Three New Resveratrol Oligomers from the Stem Bark of *Vatica pauciflora*

Tetsuro Ito,*,† Toshiyuki Tanaka,† Munekazu Iinuma,‡ Ken-ichi Nakaya,† Yoshikazu Takahashi,§ Ryuichi Sawa,§ Jin Murata,⊥ and Dedy Darnaedi||

Gifu Prefectural Institute of Health and Environmental Sciences, 1-1 Naka-fudogaoka, Kakamigahara 504-0838, Japan, Gifu Pharmaceutical University, 5-6-1, Mitahora-higashi, Gifu 502-8585, Japan, Microbial Chemistry Research Center, 3-14-23 Kamiosaki, Shinagawa-ku, Tokyo 141-0021, Japan, Botanical Gardens, Koishikawa, Graduate School of Science, University of Tokyo, 3-7-1, Hakusan, Bunkyo-Ku, Tokyo, 112-0001, Japan, and Indonesian Institute of Sciences, Jalan Ir. H. Juanda 13, Bogor 16122, Indonesia

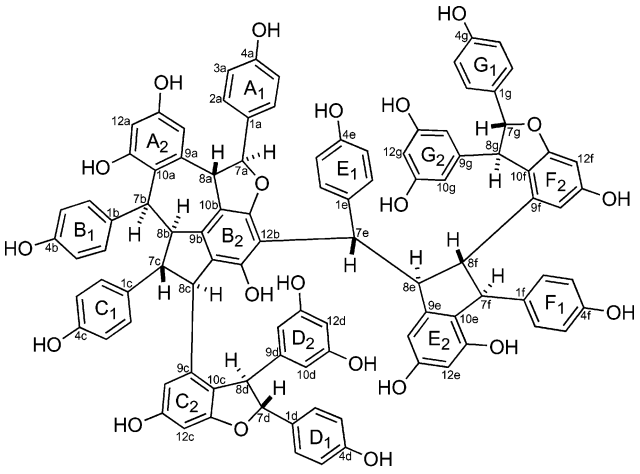
Received May 21, 2003

Three new stilbene oligomers (**1**−**3**) were isolated from the stem bark of *Vatica pauciflora*. The structures of a resveratrol heptamer (pauciflorol D) (**1**), a resveratrol dimer (pauciflorol E) (**2**), and an indanone derivative (pauciflorol F) (**3**) were elucidated by means of spectroscopic data interpretation, especially HMBC and NOESY NMR experiments.

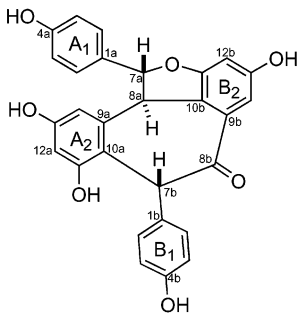
A number of resveratrol (3,5,4′-trihydroxystilbene) oligomers have been recently discovered in plants belonging to the Dipterocarpaceae.[1−6] Much attention has been paid to resveratrol and its oligomers because of their multifunctional bioactivities, e.g., cytotoxic,[3,4] antibacterial,[5,6] and anti-HIV effects.[4] *Vatica*, a genus comprising 65 species, belongs to the largest subfamily of Dipterocarpoideae in the Dipterocarpaceae, most of which are natural to Southeast Asia.[7] The genus *Vatica* is well known for its abundance of resveratrol oligomers.[3,8−10] In our preceding papers, the structures of resveratrol oligomers in the stem bark of *V. rassak* and *V. pauciflora* were described.[11−15] To further reveal the variation of resveratrol oligomers in this genus, an acetone extract of *V. pauciflora* Korth. was investigated and yielded a novel resveratrol heptamer, pauciflorol D (**1**), a new resveratrol dimer, pauciflorol E (**2**), and an indanone derivative, pauciflorol F (**3**). The structures of isolates **1**−**3** were elucidated by means of 2D NMR techniques such as ^{1}H−^{1}H COSY, ^{13}C−^{1}H COSY, and HMBC, and their stereostructures have been proposed by analysis of the NOESY spectra.

Results and Discussion

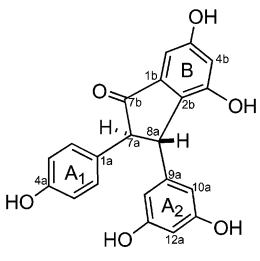
Pauciflorol D (**1**), a dark yellow amorphous powder, showed a positive reaction to Gibbs reagent. The molecular weight was determined to be 1586 based on a $[M + Na]^+$ ion at *m*/*z* 1609 in the positive-ion ESIMS. The molecular formula of $C_{98}H_{74}O_{21}$ was confirmed by HRESIMS (*m*/*z* $[M + Na]^+$ 1609.4583). The UV spectrum displayed an absorption maximum at 284 nm, which was consistent with one or more nonconjugated phenyl rings. The ^{1}H and ^{13}C NMR spectral data and analysis of ^{1}H−^{1}H COSY, ^{13}C−^{1}H COSY, and HMBC spectra [Tables 1 and S1 (Supporting Information)] exhibited the presence of seven 4-hydroxyphenyl groups (designated as A_1−G_1), two 3,5-dihydroxyphenyl groups (D_2 and G_2), four 3,5-dioxygenated-1,2-disubstituted benzene rings (A_2, C_2, E_2, and F_2), and five series of aliphatic protons, in the order H-7a/H-8a, H-7b/H-8b/H-7c/H-8c, H-7d/H-8d, H-7e/H-8e/H-8f/H-7f, and H-7g/H-8g.



