Supporting Information

Isolation of antipodal (-)-versicolamide B and notoamides L-N from a marine-derived *Aspergillus* sp.

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List of Supporting Information

General experimental conditions. Optical rotations were determined with a HORIBA SEPA-300 high sensitive polarimeter or a JASCO P-1020 polarimeter in MeOH. UV-1600 UV-visible spectrophotometer. CD spectra were measured on a JASCO J-720 spectropolarimeter in MeOH. IR spectra were recorded on a Shimadzu IR-460 infrared spectrophotometer. NMR spectra were recorded on a JEOL GSX500 or Bruker Avance500 NMR spectrometers in acetone-d_6 or CD_3OD. Chemical shifts were referenced to the residual solvent peaks (δ_H 2.04 and δ_C 29.8 for acetone-d_6 or δ_H 3.30 and δ_C 49.0 for CD_3OD). Mass spectra were measured on a JEOL SX-102 mass spectrometer.

Isolation of (-)-versicolamide B (10) and notoamides L-N (11-13). The cultured plates (1800 plates) were extracted with EtOH. The extract was concentrated under reduced pressure and extracted with EtOAc, and then *n*-BuOH. The EtOAc layer was partitioned between hexane and 90% MeOH-H_2O. The aqueous MeOH fraction (2.5 g) and *n*-BuOH fraction (1.4 g) were combined and subjected to ODS chromatography with MeOH-H_2O. The fraction eluted with 80% MeOH-H_2O was purified by reversed-phase HPLC with MeOH-H_2O to afford (-)-versicolamide B (**10**, 1.68 mg) and notoamides L (**11**, 1.17 mg), M (**12**, 3.39 mg), and N (**13**, 1.59 mg).

(-)-Versicolamide B (10): $[\alpha]_D^{26}$ -22° (*c* 0.050, MeOH); UV (MeOH) λ_{max} (log ε) 245 nm (4.2), 274 (sh, 3.7), 293 (sh, 3.5), 310 (sh, 3.0), 334 (sh, 3.0); CD (MeOH), see Figure S6; IR (film) ν_{max} 3600, 1700, 1500 cm^{-1}; NMR data (acetone-d_6), see Table S1; NOESY cross peaks: H-4/H-5, H-10β (δ 2.18), H_3-24; H-19/H-10β, H_3-24; H-10β/H-10α (δ 3.08), H-4, H-19; H-21/H-20α (δ 1.91); H_3-24/H-4, H-19, H-20β (δ 1.76), H_3-23; H-19/H-10β, H_3-24; H_3-23/H-21, H_3-24 (Figure S26); FABMS (positive) *m/z* 448 $[M + H]^+$; HRFABMS $[M + H]^+$ *m/z* 448.2235 ($C_{26}H_{30}N_3O_4$, Δ -0.1 mmu).

Notoamide L (11): $[\alpha]_D^{23}$ -17° (*c* 0.77, MeOH); UV (MeOH) λ_{max} (log ε) 242 nm (3.8), 271 (3.6), 360 (3.2); CD (MeOH), see Figure S12; IR (film) ν_{max} 3400, 1700, 1650 cm^{-1}; NMR data (acetone-d_6), see Table S2; NOESY cross peaks: H-4/H_2-10; H-21/H-10 (δ 3.44), H-20 (δ 2.22), H–24 (δ 4.79); H_3-

23/H24; H-20 (δ 1.88)/H-24; FABMS (positive) *m/z* 436 $[M + H]^+$; HRFABMS $[M + H]^+$ *m/z* 436.2235 ($C_{25}H_{30}N_3O_4$, Δ -0.1 mmu).

Notoamide M (12): $[\alpha]_D^{23}$ +51° (*c* 1.7, MeOH); UV (MeOH) λ_{max} (log ε) 248 nm (4.4), 280 (sh, 4.0), 295 (sh, 3.8), 323 (sh, 3.2); CD (MeOH), see Figure S18; IR (film) ν_{max} 3400, 1700, 1650 cm^{-1}; NMR data (CD_3OD), see Table S3; FABMS (positive) *m/z* 466 $[M + H]^+$; HRFABMS $[M + H]^+$ *m/z* 466.2338 ($C_{26}H_{32}N_3O_5$, Δ -0.4 mmu).

Notoamide N (13): $[\alpha]_D^{24}$ -54° (*c* 0.63, MeOH); UV (MeOH) λ_{max} (log ε) 245 nm (4.3), 274 (sh, 3.9), 287 (sh, 3.8), 325 (sh, 3.3); CD (MeOH), see Figure S25. IR (film) ν_{max} 3500, 1700, 1650 cm^{-1}; NMR data (acetone-d_6), see Table S4; NOESY cross peaks: H-4/H-10β (δ 3.01), H_3-24; H-19/H-21, H-26α (δ 2.26); H_3-23/H-21 (Figure S2); FABMS (positive) *m/z* 482 $[M + H]^+$; HRFABMS $[M + H]^+$ *m/z* 482.1855 ($C_{26}H_{29}{}^{35}ClN_3O_4$, Δ +0.8 mmu).

Synthesis of notoamide N (13). To a solution of *d,l*-notoamide B (7.2 mg, 0.016 mmol) in CH_2Cl_2 (1.5 mL) at 0 ºC was added *t*-BuOCl (3.5 mg, 0.032 mmol). The mixture was slowly warmed to rt over 1.5 h and stirred at rt an additional 5 h. The resulting solution was quenched with 10% aqueous Na_2SO_3 and extracted with CH_2Cl_2. The combined extracts were dried (Na_2SO_4) and concentrated. Purification by preparative TLC (CH_2Cl_2 : MeOH, 9 : 1) afforded **13** as a white powder (7.2 mg, 93%); ^1H NMR (400 MHz, acetone-d_6) δ 0.83 (s, 3H), 0.85 (s, 3H), 1.46 (s, 3H), 1.47 (s, 3 H), 1.80 – 2.08 (m, 5H), 2.25 (d, *J* = 14.4 Hz, 1H), 2.65 (m, 1H), 3.01 (d, *J* = 14.4 Hz, 1H), 3.30 (dd, *J* = 8.3, 10.2 Hz, 1H), 3.42 – 3.56 (m, 2H), 5.85 (d, *J* = 10.0 Hz, 1H), 6.67 (d, *J* = 10.0 Hz, 1H), 8.06 (s, 1 H), 9.63 (s, 1 H); ESI/APCI-HRMS $[M+Na^+]$ *m/z* 504.1658 ($C_{26}H_{28}{}^{35}ClN_3NaO_4$, Δ -0.8 mmu).

Possible biosynthetic pathway of notoamide L (11). Notoamide L (**11**) might be derived from (+)-stephacidin A (**5**) (Scheme S1). Singlet oxygen reaction at the indole 2,3-position of **5** would afford a dioxetane intermediate **21** followed by fragmentation to kynurenine **22**. Hydrolysis of the amide bond of **22** would afford **23**. Oxidation at C-24 followed by protonation would afford **25**. Decarboxylation and successive dehydration would afford **11**.

Table S1. ^{1}H and ^{13}C NMR data for (-)-versicolamide B (**10**) in acetone-d_6.

No.	δ_H *J* (Hz)	δ_c	HMBC
1	9.48 br s		
2		183.2 C	
3		63.2 C	
4	7.18 d 8.5	127.3 CH	C-6, C-8
5	6.38 d 8.5	109.4 CH	C-6, C-7, C-9
6		153.8 C	
7		105.7 C	
8		139.4 C	
9		122.6 C	
10	2.18 d 15.7	35.6 CH_2	C-2, C-9, C-11
	3.08 d 15.7		C-2, C-11, C-12, C-22
11		68.4 C	
12		170.1 C	
14	3.36 (2H) t 11.5	44.1 CH_2	C-16
15	1.91 m	25.5 CH_2	
	1.97 m		
16	1.82 m	29.8 CH_2	C-15
	2.60 m		
17		69.7 C	
18		173.4 C	
19	7.69 br s		
20	1.76 m	29.8 CH_2	C-21, C-22
	1.91 m		C-11, C-18
21	3.32 m	51.3 C	C-20, C-22, C-24
22		48.0 C	
23	0.80 (3H) s	23.6 CH_3	C-3, C-21, C-22, C-24
24	1.11 (3H) s	21.1 CH_3	C-3, C-21, C-22, C-23
25	6.66 d 10.0	117.6 CH	C-6, C-7, C-8, C-27
26	5.75 d 10.0	131.1 CH	C-7, C-27
27		76.6 C	
28	1.39 (3H) s	28.0 CH_3	C-26, C-27, C-29
29	1.41 (3H) s	28.0 CH_3	C-26, C-27, C-28

Table S2. ^{1}H and ^{13}C NMR data for notoamide L (**11**) in acetone-d_6.

No.	δ_H J (Hz)	δ_c	HMBC
1			
3		199.1 C	
4	7.70 d 9.0	134.1 CH	C-3, C-6, C-8, C-9
5	6.12 d 9.0	106.1 CH	C-6, C-7, C-9
6		159.3 C	
7		107.1 C	
8		149.4 C	
9		113.6 C	
10	3.24 d 18.0	37.1 CH_2	C-3, C-11, C-12
	3.44 d 18.0		C-3, C-12, C-21
11		63.7 C	
12		168.6 C	
14	3.46 (2H) m	44.5 CH_2	C-15, C-16, C-17
15	1.94 m	25.0 CH_2	C-14, C-16, C-17
	2.10 m		C-16, C-17
16	1.85 m	29.6 CH_2	C-14, C-15, C-17, C-18, C-20
	2.65 ddd 13.0, 7.5, 6.0		C-14, C-15, C-17, C-18, C-20
17		67.0 C	
18		173.1 C	
19	7.34 br s		
20	1.88 m	36.6 CH_2	C-16, C-21, C-22
	2.22 dd 13.5, 10.5		C-21, C-22
21	3.31 dd 10.5, 5.5	51.9 C	C-11, C-12, C-20, C-22, C-23, C-24
22		144.7 C	
23	1.64 (3H) s	19.2 CH_3	C-21, C-22
24	4.79 d 1.0	116.2 CH_2	C-21, C-23
	4.83 d 1.0		C-21, C-23
25	6.67 d 10.0	116.9 CH	C-6, C-7, C-8, C-27
26	5.67 d 10.0	128.5 CH	C-7, C-27, C-28, C-29
27		77.0 C	
28	1.39 (3H) s	27.9 CH_3	C-26, C-27, C-29
29	1.40 (3H) s	27.8 CH_3	C-26, C-27, C-28

Table S3. ^{1}H and ^{13}C NMR data for notoamide M (**12**) in CD_3OD.

