Flexuosol A, a New Tetrastilbene from *Vitis flexuosa*

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A novel tetrastilbenoid, flexuosol A (**1**), was isolated from the stems of *Vitis flexuosa* together with the known gnetin A, (+)-ϵ-viniferin, vitisin A, and hopeaphenol. The structure of **1** was elucidated using spectral methods.

Vitis flexuosa Thunb.(Vitaceae), a perennial herb growing in mainland China, is used in the treatment of diseases of the viscera and for quenching thirst.[1] Plants in the genus *Vitis* commonly contain oxidative oligomers of resveratrol.[2,3] Although the chemical composition of *V. flexuosa* has not been investigated previously, we now report the isolation and structure elucidation of a new tetrastilbenoid, flexuosol A (**1**), along with two distilbenoids, gnetin A[4] and (+)-ϵ-viniferin,[3] and two tetrastilbenoids, vitisin A[2] and hopeaphenol,[5−9] from the stems of this species.

Flexuosol A (**1**) was obtained as a brown solid, $[\alpha]_D$ −99.6° (*c* 0.15, MeOH). It exhibited an $[MH]^+$ ion at *m*/*z* 907 in its positive FABMS, which along with the analysis of its ^1H and ^{13}C NMR data, led to the molecular formula $C_{56}H_{42}O_{12}$, which corresponded to that of a tetrastilbenoid. The UV (284, 322 nm) and IR (3434, 1614, 1605, 1515, 1448, 960 cm^{-1}) spectra of **1** showed similar patterns to those of other oligostilbenes.[2,3] The ^1H NMR spectrum indicated the presence of eight sets of *ortho*-coupled aromatic proton signals [δ 6.52, 6.55; 6.57, 6.72; 6.76, 7.04; 6.80, 7.19 (each 2H, d, J = 8.6 Hz)], two sets of AX_2-type *meta*-coupled aromatic proton signals [δ 6.11 (2H, d, J = 2.0 Hz) and 6.18 (1H, t, J = 2.0 Hz); δ 6.20 (2H, d, J = 2.0 Hz) and 6.17 (1H, t, J = 2.0 Hz)], one set of *meta*-coupled aromatic proton signals [δ 6.08, 6.30 (each 1H, d, J = 2.0 Hz)], and a single aromatic proton signal [δ 6.43-(1H, s)], as well as three sets of mutually coupled aliphatic proton signals [δ 4.42, 5.13 (each 1H, br s); δ 4.49, 5.32 (each 1H, d, J = 5.0 Hz); δ 4.50, 5.42 (each 1H, d, J = 6.0 Hz)]. In addition, the ^1H NMR spectrum also exhibited a signal at δ 6.50 (2H, br s) for olefinic protons present in the resveratrol unit. Furthermore, the UV (322 nm) and IR (960 cm^{-1}) spectrum demonstrated that the olefinic protons of **1** could be in *trans*-orientation.[2,10−11]

When the ^1H NMR and ^{13}C NMR data of **1** were compared with those of miyabenol C[12] and ampelopsin E,[13] the data for substituents in rings A1−3, B1−3, and C1 in **1** were found to be similar to those of miyabenol C,[12] while the data for substituents in rings D1−3, C1−2, and B1−2 in **1** were similar to those of ampelopsin E.[13] Therefore, it was assumed that **1** was formed by the coupling of one miyabenol C or ampelopsin E molecule and one resveratrol molecule. The 2D NMR spectra of **1** including H−H COSY, C−H COSY and COLOC allowed the assignment of all proton and carbon signals (Table 1). In the H−H COSY spectrum of **1**, several significant correlations were detected: δ 4.42→5.13, δ 4.49→5.32, and δ 4.50→5.42. The C−H COSY spectrum of **1** showed signals for six carbons at

Table 1. ^1H and ^{13}C NMR Spectral Data for **1** in Me_2CO-d_6

position	δ_H (mult., J)	H−H COSY	δ_c (mult.)[a]	COLOC
1a			133.0 (s)	H-8a
2 (6)a	7.04 (d, 8.6)	H-3 (5)a	128.0 (d)	
3 (5)a	6.76 (d, 8.6)	H-2 (6)a	116.4 (d)	
4a			158.2 (s)	
7a	5.32 (d, 5)	H-8a	94.2 (d)	
8a	4.49 (d, 5)	H-7a	57.1 (d)	
9a			147.6 (s)	H-7a, 8a
10 (14)a	6.11 (d, 2)	H-12a	106.9 (d)	
11 (13)a			160.3 (s)	
12a	6.18 (t, 2)	H-10 (14)a	102.2 (d)	
1b			133.1 (s)	H-8b
2 (6)b	6.52 (d, 8.6)	H-3 (5)b	127.7 (d)	
3 (5)b	6.55 (d, 8.6)	H-2 (6)b	115.7 (d)	
4b			157.7 (s)	
7b	5.13 (br s)	H-8b	92.2 (d)	
8b	4.42 (br s)	H-7b	51.3 (d)	
9b			143.0 (s)	H-7b, 8b
10b			118.7 (s)	H-8b
11b			162.5 (s)	H-12b
12b	6.30 (d, 2)	H-14b	96.6 (d)	
13b			160.1 (s)	H-12b
14b	6.08 (d, 2)	H-12b	107.9 (d)	
1c			133.1 (s)	
2 (6)c	6.72 (d, 8.6)	H-3 (5)c	128.5 (d)	
3 (5)c	6.57 (d, 8.6)	H-2 (6)c	116.5 (d)	
4c			158.0 (s)	
7c	6.50 (br s)		133.4 (d)	
8c	6.50 (br s)		122.6 (d)	
9c			129.6 (s)	
10c			121.5 (s)	H-7/8c, H-7, 8b
11c			162.2 (s)	H-7b, 8b
12c	6.43(s)		91.9 (d)	
13c			162.4 (s)	
14c			120.4 (s)	H-7/8c
1d			133.6 (s)	H-3/5d
2 (6)d	7.19 (d, 8.6)	H-3 (5)d	128.2 (d)	
3 (5)d	6.80 (d, 8.6)	H-2 (6)d	116.2 (d)	
4d			158.2 (s)	H-2/6d
7d	5.42 (d, 6)	H-8d	94.5 (d)	
8d	4.50 (d, 6)	H-7d	58.0 (d)	
9d			146.7 (s)	
10 (14)d	6.20 (d, 2)	H-12d	107.2 (d)	
11 (13)d			159.8 (s)	H-10/14d
12d	6.17 (t, 2)	H-10 (14)d	102.6 (d)	