1



2



3

The ^{1}H NMR spectrum exhibited signals for 18 phenolic hydroxyl groups (δ 4.70−8.53), which disappeared upon addition of D_2O. Considering the molecular formula, the remaining three oxygens could be allotted to ether linkages. In the HMBC spectrum (Table S1), significant ^3J correlations were observed between H-7a/C-2a(6a), H-14a/C-8a, H-7b/C-2b(6b), H-7c/C-2c(6c), H-8c/C-14c, H-7d/C-2d(6d), H-8d/C-10d(14d), H-7e/C-2e(6e), H-8e/C-10e, H-7f/C-2f(6f), H-8f/C-14f, H-7g/C-2g(6g), and H-8g/C-10g(14g), indicating that rings A_1, A_2, B_1, C_1, C_2, D_1, D_2, E_1, E_2, F_1, F_2, G_1, and G_2 are attached at C-7a, C-8a, C-7b, C-7c, C-8c, C-7d, C-8d, C-7e, C-8e, C-7f, C-8f, C-7g, and C-8g, respectively. Further correlations were observed between H-7b/C-11a, H-7d/C-10c, H-7f/C-11e, and H-7g/C-10f, which supported the

* To whom correspondence should be addressed. Tel: +81-583-80-2100. Fax: +81-583-71-5016. E-mail: tecchan.ito@nifty.ne.jp.
† Gifu Prefectural Institute of Health and Environmental Sciences.
‡ Gifu Pharmaceutical University.
§ Microbial Chemistry Research Center, Tokyo.
⊥ Botanical Gardens, Koishikawa, University of Tokyo.
|| Indonesian Institute of Sciences, Bogor.

10.1021/np030236r CCC: $27.50
Published on Web 05/12/2004

connections between C-7b/C-10a, C-8d/C-10c, C-7f/C-10e, and C-8g/C-10f, respectively. After complete assignment of all the quaternary carbons in rings A_1−G_1, A_2, and C_2−G_2, the remaining six quaternary aromatic carbons (C-9b−C-14b) in the ^{13}C NMR spectrum (δ_C 138.26, 116.01, 155.48, 113.90, 150.73, 119.62) were assigned to those of a 1,3-dioxygenated benzene ring (B_2). Similar patterns were also observed in vaticanols I and J,[11] where one of the aromatic rings was fully substituted and based on a 1,3-dioxygenated pattern. Two oxygenated carbon signals (C-11b and C-13b) correlated with H-7e, which indicated that C-7e was linked to C-12b. The other C−C linkages attached to ring B_2 (C-8a−C-10b, C-8b−C-9b, and C-8c−C-14b) were substantiated by the correlations of H-8a/C-10b, H-7b/C-9b, and H-8c/C-13b, respectively. Additional cross-peaks observed between H-7d/C-11c and H-7g/C-11f supported the presence of two ether linkages (C-7d/O/C-11c and C-7g/O/C-11f), both of which formed dihydrobenzofuran rings (C-7d/C-8d/C-10c/C-11c/O and C-7g/C-8g/C-10f/C-11f/O). Although no long-range correlation between H-7a/C-11b was observed, the presence of another dihydrobenzofuran ring (C-7a/C-8a/C-10b/C-11b/O) was deduced after considering the carbon chemical shifts and the molecular formula. The planar structure of pauciflorol C, which included three dihydrobenzofuran rings, was concluded to be **1**. The other correlations in the HMBC spectrum, as summarized in Table S1, were in accordance with this proposed planar structure. The structure is a resveratrol heptamer and can be regarded as a complex product composed of a resveratrol tetramer unit [resveratrols A−D (resveratrol A: ring A_1−C-7a−C-8a−ring A_2)] and a resveratrol trimer unit (resveratrols E−G). The planar structure of the tetrameric unit is identical to four known diastereomeric resveratrol tetramers of vaticaphenol A[3] (vaticanol B[14]) (**4**), isovaticanol B,[15] and viniferols B and C.[16]

The stereostructure of **1** was determined by analysis of the NOESY spectrum (Table S1). The *trans* orientations of H-7a/H-8a and H-7d/H-8d on the dihydrobenzofuran rings in the tetrameric unit were confirmed by the distinctive NOEs between H-7a/H-14a, H-8a/H-2a(6a), H-7d/H-10d(14d), and H-8d/H-2d(6d). The chemical shift of H-8a (δ 4.61) was regarded as a typical value observed when H-8a and H-7b occupy *anti* positions on a dibenzo[2,1]-heptadiene ring (C-8a/C-9a/C-10a/C-7b/C-8b/C-9b/C-10b).[3] Further evidence for this relationship was the distinctive NOE between H-8a/H-2b(6b). Significant NOEs between H-2c(6c)/H-8b and H-2c(6c)/H-8c indicated that H-8b and H-8c were of *syn* orientation on a benzocyclopentane ring (C-8b/C-9b/C-14b/C-8c/C-7c). The large coupling constant values of H-8b/H-7c (J = 11.1 Hz) and H-7c/H-8c (J = 11.1 Hz) also supported the *trans* stereo-relationship of H-8b/H-7c and H-7c/H-8c.[3,6] In addition, the *syn* orientation of ring B_1, H-7c, and ring C_2 was supported by NOEs between H-2b(6b)/H-7c, H-7c/H-14c, and H-2b(6b)/H-14c. The orientations of four sequential methine protons (H-7b, H-8b, H-7c, and H-8c) were finally determined as α, α, β, and α, respectively. In this experiment, the NOEs observed in the tetrameric unit were similar to those of vaticaphenol A.[3] The signals have close similarity to those of vaticaphenol A. In a dihydrobenzofuran ring of the trimeric unit, NOE interactions between H-7g/H-10g(14g) and H-8g/H-2g(6g) indicated that the orientations of protons (H-7g and H-8g) were *trans*. Small coupling constant values of three vicinal methine protons (H-8e, H-8f, and H-7f) on the benzocyclopentane ring (C-8e/C-9e/C-10e/C-7f/C-8f) suggested that all the protons were equatorial and that all of their dihedral angles were approximately 90°. These signals are similar

