*Tetrahedron* Vol. 45, No. 18, pp. 5987 to 5994, 1989
Printed in Great Britain.

0040–4020/89 $3.00+.00


# THREE NEW BROMO ETHERS FROM THE RED ALGA LAURENCIA OBTUSA

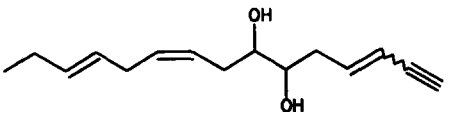
Manuel Norte*, José J. Fernández and José Z. Ruano.

C.P.N.O."Antonio González", Instituto Universitario de Bio-orgánica, Universidad de La Laguna, La Laguna 38206, Tenerife, SPAIN.

(*Received in UK* 19 *June* 1989)

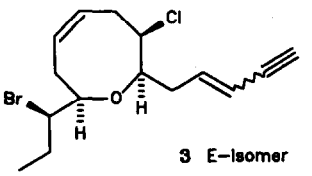
**Summary**: Three new bromo ethers **9**, **10** and **11** having a bromo propargylic moiety, have been isolated from the red alga **Laurencia obtusa**. Their structures and absolute configurations have been determined by spectroscopical and chemical methods.

The genus **Laurencia** produces a great variety of nonterpenoid C-15 compounds which arise from fatty acid metabolism. This type of compounds have aroused considerable interest in the last decade because of their structural features as well as their promising biological activity[1]. Examples include the lauredіols **1**,**2** from **L. nipponica**[2], the pinnatifidenines **3**,**4** from **L. pinnatifida**[3], the obtusin **5** from **L. obtusa**[4] and the deoxyokamurallene **6** from **L. okamurai**[5]



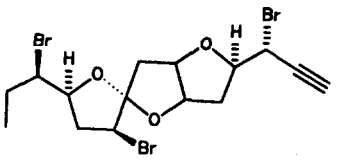

**1** E–Isomer

**2** Z–Isomer

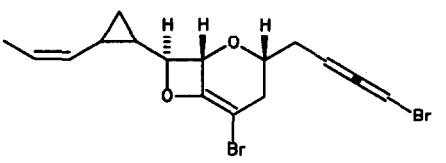



**3** E–Isomer

**4** Z–Isomer




**5**



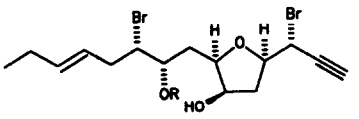

**6**

We have focused our attention on this type of compounds during our continuing research into the secondary metabolites of **Laurencia** species collected at the Canary Islands. Members of this group are unbranched, either lineal or cyclic C-15, with an enyne, bromopropargylic or bromoallenic side chain. The heterocycle rings are oxane, with sizes ranging from oxolane to oxonane, and they can be isolated, fused or in spiro arrangements. These structural properties are very interesting because they are present in the more complex polyether toxins isolated from marine organisms such as brevetoxins[6], yessotoxin[7] and okadaic acid[8]. The spectroscopical conclusions obtained from the study of these simpler systems could be expanded to more complex polyethers and then applied to unknown toxins.

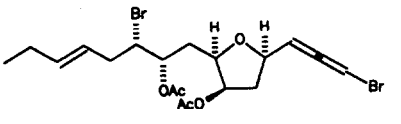
Although NMR spectroscopy has been a useful tool for studying this type of compounds, the field is fraught with difficulties. The assignment of signals presents great difficulties, especially those from the heteroatom methines, such assignments being essential in order to determine the position and size o the heterocyclic components of the molecule. Thus, the structures of most of these interesting compounds had been determined by X-ray analysis, while the non crystalline compounds were elucidated by chemical correlations with the former group. However the explosive advances in NMR techniques, especially the new pulse sequences in two-dimensional NMR spectroscopy, have dramatically facilitated structural studies of this type of molecules.

We wish to report in this paper the isolation and structural elucidation of three new C-15 acetogenins from **Laurencia obtusa.** Their structures were established by using 2D NMR homo- and heteronuclear experiments. We would like to emphasize the utility of these experiments because they permit the heteroatom positions in the molecule to be unambiguously assigned.

