Pergamon

Tetrahedron Letters, Vol. 35, No. 26, pp. 4607-4610, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00837-X

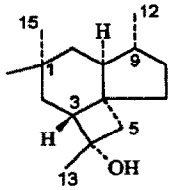
Viridianol, a Rearranged Sesquiterpene with a Novel Carbon Skeleton from *Laurencia viridis*.

Manuel Norte, José J. Fernández, and M. L. Souto

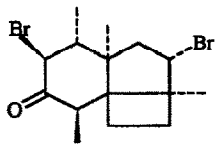
Institute of Bioorganic Chemistry, University of La Laguna, 38206 La Laguna, Tenerife, Spain

Abstracts: Viridianol **1**, a new rearranged sesquiterpene with a novel carbon skeleton has been isolated from the red seaweed *Laurencia viridis*. The structure was determined through the interpretation of 2D NMR spectra as a 3,6-cycloprecapnellane carbon skeleton. The relative stereochemistry is proposed on the basis of ROESY and NOEDIFF data.

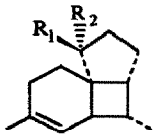
Red seaweeds of the genus *Laurencia* are known to produce regular and irregular terpenoids which contain halogens[1]. Structurally, most of them appear to be the product of a bromonium ion induced cyclization of acyclic precursors. In this article, we wish to report the isolation and structure determination of a new sesquiterpene **1** isolated from *Laurencia viridis*[2], and which did not contain the expected halogen substituents which are characteristic of metabolites isolated from this source. This compound is a new type of sesquiterpene which possesses a previously unreported fused 4,5,6 tricyclic carbon skeleton. Only a few examples of sesquiterpenes with this kind of carbon arrangement have been reported, the group of perforatane, represented by perforatone **2**, an halogenated sesquiterpene isolated from *Laurencia perforata*[3]; the group of italicane represented by italicene **3** and iso-italicene **4** isolated from *Helichrysum italicum*[4] and, finally, the group of panasinsane, isolated from the roots of *Panax ginseng*[5] and represented by α– and β-panasinene and by panasinsanols A **5** and B **6**, these last being isomers of compound **1**.



1

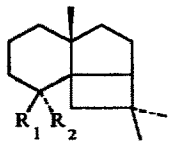


2



3 R_1= Me; R_2= H

4 R_1= H; R_2= Me



5 R_1: Me; R_2: OH

6 R_1: OH; R_2: Me

Viridianol **1**, $[\alpha]^{25}_D$= + 4.5 (c, 0.15, Cl_3CH)[6], isolated as an amorphous white solid, showed a M^+ peak in the HREIMS at m/z 222.19629 indicating a molecular formula of $C_{15}H_{26}O$, which established the presence of three degrees of unsaturation in the molecule. The absorption at 3590 cm^{-1} in the I.R spectrum and a dehydration ion at m/z 204 in the MS of **1** indicated the presence of a hydroxy group, and a quaternary carbon signal at δ 70.72 in the ^{13}C-NMR spectrum indicated that the hydroxy group was tertiary. These data together with the absence of proton and carbon olefinic signals in the NMR spectral data clearly established that compound **1** possessed three rings in its structure. The most prominent feature in the ^{1}H-NMR spectrum is

the presence of all chemical shifts as a cluster of signals in a narrow field of the spectrum, between δ 0.86 and 2.08, with three tertiary methyl groups at δ 0.86, 0.98 and 1.46, this last being α– to the hydroxy group, and a secondary methyl group at δ 0.92. The ^{13}C-NMR spectrum showed the presence of four, five and three methyl, methylene and methine groups, together with three quaternary carbon centres.

n° C	δ ^{13}C	δ ^{1}H	J (Hz)	n° C	δ ^{13}C	δ ^{1}H	J (Hz)
1	29.15			8	33.58	α 1.05	7; 8.5; 11; 12
2	36.35	β 1.39	12.9; 13.5			β 1.78	2.5; 7; 7; 12
		α 1.32	7.1; 12.9	9	40.49	1.48	5; 6.7; 6.7; 6.7; 7; 8.5
3	49.44	1.98	3.5; 7.1; 12.9	10	50.90	1.28	5; 5.8; 11.6
4	70.72			11	42.59	α 1.30	5.8; 14.8
5	50.91	1.97	3.5; 12			β 0.99	11.6; 14.8
		2.08	12	12	21.17	0.92	6.7
6	38.75			13	29.05	1.46	
7	39.26	β 1.67	7; 11; 12	14	29.11	0.86	
		α 1.88	2.5; 7; 12	15	21.17	0.98	

