

## REFERENCES

1. Caputo, R., Mangoni, L., Monaco, P. and Palumbo, G. (1978) *Phytochemistry* **18**, 896.
2. Aynechi, Y., Caputo, R., Mangoni, L., Monaco, P. and Palumbo, G. (1979) Work presented at 11th Organic Chemistry Meeting of Italian Chemical Society, Sorrento.
3. Bodenheimer, F. S. and Swirski, E. (1957) *The Aphidoidae of the Middle East*, The Weizmann Science Press of Israel.
4. Caputo, R., Mangoni, L., Monaco, P., Palumbo, G., Aynechi, Y. and Bagher, M. (1978) *Phytochemistry* **17**, 815.
5. Taylor, D. A. H. (1967) *J. Chem. Soc.* 490.
6. Barton, D. H. R., Boar, R. B., Knight, D. C. and McGhie, J. F. (1970) *J. Chem. Soc. C*, 678.
7. Mangoni, L., Monaco, P. and Previtera, L. (1982) *Phytochemistry* **21**, 811.
8. Harborne, J. B. (1977) *Introduction to Ecological Biochemistry*, p. 167. Academic Press, New York.
9. Wertheim, G. (1954) *Trans. R. Ent. Soc. Lond.* **105**, 79.

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## A HALOGENATED CHAMIGRANE EPOXIDE AND SIX RELATED HALOGEN-CONTAINING SESQUITERPENES FROM THE RED ALGA *LAURENCIA OKAMURAI*

MAKOTO OJIKI, YOSHIKAZU SHIZURI and KIYOSUKI YAMADA

Department of Chemistry, Faculty of Science, Nagoya University, Chikusa, Nagoya 464, Japan

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**Key Word Index**—*Laurencia okamurai*; Rhodomelaceae; red alga; sesquiterpenes; halogenated chamigranes; 4, 10-dibromo-3-chloro-7 $\alpha$ , 8 $\alpha$ -epoxy- $\alpha$ -chamigrene.

**Abstract**—From the red alga *Laurencia okamurai* a new chamigrane epoxide and six known halogenated chamigranes were isolated. The structure of the new epoxide was established by spectral and chemical means.

### INTRODUCTION

Previous investigation of the red alga *Laurencia okamurai* (Rhodomelaceae, Rhodophyta) has revealed that the aromatic sesquiterpenes of the laurane- and cuparane-types are characteristic metabolites of the alga, fifteen such compounds having been isolated [1–3]. Johnstonol was a sole member of the chamigrane-type sesquiterpene that was previously isolated in a minute amount from *L. okamurai* [1, 4]. We now describe the isolation from this alga of a new halogenated chamigrane (1) and six halogenated chamigranes, 4,10-dibromo-3-chloro- $\alpha$ -chamigrene (2) [5, 6], 4,10-dibromo-3-chloro-9-hydroxy- $\alpha$ -chamigrene (3) [7], prepacifenol epoxide (4) [8], prepacifenol (5) [9], 1-deoxyrepacifenol (6) [10] and nidificene (7) [11], together with aromatic sesquiterpenes of the laurane-type such as aplysin [1, 3, 12], debromoaplysin [1, 3, 12], laurinterol [2, 3, 13], and isolaurinterol [2, 3, 13].

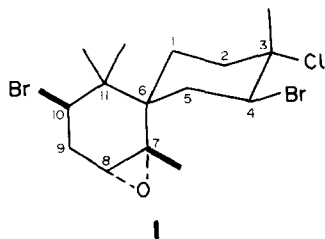
### RESULTS

The fresh alga was extracted with acetone and the resulting extract was further extracted with benzene-ethyl acetate. The oily extract was separated by CC

on Si gel and prep. TLC (Si gel) to give the new compound (1), 2, 3, 6, 7, johnstonol (8) [4], and pacifenol (9) [14].

Since 4 and 5 were found to be transformed partially or completely into 8 and 9, respectively, during CC and TLC, the crude extract of the fresh alga was subjected to separation employing prep. HPLC with a column of the reversed phase [LiChrosorb RP-8 and RP-18; methanol–water (4:1)] to afford 4 and 5. Johnstonol (8) and pacifenol (9) were not detected by analytical TLC of the crude extract, and therefore 8 and 9, obtained after chromatographic separation, must be artifacts.

