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DITERPENES FROM *SIDERITIS DENDROCHAHORRA* AND *S. CYSTOSIPHON*

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Key Word Index *Sideritis dendrochahorra*; *S. cystosiphon*; Lamiaceae; diterpenes; sidendrodiol; epicandicandiol; ^{13}C NMR.

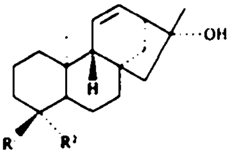
Abstract –A new diterpene, sidendrodiol (ent-16β,18-dihydroxykaur-11-ene), has been isolated from *Sideritis dendrochahorra*. From *S. cystosiphon* two new diterpenic esters, the 18-palmitate of epicandicandiol and the diacetate of epicandicandiol have been identified. The ^{13}C NMR spectra of ent-16β-hydroxykaur-11-ene and ent-16β-hydroxykaurane derivatives have been assigned.

INTRODUCTION

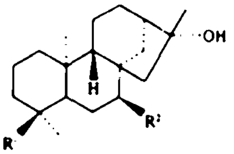
The genus *Sideritis* is represented in the Canary Islands by more than 20 species. We have been interested in their phytochemistry for several years [1–4]. In continuation of this work we have now investigated the aerial parts of *S. cystosiphon* Svent and completed an early study of *S. dendrochahorra* Bolle [2]. Both species are endemic to the island of Tenerife.

RESULTS AND DISCUSSION

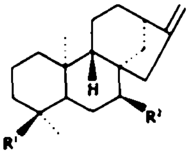
From *S. dendrochahorra* we isolated a new diterpene sidendrodiol (**1**), as its acetate (**2**), by acetylation and purification of several chromatographic fractions of the extract. The IR spectrum of **2** has typical bands for hydroxyls and acetyl groups, and the ^{1}H NMR spectrum shows signals of three methyl groups at δ0.78, 0.92 and 1.29. The chemical shift of the latter indicated that this methyl must be on a carbon united to an oxygen function, in this case a tertiary hydroxyl group. A pair of doublets centred at δ3.62 and 3.83 are characteristic of an equatorial CH$_2$OAc at C-4 in a polycyclic diterpene, without other oxygenated functions or double bonds in ring A [5]. This spectrum also shows a pair of double doublets at δ5.50 and 5.89, revealing the presence in the molecule of two adjacent vinyl hydrogens, each of these being coupled with a methynic proton. These spectral data



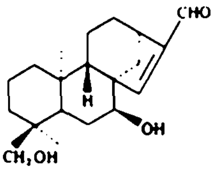
1 R^1 = CH$_2$OH R^2 = Me
2 R^1 = CH$_2$OAc R^2 = Me
3 R^1 = Me R^2 = CO$_2$Me



4 R^1 = CH$_2$OH R^2 = H
5 R^1 = CH$_2$OAc R^2 = H
6 R^1 = Me R^2 = H
7 R^1 = Me R^2 = OH



8 R^1 = CH$_2$OH R^2 = H
9 R^1 = CH$_2$OH R^2 = OAc
10 R^1 = CH$_2$OH R^2 = OH
11 R^1 = CH$_2$OAc R^2 = OAc
12 R^1 = CH$_2$O—CO—(CH$_2$)$_{14}$—CH$_3$ R^2 = OH



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permitted the assignment to this compound of structure **2** and to the natural substance the structure ent-16β,18-dihydroxykaur-11-ene (**1**). **1** could be obtained by alkaline hydrolysis of **2**. The ^{13}C NMR spectra of **1** and **2** are assigned in Table 1 together with those of another compound **3** with the same skeleton isolated from *Helianthus angustifolius* [6].

Hydrogenation of sidendrodiol (**1**) in the presence of platinum oxide as catalyst gave **4**, identical with vierol, a compound isolated from *Sideritis canariensis* [7]. In Table 2 the ^{13}C NMR data of vierol monoacetate (**5**) [7], ent-kauranol (**6**) [8] and powerol (**7**) [7] are given. The chemical shifts were assigned to individual carbon atoms by their multiplicities and by comparison with the spectra of ent-16β-hydroxykaur-11-ene derivatives (Table 1) and ent-18-hydroxykaur-16-ene derivatives [9].

