Electronic Supplementary Information

New dictyodendrins as BACE inhibitors from a southern Australian marine sponge, *Ianthella* sp.

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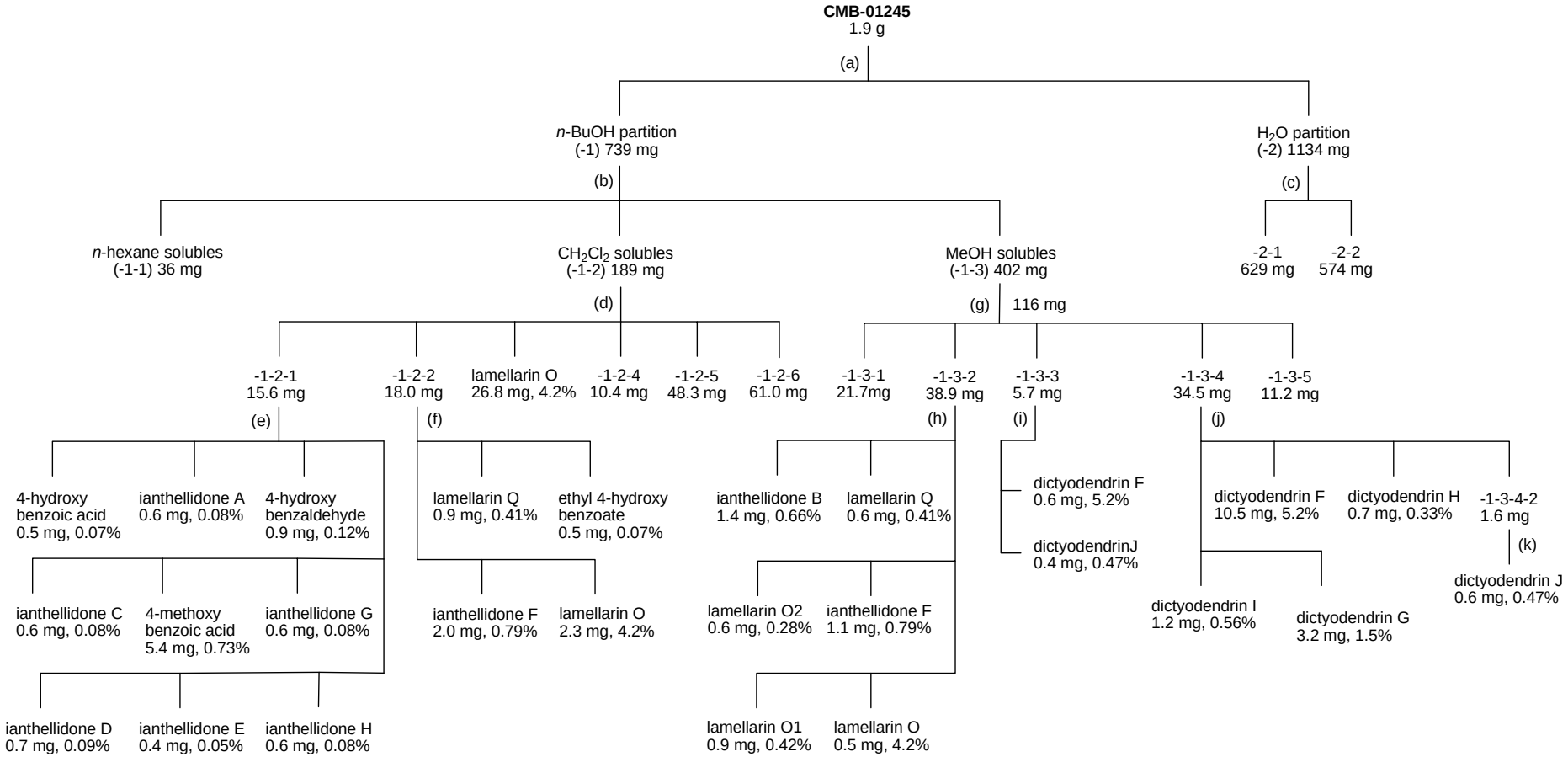
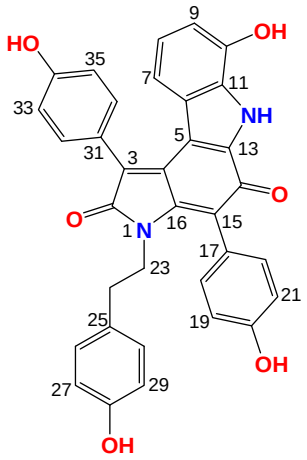
Scheme 1. Fractionation of *Ianthella* sp.



(a) Partition [*n*-BuOH (-1) and H_2O (-2)].
(b) Trituration [*n*-hexane (-1-1), CH_2Cl_2 (-1-2), and MeOH (-1-3)].
(c) Trituration [MeOH (-2-1), H_2O (-2-2)].
(d) SPE fractionation [Alltech 5g C18 SPE cartridge, from 30% MeOH/H_2O with 10% increment to MeOH, each 10 mL elution]
(e) HPLC separation [Zorbax SB-C18, 4 mL/min., 20-40% MeCN/H_2O (0.01% TFA) in 15 min, detect at 230, 254, 280 and 330 nm]
(f) HPLC separation [Zorbax SB-C18, 4 mL/min., 30-45% MeCN/H_2O in 15 min. then change to 60% MeCN/H_2O in 1min. and then hold for 4 min, detect at 230, 254, 280 and 330 nm]
(g) SPE fractionation [Alltech 5g C18 SPE cartridge, from 30% MeOH/H_2O with 10% increment to MeOH, each 10 mL elution]
(h) HPLC separation [Zorbax SB-C18, 4 mL/min., 25-50% MeCN/H_2O in 15 min, detect at 210, 230 and 330 nm]
(i) HPLC separation [Zorbax SB-C18, 4 mL/min., 40-60% MeCN/H_2O in 15 min, detect at 210, 230 and 330 nm]
(j) HPLC separation [Zorbax SB-C18, 4 mL/min., 40-60% MeCN/H_2O in 15 min, detect at 230, 254, 280 and 330 nm]
(k) HPLC separation [Sc-C18-A1, 1 mL/min., 60-90% MeOH/H_2O (0.01% TFA) in 15 min, detect at 210, 230 and 330 nm]

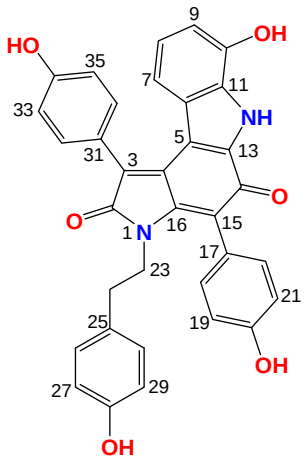


dictyodendrin F (**1**)

Table S1a. ^{1}H NMR (methanol-d_4, 600 MHz) data for dictyodendrin F (**1**).

No	**1 (Experimental)** δ_H (m, *J* (Hz))	**1 (Literature)**[1] δ_H (m, *J* (Hz))
7	5.83 (dd, 7.8, 1.2)	5.82 (dd, 7.3, 1.9)
8	6.55-6.60*	6.58 (t, 7.3)
9	6.55-6.60*	6.57 (dd, 7.3, 1.9)
18/22	7.25 (d, 8.6)	7.24 (d, 8.5)
19/21	6.94 (d, 8.6)	6.93 (d, 8.5)
23	3.43 (t like, 7.8)	3.42 (t, 7.8)
24	2.41 (t like, 7.8)	2.40 (t, 7.8)
26/30	6.55-6.60*	6.56 (d, 8.5)
27/29	6.66 (d, 8.5)	6.66 (d, 8.5)
32/36	7.32 (d, 8.6)	7.31 (d, 8.5)
33/35	6.90 (d, 8.6)	6.89 (d, 8.5)

* Overlapping signals

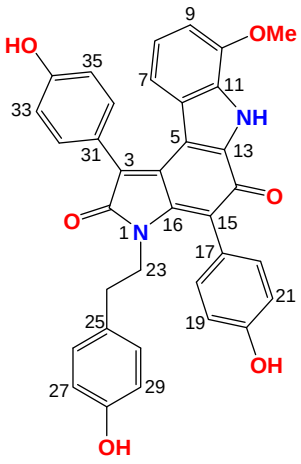


dictyodendrin F (**1**)

Table S1b. 1D and 2D NMR (pyridine-d_5, 600 MHz) data for dictyodendrin F (**1**).

No.	δ_C [A]	δ_H [B] (m, *J* (Hz))	COSY	HMBC (^{1}H to ^{13}C)
2	172.3			
3	128.9			
4	134.9[C]			
5	114.0			
6	126.7			
7	116.4	6.66 (d, 8.2)	H-8	C-5, C-6, C-9, C-11
8	122.9	6.96 (dd, 8.2, 7.5)	H-7, H-9	C-6, C-10
9	109.9	7.05 (d, 7.5)	H-8	C-7, C-10, C-11
10	147.1			
11	131.7			
13	134.2[C]			
14	180.4			
15	118.5			
16	149.6			
17	124.2			
18/22	133.9	7.65 (d, 8.3)	H-19/21	C-15, C-19/21, C-20
19/21	116.3	7.36 (d, 8.3)	H-18/22	C-17, C-20
20	159.8			
23	44.0	3.86 (t, 8.1)	H-24	C-2, C-16, C-24, C-25
24	35.0	2.76 (t, 8.1)	H-23	C-23, C-25, C-26/30
25	129.6			
26/30	130.9	7.05 (d, 8.3)	H-27/29	C-24, C-28
27/29	116.6	7.09 (d, 8.3)	H-26/30	C-25, C-28
28	157.9			
31	123.7			
32/36	133.8	7.92 (d, 8.3)	H-33/35	C-3, C-33/35, C-34
33/35	116.6	7.38 (d, 8.3)	H-32/36	C-31, C-34
34	160.8			

[A] ^{13}C NMR assignments were supported by HSQC experiment; [B] 12-NH and 10, 20, 28 and 34-OH were all resolved as very broadened peaks at 14.54, 12.46, 12.18, 11.90 and 11.28 ppm, respectively, and could not be assigned; [C] Interchangeable signals within the column.

