

Chemical Constituents of *Avicennia alba*. Isolation and Structural Elucidation of New Naphthoquinones and Their Analogues¹⁾

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Three new naphthoquinones and their analogues, named avicequinone-A (1), -B (2), -C (3), and avicenol-A (4), -B (5), -C (6), respectively, were isolated from the stem bark of *Avicennia alba* (Avicenniaceae) collected in Singapore, and their structures were elucidated by means of spectral methods.

Gillan and co-workers have proposed that the structures of the new phytoalexins isolated from *Avicennia marina* are 1,2-naphthoquinones 8 and 9. Our synthetic and spectrometric studies showed that these structures should be revised respectively to 1,4-naphthoquinones 2 and 3, named avicequinone-B and -C by us.

Key words *Avicennia alba*; naphthoquinone; phytoalexin; avicequinone; avicenol; Avicenniaceae

Avicennia alba BLUME, belonging to the family Avicenniaceae,²⁾ is known to be a type of mangrove tree and grows in the tidal forests at the mouth of rivers. This species is found far away from salt water, unlike other species, e.g. *A. marina* which grows on the shore of very saline seas.³⁾ Some species of this genus are found in the tropics and their chemical constituents have been studied.^{4–10)}

This paper is the first study of constituents of *A. alba* and describes the isolation and structural elucidation of three new naphthoquinones and their analogues along with a known naphthoquinone from the stem bark of this plant.

Results and Discussion

The acetone extract of the stem bark of the plant was fractionated by a combination of silica-gel column chromatography and preparative TLC to give new 1,4-naphthoquinones and their analogues along with a known naphthoquinone.

Structures of Avicequinones The presence of a 1,4-naphthoquinone nucleus with no substituent on the aromatic

ring in avicequinone-A (1), -B (2), and -C (3) was suggested by the following UV, IR, ¹H- (Table 1), and ¹³C-NMR (Table 2) spectral data: 1) One or two strong and sharp UV bands at 244–251 nm, a medium intensity band at 286–292 nm, a broad band at 334–336 nm, and a shoulder band at 374–380 nm; 2) Strong IR bands at 1672–1685 cm⁻¹ and 1587–1595 cm⁻¹; 3) Two typical carbonyl carbon signals at δ_C 173.27–178.14 and 180.54–182.65 ppm in the ¹³C-NMR spectrum; 4) Four contiguous aromatic proton signals at δ_H 8.08–8.24 (2H) and 7.71–7.77 (2H) assignable to two deshielded protons (H-5, H-8) *peri*-located to the carbonyl groups and other two aromatic protons (H-6, H-7), respectively; 5) Three-bond C–H long-range correlations in the ¹H-detected heteronuclear multiple bond connectivity (HMBC) spectrum between carbonyl carbons (C-4, C-1) and deshielded protons (H-5, H-8). The structure of the remaining parts of these compounds will be discussed below.

Structure of Avicequinone-A (1) Avicequinone-A (1) was obtained as a yellow oil, [α]_D +35° (CHCl₃). The high-

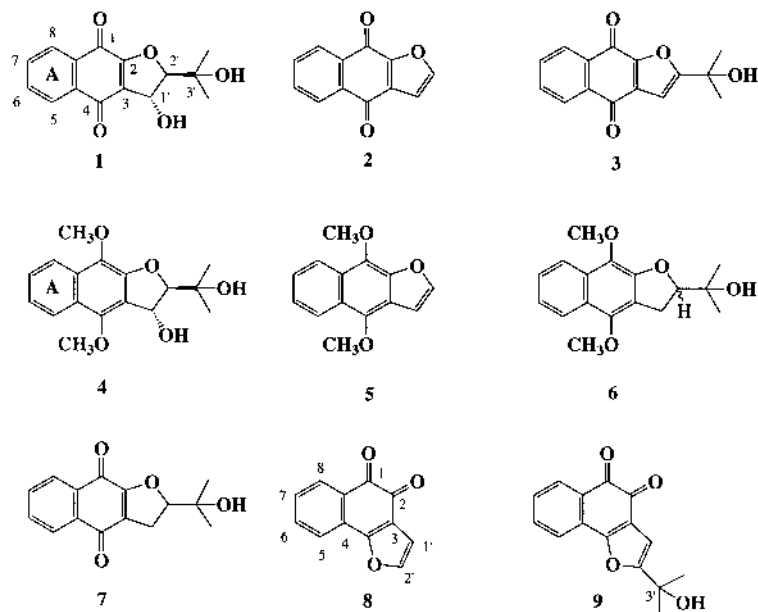


Chart 1

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Table 1. ^1H -NMR Data for the New Naphthoquinones and Their Analogues in CDCl_3

