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CAULERPENYNE, AN UNUSUAL SEQUITERPENOID FROM THE GREEN ALGA *CAULERPA PROLIFERA*

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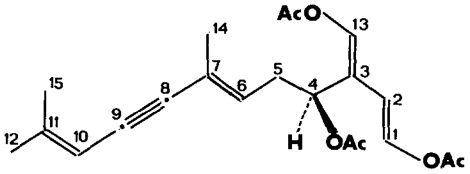
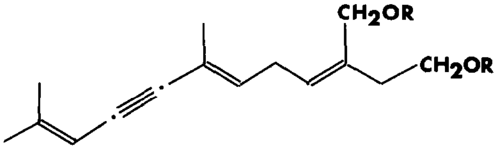
Investigation of marine algae of the genus *Caulerpa* has resulted in the isolation of diterpenes,[1] triterpenes[2] and nitrogenous compounds.[3] As part of a study of the metabolites of Mediterranean seaweeds,[4] we have investigated the green alga *Caulerpa prolifera* (Forsk.) Lamour. We wish to report here that this plant produces the acetylenic sesquiterpenoid caulerpenyne, 1.



1



2 R=H
3 R=OAc

Repeated silica gel chromatography of the chloroform extract of the alga (collected Syracuse, Sicily, Italy, July, 1977) resulted in the isolation, in yield of 0.35% based on fresh seaweed weight, of caulerpenyne, m.p. 57-58°, $[\alpha]_D^{20} = +7.1°$ (c 1 in EtOH) as colourless prisms purified by recristallization from ethanol. The elemental composition of compound 1, which was by far the most abundant component (22%) of the lipid extract, was determined as $C_{21}H_{26}O_6$ by elemental analysis. In the mass spectrum the molecular ion was not discernible and fragments were observed at m/e 314 (M^+-HOAc), 230 (M^+-HOAc-$2CH_2CO$) and 212 (M^+-2HOAc-CH_2CO), which pointed to the presence of three acetoxy groups. The i.r. spectrum exhibited carbonyl absorption at 1750 (vinyl acetate) and 1735 (acetate), and a weak C≡C stretch band at 2200 cm^{-1}, while the u.v. spectrum showed λ_{max}^{EtOH} 252, 265 (sh) and 280 (sh) nm with ε 33100, 27900 and 17000. The c.m.r. spectrum confirmed the presence of a non-terminal acetylenic group (singlets at 93.8 and 84.9 ppm) and three acetoxy groups (singlets at 169.3, 167.3 and 166.5 for the ester carbonyls), two attached to olefinic carbons (doublets at 136.7 and 133.9) and the third to a secondary saturated carbon atom (doublet at 68.5). This spectrum also comprised six additional olefinic carbons (147.5, s; 129.4, d; 121.2, s; 118.4, s; 108.8, d; 105.1, d), a methylene carbon (31.7, t) and six methyl quartets (24.4; 20.5; 20.5; 20.2; 20.2; 17.3). These data suggested that caulerpenyne is an acyclic sesquiterpenoid containing one triple and four double bonds. The p.m.r. spectrum (270 MHz, $CDCl_3$) exhibited signals representative of three acetoxymethyls at δ 2.18, 2.15 and 2.07 (3H each, s) and, in the olefinic region, three 1H double doublets at δ 7.64 (J=12.5 and 0.8 Hz), 5.83 (J=12.5 and 0.7 Hz) and 7.26 (J=0.8 and 0.7 Hz), consistent with expected chemical shifts[5] for protons at C_1, C_2 and C_{13} respectively. The observed J values are also in accordance with those recorded for a trans, trans-1,4-diacetoxy-1,3-butadiene system.[5] The acetoxymethine proton at C_4 was seen as a triplet at δ 5.87 (J=7.5 Hz), while the methylene protons appeared as two symmetrical double double doublets (J=15, 7.5 and 7.5 Hz) at δ 2.64 and 2.47. A one-proton double double quartet (J=7.5, 7.5 and 1.4 Hz) at δ 5.69 was assigned to 6-H and a 3H doublet (J=1.4 Hz) at δ 1.83 to 7-Me. The other protons in the molecule were accounted for by two 3H doublets at δ 1.89 (J=1.1 Hz, cis-11-Me) and 1.81 (J=1.1 Hz, trans-11-Me), and a 1H quartet of quartets (J=1.1 and 1.1 Hz) at δ 5.35 (10-H). These attributions, which were confirmed by extensive decouplings, allowed to clarify the proton sequences C_1-C_3, C_4-C_7 and C_{10}-C_{12}. Ozonolysis of 1 (in EtOAc at 0°, 20 min) followed by reduction with excess LAH in refluxing Et_2O afforded pentane-1,2,3,5-tetraol (isolated as the tetraphenylurethane); this established the attachment of C_3 to C_4 and consequently the formula 1 for caulerpenyne was unambiguously determined.

