PERGAMON

Phytochemistry 52 (1999) 501–509

PHYTOCHEMISTRY

Ptychantols A–C, macrocyclic bis(bibenzyls), possessing a *trans*-stilbene structure from the liverwort *Ptychanthus striatus*

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Received 22 February 1999; accepted 26 March 1999

Abstract

Three novel macrocyclic bis(bibenzyls) named ptychantols A–C possessing a *trans*-stilbene structure, have been isolated from the liverwort *Ptychanthus striatus*. Their structures were established by a combination of two-dimension NMR spectra, X-ray crystallographic analysis and chemical degradation. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: *Ptychanthus striatus*; Liverwort; Lejeuneaceae; Macrocyclic bis(bibenzyls); Ptychantol A; Ptychantol B; Ptychantol C; Two-dimension NMR; X-ray crystallographic analysis

1. Introduction

Liverworts are rich sources of both terpenoids and aromatic compounds with biological activities (Asakawa, 1982, 1990a,b, 1993, 1995, 1997, 1998; Hashimoto et al., 1995; Schwarter et al., 1995; Toyota, Tanimura & Asakawa, 1998). We have reported the distribution of a number of new terpenoids and aromatic compounds in more than 200 species of the liverworts (Asakawa, 1982, 1995; Hashimoto et al., 1995). In our previous paper, we isolated eight novel labdane-type diterpenoids, ptychantins A–H closely related to forskolin from the ether extract of the liverwort *Ptychanthus striatus*, belonging to the Lejeuneaceae and elucidated their stereostructures (Hashimoto et al., 1994; Hashimoto, Horie, Takaoka, Tori & Asakawa, 1995). Further fractionation of the MeOH extract of *P. striatus* resulted in the isolation of three novel macrocyclic bis(bibenzyls), named ptychantols A (**1**), B (**2**) and C (**3**). We now report on the structure elucidation of the three new compounds by two-dimension NMR spectra, X-ray crystallographic analysis and chemical degradation.

2. Results and discussion

2.1. Isolation of ptychantols A–C

P. striatus was extracted with Et_2O and followed with MeOH. The column chromatography of the Et_2O extract yielded kelosene (**4**) (König & Wright, 1997; Nabeta, Yamamoto, Hashimoto, Kashino, Funatsuki, & Katoh, 1998), striatene (**5**) (Takeda & Katoh, 1983), ptychantins A (**6**) (Asakawa, 1990), B (**7**) (Asakawa, 1990) and C (**8**) (Asakawa, 1990). The MeOH extract was subjected to column chromatography using silica gel and Sephadex LH-20, and HPLC to afford ptychantols A–C (**1**–**3**).

2.2. Ptychantol A (*1*)

Compound **1** was obtained as colorless prisms, m.p. 260–262°C, whose molecular formula, $C_{28}H_{22}O_4$ was established by high resolution mass spectrum (HRMS) ($[M]^+$ m/z 422.1509). The IR and UV spectra of **1** indicated the presence of a phenolic hydroxyl group (ν

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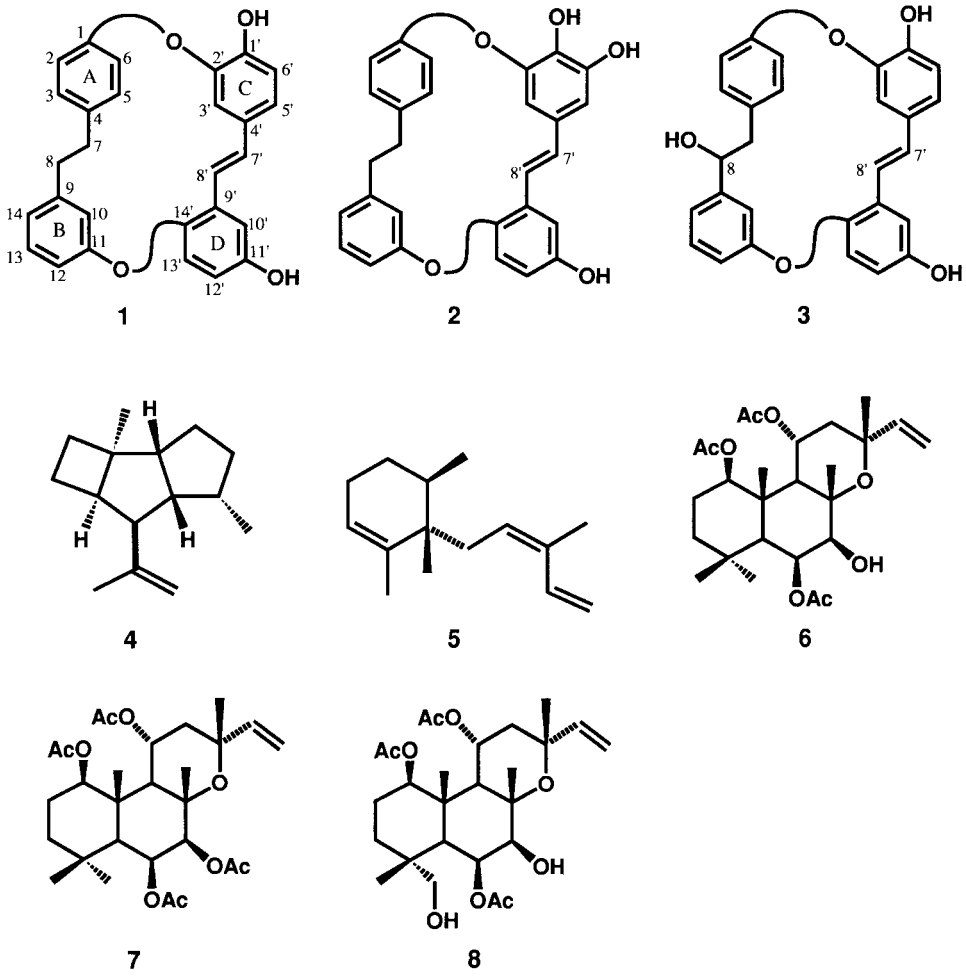
PII: S0031-9422(99)00227-7



