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STILBENE DERIVATIVES IN THE STEM OF *PARTHENOCISSUS QUINQUEFOLIA*

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Key Word Index—*Parthenocissus quinquefolia*; Vitaceae; stilbenoid; resveratrol; parthenocissin A; parthenocissin B.

Abstract—From the stem of *Parthenocissus quinquefolia*, two new resveratrol oligomers, parthenocissins A and B, were isolated in addition to three known stilbenes. The structures, 1*Z*-2α,3β-2-(3,5-dihydroxyphenyl)-2,3-dihydro-3-(4-hydroxyphenyl)-1-[(4-hydroxyphenyl)methylene]-1*H*-indene-4,6-diol (parthenocissin A) and 1*Z*,2α,3β,4′α,5′β-2-(3,5-dihydroxyphenyl)-2,3-dihydro-3(4-hydroxyphenyl)-1-[{4′-(3,5-dihydroxyphenyl)-3′-(4-hydroxyphenyl)-4,5-dihydrofurano(2′,3′:4,3)-phenyl}methylene]-1*H*-indene-4,6-diol (parthenocissin B), were elucidated by the analysis of spectral data including 2D-NMR and NOE experiment.

INTRODUCTION

Many stilbene derivatives have been isolated from Vitaceous plants, and biological activities such as chemopreventive [1] and hepatoprotective [2] have been shown for resveratrol. Stilbenoids are, therefore, potentiality useful lead compounds. Vitaceous plants which are known to be good sources of stilbenoids are classified to 11 genera and about 700 species. Nevertheless, phytochemical studies of these plants are few. Previously, we have reported on the isolation and structural elucidation of stilbene derivatives from *Parthenocissus tricuspidata* (Siebold et Zucc.) Planch. [3]. In this paper, we now wish to report on the structures of five stilbene derivatives from the stem of *P. quinquefolia* (L.) Planch. which is native in North America and is sometimes planted as a cover crop in other areas.

RESULTS AND DISCUSSION

An acetone extract of the stem of *P. quinquefolia* was chromatographed on silica gel and purified by silica gel and preparative TLC to give two stilbene oligomers, parthenocissins A (**1**) and B (**2**), in addition to three known stilbenes (**3**–**5**).

Compound **1**, parthenocissin A, gave a $[M-H]^-$ peak at *m/z* 453 on negative ion FABMS corresponding to the molecular formula $C_{28}H_{22}O_6$. Its UV spectrum suggested that **1** was a resvertrol dimer. The ^1H NMR spectrum showed the presence of six phenolic hydroxyl groups [δ 7.73, 8.08, 8.10 (×2), 8.13 and 8.20], which was supported by methylation of **1** to produce a hexamethyl ether (**1a**: $[M-H]^-$ *m/z* 547). The ^1H NMR spectrum of **1a** (Table 1) contained two sets of *ortho*-coupled protons assignable to two *para*-methoxyphenyl groups in an AA′XX′ type of arrangement [δ 7.53 (2H, *d*, *J* = 8.8 Hz, H-2a and 6a), 6.95 (2H, *d*, *J* = 8.8 Hz, H-3a and 5a); 7.06 (2H, *d*, *J* = 8.8 Hz, H-2b and 6b), 6.81 (2H, *d*, *J* = 8.8 Hz, H-3b and 5b)], protons of a 3,5-dimethoxyphenyl group in an AX_2 type of arrangement [δ 6.36 (2H, *d*, *J* = 2.0 Hz, 10b and 14b), 6.34 (1H, *t*, *J* = 2.0 Hz, H-12b)], a set of *meta*-coupled two protons on a 1,2,3,5-tetra-substituted benzene ring [δ 6.40 (1H, *d*, *J* = 2.0 Hz, H-12a), 6.54 (1H, *d*, *J* = 2.0 Hz, H-14a), an olefinic proton [δ 6.44 (1H, *br s*, H-7a)] and two mutually coupled aliphatic protons [δ 4.30 (1H, *d*, *J* = 2.4 Hz, H-7b), 3.81 (1H, *br s*, H-8b)]. All protonated carbon signals in the ^{13}C NMR spectrum were assigned by the CH COSY spectrum (Table 2). In the HH long-range COSY spectrum, a correlation was observed between H-7a and H-8b. H-8b was changed to a doublet (*J* = 2.4 Hz) when H-7a was irradiated in the homogated decoupling experiment, and H-7a was sharpened on irradiation of H-8b. In the COLOC spectrum (Fig. 1), Significant CH long range correlations were observed between H-7a and three carbon signals [δ 130.75 (C-1a), 142.29 (C-9a) and 64.07 (C-8b)]. The olefinic proton could be assigned to that

