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# PRENYLFLAVONOIDS OF *ARTOCARPUS HETEROPHYLLUS*

MEI-ING CHUNG,* CHAI-MING LU,* PAO-LIN HUANG† and CHUN-NAN LIN*‡

*School of Pharmacy, Kaohsiung Medical College, Kaohsiung, Taiwan 807, †Ta-Jen Junior Pharmaceutical College, Ping Tung Hsieng, Taiwan 907

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**Key Word Index**—*Artocarpus heterophyllus*; Moraceae; prenylflavonoids; flavonoids; 8-(γ,γ-dimethylallyl)-5,4′-dihydroxy-7,2′-dimethoxyflavone; 3,3′-di-(γ,γ-dimethylallyl)-5,7,2′,5′-tetrahydroxy-4′-methoxyflavone; artocarpetin B; heteroartonin A.

**Abstract**—Six prenylflavonoids, including two new compounds, have been isolated from the root bark of *Artocarpus heterophyllus*. The new prenylflavones have been characterized as 8-(γ,γ-dimethylallyl)-5,4′-dihydroxy-7,2′-dimethoxyflavone and 3,3′-di-(γ,γ-dimethylallyl)-5,7,2′,5′-tetrahydroxy-4′-methoxyflavone, respectively.

## INTRODUCTION

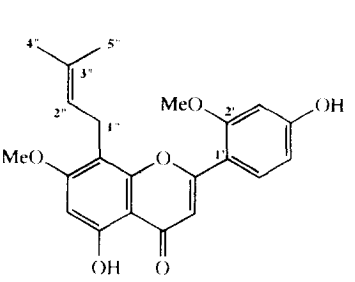
In previous papers [1–4], we reported a series of flavonoids isolated from the root of *Artocarpus heterophyllus* Lamk. In a continuing study of this plant, two new prenylflavones named artocarpetin B (**1**) and heteroartonin A (**2**), respectively, and four known prenylflavonoids, kuwanon T (**3**), artonin A (**4**), artonin and B (**5**) and heterophyllin (**6**) have been isolated from the root bark. In this paper, we now report the structural characterization of the two new compounds and **2** by NMR, MS and UV spectroscopy.

## RESULTS AND DISCUSSION

The IR spectrum of **1** showed hydroxy and chelated carbonyl absorption bands at 3350 and 1655 $cm^{-1}$, respectively. The UV spectrum of **1**, showed similar absorption maxima to those of artocarpetin and artocarpetin A [4], and the aluminium chloride and sodium methoxide induced bathochromic shifts indicated that **1** was a 5,4′-dihydroxylated flavonoid [5]. The $^1H$ NMR (pyridine-$d_5$) spectrum of **1** showed one set of γ,γ-dimethylallyl signals at δ1.69, 1.88 (each 3H, *s*, Me), 3.71 (2H, *br d*, $J$ = 6.9 Hz, $CH_2$) and 5.50 (1H, *m*, CH=), two methoxy signals at δ3.72 and 3.80 (each 3H, *s*), and two phenolic signals at δ13.30 (*br*) and 13.92 (*s*, chelated C-5 OH). The ABC type coupled aromatic proton signals appeared at δ6.79 (1H, *dd*, $J$ = 8.8, 2.4 Hz), 6.84 (1H, *d*, $J$ = 2.4 Hz) and 8.17 (1H, *d*, $J$ = 8.8 Hz) could be reasonably assigned to the H-5′, H-2′ and H-6′ of a 2′,4′-dioxygenated flavone, respectively. The other two aromatic singlets at δ7.81 and 6.67 could be assigned as the H-3 and H-6 or H-8 signals of a flavone as in artocarpetin A [4]. In the EI mass spectrum of **1**, a molecular ion appeared at *m/z* 382 (base peak) and an intense peak at *m/z* 351 $[M - 31]^+$ could be due to the loss of the C-2′ methoxy [6]. The intense peaks at *m/z* 367 $[M - 15]^+$ and 314 $[M - 68]^+$ indicated the existence of a γ,γ-dimethylallyl group and was located at C-8 of a C-7 methoxylated flavone [7]. The significant retro-Diels–Alder fragmentation peaks at *m/z* 233, 219, 191, 179, 151, 149, 148 and 133 also supported the two methoxyl groups located at A(C-7) and B(C-2′) ring, respectively [6, 7]. Based on the above evidence and the aluminium chloride and the sodium methoxide induced bathochromic shifts in the UV spectra, the structure of artocarpetin B was characterized as 8-(γ,γ-dimethylallyl)-5,4′-dihydroxy-7,2′-dimethoxyflavone (**1**) [5, 8]. The $^{13}C$ NMR (Table 1) spectrum of **1** was assigned by $^1H$-decoupled spectra, DEPT pulse sequence, comparison with those of artocarpetin A [4] and methylation induced shifts [9]. The characterization of **1** was supported by the $^{13}C$ NMR spectrum.

