

AN ENT-KAURANE FROM *SIDERITIS HUBER-MORATHII*

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**Key Word Index**—*Sideritis huber-morathii*; *S. caesarea*; Labiatae; ent-kaurane diterpenoids; 3,7,18-triacetyl-foliol.

**Abstract**—A new ent-kaurane diterpenoid, 3,7,18-triacetyl-foliol, was isolated from *Sideritis huber-morathii*, together with known diterpenes. Two known ent-kauranoids were found in *S. caesarea*. Copyright © 1996 Elsevier Science Ltd

## INTRODUCTION

The genus *Sideritis* numbers more than 120 species [1], occurring mainly in the Mediterranean area. In the last 30 years several species were found to contain diterpenoids and flavonoids. We report here on the investigation of two species growing in Turkey, namely *S. huber-morathii* Greuter and Burdet [2] and the new species *S. caesarea* Duman, Aytac et Baser [3].

## RESULTS AND DISCUSSION

From an acetone extract of the aerial parts of *S. huber-morathii*, we isolated five known ent-kaurane diterpenoids: siderol (1) [4], sideridiol (2) [4], sidol (3) [5], linearol (4) [5] and candicandiol (5) [6, 7]. Two other derivatives were also isolated: 3,7,18-triacetyl-foliol (6) and the 3,18-acetonide of foliol (7).

The triacetyl derivative 6, previously known only as a synthetic product [5], has now been isolated as a natural product. Its structure was confirmed by spectroscopic methods and by its preparation through acetylation of 3 and 4.

Compound 7 could be an extraction artifact; however, not even traces of free foliol (8) were detected in the extract of *S. huber-morathii*. Thus, doubt remains if 7 is an artefact or a natural product.

From the acetone extract of the aerial parts of *S. caesarea* only two known ent-kaurane derivatives were obtained, 1 and epoxy-siderol (9) [8].

Only the  $^{13}\text{C}$  NMR spectra of 2 [9], 4 [10] and triacetyl-foliol [10] were reported previously. We present the spectra of 1, 3, 5, 9 and 7 in Table 1.

We report in Table 2 also the complete assignments (by HETCOR correlations) of the protons and carbon atoms of 4. The chemical shifts of the  $^{13}\text{C}$  spectrum of 4 are in general agreement with those reported, except that the previous [10] assignments to C-4 and C-5 are reversed, as proved by DEPT pulse frequency determination.

The data from our spectrum of 2 were in general agreement with those reported previously [9]; however, the proposed assignments of C-5 and C-14 must be reversed, as proved by DEPT pulse frequency determination. So the C-5 methine resonates at  $\delta$  44.1 instead of  $\delta$  39.2, and the C-14 methylene resonates at  $\delta$  39.9 instead of  $\delta$  44.1.

The finding of these compounds is in agreement with previous reports that *Sideritis* species from the eastern Mediterranean area contain almost exclusively ent-kaurane diterpenoids, whereas the species from the western Mediterranean area and Canary Islands also contain labdane, atisane, trachilobane and beyerane diterpenoids beside ent-kaurane derivatives.

## EXPERIMENTAL

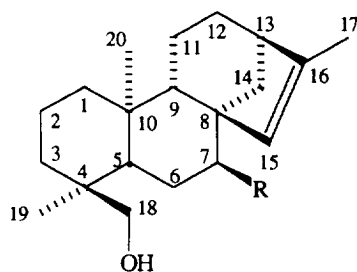
**General.** NMR ( $\text{CDCl}_3$ ): 250 MHz ( $^1\text{H}$ ) and 62.5 MHz ( $^{13}\text{C}$ ); chemical shifts are relative to residual  $\text{CHCl}_3$  ( $\delta$  7.25) and  $\text{CDCl}_3$  signals (77.0 ppm); multiplicities of  $^{13}\text{C}$  were determined by DEPT. EIMS: 70 eV. IR: nujol mull. Mps: uncorr. Petrol refers to the 50°–70° fr. Known products were identified by conventional methods (physical and spectral data, comparison with authentic samples).