No.	δ_H *J* (Hz)	δ_c	HMBC
1			
2		183.8 C	
3		57.1 C	
4	6.89 d 8.5	129.7 CH	C-6, C-8
5	6.31 d 8.5	109.3 CH	C-6, C-7, C-9
6		154.3 C	
7		106.3 C	
8		140.1 C	
9		121.0 C	
10	2.69 dd 15.0, 6.5	33.7 CH_2	C-2, C-3, C-9, C-11, C-12
	2.81 dd 15.0, 3.0		C-2, C-3, C-11, C-12, C-22
11	4.15 dd 6.5, 3.0	55.3 CH	C-3, C-10, C-12
12		167.4 C	
14	3.36 m	45.7 CH_2	C-15
	3.37 m		C-15
15	1.68 m	19.7 CH_2	C-17
	1.91 m		C-16
16	1.35 m	36.4 CH_2	
	1.95 m		C-14, C-16, C-17
17		87.6 C	
18		168.7 C	
19			
20	4.99 dd 17.5, 1.0	114.3 CH_2	C-21, C-22
	5.07 dd 10.5, 1.0		C-22
21	6.05 dd 17.5, 10.5	144.4 CH	C-22, C-23, C-24
22		43.7 C	
23	0.99 (3H) s	21.9 CH_3	C-3, C-21, C-22, C-24
24	1.08 (3H) s	22.7 CH_3	C-3, C-21, C-22, C-23
25	6.46 d 10.0	117.6 CH	C-6, C-7, C-8, C-27
26	5.69 d 10.0	131.5 CH	C-7, C-27, C-28, C-29
27		77.3 C	
28	1.38 (3H) s	27.9 CH_3	C-26, C-27, C-29
29	1.41 (3H) s	27.8 CH_3	C-26, C-27, C-28

Table S4. ^{1}H and ^{13}C NMR data for notoamide N (**13**) in acetone-d_6.

No.	δ_H J (Hz)	δ_c	HMBC
1	9.60 br s		
2		182.6 C	
3		62.0 C	
4	7.19 s	127.4 CH	C-5, C-6, C-8
5		113.3 C	
6		148.5 C	
7		106.6 C	
8		137.6 C	
9		124.0 C	
10	2.26 d 14.0	35.0 CH_2	C-2, C-3, C-11, C-12, C-21, C-22
	3.01 d 14.0		C-2, C-9, C-11, C-12, C-21
11		67.0 C	
12		170.0 C	
14	3.47 m	44.3 CH_2	C-16
	3.50 m		C-16
15	1.90 m	25.4 CH_2	
	2.04 m		
16	1.84 m	30.5 CH_2	C-16, C-17
	2.65 m		
17		69.8 C	
18		173.3 C	
19	8.04 br s		
20	1.85 m	30.9 CH_2	C-17, C-18, C-22
	2.03 m		
21	3.30 dd 10.5, 8.5	56.7 CH	C-11, C-20, C-22, C-23, C-24
22		46.8 C	
23	0.82 (3H) s	24.3 CH_3	C-3, C-21, C-22, C-24
24	0.84 (3H) s	20.6 CH_3	C-3, C-21, C-22, C-23
25	6.66 d 10.0	117.0 CH	C-6, C-7, C-27
26	5.85 d 10.0	131.5 CH	C-7, C-27
27		78.0 C	
28	1.45 (3H) s	28.1 CH_3	C-26, C-27, C-29
29	1.46 (3H) s	28.1 CH_3	C-26, C-27, C-28

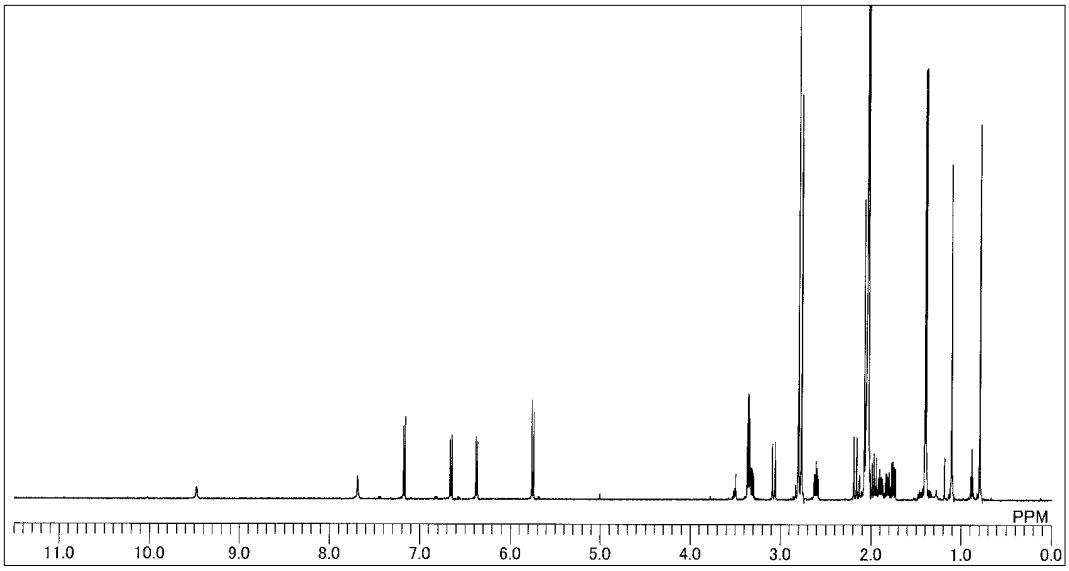


Figure S1. ^{1}H NMR spectrum of (-)-versicolamide B (**10**) in acetone-d_6.

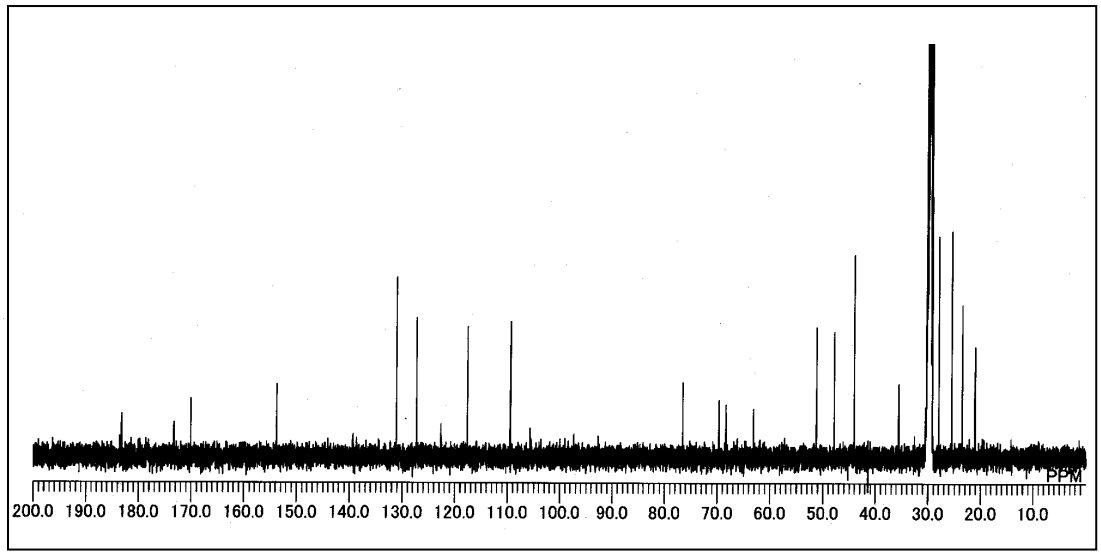


Figure S2. ^{13}C NMR spectrum of (-)-versicolamide B (**10**) in acetone-d_6.

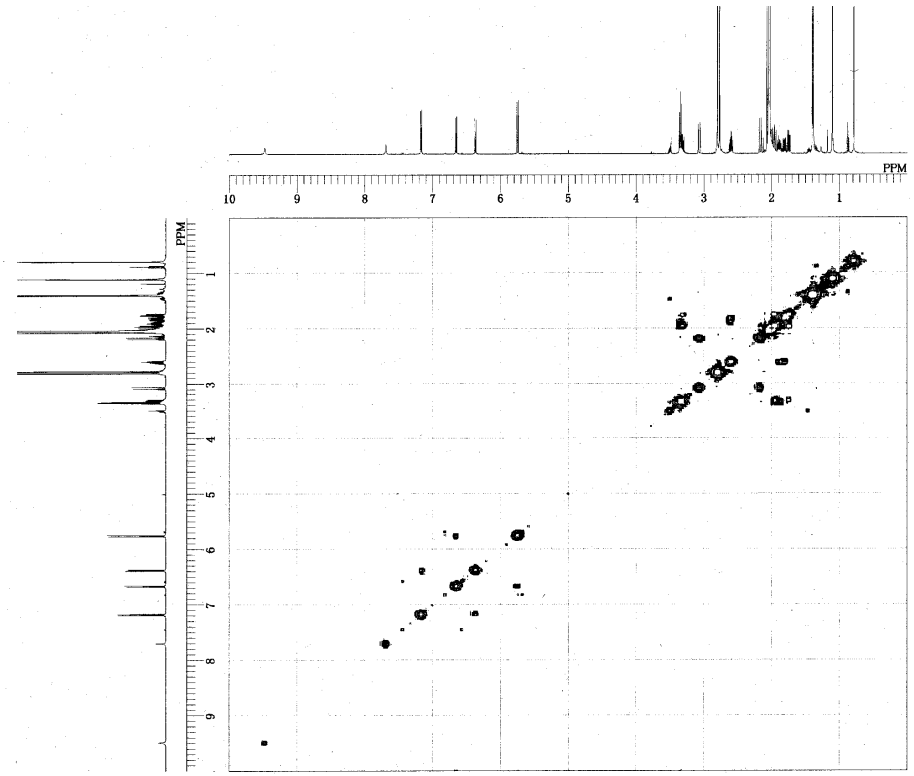


Figure S3. COSY spectrum of (-)-versicolamide B (**10**) in acetone-d_6.

