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(–)-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 (+)-ε-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).[2,3] 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).[4] 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**.[4] Recently, we have isolated a hydroxystilbene dimer (**3**) from the corks of *Vitis vinifera* 'Kyohou' (Vitaceae). The ^{1}H and ^{13}C NMR data of **3** are very similar to those of **1** (the spectra were taken in acetone-d_6) and **2** (the spectra were taken in methanol-d_4). 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

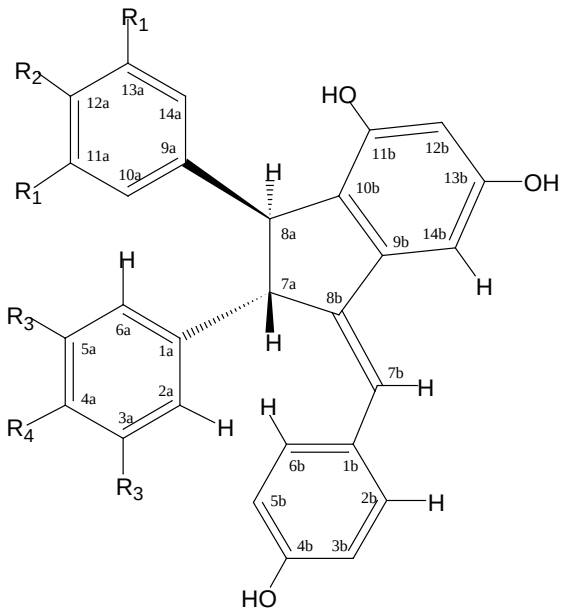
Compound (**3**) isolated from *Vitis vinifera* 'Kyohou', $[\alpha]_D^{22}$ –5° (*c* 0.27, MeOH, cell length = 100 mm); HRFABMS *m/z* 455.1498 (calcd for $C_{28}H_{23}O_6$, 455.1495) showed very similar NMR data to those of (–)-ampelopsin D (**1**) and (–)-quadrangularin A (**2**), respectively.[1,3] 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_4 (**A**) and in Acetone-d_6 (**B**)

	A			**B**		
Carbon number	^{13}C		^{1}H	^{13}C		^{1}H
1a	138.0	s[a]		137.3	s[a]	
2a,6a	129.1	d	7.02 d (8.8)[b]	128.8	d	7.11 d (8.8)[b]
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)

[a]multiplicity of ^{13}C signals.

[b]*J* (Hz) in parentheses.



(-)-Ampelopsin D (**1**) : R_1=OH, R_2=H, R_3=H, R_4=OH

(-)-Quadrangularin A (**2**) : R_1=H, R_2=OH, R_3=OH, R_4=H

basis of the NMR spectra taken in methanol-d_4.[5] 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_{7b} = C_{8b} – C_{7a}- 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 ^{1}H-^{1}H COSY spectrum, were respectively observed. The long-range coupling between H-7a and H-7b was also confirmed by decoupling experiments.[6] 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 ^{1}H-^{1}H coupling constant value of H-2a (H-6a) is 8.8 Hz, which corresponds to a value of *ortho*-coupling.[7] This means that the structure of compound (**3**) is characterized as **1**.[8]

Absolute Configuration of (–)-Ampelopsin D (+)-ε-Viniferin (**4**) ($[\alpha]_D^{22}$ +49.1° (*c* 1.85, MeOH, cell length = 100 mm), whose absolute configuration is known,[9] was treated with trifluoromethanesulfonic acid in methanol under reflux for 7 days to give (–)-ampelopsin D (**1**) and its regio-isomer (**5**)[10] based on a double bond, in yields of 7 % and 10 %, respectively. According to the reaction mechanism in Figure 1, (+)-ε-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.

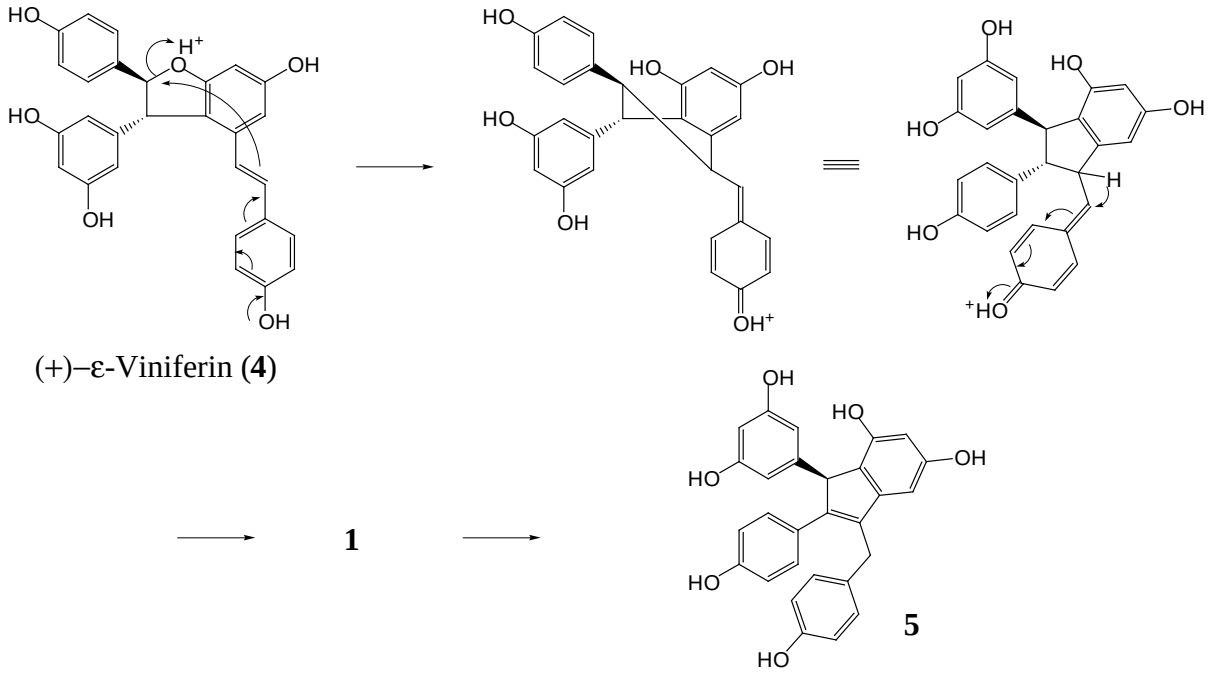


Figure 1. A reaction pathway of (+)-ε-viniferin (**4**) to (–)-ampelopsin D (**1**) and its isomer (**5**)

Consequently, the ^{1}H and ^{13}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.*[2]
7. The value of H-2a (H-6a) of (–)-quadrangularin A (**2**) was reported as 2 Hz.[4]
8. The ^{1}H NMR spectrum in acetone-d_6 of **3** was identical with that in acetone-d_6 of **1** sent by Prof. Y. Oshima.
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10. **5**: $[\alpha]_D^{22}$ –227.0° (*c* 0.39, MeOH, cell length = 100 mm); HRFABMS *m/z* 455.1499 (calcd for $C_{28}H_{23}O_6$, 455.1495); ^{1}H NMR (600 MHz, MeOH-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 (150 MHz, MeOH-d_4) δ 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).