Stilbene Derivatives from *Cissus quadrangularis*

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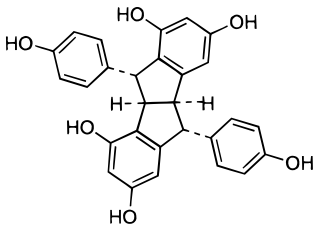
Three new stilbene derivatives, quadrangularins A, B, and C (**2**−**4**), have been isolated from the stems of *Cissus quadrangularis*, together with four known ones: resveratrol, piceatannol, pallidol (**1**), and parthenocissine A (**5**). Structure elucidation of the new compounds was achieved using 2D NMR experiments.

Previous studies on *Cissus quadrangularis* L. (Vitaceae) had led to the isolation of tetracyclic triterpenoids.[1,2] We report here the isolation from the stems of this plant of the known stilbenes resveratrol, piceatannol, and pallidol (**1**), together with three new related stilbene derivatives, quadrangularins A, B, and C (**2**−**4**). Another related stilbene parthenocissin A (**5**), which has been found recently in *Parthenocissus quinquefolia*,[3] and the known flavonols, quercetin and kaempferol, were further isolated.



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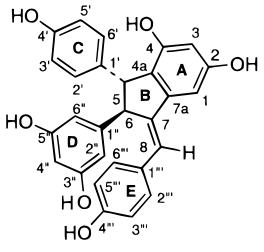

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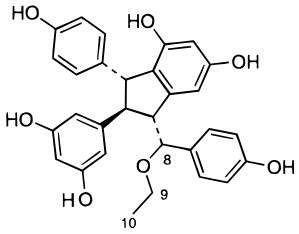
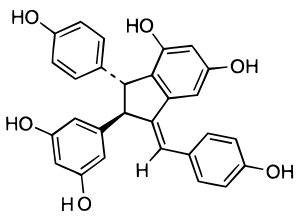


3 8*S*
4 8*R*



5

Quadrangularin A (**2**) gave a molecular peak in the HREIMS at *m*/*z* 454.1418, indicating the molecular formula $C_{28}H_{22}O_6$ to be isomeric with pallidol (**1**) and parthenocissin A (**5**). The ^{1}H NMR spectrum showed signals similar to those of **1**: an AA′BB′ system at *δ* 6.87 and 6.62 (2H, d, *J* = 8.5 Hz) corresponding to the *p*-disubstituted phenyl ring C along with two meta-coupled protons (*δ* 6.69 and 6.16, d, *J* = 2 Hz) and two aliphatic protons (*δ* 4.16, 4.02, s) of an indene AB ring system. The same signals were also found in **5**. Additional resonances in **2** indicated the presence of two other benzene rings: the 1,3,5 trisubstituted ring D (*δ* 6.21, 2H, d, *J* = 2 Hz and *δ* 6.09, t, *J* = 2 Hz) and the *p*-disubstituted ring E (*δ* 7.11 and 6. 59, 2H, d, *J* = 8.5 Hz), together with an olefinic proton singlet at *δ* 6.97. Similar signal patterns were observed in the spectrum of parthenocissin A (**5**), with somewhat different chemical shifts. These results suggested that **2** was the *E* isomer of compound **5**. The *E* geometry of the double bond was supported by the NOESY correlations H-8/H-1 and H-6/H-2‴, while the ^{13}C and the whole 2D NMR spectra (Table 1) entirely confirmed structure **2**. Especially, the HMBC correlations H-5/C-4, C-1′, H-6/C-2″, and H-8/C-6,C-2‴ showed unambiguously the positions of the aromatic rings on the five-membered B ring. In addition, the NOESY cross-peak H-6/H-2′ and H-5/H-2″ indicated that the relative stereochemistry at C-5 and C-6 was trans (depicted 5*β* and 6α as for **1** and **5**). A compound named ampelopsin D has been described previously,[4] whose NMR data are quite similar to those of **2**. The only structural variation from **2** was the relative position of rings B and C, which were interconverted. In fact, the reported structure of ampelopsin D is probably not exact and should be **2**.

Quadrangularin B (**3**) showed aromatic ^{1}H NMR signals similar to those of **2**, but the olefin signal was absent. Instead, additional resonances appeared in the aliphatic region, especially those of an C_2H_5O group: the Me triplet resonated at *δ* 0.96 (*J* = 7 Hz) and the two methylene protons at *δ* 2.96 and 3.20, respectively. This suggested that quadrangularin B (**3**) resulted from the addition of ethanol on either the olefinic derivative **2** or **5**. The mass spectrum showed no molecular ion peak, but a peak at *m*/*z* 454 [M − C_2H_5OH]$^+$. The structure of quadrangularin B was supported by its ^{13}C and 2D spectra (Table 1). The relative stereochemistry at C-5 and C-6 was similar to that of **3** as shown by the NOESY cross-peaks H-6/H-2′ and H-5/H-2″. To establish the configuration of C-7 and C-8, a NOESY spectrum was run at low temperature, so that the compound adopts a preferred conformation. The correlations H-7/H-2″ was diagnostic of a H-7*β* configuration, while the correlation H-1/H-2‴ indicated the proximity of the A and E rings. An additional cross-peak H-8/H-2′ was observed, and examination of molecular models showed that only the C-8*S* isomer could adopt a conformation at C-8 in accordance with the two latter-mentioned NOEs.

