Prenyl Coumarins from *Fatoua pilosa*

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Six new prenylcoumarins, (+)-fatouain A (**1**), (−)-fatouain B (**2**), (+)-fatouain C (**3**), (−)-fatouain D (**4**), (+)-fatouain E (**5**), and (−)-fatouain F (**6**), along with two new bis-prenylcoumarins, (+)-fatouain G (**7**) and (+)-fatouain H (**8**), have been isolated from whole plants of *Fatoua pilosa*. The relative configurations of **1**, **3**, and **4** were confirmed by their acetonides on the basis of NOEDIF experiments, the results providing additional support for the relative configurations of **2**, **5**, **6**, **7**, and **8**.

Fatoua pilosa Gaud.[1] (Moraceae) is a small perennial herb distributed throughout the Philippines, Moluccas, New Guinea, and Taiwan. There are only three species of *Fatoua* in the world, with two of them in Taiwan.[2] The chemical constituents and bioactivity of *Fatoua* species have not been previously studied, with the exception of bergapten, which was isolated from *F. villosa*.[3] Investigation of the EtOAc-soluble fraction of the whole plants of *F. pilosa* led to the isolation of six new prenylcoumarins, (+)-fatouain A (**1**), (−)-fatouain B (**2**), (+)-fatouain C (**3**), (−)-fatouain D (**4**), (+)-fatouain E (**5**), and (−)-fatouain F (**6**), together with two new bis-prenylcoumarins, (+)-fatouain G (**7**) and (+)-fatouain H (**8**).

(+)-Fatouain A (**1**) was obtained as optically active colorless needles with $[\alpha]^{25}_{D}$ +37.9 (*c* 0.085, $CHCl_3$). The ESIMS of **1** afforded an $[M + Na]^+$ ion at *m/z* 329, implying a molecular formula of $C_{16}H_{18}O_6$, which was confirmed by HRESIMS. The presence of a 7,8-dioxygenated coumarin skeleton was inferred from the UV absorption (λ_{max} 211, 228 sh, 252 sh, 300 nm).[4] The IR absorptions indicated the existence of a hydroxy group and carbonyl group (3417, 1727 cm^{-1}). The ^1H NMR spectrum (Table 1) showed a characteristic pair of doublets [δ 6.33, 7.66 (each 1H, d, $J = 9.3$ Hz)] for the C-3 and C-4 protons of the coumarin nucleus. The chemical shift of H-4 was less than 8.0 ppm, which was consistent with a lack of functionalization at C-5.[5,6] Consequently, δ 7.31 (1H, s) was assigned to H-5. The ^{13}C NMR spectrum (Table 2) revealed six carbon signals including one singlet at δ 160.2 assignable to a carbonyl carbon of the coumarin nucleus. Furthermore, residual signals in the ^1H NMR spectrum revealed one vinyl methyl group at δ 1.83 (3H, s, H-5′), two methoxy groups at δ 4.01 (3H, s, OCH_3-8) and 4.06 (3H, s, OCH_3-7), one aliphatic methine proton at δ 4.24 (1H, brd, $J = 4.8$ Hz, H-2′), one benzylic methine proton at δ 5.00 (1H, brd, $J = 4.8$ Hz, H-1′), an *exo*-methylene group at δ 4.97 (1H, brd, $J = 0.6$ Hz, Ha-4′) and 4.99 (1H, brd, $J = 0.6$ Hz, Hb-4′), and two hydroxy groups at δ 2.34 (d, $J = 4.5$ Hz, OH-1′) and 2.74 (d, $J = 4.5$ Hz, OH-2′). The COSY spectrum (Figure 1, Supporting Information) showed correlations between H-1′ (δ 5.00) and H-2′ (δ 4.24), and the HMBC spectrum (Figure 1, Supporting Information) revealed that OCH_3-7 (δ 4.06) had a ^3J correlation with C-7 (δ 152.9) and ^3J and ^2J correlations between H-1′ (δ 5.00) and C-5 (δ 120.9), C-7 (δ 152.9), and C-6 (δ 130.5). This suggests that the proton at δ 5.00 and a methoxy group at δ 4.06 must be at C-1′ and C-7, respectively, with the isopentenyl substituent attached to C-6. The planar structure of (+)-fatouain A was elucidated as **1**.[4,7,8] Furthermore, treatment of **1** with acetone in the presence of a catalytic amount of toluene-*p*-sulfonic acid gave the corresponding acetonide (**1a**).[9−16] For the reciprocal differential NOE between H-1′ (δ 5.00) and H-2′ (δ 4.24) of the derived acetonide (**1a**), no NOE enhancement was observed, by irradiation either of H-1′ at δ 5.00 or of H-2′ at δ 4.24. Thus, (+)-fatouain A-acetonide (**1a**) should be of the *threo* form. On the basis of the above evidence, the relative configuration of **1** was proposed as (+)-*threo*-6-(1,2-dihydroxy-3-methylbut-3-enyl)-7,8-dimethoxy-[2*H*]-chromen-2-one, namely, (+)-fatouain A.