	1	2	3	4	5	6
5	8.08 (dd, 7.7, 1.5)	8.21 (m)	8.14 (m)	8.04 (br d, 8.4)	8.24 (d, 8.4)	8.02 (br d, 8.4)
6	7.76 (dt, 1.5, 7.7)	7.77 (m)	7.73 (m)	7.46 (br t, 8.4)	7.47 (t, 8.4)	7.41 (br t, 8.4)
7	7.71 (dt, 1.5, 7.7)	7.77 (m)	7.73 (m)	7.33 (br t, 8.4)	7.45 (t, 8.4)	7.31 (br t, 8.4)
8	8.10 (dd, 7.7, 1.5)	8.24 (m)	8.18 (m)	8.04 (br d, 8.4)	8.27 (d, 8.4)	8.00 (br d, 8.4)
1'	5.62 (d, 5.1)	7.01 (d, 1.5)	6.80 (s)	4.44 (d, 4.0)	7.04 (d, 2.2)	3.38 (2H, d, 8.4)
2'	4.54 (d, 5.1)	7.78 (d, 1.5)		5.69 (d, 4.0)	7.64 (d, 2.2)	4.71 (t, 8.4)
3'-CH ₃	1.35 (3H, s)		1.67 (6H, s)	1.33 (3H, s)	-	1.26 (3H, s)
	1.44 (3H, s)			1.35 (3H, s)		1.39 (3H, s)
Others	3.04 (br s, OH)			4.03 (3H, s, 1'-OCH ₃)	4.27 (3H, s, 1'-OCH ₃)	3.96 (3H, s, 1'-OCH ₃)
	1.85 (br s, OH)			4.12 (3H, s, 4'-OCH ₃)	4.17 (3H, s, 4'-OCH ₃)	4.01 (3H, s, 4'-OCH ₃)
						1.90 (br s, OH)

Values in (δ) ppm. The coupling constants (J) in parentheses are in Hz. All signals correspond to 1H, and were observed as a singlet, unless otherwise stated.

Table 2. ^{13}C -NMR Data for the New Naphthoquinones and Their Analogues in CDCl_3

	1	2	3	4	5	6
C-1	178.14 (s)	173.59 (s)	173.27 (s)	148.70 (s)	134.43 (s)	147.54 (s)
C-2	160.61 (s)	152.69 (s)	151.60 (s)	147.18 (s)	143.72 (s)	147.24 (s)
C-3	124.84 (s)	130.46 (s)	131.24 (s)	119.93 (s)	119.09 (s)	118.53 (s)
C-4	182.65 (s)	180.54 (s)	180.71 (s)	132.34 (s)	143.27 (s)	132.19 (s)
C-4a	132.86 (s)	133.20 (s)	132.89 (s)	130.43 (s)	125.12 (s)	129.27 (s)
C-5	126.13 (d)	127.05 (d)	126.83 (d)	121.20 (d)	121.87 (d)	120.99 (d)
C-6	134.56 (d)	133.94 (d)	133.86 (d)	126.71 (d)	123.87 (d)	125.82 (d)
C-7	133.35 (d)	133.86 (d)	133.68 (d)	123.53 (d)	124.78 (d)	123.32 (d)
C-8	126.65 (d)	126.93 (d)	126.75 (d)	122.27 (d)	121.74 (d)	121.71 (d)
C-8a	131.75 (s)	132.43 (s)	132.38 (s)	123.96 (s)	123.62 (s)	124.08 (s)
C-1'	71.94 (d)	108.64 (d)	102.55 (d)	71.87 (d)	104.34 (d)	28.81 (t)
C-2'	98.48 (d)	148.59 (d)	168.14 (s)	97.24 (d)	145.60 (d)	90.25 (d)
C-3'	71.07 (s)		69.27 (s)	71.39 (s)		71.73 (s)
3'-CH ₃	25.81 (q)		28.67 (q $\times$ 2)	24.93 (q)		24.32 (q)
	24.46 (q)			25.70 (q)		26.06 (q)
Other				60.68 (1'-OCH ₃)	61.24 (1'-OCH ₃)	60.32 (1'-OCH ₃)
				61.15 (4'-OCH ₃)	61.47 (4'-OCH ₃)	60.55 (4'-OCH ₃)

Values in (δ) ppm.

resolution (HR)-MS spectrum of avicequinone-A showed a molecular ion at m/z 274.0847, corresponding to the formula $\text{C}_{15}\text{H}_{14}\text{O}_5$. The presence of a 1-hydroxy-1-methylethyl side-chain in the molecule was prompted by the observation of two 3H singlets at δ_{H} 1.35 and 1.44 due to methyls attached to a quaternary carbon linked to an oxygen atom in the ^1H -NMR spectrum, the ^{13}C -NMR signal at δ_{C} 71.07 (C-3'), and a significant mass fragment ion at m/z 216 ($\text{M}-59+\cdot\text{H}$)⁺ with the loss of $\text{C}_3\text{H}_7\text{O}$ followed by $\cdot\text{H}$ transfer in the EI-MS. The remaining two protons appeared as AB-type doublets ($J=5.1$ Hz) at δ_{H} 4.54 (H-2') and 5.62 (H-1') and were assigned to vicinal methine protons, both attached to oxygen-bearing carbons, on the basis of their chemical shifts. Furthermore, in the HMBC spectrum of **1**, as shown by arrows in Fig. 1, these two methine protons [δ_{H} 5.62 (H-1'), 4.54 (H-2')] showed three-bond correlations with the sp^2 carbon (δ_{C} 160.61, C-2) linked both with a carbonyl group and an oxygen atom, suggesting the presence of a vicinal methine unit fused to the naphthoquinone nucleus as a dihydrofuran ring. The location of the side-chain at C-2' was revealed by the three-bond correlations between two methyl protons (δ_{H} 1.35, 1.44) and the carbon at δ_{C} 98.48 (C-2') with a proton at δ_{H} 4.54, indicating a hydroxyl group attached to the remaining site (C-1'). *trans*-Orientation of these moieties on the dihydrofuran ring was proposed from the coupling constants ($J=5.1$ Hz) of the AB-type doublets¹¹⁾ and no nuclear Over-

