Supporting Information

Rec. Nat. Prod. 14:3 (2020) 171-176

A New Sesquiterpene from *Schisandra sphenanthera*

Nguyen Thi Mai[1], Hoang Thi Tuyet Lan[1], Bui Thi Mai Anh[1],

Vu Van Doan[2], Bui Huu Tai[2,3] and Phan Van Kiem[2,3*]

[1]University of Transport and Communications, 3 Cau Giay, Dong Da, Ha Noi, Vietnam

[2]Institute of Marine Biochemistry, Vietnam Academy of Science and Technology (VAST), 18 Hoang Quoc Viet, Cau Giay, Hanoi, Vietnam

[3]Graduate University of Science and Technology, VAST, 18 Hoang Quoc Viet, Cau Giay, Hanoi, Vietnam

Table of Contents	**Page**

TD-DFT calculations ECD of compound 1

Conformational searches carried out on Spartan 14 program (Wavefunction Inc., Irvine, CA, USA). Possible conformations were optimized and subjected to TDDFT calculation on Gaussian 09 program [1]. The calculated ECD spectra were composed after correction based on the Boltzmann distribution of the stable conformers using SpecDis v1.64 software [2]. Particularly, enantiomers **1a-1d** were submitted to conformational searches at ground state with semi-empirical AM1 set. The initial stable conformers (Boltzmann distributions over 1.0%) were optimized by DFT calculations at the B3LYP/6-31G(d,p) basic set and polarizable continuum model (PCM) calculation of the solvent methanol. Optimized conformers were subjected to TD-DFT calculation at the B3LYP/6-31G(d,p) level and methanol as a PCM. The ECD spectra at 30 excited states for each conformer were collected and summed to obtain theoretical ECD spectra of each stereoisomer. Half-band was taken at ζ = 0.3 eV. The calculated ECD spectra of each stereoisomer was obtained and compared with experimental ECD spectra without any UV corrections.

References

[1] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, Williams, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman and D. J. Fox (2009). Gaussian 09, Rev. D. 01, Gaussian, *Inc, Wallingford, CT*.

[2] T. Bruhn, A. Schaumloffel, Y. Hemberger and G. Bringmann (2013). SpecDis: quantifying the comparison of calculated and experimental electronic circular dichroism spectra, *Chirality*. **25**,243–249.

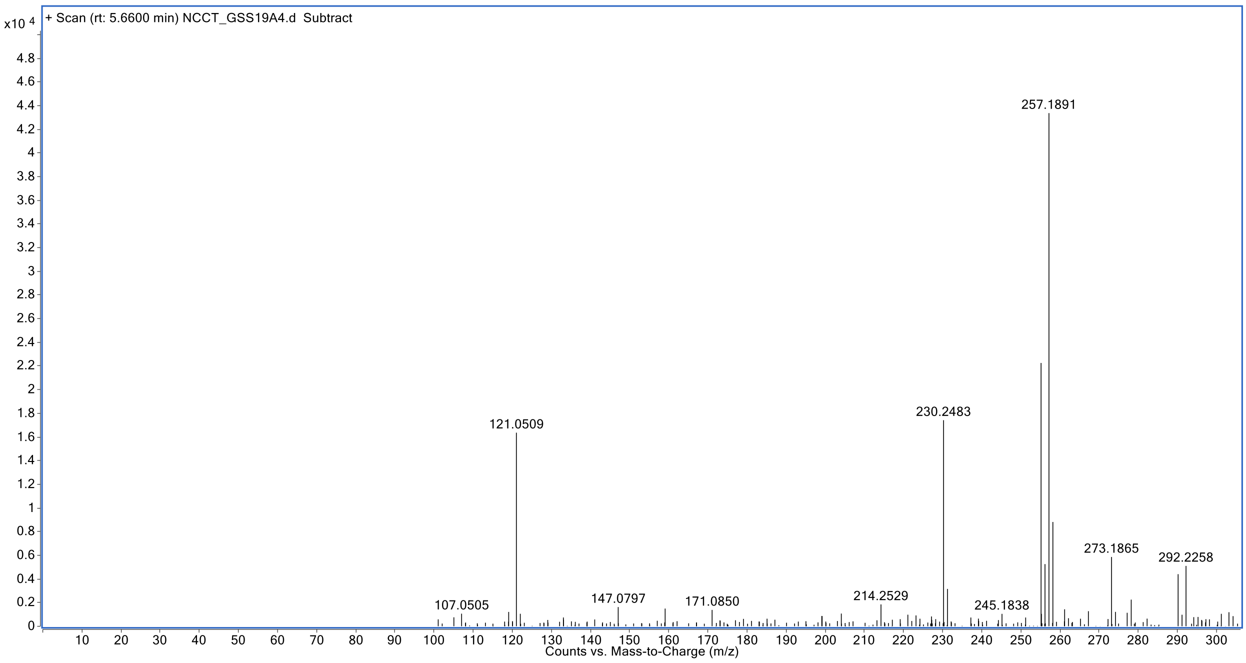

Figure S1: HR-ESI-MS spectrum of compound **1** (Schisandrathera E)

