SUPPLEMENTARY MATERIAL

Potential Role of a Novel Biphenanthrene Derivative Isolated from *Aerides falcata* in Central Nervous System Diseases

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KEYWORDS: *Aerides falcata*, Orchidaceae, biphenanthrene, CNS diseases,

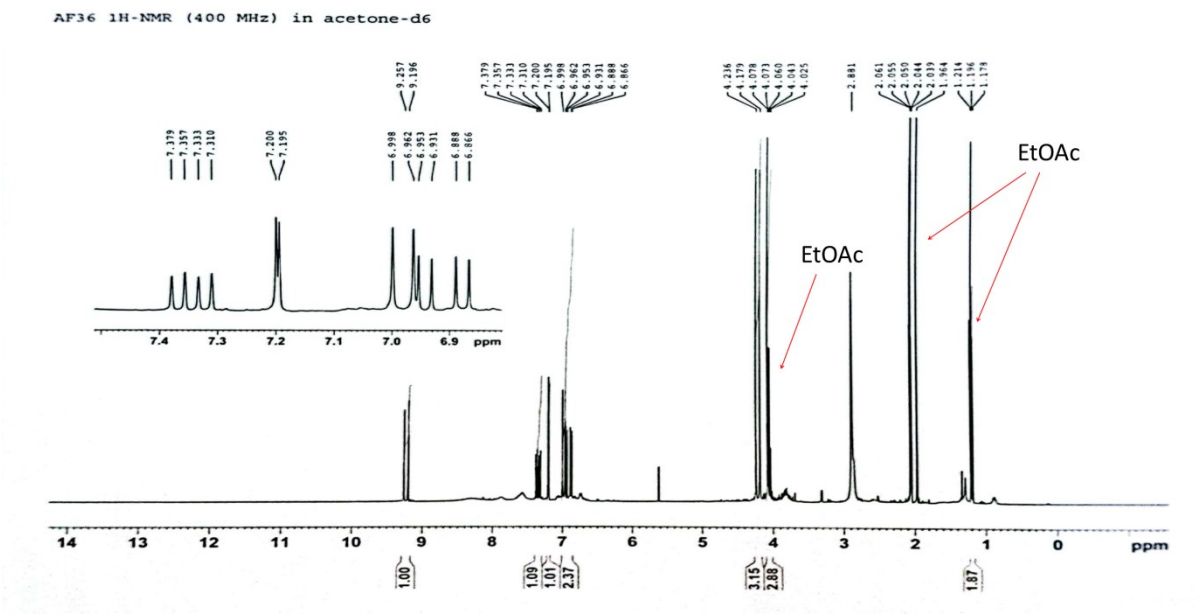

Figure S1. ^{1}H NMR spectrum of **1** (400 MHz) in acetone-d_6

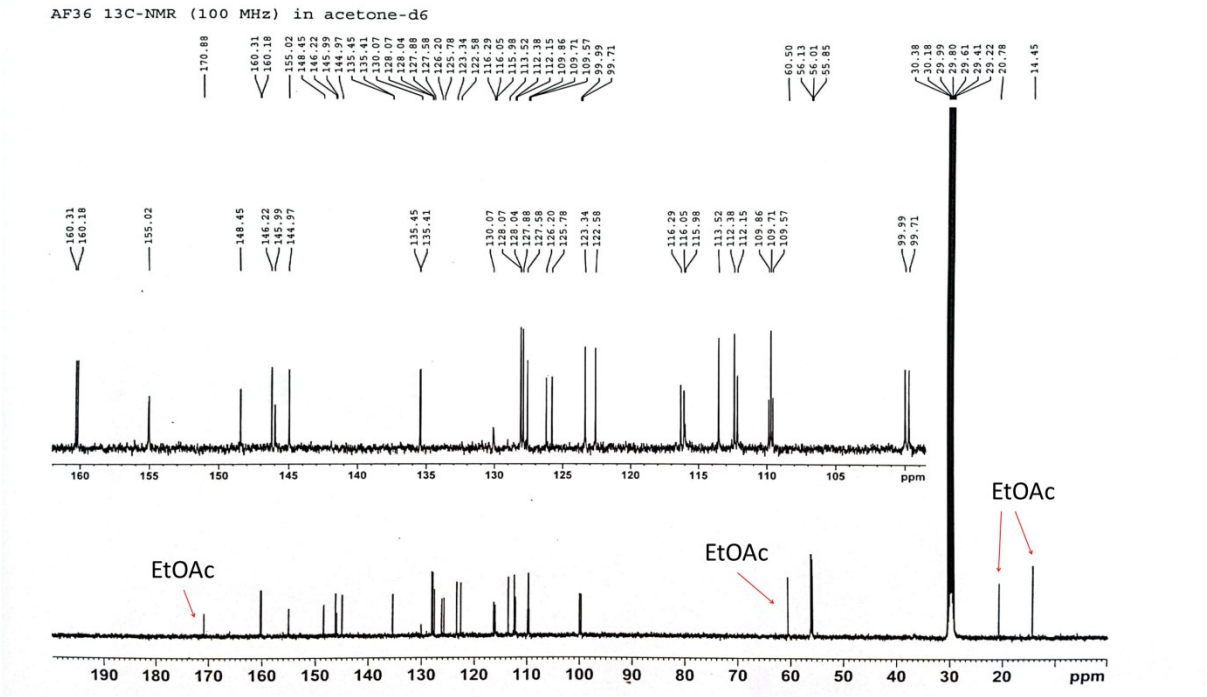

Figure S2. ^{13}C NMR spectrum of **1** (100 MHz) in acetone-d_6

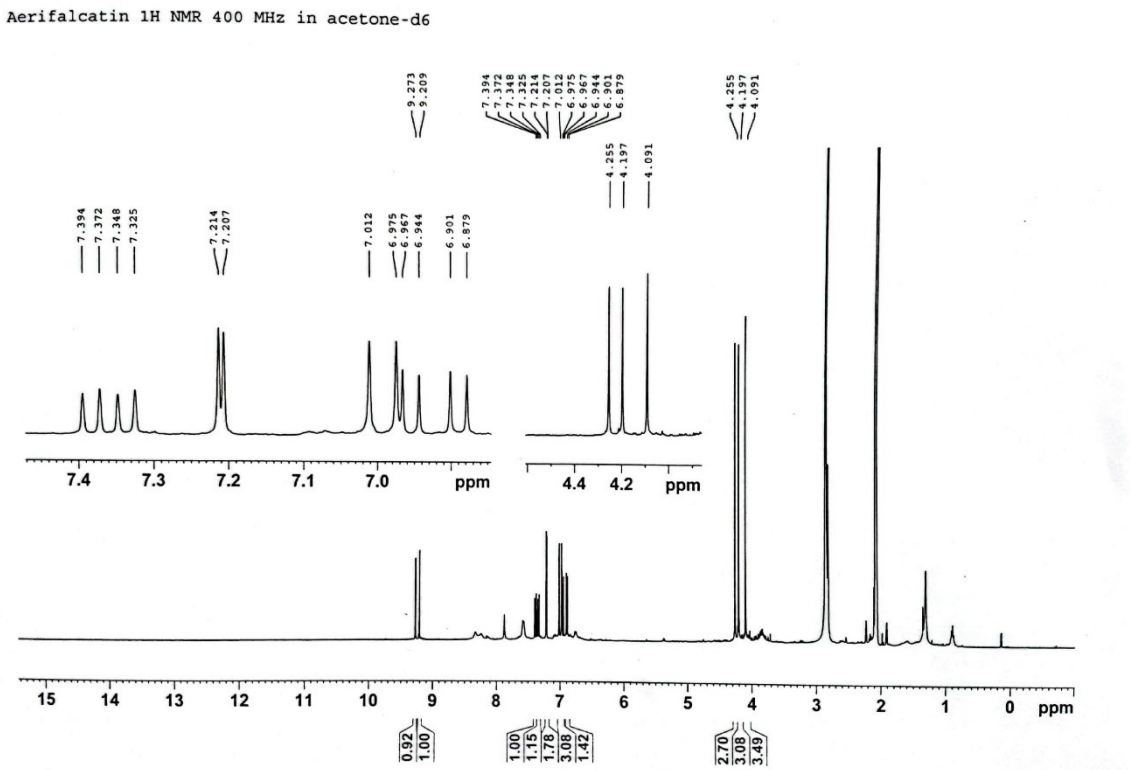

Figure S3. ^{1}H NMR spectrum of **1** (400 MHz) in acetone-d_6 (dried sample)

