Phytochemistry, Vol. 22, No. 12, pp. 2779–2781, 1983.
Printed in Great Britain.

0031–9422/83 \$3.00 + 0.00

DITERPENOIDS FROM *SIDERITIS HIRSUTA* SUBSP. *NIVALIS**

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(*Received* 4 *March* 1983)

Key Word Index—*Sideritis hirsuta* subsp. *nivalis*; Labiatae; new *ent*-13(16),14-labdadiene derivative; ^{13}C NMR data.

Abstract—From *Sideritis hirsuta* subsp. *nivalis* several known *ent*-kaurenes, *ent*-13-epi-manoyl oxides and *ent*-labdadienes have been isolated. In addition *ent*-8α-hydroxyladba-13(16),14-diene, a new natural product, has been isolated, its structure being confirmed by high resolution ^{13}C NMR spectroscopy.

INTRODUCTION

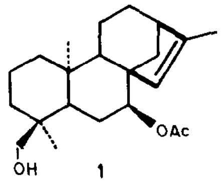
In our systematic examination of the diterpenes of the endemic *Sideritis* sp. growing in Andalusia we have examined the aerial parts of *Sideritis hirsuta* L. subsp. *nivalis*. This plant grows in areas of south-east Spain (Sierra de Baza, Granada). Traditional folk medicine has ascribed anti-inflammatory and vulneraria properties to this plant, and it is used as a home remedy for gastrointestinal disturbances.

The *Sideritis hirsuta* has been studied long ago, and only *ent*-kaur-15-enes and *ent*-kaur-16-enes were found [1]. Elsewhere, there are numerous plants under the denomination of *S. hirsuta* 'grex', which are under botanical revision, and we are making a phytochemical study of them.

RESULTS AND DISCUSSION

Several diterpenoids isolated from *Sideritis hirsuta* subsp. *nivalis* are previously known *ent*-kaurenic compounds: *ent*-7α-acetoxy-18-hydroxykaur-15-ene (siderol, **1**), *ent*-3β,7α-dihydroxy-18-acetoxykaur-16-ene (linearol, **2**), *ent*-7α,18-dihydroxy-3β-acetoxy-kaur-16-ene (sidol, **3**), *ent*-3β,7α,15-trihydroxy-18-acetoxykaur-18-ene (18-acetilleucanthol, **4**), *ent*-3β,7α,18-trihydroxykaur-16-ene (foliol, **5**) and *ent*-3β,7α,15β,18-tetrahydroxykaur-16-ene (leucanthol, **6**). In addition, *ent*-3β-hydroxy-13-epi-manoyl oxide (ribenol, **7**) and *ent*-8α,18-dihydroxylabda-13(16),14-diene (6-deoxyandalusol, **8**) have been isolated. The physical and spectroscopic properties of products **1**–**8** are identical with those reported previously for them [1–5]. Ribenol (**7**) and 6-deoxyandalusol (**8**) are rare products, isolated only from *Sideritis* sp. growing in the Canary Island (compound **7**) [6], *S. arborescens* (compound **8**) [5] and *S. varoi* (compounds **7** and **8**) [7].

Another product, compound **9**, isolated from *S. hirsuta* subsp. *nivalis* had an MW of 290, in accordance with a molecular formula $C_{20}H_{34}O$. The IR spectrum of this substance showed hydroxyl (3450 cm^{-1}) and conjugated double bond (1600 cm^{-1}) absorbtions. The UV spectrum showed absorption at λ_{max}^{hexane} 226 nm (ε 11 000) characteristic of a conjugated double bond. The ^{1}H NMR spectrum of **9** (see Experimental) showed an A_2B_2X system similar to that shown by 6-deoxyandalusol (**8**), and four methyl singlet signals at δ 1.10 (3H), 0.85 (3H) and 0.80 (6H). These data suggest for product **9** the structure of 8-hydroxylabda-13(16),14-diene. Moreover, biogenetic considerations suggest the *ent*-configuration for product **9** and an equatorial configuration for the tertiary hydroxyl group at C-8, this last point being confirmed by high resolution ^{13}C NMR spectroscopy of product **9**.



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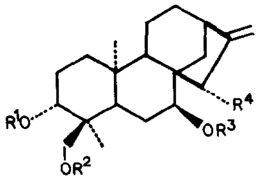

	R^1	R^2	R^3	R^4
2	H	Ac	H	H
3	Ac	H	H	H
4	H	Ac	H	OH
5	H	H	H	H
6	H	H	H	OH

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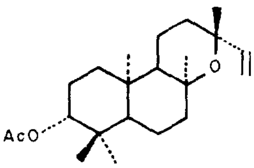
*Part 16 in the series "Terpenic Components of Spanish Labiatae". For part 15 see García-Granados, A., Martinez, A., Onorato, E, and Socorro, O. *Phytochemistry* (in press).



