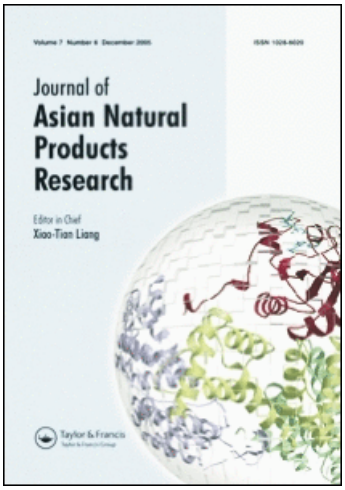

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New dibenz[*b, f*]oxepins from *Cercis chinensis* Bunge

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Three new dibenz[*b,f*]oxepins: 6-methoxy-7-methyl-8-hydroxydibenz[*b, f*]oxepin (**1**), 1,8-dimethoxy-6-hydroxy-7-methyldibenz[*b, f*]oxepin (**2**), and 1-hydroxy-6,8-dimethoxy-7-methyldibenz[*b,f*]oxepin (**3**), along with two known dibenz[*b,f*]oxepins pacharin (**4**) and bauhiniastatin 4 (**5**), were isolated from *Cercis chinensis* Bunge (Leguminosae). Their structures were elucidated on the basis of spectroscopic evidence (EI-MS, UV, IR, ^{1}H, ^{13}C and 2D NMR). Compounds **1**–**5** were isolated from the *Cercis* genus for the first time.

Keywords: *Cercis chinensis* Bunge; Leguminosae; Dibenz[*b, f*]oxepins

1. Introduction

The genus *Cercis* of Leguminosae comprises eight species distributed in temperate zones. *Cercis chinensis* Bunge is widely distributed in the southeast of China [1]. The barks and woods of this tree have been used in traditional medicines for activating blood, restoring menstrual flow, subduing swelling and detoxicating. Its flowers are used to treat rheumatic ache, and its fruits are used to treat coughs [2]. Earlier chemical investigations on *Cercis chinensis* Bunge revealed the presence of phenolic compounds [3–6]. To expand the medicinal sources and find active components, the aerial part of this plant has been investigated, resulting in the isolation of three new dibenz[*b,f*]oxepins (**1**–**3**) and two known dibenz[*b,f*]oxepins: pacharin (**4**) [7] and bauhiniastatin 4 (**5**) [8] (see figure 1). In this paper, we report the isolation and structural elucidation of these constituents.

2. Results and discussion

Compound **1** was obtained as an amorphous powder. The HREI-MS showed a molecular ion peak at *m/z* 254.0969, corresponding to the molecular formula $C_{16}H_{14}O_3$. The UV spectrum showed the presence of a *cis*-stilbene conjugated system (292 and 248 nm). The IR spectrum displayed the absorption of hydroxyls (3400 cm^{-1}) and olefinic bond and aromatic groups

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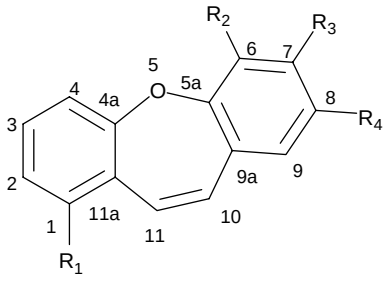

	R1	R2	R3	R4
1	H	OMe	Me	OH
2	OMe	OH	Me	OMe
3	OH	OMe	Me	OMe
4	OH	OH	Me	OMe
5	OH	OMe	Me	OH

Figure 1. Structures of compounds **1**–**5** isolated from *Cercis chinensis*.

