New Prenylflavones and Dibenzoylmethane from Glycyrrhiza inflata

Kiichiro Kajiyana, Sachio Demizu, Yukio Hiraga,
Kaoru Kinoshita, Kiyotaka Koyama, Kunio Takahashi,
Yukiyoshi Tamura, Kenzo Okada, and Takeshi Kinoshita

More About This Article

The permalink http://dx.doi.org/10.1021/np50087a005 provides access to:

- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

NEW PRENYLFLAVONES AND DIBENZOYLMETHANE
FROM *GLYCYRRHIZA INFLATA*

KIICHIRO KAJIYAMA, SACHIO DEMIZU, YUKIO HIRAGA,*

Meiji College of Pharmacy at Setagaya, 1-35-23 Nozawa, Setagaya-ku, Tokyo 154, Japan

KAORU KINOSHITA, KIYOTAKA KOYAMA, KUNIO TAKAHASHI,

Meiji College of Pharmacy at Tanashi, 1-22-1 Yato-cho, Tanashi 188, Japan

YUKIYOSHI TAMURA, KENZO OKADA,

Research Laboratory, Maruzen Kasei Co., Ltd., 14703-10 Mukaihigashi-cho, Onomichi 722, Japan

and TAKESHI KINOSHITA

*Faculty of Pharmaceutical Sciences, Teikyo University, 1091-1 Suarashi,
Sagamiko-machi, Tsukui-gun, Kanagawa 199-01, Japan*

ABSTRACT.—Two new prenylflavones, licoflavones B [1] and C [2], and one new diben-zoylmathane, glycyrdione C [4], were isolated from the root of *Glycyrrhiza inflata* (Leguminosae) together with two known flavones, licoflavone A and 4',7-dihydroxyflavone. Their structures were elucidated on spectroscopic evidence as 4',7-dihydroxy-3',6-diprenyl-flavone [1], 8-prenyl-4',5,7-trihydroxyflavone [2], and 1-(2,2-dimethyl-7-hydroxy-2*H*-1-benzopyran-6-yl)-3-(4-hydroxy-3-prenyl-phenyl)-1,3-propanedione [4]. The structure of a prenylflavone that was isolated from *Marshalli grandiflora*, previously determined as 4',5,7-trihydroxy-8-(3,3-dimethylallyl)-flavone, was revised to 6-prenyl-4',5,7-trihydroxyflavone [3].

The roots of *Glycyrrhiza uralensis* Fisch., *Glycyrrhiza glabra* L., and *Glycyrrhiza inflata* Batalin (Leguminosae) are known to contain the sweetening principle glycyrrhizin. The root of *G. uralensis* is called "kanzo" or "gancao," which literally means "sweet herb" in Japanese and Chinese, respectively, and is commonly found as one of the main ingredients in traditional Chinese mixed herbal medicines (Kampo medicine). The dried root of *G. glabra*, which occurs in Europe and its vicinity, has found medicinal use as the crude drug licorice since ancient times. However, *G. glabra* and *G. inflata* are not considered medicinal in Japan and are used mostly for extraction of glycyrrhizin, whose derivatives are of medicinal use as therapeutic agents. The crude extracts of these two *Glycyrrhiza* species are also used as food additives.

It has long been conceived that glycyrrhizin, which is well known for its anti-inflammatory, antiallergic, and antihepatotoxic activity, is the only constituent underwriting the pharmacological efficacy of licorice. However, the anti-gastric-ulcer effect of licorice extracts (from *G. uralensis*) was ascribed to glycyrrhizin-free fractions abounding in flavonoids (1), and later various types of phenolic compounds were isolated as antimicrobial principles from the root of *G. glabra* and other *Glycyrrhiza* species (2–6). These findings may verify that the phenolics also make up part of the pharmacological efficacy of licorice. These research developments have incited us to work on a research program for isolation and identification of licorice constituents with the guidance of the antimicrobial and antioxidant activities, and we have reported the isolation of several phenolic constituents from the roots of *G. uralensis*, *G. glabra*, and *G. inflata* as active principles (7,8). Continuing efforts have been made to isolate minor constituents, especially in non-medicinal *Glycyrrhiza* roots, because they are known to abound in various types of phenolic constituents that chemotaxonomically characterize species of the genus *Glycyrrhiza* (9). We previously reported the isolation and structure elucidation of three dibenzoylmethanes and also referred to their biogenetic significance in relation to

the chemotaxonomy of the genus *Glycyrrhiza* (10). In this report we describe properties and structural assignments of novel prenylflavones and a dibenzoylmethane.