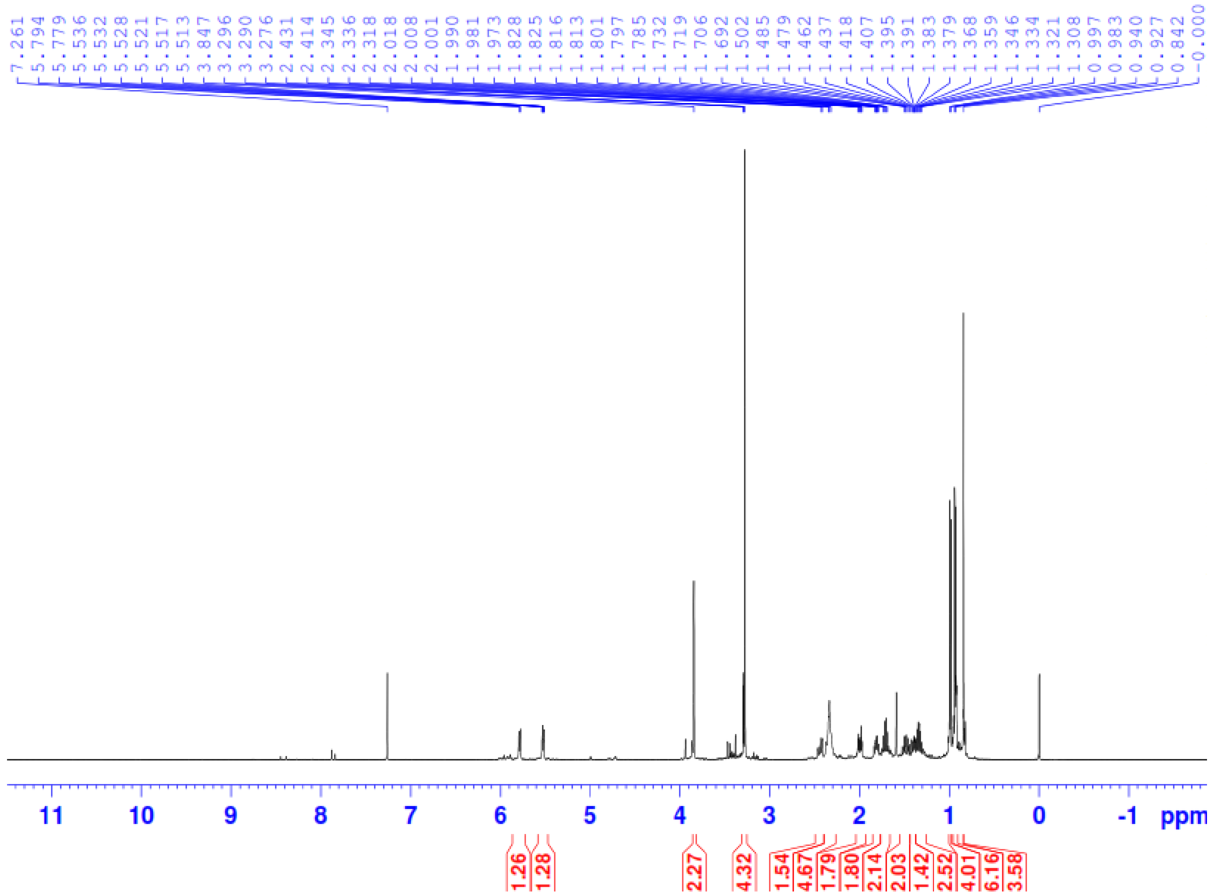

Figure S2: ^{1}H-NMR spectrum of compound **1** (Schisandrathera E)

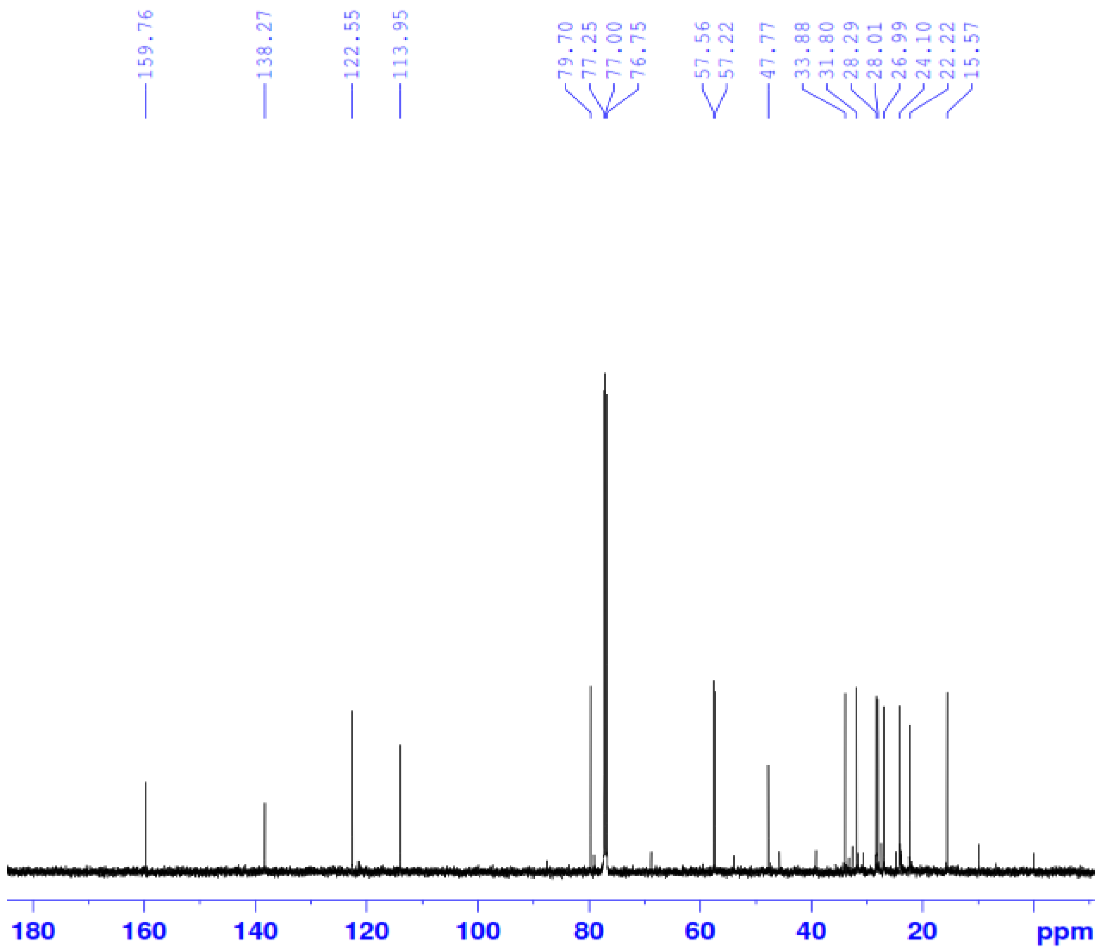

Figure S3: ^{13}C-NMR spectrum of compound **1** (Schisandrathera E)

