Three New Prenylflavones from Artocarpus altilis

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THREE NEW PRENYLFLAVONES FROM *ARTOCARPUS ALTILIS*

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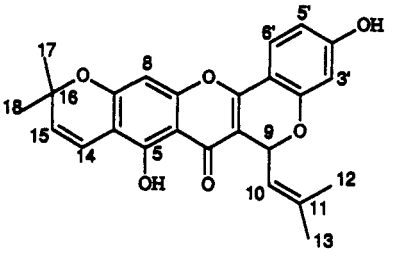
ABSTRACT.—Three new prenylflavones, isocyclomorusin [**1**], isocyclomulberrin [**3**], and cycloaltilisin [**5**], together with three known flavonoids, cyclomorusin [**2**], cyclomulberrin [**4**], and engeletin, were isolated from the stems of *Artocarpus altilis* (Moraceae). The structures of the new prenylflavones were determined by comparison with known related compounds and spectral analyses.

The stems and roots of *Artocarpus altilis* Fosberg (Moraceae) have been used traditionally for the treatment of liver cirrhosis and hypertension in Taiwan, where the plant also has been reported to possess anti-inflammatory and detoxifying effects (1). Previously, flavonoids and triterpenoids have been isolated from various parts of the plant (2–4). As part of our systematic chemical analysis of Taiwanese medicinal plants, we now report the isolation of three novel prenylflavones, together with three known flavonoids, cyclomorusin [**2**] (5,6), cyclomulberrin [**4**] (5,6), and engeletin (7), from *A. altilis*. The structural elucidations of the three new prenylflavones, isocyclomorusin [**1**], isocyclomulberrin [**3**], and cycloaltilisin [**5**], are described by comparison with known related compounds and with the aid of spectral analyses.



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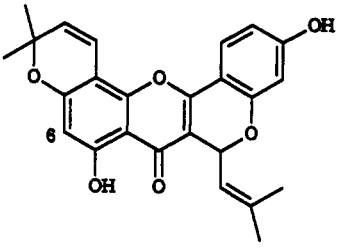

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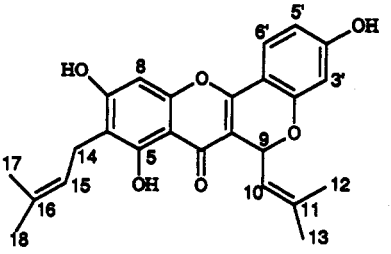
RESULTS AND DISCUSSION

Compound **1** was obtained as yellow prisms, $[M]^+$ 418. The ^{1}H-nmr data closely resembled those of cyclomorusin [**2**] (6). The ^{1}H nmr indicated the presence of a 2,2-dimethylchromene group (8) by characteristic signals of two vinyl protons at δ 6.60 (d, J=10.1 Hz, H-14) and 5.53 (H-15) and a six-proton singlet at δ 1.37. The presence of ring D, resulting from oxidative cyclization of 2′-hydroxyl group with the allylic methylene of a prenyl group at C-3, was indicated by ^{1}H-nmr signals at δ 1.61 (H-13) and 1.88 (H-12) for two vinyl Me protons, a broad doublet at δ 5.36 (H-10), and a doublet at δ 6.13 (H-9) (5, 9–12). Ring



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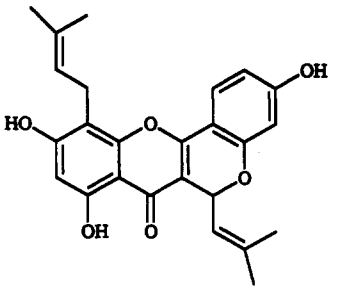

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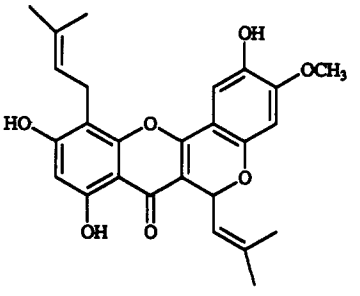

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D was substantiated by the chemical shift of H-6′ [δ 7.55 (1H, d, J=8.4 Hz)], which is downfield from H-6′ signal of mulberrin (5, 9–12). Sharp singlets at δ 13.03 (5-OH) and 6.28 (H-8) indicated that substituents were present at C-5, -6, and -7. Analyses of the 1D DEPT and 2D ^{1}H-^{13}C COSY spectra of **1** indicated that a tertiary aromatic carbon signal at δ 94.9 was assigned to C-8 (6,13). Thus, a 2,2-dimethylchromene group was determined as shown in **1**, and, consequently, compound **1** was named isocyclomorusin.

