

Kaurane Diterpenoids from Three *Sideritis* Species

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Some kaurane diterpenoids were isolated from 3 species of the genus *Sideritis* (Lamiaceae) growing in the Eastern Mediterranean region. *Sideritis libanotica* subsp. *libanotica* contained siderol **2** and sideridiol **3**. *Sideritis erythrantha* var. *erythrantha* yielded sideridiol **3**. *Sideritis perfoliata* gave siderol **2**, sideridiol **3** and sideritriol **4**. The products are known as they occur in another species of *Sideritis* growing in Italy and in other species growing also in Turkey. The products are isolated for the first time from these 3 species. The taxonomic significance of these results is discussed.

Key Words: Lamiaceae, *Sideritis libanotica* subsp. *libanotica*, *Sideritis erythrantha* var. *erythrantha*, *Sideritis perfoliata*, diterpenoids, kaurane.

Introduction

The genus *Sideritis* (Lamiaceae) consists of more than 150 species, occurring mainly in the Eastern and Western Mediterranean regions^{1–3} and has been the subject of wide chemotaxonomic investigations for 40 years, for the study of different types of diterpenoids isolated from the aerial parts.

Many species of the genus have been used for a long time in the traditional folk medicine of several countries^{3–8}, especially in the Middle East, as a herbal tea to treat different illnesses. Laboratory research discovered interesting properties of the extracts of some species^{9–12}. Kaurane diterpenoids have been studied for antimitotic and antitumour activity¹³.

Continuing our research on this genus, we report on the presence of some diterpenoids in the aerial parts of the species *S. erythrantha* var. *erythrantha*, *S. libanotica* subsp. *libanotica* and *S. perfoliata*. *S. erythrantha* var. *erythrantha* and *S. libanotica* subsp. *libanotica* have not previously been investigated for diterpenes. From *S. perfoliata*, collected in southern Turkey near Antalya, only one labdane diterpenoid, *ent*-2 α -hydroxy-13-*epi*-manoyl oxide **1** had been isolated¹⁴.

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Experimental

S. perfoliata L. was collected on 24-7-1997 in the Ehden forest (Northern Lebanon) at 1700 msl; a voucher specimen (leg. and det. N.Arnold *s.n.*, confirm. Th.Raus) is deposited in the Herbarium of the Botanische Garten, Berlin Universitat. *S. libanotica* Labill. subsp. *libanotica* (Hand-Mazz.) Huber-Morath was collected on 8-7-1998 on Mount Kneissé at 1600 msl; a voucher specimen (leg. and det. N.Arnold *s.n.*, confirm. Th.Raus) is deposited in the Herbarium of the Botanische Garten, Berlin Universitat. *S. erythrantha* (Benth) Boiss. et Heldr. var. *erythrantha* was collected in July 1995 in Isparta province, at Sütçüler, Candir-Akcal (fire tower road) at 1675 msl; a voucher specimen is kept at the Herbarium of the Faculty of Pharmacy, Anadolu University in Eskisehir, Turkey, with the number ESSE 11488.

Ground aerial parts of *S. libanotica* subsp. *libanotica* (270 g dwt) were extracted with acetone (3 x 3 L) over 1 week. The crude extract (14.7 g) was adsorbed on 50 g of silica gel (Merck 7734, deactivated with 15% H₂O) and subjected to preparative chromatography over 200 g of the same absorbent on a 3 cm diameter column with 100 mL fractions being collected as follows: eluent petrol (fr. 1-7), petrol/AcOEt 7:3 (fr. 8-15), petrol/AcOEt 1:1 (fr. 16-21). From fractions 12-13, 24 mg of siderol **2** were isolated. From fractions 16-17, 40 mg of sideridiol **3** were obtained.

Identical treatment of aerial parts of *S. erythrantha* (190 g dwt) afforded a crude extract (4.6 g) that was chromatographed in the same way; the fractions eluted with petrol/AcOEt 7:3 yielded 23 mg of sideridiol **3**. Identical treatment of the aerial parts of *S. perfoliata* (500 g dwt) gave a crude extract (26.2 g) that was chromatographed in the same way. Fractions eluted with petrol/AcOEt 7:3 gave 42 mg of siderol **2**. Fractions eluted with petrol/AcOEt 1:1 yielded 55 mg of sideridiol **3**. From fractions eluted with AcOEt 14 mg of sideritriol **4** were isolated.

Products **2-4** were identified by physical and spectroscopic literature data and by direct comparison with pure specimens. Due to the low solubility in CDCl₃ of **4**, and in order to compare its spectroscopic data with those in the literature, the ¹H NMR spectrum was registered on its triacetyl derivative (**5**).

