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OBTUSADIOL, A UNIQUE BROMODITERPENOID FROM THE MARINE RED ALGA *LAURENCIA OBTUSA*

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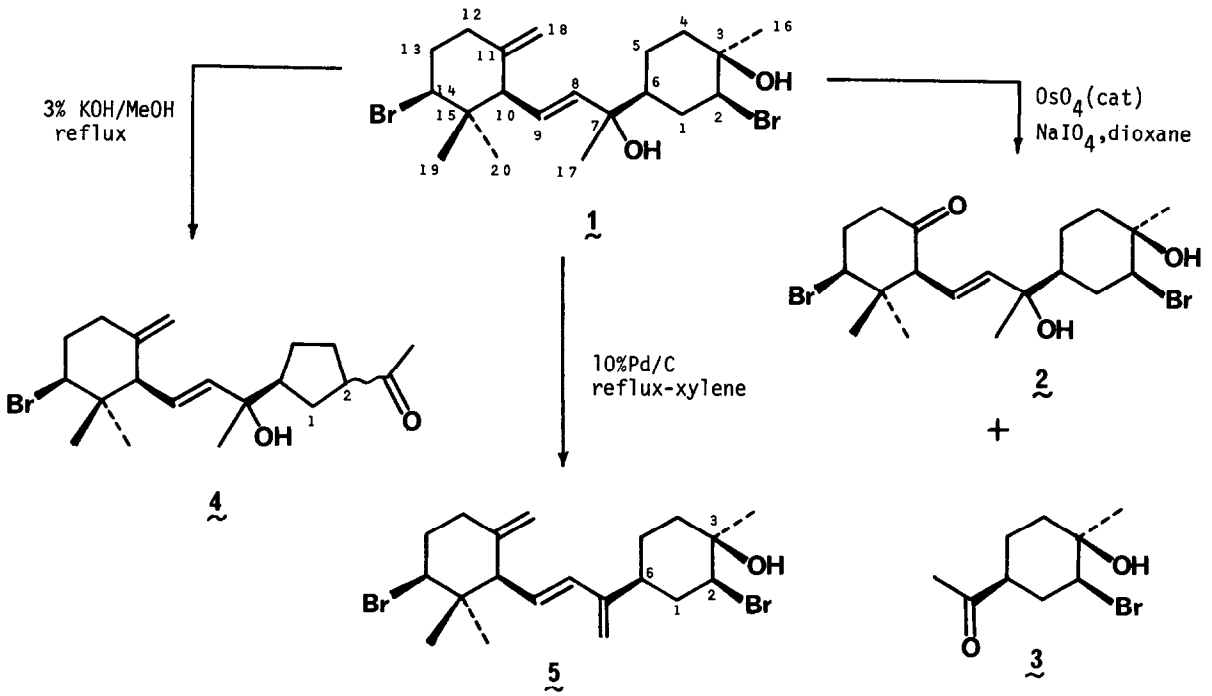
The widely distributed red seaweed *Laurencia* is known as a unique source of halogenated C_{15} nonterpenoid ethers and halogenated and nonhalogenated sesqui- and diterpenoid compounds[1]. More recently this source has also been shown to produce a interesting bromine-containing squalene derivative[2]. The diterpenoids from *Laurencia* consist of aplysin-20[3,4], concinndiol[5] and neo-concinndiol hydroperoxide[6], which are structures closely related to the rather commonly observed labdane diterpenoids[7], as well as the irieols[8], dibromoditerpenoids of unique composition. In this communication we wish to report the isolation and structure elucidation of an unprecedented new dibromoditerpenoid, obtusadiol (1). Obtusadiol was isolated, along with α-snyderol acetate, brasilenol[9], epibrasilenol[9] and guaiazulene from the Mediterranean alga *L. obtusa* (Huds.) Lamouroux[10].

The $CHCl_3$/MeOH (1/1) extract of air-dried *L. obtusa* (collected Rafina, Greece, June 1975) was fractionated by conventional silica gel column chromatography (Grace 62, Et_2O elution) to obtain obtusadiol (1), an oil, $[\alpha]_D^{25}$-24.5°(c 3.1, $CHCl_3$), in 0.1% yield of the dry algae. High resolution mass spectrometry established the elemental composition $C_{20}H_{30}Br_2O$ (observed 444.0664, calc. 444.0665) for the M^+-H_2O fragment. The thin-film infrared spectrum contained absorptions at 3500, 1650 and 1370, 1390 cm^{-1}, which were assigned to hydroxyl, terminal olefin and gem-dimethyl substituents. ^1H and ^{13}C NMR data were of great utility in determining the structure



