Two Novel Resveratrol Trimers from *Dipterocarpus grandiflorus*

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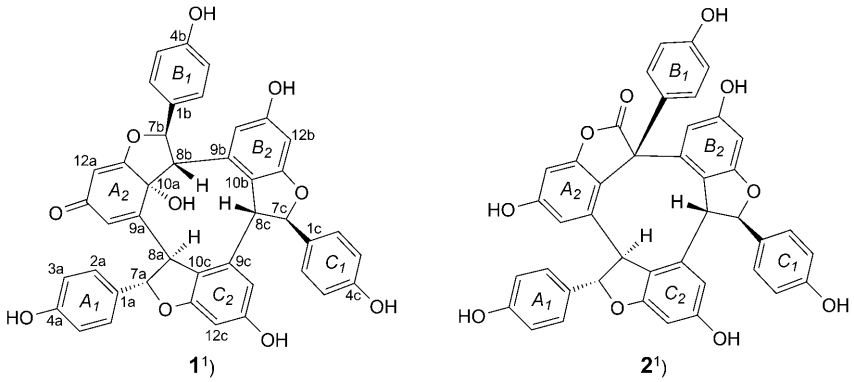
Two new resveratrol (= 5-[(*E*)-2-(4-hydroxyphenyl)ethenyl]benzene-1,3-diol) trimers, grandiphenols C (**1**) and D (**2**), were isolated from the stem of *Dipterocarpus grandiflorus* (Dipterocarpaceae). The structures of **1** and **2** were elucidated by spectral analysis including 1D- and 2D-NMR experiments and by computer-aided molecular modeling. The NMR characteristics caused by the steric hindrance and the biogenetic relationship of the isolates are also discussed in this work.

Introduction. – In the course of our research studies directed towards the isolation and identification of bioactive polyphenols in plants, we have previously reported the structural variety of resveratrol oligomers from the family of Dipterocarpaceae [1]. Lately, resveratrol and its oligomers have received notice because of their multifunctional bioactivity [2]. Our laboratory has reported the occurrence of resveratrol oligomers in a series of Dipterocarpaceaeous plants since 2001 [3]. Interest in the bioactivity of resveratrol oligomers of the Dipterocarpaceae family led us to the current phytochemical study of *Dipterocarpus grandiflorus*. In our previous studies of chemical constituents of this species, the structures of resveratrol oligomers were characterized [3c]. A detailed examination of *D. grandiflorus* yielded two novel resveratrol trimers, grandiphenols C (**1**) and D (**2**). The structures of **1** and **2** were elucidated using 2D-NMR techniques such as ^{1}H,^{1}H- and ^{13}C,^{1}H-COSY, and ^{1}H,^{13}C-HMBC. The relative configurations were determined by the ^{1}H,^{1}H-NOESY NMR technique and clarified by computer-aided molecular modeling.

Results and Discussion. – 1. *Structure Elucidation*. Grandiphenols C (**1**) and D (**2**) were isolated from the acetone extract of *D. grandiflorus* stems by column chromatography and preparative thin-layer chromatography.

Grandiphenol C (**1**), a pale yellow solid, had the molecular formula $C_{42}H_{30}O_{10}$, as deduced by the HR-FAB-MS ($[M+H]^+$ at m/z 695.1925; calc. 695.1917 for $C_{42}H_{31}O_{10}^+$) and ^{13}C-NMR spectroscopy. A signal at δ(C) 188.1 found in the ^{13}C-NMR spectrum



indicated the presence of a C=O group (C(13a)[1]). The ^{1}H- and ^{13}C-NMR spectra of **1** (*Table 1*), and the corresponding ^{1}H,^{1}H- and ^{13}C,^{1}H-COSY as well as ^{1}H,^{13}C-HMBC spectra (*Table 1* and *Fig. 1*) were recorded at room temperature in (D_6)acetone.

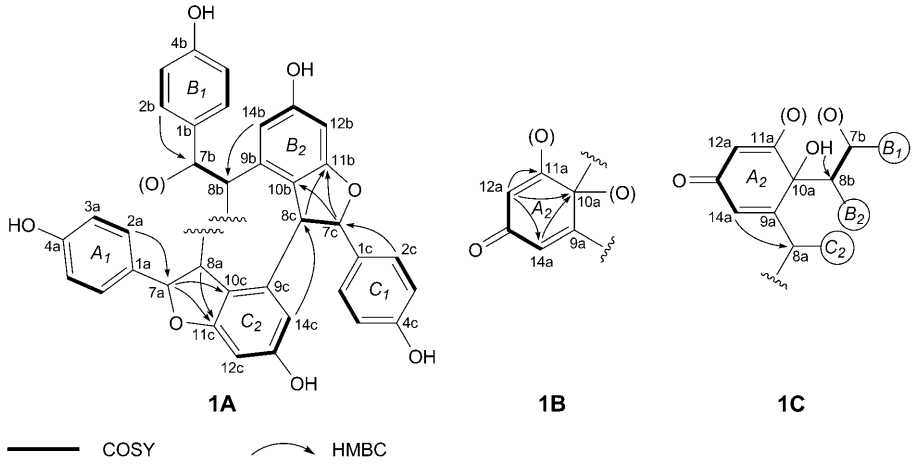


Fig. 1. *Selected correlations in the 2D-NMR spectra of the partial structures* **1A**–**1C** *of* **1**

The presence of three 4-hydroxyphenyl groups (rings A_1 – C_1) and two 3,5-dioxygenated 1,2-disubstituted benzene rings (rings B_2 and C_2) were revealed by the data analyses. Two olefinic H-atoms (H–C(12a) and H–C(14a)), two pairs of mutually coupled aliphatic H-atoms (H–C(7b)/H–C(8b) and H–C(7c)/H–C(8c)), and two non-coupled aliphatic H-atoms (H–C(7a)/H–C(8a)) were also evident (*Fig. 1*). The ^{1}H-NMR spectrum exhibited the signals for an aliphatic OH and five

[1]) Arbitrary atom numbering. For systematic names, see *Exper. Part*.

