Eight New 2-(2-Phenylethyl)chromone (= 2-(2-Phenylethyl)-4*H*-1-benzopyran-4-one) Derivatives from *Aquilaria malaccensis* Agarwood

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Eight new and eight known 2-(2-phenylethyl)chromone (=2-(2-phenylethyl)-4*H*-1-benzopyran-4-one) derivatives, *i.e.*, **1**–**8** and **9**–**16**, respectively, together with the two known sesquiterpenoids **17** and **18** were isolated from a 70% MeOH extract of *Aquilaria malaccensis* (AM) agarwood chips. Their structures were determined based on extensive spectroscopic analysis and comparison with reported data.

Introduction. – *Aquilaria malaccensis* (Thymelaeaceae) is a species of a medium-sized evergreen tree found in the rain forests of Southeast Asia and New Guinea. This species, as other species of the *Aquilaria* genus, can produce a dark aromatic resin mainly in response to the infection by *Phaeoacremonium parasiticum*, a parasitic ascomycetous mould, which results in a resin-suffused heartwood well known as agarwood [1]. The agarwood has been used as incense as well as sedative, analgesic, and digestive medicine in traditional herb therapies [2]. Previous phytochemical research on this genus led to the isolation of many (phenylethyl)chromone derivatives [2–10] and sesquiterpenoids [11–15]. Our ongoing investigation of *A. malaccensis* agarwood led to the isolation of eight new and ten known compounds, *i.e.*, **1**–**8** and **9**–**18**, respectively (*Fig. 1*). In this article, we present the isolation and structure elucidation of them.

Results and Discussion. – The 70% MeOH extract of *A. malaccensis* agarwood was partitioned with Et_2O, BuOH, and H_2O, as previously reported [15]. The BuOH fraction and Et_2O fraction were then each subjected to repeated column chromatographic separation to afford eighteen compounds, including **1**–**8** as new 2-(2-phenylethyl)chromone (=(2-phenylethyl)-4*H*-1-benzopyran-4-one) derivatives.

Compound **1** was obtained as brown amorphous powder, and its molecular formula $C_{19}H_{18}O_5$ was deduced from HR-ESI-MS (*m*/*z* 327.1232 ($[M+H]^+$). The IR absorption at 1637 cm^{-1} indicated the presence of a trisubstituted γ-pyrone (=4*H*-pyran-4-one) [3]. In the aromatic region of the ^{1}H-NMR spectrum (*Table 1*), two *s*s at δ(H) 7.52 and 6.93 (each 1 H) and two *d*s at δ(H) 7.09 and 6.80 (each J = 8.6 Hz, 2 H) were attributable to a tetrasubstituted and a *para*-disubstituted benzene ring, respectively. Besides that, a comprehensive consideration of the ^{1}H- and ^{13}C-NMR data (*Table 1*) revealed the presence of one C=O, one olefinic CH, two CH_2, one OH, and two MeO

