

Resveratrol Tetramers from the Roots of *Ampelopsis sinica*

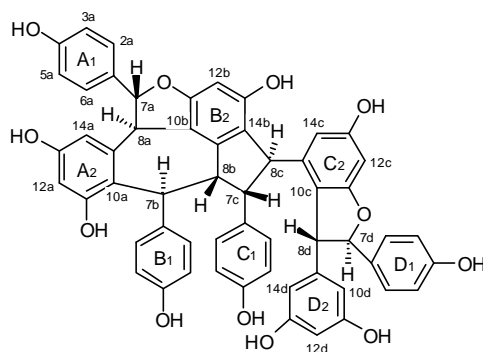
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Abstract: A new resveratrol tetramer, sinicin A was isolated from the roots of *Ampelopsis sinica*, with four known tetramers: vitisin A, *cis*-vitisin B, ampelopsin H and hopeaphenol. The structure and stereochemistry of sinicin A have been established on the basis of 1D and 2D NMR spectroscopic techniques.

Keywords: *Ampelopsis sinica*, Vitaceae, resveratrol tetramer.

Various biological activities of stilbenoids have been described, such as antifungal and antibacterial activities¹, antihepatotoxic activity²⁻⁴, anti-HIV activity⁵. Stilbenoids mainly existed in Vitaceae, Dimerocarpaceae, Gnetaceae, Cyperaceae, Leguminaceae¹. Many oligostilbenes have been isolated from Vitaceae plants. But, there was no report on the stilbenoids in *Ampelopsis sinica* (Miq.) W. T. Wang which was traditionally used to treat arthritis⁶. In our study on the constituents of the roots of *A. sinica*, a new and four known resveratrol tetramers were isolated. In this paper, we report the isolation and structure determination of the new tetramer—sinicin A.



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Roots of *A. sinica* were extracted with 95% EtOH. The alcohol extract was extracted in Soxhlet apparatus with CHCl₃, EtOAc, acetone and methanol, respectively. The EtOAc fraction was subjected to silica gel column chromatography eluted with cyclohexane-acetone and CHCl₃-CH₃OH, MPLC with CH₃OH-H₂O to provide five compounds.

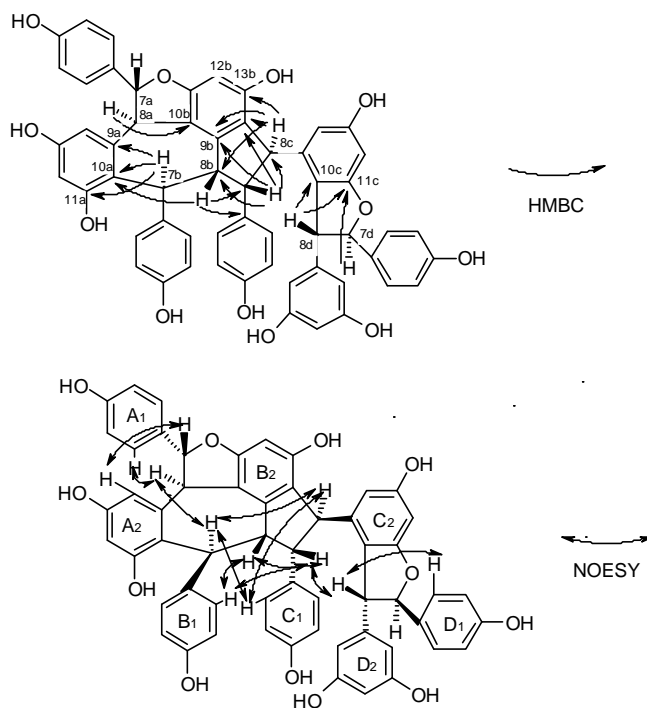
Compound **1**, obtained as a brown amorphous powder, exhibited strong blue violet fluorescence under UV light at 254 nm. The compound **1** gave an [M+H]⁺ ion peak at *m/z* 907 in FABMS corresponding to the molecular formula C₅₆H₄₂O₁₂, which suggested that **1** was a resveratrol tetramer. Its ¹H NMR spectrum showed the presence of four sets of *ortho*-coupled aromatic protons assignable to four 4-hydroxyphenol groups [δ 7.60 (*d*, 2H, *J* = 8.4 Hz, H-2a, 6a) and 6.92 (*d*, 2H, *J*=8.4 Hz, H-3a, 5a); δ 6.92 (*d*, 2H, *J*=8.4 Hz, H-2b, 6b) and 6.53 (*br. d*, 2H, *J*=8.4 Hz, H-3b, 5b); δ 6.15 (*d*, 2H, *J*=8.7 Hz, H-2c, 6c) and 6.21 (*d*, 2H, *J*=8.7 Hz, H-3c, 5c); δ 7.36 (*d*, 2H, *J*=8.4 Hz, H-2d, 6d) and 7.03 (*d*, 2H, *J* = 8.4 Hz, H-3d, 5d)]. The ¹H NMR spectrum also displayed the presence of a 3, 5-dihydroxyphenol group [δ 5.93 (*d*, 2H, *J*=2.1 Hz, H-10d, 14d) and 6.05 (*t*, 1H, *J*=2.1 Hz, H-12d)], two sets of *meta*-coupled aromatic protons on a 1, 2, 3, 5-tetra-substituted benzene ring [δ 6.04 (*d*, 1H, *J*=2.4 Hz, H-12a) and 6.29 (*d*, 1H, *J*=2.4 Hz, H-14a); δ 6.29 (*d*, 1H, *J*=2.4 Hz, H-12c) and 6.00 (*d*, 1H, *J*=2.4 Hz, H-14c)], an isolated aromatic proton on a penta-substituted benzene ring [δ 6.22 (*s*, 1H, H-12b)], two sets of mutually coupled aliphatic protons assignable to the dihydrofuran rings [δ 5.94 (*d*, 1H, *J*=10.5 Hz, H-7a) and 5.20 (*d*, 1H, *J*=10.5 Hz, H-8a); δ 5.32 (*d*, 1H, *J*=3.0 Hz, H-7d) and 4.50 (*d*, 1H, *J*=3.0 Hz, H-8d)] and a sequence of four aliphatic methine protons successively in the ¹H-¹H COSY spectrum [δ 4.32 (*d*, 1H, *J*=12.0 Hz, H-7b), 4.00 (*m*, 1H, H-8b), 3.78 (*d*, 1H, *J*=6.0 Hz, H-7c) and 4.00 (*s*, 1H, H-8c)]. The ¹³C NMR spectrum exhibited twenty-four quaternary carbons and thirty-two methine carbons which could be assignable by the HMQC spectrum (**Table 1**). The planar structure could be determined by the long-range correlations in the HMBC spectrum (**Figure 1** and **Table 1**). To clarify the relative stereochemistry of **1**, NOESY spectrum has been carried out. In the NOESY spectrum (**Figure 1** and **Table 1**), the NOEs between H-7a/H-14a, H-8a/H-2(6)a; H-8c/H-2(6)c; H-7d/H-10(14)d, H-8d/H-2(6)d revealed a *trans* orientation of ring A₁ and A₂, C₁ and C₂, D₁ and D₂, respectively. The NOEs between H-8a/H-7b, H-7b/H-8c suggested a *cis* orientation of H-8a, H-7b and H-8c. The NOEs between H-8b/H-7c, H-7c/H-8d suggested a *cis* orientation of H-8b, H-7c and H-8d. Thus, the stereochemistry of **1** was determined (shown in **Figure 1**) and the relative configuration is (7aR, 8aR, 7bS, 8bR, 7cR, 8cR, 7dR, 8dR).