Quadrangularin C (**4**) was a stereoisomer of quadrangularin B, as shown by its 1D NMR data (Table 1), which were close to those of compound **3**. Again, the molecular ion peak could not be obtained, and only a peak at *m*/*z* 454 [M − C_2H_5OH]$^+$ was observed. The relative stereochemistry

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Table 1. ^{13}C (62.5 MHz) and ^{1}H NMRData (400 MHz) for Compounds **2**−**4** in CD_3OD[a]

	2				**3**				**4**			
position	δ_C	δ_H (*J* Hz)	HMBC	NOESY[b]	δ_C	δ_H (*J* Hz)	HMBC	NOESY[b]	δ_C	δ_H (*J* Hz)	HMBC	NOESY
1	98.5	6.69 d (2)	2,3,4a,7	8	106.3	5.62 d (2)	3,4a	7,2‴	106.6	6.67 d (2)	4a	7
2	159.6				158.5				159.0			
3	103.8	6.16 d (2)	1,2,4,4a		102.5	6.12 d (2)	1,2,4,4a		102.6	6.24 d (2)	1,2,4,4a	
4	156.1				155.3				155.3			
4a	125.9				123.8				123.3			
5	58.1	4.16 s	4,4a,6,7,7a,-1′,2′,1″	2′,2″	56.0	4.21 d (3)	4a,6,7a,-1′,2′,1″	6,2′,2″	56.0	4.17 d (2.5)	4,4a,6,7,7a,1′,2′	6,2′,2″
6	61.2	4.02 s	4a,5,7,7a,8,-1′,1″,2″	2′,2″,2‴	60.0	3.39 m	4a,7a	8,2′,2″	60.0	2.74 dd (3,2.5)	1,4a,5,7,7a,8,1′,1″	8,2′,2″, 2‴
7	143.4				61.7	3.31 m	7a,1″	8,2″,2‴	61.1	3.27 m	4a,5,6,7a,8,1″	8,2‴
7a	147.7				147.3				149.8			
8	123.1	6.97 s	6,7,7a,2‴		85.8	3.95 d (8.5)	6,7,7a,9,2″	9b,2′,2‴	86.8	3.95 d (9.5)	7,7a,9,1″,2″	2′,2‴
9					64.6	a 2.96 dq (9.7)		9b,10	65.0	a 3.14 dq (9.5,7)	8,10	9b
						b 3.20 dq (9,7)		10		b 3.28 dq (9.5,7)	8,10	10
10					15.3	0.96 t (7)	9		15.2	1.09 t (7)	9	
1′	138.5				138.5				138.2			
2′,6′	128.9	6.87 d (8.5)	5,3′,4′,6′	3′	129.5	6.81 d (8.5)	5,4′,6′		129.6	6.79 d (8.5)	5,4′,6′	
3′,5′	116.0	6.62 d (8.5)	1′,4′,5′		115.8	6.65 d (8.5)	1′,4′,5′		115.8	6.68 d (8.5)	1′,4′,5′	
4′	156.6				156.3				156.5			
1″	149.8				151.6				151.5			
2″,6″	106.6	6.21 d (2)	6,3″,4″,6″	2‴	106.6	6.09 d (2)	6,3″,4″,6″		106.2	5.73 d (2)	6,3″,4″,6″	
3″,5″	159.6				159.3				159.2			
4″	101.6	6.09 t (2)	2″,3″		101.3	6.07 t (2)	2″,3″		101.2	5.99 t (2)	2″,3″	
1‴	130.3				132.8				133.3			
2‴,6‴	131.2	7.11 d (8.5)	8,4‴,6‴	3‴	130.5	6.95 d (8.5)	8,4‴,6‴		130.5	6.66 d (8.5)	8,3‴,4‴,6‴	
3‴,5‴	116.0	6.59 d (8.5)	1‴,4‴,5‴		115.8	6.12 d (8.5)	1‴,4‴,5‴		115.8	6.60 d (8.5)	1‴,4‴,5‴	
4‴	156.5				158.0				157.9			

[a] Assignments based on 2D experiments. [b] Spectrum measured at 0 °C.

