Two New Resveratrol (= 5-[(1*E*)-2-(4-Hydroxyphenyl)ethenyl]-benzene-1,3-diol) Tetramers with a Tetrahydrofuran Ring from *Dipterocarpus grandiflorus*

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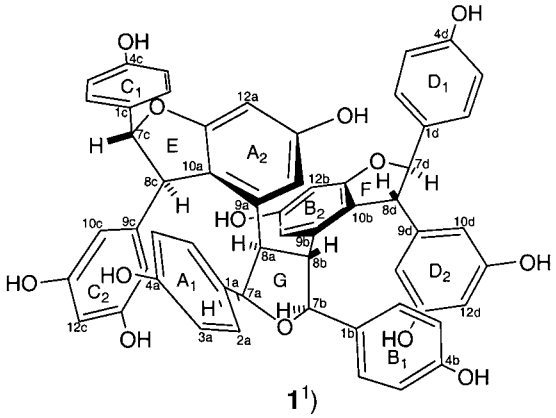
Two new stilbene tetramers, grandiphenols A (**1**) and B (**2**), along with ten known stilbene oligomers and bergenin were isolated from the stem of *Dipterocarpus grandiflorus*. The structures of **1** and **2** composed of four resveratrol (= 5-[(1*E*)-2-(4-hydroxyphenyl)ethenyl]benzene-1,3-diol) units had eight asymmetric C-atoms in the partial structures of a tetrahydrofuran and two dihydrobenzofuran moieties. Detailed spectroscopic analyses, especially HMBC and NOESY experiments, allowed to differentiate the configurations of **1** and **2**.

Introduction. – The chemistry of stilbenoids is well-studied owing to the variety of skeletons including heterocyclic systems, complexity of configuration, and various degrees of oligomerization. The varieties of stilbenoid compounds encountered in nature result from various bioactivities. In spite of chemical diversity, occurrence of stilbenoids in the plant kingdom is restricted, and the ecological roles have not always been clarified. Much attention has been paid to stilbenoids with respect to the recent discovery of functional bioactivity. One well-known example is so called French Paradox, which resulted in the study of one of several polyphenols, *i.e.*, of resveratrol (3,5,4′-trihydroxystilbene = 5-[(1*E*)-2-(4-hydroxyphenyl)ethenyl]benzene-1,3-diol) [1]. Some resveratrol oligomers also displayed bioactivities, *e.g.*, anti-HIV activity [2], cytotoxicity [3], and anti-inflammatory effects [4]. Wide-range bioactive screening of resveratrol oligomers requires to progress with their chemical pool after exact structural elucidation. Thus, we have revealed the structures of stilbene oligomers in some Dipterocarpaceous genera of *Vatica* [5], *Vateria* [6], *Shorea* [7], and *Hopea* [8]. The isolates studied up to the present were composed of all resveratrol oligomers, ranging from monomer to octamer, except for the pentamer. Further interest in the diversity of resveratrol oligomers led to the current research on *Dipterocarpus grandiflorus* (BLANCO), the genus of which comprises 53 species distributed only in Southeast Asia [9]. Detailed phytochemical information has not been reported yet. The examination of the acetone extract of stem resulted in the isolation of two new diastereoisomeric resveratrol tetramers, grandiphenols A (**1**) and B (**2**), the skeleton of

which bear a tetrahydrofuran and two dihydrobenzofuran moieties. Eleven known stilbenoids, vaticanols B (**3**) and C (**4**), hemsleyanol D (**5**), (−)-hopeaphenol (**6**), (+)-α-viniferin (**7**), miyabenol C (**8**), (−)-ε-viniferin (**9**), (−)-ampelopsin A (**10**), (−)-ampelopsin F (**11**), isoampelopsin F (**12**), and shorealactone (**13**), as well as bergenin (**14**) were also isolated, and their structures were identified. This report deals with the structure elucidation of **1** and **2**, in particular configurations, which were investigated by spectroscopy and by comparison with related tetramers.



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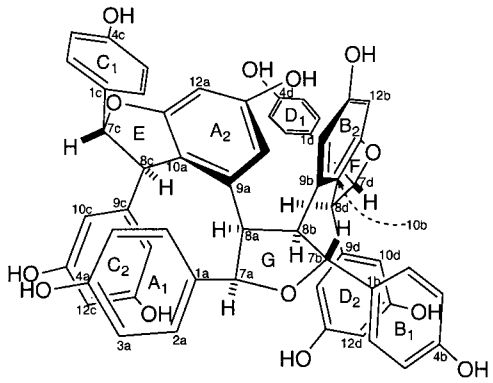

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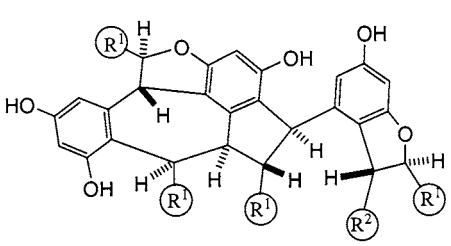
Results and Discussion. – The optically active grandiphenols A (**1**) and B (**2**) were isolated from the acetone extract of stem of *D. grandiflorus* by column chromatography (silica gel, *Sephadex LH-20*, ODS) and prep. TLC. Both compounds were obtained as pale yellow amorphous powders and showed positive reactions to the *Gibbs* reagent. The UV spectra of both **1** and **2**, displayed an absorption maximum at 284 nm, which is consistent with the presence of one or more nonconjugated phenyl rings. Their compositions were deduced to be $C_{56}H_{44}O_{13}$ from the pseudomolecular ion $[M+Na]^+$ observed at *m*/*z* 947.2653 (**1**) and 947.2668 (**2**) in the positive-ion HR-ESI-MS.



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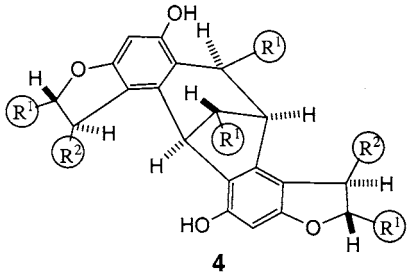

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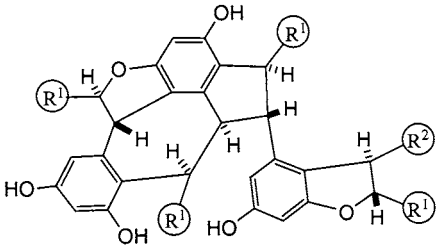

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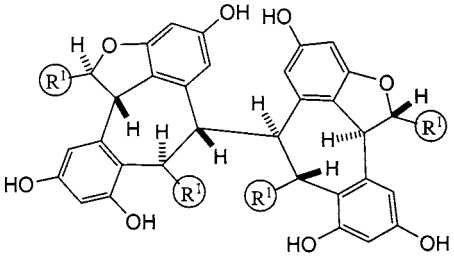

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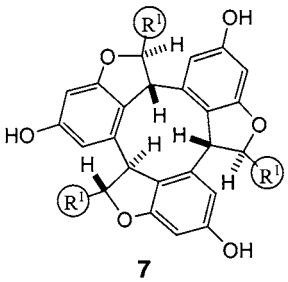

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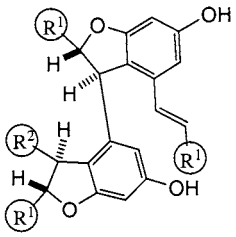

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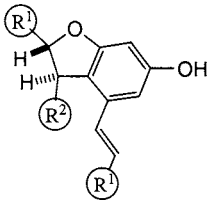

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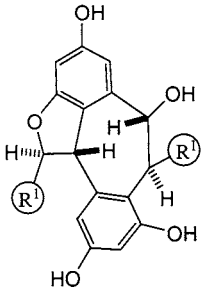

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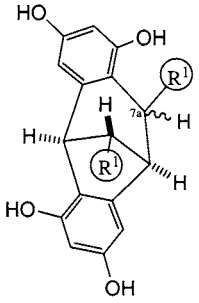
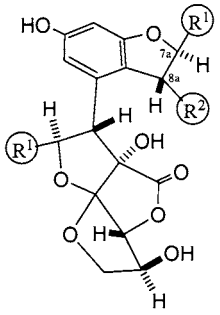


