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 spe-
cially of the genus Ballota, we have started with the investiga-
tion of Ballota hispanica Neck. ex Nym. (= Ballota hirsuta Benth.)
growing in Spain. We refer here on the structure of a new furano-
diterpene, hispanolone, occurring in this species.

Hispanolone is a crystalline product, m.p. 142–144° (from pet.
ether-AcOEt), $[\alpha]_D^{22}\circ = 17.6°$ (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 occur-
rence of a $\beta$-substituted furan ring is supported by the typical
NMR signals (100 MHz, CDCl$_3$) at 6.22, 7.18 and 7.30 $\delta$; other sig-
nals include three singlets of tertiary methyl groups at 0.87,
0.90 and 1.17 $\delta$, a doublet for a secondary methyl at 1.11 $\delta$ (J
6.5 Hz) coupled with a quartet of a methine proton at 2.72 $\delta$;
this signal collapses into a singlet on irradiation at 1.11 $\delta$;
a complex pattern for two protons (AB part of an ABX system) oc-
curs in the 2.27–2.59 $\delta$ 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*) contain¹⁻³ 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 determination⁵ of CD on hispanolone shows a negative Cotton effect at 287 nm, $\Delta$ε₂₈⁷ = -0.98°, [θ]₂₈⁷ = -3210° (EtOH; c, 0.259); this result is better consistent with an equatorial 8α-CH₃ than with an axial 8β-CH₃ configuration: compare the data reported⁴ for product [II], $[\theta]_{290}^{20}= -1820°$ (MeOH) and for product [III], $[\theta]_{289}^{20} = -6570°$ (MeOH).

The reduction of hispanolone with NaBH₄ 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), $[\alpha]_{D}^{27}= 6.6°$ (CHCl₃; c, 0.21); MS 320 m/e (M⁺); IR 3300 cm⁻¹ (broad, OH), no C=O absorption; NMR (100 MHz, CDCl₃) 3.84 δ (four lines, $J_{aa}= J_{aa''}= J_{ee} = 3.5$ Hz, equatorial 7b-H): hence the product has the structure [IV]. The second product (40% yield) has m.p. 102-105° (from hexane), $[\alpha]_{D}^{27}= +13.8°$ (CHCl₃; c, 0.18); MS 320 m/e (M⁺); IR 3450 cm⁻¹ (OH), no C=O absorption; NMR (100 MHz, CDCl₃) 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] \( R = 0 \)

[IV] \( R = 7\alpha\text{-OH, }7\beta\text{-H} \)

[V] \( R = 7\alpha\text{-H, }7\beta\text{-OH} \)

[VI] \( R = 0 \)

[VII] \( R = 7\alpha\text{-OH, }7\beta\text{-H} \)

[VIII] \( R = 7\alpha\text{-H, }7\beta\text{-OH} \)

[II] \( 8\alpha\text{-CH}_3 \)

[III] \( 8\beta\text{-CH}_3 \)

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

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

Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>[α]</th>
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</thead>
<tbody>
<tr>
<td>hispanolone [I]</td>
<td>-17.6°</td>
</tr>
<tr>
<td>7α-OH alcohol [IV]</td>
<td>-6.6°</td>
</tr>
<tr>
<td>7β-OH alcohol [V]</td>
<td>+13.8°</td>
</tr>
<tr>
<td>villenolone [VI]</td>
<td>-4.1°</td>
</tr>
<tr>
<td>7α-OH alcohol [VII]</td>
<td>-10.4°</td>
</tr>
<tr>
<td>7β-OH alcohol [VIII]</td>
<td>+22.9°</td>
</tr>
</tbody>
</table>

A product with structure [I] had been obtained by Li/NH₃ reduction 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 [α]D° = 19° (CHCl₃; c, 0.96), are in good agreement with those of hispanolone. As this product had been directly transformed 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 C₁₁H₁₄O₃ fragment [X] arising from the retro Diels-Alder cleavage of the Δ₇,8 enolic form of [I].

All the products reported gave satisfactory elemental analyses.

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References

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