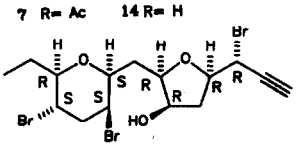
The alga **L. obtusa** was collected at La Graciosa (Canary Islands) in September 1986. Extraction o the air-dried algae with acetone and diethyl ether, followed by chromatography on silica gel and Sephadex LH-20, afforded the C-15 acetogenins, the obtusin **5**, the graciosin **7**, and graciosallene **8**[10], previously reported, and the three novel compounds **9, 10 and 11.** The compounds were isolated as a mixture by the silica gel chromatography in the n-hexane-ethyl acetate (70:30) eluent. The mixture was rechromatographed on a Sephadex LH-20 column using n-hexane:$CHCl_3$:MeOH (2:1:1) as mobile phase and yielded the pure compound **11** and the mixture of compounds **9** and **10.** These were finally separated by chromatography on the reverse-phase column Lichroprep RP-8 using EtOH:$H_2O$ (85:15) as eluent. Compounds **9** and **10** showed similar spectroscopical data. Both compounds gave in the E.I. mass spectrometry a peak at *m/z* 409 with the characteristic isotope pattern consistent with the presence o two bromine atoms. This fragment arises from the $\alpha$-cleavage to a bromine atom. The HRMS confirmed this hypothesis and established the molecular formula of $C_{15}H_{21}O_3Br_3$ for these compounds. The ions formed by simple fragmentation of the molecular ion are as follows: 1) *m/z* 486, 488, 490, 492 (n/o) → *m/z* 407, 409, 411 → *m/z* 389, 391, 393 → *m/z* 309, 311 formed by losses of bromine, water and then the bromopropargylic moiety. 2) *m/z* 407, 409, 411 → *m/z* 247 by the loss of two HBr molecules. 3) m/z 486, 488, 490, 492 → *m/z* 269, 271, 273 and *m/z* 217, 219 which are due to the ion radicals $(C_7H_{11}OBr_2)^+$ and $(C_6H_{10}O_2Br)^+$ from the C-7 - C-8 bond fragmentation.



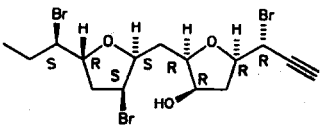
7 R= Ac 14 R= H



8



9



10

**Table I. NMR Spectral Data of 9, 10, and 11**

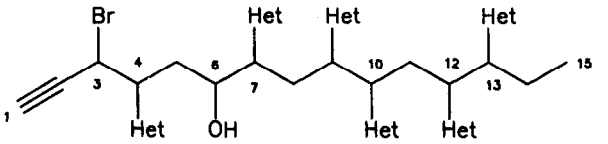
| | $^{13}C$ a) | | | $^{1}H$ b) | | |
|---|---|---|---|---|---|---|
| C | 9 | 10 | 11 | 9 | 10 | 11 |
| 1 | 76.66 | 77.17 | 76.42 | 2.72 d, 2.3 | 2.69 d, 2.4 | 2.66 d, 2.5 |
| 2 | 80.72 | 80.74 | 79.82 | -- | -- | -- |
| 3 | 37.78 | 38.24 | 39.31 | 4.64 dd, 2.3;5.8 | 4.65 dd, 2.4;6.3 | 4.56 dd, 2.5;8 |
| 4 | 79.79 | 80.06 | 80.41 | 4.19 ddd, 2.3;5.8;5.9 | 4.19 ddd, 5.6;3.8;5 | 4.14 ddd, 5.1;8;8 |
| 5 | 38.63 | 38.77 | 34.87 | 2.47 ddd, 5.9;8.5;14.5 | 2.45 ddd, 5.8;8.5;14.3 | 2.47 m |
| | | | | 2.11 m | 2.18 ddd, 5.8;6;14.3 | 2.22 |
| 6 | 72.01 | 72.18 | 76.43 | 4.26 m | 4.29 ddd, 3,6;5.8;7.6 | 4.44 m |
| 7 | 80.79 | 81.43 | 82.01 | 3.92 ddd, 3.4;6.5;7 | 3.94 ddd, 3,6;6;9.8 | 4.08 m |
| 8 | 34.29 | 33.49 | 38.05 | 2.17 ddd, 6;8;14.5 | 2.18 ddd, 6;7.7;14.2 | 2.45 m |
| | | | | 1.98 ddd, 4.9;7;14.5 | 2.00 m | 1.90 m |
| 9 | 75.58 | 78.82 | 71.44 | 3.71 ddd, 2;4.9;8 | 4.25 m | 3.49 d, 7.9 |
| 10 | 55.53 | 55.63 | 61.93 | 4.26 ddd, 2;3.1;3.4 | 4.57 ddd, 2.8;2.8;2.9 | 4.68 dd, 0.9;10.9 |
| 11 | 44.41 | 42.22 | 32.25 | 2.82 ddd, 3.1;4.4;14.4 | 2.59 dd, 2.8;7.8 | 2.47 m |
| | | | | 2.53 ddd, 3.4;11.7;14.4 | | 2.18 m |
| 12 | 46.75 | 80.19 | 71.44 | 4.20 ddd, 4.4;11.7;10.3 | 4.46 ddd, 7.6;7.8;7.8 | 4.40 m |
| 13 | 83.88 | 61.89 | 61.10 | 3.45 ddd, 2.5;7.8;10.3 | 4.05 ddd, 3.6;7.6;9.7 | 4.06 m |
| 14 | 26.19 | 28.64 | 29.02 | 2.02 ddq, 2.5;7.3;14.4 | 1.94 ddq, 3.6;7.2;14.6 | 1.93, ddq, 3.5;7.2;14.5 |
| | | | | 1.62 ddq, 7.3;7.8;14.4 | 1.68 ddq, 7.2;9.7;14.6 | 1.80, ddq, 7.2;9.1;14.5 |
| 15 | 9.30 | 12.14 | 11.84 | 0.98 t, 7.3 | 1.07 t, 7.2 | 1.09 t, 7.2 |