11[1]) H–(C7a) = α

12[1]) H–C(7a) = β



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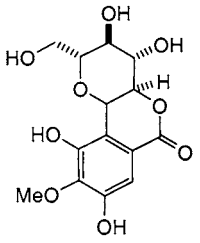

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R^1 = 4-hydroxyphenyl, R^2 = 3,5-dihydroxyphenyl

The structure of **1**[1]) was determined as follows. Its ^{1}H-NMR spectrum in (D_6)acetone at room temperature (*Table 1*) exhibited signals for ten OH H-atoms (δ 7.75–8.31) that disappeared on addition of D_2O. The remaining three O-atoms of the molecular formula were attributed to ether linkages. The ^{1}H- and ^{13}C-NMR, ^{1}H,^{1}H-COSY, ^{13}C,^{1}H-COSY, and HMBC data (*Table 1*) were consistent with the presence of four 4-hydroxyphenyl groups (designated as A_1–D_1), two 3,5-dihydroxyphenyl groups (C_2 and D_2), and two 3,5-dioxygenated-1,2-disubstituted benzene rings (A_2 and B_2). The presence of two sets of mutually coupled aliphatic H-atoms (H–C(7c) and H–C(8c); H–C(7d) and H–C(8d)) and a sequence of four aliphatic H-atoms (H–C(7a), H–C(8a), H–C(8b), and H–C(7b)) were also shown. The chemical shifts of the C-atoms bonded to the former H-atoms (93.39 (C(7c)), 55.54 (C(8c)), 94.55 (C(7d)), 55.00 (C(8d))) were typical for C-atoms of a dihydrobenzofuran moiety [5a], and those of the C-atoms bonded to the latter H-atoms (81.86 (C(7a)), 58.76 (C(8a)), 84.84 (C(7b)), 52.95 (C(8b))) were also similar to those of a tetrahydrofuran moiety such as that of kobophenol A (**15**) [10]. Several stilbene oligomers containing a tetrahydrofuran structure including **15** have been reported hitherto, and they are all resveratrol oligomers (tricuspidatol A (**16**) [11]; compound **17** [12]). Their relative configurations and the summarized NMR spectral data are given with their formulae in *Fig. 1*. Comparison with these data confirmed that the three remaining O-atoms of the molecular formula of **1** and **2** were involved in two dihydrobenzofuran and a tetrahydrofuran moiety. The results obtained from ^{1}H-NMR spectra at various temperatures implied that ring D_2 of **1** does not rotate freely, because of the steric hindrance due to neighboring substituent(s) and(or) other factors. In the structure of **1**, the conformation of ring G and the restricted free rotation of ring B_2 might be the important factors that are reflected in the spectral behavior of ring D_2. A similar phenomenon was also observed in ring A_1. The signals (δ(H) 6.78 (H–C(2a,6a)), 6.65 (H–C(3a,5a))) gradually became broad and weakened on lowering the temperature to $-60°$ (see below, *Fig. 8*) and reappeared at $-80°$ (not shown). As mentioned below, the behavior of some H-atoms in the stilbene oligomers are very complicated. Therefore, further spectral evidence in connection with steric factors are required for the accurate determination of the configuration in the stilbene oligomers such as **1** and related compounds.

Complete assignment of all quaternary C-atoms of the rings of **1** (A_1–D_1 and A_2–D_2) was established by the HMBC spectrum (*Table 1*). The connection of partial structures was deduced as follows. The significant ^3J long-range correlations were observed for H–C(2a,6a)/C(7a), H–C(14a)/C(8a), H–C(2b,6b)/C(7b), H–C(14b)/C(8b), H–C(2c,6c)/C(7c), H–C(10c,14c)/C(8c), H–C(2d,6d)/C(7d), and H–C(8d)/C(10d,14d) (*Fig. 2*), indicating that the rings A_1, A_2, B_1, B_2, C_1, C_2, D_1, and D_2 are attached at C(7a), C(8a), C(7b), C(8b), C(7c), C(8c), C(7d), and C(8d), respectively. Thus **1** is composed of four resveratrols A–D (resveratrol A: ring A_1–C(7a)–C(8a)–ring A_2). Long-range correlations were further observed between the aliphatic methine H-atoms and the quaternary C-atoms of ring A_2 (H–C(8c)/C(11a); H–C(7c)/C(11a)), which implied the presence of a dihydrobenzofuran moiety (C(10a)–C(11a)-O–C(7c)–C(8c): ring E). On the basis of similar considerations, the presence of another dihydrobenzofuran moiety (C(10b)–C(11b)-O–C(7d)–C(8d): ring F) was confirmed. Although no long-range correlation between H–C(7a)/C(7b) and/or H–C(7b)/C(7a) was observed, the presence of the central tetrahydrofuran ring (C(7a)–C(8a)–(8b)–C(7b)–O: ring G) is

[1]) Arbitrary numbering; for systematic names of **1** and **2**, see *Exper. Part*.

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

H-Atom	δ(H)	C-Atom	δ(C)	HMBC
		C(1a)	133.21	
H–C(2a,6a)	6.78 (d, J = 8.6)	C(2a,6a)	128.98	C(4a), C(7a)
H–C(3a,5a)	6.65 (d, J = 8.6)	C(3a,5a)	114.99	C(1a), C(4a)
		C(4a)	156.69	
H–C(7a)	4.71 (d, J = 9.3)	C(7a)	81.86	C(1a), C(2a,6a)
H–C(8a)	3.94 (dd, J = 11.9, 9.3)	C(8a)	58.76	C(1a), C(7a), C(9a), C(10a), C(14a), C(9b)
		C(9a)	136.33	
		C(10a)	123.07	
		C(11a)	159.90	
H–C(12a)	5.92 (d, J = 2.0)	C(12a)	96.39	C(10a), C(11a), C(13a), C(14a)
		C(13a)	157.72	
H–C(14a)	5.67 (d, J = 2.0)	C(14a)	110.18	C(8a), C(10a), C(12a), C(13a)
		C(1b)	129.81	
H–C(2b,6b)	6.76 (d, J = 8.4)	C(2b,6b)	129.16	C(4b), C(7b)
H–C(3b,5b)	6.58 (d, J = 8.4)	C(3b,5b)	115.64	C(1b), C(4b)
		C(4b)	158.04[a])	
H–C(7b)	5.01 (d, J = 10.2)	C(7b)	84.84	C(8a), C(1b), C(2b,6b), C(8b)
H–C(8b)	3.60 (dd, J = 11.9, 10.2)	C(8b)	52.95	C(8a), C(9a), C(1b), C(7b), C(9b), C(10b),
		C(9b)	138.49	C(14b)
		C(10b)	122.56	
		C(11b)	161.40	
H–C(12b)	6.17 (d, J = 2.0)	C(12b)	95.93	C(10b), C(11b), C(13b), C(14b)
		C(13b)	159.39	
H–C(14b)	6.65 (d, J = 2.0)	C(14b)	105.32	C(8b), C(10b), C(12b), C(13b)
		C(1c)	133.31	
H–C(2c,6c)	6.88 (d, J = 8.6)	C(2c,6c)	128.77	C(4c), C(7c)
H–C(3c,5c)	6.67 (d, J = 8.6)	C(3c,5c)	115.90	C(1c), C(4c)
		C(4c)	157.97[a])	
H–C(7c)	5.23 (d, J = 5.1)	C(7c)	93.39	C(10a), C(11a), C(1c), C(2c,6c), C(8c), C(9c)
H–C(8c)	4.08 (d, J = 5.1)	C(8c)	55.54	C(9a), C(10a), C(11a), C(1c), C(7c), C(9)c,
		C(9c)	148.25	C(10c,14c)
H–C(10c,14c)	6.23 (d, J = 2.2)	C(10c,14c)	106.97[b])	C(8c), C(11c,13c), C(12c)
		C(11c,13c)	159.67	
H–C(12c)	6.33 (t, J = 2.2)	C(12c)	101.81	C(10c,14c), C(11c,13c)
		C(1d)	133.16	
H–C(2d,6d)	6.68 (d, J = 8.6)	C(2d,6d)	128.35	C(4d), C(7d)
H–C(3d,5d)	6.54 (d, J = 8.6)	C(3d,5d)	115.71	C(1d), C(4d)
		C(4d)	157.43	
H–C(7d)	5.09 (d, J = 4.8)	C(7d)	94.55	C(10b), C(11b), C(1d), C(2d,6d), C(8d), C(9d)
H–C(8d)	3.94 (d, J = 4.8)	C(8d)	55.00	C(9b), C(10b), C(11b), C(1d), C(7d), C(9d),
		C(9d)	147.94	C(10d,14d)
H–C(10d,14d)	6.03 (br. s)	C(10d,14d)	106.97[b])	
		C(11d,13d)	159.57	
H–C(12d)	6.28 (t, J = 2.2)	C(12d)	101.97	C(10d,14d), C(11d,13d)
OH groups	8.31 (br. s, 4 OH)			
	8.18 (br. s, 1 OH)			
	8.08 (br. s, 2 OH)			
	7.99 (br. s, 2 OH)			
	7.75 (br. s, 1 OH)			

