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A New Prenylated Flavone from *Artocarpus champeden*

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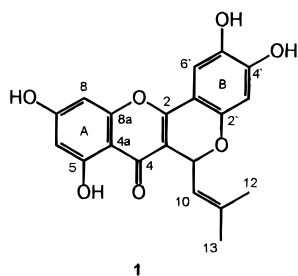
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A new prenylated flavone, named cyclochampedol (**1**), together with four known triterpenes—cycloeucalenol, glutinol, cycloartenone, and 24-methylenecycloartanone—as well as β -sitosterol were isolated from *Artocarpus champeden*. The structure of the new compound was determined on the basis of spectral evidence and by comparison with known related compounds. Compound **1** is active in the brine shrimp lethality assay.

In the Indonesian indigenous system of medicine, several *Artocarpus* plants (Moraceae) such as *A. communis* and *A. elastica* have established use, while the fruits of *A. champeden* Spreng (Moraceae) are eaten as a staple food and its wood is used commercially as timber.¹ As part of our continuing investigation of Indonesian tropical plants,^{2,3} we now report the isolation of a new prenylated flavone, together with the known triterpenes, cycloeucalenol,^{4,5} glutinol,⁶ a mixture of cycloartenone⁷ and 24-methylenecycloartanone,⁸ and the sterol, β -sitosterol, from the tree bark of *A. champeden*, an endemic species found throughout the Indonesian archipelago. The structure of the new compound **1**, named cyclochampedol, was determined on the basis of spectroscopic evidence.



The dried, powdered tree bark of *A. champeden* was extracted with hexane and then with Me₂CO. The CHCl₃-soluble portion of the Me₂CO extract was fractionated by vacuum–liquid chromatography (VLC) to give a number of fractions that contained a major compound. Repeated flash chromatography of the combined fractions yielded cyclochampedol (**1**) as yellow crystals, mp 205–206 °C. The HRFABMS gave an [MH]⁺ ion at *m/z* 369.0979 (calcd 369.0975) consistent with a molecular formula of C₂₀H₁₆O₇. The IR spectrum showed absorptions for hydroxyl (3568 cm⁻¹) and conjugated carbonyl (1701, 1626 cm⁻¹) functionalities and the UV spectrum [269 nm (log ϵ 4.42), 315 (3.98), 399

(4.29)] was consistent with the presence of a flavone structure. The ¹H-NMR spectrum included signals for an isoprenyl group (δ 1.65, 1.89, each a doublet, *J* = 1.2 Hz) in which the vinylic proton (δ 5.39, br d, *J* = 9.5 Hz) was coupled to a benzylic oxymethine (δ 6.05, d, *J* = 9.5 Hz), similar to the arrangement found for a related compound, cyclocommunol.⁹ The remaining signals in the ¹H-NMR spectrum indicated the presence of two meta-coupled protons, consistent with a 5,7-dihydroxy substitution of the A-ring,¹⁰ and two uncoupled protons in accord with a 1,2,4,5-tetrasubstituted B-ring.¹¹ HMBC measurements allowed the quaternary carbons observed at δ 153.1 and 141.9 to be assigned to C-4' and C-5', respectively. Supporting evidence for the structure assigned to cyclochampedol (**1**) came from comparison of the ¹³C-NMR spectrum, assigned with the aid of HMQC and HMBC measurements, to those reported for the related compounds cyclocommunol⁹ and cycloaltisin,¹¹ and from UV and MS data¹² (see Experimental Section). Cyclochampedol (**1**) is active (LC₅₀ 15.1 μ g/mL) in the *Artemia salina* shrimp bioassay,¹³ suggesting that it is comparable to other prenylated flavonoids isolated from *A. communis*, which have been reported to exhibit strong cytotoxic activity.¹⁴

Experimental Section

General Experimental Procedures. All melting points were determined on a micro-melting point apparatus and are uncorrected. UV and IR spectra were measured with Beckman DU-7000 and Shimadzu FT-IR 8501 spectrophotometers, respectively. ¹H- and ¹³C-NMR spectra were recorded with either a Bruker AM 300 spectrometer, operating at 300.1 MHz (¹H-) and 75.4 MHz (¹³C-), or a JEOL JNM A5000 spectrometer, operating at 500 MHz (¹H-) and 125.6 MHz (¹³C-), using TMS as an internal standard. MS were obtained with either a VG Autospec mass spectrometer using the EI mode (8000 V) or a JMS-HM20 mass spectrometer. VLC was carried out using Merck Si gel 60 GF₂₅₄, flash chromatography with Merck Si gel 60 (230–400 mesh), and TLC analysis on precoated Si gel plates (Merck Kieselgel 60 F₂₅₄, 0.25 mm).