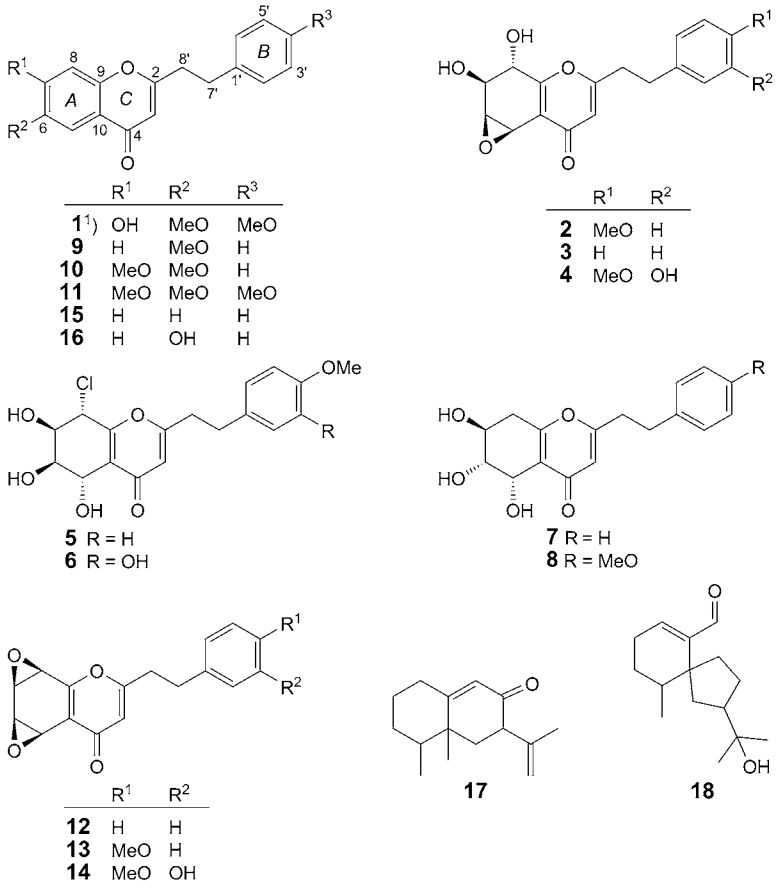

Fig. 1. *New and known compounds,* i.e., **1**–**8** *and* **9**–**18**, *respectively, isolated from* Aquilaria malaccensis *agarwood*

groups. The above findings suggested a (phenylethyl)chromone skeleton for **1**, which was further confirmed by the ^{1}H,^{1}H-COSY and HMBC data (*Fig. 2*). The H-atom at δ(H) 7.52 should be assigned to H–C(5) because of its HMBC cross-peak with C(4)=O. Three signals at δ(C) 145.1, 151.2, and 158.2 arising from O-bearing aromatic C-atoms were attributable to C(6), C(7), and C(4′) respectively, by related HMBC and comparison with a structurally similar known compound [4]. Two MeO groups were determined to be positioned at C(6) and C(4′), based on the HMBC cross-peaks between the MeO H-atoms and corresponding C-atoms. Thus, the OH group should be linked to the last open position at C(7). Consequently, the structure of **1** was elucidated as shown in *Fig. 1*.[1])

Compound **2** was obtained as pale yellow amorphous powder, and its molecular formula was determined to be $C_{18}H_{18}O_6$ by HR-FAB-MS (*m*/*z* 331.1187 ($[M+H]^+$). Its

[1]) Trivial atom numbering; for systematic names, see *Exper. Part.*

Table 1. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$, 500 MHz) *of Compounds* **1** *and* **2**[1]). δ in ppm, J in Hz

Position	**1**		**2**	
	δ(H)	δ(C)	δ(H)	δ(C)
C(2)		167.9		169.2
H–C(3)	6.06 (*s*)	109.4	6.10 (*s*)	114.2
C(4)		177.7		180.8
H–C(5)	7.52 (*s*)	104.3	3.76 (*d*, J = 4.4)	49.5
C(6) or H–C(6)		145.1	3.83 (*d*, J = 4.4)	54.8
C(7) or H–C(7)		151.2	4.10 (*d*, J = 7.7)	72.8
H–C(8)	6.93 (*s*)	102.7	4.69 (*d*, J = 7.7)	69.0
C(9)		152.8		158.5
C(10)		117.0[a])		120.3
C(1′)		131.8		131.1
H–C(2′)	7.09 (*d*, J = 8.6)	129.2	7.06 (*d*, J = 8.5)	129.1
H–C(3′)	6.80 (*d*, J = 8.6)	114.0	6.83 (*d*, J = 8.5)	114.2
C(4′)		158.2		158.4
H–C(5′)	6.80 (*d*, J = 8.6)	114.0	6.83 (*d*, J = 8.5)	114.2
H–C(6′)	7.09 (*d*, J = 8.6)	129.2	7.06 (*d*, J = 8.5)	129.1
CH_2(7′)	2.96 (*dd*, J = 8.2, 7.2)	32.2	2.91 (*m*)	32.0
CH_2(8′)	2.85 (*dd*, J = 8.2, 7.2)	36.3	2.82 (*m*)	35.4
*Me*O–C(6)	3.97 (*s*)	56.5		
*Me*O–C(4′)	3.76 (*s*)	55.3	3.77 (*s*)	55.3

[a]) The chemical shift was obtained from the HMBC coupling position (the peak of this C-atom could not be seen in the ^{13}C-NMR spectrum due to the weakness of the signal).