RESULTS AND DISCUSSION

The CHCl$_3$ extract of the root of *G. inflata* was chromatographed on a Si gel column using C$_6$H$_6$ with an increasing precentage of Me$_2$CO for elution. Four flavones were isolated by a series of chromatographic separations. Two of these four flavones were new natural products and named licoflavones B [1] and C [2], and the other two were identified as the known compounds licoflavone A (11) and 4',7-dihydroxyflavone (12), respectively, by comparison with reported spectral data. One of the less polar fractions yielded a new dibenzoylmethane named glycyrdione C [4].

Licoflavone B [1] was obtained as pale yellow needles, mp 210°. Acetylation of licoflavone B with Ac$_2$O/pyridine furnished a diacetate, mp 148°. The molecular formula of 1 was determined to be C$_{25}$H$_{26}$O$_4$ based upon the elementary analysis and ms, which was further confirmed by hrms. The close similarity of the uv spectrum to those of licoflavone A and 4',7-dihydroxyflavone indicated the presence of the same chromophoric unit, which was further substantiated by bathochromic shifts observed on addition of NaOAc and NaOMe. The ^{1}H-nmr spectrum exhibited the presence of two γ,γ-dimethylallyl groups [δ 1.74, 1.76 (6H each, s), 3.41 (4H, d, *J* = 7.2 Hz), 5.40 (2H, m)], ABX aromatic protons [δ 7.01 (1H, d, *J* = 8.6 Hz), 7.73 (1H, dd, *J* = 2.3, 8.6 Hz), 7.78 (1H, d, *J* = 2.3 Hz)], two singlet protons (δ 6.60, 7.06), and one deshielded aromatic proton (δ 7.84). The above evidence suggested that licoflavone B is diprenyl-4',7-dihydroxyflavone. The location of the prenyl groups was readily assigned at C-3' and C-6 from the ^{1}H- and ^{13}C-nmr spectra (Table 1).

Licoflavone C [2] was obtained as pale yellow needles, mp 239°. The uv spectrum suggested it to be a typical flavone, showing absorption maxima at 274, 305, and 326
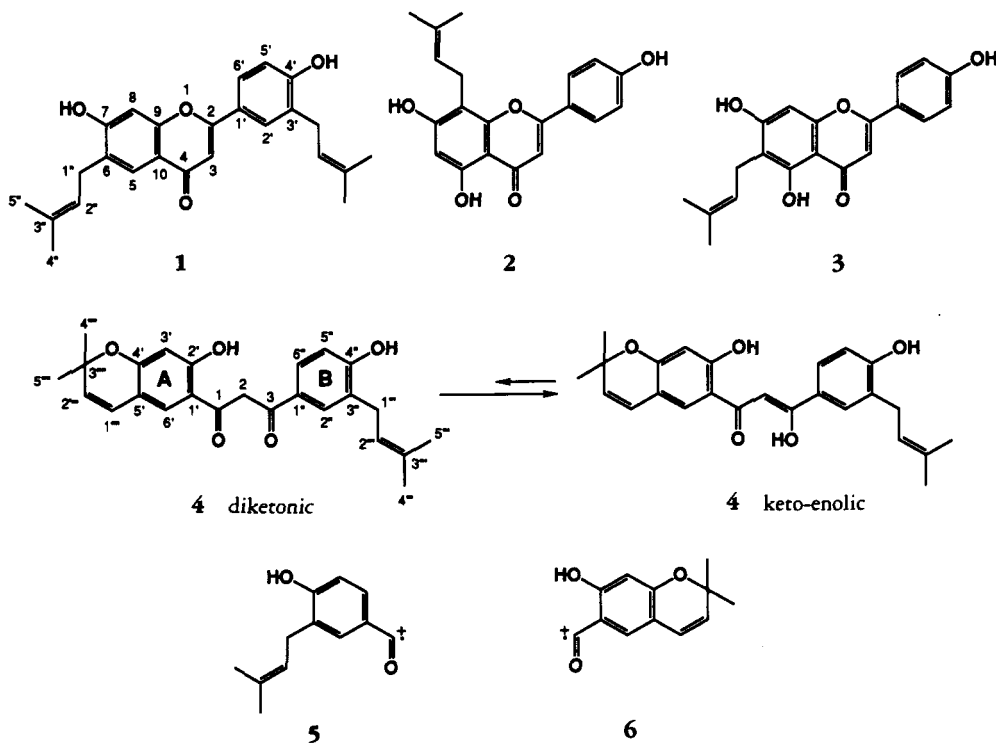