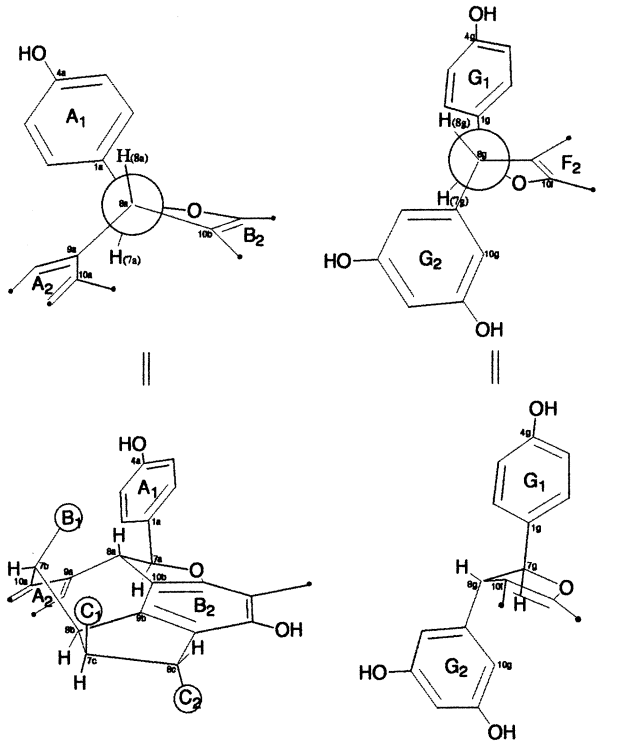


Figure 1. Stereostructure of dihydrobenzofuran rings in the molecular model of **1**.

to those of davidiol B[17] and vateriaphenol A,[18] both of which have benzocyclopentane moieties with equatorial protons. Further NOEs were observed between H-2f(6f)/8f and H-7f/H-14f, leading to the conclusion that the relative stereochemistry of the benzocyclopentane ring is the same as those of davidiol B and vateriaphenol A [H-8e(β), H-7g(α), and H-8g(β)]. The relationship between H-7e and H-8e was *trans* on the basis of the J value (12.5 Hz). The relative stereochemistry of the trimeric unit was elucidated. Therefore, the structure of pauciflorol D can be represented as **1** including relative stereochemistry.

Although three dihydrobenzofuran rings in **1** have the same orientation (*trans*), the ^1H−^1H coupling constants of the methine protons were quite different (H-7a/H-8a, J = 11.9 Hz; H-7d/H-8d, J = 3.7 Hz; H-7g/H-8g, J = 2.2 Hz). The conformational differences based on a molecular model are shown in Figure 1. The dihydrobenzofuran ring bearing H-7a and H-8a (C-7a/C-8a/C-10b/C-11b/O: furan A) was condensed to the dibenzobicyclo[5.3.0]decadiene system (C-8a/C-9a/C-10a/C-7b/C-8b/C-7c/C-8c/C-14b/C-9b/C-10b), while the furans D and G (C-7d/C-8d/C-10c/C-11c/O and C-7g/C-8g/C-10f/C-11f/O) were not condensed to additional rings. In the case of the furan A (left figure), the relative stereochemistry of the decadiene system and placement of ring A_2 requires a nearly *trans* diaxial conformation between H-7a and H-8a. As a result, rings A_1 and A_2 may be situated near one another. The distinct NOE between H-2a(6a)/H-14a and the coupling constant (J = 11.9 Hz) were well compatible. On the other hand, the protons on the furan rings D and G displayed small values (J = 3.7 Hz and J = 2.2 Hz). In these cases, the nearly *trans* diaxial conformation of the rings D_1/D_2 [G_1/G_2 (right figure)] resulted in much smaller angles of H-7d/H-8d (H-7g/H-8g). As a result, the lack of an NOE between H-2d(6d)/H-10d(14d) and H-2g(6g)/H-10g(14g) was reasonable. The C-8 position (C-8a, C-8d, and C-8G) of the dihydrobenzofuran rings behaved like an envelope.