**Plant material.** *Sideritis huber-morathii* Greuter et Burdet was collected from Hatay province, road from Vayladagi to Senkoy in August 1993. *S. caesarea*

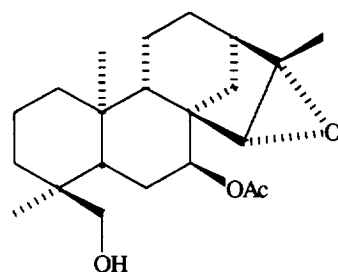
‡Author to whom correspondence should be addressed.

Table 1.  $^{13}\text{C}$  NMR chemical shifts of siderol (1) sidol (3), candicandiol (5), epoxy-siderol (9) and foliol acetone (7)

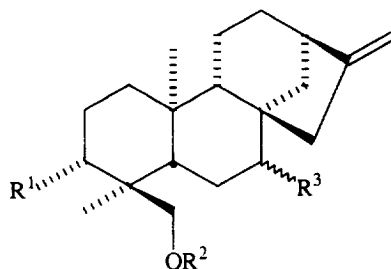
C	1	3	5	9	7
1	42.0	38.4	39.7	39.8	39.7
2	18.3	23.4	17.9	17.6	24.4
3	35.2	77.0	38.3	35.1	78.3
4	37.0	41.7	37.1	36.9	42.9
5	44.5	37.3	38.6	39.4	42.1
6	23.5	26.6	26.9	23.1	27.4
7	78.2	74.5	77.3	75.4	77.5
8	51.8	48.0	48.2	46.6	49.0
9	44.8	50.1	50.5	46.5	51.0
10	39.1	38.5	38.9	38.8	36.9
11	17.9	17.9	17.8	17.8	18.3
12	24.7	33.6	33.6	27.2	34.2
13	39.8	43.6	43.7	38.9	44.4
14	39.8	38.2	34.9	30.9	38.9
15	129.8	45.0	45.2	63.5	45.8
16	143.8	155.0	155.1	78.4	155.2
17	15.3	103.5	103.4	17.4	104.5
18	71.4	64.0	70.6	71.1	73.3
19	17.3	12.6	17.7	17.5	13.0
20	17.7	17.9	17.7	14.4	19.4
Ac-Me	21.4	21.2	—	21.4	—
Ac-CO	170.8	171.8	—	178.8	—
Acet-C	—	—	—	—	99.66
Acet-Me	—	—	—	—	30.53–20.04



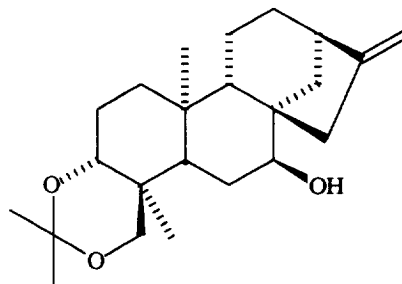
1 R = OAc  
2 R = OH



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3 R<sup>1</sup> = OAc; R<sup>2</sup> = H; R<sup>3</sup> =  $\beta$ -OH  
4 R<sup>1</sup> = OH; R<sup>2</sup> = Ac; R<sup>3</sup> =  $\beta$ -OH  
5 R<sup>1</sup> = H; R<sup>2</sup> = H; R<sup>3</sup> =  $\alpha$ -OH  
6 R<sup>1</sup> = OAc; R<sup>2</sup> = Ac; R<sup>3</sup> =  $\beta$ -AC  
8 R<sup>1</sup> = OH; R<sup>2</sup> = H; R<sup>3</sup> =  $\beta$ -OH



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Table 2. HETCOR correlation H/C of linearol (4)

C	$\delta_{\text{H}}$	$\delta_{\text{C}}$
1	1.16*, 1.89*	38.2 t
2	1.70*	26.0 t
3 $\beta$	3.58 dd (4, 9)	71.5 d
4	—	41.2 s
5	1.82 t (9)	37.9 d
6	1.55*, 1.80*	26.9 t
7 $\alpha$	3.56 t (3.8)	76.3 d
8	—	47.6 s
9	1.48*	49.9 d
10	—	38.4 s
11	1.60*	17.5 t
12	1.53*, 1.73*	33.2 t
13	2.68 s	43.4 d
14	1.03 m, 1.87*	38.0 t
15	2.27 s	44.7 t
16	—	154.9 s
17	4.80 d (9)	103.0 t
18	3.97 q (12)	65.8 t
Me-19	0.76 s	11.6 q
Me-20	1.08 s	17.6 q
Me-Ac	2.09 s	20.5 q
CO-Ac	—	172.2 s

J in parentheses.

