# A New Chalcone, Xanthones, and a Xanthonolignoid from *Hypericum geminiflorum*

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*Received November 23, 1998*

A new prenyl chalcone, gemichalcone C (**1**), was isolated from the heartwood and root of *Hypericum geminiflorum*. Three new xanthones—6,7-dihyroxy-1,3-dimethoxyxanthone (**2**), 4-hydroxy-1,2-dimethoxyxanthone (**3**), and gemixanthone A (**4**)—and four known xanthones were isolated from the leaves and stems of the same plant.

Recently we isolated and characterized several constituents of the heartwood and root of *Hypericum geminiflorum* (Guttiferae).[1] Continuing studies on this plant have resulted in the isolation of a new prenyl chalcone, gemichalcone C (**1**); three new xanthones, 6,7-dihydroxy-1,3-dimethoxy xanthone (**2**), 4-hydroxy-1,2-dimethoxyxanthone (**3**), and gemixanthone A (**4**); and four known xanthones, toxyloxanthone B,[2] 1,5,6-trihydroxy-3-methoxyxanthone,[3] 3,8-dihydroxy-1,2-dimethoxyxanthone,[4] and 1,3,5,6-tetrahydroxy xanthone.[5] In the present paper we report the isolation and the stuctural characterization of compounds **1**−**4**.

Compound **1** possessed the molecular formula $C_{30}H_{28}O_9$, as determined from FABMS ($[M + 1]^+$ at *m*/*z* 533). Its IR spectrum showed absorption for an ester group (1720 $cm^{-1}$), and the UV spectrum exhibited absorption maxima similar to those of morachalcone A.[6] The $^1H$ NMR spectrum of **1** showed a vinyl methyl signal at $\delta$ 1.74 (s), a methylene signal at $\delta$ 3.50, a singlet of $OCH_2$ signal at $\delta$ 4.96, an olefinic proton signal at $\delta$ 5.58, a methoxyl signal at $\delta$ 3.93, a 1,2,4-trisubstituted phenyl moiety ($\delta$ 6.52, 6.46, and 7.69); a 1′,2′,3′,4′-tetrasubstituted phenyl moiety ($\delta$ 6.54, and 7.94); $\alpha$ and $\beta$ proton signals in a chalcone skeleton ($\delta$ 7.80 and 8.22),[1]ABX-type signals at $\delta$ 6.87, 7.16, and 7.37; a cinnamoyl moiety indicated by doublets at $\delta$ 6.44 (H-8″) and 7.62 (H-7″);[1] and a hydrogen-bonded hydroxyl signal ($\delta$ 14.21). Based on above evidence, and the absence of a bathochromic shift induced by $AlCl_3$, **1** was concluded to be a 3″-methoxylated 3″,4″-dioxygenated or 4″-methoxylated 3″,4″-dioxygenated cinnamoyl ester of a 3′-substituted 2′,4′,2,4-tetrahydroxychalcone.

The $^{13}C$ NMR spectrum (Table 1) was assigned by, DEPT, $^1H-^1H$ COSY, NOESY, and comparison of chemical shift values with those of corresponding data of morachalcone A and gemichalcone A.[1,8] The NOESY spectrum showed intense interaction between H-2″ and OMe. Therefore, **1** was characterized as 3′-[$\gamma$-hydroxymethyl-(*z*)-$\gamma$-methylallyl]-2′,4′,2,4-tetrahydroxychalcone 11′-*O*-ferulate, named gemichalcone C.

The HREIMS of **2** indicated a molecular ion peak at *m*/*z* 288.0635, which corresponded to the molecular formula $C_{15}H_{12}O_6$. Its IR spectrum showed absorption bands for hydroxyl (3330 $cm^{-1}$), conjugated carbonyl (1633 $cm^{-1}$), and aromatic rings (1581 $cm^{-1}$), and the UV spectrum exhibited absorption maxima similar to those of tripteroside.[9] The $^1H$ NMR spectrum showed two methoxyl signals at $\delta$ 3.70 and 3.86 and four aromatic proton signals at $\delta$ 6.71, 6.81, 7.16, and 8.04. This evidence and the UV spectrum showing a bathochromic shift with NaOAc and NaOAc−$H_3BO_3$, but not on addition of $AlCl_3$, indicated that **2** is 6,7-dihydroxy-1,3-dimethoxyxanthone. The $^{13}C$ NMR signals were assigned by DEPT and comparison with corresponding data in the literature.[10] The $^{13}C$ NMR and MS data also support structure **2**.