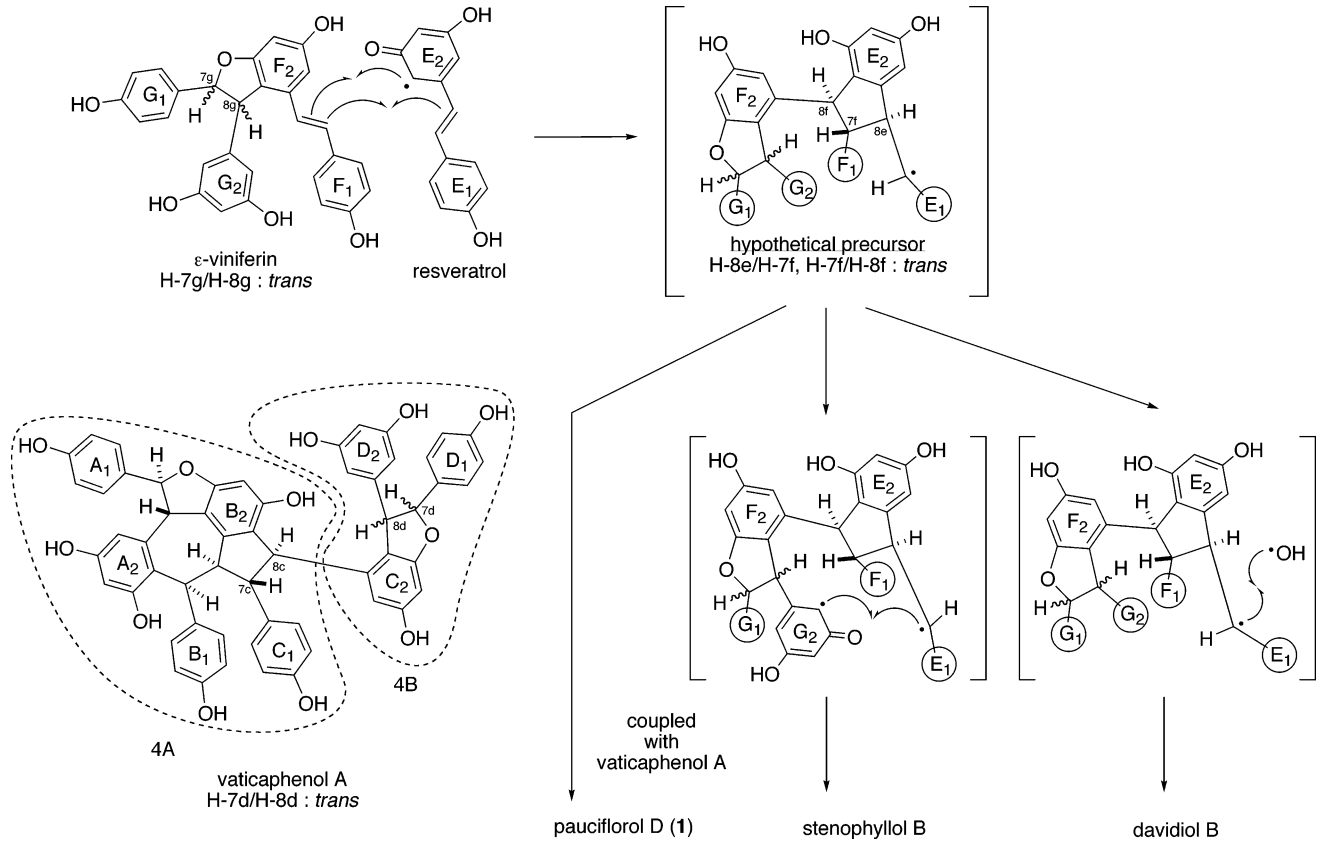


Figure 2. Possible biosynthetic formation of **1**, stenophyllol B, and davidiol B.

Previously, the relative stereochemistry of vaticaphenol A isolated from the stems of *V. diospyroides* was proposed by analysis of the NOESY spectrum and computer-aided energy-minimized stereostructures.[3] We have also reported the same oligomer named vaticanol B as a major constituent in the stem bark of *V. rassak*.[14] However, the stereo-relationship between 4A and 4B in Figure 2 has not been dealt with in both papers. The differences of stereochemistry at H-7d and H-8d being either α and *β* or *β* and α were not resolved by analysis of NOESY spectra, and therefore the stereo-relationship in pauciflorol D (**1**) still remains unclear. Biogenetically, pauciflorol D (**1**) is presumed to be formed by the oxidative coupling of the tetrameric unit (vaticaphenol A) and the trimeric unit that could be regarded as a hypothetical precursor of resveratrol trimers (Figure 2). The relative stereochemistry of the dihydrobenzofuran ring and the benzocyclopentane ring in the trimeric unit is the same as those of a hypothetical precursor of resveratrol trimers (stenophyllol B[19] and davidiol B[17]), all of which are constituents of *V. pauciflora*.[15] The occurrence of various resveratrol trimers and vaticaphenol A suggested that a resveratrol heptamer such as pauciflorol D (**1**) might be biologically synthesized by coupling these cognates. The occurrence of pauciflorol D is the second instance of a resveratrol heptamer. The first was vaticanol J isolated from the stem bark of *V. rassak*.[11]

