Pergamon

PII: S0031-9422(96)00293-2

Phytochemistry, Vol. 43, No. 3, pp. 691–694, 1996

0031-9422/96 $15.00 + 0.00

PRENYLFLAVONOIDS FROM *ARTOCARPUS ELASTICUS*

ANAKE KIJJOA, HONORINA M. CIDADE,* MADALENA M. M. PINTO* MARIA JOSÉ T. G. GONZALEZ,* CHOOJIT ANANTACHOKE,† THOMAS E. GEDRIS‡ and WERNER HERZ‡§

Department of Chemistry, Instituto dé Ciências Biomédicas de Abel Salazar, Universidade do Porto, 4050 Porto, Portugal; *Centro dos Estudos de Química Orgânica, Fitoquímica e Farmacologia de Universidade do Porto, 4050 Porto; †Wood Products Research Division, Royal Forest Department, Paholyothin Road, Bangkok, Thailand; ‡Department of Chemistry, The Florida State University, Tallahassee, FL 32306-3006, U.S.A.

(*Received* 6 *March* 1996)

Key Word Index—*Artocarpus elasticus*; Moraceae; wood; prenylated flavones.

Abstract—Three new prenylated flavones, artelastin, artelastochromene and artelasticin, along with the known artocarpesin, were isolated from the wood of *Artocarpus elasticus*. Structures were elucidated by spectroscopic techniques. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Wood and bark from *Artocarpus* species, a Southeast Asian genus of *ca* 50 arboreal species, are rich in prenylated flavonoids and derivatives thereof [1–12]. In this article, we describe isolation for the wood of *A. elasticus* of three new members of this class, which we have named artelastin (**1a**), artelastochromene (**2a**) and artelasticin (**3a**). Artocarpesin (**4a**) and β-sitosterol were also found. Other workers [13] have reported the prenylated flavones, artocarpin, cycloartocarpin, norartocarpin, cycloartocarpesin and integrin, and also β-sitosterol, from heartwood of the same species.

RESULTS AND DISCUSSION

Mass, ^{1}H and ^{13}C NMR spectra of artelastin (**1a**) indicated that it was a derivative of cyclomulberrin containing an additional γ,γ-dimethylallyl group on C-6 of ring A. The latter was completely substituted and exhibited the signal of a bonded hydroxyl on C-9 at δ 13.0. In the ^{1}H NMR spectrum, ring B exhibited the usual signals of 1′,2′,4′-substitution with H-3′,H-5′ and H-6′ at δ 6.40 (*d*, $J = 2.5$ Hz), 6.52 (*dd*, $J = 8.5$, 2.5 Hz) and 7.62 (*d*, $J = 8.5$ Hz), respectively, while the characteristic signals of the prenyl side-chain on C-3 linked by a C-9 oxygen to C-2′ of ring B appeared at δ 6.24 (H-9), 5.39 (H-10), 1.95 (3p, H-12) and 1.67 (3p. H-13). Acetylation at room temperature converted compound **1a** to a monoacetate, **1b**, which retained the bonded hydroxyl on C-5. Complete ^{1}H and ^{13}C NMR data are listed in the Experimental.

Artelastochromene (**2a**) was similar to artelastin but contained a 2,2-dimethylchromene attached to ring A, as indicated by the mass spectrum and the ^{1}H NMR spectrum, which exhibited two mutually coupled doublets ($J = 10$ Hz) at δ 6.70 (H-14) and δ 5.58 (H-15) and two methyl singlets at δ 1.44 and δ 1.43 (H-17, H-18) but was otherwise essentially identical with that of compound **1a**. The ^{13}C NMR spectrum (Experimental) agreed with this deduction. Acetylation at room temperature gave a monoacetate **2b**, which retained the bonded hydroxyl group on C-5, but acetylation under somewhat more stringent conditions resulted in formation of a diacetate **2c** and also some **2b**. These were easily separated by TLC.