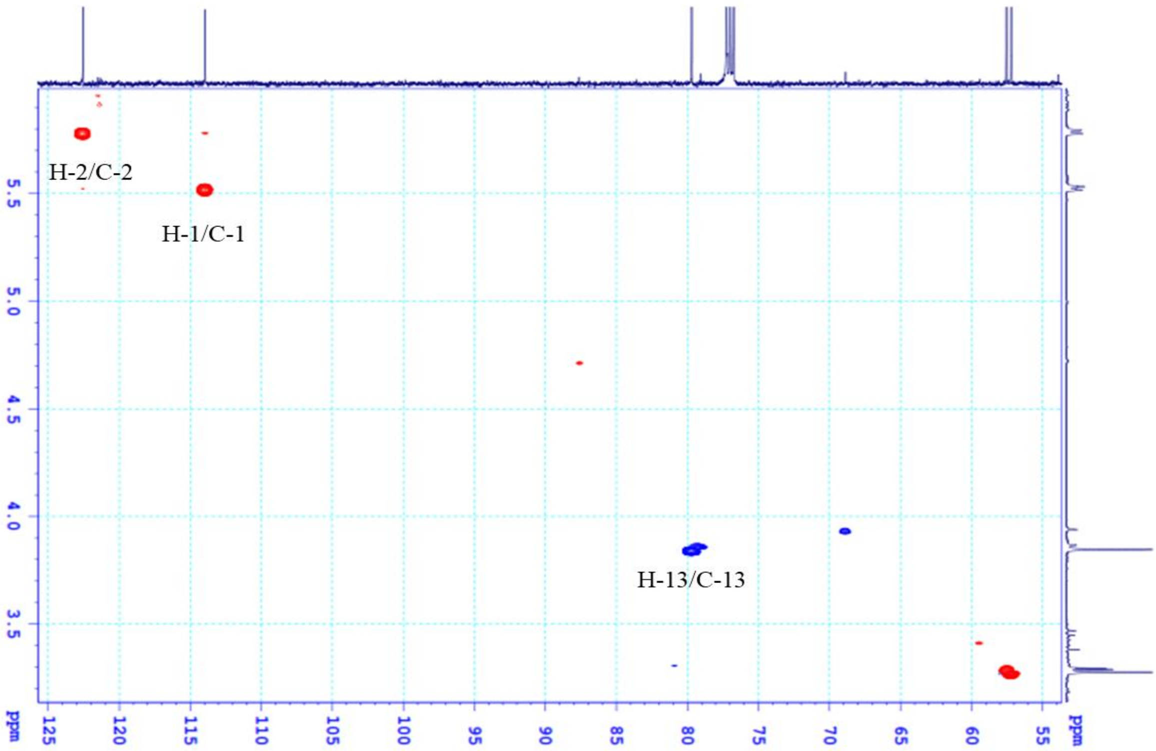

Figure S4: HSQC spectrum of compound **1** (Schisandrathera E) (From 55 to 125 ppm)