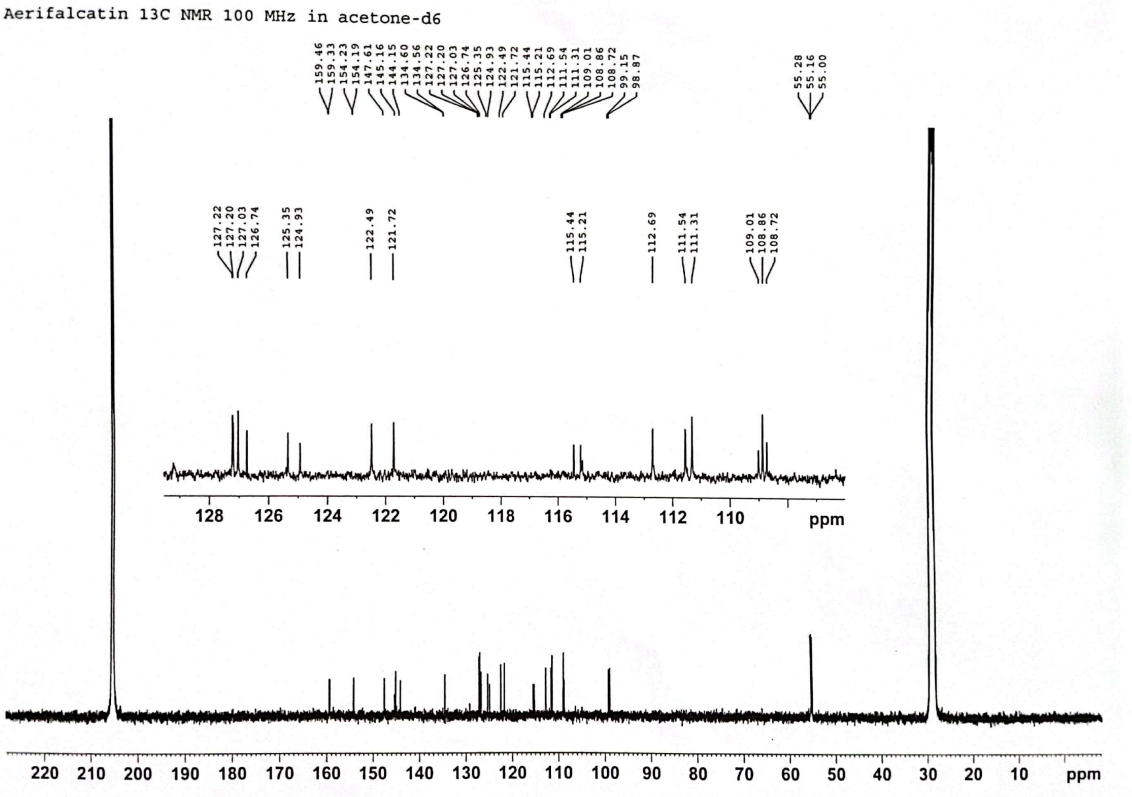

Figure S4. ^{13}C NMR spectrum of **1** (100 MHz) in acetone-d_6 (dried sample)