Compound **2** showed similar UV absorption maxima to those of 5,7,2′,4′,5′-pentaoxygenated flavone, artonin E [10]. The aluminium chloride and sodium methoxide induced bathochromic shifts in the UV spectra indicated

‡Author to whom correspondence should be addressed.

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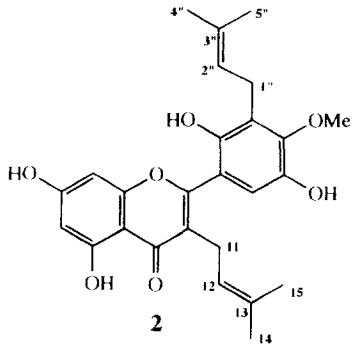


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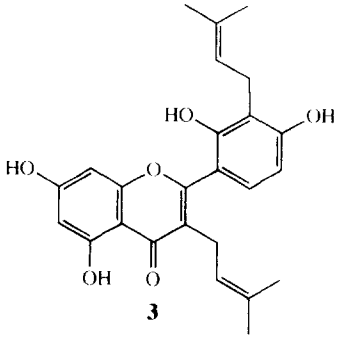


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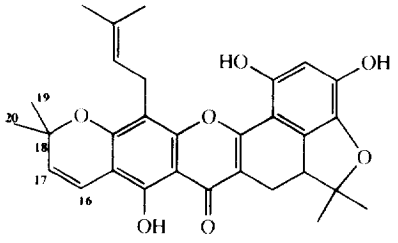


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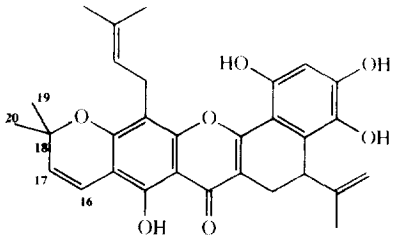


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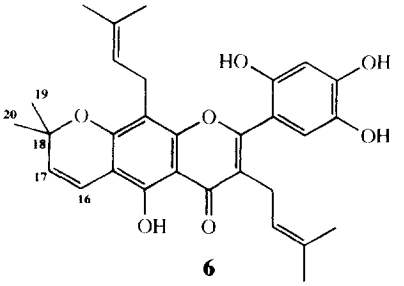


6

that **2** was 5,7-dihydroxylated flavone [5]. The IR spectrum of **2** showed hydroxyl absorption bands at 3520 and 3330 $cm^{-1}$ and chelated carbonyl absorption band at 1655 $cm^{-1}$. The $^1H$ NMR spectrum of **2** showed two sets of $\gamma,\gamma$-dimethylallyl groups at $\delta$1.38 (3H, *s*, Me), 1.78 (3H, *s*, Me), 3.08 (2H, *br d*, $J$ = 7 Hz, $CH_2$) and 5.09 (1H, *m*, CH=); $\delta$1.57 (3H, *d*, $J$ = 1.2 Hz, Me), 1.67 (3H, *d*, $J$ = 1.2 Hz, Me), 3.44 (2H, *br d*, $J$ = 7 Hz, $CH_2$), and 5.27 (1H, *m*, CH=); a methoxy signal at $\delta$3.84, and three phenolic signals at $\delta$7.84 (2H, *br*), 9.44 (1H, *br*) and 13.07 (1H, *s*, chelated). The *meta* coupled aromatic protons at $\delta$6.24 and 6.32 (each 1H, *d*, $J$ = 2.2 Hz) could be reasonably assigned to the H-6 and H-8 of a 5,7-dioxygenated flavone, respectively, and the singlet at $\delta$6.75 could be assigned to the H-6′ of the tetra-substituted B ring of **2**. In the $^{13}C$ NMR spectrum of **2** (Table 1), a methoxy signal appeared at $\delta$61.5 which indicated the methoxyl group was located at C-2′ or 4′ [11]. In addition to the above evidence, the absence of sodium methoxide–boric acid-induced bathochromic shift in the UV spectra of **2** clearly showed that the methoxy group was located at C-4′ of **2**. The EI mass spectrum of **2** showed a molecular ion at *m/z* 452 (base peak) and an intense peak at *m/z* 435 $[M-17]^+$ indicated that **2** was a C-2′ hydroxylated flavone [6]. The significant peaks at *m/z* 437 $[M-15]^+$, 409 $[M-43]^+$, 395 $[M-57]^+$, 384 $[M-68]^+$, 383, 381, 379, 365, 353 and 341 indicated the existence of two $\gamma,\gamma$-dimethylallyl groups. The intense peaks at *m/z* 297 and 153 also indicated that the A ring was dihydroxylated and that the two $\gamma,\gamma$-dimethylallyl groups were attached to the B ring and C-3, respectively [6]. Based on the above evidences, the structure of **2** was characterized as 3,3′-di-($\gamma,\gamma$-dimethylallyl)-5,7,2′,5′-tetrahydroxy-4′-methoxyflavone. The $^{13}C$ NMR spectrum of **2** (Table 1) was assigned by $^1H$-decoupled spectra, DEPT pulse sequence, comparison with those of heterophyllin (**6**) and kuwanon T (**3**), and methylation induced shifts [9]. The $^{13}C$ NMR spectrum of **2** supported the characterization of **2**.

