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Biogenetic reactions on stilbenetetramers from Vitaceaeous plants

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Abstract—The absolute configurations of stilbenetetramers, (+)-hopeaphenol, (−)-isohopeaphenol, (+)-vitisin A and (+)-vitisin D, from Vitaceaeous plants were respectively determined on the basis of chemical evidence. © 2002 Published by Elsevier Science Ltd.

1. Introduction

Many oligostilbenes with various types of the molecular skeleton have been isolated mainly from the following plant families: Vitaceae, Dipterocarpaceae, Leguminosae, Cyperaceae and Gnetaceae.[1] But, oligostilbenes isolated from Vitaceaeous plants are chemically different from those from other families as shown in the cases of ε-viniferin (a resveratrol dimer) and hopeaphenol (a resveratrol tetramer). (+)-ε-Viniferin (**1**) has been isolated from only Vitaceaeous plants, but (−)-ε-viniferin has been isolated from the plants of other families. Furthermore, (+)-hopeaphenol (**2**) has been isolated from only Vitaceous plants,[2] but (−)-hopeaphenol has been isolated from the plants of Dipterocarpaceae, Leguminosae and Cyperaceae, respectively. Therefore, Vitaceaeous plants have a specific biosynthetic pathway distinguished from those of such plants as Dipterocarpaceae, Leguminosae and Cyperaceae. (+)-ε-Viniferin (**1**) seems to be a biogenetically important precursor of many oligostilbenes isolated from Vitaceaeous plants as shown in Fig. 1. Namely, isomerization and/or rearrangement of ε-viniferin (**1**) give (+)-ampelopsin B (**13**), (−)-ampelopsin D (**14**) and (+)-ampelopsin F (**16**). Moreover, oxidative coupling accompanied with isomerization can transforms (+)-ε-viniferin (**1**) to resveratrol tetramers, e.g. (+)-hopeaphenol (**2**),[2] (+)-vitisin A (**3**), (−)-vitisin B (**5**), (+)-vitisin C (**6**),[3] (−)-isohopeaphenol (**8**),[2] and (+)-viniferol A (**9**).[7]

We describe here, according to the biogenetic pathways of the oligostilbenes, the regiospecific and stereospecific transformations of (+)-ε-viniferin (**1**) to (+)-hopeaphenol (**2**) and (−)-isohopeaphenol (**8**) as well as (−)-vitisin B (**5**) and (+)-vitisin C (**6**),[4] **5** to (+)-vitisin A (**3**), and **3** to (+)-vitisin D (**7**) and three novel compounds (**10**–**12**) undiscovered yet from natural sources. In a previous paper, we reported the absolute structures of the stilbenetetramers (**3**–**7**) isolated from Vitaceaeous plants.[3] These absolute structures were determined on the basis of the CD spectra of the degradation products of the corresponding compounds. The transformations mentioned in this report provide us information of the reactivity based on the biogenetic path and further confirmation of the absolute structures of the resveratrol oligomers.

2. Results and discussion

2.1. Oxidation of (+)-ε-viniferin (1)

The reaction of (+)-ε-viniferin (**1**), whose absolute configuration is known,[5] with horseradish peroxidase and hydrogen peroxide in aqueous acetone was already reported.[4,6] The reinvestigation of the reaction under the same conditions led to give (+)-hopeaphenol (**2**) and (−)-isohopeaphenol (**8**) in 9.4 and 1.2% yields, respectively, together with (−)-vitisin B (**5**) and (+)-vitisin C (**6**) in 5.7 and 2.9% yields.[3] These chemical results show the absolute configurations of (+)-hopeaphenol and (−)-isohopeaphenol to be **2** and **8**, respectively. Although the biogenetic pathways in Fig. 2 show the possibilities of formation of (+)-vitisin A (**3**)[3] and (+)-viniferol A (**9**),[7] they (**3**, **9**) could not be found in the reaction products even by HPLC analysis.

2.2. Acid-catalyzed reaction of (−)-vitisin B (5)

As reported previously,[8] (+)-ε-viniferin (**1**) was converted to (+)-ampelopsin B (**13**), having a seven-membered ring, by treatment with hydrochloric acid. So the formation of a seven-membered ring was tried using (−)-vitisin B (**5**), which has the same partial structure as that of **1**. (−)-Vitisin

Keywords: absolute configuration; (+)-hopeaphenol; (−)-isohopeaphenol; (+)-vitisin A; (+)-vitisin D; oligostilbene; resveratrol tetramer; biogenetic reaction.

