Two Novel Resveratrol Derivatives from the Leaves of *Vateria indica*

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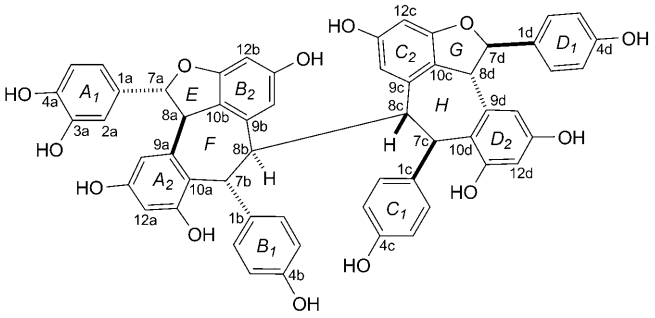
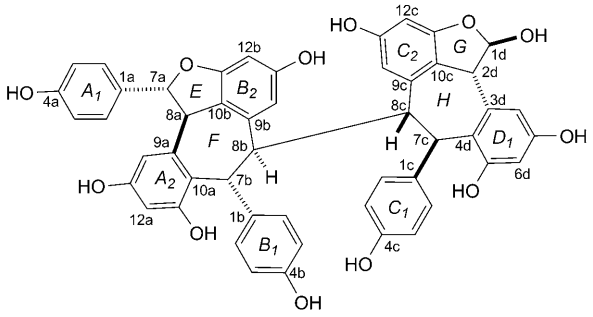
Two new resveratrol (=5-[(*E*)-2-(4-hydroxyphenyl)ethenyl]benzene-1,3-diol) derivatives, vateriaphenols D (**1**) and E (**2**), were isolated from the leaves of *Vateria indica* (Dipterocarpaceae), together with six known resveratrol oligomers (**3**–**8**), a isocoumarin (bergenin, **9**), and a benzophenone (**10**). The structures of the isolates were established on the basis of spectroscopic analyses, including a detailed NMR spectroscopic investigation. Compound **1** is composed of three resveratrol units and a piceatannol (=5-[(*E*)-2-(3,4-dihydroxyphenyl)ethenyl]benzene-1,3-diol) unit, and is the first instance of a heterogeneous coupled stilbene tetramer in dipterocarpaceaeous plants. Compound **2** bears a rare 2,3-dihydrobenzofuran-2-ol skeleton in the framework.

Introduction. – Stilbenoids represented by resveratrol (=5-[(*E*)-2-(4-hydroxyphenyl)ethenyl]benzene-1,3-diol) have drawn much attention to the important role in food or beverage and to the diverse biological activities. The compounds are typically present as stilbenoid oligomers in limited plant families such as Dipterocarpaceae [1], Vitaceae [2], Cyperaceae [3], and Gnetaceae [4]. Recent results of the structural variation and the multifunctional bioactivity need to add stilbenoid oligomers to the further detailed phytochemical investigation. Dipterocarpaceaeous plants are well-known to contain resveratrol oligomers, and their occurrences in *Vatica* [5], *Vateria* [6], *Shorea* [7], *Upuna* [8], *Dipterocarpus* [9], *Cotylelobium* [10], and *Hopea* [11] genera have been disclosed in our previous works.

The genus *Vateria*, which belongs to the tribe Dipterocarpeae in the largest subfamily Dipterocarpoideae, comprises two species and is distributed in India and Sri Lanka [12]. *Vateria indica*, a slow-growing species, found primarily in the west coast evergreen forests in India, produces useful timber to be used for varnishes and incenses. The bark, resin, and fruit have been used for various medicinal purposes [12]. We previously reported the structural variety of the resveratrol oligomers [5–11] and their antitumor effects [13]. The bioactive resveratrol oligomers in the stem bark are vaticanol B (a resveratrol tetramer, anti-inflammatory [14]), and vaticanol C (a resveratrol tetramer, anticancer [15]). The correction of the material (stem bark, stem wood, and root) causes serious damage to plants themselves and to natural environment, but the leaves are reproducible material. On the standpoint of additional phytochemical and bioactive study, a detailed study of the acetone extract was examined and yielded two novel stilbene derivatives, vateriaphenols D (**1**) and E (**2**), and eight known compounds (**3**–**10**). The structures of the isolates **1** and **2** were



1



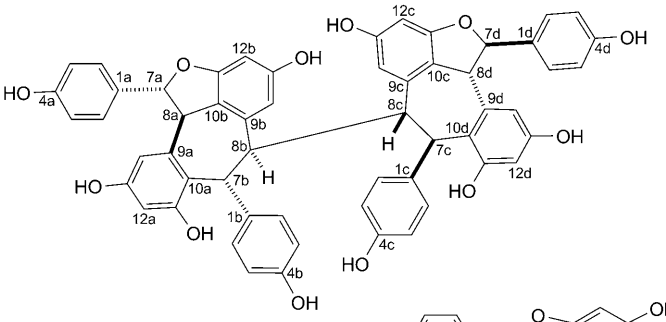
2

elucidated by means of 2D-NMR techniques such as ^{1}H,^{1}H-DQF-COSY, ^{1}H,^{13}C-HMQC, and ^{1}H,^{13}C-HMBC, and the configurations were proposed by analysis of the ROESY spectra.

Results and Discussion. – *Structure Elucidation*. Vateriaphenols D (**1**) and E (**2**) were isolated from the acetone extract of the leaves of *V. indica* by column chromatography (CC), preparative TLC, and *Sephadex LH-20* CC.

Vateriaphenol D (**1**), a pale yellow solid, had the molecular formula $C_{56}H_{42}O_{13}$, as deduced by the HR-ESI-MS ($[M-H]^-$ at m/z 921.2531, calc. for $C_{56}H_{41}O_{13}$: 921.2542) and ^{13}C-NMR spectroscopy. The ^{1}H- and ^{13}C-NMR spectra of **1** (*Table 1*), and the corresponding ^{1}H,^{1}H-DQF-COSY, ^{1}H,^{13}C-HMQC, as well as the ^{1}H,^{13}C-HMBC spectra (*Table 2* and *Fig. 1*) were recorded at various temperatures. Reducing the temperature resulted in some changes in the spectral features. When the spectrum was measured at $-20°$, OH signals sharpened and the interpretation of the spectrum enabled us to determine the structure of **1**. The NMR spectral patterns were very similar to those of (−)-hopeaphenol (**3**) (*Table 1*) [1c][2b], except for appearance of a 3,4-hydroxyphenyl group instead of a 4-hydroxyphenyl group.

