# Tetranortriterpenoids from *Swietenia macrophylla*

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Received September 18, 1997; accepted November 10, 1997

**Five new tetranortriterpenoids, methyl 3β-tigloyloxy-2,6-dihydroxy-1-oxo-meliac-8(30)-enate, methyl 3β-tigloyloxy-2-hydroxy-1-oxo-meliac-8(30)-enate, methyl 3β-tigloyloxy-2-hydroxy-8α,30α-epoxy-1-oxo-meliacate, methyl 3β-acetoxy-2,6-dihydroxy-8α,30α-epoxy-1-oxo-meliacate and methyl 3β-isobutyryloxy-2,6-dihydroxy-8α,30α-epoxy-1-oxo-meliacate, were isolated from the seeds of *Swietenia macrophylla*. The structure of these five tetranortriterpenoids was established by comprehensive spectral analysis.**

**Key words** *Swietenia macrophylla*; Meliaceae; tetranortriterpenoid

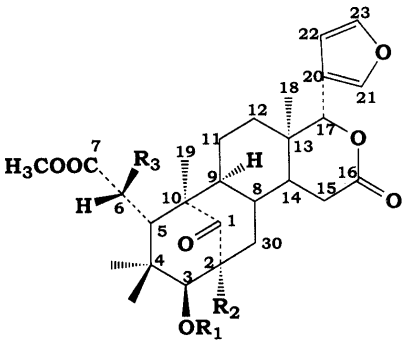
*Swietenia macrophylla* KING (Meliaceae) is a valuable timber tree in Mexico, India and Malaysia. In Mexico, the mahogany tree is called "caoba". *S. macrophylla* is closely related to *S. mahagoni* and this species is probably the most important caoba and produces an excellent wood.[1-4] The seeds of this plant are rich in fat, and the composition of this seed fat has been reported together with the possibility of using the oil.[5,6] In Malaysia, the seeds are used as a folk medicine for treatment of hypertention.[7] The presence of swietenine (**1**),[2-4,8] swietenolide (**2**),[9,10] swietenine acetate (**3**),[11] swietenolide tiglate (**4**),[11] swietenolide diacetate (**5**)[7,11] and 8, 30 epoxy swietenine acetate (**6**)[11] in the seeds of *S. macrophylla* has been reported. In the course of our investigations of biologically significant substances from medicinal plants found in Mexico, we have isolated five new tetranortriterpenoids (**7**—**11**) with two known ones (**12**, **13**) from the seeds of *S. macrophylla*.

The seeds were extracted with $CHCl_3$, $Me_2CO$ and MeOH successively, and these extracts were treated in the usual manner including normal-phase and reversed-phase column chromatography; **7**—**13** were isolated from the $CHCl_3$ and $Me_2CO$ extracts, sucrose and raffinose were isolated from the MeOH extract.

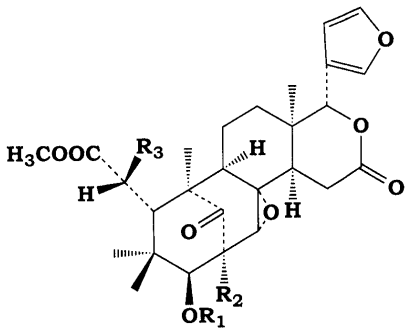
Compound **12** was identified as swietenine C isolated from *S. mahagoni*,[12-14] and **13** was humilin B isolated from *S. humilis*,[15] by comparison with reported data.

Compound **10** showed a $[M+H]^+$ peak at *m/z* 589.2643 ($C_{31}H_{41}O_{11}$). The presence of four *tert*-methyl groups ($\delta_H$ 0.85, 1.06, 1.08, 1.44), three methylene signals ($\delta_C$ 20.5, 32.2, 32.6), a β-substituted furan ($\delta_H$ 6.37, 7.43, 7.44; $\delta_C$ 109.7, 120.8, 140.7, 143.6), a lacton ($\delta_C$ 170.6), and a methylester ($\delta_H$ 3.92; $\delta_C$ 53.6) in the $^1$H- and $^{13}$C-NMR spectra, indicated that **10** was swietenine-type tetranortriterpenoid.

