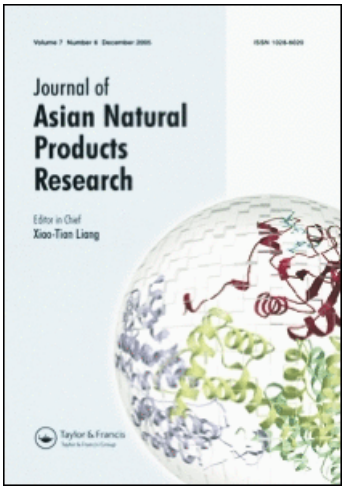

Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

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Hao-Fu Dai[a]; Jun Liu[a]; Zhuang Han[a]; Yan-Bo Zeng[a]; Hui Wang[a]; Wen-Li Mei[a]
[a] Key Laboratory of Tropical Crop Biotechnology, Ministry of Agriculture, Institute of Tropical Bioscience and Biotechnology, Chinese Academy of Tropical Agricultural Sciences, Haikou, China

Online publication date: 04 February 2010

To cite this Article Dai, Hao-Fu , Liu, Jun , Han, Zhuang , Zeng, Yan-Bo , Wang, Hui and Mei, Wen-Li(2010) 'Two new 2-(2-phenylethyl)chromones from Chinese eaglewood', Journal of Asian Natural Products Research, 12: 2, 134 — 137
To link to this Article: DOI: 10.1080/10286020903508424
URL: http://dx.doi.org/10.1080/10286020903508424

Journal of Asian Natural Products Research
Vol. 12, No. 2, February 2010, 134–137

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Two new 2-(2-phenylethyl)chromones from Chinese eaglewood

Hao-Fu Dai, Jun Liu, Zhuang Han, Yan-Bo Zeng, Hui Wang and Wen-Li Mei*

Key Laboratory of Tropical Crop Biotechnology, Ministry of Agriculture, Institute of Tropical Bioscience and Biotechnology, Chinese Academy of Tropical Agricultural Sciences, Haikou 571101, China

(*Received 9 October 2009; final version received 24 November 2009*)

Two new 2-(2-phenylethyl)chromones, (5*S**,6*R**,7*S**)-5,6,7-trihydroxy-2-(3-hydroxy-4-methoxyphenethyl)-5,6,7,8-tetrahydro-4*H*-chromen-4-one (**1**) and (5*S**,6*R**,7*R**)-5,6,7-trihydroxy-2-(3-hydroxy-4-methoxyphenethyl)-5,6,7,8-tetrahydro-4*H*-chromen-4-one (**2**), were isolated from the Chinese eaglewood of *Aquilaria sinensis* (Lour.) Gilg. Their structures were established by detailed MS and NMR spectroscopic analysis, as well as comparison with the literature data.

Keywords: Chinese eaglewood; *Aquilaria sinensis*; chromone

1. Introduction

The resinous part of agarwood is formed by injury of cutting, moth-eaten, fire, and micro-organism of the tree of the *Aquilaria* species (Thymelaeaceae). Chinese eaglewood ('Chenxiang' in Chinese) is also a kind of agarwood, which is not only a famous incense but also a famous traditional Chinese medicine used as a sedative, analgesic, and digestive [1]. Previous phytochemical investigation on Chinese eaglewood revealed characteristic sesquiterpenes and chromone derivatives [2–4], which composed a pleasant odor when agarwood was burnt. Up to now, the formation process of agarwood has not been understood in detail. Examination of the chemical constituents of the damaged wood is necessary to discover the bio-organic process of agarwood formation. In our previous study on the chemical constituents from Chinese eaglewood, a new 2-(2-phenylethyl)chromone has been isolated [5]. In the present paper, we describe the isolation and structural elucidation of two new chromone derivatives (**1** and **2**) from the EtOH extract of the withered wood of *Aquilaria sinensis*, an original plant of agarwood (Figure 1).