The data analysis revealed the presence of a 3,4-hydroxyphenyl group (ring A_1), three 4-hydroxyphenyl groups (rings B_1, C_1, and D_1), four 3,5-dioxygenated 1,2-disubstituted benzene rings (A_2, B_2, C_2, and D_2). The presence of two sets of mutually coupled aliphatic H-atoms (H−C(7a)/H−C(8a); H−C(7d)/H−C(8d)) and a sequence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HO
O
7d
1d
4d
OH
12b
OH
1a
7a
O
9c
10c
8d
9d
HO
4a
8a
10b
9b
8c
H
10d
OH
9a
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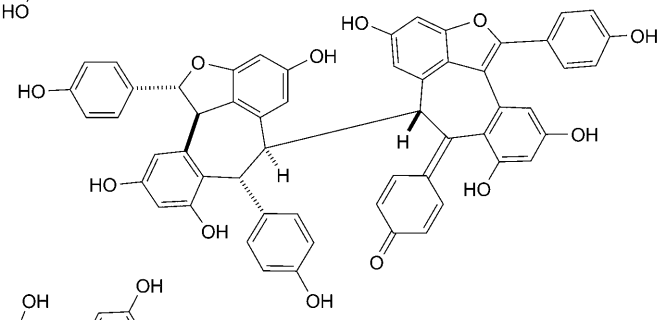
12a
OH
1b
4c
HO
4b
OH

3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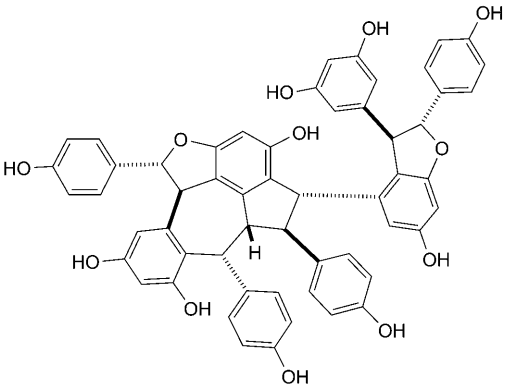
OH
OH
O

4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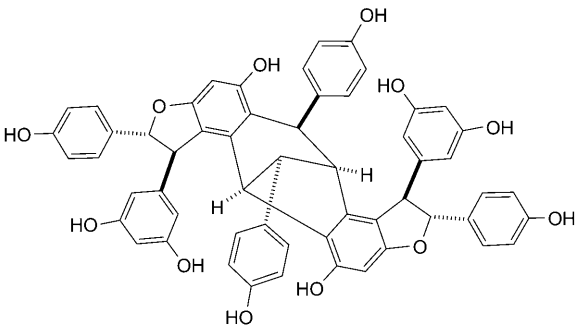
OH

5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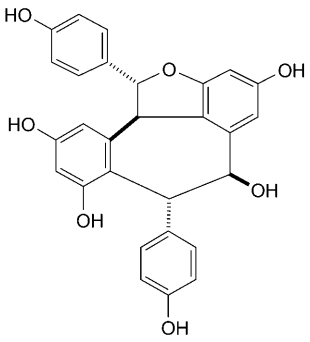
HO

6


HO
O
OH
HO
OH
OH
OH

7

Table 1. *^{1}H- and ^{13}C-NMR Spectral Data of* **1** *and* **3**. δ in ppm, J in Hz.

Position	**1**[a])			**3**[b])	
	$-20°$		r.t.	r.t.	
	δ(H)	δ(C)	δ(H)	δ(H)	δ(C)
1a		131.1			131.0
2a	6.83 (d, J = 1.6)	116.2	6.84 (d, J = 2.0)	7.09 (d, J = 8.8)	130.5
3a		145.6		6.72 (d, J = 8.8)	116.2
4a		146.0			158.8
5a	6.75 (d, J = 8.4)	115.8	6.75 (d, J = 8.6)	6.72 (d, J = 8.8)	116.2
6a	6.62 (dd, J = 8.4, 1.6)	120.1	6.62 (dd, J = 8.6, 2.0)	7.09 (d, J = 8.8)	130.5
7a	5.67 (d, J = 12.2)	88.3	5.69 (d, J = 12.0)	5.80 (d, J = 12.5)	89.0
8a	4.20 (d, J = 12.2)[c])	49.1	4.22 (d, J = 12.0)[c])	4.12 (d, J = 12.5)	49.9
9a		142.1			142.5
10a		120.6[d])			122.0
11a (OH)	8.80 (br. s)[c])	158.7[c])			159.4
12a	6.53 (br. s)[c])	100.7[c])	6.53 (br. s)[c])	6.36 (d, J = 2.2)	101.0
13a (OH)	8.51 (br. s)[c])	156.98[c])			157.2
14a	6.24 (br. s)[c])	106.0[d])	6.29 (br. s)[d])	6.21 (d, J = 2.2)	106.3
1b		134.74[d])			136.0
2b, 6b	6.86 (d, J = 8.6)[d])	129.02[d])	6.89 (d, J = 8.6)[d])	6.89 (d, J = 8.8)	129.7
3b, 5b	6.54 (d, J = 8.6)[c])	114.96[d])	6.54 (d, J = 8.6)[c])	6.54 (d, J = 8.8)	115.3
4b (OH)	8.31 (br. s)[c])	155.38[c])			155.5
7b	5.80 (br. s)[c])	40.8[c])	5.81 (br. s)[c])	5.75 (br. s)	41.5
8b	3.90 (br. s)[c])	47.8	3.91 (br. s)[c])	3.85 (br. s)	48.6
9b		140.2[c])			141.2
10b		118.2[c])			119.6
11b		158.97[d])			159.3
12b	5.69 (d, J = 2.0)[c])	94.9[c])	5.71 (d, J = 2.0)[c])	5.73 (d, J = 2.2)	95.3
13b (OH)	7.77 (br. s)[c])	156.89[d])			157.0
14b	5.14 (d, J = 2.0)[d])	110.9[c])	5.15 (d, J = 2.0)[d])	5.07 (d, J = 2.2)	111.8
1c		134.82[d])			136.0
2c, 6c	6.87 (d, J = 8.6)[d])	129.09[d])	6.91 (d, J = 8.6)[d])	7.09 (d, J = 8.8)	129.7
3c, 5c	6.54 (d, J = 8.6)[c])	115.00[d])	6.54 (d, J = 8.6)[c])	6.72 (d, J = 8.8)	115.3
4c (OH)	8.31 (br. s)[c])	155.38[c])			155.5
7c	5.80 (br. s)[c])	40.8[c])	5.81 (br. s)[c])	5.80 (d, J = 12.5)	41.5
8c	3.90 (br. s)[c])	47.9	3.91 (br. s)[c])	4.12 (d, J = 12.5)	48.6
9c		140.2[c])			141.2
10c		118.2[c])			119.6
11c (OH)		158.99[d])			159.3
12c	5.69 (d, J = 2.0)[c])	94.9[c])	5.71 (d, J = 2.0)[c])	6.36 (d, J = 2.2)	95.3
13c (OH)	7.77 (br. s)[c])	156.93[d])			157.0
14c	5.16 (d, J = 2.0)[d])	110.9[c])	5.17 (d, J = 2.0)[d])	6.21 (d, J = 2.2)	111.8
1d		130.5			131.0
2d, 6d	7.13 (d, J = 8.6)	130.2	7.13 (d, J = 8.6)	6.89 (d, J = 8.8)	130.5
3d, 5d	6.79 (d, J = 8.6)	115.8	6.78 (d, J = 8.6)	6.54 (d, J = 8.8)	116.2
4d		158.3			158.8
7d	5.72 (d, J = 12.4)	88.0	5.74 (d, J = 12.2)	5.75 (br. s)	89.0
8d	4.20 (d, J = 12.2)[c])	49.4	4.22 (d, J = 12.0)[c])	3.85 (br. s)	49.9
9d		142.0			142.5
10d		120.7[d])			122.0