Table 1. *NMR Data of Grandiphenol C* (**1**)[1]). In (D_6)acetone; at 300 (^1H) and 75 MHz (^{13}C), resp.; δ in ppm, J in Hz.

	δ(H)	δ(C)	HMBC
C(1a)		132.4	
H–C(2a,6a)	6.94 (*d*, J = 8.6)	127.9	C(4a), C(7a)
H–C(3a,5a)	6.65 (*d*, J = 8.6)	115.7	C(1a), C(4a)
C(4a)		158.33[a])	
H–C(7a)	5.49 (*s*)	91.3	C(10c), C(11c), C(1a), C(2a,6a), C(8a), C(9a)
H–C(8a)	4.02 (*s*)	44.7	C(10c), C(11c), C(1a), C(9a), C(10a), C(14a)
C(9a)		159.46[b])	
C(10a)		73.4	
C(11a)		179.2	
H–C(12a)	5.36 (*d*, J = 1.5)	99.3	C(9a)[c]), C(10a), C(11a), C(14a)
C(13a)		188.1	
H–C(14a)	6.20 (*d*, J = 1.5)	125.9	C(8a), C(10a), C(12a)
C(1b)		132.7	
H–C(2b,6b)	7.32 (*d*, J = 8.5)	129.4	C(4b), C(7b)
H–C(3b,5b)	6.80 (*d*, J = 8.5)	116.1[d])	C(1b), C(4b)
C(4b)		158.9	
H–C(7b)	6.16 (*d*, J = 10.0)	89.2	C(8b), C(2b,6b)
H–C(8b)	3.76 (*d*, J = 10.0)	56.7	C(1b), C(9b), C(10b)
C(9b)		128.7	
C(10b)		119.75	
C(11b)		161.6	
H–C(12b)	6.20 (*d*, J = 2.0)	98.2	C(10b), C(11b), C(13b), C(14b)
C(13b)		159.51[b])	
H–C(14b)	6.93 (*d*, J = 2.0)	109.5	C(8b), C(10b), C(12b), C(13b)
C(1c)		133.4	
H–C(2c,6c)	6.93 (*d*, J = 8.6)	128.4	C(4c), C(7c)
H–C(3c,5c)	6.69 (*d*, J = 8.6)	116.1[d])	C(1c), C(4c)
C(4c)		158.06[a])	
H–C(7c)	5.61 (*d*, J = 1.6)	95.6	C(10b), C(11b), C(1c), C(2c,6c), C(8c), C(9c)
H–C(8c)	4.69 (br. *s*)	52.0	C(10b), C(11b), C(1c), C(7c), C(9c), C(10c), C(14c)
C(9c)		142.3	
C(10c)		121.4	
C(11c)		160.9	
H–C(12c)	6.31 (*d*, J = 2.0)	98.0	C(10c), C(11c), C(13c), C(14c)
C(13c)		159.3	
H–C(14c)	6.38 (*d*, J = 2.0)	108.9	C(8c), C(10c), C(12c), C(13c)
HO–C(10a)	5.64 (br. *s*)		C(8b), C(12a)[e])
5 OH groups	8.28 (br. *s*), 8.42 (br. *s*), 8.44 (br. *s*), 8.58 (br. *s*), 8.73 (br. *s*)		

[a]), [b]) Interchangeable. [c]) Long-range correlation *via* ^4J. [d]) Overlapping. [e]) Long-range correlation *via* ^4J.

phenolic OH groups at δ(H) 5.64–8.73, which disappeared upon addition of D_2O. An NMR signal at δ(C) 73.4 was assigned to a quaternary aliphatic C-atom (C(10a)).

The significant ^3J long-range correlations observed between H–C(2a,6a)/C(7a), H–C(7a)/C(10c), H–C(2c,6c)/C(7c), H–C(14c)/C(8c), H–C(8c)/C(11b), H–C(2b,6b)/

C(7b), and H–C(14b)/C(8b) (see *Fig. 1*) indicated the presence of C–C bonds between C(1a)/C(7a), C(8a)/C(10c), C(1c)/C(7c), C(8c)/C(9c), C(8c)/C(10b), C(1b)/C(7b), and C(8b)/C(9b), respectively (partial structure **1A**). Cross-peaks observed between H–C(7a)/C(11c) and H–C(7c)/C(11b) supported two ether linkages of C(7a)–O–C(11c) and C(7c)–O–C(11b) to form dihydrobenzofuran rings. The remaining ring system (**1B**) and the connectivity in the molecule were determined as follows. The presence of a six-membered ring system was apparent from the signals of C(9a)–C(14a) in the ^{13}C-NMR spectrum (*Table 1*). The ring was composed of three quaternary sp^2 C-atoms (δ(C) 159.46, 179.2, 188.1 (CO)), one O-bearing quaternary sp^3 C-atom (δ(C) 73.4), and two protonated sp^2 C-atoms ((δ(C) 99.3 and 125.9), which suggested that the ring formed a cyclohexa-2,5-dienone system (ring A_2). The ring system was also supported by the cross-peaks of H–C(12a)/C(10a), C(11a), and C(14a), and H–C(14a)/C(10a). Similar ^{13}C-NMR spectral patterns in a cyclohexa-2,5-dienone system were observed in upunaphenol F (δ(C) 155.3, 72.7, 178.9, 99.0, 185.8, 140.2) [3b] (*Fig. 2*). The correlations between HO–C(10a) and C(8b), and H–C(14a) and C(8a) established the position of HO–C(10a) and the C–C bonds C(10a)–C(8b) and C(8a)–C(9a) (partial structure **1C**; *Fig. 1*). The established structures accounted for 27 of the 28 required degrees of unsaturation. Although no long-range correlation between H–C(7b) and C(11a) was observed, an ether linkage (C(7b)–O–C(11a)) was assumed. Thus, the structure of grandiphenol C (**1**) could be drawn from these data.