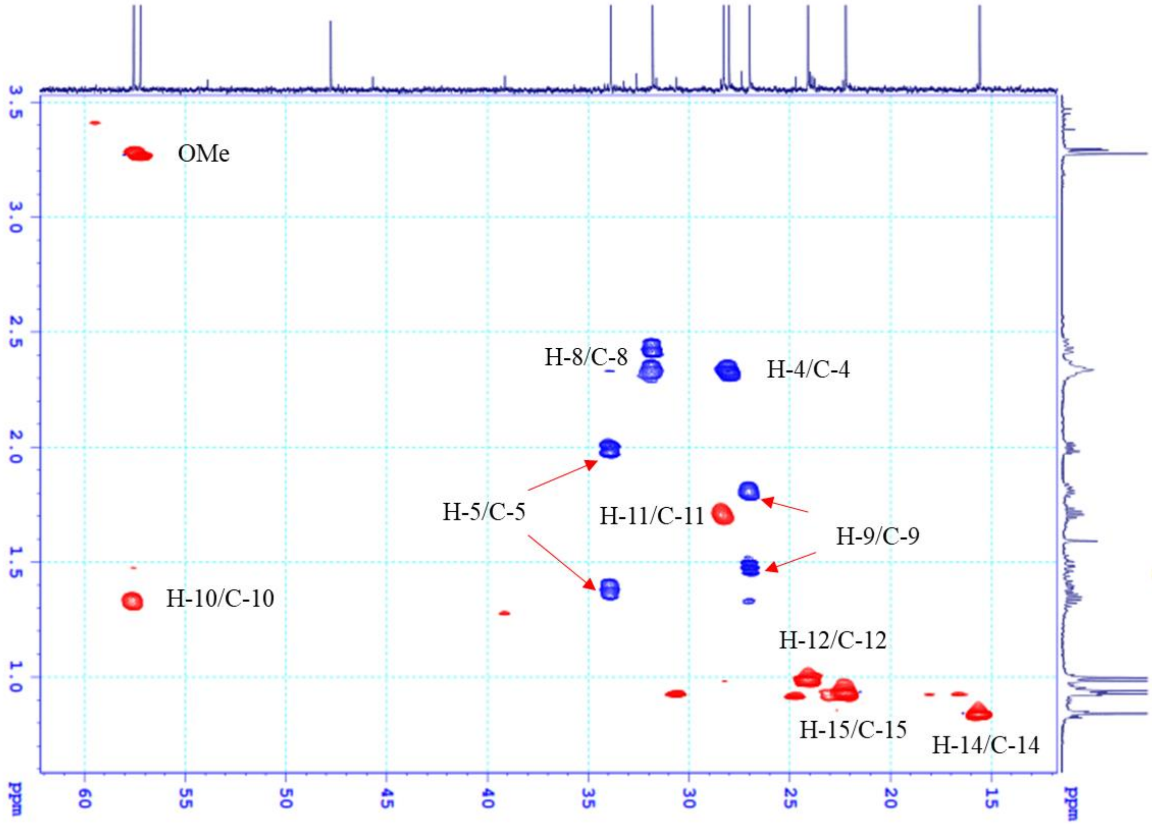

Figure S5: HSQC spectrum of compound **1** (Schisandrathera E) (From 15 to 60 ppm)

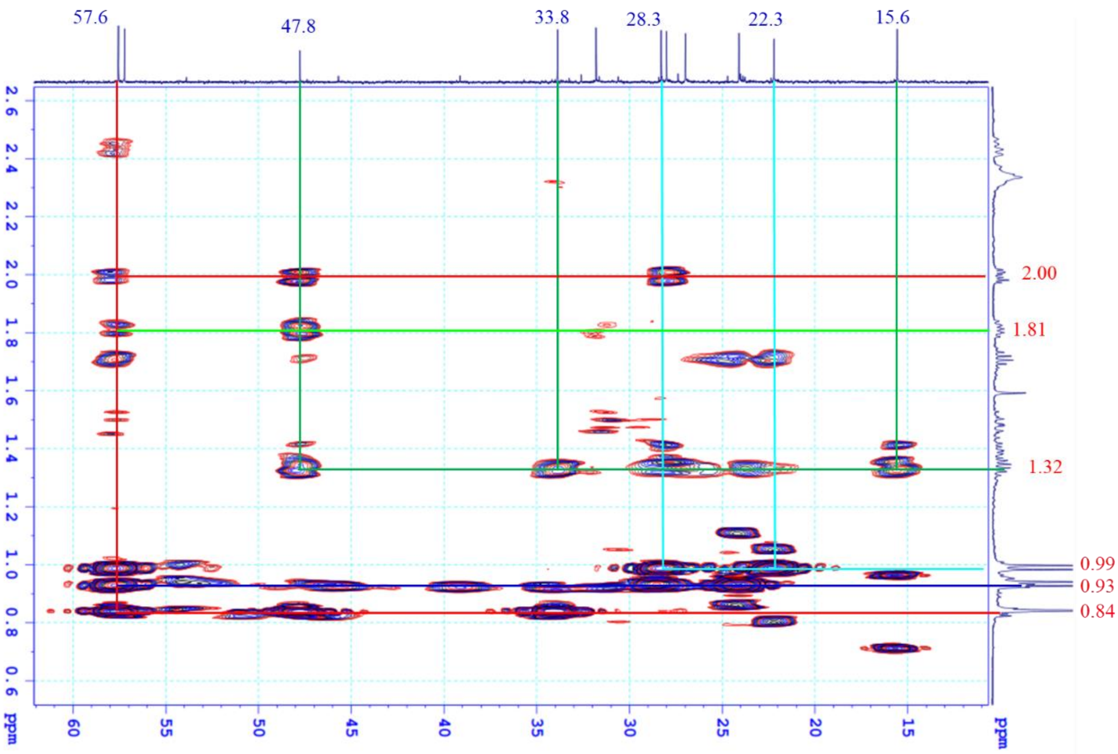

Figure S6: HMBC spectrum of compound **1** (Schisandrathera E) (From 15 to 60 ppm)

