HETEROCYCLES, Vol. 55, No. 4, 2001, pp. 729 - 740, Received, 29th January, 2001

SIX NEW HETEROCYCLIC STILBENE OLIGOMERS FROM STEM BARK OF *SHOREA HEMSLEYANA*

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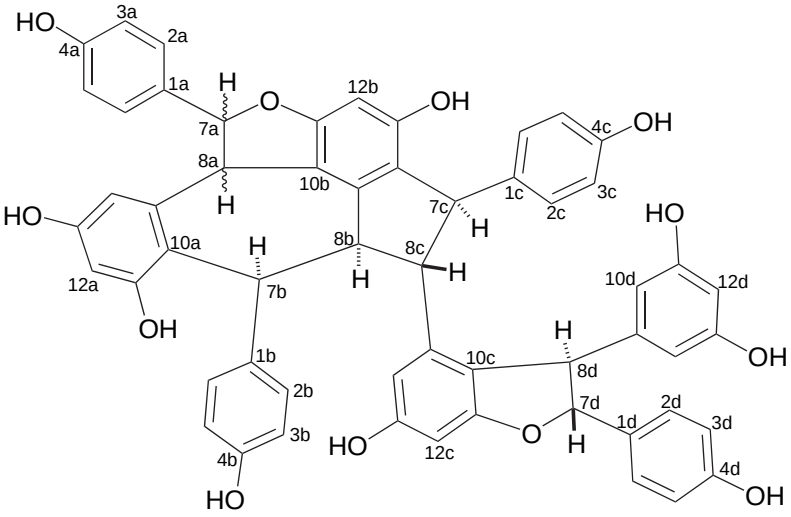
Abstract - From the stem bark of *Shorea hemsleyana* (Dipterocarpaceae), four new stilbenoids with one or two dihydrofuran ring(s) [hemsleyanols C, D, hemsleyanosides E, F, and (-)-ampelopsin H] and a new stilbenoid with a carbonyl group (hemsleyanol E) were isolated. The structures including the relative configuration were elucidated on the basis of spectroscopic and chemical evidence.

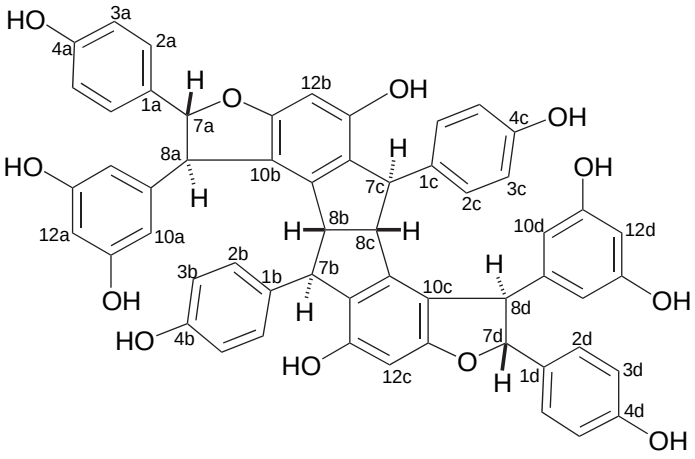
Stilbenoids are known to being abundantly distributed in Dipterocarpaceaeous plants as a variety of resveratrol (3,5,4'-trihydroxystilbene) oligomers after the homogeneous oligomeriztion.[1, 2] Some of their derivatives displayed the biological properties such as chemopreventive activity of cancer, [3] anti-inflammatory activity, [4] inhibition of histamine release[5] and gastric ATPase[6]. Stilbenoids are, therefore, useful resource of lead compounds for drug development. In continuation of our phytochemical studies on Dipterocarpaceous plant, the structures of stilbenoids in *Hopea*,[7] *Vatica*, [8, 9] and *Shorea*[10, 11] were characterized. The distinctive cytotoxicty found in some stilbenoids was discussed. [12]

In the preceding paper, the structures of stilbene oligomers, hemsleyanols A-C[10] and *C*-glycosyl stilbene oligomers, hemsleyanosides A-D [11] composed of some resveratrol units in the bark of *Shorea hemsleyana*, were revealed. Further investigation of an acetone extract of the bark resulted in isolation of six new stilbenoids named hemsleyanols C (**1**), D (**2**) and E (**4**) and hemsleyanosides E (**5**) and F (**6**) together with (-)-ampelopsin H (**3**). This paper deals with their structure elucidation including the relative configuration.

Hemsleyanol C (**1**), a brown amorphous powder, showed a positive reaction in the Gibbs reagent. The absorption band (285 nm) in the UV spectra showed the presence of aromatic rings. The $[M-H]^-$ ion



1 : H-7a = β, H-8a = α
2 : H-7a = α, H-8a = β



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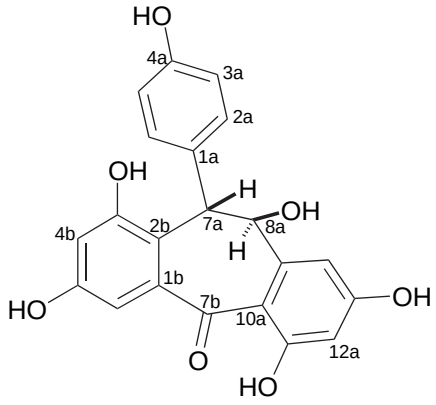