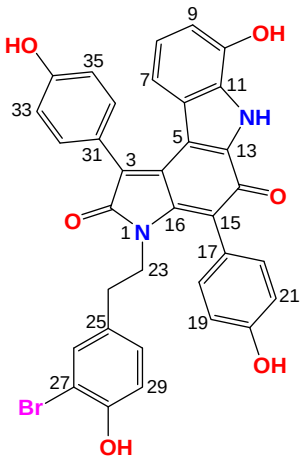


dictyodendrin G (**2**)

Table S2. 1D and 2D NMR (pyridine-d_5, 600 MHz) data for dictyodendrin G (**2**).

No.	δ_C [A]	δ_H (m, *J* (Hz))	COSY	HMBC (^{1}H to ^{13}C)
2	172.2			
3	129.2			
4	134.6[B]			
5	113.9			
6	126.0			
7	117.7	6.64 (d, 8.3)	H-8	C-5, C-6, C-9, C-11
8	122.4	6.91 (dd, 8.3, 7.7)	H-7, H-9	C-6, C-9, C-10
9	105.5	6.76 (d, 7.7)	H-8	C-7, C-10, C-11
10	148.4			
11	131.0			
13	134.2[B]			
14	180.2			
15	118.5			
16	149.4			
17	124.0			
18/22	133.8	7.62 (d, 8.2)	H-19/21	C-15, C-19/21, C-20
19/21	116.3	7.35 (d, 8.2)	H-18/22	C-17, C-20
20	159.7			
23	43.9	3.83 (t, 8.1)	H-24	C-2, C-16, C-24, C-25
24	35.0	2.73 (t, 8.1)	H-23	C-23, C-25, C-26/30
25	129.4			
26/30	130.8	7.03 (d, 8.3)	H-27/29	C-24, C-28
27/29	116.5	7.09 (d, 8.3)	H-26/30	C-25, C-28
28	157.8			
31	123.5			
32/36	133.7	7.88 (d, 8.4)	H-33/35	C-3, C-33/35, C-34
33/35	116.6	7.39 (d, 8.4)	H-32/36	C-31, C-34
34	160.8			
10-OMe	55.8	3.86 (s)		C-10

[A] ^{13}C NMR assignments were supported by HSQC experiment; [B] Interchangeable signals within the column.

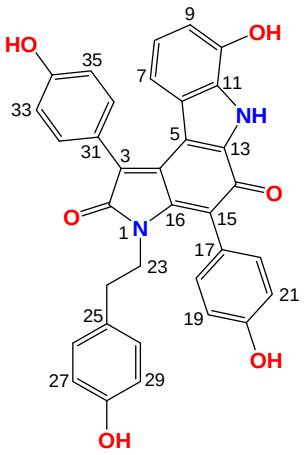


dictyodendrin H (**3**)

Table S3. 1D and 2D NMR (pyridine-d_5, 600 MHz) data for dictyodendrin H (**3**).

No.	δ_C [A]	δ_H (m, *J* (Hz))	COSY	HMBC (^{1}H to ^{13}C)
2	172.1			
3	128.8			
4	ND			
5	113.8			
6	126.6			
7	116.3	6.64 (d, 8.2)	H-8	C-5, C-9, C-11
8	122.9	6.94 (dd, 8.2, 7.6)	H-7, H-9	C-6, C-9, C-10
9	109.9	7.06 (d, 7.6)	H-8	C-7, C-10, C-11
10	146.9			
11	131.5			
13	ND			
14	ND			
15	118.4			
16	149.2			
17	124.0			
18/22	133.8	7.63 (d, 8.5)	H-19/21	C-15, C-20
19/21	116.3	7.38 (d, 8.5)	H-18/22	C-17, C-20
20	159.7			
23	43.6	3.81 (t, 8.2)	H-24	C-2, C-16
24	34.5	2.69 (t, 8.2)	H-23	C-23, C-25, C-26, C-30
25	131.1			
26	134.1	7.37 (d, 2.1)		C-24, C-27, C-28, C-30
27	111.3			
28	154.4			
29	117.0	7.08 (d, 8.2)	H-30	C-25, C-27
30	129.8	6.92 (dd, 8.2, 2.1)	H-29	C-24, C-26, C-28
31	123.6			
32/36	133.8	7.91 (d, 8.6)	H-33/35	C-3, C-34
33/35	116.6	7.39 (d, 8.6)	H-32/36	C-31, C-34
34	160.7			

[A] ^{13}C NMR assignments were supported by HSQC experiment; [ND] Signals not detected.

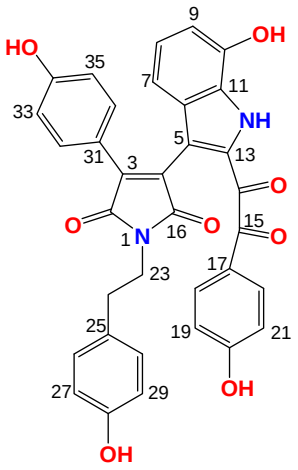


dictyodendrin I (**4**)

Table S4. 1D and 2D NMR (pyridine-d_5, 600 MHz) data for dictyodendrin I (**4**).

No.	δ_C [A]	δ_H (m, *J* (Hz))	COSY	HMBC (^{1}H to ^{13}C)
2	172.3			
3	128.8			
4	134.9[B]			
5	113.9			
6	126.6			
7	116.4	6.65 (d, 8.2)	H-8	C-5, C-6, C-9, C-11
8	123.0	6.93 (dd, 8.2, 7.6)	H-7, H-9	C-6, C-9, C-10
9	109.9	7.06 (d, 7.6)	H-8	C-7, C-10, C-11
10	147.0			
11	131.6			
13	134.1[B]			
14	180.3			
15	118.5			
16	149.4			
17	124.0			
18/22	133.8	7.62 (d, 8.3)	H-19/21	C-15, C-20
19/21	116.3	7.38 (d, 8.3)	H-18/22	C-17, C-20
20	159.8			
23	43.7	3.81 (t, 8.1)	H-24	C-2, C-16, C-24
24	34.3	2.68 (t, 8.1)	H-23	C-23, C-25, C-26, C-30
25	131.8			
26	140.3	7.66 (d, 1.9)		C-24, C-27, C-28, C-30
27	86.3			
28	157.2			
29	115.8	7.02 (d, 8.2)	H-30	C-25, C-27, C-28[W]
30	130.8	6.95 (dd, 8.2, 1.9)	H-29	C-24, C-26, C-28
31	123.6			
32/36	133.8	7.92 (d, 8.5)	H-33/35	C-3, C-34
33/35	116.5	7.39 (d, 8.5)	H-32/36	C-31, C-34
34	160.7			

[A] ^{13}C NMR assignments were supported by HSQC experiment; [B] Interchangeable signals within the column.



dictyodendrin J (**5**)

Table S5. 1D and 2D NMR (MeOH-d_4, 600 MHz) data for dictyodendrin J (**5**).

No.	δ_C [A]	δ_H (m, *J* (Hz))	COSY	HMBC (^{1}H to ^{13}C)
2	172.3			
3	138.5			
4	129.6 [B]			
5	114.8			
6	129.4			
7	114.2	6.53 (dd, 8.1, 0.7)	H-8	C-5, C-6, C-9, C-11
8	123.7	6.82 (dd, 8.1, 7.5)	H-7, H-9	C-6, C-10
9	111.2	6.71 (dd, 7.5, 0.7)	H-8	C-7, C-10, C-11
10	145.9			
11	130.6			
13	[B, ND]			
14	187.0			
15	192.4			
16	172.3			
17	126.0			
18/22	134.3	7.76 (d, 8.9)	H-19/21	C-15, C-20
19/21	116.8	6.79 (d, 8.9)	H-18/22	C-17, C-20
20	165.5			
23	41.0	3.57 (t, 7.6)		C-2, C-16, C-24, C-25
24	34.8	2.58 (br s)		
25	130.5			
26/30	131.0	6.96 (d, 8.5)	H-27/29	C-24, C-27/29, C-28
27/29	116.4	6.70 (d, 8.5)	H-26/30	C-25, C-28
28	157.2			
31	121.9			
32/36	132.9	7.35 (d, 8.9)	H-33/35	C-3, C-34
33/35	116.4	6.59 (d, 8.9)	H-32/36	C-31, C-34
34	160.8			

[A] ^{13}C NMR assignments were supported by HSQC experiment; [B] Interchangeable signals within the column; [ND] Signals not detected.

Figure S1a. ^{1}H NMR (methanol-d_4, 600 MHz) spectrum for dictyodendrin F (**1**).