The presence of a trisubstituted epoxide at C-8/C-30 was confirmed by the appropriate $^1$H ($\delta_H$ 3.41) and $^{13}$C ($\delta_C$ 62.8, 67.2) signals. The signals due to H-30 and H-3 ($\delta_H$ 4.97) appeared as singlets, suggesting that C-2 was fully substituted and, from this and the chemical shift of C-2, we deduced that C-2 was substituted by a hydroxy group. One hydroxy methine signal was assigned as C-6 ($\delta_H$ 4.43; $\delta_C$ 72.1). The substituent was identified as an isobutyryl group on the basis of the chemical shifts in the



| | | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|---|
| 1 | $\Delta^{8,30}$ | tigloyl | H | OH |
| 2 | $\Delta^{8,14}$ | H | H | OH |
| 3 | $\Delta^{8,30}$ | tigloyl | H | OAc |
| 4 | $\Delta^{8,14}$ | tigloyl | H | OH |
| 5 | $\Delta^{8,14}$ | Ac | H | OAc |
| 7 | $\Delta^{8,30}$ | tigloyl | OH | OH |
| 8 | $\Delta^{8,30}$ | tigloyl | OH | H |
| 12 | $\Delta^{8,30}$ | isobutyryl | H | OH |



| | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| 6 | tigloyl | H | OAc |
| 9 | Ac | OH | OH |
| 10 | isobutyryl | OH | OH |
| 11 | tigloyl | OH | H |
| 13 | isobutyryl | OH | H |

tigloyl = -CO-C(CH3)=CH (1' 2' 3')

isobutyryl = -CO-C(CH3)2-CH3 (1' 2' 3')

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NMR ($\delta_H$ 1.28, 1.32, 2.75; $\delta_C$ 18.8, 19.6, 34.2, 175.5). Confirmation of the position of the isobutyryl group was possible by application of the heteronuclear multiple bond correlation (HMBC) technique and a correlation peak was observed from the H-3 and CO of the isobutyryl group. The relative stereochemistry of **10** was determined on the basis of the results of a nuclear Overhauser effect spectroscopy (NOESY) experiment. As shown in Fig. 1, from the NOESY spectrum, cross-peaks were observed from the following pairs: H-3/H-28, H-5/H-29, H-5/H-6, H-6/H-19, H-9/H-19, H-14/H-30, H-17/H-18, H-17/H-22, H-18/H-22, H-22/H-23 and H-30/H-3′. The configration of C-6 was determined by comparison of the chemical shifts with reported literature data on related compounds.[8,12] Therefore, the structure of **10** was assigned as methyl 3$\beta$-isobutyryloxy-2,6-dihydroxy-8$\alpha$,30$\alpha$-epoxy-1-oxo-meliacate.

Compound **9** had an $[M+H]^+$ peak at *m/z* 561.2351 ($C_{29}H_{37}O_{11}$). The NMR spectra of **9** were similar to those of **10** except for the appearance of signals ascribable to an acetyl residue ($\delta_H$ 2.26; $\delta_C$ 20.7, 175.3) instead of signals due to an isobutyryl residue in **10**. Based on these spectral data, **9** was determined to be methyl 3$\beta$-acetoxy-2,6-dihydroxy-8$\alpha$,30$\alpha$-epoxy-1-oxo-meliacate.

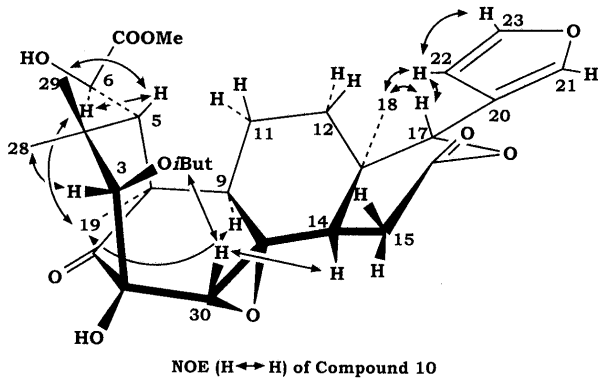


Fig. 1

Compound **11** showed an $[M+H]^+$ peak at *m/z* 585.2706 ($C_{32}H_{41}O_{10}$), and gave rise to $^1$H- and $^{13}$C-NMR spectra that were similar to those of **10**, except for the appearance of one more methylene signal ($\delta_C$ 33.2) assigned to C-6 instead of the hydroxy methine signal in **10**, and the appearance of signals ascribable to a tigloyl residue ($\delta_H$ 1.93, 1.97, 7.04; $\delta_C$ 12.6, 14.7, 127.8, 139.8, 167.0) instead of the signals due to the isobutyryl residue in **10**. Based on these spectral data, **11** was assigned as methyl 3$\beta$-tigloyloxy-2-hydroxy-8$\alpha$,30$\alpha$-epoxy-1-oxo-meliacate.