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

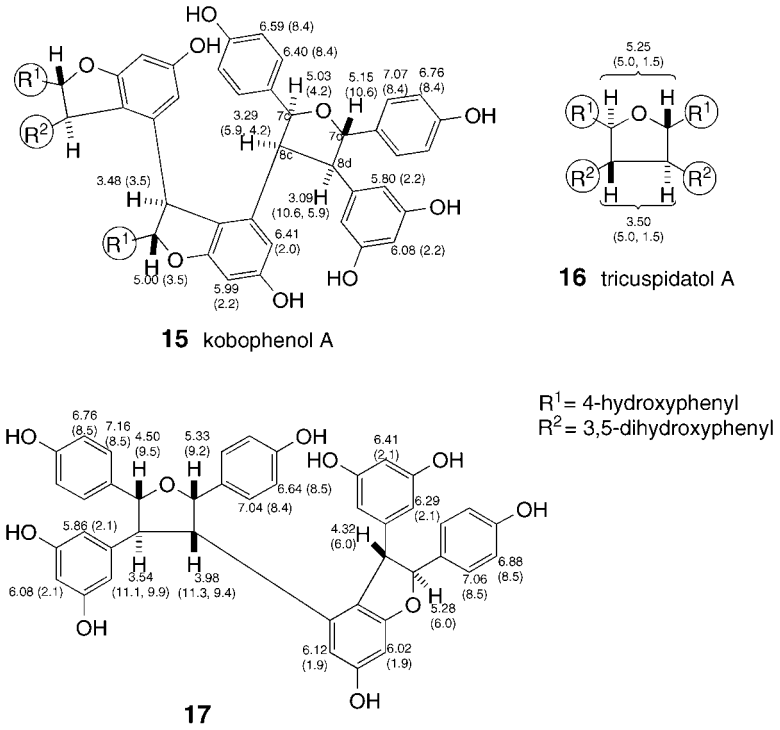


Fig. 1. *Structures and* ^{1}*H-NMR data* ((D$_6$)acetone) *of compounds* **15**–**17**. δ in ppm, J values in Hz in the parentheses.

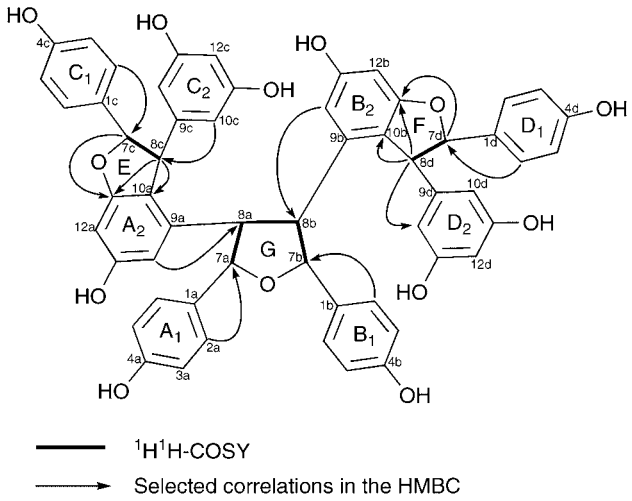


Fig. 2. *Main connectivities from the HMBC and* ^{1}*H,*^{1}*H-COSY experiments with* **1**

proposed to accommodate the remaining ether linkage. The planar structure of grandiphenol A was then determined to be **1** as shown in *Fig. 2*.

The configuration of **1** was established by the NOESY data (see *Exper. Part*; selected data in *Figs. 3–6*). Significant NOEs were observed for H–C(2c,6c)/H–C(8c), H–C(10c,14c)/H–C(7c), H–C(2d,6d)/H–C(8d), and H–C(10d,14d)/H–C(7d) (*Fig. 3*), suggesting that the two methine H-atoms at both ring E and F (H–C(7c)/H–C(8c); H–C(7d)/H–C(8d)) are *trans* to each other. H–C(7b) displayed NOEs with H–C(7a) and H–C(8a), which can be observed only when these three atoms are situated on the same side of a reference plane (α-configuration) and the O-atom or C(8b) of ring G form the flap of the envelope conformation (*Fig. 4*). The key point for the differentiation of the two envelopes was an NOE H–C(7a)/H–C(14b). In the former case (*Fig. 4*, left), the H-atoms (H–C(7a), H–C(14b)) are neighbors, while in the latter case (*Fig. 4*, right), they are never in such a situation; thus the conformation of the tetrahydrofuran ring (ring G) is an envelope with the O-atom as flap (*Fig. 4*, left). Additional NOEs (H–C(2b,6b)/H–C(8b); H–C(14a)/H–C(8b)) confirmed the *trans* relationship of H–C(7b) and H–C(8b). The large values of J(7b,8b) (= 10.2 Hz) and J(8b,8a) (= 11.9 Hz) further supported this conformation. The relationships H–C(7b)/H–C(8b) and H–C(8b)/H–C(8a) are both *trans* diaxial. Although a large J(7a,8a) (= 9.3 Hz) was observed, an eclipsed *cis* relationship was suggested for the involved protons (*Fig. 4*, left). Similar spectral data have been reported for the tetrahydrofuran rings of **17**. Therefore, the relative configuration of **17** and **1** are identical.

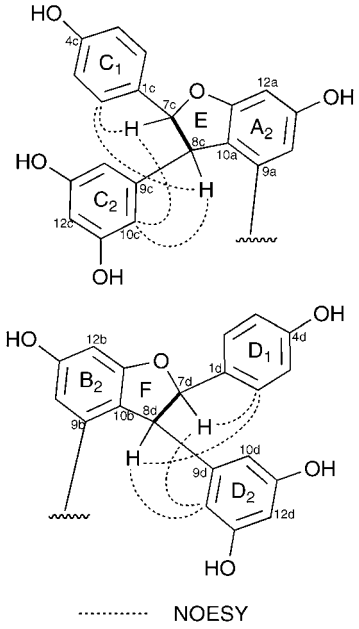


Fig. 3. *NOEs observed for the dihydrobenzofuran moieties of* **1**

The configurational relationships of the three partial structures **1A**–**1C** were determined as follows. Methine H-atoms and aromatic H-atoms generally displayed strong NOEs when positioned on the same side of a reference plane (β-configuration), such as found for H–C(2a,6a)/H–C(7a), H–C(2b,6b)/H–C(7b), and so on. But no NOE was observed for H–C(8a)/H–C(14a) and H–C(8b)/H–C(14b). These results strongly indicated that the rings A_2 and B_2 are not permitted to rotate freely due to steric hindrance (*Fig. 5*). This steric hindrance around ring G was confirmed by the distinct NOEs (H–C(8a)/H–C(14b), H–C(14a)/H–C(8b), and H–C(7b)/H–C(14b) and the absence of an NOE H–C(14a)/H–C(14b).