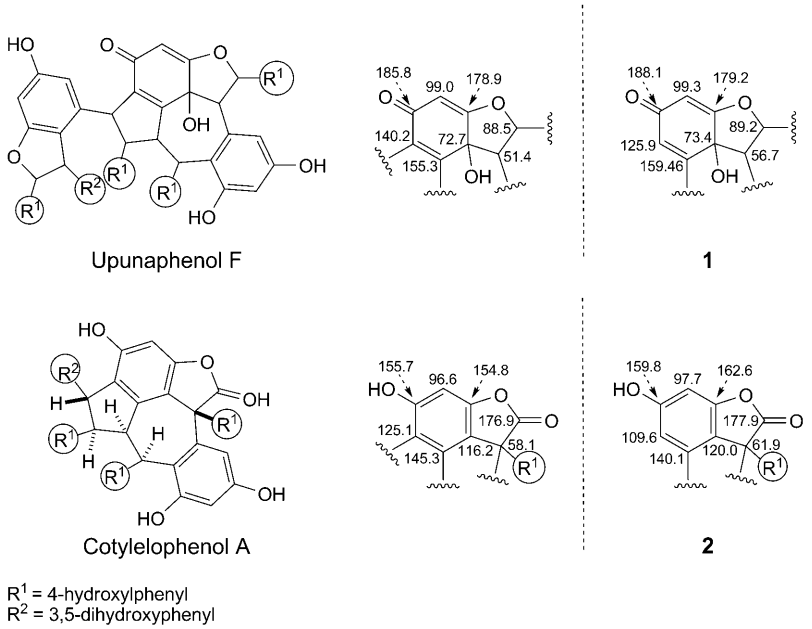
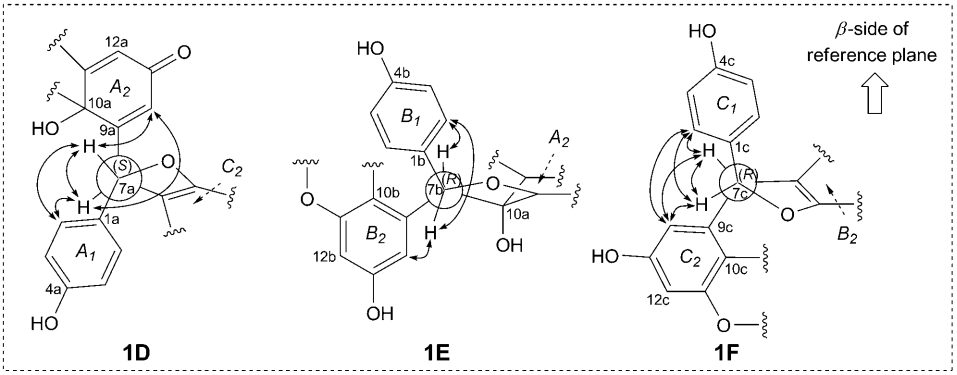


Fig. 2. *Structure and ^{13}C-NMR data of the dihydrobenzofuranone moiety* (upunaphenol F, cotylelophenol A, **1**, and **2**)

The relative configuration of **1** was determined by a NOESY experiment (*Fig. 3*) with the assistance of computer-aided molecular modeling [4]. *trans*-Orientations of H–C(7a)/H–C(8a), H–C(7b)/H–C(8b), and H–C(7c)/H–C(8c) on the dihydrobenzofuran rings (**1D**, **1F**) or the dihydrobenzofuranone ring (**1E**) were confirmed by the distinctive NOEs of H–C(7a)/H–C(14a), H–C(8a)/H–C(2a,6a), H–C(7b)/H–C(14b), H–C(8b)/H–C(2b,6b), H–C(7c)/H–C(14c), and H–C(8c)/H–C(2c,6c). Small coupling-constant values of vicinal CH H-atoms (*ca.* 0 Hz for H–C(7a)/H–C(8a); 1.6 Hz for H–C(7c)/H–C(8c)) on the rings suggested that these H-atoms had all *trans* equatorial orientations, while the large coupling constant values of H–C(7b)/H–C(8b) (10.0 Hz) supported the *trans* diaxial orientation of the latter [3d]. When the conformation of the three five-membered rings are considered, the flaps of envelope must be C(7a), C(10a), and C(7c). The relationships among **1A** – **1C** and C(10a) were determined as follows. The NOE interactions of H–C(2b,6b)/H–C(8c) and H–C(8b)/H–C(8c) indicated that H–C(8b), H–C(8c), and the ring B_1 are on the same side of the reference plane (β-side). Considering the forms of rigid nonacyclic system and the NOEs of HO–C(10a) with H–C(2a,6a) and H–C(8a),



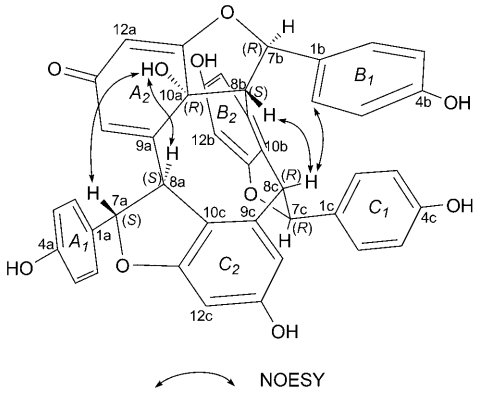


Fig. 3. *Partial structures* **1D**–**1F** *and NOEs observed in the NOESY experiment of* **1**

HO–C(10a), H–C(8a), and the ring A_1 must be α-oriented. From these data, the energy-minimized conformation of **1** (*Fig. 4*) showed dihedral angles of 101.0° and 123.1° for H–C(7a)/H–C(8a) and H–C(7c)/H–C(8c), respectively, which corresponded to the expectation of a very small coupling constant in each case from the vicinal *Karplus* correlation graph [5]. An angle of 164.4° for H–C(7b)/H–C(8b) is acceptable for the large coupling constant. As a result, grandiphenol C (**1**) is proposed as a novel resveratrol trimer.