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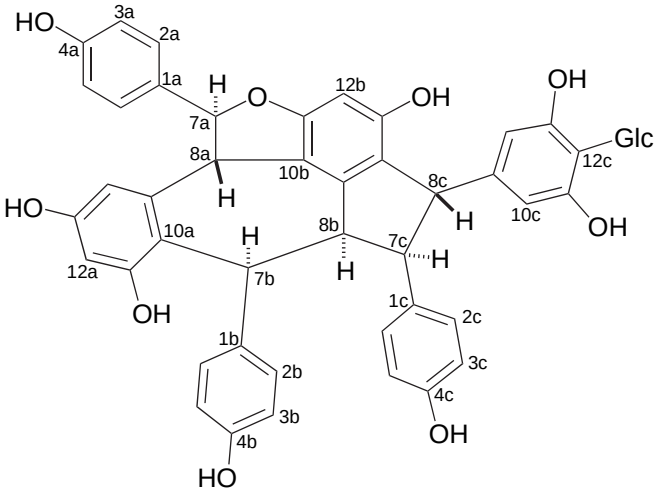

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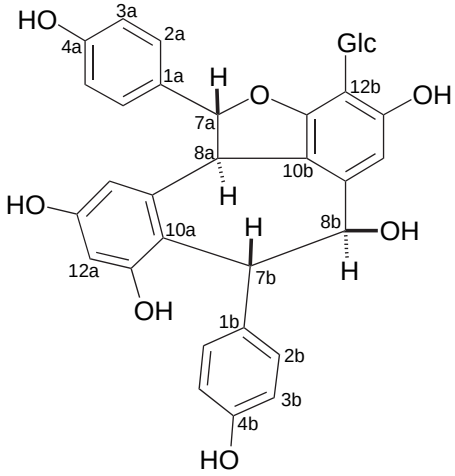

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Figure 1

peak at *m/z* 905.2607 in the high-resolution (HR) FABMS in negative ion mode corresponds to the molecular formula of $C_{56}H_{42}O_{12}$. The ^{1}H NMR spectrum (Table 1) showed the signals assignable to four 4-hydroxyphenyl groups [δ 7.51, 6.94 (2H each, d, *J*= 8.3 Hz, H-2a, 6a and H-3a, 5a); 6.05, 6.36 (2H each, d, *J*= 8.3 Hz, H-2b, 6b and H-3b, 5b); δ 5.89, 6.15 (2H each, d, *J*= 8.3 Hz, H-2c, 6c and H-3c, 5c); δ 7.02, 6.82 (2H each, d, *J*= 8.3 Hz, H-2d, 6d and H-3d, 5d)]. The presence of a 3,5-dihydroxyphenyl group [δ 5.84 (2H, d, *J*= 2.0 Hz, H-10d and 14d), 6.19 (1H, t, *J*= 2.0 Hz, H-12d)], two sets of *meta*-coupled aromatic protons on 1,2,3,5-tetrasubstituted benzene rings [δ 6.15 (1H, d, *J*= 2.0 Hz, H-12a), 5.98 (1H, br d, *J*= 2.0 Hz, H-14a); 6.25, 6.43 (1H each, d, *J*= 2.0 Hz, H-12c and 14c)] was also exhibited. The spectrum further showed the signals due to an aromatic proton on a pentasubstituted benzene ring [δ 5.95 (1H, s, H-12b)], a sequence of four aliphatic methine protons coupled successively in the ^{1}H-^{1}H COSY spectrum (Figure 1) in this order [δ 4.35 (1H, d, *J*= 3.2 Hz, H-7b), 4.11 (1H, dd, *J*= 5.3, 3.2 Hz, H-8b), 3.13 (1H, t, *J*= 5.3 Hz, H-8c), 3.82 (1H, d, *J*= 5.3 Hz, H-7c)] and two sets of mutually coupled aliphatic protons [δ 5.63, 5.29 (1H each, d, *J*= 10.0 Hz, H-7a and 8a); δ 5.03, 3.58 (1H each, d, *J*= 2.7 Hz, H-7d and 8d)] in addition to ten phenolic hydroxyl groups (δ 6.46 – 8.57). These results suggested that **1** is a stilbene tetramer composed of four resveratrol units [resveratrol A (ring A_1-7a-8a-ring A_2) – resveratrol D (ring D_1-7d-8d-ring D_2)]. Analysis of the HMQC and HMBC spectrum enabled the complete assignment of all protonated carbons and quarternary carbons corresponding to respective resveratrol units (A-D) as shown in Table 1. In the HMBC spectrum (Figure 2), distinct cross peaks were observed between the methine protons and the aromatic carbons as follows; H-7a/C-2a(6a), H-8a/C-14a, H-7b/C-2b(6b), H-8b/C-14b, H-7c/C-2c(6c), H-8c/C-10c, H-7d/C-2d(6d) and H-8d/C-10d(14d), which indicated the respective connections of C-1a/C-7a, C-8a/C-9a, C-1b/C-7b, C-8b/C-9b, C-1c/C-7c, C-8c/C-9c, C-1d/C-7d and C-8d/C-9d. The spectrum also displayed significant correlations such as H-8a/C-10b; H-8a/C-11b; H-7d/C-11c; H-8d/C-10c; H-8d/C-11c, which indicated that the resveratrols A and