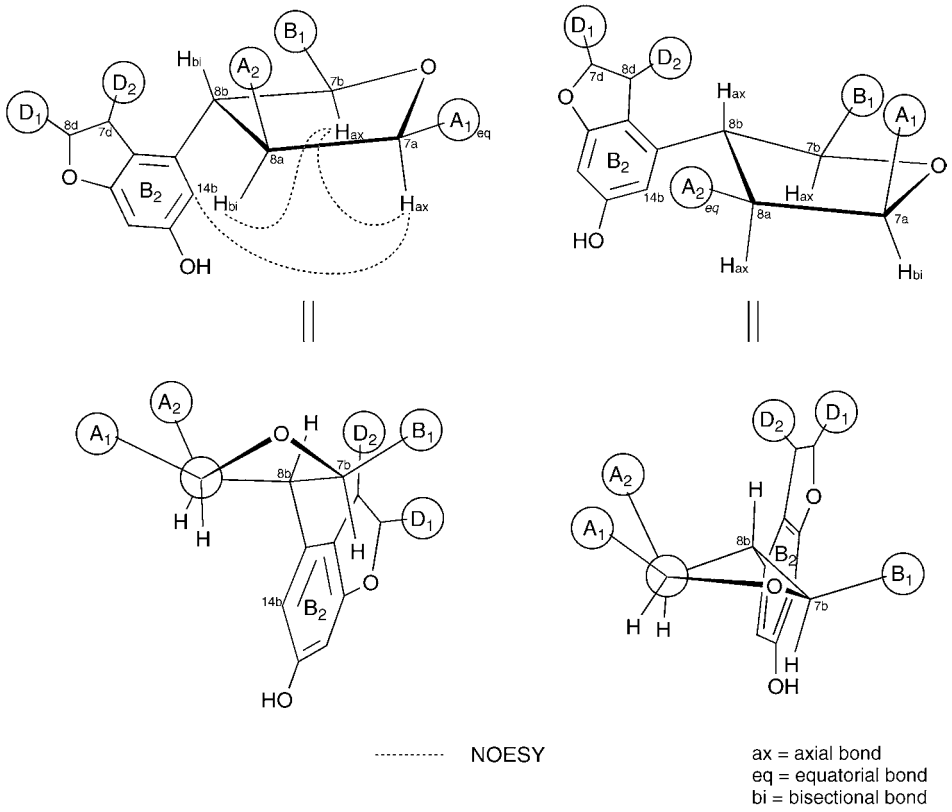
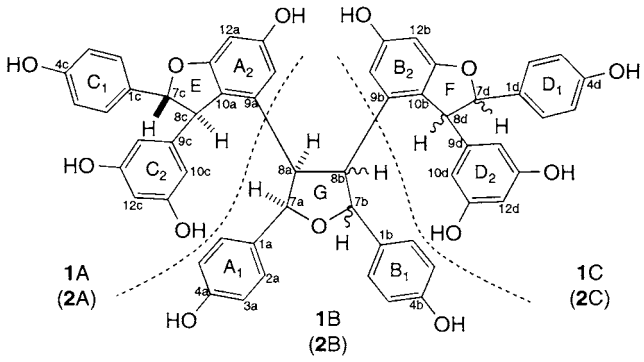


Fig. 4. *Two possible conformational isomers of the tetrahydrobenzofuran moiety of* **1** (left: O-atom as flap of the envelope, right: C(8b) as flap of the envelope) *and observed NOEs*



1 H–C(7b), H–C(7d) = α ; H–C(8b), H–C(8d) = β
2 H–C(7b), H–C(7d) = β ; H–C(8b), H–C(8d) = α

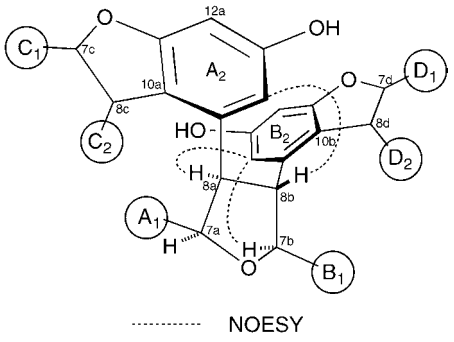


Fig. 5. *Restricted rotation of the rings A_2 and B_2 in* **1**

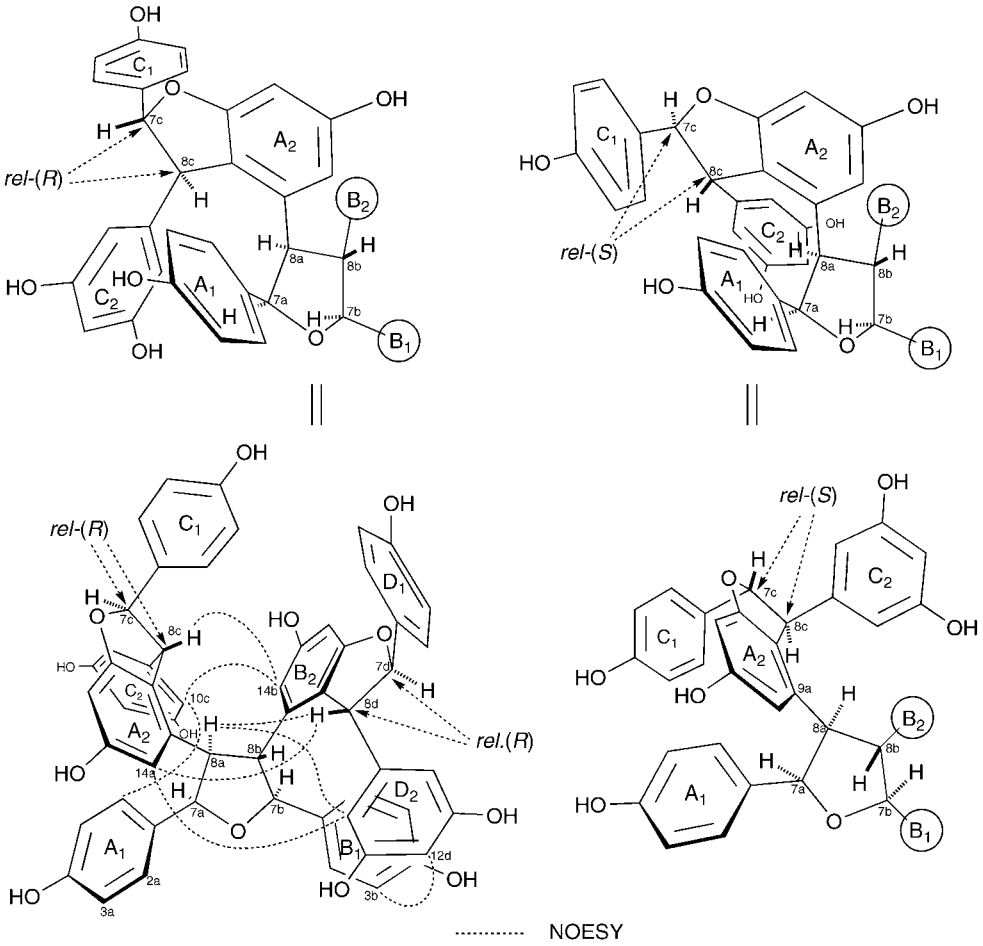


Fig. 6. *Two possibilities of the configurational relation among* **1A** – **1C** (left: *rel*-(*R*) configuration of C(7c) and C(8c); right: *rel*-(*S*) configuration of C(7c) and C(8c)) *and NOEs essential for differentiation*

Another distinct NOE was observed for H–C(8c)/H–C(14b), suggesting that C(8c) has the relative *R* configuration (*rel*-(*R*)) (C(7c) also *rel* (*R*)); *Fig. 6*, left). Although an NOE H–C(10c,14c)/H–C(14b) was observed, an NOE H–C(8c)/H–C(14b) could hardly occur if C(8c) has *rel*-(*S*) configuration (C(7c) also *rel*-(*S*); *Fig. 6*, right). The distinct NOE H–C(2a,6a)/H–C(10c,14c) also supported this relation between partial structures **1A** and **1B**. Similarly, C(8d) was determined to have the *rel*-(*R*) configuration (C(7d) also *rel*-(*R*)) by the NOEs H–C(8d)/H–C(14a), H–C(10d,14d)/H–C(14a), and H–C(3b,5b)/H–C(12d) (*Fig. 6*, left). Therefore, the relative configuration of grandiphenol A (**1**) as depicted in its formula could be deduced. The fixation of rings A_2 and B_2 played an important role for determination of the relationship among the partial structures **1A**–**1C**. In general, the free rotation of bulky substituents, here of **1A** and **1C**, render the determination of the configurational relationship difficult. An example is vateriaphenol A (**18**) [6] for which the configurational relationship of the partial structures **18A**–**18C** is still undetermined (*Fig. 7*).

