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HISPANOLONE, A NEW FURANODITERPENE

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Hispanolone, a new furanoditerpene occurring in Ballota hispanica (Labiatae), is attributed the structure [I] with normal labdane skeleton.

Continuing our examination of Mediterranean Labiatae and specially of the genus Ballota, we have started with the investigation of Ballota hispanica Neck. ex Nym. (= Ballota hirsuta Benth.) growing in Spain. We refer here on the structure of a new furanoditerpene, hispanolone, occurring in this species.

Hispanolone is a crystalline product, m.p. 142-144° (from pet. ether-AcOEt), $[\alpha]_D^{22°}$ - 17.6° ($CHCl_3$; c, 0.33). Elemental analysis and MS agree with the $C_{20}H_{30}O_3$ formula. The IR spectrum shows bands at 3450 (OH), 1690 (C=O) and 875 cm^{-1} (furan). The occurrence of a β-substituted furan ring is supported by the typical NMR signals (100 MHz, $CDCl_3$) at 6.22, 7.18 and 7.30 δ; other signals include three singlets of tertiary methyl groups at 0.87, 0.90 and 1.17 δ, a doublet for a secondary methyl at 1.11 δ (J 6.5 Hz) coupled with a quartet of a methine proton at 2.72 δ; this signal collapses into a singlet on irradiation at 1.11 δ; a complex pattern for two protons (AB part of an ABX system) occurs in the 2.27-2.59 δ region.

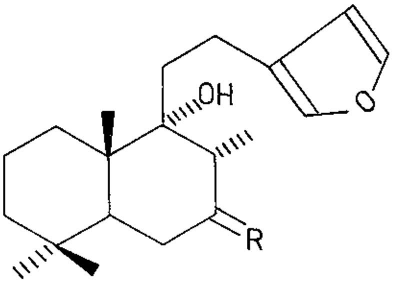
The mass spectrum of hispanolone shows prominent peaks at 318 (M^+), 194, 123, 109, 95 and 81 m/e.

As other species of the same genus (B.nigra subsp. foetida and B.rupestris) contain[1-3] furanoditerpenes similar to marrubiin and marrubenol but carrying an additional keto group on position C-7, the above reported data suggest the structure and the stereochemistry depicted in [I] for hispanolone.

The configuration of the secondary methyl on C-8 must be equatorial, as supported by the coupling constant of the doublet (J 6.5 Hz): an axial methyl group should have a larger value (J 8 Hz)[4]. The determination[5] of CD on hispanolone shows a negative Cotton effect at 287 nm, $\Delta\varepsilon_{287} = -0.98°$, $[\theta]_{287} = -3210°$ (EtOH; c, 0.259); this result is better consistent with an equatorial 8α-CH_3 than with an axial 8β-CH_3 configuration: compare the data reported[4] for product [II], $[\theta]_{290} = -1820°$ (MeOH) and for product [III], $[\theta]_{289} = -6570°$ (MeOH).

The reduction of hispanolone with $NaBH_4$ in EtOH-dioxane (1:1) solution gives a mixture of the two epimeric alcohols, separable by preparative TLC. The first product (60% yield) has m.p. 128-130° (from acetone-hexane), $[\alpha]_D^{27°}$ - 6.6° ($CHCl_3$; c, 0.21); MS 320 m/e (M^+); IR 3300 cm^{-1} (broad, OH), no C=O absorption; NMR (100 MHz, $CDCl_3$) 3.84 δ (four lines, $J_{ea'} = J_{ea''} = J_{ee} = 3.5$ Hz, equatorial 7β-H): hence the product has the structure [IV]. The second product (40% yield) has m.p. 102-105° (from hexane), $[\alpha]_D^{27°}$ + 13.8° ($CHCl_3$; c, 0.18); MS 320 m/e (M^+); IR 3450 cm^{-1} (OH), no C=O absorption; NMR (100 MHz, $CDCl_3$) 3.43 δ (six lines, $J_{aa'} = J_{aa''} = 10.5$ Hz, $J_{ae} = 5$ Hz, axial 7α-H): hence the product has structure [V].

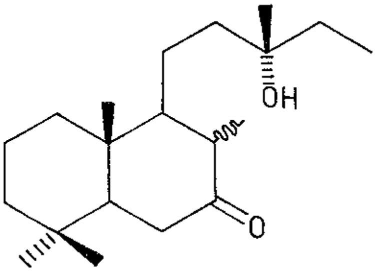
It is interesting to remark that the $[\alpha]_D$ values and the 7-H pattern of hispanolone and its reduction products closely parallel the values and the pattern found for villenolone [VI], a diterpene



[I] R = O

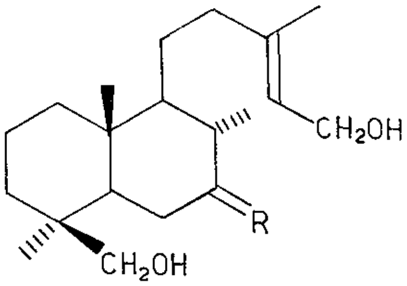
[IV] R = 7α-OH, 7β-H

[V] R = 7α-H, 7β-OH



[II] 8α-CH_3

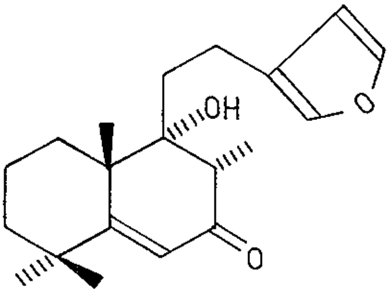
[III] 8β-CH_3



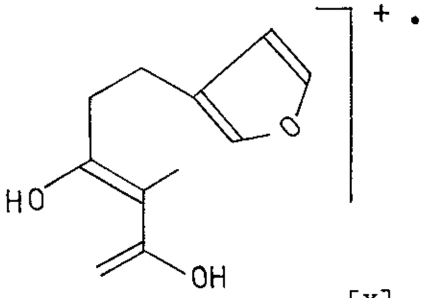
[VI] R = O

[VII] R = 7α-OH, 7β-H

[VIII] R = 7α-H, 7β-OH



[IX]



[X]

occurring in Sideritis chamaedryfolia (Labiatae), and for its reduction products, whose structures have been fully elucidated[6] as [VII] and [VIII].

As the absolute configuration of villenolone was proved[6] to be normal, these data bring further support to assign hispanolone the absolute configuration [I].

Table 1

[α] values for hispanolone, villenolone and their derivatives

hispanolone [I]	[α]	- 17.6°
7α-OH alcohol [IV]		- 6.6°
7β-OH alcohol [V]		+ 13.8°
villenolone [VI]		- 4.1°
7α-OH alcohol [VII]		- 10.4°
7β-OH alcohol [VIII]		+ 22.9°

A product with structure [I] had been obtained by Li/NH_3 reduction[7] of "Leonotis compound Y" [IX], a diterpenoid occurring in Leonotis leonurus (Labiatae). The data of this reduction product, m.p. 145-146° (from benzene-hexane) and $[\alpha]_D^{20°}$ - 19° ($CHCl_3$; c, 0.96), are in good agreement with those of hispanolone. As this product had been directly transformed[7] into isoambreinolide, the absolute stereochemistry of hispanolone [I] is therefore proved.

We wish to draw the attention on the very strong peak occurring in the MS of hispanolone at 194 m/e: it has to be attributed to the $C_{11}H_{14}O_3$ fragment [X] arising from the retro Diels-Alder cleavage of the $\Delta_{7,8}$ enolic form of [I].

All the products reported gave satisfactory elemental analyses.

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