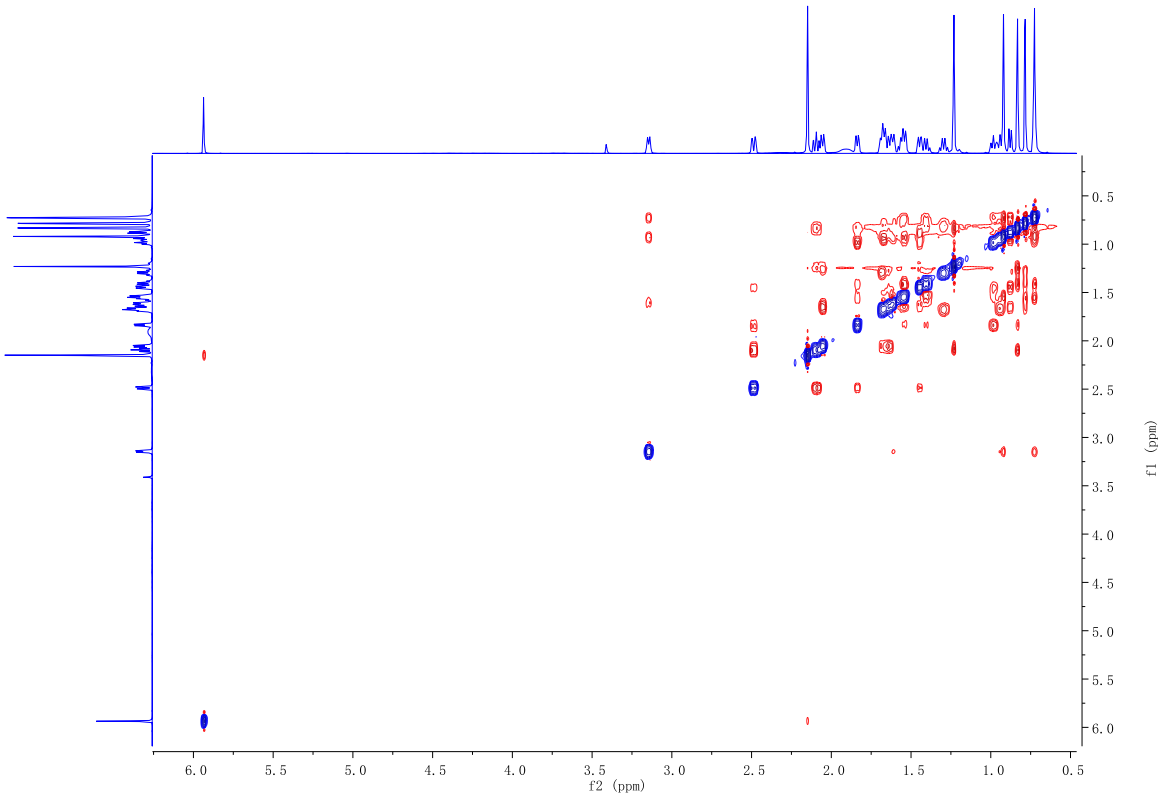


Figure S8. ROESY spectrum of chevalone E (**1**)

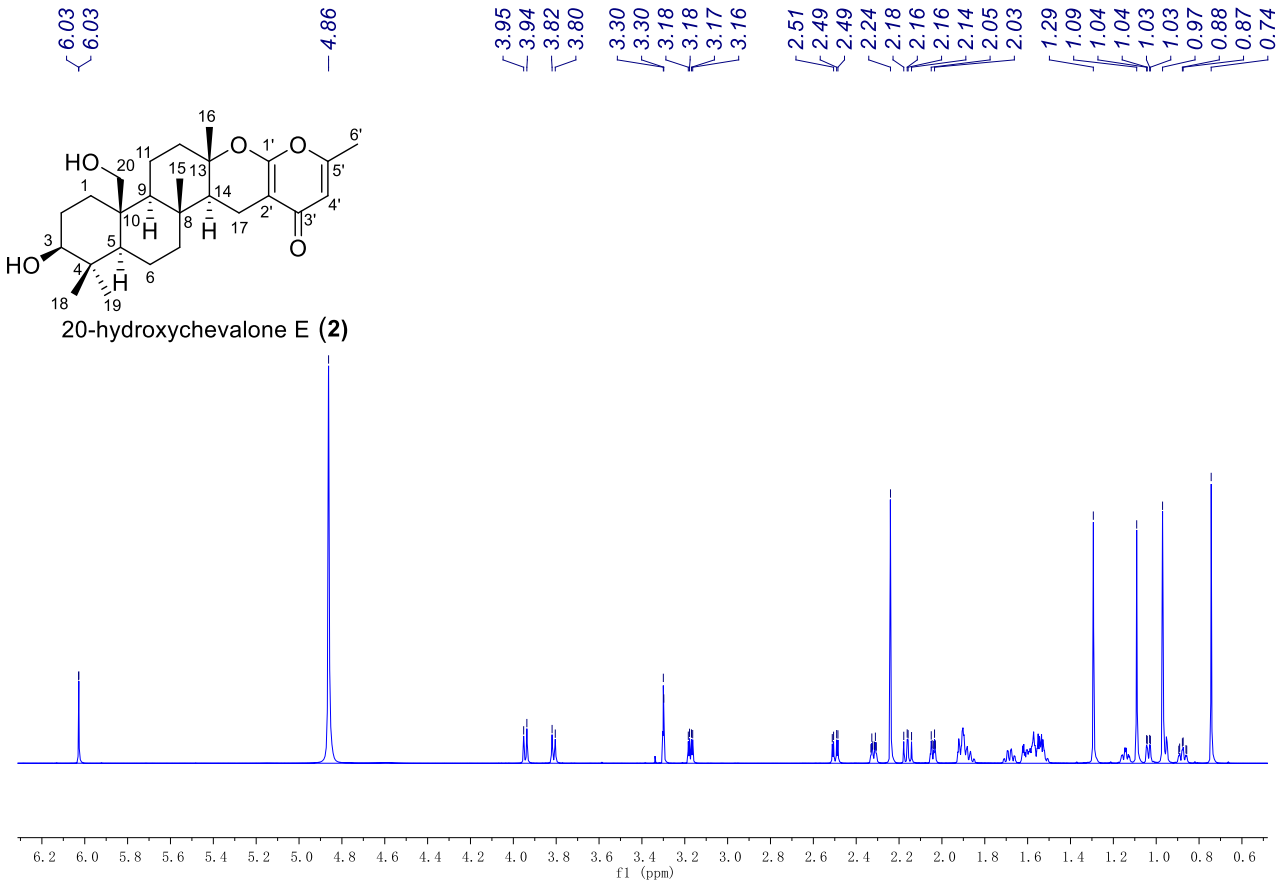


Figure S9. ^{1}H NMR spectrum of 20-hydroxychevalone E (**2**)

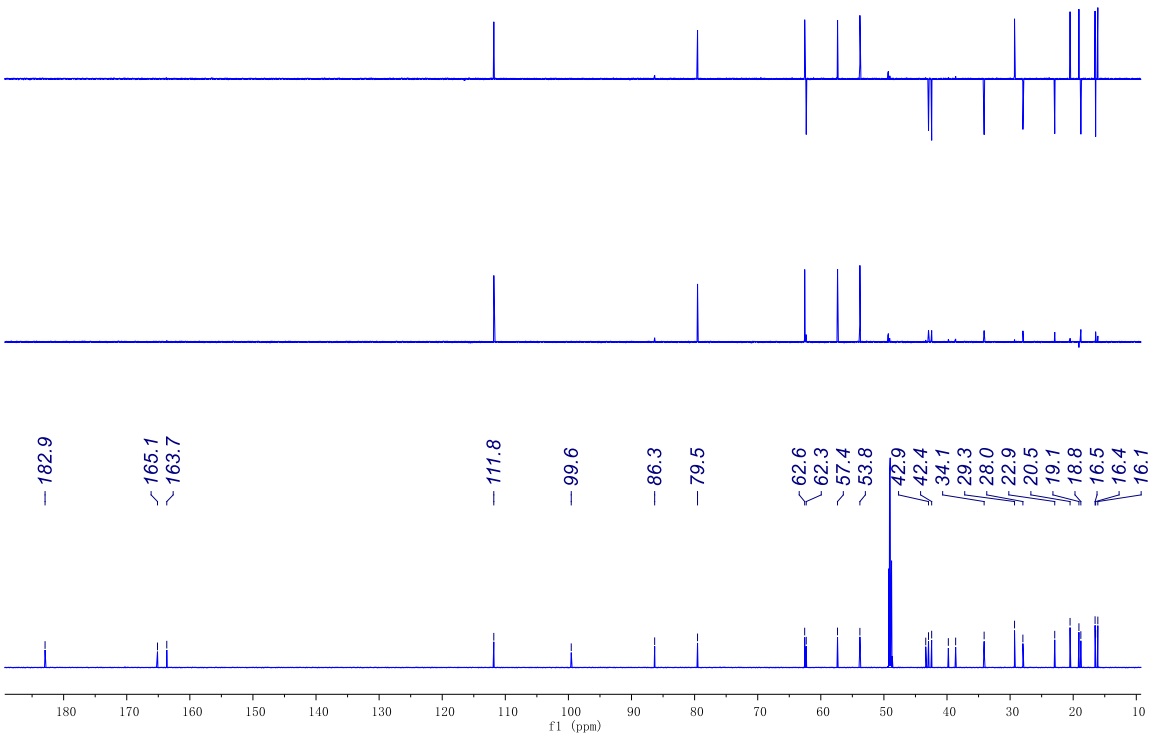


Figure S10. ^{13}C NMR spectrum of 20-hydroxychevalone E (**2**)

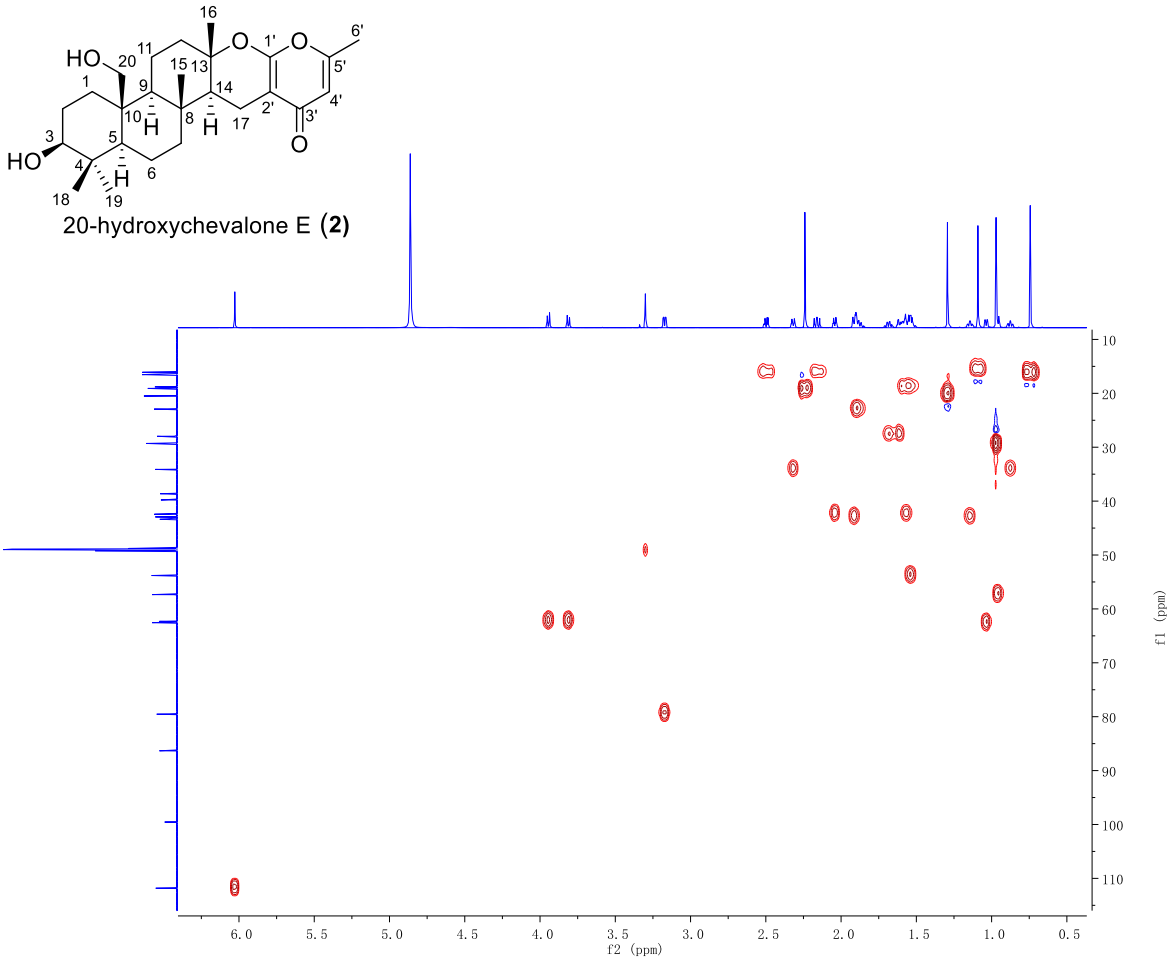


Figure S11. HSQC spectrum of 20-hydroxychevalone E (**2**)

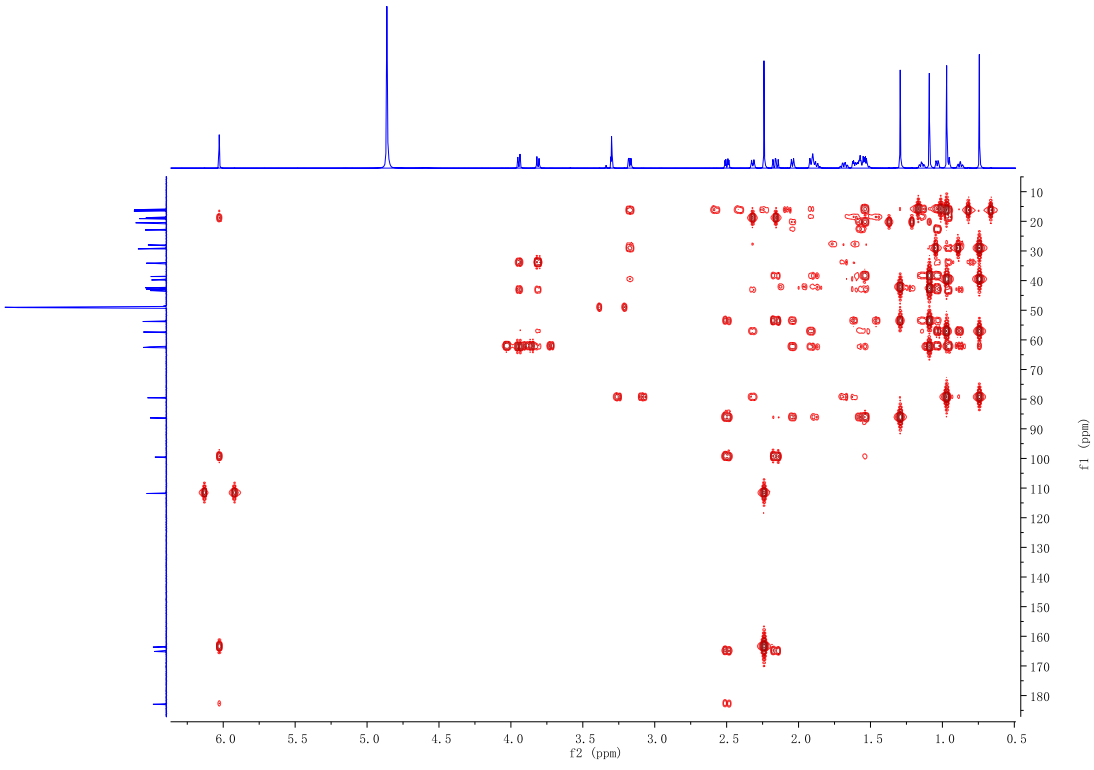


Figure S12. HMBC spectrum of 20-hydroxychevalone E (**2**)

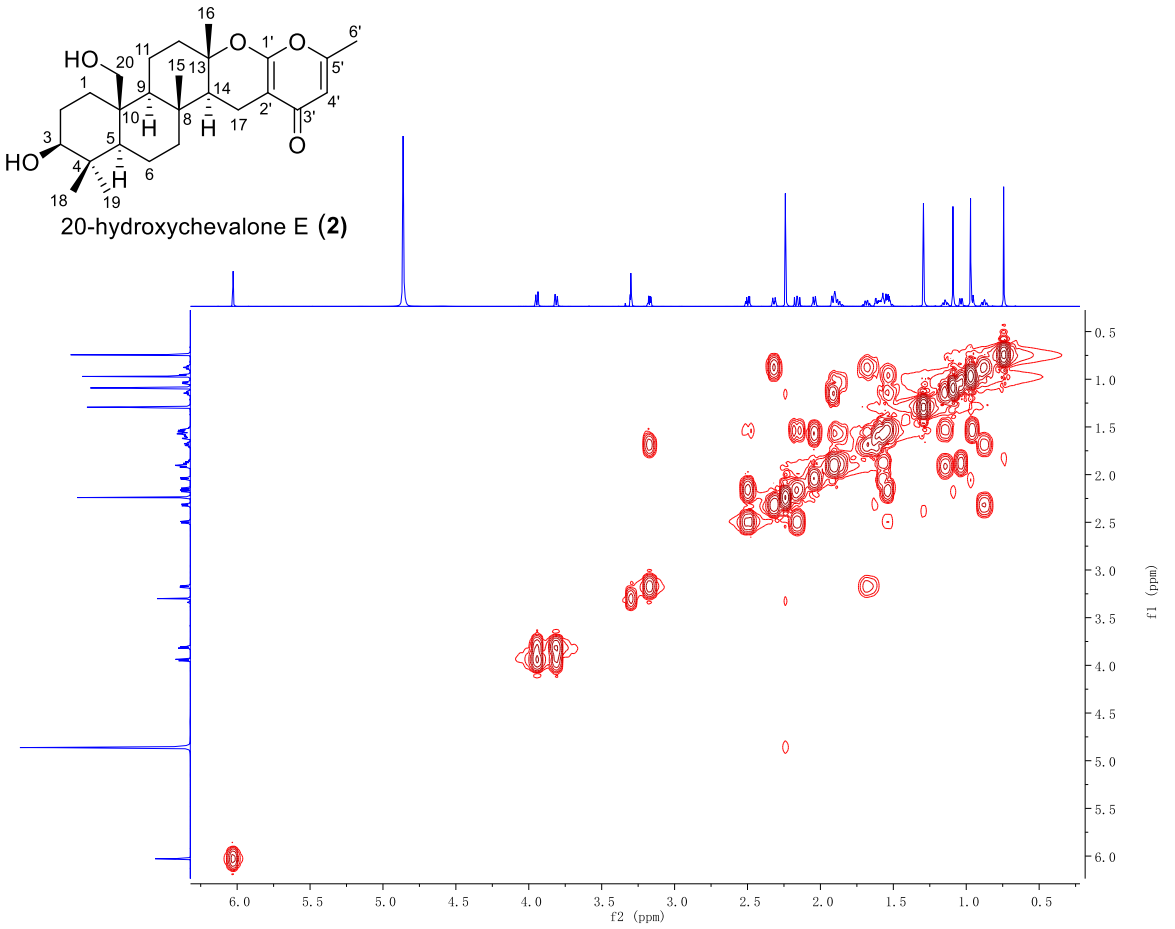


Figure S13. ^{1}H-^{1}H COSY spectrum of 20-hydroxychevalone E (**2**)

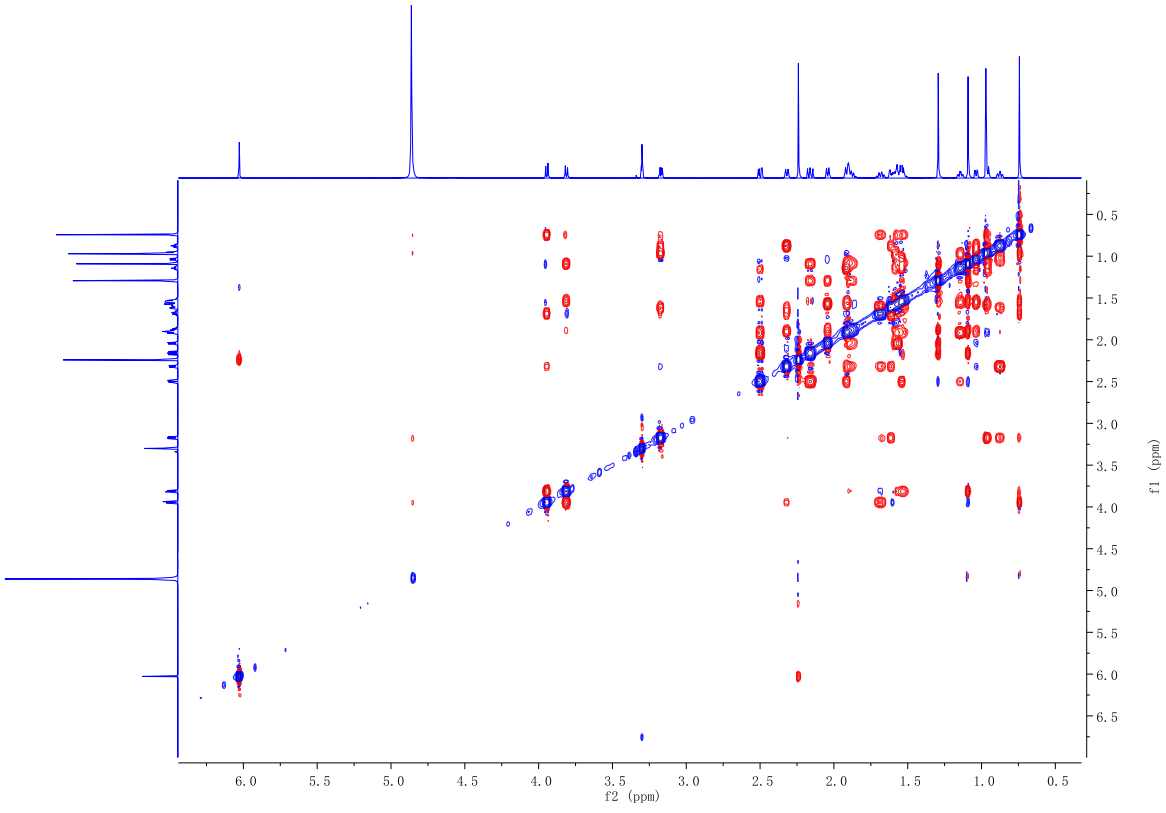


Figure S14. ROESY spectrum of 20-hydroxychevalone E (**2**)