[a] Multiplicities were determined by DEPT.

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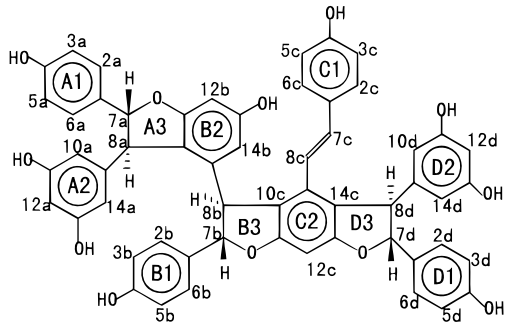
δ 51.3, 92.2; 57.1, 94.2; and 58.0, 94.5, which had cross peaks to six aliphatic methine protons at δ 4.42, 5.13; δ 4.49, 5.32; and δ 4.50, 5.42, respectively. It also showed the following additional correlations: δ 91.9→6.43 and δ 122.6, 133.4→6.50. The planar structure was deduced mainly from the COLOC results such as the following correlations: δ 133.0 (C-1a)→4.49 (H-8a); δ 147.6 (C-9a)→5.32 (H-7a) and 4.49 (H-8a); δ 118.7 (C-10b)→4.42 (H-8b); δ 143.0 (C-9b)→4.42 (H-8b) and 5.13 (H-7b); δ 133.1 (C-1b)→4.42 (H-8b); δ 121.5 (C-10c)→6.50 (H-7c, 8c), 4.42 (H-8b), and 5.13 (H-7b); and δ 120.4 (C-14c)→6.50 (H-7/8c).

The relative configuration of **1** was established by NOESY. The *trans*-orientation of the two aryls on ring A3 was deduced from the NOEs between H-7a/H-10(14)a and H-8a/H-2 (6)a. Two similar relationships were observed for the protons on ring B3 and D3. The presence of NOEs between H-8a and H-8b indicated the spatial vicinity of these protons. In addition, the fact that the ^{1}H NMR signals of H-10 (14)a and H-2 (6)b appeared at relatively high fields was accounted for by overlapping of rings A2 and B1. Therefore, we determined that the relative configuration between ring A3 and B3 was rel-(8a*R*,8b*S*). The coexistence of **1** with gnetin A, (+)-ϵ-viniferin, vitisin A, and hopeaphenol in the same plant also gave some biogenetic support to this structure. Thus, the structure of **1** was concluded to be as shown.



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Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin−Elmer-241 polarimeter. UV spectra were recorded on a Cintra 20 UV−vis spectrometer and IR spectra on a Nicolet MX-1 spectrophotometer. NMR spectra were recorded using a Bruker AM-400 system at normal probe temperature (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz). FABMS were recorded on a VG AutoSpec-3000 instrument.

Plant Material. The stems of *V. flexuosa* Thunb. were collected in Xinjin, Sichuan Province, People's Republic of China, in September 1996, and identified by Prof. C. L. Li, Chengdu Institute of Biology, The Chinese Academy of Sciences, where a voucher specimen was deposited.

Extraction and Isolation. Dried and finely powdered stems of *V. flexuosa* (980 g) were extracted with Me_2CO at room temperature. The Me_2CO extract (90 g) was partitioned with EtOAc (2 L) and H_2O (2 L) to yield the EtOAc fraction (58 g) and a water-soluble extract. The EtOAc residue (20 g) was subjected to column chromatography over Si gel with the column eluted successively with *n*-hexane−EtOAc mixtures of increasing polarity. The *n*-hexane−EtOAc (1:4) eluting fraction was then chromatographed over Si gel with $CHCl_3$−MeOH (10:0−10:3) mixtures, the $CHCl_3$−MeOH (10:1.5) fraction was followed by preparative TLC [$CHCl_3$−MeOH (4:1); R_f = 0.37] to yield **1** (160 mg), gnetin A (9 mg), (+)-ϵ-viniferin (820 mg), vitisin A (230 mg), and hopeaphenol (150 mg).

Flexuosol A (1): brown amorphous solid; $[\alpha]_D$ −99.6° (*c* 0.15, MeOH); UV λ_{max} (MeOH) (log ϵ) 322 (4.44), 284 (4.52) nm; IR (KBr) 3434, 1614, 1605, 1515, 1448, 1241, 1241, 1171, 1157, 1122, 1003, 960, 832 cm^{-1}; NMR data, see Table 1; FABMS (positive) *m/z* 907 ([M + H]$^+$), 813, 663, 453, 347, 282, 219, 147, 111.

The spectroscopic data of gnetin A,[4] (+)-ϵ-viniferin,[3] and vitisin A[2], and hopeaphenol[5−9] were consistent with those publications in the literatures.

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