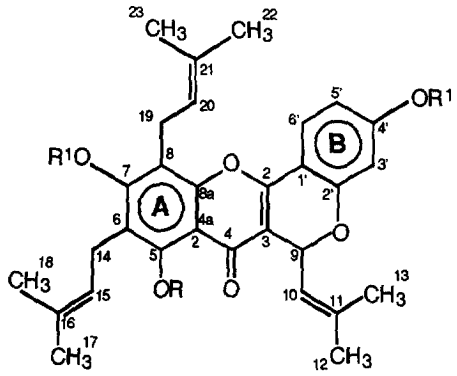
To decide between angular and linear orientation of the dimethylchromene ring we used the method of Arnone *et al.* [14], which depends on the changes in the chemical shifts of the vinylic protons in a linearly oriented 2,2-dimethylchromene upon acetylation of a 5-hydroxyl group. The relevant signals in the ^{1}H NMR spectra of compounds **2b** and **2c** run under identical conditions ($CDCl_3$, 300 MHz) within the same time period are listed in table 1 and demonstrated that the dimethylchromene ring of artelastochromene is linearly oriented. Thus, artelastochromene is the 8-γ,γ-dimethylallyl derivative of cudraflavone A [15].

Artelasticin (**3a**), the third new member of this group, was easily identified as 6-γ,γ-dimethylallylmulberrin by its spectroscopic properties, which are de-

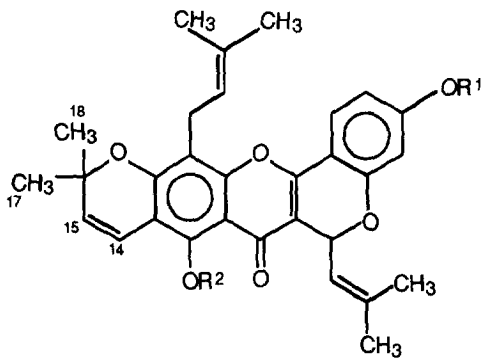
Table 1. Relevant signals from the ^{1}H NMR spectra of compounds **2b** and **2c**

H	**2b**	**2c**	$\Delta\nu$
14	6.65 *d* (10)	6.41 *d* (10)	+0.24
15	5.55 *d* (10)	5.69 *d* (10)	−0.14

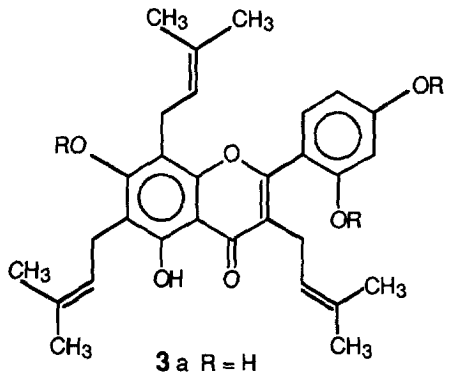
§Author to whom correspondence should be addressed.



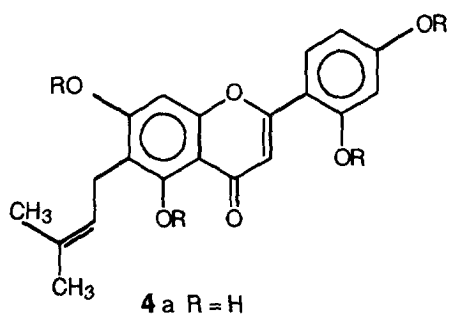
1 a $R^1, R^2 = H$
b $R^1 = Ac, R^2 = H$



2 a $R^1, R^2 = H$
b $R^1 = Ac, R^2 = H$
c $R^1, R^2 = Ac$



3 a R = H
b R = Ac



4 a R = H
b R = Ac

tailed in the Experimental. Acetylation at room temperature yielded a diacetate, **3b**, whose ^{1}H NMR spectrum retained the signal of the bonded hydroxyl on C-5.

EXPERIMENTAL

Plant material. Wood of *A. elasticus* Reinw. *ex* Blume was collected in Trang Province, Southern Thailand, in January 1991. A voucher specimen is on deposit in the Royal Forestry Department, Bangkok, Thailand.