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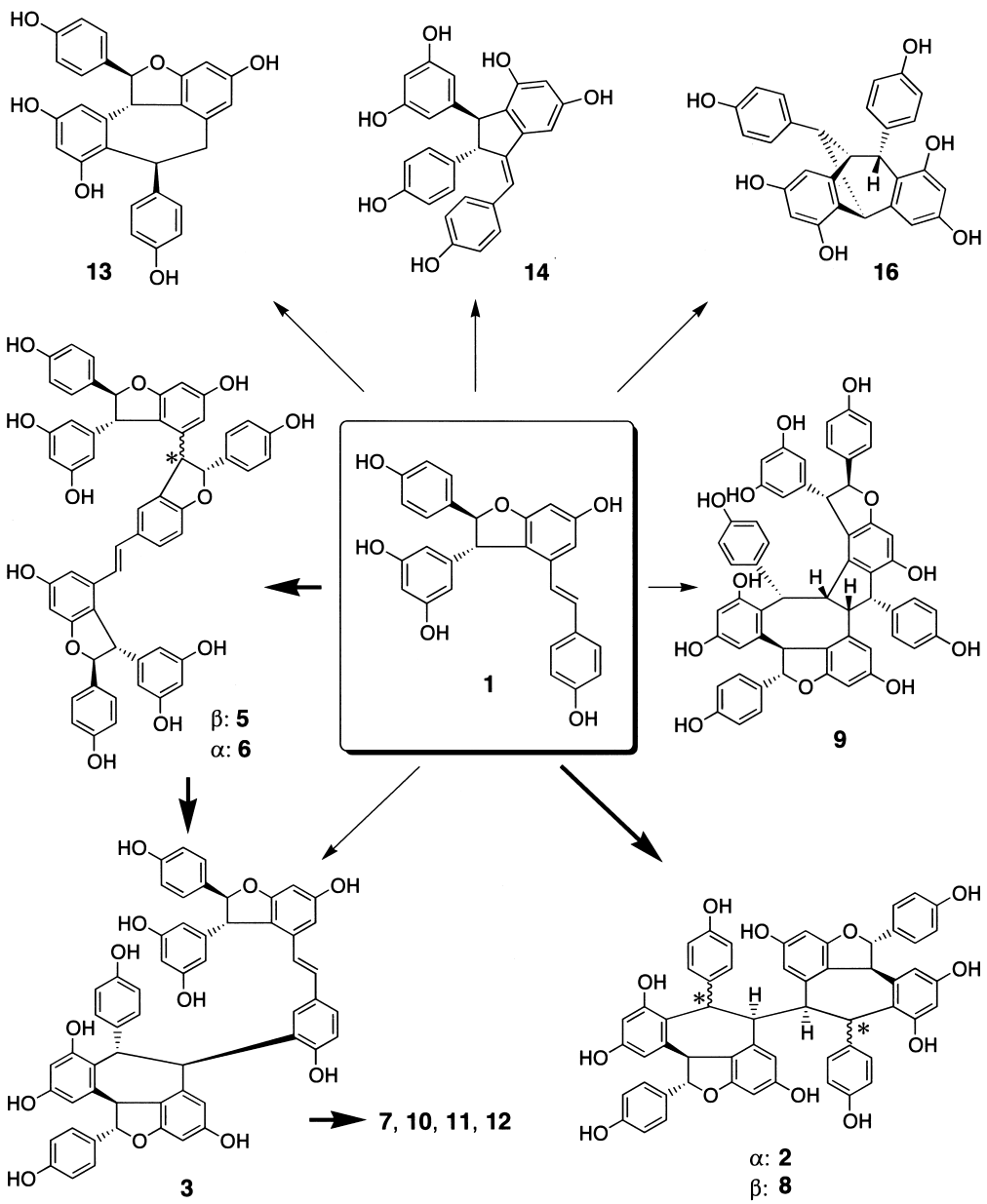


Figure 1. Biogenetic correlations of (+)-ε-viniferin with some oligostilbenes from Vitaceaeous plants. Bold arrows indicate that the transformations are demonstrated in this report.

B (**5**) was treated with hydrochloric acid at room temperature to give (+)-vitisin A (**3**) in a quantitative yield.

2.3. Acid-catalyzed reaction of (+)-vitisin A (3)

(+)-Vitisin A (**3**) was treated with sulfuric acid in methanol under reflux to give (+)-vitisin D (**7**) as a main product in 37.4% yield together with three minor products (**10**–**12**), having a novel molecular skeleton, in 2.2, 3.0 and 2.7% yields, respectively. The structures of compounds **10**–**12** were elucidated by some spectral means including HMBC and NOESY. Although the three compounds **10**–**12** have not been found yet in natural sources, their isolation will be reported in the near future.