3194 cm^{-1}) and a benzene ring (ν 1572 cm^{-1}), which was conjugated with a double bond [λ_{max} 342 nm (log $\varepsilon = 4.35$)]. The ^1H and ^{13}C NMR spectra (Table 1) of **1** in acetone-d_6 indicated the presence of two benzyl methylenes [δ_H 3.10 (4H, m, 7 and 8-H_2); δ_C 35.9 (C-7), 37.0 (C-8)], *trans*-olefine [δ_H 6.49 (1H, d, J = 16.5 Hz, 8′-H), 6.97 (1H, d, J = 16.5 Hz, 7′-H); δ_C 119.7 (C-8′), 128.9 (C-7′)], two phenolic protons [δ_H 8.25, 8.40 (each 1H, br. s)] and 14 aromatic protons on four benzene rings. The methylation (MeI/K_2CO_3/reflux) of **1** afforded a dimethyl ether (**9**) [$C_{30}H_{26}O_4$; δ_H 3.85, 3.95 (each 3H, s, –OMe)] indicating that two of the four oxygen atoms in **1** were phenolic hydroxyl groups and the remaining two oxygens were the ether oxygens since neither carbonyl nor hydroxyl absorption bands were observed in the IR spectrum of **9**. Compound **9** showed the NOEs between (i) 1′-OMe and H-6′, (ii) 11′-OMe and H-10′, (iii) 11′-OMe and H-12′ in the NOESY spectrum (Fig. 1 and Table 2) indicating that the two hydroxyl groups were located at C-1′ and C-11′. The hydrogenation (10% Pd–C/H_2) of **5** afforded a dihydro derivative **10** [$C_{30}H_{28}O_4$; δ_H 2.49 (2H, m, H-8′), 2.61 (2H, m, H-7′)] indicating that **1** contained one olefinic group. Compound **10** showed the NOEs between (i) H-3′ and H-7′, (ii) H-5′ and H-7′ and (iii) H-8′ and H-10′ in the NOESY spectrum (Fig. 1 and Table 2). The linkage between a bibenzyl and a stilbene was suggested to be C_1–O–C_2′ and C_{11}–O–C_{10}′ from careful analysis of its 2D NMR spectra including HMBC (Table 1) and NOESY spectra (Table 1) of **1**. From the above spectral and chemical evidence, the structure of ptychantol A (**1**) was deduced and finally established by X-ray crystallographic analysis of **1** as shown in Fig. 2.

2.3. Ptychantol B (2)

Compound **2** was obtained as a white powder, m.p. 235–237°C, whose molecular formula, $C_{28}H_{22}O_5$ was established by HRMS spectrum ($[M]^+$ m/z 438.1494). The spectral data of **2** resembled those of **1**. The ^1H and ^{13}C NMR spectra (Table 3) of **2** in acetone-d_6 showed the presence of two benzyl methylenes [δ_H 3.08 (4H, m, 7 and 8-H_2); δ_C 35.9 (t), 37.0 (t)], *trans*-olefine [δ_H 6.50 (1H, d, J = 16.2 Hz, 8′-H), 6.93 (1H, d, J = 16.2 Hz, 7′-H); δ_C 120.1 (C-8′), 129.0 (C-7′)] and

Table 1
^{1}H NMR and ^{13}C NMR assignments and HMBC and NOESY correlations of ptychantol A (**1**)[a]

Position No.	^{1}H (δ)	^{13}C (δ)	HMBC	NOESY
A-1		153.7 (s)	H-2, H-3, H-5, H-6	
A-2, 6	6.89 (d, J = 8.2)	122.4 (d)	H-3, H-5	H-3, H-5, H-3′
A-3, 5	7.17 (d, J = 8.2)	131.4 (d)	H-2, H-6, H-7	H-2, H-6, H-7, H-10
A-4		138.5 (s)	H-2, H-6, H-7	
7	3.10 (m)	35.9 (t)	H-3, H-5	H-3, H-5
8	3.10 (m)	37.0 (t)	H-10, H-14	H-10, H-14
B-9		143.6 (s)	H-7, H-8, H-13	
B-10	6.63 (dd, J = 1.9, 1.9)	118.7 (d)	H-8, H-12, H-14	H-3, H-8
B-11		160.3 (s)	H-10, H-12, H-13	
B-12	6.09 (ddd, J = 8.0, 1.9, 1.9)	109.9 (d)	H-10, H-13, H-14	H-13, H-13′
B-13	7.06 (dd, J = 8.0, 8.0)	129.9 (d)		H-12, H-14
B-14	6.99 (ddd, J = 8.0, 1.9, 1.9)	121.9 (d)	H-8, H-10, H-12	H-8, H-13
C-1′		147.5 (s)	1′-OH, H-3′, H-5′,	
C-2′		149.8 (s)	1′-OH, H-3′, H-6′	
C-3′	6.41 (d, J = 1.9)	109.8 (d)	H-5′, H-7′	H-6, H-8′
C-4′		129.8 (s)	H-3′, H-6′, H-8′	
C-5′	6.82 (dd, J = 8.0, 1.9)	124.2 (d)	H-3′, H-7′	H-6′, H-7′
C-6′	6.86 (d, J = 8.0)	116.7 (d)		1′-OH, H-5′
1′-OH	8.25 (br, s)			H-6′
7′	6.97 (d, J = 16.5)	128.9 (d)	H-3′, H-5′	H-5′, H-10′
8′	6.49 (d, J = 16.5)	119.7 (d)	H-7′, H-10′	H-3′
D-9′		132.1 (s)	H-7′, H-13′	
D-10′	7.27 (d, J = 3.0)	111.8 (d)	H-8′, 11′-OH, H-12′	H-7′, 11′-OH
D-11′		155.8 (s)	H-10′, 11′-OH, H-12′ H-13′	
D-12′	6.81 (dd, J = 8.5, 3.0)	116.4 (d)	H-10′, 11′-OH, H-13′	11′-OH, H-13′
D-13′	6.91 (d, J = 8.5)	125.0 (d)	H-12′	H-12, H-12′
D-14′		144.7 (s)	H-10′, H-12′, H-13′	
11′-OH	8.40 (br. s)			H-10′, H-12′

