Tetrahedron Letters,Vol.24,No.31,pp 4063-4066,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

THE ISOLATION AND STRUCTURE DETERMINATION OF CHILENONE A, A PUTATIVE DIMER OF 2-METHYL-3(2H)-FURANONE FROM THE MARINE ALGA *LAURENCIA CHILENSIS*

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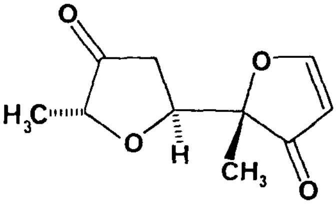
Summary: The isolation of chilenone A from *Laurencia chilensis* and the determination of its structure by spectral and x-ray crystallographic techniques is described.

Red marine algae of the genus *Laurencia* have been the subject of a large number of recent chemical investigations. These plants have been a rich source of new natural products and many halogenated terpenes[1] and linear C_{15} acetylenes[2] have been reported. An earlier communication has dealt with *Laurencia chilensis* and the isolation of 3-hydroxy-4-methylacetophenone was reported.[3] In this preliminary communication we wish to point out that a rather different array of secondary metabolites occurs in this alga. Specifically, we wish to report on the isolation and structure proof of chilenone A (**1**).



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A 5.4 kg collection of Laurencia chilensis was obtained at Horcones Bay, Chile in January 1982. Voucher specimens are available from the Museo de Historia Natural de Chile. The dried, ground plant material was extracted with acetone (Soxhlet) to give 180 g of extract. This extract was chromatographed on silica gel (70-230 mesh) using open column chromatography and petroleum ether-ethyl acetate mixtures of increasing polarity. The first fraction was mostly a mixture of steroids and the second fraction was a mixture of at least three compounds. The second fraction was rechromatographed on silica gel using 40% petroleum ether-ethyl acetate to give three pure compounds, one of which crystallized. This crystalline compound, chilenone A (1), was further purified by crystallization to a m.p. of 51 °C

A formula of $C_{10}H_{12}O_4$ was deduced for chilenone A from mass spectrometry. This was confirmed by ^1H and ^{13}C NMR spectroscopy and ultimately by a single crystal x-ray diffraction experiment. Preliminary x-ray photographs showed orthorhombic symmetry and accurate lattice constants of $\mathbf{a}$=7.916(2), $\mathbf{b}$=24.676(4) and $\mathbf{c}$=10.054(2) Å were determined from a least squares fit of fifteen diffractometer measured 2Θ-values. The systematic extinctions and estimated crystal density were uniquely consistent with space group Pbca with one molecule of $C_{10}H_{12}O_4$ forming the asymmetric unit. It should be noted that this space group requires chilenone A to be either an achiral molecule or a racemic mixture. Upon successful refinement (vide infra) the latter description was shown to be correct. That chilenone A is a racemic mixture is also consistent with our inability to observe a measurable optical rotation for chilenone A. All unique diffraction maxima with $2\theta \lesssim 114°$ were collected on a computer controlled four-circle diffractometer using a variable speed, 1° ω-scan and graphite monochromated CuK$\bar{\alpha}$ radiation (1.54178 Å). After correction for Lorentz, polarization and background effects, 970 (62%) of the 1573 reflections were judged observed ($|F_o| \gtrsim 3\sigma(F_o)$). A phasing model was readily achieved using a multisolution sign determining procedure.[4] All nonhydrogen atoms were revealed on the first E-synthesis and eleven of the twelve hydrogens were located on a subsequent difference synthesis following partial refinement of the nonhydrogen atoms. The twelfth hydrogen was included at a calculated position. Block diagonal least squares refinements with anisotropic nonhydrogen atoms and isotropic hydrogens have converged to a standard crystallographic residual of 0.064.[5] A computer-generated perspective drawing of the final x-ray model is given in Figure 1.

The ^1H and ^{13}C NMR spectra are fully consistent with this structure. The alkene protons, H5 and H4, appear at δ 8.22 and 5.71 respectively with a 2.4 Hz coupling constant. The quaternary methyl protons, $C6H_3$, are a singlet at 1.50. The proton attached to C5', H5' is a double doublet at 4.47 with an 8.5 Hz cis coupling constant and a 3.7 Hz trans coupling constant. The methylene protons attached to C4' resonate at 2.14 and 2.49 as double doublets with a geminal coupling constant of 18.3 Hz. The proton giving rise to the 2.14 signal is cis to the 3(2H)-furanone substituent. The methine proton on C2', H2', is a quartet at 4.12 with a 6.8 Hz coupling constant and the remaining methyl group, C6'H_3, is a doublet at 1.26 with the same coupling constant. These assignments were confirmed with selected decoupling experiments. The ^{13}C NMR is assigned as follows: δ 214.1 (s, C3'); 204.5 (s,C3); 177.6 (d, C5); 107.3 (d, C4); 91.6 (s, C2); 76.2 and 75.6 (both d's, C2' and C5'); 35.47 (t, C4'); 18.6 and 16.6 (both q's, C6 and C6'). Chilenone A showed carbonyl absorptions in the IR at 1775 and 1705 cm^{-1}.