2.4. Structure of (+)-compound 10

(+)-Compound **10**, $[\alpha]_D$=+122.5° (*c* 0.32, MeOH), was found to have the molecular formula $C_{56}H_{42}O_{12}$ determined by high-resolution FABMS. The ^1H and ^{13}C NMR spectral data, indicated that (+)-compound **10** consists of two moieties of (+)-ampelopsin B (**13**)[9] and (−)-ampelopsin D (**14**),[10,11] as shown in Tables 1 and 2. In particular, the olefinic signal at $\delta_{H\text{-}7c}$ 6.50 (1H, s) [$\delta_{C\text{-}7c}$ 124.2 (d)] is characteristic of the moiety of **14**.

2.5. Structure of (+)-compound 11

(+)-Compound **11**, $[\alpha]_D$=+74.8° (*c* 0.28, MeOH), was found to have the molecular formula $C_{56}H_{42}O_{12}$ determined by high-resolution FABMS. The ^1H and ^{13}C NMR spectral data indicated that (+)-compound **11** consists of two moieties of (+)-ampelopsin B (**13**) and (−)-isoampelopsin D (**15**),[11,12] as shown in Tables 1 and 2. In particular, the methylenic signals at $\delta_{H\text{-}7c}$ 3.26

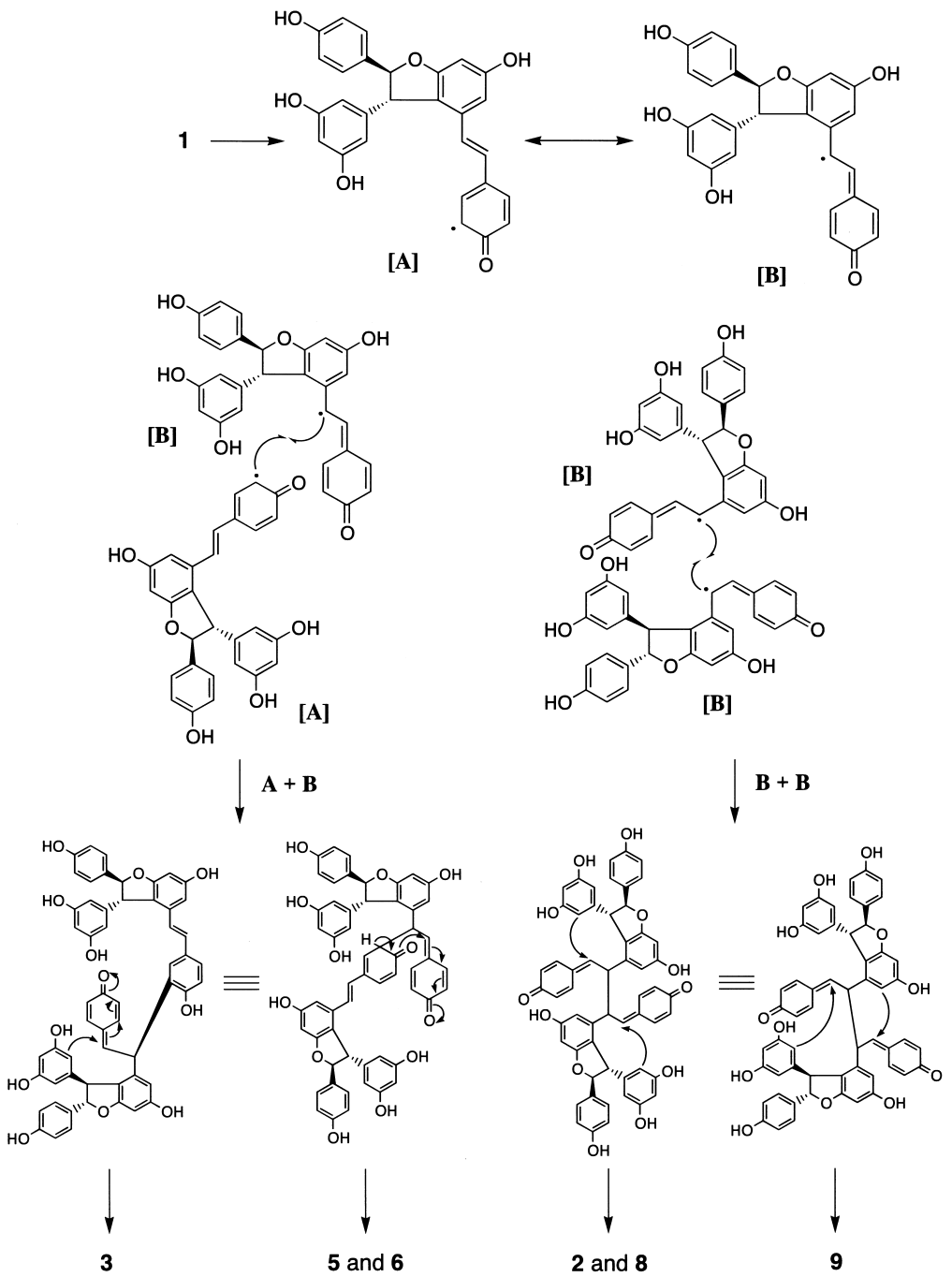


Figure 2. Plausible biogenetic pathways of some stilbenetetramers from (+)-ε-viniferin.

