New Phenolic Principles from *Hypericum sampsonii*

Ming-Jaw Don, Yeh-Jeng Huang, Ray-Ling Huang, and Yun-Lian Lin*

National Research Institute of Chinese Medicine; Taipei 112, Taiwan.
Received February 12, 2004; accepted March 27, 2004

Using the anti-hepatitis B virus (HBV)-producing cell line MS-G2 *in vitro* cultural system-guided screening was performed, and two new benzophenones, 2,6-dihydroxy-4-[(*E*)-5-hydroxy-3,7-dimethylocta-2,7-dienyloxy]benzophenone (1) and 2,6-dihydroxy-4-[(*E*)-7-hydroxy-3,7-dimethylocta-2-enyloxy]benzophenone (2), a new xanthone, hyperxanthone (3), a new bisanthraquinone glycoside, *R*-(−)-skyrin-6-*O*-β-D-xylopyranoside (4), and 2-caffeoyloxy-3-hydroxy-3-(3,4-dihydroxyphenyl)propyl alcohol (5), and 16 known compounds were isolated from the anti-HBV active fraction of the whole herbs of *Hypericum sampsonii*. Their structures were elucidated using spectroscopic methods, mainly 2D NMR and MS spectrometry. Circular dichroism was used to determine the stereochemistry of bisanthraquinone glycosides.

Key words *Hypericum sampsonii*; benzophenone; xanthone; antraquinone; flavone

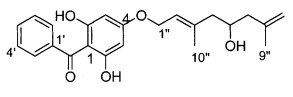
The phytochemistry and antidepressant activity of *Hypericum perforatum* (St. John's wort) have attracted much attention to the *Hypericum* genus and several biologically active components have been isolated.[1—8] *Hypericum sampsonii* (Guttiferae) is a herbal medicine used in the treatment of blood stasis, to relieve swelling, and as an antitumor herb in Taiwan.[9] Xanthones[10] and series of polyprenylated benzophenone derivatives[11—15] were previously isolated from this plant. In a continuation of our search for active components similar to *H. perforatum* in *H. sampsonii*,[15] We report here the isolation and structural determination of five new phenolic compounds together with 16 known compounds from the whole herbs of *H. sampsonii*.

Results and Discussion

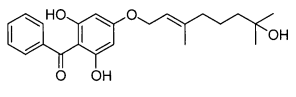
The ethanolic extract of the whole herbs was successively partitioned with ethyl acetate and *n*-butanol. The ethyl acetate and BuOH-soluble fractions were chromatographed on silica gel and Sephadex LH-20 to give two new benzophenones, 2,6-dihydroxy-4-[(*E*)-5-hydroxy-3,7-dimethylocta-2,7-dienyloxy]benzophenone (**1**) and 2,6-dihydroxy-4-[(*E*)-7-hydroxy-3,7-dimethylocta-2-enyloxy]benzophenone (**2**), a new xanthone, hyperxanthone (**3**), a new bisanthraquinone glycoside, *R*-(−)-skyrin-6-*O*-β-D-xylopyranoside (**4**), and 2-caffeoyloxy-3-hydroxy-3-(3,4-dihydroxyphenyl)propyl alcohol (**5**), together with 2,4,6-trihydroxybenzophenone 4-*O*-geranyl ether,[16] 1,6-dihydroxyxanthone,[17] 1,3,5,6-tetrahydroxyxanthone,[18] 1,3,6,7-tetrahydroxyxanthone (norathyriol),[17] padiaxanthone,[19] toxyloxanthone B,[5] 1,3,5,6-tetrahydroxy-2-prenylxanthone,[1] neolancerin,[20] mangiferin,[10] and *R*-(−)-skyrin-6-*O*-β-D-glucopyranoside[6] and *S*-(−)-skyrin-6-*O*-β-D-glucopyranoside,[6] emodin,[21] kaempferol,[22] quercetin,[23] kaempferol 3-*O*-glucopyranoside,[22] and quercetin 3-*O*-glucopyranoside.[23]

