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Chemical determination of the absolute structures of resveratrol dimers, ampelopsins A, B, D and F

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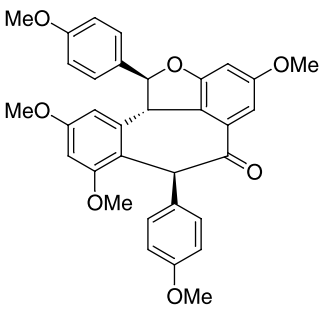
Abstract—The absolute configurations of four stilbenedimers, (+)-ampelopsins A, (+)-ampelopsins B, (−)-ampelopsins D and (+)-ampelopsins F were respectively determined on the basis of chemical evidence.

1. Introduction

In the course of the structural determination of stilbene-oligomers, we reported the absolute structure of a stilbenedimer, (+)-ampelopsin A (**1**),[1] on the basis of spectral evidence.[2] Namely, based on the evidence that the CD spectrum of the methylated ketone (**2**) derived from (+)-ampelopsin A (**1**)[1] showed a positive Cotton effect at 357 nm, the absolute structure of (+)-ampelopsin A was determined to be **1**. The absolute structure of (+)-ampelopsin B was also characterized to be **3**, because of the similarity of the CD spectrum to that of (+)-ampelopsin A (**1**).[1,2] Thereafter, we received some inquiries about the validity of the assignment at the wavelength. So, we undertook to confirm chemically the absolute structures of (+)-ampelopsin A (**1**) and (+)-ampelopsin B (**3**). (+)-ε-Viniferin (**4**), of which the absolute structure is known,[3] is regarded as an important biogenetic precursor of many stilbenedimers from Vitaceaeous plants including (+)-ampelopsin A (**1**) and (+)-ampelopsin B (**3**). In the present paper, we describe the regiospecific and stereospecific transformation of (+)-ε-viniferin (**4**) to (+)-ampelopsin A (**1**), (+)-ampelopsin B (**3**), (−)-ampelopsin D (**5**),[4] and (+)-ampelopsin F (**6**).[5] These chemical results gave the absolute structures of these compounds. Furthermore, the transformation of (+)-ε-viniferin (**4**) to (−)-ampelopsin D (**5**) clearly resolves any doubt about the structure of (−)-ampelopsin D as raised by Adesanya et al.[1,6]



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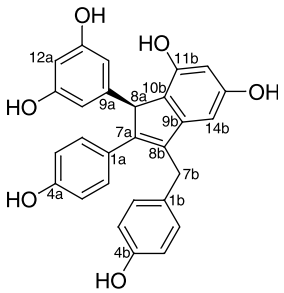

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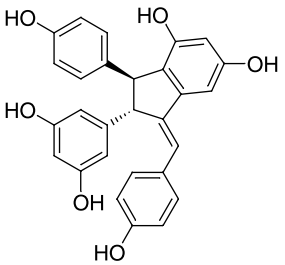

(–)-quadrangularin A (**8**)

2. Results and discussion

2.1. Acid-catalyzed reactions of (+)-ε-viniferin

(+)-ε-Viniferin (**4**) seems to be the biogenetically important precursor of (+)-ampelopsin A (**1**), (+)-ampelopsin B (**3**), (−)-ampelopsin D (**5**) and (+)-ampelopsin F (**6**), as shown in Scheme 1. The difference of the products apparently is due to the difference of the position of protonation at the initial stage of the reaction. In the case of path ***a***, the reaction starts with the protonation of the double bond, followed by cyclization to form a seven-membered ring to give (+)-ampelopsin A (**1**). In the cases of both paths ***b*** and ***c***, an acid protonates the oxygen atom on the dihydrofuran ring,

Keywords: (+)-ampelopsin A; (+)-ampelopsin B; (−)-ampelopsin D; (+)-ampelopsin F; oligostilbene; resveratrol dimer; biogenetic reaction.

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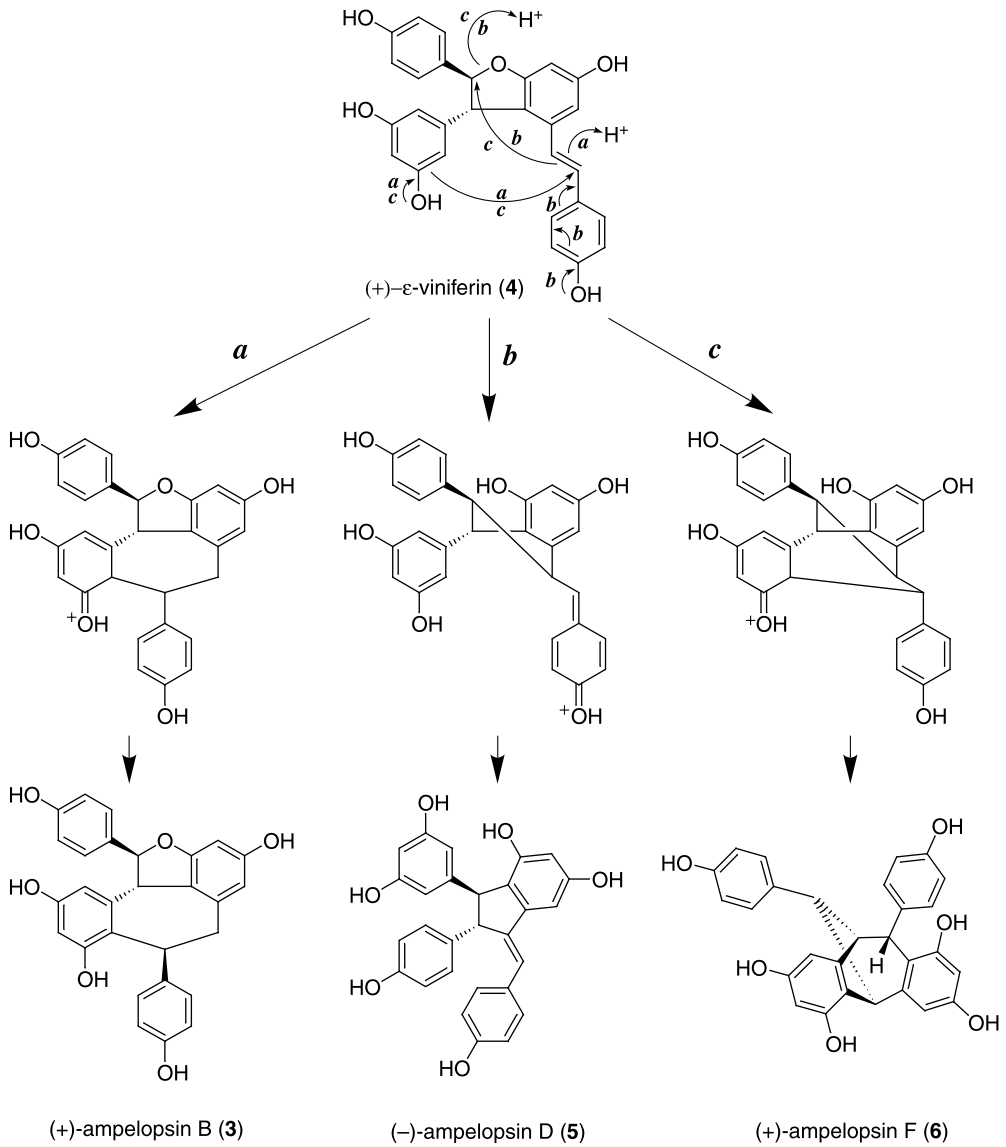


