

## (-)-AMPELOPSIN D IS DIFFERENT FROM (-)-QUADRANGULARIN A

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**Abstract** — The structure of (-)-ampelopsin D, hydroxystilbene dimer, was reinvestigated using spectroscopic methods. Furthermore, the relative and absolute stereostructures were discussed on the basis of chemical transformation of (+)- $\epsilon$ -viniferin to (-)-ampelopsin D.

In 1993, Y. Oshima *et al.* reported the isolation and structure of a hydroxystilbene dimer named (-)-ampelopsin D (**1**) as a hepatoprotective substance from the roots of *Ampelopsis brevipedunculata* var. *hancei* (Vitaceae).<sup>2,3</sup> In 1999, S. A. Adesanya *et al.* reported the isolation and structure of a hydroxystilbene dimer named (-)-quadrangularin A (**2**) from the stems of *Cissus quadrangularis* (Vitaceae).<sup>4</sup> In their paper, it was described that the NMR data of ampelopsin D (**1**) are quite similar to those of quadrangularin A (**2**) and the reported structure of ampelopsin D is probably erroneous and should be **2**.<sup>4</sup> Recently, we have isolated a hydroxystilbene dimer (**3**) from the corks of *Vitis vinifera* 'Kyohou' (Vitaceae). The <sup>1</sup>H and <sup>13</sup>C NMR data of **3** are very similar to those of **1** (the spectra were taken in acetone-d<sub>6</sub>) and **2** (the spectra were taken in methanol-d<sub>4</sub>). We, therefore, studied the structure of compound (**3**) in detail. In this communication we describe that the relative and absolute structure of (-)-ampelopsin D is **1** and not **2**.

### Structure Review of Ampelopsin D

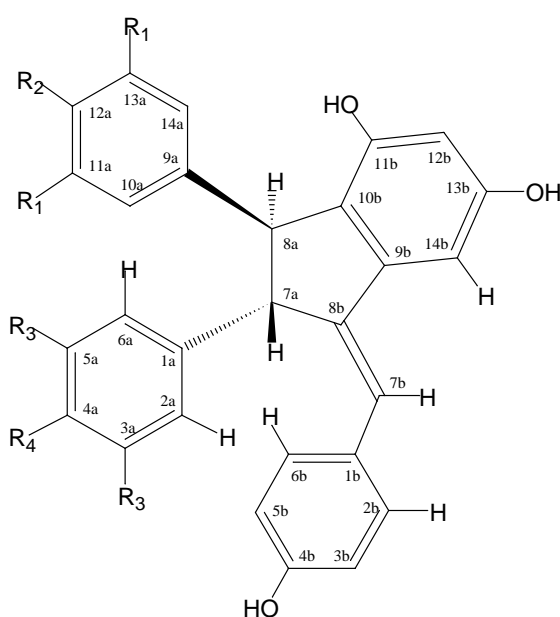
Compound (**3**) isolated from *Vitis vinifera* 'Kyohou', [ $\alpha$ ]<sub>D</sub><sup>22</sup> -5° (c 0.27, MeOH, cell length = 100 mm); HRFABMS *m/z* 455.1498 (calcd for C<sub>28</sub>H<sub>23</sub>O<sub>6</sub>, 455.1495) showed very similar NMR data to those of (-)-ampelopsin D (**1**) and (-)-quadrangularin A (**2**), respectively.<sup>1,3</sup> The most important difference between (-)-ampelopsin D (**1**) and (-)-quadrangularin A (**2**) is whether H-2a (H-6a) shows an *ortho*-coupling or a *meta*-coupling. For the structure reviews of **1** and **2**, the structure of compound (**3**) was examined on the

Table 1. NMR Data of Compound (**3**) in Methanol-d<sub>4</sub> (**A**) and in Acetone-d<sub>6</sub> (**B**)

