

A NEW LABILE BROMOTERPENOID FROM THE RED ALGA *LAURENCIA MAJUSCULA*:  
DEHYDROCHLOROPREPAFENOL

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(Received in UK 14 September 1987)

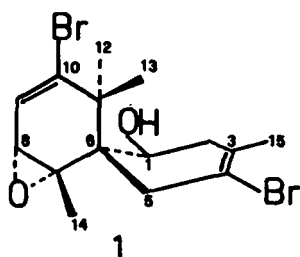
**Abstract** - A new labile brominated chamigrene, dehydrochloroprepacifenol, was isolated from the red alga *Laurencia majuscula*. The structure of this compound was determined by its spectral properties and low-temperature X-ray diffraction analysis.

The red seaweed genus *Laurencia* is a rather prolific source of halogenated metabolites<sup>1,2</sup>. Among the sesquiterpenes, new halogenated chamigrenes continue to be disclosed with surprising frequency from already investigated species of this genus. This fact can be explained by the usual dominance of one very major metabolite in a species associated with several minor components hardly separable, and by the marked variability of the constituents from the same species collected at different sites<sup>3</sup>.

As a part of our study in isolating halogenated and antimicrobial metabolites from *Laurencia* species collected in the Mediterranean Sea<sup>3-6</sup>, we became interested in *L. majuscula* because of the distinct antimicrobial activity of its extract against *Bacillus subtilis* and *Escherichia coli* and since two compounds only are reported from this species collected in Japanese waters<sup>7</sup>.

In this paper we wish to describe the structure of a new chamigrene derivative, isolated as a minor component from the above species and unstable at room temperature to the X-rays and acidic solvent.

The fresh alga *Laurencia majuscula* was soaked in *i*-PrOH. Then, the concentrate from the *i*-PrOH/sea water solution was partitioned between Et<sub>2</sub>O and NaNO<sub>3</sub> solution. The yield of the ether extract obtained with this procedure was much higher than that from a previous procedure that started from dried alga<sup>5</sup>. In our opinion, in this way the cellular lysis of the turgid seaweed that releases a liquor containing metabolites during the drying is avoided. The ether extract was chromatographed on a silica gel column to obtain from some pooled fractions dehydrochloroprepacifenol **1**, crystallized from dichloromethane/hexane, m.p. 124-125°,  $[\alpha]_D^{20} +51.7^\circ$ , 0.16% extract. High resolution electron-impact mass spectrometry established the elemental composition C<sub>15</sub>H<sub>18</sub>Br<sub>2</sub>O for the M-H<sub>2</sub>O<sup>+</sup> fragment. The molecular ion was too weak to measure but it was clearly detected at *m/z* 390 (C<sub>15</sub>H<sub>20</sub><sup>79</sup>Br<sub>2</sub>O<sub>2</sub>) by field desorption mass spectrometry and at M+H<sup>+</sup> by FAB MS. The IR spectrum exhibited significant ab-



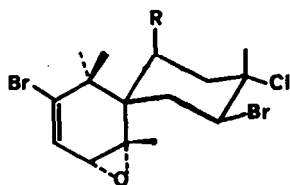
sorptions ( $\text{cm}^{-1}$ ) for hydroxyl (3630), a quaternary carbon bearing two methyls (1195), isolated double bonds (1640, 800), epoxide (1295, 875, 860) and further illustrated the absence of carbonyl functionality. A strong absorption at  $1380\text{ cm}^{-1}$  flanked by small bands at 1395 and 1370 is characteristic of a spiro carbon skeleton<sup>8,9</sup>. Only end absorption was noted in the UV spectrum.

