Available online at www.sciencedirect.com
ScienceDirect
Chinese Chemical Letters 22 (2011) 961–963
CHINESE CHEMICAL LETTERS
www.elsevier.com/locate/cclet

A new phenylethanoid glycoside from *Isodon sculponeatus*

Li Mei Li [a], Jian Xin Pu [b], Wei Lie Xiao [b], Han Dong Sun [b,*]

[a] *Scientific Research Center, Chengdu Medical College, Chengdu 610083, China*
[b] *State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650204, China*

Received 30 September 2010
Available online 17 May 2011

Abstract

A new phenylethanoid glycoside, sculponiside (**1**) was isolated from the aerial parts of *Isodon sculponeatus* (Vaniot) Kudo, along with six known compounds martynoside (**2**), verbascoside (**3**), (+)-hydroxypinoresinol-8-*O*-*β*-D-glucoside (**4**), cedrusin (**5**), 7-megastigmene-3*S*,5*R*,6*R*,7*E*,9*S*-tetrol (**6**) and 4-oxo-*β*-ionol-*β*-D-glucopyranoside (**7**). Their chemical structures were elucidated from physicochemical data and by acidic hydrolysis.

Keywords: *Isodon sculponeatus* (Vaniot) Kudo; Labiatae; Phenylethanoid glycoside; Sculponiside

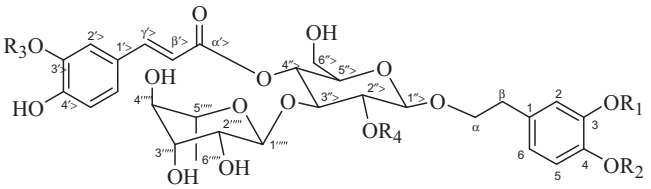
Isodon sculponeatus (Vaniot) Kudo (family Labiatae) is mainly distributed in southern China. Its stems and leaves have long been used in traditional Chinese medicine for the treatment of diarrhea [1]. Bioactive *ent*-kaurane diterpenoids were reported from the aerial parts of *I. sculponeatus* recently [2,3]. On continuing further chemical analysis, a new phenylethanoid glycoside, sculponiside (**1**) and six known compounds martynoside (**2**) [4], verbascoside (**3**) [4], (+)-hydroxypinoresinol-8-*O*-*β*-D-glucoside (**4**) [5], cedrusin (**5**) [6], 7-megastigmene-3*S*,5*R*,6*R*,7*E*,9*S*-tetrol (**6**) [7] and 4-oxo-*β*-ionol-*β*-D-glucopyranoside (**7**) [8] were isolated and identified from the aerial parts of *I. sculponeatus*. All these compounds are reported for the first time in this genus.

The air-dried powdered aerial parts of *I. sculponeatus* (1.5 kg) were extracted at room temperature with acetone and filtered. The filtrate was evaporated *in vacuo* to afford a residue, which was partitioned by a liquid–liquid extraction between EtOAc and H_2O (1500 mL of each). The EtOAc extract (45 g) was decolorized using MCI gel, eluted with 90% MeOH–H_2O, to yield a yellowish gum (39 g). The gum was separated on a silica gel column, eluted with a $CHCl_3$–Me_2CO step gradient (1:0 to 0:1), to obtain ten fractions, A–J.

Fraction F (6 g) was chromatographed over silica gel eluted with a $CHCl_3$–MeOH step gradient (10:1 to 5:1) to give three subfractions F1–F3. Compound **1** (15 mg) was purified from subfraction F1 by preparative HPLC (35% MeOH–H_2O). Subfraction F2 was applied to RP-18 with 30% MeOH–H_2O eluent to afford compounds **2** (11 mg) and **3** (110 mg), respectively. Fraction H (2.4 g) was subjected to Sephadex LH-20 eluting with MeOH followed by semipreparative HPLC eluting with 20% MeCN–H_2O to give compounds **5** (5 mg) and **6** (6 mg), respectively. Fraction

* Corresponding author.
E-mail address: hdsun@mail.kib.ac.cn (H.D. Sun).

1001-8417/$ – see front matter
doi:10.1016/j.cclet.2011.01.029



	R_1	R_2	R_3	R_4
1	H	CH_3	CH_3	$COCH_3$
2	H	CH_3	CH_3	H
3	H	H	H	H

Fig. 1. The structures of compounds **1**–**3**.

I (5.5 g) was fractionated over silica gel eluted with $CHCl_3$–MeOH (6:1 to 4:1) followed by semipreparative HPLC with 15% MeCN–H_2O eluent to provide compounds **4** (11 mg) and **7** (8 mg), respectively.

