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ISOLATION OF (2S,8R)-GERMACRA-1(11),5(12),E6-TRIEN-2-OL ACETATE FROM THE BROWN ALGA *DILOPHUS FASCIOLA*

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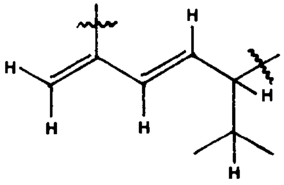
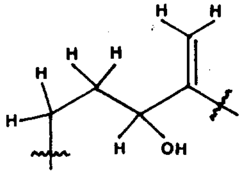
Brown algae of the family Dictyotaceae have provided a host of natural products.[1] Our recent study[2] on the constituents of a member of this family, namely *Dilophus fasciola*, has resulted in the isolation of a number of sesquiterpenes based on the cadalane skeleton. Further investigation of this species has turned up the novel sesquiterpene, (2S,8R)-germacra-1(11),5(12),E6-trien-2-ol acetate (1), a possible precursor of the cadalane constituents. Compound 1, isolated by careful silica gel chromatography of a chloroform extract as a colourless optically active oil (0.05% dry weight), $[\alpha]_D = -106.5°$ (*c* 1 in $CHCl_3$), λ_{max} 235 nm (ε 7890, conjugated diene), has the molecular formula $C_{17}H_{26}O_2$. An intense fragment at *m/e* 202 (M^+ -60) indicated the presence of an acetoxy group, which was corroborated by ir (1740, 1242 cm^{-1}); pmr [$CDCl_3$, δ 1.97 (3H, s, $C\underline{H}_3$-CO-) 5.07 (1H, dd, J=13 and 4.5 Hz, >C$\underline{H}$-OAc)] and cmr (170.5, s, CH_3-$\underline{C}$OO- and 52.5 ppm, d, >$\underline{C}$H-OAc) data showed it to be secondary. Alkaline hydrolysis of 1 afforded the alcohol 2, $C_{15}H_{24}O$, $[\alpha]_D = -180.3°$, from which 1 could be regenerated by acetylation (Ac_2O/Py). The cmr spectrum of 1 comprised, in addition to the acetate carbonyl, six sp^2 carbons (149.3, s, C_1; 146.2, s, C_5; 138.3, d, C_7; 129.6, d, C_6; 114.0, t, C_{11} or C_{12}; 113.3, t, C_{12} or C_{11}; ppm). Therefore, the five degrees of unsaturation implied by the formula of 1 must be due to an ester function, three double bonds and a ring. Selenium aromatization of 1 to cadalene pointed to a ten-membered monocyclic system of the germacrane type. Complete elucidation of the structure of the algal metabolite was essentially based on spectral data, mainly nmr spectra of the alcohol 2. That the conjugated diene system was part of the structural unit I was inferred from the pmr spectrum of 2 (270 MHz, C_6D_6, δ-scale) which



I

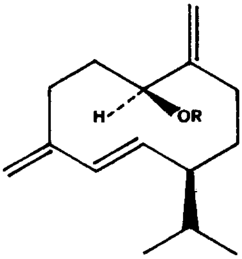


II

contained a doublet (1H, J=15 Hz) at 5.99 ($H-C_6$), a double doublet (1H, J=15 and 9 Hz) at 5.50 ($H-C_7$) and two singlets (1H each) at 5.0 and 4.97 (H_2-C_{12}), all of them with long-range couplings, an octet at 1.43 (1H, J=6.5 Hz, $H-C_{13}$), two 3-protons doublets at 0.89 and 0.93 (J=6.5 Hz, H_3-C_{14} and H_3-C_{15}) and a multiplet, partly obscured by overlapping with other resonances, at 1.71 ($H-C_8$). These attributions were confirmed by spin decoupling experiments. Irradiation at 5.99 caused the double doublet at 5.50 to collapse to a doublet (J=9 Hz) and sharpened the singlets at 5.0 and 4.97, while irradiation at 5.50 converted the signal at 5.99 into a broad singlet, simplified the multiplet at 1.71 and sharpened the singlets at 5.0 and 4.97. Saturation of the proton signal at 1.71 converted the double doublet at 5.50 to a doublet (J=15 Hz), and the octet at 1.43 to a heptet (J=6.5 Hz). Finally, irradiation at 1.43 not only collapsed the doublets at 0.89 and 0.93 to singlets, but at the same time simplified the multiplet at 1.71.

The presence of the partial formula II in 2 was also deduced from the pmr spectrum, which displayed two 1H singlets, finely splitted by long-range coupling, at 5.15 and 4.88 (H_2-C_{11}), a one-proton double doublet (J=11 and 4.5 Hz, $H-C_2$) at 3.83, two double double doublets at 2.45 (J=13.5, 13.5 and 5.3 Hz) and 2.14 (J=13.5, 6.0 and 3.5 Hz) for H_2-C_4 and two one-proton multiplets at 1.94 and 1.74 (H_2-C_3). Irradiation at

3.83 simplified the multiplets at 5.15 and 4.88, and sharpened the singlets at 1.94 and 1.74, while irradiation at 2.14 caused the double double doublet at 2.45 to collapse to a double doublet (J=13.5 and 5.3 Hz) and conversely irradiation at 2.45 simplified the double double doublet at 2.14 into a double doublet (J=6.0 and 3.5 Hz). The signals at 3.83, 2.45 and 2.14 were simplified on irradiation at 1.94 into a doublet (J=4.5 Hz), a double doublet (J=13.5 and 13.5 Hz) and a double doublet (J=13.5 and 6.0 Hz) respectively, while on irradiation at 1.74 the same signals were converted into a doublet (J=11 Hz), a double doublet (J=13.5 and 5.3 Hz) and a double doublet (J=13.5 and 3.5 Hz). The remaining carbon atoms implied by the molecular formula of 2 were accounted for by two methylenes, since the cmr spectrum of 1 included in the sp^3 region, in addition to three methyl quartets at 20.71, 20.71 and 20.56, and two methine doublets at 31.80 (C_{13}) and 21.42 (C_8), four methylene triplets at 35.91, 34.44, 32.94 and 29.70. Taken together, the above spectral properties and the aromatization to cadalene led unambiguosly to structure 2 for the alcohol and structure 1 for the natural compound.



1, R = Ac
2, R = H

Permanganate-periodate oxidation[3] of 2 afforded laevorotatory isopropylglutaric acid, which is known to have the R absolute configuration,[4] thus revealing the stereochemistry at C_8. Chirality at C_2 was established as S by the application of the Horeau method[5] which gave a preponderance of (-) α-phenylbutyric acid (optical yield 21%). The E stereochemistry of the cyclic double bond was indicated by the high value (15 Hz) of the coupling constant between the pertinent olefinic protons.

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