(−)-Fatouain B (**2**) was obtained as optically active colorless needles with $[\alpha]^{25}_{D}$ −39.9 (*c* 0.08, $CHCl_3$). Using HRESIMS the molecular formula was determined to be $C_{16}H_{18}O_6$. The presence of a 7,8-dioxygenated coumarin skeleton was also suggested by UV, IR, and ^1H NMR [δ 6.33 and 7.65 (each 1H, d, $J = 9.6$ Hz, H-3, 4)] spectra. The $^1H/^{13}C$ NMR (Tables 1 and 2), COSY (Figure 1, Supporting Information), HSQC, and HMBC spectra (Figure 1, Supporting Information) of **2** were similar to those of **1**, except that the H-1′ and H-2′ signals shifted from δ 5.00 and 4.24 of **1** to δ 5.06 and 4.33 of **2**, respectively. Due to the negative value of optical rotation in comparison with that of **1**, the relative configuration of **2** was considered to be of the *erythro* form. Compounds **1** and **2** are diastereoisomeric compounds. According to the above data, the structure of **2** was elucidated as (−)-*erythro*-6-(1,2-dihydroxy-3-methylbut-3-enyl)-7,8-dimethoxy-[2*H*]-chromen-2-one and designated as (−)-fatouain B.

(+)-Fatouain C (**3**) was obtained as optically active colorless needles with $[\alpha]^{25}_{D}$ +31.6 (*c* 0.08, acetone). The molecular formula of $C_{15}H_{16}O_6$ was established by HRESIMS. The $^1H/^{13}C$ NMR spectra of **3** were similar to those of **1**, except that a hydroxy group at C-8 in **3** replaced a methoxy group in **1**. Furthermore, treatment of **3** with acetone in the presence of a catalytic amount of toluene-*p*-sulfonic acid gave the corresponding acetonide (**3a**). For the reciprocal differential NOE between H-1′ (δ 5.02) and H-2′ (δ 4.18), no NOE was observed, by irradiation either of H-1′ at δ 5.02 or of H-2′ at δ 4.18. Thus, (+)-fatouain C-acetonide (**3a**) should be of the *threo* form.[9−16] On the basis of the above data, the structure of **3** was elucidated as (+)-*threo*-6-(1,2-dihydroxy-3-methylbut-3-enyl)-8-hydroxy-7-methoxy-[2*H*]-chromen-2-one, namely, (+)-fatouain C, which was further confirmed by HSQC, HMBC (Figure 1, Supporting Information), and NOESY (Figure 2, Supporting Information) experiments.

(−)-Fatouain D (**4**) was obtained as optically active colorless needles with $[\alpha]^{25}_{D}$ −13.4 (*c* 0.07, acetone) and had a molecular formula of $C_{15}H_{16}O_6$ according to the HRESIMS results. The presence of a 7,8-dioxygenated coumarin skeleton was also

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Table 1. ^{1}H NMR Data for Compounds **1**−**6**[a]

position	δ_H (J in Hz)					
	1	**2**	**3**	**4**	**5**	**6**
3	6.33, d (9.3)	6.33, d (9.6)	6.27, d (9.6)	6.27, d (9.6)	6.33, d (9.6)	6.33, d (9.3)
4	7.66, d (9.3)	7.65, d (9.6)	7.90, d (9.6)	7.90, d (9.6)	7.68, d (9.6)	7.68, d (9.3)
5	7.31, s	7.34, s	7.27, s	7.29, s	7.06, s	7.13, s
1′	5.00, brd (4.8)	5.06, dd (6.0, 4.2)	5.02, d (5.4)	5.08, d (6.4)	4.61, d (6.8)	4.73, d (5.7)
2′	4.24, brd (4.8)	4.33, dd (6.0, 4.2)	4.18, d (5.4)	4.29, d (6.4)	4.14, d (6.8)	4.34, d (5.7)
CH_3-3′	1.83, s	1.74, s	1.78, s	1.76, s	1.76, s	1.78, s
4′	4.99, brd (0.6)	4.97, brd (1.4)	4.81, brd (1.4)	4.81, brd (1.3)	4.80, brd (1.2)	4.87, brd (1.2)
	4.97, brd (0.6)	4.94, brd (1.4)	4.74, brd (1.4)	4.77, brd (1.3)	4.71, brd (1.2)	4.81, brd (1.2)
OCH_3-7	4.06, s	4.05, s	3.98, s	3.98, s	4.01, s	4.03, s
OCH_3-8	4.01, s	4.01, s				
OH-8[b]			8.79, brs		6.11, br s	6.20, brs
OCH_3-1′					3.29, s	3.28, s
OH-1′[b]	2.34, d (4.5)	2.16, d (4.2)	4.05, brs			
OH-2′[b]	2.74, d (4.5)	2.61, d (4.2)	4.26, brs		3.01, br s	2.31, brs

[a] ^{1}H NMR data (δ) were measured in $CDCl_3$ at 400 MHz for **5**, at 600 MHz for **1**, **2**, and **6**, and in acetone-d_6 at 400 MHz for **3** and **4**. The assignments are based on DEPT, ^{1}H−^{1}H COSY, HSQC, and HMBC spectra. [b] D_2O exchangeable.

