Journal of Molecular Structure 1049 (2013) 299–302

Contents lists available at SciVerse ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Two new phenylpropanoid glycosides with interesterification from *Scrophularia dentata* Royle ex Benth

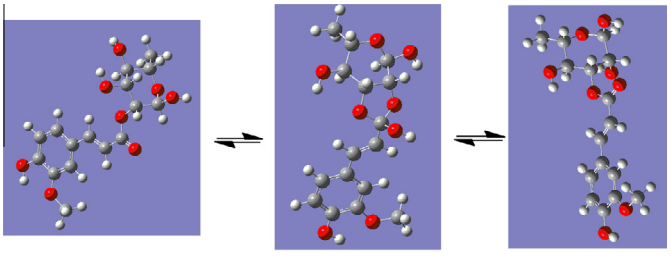
Liuqiang Zhang [a], Zhuo Yang [b], Qi Jia [a], Gaawe Dorje [c], Zhili Zhao [a], Fujiang Guo [a,*], Yiming Li [a,*]

[a] School of Pharmacy, Shanghai University of Traditional Chinese Medicine, 1200 Cailun Road, Shanghai 201203, China
[b] Drug Discovery and Design Center, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China
[c] Tibetan Traditional Medical College, Lhasa 850000, China

HIGHLIGHTS

- First phytochemical investigation of *Scrophularia dentata* Royle ex Benth.
- Two new phenylpropanoid glycosides along with seven known ones were isolated.
- Compounds **1** and **2** failed to be separated, the interesterification mechanism was presumed and discussed firstly.
- The quantum chemical calculation was applied to elucidate the interesterification mechanism.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 3 May 2013
Received in revised form 20 May 2013
Accepted 20 May 2013
Available online 24 June 2013

Keywords:
Scrophularia dentata
Phenylpropanoid glycosides
Acetyl migration
DFT calculations

ABSTRACT

Two new phenylpropanoid glycosides (**1**–**2**), along with seven known ones (**3**–**9**), were isolated from the whole plant of *Scrophularia dentata* Royle ex Benth. Their structures were elucidated by spectroscopic methods. Among them, compounds **1** and **2** failed to separated, because they can easily transform into each other by acyl migrant reaction. In this paper, the interesterification mechanism was discussed firstly and the rule can be used in the similar structure elucidation in future.

1. Introduction

The genus *Scrophularia* (Scrophulariaceae), comprising of more than two hundred species, is widely distributed in the world. Some of them have been used as medicinal herbs worldwide which can be learned from the genus name *Scrophularia* comes from a disease named "scrofula". About 36 species of this genus grow in China, some of which have been used as traditional Chinese medicine (TCM), such as the roots of *Scrophularia ningpoensis*, a popular TCM named "Xuan-Shen", for the treatment of fever, swelling, constipation, pharyngitis and laryngitis [1]. *Scrophularia dentata* Royle ex Benth is the only plant of this genus growing in high altitude (4000–6000 m) areas, which is recorded in Tibetan volume of Chinese Materia Medica. The whole plant of *S. dentata* is used as the main resource of Tibetan herb "Ye-Xin-Ba", which is used in the treatment of smallpox, measles disease, high heat plague, poisoning, etc.

Relevant pharmacological studies demonstrated that the plant extracts or their constituents from *Scrophularia* genus showed antimicrobial, antiinflammatory, antitumor, improving heart function and neuroprotective activity, etc. [2]. Meanwhile, many species of this genus have been chemically investigated. The mainstream characteristic constituents reported are iridoid and phenylpropanoid glycosides, which reflect their consistency in plant chemotaxonomy.

* Corresponding authors. Tel.: +86 21 51322191; fax: +86 21 51322193.
E-mail addresses: guofj1972@hotmail.com (F. Guo), ymlius@163.com (Y. Li).

