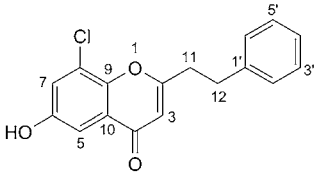
Two New 2-(2-Phenylethyl)chromen-4-ones from *Aquilaria sinensis* (LOUR.) GILG

by **You-Heng Gao***, **Jun-Min Liu**, **Hai-Xiao Lu**, and **Zhi-Xiong Wei**

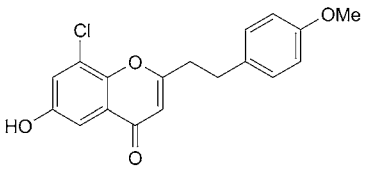
Department of Phytochemistry, School of Chinese Medica, Guangzhou University of Chinese Medicine, Guangzhou 510006, P. R. China (phone: +86-20-39358083; e-mail: gaoyouheng@yahoo.com.cn)

Two new compounds, 8-chloro-6-hydroxy-2-(2-phenylethyl)chromen-4-one (**1**) and 8-chloro-6-hydroxy-2-[2-(4-methoxyphenyl)ethyl]chromen-4-one (**2**), were isolated from the *Aquilaria sinensis* (LOUR.) GILG. Their structures were elucidated on the basis of spectroscopic methods including 1D- and 2 D-NMR analysis.

Introduction. – *Aquilaria sinensis* (LOUR.) GILG is distributed in Southern China in Hainan, Guangxi, and some other provinces. The resin-deposited part of *Aquilaria sinensis* (LOUR.) GILG is called Chinese eaglewood. It has been used as incense as well as sedative, analgesic, and digestive medicine in traditional Chinese medicine [1]. Several sesquiterpenes, triterpenes, and chromen-4-one derivatives have been reported [2–6]. In the course of our studies to evaluate the quality of Chinese eaglewood products, we have reported the structures of two new chromen-4-one derivatives in 2006 and 2007 [7][8]. Continuing our search for new bioactive natural products from this plant, we have investigated the Chinese eaglewood collected from the Hainan Province, P. R. China, which led to the isolation of two new 2-(2-phenylethyl)chromen-4-ones, whose structures were unambiguously elucidated as 8-chloro-6-hydroxy-2-(2-phenylethyl)chromen-4-one (**1**) and 8-chloro-6-hydroxy-2-[2-(4-methoxyphenyl)-ethyl]chromen-4-one (**2**). Here, we describe the isolation and structure elucidation of these new compounds.



1[1])



2

Results and Discussion. – Compound **1** was obtained as yellowish needles. HR-EI-MS Analysis revealed the presence of a Cl-atom, and the molecular formula was determined as $C_{17}H_{13}ClO_3$ (300.0548 (M^+)). The UV absorption maxima at 322 and 242 nm, and the IR absorption at 1633, 1594, 1480, 1458, 1250, 750, and 700 cm^{-1}

[1]) Arbitrary atom numbering. For systematic names, see *Exper. Part.*

suggested the presence of a chromen-4-one skeleton [2]. Compound **1** gave the base peak (*m/z* 91) corresponding to C_7H_7 (arising from bond cleavage of the C(11)–C(12) bond) in the EI-MS spectrum, which suggested **1** to be a chromen-4-one derivative with no substituent in the phenyl group. The ^{1}H-NMR spectrum (*Table*) of **1** revealed the presence of a OH group (δ(H) 9.15), and a *meta*-coupling system (δ(H) 7.37 (*d*, *J* = 2.8, 1 H), 7.35 (*d*, *J* = 2.8, 1 H)), indicating a 6,8-disubstituted chromen-4-one moiety. The ^{13}C-NMR spectrum (*Table*) of **1** displayed signals of two CH_2 groups at δ(C) 36.2 and 33.3, of a 2-substituted C=C bond at δ(C) 169.1 (*s*) and 110.0 (*d*), and of a C=O group at δ(C) 176.9. The HMBC and NOESY correlations (*Fig. 1*) evidenced that the OH group was located at C(6), because the OH H-atom (δ(H) 9.15) showed a correlation with the C(6)-atom (δ(C) 155.1). Accordingly, the Cl-atom was located at C(8). Thus, compound **1** was identified as 8-chloro-6-hydroxy-2-(2-phenylethyl)chromen-4-one.

Table. *^{1}H- and ^{13}C-NMR Data* (400 and 100 MHz, resp.; in CD_3OD) *of Compounds* **1** *and* **2**[1]). δ in ppm, *J* in Hz.