The IR spectrum of compound **1** showed the presence of hydroxyl groups (3450—3050 cm^{-1}), conjugated carbonyl (1630 cm^{-1}), and aromatic (1588, 1517 cm^{-1}) absorption bands. The molecular formula of compound **1** was established to be $C_{23}H_{26}O_5$ by high-resolution (HR)-EI-MS at *m*/*z* 382.1998. The ^{1}H- and ^{13}C-NMR spectra (Table 1) suggested that **1**: related to a benzophenone derivative. The ^{1}H-NMR spectrum revealed the presence of a phenolic hydroxyl group [δ_H 8.93 (br s)], phenyl group, two proton singlet, hydroxygeranyl group with a terminal methylene, and a hydroxymethine group [δ_H 4.54 (2H, d, J=7.5 Hz, H-1″), 5.49 (1H, t, J=7.5 Hz, H-2″), 2.16 (2H, m, H-4″), 4.07 (1H, t, J=6.5 Hz, H-5″), 1.70 (2H, m, H-6″), 4.87 and 4.95 (1H each, br s, H-8″), 1.72 and 1.73 (3H each, s)]. The two symmetric phenyl protons and the lower field shift of 1″-methylene protons suggested that the side chain: linked to the C-4 hydroxyl group. This fragment was determined by analysis of COSY, NOESY, and HMBC spectra. The structure of **1** was deduced from NOE correlations: H-1″ and H-3 (-5), H-10″; and H-6″ and H-8″, -9″, and HMBC correlations: H-2′ (6′) and C-7 (δ_C 197.8); H-3 (5) and C-2 (6) (δ_C 162.7), C-1 (δ_C 104.8); OH and C-2 (6), C-1, C-3 (5) (δ_C 95.8); and H-1″ and C-4 (δ_C 166.5). Therefore compound **1** was established as 2,6-dihydroxy-4-(5-hydroxy-3,7-dimethylocta-2,7-dienyloxy)benzophenone. However, the orientation of the hydroxyl at C-5″ remains undetermined.

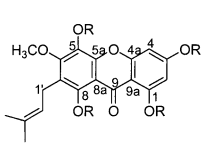
Compound **2** has the molecular formula $C_{23}H_{28}O_5$ based on HR-EI-MS. A comparison of the ^{1}H- and ^{13}C-NMR spectra of **2** with those of **1** revealed that the only difference was in the side chain. The ^{1}H-NMR spectrum showed that the terminal methylene group in **1**: replaced by two methyl groups and one hydroxyl group in **2**. HMBC connectivities of H-8″ (δ_H 1.10) to C-6″ (δ_C 29.5), C-7″ (δ_C 73.5), and C-9″ (δ_C



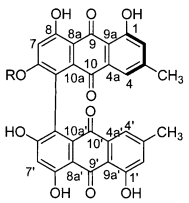
1



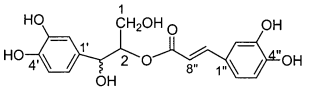
2



3 R=H
3a R=Ac



4: R=β-D-xylopyranosyl



5

* To whom correspondence should be addressed. e-mail: yllin@cma23.nricm.edu.tw

Table 1. ^{1}H- and ^{13}C-NMR Spectral Data for Compounds **1** and **2** in $CDCl_3$

Position	**1**		**2**	
	^{1}H	^{13}C	^{1}H	^{13}C
1		104.8 s		104.8 s
2		162.7 s		162.6 s
3	6.01 s	95.8 d	5.95 s	96.1 d
4		166.5 s		166.3 s
5	6.01 s	95.8 d	5.95 s	96.1 d
6		162.7 s		162.6 s
1′		140.2 s		140.1 s
2′	7.56 t (7.0)[a)]	129.3 d	7.56 t (7.0)	128.1 d
3′	7.41 t (7.0)	128.1 d	7.41 t (7.0)	128.7 d
4′	7.52 d (7.0)	132.5 d	7.52 d (7.0)	132.5 d
5′	7.41 t (7.0)	128.1 d	7.41 t (7.0)	128.7 d
6′	7.56 t (7.0)	129.3 d	7.56 t (7.0)	128.1 d
1″	4.54 d (7.5)	65.4 t	4.44 d (7.5)	65.5 t
2″	5.49 t (7.5)	119.1 d	5.42 t (7.5)	119.5 d
3″		142.0 s		142.0 s
4″	2.16 m	39.7 t	2.27 m	36.7 t
5″	4.07 t (6.5)	75.7 d	1.67 m	29.6 t
6″	1.70 m	32.9 t	2.12 m	29.5 t
7″		147.4 s		73.5 s
8″	4.87, 4.95 br s each	111.6 t	1.10 s	26.7 q
9″	1.72 s	17.8 q	1.14 s	23.5 q
10″	1.73 s	17.0 q	1.68 s	16.9 q
C=O		197.8 s		197.5 s
OH	8.93 br s		8.87 br s	

a) Coupling constants are presented in Hz.