The $^{13}C$ NMR spectrum of **5** (Table 1) was assigned by $^1H$-decoupled spectra, DEPT pulse sequence, long range HETCOR spectrum and comparison with that of hetero-

Table 1. $^{13}C$ NMR chemical shift assignment of the flavonoids **1–6***

| No. C | 1† | 2‡§ | 3‡ | 4‡ | 5† | 6‡ |
|---|---|---|---|---|---|---|
| 2 | 163.0¶ | 162.1 | 162.8 | 162.1 | 162.4 | 162.9 |
| 3 | 108.6 | 122.8 | 123.0 | 124.3 | 111.9 | 122.0 |
| 4 | 183.9 | 183.7 | 183.8 | 182.3 | 182.1 | 184.2 |
| 5 | 160.2 | 160.0 | 160.1 | 155.9 | 155.8 | 155.9¶ |
| 6 | 95.4 | 99.9 | 99.8 | 105.9 | 106.0 | 106.2 |
| 7 | 163.8 | 165.5 | 165.5 | 157.6 | 157.6 | 157.8 |
| 8 | 107.9 | 94.8 | 94.9 | 108.9 | 108.9 | 112.4 |
| 9 | 161.3 | 164.1 | 164.0 | 155.1 | 155.2 | 156.4¶ |
| 10 | 105.4 | 106.0 | 106.0 | 105.7 | 108.9 | 106.1 |
| 11 | | 25.1 | 25.2 | 21.1 | 23.0 | 25.3 |
| 12 | | 124.5 | 124.4 | 48.2 | 38.7 | 123.3 |
| 13 | | 132.4 | 132.1 | 94.4 | 146.0 | 132.4 |
| 14 | | 26.5 | 26.6 | 23.6 | 112.5 | 26.5 |
| 15 | | 18.2 | 18.6 | 29.0 | 22.6 | 18.3 |
| 16 | | | | 117.1 | 117.0 | 117.1 |
| 17 | | | | 129.5 | 129.5 | 129.6 |
| 18 | | | | 79.0 | 79.0 | 79.1 |
| 19 | | | | 29.0 | 29.0 | 28.9 |
| 20 | | | | 29.0 | 29.0 | 28.9 |
| 1′ | 112.2 | 117.3 | 113.8 | 106.5 | 107.6 | 108.5 |
| 2′ | 154.8 | 150.1 | 155.0 | 152.1 | 152.1 | 150.4 |
| 3′ | 102.9 | 125.7 | 122.9 | 106.0 | 104.2 | 105.3 |
| 4′ | 162.7¶ | 147.3 | 159.4 | 147.6 | 151.5 | 150.0 |
| 5′ | 106.3 | 145.0 | 108.8 | 138.6 | 137.3 | 139.7 |
| 6′ | 130.5 | 115.8 | 129.3 | 132.3 | 130.4 | 117.8 |
| 1″ | 22.2 | 24.8 | 23.8 | 22.7 | 22.7 | 22.6 |
| 2″ | 123.7 | 122.8 | 123.0 | 124.5 | 124.1 | 123.7¶ |
| 3″ | 131.7 | 133.0 | 132.9 | 134.3 | 132.4 | 132.8¶ |
| 4″ | 25.7 | 26.5 | 26.5 | 26.6 | 26.6 | 26.5 |
| 5″ | 18.0 | 18.6 | 18.2 | 18.8 | 18.8 | 18.6 |
| OMe | 55.3, 56.1 | 61.5 | | | | |

* The number of directly attached protons to each carbons were verified with DEPT pulse sequence.
† Detected in pyridine-$d_5$.
‡ Detected in acetone-$d_6$.
§ These signals were obtained by long-range HETCOR technology.
¶ These signals may be reversed in each column.
‖ These two signals were revised by the long-range HETCOR spectrum.

phyllin (**6**). In the assignment of $^{13}C$ NMR spectrum of **5**, we found that the chemical shift values of C-13 and C-4′, reported in literature [12], should be exchanged.