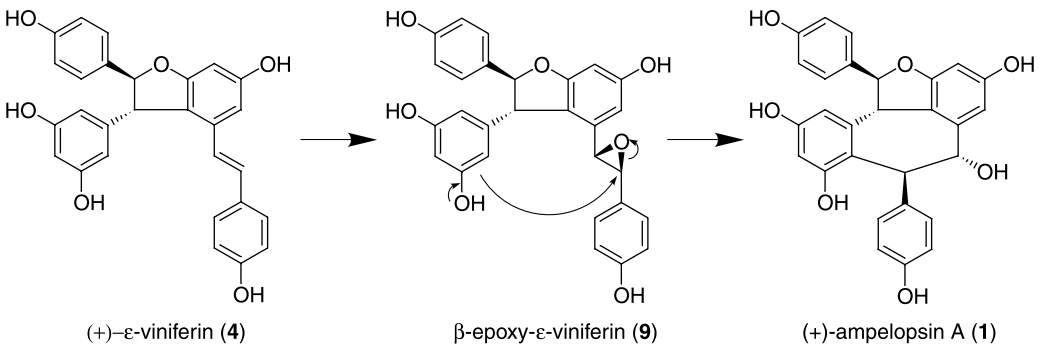
Scheme 1. Plausible biogenetic pathways of (+)-ampelopsin B (**2**), (−)-ampelopsin D (**5**) and (+)-ampelopsin F (**6**) from (+)-ε-viniferin (**4**).

followed by nucleophilic attack of the double bond; then, a five-membered ring intermediate is formed. In the case of path ***b***, the subsequent deprotonation of the intermediate gives (−)-ampelopsin D (**5**). In the case of path ***c***, the second nucleophilic attack of the double bond against the intermediate and the subsequent deprotonation gives (+)-ampelopsin F (**6**). All reactions above should be carried out concertedly.

(+)-ε-Viniferin (**4**) ($[\alpha]_D^{22}$=+49.1°) was treated with hydrochloric acid in H_2O at room temperature for 50 h to give a mixture of (+)-ampelopsin B (**3**) ($[\alpha]_D$=+176.4°)[1] and (+)-ampelopsin F (**6**) ($[\alpha]_D$=+19.0°)[5] in 38 and 8% yields, respectively. Next, treatment of (+)-ε-viniferin (**4**) with trifluoromethanesulfonic acid in nitromethane at room temperature for 10 h gave a single product, (+)-ampelopsin F (**6**) in 38% yield. Trifluoromethanesulfonic acid in methanol transformed (+)-ε-viniferin (**4**) to a mixture of (−)-ampelopsin D (**5**) ($[\alpha]_D$=−5°),[4] its regioisomer (**7**) ($[\alpha]_D$=−227.0°),[7] and (+)-ampelopsin F (**6**) in 14, 8 and 21% yields, respectively, under reflux for 7 days. Treatment of **4** with sulfuric acid in methanol under reflux for 5 days afforded a mixture of four compounds, **3**, **5**, **6** and **7** in 13, 6, 19, and 10% yields, respectively.

2.2. Confirmation of the structure of (−)-ampelopsin D

Oshima et al. reported the isolation and structure of (−)-ampelopsin D (**5**) from the root of *Ampelopsis brevpedunculata* var. *hancei* (Vitaceae) in 1993,[4] and Adesanya et al. reported the isolation and structure of (−)-quadrangularin A (**8**) from the stem of *Cissus quadrangularis* (Vitaceae) in 1999.[6] The latter authors described that the reported structure of ampelopsin D is probably erroneous and should be **8** on the basis of the similarity of the NMR data in their paper.[6] Their claim was based only on a comparison of their NMR data. But our product (**5**) from (+)-ε-viniferin was completely identical with the natural (−)-ampelopsin D by comparison of the IR, ^{1}H NMR, and ^{13}C NMR spectra and the sign of the optical rotation[7] with those reported by Oshima et al.[4] Furthermore, according to the reaction mechanism in