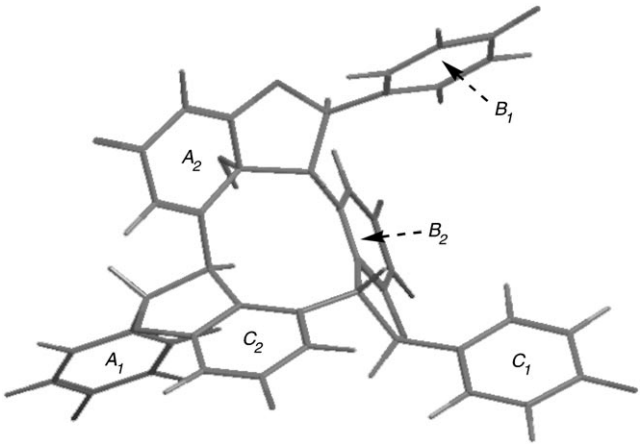


Fig. 4. *Energy-minimized configuration of* **1** (MMFF 94 calculation using the Pcmodel 9.1 molecular modeling program)

Grandiphenol D (**2**) was obtained as a pale yellow solid. The molecular formula was deduced to be $C_{42}H_{28}O_{10}$ from the HR-FAB-MS *pseudo*-molecular-ion peak ($[M + H]^+$) at *m/z* 693.1754 (calc. 695.1760 for $C_{42}H_{29}O_{10}^+$), and the ^{13}C-NMR spectrum (*Table 2*). A NMR signal at δ(C) 177.9 indicated the presence of an ester C=O group (C(7b)). An atom, C(8b), was identified to be quaternary. The 1D- and 2D-NMR spectral data (*Table 2*) revealed the presence of six aromatic rings (rings $A_1 - C_1$ and $A_2 - C_2$), two pairs of mutually coupled aliphatic H-atoms (H–C(7a)/H–C(8a) and H–C(7c)/H–C(8c)), and six phenolic OH groups. The signals attributed to the ring B_1 among the aromatic rings were observed as four double *doublet*s in the ^{1}H-NMR spectrum, the behavior of which was also equal to a 4-hydroxyphenyl group in isoampelopsin F [6].

The 2D-NMR analysis of **2** (*Table 2* and *Fig. 5*) showed that partial structures are composed of five rings (rings A_1, A_2, B_2, C_1, and C_2), four CH groups (H–C(7a), H–C(8a), H–C(7c), and H–C(8c), and a quaternary C-atom (C(8b)) connected analogously as in **1** (**2A**). The presence of ring B_1 and the bond C(1b)–C(8b) were also supported by these data (**2B**). Considering the required degrees of unsaturation of 29, the remaining ring system was deduced as a five membered lactone ring fused to a nonacyclic system (**2C**). Similar ^{13}C-NMR spectral patterns in the same partial structure were also observed in cotylelophenol A [3a] (*Fig. 2*). These data allowed to determine the configuration of grandiphenol D as **2**.

Table 2. *NMR Data of Grandiphenol D* (**2**). In (D_6)acetone; at 300 (^1H) and 75 MHz (^{13}C); δ in ppm, J in Hz.

	δ(H)	δ(C)	HMBC
C(1a)		131.8	
H–C(2a,6a)	6.96 (*d*, *J* = 8.6)	127.6	C(4a), C(7a)
H–C(3a,5a)	6.70 (*d*, *J* = 8.6)	115.5	C(1a), C(4a)
C(4a)		157.6	
H–C(7a)	6.20 (*s*)	86.2	C(10c), C(11c), C(1a), C(2a,6a), C(8a), C(9a)
H–C(8a)	3.96 (*s*)	47.1	C(10c), C(11c), C(1a), C(9a)
C(9a)		136.5	
C(10a)		119.96[a])	
C(11a)		154.2	
H–C(12a)	6.67 (*d*, *J* = 2.0)	97.7	C(10a), C(11a), C(13a), C(14a)
C(13a)		159.4	
H–C(14a)	7.19 (*d*, *J* = 2.0)	110.1	C(8a), C(10a), C(12a), C(13a)
C(1b)		129.7	
H–C(2b)	5.65 (*dd*, *J* = 8.6, 2.5)	128.8	C(4b), C(6b), C(8b)
H–C(3b)	6.14 (*dd*, *J* = 8.6, 2.5)	115.1	C(1b), C(5b)
C(4b)		158.15[b])	
H–C(5b)	6.73 (*dd*, *J* = 8.6, 2.5)	116.4	C(1b), C(3b)
H–C(6b)	7.41 (*dd*, *J* = 8.6, 2.5)	131.2	C(4b), C(2b), C(8b)
C(7b)		177.9	
C(8b)		61.9	
C(9b)		140.1[c])	
C(10b)		120.00[a])	
C(11b)		162.6	
H–C(12b)	6.29 (*d*, *J* = 2.2)	97.7	C(10b), C(11b), C(13b), C(14b)
C(13b)		159.8	
H–C(14b)	6.21 (*d*, *J* = 2.2)	109.6	C(8b), C(10b), C(12b), C(13b)
C(1c)		131.5	
H–C(2c,6c)	6.88 (*d*, *J* = 8.6)	129.2	C(4c), C(7c)
H–C(3c,5c)	6.77 (*d*, *J* = 8.6)	115.7	C(1c), C(4c)
C(4c)		158.23[b])	
H–C(7c)	4.34 (*d*, *J* = 8.5)	94.5	C(11b), C(1c), C(2c,6c), C(8c), C(9c)
H–C(8c)	3.75 (*d*, *J* = 8.5)	57.4	C(10b), C(11b), C(1c), C(7c), C(9c), C(10c), C(14c)
C(9c)		140.1[c])	
C(10c)		116.5	
C(11c)		161.5	
H–C(12c)	6.16 (*d*, *J* = 2.0)	97.3	C(10c), C(11c), C(13c), C(14c)
		158.9	
H–C(14c)	4.95 (*d*, *J* = 2.0)	107.8	C(8c), C(10c), C(12c), C(13c)
HO–C(4a)	8.31 (br. *s*)		C(3a,5a), C(4a)
HO–C(13a)	8.98 (br. *s*)		C(12a), C(13a), C(14a)
HO–C(4b)	8.30 (br. *s*)		C(3b,5b), C(4b)
HO–C(13b)	8.52 (br. *s*)		C(12b), C(13b), C(14b)
HO–C(4c)	8.45 (br. *s*)		C(3c,5c), C(4c)
HO–C(13c)	8.01 (br. *s*)		C(12c), C(13c), C(14c)

[a]), [b]) Interchangeable. [c]) Overlapping.