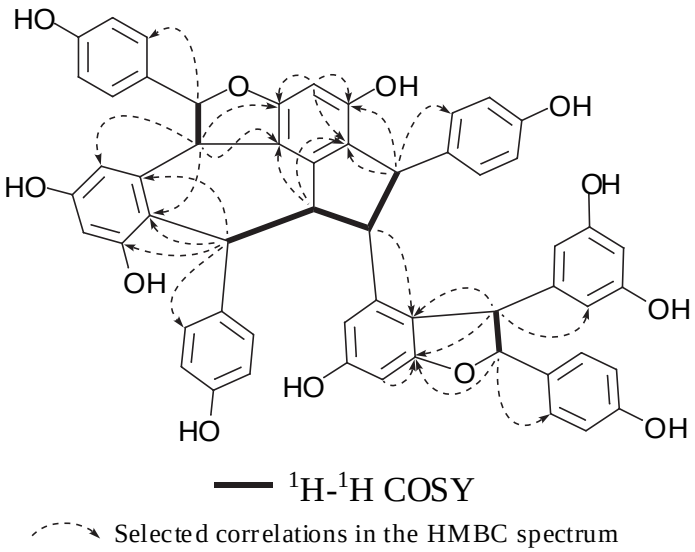

Figure 2 Connection of partial structures of **1**

Table 1 ^{1}H and ^{13}C NMR Spectral Data of **1** and **2**

No.	**1***		**2****	
	δH	δC	δH	δC
1a		133.1		130.9
2a. 6a	7.51 (d, *J* = 8.3)	131.0	7.22 (d, *J* = 8.5)	130.3
3a, 5a	6.94 (d, *J* = 8.3)	116.5	6.78 (d, *J* = 8.5)	116.2
4a (OH)	8.57 (br s)	158.7		158.7 [a]
7a	5.63 (d, *J* = 10.0)	94.7	5.77 (d, *J* = 11.5)	90.6
8a	5.29 (d, *J* = 10.0)	51.8	4.41 (d, *J* = 11.5)	48.9
9a		138.9		141.9
10a		123.0		125.0
11a (OH)	7.72 (br s)	157.8		155.9
12a	6.15 (d, *J* = 2.0)	102.0	6.36 (d, *J* = 2.0)	101.8
13a (OH)	7.82 (br s)	156.3		156.9
14a	5.98 (br d, *J* = 2.0)	107.9	6.12 (d, *J* = 2.0)	105.9 [c]
1b		133.4		133.6
2b, 6b	6.05 (d, *J* = 8.3)	133.5	6.94 (d, *J* = 8.3)	130.8
3b, 5b	6.36 (d, *J* = 8.3)	114.8	6.48 (d, *J* = 8.3)	116.3 [d]
4b (OH)	7.78 (br s)	156.0		158.1 [a]
7b	4.35 (d, *J* = 3.2)	46.2	5.29 (d, *J* = 3.4)	37.5
8b	4.11 (dd, *J* = 5.3, 3.2)	55.4	3.38 (br d, *J* = 11.2)	55.5 [b]
9b		144.3		143.1
10b		115.2		116.3
11b		160.0		159.5
12b	5.95 (s)	96.2	6.01 (s)	96.8
13b (OH)	6.46 (br s)	154.7		154.8
14b		122.8		121.6
1c		136.3		132.6
2c, 6c	5.89 (d, *J* = 8.3)	129.5	6.72 (d, *J* = 8.3)	129.4
3c, 5c	6.15 (d, *J* = 8.3)	115.5	6.52 (d, *J* = 8.3)	115.7
4c (OH)	7.81 (br s)	156.1		156.8 [a]
7c	3.82 (d, *J* = 5.3)	61.2	4.55 (d, *J* = 11.7)	54.1
8c	3.13 (t, *J* = 5.3)	56.6	3.89 (dd, *J* = 11.7, 11.2)	57.4
9c		147.5		141.1
10c		119.1		116.3 [d]
11c		162.8		162.2
12c	6.25 (d, *J* = 2.0)	95.4	6.23 (d, *J* = 2.0)	96.0
13c (OH)	8.21 (br s)	160.2		159.5
14c	6.43 (d, *J* = 2.0)	106.4	6.78 (d, *J* = 2.0)	105.9 [c]
1d		134.6		135.0
2d, 6d	7.02 (d, *J* = 8.3)	127.5	7.07 (d, *J* = 8.5)	128.1
3d, 5d	6.82 (d, *J* = 8.3)	116.0	6.82 (d, *J* = 8.5)	116.2
4d (OH)	8.36 (br s)	158.0		155.8 [a]
7d	5.03 (d, *J* = 2.7)	93.9	4.92 (br s)	94.5
8d	3.58 (d, *J* = 2.7)	56.2	3.50 (br s)	55.6 [b]
9d		148.3		148.1
10d, 14d	5.84 (d, *J* = 2.0)	106.6	5.34 (d, *J* = 2.0)	106.5
11d, 13d (OH)	8.10 (br s)	160.1		159.1
12d	6.19 (t, *J* = 2.0)	102.3	6.07 (t, *J* = 2.0)	102.3
OH			7.59-8.54 (br s, 9 x OH) 5.89 (br s, 1 x OH)	

Measured in (CD3)2CO.* 500 MHz (^{1}H) and 125 MHz (^{13}C). ** 400 MHz (^{1}H) and 100 MHz (^{13}C).
a, b : interchangeable. c, d : overlapping.