The  $^{13}\text{C}$  NMR spectrum (Table 1) revealed six quaternary carbons with three of them involved in substituted olefinic bonds ( $\delta$ 144.1, 130.0 and 116.0), one confirming the  $\text{R}_2\text{-C-(CH}_3)_2$  moiety (45.6), one oxygen-bearing

Table 1.  $^1\text{H}$  and  $^{13}\text{C}$  NMR data for dehydrochloroprepacifenol (1) (see Experimental section for details)

| Position | $\delta_{\text{C}}$ | $\delta_{\text{H}}$ (J)  | Protons correlated   |
|----------|---------------------|--|--|
| 1        | 68.3 d              | 3.96 m   | $\text{H}_{2a}, \text{H}_{2b}$   |
| 2        | 41.6 t              | $\begin{cases} \text{H}_a & 2.99 \text{ br d} \\ \text{H}_b & 2.11 \text{ br d} \end{cases}$ | $\text{H}_1, \text{H}_{2b}, \text{H}_{15}$<br>$\text{H}_1, \text{H}_{2a}, \text{H}_{15}$ |
| 3        | 116.0 s             |  |  |
| 4        | 130.0 s             |  |  |
| 5        | 37.0 t              | $\begin{cases} \text{H}_a & 2.93 \text{ br d} \\ \text{H}_b & 2.52 \text{ br d} \end{cases}$ | $\text{H}_{5b}$<br>$\text{H}_{5a}$   |
| 6        | 50.9 s              |  |  |
| 7        | 60.9 s              |  |  |
| 8        | 57.6 d              | 2.95 d (3.0)   | $\text{H}_9$   |
| 9        | 124.6 d             | 6.29 d (3.0)   | $\text{H}_8$   |
| 10       | 144.1 s             |  |  |
| 11       | 45.6 s              |  |  |
| 12       | 26.9 q              | 1.39 s   | $\text{H}_{13}$  |
| 13       | 27.2 q              | 1.20 s   | $\text{H}_{12}$  |
| 14       | 22.4 q              | 1.42 s   |  |
| 15       | 22.7 q              | 1.83 s   | $\text{H}_{2a}, \text{H}_{2b}$   |
| OH       |                     | 1.34 d (6.0)   |  |

(60.9) and a spiro carbon resonating at 50.9 ppm that agrees with other chamigrenes data<sup>10</sup>. The resonance at 116 ppm could be, in principle, attributed to a ketal quaternary carbon; however this possibility can be ruled out because one of the two oxygen atoms contained in the molecule forms an hydroxyl. One of the three tertiary carbons is part of an olefinic bond (124.6), the remaining two can be assigned to  $\text{R}_2\text{CHOH}$  (68.3) and  $\text{R}_2\text{CHOR}$  (57.6) analogously to reported chamigrenes data<sup>10</sup>. The two secondary carbons (41.6 and 37.0) are strongly  $\alpha$ -deshielded. The remaining four resonances in the range  $27.2 + 22.7$  ppm are due to methyl singlets and are diagnostic of a sesquiterpene skeleton. Multiplicities of the  $^{13}\text{C}$  NMR resonances were determined by INEPT experiments. The  $^1\text{H}$  NMR spectrum (Table 1) indicate at  $\delta$ 3.96 (m, X of ABX) one proton  $\alpha$  to hydroxyl, at  $\delta$ 2.11 (broad d) and  $\delta$ 2.99 (br d) two methylene protons AB of ABX, at  $\delta$ 2.52 (br d) and  $\delta$ 2.93 (br d) two protons of an isolated AB methylene system. The spectrum also contained four methyl singlets characteristic of sesquiterpenoids at  $\delta$ 1.20, 1.39, 1.42 and 1.83, the last signal indicative of a methyl group downfield shifted by a vicinal double bond or bromine, and an hydroxylic proton at  $\delta$ 1.34 (d,  $J = 6$  Hz). A key feature of the  $^1\text{H}$  NMR spectrum is the presence of only one olefinic proton at  $\delta$ 6.29 coupled ( $J = 3$  Hz) with an  $\alpha$ -oxygen proton resonating at  $\delta$ 2.95 (d). Since this oxygen atom is involved in an epoxide ring, the moiety  $\text{Br-C=CH-CH-O}$  can be suggested.