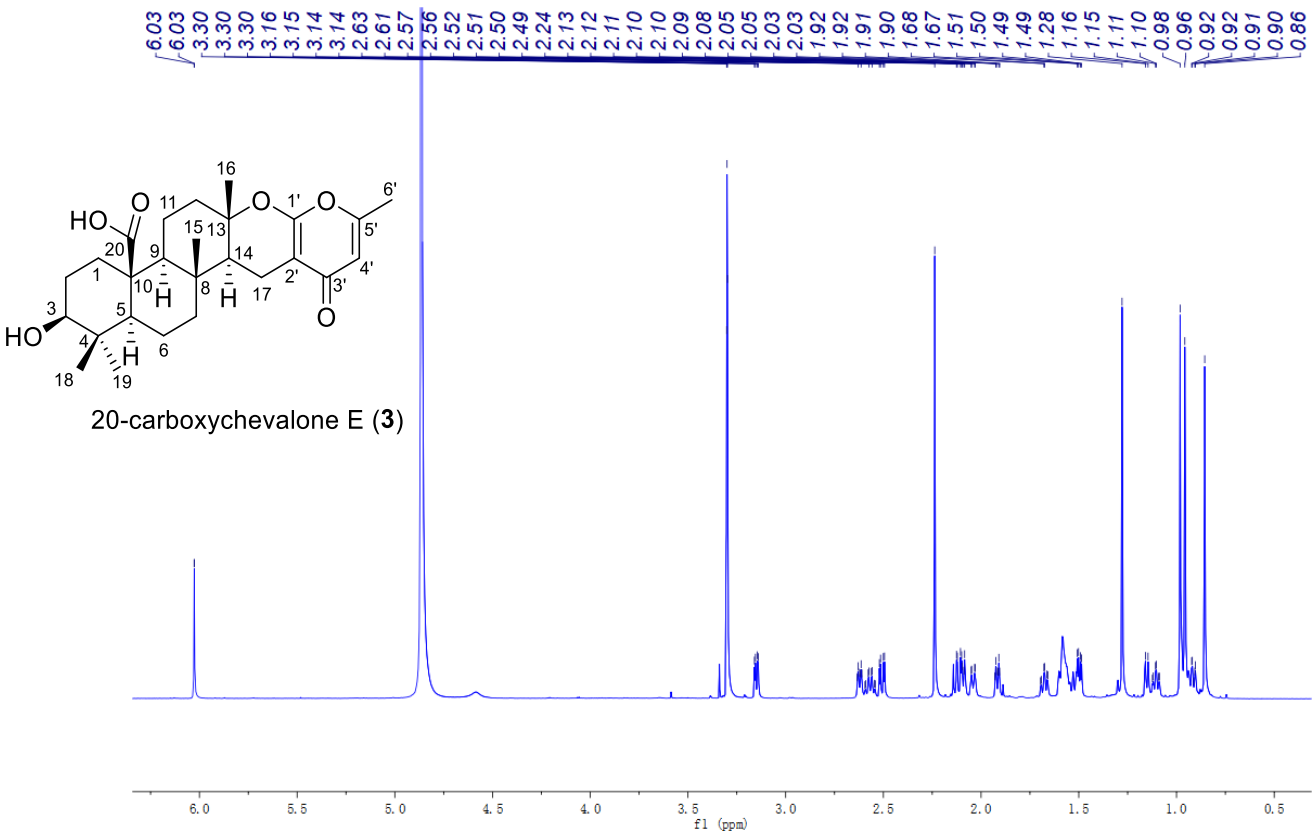


Figure S15. ^{1}H NMR spectrum of 20-carboxychevalone E (**3**)

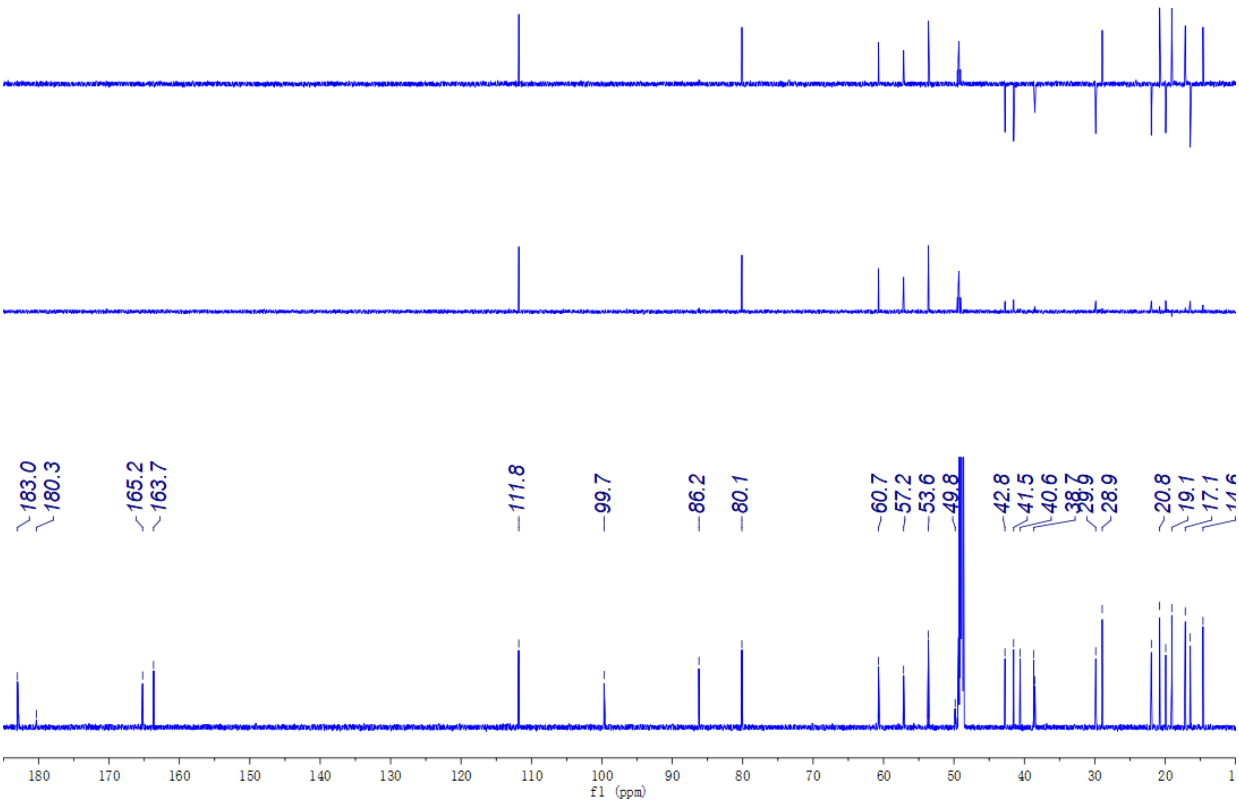


Figure S16. ^{13}C NMR spectrum of 20-carboxychevalone E (**3**)

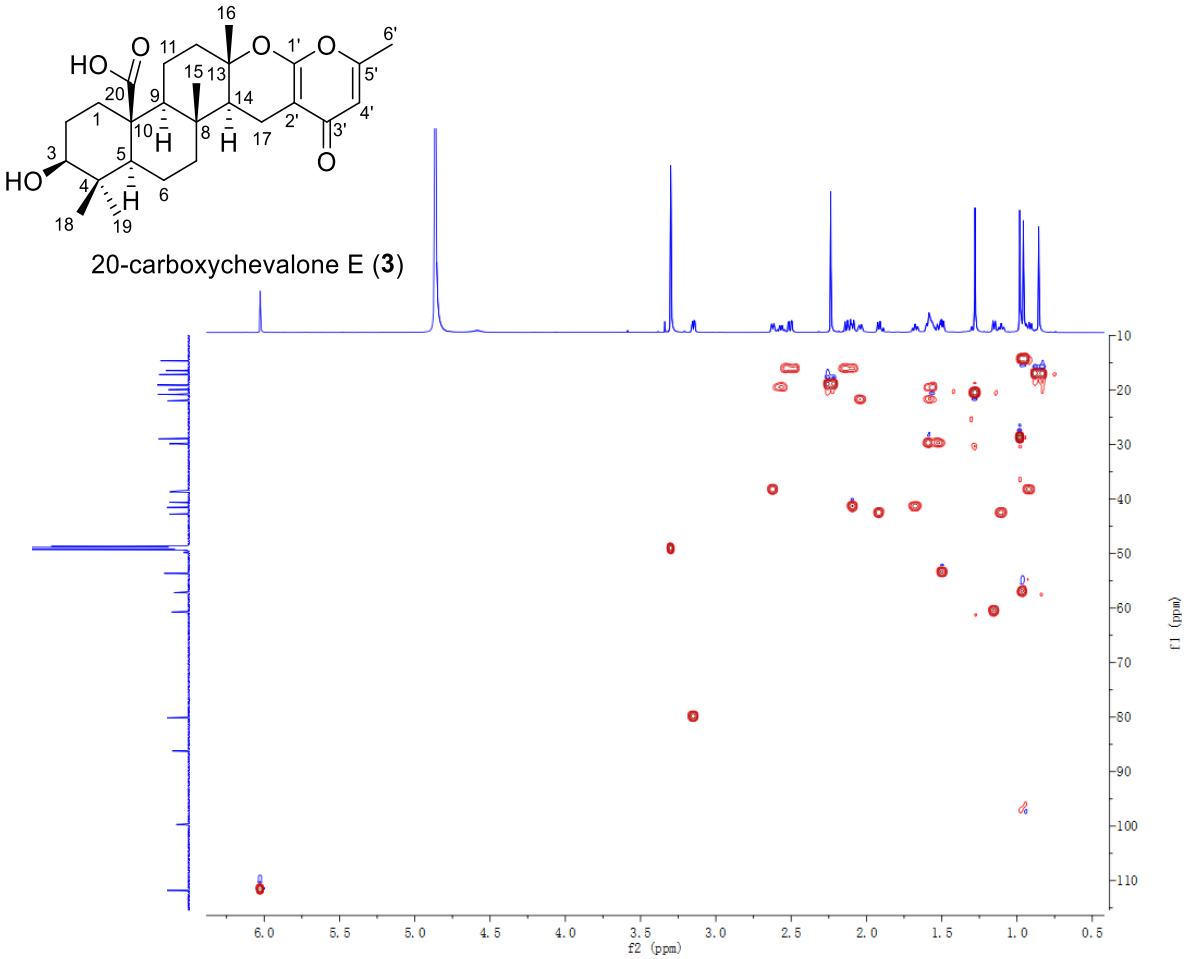


Figure S17. HSQC spectrum of 20-carboxychevalone E (**3**)

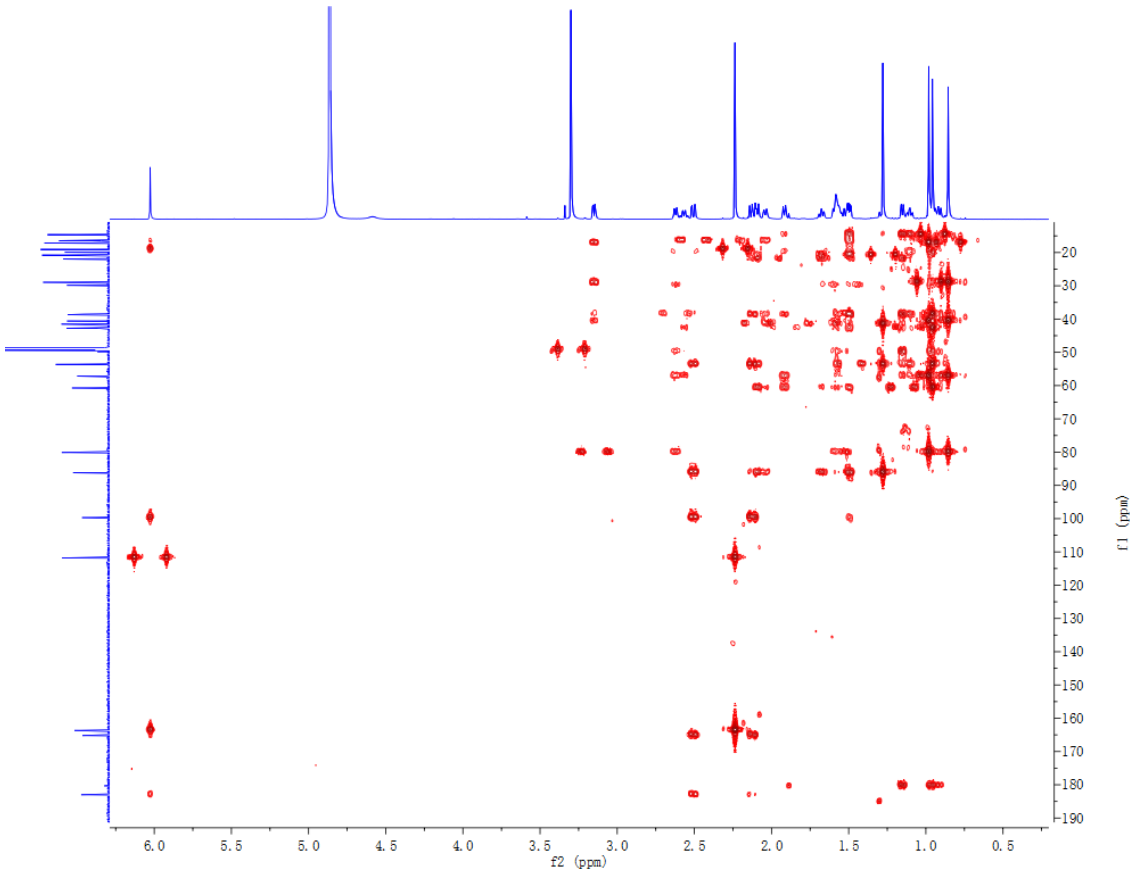
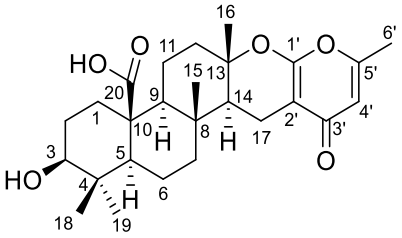


Figure S18. HMBC spectrum of 20-carboxychevalone E (**3**)



20-carboxychevalone E (**3**)

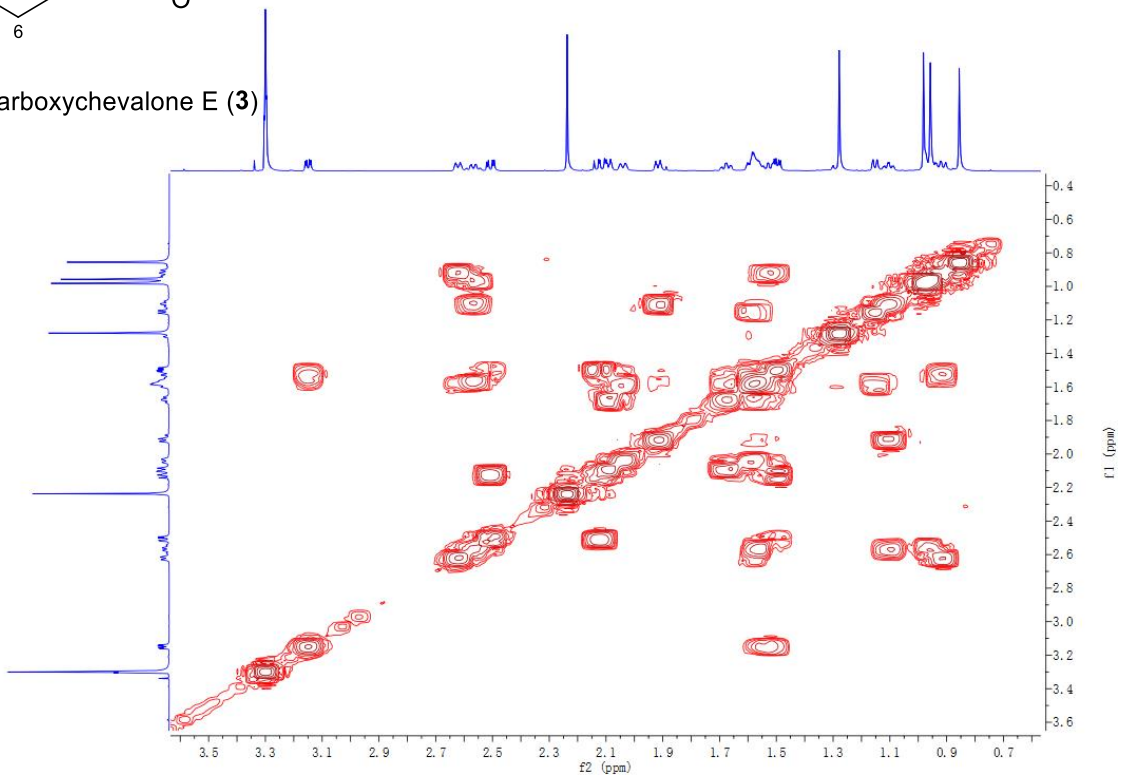


Figure S19. ^{1}H-^{1}H COSY spectrum of 20-carboxychevalone E (**3**)

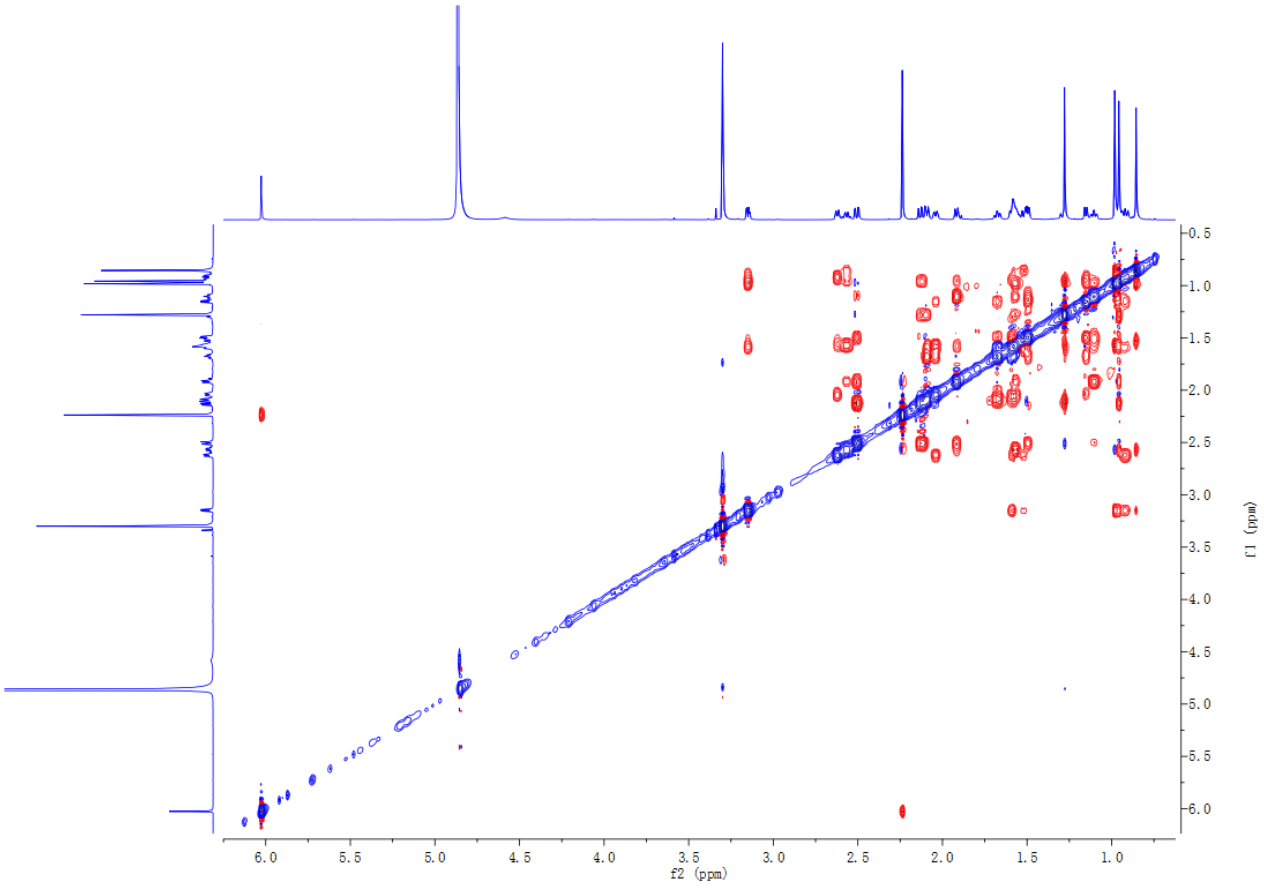


Figure S20. ROESY spectrum of 20-carboxychevalone E (**3**)

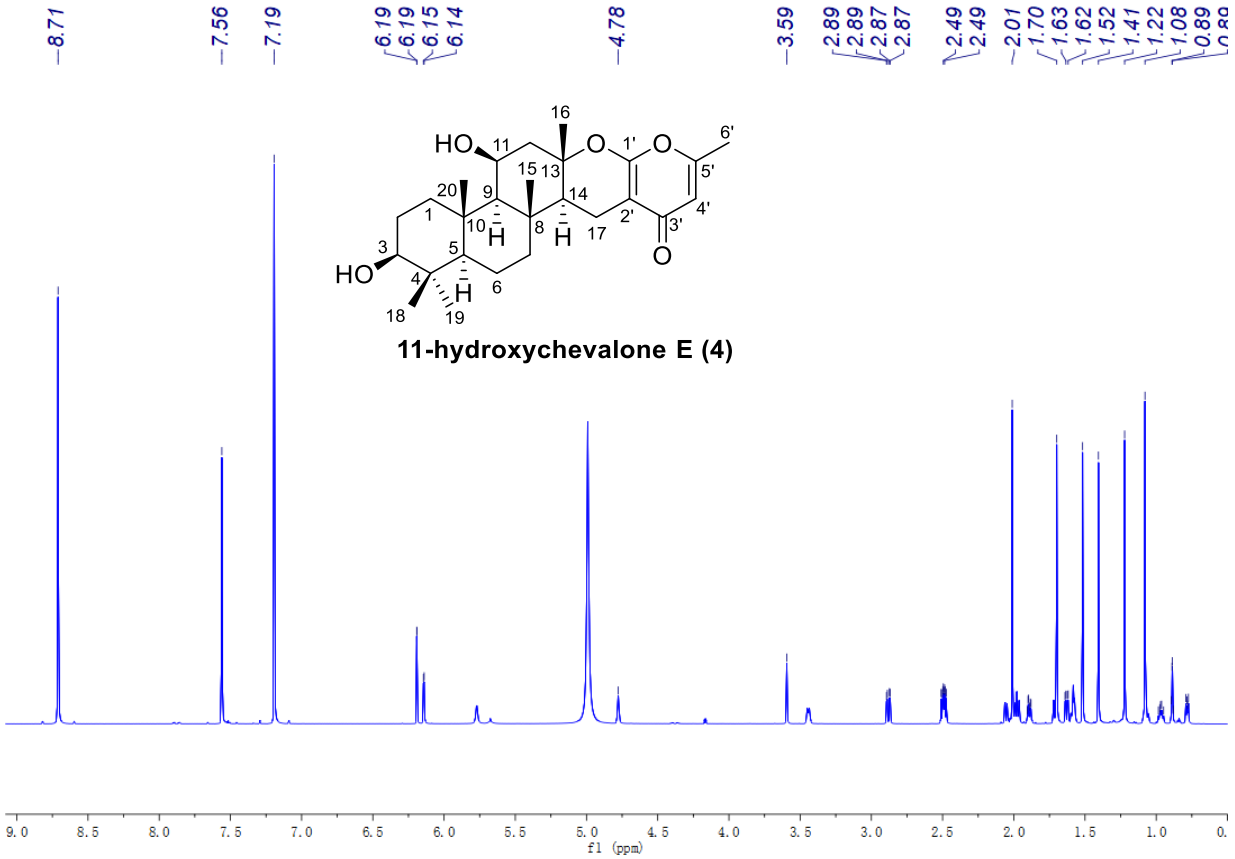


Figure S21. ^{1}H NMR spectrum of 11-hydroxychevalone E (**4**)