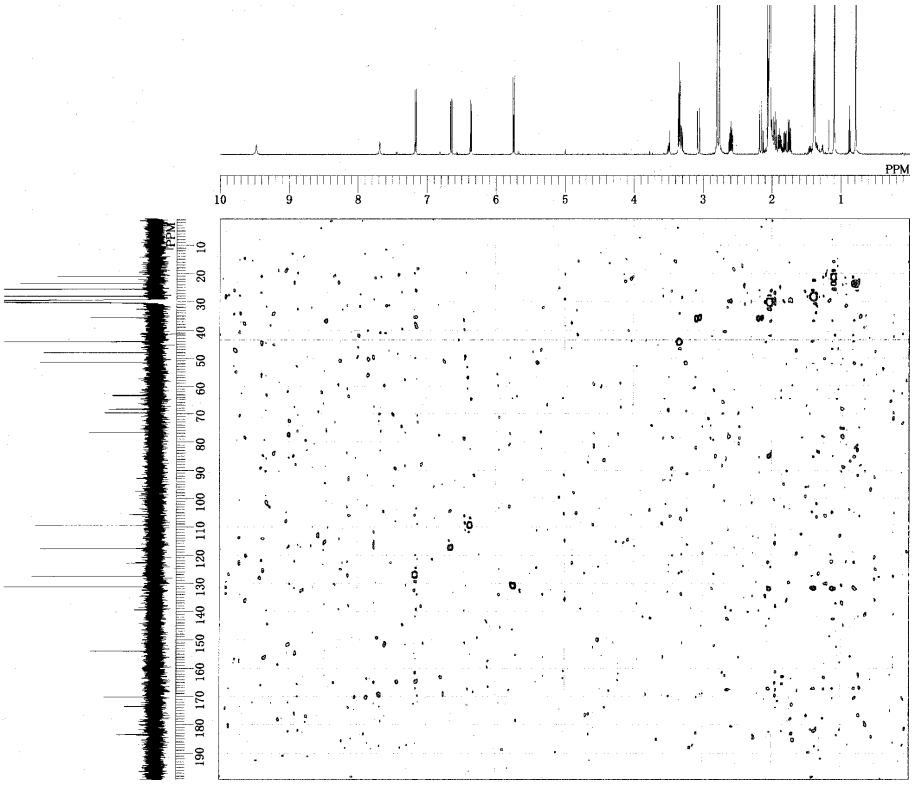


Figure S4. HMQC spectrum of (-)-versicolamide B (**10**) in acetone-d_6.

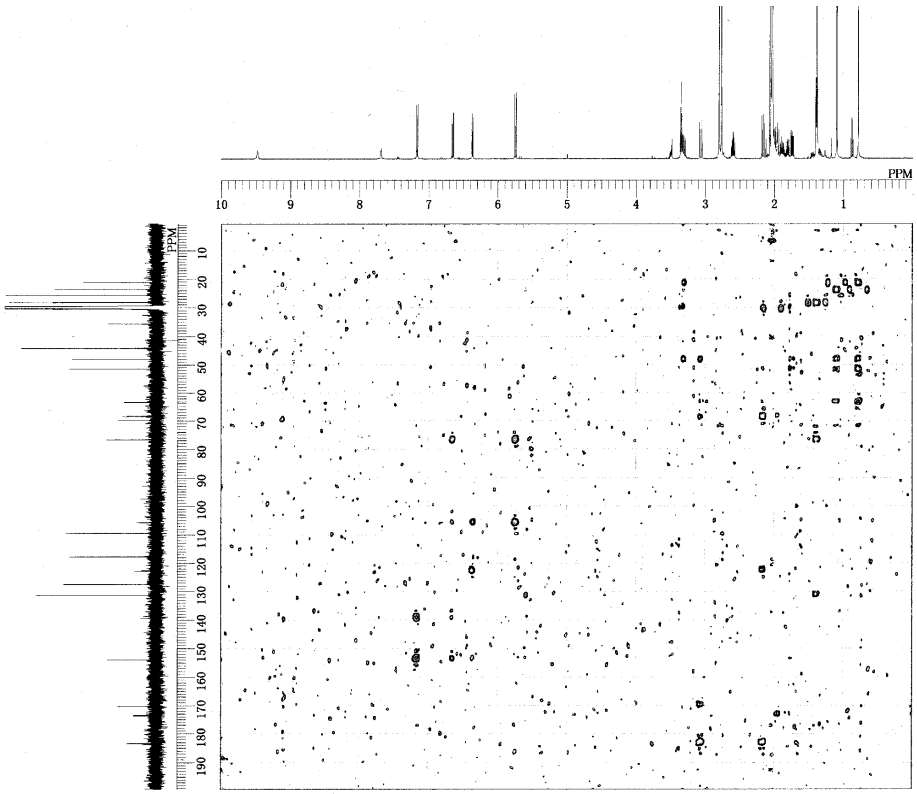


Figure S5. HMBC spectrum of (-)-versicolamide B (**10**) in acetone-d_6.

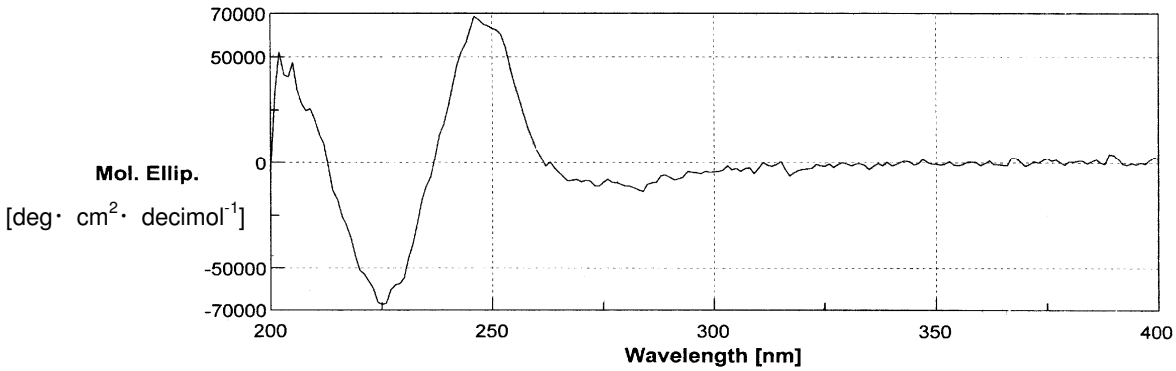


Figure S6. CD spectrum of (-)-versicolamide B (**10**) in MeOH.

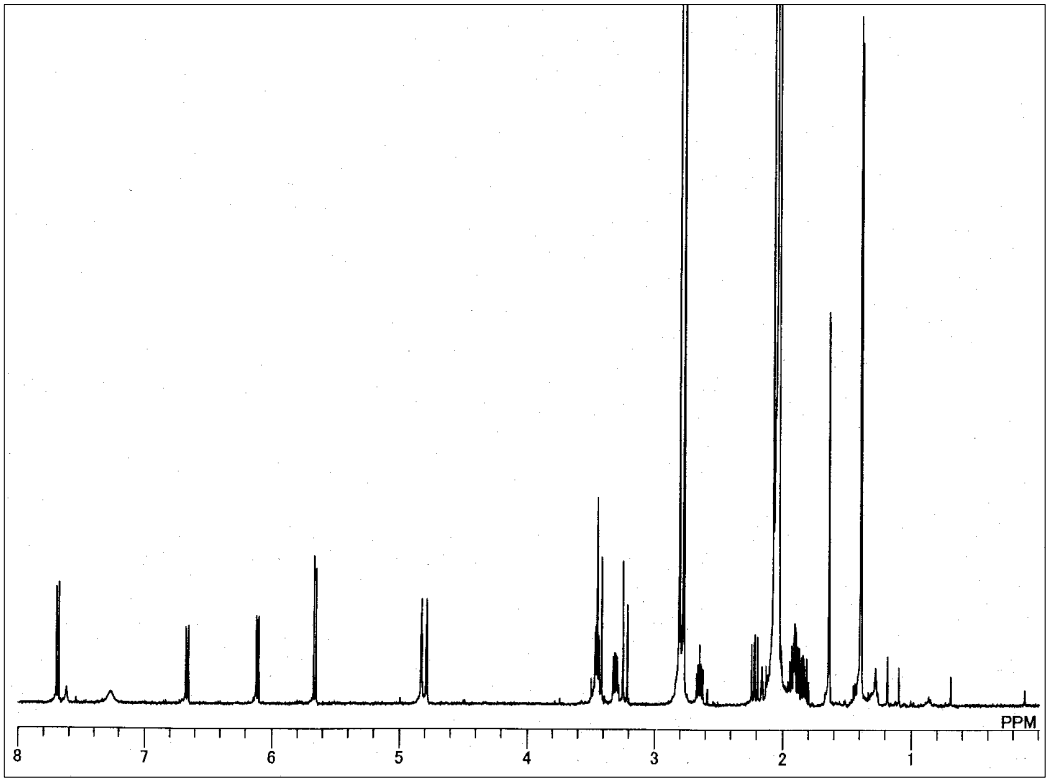


Figure S7. ^{1}H NMR spectrum of notoamide L (**11**) in acetone-d_6.