(1H, d, J=15.8 Hz) and 3.59 (1H, d, J=15.8 Hz) [$\delta_{C\text{-}7c}$ 32.1 (t)] are characteristic of the moiety of **15**.

2.6. Structure of (+)-compound 12

(+)-Compound **12**, $[\alpha]_D$=+162.7° (c 0.14, MeOH), was found to have the molecular formula $C_{56}H_{42}O_{12}$ determined by high-resolution FABMS. The ^1H and ^{13}C NMR spectral data indicated that (+)-compound **12** consists of two moieties of (+)-ampelopsin B (**13**) and (+)-ampelopsin F (**16**),[13] as shown in Tables 1 and 2. In particular, four methinic signals at $\delta_{H\text{-}7c}$ 3.68 (1H, brs) [$\delta_{C\text{-}7c}$ 46.2 (d)], $\delta_{H\text{-}8c}$ 3.15 (1H, brs) [$\delta_{C\text{-}8c}$ 59.5 (d)], $\delta_{H\text{-}7d}$ 2.79 (1H, s) [$\delta_{C\text{-}7d}$ 50.6 (d)], and $\delta_{H\text{-}8d}$ 3.97 (1H, s) [$\delta_{C\text{-}8d}$ 49.8 (d)] are characteristic of the moiety of **16**.

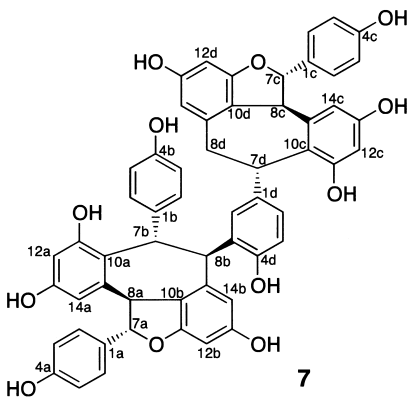
2.7. Absolute configurations

On the basis of the absolute configuration of (+)-ε-viniferin (**1**),[5] and the transformation reaction mechanisms of (+)-ε-viniferin (**1**) and (−)-vitisin B (**5**) shown above, the absolute configurations of (+)-hopeaphenol, (−)-isohopeaphenol, (+)-vitisin A and (+)-vitisin D were clearly determined as **2**, **8**, **3** and **7**, respectively.

Structures of (+)-vitisin D (**7**), compounds **10**–**12**, and (−)-isoampelopsin D (**15**) are given below.