of obtusadiol: ^{1}H NMR (220 MHz, $CDCl_3$) δ 5.80(1H) dd J=15, 10Hz; 5.56(1H) d J=15; 4.86(1H) s; 4.64(1H) s; 4.18(2H) dd J=12, 4; 2.54(1H) d J=10; 1.34(3H) s; 1.29(3H) s; 1.09(3H) s; 0.96(3H) s; ^{13}C NMR (20 MHz, $CDCl_3$) 147.2 s (C-11), 139.1 d (C-8), 126.8 d (C-9), 110.3 t (C-18), 74.3 s (C-7) 70.3 s (C-3), 66.4 d (C-14), 66.2 d (C-2), 56.5 d (C-10), 49.7 d (C-6), 41.1 s (C-15), 37.5 t (C-12), 36.6 t (C-1), 34.9 t (C-4), 34.8 t (C-5), 30.4 q (C-17), 29.5 q (C-16), 26.1 q (C-20), 22.0 t (C-13), 16.1 q (C-19). Analysis of these data revealed that 1 contained an isolated *trans*-disubstituted olefin adjacent to an isolated methine carbon (^{1}H NMR decoupling at δ 5.80, 5.56 and 2.54), an exocyclic double bond (2 broad singlets, δ 4.86 and 4.64), two secondary bromine substituents oriented equatorial in chair cyclohexane rings (two bands centered at δ 4.18, each J=12, 4 Hz), and two methyl-substituted tertiary alcohols (^{1}H methyl singlets at δ 1.34 and 1.29 and ^{13}C off-resonance singlets at 74.3 and 70.3 PPM). ^{13}C off-resonance data confirmed the molecular composition of $C_{20}H_{32}Br_2O_2$, the terminal olefin substituent (110.3 PPM triplet and 147.2 PPM singlet), and illustrated that 1 is bicyclic.

Oxidative cleavage of obtusadiol with OsO_4 (cat.)/$NaIO_4$ gave the cyclohexyl ketone 2 and the cleavage product 3 (10:1 ratio) in modest yield. As a consequence of the selective cleavage of the exomethylene group in 1, the C-10 methine proton, which appears at δ 2.54 in 1, was shifted

to δ 2.90 (d, J=10) in 2, thus confirming the structural assignment of the natural product. Treatment of the ketone 2 with 3% KOH/MeOH under reflux for 1 hr. failed to epimerize the C-10 methine center; therefore, we assign the C-10 proton as axial, consistent with a more stable equatorial substituent. We assign the bromine-bearing carbon as C-14 since a close correlation exists between the comparable ^{13}C NMR bands of 1 and those of β-snyderol[12]. Also, the infrared absorption for the C-11 carbonyl in 2 is normal for cyclohexanone (1715 cm^{-1}), and precludes the placement of equatorial halogen at C-12 by virtue of the expected shift of 20 cm^{-1} [13]. The structure of compound 3, $C_9H_{15}O_2Br$, $\nu_{C=O}$ 1715 cm^{-1}, was established, without stereochemistry, based upon its ^1H NMR characteristics: δ 4.14(1H) dd J=12, 4; 2.45(1H) m; 2.14(3H) s; 1.34(3H) s and 1.2 - 2.0(6H) m. The isolation of a monocyclic compound, (3), as well as the existence of a *trans* olefin, illustrates that the 6-membered rings in 1 are not mutually interconnected as in bicyclo[4·4·0]decane or spiro[5·5]undecane systems, but result from independent cyclizations at the termini of an acyclic precursor. Hence, the aforementioned spectral data and chemical transformations led to the assignment of obtusadiol as the regular terpenoid structure 1. However, stereochemical assignments at C-3 and C-6 of the bromohydrin-containing ring could not be deduced from these data.

Reaction of obtusadiol with refluxing 3% KOH/MeOH gave, in quantitative yield, the ring contracted methyl ketone 4 as an epimeric mixture at C-2. The ketone showed an infrared carbonyl band at 1715 cm^{-1} and ^1H NMR bands characteristic of the ring-substituted methyl ketone: δ 2.14 (3H) s; 2.91(1H) m. The facile ring contraction and lack of epoxide formation from this reaction strongly suggest that 1 is a *cis*-1,2-bromohydrin with axial hydroxyl[14].

In an attempt to aromatize the bromohydrin-containing ring, 1 was refluxed in toluene over 10% Pd/C. Unexpectedly, these conditions led to a regiospecific dehydration to the diene 5. Compound 5 showed UV absorption at 236 nm (ε=8,400, Et_2O) and ^1H NMR bands which confirmed the terminal olefin assignment [δ 5.03(1H) s; 4.99(1H) s]. By virtue of the sole hydroxyl function in 5, $Eu(fod)_3$ shifted ^1H NMR experiments gave substantive information. Of particular interest was the intense deshielding effects on the C-1 and C-5 axial protons from 1,3 diaxial interactions, which confirmed the C-3 hydroxyl as axial. The strong shifts noted for the C-1 axial proton allowed this band to be fully resolved. Irradiation of the C-2 methine proton allowed the aforementioned band to be fully interpreted as a multiplet with couplings of 14 Hz (geminal), 12 Hz (C-1 ax - C-2 ax), and 12 Hz (C-1 ax - C-6 ax). The lack of small (a,e) coupling in this multiplet established the adjacent center (C-6) to bear an equitorial substituent.

Acknowledgments

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10. *Laurencia obtusa* is considered to be widely distributed throughout the Atlantic Ocean with specimens found in abundance in the equatorial Atlantic (Caribbean Sea) as well as north temperate zones (British Isles). Chemical studies of *L. obtusa* from two habitats have been reported with little comparison of chemical components[11]. In the Mediterranean at least four morphologically distinct forms exist, each of which also exhibits different constituents. We conclude that the taxonomy of this complex group should be re-evaluated.

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