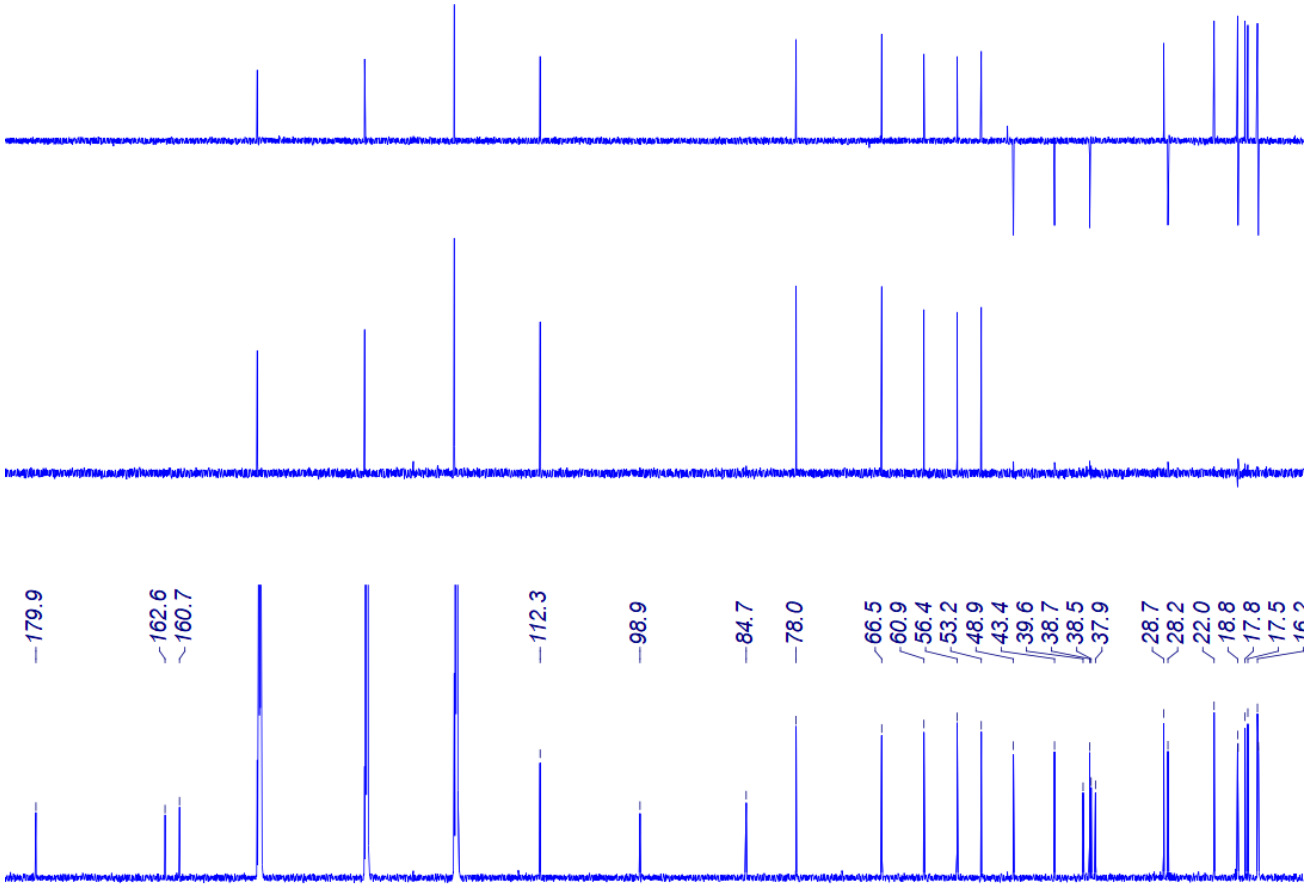


Figure S22. ^{13}C NMR spectrum of 11-hydroxychevalone E (**4**)

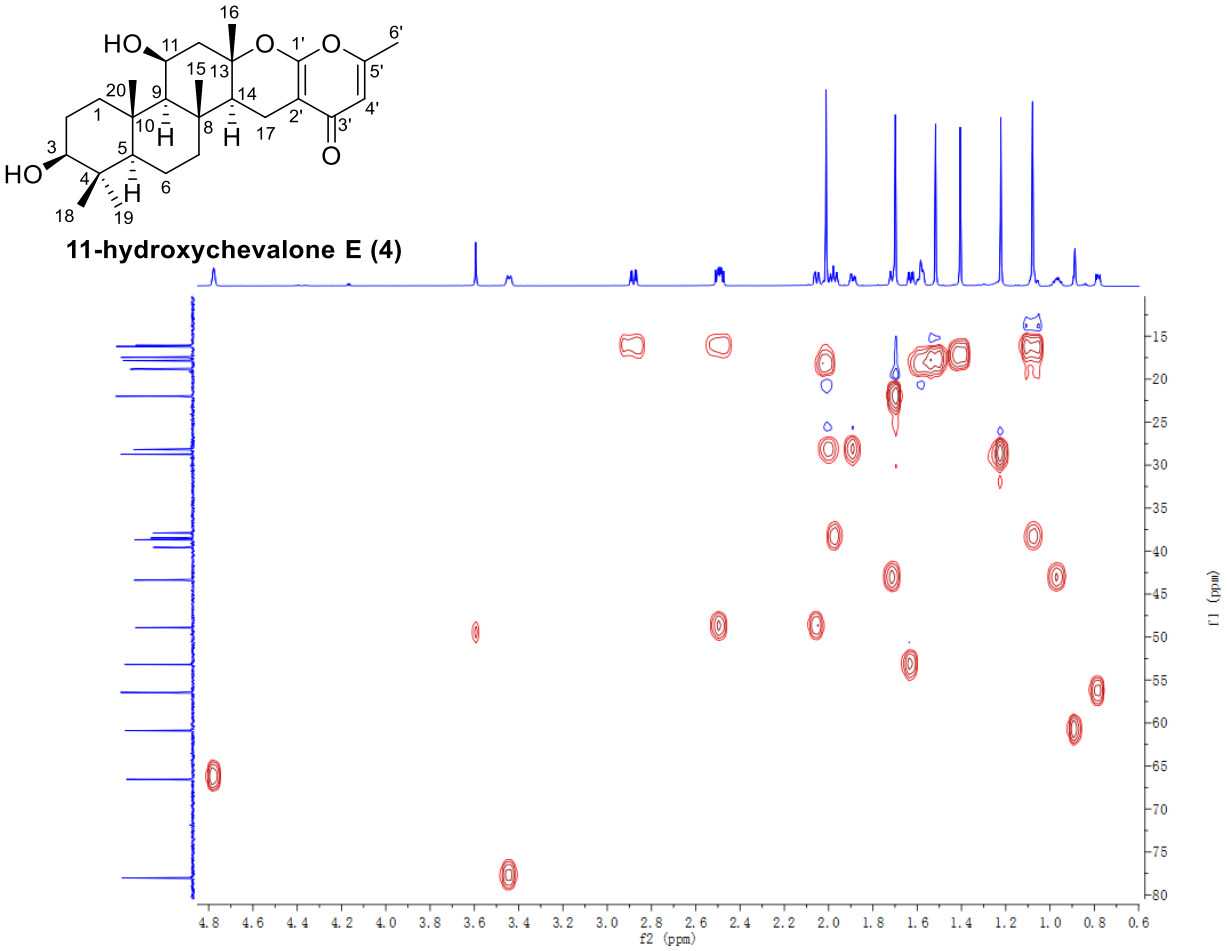


Figure S23. HSQC spectrum of 11-hydroxychevalone E (**4**)

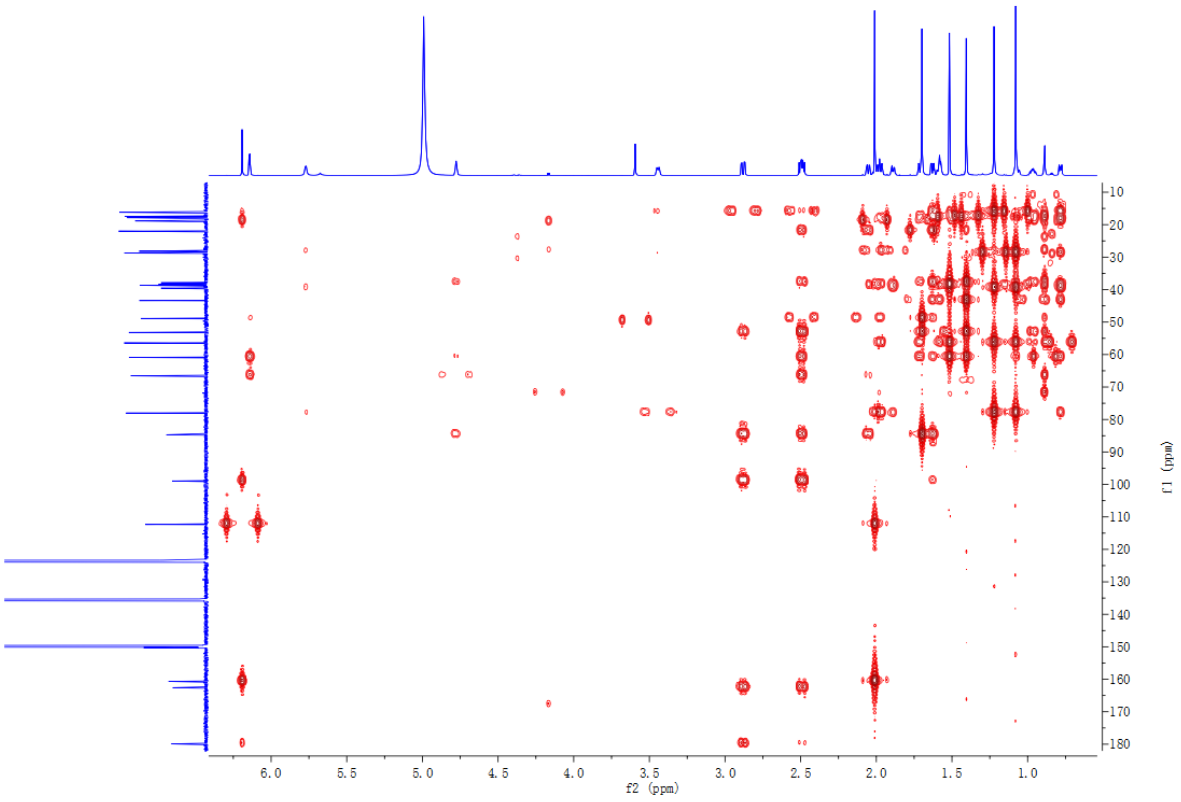


Figure S24. HMBC spectrum of 11-hydroxychevalone E (**4**)

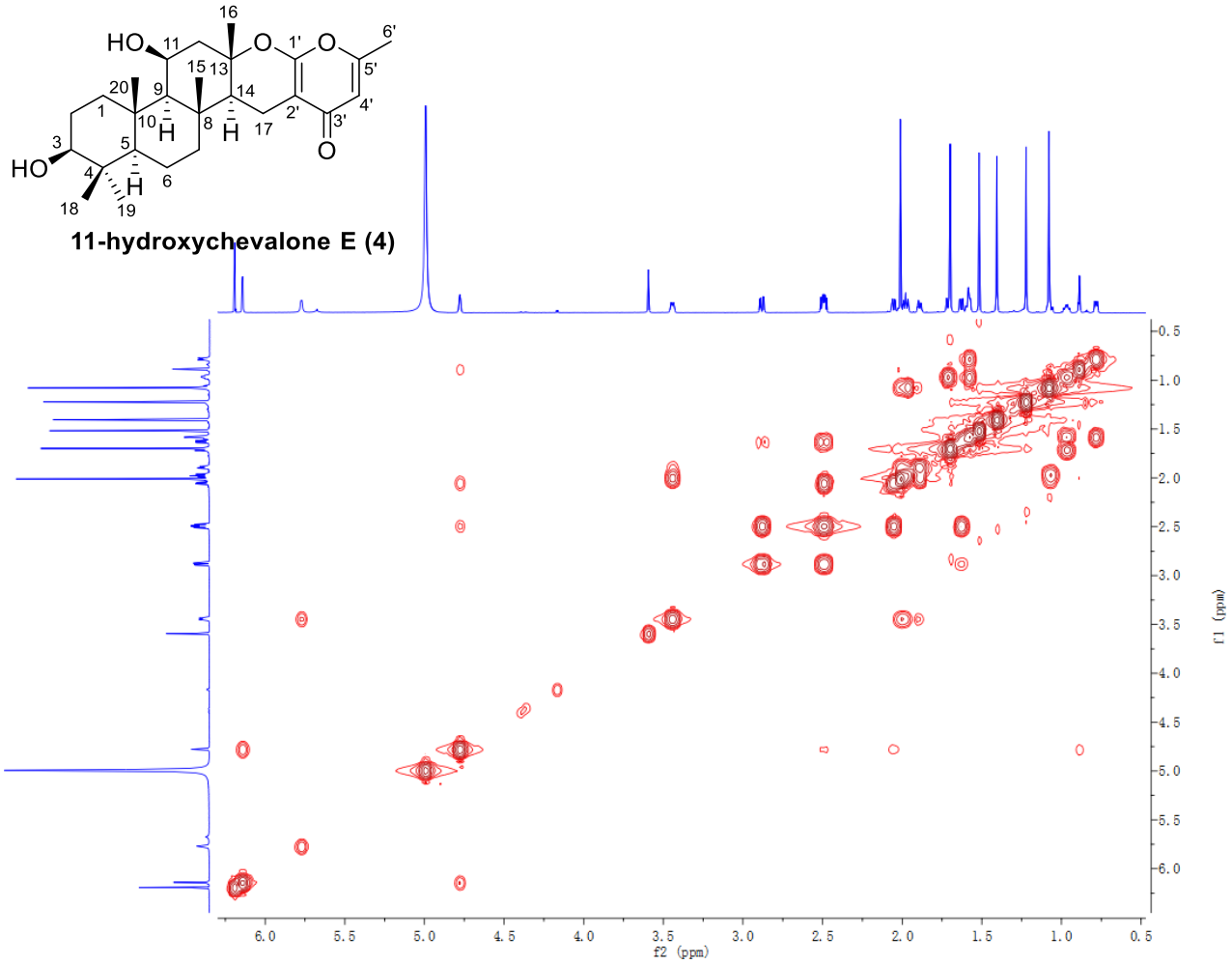


Figure S25. ^{1}H-^{1}H COSY spectrum of 11-hydroxychevalone E (**4**)

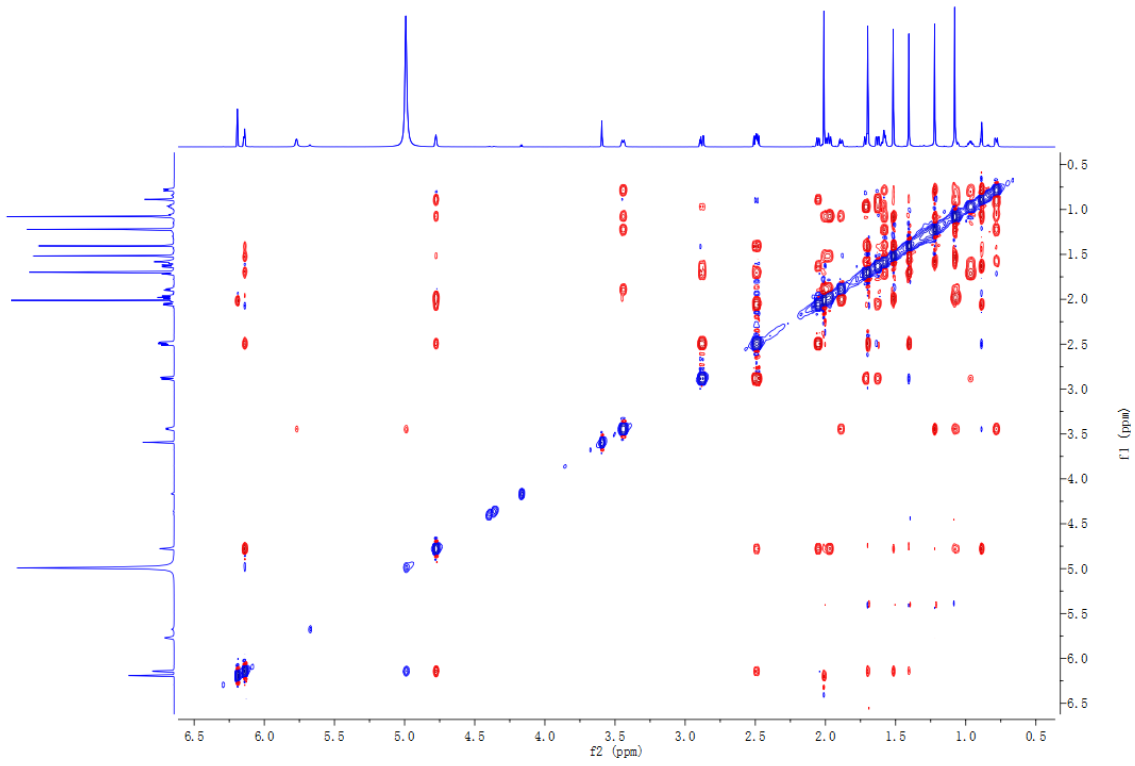
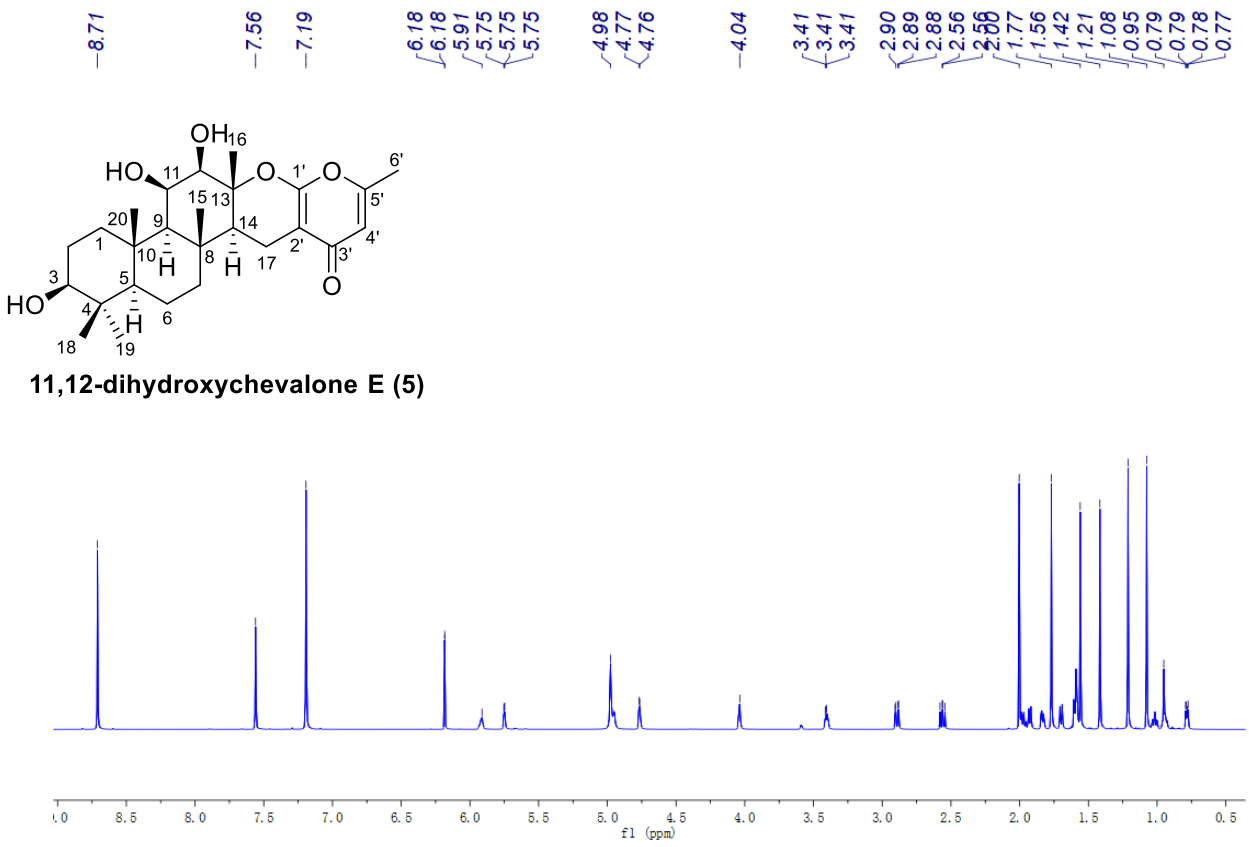


Figure S26. ROESY spectrum of 11-hydroxychevalone E (**4**)



11,12-dihydroxychevalone E (5)

Figure S27. ^{1}H NMR spectrum of 11,12-dihydroxychevalone E (**5**)

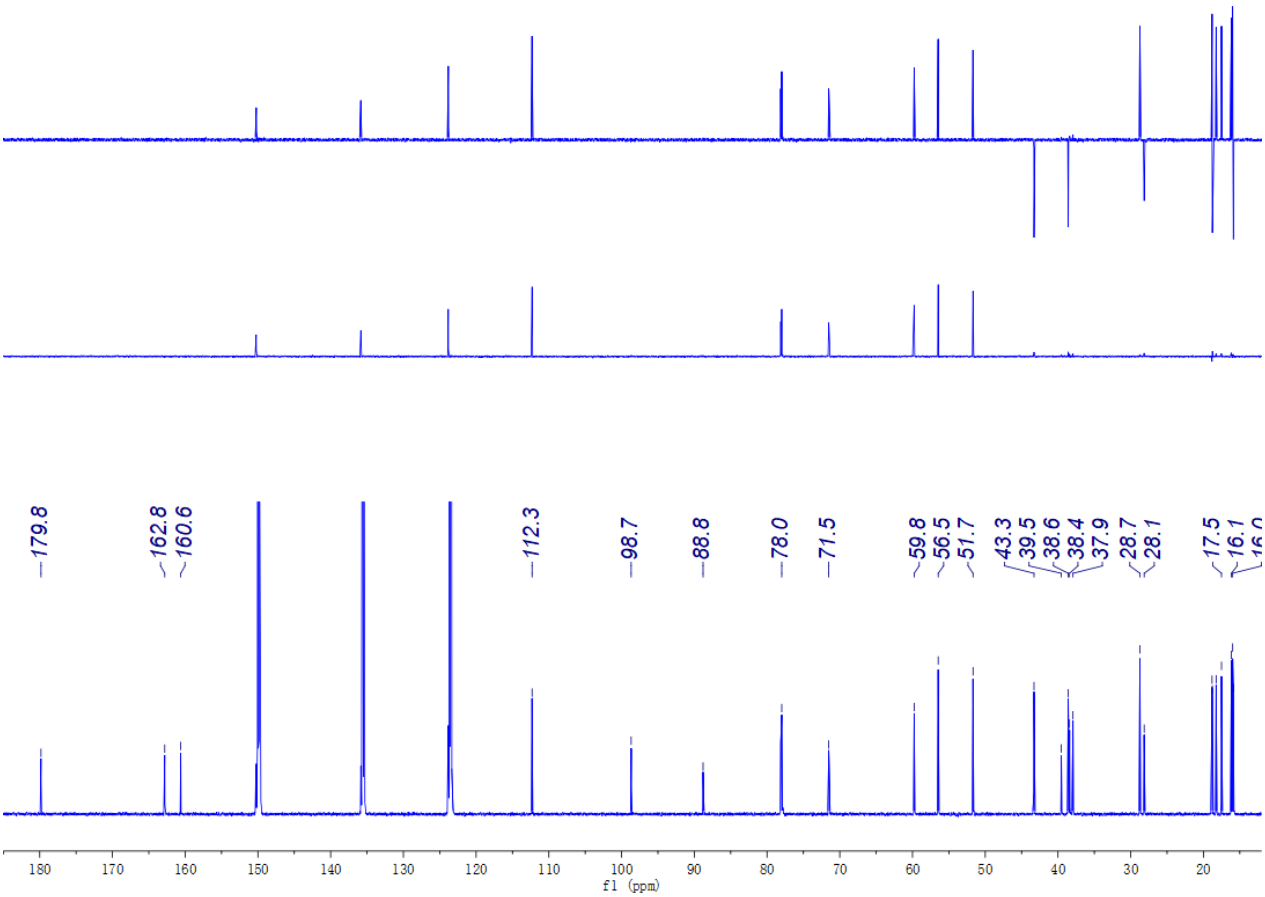
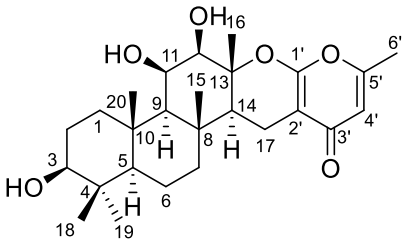