[a] Chemical shifts from TMS (multiplicity, J in Hz) in acetone-d_6.

three phenolic protons [δ_H 7.86, 8.00, 8.42 (each 1H, br. s)] signals and were very similar to those (Table 1) of **1** except for the chemical shifts of benzene ring C. The methylation (MeI/K_2CO_3/reflux) of **2** afforded a trimethyl ether (**11**) [δ_H 3.85, 3.90, 3.97 (each 3H, s, –OMe)] indicating that **2** contained three phenolic hydroxyl groups. Compound **11** showed the NOEs between (i) 6′-OMe and H-5′, (ii) 11′-OMe and H-10′, (iii) 11′-OMe and H-12′ in the NOESY spectrum (Fig. 1 and Table 2) indicating that the three hydroxyl groups were located at C-1′, C-6′ and C-11′. The hydrogenation (10% Pd–C/H_2) of **11** afforded a dihydro derivative **12** [δ_H 2.51, 2.60 (4H, m, 7′ and 8′-H_2), 2.97 (4H, m, 7 and 8-H_2)]. From the HMBC and NOESY spectra (Table 3) of **2** and NOESY spectra (Fig. 3 and Table 4) of **11** and **12**, the structure of ptychantol B was determined as a C-6′ hydroxylated derivative of ptychantol A (**1**) and represented as **2**.

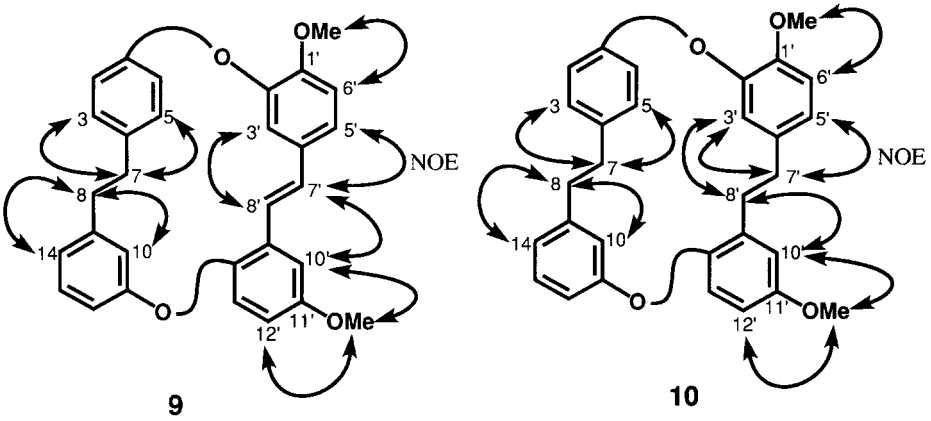


Fig. 1. 2D-NOESY experiments of **9** and **10**.

Table 2
^{1}H NMR and ^{13}C NMR assignments and HMBC and NOESY correlations of ptychantol B (**2**)[a]

Position No.	^{1}H (δ)	^{13}C (δ)	HMBC	NOESY
A-1		154.0 (s)	H-2, H-3, H-5, H-6	
A-2, 6	6.89 (d, J = 8.5)	122.5 (d)	H-3, H-5	H-3, H-5, H-3′
A-3, 5	7.14 (d, J = 8.5)	131.3 (d)	H-2, 6-H, 7-H	H-2, H-6, H-7, H-10
A-4		138.3 (s)	H-2, H-6, H-7	
7	3.10 (m)	35.9 (t)	H-3, H-5	H-3, H-5
8	3.10 (m)	37.0 (t)	H-10, H-14	H-10, H-14
B-9		143.5 (s)	H-7, H-8, H-13, H-14	
B-10	6.62 (dd, J = 1.9, 1.9)	118.7 (d)	H-8, H-12, H-14	H-3, H-8
B-11		160.3 (s)	H-10, H-12, H-13	
B-12	6.08 (ddd, J = 8.0, 1.9, 1.9)	109.9 (d)	H-10, H-13, H-14	H-13, H-13′
B-13	7.06 (dd, J = 8.0, 8.0)	129.9 (d)		H-12, H-14
B-14	6.99 (ddd, J = 8.0, 1.9, 1.9)	121.9 (d)	H-8, H-10, H-12	H-8, H-13
C-1′		134.9 (s)	1′-OH, H-3′, H-5′, 6′-OH	
C-2′		150.3 (s)	1′-OH, 3′-H	
C-3′	5.96 (d, J = 1.9)	101.8 (d)	H-5′, H-7′	H-6, H-8′
C-4′		129.0 (s)	H-3′, H-8′	
C-5′	6.53 (d, J = 1.9)	111.6 (d)	H-3′, 6′-OH, H-7′	6′-OH, H-7′
C-6′		146.8 (s)	H-5′, 6′-OH	
1′-OH	8.00 (br. s)			
6′-OH	7.86 (br. s)			H-5′
7′	6.89 (d, J = 16.2)	129.2 (d)	H-3′, H-5′	H-5′, H-10′
8′	6.50 (d, J = 16.2)	120.1 (d)	H-7′, H-10′	H-3′
D-9′		132.0 (s)	H-7′, H-13′	
D-10′	7.26 (d, J = 2.7)	111.8 (d)	H-8′, 11′-OH, H-12′	H-7′, 11′-OH
D-11′		155.8 (s)	H-10′, 11′-OH, H-12′ H-13′	
D-12′	6.80 (dd, J = 8.5, 2.7)	116.4 (d)	H-10′, 11′-OH, H-13′	11′-OH, H-13′
D-13′	6.91 (d, J = 8.5)	125.0 (d)	H-12′	H-12, H-12′
D-14′		144.6 (s)	H-10′, H-12′, H-13′	
11′-OH	8.42 (br. s)			H-10′, H-12′