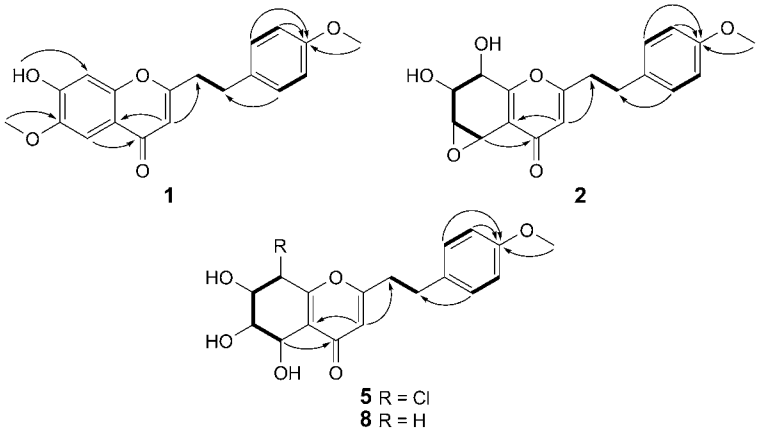

Fig. 2. *Key ^{1}H,^{1}H-COSY* (—) *and HMBC* (H → C) *features of* **1**, **2**, **5**, *and* **8**

^{13}C-NMR spectrum (*Table 1*) closely resembled that of oxidoagarochromone B (=(+)-*rel*-(1a*R*,1b*R*,2a*R*,6b*R*)-1a,1b,2a,6b-tetrahydro-4-[2-(4-methoxyphenyl)ethyl]-6*H*-bisoxirenol[*f*,*h*][1]benzopyran-6-one) reported by *Honda* and co-workers [2], except for three strongly downfield-shifted signals at δ(C) 72.8, 69.0, and 54.8, probably due to the presence of a vicinal diol group instead of an epoxy group in this region. This

speculation was also supported by the molecular mass of **2**, which showed an increase of 18 mass units compared to that of oxidoagarochromone B. Careful examination of the ^{1}H,^{1}H-COSY (*Fig. 2*) and HSQC data (not shown) allowed the assignment of four consecutive O-bearing CH groups from C(5) to C(8), as shown in *Table 1*. The H-atom resonating at δ(H) 3.76, located at one end of this chain, was assigned to H–C(5) because of its correlation with the C=O in the HMBC spectrum. When considering the relative configuration of **2**, a half-chair conformation with minimum total energy was assumed for the cyclohexene ring (ring *A*). The large *J* value (7.7 Hz) of H–C(8) and H–C(7) indicated their *trans* axial relationship, whereas a very small coupling constant (almost zero) between H–C(7) and H–C(6) could be explained by the approximate 90° dihedral angle between them, which could be achieved by an equatorial orientation of H–C(6). This configuration was further confirmed by the NOESY correlation between H–C(6) and H–C(7). Since the O-atom took an axial position at C(6), the epoxide could be formed only when this atom took the *cis*-equatorial position at C(5), thus the H–C(5) must be axially oriented. Therefore, assuming a β-orientation of H–C(8), all of the other three H-atoms in ring *A* should be positioned on the α-face. Based on all these informations, the structure of **2** was determined as depicted in *Fig. 1*.

Compounds **3** and **4** possessed the same molecular skeleton as **2**, including the relative configuration, as indicated by their ^{1}H- and ^{13}C-NMR spectra (*Table 2*). The differences among them appeared in the substitution pattern of benzene ring *B*. In the ^{1}H-NMR spectrum of **3**, the *m*s at δ(H) 7.16 (2 H), 7.22 (1 H), and 7.30 (2 H) corresponded to an unsubstituted phenyl group, compared to a disubstituted one in **4** as demonstrated by a diagnostic peak combination at δ(H) 6.60 (*dd*, $J = 8.0$ and 1.6 Hz, H–C(6′)), 6.74 (*d*, $J = 1.6$ Hz, H–C(2′)), and 6.75 (*d*, $J = 8.0$ Hz, H–C(5′)). The full

Table 2. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$, 500 MHz) *of Compounds* **3** *and* **4**[1]). δ in ppm, *J* in Hz.