In an earlier study of *S. dendrochahorra* the known terpenoids squalene, ent-13-epi-manoyloxide, α- and β-amyrin, β-sitosterol, the 7β-monoacetates of epicandicandiol and trachinodiol, oleanolic and ursolic acids, candidiol, candicandiol and epicandicandiol were isolated [2].

It is interesting to note, from the biosynthetic point of view, that ent-16β-hydroxykaur-11-ene derivatives are rare in nature and have only been found in plants from which diterpenes with a trachylobane skeleton have also been isolated [6, 10]. Thus sidendrodiol (**1**) can be formed by enzymatic abstraction of a hydrogen at C-11 in **14**, assisting the cleavage of the cyclopropane ring and forming the carbenium ion **15**, which after neutralization with water gives **1**. Compound **14** was not found in *S. dendrochahorra* but it may also be a biosynthetic precursor of trachinodiol monoacetate (**16**), obtained with **1** from this species.

Table 1. ^{13}C NMR spectral data (50.32 MHz) of ent-16β-hydroxykaur-11-ene derivatives

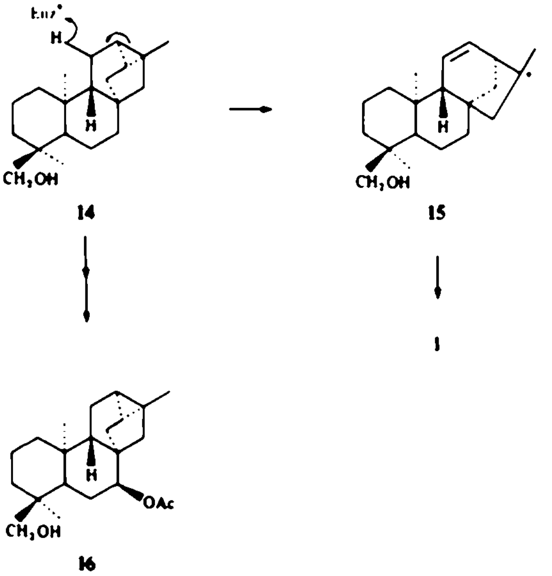
C	1	2	3
1	39.40	39.23	39.9
2	17.96	17.78	19.1
3	35.50	35.96	38.0
4	37.96	36.62	44.0
5	48.30	49.15	51.2*
6	20.19	20.33	21.9
7	41.05	40.97	41.4
8	43.45	43.57	43.3
9	62.35	62.26	61.3
10	38.43	38.42	38.8
11	127.29	127.11	127.1
12	132.63	132.73	132.7
13	50.43	50.37	50.1*
14	34.68	34.56	34.5
15	59.29	59.13	58.6
16	83.94	83.96	83.8
17	25.97	25.94	25.8
18	72.39	73.25	28.7
19	18.01	17.97	178.1
20	17.70	17.60	15.3

*These values can be interchanged.

Table 2. ^{13}C NMR spectral data (50.32 MHz) of ent-16β-hydroxykaurane derivatives

C	5	6	7
1	39.96	40.62	40.30
2	17.94	18.81	18.74
3	35.96	42.34	42.15
4	36.62	33.44	32.86
5	50.30*	56.48	50.30*
6	20.46	20.63	27.76
7	41.78	42.30	77.57
8	45.38	45.59	48.90
9	56.99	57.19	46.37
10	39.33	39.60	39.31
11	18.13	18.18	17.60
12	37.78	37.93	36.60
13	49.13*	49.30	49.50*
14	27.01	27.13	27.35
15	58.12	58.43	54.25
16	79.36	79.46	79.39
17	24.59	24.61	24.59
18	73.22	33.76	33.49
19	17.50	21.74	21.70
20	18.28	17.94	17.72

*These values can be interchanged.