Figure S28. ^{13}C NMR spectrum of 11,12-dihydroxychevalone E (**5**)



11,12-dihydroxychevalone E (5)

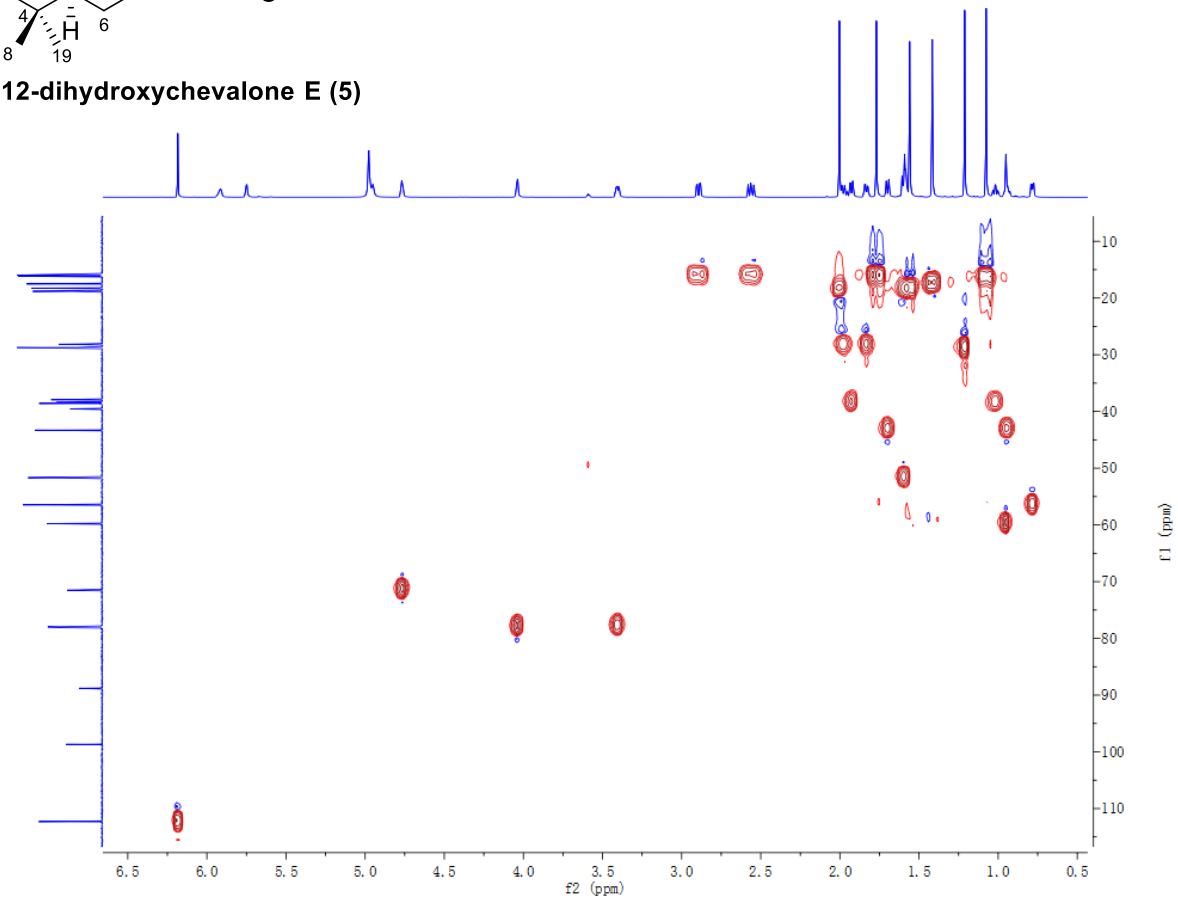


Figure S29. HSQC spectrum of 11,12-dihydroxychevalone E (**5**)

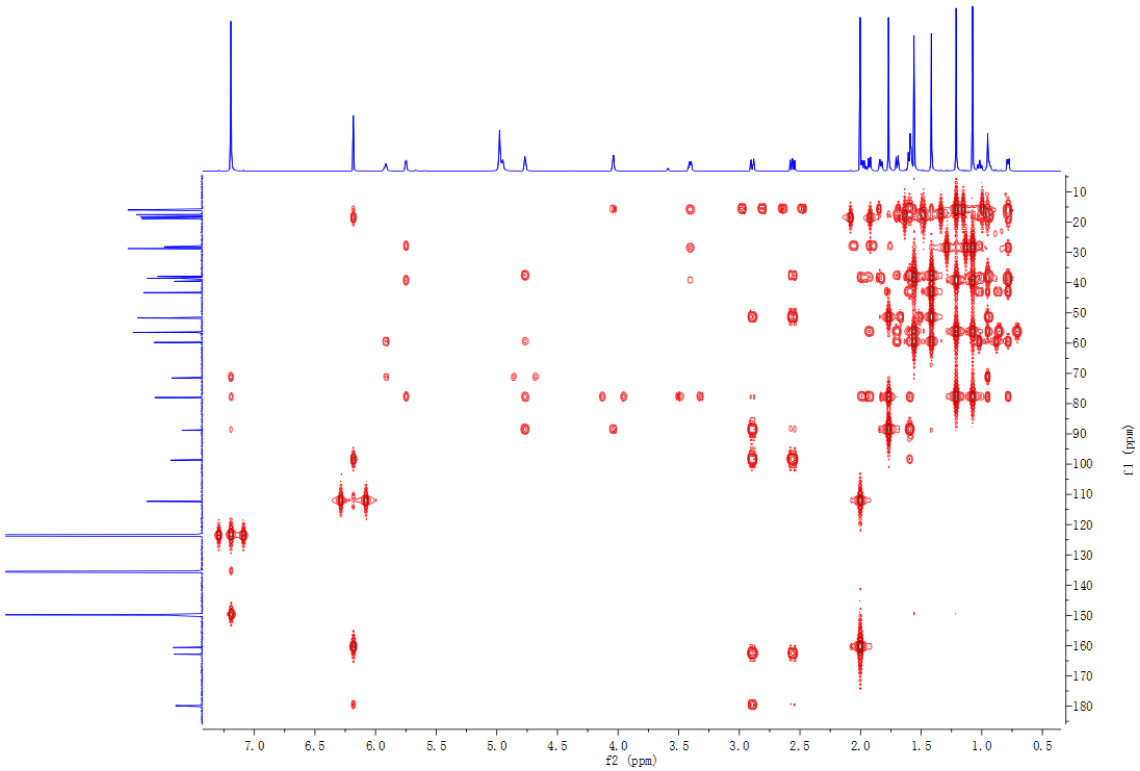


Figure S30. HMBC spectrum of 11,12-dihydroxychevalone E (**5**)

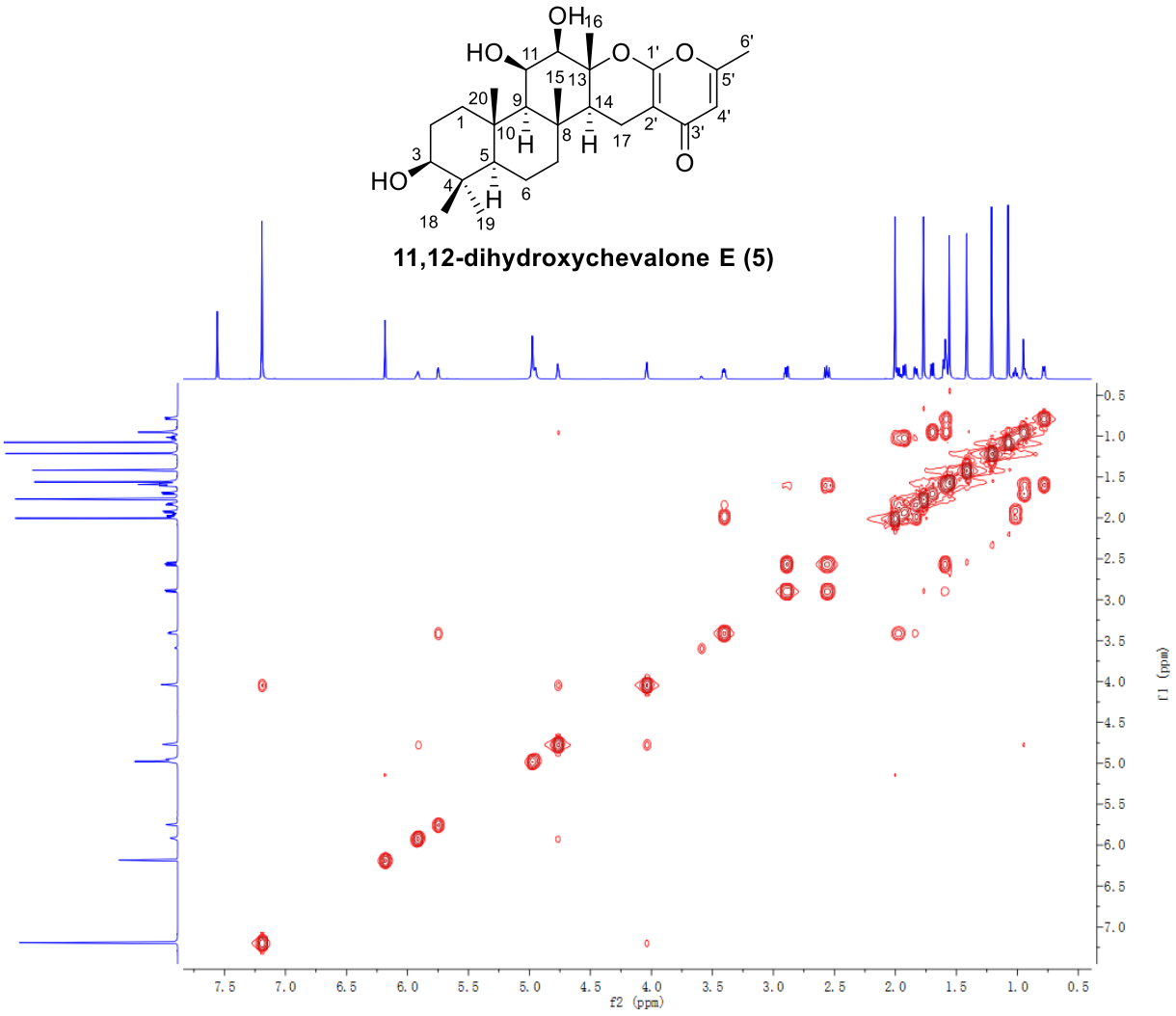


Figure S31. ^{1}H-^{1}H COSY spectrum of 11,12-dihydroxychevalone E (**5**)

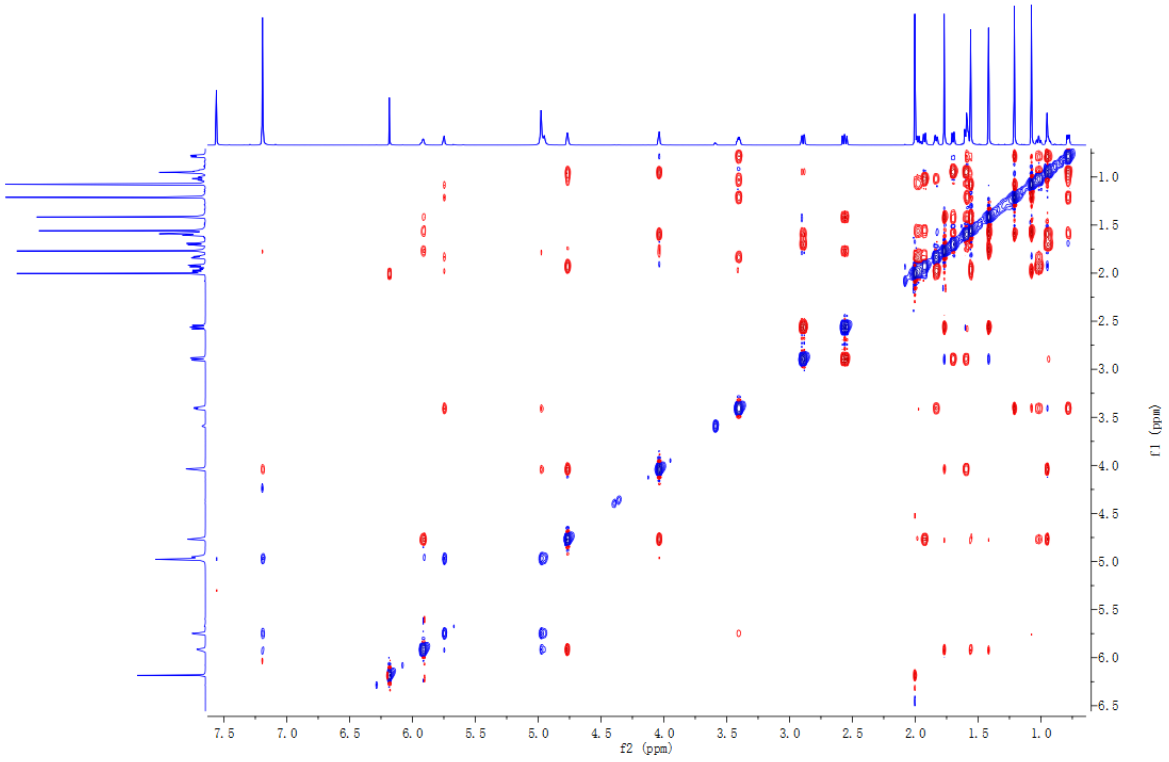


Figure S32. ROESY spectrum of 11,12-dihydroxychevalone E (**5**)

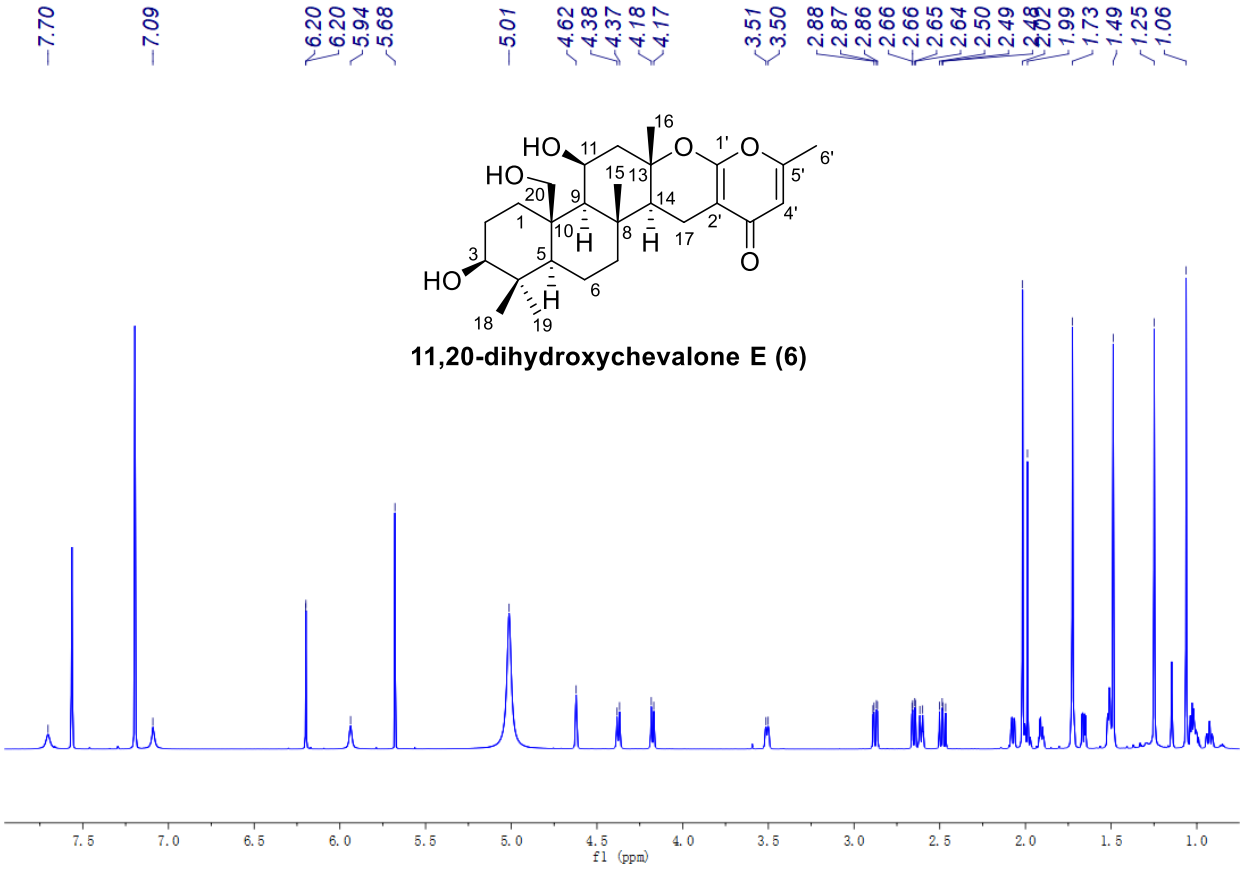


Figure S33. ^{1}H NMR spectrum of 11,20-dihydroxychevalone E (**6**)

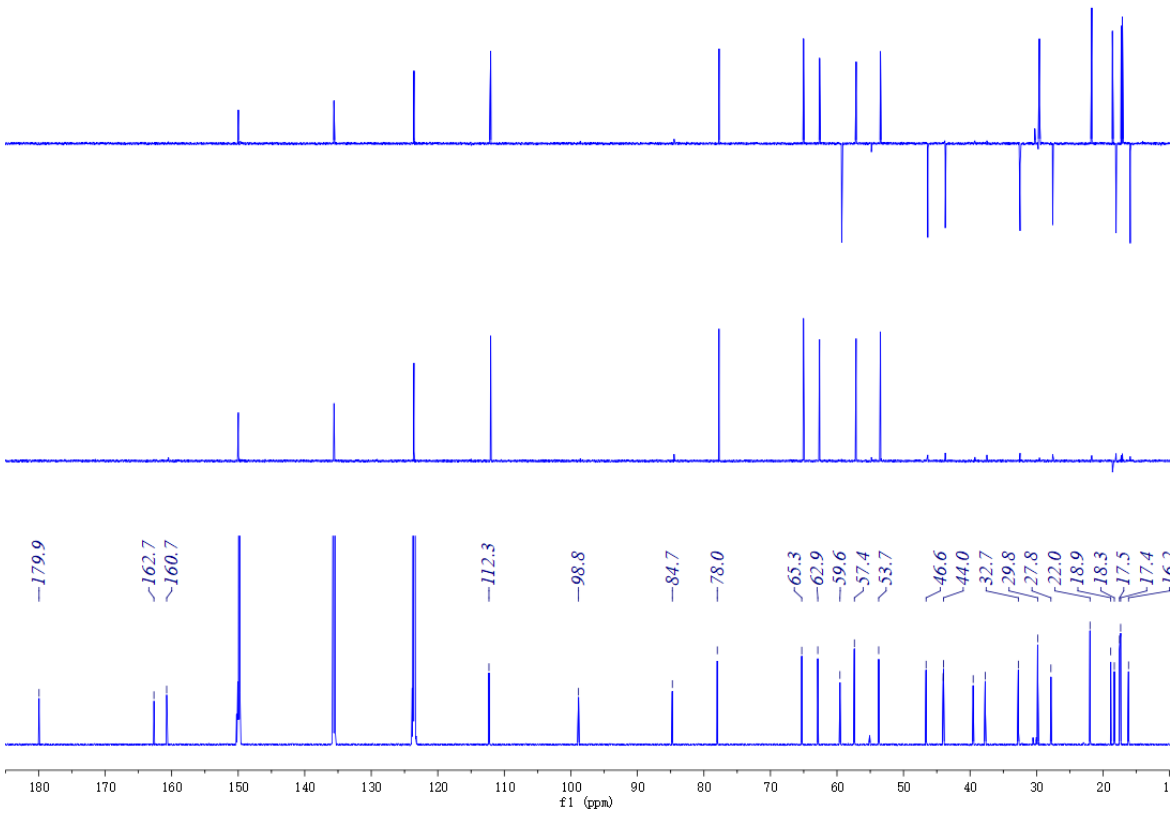
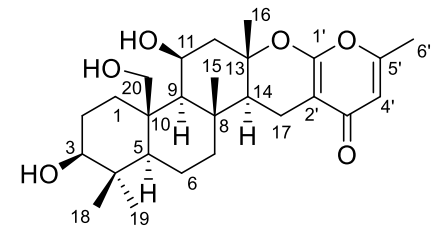


Figure S34. ^{13}C NMR spectrum of 11,20-dihydroxychevalone E (**6**)



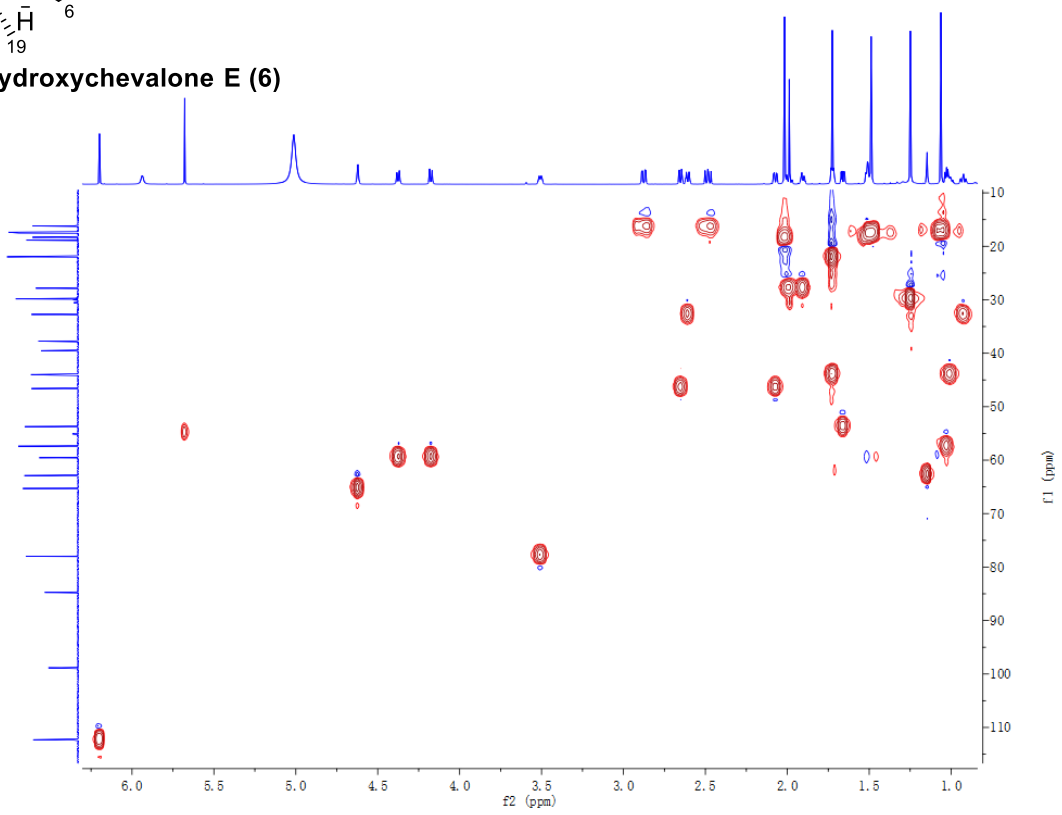


Figure S35. HSQC spectrum of 11,20-dihydroxychevalone E (**6**)

