

A NEW CHAMIGRANE FROM LAURENCIA GLOMERATA

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ABSTRACT.—From the red alga *Laurencia glomerata* four halogenated chamigranes have been isolated, one of which is new. The new metabolite, 4,10-dibromo-3-chloro-7,8-epoxy-9-hydroxy- α -chamigrane [4] was identified by spectroscopic methods.

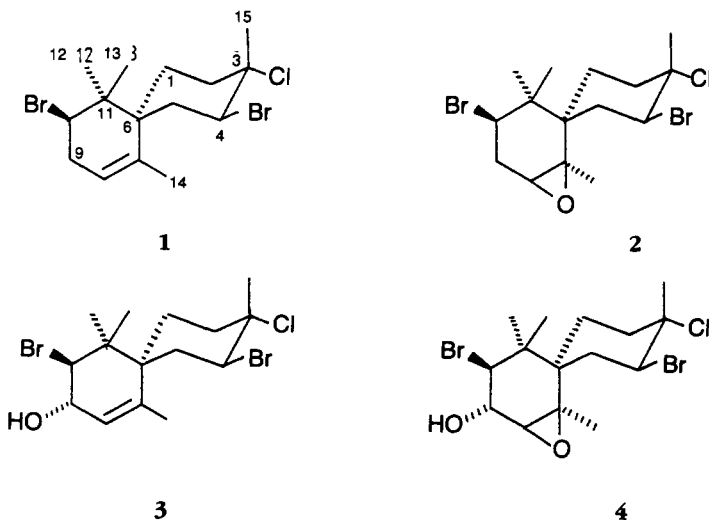
Numerous chamigranes have been isolated from the red seaweed genus *Laurencia* which grows in many geographical areas (1-5). In a first examination of a South African species, *L. glomerata* Kütz. (Rhodomelaceae), we have again encountered a group of chamigranes of which one is new.

The crude PhMe/MeOH extract was fractionated by cc and plc to give the known compounds **1** (6,8,9), **2** (6,7,9,10), and **3** (11,12) isolated previously from other *Laurencia*. They were identified by comparison with literature spectroscopic data and by direct comparison (except for **3**).

The new metabolite **4**, C₁₅H₂₃Br₂ClO₂, contains one atom of oxygen more than **2** and **3** and is related to both. The nmr spectra revealed characteristic chamigrane features such as four methyl singlets

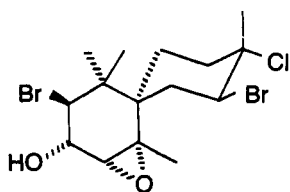
and quaternary carbon signals at δ 44.52 and 42.83 corresponding to C-6 and C-11, respectively. Ring B in **4** was the same as in **1-3**, as indicated by the methyl singlet at δ 1.72 for 3-Me_{ax}, the quaternary carbon signal at δ 70.73 corresponding to C-3 with equatorial chlorine, and the methine carbon at 61.83 indicating equatorial bromine at C-4 (13). The signal at δ 4.78 ($J = 13.1, 5.3$ Hz) coupled to a methylene group can be assigned to H-4_{ax}, and an isolated -CH₂CH₂- group, revealed by decoupling experiments, completes the ring.

In ring A a quaternary carbon signal at δ 64.41 and a methine carbon at 65.14 suggest an epoxide function at C-7-C-8. The bromine occupies its usual equatorial position at C-10 with the H-10_{ax} signal a doublet at δ 3.94 coupled to H-9 (δ 4.22) on the hydroxyl-bearing



carbon ($\nu_{\text{HO}} 3437 \text{ cm}^{-1}$). The coupling constant ($J = 9.2 \text{ Hz}$) is the same as that for H-10 in **3**, suggesting the same trans diequatorial stereochemistry of Br and OH substituents. However, in **4** H-9 is only a doublet, and the epoxy proton signal, H-8, is a singlet at $\delta 3.02$. Examination of a Dreiding model of **4** shows that the dihedral angle between H-8 and H-9 is near to 90° , and zero Hz coupling may be expected. Confirmation of the epoxide environment was obtained by nOe experiments. Irradiation of the 7-methyl proton at $\delta 1.51$ produced a 14% enhancement of each of the signals from H-4, H-5_{eq}, and H-8, while H-8 and H-9 showed mutual enhancement of 3%. Thus, all the spectroscopic data are consistent with the 7 β ,8 β -epoxy- α -chamigrane structure **4** (relative stereochemistry).