23.5), and of H-10″ (δ_H 1.68) to C-2″ (δ_C 119.5), C-3″ (δ_C 142.0), and C-4″ (δ_C 36.7) confirmed that two methyl groups are in an oxygenated position at C-7″. Additional spectroscopic ^{1}H–^{1}H-COSY, HMBC, HMQC, and NOESY data confirmed the proposed structure of **2**.

Compound **3** was obtained as a yellow amorphous powder. The IR spectrum suggested the presence of hydroxyl (3369 cm^{-1}), conjugated carbonyl (1654 cm^{-1}), and aromatic (1597, 1509 cm^{-1}) absorption bands. Its UV absorption bands and bathochromic shifts on the addition of $AlCl_3$ and NaOAc indicated that compound **3**: a xanthone with 1- and 8-; and 3- and/or 6-hydroxyl groups.[24,25)] HR-EI-MS established the molecular formula to be $C_{19}H_{18}O_7$ (*m/z* 358.1371 [M^+]). The ^{1}H-NMR spectrum exhibited an isoprenyl [δ 3.93 (2H, d, J=6.5 Hz), 5.15 (1H, t, J=6.5 Hz), 1.61 and 1.62 (3H each, s)], a methoxyl group [δ 3.69 (3H, s)], two *meta*-coupled phenyl protons [δ 6.12 and 6.34 (1H each, d, J=2.0 Hz)], and chelated hydroxyl groups [δ 13.47 (br s)]. The ^{13}C-NMR spectrum of **3** showed 19 carbon signals for a carbonyl, 11 quarternary carbons, three methines, a methylene, a methoxyl, and two methyl groups. Acetylation of **3** with acetic anhydride and pyridine yielded tetraacetate (**3a**). Two lower field shifts of *meta*-coupled protons δ 6.71 and 7.08 (d, J=2.0 Hz) and the NOESY correlations of methoxyl protons with H-1′ and one of the acetyl groups [δ_H 2.31 (3H, s)] indicated that the methoxyl group presented between one of the hydroxyl group and isoprenyl group. This established compound **3** as 1,3,5,8-tetrahydroxy-6-methoxy-7-isoprenylxanthone or 1,3,5,8-tetrahydroxy-7-methoxy-6-isoprenylxanthone. HMBC correlations were found between the chelated hydroxyl group and C-1, between H-1′ and C-6 (δ_C 144.9), C-7 (δ_C 126.7), and C-8 (δ_C 146.2), between methoxyl protons and C-6, between H-2 and C-1, C-3, C-4, and C-9a, and between H-4 and C-2, C-3, C-4a, and C-9a. Based on the above evidence, the structure of **3** was confirmed to be 1,3,5,8-tetrahydroxy-6-methoxy-7-isoprenylxanthone, and designated hyperxanthone.

