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OXOCRINOL AND CRINITOL, NOVEL LINEAR TERPENOIDS FROM THE BROWN ALGA *CYSTOSEIRA CRINITA*

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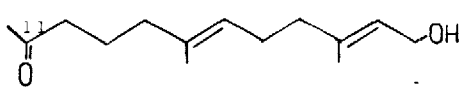
In connection with our systematic investigation of Mediterranean algae[1], we examined *Cystoseira crinita* Bory (Cystoseiraceae), a brown seaweed rather common along the Sicilian coasts This paper describes the isolation and structure elucidation of two novel linear terpenoid alcohols, oxocrinol (I) and crinitol (2)

Fresh seaweed collected near Catania was freeze-dried and exhaustively extracted with chloroform Concentration of the extracts gave a green-brown oil which was saponified, and the non-saponifiable fraction isolated in the customary way Chromatography on a Si gel column (eluent benzene-ether 4 I) afforded a mixture of I and 2 which, following acetylation, was further submitted to rechromatography over Si gel (eluent benzene-ether 49 I) From the pertinent acetates, oxocrinol and crinitol were recovered by alkaline hydrolysis



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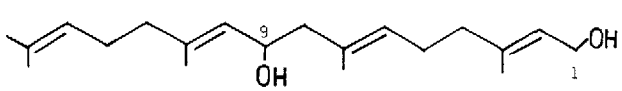


2

Oxocrinol was isolated as an optically inactive, colourless oil (0 43% dry weight of alga), n_D I 4923 (30°) High resolution mass spectrometry on the

molecular ion of oxocrinol gave a formula of $C_{14}H_{24}O_2$ (measured mass 224 1781, calculated 224 1776) A band at 1720 cm^{-1} in the IR spectrum (CCl_4) and signals in the NMR spectrum (CCl_4) at δ 2 02 (3H, s, CH_3CO-) and 2 30 (2H, t, J 7Hz, -$COC\underline{H}_2CH_2$-) were indicative for partial structure $CH_3COCH_2CH_2$- Evidence for a -$C(CH_3)$=$CHCH_2OH$ fragment was also provided by IR-NMR data {ν_{max} 3300 cm^{-1}, δ 1 64 (3H, bs, -$C(CH_3)$=), 2 53 (1H, b, D_2O-exchangeable, -OH), 3 98 (2H, d, J 7Hz, =$CHC\underline{H}_2OH$), 5 30 (1H, bt, J 7Hz, >C=$C\underline{H}CH_2OH$)} Upon irradiation at δ 5 30 the doublet at δ 3 98 collapsed into a singlet and, conversely, irradiation at δ 3 98 produced at δ 5 30 a singlet broadened by long range coupling Lastly, proof for the presence of part structure -$C(CH_3)$=$CHCH_2$- was adduced by NMR signals at δ 5 06 (1H, bt, J 6Hz, >C=$C\underline{H}CH_2$-) and 1 58 (3H, bs, -$C(CH_3)$=C<)

Additional structural information was obtained by the ozonolysis of oxocrinol acetate, n_D 1 4794 (26°), which afforded, after oxidative decomposition (H_2O_2) followed by treatment with CH_2N_2, laevulinic acid methyl ester, 2,6-heptanedione and acetylglycolic acid methyl ester, identified by co-GLC (1% SE 30 at 80°) with authentic samples