Position	**3**		**4**	
	δ(H)	δ(C)	δ(H)	δ(C)
C(2)		169.0		169.2
H–C(3)	6.12 (*s*)	114.2	6.10 (*s*)	114.2
C(4)		180.7		180.8
H–C(5)	3.76 (*d*, $J = 4.2$)	49.5	3.77 (*d*, $J = 4.2$)	49.5
H–C(6)	3.83 (*d*, $J = 4.2$)	54.7	3.83 (*d*, $J = 4.2$)	54.8
H–C(7)	4.10 (*d*, $J = 7.7$)	72.9	4.10 (*d*, J = 7.8)	72.9
H–C(8)	4.69 (*d*, $J = 7.7$)	69.0	4.69 (*d*, J = 7.8)	69.0
C(9)		158.5		158.5
C(10)		120.3		120.3
C(1′)		139.1		132.3
H–C(2′)	7.16 (*m*)	128.2	6.74 (*d*, $J = 1.6$)	114.3
H–C(3′) or C(3′)	7.30 (*m*)	128.8		145.8
H–C(4′) or C(4′)	7.22 (*m*)	126.8		145.4
H–C(5′)	7.30 (*m*)	128.8	6.75 (*d*, $J = 8.0$)	110.8
H–C(6′)	7.16 (*m*)	128.2	6.60 (*dd*, $J = 8.0$, 1.6)	119.6
CH_2(7′)	2.98 (*m*)	32.9	2.88 (*m*)	32.2
CH_2(8′)	2.86 (*m*)	35.1	2.82 (*m*)	35.2
*Me*O–C(4′)			3.85 (*s*)	56.0

assignment of the H- and C-atom signals was accomplished on the basis of HMBC spectra and comparison with reported data of similar compounds [2].

Compound **5** was obtained as pale brown amorphous powder, and its molecular formula $C_{18}H_{19}ClO_6$ was deduced from the HR-ESI-MS (*m/z* 367.0931 ($[M+H]^+$, $C_{18}H_{20}ClO_6^+$). The existence of a Cl-atom could be confirmed by the *ca.* 3:1 peak-intensity ratio of the ions $[M+H]^+/[M+2+H]^+$. The diagnostic signals at δ(H) 6.82 (*d*, *J* = 8.5 Hz, 2 H) and 7.06 (*d*, *J* = 8.5 Hz, 2 H) in the ^{1}H-NMR spectrum (*Table 3*) indicated the presence of a 4-substituted phenyl group. Careful examination of the ^{1}H- and ^{13}C-NMR data led to the identification of one olefinic and three O-bearing CH groups, together with one MeO and two CH_2 groups, suggesting the existence of a highly oxygenated (phenylethyl)chromone skeleton [3]. This speculation was further confirmed by the analysis of the ^{1}H,^{1}H-COSY, HSQC, and HMBC data. Comprehensive consideration of the ^{1}H,^{1}H-COSY (*Fig. 2*) and HSQC data (not shown) allowed the assignment of four consecutive CH groups from C(5) to C(8), as shown in *Table 3*. The H-atom resonating at δ(H) 4.90, located at one end of this chain, was assigned to H–C(5) because its signal correlated with that of C(4) in the HMBC spectrum (*Fig. 2*). The linkage of C(8) to a Cl-atom was revealed by the upfield shift of its signal in the ^{13}C-NMR spectrum (*Table 3*), comparing to those of the O-bearing C-atoms. The MeO group was connected to C(4′), as indicated by a corresponding HMBC cross-peak (*Fig. 2*). Based on the above analysis, the planar structure of **5** could be established unambiguously. When considering the relative configuration of **5**, a half-chair conformation with minimum total energy was assumed for the cyclohexene ring (ring

Table 3. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$, 500 MHz) *of Compounds* **5** *and* **6**[1]). δ in ppm, *J* in Hz.

Position	**5**		**6**	
	δ(H)	δ(C)	δ(H)	δ(C)[a])
C(2)		169.7		172.2
H–C(3)	6.08 (*s*)	113.6	6.07 (*s*)	115.1
C(4)		180.6		182.3
H–C(5)	4.90 (*d*, *J* = 7.2)	68.0	4.89 (*d*, *J* = 7.2)	67.3
H–C(6)	4.25 (*dd*, *J* = 7.2, 2.1)	70.4	4.25 (*dd*, *J* = 7.2, 2.2)	74.4
H–C(7)	4.36 (*dd*, *J* = 3.5, 2.1)	73.2	4.36 (*dd*, *J* = 3.5, 2.2)	74.4
H–C(8)	4.71 (*d*, *J* = 3.5)	53.9	4.71 (*d*, *J* = 3.5)	58.9
C(9)		157.3		161.9
C(10)		121.2		123.7
C(1′)		131.2		134.7
H–C(2′)	7.06 (*d*, *J* = 8.5)	129.2	6.74 (*d*, *J* = 2.0)	117.2
H–C(3′)	6.82 (*d*, *J* = 8.5)	114.2		148.5
C(4′)		158.4		148.4
H–C(5′)	6.82 (*d*, *J* = 8.5)	114.2	6.74 (*d*, *J* = 8.2)	113.8
H–C(6′)	7.06 (*d*, *J* = 8.5)	129.2	6.60 (*dd*, *J* = 8.2, 2.0)	121.4
CH_2(7′)	2.91 (*m*)	32.0	2.88 (*m*)	34.0
CH_2(8′)	2.82 (*m*)	35.6	2.81 (*m*)	37.2
*Me*O–C(4′)	3.77 (*s*)	55.3	3.85 (*s*)	57.3