a) Assignments made by $^{1}H$-$^{13}C$ heteronuclear COSY

b) Assignments made by homonuclear decoupling and $^{1}H$-$^{1}H$ COSY

The I.R. of compounds **9** and **10** showed the presence in the compounds of an hydroxyl group (3400 $cm^{-1}$) and a characteristic terminal acetylenic group (3300 $cm^{-1}$). The presence of bromopropargylic moiety in these molecules was confirmed by the $^{1}H$-NMR resonances for 1-H at $\delta$ 2.70 and for 3-H at $\delta$ 4.64 and the $^{13}C$-NMR signals at $\delta$ 76.6, 80.7 and 37.8 corresponding to C-1, C-2 and C-3 respectively.

In addition, the $^{1}H$-NMR spectra of these compounds were very similar and showed signals for seven heteroatom-methine protons and a terminal methyl group (see Table 1). The signals at $\delta$ 4.26 for compound **9** and at $\delta$ 4.29 for compound **10**, were assigned to the hydroxy group methine by the formation of their acetate derivatives. The COSY maps of the compounds showed the familiar cross peak correlating all the protons in the molecule.




The $^{1}H$-$^{13}C$ correlations provide by the COSY(HETCOR) experiments led us to establish the nature of the heteroatoms at the carbons C-4, C-7, C-9, C-10, C-12 and C-13 of these compounds[11]. For compound **9**, the COSY(HETCOR) map (Fig. 1a) established correlations between 4-H at $\delta$ 4.19 and C-4 at $\delta$ 79.79; 7-H at $\delta$ 3.92 and C-7 at $\delta$ 80.79; 9-H at $\delta$ 3.71 and C-9 at $\delta$ 75.58; 10-H at $\delta$ 4.26 and C-10 at $\delta$ 55.53; 12-H at $\delta$ 4.20 and C-12 at $\delta$ 46.75; 13-H at $\delta$ 3.45 and C-13 at $\delta$ 83.88. These results

