

IRIEOL A AND IRIEDIOL, DIBROMODITERPENES OF A
NEW SKELETAL CLASS FROM LAURENCIA

William Fenical* and Bruce Howard
Institute of Marine Resources
Scripps Institution of Oceanography
La Jolla, California 92093

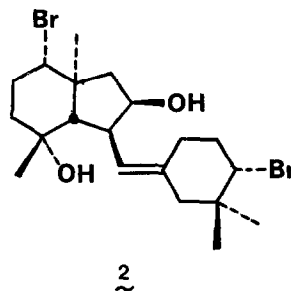
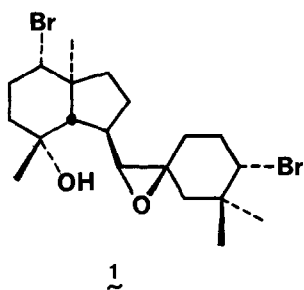
and

Kirsten B. Gifkins and Jon Clardy*
Ames Laboratory-USERDA and Department of Chemistry
Iowa State University
Ames, Iowa 50010

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Red seaweeds of the genus Laurencia are unique in their diverse biosynthesis of non-terpenoid compounds related to laurediol, as well as sesquiterpenes of the chamigrene, cuparene, bisabolene and oppositol ring systems¹. In addition, some methyl-rearranged sesquiterpenes, isolaurinterol², laurene³, perforatone⁴ and perforone A and B⁴, have been reported. One diterpene, concinndiol, of the rather common labdane ring system, is also known from a Laurencia species⁵. In our continuing studies of the halogen-containing metabolites from this fascinating genus⁶, we have isolated a series of dibromoditerpenes with a new diterpene ring system. Reported herein are the structures of two members of this new group, irieol A (1) and iriedioli (2), which have been determined by X-ray diffraction methods. Interestingly, part of these diterpenes, including relative stereochemistries, are identical in structure to the Laurencia sesquiterpene oppositol⁷.

Silica gel column chromatography of the chloroform extract of the air-dried alga⁸ gave crystalline samples of both 1 and 2. Irieol A (1) (benzene elution)



mp. 142-4° (CHCl₃) [α]_D²⁵ 0° (c 1.73, CHCl₃) was isolated in 0.008% (dry wt. basis) and had the following nmr characteristics: (220 MHz, CDCl₃) δ 4.36 (bs, 1H), 3.97 (d of d, J = 12,5Hz, 1H), 2.61 (d, J = 10 Hz, 1H), 1.3-2.5 (m, 17H), 1.27 (s, 1H), 1.24 (s, 3H), 1.20 (s, 3H), 1.09 (s, 3H). The mass spectrum of 1 showed only an M⁺-H₂O fragment at m/e 444/446/448 for C₂₀H₃₀Br₂O. Iriediol (2) (5% ether in benzene elution) mp. 103-105° dec. (CHCl₃) [α]_D²³ - 183° (c, 0.25, CHCl₃) was isolated in 0.11% yield and had the following nmr characteristics: (220 MHz, CDCl₃) δ 5.05 (d, J = 10 Hz, 1H), 4.14 (d of d, J = 9,4Hz, 1H), 3.91 (d of d, J = 12,4 Hz, 1H), 3.84 (m, 1H), 3.06 (m, 1H), 2.68 (m, 1H), 2.34 (m, 1H), 1.5-2.2 (m, 13H), 1.41 (s, 3H), 1.20 (s, 3H), 1.07 (s, 3H), 0.93 (s, 3H). The mass spectrum of 2 was analogous to 1 in that the largest fragment was clearly M⁺-H₂O at 444/446/448.

Crystals of irieol A (1) belong to the space group P₂₁ with $a = 7.45(1)$, $b = 11.41(2)$, $c = 12.06(2)$ Å and $\beta = 85.21(5)^\circ$ and one molecule of composition C₂₀H₃₂Br₂O₂ per asymmetric unit. A total of 1490 unique reflections with $\theta \leq 57^\circ$ were measured using graphite monochromated CuK α radiation. Periodically monitored check reflections indicated an 18% decline in intensities. After correction for crystal decay, Lorentz and polarization effects, 1284 reflections were judged observed ($F_o \geq 3\sigma(F_o)$).

The structure was solved routinely by deconvolution of the Patterson to yield Br positions and the nonhydrogen atoms were located with Br-phased

electron density synthesis. Full-matrix, least squares refinement with anisotropic temperature factors for nonhydrogen atoms and isotropic temperature factors for hydrogen converged to a minimum unweighted crystallographic residual of 0.057⁹.

Crystals of iriediol belong to the common and unambiguously determined orthorhombic space group $P2_12_12_1$ with $a = 15.47(4)$, $b = 16.80(3)$ and $c = 7.90(1)$ Å with one molecule of $C_{20}H_{32}Br_2O_2$ per asymmetric unit. A total of 1580 unique reflections with $\theta \leq 45$ were measured on a fully automated four-circle diffractometer using monochromated Mo $K\alpha$ (0.7107 Å) radiation. Periodically monitored standard reflections declined 5% for which no correction was made. After Lorentz, polarization and background corrections, 1456 reflections were judged observed ($F_o \geq 3\sigma(F_o)$).

Normalized structure factors were computed and phase angles assigned to the 499 E's larger than 1.06 by a multiple solution, weighted tangent formula procedure¹⁰. The phased three-dimensional E-synthesis revealed both bromines and ten carbons. A subsequent F-synthesis revealed all nonhydrogen atoms. Full-matrix least-squares refinements smoothly converged to an unweighted crystallographic residual of 0.081 (*vide infra*)⁹.

All bond distances and angles for $\underline{1}$ and $\underline{2}$ agree well with generally accepted values¹¹. There are no unusually short intermolecular contacts.

Attempts to define the absolute stereochemistries of $\underline{1}$ and $\underline{2}$ have led to puzzling results. Inclusion of the anomalous scattering contribution for Br and refinement of the structure and its enantiomer indicated that irieol A has the absolute stereochemistry shown ($R = 0.057$, $wR = 0.056$ for $\underline{1}$ and $R = 0.059$, $wR = 0.058$ for the enantiomer of $\underline{1}$) but iriediol has the opposite absolute stereochemistry ($R = 0.081$, $wR = 0.098$ for $\underline{2}$ and $R = 0.070$, $wR = 0.084$ for the enantiomer of $\underline{2}$)¹². A careful remeasurement of the most enantiomorph sensitive reflections of both $\underline{1}$ and $\underline{2}$ (20 reflections each using Mo $K\alpha$ radiation) also supports this assignment. Since the effects are small, we regard these assignments as tentative.

There exists the additional possibility, based upon our current inability to

observe any optical rotation for irieol A, that irieol A is racemic. The crystals, however, unambiguously belong to a chiral space group, and intensity differences in Friedel pairs, although small, are clearly measurable. Hence, if racemic, irieol A spontaneously resolves upon crystallization, and both single crystals that we have examined fortuitously represent the same enantiomer.

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6. The Laurencia species under consideration here is among a group of algae which appear to be undescribed entities from the Gulf of California. The taxonomic assignment of this alga is in preparation and will appear elsewhere. Also see: W. Fenical, J. N. Norris, J. Phycol. **11**, 104 (1975) for a more detailed description of the Laurencia sp. under question. Irieol A and iriediol were named in honor of Professor Toshi Irie, Hokkaido University, because of his pioneering work in Laurencia metabolites.
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