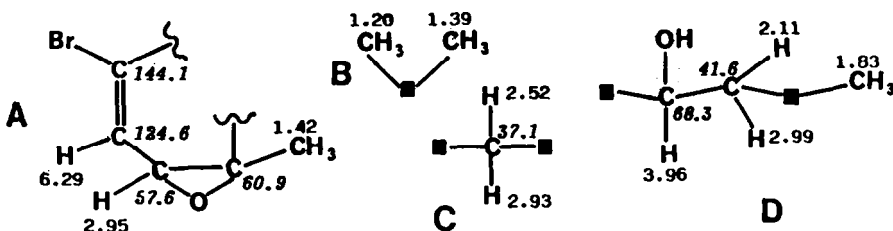


2 R=H  
3 R=OH

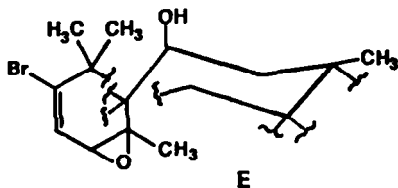
This fragment is present in the naturally occurring chamigrene derivatives 2 and 3 from *Laurencia*;  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra show a close similarity for A-ring resonances of 1, 2<sup>10,11</sup> and 3<sup>12</sup> ( $^{13}\text{C}$  NMR data of 3 are curiously unreported).

Bidimensional NMR gave additional information on the structure. Table 1 shows in fact the observed  $^1\text{H}$ - $^1\text{H}$  shift correlations. Also, the one bond  $^1\text{H}$ - $^{13}\text{C}$  correlations afforded the unequivocal assignments of the protonated carbons in the  $^{13}\text{C}$  NMR spectrum of 1.

The spectral features were all combined to define the partial structures A, B, C and D, where numbers designate pertinent resonances for protons and carbons (in italics) and ■ denotes a quaternary carbon. Taking into account that we observe six quaternary carbons and that the compound possesses

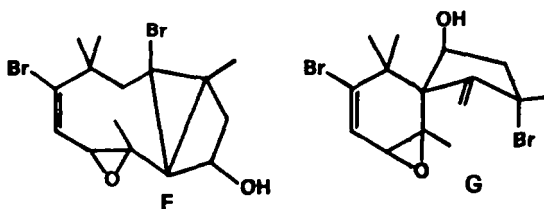


a sesquiterpene skeleton, combination of the above partial structures leads to the substructure E.



Since the NMR data indicate the presence of an additional tetrasubstituted double bond and of an additional bromine bonded to a quaternary carbon, and the IR spectrum indicates the presence of a spiro carbon atom and the elemental composition requires five degrees of unsaturation, the atoms must be linked to lead unavoidably to structure 1 (devoid of stereochemistry) for dehydrochloroprepacifenol. Alternative structures derived through appropriate linkages from the substructure E, as F and G, satisfy to the observed carbons multiplicities and to the required unsaturations: however, structure F does not possess a tetrasubstituted double bond including a downfield methyl group, as required by  $^1\text{H}$  and  $^{13}\text{C}$  NMR data; structure G does not possess the tetrasubstituted double bond, showing instead an unobserved exocyclic methylene group. They can be thus ruled out.

Dehydrochloroprepacifenol, when left in a NMR tube in  $\text{CDCl}_3$  for two days, converted spontaneously to an unidentified compound. The  $^1\text{H}$  NMR spectrum of it indicates that a bridged O(1) - C(10) ether was formed, lacking the epoxide ring and having a 8,9-disubstituted double bond. This proposed cyclization is the same as the observed formation of pacifenol from prepacifenol<sup>12</sup>.



Confirmation of this delucidation, including absolute stereochemistry, was provided by single-crystal X-ray structure determination. Because of the thermolability of 1, after a failed attempt at room temperature, it was necessary to make X-ray measurement at  $-43^\circ\text{C}$ .

The skeleton of the molecule is constituted by two nearly orthogonal cyclohexene rings which share a common tetrahedral carbon atom. Each of them carry one bromine and one oxygen atom as shown

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in Figure 1. Neglecting the methyl substituents, the two rings are almost similar; their conformations are essentially determined by the presence of the ethylenic bond. In both rings, the rigid group tend to constrain half of the ring in a planar arrangement while the tetrahedral carbon chain favor a flexible off-plane disposition similar to cyclohexane.