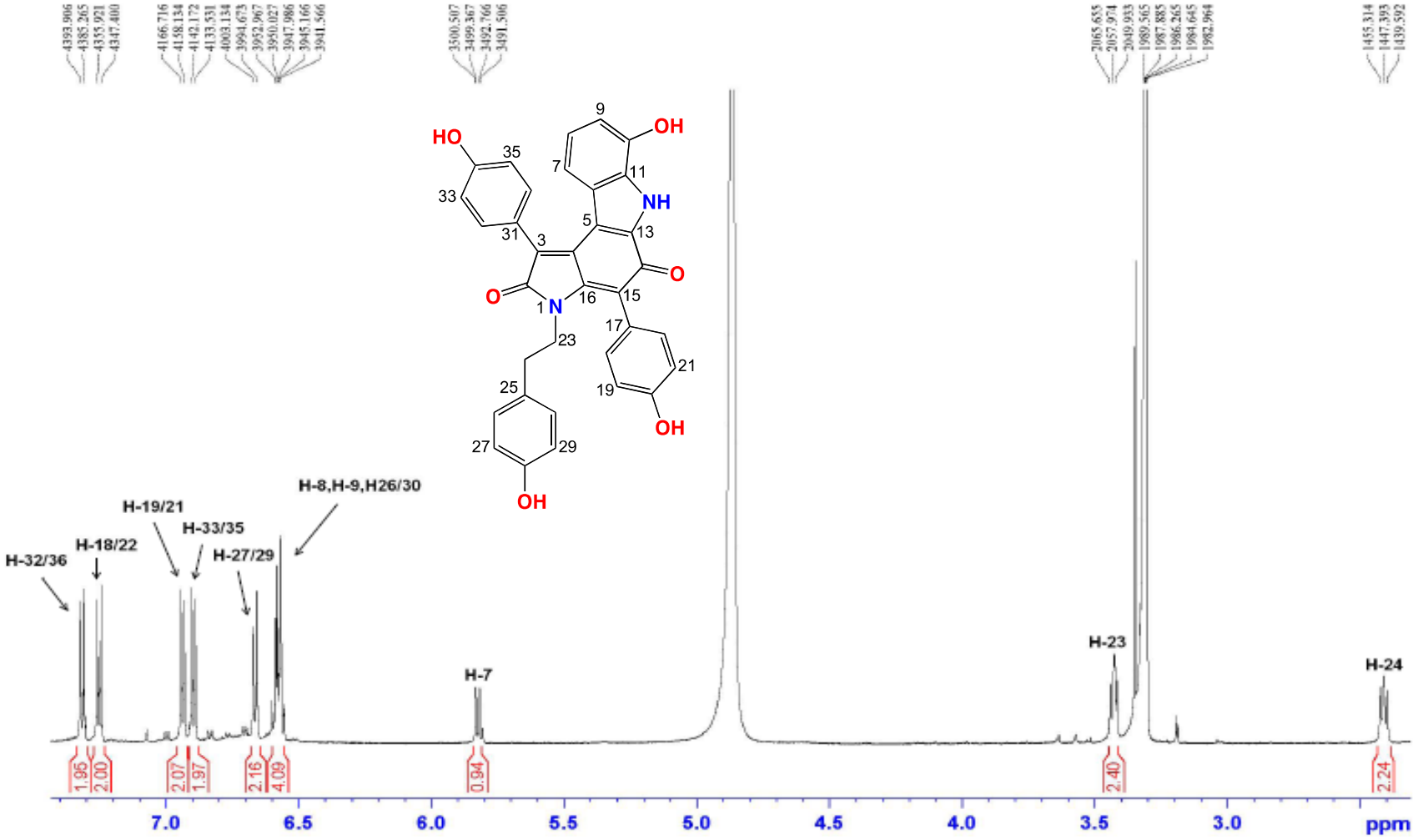


Figure S1b. ^{1}H NMR (pyridine-d_5, 600 MHz) spectrum for dictyodendrin F (**1**).

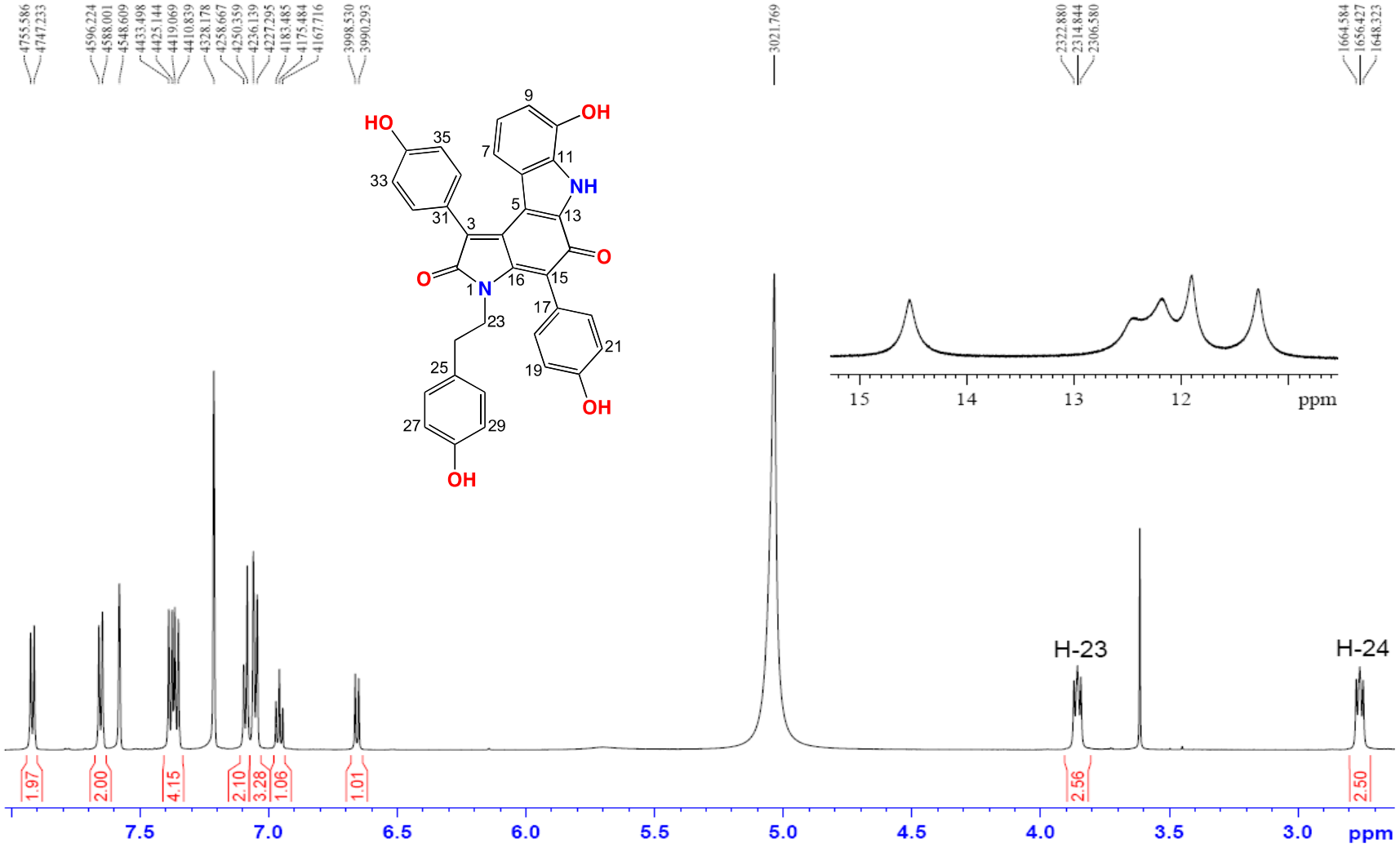


Figure S1c. ^{1}H NMR (pyridine-d_5, 600 MHz) expansion for dictyodendrin F (**1**).

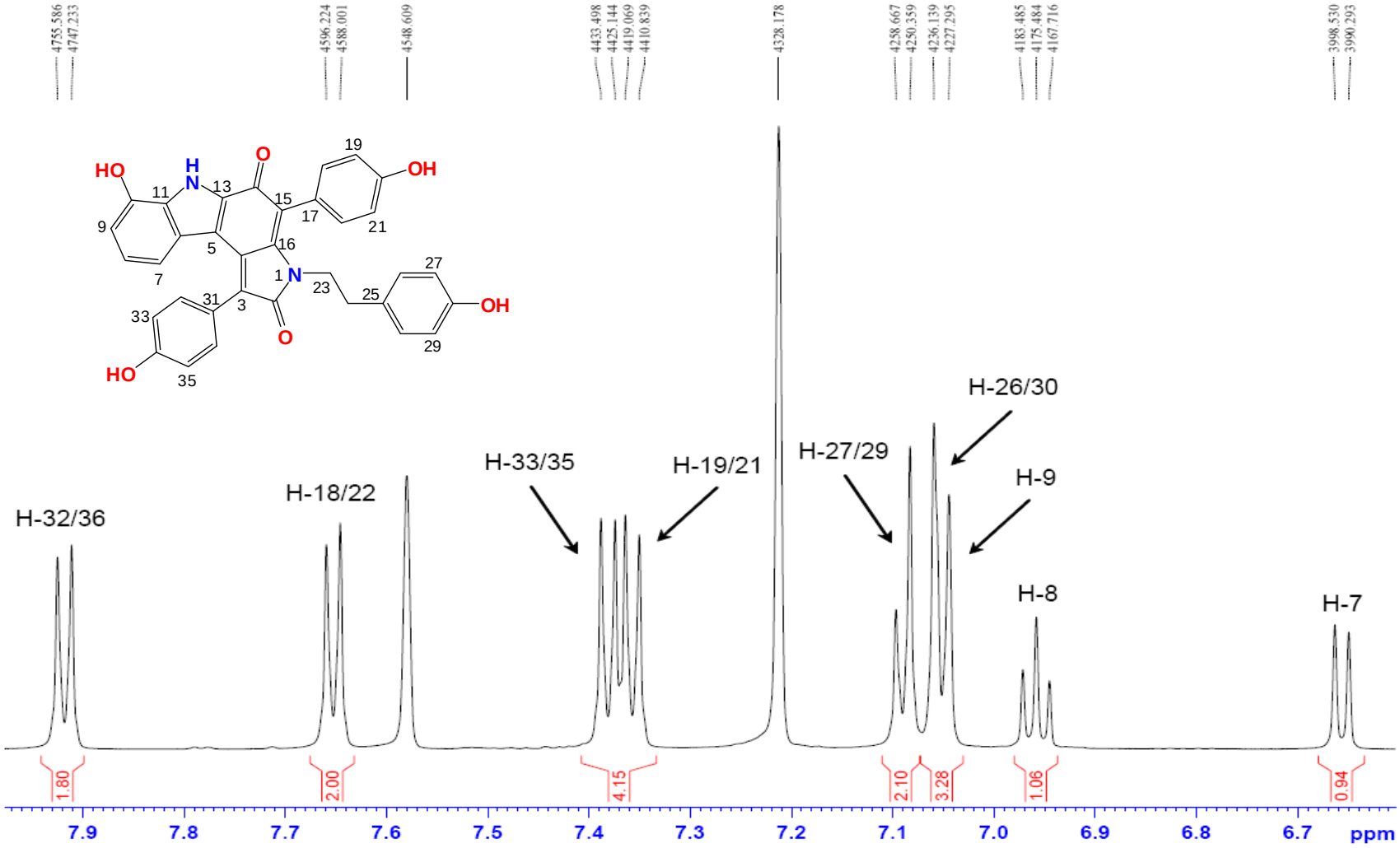


Figure S1d. ^{13}C NMR (pyridine-d_5, 150 MHz) spectrum for dictyodendrin F (**1**).