Pauciflorol E (**2**), a yellow amorphous powder, showed a positive reaction to Gibbs reagent. The $[M - H]^-$ ion peak at *m/z* 467.1136 in the HRFABMS in the negative-ion mode corresponded to a molecular formula of $C_{28}H_{20}O_7$. An absorption band in the IR spectrum (1659 cm^{-1}) and a signal in the ^{13}C NMR spectrum (δ_C 195.26) indicated the presence of a carbonyl group (C-8b) in the molecule. The ^1H and ^{13}C NMR spectra, supported by $^1H-^1H$ COSY, $^{13}C-^1H$ COSY, and HMBC spectra (Table 2), revealed the presence of two 4-hydroxyphenyl groups (rings A_1 and B_1), two 1,2,3,5-tetrasubstituted benzene rings (rings A_2 and B_2), and a set of mutually coupled aliphatic protons (H-7a/H-8a). The spectrum further showed signals due to a methine proton (H-7b) and five phenolic hydroxyl groups (δ 8.42−8.94). Their positions on four aromatic rings (A_1, B_1, A_1, and B_2) were established by analysis of correlations in the HMBC spectrum. Considering the molecular formula, the remaining oxygen was attributable to an ether linkage. In the HMBC spectrum (Table 2), the correlations between H-2a(6a)/C-7a, H-14a/C-8a, H-2b(6b)/C-7b, H-14b/C-8b, and H-7b/C-11a revealed the linkages between C-1a/C-7a, C-8a/C-9a, C-1b/C-7b, C-8b/C-9b, and C-7b/C-10a, respectively. The spectrum also displayed significant correlations between H-7b/C-8b and H-7b/C-9b, which confirmed the linkages between C-8b/C-9b. Although no long-range correlation between H-7a/C-11b was observed, the presence of a dihydrobenzofuran ring [C-7a/C-8a/C-10b/C-11b/O] was clear considering the existence of an ether linkage. The planar structure of pauciflorol E was thus determined. To confirm the relative stereochemistry, a NOESY experiment was conducted (Table 2). Cross-peaks between H-7a/H-14a, H-8a/H-2a(6a), and H-2a(6a)/H-14a were observed, and cross-peaks substantiated the relative stereochemistry of the methine protons as *trans*. The relationship between H-7b and H-8a was determined to be *anti* on the basis of an NOE interaction between H-8a/H-2b(6b). The relative stereostructure of **2** was fully established.

Pauciflorol F (**3**), a yellow amorphous powder, showed a positive reaction to Gibbs reagent. The $[M]^+$ ion peak at *m/z* 364.0938 in the HREIMS corresponded to a molecular formula of $C_{21}H_{16}O_6$. Analysis of the ^1H and ^{13}C NMR, $^1H-^1H$ COSY, $^{13}C-^1H$ COSY, and HMBC spectra (Table 3) indicated that **3** had the following partial structures; a 4-hydroxyphenyl group (ring A_1), a 3,5-dihydroxyphenyl group (ring A_2), a 1,2,3,5-tetrasubstituted benzene ring

Table 1. ^{1}H and ^{13}C NMR Spectral Data of **1**[a]

position	δ_H	δ_C	position	δ_H	δ_C
1a		130.1	1e		136.9
2a, 6a	7.37 (d, 8.6)	129.4	2e, 6e	6.78 (d, 8.6)	129.5
3a, 5a	6.76 (d, 8.6)	115.3[b]	3e, 5e	6.19 (d, 8.6)	115.2
4a (OH)	7.89 (br s)	157.5[c]	4e		154.8
7a	5.75 (d, 11.9)	89.2	7e	4.18 (d, 12.5)	46.0
8a	4.61 (br d, 11.9)	48.1	8e	4.10 (d, 12.5)	56.1
9a		140.9	9e		148.1[f]
10a		123.9	10e		122.7
11a (OH)	8.15 (br s)	154.5	11e (OH)	7.52 (br s)	153.3
12a	6.25 (d, 2.0)	100.8	12e	6.35 (d, 2.0)	101.6[c]
13a (OH)	8.02 (br s)	155.7	13e (OH)	8.05 (br s)	157.5[c]
14a	6.12 (br d, 2.0)	105.2	14e	6.37 (d, 2.0)	106.2[d]
1b		132.6	1f		136.3
2b, 6b	7.20 (d, 8.6)	129.9	2f, 6f	6.08 (d, 8.6)	129.1
3b, 5b	6.89 (d, 8.6)	115.3[b]	3f, 5f	6.54 (d, 8.6)	114.4
4b		154.9	4f		154.7
7b	5.15 (d, 3.7)	36.1	7f	4.01 (s)	53.3
8b	3.01 (br d, 11.1)	52.2	8f	3.03 (s)	54.6
9b		138.3	9f		150.3[f]
10b		116.0	10f		118.2
11b		155.5	11f		160.6
12b		113.9	12f	6.16 (d, 2.0)	94.4
13b (OH)	4.70 (s)	150.7	13f (OH)	8.24 (br s)	158.9
14b		119.6	14f	5.92 (d, 2.0)	103.8
1c		129.7	1g		133.8
2c, 6c	6.34 (d, 8.6)	128.3	2g, 6g	7.01 (d, 8.6)	126.7
3c, 5c	6.45 (d, 8.6)	115.0	3g, 5g	6.87 (d, 8.6)	115.3[b]
4c		155.2	4g		156.8
7c	3.95 (t, 11.1)	57.0	7g	5.11 (d, 2.2)	92.7
8c	4.32 (d, 11.1)	49.1	8g	3.22 (d, 2.2)	54.0
9c		139.4	9g		149.0
10c		120.1	10g, 14g	5.90 (d, 2.2)	106.3
11c		162.0	11g, 13g		158.6
12c	6.44 (d, 2.2)	96.0	12g	6.42 (t, 2.2)	101.0
13c (OH)	8.53 (br s)	160.0			
14c	6.51 (d, 2.2)	106.9	OH	8.49 (2H), 8.41(2H), 8.34 (1H),	
1d		133.5		8.04 (1H), 7.94 (1H), 7.62 (1H)	
2d, 6d	7.10 (d, 8.6)	126.2		(each, br s)	
3d, 5d	6.81 (d, 8.6)	115.6		[OH-4b, 4c, 4d, 4e, 4f, 4g, 11g, 13g]	
4d		156.7			
7d	5.43 (d, 3.7)	93.7			
8d	4.14 (d, 3.7)	57.1			
9d		146.4			
10d, 14d	5.95 (d, 2.0)	106.2[d]			
11d, 13c (OH)	8.05 (br s)	159.0			
12d	6.26 (t, 2.0)	101.6[e]			

[a] Measured in CD_3COCD_3 at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR). [b–e] Overlapping signals. [f] Interchangeable.

