Limonoids of the Phragmalin Type from *Swietenia macrophylla* and Their Chemotaxonomic Significance

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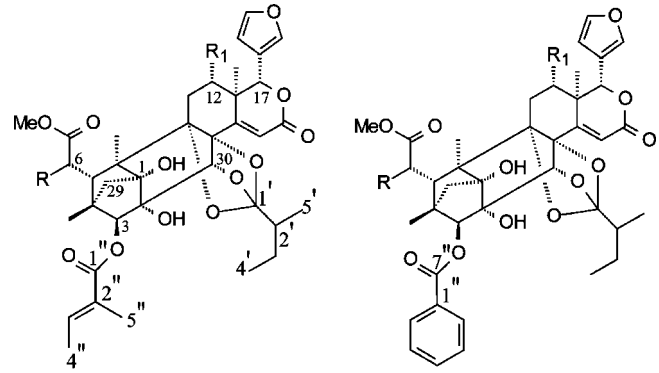
Species of *Swietenia* elaborate limonoid chemistry along only one route, which leads to the mexicanolide type in most species and the phragmalin type in *S. mahogani*. A hexane extract from leaves of *S. macrophylla* afforded six new phragmalins with a 8,9,30-ortho-ester unit, namely, 6-*O*-acetylswietephragmin E (**1**), 3*β*-*O*-destigloyl-3*β*-*O*-benzoyl-6-*O*-acetylswietephragmin E (**2**), 12α-acetoxyswietephragmin C (**3**), 3*β*-*O*-destigloyl-3*β*-*O*-benzoyl-12α-acetoxyswietephragmin C (**4**), 12α-acetoxyswietephragmin D (**5**), and 3*β*-*O*-destigloyl-3*β*-*O*-benzoyl-12α-acetoxyswietephragmin D (**6**). This appears to be the first record of phragamalins from *S. macrophylla*, and this study shows the potential of tricyclic [3.3.$1^{2,10}$.$1^{1,4}$]-decane limonoids as taxonomically useful chemical markers in the Meliaceae.

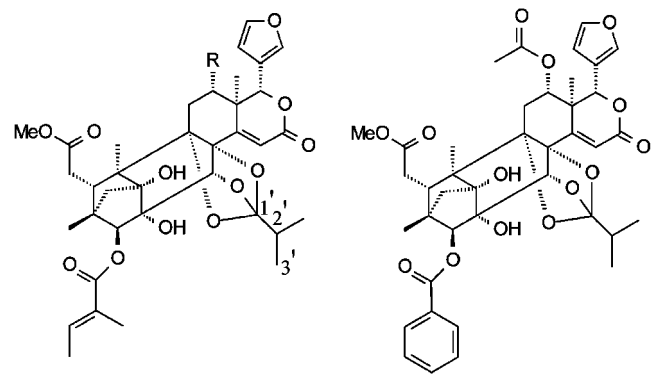
The family Meliaceae, comprising about 50 genera, provides valuable timber, such as mahogany (*Swietenia*) and cedar (*Cedrela*). The name "mahogany" refers to the red-brown wood of the species *Swietenia mahogani*, known as West Indian mahogany. Closely related to this is *S. macrophylla*, known as South American mahogany, which is also a highly valued timber species. This genus consists of three species, *S. mahogani* Jacq., *S. macrophylla* King, and *S. humilis* Zucc., and two natural hybrids. One is a product of a cross between *S. macrophylla* and *S. humilis* and is found in the areas of the distribution range in which these two species overlap. The second is a cross between *S. macrophylla* and *S. mahogani*, named *S.* x *aubrevilleana*.[1]

