Three New 2-Phenoxychromones from the Leaves of Epimedium sagittatum

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THREE NEW 2-PHENOXYCHROMONES FROM THE LEAVES OF *EPIMEDIUM SAGITTATUM*

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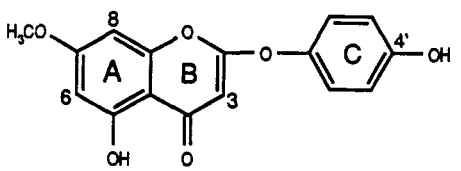
ABSTRACT.—Three new 2-phenoxychromones, 6-demethoxy-7-methylcapillarisin [**1**], 6-demethoxy-4′-methyl-8-isopentenylcapillarisin [**2**], and 6-demethoxy-7-isopentenylcapillarisin [**3**], were isolated from the leaves of *Epimedium sagittatum* (Berberidaceae). The structures of these compounds were established by spectral methods.

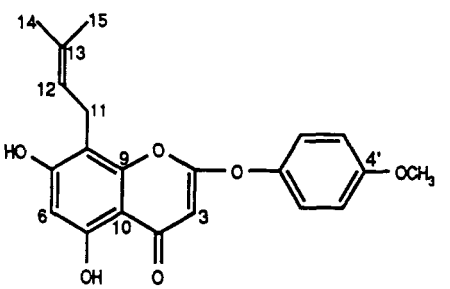
The aerial parts of *Epimedium* plants (Berberidaceae) or "yinyanghuo," are used in China for impotence, atrophy, neurasthenia, amnesia, and climacteric hypertension. Previous studies on the aerial parts of *Epimedium* species have reported the presence of alkaloids, lignans, terpenoids, and flavonoid glycosides (1–6). Recently, we reinvestigated the leaves of *Epimedium sagittatum* Maxim. with attention to less polar fractions. As a result, three new 2-phenoxychromones **1–3** were isolated.

From the analysis of spectral data, compounds **1–3** were identified as members of the 2-phenoxychromone class, which possesses a flavone-like skeleton with the A/B ring system linked to the C ring via an oxygen atom (7–9).

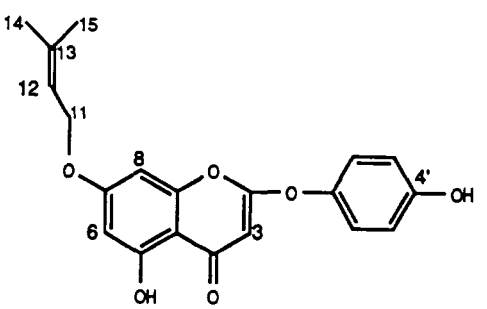
6-Demethoxy-7-methylcapillarisin [**1**] was obtained as colorless needles. The hreims of compound **1** displayed the molecular ion peak at *m/z* 300.0613 (calcd 300.0633), consistent with the molecular formula $C_{16}H_{12}O_6$. In the ^{1}H-nmr spectrum, the singlet at δ 5.08 was characteristic of the H-3 signal in 2-



1



2



3

phenoxychromone (7–9). The singlet at δ 12.86, due to a chelated 5-OH group, and two doublets ($J=2.1$ Hz), at δ 6.38 (1H, H-6), and 6.57 (1H, H-8), suggested that compound **1** was 5,7-disubstituted in ring A. Furthermore, a typical A_2B_2 system at δ 6.86 (2H, d, $J=8.0$ Hz) and 7.18 (2H, d, $J=8.0$ Hz) showed the presence of four aromatic protons on ring C. The location of the MeO group at δ 3.84 (3H, s) was established through nOe experiments. Irradiation of the MeO protons enhanced the signals at δ 6.38 (H-6) and 6.57 (H-8) by 24%. On the basis of above spectral evidence, the structure of **1** was identified as 6-demethoxy-7-methylcapillarisin.