The HREIMS of **3** indicated $[M]^+$ at *m*/*z* 272.0681, which corresponded to molecular formula $C_{15}H_{12}O_5$ . Its IR spectrum showed absorption bands for hydroxyl (3286 $cm^{-1}$), conjugated carbonyl (1656 $cm^{-1}$ ), and aromatic rings (1600 $cm^{-1}$), and the UV spectrum exhibited absorption maxima characteristic of xanthones.[11] The $^1H$ NMR spectrum showed two methoxyl signals at $\delta$ 3.88 and 3.89 and five aromatic proton signals at $\delta$ 7.19, 7.24, 7.62, 7.80, and 8.18. The absence of a bathochromic shift with $AlCl_3$, NaOAc, and NaOAc−$H_3BO_3$ in the UV spectrum and the presence of an *ortho*-dimethoxyl group ($\delta$ 57.1 and 61.9) in the $^{13}C$ NMR spectrum indicated that **3** is 4-hydroxy-1,2-dimethoxyxanthone (**3**).[12] The $^{13}C$ NMR spectrum was assigned by DEPT and comparison with corresponding data in the literature.[12,13] The $^{13}C$ NMR and MS data also support structure **3**.

Compound **4** was acetylated because we were unable to isolate it in pure form. The HREIMS of peracetate (**5**) indicated a molecular ion peak at *m*/*z* 638.1675, which corresponded to molecular formula $C_{32}H_{30}O_{14}$. Its IR spectrum showed absorption bands for ester (1775 $cm^{-1}$), conjugated carbonyl (1660 $cm^{-1}$), and aromatic (1660 $cm^{-1}$) rings, and the UV spectrum exhibited absorption characteristic of a xanthone.[11] The $^1H$ MNR spectrum (Table 1) indicated three acetyl proton signals at $\delta$ 2.10, 2.34, and 2.35; four methoxyl proton signals at $\delta$ 3.84, 3.95, and 4.00; and five aromatic proton signals at $\delta$ 6.57, 6.66, 7.01, and 7.36.[14] The spectrum of **5** also showed trans diaxial dioxane proton signals at $\delta$ 4.39 (H, ddd, $J$ = 7.5, 4.3, 3.4 Hz) and 5.04 (1H, d, $J$ = 7.5 Hz).[14,15] The deshielded doublet ($\delta$ 5.04) typical of a benzylic methylene substituted by oxygen and its typical trans-coupling ($J$ = 7.5 Hz) implied the existence of a trans-substituted 1,4-dioxane ring between the xanthone moiety and the phenyl ring. A significant peak at *m*/*z* 252 could be rationalized in terms of a retro-Diels−Alder reaction in the dioxane ring.[14,15] The ions at *m*/*z* 252, 210, 209, 192, 182, and 181 indicated that an acetyl group and two methoxyl groups were present on the phenyl ring.[14,15] The $^1H$ NMR spectrum of **5** also showed two aliphatic proton signals of $-CH_2O-$ group at $\delta$ 4.15 (dd, $J$ = 12.3, 4.3 Hz) and 4.49 (dd, $J$ = 12.3, 3.4 Hz). The NOESY

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10.1021/np980533+ CCC: $18.00 © 1999 American Chemical Society and American Society of Pharmacognosy
Published on Web 05/29/1999