Table 2. ^{13}C NMR Data for Compounds **1**−**6**[a]

position	**1**	**2**	**3**	**4**	**5**	**6**
2	160.2	160.2	161.0	161.1	159.8	159.9
3	114.7	114.8	115.6	115.5	114.4	114.4
4	143.8	143.8	146.0	146.0	144.1	144.3
5	120.9	121.0	118.1	118.7	117.0	117.4
6	130.5	130.1	134.1	134.2	128.7	128.6
7	152.9	153.4	149.7	150.4	148.6	148.8
8	139.5	139.5	138.1	138.4	135.7	135.7
9	147.9	147.8	144.4	144.4	143.0	142.4
10	115.1	115.3	116.4	116.5	114.5	114.6
1′	69.8	70.0	70.7	70.9	79.0	78.8
2′	77.8	78.8	79.9	80.0	79.2	77.7
3′	143.9	144.3	146.8	147.3	143.0	144.1
4′	112.9	114.4	113.1	113.8	113.9	113.5
CH_3-3′	18.9	18.5	19.6	19.5	18.3	18.8
OCH_3-7	61.2	61.4	61.7	61.9	60.8	61.0
OCH_3-8	61.5	61.5				
OCH_3-1′					57.3	57.4

[a] ^{13}C NMR data (δ) were measured in $CDCl_3$ at 100 MHz for **5**, at 150 MHz for **1**, **2**, and **6**, and in acetone-d_6 at 100 MHz for **3** and **4**. The assignments are based on DEPT, ^{1}H−^{1}H COSY, HSQC, and HMBC spectra.

suggested by the UV, IR, and ^{1}H NMR [δ 6.27 and 7.90 (each 1H, d, J = 9.6 Hz, H-3, 4)] spectra. The ^{1}H NMR spectrum of **4** was similar to that of **3**, except that the signals of H-1′ and H-2′ shifted from δ 5.02 and 4.18 of **3** to δ 5.08 and 4.29 of **4**, respectively. Treatment of **4** with acetone in the presence of a catalytic amount of toluene-*p*-sulfonic acid gave the corresponding acetonide (**4a**). For the reciprocal differential NOE between H-1′ (δ 5.08) and H-2′ (δ 4.29), 4.11% and 3.27% enhancements were observed. Thus, (−)-fatouain D-acetonide (**4a**) should be of the *erythro* form.[9−16] On the basis of the above data, the structure of **4** was elucidated as (−)-*erythro*-6-(1,2-dihydroxy-3-methylbut-3-enyl)-8-hydroxy-7-methoxy-[2*H*]-chromen-2-one, namely, (−)-fatouain D, which was further confirmed by DEPT, COSY (Figure 1, Supporting Information), HSQC, HMBC (Figure 1, Supporting Information), and NOESY (Figure 2, Supporting Information) experiments.

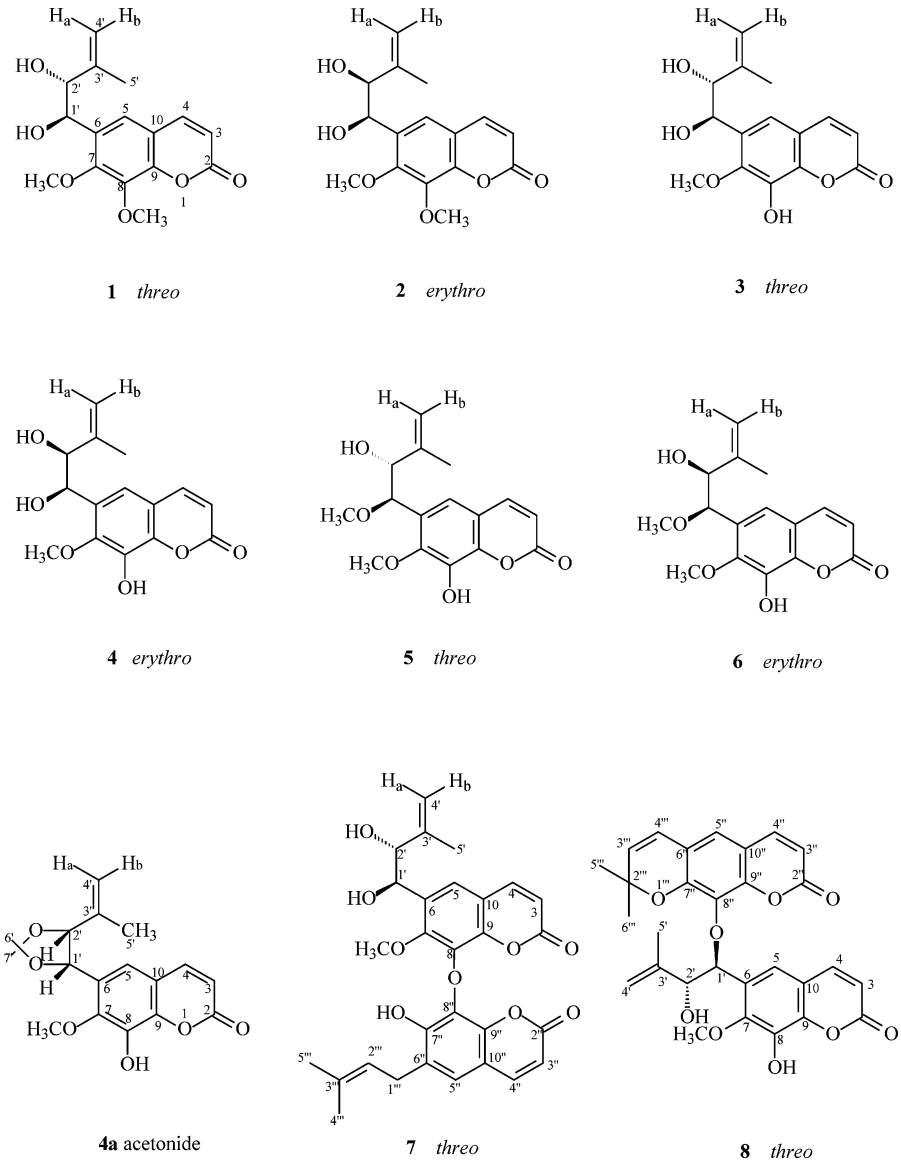
(+)-Fatouain E (**5**) was obtained as optically active colorless needles with $[\alpha]^{25}_D$ +54.3 (*c* 0.11, $CHCl_3$). The molecular formula of **5** was determined as $C_{16}H_{18}O_6$ using HRESIMS. Similar to **1**−**4**, their UV, IR, ^{1}H NMR, and ^{13}C NMR spectra (Tables 1 and 2) also revealed the presence of a 7,8-dioxygenated coumarin skeleton. The ^{1}H/^{13}C NMR spectra of **5** were similar to those of **1**, except that the methoxy group at C-8 and the hydroxy group at C-1′ of the latter were replaced by a hydroxy group at C-8 and a methoxy group at C-1′ in **5**. The planar structure of (+)-fatouain E was elucidated as **5**.[4,7,8] Due to the dextrorotatory specific rotation, and by comparison with the relative configuration of (+)-fatouain A (**1**), the relative configuration of **5** was considered to be of the *threo* form. On the basis of the above data, the structure of **5** was identified as (+)-*threo*-8-hydroxy-6-(2-hydroxy-1-methoxy-3-methylbut-3-enyl)-7-methoxy-[2*H*]-chromen-2-one, which was further confirmed by NOESY (Figure 2, Supporting Information) and HMBC (Figure 1, Supporting Information) techniques, and this compound was named (+)-fatouain E.