[a]) The ^{13}C-NMR spectrum of **6** was recorded in CD_3OD due to the poor solubility of this compound in $CDCl_3$

A). The large *J* value (7.2 Hz) of H–C(5) and H–C(6) indicated their *trans*-axial relationship, whereas a small coupling constant (2.1 Hz) between H–C(6) and H–C(7) could be explained by the axial-equatorial relationship of them. The absence of a NOESY interaction between H–C(6) and H–C(8) suggested the pseudoequatorial orientation of H–C(8). Therefore, assuming a β-configuration of H–C(8), H–C(5) should also be β-oriented, while H–C(7) and H–C(6) were positioned on the α-face. Consequently, the structure of **5** was determined as shown in *Fig. 1*.

Compound **6** was isolated as white amorphous powder. Its HR-ESI-MS exhibited a $[M+H]^+$ peak at *m/z* 383.0888 ($C_{18}H_{20}ClO_7^+$) in accordance with the molecular formula $C_{18}H_{19}ClO_7$. The structure of **6** was very similar to that of **5**, except for one more OH group substituting ring *B*. The NOESY correlations H–C(2′)/CH_2(7′), H–C(6′)/CH_2(7′), H–C(5′)/MeO–C(4′), as well as the absence of a NOESY coupling H–C(2′)/MeO–C(4′) established that the OH group was attached to C(3′). The full assignment of the H- and C-atom signals, as shown in *Table 3*, was accomplished on the basis of 2D-NMR spectra and by comparison with **5**.

An inseparable pair of compounds **7**/**8** was obtained as brown amorphous powder. The molecular formulas of **7** and **8** were determined to be $C_{17}H_{18}O_5$ (*m/z* 303.1220 ($[M+H]^+$, $C_{17}H_{19}O_5^+$) and $C_{18}H_{20}O_6$ (*m/z* 333.1326 ($[M+H]^+$, $C_{18}H_{21}O_6^+$), respectively, by HR-ESI-MS. Two sets of signals, arising from these two compounds, were observed in the ^{1}H-NMR spectrum (*Table 4*), with differences mainly in the aromatic region. The three *m*s resonating at δ(H) 7.27 (2 H), 7.19 (1 H), and 7.14 (2 H) were attributed to an unsubstituted phenyl group in **7**, while two correlated *d*s at δ(H) 7.05 (2 H) and 6.81 (2 H) could be ascribed to a *para*-substituted one in **8**. The skeletons of **7**

Table 4. *^{1}H- and ^{13}C-NMR Data* ($CDCl_3$, 500 MHz) *of Compounds* **7** *and* **8**[1]). δ in ppm, *J* in Hz.

Position	**7**		**8**	
	δ(H)	δ(C)	δ(H)	δ(C)
C(2)		168.8		168.9
H–(3)	6.10 (*s*)	113.0	6.08 (*s*)	113.0
C(4)		180.5		180.5
H–(5)	4.88 (br. *s*)	65.8	4.88 (br. *s*)	65.8
H–(6)	4.05 (br. *s*)	69.6	4.05 (br. *s*)	69.6
H–(7)	4.08 (br. *s*)	67.8	4.08 (br. *s*)	67.8
CH_2(8)	2.77 (*m*), 2.94 (*m*)	33.5	2.77 (*m*), 2.94 (*m*)	33.5
C(9)		162.3		162.3
C(10)		119.8		119.6
C(1′)		139.4		131.4
H–(2′)	7.14 (*m*)	128.2	7.05 (*d*, *J* = 8.5)	129.1
H–(3′)	7.27 (*m*)	128.6	6.81 (*d*, *J* = 8.5)	114.1
H–(4′) or C(4′)	7.19 (*m*)	126.6		158.3
H–(5′)	7.27 (*m*)	128.6	6.81 (*d*, *J* = 8.5)	114.1
H–(6′)	7.14 (*m*)	128.2	7.05 (*d*, *J* = 8.5)	129.1
CH_2(7′)	2.92 (*m*)	32.9	2.86 (*m*)	32.0
CH_2(8′)	2.79 (*m*)	35.1	2.76 (*m*)	35.4
*Me*O–C(4′)			3.75 (*s*)	55.2