Pennington and Styles classified the Meliaceae genera into four subfamilies, the Swietenioideae, Melioideae, Quivisianthoideae, and Capuronianthoideae.[1] Chemically, the family Meliaceae is distinguished by the frequent occurrence of characteristic limonoids, which are derived from tirucallol (20αH) or euphol (20*β*H) precursors, by oxidative opening either of rings D (**1.1**), B (**1.2**), or C (**1.3**), or both rings B/D (**1.1.1**) or A/B (**1.2.1**), as shown in Figure S1, Supporting Information.[2−5] Genera of the Melioideae subfamily are the most prolific in the production of A,B-*seco* limonoids (**1.2.1**) but relatively deficient in the mexicanolide type (**1.1.1.1**). The C-*seco* limonoids (**1.3**) have so far been recorded only in genera of the Melioideae. In contrast, genera of the Swietenioideae contain mainly limonoids of the mexicanolide (**1.1.1.1**) and phragmalin groups (**1.1.1.1.1**).[2−5] Quivisianthoideae and Capuronianthoideae are related phytochemically to normal members of the Swietenioideae, which also accumulate limonoids of the mexicanolide group (**1.1.1.1**).[6,7]

Limonoids with an intact carbon skeleton (**1**), B,D-*seco* (**1.1.1**; Figures S1 and S2, Supporting Information) and mexicanolides (**1.1.1.1**, Figures S1 and S3, Supporting Information) have been reported from *Swietenia* species, but the phragmalin type (**1.1.1.1.1**, Figures S1 and S4, Supporting Information) appears to be present only in *S. mahogani* (Table S1, Supporting Information). However, phragmalins have been found only in the leaves and stem bark of *S. mahogani*, which were not studied in other species (Table S1). We describe herein the isolation and structural elucidation of six new limonoids, **1**−**6**, possessing an ortho-ester group at the 8,9,30 positions, similar to swietephragmins C−E,[8] from the leaves of *S. macrophylla*.



1: R = OAc, R_1 = H
2: R = OAc, R_1 = H
3: R = H, R_1 = OAc
4: R = H, R_1 = OAc



5: R = OAc
6

Results and Discussion

The hexane extract from leaves of *S. macrophylla* after repetitive chromatographic separation afforded six new limonoids, **1**−**6**.

Limonoid **1** gave a molecular formula of $C_{39}H_{48}O_{14}$ as determined from the pseudomolecular ion peak at *m*/*z* 763.6 [M + Na]$^+$ in the positive ESIMS and by elemental analysis. The ^{1}H NMR spectrum (Table 1) indicated the presence of three tertiary methyl groups (δ_H 1.31, 1.27, 0.98), a methyl group of

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Table 1. ^{1}H NMR Chemical Shifts of Compounds **1**−**6**[a]