1   2   3

4   diketonic   4   keto-enolic

5   6

TABLE 1. ^{13}C-nmr Data of Flavones Isolated from Root of *Glycyrrhiza inflata* (100 MHz, δ ppm, TMS as internal standard).[a]

Carbon	Compound			
	Licofavone A (CD$_3$OD)	1 [(CD$_3$)$_2$CO]	2 [(CD$_3$)$_2$CO]	4',7-Dihydroxyflavone [(CD$_3$)$_2$SO]
C-2	165.7	163.9	165.0	162.5[b]
C-3	102.6	102.9	103.9	102.4
C-4	180.4	177.5	183.5	176.2
C-5	126.0	126.2	161.0	126.4
C-6	129.9	129.8	99.3	114.7
C-7	162.7[b]	161.0	162.2	160.6
C-8	105.1	105.7	105.4	104.4
C-9	158.0	157.1	156.0	157.3
C-10	nf	117.7	107.4	116.1
C-1'	123.7	124.0	123.7	121.8
C-2'	129.3	126.2	129.3	128.1
C-3'	116.9	128.4	116.9	115.9
C-4'	162.4[b]	159.1	161.9	162.4[b]
C-5'	116.9	116.3	116.9	115.9
C-6'	129.3	128.6	129.3	128.1
[prenyl]				
C-1''	28.9	28.7, 29.1	22.4	—
C-2''	122.7	122.8, 123.1	123.6	—
C-3''	134.3	133.2, 133.5	132.1	—
C-4''	26.0	25.9 (2C)	25.8	—
C-5''	17.9	17.9 (2C)	18.1	—

[a]nf indicates that the corresponding signal was missing.
[b]Signals in the same column may be interchangeable.

nm. Uv shifts with NaOAc and AlCl$_3$ indicated the location of the A ring hydroxyl groups at C-7 and C-5, respectively. The ^{1}H-nmr spectrum exhibited the presence of the γ,γ-dimethylallyl group {δ 1.67 (3H, s), 1.82 (3H, s), 3.57 (2H, d, J = 6.8 Hz), 5.30 (1H, br t, J = 6.8 Hz)], A$_2$B$_2$ aromatic protons [δ 7.05 (2H, d, J = 9.0 Hz), 7.96 (2H, d, J = 9.0 Hz)] assignable to the B ring, a singlet proton [δ 6.63 (1H, s)] at C-3, and one singlet aromatic proton [δ 6.34 (1H, s)]. From the above evidence, the structure of licoflavone C was elucidated as either 6- or 8-prenyl-4',5,7-trihydroxyflavone. The location of the prenyl group was determined at C-8 by comparison of ^{13}C-nmr chemical shifts of C-6 and C-8 with those of apigenin and 6- or 8-substituted-5,7-hydroxyflavones (13). The resonances for unsubstituted C-6 and C-8 in these compounds usually appear approximately at 99 ppm and 94 ppm, respectively, and are quite distinct. Furthermore, substitution at C-6 or C-8 is known not to alter markedly the chemical shift of the unsubstituted aromatic methine carbon atom. Therefore, whether a prenyl group is substituted at C-6 or C-8 in 4',5,7-trihydroxyflavone can be unambiguously determined. The chemical shifts of C-6 and C-8 for licoflavone C were observed at 99.3 and 105.4, respectively. The marked downfield shift (ca. 11 ppm) of C-8 and the almost unchanged chemical shift of C-6 revealed the prenyl group to be located at C-8. This location was further substantiated by the following irradiation experiments. A singlet at δ 6.34 was significantly sharpened upon irradiation of a singlet at δ 13.0 assigned to a chelated 5-OH, while other signals were unchanged. This indicated the occurrence of a small coupling between both signals; therefore, a singlet proton signal at δ 6.34 was unequivocally assigned to H-6. Irradiation of the 5-OH also resulted in a 3% nOe (based on a difference spectrum) on H-6.

