CHAPTER II
RESULTS AND DISCUSSION

2.1 Extraction and Isolation

Sequential extraction of air-dried mycelial mat of *C. elatum* (210 g) and *C. lucknowense* (282 g) with hexane, EtOAc, and MeOH gave six crude extracts. The extracts obtained from *C. elatum* were crude hexane 8.4 g (4.00%), crude EtOAc 21.7 g (10.33%) and crude MeOH 28.5 g (13.57%), while the *C. lucknowense* extracts yielded crude hexane 8.4 g (2.98%), crude EtOAc 18.0 g (6.38%), and crude MeOH 45.3 g (16.06%). The crude extracts were then separated by column chromatography and PLC, using the solvent systems of hexane, CH_2Cl_2, EtOAc, and MeOH, respectively. Separation of the crude extracts from *C. elatum* afforded twelve compounds, **I-XI** and **XIX**, while the separation of crude extracts from *C. lucknowense* yielded ten compounds, **I**, **II** and **XII-XIX**. The quantity of the isolation compounds from *C. elatum* was **I** (370.1 mg), **II** (52.1 mg), **III** (4123.4 mg), **IV** (67.1 mg), **V** (19.6 mg), **VI** (9.3 mg), **VII** (204.2 mg), **VIII** (43.8 mg), **IX** (21.0 mg), **X** (43.4 mg), **XI** (10.9 mg), and **XIX** (1247.3 mg). The amount of isolated compounds from *C. lucknowense* was **I** (47.6 mg), **II** (86.0 mg), **XII** (193.9 mg), **XIII** (54.6 mg), **XIV** (137.0 mg), **XV** (188.3 mg), **XVI** (705.0 mg), **XVII** (30.0 mg), **XVIII** (479.5 mg), and **XIX** (729.3 mg). Among these, compounds **I**, **II**, and **XIX** were isolated from both fungi. The structures of these compounds were determined on the basis of spectroscopic method, IR, UV, MS, 1D NMR (^1H, ^{13}C and DEPT) spectral data, including 2D NMR techniques (COSY, HSQC, HMBC and NOESY).

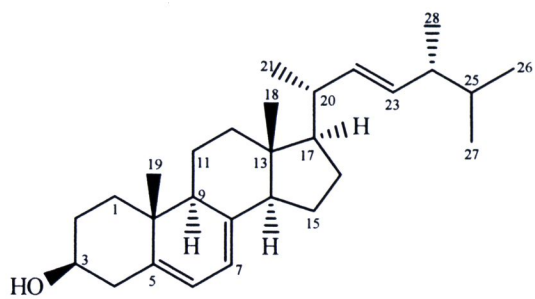
2.2 Structural Identification

Compound I was obtained as a white solid. The IR spectrum (Figure 1 in Appendix) showed a broad absorption band at 3423 cm^{-1} indicated the O-H stretching of a hydroxyl group. The very weak absorption bands of alkene were appeared at 3044 and 1654, 1605 cm^{-1} due to its =C-H and C=C stretching, respectively. The set of strong absorption bands at 2954, 2871 and weak absorption bands at 1460, 1383,

and 1368 cm^{-1} were characterized as saturated the C-H stretching and bending, respectively. The two medium absorption bands at 1056 and 1037 cm^{-1} were assigned to C-O stretching.

The ^{1}H and ^{13}C NMR spectra (Figures 2 and 3 in Appendix and Table 2.1) showed the characteristic signals of a steroid skeleton. The ^{1}H NMR spectra data showed the resonance signals of four olefinic protons at δ 5.50, 5.32 and 5.14. An oxymethine proton displayed at δ 3.56 while a set of chemical shift between 2.40-1.18 was signals of methine and methylene protons. The resonance signals of methyl protons displayed at δ 0.97, 0.88, 0.84, 0.77, 0.75 and 0.56.

The ^{13}C NMR and DEPT spectra (Figures 3 and 4 in Appendix and Table 2.1) indicated that compound **I** contain 28 carbons, contributable to six methyl, seven methylene, eleven methine and four quaternary carbons. The ^{13}C NMR spectra data showed the presence of olefinic carbons at δ 140.3, 138.8, 134.6, 131.0, 118.6 and 115.3. The resonance signal of carbon attaching to the oxygen atom appeared at δ 69.4 while quaternary, methine, methylene, and methyl carbons exhibited the resonance signals at chemical shifts between 54.7-11.0. According to ^{1}H and ^{13}C NMR spectra data suggested that compound **I** possessed a steroid structure and was then identified as ergosterol by comparison of its mixed-mp (156-158 °C) with the authentic sample and its spectral data with those reported from literature.[56-58]



Ergosterol (I)

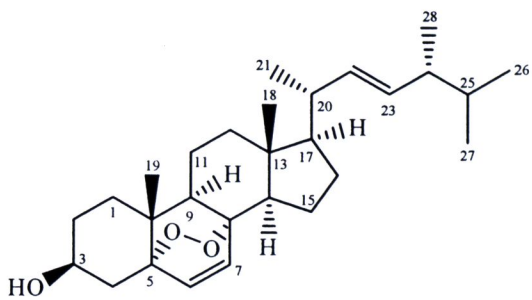
Table 2.1 ^{1}H and ^{13}C NMR and DEPT spectral data of compound **I** (400 MHz, $CDCl_3$)[a]

position	δ_H	δ_C	DEPT
1	1.21 m, 1.80 m	37.4	CH_2
2	1.42 m, 1.80 m	31.0	CH_2
3	3.56 m	69.4	CH
4	2.20 m, 2.40 m	40.0	CH_2
5		138.8	C
6	5.50 dd (2.2, 5.5)	118.6	CH
7	5.32 dd (2.4, 5.6)	115.3	CH
8		140.3	C
9	1.89 m	45.2	CH
10		36.0	C
11	1.5.0 m, 1.64 m	20.1	CH_2
12	1.18 m, 1.98 m	38.1	CH_2
13		41.8	C
14	1.81 m	53.6	CH
15	1.28 m, 1.58 m	22.0	CH_2
16	1.22 m, 1.66 m	27.3	CH_2
17	1.18 m	54.7	CH
18	0.56 s	11.0	CH_3
19	0.88 s	15.3	CH_3
20	1.97 m	39.4	CH
21	0.97 d (6.6)	20.1	CH_3
22	5.14 dd (7.3, 15.0)	134.6	CH
23	5.14 dd (7.3, 15.0)	131.0	CH
24	1.78 m	41.8	CH
25	1.40 m	32.1	CH
26	0.77 d (6.3)	18.9	CH_3
27	0.75 d (6.5)	18.6	CH_3
28	0.84 d (6.8)	16.6	CH_3

[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound II was obtained as a white solid. The IR spectrum (Figure 5 in Appendix) exhibited the absorption bands at 3521 and 3300 cm^{-1} were due to the hydroxyl group. The absorption bands due to =C-H and C=C stretching of alkene were displayed at 3065 and 1653 cm^{-1}. The absorption bands at 2955 and 2869 cm^{-1} were due to C-H stretching, while two absorption bands at 1459 and 1381 cm^{-1} were characteristic of C-H bending. The absorption bands at 1074 and 1047 cm^{-1} were characteristic of C-O stretching.

The ^{1}H and ^{13}C NMR spectra (Figures 6 and 7 in Appendix and Table 2.2) showed the characteristic signals of the steroid unit similar to those of compound **I**, except for the difference of the their chemical shifts of C-5 (δ 82.2) and C-8 (δ 79.4) which confirmed the connection of these carbons to oxygen atoms. Analysis of its ^{13}C NMR and DEPT spectra (Figures 7 and 8 in Appendix and Table 2.2) indicated that compound **II** containing 28 carbons, attributable to six methyl, seven methylene, eleven methine and four quaternary carbons. According to ^{1}H and ^{13}C NMR spectral data suggested that compound **II** possessed a steroid structure and was then identified as, ergosterol peroxide, 24(*R*)-5α,8α-epidioxyergosta-6-22-diene-3β-ol by comparison of its mixed-mp (180-181 °C) with the authentic sample and its spectral data with those reported from literature.[58-61]



24(*R*)-5α,8α-epidioxyergosta-6-22-diene-3β-ol (II)

Table 2.2 ^{1}H and ^{13}C NMR and DEPT spectral data of compound **II** (400 MHz, $CDCl_3$)[a]

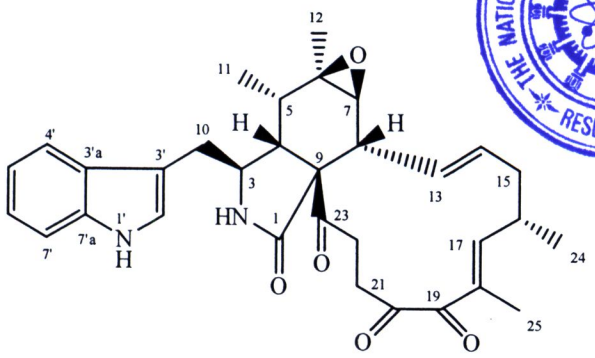
position	δ_H	δ_C	DEPT
1	1.24 m, 1.95 m	39.4	CH_2
2	1.50 m, 1.82 m	30.1	CH_2
3	3.96 m	66.5	CH
4	1.86 m, 2.11 m	36.9	CH_2
5		82.2	C
6	6.49 d (8.7)	130.8	CH
7	6.23 d (8.7)	135.4	CH
8		79.4	C
9	1.47 m	51.1	CH
10		36.9	C
11	1.67 m, 1.91 m	34.7	CH_2
12	1.38 m, 1.57 m	20.6	CH_2
13		44.6	C
14	1.55 m	51.7	CH
15	1.34 m, 1.75 m	28.6	CH_2
16	1.21 m, 1.49 m	23.4	CH_2
17	1.22 m	56.2	CH
18	0.81 s	12.9	CH_3
19	0.87 s	18.1	CH_3
20	2.02 m	39.7	CH
21	1.00 d (6.6)	20.9	CH_3
22	5.20 dd (7.2, 15.3)	132.3	CH
23	5.18 dd (8.1, 15.3)	135.2	CH
24	1.83 m	42.8	CH
25	1.38 m	33.1	CH
26	0.84 d (6.6)	19.9	CH_3
27	0.82 d (6.6)	19.6	CH_3
28	0.91 d (7.0)	17.6	CH_3

[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound III was obtained as a white solid and showed a molecular ion in the HRESITOFMS (Figure 9 in Appendix) at *m/z* 551.2522 ($[M+Na]^+$), indicating a molecular formula $C_{32}H_{36}N_2O_5$. The UV spectra exhibited the absorption maximum of indole chromophore at 221, 274, 280, 290 nm.[21] The IR spectrum (Figure 10 in Appendix) showed characteristic absorption bands of secondary amine (3462 cm^{-1}), amide (3316 cm^{-1}), aromatic ring (3122, 3085, 3059, and 1624 cm^{-1}), the ketone carbonyl (1714, and 1703 cm^{-1}), an α,β-unsaturated ketone (1688 cm^{-1}), and carbonyl of amide (1647 cm^{-1}). The absorption bands at 2938, 2869, and 1458, 1389 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively. Three absorption bands at 1355, 1263, and 1102 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^1H and ^{13}C NMR spectra (Figures 11 and 12 in Appendix and Table 2.3) which indicated a total of 32 carbons and 36 hydrogens resonances. The ^1H NMR spectrum displayed five low-field signals of an indole group at δ 6.93 (s, H-2′), 7.06 (t, J = 7.9 Hz, H-5′), 7.12 (t, J = 7.7 Hz, H-6′), 7.31 (d, J = 8.0 Hz, H-7′), and 7.46 (d, J = 7.7 Hz, H-4′), two signals of *trans*-double bond coupled protons at δ 5.03 (ddt, J = 2.6, 11.3, 14.5 Hz, H-14) and 6.03 (ddd, J = 1.5, 11.3, 15.1 Hz, H-13), an olefinic proton at δ 5.93 (d, J = 10.1 Hz, H-17), and four methyl group signals at δ 0.98 (d, J = 6.7 Hz, H-24), 1.07 (d, J = 7.3 Hz, H-11), 1.22 (s, H-12), and 1.73 (s, H-25). The ^1H and ^{13}C NMR spectra and DEPT experiments (Figures 11-13 in Appendix and Table 2.3) indicated that **III** contained 32 carbons, attributable to four carbonyl, four sp^2 quaternary, eight sp^2 methine, two sp^3 quaternary, six sp^3 methine, four sp^3 methylene, and four methyl carbons. The appearance of the signals due to a sp^3 methine at δ_H 3.80 (m, H-3) and δ_C 53.1 implied that one of the six sp^3 methines linked to an amide group. The methine proton (H-7), coupling to H-8 as a doublet, was assigned as epoxidemethine on the basis of its chemical shifts at δ_H 2.70 and δ_C 61.3. Two singlet signals at δ 1.22 (H-12) and 1.73 (H-25) were assigned to methyl groups bearing to the epoxide ring and alkene, respectively, whereas the other two methyl groups showed as doublet at δ 1.07 (H-11) and 0.98 (H-24). The ^{13}C NMR spectrum showed conjugated ketone and amide carbons at δ 196.7 and 175.6, respectively.

The structure of **III** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 14-17 in Appendix and Table 2.3). The four partial structural units were assigned by analysis of the COSY spectrum as shown as bold lines in Figure 2.1. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-4 and H-5; H-5 and H-11; H-7 and H-8; H-8 and H-13; H-13 and H-14; H-14 and H-15; H-15 and H-16; H-16 and H-17, H-24; H-21 and H-22; H-4′ and H-5′; H-5′ and H-6′; H-6′ and H-7′; and long-range correlations between H-17 and H-25 (Figure 2.1 and Table 2.3). The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.1 Hz) of olefinic protons. The HMBC spectrum confirmed the connection of these four units by showing correlations of H-3 to C-3′; H-8 to C-1, C-7, C-9, C-13, C-14, and C-23; H-12 to C-5, C-6, and C-7; H-21 to C-19 and C-20; H-22 to C-20 and C-23; H-25 to C-17, C-18, and C-19; H-2′ to C-3′, C-3′a, and C-7′a; H-4′ to C-6′ and C-7′a; and H-7′ to C-3′a and C-5′ (Figure 2.2 and Table 2.3). The NOESY spectrum showed the correlations between H–3 and H–10, H-11, H-12; H-4 and H-5, H-11; H–7 and H–12; H–11 and H–12 as depicted in Figure 2.3. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[22,24,27,62] as well as the assignment made by 2D NMR experiments, compound **III** was then identified as the known chaetoglobosin C.



Chaetoglobosin C (III)

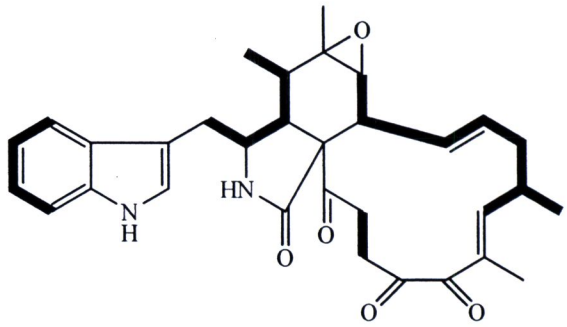


Figure 2.1 COSY correlations (bold lines) of **III**.

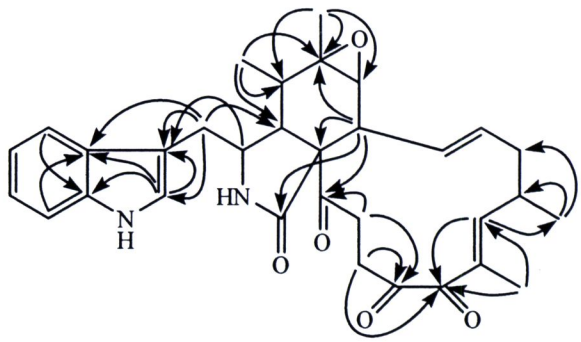


Figure 2.2 HMBC correlations of **III**.

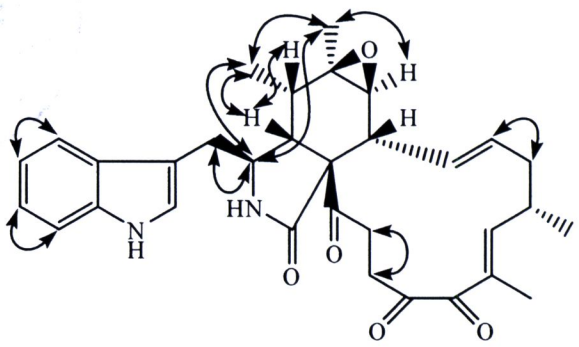


Figure 2.3 NOESY correlations of **III**.

Table 2.3 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **III** (400 MHz, CD_3OD in $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		175.6	C			
3	3.80 m	53.1	CH	H-4, 10	C-3′	H-10, 11, 12
4	2.40 dd (2.7, 5.3)	49.3	CH	H-3, 5	C-5	H-5, 11
5	1.79 m	36.4	CH	H-4, 11	C-11	H-4
6		57.4	C			
7	2.70 d (6.2)	61.3	CH	H-8	C-8	H-12
8	2.27 dd (5.9, 9.8)	48.9	CH	H-7, 13	C-1, 7, 9, 13, 14, 23	
9		63.0	C			
10a	2.70 dd (3.5, 11.7)	32.5	CH_2	H-3, 10b	C-3, 2′, 3′, 3′a	H-3
10b	2.93 dd (4.9, 14.7)			H-3, 10a	C-3, 4, 2′, 3′, 3′a	H-10a
11	1.07 d (7.3)	12.6	CH_3	H-5	C-4, 5, 6	H-12
12	1.22 s	19.3	CH_3		C-5, 6, 7	H-11
13	6.03 ddd (1.5, 11.3, 15.1)	126.4	CH	H-8, 14		
14	5.03 ddt (2.6, 11.3, 14.5)	134.5	CH	H-13, 15		H-15
15	1.82 m, 2.33 m	39.9	CH_2	H-14, 15, 16		
16	2.63 m	33.3	CH	H-15, 17, 24		
17	5.93 d (10.1)	156.5	CH	H-16, 25	C-24	
18		131.8	C			
19		196.7	C			
20		205.3	C			
21	1.76 m, 2.76 m	32.3	CH_2	H-21, H-22	C-19, 20	H-22
22	1.66 m, 1.71 m	37.9	CH_2	H-21, 22	C-20, 23	H-21
23		208.2	C			
24	0.98 d (6.7)	19.1	CH_3	H-16	C-15, 16, 17	
25	1.73 s	10.0	CH_3	H-17	C-17, 18, 19	
2′	6.93 s	124.5	CH		C-3′, 3′a, 7′a	
3′		108.2	C			
3′a		127.4	C			
4′	7.46 d (7.7)	118.1	CH	H-5′	C-6′, 7′a	H-5′
5′	7.06 t (7.9)	119.6	CH	H-4′		H-4′
6′	7.12 t (7.7)	121.9	CH	H-7′		H-7′
7′	7.31 d (8.0)	111.5	CH	H-6′	C-3′a, 5′	H-6′
7′a		136.2	C			

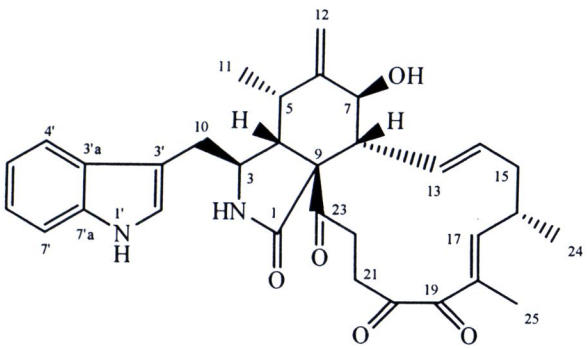
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound IV was obtained as a white solid and showed a molecular ion in the HRESITOFMS (Figure 18 in Appendix) at *m/z* 551.2522 ($[M+Na]^+$), indicating a molecular formula $C_{32}H_{36}N_2O_5$. The UV spectra exhibited the absorption maximum of indole chromophore at 220, 252, 282, and 290 nm.[21] The IR spectrum (Figure 19 in Appendix) showed characteristic absorption bands of hydroxyl group (3542 cm^{-1}), secondary amine (3454 cm^{-1}), amide (3329 cm^{-1}), aromatic ring (3083, 3061, 1648, and 1623 cm^{-1}), the ketone carbonyl (1713 and 1703 cm^{-1}), an α,β-unsaturated ketone (1685 cm^{-1}), and carbonyl of amide (1648 cm^{-1}). The absorption bands at 2926, 2867, and 1459, 1390 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively, while the absorption bands at 1330, 1265, and 1103 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^1H and ^{13}C NMR spectra (Figures 20 and 21 in Appendix and Table 2.4) which exhibited a total of 32 carbon resonances and a sum of 36 hydrogens. The ^1H NMR spectrum displayed five low-field signals of an indole group at δ 6.97 (s, H-2′), 7.05 (t, J = 7.5 Hz, H-5′), 7.12 (t, J = 7.7 Hz, H-6′), 7.31 (d, J = 7.9 Hz, H-7′), and 7.46 (d, J = 7.8 Hz, H-4′), two signals of *trans*-double bond coupled protons at δ 5.04 (ddt, J = 2.5, 11.2, 14.4 Hz, H-14) and 5.81 (dd, J = 9.8, 15.3 Hz, H-13), two singlets signal of terminal alkene protons at δ 5.10 (s, H-12a) and 5.31 (s, H-12b), an olefinic proton at δ 5.93 (d, J = 10.0 Hz, H-17), and three methyl group signals at δ 0.97 (d, J = 6.5 Hz, H-24), 1.08 (d, J = 6.6 Hz, H-11), and 1.75 (s, H-25). The ^1H and ^{13}C NMR spectra and DEPT experiments (Figures 20-22 in Appendix and Table 2.4) indicated that **IV** contained 32 carbons, attributable to four carbonyl, five sp^2 quaternary, eight sp^2 methine, one sp^2 methylene, one sp^3 quaternary, six sp^3 methine, four sp^3 methylene, and three methyl carbons. The appearance of the signals due to a sp^3 methine at δ_H 3.46 (m, H-3) and δ_C 53.0 implied that one of the six sp^3 methines is linked to an amide group. The methine proton (H-7), coupling to H-8 as a doublet, was assigned a hydroxylmethine on the basis of its chemical shift at δ_H 3.78 and δ_C 69.2. A singlet signal at δ 1.75 (H-25) was assigned to methyl groups bearing to an alkene, whereas the other two methyl groups showed as doublet at δ 1.08 (H-11) and 0.97 (H-24). The

^{13}C NMR spectrum showed conjugated ketone and amide carbons at δ 196.5 and 175.3, respectively.