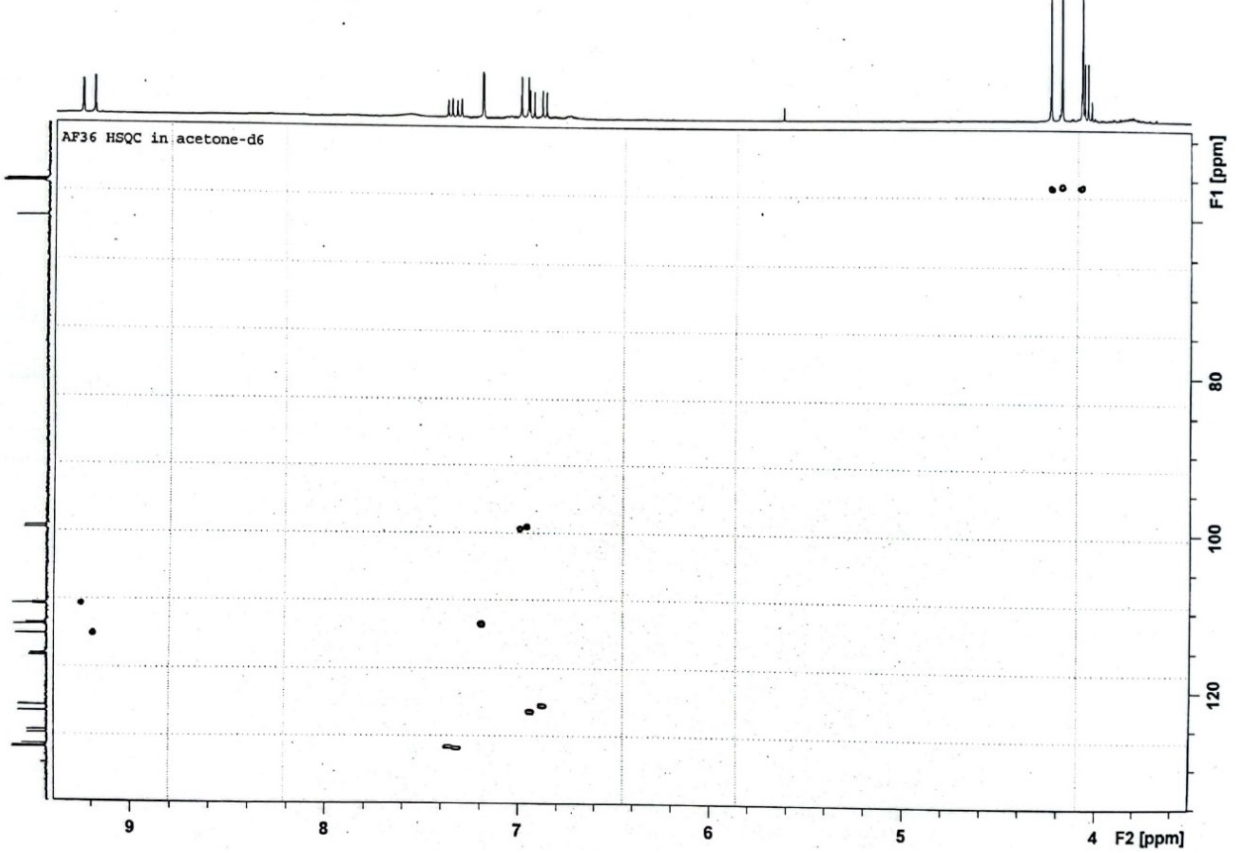

Figure S5. HSQC (1) correlation of **1** in acetone-d_6

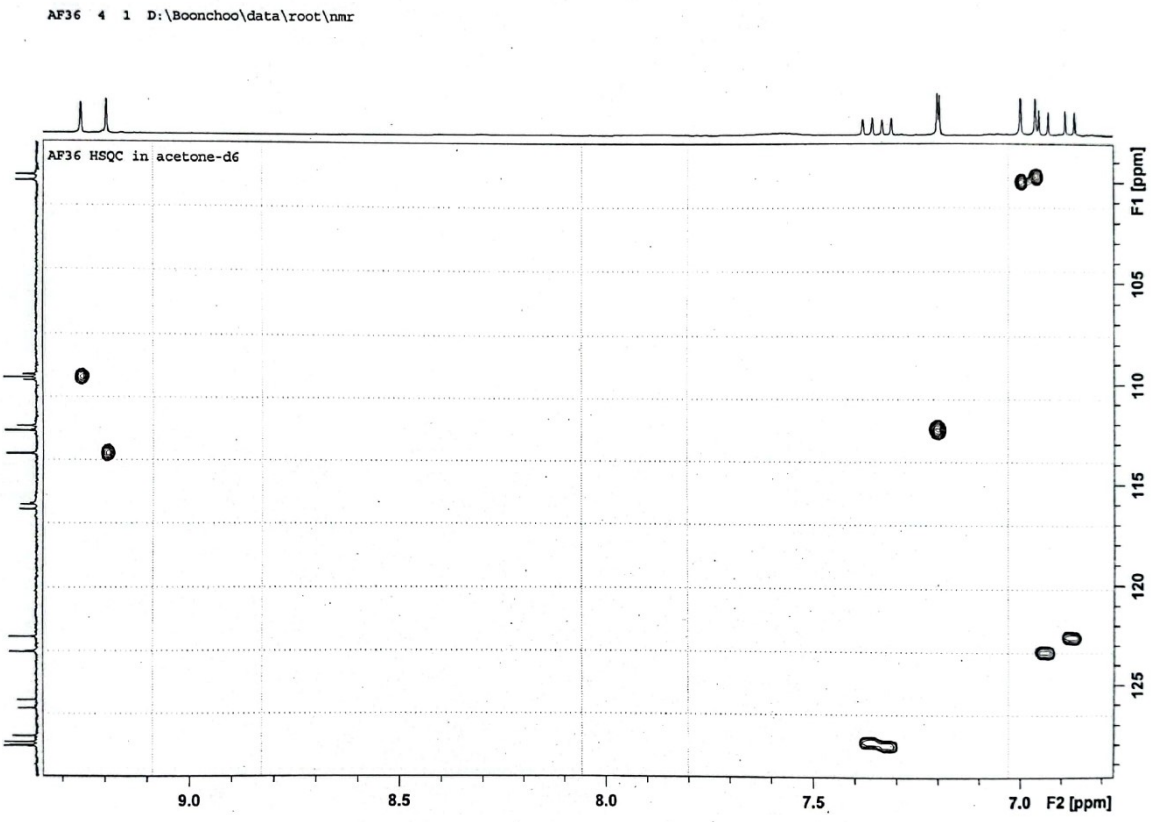

Figure S6. HSQC (2) correlation of **1** in acetone-d_6

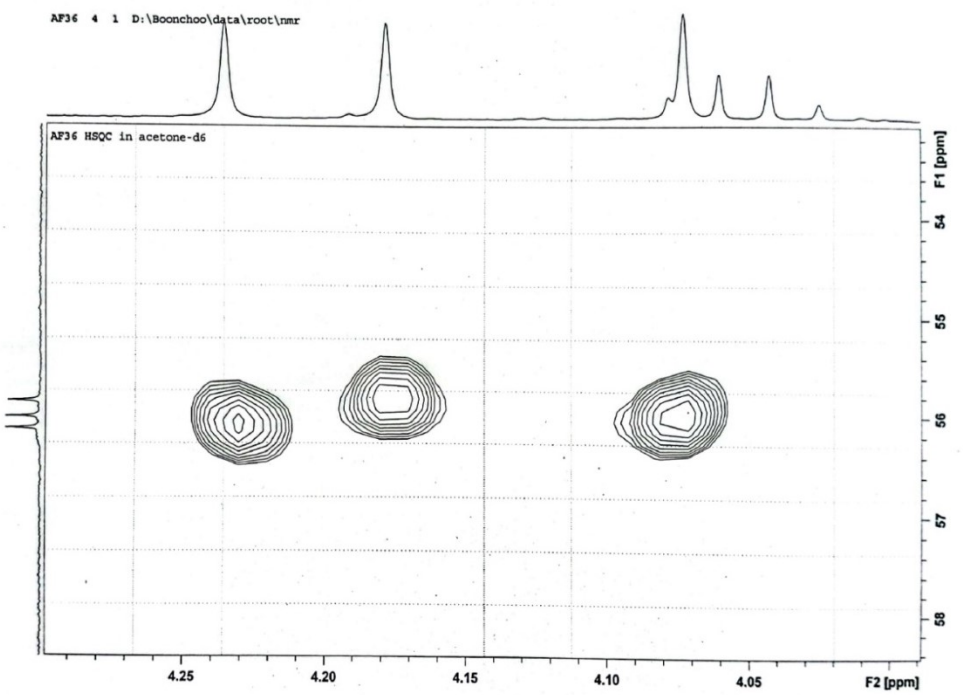

Figure S7. HSQC (3) correlation of **1** in acetone-d_6

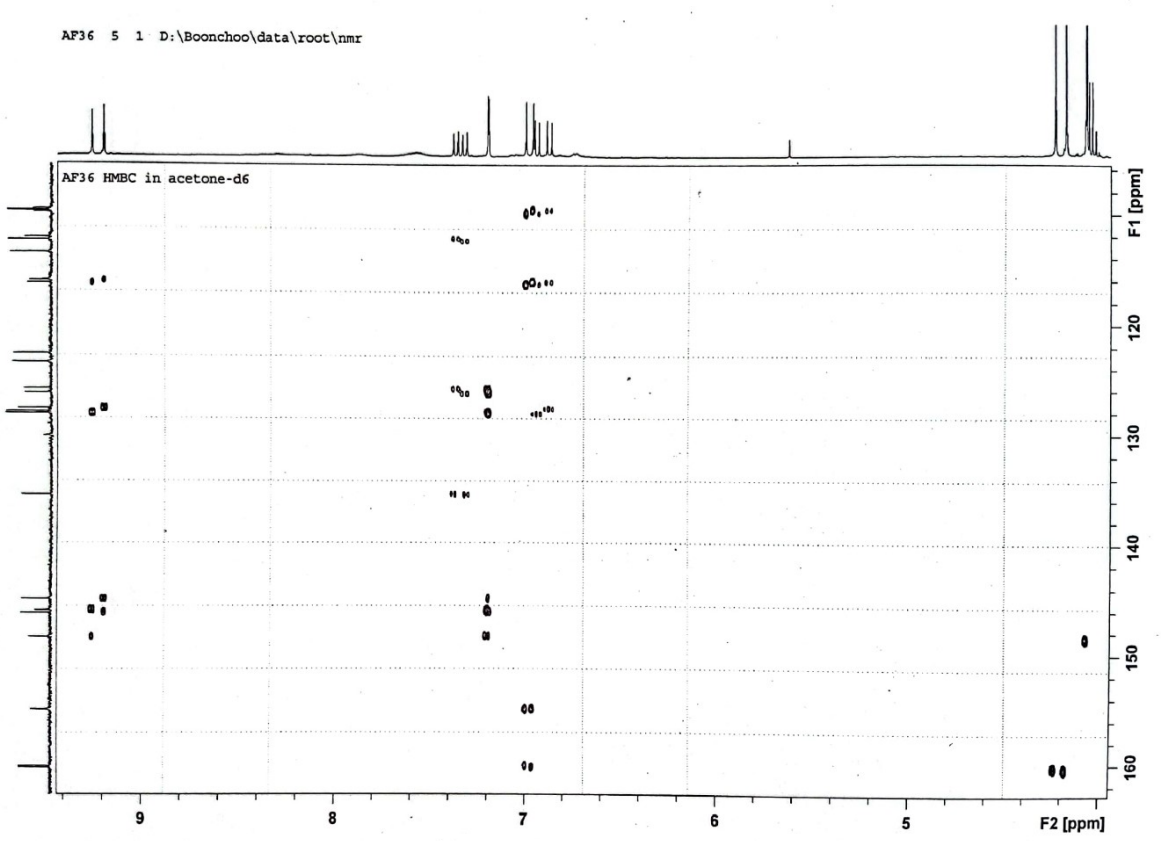

Figure S8. HMBC (1) correlation of **1** in acetone-d_6

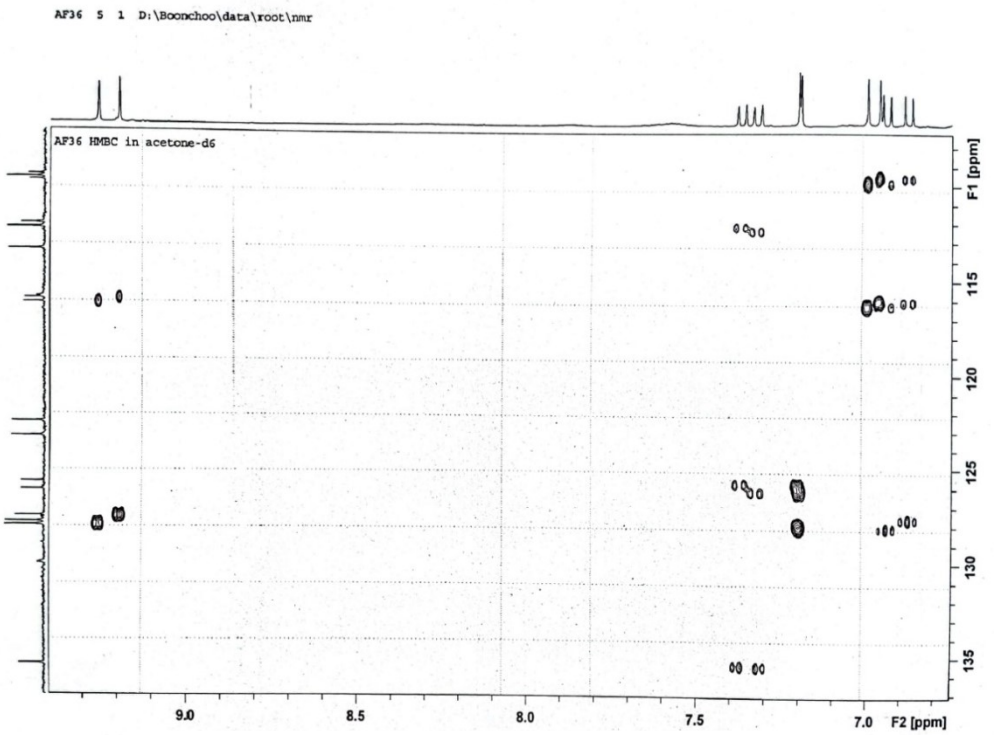

Figure S9. HMBC (2) correlation of **1** in acetone-d_6

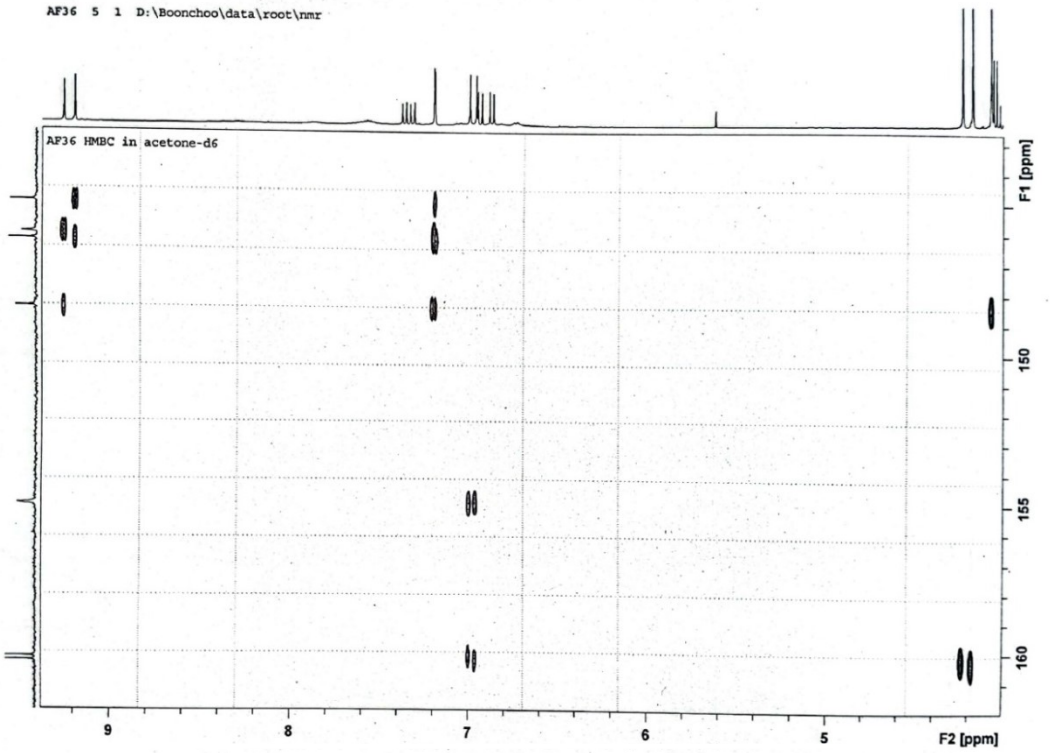

Figure S10. HMBC (3) correlation of **1** in acetone-d_6

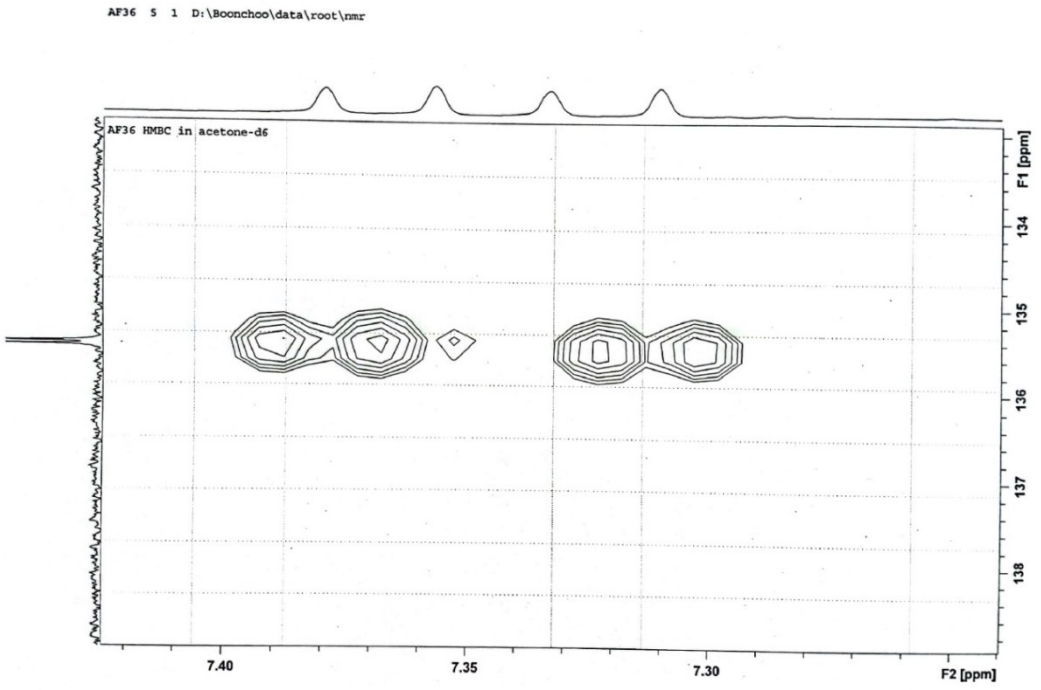

Figure S11. HMBC (4) correlation of **1** in acetone-d_6

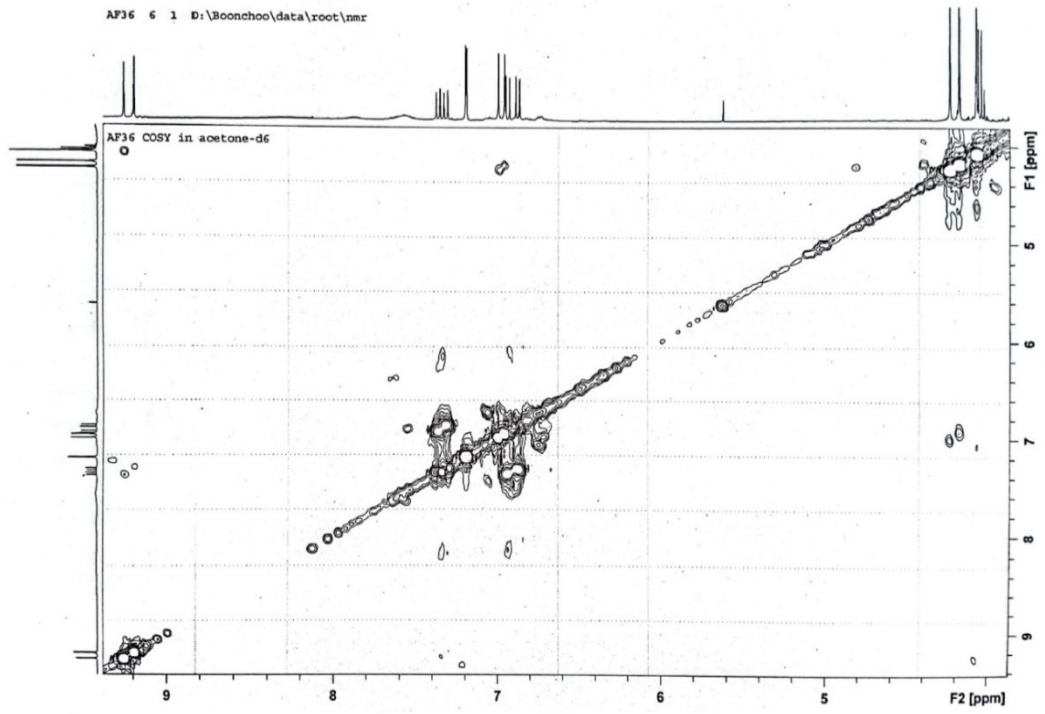

Figure S12. COSY correlation of **1** in acetone-d_6

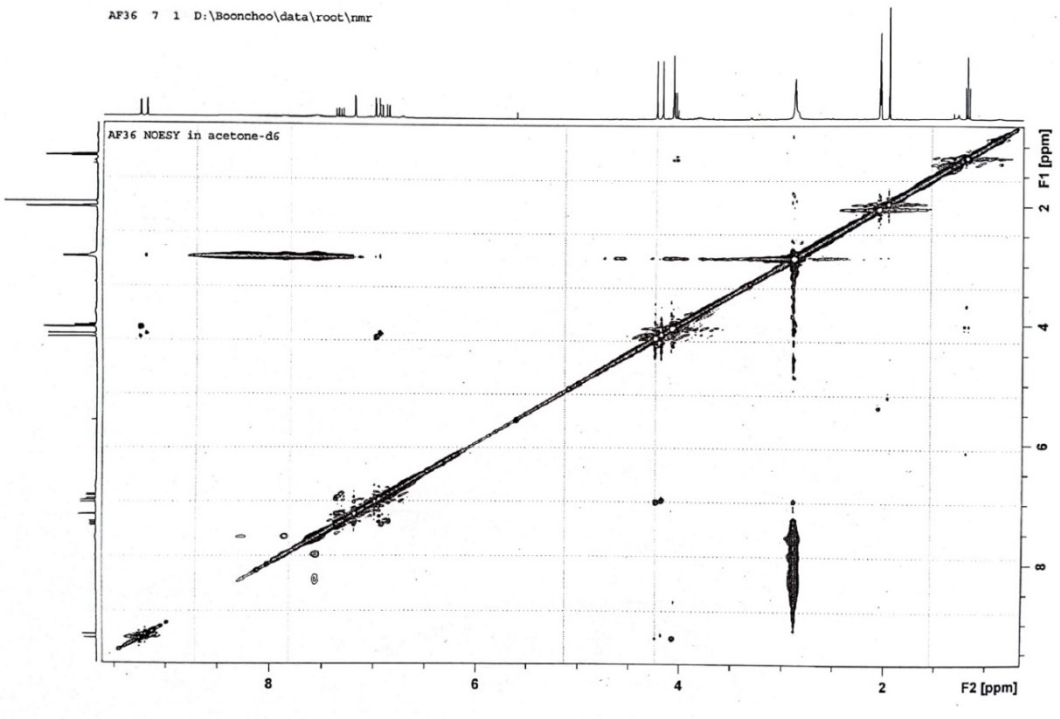

Figure S13. NOESY correlation of **1** in acetone-d_6

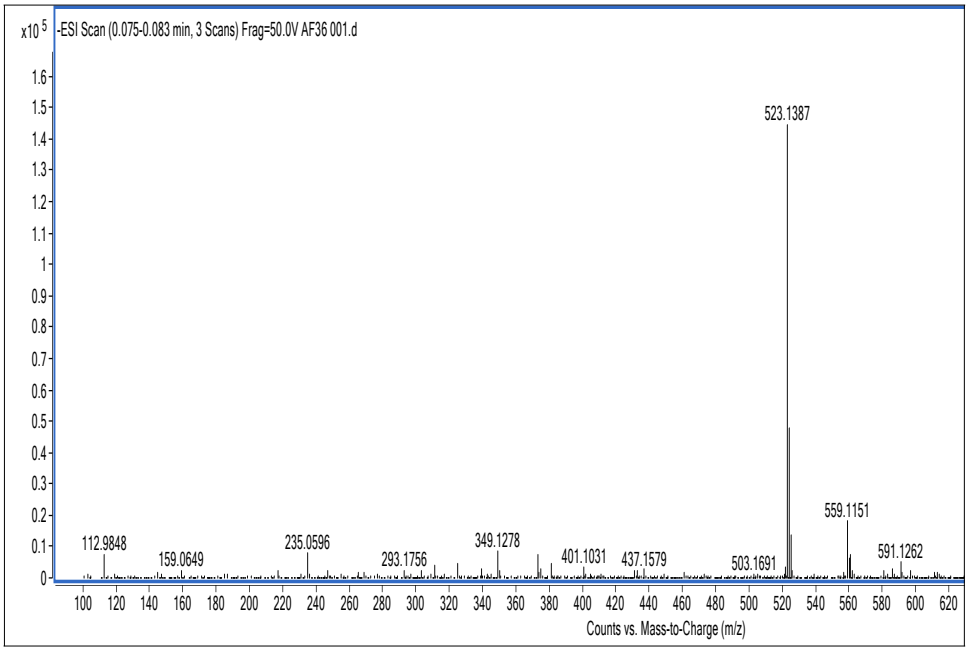

Figure S14. HRESIMS spectrum of **1**

Table S1. NMR spectral data of **2** and n-eicosyl-trans ferulate

Position	Compound **2** (acetone-d_6)		n-eicosyl-trans ferulate* ($CDCl_3$)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	-	127.9	-	127.1
2	7.14 (dd, J = 2, 8 Hz)	124.0	7.07 (dd, J = 2,8 Hz)	122.9
3	6.87 (d, J = 8.4 Hz)	116.1	6.91 (d, J = 8 Hz)	114.6
4	-	150.3	-	146.7
5	-	149.0	-	147.8