position	1	2	3	4	5	6
3	4.78 s	5.00 s	4.83 s	5.03 s	4.83 s	5.04 s
5	2.81 brs	2.97 brs	2.41 brs	2.58 d (12)	2.42 d (12.2)	2.58 d (12)
6	5.48 brs	5.55 s	3.19 d 2.36 d (15.8)	3.25 d (16.5) 2.41 dd (16.5, 12)	3.19 d (15.6) 2.37 m	3.26 d (16.7) 2.41 dd (16.7, 12)
11		2.17 m	2.21 m 1.90 m		2.18 m	2.23 dd (13.4, 4.0) 1.90 m
12	1.19 m 1.68 m	1.75 m 1.21 m	4.79 dd (13.5, 4.0)	4.79 dd (13.2, 4.2)	4.79 dd (13.2, 3.9)	4.84 dd (13.4, 4.0)
15	5.94 s	5.75 s	6.01 s	6.02 s	6.02 s	5.83 s
17	5.64 s	5.74 s	5.82 s	5.83 s	5.83 s	5.91 s
Me-18	1.31 s	1.24 s	1.51 s	1.51 s	1.51 s	1.43 s
Me-19	1.27 s	1.31 s	1.31 s	1.31 s	1.31 s	1.35 s
21	7.50 brs	7.52 brs	7.46 d (1.0)	7.52 brs	7.41 t (1.7)	7.49 brs
22	6.45 d (1.0)	6.43 d (1.1)	6.55 d (1.1)	6.42 brs	6.55 d (1.2)	6.50 d (1.3)
23	7.43 t (1.5)	7.44 m	7.41 t (1.7)	7.44 m	7.46 brs	7.40 t (1.6)
Me-28	0.98 s	1.07 s	0.82 s	0.82 s	0.82 s	0.92 s
29	2.08 d (10.8) 1.79 m	2.16 d 1.89 d (11.1)	2.43 d 1.78 d (11.3)	1.89 m	1.85 m	1.93 d 1.85 d (10.1)
30	4.47 s	4.52 s	4.48 s	4.52 s	4.49 s	4.54 s
$\underline{CH_3}CO$	2.22 s	2.25 s	1.53 s	1.52 s	1.53 s	1.53 s
2′	1.92 m	1.88 m	1.92 m	1.92 m	2.19 m	2.18 m
3′	1.70 m	1.69 m	1.70 m 1.22 m		1.04 d (6.6)	1.04 d (6.8)
4′	0.92 t (7.5)	0.91 t (7.4)	0.93 t (7.5)	0.93 t (7.8)	1.04 d (6.6)	1.04 d (6.8)
5′	1.01 d (6.6)	1.01 d (6.8)	1.02 d (6.9)	1.01 d (6.9)		
2”		7.99 dd (7.5, 1.8)		8.08 dd (8.5, 1.5)		8.08 dd (8.5, 1.3)
3”	6.76 dq (7.2, 1.1)	7.44 m	6.93 qq (7.0, 1.4)	7.45 m	6.94 qq (7.0, 1.5)	7.44 t (7.9)
4”	1.73 dd (7.2, 1.1)	7.59 t (7.5)	1.72 dd (7.0, 1.1)	7.45 m	1.73 dd (7.0, 1.1)	7.57 t (7.9)
5”	1.83 t (1.1)	7.44 m	1.84 dd (1.4, 1.1)	7.45 m	1.84 brs	7.44 t (7.9)
6”		7.99 dd (7.5, 1.8)		8.08 dd (8.5, 1.5)		8.08 dd (8.5, 1.3)
1-OH	3.51 s	3.56 s	3.40 s	3.72 s	3.41 s	3.44 s
2-OH	3.54 s	3.62 s	3.56 s	3.44 s	3.58 s	3.58 s
$O\underline{CH_3}$	3.75 s	3.82 s	3.74 s	3.79 s	3.74 s	3.80 s

[a] Spectra of **1**−**6** were run in $CDCl_3$ and coupling constants are in Hz.

an acetate function (δ_H 2.22), a methoxyl singlet (δ_H 3.75 s), two signals for vinylic methyls (δ_H 1.83 t, J = 1.1 Hz; 1.73 dd, J = 7.0 and 1.1 Hz), three downfield shifted signals attributable to a β-substituted furan ring (δ_H 7.50, 7.43, 6.45), four signals characteristic of protons attached to a carbon adjacent to an oxygen atom (δ_H 5.64 s; 4.78 s; 5.48 brs; 4.47 s), two olefinic protons (δ_H 5.94 s; 6.76 dq, J = 7.2 and 1.1 Hz), an AB-type methylene (δ_H 2.08 d, J = 10.8 Hz; 1.79 m), and four signals characteristic of a 2-substituted-butyl group (δ_H 1.01 d, J = 6.6 Hz; 1.92 m; 1.70 m; 0.92 t, J = 7.5 Hz). The ^{13}C NMR spectrum revealed 39 carbon signals, which were assigned by DEPT and HETCOR experiments (Table 2). The HMBC spectrum of **1** showed correlation characteristics of a furan ring at C-17 of a D-ring α,β-unsaturated δ-lactone limonoid. The principal correlations observed were between H-17 (δ_H 5.64, δ_C 79.8)/C-21 (δ_C 141.8); H_3-18 (δ_H 1.31, δ_C 19.7)/C-17, C-12 (δ_C 29.3), C-13 (37.8), and C-14 (δ_C 152.7); and H-15 (δ_H 5.94)/C-16 (δ_C 162.8). Moreover, the correlations observed between H-15/C-8 (δ_C 83.6) and 2H-12 (δ_H 1.19 and 1.68)/C-9 (δ_C 86.8) indicated a tertiary hydroxyl or ether substituent at C-8 and C-9. The oxymethine proton at δ_H 4.47 showed a one-bond correlation with the ^{13}C NMR signals at δ_C 77.7 and cross-peaks with δ_C 122.5 and C-8, thus indicating the presence of an ether function at C-30 and permitting the assignment of the signals at δ_H 4.47 to H-30, δ_C 77.7 to C-30, and δ_C 122.5 to an ortho-carbon. The HMBC spectrum suggested the presence of an isolated structural unit, $-CH(CH_3)CH_2CH_3$ (δ_H 1.01 d, 3H, J = 6.6 Hz; 1.92 m, 1H; 1.70 m, 2H; 0.92 t, 3H, J = 7.5 Hz). The methyl signal at δ_H 1.01 showed a cross-peak with the ^{13}C NMR signal at δ_C 122.5, characteristic of an ortho-carbon, identified as a 2-methylbutanoate group, which was located at the positions C-8, C-9, and C-30.

