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α- and β-SNYDEROL; NEW BROMO-MONOCYCLIC SESQUITERPENES FROM THE SEAWEED LAURENCIA

Bruce M. Howard and William Fenical*
Institute of Marine Resources
Scripps Institution of Oceanography
La Jolla, California 92093

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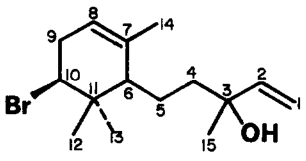
Brominated bicyclic sesquiterpenes of the chamigrene ring system are common metabolites found in many species of the marine red alga *Laurencia*[1]. The biosynthesis of these compounds has been generally predicted[1,2] to involve the intermediacy of a brominated monocyclo-farnesol derivative in analogy to the probable biosynthesis of the parent hydrocarbon[3]. To support these contentions, we wish to report that at least two species of *Laurencia* contain bromo monocyclonerolidol derivatives closely related to the proposed biosynthetic precursor.

Standard chromatographic procedures resulted in the isolation of α-snyderol (1) from *L. obtusa* (Huds.) Lamouroux (15% CHCl$_3$ extract) and β-snyderol (2) from *L. snyderae* Dawson (25% CHCl$_3$ extract). *L. obtusa* was collected in May, 1975 along the eastern Spanish coast in Tossa de Mar, while *L. snyderae*, a local species, was collected in June, 1974 in La Jolla, California.



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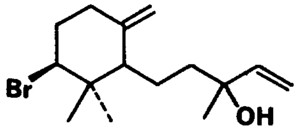

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α-Snyderol (1), an oil, $[\alpha]_D$ 10.4° (c, 4.65, $CHCl_3$), showed a strong M^+-H_2O fragment at m/e 282/284 for $C_{15}H_{23}Br$ in the mass spectrum and hydroxyl (3600 cm^{-1}) and terminal vinyl absorptions (999, 921 cm^{-1}) in the infrared. Proton and carbon-13 nmr spectra were clearly illustrative of the structural features of this sesquiterpene. ^1H nmr (220 MHz, CCl_4) δ 5.84 (1H) dd, J = 17, 10 Hz; 5.16 (1H) d, J = 17; 5.16 (1H) bs; 5.00 (1H) d, J = 10; 4.05 (1H) dd, J = 9, 7; 2.48 (2H) bs; 1.66 (3H) s; 1.23 (3H) s; 1.09 (3H) s; 0.89 (3H) s; 1.2-1.9 (5H) multiple bands. ^{13}C nmr (20 MHz, $CDCl_3$, PPM rel. to TMS) 145.1, d, J = 155.8; 137.0, s; 120.7, d, J = 155.7; 112.0, t, J = 156.7; 73.4, s; 65.0, d, J = 150.5; 50.5, d, J = 124.5; 44.4, t, J = 123.6; 39.2, s; 35.4, t, J = 130.6; 28.5, q; 27.7, q; 23.5, q; 22.2, q; and 15.7, q[4].

β-Snyderol (2), also isolated as an oil, showed $[\alpha]_D$ 14.6° (c, 3.9, $CHCl_3$) and behaved similarly to 1 in presenting only an M^+-H_2O fragment in its mass spectrum (m/e = 282.0992 ± .0014 for $C_{15}H_{23}Br$, calc. 282.0983). Infrared absorptions at 3600, 999 and 923 cm^{-1} showed the analogous hydroxyl and vinyl functions as in 1. In addition, strong bands at 1650 and 881 cm^{-1} showed the presence of an exocyclic double bond. Proton and carbon nmr spectra were comparable with 1 except for features generated by carbons 7, 8 and 14 and their respective protons. ^1H nmr (220 MHz, CCl_4) δ 5.88 (1H) dd, J = 18, 10 Hz; 5.14 (1H) d, J = 18; 4.98 (1H) d, J = 10; 4.82 (1H) bs; 4.55 (1H) bs; 4.00 (1H) dd, J = 11, 5; 1.23 (3H) s; 1.16 (3H) s; 0.81 (3H) s; 1.10-2.30 (10 H) multiple bands. ^{13}C nmr (20 MHz, $CDCl_3$) PPM 145.6, s; 144.9, d, J = 157.6; 111.8, t, J = 157.0; 109.0, t, J = 157.0; 73.3, s; 67.1, d, J = 150.0; 53.1, d, J = 124.0; 41.9, s; 41.3, t; 37.4, t; 35.9, t; 28.4, q; 28.1, q; 20.6, q; and 16.4, q[4].

Since each isomer contains 3 degrees of unsaturation by mass spectrometry, and both show 2 double bonds in their ^{13}C nmr spectra, these metabolites must be monocyclic terpenes. Hydrogenation of both snyderol isomers served to conclusively relate these two metabolites. Treatment of (1) with hydrogen and platinum catalyst in ether gave a single perhydro derivative, $[\alpha]_D$ 14.9° (c, 3.56, $CHCl_3$) as determined by its GC homogeniety and nmr characteristics (a single methyl doublet at δ 0.95, J = 8 Hz). Consistent treatment of β-snyderol (2) gave the identical perhydro derivative, $[\alpha]_D$ 14.3^{o} (c, 4.0, $CHCl_3$). Since the optical rotations of both perhydro compounds are comparable, it appears that the absolute stereochemistries of the asymmetric carbons 3, 6 and 10 are identical in 1 and 2. In addition, the coupling constants observed (12, 4 Hz) for the deshielded proton on C-10 in this cyclohexane derivative (bromine-bearing carbon) clearly indicate an axial proton and hence an equitorial bromine atom. Therefore, the bromine substituent in both 1 and 2 must occupy a pseudo-equatorial position.

Since Δ^6-ene (tetrasubstituted) monocyclo-farnesol derivatives are known[3,5] to cyclize in low yield, under acid catalysis, to chamigrene derivatives, cyclization reactions of 1 and 2 were attempted with I_2 in benzene, BF_3 etherate and p-toluenesulfonic acid in benzene. With each reagent, α-snyderol (1) gave complex mixtures of bromine-containing hydrocarbons, none of which were 10-bromo-α-chamigrene[6], by GC-MS comparison. Treatment of β-snyderol with BF_3 etherate and p-toluenesulfonic acid gave complex mixtures, also lacking 10-bromo-α-chamigrene by analogous comparisons. However, I_2 treatment gave a single bicyclic hydrocarbon (3) mixture, epimeric at C-3 (60/40), resulting from cyclization at the exocyclic carbon in 2. These combined results suggest that acid catalyzed double bond migration to the more favorable Δ^6 position in these isomers is slow, relative to cyclization reactions initiated by carbonium ion formation at C-3. Careful investigations of the extracts of these seaweeds failed to show the presence of chamigrene derivatives or the Δ^6 olefin isomer.

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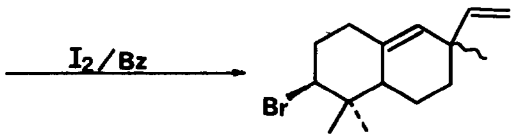

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The structures of **1** and **2** lend support to the contention[1,2] that bromocyclization reactions occur with acyclic precursors in Laurencia. While these and previous results[3,5] support analogous Δ^6 olefin intermediates in bromochamigrene biosynthesis, the monocarbocyclic Laurencia sesquiterpenes caespitol and isocaespitol[7] illustrate the existence of an alternative biosynthetic path involving a γ-bisabolene intermediate. Neither pathway can be discounted.

Acknowledgements

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