Compound **4** was isolated as an orange-red amorphous powder. The molecular formula was determined as $C_{35}H_{26}O_{14}$ based on HR-FAB-MS, ^{13}C-NMR, and DEPT spectra, with 23 indices of hydrogen deficiency. The ^{1}H-NMR spectrum indicated six aromatic protons, two aromatic methyl protons [δ 2.34, 2.37 (3H each, s)], and an anomeric proton. The sugar moiety was identified as a β-xylopyranose by ^{1}H-NMR [δ 3.03 (1H, dd, J=8.5, 7.2 Hz), 3.26 (1H, dd, J=9.0, 8.5 Hz), 3.40 (1H, m), 3.43 (1H, m), 3.92 (1H, dd, J=11.0, 5.0 Hz), and 4.86 (1H, d, J=7.5 Hz)] and ^{13}C-NMR [δ_C 65.4, 69.4, 72.8, 76.0, 101.2] spectral data as well as 1D TOCSY and comparison with data reported in the literature.[26)] The assignment of 35 individual discrete signals in the ^{13}C-NMR spectrum was based on the results of 2D experiments (HMQC, HMBC, NOESY). The HMBC spectrum showed a long-range correlations: anomeric proton δ 4.86 (d, J= 7.5 Hz) and C-6 (δ 163.2); H-4 [δ 7.35 (d, J=2.0 Hz)] and C-2 (δ 123.3), C-3 (δ 148.7), C-9a (δ 117.6), C-4a (δ 134.1), C-10 (δ 183.2), and methyl (δ 20.8); and H-4′ [δ 7.30 (d, J=2.0 Hz)] and C-2′ (δ 122.9), C-3′ (δ 146.5), C-9a′ (δ 117.0), C-4a′ (δ 134.1), C-10′ (δ 182.5); and methyl (δ 20.7); and H-7 [δ 7.02 (s)] and C-8a (δ 114.1), C-8 (δ 165.3), C-6 (δ 163.2), and C-5 (δ 132.0); and H-7′ [δ 6.62 (s)] and C-8a′ (δ 113.5), C-8′ (δ 164.6), C-6′ (δ 162.9), and C-5′ (δ 131.5) which indicated glycosidation at C-6-OH. Comparison of the ^{1}H- and ^{13}C-NMR data of **4** are similar to those of *S*-(−)-skyrin-6-*O*-β-xylopyranoside with almost identical MS, IR, and UV absorption bands but opposite CD curves.[6)] The CD spectrum of **4** revealed strong negativity ($\Delta\varepsilon$) at 262 nm (−17.04) and positivity at 248 nm (+4.38), indicating a different anisotropic effect with *S*-(−)-skyrin-6-*O*-β-xylopyranoside in the two atropisomeric forms.

Compound **5** was optically active, $[\alpha]_D^{25}$ +35°. It was suggested to have the molecular formula of $C_{18}H_{18}O_8$ based on HR-FAB-MS. The IR spectrum revealed hydroxyl (3378 cm^{-1}), and conjugated ester (1682, 1272 cm^{-1}) absorptions. The UV spectrum showed absorption maxima characteristic of an ester of 3-(3,4-dihydroxyphenyl)-2-propenoic acid.[27)] Its ^{1}H-NMR spectrum gave signals attributed to two 1,3,4-trisubstituted benzene rings, two *trans*-olefinic protons, two oxygenated methylene protons, and two oxymethine protons. The 1D-TOCSY experiment showed the proton sequence of H-3/H-2/H-1. H-2 and H-3 were assigned to be *trans*-diaxial based on their coupling constants. The NOE correlations between H-3 and H-2′ and H-6′, and between H-7″ and H-2″, and H-6″, and HMBC correlations between H-3 and C-1, and C-2, and C-1′, between H-7″ and C-1″, C-2″, C-6″, C-8″, and C-9″ allowed assignment of the connectivity of compound **5** as shown in the structure chart.

Experimental

General IR spectra were recorded on a Nicolet avatar 320 FT-IR spectrophotometer. Optical rotations were recorded on a JASCO DIP-370 polarimeter. UV spectra were measured on a Hitachi U-3200 spectrophotometer. NMR were obtained with a Varian unity INOVA-500 spectrometer. Mass spectra (EI-MS and FAB-MS) were recorded on a JEOL JMS-HX300 and a JEOL SX-102A mass spectrometer, respectively. CD spectra were recorded

in $CHCl_3$ on a JASCO J-715 spectropolarimeter using constant N_2 flushing at 25 °C. Stoppered cuvettes (0.1 cm) were employed. Data were plotted as Vε against wavelength. Column chromatography was performed on silica gel (Merck, 70—230 mesh) and Sephadex LH-20 (Pharmacia) for the ethyl acetate-soluble fraction, and on Diaion HP-20 and Sephadex LH-20 (Pharmacia) for the *n*-BuOH-soluble fraction. Silica gel $60F_{254}$ (Merck) was used for TLC and 5% and 15% MeOH/$CHCl_3$ as the developing solvent.

Plant Material The dried whole herbs of *H. sampsonii* were purchased from a local herbal drugstore, Taipei, Taiwan, in 2001. The plant was identified by comparison with the voucher specimens already deposited in the Herbarium of the Department of Botany, National Taiwan Unversity, Taipei, Taiwan (no. 077152).