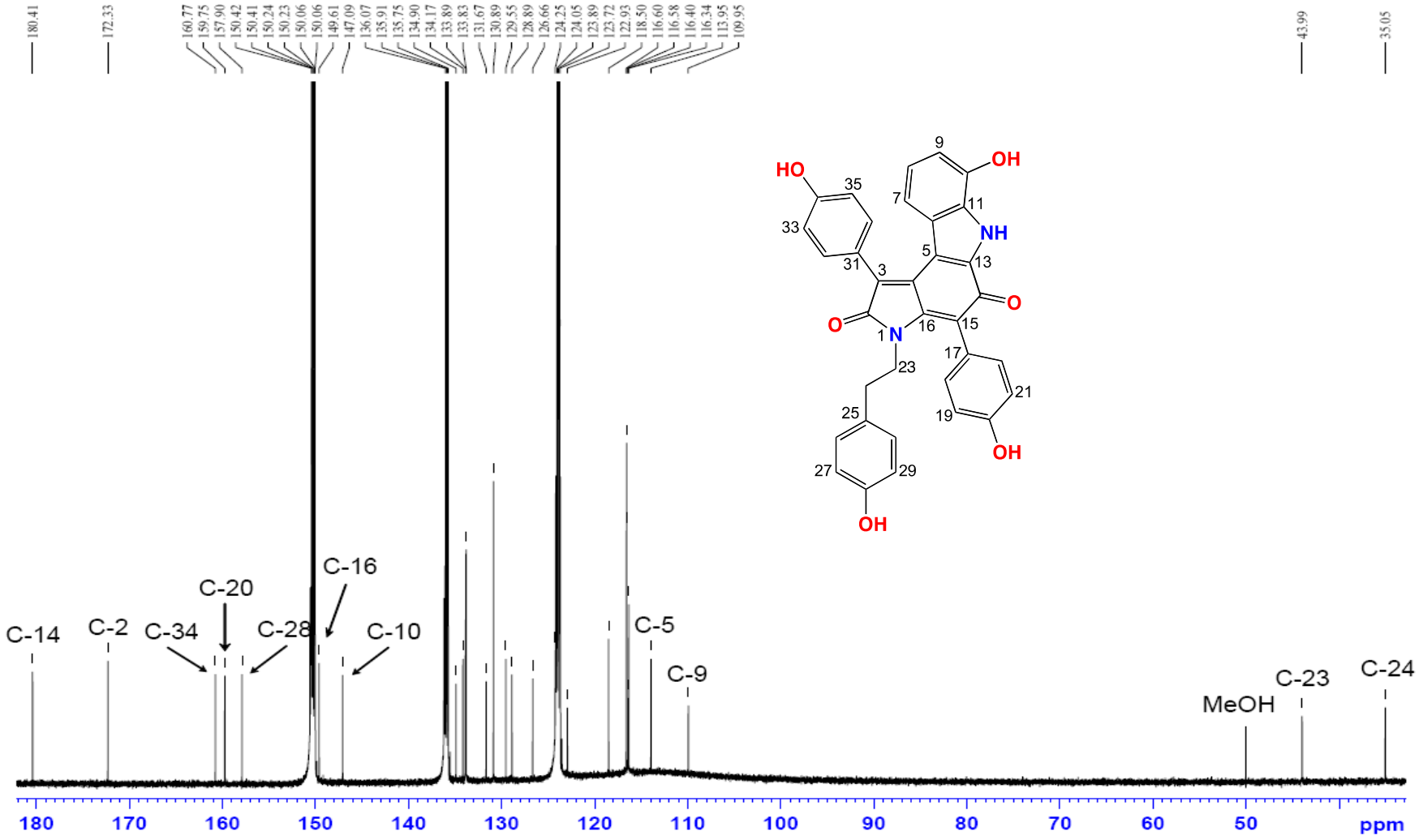


Figure S1e. ^{13}C NMR (pyridine-d_5, 150 MHz) expansion for dictyodendrin F (**1**).

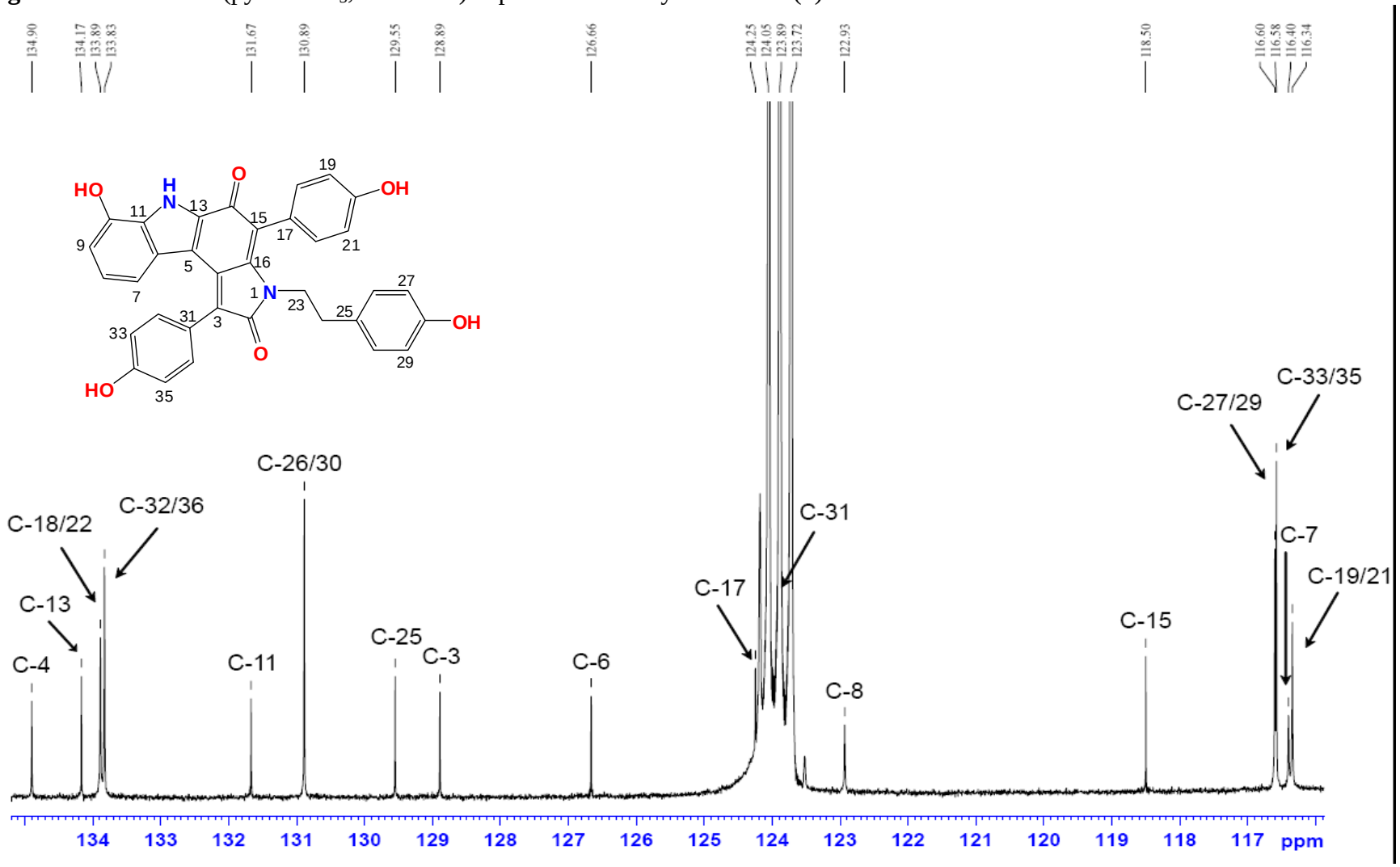
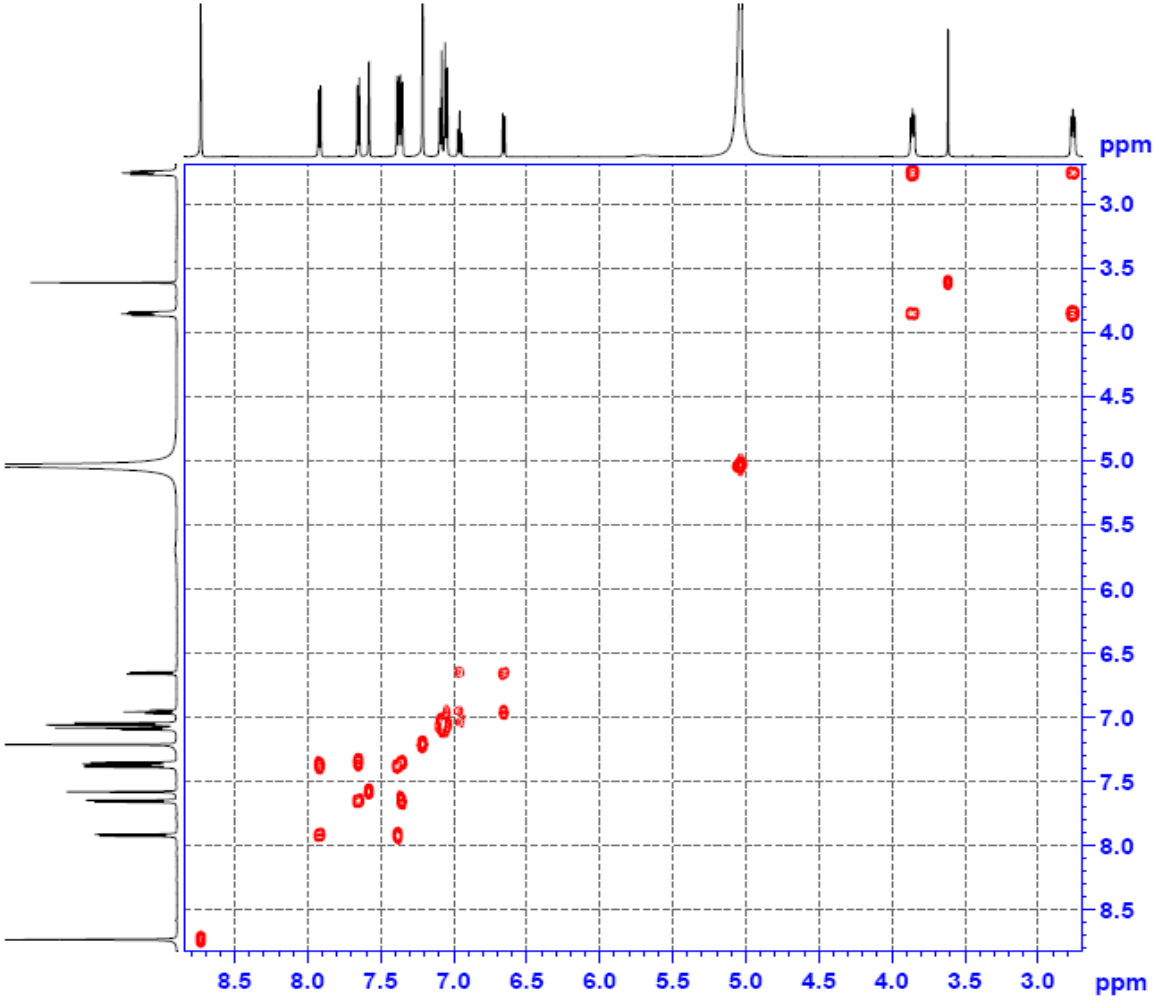


Figure S1f. gCOSY (pyridine-d_5, 600 MHz) spectrum for dictyodendrin F (**1**).