0022-2860/$ - see front matter
http://dx.doi.org/10.1016/j.molstruc.2013.05.039

So far, there was no chemical constituent reported on this plant. Herein, we reported the isolation and structure elucidation of two new phenylpropanoid glycosides (**1**–**2**) along with seven known ones (**3**–**9**). After purification, **1** and **2** were quickly transformed to each other and existed in a mixture form. Here, according to Hammond hypothesis, we presumed the reason was the acyl groups' migrating between C-2′ and C-3′, which was further confirmed by computational chemistry.

2. Experimental

2.1. General experimental procedures

Optical rotations were determined on a Perkin–Elmer 341 polarimeter. IR spectra were recorded on a Nicolet Magna-750-FTIR spectrometer with KBr tablet. NMR spectra were acquired on a Bruker AM-400 spectrometer. ESI-MS and HR-ESI-MS were obtained on an Esquire 3000 plus and a Q-TOF-Ultima mass spectrometer, respectively. Silica gel (200–300 mesh, Qingdao Haiyang Chemical Co., Ltd., Qingdao, China), D-1400 macroporous resin (Yangzhou Pharmaceutical Factory, Yangzhou, China), C_{18} reversed phase silica gel (150–200 mesh, Fuji Silysia Chemical Ltd., Aichi, Japan), MCI gel (CHP20P, 75–150 μM, Mitsubishi Chemical Industries Ltd., Tokyo, Japan), and Sephadex LH-20 gel (Pharmacia Biotech AB, Uppsala, Sweden) were used for column chromatography (CC).

2.2. Plant material

The whole plant of *S. dentata* Royle ex Benth was collected from Tibet, China in October 2010. It was identified by Professor Zhili Zhao, School of Pharmacy, Shanghai University of Traditional Chinese Medicine. The voucher specimen (No. CX2010) was deposited at the Herbarium of the Department of TCM Chemistry, School of Pharmacy of Shanghai University of Traditional Chinese Medicine (Shanghai, China).

2.3. Extraction and isolation

Dried whole plant of *S. dentata* (4.2 kg) were extracted for 2 h with 95% EtOH (3×, each 6 L), using a reflux apparatus that yielded an extract (570 g) upon removal of the solvent under reduced pressure. This extract was suspended in water and extracted with petether (b.p. 60–90 °C), EtOAc and n-butanol, successively. The EtOAc extract was evaporated to dryness under reduced pressure and the resultant EtOAc fraction (48.8 g) was subjected to a silica gel column chromatography eluting with gradient solvents of petroleum ether–EtOAc (1:0–0:1) and then pure methanol to afford fractions A–G. Fr.D was separated by CC of MCI gel (MeOH/H_2O 20, 30, 40, 50, 60, 70, 100, v/v) to afford sub-fractions D1-D6 Fr.D3 was purified using Rp-18 column (MeOH/H_2O, 30:70-40:60, v/v), Sephadex LH-20 (MeOH/H_2O, 35:65, v/v) columns and preparative HPLC on a *Agilent Eclipse* XDB-C_{18} column (5 μm, 9.4 × 250 μm), eluting with CH_3OH–H_2O (35:65), to obtain the mixture of compounds **1** and **2**(44 mg). By the same procedure, compound **3** (287 mg) and **4** (58 mg) were obtained from Fr.D2 and Fr. D5, respectively. Fr.E was separated by CC of MCI gel (MeOH/H_2O 20, 30, 40, 50, 60, 70, 100, v/v) to afford sub-fractions E1–E5, Fr.E3 was purified using Rp-18 column (MeOH/H_2O, 35:65-40:60, v/v) repeatedly, to obtain **5** (23 mg), **6** & **7** (11 mg) and **8** (26 mg). Fr.F was separated by CC of MCI gel (MeOH/H_2O 10, 20, 30, 40, 50, 100, v/v) to afford sub-fractions F1–F5, Fr.F2 was purified using Rp-18 column (MeOH/H_2O, 15:85-25:75, v/v) and preparative HPLC on a *Agilent Eclipse* XDB-C_{18} column (5 μm, 9.4 × 250 μm), eluting with CH_3OH–H_2O (20:80), to obtain **9** (83 mg).

