on further chromatographic separation afforded the former (110 mg) in a pure form, mp 117°, $[\alpha]_D^{32}$ + 60° (lit. [1] $[\alpha]_D$ 65°, mp 118–119°). IR ν_{max}^{Nujol} cm^{-1}: 3400, (OH) NMR: δ 0.75 and 0.87 (3H, each *d*, $J = 7$ Hz, Me_2CH—), 1.02 and 1.21 (6H, *s*, 2 × Me).

Acknowledgement—The work was financially supported by the Pubjab State Government (India) under the scheme 'Chemistry of some Natural Products and Their Significance in Agriculture'.

REFERENCES

1. Rao, A. A., Surve, K. L., Chakravarti, K. K. and Bhattacharyya, S. C. (1963) *Tetrahedron* **19**, 233.
2. Tirodkar, S. V., Paknikar, S. K. and Chakravarti, K. K. (1969) *Sci. Cult. (India)* **35**, 27.
3. Kalsi, P. S., Chakravarti, K. K. and Bhattacharyya, S. C. (1963) *Tetrahedron* **19**, 1073.
4. Shaligram, A. M., Rao, A. S. and Bhattacharyya, S. C. (1962) *Tetrahedron* **18**, 969.
5. Kalsi, P. S., Kohli, J. C. and Wadia, M. S. (1965) *Indian J. Chem.* **3**, 324.
6. Kalsi, P. S., Gupta, B. C., Chahal, S., Mehta, Y. K. and Wadia, M. S. (1979) *Bull. Soc. Chem.* (in press).
7. Anderson, N. H. (1970) *Phytochemistry* **9**, 145.
8. Seshadri, R., Kalsi, P. S., Chakravarti, K. K. and Bhattacharyya, S. C. (1967) *Tetrahedron* **23**, 1267.
9. Cross, A. D. (1960) *Q. Rev. London* **14**, 317.
10. Aggarwal, R. C., Trivedi, G. K. and Bhattacharyya, S. C. (1975) *Indian J. Chem.* **13**, 876.
11. Trivedi, G. K., Wagh, A. D., Paknikar, S. K., Chakravarti, K. K. and Bhattacharyya, S. C. (1966) *Tetrahedron* **22**, 1961.
12. Aggarwal, S. K., Wadia, M. S., Bhatia, I. S. and Kalsi, P. S. (1970) *Riechst. Aromen* **20**, 169.

Phytochemistry, 1979, Vol. 18, pp. 1224–1225. © Pergamon Press Ltd. Printed in England. 0031-9422/79/0701-1224 $02.00/0

GUADALUPOL AND EPIGUADALUPOL, REARRANGED SESQUITERPENE ALCOHOLS FROM *LAURENCIA SNYDERIAE* VAR. *GUADALUPENSIS*

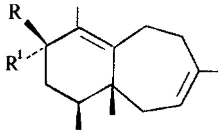
Bruce M. Howard* and William Fenical

Institute of Marine Resources, Scripps Institution of Oceanography, La Jolla, CA 92093, U.S.A.

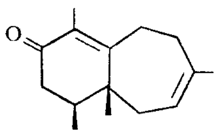
(*Received* 26 *October* 1978)

Key Word Index—*Laurencia synderiae* var. *guadalupensis*; Rhodomelaceae; marine natural products; chemistry; perforenone; sesquiterpene alcohols.

Examinations of the natural products chemistry of the marine alga *Laurencia snyderiae* Dawson (Rhodomelaceae, Rhodophyta) from various habitats have resulted in the isolation of the brominated sesquiterpenoid β-snyderol [1] from the La Jolla, California population, and the unique diterpenoid neocincinndiol hydroperoxide [2] from the Santa Catalina Island, California population. Investigation of the lipid components of *Laurencia snyderiae* var. *guadalupensis*, collected from Isla Guadalupe, Mexico, has now resulted in the isolation of two new epimeric sesquiterpene alcohols, guadalupol (**1**) and epiguadalupol (**2**), the structures of which are reported here.