The structural elucidation of the new compound (1) is as follows. High resolution mass spectral data of 1 established a molecular formula of C<sub>15</sub>H<sub>23</sub>OBr<sub>2</sub>Cl. <sup>1</sup>H NMR spectral data of 1 was similar to but not identical with 4,10-dibromo-3-chloro-7 $\beta$ ,8 $\beta$ -epoxy- $\alpha$ -chamigrene (10) [5], isolated previously from the same algal genus. Based on the spectral data, the new compound was deduced to have structure 1. This was confirmed by direct comparison with a sample of 1 obtained by oxidation of 2 with *m*-chloroperbenzoic acid. Synthesis of 1 from 2 was reported previously [5], but this is the first time that 1 has been isolated as a natural product.



### EXPERIMENTAL

Mps were uncorr. Si gel BW-80 (Fuji-Davison) for CC and Si gel 60 (Merck) for TLC were used, respectively. HPLC was performed on a Jasco Tri Rotar-II liquid chromatograph using a refractive index detector. The isolated yield is based on fr. wt of the alga.

**Extraction.** The alga (*L. okamurai*) was collected in July 1980 at Yasurihama, Mie Prefecture, Japan. The fresh alga (3.2 kg) was extracted with Me<sub>2</sub>CO, and the extract concd to give 2 l. of a dark green soln. The soln was extracted with C<sub>6</sub>H<sub>6</sub> (2 × 1 l.) and EtOAc (1 l.), and the combined extracts were concd to leave a dark green oil (12.5 g).

**Isolation.** (a) A portion of the oil (11 g) was chromatographed on Si gel (330 g) with 3 l. hexane-C<sub>6</sub>H<sub>6</sub> (4:1), 3 l. hexane-C<sub>6</sub>H<sub>6</sub> (1:1) and 9.5 l. C<sub>6</sub>H<sub>6</sub>, successively. The fraction eluted with hexane-C<sub>6</sub>H<sub>6</sub> (4:1) was further separated by prep. TLC with hexane-C<sub>6</sub>H<sub>6</sub> (4:1) to give **2** (142 mg, 4.8 × 10<sup>-3</sup>%) and **7** (12 mg, 3.9 × 10<sup>-4</sup>%). Separation of the eluates from hexane-C<sub>6</sub>H<sub>6</sub> (1:1) by prep. TLC with C<sub>6</sub>H<sub>6</sub> afforded **6**, mp 125–125.5° (lit. [10] mp 125°) (62 mg, 2.1 × 10<sup>-3</sup>%). The early fractions eluted by C<sub>6</sub>H<sub>6</sub> were separated twice by prep. TLC with hexane-Et<sub>2</sub>O (17:3) and with C<sub>6</sub>H<sub>6</sub> to give **1**, mp 123.5–124°, [ $\alpha$ ]<sub>D</sub><sup>25</sup> + 13° (CHCl<sub>3</sub>; c 0.4) (5 mg, 1.6 × 10<sup>-4</sup>%). **1**: IR  $\nu_{\text{max}}^{\text{CCl}_4}$  cm<sup>-1</sup>: 879, 845, 821; <sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>):  $\delta$  0.94 (3H, s), 1.10 (3H, s), 1.55 (3H, s), 1.71 (3H, s), 1.8–2.8 (8H, m), 2.95 (1H, br s), 4.10 (1H, dd, J = 11, 6 Hz), 4.86 (1H, dd, J = 11, 7 Hz); MS 70 eV m/z 418 (0.5), 416 (2.9), 414 (3.4), 412 (2.1) [M]<sup>+</sup>, 337 (5.2), 335 (22), 333 (16) [M - Br]<sup>+</sup>, 119 (100); high resolution MS m/z 414 [M]<sup>+</sup>. Found 413.9797; calc. for C<sub>15</sub>H<sub>23</sub>O <sup>79</sup>Br<sup>81</sup>Br<sup>35</sup>Cl 413.9785. The middle fractions of the C<sub>6</sub>H<sub>6</sub> eluates afforded **9**, mp 150–151° (lit. [14] mp 149–150.5°) (1350 mg, 4.5 × 10<sup>-2</sup>%). The later fractions of the C<sub>6</sub>H<sub>6</sub> eluates gave **8**, mp 176–179° (lit. [4] mp 178°) (940 mg, 3.2 × 10<sup>-2</sup>%) and separation of the mother liquor by prep. TLC with hexane-EtOAc (3:1) yielded **3**, mp 118.5–119° (lit. [7] mp 120–121°) (211 mg, 7.1 × 10<sup>-3</sup>%).