Table 1. ^{1}H NMR data of oligostilbenes **10**–**16**

Position	**10**	**11**	**12**	**13**	**14**	**15**	**16**
2a, 6a	7.06 (2H, d, 8.8)	7.15 (2H, d, 8.8)	7.12 (2H, d, 8.8)	7.00 (2H, d, 8.8)			
3a, 5a	6.68 (2H, d, 8.8)	6.77 (2H, d, 8.8)	6.70 (2H, d, 8.8)	6.68 (2H, d, 8.8)			
7a	5.73 (1H, d, 11.7)	5.88 (1H, d, 11.7)	5.58 (1H, d, 12.1)	5.64 (1H, d, 11.4)			
8a	4.05 (1H, d, 11.7)	4.31 (1H, d, 11.7)	4.00 (1H, d, 12.1)	4.04 (1H, d, 11.4)			
12a	5.92 (1H, d, 2.2)	6.26 (1H, d, 2.2)	5.64 (1H, d, 2.2)	6.28 (1H, d, 2.2)			
14a	6.03 (1H, d, 2.2)	6.33 (1H, d, 2.2)	5.83 (1H, d, 2.2)	6.08 (1H, d, 2.2)			
2b, 6b	6.95 (2H, d, 8.4)	7.09 (2H, d, 8.4)	6.99 (2H, d, 8.4)	6.88 (2H, d, 8.4)			
3b, 5b	6.59 (2H, d, 8.4)	6.69 (2H, d, 8.4)	6.58 (2H, d, 8.4)	6.58 (2H, d, 8.4)			
7b	5.23 (1H, d, 3.7)	5.48 (1H, d, 4.4)	5.27 (1H, d, 4.4)	5.13 (1H, t, 4.0)			
8b	5.36 (1H, d, 3.7)	5.58 (1H, d, 4.4)	5.43 (1H, d, 4.4)	3.52 (1H, dd, 17.7, 4.0) 3.15 (1H, brd, 17.7)			
12b	6.10 (1H, d, 2.2)	6.11 (1H, d, 2.2)	6.03 (1H, d, 2.2)	5.99 (1H, d, 2.2)			
14b	6.03 (1H, d, 2.2)	6.19 (1H, d, 2.2)	6.02 (1H, d, 2.2)	6.25 (1H, d, 2.2)			
2c	5.96 (1H, d, 2.2)	6.19 (1H, d, 2.2)	5.89 (1H, d, 2.2)		7.08 (1H, d, 8.8)	7.10 (1H, d, 8.8)	6.97 (1H, d, 7.5)
3c					6.56 (1H, d, 8.8)	6.72 (1H, d, 8.8)	6.63 (1H, d, 7.5)
5c	6.49 (1H, d, 8.4)	6.68 (1H, d, 8.4)	6.75 (1H, d, 8.4)		6.56 (1H, d, 8.8)	6.72 (1H, d, 8.8)	6.63 (1H, d, 7.5)
6c	6.80 (1H, dd, 8.4, 2.2)	6.81 (1H, dd, 8.4, 2.2)	6.93 (1H, dd, 8.4, 2.2)		7.08 (1H, d, 8.8)	7.10 (1H, d, 8.8)	6.97 (1H, d, 7.5)
7c	6.50 (1H, s)	3.26 (d, 1H, 15.8)	3.68 (1H, brs)		6.96 (1H, d, 2.2)	3.85 (1H, d, 16.1)	4.07 (1H, brs)
8c		3.59 (d, 1H, 15.8)″	3.15 (1H, brs)			3.81 (1H, d, 16.1)	3.23 (1H, brs)
12c	6.09 (1H, d, 2.2)		5.93 (1H, d, 2.2)		6.18 (1H, d, 2.2)		5.94 (1H, d, 2.5)
14c	6.50 (1H, d, 2.2)		6.17 (1H, d, 2.2)		6.69 (1H, d, 2.2)		6.39 (1H, d, 2.5)
1d		6.17 (1H, d, 2.2)				6.17 (1H, d, 2.2)	
2d, 6d	6.84 (2H, d, 8.8)		6.68 (2H, d, 8.8)		7.02 (2H, d, 8.8)		6.66 (2H, d, 7.5)
3d, 5d	6.63 (2H, d, 8.8)	7.13 (2H, d, 8.8)	6.53 (2H, d, 8.8)		6.67 (2H, d, 8.8)	7.06 (2H, d, 8.8)	6.44 (2H, d, 7.5)
4d		6.66 (2H, d, 8.8)				6.65 (2H, d, 8.8)	
7d	3.93 (1H, brs)		2.79 (1H, s)		4.17 (1H, brs)		3.52 (1H, brs)
8d	3.94 (1H, brs)		3.97 (1H, s)		4.05 (1H, brs)		4.01 (1H, brs)
9d		4.88 (1H, d, 1.8)				4.79 (1H, d, 1.8)	
10d	6.03 (1H, d, 2.2)				6.06 (1H, d, 2.2)		
11d		6.16 (1H, d, 2.2)				6.06 (1H, d, 2.2)	
12d	6.07 (1H, t, 2.2)		5.83 (1H, d, 2.2)		6.04 (1H, t, 2.2)		6.03 (1H, d, 2.5)
13d		6.04 (1H, t, 2.2)				5.98 (1H, d, 2.2)	
14d	6.03 (1H, d, 2.2)		6.35 (1H, d, 2.2)		6.06 (1H, d, 2.2)		6.32 (1H, d, 2.5)



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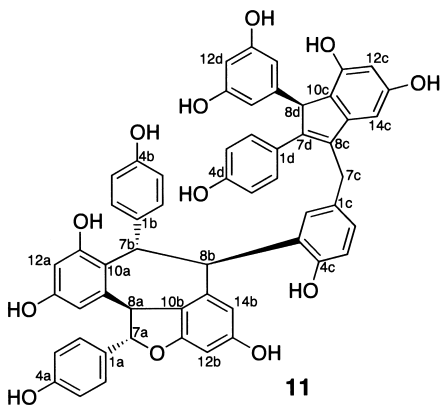

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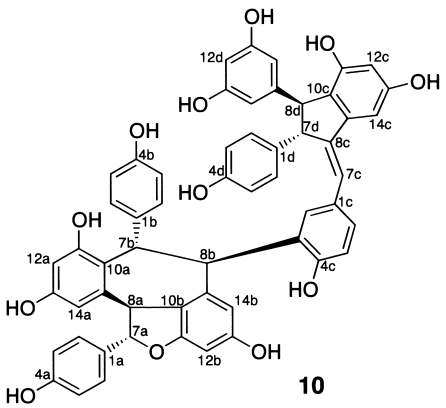