**Table 1.** $^{13}C$ NMR Data for **1** and **5**[a] and $^{1}H$ NMR Data for **5**

| C | **1**($\delta$ $^{13}C$) (100 MHz, $Me_2CO$-$d_6$) | C | **5**[b]($\delta$ $^{13}C$) (100 MHz, $CDCl_3$) | **5**[b]($\delta$ $^{1}H$) (400 MHz, $CDCl_3$) |
|---|---|---|---|---|
| 1 | 116.6 | 5 | 77.3 | 5.04, 1H, d (7.5) |
| 2 | 163.5[c] | 6 | 75.3 | 4.39, 1H, ddd (7.5, 4.3, 3.4) |
| 3 | 104.3 | 1′ | 97.6 | 7.36, 1H, s |
| 4 | 163.5 [c] | 2′ | 146.0 | |
| 5 | 109.9 | 3′ | 138.5 | |
| 6 | 132.4 | 4′ | 131.6 | |
| α | 119.0 | 4′a | 140.7 | |
| *β* | 146.0 | 10′a | 158.4 | |
| CO | 193.7 | 5′ | 103.4 | 7.10, 1H, d (2.0) |
| 1′ | 115.7 | 6′ | 154.9 | |
| 2′ | 165.8 | 7′ | 100.1 | 6.57, 1H, d (2.0) |
| 3′ | 115.0 | 8′ | 161.7 | |
| | | 8′a | 110.2 | |
| 4′ | 163.5 | 9′ | 174.7 | |
| 5′ | 108.6 | 9′a | 116.4 | |
| 6′ | 131.0 | 1″ | 129.6 | |
| 7′ | 22.8 | 2″ | 104.1 | 6.66, 1H, s |
| 8′ | 129.2 | 3″ | 152.8 | |
| 9′ | 131.7 | 4″ | 133.0 | |
| 10′ | 22.3 | 5″ | 152.8 | |
| 11′ | 64.2 | 6″ | 104.1 | 6.66, 1H,s |
| 1″ | 128.2 | $CH_2O$ | 62.5 | 4.15, 1H, dd (12.3, 4.3) |
| 2″ | 112.0 | | | 4.49, 1H, dd (12.3, 3.4) |
| 3″ | 149.5 | $CH_2OCOCH_3$ | 170.3 | |
| 4″ | 150.7 | $COCH_3$−6′ | 168.4 | |
| 5″ | 116.6 | $COCH_3$−4″ | 168.4 | |
| 6″ | 124.6 | MeO-2′ | 56.6 | 3.95, 3H, s |
| 7″ | 146.3 | MeO-8′ | 56.6 | 4.00, 3H, s |
| 8″ | 116.6 | MeO-3″ and 5″ | 56.3 | 3.84, 6H, s |
| 9″ | 168.3 | $CH_2OCOCH_3$ | 20.7 | 2.10, 3H, s |
| OMe | 57.0 | $COCH_3$-6′ | 21.1 | 2.35, 3H, s |
| | | $COCH_3$-4″ | 20.7 | 2.34, 3H, s |

[a] The number of protons directly attached to each carbon was verified by DEPT. [b] Signals obtained by $^{1}H-^{1}H$ COSY, HMQC, HMBC, and NOESY spectra. [c] Assignments may be reversed. Coupling constants ($J$ in Hz) are given in parentheses.

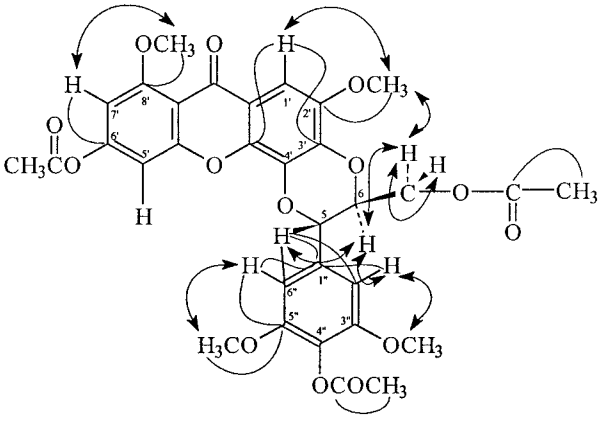
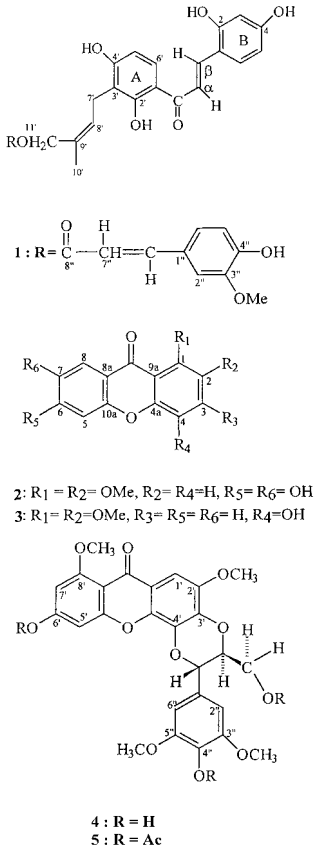


**Figure 1.** $^{13}C-^{1}H$ long-range correlations of **5** obtained from HMBC spectra (—) and NOEs observed in phase-sensitive NOESY of **5** (↔).