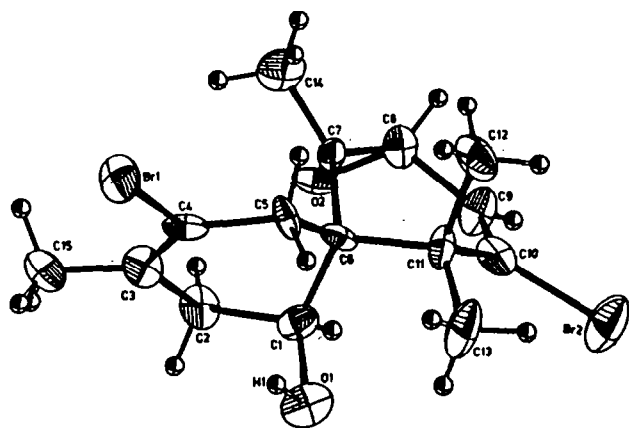


Fig. 1. View of the absolute configuration of **1** indicating the numbering scheme.

The internal bond angles (Table 2) and the deviations from the weighted least-squares planes (Table 3) reveal that a compromise is adopted between the two extreme solutions. This compromise is more evident from the puckering coordinates<sup>13</sup>. In the first ring C(1)-C(6) the half-chair conformation <sup>1</sup>H<sub>6</sub> ( $\varphi = -29(2)^\circ$ ,  $\phi = 52(2)^\circ$  and  $Q = 0.48(2)$ ) is adopted while for the second, C(6)-C(11), the screw-boat <sup>6</sup>S<sub>1</sub> ( $\varphi = 156(2)^\circ$ ,  $\phi = 114(2)^\circ$  and  $Q = 0.52(2)$ ) is favored with almost the same deviation from planarity.

Table 2. Bond distances (Å) and angles (°)

|                     |         |                       |         |
|---------------------|---------|-----------------------|---------|
| Br(1) - C(4)        | 1.89(1) | C(4) - C(5)           | 1.52(2) |
| Br(2) - C(10)       | 1.91(2) | C(5) - C(6)           | 1.53(2) |
| O(1) - C(1)         | 1.43(2) | C(6) - C(7)           | 1.57(2) |
| O(1) - H(1)         | .94(15) | C(6) - C(11)          | 1.58(2) |
| O(2) - C(7)         | 1.46(2) | C(7) - C(8)           | 1.44(2) |
| O(2) - C(8)         | 1.43(2) | C(7) - C(14)          | 1.50(2) |
| C(1) - C(2)         | 1.51(2) | C(8) - C(9)           | 1.48(2) |
| C(1) - C(6)         | 1.52(2) | C(9) - C(10)          | 1.30(2) |
| C(2) - C(3)         | 1.48(2) | C(10) - C(11)         | 1.51(2) |
| C(3) - C(4)         | 1.34(2) | C(11) - C(12)         | 1.58(2) |
| C(3) - C(15)        | 1.46(2) | C(11) - C(13)         | 1.56(2) |
| C(1) - O(1) - H(1)  | 98(9)   | O(2) - C(7) - C(6)    | 115(1)  |
| C(7) - O(2) - C(8)  | 60(1)   | C(6) - C(7) - C(14)   | 120(1)  |
| O(1) - C(1) - C(6)  | 114(1)  | C(6) - C(7) - C(8)    | 117(1)  |
| O(1) - C(1) - C(2)  | 109(1)  | O(2) - C(7) - C(14)   | 112(1)  |
| C(2) - C(1) - C(6)  | 111(1)  | O(2) - C(7) - C(8)    | 59(1)   |
| C(1) - C(2) - C(3)  | 117(1)  | C(8) - C(7) - C(14)   | 119(1)  |
| C(2) - C(3) - C(15) | 118(1)  | O(2) - C(8) - C(7)    | 61(1)   |
| C(2) - C(3) - C(4)  | 117(1)  | C(7) - C(8) - C(9)    | 121(1)  |
| C(4) - C(3) - C(15) | 125(2)  | O(2) - C(8) - C(9)    | 118(1)  |
| Br(1) - C(4) - C(3) | 121(1)  | C(8) - C(9) - C(10)   | 118(1)  |
| C(3) - C(4) - C(5)  | 125(1)  | Br(2) - C(10) - C(9)  | 117(1)  |
| Br(1) - C(4) - C(5) | 114(1)  | C(9) - C(10) - C(11)  | 124(1)  |
| C(4) - C(5) - C(6)  | 114(1)  | Br(2) - C(10) - C(11) | 119(1)  |
| C(1) - C(6) - C(5)  | 108(1)  | C(6) - C(11) - C(10)  | 110(1)  |
| C(5) - C(6) - C(11) | 109(1)  | C(10) - C(11) - C(13) | 111(1)  |
| C(5) - C(6) - C(7)  | 112(1)  | C(10) - C(11) - C(12) | 107(1)  |
| C(1) - C(6) - C(11) | 114(1)  | C(6) - C(11) - C(13)  | 114(1)  |
| C(1) - C(6) - C(7)  | 108(1)  | C(6) - C(11) - C(12)  | 110(1)  |
| C(7) - C(6) - C(11) | 106(1)  | C(12) - C(11) - C(13) | 105(1)  |

