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LAURENCIENYNE, A NEW ACETYLENIC CYCLIC ETHER FROM THE MARINE RED ALGA LAURENCIA OBTUSA

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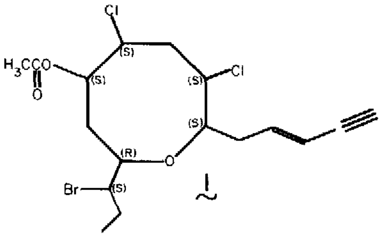
ABSTRACT: The structure and absolute stereochemistry of laurencienyne, a non-isoprenoid cyclic ether isolated from *Laurencia obtusa*, has been established by X-ray and spectroscopic studies.

In our continuing effort to screen marine algae from Eastern Sicily for antimicrobial activity and to isolate the active components, we have investigated several species of the *Laurencia* genus (Rhodophyta).[1,2] *Laurencia obtusa* (Huds.) Lamour., a widespread Mediterranean alga whose lipid extract inhibited *Bacillus subtilis* and *Escherichia coli*,[2] was found to contain several halogenated sesquiterpenes[3] and interest in this species has been sustained by recent reports of new compounds--a dibrominated diterpene,[4] an acetylenic 9-membered cyclic ether,[5] and a brominated polycyclic ketal[6]--as well as by revisions by X-ray analyses of previously published structures.[7] The present work describes the characterization and identification of laurencienyne (1), an interesting modification of the *Laurencia*-derived acetylenes.



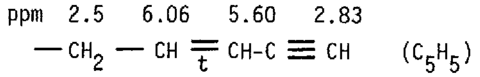
1

Laurencia obtusa was collected intertidally at Castelluccio, 40 km south of Catania, Sicily, in May, 1979. Room temperature extraction of the air-dried material (274 g) with methanol-toluene (3:1) gave, after rotary evaporation, a residue which was partitioned between sodium nitrate (1 M) and ethyl ether. After drying over sodium sulfate and rotary evaporation, the organic layer gave a deep-green semisolid oil (6.7 g), which was chromatographed over silica gel. Fractions eluted with petroleum ether-ether (80:20) yielded laurencienyne (75 mg, 1.1% of lipid weight), mp 119-120 °C (from *n*-hexane-benzene), $[\alpha]_D^{24}$ +50.3° (*c* 1.1, $CHCl_3$), active *vs*. *B. subtilis* and *E. coli*.

High resolution electron impact (HREI) mass spectrometry established, by peak matching, the elemental composition $C_{17}H_{23}{}^{79}Br^{35}Cl_2O_3$ (Varian MAT 731, observed 424.0204; Δ -0.4 mmu) as well as fragment peaks at m/z 358.9818 (Δ 0.1, M - C_5H_5), 345.1021 (Δ -0.4, M - Br) and 303.0553 (Δ -0.2, M - C_3H_6Br). Although the molecular ion was the most intense in the field desorption mass spectrum, its intensity was very low by EI (<1% of the base peak at m/z 43), suggesting the presence of easily cleaved side chains, C_5H_5 and C_3H_6Br.

The system **a** was established by irradiation at 2.6 ppm, which converted the olefinic

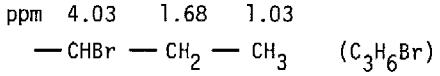
a:



$$\begin{array}{l}\text{ppm}\quad 2.5\quad 6.06\quad 5.60\quad 2.83\\ -CH_2-CH\underset{t}{=}CH-C\equiv CH\qquad (C_5H_5)\end{array}$$

protons to an ABX system [δ_A = 6.06 ppm (d), δ_B = 5.60 ppm (q), δ_X = 2.83 ppm (d), J_{AB} = 15 Hz, J_{AX} = 0, J_{BX} = 2 Hz] and by irradiation in the AB region, which collapsed the acetylenic doublet at 2.83 ppm to a singlet. The system **b** was identified in the ^1H NMR spectrum by irradiation at

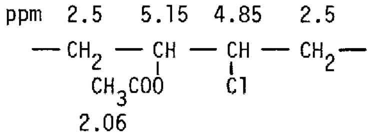
b:



$$\begin{array}{l}\text{ppm}\quad 4.03\quad 1.68\quad 1.03\\ -CHBr-CH_2-CH_3\qquad (C_3H_6Br)\end{array}$$

1.68 ppm, which collapsed the triplet at 1.03 ppm (3 H, J = 7 Hz) to a singlet and simplified the multiplet at 4.03 ppm (1 H). Another recognizable structural unit is **c**, since irradiation