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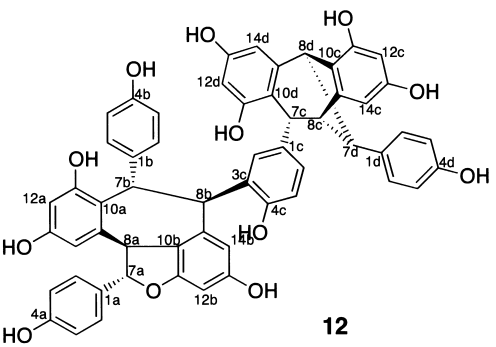

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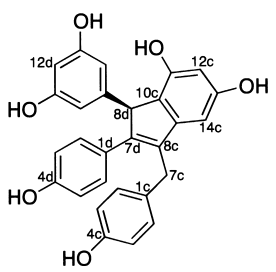
Table 2. ^{13}C NMR data of oligostilbenes **10**–**16**

Position	10	11	12	13	14	15	16
1a	131.3 (s)	130.9 (s)	131.1 (s)	131.1 (s)			
2a, 6a	130.4 (d)	130.6 (d)	130.7 (d)	130.2 (d)			
3a, 5a	116.4 (d)	116.0 (d)	116.1 (d)	116.2 (d)			
4a	158.8 (s)	158.8 (s)	158.7 (s)	157.2 (s)			
7a	88.7 (d)	88.5 (d)	89.1 (d)	89.0 (d)			
8a	49.8 (d)	49.6 (d)	49.8 (d)	49.5 (d)			
9a	141.4 (s)	142.2 (s)	142.8 (s)	142.9 (s)			
10a	121.0 (s)	120.9 (s)	121.0 (s)	123.6 (s)			
11a	158.4 (s)	158.5 (s)	157.6 (s)	158.82 (s)			
12a	100.8 (d)	101.54 (d)	101.66 (d)	101.5 (d)			
13a	156.1 (s)	156.1 (s)	156.3 (s)	157.0 (s)			
14a	104.6 (d)	105.0 (d)	106.3 (d)	105.2 (d)			
1b	136.3 (s)	132.9 (s)	136.2 (s)	135.5 (s)			
2b, 6b	129.1 (d)	128.9 (d)	129.4 (d)	128.9 (d)			
3b, 5b	115.5 (d)	115.4 (d)	115.4 (d)	115.7 (d)			
4b	155.9 (s)	156.0 (s)	155.7 (s)	156.0 (s)			
7b	41.1 (d)	40.9 (d)	41.3 (d)	36.3 (d)			
8b	42.0 (d)	41.6 (d)	42.0 (d)	34.0 (t)			
9b	142.4 (s)	141.4 (s)	141.7 (s)	138.7 (s)			
10b	121.6 (s)	120.2 (d)	120.5 (s)	119.6 (d)			
11b	160.4 (s)	160.3 (s)	160.3 (s)	160.5 (s)			
12b	96.2 (d)	96.1 (d)	95.9 (d)	95.6 (d)			
13b	156.2 (s)	158.1 (s)	157.6 (s)	158.79 (s)			
14b	110.4 (d)	110.1 (d)	110.3 (d)	109.2 (d)			
1c	129.3 (s)	129.9 (s)	135.7 (s)		130.2 (s)	132.1 (s)	138.7 (s)
2c	133.6 (d)	132.5 (d)	133.7 (d)		131.2 (d)	132.2 (d)	130.3 (d)
3c	133.0 (s)	135.2 (s)	132.1 (s)		116.0 (s)	116.3 (d)	116.0 (s)
4c	154.9 (s)	153.6 (s)	153.0 (s)		157.4 (s)	156.5 (s)	156.4 (s)
5c	114.7 (d)	115.0 (d)	115.4 (d)		116.0 (s)	116.3 (d)	116.0 (s)
6c	127.4 (d)	125.8 (d)	126.6 (d)		131.2 (d)	132.2 (d)	130.3 (d)
7c	124.2 (d)	32.1 (t)	46.2 (d)		122.9 (d)	32.1 (t)	47.5 (d)
8c	141.8 (s)	149.5 (s)	59.5 (d)		143.7 (s)	149.9 (s)	58.5 (d)
9c	148.2 (s)	135.9 (s)	147.5 (s)		147.9 (s)	136.6 (s)	147.7 (s)
10c	124.1 (s)	125.2 (s)	129.8 (s)		124.7 (s)	125.4 (s)	128.2 (s)
11c	158.7 (s)	157.9 (s)	152.7 (s)		156.3 (s)	154.0 (s)	153.4 (s)
12c	103.3 (d)	100.8 (d)	101.72 (d)		103.8 (d)	101.1 (d)	102.3 (d)
13c	159.5 (s)	153.4 (s)	158.0 (s)		159.8 (s)	158.9 (s)	158.8 (s)
14c	98.3 (d)	101.0 (d)	104.5 (d)		98.3 (d)	100.8 (d)	104.6 (d)
1d	137.9 (s)	128.0 (s)	136.8 (s)		138.0 (s)	128.9 (s)	135.7 (s)
2d, 6d	129.0 (d)	130.1 (d)	129.7 (d)		129.1 (d)	131.1 (d)	129.6 (d)
3d, 5d	116.1 (d)	115.8 (d)	115.4 (d)		116.5 (d)	115.8 (d)	115.9 (d)
4d	156.4 (s)	157.4 (s)	155.7 (s)		156.7 (s)	157.5 (s)	156.4 (s)
7d	59.4 (d)	149.5 (s)	50.6 (d)		60.0 (d)	150.4 (s)	50.8 (d)
8d	59.3 (d)	55.7 (d)	49.8 (d)		59.2 (d)	56.8 (d)	49.1 (d)
9d	149.9 (s)	143.6 (s)	147.1 (s)		149.9 (s)	144.0 (s)	147.9 (s)
10d	106.9 (d)	107.7 (d)	113.4 (s)		106.7 (d)	108.2 (d)	113.8 (s)
11d	159.0 (s)	158.9 (s)	158.2 (s)		159.2 (s)	158.8 (s)	158.1 (s)
12d	101.3 (d)	101.53 (d)	101.66 (d)		101.3 (d)	101.5 (d)	102.3 (d)
13d	159.0 (s)	158.9 (s)	156.5 (s)		159.2 (s)	158.8 (s)	157.3 (s)
14d	106.9 (d)	107.7 (d)	106.4 (d)		106.7 (d)	108.2 (d)	106.1 (d)