The AB-type methylene protons at δ_H 2.08 and 1.79 were attributed to H_2-29 by their correlation with the C-1 signal at δ_C 84.6 and suggested that **1** is a phragmalin-type limonoid. The methyl proton signal at δ_H 0.98 and the H_2-29 signals showed cross-peaks with the ^{13}C NMR signal at δ_C 86.9, which exhibited a one-bond correlation with the ^{1}H NMR signal at δ_H 4.78 and a long-range correlation to the ^{13}C NMR signal at δ_C 167.6, thus indicating that an ester substituent occurred at C-3 and leading to their assignments as H_3-28, C-3, and H-3, respectively. The HMBC correlations between H-3″ (δ_H 6.76, δ_C 139.5)/C-1″ (δ_C 167.6), C-2″ (δ_C 129.9); H_3-5″ (δ_H 1.83)/C-1″; and H_3-4″ (δ_H 1.73, δ_C 12.4)/C-3″ (δ_C 139.5), C-2″ suggested a tigloyl ester at C-3. A hydroxyl must be connected to C-2 due to the observed correlation between the H-3 signal and ^{13}C NMR quaternary signal at δ_C 75.6.

The oxymethine proton at δ_H 5.48 showed a one-bond correlation with the ^{13}C NMR signal at δ_C 71.4 and long-range correlation with the signal for C-5 and the ^{13}C NMR signals at δ_C 169.8 and 171.0. The methoxyl singlet at δ_H 3.75 showed a cross-peak with the ^{13}C NMR signal at δ_C 171.0, and a methyl signal at δ_H 2.22 correlated to δ_C 169.8, indicating the presence of a carbomethoxy group at C-7 and an acetoxyl substituent at C-6.

The structural assignment was also supported by comparison of the ^{13}C NMR spectrum of **1** (Table 2) with that of swietephragmin E.[8] The stereochemistry suggested for **1** was based on the biosynthesis of limonoids.[3] However, for H-3 and H-30 the configurations were assigned by g-NOESY 1-D experiments, which showed a NOE between H-30 (δ_H 4.47) and H-15 (δ_H 5.94), requiring H-30 to be on the β-side of the molecule. Inspection of a model for **1** showed that when H-30 is on the β-side of the molecule, the formation of a less strained 8,9,30-*ortho*-2-methylbutanoate group is allowed only on the α-side. In addition, irradiation of the H-3 signal at δ_H 4.78 showed a NOE with the H-29 signal at δ_H 1.79, showing that H-3 is thus on the α-side of the molecule. The new natural product was, therefore, assigned as 6-*O*-acetylswietephragmin E (**1**).

Limonoid **2** showed spectroscopic characteristics similar to those of **1**. The principal changes observed in the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of **2** were due to the replacement of the resonances for a tigloyl ester by signals for a benzoate group (δ_H 7.99 dd, J = 7.5 and 1.8 Hz, 2H; 7.44 m, 2H; 7.59 t, J = 7.5 Hz; 166.5, 139.4; 129.7, 2C; 129.0, 2C; 134.2). An HMBC experiment, in addition to showing correlations similar to those of **1**, revealed a cross-peak of the ^{1}H NMR signal at δ_H 5.00, assigned to H-3, with the ^{13}C NMR signal at δ_C 166.5, aiding the location of the benzoate group at C-3. This conclusion was supported by the observed correlation between the aromatic ^{1}H NMR signals and ^{13}C NMR

