Isoangoroside C, a Phenylpropanoid Glycoside from *Scrophularia scorodonia* Roots

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Isoangoroside C, *Scrophularia scorodonia,* Phenylpropanoid Glycoside

A new phenylpropanoid glycoside isoangoroside C was isolated from the roots of *Scrophularia scorodonia*. Its structure was determined on the basis of spectral data as: 3-hydroxy-4-methoxy-β-phenylethoxy-O-α-L-arabinopyranosyl-(1→6)α L-rhamnopyranosyl-(1→3)-4-O-*Z*-feruloyl-ß-D -glucopyranoside. Additionally, one known phenylpropanoid, angoroside C, and five known iridoid glycosides, harpagoside, bartsioside, 8-O-acetyl-harpagide, aucuboside and harpagide were isolated and identified.

The genus *Scrophularia* is known to contain a variety of phenolic compounds. We report the isolation and structural identification of a new phenylpropanoid glycoside named isoangoroside C (**2**) together with the known angoroside C (**1**) from the roots of *Scrophularia scorodonia.*

In addition this paper deals with the isolation of harpagoside, bartsioside, 8-O-acetyl-harpagide, aucuboside and harpagide from *Scrophularia scorodonia* roots. In a previous paper, we have reported the isolation and structure elucidation of these iridoids from the aerial parts of *Scrophularia scorodonia* (Fernández *et al*; 1995) except for harpagide. This compound has been isolated for the first time from this species.

Material and Methods

Roots of *Scrophularia scorodonia* were collected in November 1993 from the vicinity of Jaén (Spain). A voucher specimen (J. D. S. 93) is deposited at the Pharmacognosy Department of the University of Alcalá de Henares. Plant material was identified by Carmen Bartolomé (Department of Vegetal Biology, Faculty of Sciences, Alcalá de Henares, Madrid, Spain).

Powdered roots (400 g) were extracted with acetone to obtain an extract (17.6 g dry weight). The marc was percolated with MeOH. The MeOH extract obtained was concentrated in a vacuum, and fractionated by flash chromatography on silicagel using different mixtures of $CHCl_3$-MeOH (90:10, 80:20 v/v) and pure MeOH yielding four fractions (A1-A4).

Fractions A2, A3 and A4 (1.46 g dry weight) were fractionated by Medium Pressure Liquid Chromatographic (MPLC) (Lichroprep RP_{18}, 26–40 μ, H_2O-MeOH gradient). Fractions obtained between 40%-50% MeOH were combined and subjected to MPLC to obtain the following mixture of the two isomers of angoroside C (45% MeOH, 10.7 mg).

The acetone extract obtained (17.6 g) was concentrated under vacuum, and fractionated by chromatography on silicagel column using different mixtures of $CHCl_3$-MeOH-H_2O (65:30:3, 65:45:3, 55:37:7 v/v) and pure MeOH to give thirteen fractions (A′1-A′13).

Fractions obtained with $CHCl_3$-MeOH-H_2O 65:30:3 v/v (A′4-A′9) were also purified by MPLC (Lichroprep RP_{18}, 26–40 μ, H_2O-MeOH gradient): Fraction A′4 yielded harpagoside (45% MeOH, 17.8 mg); Fraction A′5 yielded bartsioside (40% MeOH, 7.6 mg); Fraction A′6 yielded 8-O-acetyl-harpagide (45% MeOH, 13.1 mg); Fraction A′8 yielded aucubin (30%/40% MeOH, 13.1 mg) and fraction A′9 yielded harpagide (15% MeOH, 16.5 mg). Identification and assignment of the iso-

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lated compounds were performed by a comparison of their spectroscopic data (UV, ^{1}H-NMR, and ^{13}C-NMR) with those of authentic samples and/or previously reported data (Fernández *et al.*, 1995; Weinges and Von der Eltz, 1978).

^{1}H-NMR and ^{13}C-NMR spectra (in CD_3OD, TMS as internal standard; chemical shifts in δ ppm) were obtained using a Bruker WM 300 spectrometer [300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR)]. MPLC Supercosil RP-18 column (26–

Table I. ^{13}C and ^{1}H NMR data of compounds **1** and **2**.

