SHORT REPORT

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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.*

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 δ-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 H_2O. The *n*-BuOH phase was concentrated under reduced pressure and partitioned between MeOH-H_2O (8:2) and hexane. The hydromethanolic phase was then diluted to MeOH- H_2O (7:3) and further partitioned with CH_2Cl_2. The CH_2Cl_2 phase (5.0 g) was chromatographed on a RP-18 silica gel column using MeOH-H_2O (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 [$CHCl_3$→ $CHCl_3$-MeOH (9:1), followed by reversed-phase semipreparative HPLC on RP-18 column (5 μm, 21.6x250 mm) using CH_3CN-H_2O (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]. ^{1}H and ^{13}C 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 with 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. Addingly, 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 andirobine-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; $[\alpha]_D^{20}$ = – 88.10 (*c* = 0.09, $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD): 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, brs, H-4'), 1.72 (3H, d, *J* = 6.5 Hz, H-5'), 2.18 (3H, s, OAc), 3.72 (3H, s, H-1''); ^{13}C NMR (75 MHz, CD_3OD): 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 (CH_2, C-11), 35.3 (CH_2, C-12), 37.9 ($C_,$ C-13), 45.8 (CH, C-14), 30.5 (CH_2, C-15), 171.6 ($COO_,$ C-16), 78.7 ($CH_,$ C-17), 21.7 (CH_3, C-18), 16.0 (CH_3, C-19), 122.4 ($C_,$ C-20), 142.6 ($CH_,$ C-21), 110.6 ($CH_,$ C-22), 144.7 ($CH_,$ C-23), 22.6* (CH_3, C-28), 22.8* (CH_3, C-29), 129.9 ($CH_,$ C-30), 168.1($COO_,$ C-1'), 128.8 ($C_,$ C-2'), 140.4 ($CH_,$ C-3'), 12.2 (CH_3, C-4'), 14.7 (CH_3, C-5'), 171.3 (COO, OAc), 20.8 (CH_3, OAc), 53.8 ($OMe_,$ C-1'') *interchangeable signals; EIMS (70 eV) *m/z* 626 ($M^{+\cdot}$).

*Methyl 2-hydroxy-3β-tigloyloxy-1-oxomeliac-8(30)-enate **(2)**:* amorphous solid; $[\alpha]_D^{20}$ = – 46.17 (*c* = 0.08 $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD): δ (ppm) = 4.94 (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

Hz, H-5'), 3.72 (3H, s, H-1''); ^{13}C NMR (75 MHz, CD_3OD): δ (ppm) = 216.5 (CO, C-1), 78.9 (C, C-2), 85.9 ($CH_,$ C-3), 40.9 ($C_,$ C-4), 42.6 (CH, C-5), 33.4 ($CH_2,$ C-6), 176.1 ($COO_,$ C-7), 139.3 ($C_,$ C-8), 57.7 ($CH_,$ C-9), 51.0 ($C_,$ C-10), 22.5 ($CH_2,$ C-11), 35.4 ($CH_2,$ C-12), 38.1 ($C_,$ C-13), 45.9 (CH, C-14), 30.6 ($CH_2,$ C-15), 172.0 ($COO_,$ C-16), 78.7 ($CH_,$ C-17), 21.7 ($CH_3,$ C-18), 15.9 (CH_3, C-19), 122.2 ($C_,$ C-20), 143.3 ($CH_,$ C-21), 110.8 ($CH_,$ C-22), 144.5 ($CH_,$ C-23), 20.1* ($CH_3,$ C-28), 22.0* ($CH_3,$ C-29), 129.6 ($CH_,$ C-30), 168.4 ($COO_,$ C-1'), 128.8 ($C_,$ C-2'), 140.5 ($CH_,$ C-3'), 12.0 ($CH_3,$ C-4'), 14.7 ($CH_3,$ C-5'), 52.6 ($OMe_,$ C-1'') *interchangeable signals; EIMS (70 eV) *m/z* 568 ($M^{+\cdot}$).

Swietenine acetate ***(3)****:* amorphous solid; $[\alpha]_D^{20}$ = – 52.61 (*c* = 0.06 MeOH); ^{1}H NMR (300 MHz, CD_3OD): δ (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_3OD): δ (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 ($CH_3,$ C-18), 16.2 (CH_3, C-19), 122.5 ($C_,$ 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 ($M^{+\cdot}$).

Methyl angolensate ***(4)****:* amorphous solid; $[\alpha]_D^{20}$ = – 26.81 (*c* = 0.25 MeOH); ^{1}H NMR (300 MHz, CD_3OD): δ (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_3OD): δ (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_2, 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 ($M^{+\cdot}$).

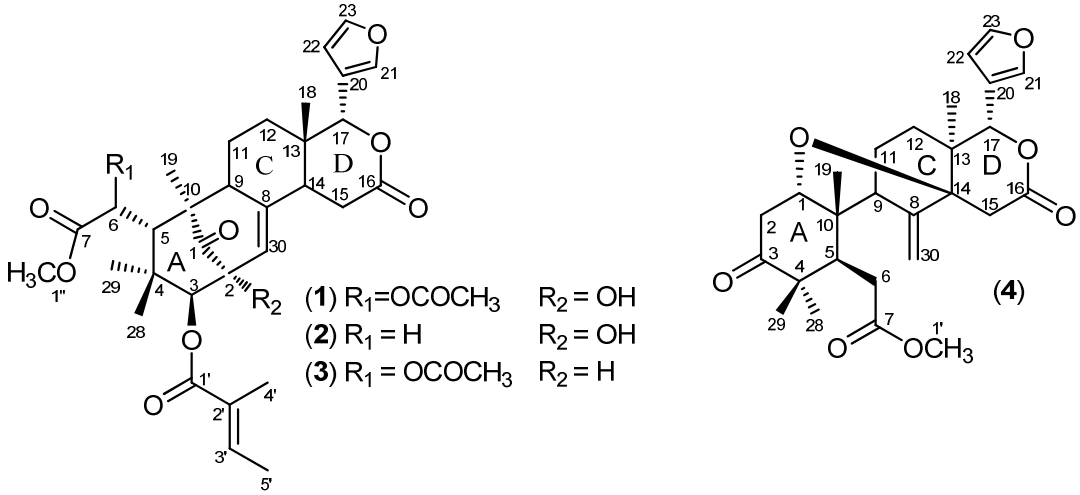

Figure 1. Structures of limonoids 1-4 isolated from *G. kunthiana*.

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