6-Demethoxy-4′-methyl-8-isopentenylcapillarisin [**2**] was obtained as colorless needles. The hreims of compound **2** displayed the molecular ion peak at *m/z* 368.1238 (calcd 368.1260), consistent with the molecular formula $C_{21}H_{20}O_6$. The characteristic singlet of H-3 at δ 5.15 was also observed in its ^{1}H-nmr spectrum. One MeO group (δ 3.85) appeared in **2**. The signals at δ 1.67 (3H, s), 1.71 (3H, s), 3.33 (2H, d, $J=7.1$ Hz) and 5.14 (1H, m) showed the presence of a γ,γ-dimethylallyl group (10,11). The chemical shifts of aromatic protons at δ 7.08 (2H, d, $J=7.8$ Hz), 7.32 (2H, d, $J=7.8$ Hz), and 6.32 (1H, s) indicated that **2** also contained an A_2B_2 system in ring C, but only one unsubstituted proton in ring A. Irradiation at δ 3.85 (Ar-OMe) enhanced the signal at δ 7.08 (H-3′ and H-5′) by 18%, showing that the MeO group was located at C-4′. The position of the γ,γ-dimethylallyl group was assigned by HMBC (heteronuclear multiple bond correlation) experiments. As shown in Figure 1, the proton at δ 12.83 (5-OH) showed cross peaks with the carbons at δ 99.7 (C-6) and 103.4 (C-10); the proton at δ 6.32 (H-6) showed cross peaks with the carbons at δ 103.4 (C-10) and 107.5 (C-8). From these results, the position of the γ,γ-dimethylallyl group of **2** was concluded to be at C-8, and the structure of **2** was assigned as 6-demethoxy-4′-methyl-8-isopentenylcapillarisin.

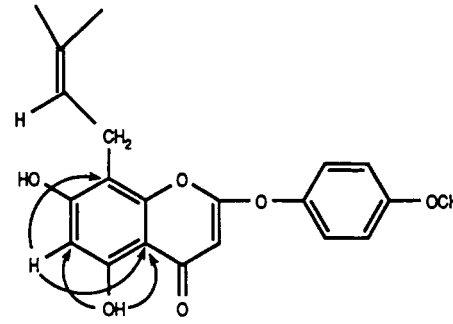


FIGURE 1. Correlations in the HMBC spectrum of **2**.

6-Demethoxy-7-isopentenylcapillarisin [**3**] was obtained as pale pink needles. The hreims of compound **3** displayed the molecular ion peak at *m/z* 354.1109 (calcd 354.1103), consistent with the molecular formula $C_{20}H_{18}O_6$. In the ^{1}H-nmr spectrum, the singlet at δ 5.10 was assigned to H-3 (7–9). The signals at δ 1.76 (3H, s), 1.78 (3H, s), 4.66 (2H, d, $J=6.6$ Hz), and 5.47 (1H, m) showed the presence of an isopentenoxyl group. Furthermore, irradiation of the C-11 protons at δ 4.66 enhanced the signals at δ 6.32 (H-6) and 6.50 (H-8) by 16% and 12%, respectively. This clearly indicated that the isopentenoxyl group was located at C-7. As for the remaining signals, δ 6.97 (2H, d, $J=9.0$ Hz) was assigned to H-3′ and H-5′, and δ 7.20 (2H, d, $J=9.0$ Hz) was for H-2′ and H-6′. From the above spectral data, the structure of **3** was established as 6-demethoxy-7-isopentenylcapillarisin.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Mp's were measured on Yanaco Micro Melting Point Apparatus and were uncorrected. The ir spectra were recorded on a JASCO-IR-100 Spectrometer. ^{1}H- and ^{13}C-nmr spectra were taken on Bruker AM-300 WB (300 MHz) FT-NMR. Hreims and eims were obtained on JEOL SX-102A and JEOL JMS-HX100 spectrometers, respectively.

PLANT MATERIAL.—Plant material, named "yinyanghuo," used in this research was obtained at a market in Taipei and was identified as the leaves of *E. sagittatum* by Mr. M.T. Kao (National Research Institute of Chinese Medicine). A voucher specimen is deposited in the herbarium of our institution.

EXTRACTION AND SEPARATION.—The dried leaves (15 kg) were extracted with Me_2CO. After evaporation, the residue was chromatographed on a Si gel column and eluted with a gradient of *n*-hexane and *n*-hexane–Me_2CO (10:1→1:1) to give several fractions. The fractions eluted with *n*-hexane–Me_2CO (5:1) were evaporated, and the residue was further separated on a Si gel column (230–400 mesh) using *n*-hexane–EtOAc (4:1→2:1) as the eluent to afford four fractions. Each fraction was further purified by preparative tlc on Si gel using CH_2Cl_2-MeOH (13:1) as the solvent system to give 6-demethoxy-7-methylcapillarisin [**1**] (250 mg), 6-demethoxy-4′-methyl-8-isopentenyl-capillarisin [**2**] (25 mg), and 6-demethoxy-7-isopentenylcapillarisin [**3**] (120 mg).