6	7.34 (d, J = 2 Hz)	111.3	7.03 (d, J = 2 Hz)	109.3
7	7.59 (d, J = 16 Hz)	145.6	7.61 (d, J = 16 Hz)	144.6
8	6.39 (d, J = 16 Hz)	116.0	6.29 (d, J = 16 Hz)	115.6
9	-	167.5	-	167.3
1′	4.15 (t)	64.7	4.18 (t)	64.6
2′	1.58 (m)	29.6	1.64 (m)	31.8
3′	1.42 (m)	26.8	1.64 (m)	25.9
-$(CH_2)_{14}$-	1.28 (m)	23.4 -29.6	1.25 (m)	25.9-29.6
n-2	1.28 (m)	32.7	1.25 (m)	31.9
n-1	1.28 (m)	23.4	1.25 (m)	22.7
Me	0.87 (t)	14.4	0.86 (t)	14.1
MeO-5	3.92 (s)	56.42	3.92 (s)	55.9

*A. M. Baldé, M. Claeys, L. A. Pieters, V. Wray and A. J. Vlietinck, Ferulic acid ester from stem bark of *Pavetta owariensis*, *Phytochemistry.*, 1991, **30**, 1024-1026.

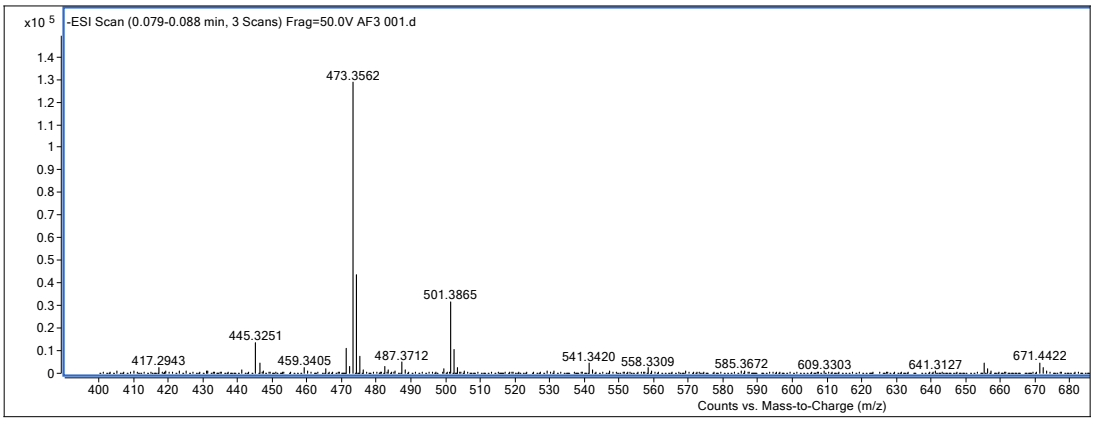

Figure S15. HRESIMS spectrum of **2**

Table S2. NMR spectral data of **3** and denthyrsinin

Position	Compound **3** (acetone-d_6)	Denthyrsinin* ($CDCl_3$)

	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	7.25 (s)	105.9	7.09 (s)	104.9
2	-	148.7	-	146.8
3	-	141.2	-	139.4
4	-	145.4	-	144.0
4a	-	120.4	-	119.2
4b	-	124.8	-	124.2
5	9.15 (d, *J* = 9.2 Hz)	124.2	9.16 (d, *J* = 9.2 Hz)	124.0
6	7.24 (d, *J* = 9.2 Hz)	117.9	7.30 (d, *J* = 9.2 Hz)	116.1
7	-	147.3	-	145.6
8	-	142.2	-	140.8
8a	-	128.5	-	125.7
9	7.85 (d, *J* = 9.2 Hz)	118.6	7.82 (d, *J* = 9.2 Hz)	117.9
10	7.67 (d, *J* = 8.8 Hz)	128.7	7.63 (d, *J* = 9.2 Hz)	127.5
10a	-	126.4	-	126.6
MeO-2	3.99	56.3	4.05 (s)	56.1