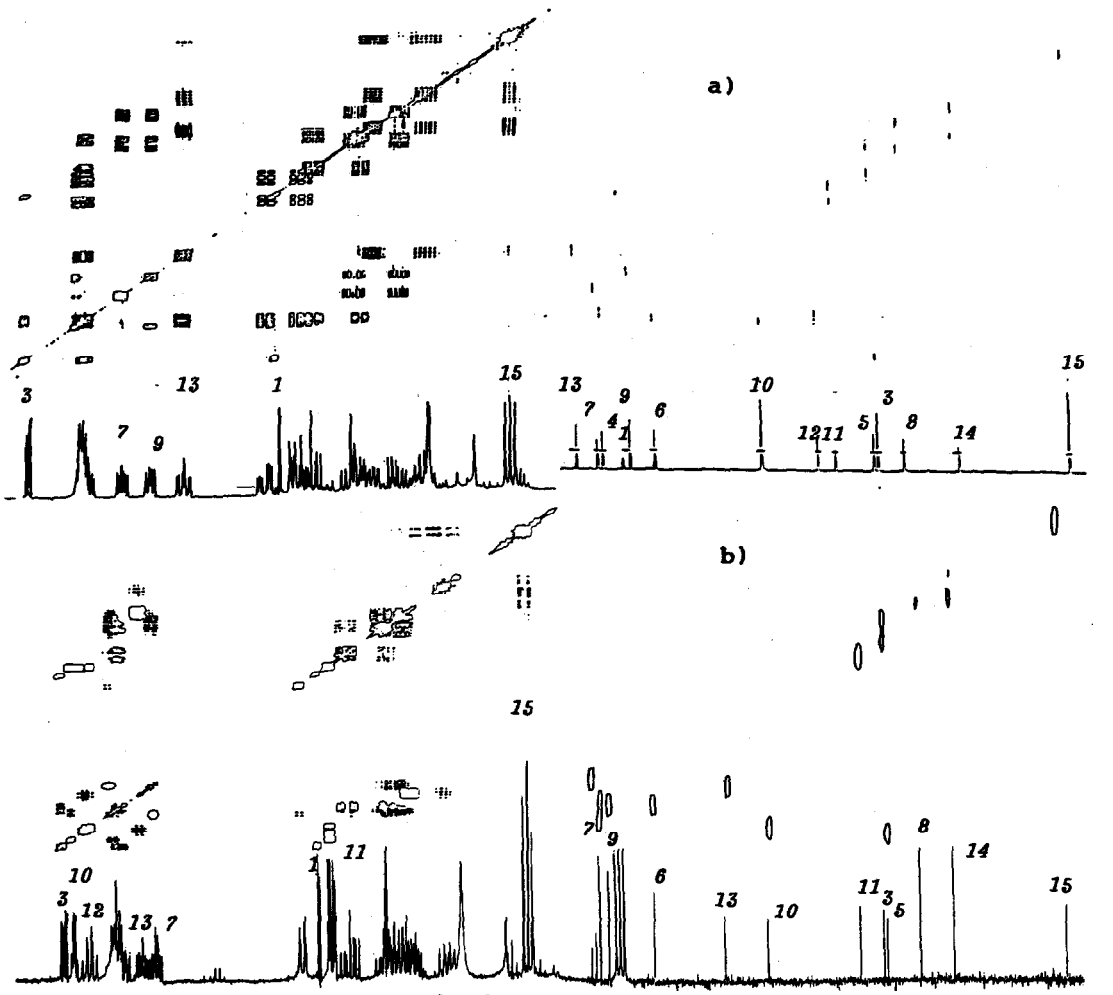
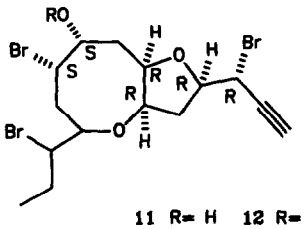


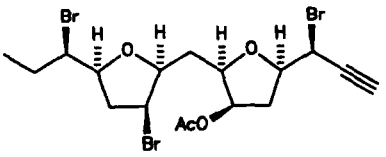

Fig.1.- COSY $^{1}H$-$^{1}H$ and one-bond $^{1}H$-$^{13}C$ correlations of compounds **9** (1a) and **10** (1b)

suggested the presence of C-4 - C-7 and C-9 - C-13 ether linkages and two bromine atoms at C-10 and C-12, respectively. For compound **10** the $^{1}H$-$^{13}C$ correlations in the COSY(HETCOR) map (Fig. 1 b) were as follows: 4-H at $\delta$ 4.19 and C-4 at $\delta$ 80.06; 7-H at $\delta$ 3.94 and C-7 at $\delta$ 81.43; 9-H at $\delta$ 4.25 and C-9 at $\delta$ 78.82; 10-H at $\delta$ 4.57 and C-10 at $\delta$ 55.63; 12-H at $\delta$ 4.46 and C-12 at $\delta$ 80.19; 13-H at $\delta$ 4.05 and C-13 at $\delta$ 61.89. These results, also support the presence of a bromine atom at C-10 and an ether linkage between C-4 and C-7 . However, the second bromine atom is now placed at C-13 and the ether linkage is established between C-9 - C-12. Consequently, we can conclude that compounds **9** and **10** have two isolated oxane rings: oxolane and oxixane for compound **9** and two oxolanes for compound **10**. The stereochemistry of these compounds will be discussed later.