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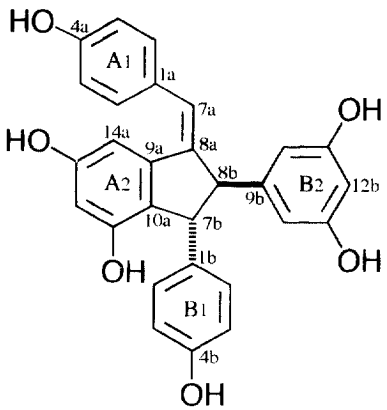

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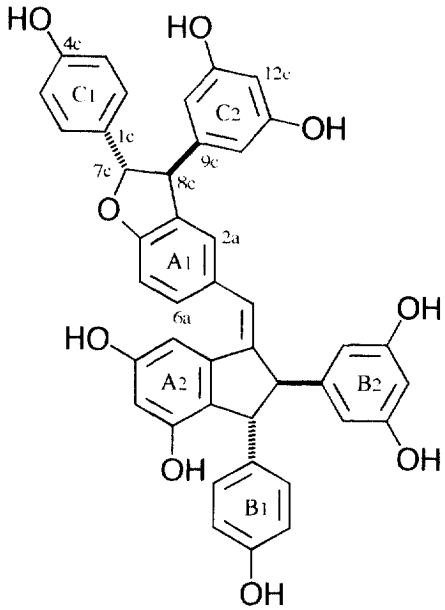

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Table 1. ^{1}H NMR spectral data of compounds **1** and **2** and their permethyl ethers (**1a** and **2a**)

H	**1**	**1a**	**2**	**2a**
2a	7.20 (*d*, 8.3)	7.53 (*d*, 8.8)	6.98 (*br d*, 1.0)	7.06 (*br d*, 1.0)
3a	6.72 (*d*, 8.3)	6.95 (*d*, 8.8)		
5a	6.72 (*d*, 8.3)	6.95 (*d*, 8.8)	6.96 (*d*, 8.3)	6.95 (*d*, 8.3)
6a	7.20 (*d*, 8.3)	7.53 (*d*, 8.8)	7.33 (*br dd*, 8.3, 1.0)	7.29 (*br dd*, 8.3, 1.0)
7a	6.31 (*br s*)	6.44 (*br s*)	6.34 (*br s*)	6.43 (*br s*)
12a	6.26 (*d*, 1.5)	6.40 (*d*, 2.0)	6.29 (*d*, 1.5)	6.38 (*d*, 2.0)
14a	6.52 (*d*, 1.5)	6.54 (*d*, 2.0)	6.61 (*d*, 1.5)	6.50 (*d*, 2.0)
2b(6b)	6.99 (*d*, 8.8)	7.06 (*d*, 8.8)	6.96 (*d*, 8.8)	7.03 (*d*, 8.3)
3b(5b)	6.80 (*d*, 8.8)	6.81 (*d*, 8.8)	6.71 (*d*, 8.8)	6.78 (*d*, 8.3)
7b	4.26 (*d*, 1.8)	4.30 (*d*, 2.4)	4.27 (*d*, 1.7)	4.28 (*d*, 2.3)
8b	3.45 (*br s*)	3.81 (*br s*)	3.75 (*br s*)	3.89 (*m*)
10b(14b)	6.19(*br s*)	6.36 (*d*, 2.0)	6.18 (*d*, 2.0)	6.33 (*m*)
12b	6.19 (*br s*)	6.34 (*t*, 2.0)	6.19 (*t*, 2.0)	6.33 (*m*)
2c(6c)			7.26 (*d*, 8.3)	7.33 (*d*, 8.8)
3c(5c)			6.98 (*d*, 8.3)	6.94 (*d*, 8.8)
7c			5.43 (*d*, 8.3)	5.62 (*d*, 7.8)
8c			4.90 (*br d*, 8.3)	4.56 (*d*, 7.8)
10c(14c)			6.20 (*d*, 2.0)	6.41 (*d*, 2.0)
12c			6.23 (*t*, 2.0)	6.42 (*t*, 2.0)
OH	7.73, 8.08 8.10 (×2) 8.13, 8.20			
OMe		3.57 (C-13a) 3.61 (C-11a) 3.74 (C-4a) 3.78 (C-11b, 13b) 3.81 (C-4b)		3.53 (C-13a) 3.60 (C-11a) 3.69 (C-11b, 13b) 3.72 (C-11c, 13c) 3.74 (C-4b) 3.84 (C-4c)