[a] Chemical shifts from TMS (multiplicity, J in Hz) in acetone-d_6.

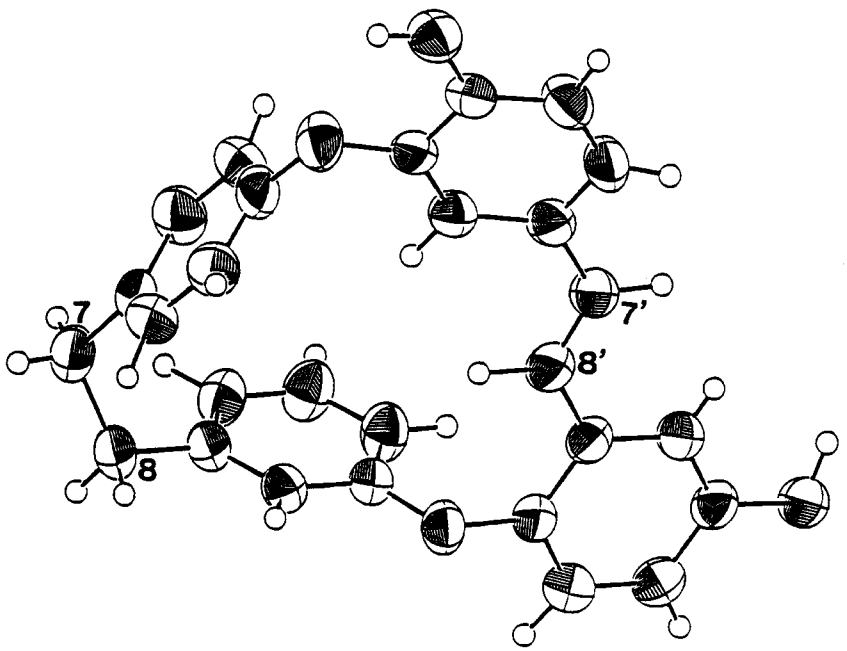


Fig. 2. The ORTEP drawing of ptychantol A (**1**).

Table 3
^{1}H NMR and ^{13}C NMR assignments and HMBC and NOESY correlations of ptychantol C (**3**)[a]

Position No.	^{1}H (δ)	^{13}C (δ)	HMBC	NOESY
A-1		154.1 (s)	H-2, H-3, H-5, H-6	
A-2	6.96 (dd, J = 8.5, 2.5)	122.2 (d)	H-3, H-6	H-3, H-3′
A-3	7.27 (dd, J = 8.5, 2.2)	132.8 (d)	H-2, H-5, H-7	H-2, H-7, H-8, H-10
A-4		135.7 (s)	H-2, H-6, H-7	H-6, H-7
A-5	7.06 (dd, J = 8.5, 2.2)	131.4 (d)	H-3, H-6, H-7	H-5
A-6	6.79 (dd, J = 8.5, 2.5)b	122.2 (d)	H-2, H-5	H-6
7	3.13 (dd, J = 12.9, 8.8) 3.40 (dd, J = 12.9, 4.7)	44.7 (t)	H-3, H-5	H-3, H-5, H-8, H-14
8	5.08 (dd, J = 8.8, 4.7)	75.4 (d)	H-7, H-10, H-14	H-3, H-7, H-10
B-9		147.1 (s)	H-7, H-13	
B-10	6.78 (dd, J = 2.2, 2.2)	116.6 (d)	H-12, H-14	H-3, H-8
B-11		160.2 (s)	H-10, H-12, H-13	
B-12	6.27 (ddd, J = 8.0, 2.2, 2.2)	110.9 (d)	H-10, H-13, H-14	H-13, H-13′
B-13	7.14 (dd, J = 8.0, 8.0)	130.0 (d)		H-12, H-14
B-14	7.17 (ddd, J = 8.0, 2.2, 2.2)	119.6 (d)	H-10, H-12	H-7, H-13
C-1′		147.6 (s)	1′-OH, H-3′, H-5′	
C-2′		149.6 (s)	1′-OH, H-3′, H-6′	
C-3′	6.43 (d, J = 2.2)	109.9 (d)	H-5′, H-7′	H-6, H-8′
C-4′		129.8 (s)	H-3′, H-6′, H-8′	
C-5′	6.82 (dd, J = 8.2, 2.2)	124.2 (d)	H-3′, H-7′	H-6′, H-7′
C-6′	6.86 (d, J = 8.2)	116.8 (d)		1′-OH, H-5′
1′-OH	8.30 (br. s)			H-6′
7′	6.97 (d, J = 16.5)	128.8 (d)	H-3′, H-5′, H-8′	H-5′, H-10′
8′	6.48 (d, J = 16.5)	119.7 (d)	H-7′, H-10′	H-3′
D-9′		132.1 (s)	H-7′, H-10′, H-13′	
D-10′	7.26 (d, J = 2.7)	111.7 (d)	H-8′, 11′-OH, H-12′	H-7′, 11′-OH
D-11′		155.9 (s)	H-10′, 11′-OH, H-12′, H-13′	
D-12′	6.80 (dd, J = 8.5, 2.7)	116.5 (d)	H-10′, 11′-OH, H-13′	11′-OH, H-13′
D-13′	6.91 (d, J = 8.5)	124.9 (d)	H-12′	H-12, H-12′
D-14′		144.6 (s)	H-10′, H-12′, H-13′	
11′-OH	8.48 (br. s)			H-10′, H-12′

[a] Chemical shifts from TMS (multiplicity, J in Hz) in acetone-d_6.