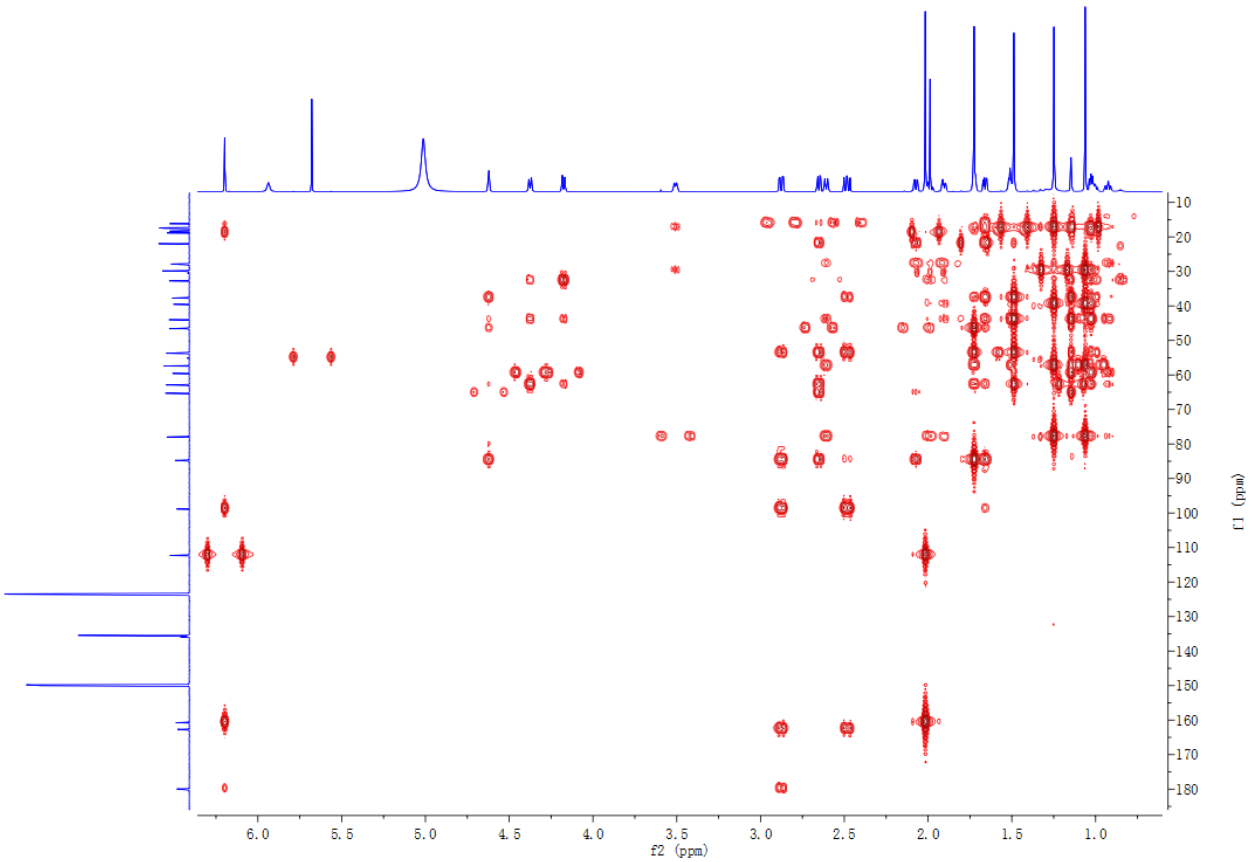


Figure S36. HMBC spectrum of 11,20-dihydroxychevalone E (**6**)

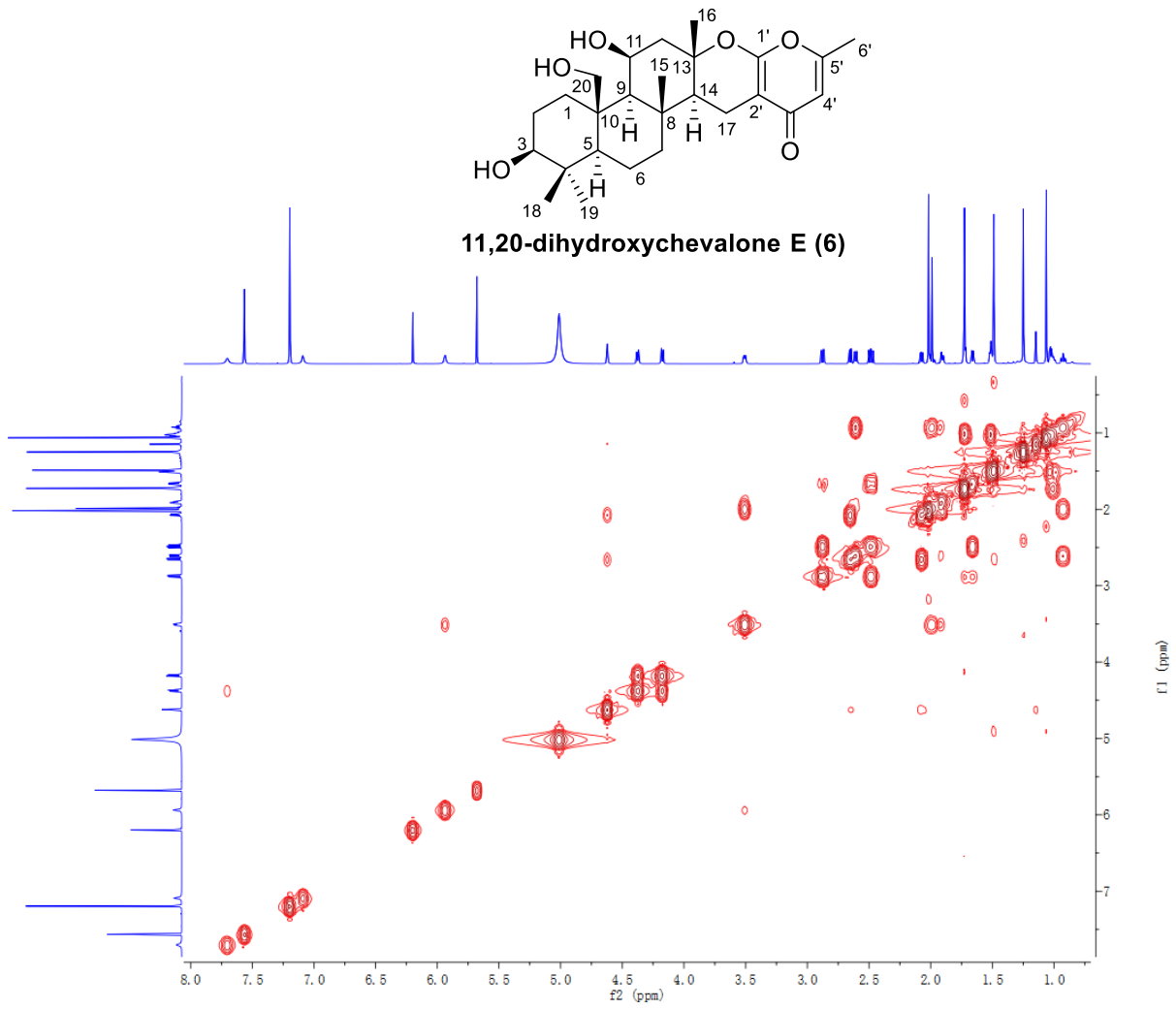


Figure S37. ^{1}H-^{1}H COSY spectrum of 11,20-dihydroxychevalone E (**6**)

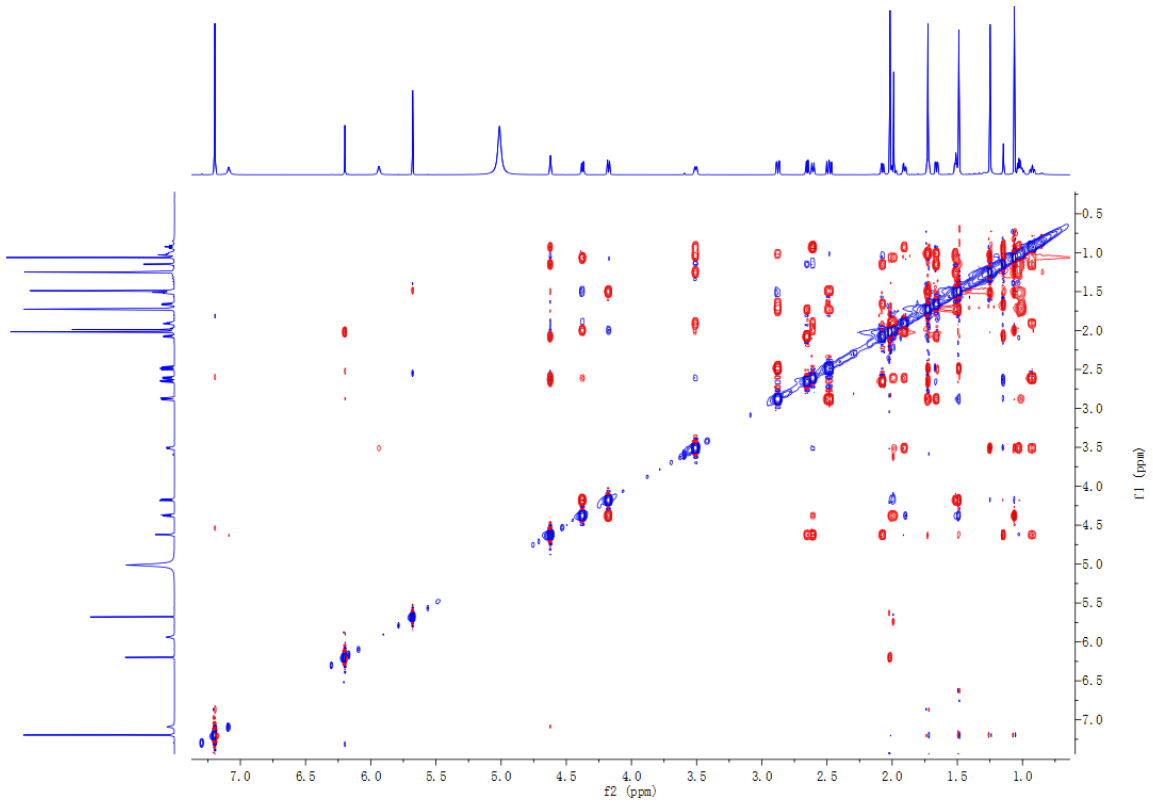


Figure S38. ROESY spectrum of 11,20-dihydroxychevalone E (**6**)

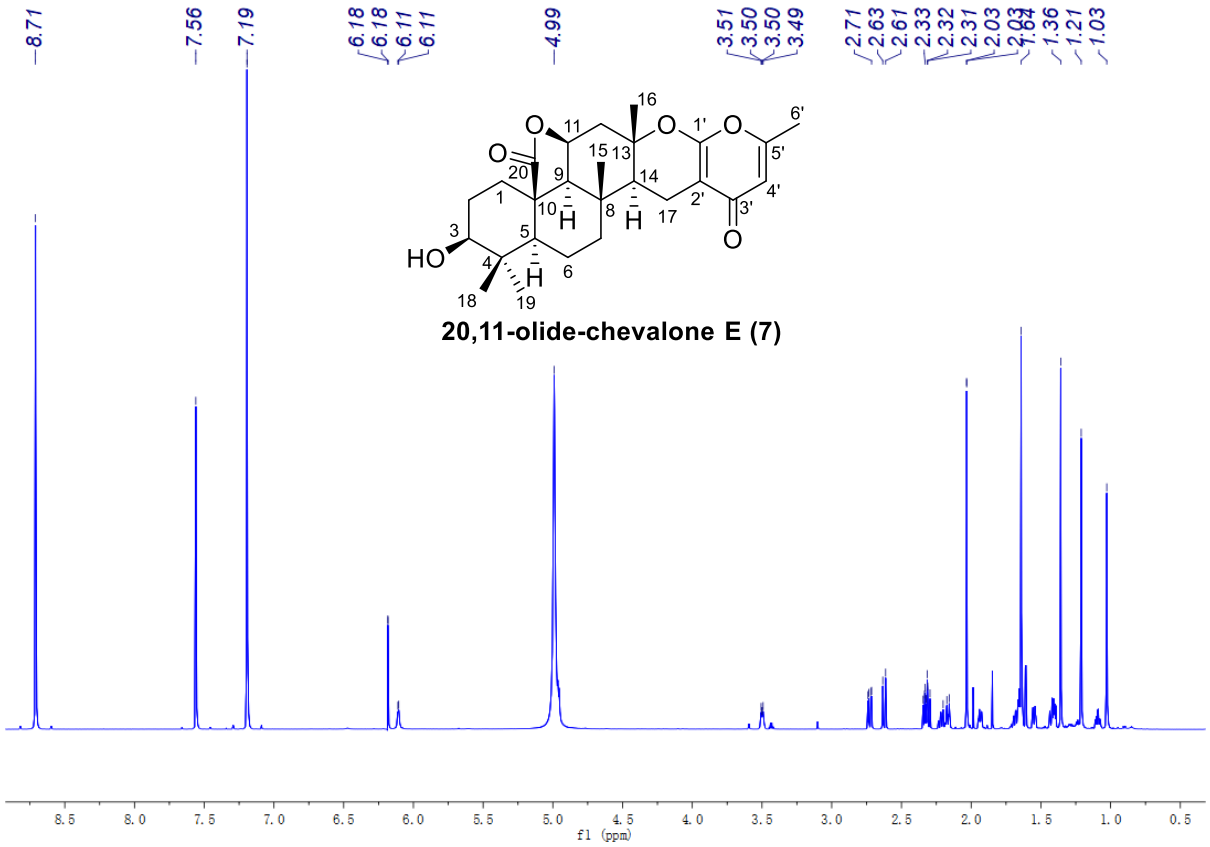


Figure S39. ^{1}H NMR spectrum of 20,11-olide-chevalone E (**7**)

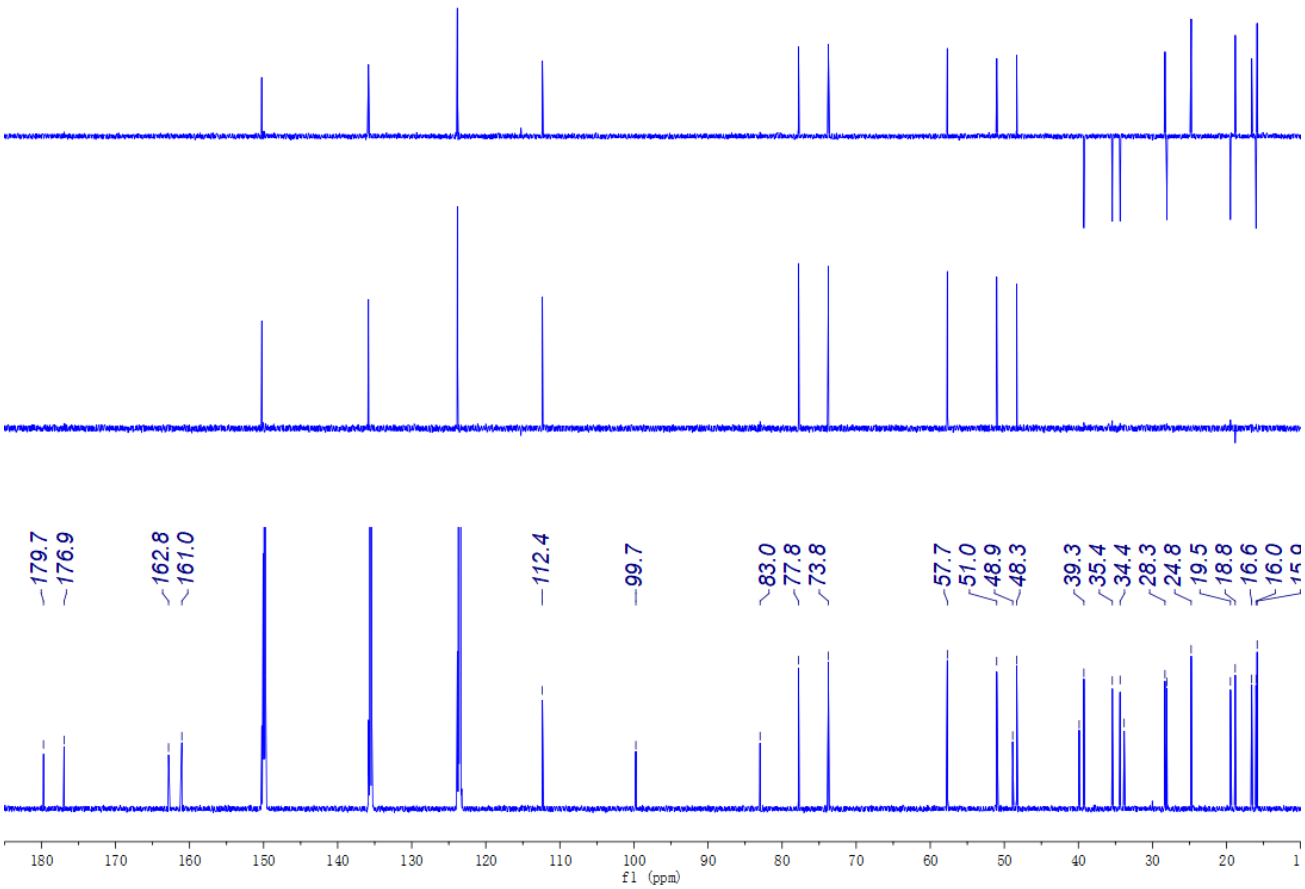


Figure S40. ^{13}C NMR spectrum of 20,11-olide-chevalone E (**7**)

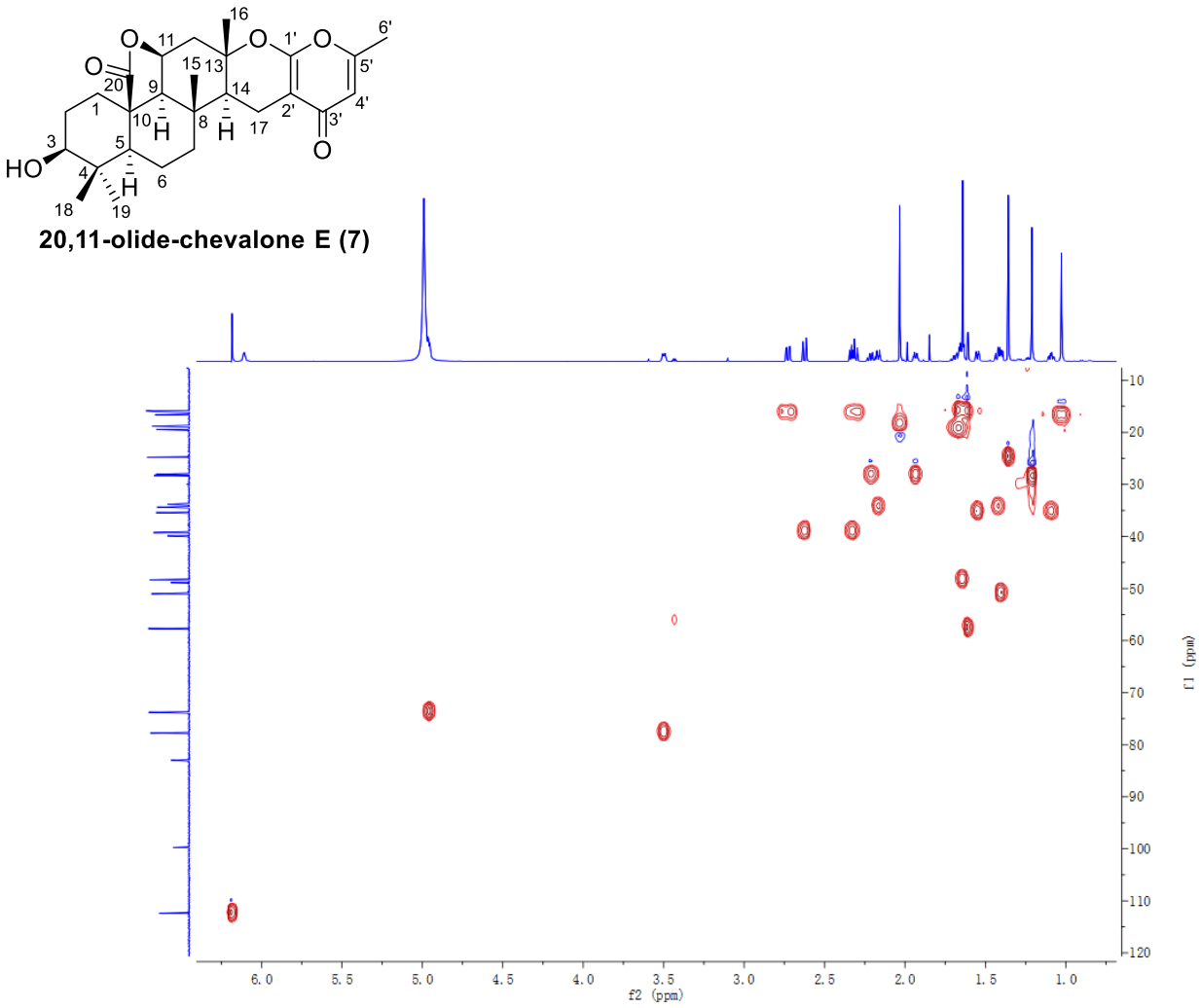


Figure S41. HSQC spectrum of 20,11-olide-chevalone E (**7**)

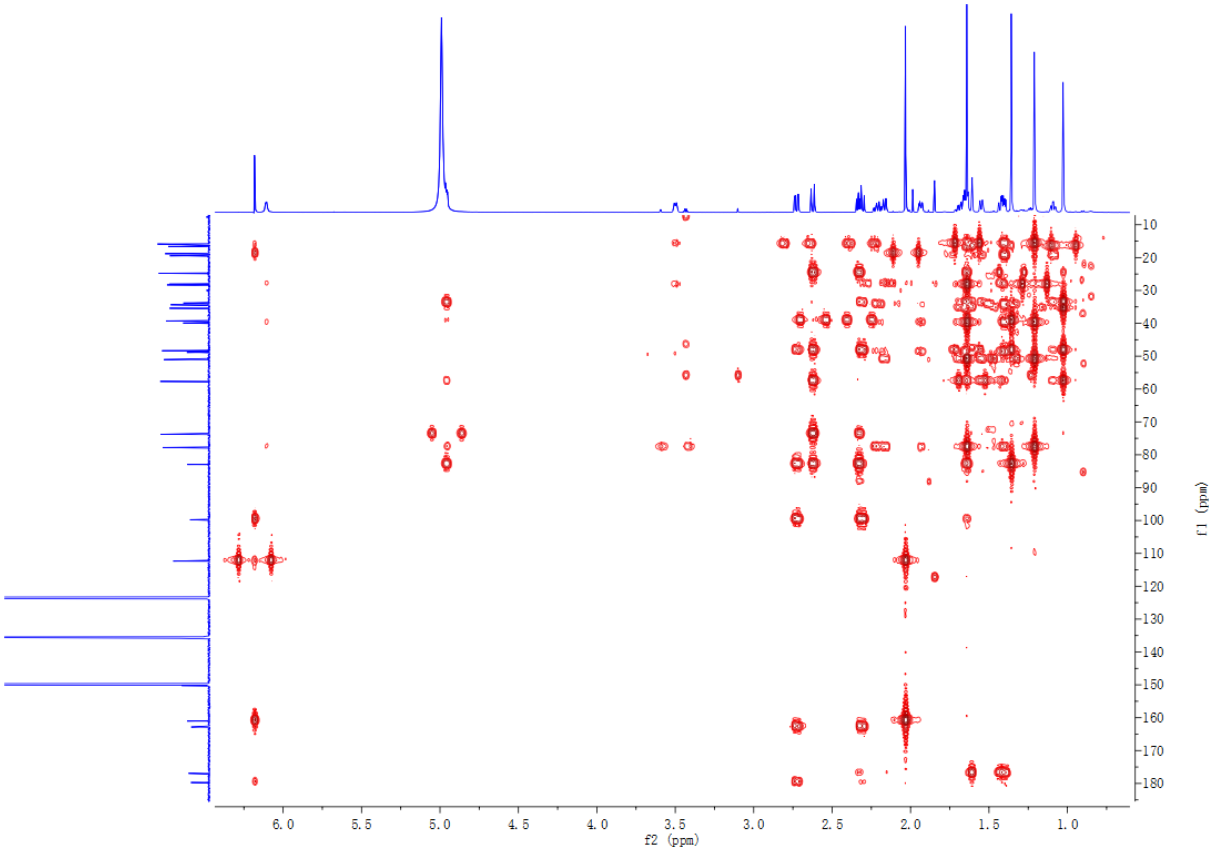


Figure S42. HMBC spectrum of 20,11-olide-chevalone E (**7**)