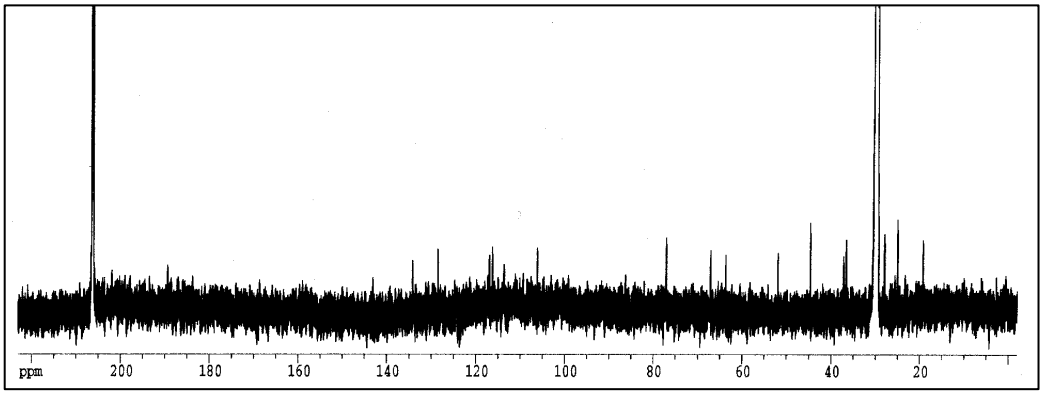


Figure S8. ^{13}C NMR spectrum of notoamide L (**11**) in acetone-d_6.

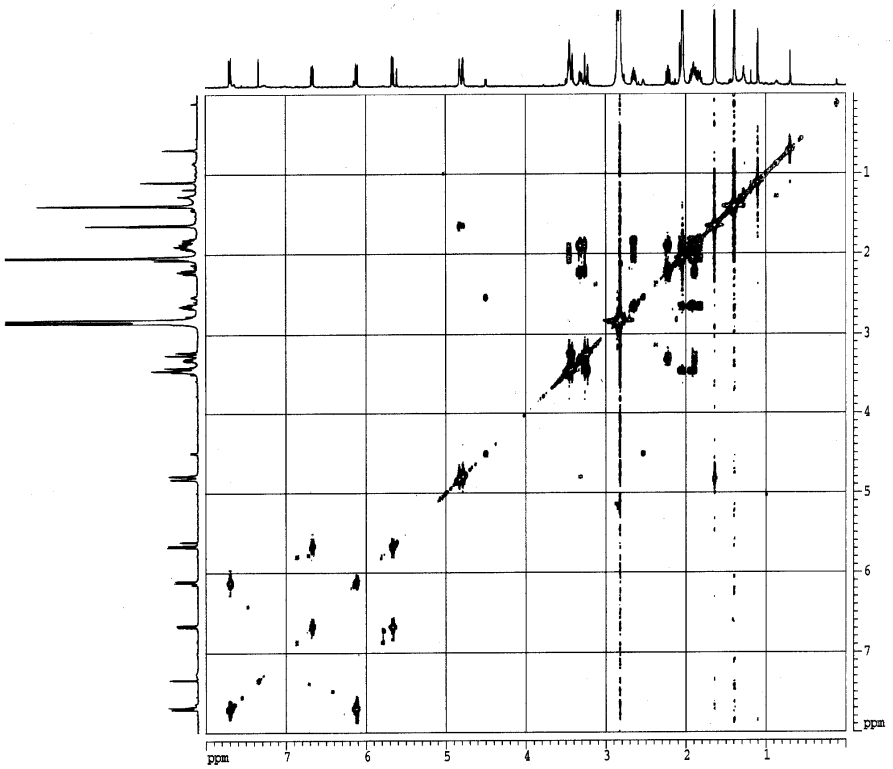


Figure S9. COSY spectrum of notoamide L (**11**) in acetone-d_6.

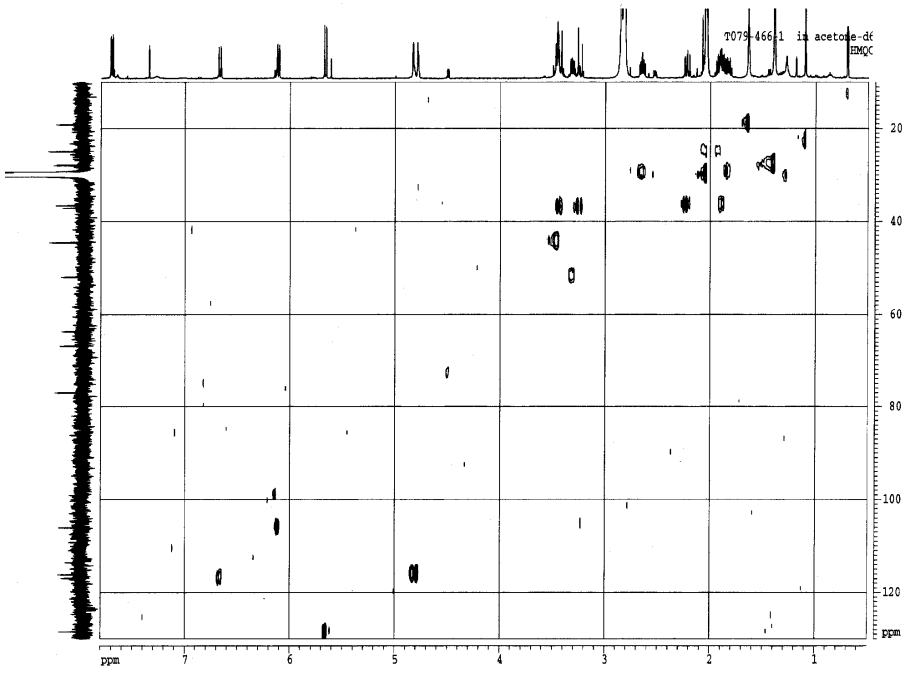


Figure S10. HMQC spectrum of notoamide L (**11**) in acetone-d_6.

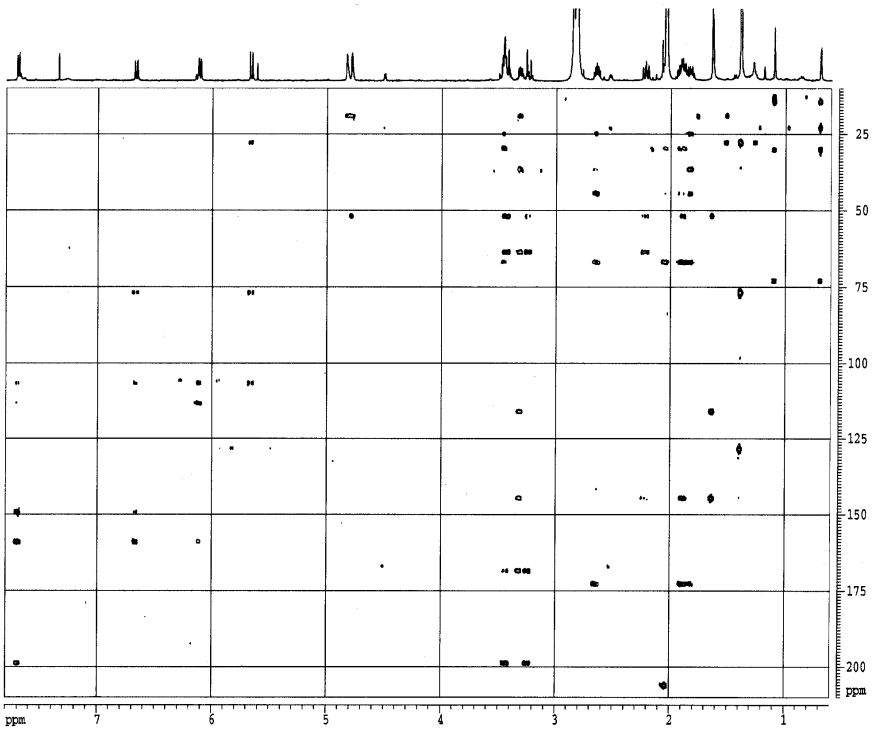


Figure S11. HMBC spectrum of notoamide L (**11**) in acetone-d_6.

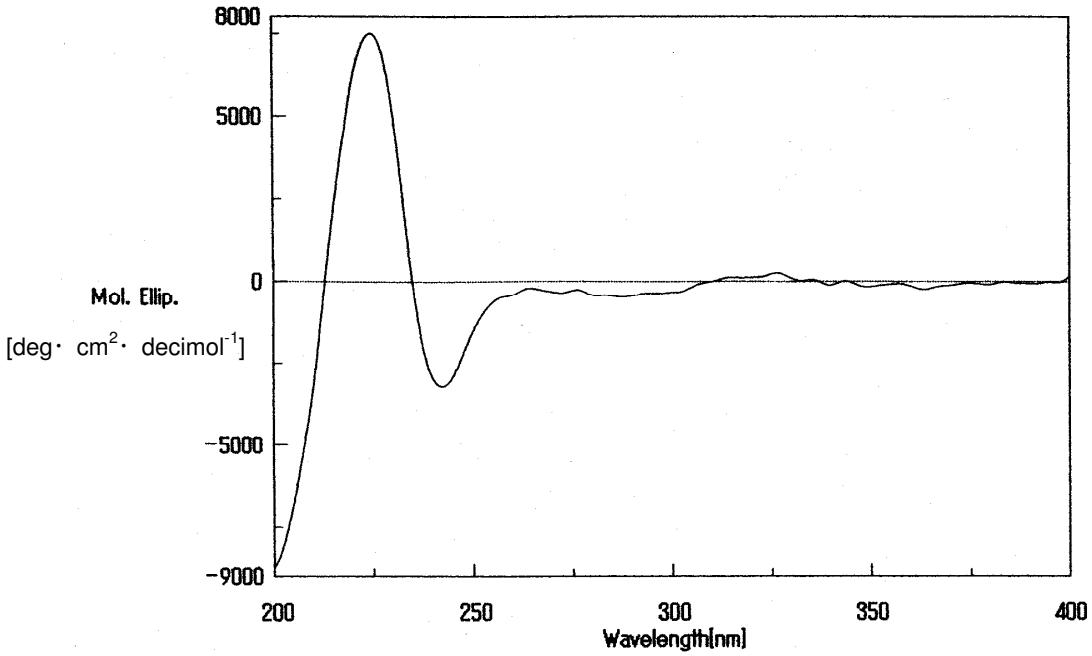


Figure S12. CD spectrum of notoamide L (**11**) in MeOH.