A flavone derivative whose structure was established as 4',5,7-trihydroxy-8-(3,3-dimethylallyl)-flavone has been isolated from *Marshallia grandiflora* (Compositae) in small quantity and uncrystallized form (14). However, the reported data did not agree with those of licoflavone C although these two compounds have the same nominal structure. Chemical shifts of H-3 and H-6 were 6.64 and 6.63, respectively, whereas they were observed at 6.63 and 6.34, respectively, for licoflavone C. On the other hand, chemical shifts of H-3 and H-8 in gancaonin Q (3',6-diprenyl-4',5,7-trihydroxy-flavone), a closely related prenylflavone isolated from *G. uralensis* (15) having identical partial structure of the A and C rings, were reported to be 6.61 and 6.60, respectively, with which 4',5,7-trihydroxy-8-(3,3-dimethylallyl)-flavone was in good agreement. It is apparent from this evidence that the structure of a prenylflavone isolated from *M. grandiflora* was erroneously elucidated and should be revised to 4',5,7-trihydroxy-6-(3,3-dimethylallyl)-flavone [3] as far as it can be deduced from its reported ^{1}H-nmr data. Since a further search of the literature has revealed that 8-prenyl-4',5,7-trihydroxyflavone has not yet been known as a natural product, the new name of licoflavone C was proposed.

Glycyrdione C [4] did not crystallize though it was purified by repeated sets of chromatography including hplc. However, its spectroscopic data revealed that it is pure. Its molecular formula was deduced to be $C_{25}H_{26}O_5$ from the hrms. Its β-hydroxychalcone nature was suggested by the ir, v max cm^{-1} 3000 (OH), 1600, 1570 [C(OH)=CH-CO], and uv (λ max 266, 350, 402) spectra, which is also consistent with the positive color reaction with Mg-HCl and FeCl$_3$. These features closely resemble those of licodione, a constituent of *G. echinata* callus (11), and dibenzoylmethane derivatives previously isolated by us from *G. inflata* root (10), suggesting that glycyrdione C is one of their analogues. Nearly all signals of the ^{1}H- and ^{13}C-nmr spectra appeared as pairs, indicating its existence in solution as an equilibrium mixture of two tautomeric forms. The dibenzoylmethane has been known to constitute two tautomers, diketonic (dibenzoylmethane) and keto-enolic (β-hydroxychalcone) forms (10,11). A singlet proton at δ 6.58 which integrates for 0.70 H was assigned to the vinyl methine, while a singlet proton at δ 4.46 (0.60 H) was attributed to methylene protons of the diketonic form. The assignments of ^{1}H and ^{13}C signals of glycyrdione C are shown in Table 2. It should be noted that assignments of some aromatic carbons of glycyrdiones A and B reported in a previous paper (10) were revised based upon the long range ^{13}C-^{1}H COSY analysis of glycyrdione C (data not shown). The ratio of two tautomers was found to be 70:30 in excess of keto-enolic form, based upon the integration of the above signals. The presence of C$_5$ units, one γ,γ-dimethylallyl and one chromene, was also indicated by the ^{1}H- and ^{13}C-nmr spectra. The position of C$_5$ attachments was readily deduced from analysis of ^{1}H- and ^{13}C-nmr signals and mass fragment ions. In general, the dibenzoylmethane gives rise to two predominant ion peaks derived from either A or B ring in the ms. The prominent ion peaks at 189 and 203 amu in the ms of glycyrdione C, which were assigned to **5** and **6**, respectively, indicated that the chromene occurs on the A ring while the prenyl unit is substituted on the B ring. From this evidence, the structure of glycyrdione C was elucidated as **4**, a regio isomer of glycyrdione B.