MeO-4	3.91	59.6	3.94 (s)	59.8
MeO-8	3.92	61.3	3.98 (s)	61.9
HO-3	7.96 (s)	-	5.79 (s)	-
HO-7	8.31 (s)	-	6.01 (s)	-

* M. Ono, Y. Ito, C. Masuoka, H. Koga and T. Nohar, Antioxidative constituents from *Dendrobii herba* (stems of *Dendrobium* spp.), *Food. Sci. Technol. Int*., 1995, **1**, 115-120.

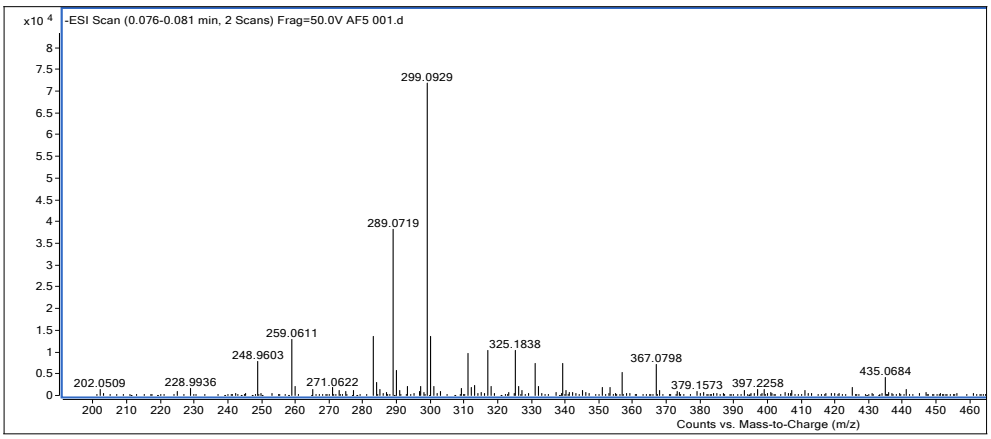

Figure S16**.** HRESIMS spectrum of **3**

Table S3. NMR spectral data of **4** and 2,4-dimethoxy-3,7-dihydroxyphenanthrene

Position	Compound 4 (acetone-d_6)		2,4-dimethoxy-3,7-dihydroxyphenanthrene (CDCl3)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	7.22 (s)	105.9	7.12 (s)	105.0
2	-	148.4	-	147.7
3	-	141.1	-	139.9
4	-	145.3	-	144.5
4a	-	120.0	-	119.1
4b	-	123.9	-	123.0
5	9.34 (d, J = 9.2 Hz)	129.1	9.27 (d, J = 9.0 Hz)	128.0
6	7.18 (dd, J = 9.2, 2.8Hz)	117.4	7.09 (dd, J = 9.0, 2.5Hz)	116.1
7	-	155.9	-	154.8
8	7.24 (d, J = 2.8 Hz)	112.2	7.14 (d, J = 2.5 Hz)	111.1
8a	-	135.0	-	134.2
9	7.45 (d, J = 8.8 Hz)	125.3	7.52 (d, J = 9.0 Hz)	124.3
10	7.59 (d, J = 8.8 Hz)	128.1	7.39 (d, J = 9.0 Hz)	127.0
10a	-	126.4	-	125.8
MeO-2	3.98 (s)	56.3	3.87 (s)	55.2
MeO-4	3.92 (s)	59.6	3.97 (s)	58.6

*K. W. Woo, J. E. Park, S. U, Choi, K. H. Kim and K. L. Lee, Phytochemical constituents of *Bletilla striata* and their cytotoxic activity, *Nat. Prod. Sci*., 2014, **20**, 91-94.

