

STRUCTURE AND STEREOCHEMISTRY OF THALICSILINE, A NEW ANTIINFLAMMATORY C_{20} -
DITERPENOID ALKALOID FROM THALICTRUM SESSILE.

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Abstract - Antiinflammatory thalicsiline, the first ajaconine-type alkaloid bearing an oxygen function at C_6 , has been isolated from Thalictrum sessile, and its structure and stereochemistry have been established by spectral data and a single-crystal X-ray analysis.

We reported recently on the isolation of thalicsessine (1), a spiradine-type C_{20} -diterpenoid alkaloid from the roots of Thalictrum sessile Hayata.¹ Further investigations on bioactive compounds with novel structures from this same plant have now resulted in the isolation of a new ajaconine-type² C_{20} -diterpenoid alkaloid, thalicsiline (2), which was characterized on the basis of spectral data in conjunction with a single-crystal X-ray analysis. Thalicsiline demonstrated significant antiinflammatory activity in rats.³

Thalicsiline (2) [$C_{24}H_{35}NO_5$, m/z 417.2481 (M^+), mp 183-186 °C, $[\alpha]_D^{20}$ -11.4° (c 0.1, MeOH) was isolated in 0.00021% yield and showed ir bands (Nujol) at 3540 (OH), 1720 and 1240 (acetyl), and 1100 cm^{-1} (ether). The presence of an ajaconine-type [C(7)-C(20) carbinolamine ether linkage] skeleton in 2 was indicated by comparison of the ^{13}C nmr chemical shift values⁴ with literature data.^{5,6} The 1H nmr spectrum (400 MHz, $CDCl_3$) of 2 is in accord with the assigned structure. Presence of an oxazolidine ring system was revealed by a five-proton multiplet pattern between