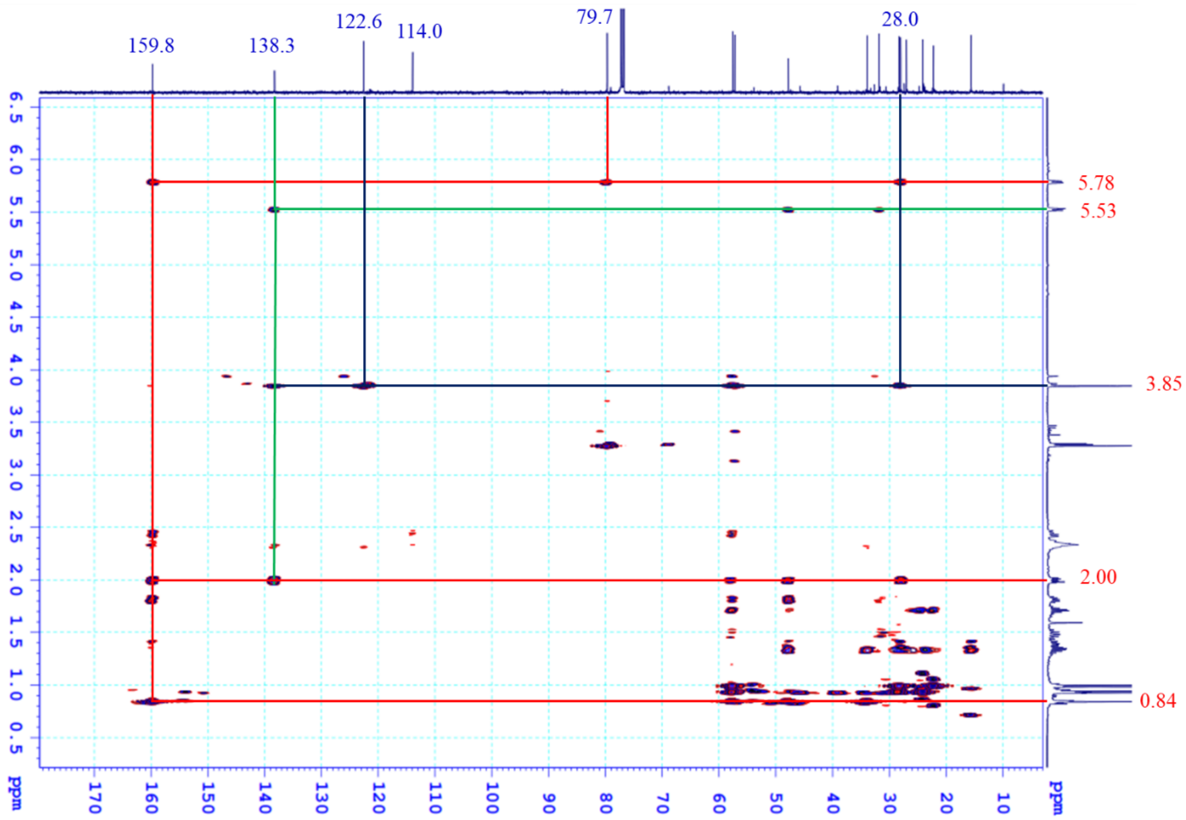

Figure S7: HMBC spectrum of compound **1** (Schisandrathera E)

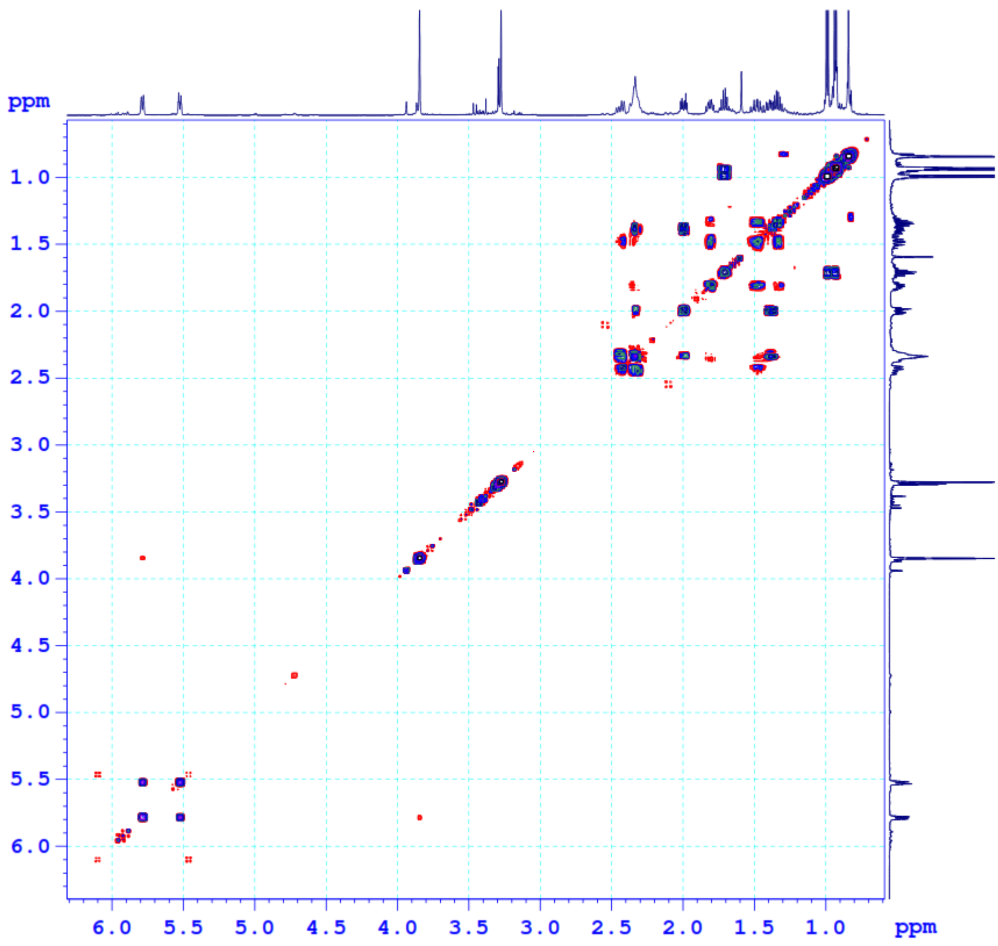

Figure S8: COSY spectrum of compound **1** (Schisandrathera E)