(ring B), and a set of mutually coupled aliphatic protons (H-7a/H-8a). The presence of five hydroxyl groups and a carbonyl group was deduced from its IR bands (3369, 1694 cm^{-1}) and the five broad signals due to hydroxyl groups (δ 8.02−8.76) in the ^{1}H NMR spectrum. In the HMBC spectrum (Table 3), significant ^3J long-range correlations were observed between H-2a(6a)/C-7a, H-10a(14a)/C-8a, and H-8a/C-3b, indicating that three rings (A_1, A_2, and B) and two methine carbons (C-7a and C-8a) were connected by three C−C bonds (C-1a/C-7a, C-8a/C-9a, and C-8a/C-2b). Other ^3J long-range correlations between H-8a/C-7b, H-7a/C-1b, and H-6b/C-7b suggested that the carbons were connected in the order C-7b, C-1b, and C-6b. The planar structure of pauciflorol F, which had an indanone skeleton, was thus determined. The orientation of two methine protons (H-7a and H-8a) was determined to be *trans* on the basis of NOESY data (Table 3). Previously Oshima et al. in the course of their structure elucidation[20] reported a permethyl ether of **3** that is afforded by methylation of a resveratrol dimer (ampelopsin D) followed by ozonolysis. As described in our latest report, ampelopsin D is one of the constituents in this plant.[15] Biogenetically, the oxidative elimination of a C_6−C_1 unit from ampelopsin D and/or related cognates might produce pauciflorol F (**3**).

In our previous paper, variations of 25 resveratrol derivatives ranging from monomers to tetramers in the same extract have been disclosed.[15] The representative skeletons consist of dihydrobenzofuran rings, benzocyclopentane rings, dibenzo[2.1]octadiene systems, dibenzobicyclo[3.2.1]octadiene systems, and tribenzobicyclo[3.3.2]octatriene systems. Isolation of pauciflorols D (**1**)−F (**3**) adds complexity to the constituents due to their much higher order condensation (pauciflorol D) and the presence of a dibenzo[2.1]octadienone system (pauciflorol E) and an indanone skeleton (pauciflorol F).

Experimental Section

General Experimental Procedures. The following instruments were used: optical rotations, JASCO P-1020 polarimeter; UV spectra, Shimadzu UV-2200 spectrophotometer (in methanol solution); IR spectra, JASCO FT-IR-8000 spectrophotometer (KBr microplate); ^{1}H and ^{13}C NMR spectra, JEOL JNM LA-300 (chemical shift values in ^{1}H NMR spectra are presented as δ values with TMS as internal standard); EIMS and FABMS, JEOL JMS-DX-300 instrument; ESIMS, JEOL JMS-T100LC mass spectrometer. The following adsorbents were used for purification: analytical TLC, Merck Kieselgel 60 F_{254} (0.25 mm); preparative TLC, Merck Kieselgel

Table 2. ^{1}H and ^{13}C NMR Spectral Data of **2**[a]

position	δ_H	δ_C	HMBC	NOESY
1a		130.1		
2a, 6a	7.19 (d, 8.5)	129.5	4a, 7a	7a, 8a, 14a
3a, 5a	6.83 (d, 8.5)	115.9	1a	
4a (OH)	8.71 (br s)	158.2	3a(5a), 4a	
7a	5.94 (d, 10.8)	88.4	2a(6a), 8a, 9a	2a(6a), 14a
8a	4.52 (d, 10.8)	50.8	7a, 9a, 10a, 10b	2a(6a), 2b(6b)
9a		142.0		
10a		113.9		
11a (OH)	8.94 (br s)	159.0	10a, 11a, 12a	12a, 7b
12a	6.49 (br d, 2.2)	101.7	10a, 11a, 13a, 14a	OH-11a, OH-13a
13a (OH)	8.57 (br s)	158.0	12a, 13a, 14a	12a, 14a
14a	6.39 (br s)	105.3	8a, 10a, 12a, 13a	2a(6a), 7a, OH-13a
1b		128.2		
2b, 6b	6.77 (dd, 8.5, 1.1)	128.0	4b, 7b	8a, 7b
3b, 5b	6.70 (d, 8.5)	115.8	1b	OH-4b
4b (OH)	8.42 (br s)	156.8	3b(5b), 4b	3b(5b)
7b	6.06 (br s)	54.8	9a, 10a, 11a, 2b(6b), 8b, 9b	2b(6b), OH-11a
8b		195.3		
9b		133.7		
10b		123.9		
11b		160.4		
12b	6.45 (d, 2.4)	102.2	10b, 11b, 13b, 14b	OH-13b
13b (OH)	8.84 (br s)	158.5	12b, 13b, 14b	12b, 14b
14b	7.12 (d, 2.4)	106.5	8b, 10b, 12b, 13b	OH-13b

[a] Measured in CD_3COCD_3 at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR).