2.4. Ptychantol C (3)

Compound **3** was obtained as colorless needles; m.p. 155–158°C, whose molecular formula, $C_{28}H_{22}O_5$ was established by HRMS spectrum ([M]$^+$ m/z 438.1494). Compound **3** was optically active compound by a specific rotation {[α]$_D$ −14.8° (c 0.66, MeOH)} and Cotton effect [289 nm ($\Delta\varepsilon$ +10.6), 270 nm ($\Delta\varepsilon$ −3.0), 253 nm ($\Delta\varepsilon$ +21.2), 235 nm ($\Delta\varepsilon$ −30.8)] in CD spectrum. The ^{1}H and ^{13}C NMR spectra (Table 5) of **3** were similar to those (Table 1) of ptychantol A (**1**) except for the presence of a benzyl methylene [δ_H 3.13 (1H, dd, J = 12.9, 8.8, 7-H), 3.40 (1H, dd, J = 12.9, 4.7, 7-H); δ_C 35.9 (t)] and a secondary alcohol [δ_H 5.08 (1H, dd, J = 8.8, 4.7 Hz, 8-H); δ_C 75.4 (d)] signals. In the HMBC spectrum (Table 5) of **3**, the cross-peaks

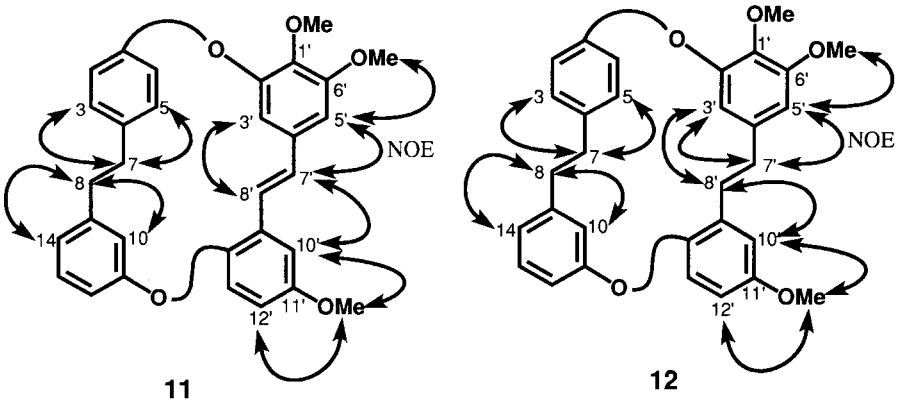


Fig. 3. 2D-NOESY experiments of **11** and **12**.

Table 4
600 MHz ^{1}H NMR assignments and NOESY correlations of compound **9** and **10**[a]

Position No.	Compound **9**		Compound **10**	
	^{1}H NMR	NOESY	^{1}H NMR	NOESY
A-2, 6	6.93 (d, J = 8.5)	H-3, H-5, H-3′	6.92 (br. s)	H-3′
A-3, 5	7.06 (d, J = 8.5)	H-2, H-6, H-7, H-10	6.92 (br. s)	H-7, H-10
7	3.07 (m)	H-3, H-5	2.97 (m)	H-3, H-5
8	3.07 (m)	H-10, H-14	2.97 (m)	H-10, H-14
B-10	6.63 (dd, J = 2.4, 1.6)	H-3, H-3	6.33 (dd, J = 2.5, 1.9)	H-3, H-8
B-12	6.13 (ddd, J = 8.2, 2.4, 0.8)	H-13, H-13′	6.26 (ddd, J = 8.0, 2.5, 0.8)	H-13, H-13′
B-13	7.05 (dd, J = 8.2, 8.2)	H-12, H-14	7.09 (dd, J = 8.0, 8.0)	H-12, H-14
B-14	6.93 (ddd, J = 8.2, 1.6, 0.8)	H-8, H-13	6.91 (ddd, J = 8.0, 1.9, 0.8)	H-8, H-13
C-3′	6.49 (d, J = 1.9)	H-6, H-8′	6.21 (d, J = 1.9)	H-6, H-7′, H-8′
C-5′	6.82 (dd, J = 8.2, 1.9)	H-6′, H-7′	6.72 (dd, J = 8.2, 1.9)	H-6, H-7′, H-8′
C-6′	6.85 (d, J = 8.2)	1′-OMe, H-5′	6.83 (d, J = 8.2)	1′-OMe, H-5′
1′-OMe	3.95 (s)	H-6′	3.93 (s)	H-6′
7′	6.87 (d, J = 16.5)	H-5′, H-10′	2.61 (m)	H-3′, H-5′
8′	6.54(d, J = 16.5)	H-3′	2.49 (m)	H-3′, H-10′
D-10′	7.21 (d, J = 3.0)	H-7′, 11′-OMe	6.80 (d, J = 3.0)	H-8′, 11′-OMe
D-12′	6.81 (dd, J = 8.8, 3.0)	11′-OMe, H-13′	6.72 (dd, J = 8.8, 3.0)	11′-OMe, H-13′
D-13′	6.98 (d, J = 8.8)	H-12, H-12′	6.87 (d, J = 8.8)	H-12, H-12′
11′-OMe	3.85 (s)	H-10′, H-12′	3.80 (s)	H-10′, H-12′