Table 1 (cont.)

Position	**1**[a])			**3**[b])	
	−20°		r.t.	r.t.	
	δ(H)	δ(C)	δ(H)	δ(H)	δ(C)
11d (OH)	8.80 (br. *s*)[c])	158.7[c])			159.4
12d	6.53 (br. *s*)[c])	110.7[c])	6.53 (br. *s*)[c])	5.73 (*d*, *J* = 2.2)	101.0
13d (OH)	8.51 (br. *s*)[c])	156.98[c])			157.2
14d	6.24 (br. *s*)[c])	106.2[d])	6.30 (br. *s*)[d])	5.07 (*d*, *J* = 2.2)	106.3
OH	8.30, 8.40, 8.55		7.42, 7.44, 8.01 (4 OH), 8.22 (2 OH), 8.51, 8.53, 8.55	7.47, 8.04, 8.26 (each 2 OH), 8.57 (4 OH)	

[a]) Measured in (D_6)acetone at 600 MHz (^{1}H) and 150 MHz (^{13}C). [b]) Measured in (D_6)acetone at 400 MHz (^{1}H). [c]) Overlapping signals. [d]) Interchangeable signals.

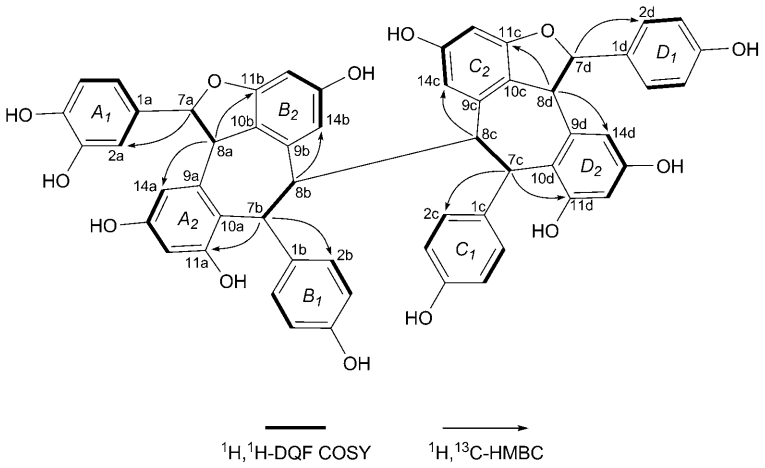


Fig. 1. *Selected 2D-NMR correlations for* **1**

of four aliphatic H-atoms (H–C(7b), H–C(8b), H–C(8c), and H–C(7c)) were also confirmed (*Fig. 1*). The ^{1}H-NMR spectrum exhibited signals for 11 phenolic OH groups in the range of δ(H) 7.77–8.80, which disappeared upon addition of D_2O.

The connection of the partial structures was established as follows. The significant ^3J long-range correlations observed between H–C(7a)/C(2a), H–C(8a)/C(14a), H–C(8a)/C(11b), H–C(7b)/C(2b,6b), H–C(7b)/C(11a), H–C(8b)/C(14b), H–C(7c)/C(2c,6c), H–C(7c)/C(11d), H–C(8c)/C(14c), H–C(7d)/C(2d,6d), H–C(8d)/C(14d), and H–C(8d)/C(11c) (*Fig. 1*) indicated C–C bonds between C(1a)/C(7a), C(8a)/C(9a), C(8a)/C(10b), C(1b)/C(7b), C(7b)/C(10a), C(8b)/C(9b), C(1c)/C(7c), C(7c)/C(10d), C(8c)/C(9c), C(1d)/C(7d), C(8d)/C(9d), and C(8d)/C(10c), respectively. Although long-range correlations (H–C(7a)/C(11b), H–C(7d)/C(11c)) were not observed, the presence of two ether linkages (C(7a)–O–C(11b) and

Table 2. *2D-NMR Data of* **1**[1])