2. Results and discussion

Compound **1** was isolated as a white amorphous powder, with mp 90–92°C and $[\alpha]_D^{18}$ −48 ($c = 0.5$, MeOH). The pseudo-molecular ion at *m/z* 371.1101 $[M+Na]^+$ in the HR-ESI-MS corresponded to the molecular formula $C_{18}H_{20}O_7$. This formula can also be validated through ^{1}H NMR, ^{13}C NMR, and DEPT spectra. Its IR spectrum showed the presence of hydroxyl (3403 cm^{-1}), unsaturated carbonyl (1659 cm^{-1}), and phenyl groups (1583, 1514, 1452 cm^{-1}). The ^{1}H NMR spectrum (Table 1) of **1** showed the presence of one

*Corresponding author. Email: meiwenli@yahoo.com.cn

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020903508424
http://www.informaworld.com

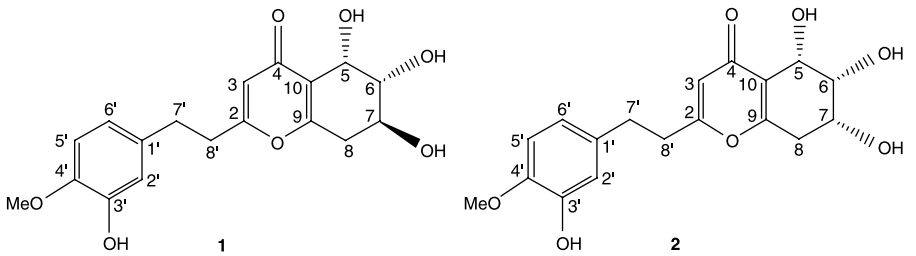

Figure 1. Structures of compounds **1** and **2**.

methoxyl group at δ_H 3.71 (3H, s), three consecutive methine protons [δ_H 3.68 (1H, dd, $J = 6.9$, 4.6 Hz, H-6), 4.45 (1H, d, $J = 4.6$ Hz, H-5), 3.90 (1H, m, H-7)], three methylene groups at δ_H 2.76 (4H, overlapped, H-7′, 8′) and δ_H 2.83, 2.55 (each 1H, H-8), and one 1,3,4-trisubstituted phenyl group at δ_H 6.80 (1H, d, $J = 8.2$ Hz, H-5′), 6.66 (1H, d, $J = 2.0$ Hz, H-2′), and 6.59 (1H, dd, $J = 8.2$, 2.0 Hz, H-6′). The ^{13}C NMR spectrum (Table 1) of **1** showed the presence of three methylene groups at δ_C 31.3, 34.2, and 33.0, one methoxyl at δ_C 55.7, and three consecutive methine carbons at δ_C 67.0, 71.8, and 67.2. Based on the above evidence, compound **1** was presumed to be a 2-(2-phenylethyl)chromone derivative. The ^{13}C NMR spectrum of **1** was similar to that of 8-chloro-5,6,7-trihydroxy-2-(3-hydroxy-4-methoxyphenethyl)-5,6,7,8-tetrahydro-4*H*-chromen-4-one [5], except that C-8 was a methylene group instead of a methine group, which was confirmed by the long-distance correlations from H-8 (δ_H 2.55, 2.83) to C-9

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1** and **2** (^{1}H: 400 MHz; ^{13}C: 100 MHz; in CD_3OD).