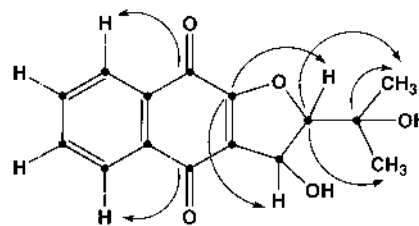


Fig. 1. C-H Long-Range Correlations in the HMBC Spectrum of Avicequinone-A (**1**) in CDCl_3

hauser effect (NOE) enhancement between these two methine proton signals. Based on these results, the structure of avicequinone-A was concluded to be **1**, corresponding to the hydroxy derivative of stenocarpoquinone-B (**7**) isolated from *Stenocarpus salignus*,¹²⁾ leaving the absolute stereochemistry undetermined.

Structure of Avicequinone-B (2) The molecular formula $\text{C}_{12}\text{H}_6\text{O}_3$ was established by HR-MS. In the ^1H - and ^{13}C -NMR spectra, only AB-type olefinic protons at δ_{H} 7.78, 7.01 (each 1H, d, $J=1.5$ Hz) and sp^2 carbon signals at δ_{C} 148.59, 108.64 were observed, in addition to signals due to the 1,4-naphthoquinone skeleton. Based on the J -value (1.5 Hz) of the AB-type signals and the appearance of three-bond C-H long-range correlations between C-2 and C-3 carbons

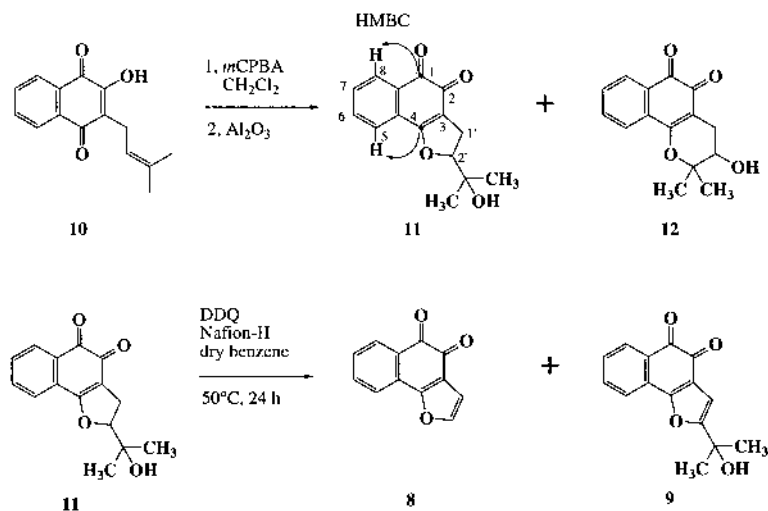


Chart 2

Table 3. ^1H -NMR Data for Phytoalexins and the Corresponding Naphthoquinones in $\text{MeOD}-d_4$

	Phytoalexin (8')	8	2	Phytoalexin (9')	9	3
5	8.22 (m)	8.05 (br d, 7.7)	8.18 (m)	8.21 (m)	8.00 (br d, 7.7)	8.11 (m)
6	7.85 (m)	7.53 (br t, 7.7)	7.82 (m)	7.86 (m)	7.49 (br t, 7.7)	7.78 (m)
7	7.85 (m)	7.73 (br t, 7.7)	7.82 (m)	7.86 (m)	7.70 (br t, 7.7)	7.78 (m)
8	8.22 (m)	7.79 (br d, 7.7)	8.18 (m)	8.21 (m)	7.76 (br d, 7.7)	8.11 (m)
1'	7.08 (d, 1.6)	6.90 (d, 1.8)	7.05 (d, 1.5)	6.90 (s)	6.65 (s)	6.82 (s)
2'	8.06 (d, 1.6)	7.75 (d, 1.8)	8.03 (d, 1.5)			
3'-CH ₃				1.66 (6H, s)	1.63 (6H, s)	1.64 (6H, s)

Values in (δ) ppm. The coupling constants (*J*) in parentheses are in Hz. All signals correspond to 1H, and were observed as a singlet, unless otherwise stated.

(δ_{C} 152.69 and 130.46, respectively) on the 1,4-naphthoquinone nucleus and these olefinic protons (δ_{H} 7.78 and 7.01) in the HMBC spectrum, the structure of avicequinone-B was proposed as **2**. Although synthesis of this compound has already been reported by Tanaka and co-workers,¹³⁾ this is its first isolation from a natural source.