H-Atom	HMBC (C-Atom)	ROESY (H-Atom)
2a	4a, 6a, 7a	7a, 8a
5a	1a, 3a, 6a	
6a	2a, 4a, 7a	7a, 8a
7a	1a, 2a, 6a, 8a, 9a	2a, 6a, 14a
8a	1a, 7a, 9a, 10a, 14a, 9b, 10b, 11b	2a, 6a, 14a, 2b(6b)
11a (OH)	10a, 11a, 12a	12a, 2c(6c), 7b
12a	10a, 11a, 13a, 14a	OH-11a, OH-13a
13a (OH)	12a, 13a, 14a	12a, 14a
14a	8a, 10a, 12a, 13a	7a, 8a, OH-13a
2b, 6b	2b(6b), 4b, 7b	8a, OH-11d, 7b, 8b, 14c
3b, 5b	1b, 3b(5b), 4b	
4b (OH)	3b(5b)	
7b	9a, 10a, 11a, 1b, 2b(6b), 8b, 9b, 8c	OH-11a, 2b(6b), 8b, 8c
8b	10a, 7b, 9b, 10b, 14b, 7c, 8c	2b(6b), 7b, 14b, 2c(6c), 7c
12b	10b, 11b, 13b, 14b	OH-13b
13b (OH)	12b, 13b, 14b	12b, 14b
14b	8b, 10b, 12b, 14b	8b, OH-13b, 2c(6c)
2c, 6c	2c(6c), 4c, 7c	OH-11a, 14b, 7c, 8c, 8d
3c, 5c	1c, 3c(5c), 4c	
4c (OH)	3c(5c)	
7c	9d, 10d, 11d, 1c, 2c(6c), 8c, 9c, 8b	8b, 2c(6c), 8c, OH-11d
8c	10d, 7c, 9c, 10c, 14c, 7b, 8b	2b(6b), 7b, 7c, 14c
12c	10c, 11c, 13c, 14c	OH-13c
13c (OH)	12c, 13c, 14c	12c, 14c
14c	8c, 10c, 12c, 14c	2b(6b), 8c, OH-13c
2d, 6d	2c(6c), 4c, 7c	7d, 8d, 14d
3d, 5d	1c, 3c(5c), 4c	
4d (OH)	3c(5c)	
7d	1d, 2d, 6d, 8d, 9d	2d(6d), 14d
8d	1d, 7d, 9d, 10d, 14d, 9c, 10c, 11c	2c(6c), 2d(6d), 14d
11d (OH)	10d, 11d, 12d	2b(6b), 7c, 12d
12d	10d, 11d, 13d, 14d	OH-11d, OH-13d
13d (OH)	12d, 13d, 14d	12d, 14d
14d	8d, 10d, 12d, 13d	2d(6d), 7d, 8d, OH-13d

[a]) Measured in (D_6)acetone at $-20°$.

C(7d)–O–C(11c)) was proposed after consideration of the molecular formula. From these data, a structure of vateriaphenol D could be proposed.

The relative configuration of **1** was determined by ROESY experiments (*Table 2* and *Fig. 2*), as well as by the analysis of the coupling constants. The significant ROE correlations observed between H–C(2a)/H–C(8a), H–C(7a)/H–C(14a), H–C(2d,6d)/H–C(8d), and H–C(7d)/H–C(14d) suggested that the two sets of CH H-atoms in the two dihydrobenzofuran rings (ring *E:* H–C(7a)/H–C(8a); ring *G:* H–C(7d)/H–C(8d)) were *trans*-oriented. The coupling constant ($J = 12.2$ Hz) between H–C(7a)/H–C(8a) and H–C(7d)/H–C(8d) was in agreement with diaxial orientations [5a]. The CH H-atoms (H–C(8a) and H–C(8b)) also showed ROE

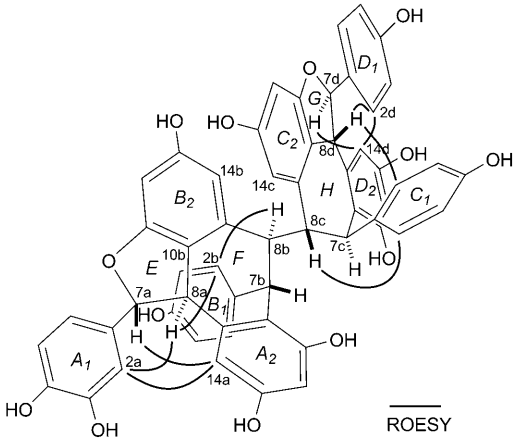


Fig. 2. *Selected ROEs observed for* **1**

interactions with the aromatic H-atoms (H–C(2b,6b)) on *ring* B_1, which indicated that ring B_1, H–C(8a), and H–C(8b) are *syn*-oriented. The small value of the vicinal coupling constant of the CH H-atoms (H–C(7b) and H–C(8b)) indicated the dihedral angle of them to be near 90°. When the difference in the conformation of the dibenzo[2,1]heptadiene ring (*ring F*) was considered (*Fig. 3*), the *pseudo*-boat conformation (left figure) and *pseudo*-chair conformation (right figure) were supported. It was found that the *pseudo*-boat conformation of the ring system agreed with the ROE correlations (H–C(2b,6b)/H–C(8a) and H–C(2b,6b)/H–C(8b)) and the angle of H–C(7b)/H–C(8b), while the *pseudo*-chair conformation did not agree with them, as shown in *Fig. 3*. With the same arguments as described for ring *F*, the orientation of ring C_1 and H–C(8c) on ring *H* were both found to be *syn* to H–C(8d). The relative configuration of H–C(8b) and H–C(8c) is discussed as follows. (–)-Hopeaphenol (**3**) should be represented as (1*R*,6*S*,7*R*,11b*R*)-1-(3,4-dihydroxyphen-