Epoxidation of **3** with *m*-chloroperoxybenzoic acid did not yield **4** but the isomeric 7 α ,8 α -epoxide **5**, as expected. Spectroscopically, **5** is very similar to **4**, but the H-8 signal is a doublet at $\delta 3.21$ ($J = 3.0 \text{ Hz}$) coupled to H-9 at 4.12 ($J = 9.5, 3.0 \text{ Hz}$). The ^{13}C -nmr spectrum of **5** is in good agreement with that reported by Sims *et al.* (13: table 14, no other information is available). It has been shown that epoxidation of **1** gives the 7 α ,8 α -epoxy isomer of **2** quantitatively as steric constraints clearly favor attack on the double bond from the α side (6,14). Further, it is known that an allylic hydroxyl group directs epoxidative attack on a double bond from the side of the hydroxyl (15). This dictates the conversion of **3** to **5** isomeric with **4**.



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EXPERIMENTAL

PLANT MATERIAL.—*L. glomerata* (5.60 kg wet wt) was collected at Buffels Bay, Cape Point, and identified by Mr. R.H. Simons, Department of Environment Affairs, Rogge Bay, Cape Town. A specimen has been deposited in the Bolus Herbarium, University of Cape Town.

ISOLATION.—The wet seaweed was washed briefly with fresh H_2O and immediately immersed in MeOH. In the laboratory the MeOH was drained off, the plant material was macerated with PhMe (4 liters) in a blender, and then left overnight. After draining, the seaweed was steeped overnight (twice) in a mixture of PhMe-MeOH (1:3, 4 liters). All extracts were evaporated at $<50^\circ$ to low volume, combined, and dried (MgSO_4). The residual dark green and viscous gum (16.2 g) was transferred to a Florisil column (236 g) and eluted with petroleum ether (bp $70\text{--}85^\circ$) followed with increasing amounts of EtOAc. The petroleum ether fraction after plc on silica in EtOAc-petroleum ether (1:9, bp $60\text{--}80^\circ$) gave **1** as a gum (115 mg). The petroleum ether-EtOAc (9:1) fraction, after plc in EtOAc-petroleum ether (15:85) afforded compound **2**: 90 mg, mp $142\text{--}143^\circ$ (from $\text{C}_6\text{H}_{12}/\text{Et}_2\text{O}$) [lit. (6) $142\text{--}144^\circ$]. The petroleum ether-EtOAc (8:1) fraction yielded, after plc in CHCl_3 and then EtOAc-petroleum ether (15:85), cholesterol (10 mg) and compound **3**: 210 mg, mp $118\text{--}119^\circ$ (from petroleum ether) [lit. (11) $120\text{--}121^\circ$]. The petroleum ether-EtOAc (7:1) fraction gave **4**, obtained as a gum (22 mg) after plc in EtOAc- C_6H_6 (1:3) followed by Me_2CO -petroleum ether (1:5).