[a] Chemical shifts from TMS (multiplicity, J in Hz) in $CDCl_3$.

due to long range ^{1}H–^{13}C coupling were observed for H-7/C-8, H-10/C-8, H-14/C-8, H-3/C-7 and H-5/C-7, respectively. Compound **3** showed NOEs between (i) H-7 and H-3, 5, (ii) H-8 and H-10, (iii) H-8 and H-14, (iv) 1′-OH and H-6′, (v) H-3′ and H-8′, (vi) H-5′ and H-7′, (vii) H-7′ and H-10′, (viii) 11′-OH and H-10′ and (ix) 11′-OH and H-12′ in the NOESY spectrum (Table 5). Thus, the structure of ptychantol C was determined as a C-8 hydroxylated derivative of ptychantol A (**1**) and depicted as **3**. The absolute structure of ptychantol C remains to be identified.

2.5. Bis(bibenzyls) possessing a stilbene moiety

The cyclic bis(bibenzyls) are one of the most important chemical markers of the Hepaticae (Asakawa,

Table 5
600 MHz ^{1}H NMR assignments and NOESY correlations of compound **11** and **12**[a]

Position No.	Compound **11**		Compound **12**	
	^{1}H NMR	NOESY	^{1}H NMR	NOESY
A-2, 6	6.91 (d, J = 8.5)	H-3, H-5, H-3′	6.90 (br. s)	H-3′
A-3, 5	7.06 (d, J = 8.5)	H-2, H-6, H-7, H-10	6.90 (br. s)	H-7, H-10
7	3.06 (m)	H-3, H-5	2.97 (m)	H-3, H-5
8	3.06 (m)	H-10, H-14	2.97 (m)	H-10, H-14
B-10	6.61 (dd, J = 2.4, 1.6)	H-3, H-8	6.31 (dd, J = 2.4, 1.6)	H-3, H-8
B-12	6.12 (ddd, J = 8.2, 2.4, 0.8)	H-13, H-13′	6.26 (ddd, J = 8.0, 2.4, 0.8)	H-13, H-13′
B-13	7.05 (dd, J = 8.2, 8.2)	H-12, H-14	7.09 (dd, J = 8.0, 8.0)	H-12, H-14
B-14	6.92 (ddd, J = 8.2, 1.6, 0.8)	H-8, H-13	6.91 (ddd, J = 8.0, 1.6, 0.8)	H-8, H-13
C-3′	6.15 (d, J = 1.9)	H-6, H-8′	5.86 (d, J = 1.9)	H-6, H-7′, H-8′
C-5′	6.48 (dd, J = 8.2, 1.9)	6′-OMe, H-7′	6.44 (d, J = 1.9)	6-OMe, H-7′
1′-OMe	3.97 (s)		3.95 (s)	
6′-OMe	3.90 (s)	H-5′	3.93 (s)	H-5′
7′	6.84 (d, J = 16.2)	H-5′, H-10′	2.61 (m)	H-3′, H-5′
8′	6.54(d, J = 16.2)	H-3′	2.51 (m)	H-3′, H-10′
D-10′	7.21 (d, J = 3.0)	H-7′, 11′-OMe	6.80 (d, J = 3.3)	H-8′, 11′-OMe
D-12′	6.83 (dd, J = 8.8, 3.0)	11′-OMe, H-13′	6.73 (dd, J = 8.8, 3.3)	11′-OMe, H-13′
D-13′	6.99 (d, J = 8.8)	H-12, H-12′	6.87 (d, J = 8.8)	H-12, H-12′
11′-OMe	3.85 (s)	H-10′, H-12′	3.81 (s)	H-10′, H-12′

[a] Chemical shifts from TMS (multiplicity, J in Hz) in $CDCl_3$.

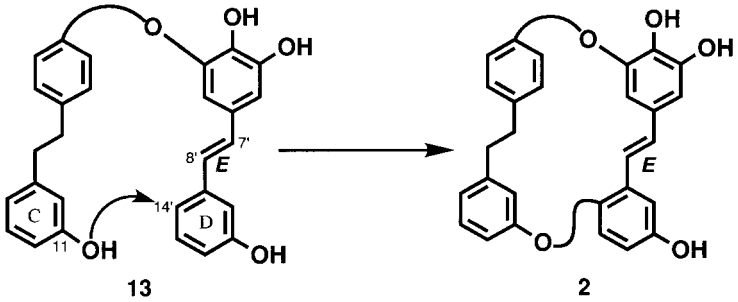
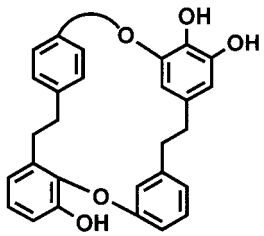


Fig. 4. Possible biogenetic pathway of ptychantol B (**2**).

1995). Most of them possess two ether linkages between two bibenzyl groups. The Hepaticae also produce several bis(bibenzyls) with one ether and one bipheny linkage or two biphenyl bonds. Some Jungermanniales species of the Hepaticae biosynthesize bis(bibenzyls) with a *cis*-stilbene. Novel bis(bibenzyls) possessing a *cis*-stilbene moiety, isoplagiochins A–C were first isolated from the liverwort *Plagiochila fruticosa* (Hashimoto et al., 1994; Hashimoto, Kanayama, Kan, Tori & Asakawa, 1996). Later, isoplagiochin C from the European *Plagiochila* species (Anton, Kraut, Mues & Morales, 1997) and chlorinated isoplagiochin C analogues, bazzanines from *Bazzania trilobata* (Martini, Zapp & Becker, 1998) were isolated, respectively.