at C-5 and C-6 was similar to those of compounds **2** and **3** owing to the NOESY cross-peaks H-6/H-2′ and H-5/H-2″. In the spectrum at low temperature, the correlation between H-1 and and H-2‴ was absent, indicating that the E ring was no longer close to ring A. This was also supported by the lowfield shift (about 1 ppm) of H-1 in **4** compared to H-1 in **3**. Conversely, ring E was close to ring D as shown by the correlations H-6/H-2‴ and H-6/H-8. These correlations further indicated a H-7β configuration similar to that of **3**. Therefore, compound **4** varied from **3** only by the configuration of C-8. The C-8*R* configuration was confirmed by the cross-peak H-7/H-2‴ and H-8/H-2′, which, in addition to those mentioned above, could be observed only for the C-8*R* isomer. Compounds **3** and **4** may be artifacts derived from **2** and/or **5** by addition of EtOH during extraction.

Experimental Section

General Experimental Procedures. Optical rotations at 20 °C were obtained on a Perkin−Elmer 241 polarimeter. Spectra were recorded as follows: UV (MeOH), Varian Cary 100; NMR, Bruker AC 250 (^{1}H and ^{13}C NMR spectra) and AMX 400 (2D NMR spectra); HREIMS, Kratos MS 9. Vacuum-liquid chromatography (VLC) and column chromatography, Si gel Merck 60 H. Semipreparative HPLC, column Ultrasphere C_{18} (10 × 250 mm), MeOH−H_2O (40:60), flow rate 3 mL/mn, UV detection.

Plant Material. Climbing stems of *Cissus quadrangularis* (Vitaceae) were collected in June 1997, on Ondo Road, Ife-Ife, Nigeria. The material was identified and authenticated by Mr. G. A. Adesakin of the Herbarium, Department of Pharmacognosy, Obafemi Awolowo University, Ile-Ife, Nigeria. A voucher specimen (CQ/Pharm cog/12) is deposited at the Herbarium of the Department of Pharmacognosy, Obafemi Awolowo University, Ile-Ife, Nigeria.

Extraction and Isolation. The dried plant material (10 kg) was extracted with with EtOH−H_2O (4:1), yielding a crude extract (87 g) that was partitioned beween H_2O and *n*-hexane, CH_2Cl_2, EtOAc, and BuOH, successively. The CH_2Cl_2 extract (4 g) afforded an insoluble fraction, which was recrystallized from CH_2Cl_2, yielding quercetin (210 mg). The EtOAc extract (28 g) was fractionated by VLC using CH_2Cl_2 containing increasing amounts of MeOH. The fraction eluted with CH_2Cl_2−MeOH (95:5) was chromatographed on a Si gel column with *n*-heptane−EtOAc (4:1) yielding resveratrol (50 mg), piceatannol (20 mg), and kaempferol (30 mg). The fraction eluted with CH_2Cl_2−MeOH (90−10) was submitted to successive column chromatography and HPLC, yielding quadrangularin A (**2**) [90 mg; (1) column chromatography EtOAc−MeOH 99:1; (2) semipreparative HPLC], a mixture of quadrangularins B (**3**) and C (**4**) [60 mg; (1) column chromatography CH_2Cl_2−MeOH 99:1; (2) semipreparative HPLC], parthenocissin A (**2**) [70 mg; (1) column chromatography EtOAc−MeOH 99:1. (2) semipreparative HPLC], and pallidol (**1**) (55 mg; (1) column chromatography EtOAc−MeOH 98:2; (2), semipreparative HPLC]. The mixture of **3** and **4** was further separated by semipreparative HPLC on an analytical column (Novapak C_{18}, 4 × 125, CH_2Cl_2−MeOH 35:75, flow rate 1 mL/mn, UV detection) yielding **3** (4 mg) and **4** (8 mg). The known stilbenes resveratrol, piceatannol, and pallidol were identified by comparison of their NMR data with those reported.[5−7]

Quadrangularin A (2): amorphous gum, $[\alpha]_D$ −2° (MeOH); UV λ_{max} (log ϵ) 226 (sh) (4.68), 290 (sh) (4.25), 322 (4.39), 345 (sh) (4.25) nm; ^{1}H and ^{13}C NMR, see Table 1; HREIMS *m*/*z* 454.1418, M^+ ($C_{28}H_{22}O_6$, Δ 0.2 mmu).

Quadrangularin B (3): amorphous gum, $[\alpha]_D$ 0° (MeOH); UV λ_{max} (log ϵ) 226 (sh) (4.68), 280 (3.87) nm; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m*/*z* 454, $[M - C_2H_5OH]^+$.

Quadrangularin C (4): amorphous gum, $[\alpha]_D$ −1° (MeOH); UV λ_{max} (log ϵ) 226 (sh) (4.68), 280 (3.87) nm; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m*/*z* 454, $[M - C_2H_5OH]^+$.

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