Measured in acetone-d_6 (400 MHz). All protons were assigned by aid of HH and HH long-range COSY spectrum. Methoxyl protons were assigned by the difference NOE experiments.

Table 2. ^{13}C NMR spectral data of compounds **1** and **2** and their permethyl ethers (**1a** and **2a**)

C	1	1a	2	2a
1a	129.87	130.75	133.84	133.84
2a	130.57	130.66	126.47	126.16
3a	115.86	114.66	132.27	133.84
4a	157.15	159.86	159.77	159.81
5a	115.86	114.51	109.77	109.97
6a	130.57	130.66	129.76	130.29
7a	125.19	125.48	125.32	125.75
8a	149.86	149.26	149.55	149.31
9a	142.86	142.29	142.75	142.27
10a	128.04	130.42	128.67	130.47
11a	155.37	158.04	155.42	158.04
12a	104.12	100.12	104.42	100.25
13a	158.47	161.42	158.05	161.46
14a	103.12	100.81	103.48	100.59
1b	137.39	138.39	137.26	138.39
2b(6b)	128.92	128.76	128.95	128.76
3b(5b)	115.81	114.40	115.83	114.40
4b	156.48	159.02	156.52	159.02
7b	54.93	55.25	54.87	55.27
8b	64.44	64.07	64.46	63.89
9b	145.60	145.87	146.12	146.04
10b(14b)	106.94	106.35	106.61	106.30
11b(13b)	159.33	161.93	159.37	161.91
12b	101.45	98.34	101.53	98.36
1c			131.53	131.60
2c(6c)			128.74	128.17
3c(5c)			116.14	114.77
4c			158.42	160.68
7c			93.97	93.11
8c			57.87	58.26
9c			144.75	145.25
10c(14c)			107.49	106.94
11c(13c)			159.66	162.22
12c			102.44	99.44
OMe		55.42 (C-13a,4b)		55.40 (C-11c,13c)
		55.55 (C-4a,11a,11b,13b)		55.44 (C-4b)
				55.53 (C-13a,11b,13b)
				55.57 (C-11a,4c)

Measured in acetone-d_6 (100 MHz). All carbons were assigned by the aid of CH COSY and COLOC spectrum except **1**.