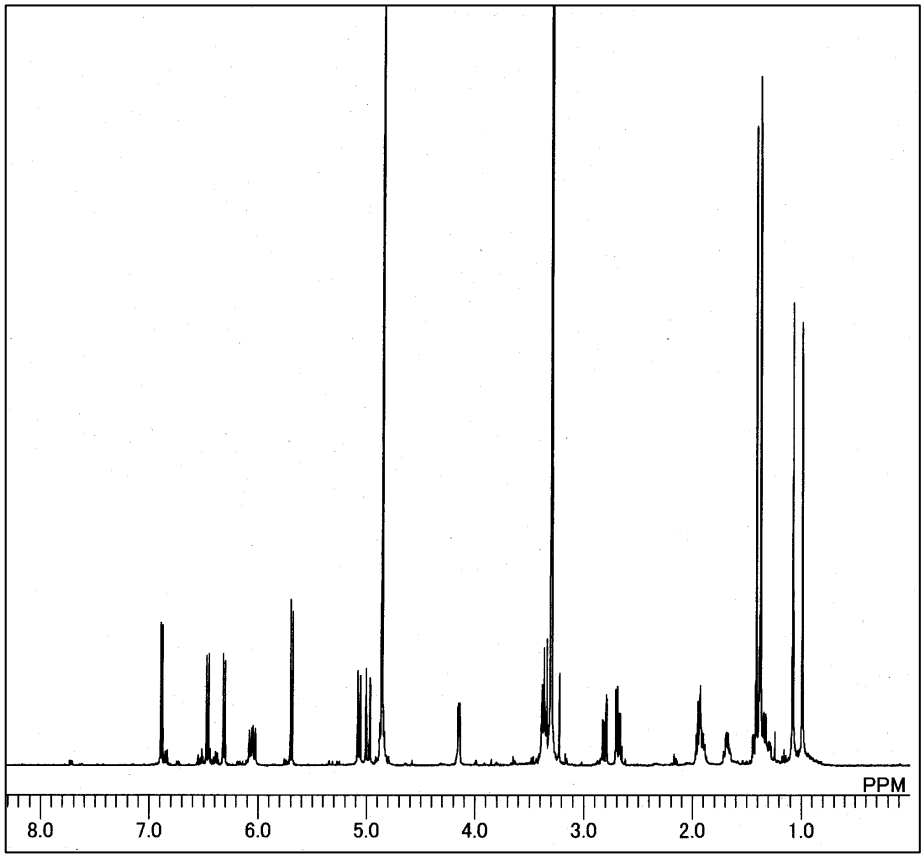


Figure S13. ^{1}H NMR spectrum of notoamide M (**12**) in CD_3OD.

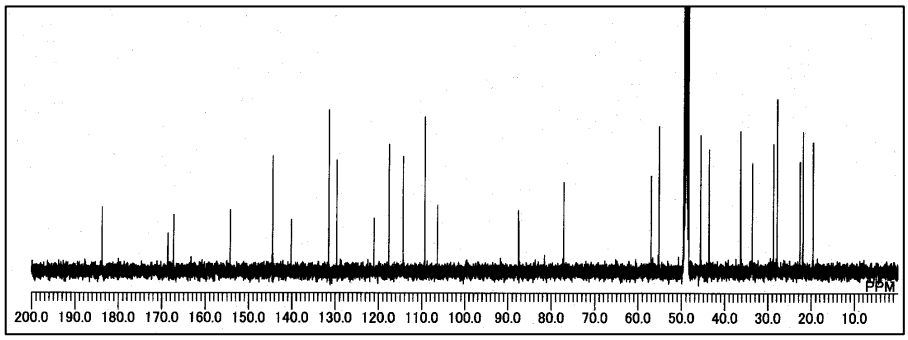


Figure S14. ^{13}C NMR spectrum of notoamide M (**12**) in CD_3OD.

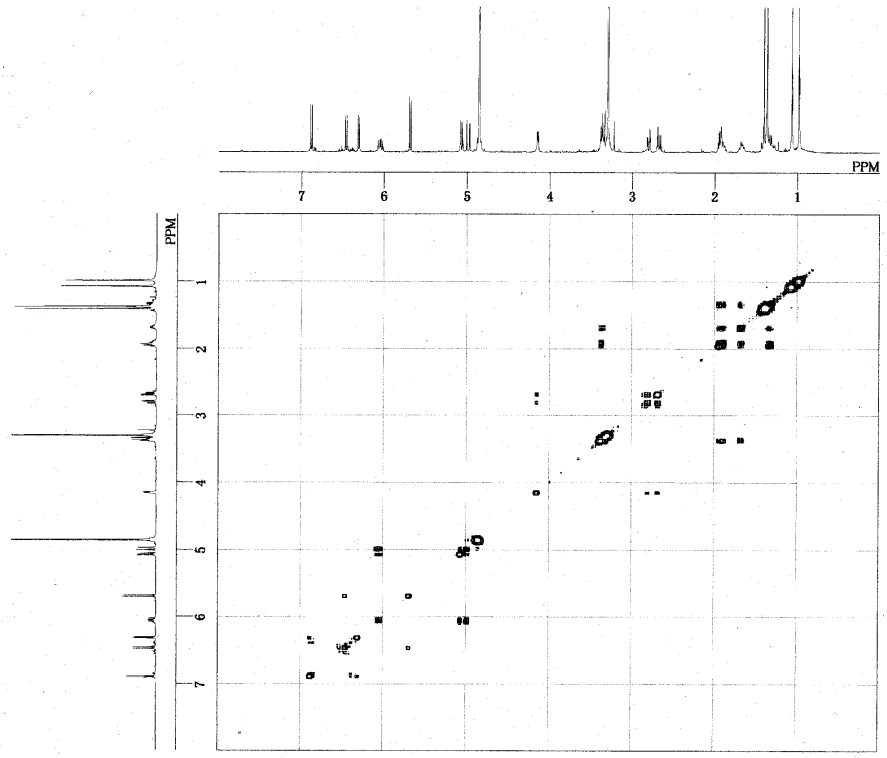


Figure S15. COSY spectrum of notoamide M (**12**) in CD_3OD.

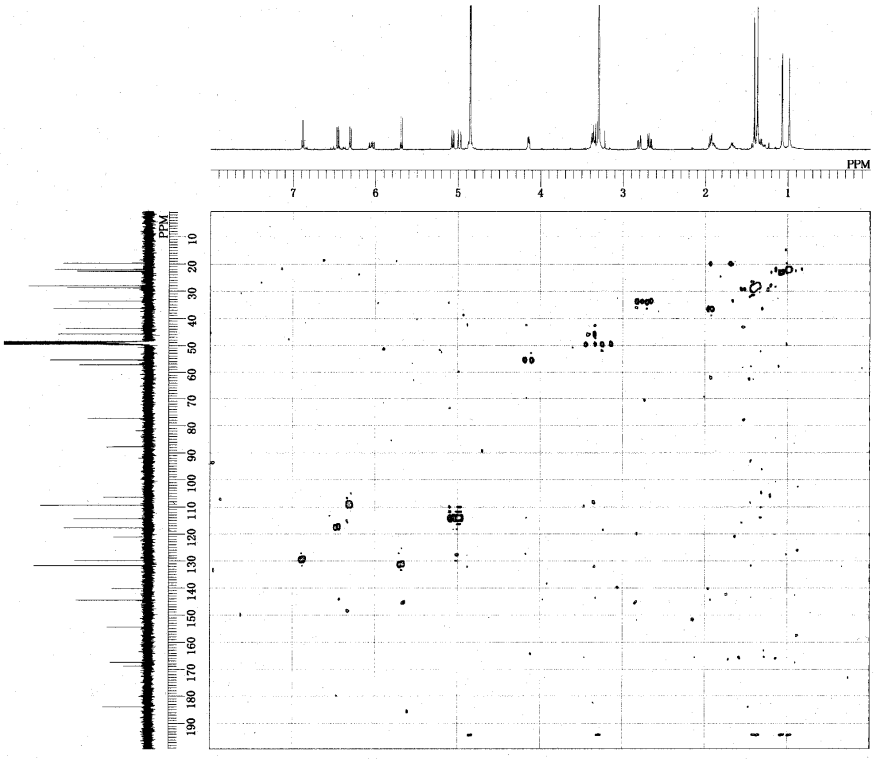


Figure S16. HMQC spectrum of notoamide M (**12**) in CD_3OD.