1 R' = OH; R = H
2 R' = H; R = OH
3 R' = OAc; R = H
4 R' = H; R = OAc

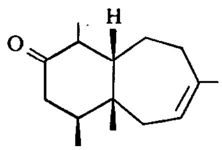


5

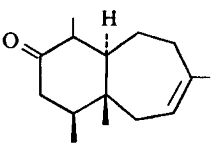
Open column silica gel chromatography of the chloroform–methanol (1:1) extract of the fresh alga gave, upon benzene elution, fractions which contained a mixture of **1** and **2** as oils in equal amounts. Both alcohols exhibited prominent $M^+ - H_2O$ fragments at *m/e* 202 for $C_{15}H_{22}$ in their mass spectra, and hydroxyl absorptions (3500 cm^{-1}) in their IR spectra. Treatment of **1** and **2** with acetic anhydride–pyridine gave the acetates **3** and **4** which suggested these alcohols to be secondary. The ^{1}H NMR spectrum of **1** illustrated a vinyl proton (δ 5.15, *bm*), an α-hydroxy methine proton (δ 3.61, *s*), a methyl doublet (δ 0.86, *d*, $J = 7$ Hz) and six protons between 1.70 and 2.50. The epimeric alcohol **2** provided a ^{1}H NMR spectrum which also exhibited a vinyl proton (δ 5.20, *bm*), a high field methyl (δ 0.75, *s*), a methyl doublet (δ 0.86, *d*, $J = 7$ Hz) and six protons between 1.70 and 2.50. Jones' oxidation of **1** and **2** at +5° yielded the same α,β-unsaturated ketone, **5**, (IR, $\gamma_{C=O}$ 1670 cm^{-1}) which

---

* Present address: Department of Chemistry, San Francisco State University, 1600 Holloway Ave, San Francisco, CA 94132, U.S.A.



6



7

established their epimeric relationship. Lithium in ammonia reduction of **5** gave the *cis* and *trans* ketones **6** and **7**, respectively, which exhibited IR carbonyl stretching absorptions at 1715 cm^{-1}, thus placing the carbonyl group in a six-membered ring or acyclic. The coupling constants for the alcohol methine protons established the stereochemistries of the alcohol groups in both **1** and **2**. In **1**, the alcohol was assigned as pseudo-axial based upon the small coupling constants for the δ 3.61 signal, which imply ax-eq and eq-eq proton couplings. In **2**, the alcohol was assigned as pseudo-equatorial since the larger coupling constants of the δ 4.00 signal more closely compare with ax-ax and ax-eq couplings. Estimates of the dihedral angles of these protons from molecular models and comparison of the observed and calculated coupling constants support these assignments.

Investigation of the non-polar column chromatography fractions from this alga resulted in the isolation of the ketone **5** (perforenone) as a natural product. While this work was in progress, González *et al.* [3], reported the isolation of **5** from the related *Laurencia perforata* and secured its structure by total synthesis [4]. In that study, compounds **1** and **2** were not observed, but their isolation here supports the proposal that these alcohols are intermediates in the interconversion of the perforenone and perforatol ring systems [4].

EXPERIMENTAL

Isolation of guadalupol and epiguadalupol. Freshly collected *Laurencia snyderiae* var. *guadalupensis* (10 kg) was homogenized with MeOH and the homogenate repeatedly extracted with $CHCl_3$ to yield 60 g of crude extract after solvent removal *in vacuo*. Fractionation over Si gel (Grace Chemical, grade 62) gave, upon C_6H_6 elution, fractions which contained mixtures of **1** and **2** (1.5 g). Separation of these mixtures by high pressure liquid chromatography (HPLC) on μ-porasil (CH_2Cl_2) gave purified samples of each compound. For guadalupol (**1**): ^1H NMR (220 MHz, CCl_4) δ 5.15 (1H, *bm*), 3.61 (1H, *bs*), 1.72 (3H, *s*), 1.57 (3H, *s*), 0.86 (3H, *d*, J = 7,7 Hz), 0.73 (3H, *s*); IR (film): 3500, 2950, 1470, 1400, 1250, 1070, 1020, 940, 910, 885, 850, 800 cm^{-1}; MS (70 ev): $M^+ - H_2O$ *m/e* = 202 for $C_{15}H_{22}$. For epiguadalupol (**2**): ^1H NMR (60 MHz, CCl_4) δ 5.20 (1H, *bm*), 4.00 (1H, *dd*, J = 7,7 Hz), 1.70 (3H, *s*), 1.57 (3H, *bs*), 0.86 (3H, *d*, J = 7 Hz), 0.75 (3H, *s*); IR (film): 3450, 2950, 1470, 1250 cm^{-1}; MS (70 eV): $M^+ - H_2O$ *m/e* 202 for $C_{15}H_{22}$.