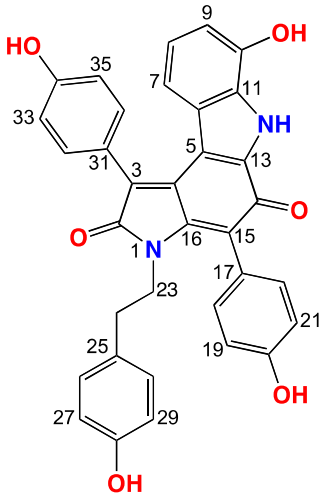


Figure S1g. HSQC (pyridine-d_5, 600 MHz) spectrum for dictyodendrin F (**1**).

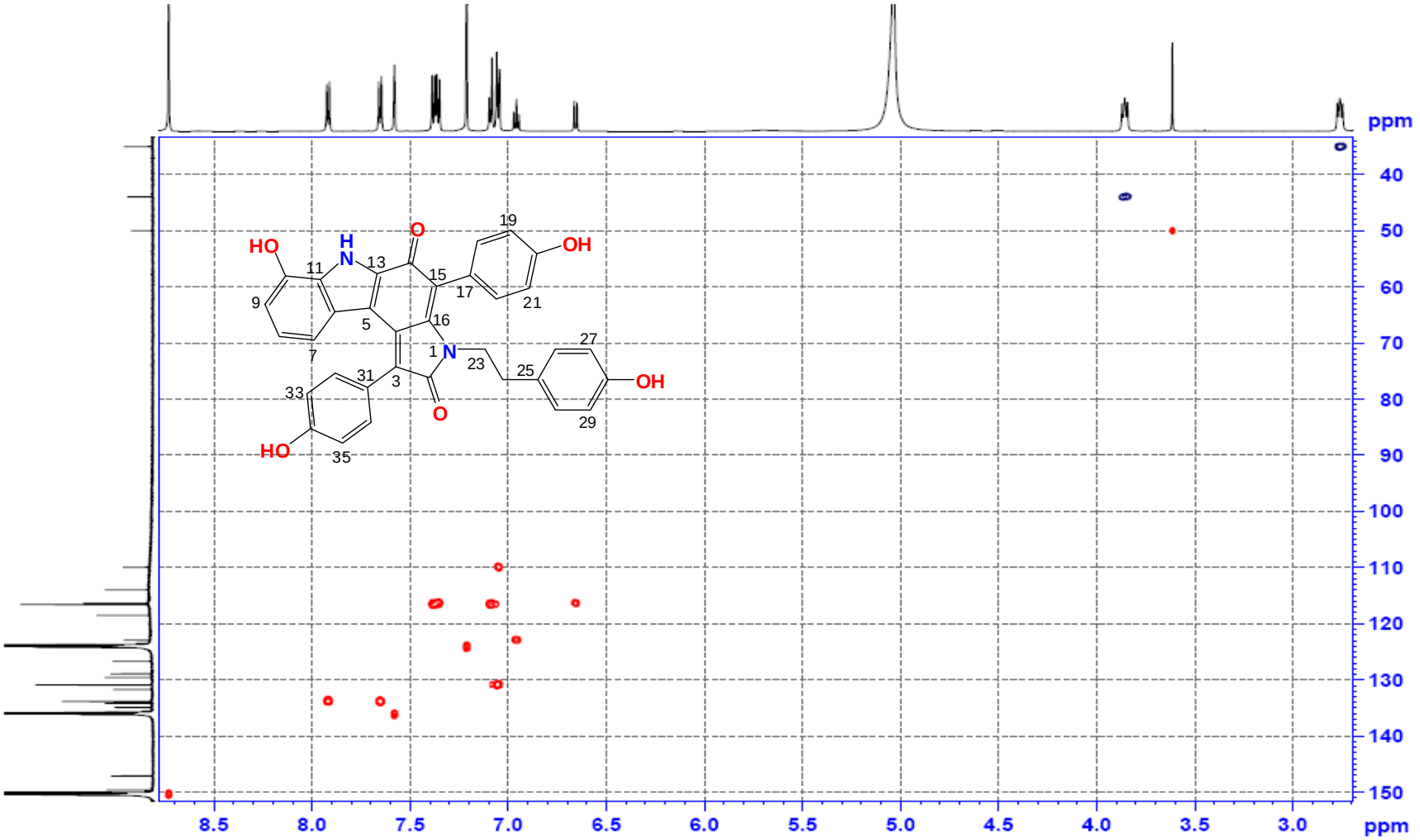


Figure S1h. HSQC (pyridine-d_5, 600 MHz) expansion for dictyodendrin F (**1**).

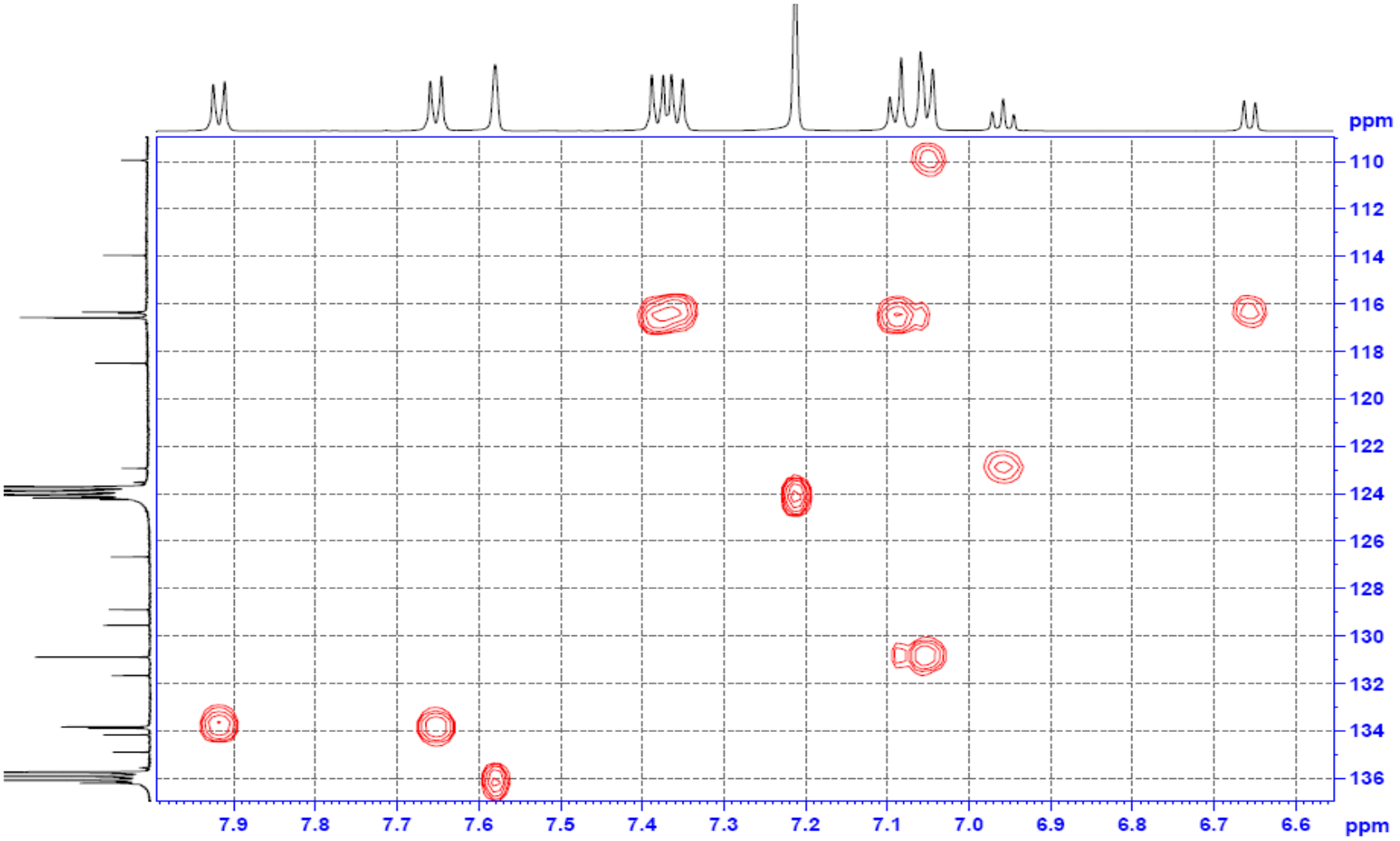


Figure S1i. HMBC (pyridine-d_5, 600 MHz) spectrum for dictyodendrin F (**1**).