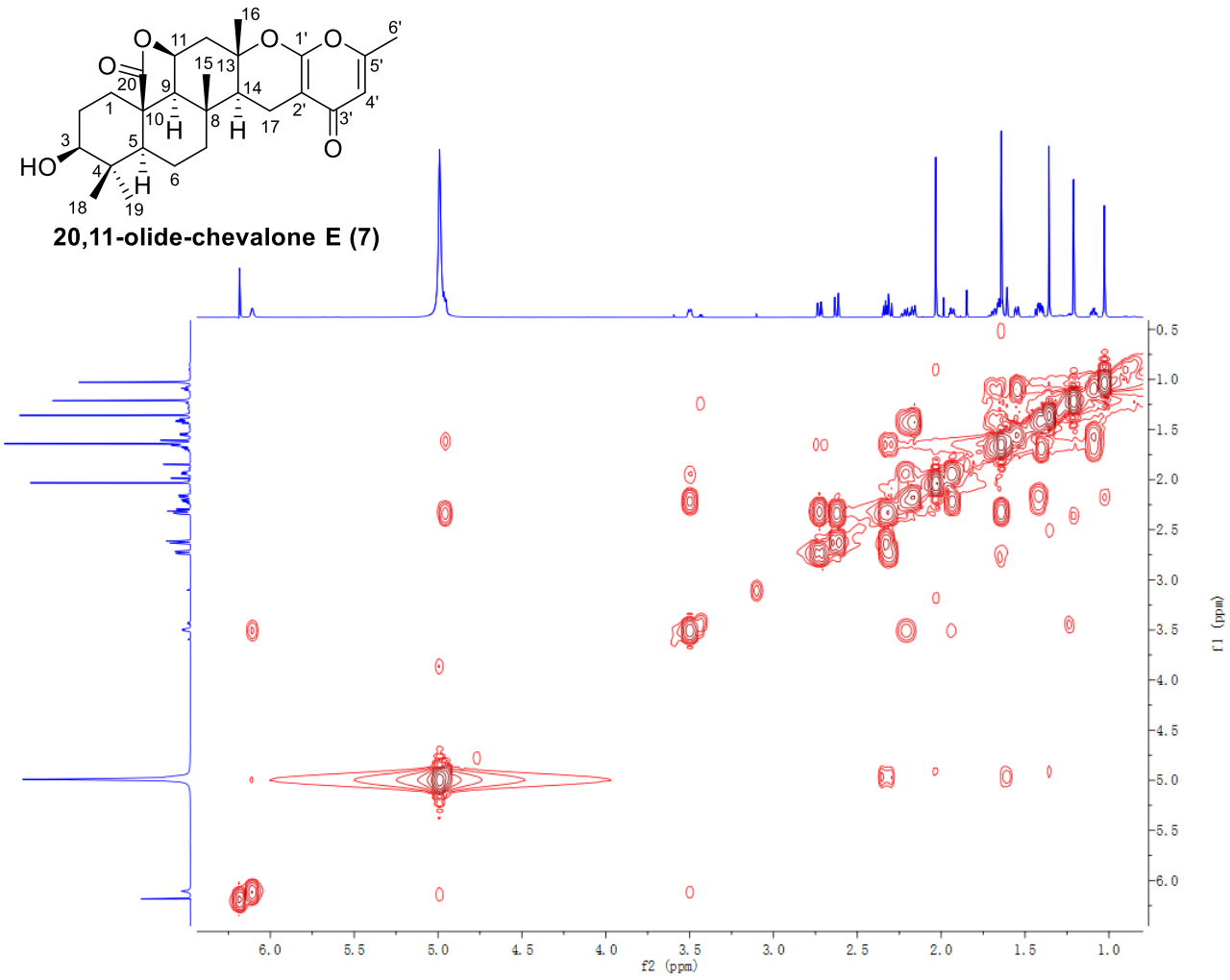


Figure S43. ^{1}H-^{1}H COSY spectrum of 20,11-olide-chevalone E (**7**)

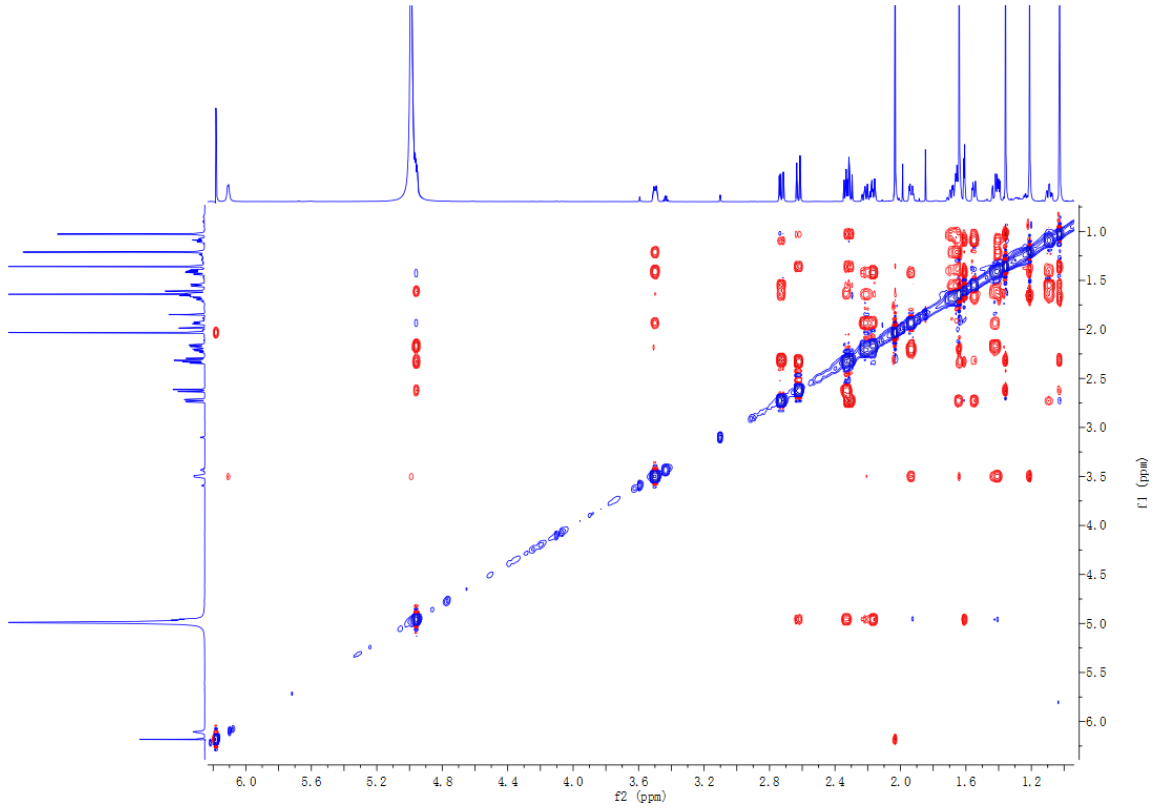


Figure S44. ROESY spectrum of 20,11-olide-chevalone E (**7**)

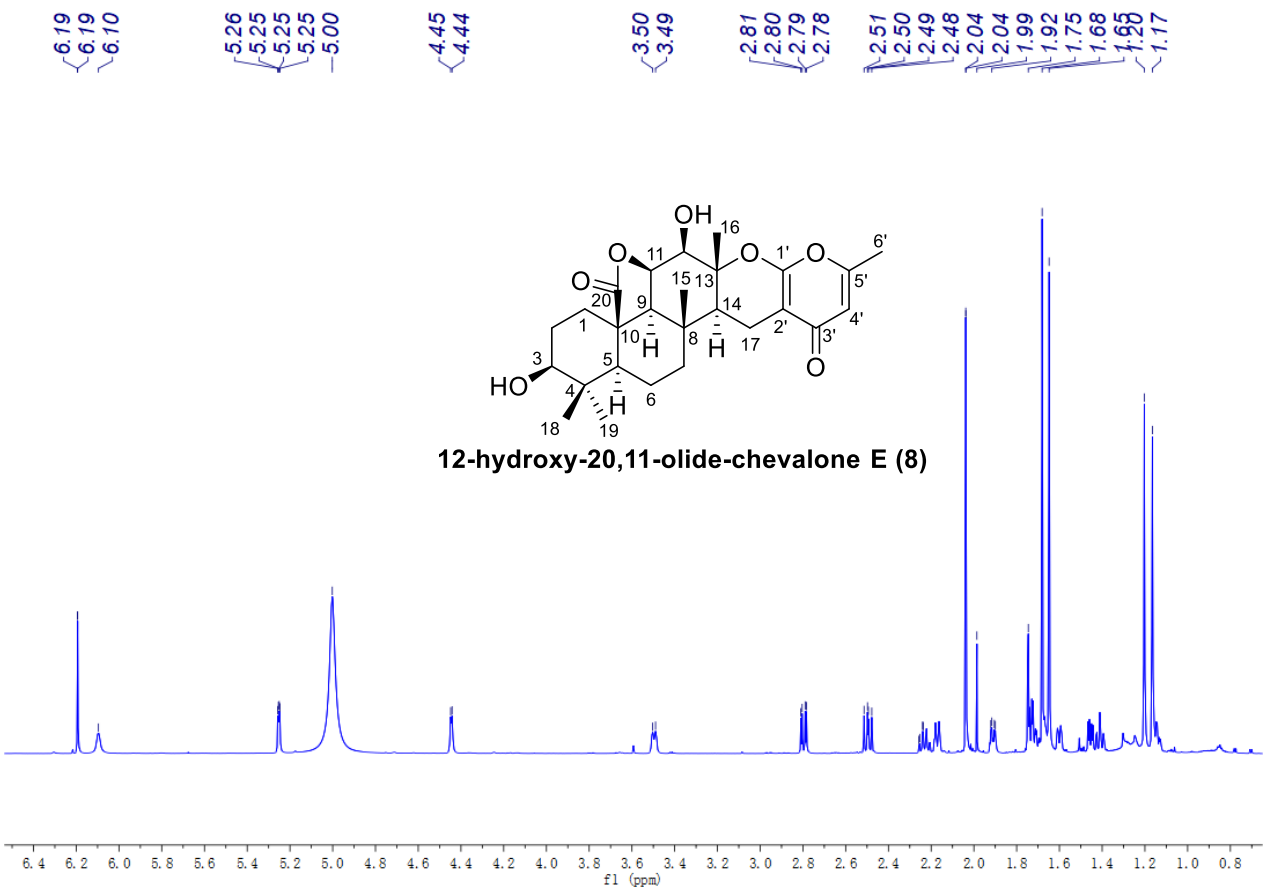


Figure S45. ^{1}H NMR spectrum of 12-hydroxy-20,11-olide-chevalone E (**8**)

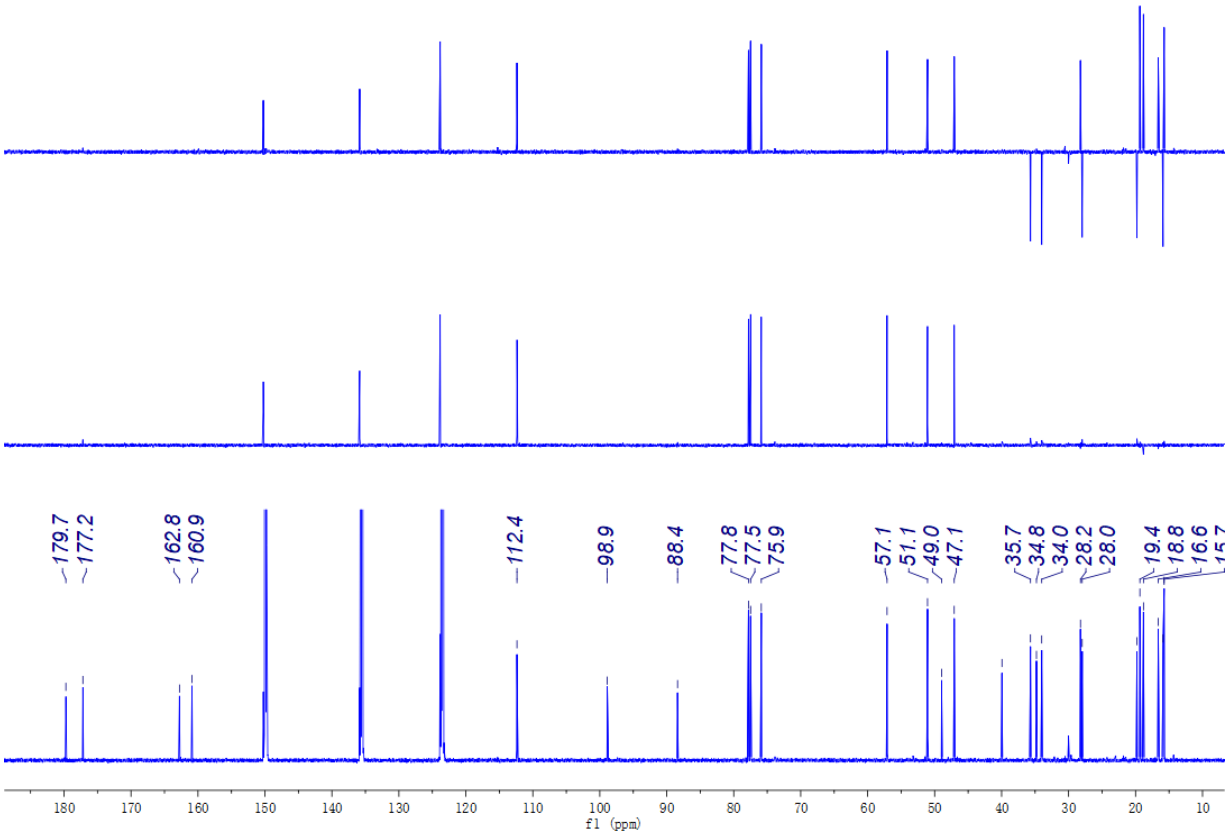
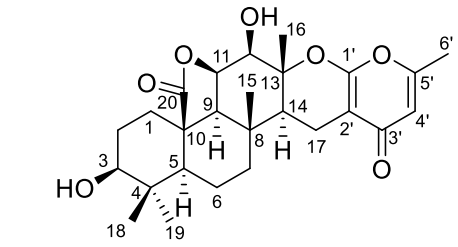


Figure S46. ^{13}C NMR spectrum of 12-hydroxy-20,11-olide-chevalone E (**8**)



12-hydroxy-20,11-olide-chevalone E (8)

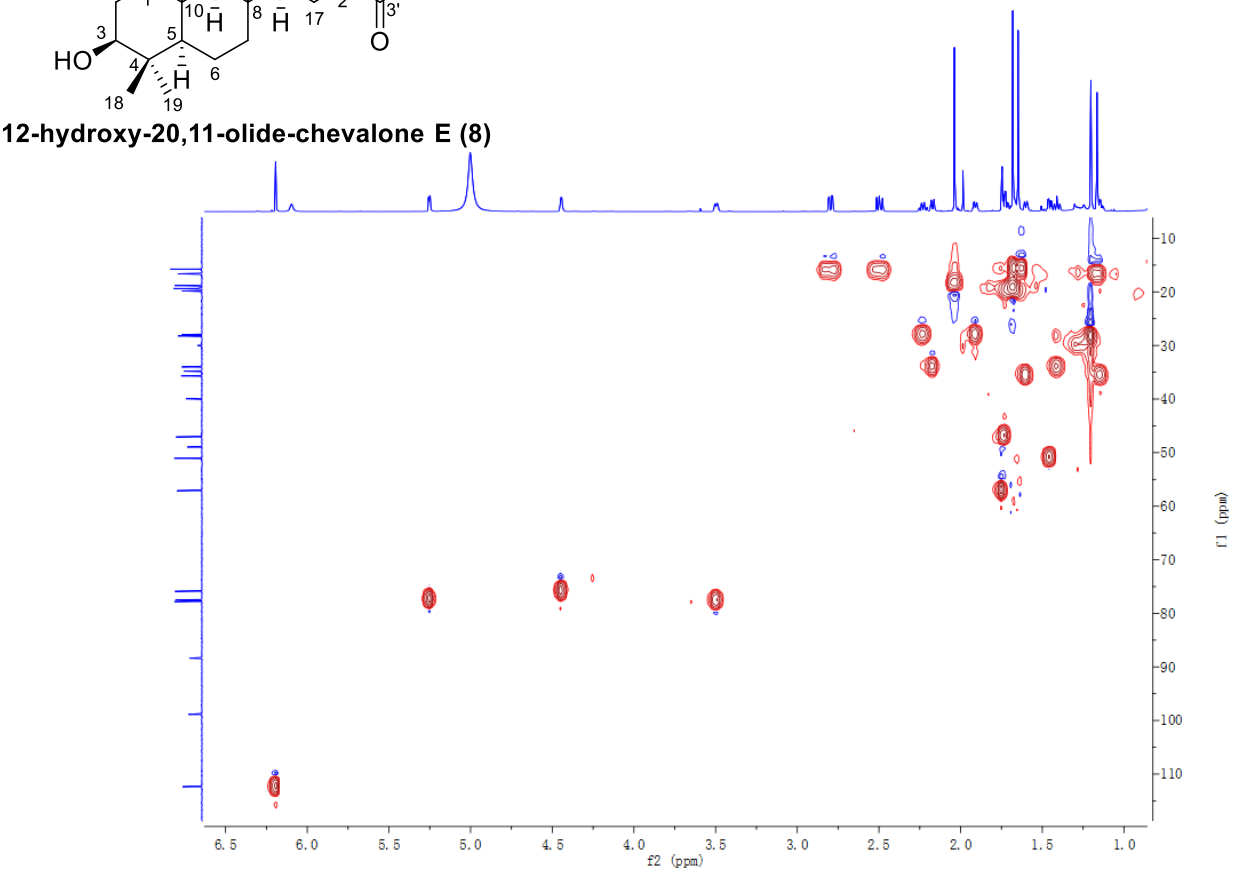


Figure S47. HSQC spectrum of 12-hydroxy-20,11-olide-chevalone E (**8**)

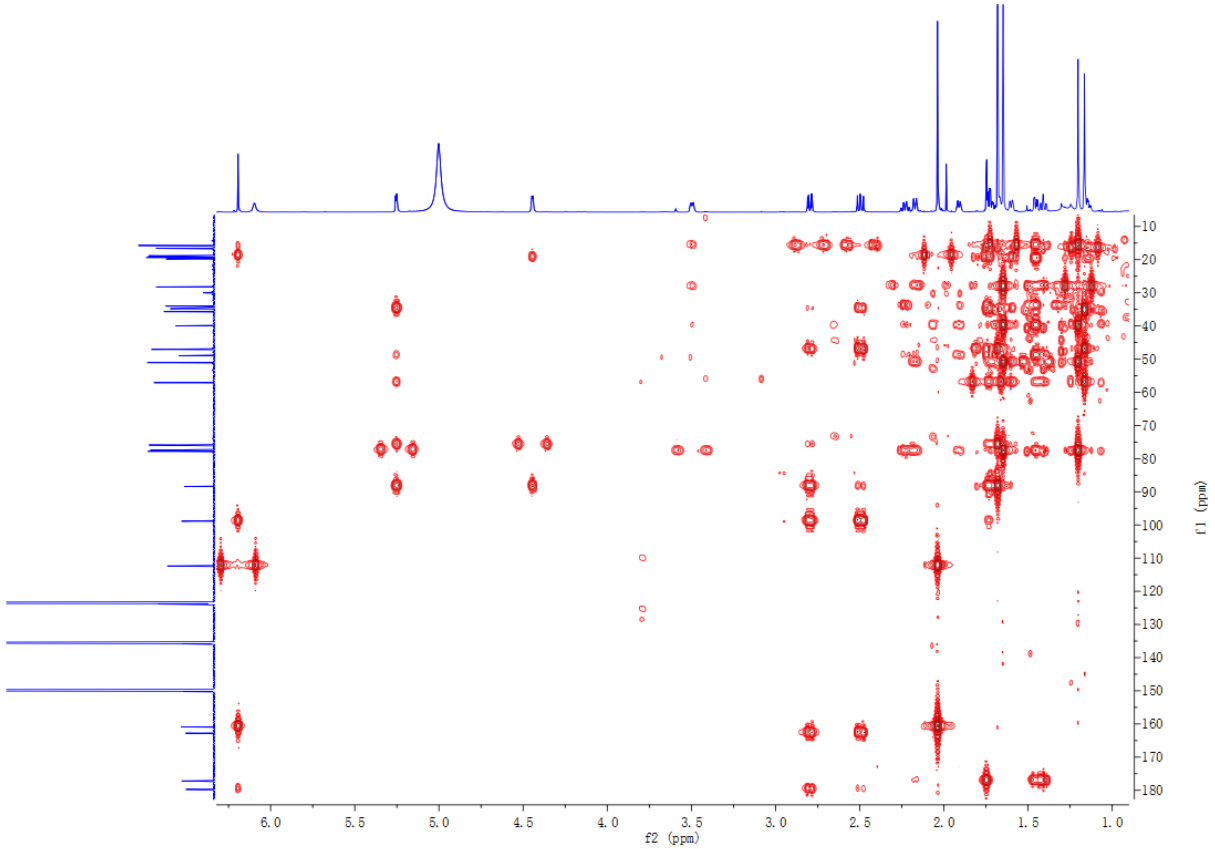


Figure S48. HMBC spectrum of 12-hydroxy-20,11-olide-chevalone E (**8**)