Extraction and isolation. Powdered wood was percolated with cold EtOH to exhaustion. Evapn of the extract at red. pres. gave 110 g of residue which was taken up in $CHCl_3$. Evapn of the $CHCl_3$ sol at red. pres. gave 61 g of crude material. Half of this (30 g) was chromatographed on silica gel 60 (200 g), eluents petrol–$CHCl_3$ and $CHCl_3$–Me_2CO (500 ml frs) as follows: frs 1–12 (petrol–$CHCl_3$, 3:2), frs. 13–27 (petrol–$CHCl_3$, 2:3), frs 28–50 (petrol–$CHCl_3$, 3:7), frs 51–77 (petrol–$CHCl_3$, 1:9), frs 78–114 ($CHCl_3$–Me_2CO, 9:1) and frs 115–130 ($CHCl_3$–Me_2CO, 4:1). Frs 1–5 contained a mixt. of hydrocarbons. Frs 6–12 contained mainly β-sitosterol. Recrystallization of the combined residues gave 0.5 g of β-sitosterol. Frs 13–22 contained oily apolar mixts and were not investigated further. Frs 23–46 (1.2 g) were combined. TLC (silica gel GF 254, petrol-EtOAc-HCO_2H, 70:30:1) yielded compounds **2a** (400 mg) and **1a** (300 mg). Frs 47–56 (600 mg) were combined; TLC as above, as yielded additional **2a** (100 mg) and **1a** (40 mg). Combination of frs 57–81 (2 g) followed by TLC (silica gel GF254, $CHCl_3$–Me_2CO–HCO_2H, 90:10:1) gave 1.2 g of **3a**. Frs 82–90 (1.2 g), which contained a mixt. of compound **3a** and several others with very similar R_f values and frs 91–97 (500 mg, also a complex mixt.) were not studied further. Frs 98–115 (800 mg) were combined and taken up in Me_2CO, which was then diluted with 3× its vol. of $CHCl_3$. The ppt. was purified by TLC (silica gel GF254, $CHCl_3$–Me_2CO–HCO_2H, 90:10:1) to give artocarpesin (**4a**, 0.25 g), identified by MS, ^{1}H NMR and conversion to the triacetate, **4b** whose previously unreported ^{1}H NMR ($CDCl_3$, 500 MHz) exhibited signals at δ 7.73 (*d*, J = 8.5 Hz, H-6′), 7.16 (*dd*, J = 8.5, 2 Hz, H-5′), 7.06 (*d*, J = 2 Hz, H-2′), 6.70 and 6.56 (both *s*, H-3, H-8), 5.12 (*br t*, J = 7 Hz, H-2″), 3.31 (2p, *d*, J = 7 Hz, H-1″a,b), 2.32, 2.31, 2.28 (each *s* and 3p, Ac), 1.76 and 1.67 (each *br s* and 3p, H-4″ and H-5″). The material remaining in soln was a mixt. of substances with very similar R_f values.

Artelastin (**1a**). Orange–red gum. MS PCI *m/z* (rel. int.): 489 (100, $C_{30}H_{32}O_6 + H^+$). IR ν^{KBr} cm^{-1} 3600–