Carbon number	<b>A</b>			<b>B</b>		
	<sup>13</sup> C		<sup>1</sup> H	<sup>13</sup> C		<sup>1</sup> H
1a	138.0	s <sup>a</sup>		137.3	s <sup>a</sup>	
2a,6a	129.1	d	7.02 d (8.8) <sup>b</sup>	128.8	d	7.11 d (8.8) <sup>b</sup>
3a,5a	116.5	d	6.67 d (8.8)	116.3	d	6.74 d (8.8)
4a	156.7	s		156.7	s	
7a	60.0	d	4.17 brs	59.5	d	4.27 brs
8a	59.2	d	4.05 brs	58.7	d	4.14 brs
9a	149.9	s		149.9	s	
10a,14a	106.7	d	6.06 d (2.2)	106.4	d	6.10 d (2.2)
11a,13a	159.2	s		159.3	s	
12a	101.3	d	6.04 t (2.2)	101.3	d	6.11 t (2.2)
1b	130.2	s		129.7	s	
2b,6b	131.2	d	7.08 d (8.8)	131.0	d	7.17 d (8.8)
3b,5b	116.0	d	6.56 d (8.8)	116.0	d	6.65 d (8.8)
4b	157.4	s		157.3	s	
7b	122.9	d	6.96 d (2.2)	122.6	d	7.03 d (2.2)
8b	143.7	s		143.1	s	
9b	147.9	s		147.5	s	
10b	124.7	s		123.8	s	
11b	156.3	s		156.1	s	
12b	103.8	d	6.18 d (2.2)	103.8	d	6.29 d (2.2)
13b	159.8	s		159.7	s	
14b	98.3	d	6.69 d (2.2)	98.4	d	6.79 d (2.2)

<sup>a</sup>multiplicity of <sup>13</sup>C signals.

<sup>b</sup>*J* (Hz) in parentheses.



(-)-Ampelopsin D (**1**) : R<sub>1</sub>=OH, R<sub>2</sub>=H, R<sub>3</sub>=H, R<sub>4</sub>=OH  
 (-)-Quadrangularin A (**2**) : R<sub>1</sub>=H, R<sub>2</sub>=OH, R<sub>3</sub>=OH, R<sub>4</sub>=H

basis of the NMR spectra taken in methanol- $d_4$ .<sup>5</sup> In DIF-NOE experiments of **3**, the NOEs between H-7b and H-14b (4.0%), H-7b and H-2b (H-6b) (2.6%), and H-6b (H-2b) and H-7a (7.0%) were respectively observed. These observations indicated H-7a to be an allylic hydrogen of an Ar - C<sub>7b</sub> = C<sub>8b</sub> - C<sub>7a</sub>-grouping. This was further supported by the following observations. The correlations between H-7a and C-7a in the HMQC spectrum, between H-7b and C-7a in the HMBC spectrum, and between H-7a and H-7b in the <sup>1</sup>H-<sup>1</sup>H COSY spectrum, were respectively observed. The long-range coupling between H-7a and H-7b was also confirmed by decoupling experiments.<sup>6</sup> The broad singlet signal of H-7a changed to a sharp signal by irradiation of H-7b, and the doublet signal of H-7b changed to a singlet signal by irradiation of H-7a. This evidence confirmed the assignments of H-7a and C-7a. Next, the correlations between H-7a and C-2a (C-6a), and between H-2a (H-6a) and C-7a were respectively observed in the HMBC spectrum. The <sup>1</sup>H-<sup>1</sup>H coupling constant value of H-2a (H-6a) is 8.8 Hz, which corresponds to a value of *ortho*-coupling.<sup>7</sup> This means that the structure of compound (**3**) is characterized as **1**.<sup>8</sup>

**Absolute Configuration of (-)-Ampelopsin D**      (+)- $\epsilon$ -Viniferin (**4**) ( $[\alpha]_D^{22} +49.1^\circ$  ( $c$  1.85, MeOH, cell length = 100 mm), whose absolute configuration is known,<sup>9</sup> was treated with trifluoromethanesulfonic acid in methanol under reflux for 7 days to give (-)-ampelopsin D (**1**) and its regio-isomer (**5**)<sup>10</sup> based on a double bond, in yields of 7 % and 10 %, respectively. According to the reaction mechanism in Figure 1, (+)- $\epsilon$ -viniferin (**4**) will give a product having the structure of **1** and not a product having the structure of **2**, under the above reaction conditions. From the above-mentioned results, (-)-ampelopsin D should be represented as **1**, including the absolute configuration.