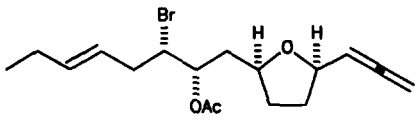
The more polar component in the acetylenic fractions was compound **11**. Its acetate derivative **12** had been isolated in a previous study of this alga and it was published as 13[9]. This compound is an example of the difficulties encountered in establishing unambiguously the structure of this type of C-15 aceto



11 R= H 12 R= Ac



13



15

genins by using monodimensional techniques and without the aid of bidimensional NMR experiments as we have remarked above. We wish here to reassign its structure as **12** by the study of the new metabolite **11** which was correlated with **12** by treatment with $Ac_2O$/Py at rt. The COSY map of **11** established the same correlations found in compounds **9** and **10**. However, the secondary hydroxyl group is now at C-9 in accordance with the signal for its α-methine 9-H at δ 3.49, which shifted to δ 4.54 in **12**. Its COSY(HETCOR), $^1H$-$^{13}C$, (Fig. 2), showed the following relevant correlations: 4-H at δ 4.14 and C-4 at δ 80.41; 6-H at δ 4.4 and C-6 at δ 76.43; 7-H at δ 4.42 and C-7 at δ 82.01; 9-H at δ 3.49 and C-9 at δ 71.44; 10-H at δ 4.68 and C-10 at δ 61.93; 12-H at δ 4.4 and C-12 at δ 71.44; 13-H at δ 4.42 and C-13 at δ 61.10. These correlations established that a bromhydrin system was placed at C-9 - C-10, which precluded the proposed structure **13**, an additional bromine at C-13 and two ether linkages between C-6 - C-13 and C-7 - C-4 according with the presence of an oxocane and oxolane fused system.

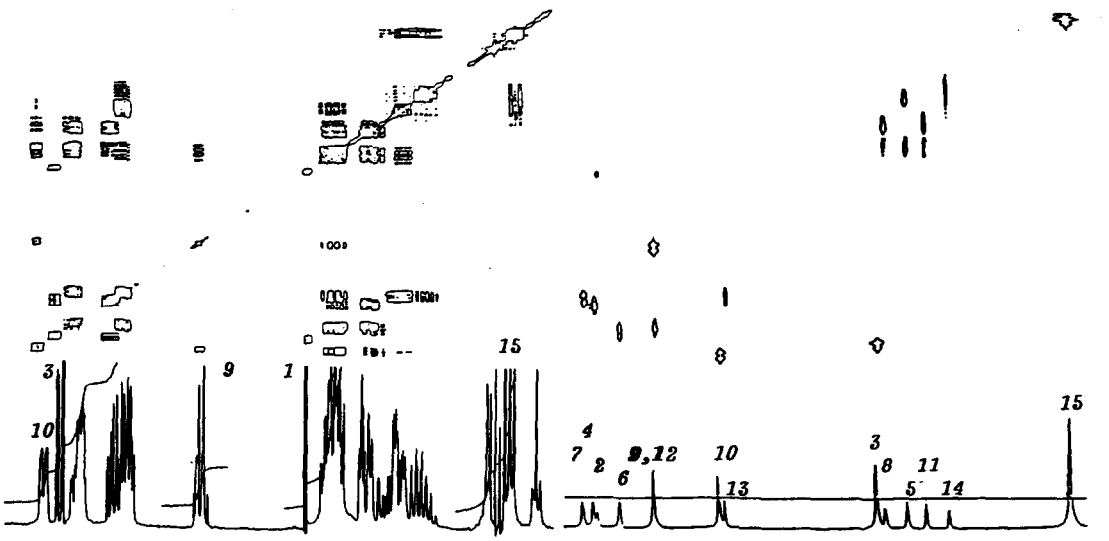
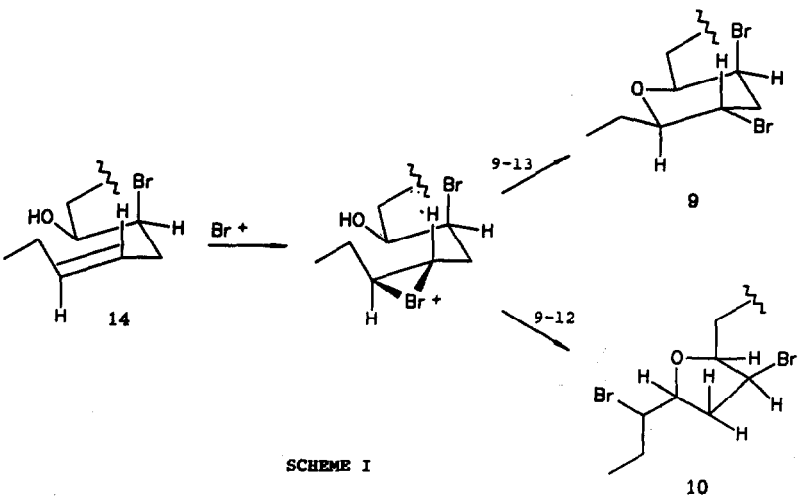



Fig.2.- COSY $^1H$-$^1H$ and one-bond $^1H$-$^{13}C$ correlations of compound 11

The stereochemistry of compounds **9**, **10** and **11** was established by chemical correlations of these compounds with deacetoxygraciosin **14** whose absolute configuration was established by X-ray analysis[10].