(1610, 1576, 1485, 1450, 1088, 685 cm^{-1}). The ^1H NMR spectrum of **1** (table 1) showed signals assignable to a set of *ortho*-disubstituted benzene ring system at δ 7.20 (1H, ddd, $J = 7.5, 7.5, 1.0$ Hz, H-3), 7.14 (1H, br d, $J = 7.5$ Hz, H-4), 7.10 (1H, dd, $J = 7.5, 1.0$ Hz, H-1) and 7.02 (1H, ddd, $J = 7.5, 7.5, 1.0$ Hz, H-2), two *cis* olefinic protons at δ 6.59 (1H, d, $J = 11.5$ Hz, H-11) and 6.52 (1H, d, $J = 11.5$ Hz, H-10), a singlet representing one aromatic proton at δ 6.29 (1H, s, H-9), one methoxyl at δ 3.86 (3H, s, OCH_3) and one methyl at 2.05 (3H, s, CH_3). The ^{13}C NMR spectrum of **1** showed signals for 14 carbons at δ110.4–159.1 except for the signals due to one methoxyl at δ 61.9 (OCH_3) and one methyl at δ 9.3 (CH_3). The ^1H NMR and ^{13}C NMR signals (table 1) were assigned by means of HMQC. By comparing the ^1H NMR and ^{13}C NMR data of **1** with those of bauhiniastatin 4 (**5**), **1** was

Table 1. ^1H NMR and ^{13}C NMR data for compounds **1**–**3**.

Position	***1***		***2***		***3***	
	δ_C[†]	δ_H[†]	δ_C[‡]	δ_H[‡]	δ_C[†]	δ_H[†]
1	130.4	7.10 dd (7.5, 1.0)	157.4		157.7	
2	125.7	7.02 ddd (7.5,7.5,1.0)	101.1	6.68 d (7.5)	113.1	6.52 d (8.0)
3	130.6	7.20 ddd (7.5,7.5,1.0)	124.1	7.22 t (7.5)	131.2	7.00 t (8.0)
4	122.5	7.14 d (7.5)	113.1	6.76 d (7.5)	113.6	6.63 d (8.0)
4a	159.1		158.5		161.5	
5a	144.4		138.3		145.7	
6	151.9		146.1		152.3	
7	120.9		113.7		122.3	
8	153.6		154.9		156.5	
9	110.4	6.29 s	107.2	6.17 s	106.6	6.42 s
9a	132.2		127.2		131.6	
10	131.1	6.52 d (11.5)	129.8	6.70 d (11.5)	129.7	6.58 d (11.5)
11	130.3	6.59 d (11.5)	129.3	7.00 d (11.5)	126.5	6.91 d (11.5)
11a	132.2		119.6		120.5	
OMe-6	61.9	3.86 s			62.4	3.85 s
Me-7	9.3	2.05 s	8.5	2.12 s	9.7	2.13 s
OMe-8			55.7	3.76 s	59.7	3.71 s
OMe-1			55.9	3.84 s		

[†] δ (ppm); ^1H (500 MHz) and ^{13}C (125 MHz); CD_3OD; J (Hz) in parentheses.
[‡] [b] δ (ppm); ^1H (500 MHz) and ^{13}C (125 MHz); $CDCl_3$; J (Hz) in parentheses.

also elucidated as a dibenz[*b,f*]oxepin. In the NOE experiment, irradiation of 6-OCH_3 (δ 3.86) resulted in enhancement at 7-CH_3 (δ 2.05) and H-4 (δ 7.14), irradiation of H-9 (δ 6.29) showed enhancement at H-10 (δ 6.52), which proved that methoxyl and methyl were located at C-6 and C-7, respectively. From these data, compound **1** was elucidated as 6-methoxy-7-methyl-8-hydroxydibenz[*b,f*]oxepin.

