THE STRUCTURE OF TAMARISCOL, A NEW PACIFIGORGIANE

SESQUITERPENOID ALCOHOL FROM THE LIVERWORT FRULLANIA TAMARISCI

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Summary  Tamariscol, a new sesquiterpenoid alcohol with the rare pacifigorgiane carbon skeleton, is a major constituent of the liverwort Frullania tamarisci, collected in Scotland.  It has been assigned the structure and relative configuration (1) on the basis of $^{13}$C (including 2D INADEQUATE) and $^{1}$H nmr spectroscopic evidence.

The liverwort Frullania tamarisci is associated with the incidence of allergenic contact dermatitis among lumberjacks.[1]  The main active principle is the sesquiterpenoid lactone (-)-frullanolide (2).  Several other sesquiterpenoid lactones have also been reported from the same source.[1]  Reinvestigation of F. tamarisci collected in various locations in Scotland, mainly from roadside dry-stone walls, has revealed the presence, in addition to the known lactones frullanolide (2) (0.030%), γ-cyclocostunolide (0.005%) and costunolide (0.002%), of a new major constituent, tamariscol, a pungent oil (0.032% of dried plant material), which has been assigned structure (1).  The only other recorded example of a sesquiterpenoid with this carbon skeleton is the ichthyotoxin pacifigorgiol (3) from the gorgonian Pacifigorgia adamsii.[2]

Tamariscol (1) $[\alpha]_D$ + 19.7 (c, 1.1 in CHCl$_3$), $\nu_{max}$ (CCl$_4$) 3620 cm$^{-1}$, m/z 222.1991 (C$_{15}$H$_{26}$O requires m/z 222.1984) shows in its nmr spectra (CDCl$_3$ solution) a trisubstituted double bond [$\delta_H$ 5.07 (sept., J 1.5 Hz, H-10); $\delta_C$ 121.9 (d, C-10) and 136.4 (s, C-11)], a tertiary alcohol [$\delta_C$ 79.0 (s, C-2)], two vinyl methyl groups [$\delta_H$ 1.88 (d, J 1.5 Hz, 3H-13) and 1.75 (d, J 1.5 Hz, 3H-12); $\delta_C$ 28.5 (C-12) and 20.3 (C-13)], two secondary methyl groups [$\delta_H$ 0.92 (d, J. 6.6 Hz, 3H-15) and 0.87 (d, J 6.6 Hz, 3H-14); $\delta_C$ 15.4 (C-14) and 19.2 (C-15)] which together with four methines [$\delta_C$ 59.0 (C-1), 46.0 (C-3), 50.3 (C-6) and 40.1 (C-7)] and four methylenes [$\delta_C$ 33.3 (C-4), 30.6 (C-5), 32.2 (C-8) and 24.3 (C-9)] constitute a bicarbocyclic system.  At first sight the presence of an isobutenyl group and two secondary methyls suggested a ring-contracted cadinane skeleton as in  mutisianthol (4)[3] or a ring-contracted guaiane skeleton as in valeren-enol (5).[4]  However the 2D INADEQUATE $^{13}$C nmr spectrum[5,6] of tamariscol clearly established the basic carbon skeleton as in (1) and also allowed unambiguous assignment of all the $^{13}$C resonances.

The 360 MHz $^{1}$H nmr spectrum of tamariscol was not sufficiently resolved to reveal the relative stereochemistry.  Addition of Eu(fod)$_3$ [100 MHz spectrum, CDCl$_3$ solution, 135 mM tamariscol, 75 mM Eu(fod)$_3$] caused significant downfield shifts of the vinyl proton (H-10, Δδ 2.61), a vinyl methyl (3H-13, Δδ 2.90), a secondary methyl (3H-14, Δδ 2.65) and its associated methine (H-3, Δδ 5.21), and one other methine (H-1, Δδ 5.63), the ring junction proton α to the hydroxyl group. H-3 (ddq, J 4.5, 12.0, 6.5 Hz) has a large coupling to a neighbouring proton (H-4β) and is therefore axial (α).  The hydroxyl group must be equatorial (α) to account for the large shift of H-3 on addition of Eu(fod)$_3$.  H-1 (dt, J 8.0, 11.0 Hz) is also axial (α) as indicated by its

large couplings which also suggest that the ring junction is <u>trans</u>. The H-6 and H-7 methines could not be identified clearly even at 360 MHz in different solvents and it was not possible to observe the size of $J_{6,7}$. However the $^{13}C$ shift of the methyl group attached to C-7 ($\delta$ 19.2) is virtually identical to the corresponding methyl in pacifigorgiol ($\delta$ 19.0 or 19.4) indicating that it must be $\beta$. An $\alpha$-methyl group would be expected to be considerably more shielded than in pacifigorgiol as a result of two additional $\gamma$-gauche interactions (with C-1 and C-9). Thus tamariscol has the relative configuration as shown in (1).

The biogenesis of the pacifigorgiane carbon skeleton is a matter for speculation. One possible derivation is from a caryophyllene precursor (6, arrows). It is of interest to note that $\beta$-caryophyllene (of unknown absolute configuration) is the most widespread sesquiterpene in the Frullaniaceae although it has not been observed in <u>F. tamarisci</u>.[1] The occurrence of pacifigorgiane and dolabellane[7] terpenoids in both marine organisms and liverworts may be of significance in terms of the evolutionary origin of the Hepaticae.
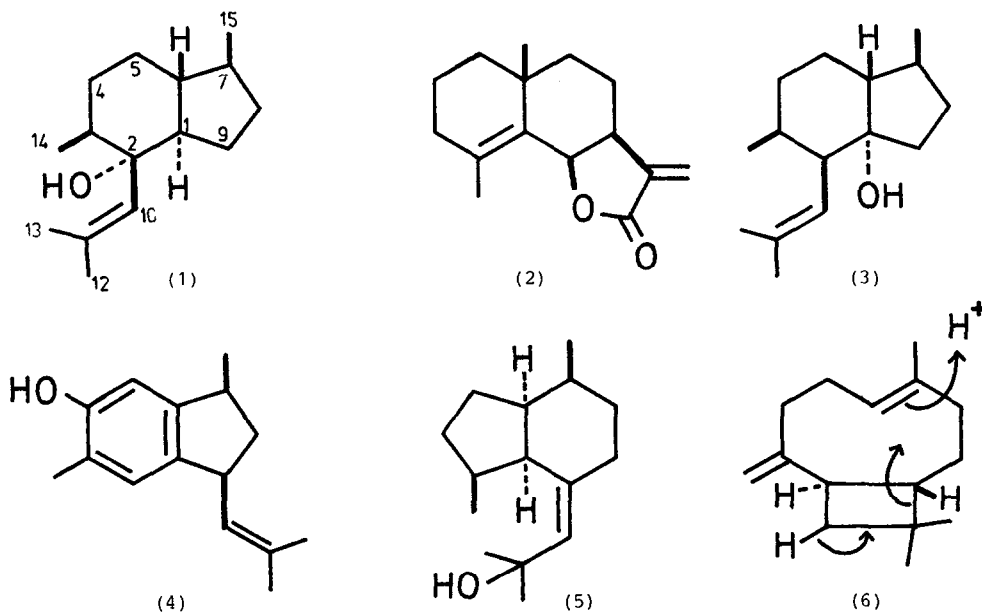


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