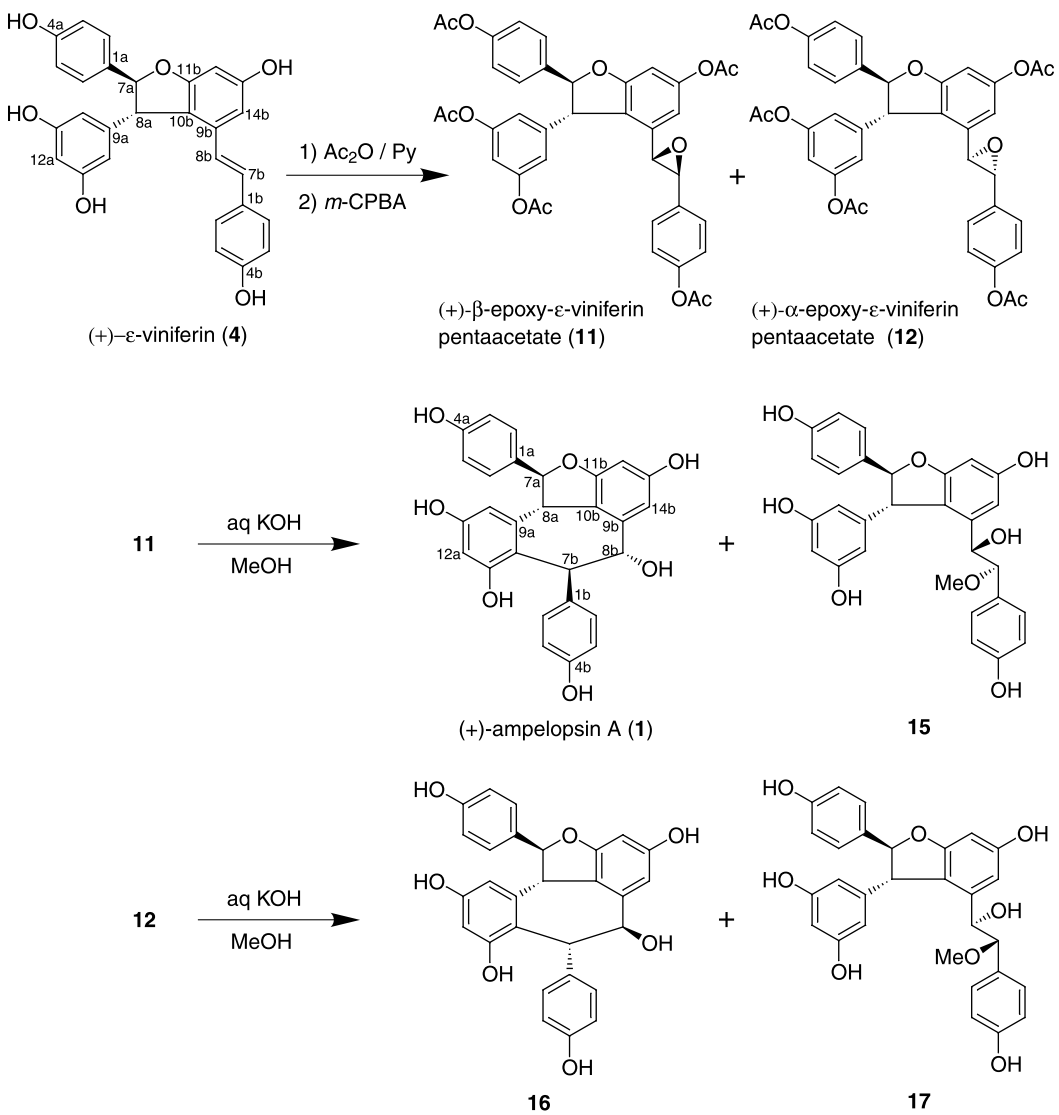


Scheme 2. Formation of (+)-ampelopsin A (**1**) from (+)-ε-viniferin (**4**) via its (+)-β-epoxide (**9**).

Scheme 1, (+)-ε-viniferin would give (−)-ampelopsin D (**5**) and would not, in any event, give (−)-quadrangularin A (**8**). From the above evidence, we have concluded that the structure of (−)-ampelopsin D (**5**) as reported by Oshima et al. is correct, and (−)-ampelopsin D (**5**) is a different compound from (−)-quadrangularin (**8**), though the ^{1}H and ^{13}C NMR data of both compounds are very similar.[4,6,7]

2.3. Base-promoted reactions of (+)-β-epoxy-ε-viniferin

As shown in Scheme 2, (+)-β-epoxy-ε-viniferin (**9**) seems to be the important precursor of (+)-ampelopsin A (**1**). So we tried to transform (+)-ε-viniferin (**4**) to **9**. Any trials of epoxidation of (+)-ε-viniferin (**4**) to (+)-β-epoxy-ε-viniferin (**9**) gave no good results. Therefore, (+)-ε-viniferin



Scheme 3. Transformation of (+)-ε-viniferin (**4**) by the biomimic pathways.

pentaacetate (**10**) derived from **4** with acetic anhydride in pyridine was epoxidated with *m*-chloroperbenzoic acid to afford two epoxides **11** and **12** in 49 and 23% yields, respectively. Both epoxides (**11** and **12**) were respectively treated with hydrochloric acid or trifluoroacetic acid in a mixture of methanol and H_2O to give no cyclized product but the corresponding epoxide-ring cleaved products **13** and **14**. As shown in Scheme 3, epoxide **11** was treated with potassium hydroxide in methanol to give (+)-ampelopsin A (**1**) together with a methyl ether product (**15**) in 55 and 31% yields, respectively. On the other hand, epoxide **12** was treated under the same conditions to give a cyclized product (**16**) and a methyl ether (**17**) in 41 and 52% yields, respectively. The stereochemistry osf compound **16** was characterized on the basis of ^{1}H NMR data. The chemical shift value $\delta_{H\text{-}8a}$ 5.37 indicated the *anti*-configuration between H-8a and 4-hydroxyphenyl group at the C-7b position,[8] as is observed in isohopeaphenol.[9]

2.4. Absolute configurations

On the basis of the absolute configuration of (+)-ε-viniferin (**4**)[3] and the reaction mechanisms of the isomerization of (+)-ε-viniferin (**4**) shown above, the absolute configurations of (+)-ampelopsin A, (+)-ampelopsin B, (−)-ampelopsin D and (+)-ampelopsin F were determined as **1**, **3**, **5** and **6**, respectively.