H(1)...O(2) 2.04(16) O(1)...O(2) 2.85(1) O(1)...H(1)...O(2) 144(13)

Both rings exhibit however some tensions that, with the epoxyde group, might explain the thermal instability of this compound observed during the X-ray analysis and found for other similar structure<sup>14</sup>. These considerations are confirmed by the geometry of both ethylene fragments, which is signi

ificantly distorted from the ideal conformation (slightly more in the second ring), as shown by the plane 3 and 4 in Table 3. In the first ring it is interesting to observe the short length of the C(9)-C(10) double bond caused by the methyl substituent in *cis* position to the bromine atom.

Table 3. Selected weighted least-squares planes<sup>1</sup> with deviations (Å)<sup>2</sup> and dihedral angles (°)

|          |         |          |         |         |         |         |        |       |        |       |
|----------|---------|----------|---------|---------|---------|---------|--------|-------|--------|-------|
| plane 1: | C(1)*   | -.34     | C(2)*   | .12     | C(3)*   | .08     | C(4)*  | -.05  | C(5)*  | -.12  |
|          | C(6)*   | .28      | Br(1)   | -.19    | C(15)   | .24     | O(1)   | -1.77 | H(1)   | -1.91 |
|          | C(7)    | 1.84     | C(11)   | -.14    |         |         |        |       |        |       |
| plane 2: | C(7)*   | -.10     | C(8)*   | -.14    | C(9)*   | .15     | C(10)* | .05   | C(11)* | -.31  |
|          | C(6)*   | .34      | Br(1)   | .15     | O(2)    | .94     | C(12)  | -1.88 | C(13)  | .06   |
|          | C(14)   | -.96     | C(1)    | 1.86    | C(5)    | -.15    |        |       |        |       |
| plane 3: | C(5)*   | .04      | Br(1)*  | .00     | C(4)*   | .02     | C(3)*  | .00   | C(15)* | -.06  |
|          | C(2)    | -.06     | C(1)    | -.43    | C(6)    | .35     | O(1)   | -1.85 |        |       |
| plane 4: | C(8)*   | -.09     | C(9)*   | .07     | C(10)*  | .08     | Br(2)* | .00   | C(11)* | -.01  |
|          | C(12)   | -1.55    | C(13)   | .45     | C(7)    | .20     | C(14)  | -.53  | O(2)   | 1.09  |
|          | C(6)    | .77      |         |         |         |         |        |       |        |       |
| plane 5: | C(7)*   | .00      | C(8)*   | .00     | O(2)*   | .00     | C(6)   | -1.36 | C(14)  | 1.30  |
|          | C(9)    | -1.22    |         |         |         |         |        |       |        |       |
|          | 1 - 2 = | 67.2(5)  | 1 - 3 = | 6.6(3)  | 1 - 4 = | 63.2(5) |        |       |        |       |
|          | 1 - 5 = | 23.9(7)  | 2 - 3 = | 60.6(4) | 2 - 4 = | 10.1(5) |        |       |        |       |
|          | 2 - 5 = | 121.7(7) | 3 - 4 = | 56.7(4) | 3 - 5 = | 21.3(7) |        |       |        |       |
|          | 4 - 5 = | 121.2(7) |         |         |         |         |        |       |        |       |

<sup>1</sup>the atoms defining the plane are characterized by \*.