Extraction and Isolation The whole herbs of *H. sampsonii* (12 kg) were extracted with EtOH (each 100 l, ×3) at 60 °C (overnight). The EtOH extracts were combined and evaporated under reduced pressure to give a residue. The concentrate was suspended in H_2O and partitioned successively with EtOAc (each 1 l, ×3) and *n*-butanol. The EtOAc-soluble fraction was subjected to column chromatography over silica gel using an *n*-hexane–EtOAc–MeOH gradient. Fractions of the EtOAc and 50% EtOAc/MeOH eluate were further purified on a Sephadex LH-20 column with methanol elution to yield benzophenones **1** (18 mg) and **2** (22 mg), hyperxanthone (25 mg) (**3**), and 2,4,6-trihydroxybenzophenone 4-*O*-geranyl ether (1.65 g), emodin (37 mg), betulinic acid (3.58 g), 1,6-dihydroxyxanthone (67 mg), padiaxanthone (27 mg), and toxyloxanthone B (16 mg). The *n*-BuOH-soluble fraction was chromatographed on a Diaion HP-20 column with a 50% MeOH/H_2O–MeOH gradient, and the 50% MeOH/H_2O eluate was further purified on a Sephadex LH-20 column using methanol elution to give neolancerin (38 mg) and mangiferin (6.5 g). The 75% MeOH/H_2O eluate was purified on a Sephadex LH-20 column to give the bisanthraquinone glycosides *R*-(−)-skyrin-6-*O*-β-D-xylopyranoside (**4**) (23 mg), *R*-(−)-skyrin-6-*O*-β-D-glucopyranoside (26 mg), and (*S*)-(−)-skyrin-6-*O*-β-D-glucopyranoside (21 mg), kaempferol 3-*O*-glucopyranoside (125 mg), and quercetin 3-*O*-glucopyranoside (175 mg). The MeOH eluate was purified on a Sephadex LH-20 column and yielded 2-caffeoyloxy-3-hydroxy-3-(3,4-dihydroxyphenyl)propyl alcohol (31 mg) (**5**), together with 1,3,5,6-tetrahydroxyxanthone (18 mg), 1,3,6,7-tetrahydroxyxanthone (norathyriol) (65 mg), 1,3,5,6-tetrahydroxy-2-prenylxanthone (21 mg), kaempferol (57 mg), and quercetin (95 mg).

Compound **1**: Yellow amorphous powder. $[\alpha]_D^{25}$ −20° (*c*=0.2, MeOH). IR ν_{max} (KBr) cm^{-1}: 3450—3050, 1630, 1588, 1517, 1291, 1165, 1073, 758. UV λ_{max} (MeOH) nm (log ε): 254 (3.91), 306 (3.96). ^{1}H-NMR (500 MHz, $CDCl_3$) see Table 1. ^{13}C-NMR (125 MHz ,$CDCl_3$): see Table 1. Key HMBC correlations: H-2′ (6′)/C-7, C-3′(5′), C-4′; H-3(5)/C-1, C-2(6), C-4; H-1″/C-4, C-2′, C-3″; H-10″/C-2″, C-3″, C-4″; H-9″/C-6″, C-7″, C-8″; H-5″/C-C-3, C-4, C-6C-7. Key NOE correlations: H-1″/H-3 (-5), -10″; H-6″/H-8″, -9″. EI-MS *m/z*: 382 $[M]^+$ (10), 364 (M^+-H_2O, 25), 296, 281, 255, 243. (100). HR-EI-MS *m/z*: 382.1998 (Calcd for $C_{23}H_{26}O_5$: 382.2006).

Compound **2**: Yellow amorphous powder. $[\alpha]_D^{25}$ +30° (*c*=0.3, MeOH); IR ν_{max} (KBr) cm^{-1}: 3410, 1632, 1590, 1514, 1290, 1164, 1067, 762. ^{1}H-NMR (500 MHz, $CDCl_3$): see Table 1. ^{13}C-NMR (125 MHz, $CDCl_3$): see Table 1. Key HMBC correlations: H-6″/C-4″, C-5″, C-7″, C-8″, C-9″; H-10″/C-2″, C-3″, C-4″; H-1″/C-4, C-2″, C-3″. EI-MS *m/z*: 384 $[M]^+$ (10), 366 (M^+-H_2O, 10), 229 ($M^+-C_{10}H_{19}O$, 100). HR-EI-MS *m/z*: 384.2202 (Calcd for $C_{23}H_{28}O_5$: 384.2202).