6-Demethoxy-7-methylcapillarisin [**1**].—Colorless needles: mp 245–246°; ir (KBr) 3200, 1670, 1610, 1490 cm^{-1}; eims *m/z* (%) $[M]^+$ 300 (100), 721 (23), 167 (33), 134 (11); hreims 300.0613 (calcd for $C_{16}H_{12}O_6$, 300.0633); ^1H nmr (DMSO-d_6) δ 3.84 (3H, s, 7-OMe), 5.08 (1H, s, H-3), 6.38 (1H, d, J = 2.1 Hz, H-6), 6.57 (1H, d, J = 2.1 Hz, H-8), 6.86 (2H, d, J = 8.0 Hz, H-3′ and H-5′), 7.18 (2H, d, J = 8.0 Hz, H-2′ and H-6′), 12.86 (1H, s); ^{13}C nmr see Table 1.

6-Demethoxy-4′-methyl-8-isopentenylcapillarisin [**2**].—Colorless needles: mp 155–156°; ir (KBr) 3200, 1650, 1615, 1590, 1505 cm^{-1}; eims *m/z* (%) $[M]^+$ 368 (84), 353 (100), 313 (64), 300 (47), 153 (3), 148 (16); hreims 368.1238 (calcd for $C_{21}H_{20}O_6$, 368.1260); ^1H nmr (Me_2CO-d_6) δ 1.67 (3H, s, H-14), 1.71 (3H, s, H-15), 3.33 (2H, d, J = 7.1 Hz, H-11), 3.85 (3H, s, 4′-OMe), 5.14 (1H, br t, J = 7.1 Hz, H-12), 5.15 (1H, s, H-3), 6.32 (1H, s, H-6), 7.08 (2H, d, J = 7.8 Hz, H-3′ and H-5′), 7.32 (2H, d, J = 7.8 Hz, H-2′ and H-6′), 12.83 (1H, s); ^{13}C nmr see Table 1.

6-Demethoxy-7-isopentenylcapillarisin [**3**].—Pale pink needles: mp 170–172°; ir (KBr) 3200, 1650, 1585, 1505 cm^{-1}; eims *m/z* (%) $[M]^+$ 354 (6), 286 (100), 153 (29), 134 (20); hreims 354.1109 (calcd for $C_{20}H_{18}O_6$, 354.1103); ^1H nmr (Me_2CO-d_6) δ 1.76 (3H, s, H-14), 1.78 (3H, s, H-15), 4.66 (2H, d, J = 6.6 Hz, H-11), 5.10 (1H, s, H-3), 5.47 (1H, br s, J = 6.6 Hz, H-12), 6.32 (1H, d, J = 2.0 Hz, H-6), 6.50 (1H, d, J = 2.0 Hz, H-8), 6.97 (2H, d, J = 9.0 Hz, H-3′ and H-5′), 7.20 (2H, d, J = 9.0 Hz, H-2′ and H-6′), 12.86 (1H, s); ^{13}C nmr see Table 1.

TABLE 1. ^{13}C-nmr Data for Compounds **1**, **2**, and **3**.[a]

Carbon	Compound		
	1	**2**	**3**
C-2	168.8	168.7	169.5
C-3	87.6	88.0	88.1
C-4	183.6	184.7	184.5
C-5	161.8	162.4	163.0
C-6	98.7	99.7	99.6
C-7	165.3	162.4	165.5
C-8	93.2	107.5	93.9
C-9	155.2	153.6	156.2
C-10	103.3	103.4	104.2
C-1′	143.6	145.9	145.0
C-2′	122.3	122.8	122.7
C-3′	117.0	116.1	117.5
C-4′	156.3	159.2	157.1
C-5′	117.0	116.1	117.5
C-6′	122.3	122.8	122.7
C-11		22.0	66.3
C-12		122.9	120.0
C-13		132.0	139.0
C-14		25.8	25.8
C-15		17.8	18.2
-OMe	56.5	56.0	

[a]300 MHz, Me_2CO-d_6. The chemical shifts were assigned on the basis of ^1H-^{13}C COSY spectra.

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