	1		**2**	
Position	δ_H (J, Hz)	δ_C	δ_H (J, Hz)	δ_C
2		168.0		168.0
3	6.09 (1H, s)	112.7	6.10 (1H, s)	112.5
4		178.4		178.6
5	4.45 (1H, d, 4.6)	67.0	4.61 (1H, d, 4.0)	65.0
6	3.68 (1H, dd, 6.9, 4.6)	71.8	3.70 (1H, dd, 4.0, 1.8)	69.0
7	3.90 (1H, m)	67.2	3.96 (1H, m)	67.4
8	2.83 (1H, dd, 17.8, 4.9), 2.55 (1H, dd, 17.8, 5.1)	33.0	2.74 (2H, overlapped)	34.0
9		161.5		162.0
10		120.6		120.5
1′		132.5		132.4
2′	6.66 (1H, d, 2.0)	115.6	6.65 (1H, d, 1.6)	115.6
3′		146.1		146.0
4′		146.3		146.3
5′	6.80 (1H, d, 8.2)	112.3	6.80 (1H, d, 8.2)	112.2
6′	6.59 (1H, dd, 8.2, 2.0)	118.8	6.59 (1H, dd, 8.2, 1.6)	118.6
7′	2.76 (2H, overlapped)	31.3	2.76 (2H, overlapped)	31.3
8′	2.76 (2H, overlapped)	34.2	2.76 (2H, overlapped)	34.1
4′-OCH_3	3.71 (3H, s)	55.7	3.80 (1H, s)	55.6

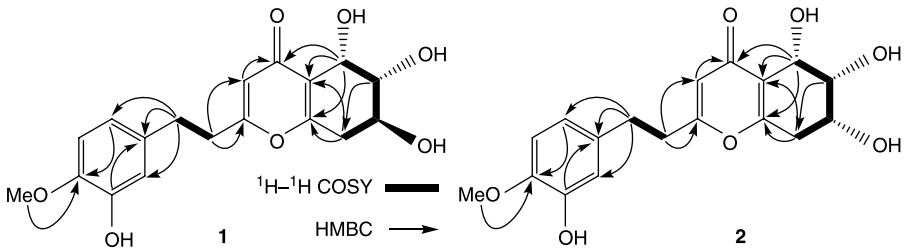

Figure 2. Key HMBC and ^{1}H–^{1}H COSY correlations of compounds **1** and **2**.

(δ_C 161.5) and C-10 (δ_C 120.6) in the HMBC spectrum (Figure 2). The relative stereochemistry was determined by ^{1}H–^{1}H coupling constants. The relatively small coupling constant between H-5 and H-6 revealed the *cis* relationship between H-5 and H-6. While the relatively large coupling constant between H-6 and H-7 revealed the *trans* relationship between them [6]. In the ROESY spectrum, the cross-peak from H-5 to H-7 was not observed, which indicated that H-5 and H-7 were at the different side. Consequently, the structure of **1** was established as (5*S**,6*R**,7*S**)-5,6,7-trihydroxy-2-(3-hydroxy-4-methoxyphenethyl)-5,6,7,8-tetrahydro-4*H*-chromen-4-one.

Compound **2** was obtained as a white amorphous powder, with mp 134–136°C and $[\alpha]_D^{18}$ −68 ($c = 0.5$, MeOH). The $[M+Na]^+$ at *m/z* 371.1101 in the HR-ESI-MS corresponded to the molecular formula $C_{18}H_{20}O_7$. This formula can also be validated through ^{1}H NMR, ^{13}C NMR, and DEPT spectra. A careful comparison of the ^{13}C and ^{1}H NMR spectral data (Table 1) of compound **2** with those of compound **1** indicated that the two structures were very similar except for the different coupling constants between H-6 and H-7 in **1** ($J_{6,7} = 6.9$) and **2** ($J_{6,7} = 1.8$), which suggested that **2** was an epimer of **1** [6]. The relative stereochemistry of compound **2** was also confirmed by the ROESY experiment. The cross-peak from H-5 to H-7 indicated that H-5 and H-7 were at the same side. Based on the above evidence, the structure of **2** was established as (5*S**,6*R**,7*R**)-5,6,7-trihydroxy-2-(3-hydroxy-4-methoxyphenethyl)-5,6,7,8-tetrahydro-4*H*-chromen-4-one.