Treatment of compound **11** with Zn/AcOH at 0º C and subsequently with $Ac_2O$/Py yielded compound **15**, identical with that obtained from graciosin **7** by its reaction with Zn/AcOH at Oº C, followed by acetylation These results led necessarily to the conclusion that the absolute configurations at carbons C-4, C-6, C-7, C-9 and C-10 are **R**, **R**, **R**, **S** and **S**, respectively. Since the C-3 methine displayed the same $^1$H-NMR couplings in **11** as in graciosin **7** its absolute configuration was established as **R**. Attempts to solve the stereochemistry at C-12 and C-13 failed because the $^1$H-NMR signals for the methines at these carbons were unresolved and their chemical shifts too close to perform nOe experiments.

For compounds **9** and **10**, the chemical correlations with the deacetoxygraciosin **14** were established by bromocyclization. Treatment of a dichloromethane solution of deacetoxygraciosin with NBS at -40 ºC and then at rt, afforded two compounds on reverse phase tlc, which were isolated by reverse phase HPLC. These compounds showed physical and spectroscopical properties identical with those of compounds **9** and **10**. Consequently, the reaction was stereoselective and established the absolute configurations for all the chiral centers of these compounds except at the carbons C-12 and C-13 which were formed during the cyclization. The chirality of those carbons in compound **9** was established in accordance with the coupling constant values observed for the protons in the oxixane ring, $J_{9\text{-}10}$= 2 Hz; $J_{10\text{-}11}$= 3.4 Hz; $J_{11\alpha\text{-}12}$= 11.7 Hz; $J_{11\beta\text{-}12}$= 4.4 Hz and $J_{12\text{-}13}$= 10.3 Hz. Such values agree with a trans diequatorial relationship between the bromine at C-12 and the ethyl side chain at C-13, the methine being α-axial at C-13, as shown in Scheme I. Moreover, the stereochemistry at the oxolane ring resulting from this cyclization is in accordance with the coupling constant values observed for the methines at C-10 and C-12 and for the methylene at C-11 (see Table I). Accordingly, the absolute configurations at C-12 and C-13 were **S** and **R** for compound **9**, respectively, and **R** and **S** for compound **10**.




SCHEME I

## EXPERIMENTAL PART

Infrared espectra were recorded on a Perkin-Elmer Mod. 257. Optical rotations were determined for solution in chloroform with a Perkin-Elmer Mod. 241 polarimeter. $^1$H-NMR and $^{13}$C-NMR spectra were recorded on a Bruker Mod. WP-200 SY (200 MHz), chemical shift are reported relative to $Me_4Si$( 0) and coupling constants are given in hertz. The 2D-NMR spectra were obtained using Bruker's micro-programs. Low and high resolution mass spectra were obtained from a VG micromass ZAB-2F spectro-photometer. Silica gel chromatography was perfomed on silica gel 60 G, TLC and PLC obtained from Merck products. The TLC plates were developed by sprayin with 6-N sulphuric acid and heating. Sephadex LH -20 obtained from Pharmacia was used for gel filtration chromatography and Licroprep RP-8 Merck was used for reverse-phase chromatography. Preparative HPLC purifications were carried out on Water apparatus equiped with a RP C18 -Bondapak colum and with an R.I. detector. All sol-vents were purified by standard techinques. Anhidrous sodium sulfate was used for dryind solution.

**Collection, extraction and chromatographic separation.**

**Laurencia obtusa** was collected in shallow water at low tide in the Island of La Graciosa in Septem-ber 1986. The air-dried alga (5 kg) was extracted with acetone and diethyl ether, the solvents were evaparated in vacuo to afford 62 gr of crude extract. This extract was chromatographed on silica gel column eluted with a mixture of n-hexane:ethyl acetate of increasing polarity and 50 fractions of 1l each were collected. The fractions eluted with n-hexane:ethyl acetate 70:30 afford after solvent evapo-ration the products **1**, **2**, **3**, graciosin, **7**, and graciosallene, **8**, in the crude extract. This was chromato-graphed on Sephadex LH-20 column with chloroform:methanol:n-hexane 1:1:2 to give pure product **3** (50 mg), graciosin (200 mg), graciosallene (23 mg) and the mixture of products **1** and **2** (94 mg). This mixture was chromatographed on Licroprep RP-8 using methanol: water 85:15 affording pure the products **1** (61 mg) and **2** (33 mg).