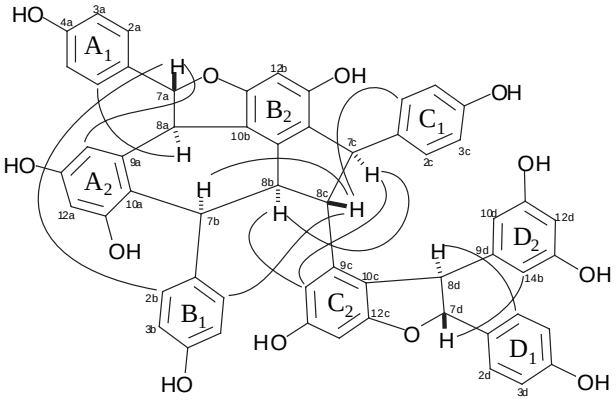

Figure 3 NOEs in the NOESY spectrum of **1**

D form dihydrofuran rings with rings B_2 and C_2, respectively. As the proton signal at δ 4.35 (H-7b) had cross peaks with C-9a, C-10a and C-11a, the linkage between C-10a and C-7b was confirmed. The linkage between C-7c and C-14b was deduced by the correlation such as H-7c/C-14b. Finally, the planar structure of **1** was determined as shown in Figure 2. For confirmation of the relative stereochemistry, NOESY was examined (Figure 3). In this experiment, **1** showed NOEs between H-7a/H-14a, H-8a/H-2a(6a), H-7d/H-10d(14d) and H-8d/H-2d(6d), suggesting that the orientation of the both dihydrofuran rings are *trans*. The aromatic protons on ring B_1 [H-2b(6b)] showed NOE interactions with the methine hydrogen signals (H-7a and H-8c), which can be observed only when H-7a and H-8c are situated in *cis* toward ring B_1. The correlations between H-14c/H-8b and H-14c/H-7c supported that the configuration of H-8b and H-7c are α. On the basis of these results, the relative structure of hemsleyanol C was characterized as shown in Figure 3. The relative configuration mentioned above [7b(α), 8b(α), 7c(α) and 8c(β)] can well explain the anisotropic effect of rings B_2, B_1 and C_1, which causes the upper field shift of H-2b(6b), H-2c(6c) and OH-13b, respectively.

Hemsleyanol D (**2**), a brown amorphous powder, reacted positive to the Gibbs reagent and had the molecular formula of $C_{56}H_{42}O_{12}$ supported by the HR-FABMS ($[M-H]^-$: m/z 905.2612). Analysis of the ^{1}H-^{1}H COSY, ^{1}H-^{1}H long-range COSY, ^{13}C-^{1}H COSY and COLOC spectrum (Table 1 and Figure 4) indicated that **2** had a same planar structure as **1**. In the NOESY experiment (Figure 5), the results of NOE which are similar to those of **1** [H-7a/H-14a, H-8a/H-2a(6a), H-7d/H-10d(14d), H-8d/H-2d(6d), H-8c/H-2b(6b), H-14c/H-8b and H-14c/H-7c] were obtained, which suggested that the orientation of the protons on two dihydrofuran rings is *trans* and the sequence of four methine protons (H-7b, H-8b, H-8c and H-7c) has an identical orientation with that of **1**. The main difference from **1** was NOE between H-2b(6b) and H-8a, which indicated that the orientation of two methine protons on the resveratrol A (H-7a and H-8a) is located in opposite to that of **1**. Therefore, hemsleyanol E was elucidated to be a stereoisomer of hemsleyanol D due to C-7a and C-8a.

Compound (**3**), a yellow amorphous powder, was found to have a same relative structure as (+)-ampelopsin H isolated from *Ampelopsis brevipedunculata*.[13] The optical rotation of **3** showed -76°, the

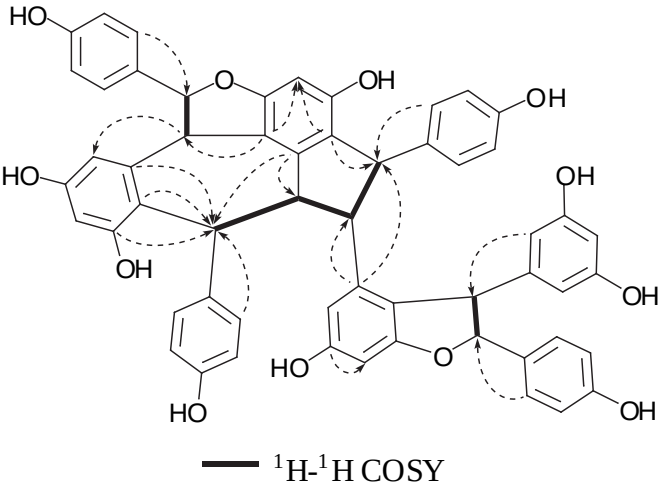

Figure 4 Correlations in the ^{1}H-^{1}H COSY and COLOC spectrum of **2**

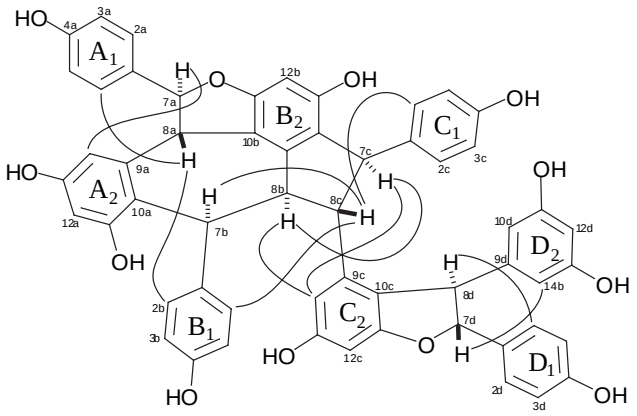

Figure 5 NOEs in the NOESY spectrum of **2**

value of which was opposite to that of (+)-ampelopsin H. Therefore, **3** is an enantiomer of (+)-amplelopsin H. Detail NMR spectral data assigned by the aid of 2D-NMR are presented in experimental section. Hemsleyanol E (**4**), obtained as a yellow amorphous powder, gave an $[M-H]^-$ ion at *m/z* 379.0825 in the HR-FABMS corresponding to the molecular formula of $C_{21}H_{16}O_7$. The ^{1}H NMR spectral data (see experimental section) showed the presence of a set of *ortho*-coupled aromatic protons assignable to a 4-hydroxyphenyl group [δ 6.80, 6.56 (2H each, d, *J*= 8.6 Hz, H-2a, 6a and H-3a, 5a)] and two sets of *meta*-coupled aromatic protons on a 1,2,3,5-tetrasubstituted benzene rings [δ 6.18, 6.04 (1H each, d, *J*= 2.0 Hz, H-12a and 14a); 6.69, 7.44 (1H each, d, *J*= 2.0 Hz, H-4b and 6b)]. An alcoholic hydroxyl group [δ 4.53 (1H, br s, OH-8a)] and five phenolic hydroxyl groups [δ 8.50 (3H, br s), 8.02 (1H, br s) and 13.34 (1H, s, chelated)] were also exhibited in the spectrum. Two mutually coupled benzylic methine protons were furthermore observed at δ 6.24 (1H, d, *J*= 6.2 Hz) and 5.14 (1H, br d, *J*= 6.2 Hz). In the ^{13}C NMR