3. Experimental

3.1 General experimental procedures

Melting points were obtained on a Beijing Taike X-5 stage apparatus and are uncorrected. Optical rotation was recorded using a Rudolph Autopol III polarimeter (Rudolph Research Analytical, Hackettstown, NJ, USA). The UV spectra were measured on a Shimadzu UV-2550 spectrometer. The IR spectra were obtained on a Nicolet 380 FT-IR instrument, as KBr pellets. The NMR spectra were recorded on a Bruker AV-400 spectrometer, using TMS as an internal standard. The HR-ESI-MS spectra were measured with an API QSTAR Pulsar mass spectrometer. Column chromatography was performed with silica gel (Marine Chemical Industry Factory, Qingdao, China), Sephadex LH-20, and Rp-18 gel (Merck, Darmstadt, Germany). TLC was performed with silica gel GF254 (Marine Chemical Industry Factory).

3.2 Plant material

The material of Chinese eaglewood was collected in Ding'an County of Hainan Province, China, in May 2006, and identified by Prof. Hao-Fu Dai. A voucher specimen (No. CX20060501) is deposited

in the Institute of Tropical Bioscience and Biotechnology, Chinese Academy of Tropical Agricultural Sciences.

3.3 Extraction and isolation

The material of Chinese eaglewood (35.4 kg) was exhaustively extracted with 95% EtOH three times at room temperature and filtered. After evaporation, the residue was suspended in H_2O and partitioned with EtOAc to afford EtOAc extract. The H_2O part was applied to a D101 reticular resin column eluted with H_2O and MeOH. The MeOH eluent was concentrated *in vacuo* to give a residue (147.3 g), which was chromatographed on a silica gel column (200–300 mesh) with gradient elution utilizing $CHCl_3$–MeOH as a solvent system to give nine fractions. Fraction 5 (21.0 g) was chromatographed on an RP-18 column with gradient elution of MeOH–H_2O as the solvent system to give 11 fractions (5-1–11). Fraction 5-4 (2.99 g) was subjected to column chromatography over Sephadex LH-20 eluted with 95% EtOH and further purified by silica gel column chromatography eluted with EtOAc–MeOH (20:1) to afford compounds **1** (16.8 mg) and **2** (77.7 mg).

3.3.1 (5S,6R*,7S*)-5,6,7-Trihydroxy-2-(3-hydroxy-4-methoxyphenethyl)-5,6,7,8-tetrahydro-4H-chromen-4-one (**1**)*

A white amorphous powder, $C_{18}H_{20}O_7$, mp 90–92°C, $[\alpha]_D^{18}$ −48 ($c = 0.5$, MeOH). IR (KBr) ν_{max} (cm^{-1}): 3403, 2464, 1659, 1583, 1514, 1452, 1280, 1069. ^1H and ^{13}C NMR spectral data: see Table 1. HR-ESI-MS *m/z*: 371.1101 $[M+Na]^+$ (calcd for $C_{18}H_{20}O_7Na$, 371.1107).

3.3.2 (5S,6R*,7R*)-5,6,7-Trihydroxy-2-(3-hydroxy-4-methoxyphenethyl)-5,6,7,8-tetrahydro-4H-chromen-4-one (**2**)*

A white amorphous powder, $C_{18}H_{20}O_7$, mp 134–136°C, $[\alpha]_D^{18}$ −68 ($c = 0.5$, MeOH). IR (KBr) ν_{max} (cm^{-1}): 3414, 2446, 1657, 1570, 1514, 1448, 1279, 1107. ^1H and ^{13}C NMR spectral data: see Table 1. HR-ESI-MS *m/z*: 371.1103 $[M+Na]^+$ (calcd for $C_{18}H_{20}O_7Na$, 371.1107).

Acknowledgements

This research was financially supported by the National Nonprofit Institute Research Grant of CATAS-ITBB (No. ITBBZD2007-4-3) and the Science and Technology Foundation of Chinese Academy of Tropical Agricultural Sciences (No. RKY0726).

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