The structure of **IV** was then confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 23-26 in Appendix and Table 2.4). The four partial structural units were assigned by analysis of the COSY spectrum shown as bold lines in Figure 2.4. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-5 and H-4, H-11; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-15, H-17, H-24; H-21 and H-22; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations between H-17 and H-25 (Figure 2.4 and Table 2.4). The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.3 Hz) of olefinic protons. The HMBC spectrum confirmed the connection of these four unist by showing correlations of H-3 to C-1, C-4, C-5, and C-3′; H-8 to C-1, C-7, C-9, C-13, C-14, and C-23; H-12 to C-7; H-21 to C-20 and C-23; H-22 to C-20 and C-23; H-25 to C-17, C-18, and C-19; H-2′ to C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-6′, C-3′a, and C-7′a; and H-7′ to C-5′ and C-3′a (Figure 2.5 and Table 2.4). The NOESY spectrum showed the correlations between H–3 and H-11; H-4 and H-11; H-5 and H-4, H-11; H–12 and H–11; H–16 and H–24, H-25 depicted in Figure 2.6. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[3,35,62] as well as the assignment made by 2D NMR experiments, compound **IV** was then identified to be the known isochaetoglobosin D.



Isochaetoglobosin D (IV)

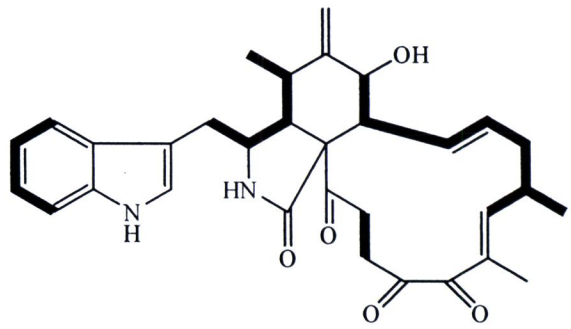


Figure 2.4 COSY correlations (bold lines) of **IV**.

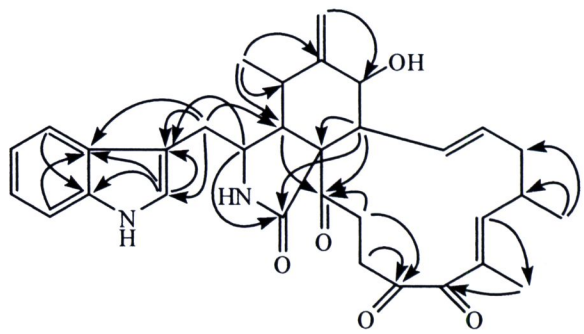


Figure 2.5 HMBC correlations of **IV**.

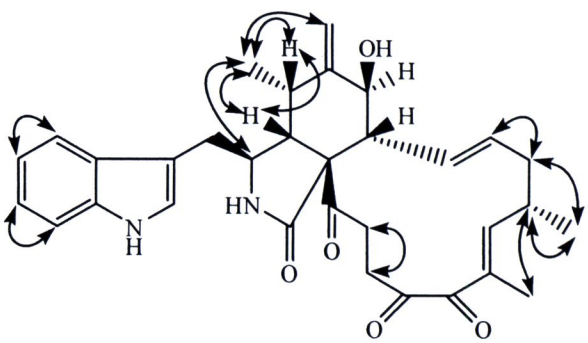


Figure 2.6 NOESY correlations of **IV**.

Table 2.4 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **IV** (400 MHz, CD_3OD in $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		175.3	C			
3	3.46 m	53.0	CH	H-4, 10	C-1, 4, 5, 3′	H-11
4	2.35 t (4.3)	46.8	CH	H-3, 5	C-1, 5, 6, 9, 10, 23	H-11
5	2.83 m	32.2	CH	H-4, 11		H-4, 11
6		148.7	C			
7	3.78 d (11.3)	69.2	CH	H-8		
8	2.73 t (10.1, 20.9)	49.2	CH	H-7, 13	C-1, 7, 9, 13, 14, 23	
9		61.4	C			
10	2.68 dd (4.1, 15.1) 2.99 dd (3.9, 15.1)	31.2	CH_2	H-3, 10	C-3, 4, 2′, 3′, 3′a	H-10
11	1.08 d (6.6)	13.6	CH_3	H-5	C-4, 5, 6	H-5
12	5.10 s, 5.31 s	114.2	CH_2	H-12	C-7	H-11, 12
13	5.81 dd (9.8, 15.3)	126.2	CH	H-8, 14	C-15	
14	5.04 ddt (2.5, 11.2, 14.4)	135.6	CH	H-13, 15		
15	1.81 dd (10.6, 14.7) 2.31 m	39.9	CH_2	H-14, 15, 16		H-15, 24
16	2.66 m	33.3	CH	H-17, 24		H-24, 25
17	5.93 d (10.0)	156.3	CH	H-16, 25	C-25	
18		131.6	C			
19		196.5	C			
20		205.3	C			
21	1.67 m 2.55 dd (8.4, 15.3)	32.4	CH_2	H-21, 22	C-20, 23	H-21, 22
22	1.41 dd (6.5, 17.8) 2.55 dd (8.4, 15.3)	37.4	CH_2	H-21, 22	C-20, 23	H-21, 22
23		208.0	C			
24	0.97 d (6.5)	19.1	CH_3	H-16	C-15, 16, 17	H-15
25	1.75 s	10.0	CH_3	H-17	C-17, 18, 19	H-16
2′	6.97 s	124.6	CH		C-3′, 3′a, 7′a	
3′		108.6	C			
3′a		127.6	C			
4′	7.46 d (7.8)	118.2	CH	H-5′	C-3′, 6′, 3′a, 7′a	H-5′
5′	7.05 t (7.5)	119.6	CH	H-4′, 6′		H-4′
6′	7.12 t (7.7)	121.8	CH	H-5′, 7′	C-4′, 7′	H-7′
7′	7.31 d (7.9)	111.4	CH	H-6′	C-5′, 3′a	H-6′
7′a		136.1	C			

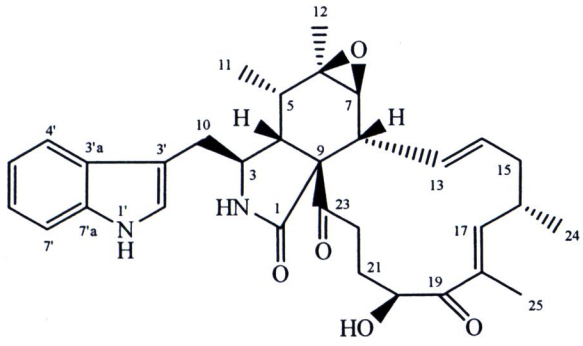
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound V was obtained as a white solid and showed a molecular ion in the HRESITOFMS (Figure 27 in Appendix) at *m/z* 553.2678 ($[M+Na]^+$), indicating a molecular formula $C_{32}H_{38}N_2O_5$. The UV spectra exhibited the absorption maximum of indole chromophore at 221, 274, 280, 290 nm.[21] The IR spectrum (Figure 28 in Appendix) showed characteristic absorption bands of secondary amine (3421 cm^{-1}), amide (3361 cm^{-1}), aromatic ring (1619 cm^{-1}), an α,β-unsaturated ketone (1695 cm^{-1}), and carbonyl of amide (1677 cm^{-1}). The absorption bands at 2929, 2851, and 1455, 1385 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively. Three absorption bands at 1261, 1232 and 1111 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^1H and ^{13}C NMR spectra and DEPT experiments (Figures 29-31 in Appendix and Table 2.5) which exhibited a total of 32 carbon resonances and a sum of 38 hydrogens. The ^1H and ^{13}C NMR spectra of **V** showed the characteristic signals of the chaetoglobosin unit similar to those of **III** except the carbonyl group at C-20 was replaced by hydroxyl group. The chemical shifts of C-20 confirmed the connection of the carbon to oxygen atoms at δ_H 4.58 (t, J = 4.7 Hz, H-20) and δ_C 71.5. The ^1H and ^{13}C NMR spectra and DEPT experiments indicated that **V** contained 32 carbons, attributable to three carbonyl, four sp^2 quaternary, eight sp^2 methine, two sp^3 quaternary, seven sp^3 methine, four sp^3 methylene, and four methyl carbons. The ^{13}C NMR spectrum showed conjugated ketone and amide carbons at δ 203.8 and 175.3, respectively.

The structure of **V** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 32-35 in Appendix and Table 2.5). The four partial structural units were assigned by analysis of the COSY spectrum shown as bold lines in Figure 2.7. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-5 and H-4, H-11; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-17, H-24; H-21 and H-20, H-22; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations between H-17 and H-25 (Figure 2.7 and Table 2.5). The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.0 Hz) of olefinic protons. The HMBC spectrum confirmed the connection of these four units by showing correlations of H-8 to C-1, C-4, C-7, C-9, C-13, C-14, and C-23; H-12 to C-5, C-6, and C-7; H-20 to C-21 and C-22; H-22 to C-23; H-25 to C-17, C-18, and C-19; H-2′ to C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-6′, C-3′a and C-7′a; and H-7′

to C-3′a and C-5′ (Figure 2.8 and Table 2.5). The NOESY spectrum showed the correlations between H–3 and H–10; H-4 and H-5, H-10, H-11; H–7 and H–12; H-8 and H-5; H–10 and H–4; H–12 and H–3, H-11; H-17 and H- 20; H-24 and H-15 depicted in Figure 2.9. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[24,30,62] as well as the assignment made by 2D NMR experiments, compound **V** was then identified to be the known chaetoglobosin F.



Chaetoglobosin F (V)

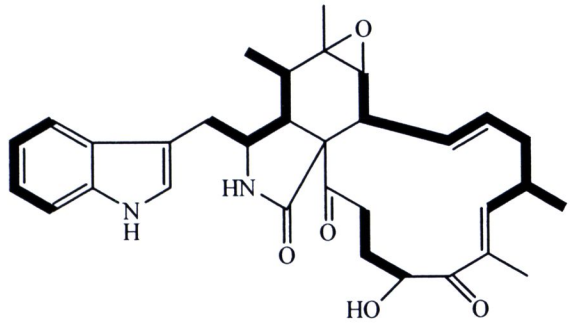


Figure 2.7 COSY correlations (bold lines) of **V**.

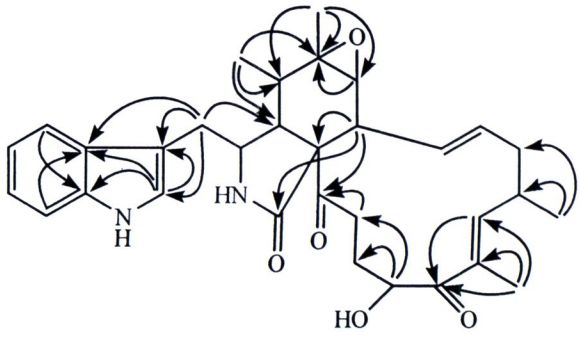


Figure 2.8 HMBC correlations of **V**.

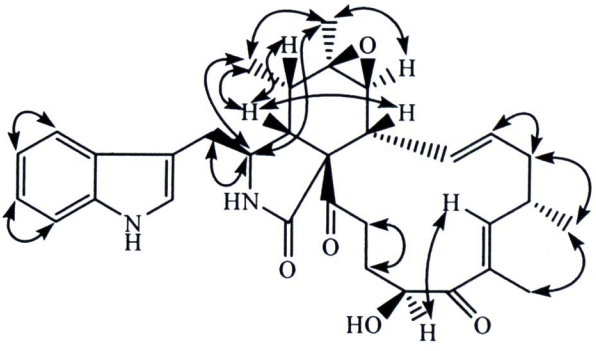


Figure 2.9 NOESY correlations of **V**.

Table 2.5 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **V** (400 MHz, CD_3OD in $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		175.3	C			
3	3.74 m	52.8	CH	H-4, 10		H-10
4	2.55 dd (1.8, 5.7)	48.6	CH	H-3, 5		H-5, 10, 11
5	1.70 m	36.3	CH	H-4, 11		H-4, 8
6		57.8	C			
7	2.73 d (5.8)	61.9	CH	H-8	C-6, 8, 12, 13	H-12
8	2.11 dd (5.8, 10.0)	48.4	CH	H-7, 13	C-1, 4, 7, 9, 13, 14, 23	H-5
9		64.4	C			
10	2.75 d (5.9) 2.78 d (5.5)	32.9	CH_2	H-3	C-3, 4, 2′, 3′, 3′a	H-4
11	0.98 d (6.6)	12.4	CH_3	H-5	C-4, 5, 6	H-4
12	1.18 s	19.1	CH_3		C-5, 6, 7	H-3, 11
13	6.26 ddd (1.5, 9.8, 15.0)	128.3	CH	H-8, 14		H-14
14	5.16 ddt (2.8, 11.0, 14.3)	133.4	CH	H-13, 15		H-13
15	2.00 m 2.39 m	40.9	CH_2	H-14, 15, 16	C-13, 14, 16	H-15, 24
16	2.66 m	33.1	CH	H-15, 17, 24	C-21	H-25
17	6.08 d (8.9)	149.2	CH	H-16, 25	C-19, 25	H-20
18		134.5	C			
19		203.8	C			
20	4.58 t (4.7)	71.5	CH	H-21	C-21, 22	H-17
21	1.46 m	30.7	CH_2	H-20, 22		
22	2.03 m, 2.07 m	37.8	CH_2	H-21	C-23	H-4, 16
23		208.3	C			
24	1.00 d (7.2)	19.5	CH_3	H-16	C-15, 16, 17	H-15
25	1.75 s	11.9	CH_3	H-17	C-17, 18, 19	H-16, 24
2′	6.92 s	124.0	CH		C-3′, 3′a, 7′a	
3′		108.7	C			
3′a		127.4	C			
4′	7.44 d (7.9)	117.9	CH	H-5′	C-3′, 6′, 3′a, 7′a	H-5′
5′	7.05 t (7.4)	119.3	CH	H-4′	C-4′, 7′	H-4′, 6′
6′	7.11 t (7.6)	121.7	CH	H-7′	C-7′	H-5′, 7′
7′	7.32 d (7.9)	111.6	CH	H-6′	C-3′a, 5′	H-6′
7′a		136.3	C			

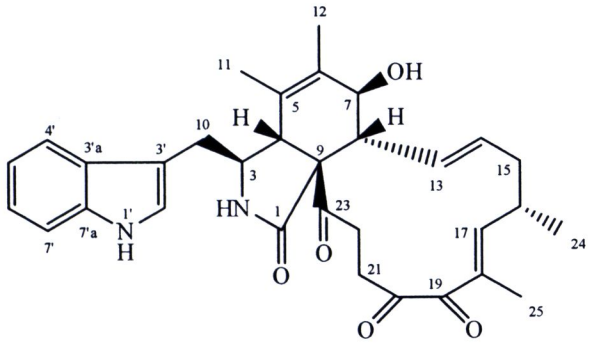
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound VI was obtained as a white solid and showed a molecular ion in the HRESITOFMS (Figure 36 in Appendix) at *m/z* 551.2522 ($[M+Na]^+$), indicating a molecular formula $C_{32}H_{36}N_2O_5$. The UV spectra exhibited the absorption maximum of indole chromophore at 221, 274, 281, and 290 nm.[21] The IR spectrum (Figure 37 in Appendix) showed characteristic absorption bands of hydroxyl group (3550-3400 cm^{-1}), secondary amine (3508 cm^{-1}), amide (3436 cm^{-1}), aromatic ring (1624 cm^{-1}), the ketone carbonyl (1725, and 1713 cm^{-1}), an α,β-unsaturated ketone (1691 cm^{-1}), and carbonyl of amide (1651 cm^{-1}). The absorption bands at 2927, 2896, and 1457, 1414 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively, while the absorption bands at 1257, 1228, and 1125 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^1H and ^{13}C NMR spectra and DEPT experiments (Figures 38-40 in Appendix and Table 2.6) which exhibited a total of 32 carbon resonances and a sum of 36 hydrogens. The ^1H and ^{13}C NMR spectra of **VI** displayed the characteristic signals of the chaetoglobosin unit similar to those of **IV** except for the terminal alkene at C-12 was replaced by methyl group, δ_H 1.59 (s, H-12) and δ_C 13.9. Compound **VI** is found to be a isomer of **IV**, *via* a tautomerization between the C-5 and C-12. The ^1H and ^{13}C NMR spectra and DEPT experiments indicated that **VI** contained 32 carbons, attributable to four carbonyl, six sp^2 quaternary, eight sp^2 methine, one sp^3 quaternary, five sp^3 methine, four sp^3 methylene, and four methyl carbons. The ^{13}C NMR spectrum showed conjugated ketone and amide carbons at δ 197.1 and 175.7, respectively.

The structure of **VI** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 41-44 in Appendix and Table 2.6). The four partial structural units were assigned by analysis of the COSY spectrum shown as bold lines in Figure 2.10. The COSY spectrum displayed correlations in bold line between H-3 and H-4, H-10; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-15, H-17, H-24; H-21 and H-22; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations between H-17 and H-25 (Figure 2.10 and Table 2.6). The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.0 Hz) of olefinic protons. The connection of these four units and the

remaining functional groups was determined on the basis of the HMBC correlations of H-3 to C-1, C-4, and C5; H-8 to C-1, C-6, C-7, C-9, C-13, and C-14; H-12 to C-5, C-6, and C-7; H-21 to C-23; H-22 to C-20 and C-23; H-25 to C-17, C-18, and C-19; H-2′ to C-10, C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-6′, C-3′a, and C-7′a; and H-7′ to C-5′, C-6′, and C-3′a (Figure 2.11 and Table 2.6). The NOESY spectrum showed the correlations between H–3 and H–10, H-11; H-4 and H-11; H–8 and H–14; H–11 and H–12; H–16 and H–22, H-24, H-25 depicted in Figure 2.12. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[23,24,30,62] as well as the assignment made by 2D NMR experiments, compound **VI** was then identified to be the known chaetoglobosin G.



Chaetoglobosin G (VI)

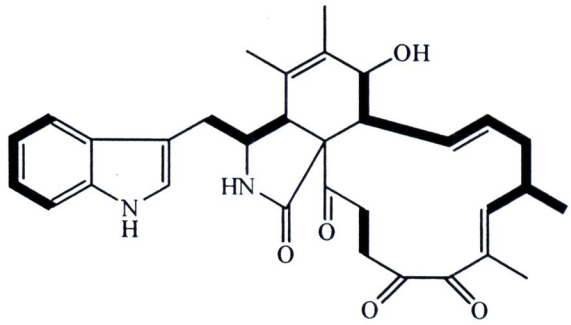


Figure 2.10 COSY correlations (bold lines) of **VI**.

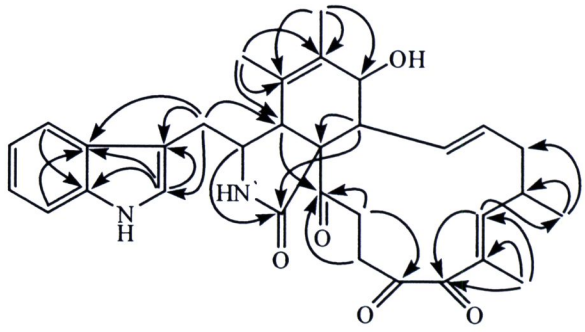


Figure 2.11 HMBC correlations of **VI**.