Table 3. ^{1}H and ^{13}C NMR Spectral Data of **3**[a]

position	δ_H	δ_C	HMBC	NOESY
1a		130.9		
2a, 6a	6.82 (d, 8.6)	128.7	4a, 7a	7a, 8a, 10a(14a)
3a, 5a	6.65 (d, 8.6)	115.4	1a, 4a	OH-4a
4a (OH)	8.25 (br s)	156.4	3a(5a), 4a	3a(5a)
7a	3.36 (d, 2.6)	64.4	1a, 2a(6a), 8a, 9a, 1b, 2b, 7b	2a(6a), 10a(14a)
8a	4.23 (d, 2.6)	51.2	1a, 7a, 9a, 10a(14a), 1b, 2b, 3b	2a(6a), 10a(14a)
9a		146.5		
10a, 14a	5.89 (d, 2.2)	105.4	8a, 11a(13a), 12a	2a(6a), 7a, 8a, OH-11a(13a)
11a, 13a (OH)	8.02 (br s)	158.6	10a(14a), 11a(13a), 12a	10a(14a)
12a	6.05 (t, 2.2)	100.8	10a(14a), 11a(13a)	
1b		139.1		
2b		133.9		
3b (OH)	8.48 (br s)	155.8	2b, 3b, 4b	
4b	6.58 (s)	109.4	2b, 3b, 5b, 6b	
5b (OH)	8.76 (br s)	159.4		
6b	6.58 (s)	99.6	2b, 4b, 5b	
7b		204.8		

[a] Measured in CD_3COCD_3 at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR).

60 F_{254} (0.5 mm); column chromatography, Merck Kieselgel 60, Pharmacia Fine Chemicals AB, Sephadex LH-20, and Fuji Silysia Chemical Chromatorex, Waters Sep-Pak C_{18} cartridges; vacuum-liquid chromatography (VLC), Merck Kieselgel 60.

Plant Material. *Vatica pauciflora* was cultivated at Bogor Botanical Garden, Bogor, Indonesia, and its stem bark was collected in May 2000 with identification by one of the coauthors (D.D.), and a voucher specimen (number DP-011) was deposited at the herbarium of Gifu Prefectural Institute of Health and Environmental Sciences.

Extraction and Isolation. Dried and ground stem bark (500 g) of *V. pauciflora* was extracted successively with acetone (2 L × 24 h × 3), MeOH (2 L × 24 h × 3), and 70% MeOH (2 L × 24 h × 2) at room temperature. The solvent was removed to yield the following residues: 38 g (acetone), 23 g (MeOH), and 15 g (70% MeOH). The acetone extract (37 g) was subjected to column chromatography on silica gel eluted with a mixture of $CHCl_3$−MeOH increasing in polarity to give a total of 60 fractions (Fr. 1−60). The combined fractions of Fr. 42−Fr. 46 [$CHCl_3$−MeOH (4:1), 910 mg] were further subjected to Sephadex LH-20 column chromatography (MeOH) to give 22 fractions (Fr. 42−46A−Fr.42−46V). The combined fractions of Fr. 42−46Q−Fr. 42−46V (450 mg) were further subjected to reversed-phase column chromatography (H_2O−MeOH gradient system, 20%−60% MeOH) to give 10 fractions. Compound **1** (60 mg) was purified from the 10th fraction (80 mg) after purification by preparative TLC [EtOAc−$CHCl_3$−MeOH−H_2O (15:8:4:1)]. Compounds **2** (4 mg) and **3** (2 mg) were obtained from Fr. 13 [$CHCl_3$−MeOH (10:1), 90 mg] after separation by VLC [EtOAc−$CHCl_3$−MeOH−H_2O (240:60:11:2)] and preparative TLC [EtOAc−$CHCl_3$−MeOH−H_2O (80:40:11:2)].

Pauciflorol D (1): dark yellow amorphous powder; $[\alpha]^{25}_D$ −69° (*c* 0.1 MeOH); UV (MeOH) λ_{max} (log ϵ) 223 (5.2), 284 (4.1) nm; IR (KBr) ν_{max} 3360, 1612, 1513, 1450 cm^{-1}; ^{1}H and ^{13}C NMR spectral data, see Table 1; HMBC and NOESY correlations, see Table S1 (Supporting Information); ESIMS *m/z* 1609 $[M + Na]^+$; HRESIMS *m/z* 1609.4583 (calcd for $C_{98}H_{74}NaO_{21}$, 1609.4620) $[M + Na]^+$.

Pauciflorol E (2): yellow amorphous powder; $[\alpha]^{25}_D$ −228° (*c* 0.1 MeOH); UV (MeOH) λ_{max} (log ϵ) 223 (4.6), 276 (4.1), 342 (3.7) nm; IR (KBr) ν_{max} 3371, 1659, 1611, 1513, 1449 cm^{-1}; ^{1}H and ^{13}C NMR spectral data and HMBC and NOESY correlations, see Table 2; FABMS *m/z* 467 $[M - H]^-$; HRFABMS *m/z* 467.1136 (calcd for $C_{28}H_{19}O_7$, 467.1130).