Table 2. ^{13}C NMR Chemical Shifts of Compounds **1**−**6**[a]

carbon	1	2	3	4	5	6
1	84.6	84.6	84.5	84.5	84.4	84.5
2	75.6	75.6	75.7	75.7	75.7	75.7
3	86.9	87.4	86.6	87.1	86.5	86.4
4	43.6	43.7	43.8	43.9	43.8	43.9
5	44.8	44.9	40.7	40.8	40.6	40.8
6	71.4	71.5	32.9	33.0	32.9	33.0
7	171.0	171.2	174.6	174.7	174.5	174.7
8	83.6	83.7	83.3	83.4	83.4	83.6
9	86.8	86.8	86.3	86.3	86.3	87.2
10	48.4	48.4	47.3	47.4	47.3	47.4
11	25.6	25.6	32.0	32.1	32.0	32.1
12	29.3	29.3	68.6	68.6	68.6	68.6
13	37.8	38.0	42.7	42.8	42.7	42.9
14	152.7	152.7	151.3	151.3	151.2	151.3
15	122.4	122.2	123.9	123.6	123.9	123.7
16	162.8	161.8	162.4	161.3	162.4	161.3
17	79.8	79.7	78.2	78.1	78.2	78.0
Me-18	19.7	19.5	14.5	14.4	14.4	14.3
Me-19	16.3	16.4	15.5	15.5	15.5	15.5
20	119.5	119.6	121.3	121.4	121.2	121.4
21	141.8	141.7	141.9	141.8	143.1	141.8
22	110.0	110.0	110.3	110.3	110.2	110.3
23	143.1	143.0	143.0	143.0	143.1	143.0
Me-28	15.5	15.5	14.4	14.3	14.3	14.4
29	39.8	39.8	38.9	38.9	38.9	39.8
30	77.7	77.6	78.1	78.0	78.1	78.2
$\underline{C}H_3CO$	21.0	21.1	19.8	19.8	19.8	19.8
$CH_3\underline{C}O$	169.8	169.7	170.4	170.5	170.4	170.4
1″	167.6	139.4	167.8	129.6	167.8	129.7
2″	129.9	129.7	130.0	129.7	130.0	129.8
3″	139.5	129.0	139.8	129.1	139.8	129.0
4″	12.4	134.2	12.4	134.1	12.4	134.1
5″	14.3	129.0	14.6	129.1	14.5	129.0
6″		129.7		129.7		129.8
7″		166.5		166.7		166.7
1′	122.5	122.4	122.7	122.7	122.7	122.7
2′	35.5	35.5	35.5	35.5	28.9	29.0
3′	23.7	23.7	23.7	23.7	16.7	16.6
4′	11.6	11.6	11.6	11.6	16.8	16.7
5′	13.3	13.5	13.3	13.3		
$\underline{C}H_3O$	53.2	53.4	52.1	52.2	52.1	52.2
$\underline{C}H_3CO$						
$CH_3\underline{C}O$						

[a] The spectra of **1**−**10** were run in $CDCl_3$. Assignments are based on HETCOR, HSQC, and HMBC experiments.

signal at δ_C 166.5. In a g-NOESY 1D experiment, NOE interactions of H-30 at δ_H 4.52 with H-15 (δ_H 5.75) and H-5 (δ_H 2.97; weak) required H-30 to be on the β-side of the molecule. This implied that the 8,9,30-*ortho*-2-methylbutanoate group is thus in the α-orientation. In the same way, a NOE interaction of H-29 at δ_H 1.89 with H-3 at δ_H 5.00 showed that H-3 is thus on the α-side of the molecule. Elemental analysis and ESIMS confirmed the molecular formula as $C_{41}H_{46}O_{14}$. The structure of the new natural product **2** was thus established as 3β-*O*-destigloyl-3β-*O*-benzoyl-6-*O*-acetylswietephragmin E.