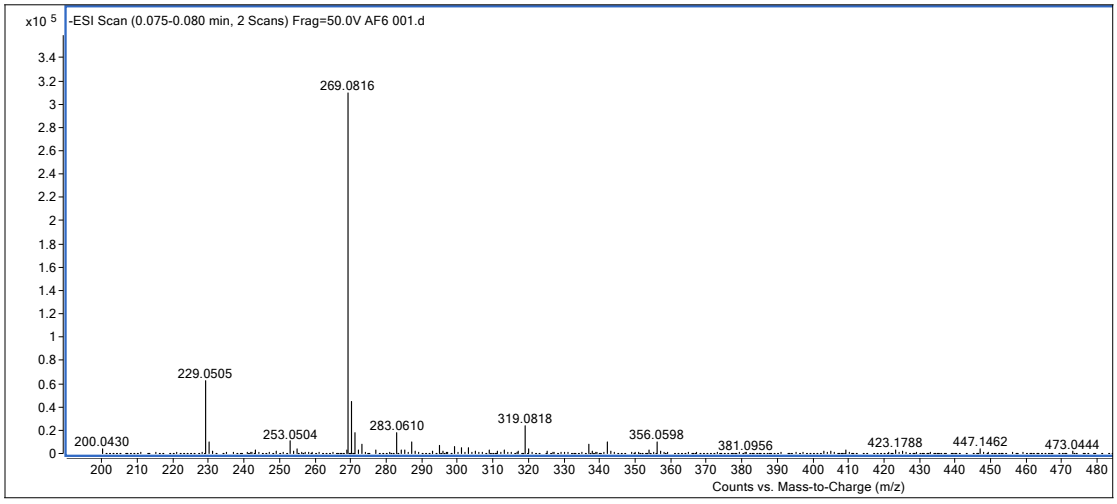

Figure S17. HRESIMS spectrum of **4**

Table S4. NMR spectral data of **5** and 2,7-dihydroxy-3,4,6-trimethoxyphenanthrene

Position	Compound 5 (acetone-d_6)		2,7-dihydroxy-3,4,6-trimethoxyphenanthrene*
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)
1	7.14 (s)	109.7	2.78 (s)
2	-	150.0	-
3	-	142.6	-
4	-	152.1	-
4a	-	118.8	-
4b	-	124.7	-
5	9.04 (s)	108.2	1.09 (s)
6	-	148.7	-
7	-	146.5	-
8	7.25 (s)	112.7	2.91 (s)
8a	-	128.4	-
9	7.48 (d, J = 8.8 Hz)	126.7	2.63 (2H)
10	7.43 (d, J = 8.8 Hz)	125.4	2.63 (2H)
10a	-	130.7	-
MeO-3	4.01 (s)	61.3	5.96 (s)
MeO-4	4.02 (s)	60.4	6.00 (s)
MeO-6	4.04 (s)	56.1	6.07 (s)
HO-2	7.29 (s)	-	4.10 (s)
HO-7	8.28 (s)	-	4.10 (s)

*R. M. Letcher and L. R. M. Nhamo, Chemical constituents of the *Combretaceae.* part III. substituted phenanthrenes, 9,10-dihydrophenanthrenes, and bibenzyls from the heartwood of *Combreturn psidioides, J. Chem. Soc., Perkin. Trans. 1.,* 1972, 2941-2946.

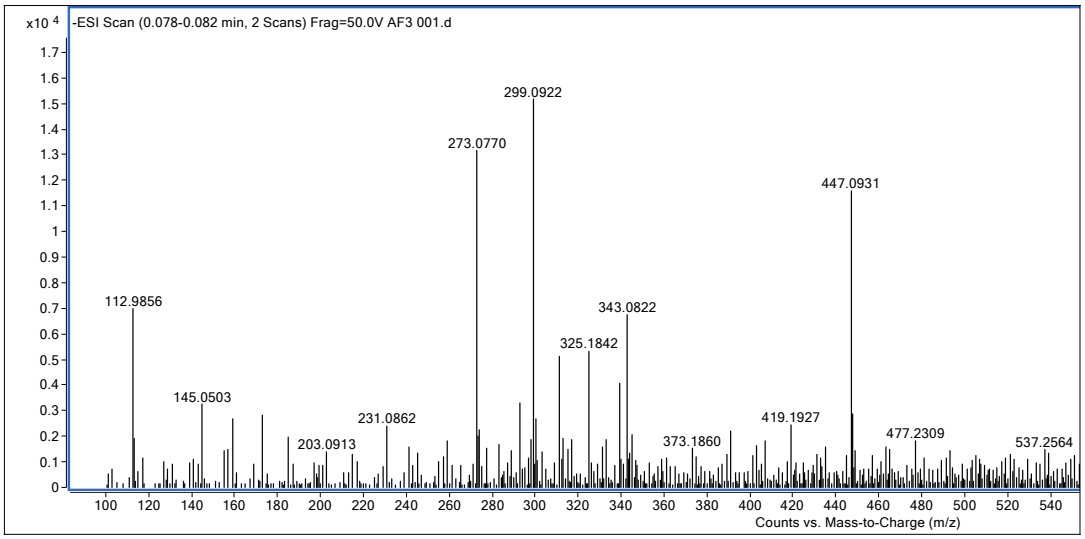

Figure S18. HRESIMS spectrum of **5**

Table S5. NMR spectral data of **6** and 3,7-dihydroxy-2,4,6-trimethoxyphenanthrene

Position	Compound **6** (acetone-d_6)		3,7-dihydroxy-2,4,6-trimethoxyphenanthrene* ($CDCl_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	7.22 (s)	105.6	6.97 (s)	103.6
2	-	144.9	-	146.5
3	-	140.6	-	138.3
4	-	148.3	-	143.0
4a	-	126.7	-	117.4
4b	-	124.2	-	122.2
5	9.06 (s)	108.1	8.95 (s)	106.1
6	-	148.4	-	146.6
7	-	146.5	-	144.3
8	7.25 (s)	105.9	7.19 (s)	110.4
8a	-	128.8	-	126.9
9	7.45 (d, *J* = 8.8 Hz)	124.9	7.31(s)	122.8
10	7.51 (d, *J* = 8.8 Hz)	125.7	7.31(s)	123.7
10a	-	119.5	-	124.9
MeO-2	4.04 (s)	59.8	3.88 (s)	54.0
MeO-4	3.99 (s)	56.2	3.85 (s)	57.8
MeO-6	3.98 (s)	56.0	3.97 (s)	53.8

*Y. Chen, J. Xu, H. Yu, C. Qing, Y. Zhang, Y. Liu and J. Wang. 3,7-Dihydroxy-2,4^6-trimethoxyphenanthrene, A New Phenanthrene from *Bulbophyllum odoratissimum, J. Korean Chem. Soc.*, 2007, **51**, 352-355.

