Tetrahedron Letters,Vol.23,No.38,pp 3847-3850,1982 0040-4039/82/383847-04$03.00/0
Printed in Great Britain

NEOIRIEONE, A DITERPENOID OF A NEW SKELETAL CLASS FROM THE RED MARINE ALGA *LAURENCIA* CF *IRIEII*

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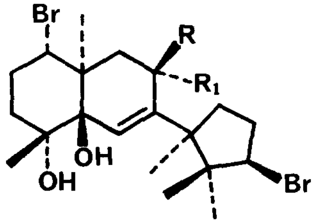
Summary Neoirieone, a dibrominated diterpenoid of a new skeletal class, related to the irieol diterpenoids, has been isolated from *Laurencia* cf *irieii* The structure of neoirieone was elucidated by x-ray crystallographic analysis of its corresponding reduction product, neoirieol (7)

Red marine algae of the genus *Laurencia* are noted for their prolific and diverse synthesis of halogenated and rearranged terpenoids.[1] In the past 15 years over 25 terpene-derived ring systems have been reported from this source As a consequence of our long term interest in the diterpenoids from this source, we wish to describe here the structure of a new diterpenoid, neoirieone (1) The skeletal name neoirieane, as in 2, is suggested for this new class based upon its structural similarity and potentially related biosynthesis to the irieane (3) diterpenoid class [2]

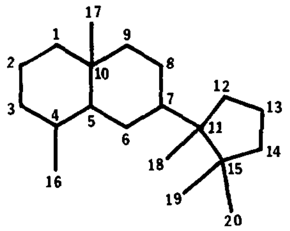
As part of our chemotaxonomic studies of various *Laurencia* species,[3] we investigated *L* cf *irieii* over its distributional range within the Gulf of California One particular collection, made at Bahia de Los Angeles, was found to contain several of the previously reported irieols,[2] irieol C (4), irieol D (5), and irieol E (6), but the major metabolite of this collection (10% extract) was found to be a new tricyclic dibromoditerpenoid of a unique structure class

Fractionation of the crude $CHCl_3$/MeOH extract of the alga on silica gel, followed by silica HPLC purification, yielded neoirieone (1) as a viscous oil Analysis of the spectral features of 1[4] allowed a basic formulation of the structure of this compound Details of the full stereochemistry at C5, C11 and C14 could not be extracted from these data In order to produce a crystalline derivative for x-ray analysis, the ketone 1 was reduced with $NaBH_4$ in methanol to yield the crystalline neoirieol (7) [5] Preliminary x-ray photographs revealed that neoirieol possessed orthorhombic symmetry, and accurate lattice constants, determined from a least-squares fitting of fifteen 2θ-values, were a = 10 817(92), b = 11 756(85), and c = 16 185(62)Å Systematic extinctions, density considerations and the presence of chirality were uniquely accommodated by space group $P2_12_12_1$ with one molecule of $C_{20}H_{32}Br_2O_3$ forming the asymmetric unit All unique diffraction maxima with 2θ ≦ 114° were collected on a four-circle diffractometer using a variable



1, R=R1=O

7, R=OH,R1=H



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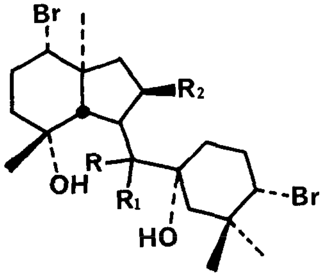
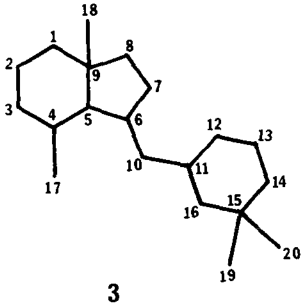


4, R=R1=R2=H

5, R=OH,R1=H,R2=OAc

6, R=R2=H, R1=OH



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speed ω-scan and graphite monochromated CuKα radiation (1 54178Å) Of the 1619 data recorded in this manner, 1489 (92%) were judged observed (|Fo| ≧ 3σ(Fo)) after correction for Lorentz, polarization and background effects Periodically monitored check reflections showed an approximate 10% decrease but this decomposition was not used in the data reduction

A phasing model consisting of two bromines was found by deconvoluting the Patterson and subsequent electron density syntheses eventually showed all of the nonhydrogen atoms[6] A difference electron density synthesis after partial least-squares refinement showed the hydrogen atoms Full-matrix least-squares refinements with anisotropic nonhydrogen atoms and isotropic hydrogens and an anomalous dispersion correction for bromine have converged to a conventional discrepancy index of 0.036 for the structure and 0.043 for the enantiomer[7]

Figure 1 illustrates the computer-generated structure of neoirieol (7) with absolute stereochemistry as deduced using the anomalous scattering of bromine The two six-membered rings are joined in a *trans* manner The cyclohexane ring is in the chair conformation with -C(16)H_3 and -Br(1) in equatorial orientations The hydroxyls, -O(1)H and -O(2)H, are in axial orientations with a 177° dihedral angle between them The cyclohexene ring has a 1,2-diplanar conformation The double bond, C(6)=C(7) has a negligible dihedral angle and the C(6)-C(7)-C(8)-C(9) dihedral