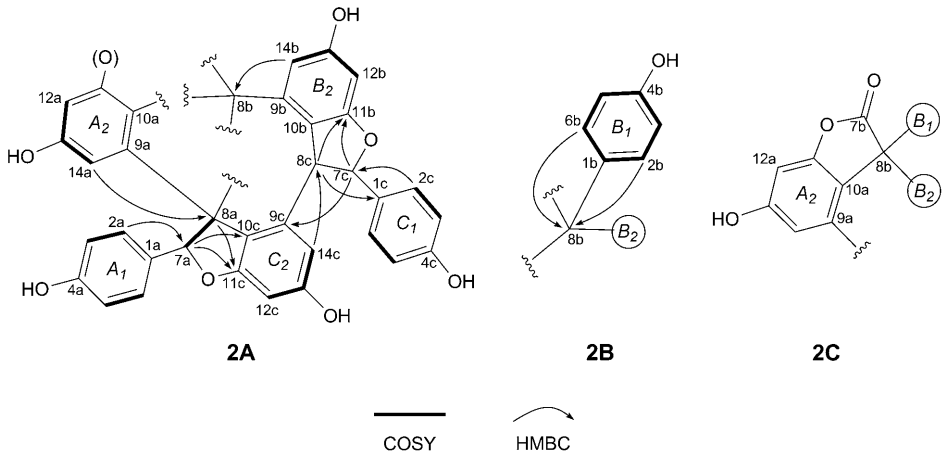


Fig. 5. *Selected correlations in the 2D-NMR spectra of* **2**

The relative configuration of **2** was proposed on the basis of NOESY spectrum analysis (*Fig. 6*) and the computer-aided energy-minimized conformations (*Fig. 7*) [4]. The configuration of the CH groups H–C(7a) and H–C(8a) was *trans* di-equatorial, which is supported by a computer-aided calculation for the dihedral angles (84.5°), and results in a coupling constant with a small value according to the vicinal *Karplus* correlation graph [5]. The dihedral angle between H–C(7c) and H–C(8c) was computed as 154°, corresponding to a large constant (8.5 Hz). Thus, a *tran*s diaxial orientation of H–C(7c)/H–C(8c) is supported. The *cis* relative disposition for H–C(8a) and H–C(7c) is inferred from the NOE between both H-atoms. Another

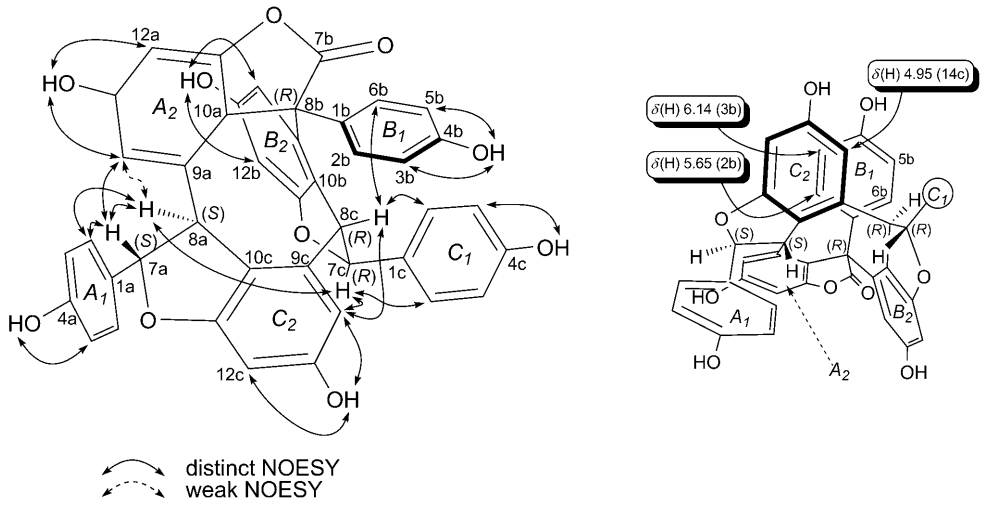


Fig. 6. *NOEs observed in the NOESY experiment of* **2** (left) *and upper field shift of aromatic H-atoms caused by anisotropy* (right)

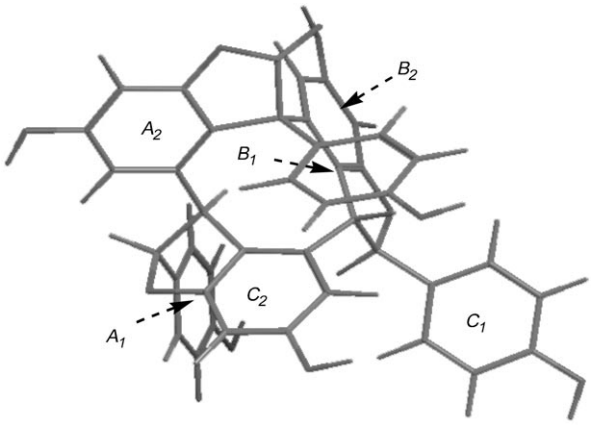


Fig. 7. *Energy-minimized configuration of* **2** (MMFF 94 calculation using the Pcmodel 9.1 molecular modeling program)

distinct NOE was observed for H–C(8c)/H–C(6b), suggesting that C(8b) has the relative (*R*)-configuration. Consequently, the relative configuration of grandiphenol D was established as shown in **2**.

In **2**, the ring B_1 is situated above the ring C_2, which disturbs the free rotation of the ring B_1 by strong steric hindrance (*Fig. 6*). As a result, originally equal (equivalent) H-atoms (H–C(2b) and H–C(6b), as well as H–C(3b) and H–C(5b)) are situated in different chemical environments and the H-atoms appeared as distinct double *doublet*s. The high-field shifts of H–C(2b) (δ(H) 5.65), H–C(3b) (δ(H) 6.14), and H–C(14c) (δ(H) 4.95) can be reasonably explained by the anisotropic effects of rings C_2 (to H–C(2b) and H–C(3b)) and B_1 (to H–C(14c)).