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). ^{1}H and ^{13}C NMR spectra were recorded on JEOL ALPHA-600 (^{1}H: 600 MHz and ^{13}C: 150 MHz). Chemical shifts for ^{1}H and ^{13}C NMR are given in parts per million (δ) relative to TMS or solvent signal (methanol-d_4: δ_H 3.30 and δ_C 49.0, acetone-d_6: δ_H 2.04 and δ_C 24.9) as internal standards, respectively. LR and HR FAB-MS were obtained with JEOL JMS HX-110 using *m*-nitrobenzylalcohol as matrix. Analytical TLC was performed on silica gel 60 F254 (Merck). Column chromatography was carried out on silica gel BW-820 MH (Fuji Silysia Chemicals, Co. Ltd.).

3.2. Material

(+)-ε-Viniferin (**4**) was obtained from corks of *Vitis vinifera* 'Kyohou'.[10]

3.2.1. Compound 4. $[\alpha]_D$=+49.1° (*c* 1.9, MeOH). Other spectral and physical data were identical with those reported.[3]

3.3. Reaction of (+)-ε-viniferin (4) with 1 M HCl

A mixture of (+)-ε-viniferin (**4**) (11.1 mg) in 1 M HCl (1.5 ml) was stirred under nitrogen atmosphere at room temperature for 50 h. The reaction mixture was extracted twice with ethyl acetate (10 ml each), washed with brine and then dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was subjected to preparative HPLC [YMC-C8 (∅ 20×250 mm), MeOH–H_2O (6:4), flow rate: 3.0 ml/min] to give (+)-ampelopsin B (**3**) (4.2 mg, 38%), (+)-ampelopsin F (**6**) (0.8 mg, 8%), and the starting material (**4**) (0.9 mg).

3.3.1. Compound 3. $[\alpha]_D^{22}$=+176.4° (*c* 0.10, MeOH), FABMS *m/z*: 455 (MH^+; $C_{28}H_{23}O_6$); ^{1}H NMR (acetone-d_6) δ_H 7.08 (2H, d, *J*=8.8 Hz; H-2a,6a), 6.92 (2H, d, *J*=8.8 Hz; H-2b,6b), 6.75 (2H, d, *J*=8.8 Hz; H-3a,5a), 6.63 (1H, d, *J*=8.8 Hz; H-3b,5b), 6.42 (1H, d, *J*=1.8 Hz; H-12a), 6.31 (1H, d, *J*=2.2 Hz; H-14b), 6.21 (1H, d, *J*=1.8 Hz; H-14a), 6.04 (1H, d, *J*=2.2 Hz; H-12b), 5.71 (1H, d, *J*=11.4 Hz; H-7a), 5.20 (1H, t, *J*=4.0 Hz; H-7b), 4.16 (1H, d, *J*=11.4 Hz; H-8a), 3.58 (1H, dd, *J*=17.6, 4.0 Hz; H-8b), 3.17 (1H, brd, *J*=17.6 Hz; H-8b); ^{13}C NMR (acetone-d_6) δ_C 160.4* (s; C-11b), 158.7* (s; C-11a), 158.4* (s; C-13b), 157.1* (s; C-4a), 156.5 (s; C-13a), 156.0 (s; C-4b), 142.5 (s; C-9a), 138.1 (s; C-9b), 134.7 (s; C-1b), 131.0 (s; C-1a), 130.0 (2C, d; C-2a,6a), 128.5 (2C, d; C-2b,6b), 122.8 (s; C-10a), 118.9 (s; C-10b), 115.9 (2C, d; C-3a,5a), 115.5 (2C, d; C-3b,5b), 108.9 (d; C-14b), 105.4 (d; C-14a), 101.4 (d; C-12a), 95.6 (d; C-12b), 88.3 (d; C-7a), 49.2 (d; C-8a), 35.8 (d; C-7b), 33.7 (t; C-8b), (* data can be interchanged within the group).

3.3.2. Compound 6. $[\alpha]_D^{22}$=+19.0° (*c* 0.30, MeOH), FABMS *m/z*: 455 (MH^+; $C_{28}H_{23}O_6$); ^{1}H NMR (acetone-d_6) δ_H 7.08 (2H, d, *J*=8.1 Hz; H-2a,6a), 6.78 (2H, d, *J*=8.8 Hz; H-2b,6b), 6.75 (2H, d, *J*=8.1 Hz; H-3a,5a), 6.56 (2H, d, *J*=8.8 Hz; H-3b,5b), 6.51 (1H, d, *J*=2.2 Hz; H-14a), 6.44 (1H, d, *J*=2.2 Hz; H-14b), 6.15 (1H, d, *J*=2.2 Hz; H-12b), 6.06 (1H, d, *J*=2.2 Hz; H-12a), 4.19 (1H, d, *J*=1.5 Hz; H-7a), 4.12 (1H, brs; H-8b), 3.64 (1H, brs; H-7b), 3.36 (1H, brs; H-8a); ^{13}C NMR (acetone-d_6) δ_C 158.6 (s; C-13a), 157.8 (s; C-11b), 157.1 (s; C-13b), 156.2* (s; C-4a), 156.1* (s; C-4b), 153.1 (s; C-11a), 147.6 (s; C-9b), 147.3 (s; C-9a), 138.4 (s; C-1a), 135.4 (s; C-1b), 129.9 (2C, d; C-2a,6a), 129.2 (2C, d; C-2b,6b), 127.8 (s; C-10a), 115.6 (2C, d; C-3a,5a), 115.5 (2C, d; C-3b,5b), 113.3 (s; C-10b), 105.7 (d; C-14b), 104.2 (d; C-14a), 101.9** (d; C-12a), 101.8** (d; C-12b), 58.1 (d; C-8a), 50.4 (d; C-7b), 49.7 (d; C-8b), 47.1 (d; C-7a) (*, ** data can be interchanged within the group).