Structure of Avicequinone-C (3) The molecular formula, $\text{C}_{15}\text{H}_{12}\text{O}_4$, with a difference of $\text{C}_3\text{H}_6\text{O}$ compared with that of **2**, was determined by HR-MS. The ^1H -NMR spectrum of this compound was similar to that of **2**, except for the appearance of a 6H singlet at δ_{H} 1.67, due to two methyls, and a 1H sharp singlet at δ_{H} 6.80, instead of the AB-type olefinic proton signals in the spectrum of **2**. The presence of a 1-hydroxy-1-methylethyl side-chain in the molecule was prompted by the observation of a quarternary carbon signal at δ_{C} 69.27 (C-3') assignable to an oxygen-bearing carbon in the ^{13}C -NMR spectrum, a 6H singlet (δ_{H} 1.67) in the ^1H -NMR spectrum, and a base fragment ion at m/z 241 produced by loss of a methyl radical from the molecular ion. The location of the side-chain at C-2' was suggested by the chemical shifts of a sharp singlet at δ_{H} 6.80 (H-1', not H-2') and the carbon (δ_{C} 102.55, C-1') with this proton. On the basis of these spectral data, we proposed structure **3** for avicequinone-C.

Gillan and co-workers reported the isolation of phytoalexins for fungus belonging to the genus *Phytophthora*¹⁴⁾ from *Avicennia marina*, and proposed their structures to be 1,2-naphthoquinones (naphtho[1,2-*b*]furan-4,5-diones) (**8**) and (**9**). Strangely, we found that the ^1H -NMR data of the phytoalexins assigned to 1,2-naphthoquinones reported in the lit-

erature¹⁴⁾ showed close similarity to that of **2** and **3**, determined as 1,4-naphthoquinones by us, as shown in Table 3. To clarify this discrepancy, synthesis of the 1,2-naphthoquinones (**8**) and (**9**) proposed by Gillan and co-workers was carried out as outlined in Chart 2.

Lapachol (**10**), which is commercially available, was treated with *m*-chloroperbenzoic acid (*m*CPBA) in CH_2Cl_2 followed by treatment with Al_2O_3 to give two cyclization products, dihydrofuran **11** and dihydropyran **12** in a ratio of 1:1.^{12,15)}

The *ortho*-quinoid structure of **11** was confirmed by the HMBC spectrum. Of the two carbonyl carbons of **11**, C-1 at δ_{C} 180.93 showed a three-bond long-range correlation with a lower field aromatic proton at δ_{H} 8.04 (H-8), and the other carbonyl carbon at δ_{C} 175.26 (C-2) had no correlation with any aromatic protons. Instead, the sp^2 carbon (C-4) with an oxygen atom at δ_{C} 169.73 showed a correlation with one of the four aromatic protons at δ_{H} 7.66 (H-5). Treatment of **11** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in the presence of Nafion-H in dry benzene afforded the corresponding dehydro compound **9** and the dealkylation product **8**.¹⁶⁾

As shown in Table 3, the ^1H -NMR data of the synthetic compounds were clearly different from that of the phytoalexins reported by Gillan and co-workers.^{14,17)} From these results, we concluded that the structures of the phytoalexins isolated from *A. marina* by Gillan and co-workers must be revised to *para*-quinoid structures **2** and **3**, named avicequinone-B and -C by us, respectively.

Structures of Avicenols Three additional new com-

pounds, avicenol-A (**4**), -B (**5**), and -C (**6**) were isolated and shown to have a 1,4-naphthoquinol chromophore, based on the similarities in their UV spectra with a high-intensity band at $\lambda_{\max}$ 239–246 nm and low-intensity bands with fine-structures over the range 286 to 338 nm, although a hyperchromic shift of the bands in avicenol-B was observed.

Structure of Avicenol-A (4) Avicenol-A (**4**) was obtained as a colorless oil, $[\alpha]_D^{25} +5.1^\circ$ (CHCl₃). The molecular formula was established as C₁₇H₂₀O₅ by HR-MS. In the ¹H-NMR spectrum, observation of symmetrical four-spin proton signals, analyzed as an AA'BB'-type [δ_H 8.04 (2H, d, $J=8.4$ Hz), 7.46 (1H, t, $J=8.4$ Hz), 7.33 (1H, t, $J=8.4$ Hz)], and two 3H singlets due to methoxys (δ_H 4.12, 4.03), together with 4 and 3% NOE enhancement of the 2H-doublet at δ_H 8.04 on irradiation of each methoxyl at δ_H 4.12 and 4.03, respectively, suggested the presence of a 1,4-dimethoxynaphthol nucleus having no substituents on the A-ring. The presence of a 2-(1-hydroxy-1-methylethyl)-3-hydroxydihydrofuran ring fused to the naphthol skeleton, as shown in formula **4**, was proposed from the ¹H- and ¹³C-NMR spectral data: a) Appearance of two 3H singlets at δ_H 1.33 and 1.35, a quarternary carbon linked to an oxygen atom at δ_C 71.39, AB-type doublets at δ_H 4.44 and 5.69 ($J=4.0$ Hz) which bonded to carbons at δ_C 71.87 and 97.24, respectively. b) C–H long-range correlations in the HMBC spectrum of the carbons at δ_C 97.24 (C-2') and 71.39 (C-3') with two methyls at δ_H 1.33 (3'-CH₃) and 1.35 (3'-CH₃). Another possible 6-membered ring system (2,2-dimethyl-3,4-dihydroxyfuran ring) was excluded by consideration of the typical chemical shift values of the quarternary carbon (δ_C 71.39) and the methine carbon (δ_C 97.24) linked to the side-chain. *trans*-Configuration of two substituents on the dihydrofuran ring was proposed based on the coupling constants ($J=4.0$ Hz) of the AB-type doublets and no NOE enhancement between the two methine doublets at δ_H 4.44 and 5.69, as in the case of **1**. Thus, the structure of avicenol-A is that depicted by formula **4**.