To further explore the stable conformations of the molecule and free rotation pertaining to the aromatic rings (rings $A_1 - C_1$) of **2**, computational calculations were performed. The observed evidence is that hindered rotation along the C–C bond (C(1b)–C(8b)) can cause a difference in the magnetic environment in the overall structure, and hence distinct signals in the NMR spectrum for all H- and C-atoms can be observed. To gain an insight into this issue, the conformational dynamics of **2** were studied. The minimum-energy conformation of **2** was obtained using the PCMODEL suite of programs with MMFF's force field (MM2 type) [4]. The energy-minimized conformation (total energy 206.5 kcal/mol) shows that the structure adopts a conformation where the rings B_1 and C_2 are co-facial. In order to visualize the effect of rotation along C–C bonds of all rotable aromatic rings (rings $A_1 - C_1$) on the overall energy (potential energy) of the molecule, a conformational search was carried out employing macromodel module, dihedral drive with an increment of 1° rotation over 180° of angles of O–C(7a)–C(1a)–C(2a) (ring A_1), C(7b)–C(8b)–C(1b)–C(2b) (ring B_1), and O–C(7c)–C(1c)–C(2c) (ring C_1) (*Fig. 8*). An inspection of the results reveals that the dip in *Fig. 8* (104°; 202.8 kcal/mol) almost corresponds to the energy-minimized model in *Fig. 7* (103.0°; 206.6 kcal/mol). The ring B_1 in **2** lies above the ring C_2 as predicted earlier by the NMR study. The above discussed results clearly corroborate the appearance of distinct NMR signals for all H- and C-atoms of ring B_1.

The $\delta G^{\ddagger}$ values for rings $A_1 - C_1$ (*Fig. 8*) show that the rings A_1 and C_1 can freely rotate due to their low energy barrier (3.5 kcal/mol for ring A; 5.8 kcal/mol for ring C), while the ring B_1 can not rotate due to its much higher energy barrier of 43.1 kcal/mol. An increase in restriction of the rotation may be attributed to closer location of the ring B_1 to the ring C_2.

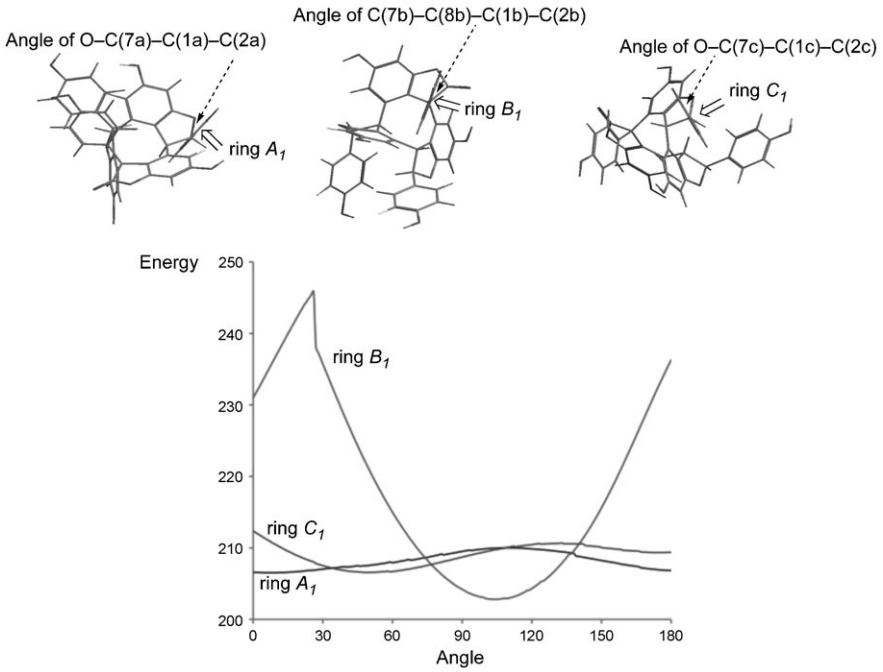
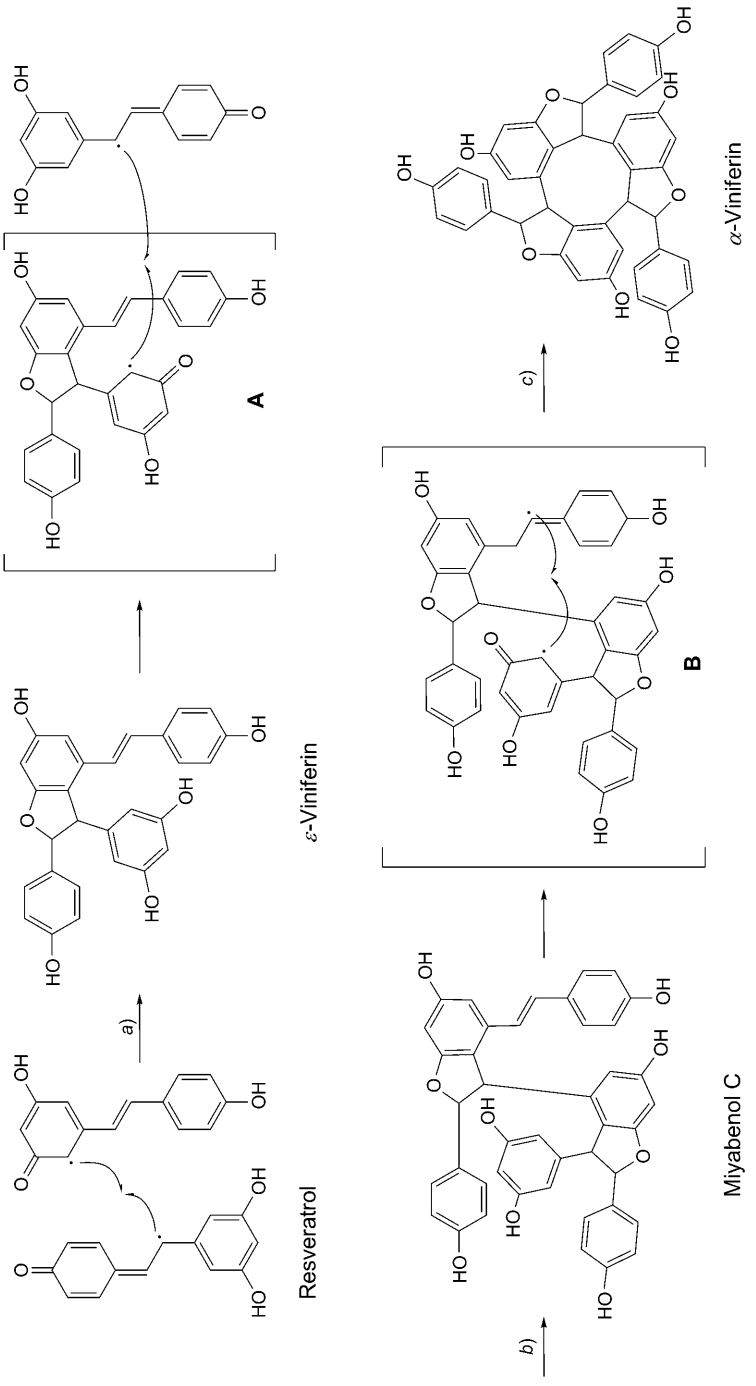