(−)-Fatouain F (**6**) was isolated as optically active colorless needles with $[\alpha]^{25}_D$ −75.7 (*c* 0.08, $CHCl_3$). The molecular formula was established as $C_{16}H_{18}O_6$ by ESIMS and HRESIMS analysis (329.1000 $[M + Na]^+$). The ^{1}H NMR spectrum of **6** was similar to that of **5**, except that the H-1′ and H-2′ signals shifted from δ 4.61 and 4.14 of **5** to δ 4.73 and 4.34 of **6**, respectively. Due to the levorotatory specific rotation, and referring to the relative configuration of (−)-fatouain B, the relative configuration of **6** was considered to be of the *erythro* form. According to the above evidence, the structure of **6** was elucidated as (−)-*erythro*-8-hydroxy-6-(2-hydroxy-1-methoxy-3-methylbut-3-enyl)-7-methoxy-[2*H*]-chromen-2-one, which has been designated as (−)-fatouain F.

(+)-Fatouain G (**7**) was obtained as optically active colorless needles with $[\alpha]^{25}_D$ +42.5 (*c* 0.08, $CHCl_3$), and its molecular formula was established as $C_{29}H_{28}O_9$ by HRESIMS. The presence of a 7,8-dioxygenated coumarin skeleton was suggested by the UV absorptions [λ_{max} 230 sh, 260, 312 nm]. The IR absorptions indicated the existence of a hydroxy group (3410 cm^{-1}) and a carbonyl group (1719 cm^{-1}). The ^{1}H NMR spectrum showed a pair of doublets [δ 6.33, 7.71 (each 1H, d, J = 9.6 Hz)] characteristic of the C-3 and C-4 protons of the coumarin nucleus. The ^{1}H NMR spectrum showed one vinyl methyl at δ 1.66 (3H, s, H-5′), one methoxy group at δ 3.88 (3H, s, OCH_3-7), an *exo*-methylene at δ 4.81 (1H, brs, Ha-4′) and 4.93 (1H, brs, Hb-4′), one aliphatic methine proton at δ 4.88 (1H, d, J = 8.1 Hz, H-2′), one benzylic methine proton at δ 5.05 (1H, d, J = 8.1 Hz, H-1′), one aromatic proton at δ 7.24 (1H, s, H-5), and three hydroxy singlets at δ 2.90, 6.02, and 9.05. The data suggested the partial structure of **7**, with a coumarin moiety similar to **1**−**6**. However, there was no signal for H-8.

The remaining signals in the ^{1}H NMR spectrum revealed signals of an isoprenyl group at δ 3.38 (2H, dd, J = 16.2, 7.2 Hz, H-1‴), 5.33 (1H, brt, J = 7.2 Hz, H-2‴), 1.72 (3H, s, H-4‴), and 1.78 (3H, s, H-5‴), one aromatic proton at δ 6.94 (1H, *s*, H-5″), and C-3 and C-4 protons of the coumarin nucleus at δ 5.98, 7.47 (each 1H, d, J = 9.3 Hz). The HMBC spectrum revealed H-1‴ (δ 3.38) giving ^3J and ^2J correlations with C-7″ (δ 151.8) and C-6″ (δ 126.2). Thus, the isoprenyl substituent was attached to C-6″. The above-mentioned proton signals suggested that the residual moiety was also a coumarin moiety. As there was no signal at H-8″, this suggested that the two coumarin moieties are linked via an oxygen at C-8 and C-8′.