3100, 2980, 2936, 1623, 1567, 1453, 1397, 1220. UV λ_{max}^{MeOH} (log ε) 207 (4.8), 260 (4.2), 276 (4.2), 369 (4.1); $\lambda_{max}^{MeOH+NaOH}$ 268 (4.3), 403 (4.2); $\lambda_{max}^{MeOH+AlCl_3}$ 207 (4.8), 260 (4.2), 276 (4.2), 369 (4.1), 420 (3.7). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 13.0 (5-OH), 7.62 (*d*, J = 8.5 Hz, H-6'), 6.52 (*dd*, J = 8.5, 2.5 Hz, H-5'), 6.40 (*d*, J = 2.5 Hz, H-3'), 6.28 (br s, 7-OH), 6.24 (*d*, J = 9.5 Hz, H-9), 5.39 (dsept, J = 9.5, 1.5 Hz, H-10), 5.27 and 5.23 (each *br t*, J = 7 Hz, H-15, H-20), 3.53 and 3.41 (each 2p and *br d*, J = 7 Hz, H-14ab, H-19a,b), 1.95 (3p, *br s*, H-18 and H-23). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 1.78*s* (C-4), 161.0*s*, 159.0*s*, 158.0*s*, 157.1*s* (C-2, 5, 7, 8a, 2', 4'; two signals unobs.), 139.2*s* (C-11), 135.4*s*, 134.0*s* (C-16, 21), 125.3*d* (C-15), 121.7*d*, 121.4*d*, 121.1*d* (C-6', 10, 20), 110.0*s*, 109.5*s*, 109.0*s*, 105.5*s*, 104.5*s* (C-3, 4a, 6, 8, 1'), 109.5*d* (C-5'), 104.5*d* (C-3'), 69.9*d* (C-9), 25.9*q*, 25.6*q* (C-12, 18, 22), 22.0*q*, 21.6*q* (C-14, 19), 18.7*q*, 18.0*q*, 17.3*q* (C-13, 17, 23).

Acetylation of **1a** (30 mg) with Ac_2O–pyridine at room temp. and work-up in the usual manner yielded 22 mg of **1b**. orange–red crystals, mp 181–183° ($CHCl_3$). MS PCI *m/z* (rel. int.): 573 (100, $C_{34}H_{36}O_8 + H^+$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.92 (5-OH), 7.72 (*d*, J = 8.5 Hz, H-6'), 6.80 (*dd*, J = 8.5, 2.5 Hz, H-5'), 6.71 (*d*, J = 2.5 Hz, H-3'), 6.28 (*d*, J = 9.5, H-9), 5.40 (*br d*, J = 9.5 Hz, H-10), 5.15 and 5.10 (each *br t*, J = 7 Hz, H-15, 19), 2.32 and 2.29 (each *s* and 3p, Ac), 1.95 (3p, *d*, J = 1.5 Hz, H-12), 1.78, 1.73, 1.68, 1.68, 1.66 (5 vinyl Me). ^{13}C NMR ($CDCl_3$, 67.89 MHz): δ 179.4*s* (C-4), 168.5*s*, 168.2*s* (acetate C = 0), 157.6*s*, 157.5*s*, 155.4*s*, 154.9*s*, 152.8*s*, 152.8*s*, (C-2, 5, 7, 8a, 2', 4'), 139.6*s* (C-11), 132.2*s*, 132.2*s* (C-16, 21), 124.6*d* (C-15), 121.8*d*, 121.4*d*, 120.8*d* (C-10, 20, 6'), 115.1*d* (C-5'), 111.4*d* (C-3'), 117.9*s*, 113.4*s*, 112.8*s*, 111.7*s*, 109.4*s* (C-3, 4a, 6, 8, 1'), 70.2*d* (C-9), 25.9*q*, 25.6*q*, 25.6*q* (C-12, 18, 22), 23.4*t*, 22.9*t* (C-14, 19), 21.1q, 20.5*q* (Me of Ac), 18.7*q*, 18.1*q*, 17.8*q* (C-13, 17, 21).