Pauciflorol F (3): yellow amorphous powder; $[\alpha]^{25}_D$ −80° (*c* 0.1 MeOH); UV (MeOH) λ_{max} (log ϵ) 224 (4.6), 274 (4.0), 336 (3.5) nm; IR (KBr) ν_{max} 3369, 1694, 1609, 1513, 1471 cm^{-1}; ^{1}H and ^{13}C NMR spectral data and HMBC and NOESY correlations, see Table 3; EIMS *m/z* (rel int) 364 (M^+, 100), 362 (33),

345 (6), 270 (28), 258 (31), 242 (6), 213 (8); HREIMS *m/z* 364.0938 (calcd for $C_{21}H_{16}O_6$, 364.0947); FABMS *m/z* 363 [M − H]$^-$; HRFABMS *m/z* 363.0876 (calcd for $C_{21}H_{15}O_6$, 363.0868).

Acknowledgment. The authors are grateful to Mr. Y. Doke of Gifu Prefectural Institute of Industrial Product Technology for his constant technical support during the course of these studies for NMR spectra. We also express our appreciation to Mrs. M. Hosokawa and Mrs. M. Hayashi of Gifu Pharmaceutical University for measurement of FABMS and EIMS data.

Supporting Information Available: Table of HMBC and NOESY data for compound **1**. This information is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Sotheeswaran, S.; Pasupathy, V. *Phytochemistry* **1993**, *32*, 1083−1092.
(2) Gorham, J. *The Biochemistry of Natural Products Series 1: The Biochemistry of the Stilbenoids*; Chapman & Hall: London, 1995; pp 71−72.
(3) Seo, E.-K.; Chai, H.; Constant, H. L.; Santisuk, T.; Reutrakul, V.; Beecher, C. W. W.; Farnsworth, N. R.; Cordell, G. A.; Pezzuto, J. M.; Kinghorn, A. D. *J. Org. Chem*. **1999**, *64*, 6976−6983.
(4) Dai, J.-R.; Hallock, Y. F.; Cardellina, J. H., II; Boyd, M. R. *J. Nat. Prod*. **1998**, *61*, 351−353.
(5) Samaraweera, U.; Sotheeswaran, S.; Sultanbawa, M. U. S. *Phytochemistry* **1982**, *21*, 2585−2587.
(6) Nitta, T.; Arai, T.; Takamatsu, H.; Inatomi, Y.; Murata, H.; Iinuma, M.; Tanaka, T.; Ito, T.; Asai, F.; Ibrahim, I.; Nakanishi, T.; Watabe, K. *J. Health Sci*. **2002**, *48*, 273−276
(7) Ashton, P. S. *Flora Malesiana*, Ser. I, *Spermatophyta*; Steenis, C. G. G. J., Ed.; Martivus Nijhoff Publishers: Leiden, The Netherlands, 1982; Vol. 9, pp 237−552.
(8) Sotheeswaran, S.; Diyasena, M. N. C.; Gunatilaka, A. A. L.; Bokel, M.; Kraus, W. *Phytochemistry* **1987**, *26*, 1505−1507.
(9) Sotheeswaran, S.; Sultanbawa, M. U. S.; Surendrakumar, S.; Balasubramaniam, S.; Bladon, P. *J. Chem. Soc., Perkin Trans. 1* **1985**, 159−162.
(10) Sultanbawa, M. U. S.; Surendrakumar, S.; Wazeer, I. M. *J. Chem. Soc., Chem. Commun*. **1981**, 1204−1206.
(11) Ito, T.; Tanaka, T.; Nakaya, K.; Iinuma, M.; Takahashi, Y.; Naganawa, H.; Ohyama, M.; Nakanishi, Y.; Bastow, K. F.; Lee, K.-H. *Tetrahedron* **2001**, *57*, 7309−7321.
(12) Ito, T.; Tanaka, T.; Ido, Y.; Nakaya, K.; Iinuma, M.; Takahashi, Y.; Naganawa, H.; Riswan, S. *Heterocycles* **2001**, *55*, 557−567.
(13) Tanaka, T.; Ito, T.; Nakaya, K.; Iinuma, M.; Takahashi, Y.; Naganawa, H.; Matsuura N.; Ubukata, M. *Tetrahedron Lett*. **2000**, *41*, 7929−7932.
(14) Tanaka, T.; Ito, T.; Nakaya, K.; Iinuma, M.; Riswan, S. *Phytochemistry* **2000**, *54*, 63−69.
(15) Ito, T.; Tanaka, T.; Iinuma, M.; Iliya, I.; Nakaya, K.; Ali, Z.; Takahashi, Y.; Sawa, R.; Shirataki, Y.; Murata, J.; Darnaedi, D. *Tetrahedron* **2003**, *59*, 5347−5363.
(16) Yan, K.-X.; Terashima, K.; Takaya, Y.; Niwa, M. *Tetrahedron* **2002**, *58*, 6931−6935.
(17) Tanaka, T.; Ito, T.; Iinuma, M.; Ohyama, M.; Ichise, M.; Tateishi, Y. *Phytochemistry* **2000**, *53*, 1009−1014.
(18) Ito, T.; Tanaka, T.; Iinuma, M.; Nakaya, K.; Takahashi, Y.; Sawa, R.; Naganawa, H.; Chelladurai, V. *Tetrahedron* **2003**, *59*, 1255−1264.
(19) Ohyama, M.; Tanaka, T.; Iinuma, M.; Burandt, C. L., Jr. *Chem. Pharm. Bull*. **1998**, *46*, 663−668.
(20) Oshima, Y.; Ueno, Y. *Phytochemistry* **1993**, *33*, 179−182.

NP030236R