\*Overlapped signals.

Duman, Aytac et Baser was collected from Sariz, province of Kayseri in August 1992. Voucher specimens are deposited at the Herbarium of the Faculty of Pharmacy of Anadolu University at Eskisehir, Turkey (ESSE 10089 and 9571, resp.).

*Extraction of S. huber-morathii.* Aerial parts (750 g) were dried, finely powdered and extracted with Me<sub>2</sub>CO (3 × 51) at room temp. for 1 week. The crude gum (39 g) was adsorbed on silica gel (50 g, Merck No. 7734, deactivated with 15% H<sub>2</sub>O) and subjected to CC over 400 g of the same adsorbent, 250 ml frs being collected as follows: frs 1–6 (petrol), 7–13 (petrol–EtOAc, 7:3), 14–21 (petrol–EtOAc, 1:1), 22–35 (petrol–EtOAc, 3:7), 36–43 (petrol–EtOAc, 1:4), 44–50 (EtOAc), 51–60 (EtOAc–MeOH, 9:1).

Frs 9–10 were rechromatographed over silica gel (petrol–EtOAc, 9:1) and by radial chromatography (Chromatotron: silica gel Merck No. 7749; petrol–EtOAc, 9:1) to give 15 mg **6**. Frs 11–12 were subjected to CC (petrol–EtOAc, 7:3) giving a fr. containing 2 products which were dissolved in petrol–EtOAc (7:3) and, on refrigeration (–20°), deposited 10 mg **1**. The mother liquors were purified by radial chromatography (petrol–EtOAc, 7:3) to give 5 mg more of **1** and 4 mg **7** as an amorphous solid. Rechromatography (petrol–EtOAc, 7:3) of frs 13–16 gave a mixt. of three compounds which were separated by radial chromatography (CHCl<sub>3</sub>–MeOH 97:3) to give 70 mg **5** 20 mg **2** and 30 mg **3**. Frs 26–35, dissolved in petrol–EtOAc (1:1), on refrigeration (–20°), deposited ca 1 g **4**.

*Extraction of S. caesarea.* Aerial parts (1100 g) were, dried, finely powdered and extracted with Me<sub>2</sub>CO (3 × 61) at room temp. for 1 week. The crude extract (11 g) was adsorbed on silica gel (20 g) as above and subjected to CC over 200 g of the same adsorbent, 250 ml frs being collected as follows: frs 1–5 (petrol), 6–15 (petrol–EtOAc, 4:1), 16–26 (petrol–EtOAc, 7:3), 27–34 (petrol–EtOAc, 3:2), 35–43 (petrol–EtOAc, 1:1), 44–51 (petrol–EtOAc, 3:7), 52–64 (EtOAc), 65–72 (EtOAc–MeOH, 9:1). Frs 18–21 were purified by CC (petrol–EtOAc, 7:3) to give 2 frs which were subjected to radial chromatography (CHCl<sub>3</sub>) yielding 25 mg **1** and 20 mg **9**.

*3,7,18-Triacetyl-foliol (6).* Mp, [ $\alpha$ ]<sub>D</sub> and <sup>1</sup>H NMR spectrum identical with those reported previously [5] for the synthetic product. Also, the <sup>13</sup>C NMR spectrum is identical with the reported one [10].

*Acetylation of 3 and 4.* Compounds **3** and **4** (10 mg each) were treated separately with 1 ml pyridine and 1.5 ml Ac<sub>2</sub>O at room temp. for 3 hr. Usual work-up yielded 8 mg each of product **6**.

*3,18-Acetonide of foliol (7).* Amorphous solid, no definite mp. <sup>13</sup>C NMR: Table 1.

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