	δ ppm (^{13}C NMR)		δ ppm (^{1}H NMR)	
C/H	**1**	**2**	**1**	**2**
AGLYCONE				
C-1	132.99	132.99		
CH-2	112.84	112.84	6.77 d (*J*=1.9 Hz)	6.77 d (*J*=1.9 Hz)
C-3	147.55[a]	147.55[a]		
C-4	147.36[a]	147.36[a]		
CH-5	117.07	117.07	6.84 d (*J*=8.3 Hz)	6.83 d (*J*=8.3 Hz)
CH-6	121.22	121.22	6.70 dd (*J*=8.3/1.9 Hz)	6.72 dd (*J*=8.3/1.9 Hz)
CH_2-a	72.23	72.23	A=4.06 m	A=4.06 m
			B=3.73 m	B=3.73 m
CH_2-b	36.56	36.56	2.82 t (*J*=7.0 Hz)	2.82 t (*J*=7.0 Hz)
OCH_3	56.47	56.47	3.80 S	3.80 S
FERULOYL MOIETY				
C-1′	127.62	127.95		
CH-2′	111.78	112.94	7.22 d (*J*=2.0 Hz)	7.91 d (*J*=2.0 Hz)
C-3′	149.42	148.31[b]		
C-4′	150.93	149.80[b]		
CH-5′	116.51	115.62[c]	6.82 d (*J*=8.3Hz)	6.78 d (*J*=8.3Hz)
CH-6′	124.43	127.48	7.10 dd (*J*=8.3/2.0 Hz)	7.17 dd (*J*=8.3/2.0 Hz)
CH-a′	115.04	115.43[c]	6.39 d (*J*=15.9 Hz)	5.82 d (*J*=12.9 Hz)
CH-b′	148.10	147.78	7.68 d (*J*=15.9)	6.96 d (*J*=12.9)
CO	168.30	166.94		
OCH_3	56.47	56.47	3.90 s	3.90 s
GLUCOSE				
CH-1″	105.06	105.06	4.40 d (*J*=7.8 Hz)	4.38 d (*J*=7.8 Hz)
CH-2″	76.15	76.03	3.3–3.5	3.3–3.5
CH-3″	81.50	81.91	3.7–3.9	3.7–3.9
CH-4″	70.45	70.45	4.97 t (9.5 Hz)	4.90 t (9.5 Hz)
CH-5″	74.99	75.04	3.7–3.9	3.7–3.9
CH_2-6″	69.04	68.97	A=3.5–3.7	A=3.5–3.7
			B=3.7–3.9	B=3.7–3.9
RHAMNOSE				
CH-1‴	103.03	103.24	5.22 d (*J*=1.7 Hz)	5.17 d (*J*=1.7 Hz)
CH-2‴	72.36	72.36	3.8–4.0	3.8–4.0
CH-3‴	72.36	72.36	3.5–3.7	3.5–3.7
CH-4‴	74.07	74.07	3.2–3.4	3.2–3.4
CH-5‴	70.45	70.45	3.5–3.7	3.5–3.7
CH_3-6‴	18.44	18.24	1.12 d (*J*=6.3 Hz)	1.20 d (*J*=6.3 Hz)
ARABINOSE				
CH-1⁗	104.16	104.11	4.26 d (*J*=6.5 Hz)	4.23 d (*J*=6.5 Hz)
CH-2⁗	72.06	72.15	3.5–3.7	3.5–3.7
CH-3⁗	73.76	73.76	3.4–3.5	3.4–3.5
CH-4⁗	69.47	69.47	3.7–3.9	3.7–3.9
CH_2-5⁗	66.77	66.77	3.4–3.9	3.4–3.9

a,b,c: Signals are interchangeable within the same column.

40 μm; i.d. 4.6x15 mm); Flash chromatography on silicagel (32–63 μm, 60 Å, 500–550 m^2/g silica).

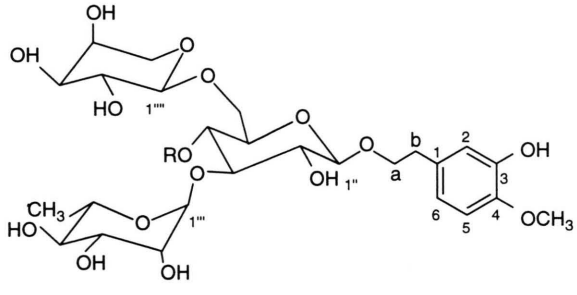
Results and Discussion

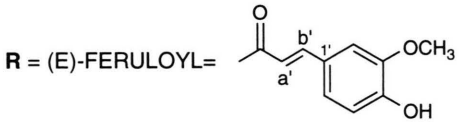
Angoroside C (**1**) and *isoangoroside C* (**2**) were obtained as an amorphous powder. For ^{1}H-NMR and ^{13}C-NMR data see Table I.

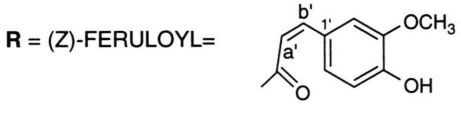
Compounds **1** and **2** were obtained as a mixture. The ratio of **1** to **2** was determined as 2:3 by the intensities of the corresponding proton signals in the ^{1}H NMR spectrum. Compound **1** was identified as angoroside C by comparison of the ^{1}H and ^{13}C-NMR data with those of the literature (Calis *et al.*, 1988) (Fig. 1).

The ^{1}H-NMR spectrum of **2** (Table I) exhibited two doublets at δ 6.96 and δ 5.82 with a coupling constant of 12.9 Hz, assignable to two olefinic protons of a *cis* double bond. Apart from the olefinic proton signals the ^{1}H-NMR spectra of **1** and **2** differed only in the chemical shifts of the aromatic protons. The H-2′ signals showed the highest difference: the spectrum of **2** showed a signal at δ 7.91 ppm whereas the H-2′ signal of **1** was observed at δ 7.22 ppm. Smaller difference were observed for the aromatic protons H-5′ and H-6′: the H-5′ signal of **2** showed an upfield shift of 0.04 ppm and the H–6′ signal of **2** a downfield shift of 0.07 ppm compared to **1**. These differences are in agreement with the differences expected for *trans* and *cis* feruloyl moieties. Indeed, the ^{1}H-NMR data of the acyl moiety in **2** are identical with those of the cis-feruloyl moiety reported in the literature (Kikuzaki *et al.*, 1996).

The assignments of methoxyl groups of compound **2** were carried out by using the 2D ^{1}H-^{1}H NOESY experiment, which showed a series of bidirectional NOESY interactions between the H-2′ proton at 7.91 ppm and the methoxyl group (δ 3.90) and H-β′ proton (δ 6.96). Furthermore, NOESY interactions were displayed between the methoxyl group at 3.80 ppm and the H-5 proton (δ 6.72). Therefore, the structure of compound **2** was determined as *cis* isomer in the feruloyl moiety of the angoroside C (**1**).







	R	NAME
1	(E)-FERULOYL	ANGOROSIDE C
2	(Z)-FERULOYL	ISOANGOROSIDE C

Fig. 1.

Acknowledgements

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