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FURTHER PRENYLFLAVONOIDS FROM *ARTOCARPUS ELASTICUS*

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

Abstract—Further study of one of the fractions from the wood of *Artocarpus elasticus* gave two new prenylated flavones artelastinin and artelastofuran in addition to artelasticin and cyclocommunin. Structures were elucidated by spectroscopic techniques. © 1998 Published by Elsevier Science Ltd. All rights reserved

INTRODUCTION

In an earlier article [1] we reported the isolation from wood of *Artocarpus elasticus* Reinw. *ex* Blume (Moraceae) of three new prenylated flavonoids artelastin (**1**), artelastochromene (**2**) and artelasticin (**3**) as well as the previously known artocarpesin (6-prenyl-5,7,2′,4′-tetrahydroxyflavone). Further study of one of the fractions has now yielded two more new members of this class which we have named artelastinin (**4**) and artelastofuran (**5a**). Cyclocommunin (isocyclomulberrin) (**6**) previously isolated from *Artocarpus communis* [2] and *Artocarpus altilis* [3] was also found.

RESULTS AND DISCUSSION

The ring A substitution of artelastinin (**4**), with a bonded hydroxyl group on C-5, a second hydroxyl on C-7 and two γ,γ-dimethylallyl groups on C-6 and C-8 paralleled that of artelastin (**1**) as was apparent from the ^{1}H and ^{13}C NMR spectra, the latter in Table 1. However instead of the 6-membered ring linking C-9 of the prenyl group on C-3 to the oxygen on C-2′ of ring B, artelastinin was an analogue of chaplashin from *Artocarpus chaplasha* [4], oxycyclointegrin from *Artocarpus integer* [5] and a related compound from *Morus alba* [6], all of which posess a hydroxyisopropyloxepin ring linking C-3 and C-2′ of the flavone skeleton as in **4**. This could be deduced from the ^{1}H NMR spectrum which exhibited a *dd* (J = 9 and 2 Hz) at δ 3.78 (H-10) coupled, as shown by COSY, to two mutually coupled signals of H-9a and H-9b (J = 16.8 Hz) at δ 2.37 and 3.3, the latter under the H_2O peak in the DMSO-d_6 solvent. The hydroxyisopropyl residue was represented in the ^{1}H NMR spectrum by two methyl singlets at δ 1.23 and 1.19 (H-12 and H-13) and in the ^{13}C NMR spectrum (Table 1) by a singlet at δ 72.0 and two quartets at δ 27.4 and δ 24.2 identified by HETCOR. The oxygen atom of the oxepin ring was attached to C-2′ of ring B which as in **1** carried a hydroxyl group on C-4′ as was evident from the ^{1}H NMR spectrum which exhibited signals of three aromatic protons at δ 7.79 (*d*,J = 8.8 Hz), 6.59 (*dd*,J = 8.8, 2.2 Hz) and 6.48 (*d*,J = 2.2 Hz) corresponding to H-6′, H-5′ and H-3′, respectively.

An attempt to characterize **4** further by conversion to a diacetate under the usual conditions (Ac_2O-Py, room temperature) resulted in a rearrangement, ***cum*** acetylation, to a substance whose nature became clear only in conjunction with structure elucidation of artelastofuran (**5a**), the second new constituent; its discussion will, therefore, be deferred until we have dealt with **5a**. Like artelasticin (**3**), **5a** incorporated a 3,3-dimethylallyl group on C-3, as shown by the characteristic signal of the *syn* 13-methyl group at δ 1.37, and a 2′,4′-dihydroxylated ring B since the chemical shifts of H-3′, H-5′ and H-6′ at δ 6.38, 6.25 and 7.03 compared with those of **3**, a bonded hydroxyl group on C-5 and a second 3,3-dimethylallyl group in ring B. A third prenyl residue was involved in formation of a furan ring with the oxygen function on C-7, as shown by characteristic ^{1}H NMR signals of a triplet (eventually shown to be that of H-20) at δ 4.71 (J = 8.6 Hz) coupled, as shown by COSY, to a *dd* (H-19a) under the DMSO-d_6 H_2O peak and a *dd* (J = 15.4, 8.6 Hz) at δ 3.12 (H-19b) [7]; in the spectrum of the diacetate **5b** these three signals were clearly visible at δ 4.75, 3.16 and 3.09, respectively.