Compound **8** showed an $[M+H]^+$ peak at *m/z* 569.2762 ($C_{32}H_{41}O_9$). The NMR spectral pattern resembled that of **11**, but it was characterized by the appearance of signals assignable to a trisubstituted olefinic linkage at C-8/C-30 ($\delta_H$ 5.36; $\delta_C$ 129.1, 136.8) instead of the epoxide in **11**. Thus, the structure of **8** was assigned as methyl 3$\beta$-tigloyloxy-2-hydroxy-1-oxo-meliac-8(30)-enate.

Compound **7** had an $[M+H]^+$ peak at *m/z* 585.2709 ($C_{32}H_{41}O_{10}$). The NMR spectrum of **7** was similar to that of **8** except for the appearance of hydroxy methine signals at C-6 instead of the methylene signal in **8**. Based on these spectral data, **7** was determined to be methyl 3$\beta$-tigloyloxy-2,6-dihydroxy-1-oxo-meliac-8(30)-enate.

## Experimental

**General Procedures** NMR spectra were recorded on a JEOL JNM-A500 spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. FAB-MS spectra were recorded on a JEOL JMS-DX300 spectrometer. Optical rotations were measured with a JASCO DIP-4 digital polarimeter.

Table 1. $^1$H-NMR Spectral Data of Compounds **7**—**11** in $CDCl_3$

| | **7** | **8** | **9** | **10** | **11** |
|---|---|---|---|---|---|
| 3 | 4.73 (1H, s) | 4.92 (1H, s) | 4.95 (1H, s) | 4.97 (1H, s) | 5.14 (1H, s) |
| 5 | 3.42 (1H, s) | 3.39 (1H, br d) | 3.17[a] | 3.19 (1H, s) | 3.23 (1H, dd, $J$=9, 2 Hz) |
| 6 | 4.55 (1H, s) | 2.37 (2H, m) | 4.44 (1H, s) | 4.43 (1H, s) | 2.35 (1H, m) |
| 9 | 2.32 (1H, m) | 2.11[a] | 1.97 (1H, m) | 1.98 (1H, dd, $J$=15, 5 Hz) | 1.91[a] |
| 11 | 2.04 (2H, m) | 1.65 (2H, m) | 2.11 (2H, m) | 1.79 (1H, m) | 1.79 (1H, m) |
| | | | | 1.92 (1H, m) | 1.90 (1H, m) |
| 12 | 1.47 (1H, m) | 1.32[a] | 1.39 (1H, m) | 1.39 (1H, m) | 1.44 (1H, m) |
| | 1.80 (1H, m) | 2.10[a] | 2.09 (1H, m) | 2.12 (1H, m) | 1.99[a] |
| 14 | 2.25 (1H, m) | 2.23 (1H, m) | 1.63 (1H, dd, $J$=12, 7 Hz) | 1.63 (1H, m) | 1.61 (1H, m) |
| 15 | 2.82 (1H, br s) | 2.84 (1H, br s) | 2.87 (1H, m) | 2.88 (1H, m) | 2.83 (1H, br d) |
| | 2.83 (1H, br s) | 2.85 (1H, br s) | 3.17[a] | 3.16[a] | 3.48 (1H, br d) |
| 17 | 5.55 (1H, s) | 5.63 (1H, s) | 5.15 (1H, s) | 5.12 (1H, s) | 5.18 (1H, s) |
| 21 | 7.57 (1H, br s) | 7.83 (1H, br s) | 7.44[a] | 7.43 (1H, br d) | 7.49 (1H, br s) |
| 22 | 6.39 (1H, br s) | 6.48 (1H, br s) | 6.39 (1H, br d) | 6.37 (1H, br d) | 6.45 (1H, br s) |
| 23 | 7.45 (1H, br s) | 7.43 (1H, br s) | 7.44[a] | 7.44 (1H, t, $J$=2 Hz) | 7.43 (1H, br s) |
| 18 | 0.99 (3H, s) | 1.09 (3H, s) | 1.05 (3H, s) | 1.06 (3H, s) | 1.00 (3H, s) |
| 19 | 1.54 (3H, s) | 1.24 (3H, s) | 1.43 (3H, s) | 1.44 (3H, s) | 1.17 (3H, s) |
| 28 | 1.11 (3H, s) | 0.84 (3H, s) | 1.07 (3H, s) | 1.08 (3H, s) | 0.79 (3H, s) |
| 29 | 0.88 (3H, s) | 0.79 (3H, s) | 0.85 (3H, s) | 0.85 (3H, s) | 0.81 (3H, s) |
| 30 | 5.32 (1H, s) | 5.36 (1H, s) | 3.40 (1H, s) | 3.41 (1H, s) | 3.51 (1H, s) |
| COOMe | 3.76 (3H, s) | 3.73 (3H, s) | 3.92 (3H, s) | 3.92 (3H, s) | 3.74 (3H, s) |
| 2′ | | | 2.26 (3H, s) | 2.75 (1H, m) | |
| 2′Me | 1.83 (3H, br s) | 2.02 (3H, s) | | 1.28[a] | 1.97 (3H, br s) |
| 3′ | 6.89 (1H, m) | 6.95 (1H, m) | | 1.32[a] | 7.04 (1H, m) |
| 3′Me | 1.74 (3H, d, $J$=6 Hz) | 1.75 (3H, d, $J$=8 Hz) | | | 1.93[a] |