The isolation of prenylated 4',7-dihydroxyflavones is of interest in view of their biogenetic relation to dibenzoylmethanes previously isolated from the same licorice (10). For instance, 5-prenyl-licodione and glycyrdione A would give rise to licoflavones A and B if they undergo cyclization and dehydration, respectively. In a previous paper, we discussed the intermediacy of 2-hydroxyflavanone as a common precursor for both flavones and dibenzoylmethanes (10). The co-occurrence of dibenzoylmethanes and their structurally related flavones in the same plant lends support to this hypothesis.

TABLE 2. ^{1}H- and ^{13}C-nmr Data of Glycyrdione C [**4**] (400 MHz for ^{1}H, 100 MHz for ^{13}C, δ ppm in CDCl$_3$, TMS as internal standard. Assignments of carbon resonances were confirmed by the long range ^{1}H-^{13}C COSY).

Position	^{1}H nmr		^{13}C nmr	
	keto-enolic	diketonic	keto-enolic	diketonic
1			193.4	198.0
2	6.58 (0.70 H, s)	4.46 (0.60 H, s)	90.4	49.5
3			176.7	193.0
1′			113.8	112.7
2′			164.6	165.5
3′	6.36 (0.70 H, s)	6.32 (0.30 H, s)	104.8	104.4
4′			159.8	161.1
5′			113.9	113.7
6′	7.35 (0.70 H, s)	7.41 (0.30 H, s)	126.2	128.9
1″			125.7[a]	
2″	7.71 (0.70 H, d, $J = 2.3$ Hz)	7.83 (0.30 H, d, $J = 2.3$ Hz)	128.8	131.2
3″			127.7	127.9
4″			158.3	159.9
5″	6.88 (0.70 H, d, $J = 9.0$ Hz)	6.86 (0.30 H, d, $J = 9.0$ Hz)	115.7	115.4
6″	7.70 (0.70 H, dd, $J = 9.0, 2.3$ Hz)	7.82 (0.30 H, dd, $J = 9.0, 2.3$ Hz)	126.5	129.4
[prenyl]				
1‴	3.43 (1.40 H, d, $J = 7.2$ Hz)	3.38 (0.60 H, d, $J = 7.2$ Hz)	29.3	28.9
2‴	5.34 (0.70 H, m)	5.31 (0.30 H, m)	121.3	120.8[b]
3‴			134.8	134.9
4‴	1.7–1.8 (4.2 H, s)	1.7–1.8 (1.8 H, s)	25.7	25.7
5‴	1.7–1.8 (4.2 H, s)	1.7–1.8 (1.8 H, s)	17.9	17.8
[chromene]				
1‴‴	6.32 (0.70 H, d, $J = 9.7$ Hz)	6.27 (0.30 H, d, $J = 9.7$ Hz)	121.1	120.9[b]
2‴‴	5.58 (0.70 H, d, $J = 9.7$ Hz)	5.57 (0.30 H, d, $J = 9.7$ Hz)	128.8	128.8
3‴‴			77.7	78.2
4‴‴,5‴‴	1.45 (4.2 H, s)	1.43 (1.8 H, s)	28.5	28.4
[hydroxyls]				
3-OH	15.57 (0.70 H, s)			
2′-OH	12.62 (0.70 H, s)	12.45 (0.30 H, s)		
4″-OH	6.12 (0.70 H, br s)	6.40 (0.30 H, br s)		

[a]One of pair signals is missing or overlapped.
[b]Signals may be interchangeable.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All mp's were measured on a Yanagimoto mp apparatus and are uncorrected. Spectral data were obtained using the following apparatus: ^{1}H and ^{13}C nmr spectra with JEOL JMN GSX-400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometer with TMS as internal standard; ms with JEOL JMS-D300 mass spectrometer; ir spectra with a JASCO DS-701G infrared spectrometer; uv spectra with a Hitachi 340 uv spectrometer. Cc was carried out with the following materials; Wakogel C-200 or Merck Kieselgel 60 (eluted with C_6H_6/Me$_2$CO or hexane/EtOAc), Sephadex LH-20 (Pharmacia, column size; 3.6 × 30 cm; eluted with MeOH or MeOH/CHCl$_3$). Tlc was conducted on a 0.25 mm pre-coated Si gel plate (60GF$_{254}$, Merck). All chromatographic fractions were monitored by tlc, and spots were detected either by inspection under short (254 nm) or long (360 nm) wavelength uv lights, or by the colors developed with 10% H$_2$SO$_4$ spraying followed by heating on a hot plate. Hplc was carried out on RF-535 (Shimadzu Co., Kyoto, Japan) using μ-Bondapak C-18 column (4.6 × 30 cm, Waters).