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Table 1. ^{13}C NMR spectra of **4**, **5a**, **b** and **7** (75 MHz)*

C	**4** (DMSO-d_6)†	**5a** (DMSO-d_6)†	**5b** ($CDCl_3$)	**7** ($CDCl_3$)
2	159.3*s*[a]	158.4*s*[a]	157.4*s*‡	158.4*s*‡
3	114.1*s*[b]	119.4*s*	121.5*s*	121.1*s*
4	177.5*s*	181.7*s*	181.9*s*	182.3*s*
4a	105.3*s*	103.7*s*	104.9*s*‡	105.6*s*‡
5	155.7*s*‡	[a]	159.6*s*‡	154.5*s*‡
6	111.8*s*‡	105.7*s*	107.3*s*‡	108.2*s*‡
7	161.4*s*	164.2*s*	164.3*s*‡	163.9*s*‡
8	113.9*s*[b]	102.5*s*	102.2*s*‡	101.8*s*
8a	154.2*s*[c]	150.6*s*	150.8*s*	155.2*s*
9	24.5*t*	23.8*t*	24.1*t*	23.8*t*
10	87.9*d*	121.7*d*	121.2*d*	121.4*d*
11	77.0*s*	131.0*s*	132.7*s*[a]	132.6*s*[a]
12	27.4*q*	25.5*q*[b]	25.8*q*	25.7*q*
13	24.2*q*	17.4*q*	17.6*q*[b]	17.6*q*[b]
14	22.0*t*	21.5*t*	21.8*t*	27.1*t*‡
15	125.1*d*[a]	122.0*d*	121.0*d*	91.2*d*‡
16	128.5*s*[c]	131.0*s*	132.2*s*[a]	71.9*s*‡
17	25.6*q*[f]	25.5*q*	25.6*q*[c]	25.6*q*[c]
18	18.0*q*[g]	17.6*q*[c]	17.8*q*[b]	23.8*q*
19	21.9*t*	26.5*t*	27.2*t*	21.8*t*
20	125.5*d*	90.8*d*	91.1*d*	120.9*d*
21	128.1*s*[c]	70.2*s*	72.0*s*	132.0*s*[a]
22	25.5*q*[f]	26.1*q*[b]	25.8*q*[c]	25.7*q*[c]
23	17.8*q*[g]	24.2*q*	23.8*q*	17.6*q*[b]
1′	97.5*s*	110.8*s*	123.5*s*	123.5*s*‡
2′	153.3*s*[c]	162.0*s*[b]	152.4*s*‡	152.3*s*‡
3′	107.5*d*	101.1*d*	117.0*d*	116.8*d*
4′	[a]	161.3*s*[b]	148.9*s*‡	148.8*s*‡
5′	110.9*d*	105.1*d*	119.2*d*	119.1*d*
6′	129.2*d*	130.9*d*	131.0*d*	130.9*d*
Ac			168*s*, 168.4*s*	168.6*s*, 168.1*s*
			21.1*q*, 20.8*q*	21.1*q*, 20.8*q*

*Multiplets assigned by HETCOR.
†One singlet not observed.
‡Assigned by selective INEPT.
[a,b,c,d,e,f]Assignments with the same superscript are interchangeable within the same column.

A priori two structures, the angularly fused benzofuran **5a** or the linearly fused desacetyl derivative of **7** were possible structures for artelastofuran. To our surprise the other possible diacetate, **7** or **5b**, had been formed by acetylation of **4** at room temperature concomitant with liberation of the prenyl residue on C-3, as evidenced in the ^1H NMR spectrum by appearance of the *syn* 13-methyl resonance at δ 1.35, acetylation of the hydroxyl group on C-4′ and the newly freed hydroxyl on C-2′ and shifts of the signals of H-9a,b and H-10 of **4** to frequencies similar to but not identical with, those of **5b** at δ 4.69 (*dd*, J = 9.5, 8 Hz), 31.5 (*dd*, J = 16, 9.5 Hz) and 3.06 (*dd*, J = 16, 8 Hz). In the ^{13}C NMR spectra of the two acetates (Table 1) the signals tentatively attributed to C-2 through C-4a, and C-1′ through C-6′, coincided, but there were significant differences in the chemical shifts of C-5 and C-8a.

