



Diterpenes from *Sideritis argyrea*

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Abstract

The known *ent*-kaurene diterpenes **1–9** and a new *ent*-labdane, *ent*-6 β ,8 α -dihydroxyl-abda-13(16),14-diene (**10**), were isolated from the whole plant of *Sideritis argyrea*. Their structures were elucidated based on one- and two-dimensional NMR techniques and HRMS. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: *Sideritis argyrea*; Diterpenes

1. Introduction

Sideritis species have been used in folk medicine for their anti-inflammatory, antirheumatic, digestive and antimicrobial activities in Turkey as well as in Europe [1,2]. *Sideritis* species are also often used for herbal teas in Turkey. Forty-five *Sideritis* species are known in the flora of Turkey, with 10 subspecies and two varieties. Among them, 34 species, four subspecies and two varieties are endemic [3,4]. We report here on the constituents of *Sideritis argyrea* P.H. Davis (Lamiaceae) [5], collected in the Alanya region of Turkey.

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2. Experimental

2.1. Plant material

Sideritis argyrea whole plant was collected from Alanya (Antalya, Turkey) in June 1995 and identified by Prof. Dr K.H.C. Baser (Eskisehir). A voucher specimen was deposited in the Herbarium of the Faculty of Pharmacy, Anadolu University (ESSE 1072).

2.2. Extraction and isolation

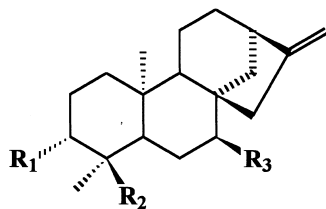
The powdered whole plant (1.5 kg) was extracted successively with hexane and MeOH to give 50 and 65 g of extracts, respectively. A Si-gel CC of the hexane extract was eluted with hexane and gradients of chloroform, acetone and MeOH, provided in succession compounds **1** (20 mg), **5** (2 g), **6** (60 mg), **2** (2.3 g), **3** (2.3 mg), and **10** (35 mg). The Si-gel CC of the MeOH extract provided compounds **4** (372 mg), **7** (25 mg), **8** (43 mg) and **9** (38 mg).

Ent-6 β ,8 α -dihydroxylabda-13(16),14-diene (**10**). UVmax (CHCl₃): 225 nm (ϵ , 9800); IR bands (CHCl₃): 3450 (OH) 3075, 1640 (C=C) 1600, 1040 (C–O), 995, 930, 890 cm⁻¹; ¹H-NMR (200 MHz, CDCl₃): δ 6.37 (1H, *dd*, *J* 11 and 17.5 Hz, H-14), 5.07 (1H, *br d*, *J* 11 Hz, H-15), 5.31 (1H, *br d*, *J* 17.5 Hz, H-15), 5.01 (2H, *br s*, H-16), 4.52 (1H, *br dd*, *J* 3 and 6 Hz, H-6), 1.40 (3H, *s*, Me-17), 1.19 (3H, *s*, Me-18), 1.18 (3H, *s*, Me-19) and 0.99 (3H, *s*, Me-20); ¹³C-NMR (50.34 MHz, CDCl₃): 41.904 (C-1), 18.591 (C-2), 44.143 (C-3), 34.133 (C-4), 62.018 (C-5), 68.846 (C-6), 51.704 (C-7), 73.304 (C-8), 57.031 (C-9), 40.081 (C-10), 24.266 (C-11), 35.078 (C-12), 147.255 (C-13), 138.798 (C-14), 115.601 (C-15), 113.475 (C-16), 25.580 (C-17), 33.245 (C-18), 24.007 (C-19), 16.591 (C-20); EIMS (70 eV) *m/z*: 306.3 (M⁺ 5%), 288.3 [M–H₂O]⁺ (20), 273.3 [M–H₂O–Me]⁺ (26); 255.3 [M–H₂O–Me–H₂O]⁺ (26), 248.2 (4), 227.2 (4), 217.2 (8), 206.2 (33), 191.2 (66), 175.1 (21), 164.2 (52), 153.1 (48), 135.1 (44), 125.2 (42), 120.1 (77), 109.0 (92), 69 (100); HREIMS: 306.2551 (calc. for C₂₀H₃₄O₂: 306.2558).

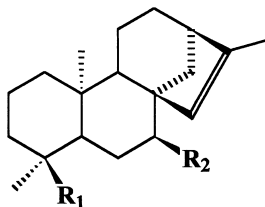
3. Result and discussion

From the whole plant of *S. argyreae*, the known *ent*-kaurenes **1–9** and a new labdane **10** (Fig. 1) were isolated. Their structures were identified as candol B (**1**) [6,7], 7-epicandicandiol (**2**), *ent*-7 α -acetoxy-18-hydroxykaur-16-ene (**3**), foliol (**4**), linearol (**5**), sidol (**6**) [6,8–10], 7-epicandicandiol 18-monoacetate (**7**) [6], siderol (**8**) [11,12], sideridiol (**9**) [11], and *ent*-6 β ,8 α -dihydroxylabda-13(16),14-diene (**10**), based on IR, ¹H- and ¹³C-NMR and MS spectral data. 7-Epicandicandiol, linearol and foliol were isolated in 0.15, 0.13 and 0.025% yields, respectively.