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From *S. cystosiphon* we have isolated the known diterpenes candol B (**8**) [11], the 7β-monoacetate of epicandicandiol (**9**) [11], epicandicandiol (**10**) [12, 13], candidiol [12] and episinfernal (**13**) [4], and the new ones, the diacetate of epicandicandiol (**11**) and the 18-palmitate of epicandicandiol (**12**). The structure of **11** was determined by comparison of its spectral data with those of a synthetic sample obtained by acetylation of epicandicandiol (**10**) [12, 13] or of its monoacetate (**9**) [11]. The mass spectrum of epicandicandiol 18-palmitate (**12**) is in accordance with the formula $C_{36}H_{62}O_3$. This spectrum also shows two fragments at *m/z* 524 and 286, formed from the [M]$^+$ by loss of water and palmitic acid, respectively. The ^{1}H NMR spectrum of **12** shows the resonances of the two angular methyl groups (δ0.82 and 1.06), of the linear chain of the methylene groups (δ1.25, *s*), of the esterified hydroxymethylene group at C-18 (δ3.49 and 4.06, each *d*, *J* = 11 Hz), of the proton geminal to the alcohol group at C-7 (δ3.57, *br s*) and of the exocyclic double bond (δ4.81, *br s*).

EXPERIMENTAL

Mps are uncorr.; NMR: $CDCl_3$, except where otherwise indicated; IR: $CHCl_3$; MS: 70 eV (probe); column and dry column chromatography silica gel 0.063–0.2 mm.

Isolation of sidendrodiol (**1**) *from* S. dendrochahorra. Air-dried aerial parts of the plant (8 kg), collected near Taganana (Island of Tenerife) in May, were used for this work. A voucher has been deposited at the Herbarium of the Instituto Canario de Investigaciones Agrarias (ORT 29242).

A general description of the procedure to isolate the terpenoid substances of species of the genus *Sideritis* has been published previously [2]. In this way several terpenoids were isolated and identified as squalene, ent-13-epi-manoyloxide, α- and β-amyrin, β-sitosterol, the 7β-monoacetates of epicandicandiol and trachinodiol, oleanolic and ursolic acids, candidiol, candicandiol and epicandicandiol [2]. Sidendrodiol (**1**) (40 mg) was obtained in acetate form (**2**) by acetylation of several fractions that contain it and the 7β-monoacetate of trachinodiol [2]. The diacetate of sidendrodiol was also formed, in poor yield, in this acetylation.

Sidendrodiol monoacetate (**2**). Mp 139 142°; $[M-H_2O]^+$ at 328.2399, $C_{22}H_{32}O$ requires 328.2401; ^1H NMR (200 MHz): δ0.78, 0.92 and 1.29 (each 3H, *s*), 2.05 (3H, *s*), 2.17 (1H, *dd*, *J* = 7 and 3 Hz, H-13), 3.62 and 3.83 (each 1H, *d*, *J* = 11 Hz, H-18), 5.50 (1H, *dd*, *J* = 10 and 4 Hz, H-11), 5.89 (1H, *br dd*, *J* = 10 and 7 Hz, H-12); EIMS *m/z* (rel. int.): 328 [M − 18] (2), 313 (1), 288 (68), 273 (2), 255 (4), 253 (3), 228 (30), 213 (15), 199 (9).

Sidendrodiol (**1**). Mp 116–118°; $[M-H_2O]^+$ at 286.2305, $C_{20}H_{30}O$ requires 286.2294; ^1H NMR (200 MHz): δ0.72, 0.94 and 1.29 (each 3H, *s*), 2.17 (1H, *dd*, *J* = 7 and 3 Hz, H-13), 3.08 and 3.40 (each 1H, *d*, *J* = 11 Hz, H-18), 5.51 (1H, *dd*, *J* = 10 and 4 Hz, H-11), 5.89 (1H, *br dd*, *J* = 10 and 7 Hz, H-12); EIMS *m/z* (rel. int.): 286 $[M-18]^+$ (2), 274 (2), 273 (7), 256 (3), 255 (7), 247 (17), 246 (85), 231 (6), 215 (17), 199 (3).