Structure of Avicenol-B (5) Avicenol-B (**5**) was isolated as a colorless oil, C₁₄H₁₂O₃. Some red-shift in the UV absorption spectrum of this compound compared with that of **4**, suggested the presence of an additional conjugated system. In the ¹H-NMR spectrum, lack of two methyl signals (δ_H 1.33, 1.35) in the high-field and aliphatic vicinal protons [δ_H 4.44, 5.69 ($J=4.0$ Hz)] adjacent to the oxygen atoms in **4**, and the appearance of two doublets at δ_H 7.04 and 7.64 ($J=2.2$ Hz) coupled to each other, along with four contiguous aromatic proton signals and two methoxy signals, indicated that **5** was the structure of avicenol-B.

Structure of Avicenol-C (6) Avicenol-C (**6**) was also isolated as a colorless oil, $[\alpha]_D^{25} +22^\circ$ (CHCl₃). The molecular formula C₁₇H₂₀O₄, a difference of an oxygen atom compared with **4**, was established by HR-MS. The ¹H- and ¹³C-NMR spectra (Tables 1, 2) were very similar to those of **4**, except for the proton signals at δ_H 3.38 (2H, d, $J=8.4$ Hz) and 4.71 (1H, t, $J=8.4$ Hz) coupled to each other, instead of the two doublets at δ_H 4.44 and 5.69 ($J=4.0$ Hz) in **4**, and the displacement of a methine carbon signal having a hydroxyl group at δ_C 71.87 in **4** to a high-field methylene carbon signal at δ_C 28.81 in the ¹³C-NMR spectrum of **6**. These facts together with the results of the HMBC spectrum (see Experimental) led us to conclude that **6** was the structure of avi-

cenol-C, although the absolute stereochemistry remained undetermined.

Another naphthoquinone isolated from this plant material was characterized as stenocarpoquinone-B (**7**) by comparison of the ¹H-NMR and IR data with that reported in the literature.¹²⁾

Experimental

The ¹H- and ¹³C-NMR, H–H correlation spectroscopy (COSY), NOE, and HMBC ($J=8$ Hz) spectra were recorded on an A-400 or A-600 (JEOL) spectrometer in CDCl₃, unless otherwise stated. Chemical shifts are shown in δ values (ppm) with tetramethylsilane (TMS) as an internal reference. All MS were recorded under electron impact (EI) conditions using an M-80 instrument (Hitachi) having a direct inlet system. UV spectra were recorded on a UVDEC-610C double-beam spectrophotometer (JASCO) in methanol, IR spectra on an IR-230 instrument (JASCO) in CHCl₃, and optical rotations on a DIP-370 instrument (JASCO) in CHCl₃ at 25 °C. Preparative TLC was carried out on Kieselgel 60 F₂₅₄ (Merck).

Plant Material *A. alba* BLUME (Avicenniaceae) stem bark from young trees was collected on August 1995. Dr. H.T.W. Tan identified the material using keys or by comparison with herbarium sheet specimens at the Herbarium, Department of Biological Sciences, the National University of Singapore (SINU) or the Herbarium, Botanic Gardens, Singapore (SING). A voucher specimen has been deposited at SINU.

Extraction and Isolation The dried stem bark (1.63 kg) of *A. alba* collected in Singapore was extracted with acetone. The acetone extract (9.0 g) was subjected to silica-gel column chromatography, eluting with hexane–acetone (19:1, 18:2, 17:3, 4:1, 7:3, 1:1, 1:2), acetone, CH₂Cl₂–MeOH (3:1), and MeOH, successively, to give 10 fractions. Each fraction was further subjected to silica-gel column and preparative thin-layer chromatographies with appropriate combinations of hexane, CH₂Cl₂, iso-Pr₂O, EtOAc, benzene, CHCl₃, acetone, and MeOH as developing solvents to give three new naphthoquinones and their analogues, along with a known naphthoquinone, as stated below. From the hexane–acetone (19:1) eluate: avicequinone-B (**2**) (2.6 mg) and avicenol-B (**5**) (1.6 mg). From the hexane–acetone (17:3) eluate: avicenol-C (**6**) (20.7 mg). From the hexane–acetone (4:1) eluate: avicequinone-C (**3**) (14.3 mg) and stenocarpoquinone-B (**7**) (13.8 mg). From the hexane–acetone (7:3) eluate: avicenol-A (**4**) (10.2 mg). From the hexane–acetone (1:1) eluate: avicequinone-A (**1**) (3.7 mg).