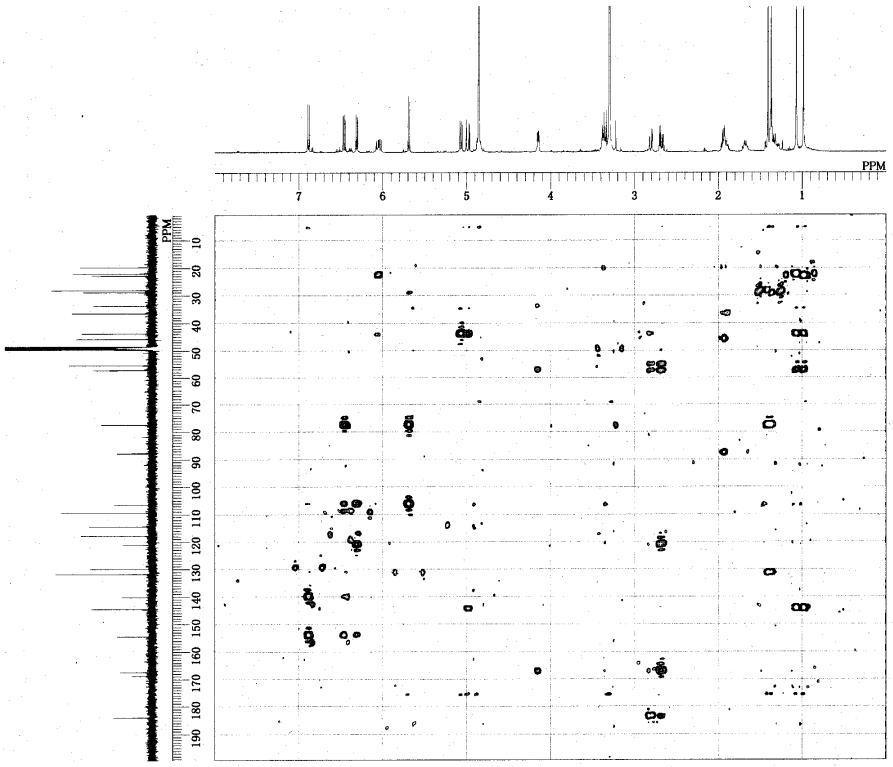


Figure S17. HMBC spectrum of notoamide M (**12**) in CD_3OD.

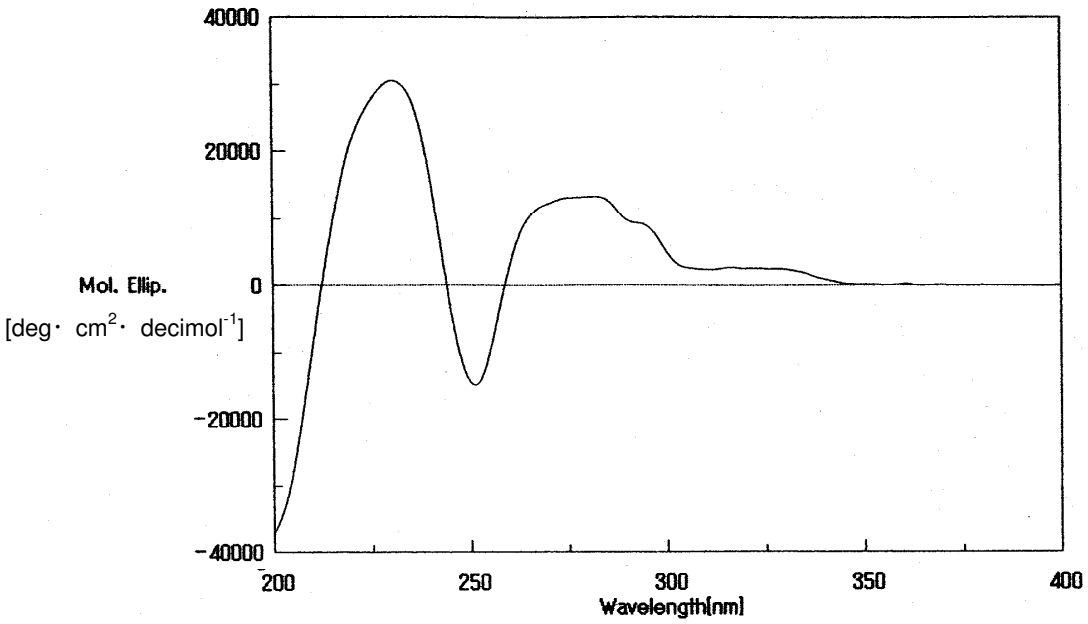
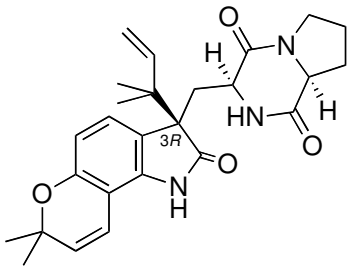
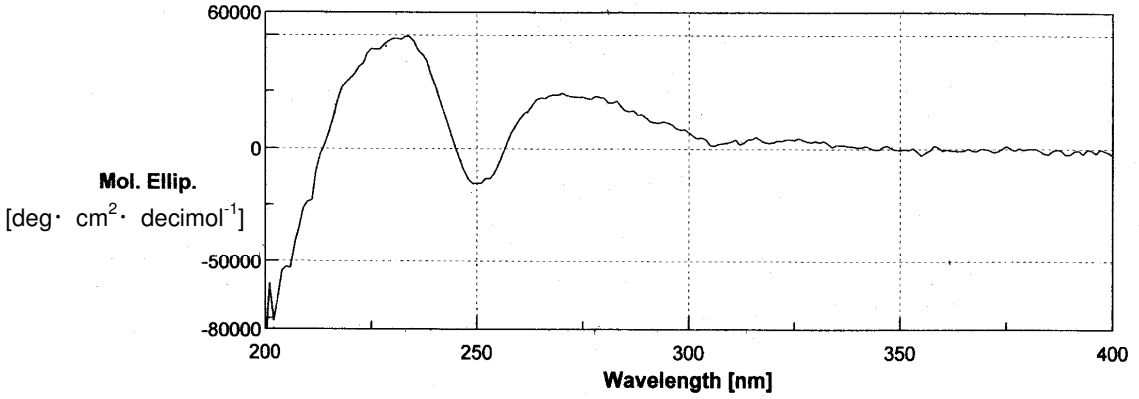


Figure S18. CD spectrum of notoamide M (**12**) in MeOH.

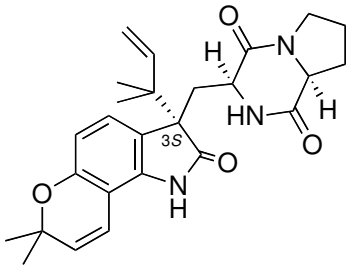
(a)



notoamide C (**3**)



(b)



3-*epi*-notoamide C (**14**)

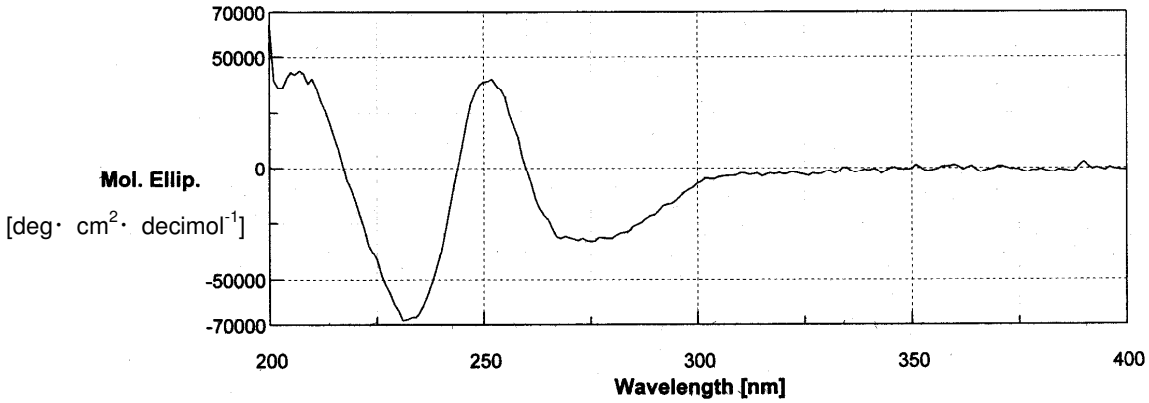


Figure S19. CD spectra of (a) notoamide C (**3**) and (b) 3-*epi*-notoamide C (**14**) in MeOH.

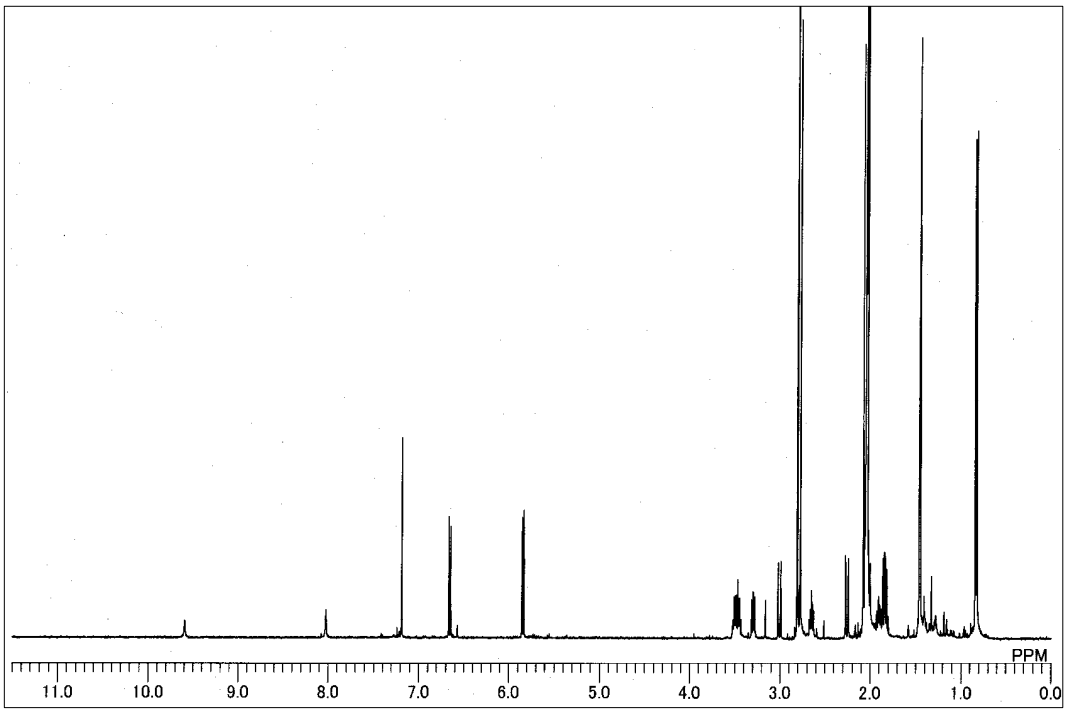


Figure S20. ^{1}H NMR spectrum of notoamide N (**13**) in acetone-d_6.