To differentiate the two diacetates we resorted to selective INEPT experiments. Thus irradiation at the frequency of the bonded -OH signal (δ 12.92) of the diacetate formed from **4** enhanced three carbon signals at δ 154.5, 108.2 and 105.6 which were, therefore, assigned to C-5, C-6 and C-4a, respectively. Irradiation at the frequency of the proton *alpha* to the furan oxygen at δ 4.69 enhanced two carbon signals at δ 163.9 and δ 108.2. Since the latter had already been identified as the signal of C-6, the former had to be associated with C-7 and the structure of the rearranged diacetate from **4** was **7** with a linearly fused tetrahydrofuran ring. Most of the remaining carbon singlets in the ^{13}C spectrum of **7** could be identified in a similar fashion while the multiplets were identified by HETCOR. Thus **7** was a diacetate of the unknown 8-(3,3-dimethylallyl)mulberranol.

By exclusion the structure of artelastofuran was **5a**. This was confirmed by irradiation at the frequency of the bonded -OH of **5b** which enhanced the carbon singlets at δ 159.6 (C-5), 107.3 (C-6) and 104.9 (C-4a) but none of the these was affected by irradiation at δ 4.75, the signal of H-20. The other carbon singlets were assigned by comparison with those of **7** while the

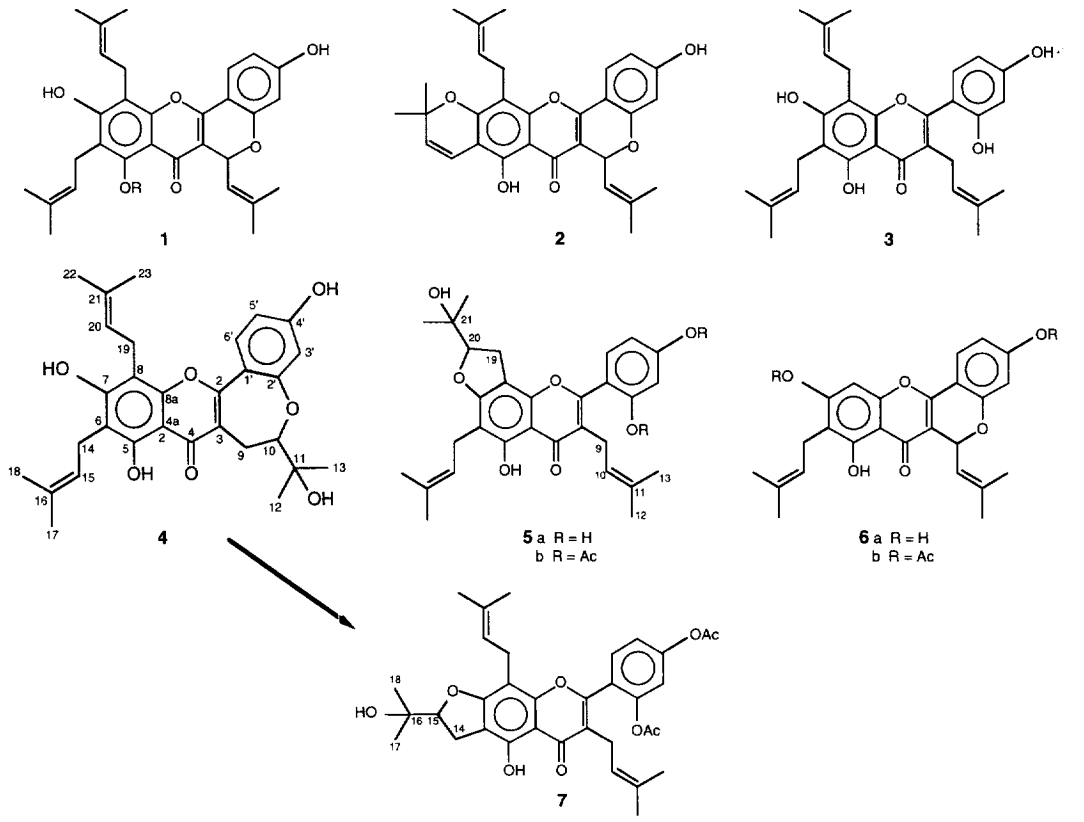

Fig. 1

multiplets were identified by HETCOR as were those of **4**.