spectrum, signals due to 21 carbon atoms were observed and one of them at δ 196.4 was assigned to a carbonyl group. These spectral data resembled those of parviflorol isolated from bark of *Hopea parviflora* in our preceding study,[7] the molecule of which consists of a resveratrol and a 3,5-dihydroxy benzoyl moiety. The correlation between the methine proton (H-7a) and H-2a(6a) on ring A_1 in the ^{1}H-^{1}H long-range COSY spectrum supported that the planer structure of **4** was identical with that of parviflorol. All carbons were assigned by ^{13}C-^{1}H COSY spectrum and/or by comparison with the spectral data of parviflorol. The relative configuration of C-8a [H-8a(α), OH-8a(β)] was deduced by an NOE between H-2a(6a) and H-8a in the DIFNOE experiment, where both functions are situated in opposite to those of paviflorol [H-8a(β), OH-8a(α)]. Therefore the relative stereostructure of **4** was confirmed as shown in Figure 1.

Hemsleyanoside E (**5**), a brown amorphous powder, showed a positive reaction in the Gibbs reagent and has the molecular formula of $C_{48}H_{42}O_{14}$, supported by the HR-FABMS ([M-H]$^-$: *m/z* 841.2482). The ^{1}H and ^{13}C NMR spectrum (Table 2) showed a presence of a *C*-glucopyranosyl unit [δ_H 4.83 (1H, d, *J* = 9.2 Hz, anomeric proton), δ_C 82.4, 79.9, 76.6, 73.3, 71.4 and 62.5]. These results indicated that **5** is a resveratrol trimer with a *C*-glucopyranosyl moiety. The ^{1}H NMR spectrum showed the presence of three sets of *ortho*-coupled aromatic protons assignable to three 4-hydroxyphenyl groups [δ 7.11, 6.69 (2H each, d, *J*= 8.6 Hz, H-2a, 6a and H-3a,5a); δ 6.48, 6.12 (2H each, d, *J*= 8.6 Hz, H-2b, 6b and H-3b, 5b); δ 6.94, 6.38 (2H each, d, *J*= 8.4 Hz, H-2c, 6c and H-3c, 5c)] and a set of *meta*-coupled aromatic protons on a 1,2,3,5-tetrasubstituted benzene ring [δ 6.25 (1H, d, *J*= 2.2 Hz, H-12a) and 5.92 (1H, br s, H-14a)]. The spectrum also exhibited an aromatic proton on a pentasubstituted benzene ring [δ 6.20 (1H, s, H-12b)], two aromatic protons on a 1,3,4,5-tetrasubstituted benzene ring [δ 6.05 (2H, br s, H-10c and 14c)] and a set of mutually coupled aliphatic protons [δ 5.68 (1H, d, *J*= 11.5 Hz, H-7a) and 4.35 (1H, br d, *J*= 11.5 Hz, H-8a)] in addition to a sequence of four aliphatic methine protons connected successively in this order [δ 5.42 (1H, d *J*= 3.3 Hz, H-7b), 3.92 (1H, m, H-8b), 3.66 (1H, br d, *J*= 7.7 Hz, H-7c) and 4.73 (1H,