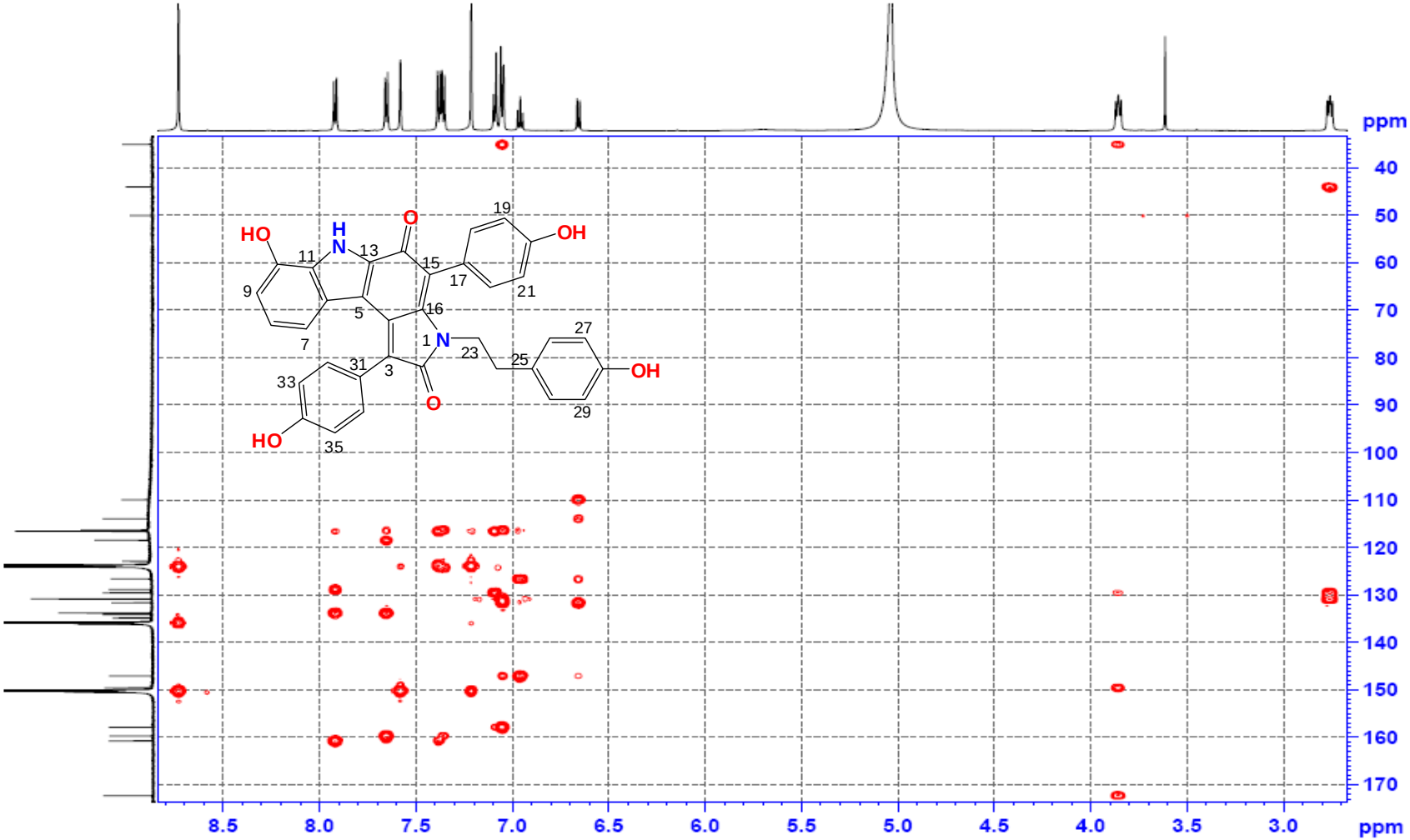


Figure S1j. HMBC (pyridine-d_5, 600 MHz) expansion for dictyodendrin F (**1**).

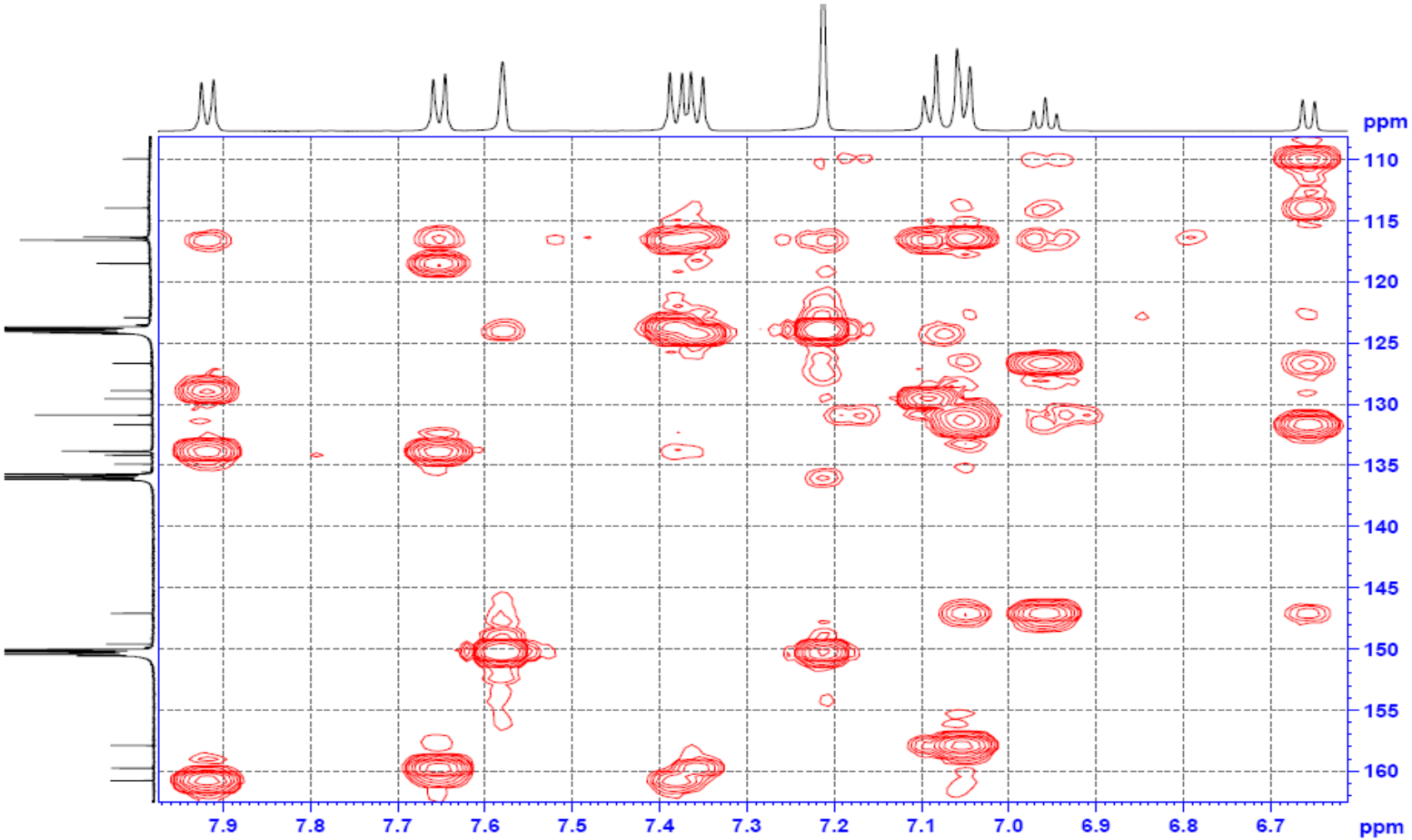


Figure S2. ^{1}H NMR (pyridine-d_5, 600 MHz) spectrum for dictyodendrin G (**2**).

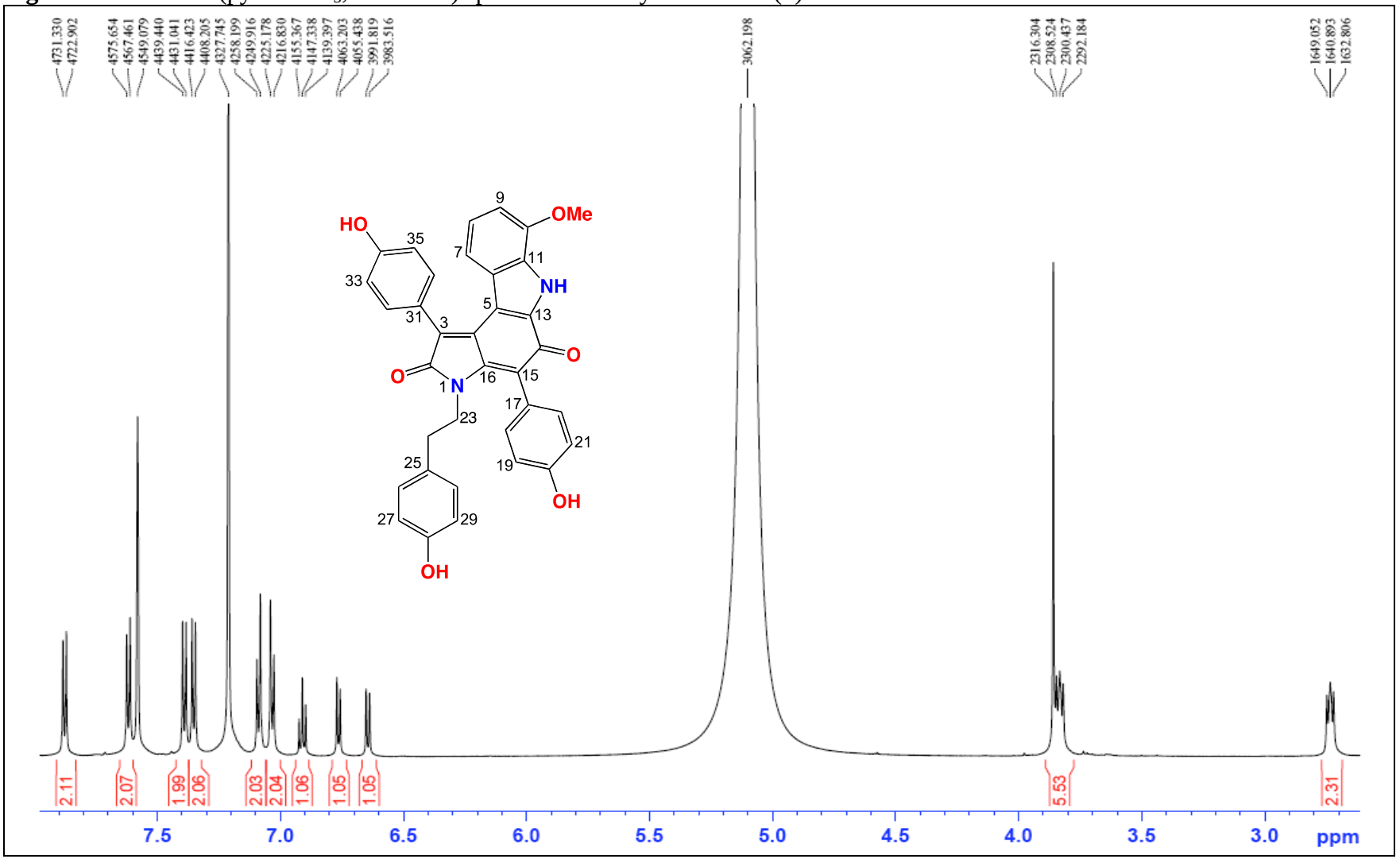


Figure S3 ^{1}H NMR (pyridine-d_5, 600 MHz) spectrum for dictyodendrin H (**3**).