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3. Experimental

3.1. General

UV and IR spectra were recorded on JASCO Ubest V-560 (cell length 10 mm) and FT/IR-410 spectrometers, respectively. Optical rotations were measured with a JASCO P-1020 polarimeter (cell length 100 mm). ^1H and ^{13}C NMR spectra were recorded on JEOL ALPHA-600 (^1H: 600 MHz and ^{13}C: 150 MHz). Chemical shifts for ^1H and ^{13}C NMR are given in parts per million (δ) relative to the solvent signal (methanol-d_4: δ_H 3.30 and δ_C 49.0,) as internal standards, respectively. LR and HR FAB-MS were obtained with JEOL JMS HX-110 using *m*-nitrobenzyl alcohol as matrix. Analytical TLC was performed on silica gel 60 F254 (Merck). Column chromatography was carried out on silica gel BW-820MH (Fuji Silysia Chemicals, Co. Ltd.).

3.2. Material

(+)-ε-Viniferin (**1**) was provided by Professor Oshima (Graduate School of Pharmaceutical Sciences, Tohoku University), which was originated in *Vitis coignetiae*.

Compound **1**: $[\alpha]_D^{26}$=+31.0° (*c* 3.1, MeOH), FABMS *m/z*: 455 (MH^+; $C_{28}H_{23}O_6$), and other spectral data were identical with those reported.[4]

3.2.1. Reaction of (+)-ε-viniferin (1) with peroxidase and hydrogen peroxide. To a solution of (+)-ε-viniferin (**1**) (72 mg) in 50% aqueous acetone (4.2 ml), a suspension of horseradish peroxidase (0.1 mg) (Wako Pure Chemical Industries Ltd., Osaka, Japan) in 50% aqueous acetone (3.0 ml) was added at 25°C, and after 5 min stirring, 30% hydrogen peroxide (18 μl) was added. After stirring for 15 min, the reaction mixture was diluted with ethyl acetate (15 ml), washed with brine, and then dried over anhydrous magnesium sulfate. After evaporation of the solvent, the residue (73 mg) was subjected to column chromatography over silica gel (7 g, ϕ1.0×40 cm) using a mixture of chloroform–methanol (9:1) to give six fractions (F-1: 1.5 mg, F-2: 4.2 mg, F-3: 9.4 mg, F-4: 11 mg, F-5: 9.6 mg and F-6: 35 mg). Fraction 3 gave (−)-vitisin B (**5**) (4.1 mg, 5.7%) and (+)-vitisin C (**6**) (2.1 mg, 2.9%) by preparative recycled HPLC using a column (Develosil C8-5, ϕ20×250 mm, Nomura Chemical Co. Ltd.) and a mixed solvent of methanol–water (55:45) at a flow rate (3.0 ml/min). Fraction 6 was subjected to preparative recycle HPLC using a column (YMC-Pack C-8, ϕ20×250 mm, YMC Co. Ltd.) and a mixed solvent of methanol–water (6:4), flow rate (3.0 ml/min) give (+)-hopeaphenol (**2**) (6.8 mg) and (−)-isohopeaphenol (**8**) (0.9 mg) in 9.4 and 1.2% yields, respectively. (+)-Hopeaphenol (**2**), (−)-vitisin B (**5**), (+)-vitisin C (**6**) and (−)-isohopeaphenol (**8**) were identified by comparison of the spectral data of each authentic sample.

