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A NEW BERGENIN DERIVATIVE FROM *Corylopsis willmottiae*

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*A new bergenin derivative, 11-*O*-(3′-*O*-methylgalloyl)-bergenin, was isolated from the whole plants of* Corylopsis willmottiae *Rehd. et Wils, along with 11-*O*-galloylbergenin, 11-*O*-syringylbergenin, bergenin, 4-*O*-galloylbergenin, and 4,11-di-*O*-galloylbergenin. They were identified on the basis of spectral evidence.*

Keywords: *Corylopsis willmottiae*, Hamamelidaceae, bergenin.

Corylopsis willmottiae Rehd. et Wils (Hamamelidaceae) is widely distributed in China, Japan, Korea, India, and Bhutan [1]. It is cultivated as an ornamental plant in China. Its chemical study has not been reported. Some species of the genus *Corylopsis*, such as *Corylopsis sinensis* Hemsl., a traditional Chinese medicine, contain bergenin, which is used to treat chronic bronchitis [2]. In the search for new bioactive constituents from wild plants, we initiated chemical studies of the whole plants of *C. willmottiae*, which led to the isolation of a new bergenin derivative 11-*O*-(3′-*O*-methylgalloyl)-bergenin (**1**), together with 11-*O*-galloylbergenin (**2**) [3–6], 11-*O*-syringylbergenin (**3**) [3], bergenin (**4**) [3–6], 4-*O*-galloylbergenin (**5**) [4–6], and 4,11-di-*O*-galloylbergenin (**6**) [4].

Compound **1** was obtained as a white amorphous powder and gave a brown coloration with ferric chloride on TLC. The IR bands at 3361 (strong), 1709, 1616, and 1517 cm^{-1} suggested the presence of hydroxyl, lactone, and the aromatic ring. The HR-ESI-MS exhibited a quasi-molecular ion peak at *m*/*z* 493.1005 $[M - H]^-$, corresponding to the molecular formula $C_{22}H_{22}O_{13}$.

From its ^1H NMR spectrum, the signals of three aromatic protons at δ 7.24 (br.s), 7.23 (br.s), and 7.09 (s); two methoxyl singlets at δ 3.91 and 3.87; two sets of doublets of doublets of the ABX pattern at δ 4.94 (J = 12, 1.9 Hz) and 4.31 (J = 12, 7.5 Hz); and five oxygenated protons at δ 3.97, 3.52, 3.85, 4.11, and 5.04 were observed. ^{13}C NMR further differentiated the skeleton carbons of **1** as two ester carbonyls (δ 166.5 and 164.2), two aromatic rings (δ 151.1, 148.0, 147.8, 145.0, 140.9, 139.6, 119.6, 118.1, 115.6, 110.8, 109.8 and 104.8), and two methoxyls (δ 59.5 and 55.4). Compared to the spectral data of compounds **2–6**, compound **1** was similar to 11-*O*-galloylbergenin, 11-*O*-syringylbergenin, and 4-*O*-galloylbergenin, indicating it was a bergenin derivative with a galloyl moiety. Thus, the signals of the aromatic proton at δ 7.09 (s, H-7) and the seven oxygenated protons at δ 3.97 (ddd, H-2), 3.52 (t, H-3), 3.85 (dd, H-4), 4.11 (t, H-4a), 4.31 (dd, H-11), 4.94 (dd, H-11), and 5.04 (d, H-10b) were easily attributed to the bergenin moiety, and the signals of the two aromatic protons at δ 7.24 (br.s, H-6′) and 7.23 (br.s, H-2′) were attributed to an asymmetrically substituted galloyl group.

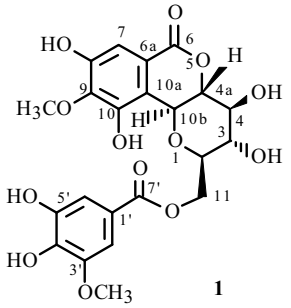

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TABLE 1. Chemical Shifts of C and H Atoms and Parameters of HSQC, HMBC, and NOESY Spectra of Compound **1** (MeOH-d_4, δ, ppm, J/Hz)

C atom	δ_C	δ_H	HMBC (H atoms)	NOESY (H atoms)
2	79.2	3.97 (ddd, J = 9.3, 7.5, 1.9)	11 (δ 4.31)	3, 10b, 11 (δ 4.94)
3	70.8	3.52 (t, J = 9.3)	4	2, 4, 4a, 11 (δ 4.31)
4	74.1	3.85 (dd, J = 10.5, 9.3)	10b	3, 4a, 10b
4a	79.9	4.11 (t, J = 10.5)	2, 4, 10b	3, 4, 10b
6	164.2		7	
6a	118.1			
7	109.8	7.09 s		
8	151.1		7	
9	140.9		7, 9-OMe	
10	148.0			
10a	115.6		7, 10b	
10b	72.9	5.04 (d, J = 10.5)	4a	2, 4, 4a
11	63.6	4.94 (dd, J = 12.0, 1.9)		2, 11 (δ 4.31)
		4.31 (dd, J = 12.0, 7.5)		3, 11 (δ 4.94)
9-OMe	59.5	3.87 s		
1′	119.6		2′, 6′	
2′	104.8	7.23 br.s	6′	3′-OMe
3′	147.8		2′, 3′-OMe	
4′	139.6		2′, 6′	
5′	145.0		6′	
6′	110.8	7.24 br.s	2′	
7′	166.5		2′, 6′, 11 (δ4.31)	
3′-OMe	55.4	3.91 s		2′

The galloyl moiety could be located at C-11 on the basis of the HMBC correlation of H-11 with C-7′. One methoxyl group at δ 3.87 was assigned to C-9 in view of the HMBC cross signal at δ 3.87/140.9 (C-9), and the other methoxyl group at δ 3.91 was assigned to C-3′ in view of the NOESY cross signal at 3.91/7.23 (H-2′). The HSQC and ^{1}H–^{1}H COSY correlations further confirmed the proposed structure and allowed the assignment of all signals in the ^{1}H and ^{13}C NMR spectra. Thus, compound **1** was finally identified as 11-*O*-(3′-*O*-methylgalloyl)-bergenin.