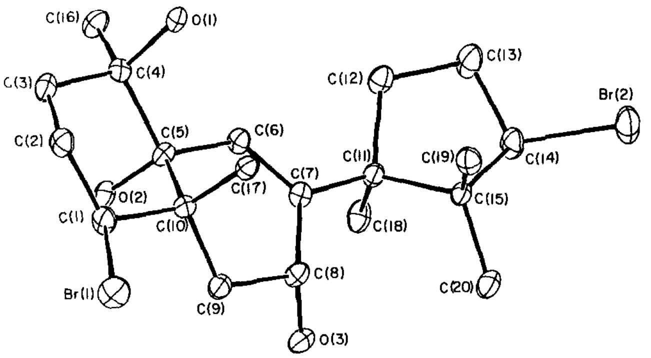
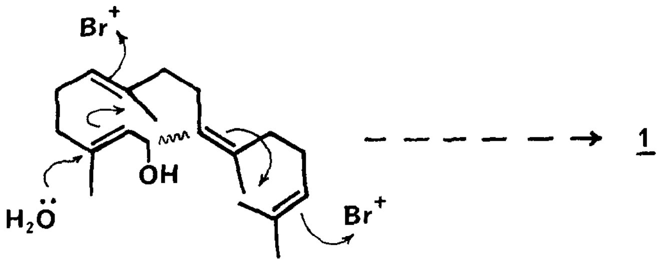
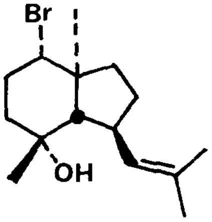


Figure 1

angle is also zero The cyclopentane ring is rotated so that the -C(18)H_3 group is perpendicular to the C(6), C(7), C(8) plane It has an envelope conformation with C(15) serving as the flap Br(2), C(7) and C(20) are in pseudoequatorial positions and C(18) and C(19) are in axial positions The stereochemical descriptors are C(1)*S*, C(4)*R*, C(8)*R*, C(10)*S*, C(11)*R*, and C(14)*R*

On structural grounds, neoirieone appears to be the biosynthetic product of two bromonium-ion-induced cyclizations of a typical linear diterpenoid precursor, as illustrated below[9] The irieane and neoirieane diterpenoid skeletons appear related in much the same way as the *Laurencia*-derived sesquiterpenoids oppositol (**8**)[10] and selinane **9**[11] A plausible intermediate relating these sesqui- and diterpenoid systems could be structure **10** which is converted to the rearranged skeletons (as in **8** and **3**) via an acid catalysed ring opening of the cyclopropane ring at C9-C10





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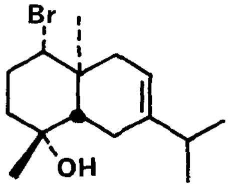

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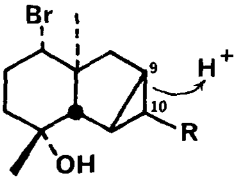

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Acknowledgements

Research at the Scripps Institution was supported by NSF, Oceanography Division under grant OCE 80 14167 Research at Cornell University was supported by the NIH under grant CA 24487 BMH wishes to acknowledge NSF grant TFI80-19267 for HPLC equipment support

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4 Neoirieone, $[\alpha]_D^{20}$ +1 0° (c 1 5, $CHCl_3$) IR ($CHCl_3$) 3300, 2950, 1680, 1480, 1380, 1200, 1000, 960 cm^{-1}, LRMS m/z 458/460/462, M^+-H_2O ($C_{20}H_{28}Br_2O_2$), ^1H NMR (220 MHz, $CDCl_3$) δ 7 00 (1 H, s), 4 59(1H, dd, *J* = 12, 4 Hz), 4 34 (1 H, dd, *J* = 7, 7 Hz), 2 80 (1 H, d, *J* = 17 Hz), 1 5-2 60 (11 H, m), 1 43 (3 H, s), 1 34 (3 H, s), 1 30 (3 H, s), 1 11 (3 H, s) and 0 87 (3 H, s) ^{13}C NMR ($CDCl_3$) δ 200 1 (s), 148 1 (s), 144 9 (d), 75 7 (s), 73 5 (s), 64 1 (d), 60 7 (d), 51 8 (t), 49 2 (s), 47 6 (s), 45 2 (s), 37 5 (t), 35 7 (t), 31 2 (t), 29 8 (t), 25 7 (q), 24 7 (q), 23 5 (q), 22 4 (q), 19 9 (q)

5 For neoirieol (acetate derivative) ^1H NMR ($CDCl_3$, 220 MHz) δ 5 34 (1 H, d, *J* = 5 Hz), 4 45 (1 H, dd, *J* 12, 5 Hz), 4 23 (1 H, dd, *J* = 7, 7 Hz), 2 02 (3 H, s), 1 30 (3 H, s), 1 25 (3 H, s), 1 18 (3H, s), 1 07 (3 H, s) and 0 86 (3 H, s)

6 All crystallographic calculations were done on a Prime 400 computer, operated by the Materials Science Center, Cornell University The principal programs used were as follows REDUCE and UNIQUE, data reduction programs, M E Leonowicz, Cornell University, 1978, BLS, block-diagonal least-squares refinement, K Hirotsu, Cornell Univesity, 1978, ORFLS (modified) full-matrix, least-squares, W R Busing, K O Martin, and H S Levy, Oak Ridge National Laboratory Report No ORNL-TM305, ORTEP, crystallographic illustration program C Johnson, Oak Ridge National Laboratory No ORNL-3794, BOND, structural parameters and errors, K Hirotsu, Cornell University, 1978, MULTAN-76 direct methods and fast fourier transform, G Germain, P Main and M Woolfson, University of York

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8 Supplementary crystallographic information defining the structure of neoirieol (1) have been deposited with the Cambridge Crystallographic Data Center

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(Received in USA 8 June 1982)