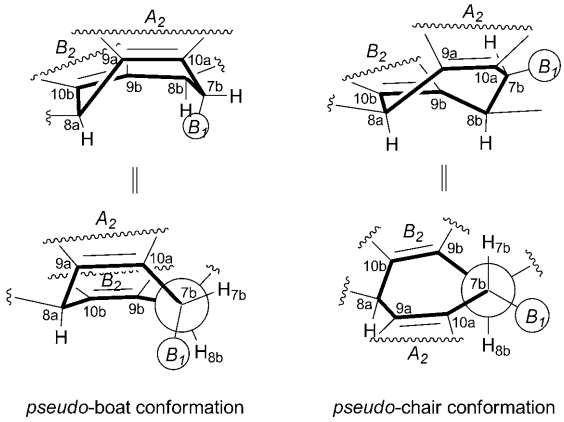


Fig. 3. *Possible conformation of ring* F (bold line) *for* **1**

yl)-1,6,7,11b-tetrahydro-6-[(1*R*,6*S*,7*R*,11b*R*)-1,6,7,11b-tetrahydro-4,8,10-trihydroxy-1,7-bis(4-hydroxyphenyl)benzo[6,7]cyclohepta[1,2,3-*cd*]benzofuran-6-yl]-7-(4-hydroxyphenyl)benzo[6,7]cyclohepta[1,2,3-*cd*]benzofuran-4,8,10-triol or (1*R*,6*S*,7*R*,11b*R*)-1-(3,4-dihydroxyphenyl)-1,6,7,11b-tetrahydro-6-[(1*S*,6*R*,7*S*,11b*S*)-1,6,7,11b-tetrahydro-4,8,10-trihydroxy-1,7-bis(4-hydroxyphenyl)benzo[6,7]cyclohepta[1,2,3-*cd*]benzofuran-6-yl]-7-(4-hydroxyphenyl)benzo[6,7]cyclohepta[1,2,3-*cd*]benzofuran-4,8,10-triol, except for the absolute configuration. The skeleton of the former has no symmetrical plane as seen in the case of (−)-hopeaphenol ($[\alpha]_D^{28} = -402.9$) [1d], while the skeleton of the latter has a symmetrical plane as seen in the case of neohopeaphenol ($[\alpha]_D = 0$) [16]. Therefore, vateriaphenol D (**1**) ($[\alpha]_D^{25} = -346$) was supposed to have the same configuration as (−)-hopeaphenol.

Supporting evidences for the conformation and the ROE results were rationalized by a molecular mechanics calculation. A 3D structure of **1** was generated with the PCMODEL (version 9.1) software [17], using MMFF's (an MM2 type) force field for energy minimization. The structure (*Fig. 4*) has much the correspondence to the configuration discussed above. The dihedral angle of H−C(8b)−H−C(8c) was calculated to 139.3° in the model, which causes special approaches among the four resorcinol rings (rings A_2–D_2) and can reasonably explain the anisotropic effects as follows. The shifts of the aromatic H-atoms, H−C(14b) (δ(H) 5.14) on the ring B_2 and H−C(14c) (δ(H) 5.16) on the ring C_2 to higher field are well-explained by the anisotropic effects caused by the rings D_2 and A_2, respectively. The exact understanding of such upfield chemical shifts due to anisotropic effects is essential to determine the configuration. Vateriaphenol D (**1**) has such a common structure and the optical rotation as (−)-hopeaphenol (**3**), which is one of major components in this plant. The absolute configuration of **3** was confirmed by the aid of X-ray crystallography. From the above data, vateriaphenol D (**1**) was determined as (1*R*,6*S*,7*R*,11b*R*)-1-(3,4-dihydroxyphenyl)-1,6,7,11b-tetrahydro-6-[(1*R*,6*S*,7*R*,11b*R*)-1,6,7,11b-tetrahydro-4,8,10-

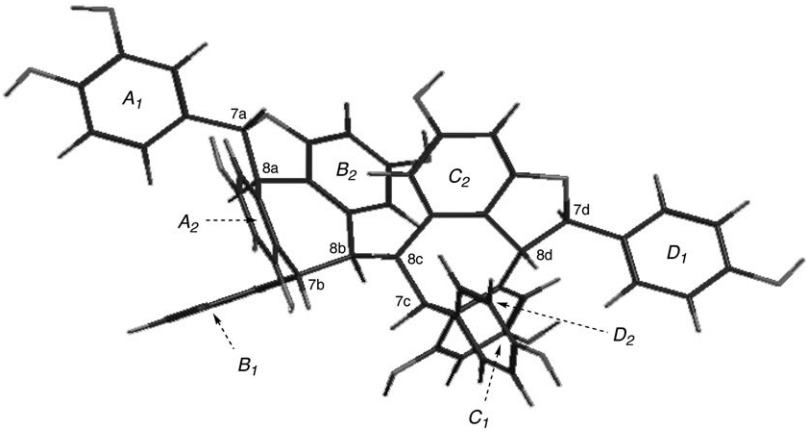


Fig. 4. *Energy-minimized configuration of* **1** (MMFF94 calculation using the PCMODEL v. 9.0 molecular modeling program)

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

trihydroxy-1,7-bis(4-hydroxyphenyl)benzo[6,7]cyclohepta[1,2,3-*cd*]benzofuran-6-yl]-7-(4-hydroxyphenyl)benzo[6,7]cyclohepta[1,2,3-*cd*]benzofuran-4,8,10-triol[1]).

Vateriaphenol E (**2**) was obtained as a yellow amorphous powder. The molecular formula was deduced to be $C_{50}H_{38}O_{12}$ by the $[M-H]^-$ ion peak observed at *m/z* 829.2278 in the HR-ESI-MS (calc. for $C_{50}H_{37}O_{12}$: 829.2280). The patterns of the NMR spectral data of **2** (*Table 3*) were closely similar to those of **3**, and in particular, in the partial structure of resveratrols A–C (resveratrol A: ring A_1–C(7a)–C(8a)–ring A_2) including ring D_1. By detailed analysis of the 2D-NMR spectra (*Table 4*), they were found to have identical partial structures in the molecule. The structural differences between **2** and **3** were attributable to a 2,3-dihydrobenzofuran-2-ol skeleton (ring *G*-ring C_2) in **2** instead of a 2-aryl-2,3-dihydrobenzofuran (ring D_1-ring *G*-ring C_2) in **3**. The HMBC spectrum and ROESY spectrum explained the structure of **2** rather well, including its configuration. For the same reasons as described for the configuration of **1**, the relative configuration of vateriaphenol E was elucidated as shown in the formula for **2**. As the $[\alpha]_D$ value of **2** was −348, the absolute configuration is concluded to be analogous to **3**. Therefore, vateriaphenol E (**2**) was determined as (1*R*,6*S*,7*R*,11b*R*)-1,6,7,11b-tetrahydro-1-hydroxy-6-[(1*R*,6*S*,7*R*,11b*R*)-1,6,7,11b-tetrahydro-4,8,10-trihydroxy-1,7-bis(4-hydroxyphenyl)benzo[6,7]cyclohepta-[1,2,3-*cd*]benzofuran-6-yl]-7-(4-hydroxyphenyl)benzo[6,7]cyclohepta[1,2,3-*cd*]benzofuran-4,8,10-triol[1]).