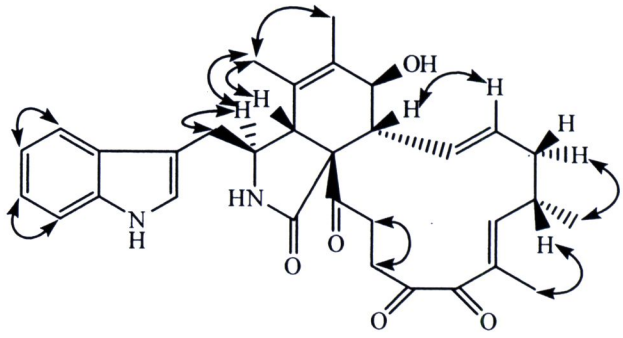


Figure 2.12 NOESY correlations of **VI**.

Table 2.6 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **VI** (400 MHz, CD_3OD in $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		175.7	C			
3	3.50 t (7.0)	58.2	CH	H-4	C-1, 4, 5	H-10, 11
4	2.90 s	50.9	CH	H-3	C-23	H-11
5		126.6	C			
6		132.6	C			
7	3.75 d (9.2)	68.0	CH	H-8		
8	2.19 t (10.1)	52.5	CH	H-7, 13	C-1, 6, 7, 9, 13, 14	H-14
9		61.4	C			
10	2.59 dd (7.7, 14.3) 2.76 dd (6.5, 14.3)	32.3	CH_2	H-3	C-3, 4, 2′, 3′, 3′a	H-3, 10
11	1.30 s	16.9	CH_3		C-4, 5, 6	H-3, 4, 12
12	1.59 s	13.9	CH_3		C-5, 6, 7	H-11
13	6.11 ddd (0.9, 10.0, 15.0)	126.7	CH	H-8, 14	C-15	
14	5.10 ddt (2.6, 11.2, 14.5)	136.1	CH	H-13, 15		
15	1.92 m, 2.40 m	40.3	CH_2	H-14, 16	C-13, 14	H-15, 24
16	2.70 m	33.4	CH	H-15, 17, 24		H-22, 24, 25
17	6.02 d (9.9)	156.7	CH	H-16, 25	C-15, 19, 24	
18		132.3	C			
19		197.1	C			
20		205.5	C			
21	2.29 m, 3.27 m	32.7	CH_2	H-21, 22	C-23	H-21, 22
22	2.90 m, 3.04 m	37.8	CH_2	H-21, 22	C-20, 23	H-16, 21, 22
23		208.4	C			
24	1.03 d (6.7)	19.2	CH_3	H-16	C-15, 16, 17	H-16
25	1.79 s	10.0	CH_3	H-17	C-17, 18, 19	H-16. 24
2′	6.94 s	123.5	CH		C-10, 3′, 3′a, 7′a	
3′		109.6	C			
3′a		126.9	C			
4′	7.41 d (7.8)	117.9	CH	H-5′	C-3′, 6′, 3′a, 7′a	H-5′
5′	7.04 t (7.7)	119.2	CH	H-4′, 6′	C-7′, 3′a, 7′a	H-4′, 6′
6′	7.12 t (7.9)	121.8	CH	H-5′, 7′	C-4′, 7′, 7′a	H-5′, 7′
7′	7.33 d (8.0)	111.5	CH	H-6′	C-5′, 6′, 3′a	H-6′
7′a		136.5	C			

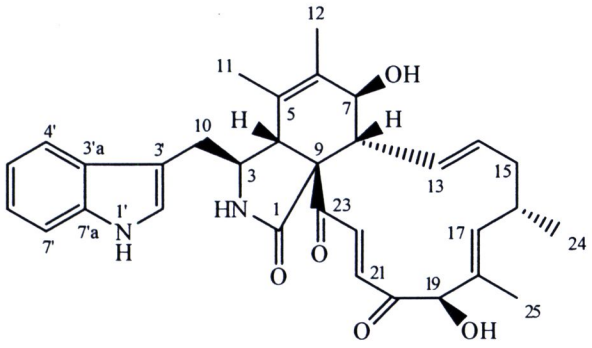
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound VII was obtained as a white solid and showed a molecular ion in the HRESITOFMS (Figure 45 in Appendix) at *m/z* 551.2522 ([M+Na]$^+$), indicating a molecular formula $C_{32}H_{36}N_2O_5$. The UV spectra exhibited the absorption maximum of indole chromophore at 221, 274, 280, and 290 nm.[21] The IR spectrum (Figure 46 in Appendix) showed characteristic absorption bands of hydroxyl group (3500-3400 cm^{-1}), secondary amine (3416 cm^{-1}), aromatic ring (1619 cm^{-1}), an α,β-unsaturated ketone (1694 cm^{-1}), and carbonyl of amide (1675 cm^{-1}). The absorption bands at 2920, 2895, and 1457, 1385 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively. Three absorption bands at 1250, 1230, and 1098 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^{1}H and ^{13}C NMR spectra and DEPT experiments (Figures 47-49 in Appendix and Table 2.7) which exhibited a total of 32 carbon resonances and a sum of 36 hydrogens. The ^{1}H and ^{13}C NMR spectra of **VII** displayed the characteristic signals of the chaetoglobosin unit similar to those of **VI** except the carbonyl group at C-19 and two sp^3 methylene groups at C-21 and C-22. The carbonyl group at C-19 was replaced by hydroxyl group which confirmed the connection of the carbon to oxygen atoms at δ_H 5.05 (s, H-19) and δ_C 82.0. In addition, two sp^3 methylene groups at C-21 and C-22 were changed by sp^2 methine alkene group (δ_H 6.74 (d, J = 16.4 Hz, H-21) and δ_C 133.0, and δ_H 7.73 (d, J = 16.4 Hz, H-22) and δ_C 136.0). The ^{1}H and ^{13}C NMR spectra and DEPT experiments indicated that **VII** contained 32 carbons, attributable to three carbonyl, six sp^2 quaternary, ten sp^2 methine, one sp^3 quaternary, six sp^3 methine, two sp^3 methylene, and four methyl carbons. The ^{13}C NMR spectrum showed two conjugated ketone and one amide carbons at δ 197.3, 201.3 and 172.9, respectively.

The structure of **VII** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 50-53 in Appendix and Table 2.7). The six partial structural units were assigned by analysis of the COSY spectrum shown as bold lines in Figure 2.13. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-15, H-17, H-24; H-19 and 19-OH; H-21 and H-22; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations between H-4 and H-12; H-17 and H-25 (Figure 2.13

and Table 2.7). The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.6 Hz) of olefinic protons. The HMBC spectrum confirmed the connection of these six units by showing correlations of H-2 to C-3, C-4, and C-9; H-8 to C-1, C-6, C-7, C-9, C-13, C-14, and C-23; H-12 to C-5, C-6, and C-7; H-21 to C-19, C-20,C-22, and C-23; H-22 to C-20, C-21, and C-23; H-25 to C-17, C-18, and C-19; H-2′ to C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-3′a, C-6′ and C-7′a; and H-7′ to C-3′a, C-4′, and C-5′ (Figure 2.14 and Table 2.7). The NOESY spectrum showed the correlations between H–3 and H2, H–10, H-11; H-4 and H-10, H-11; H–7 and H–13, H-14, H-15; H–15 and H–14, H-24; H–17 and H–19, H-24 depicted in Figure 2.15. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[21,24,30,62] as well as the assignment made by 2D NMR experiments, compound **VII** was then identified to be the known chaetoglobosin B.



Chaetoglobosin B (VII)

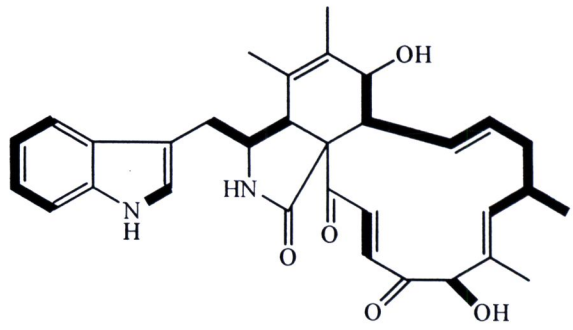


Figure 2.13 COSY correlations (bold lines) of **VII**.

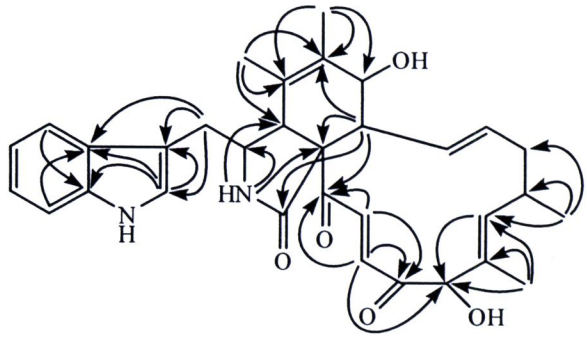


Figure 2.14 HMBC correlations of **VII**.

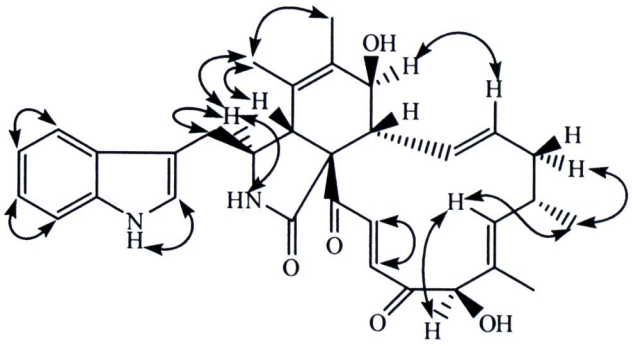


Figure 2.15 NOESY correlations of **VII**.

Table 2.7 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **VII** (400 MHz, $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		172.9	C			
2	5.82 s				C-3, 4, 9	H-3
3	3.55 t (6.6)	58.1	CH	H-4, 10		H-2, 10, 11
4	3.41 s	47.7	CH	H-3, 7, 12		H-10, 11
5		126.1	C			
6		131.9	C			
7	3.93 d (9.4)	68.7	CH	H-4, 8, 11		H-13, 14, 15
8	2.04 t (3.1)	52.5	CH	H-7, 13	C-1, 6, 7, 9, 13, 14, 23	
9		61.3	C			
10	2.65 dd (8.6, 14.0) 2.88 dd (5.5, 14.4)	33.1	CH_2	H-3, 10	C-2′, 3′, 3′a	H-3, 10
11	1.65 s	17.9	CH_3	H-7	C-4, 5, 6	H-3, 4
12	1.73 s	13.9	CH_3	H-4	C-5, 6, 7	
13	6.18 dd (10.1, 15.6)	127.8	CH	H-8, 14	C-15	H-14
14	5.34 ddt (3.5, 10.1, 14.4)	137.2	CH	H-13, 15	C-8, 15	H-13, 15
15	2.10 m 2.31 d (13.6)	41.4	CH_2	H-14, 15, 16	C-13, 14	H-14, 15, 24
16	2.51 m	32.2	CH	H-15, 17, 24		H-15, 24, 25
17	5.59 d (9.4)	140.0	CH	H-16, 25	C-15, 19, 25	H-19, 24
18		132.3	C			
19	5.05 s	82.0	CH	C19-OH	C-17, 18, 20, 25	H-17, 22
19-OH	3.82 s			H-19		
20		201.3	C			
21	6.74 d (16.4)	133.0	CH	H-22	C-19, 20, 22, 23	H-22
22	7.73 d (16.4)	136.0	CH	H-21	C-20, 21, 23	H-19, 21
23		197.3	C			
24	1.02 d (6.6)	21.0	CH_3	H-16	C-15, 16, 17	H-15, 16, 17
25	1.37 s	10.7	CH_3	H-17	C-17, 18, 19	H-17
1′	8.19 s			H-2′		H-2′
2′	6.98 s	122.9	CH	H-1′	C-3′, 3′a, 7′a	H-1′
3′		111.0	C			
3′a		126.8	C			
4′	7.48 d (7.8)	118.4	CH	H-5′	C-3′, 3′a, 6′, 7′a	H-5′
5′	7.12 t (7.8)	119.9	CH	H-4′, 6′	C-3′a, 4′, 7′	H-4′, 6′
6′	7.20 t (7.8)	122.4	CH	H-5′, 7′	C-4′, 7′a	H-5′, 7′
7′	7.36 d (8.2)	111.5	CH	H-6′	C-3′a, 4′, 5′	H-6′
7′a		136.4	C			

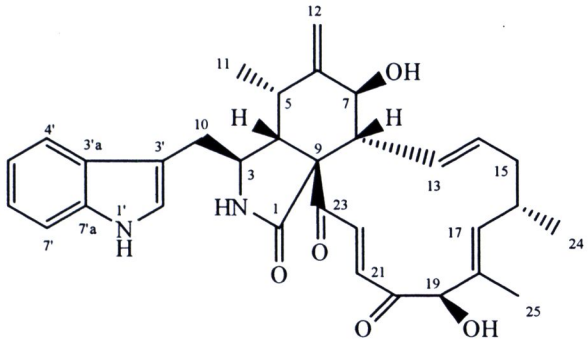
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound VIII was obtained as a pale yellow crystals and showed a molecular ion in the HRESITOFMS (Figure 54 in Appendix) at *m/z* 551.2522 ($[M+Na]^+$), indicating a molecular formula $C_{32}H_{36}N_2O_5$. The UV spectra exhibited the absorption maximum of indole chromophore at 221, 274, 280, and 290 nm.[21] The IR spectrum (Figure 55 in Appendix) showed characteristic absorption bands of hydroxyl group (3500-3300 cm^{-1}), secondary amine (3461 cm^{-1}), amide (3297 cm^{-1}), aromatic ring (3101, 3061 and 1606 cm^{-1}), an α,β-unsaturated ketone (1695 cm^{-1}), and carbonyl of amide (1664 cm^{-1}). The absorption bands at 2923, 2879, and 1454, 1377 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively, while the absorption bands at 1251, 1232, and 1088 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^1H and ^{13}C NMR spectra and DEPT experiments (Figures 56-58 in Appendix and Table 2.8) which exhibited a total of 32 carbon resonances and a sum of 36 hydrogens. The ^1H and ^{13}C NMR spectra of **VIII** exhibited the characteristic signals of the chaetoglobosin unit similar to those of **VII** except for the methyl group at C-12 was replaced by the terminal alkene, δ_H 5.10 (s, H-12), 5.31 (s, H-12) and δ_C 112.7. It was found that compound **VIII** is a isomer of **VII**, which could be explained by a tautomerization between the C-5 and C-12. The ^1H and ^{13}C NMR spectra and DEPT experiments indicated that **VIII** contained 32 carbons, attributable to three carbonyl, five sp^2 quaternary, ten sp^2 methine, one sp^2 methylene, one sp^3 quaternary, seven sp^3 methine, two sp^3 methylene, and three methyl carbons. The ^{13}C NMR spectrum showed two conjugated ketone and one amide carbons at δ 197.9, 201.1 and 173.2, respectively.

The structure of **VIII** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 59-62 in Appendix and Table 2.8). The four partial structural units were assigned by analysis of the COSY spectrum shown as bold lines in Figure 2.16. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-5 and H-4, H-11; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-17, H-24; H-21 and H-22; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations of H-17 to H-25 (Figure 2.16 and Table 2.8).

The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.4 Hz) of olefinic protons. The connection of these four units and the remaining functional groups was determined on the basis of the HMBC correlations of H-3 to C-4 and C-5; H-8 to C-1, C-6, C-7, C-9, C-13, C-14, and C-23; H-12 to C-5 and C-7; H-21 to C-19, C-22, and C-23; H-22 to C-20 and C-23; H-25 to C-17, C-18, and C-19; H-2′ to C-10, C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-6′, C-3′a, and C-7′a; and H-7′ to C-5′ and C-3′a (Figure 2.17 and Table 2.8). The NOESY spectrum showed the correlations between H–3 and H–4, H-10; H-5 and H-8; H–7 and H–12, H-13; H-17 and H-19; H–24 and H–15, H-16; H–25 and H–16 depicted in Figure 2.18. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[22,24,27] as well as the assignment made by 2D NMR experiments, compound **VIII** was then identified to be the known chaetoglobosin D.



Chaetoglobosin D (VIII)

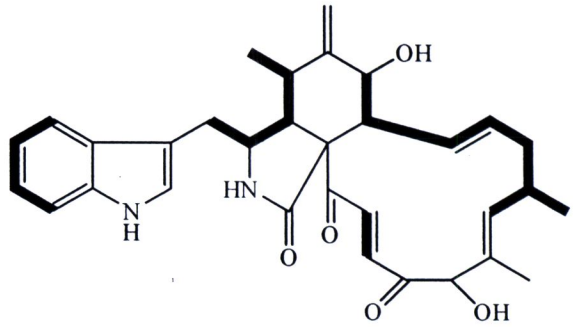


Figure 2.16 COSY correlations (bold lines) of **VIII**.

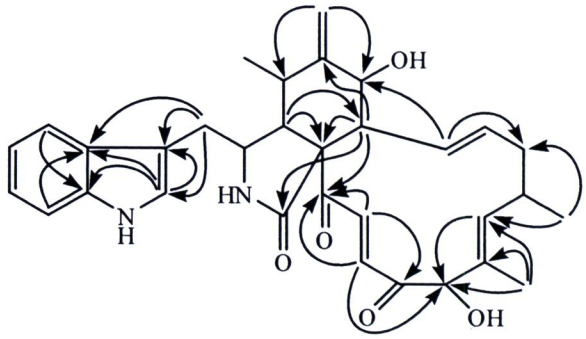


Figure 2.17 HMBC correlations of **VIII**.

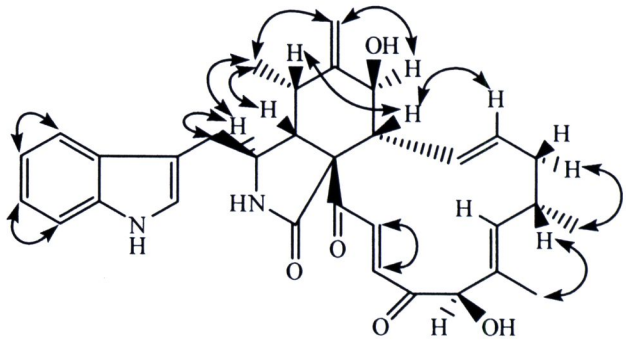


Figure 2.18 NOESY correlations of **VIII**.

Table 2.8 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **VIII** (400 MHz, CD_3OD in $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		173.2	C			
3	3.46 m	52.7	CH	H-4, 10	C-4, 5	H-4, 10
4	2.86 t (4.4)	45.3	CH	H-3, 5, 10	C-3, 5, 8, 9, 10, 11	H-3
5	2.77 m	32.2	CH	H-4, 11		H-8
6		149.5	C			
7	3.89 d (10.6)	70.5	CH	H-8	C-6, 12, 13	H-12, 13
8	2.30 t (10.1)	50.2	CH	H-7, 13	C-1, 6, 7, 9, 13, 14, 23	H-7, 14
9		62.4	C			
10	2.66 dd (6.6, 14.5) 2.90 dd (4.0, 14.5)	32.7	CH_2	H-3	C-3, 4, 2′, 3′, 3′a	H-3, 4, 10
11	1.14 d (6.6)	14.2	CH_3	H-5	C-4, 5, 6	H-3, 4, 5, 12
12	5.10 s, 5.31 s	112.7	CH_2	H-12	C-5, 7	H-12
13	5.79 dd (9.8, 15.4)	128.4	CH	H-8, 14	C-7, 15	H-14
14	5.15 ddt (4.0, 11.0, 14.9)	134.5	CH	H-15	C-8, 15	H-13
15	1.98 m 2.25 d (14.1)	41.8	CH_2	H-14, 16	C-13, 14	H-14, 15
16	2.42 m	32.0	CH	H-15, 17, 24		H-15
17	5.54 d (8.8)	140.3	CH	H-16, 25	C-15, 19, 25	H-19
18		132.3	C			
19	5.03 s	81.5	CH		C-17, 18, 21, 25	H-17
20		201.1	C			
21	6.23 d (16.7)	131.3	CH	H-22	C-19, 22, 23	H-22
22	7.68 d (16.7)	136.4	CH	H-21	C-20, 23	H-17, 19, 21
23		197.9	C			
24	0.95 d (6.6)	20.5	CH_3	H-16	C-15, 16, 17	H-15, 16, 17
25	1.30 s	10.1	CH_3	H-17	C-17, 18, 19	H-16
2′	6.90 s	123.7	CH		C-10, 3′, 3′a, 7′a	
3′		109.3	C			
3′a		127.2	C			
4′	7.42 d (7.5)	118.2	CH	H-5′	C-3′, 6′, 3′a, 7′a	H-5′
5′	7.01 t (7.5)	119.0	CH	H-4′	C-3′a, 7′a	H-4′
6′	7.06 t (8.3)	121.5	CH	H-7′	C-4′, 7′, 7′a	H-7′
7′	7.30 d (7.9)	111.4	CH	H-6′	C-5′, 3′a	H-6′
7′a		136.5	C			

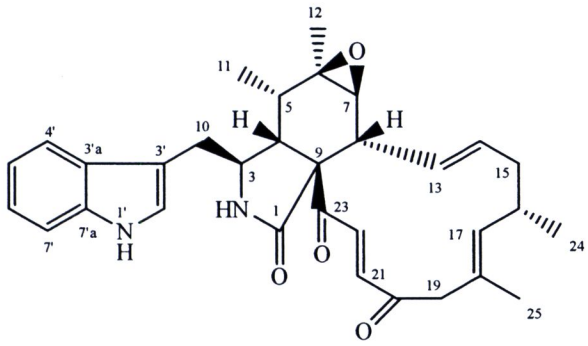
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound IX was obtained as a yellow solid and showed a molecular ion in the HRESITOFMS (Figure 63 in Appendix) at *m/z* 535.2573 ([M+Na]$^+$), indicating a molecular formula $C_{32}H_{36}N_2O_4$. The UV spectra exhibited the absorption maximum of indole chromophore at 222, 280, and 290 nm.[21] The IR spectrum (Figure 64 in Appendix) showed characteristic absorption bands of secondary amine (3420 cm^{-1}), aromatic ring (1610 cm^{-1}), an α,β-unsaturated ketone (1694 and 1680 cm^{-1}), and carbonyl of amide (1659 cm^{-1}). The absorption bands at 2967, 2925, and 1457, 1384 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively. Three absorption bands at 1251, 1091, and 1053 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^{1}H and ^{13}C NMR spectra and DEPT experiments (Figures 65-67 in Appendix and Table 2.9) which exhibited a total of 32 carbon resonances and a sum of 36 hydrogens. The ^{1}H and ^{13}C NMR spectra of **IX** displayed the characteristic signals of the chaetoglobosin unit similar to those of **III** except for the absence of carbonyl group at C-19 (δ_H 2.96 (d, J = 14.1 Hz, H-19), 3.50 (d, J = 13.6 Hz, H-19) and δ_C 53.2) and two sp^3 methylene groups (C-21 and C-22) were replaced by sp^2 methine alkene group (δ_H 6.41 (d, J = 16.4 Hz, H-21) and δ_C 135.4, and δ_H 7.59 (d, J = 16.4 Hz, H-22) and δ_C 134.9). The ^{1}H and ^{13}C NMR spectra and DEPT experiments indicated that **IX** contained 32 carbons, attributable three carbonyl, four sp^2 quaternary, ten sp^2 methine, two sp^3 quaternary, six sp^3 methine, three sp^3 methylene, and four methyl carbons. The ^{13}C NMR spectrum showed two conjugated ketone and one amide carbons at δ 197.3, 201.4 and 173.6, respectively.

