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Artoindonesianins A and B, Two New Prenylated Flavones from the Root of *Artocarpus champeden*

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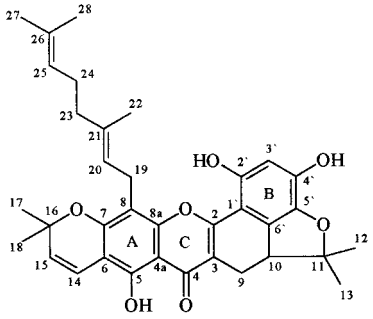
Two new prenylated flavones, named artoindonesianin A (**1**) and artoindonesianin B (**2**), were isolated from the root of *Artocarpus champeden*, together with a known prenylated flavone, artonin A. The structures of artoindonesianins A and B were determined on the basis of spectral evidence (MS, ^{1}H and ^{13}C NMR) and by comparison with known related compounds. Compounds **1** and **2** exhibited cytotoxic activity against murine leukemia (P-388) cells.

In continuation[1−3] of work on the genus *Artocarpus*, two new cytotoxic prenylated flavones, named artoindonesianin A (**1**) and artoindonesianin B (**2**), and a known compound, artonin A, were further isolated from the root of *Artocarpus champeden* Spreng., one of the endemic species of the genus *Artocarpus* (Moraceae). In this paper, we report the isolation and structure elucidation of these compounds on the basis of spectroscopic evidence.



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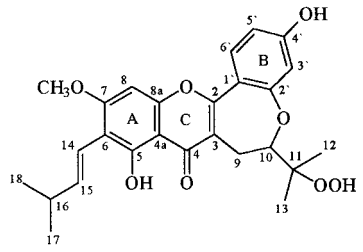

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Artoindonesianin A (**1**) was isolated as a yellow powder. The HRFABMS gave an $[MH]^+$ ion at *m/z* 571.2694, consistent with a molecular formula of $C_{35}H_{38}O_7$. The ^{13}C NMR spectrum revealed the presence of 35 carbons, including seven methyl groups and a carbonyl group (δ 180.2), corresponding to a tetraprenylated flavonoid. The IR spectrum showed absorptions typical of hydroxyl, conjugated carbonyl, and benzene ring functionalities, and the UV spectrum was consistent with the presence of a flavone structure. The analysis of its NMR data, including DEPT, HMQC, and HMBC spectra, allowed for an unambiguous assignment of all proton and carbon signals. The ^{1}H NMR spectrum had resonances associated with two methyl groups, δ 1.23, 1.58 (each 3H, s) and an ABX spin system δ 2.27, 3.10, 3.34 attributed to the isoprenyl moiety located at the C-3 position, similar to the arrangement found for related compounds, artonin A[4] and cycloartobiloxanthone.[5] In addition to the pyrano-xanthonoid moiety, the ^{1}H NMR spectrum also indicated the presence of two methyl groups at δ 1.38, 1.39 (each 3H, s) and the olefinic protons at δ 5.74 and 6.57 (each 1H, d, J = 10.0 Hz), attributed to the 2,2-dimethylchromene ring. Of the remaining signals in the ^{1}H NMR spectrum, those at δ 1.45, 1.53, 1.79, 1.88, 1.97, 3.35, 3.55, 4.98, and 5.26 indicated the presence of a geranyl group. An aromatic singlet at δ 6.28 was consistent with a 1,2,4,5,6-pentasubstituted B-ring, and a downfield signal at δ 13.70 indicated a chelated hydroxyl group. The order of the substitution on the A and B rings was deduced from HMBC experiments. The HMBC measurements showed long-range correlations between the singlet at δ 10.15 (OH-4′), methine carbon at δ 104.0 (C-3′), and two quaternary carbons at δ 136.2 (C-5′) and 140.5 (C-4′), and between the singlet at δ 9.83 (OH-2′) and two quaternary carbons at δ 103.1 (C-1′) and 151.1 (C-2′), thus establishing the location of the one unsubstituted position on the B ring at carbon C-3′. The HMBC experiments also showed the connectivities between the vinyl proton at δ 6.57 (H-14) and three quaternary carbons at δ 153.5 (C-5), 104.5 (C-6), and 155.6 (C-7). Long-range correlations were observed for the methylene protons at δ 3.4−3.6 (H-19) to three quaternary carbons at δ 155.6 (C-7), 107.0 (C-8), and 152.9 (C-8a). These results provided support for the presence of the geranyl substituent at C-8, and the 2,2-dimethylchromene ring fused to C-6 and C-7. Further evidence for the structure assigned to **1** came from comparison of the ^{13}C NMR spectrum, assigned with the aid of HMQC and HMBC data, to that reported for the related compound artonin A,[4] and from UV and MS data.[6−9] Consequently, artoindonesianin A was assigned structure **1**.