Compound **3** was obtained in form of yellow prisms, $[M]^{+}$ 420. The ^{1}H nmr of **3** closely resembled that of cyclomulberrin [**4**] (5,6). The ^{1}H-nmr spectrum of **3** showed the characteristic signals for a γ,γ-dimethylallyl group [δ 1.62 and 1.66 (each 3H, s, H-17 and H-18), 3.31 (2H, d, J=7.2 Hz, H-14), 5.24 (1H, t, J=7.2 Hz, H-15)]. The presence of ring D, as in **1**, was substantiated by the presence of two vinyl Me protons at δ 1.75 (3H, s, H-13) and 1.93 (3H, s, H-12), a doublet at δ 5.45 (J=9.4 Hz, H-10), and a doublet at δ 6.19 (J=9.4 Hz, H-9). A sharp singlet at δ 13.12 indicated a chelated OH group. The aromatic protons of ring B showed the characteristic ABX pattern [δ 6.41 (1H, d, J=2.3 Hz), 6.58 (1H, dd, J=2.3, 8.3 Hz), 7.65 (1H, d, J=8.3 Hz)]. The singlet at δ 6.59 was assigned to H-8. Analyses of the 1D DEPT and 2D ^{1}H-^{13}C COSY spectra of **3** showed C-6 and C-8 at δ 108.2 and 93.3, respectively; these data were in good agreement with those of C-6 substituted flavones (6,13). These spectral analyses led to structure **3**, which was named isocyclomulberrin.

Structures **1** and **3** were reported from *Morus alba* (5), but these structures were later revised to structures **2** and **4**, respectively (6).

Compound **5** was obtained in form of yellow prisms, $[M]^{+}$ 450. The ^{1}H-nmr spectrum of **5** showed the characteristic signals for a γ,γ-dimethylallyl group [δ 1.66 (6H, s, H-17 and H-18), 3.54 (2H, m, H-14), 5.29 (1H, t, J=7.2 Hz, H-15)]. The presence of ring D, as in **1**, was substantiated by the presence of two vinyl Me protons at δ 1.82 (H-13) and 1.92 (H-12), together with vinyl protons at δ 5.50 (d, J=9.4 Hz, H-10) and 6.16 (d, J=9.4 Hz, H-9). The ^{1}H-nmr spectrum of **5** also showed three singlets of aromatic proton signals at δ 6.34 (H-6), 6.56 (H-3′), and 7.26 (H-6′) (5, 9–12), an MeO proton signal at δ 3.91, and a chelated OH proton at δ 12.79. NOe difference experiment revealed that the MeO group in **5** was located at C-4′, since irradiation of the MeO signal at δ 3.91 induced a 42% nOe effect in the H-3′ at δ 6.56. In the ^{13}C-nmr spectrum, the chemical shift values of the C-6 (δ 98.5) and C-8 (δ 103.6) signals of **5** were in good agreement with those of the C-8 substituted flavones (6,13). From the above data, structure **5** is proposed for the new flavone, namely cycloaltilisin.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were measured on Yanaco Micro Melting Point Apparatus and are uncorrected. Hreims and eims were obtained on JEOL SX-102A and JEOL

JMS-HX100 mass spectrometers, respectively. The ir spectra were recorded on a Jasco IR-100 ir spectrometer. ^{1}H- and ^{13}C-nmr spectra were taken on a Bruker AM-300WB FT-NMR spectrometer.

PLANT MATERIAL.—The stems of *A. altilis* were collected and identified at the Botanical Garden of Taipei in May 1989. A voucher specimen is deposited in the National Research Institute of Chinese Medicine, Republic of China.