of trisubstituted ethylene. In the COLOC spectrum, a CH long-range correlation through ^3J was observed between C-8b and H-10b(14b). Therefore, the 3,5-dimethoxyphenyl group (ring B2) was connected at C-8b. A quaternary carbon [δ 138.39 (C-1b)] gave correlations with H-7b, H-8b and H-3b(5b). The *para*-methoxyphenyl group (Ring B1) was connected at C-7b. Considering the number of unsaturations and the other correlations which were observed in the COLOC spectrum (Fig. 1), a five-membered ring was present in **1a** and another *para*-methoxyphenyl group (ring A1) was connected at C-7a. In the difference NOE (DIFNOE) experiments, NOEs were observed between H-7a/H-8b and H-2a(6a)/H-14a. These results indicated the configuration of double bond to be *Z*. NOEs observed between H-8b/H-2b(6b) and H-7b/H-10b(14b) suggested that rings B1 and B2 were *trans*. Thus the total structures of parthenocissin A, and its hexamethyl ether were characterized as 1*Z*-2α,3β-2-(3,5-dihydroxyphenyl)-2,3-dihydro-3-(4-hydroxyphenyl)-1-[(4-hydroxyphenyl)-methylene]-1*H*-indene-4,6-diol (**1**) and **1a**, respectively.

Compound **2**, parthenocissin B, gave a $[M-H]^-$ peak at *m/z* 679 on negative ion FABMS which corresponds to the molecular formula $C_{42}H_{32}O_9$. Methylation of **2** gave a heptamethyl ether (**2a**: $[M-H]^-$ *m/z* 781), indicating that **2** was a resveratrol trimer. The ^1H NMR spectrum of **2** showed the presence of two sets of *ortho*-coupled aromatic protons in an AA′XX′ type arrangement assignable to two *para*-hydroxyphenyl groups [δ 6.96 (2H, *d*, *J* = 8.8 Hz, H-2b(6b), 6.71 (2H, *d*, *J* = 8.8 Hz, H-3b and 5b); 6.98 (2H, *br d*, *J* = 8.3 Hz, H-3c and 5c), 7.26 (2H, *d*, *J* = 8.3 Hz, H-2c and 6c)], aromatic protons due to

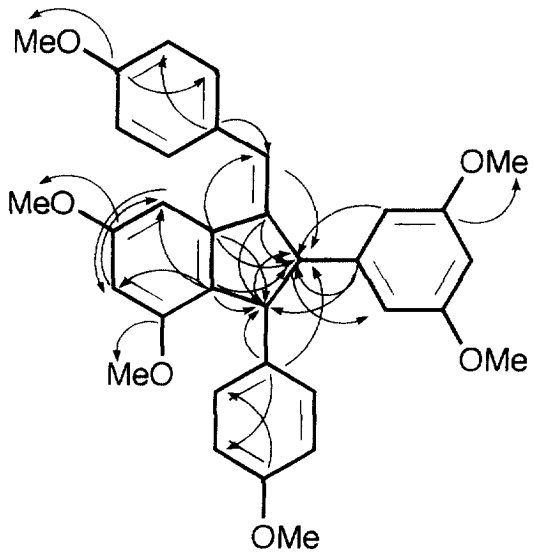

Fig. 1. CH long-range correlations in the COLOC spectrum (J = 10 Hz) of **1a**.

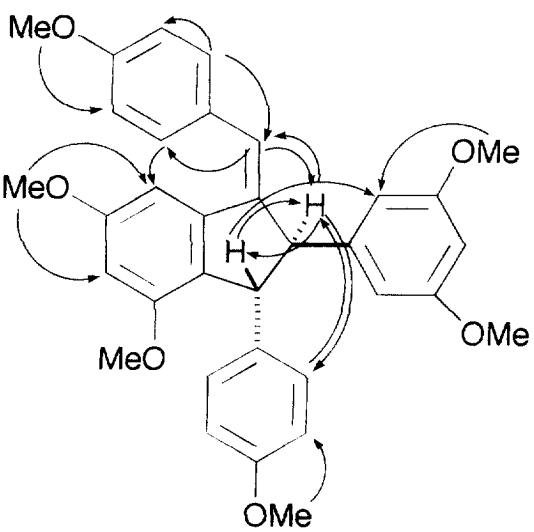

Fig. 2. NOE interactions in the difference NOE experiments of **1a**.