The structure of **IX** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 68-71 in Appendix and Table 2.9). The five partial structural units were assigned by analysis of the COSY spectrum shown as bold lines in Figure 2.19. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-5 and H-4, H-11; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-17, H-24; H-21 and H-22; H-1′ and H-2′; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations of H-25 to H-17, 19 (Figure 2.19 and Table 2.9). The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.2 Hz) of olefinic protons. The HMBC spectrum confirmed the

connection of these five units by showing correlations of H-2 to C-3, C-4, and C9; H-3 to C-1, C-4, C-5, C-9, and C-3′; H-8 to C-1, C-4, C-7, C-9, C-13, C-14, and C-23; H-12 to C-5, C-6, C-7, and C-11; H-21 to C-19, C-20, C-22, and C-23; H-22 to C-9, C-20, C-21, and C-23; H-25 to C-17, C-18, C-19, and C-24; H-2′ to C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-6′, C-7′, C-3′a, and C-7′a; and H-7′ to C-4′, C-5′, and C-3′a (Figure 2.20 and Table 2.9). The NOESY spectrum showed the correlations between H–3 and H–10, H-11, H-12; H-4 and H-5, H-11; H–7 and H-8, H–12; H–14 and H–13, H-19, H-24; H–16 and H–24, H-25 depicted in Figure 2.21. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[52,63] as well as the assignment made by 2D NMR experiments, compound **IX** was then identified to be the new natural product, which we named prochaetoglobosin III.



Prochaetoglobosin III (IX)

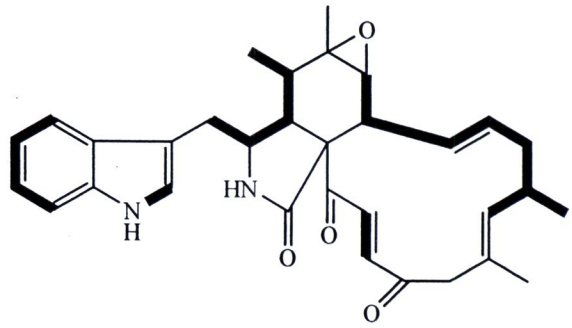


Figure 2.19 COSY correlations (bold lines) of **IX**.

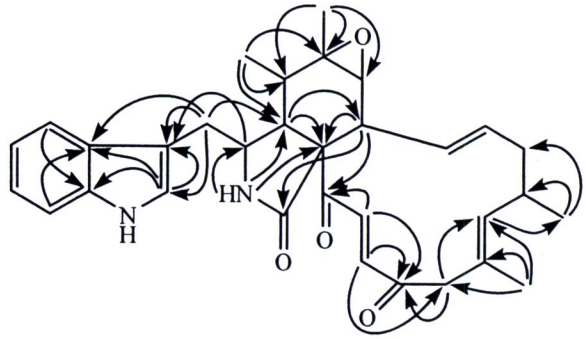


Figure 2.20 HMBC correlations of **IX**.

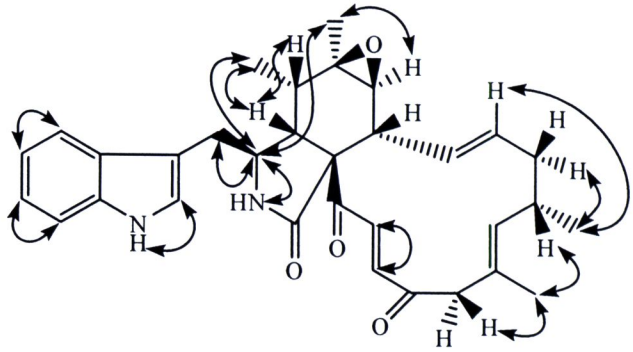


Figure 2.21 NOESY correlations of **IX**.

Table 2.9 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **IX** (400 MHz, $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		173.6	C			
2	6.25 s				C-3, 4, 9	H-3
3	3.79 t (3.5)	52.7	CH	H-4, 10	C-1, 4, 5, 9, 3′	H-10, 11, 12
4	2.98 s	47.2	CH	H-5	C-1, 3, 5, 6, 8, 9, 10, 11, 23	H-5, 11
5	1.83 t (6.6)	36.1	CH	H-4, 11	C-3, 4, 6, 11, 12	H-4, 8, 11
6		58.0	C			
7	2.78 d (5.5)	62.4	CH	H-8	C-6, 8, 9, 12, 13	H-8, 12
8	2.14 dd (5.1, 10.1)	48.6	CH	H-7, 13	C-1, 4, 7, 9, 13, 14, 23	H-5
9		63.4	C			
10	2.64 dd (7.8, 14.4) 2.89 dd (3.9, 14.8)	34.1	CH_2	H-3, 10	C-3, 4, 2′, 3′, 3′a	H-3, 10
11	1.20 d (7.4)	13.4	CH_3	H-5	C-4, 5, 6	H-3, 5
12	1.27 s	19.8	CH_3		C-5, 6, 7, 11	H-3, 7
13	6.06 dd (9.7, 15.2)	127.8	CH	H-8, 14	C-7, 8, 15	H-14
14	5.22 ddt (3.5, 11.3, 15.2)	134.1	CH	H-13	C-7, 8, 16	H-13, 19, 24
15	1.98 m, 2.23 m	41.7	CH_2	H-14, 15, 16	C-13, 14, 16, 17, 24	H-15, 24
16	2.42 m	32.3	CH	H-15, 17, 24	C-17	H-24, 25
17	5.20 d (9.0)	138.3	CH	H-16, 25	C-15, 19, 24, 25	
18		128.0	C			
19	2.96 d (14.1) 3.50 d (13.6)	53.2	CH_2	H-19, 25	C-17, 18, 20, 25	H-19, 25
20		201.4	C			
21	6.41 d (16.4)	135.4	CH	H-22	C-19, 20, 22, 23	H-22
22	7.59 d (16.4)	134.9	CH	H-21	C-9, 20, 21, 23	H-21
23		197.3	C			
24	0.94 d (6.6)	21.2	CH_3	H-16	C-15, 16, 17	H-15, 16
25	1.48 s	16.1	CH_3	H-17, 19	C-17, 18, 19, 24	H-16
1′	8.47 s			H-2′	C-3′a	
2′	6.94 d (1.6)	123.3	CH	H-1′	C-3′, 3′a, 7′a	H-1′
3′		110.3	C			
3′a		127.1	C			
4′	7.49 d (7.8)	118.3	CH	H-5′	C-3′, 6′, 7′, 3′a, 7′a	H-5′
5′	7.12 t (7.0)	119.8	CH	H-4′, 6′	C-4′, 6′, 7′, 3′a, 7′a	H-4′
6′	7.18 t (7.0)	122.3	CH	H-5′, 7′	C-4′, 5′, 7′a	H-7′
7′	7.34 d (8.2)	111.6	CH	H-6′	C-4′, 5′, 3′a	H-6′
7′a		136.4	C			

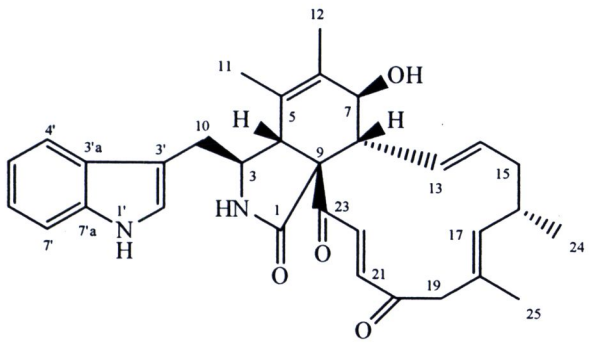
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound X was obtained as a pale yellow solid and showed a molecular ion in the HRESITOFMS (Figure 72 in Appendix) at *m/z* 535.2573 ($[M+Na]^+$), indicating a molecular formula $C_{32}H_{36}N_2O_4$. The UV spectra exhibited the absorption maximum of indole chromophore at 222, 280, and 290 nm.[21] The IR spectrum (Figure 73 in Appendix) showed characteristic absorption bands of secondary amine (3410 cm^{-1}), aromatic ring (1617 cm^{-1}), and an α,β-unsaturated ketone (1693 cm^{-1}). The absorption bands at 2952, 2922, and 1457, 1387 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively, while the absorption bands at 1251, 1095, and 1036 cm^{-1} were characteristic of C-O stretching.

The molecular formula assignment was reinforced by its ^1H and ^{13}C NMR spectra and DEPT experiments (Figures 74-76 in Appendix and Table 2.10) which exhibited a total of 32 carbon resonance lines and a sum of 36 hydrogens. The ^1H and ^{13}C NMR spectra of **X** displayed the characteristic signals of the chaetoglobosin unit similar to those of **VII** except for the absence of hydroxyl group at C-19, δ_H 2.92, 3.46 (d, J = 12.9 Hz, H-19) and δ_C 53.2. The ^1H and ^{13}C NMR spectra and DEPT experiments indicated that **X** contained 32 carbons, attributable three carbonyl, six sp^2 quaternary, ten sp^2 methine, one sp^3 quaternary, five sp^3 methine, three sp^3 methylene, and four methyl carbons. The ^{13}C NMR spectrum showed two conjugated ketone and one amide carbons at δ 198.4, 201.1 and 173.9, respectively.

The structure of **X** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 77-80 in Appendix and Table 2.10). The five partial structural units were assigned by analysis of the COSY spectra shown as bold lines in Figure 2.22. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-17, H-24; H-21 and H-22; H-1′ and H-2′; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations of H-4 and H-7, H-11, H-12; H-17 and H-19, H-25 (Figure 2.22 and Table 2.9). The *E*-geometry of the double bond was deduced from a coupling constant ($J_{13,14}$ = 15.2 Hz) of olefinic protons. The connection of these five units and the remaining functional groups was determined on the basis of the HMBC correlations of H-3 to C-5 and C-3′; H-8 to C-1, C-6, C-7, C-9, C-13, C-14, and C-23; H-12 to C-5, C-6, and C-7; H-21 to C-20, C-22, and C-23; H-22 to C-20, C-21, and

C-23; H-25 to C-17 and C-18; H-2′ to C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-6′, C-7′, C-3′a, and C-7′a; and H-7′ to C-4′, C-5′, C-6′, and C-3′a (Figure 2.23 and Table 2.10). The NOESY spectrum showed the correlations between H–3 and H-4, H–7, H-10, H-11; H-4 and H-8, H-10, H-11; H–7 and H-3, H-8, H–12, H-13; H–10 and H–3, H-4, H-2′; H–19 and H–25 depicted in Figure 2.24. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[63] as well as the assignment made by 2D NMR experiments, compound **X** was then identified to be the new natural product, which we named prochaetoglobosin IIIed.



Prochaetoglobosin IIIed (X)

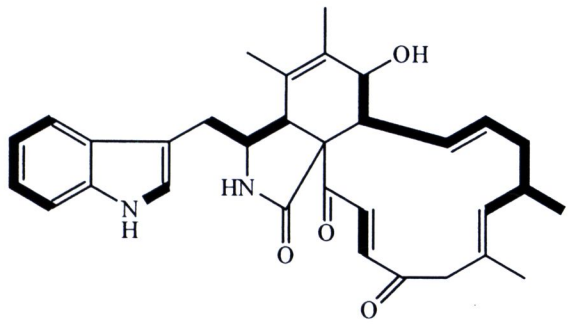


Figure 2.22 COSY correlations (bold lines) of **X**.

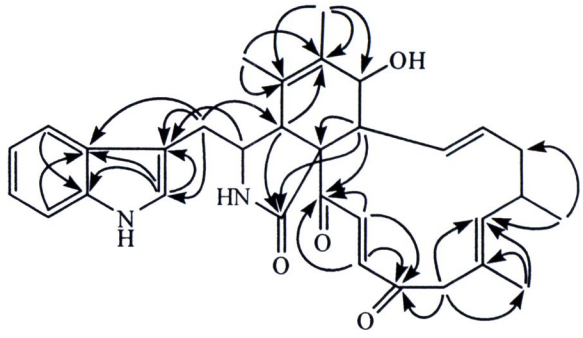


Figure 2.23 HMBC correlations of **X**.

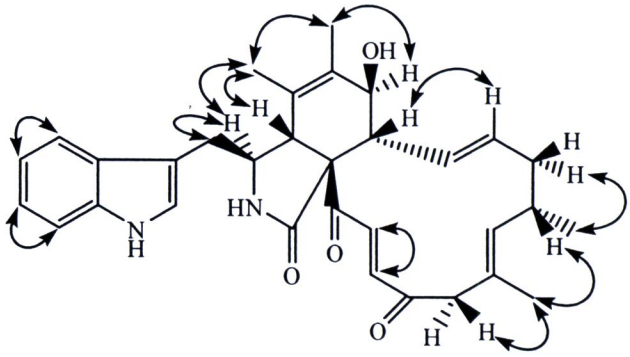


Figure 2.24 NOESY correlations of **X**.

Table 2.10 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **X** (400 MHz, CD_3OD in $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		173.9	C			
3	3.48	58.2	CH	H-4, 10	C-5, 3′	H-4, 7, 10, 11
4	3.24 s	47.7	CH	H-3, 7, 11, 12	C-1, 5, 6, 23	H-8, 10, 11
5		126.2	C			
6		132.2	C			
7	3.83 d (9.7)	68.6	CH	H-8, 11, 12		H-3, 8, 12, 13
8	2.03 t (9.7)	52.0	CH	H-7, 13	C-1, 6, 7, 9, 13, 14, 23	H-4, 14
9		61.5	C			
10	2.68 m	32.4	CH_2	H-3	C-2′, 3′, 3′a	H-3, 4, 2′
11	1.44 s	17.5	CH_3	H-4, 7, 12	C-5, 6	H-3, 4, 12
12	1.62 s	13.9	CH_3	H-4, 7, 12	C-5, 6, 7	H-7, 11
13	6.0.3 dd (10.1, 15.2)	127.2	CH	H-8, 14, 15	C-7, 8, 15	H-7, 14, 15
14	5.22 ddt (3.1, 10.5, 14.8)	136.7	CH	H-13, 15	C-8, 15	H-8
15	1.94 d (11.3) 2.23 d (13.6)	41.4	CH_2	H-14, 15, 16	C-13, 14, 17, 24	H-15, 24
16	2.43 m	32.5	CH	H-15, 17, 24	C-24	H-15, 17, 24
17	5.16 d (9.4)	138.5	CH		C-19, 25	H-13, 15, 16, 22, 24
18		127.7	C			
19	2.92 d (12.9) 3.46	53.4	CH_2	H-17, 19, 25	C-17, 18, 20, 24, 25	H-19,25
20		201.1	C			
21	6.63 d (16.0)	136.8	CH	H-22	C-20, 22, 23	H-22
22	7.46 d (16.4)	134.5	CH	H-21	C- 20, 21, 23	H-21
23		198.4	C			
24	0.90 d (6.6)	21.1	CH_3	H-16	C-15, 17	H-15, 16, 17, 25
25	1.47 s	16.13	CH_3	H-17, 19	C-17, 18	H-16. 19, 24
1′	9.31 s			H-2′		
2′	6.93 s	123.2	CH	H-1′	C-3′, 3′a, 7′a	H-4, 10
3′		110.2	C			
3′a		126.9	C			
4′	7.43 d (8.5)	118.2	CH	H-5′	C-3′, 6′, 7′, 3′a, 7′a	H-5′
5′	7.02 t (7.4)	119.2	CH	H-4′, 6′	C-6′, 3′a	H-4′, 6′
6′	7.09 t (7.0)	121.8	CH	H-5′, 7′	C-4′, 7′, 3′a, 7′a	H-5′, 7′
7′	7.29 d (8.5)	111.4	CH	H-6′	C-4′, 5′, 6′, 3′a	H-6′
7′a		136.4	C			

[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound XI was afforded as a white solid and showed a molecular ion in the HRESITOFMS (Figure 81 in Appendix) at *m/z* 521.2780 ($[M+Na]^+$), indicating a molecular formula $C_{32}H_{38}N_2O_3$. The UV spectra exhibited the absorption maximum of indole chromophore at 222, 280, and 290 nm.[21] The IR spectrum (Figure 82 in Appendix) showed characteristic absorption bands of hydroxyl group (3530-3250 cm^{-1}), secondary amine (3522 cm^{-1}), amide (3330 cm^{-1}), aromatic ring (1616 cm^{-1}), an α,β-unsaturated ketone (1704 cm^{-1}), and carbonyl of amide (1657 cm^{-1}). The absorption bands 2951, 2917 and 1456, 1384 cm^{-1} were assigned to aliphatic C-H stretching and bending, respectively. Three absorption bands at 1259, 1233, and 1036 cm^{-1} were characteristic of C-O stretching.

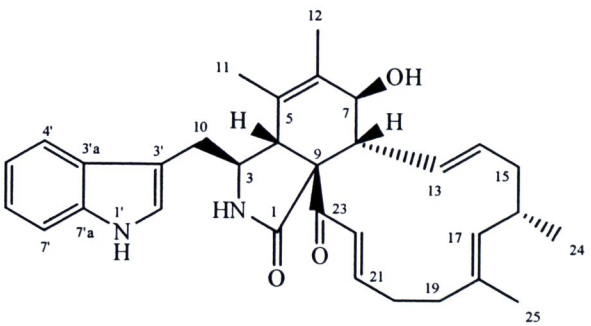
The molecular formula assignment was reinforced by its ^1H and ^{13}C NMR spectra (Figures 83 and 84 in Appendix and Table 2.11) which exhibited a total of 32 carbon resonances and a sum of 38 hydrogens. The ^1H NMR spectrum displayed two singlet signal of secondary amine protons at δ 8.47 (s, H-2) and 9.53 (s, H-1′), five low-field signals of an indole group at δ 6.94 (s, H-2′), 6.97 (t, J = 8.2 Hz, H-5′), 7.07 (t, J = 7.8 Hz, H-6′), 7.29 (d, J = 8.2 Hz, H-7′) and 7.44 (d, J = 7.8 Hz, H-4′), four signals of *trans*-double bond protons at δ 5.16 (ddd, J = 2.3, 10.1, 15.2 Hz, H-14), 5.92 (ddd, J = 1.6, 9.7, 15.2 Hz, H-13), 6.33 (d, J = 15.2 Hz, H-22) and 6.81 (ddt, J = 5.5, 9.7, 15.2 Hz, H-21), one olefinic proton at δ 4.60 (d, J = 9.7 Hz, H-17), and four methyl group signals at δ 0.85 (d, J = 6.6 Hz, H-24), 1.34 (s, H-12), 1.50 (s, H-25) and 1.60 (s, H-11). The ^1H and ^{13}C NMR spectra and DEPT experiments (Figures 83-85 in Appendix and Table 2.11) indicated that **XI** contained 32 carbons, attributable to two carbonyl, six sp^2 quaternary, ten sp^2 methine, one sp^3 quaternary, five sp^3 methine, four sp^3 methylene, and four methyl carbons. The appearance of the signals due to a sp^3 methine at δ_H 3.46 (t, J = 7.8 Hz, H-3) and δ_C = 58.6 implied that one of the four sp^3 methines is linked to an amide group. The methine proton (H-7), coupling to H-8 as a doublet, was assigned a hydroxymethine on the basis of its chemical shift at δ_H 3.78 and δ_C 68.1. The appearance of three allylic methyl proton singlets at δ 1.34 (H-12), 1.50 (H-25), and 1.60 (H-11) and three quaternary carbon signals at δ 126.0 (C-5), 130.7 (C-18), and 133.5 (C-6) implied the presence of a tetrasubstituted double bond linked to three methyl groups, whereas the other methyl

group showed as doublet at δ 0.85 (H-24). The ^{13}C NMR spectrum showed conjugated ketone and amide carbons at δ 198.0 and 175.2, respectively.