<sup>2</sup>all the deviation E.S.D. are in the range 0.02-.002.

The C-C single bond distances show a relatively large range 1.44-1.58 Å with a mean value of 1.52 Å. The largest value is observed between the two carbon atoms of the epoxyde bond as expected. The carbon-oxygen bonds have a mean value close to 1.43 Å. In the epoxyde fragment C(7)-O(2)-C(8) the geometry is almost a regular triangle; the O(2)-C(7) distance is slightly longer. This is probably due to the difference in substitution between C(7) and C(8). This structure is similar to the analogous molecule reported by Suzuki et al.<sup>15</sup>. In the present structure, the epoxide and C-Br bonds are shorter. For the bromine distance, the difference is significant. The close double bond which causes an electron delocalization in the planar C=C-Br system might be a possible explanation.

The crystal packing is characterized by the existence of an intermolecular hydrogen bond between the hydroxyl oxygen O(1) and the epoxyde O(2), (see Table 2). Each molecule is connected by hydrogen bridges to the two nearest neighbours related by the transformation  $-x; y-1/2; -z+3/2$  and  $-x; y+1/2; -z+3/2$ ; They form infinite chains along the *b* direction (see Figure 2; only the hydroxyl hydrogen is reported).

It would be interesting to know if compound 1 is a biosynthetic precursor of the prepaçifanol 3 or is derived by loss of hydrogen chloride from the prepaçifanol. Among the marine natural sesquiterpenes there are two reported structures presumably derived by loss of hydrogen bromide, bicyclocalaurone<sup>16</sup> from  $\alpha$ -snyderol and nidifidiene<sup>17</sup> from nidificene respectively, and only one structure derived by loss of hydrogen chloride, 10-bromo-3,4-epoxy- $\alpha$ -chamigrene<sup>15</sup> from glanduliferol.

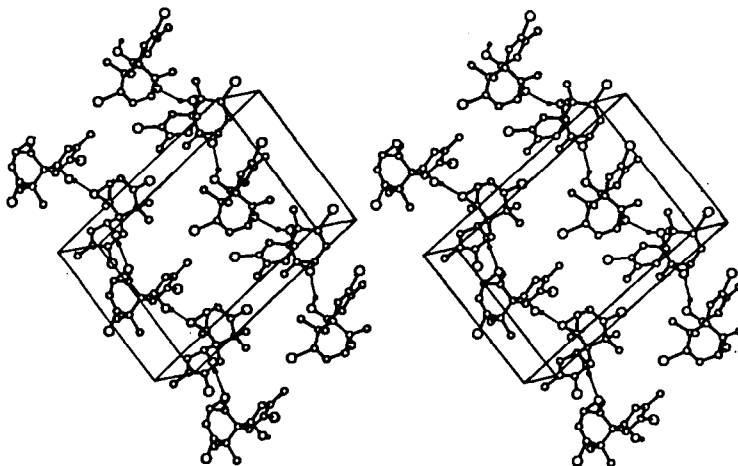


Fig. 2. Stereoscopic view of the crystal packing and hydrogen bond. Calculated H-atoms have been omitted for clarity.