3.4. Reaction of (+)-ε-viniferin (4) with CF_3SO_3H in nitromethane

A mixture of (+)-ε-viniferin (**4**) (11.0 mg) and trifluoromethanesulfonic acid (2.2 μl) in nitromethane (1.0 ml) was stirred under nitrogen atmosphere at room temperature for 10 h. The reaction mixture was diluted by water (5 ml), and then extracted with ethyl acetate (5 ml×2). The extract was washed with brine and then dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was subjected to preparative HPLC [YMC-C8 (∅ 20×250 mm), MeOH–H_2O (6:4), flow rate: 3.0 ml/min] to give (+)-ampelopsin F (**6**) (4.2 mg, 38%) and the starting material (**4**) (2.5 mg).

3.5. Reaction of (+)-ε-viniferin (4) with CF_3SO_3H in methanol

A mixture of (+)-ε-viniferin (**4**) (10.3 mg) and trifluoro-

methanesulfonic acid (2.2 μl) in methanol (1.0 ml) was stirred under nitrogen atmosphere under reflux for 7 days. The reaction mixture was diluted with water (5 ml), and then passed through Sep-Pak C_{18} (Waters). The absorbed product was eluted by methanol, and the eluate was concentrated in vacuo. The residue was subjected to preparative HPLC [YMC-C8 (∅ 20×250 mm), MeOH–H_2O (6:4), flow rate: 3.0 ml/min] to give (−)-ampelopsin D (**5**) (1.4 mg, 14%), (+)-ampelopsin F (**6**) (2.1 mg, 20%), compound **7** (0.8 mg, 8%), and the starting material (**4**) (0.3 mg).

3.5.1. Compound 5. $[\alpha]_D^{22}=-5.0°$ (*c* 0.27, MeOH); HRFABMS *m/z* 455.1498 (calcd for $C_{28}H_{23}O_6$, 455.1495); ^{1}H NMR (acetone-d_6) δ 7.17 (2H, d, *J*=8.8 Hz; H-2b,6b), 7.11 (2H, d, *J*=8.8 Hz; H-2a,6a), 7.03 (1H, d, *J*=2.2 Hz; H-7b), 6.79 (1H, d, *J*=2.2 Hz; H-14b), 6.74 (2H, d, *J*=8.8 Hz; H-3a,5a), 6.65 (2H, d, *J*=8.8 Hz; H-3b,5b), 6.29 (1H, d, *J*=2.2 Hz; H-12b), 6.11 (1H, t, *J*=2.2 Hz; H-12a), 6.10 (2H, d, *J*=2.2 Hz; H-10a,14a), 4.27 (1H, brs; H-7a), 4.14 (1H, brs; H-8a); ^{13}C NMR (acetone-d_6) δ 159.7 (s; C-13b), 159.3 (s; C-11a,13a), 157.3 (s; C-4b), 156.7 (s; C-4a), 156.1 (s; C-11b), 149.9 (s; C-9a), 147.5 (s; C-9b), 143.1 (s; C-8b), 137.3 (s; C-1a), 131.0 (d; C-2b,6b), 129.7 (s; C-1b), 128.8 (d; C-2a,6a), 123.8 (s; C-10b), 122.6 (d; C-7b), 116.3 (d; C-3a,5a), 116.0 (d; C-3b,5b), 106.4 (d; C-10a,14a), 103.8 (d; C-12b), 101.3 (d; C-12a), 98.4 (d; C-14b), 59.5 (d; C-7a), 58.7 (d; C-8a).

3.5.2. Compound 7. $[\alpha]_D^{22}=-227.0°$ (*c* 0.39, MeOH); HRFABMS *m/z* 455.1499 (calcd for $C_{28}H_{23}O_6$, 455.1495); ^{1}H NMR (methanol-d_4) δ 3.81 (1H, d, *J*=16.1 Hz; H-7b), 3.86 (1H, d, *J*=16.1 Hz; H-7b′), 4.79 (1H, s, H-8a), 5.98 (1H, t, *J*=2.2 Hz; H-12a), 6.06 (3H, d, *J*=2.2 Hz; H-10a,14a, H-12b), 6.17 (1H, d, *J*=2.2 Hz; H-14b), 6.65 (2H, d, *J*=8.5 Hz; H-3a,5a), 6.72 (2H, d, *J*=8.5 Hz; H-3b,5b), 7.06 (2H, d, *J*=8.5 Hz; H-2a,6a), 7.10 (2H, d, *J*=8.5 Hz; H-2b,6b); ^{13}C NMR (methanol-d_4) δ 158.9 (s, C-13b), 158.8 (s, C-11a,13a), 157.5 (d, C-4a), 156.5 (s, C-4b), 154.0 (s, C-11b), 150.4 (s, C-7a), 149.9 (s, C-9b), 144.0 (s, C-9a), 136.6 (s, C-8b), 132.1 (s, C-1b), 131.1 (d, 2a,6a), 130.2 (d, 2b,6b), 128.9 (s, C-1a), 125.4 (s, C-10b), 116.3 (d, C-3b,5b), 115.8 (s, C-3a,5a), 108.2 (d, C-10a,14a), 101.5 (d, C-12a), 101.1 (d, C-12b), 100.8 (d, C-14b), 56.8 (d, C-8a), 32.2 (t, C-7b).

3.6. Reaction of (+)-ε-viniferin (4) with H_2SO_4 in methanol

To a mixture of (+)-ε-viniferin (**4**) (54 mg) and methanol (5.0 ml) was added H_2SO_4 (7.2 μl), and the solution was refluxed under nitrogen atmosphere for 5 days. The reaction mixture was diluted by water (12 ml), and then passed through Sep-Pak C_{18}. The absorbed product was eluted by methanol, and the eluate was concentrated in vacuo. The residue was subjected to preparative HPLC [YMC-C8 (∅ 20×250 mm), MeOH–H_2O (6:4), flow rate: 3.0 ml/min] to give (+)-ampelopsin B (**3**) (7.0 mg, 13%), (−)-ampelopsin D (**5**) (3.5 mg, 6%), (+)-ampelopsin F (**6**) (10 mg, 19%), compound **7** (5.4 mg, 10%), and the starting material (**4**) (1.4 mg), respectively.