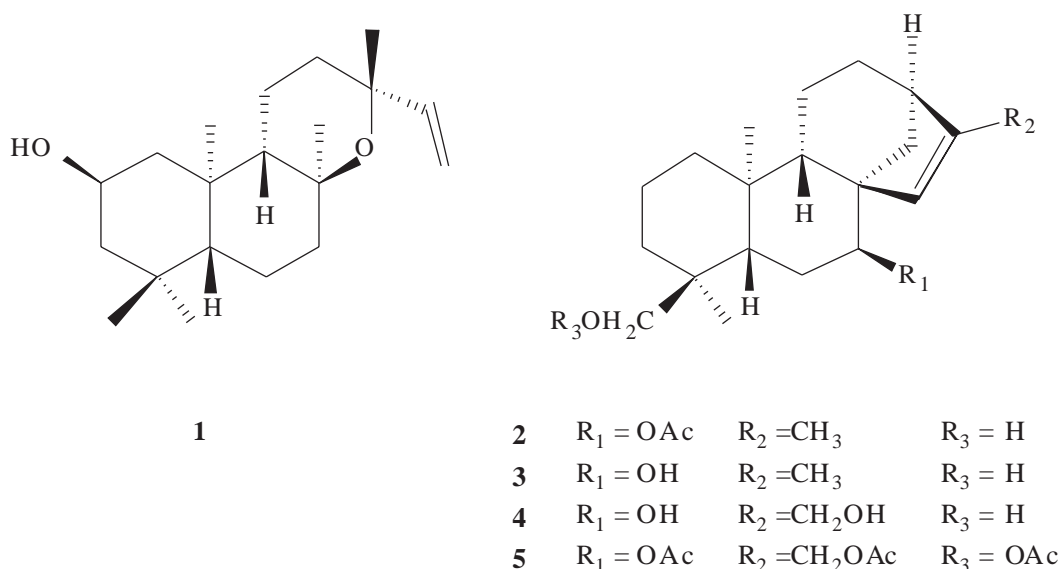
IR spectra were determined with a Perkin Elmer 257 instrument. ¹H spectra were obtained on a Bruker AC-250E. Measurements were obtained from solution in CDCl₃, chemical shifts were referred to TMS set at 0 ppm, and coupling constants are given in hertz. MS were recorded on a Finnigan TSQ70 instrument (70 eV, direct inlet). Flash chromatography was performed using silica gel (Merck, 0.040-0.063 mesh).

Compound **2**, siderol. IR (film) ν_{max} cm⁻¹: 3500, 3060, 1715, 1648, 1265, 820. ¹H NMR δ 0.71 (3H, s, Me-19), 1.08 (3H, s, Me-20), 1.72 (3H, d, $J = 1$, Me-17), 2.08 (3H, s, OAc), 3.03 and 3.35 (each 1H, d, $J = 12$ Hz, H-18), 4.71 (1H, brs, H-7), 5.28 (1H, brs, H-15). EIMS m/z : 346 [M]⁺ (C₂₂H₃₄O₃), 331, 315, 286.

Compound **3**, sideridiol. IR (film) ν_{max} cm⁻¹: 3560, 3460, 3055, 1645, 830. ¹H NMR δ 0.68 (3H, s, Me-19), 1.08 (3H, s, Me-20), 1.72 (3H, d, $J = 1$, Me-17), 2.90 and 3.49 (each 1H, d, $J = 12$ Hz, H-18), 3.60 (1H, brs, H-7), 5.50 (1H, brs, H-15). EIMS m/z : 304 [M]⁺ (C₂₀H₃₂O₂), 289, 286, 273.

Compound **4**, sideritriol. IR (film) ν_{max} cm⁻¹: 3520, 3420, 3380, 3060, 1640, 840. EIMS m/z : 320 [M]⁺ (C₂₀H₃₂O₃), 302, 284, 271, 251.

Compound **5**, triacetylsideritriol. ¹H NMR δ 0.79 (3H, s, Me-19), 1.06 (3H, s, Me-20), 2.03, 2.05, and 2.06 (each 3H, s, OAc), 3.63 and 3.70 (each 1H, d, $J = 12$ Hz, H-18), 4.55 and 4.65 (each 1H, d, $J = 14$ Hz, H-17), 4.73 (1H, brs, H-7), 5.56 (1H, brs, H-15).



Results and Discussion

The acetone extract of *S. libanotica* subsp. *libanotica* yielded the known¹⁵ kaurane diterpenoids siderol **2** and sideridiol **3**. No other products were isolated.

From the acetone extract of *S. erythrantha* var. *erythrantha* only the kaurane derivative sideridiol **3** was obtained.

In the acetone extract of *S. perfoliata* 3 kauranes occurred: siderol **2**, sideridiol **3** and sideritriol¹⁶ **4**. No other diterpenoid was detected; in particular the manoyl oxide **1** was absent.

The 3 species investigated here belong to the section Empedoclia. The 3 kaurane diterpenoids had been isolated previously¹⁵⁻¹⁶ from the species *S. italica* (formerly *S. sicula*) growing in Sicily and also belonging to the section Empedoclia. As for the chemotaxonomic significance, these results confirm that the species occurring in the Eastern Mediterranean region contain almost exclusively diterpenes having the kaurane skeleton. The case of *S. perfoliata* is worthy of remark: whereas the material collected in southern Turkey was reported¹⁴ to contain only 1 diterpene, a labdane derivative, our material harvested in Lebanon yielded 3 kaurane derivatives, with total absence of the labdane product. This can probably be attributed to the different geographic origin of the plant.

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