Additional evidence to confirm structure 1 was also obtained by sodium borohydride reduction to the expected diol 2, oily, $C_{15}H_{22}O_2$, M^+ 234, ν_{max}^{film} 3300 (OH) and 2170 cm^{-1} (C≡C), λ_{max}^{EtOH}255 (sh), 267, 283 with ε 18000, 22800 and 18000. Its p.m.r. spectrum (90 MHz, $CDCl_3$) showed signals at δ 1.82 (6H, 7-Me and trans-11-Me), 1.90 (3H, s, cis-11-Me), 2.43 (2H, t, J=6 Hz, 2-H_2), 2.90br (2H, t, J=7 Hz, 5-H_2), 3.52 (2H, D_2O-exchangeable, 2 OH), 3.76 (2H, t, J=6 Hz, 1-H_2), 4.08 (2H, s, 13-H_2), 5.40br (1H, s, 10-H), 5.55 (1H, t, J=7 Hz, 4-H) and 5.80 (1H, t, J=7 Hz, 6-H). On acetylation (Ac_2O/Py, 12 hr at room temp.), 2 gave the diacetate 3 (OH absorption absent in the i.r.), $C_{19}H_{26}O_4$, M^+ 318, whose p.m.r. spectrum exhibited two acetoxymethyl signals at δ 2.03 and 2.06 and the carbinol methylenes appeared at 4.15 (2H, t, J=6 Hz, 1-H_2) and 4.54 (2H, s, 13-H_2) showing downfield shifts of 0.39 and 0.46 ppm, respectively.

Assignment of E configuration to C_6 double bond in 1 was made by application of nuclear Overhauser effect; irradiation at the frequency of 7-Me resulted in a 20% enhancement of the integrated absorption of the methylene signal, whereas the 6-H signal was not significantly affected. The Z configuration of C_3 double bond was also confirmed by n.o.e.; irradiation at δ 7.26, the frequency of 13-H, increased the intensity of the signal at δ 5.82 (2-H) by ca. 25%, whereas the triplet at δ 5.87 (4-H) was unaffected, a result which shows in addition that the preferred conformation of the diacetoxy-1,3-butadiene system is trans-coplanar with respect to C_2-C_3 single bond. Also the values of the europium induced shifts, which are summarized in Table 1, were in agreement with the proposed structure.

Table 1. ^{1}H Induced Shifts of Caulerpenyne in the presence of Eu(fod)$_3$

Proton	1	2	4	5	6	10	12	13	14	15	AcO
$\Delta\delta^{a}$	7.19	4.12	10.75	2.54	2.73	0.21	0.80	6.93	1.34	-0.61	2.89 3.33 4.30

a = solvent $CDCl_3$; LSR/Substrate = 1

The chirality at C_4 was established by the following observation. Pentane-1,2,3,5-tetraol tetraphenylurethane obtained as above was shown to be a levorotatory mixture ($[\alpha]_D^{20}$ = -21°, c 1 in dioxane) of two diastereoisomers, evidently epimers at C_2, which were not separated on account of the small amounts available. Nonetheless, considering that both 2(R)-3(S)- and 2(S)-3(S)-diastereoisomers are levorotatory,[6] this result shows that chirality at C_4 in 1 is S.

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