Ptychantols A–C (**1**–**3**) from the liverwort *P. striatus* and 7′,8′-dehydroperrottein F (**13**) (Asakawa, 1995) from the liverwort *L. cruciata* possess a C7′– C8′ *trans*-stibene structure. Ptychantols A–C are the first macrocyclic bis(bibenzyls) possessing a *trans*-stilbene moiety.

A biosynthetic study of the cyclic bis(bibenzyls), marchantin A (**14**) isolated from the liverwort *Marchantia polymorpha*, has been carried out by Friederich, Maier, Deus-Neumann, Asakawa and Zenk (1999). A phenylpropane/polymalonate pathway has been proposed for the biosynthesis of marchantin A (**14**) by feeding experiments using radioactive and ^{13}C labelled precursors. Ptychantol B (**2**) might be biosynthesized from **13** by phenolic oxidation as shown in Fig. 4.



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3. Experimental

3.1. General

IR spectra were measured on a Jasco FT-IR 500 spectrophotometer. ^{1}H and ^{13}C NMR were recorded on a Varian Unity 600 (^{1}H; 600 MHz, ^{13}C; 150 MHz) or a Varian Unity 200 (^{1}H; 200 MHz, ^{13}C; 50 MHz) spectrometer. The solvent used for NMR spectra was $CDCl_3$ unless otherwise stated. MS spectra were measured on a JEOL JMS HX-100 or a JEOL AX-500 spectrometer. The specific rotation and the CD spectra were taken on a JASCO DIP-140 polarimeter and a JASCO J-500 spectrometer, respectively. Silica gel 60 for column chromatography was purchased from Merk.

3.2. Plant material

P. striatus was collected in Tokushima, Japan, in April, 1998 and identified by Y. A. A voucher specimen was deposited at the Institute of Pharmacognosy, Tokushima Bunri University.

3.3. Extraction and isolation

Air-dried material (0.92 kg) of *P. striatus* was extracted with Et_2O (10 l) for 1 week at RT. The Et_2O extract (44.45 g) was chromatographed on silica gel (500 g) with a gradient solvent system of *n*-hexane–EtOAc to afford kelosene (**4**) (König & Wright, 1997; Nabeta et al., 1998) (36 mg), striatene (**5**) (Takeda & Katoh, 1983) (2.17 g), ptychantins A (**6**) (Asakawa, 1990) (4.31 g), B (**7**) (Asakawa, 1990) (1.07 g) and C (**8**) (Asakawa, 1990) (0.65 g). *P. striatus* was further extracted with MeOH (10 l) for 2 weeks at RT. The MeOH extract (27.4 g) was subjected repeatedly to column chromatography using silica gel with a gradient solvent system of $CHCl_3$–MeOH increasing the amount of 2% portions MeOH stepwise, Sephadex LH-20 ($CHCl_3$: MeOH = 1:1) and HPLC (diol, 3% MeOH–$CHCl_3$) to afford ptychantols A (**1**) (365 mg), B (**2**) (194 mg) and C (**3**) (18 mg).

3.3.1. Ptychantol A (*1*)

Colorless prisms; m.p. 260–262°C, $[\alpha]_D^{22}$ ±0° (*c* 0.29, MeOH); HR-MS: *m*/*z* 422.1509, $C_{28}H_{22}O_4$ requires 422.1518; EI-MS: *m*/*z* 422 (M^+, 100%), 223, 211, 181,

107; FT-IR (KBr) cm^{-1}: 3409 (OH), 1589, 1507, 1202; UV (EtOH) λ_{max} nm (log ε): 342 (4.35), 204 (4.72).

3.3.2. Ptychantol B (2)

Pale brown powder; m.p. 235–237°C, $[\alpha]_D^{22}$ ±0° (*c* 0.35, MeOH); HR-MS: *m/z* 438.1494, $C_{28}H_{22}O_5$ requires 438.1468; EI-MS: *m/z* 438 (M^+, 100%), 219, 197, 107; FT-IR (KBr) cm^{-1}: 3354 (OH), 1613, 1505, 1206; UV (EtOH) λ_{max} nm (log ε): 341 (4.32), 205 (4.57).

3.3.3. Ptychantol C (3)

Colorless needles; m.p. 155–158°C, $[\alpha]_D^{22}$ −14.8° (*c* 0.66, MeOH); HR-MS: *m/z* 438.1494, $C_{28}H_{22}O_5$ requires 438.1468; EI-MS: *m/z* 438 (M^+, 100%), 420 (M^+–H_2O), 210, 197, 107; FT-IR (KBr) cm^{-1}: 3360 (OH), 1589, 1512, 1202; UV (EtOH) λ_{max} nm (log ε): 342 (4.02), 203 (4.70); CD (MeOH) λ_{max} nm ($\Delta\varepsilon$): 289 (+10.6), 270 (−3.0), 253 (+21.2), 235 (−30.8).

3.3.4. The crystal data for ptychantol A (1)

Triclinic, space group $P2_1/c$, a = 14.619 (0) Å, b = 8.942 (0) Å, c = 21.639 (0) Å, V = 2730 (0) $Å^3$, β = 105.175 (0) Å, Z = 4, D_x = 1.530 Mg m^{-3}, D_m = 1.500 Mg m^{-3}, μ (Cu Kα) = 0.753 mm^{-1}, Final R and R_w were 0.065 and 0.084 for 2632 reflections with $I > 3\sigma(I)$. The structure was solved by direct method (Monte-Carlo Multan) and refined by full-matrix least-squares techniques. Diffraction data were obtained using a Mac Science MXC18 diffractiometer at rt. All diagrams and calculations were performed using CRYSTAN (Mac Science, Japan).