A known compound, stenocarpoquinone-B, was fully characterized by comparison of the ¹H-NMR and IR data with that reported in the literature.¹²⁾

Avicequinone-A (1): Yellow oil. $[\alpha]_D^{25} +35^\circ$ ($c=0.108$). UV $\lambda_{\max}$ nm: 206, 245, 251, 286, 334. IR $\nu_{\max}$ cm^{−1}: 3587, 3406 (br), 1685, 1653, 1635, 1595. EI-MS m/z (%): 274 (M^+ , 2), 241 (14), 216 (12), 198 (10), 173 (10), 146 (10). HR-MS Calcd for C₁₅H₁₄O₅: 274.0840. Found: 274.0847. NOE: No enhancement of any proton signal was observed on irradiation of the methine proton at δ_H 5.62 and 4.54.

Avicequinone-B (2): Pale yellow powder. UV $\lambda_{\max}$ nm: 244, 248, 286, 336. IR $\nu_{\max}$ cm^{−1}: 1682, 1587. EI-MS m/z (%): 198 (M^+ , 100), 170 (54), 142 (21), 114 (76). HR-MS Calcd for C₁₂H₈O₃: 198.0315. Found: 198.0277. HMBC C–H correlations: C-1→H-8; C-2→H-1', H-2'; C-3→H-1', H-2'; C-4→H-5; C-4a→H-6; C-5→H-7; C-6→H-8; C-7→H-5; C-8→H-6; C-8a→H-7; C-1'→H-2'; C-2'→H-1'.

Avicequinone-C (3): Yellow powder. UV $\lambda_{\max}$ nm: 249, 292, 335, 374. IR $\nu_{\max}$ cm^{−1}: 3589, 3450 (br), 1672, 1595, 1537. EI-MS m/z (%): 256 (M^+ , 12), 241 (100), 214 (18), 199 (10), 129 (10), 115 (17), 105 (22). HR-MS Calcd for C₁₅H₁₂O₄: 256.0734. Found: 256.0723. HMBC C–H correlations: C-1→H-8; C-2→H-1'; C-3→H-1'; C-4→H-5; C-4a→H-6; C-5→H-7; C-6→H-8; C-7→H-5; C-8→H-6; C-8a→H-7; C-2'→H-1', 3'-CH₃; C-3'→3'-CH₃.

Reaction of Lapachol with mCPBA To a solution of lapachol (**10**) (30 mg) in dry CH₂Cl₂ (2 ml) was added a solution of mCPBA (30 mg) in CH₂Cl₂ (1 ml). After 10 min, the reaction mixture was treated with Al₂O₃ (10 mg) for 5 min. The mixture was then filtered through a short column of Al₂O₃, and eluted with MeOH. On evaporation, the combined eluates gave a crude orange oil. This was subjected to preparative TLC with iso-Pr₂O–MeOH (24:1) as the developing solvent to give a dihydrofuran **11** (13.1 mg) and a dihydropyran **12** (13.2 mg). Dihydropyran **12** was found to be identical to stenocarpoquinone-A¹²⁾ and dihydrofuran **11** to hydroxyiso- β -lapachone¹²⁾ by comparison of the ¹H-NMR, UV, and IR spectra.

Dihydrofuran 11: Red oil. ¹H-NMR (400 MHz, CDCl₃) δ : 8.04 (1H, d,

$J=7.3$ Hz, H-8), 7.66 (2H, m, H-5, 6), 7.57 (1H, br t, $J=7.3$ Hz, H-7), 4.93 (1H, t, $J=9.2$ Hz, H-2'), 3.08 (2H, d, $J=9.2$ Hz, H-1'), 1.43 (3H, s, 3'-CH₃), 1.29 (3H, s, 3'-CH₃); ¹³C-NMR (100 MHz, CDCl₃) δ : 180.93 (C-1), 175.26 (C-2), 169.73 (C-4), 134.50 (C-6), 131.93 (C-7), 130.59 (C-8a), 129.43 (C-8), 127.26 (C-4a), 124.41 (C-5), 115.96 (C-3), 93.50 (C-2'), 71.69 (C-3'), 27.40 (C-1'), 25.70 (3'-CH₃), 24.41 (3'-CH₃). HMBC C-H correlations: C-1→H-8; C-3→H-1'; C-4→H-5, H-1'; C-4a→H-6, H-8; C-5→H-7; C-6→H-8; C-8a→H-5, H-7; C-2'→3'-CH₃; C-3'→3'-CH₃; 3'-CH₃→H-2'.