and **8** could easily be established as (phenylethyl)chromones on the basis of their ^{1}H- and ^{13}C-NMR spectra. In both **7** and **8**, a chain consisting of three consecutive O-bearing CH groups and one CH_2 group was identified with the assistance of the ^{1}H,^{1}H-COSY and HSQC experiments, as shown in *Fig. 2*. The signal at δ(H) 4.88 in the ^{1}H-NMR spectrum was assigned to H–C(5) because of its correlation with the C(4) signal in the HMBC spectrum (*Fig. 2*). Based on all these information, the planar structures of **7** and **8** were characterized as shown in *Fig. 1*. Assuming a half-chair conformation for the ring *A* of **7** (or **8**) (*Fig. 3*), the orientation of H–C(7) should be equatorial since no large coupling constant was observed between this H-atom and either H-atom at C(8). The H–C(6) was also equatorially oriented, as revealed by the absence of a NOESY interaction H–C(6)/CH_2(8). For stability reasons, it was most indicated to propose an axial orientation for H–C(5) to avoid the presence of three axial OH groups in ring *A*. The equatorial OH–C(5) was able to form a H-bond with the C=O group at C(4) [6][7], which further stabilized this conformation. Therefore, the relative configurations of **7** and **8** were unambiguously established (*Fig. 1*).

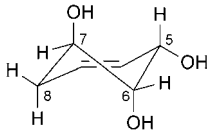

Fig. 3. *Conformation of the cyclohexene moiety* (ring *A*) *of compound* **7** (or **8**)

The absolute configurations of compounds **2**–**8** were not determined due to the scarcity of the samples.

The known compounds isolated were identified as 6-methoxy-2-(2-phenylethyl)-chromone (**9**) [4][10], 6,7-dimethoxy-2-(2-phenylethyl)chromone (**10**) [4][10], 6,7-dimethoxy-2-[2-(4-methoxyphenyl)ethyl]chromone (**11**) [8], 5,6:7,8-diepoxy-5,6,7,8-tetrahydro-2-(2-phenylethyl)chromone (**12**) [2], 5,6:7,8-diepoxy-5,6,7,8-tetrahydro-2-[2-(4-methoxyphenyl)ethyl]chromone (**13**) [2], 5,6:7,8-diepoxy-5,6,7,8-tetrahydro-2-[2-(3-hydroxy-4-methoxyphenyl)ethyl]chromone (**14**) [2], 2-(2-phenylethyl)chromone (**15**) [5][9], 6-hydroxy-2-(2-phenylethyl)chromone (**16**) [4], neopetasane (**17**) [14], and baimuxinal (**18**) [13] by comparing their spectroscopic data with the reported ones. Among them, **12**–**14** were obtained for the first time from the *A. malaccensis* species.

Experimental Part

General. Column chromatography (CC): *silica gel 60* (70–230 mesh (No. *107734*); 230–400 mesh (No. *109385*); *Merck*) and *Sephadex^{TM} LH-20* (*GE Healthcare*, Sweden). Anal. TLC: silica gel *60* F_{254} (SiO_2; *Merck*). Semi-prep. HPLC: *Hitachi* instrument with a *Gemini RP* C_{18} column (250 × 10 mm, 5 μm). Optical rotations: *Jasco-P-1020* polarimeter (Japan). UV Spectra: *Hitachi-U-3010* spectrophotometer (Japan); λ_{max} (log ε) in nm. IR Spectra: *Jasco-FT/IR-4200* spectrometer (Japan); $\tilde{\nu}$ in cm^{-1}. NMR Spectra: *Bruker-Avance* (500 MHz) FT-NMR spectrometer (Germany); δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *Bruker-micrOTOF-Q-II* mass spectrometer (Germany); in *m*/*z*.

Plant Material. The agarwood chips of *A. malaccensis* were purchased from *Industrial Plantation Co.*, Vientiane, Laos, in January 2010. The voucher specimen was deposited with the Herbarium of the Natural Product Research Institute, Seoul National University.