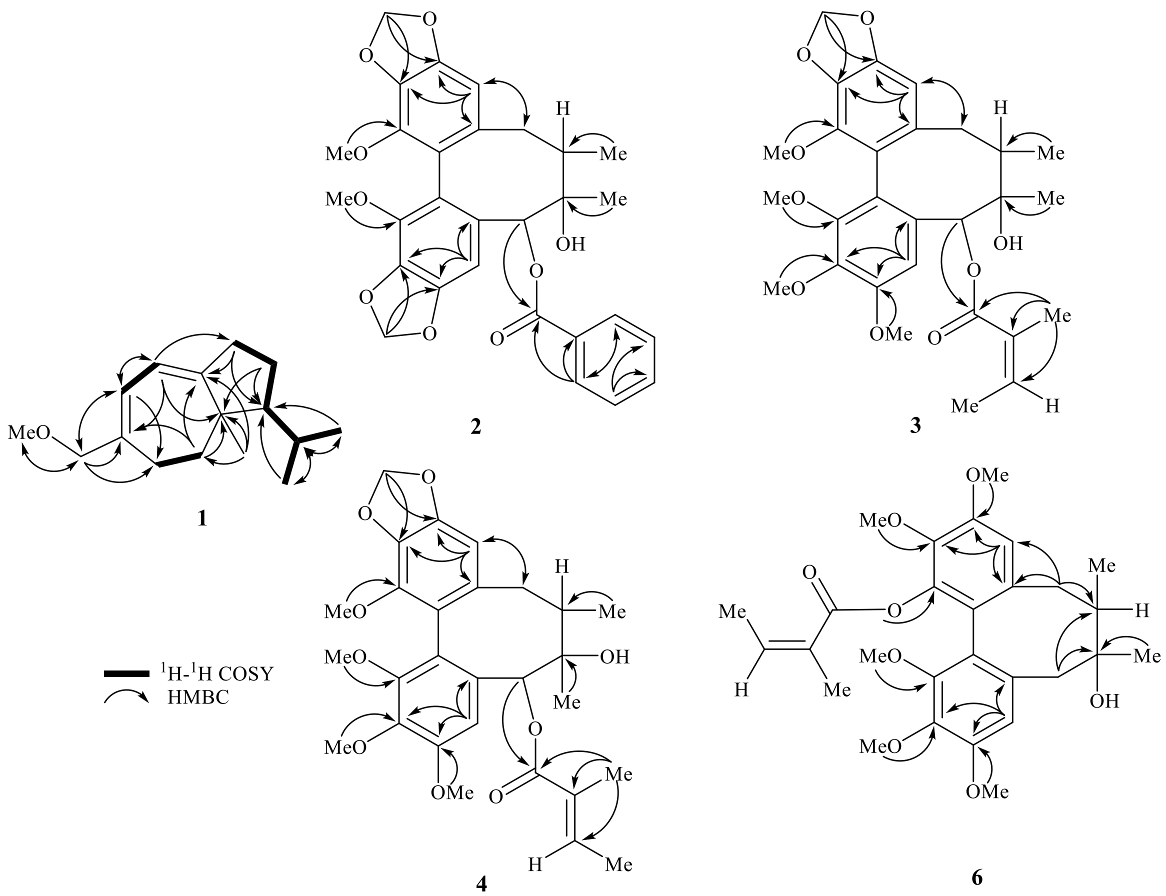

Figure S9: Selected HMBC and COSY correlations in compounds **1**, **2**, **3**, **4**, and **6**.

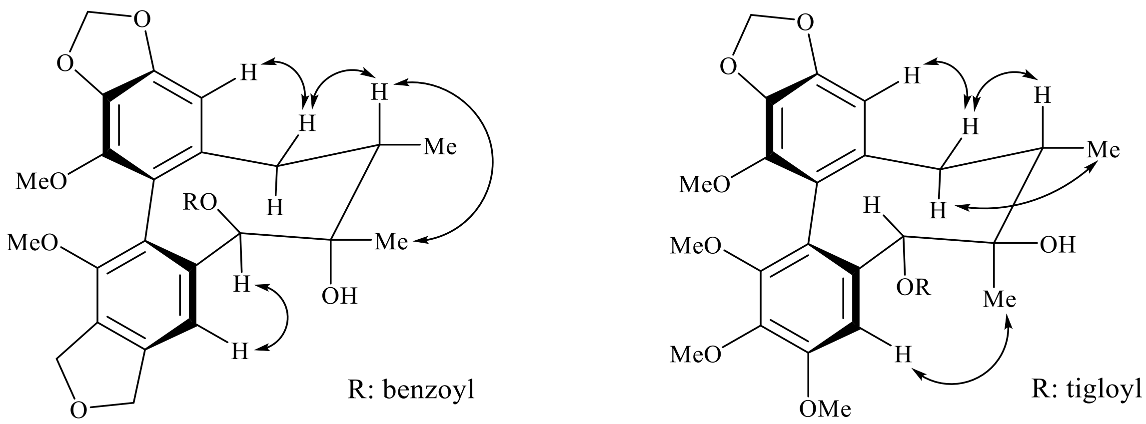

Figure S10: Selected NOESY correlations in compounds **2** and **4**.

Table S1. NMR comparison between compound **1** and Hortonone B

Pos.	[5]δ_C	a,bδ_C	a,cδ_H (mult., J = Hz)
1	204.5 (C)	113.9 (CH)	5.52 (1H, dt, J = 7.5, 2.0 Hz)
2	126.1 (CH)	122.5 (CH)	5.78 (1H, d, J = 7.5 Hz)
3	159.9 (C)	138.3 (C)	-
4	27.7 (CH_2)	28.0 (CH_2)	2.34 (2H, m)
5	40.9 (CH_2)	33.9 (CH_2)	2.00 (1H, m) 1.39 (1H, m)
6	48.3 (C)	47.8 (C)	-
7	65.0 (CH)	159.8 (C)	-
8	22.7 (CH_2)	31.8 (CH_2)	2.44 (1H, dd, J = 17.5, 8.5 Hz) 2.32 (1H, m)
9	30.0 (CH_2)	27.0 (CH_2)	1.81 (1H, m) 1.48 (1H, m)
10	55.1 (CH)	57.6 (CH)	1.32 (1H, m)
11	29.8 (CH)	28.3 (CH)	1.71 (1H, m)
12	23.1 (CH_3)	24.1 (CH_3)	0.99 (3H, d, J = 7.0 Hz)
13	66.4 (CH_2)	79.7 (CH_2)	3.85 (2H, s)
14	20.9 (CH_3)	15.6 (CH_3)	0.84 (3H, s)
15	23.1 (CH_3)	22.3 (CH_3)	0.93 (3H, d, J = 7.0 Hz)
OMe		57.2 (CH_3)	3.28 (3H, s)

Measured in a)$CDCl_3$, b)125 MHz, c)500 MHz, [5]δ_C of hortonone B in CD_2Cl_2 at 600 MHz.