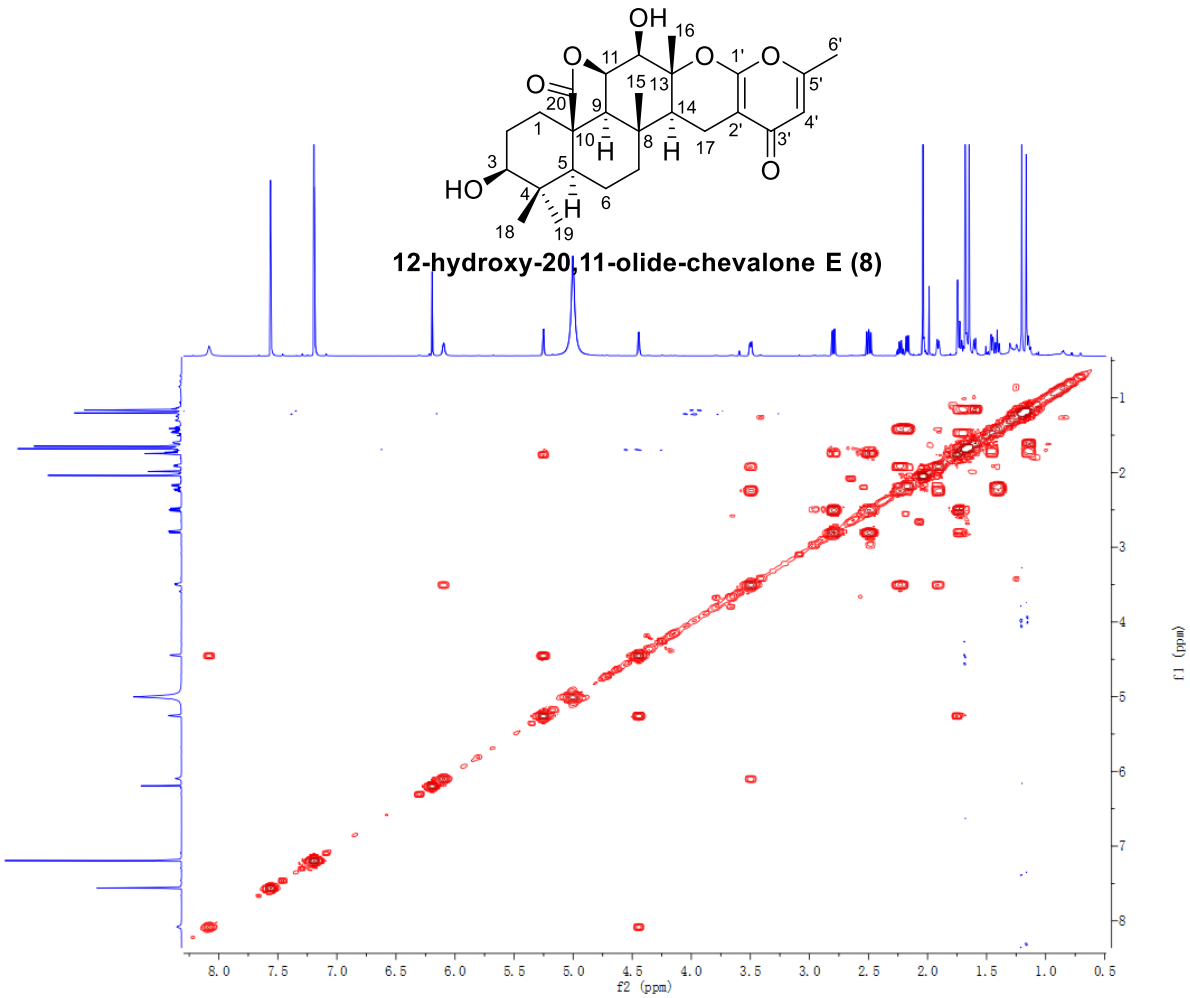


Figure S49. ^{1}H-^{1}H COSY spectrum of 12-hydroxy-20,11-olide-chevalone E (**8**)

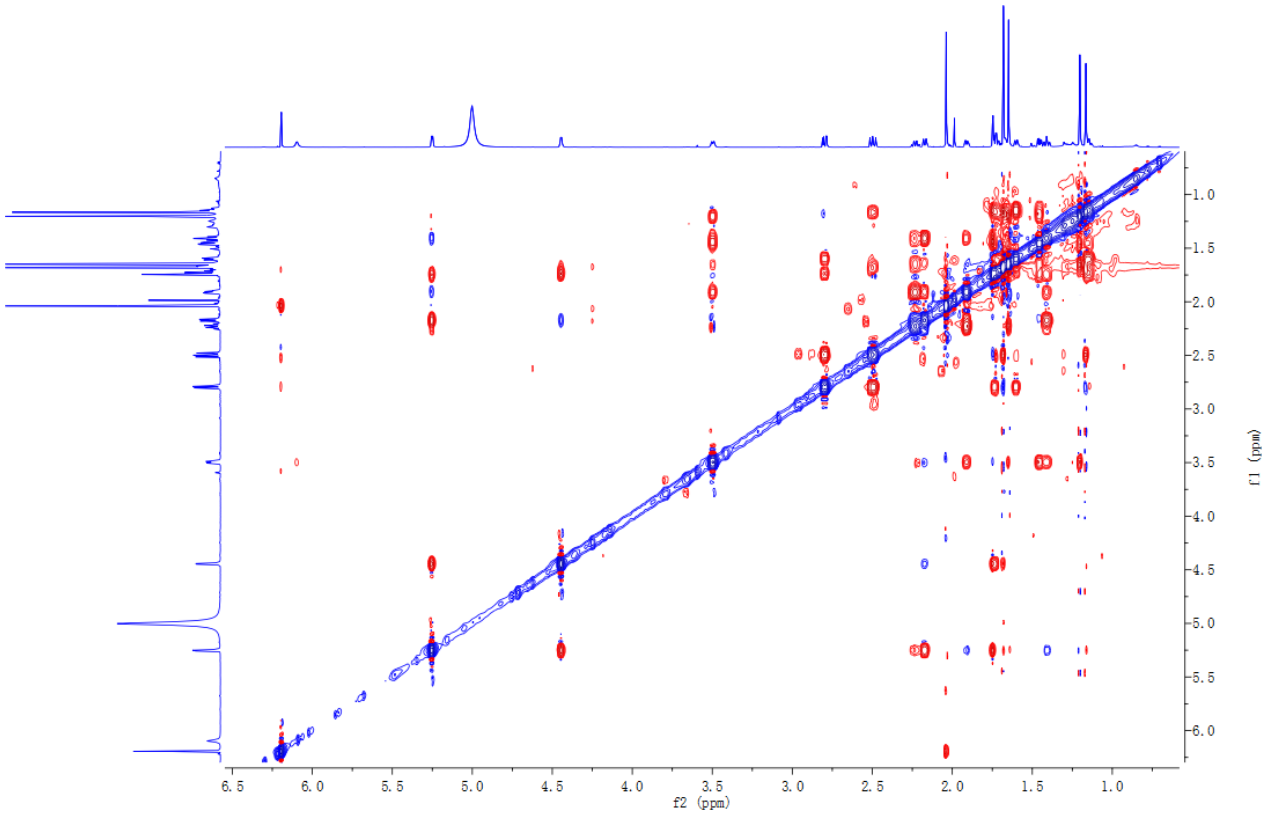


Figure S50. ^{1}H-^{1}H COSY spectrum of 12-hydroxy-20,11-olide-chevalone E (**8**)

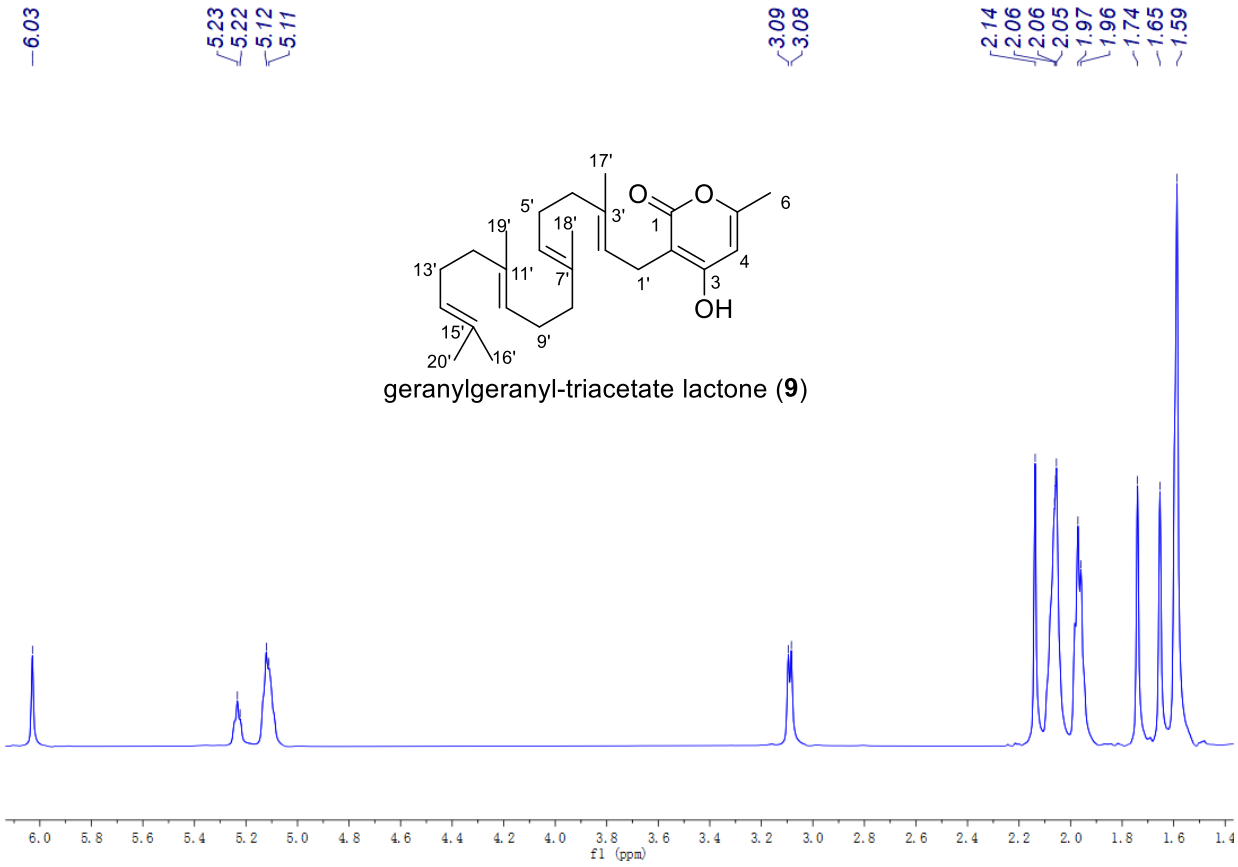


Figure S51. ^{1}H NMR spectrum of geranylgeranyl-triacetate lactone (**9**)

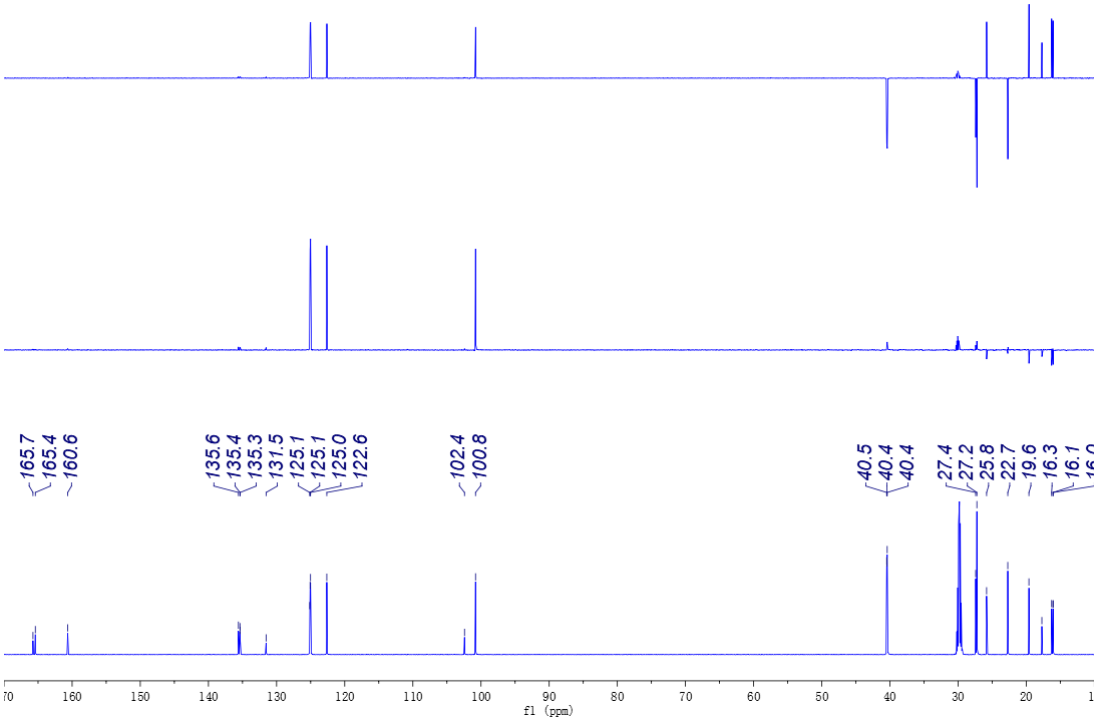
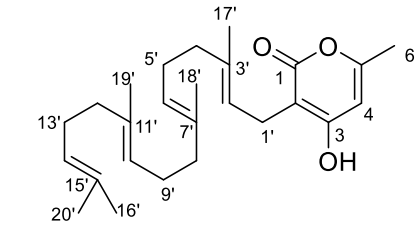


Figure S52. ^{13}C NMR spectrum of geranylgeranyl-triacetate lactone (**9**)



geranylgeranyl-triacetate lactone (**9**)

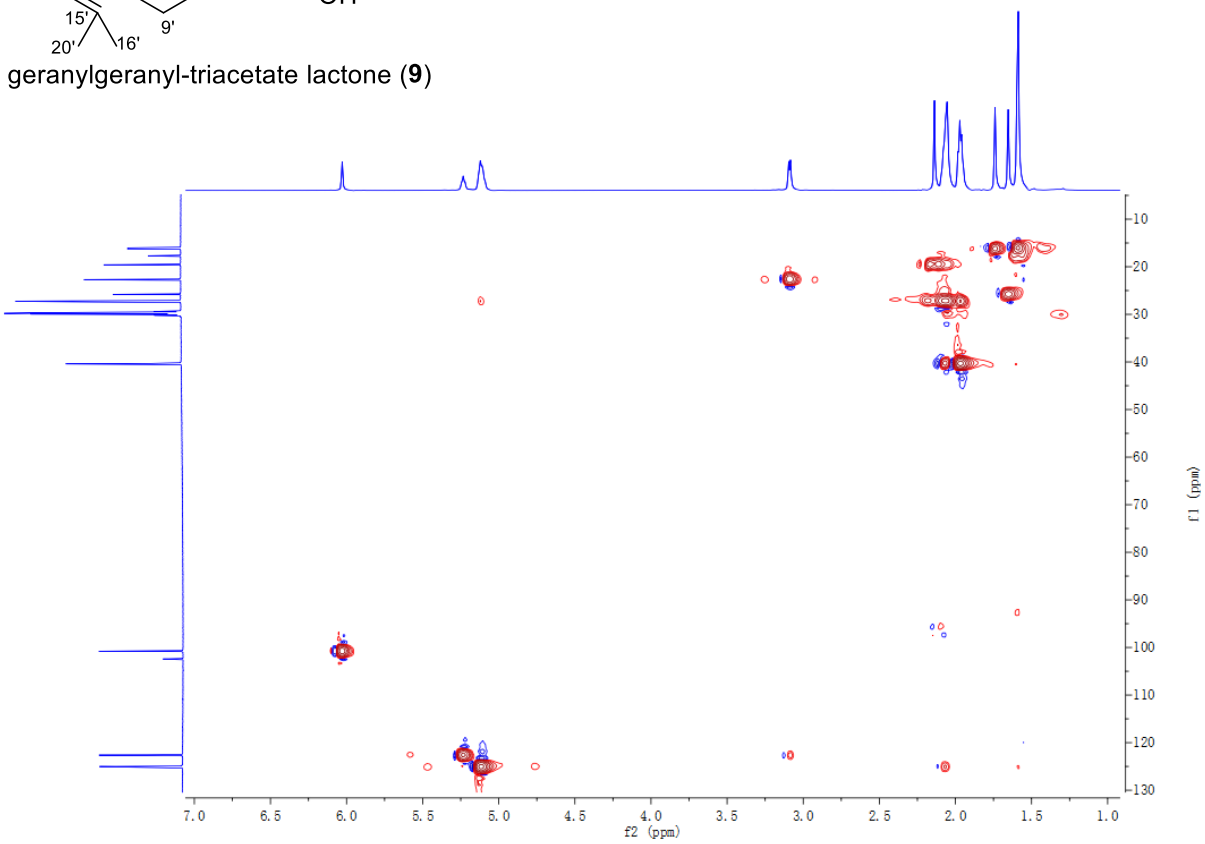


Figure S53. HSQC spectrum of geranylgeranyl-triacetate lactone (**9**)

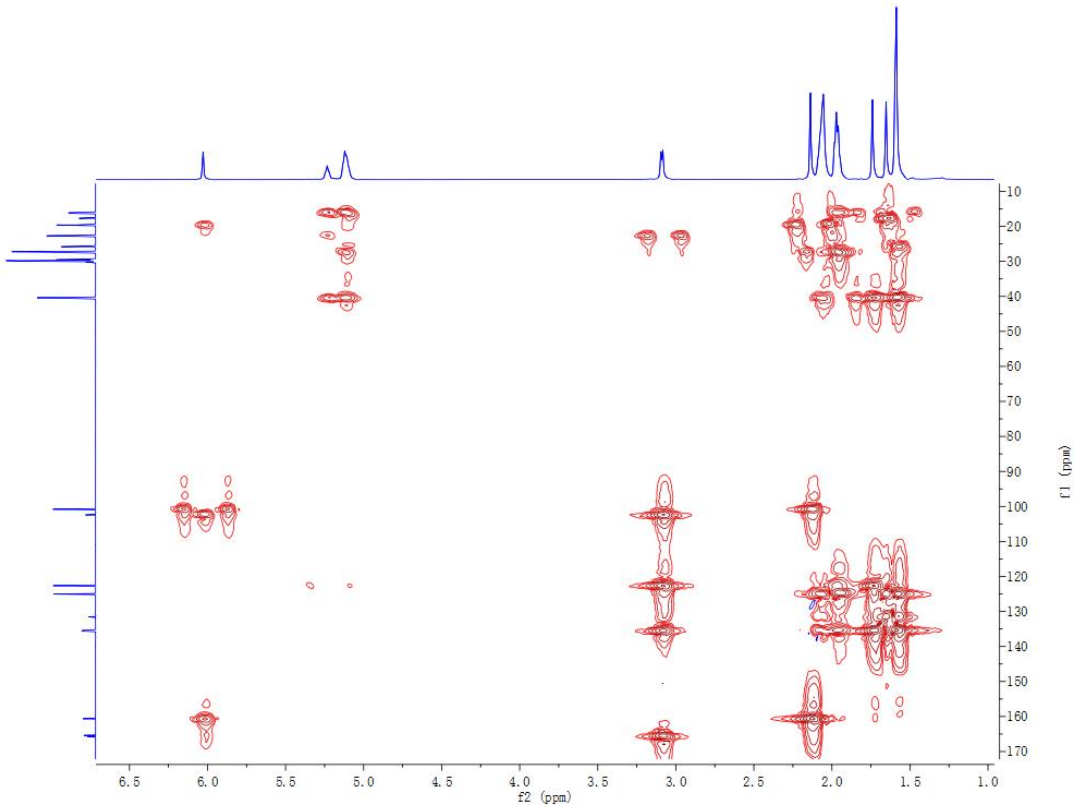


Figure S54. HMBC spectrum of geranylgeranyl-triacetate lactone (**9**)

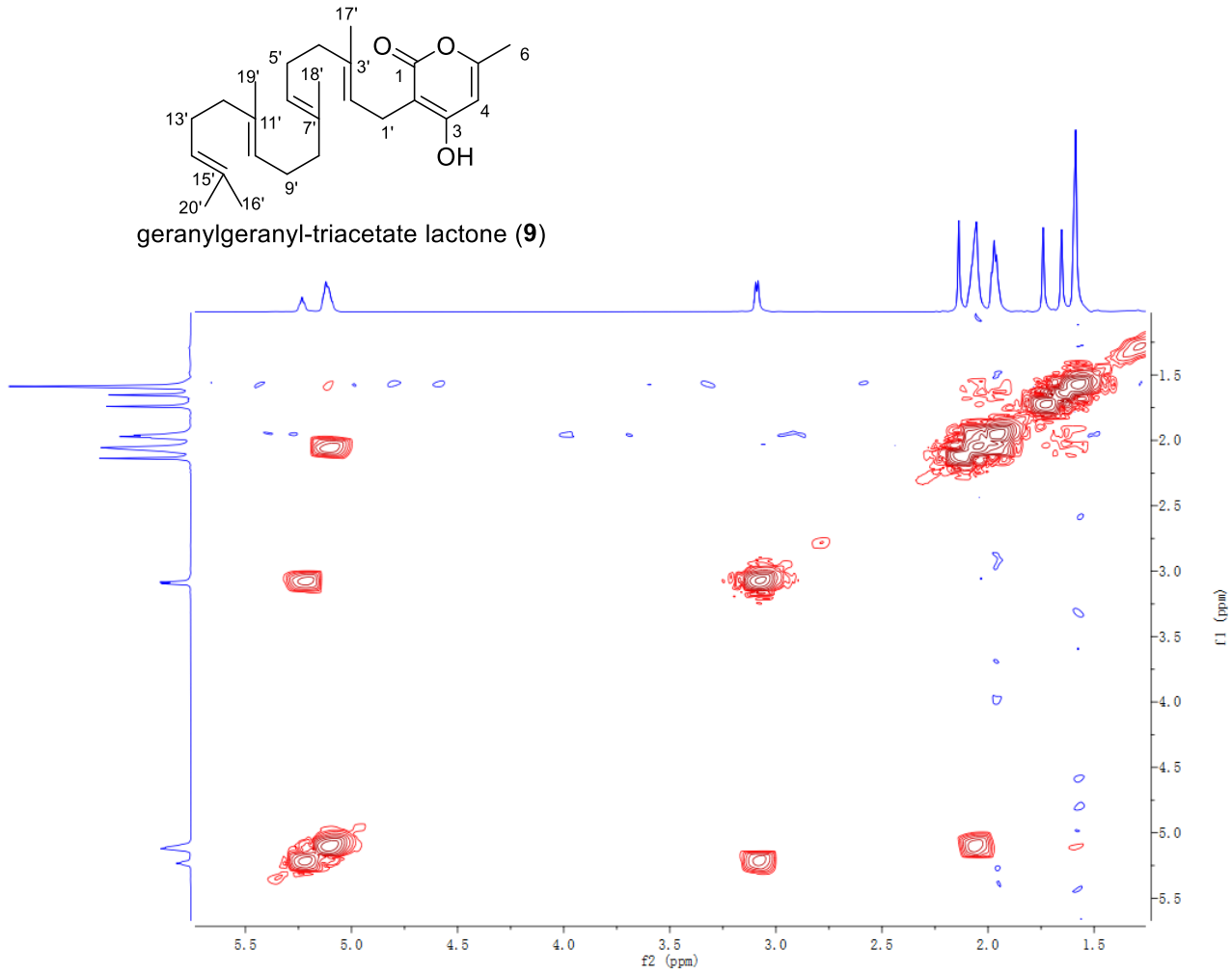


Figure S55. ^{1}H-^{1}H COSY spectrum of geranylgeranyl-triacetate lactone (**9**)