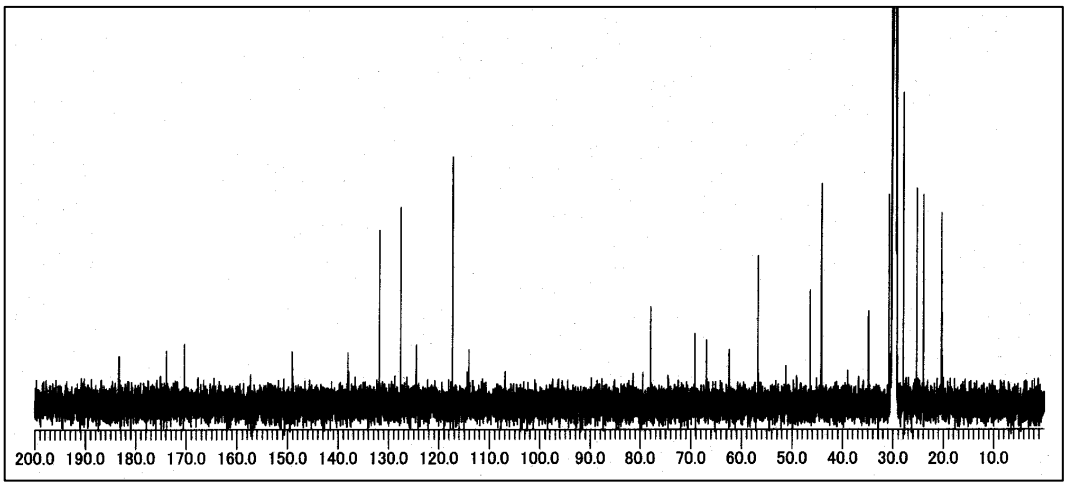


Figure S21. ^{13}C NMR spectrum of notoamide N (**13**) in acetone-d_6.

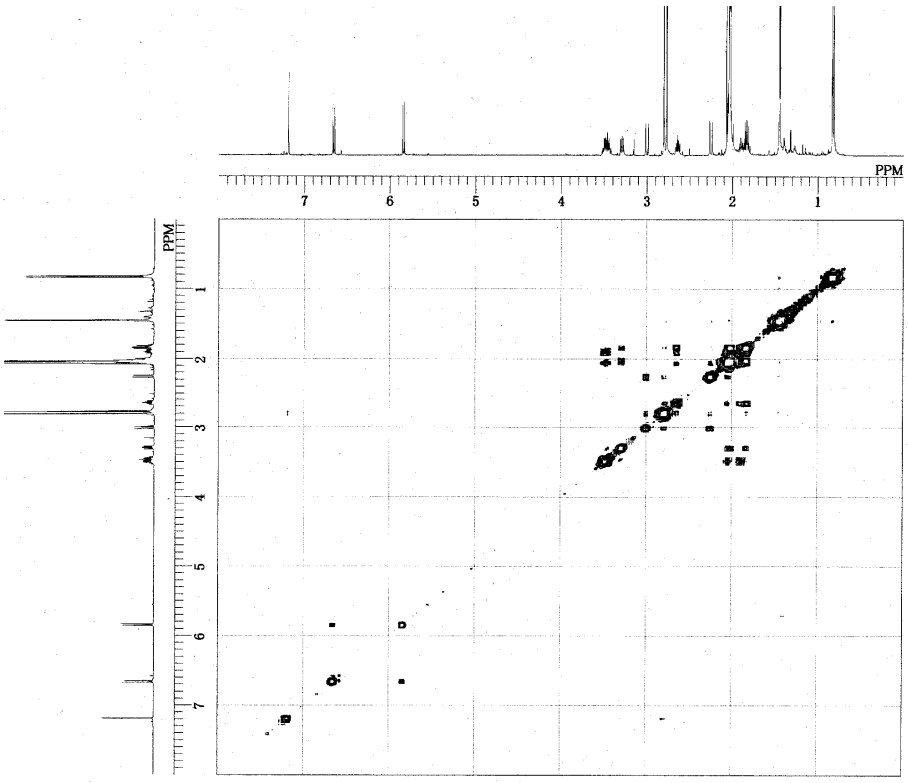


Figure S22. COSY spectrum of notoamide N (**13**) in acetone-d_6.

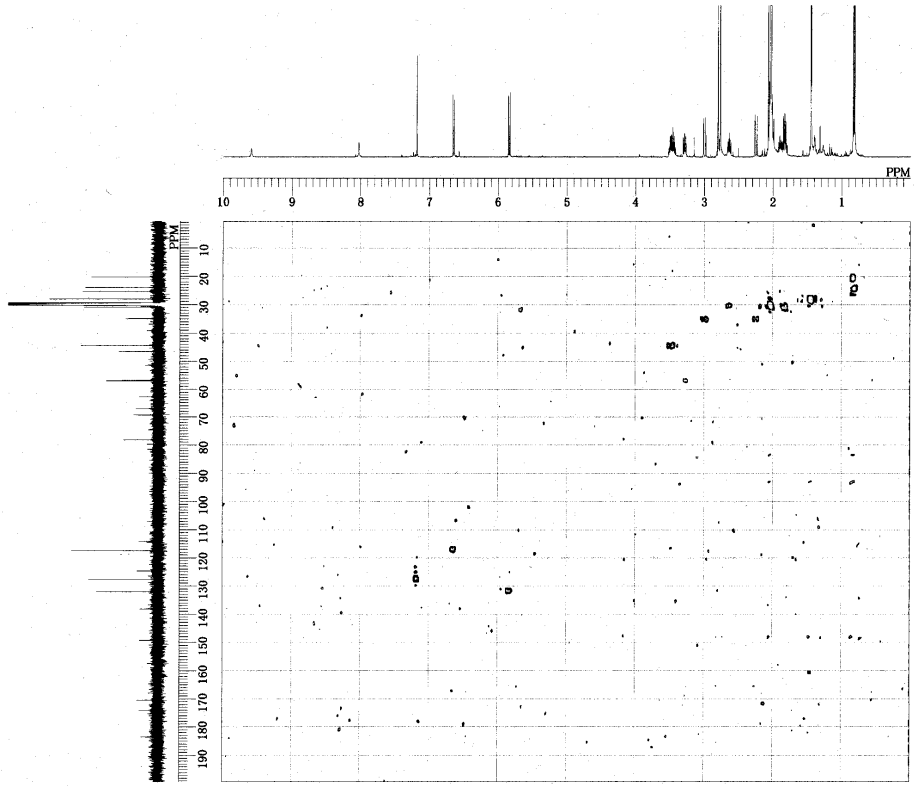


Figure S23. HMQC spectrum of notoamide N (**13**) in acetone-d_6.

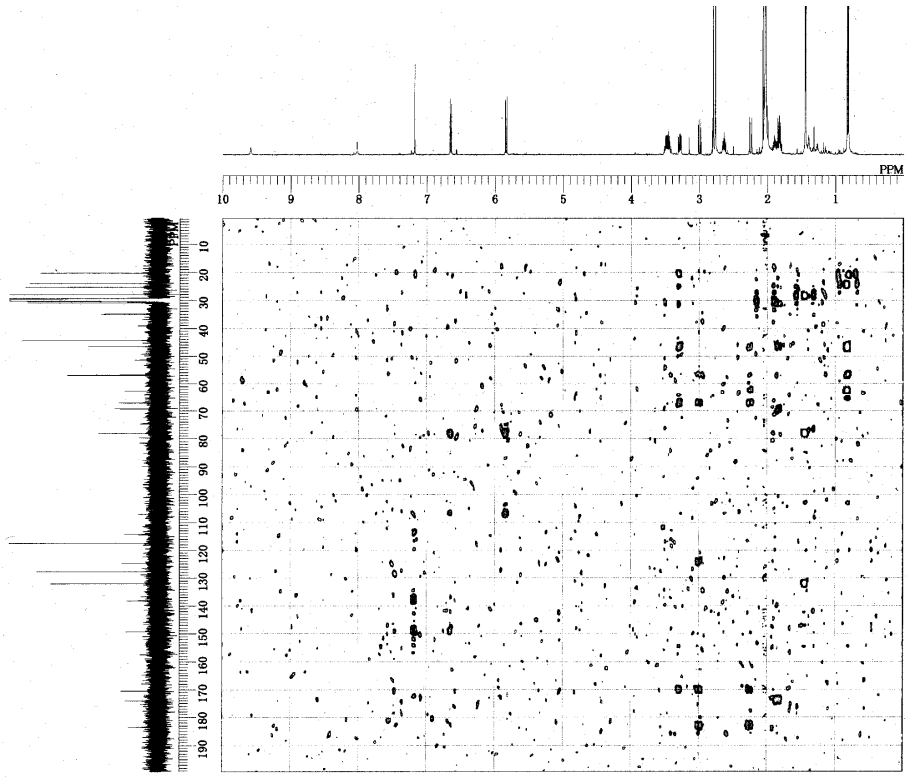


Figure S24. HMBC spectrum of notoamide N (**13**) in acetone-d_6.