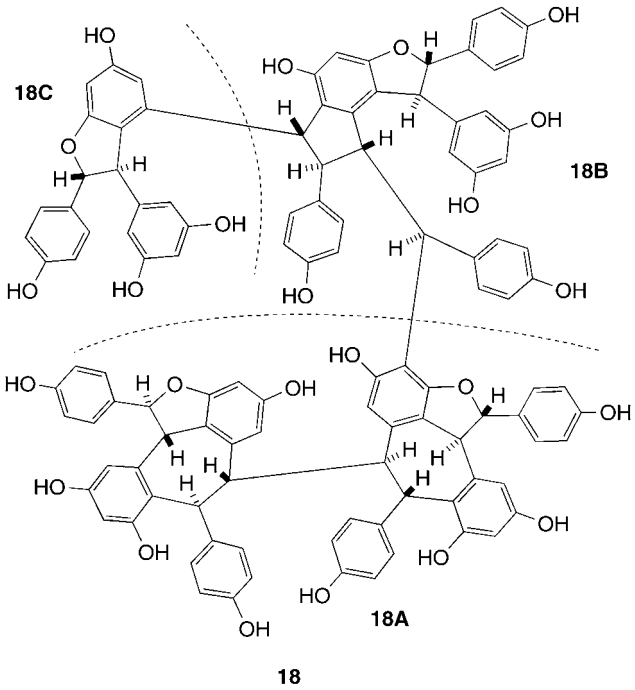
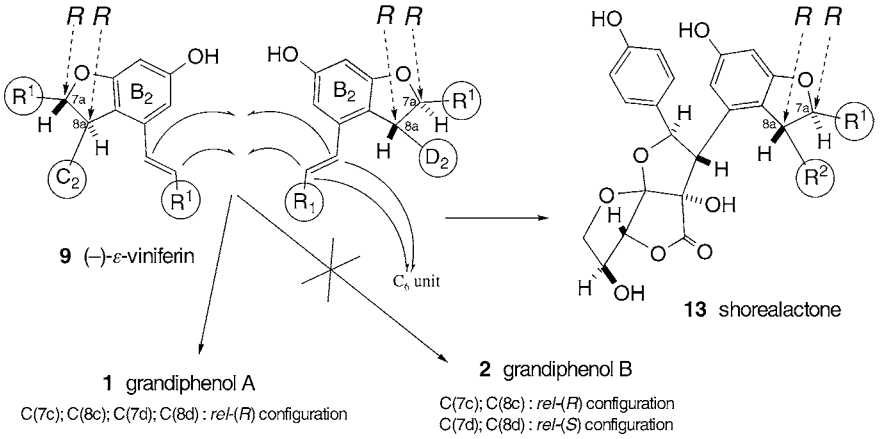


Fig. 7. *Partial structures* **18A**–**18C** *of vateriaphenol A* (**18**)

In the ^{1}H-NMR spectrum of **1** at room temperature, the aromatic H–C(10d) and H–C(14d) were observed as a broad signal. Similar behavior of H-atoms of a 3,5-dihydroxyphenyl group of some stilbene oligomers (vaticanol B (**3**); isovaticanol B) has been reported in the previous paper [5a]. In their ^{1}H-NMR spectra, the two equivalent H-atoms (H–C(10d) and H–C(14d) of the 3,5-dihydroxyphenyl group have been observed as two independent broad *s* at $-20°$ (or $-40°$), which was caused by steric hindrance. In the ^{1}H-NMR spectra of **1** at variable temperature (25 to $-60°$; *Fig. 8*), the signals of H–C(10d) and H–C(14d) gradually diminished and disappeared at $-10°$, appeared again at $-30°$ as independent signals, and became sharp signals at $-60°$. The mutual coupling of H–C(10d) and H–C(14d) was confirmed by a ^{1}H,H-COSY experiment at $-55°$. The chemical shifts of the independent signals were quite different between -30 and $-90°$, *e.g.* δ(H), 5.69 (H–C(10d)) and 6.56 (H–C(14d)) at $-55°$ (for the assignment, see *Exper. Part*), which strongly suggested that they were located in a different environment. At $-55°$, where H–C(14d) gave the clearest signal separated from the neighboring ones (*Fig. 8*, *e*), an NOE was observed for H–C(8d)/H–C(14d) but not for H–C(8d)/H–C(10d) (*Fig. 9*). In this experiment, further NOEs were observed for H–C(7d)/H–C(10d) but not for

Scheme



H–C(8d)/H–C(14d), and for H–C(8b)/H–C(14d) but not for H–C(8b)/H–C(10d); if ring D_2 rotated freely at −55°, these NOEs should be observed. The signals of OH–C(11d) and OH–C(13d) of **1** behaved in a manner analogous to H–C(10d) and H–C(14d) (*Fig. 8*).

The structure of **2** was determined in the same manner as that of **1**. Analysis of the ^{1}H- and ^{13}C-NMR, ^{1}H,^{1}H-COSY, ^{13}C,^{1}H-COSY, and HMBC data (*Table 2*) confirmed that **2** had the same planar structure as **1**. The configuration of **2** was determined by the NOESY data (see *Exper. Part*; selected data in *Figs. 10* and *11*).

The NOEs for H–C(2c,6c)/H–C(8c), H–C(10c,14c)/H–C(7c), H–C(2d,6d)/H–C(8d), and H–C(14d)/H–C(7d) suggested that the two methine H-atoms at both ring E and F (H–C(7c)/H–C(8c); H–C(7d)/H–C(8d)) are in *trans* position to each other. The relative configuration of ring G was determined as follows. H–C(7a) displayed NOEs with H–C(2b,6b) and H–C(8b), which indicated that H–C(7a), ring B_1, and H–C(8b) are situated on the same side of a reference plane (α-configuration). A further NOE for H–C(14a)/H–C(7b) was observed, which implied that H–C(7b) and ring A_2 are *cis* oriented to each other (β-configuration). The NOEs, especially H–C(7a)/H–C(2b,6b), supported that C(8a) is the flap of the envelope conformation of ring G (see *Fig. 10*). The coupling-constant patterns among H–C(7a), H–C(8a), H–C(7b), and H–C(8b) of **2** have similarity to those of a same moiety of kobophenol A (**15**; *Fig. 1*).

The configurational relationship among the three partial structures **2A**–**2C** (see above) was determined as follows. The observation of distinct NOEs for H–C(14a)/H–C(7b) and H–C(7b)/H–C(14b) and not for H–C(8a)/H–C(14a) and H–C(8b)/H–C(14b) (*Fig. 11*) implied that the restriction of free rotation applies to rings A_2 and B_2 of **2**, similar to **1**. A molecular model confirmed an NOE for H–C(14a)/H–C(14b). The NOE for H–C(8c)/H–C(8d) established the *rel*-(*S*) and *rel*-(*R*) configuration for C(8c) and C(8d), respectively (*Fig. 11*). This relationship among the partial structures **2A**–**2C** was well supported by the NOEs for H–C(2a,6a)/H–C(10c,14c), H–C(3c,5c)/H–C(3d,5d), and H–C(2b,6b)/H–C(10d,14d) (not shown in *Fig. 11*).