	1		**2**	
	δ(H)	δ(C)	δ(H)	δ(C)
C(2)	–	169.1 (*s*)	–	169.3 (*s*)
H–C(3)	6.10 (*s*)	110.0 (*d*)	6.08 (*s*)	110.0 (*d*)
C(4)	–	176.9 (*s*)	–	177.0 (*s*)
H–C(5)	7.37 (*d*, *J* = 2.8)	108.5 (*d*)	7.37 (*d*, *J* = 2.8)	108.5 (*d*)
C(6)	–	155.1 (*s*)	–	155.3 (*s*)
H–C(7)	7.35 (*d*, *J* = 2.8)	123.1 (*d*)	7.35 (*d*, *J* = 2.8)	123.2 (*d*)
C(8)	–	123.9 (*s*)	–	123.9 (*s*)
C(9)	–	146.9 (*s*)	–	146.9 (*s*)
C(10)	–	126.6 (*s*)	–	126.5 (*s*)
CH_2(11)	3.02 – 3.06 (*m*)	36.2 (*t*)	3.01 – 3.05 (*m*)	36.5 (*t*)
CH_2(12)	3.10 – 3.15 (*m*)	33.3 (*t*)	2.99 – 3.00 (*m*)	32.5 (*t*)
C(1′)	–	141.0 (*s*)	–	132.8 (*s*)
H–C(2′)	7.20 – 7.30 (*m*)	129.3 (*d*)	7.19 (*dd*, *J* = 2.0, 6.4)	130.2 (*d*)
H–C(3′)	7.20 – 7.30 (*m*)	129.3 (*d*)	6.82 (*dd*, *J* = 2.0, 6.4)	130.2 (*d*)
H–C(4′) or C(4′)	7.15 – 7.19 (*m*)	127.1 (*d*)	–	159.3 (*s*)
H–C(5′)	7.20 – 7.30 (*m*)	129.2 (*d*)	6.82 (*dd*, *J* = 2.0, 6.4)	114.7 (*d*)
H–C(6′)	7.20 – 7.30 (*m*)	129.2 (*d*)	7.19 (*dd*, *J* = 2.0, 6.4)	114.7 (*d*)
*Me*O–C(6′)	–	–	3.70 (*s*)	55.4 (*q*)
HO–C(6)	9.15 (*s*)	–	9.40 (*s*)	–

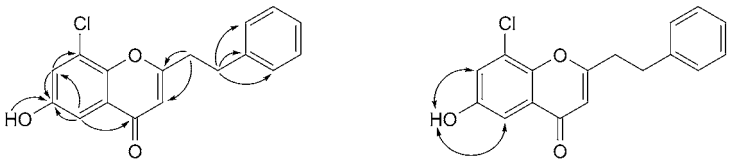


Fig. 1. *Selected HMBC* (H → C) *and key ROESY* (H ↔ H) *correlations of* **1**

Compound **2**, colorless needles, exhibited the M^+ peak at *m/z* 330.0655 in HR-EI-MS, which was consistent with the molecular formula $C_{18}H_{14}ClO_4$. Compound **2** indicated as 2-(2-phenylethyl)chromen-4-one by its IR and UV spectra which exhibited

strong absorption maxima due to a γ-pyrone ring. Compound **2** exhibited the base peak (*m*/*z* 121) corresponding to C_8H_9O (arising from the cleavage of the C(11)–C(12) bond) in the EI-MS spectrum, which suggested **2** to be a chromen-4-one derivative with a MeO substituent in the phenyl group. The ^{1}H-NMR spectrum (*Table*) of **2** showed the signal of a OH group at δ(H) 9.40, a *meta*-coupling system (δ(H) 7.37 (*d*, *J* = 2.8, 1 H), 7.35 (*d*, *J* = 2.8, 1 H)), and an *AA′XX′* system (δ(H) 7.19 (*dd*, *J* = 2.0, 6.4, 2 H), 6.82 (*dd*, *J* = 2.0, 6.4, 2 H)), indicating that C(4′), C(6), and C(8) were substituted. The ^{13}C-NMR spectrum (*Table*) of **2** displayed the signals of two CH_2 groups at δ(C) 36.5 and 32.5, of a 2-substituted C=C bond at δ(C) 110.0 (*d*) and 169.3 (*s*), and of a C=O group at δ(C) 177.0. Comparison of the NMR data with those of **1** revealed that the only difference between these two compounds was an additional MeO group at C(4′) (δ(C) 159.3) of **2**. Thus, compound **2** was determined as 8-chloro-6-hydroxy-2-[2-(4-methoxyphenyl)ethyl]chromen-4-one.

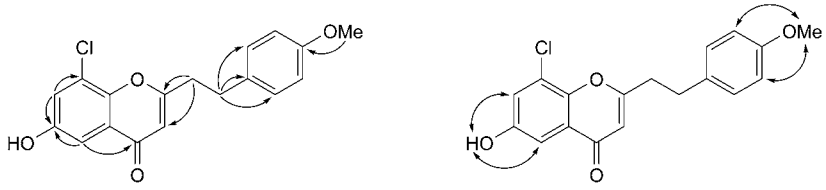


Fig. 2. *Selected HMBC* (H → C) *and key ROESY* (H ↔ H) *correlations of* **2**

Experimental Part

General. Column chromatography (CC): silica gel (SiO_2; 200–300 mesh; *Qingdao Marine Chemical Factory*, Qingdao, P. R. China). *RP-18* gel (75 μm, *YMC. Co., Ltd.*, Japan), and *Sephadex LH-20* (*GE Healthcare Bio-Sciences AB*, Switzerland). TLC: SiO_2 GF_{254}. M.p.: *XT-4A* micro melting-point apparatus; uncorrected. UV Spectra: *Agilent-8453E* spectrophotometer; λ_{max} (log ε) in nm. IR Spectra: *Analect RFX-65A* FT-IR spectrophotometer; KBr pellets; $\tilde{\nu}$ in cm^{-1}. 1D- and 2D-NMR spectra: *Bruker DRX-400* spectrometer; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-ESI-MS: *Thermo MAT95XP* mass spectrometer; in *m*/*z*.