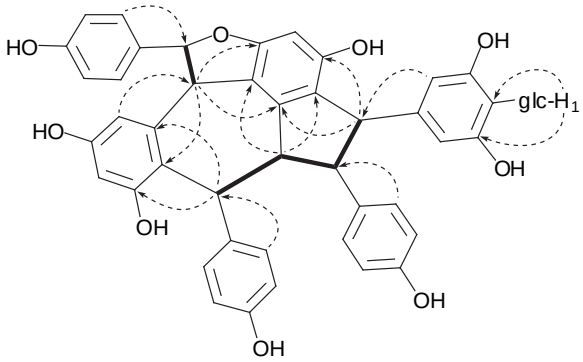

Figure 6 Connection of partial structures of **5**

Table 2 ^{1}H and ^{13}C NMR Spectral data of **5** and **6**

No.	**5**		**6**	
	δH	δC	δH	δC
1a		130.7 [a]		133.0
2a, 6a	7.11 (d, *J*= 8.6)	130.4	7.05 (d, *J*= 8.8)	130.3
3a, 5a	6.69 (d, *J*= 8.6)	116.2	6.69 (d, *J*= 8.8)	116.2
4a		158.9		157.5 [c]
7a	5.68 (d, *J*= 11.5)	91.5	5.77 (d, *J*= 11.4)	89.1
8a	4.35 (br d, *J*= 11.5)	48.7	4.06 (br d, *J*= 11.4)	50.1
9a		141.8		143.4
10a		126.8		118.9
11a		155.2		158.9 [c]
12a	6.25 (d, *J*= 2.2)	101.8	6.31 (d, *J*= 1.8)	101.6
13a		156.6		159.3 [c]
14a	5.92 (br s)	105.8	6.14 (br s)	108.0 [d]
1b		133.9		131.1
2b, 6b	6.48 (d, *J*= 8.6)	130.7 [a]	6.82 (d, *J*= 8.4)	129.0
3b, 5b	6.12 (d, *J*= 8.6)	114.2	6.57 (d, *J*= 8.4)	115.7
4b		154.5		157.9 [c]
7b	5.42 (d, *J*= 3.3)	39.7	5.37 (br s)	44.1
8b	3.92 (m)	49.0	5.38 (br s)	71.7 [b]
9b		144.6		139.5
10b		122.7		120.1
11b		160.2		159.4 [c]
12b	6.20 (s)	96.2		111.5
13b		155.0		156.3 [c]
14b		117.3	6.56 (s)	105.4 [d]
1c		135.4		
2c, 6c	6.94 (d, *J*= 8.4)	130.8		
3c, 5c	6.38 (d, *J*= 8.4)	115.5		
4c		156.5		
7c	3.66 (br d, *J*= 7.7)	61.0		
8c	4.73 (br s)	54.3		
9c		147.8		
10c, 14c	6.05 (br s)	107.7		
11c, 13c		158.0		
12c		110.0		
glc-1	4.83 (d, *J*= 9.2)	76.6	4.60 (d, *J*= 9.9)	76.5
glc-2	3.97 (dd, *J*= 9.2)	73.3	4.04 (t, *J*= 9.9)	72.8
glc-3	3.43 (dd, *J*= 9.2)	79.9	3.38 (dd, *J*= 9.9, 8.7)	80.0
glc-4	3.45 (dd, *J*= 9.2)	71.4	3.42 (m)	71.7 [b]
glc-5	3.35 (m)	82.4	3.33 (m)	82.4
glc-6	3.72 (dd, *J*= 12.1, 4.5)	62.5	3.69 (dd, *J*= 12.0, 4.6)	62.5
	3.82 (dd, *J*= 12.1, 2.3)		3.82 (dd, *J*= 12.0, 2.6)	62.9

Measured in CD3OD. 300 MHz (^{1}H) and 75 MHz (^{13}C). a, b : overlapping. c, d : interchangeable.

br s, H-8c)]. The ^{13}C-^{1}H COSY spectrum supplied complete assignment of all protonated carbons as shown in Table 2. In the HMBC spectrum (Figure 6), the correlations were observed between H-2a(6a)/C-7a, H-14a/C-8a, H-7b/C-11a, H-2b(6b)/C-7b, H-8b/C-14b, H-2c(6c)/C-7c, H-10c(14c)/C-8c, H-8c/C-13b and H-8a/C-11b, which supported the linkages of C-1a/C-7a, C-8a/C-9a, C-7b/C-10a, C-1b/C-7b, C-8b/C-9b, C-1c/C-7c, C-8c/C-9c, C-8c/C-14b and C-8a/C-10b, respectively. Although no long-range correlation between H-7a/C-11b was observed, the presence of a dihydrofuran ring in **5** could

be considered by the molecular formula. The planar structure of the aglycone moiety could then be depicted as shown in Figure 6. The position of the glucose moiety was confirmed to be at C-12c by correlation of H-glc-1/C-11c(13c) in the HMBC spectrum. The relative stereochemistry of **5** was characterized by analyzing the NOESY spectrum (Figure 7). In this study, **5** showed significant NOEs between H-7a/H-14a and H-8a/H-2a(6a), suggesting that the orientation of the dihydrofuran ring is *trans*. NOE interactions [H-2b(6b)/H-8a, H-10c(14c)/H-8b, H-10c(14c)/H-7c, H-2c(6c)/H-8c, H-7b/H-7c and H-2b(6b)/H-8c] indicated that the relative configuration of methine hydrogens at C-8a, C-7b, C-8b, C-7c and C-8c are *β, α, α, α* and *β,* respectively. The relative stereostructure of **5** then was determined as shown in Figure 7.

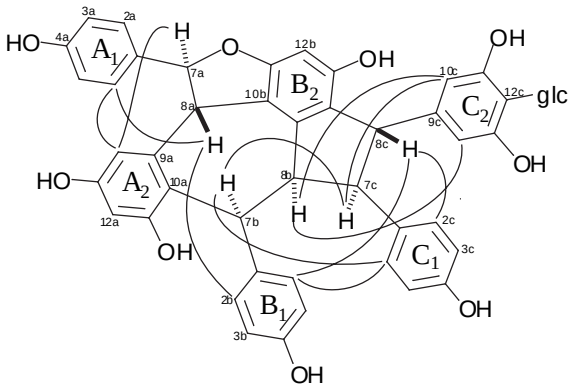

Figure 7 NOEs in the NOESY spectrum of **5**

Hemsleyanoside F (**6**) was obtained as a dark brown amorphous powder. An $[M-H]^-$ ion peak at *m/z* 631 in the FABMS is corresponding to the molecular formula of $C_{34}H_{32}O_{12}$. The ^1H and ^{13}C NMR spectral data (Table 2) showed similarity of signals to those of (-)-ampelopsin A[7, 14] except for the presence of a *C-β*-glucopyranosyl moiety [δ_H 4.60 (1H, d, J = 9.9 Hz, H-glc-1) and δ_C 82.4, 80.0, 76.5, 72.8, 71.7 and 62.9] and the absence of an aromatic proton due to H-12b. Therefore, the glucosyl moiety in **6** should be attached to C-12b. The structure of **6** was then concluded to be ampelopsin A 12b-*C-β*-glucopyranoside.

EXPERIMENTAL

General Method

The following instruments were used: FABMS spectra, JEOL JMS-DX-300 instrument; ^1H and ^{13}C NMR spectra, JEOL JNM A-500, EX-400 and LA-300 (TMS as internal standard); UV spectra, Shimadzu UV-2200 spectrophotometer (in methanol solution); optical rotations, JASCO P-1020 polarimeter (in methanol solution). The following adsorbents were used for purification: analytical TLC, Merck Kieselgel 60 F_{254} (0.25 mm); preparative TLC, Merck Kieselgel 60 F_{254} (0.5 mm); column chromatography, Merck Kieselgel 60, Pharmacia Fine Chemicals AB Sephadex LH-20 and Fuji Silysia Chemical Chromatorex; vacuum liquid chromatography (VLC), Merck Kieselgel 60.

