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MOLECULAR STRUCTURE OF ACETOXYINTRICATOL: A NEW BROMO COMPOUND FROM LAURENCIA INTRICATA.

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As a result of a preliminary survey[1] conducted during the past year, halogenated compounds have been found to occur widely in marine organisms. As has been previously reported,[2] members of the genus Laurencia, family Rhodomelaceae, have been found to contain consistently large amounts of halogenated materials. The present work describes the characterization and identification of a sesquiterpene (I), for which we propose the name acetoxyintricatol, one of seventeen new halogenated compounds isolated from Laurencia intricata. On the basis of chemical, spectroscopic, and X-ray diffraction studies, the structure of acetoxyintricatol has been established as that shown in Figure 1.

Benzene-methanol extracts of the fresh seaweed were chromatographed on a standard silica gel column and assayed for organic halogen. From the hexane-ether (50:50) eluent was obtained 76 mg of compound (I) in 1.4% yield from the oil. Acetoxyintricatol (I) had analytical data corresponding to $C_{17}H_{27}O_3Br_2Cl$, m/e 472, 474, 476, 478; high resolution $M^+ - CH_3 - HOAc$, m/e = 398.9568 (calcd for $C_{14}H_{20}OCl^{35}Br^{79}Br^{81}$ 398.9550) and $M^+ - Br - HOAc$, m/e = 333.0617 (calcd $C_{15}H_{23}OCl^{35}Br^{79}$ 333.0621). The IR spectra ($\bar{\nu}$ = 3500, 1720, and 1250 cm^{-1}) showed the presence of a hydroxyl group and an acetate ester. The PMR spectrum (100 MHz, $CDCl_3$, δ scale) displayed signals at 5.31 (1H, dd, J = 5.8 and 11.8 Hz, $C\underline{H}OC(=O)-CH_3$), 5.06 (1H, dd, J = 4.0 and 13.2 Hz, $Cl-C-C(Br)-\underline{H}$), 4.22 (1H, dd, J = 5.6 and 10.6 Hz, $C\underline{H}-Br$), 3.20 (1H, bd t, J = 11.9 Hz, $CH_3C(=O)-O-C-C-\underline{H}$). In addition, four tertiary methyl signals were observed at 1.78 ($\underline{Me}-C-Cl$), 1.52 ($\underline{Me}-C-OH$), 1.15 and 1.16 (gem dimethyl) and an acetate methyl appeared at 2.12. One D_2O exchangeable proton occurred at 1.6. Consideration of the above information led to the conclusion that the molecule contains a bicyclic system. From a comparison of

the above data with those from materials previously isolated from other Laurencia species, pacifenol,[3] johnstonol,[4] prepacifenol,[5] and caespitol,[6] structure (I) was proposed.

Crystals of (I) suitable for X-ray work were obtained from hexane-carbon tetrachloride (50:50). The colorless brick-shaped crystals are orthorhombic, $\underline{a}$ = 14.80(5), $\underline{b}$ = 7.73(3), and $\underline{c}$ = 17.25(3) Å, the space group is $P2_12_12_1$ and there are four molecules per unit cell. A total of 1,264 non-zero reflections was collected on a Picker FACS-1 diffractometer using CuK_α radiation. The intensity of the standards decreased quite rapidly with time; hence, it was necessary to use two crystals to accumulate the data. The structure was solved by heavy atom methods. The positions of all non-hydrogen atoms were refined by full-matrix least squares methods (with the bromine and chlorine atoms being allowed to vibrate anisotropically) to an R-factor of 0.115 on all non-zero reflections. The largest peaks on a final difference map were at positions expected for hydrogen atoms. The final coordinates are listed in Table 1. The enantiomer shown in Figure 1 was choosen to agree with the absolute configuration found for pacifenol[3] and johnstonol.[4]