3.7. Reaction of (+)-ε-viniferin (4) with acetic anhydride in pyridine

A mixture of (+)-ε-viniferin (**4**) (209 mg) and acetic anhydride (2 ml) in pyridine (4 ml) was stirred at room temperature for 16 h. The reaction mixture was evaporated to dryness, and the residue was subjected to silica-gel column chromatography using chloroform as eluant to give (+)-ε-viniferin pentaacetate (**10**) (253 mg, 83%).

3.7.1. Compound 10. $[\alpha]_D^{25}=+4.6°$ (*c* 0.54, $CHCl_3$), FABMS *m/z*: 665.2010 (MH^+; 665.2023 for $C_{38}H_{33}O_{11}$); IR ν_{max} (film) cm^{-1}: 1768, 1198; ^{1}H NMR ($CDCl_3$) δ 7.32 (2H, d, *J*=8.8 Hz; H-2a,6a), 7.16 (2H, d, *J*=8.8 Hz; H-2b,6b), 7.08 (2H, d, *J*=8.8 Hz; H-3a,5a), 6.96 (2H, d, *J*=8.8 Hz; H-3b,5b), 6.93 (1H, d, *J*=2.2 Hz; H-14b), 6.88 (1H, t, *J*=2.2 Hz; H-12a), 6.86 (1H, d, *J*=16.1 Hz; H-8b), 6.84 (2H, d, *J*=2.2 Hz; H-10a,14a), 6.63 (1H, d, *J*=2.2 Hz; H-12b), 6.52 (1H, d, *J*=16.1 Hz; H-7b), 5.59 (1H, d, *J*=6.6 Hz; H-7a), 4.58 (1H, d, *J*=6.6 Hz; H-8a), 2.32, 2.28, 2.25 (each 3H, s; C*H*$_3$CO), 2.24 (6H, s; C*H*$_3$CO); ^{13}C NMR ($CDCl_3$) δ 161.0 (s; C-11b), 152.2 (s; C-13b), 151.7 (2C, s; C-11a,13a), 150.7 (s; C-4a), 150.4 (s; C-4b), 144.4 (s; C-9a), 138.1 (s; C-1a), 135.4 (s; C-9b), 134.5 (s; C-1b), 130.4 (d; C-8b), 127.8 (2C, d; C-2b,6b), 126.8 (2C, d; C-2a,6a), 124.1 (d; C-7b), 123.9 (s; C-10b), 122.0 (2C, d; C-3a,5a), 121.8 (2C, d; C-3b,5b), 118.6 (2C, d; C-10a,14a), 114.9 (d; C-12a), 110.7 (d; C-14b), 102.9 (d; C-12b), 92.8 (d; C-7a), 56.7 (d; C-8a), 169.5, 169.42, 169.39 (each s; CH_3*C*O), 168.8 (2C, s; CH_3*C*O), 21.3 (q; *C*H_3CO), 21.2, 21.1 (each 2C, q; *C*H_3CO).

3.8. Reaction of (+)-ε-viniferin pentaacetate (4) with *m*-chloroperbenzoic acid in dichloromethane

A mixture of (+)-ε-viniferin pentaacetate (**10**) (150 mg) and *m*-chloroperbenzoic acid (118 mg) in dichloromethane (5 ml) was stirred at room temperature for 16 h. A saturated sodium bicarbonate aqueous solution (20 ml) was added to the reaction solution, and the mixture was extracted with chloroform (10 ml×2). The extract was washed with water and brine, and then dried over sodium sulfate. After evaporation of the solvent, the residue was subjected to preparative silica-gel TLC using chloroform–acetone (99:1) as solvent to give β-epoxide (**11**) (75 mg, 49%), α-epoxide (**12**) (36 mg, 23%) and recovered starting material (**10**) (17 mg).

3.8.1. Compound 11. $[\alpha]_D^{25}=+40.3°$ (*c* 0.74, $CHCl_3$); FABMS *m/z*: 681.2009 (MH^+; 681.1972 for $C_{38}H_{33}O_{12}$); IR ν_{max} (film) cm^{-1}: 1767, 1201; ^{1}H NMR ($CDCl_3$) δ 7.28 (2H, d, *J*=8.8 Hz; H-2a,6a), 7.06 (2H, d, *J*=8.8 Hz; H-3a (5a)), 6.89 (2H, brs; H-3b,5b), 6.89 (2H, brs; H-2b,6b), 6.69 (1H, d, *J*=2.2 Hz; H-12b), 6.66 (1H, t, *J*=2.2 Hz; H-12a), 6.64 (2H, d, *J*=2.2 Hz; H-10a,14a), 6.61 (1H, d, *J*=2.2 Hz; H-14b), 5.59 (1H, d, *J*=6.6 Hz; H-7a), 4.51 (1H, d, *J*=6.6 Hz; H-8a), 3.43 (1H, d, *J*=1.8 Hz; H-8b), 3.40 (1H, d, *J*=1.8 Hz; H-7b), 2.29, 2.27, 2.26 (each 3H, s; C*H*$_3$CO), 2.23 (6H, s; C*H*$_3$CO); ^{13}C NMR ($CDCl_3$) δ 160.4 (s; C-11b), 152.4 (s; C-13b), 151.5 (2C, s; C-11a,13a), 150.63* (s; C-4a), 150.58* (s; C-4b), 143.9 (s; C-9a), 137.9 (s; C-1a), 135.3 (s; C-9b), 133.4 (s; C-1b), 126.5 (2C, d; C-2a,6a), 126.5 (2C, d; C-2b,6b), 124.2 (d; C-10b), 122.0 (2C, d; C-3a,5a), 121.5 (2C, d; C-3b,5b), 117.9 (2C, d; C-10a,14a), 114.4 (d; C-12a), 109.9 (d; C-14b), 103.6 (d; C-12b), 93.0 (d; C-7a), 61.6 (d; C-7b), 60.0 (d; C-8b), 56.2 (d; C-8a),

169.3, 169.5 (each 2C, s; CH_3CO), 169.1 (s; CH_3CO), 21.07, 21.12 (each 2C, q; CH_3CO), 25.7 (q; CH_3CO).