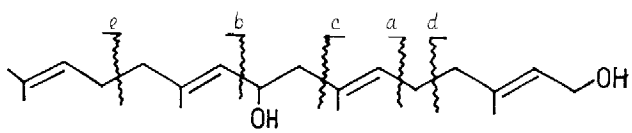
All in all, the above data established the structure of oxocrinol except for the location of one double bond, which could be assigned Δ^6 or Δ^7 positions The latter position could be eliminated on the basis of double irradiation experiments performed on oxocrinol acetate ν_{max} (CCl_4) 1720 (>CO ketone), 1740 and 1235 (acetate), m/e 266 (M^+), 206, 179, 173, 163, 161, 159, 149, 148, 145, 143, 142, 121, 95, 93, 81, δ 5 28 (1H, bt, J 7Hz, H-C_2), 5 04 (1H, bt, J 6Hz, H-C_6), 4 48 (2H, d, J 7Hz, H_2-C_1), 2 29 (2H, t, J 7Hz, H_2-C_{10}), 2 03 (3H, s, H_3-C_{12}), 1 95 (3H, s, CH_3COO-), 1 70 (3H, s, CH_3-C_3) and 1 57 (3H, s, CH_3-C_7)} By irradiation at δ 4 48 the triplet at δ 5 28 collapsed into a singlet broadened by long range coupling, irradiation at δ 1 59 produced at δ 2 29 a singlet, while the vinyl proton signal at δ 5 04 was unaffected Therefore, the structure of oxocrinol may be unambiguously represented by formula I The stereochemistry was assigned on the basis of the chemical shifts of both vinylic methyl groups (δ 1 58 and 1 64) in the NMR spectrum of I, which are consistent with these groups being *trans* to the olefinic protons[2]

Crinitol (2, 0 13% dry weight of alga), $[\alpha]_D$ -3°, n_D 1 4975, gave elemental analyses in good agreement with the molecular formula $C_{20}H_{34}O_2$ (hig reso-lution mass measurement on the ion $M^+ - H_2O$ gave m/e 288 2458, calculated 288 2453) Its NMR spectrum (CCl_4) indicated the presence of five vinylic methyl

groups (a set of five overlapping signals from δ I 56 to I 70, I5H), four olefinic protons (δ 5 55-4 95, 4H, complex signals) and in addition one primary and one secondary allylic hydroxyl groups {δ 2 65 (2H, bs, D_2O exchangeable, 2 -OH), 4 24 (IH, q, J 7Hz, H-C_9) and 3 98 (2H, d, J 7Hz, H-C_1)}. The presence of two -OH groups was confirmed by the formation of the diacetate {n_D I 49I6, $[\alpha]_D$ = -2°, ν_{max} I740, I240 cm^{-1}, δ 5 65-4 I5 (5H, complex signals), 4 49 (2H, d, J 7Hz, H-C_1), I 98 (6H, s, $2CH_3$-CO-), I 74-I 60 (I5H, singlets), m/e 330 (M^+ -CH_3COOH)}

Reduction of crinitol with Na in liquid ammonia at -45° gave, after conventional work-up, an oily product from which the major component (M^+/e 274) was isolated by $AgNO_3$-Si gel (I 3) chromatography (benzene as eluent) and identified as 2,6,IO,I4-tetramethylhexadeca-2,6,IO,I4-tetraene by comparison of its chromatographic {GLC (I% SE 30 on chromosorb W at IIO°), TLC on Si gel (eluent *n*-hexane) and argentation TLC (eluent benzene)} and spectral (MS and NMR) properties with those of an authentic specimen. Thus, the basic skeleton and the location of double bonds in crinitol were firmly established along with the position of primary hydroxyl group which must be C-I.

The position of the secondary hydroxyl group was deduced on the basis of the following considerations. Multiplicity of the NMR signal of the C<u>H</u>OH proton and NMDR experiments (the quartet at δ 4 24 collapsed to a doublet by irradiation at δ I 9I and was simplified to a triplet by irradiation at δ 5 09) excluded positions 4, 8 and I2. Of the remaining three possible positions, only position 9 was consistent with the fragmentation pattern in the mass spectrum, which displayed intense diagnostically important peaks at m/e 288 (M^+ - H_2O), I89 (*a* - H_2O), I23 (*b*), I2I (*c* - H_2O), 85 (*d*) and 69 (*e*). Crinitol, therefore, could be formulated as <u>2</u>



An examination of the chloroform extract from the alga prior to saponification by column chromatography over Si gel followed by GLC (2 5% SE 30 at I80°) of the fractions thus obtained showed that crinitol occurs in the plant in the free state, while oxocrinol is present as the acetate.

The two new terpenoid alcohols, oxocrinol and crinitol, appear to be related biogenetically to farnesol and geranylgeraniol, respectively However, other possibilities must be taken into considerations for the biogenesis of oxocrinol, which could also originate, for instance, from a monoterpene by addition of two acetate units or from geranylgeraniol by oxidative eleimination of a C_6 fragment

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