Hyperxanthone (**3**): Yellow amorphous powder. IR ν_{max} (KBr) cm^{-1}: 3369, 1654, 1597, 1509, 1167, 1081, 1031, 831. UV λ_{max} (MeOH) nm (log ε): 326 (3.90), 276 (3.70), 254 (4.14); λ_{max} (+$AlCl_3$) nm (log ε): 390 (3.88), 269 (3.98), 242 (3.92); λ_{max} (+$AlCl_3$+HCl) nm (log ε): 355 (3.89), 269 (3.99), 236 (3.91); λ_{max} (+NaOAc) nm (log ε): 382 (3.80), 354 (3.82), 274 (3.90), 247 (3.98); λ_{max} (+NaOAc+H_3BO_3) nm (log ε): 382 (3.80), 350 (3.83), 290 sh (3.85), 254 (3.94); λ_{max} (+NaOMe) nm (log ε): 370 (3.81), 297 (3.72), 264 (3.92), 242 (3.90). ^{1}H-NMR (500 MHz DMSO-d_6) δ: 1.61 and 1.62 (3H each, s, C$\underline{H}_3$), 3.69 (3H, s, OC$\underline{H}_3$), 3.93 (2H, d, *J*=6.5 Hz, H-1′), 5.15 (1H, t, *J*=6.5 Hz, H-2′), 6.12 (1H, d, *J*=2.0 Hz, H-2), 6.34 (1H, d, *J*=2.0 Hz, H-4), 13.47 (1H, br s, OH). ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 16.6 (q, C-4′), 25.7 (t, C-1′), 26.2 (q, C-5′), 61.1 (q, O$\underline{C}H_3$), 93.8 (d, C-4), 98.4 (d, C-2), 102.8 (s, C-9a), 110.1 (s, C-8a), 125.1 (d, C-2′), 126.7 (s, C-7), 130.4 (s, C-3′), 132.5 (s, C-5), 144.1 (s, C-4b), 144.9 (s, C-6), 146.2 (s, C-8), 157.1 (s, C-3), 163.7 (s, C-4a), 165.3 (s, C-1), 182.4 (s, C-9). Key HMBC correlations: OH (δ 13.47)/C-1, -2, -9a; H-2/C-1, -3, -4, -9a; OMe/C-6; H-1′/C-6, -7, -2′, -3′, -8. EI-MS *m/z*: 358 (M^+, 15), 315 (100), 300 (25), 273 (25). HR-EI-MS *m/z*: 358.1371 (Calcd for $C_{19}H_{18}O_7$: 358.1367).

Acetylation of 3 A solution of **3** (5 mg) in pyridine (0.5 ml) and Ac_2O (0.5 ml) was left at room temperature overnight. The solvent and excess reagent were removed with a high-vacuum pump. Purification by preparative TLC gave **3a** (4 mg). **3a**: Colorless amorphous powder. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.61 and 1.74 (3H each, s, H-4′, 5′), 2.24, 2.31, 2.34, 2.36 (3H each, s, OAc), 3.70 (3H, s, OMe), 3.96 (2H, d, *J*=6.5 Hz, H-1′), 5.09 (1H, t, *J*=6.5 Hz, H-2′), 6.71 and 7.08 (1H each, d, *J*=2.0 Hz, H-2, -4). NOE correlations: OMe/H-1′, OMe/H-4′, -5′, OMe/OAc (δ 2.31).