3.8.2. Compound 12. $[\alpha]_D^{25}=+24.0°$ (*c* 0.51, $CHCl_3$); FABMS *m/z*: 681.1994 (MH^+; 681.1972 for $C_{38}H_{33}O_{12}$); IR ν_{max} (film) cm^{-1}: 1768, 1215; ^1H NMR ($CDCl_3$) δ 7.28 (2H, d, *J*=8.8 Hz; H-2a,6a), 7.10 (2H, d, *J*=8.8 Hz; H-2b,6b), 7.05 (2H, d, *J*=8.8 Hz; H-3a,5a), 6.98 (2H, d, *J*=8.8 Hz; H-3b,5b), 6.89 (1H, t, *J*=2.2 Hz; H-12a), 6.72 (2H, d, *J*=2.2 Hz; H-10a,14a), 6.71 (1H, d, *J*=2.2 Hz; H-12b), 6.61 (1H, d, *J*=2.2 Hz; H-14b), 5.61 (1H, d, *J*=6.2 Hz; H-7a), 4.47 (1H, d, *J*=6.2 Hz; H-8a), 3.54 (1H, d, *J*=1.8 Hz; H-7b), 3.41 (1H, d, *J*=1.8 Hz; H-8b), 2.29, 2.27, 2.26 (each 3H, s; CH_3CO), 2.23 (6H, s; CH_3CO); ^{13}C NMR ($CDCl_3$) δ 160.7 (s; C-11b), 152.3 (s; C-13b), 151.6 (2C, s; C-11a,13a), 150.7* (s; C-4a), 150.6* (s; C-4b), 143.8 (s; C-9a), 138.0 (s; C-1a), 135.5 (s; C-9b), 133.7 (s; C-1b), 126.9 (2C, d; C-2b,6b), 126.4 (2C, d; C-2a,6a), 123.9 (d; C-10b), 122.0 (2C, d; C-3a,5a), 121.7 (2C, d; C-3b,5b), 118.3 (2C, d; C-10a,14a), 114.9 (d; C-12a), 110.7 (d; C-14b), 103.7 (d; C-12b), 92.7 (d; C-7a), 61.2 (d; C-7b), 59.3 (d; C-8b), 56.9 (d; C-8a), 168.7 (2C, s; CH_3CO), 169.34, 169.29, 169.26 (each s; CH_3CO), 21.0, 21.1 (each 2C, q; CH_3CO), 29.2 (q; CH_3CO), (* data can be interchanged within the group).

3.9. Reaction of (+)-epoxy-ε-viniferin pentaacetate (11 and 12) with potassium hydroxide in methanol

A mixture of compound **11** (18 mg) and potassium hydroxide (8.9 mg) in methanol (2 ml) was stirred in an ice bath for 30 min. Then the mixture was acidified with 2 M hydrochloric acid aqueous solution and extracted with ethyl acetate (5 ml×2). The extract was washed with water and brine, and dried over anhydrous sodium sulfate. The solvent was removed by evaporation, and the residue was subjected to preparative silica-gel TLC using chloroform–methanol–H_2O (40:10:1) as solvent to give (+)-ampelopsin A (**1**) (9.7 mg, 55%) and 8*b*-hydroxy-7*b*-methoxy-ε-viniferin (**15**) (5.8 mg, 31%).

In almost the same manner, compound **12** (8.9 mg) was treated to give compound **16** (2.5 mg, 41%) and compound **17** (3.4 mg, 52%).

3.9.1. Compound 1. $[\alpha]_D^{25}=+191.9°$ (*c* 0.96, MeOH); FABMS *m/z*: 471.1479 (MH^+; 471.1444 for $C_{28}H_{23}O_7$); IR ν_{max} (film) cm^{-1}: 3333, 1613, 1515, 1455; ^1H NMR (acetone-d_6) δ_H 7.10 (2H, d, *J*=8.4 Hz; H-2a,6a), 6.88 (2H, d, *J*=8.8 Hz; H-2b,6b), 6.77 (2H, d, *J*=8.4 Hz; H-3a,5a), 6.63 (2H, d, *J*=8.4 Hz; H-3b,5b), 6.60 (1H, d, *J*=2.2 Hz; H-14b), 6.42 (1H, d, *J*=2.2 Hz; H-12a), 6.22 (1H, brs; H-14a), 6.14 (1H, d, *J*=2.2 Hz; H-12b), 5.75 (1H, d, *J*=11.4 Hz; H-7a), 5.44 (1H, d, *J*=4.8 Hz; H-7b), 5.40 (1H, d, *J*=4.8 Hz; H-8b), 4.15 (1H, d, *J*=11.4 Hz; H-8a); ^{13}C NMR (acetone-d_6) δ 159.8 (s; C-13a), 159.8 (s; C-11b), 158.5 (s; C-13b), 158.1 (s; C-4b), 156.9 (s; C-4a), 155.7 (s; C-11a), 142.7 (s; C-9a), 140.1 (s; C-9b), 132.3 (s; C-1a), 130.6 (s; C-1b), 129.6 (2C, d; C-2a,6a), 128.3 (2C, d; C-2b,6b), 118.5 (d; C-10a), 118.0 (s; C-10b), 115.6 (2C, d; C-3a,5a), 115.0 (2C, d; C-3b,5b), 110.1 (d; C-14b), 105.1 (d; C-14a), 101.1 (d; C-12a), 97.0 (d; C-12b), 88.1 (d; C-7a), 70.7 (d; C-8b), 49.2 (d; C-8a), 43.5 (d; C-7b).