Compound **2** was obtained as an amorphous powder. The UV spectrum showed absorption bands at 301 and 220 nm due to a stilbene conjugated system. The IR spectrum displayed the absorption of hydroxyls (3477 cm^{-1}) and olefinic bond and aromatic groups (1680, 1601, 1577, 1466, 1132, 1095, 739, 669 cm^{-1}). The molecular formula was determined to be $C_{17}H_{16}O_4$ based on HREI-MS at *m/z* 284.1051 $[M]^+$. The overlapped and duplicated signals on the ^1H NMR and ^{13}C NMR spectra between compound **2** (table 1) and bauhiniastatin 4 (**5**) indicated that **2** was also a dibenz[*b,f*]oxepin. Furthermore, the ^1H NMR and ^{13}C NMR spectra of **2** exhibited two methoxyl and one methyl groups. In the NOE experiment, irradiation of 8-OCH_3 (δ 3.76) created NOE enhancement at 7-CH_3 (δ 2.12) and H-9 (δ 6.17), irradiation of 1-OCH_3 (δ 3.84) showed NOE enhancement at H-2 (δ 6.68), indicating the presence of 1,8-dimethoxyl and 7-CH_3 groups. So compound **2** was elucidated as 1,8-dimethoxy-6-hydroxy-7-methyldibenz[*b,f*]oxepin.

Compound **3** was obtained as an amorphous powder. The HREI-MS showed it had the same molecular formula $C_{17}H_{16}O_4$ with compound **2**. The UV absorption bands at 293 and 247 nm suggested that **3** had a stilbene conjugated system. The IR spectrum displayed the absorption of hydroxyls (3450 cm^{-1}) and olefinic bond and aromatic groups (1676, 1606, 1572, 1458, 1126, 771, 739 cm^{-1}). By comparing the ^1H NMR and ^{13}C NMR signals (table 1) with those of compound **2**, **3** was also a dibenz[*b,f*]oxepin. In the NOE experiment, irradiation of 7-CH_3 (δ 2.13) resulted in enhancement at 8-OCH_3 (δ 3.71) and 6-OCH_3 (δ 3.85), irradiation of 8-OCH_3 (δ 3.71) showed NOE enhancement at H-9 (δ 6.42), which proved that the two methoxyls were located at C-6 and C-8, and the methyl at C-7. The structure of compound **3** was elucidated as 1-hydroxy-6,8-dimethoxy-7-methyldibenz[*b,f*]oxepin.

3. Experimental

3.1 General experimental procedures

The optical rotation was determined on a Perkin Elmer Model 341 LC digital polarimeter. Melting points were determined on an XT-4 micro-melting point apparatus and were uncorrected. UV spectra were taken on a Shimadzu UV-260 spectrophotometer. IR spectra were recorded on an IMPACT 400 spectrometer as KBr pellets. NMR spectra were run on an INOVA-500 spectrometer. HR-MS spectra were performed on VG-Autospec-300 mass spectrometer. ESI-MS were obtained using an Agilent 1100 series LC/MSD Trap SL mass spectrometer. Reversed-phase HPLC was performed on a YMC-Pack ODS-A (YMC Co., Ltd.) column (250 × 20 mm). Sephadex LH-20 (Pharmacia Biotech Co., Ltd.) and silica gel (60–100, 100–200 and 200–300 mesh, Qingdao Haiyang Chemical Co. Ltd, China) were used for column chromatography. TLC was prepared with silica gel GF_{254} (Qingdao Haiyang Chemical), and the spots were detected by UV light at 365 nm and/or by spraying with 10% H_2SO_4 and then heating.

3.2 Plant material

The aerial parts of *Cercis chinensis* Bunge were collected in Guangxi province (China) in November of 2003. The plant material was identified by Engineer Long Guang-ri (Guangxi province Forestry Administration, Liuzhou, China). A voucher specimen was deposited in Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing.

3.3 Extraction and isolation

The air-dried and powdered aerial parts of *Cercis chinensis* Bunge (10 kg) were extracted with 95% EtOH under reflux, and the crude extract (800 g) was obtained after removing the solvent *in vacuo*. The mixture of the extract and silica-gel (60–100 mesh) was put into a Soxhlet Extractor and extracted with petroleum ether, $CHCl_3$, EtOAc, acetone, EtOH and MeOH successively. The EtOAc extract (25 g) was subjected to silica-gel column chromatography, eluted with $CHCl_3$-MeOH (100:1, 4:1, v/v) to provide 78 fractions. Compound **4** (100 mg) crystallised from fractions 18–25. Fraction 37 was subjected to Sephadex LH-20 column, eluted with MeOH to provide compound **5** (5 mg); The extract of chloroform (20 g) was subjected to silica-gel column chromatography, eluted with Acetone - EtOAc (100:1, 4:1, v/v) to provide 59 fractions. Fractions 31–36, 11–13 and 42–49 were subjected to preparative HPLC to provide compounds **1** (16 mg), **2** (2 mg) and **3** (6 mg) respectively.