two 3,5-dihydroxyphenyl groups in an AX_2 type arrangement [δ 6.18 (2H, *d*, J = 2.0 Hz, H-10b and 14b), 6.19 (1H, *t*, J = 2.0, H-12b); 6.20 (2H, *d*, J = 2.0 Hz, H-10c and 14c), 6.23 (1H, *t*, J = 2.0 Hz, H-12c), protons in an ABX type [δ 6.98 (1H, *br d*, J = 1.0 Hz, H-2a), 6.96 (1H, *d*, J = 8.3 Hz, H-5a), 7.33 (1H, *br dd*, J = 8.3, 1.0 Hz, H-6a)], two *meta*-coupled protons of a 1,2,3,5-tetrasubstituted benzene ring [δ 6.29 (1H, *d*, J = 1.5 Hz, H-12a), 6.61 (1H, *d*, J = 1.5 Hz, H-14a)], an olefinic proton [δ 6.34 (1H, *br s*, H-7a)] and two sets of mutually coupled protons [δ 4.27 (1H, *d*, J = 1.7 Hz, H-7b), 3.75 (1H, *br s*, H-8b); 5.43 (1H, *d*, J = 8.3 Hz, H-7c), 4.90 (1H, *br d*, J = 8.3 Hz, H-8c)].

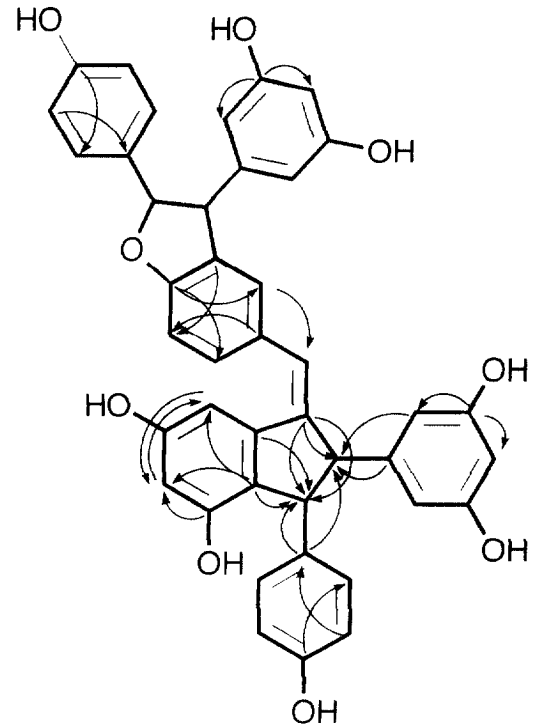

Fig. 3. CH long-range correlations in the COLOC spectrum (J = 10 Hz) of **2**.

The ^{1}H NMR spectral data of **2a** and all protonated carbon signals in the ^{13}C NMR spectrum assigned by the CH COSY spectrum are listed in Tables 1 and 2. In the HH long-range COSY spectrum, the olefinic proton was correlated with H-8b, H-2a and H-6a, respectively. Detailed analysis of the ^{1}H and ^{13}C NMR spectra including the HH long-range COSY, COLOC spectrum (Figs 3 and 4), DIFNOE and homogated decoupling experiments of **2** and **2a** revealed that **2** possessed one more resveratrol unit than **1** and that this resveratrol unit (ring C1—C-7-C-8—ring C2) formed a 2,3-dihydro-2,3-diarylbenzofuran next to ring A1. H-8 gave long-range correlations with C-1c and C-10c(14c) in the COLOC spectrum of **2a** (Fig. 4). Thus the *para*-hydroxyphenyl group in the resveratrol was substituted at C-7c and the 3,5-dihydroxyphenyl group was at C-8c. NOEs in the DIFNOE experiments were observed between H-7c/H-10c(14c) and H-8c/H-2c(6c). The configuration of the dihydrobenzofuran ring was thus deduced to be *trans*. Finally, the structure of parthenocissin B was characterized as 1*Z*,2α,3β,-4′α,5′β-2-(3,5-dihydroxyphenyl)-2,3-dihydro-3-(4-hydroxyphenyl)-1-[{4′-(3,5-dihydroxyphenyl)-3′-(4-hydroxyphenyl)-4,5-dihydrofurano(2′,3′:4,3)-phenyl}methylene]-1H-indene-4,6-diol (**2**).