Artelastochromene (**2a**). Yellow solid, mp 238–240° ($CHCl_3$). MS *m/z* (rel. int.): 486 (74.9, $C_{30}H_{32}O_6$), 471 (60.2), 194 (100), 149 (39.4), 109 (31.0). IR ν^{KBr} cm^{-1} 3500–3100, 2920, 1652, 1617, 1590, 1548, 1465, 1350, 1298, 1240, 1215, 1187, 1140. UV λ_{max}^{MeOH} (log ε) 202 (5.2), 296 (4.3), 375 (4.2); $\lambda_{max}^{MeOH+NaOH}$ 277 (4.3), 412 (4.2); $\lambda_{max}^{MeOH+AlCl_3}$ 202 (5.2), 296 (4.3), 375 (4.2), 440 (3.7). ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.92*s* (5-OH), 7.63 (*d*, J = 8 Hz, H-6'), 6.70 (*d*, J = 10 Hz, H-14), 6.53 (*dd*, J = 8.5, 2.5 Hz, H-3'), 6.41 (*d*, J = 2.5 Hz, H-5'), 6.23 (*d*, J = 9.5 Hz, H-9), 5.58 (*d*, J = 10 Hz, H-15), 5.41 (*d*, J = 9.5 Hz, H-10), 5.23 (*br t*, J = 7 Hz, H-20), 3.46 (2p, *br d*, J = 7 Hz, H-19a,b), 1.95 (3p, *br s*, H-12) 1.83 (*br s* and 3p, H-21), 1.68, 1.67 (each *br s*, and 3p, H-13, H-22), 1.44*s*, 1.43*s* (each 3p, H-17, H-18). ^{13}C NMR ($CDCl_3$, 67.89 MHz) δ 178.9*s* (C-4), 160.8*s* (C-2), 158.2*s*, 156.6*s*, 155.1*s*, 154.7*s*, 153.8*s* (C-5, 7, 8a, 2', 4'), 139.1*s* (C-11), 131.5*s* (C-21), 127.8*d* (C-15), 125.3*d*, 122.4*d*, 121.3*d* (C-6', 10, 20), 116.0*d* (C-14), 109.6*d* (C-5'), 104.6*d* (C-3'), 109.8*s*, 109.3*s*, 107.6*s*, 105.5*s* (C-3, 4a, 6, 8, 1', one signal signal not obs.), 77.8*s* (C-16), 70.0*d* (C-9), 28.3*q*, 28.2*q* (C-17, 18), 21.6*t* (C-19), 18.7*q*, 18.1*q* (C-13, 23).

Acetylation of **2a** (30 mg) with Ac_2O–pyridine at room temp. and work-up in the usual manner yielded 25 mg of monoacetate **2b**. Yellow solid, mp 185–187° ($CHCl_3$). MS PCI *m/z* (rel. int.): 529 (100, $C_{32}H_{34}O_7 + H^+$). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 12.91 (5-OH), 7.74 (*d*, J = 8.5 Hz, H = 6'), 6.79 (*dd*, J = 8.5, 2.5 Hz, H-5'), 6.71 (*d*, J = 2.5 Hz, H-3'), 6.70 (*d*, J = 10 Hz, H-14), 6.26 (*d*, J = 9.5 Hz, H-9), 5.59 (*d*, J = 10 Hz, H-15), 5.42 (*br d*, J = 9.5 Hz, H-10), 5.22 (*br t*, J = 7 Hz, H-20), 3.47 (2p, *br t*, J = 7 Hz, H-19a,b), 2.23 (3p, *s*, Ac), 1.96 (*br s*, 3p, H-12), 1.83 (*br s*, 3p, H-21), 1.68, 1.67 (each *br s* and 3p, H-13, H-22), 1.44 and 1.435 (each *s* and 3p, H-17, H-18). Acetylation of **2a** (50 mg) with Ac_2O–pyridine at 60° for 30 min and subsequently keeping the mixt. at room temp. for 1 week followed by the usual work-up gave a mixt. which was sepd by prep. TLC (silica gel 6254, petrol–EtOAc–HCO_2H, 70:30:1) to give the less polar monoacetate **2b** (25 mg) and the diacetate **2c** (27 mg). The latter had mp 215–218° ($CHCl_3$). EI-MS *m/z* (rel. int.): 570 ($[M]^+$, $C_{34}H_{36}O_8$, 62), 528 (72), 486 (80), 471 (40), 194 (100). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (*d*, J = 8.5 Hz, H = 6'), 6.74 (*d*, J = 8.5, 2 Hz, H-5'), 6.63 (*d*, J = 2 Hz, H-3'), 6.41 (*d*, J = 10 Hz, H-15), 5.30 (*br d*, J = 9.2 Hz, H-10), 5.20 (*br t*, J = 7 Hz, H-20), 3.50 (2p, *br d*, J = 7 Hz, H-19a,b), 2.38 and 2.24 (each *s* and 3p, Ac), 1.88, 1.79, 1.63, 1.59 (each *br s* and 3p, H-12, H-21, H-13, H-22), 1.41 and 1.40 (each *s* and 3p, H-17, H-18).