Compound **1** was isolated as a white amorphous powder. The HRESIMS displayed quasi-molecular ion peak $[M-H]^-$ at *m/z* 693.2390 corresponding to the formula $C_{33}H_{41}O_{16}$ (calcd. for $C_{33}H_{41}O_{16}$, 693.2394). The IR spectrum showed significant absorption bands due to hydroxyl groups (3433 cm^{-1}), an ester group (1733 cm^{-1}), an α,β-conjugated ester group (1630, 1711 cm^{-1}) and aromatic rings (1593, 1515 cm^{-1}). The ^1H NMR signals at δ_H 7.19 (d, 1H, *J* = 1.8 Hz), 7.08 (dd, 1H, *J* = 8.2, 1.8 Hz), 6.81 (d, 2H, *J* = 8.2 Hz), 6.68 (d, 1H, *J* = 2.0 Hz) and 6.64 (dd, 1H, *J* = 8.2, 2.0 Hz) suggested the presence of two 1,3,4-trisubstituted phenyl groups. The ^1H NMR spectrum of **1** also showed two *trans* olefinic protons at δ_H 7.66 (d, 1H, *J* = 15.9 Hz) and 6.38 (d, 1H, *J* = 15.9 Hz). The evidence mentioned above and the following signals at δ_H 4.10 (m, 2H), 2.73 (m, 2H), 3.88 (s, 3H), 3.81 (s, 3H), and δ_C 71.6 (t), 36.3 (t), 56.5 (q) and 56.4 (q) indicated the presence of one 3,4-disubstituted phenylethanol and one *trans* feruloyl groups in compound **1**. The two sugar units were revealed by the signals for two anomeric carbons at δ_C 101.7 (d) and 103.3 (d), correlated by the HSQC spectrum with the corresponding signals of anomeric protons at δ_H 4.53 (d, 1H, *J* = 8.1 Hz) and 4.87 (overlap, 1H). Additionally, the signals of δ_H 1.07 (d, 3H, *J* = 6.2 Hz) and δ_C 18.5 (q) further suggested the presence of one rhamnose. Acid hydrolysis of **1** gave D-glucose and L-rhamnose in the ration of 1:1 as component sugars, which were confirmed by GC–MS analysis of their corresponding trimethylsilylated L-cysteine adducts. Therefore, compound **1** was a phenylethanoid glycoside, similar to compound **2** (Fig. 1). The main difference was that compound **1** possessed an acetyl group at δ_H 1.98 (s, 3H) and δ_C 171.4 (s) and 20.9 (q). In the HMBC spectrum of compound **1**, correlations of H-α (δ_H 4.10) to C-1″ (δ_C 101.7) and H-1″ (δ_H 4.53) to C-α (δ_C 71.6) suggested that the C-1 of glucose was linked to the C-α of aglycon. The HMBC correlation between H-4″ (δ_H 4.92) and C-α′ (δ_C 168.0) indicated that the *trans* feruloyl group was located at C-4″. The H-3″ (δ_H 4.00) correlating to C-1‴ (δ_C 103.3) proved that the sugar chain was rha(1→3)-glc-. Moreover, the acetyl group was placed at C-2″ from the HMBC correlation between H-2″ (δ_H 4.88) and the carbonyl carbon at δ_C 171.4 (Fig. 2). Meanwhile, the positions of the two methoxyl groups were confirmed by a NOESY experiment (Fig. 2). Therefore, the structure of **1** was elucidated as 3-hydroxy-4-methoxy-β-phenylethoxy-*O*-[α-L-rhamnopyranosyl-(1→3)]-2-*O*-acetyl-4-*O*-feruloyl-β-D-glucopyranoside and was named sculponiside.

Compound **1** is a natural product, as it was detected in the ethanol extract of the title plant by both TLC ($CHCl_3$–MeOH, 2:1, R_f = 0.35) and HPLC (0–100% MeOH–H_2O in 40 min, gradient system, R_t = 14.8 min) conditions.

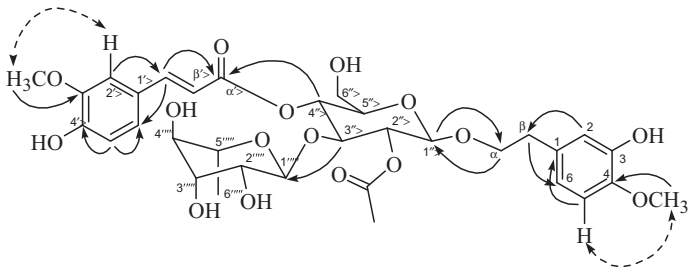


Fig. 2. The key HMBC (plain) and NOESY (dashed) correlations of compound **1**.

Table 1
^{1}H and ^{13}C NMR data of compound **1** (400 and 100 MHz, in CD_3OD).