Plant material

Stem bark of *Shorea hemsleyana* was collected in Indonesia in October, 1997.

Extraction and isolation

The dried and ground stem bark (1 kg) of *Shorea hemsleyana* was extracted successively with acetone (3 L x 24 h x 3), MeOH (3 L x 24 h x 3) and 70% MeOH (3 L x 24 h x 3) at rt. Concentrated extracts gave respective residues [47 g (acetone), 42 g (MeOH) and 26 g (70% MeOH)]. A part (40 g) of the acetone extract was subjected to chromatography on silica gel column eluted with a mixture of $CHCl_3$-MeOH increasing polarity to give 34 fractions (Fr. 1 - 34). The Fr. 22 [$CHCl_3$-MeOH (10 : 1), 55 mg] was further chromatographed by column on Sephadex LH 20 (acetone) and by PTLC [$CHCl_3$-MeOH = 10 : 1] to give **4** (2 mg). Compound (**3)** (5 mg) was obtained from the Fr. 23 [$CHCl_3$-MeOH (8 : 1), 122 mg] after VLC ($CHCl_3$-MeOH system), Sephadex LH-20 column (acetone-H_2O = 10 : 1) and PTLC (benzene-EtOAc-MeOH = 4 : 2 : 1). The Fr. 25 [$CHCl_3$-MeOH (8 : 1) fraction, 1.5 g] was further chromatographed by vacuum liquid chromatography (VLC) using $CHCl_3$-MeOH mixtures. The $CHCl_3$-MeOH (5 : 1) fraction afforded to **1** (6 mg) and **2** (30 mg) after purification by Sephadex LH 20 column (MeOH) and PTLC [$CHCl_3$-MeOH-H_2O-AcOH system]. The Fr. 31 [$CHCl_3$-MeOH (5 : 1), 2.2 g] was further subjected to chromatography on reversed-phase ODS column eluted with a mixture of H_2O-MeOH mixture (5% – 40% MeOH) to give 5 fractions. Compounds **5** (13 mg) and **6** (5 mg) were obtained in a pure form from the third fraction (30% MeOH, 560 mg) after purification by Sephadex LH 20 column [acetone-H_2O (20 : 1) and MeOH] and preparative TLC (EtOAc-$CHCl_3$-MeOH-H_2O = 20 : 10 : 11 : 5).

Hemsleyanol C (1) : A brown amorphous powder. Negative ion HR-FAB-MS: $[M-H]^-$ *m/z* 905.2607 (Calcd 905.2598 for $C_{56}H_{41}O_{12}$); Negative ion FABMS: $[M-H]^-$ *m/z* 905; UV λ max (MeOH) nm: 214, 285; $[\alpha]_D$ -30° (*c*= 0.1, MeOH); The ^1H and ^{13}C NMR spectral data are listed in Table 1.

Hemsleyanol D (2) : A brown amorphous powder. Negative ion HR-FAB-MS: $[M-H]^-$ *m/z* 905.2612 (Calcd 905.2598 for $C_{56}H_{41}O_{12}$); Negative ion FAB-MS: $[M-H]^-$ *m/z* 905; UV λ max (MeOH) nm: 216, 284; $[\alpha]_D$ +29° (*c*= 0.1, MeOH); The ^1H and ^{13}C NMR spectral data are shown in Table 1.

(-)-Ampelopsin H (3) : A yellow amorphous powder. Negative ion FAB-MS: $[M-H]^-$ *m/z* 905; UV λ max (MeOH) nm: 216, 285; $[\alpha]_D$ -76° (*c*= 0.06, MeOH); ^1H NMR [300 MHz, $(CD_3)_2CO$] δ: 3.47 (2H, s, H-8c, 8d), 4.57 (2H, s, H-7c,7d), 4.82 (2H, d, *J* = 7.7 Hz, H-8a, H-8d), 5.23 (2H, d, *J* = 7.7 Hz, H-7a, H-7d), 6.20 (2H, s, H-12b, 12c), 6.21 (4H, d, *J* = 2.2 Hz, H-10a, 14a, 10d, 14d), 6.25 (2H, t, *J* = 2.2 Hz, H-12a, 12d), 6.34 (4H, d, *J* = 8.8 Hz, H-2b, 6b, 2c, 6c), 6.42 (4H, d, *J* = 8.8 Hz, H-3b, 5b, 3c, 5c), 6.84 (4H, d, *J* = 8.6 Hz, H-2a, 6a, 2d, 6d), 7.21 (4H, d, *J* = 8.6 Hz, H-3a, 5a, 3d, 5d), 7.75 (2H, br s, OH-C-4b,4c), 7.88 (2H, br s, OH-C-13b, 13c), 8.11 (4H, br s, OH-C-11a, 13a, 11d, 13c), 8.41 (2H, br s, OH-C-4a, 4d); ^{13}C NMR [75 MHz, $(CD_3)_2CO$] δ: 49.4 (C-7c, 7d), 57.6 (C-8a, 8d), 59.4 (C-8c, 8d), 94.7 (C-7a, 7d), 96.9 (C-12b, 12c), 102.3 (C-12a, 12d), 107.5 (C-10a, 14a, 10d, 14d), 115.4 (C-3b, 5b, 3c, 5b), 116.2 (C-3a, 5a, 3d, 5d), 116.5 (C-10b, 10c), 125.3 (C-14b, 14c), 128.7 (C-2a, 6a, 2d, 6d), 129.1 (C-2b, 6b, 2c, 6c), 133.3

(C-1a, 1d), 136.5 (C-1b, 1c), 145.2 (C-9b, 9c), 145.4 (C-9a, 9d), 155.4 (C-13b, 13c), 156.0 (C-4b, 4c), 158.3 (C-4a, 4d), 160.0 (C-11a, 13a, 11d, 13d), 162.8 (C-11b, 11c).