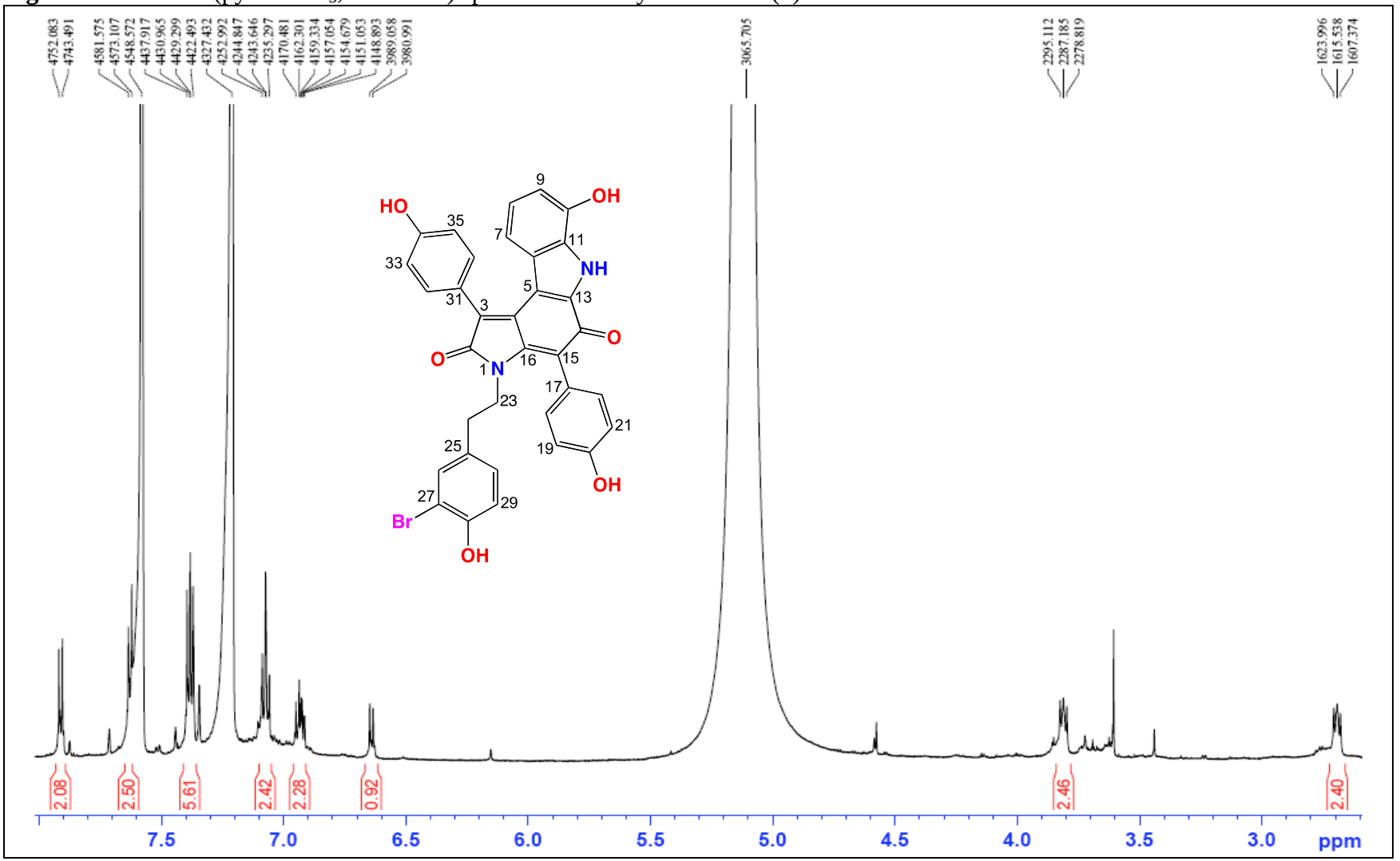


Figure S4 ^{1}H NMR (pyridine-d_5, 600 MHz) spectrum for dictyodendrin I (**4**).

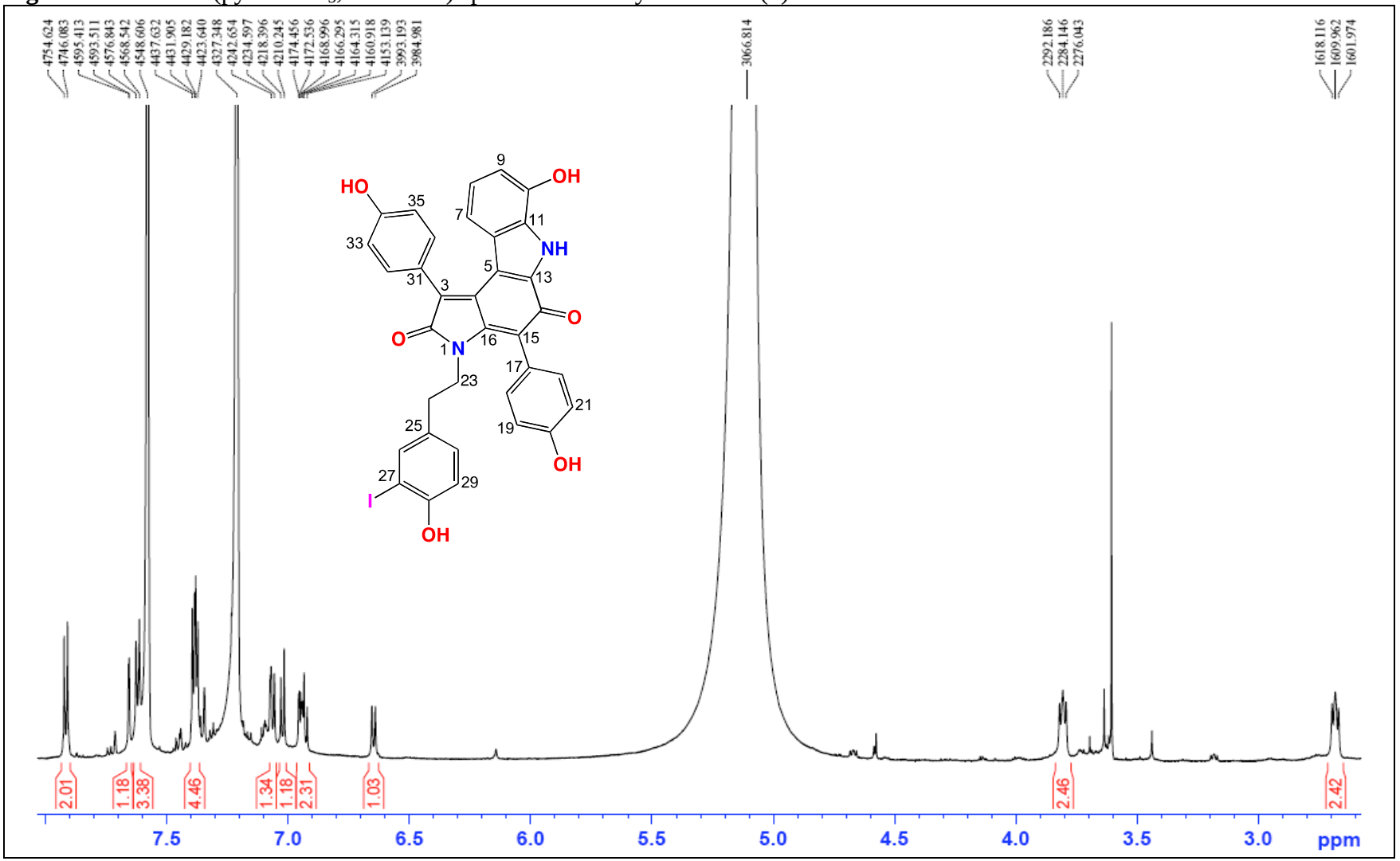


Figure S5 ^{1}H NMR (MeOH-d_4, 600 MHz) spectrum for dictyodendrin J (**5**).