Table 1.- ^{13}C and ^{1}H-NMR Chemical Shift data ($CDCl_3$) for Viridianol **1**

The DQF-COSY experiment may be conveniently started from the α-methine to the secondary methyl group H-9 (δ 1.48), which is coupled to the methine group H-10 (δ 1.28) and to the methylene group, H-8s (δ 1.05 and 1.78). The latter protons were coupled with H-7s (δ 1.67 and 1.88) and H-10 with H-11s (δ 1.30 and 0.99), the system of coupled protons in this region terminating with the presence of quaternary centres at C-1 and C-6. The remaining methine group in the molecule, H-3 (δ 1.98) showed to be connected with the methylene group H-2s (δ 1.32 and 1.39), while the last methylene group, H-5s, was present as an isolated AB system centred at δ 1.97 and 2.08. In the molecule, these connectivities defined the presence of two separate directly proton-coupled systems, ■-CH_2-CH-CH(Me)-CH_2-CH_2-■ and ■-CH-CH_2-■; together with an isolated methylene group. After the carbon assignments through the NMR-HMQC experiment, these fragments were connected on the basis of the NMR-HMBC experiment. Thus the HMBC correlation between the quaternary carbon C-1 and the H-11s and H-2s methylene protons together with those between C-1and the *gem*-dimethyl at δ 0.86 and 0.98, connect one end of each of the two observed fragments with the carbon

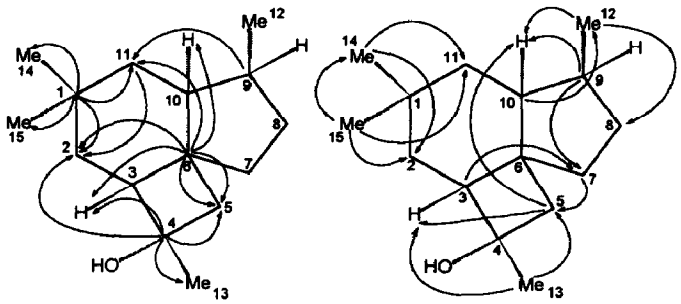


Figure 1. Significant HMBC correlations of the Viridianol **1**

bearing the *gem*-dimethyl group. In addition, the other two ends of the above fragments, H-3 and H-7, showed to be correlated with the quaternary carbon C-6 at δ 38.75 which, in turn, was also correlated with the methine H-10 and with the methylene protons H-5. This last methylene group was, together with the methine H-3, correlated with the α-hydroxyl methyl group Me-12 at δ 21.17. Finally carbon C-4 was correlated with H-5, H-3 and Me-13. These observed correlations in the HMBC experiment support the proposed structure for compound **1**, which was reinforced by the other correlations summarized in Fig. 1.

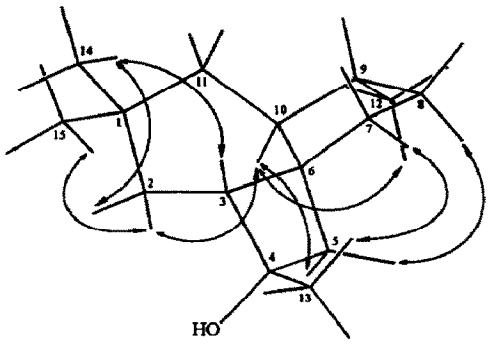
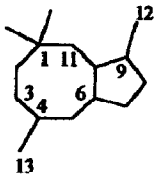
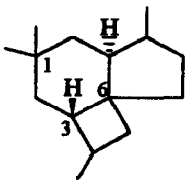