The structure of **XI** was confirmed by analysis of the 2D NMR spectra including COSY, HSQC, HMBC, and NOESY (Figures 86-89 in Appendix and Table 2.11). The four partial structural units were assigned by analysis of the COSY spectra shown as bold lines in Figure 2.25. The COSY spectrum displayed correlations between H-3 and H-4, H-10; H-8 and H-7, H-13; H-14 and H-13, H-15; H-16 and H-17, H-24; H-20 and H-19, H-21; H-21 and H-22; H-5′ and H-4′, H-6′; H-6′ and H-7′; and long-range correlations between H-4 and H-7, H-11, H-12; H-17 and H-19, H-25 (Figure 2.25 and Table 2.11). The *E*-geometry of both double bonds were deduced from coupling constant ($J_{13,14}$ and $J_{21,22}$ = 15.2 Hz) of olefinic protons. The connection of these four units and the remaining functional groups was determined on the basis of the HMBC correlations of H-3 to C-1, C-4, C-5, C-9, and C-3′; H-8 to C-4, C-7, and C-9; H-12 to C-4 and C-6; H-21 to C-23; H-22 to C-20 and C-23; H-25 to C-17, C-18, and C-19; H-2′ to C-10, C-3′, C-3′a, and C-7′a; H-4′ to C-3′, C-6′, C-3′a, and C-7′a; and H-7′ to C-5′, C-6′, and C-3′a (Figure 2.26 and Table 2.11). The NOESY spectrum showed the correlations between H–3 and H-4, H-10, H-12; H-4 and H-8, H-10, H-12; H–7 and H-11, H-13; H–10 and H–3, H-4, H-10, H-2′; H–19 and H-17, H-21, H–25 depicted in Figure 2.27.

The relative stereochemistry of compound **XI** was determined by comparing its ^{13}C NMR and NOESY spectra with those of its reported congener, chaetoglobosin A,[24,63,64] whose absolute configulations were established by X-ray diffraction analysis. ^{13}C NMR spectrum of **XI** showed the chemical shifts of C-1 through C-23 and of C-2′ through C-7′ nearly identical to those of chaetoglobosin B (**VII**), chaetoglobosin E, prochaetoglobosin IIIed (**X**), and prochaetoglobosin IV.[24,63] In addition, the substructure of **XI** shared the absolute configulations with those of the four related compounds. This was further substantiated by the full detection of the anticipated NOESY correlations. The observed coupling constants and NOESY (Table 2.11) showed that the relative stereochemistry of **XI** is the same as prochaetoglobosin IIIed (**X**). The coupling constant (8.5 Hz) of H-7 to H-8 implied that H-7 is arranged axial and *trans* to H-8.[22,64] The NOESY spectrum showed correlations between H-8 and

H-4, indicating that H-4 was axial and *cis* to H-8. The observed NOESY correlations for H-17 and H-15a, H-17 and H-16, H-17 and H-19, H-19 and H-20b, and H-20b and H-15 revealed that the conformation of macrocyclic ring. Finally, the absolute configulations of **XI** were compared with chaetoglobosin E and chaetoglobosin G (**VI**) as 3*S*, 4*R*, 7*S*, 8*R*, and 16*S*.[62] Compound **XI** was then identified to be the new cytochalasans compound, which we named chaetoglobosin V.



Chaetoglobosin V (XI)

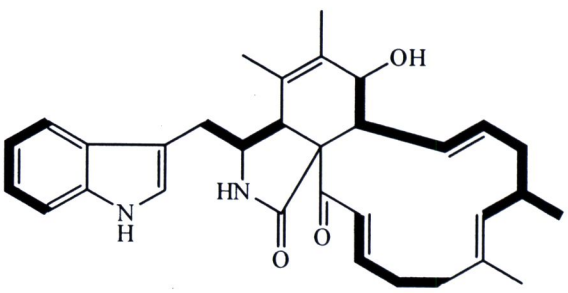


Figure 2.25 COSY correlations (bold lines) of **XI**.

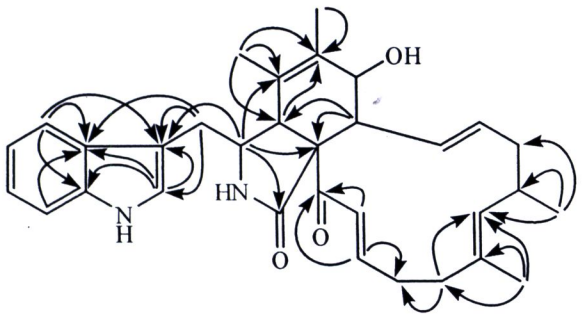


Figure 2.26 HMBC correlations of **XI**.

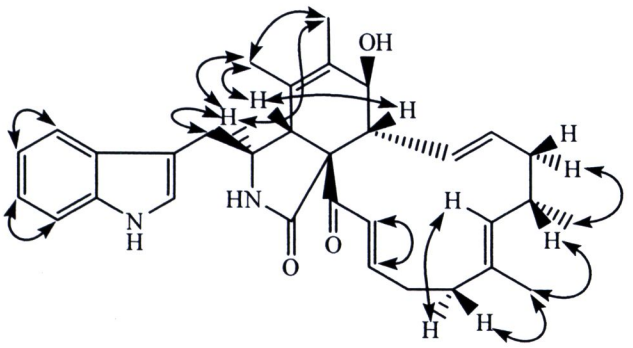


Figure 2.27 NOESY correlations of **XI**.

Table 2.11 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **XI** (400 MHz, CD_3OD in $CDCl_3$)[a]

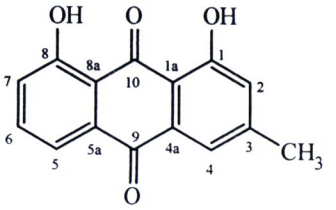
position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1		175.2	C			
2	8.47					
3	3.46 t (7.8)	58.6	CH	H-4, 10a, 10b	C-1, 4, 5, 9, 3′	H-4, 10a, 10b, 12, 2′, 4′
4	2.90 s	48.1	CH	H-3, 7, 11, 12	C-6	H-3, 8, 10a, 12, 22, 2′
5		126.0	C			
6		133.5	C			
7	3.78 d (8.5)	68.1	CH	H-4,8,11,12		H-11, 13
8	2.24 m	50.6	CH		C-4, 7, 9	H-4
9		60.8	C			
10a	2.67 dd (7.6, 14.2)	31.6	CH_2	H-3, 10b	C-3, 2′, 3′, 3′a	H-3, 4, 10b, 2′, 4′
10b	2.73 dd (7.8, 14.2)			H-3, 10a	C-3, 2′, 3′, 3′a	H-3, 4, 10a, 2′
11	1.60 s	14.1	CH_3	H-4, 7, 12	C-3, 4, 6, 7, 12,	H-7, 12
12	1.34 s	17.2	CH_3	H-4, 7, 11	C-4, 5, 6	H-3, 4, 11, 14, 16, 19, 20a
13	5.92 ddd (1.6, 9.7, 15.2)	124.8	CH	H-8, 14	C-15	H-7, 14, 15a
14	5.16 ddd (2.3, 10.1, 15.2)	138.4	CH	H-13, 15a, 15b		H-12, 13, 15b, 16, 25
15a	1.74 m	39.8	CH_2	H-14, 15b	C-13, 14, 16, 17	H-13, 15b, 17, 19, 24
15b	2.22 m			H-14, 15a, 16	C-17	H-7, 15a, 24
16	2.43 m	32.9	CH	H-17, 24	C-24	H-14, 17, 24, 25
17	4.60 d (9.7)	132.4	CH	H-16, 19, 25	C-16, 19, 24, 25	H-15a, 16, 19, 24
18		130.7	C			
19	2.16 m	38.3	CH_2	H-17, 20b	C-17, 18, 20, 25	H-17, 20b, 21, 25
20a	2.25 m	30.1	CH_2	H-19, 20b	C-22	H-20b, 25
20b	2.35 m			H-20a	C-18, 21, 22	H-15b, 20a, 21
21	6.81 ddt (5.5, 9.7, 15.2)	150.1	CH	H-20a, 20b, 22	C-23	H-19, 20, 22
22	6.33 d (15.2)	126.0	CH	H-21	C-20, 23	H-4, 15b, 21
23		198.0	C			
24	0.85 d (6.6)	21.3	CH_3	H-16	C-15, 16, 17	H-15a, 15b, 16, 17, 25
25	1.50 s	16.2	CH_3	H-17	C-17, 18, 19	H-14, 16. 19, 20a, 24
1′	9.53 s					
2′	6.94 s	123.2	CH		C-10, 3′, 3′a, 7′a	H-3, 4, 10a, 10b
3′		110.7	C			
3′a		127.0	C			
4′	7.44 d (7.8)	118.3	CH	H-5′	C-3′, 6′, 3′a, 7′a	H-3, 10a, 5′
5′	6.97 t (8.2)	119.0	CH	H-4′, 6′	C-7′, 3′a	H-4′, 6′
6′	7.07 t (7.8)	121.6	CH	H-5′, 7′	C-4′, 7′, 3′a, 7′a	H-5′, 7′
7′	7.29 d (8.2)	111.3	CH	H-6′	C-5′, 6′, 3′a	H-6′
7′a		136.4	C			

[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound XII was obtained as orange needles. The UV spectrum displayed the absorption maxima at 229, 259, 290, and 432 nm indicating the presence of an extended conjugated system. The IR spectrum (Figure 90 in Appendix) showed the O-H stretching of hydroxyl group at 3433 cm^{-1}. A set of absorption band at 2922 and 1477, 1458, 1386 cm^{-1} was assigned to C-H stretching and bending, respectively. The characteristic absorption bands of aromatic system appeared at 3064, 1607, 1593, and 1573 cm^{-1}, while the absorption bands at 1672 and 1630 cm^{-1} were characteristic of carbonyl ketone and chelating carbonyl ketone, respectively.

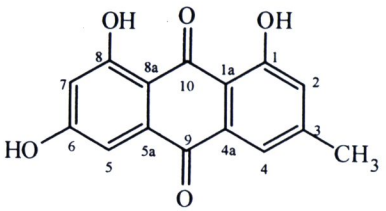
The ^{1}H and ^{13}C NMR spectrum (Figures 91 and 92 in Appendix and Table 2.12) showed the characteristic signals of a hydroxyantraquinone skeleton. The ^{1}H NMR spectrum indicated the presence of two hydroxyl groups as two singlet signals at δ 12.00 (1-OH) and 12.11 (8-OH). The signals of aromatic protons appeared as two singlets at δ 7.09 (H-2) and 7.64 (H-4), two doublet of doublets at δ 7.81 (J = 1.1, 7.5 Hz, H-5), 7.28 (J = 1.1, 8.4 Hz, H-7) and one triplet at δ 7.66 (J = 8.1 Hz, H-6). A methyl substitute attached to the 3-position of aromatic ring displayed as a singlet at δ 2.46.

Analysis of its ^{13}C NMR and DEPT spectrum (Figures 92 and 93 in Appendix and Table 2.12) indicated fifteen carbons of two carbonyl, seven sp^2 quaternary, five sp^2 methine, and one methyl carbons. The ^{13}C NMR spectral data showed signals at δ 162.7 (C-1) and 162.4 (C-8) on the aromatic ring which were corresponding to the hydroxyl bearing carbons at the 1 and 8 positions of anthraquinone, respectively. The resonance signals at δ 182.0 and 192.5 were assigned to the carbonyl carbon atoms of C-9 and C-10 of anthraquinone, respectively. Comparison of the NMR data of **XII** with those of the known compound reported from *C. globosum* KMITL-N0802,[3,35] the structure of **XII** was deduced as a known dihydroxyantraquinone, chrysophanol.



Chrysophanol (XII)

Compound XIII was obtained as an orange solid. The UV spectrum appeared the presence of an extended conjugated system due to the maximum absorption bands at 253, 266, 289, and 436 nm. The IR spectrum (Figure 94 in Appendix) showed characteristic absorption bands of hydroxyl group (3367 cm^{-1}), aromatic ring (3050 and 1588 cm^{-1}), and chelating carbonyl ketone (1630 cm^{-1}). The ^{1}H and ^{13}C NMR spectral features (Figures 95 and 96 in Appendix and Table 2.12) of **XIII** were similar to those of chrysophanol (**XII**) except for the presence of the hydroxyl group at C-6 (δ 165.4). From these spectroscopic evidence and by comparison with dihydroxy-antraquinone in literature data of *Heterodermia obscurata*,[65] compound **XIII** was then identified as a known emodin.



Emodin (XIII)

Table 2.12 ^{1}H and ^{13}C NMR spectral data of **XII** and **XIII** (400 MHz, $CDCl_3$ and CD_3OD in $CDCl_3$, respectively)[a]

position	XII		XIII	
	^{1}H	^{13}C	^{1}H	^{13}C
1		162.7		161.8
1a		113.7		113.5
2	7.09 (s)	124.3	7.01 (s)	124.2
3		149.3		147.9
4	7.64 (s)	121.3	7.52 (s)	120.9
4a		133.3		132.9
5	7.81 (dd, 1.1, 7.5)	119.9	7.17 (d, 2.4)	109.2
5a		133.6		135.1
6	7.66 (t, 8.1)	136.9		165.2
7	7.28 (dd, 1.1, 8.4)	124.5	6.56 (d, 2.4)	108.2
8		162.4		164.8
8a		115.9		108.2
9		182.0		182.5
10		192.5		190.2
1-OH	12.00 (s)		12.15 (s)	
3-CH_3	2.46 (s)	22.2	2.38 (s)	21.7
6-OH			12.25 (s)	
8-OH	12.11 (s)			

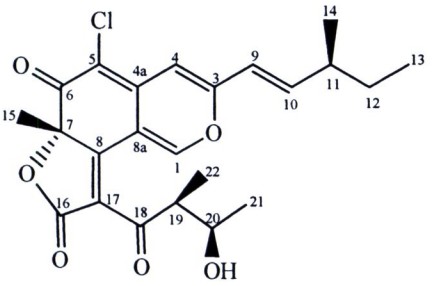
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound XIV was obtained as red-orange needles. The UV spectrum displayed absorption maxima at 229, 306 and 366 nm, indicating the presence of an extended conjugated system. Its IR spectrum (Figure 97 in Appendix) showed a broad absorption band at 3421 cm^{-1} corresponding to the O-H stretching of a hydroxyl group. The weak absorption band at 2971 cm^{-1} was assigned to C-H stretching of the alkene. The strong absorption band at 1773 cm^{-1} was characterized as α,β-unsaturated-γ-lactone, while conjugated ketone appeared at 1680 and 1649 cm^{-1}.

The ^{1}H and ^{13}C NMR spectra (Figures 98 and 99 in Appendix and Table 2.13) exhibited a total of 23 carbons and 25 hydrogens. The ^{1}H NMR spectrum revealed a low-field resonance of an olefinic proton at δ 8.76 (s, H-1), three olefinic protons at δ 6.07 (d, J = 15.7 Hz, H-9), 6.55 (s, H-4), and 6.60 (dd, J = 8.0, 15.7 Hz, H-10), and five signals of methyl groups at δ 0.91 (t, J = 7.4 Hz, H-13), 1.09 (d, J = 6.7 Hz, H-14), 1.17 (d, J = 6.2 Hz, H-21 and H-22), and 1.70 (s, H-15). The ^{1}H and ^{13}C NMR spectra and DEPT experiments (Figures 98-100 in Appendix and Table 2.13) indicated three carbonyl, six sp^2 quaternary, four sp^2 methine, one sp^3 quaternary, three sp^3 methine, one sp^3 methylene, and five methyl carbons. The ^{13}C NMR spectrum showed conjugated ketone carbonyls at δ 183.3 and 201.1 and a lactone carbonyl at δ 167.9.

The structure of **XIV** was then elucidated to be an azaphilone bearing a five-membered-ring lactone from 2D NMR analysis, including COSY, HSQC, HMBC and NOESY experiments (Figures 101-104 in Appendix and Table 2.13). The three partial structural units were assigned by analysis of the COSY spectrum (Figure 2.28). The 3-methyl-1-pentenyl and 2-butanol-3-yl groups were established by COSY correlations (Figure 2.28) between H-9 and H-10; H-11 and H-12, H-14; H-12 and H-13; H-19 and H-20, H-22; and H-20 and H-21. The HMBC spectrum (Figure 2.29 and Table 2.13) confirmed the connection of these three units by demonstrating ^{3}J correlations of H-1 to C-3, C-4a, and C-8; H-4 to C-5, and C-9; H-9 to C-4, and C-11; H-10 to C-3, C-12, and C-14; H-15 to C-8; H-21 to C-22; H-21 to C-19; and H-22 to C-18. The configurations of the C-9 and C-10 double bond were found to be *E*, on the basis of coupling constants (Table 2.13) and observation of NOESY correlation (Figure 2.30). The HMBC spectrum exhibited correlations of H-9 and H-10 to C-3, confirming the connection of this unit at C-3. Base on the analysis of the above data

and from a comparison of the physical properties with those reported in the literature,[31] compound **XIV** was deduced as a known chaetoviridin A.



Chaetoviridin A (XIV)

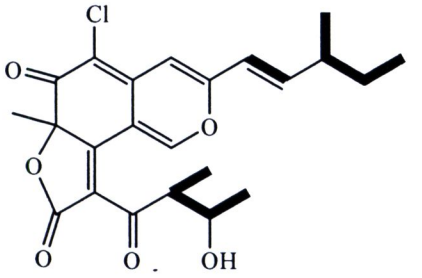


Figure 2.28 COSY correlations (bold lines) of **XIV**.

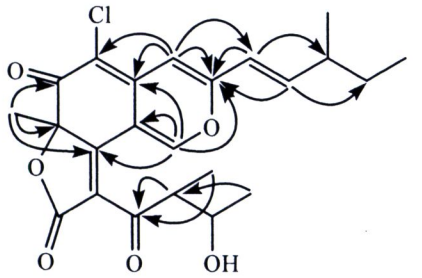


Figure 2.29 HMBC correlations of **XIV**.

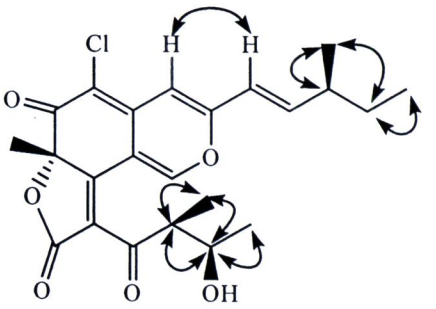


Figure 2.30 NOESY correlations of **XIV**.

Table 2.13 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **XIV** (400 MHz, $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1	8.76 s	151.5	CH		C-3, 8, 4a, 8a	
3		157.0	C			
4	6.55 s	105.4	CH		C-3, 5, 9, 4a	H-9
4a		139.6	C			
5		109.0	C			
6		183.3	C			
7		87.6	C			
8		162.9	C			
8a		110.4	C			
9	6.07 d (15.7)	119.7	CH	H-10	C-3, 4, 10, 11	H-4
10	6.60 dd (8.0, 15.7)	148.0	CH	H-9	C-3, 11, 12, 14	
11	2.29 m	40.0	CH	H-12, 14		H-14
12	1.45 quint (7.6)	29.1	CH_2	H-11, 13	C-10, 11, 13, 14	H-13, 14
13	0.91 t (7.4)	11.7	CH_3	H-12	C-11, 12	H-12
14	1.09 d (6.7)	19.2	CH_3	H-11	C-10, 11, 12	H-11, 12
15	1.70 s	26.3	CH_3		C-6, 7, 8	
16		167.9	C			
17		124.9	C			
18		201.1	C			
19	3.63 quint (6.8)	50.9	CH	H-20, 22	C-18, 20	H-20, 21, 22
20	3.86 quint (6.3)	70.9	CH	H-19, 21	C-19, 21	H-19, 21, 22
21	1.17 d (6.2)	21.5	CH_3	H-20	C-19, 20	H-19, 20
22	1.17 d (6.2)	13.5	CH_3	H-19	C-18, 19, 20	H-19, 20

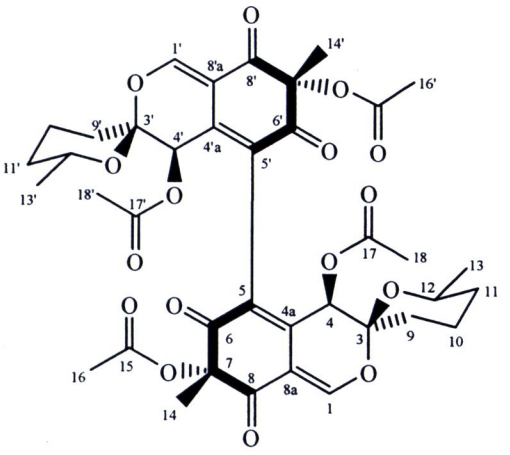
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound XV was obtained as a pale yellow solid, and was assigned the molecular formula $C_{38}H_{42}O_{16}$, as deduced from the HRESITOF mass spectrum (Figure 105 in Appendix) (observed *m/z* 777.2371 $[M+Na]^+$) indicating 18 degrees of unsaturation. The UV spectrum displayed an absorption maximum due to $\alpha,\beta,\gamma,\delta$-conjugated ketone at 230, 299, and 334 nm. The IR spectrum (Figure 106 in Appendix) showed absorption bands at 3060, 1605, and 1582 cm^{-1} due to C-H and C=C stretching. The absorption bands at 1766 and 1741 cm^{-1} were characterized to the esters carbonyl, whereas the absorption bands at 1712 and 1675 cm^{-1} were assigned to an α,β-unsaturated and $\alpha,\beta,\gamma,\delta$-conjugated ketone groups.