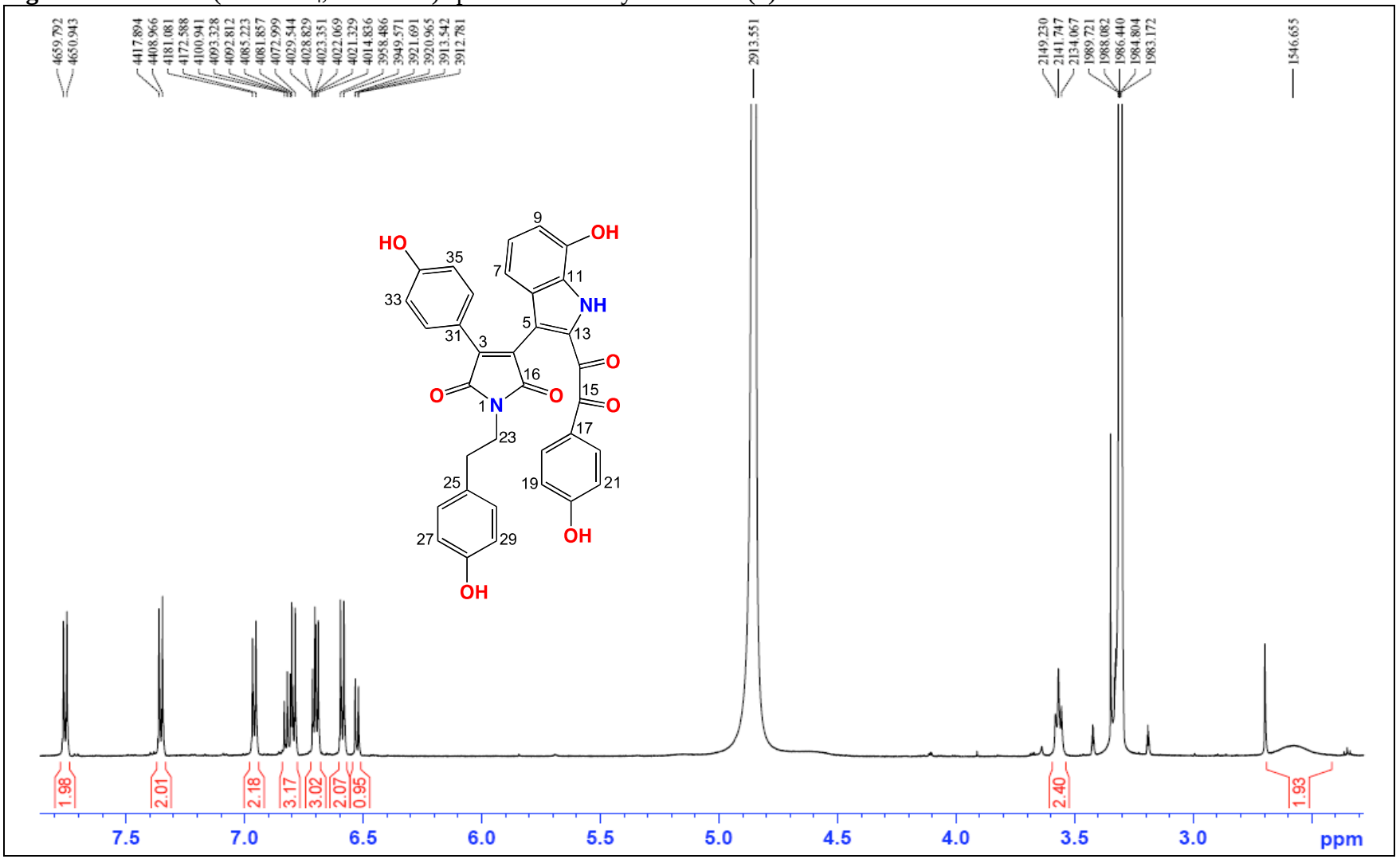


Figure S6 BACE assay data for compounds **1–5**.

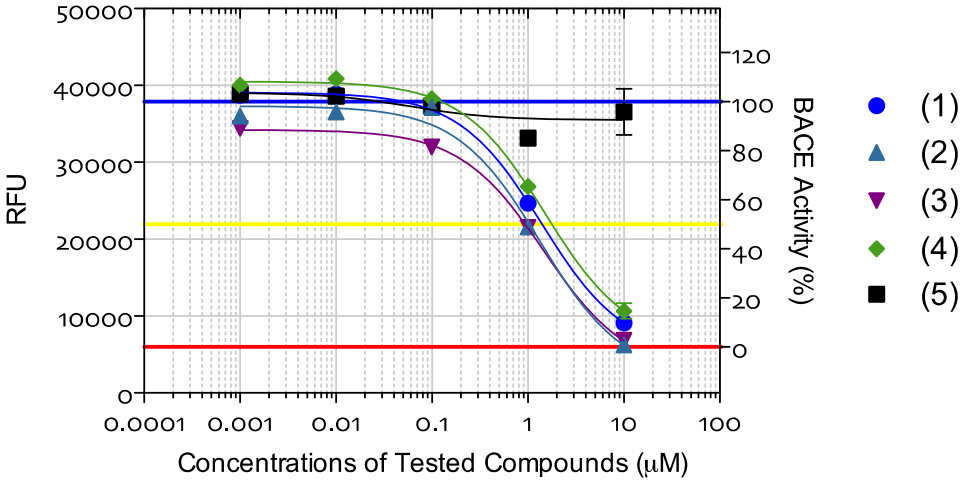
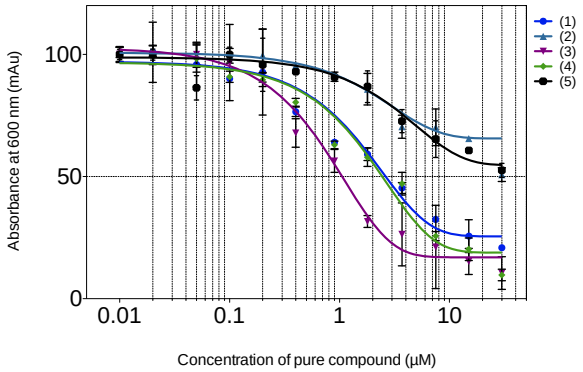
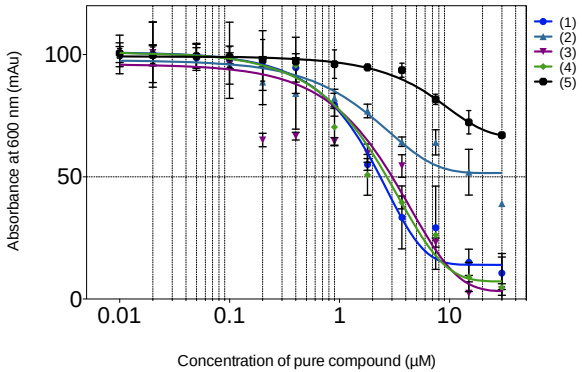


Figure S7 Antibacterial and antifungal screening results for compounds **1–5**.

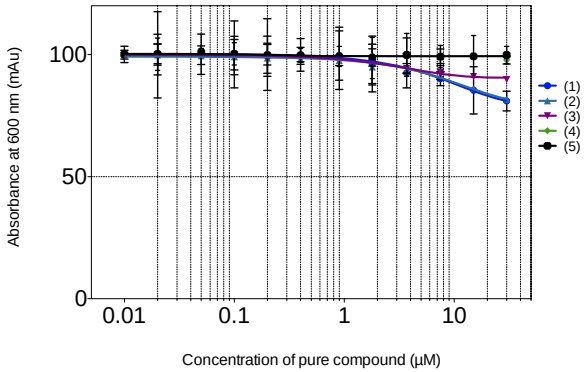
Bacillus subtilis ATCC 6051



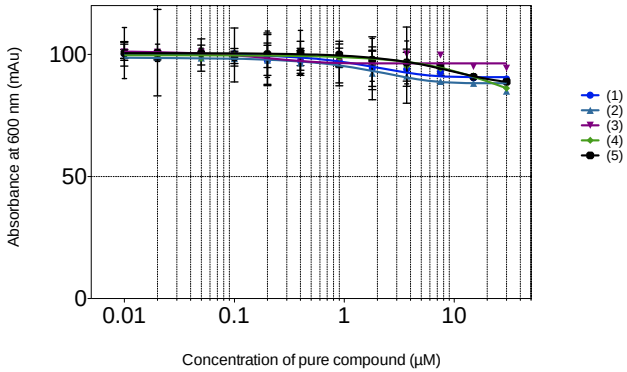
Bacillus subtilis ATCC 6633



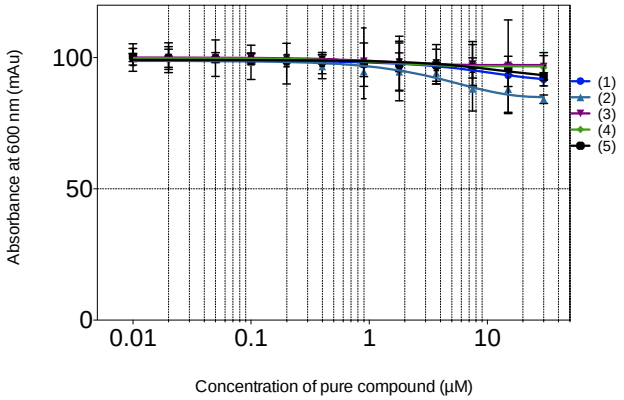
Staphylococcus aureus ATCC 9144



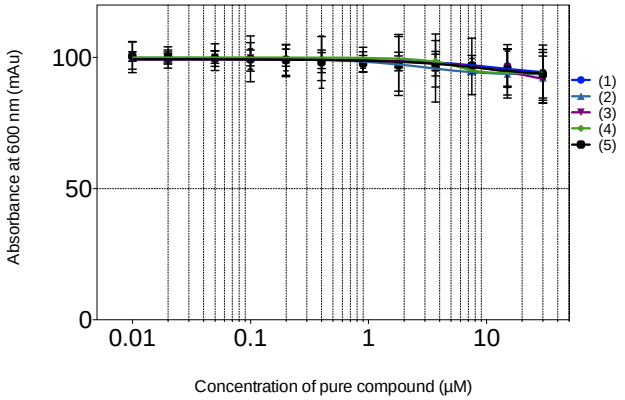
Staphylococcus aureus ATCC 25923



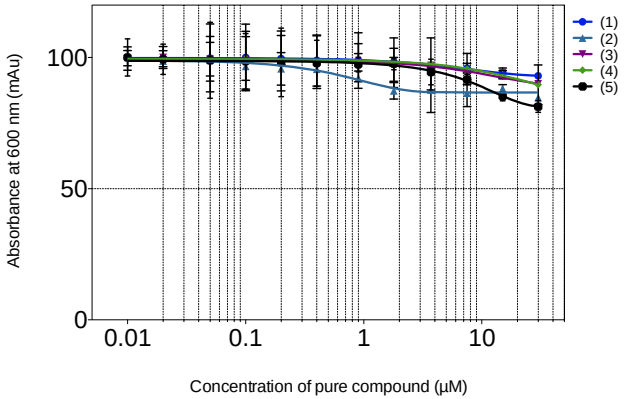
Escherichia coli ATCC 11775



Pseudomonas aeruginosa ATCC 10145



Candida albicans ATCC 90028



	***Escherichia coli* ATCC 11775**		***Pseudomonas aeruginosa* ATCC 10145**		***Staphylococcus aureus* ATCC 25923**		***Staphylococcus aureus* ATCC 9144**		***Bacillus subtilis* ATCC 6051**		***Bacillus subtilis* ATCC 6633**		***Candida albicans* ATCC 90028**	
Compounds	**MIC (μM)**	**IC_{50} (μM)**	**MIC (μM)**	**IC_{50} (μM)**	**MIC (μM)**	**IC_{50} (μM)**	**MIC (μM)**	**IC_{50} (μM)**	**MIC (μM)**	**IC_{50} (μM)**	**MIC (μM)**	**IC_{50} (μM)**	**MIC (μM)**	**IC_{50} (μM)**
(1)	--	--	--	--	--	--	--	--	7.5	2.7	3.7	2.3	--	--
(2)	--		--	--	--	--	--	--	--	--	--	--	--	--
(3)	--		--	--	--	--	--	--	1.8	1.2	7.5	3.1	--	--
(4)	--	--	--	--	--	--	--	--	7.5	2.5	3.7	2.8	--	--
(5)	--	--	--	--	--	--	--	--	--	--	--	--	--	--