Extraction and Isolation. Air-dried *A. malaccensis* agarwood chips (450 g) were crushed and exhaustively extracted by refluxing with 70% MeOH. The extract was concentrated to give a residue of 68.2 g, which was successively partitioned with Et_2O, BuOH, and H_2O [15]. The BuOH fraction (31.0 g) was subjected to CC (SiO_2, AcOEt/MeOH 50:1 → 10:1): *BFrs. 1–5*. *BFr. 2* was further separated by CC (SiO_2, hexane/AcOEt 2:1 → 1:2): *BFrs. 2.1–2.9*. *BFr. 2.1* was applied to CC (SiO_2, hexane/$CHCl_3$ 10:1 → 3:1): **9** (17 mg). *BFr. 2.2* was subjected to CC (SiO_2, $CHCl_3$/AcOEt 20:1): **10** (15 mg). *BFr. 2.3* was applied to CC (SiO_2, hexane/$CHCl_3$ 10:1 → 1:1): **11** (9 mg). Compounds **1** (11 mg), **12** (28 mg), **13** (17 mg), and a mixture **2**/**3** were obtained from *BFr. 2.5* after CC (SiO_2, $CHCl_3$/AcOEt 20:1 → 3:1). Separation of **2** and **3** was finally achieved by CC (SiO_2, $CHCl_3$): **2** (14 mg) and **3** (33 mg). *BFr. 2.6* was subjected to CC (SiO_2, $CHCl_3$): **14** (25 mg). *BFr. 2.7* was applied to CC (SiO_2, $CHCl_3$/AcOEt 20:1 → 5:1): **4** (22 mg). *BFr. 2.8* was applied to CC (SiO_2, $CHCl_3$/AcOEt 5:1 → 3:1, $CHCl_3$/MeOH 40:1 → 20:1): *BFrs. 2.8.1–2.8.5*. *BFr. 2.8.3* was subjected to CC (SiO_2, $CHCl_3$/MeOH 100:1 → 60:1): **5** (11 mg). *BFr. 2.8.*4 was applied to CC (SiO_2, $CHCl_3$/MeOH 80:1 → 35:1): **6** (5 mg). *BFr. 3* was separated by CC (SiO_2, $CHCl_3$/MeOH 40:1 → 10:1): *BFrs. 3.1–3.5*. A mixture **7**/**8** (21 mg) was obtained from *BFr. 3.3* by CC (SiO_2, $CHCl_3$/MeOH 80:1 → 10:1). Although different solvent combinations and several kinds of columns (including C_{18} semi-prep. HPLC columns) were tried, separation of **7**/**8** was not successful due to the structural similarity of them. The Et_2O fraction (21.5 g) was also subjected to CC (SiO_2, hexane/AcOEt 40:1 → 1:1): *EFrs. 1–14*. *EFr. 1* was purified by CC (*Sephadex LH-20*, MeOH): **17** (36 mg). Compounds **15** (42 mg) and **18** (12 mg) were obtained from *EFr. 4* after separation by CC (SiO_2, $CHCl_3$). Compound **16** (86 mg) was isolated from *EFr. 14* by recrystalization in MeOH. All the isolated compounds were further purified by CC (*Sephadex LH-20*) or semi-prep. reversed-phase HPLC.

*7-Hydroxy-6-methoxy-2-[2-(4-methoxyphenyl)ethyl]-4*H*-1-benzopyran-4-one* (**1**): Brown amorphous powder. UV (MeOH): 317 (3.65), 278 (3.71), 228 (4.15), 205 (4.18). IR (film): 2929, 1736, 1637, 1513, 1475, 1383, 1279, 1247, 1217, 1179, 1116, 1081, 1034. ^{1}H- and ^{13}C-NMR*: Table 1*. HR-ESI-MS (pos.): 327.1232 ($[M+H]^+$, $C_{19}H_{19}O_5^+$; calc. 327.1227).

rel-*(1a*R*,2*R*,3*R*,7b*S*)-1a,2,3,7b-Tetrahydro-2,3-dihydroxy-5-[2-(4-methoxyphenyl)ethyl]-7*H*-oxireno[*f*][1]benzopyran-7-one* (**2**): Pale yellow amorphous powder. $[\alpha]_D^{25} = +18.0$ ($c = 0.178$, MeOH). UV (MeOH): 253 (4.00), 223 (4.18), 203 (4.23). IR (film): 3398, 1658, 1600, 1513, 1458, 1247, 1184, 1060. ^{1}H- and ^{13}C-NMR*: Table 1*. HR-FAB-MS (pos.): 331.1187 ($[M+H]^+$, $C_{18}H_{19}O_6^+$; calc. 331.1182).