Compounds **3**–**5** were determined as resveratrol (**3**), piceatannol (**4**) and resveratrol 3-*O*-β-glucopyranoside (**5**) by analysis of the spectral data and comparison of the authentic samples.

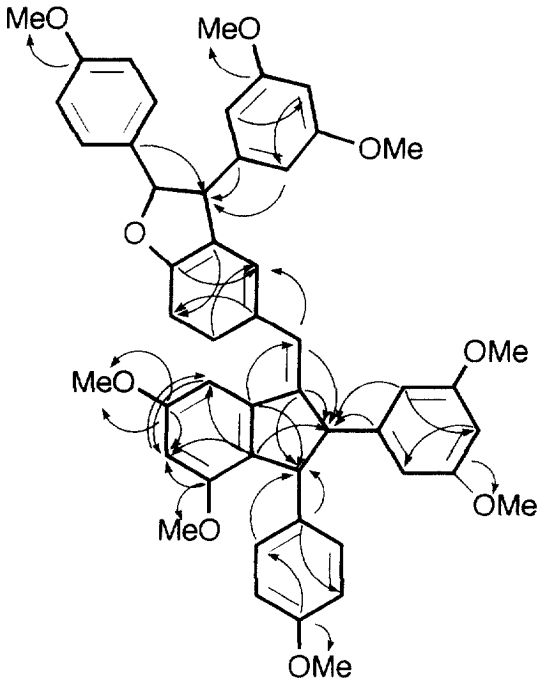

Fig. 4. CH long-range correlations in the COLOC spectrum ($J = 10$ Hz) of **2a**.

EXPERIMENTAL

Plant material

Stems of *Parthenocissus quinquefolia* grown in the herbal garden of the Setsunan University were collected in June 1996. The voucher specimen was deposited in the Herbarium of the Setsunan University.

Extraction and isolation

The dried and powdered stems of *P. quinquefolia* (250 g) were successively extracted with Me_2CO and MeOH at room temp. After concentration, the Me_2CO extract (20 g) was chromatographed on silica gel eluted with a $CHCl_3$–MeOH mixture. The $CHCl_3$–MeOH (8:1) fr. was further chromatographed by VLC and purified by prep TLC (PTLC) to give **3** (135 mg) and **4** (12 mg). The $CHCl_3$–MeOH (6:1) fr. was rechromatographed by VLC ($CHCl_3$–MeOH 5:1) and PTLC ($CHCl_3$–MeOH 4:1) to give **1** (130 mg), **2** (165 mg) and **5** (8 mg) in pure form.

Compound **1** (*parthenocissin A*). Colorless amorphous powder $[\alpha]_D -25°$ (MeOH, $c = 0.13$). UV (nm, MeOH): 216, 287, 315; Negative ion FABMS *m/z* 453 $[M-H]^-$.

Compound **2** (*parthenocissin B*). Colorless amorphous powder $[\alpha]_D -39°$ (MeOH, $c = 0.13$). UV (nm, MeOH): 225, 314, 335 *sh*; Negative ion FABMS *m/z* 679 $[M-H]^-$.

Methylation of **1** *and* **2**. Compounds **1** and **2** (each 30 mg) were heated with MeI/K_2CO_3 in dry Me_2CO (10 ml) under reflux for 6 h. After usual work-up, the resulting products were purified by PTLC (C_6H_6–Me_2CO) (20:1) to give **1a** (23 mg) and **2a** (28 mg) as colorless solids, respectively.

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