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OBTUSENOL, A SESQUITERPENE FROM *LAURENCIA OBTUSA*

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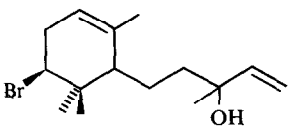
Key Word Index—*Laurencia obtusa*; Rhodomelaceae; brominated sesquiterpene; obtusenol.

The *Laurencia* genus of red algae is a particularly rich source of halogenated metabolites, especially sesquiterpenes. The widely distributed species *L. obtusa* is known to elaborate the following compounds: α-snyderol (**1**) [1] and its acetate, [2], 3-bromo-8-epicaparrapi oxide (**2**) [3], a family of chamigrenes, [4–7], brasilenol and epibrasilenol [2,8], guaiazulene [2], the diterpene obtusadiol [2], and the C_{15} cyclic ether acetylenes obtusenyne [9] and obtusin [10]§. In continuing our work on *L. obtusa* we can now add further compounds to this list, including obtusenol, a new sesquiterpene.

Air-dried alga, collected on Gökçeada, an island in the Aegean Sea, was extracted with ether giving an oil which was chromatographed on silica gel. The main component, obtusenol (**3**) was obtained as an oil, $C_{15}H_{26}Br_2O_2$, $[\alpha]_D^{16.4}$ − 50.2° (*c* 1.74, $CHCl_3$). The IR showed significant bands for tertiary hydroxyl (3610, 1410, 1103 cm^{-1}), vinyl (3090, 1640, 920), gem-dimethyl (1377, 1368), and cyclic ether (1125) functions. The ^1H NMR spectrum (220 MHz, $CDCl_3$) revealed signals for four tertiary methyl groups attached to carbons bearing oxygen (δ 1.57, 1.40, 1.34, 1.30, each 3 H, *s*), an isolated vinyl group (5.90, 1 H, *dd*, *J* = 18 and 11 Hz; 5.22, 1 H, *dd*, *J* = 18 and 2.5 Hz; 5.08, 1 H, *dd*, *J* = 11 and 2.5 Hz), two >CHBr groups (3.86, 1 H, *dd*, *J* = 12 and 5 Hz; 3.74, 1 H, *dd*, *J* = 10 Hz) the former indicating an equatorial bromo substituent attached to a 6-membered ring in chair conformation, and three multiplets centred at 2.20, 1.93, and 1.57 for eight methylene protons. Supporting data were obtained from the ^{13}C NMR spectrum which also established the presence of three quaternary carbons attached to oxygen. All the constituent groups in obtusenol are thus defined by the foregoing spectroscopic evidence. The manner in which they are assembled was deduced as follows.

Conversion to the 3,5-dinitrobenzoate gave an oil whose ^1H NMR spectrum was very similar to that of obtusenol except that the methyl signal at δ 1.57 was shifted downfield to 1.77 and the vinyl proton signals had also moved 0.14–0.23 ppm downfield. The same deshielding effects on the adjacent methyl and vinyl groups are observed [11] when the tert.-alcohol function in manoöl is converted into the 3,5-dinitrobenzoate which indicates the structure of the terminal allylic alcohol function (cf. **1**).

In the mass spectrum of obtusenol, the base peak arises from a fragmentation occurring as shown (**3**) to give a doublet at *m/e* 205/207 (Found: 205.0226; required for $C_8H_{14}{}^{79}BrO$ 205.0227). Ions at higher mass than 207 are all weak but a significant sequence is $M^{+\cdot}$ − Me − HBr − Me_2CO to give *m/e* 241/243 ($C_{12}H_{18}Br$). On this basis the molecule should contain two isolated $-CHBrCH_2CH_2-$ moieties which was confirmed by a study of the lanthanide-shifted ^1H NMR spectrum. At a concentration of 8.8 mg $Eu(fod)_3$ to 23 mg of **3** the spectrum of the entire side chain was shifted downfield becoming approximately first order, while the remainder of the spectrum was little changed. Notably the broad doublet at δ 3.74 (H-6) (farnesol numbering) moved to 4.12, i.e. downfield instead of upfield of the other >CHBr signal at 3.86. Sequential irradiation of the shifted spectral bands allowed us to correlate the signals and, in particular, irradiation of a methylene resonance at δ 2.48 collapsed another methylene multiplet at 3.2 and also the lower field >CHBr doublet at 4.12. Thus the signal at δ 2.48 arises from H-5 and that at 3.2 from the methylene



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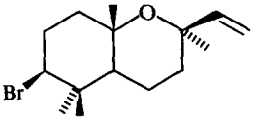

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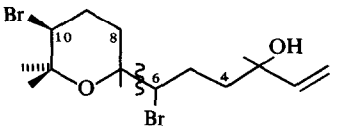

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§Not to be confused with the anthraquinone, obtusin [Takido, M. (1960) *Chem. Pharm. Bull. (Tokyo)* **8**, 246].

at C-4; the side chain is therefore $-CHBrCH_2CH_2CMe(OH)CH{=}CH_2$. As the signal from the other $>CHBr$ proton is a double doublet it has to be located at C-8 or C-10, and on biogenetic reasoning it must be at C-10 as in **3**.