The ^1H NMR spectrum (Figure 107 in Appendix and Table 2.15) showed half number of resonance signals expected for 42 protons. Therefore, the structure must be a symmetrical dimer. The monomeric unit showed the presence of an olefinic proton at δ 7.82 (s, H-1/H-1′), an oxymethine proton at δ 4.16 (m, H-12/H-12′), a methane proton at δ 5.85 (s, H-4/H-4′), three methylene protons at δ 1.36 and 2.35 (m, H-9/H-9′); 1.77 (m, H-10/H-10′); and 1.21 and 1.76 (m, H-11/H-11′), and four methyl groups at δ 2.11 (s, H-16/H-16′), 1.93 (s, H-18/H-18′), 1.59 (s, H-14/H-14′) and 1.15 (d, J = 6.2 Hz, H-13/H-13′). The ^{13}C NMR and DEPT spectral (Figures 108 and 109 in Appendix and Table 2.15) showed only 19 signals attributable to four carbonyl (δ 168.5, 169.1, 190.9, 193.6), three sp^2 quaternary (δ 109.6, 124,7, 140.3), one sp^2 methine (δ 158.5), two sp^3 quaternary (δ 84.9 and 103.4), two sp^3 methine (oxymethine, δ 66.8, 69.3), three sp^3 methylene (δ 18.2, 28.9, 31.9) and four methyl carbons (δ 19.8, 19.9, 21.5, 22.3). The siglet signal at δ_H 5.85 (H-4/H-4′) which correlated to acetate carbonyl C-17/C-17′ (δ_C 168.5) in the HMBC experiment revealed that the acetoxy group was located at C-4/C-4′.

The structural connectivity of **XV** was then confirmed by 2D NMR spectroscopic analysis, including COSY, HSQC, HMBC, and NOESY experiments (Figures 110-113 in Appendix and Table 2.14). The HMBC spectrum (Figure 2.31) showed the connectivity of its skeleton by demonstrating correlations of H-1 to C-3, C-4a, C-8, and C-8a; H-4 to C-4a, C-5, C-8a, and C-17; H-9 to C-11; H-13 to C-11, and C-12; H-14 to C-6, C-7, and C-8; H-16 to C-15; and H-18 to C-17. The COSY spectrum displayed correlations of the tetrahydropyran ring protons between H-9 and H-10, H-10 and H-11, H-11 and H-12, and H-12 and H-13. The NOESY spectrum

(Figure 2.32) displayed correlations of oxymethine and the tetrahydropyran ring protons between H-4 and H-9, H-9 and H-10, H-9 and H-11, H-10 and H-11, H-10 and H-12, and H-12 and H-13. According to the analysis of the above data and comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported in literature[66] as well as the assignment made by 2D NMR experiments, compound **XV** was then identified to be the known cochliodone D, which previously isolated from *C. cochliodes* CTh05.



Cochliodone D (XV)

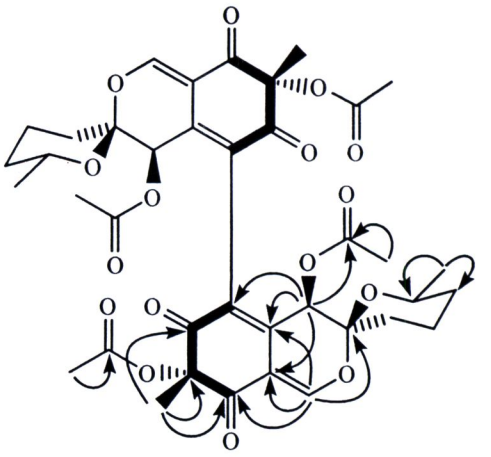


Figure 2.31 HMBC correlations of **XV**.

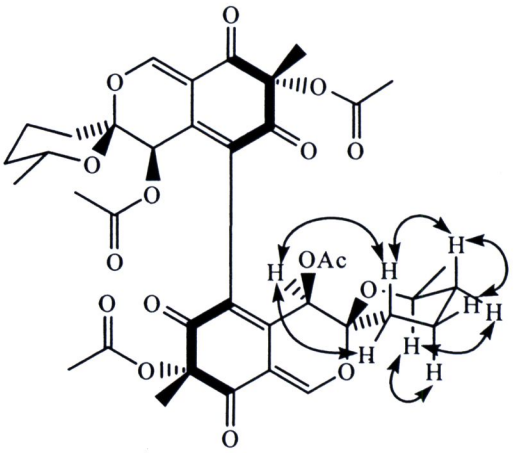


Figure 2.32 NOESY correlations of **XV**.

Table 2.14 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **XV** (400 MHz, $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
1, 1′	7.82 (s)	158.5	CH		C-3, 8, 4a, 8a	
3, 3′		103.4	C			
4, 4′	5.85 (s)	66.8	CH		C-5, 6, 8, 9, 4a, 8a, 17	
4a, 4′a		109.6	C			
5, 5′		124.7	C			
6, 6′		193.6	C			
7, 7′		84.9	C			
8, 8′		190.9	C			
8a, 8′a		140.3	C			
9, 9′	1.36 (m) 2.35 (m)	28.9	CH_2	H-10	C-3, 10, 11	H-4, 10, 11
10, 10′	1.77 (m)	18.2	CH_2	H-9, 11	C-3, 11, 12	H-9, 11
11, 11′	1.21 (m) 1.76 (m)	31.9	CH_2	H-10, 12	C-10, 12	H-9, 10
12, 12′	4.16 (m)	69.3	CH_2	H-11, 13		H-13
13, 13′	1.15 (d, 6.4)	21.5	CH_3	H-12	C-11, 12	H-11, 12
14, 14′	1.59 (s)	22.3	CH_3		C-6, 7, 8	H-6,8, 11
15, 15′		169.1	C			
16, 16′	2.11 (s)	19.8	C			
17, 17′		168.5	C			
18, 18′	1.93 (s)	19.9	C			

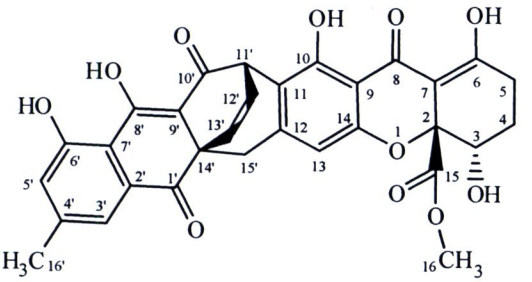
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound XVI was isolated as a pale yellow solid and assigned the molecular formula $C_{31}H_{24}O_{11}$ (*m/z* observed 595.1215 $[M+Na]^+$), as deduced from the HRESITOF mass spectrum (Figure 114 in Appendix), indicating 20 degrees of unsaturation. The UV spectrum displayed absorption maxima at 254, 274, 339, and 379 nm, indicating the presence of an extended conjugated system. The IR spectrum (Figure 115 in Appendix) showed characteristic of hydroxyl (3436 cm^{-1}), and chelating carbonyl (1741, 1687, and 1610 cm^{-1}) groups.

The ^1H NMR spectrum (Figure 116 in Appendix and Table 2.15) showed two phenolic hydroxyl protons at δ 11.93 (10-OH) and 11.68 (6′-OH), two hydroxyl of an enol at δ 14.80 (8′-OH) and 13.91 (6-OH), and the hydroxyl group of C-3 at δ 2.65. Three aromatic protons appeared as singlet resonances at δ 7.55 (H–3′), 7.06 (H–5′), and 6.06 (H–13). The resonance signals of the *cis* vinyl protons showed the coupling of H–13′ at δ = 6.65 (d, J = 8.3 Hz) to H–12′ at δ 6.46 (dd, J = 8.4, 6.6 Hz) whereas the latter signal further coupled to H–11′ at δ 4.78 (d, J = 6.6 Hz). An AB quartet confirmed the resonance signals of the methylene protons, H–15′α and H–15′β at δ 2.87 (d, J = 17.6 Hz) and 3.03 (d, J = 17.6 Hz), respectively. The oxymethine proton (H-3) resonated at δ 4.26 (d, J = 1.8 Hz), while two methylene protons appeared at δ 2.79 (ddd, J = 19.3, 11.9, 4.4 H-5β), 2.37 (dd, J = 19.3, 6.6 H-5α), 2.11 (m, H-4β), and 1.92 (m, H-4α). The ^{13}C NMR spectrum and DEPT experiments (Figures 117 and 118 in Appendix and Table 2.15) revealed the presence of thirty one carbons attributable to four carbonyl, thirteen sp^2 quaternary, five sp^2 methine, two sp^3 quaternary, two sp^3 methine, three sp^3 methylene, and two methyl carbons. The ^{13}C NMR data showed signals at δ 195.5, 189.0, 186.6, and 171.0 corresponding to carbonyl carbons of the quinone, xanthone, and ester, respectively.

The structural connectivity of **XVI** was then confirmed by 2D NMR spectroscopic analysis, including COSY, HSQC, HMBC, and NOESY experiments (Figures 119-122 in Appendix and Table 2.15). The COSY spectrum (Figure 2.33) displayed correlations between H-4 and H-3, H-5; H-12′ and H-11′, H-13′; H-15′α and H-15′β; and long-range correlations of H-13 and H15′; H-3′ and H-5′, H-16′; H-5′ and H-16′. Information of the HMBC spectrum (Figure 2.34 and Table 2.15) clearly demonstrated two sets of correlations between methylene protons H-15′ to C-11, C-

12, C-13, C-1′, C-9′, C-13′, and C-14′ and between methine proton H-11′ to C-10, C-11, C-12, C-9′, C-10′, C-12′, and C-13′ which fixed the linkage between the anthraquinone unit and the chromanone unit. The NOESY spectrum (Figure 2.35) showed correlations between H–3 and H–4; H–4 and H–5; H–13 and H–15′; H–16′ and H–3′, H–5′; indicating that those protons are located on the same face of molecule. In comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[67] and the assignment made by 2D NMR experiments, compound **XVI** was then identified to be the known xanthoquinodin A1.



Xanthoquinodin A1 (XVI)

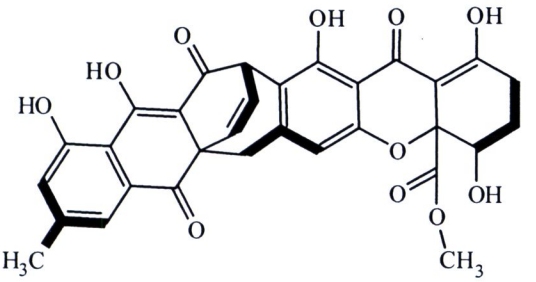


Figure 2.33 COSY correlations (bold lines) of **XVI**.

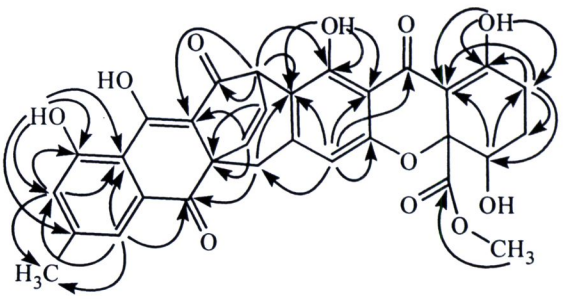


Figure 2.34 HMBC correlations of **XVI**.

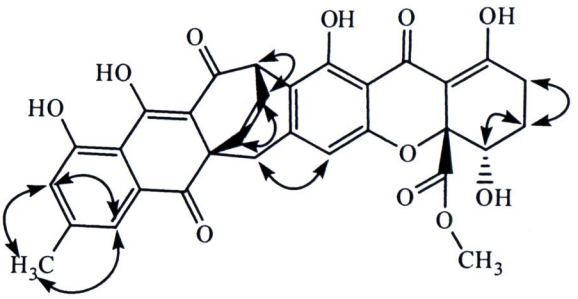


Figure 2.35 NOESY correlations of **XVI**.

Table 2.15 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **XVI** (400 MHz, $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
2		83.9	C			
3	4.26 d (1.8)	66.8	CH	H-4	C-5, 7	H-4
3-OH	2.65 bs					
4α	1.92 m	23.0	CH_2	H-3, 4, 5		H-3, 5
4β	2.11 m					
5α	2.37 dd (6.6, 19.3)	24.4	CH_2	H-4, 5	C-3, 4, 6, 7	H-5
5β	2.79 ddd (4.4, 11.9, 19.3)					
6		179.8	C			
6-OH	13.91 s				C-5, 6, 7	
7		100.1	C			
8		186.6	C			
9		105.0	C			
10		158.7	C			
10-OH	11.93 s				C-9, 10, 11	
11		116.5	C			
12		146.5	C			
13	6.06 s	110.4	CH	H-15′	C-8, 9, 11, 14, 15′	H-15′
14		156.1	C			
15		171.0	C			
16	3.68 s	53.5	CH_3		C-15	
1′		195.5	C			
2′		132.2	C			
3′	7.55 s	121.0	CH	H-5′, 16′	C-1′, 5′, 7′, 16′	H-16′
4′		147.5	C			
5′	7.06 s	124.3	CH	H-3′, 16′	C-3′, 6′, 7′, 16′	H-3′, 16′
6′		161.4	C			
6′-OH	11.68 s				C-4′, 5′, 6′, 7′	
7′		115.1	C			
8′		182.8	C			
8′-OH	14.80 bs					
9′		106.5	C			
10′		189.0	C			
11′	4.78 d (6.6)	37.8	CH	H-12′	C-10, 11, 12, 9′, 10′, 12′, 13′	H-12′
12′	6.46 dd (6.6, 8.4)	131.4	CH	H-11′, 13′	C-10′, 11′, 14′	H-11′, 13′
13′	6.65 d (8.3)	132.7	CH	H-12′	C-11, 1′, 9′, 11′, 14′	H-12′
14′		50.0	C		-	
15′α	2.87 d (17.6)	38.9	CH_2	H-13, 15′	C-11, 12, 13, 1′, 9′, 13′, 14′	H-13
15′β	3.03 d (17.6)					
16′	2.43 s	22.0	CH_3	H-3′, 5′	C-3′, 4′, 5′, 7′	H-3′, 5′

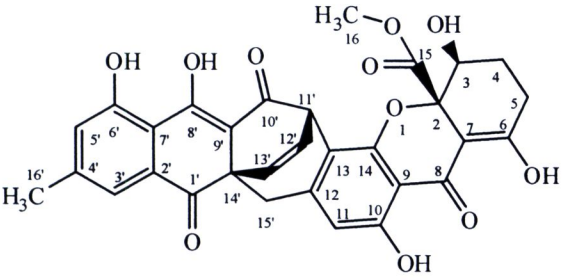
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound XVII was isolated as a pale yellow solid and assigned the molecular formula $C_{31}H_{24}O_{11}$ (*m/z* observed 595.1220 $[M+Na]^+$), as deduced from the HRESITOF mass spectrum (Figure 123 in Appendix), indicating 20 degrees of unsaturation. The UV spectrum displayed absorption maxima at 208, 237, 274, and 362 nm, indicating the presence of an extended conjugated system. The IR spectrum (Figure 124 in Appendix) showed characteristic of hydroxyl (3430 cm^{-1}), and chelating carbonyl (1623, and 1596 cm^{-1}) groups.

The ^1H NMR spectrum (Figures 125 in Appendix and Table 2.16) showed two phenolic hydroxyl protons at δ 11.74 (10-OH) and 13.94 (6′-OH) and three aromatic protons appeared as three singlet resonances at δ 7.40 (H–3′), 6.88 (H–5′), and 5.59 (H–13). The resonance signals of the *cis* vinyl protons showed the coupling of H–13′ at δ 6.51 (d, J = 8.3 Hz) to H–12′ at δ 6.16 (dd, J = 15.4, 7.5 Hz) whereas the latter signal further coupled to H–11′ at δ 4.54 (d, J = 6.6 Hz). An AB quartet confirmed the resonance signals of the methylene protons, H–15′α and H–15′β, at δ 2.77 (d, J = 17.6 Hz) and 2.99 (d, J = 17.6 Hz), respectively. The oxymethine proton (H-3) resonated at δ 4.09 (dd, J = 12.3, 4.4 Hz), while two methylene protons appeared at δ 2.59 (m, H-5β), 2.40 (dd, J = 18.0, 5.7 H-5α), 2.03 (m, H-4β), and 1.94 (m, H-4α). The ^{13}C NMR and DEPT experiments (Figures 126 and 127 in Appendix and Table 2.16) revealed the presence of thirty one carbons attributable to four carbonyl, thirteen sp^2 quaternary, five sp^2 methine, two sp^3 quaternary, two sp^3 methine, three sp^3 methylene, and two methyl carbons. The ^{13}C NMR spectral data showed signals at δ 198.6, 197.3, 178.5, and 175.0 corresponding to carbonyl carbons of the quinone, xanthone, and ester, respectively.

The structural connectivity of **XVII** was then confirmed by 2D NMR spectroscopic analysis, including COSY, HSQC, HMBC, and NOESY experiments (Figures 128-131 in Appendix and Table 2.16). The COSY spectrum (Figure 2.36) displayed correlations between H-4 and H-3, H-5; H-12′ and H-11′, H-13′; H-15′α and H-15′β; and long-range correlations of H-11 and H15′; H-3′ and H-5′, H-16′; H-5′ and H-16′. Information of the HMBC spectrum (Figure 2.37 and Table 2.16) clearly demonstrated two sets of correlations between methylene protons H-15′ to C-11, C-12, C-13, C-1′, C-9′, C-13′, and C-14′ and between methine protons H-11′ to C-12, C-

13, C-14, C-9′, C-10′, C-12′, and C-13′ which fixed the linkage between the anthraquinone unit and the chromanone unit. The NOESY spectrum (Figure 2.38) showed correlations between H–3 and H–4; H–11 and H–15′; H–16′ and H–3′, H–5′; indicating that those protons are located on the same face of molecule. In comparison of the ^{1}H and ^{13}C NMR spectral data with those values reported from literature[67] and the assignment made by 2D NMR experiments, compound **XVII** was then identified to be the known xanthoquinodin B2.



Xanthoquinodin B2 (XVII)

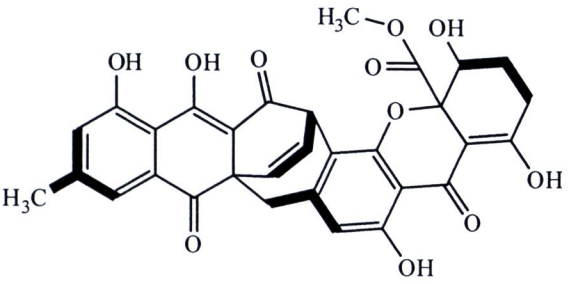


Figure 2.36 COSY correlations (bold lines) of **XVII**.

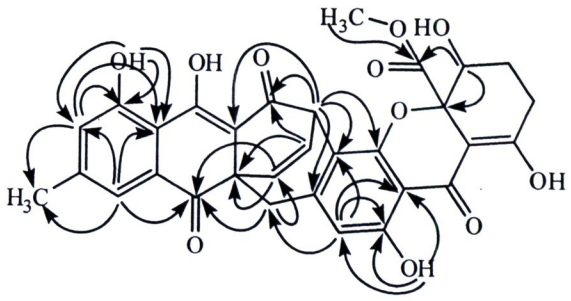


Figure 2.37 HMBC correlations of **XVII**.

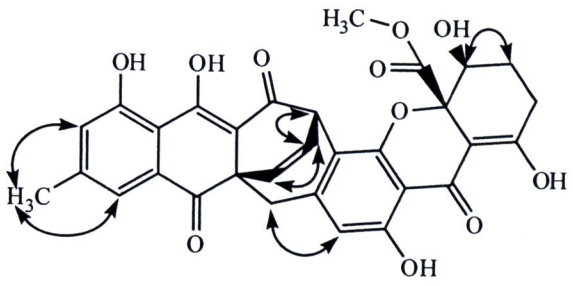


Figure 2.38 NOESY correlations of **XVII**.