Position	δ_H (mult., J in Hz)	δ_C (mult.)	Position	δ_H (mult., J in Hz)	δ_C (mult.)
1		133.2 (s)	1″	4.53 (d, 1H, 8.1)	101.7 (d)
2	6.68 (d, 1H, 2.0)	117.1 (d)	2″	4.88 (overlap, 1H)	75.1 (d)
3		147.5 (s)	3″	4.00 (m, 1H)	80.4 (d)
4		147.3 (s)	4″	4.92 (m, 1H)	70.6 (d)
5	6.81 (d, 1H, 8.2)	112.7 (d)	5″	3.49–3.68 (overlap, 1H)	76.1 (d)
6	6.64 (dd, 1H, 8.2, 2.0)	121.2 (d)	6″	3.49–3.68 (overlap, 2H)	62.2 (t)
α	4.10 (m, 2H)	71.6 (t)	1‴	4.87 (overlap, 1H)	103.3 (d)
β	2.73 (m, 2H)	36.3 (t)	2‴	3.49–3.68 (overlap, 1H)	71.8 (d)
1′		127.6 (s)	3‴	3.49–3.68 (overlap, 1H)	72.6 (d)
2′	7.19 (d, 1H, 1.8)	111.7 (d)	4‴	3.31 (m, 1H)	73.6 (d)
3′		149.4 (s)	5‴	3.49–3.68 (overlap, 1H)	70.8 (d)
4′		150.9 (s)	6‴	1.07 (d, 3H, 6.2)	18.5 (q)
5′	6.81 (d, 1H, 8.2)	116.5 (d)	OCH_3	3.88 (s, 3H)	56.5 (q)
6′	7.08 (dd, 1H, 8.2, 1.8)	124.4 (d)	OCH_3	3.81 (s, 3H)	56.4 (q)
α′		168.0 (s)	$CO\underline{CH_3}$	1.98 (s, 3H)	20.9 (q)
β′	6.38 (d, 1H, 15.9)	114.9 (d)	$\underline{CO}CH_3$		171.4 (s)
γ′	7.66 (d, 1H, 15.9)	148.0 (d)			

Sculponiside (**1**): a white amorphous powder; $[\alpha]_D^{24}$ −76.4 (*c* 0.34, MeOH); UV (MeOH) λ_{max} (log ε): 204 (4.57), 218 (4.26), 329 (4.22) nm; IR (KBr) υ_{max}: 3433, 2937, 2843, 1733, 1711, 1630, 1593, 1515, 1431, 1376, 1273, 1245, 1158, 1131, 1034 cm^{-1}; ^{1}H and ^{13}C NMR data are in Table 1; ESIMS *m/z*: 693 $[M-H]^-$, 729 $[M+Cl]^-$; HRESIMS *m/z*: 693.2390 (calcd. for $C_{33}H_{41}O_{16}$ $[M-H]^-$, 693.2394).

Acid hydrolysis: A solution of **1** (2 mg) in 1 mol/L HCl/dioxane (1:1, v/v, 2 mL) was refluxed on a H_2O bath for 6 h. After dioxane was removed, the solution was extracted with EtOAc (3 mL × 3). The H_2O layer was neutralized with Amberlite MB-3 and concentrated to dryness to yield a mixture of sugars. The configuration of glucose and rhamnose was determined by GC–MS analysis using the method described previously [9].

Acknowledgments

This work was supported financially by the NSFC (Nos. 30772637 to H.D. Sun, and 30830119 to S.J. Chen), the NSFC-Joint Foundation of Yunnan Province (No. U0832602 to H.D. Sun), the Major State Basic Research Development Program of China (No. 2009CB522300 and 2009CB940900), the Natural Science Foundation of Yunnan Province (No. 2008CD162), and the Science and technology plan project of Yunnan Province (No. 2008IF010).

References

[1] Compiling Groups of Compilation of Countrywide Herbal Medicine of China, Compilation of Countrywide Herbal Medicine of China, People's Medical Publishing House, Beijing, 1996, p. 853.
[2] L.M. Li, G.Y. Li, L.S. Ding, et al. Tetrahedron Lett. 48 (2007) 9100.
[3] L.M. Li, G.Y. Li, J.X. Pu, et al. J. Nat. Prod. 72 (2009) 1851.
[4] T. Miyase, A. Koizumi, A. Ueno, et al. Chem. Pharm. Bull. 30 (1982) 2732.
[5] T. Tanahashi, N. Nagakura, K. Inoue, et al. Chem. Pharm. Bull. 35 (1987) 5032.
[6] P.K. Agrawal, S.K. Agarwal, R.P. Rastogi, Phytochemistry 19 (1980) 1260.
[7] Y. Takeda, Y. Okada, T. Masuda, et al. Chem. Pharm. Bull. 48 (2000) 752.
[8] A. Pabst, D. Barron, E. Sémon, et al. Phytochemistry 31 (1992) 4187.
[9] J.M. Jin, Y.J. Zhang, H.Z. Li, et al. J. Nat. Prod. 67 (2004) 1992.