Other components obtained from the ether extract besides obtusenyne [9] were laurinterol [12], epibrasilenol [2, 8] and *cis*-isodihydrorhodophytin ([13] and W. Fenical, personal communication).

EXPERIMENTAL

Powdered air-dried *Laurencia obtusa* (a voucher specimen (ref. No. 56) is kept at the Herbarium, Department of Systematic Botany, Faculty of Science, University of Ege, Izmir, Turkey) (2 kg) was extracted with ether. Evapn gave a residual brown-green oil which was chromatographed on a Si gel column eluting successively with petrol, petrol–C_6H_6, C_6H_6 and C_6H_6–$CHCl_3$ mixtures. Elution with petrol–C_6H_6 (10:1) gave an oil which was separated by PLC on Si in petrol–C_6H_6 (1:1) to give obtusenyne (365 mg) and *cis*-isodihydrorhodophytin (25 mg), an oil, $C_{15}H_{20}BrClO$, $[\alpha]_D^{23}$ + 69.6° (*c* 0.46, $CHCl_3$), identical (TLC, IR, NMR, MS) by direct comparison with an authentic sample; this compound was found recently [13] in the sea hare *Aplysia brasiliana* and also in *L. obtusa* (W. Fenical, personal communication). The fractions obtained using petrol–C_6H_6 (6:1) yielded laurinterol, mp 53–54° (from MeOH) (485 mg) identical (mmp, IR, NMR) with an authentic sample [12]. The residue from the C_6H_6 eluate was repeatedly chromatographed on Si plates in $CHCl_3$ to give epibrasilenol (370 mg) and obtusenol (350 mg). Epibrasilenol was an oil, $C_{15}H_{26}O$, $[\alpha]_D^{17}$ 93.1° (*c* 0.32, $CHCl_3$) identical (TLC, IR, NMR, MS) by direct comparison with authentic material. Sarett oxidation gave brasilenone [8], $C_{15}H_{24}O$, λ_{max} (MeOH) 252 nm, ν_{max} (CCl_4) 1662, 1625 cm^{-1}; the acetate, an oil, ν_{max} 1730 cm^{-1}, was very similar to the epimer except for $>C\underline{H}OAc$ at δ 4.97 *br.s* (cf. 5.36 *m* for brasilenol acetate [8]).

Obtusenol was obtained as an oil, $C_{15}H_{26}Br_2O_2$ [Found: 381.0068; required for $^{79}M^+ - Me$, 381.0073. In the CI mode $M^+ + 1$ was observed at 397 (1%)]; IR (CCl_4) 3610, 3090, 2960, 2920, 2860, 1702, 1640, 1450, 1410, 1377, 1368, 1350, 1125, 1103, 920 cm^{-1}; ^{13}C NMR (20 MHz, $CDCl_3$), 144.8 (*d*), 112.0 (*t*), 76.2 (*s*), 75.7 (*s*), 73.3 (*s*), 68.4 (*d*), 57.8 (*d*), 40.5 (*t*), 38.2 (*t*), 30.9 (*q*), 28.5 (*q*), 28.4 (*q*), 27.5 (*q*), 23.5 (*t*), 19.8 (*t*) ppm; ^1H NMR in the text. MS 385, 383, 381 (M^+, <0.3%), 301 (8), 299 (8), 243 (3), 241.0589 (3; $C_{12}H_{18}{}^{79}Br$ requires 241.0591), 219 (3), 212 (25), 207 (100), 205 (100), 195 (14), 166 (11), 161 (9), 147 (17), 135 (56), 125 (70), 107 (65), 93 (70). Obtusenol (50 mg) in pyridine (0.5 ml) containing 4-dimethylaminopyridine (5 mg) was added to freshly prepared 3,5-dinitrobenzoyl chloride (70 mg) in pyridine (0.5 ml) and warmed at 50–60° for 1.5 hr. The dinitrobenzoate was obtained as an oil, ν_{CO} 1715 cm^{-1}; ^1H NMR δ 9.21 (1 H, *d*, *J* = 2.5 Hz), 9.12 (2 H, *d*, *J* = 2.5 Hz), 6.13 (1 H, *dd*, *J* = 17 and 11 Hz), 5.36 (1 H, *d*, *J* = 11 Hz), 5.29 (1 H, *d*, *J* = 3 Hz), 3.85 (1 H, *dd*, *J* = 11 and 4 Hz), 3.70 (1 H, *d*, *J* = 11 Hz), 2.4–1.5 (8 H, *m*), 1.77, 1.48, 1.45, 1.23 (each 3 H, *s*).

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