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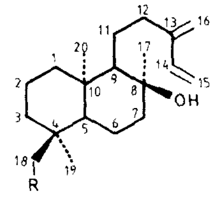
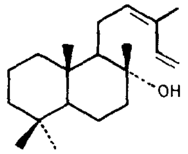


8 R = OH

9 R = H



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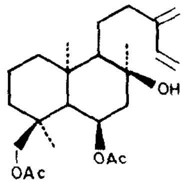

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The chemical shifts for the carbons of the rings of product **9** are consistent with those published for products with similar ring structures (**10**) [8]. In addition, the chemical shifts of the chain carbons are also in accordance for products with a similar chain (i.e. product **11** [9]). Thus, we conclude that product **9** must be *ent*-8α-hydroxylabda-13(16),14-diene, a new natural product.

EXPERIMENTAL

Mps were determined in a Kofler apparatus and are uncorr. ^{1}H NMR spectra were measured at 60 MHz ($CDCl_3$ soln with TMS as int. standard). ^{13}C NMR spectra were determined at 90.6 MHz on a Bruker WM-360 spectrometer, also in $CDCl_3$ soln (which also provided the lock signal) with TMS added as internal reference. Assignments of ^{13}C NMR chemical shifts were made with the aid of broad-band proton decoupling and SFORD experiments, setting the decoupler frequency in the middle of the proton range in the former and 2 ppm to the right of the TMS in the latter. Silica gel Merck 7729 (less than 0.08 mm) was used for CC. Plant material was collected in June 1980 on Sierra de Baza (Granada) and voucher specimens were deposited in the Herbarium of the Faculty of Pharmacy (University of Granada).

Extraction and isolation of the diterpenoids. Dried and finely powdered plants of *Sideritis hirsuta* L. subsp. *nivalis* (1.5 kg) were extracted with hexane (4 l.) in a Soxhlet and processed as indicated in ref. [7], to give 28 g of a yellowish residue, 15 g of which was chromatographed on a silica gel column and eluted with increasing polarity CH_2Cl_2–Me_2CO mixtures. The homogeneous fractions were repeatedly chromatographed on 10% $AgNO_3$–silica gel columns and eluted with CH_2Cl_2–Me_2CO mixtures of increasing polarity, yielding the following compounds in order of elution: *ent*-8α-hydroxylabda-13(16),14-diene (400 mg, **9**), ribenol (950 mg, **7**), siderol (160 mg, **1**), linearol (900 mg, **2**), sidol (700 mg, **3**), 6-deoxiandalusol (510 mg, **8**), 18-acetylleucanthol (900 mg, **4**), foliol (200 mg, **5**) and leucanthol (100 mg, **6**), identified as the diacetone derivative.

ent-8-*Hydroxylabda*-13(16),14-*diene* (**9**). Mp 50–51° C. $[\alpha]_D^{20} = -0.49°$ (*c* 1, $CHCl_3$). UV λ_{max}^{hexane} nm: 226 (ε 11 000). IR ν_{max}^{KBr} cm^{-1}: 3370, 2040, 1600, 990, 915, 890. ^{1}H NMR (60 MHz): δ 6.31 (1H, *dd*, part X of an A_2B_2X system, $J_{AX} + J_{BX} = 29$ Hz, H-14), 4.80–5.50 (4H, part A_2B_2 of an A_2B_2X system, 2H-15 and 2H-16), 1.10 (3H), 0.85 (3H) and 0.80 (6H) (singlet signals of Me groups at C-17, C-18, C-19 and C-20). ^{13}C NMR: see Table 1. MS: 290 $[M]^+$, 271 $[M-17]^+$. (Found: C, 82.53; H, 11.91. Requires: C, 82.70; H, 11.80%.)

Table 1. ^{13}C NMR chemical shifts of product **9** and reference compounds **10** and **11**

Carbon No.	**9**	**10***	**11†**
1	39.76	40.2	—
2	18.50	18.6	—
3	42.03	41.9	—
4	33.29	33.1	—
5	56.19	56.2	—
6	20.60	20.3	—
7	44.62	44.0	—
8	74.28	74.3	—
9	61.28	62.2	—
10	39.17	39.0	—
11	24.75	—	24.5
12	35.13	—	34.7
13	147.47	—	146.9
14	138.82	—	138.5
15	115.60	—	115.6
16	113.51	—	113.5
17	24.05	24.4	—
18	33.43	33.5	—
19	31.52	21.6	—
20	15.50	15.5	—

All ^{13}C chemical shifts are given in ppm relative to TMS.

*See reference [8].

†See reference [9].

Acknowledgements—We thank Dr. O. Socorro (Departamento de Botánica, Universidad de Granada) for the identification of plant material. We are deeply indebted to Dr. J. Santoro (Instituto de Estructura de la Materia, C.S.I.C., Madrid) for ^{13}C NMR spectra. This work was supported by a grant from Comisión Asesora de Investigación Científica y Técnica.

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