2.3.1. 2-O-trans-feruloylrhamnopyranose & 3-O-trans-feruloylrhamnopyranose

Yellow amorphous powder; $[\alpha]_D^{22} = 48.8$ (c = 0.125 g/100 ml, MeOH); IR (KBr)υ_{max}: 3423, 2975, 2937, 1693, 1631, 1596, 1515, 1429, 1382, 1270, 1178, 1058, 979, 817, 601 cm^{-1}; UV λ_{max}^{MeOH} nm: 217, 236, 302, 326; ESI-MS (pos.): 363 $[M + Na]^+$, 703 $[2\,M + Na]^+$; ESI-MS (neg.): 339 $[M - H]^-$. HR-ESI-MS: 363.1048 (calc. for $C_{16}H_{20}O_8Na^+$, 363.1056); ^1H & ^{13}C NMR spectral data see Table 1.

2.3.2. Identification of compounds 3–9

The structures of the known compounds were identified as diacetylmartynoside (**3**) [8], Acteoside (**4**) [9], Lipedosides A-I (**5**) [10], (*E*, *Z*)-martynoside (**6, 7**) [11], Osmanthuside B (**8**) [12], Isoacteoside (**9**) [13] by comparison with spectroscopical data and MS values in literature. Among them, compounds **3** and **8** were firstly isolated from this genus.

2.4. Theoretical methods

The compounds **1**, **2** and **10** were optimized by using DFT method, starting from the experimental structures. DFT calculations with a hybrid functional B3LYP (Becke's three parameter hybrid functional using the LYP correlation functional) at 6-31G (d,p) basis set using the Berny method [14] were performed with the Gaussian 03 software package [15], and Gauss-view visualization program [16].

Table 1
^1H and ^{13}C NMR data of compounds **1** and **2** (CD_3OD, δ, J in Hz).

No.	1		2		Isoferuloyl	Feruloyl
	δ_C	δ_H(J in Hz)	δ_C	δ_H(J in Hz)	δ_C	δ_C
1	127.7	–	127.9	–	129.1	127.8
2	111.8	7.21 (1H, d, 1.8)	111.7	7.19 (1H, d, 1.8)	112.7	111.9
3	149.6	–	149.6	–	151.6	149.5
4	151.1	–	151.0	–	148.1	150.9
5	115.4	6.81 (1H, d, 8.2)	115.8	6.81 (1H, d, 8.2)	115.0	115.4
6	124.5	7.07 (1H, dd, 1.8/8.2)	124.2	7.09 (1H, dd, 1.8/8.2)	122.8	124.4
7	147.4	7.65 (1H, d, 15.9)	147.1	7.69 (1H, d, 15.9)	147.0	147.3
8	116.7	6.43 (1H, d, 15.9)	116.7	6.42 (1H, d, 15.9)	116.6	116.6
9	169.0	–	169.1	–	168.7	169.2
OMe	56.6	3.89 (3H, s)	56.6	3.89 (3H, s)	56.5	56.5
Rha-1′	93.3	5.05 (1H, d, 1.5)	96.0	5.02 (1H, d, 1.7)		
2′	75.2	5.08 (1H, dd, 1.5/3.4)	71.2	4.01 (1H, dd, 1.7/3.2)		
3′	70.5	3.94 (1H, dd, 3.4/9.6)	75.5	5.15 (1H, dd, 3.2/9.9)		
4′	74.7	3.45 (1H, t, 9.6)	71.8	3.65 (1H, t, 9.9)		
5′	69.6	3.87 (1H, dd, 6.2/9.6)	69.4	3.95 (1H, dd, 6.2/9.9)		
6′	18.3	1.29 (3H, d, 6.2)	18.3	1.30 (3H, d, 6.2)		