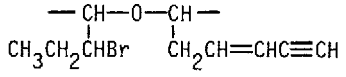
c:



$$\begin{array}{l}\text{ppm}\quad 2.5\quad 5.15\quad 4.85\quad 2.5\\ -CH_2-\underset{\underset{\displaystyle 2.06}{CH_3COO}}{CH}-\underset{Cl}{CH}-CH_2-\end{array}$$

at 2.5 ppm collapsed the two central protons (5.15 ppm, d of t, J = 8, 3 Hz; 4.85 ppm, t of d, J = 9, 2 Hz) to another AB system (δ_A = 5.15, δ_B = 4.85, J_{AB} = 9 Hz), with some residual coupling of both the A (db, J < 1 Hz) and B (dd, J = 2 Hz) protons. The remainder of the ^1H NMR spectrum consists of an additional two protons in the 2.3-2.6 ppm region (m, $-CH_2-$) and three in the 3.8-4.4 ppm region (m, $-\underset{|}{C}H-O-$, $-\underset{|}{C}H-O-$, -CHCl-). If one assumes from the mass spectrometric fragmentations a cyclic ether flanked by the two easily lost fragments **a** and **b**, i.e., **d**, then

d:



$$-\underset{CH_3CH_2CHBr}{CH}-O-\underset{CH_2CH=CHC\equiv CH}{CH}-$$

only four structures are possible from linking **c** and **d** at one end and inserting the remaining -CHCl- unit between **c** and **d** at the other end.

Ultraviolet [λ_{max}^{MeOH} 225 nm (ε 15,000) and 232 (shoulder, 13,100)] and infrared ($\tilde{\nu}_{max}^{KBr}$ 3280, 2980, 1740, 1235, 1080, 1060, 970 cm^{-1}) data agree with the conjugated _trans_-enyne and acetate functionalities. The total degree of unsaturation and the data above argue that laurencienyne is a non-isoprenoid cyclic ether similar to those isolated by Irie, Kurosawa, _et al_., from Japanese _Laurencia_[8] or to obtusenyne.[5]

The ^{13}C NMR spectrum (JEOL FX60, CD_2Cl_2) of **1** showed seventeen resolved carbons. Signals at 170.1 (s), 140.4 (d), 113.1 (d), 82.0 (s), 21.0 (t) and 12.4 ppm (q) are attributed to the acetate carbonyl, the two olefinic carbons, the quaternary alkyne carbon, and the terminal ethyl carbons, respectively. The remainder of the spectrum showed signals at 77.4, 75.9, 74.1, 72.4, 62.8, 62.1, 57.7, 42.7, 38.9, 30.4 and 29.7 ppm, with difficultly assignable multiplicity in routine off-resonance spectra due to overlapping of signals. A decision among the four potential structures and assignment of the stereochemistry were effected by X-ray crystallographic techniques.

Crystals of **1** suitable for X-ray analysis were obtained from n-hexane-benzene (80:20). Crystal data: orthorhombic, a = 5.243(1)Å, b = 17.175(5)Å, c = 21.541(7)Å, V = 1940Å^3, Z = 4, ρ_{calc} = 1.46 g cm^{-3}, space group $P2_12_12_1$. The structure was solved using the MULTAN program[9] and has been refined to an R-factor of 0.073 on 1668 intensities (2σ-level) collected on a Syntex $P2_1$ diffractometer (MoK_α). The absolute configuration was established by anomalous dispersion methods [R_2(+) = 0.075, R_2(-) = 0.087]. Further details of the X-ray work will be published elsewhere.[10] A stereoscopic view of the molecule is shown in Figure 1.

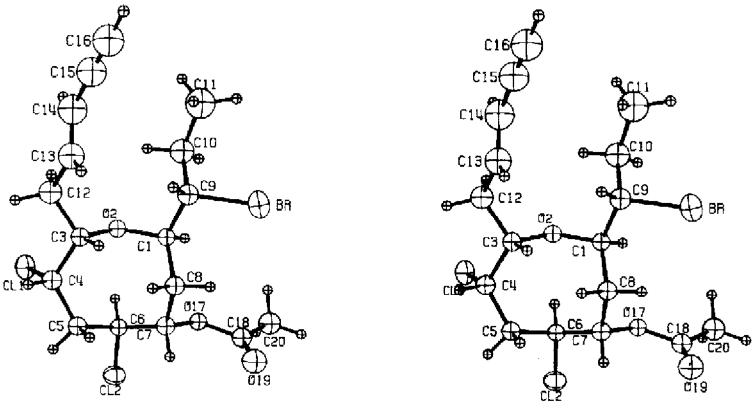


Figure 1. Stereoscopic view of a single molecule of laurencienyne

Although laurencienyne has some structural features in common with isolaureatin (8-ring with identical side chains),[11] and some (presence of chlorine) in common with obtusenyne[5] and chondriol,[12] it is the first compound in this series found to contain two chlorine atoms.

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