Table 2.16 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **XVII** (400 MHz, CD_3OD in $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
2		86.2	C			
3	4.09 dd (4.4, 12.3)	72.8	CH	H-4	C-2, 15	H-4
4α 4β	1.94 m 2.03 m	24.5	CH_2	H-3, 4, 5		
5α 5β	2.40 dd (5.7, 18.0) 2.59 m	34.6	CH_2	H-4, 5		H-5
6		175.3	C			
7		99.1	C			
8		178.5	C			
9		104.2	C			
10		159.1	C			
10-OH	11.74 s				C-9, 10, 11	
11	5.59 s	112.7	CH	H-15′	C-9, 10, 13, 15′	H-15′
12		144.3	C			
13		112.8	C			
14		153.7	C			
15		175.0	C			
16	3.56 s	52.9	CH_3		C-15	
1′		198.6	C			
2′		131.9	C			
3′	7.40 s	119.5	CH	H-5′, 16′	C-1′, 5′, 7′, 16′	H-16′
4′		144.6	C			
5′	6.88 s	123.6	CH	H-3′, 16′	C-3′, 6′, 7′, 16′	H-16′
6′		161.0	C			
6′-OH	13.94 s				C-5′, 6′, 7′	
7′		117.5	C			
8′		189.0	C			
9′		105.4	C			
10′		197.3	C			
11′	4.54 d (6.6)	44.6	CH	H-12′	C-12, 13, 14, 9′, 10′, 12′, 13′	H-12′
12′	6.16 t (7.5)	131.4	CH	H-11′, 13′	C-10′, 11′, 14′	H-13′
13′	6.51 d (8.3)	132.8	CH	H-12′	C-13, 1′, 9′, 11′, 14′	H-12′
14′		51.8	C			
15′α 15′β	2.77 d (17.6) 2.99 d (17.6)	40.7	CH_2	H-11, 15′	C-11, 12, 13, 1′, 9′, 13′, 14′	H-11
16′	2.33 s	21.6	CH_3	H-3′, 5′	C-3′, 4′, 5′, 7′	H-3′, 5′

[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

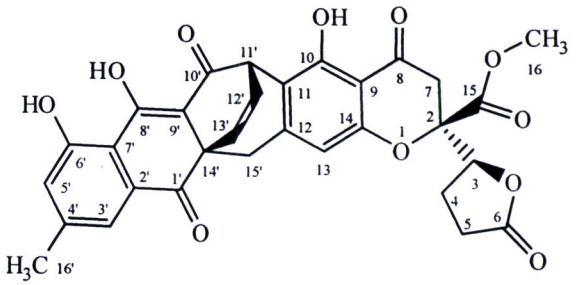
Compound XVIII was obtained as yellow crystals and assigned the molecular formula $C_{31}H_{24}O_{11}$, as deduced from the HRESITOF mass spectrum (Figure 132 in Appendix) (observed *m/z* 595.1226 $[M+Na]^+$), indicating 20 degrees of unsaturation. The UV spectrum showed absorption maxima at 239, 281 and 382 nm which indicating the presence of an extended conjugated system. The IR spectrum (Figure 133 in Appendix) showed a broad absorption band at 3421 cm^{-1} corresponding to the O-H stretching of a hydroxyl group. The absorption bands at 1784 and 1748 cm^{-1} confirmed the presence of lactone and ester, while those at 1684 and 1647 cm^{-1} corresponded to the presence of chelating carbonyl groups. The characteristic absorption band at 1563 cm^{-1} was assigned to C=C stretching.

The ^1H NMR spectrum (Figure 134 in Appendix and Table 2.17) displayed two downfield singlet signals at δ 11.65, and 11.98 due to phenolic hydroxyl protons. Three singlet signals at δ 7.57, 7.07, and 6.14 corresponded to three aromatic protons of H-3′, H-5′, and H-13, respectively. The *cis* vinyl protons appeared as a doublet signal of H-13′ at δ 6.68 (d, J = 8.6 Hz) and a doublet of doublet signal of H-12′ at δ 6.47 (dd, J = 8.2, 6.6 Hz) which couple to a bridge-head proton, H-11′, at δ 4.76 (d, J = 6.2 Hz). A singlet signal of methyl substituent attached to the 4′-position of the aromatic ring appeared at δ 2.44 (H-16′) whereas the singlet methyl signal at δ 3.74 (H-16) corresponded to that of the methyl ester group. The two sets of AB quartet at δ 2.92 and 3.11 (d, J = 17.2 Hz), and 2.90 and 3.07 (d, J = 17.6 Hz) were assigned to the two germinal methylene protons of H-7α, H-7β and H-15′α, H-15′β, respectively. Two methylene of the lactone ring, H-4 and H-5, appeared as multiplet signals at δ 2.35 and 2.58, respectively. An oxymethine proton (H-3) appeared as a triplet signal at δ 4.82 (t, J = 6.6 Hz). The ^{13}C NMR and DEPT spectral data (Figures 135 and 136 in Appendix and Table 2.17) contained thirty one signals which were classified into five carbonyl, eleven sp^2 quaternary, five sp^2 methine, two sp^3 quaternary, two sp^3 methine, four sp^3 methylene, and two methyl carbons. The ^{13}C NMR spectrum exhibited five carbonyl resonances at δ 195.3, 193.2, 182.9, 175.3, and 168.6 which indicated the presence of quinone, chromanone, γ-lactone, and ester, respectively.

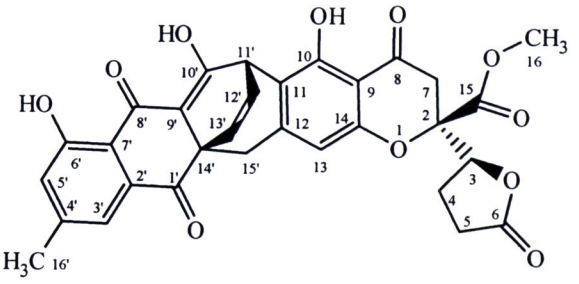
The structure of **XVIII** was then confirmed by 2D NMR techniques: COSY, HSQC, HMBC, and NOESY (Figures 137-140 in Appendix and Table 2.17). The COSY spectrum (Figure 2.39) displayed correlations between H-3 and H-4, H-4 and

H-5, H-7α and H-7β, H-15′α and H-15′β; and long-range correlations of H-13 to H15′, H-3′ to H-5′, H-16′, and H-5′ to H-3′, H-16′. Information of the HMBC spectrum (Figure 2.40 and Table 2.17) clearly demonstrated two sets of correlations between methylene protons H-15′ to C-11, C-12, C-13, C-1′, C-9′, C-13′ and C-14′ and between methine proton H-11′ to C-10, C-11, C-12, C-9′, C-10′, C-12′, and C-13′ which fixed the linkage between the anthraquinone unit and the chromanone unit. The ^{1}H and ^{13}C NMR spectral data of **XVIII** were similar to those reported for xanthoquinodin A3[67] (Table 2.17). However, there were some differences between these two compounds. The dihydroxy and keto groups in xanthoquinodin A3 located at C-6′, C-8′, and C-10′, respectively, were confirmed by NOESY correlation between the C-6′ and C-8′ hydroxyl protons, whereas compound **XVIII** has dihydroxy groups at C-6′ and C-10′, and a keto group at C-8′ base on the X-ray crystallographic analysis.[68] The distance between C-6′ and C-10′ hydroxyl protons was 3.035 Å from X-ray analysis corresponding to NOESY correlation in the range of 4.2 Å.[68] The NOESY spectrum (Figure 2.41) of **XVIII** displayed no correlation between the C-6′ and C-10′ hydroxyl protons.

The relative stereochemistry was assigned by analysis of the NOESY spectral data (Figure 2.50). Compound **XVIII** exhibited a positive sign of specific rotation [+54° (*c* 0.1, MeOH)] similar to that of xanthoquinodin A3 [+20 (*c* 0.10, MeOH)],[67] implying that **XVIII** possessed the same configuration as xanthoquinodin A3. From the above evidence, compound **XVIII** was proposed as the keto-enol form of xanthoquinodin A3. It could be concluded that in the solid state it preferred the form **XVIII** while in solution it preferred the xanthoquinodin A3 structure.



Xanthoquinodin A3



XVIII

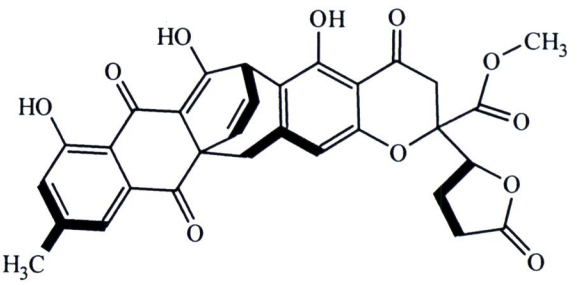


Figure 2.39 COSY correlations (bold lines) of **XVIII**.

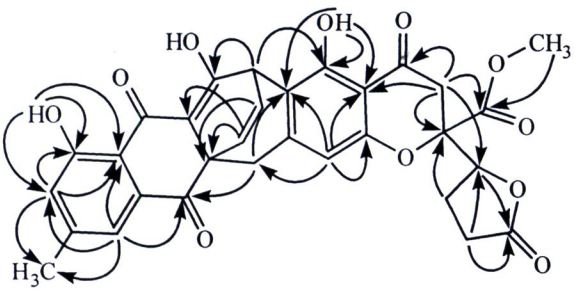


Figure 2.40 HMBC correlations of **XVIII**.

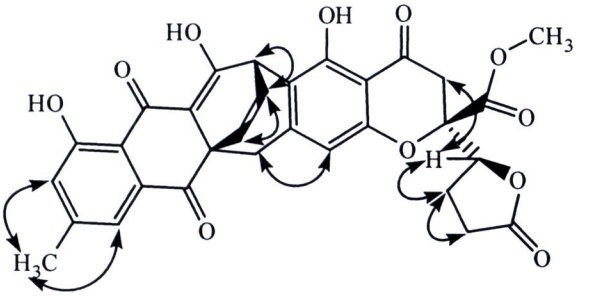


Figure 2.41 NOESY correlations of **XVIII**.

Table 2.17 ^{1}H and ^{13}C NMR, DEPT, COSY, HMBC, and NOESY spectral data of compound **XVIII** (400 MHz, $CDCl_3$)[a]

position	δ_H	δ_C	DEPT	COSY	HMBC	NOESY
2		84.0	C			
3	4.82 t (6.6)	80.7	CH	H-4	C-6	H-4, 7
4	2.35 m	22.1	CH_2	H-3, 5	C-2, 5, 6	H-3, 5
5	2.58 m	27.5	CH_2	H-4	C-3, 6	H-4
6		175.3	C			
7α 7β	2.92 d (17.2) 3.11 d (17.2)	39.3	CH_2	H-7β H-7α	C-2, 3, 8, 9, 15	
8		193.2	C			
9		105.7	C			
10		158.5	C			
10-OH	11.98				C-9, 10, 11	
11		116.0	C			
12		148.3	C			
13	6.14 s	110.2	CH	H-15′	C-8, 9, 11, 14, 15′	H-15′
14		157.5	C			
15		168.6	C			
16	3.74 s	53.7	CH_3		C-15	
1′		195.3	C			
2′		132.2	C			
3′	7.57 s	121.1	CH	H-5′, 16′	C-1′, 5′, 7′, 16′	H-16′
4′		147.7	C			
5′	7.07 s	124.3	CH	H-3′, 16′	C-3′, 6′, 7′, 16′	H-16′
6′		161.4	C			
6′-OH	11.65 s				C-4′, 5′, 6′, 7′	
7′		115.0	C			
8′		182.9	C			
9′		106.5	C			
10′		188.9	C			
11′	4.76 d (6.2)	37.8	CH	H-12′	C-10, 11, 12, 9′, 10′, 12′, 13′	H-12′
12′	6.47 dd (8.2, 6.6)	131.3	CH	H-11′, 13′	C-10′, 11′, 13′, 14′	H-11′, 13′
13′	6.68 d (8.6)	132.8	CH	H-12′	C-11, 1′, 9′, 11′, 12′, 14′	H-12′
14′		49.9	C			
15′α 15′β	2.90 d (17.9) 3.07 d (17.2)	39.0	CH_2	H-15′	C-11, 12, 13, 1′, 9′, 13′, 14′	H-13
16′	2.44 s	21.9	CH_3	H-3′, 5′	C-3′, 4′, 5′, 7′	H-3′, 5′

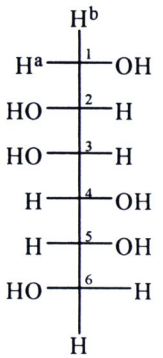
[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Table 2.18 Comparison of ^{1}H and ^{13}C NMR spectral data of **XVIII** and xanthoquinodin A3[a]

position	XVIII		Xanthoquinodin A3	
	δ_H	δ_C	δ_H	δ_C
2		83.97		83.99
3	4.82 t (6.6)	80.70	4.83 dd (7.0, 7.0)	80.72
4	2.35 m	22.06	2.36 m	21.97
5	2.58 m	27.51	2.54 m, 2.60 m	27.55
6		175.30		175.30
7α 7β	2.92 d (17.2) 3.11 d (17.2)	39.29	2.93 d (17.0) 3.12 d (17.0)	39.34
8		193.22		193.21
9		105.68		105.71
10		158.49		158.52
10-OH	11.98		12.00 s	
11		116.00		116.04
12		148.28		147.70
13	6.14 s	110.25	6.15 s	110.28
14		157.50		157.52
15		168.64		168.65
16	3.74 s	53.71	3.75 s	53.75
1′		195.32		195.34
2′		132.22		132.25
3′	7.57 s	121.08	7.58 d (1.0)	121.11
4′		147.68		148.31
5′	7.07 s	124.30	7.08 d (1.0)	124.33
6′		161.39		161.42
6′-OH	11.65 s		11.68 s	
7′		114.98		115.01
8′		182.86		182.89
9′		106.48		106.50
10′		188.92		188.93
11′	4.76 d (6.2)	37.80	4.77 dd (0.1, 6.2)	37.84
12′	6.47 dd (6.6, 8.2)	131.28	6.48 dd (6.2, 8.4)	131.31
13′	6.68 d (8.6)	132.85	6.69 dd (0.1,8.4)	132.87
14′		49.92		49.95
15′α 15′β	2.90 d (17.6) 3.07 d (17.6)	38.99	2.91 d (17.0) 3.08 d (17.0)	39.03
16′	2.44 s	21.94	2.45 s	22.11

[a]Chemical shift values are in ppm, and *J* values (in Hz) are presented in parentheses.

Compound XIX was obtained as a white solid. The IR spectrum (Figure 141 in Appendix) showed broad absorption bands at 3389 and 3289 cm^{-1} corresponding to hydroxyl group. The C-H aliphatic stretching appeared at 2970, 2954, 2939 and 2917 cm^{-1} while its bending displayed at 1458, 1429, 1388 and 1317 cm^{-1}. The strong absorption bands at 1080 and 1019 cm^{-1} were characteristic of C-O asymmetric stretching of 2° and 1° alcohols, respectively. The ^{1}H NMR spectrum (Figure 142 in Appendix) showed that all methine and methylene protons were attaching to hydroxyl groups. Two doublet of doublet signals at δ 3.77 (J = 12.0, 2.3 Hz) and δ 3.57 (J = 12.0, 6.0 Hz) were assigned to H-1b and H-1a, respectively, whilst signals of H-2 and H-3 appeared at δ 3.71-3.64 as multiplet. The ^{13}C NMR spectrum (Figure 143 in Appendix) exhibited three carbon signals at δ 70.8, 69.2 and 63.2 which were assigned to the carbons of a symmetric monosaccharide sugar. According to the above spectral evidences and comparison with the spectral data reported in the literature,[69] compound **XIX** was then deduced to a D-mannitol.



D-mannitol (**XIX**)

2.3 Proposed Biosynthetic Pathway of Cytochalasans, III-XI

From the previous studies, the biosynthetic pathway of 10[indolcytochalasan type such as chaetoglobosin A (**20**) has been proposed *via* a coupling between one molecule of tryptophan and one polyketide from one molecule of starter acetate, eight molecules of malonate and three C_1 units from methionine.[24,27] Incorporation studies using ^{2}H- and ^{13}C-labelled acetates and methionine as well as ^{2}H-, ^{14}C-, and ^{15}N-labelled tryptophan indicate the pathway for the biosynthesis of chaetoglobosin A (**20**) and 19-*O*-acetylchaetoglobosin A (**8**) in *C. globosum*.[27] Indirect evidence for the Diels-Alder mediated biosynthesis of the cytochalasins was obtained by feeding[70] and inhibition[63] experiments with *C. subaffine*, which produces chaetoglobosin A (**20**, Figure 2.29). A feeding experiment with [1-^{13}C,2-$^{2}H_3$]acetate showed retention of the deuterium labels at C-11, C-8, and C-14.[70] Retention of deuterium at C-8 and C-14 precludes formation of the perhydroisoindole and macrocycle through a proposed formation of a carbon-carbon in which a carbonyl group is located at C-14. A feeding experiment with [1-^{13}C,1-$^{18}O_2$]acetate established that the oxygen atoms at C-1 and C-23 originate from the acetate, while incubation in an $^{18}O_2$-enriched atmosphere displayed an upfield shift of the C-6, C-7, and C-20 signals in the NMR spectrum. An inhibition experiment with the cytochrome P450 inhibitor metapyrone led to the formation of the metabolites **131-133**, **IX** and **131** was a major product.[63] These results led to the biosynthetic proposal for the formation of **20** outline in Figure 2.42. An intramolecular Diels-Alder reaction of the putative hexane **130** would provide **131** which could then undergo a stepwise oxidation to provide chaetoglobosin A (**20**).

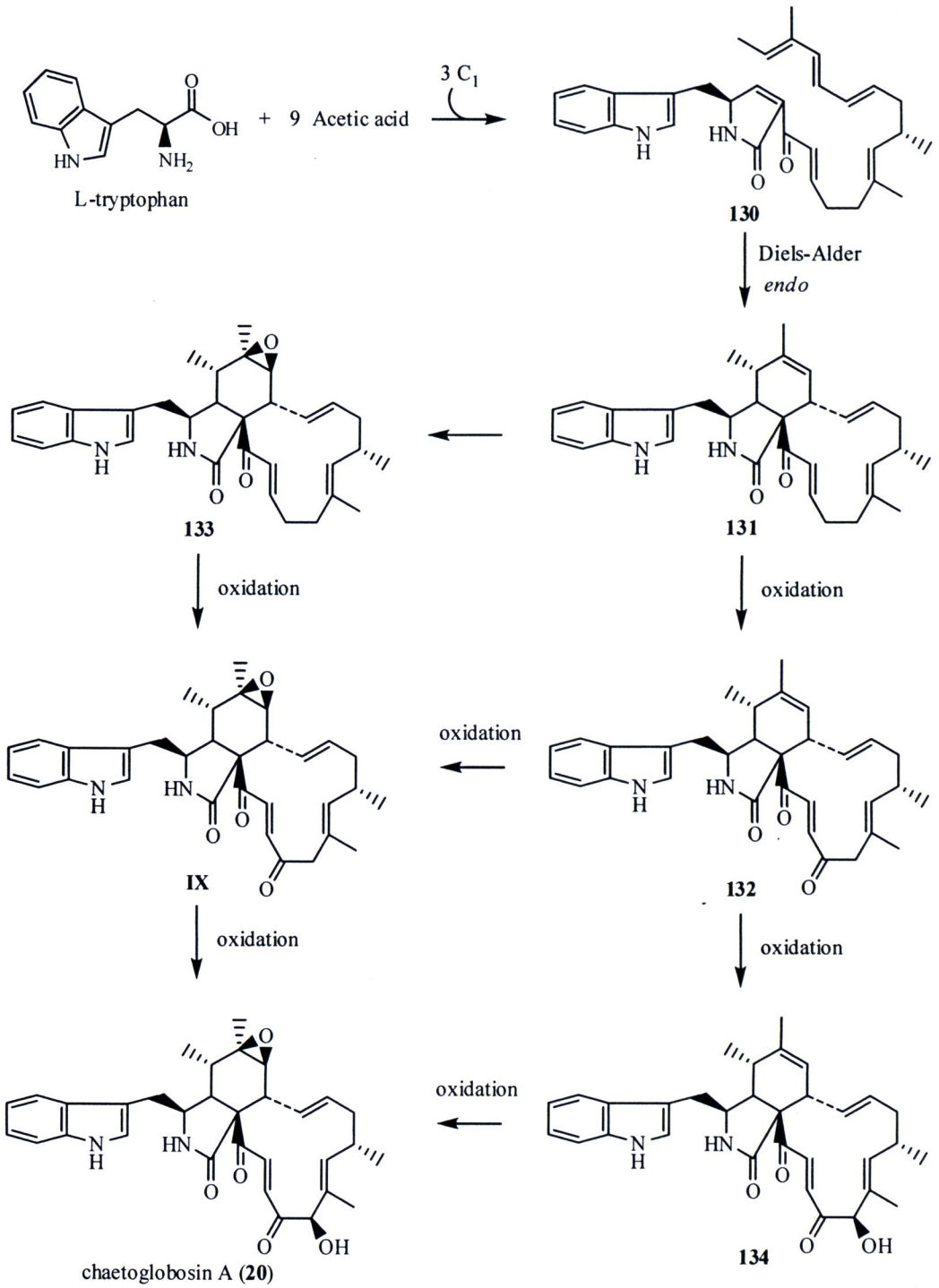


Figure 2.42 Proposed biosynthesis pathway of chaetoglobosin A (**20**).[70]

The possibility for enzymatic involvement in the proposed Diels-Alder cyclization of the cytochalasans was evidenced by the retro-Diels-Alder reaction of **131** (Figure 2.43). Instead of forming the expected triene **130**, pyrolysis (180 °C, sealed tube) of **131** produced equal amounts of starting material and the diastereomer **135**.[70] The lack of stereoselectivity in the thermal Diels-Alder reaction supports the hypothesis that an enzyme preorganizes the substrate conformation to favor the *endo*-transition state in the biological system, which results in exclusive formation of **131**.[70] Compound **133** was converted to cytochalasans (**III-XI**) which **III** was a major metabolites (Figure 2.44). Oxidation of **133** afforded prochaetoglobosin III (**IX**) which was further oxidation to yield chaetoglobosin A (**20**). The open epoxide-ring of **133** to yield chaetoglobosin V (**XI**) which was oxidation to prochaetoglobosin IIIed (**X**). Convert prochaetoglobosin III (**IX**) by open epoxide-ring to yield prochaetoglobosin IIIed (**X**) which was oxidation to chaetoglobosin B (**VII**). In contrast, oxidation of prochaetoglobosin III (**IX**) afforded compound **20** which was converted to chaetoglobosin B (**VII**) by open epoxide-ring. The open epoxide-ring of compound **20** afforded chaetoglobosin D (**VIII**) and was converted to chaetoglobosin C (**III**). Reduction of chaetoglobosin C (**III**) afforded chaetoglobosin F (**V**) and open epoxide-ring pathway of **III** was converted to isochaetoglobosin D (**IV**) and G (**VI**). However, this proposed biosynthesis pathway need experimental proof.