spectrum indicated correlations between H-1′ and the methoxyl signal at $\delta$ 3.95, the methoxyl signal at $\delta$ 3.95 and the ($-CH_2O-$) signal at $\delta$ 4.15, and the alphatic proton ($-CH_2O-$) signal at $\delta$ 4.15 and the dioxane proton signal at $\delta$ 4.39 (Figure 1). Acetyl signals were absent in the $^{1}H$ NMR spectra of impure **4**, thus, the xanthonolignoid, gemixanthone A (**4**), could be characterized as (5*S*,6*S*)-6-hydroxymethyl-5-(4″-hydroxy-3″,5″-dimethoxyphenyl)-2,3:3′, 4′-(6′-hydroxy-2′, 8′-dimethoxyxanthone)-1,4-dioxane. The $^{13}C$ NMR spectral data (Table 1) of **5** were consistent with the proposed structure **4**.



**2**: $R_1 = R_2 =$ OMe, $R_2 = R_4 =$H, $R_5 = R_6 =$ OH
**3**: $R_1 = R_2 =$OMe, $R_3 = R_5 = R_6 =$ H, $R_4 =$OH

**4 : R = H**
**5 : R = Ac**

## Experimental Section

**General Experimental Procedures.** Melting points reported are uncorrected. The optical rotation was obtained on a JASCO model DIP-370 digital polarimeter. UV spectra were obtained on a JASCO model 7800 UV/vis spectrophotometer, and IR spectra were recorded on a Hitachi model 260−30 spectrophotometer. $^{1}H$ (400 MHz) and $^{13}C$ (100 MHz) NMR

spectra were recorded on a Varian Unity-400 spectrometer, and MS were obtained on a JMS−HX 100 mass spectrometer.

**Plant Material.** Whole plants of *H. geminiflorum* were collected at Ping Tung Hsieng, Taiwan, during November 1993, and a voucher specimen (9302) has been deposited at the Department of Medicinal Chemistry, School of Pharmacy, Kaohsiung Medical College.

**Extraction and Isolation.** The heartwood and root (3 kg) were chipped and extracted with MeOH and $Me_2CO$, succcessively. The $Me_2CO$ extract (55 g) was chromatographed over Si gel. Elution with hexane−$CHCl_3$−$Me_2CO$−MeOH (1:7:2:0.2) yielded **1** (6 mg). The leaf (3 kg) was chipped and extracted with MeOH. The MeOH extract (50 g) was chromatographed over Si gel. Elution with hexane−EtOAc−MeOH (7: 12: 1) yielded fraction A. Fraction A was chromatographed over Si gel, and elution with $CH_2Cl_2$−MeOH (15:1) yielded toxyloxanthone B (3 mg), 1,5,6-trihydroxy-3-methoxy xanthone (3 mg), 3,8-dihydroxy-1,2-dimethoxy xanthone (2.6 mg), and **2** (2.5 mg); $CH_2Cl_2$−MeOH (9:1) yielded **3** (3 mg), 1,3,5,6-tetrahydroxy xanthone (2 mg), and **4** (10 mg). The known compounds were identified by spectroscopic methods and by comparison with authentic samples or reported data. [2−4]

**Gemichalcone C** (**1**): yellow powder (MeOH); UV (MeOH) $\lambda_{max}$ (log $\epsilon$) 295 (sh) (4.09), 3.18 (4.17), 388 (4.15) nm; + $AlCl_3$: unchanged; + NaOAc 290 (sh), 323, 398 nm; + NaOAc−$H_3BO_3$: unchanged; + NaOMe: 298 (sh), 367, 481 nm; IR (KBr) $\nu_{max}$ 3350, 1720, 1630 $cm^{-1}$; $^1H$ MNR ($Me_2CO$-$d_6$, 400 MHz), see text; $^{13}C$ NMR ($Me_2CO$-$d_6$, 100 MHz), Table 1; FABMS (positive mode) *m/z* 533 $[M + H]^+$ (0.3), 391 (0.1), 339 (0.4), 307 (1), 289 (1), 203 (3), 176 (8), 154 (23), 136 (21), 107 (21), 95 (38), 69 (65), 55 (100).

