Mexicanolide- and Andirobine-type Limonoids from the Fruits of

*Guarea kunthiana*

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**Abstract:** Four limonoids, humilinolide E (1), methyl 2-hydroxy-3β-tigloyloxy-1-oxomeliac-8(30)-enate (2), swietenine acetate (3) and methyl angolensate (4) were isolated from the fruits of *Guarea kunthiana*. Compounds 1-3 are being reported for the first time in the genus *Guarea*, while 4 has been previously described in only one species of this genus. The isolated compounds were identified by spectral methods (1D-, 2D-NMR and EIMS).

**Keywords:** Limonoids; Meliaceae; *Guarea kunthiana*. © 2014 ACG Publications. All rights reserved.

1. **Plant Source**

In our continuing phytochemical study of Meliaceous representatives occurring in the “Cerrado” of the Central-western region of Brazil, we have investigated the fruits of *Guarea kunthiana* A. Juss. Herein, we report the isolation of three mexicanolide limonoids, humilinolide E (1), methyl 2-hydroxy-3β-tigloyloxy-1-oxomeliac-8(30)-enate (2), swietenine acetate (3) and one andirobin-type limonoid, methyl angolensate (4) from this plant (Figure 1).

*G. kunthiana* was collected in Campo Grande, MS, Brazil, in August 2007, and identified by MSc. Ubirazilda M Resende (Federal University of Mato Grosso do Sul, Brazil). A voucher specimen (No. 11217) has been deposited at the CGMS herbarium of the Federal University of Mato Grosso do Sul, Brazil.

2. **Previous Studies**

Although members of the Meliaceae are known for the occurrence of limonoids, they have not been detected in the leaves of a previously studied Brazilian specimen of *G. kunthiana*, from which diterpenes, sesquiterpenes, α- and β-tocopherols and polyprenol-12 have been isolated [1], while only one B, D-ring seco-limonoid, ecuadorin, has been obtained from the aerial parts of *G. kunthiana* growing in Ecuador [2].

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3. Present Study

The fruits of *G. kunthiana* (2.5 kg) were extracted with hexane at room temperature for 2 hours and subsequently with EtOH at room temperature for seven days. After concentration under reduced pressure, a portion of the crude EtOH extract (40.0 g) was partitioned between n-BuOH and H₂O. The n-BuOH phase was concentrated under reduced pressure and partitioned between MeOH-H₂O (8:2) and hexane. The hydromethanolic phase was then diluted to MeOH-H₂O (7:3) and further partitioned with CH₂Cl₂. The CH₂Cl₂ phase (5.0 g) was chromatographed on a RP-18 silica gel column using MeOH-H₂O (1:9, 2:8, 4:6, 6:4, 8:2, 9:1) and MeOH as eluents, to give seven fractions, respectively (F1→F7). Fraction F5 (1.7 g) was further subjected to column chromatography on Sephadex LH-20 with MeOH to yield six subfractions (F5.1→F5.6). Subfraction F5.4 (686.9 mg), after column chromatography on silica gel (230-400 mesh) using gradient solvent system [CHCl₃→CHCl₃-MeOH (9:1)], followed by reversed-phase semipreparative HPLC on RP-18 column (5 μm, 21.6x250 mm) using CH₃CN-H₂O (55:45) as eluent, afforded humilinolide E (1, 49.7 mg) [3], methyl 2-hydroxy-3β-tigloyloxy-1-oxomeliac-8(30)-enate (2, 52.2 mg) [3], swietenine acetate (3, 4.1 mg) [4] and methyl angolensate (4, 3.0 mg) [4]. ¹H and ¹³C NMR data of compounds 1-4 were in agreement with those reported in the literature [3, 4].

Plants belonging to the Meliaceae are known as a rich source of limonoids, many of which have significant biological properties, namely antifeedant and insecticidal activities and cytotoxicity against human cancer cell lines [5]. However, this class of secondary metabolites is scarcely reported in the genus *Guarea*, as compared to other representative genera within this family. To date, less than 20 limonoids bearing A,B-, B,D- and/or D- ring seco-type skeletons have been isolated from six amongst the 16 *Guarea* species that have been chemically investigated [2, 3, 5-11]. So, the presence of the rearranged limonoids belonging to the mexicanolide-class 1-3 in *G. kunthiana* is noteworthy, since no records related to the isolation of these limonoids have hitherto been reported in this genus. Additionally, there are very few reports concerning the occurrence of 1-3 in higher plants. Humilinolide E (1) was only found in the Meliaceous species *Swietenia humilis* [3], while methyl 2-hydroxy-3β-tigloyloxy-1-oxomeliac-8(30)-enate (2) and swietenine acetate (3) were previously isolated only from three and two Meliaceous species, respectively, belonging to the genera *Swietenia* and *Capuronianthus*, namely *S. humilis*, *S. macrophylla* and *C. mahafalensis* (2) [3, 12, 13] and *S. macrophylla* and *S. mahogani* (3) [4,13]. Although the androbinone-type limonoid methyl angolensate (4) is well distributed in the Meliaceae, especially in the genus *Khaya* [5], its occurrence in the genus *Guarea* has hitherto been described only in *Guarea thompsonii* [14].