PLANT MATERIAL.—The root of *G. inflata* (commercial name: shinkyo kanzo in Japanese; Xinjiang Gancao in Chinese) was imported from Xinjiang Province, China through Maruzen Kasei Co., Onomichi, Japan. A voucher specimen is deposited at Meiji College of Pharmacy, Setagaya, Japan.

EXTRACTION AND ISOLATION.—The crushed roots of *G. inflata* (3 kg) were extracted with $CHCl_3$ at room temperature, and the extract was evaporated to dryness under reduced pressure to yield a semisolid residue (110 g). A portion of the residue (75 g) was dissolved in Me_2CO and adsorbed on Si gel (75 g). The adsorbed material was transferred to a Si gel column (750 g; column size 7 × 40 cm) packed in C_6H_6. The column was eluted with a gradient solvent system of C_6H_6/Me_2CO increasing the amount of Me_2CO stepwise to give a number of fractions, which were combined into 13 fractions on the basis of their tlc patterns: fraction I (1.4 g) with 100% C_6H_6; fraction II (0.4 g) with C_6H_6-Me_2CO (98:2); fraction III (3.3 g) with C_6H_6-Me_2CO (96:4); fractions IV (3.5 g), V (9.9 g), and VI (1.7 g) with C_6H_6-Me_2CO (94:6); fraction VII (16.6 g) with C_6H_6-Me_2CO (92:8); fractions VIII (2.5 g) and IX (3.7 g) with C_6H_6-Me_2CO (90:10); fractions X (2.4 g) and XI (4.9 g) with C_6H_6-Me_2CO (88:12); fraction XII (3.2 g) with C_6H_6-Me_2CO (86:14); and fraction XIII (1.6 g) with C_6H_6-Me_2CO (84:16). Fraction III was chromatographed over Si gel (column size 3.2 × 40 cm) on elution with a C_6H_6/Me_2CO mixture increasing the amount of Me_2CO stepwise (0, 2, 4, 6, 8%) to give 24 fractions. Fractions (2.4 g) eluted with 4% C_6H_6/Me_2CO were combined and successively chromatographed over Sephadex LH-20 (MeOH) and Si gel [hexane-EtOAc (9:2)] to afford crude glycyrdione C [4]. This was finally purified by hplc on elution with $MeOH-H_2O$ (9:1) to give pure glycyrdione C [4] (60 mg). Fraction VIII was repeatedly chromatographed over Sephadex LH-20 on elution with $MeOH-CHCl_3$ (2:1) to give licoflavone C [2] (45 mg). Fractions X and XII were chromatographed over Sephadex LH-20 [$MeOH-CHCl_3$ (2:1)] to yield licoflavones B [1] (260 mg), and A (110 mg), respectively. Fraction XIII yielded yellow precipitates, which, upon recrystallization from $MeOH/H_2O$, gave pure 4',7-dihydroxyflavone (40 mg).

Licoflavone A.—Pale yellow needles from MeOH: mp 236°; uv λ max (MeOH, log ε) 258 (3.95), 330 (4.39); λ max (MeOH + NaOAc) 262, 330; λ max (MeOH + NaOMe) 266, 334, 396; ir ν max (KBr) 3100, 1620, 1606, 1560, 1498, 1475, 1440, 1368; ^1H nmr (CD_3OD, 400 MHz) δ 1.73 (3H, s, Me-4″), 1.78 (3H, s, Me-5″), 3.35 (2H, d, $J = 7.3$ Hz, CH_2-1″), 5.36 (1H, br t, $J = 7.3$ Hz, H-2″), 6.63 (1H, s, H-3), 6.92 (2H, d, $J = 9.0$ Hz, H-3′ and H-5′), 6.93 (1H, s, H-8), 7.78 (1H, s, H-5), 7.82 (2H, d, $J = 9.0$ Hz, H-2′ and H-6′); eims *m/z* [M]$^+$ 322 (100%), 307 (68%), 293 (17%), 267 (86%), 149 (17%); hrms 322.1222 ($C_{20}H_{18}O_4$ requires 322.1205). Found C 74.29, H 5.66 ($C_{20}H_{18}O_4$ requires C 74.52, H 5.63).