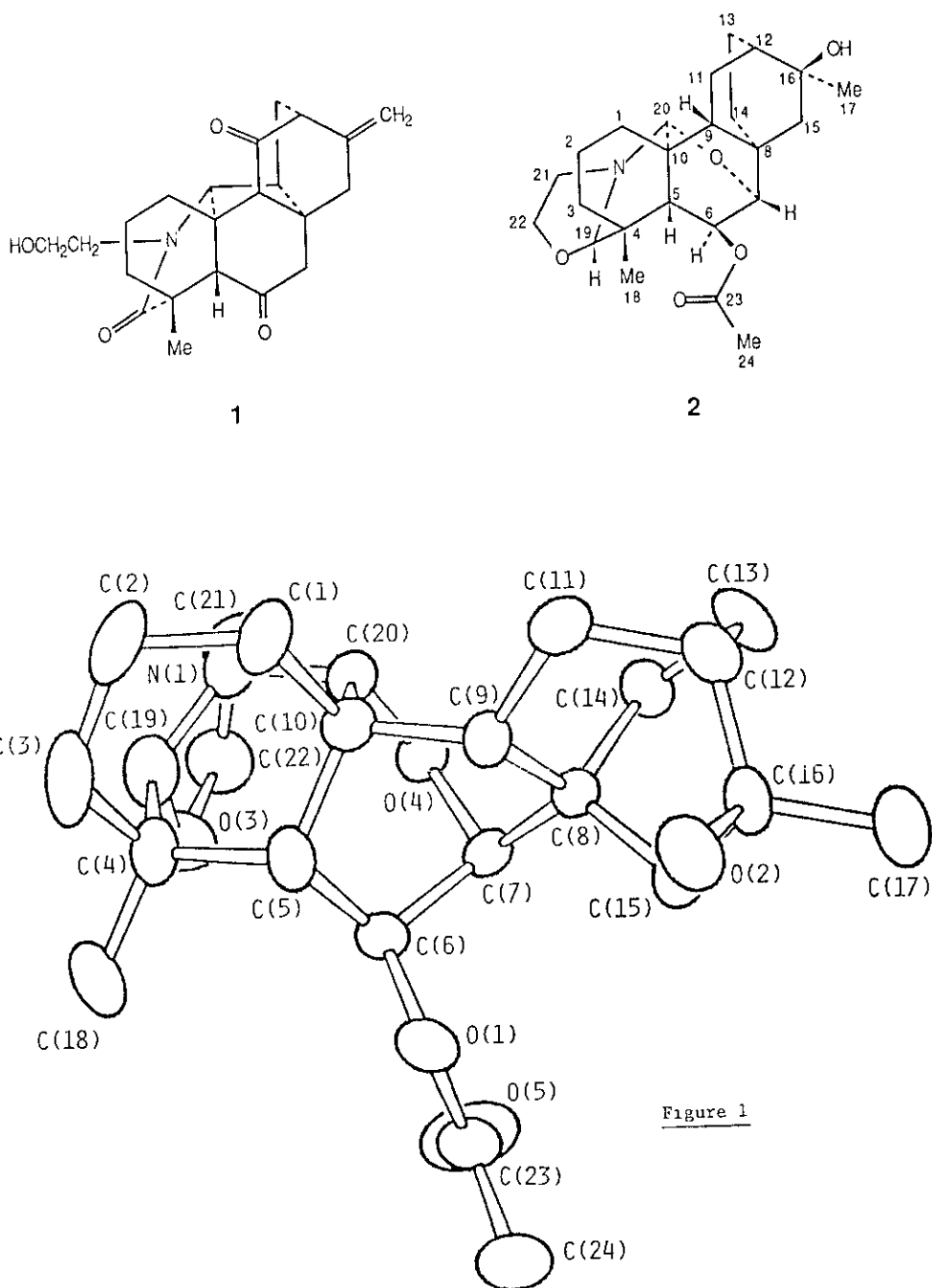


Figure 1

δ3.00 and 4.10, in which the proton at C(19) occurs as a distinct epimeric pair of signals at δ4.11 [(S)] and 3.86 [(R)] in a ratio of ca. 1:3, a phenomenon which is also common in the spirasine series.⁷ Other epimeric pairs, a doublet of doublets ($J = 2.40$ Hz) at δ5.32 and 5.67 as well as singlets at δ2.05 and 2.06, in approximately the same ratio of 1:3 for each, were assigned to H-C(6) and MeCOO-C(6), respectively. The rest of the characteristic pairs of signals (all ca. 1:3) was assigned as follows: δ4.82 and 4.58 [H-C(20)], 1.31 and 1.30 [Me-C(16)], and 0.94 and 1.11 [Me-C(4)].

The complete structure and relative stereochemistry of **2** were defined unequivocally by a single-crystal X-ray analysis. Crystal data. $C_{24}H_{35}NO_5$ (**2**), $M = 417.55$, monoclinic, space group $P2_1$, $a = 10.000(3)$, $b = 12.983(2)$, $c = 8.879(2)$ Å, $\beta = 107.86(2)^\circ$, $V = 1097.2$ Å³, $Z = 2$, $D_c = 1.264$ g cm⁻³, μ (Cu-K α radiation, $\lambda = 1.5418$ Å) = 6.7 cm⁻¹. Intensity data ($+h$, $+k$, $\pm l$; 2051 independent forms) from a crystal of dimensions 0.12 x 0.14 x 0.05 mm were recorded on an Enraf-Nonius CAD-4 diffractometer (Cu-K α radiation, incident-beam graphite monochromator; ω -2 θ scans, $\theta_{max} = 67^\circ$). The crystal structure was solved by direct methods (MULTAN11/82). Hydrogen atoms were located in a difference Fourier synthesis. Full-matrix least-squares refinement (Enraf-Nonius SDP) of non-hydrogen atom positional and anisotropic thermal parameters, with hydrogen atoms included at their calculated positions, converged at $R = 0.042$ [$R_w = 0.055$, $w = 1/\sigma^2 (F_o)$] over 1284 reflections with $I > 3.0\sigma(I)$.⁸ A view of the solid-state conformation is provided in Figure 1. In the crystals, molecules of **2** related by unit-translation along c are associated by an O-H . . . O hydrogen bond [O(26) . . . O(29) 2.924(5) Å].

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4. ^{13}C Nmr (δ) data (25.0 MHz; CDCl_3) for 2: C(1) 40.54, C(2) 22.70, C(3) 47.21, C(4) 35.16, C(5) 52.18, C(6) 70.79, C(7) 70.91, C(8) 36.27, C(9) 42.53, C(10) 35.28, C(11) 29.02, C(12) 38.26, C(13) 26.68, C(14) 23.52, C(15) 20.24, C(16) 73.83, C(17) 30.19, C(18) 22.58, C(19) 94.60, C(20) 85.59, C(21) 51.01, C(22) 63.30, C(23) 169.72, C(24) 21.41.
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