JOURNAL OF NATURAL PRODUCTS

Subscriber access provided by ISTANBUL TEKNIK UNIV

Ajureptoside, a Novel C Iridoid Glucoside from Ajuga reptans

Noboru Shoji, Akemi Umeyama, Nobuyuki Sunahara, and Shigenobu Arihara

J. Nat. Prod., **1992**, 55 (7), 1004-1006• DOI:
10.1021/np50085a030 • Publication Date (Web): 01 July 2004

Downloaded from http://pubs.acs.org on April 4, 2009

More About This Article

The permalink http://dx.doi.org/10.1021/np50085a030 provides access to:

- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

ACS Publications
High quality. High impact.

Journal of Natural Products is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Journal of Natural Products
Vol. 55, No. 7, pp. 1004-1006, July 1992

AJUREPTOSIDE, A NOVEL C_9 IRIDOID GLUCOSIDE FROM *AJUGA REPTANS*

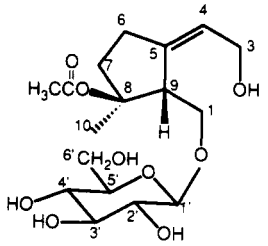
NOBORU SHOJI,* AKEMI UMEYAMA, NOBUYUKI SUNAHARA, and SHIGENOBU ARIHARA

Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Tokushima-shi, Tokushima 770, Japan

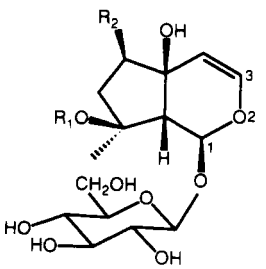
ABSTRACT.—A novel C_9 iridoid glucoside, named ajureptoside [**1**], has been isolated from *Ajuga reptans* (Labiatae) and characterized on the basis of spectroscopic data.

Ajuga reptans L. (Labiatae), indigenous to Europe, is cultivated world-wide as a ground cover plant. Our phytochemical interest in the species led to isolation of a novel C_9 iridoid glucoside, named ajureptoside [**1**], along with three known analogues, reptoside [**2**] (1), harpagide [**3**] (2), and 8-acetylharpagide [**4**] (3). This paper deals with the structural elucidation of compound **1**.

Compound **1**, amorphous, $[\alpha]^{25}D$ $-14.17°$ ($c=4.4$, MeOH), was obtained in a yield of 0.007%. The ir spectrum showed a carbonyl band at 1710 cm^{-1}. The uv spectrum displayed only end absorption. The empirical formula of $C_{17}H_{28}O_9$, established by the $[M+Na]^+$ peak at *m/z* 399 in the fabms spectrum, differs from that of compound **2** ($C_{17}H_{26}O_{10}$) by two hydrogen atoms and one oxygen atom. The ^1H- and ^{13}C-nmr spectra of compound **1** showed one tertiary methyl (δ 1.74, 3H, s; δ 20.1), one acetyl (δ 1.90, 3H, s; δ 22.1 and 170.7), and one double bond (δ 5.91, 1H, t; δ 125.8 and 143.9) as in compound **2**. These values suggested that compound **1** must be a monocyclic C_9 iridoid glucoside. The ^{13}C-nmr spectra proved that a disubstituted double bond (δ 110.3 and 141.1) in compound **2** was replaced by trisubstituted one (δ 125.8 and 143.9) in compound **1**. The lack of an angular hydroxyl in compound **1** explained the reduction of one oxygen functionality compared to compound **2**. An olefinic proton at δ 5.91 was coupled with methylene protons at δ 4.45 and 4.61 on an oxygenated carbon (δ 60.4). The ^{13}C-nmr spectrum showed nine oxygenated carbons, six of which were assignable to the glucose moiety (δ 62.8, 71.6, 75.1, 78.4, 78.5, and 104.6) and the rest to two methylene carbon atoms and one quarternary carbon (δ 60.4, 69.8, and 92.0, respectively). Therefore, one of the two remaining methylene groups should be bonded to the sugar, suggesting that compound **1** should be a ring-opened analogue of compound **2** between C-1 and O-2, as depicted. The structure was confirmed by the HMBC spectrum, in which the methylene protons on an oxygen-bearing carbon (C-1) at δ 69.8 were correlated with three carbons at δ 49.7, 92.0, and 143.9 (C-9, C-8, and C-5, respectively). The geometry of the double



1



2 R_1=Ac, R_2=H
3 R_1=H, R_2=OH
4 R_1=Ac, R_2=OH

bond was determined by nOe difference spectra. On irradiation of the olefinic proton at δ 5.91 (C-4), the methylene protons at δ 2.49 (C-6) adjacent to the double bond were enhanced, and vice versa. The β-glycosidic linkage was derived from the coupling constant of 8.06 Hz. The stereochemistry at the two chiral carbon atoms was determined from the biosynthetic point of view. All the C_9 iridoid glucosides isolated so far have an 8α-methyl group and a 9β-hydrogen in common. In addition, compounds **2–4** co-occurred in the same plant. These facts suggest that compound **1** should have the same stereochemistry. Some nmr nOe difference measurements were obtained on compound **1** to confirm this assumption. The nOe was observed between C-10 methyl protons and C-1 methylene protons, but not between C-10 methyl protons and the C-9 methine proton, supporting α-orientation of the methyl group. In conclusion, the stereostructure shown is assigned to ajureptoside [**1**]. Gelsemiol 1-glucoside, from *Gelsemium sempervirens* L., is the only C_{10} iridoid glucoside ring-opened between C-1 and O-2 reported so far (4). To the best of our knowledge, ajureptoside is the first C_9 iridoid glucoside of the same type.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—*A. reptans* plants were cultivated by Mrs. S. Motoki in her garden and harvested in October. A voucher specimen is on deposit in our laboratory. Si gel F_{254} (Merck, art. 5715) plates were used for tlc. Si gel 60 (Merck, art. 9583) and Sephadex LH-20 (Pharmacia) were used for cc. The solvent system $CHCl_3$-MeOH-H_2O (65:30:4) was employed for Si gel tlc. The following instruments were used: Shimadzu IR-27G photometer (ir), Hitachi 200-20 spectrophotometer (uv), Jasco DIP-180 digital polarimeter (optical rotation), JEOL JMS-HX-100 mass spectrometer (hrms), and JEOL JNM-GX-400FT NMR spectrometer (^1H and ^{13}C nmr).