In addition to grandiphenols A (**1**) and B (**2**), 11 known resveratrol oligomers were isolated, and their structures were identified as vaticanols B (**3**) and C (**4**) [5c], hemsleyanol D (**5**) [7b], (–)-hopeaphenol (**6**) [13], (+)-α-viniferin (**7**) [14], miyabenol C (**8**) [15], (–)-ε-viniferin (**9**) [16], (–)-ampelopsin A (**10**) [8b], (–)-ampelopsin F (**11**) [17], isoampelopsin F (**12**) [18] and shorealactone (**13**) [7a]. For shorealactone (**13**), the absolute structure has been established by means of X-ray crystallographic analysis

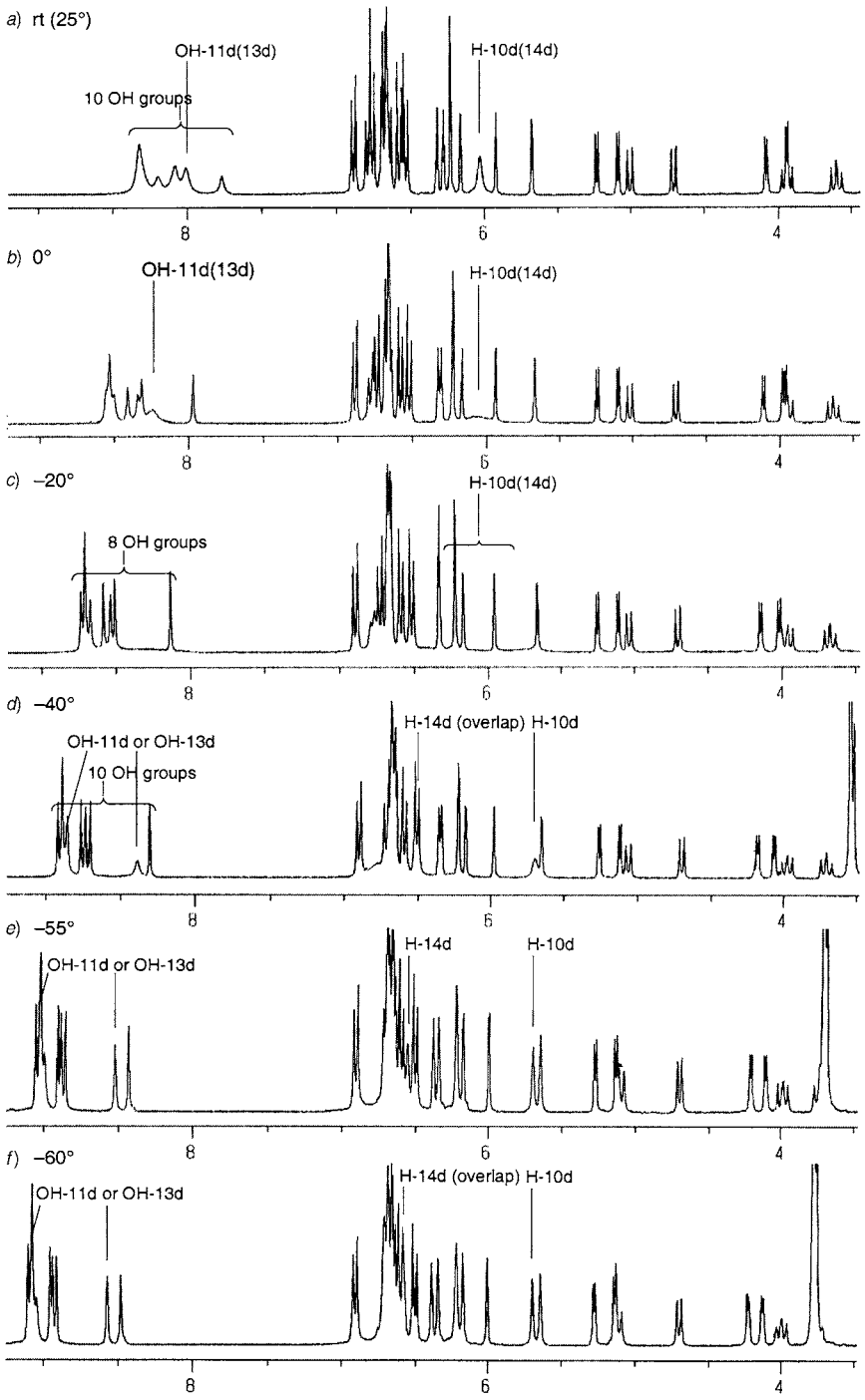


Fig. 8. *^{1}H-NMR Spectra* (D_6(acetone), 300 MHz) *of* **1** *at variable temperatures.* OH-11d(13d) = OH–C(11d) and OH–C(13d), H-10d(14d) = H–C(10d) and H–C(14d).

Table 2. *NMR Data for Grandiphenol B* (**2**). (D_6)Acetone solution; at 300 (^1H) and 75 MHz (^{13}C). δ in ppm, J in Hz.

H-Atom	δ(H)	C-Atom	δ(C)	HMBC
		C(1a)	131.20	
H–C(2a,6a)	6.52 (d, J = 8.8)	C(2a,6a)	127.52	C(4a), C(7a)
H–C(3a,5a)	6.42 (d, J = 8.8)	C(3a,5a)	115.14	C(1a), C(4a)
		C(4a)	155.94	
H–C(7a)	5.34 (d, J = 5.5)	C(7a)	85.53	C(1a), C(2a,6a), C(9a)
H–C(8a)	3.44 (t, J = 5.5)	C(8a)	50.46	C(10a), C(14a), C(7b), C(8b)
		C(9a)	136.39	
		C(10a)	124.09	
		C(11a)	160.64[a])	
H–C(12a)	6.09 (d, J = 2.1)	C(12a)	96.09	C(10a), C(11a), C(13a), C(14a)
		C(13a)	158.75	
H–C(14a)	6.48 (d, J = 2.1)	C(14a)	110.27	C(8a), C(10a), C(12a), C(13a)
		C(1b)	134.11[b])	
H–C(2b,6b)	7.03 (d, J = 8.8)	C(2b,6b)	127.78	C(4b), C(7b)
H–C(3b,5b)	6.79 (d, J = 8.8)	C(3b,5b)	115.76	C(1b), C(4b)
		C(4b)	157.79	
H–C(7b)	5.12 (d, J = 10.6)	C(7b)	86.95	C(2b,6b), C(8b)
H–C(8b)	3.83 (dd, J = 10.6, 5.5)	C(8b)	57.22	C(8a), C(1b), C(7b), C(10b), C(14b)
		C(9b)	135.39	
		C(10b)	122.91	
		C(11b)	160.84[a])	
H–C(12b)	6.19 (d, J = 2.1)	C(12b)	96.77[c])	C(10b), C(11b), C(13b), C(14b)
		C(13b)	159.03	
H–C(14b)	5.53 (d, J = 2.1)	C(14b)	108.5	C(8b), C(10b), C(12b), C(13b)
		C(1c)	134.03[b])	
H–C(2c,6c)	6.90 (d, J = 8.8)	C(2c,6c)	128.63	C(4c), C(7c)
H–C(3c,5c)	6.74 (d, J = 8.8)	C(3c,5c)	116.03[e])	C(1c), C(4c)
		C(4c)	158.19	
H–C(7c)	5.15 (d, J = 3.1)	C(7c)	94.08[c])	C(11a), C(1c), C(2c,6c), C(8c), C(9c)
H–C(8c)	3.70 (d, J = 3.1)	C(8c)	55.37	C(10a), C(11a), C(1c), C(9c), C(10c,14c)
		C(9c)	148.36[d])	
H–C(10c,14c)	5.97 (d, J = 2.0)	C(10c,14c)	107.08	C(8c), C(11c,13c), C(12c)
		C(11c,13c)	159.47	
H–C(12c)	6.24 (t, J = 2.0)	C(12c)	101.52	C(10c,14c), C(11c,13c)
		C(1d)	132.95	
H–C(2d,6d)	6.75 (s)	C(2d,6d)	128.76	C(4d), C(7d)
H–C(3d,5d)	6.75 (s)	C(3d,5d)	116.03[e])	C(1d), C(4d)
		C(4d)	157.90	
H–C(7d)	5.15 (d, J = 6.1)	C(7d)	93.97	C(11b), C(2d,6d), C(9d)
H–C(8d)	3.55 (d, J = 6.1)	C(8d)	56.22	C(10b), C(11b), C(1d), C(7d),
		C(9d)	148.26[d])	C(9d), C(10d,14d)
H–C(10d,14d)	6.18 (d, J = 2.0)	C(10d,14d)	107.50	C(8d), C(11d,13d), C(12d)
		C(11d,13d)	159.06	
H–C(12d)	6.37 (t, J = 2.0)	C(12d)	102.87	C(10d,14d), C(11d,13d)
	8.31 (br. s, OH)			
	8.18 (br. s, OH)			
	8.01 (br. s, OH)			
OH groups	7.90 (br. s, OH)			

[a]) – [d]) Interchangeable. [e]) Overlapping.