[5] G. Carr, D. E. Williams, R. Ratnayake, R. Bandara, S. Wijesundara, T. Tarling, A. D. Balgi, M. Roberge, R. J. Andersen and V. Karunaratne (2012). Hortonones A to C, hydroazulenones from the genus *Hortonia*, *J. Nat. Prod*. **75**,1189-1191.

Table S2. ^{1}H-NMR data for compounds **2-5**

Pos.	2	3	4	5
	a,bδ_H (mult., J = Hz)	a,bδ_H (mult., J = Hz)	a,bδ_H (mult., J = Hz)	a,bδ_H (mult., J = Hz)
4	6.78 (s)	6.77 (s)	6.96 (s)	6.53 (s)
6	5.75 (s)	5.61 (s)	5.51 (s)	3.78 (m)
7				1.72 (m)
8	2.07 (m)	1.94 (m)	1.88 (m)	1.84 (m)
9	2.20 (d, 14.0) 2.64 (dd, 10.0, 14.0)	2.14 (d, 14.0) 2.30 (dd, 9.5, 14.0)	2.08 (d, 13.5) 2.23 (dd, 10.0, 13.5)	2.32 (d, 14.0) 1.92 (dd, 10.0, 14.0)
11	6.62 (s)	6.46 (s)	6.58 (s)	6.51 (s)
17	1.23 (d, 7.0)	1.13 (d, 7.0)	1.11 (d, 7.0)	0.87 (d, 7.0)
18	1.36 (s)	1.33 (s)	1.14 (s)	0.90 (d, 7.0)
1-OMe	3.77 (s)	3.55 (s)	3.55 (s)	3.52 (s)
2-OMe		3.90 (s)	3.87 (s)	3.91 (s)
3-OMe		3.90 (s)	3.88 (s)	3.91 (s)
6-OMe				3.02 (s)
13-OMe				3.91 (s)
14-OMe	3.30 (s)	3.73 (s)	3.79 (s)	3.73 (s)
OCH_2O	6.02 (brs)	5.86 (d, 1.5) 5.89 (d, 1.5)	5.96 (d, 1.5) 5.97 (d, 1.5)	
OCH_2O	5.73 (brs) 5.82 (d, 1.5)			
2′	7.48 (d, 8.0)			
3′	7.40 (t, 8.0)	5.99 (m)	7.00 (m)	
4′	7.60 (t, 8.0)	1.85 (dd, 1.5, 7.0)	1.83 (dd 7.0, 1.5)	
5′	7.40 (t, 8.0)	1.39 (dd, 1.5, 1.5)	1.88 (dd 1.5, 1.5)	
6′	7.48 (d, 8.0)			

Recorded in a)CD_3OD, b)500 MHz.

Table S3. ^{13}C-NMR data for compounds **2-5**

Pos.	2		3		4		5	
	[$]$\delta_C$	a,cδ_C	[#]δ_C	a,cδ_C	[Δ]δ_C	a,cδ_C	[‡]δ_C	a,cδ_C
1	141.6	142.4	152.1	152.1	151.1	152.1	148.9	151.9
2	136.9	137.3	141.8	141.8	141.1	142.8	139.1	141.9
3	148.1	149.1	151.9	151.9	152.3	153.8	148.3	151.4
4	102.4	107.8	110.0	110.0	106.2	107.9	110.0	111.5
5	120.6	122.8	130.6	130.7	133.0	135.3	131.5	133.8
6	84.9	86.6	84.4	84.5	77.6	78.5	89.9	90.5
7	72.2	73.3	72.2	72.3	75.2	75.8	40.1	38.5
8	42.7	44.2	42.5	42.5	46.6	47.9	38.2	36.7
9	36.4	37.3	36.5	36.5	36.7	37.4	39.2	38.3
10	121.4	122.4	135.2	135.2	136.7	138.4	134.8	137.5
11	105.9	103.4	102.7	102.7	103.0	103.9	107.8	109.1
12	148.8	150.3	148.7	148.8	149.4	150.9	145.8	148.6
13	133.9	135.4	134.3	134.3	135.6	136.9	134.8	137.5
14	140.2	141.5	140.6	140.6	141.5	142.3	147.5	150.6
15	135.3	134.3	122.3	122.3	122.9	121.0	119.8	121.7
16	129.1	131.7	121.2	121.3	119.6	124.3	122.0	124.0
17	18.8	19.2	18.9	18.9	17.5	17.4	19.6	17.3
18	28.3	29.0	28.2	28.2	18.8	19.0	19.6	17.3
OMe								
1	*	60.0	60.6	60.6	60.6	61.0	60.6	60.2
2			60.8	60.8	60.9	61.3	61.6	60.9
3			55.9	55.9	55.9	56.6	56.9	56.1
6							56.6	55.8
13							61.4	60.1
14	*	59.0	59.0	59.0	60.2	60.2	60.9	59.9
OCH_2O	*	102.5	100.5	100.6	101.0	102.4		
OCH_2O		101.7						
1′	129.1	130.8	165.8	165.8	166.6	168.0		
2′	132.8	130.5	127.1	127.1	128.8	130.0		
3′	127.8	129.1	139.8	139.8	137.5	138.6		
4′	129.5	134.3	15.7	15.7	14.4	14.4		
5′	127.8	129.1	19.7	19.7	12.2	12.3		
6′	132.8	130.5						
C=O	164.6	166.3						

Recorded in a) CD_3OD, c)125 MHz, $δ of schisantherin D in $CDCl_3$, &δ of schirubrisin B in $CDCl_3$, #δ of schisantherin B in $CDCl_3$, Δδ of tigloylgomisin P in $CDCl_3$, ‡δ of schisphenin E in $CDCl_3$.

