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NEW FURANOID DITERPENES FROM TEUCRIUM GNAPHALODES L'HER.

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The chemistry of the diterpene lactones extracted from several Teucrium species (Labiatae) has received a great deal of attention in the last few years. We wish to report here our latest results on some products isolated from T.gnaphalodes L'Hér., a Spanish species.

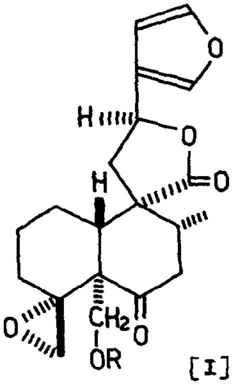
To gnaphalin and 19-acetylgnaphalin, two of the diterpenoids extracted from T.gnaphalodes, we attributed the structures [I] and [II] respectively on the basis of the evidence reported below.

Gnaphalin [I], $C_{20}H_{24}O_6$, has m.p. 172°-174°, $[\alpha]_D^{22°}$ +46.6° ($CHCl_3$; c, 0.51). MS: m/e 360 (M^+), 185 (base peak), 134, 96, 95, 81. IR (KBr): 3575 cm^{-1} (OH), 1756 (γ-lactone), 1720 (ketone), 880 (furan ring). ^1H-NMR ($CDCl_3$, 100 MHz): δ 1.07 (3H, d, J 6.5 Hz, s.CH_3), 3.73 (1H, m, epoxide proton), 4.36 and 5.02 (2H, q_{AB}, J 12 Hz, $C\underline{H}_2OH$), 5.46 (1H, t, J 8.5 Hz, H-12), 6.40 (1H, m, β-furan proton), 7.49 (2H, m, α-furan protons).

19-Acetylgnaphalin [II], $C_{22}H_{26}O_7$, has m.p. 227°-229°, $[\alpha]_D^{22°}$ +82° ($CHCl_3$; c, 0.315)(Found, C% 65.42, H% 6.62; Calcd, C% 65.66, H% 6.66). Its ^1H-NMR spectrum is quite similar to the spectrum of gnaphalin, except that a singlet at 2.07 δ occurs (3H, CH_3COO) and the AB quartet of CH_2OAc is shifted downfield to 5.05 and 5.49 δ. MS: m/e 402 (M^+), 330, 311 (base peak), 95, 81. IR (KBr): 1748 cm^{-1} (γ--lactone), 1766 and 1255 (acetate), 1715 (ketone), 880 (furan ring).

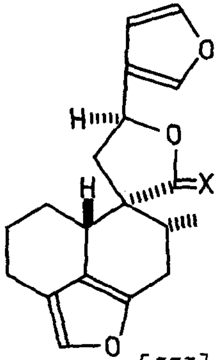
Treatment of gnaphalin [I] with Ac_2O-pyridine gave 19-acetylgnaphalin [II], identical with the natural product described above.

CD measurements on [I] and [II] showed the occurrence of negative Cotton effects, $\Delta\varepsilon_{299}$ -0.89 for [I] and $\Delta\varepsilon_{298.5}$ -0.48 for [II]. This behaviour agrees with a 6-keto structure with normal (i.e. 5α, 10β) configuration, as observed for fruticolone[1] and for ajugarins[2] derivatives.



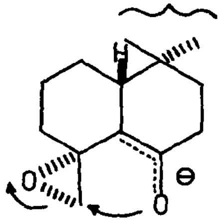
[I] R = H

[II] R = Ac

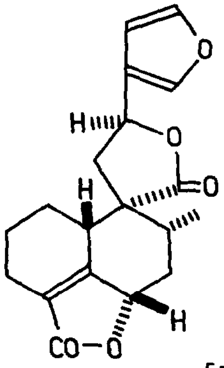


[III] X = O

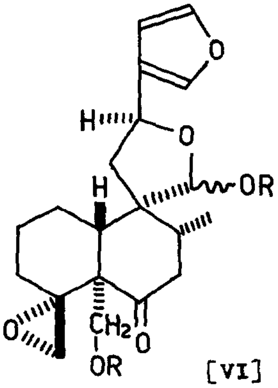
[VIII] X = H,OH



[IV]

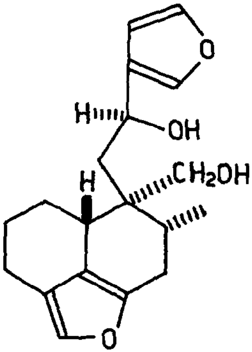


[V]



[VI] R = Ac

[VII] R = H



[IX]

When [II] was treated with methanolic OH$^-$, a $C_{19}H_{20}O_4$ product was obtained; the same substance was formed in quantitative yield merely by standing a solution of [I] over silica gel. It has m.p. 126°-127°, $[\alpha]_D^{27°}$ +115° ($CHCl_3$; c, 0.59). MS: m/e 312 (M^+), 185 (base peak), 134, 96. ^{1}H-NMR ($CDCl_3$, 60 MHz): δ 1.16 (3H, d, J 6.5 Hz, s.CH_3), 5.42 (1H,t, J 8.5 Hz, H-12), 6.38 (1H, m, β-furan proton), 7.02 (1H, broad s, α-furan proton), 7.40 (2H, m, α-furan protons). IR (nujol): 1745 cm^{-1} (γ-lactone), 875 (furan ring). These data support the structure [III], arising from a retroaldolic cleavage with loss of C-19 as formaldehyde and from an attack of the hydrid ion [IV] on C-18 with opening of the epoxide ring and dehydration; the occurrence of a keto group at C-6 is a necessary condition for this reaction. A similar furan synthesis was reported previously[3].