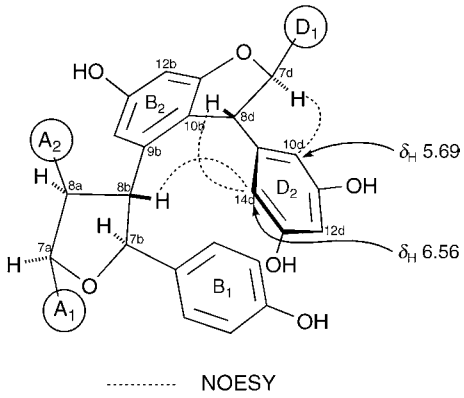


Fig. 9. *Selected NOEs observed in the NOESY experiment with* **1** *at* $-55°$

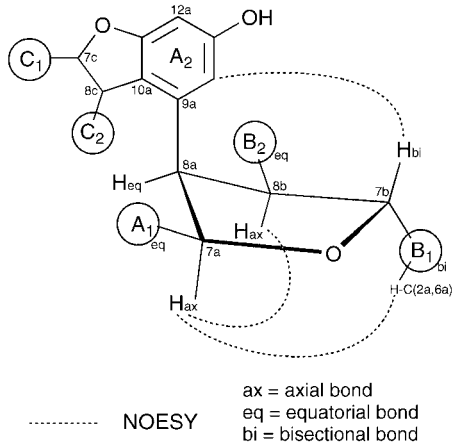


Fig. 10. *Conformation of the tetrahydrobenzofuran moiety of* **2**

of its 4-bromobenzoyl derivative by using anomalous scattering of the Br-atom [7a]. Compound **13** has the same partial structures as (−)-ε-viniferin (**9**), which undergoes addition following conjecture of a plausible biogenetic pathway and information on the configuration of several cognates in Dipterocarpaceae. As shown in the *Scheme*, **9** can be regarded as a precursor of **13**, and C(7a) and C(8a) of both compounds have the absolute (*R*) configuration. As already reported, **9** can be regarded as one of the major intermediates of various resveratrol oligomers of the same family [6a]. The present information on the configuration of **1** and **2** definitely call this hypothesis into question. Indeed, if this hypothesis were to be applied to the biogenetic formation of **1** and **2**, all C-atoms of the dihydrobenzofuran moiety, *i.e.*, C(7c), C(8c), C(7d), and C(8d), would have the same configuration (in this case, absolute (*R*)-configuration). Actually, in **2**, C(7d) and C(8d) have configurations opposite to those of C(7c) and (8c). This contradiction suggests the existence of other pathways of formation. For example,

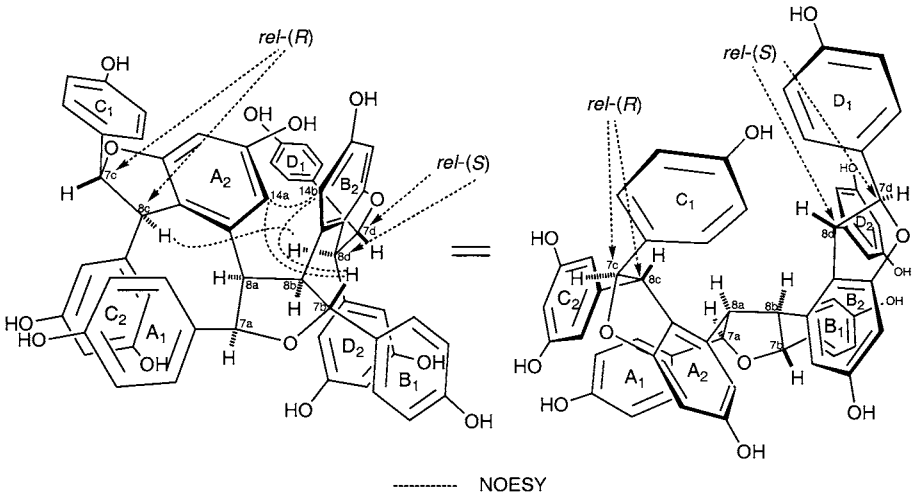


Fig. 11. *NOEs essential for the determination of the configurational relation among* **2A** – **2C**

resveratrols could be condensed step by step, the oligomerization of which could explain the configuration of the encountered tetramers.

Most of the stilbenoids are not crystalline, which hampers the confirmation of their configuration by X-ray crystallography. Until now, the detailed spectral data based on 2D NMR are essential for structural determination of resveratrol oligomers. Further advanced and accumulated data is required to better understand the chemistry of stilbene oligomers.

The authors are grateful to Mr. *Y. Doke* of Gifu Prefectural Institute of Industrial Product Technology for his constant technical support for NMR spectra.

Experimental Part

General. Anal. TLC: *Merck* silica gel F_{254} (0.25 mm). Prep. TLC: *Merck* silica gel F_{254} (0.5 mm). Column chromatography (CC): *Merck* silica gel *60* (70–230 mesh), *Sephadex LH-20*. Optical rotation: *Jasco P-1020* polarimeter. UV Spectra: *Shimadzu UV-2200* spectrophotometer; λ_{max} (log ε) in nm. ^{1}H- and ^{13}C-NMR Spectra: *Jeol JNM-LA-300* spectrometer; (D_6)acetone soln.; δ(H) in ppm rel. to Me_4Si (= 0 ppm) as internal ref., δ(C) in ppm rel. to solvent (carbonyl C-atom, 206.0 ppm), coupling constants *J* in Hz. ESI-MS: *Jeol JMS-T100LC* mass spectrometer; in *m*/*z* (rel. %).

Plant Material. D. grandiflorus (BLANCO) was cultivated at the Bogor Botanical Garden, Bogor, Indonesia, from which the stem was collected and identified by one of us (*D. D*) in May 2000, and a voucher specimen is deposited at the Gifu Prefectural Institute of Health and Environmental Sciences, Gifu, Japan.