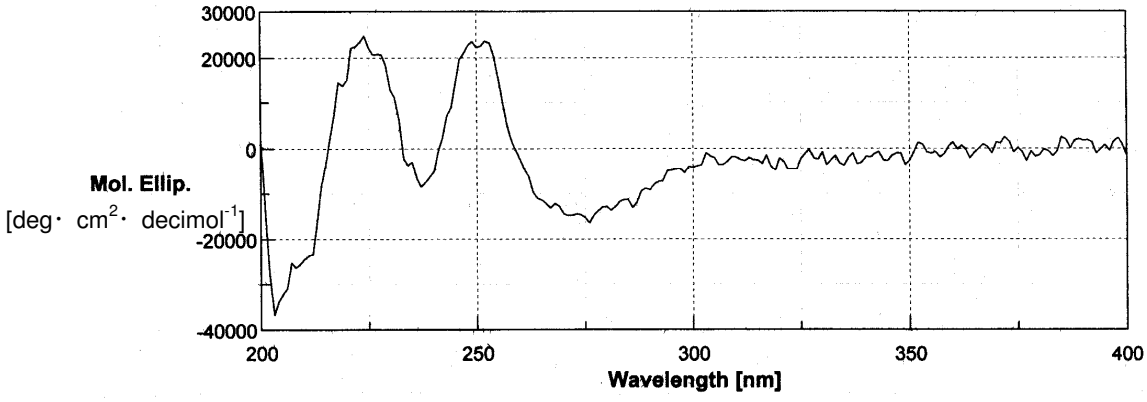


Figure S25. CD spectrum of notoamide N (**13**) in MeOH.

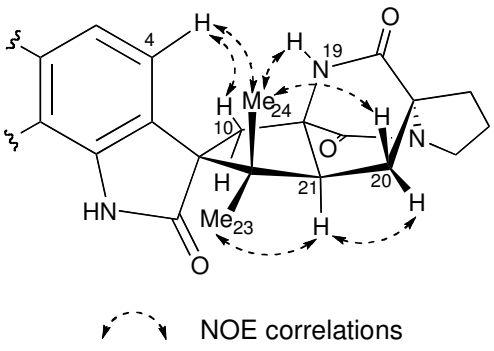


Figure S26. NOE correlations for (-)-versicolamide B (**10**).

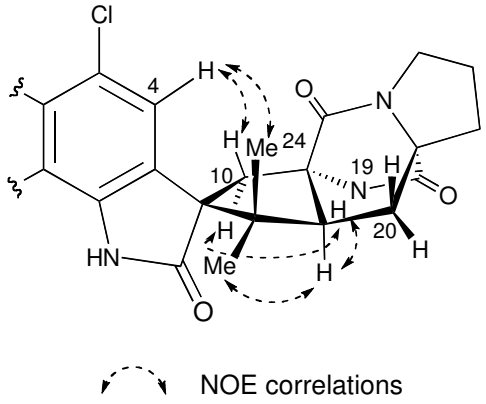
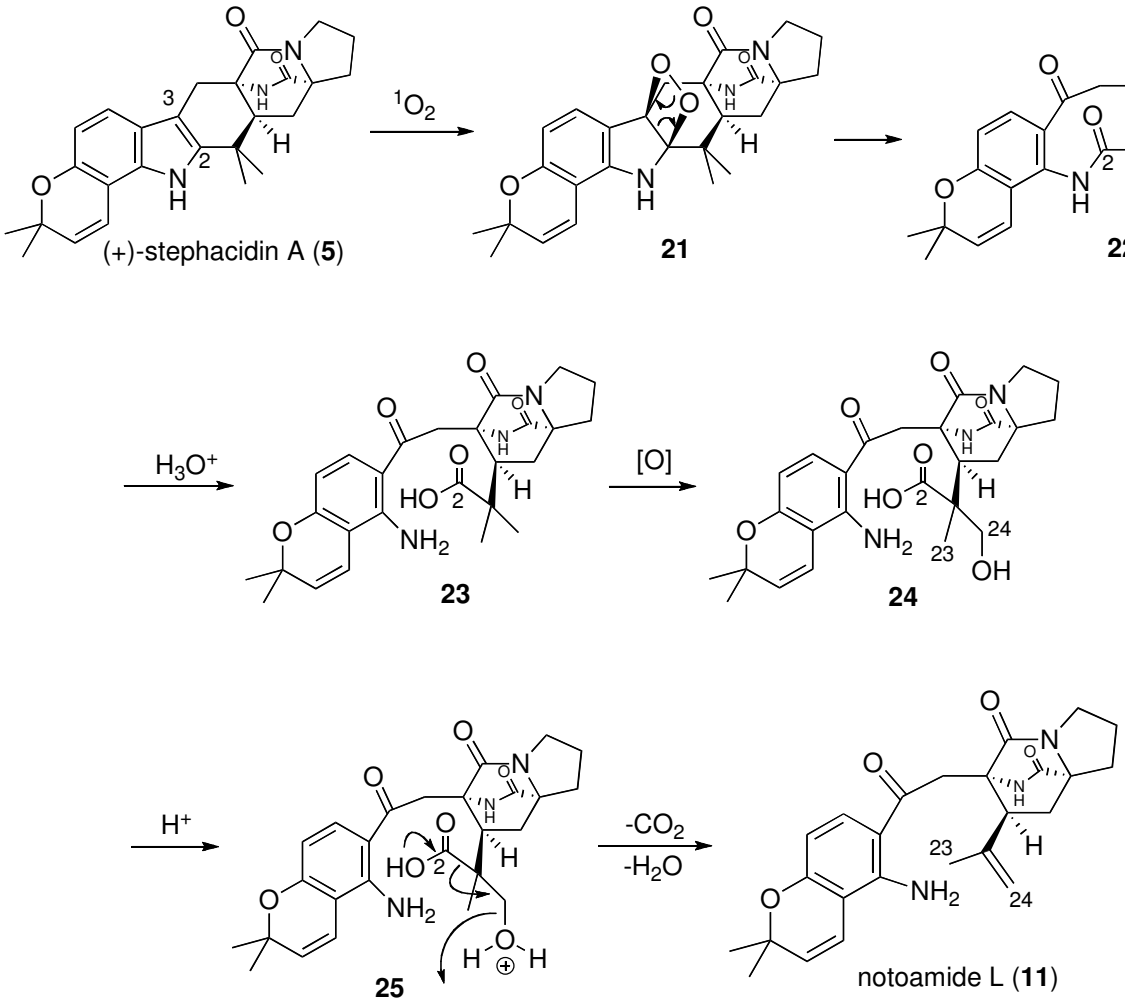
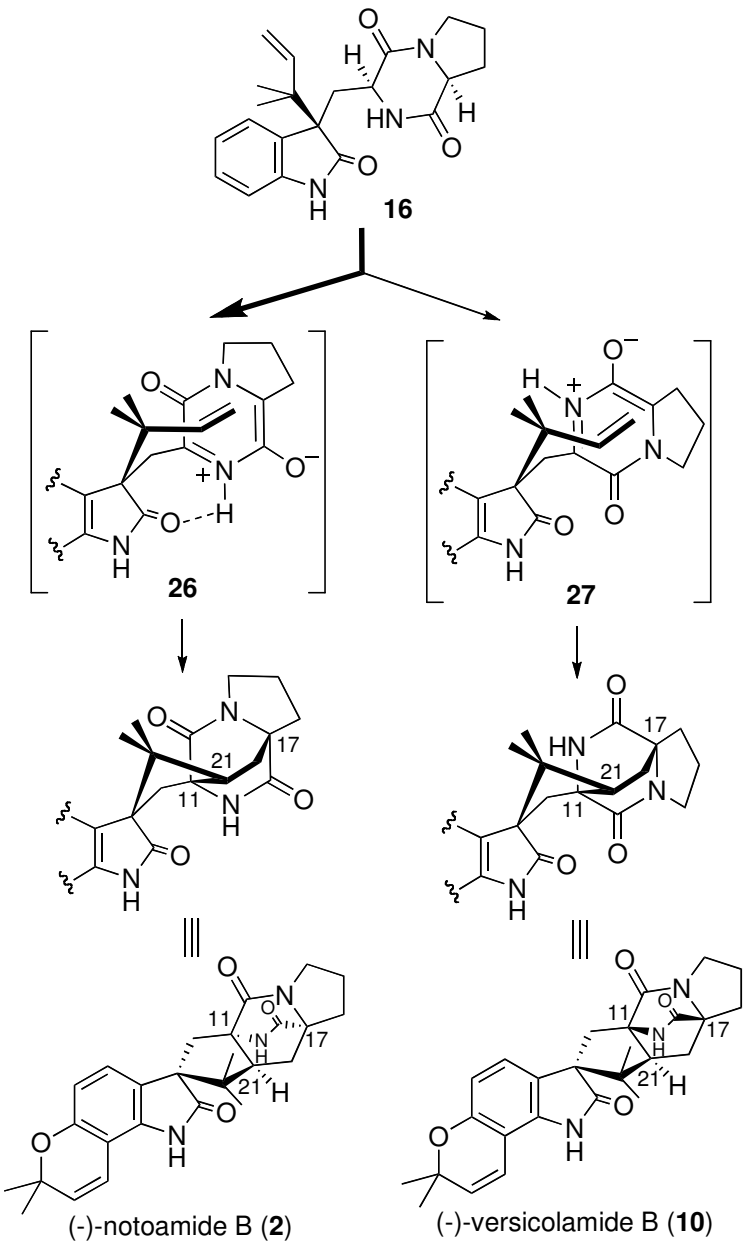


Figure S27. NOE correlations for notoamide N (**13**).



Scheme S1. Possible biosynthetic pathway of notoamide L (**11**).



Scheme S2. Possible intermediates **26** and **27** derived from **16**.