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Plant Material. Samples of the tree bark of *A. champeden* were collected in July, 1994, from plantation trees growing in Bogor District, West Java, Indonesia. The plant was identified by staff at the Herbarium Bogoriense, Bogor Botanical Garden, Bogor, Indonesia, and a voucher specimen has been deposited at the herbarium.

Extraction and Isolation. The milled, dried bark (0.96 kg) was extracted exhaustively with hexane and then with Me₂CO. The Me₂CO extract, on removal of solvent under reduced pressure, gave a light brown residue (42.0 g, 4.4%). The residue was solubilized in a mixture of H₂O–Me₂CO (75:25), and the soluble portion extracted with CHCl₃. A portion (7 g) of the total CHCl₃ extract (32 g) was fractionated by Si gel VLC (95 g, 6.5 × 7.5 cm, CHCl₃, CHCl₃–EtOAc, EtOAc, EtOAc–Me₂CO, Me₂CO, in order of increasing polarity) to give 35 fractions. This chromatographic step was repeated five times on portions of 5 g each of the CHCl₃ extract. Nine fractions were ultimately obtained on combining the eluates on the basis of TLC. The sixth fraction (2.1 g) was further fractionated by Si gel VLC (44 g, 4.5 × 5.5 cm, hexane, hexane–EtOAc, EtOAc, in order of increasing polarity) to afford 75 fractions. From fractions 29–34 a precipitate was obtained (180 mg), which was further purified by Si gel flash chromatography [29 g, 2.5 × 15 cm, CHCl₃–MeOH (93:7)] to yield a crude compound (75 mg), which was crystallized from CHCl₃–MeOH to afford cyclochampedol (**1**) (11 mg). Using the same methods, five known compounds were identified from the hexane extract: cycloeucalenol,^{4,5} glutinol,⁶ cycloartenone,⁷ 24-methylenecycloartanone⁸ and β -sitosterol.

Cyclochampedol (1): obtained as yellow crystals; mp 205–206 °C; $[\alpha]^{25}_D +141.6^\circ$ (c 0.12, MeOH); IR (KBr) ν max 3568 (OH), 1701 (C=O, ketone), 1626, 1599, 1512, 1454 cm⁻¹; UV (MeOH) λ max (log ϵ) 212 (4.64), 269 (4.42), 315 (sh, 3.98), 399 (4.29) nm; (MeOH + NaOH) 214 (4.99), 276 (4.49), 305 (sh, 4.25), 315 (sh, 4.26), 4.38 (4.54) nm; (MeOH + AlCl₃) 212 (4.68), 278 (4.33), 303 (sh, 3.98), 338 (sh, 3.91), 470 (4.43) nm; (MeOH + NaOAc) 214 (4.87), 270 (4.36), 421 (4.33) nm; ¹H NMR (CD₃OD, 500 MHz) δ 7.09 (1H, s, H-6'), 6.33 (1H, d, J = 2.2 Hz, H-8), 6.30 (1H, s, H-3'), 6.12 (1H, d, J = 2.2 Hz, H-6), 6.05 (1H, d, J = 9.5 Hz, H-9), 5.39 (1H, br d,

J = 9.5 Hz, H-10), 1.89 (3H, d, J = 1.2 Hz, Me-12), 1.65 (3H, d, J = 1.2 Hz, Me-13); ¹³C NMR (CD₃OD, 125.6 MHz) δ 179.5 (s, C-4), 165.4 (s, C-7), 163.3 (s, C-8a), 158.6 (s, C-5), 157.6 (s, C-2), 153.1 (s, C-4'), 152.5 (s, C-2'), 141.9 (s, C-5'), 139.5 (s, C-11), 122.4 (d, C-10), 110.5 (s, C-3), 109.9 (d, C-6'), 107.8 (s, C-1'), 105.6 (s, C-4a), 105.4 (d, C-3'), 99.9 (d, C-6), 95.0 (d, C-8), 70.2 (d, C-9), 26.0 (q, C-13), 18.7 (q, C-12); EIMS m/z [M]⁺ 368 (16), 353 (22), 313 (38), 153 (13), 69 (16), 56 (67), 41 (100); HRFABMS (glycerol) m/z [MH]⁺ 369.0979 (calcd for C₂₀H₁₇O₇, 369.0975).

Biological Evaluation. Compound **1** exhibited an LC₅₀ of 15.1 μ g/mL when evaluated in the brine shrimp lethality assay as described by Meyer *et al.*¹³

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