R-(−)-Skyrin-6-*O*-β-xylopyranoside (**4**): Orange-red amorphous powder. IR ν_{max} (KBr) cm^{-1}: 3396, 1625, 1598, 1198, 1041, 800, 746. UV λ_{max} (MeOH) nm (log ε): 294 (4.01), 258 (3.95), 221 (3.87). ^{1}H-NMR (500 MHz, CD_3OD) δ: 2.34 and 2.37 (3H each, s, C$\underline{H}_3$), 3.03 (1H, dd, *J*=8.5, 7.5 Hz, H-2″), 3.26 (1H, dd, *J*=9.0, 8.5 Hz, H-3″), 3.40 (1H, m, H-4″), 3.43 (1H, m, H-5″), 3.92 (1H, dd, *J*=11.0, 6.0 Hz, H-5″), 4.86 (1H, d, *J*=7.5 Hz, H-1″), 6.62 (1H, s, H-7′), 7.02 (1H, d, *J*=2.0 Hz, H-2′), 7.02 (1H, s, H-7), 7.08 (1H, d, *J*=2.0 Hz, H-2), 7.30 (1H, d, *J*=2.0 Hz, H-4′), 7.35 (1H, d, *J*=2.0 Hz, H-4). ^{13}C-NMR (125 MHz, CD_3OD) δ: 20.7 (q, Me-3′), 20.8 (q, Me-3), 65.4 (t, C-5″), 69.4 (d, C-4″), 72.8 (d, C-2″), 76.0 (d, C-3″), 102.4 (d, C-1″), 107.4 (s, C-7′), 107.9 (s, C-7), 113.5 (s, C-8a′), 114.1 (s, C-8a), 117.0 (s, C-9a′), 117.6 (s, C-9a), 120.3 (d, C-4′), 120.4 (d, C-4), 122.9 (d, C-2′), 123.3 (d, C-2), 131.5 (s, C-5′), 132.0 (s, C-5), 133.6 (s, C-4b′), 133.6 (s, C-4b), 134.1 (s, C-4a′), 134.1 (s, C-4a), 146.5 (s, C-3′), 148.7 (s, C-3), 161.7 (s, C-1′), 162.0 (s, C-1), 162.9 (s, C-6′), 163.2 (s, C-6), 164.6 (s, C-8′), 165.3 (s, C-8), 182.5 (s, C-10′), 183.2 (s, C-10), 191.3 (s, C-9), 192.5 (s, C-9′). CD λ_{max} (MeOH) nm ($\Delta\varepsilon$): 236 (−0.46), 248 (+4.38), 262 (−17.04), 309 (3.12). Key HMBC correlations: H-1″/C-6; H-2/C-1, -3, -4, -9a; H-2′/C-1′, -3′, -4′, -9a′; H-4/C-2, -3, -4a, -9a, -10, -C$\underline{H}_3$; H-4′/C-2′, -3′, -4a′, -9a′, -10, -C$\underline{H}_3$; H-7/C-8a, -8, -6, -5; H-7′/-8a′, -8′, -6′, -5′. Key NOE correlations: CH_3 (δ 2.37)/H-2, -4; CH_3 (δ 2.34)/H-2′, -4′. Positive-ion FAB-MS *m/z*: 671 $[M+H]^+$. HR positive FAB-MS *m/z*: 671.2064 (Calcd for $C_{35}H_{27}O_{14}$: 671.2068).

2-Caffeoyloxy-3-hydroxy-3-(3,4-dihydroxyphenyl)propyl alcohol (**5**): Colorless amorphous powder. $[\alpha]_D^{25}$ +35° (*c*=1.0, MeOH). IR ν_{max} (KBr) cm^{-1}: 3378, 1682, 1620, 1609, 1593, 1507, 1272, 1115, 1035, 809. UV λ_{max} (MeOH) nm (log ε): 313 (3.80), 285 (3.84), 261 (3.90), 235 (3.95). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 3.33 (1H, dd, *J*=12.0, 4.5 Hz, H-1), 3.54 (1H, dd, *J*=12.0, 2.5 Hz, H-1), 4.10 (1H, m, H-2), 4.84 (1H, d, *J*=7.5 Hz, H-3), 6.35 (1H, d, *J*=15.5 Hz, H-7″), 6.70 (1H, dd, *J*=8.0, 2.0 Hz, H-6′), 6.75 (1H, d, *J*=8.0 Hz, H-5′), 6.80 (1H, d, *J*=2.0 Hz, H-2′), 6.95 (1H, d, *J*=8.5 Hz, H-5″), 7.20 (1H, dd, *J*=8.5, 2.0 Hz, H-6″), 7.26 (1H, d, *J*=2.0 Hz, H-2″), 7.47 (1H, d, *J*=15.5 Hz, H-8″). ^{13}C-NMR (125 MHz, DMSO-d_6) δ: 60.1 (t, H-1), 75.6 (d, C-3), 78.6 (d, C-2), 115.0 (d, C-2′), 115.5 (d, C-5′), 116.3 (d, C-2″), 117.0 (d, C-5″), 117.3 (d, C-7″), 118.9 (d, C-6′), 121.9 (d, C-6″), 127.4 (s, C-1′), 127.6 (s, C-1″), 143.5 (d, C-8″), 143.8 (s, C-3″), 145.42 (s, C-3′), 145.3 (s, C-4″), 145.9 (s, C-4′), 167.8 (s, C-9″). Key HMBC correlations: H-7″/C-1″, -2″, -6″, 8″, C-9″; H-3/C-1′, -2, -2′, -3, -6′. Positive-ion FAB-MS *m/z*: 363 $[M+H]^+$ (35), 344 (M^+-H_2O-H, 95). HR positive FAB-MS *m/z*: 363.1446 (Calcd for $C_{18}H_{19}O_8$: 363.1441).

