Chemical Constituents of *Avicennia alba*. Isolation and Structural Elucidation of New Naphthoquinones and Their Analogues[1)]

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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, ^{1}H- (Table 1), and ^{13}C-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 ^{13}C-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 ^{1}H-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 dicussed below.

Structure of Avicequinone-A (1) Avicequinone-A (**1**) was obtained as a yellow oil, $[\alpha]_D$ +35° (CHCl$_3$). The high-

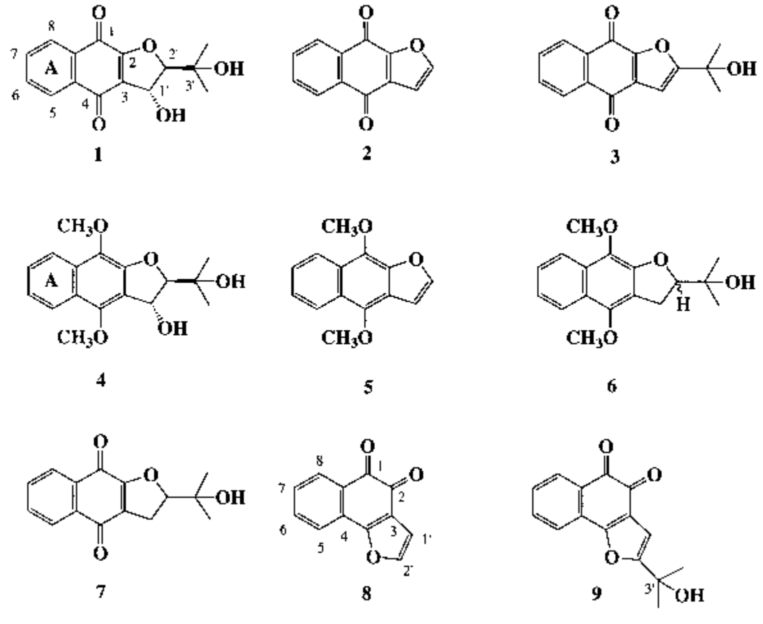

Chart 1

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Table 1. ^{1}H-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) 1.44 (3H, s)		1.67 (6H, s)	1.33 (3H, s) 1.35 (3H, s)	-	1.26 (3H, s) 1.39 (3H, s)
Others	3.04 (br s, OH) 1.85 (br s, OH)			4.03 (3H, s, 1′-OCH_3) 4.12 (3H, s, 4′-OCH_3)	4.27 (3H, s, 1′-OCH_3) 4.17 (3H, s, 4′-OCH_3)	3.96 (3H, s, 1′-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) 24.46 (q)		28.67 (q×2)	24.93 (q) 25.70 (q)		24.32 (q) 26.06 (q)
Other				60.68 (1′-OCH_3) 61.15 (4′-OCH_3)	61.24 (1′-OCH_3) 61.47 (4′-OCH_3)	60.32 (1′-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 $C_{15}H_{14}O_5$. 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 quarternary carbon linked to an oxygen atom in the ^{1}H-NMR spectrum, the ^{13}C-NMR signal at δ_C 71.07 (C-3′), and a significant mass fragment ion at m/z 216 $(M-59+\cdot H)^+$ with the loss of C_3H_7O followed by $\cdot$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 doublets[11] and no nuclear Overhauser 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.

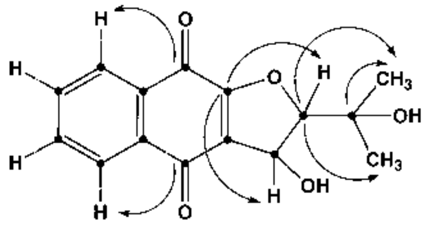

Fig. 1. C–H Long-Range Correlations in the HMBC Spectrum of Avicequinone-A (**1**) in $CDCl_3$

Structure of Avicequinone-B (2) The molecular formula $C_{12}H_6O_3$ was established by HR-MS. In the ^{1}H- 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

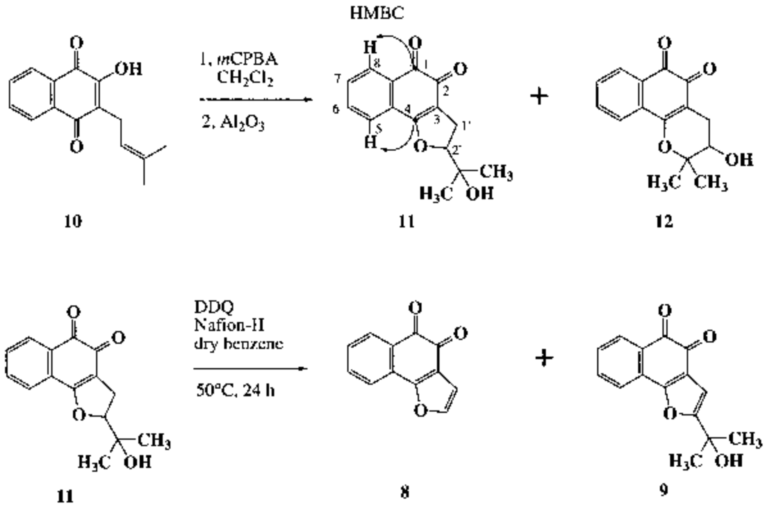

Chart 2

Table 3. ^{1}H-NMR Data for Phytoalexins and the Corresponding Naphthoquinones in 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, $C_{15}H_{12}O_4$, with a difference of C_3H_6O compared with that of **2**, was determined by HR-MS. The ^{1}H-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 cabon 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 ^{1}H-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 ^{1}H-NMR data of the phytoalexins assigned to 1,2-naphthoquinones reported in the literature[14] 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 ^{1}H-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 compounds, 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 λ_{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, $[\alpha]_D$ +5.1° ($CHCl_3$). The molecular formula was established as $C_{17}H_{20}O_5$ by HR-MS. In the ^{1}H-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 methoxyls (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 ^{1}H- and ^{13}C-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′-CH_3) and 1.35 (3′-CH_3). Another possible 6-membered ring system (2,2-dimethyl-3,4-dihydroxypyran 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, $C_{14}H_{12}O_3$. 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 ^{1}H-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, $[\alpha]_D$ +22° ($CHCl_3$). The molecular formula $C_{17}H_{20}O_4$, a difference of an oxygen atom compared with **4**, was established by HR-MS. The ^{1}H- and ^{13}C-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 ^{13}C-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 avicenol-C, although the absolute stereochemistry remained undetermined.