**Humilinolide E (1):** amorphous solid; [α]D²⁰ = 88.10 (c = 0.09, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ (ppm) = 4.81 (1H, s, H-3), 3.66 (1H, brs, H-5), 5.63 (1H, s, H-6), 2.38 (1H, m, H-9), 1.56 (2H, m, H-12), 2.41 (1H, brd, J = 6.0 Hz, H-14), 2.79 (1H, brd, J = 18.0 Hz, H-15a), 2.95 (1H, dd, J = 18.0 and 6.0 Hz, H-15b), 5.68 (1H, s, H-17), 1.05 (3H, s, H-18), 1.26 (3H, s, H-19), 7.78 (1H, brs, H-21), 6.55 (1H, brs, H-22), 7.56 (1H, brs, H-23), 1.12 (3H, s, H-28), 0.90 (3H, s, H-29), 5.23 (1H, brs, H-30), 6.92 (1H, qq, J = 6.5 and 1.5 Hz, H-3'), 1.81 (3H, s, H-4'), 1.73 (3H, s, H-4''), 1.72 (3H, s, H-6'), 2.18 (3H, s, OAc), 3.72 (3H, s, H-1''); ¹³C NMR (75 MHz, CDCl₃): δ (ppm) = 215.2 (COO, C-18), 78.9 (C, C-2), 86.6 (CH C-3), 41.3 (C, C-4), 45.8 (CH C-5), 73.8 (CH C-6), 172.8 (COO C-7), 139.0 (C, C-8), 58.1 (CH C-9), 51.1 (C, C-10), 22.3 (CH₂ C-11), 35.3 (CH₂ C-12), 37.9 (C, C-13), 45.8 (CH, C-14), 30.5 (CH₂ C-15), 171.6 (COO, C-16), 78.7 (CH C-17), 21.7 (CH₃ C-18), 16.0 (CH₂, C-19), 122.4 (C C-20), 142.6 (CH C-21), 110.6 (CH C-22), 144.7 (CH C-23), 22.6* (CH₃ C-28), 22.8* (CH₃ C-29), 129.9 (CH C-30), 168.1(COO C-1'), 128.8 (C, C-2'), 140.4 (CH C-3'), 12.2 (CH₂ C-4'), 14.7 (CH₂ C-5'), 171.3 (COO, OAc), 20.8 (CH₃ OAc), 53.8 (OMe, C-1'') *interchangeable signals; EIMS (70 eV) m/z 626 (M⁺).