Artoindonesianin B (**2**) was isolated as a yellow powder. The HRFABMS gave an $[MH]^+$ ion at *m/z* 469.1883, consistent with a molecular formula of $C_{26}H_{28}O_8$. The ^{13}C NMR spectrum indicated the presence of 26 carbons,

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Me-13), 1.53 (3H, s, Me-27), 1.45 (3H, s, Me-28), 1.39 (3H, s, Me-17), 1.38 (3H, s, Me-18), 1.23 (3H, s, Me-12); ^{13}C NMR (DMSO-d_6, 125.7 MHz) δ 180.2 (s, C-4), 160.7 (s, C-2), 155.6 (s, C-7), 153.5 (s, C-5), 152.9 (s, C-8a), 151.1 (s, C-2′), 140.5 (s, C-4′), 136.2 (s, C-5′), 134.1 (s, C-21), 132.3 (s, C-6′), 130.6 (s, C-26), 128.5 (d, C-15), 124.1 (d, C-25), 122.3 (d, C-20), 115.1 (d, C-14), 110.9 (s, C-3), 107.0 (s, C-8), 104.5 (s, C-6), 104.0 (d, C-3′), 103.8 (s, C-4a), 103.1 (s, C-1′), 92.4 (s, C-11), 77.5 (s, C-16), 46.2 (d, C-10), 39.3 (t, C-23), 27.9 (q, Me-13), 27.8 (q, Me-17), 27.7 (q, Me-18), 26.1 (t, C-24), 25.4 (q, Me-27), 22.6 (q, Me-12), 20.9 (t, C-19), 19.5 (t, C-9), 17.5 (q, Me-28), 16.1 (q, Me-22); FABMS *m*/*z* [MH]$^+$ 571 (36.8), 570 (24.4), 489 (14.0), 467 (12.4), 447 (20.2), 446 (13.6), 316 (23.2), 315 (100), 314 (10.8); HRFABMS *m*/*z* [MH]$^+$ 571.2694 (calcd for $C_{35}H_{39}O_7$, 571.2696).

Artoindonesianin B (2): obtained as yellow powder; mp 165−166 °C; $[\alpha]^{22}_D$ +8.6° (*c* 0.18, MeOH); IR (KBr) ν_{max} 3500 (OH), 1649 (C═O, ketone), 1606, 1548, 1475 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 252 (3.87), 294 (4.26), 346 (4.26) nm; (MeOH + NaOH) 214 (4.63), 273 (4.40), 286 (4.41), 388 (4.57), 486 (3.95) nm; ^{1}H NMR (Me_2CO-d_6, 399.7 MHz) δ 13.83 (1H, s, OH-5), 10.35 (1H, s, OOH-11), 9.20 (1H, s, OH-4′), 8.06 (1H, d, J = 8.8 Hz, H-6′), 6.77 (1H, s, H-8), 6.75 (1H, dd, J = 2.4 and 8.8 Hz, H-5′), 6.71 (1H, dd, J = 7.0, 16.2 Hz, H-15), 6.62 (1H, d, J = 2.4 Hz, H-3′), 6.59 (1H, dd, J = 1.0, 16.2 Hz, H-14), 4.36 (1H, dd, J = 2.0, 10.0 Hz, H-10), 3.99 (3H, s, OMe-7), 3.49 (1H, dd, J = 2.0, 17.1 Hz, H-9), 2.63 (1H, dd, J = 10.0, 17.1 Hz, H-9), 2.43 (1H, m, H-16), 1.45 (3H, s, Me-12), 1.30 (3H, s, Me-13), 1.08 (6H, each d, J = 6.8 Hz, Me-17 and Me-18); ^{13}C NMR (Me_2CO-d_6, 100.4 MHz) δ 182.0 (s, C-4), 164.0 (s, C-7), 162.5 (s, C-4′), 161.5 (s, C-2′), 159.6 (s, C-5), 158.6 (s, C-2), 156.7 (s, C-8a), 142.3 (d, C-15), 131.3 (d, C-6′), 117.6 (s, C-3), 117.0 (d, C-14), 114.6 (s, C-1′), 112.1 (d, C-5′), 110.0 (s, C-6), 108.5 (d, C-3′), 104.4 (s, C-4a), 90.5 (d, C-8), 86.2 (d, C-10), 83.4 (s, C-11), 56.7 (q, OMe-7), 34.0 (d, C-16), 25.9 (t, C-9), 23.1 (q, Me-17), 23.1 (q, Me-18), 22.5 (q, Me-13), 20.1 (q, Me-12); FABMS *m*/*z* [MH]$^+$ 469 (100), 468 (70.8), 453 (24.2), 393 (33.3), 337 (31.7), 321 (18.3), 307 (14.2), 233 (6.7), 179 (8.3), 79 (5.4), 57 (6.8), 41 (3.7); HRFABMS *m*/*z* [MH]$^+$ 469.1883 (calcd for $C_{26}H_{29}O_8$, 469.1863).

Cytotoxicity Assay. Both **1** and **2** were tested against murine leukemia (P-388) cells using established protocols.[15] Compounds **1** and **2** exhibited cytotoxic activity, IC_{50} 21.0 and 3.9 μg/mL, respectively.

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