Limonoid **3** also showed spectroscopic characteristics of an 8,9,30-*ortho*-2-metylbutanoate of 1,2-dihydroxy-3β-*O*-tigloylphragmalin. Elemental analysis and ESIMS indicated the molecular formula to be $C_{39}H_{48}O_{14}$, which strongly suggested this compound to be an isomer of **1**. However, the methyl proton at δ_H 1.51 showed long-range correlations with the C-17 signal (δ_C 78.2) and the ^{13}C NMR signals at δ_C 68.6 (CH, by HETCOR and DEPT 135°), 42.7 (quaternary), and 151.3, thus indicating a double bond at C-14 and a secondary hydroxyl or ester substituent at C-12 and leading to their assignments as H_3-18, C-12, C-13, and C-14, respectively. The C-12 signal at δ_C 68.6 showed one-bond correlations with the ^1H NMR signals at δ_H 4.79 (dd, J = 13.5 and 4.0 Hz), which was coupled to the ^1H NMR signals at δ_H 2.21 and 1.90 (m), permitting their assignment to 2H-11. The ^1H NMR signals at δ_H 4.79 and a methyl signal at δ_H 1.53 showed a long-range correlation with the ^{13}C NMR signals at δ_C 170.4, indicating an acetoxyl group at C-12. The ^1H NMR and HMBC experiments suggested the presence of the structural unit $-CH_2COOMe$ (δ_H 3.19, d; 2.36 d, J = 15.8 Hz; 2H-6; 3.74, s) for C-6 and C-7. The NOESY experiments showed correlations between H-12 and H-17 (δ_H 5.82), H-5 (δ_H 2.41), and Hβ-6 (δ_H 3.19), indicating a β-orientation for these four hydrogens. In addition, the signal of H-29 (δ_H 1.78) showed cross-peaks with the signals of H-3, thereby requiring H-3 to be on the α-side of the molecule. The structural assignment was also supported by comparison of the ^{13}C NMR spectrum (Table 2) with that of swietephragmin C.[8] Thus, the structure of compound **3** was proposed as 12α-acetoxyswietephragmin C.

Limonoid **4** exhibited similar NMR spectra to those of an 8,9,30-*ortho*-2-metylbutanoate of 1,2-dihydroxy-3β-*O*-benzoylphragmalin. Elemental analysis and ESIMS indicated the molecular formula to be $C_{41}H_{46}O_{14}$, which suggested it to be an isomer of **2**. However, a long-range correlation observed between the methyl proton signal at δ_H 1.51 and the C-17 signal (δ_C 78.1) and the ^{13}C NMR signals at δ_C 68.6 (CH, by HETCOR and DEPT 135°) thus indicated a secondary acetoxyl substituent now affixed to C-12, similar to **3**. The coupling constants for H-12 (δ_H 4.79 dd, J = 13.2 and 4.2 Hz) were in agreement with a pseudoaxial orientation as in **3** and in xyloccensin Q (δ_H 4.80 dd, J = 4.0, 13.5 Hz). The structural assignment was also supported by comparison of the ^{13}C NMR spectrum (Table 3) with those of **2**, **3**, and xyloccensin Q.[9] In the

g-NOESY experiments, the observed NOE interactions were similar to those found for **3**. The new natural product **4** was proposed as 3β-*O*-destigloyl-3β-*O*-benzoyl-12α-acetoxyswietephragmin C.

Limonoid **5** showed spectroscopic characteristics similar to those of **3**. The principal changes observed in the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of **5** were the replacement of resonances for an *ortho*-2-methylbutanoate group by signals for an *ortho*-isobutylate (δ_H 2.19 m; 1.04 d, 6H, J = 6.6 Hz; δ_C 122.7; 28.9; 16.7; 16.8). The HMBC experiments, in addition to showing correlations similar to those for **3**, revealed a cross-peak of the ^{1}H NMR signal at δ_H 4.49, assigned to H-30, with the ^{13}C NMR signal at δ_C 122.7. The methyl signal (6H) resonating at δ_H 1.04 showed a cross-peak with the ^{13}C NMR signal at δ_C 122.7, characteristic of an ortho-carbon, identified as an isobutylate group, which was located at positions C-8, C-9, and C-30. In a g-NOESY 1D experiment, the NOE interaction of H-30 at δ_H 4.49 with H-15 (δ_H 6.02) and H-5 (δ_H 2.42; weak) required H-30 to be on the β-side of the molecule. This implied that the 8,9,30-*ortho*-isobutylate group is thus in an α-orientation. A NOE interaction of the H-12 signal at δ_H 4.79, coming from H-17 at δ_H 5.83 and H-5 at δ_H 2.42, showed that H-12 was thus on the β-side of the molecule. Elemental analysis and ESIMS confirmed the molecular formula as $C_{38}H_{46}O_{14}$. The structural assignment was also supported by comparison of the ^{13}C NMR spectrum (Table 3) with that of swietephragmin D.[8] Thus, the structure of the new natural product **5** was thus established as 12α-acetoxyswietephragmin D.