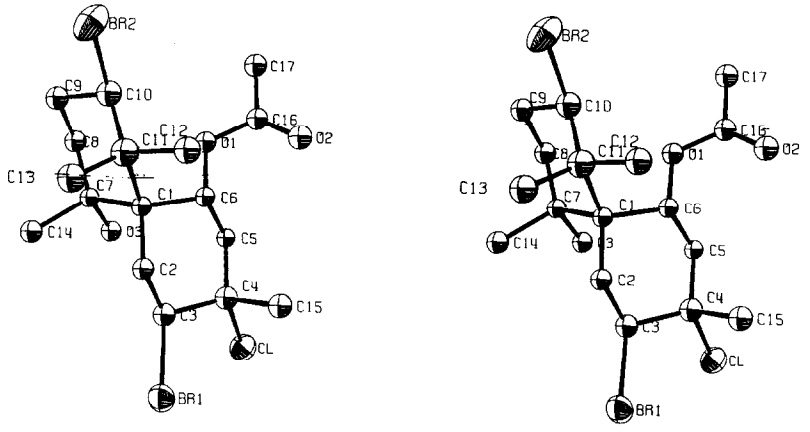
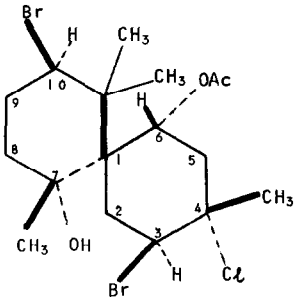
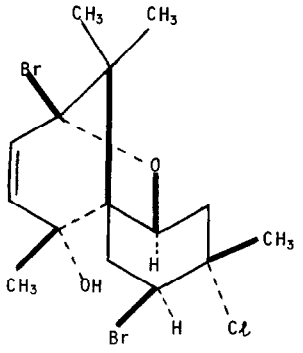


Figure 1: A stereoscopic view of a molecule of (I).



(I)



(II)

The bond lengths and angles are not unusual. Both spiro-cyclohexane rings are in a chair conformation. The hydroxyl oxygen O(3) forms a hydrogen bond with O(2) in the molecule at -1/2 + x, 1 1/2 - y, 1 - z to give an infinite chain of molecules along the x-direction in the crystal. The O(3)---O(2) distance is 2.93(2) Å and the C(7) — O(3)---O(2) angle is 105(1)°. There is a possibility that the bromine atom in the molecule at 1 - x, 1/2 - y, 1/2 - z also serves as an acceptor for this hydrogen bond, to give it partial bifurcated character.

The structure of acetoxyintricatol (I) resembles that of pacifenol (II), the difference being loss of the double bond between C(8) and C(9), and opening of the oxygen-containing ring in pacifenol, plus replacement of the ether oxygen by an acetate ester with change of configuration at C(6) in acetoxyintricatol. In as much as Laurencia intricata was obtained from the Atlantic Ocean and Laurencia pacifica from the Pacific, these small differences in chemical structures of (I) and (II) may be of particular interest to marine biologists.[7]

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References

1. R. H. White, Ph.D. Thesis, University of Illinois, Urbana, Illinois, January 1974.
2. J. F. Siuda, and J. F. DeBernardis, Lloydia, 36, 107 (1973).
3. J. J. Sims, W. Fenical, R. M. Wing, and P. Radlick, J. Amer. Chem. Soc., 93, 3774 (1971).
4. J. J. Sims, W. Fenical, R. M. Wing, and P. Radlick, Tetrahedron Letters, 195 (1972).
5. J. J. Sims, W. Fenical, R. M. Wing, and P. Radlick, J. Amer. Chem. Soc., 95, 972 (1973).

6. A. G. Gonzaliz, J. Darias, and J. D. Martin, Tetrahedron Letters, 2381 (1973).

7. Algae were collected in early July, 1973 in shallow water at Key Largo, Florida, lat. 80° 37.9'; long. 24° 50.0'.

Table 1. Final atomic co-ordinates for acetoxyintricatol. Standard deviations in parentheses.

Atom	x	y	z
Br(1)	.5930(2)	.4599(5)	.2219(2)
Br(2)	.5134(3)	.1284(4)	.6737(2)
Cℓ	.6704(6)	.8518(11)	.2884(4)
O(1)	.6194(10)	.6500(20)	.5618(8)
O(2)	.7716(12)	.6462(23)	.5690(9)
O(3)	.4560(11)	.7180(21)	.4400(8)
C(1)	.548 (2)	.454 (3)	.465 (1)
C(2)	.565 (1)	.395 (3)	.384 (1)
C(3)	.577 (2)	.553 (3)	.328 (1)
C(4)	.662 (2)	.657 (3)	.353 (1)
C(5)	.649 (1)	.731 (3)	.436 (1)
C(6)	.632 (2)	.572 (3)	.485 (1)
C(7)	.447 (1)	.548 (3)	.480 (1)
C(8)	.414 (2)	.572 (3)	.557 (1)
C(9)	.414 (2)	.397 (3)	.603 (1)
C(10)	.509 (2)	.332 (3)	.603 (1)
C(11)	.547 (2)	.284 (4)	.525 (2)
C(12)	.650 (2)	.223 (3)	.525 (1)
C(13)	.496 (2)	.130 (3)	.485 (2)
C(14)	.372 (2)	.448 (3)	.428 (1)
C(15)	.758 (2)	.562 (3)	.346 (1)
C(16)	.698 (2)	.685 (3)	.596 (1)
C(17)	.682 (2)	.769 (3)	.676 (1)