3.3.5. Methylation of ptychantol A (1)

A solution of **1** (68 mg) in dry $(CH_3)_2CO$ (20 ml) was treated with K_2CO_3 (5.0 g) and MeI (3.0 ml). The reaction mixture was refluxed for 2 h and filtrated. The filtrate was evapd in vacuo to give a colorless oil (159 mg). The crude product was recrystallized from Et_2O to afford ptychantol A dimethyl ether (**9**) (54 mg; 74%) as colorless needles, m.p. 231–233°C; HR-MS: *m/z* 450.1826, $C_{30}H_{26}O_4$ requires 450.1831; EI-MS: *m/z* 450 (M^+, 100%), 435, 225, 211, 195, 165; FT-IR (KBr) cm^{-1}: 3003, 1611, 1584, 1512, 1263, 1209; UV (EtOH) λ_{max} nm (log ε); 338 (3.84), 203 (4.36); ^{13}C NMR ($CDCl_3$): δ 35.6 (t), 36.7 (t), 55.6 (q, –OMe), 56.0 (q, –OMe), 109.4 (d), 109.7 (d), 111.4 (d), 114.2 (d), 118.1 (d), 119.9 (d), 121.1 (d), 122.0 (d), 122.7 (d), 124.4 (d), 128.0 (d), 129.1 (d), 129.8 (d), 130.4 (d), 131.3 (s), 137.2 (s), 142.5 (s), 144.8 (s), 148.9 (s), 150.1 (s), 152.9 (s), 157.1 (s), 159.3 (s).

3.3.6. Catalytic reduction of ptychantol A dimethyl ether (9)

Compound **9** (22 mg) was hydrogenated over 10% Pd–C (70 mg) in MeOH (10 ml) and EtOAc (15 ml) at RT for 1 h. After removal of the catalyst, the filtrate was concd in vacuo. The residue (69.6 mg) was subjected to CC on silica gel with *n*-hexane–EtOAc gradient to afford dihydroptychantol A dimethyl ether (**10**) (12 mg; 55%) as colorless needles, m.p. 204–205°C; HR-MS: *m/z* 452.1960, $C_{30}H_{28}O_4$ requires 452.1987; EI-MS: *m/z* 452 (M^+, 100%), 345, 315, 239, 227, 211; FT-IR (KBr) cm^{-1}: 3032, 1611, 1584, 1505, 1231, 1209; UV (EtOH) λ_{max} nm (log ε); 280 (3.62), 214 (4.47); ^{13}C NMR ($CDCl_3$): δ 34.8 (t), 36.9 (t), 37.3 (t), 37.9 (t), 55.6 (q, –OMe), 56.2 (q, –OMe), 110.4 (d), 111.6 (d), 112.4 (d), 115.4 (d), 115.7 (d), 119.1 (d), 120.9 (d), 121.6 (d), 121.8 (d), 121.9 (d), 129.0 (d), 130.4 (d), 134.9 (s), 135.7 (s), 137.1 (s), 142.7 (s), 146.4 (s), 147.2 (s), 149.8 (s), 153.4 (s), 156.3 (s), 158.3 (s).

3.3.7. Methylation of ptychantol B (2)

A solution of **2** (38 mg) in dry $(CH_3)_2CO$ (20 ml) was treated with K_2CO_3 (4.5 g) and MeI (2.0 ml). The reaction mixture was refluxed for 24 h and filtered. The filtrate was evapd in vacuo to give a colorless oil (97 mg) which was subjected to Sephadex LH-20 CC with $CHCl_3$: MeOH = 1:1 to afford ptychantol B trimethyl ether (**11**) (14.6 mg; 35%) as colorless needles, m.p. 207–208°C; HR-MS: *m/z* 480.1906, $C_{31}H_{28}O_5$ requires 480.1936; EI-MS: *m/z* 480 (M^+,100%), 465, 375, 240, 224; FT-IR (KBr) cm^{-1}: 2941, 1582, 1244, 1211; UV (EtOH) λ_{max} nm (log ε); 334 (4.28), 222 (4.49).

3.3.8. Catalytic reduction of ptychantol B trimethyl ether (11)

Compound **11** (22 mg) was hydrogenated over 10% Pd–C (32 mg) in MeOH (5 ml) and AcOEt (10 ml) at RT for 1 h. After removal of the catalyst, the filtrate was concd in vacuo. The residue (69.6 mg) was subjected to CC on silica gel with *n*-hexane–EtOAc gradient to afford dihydroptychantol B trimethyl ether (**12**) (7.8 mg; 72%) as colorless oil, HR-MS: *m/z* 482.2065, $C_{31}H_{30}O_5$ requires 482.2093; EI-MS: *m/z* 482 (M^+, 100%), 467, 375, 257, 243, 225; FT-IR (KBr) cm^{-1}: 3020, 1597, 1246, 1209; UV (EtOH) λ_{max} nm (log ε); 280 (3.34), 206 (4.49); ^{13}C NMR ($CDCl_3$): δ 34.6 (t), 36.9 (t), 37.9 (t), 55.6 (q, –OMe), 56.2 (q, –OMe), 61.2 (q, –OMe), 105.8 (d), 108.9 (d), 110.4 (d), 112.2 (d), 115.6 (d), 119.1 (d), 121.6 (d), 121.7 (d), 122.0 (d), 129.0 (d), 130.3 (d), 135.6 (s), 137.0 (s), 137.8 (s), 142.7 (s), 146.4 (s), 153.2 (s), 153.8 (s), 156.3 (s), 158.3 (s).

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