Compound **2**: $[\alpha]_D^{26}$=+405.6° (*c* 1.6, MeOH), FABMS *m/z*: 907 (MH^+; $C_{56}H_{43}O_{12}$).

Compound **5**: $[\alpha]_D^{26}$=−83.3° (*c* 0.68, MeOH), FABMS *m/z*: 907 (MH^+; $C_{56}H_{43}O_{12}$).

Compound **6**: $[\alpha]_D^{26}$=+233.1° (*c* 0.68, MeOH), FABMS *m/z*: 906 (M^+; $C_{56}H_{42}O_{12}$).

Compound **8**: $[\alpha]_D^{26}$=−116.8° (*c* 0.64, MeOH), FABMS *m/z*: 907 (MH^+; $C_{56}H_{43}O_{12}$).

3.2.2. Reaction of (−)-vitisin B (5) with diluted HCl. A mixture of (−)-vitisin B (**5**) (11 mg) in 10% HCl (1.5 ml) was stirred under nitrogen atmosphere at room temperature for 50 h. The reaction mixture was diluted by ethyl acetate (20 ml), washed with brine and then dried over anhydrous sodium sulfate. The resulted crude product was purified by preparative HPLC [YMC-C8 (ϕ20×250 mm), MeOH–H_2O (6:4), flow rate: 3.0 ml/min] to give (+)-vitisin A (**3**) (11 mg, quant).

3.2.3. Reaction of (+)-vitisin A (3) with H_2SO_4. A mixture of (+)-vitisin A (**3**) (200 mg) and sulfuric acid (14 μl) in methanol (5 ml) was refluxed under nitrogen atmosphere for 14 h. The reaction mixture was diluted by ethyl acetate (10 ml), washed with brine and then dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was subjected to medium-pressure column chromatography on silica gel [Fuji Silysia CQ-3, 15 g (ϕ20×100 mm), $CHCl_3$–MeOH (7:1), flow rate: 2.0 ml/min] to give eight fractions (F-1: 15 mg, F-2: 30 mg, F-3: 50 mg, F-4: 11 mg, F-5: 27 mg, F-6: 7.5 mg, F-7: 6.7 mg, F-8: 27 mg). Fractions 2–4 were purified by preparative HPLC [Develosil C8-5 (ϕ20×250 mm), MeOH–H_2O (6:4), flow rate: 3.0 ml/min] to give (+)-vitisin D (**7**) (75 mg, 37.4%). Fraction 5 was subjected to recycled preparative HPLC [Develosil C8-5 (ϕ20×250 mm), MeOH–H_2O (6:4), flow rate: 3.0 ml/min] to give compounds **10** (5.4 mg, 2.7%), **11** (4.4 mg, 2.2%) and **12** (6.0 mg, 3.0%), respectively.

Compound **10**: $[\alpha]_D^{25}$=+122.5° (*c* 0.32, MeOH), HRFABMS *m/z*: 907.2726 (MH^+; 907.2755 for $C_{56}H_{43}O_{12}$); IR ν_{max} (film) cm^{-1}: 3406, 1608, 1509, 1455. ^1H NMR and ^{13}C NMR in CD_3OD are shown in Tables 1 and 2, respectively.

Compound **11**: $[\alpha]_D^{25}$=+74.8° (*c* 0.28, MeOH), HRFABMS *m/z*: 907.2769 (MH^+; 907.2755 for $C_{56}H_{43}O_{12}$); IR ν_{max} (film) cm^{-1}: 3335, 1607, 1509, 1453. ^1H NMR and ^{13}C NMR in CD_3OD are shown in Tables 1 and 2, respectively.

Compound **12**: $[\alpha]_D^{25}$=+162.7° (*c* 0.14, MeOH), HRFABMS *m/z*: 907.2762 (MH^+; 907.2755 for $C_{56}H_{43}O_{12}$); IR ν_{max} (film) cm^{-1}: 3371, 1609, 1509, 1458. ^1H NMR and ^{13}C NMR in CD_3OD are shown in Tables 1 and 2, respectively.

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