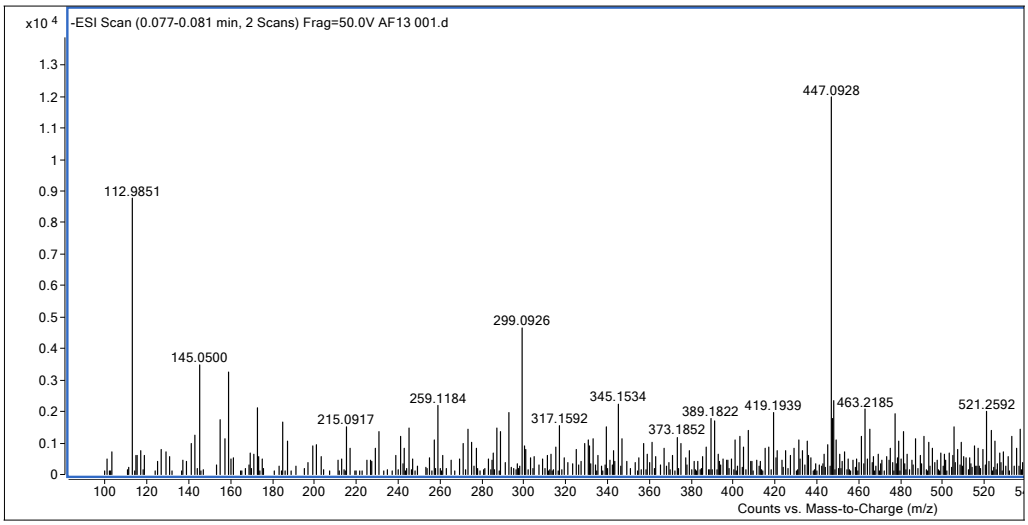

Figure S19. HRESIMS spectrum of **6**

Table S6. NMR spectral data of **7** and agrostonin

Position	Compound 7 (acetone-d_6)		Agrostonin* (acetone-d_6)	
	δ_H (mult., J in Hz)	δ_C	δ_H (mult., J in Hz)	δ_C
1	-	109.1	-	109.8
2	-	154.1	-	155.1
3	7.02 (s)	99.1	7.00 (s)	100.0
4	-	159.3	-	160.2
4a	-	115.4	-	116.3
4b	-	125.0	-	125.8
5	9.27 (s)	159.0	9.25 (s)	109.7
6	-	147.7	-	148.5
7	-	145.2	-	146.0
8	7.21 (s)	111.3	7.19 (s)	112.2
8a	-	127.1	-	128.1
9	7.37 (d, J = 8.8 Hz)	127.0	7.36 (d, J = 9.2 Hz)	127.9
10	6.92 (d, J = 9.2 Hz)	122.5	6.93 (d, J = 9.2 Hz)	123.3
10a	-	134.6	-	135.4
1′	-	109.1	-	109.8
2′	-	154.1	-	155.1
3′	7.02 (s)	99.1	7.00 (s)	100.0
4′	-	159.3	-	160.2
4a′	-	115.4	-	116.3
4b′	-	125.0	-	125.8
5′	9.27 (s)	159.0	9.25 (s)	109.7
6′	-	147.7	-	148.5
7′	-	145.2	-	146.0

8′	7.21 (s)	111.3	7.19 (s)	112.2
8a′	-	127.1	-	128.1
9′	7.37 (d, *J* = 8.8 Hz)	127.0	7.36 (d, *J* = 9.2 Hz)	127.9
10′	6.92 (d, *J* = 9.2 Hz)	122.5	6.93 (d, *J* = 9.2 Hz)	123.3
10a′	-	134.6	-	135.4
MeO-4	4.25 (s)	55.3	4.23 (s)	55.6
MeO-6	4.09 (s)	55.2	4.07 (s)	56.0
MeO-4′	4.25 (s)	55.3	4.23 (s)	56.1
MeO-6′	4.09 (s)	55.2	4.07 (s)	56.0

*C. Lin, T. Hwang, F. Chen, C. Huang, H. Hung and T. Wu, Chemical constituents of the rhizomes of *Bletilla formosana* and their potential anti-inflammatory activity, *J. Nat. Prod.,* 2016, **79,** 1911-1921.

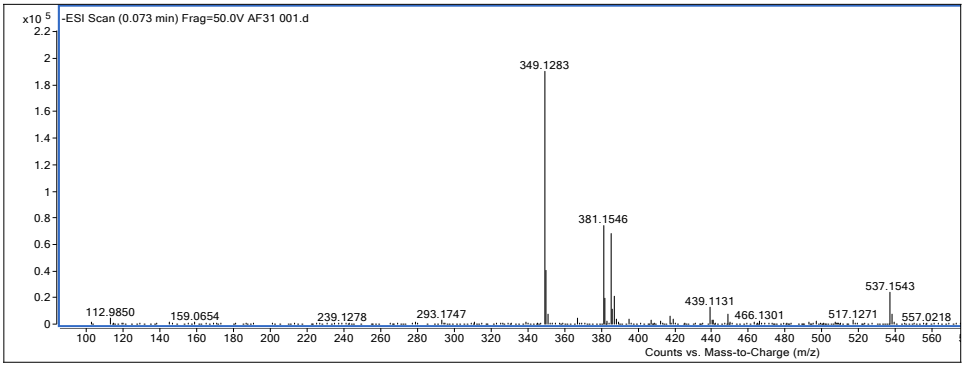

Figure S20. HRESIMS spectrum of **7**

Table S7. NMR spectral data of **8** and trans-n-coumaroyltyramine

Position	Compound 8 (acetone-d_6)		Trans-N-coumaroyltyramine*(CD_3OD)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	127.8	-	127.7
2	7.41 (d, *J* = 6.8 Hz)	130.1	7.41 (d, *J* = 8.4 Hz)	130.5
3	6.85 (d, *J* = 6.8 Hz)	116.5	6.80 (d, *J* = 8.4 Hz)	116.2
4	-	160.0	-	160.5
5	6.85 (d, *J* = 6.8 Hz)	116.5	6.80 (d, *J* = 8.4 Hz)	116.2
6	7.41 (d, *J* = 6.8 Hz)	130.1	7.41 (d, *J* = 8.4 Hz)	130.5
7	7.45 (d, *J* = 15.6 Hz)	140.0	6.38 (d, *J* = 15.5 Hz)	141.8
8	6.47 (d, *J* = 15.6 Hz)	119.7	7.44 (d, *J* = 15.5 Hz)	118.4
9	-	166.4	-	169.2
1′	-	131.1	-	131.3
2′	7.06 (d, *J* = 7.2 Hz)	130.5	7.06 (d, *J* = 8.6 Hz)	130.7
3′	6.76 (d, *J* = 6.4 Hz)	116.0	6.73 (d, *J* = 8.6 Hz)	116.7
4′	-	156.7	-	156.9
5′	6.76 (d, *J* = 6.4 Hz)	116.0	6.73 (d, *J* = 8.6 Hz)	116.7
6′	7.06 (d, *J* = 7.2 Hz)	130.5	7.06 (d, *J* = 8.6 Hz)	130.7

7′	2.74 (t, *J* =7.2 Hz)	35.7	2.75 (t, *J* = 7.5 Hz)	35.8
8′	3.45 (t, *J* =7.2 Hz)	41.9	3.46 (t, *J* = 7.5 Hz)	42.5

*A. M. Al-Taweel, S. Perveen, A. M. El-Shafae, G. A. Fawzy, A. Malik, N. Afza, L. Iqbal and M. Latif, Bioactive phenolic amides from *Celtis africana*, *Molecules*, 2012, **17**, 2675-2682.

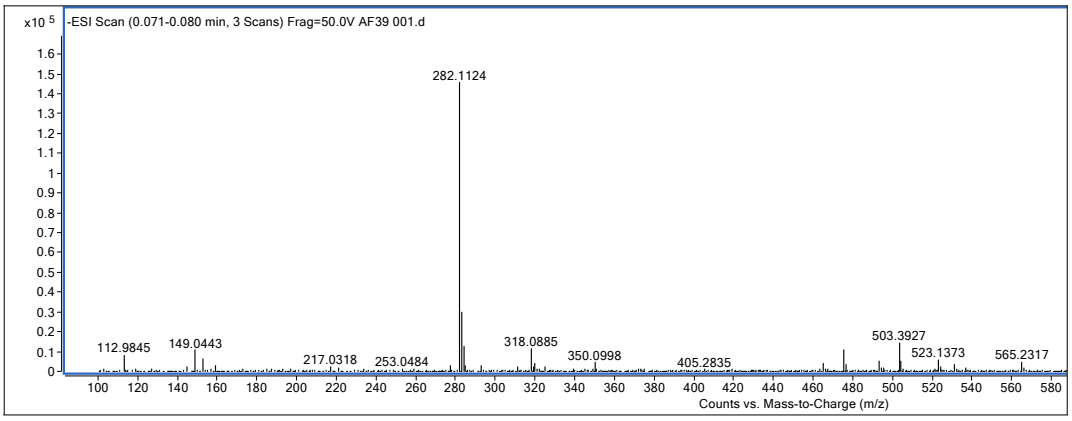

Figure S21. HRESIMS spectrum of **8**

Table S8. NMR spectral data of **9** and syringaresinol

Position	Compound 9 (acetone-d_6)		Syringaresinol* ($CDCl_3$)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	113.2	-	132.1
2	6.68 (s)	104.4	6.59 (s)	102.8
3	-	148.6	-	147.2
4	-	136.2	-	134.4
5	-	148.6	-	147.2
6	6.68 (s)	104.4	6.59 (s)	102.8
7	4.67 (d, *J* = 4 Hz)	86.8	4.73 (d, *J* = 4.3 Hz)	86.0
8	3.09 (m)	55.3	3.10 (m)	54.3
9a	4.22 (dd)	72.3	4.28 (dd, *J* = 8.8, 6.4 Hz)	71.8
9b	3.84	72.3	3.92	71.8
1′	-	113.2	-	132.1
2′	6.68 (s)	104.4	6.59 (s)	102.8
3′	-	148.6	-	147.2
4′	-	136.2	-	134.4
5′	-	148.6	-	147.2
6′	6.68 (s)	104.4	6.59 (s)	102.8
7′	4.67 (d, *J* = 4 Hz)	86.8	4.73 (d, *J* = 4.3 Hz)	86.0

8′	3.09 (m)	55.3	3.10 (m)	54.3
9′a	4.22 (dd)	72.3	4.28 (dd, *J* = 8.8, 6.4 Hz)	71.8
9′b	3.84	72.3	3.92	71.8
MeO-3	3.83 (s)	56.6	3.89 (s)	56.4
MeO-5	3.82 (s)	56.6	3.89 (s)	56.4
MeO-3′	3.83 (s)	56.6	3.89 (s)	56.4
MeO-5′	3.82 (s)	56.6	3.89 (s)	56.4

*M. Ono, Y. Ito, C. Masuoka, H. Koga and T. Nohar, Antioxidative constituents from *Dendrobii herba* (stems of *Dendrobium* spp.), *Food. Sci. Technol. Int*., 1995, **1**, 115-120.