Chart 1



Due to its dextrorotatory optical rotation, the relative configuration of **7** was considered to be of the *threo* form. On the basis of the above evidence, the structure of **7** was elucidated as (+)-*threo*-6-(1,2-dihydroxy-3-methylbut-3-enyl)-8-(7-hydroxy-6-(3-methylbut-2-enyl)-2-oxo-[2*H*]-chromen-8-yloxy)-7-methoxy-[2*H*]-chromen-2-one, which has been designated as (+)-fatouain G. This was further confirmed by DEPT, COSY (Figure 1, Supporting Information), HSQC, HMBC (Figure 1, Supporting Information), and NOESY (Figure 2, Supporting Information) experiments.

(+)-Fatouain H (**8**) was obtained as optically active colorless needles with $[\alpha]^{25}_{D}$ + 21.0 (*c* 0.075, $CHCl_3$). ESIMS and HRESIMS data were used to determine the molecular formula as $C_{29}H_{26}O_9$. The presence of a 7,8-dioxygenated coumarin skeleton was suggested from the UV absorptions [λ_{max} 229, 263, 312 nm]. The IR absorptions indicated the existence of a hydroxy group and carbonyl group (3461, 1729 cm^{-1}, respectively). The ^{1}H NMR spectrum showed a pair of doublets [δ 6.10, 7.46 (each 1H, d, J = 9.6 Hz)] characteristic for the C-3″ and C-4″ protons of the coumarin nucleus. The ^{1}H NMR spectrum showed two methyl groups at δ 1.54, 1.58 (each 3H, s, H-5‴, 6‴), one aromatic proton at δ 6.81 (1H, s, H-5″), and two aromatic *ortho* protons at δ 5.72, 6.32 (each 1H, d, J = 9.9 Hz, H-3‴, H-4‴). The data suggested the partial structure of **8**, with a coumarin moiety of the pyranocoumarin: xanthyletin type. However, no resonance for H-8″ was observed.

The remaining signals in the ^{1}H NMR spectrum revealed signals of an isopentenyl group at δ 1.77 (3H, s, H-5′), 4.53 (1H, d, J = 8.1 Hz, H-2′), 4.75 (1H, brs, Ha-4′), 4.78 (1H, brs, Hb-4′), 5.61 (1H, d, J = 8.1 Hz, H-1′), one methoxy group at δ 3.81 (3H, s, OCH_3-7), one aromatic proton at δ 7.62 (1H, s, H-5), and the C-3 and C-4 protons of a coumarin nucleus at δ 6.32, 7.83 (each 1H, d, J = 9.6 Hz). The above-mentioned proton signals revealed that the residual moiety was similar to **1**−**6**. The HMBC spectrum revealed ^3J correlations between H-1′ (δ 5.61) and C-8″ (δ 133.2). This suggests that two coumarin moieties are linked via an oxygen at C-1′ and C-8″. Due to the dextrorotatory optical rotation, the relative configuration of **8** was considered to be of the *threo* form. On the basis of the evidence above, the structure of **8** was elucidated as (+)-*threo*-10-(2-hydroxy-1-(8-hydroxy-7-methoxy-2-oxo-[2*H*]-chromen-6-yl)-3-methylbut-3-enyloxy)-8,8-dimethylpyrano[3,2-*g*]chromen-2(8*H*)-one. This was further confirmed by DEPT, COSY (Figure 1, Supporting Information), HSQC, NOESY (Figure 2, Supporting Information) and HMBC (Figure 1, Supporting Information) experiments, and this compound was named (+)-fatouain H.

All the compounds are coumarins with high polarity. In other Formosan Moraceous plants, such as *Broussonetia papyrifera*,[17–21] *Ficus benjamina*,[22,23] *F. microcarpa*,[24] *F. pumila*,[25] *F. ruficaulis* var. *antaoensis*,[26,27] *F. septica*,[28] and *Morus australis*,[29] coumarins were more randomly distributed and were also the more common coumarins such as umbelliferone, marmesin, bergapten, psoralen, and coumarin glycosides (scopolin, cichoriin, and xeroboside). The coumarins isolated in this study had a 7,8-dioxygenated-6-prenyl substitution pattern not previously observed in other Formosan Moraceous species, which could be of chemotaxonomic interest.

Experimental Section

General Experimental Procedures. All melting points were determined on a Yanaco micromelting point apparatus and are uncorrected. Optical rotations were measured on a JASCO P-1020 digital polarimeter. UV spectra were obtained on a JASCO UV-240 spectrophotometer in MeOH. IR spectra (KBr or neat) were taken on a Perkin-Elmer System 2000 FT-IR spectrometer. 1D (^{1}H, ^{13}C, DEPT) and 2D (COSY, NOESY, HSQC, HMBC) NMR spectra using $CDCl_3$ or acetone-d_6 as solvent were recorded on a Varian Unity Plus 400 (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) and a Varian INOVA-600 (600 MHz for ^{1}H NMR, 150 MHz for ^{13}C NMR) spectrometer. Chemical shifts were internally referenced to the solvent signals in $CDCl_3$ (^{1}H, δ 7.26; ^{13}C, δ 77.0), with TMS as the internal standard. Low-resolution ESIMS were obtained on an API 3000 (Applied Biosystem); high-resolution ESIMS on a Bruker Daltonics APEX II 30e spectrometer. Silica gel (70−230, 230−400 mesh) (Merck) was used for column chromatography, and silica gel 60 F-254 (Merck) was used for analytical and preparative TLC. Medium-pressure liquid chromatography was used for chromatograpy.