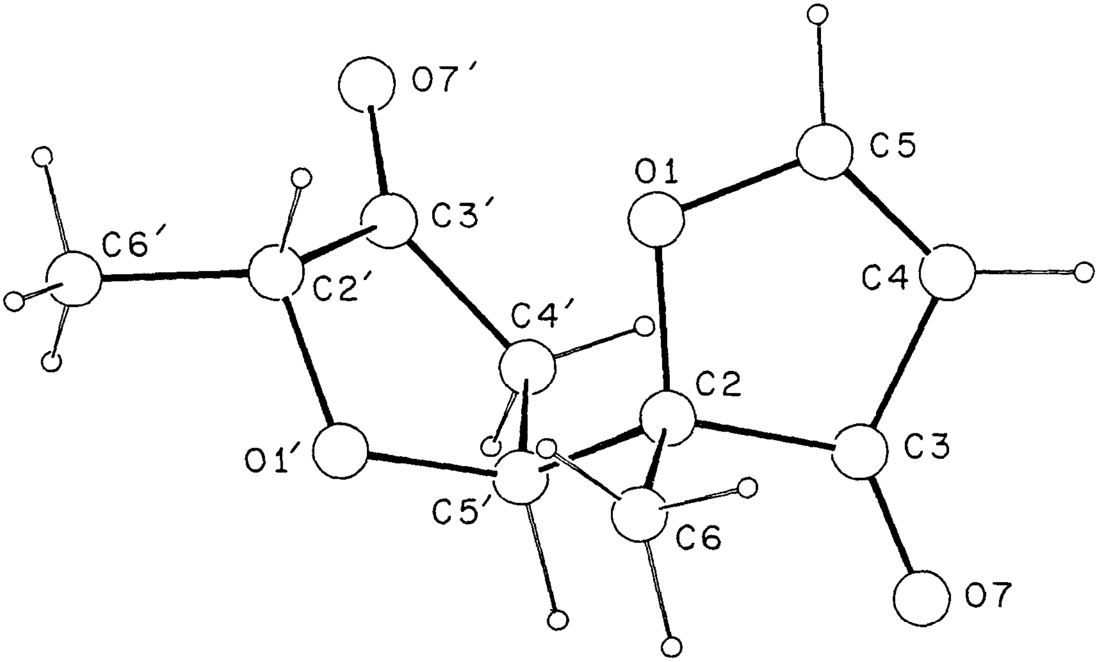

Figure 1. A computer generated perspective drawing of chilenone A including hydrogens. The compound was isolated as a racemic mixture.

A computer generated perspective drawing of the final x-ray model of chilenone A is given in Figure 1. Bond distances and angles agree well with generally accepted values.[5] The 3(2H)-furanone ring is virtually planar with all torsional angles being less than 3.5°. The tetrahydrofuran ring is best described as adopting an envelope conformation with C5' serving as the flap.

The structure of chilenone A is unusual and we are not aware of any published precedents. It could very plausibly arise from the dimerization of 2-methyl-3(2H)-furanone by a conjugate addition of the derived enolate. This biogenesis is especially attractive because of the racemic nature of chilenone A and the trans relationship of the substituents on the saturated ring. The potential precursor, 2-methyl-3(2H)-furanone has been known since 1929 when it was prepared in poor yield from $CH_3CO(CHOH)_3CO_2H$.[6] It has not been reported from any natural sources. The saturated compound, 2-methyltetrahydrofuran-3-one has been reported as one of the volatile constituents of roasted coffee.[7]

ACKNOWLEDGMENTS. We wish to thank DDI, University of Chile, and Organizacion Estados Americanos for support of the work in Chile and NIH-CA-24487 and the New York State Sea Grant for support of the work at Cornell.

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4. All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, a system of computer programs for the automatic solution of crystal structures from x-ray diffraction data which were locally modified to perform all Fourier calculations including Patterson syntheses written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq and M. M. Woolfson, University of York, England, 1978; NQEST, CYBER 173 version of the negative quartets figure of merit estimate written by C. M. Weeks at the Medical Foundation of Buffalo, Inc., 1976; BLS78A, an anisotropic block diagonal least squares refinement written by K. Hirotsu, and E. Arnold, Cornell University, 1980; ORTEP, an crystallographic illustration program written by C. K. Johnson, Oak Ridge National Laboratory, 1965; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu, Cornell University, 1978.

5. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, Lensfield Rd., Cambridge, England.

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