The important observations of the spectral data through the present study are summarized as follows: *1*) Differently from **3**, which has two equivalent units in the molecule, many NMR signals in **1** and **2** were observed as overlapped or interchangeable signals, because of the loss of equivalence (*Tables 1* and *3*); *2*) in the HMBC spectrum (*Tables 2* and *4*), the overlapping signals in the ^{13}C-NMR spectrum caused overlapping cross-peaks. Although this is the case for H–C(8b)/C(9c) and H–C(8b)/C(9b) in **1**, the overlapping chemical shifts of C(9b) and C(9c) (δ(C) both 140.2) would cause masking of the ^3J correlation by the large ^2J one, respectively. In the current experiment, the C–C bond between C(8b) and C(8c) could, thus, not be corroborated directly. The experimental mode of *J*-resolved HMBC experiments [18] would detect and extract from the overlapping cross peaks; *3*) generally, systems that give rise to small ^4J(H,C)-NMR coupling can be readily detected by NMR. When the geometry of the pertinent bonds is fixed in a *W*-letter conformation, ^4J(H,C)-NMR coupling can be detected by NMR, which is in the case for H–C(8a)/C(11a), H–C(8a)/C(14b), H–C(2d)/C(8c), and H–C(2d)/C(5d) in **2**; *4*) structure elucidation of **3** required the results of NOEs (ROEs) not only in the half unit but in the whole molecule. Although **1** and **2** are different from **3**, their NMR signal duplication caused new problems. For example, the differentiation between the correlations of H–C(2b,6b)/H–C(8a) and H–C(2b,6b)/H–C(8d) had to be discussed in **1**. When the bond (C(8b)–C(8c)) has equatorial orientation, and one unit (rings A_1, A_2, B_2, B_2, *E*, *F:* unit *A*) lies horizontally relative to the other one (rings C_1, C_2, D_2, D_2, *G*, *H:* unit *B*), an extended molecule can be considered (*Fig. 5*, left figure), and the differentiation is easy. ROEs between units *A* and *B* could hardly be observed in an extended molecule. But in case that the C(8b)–C(8c) bond is in axial orientation, and unit *A* lies vertically relative to unit *B*, and the compound froms a compact molecule (*Fig. 5*, right figure), the ROEs between the units would essentially have to be considered.

Table 3. *^{1}H- and ^{13}C-NMR Spectral Data of* **2**[a]). δ in ppm, J in Hz.

Position	− 20°		r.t.
	δ(H)	δ(C)	δ(H)
1a		130.5	
2a, 6a	7.12 (*d*, *J* = 8.8)	130.2	7.12 (*d*, *J* = 8.8)
3a, 5a	6.78 (*d*, *J* = 8.8)	115.8	6.77 (*d*, *J* = 8.8)
4a (OH)	8.83 (br. *s*)	158.3	8.48 (br. *s*)[b])
7a	5.70 (*d*, *J* = 12.2)	88.0	5.72 (*d*, *J* = 12.2)
8a	4.18 (*d*, *J* = 12.2)	49.3	4.20 (*d*, *J* = 12.2)
9a		142.0	
10a		120.7	
11a (OH)	8.78 (br. *s*)	159.0	8.48 (br. *s*)[b])
12a	6.51 (br. *s*)	100.6	6.51 (br. *d*, *J* = 2.0)
13a (OH)	8.51 (br. *s*)	157.0	8.18 (br. *s*)
14a	6.23 (br. *s*)	106.0	6.27 (br. *s*)
1b		134.79	
2b, 6b	6.85 (*d*, *J* = 8.8)	129.0	6.88 (*d*, *J* = 8.8)
3b, 5b	6.54 (*d*, *J* = 8.8)	114.9[b])	6.54 (*d*, *J* = 8.8)
4b (OH)	8.31 (br. *s*)[b])	155.4	7.94 (br. *s*)[b])
7b	5.76 (br. *d*, *J* = 3.4)	40.7[b])	5.78 (br. *d*, *J* = 3.4)
8b	3.87 (br. *dd*, *J* = 7.4, 3.4)	47.93	3.89 (br. *dd*, *J* = 7.4, 3.4)
9b		140.1	
10b		118.1	
11b		156.9[b])	
12b	5.66 (br. *d*, *J* = 1.6)	94.9	5.68 (*d*, *J* = 2.0)
13b (OH)	7.75 (br. *s*)[c])	158.6[b])	7.37 (br. *s*)[b])
14b	5.09 (br. *d*, *J* = 1.6)	110.7	5.10 (*d*, *J* = 2.0)
1c		134.84	
2c, 6c	6.80 (*d*, *J* = 8.8)	129.1	6.84 (*d*, *J* = 8.8)
3c, 5c	6.50 (*d*, *J* = 8.8)	114.9[b])	6.50 (*d*, *J* = 8.8)
4c (OH)	8.31 (br. *s*)[b])	155.2	7.94 (br. *s*)[b])
7c	5.74 (br. *dd*, *J* = 7.4, 3.4)	40.7[b])	5.76 (br. *dd*, *J* = 7.4, 3.4)
8c	3.85 (br. *d*, *J* = 3.4)	47.86	3.87 (br. *d*, *J* = 3.4)
9c		140.3	
10c		110.5	
11c		156.9[b])	
12c	5.67 (br. *d*, *J* = 1.6)	95.0	5.69 (*d*, *J* = 2.0)
13c (OH)	7.74 (br. *s*)[c])	156.9[b])	7.37 (br. *s*)[b])
14c	5.10 (br. *d*, *J* = 1.6)	117.2	5.11 (*d*, *J* = 2.0)
1d	6.18 (*t*, *J* = 9.0)	107.1	6.18 (br. *t*, *J* = 9.0)
1d (OH)	6.73 (*d*, *J* = 4.5)		6.37 (br. *d*, *J* = 9.0)
2d	3.65 (*d*, *J* = 9.0)	51.2	3.68 (*d*, *J* = 9.0)
3d		141.5	
4d		120.7	
5d (OH)	8.79 (br. *s*)	158.6[b])	8.48 (br. *s*)[b])
6d	6.57 (*s*)[b])	100.7	6.58 (br. *d*, *J* = 2.0)
7d (OH)	8.58 (br. *s*)	157.2	8.23 (br. *s*)
8d	6.57 (*s*)[b])	105.5	6.61 (br. *s*)

[a]) Measured in (D_6)-acetone at 600 MHz (^{1}H) and 150 MHz (^{13}C). [b]) Overlapping signals. [c]) Interchangeable signals.