Hydrogenation of **1**. **1** (5 mg) was dissolved in EtOAc (5 ml) and hydrogenated for 36 hr over PtO_2 (4 mg) at room temp. and atm. press. In this way **4** was obtained, identical with the natural compound vierol (IR, MS and ^1H NMR data).

Isolation of the terpenoid from S. cystosiphon. Air-dried aerial parts of the plant (1.1 kg), collected near Tamaimo (Santiago del Teide, Tenerife) (voucher ORT 28644) in May, were treated as described for other species of this genus [2]. In this way several terpenoids were obtained: the 18-palmitate of epicandicandiol (**12**) (8 mg), glutinol (40 mg), candol B (**8**) (110 mg), epicandicandiol diacetate (**11**) (45 mg), β-sitosterol, 7β-monoacetate of epicandicandiol (**9**) (1.55 g), epicandicandiol (**10**) (1.6 g), candidiol (60 mg) and episinfernal (**13**) (90 mg).

18-*Palmitate of epicandicandiol* (**12**). ^1H NMR (200 MHz) δ: 0.82 and 1.06 (each 3H, *s*, Me), 1.25 (*s*, nCH_2), 3.49 and 4.06 (each 1H, *d*, *J* = 11 Hz, H-18), 3.57 (1H, *br s*, H-7), 4.81 (2H, *br s*, H-17). EIMS *m/z* (rel. int.): 542 $[M]^+$ (2), 524 (5), 509 (1), 496 (1), 328 (2), 286 (8), 270 (9), 268 (18), 255 (62), 253 (28), 239 (12), 225 (9).

Epicandicandiol diacetate (**11**). ^1H NMR (200 MHz) δ: 0.80 and 1.05 (each 3H, *s*, Me), 2.02 (6H, *s*, 2Ac), 3.63 and 3.70 (each 1H, *d*, *J* = 11 Hz, H-18), 4.76 (3H, *br*, H-7 and H-17). EIMS *m/z* (rel. int.): 328 $[M-60]^+$ (6), 313 (1), 286 (2), 268 (21), 255 (10), 253 (10), 239 (6).

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REFERENCES

1. Gonzalez, A. G., Bretón, J. L., Fraga, B. M. and Luis, J. G. (1971) *Tetrahedron Letters* 3097.
2. Gonzalez, A. G., Fraga, B. M., Hernandez, M. G., Luis, J. G. and Larruga, F. (1979) *Biochem. Syst. Ecol.* **7**, 115.
3. Fernandez, C., Fraga, B. M., Gonzalez, A. G., Hernandez, M. G., Hanson, J. R. and Hitchcock, P. B. (1985) *Phytochemistry* **24**, 188.
4. Fernandez, C., Fraga, B. M. and Hernandez, M. G. (1986) *Phytochemistry* **25**, 2825.
5. Jefferies, P. R. and Retallack, R. W. (1968) *Aust. J. Chem.* **21**, 2085.
6. Ohno, N., Gershenzon, J., Neuman, P. and Mabry, T. J. (1981) *Phytochemistry* **20**, 2393.
7. Gonzalez, A. G., Fraga, B. M., Hernandez, M. G. and Luis, J. G. (1973) *Tetrahedron* **29**, 561.
8. Hanson, J. R. (1963) *J. Chem. Soc. C* 5061.
9. Gonzalez, A. G., Fraga, B. M., Hernandez, M. G. and Hanson, J. R. (1981) *Phytochemistry* **20**, 846.
10. Herz, W., Govindan, S. V. and Watanabe, K. (1982) *Phytochemistry* **21**, 946.
11. Gonzalez, A. G., Fraga, B. M., Hernandez, M. G. and Luis, J. G. (1973) *Phytochemistry* **12**, 2721.
12. Rodriguez-Gonzalez, B., Valverde, S. and Rocha, J. M. (1970) *Anal. Quim.* **66**, 503.
13. Piozzi, F., Venturella, P., Bellino, A., Paternostro, M. P., Rodriguez, B. and Valverde, S. (1971) *Chem. Ind.* 962.