EXPERIMENTAL

Isolation and extraction. Frs. 59–61 (3.5 g) of the original chromatogram of the *Artocarpus elasticus* extraction [1] were combined and rechromatographed over Si gel, 100 ml subfrs being collected as follows. Subfrs 1–164 (petrol–$CHCl_3$, 7:3), 165–242 (petrol–$CHCl_3$, 1:1), 243–260 (petrol–$CHCl_3$, 3:7), 261–290 ($CHCl_3$), 291–301 ($CHCl_3$–Me_2CO, 4:1) and 302–304 ($CHCl_3$–Me_2CO, 1:1). Subfrs. 42–102 (900 mg) were combined and rechromatographed over Sephadex LH-20 (15 g). Elution with MeOH gave 12 10 ml frs. Frs 6–10 were combined and purified by TLC (Si gel G254, petrol–EtOAc, 7:3) to give 140 mg of artelasticin (**3**). Frs 11 and 12 were combined and purified by TLC (Si gel G254, petrol–EtOAc, 13:7) to give 26 mg of cyclocommunin (**6**).

Subfrs 125–174 (800 mg) were combined and rechromatographed over 15 g of Sephadex LH-20. Elution with MeOH gave 12 10 ml frs. Frs 4–7 were combined and purified by TLC (Si gel G 254, petrol–EtOAc) to give 200 mg of artelasticin (**3**). Frs 8–12 (62 mg) were combined and purified by TLC (Si gel G 254, petrol–EtOAc 13:7) to give 30 mg of **6**. Subfrs 191–261 (350 mg) were combined and purified by TLC (Si gel G 254, petrol–EtOAc 11:9) to give 20 mg of **6** and 30 mg of **4**. Subfrs 262–277 (140 mg) were also combined and purified by TLC (Si gel G 254, petrol–EtOAc, 3:2) to give 12 mg of **4** and 32 mg of **5a**. Cyclocommunin (**6**) was identified by MS, ^1H and ^{13}C NMR and conversion to the diacetate. The ^{13}C NMR spectrum in DMSO-d_6 tallied with that reported in [3]; in particular the frequency of the C-8 signal at δ 93.3 differentiated [8] the substance from cyclomulberrin, the isomer with the prenyl group on C-8 (δC-6 100.2) [3].

Artelastinin (**4**). Orange-red gum; MS PCI *m/z* (rel. int.) 507 (100, $C_{30}H_{34}O_7+[H]^+$), 451 (15), 395 (10), 377 (20), 335 (15), 207 (25), 185 (55), 115 (85), 93 (100); UV λ_{max}^{meOH} (nm, log ε) 337 (4.0), 272 (4.1), 214 (4.4); $\lambda_{max}^{MeOH+NaOH}$ 385 (4.1), 267 (4.1), 214 (4.6), $\lambda_{max}^{MeOH+AlCl_3}$ 364 (4.1), 280 (4.1), 216 (4.4); $\lambda_{max}^{MeOH+AlCl_3+HCl}$ 356 (4.0), 281 (4.1), 216 (4.4); ^1H NMR (300 MHz, DMSO-d_6) δ 13.17 (*s*, 5-OH), 7.79 (*d*, J = 8.8 Hz, H-6′), 6.59 (*dd*, J = 8.8, 2.2 Hz, H-5′), 6.48 (*d*, J = 2.2 Hz, H-3′), 5.19 (*t*, J = 7 Hz, H-15 or H-20), 5.12 (*t*, J = 7 Hz, H-20 or H-15), 3.78 (*dd*, J = 9.2, 2 Hz, H-10), 3.15 (*d*, J = 6.6 Hz, H-14 or H-19), 3.12 (*d*, J = 7.6 Hz, H-19 or H-14), 3.3 (H-9a, obscured by H_2O peak), 2.37 (*d*, J = 16.8, 10.1 Hz, H-9b), 1.71 and 1.69 (each *s* and 3p, H-18 and H-23), 1.57 (*s*, 6p, H-17 and H-22), 1.23 and 1.19 (each *s* and 3p, H-12 and H-13); ^{13}C NMR in Table 1.