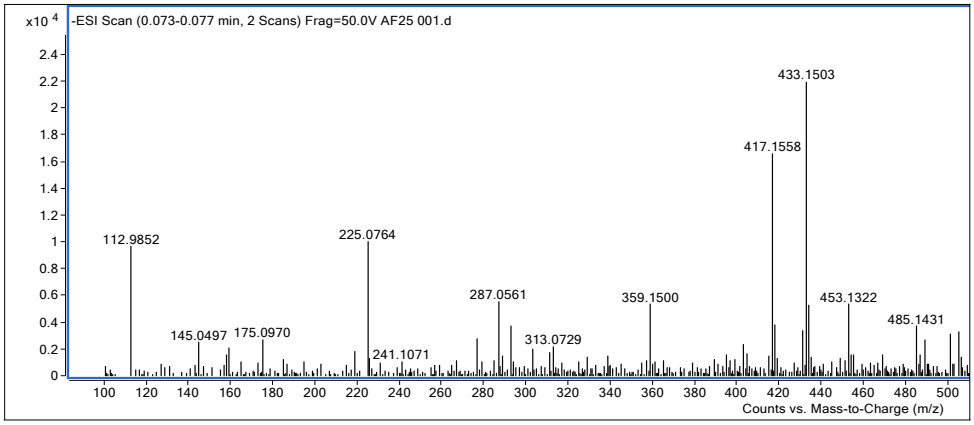

Figure S22. HRESIMS spectrum of **9**

Table S9. NMR spectral data of **10** and trans-n-feruloytyramine

Position	Compound 10 (acetone-d_6)		Trans-N-Feruloytyramine* (CD_3OD)	
	δ_H (mult., *J* in Hz)	δ_C	δ_H (mult., *J* in Hz)	δ_C
1	-	128.3	-	128.2
2	7.15 (d, *J* = 2.0 Hz)	111.2	7.13 (d, *J* = 1.2 Hz)	111.5
3	-	149.0	-	149.3
4	-	148.6	-	149.8
5	6.83 (d, *J* = 8.0 Hz)	116.0	6.81 (d, *J* = 8.5 Hz)	116.4
6	7.03 (dd, *J* = 8.0 Hz, 2.0 Hz)	122.5	7.04 (dd, *J* = 8.5, 1.2 Hz)	123.2
7	7.44 (d, *J* = 15.6 Hz)	140.2	7.44 (d, *J* = 15.6 Hz)	142.0
8	6.50 (d, *J* = 15.6 Hz)	120.0	6.41 (d, *J* = 15.5 Hz)	118.7
9	-	166.3	-	169.2
1′	-	131.2	-	131.3
2′	7.06 (d, *J* = 8.4 Hz)	130.5	7.07 (d, *J* = 8.4 Hz)	130.7
3′	6.75 (d, *J* = 8.4 Hz)	116.0	6.73 (d, *J* = 8.4 Hz)	116.2
4′	-	156.7	-	156.9
5′	6.75 (d, *J* = 8.4 Hz)	116.0	6.73 (d, *J* = 8.4 Hz)	116.2
6′	7.06 (d, *J* = 8.4 Hz)	130.5	7.07 (d, *J* = 8.4 Hz)	130.7

7′	2.74 (t, *J* = 7.6 Hz)	35.0	2.76 (t, *J* = 7.5 Hz)	35.8
8′	3.48 (t, *J* = 7.6 Hz)	41.9	3.47 (t, *J* = 7.5 Hz)	42.5
MeO-3	3.88 (s)	56.2	3.85 (s)	56.4

*A. M. Al-Taweel, S. Perveen, A. M. El-Shafae, G. A. Fawzy, A. Malik, N. Afza, L. Iqbal and M. Latif, Bioactive phenolic amides from *Celtis africana*, *Molecules*, 2012, **17**, 2675-2682.

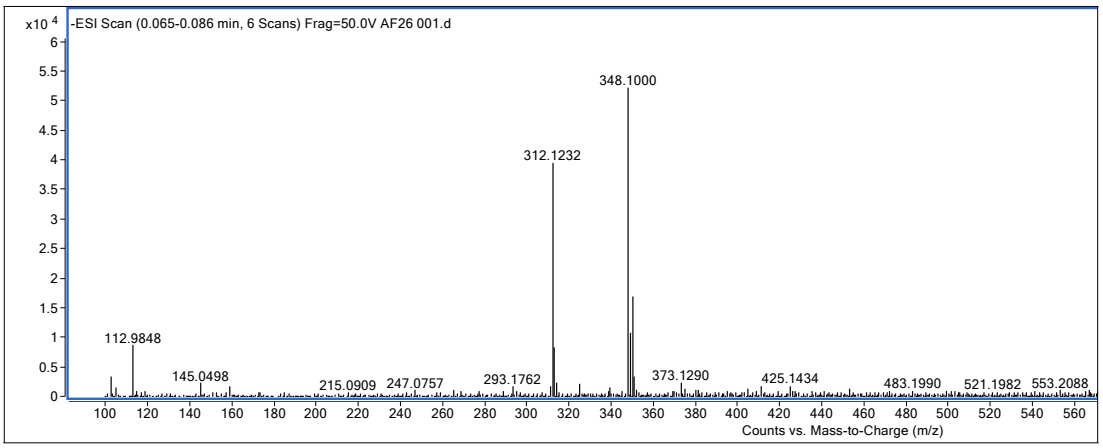

Figure S23. HRESIMS spectrum of **10**

Table S10. Effects of constituents of *Aerides falcata* on the viability of BV-2 microglial cells

Comp.	Percentage cell viability (mean ± SD) (%)					
	Vehicle	**5 µM**	**10 µM**	**20 µM**	**40 µM**	**80 µM**
1	100.0 ± 0.0	102.2 ± 4.1	44.1 ± 11.7***	19.9 ± 2.7***	15.3 ± 1.0***	13.4 ± 0.6***
2	100.0 ± 0.0	100.7 ± 1.9	97.3 ± 5.5	99.5 ± 3.9	101.3 ± 2.6	103.1 ± 0.6
3	100.0 ± 0.0	97.9 ± 3.1	101.9 ± 5.0	109.2 ± 3.5	122.7 ± 4.7	77.6 ± 7.2***
4	100.0 ± 0.0	102.3 ± 7.	104.9 ± 2.8	98.4 ± 6.4	96.1 ± 6.9	70.0 ± 1.8***
5	100.0 ± 0.0	102.2 ± 3.0	100.2 ± 5.5	102.3 ± 4.1	85.4 ± 1.4***	83.8 ± 0.2***
6	100.0 ± 0.0	100.7 ± 3.6	103.0 ± 3.6	99.2 ± 3.1	98.6 ± 5.7	84.9 ± 2.7***
7	100.0 ± 0.0	100.7 ± 4.6	94.5 ± 2.3	72.8 ± 9.1***	36.9 ± 7.3***	32.9 ± 8.6***
9	100.0 ± 0.0	98.1 ± 0.5	86.1 ± 4.4**	79.7 ± 4.3***	73.7 ± 2.8***	58.1 ± 8.3***
10	100.0 ± 0.0	99.0 ± 2.7	100.4 ± 6.6	98.5 ± 7.3	100.0 ± 2.1	82.3 ± 5.6**

The statical differences were analyzed using one-way ANOVA followed by Dunnett's post-hoc test. **p< 0.01, ***p<0.001 denote significantly reduced cell viability; vehicle (0.5% DMSO) vs. other groups of treatments.

Table S11. Effects of compounds **1**, **7**, and **9** on the viability of C6 glioblastoma cells

Comp.	Percentage cell viability (mean ± SD) (%)							
	Vehicle	**2.5 µM**	**5 µM**	**10 µM**	**20 µM**	**40 µM**	**80 µM**	**160 µM**
1	100.0 ± 0.0	96.4 ± 3.5	84.6 ± 2.2***	85.0 ± 3.2***	62.1 ± 6.3***	39.7 ± 6.8***	9.6 ± 0.5***	7.9 ± 1.0***
7	100.0 ± 0.0	96.4 ± 0.9	79.6 ± 8.3**	63.0 ± 8.4***	58.7 ± 8.4***	42.0 ± 0.2***	36.3 ± 3.4***	29.9 ± 1.7***
9	100.0 ± 0.0	98.2 ± 6.5	82.5 ± 3.8**	74.5 ± 9.2***	71.7 ± 3.7***	61.8 ± 3.6***	55.5 ± 5.7***	45.1 ± 3.0***

The statical differences were analyzed using one-way ANOVA followed by Dunnett's post-hoc test. **p< 0.001, ***p<0.001 denote significantly reduced cell viability; vehicle (0.5% DMSO) vs. other groups of treatments.