The data of [III] are in agreement with those reported recently for montanin-A, described[4] as a natural nor-diterpene occurring in Teucrium montanum L. The photo-oxidative transformation of montanin-A into teucvin[5] [V] was repeated on our product and gave [V]. This correlation confirmed the absolute configuration of [I] and [II] inferred on the basis of CD results.

A third diterpenoid was isolated from <u>T.gnaphalodes</u>, i.e. gnaphalidin [VI], $C_{24}H_{30}O_8$, m.p. 132°, $[\alpha]_D^{20°}$ -36.5° ($CHCl_3$; c, 0.14). Its MS showed prominent peaks at m/e 446 (M^+), 386, 344, 313, 95, 94 (base peak), 81. The IR spectrum lacked the γ-lactone absorption: bands occurred at 1735, 1720, 1230 cm^{-1} (acetates), 1710 (ketone), 870 (furan ring). The ^{1}H-NMR spectrum ($CDCl_3$, 60 MHz) had signals at δ 1.29 (3H, d, J 6.5 Hz, $\underline{s}.CH_3$), 1.99 and 2.11 (3H each, s, CH_3COO), 3.34 (1H, m, epoxide proton), 4.69 (2H, pseudo s, $C\underline{H}_2OAc$), 4.94 (1H, t, J 8.5 Hz, H-12), 6.29 (1H, s, H-20), 6.40 (1H, m, β-furan proton), 7.32 (2H, m, α-furan protons).

Treatment of [VI] with methanolic OH^- gave two products, identified as the deacetylated diterpene [VII] and the furanized nor-diterpene [VIII]; the former was transformed quantitatively into the latter merely by percolation through neutral Al_2O_3.

Product [VII], m.p. 182°, has formula $C_{20}H_{26}O_6$. MS: m/e 362 (M^+), 314, 185, 134 (base peak). IR (nujol): 3300 cm^{-1} (OH), 1690 (ketone), 875 (furan ring). ^{1}H-NMR (acetone-d_6, 60 MHz): 3.07 and 4.41 δ (2H, q_{AB}, J 12 Hz, $C\underline{H}_2OH$), 4.83 (1H, m, H-12), 4.98 (1H, s, H-20).

Product [VIII], oily, has formula $C_{19}H_{22}O_4$. MS: m/e 314 (M^+), 296, 185, 134. IR (nujol): 3350 cm^{-1} (OH), 875 (furan ring). The ^{1}H-NMR spectrum ($CDCl_3$, 60 MHz) showed signals at δ 4.88 (1H, m, H-12), 5.03 (1H, s, H-20), 6.42 (1H, m, β-furan proton), 6.90 (1H, s, α-furan proton), 7.36 (2H, m, α-furan protons).

The correlation of gnaphalidin [VI] with gnaphalin [I] was performed as follows. Reduction of either [III] or [VIII] with $(\underline{i}.C_4H_9)_2AlH$ in toluene gave the same diol [IX], oily, formula $C_{19}H_{24}O_4$. MS: m/e 316 (M^+), 285, 204, 134. ^{1}H-NMR ($CDCl_3$, 60 MHz): δ 3.47 (2H, q, J 12 Hz, $C\underline{H}_2OH$), 4.88 (1H, dd, J 9 Hz and 2.5 Hz, H-12), 6.30 (1H, m, β-furan proton), 6.87 (1H, s, α-furan proton), 7.21 (2H, m, α-furan protons).

The easy transformation of 6-keto-19-hydroxy-4,18-epoxy-clerodanes into furanized nor-clerodanes, and the possibility of photo-oxidation of the latter into lactones, suggests the mechanism of formation depicted below.

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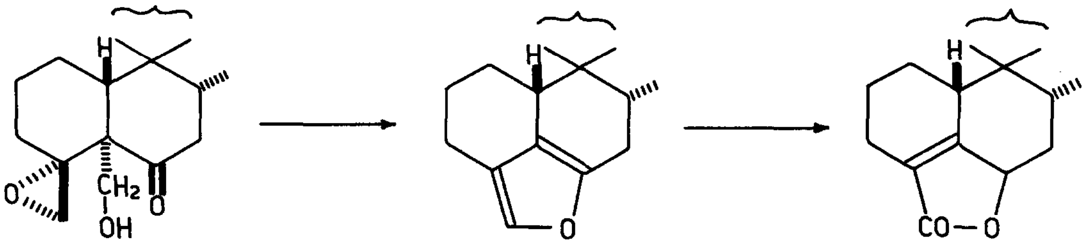

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