EPOXIDE 4.— $[\alpha]^{25}_{\text{D}} + 32.7^\circ$ ($c = 0.91$, CHCl_3); ir (KBr) ν max 3437, 2982, 2943, 1472, 1458, 1396, 1383, 1194, 1057, 845, 779, 739 cm^{-1} ; ^1H nmr (360 MHz, CDCl_3) δ 4.78 (1H, dd, $J = 13.1, 5.3 \text{ Hz}$, H-4), 4.22 (1H, d, $J = 9.2 \text{ Hz}$, H-9), 3.94 (1H, d, $J = 9.2 \text{ Hz}$, H-10), 3.02 (1H, s, H-8), 2.61 (1H, br, exchanged with D_2O , OH), 2.54 (1H, dd, $J = 14.9, 5.3 \text{ Hz}$, H-5_{eq}), 2.40 (1H, br dd, $J = 14.4, 6.0 \text{ Hz}$, H-2_{eq}), 2.35 (1H, ddd, $J = 14.3, 6.0, 2.6 \text{ Hz}$, H-1_{eq}), 2.16 (1H, dd, $J = 14.9, 13.1 \text{ Hz}$, H-5_{ax}), 2.05 (1H, dt, $J = 14.4, 14.4, 6.0 \text{ Hz}$, H-2_{ax}), 1.72 (3H, s, 3-Me), 1.68 (1H, m, H-1_{ax}), 1.51 (3H, s, Me-7), 1.34 (6H, s, 11-Me₂); ^{13}C nmr (90 MHz, CDCl_3) (DEPT) δ 20.10 (C-12), 23.94 (C-15), 25.27 (C-1), 25.37 (C-14), 28.33 (C-13), 38.76 (C-2), 39.97 (C-5), 42.83 (C-11), 44.52 (C-6), 61.83 (C-4), 64.41 (C-7), 65.14 (C-8), 69.66 (C-10), 70.59 (C-9), 70.73 (C-3); cims m/z (rel. int.) $[\text{M} + \text{NH}_4]^+$ 448 (100), 368 (85), 332 (93), 252 (63), 168 (70), 102 (90). Found $[\text{M} + \text{NH}_4]^+$ 446.00922, $\text{C}_{15}\text{H}_{27}^{79}\text{Br}_2^{35}\text{ClNO}_2$ requires 446.00974. Note: Ions m/z 448–332 appear as expected isotopic clusters and m/z 252

$[M + NH_4 \cdot HBr \cdot HCl \cdot HBr]^+$ is also a doublet, m/z 252/254, and must result from a different mode of fragmentation. The ms of **5** shows the same feature.

EPOXIDATION OF **4**.—To a solution of **4** (10 mg) in $CHCl_3$ (2 ml) was added *m*-chloroperbenzoic acid (6 mg), and the mixture was kept at 50° for 24 h. After removal of solvent the residue was purified by plc on silica in $CHCl_3$ to give the epoxide **5** as a gum (7.7 mg): ir (KBr) ν max 3476, 3414, 2978, 2937, 1472, 1385, 1101, 1051, 845, 631 cm^{-1} ; 1H nmr (360 MHz, $CDCl_3$) δ 4.88 (1H, dd, $J = 12.7, 5.6$ Hz, H-4), 4.12 (1H, dd, $J = 9.5, 3.0$ Hz, H-9), 3.90 (1H, d, $J = 9.5$ Hz, H-10), 3.21 (1H, d, $J = 3.0$ Hz, H-8), 2.33 (1H, dd, $J = 14.9, 5.6$ Hz, H-5_{eq}), 2.29 (2H, m, H-1_{eq} and H-2_{eq}), 2.18 (1H, dd, $J = 14.9, 12.7$ Hz, H-5_{ax}), 2.04 (1H, m, H-2_{ax}), 1.70 (3H, s, 3-Me), 1.62 s (3H, s, 7-Me), 1.51 (1H, m, H-1_{ax}), 1.09 and 0.94 (each 3H, s, 11-Me₂), OH not observed; ^{13}C nmr (90 MHz, $CDCl_3$) (DEPT) δ 18.19 (C-12), 24.43 (C-15), 24.76 (C-1), 25.32 (C-14)*, 25.56 (C-13)*, 39.42 (C-2), 40.11 (C-5), 43.84 (C-11), 46.15 (C-6), 62.25 (C-4), 62.71 (C-7), 65.03 (C-8), 67.34 (C-10), 70.66 (C-3), 72.23 (C-9) (* interchangeable); cims m/z (rel. int.) $[M + NH_4]^+$ 448 (100), 368 (59), 332 (98), 252 (45), 168 (71), 102 (87). Found $[M + NH_4]^+$ 446.01051, $C_{15}H_{27}^{79}Br_2^{35}ClNO_2$ requires 446.00974.

ACKNOWLEDGMENTS

We thank SERC Mass Spectrometry Centre and Edinburgh University WH-360 NMR Service for spectra and Dr. A. G. Brown for the optical rotation measurement. We are particularly grateful to Mr. R. H. Simons for locating and collecting the algae.

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Received 13 February 1989