EXTRACTION AND ISOLATION.—The dried stems (4 kg) were extracted with EtOH. The combined EtOH extracts were evaporated and further partitioned to yield $CHCl_3$, *n*-BuOH, and aqueous extracts. Chromatography of the $CHCl_3$ extract over Si gel, using a gradient of *n*-hexane and EtOAc (1:0→1:1) as eluent, afforded 4 fractions. Fraction II was chromatographed on Si gel and Sephadex LH-20 (MeOH) columns to yield **1** (13 mg) and **2** (7 mg). Fraction III was also chromatographed on Si gel [$CHCl_3$-Me_2CO (15:1)] and Sephadex LH-20 (MeOH) to yield **3** (6 mg), **4** (10 mg), and **5** (15 mg). The *n*-BuOH extract was evaporated to dryness and chromatographed on Amberlite XAD-2 eluting with H_2O, 50% MeOH, and MeOH. The MeOH eluent was chromatographed on Si gel [$CHCl_3$-MeOH (4:1)] and Sephadex LH-20 (MeOH) columns to yield engeletin (650 mg).

Isocyclomorusin [**1**].—Mp 244–245°; $[\alpha]^{25}$ +30° (*c*=0.29, Me_2CO); ir (KBr) 3400, 1650, 1620, 1580 cm^{-1}; eims *m/z* (%) $[M]^+$ 418 (41), 403 (100), 363 (21), 347 (14), 194 (9), 174 (5); hreims 418.1443 (calcd for $C_{25}H_{22}O_6$, 418.1447); ^{1}H nmr (Me_2CO-d_6) δ 1.37 (6H, s, H-17 and H-18), 1.61 (3H, s, H-13), 1.88 (3H, s, H-12), 5.36 (1H, d, *J*=9.4 Hz, H-10), 5.53 (1H, d, *J*=10.1 Hz, H-15), 6.13 (1H, d, *J*=9.4 Hz, H-9), 6.28 (1H, s, H-8), 6.37 (1H, d, *J*=2.3 Hz, H-3′), 6.51 (1H, dd, *J*=2.3, 8.4 Hz, H-5′), 6.60 (1H, d, *J*=10.1 Hz, H-14), 7.55 (1H, d, *J*=8.4 Hz, H-6′), 13.03 (1H, s, 5-OH); ^{13}C nmr see Table 1.

Cyclomorusin [**2**].—Mp 256–257°; eims *m/z* (%) $[M]^+$ 418 (55), 403 (100); ^{1}H nmr (Me_2CO-d_6) δ 1.45 (6H, s, H-17 and H-18), 1.66 (3H, s, H-13), 1.92 (3H, s, H-12), 5.45 (1H, d, *J*=9.4 Hz, H-10), 5.76 (1H, d, *J*=10.0 Hz, H-15), 6.14 (1H,

TABLE 1. ^{13}C-nmr Chemical Shifts (ppm) of Compounds **1–5**.[a]

Carbon	Compound				
	1	**2**	**3**	**4**	**5**[b]
C-2	157.9	158.4	158.3	159.0	159.0
C-3	106.2	106.3	106.5	106.7	106.6
C-4	178.0	177.7	177.5	177.7	177.6
C-4a	104.8	101.2	103.5	106.2	106.3
C-5	155.8	155.3	154.9	153.7	153.6
C-6	108.3	99.4	108.2	98.4	98.6
C-7	163.9	163.6	163.2	163.3	162.3
C-8	95.4	103.7	93.3	103.8	103.4
C-8a	163.9	163.6	163.2	163.8	162.3
C-9	69.2	68.8	68.9	68.9	68.6
C-10	121.0	120.9	121.1	121.0	121.0
C-11	138.7	138.2	137.9	137.9	137.6
C-12	18.7	18.3	18.3	18.3	18.3
C-13	17.9	17.8	17.6	17.7	17.8
C-14	114.5	114.2	20.9	21.1	21.2
C-15	128.8	128.2	122.1	122.3	122.4
C-16	78.3	78.1	130.6	125.1	130.9
C-17	27.7	27.7	25.3	25.3	25.3
C-18	27.6	27.7	25.4	25.4	25.4
C-1′	110.2	110.3	111.0	106.7	108.5
C-2′	156.1	157.6	157.4	157.5	154.6
C-3′	103.7	105.8	103.8	103.8	101.5
C-4′	158.8	164.8	161.5	161.4	150.1
C-5′	110.2	111.3	110.0	110.1	141.0
C-6′	125.4	125.8	125.4	125.1	108.5

[a]Assignments were aided by 1D DEPT, nOe, and 2D ^{1}H-^{13}C COSY experiments. The chemical shift values were given in ppm and referenced to DMSO-d_6.