Dihydropyran 12: Red oil. ¹H-NMR (400 MHz, CDCl₃) δ : 8.03 (1H, d, $J=7.7$ Hz, H-8), 7.82 (1H, d, $J=7.7$ Hz, H-5), 7.64 (1H, t, $J=7.7$ Hz, H-6), 7.50 (1H, t, $J=7.7$ Hz, H-7), 3.93 (1H, t, $J=5.1$ Hz, H-2'), 3.50 (1H, br, OH), 2.80 (1H, dd, $J=17.6$, 5.1 Hz, H-1'), 2.62 (1H, dd, $J=17.6$, 5.1 Hz, H-1'), 1.51 (3H, s, 3'-CH₃), 1.45 (3H, s, 3'-CH₃); ¹³C-NMR (100 MHz, CDCl₃) δ : 179.53 (C-1), 178.66 (C-2), 161.70 (C-4), 134.84 (C-6), 132.07 (C-8a), 130.82 (C-7), 129.93 (C-4a), 128.57 (C-8), 124.34 (C-5), 110.54 (C-3), 81.64 (C-3'), 68.05 (C-2'), 25.21 (3'-CH₃), 25.00 (C-1'), 21.99 (3'-CH₃).

Dehydrogenation of 11 with DDQ A mixture of **11** (10 mg), DDQ (15 mg), and Nafion-H (solid, Aldrich) (3.0 mg) in dry benzene (2 ml) was heated in an oil bath at 50 °C for 24 h. The reaction mixture was filtered, and the filtrate was evaporated to dryness. The residue was subjected to preparative TLC with hexane-acetone (7:3) and CHCl₃-MeOH (19:1) as developing solvents to afford 2-[2'-(2'-hydroxy)propyl]naphtho[1,2-b]furan-4,5-dione (**9**, 1 mg) and naphtho[1,2-b]furan-4,5-dione (**8**, 0.4 mg).

Naphtho[1,2-b]furan-4,5-dione (8): Red oil. UV $\lambda_{\max}$ nm: 214, 244, 261, 267 (sh), 327, 436. IR $\nu_{\max}$ cm⁻¹: 1709, 1678, 1603. EI-MS m/z (%): 198 (M⁺, 85), 170 (100), 142 (26). HR-MS Calcd for C₁₂H₆O₃: 198.0317. Found: 198.0323. ¹H-NMR (400 MHz, CDCl₃) δ : 8.10 (1H, d, $J=7.7$ Hz, H-8), 7.74 (1H, d, $J=7.7$ Hz, H-5), 7.67 (1H, t, $J=7.7$ Hz, H-6), 7.52 (1H, d, $J=2.2$ Hz, H-1'), 7.49 (1H, t, $J=7.7$ Hz, H-7), 6.88 (1H, d, $J=2.2$ Hz, H-2'); ¹³C-NMR (100 MHz, CDCl₃) δ : 180.51 (C-1), 174.48 (C-2), 160.58 (C-4), 145.07 (C-2'), 135.43 (C-6), 130.60 (C-8), 130.31 (C-7), 128.77 (C-8a), 128.44 (C-4a), 122.36 (C-5), 121.52 (C-3), 108.89 (C-1').

2-[2'-(2'-Hydroxy)propyl]naphtho[1,2-b]furan-4,5-dione (9): Red oil. UV $\lambda_{\max}$ nm: 214, 246, 264, 272 (sh), 328, 436. IR $\nu_{\max}$ cm⁻¹: 3504 (br), 1709, 1678, 1603. EI-MS m/z (%): 256 (M⁺, 31), 241 (60), 213 (51), 199 (10), 185 (8), 170 (16), 149 (46). HR-MS Calcd for C₁₅H₁₂O₄: 256.0734. Found: 256.0725. ¹H-NMR (400 MHz, CDCl₃) δ : 8.09 (1H, d, $J=7.7$ Hz, H-8), 7.74 (1H, d, $J=7.7$ Hz, H-5), 7.66 (1H, t, $J=7.7$ Hz, H-6), 7.47 (1H, t, $J=7.7$ Hz, H-7), 6.68 (1H, s, H-1'), 2.17 (1H, br s, OH), 1.68 (6H, s, 3'-CH₃); ¹³C-NMR (100 MHz, CDCl₃) δ : 180.42 (C-1), 174.48 (C-2), 163.61 (C-2'), 159.94 (C-4), 135.36 (C-6), 130.54 (C-8), 130.20 (C-7), 128.83 (C-8a), 128.41 (C-4a), 122.28 (C-5), 122.02 (C-3), 102.65 (C-1'), 68.78 (C-3'), 28.54 (3'-CH₃×2).

Avicenol-A (4): Colorless oil. [α]_D +5.1° ($c=0.392$). UV $\lambda_{\max}$ nm: 210, 239, 290, 300, 321, 335. IR $\nu_{\max}$ cm⁻¹: 3587, 3429 (br), 1639. EI-MS m/z (%): 304 (M⁺, 100), 289 (23), 286 (72), 271 (91), 253 (10), 241 (42), 232 (11), 229 (25), 217 (79), 213 (57), 211 (10), 199 (17), 189 (26), 173 (15). HR-MS Calcd for C₁₇H₂₀O₅: 304.1310. Found: 304.1310. NOE: Irradiation of 1-OCH₃ (δ 4.03) gave a 3% NOE at H-8 (δ 8.04); irradiation of 4-OCH₃ (δ 4.12) gave a 4% NOE at H-1' (δ 4.44) and a 4% NOE at H-5 (δ 8.04); No enhancement of any proton signal was observed on irradiation of the methine protons at δ _H 5.69 and 4.44. HMBC C-H correlations: C-1→H-8, 1-OCH₃; C-2→H-1'; C-4→4-OCH₃; C-4a→H-6; C-5→H-7; C-7→H-5; C-8→H-6; C-8a→H-7; C-2'→3'-CH₃; C-3'→3'-CH₃.