In addition to **1**, four known resveratrol tetramers were isolated and their structures were identified as vitisin A, *cis*-vitisin B, ampelopsin H and hopeaphenol, respectively, by the spectral analysis and comparison with respective authentic samples.

Table 1. ^1H and ^{13}C NMR spectral data for **1** (in acetone- d_6)

	δ_{H} ppm (<i>J</i> Hz)	δ_{C}	HMBC	NOESY
1a		130.6		
2,6a	7.600 d (8.4)	130.3	C-2, 6a, C-4a, C-7a	H-7a, H-8a, H-14a
3,5a	6.920 d (8.4)	116.1	C-1a, C-3, 5a, C-4a	
4a		158.6		
7a	5.941 d (10.5)	90.2	C-2, 6a, C-9a	H-2, 6a, H-14a
8a	5.197 d (10.5)	48.5	C-1a, C-9a, C-10b	H-2, 6a, H-7b
9a		142.1		
10a		121.9		
11a		158.1		
12a	6.035 d (2.4)	103.5	C-10a, C-13a, C-14a	
13a		157.2		
14a	6.289 d (2.4)	105.0	C-8a, C-10a, C-12a, C-13a	H-2, 6a, H-7a
1b		132.7		
2,6b	6.920 d (8.4)	132.1		H-7c, H-7b, H-8b
3,5b	6.533 br.d (8.4)	115.0	C-1b, C-3, 5b	
4b		156.3		
7b	4.323 d (12.0)	45.4	C-9a, C-10a, C-11a, C-2, 6b, C-8b, C-9b	H-2, 6b, H-2, 6c, H-8a, H-8c
8b	3.998 m	47.2	C-10a, C-1c, C-9b, C-14b	H-2, 6b, H-8d, H-7c
9b		147.0		
10b		117.8		
11b		159.8		
12b	6.221 s	95.9	C-10b, C-11b, C-14b	
13b		155.4		
14b		122.0		
1c		134.0		
2,6c	6.147 d (8.7)	128.9	C-2, 6c, C-4c, C-7c	H-7c, H-8c, H-7b
3,5c	6.214 d (8.7)	114.9	C-1c, C-3, 5c, C-4c	
4c		155.8		
7c	3.777 d (6.0)	61.4	C-8b, C-9b, C-14b, C-1c, C-2, 6c, C-8c, C-9c	H-2, 6b, H-2, 6c, H-8d, H-8b
8c	3.998 s	52.9	C-8b, C-9b, C-13b, C-14b, C-1c, C-7c, C-9c, C-10c, C-14c	H-2, 6c, H-14c, H-7b, H-10, 14d
9c		143.0		
10c		119.1		
11c		162.7		
12c	6.289 d (2.4)	95.9	C-10c, C-11c, C-13c, C-14c	
13c		159.4		
14c	6.004 d (2.4)	107.1	C-8c, C-10c, C-12c	H-8c
1d		134.8		
2,6d	7.356 d (8.4)	127.7	C-2, 6d, C-4d, C-7d	H-7d, H-8d
3,5d	7.029 d (8.4)	116.3	C-1d, C-3, 5d, C-4d	
4d		158.3		
7d	5.323 d (3.0)	93.9	C-11c, C-2,6d, C-9d	H-2, 6d, H-10, 14d
8d	4.504 d (3.0)	56.8	C-10c, C-11c, C-1d, C-9d, C-10, 14d	H-2,6d, H-10,14d, H-8b, H-7c
9d		146.4		
10,14d	5.926 d (2.1)	106.5	C-8d, C-10, 14d, C-11,13d, C-12d	H-7d, H-8d, H-8c
11,13d		159.4		
12d	6.054 t (2.1)	101.9	C-10, 14d, C-11,13d	

Figure 2 Significant NOE and ^{13}C - ^1H long-range correlations observed in the NOESY and HMBC spectra of **1**



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