*a*) Overlapped with other signals.

Table 2. $^{13}$C-NMR Spectral Data of Compounds **7**—**11** in $CDCl_3$

| | 7 | 8 | 9 | 10 | 11 |
|---|---|---|---|---|---|
| 1 | 214.5 | 215.1 | 212.5 | 212.6 | 213.1 |
| 2 | 77.2 | 77.5 | 77.8 | 78.1 | 78.4 |
| 3 | 86.1 | 84.9 | 86.3 | 85.8 | 84.8 |
| 4 | 39.9 | 39.5 | 40.3 | 40.5 | 40.1 |
| 5 | 45.6 | 41.8 | 46.1 | 46.1 | 42.4 |
| 6 | 72.7 | 32.7 | 72.2 | 72.1 | 33.2 |
| 7 | 175.7 | 173.9 | 170.9 | 175.3 | 174.2 |
| 8 | 136.5 | 136.8 | 62.5 | 62.8 | 63.2 |
| 9 | 57.4 | 56.7 | 54.8 | 54.6 | 55.2 |
| 10 | 49.8 | 49.3 | 49.2 | 49.3 | 49.1 |
| 11 | 21.2 | 20.5 | 20.3 | 20.5 | 19.5 |
| 12 | 34.5 | 34.4 | 32.8 | 32.6 | 33.0 |
| 13 | 36.7 | 36.9 | 35.8 | 35.8 | 36.2 |
| 14 | 44.9 | 45.0 | 44.0 | 43.6 | 45.3 |
| 15 | 29.5 | 29.7 | 32.2 | 32.2 | 33.5 |
| 16 | 168.3 | 168.6 | 169.2 | 170.6 | 171.3 |
| 17 | 76.6 | 76.6 | 80.4 | 80.8 | 79.0 |
| 20 | 121.2 | 120.7 | 120.6 | 120.8 | 120.3 |
| 21 | 140.6 | 141.9 | 140.7 | 140.7 | 141.0 |
| 22 | 109.2 | 109.7 | 109.8 | 109.7 | 110.2 |
| 23 | 143.3 | 143.1 | 143.5 | 143.6 | 143.2 |
| 18 | 21.2 | 21.7 | 26.7 | 27.0 | 26.3 |
| 19 | 16.4 | 15.7 | 17.1 | 17.1 | 16.1 |
| 28 | 22.1 | 19.7 | 22.2 | 22.4 | 22.0 |
| 29 | 22.5 | 22.1 | 22.1 | 22.0 | 20.5 |
| 30 | 129.8 | 129.1 | 67.5 | 67.2 | 67.4 |
| COOMe | 53.4 | 52.3 | 53.6 | 53.6 | 52.4 |
| 1′ | 167.1 | 167.4 | 175.3 | 175.5 | 167.0 |
| 2′ | 127.7 | 127.5 | 20.7 | 34.2 | 127.8 |
| 3′ | 139.3 | 139.9 | | 18.8 | 139.8 |
| 2′Me | 11.9 | 11.9 | | 19.6 | 12.6 |
| 3′Me | 14.6 | 14.7 | | | 14.7 |

**Plant Material** The seeds of *Swietenia macrophylla* KING were collected in Morelos, Mexico in 1987. It was identified by Dr. G. S. Ortega in the Jardin de Etno-botanico, Instituto Nacional de Antropologia e Historia, Mexico, where voucher specimens of the plant are deposited.