**Methyl 2-hydroxy-3β-tigloyloxy-1-oxomeliac-8(30)-enate (2):** amorphous solid; [α]D²⁰ = -46.17 (c = 0.08 CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ (ppm) = 4.98 (1H, s, H-3), 3.43 (1H, brd, J = 9.0 Hz, H-5), 2.51 (2H, m, H-6), 2.30 (1H, brdd, J = 12.0 and 6.0 Hz, H-9), 2.10 (2H, dd, J =12.0 and 6.0 Hz, H-11), 1.54 (2H, m, H-12), 2.39 (1H, brd, J = 6.0 Hz, H-14), 2.80 (1H, brd, J = 18.0 Hz, H-15a), 3.02 (1H, dd, J = 18.0 and 6.0 Hz, H-15b), 5.75 (1H, s, H-17), 1.11 (3H, s, H-18), 1.23 (3H, s, H-19), 7.88 (1H, brs, H-21), 6.56 (1H, brs, H-22), 7.54 (1H, brs, H-23), 0.84 (3H, s, H-28), 0.73 (3H, s, H-29), 5.25 (1H, brs, H-30), 6.96 (1H, qq, J = 6.5 and 1.3 Hz, H-3''), 1.81 (3H, brs, H-4''), 1.74 (3H, d, J = 6.5
Swietenia acetate (3): amorphous solid; $[\alpha]_D^{20} = -52.61$ (c = 0.06 MeOH); $^1$H NMR (300 MHz, CD$_3$OD); $\delta$ (ppm) = 3.45 (1H, t, J = 9.0 Hz, H-2), 4.97 (1H, d, J = 9.0 Hz, H-3), 3.74 (CH, brs, H-5), 5.62 (1H, s, H-6), 2.29 (1H, m, H-9), 1.54 (2H, m, H-12), 2.37 (1H, m, H-14), 2.75 (1H, brd, J = 18.0 Hz, H-15a), 2.95 (1H, dd, J = 18.0 and 6.0 Hz, H-15b), 5.61 (1H, s, H-17), 1.03 (3H, s, H-18), 1.20 (3H, s, H-19), 7.78 (1H, brs, H-21), 6.54 (1H, brs, H-22), 7.56 (1H, brs, H-23), 1.12 (3H, s, H-28), 0.99 (3H, s, H-29), 5.29 (1H, d, J = 7.3 Hz, H-30), 6.92 (1H, brq, J = 7.0 Hz, H-3'), 1.79 (3H, brs, H-4'), 1.70 (3H, brd, J = 7.0 Hz, H-5'), 2.18 (3H, s, OAc), 3.75 (3H, s, H-1'); $^{13}$C NMR (75 MHz, CD$_3$OD); $\delta$ (ppm) = 217.7 (CO, C-1), 50.3 (CH, C-2), 79.7 (CH, C-3), 40.1 (C, C-4), 45.9 (CH, C-5), 74.1 (CH, C-6), 172.9 (COO, C-7), 140.9 (C, C-8), 58.7 (CH, C-9), 51.4 (C, C-10), 21.7 (CH$_2$, C-11), 35.4 (CH$_2$, C-12), 38.0 (C, C-13), 46.0 (CH, C-14), 30.4 (CH$_2$, C-15), 171.7 (COO, C-16), 78.7 (CH, C-17), 22.4 (CH$_2$, C-18), 16.2 (CH$_3$, C-19), 122.5 (CH, C-20), 142.6 (CH, C-21), 110.6 (CH, C-22), 144.6 (CH, C-23), 23.5 (CH$_3$, C-28), 23.1 (CH$_3$, C-29), 123.6 (CH, C-30), 168.3 (COO, C-1'), 128.8 (C, C-2'), 140.4 (CH, C-3'), 12.0 (CH$_3$, C-4'), 14.8 (CH$_3$, C-5'), 171.3 (COO, OAc), 20.9 (CH$_3$, OAc), 53.8 (OMe, C-1'); EIMS (70 eV) m/z 610 (M$^+$).

Methyl angolensate (4): amorphous solid; $[\alpha]_D^{20} = -26.81$ (c = 0.25 MeOH); $^1$H NMR (300 MHz, CD$_3$OD); $\delta$ (ppm) = 3.63 (1H, m, H-1), 2.40 (1H, dd, J = 15.0 and 4.0 Hz, H-2a), 3.11 (1H, d, J = 15.0 Hz, H-2b); 2.86 (1H, brd, J = 12.0 Hz, H-5), 2.42 (1H, brd, J = 16.5 Hz, H-6a), 2.69 (1H, d, J = 16.5 Hz, H-6b), 2.30 (1H, brd, J = 5.1 Hz, H-9), 2.42 (1H, d, J = 18.0 Hz, H-15a), 3.13 (1H, d, J = 18.0 Hz, H-15b), 5.62 (1H, s, H-17), 0.88 (3H, s, H-18), 1.00 (3H, s, H-19), 7.52 (1H, brs, H-21), 6.43 (1H, brs, H-22), 7.48 (1H, brs, H-23), 0.96 (3H, s, H-28), 1.19 (3H, s, H-29), 4.94 (1H, s, H-30a), 5.19 (1H, s, H-30b), 3.67 (3H, s, H-1'); $^{13}$C NMR (75 MHz, CD$_3$OD); $\delta$ (ppm) = 79.1 (CH, C-1), 40.5 (CH$_2$, C-2), 216.2 (CO, C-3), 49.4 (C, C-4), 44.5 (CH, C-5), 33.5 (CH$_2$, C-6), 175.8 (COO, C-7), 147.3 (C, C-8), 51.2 (CH, C-9), 45.1 (C, C-10), 25.0 (CH$_2$, C-11), 30.9 (CH$_3$, C-12), 42.5 (C, C-13), 81.8 (C, C-14), 34.7 (CH$_2$, C-15), 173.0 (COO, C-16), 81.4 (CH, C-17), 14.4 (CH$_3$, C-18), 21.9 (CH$_3$, C-19), 122.5 (C, C-20), 142.2 (CH, C-21), 110.9 (CH, C-22), 144.3 (CH, C-23), 25.9 (CH$_3$, C-28), 21.9 (CH$_3$, C-29), 112.5 (CH$_2$, C-30), 52.5 (OMe, C-1'); EIMS (70 eV) m/z 470 (M$^+$).
References