(b) A portion of the oil (0.88 g) obtained from the C<sub>6</sub>H<sub>6</sub>-EtOAc extract of the alga was separated by HPLC under the following conditions: Lobar column (LiChrosorb PR-8, size A), MeOH-H<sub>2</sub>O (4:1), flow rate of 2 ml/min. Fractions with retention times between 18 and 36.5 min were collected and concd to give an oily mixture (297 mg). The mixture was subsequently separated by HPLC under the conditions [a column (250 × 4.6 mm) of LiChrosorb RP-18, MeOH-H<sub>2</sub>O

(7:3), flow rate of 1 ml/min] to afford **4**, mp 101–104° (lit. [8] mp 98–99°) (58 mg, 2.5 × 10<sup>-2</sup>%), and **5**, mp 129–133° (lit. [9] mp 109–126°, 147°) (77 mg, 3.4 × 10<sup>-2</sup>%).

**Transformation of 2 to 1.** A mixture of **2** (13.5 mg) and *m*-chloroperbenzoic acid (17.5 mg) in CHCl<sub>3</sub> (1 ml) was stirred at room temp. for 5 hr. After addition of NaHSO<sub>3</sub> (10 mg) the mixture was diluted with H<sub>2</sub>O (1 ml)-CHCl<sub>3</sub> (10 ml). The organic layer was separated, washed with satd NaCl soln, dried, and evaporated to give an oily mixture (24 mg). Separation of the mixture by prep. TLC with hexane-CHCl<sub>3</sub> (2:3) gave crude crystals (11.3 mg), recrystallization of which from hexane afforded **1** (5.8 mg), mp 124° (mmp with natural **1**, 123.5–124°).

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### REFERENCES

- Irie, T., Suzuki, M. and Hayakawa, Y. (1969) *Bull. Chem. Soc. Jpn.* **42**, 843.
- Suzuki, M. and Kurosawa, E. (1978) *Tetrahedron Letters* 2503.
- Suzuki, M. and Kurosawa, E. (1979) *Bull. Chem. Soc. Jpn.* **52**, 3352.
- Sims, J. J., Fenical, W., Wing, R. M. and Radlick, P. (1972) *Tetrahedron Letters* 195.
- Howard, B. M. and Fenical, W. (1975) *Tetrahedron Letters* 1687.
- Suzuki, M., Furusaki, A. and Kurosawa, E. (1979) *Tetrahedron* **35**, 823.
- Fenical, W. (1976) *Phytochemistry* **15**, 511.
- Faulkner, D. J., Stallard, M. O. and Ireland, C. (1974) *Tetrahedron Letters* 3571.
- Sims, J. J., Fenical, W., Wing, R. M. and Radlick, P. (1973) *J. Am. Chem. Soc.* **95**, 972.
- Ireland, C., Stallard, M. O., Faulkner, D. J., Finer, J. and Clardy, J. (1976) *J. Org. Chem.* **41**, 2461.
- Waraszkiewicz, S. M. and Erickson, K. L. (1974) *Tetrahedron Letters* 2003.
- Yamamura, S. and Hirata, Y. (1963) *Tetrahedron* **19**, 1485.
- Irie, T., Suzuki, M., Kurosawa, E. and Masamune, T. (1970) *Tetrahedron* **26**, 3271.
- Sims, J. J., Fenical, W., Wing, R. M. and Radlick, P. (1971) *J. Am. Chem. Soc.* **93**, 3774.