Fig. 8. *Conformational profile for* **2** *obtained for the allyl C–C bond rotation at the molecular mechanics* (MMFF) *level of theory* (ring A: angle of O–C(7a)–C(1a)–C(2a); ring B: angle of C(7b)–C(8b)–C(1b)–C(2b); ring C: angle of O–C(7c)–C(1c)–C(2c))

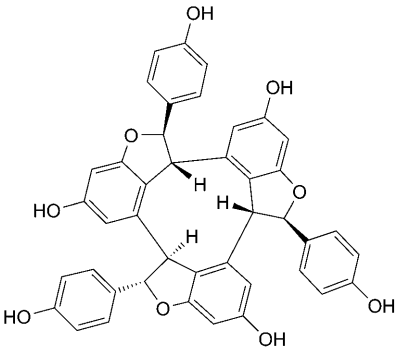
Such NMR spectral behaviors of aromatic rings had been observed in several stilbene oligomers, especially in case of 4-hydroxyphenyl groups. In **2** and isoampelopsin F [6], four signals were observed as clear *doublet* of *doublet*s at room temperature, while the signals of cotylelophenol A [3a], vaticanol G [3f], vateriaphenol A [3e], and amurensins A – D [7] displayed the same behavior only at lower temperature. These differences suggest that the 4-hydroxyphenyl group (ring B_1) in **2** or isoampelopsin F is somewhat unflexible compared to the others. The restricted rotation of the 4-hydroxyphenyl rings could not be discussed exactly only by the steric hindrance as discussed above because the skeleton of isoampelopsin F is simple. Another strong attractive force, for example CH–π and (or) OH–π interaction, may exist between a π-system and a H-atom in such molecules [8].

Resveratrol oligomers in *D. grandiflorus* are presumed to be produced by successive oxidative couplings of resveratrol (monomer) and/or ε-viniferin (dimer). A plausible mode for production of α-viniferin *via* radical precursors (**A**, **B**) is shown in *Scheme 1*. A step-by-step coupling of three resveratrols can occur *via* the formation of



Scheme 1. *Plausible Biogenetic Pathways of Resveratrol Oligomers.* Pathway to α-viniferin.

three dihydrobenzofuran rings (*a* – *c*) and a cyclonona-1,4,7-triene ring (*c*). The explanation for the relationship among the isolates in the biogenetic pathway also requires the definition of the radical precursors. When the formation of **1** and **2** is considered, α-viniferin can be regarded as their common precursor by consideration of the configurational similarity. This would result in the generation of trimeric radicals (**C** – **E**), which would react individually (*Scheme 2*). These differ in the position of the radical located in **C**, **D**, and **E** on positions C(12a), C(10a), and C(7b), respectively. Compound **2** and cotylelophenol A [3a] have a common lactone ring (3-(4-hydroxyphenyl)benzofuran-2(*3 H*)-one). The skeleton is presumed to be formed after a rearrangement of a 4-hydroxyphenyl group *via* radical **E**. Radical **D** reacts with a hydroxyl radical to form **1**. In *Scheme 2*, a plausible biogenetic pathway of some resveratrol trimers is described, which suggests that not only various skeletal isomers and stereoisomers, but also further oxidative products may co-exist in Dipterocarpaceaeous plants.