Extraction and Isolation. The dried and ground stem of *D. grandiflorus* (550 g) were successively extracted with acetone (1.5 l, 3 ×), MeOH (1.5 l, 3 ×), and 70% MeOH (2 l, 2 ×) at r.t., and the extracts were evaporated: 21 g (acetone), 7 g (MeOH), and 8 g (70% MeOH)). A part (20 g) of the acetone extract was subjected to CC (silica gel, $CHCl_3$/MeOH of increasing polarity): *Fractions 1–29*. The fractions were combined according to TLC (*Gibbs* test) as follows: *Fr. 1–9* (= *Fr. A*; $CHCl_3$/MeOH 20:1; 4.5 g), *Fr. 10–13* (= *Fr. B*; $CHCl_3$/MeOH 10:1; 620 mg), *Fr. 14–15* (= *Fr. C*; $CHCl_3$/MeOH 9:1; 230 mg), *Fr. 16–18* (= *Fr. D*; $CHCl_3$/MeOH 8:1; 960 mg), *Fr. 19–20* (= *Fr. E*; $CHCl_3$/MeOH 7:1; 850 mg). *Fr. B* was further subjected to reversed-phase CC (H_2O/MeOH gradient, 40–60% MeOH): *Fr. B.1–B.22*. Compounds **7** (320 mg), **8** (6 mg), **9** (6 mg), and **12** (0.8 mg) were obtained from the combined *Fr. 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). An acetone-insoluble part (500 mg) of *Fr. C* was dissolved in acetone/$CHCl_3$ 3:1 (20 ml) and gave **14** (420 mg) as a powder. Purification of an acetone-soluble part of *Fr. C* by CC (*Sephadex LH-20*, MeOH) resulted in the isolation of **10** (7 mg). *Fr. D* was further subjected to CC (*Sephadex LH-20*, MeOH): *Fr. D.1–D.25*. Additional quantities of **14** (460 mg), **13** (45 mg), and **1** (12 mg) were obtained from the combined *Fr. D.5–D.7*, *Fr. D.9–D.11*), and *Fr. D.13–D.14*, resp. Compounds **2** (6 mg) and **11** (2 mg) were obtained from *Fr. D.15* after purification by two successive prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1). Further purification of *Fr. D.23* by prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1) gave **5** (8 mg). Compounds **3** (25 mg), **4** (4 mg), and **6** (3 mg) were obtained from *Fr. E* after purification by CC (*Sephadex LH-20*, MeOH) and prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1).

Grandiphenol A (= rel-*5,5′-{[(2*S*,3*R*,4*R*,5*R*)-Tetrahydro-2,5-bis(4-hydroxyphenyl)furan-3,4-diyl]-bis[(2*R*,3*R*)-2,3-dihydro-6-hydroxy-2-(4-hydroxyphenyl)benzofuran-4,3-diyl]}bis[benzene-1,3-diol]*; **1**) Pale yellow amorphous powder. $[\alpha]_D = -289$ ($c = 0.1$, MeOH) UV: 229 (4.69), 278 (sh, 4.09), 284 (4.11), 295 (sh, 3.87). ^{1}H- and ^{13}C-NMR, ^{1}H,^{13}C-HMBC: *Table 1*. ^{1}H,^{1}H-NOESY (* = weak correlations): H–C(2a,6a)/H–C(7a), H–C(14a), and H–C(10c,14c); H–C(7a)/H–C(10c,14c)*, H–C(7b), and H–C(14b); H–C(8a)/H–C(8c), H–C(10c,14c), H–C(7b), and H–C(14b); H–C(14a)/H–C(8b), H–C(8d), and H–C(10d,14d); H–C(2b,6b)/H–C(7b), H–C(8b), and H–C(12d); H–C(7b)/H–C(14b); H–C(8b)/H–C(8c) and H–C(10d,14d); H–C(14b)/H–C(8c) and H–C(10c,14c); H–C(2c,6c)/H–C(7c) and H–C(8c); H–C(7c)/H–C(10c,14c); H–C(8c)/H–C(10c,14c); H–C(2d,6d)/H–C(7d) and H–C(8d); H–C(7d)/H–C(10d,14d); H–C(8d)/H–C(10d,14d). ^{1}H-NMR ((D$_6$)acetone, 300 MHz, −55°): 4.70 (*d*, *J* = 9.2, H–C(7a)); 3.99 (*dd*, *J* = 9.2, 11.7, H–C(8a)); 5.99 (br. *d*, *J* = 1.8, H–C(12a)); 5.64 (br. *d*, *J* = 1.8, H–C(14a)); 6.72 (br. *d*, *J* = 8.4, H–C(2b,6b)); 6.60 (br. *d*, *J* = 8.4, H–C(3b,5b)); 5.09 (*d*, *J* = 10.3, H–C(7b)); 3.74 (*dd*, *J* = 10.3, 11.7, H–C(8b); partly overlapped by H_2O); 6.17 (br. *d*, *J* = 1.7, H–C(12b)); 6.70 (br. *s*, H–C(14b)); 6.90 (br. *d*, *J* = 8.4, H–C(2c,6c)); 6.66 (br. *d*, *J* = 8.4, H–C(3c,5c)); 5.27 (*d*, *J* = 4.2, H–C(7c)); 4.21 (*d*, *J* = 4.2, H–C(8c)); 6.22 (br. *s*, H–C(10c,14c)); 6.34 (br. *s*, H–C(12c)); 6.67 (br. *d*, *J* = 8.4, H–C(2d,6d)); 6.51 (br. *d*, *J* = 8.4, H–C(3d,5d)); 5.13 (*d*, *J* = 4.4, H–C(7d)); 4.11 (*d*, *J* = 4.4, H–C(8d)); 5.69 (br. *s*, H–C(10d)); 6.38 (br. *s*, H–C(12d)); 6.56 (br. *s*, H–C(14d)); 8.43 (br. *s*, OH–C(13a); assigned by NOESY); 8.52 (br. *s*, OH–C(11d); assigned by NOESY); 9.00 (br. *s*, OH–C(13b); assigned by NOESY); 8.85 (br. *s*, 1 OH); 8.87 (br. *s*, OH); 8.90 (br. *s*, 1 OH); 9.02 (br. *s*, 3 OH); 9.05 (br. *s*, 1 OH). ^{1}H,^{1}H NOESY (−55°): H–C(12a)/OH–C(13a); OH–C(13a)/H–C(14a); H–C(14a)/H–C(8d); H–C(2b,6b)/H–C(7b); H–C(7b)/H–C(14b); H–C(8b)/H–C(14d); H–C(12b)/OH–C(13b); H–C(2c,6c)/H–C(7c) and H–C(8c); H–C(7c)/H–C(10c,14c); H–C(8c)/H–C(10c,14c); H–C(2d,6d)/H–C(7d) and H–C(8d); H–C(7d)/H–C(10d); H–C(8d)/H–C(14d); H–C(10d)/OH–C(11d); OH–C(11d)/H–C(12d). ESI-MS: 947 ([*M* + Na]$^+$). HR-ESI-MS: 947.2653 ([*M* + Na]$^+$; $C_{56}H_{44}NaO_{13}^+$; calc. 947.2680).

Grandiphenol B (= rel-*5-{(2*R*,3*R*)-4-{(2*R*,3*R*,4*S*,5*R*)-4-[(2*S*,3*S*)-3-(3,5-Dihydroxyphenyl)-2,3-dihydro-6-hydroxy-2-(4-hydroxyphenyl)benzofuran-4-yl]tetrahydro-2,5-bis(4-hydroxyphenyl)furan-3-yl}-2,3-dihydro-6-hydroxy-2-(4-hydroxyphenyl)benzofuran-3-yl]benzene-1,3-diol*; **2**): Pale yellow amorphous powder. $[\alpha]_D = -372$ ($c = 0.1$, MeOH). UV: 230 (4.70), 278 (sh, 4.14), 284 (4.16), 295 (sh, 3.97). ^{1}H- and ^{13}C-NMR, ^{1}H,^{13}C-HMBC: *Table 2*. ^{1}H,^{1}H-NOESY (= weak correlations): H–C(2a,6a)/H–C(7a), H–C(8a), and H–C(10c,14c); H–C(7a)/H–C(2b,6b) and H–C(8b); H–C(8a)/H–C(8c) and H–C(10c,14c); H–C(14a)/H–C(7b) and H–C(14b); H–C(2b,6b)/H–C(7b) and H–C(8b); H–C(7b)/H–C(14b); H–C(8b)/H–C(8d); H–C(12b)/H–C(2c,6c); H–C(14a)/H–C(2c,6c); H–C(2c,6c)/H–C(7c), H–C(8c), and H–C(8d)*; H–C(3c,5c)/H–C(3d,5d); H–C(7c)/H–C(10c,14c); H–C(8c)/H–C(10c,14c) and H–C(8d); H–C(2d,6d)/H–C(7d) and H–C(8d); H–C(7d)/H–C(10d,14d); H–C(8d)/H–C(10d,14d). ESI-MS: 947 ([*M* + Na]$^+$). HR-ESI-MS: 947.2668 ([*M* + Na]$^+$; $C_{56}H_{44}NaO_{13}^+$; calc. 947.2680).

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