Limonoid **6** also showed spectroscopic characteristics of an 8,9,30-*ortho*-isobutylate of 1,2-dihydroxyphragmalin. The principal change observed in the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) of **6** when compared to compound **5** was the replacement of resonances for a tigloyl ester by signals for a benzoate group (δ_H 8.08 dd, J = 8.5 and 1.3 Hz, 2H; 7.44 t; J = 7.9 Hz, 2H; 7.57 t, J = 7.9 Hz; δ_C 166.7; 129.7; 129.8; 2C; 129.0, 2C; 134.1). The HMBC experiment, in addition to showing correlations similar to those for **5**, revealed a cross-peak of the ^{1}H NMR signal at δ_H 5.04, assigned to H-3, with the ^{13}C NMR signal at δ_C 166.7, helping to determine the position of the benzoate group at C-3. This conclusion was supported by the observed correlation between the aromatic ^{1}H NMR signals and the ^{13}CNMR signal at δ_C 166.7. In a g-NOESY 1D experiment, the observed NOE interactions were similar to those found for **5**. Elemental analysis and ESIMS confirmed the molecular formula as $C_{40}H_{44}O_{14}$. The structure of the new natural product **6** was thus established as 3β-*O*-destigloyl-3β-*O*-benzoyl-12α-acetoxyswietephragmin D.

Compounds **1**−**6** show significant chemotaxonomic evidence in favor of the link between the species *S. macrophylla* and *S. mahogany*. As discussed earlier, species of *Swietenia* elaborate limonoid chemistry along only one route, which leads to compounds of the mexicanolide group (**1.1.1.1**) in all species and of the phragmalin type (**1.1.1.1.1**) only in *S. mahogani*. The present study appears to be the first record of phrgamalins from *S. macrophylla*. This study supports the use of phragmalins as taxonomically useful chemical markers in this species and clearly shows that the leaves, stems, and roots of *Swietenia* species are in need of further phytochemical work, particularly searching for limonoids with a tricyclic [3.3.1^{2,10}.1^{1,4}] decane ring system.

Experimental Section

General Experimental Procedures. Optical rotations were measured by using a Perkin-Elmer 241 spectropolarimeter. IR spectra were recorded on a Bomen-Ft/IR spectrometer. NMR spectra were recorded in $CDCl_3$ at room temperature on a Bruker DRX 400 and a Varian Mercury-300 NMR spectrometer, and the solvent resonance was used as internal shift reference (tetramethylsilane as standard). The 2D NMR spectra were recorded by using standard pulse sequence. ESIMS were recorded on a Micromass Quattro LC instrument, equipped with a "Z-spray" ion source. Elemental analyses were recorded on an EA 1108, CHNS-O (Fisons). HPLC was performed on a Shimadzu model SCL-10A.

Plant Material. *Swietenia macrophylla* was collected in Aurora do Pará, Pará State, Brazil, in April 2002, and was identified by Prof. Dr. Orlando Shigueo Ohashi from the Botany Department, Universidade Federal Rural da Amazônia, Brazil. A voucher specimen (no. 1320) was deposited at the Herbarium of the Museum Paraense Emílio Goeldi, Belém, Pará, Brazil.