**6,7-Dihydroxy-1,3-dimethoxyxanthone** (**2**): yellow needles ($CH_2Cl_2$−MeOH); mp > 300 °C; UV (MeOH) $\lambda_{max}$ (log $\epsilon$) 240 (sh) (4.11), 303 (3.84), 350 (3.78), 400 (sh) (2.85) nm; + $AlCl_3$: unchanged; + NaOAc: 263, 370 nm; + NaOAc−$H_3BO_3$: 263, 350 nm; IR (KBr) $\nu_{max}$ 3330 (OH), 1633 (CO), 1581 (C═C) $cm^{-1}$; $^1H$ NMR (pyridine-$d_5$, 400 MHz), see text; $^{13}C$ NMR (pyridine-$d_5$, 100 MHz), $\delta$ 96.1 (C-4), 96.6 (C-2), 103.4 (C-5), 106.5 (C-9a), 107.0 (C-8), 115.8 (C-8a), 146.6 (C-7), 151.7 (C-6), 154.5 (C-10a), 160.4 (C-4a), 162.2 (C-1), 164.5 (C-3), 174.1 (CO); EIMS (70 eV) *m/z* 288 $[M]^+$ (100), $[M - CO]^+$ 259 (49), 242 $[M - OH]^+$ (30); HREIMS *m/z* $[M]^+$ 288.0635 (calcd for $C_{15}H_{12}O_6$, 288.0634).

**4-Hydroxy-1,2-dimethoxyxanthone (3)**: yellow needles ($CH_2Cl_2$−MeOH); mp 200−203 °; UV (MeOH) $\lambda_{max}$ (log $\epsilon$) 237 (4.05), 256 (4.21), 350 (3.44), 400 (sh) (3.21) nm; IR (KBr) $\nu_{max}$ 3286 (OH), 1656 (CO), 1600 (C═C) $cm^{-1}$ ; $^1H$ NMR ($Me_2CO$-$d_6$, 400 MHz), see text; $^{13}C$ NMR ($Me_2CO$-$d_6$, 100 MHz), $\delta$ 97.9 (C-3), 119.0 (C-9a), 119.6 (C-5), 122.8 (C-8a), 125.4 (C-7), 127.7 (C-8), 136.0 (C-6), 141.0 (C-2 and 4a), 151.9 (C-1 and 4), 157.6 (C-10a), 176.9 (CO); EIMS (70 eV) *m/z* 272 $[M]^+$ (100) 257 (26), 229 (13), 214 (17), 183 (11), 149 (15), 102 (29), 69 (73); HREIMS *m/z* 272.0681 (calcd for $C_{15}H_{12}O_5$, 272.0685).

**Gemixanthone A Acetate (5).** A solution of **4** (4 mg) in 1 mL of anhydrous pyridine was treated with 1 mL of $Ac_2O$ in a water bath for 12 h. The reaction mixture was concentrated under reduced pressure to remove excess solvent, and $H_2O$ was added to destroy excess $Ac_2O$. The residue was concentrated under reduced pressure to give **5**. Purification by column chromatography and recrystallization from $CHCl_3$ gave a white powder (**5**, 2 mg): $[\alpha]^{26}_D$ −21°(*c* 0.07, $CHCl_3$) ; mp 241−242 °C; UV (MeOH) $\lambda_{max}$ (log $\epsilon$) 250 (4.26), 286 (3.61), 319 (3.78), 402 (sh) (3.18) nm; IR (KBr) $\nu_{max}$ 1775, 1661, 1611 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz), text and Table 1; $^{13}C$ NMR ($CDCl_3$, 100 MHz), see Table 1; EIMS (70 eV) *m/z* 638 $[M]^+$ (8), 596 $[M - COCH_2]^+$ (6), 345 $[596 - 252]^+$ (4), 303 $[345 - COCH_2]^+$ (4); 284 $[ArCHO - CHO - CH_2OAc]^+$ (2), 252 $[ArCH{=}CH - CH_2OAc]^+$ (43), 210 $[ArCH{=}CH - CH_2OH]^+$ (3), 209 $[210 - H]^+$ (7), 192 $[210 - H_2O]^+$ (3), 182 $[210 - COO]^+$ (1), 181 $[210 - HCO]^+$ (3); HREIMS *m/z* 638.1675 $[M]^+$ (calcd for $C_{32}H_{30}O_{14}$, 638.1636).

**Acknowledgment.** This work was supported by a grant from the National Science Council of the Republic of China (NSC 86-2314-B037-035).

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NP980533+