Acknowledgments This work was supported by the National Science Council of the Republic of China (NSC 92-2320-B-077-006).

References

1) Schmidt W., Abd EI-Mawla A. M. A., Wolfender J. L., Hostettmann K., Beerhues L., *Planta Med.*, **66**, 380—381 (2000).
2) Schmidt W., Peters S., Beerhues L., *Phytochemistry*, **53**, 427—431 (2000).
3) Chung M. I., Weng J. R., Wang J. P., Teng C. M., Lin C. N., *Planta Med.*, **68**, 25—29 (2002).
4) Shan M. D., Hu L. H., Chen Z. L., *J. Nat. Prod.*, **64**, 127—130 (2001).
5) Hu L. H., Yip S. C., Sim K. Y., *Phytochemistry*, **52**, 1371—1373 (1999).
6) Wirz A., Simmen U., Heilmann J., Calis I., Meier B., Sticher O., *Phytochemistry*, **55**, 941—947 (2000).
7) Kitanov G. M., Nedialkov P. T., *Phytochemistry*, **57**, 1237—1243 (2001).
8) Matsuhisa M., Shikishima Y., Takaishi Y., Honda G., Ito M., Takeda Y., Shibata H., Higuti T., Kodzhimatov O. K., Ashurmetov O., *J. Nat. Prod.*, **65**, 290—294 (2002).
9) Chiu N. Y., Chang K. H., "The Illustrated Medicinal Plants of Taiwan (II)," SMC Pubishing Inc., Taipei, 1986, p. 126.
10) Chen M. T., Chen C. M., *Heterocycles*, **23**, 2543—2548 (1985).
11) Hu L. H., Sim K. Y., *Tetrahedron Lett.*, **39**, 7999—8002 (1998).
12) Hu L. H., Sim K. Y., *Tetrahedron Lett.*, **40**, 759—762 (1999).
13) Hu L. H., Sim K. Y., *Org. Lett.*, **1**, 879—882 (1999).

14) Hu L. H., Sim K. Y., *Tetrahedron*, **56**, 1379—1386 (2000).
15) Lin Y. L., Wu Y. S., *Helv. Chim. Acta*, **86**, 2156—2163 (2003).
16) Bohlmann F., Suwita A., *Phytochemistry*, **17**, 1929—1934 (1978).
17) Noro T., Ueno A., Mizutani M., Hashimoto T., Miyase T., Kuroyanagi M., Fukushima S., *Chem. Pharm. Bull.*, **32**, 4455—4459 (1984).
18) Abou-Shoer M., Suwanborirux K., Habib A. A. M., Chang C. J., Cassady J. M., *Phytochemistry*, **34**, 1413—1420 (1993).
19) Ishiguro K., Fukumoto H., Nakajima M., Isoi K., *Phytochemistry*, **42**, 435—437 (1996).
20) Schaufelberger D., Hostettmann K., *Planta Med.*, **54**, 219—221 (1988).
21) Malhotra S., Misra K., *Phytochemistry*, **21**, 197—199 (1982).
22) Lin Y. L., Kuo Y. H., *J. Chin. Chem. Soc.*, **42**, 973—976 (1995).
23) Lin Y. L., Lee H. P., Ou J. C., Kuo Y. H., *Chin. Pharm. J.*, **46**, 115—122 (1994).
24) Li W., Chan C. L., Leung H. W., Yeung H. W., Xiao P., *Phytochemistry*, **51**, 953—958 (1999).
25) Zhou H. M., Liu Y. L., Blasko G., Cordell G. A., *Phytochemistry*, **28**, 3569—3571 (1989).
26) Hostettmann K., Due L. M., Goetz M., Jacot-Guillarmod A., *Phytochemistry*, **14**, 499—500 (1975).
27) Klosterman H. J., Muggli R. Z., *J. Am. Chem. Soc.*, **81**, 2188—2192 (1959).