Extraction and Isolation. Ground leaves (1.4 kg) from *S. macrophylla* were extracted with hexane, then CH_2Cl_2, and finally MeOH, at room temperature, three times. The concentrated hexane extract (30 g) was subjected to column chromatography over silica gel (70−230 mesh) under vacuum. Elution with a hexane−EtOAc gradient yielded four fractions. Purification of fraction 4 was carried out by applying to an ODS (C_{18}) SPE cartridge. The solvent was removed from the cartridge under vacuum. The eluent was evaporated and resuspended in MeOH and subjected to rp-HPLC (H_2O−MeOH, 28:72; detection, UV 217 nm, flow rate, 4.7 mL min^{-1}, Phenomenex Gemini C_{18} column, 250 × 10 mm i.d.), yielding compounds **1** (42 min; 13.6 mg), **2** (31 min; 24.8 mg), **3** (44 min; 26.1 mg), **4** (35 min; 10.5 mg), **5** (47 min; 15.4 mg), and **6** (38 min; 13.7 mg).

6-*O*-Acetylswietephragmin E (1): amorphous, white solid; $[\alpha]_D^{25}$ −10.6 (*c* 0.0012, $CHCl_3$); IR (film) ν_{max} 3520 (OH), 1730 (carboxyl group) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m/z* 763.6 [M + Na]$^+$ (100); *anal*. found C 63.30%, H 6.43%, calcd for $C_{39}H_{48}O_{14}$, C 63.23%, H 6.53%, O 30.24%.

3β-*O*-Destigloyl-3β-*O*-benzoyl-6-*O*-acetylswietephragmin E (2): amorphous, white solid; $[\alpha]_D^{25}$ −12.6 (*c* 0.003, $CHCl_3$); IR (film) ν_{max} 3509 (OH), 1731 (carboxyl group) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m/z* 785.3 [M + Na]$^+$ (100); *anal*. found C 64.40%, H 6.09%, calcd for $C_{41}H_{46}O_{14}$, C 64.56%, H 6.08%, O 29.36%.

12α-Acetoxyswietephragmin C (3): amorphous, white solid; $[\alpha]_D^{25}$ +54.0 (*c* 0.003, $CHCl_3$); IR (film) ν_{max} 3507 (OH), 1730 (carboxyl group) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m/z* 763.6 [M + Na]$^+$ (100); *anal*. found C 63.27%, H 6.50%, calcd for $C_{39}H_{48}O_{14}$, C 63.23%, H 6.53%, O 30.24%.

3β-*O*-Destigloyl-3β-*O*-benzoyl-12α-acetoxyswietephragmin C (4): amorphous, white solid; $[\alpha]_D^{25}$ +30.4 (*c* 0.003, $CHCl_3$); IR (film) ν_{max} 3473 (OH), 1728 (carboxyl group) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m/z* 785.3 [M + Na]$^+$ (100); *anal*. found C 64.50%, H 6.10%, calcd for $C_{41}H_{46}O_{14}$, C 64.56%, H 6.08%, O 29.36%.

12α-Acetoxyswietephragmin D (5): amorphous, white solid; $[\alpha]_D^{25}$ +23.4 (*c* 0.003, $CHCl_3$); IR (film) ν_{max} 3473 (OH), 1728 (carboxyl group) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m/z* 749.3 [M + Na]$^+$ (100); *anal*. found C 63.00%, H 6.25%, calcd for $C_{38}H_{46}O_{14}$, C 62.80%, H 6.38%, O 30.82%.

3β-*O*-Destigloyl-3β-*O*-benzoyl-12α-acetoxyswietephragmin D (6): amorphous, white solid; $[\alpha]_D^{25}$ −13.4 (*c* 0.003, $CHCl_3$); IR (film) ν_{max} 3473 (OH), 1728 (carboxyl group) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), see Table 1; ^{13}C NMR (100 MHz, $CDCl_3$), see Table 2; ESIMS *m/z* 749.3 [M + H]$^+$ (100); *anal*. found C, 64.10%, H 6.00%, calcd for $C_{40}H_{44}O_{14}$, C 64.16%, H 5.92%, O 29.91%.

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Supporting Information Available: Biogenetic pathway for limonoid types found in the family Meliaceae (Figure S1), occurrence of limonoids classified into structural types (Figures S2−S4) in *Swietenia* species (Table S1), and ^{1}H and ^{13}C NMR spectra of compounds **1**−**6** are available free of charge via the Internet at http://pubs.acs.org.

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