3.9.2. Compound 15. $[\alpha]_D^{25}=+61.9°$ (*c* 0.11, MeOH), FABMS *m/z*: 502.1644 (M^+; 502.1628 for $C_{28}H_{23}O_7$); IR ν_{max} (film) cm^{-1}: 3363, 1600; ^1H NMR (methanol-d_4) δ 7.07 (2H, d, *J*=8.8 Hz; H-2a,6a), 6.71 (2H, d, *J*=8.8 Hz; H-3a,5a), 6.66 (2H, d, *J*=8.8 Hz; H-2b,6b), 6.60 (1H, d, *J*=2.2 Hz; H-14b), 6.58 (2H, d, *J*=8.8 Hz; H-3b,5b), 6.26 (1H, d, *J*=2.2 Hz; H-12b), 6.22 (1H, t, *J*=2.2 Hz; H-12a), 6.07 (2H, d, *J*=2.2 Hz; H-10a,14a), 5.31 (1H, d, *J*=4.8 Hz; H-7a), 4.43 (1H, d, *J*=4.0 Hz; H-8b), 4.27 (1H, d, *J*=4.8 Hz; H-8a), 3.86 (1H, d, *J*=4.0 Hz; H-7b), 3.04 (3H, s, OMe); ^{13}C NMR (methanol-d_4) δ 162.3 (s; C-11b), 160.7 (2C, s; C-11a,13a), 159.8 (s; C-13b), 158.6 (s; C-4a), 157.8 (s; C-4b), 148.4 (s; C-9a), 141.2 (s; C-9b), 134.4 (s; C-1a), 131.0 (s; C-1b), 130.0 (2C, d; C-2b,6b), 127.6 (2C, d; C-2a,6a), 120.1 (d; C-10b), 116.4 (2C, d; C-3a,5a), 115.8 (2C, d; C-3b,5b), 108.8 (d; C-14b), 107.4 (2C, d; C-10a,14a), 102.4 (d; C-12a), 97.2 (d; C-12b), 89.1 (d; C-7a), 86.0 (d; C-7b), 74.4 (d; C-8b), 57.8 (d; C-8a), 57.1 (q; OMe).

3.9.3. Compound 16. $[\alpha]_D^{25}=+4.5°$ (*c* 0.14, MeOH), FABMS *m/z*: 471.1425 (MH^+; 471.1444 for $C_{28}H_{23}O_7$); IR ν_{max} (film) cm^{-1}: 3359, 1614; ^1H NMR (methanol-d_4) δ 7.45 (2H, d, *J*=8.8 Hz; H-2a,6a), 6.88 (2H, d, *J*=8.8 Hz; H-3a,5a), 6.65 (2H, d, *J*=8.8 Hz; H-2b,6b), 6.43 (2H, d, *J*=8.8 Hz; H-3b,5b), 6.16 (1H, d, *J*=2.2 Hz; H-14a), 6.14 (1H, d, *J*=2.2 Hz; H-12a), 6.00 (1H, d, *J*=2.2 Hz; H-14b), 5.72 (1H, d, *J*=9.6 Hz; H-7a), 5.67 (1H, d, *J*=2.2 Hz; H-12b), 5.37 (1H, d, *J*=9.6 Hz; H-8a), 5.03 (1H, d, *J*=5.6 Hz; H-7b), 4.69 (1H, d, *J*=5.6 Hz; H-8b); ^{13}C NMR (methanol-d_4) δ 161.0 (s; C-11b), 159.7 (s; C-4a), 159.1 (s; C-11a), 159.0 (s; C-13b), 157.0 (s; C-13a), 155.8 (s; C-4b), 141.8 (s; C-9a), 140.6 (s; C-9b), 135.7 (s; C-1b), 133.6 (s; C-1a), 130.8 (2C, d; C-2b,6b), 130.7 (2C, d; C-2a,6a), 118.6 (d; C-10a), 118.5 (d; C-10b), 116.9 (2C, d; C-3a,5a), 115.2 (2C, d; C-3b,5b), 108.9 (d; C-14b), 106.8 (d; C-14a), 102.2 (d; C-12a), 96.2 (d; C-12b), 94.4 (d; C-7a), 79.1 (d; C-8b), 53.3 (d; C-8a), 49.6 (d; C-7b).

3.9.4. Compound 17. $[\alpha]_D^{25}=+46.7°$ (*c* 0.12, MeOH), FABMS *m/z*: 503.1700 (MH^+; 503.1706 for $C_{28}H_{23}O_7$); IR ν_{max} (film) cm^{-1}: 3356, 1613; ^1H NMR (methanol-d_4) δ 6.78 (2H, d, *J*=8.7 Hz; H-2a,6a), 6.76 (2H, d, *J*=8.7 Hz; H-2b,6b), 6.73 (2H, d, *J*=8.7 Hz; H-3a,5a), 6.64 (2H, d, *J*=8.7 Hz; H-3b,5b), 6.56 (1H, d, *J*=2.3 Hz; H-14b), 6.13 (1H, d, *J*=2.3 Hz; H-12b), 6.12 (1H, t, *J*=2.3 Hz; H-12a), 5.94 (2H, d, *J*=2.3 Hz; H-10a,14a), 4.95 (1H, d, *J*=7.8 Hz; H-7a), 4.33 (1H, d, *J*=9.2 Hz; H-7b), 3.93 (1H, d, *J*=9.2 Hz; H-8b), 3.18 (1H, d, *J*=7.8 Hz; H-8a), 3.14 (3H, s; OMe); ^{13}C NMR (methanol-d_4) δ 163.2 (s; C-11b), 161.2 (2C, s; C-11a,13a), 161.0 (s; C-13b), 160.1 (s; C-4a), 160.0 (s; C-4b), 147.9 (s; C-9a), 141.4 (s; C-9b), 133.9 (s; C-1a), 131.6 (2C, d; C-2b,6b), 130.8 (s; C-1b), 130.7 (2C, d; C-2a,6a), 122.1 (s; C-10b), 117.7 (2C, d; C-3a,5a), 117.1 (2C, d; C-3b,5b), 108.9 (2C, d; C-10a,14a), 108.7 (d; C-14b), 103.6 (d; C-12a), 98.4 (d; C-12b), 96.8 (d; C-7a), 91.5 (d; C-7b), 76.5 (d; C-8b), 58.1 (q; OMe), 58.0 (d; C-8a).

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