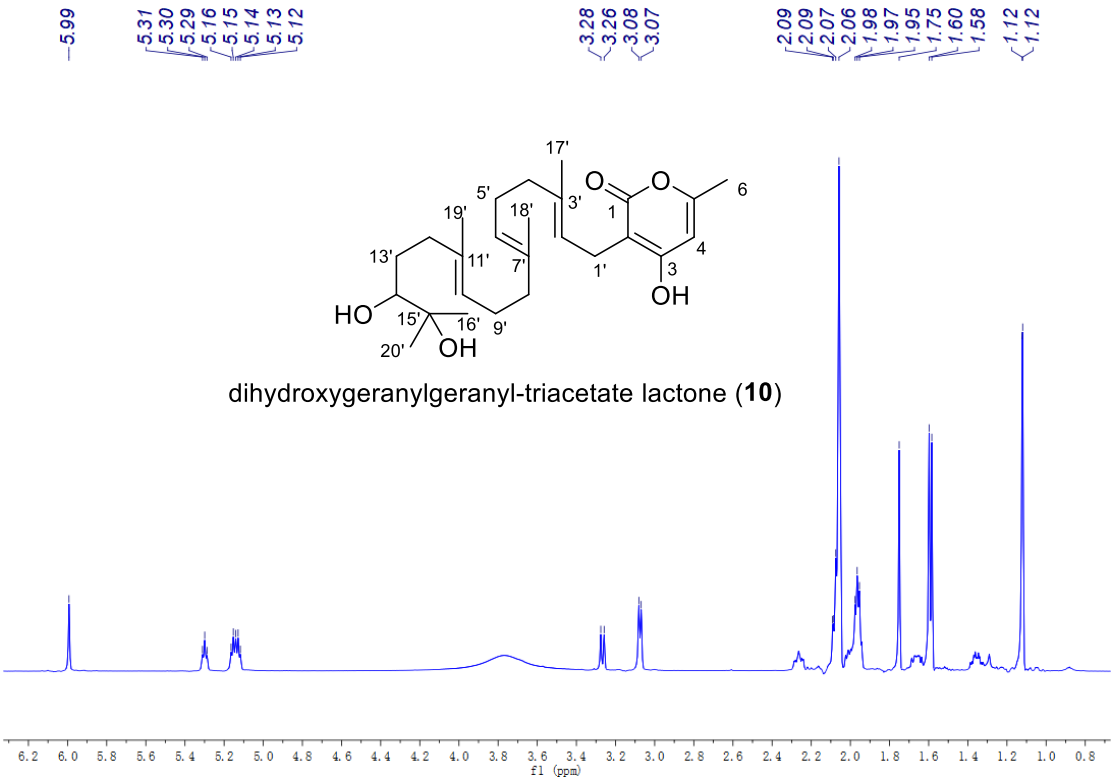


Figure S56. ^{1}H NMR spectrum of dihydroxygeranylgeranyl-triacetate lactone (**10**)

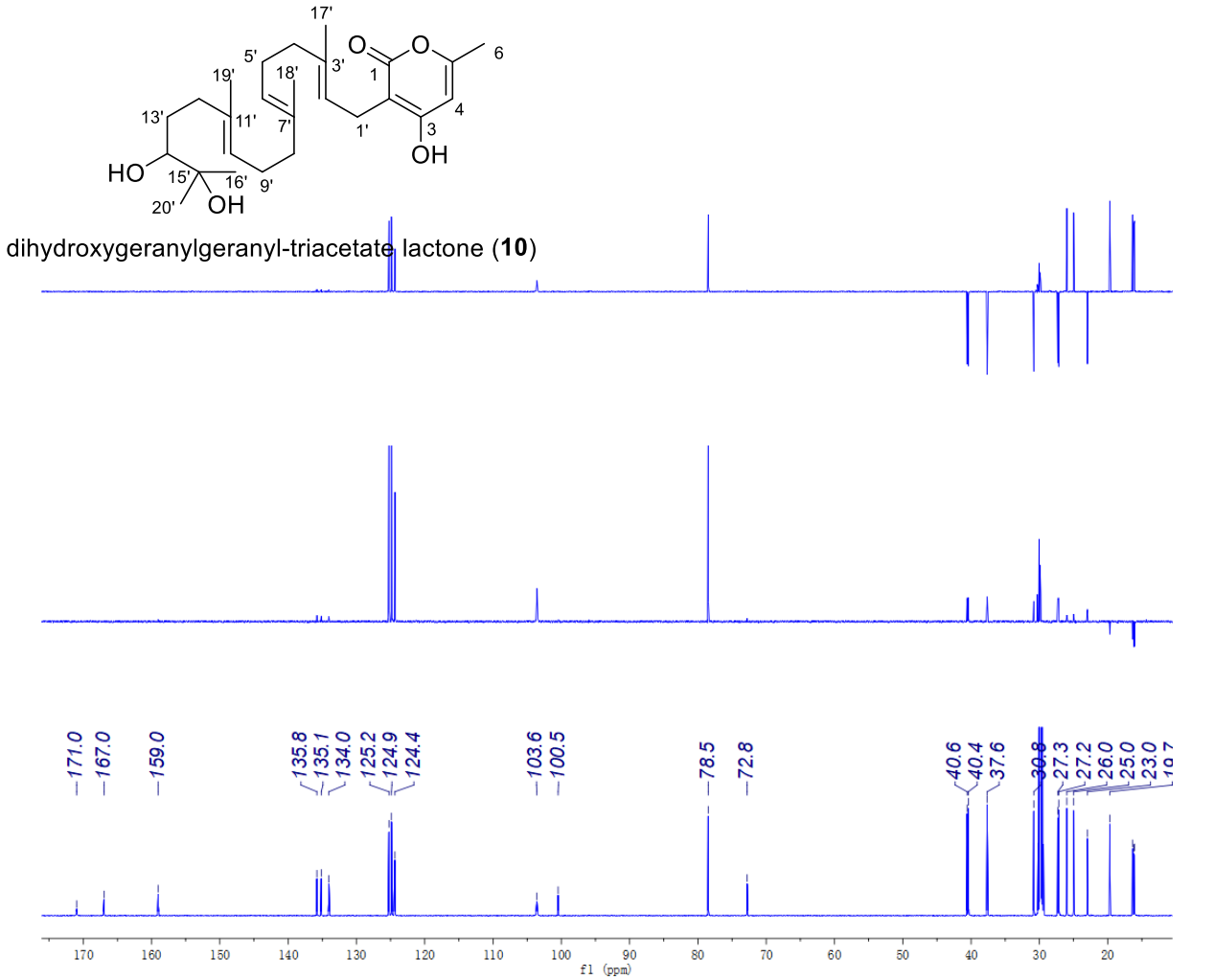


Figure S57. ^{13}C NMR spectrum of dihydroxygeranylgeranyl-triacetate lactone (**10**)

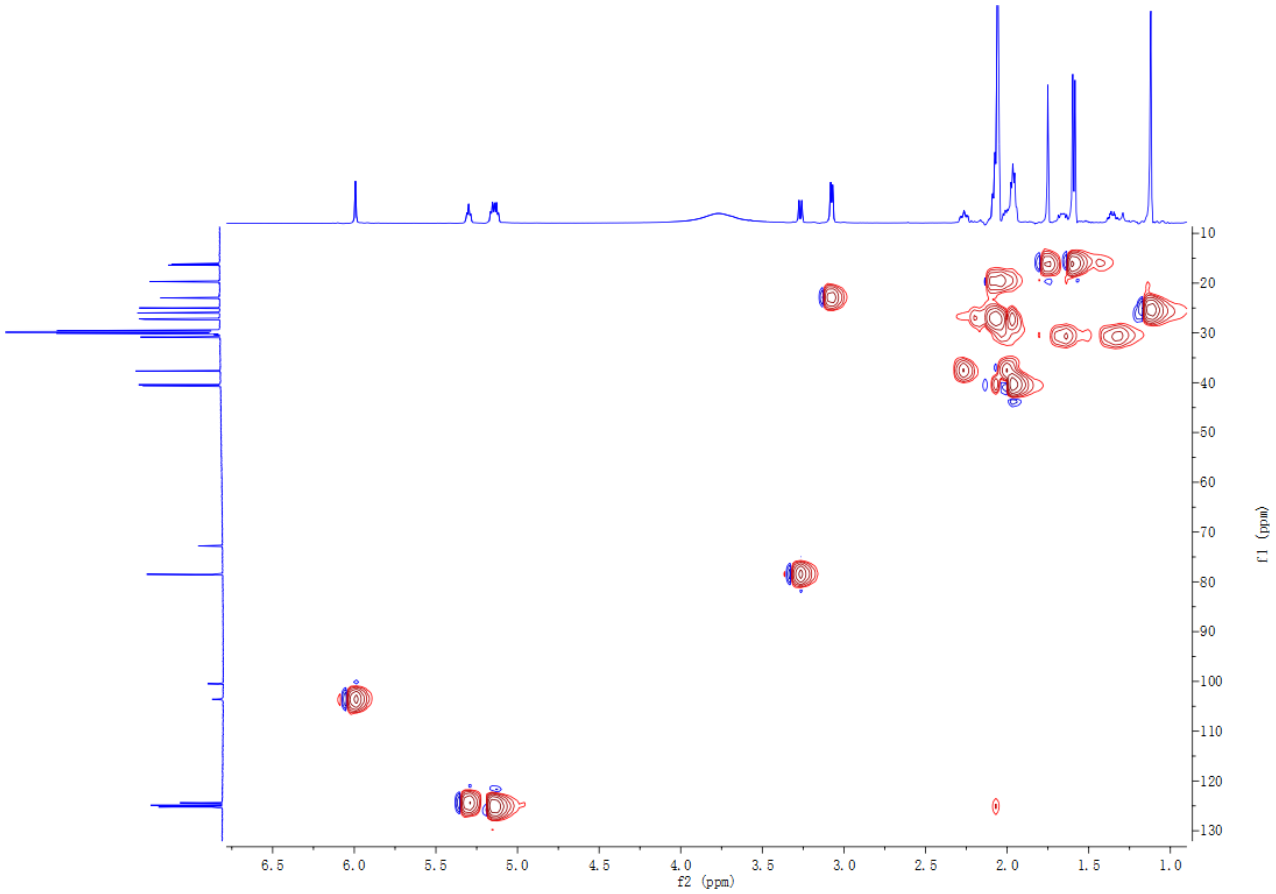
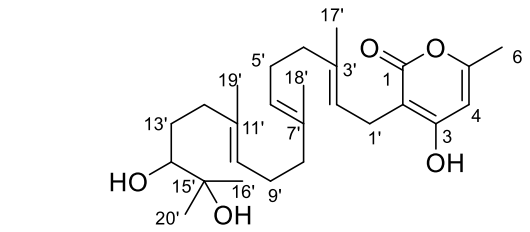


Figure S58. HSQC spectrum of dihydroxygeranylgeranyl-triacetate lactone (**10**)



dihydroxygeranylgeranyl-triacetate lactone (**10**)

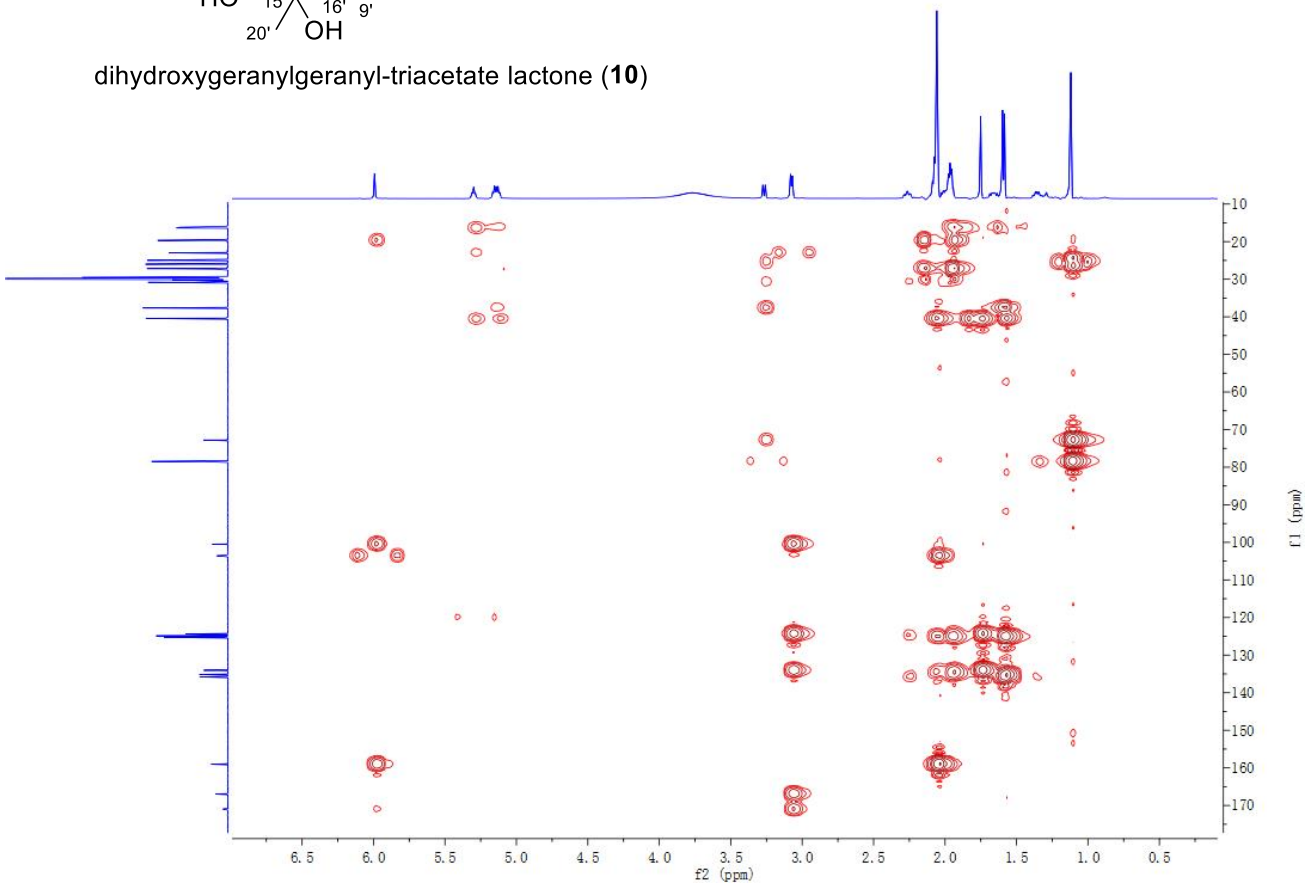


Figure S59. HMBC spectrum of dihydroxygeranylgeranyl-triacetate lactone (**10**)

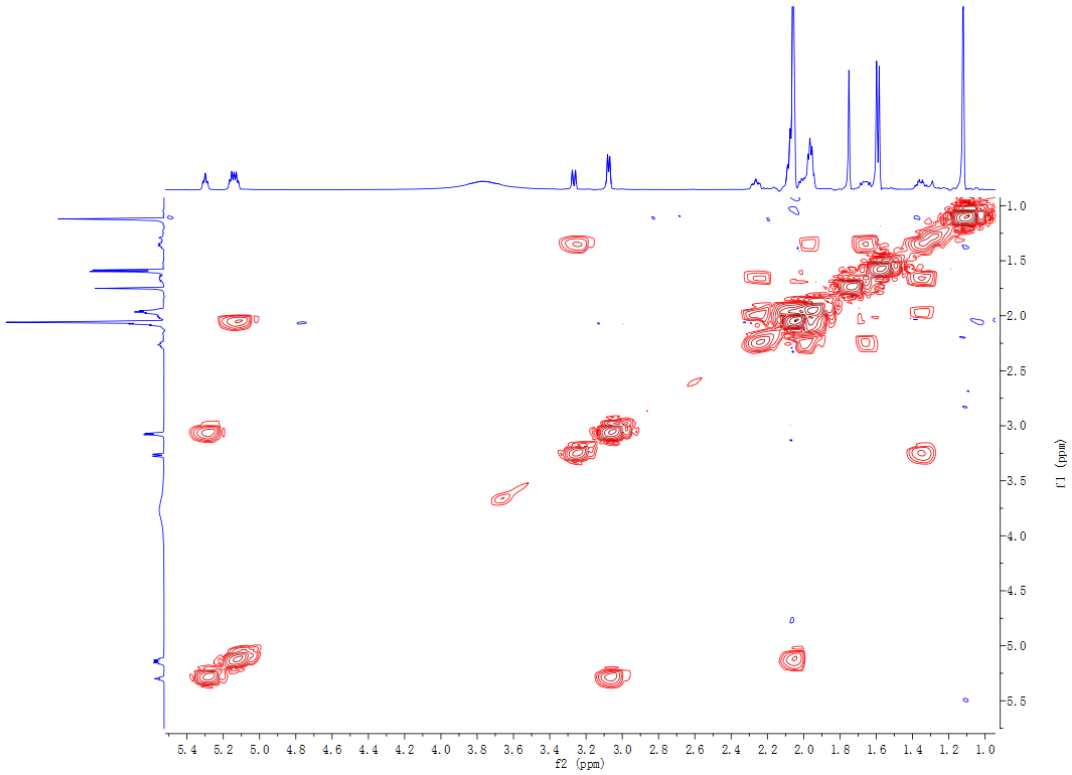


Figure S60. ^{1}H-^{1}H spectrum of dihydroxygeranylgeranyl-triacetate lactone (**10**)

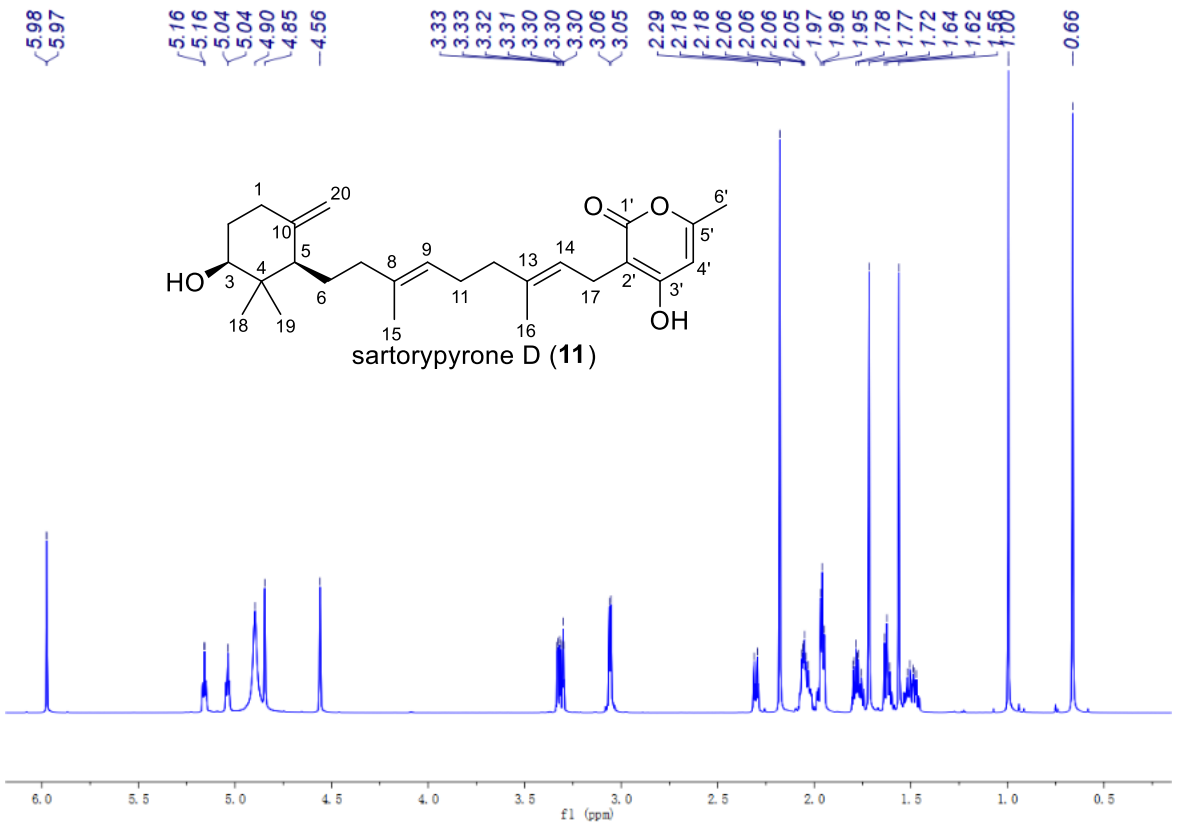


Figure S61. ^{1}H NMR spectrum of sartorypyrone D (**11**)

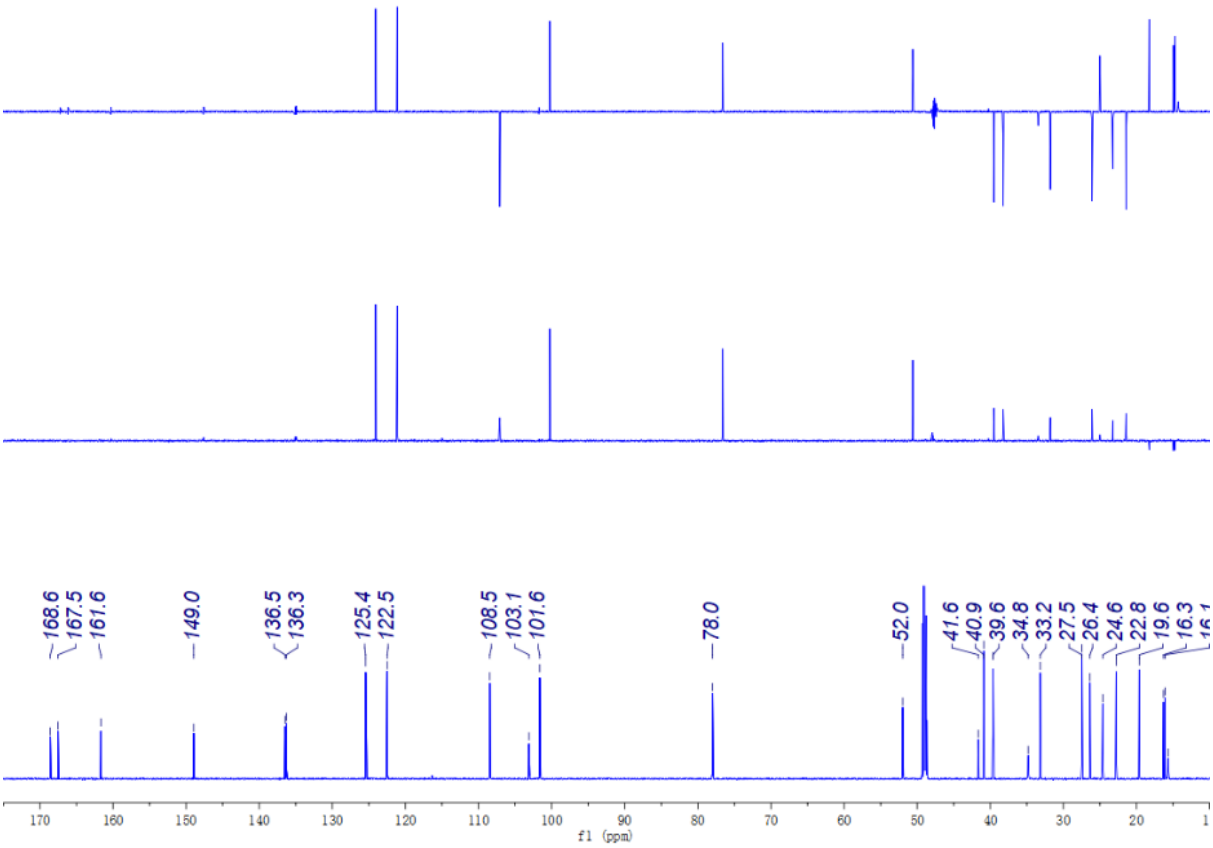


Figure S62. ^{13}C NMR spectrum of sartorypyrone D (**11**)