Table 4. *2D-NMR Data of* **2**[a])

H-Atom	HMBC (C-Atom)	ROESY (H-Atom)
2a, 6a	2a(6a), 4a, 7a	7a, 8a, 14a
3a, 5a	1a, 3a(5a), 4a	
7a	1a, 2a(6a), 8a, 9a	2a(6a), 8a, 14a
8a	1a, 7a, 9a, 10a, 11a[b]), 14a, 9b, 10b, 11b, 14b[b])	2a(6a), 7a, 14a, 2b(6b)
11a (OH)	10a, 11a, 12a	12a, 2c(6c), 7b
12a	10a, 11a, 13a, 14a	OH-11a
13a (OH)	12a, 13a, 14a	
14a	8a, 10a, 12a, 13a	2a(6a), 7a, 8a
2b, 6b	2b(6b), 4b, 7b	8a, 7b, 8c, 14c, OH-5d
3b, 5b	1b, 3b(5b), 4b	OH-4b
4b (OH)	3b(5b), 4b	3b(5b)
7b	9a, 10a, 11a, 1b, 2b(6b), 8b, 9b, 8c	OH-11a, 2b(6b), 8b, 8c
8b	10a, 7b, 9b, 10b, 14b, 7c, 8c, 9c	7b, 14c, 2c(6c), 7c
12b	10b, 11b, 13b, 14b	OH-13b
13b (OH)	12b, 13b, 14b	12b, 14b
14b	8b, 10b, 12b, 14b	OH-13b, 2c(6c), 8c
2c, 6c	2c(6c), 4c, 7c	OH-11a, 8b, 14b, 7c, 2d
3c, 5c	1c, 3c(5c), 4c	OH-4c
4c (OH)	3c(5c), 4c	3c(5c)
7c	8b, 1c, 2c(6c), 8c, 9c, 9d, 10d, 11d	8b, 2c(6c), 8c, OH-5d
8c	7b, 8b, 9b, 7c, 9c, 10c, 14c, 10d	2b(6b), 7b, 14b, 7c
12c	10c, 11c, 13c, 14c	OH-13c
13c (OH)	12c, 13c, 14c	12c, 14c
14c	8c, 10c, 12c, 14c	2b(6b), 8b, OH-13c
1d	2d, 3d	8d
1d (OH)	1d, 2d	2d
2d	8c[b]), 10c, 11c, 1d, 3d, 4d, 5d[b]), 8d	2c(6c), OH-1d
5d (OH)	4d, 5d, 6d	2b(6b), 7c
6d	4d, 5d, 7d, 8d	OH-7d
7d (OH)	6d, 7d, 8d	6d, 8d
8d	2d, 4d, 6d, 7d	1d, OH-7d

[a]) Measured in (D_6)acetone at $-20°$. [b]) ^4J Coupling.

In addition to the two compounds **1** and **2**, eight known compounds were isolated and their structures were identified as (−)-hopeaphenol (**3**) [1c][1d][2b], upunaphenol B (**4**) [8a], vaticanols B (**5**) and C (**6**) [5d], ampelopsin A (**7**) [2a][11], balanocarpol (**8**) [11], bergenin (**9**) [19], and (3,5-dihydroxyphenyl)(4-hydroxyphenyl)methanone (**10**) [20], respectively, by spectral analysis and comparison with respective authentic samples and literature. Compound **10** has been previously synthesized [20], however, the occurrence is now reported as a natural product for the first time.

The structures of **1** and **2** had a different substitution pattern at C(7a) or C(7d) than **3**, and their co-occurrence involves important biogenetic relationship. In our previous articles, new and various stilbene oligomers are composed of resveratrols [5–11]. However, vateriaphenol D (**1**) is the first stilbene tetramer bearing a piceatannol (= 5-[(*E*)-2-(3,4-dihydroxyphenyl)ethenyl]benzene-1,3-diol) unit. The occurrence of a 2,3-dihydrobenzofuran-2-ol skeleton in **2** is also the first observation of this kind. These

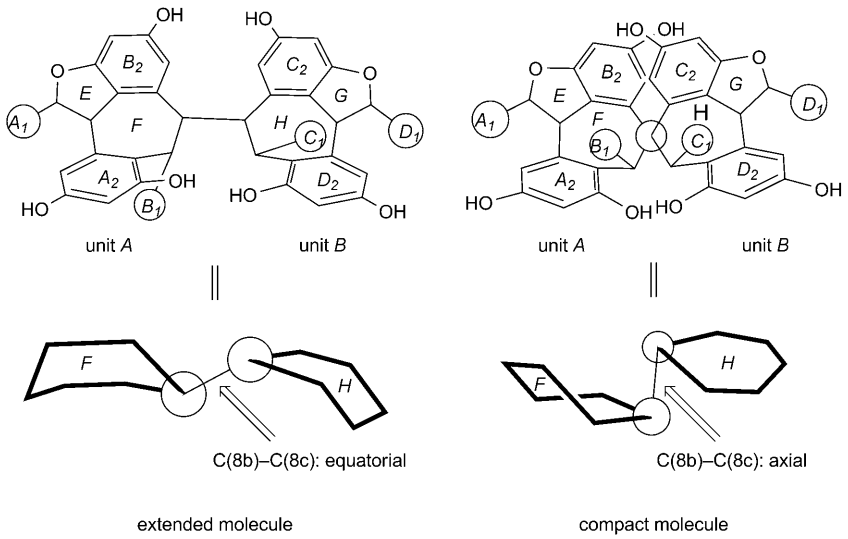
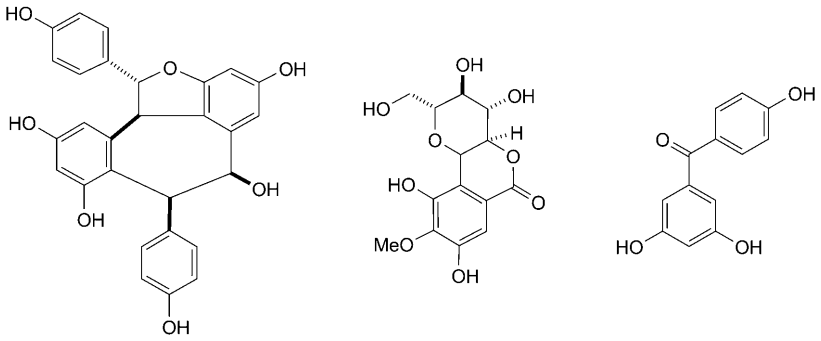


Fig. 5. *Conformational heterogeneities in a dimer of heptacyclic rings*



8 **9** **10**

findings add the structural diversity to chemical constituents in dipterocarpaceaeous plants.