**Compound 9.**- oil, $[\alpha]_D^{25}$ -4.1º ($CHCl_3$, c 0.05); IR $\nu_{max}^{cm-1}$: 3400, 3300, 3000, 2960, 2390, 1630, 1460, 1080, 1050 and 660 . $^1$H and $^{13}$C -NMR($CDCl_3$) see Table I. MS: m/z 407, 409, 411; 406.9850 ( $C_{15}H_{21}O_3{}^{79}Br_2$, requires 406.9855); 389, 391, 393; 369, 371, 373; 351, 353, 355; 327, 329.

**Compound 10.**- oil, $[\alpha]_D^{25}$ +7.5º ($CHCl_3$, c 0.03) ; I.R. $\nu_{max}^{cm-1}$: 3375,3300,3000,2390,1630 and 1460.$^1$H-NMR and $^{13}$C-NMR($CDCl_3$) see Table I. MS: m/z: 407,409,411; 410.9725 ($C_{15}H_{21}O_3{}^{81}Br_2$ requires 410.9816); 389,391,393; 309,311; 269,271,273; 247; 217,219

**Compound 11.**- oil, $[\alpha]_D^{25}$ -8.2 ($CHCl_3$, c 0.0.9); IR $\nu_{max}^{cm-1}$: 3400, 3000, 2960, 2945, 1370, 1240, 1070 and 1035 .$^1$H and $^{13}$C NMR in Table I. MS: 369, 371, 373; 368.9689 ($C_{12}$ $H_{19}O_3{}^{79}Br_2$ requires 368.9698); 351, 353, 355; 333, 335, 337; 285, 287; 271, 273; 253, 255.

**Acetylation of compound 11.**- To a solution of product **11** (10 mg, 18 $\mu$mol) in dry pyridine (250 $\mu$l) was added acetic anhidride (250 $\mu$l) and the mixture was stirred fro 5h at rt under nitrogen. Usual work up give an oil residue wich was chomatographed on silica gel to furnisch 10.6 mg of **12**. oil, $[\alpha]_D^{25}$ -29.3º ($CHCl_3$, c 0.08). IR $\nu_{max}^{cm-1}$: 3300, 3010, 2960, 1730, 1430, 1370, 1250, 1070 and 1030. $^1$H-NMR($CDCl_3$) $\delta$ : 1.05 (3H, t, 7.3); 1.73 (1H, ddq, 6.45, 7.3, 14.6); 1.85 (1H, m); 1.95 (1H, ddq, 3.7, 7.3, 14.6); 2.06 (3H, s); 2.19 (1H, m); 2.2 (1H, m); 2,35 (1H, m); 2.42 (1H, ddd, 4.3, 8.1, 14); 2.53 (1H, ddd, 0.9, 10.9, 14.3); 2.63 (1H, d, 2.45); 4.01 (1H, ddd, 3.7, 6.4, 8.8); 4.08 (1H, ddd, 4.2, 4.4, 10.8); 4.14 (1H, ddd, 4.6, 8, 8.3); 4.39 (1H, ddd, 3.6, 4.3, 4.3); 4.41 (1H, ddd, 2.6, 8.8, 10.8); 4.53 (1H, dd, 2.4, 8.4); 4.54 (1H, bd, 8). $^{13}$C-NMR ($CDC_{13}$) $\delta$ :12.01 (q); 21.2 (q); 29.4 (t); 32.5 (t); 32.9 (t); 38.3 (t); 39.25 (d); 55.3 (d); 61.4 (d); 71.8 (d); 73.1 (d); 76.27 (d); 76.5 (s); 76.6 (d); 81 (d); 82.1 (d); 170.1 (s). MS: m/z 528, 530, 532, 534; 411, 413, 415; 389, 391, 393; 351, 353, 355; 347, 349, 351; 327, 329.