Artelastin (**3a**). Orange–red gum. MS PCI *m/z* (rel. int.): 491 (100, $C_{30}H_{34}O_6 + H^+$). IR ν^{KBr} cm^{-1} 3600–3100, 2922, 2855, 1658, 1565, 1467, 1440, 1378. UV λ_{max}^{MeOH} (log ε) 269 (4.1), 271 (4.0); $\lambda_{max}^{MeOH+NaOH}$ 261 (4.0), 277 (4.1), 407 (4.2); $\lambda_{max}^{MeOH+AlCl_3}$ 285 (4.2), 383 (4.1), 415 (4.0). ^{1}H NMR (200 MHz, $CDCl_3$): δ 13.06*s* (5-OH), 7.12 (*d*, J = 8.2 Hz, H-6'); 6.52 (*s*, H-3'), 6.49 (*dd*, J = 8.2, 2.2 Hz, H-5'), 6.35 (*br s*, -OH), 5.14 (*m*, 3p, H-10, 15, 20), 3.37 (*d* = 6.8 Hz, 4p, H-14a,b, H-19a,b), 3.12 (*d* = 6.5 Hz, 2p, H-9a,b), 1.79, 1.71, 1.65, 1.65, 1.54, 1.36 (each *br s* and 3p, 6 vinyl Me). The substance underwent decomposition fairly rapidly, hence, the main portion was converted to the triacetate.

Acetylation of compound **3a** (80 mg) with Ac_2O-pyridine and work-up in the usual manner afforded 76 mg of triacetate **3c** as an orange-red gum. MS PCI *m/z* (rel. int.): 617 (100, $C_{36}H_{40}O_9 + H^+$). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 13.0 (5-OH), 7.39 (*d*, J = 8 Hz, H-6'), 7.13 (*d*, J = 2 Hz, H-3'), 7.10 (*dd*, J = 8, 2 Hz, H-5'), 5.12, 5.01, 4.99 (each *br t*, J = 7.5 Hz, H-10, 15, 20), 3.25, 3.20, 3.00 (each broad and 2p, H-9a,b, 14a,b, 19a,b), 2.31, 2.30, 2.10 (each *s* and 3p, 3 Ac), 1.74, 1.66, 1.55, 1.55, 1.48, 1.38 (each *br s* and 3p, 6 vinyl Me). ^{13}C NMR ($CDCl_3$, 67.89 MHz): δ 182.9*s* (C-4), 168.3*s*, 1.68.1*s*, 1.67.9*s*, (three acetate C=O), 158.9*s*, 157.4*s*, 152.9*s*, 152.6*s*, 149.0*s* (C-2, 5, 7, 8a, 2', 4', one signal unobserved), 132.9*s*, 132.2*s*, 131.1*s* (C-11, 16, 21), 130.8*d*, 121.5*d*, 121.3*d*, 120.7*d*, 119.0*d* (C-10, 15,

20, 3′, 6′), 116.8*d* (C-5′), 123.9*s*, 121.8*s*, 108.7*s* (C-3, 4a, 6, 8, 1′), 25.6*q*, 25.5*q*, 25.5*q* (C-12, 17, 22), 24.0*t*, 23.0*t*, 22.9*t* (C-9, 14, 19), 21.1*q*, 21.1*q*, 20.8*q* (acetate Me), 17.8*q*, 17.6*q*, 17.6*q* (C-13, 18, 23).

Acknowledgements—Work in Portugal was supported by the Junta Nacional de Investigação Cientifica e Technológica of Portugal. M.M.C. thanks NJICT for a scholarship.

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