EXPERIMENTAL

General Experimental. Melting points were measured on an X-6 melting point apparatus and are uncorrected (Beijing Fukai Science and Technology Development Company Limited); optical rotations were measured on a Perkin–Elmer 341 automatic polarimeter; UV and IR spectra were recorded on a Lambda 35 spectrometer and a Perkin-Elmer Spectrum One FT-IR spectrometer (KBr disc), respectively; mass spectra were measured on a Finnigan-LCQ^{DECA} mass spectrometer (ESI-MS); NMR spectra (^{1}H: 600 MHz; ^{13}C: 150 MHz) were recorded on a Bruker Advance 600 spectrometer with TMS as an internal standard; silica gel H (200–300 mesh, Qingdao Haiyang Chemical Group Co., China), MCI gel (CHP 20P, 75–150 μm, Mitsubishi Chemical Corporation, Japan), LiChroprep RP-18 (40–63 μm, Merck KGaA, Germany), and Sephadex LH-20 (Pharmacia Biotech, Sweden) were used for column chromatography. The plates for thin layer chromatography (TLC) were precoated with silica gel GF254 (0–40 μm, Qingdao Haiyang Chemical Group Co., China) and activated at 110°C for 1 hour.

Plant Material. The whole plants of *Corylopsis willmottiae* Rehd. et Wils were collected in Lu-Ding County of Sichuan Province, China, in July 2005. A voucher specimen (LD-3) was authenticated by Prof. Zuocheng Zhao at Chengdu Institute of Biology, Chinese Academy of Sciences, and deposited in the Herbarium of the Chengdu Institute of Biology, Chinese Academy of Sciences.

Extraction and Isolation. The air-dried and powdered whole plants of *Corylopsis willmottiae* Rehd. et Wils (8.0 kg) were soaked in 95% EtOH (20 L × 3, 10 days each) at room temperature. The EtOH was evaporated under reduced pressure to give 350.0 g residue. The residue (350.0 g) was suspended in H_2O (1 L) and partitioned with petroleum ether

(1 L × 5), EtOAc (1 L × 6), and *n*-BuOH (1 L × 5). The EtOAc extract (50.0 g) was subjected to an MCI column (4 × 60 cm) eluted with MeOH–H_2O (95%, 5 L; 100%, 3 L) to remove pigments and fractionated into five fractions (I–V) by an RP-18 gravity column (400.0 g; MeOH in H_2O, 0%, 30%, 50%, 70%, 100%, each 2.5 L). Fraction I was recrystallized in methanol to afford bergenin (**4**, 320 mg). Fraction II was repeatedly separated over Sephadex LH-20 (MeOH) column to give 11-*O*-galloylbergenin (**2**, 5.0 g) and 4,11-di-*O*-galloylbergenin (**6**, 30 mg). Fraction III was recrystallized from methanol to give 11-*O*-galloylbergenin (**2**, 7.0 g), and the mother liquor was chromatographed on a silica gel (80.0 g) column eluted with $CHCl_3$–MeOH (15:2) saturated with H_2O to give 11-*O*-galloylbergenin (**2**, 300 mg) and 4-*O*-galloylbergenin (**5**, 250 mg). Fraction IV was recrystallized from methanol to give 11-*O*-galloylbergenin (**2**, 12.0 g), and the mother liquor was chromatographed on an RP-18 silica gel column eluted with MeOH–H_2O (35%) to furnish 11-*O*-galloylbergenin (**2**, 1.2 g), 11-*O*-(3′-*O*-methylgalloyl)-bergenin (**1**, 10 mg), and 11-*O*-syringylbergenin (**3**, 40 mg).

11-*O*-(3′-*O*-Methylgalloyl)-bergenin (1). White powder, mp 164–167°C; $[\alpha]_D^{20}$ +67° (*c* 0.015, CH_3OH). IR spectrum (KBr, ν, cm^{-1}): 3361 (OH), 1709 (C=O), 1616, 1462 (Ar). UV spectrum (CH_3OH, λ_{max}, nm): 218, 275 (log ε 4.48; 4.04). Negative ESI-MS *m*/*z*: 493 $[M - H]^-$; HR-negative ESI-MS *m*/*z*: 493.1005 (calcd for $C_{22}H_{21}O_{13}$: 493.0988). ^1H NMR and ^{13}C NMR data, see Table 1.

REFERENCES

1. L. G. Fu, *Higher Plants of China* [in Chinese], Qingdao Publishing House, Qingdao, Vol. **3**, 2000, p. 710.
2. Editorial Committee of Flora of China of Chinese Academy of Science, *Flora of China* [in Chinese], Science Press, Beijing, Vol. **35**, 1979, No. 2, p. 76.
3. Zh. H. Jia, K. Mitsunaga, K. Koike, and T. Ohmoto, *Nat. Med.*, **49**, 187 (1995).
4. R. Saijo, G. I. Nonaka, and I. Nishioka, *Phytochemistry*, **29**, 267 (1990).
5. X. M. Chen, T. Yoshida, T. Hatano, M. Fukushima, and T. Okuda, *Phytochemistry*, **26**, 515 (1987).
6. T. Yoshida, K. Seno, Y. Takama, and T. Okuda, *Phytochemistry*, **21**, 1180 (1982).