**Extraction and Isolation** The seeds of *Swietenia macrophylla* (800 g) were extracted successively with $CHCl_3$, $Me_2CO$ and MeOH under reflux. After evaporation of these extracts, part of the $CHCl_3$ extract (54 g) was partitioned between hexane and 90% aq. MeOH. The 90% aq. MeOH layer was dried, the solvent was removed and the residue was chromatographed on silica gel with $C_6H_6$–$Me_2CO$ (30 : 1—1 : 1). The crude fraction was subjected to RP-18 Lobar chromatography (45% $CH_3CN$) to give **7** (7 mg), **9** (7 mg), **10** (11 mg) and **13** (6 mg). Part of the $Me_2CO$ extract (50 g) was partitioned between hexane and 90% aq. MeOH. The 90% aq. MeOH layer was dried, the solvent was removed and the residue was chromatographed on silica gel with $C_6H_6$–$Me_2CO$ (30 : 1—1 : 1). The crude fraction was subjected to RP-18 Lobar chromatography (45% $CH_3CN$) to give **8** (5 mg), **11** (8 mg) and **12** (5 mg).

Methyl 3$\beta$-Tigloyloxy-2,6-dihydroxy-1-oxo-meliac-8(30)-enate (**7**): Amorphous powder, $[\alpha]_D^{22}$: $-55.0°$ ($c=1.8$, $CHCl_3$). FAB-MS *m/z*: 585 $[M+H]^+$. High-resolution FAB-MS *m/z*: 585.2709 $[M+H]^+$ (Calcd for $C_{32}H_{41}O_{10}$: 585.2699). $^1$H- and $^{13}$C-NMR: Table 1, 2.

Methyl 3$\beta$-Tigloyloxy-2-hydroxy-1-oxo-meliac-8(30)-enate (**8**): Amorphous powder, $[\alpha]_D^{23}$: $-37.4°$ ($c=0.3$, $CHCl_3$). FAB-MS *m/z*: 569 $[M+H]^+$. High-resolution FAB-MS *m/z*: 569.2762 $[M+H]^+$ (Calcd for $C_{32}H_{41}O_9$: 569.2750). $^1$H- and $^{13}$C-NMR: Table 1, 2.

Methyl 3$\beta$-Acetoxy-2,6-dihydroxy-8$\alpha$,30$\alpha$-epoxy-1-oxo-meliacate (**9**): Amorphous powder, $[\alpha]_D^{23}$: $-15.5°$ ($c=0.7$, $CHCl_3$). FAB-MS *m/z*: 561 $[M+H]^+$. High-resolution FAB-MS *m/z*: 561.2351 $[M+H]^+$ (Calcd for $C_{29}H_{37}O_{11}$: 561.2336). $^1$H- and $^{13}$C-NMR: Table 1, 2.

Methyl 3$\beta$-Isobutyryloxy-2,6-dihydroxy-8$\alpha$,30$\alpha$-epoxy-1-oxo-meliacate (**10**): Amorphous powder, $[\alpha]_D^{22}$: $-53.9°$ ($c=0.8$, $CHCl_3$). FAB-MS *m/z*: 589 $[M+H]^+$. High-resolution FAB-MS *m/z*: 589.2643 $[M+H]^+$ (Calcd for $C_{31}H_{41}O_{11}$: 589.2649). $^1$H- and $^{13}$C-NMR: Table 1, 2.

Methyl 3$\beta$-Tigloyloxy-2-hydroxy-8$\alpha$,30$\alpha$-epoxy-1-oxo-meliacate (**11**): Amorphous powder, $[\alpha]_D^{23}$: $-25.4°$ ($c=0.8$, $CHCl_3$). FAB-MS *m/z*: 585 $[M+H]^+$. High-resolution FAB-MS *m/z*: 585.2706 $[M+H]^+$ (Calcd for $C_{32}H_{41}O_{10}$: 585.2699). $^1$H- and $^{13}$C-NMR: Table 1, 2.

**Acknowledgements** The plant material was collected with the aid of Mitsui Pharmaceuticals, Inc. Thanks are also due to Miss S. Kato and Miss K. Takahashi for NMR and MS mesurements.

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