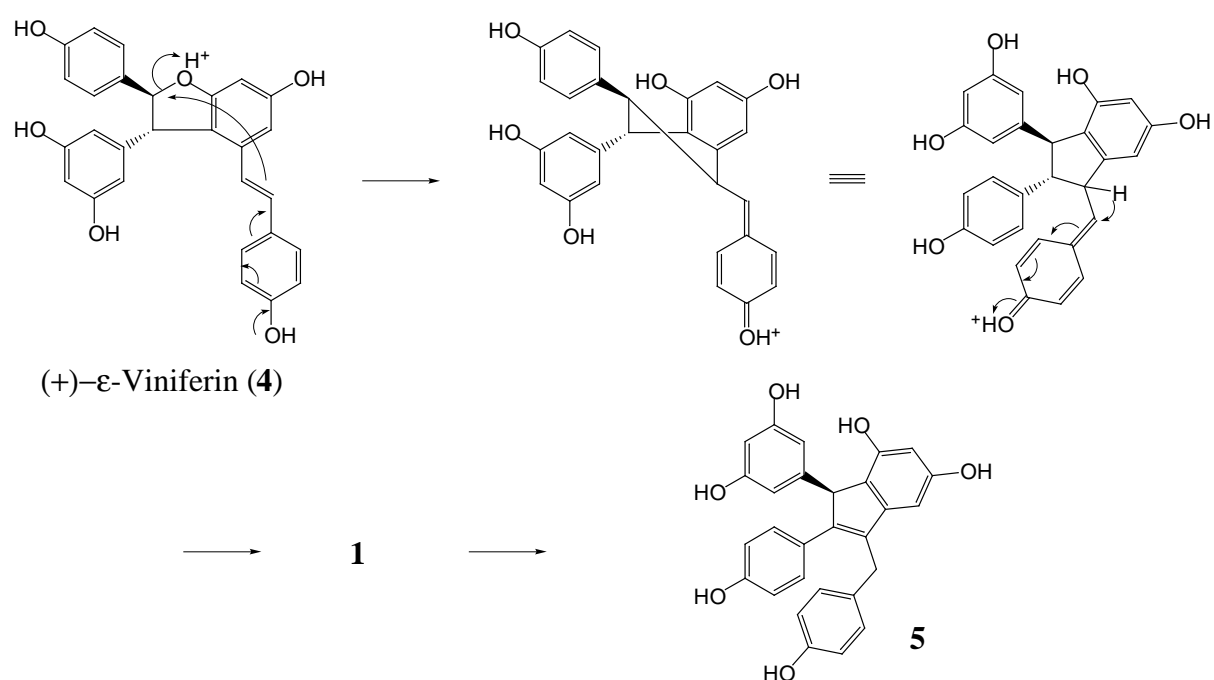


Figure 1. A reaction pathway of (+)- $\epsilon$ -viniferin (**4**) to (-)-ampelopsin D (**1**) and its isomer (**5**)

Consequently, the  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of (–)-ampelopsin D (**1**) and (–)-quadrangularin A (**2**) both are very similar, but (–)-ampelopsin D (**1**) and (–)-quadrangularin A (**2**) are a different compound from each other.

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6. The same long-range coupling was reported by Prof. Y. Oshima *et al.*<sup>2</sup>
7. The value of H-2a (H-6a) of (–)-quadrangularin A (**2**) was reported as 2 Hz.<sup>4</sup>
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10. **5**:  $[\alpha]_{\text{D}}^{22}$   $-227.0^\circ$  (*c* 0.39, MeOH, cell length = 100 mm); HRFABMS *m/z* 455.1499 (calcd for  $\text{C}_{28}\text{H}_{23}\text{O}_6$ , 455.1495);  $^1\text{H}$  NMR (600 MHz, MeOH- $\text{d}_4$ )  $\delta$  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);  $^{13}\text{C}$  NMR (150 MHz, MeOH- $\text{d}_4$ )  $\delta$  32.2 (t, C-7b), 56.8 (d, C-8a), 100.8 (d, C-14b), 101.1 (d, C-12b), 101.5 (d, C-12a), 108.2 (d, C-10a, 14a), 115.8 (s, C-3a, 5a), 116.3 (d, C-3b, 5b), 125.4 (s, C-10b), 128.9 (s, C-1a), 130.2 (d, 2b, 6b), 131.1 (d, 2a, 6a), 132.1 (s, C-1b), 136.6 (s, C-8b), 144.0 (s, C-9a), 149.9 (s, C-9b), 150.4 (s, C-7a), 154.0 (s, C-11b), 156.5 (s, C-4b), 157.5 (d, C-4a), 158.8 (s, C-11a, 13a), 158.9 (s, C-13b).