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TWO NEW ISOMERIC LIGNANS FROM *Eusideroxylon zwageri*

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Two new lignans were isolated with two other known compounds, eusiderin A and eusiderin I, from Eusideroxylon zwageri *(billian). The two new lignans have isomeric structure. The structures of the new lignans were determined to be (2*R*,3*R*,4*S*)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy (3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin and (2*R*,3*S*,4*S*)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy(3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin.*

Key words: *Eusideroxylon zwageri*, Lauraceae, durability, lignan, eusiderin.

Eusideroxylon zwageri (Indonesian name: belian), which belongs to Lauraceae, is a durable wood distributed in Indonesia, Malaysia, Philippines, etc. The yields of *n*-hexane, ether, acetone, and methanol extracts were 1.2, 0.2, 6.8, and 3.3%, respectively [1]. Matsuoka reported that billian wood has high durability, being resistant to decay by wood rotting fungi [2]. Several eusiderin derivatives were isolated from the woods of Lauraceae [3], and eusiderin I was found in billian wood [1].

In this paper, we report the isolation of four lignans containing two new lignans having isomeric structure from the wood of *Eusideroxylon zwageri*.

The two isolated compounds eusiderin A (**1**) and eusiderin I (**2**), were identified in a comparison using FD-MS, EI-MS, ^{1}H, and ^{13}C NMR spectral data in the literature [3].

Compound **3** exhibited a molecular ion peak at *m/z* 462 in the FD-MS spectrum and was assigned the formula $C_{25}H_{34}O_8$ by HR-MS. In the EI-MS spectrum of compound **3**, the ions of *m/z* (%): 462 (66), 416 (18), 376 (100), and 348 (87) were $[M]^+$, $[M–EtOH]^+$, $[M–(EtOH+C_3H_4)]^+$, and $[M–(EtOH+C_5H_8)]^+$, respectively, which were formed by deethoxylation and successive cleavages of C_3H_4 and C_5H_8 from the molecular ion (*m/z* 462).

The ^{1}H NMR spectrum (δ, ppm, J/Hz) of compound **3** revealed the presence of two methyl groups (δ 0.73, d, J = 6.89 and δ 0.83, d, J = 7.39), two methine groups (δ 2.44, m and δ 2.23, m), a methine group bearing one hydroxyl group (δ 4.57, d, J = 8.61), one ethoxyl group (δ 3.52, q, CH_2 and δ 1.28, t, CH_3) and three aromatic protons (δ 6.39, d, J = 1.48; δ 6.50, d, J = 1.48; δ 7.06, s), one hydroxyl group (δ 4.75, s) at the benzene ring, and five methoxyl groups (δ 3.63, 3.85, 3.86, 3.90, and 3.92). These data suggested the possibility that compound **3** was a tetralin-type compound bearing five methoxyl groups, two benzene rings, one ethoxyl group, and two hydroxyl groups.

The ^{13}C NMR and distortionless enhancement by polarization transfer (DEPT) spectra of compound **3** showed signals of carbon of one secondary alcohol at δ 83.4, ethoxyl group at δ 63.2 and δ 15.3, five singlets of methoxyl groups at δ 55.8, 56.3, 56.3, 60.8, and 61.1, two methine carbons at δ 43.5 and 43.9, two methyl carbons at δ 11.2 and 11.5, and two chemical shifts of two benzene rings at δ 106.2 to δ 153.0.

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TABLE 1. ^{1}H and ^{13}C NMR Spectral Data of Compound **3** and **4** ($CDCl_3$, J/Hz)

C atom	δ_H		δ_C	
	3	**4**	**3**	**4**
1	4.57 (d, J = 8.61)	4.62 (d, J = 4.68)	83.4	83.8
2	2.44 (m)	2.37 (m)	43.5	40.0
3	2.23 (m)	2.03 (m)	43.9	43.5
4			127.3	127.4
5	4.75 (s)	5.12 (d, J = 4.92)	109.7	106.2
6			153.0	152.9
7			141.2	141.2
8	7.06 (s)	6.79 (s)	106.2	104.7
9			129.2	128.2
10			136.3	137.4
11	0.73 (d, J = 6.89)	0.70 (d, J = 7.38)	11.5	14.8
12	0.83 (d, J = 7.39)	0.79 (d, J = 7.39)	11.2	8.9
1′			133.6	133.7
2′	6.50 (d, J = 1.47)	6.50 (d, J = 1.72)	108.1	108.0
3′			146.6	146.7
4′			150.7	151.2
5′			146.4	146.7
6′	6.39 (d, J = 1.48)	6.43 (d, J = 1.72)	106.6	106.6
6-OMe	3.92 (s)	3.90 (s)	55.8	61.2
7-OMe	3.90 (s)	3.89 (s)	60.8	60.8
3′-OMe	3.85 (s)	3.86 (s)	56.3	56.3
4′-OMe	3.63 (s)	3.64 (s)	61.1	62.3
5′-OMe	3.86 (s)	3.87 (s)	56.3	56.3
4-OEt(CH_2)	3.52 (q)	3.40 (q)	63.2	62.9
4-OEt(CH_3)	1.28 (t)	1.13 (t)	15.3	15.3