3.3.1 6-Methoxy-7-methyl-8-hydroxydibenz[*b*,*f*]oxepin (1). An amorphous powder. ESI-MS *m*/*z*: 277 $[M + Na]^+$. HREI-MS *m*/*z*: 254.0969 (calcd for $C_{16}H_{14}O_3$, 254.0942). UV (MeOH) λ_{max} nm (log ε): 292 (3.97), 248 (4.05) nm. IR (KBr) ν_{max} cm^{-1}: 3400, 1610, 1576, 1485, 1450, 1088, 685. ^1H NMR and ^{13}C NMR, see table 1.

3.3.2 1,8-Dimethoxy-6-hydroxy-7-methyldibenz[*b*,*f*]oxepin (2). Amorphous solid. ESI-MS *m*/*z*: 307 $[M + Na]^+$. HREI-MS *m*/*z*: 284.1051 (calcd for $C_{17}H_{16}O_4$, 284.1048). UV (MeOH) λ_{max} nm (log ε): 301 (3.83), 220 (4.09) nm. IR (KBr) ν_{max} cm^{-1}: 3477, 1680, 1601, 1577, 1466, 1132, 1095, 739, 669. ^1H NMR and ^{13}C NMR, see table 1.

3.3.3 1-Hydroxy-6,8-dimethoxy-7-methyldibenz[*b*,*f*]oxepin (3). Amorphous solid. ESI-MS *m*/*z*: 307 $[M + Na]^+$. HREI-MS *m*/*z*: 284.1046 (calcd for $C_{17}H_{16}O_4$, 284.1048). UV (MeOH) λ_{max} nm (log ε): 293 (3.79), 247.2 (3.86) nm. IR (KBr) ν_{max} cm^{-1}: 3450, 1676, 1606, 1572, 1458, 1126, 771, 739. ^1H NMR and ^{13}C NMR, see table 1.

3.3.4 Pacharin (4). Colourless needles (MeOH). ESI-MS *m*/*z*: 293 $[M + Na]^+$. ^1H NMR (500 MHz CD_3OD) δ:7.02 (1H, t, $J = 8.0$ Hz, H-3), 6.88 (1H, d, $J = 11.5$ Hz, H-10), 6.83 (1H, d, $J = 8.5$ Hz, H-4), 6.57 (1H, d, $J = 11.5$ Hz, H-11), 6.53 (1H, dd, $J = 1.0$, 8.0 Hz, H-2), 6.16 (1H, s, H-9), 3.68 (3H, S, OCH_3), 2.00 (3H, s, CH_3). ^{13}C NMR (125 MHz CD_3OD) δ:160.6 (C-4a), 156.5 (C-1), 156.0 (C-8), 148.1 (C-6), 140.2 (C-5a), 130.5 (C-10), 129.7 (C-11), 129.3 (C-9a), 125.3 (C-3), 119.8 (C-11a), 115.0 (C-7), 113.3 (C-4), 112.4 (C-9), 101.7 (C-2), 59.0 (OCH_3), 8.8 (CH_3).

3.3.5 Bauhiniastatin 4 (5). Colourless needles (MeOH), mp 217–219°C; ESI-MS *m/z*: 293 $[M + Na]^+$. HREI-MS *m/z*: 270.0918 (calcd for $C_{16}H_{14}O_4$,270.0892). UV (MeOH) λ_{max} nm (log ε): 296 (3.87), 240 (4.04) nm. IR (KBr) ν_{max} cm^{-1}: 3408, 1608, 1581, 1458, 1207, 1082, 1016, 739, 714. ^1H NMR and ^{13}C NMR data are consistent with literature values [8].

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