The authors would like to thank Mr. *Kenji Tsujimoto*, *Tsujimoto Chemical Industry Co., Ltd.*, for his help in collecting the plant material and for the preparation of the extracts.

Experimental Part

General. Anal. and prep. TLC: *Kieselgel* F_{254} (0.25 mm; *Merck*). Column chromatography (CC): silica gel *60* (70–230 mesh; *Merck*), *DMS* (100–200 mesh; *Fuji Silysia Chemical*), *ODS* (100–200 mesh; *Fuji Silysia Chemical*), or *Sephadex LH-20* (*Pharmacia*). Optical rotation: *Jasco DP-370* polarimeter. UV Spectra: *Shimadzu UV-3100* spectrophotometer; λ_{max} (log ε) in nm. ^{1}H- and ^{13}C-NMR Spectra: *Jeol JNM-ECA-600* and *Jeol JNM-AL-400* 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. ESI-MS: *Jeol JMS-T100LC* mass spectrometer; in *m*/*z*.

Plant Material. Leaves of *Vateria indica* were collected in Mangalore, India in June, 2004, and a voucher specimen is deposited with the Gifu Pharmaceutical University, Gifu, Japan.

Extraction and Isolation. The dried and well-ground leaves of *V. indica* (250 g) were successively extracted with acetone (3 × 1 l × 24 h), MeOH (3 × 1 l × 24 h), and 70% MeOH (2 × 1 l × 24 h) at r.t., and the extracts were evaporated to afford 9.9 g (from acetone), 8.5 g (from MeOH), and 11.9 g (from 70% MeOH). The other material (1.6 kg) was extracted with *EKINEN*® (EtOH/i-PrOH/EtCOMe 86:6:2) (1 × 30 l × 120 h) at r.t., and the extract was evaporated to afford 47 g. A part (9 g) of the acetone extract and a part (20 g) of *EKINEN* extract were combined and subjected to CC (*DMS*; MeOH/H_2O mixtures of decreasing polarity): *Fr. 1–43*. The particular fractions of them were combined by the indication of *Gibbs* test on TLC as follows, *Fr. 1–3* (*Fr. A:* 15% MeOH); *Fr. 4–6* (*Fr. B:* 15% MeOH); *Fr. 7–10* (*Fr. C:* 20% MeOH); *Fr. 11–14* (*Fr. D:* 30% MeOH); *Fr. 15–16* (*Fr. E:* 30% MeOH); *Fr. 17–18* (*Fr. F:* 35% MeOH); *Fr. 19–24* (*Fr. G:* 40–45% MeOH); *Fr. 25–27* (*Fr. H:* 50–55% MeOH); *Fr. 28–43* (*Fr. I:* 55% MeOH/MeOH; then $CHCl_3$). Compound **9** (20 mg) was obtained from *Fr. A* after purification by CC (*Sephadex LH-20*; MeOH). *Fr. D* was re-subjected to CC (*Sephadex LH-20*; MeOH) to afford the subfractions *Fr. Da – Df*. Compounds **2** (3 mg), **3** (50 mg), and **7** (12 mg) were obtained from *Fr. Db* after purification by CC (SiO_2; AcOEt/$CHCl_3$ 2:1) and prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1). Compound **8** (6 mg) was obtained from *Fr. De* after purification by prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1). Compound **1** (5 mg) was obtained from *Fr. E* after purification by CC (*Sephadex LH-20*; MeOH; then *ODS*; 35% MeOH) and prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1). Compounds **4** (15 mg), **5** (150 mg), **6** (18 mg), and **10** (6 mg) were obtained from *Fr. G* after purification by CC (*Sephadex LH-20*; MeOH; then *ODS*; 25–50% MeOH) and prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 15:8:4:1).

Vateriaphenol D (=*(1*R,*6*S,*7*R,*11b*R*)-1-(3,4-Dihydroxyphenyl)-1,6,7,11b-tetrahydro-7-(4-hydroxyphenyl)-6-[(1*R,*6*S,*7*R,*11b*R*)-1,6,7,11b-tetrahydro-4,8,10-trihydroxy-1,7-bis(4-hydroxyphenyl)-2-oxadibenzo[*cd,h*]azulen-6-yl]-2-oxadibenzo[*cd,h*]azulene-4,8,10-triol*; **1**). Pale yellow solid. $[\alpha]_D = -346$ (c = 0.1, MeOH). UV (log ε, MeOH): 280 (4.21). ^{1}H- and ^{13}C-NMR: see *Table 1*. ESI-MS (neg.): 921 ($[M-H]^-$). HR-ESI-MS (neg.): 921.2531 ($[M-H]^-$, $C_{56}H_{41}O_{13}^-$; calc. 921.2542).

Vateriaphenol E (=*(1*R,*6*S,*7*R,*11b*R*)-1,6,7,11b-Tetrahydro-7-(4-hydroxyphenyl)-6-[(1*R,*6*S,*7*R,*11b*R*)-1,6,7,11b-tetrahydro-4,8,10-trihydroxy-1,7-bis(4-hydroxyphenyl)-2-oxadibenzo[*cd,h*]azulen-6-yl]-2-oxadibenzo[*cd,h*]azulene-1,4,8,10-tetrol*; **2**). Pale yellow solid. $[\alpha]_D = -348$ (c = 0.1, MeOH). UV (log ε, MeOH): 283 (4.10). ^{1}H- and ^{13}C-NMR: see *Table 3*. ESI-MS (neg.): 829 ($[M-H]^-$). HR-ESI-MS (neg.): 829.2278 ($[M-H]^-$, $C_{50}H_{37}O_{12}^-$; calc. 829.2280).

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