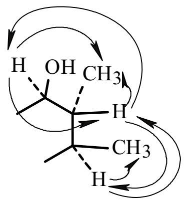
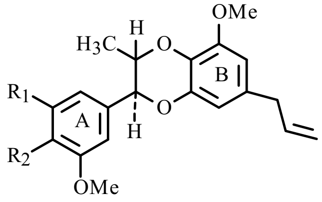


Fig.1. The partial structure of compound **3** in ^{1}H–^{1}H COSY.

In the two-dimensional homonuclear chemical shift correlated spectrum (^{1}H–^{1}H COSY) of compound **3**, the correlation of the ethoxyl group (δ 3.52, q, CH_2, and δ 1.28, t, CH_3) was observed. A correlation between the methine proton bearing a hydroxyl group (δ 4.57, d, J = 8.61, H-1) and a methine proton (δ 2.44, m, H-2) was observed. Also, a correlation between the methine proton bearing a hydroxyl group (δ 4.57, d, J = 8.61, H-1) and a methyl group (δ 0.73, d, J = 6.89, H-11) was observed. A correlation between the methine proton (δ 2.44, m, H-2) and the methine proton (δ 2.23, m, H-3) was observed, and also a correlation between the methine proton (δ 2.44, m, H-2) and the methyl group (δ 0.73, d, J = 6.89, H-11), and a correlation between the methine proton (δ 2.23, m, H-3) and the methyl group (δ 0.83, d, J = 7.39, H-12). The observed coupling constants of the H-1 and H-2 signals (J = 8.61) confirm the *trans* stereochemistry with the hydroxyl between two methine protons and two methyl protons (J = 6.89 and J = 7.39), suggesting that the partial structure of compound **3** formed the *trans* stereochemistry with hydroxyl, the methyl groups being all pseudo-equatorial, as shown in Fig. 1 [4–7].

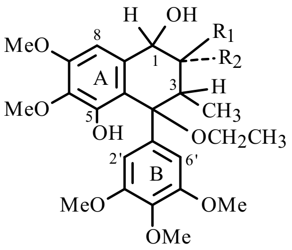
TABLE 2. The Correlations of Partial Structure of Compound **3** in HMBC

Compound **3**		Compound **3**	
H-1	C-5, C-8, C-9, C-11	H-12	C-5
H-2	C-10, C-11	Ring B	
H-8	C-6, C-7, C-9	H-2′, H-6′	C-1′, C-2′, C-3′, C-5′, C-6′



1, 2

1: $R_1 = R_2 = OMe$
2: $R_1 = R_2 = OCH_2O$



3, 4

3: $R_1 = CH_3, R_2 = H$
4: $R_1 = H, R_2 = CH_3$

In the heteronuclear multiple bond coherence (HMBC) and heteronuclear multiple quantum coherence (HQMC) spectra of compound **3**, the methine proton (δ 4.57, d) bearing one hydroxyl group was observed to correlate with three carbons at δ 129.2, 109.7, 106.2 in benzene ring A and one methyl group at δ 11.5, and the methine proton at δ 2.44 (m) was observed to correlate with δ 136.3 and one methyl group at δ 11.2. The methine proton at 2.23 (m) was observed to correlate with δ 109.7 and δ 11.2, and the methyl group at δ 11.2 with δ 109.7. The methine proton (7.06, s) of ring A was observed to correlate with δ 141.2, 129.2 and 153.0. The partial correlations of compound **3** are shown in Fig. 1. In ring B correlations were observed between methine protons at δ 6.50 and 6.39 and carbons at δ 108.1, 106.7, 133.6, 146.6, and 146.4 as shown in Table 2.

On the basis of the above-described data, compound **3** was concluded to be (2*R*,3*R*,4*S*)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy(3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin.