Acetylation of 30 mg of artelastinin at room temp. with Py-Ac_2O, work-up in the usual way and puri-

fication of the product by TLC afforded 22 mg of diacetate 7 as a gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.9 (*s*, 5-OH), 7.37 (*d*, *J* = 9 Hz, H-6′), 7.07 (*d*, *J* = 2.2 Hz, H-3′), 7.06 (*d*, *J* = 9, 2.2 Hz, H-5′), 5.02 (*m*, 2p, H-10 and H-20), 4.69 (*dd*, *J* = 9.5, 8 Hz, H-15), 3.21 (*d*, *J* = 8 Hz, 4p, H-9, 19), 31.5 (*dd*, *J* = 16, 9.5 Hz, H-14a), 3.06 (*dd*, *J* = 16, 8 Hz, H-14b), 2.26 and 2.04 (each *s* and 3p, Ac), 1.55 (*s*, 6p, H-12, H-22), 1.52 (*s*, 3p, H-23), 1.35 (*s*, 3p, H-13), 1.26 and 1.15 (each *s* and 3p, H-17, H-18); ^{13}C NMR in Table 1.

Artelastofuran (**5a**). Orange-red gum; MS PCI *m/z* (rel. int.) 507 (100, $C_{30}H_{34}O_7+[H]^+$), 451 (55), 379 (15), 343 (15), 177 (20), 115 40); MS EI *m/z* 506 (100), 491 (10), 463 (65), 451 (85), 433 (15), 391 (10), 335 (15), 189 (15); UV λ_{max}^{meOH} (nm, log ε) 315 (3.7 sh), 268 (4.2), 212 (4.4); $\lambda_{max}^{MeOH+NaOH}$ 380 (3.8), 266 (4.2), 213 (4.6); $\lambda_{max}^{MeOH+AlCl_3}$ 315 (3.9 sh), 268 (4.2), 212 (4.4); $\lambda_{max}^{MeOH+AlCl_3+HCl}$ 315 (3.38 sh), 267 (4.2), 212 (4.4); ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.60 (*s*, 5-OH), 7.03 (*d*, *J* = 8.3 Hz, H-6′), 6.38 (*d*, *J* = 2 Hz, H-3′), 6.25 (*d*, *J* = 8.3, 2 Hz, H-5′), 5.20 (*t*, *J* = 6.5 Hz, H-10), 5.03 (*t*, *J* = 6.5 Hz, H-15), 4.71 (*t*, *J* = 8.6 Hz, H-20), 3.3 (obscured by H_2O peak, H-19a), 3.20 (2p, H-9), 3.12 (*dd*, *J* = 15.4, 8.6 Hz, H-19b), 3.03 (*d*, *J* = 6.3 Hz, 2p, H-14), 1.71 (*s*, 3p, H-18), 1.62 and 1.53 (each *s* and 3p, H-12 and H-17), 1.37 (*s*, 3p, H-13), 1.13 and 1.09 (each *s* and 3p, H-22 and H-23); ^{13}C NMR in Table 1.

Acetylation of 25 mg of artelastofuran at room temp. with Ac_2O-Py, work-up in the usual way and purification of the product by TLC afforded 18 mg of diacetate **5b** as a gum; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.21 *s* (5-OH), 7.45 (*d*, *J* = 8.6 Hz, H-6′), 7.14 (*d*, *J* = 2.2 Hz, H-3′), 7.13 (*J* = 8.6, 2.2 Hz, H-5′), 5.28 (*t*, *J* = 6.5 Hz, H-10), 5.03 (*t*, *J* = 6.5 Hz, H-15), 4.75 (*t*, *J* = 8.2 Hz, H-20), 3.34 (*d*, *J* = 7 Hz, 2p, H-9), 3.16 (*dd*, *J* = 15.4, 9.3 Hz, H-19a), 3.09 (*dd*, *J* = 15.4, 8.1 Hz, H-19b), 3.07 (*d*, *J* = 7 Hz, 2p, H-14), 2.34 and 2.14 (both *s* and 3p, Ac), 1.79 (*s* and 3p, H-18), 1.69 and 1.62 (both *s* and 3p, H-12 and H-17), 1.42 (*s* and 3p, H-13), 1.34 and 1.19 (each *s* and 3p, H-22 and H-23); ^{13} C NMR in Table 1.

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