Table S4. ^{1}H- and ^{13}C- NMR data for compounds **6-8**

C	6			7			8		
	$^{[\varepsilon]}\delta_C$	$^{a,c}\delta_C$	$^{a,b}\delta_H$ (mult., *J* = Hz)	$^{[\theta]}\delta_C$	$^{a,c}\delta_C$	$^{a,b}\delta_H$ (mult., *J* = Hz)	$^{[\mu]}\delta_C$	$^{a,c}\delta_C$	$^{a,b}\delta_H$ (mult., *J* = Hz)
1	152.6	152.6	-	151.75	152.6	-	151.3	152.6	-
2	140.4	140.4	-	140.32	141.4	-	139.9	141.1	-
3	151.8	151.8	-	153.09	153.2	-	153.2	154.3	-
4	110.1	110.1	6.56 (s)	107.43	108.8	6.70 (s)	107.3	108.0	6.68 (s)
5	133.1	133.1	-	139.40	140.8	-	139.8	140.8	-
6	40.7	40.7	2.74 (d, 14.0) 2.35 (d, 14.0)	35.82	36.4	2.11 (d, 13.5) 2.48 (d, 13.5)	35.8	36.5	2.09 (d, 13.5) 2.45 (d, 13.5)
7	72.0	72.0	-	41.00	42.3	1.92 (m)	40.9	42.5	1.92 (m)
8	40.9	42.0	1.88 (m)	33.98	35.1	1.80 (m)	33.8	35.2	1.79 (m)
9	34.3	34.3	2.42 (dd, 2.0, 14.5) 2.72 (dd, 8.0, 14.5)	39.37	40.0	2.28 (dd, 10.0, 13.5) 2.65 (dd, 8.0, 13.5)	39.2	40.1	2.28 (dd, 10.0, 13.5) 2.62 (dd, 8.0, 13.5)
10	133.8	133.9	-	134.17	135.6	-	134.3	135.7	-
11	112.8	112.8	6.70 (s)	110.74	112.2	6.69 (s)	107.9	109.0	6.45 (s)
12	151.7	151.7	-	153.09	154.4	-	150.6	152.4	-
13	139.7	139.7	-	139.97	141.1	-	134.0	135.5	-
14	142.3	142.3	-	151.62	152.5	-	146.9	148.8	-
15	122.9	123.3	-	123.62	124.7	-	117.0	118.9	-
16	**127.7**	**122.9**	-	122.57	123.6	-	121.3	123.5	-
17	15.9	15.9	0.85 (d, 7.0)	12.88	12.9	1.03 (d, 7.0)	12.8	13.0	1.03 (d, 7.0)
18	29.8	29.9	1.25 (s)	21.99	22.0	0.75 (d, 7.0)	21.7	22.1	0.75 (d, 7.0)
OMe									
1				60.74	61.0	3.49 (s)	61.0	61.2	3.57 (s)
2	60.9	60.9	3.84 (s)	61.17	61.4	3.84 (s)	61.1	61.2	3.83 (s)
3	56.1	56.1	3.91 (s)	56.12	56.5	3.88 (s)	56.0	56.5	3.88 (s)
12	56.1	56.0	3.87 (s)	56.12	56.5	3.88 (s)	55.9	56.3	3.88 (s)
13	60.8	60.8	3.84 (s)	61.17	61.4	3.84 (s)	61.0	61.2	3.84 (s)
14	60.6	60.6	3.55 (s)	60.74	61.0	3.49 (s)			
Ang									
1′	165.7	165.7	-						
2′	**138.2**	**127.7**	-						
3′	137.2	137.2	5.88 (m)						
4′	15.3	15.3	1.76 (dq, 7.2, 1.0)						
5′	20.3	20.3	1.76 (s)						

Measured in $^{a)}CD_3OD$, $^{b)}$*500 MHz,* $^{c)}$*125 MHz,* $^{\varepsilon}\delta_C$ *of angeoylgomisin H in* $CDCl_3$, $^{\theta}\delta_C$ *of (+)-deoxyschizandrin in* $CDCl_3$, $^{\mu}\delta_C$ *of (+)-gomisin* K_3 *in* $CDCl_3$,

Table S5. Cytotoxic effect of compounds **1-8** toward PC3 and MCF7 cell lines

	Cell viability (%) at 30µM	
Compounds	PC3	MCF7
1	49.40 ± 0.46	29.80 ± 0.27
2	84.50 ± 0.78	45.20 ± 0.41
3	75.80 ± 0.70	62.10 ± 0.56
4	95.00 ± 0.97	83.60 ± 0.75
5	89.30 ± 0.82	74.30 ± 0.67
6	98.00 ± 1.05	74.60 ± 0.67
7	78.00 ± 0.72	35.50 ± 0.32
8	76.00 ± 0.70	31.60 ± 0.28
Capecitabine*	22.00 ± 0.92	17.00 ± 0.90

*Positive control

Table S6. IC_{50} of compounds **1, 7-8** against PC3 and MCF7 cell lines

Compounds	IC_{50} (µM)	
	PC3	MCF7
1	22.60 ± 0.48	7.80 ± 0.30
7	34.00 ± 0.20	8.30 ± 0.01
8	39.30 ± 0.50	22.20 ± 1.60
Capecitabine*	11.2 ± 1.44	7.17 ± 3.93

*Positive control