[b]The chemical shift of MeO was at δ 55.9.

s, H-6), 6.17 (1H, d, J=9.4 Hz, H-9), 6.42 (1H, d, J=2.1 Hz, H-3′), 6.61 (1H, dd, J=2.1, 8.5 Hz, H-5′), 6.90 (1H, d, J=10.0 Hz, H-14), 7.77 (1H, d, J=8.5 Hz, H-6′), 12.96 (1H, s, 5-OH); ^{13}C nmr see Table 1.

Isocyclomulberrin [**3**].—Mp 270–271°; $[\alpha]^{25}$ +53° (c=0.31, Me_2CO); ir (KBr) 3400, 1645, 1620, 1560 cm^{-1}; eims *m/z* (%) $[M]^+$ 420 (79), 365 (100), 349 (9), 321 (97), 309 (35); hreims 420.1593 (calcd for $C_{25}H_{24}O_6$, 420.1606); ^{1}H nmr (Me_2CO-d_6) δ 1.62 and 1.66 (each 3H, s, H-17 and H-18), 1.75 (3H, s, H-13), 1.93 (3H, s, H-12), 3.31 (2H, d, J=7.2 Hz, H-14), 5.24 (1H, t, J=7.2 Hz, H-15), 5.45 (1H, d, J=9.4 Hz, H-10), 6.19 (1H, d, J=9.4 Hz, H-9), 6.41 (1H, d, J=2.3 Hz, H-3′), 6.58 (1H, dd, J=2.3, 8.3 Hz, H-5′), 6.59 (1H, s, H-8), 7.65 (1H, d, J=8.3 Hz, H-6′), 13.12 (1H, s, 5-OH); ^{13}C nmr see Table 1.

Cyclomulberrin [**4**].—Mp 245–246°; eims *m/z* (%) $[M]^+$ 420 (54), 405 (100); ^{1}H nmr (Me_2CO-d_6) δ 1.64 and 1.67 (each 3H, s, H-17 and H-18), 1.82 (3H, s, H-13), 1.93 (3H, s, H-12), 3.54 (2H, dd, J=6.7, 15 Hz, H-14), 5.28 (1H, t, J=6.7 Hz, H-15), 5.45 (1H, d, J=9.4 Hz, H-10), 6.18 (1H, d, J=9.4 Hz, H-9), 6.33 (1H, s, H-6), 6.42 (1H, d, J=2.0 Hz, H-3′), 6.63 (1H, dd, J=2.0, 8.6 Hz, H-5′), 7.70 (1H, d, J=8.6 Hz, H-6′), 12.78 (1H, s, 5-OH); ^{13}C nmr Table 1.

Cycloaltilisin [**5**].—Mp 186–188°; $[\alpha]^{25}$ +99° (c=0.36, Me_2CO); ir (KBr) 3420, 1650, 1620, 1540 cm^{-1}; eims *m/z* (%) $[M]^+$ 450 (75), 435 (58), 395 (100); hreims 450.1701 (calcd for $C_{26}H_{26}O_7$, 450.1715); ^{1}H nmr (Me_2CO-d_6) δ 1.66 (6H, s, H-17 and H-18), 1.82 (3H, s, H-13), 1.92 (3H, s, H-12), 3.54 (2H, m, H-14), 3.91 (3H, s, 4′-OMe), 5.29 (1H, t, J=6.7 Hz, H-15), 5.50 (1H, d, J=9.4 Hz, H-10), 6.16 (1H, d, J=9.4 Hz, H-9), 6.34 (1H, s, H-6), 6.56 (1H, s, H-3′), 7.26 (1H, s, H-6′), 12.79 (1H, s, 5-OH); ^{13}C nmr see Table 1.

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