#### EXPERIMENTAL

M.p. was taken on a Kofler block and is uncorrected. Mass spectral analyses (EI, FAB glycerol, HR) were performed with a Kratos MS 50 instrument (direct probe). FD mass spectrum was obtained with a Finnigan MAT 731 instrument. IR and UV spectra were obtained on a Perkin-Elmer model 684 spectrophotometer, assisted by a 3600 data station, and on a Perkin-Elmer model 330 instrument, respectively.  $^1\text{H}$  NMR spectra were measured at 80 MHz, 250 MHz and 400 MHz (HOMOCOSY) on Bruker WP-80, AC-250 and AM-400 instruments, respectively.  $^{13}\text{C}$  NMR spectra were run at 62.5 MHz on a Bruker AC-250 instrument including INEPT and HETERO COSY pulse sequences. Chemical shifts are quoted in  $\delta$  (ppm) relative to TMS and solvent was  $\text{CDCl}_3$ . Optical rotation was measured with a Perkin-Elmer 141 polarimeter. HPLC was carried out on a Varian 5020 instrument, detector at 235 nm.

**Plant material.** *Laurencia majuscula* (Harvey) Lucas was collected at Castelluccio, eastern Sicily, in August 1985 and identified by Prof. Y. Saito at Hokkaido University. It grows as scattered, red-brown clumps 2-3 cm tall in littoral zones. A voucher specimen was deposited in the Herbarium of the Algology Laboratory of the Institute of Botany at the University of Catania.

**Extraction and Isolation.** The fresh alga (approximately 10 kgs wet wt.) was immediately soaked in *i*-PrOH and left steeping for three months. The material was then filtered and the algal residue was repeatedly homogenized with *i*-PrOH in a Waring blender and filtered. The exhausted dried powdered residue weighted 490 g. Room temperature rotary evaporation of the *i*-PrOH/sea water solution gave a concentrate that was taken up in  $\text{Et}_2\text{O}$  and partitioned with saturated  $\text{NaNO}_3$  solution. The ether layer was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to give 26.5 g of dark green viscous oil.

When assayed for antimicrobial activity, the crude extract inhibited the growth of *Bacillus subtilis* and *Escherichia coli* at a concentration of 100  $\mu\text{g}/6\text{mm}$  disc in the disc diffusion on agar-seeded plates test. At the same concentration, compound **1** and pacifenol (see later) turned out to be inactive. Nevertheless, bioautography of the extract suggests that its activity is due to other more polar unidentified components.

The crude extract showed in analytical HPLC several chromatographic peaks, prior to open column chromatography. That **1** is in fact a natural product was borne out spiking one of these peaks with an isolated pure sample of it in two different elution solvents.

The crude extract was applied to a silica gel column (70-230 mesh, 700 g) and chromatographed using increasing concentration of  $\text{Et}_2\text{O}$  in petroleum ether. Fractions eluted with 10%  $\text{Et}_2\text{O}$  and exhibiting similar TLC profiles were combined to give an oily residue ( $R_f$  0.24 on  $\text{SiO}_2$  plates, hexane/ $\text{Et}_2\text{O}$  (85:15) as eluant). After washing with cold pentane, this oil solidified and it was recrystallized from dichloromethane/hexane to yield colorless needles of dehydrochloroprepacifenol (42 mg, m.p. 124-125°, 0.16% extract),  $[\alpha]_D^{20}$  ( $\lambda$ , nm) +51.7 (589), +52.6 (578), +61.4 (546), +117.5 (436), +212.3 (365) (c 1.1,  $\text{EtOH}$ ); IR  $\nu_{\text{max}}^{\text{CCl}_4}$   $\text{cm}^{-1}$ : 3630, 3470, 1640, 1470, 1380, 1295, 1195, 1070, 875, 860, 800; HRMS  $\text{C}_{15}\text{H}_{18}^{79}\text{Br}_2\text{O}$  (obs.  $m/z$  371.9733,  $\Delta = 0.8$  mmu) for the  $\text{M}-\text{H}_2\text{O}^+$  fragment; MS 13 eV,  $m/z$  ( $\Sigma$ ): 372 (7), 374 (12), 376 (8), 311 (10), 313 (10), 293 (72), 295 (78), 281 (40), 279 (55), 277 (28), 265 (21), 267 (22), 251 (29), 237 (21), 213 (96), 199 (100), 97 (82), 43 (62).

HPLC  $K'$  3.45 ( $\text{CH}_2\text{Cl}_2$ , LiChrosorb Si 100, 250  $\times$  4).