Hemsleyanol E (4) : A yellow amorphous powder. Negative ion HR-FABMS: $[M-H]^-$ *m/z* 379.0825 (Calcd 379.0818 for $C_{21}H_{15}O_7$); Negative ion FAB-MS: $[M-H]^-$ *m/z* 379; UV λ max (MeOH) nm: 225, 287, 345; $[\alpha]_D$ +348° (*c*= 0.1, MeOH) ; ^{1}H NMR [400 MHz, $(CD_3)_2CO$] δ: 4.53 (1H, br s, OH-8a), 5.14 (br d, *J* = 6.2 Hz, H-8a), 6.04 (d, *J* = 2.0 Hz, H-14a), 6.18 (d, *J* = 2.0Hz, H-12a), 6.24 (d, *J* = 6.2Hz, H-7a), 6.56 (d, *J* = 8.6 Hz, H-3a, 5a), 6.69 (d, *J* = 2.0 Hz, H-4b), 6.80 (d, *J* = 8.6 Hz, H-2a, 6a), 7.44 (d, *J* = 2.0 Hz, H-6b), 8.02 (1H, br s, OH), 8.50 (3H, br s, 3xOH), 13.34 (1H, s, OH-13a); ^{13}C NMR [100 MHz, $(CD_3)_2CO$] δ: 47.5 (C-7a), 79.0 (C-8a), 103.0 (C-12a), 108.0 (C-14a), 109.8 (C-4b), 111.5 (C-10a), 111.5 (C-6b), 115.5 (C-3a, 5a), 119.5 (C-2b), 129.9 (C-2a, 6a), 132.6 (C-1a), 141.5 (C-1b), 147.0 (C-9a), 156.2 (C-4a)*, 156.9 (C-3b), 157.7 (C-5b)*, 163.5 (C-13b), 167.6 (C-11a), 196.4 (C-7b) (*interchangeable).

Hemsleyanoside E (5) : A dark brown amorphous powder. Negative ion HR-FAB-MS: $[M-H]^-$ *m/z* 841.2482 (Calcd 841.2496 for $C_{48}H_{41}O_{14}$); Negative ion FABMS: $[M-H]^-$ *m/z* 841; UV λ max (MeOH) nm: 230, 282; $[\alpha]_D$ -85° (*c*= 0.1, MeOH); The ^{1}H and ^{13}C NMR spectral data are listed in Table 2.

Hemsleyanoside F (6) : A dark blown amorphous powder. Negative ion FAB-MS: $[M-H]^-$ *m/z* 631; UV λ max (MeOH) nm: 210, 283; $[\alpha]_D$ -63° (*c*= 0.1, MeOH); The ^{1}H and ^{13}C NMR spectral data are shown in Table 2.

ACKNOWLEDGEMENT

The authors (M. I. and Y. T.) thank a Grant-in-Aid for Scientific Research on Priority Area (08281105) to support this work in part.

REFERENCES

1. J. Gorham, "*The Biochemistry of the Stilbenoids*", Chapman & Hall, London, 1995.
2. S. Sotheeswaran and V. Pasupathy, *Phytochemistry*, 1993, **32**, 1083.
3. M. Jang, L. Cai, G. O. Udeani, K. V. Slowing, C. F. Thomas, C. W. W. Beecher, H. H. S. Fong, N. R. Farnsworth, A. D. Kinghorn, R. G. Mehta, R. C. Moon, and J. M. Pezzuto, *Science*, 1997, **275**, 218.
4. S. Kitanaka, T. Ikezawa, K. Yasukawa, S. Yamanouchi, M. Takido, H. Sung, and I. Kim, *Chem. Pharm. Bull*., 1990, **38**, 432.
5. Y. Inamori, M. Ogawa, H. Tsujibo, K. Baba, M. Kozawa, and H. Nakamura, *Chem. Pharm. Bull*., 1991, **39**, 805.

6. S. Murakami, I. Arai, M. Muramatsu, S. Otomo, K. Baba, T. Kodo and M. Kozawa, *Biochem. Pharm*., 1992, **44**, 33.
7. T. Tanaka, T. Ito, Y. Ido, T.-K. Son, K. Nakaya, M. Iinuma, M. Ohyama, and V. Chelladurai, *Phytochemistry*, 2000, **53**, 1015.
8. T. Tanaka, T. Ito, K. Nakaya, M. Iinuma, and S. Riswan, *Phytochemistry*, 2000, **54**, 63.
9. T. Tanaka, T. Ito, K. Nakaya, M. Iinuma, Y. Takahashi, H. Naganawa, N. Matsuura, and M. Ubukata, *Tetrahedron Lett*., 2000, **41**, 7929.
10. T. Ito, T. Tanaka, Y. Ido, K. Nakaya, M. Iinuma, and S. Riswan, *Chem. Pharm. Bull*., 2000, **48**, 1001.
11. T. Ito, T. Tanaka, Y. Ido, K. Nakaya, M. Iinuma, and S. Riswan, *Chem. Pharm. Bull*., 2000, **48**, 1959.
12. M. Ohyama, T. Tanaka, T. Ito, M. Iinuma, K. F. Bastow, and K. Lee, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 3057.
13. Y. Oshima and Y. Ueno, *Phytochemistry*, 1993, **33**, 179.
14. Y. Oshima, Y. Ueno, and H. Hikino, *Tetrahedron*, 1990, **46**, 5121.