Licoflavone B [1].—Pale yellow needles from MeOH, mp 210°; uv λ max (MeOH, log ε) 256 sh (3.92), 336 (4.36); λ max (MeOH + NaOAc) 258, 336; λ max (MeOH + NaOMe) 256, 338, 404; ir ν max (KBr) 3200, 1620, 1600, 1560, 1492, 1418, 1367; ^1H nmr [$(CD_3)_2CO$, 400 MHz] δ 1.74, 1.76 (6H each, s, 2 × Me-4″ and 2 × Me-5″), 3.41 (4H, d, $J = 7.2$ Hz, CH_2-1″), 5.40 (2H, m, H-2″), 6.60 (1H, s, H-3), 7.01 (1H, d, $J = 8.6$ Hz, H-5′), 7.06 (1H, s, H-8), 7.73 (1H, dd, $J = 2.3, 8.6$ Hz, H-6′), 7.78 (1H, d, $J = 2.3$ Hz, H-2′), 7.84 (1H, s, H-5), 9.16, 9.77 (1H each, disappeared by the addition of D_2O, 7- and 4′-OH); eims *m/z* [M]$^+$ 390 (100%), 375 (41%), 373 (21%), 335 (97%), 149 (16%); hrms 390.1840 ($C_{25}H_{26}O_4$ requires 390.1831). Found C 76.80, H 6.76 ($C_{25}H_{26}O_4$ requires C 76.90, H 6.71). A mixture of licoflavone B (30 mg), pyridine, and Ac_2O was left overnight at room temperature, and then poured into ice-H_2O. Precipitates were collected and recrystallized from MeOH to give a diacetate as colorless needles: mp 148°; ^1H nmr ($CDCl_3$, 400 MHz) δ 1.72, 1.74, 1.76, 1.78 (3H each, s, 2 × Me-4″ and 2 × Me-5″), 2.35, 2.37 (3H each, s, Ac), 3.31 (2H, d, $J = 7.9$ Hz, CH_2-1″), 3.34 (2H, d, $J = 7.6$ Hz, CH_2-1″), 5.25 (2H, m, H-2″), 6.76 (1H, s, H-3), 7.18 (1H, d, $J = 8.6$ Hz, H-5′), 7.34 (1H, s, H-8), 7.74–7.76 (2H, m, H-2′ and H-6′), 8.08 (1H, s, H-5).

Licoflavone C [2].—Pale yellow needles from MeOH: mp 239°; uv λ max (MeOH, log ε) 274 (4.25), 305 (4.14), 326 (4.17); λ max (MeOH + NaOAc) 276; λ max (MeOH + $AlCl_3$) 284, 310, 343; λ max (MeOH + NaOMe) 284, 334, 404; ir ν max (KBr) 3430, 1660, 1606, 1565, 1552, 1510, 1468, 1425, 1362; ^1H nmr [$(CD_3)_2CO$, 400 MHz] δ 1.67 (3H, s, Me-5″), 1.82 (3H, s, Me-4″), 3.57 (2H, d, $J = 6.8$ Hz, CH_2-1″), 5.30 (1H, br t, $J = 6.8$ Hz, H-2″), 6.34 (1H, s, H-6), 6.63 (1H, s, H-3), 7.05 (2H, d, $J = 9.0$ Hz, H-3′ and H-5′), 7.96 (2H, d, $J = 9.0$ Hz, H-2′ and H-6′), 9.40 (2H, br, 7- and 4′-OH, disappeared by the addition of D_2O), 13.0 (1H, s, 5-OH, disappeared by the addition of D_2O); eims *m/z* [M]$^+$ 338 (100%), 323 (99%), 283 (35%), 270 (60%), 205 (9%), 165 (12%); hrms 338.1153 ($C_{20}H_{18}O_5$ requires 338.1154). Found C 71.27, H 5.34 ($C_{20}H_{18}O_5$ requires C 71.00, H 5.36).