α-Viniferin

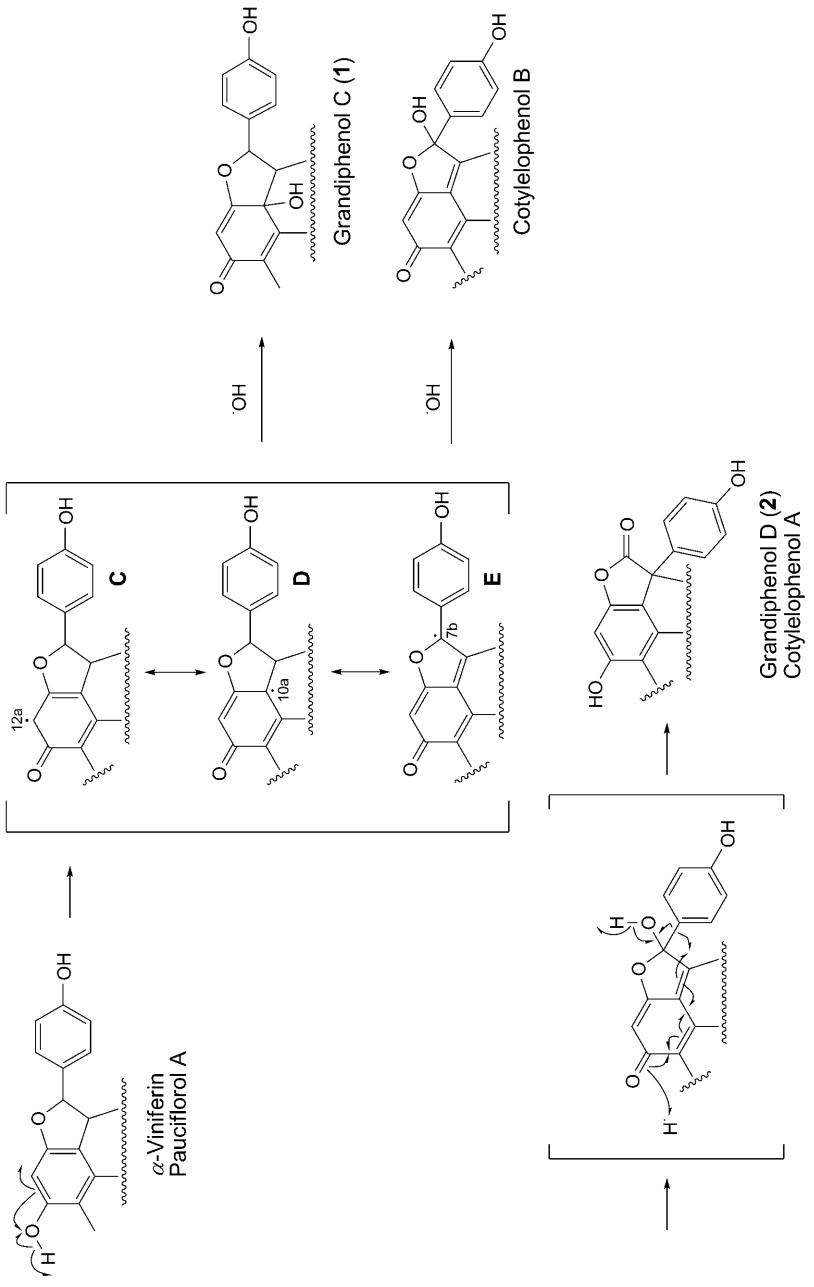
Experimental Part

General. Anal. and prep. TLC: *Kieselgel F$_{254}$* (0.25 mm; *Merck*). Column chromatography (CC): silica gel *60* (SiO_2; 70–230 mesh; *Merck*), *ODS* (100–200 mesh; *Fuji Silysia Chemical*), or *Sephadex LH-20* (*Pharmacia*). Optical rotation: *Jasco DIP-370* polarimeter. UV Spectra: *Shimadzu UV-3100* spectrophotometer; λ_{max} (log ε) in nm. ^{1}H- and ^{13}C-NMR Spectra: *Jeol JNM-LA-300* spectrometer; in (D_6)acetone; δ(H) in ppm rel. to Me_4Si (=0 ppm) as internal standard, δ(C) in ppm rel. to residual solvent signals (C=O at 206.0 ppm); coupling constants *J* in Hz. FAB- and HR-FAB-MS: *Jeol JMS-SX-102A* instrument; in *m*/*z*. All the computational calculations were performed on a PCMODEL V 9.0 software [4]. The geometry optimizations of the structures leading to energy minima and the conformational analysis were achieved by using MMFF force field.

Plant Material. Dipterocarpus grandiflorus (BLANCO) BLANCO was cultivated at Bogor Botanical Garden, Bogor, Indonesia, from which the stem was collected and identified by one of us (*D. D.*) in May 2000. A voucher specimen was deposited with the Gifu Pharmaceutical University, Gifu, Japan.

Extraction and Isolation. The extraction procedures are described in our previous work [3c]. The acetone extract (20 g) of stems of *D. grandiflorus* (550 g) was subjected to chromatography on a SiO_2 column ($CHCl_3$/MeOH gradient) to give six fractions (*Frs. A – F*). *Fr. B* ($CHCl_3$/MeOH 10:1, 620 mg) was further subjected to reversed-phase CC (H_2O/MeOH gradient, 40–60% MeOH): *Frs. B$_1$ – B$_{22}$*. Compound **1** (3 mg) was obtained from the combined *Frs. B$_7$ – B$_{12}$* after purification by repeated CC (*Sephadex LH-20*, MeOH) and prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 80:40:11:2). *Fr. D* ($CHCl_3$/

Scheme 2. *Plausible Biogenetic Pathways of Resveratrol Oligomers.* Pathway starting from α-viniferin.



MeOH 8:1, 960 mg) was further subjected to CC (*Sephadex LH-20*, MeOH): further purification of *Fr. D_{23}* by prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1) led to the isolation of **2** (6 mg).

Grandiphenol C (= rel-*(2S,2aS,5bR,7R,7aS,12R,12aR)-2,2a,7,7a,12,12a-Hexahydro-5b,9,14-trihydroxy-2,7,12-tris(4-hydroxyphenyl)bis[1]benzofuro[3′,4′:4,5,6;3″,4″:7,8,9]cyclonona[1,2,3*-cd*][1]benzofuran-4(5bH)-one*; **1**). Pale yellow solid. $[\alpha]_D^{25} = -16$ ($c = 0.1$, MeOH). UV: 279 (sh, 4.36), 284 (4.37), 292 (sh, 4.30), 314 (sh, 4.03). ^{1}H- and ^{13}C-NMR: *Table 1*. FAB-MS (pos.): 695 ($[M+H]^+$). HR-FAB-MS (pos.): 695.1925 ($[M+H]^+$, $C_{42}H_{31}O_{10}^+$; calc. 695.1917).

Grandiphenol D (= rel-*(2aR,7R,7aR,12S,12aS)-7,7a,12,12a-Tetrahydro-4,9,14-trihydroxy-2a,7,12-tris(4-hydroxyphenyl)bis[1]benzofuro[3′,4′:4,5,6;3″,4″:7,8,9]cyclonona[1,2,3*-cd*][1]benzofuran-2(2aH)-one*; **2**). Pale yellow solid. $[\alpha]_D^{25} = -6.0$ ($c = 0.1$, MeOH). UV: 286 (3.91), 294 (sh, 3.83). ^{1}H- and ^{13}C-NMR: *Table 2*. FAB-MS (pos.): 693 ($[M+H]^+$). HR-FAB-MS (pos.): 693.1754 ($[M+H]^+$, $C_{42}H_{29}O_{10}^+$; calc. 693.1760).

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