Plant Material. The whole plant of *F. pilosa* was collected from Ban-ping Mountain, Kaohsiung County, Taiwan, in August 2006, and identified by Prof. I. S. Chen. A voucher specimen (Chen 5672) was deposited in the Herbarium of School of Pharmacy, College of Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan, Republic of China.

Extraction and Isolation. Dried whole plant (2.1 kg) was sliced and extracted with cold MeOH (30 L) three times. After concentration under reduced pressure, the MeOH extract (240 g) was partitioned between EtOAc−H_2O (1:1) to obtain EtOAc-soluble (40 g) and H_2O-soluble fractions (195 g). The EtOAc fraction (40 g) was subjected to a silica gel column (230−400 mesh, 2.0 kg), eluting with a gradient of *n*-hexane−acetone, to give 18 fractions (A1−A18). Fraction A16 (3.6 g) was chromatographed on a silica gel column (230−400 mesh, 200 g), eluting with *n*-hexane−acetone (4:1), to give 11 fractions. Fraction A16-6 (0.3 g) was subjected to MPLC (SiO_2, 15 g), eluting with CH_2Cl_2−acetone (40:1), to afford (+)-fatouain E (**5**) (7.9 mg) and (−)-fatouain F (**6**) (3.2 mg). MPLC (SiO_2, 4 g) was applied to fraction A16-9 (0.08 g), eluting with CH_2Cl_2−acetone (20:1), to give six fractions. Fraction A16-9-3 (4 mg) was further purified by preparative RP-18 TLC (MeOH−H_2O, 3:1) to obtain (+)-fatouain A (**1**) (1.7 mg) and (−)-fatouain B (**2**) (1.6 mg). Fraction A16-9-5 (7 mg) was further purified by preparative TLC (*n*-hexane−acetone, 1:1) to yield (+)-fatouain H (**8**) (2.5 mg). Fraction A16-9-6 (5.2 mg) was further purified by preparative TLC (CH_2Cl_2−acetone, 40:1) to obtain (+)-fatouain G (**7**) (1.5 mg). Fraction A17 (4.50 g) was chromatographed on a silica gel column (230−400 mesh, 250 g), eluting with *n*-hexane−EtOAc (2:1), to give seven fractions. MPLC (SiO_2, 35 g) of fraction A17-2 (700 mg) involved eluting with acetone−H_2O (2:1) to give nine fractions, while fraction A17-2-2 (80 mg) was eluted with acetone−H_2O (2:1) to give four fractions. Fraction A17-2-2-1 (40 mg) was further purified by preparative RP-C_{18} TLC (acetone−H_2O, 1:3) to afford (+)-fatouain C (**3**) (8.5 mg) and (−)-fatouain D (**4**) (3.5 mg).

(+)-Fatouain A (1): colorless needles (acetone); mp 99−100 °C; $[\alpha]^{25}_D$ +37.9 (*c* 0.085, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 211 (4.42), 228 (sh) (4.17), 252 (sh) (3.57), 300 (4.12) nm; IR (KBr) ν_{max} 3417 (OH), 1727 (C=O), 1608, 1565 (benzene ring) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 150 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 150 MHz) see Table 2; ESIMS *m*/*z* 329 [M + Na]$^+$; HRESIMS *m*/*z* 329.1003 [M + Na]$^+$ (calcd for $C_{16}H_{18}O_6Na$, 329.1001).

(+)-Fatouain A-acetonide (1a). A solution of (+)-fatouain A (**1**) (2.0 mg) in acetone (1 mL) and a catalytic amount of *p*-TsOH were stirred for 20 min at room temperature. The mixture was neutralized with Et_3N, and the solvent was evaporated under reduced pressure. The residue was subjected to silica gel preparative TLC, yielding compound **1a** as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.55 (3H, s, H-6′ or 7′), 1.61 (3H, s, H-7′ or 6′), 1.84 (3H, s, H-5′), 3.95 (3H, s, OCH_3-8), 3.98 (3H, s, OCH_3-7), 4.14 (1H, d, *J* = 8.4 Hz, H-2′), 4.87 (1H, brt, *J* = 1.4 Hz, Ha-4′), 4.94 (1H, brt, *J* = 1.4 Hz, Hb-4′), 5.17 (1H, d, *J* = 8.4 Hz, H-1′), 6.33 (1H, d, *J* = 9.6 Hz, H-3), 7.37 (1H, s, H-5), 7.67 (1H, d, *J* = 9.6 Hz, H-4).

(−)-Fatouain B (2): colorless needles (acetone); mp 99−100 °C; $[\alpha]^{25}_D$ −39.9 (*c* 0.08, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 227 (sh) (4.08), 250 (3.52), 300 (3.87) nm; IR (KBr) ν_{max} 3416 (OH), 1738 (C=O),1606, 1565 (benzene ring) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 150 MHz) see Table 2; ESIMS *m*/*z* 329 [M + Na]$^+$; HRESIMS *m*/*z* 329.1004 [M + Na]$^+$ (calcd for $C_{16}H_{18}O_6Na$, 329.1001).