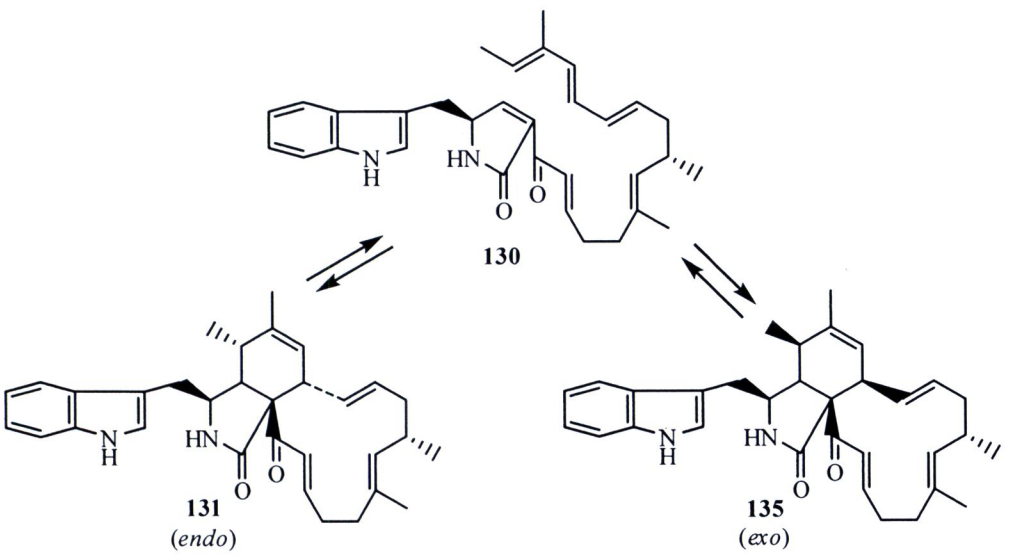


Figure 2.43 The retro-Diels-Alder reaction of **131**.[70]

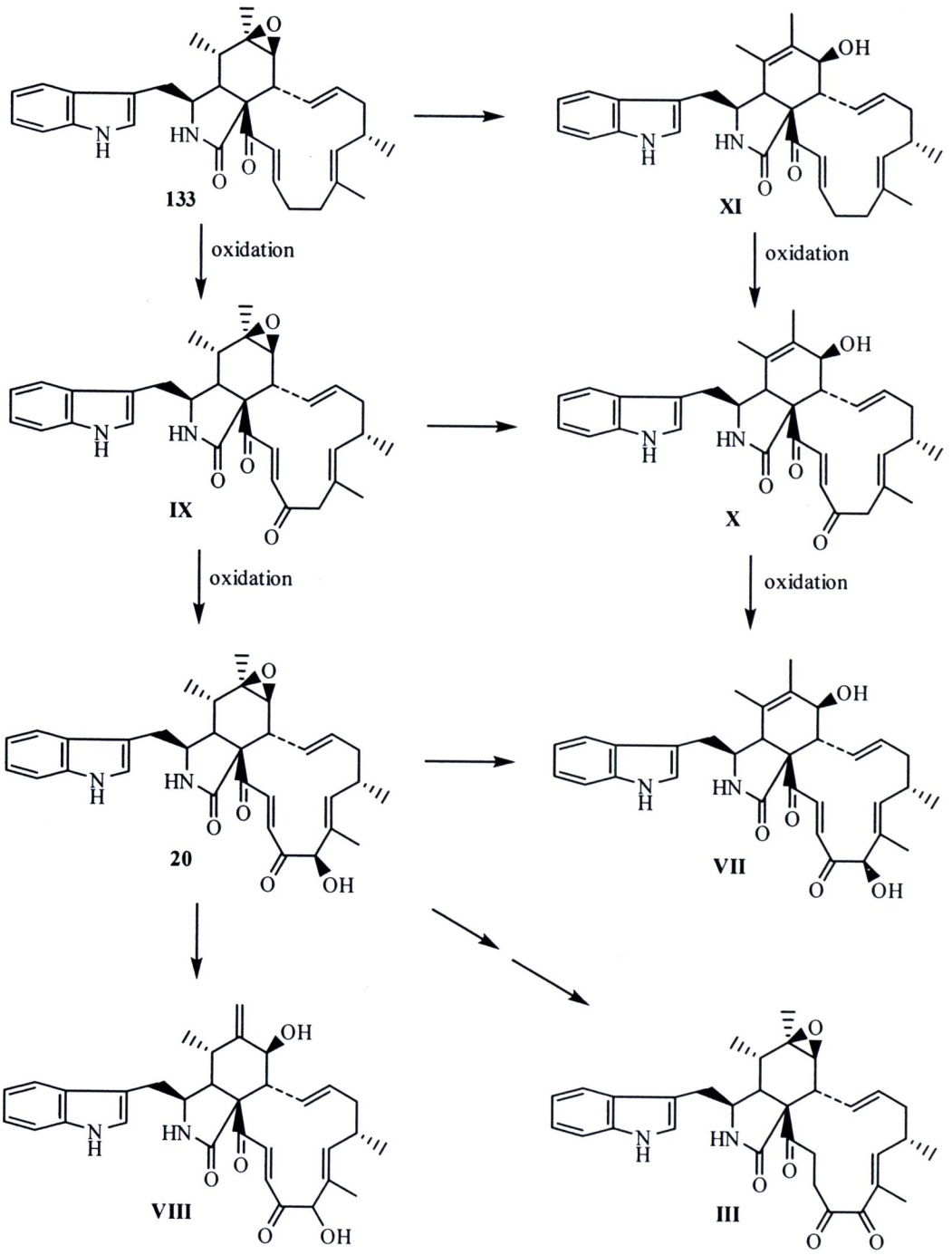


Figure 2.44 Proposed biosynthesis pathway of cytochalasans, **III-XI**.

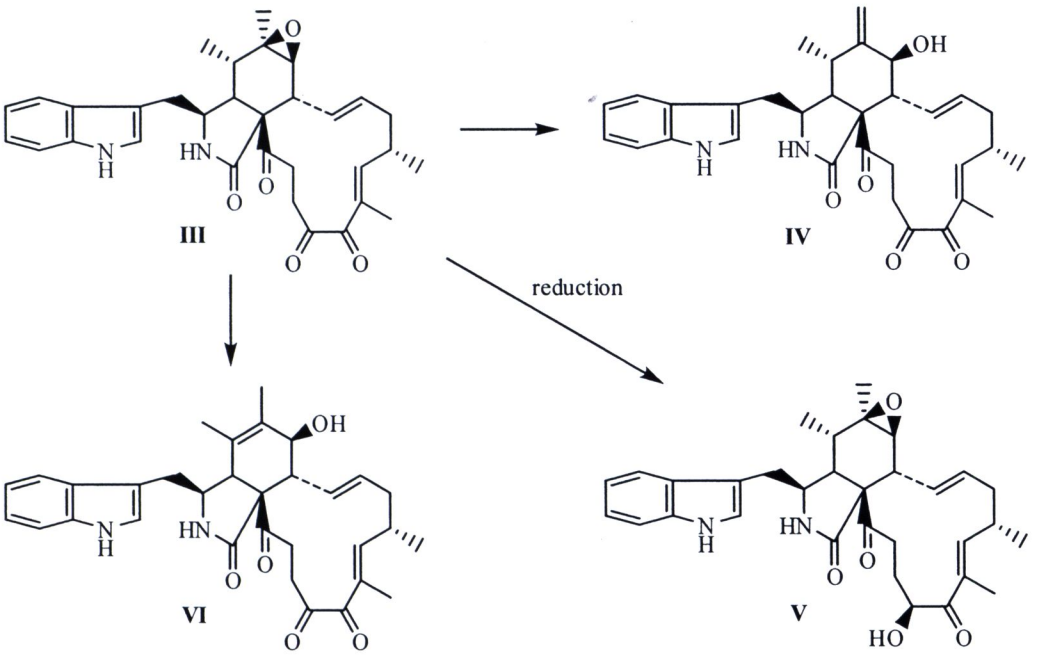


Figure 2.44 Proposed biosynthesis pathway of cytochalasans, **III-XI**. (cont.)

2.4 Proposed Biosynthetic Pathway of Xanthoquinodins, XVI-XVIII

From the chemistry point of view, the biosynthetic pathway of compounds **XVI- XVIII** could be proposed *via* a polyketide pathway.[67] For xanthoquinodins, **XVI- XVIII**, a heterodimer of an octaketide-derived xanthone and an anthraquinone moiety are linked in a unique fashion (an "end-to-body" manner). The proposed biosynthetic sequence of these three compounds is shown in Figure 2.45. Two anthraquinones (or anthrones) **137** were produced from two octaketides **136** *via* decarboxylation of the tail. One molecule of **137** is subjected to oxidative cleavage at the B ring to give hypothetical benzophenone intermediate **139**. An analogous rotation of two intermediates were proved in the [1,2-$^{13}C_2$] acetate feeding experiments.[67] The phloroglucinol moiety (C ring) of this intermediate rotates between **139a** and **139b**. The tricyclic xanthones **140** and **141** were formed from this intermediate and anthraquinone **138** is converted form **137**. The connection of anthraquinone **138** and xanthone **140** through end-to-body coupling *via* ortho to ortho coupling followed by methylation gave xanthoquinodin type A **XVI**. Compound **XVI** was converted to form γ-lactone-ring in **XVIII** (Figure 2.46).[67] Alternative

connection of anthraquinone **138** and xanthone **141** involved end-to-body coupling *via* the ortho to para position and then methylation to obtain xanthoquinodin type B **XVII**. However, this proposed biosynthetic path way needs experimental proof.

2.5 Bioactivity Assays

The isolated compounds, chaetoglobosin V (**XI**), cochliodone D (**XV**), xanthoquinodin A1 (**XVI**), xanthoquinodin B2 (**XVII**), and **XVIII** were tested for antimalarial (*Plasmodium falciparum*), antituberculosis (*Mycobacterium tuberculosis*) and cytotoxicity against NCI-H187, KB, and BC1 cell lines. Compounds **III-XI** were test for cytotoxicity against BC1 cell lines and cholangiocarcinoma (CCA) cultured cell lines (Table 2.19). The results showed that compounds **XI** and **XVI-XVIII** displayed strong activity against *P. falciparum* and activity against *M. tuberculosis*. Compounds **XI** and **XVI-XVIII** displayed cytoxicity against NCI-H187, KB, and BC1 cell lines, except that **XVIII** showed inactivity against NCI-H187. However, compounds **XIV** and **XV** displayed inactitvity for all test. Compounds **III-XI** exhibited cytoxicity against BC1 and CCA (KKU-100 and KKU-OCA17) except for **III**, **VI**, and **X** showed inactive against KKU-100, KKU-OCA17, and CCA, respectively (Table 2.19).

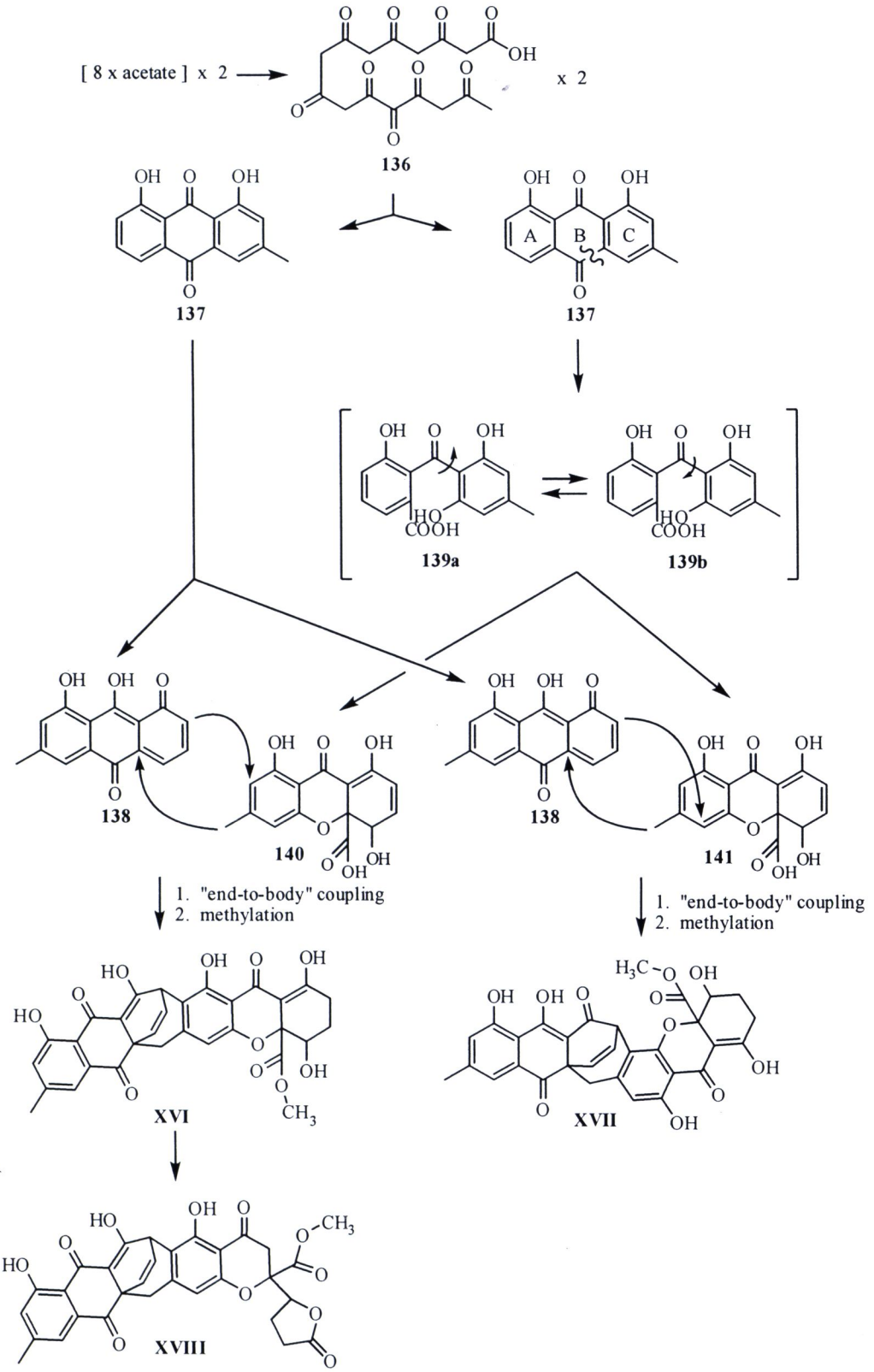


Figure 2.45 Proposed biosynthesis pathway of xanthoquinodins, **XVI-XVIII**.[67]

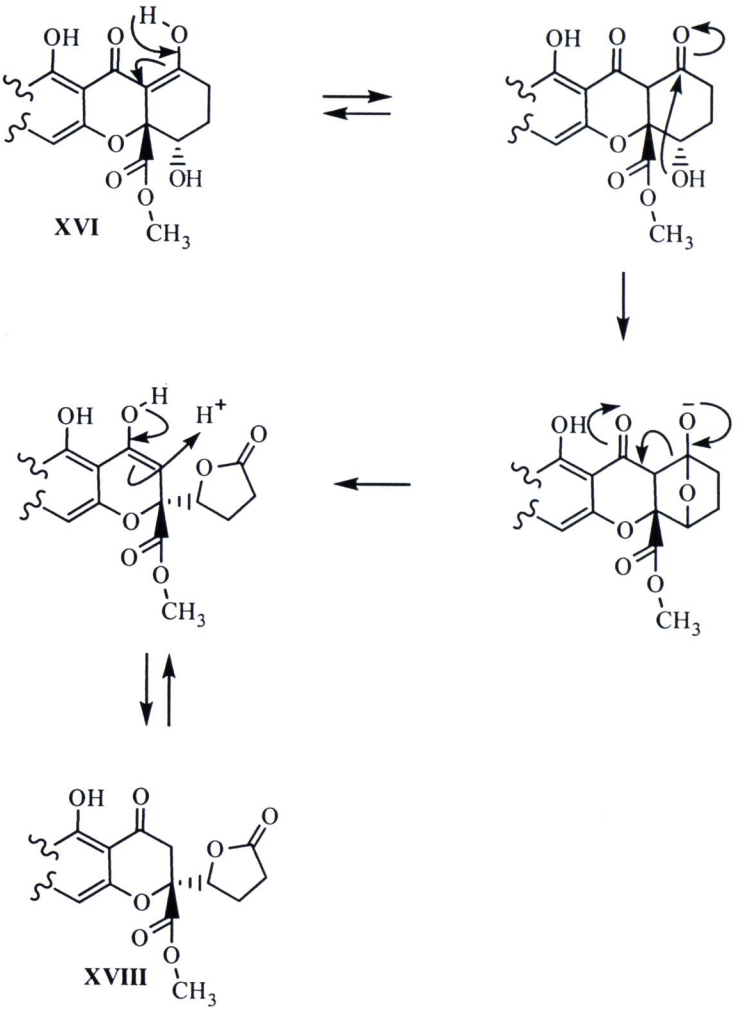


Figure 2.46 Conversion of **XVI** to γ-lactone **XVIII**.[67]

Table 2.19 Bioactivities of isolated compounds from *C. elatum* and *C. lucknowense*

Compound	Antimalarial, IC_{50} (μg/mL)	Anti-TB, MIC (μg/mL)	Cytotoxicity, IC_{50} (μg/mL)				
			NCI-H187[a]	KB[b]	BC1[c]	KKU-100[d]	KKU-OCA17[e]
III	nd[f]	nd	nd	nd	3.27	inactive[g]	15.6
IV	nd	nd	nd	nd	2.88	3.9	44.9
V	nd	nd	nd	nd	10.55	22.4	46.8
VI	nd	nd	nd	nd	5.50	15.7	inactive
VII	nd	nd	nd	nd	1.55	36.9	30.5
VIII	nd	nd	nd	nd	3.83	1.8	6.4
IX	nd	nd	nd	nd	10.96	43.9	26.6
X	nd	nd	nd	nd	1.29	inactive	inactive
XI	2.40	50	11.57	2.28	2.59	43.3	26.5
XIV	inactive	inactive	inactive	inactive	inactive	nd	nd
XV	inactive	inactive	inactive	inactive	inactive	nd	nd
XVI	1.43	12.50	0.456	2.77	10.64	nd	nd
XVII	1.70	25.00	1.03	4.01	25.23	nd	nd
XVIII	3.2	25	inactive	9.6	9.8	nd	nd
artemisinin	0.001						
isoniazid		0.05					
kanamycin sulfate		2.5					
ellipticine			0.32	0.36	0.26		
5-fluorouracil (5-FU)						45.3	0.3

[a]Human lung cancer cells,

[b]Human epidermoid carcinoma in the mouth,

[c]Human breast cancer cells,

[d]Poorly differentiated adenocarcinoma,

[e]Well differentiated adenocarcinoma,

[f]nd = not determined,

[g]inactive at > 50.0 μg/mL