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

Experimental

The ^{1}H- and ^{13}C-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 $CDCl_3$, 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 UVIDEC-610C double-beam spectrophotometer (JASCO) in methanol, IR spectra on an IR-230 instrument (JASCO) in $CHCl_3$, and optical rotations on a DIP-370 instrument (JASCO) in $CHCl_3$ at 25 °C. Preparative TLC was carried out on Kieselgel 60 F_{254} (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, CH_2Cl_2–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, CH_2Cl_2, iso-Pr_2O, EtOAc, benzene, $CHCl_3$, 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 ^{1}H-NMR and IR data with that reported in the literature.[12)]

Avicequinone-A (**1**): Yellow oil. $[\alpha]_D$ +35° (c=0.108). UV λ_{max} nm: 206, 245, 251, 286, 334. IR ν_{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 $C_{15}H_{14}O_5$: 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 λ_{max} nm: 244, 248, 286, 336. IR ν_{max} cm^{-1}: 1682, 1587. EI-MS *m/z* (%): 198 (M^+, 100), 170 (54), 142 (21), 114 (76). HR-MS Calcd for $C_{12}H_6O_3$: 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 λ_{max} nm: 249, 292, 335, 374. IR ν_{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 $C_{15}H_{12}O_4$: 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′-CH_3; C-3′→3′-CH_3.

Reaction of Lapachol with *m*CPBA To a solution of lapachol (**10**) (30 mg) in dry CH_2Cl_2 (2 ml) was added a solution of *m*CPBA (30 mg) in CH_2Cl_2 (1 ml). After 10 min, the reaction mixture was treated with Al_2O_3 (10 mg) for 5 min. The mixture was then filtered through a short column of Al_2O_3, and eluted with MeOH. On evaporation, the combined eluates gave a crude orange oil. This was subjected to preparative TLC with iso-Pr_2O–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-A[12)] and dihydrofuran **11** to hydroxyiso-β-lapachone[12)] by comparison of the ^{1}H-NMR, UV, and IR spectra.

Dihydrofuran **11**: Red oil. ^{1}H-NMR (400 MHz, $CDCl_3$) 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′-CH$_3$), 1.29 (3H, s, 3′-CH$_3$); ^{13}C-NMR (100 MHz, CDCl$_3$) 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′-CH$_3$), 24.41 (3′-CH$_3$). 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′-CH$_3$; C-3′→3′-CH$_3$; 3′-CH$_3$→H-2′.

Dihydropyran **12**: Red oil. ^{1}H-NMR (400 MHz, CDCl$_3$) 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′-CH$_3$), 1.45 (3H, s, 3′-CH$_3$); ^{13}C-NMR (100 MHz, CDCl$_3$) 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′-CH$_3$), 25.00 (C-1′), 21.99 (3′-CH$_3$).

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 CHCl$_3$–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 C$_{12}$H$_6$O$_3$: 198.0317. Found: 198.0323. ^{1}H-NMR (400 MHz, CDCl$_3$) 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′); ^{13}C-NMR (100 MHz, CDCl$_3$) 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 C$_{15}$H$_{12}$O$_4$: 256.0734. Found: 256.0725. ^{1}H-NMR (400 MHz, CDCl$_3$) 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); ^{13}C-NMR (100 MHz, CDCl$_3$) 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′-CH$_3$×2).

Avicenol-A (**4**): Colorless oil. $[\alpha]_D$ +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 C$_{17}$H$_{20}$O$_5$: 304.1310. Found: 304.1310. NOE: Irradiation of 1-OCH$_3$ (δ 4.03) gave a 3% NOE at H-8 (δ 8.04); irradiation of 4-OCH$_3$ (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-OCH$_3$; C-2→H-1′; C-4→4-OCH$_3$; C-4a→H-6; C-5→H-7; C-7→H-5; C-8→H-6; C-8a→H-7; C-2′→3′-CH$_3$; C-3′→3′-CH$_3$.

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 C$_{14}$H$_{12}$O$_3$: 228.0786. Found: 228.0811. NOE: Irradiation of 1-OCH$_3$ (δ 4.27) gave a 2% NOE at H-8 (δ 8.27); irradiation of 4-OCH$_3$ (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-OCH$_3$; C-2→H-2′; C-3→H-1′, H-2′; C-4→H-5, H-1′, 4-OCH$_3$; 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. $[\alpha]_D$ +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 C$_{17}$H$_{20}$O$_4$: 288.1360. Found: 288.1355. NOE: Irradiation of 1-OCH$_3$ (δ 3.96) gave a 2% NOE at H-8 (δ 8.00); irradiation of 4-OCH$_3$ (δ 4.01) gave a 2% NOE at H-5 (δ 8.02). HMBC C–H correlations: C-1→H-8, 1-OCH$_3$; C-2→H-1′; C-3→H-1′; C-4→H-5, 4-OCH$_3$; 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′-CH$_3$; C-3′→H-1′, 3′-CH$_3$.

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References and Notes

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