Compound **4** exhibited a molecular ion peak at *m/z* 462 in the FD-MS spectrum, and the molecular formula was determined to be $C_{25}H_{34}O_8$ using EI-HR-MS. A comparison of the ^{1}H and ^{13}C NMR spectral data of compounds **3** and **4** shows that compound **4** is an isomer of compound **3** (Table 1). In the EI-MS spectrum of compound **4**, the ions of *m/z* (%): 462 (100), 416 (26), 376 (80), and 348 (99.9) were $[M]^+$, $[M\text{-}EtOH]^+$, $[M\text{-}(EtOH+C_3H_4)]^+$, and $[M\text{-}(EtOH+C_5H_8)]^+$, respectively, which were formed by deethoxylation and successive cleavages from the molecular ion (*m/z* 462).

In the ^{1}H NMR spectra of compounds **3** and **4**, the differences in coupling constants at H-1 of compounds **3** (J = 8.61) and **4** (J = 4.68) and at H-11 of **3** (J = 6.89) and **4** (J = 7.39) suggested that the position of the methine proton and methyl group (C-11) at C-2 was changed. This shows that the methine protons at C-2 and C-3 of **4** appeared at higher field. Also, the ^{13}C NMR spectra show that the chemical shifts at C-2 and C-12 appeared at higher field than those of compound **3**, and the chemical shift at C-11 appeared at lower field than those of compound **3**. The differences between the methine proton at H-8 and the hydroxyl group at C-5 were due to the rotation of the ethoxyl group and ring B and the change of position of the proton and methyl group (C-11) at C-2.

On the basis of the above data, compound **4** was concluded to be an isomer of compound **3**, (2*R*,3*S*,4*S*)-2,3-dimethyl-6,7-dimethoxy-4-ethoxy(3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin.

EXPERIMENTAL

Analysis. The NMR spectra were measured on a Brucker AMX-500 (^{1}H : 500 MHz; ^{13}C : 125 MHz) using deuterated chloroform ($CDCl_3$) as a solvent and tetramethylsilane (TMS) as an internal standard. Two-dimensional (2D) NMR was performed by ^1H–^1H COSY, HMQC, and HMBC. FD-MS was obtained by a JEOL JMS-SX102A mass spectrometer. EI-MS and EI-HR-MS were obtained by a JEOL JMS-AX500 mass spectrometer. Thin-layer chromatography (TLC) was performed on a Wako gel B-10 and silica gel 70 Plate-Wako using the solvent SGIII (toluene–formic acid–ethyl formate, 5:1:4, v/v).

Extraction and Isolation. The sample (500 g) was obtained from state of Sarawak, Malaysia in 1996. Powdered sample (400 g) was extracted using 60% ethanol, 3 h, and reflux. The EtOH extracts were concentrated under reduced pressure. The concentrated extracts (58.16 g) were successively separated on a silica gel column chromatograph (CC, Wako gel C-200) with *n*-hexane, ether and ethyl acetate, successively. From *n*-hexane extracts (0.54 g), crude eusiderin A and eusiderin I were obtained by using a silica gel column chromatograph (Wako gel C-200), solvents, HEA (*n*-hexane–ethyl acetate, 10:1, v/v). Finally, eusiderin A (66.5 mg) and eusiderin I (6 mg) were isolated. Compounds **3** and **4** were isolated from the ether extracts (7.97 g) and separated by silica gel column chromatograph using HEA (4:1, v/v) monitored by TLC with SGIII. The yields of the isolated compound **3** and **4** were 14 mg and 10 mg, respectively. Acetylation of the isolated compounds was conducted with acetic anhydride and pyridine at 55°C for 24 h.

(2*R*,3*R*,4*S*)-2,3-Dimethyl-6,7-dimethoxy-4-ethoxy(3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin (3). FD-MS *m/z* 462; EI-HR-MS, $C_{25}H_{34}O_8$; EI-MS *m/z* (%): 462 (66) $[M]^+$, 416 (18) $[M–EtOH]^+$, 376 (100) $[M–(EtOH+C_3H_4)]^+$, 348 (87) $[M–(EtOH+C_5H_8)]^+$, 331 (35) $[M–(EtOH+C_5H_8+H_2O)]^+$. For ^1H and ^{13}C NMR, see Table 1.

(2*R*,3*S*,4*S*)-2,3-Dimethyl-6,7-dimethoxy-4-ethoxy(3′,4′,5′-trimethoxybenzene)-1,5-dihydroxytetralin (4). FD-MS *m/z* 462; EI-HR-MS, $C_{25}H_{34}O_8$; EI-MS *m/z* (%): 462 (100) $[M]^+$, 416 (26) $[M–EtOH]^+$, 376 (80) $[M–(EtOH+C_3H_4)]^+$, 348 (99) $[M–(EtOH+C_5H_8)]^+$, 331 (52) $[M–(EtOH+C_5H_8+H_2O)]^+$. For ^1H and ^{13}C NMR, see Table 1.

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