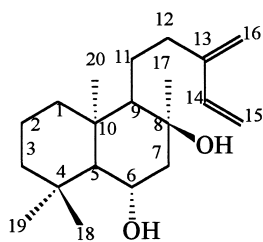
The molecular ion of the new *ent*-labdane **10** was observed at *m/z* 306.2551 in the high resolution mass spectrum, accounting for a molecular formula C₂₀H₃₄O₂. Its IR spectrum showed hydroxyl and olefinic double bond absorptions. In the ¹H-NMR spectrum an A₂B₂X system was observed [12–14] similar to that shown



	R ₁	R ₂	R ₃
1	H	CH ₂ OH	H
2	H	CH ₂ OH	OH
3	H	CH ₂ OH	OAc
4	OH	CH ₂ OH	OH
5	OH	CH ₂ OAc	OH
6	OAc	CH ₂ OH	OH
7	H	CH ₂ OAc	OH



	R ₁	R ₂
8	CH ₂ OH	OAc
9	CH ₂ OH	OH



10

Fig. 1. Structures of Isolated Diterpenes (1–10).

by *ent*-labda13(16),14-diene systems exhibiting signals at δ 6.37 (1H, *dd*, $J = 11$ and 17.5 Hz, H-14), 5.07 (1H, *br d*, $J = 11$ Hz, H-15), 5.31 (1H, *br d*, $J = 17.5$ Hz, H-15) and 5.01 (2H, *br s*, H-16). Four methyl singlets were observed at 0.99, 1.18, 1.19, and 1.40 (each 3H). A methine signal appeared at δ 4.52 (1H, *br dd*, $J = 3$ and 6 Hz) which was assigned to the C-6 proton bearing a secondary hydroxy group. A two-dimensional NOESY experiment indicated α position of the hydroxyl at C-6, which showed interactions between H-6 and H-5 (1.17, *m*) as well as H-6 and H-7 β (2.33, *ddd*, $J = 3, 6$ and 12 Hz). The ^{13}C -NMR spectrum revealed 20 carbon signals consisting of four methyl, eight methylene, four methine and four quaternary carbon atoms. Olefinic signals were observed at δ 115.60, 113.48 (methylenes), 138.79 (methine) and 147.91 (quaternary carbon), which were characteristic for opened ring C carbons of a labdane structure [13,14]. Due to the β effect of the hydroxyl proton at C-6, a C-7 signal appeared at δ 51.70 [13,15]. In a previous study, a C-6 epimeric compound was described [13], which showed H-6 at δ 3.86 (*ddd*, $J = 10, 10$ and 4 Hz). The appearance of a methylene signal at δ 51.70 could be explained assigning to the C-6 secondary hydroxy group in this structure. The HETCOR correlations allowed us to determine unambiguously the protonated carbons of the structure. In the EI-mass spectrum, the loss of two hydroxyl groups as water was observed with fragment ions at m/z 288.3 (M-H₂O) and 255.3 (M-2H₂O-Me). The above spectroscopic data supported that the structure of *ent*-6 β ,8 α -dihydroxylabda-13(16),14-diene (**10**) for the new compound.

Acknowledgements

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References

- [1] Yesilada E, Ezer N. *Phytochemistry* 1996;41:203.
- [2] Quer FP. *Planta Medicinales*. Barcelona, Spain: Ed. Labor, 1962.
- [3] Kirimer N, Kürkçüoğlu M, Özek T, Baser KHC, Tümen G. *Flavours and Fragrance J* 1996;11:315.
- [4] Kirimer N, Kürkçüoğlu M, Baser KHC, Tümen G. A Review, 13th International Congress of Flavours, Fragrances and Essential Oils, 15–19 October, Istanbul, 1995.
- [5] Mill MR. In: Davis PH, editor. *Flora of Turkey and the East Aegean islands*, 7. Edinburg: University Press, 1982:193.
- [6] Gonzalez AG, Fraga BM, Hernandez G, Luis JG. *Phytochemistry* 1973;12:2721.
- [7] Fraga BM, Hernandez MG, Fernandez C, Arteaga JM. *Phytochemistry* 1987;26:775.
- [8] Gonzalez AG, Fraga BM, Hernandez MG, Hanson JR. *Phytochemistry* 1981;20:846.
- [9] Fraga BM, Hernandez MG, Santana JMH, Arteaga JM. *Phytochemistry* 1991;30:913.
- [10] Baser KHC, Bondi ML, Bruno M et al. *Phytochemistry* 1996;43:1293.
- [11] Venturella P, Bellino A, Marino ML. *Phytochemistry* 1978;17:811.
- [12] Algarra J, Garcia-Granados A, De Bruaga AS, De Bruaga JMS. *Phytochemistry* 1983;22:1779.
- [13] Garcia-Granados A, Martinez A, Onorato ME. *Phytochemistry* 1985;24:517.
- [14] Lopez M^aA, Von Carstenne-Lichterfelde C, Rodriguez B. *J Org Chem* 1977;42:1977.
- [15] Garcia-Alvarez MC, Rodriguez B. *Phytochemistry* 1980;19:2405.