4',7-Dihydroxyflavone.—Pale yellow granules from $MeOH/H_2O$: mp >300°; uv λ max (MeOH, log ε) 254 (4.05), 313 sh (4.36), 328 (4.40); λ max (MeOH + NaOAc) 258, 313 sh, 328; λ max (MeOH + NaOMe) 256, 262 sh, 334, 392; ir ν max (KBr) 3200, 1630, 1600, 1550, 1502, 1441, 1382; ^1H nmr [$(CD_3)_2SO$, 400 MHz] δ 6.73 (1H, s, H-3), 6.91 (1H, dd, $J = 8.6$ and 2.1 Hz, H-6), 6.93 (2H, d, $J = 8.7$ Hz, H-3′ and H-5′), 6.98 (1H, d, $J = 2.1$ Hz, H-8), 7.87 (1H, d, $J = 8.6$ Hz, H-5), 7.92 (2H,

d, $J = 8.7$ Hz, H-2' and H-6'), 10.28, 10.79 (1H each, br s, 7- and 4'-OH, disappeared by the addition of D_2O).

Glycyrdione C [4].—Amorphous; uv λ max (MeOH, log ε) 266 (4.52), 350 (4.33), 402 (4.60); ir ν max (CHCl$_3$) 3000, 1600, 1570, 1490, 1370, 1261; eims *m/z* [M]$^+$ 406 (24%), 391 (34%), 203 (100%), 189 (40%); hrms 406.1769 ($C_{25}H_{26}O_5$ requires 406.1780).

ACKNOWLEDGMENTS

LITERATURE CITED

1.   K. Takagi and Y. Ishii, *Arzneim. Forsch.*, **17**, 1544 (1967).
2.   L.A. Mitscher, Y.H. Park, S. Omoto, G.W. Clark, and D. Clark, *Heterocycles*, **9**, 1533 (1978).
3.   L.A. Mitscher, Y.H. Park, D. Clark, and J.L. Beal, *J. Nat. Prod.*, **43**, 259 (1980).
4.   L.A. Mitscher, G.S.R. Rao, I. Khanna, T. Veysoglu, and S. Drake, *Phytochemistry*, **22**, 573 (1983).
5.   M. Hattori, K. Miyachi, Y.-Z. Shu, N. Kakiuchi, and T. Namba, *Shoyakugaku Zasshi*, **40**, 406 (1986).
6.   S.R. Gollapudi, H. Telikepalli, A. Keshavarz-Shokri, D. Vander, and L.A. Mitscher, *Phytochemistry*, **28**, 3556 (1989).
7.   S. Demizu, K. Kajiyama, K. Takahashi, Y. Hiraga, S. Yamamoto, Y. Tamura, K. Okada, and T. Kinoshita, *Chem. Pharm. Bull.*, **36**, 3474 (1988).
8.   K. Okada, Y. Tamura, M. Yamamoto, Y. Inoue, R. Takagaki, K. Takahashi, S. Demizu, K. Kajiyama, Y. Hiraga, and T. Kinoshita, *Chem. Pharm. Bull.*, **37**, 2528 (1989).
9.   S. Shibata and T. Saitoh, *J. Indian Chem. Soc.*, **55**, 1184 (1978).
10.   S. Demizu, K. Kajiyama, Y. Hiraga, K. Kinoshita, K. Koyama, K. Takahashi, Y. Tamura, K. Okada, and T. Kinoshita, *Chem. Pharm. Bull.*, **40**, 392 (1992).
11.   S. Ayabe, M. Kobayashi, M. Hikichi, K. Matsumoto, and T. Furuya, *Phytochemistry*, **19**, 2179 (1980).
12.   T. Hatano, H. Kagawa, T. Yasuhara, and T. Okuda, *Chem. Pharm. Bull.*, **36**, 2090 (1988).
13.   K.R. Markham and V.M. Chari, in: "The Flavonoids: Advances in Research." Ed. by J.B. Harborne and T.J. Mabry, Chapman and Hall, London & New York, 1982, Chapter 2, pp. 19–134.
14.   F. Bohlmann, C. Zdero, R.M. King, and H. Robinson, *Phytochemistry*, **18**, 1246 (1979).
15.   T. Fukai, Q.-H. Wang, and T. Nomura, *Phytochemistry*, **30**, 1245 (1991).