## EXPERIMENTAL

*Plant material, extraction and isolation.* Root bark (1 kg) of *Artocarpus heterophyllus* Lamk., collected at Ping Tung Hsieng, during July, 1992, chipped and extracted ×3 with $Me_2CO$ at room temperature. The $Me_2CO$ extract was chromatographed on Si gel. Elution with $CHCl_3$–cyclohexane–$Me_2CO$ (4:5:1) yielded artonin A (**4**); $CHCl_3$–cyclohexane–$Me_2CO$ (5:4:1) yielded artocarpetin B (**1**), heteroartonin A (**2**), kuwanon T (**3**); and $CHCl_3$–cyclohexane–$Me_2CO$ (6:3:1) yielded artonin B (**5**) and heterophyllin (**6**). These compounds were all purified by further CC and recrystallization with a suitable solvent. The known compounds were all determined by spectral methods and compared with corresponding data reported in the literature.

*Compound* **1**. $C_{22}H_{22}O_6$, yellow needles ($CHCl_3$), mp 253 ~ 257°. IR$\nu_{max}^{KBr}$ cm$^{-1}$: 3350 (OH), 1655 (chelated C=O), 1615. UV$\lambda_{max}^{MeOH}$ (log $\varepsilon$) nm: 209 (4.53), 252 (sh) (4.16), 270 (4.30), 288 (sh) (4.08), 345 (4.23); + $AlCl_3$: 212, 238, 256 (sh), 276, 295, 355, 397 and + NaOMe: 210, 268, 288 (sh), 330 (sh), 360, 400 (sh). $^1H$ NMR (pyridine-$d_5$): see text. $^{13}C$ NMR (pyridine-$d_5$): see Table 1. EIMS (direct inlet) 70 eV, *m/z* (rel. int.): 382 $[M]^+$ (100), 367 $[M-CH_3]^+$ (97), 351 $[M-OMe]^+$ (4), 327 $[M-55]^+$ (19), 326 $[M-56]^+$ (22), 314 $[M-68]^+$ (63), 233 (7), 219 (20), 203 (6), 191 (10), 179 (25), 167 (13), 161 (10), 151 (22), 149 (25), 148 (39), 133 (14), 121 (23), 120 (17), 105 (21), 91 (43), 77 (59), 69 (77), 55 (48), 43 (59). HRMS Calc. for $C_{22}H_{22}O_6$: 382.1416. Found: 382.1426.

*Compound* **2**. $C_{26}H_{28}O_7$, yellow plates (benzene), mp 206–208°. IR$\nu_{max}^{KBr}$ cm$^{-1}$: 3520 (OH), 3330 (OH), 1655 (C=O), 1620. UV$\lambda_{max}^{MeOH}$ (log $\varepsilon$) nm: 213 (4.52), 230 (sh) (4.37), 255 (4.41), 298 (4.02), 325 (sh) (3.98), 402 (sh) (2.89); + $AlCl_3$–216, 267, 313, 375; + NaOAc— 218, 260, 327, 397 (sh); + NaOAc + $H_3BO_3$— unchanged and

+ NaOMe-217, 265, 333. $^1$H NMR (acetone-$d_6$): see text. $^{13}$C NMR (acetone-$d_6$): see Table 1. EIMS (direct inlet) 70 eV, *m/z* (rel. int.): 452 $[M]^+$ (100), 437 $[M-CH_3]^+$ (6), 422 $[M-OCH_2]^+$ (7), 409 $[M-43]^+$ (63), 397 $[M-55]^+$ (6), 396 $[M-56]^+$ (8), 395 $[M-57]^+$ (32), 386 $[M-68]^+$ (4), 383 (11), 381 (16), 379 (18), 365 (10), 353 (16), 341 (21), 325 (14), 321 (12), 297 (6), 253 (4), 243 (7), 229 (6), 213 (3), 198 (5), 182 (6), 153 (69), 141 (7), 133 (7), 128 (12), 115 (16), 91 (28), 79 (11), 77 (18), 67 (15), 55 (24), 53 (15). HRMS Calc. for $C_{26}H_{28}O_7$: 452.1835. Found: 452.1820.

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