(+)-Fatouain C (3): colorless needles (acetone); mp 165−166 °C; $[\alpha]^{25}_D$ +31.6 (*c* 0.08, acetone); UV (MeOH) λ_{max} (log ε) 230 (sh) (3.97), 258 (3.73), 305 (3.85) nm; UV (MeOH+KOH) λ_{max} (log ε) 235 (sh) (3.85), 279 (4.02), 324 (3.74); IR (KBr) ν_{max} 3356 (OH), 1712 (C=O), 1614, 1569 (benzene ring) cm^{-1}; ^{1}H NMR (acetone-d_6, 400 MHz) see Table 1; ^{13}C NMR (acetone-d_6, 100 MHz) see Table 2; ESIMS *m*/*z* 315 [M + Na]$^+$; HRESIMS *m*/*z* 315.0846 [M + Na]$^+$ (calcd for $C_{15}H_{16}O_6Na$, 315.0845).

(+)-Fatouain C-acetonide (3a). Compound (**5**) (1.0 mg) was treated with *p*-TsOH and acetone under the same conditions as **3** to afford compound **5a** as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.56 (3H, s, H-6′ or 7′), 1.61 (3H, s, H-7′ or 6′), 1.83 (3H, s, H-5′), 3.97 (3H, s, OCH_3-7), 4.17 (1H, d, *J* = 8.4 Hz, H-2′), 4.88 (1H, brt, *J* = 1.5 Hz, Ha-4′), 4.94 (1H, brt, *J* = 1.5 Hz, Hb-4′), 5.18 (1H, d, *J* = 8.4 Hz, H-1′), 5.88 (1H, brs, OH-8, D_2O exchangeable), 6.34 (1H, d, *J* = 9.6 Hz, H-3), 7.22 (1H, s, H-5), 7.70 (1H, d, *J* = 9.6 Hz, H-4).

(−)-Fatouain D (4): colorless needles (acetone); mp 88−90 °C; $[\alpha]^{25}_D$ −13.4 (*c* 0.07, acetone); UV (MeOH) λ_{max} (log ε) 229 (sh) (4.02), 258 (3.80), 305 (3.88) nm; UV (MeOH+KOH) λ_{max} (log ε) 235 (3.77), 279 (3.86), 323 (3.60); IR (KBr) ν_{max} 3358 (OH), 1713 (C=O), 1614, 1571 (benzene ring) cm^{-1}; ^{1}H NMR (acetone-d_6, 400 MHz) see Table 1; ^{13}C NMR (acetone-d_6, 100 MHz) see Table 2; ESIMS *m*/*z* 315 [M + Na]$^+$; HRESIMS *m*/*z* 315.0846 [M + Na]$^+$ (calcd for $C_{15}H_{16}O_6Na$, 315.0845).

(−)-Fatouain D-acetonide (4a). Compound **4** (1.0 mg) was treated with *p*-TsOH and acetone under the same conditions as **1** to afford compound **4a** as a colorless oil: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.32 (3H, s, H-5′), 1.52 (3H, s, H-6′ or 7′), 1.69 (3H, s, H-7′ or 6′), 4.06 (3H, s, OCH_3-7), 4.69 (1H, brt, *J* = 1.4 Hz, Ha-4′), 4.92 (1H, d, *J* = 7.5 Hz, H-2′), 4.95 (1H, brt, *J* = 1.4 Hz, Hb-4′), 5.60 (1H, d, *J* = 7.5 Hz, H-1′), 6.30 (1H, d, *J* = 9.6 Hz, H-3), 7.16 (1H, s, H-5), 7.67 (1H, d, *J* = 9.6 Hz, H-4).

(+)-Fatouain E (5): colorless needles (acetone); mp 150−151 °C; $[\alpha]^{25}_D$ +54.3 (*c* 0.11, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 229 (sh) (4.01), 258 (3.76), 306 (3.88) nm; UV (MeOH+KOH) λ_{max} (log ε) 238 (sh) (3.83), 279 (4.06), 324 (3.76) nm; IR (KBr) ν_{max} 3314 (OH), 1726 (C=O), 1612, 1572 (benzene ring) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz) see Table 2; ESIMS *m*/*z* 329 [M + Na]$^+$; HRESIMS *m*/*z* 329.0999 [M + Na]$^+$ (calcd for $C_{16}H_{18}O_6Na$, 329.1001).

(−)-Fatouain F (6): colorless needles (acetone); mp 95−96 °C; $[\alpha]^{25}_D$ −75.7 (*c* 0.08, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 230 (sh) (4.06), 258 (3.83), 305 (3.93) nm; UV (MeOH+KOH) λ_{max} (log ε) 237 (sh) (3.91), 279 (4.10), 323 (3.82) nm; IR (KBr) ν_{max} 3391 (OH), 1727 (C=O), 1615, 1572 (benzene ring) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) see Table 1; ^{13}C NMR ($CDCl_3$, 150 MHz) see Table 2; ESIMS *m*/*z* 329 [M + Na]$^+$; HRESIMS *m*/*z* 329.1000 [M + Na]$^+$ (calcd for $C_{16}H_{18}O_6Na$ 329.1001).