Plant Material. The material of Chinese eaglewood was collected in Ding'an County of Hainan Province, China, in May 2006. Voucher specimens (No. 2006-HNCX-1) have been deposited with the Laboratory of Phytochemistry, Department of Phytochemistry, Guangzhou University of Chinese Medicine, and were identified by Prof. *Hong-Hua Xu*, Guangzhou University of Chinese Medicine.

Extraction and Isolation. The material of Chinese eaglewood (5.5 kg) was exhaustively extracted with 95% EtOH (3 × 10 l, 2 h) in a *DTQ-100L* multi-function extractor, and the extract was filtered. The filtrate was concentrated to give a residue, which was suspended in H_2O and partitioned with petroleum ether (PE; b.p. 60–90°), AcOEt, and BuOH to afford four extracts. The AcOEt extract (90 g) was applied to a SiO_2 column (200–300 mesh) with gradient elution with petroleum ether/AcOEt as solvent system to give nine fractions, *Frs. 1–9*. *Fr. 5* (5.8 g) was repeatingly purified by CC (SiO_2; petroleum ether/acetone 9 : 1 – 1 : 1, gradient system) to afford compound **2** (12 mg). *Fr. 6* (4.1 g) was subjected to CC (*Sephadex LH-20*; $CHCl_3$/MeOH 1 : 1) and further purified by CC (SiO_2; petroleum ether/acetone 9 : 1 – 1 : 1, gradient system) to afford compound **1** (27 mg).

8-Chloro-6-hydroxy-2-(2-phenylethyl)chromen-4-one (= *8-Chloro-6-hydroxy-2-(2-phenylethyl)-4H-1-benzopyran-4-one*; **1**): Yellowish needles (MeOH). M.p. 146.5–148.5°. UV (MeOH): 223 (4.3), 248 (4.4), 329 (3.7). IR (KBr): 3110, 1633, 1594, 1124, 1480, 1458, 1250, 849, 814, 750, 700. ^{1}H- and ^{13}C-NMR: *Table*. HR-EI-MS: 300.0548 (M^+, $C_{17}H_{13}ClO_3^+$; calc. 300.0553).

8-Chloro-6-hydroxy-2-[2-(4-methoxyphenyl)ethyl]chromen-4-one (= *8-Chloro-6-hydroxy-2-[2-(4-methoxyphenyl)ethyl]-4*H-*1-benzopyran-4-one*; **2**): Colorless needles (MeOH). M.p. 167–169°. UV (MeOH): 224 (4.5), 240 (4.4), 323 (3.8). IR (KBr): 3110, 1633, 1594, 1124, 1480, 1458, 1250, 849, 814. ^{1}H- and ^{13}C-NMR: *Table.* HR-EI-MS: 330.0655 (M^+, $C_{18}H_{14}ClO_4^+$; calc. 330.0659). EI-MS: 330, 121, 91, 77.

REFERENCES

[1] Institute of Materia Medica of Chinese Academy of Medical Sciences, 'Modern Research on Chinese Herbal Medicine', Peking Medical College and Peking Union Medical College Associationed Press, Beijing, 1997, Vol. 3, p. l.
[2] T. Yagura, M. Ito, F. Kiuchi, G. Honda, Y. Shimada, *Chem. Pharm. Bull.* **2003**, *51*, 560.
[3] T. Yagura, N. Shibayama, M. Ito, F. Kiuchi, G. Honda, *Tetrahedron Lett.* **2005**, *46*, 4395.
[4] W.-L. Mei, Y.-B. Zeng, J. Liu, H.-F. Dai, *J. Chin. Med. Mater.* **2007**, *30*, 551.
[5] J. Liu, J. Wu, Y. X. Zhao, Y. Y. Deng, W. L. Mei, H. F. Dai, *Chin. Chem. Lett.* **2008**, *19*, 934.
[6] H.-F. Dai, J. Liu, Y.-B. Zeng, Z. Han, H. Wang, W.-L. Mei, *Molecules* **2009**, *14*, 5165.
[7] J.-M. Liu, Y.-H. Gao, H.-H. Xu, H.-Y. Chen, *Chin. Tradit. Herb. Drugs* **2006**, *37*, 325.
[8] J.-M. Liu, Y.-H. Gao, H.-H. Xu, Z.-Q. Xu, *Chin. Tradit. Herb. Drugs* **2007**, *38*, 1138.

Received November 13, 2011