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(-)-Paniculatol, a New *ent*-Labdane Bromoditerpene from *Laurencia paniculata*

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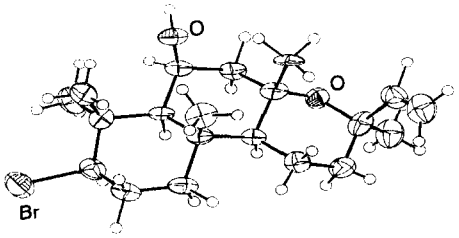
Abstract. (-)-Paniculatol, **1**, an unusual tricyclic bromoditerpene belonging to the *ent*-labdane series has been identified in the red alga *Laurencia paniculata* collected on Qatari coasts, Arabian Gulf. The structure displays an unusual tetrahydropyran ring and the absolute configuration has been determined by X-ray crystallography.

To date, bromoditerpenes from the *ent*-labdane series have only been identified in red algae belonging to *Laurencia* genus and in some herbivorous molluscs that diet on them[1]. None of these compounds have been shown to contain a dihydropyran ring or a hydroxyl group on C-6. In this paper we report on the structure and the absolute configuration of (-)-paniculatol **1**, which contains both characters.

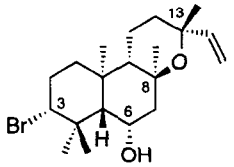
Laurencia paniculata[2] (C. Agardh) J. Agardh has been collected at Al Wakrah Bay, 30 km south of Doha, Qatar, on March 1995. Air-dried alga was extracted by MeOH/$CHCl_3$ (1/1, v/v, rt, magnetic stirring) and crude extract was partitioned between ethyl ether and water. The organic fraction (1,200 mg) was then chromatographed on silica gel column. The hexane/dichloromethane (H/D, 1/1, v/v) fraction (179 mg) was then rechromatographed on silica gel and eluted with increasing quantities of dichloromethane in hexane. The fraction H3/D7 was then purified by preparative TLC and gave 20 mg of pure **1** (1.6 % yield from crude organic extract) after recrystallization in hexane. Colourless needles, mp 172 ± 1°C (uncorrected) , $[\alpha]_D$ = -12 (c 0.006, $CHCl_3$). IR ν_{max} (cm^{-1}, KBr) 3487, 2924, 1449, 1365, 1188, 1168, 980, 918.

NMR analysis, ^1H and ^{13}C NMR ($CDCl_3$, 400 MHz) clearly displayed 4 quaternary carbons, 5 methyl, 6 methylene and 5 methine groups. Two quaternary carbons at 73.5 and 75.0 ppm were linked to an oxygen atom and a tertiary carbon at 70.6 ppm was linked to a hydroxyl group. Another tertiary carbon at 69.8 ppm was linked to a bromine atom that was confirmed by the MS spectra (EI, 70eV). Characteristic doublets at *m/z* 369-371 $(M-CH_3)^{+}$ and *m/z* 351-353 $(M-CH_3 - H_2O)^{+}$ confirmed the presence of one bromine atom. EI-HRMS gave *m/z* 384.1670 for the molecular peak (low intensity) and *m/z* 369.1429 for the $(M-CH_3)^{+}$ peak (high intensity) corresponding to $C_{20}H_{33}O_2Br$ (calculated M = 384.1663 and $(M-CH_3)$ = 369.1413). With an unsaturation degree of 4 the structure contained 3 rings and 1 double bond. The presence of a vinyl group (147.8 ppm, 6.012 ppm, 1H, dd J=11 and 18Hz 109.7 ppm; 4.970 ppm, 1H dd 11 and 1 Hz, 4.928 ppm, 1H dd 18 and 1 Hz) associated to UD = 4 strongly suggested an ether containing labdane skeleton for (-) paniculatol which was proved by an X-ray investigation[3].

(-)-Paniculatol **1** (3R,6S,8S,13R) is closely related to *ent*-isoconcinndiol **2**[1] as manoyl oxide **3** is related to sclareol **4**, two well-known labdane diterpenes from terrestrial origin[10]. EIMS fragmentations observed in **1** were analogs to those of manoyl oxide[11]. Thus, it is likely that a postulated « *epi*-paniculatol » could be related to (+)-isoconcinndiol **5** (3β-bromosclareol).



Perspective view of (-)-paniculatol, **1**



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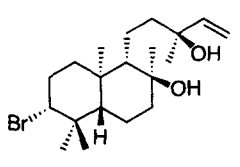

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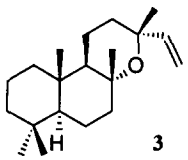

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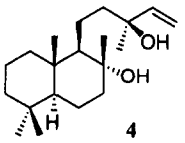

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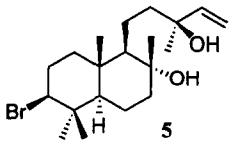

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According to Marinlit[12] it appears that (-)-paniculatol is the first tetrahydropyran containing *ent*-bromolabdane ever found in a marine organism. Another new characteristic is the 6α-hydroxyl never encountered so far on any labdane skeleton from marine origin. This unusual compound could have originated from *ent*-isoconcinndiol after internal cyclization and migration of an hydroxyl group.

Structural determinations of some other compounds from *Laurencia paniculata* are in progress.

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References and notes

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2. *Laurencia paniculata* was identified by Dr. Liliane and Max Pellegrini, Laboratoire de Biologie Marine Fondamentale et Appliquée, Faculté des Sciences de Marseille Luminy, case 901, 13288 Marseille Cedex 9 where a voucher specimen was lodged.

3. X-ray crystallography: Colourless crystal (0.15x0.20x0.25 mm), Mr = 385.39, orthorhombic, $P2_12_12_1$, a = 6.314(2), b = 12.572(2), c = 24.312(4) Å, V = 1929.7(7) $Å^{-3}$, Z = 4, D_x = 1.327 $Mg.m^{-3}$, λ(MoKα) = 0.70926 Å, μ = 3.25 cm^{-1}, F(000) = 816, T=294 K. Automatic diffractometer CAD4 ENRAF-NONIUS, graphite monochromatized MoKα radiation. Cell parameters obtained by fitting a set of 25 high-theta reflections. Data collection ($2\theta_{max}$ = 50°, scan $\omega/2\theta$ = 1, t_{max} = 60 s, range HKL : H -2,9 K -6,15 L -11,23, intensity controls without appreciable decay): 5499 reflections from which 3030 independent with $I>3\sigma(I)$. Structure solved with Direct Methods. Refinement performed by full-matrix least-square techniques (use of F magnitude ; x, y, z, β_{ij} for Cl, O, N and C atoms and x, y, z for H atoms ; 332 variables and 3030 observations ; $w = /\sigma(F_o)^2 = [\ \sigma^2(I) + (0.04F_o^2)^2\ ]^{-1/2}$) with the resulting R = 0.0288, R_w = 0.0318 and S_w = 1.077 (residual $\Delta\rho \leq 0.20$ $eÅ^{-3}$). Absolute configuration from refinement of the η parameter[4] to 1.00(2). To confirm, a refinement fixed as the opposite absolute structure gave R = 0.0301, R_w = 0.0327 and S_w = 1.106. Atomic scattering factors from International Tables for X-ray Crystallography[5]. Calculations performed on a Hewlett Packard 9000-710 for structure determination[6] and on a Digital Micro VAX 3100 computer with the MOLEN package[7] for refinement and Ortep calculations[8]. All these characteristics are very close to those of (+)-isoconcinndiol **2**[9] .

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