ISOLATION OF AJUREPTOSIDE [**1**].—Dried whole plants (1.5 kg) were extracted three times with MeOH, and the combined extracts were evaporated to dryness (524.3 g). The residue was partitioned between equal volumes of EtOAc and H_2O. The aqueous layer was separated and extracted three times with *n*-BuOH. The combined extracts were evaporated to dryness to afford a residue (214.7 g). A 100-g sample of the residue was chromatographed on a Si gel (1500 g) column, which was eluted with $CHCl_3$-MeOH-H_2O (25:8:1). Fractions of 500 ml were collected and combined using tlc monitoring. Iridoid mixtures, R_f values of which on Si gel tlc were from 0.5 to 0.2, were repeatedly subjected to cc on Si gel with $CHCl_3$-MeOH-H_2O (25:8:1) and to gel filtration with Sephadex LH-20 and MeOH, to give ajureptoside [**1**] (50 mg) along with reptoside [**2**] (2.2 g), harpagide [**3**] (5.8 g), and 8-acetylharpagide [**4**] (15.6 g). The R_f values of Si gel tlc for compounds **1–4** were 0.47, 0.47, 0.36, and 0.24, respectively.

Ajureptoside [**1**]: amorphous, $[\alpha]^{25}D$ −14.17° (c = 4.4, MeOH), ir ν max (KBr) cm^{-1} 3350, 2950, 1710, 1380, 1250, 1170, 1090, 1030; fabms *m/z* 753, 399, 377, 359, 299; ^1H nmr (C_5D_5N) δ 1.74 (3H, s, H-10), 1.90 (3H, s, Ac), 1.97 (1H, dd, J = 10.25 and 6.23 Hz, H-7), 2.30 (1H, m, $W_{1/2}$ = 16.48 Hz, H-7), 2.49 (2H, m, $W_{1/2}$ = 19.44 Hz, H-6), 3.63 (1H, dd, J = 10.53 and 5.56 Hz, H-1), 3.82 (1H, t, J = 5.56 Hz, H-9), 3.96 (1H, m, $W_{1/2}$ = 20.00 Hz, H-5′), 4.03 (1H, t, J = 8.6 Hz, H-2′), 4.22 (1H, dd, J = 8.79 and 8.69 Hz, H-3′), 4.35 (1H, dd, J = 10.53 and 5.56 Hz, H-1), 4.36 (1H, dd, J = 12.46 and 5.86 Hz, H-6′), 4.44

TABLE 1. ^{13}C-nmr Data of Ajureptoside [**1**] and Reptoside [**2**] in C_5D_5N.[a]

Carbon	Compound	
	1	**2**
C-1	69.8 (t)	94.1 (d)
C-2		
C-3	60.4 (t)	141.1 (d)
C-4	125.8 (d)	110.3 (d)
C-5	143.9 (s)	72.1 (s)
C-6	29.7 (t)	37.2 (t)
C-7	36.2 (t)	38.3 (t)
C-8	92.0 (s)	88.3 (s)
C-9	49.7 (d)	58.1 (d)
C-10	20.1 (q)	21.9 (q)
C-1′	104.6 (d)	98.6 (d)
C-2′	75.1 (d)	74.7 (d)
C-3′	78.4 (d)	78.4 (d)
C-4′	71.6 (d)	71.6 (d)
C-5′	78.5 (d)	78.6 (d)
C-6′	62.8 (t)	62.6 (t)
Ac	22.1 (q)	21.7 (q)
Ac	170.7 (s)	170.9 (s)

[a]Chemical shifts in ppm. Multiplicity in an INEPT experiment.

(1H, dd, J = 11.11 and 6.41 Hz, H-3), 4.54 (1H, dd, J = 12.46 and 8.06 Hz, H-4′), 4.54 (1H, dd, J = 12.46 and 8.06 Hz, H-6′), 4.60 (1H, dd, J = 11.11 and 6.41 Hz, H-3), 4.82 (1H, d, J = 8.06 Hz, H-1′), 5.91 (1H, t, J = 6.41 Hz, H-4); ^{13}C nmr (C_5D_5N) see Table 1.

ACKNOWLEDGMENTS

The authors thank Mrs. S. Motoki for supply of the plant material. We especially thank Dr. Masao Toyota for providing the fabms spectrum.

LITERATURE CITED

1. M. Guiso, R. Marini-Bettolo, and A. Agostini, *Gazz. Chim. Ital.*, **104**, 25 (1974).
2. H. Lichti and A. von Wartburg, *Tetrahedron Lett.*, **15**, 835 (1964).
3. M.L. Scarpati, M. Guiso, and L. Panizzi, *Tetrahedron Lett.*, **39**, 3439 (1965).
4. S.R. Jensen, O. Kirk, B.J. Nielsen, and R. Norrestam, *Phytochemistry*, **26**, 1725 (1987).

Received 30 December 1991