(+)-Fatouain G (7): yellow needles (acetone); mp 99−101 °C; $[\alpha]^{25}_D$ +42.5 (*c* 0.08, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 230 sh (4.23), 260 (4.10), 312 (4.25) nm; UV (MeOH+KOH) λ_{max} (log ε) 234 (sh) (4.19), 272 (4.16), 324 (4.21) nm; IR (KBr) ν_{max} 3410 (OH), 1719 (C=O), 1613, 1572 (benzene ring) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.66 (3H, s, H-5′), 1.72 (3H, s, H-4‴), 1.78 (3H, s, H-5‴), 2.90 (1H, brs, OH-2′, D_2O exchangeable), 3.38 (2H, dd, *J* = 16.2, 7.2 Hz, H-1‴), 3.88 (3H, s, OCH_3-7), 4.81 (1H, brs, Ha-4′), 4.88 (1H, d, *J* = 8.1 Hz, H-2′), 4.93 (1H, brs, Hb-4′), 5.05 (1H, d, *J* = 8.1 Hz, H-1′), 5.33 (1H, brt, *J* = 7.2 Hz, H-2‴), 5.98 (1H, d, *J* = 9.3 Hz, H-3″), 6.02 (1H, brs, OH-1′, D_2O exchangeable), 6.33 (1H, d, *J* = 9.6 Hz, H-3), 6.94 (1H, s, H-5″), 7.24 (1H, s, H-5), 7.47 (1H, d, *J* = 9.3 Hz, H-4″), 7.71 (1H, d, *J* = 9.6 Hz, H-4), 9.05 (1H, s, OH-7″, D_2O exchangeable); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 17.8 (C-5′), 17.9 (C-

4‴), 25.8 (C-5‴), 27.8 (C-1‴), 61.0 (O$\underline{C}$H$_3$-7), 79.5 (C-2′), 84.7 (C-1′), 111.6 (C-10″), 112.2 (C-3″), 114.4 (C-3 or 10), 114.5 (C-10 or 3), 116.0 (C-4′), 119.0 (C-5), 121.2 (C-2‴), 123.1 (C-5″), 126.2 (C-6″), 127.6 (C-6), 132.6 (C-8), 133.8 (C-3‴), 135.9 (C-8″), 142.4 (C-3′), 143.2 (C-9), 143.8 (C-4″), 144.1 (C-4), 146.3 (C-9″), 148.1 (C-7), 151.8 (C-7″), 159.8 (C-2), 159.9 (C-2″); ESIMS *m/z* 543 $[M+Na]^+$; HRESIMS *m/z* 543.1627 $[M + Na]^+$ (calcd for $C_{29}H_{28}O_9Na$, 543.1631).

(+)-Fatouain H (8): yellow needles (acetone); mp 86−88 °C; $[\alpha]^{25}_D$ +21.0 (*c* 0.075, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 229 (4.50), 263 (4.37), 312 (4.16) nm; UV (MeOH+KOH) λ_{max} (log ε) 233 (4.47), 270 (4.44), 324 (4.13) nm; IR (KBr) ν_{max} 3461 (OH), 1729 (C=O), 1616, 1565 (benzene ring) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.54 (3H, s, H-5‴), 1.58 (3H, s, H-6‴), 1.77 (3H, s, H-5′), 3.81 (3H, s, O$\underline{C}$H$_3$-7), 3.98 (1H, brs, OH-2′, D_2O exchangeable), 4.53 (1H, d, J = 8.1 Hz, H-2′), 4.75 (1H, brs, Ha-4′), 4.78 (1H, brs, Hb-4′), 5.61 (1H, d, J = 8.1 Hz, H-1′), 5.72 (1H, d, J = 9.9 Hz, H-3‴), 6.00 (1H, brs, OH-8, D_2O exchangeable), 6.10 (1H, d, J = 9.6 Hz, H-3″), 6.32 (1H, d, J = 9.9 Hz, H-4‴), 6.32 (1H, d, J = 9.6 Hz, H-3), 6.81 (1H, s, H-5″), 7.46 (1H, d, J = 9.6 Hz, H-4″), 7.62 (1H, s, H-5), 7.83 (1H, d, J = 9.6 Hz, H-4); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 18.1 (C-5′), 28.2 (C-6‴), 28.3 (C-5‴), 60.6 (O$\underline{C}$H$_3$-7), 78.6 (C-2‴), 80.0 (C-2′), 82.0 (C-1′), 112.9 (C-10″), 113.4 (C-3″), 114.1 (C-3), 114.3 (C-10), 114.8 (C-4′), 118.8 (C-6″), 119.2 (C-5), 119.7 (C-5″), 120.9 (C-4‴), 128.0 (C-6), 131.0 (C-3‴), 133.2 (C-8″), 135.0 (C-8), 142.4 (C-3′), 142.6 (C-9), 143.3 (C-4″), 144.6 (C-4), 147.8 (C-7 or 9″), 147.9 (C-9″ or 7), 148.7 (C-7″), 159.6 (C-2″), 159.9 (C-2); ESIMS *m/z* 517 $[M - H]^+$; HRESIMS *m/z* 541.1477 $[M + Na]^+$ calcd for $C_{29}H_{26}O_9Na$, 541.1474).

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Supporting Information Available: 1D and 2D NMR spectra for compounds **1**−**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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