Avicenol-B (5): Colorless oil. UV $\lambda_{\max}$ nm: 212, 246, 331, 345. IR $\nu_{\max}$ cm⁻¹: 1639, 1608. EI-MS m/z (%): 228 (M⁺, 13), 213 (28), 167 (63), 149 (100), 135 (6). HR-MS Calcd for C₁₄H₁₂O₃: 228.0786. Found: 228.0811. NOE: Irradiation of 1-OCH₃ (δ 4.27) gave a 2% NOE at H-8 (δ 8.27); irra-

diation of 4-OCH₃ (δ 4.17) gave a 3% NOE at H-1' (δ 7.04) and 1% NOE at H-5 (δ 8.24). HMBC C-H correlations: C-1→H-8, 1-OCH₃; C-2→H-2'; C-3→H-1', H-2'; C-4→H-5, H-1', 4-OCH₃; C-4a→H-6; C-5→H-7; C-6→H-8; C-7→H-5; C-8→H-6; C-8a→H-7; C-1'→H-2'; C-2'→H-1'.

Avicenol-C (6): Colorless oil. [α]_D +22° ($c=1.031$). UV $\lambda_{\max}$ nm: 210, 239, 286, 297, 326, 338. IR $\nu_{\max}$ cm⁻¹: 3587, 3442 (br), 1639, 1608. EI-MS m/z (%): 288 (M⁺, 100), 273 (19), 255 (16), 229 (7), 215 (18), 213 (32), 201 (27), 199 (17), 195 (11), 187 (13), 183 (10), 173 (63), 171 (12), 157 (16), 143 (23). HR-MS Calcd for C₁₇H₂₀O₄: 288.1360. Found: 288.1355. NOE: Irradiation of 1-OCH₃ (δ 3.96) gave a 2% NOE at H-8 (δ 8.00); irradiation of 4-OCH₃ (δ 4.01) gave a 2% NOE at H-5 (δ 8.02). HMBC C-H correlations: C-1→H-8, 1-OCH₃; C-2→H-1'; C-3→H-1'; C-4→H-5, 4-OCH₃; C-4a→H-6, H-8; C-5→H-7; C-6→H-8; C-8→H-6; C-8a→H-5, H-7; C-2'→H-1', 3'-CH₃; C-3'→H-1', 3'-CH₃.

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References and Notes

- 1) Part of this paper was presented at the 116th and 117th Annual Meetings of the Pharmaceutical Society of Japan, Kanazawa, March 1996 and Tokyo, March 1997.
- 2) A different classification of this genus has been reported by several authors. König G., Rimpler H., Hunkler D., *Phytochemistry*, **26**, 423—427 (1987), and references cited herein.
- 3) "A Dictionary of the Economic Products of the Malay Peninsula," ed. by Burkill I. H., Ministry of Agriculture and Co-Operatives, Kuala Lumpur, Malaysia, 1966, pp. 274—279.
- 4) Fauvel M.-T., Bousquet-Melou A., Moulis C., Gleye J., Jensen S. R., *Phytochemistry*, **38**, 893—894 (1995).
- 5) Fauvel M. T., Taoubi K., Gleye J., Fouraste I., *Planta Med.*, **59**, 387 (1993).
- 6) Misra S., Choudhury A., Pal P. K., Ghosh A., *Phytochemistry*, **25**, 1083—1087 (1986).
- 7) Ghosh A., Misra S., Dutta A. K., Choudhury A., *Phytochemistry*, **24**, 1725—1727 (1985).
- 8) König G., Rimpler H., *Phytochemistry*, **24**, 1245—1248 (1985).
- 9) Wannigama G. P., Volkman J. K., Gillan F. T., Nichols P. D., Johns R. B., *Phytochemistry*, **20**, 659—666 (1981).
- 10) Majumdar S. G., Patra G., *J. Indian Chem. Soc.*, **56**, 111—113 (1979).
- 11) Hayward E. C., Tarbell D. S., Colebrook L. D., *J. Org. Chem.*, **33**, 399—402 (1968).
- 12) Mock J., Murphy S. T., Ritchie E., Taylor W. C., *Aust. J. Chem.*, **26**, 1121—1130 (1973).
- 13) Koyanagi J., Yamamoto K., Nakayama K., Tanaka A., *J. Heterocyclic Chem.*, **31**, 1303—1304 (1994).
- 14) Sutton D. C., Gillan F. T., Susic M., *Phytochemistry*, **24**, 2877—2879 (1985).
- 15) Murray R. D. H., Sutcliffe M., McCabe P. H., *Tetrahedron*, **27**, 4901—4906 (1971).
- 16) Mathieson J. W., Thomson R. H., *J. Chem. Soc. (C)*, **1971**, 153—160.
- 17) The UV data could not be compared, because sufficient data were not reported in the literature.¹⁴⁾