**Hydrolysis of Graciosin, 7.** To a solution of 30 mg of graciosin, 7, in 10 ml of MeOH cooled at -25 ºC was added excess of $K_2CO_3$ (15 mg) and the mixture stirred for 6 h. The mixture was filtered off, the solvent evapored and the residue crystallized from n-hexane to give 24 mg of deacetoxygraciosin, 14, colourless crystals, mp 96 ºC; IR $\nu_{max}^{cm-1}$: 3500, 3300, 2950, 2100, 1435, 1370, 1240 and 1100. $^1$H-NMR ($CDCl_3$) $\delta$ : 0.91 (3H, t, 7.3), 2.63 (1H, d, 2.4); 3.8-4.03 (3H, m); 4.19 (2H, m); 4.57 (1H, dd, 2.4, 6.4); 5.36 (1H, ddd, 5.4, 5.4, 15); 5.53 (1H, ddd, 6.2, 7 and 15). MS: 329, 331; 311, 313; 273, 275.

**Compound 15.-** To a solution of 10 mg of 11 or 10 mg of deacetoxygraciosin, 14, in 1 ml of EtOH at 0º C, was added 10 mg of Zn powder adn 50 ml of HOAc. The mixture was stirred for 3 hr, filtered off and the solvent evaporated to give 6 mg of the allene, 15 ,oil $[\alpha]_D^{25}$ -5.5º ($CHCl_3$, 0.04). IR $\nu_{max}^{cm-1}$: 3660, 3565, 1950, 1600, 1570 and 1260. $^1$H-NMR ($CDCl_3$) $\delta$ : 0.98 (3H, t, 7.4); 4.3 (1H, m); 4.5 (1H, m); 4.8 (1H, ddd, 1.6, 2.7, 6.6); 5.3 (1H, ddd, 6.55, 6.5, 13.3); 5.42 (1H, ddd, 5.4, 5.4, 15.5); 5.54 (1H, ddd, 6.2, 7, 15.5). MS: 273, 275; 255, 257.

**Cyclization of deacetoxygraciosin.-** To a solution of deacetoxygraciosin,14, (20 mg, 44 lmol) in $CH_2Cl_2$ (2ml) at - 40º C, was added NBS (12 mg, 53 $\mu$mol) and the mixture was stirred at rt for 3 h, and the excess of the reagent was destroyed by adding several drops of thiosulphate solution. Usual work up gave, after semipreparative HPLC purification on $\mu$-Bondapak C-18 (methanol:water 85:15) the products 9 (9 mg) and 10 (7 mg). The physical and spectroscopic data of these compounds were identical with those of the natural samples.

**Acknowledgements.-** We acknowledge financial support from U.S.-Spanish Joint Committee for Scientific Cooperation Grant CCA 8510-079 and from Plan Nacional de Investigación FAR 88-0500.

## REFERENCES

1.- K.L. Erickson. **Mar. Nat. Prod.** Ed. P.J. Scheuer, 1983, Vol. V, 132.
2.- Kurosawa E., Fukusawa A., Irie T., **Tetrahedron Letters**, 1972, 2121.
3.- González A.G., Martín J.D., Martín V.S., Norte M., Pérez R., Ruano J.Z., Drexler S.A., Clardy J., **Tetrahedron**, 1982, **38**, 1009.
4.- Howard B.M., Fenical F., Clardy J., Arnold E.V., **Tetrahedron Letters**, 1979, **31**, 2841.
5.- Suzuki M., Kurosawa E., **Tetrahedron Letters**, 1981, **22**, 3853.
6.- a) Shimizu Y., Chou H.N., Bando H., Van Duyne G., Clardy J., **J. Am. Chem. Soc.**, 1986, **108**, 514.
b) Pawlak J., Tempesta M.S., Golik J., Zagorski M.G., Lee M.S., Nakanishi K., Iwashita T., Gross M.L., Tomer K.B., **J. Am. Chem. Soc.**, 1987, **109**, 1144.
7.- Murata M., Masanori K., Lee J.S.,Yasumoto T., **Tetrahedron Letters**, 1987, **28**, 5869.
8.- Yasumoto T., Murata M., Oshima Y. Sano M., Matsumoto G.K., Clardy J., **Tetrahedron**, 1985, **41**, 1019.
9.- González A.G., Martín J.D., Norte M., Rivera P., Ruano J. Z., **Tetrahedron**, 1984, **40**, 3443.
10.- Norte M. Fernández J.J., Ruano J.Z., Rodríguez M.L., Pérez R., **Phytochemistry**, 1988, **27**, 3537.
11.- Beitmaier E., Volter W., **Carbon -13 NMR Spectroscopy**, Ebel E. Ed., VCH, 1987, 107.