Chromatographic fractions eluted with 30%  $\text{Et}_2\text{O}$  in petroleum ether gave the much more abundant pacifenol (3:82 g, 15% extract), identified by comparison of its m.p. and  $^1\text{H}$  NMR spectrum with those previously reported<sup>5</sup>.

**Crystal Data.**  $\text{C}_{15}\text{H}_{20}\text{Br}_2\text{O}_2$ ,  $M = 392.130$ , Orthorhombic, Space group  $\text{P2}_12_12_1$  (ITC No. 19),  $a = 6.707(3)$ ,  $b = 12.364(4)$ ,  $c = 18.238(6)\text{\AA}$ ,  $V = 1512\text{\AA}^3$ ,  $Z = 4$ ,  $F(000) = 784$ ,  $D_c = 1.72$ , Nb-filte-

red MoK $\alpha$  radiation ( $\lambda = 0.71069 \text{ \AA}$ ),  $\mu(\text{MoK}\alpha) = 53.04 \text{ cm}^{-1}$ .

**Data Collection and Refinement.** A colourless crystal with an approximately prismatic habit and dimensions 0.45 x 0.11 x 0.14 mm was mounted on a Syntex P2<sub>1</sub> four circle diffractometer. Owing to the thermal instability under X-ray irradiation, the measurements were performed at 230 K. An asymmetric set of 1566 unique reflections was collected with  $2 < 2\theta < 50^\circ$  by the  $\phi$ - $2\theta$  scan method. Intensities were evaluated according to the Lehmann-Larsen algorithm. The 3 reference intensities, monitored at intervals of 50 measurements showed only mirror statistical fluctuations during the whole data collection. The space group was unequivocally determined by the systematic absence: h00 with h odd, 0k0 with k odd, 00l with l odd. The data reduction was performed by XRAY76<sup>18</sup>. The reflections were corrected for Lorentz, polarization and secondary extinction effects; no absorption correction was made program. The solution and refinement of the structure was obtained from SHELX76<sup>19</sup>, considering as less-than 719 reflections with  $I < 3\sigma(I)$ . The atomic scattering factors and anomalous dispersion terms were taken from the International Tables for X-ray Crystallography (1974).

**Structure Analysis.** The structure was solved by the heavy atom method, locating the two bromine positions from a three-dimensional Patterson map. Positions of the carbon and oxygen atoms were located by successive weighted difference Fourier syntheses. The structure was refined up to  $R = 0.061$  by the full matrix least squares technique based on  $F$ , with anisotropic non-hydrogen atoms. Most hydrogen atoms were located on a Difference Fourier map. Their calculated positions were included in the refinement but not refined (C-H = 0.96Å and U = 0.045Å<sup>2</sup>). The hydroxyl hydrogen was refined with constrained O-H bond length and thermal parameter (0.94Å and 0.045Å<sup>2</sup> resp.). The refinement converged finally to  $R = 0.049$  and  $R_w = 0.047$ . The weighting scheme  $w = 0.980/(\sigma^2(F) + 0.00090 F^2)$  with  $\sigma(F)$  calculated from the counting statistics were applied. The final difference Fourier indicated residues around the bromine positions (0.4-0.9 e/Å<sup>3</sup> at a distance 0.9-1.2Å); this is due to the relevant absorption effects which is not been corrected for. The refinement with a reversed chirality of the molecule converged to  $R = 0.059$  and  $R_w = 0.057$ . This result was also confirmed by the enantiomorph-polarity parameter which converged to 0.07(4) (Flack et al.<sup>20</sup>). The geometrical calculations and drawings were obtained from the programs PARST<sup>21</sup> and ORTEP<sup>22</sup> respectively. The atomic coordinates, thermal parameters, torsion angles and the list of observed and calculated structural factors are available as supplementary material and are deposited at the Cambridge Crystallographic Data Centre.

**Acknowledgments.** This work was financially supported by the Consiglio Nazionale delle Ricerche (Rome) under the scheme "Progetto Finalizzato per la Chimica Fine e Secondaria". Thanks are due to Mrs. Dora von Ow of Bruker Spectrospin AG (Zürich) for determining high field NMR spectra.

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