Guadalupol acetate (**3**) *and epiguadalupol acetate* (**4**). Standard acetylation of **1** and **2** with Ac_2O in Py for 24 hr at 25° gave the acetates **3** and **4** in near quantitative yields. For **3**: ^1H NMR (220 MHz, CCl_4) δ 5.14 (1H, *bm*), 4.93 (1H, *bs*), 1.95 (3H, *s*), 1.57 (6H, *s*), 0.84 (3H, *d*, J = 7 Hz), 0.74 (3H, *s*). For **4**: ^1H NMR (220 MHz, CCl_4) δ 5.20 (1H, *dd*, J = 7,7 Hz), 5.09 (1H, *bm*), 1.95 (3H, *s*), 1.77 (3H, *s*), 1.75 (3H, *s*), 0.86 (3H, *d*, J = 7 Hz), 0.84 (3H, *s*).

Jones' oxidation of (**1**) *and* (**2**). In separate experiments, 35 mg of **1** and **2** were dissolved in Me_2CO and maintained at $-5°$. Jones' reagent was cautiously added with stirring until the orange color persisted, at which time the reaction was diluted with Et_2O (20 ml) and poured onto ice. The Et_2O layer was washed with H_2O (2 × 25 ml) and satd $NaHCO_3$ (2 × 25 ml). The Et_2O was dried ($MgSO_4$), evapd and the crude product purified by PLC on Si gel (10% Et_2O in hexanes) to give the ketone **5**: ^1H NMR (220 MHz, CCl_4) δ 5.20 (1H, *bm*), 2.75 (1H, *m*), 1.93 (1H, *dd*, J = 18, 10 Hz), 1.70 (3H, *s*), 1.57 (3H, *s*), 0.93 (3H, *d*, J = 7 Hz), 0.91 (3H, *s*); IR (CCl_4) 2950, 1685, 1650, 1400, 1350, 1320, 1150, 1050, 850 cm^{-1}.

Lithium in ammonia reduction of the ketone (**5**). To a soln of excess Li in liquid NH_3 maintained at $-78°$ was added 25 mg of **5** in 2 ml dry Et_2O. After stirring for 2 hr, solid NH_4Cl was slowly added and the reaction mixture was allowed to warm to room temp. After all NH_3 had evapd, the residue was taken up in Et_2O, the Et_2O phase was washed with 5% HCl, followed by satd $NaHCO_3$ and finally dried. Removal of the solvent *in vacuo* gave an oily mixture of **6** and **7** which were further separated by HPLC (μ-porasil, 2% Et_2O in trimethylpentane). For **6**: ^1H NMR (220 MHz, $CDCl_3$) δ 5.27 (1H, *bm*), 1.68 (3H, *bs*), 1.02 (3H, *d*, J = 7 Hz), 0.86 (3H, *d*, J = 7 Hz), 0.82 (3H, *s*); IR (film): 2950, 1715, 1450, 1380, 950 cm^{-1}. For **7**: ^1H NMR (220 MHz, $CDCl_3$) δ 5.27 (1H, *bm*), 1.68 (3H, *bs*), 1.14 (3H, *s*), 0.93 (3H, *d*, J = 7 Hz), 0.84 (3H, *d*, J = 7 Hz).

Acknowledgements—We appreciate the financial support for this research from the National Science Foundation, Oceanography Section, under grant No. OCE 75-03824, and for NSF funding of research vessel E. B. Scripps, which enabled us to collect *Laurencia* species at Isla Guadalupe, Mexico. In addition, we wish to acknowledge our use of the NMR Center, University of California, San Diego, which is supported by an NIH grant, No. RR-408. Voucher specimens, identified as *Laurencia snyderiae* var. *guadalupensis* by Dr. Jim Norris, have been deposited in the National Herbarium, Smithsonian Institution, Washington, D.C.

REFERENCES

1. Howard, B. M. and Fenical, W. (1967) *Tetrahedron Letters* 41.
2. Howard, B. M., Fenical, W., Finer, J., Hirotsu, K. and Clardy, J. (1977) *J. Am. Chem. Soc.* **99**, 6440.
3. González, A. G., Darias, J. and Martin, J. D. (1977) *Tetrahedron Letters* 3375.
4. González, A. G., Darias, J., Martin, J. D. and Melian, M. A. (1978) *Tetrahedron Letters* 481.