rel-*(1a*R*,2*R*,3*R*,7b*S*)-1a,2,3,7b-Tetrahydro-2,3-dihydroxy-5-(2-phenylethyl)-7*H*-oxireno[*f*][1]benzopyran-7-one* (**3**). White amorphous powder. $[\alpha]_D^{25} = -38.9$ ($c = 0.141$, MeOH). UV (MeOH): 253 (4.03), 205 (4.24). IR (film): 3265, 2917, 1651, 1573, 1456, 1187, 1010. ^{1}H- and ^{13}C-NMR*: Table 2*. HR-ESI-MS (pos.): 301.1066 ($[M+H]^+$, $C_{17}H_{17}O_5^+$; calc. 301.1071).

rel-*(1a*R*,2*R*,3*R*,7b*S*)-1a,2,3,7b-Tetrahydro-2,3-dihydroxy-5-[2-(3-hydroxy-4-methoxyphenyl)ethyl]-7*H*-oxireno[*f*][1]benzopyran-7-one* (**4**): Brown amorphous powder. $[\alpha]_D^{25} = +60.9$ ($c = 0.183$, MeOH). UV (MeOH): 204 (4.47). IR (film): 3388, 2931, 1658, 1604, 1513, 1442, 1246, 1186, 1131, 1032. ^{1}H- and ^{13}C-NMR*: Table 2*. HR-ESI-MS (pos.): 347.1110 ($[M+H]^+$, $C_{18}H_{19}O_7^+$; calc. 347.1125).

rel-*(5*R*,6*S*,7*S*,8*R*)-8-Chloro-5,6,7,8-tetrahydro-5,6,7-trihydroxy-2-[2-(4-methoxyphenyl)ethyl]-4*H*-1-benzopyran-4-one* (**5**): Pale brown amorphous powder. $[\alpha]_D^{25} = -2.6$ ($c = 0.138$, MeOH). UV (MeOH): 253 (4.00), 203 (4.25). IR (film): 3399, 2917, 2849, 1734, 1657, 1610, 1513, 1438, 1247, 1180, 1099, 1033. ^{1}H- and ^{13}C-NMR*: Table 3*. HR-ESI-MS (pos.): 367.0931 ($[M+H]^+$, $C_{18}H_{20}ClO_6^+$; calc. 367.0943).

rel-*(5*R*,6*S*,7*S*,8*R*)-8-Chloro-5,6,7,8-tetrahydro-5,6,7-trihydroxy-2-[2-(3-hydroxy-4-methoxyphenyl)ethyl]-4*H*-1-benzopyran-4-one* (**6**): White amorphous powder. $[\alpha]_D^{25} = -3.9$ ($c = 0.172$, MeOH). UV (MeOH): 253 (3.91), 203 (4.37). IR (film): 3354, 2918, 2849, 1734, 1657, 1590, 1513, 1437, 1276, 1241, 1130, 1099, 1024. ^{1}H- and ^{13}C-NMR*: Table 3*. HR-ESI-MS (pos.): 383.0888 ($[M+H]^+$, $C_{18}H_{20}ClO_7^+$; calc. 383.0892).

rel-*(5*R*,6*S*,7*R*)-5,6,7,8-Tetrahydro-5,6,7-trihydroxy-2-(2-phenylethyl)-4*H*-1-benzopyran-4-one* (**7**) *and* rel-*(5*R*,6*S*,7*R*)-5,6,7,8-Tetrahydro-5,6,7-trihydroxy-2-[2-(4-methoxyphenyl)ethyl]-4*H*-1-benzopyran-4-one* (**8**): Brown amorphous powder (mixture). $[\alpha]_D^{25} = -10.6$ ($c = 0.221$, MeOH). UV (MeOH): 250, 203. IR (film): 3397, 2918, 2848, 1733, 1658, 1601, 1513, 1439, 1246, 1179, 1032. ^{1}H and ^{13}C-NMR*: Table 4*. HR-ESI-MS (pos.): 303.1220 ($[M+H]^+$, $C_{17}H_{19}O_5^+$; calc. 303.1227) for **7** and 333.1326 ($[M+H]^+$, $C_{18}H_{21}O_6^+$; calc. 333.1333) for **8**.

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