Figure 2.- Selected ROESY Correlations for **1**

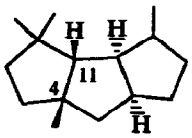
The relative stereochemistry of compound **1** was established on the basis of the ROESY and NOEDIFF experiments, the relative stereochemistry of the methine protons H-3, H-9 and H-10 being crucial for this proposal. The extensive overlap observed in the $CDCl_3$ ^{1}H-NMR spectrum for these signals was avoided by using deuterated pyridyne as solvent[5]. In fact the methine signals for H-3, H-9 and H-10 were observed as isolated signals at δ 2.08, 1.46 and 1.33, respectively . The configurational assignments in the molecule were established as follows. Starting from H-10, two cross-peaks could be labelled with confidence in the ROESY spectrum, H-10/H-2α and H-10/H-5α. Moreover, H-2α was correlated with one of the *gem*-dimethyl groups centred at δ 0.98 and H-5α, thus establishing that H-10, Me-,H-2α and H-5α, were on the same face of the molecule. Similarly ROE correlations between the other *gem*-methyl group, which was centred at δ 0.86 with H-2β and with the bridgehead methine H-3 were observed, which implies that they were in the opposite face of the molecule. In the ROESY spectrum, the ROE connectivity between the proton H-10 and the methyl group Me-12 was not clear, which was important to established their relative stereochemistry. For that reason we decided to carry out a NOEDIFF experiment by irradiation of the secondary methyl group. The enhacement of the H-10 and H-8α proton signals established that all of them were on the same face of the molecule. All the other ROE connectivities are shown in Fig. 2. These connectivities, together with the observed coupling constants values (Table 1), established that the cyclohexane ring exists in a distorted boat conformation, with the cyclobutane and the cyclopentane oriented to different faces (Fig. 2).



7



8



9

The biosynthetic origin of this carbon skeleton has not been established, although it appears to be derived from the precapnellane carbon skeleton 7 by cyclization between carbons C-3 and C-6 to give a 3,6 - cycloprecapnellane carbon skeleton 8. The other well-kown group of compounds with cyclized precapnellane skeleton is the capnellane (4,1-cycloprecapnellane) 9, which is represented by several examples isolated from *Capnella imbricata*[7].

Acknowledgements

M.N. acknowledges financial support from the Plan Nacional de Investigaciones Farmacéuticas Far 91-0827.

References and notes.

1.- **a)** Martín, J.D., Darias J., *Mar. Nat. Prod.*, Scheuer, P.J Ed., Academic Press **1973**, Vol. *I.* 125; **b)** Erickson K.L., *Mar. Nat. Prod.*, Scheuer, P.J Ed., Academic Press **1983**, Vol. *V*, 131.

2.- Gil-Rodríguez M.C., Haaroun R., *Botanica Marina*, **1992**, *35*, 227-237.

3.- **a)** González, A.G., Aguiar, J.M., Martín, J.D., Norte, M.,*Tet. Lett.*, **1975**, *29*, 2499-2502; **b)** Coll, J.C., Skelton, B.W., White, A.H., Wright, A.D., *Aust. J. Chem.*, **1989**, *42*, 1695.

4.- Leimner J, Marschall, H., Meier, N., Weyerstahl, P., *Chem. Lett.*, **1984**, 1769

5.- Iwabuchi, H., Yoshikura, M., Ikawa, Y. Kamisako, W., *Chem. Pharm. Bull.*, **1987**, *35*, 1975

6.- **Compound 1**: amorphous white solid, mp 73° C; $[\alpha]^{25}_{D}$= + 4.5° (c, 0.15, Cl_3CH); IR ν_{max} (Cl_3CH): 3590, 2980, 2930, 2900, 2840, 1450 and 1360 cm^{-1}; HRMS: M^+ at m/z: $C_{15}H_{26}O$ 222.19629 (Calc. 222.19837); MS at m/z: 222, 204, 189, 177; ^{1}H-NMR (Pyridine-d_5) δ 2.38 (H-5α), 2.08 (H-3), 2.03 (H-5β), 1.91 (H-7α), 1.88 (H-11α), 1.76 (H-8β), 1.66 (H-7β), 1.64 (3H, H-13), 1.54 (H-2β), 1.46 (H-9), 1.33 (H-10), 1.27 (H-11β), 1.07 (H-8α), 0.98 (H-11α), 0.98 (3H, H-15), 0.91 (3H, H-12), 0.87 (3H, H-14); ^{13}C-NMR (Pyridine-d_5) δ 21.28 (C-12), 29.24 (C-1), 29.32 (C-13), 30.32 (C-14), 32.30 (C-15), 33.95 (C-8), 37.15 (C-2), 38.93 (C-6), 40.02 (C-7), 40.87 (C-9), 42.73 (C-11), 50.29 (C-3), 51.33 (C-5), 51.41 (C-10), 69.74 (C-4).

7.- **a)** Schmitz F.J., Hollenbeak K., Vanderah D., *Tetrahedron*, **1978**, *34*, 2719; **b)** Kaisin, M., Braekman, J.C., Daloze, D., Tursch, B., *Tetrahedron*, **1985**, *41*, 1067

(*Received in UK* 21 *March* 1994; *revised* 25 *April* 1994; *accepted* 29 *April* 1994)