

## THE ABSOLUTE CONFIGURATIONS OF LAUREATIN AND ISOLAUREATIN

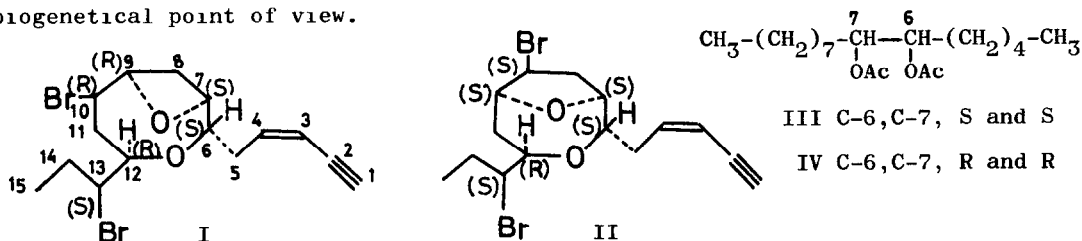
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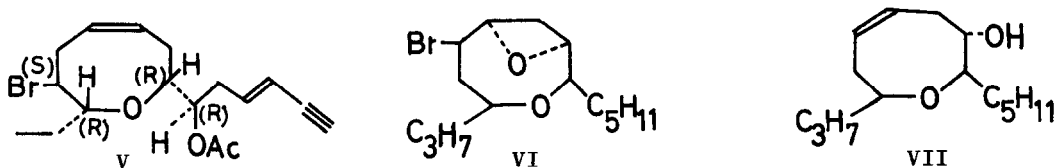
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In previous papers (1,2,3), the structures and stereochemistry of laureatin (I) and isolaureatin (II),  $C_{15}H_{20}O_2Br_2$ , isolated from Laurencia nipponica Yamada, have been proposed by the views of their physical and chemical properties and biogenetical point of view.



The configurations at C-6 and C-7 (S and S) have been determined by means of optical rotation of glycol diacetate (III), derived from I (zinc-acetic acid,  $H_2/PtO_2$  and acetylation), which was antipode of diacetate (IV) from laureatin (V) (4,5,6). The stereochemical relationship between ether oxygen at C-9 and bromine at C-10 in I was proposed as trans by the observation of zinc-acetic acid degradation of hexahydromonodebromolaureatin (VI) (1,3), yielding smoothly unsaturated cyclic ether (VII) and coupling constant (2.5 Hz) between protons at C-9 and C-10, arising from dihedral angle of  $60^\circ$ . Consequently, each center at C-9 and C-10 would be reasonably assigned as R-configuration.



On the other hand, the proton at C-12 in I was located as  $\alpha$ -configuration, because of its considerable downfield shift ( $\tau$  5.62) on nmr spectrum, which should be probably caused by situation closing to oxygen of the oxirane ring. The relative relationship concerning C-12 and C-13 has been presumed to be erythro from biogenetic point, in which laureatin (I) and laurencin (V) would be formed from the same precursor (3), hexadeca-4,7,10,13-tetraenoic acid, via the similar pathway at least concerning C-12 and C-13. Therefore, S-configuration has been assigned to C-13 in I.

Furthermore, the structural and stereochemical relationship between laureatin (I) and isolaureatin (II) has been undoubtedly established by acid-catalyzed rearrangement of I to II (7). The above presumptions concerning stereochemistry were fully confirmed by the study of crystallographic method to isolaureatin as follows.

The crystals are orthorhombic, with four molecules in a unit cell of the dimensions,  $a = 12.227$ ,  $b = 18.594$  and  $c = 7.110 \text{ \AA}$ . The space group is  $P2_12_12_1$ . The intensities of reflections with  $2\theta$  values up to  $54^\circ$  were collected on a Rigaku automatic four-circle diffractometer, using Mo  $K\alpha$  radiation monochromatized with a LiF crystal. The intensity measurement was made by use of the  $\omega$ - $2\theta$  scanning technique. The structure was solved by the heavy-atom method, and was refined by the block-diagonal-matrix least-squares method, anisotropic thermal motions being assumed for all the atoms (8). At the stage of the R factor of 10.2%, the absolute configuration of the molecule was determined by taking account of the anomalous dispersion of the bromine atoms for Mo  $K\alpha$  radiation. The R factors obtained for structure shown in Fig. 1 and its antipode were 7.1 and 10.2% , 9.0 and 10.6% and 8.0 and 9.4% for the 20, 50 and 100 reflections having the largest  $||F_c(hkl)| - |F_c(\bar{h}\bar{k}\bar{l})|| / \sigma(F_o)$  values respectively. Thus, the full structure of isolaureatin including the absolute configuration was established as shown in Fig. 1. Further least-squares refinement including the anomalous dispersion effects reduce the R factor to 9.7%. The final atomic coordinates are listed in Table 1.

Table 1. The final atomic coordinates

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
Br(1)	-0.2274	0.3733	0.5347	C(7)	-0.0326	0.4810	0.1550
Br(2)	0.0629	0.1998	0.1547	C(8)	-0.0654	0.4650	0.3580
O(1)	0.0616	0.3657	0.1201	C(9)	-0.1849	0.4374	0.3393
O(2)	-0.1191	0.4591	0.0371	C(10)	-0.1797	0.4059	0.1315
C(1)	0.1791	0.3385	-0.5018	C(11)	-0.1285	0.3309	0.1119
C(2)	0.2240	0.3643	-0.3695	C(12)	-0.0232	0.3328	0.0046
C(3)	0.2837	0.3922	-0.2178	C(13)	0.0221	0.2609	-0.0620
C(4)	0.2431	0.4374	-0.0868	C(14)	-0.0554	0.2219	-0.1897
C(5)	0.1271	0.4633	-0.0789	C(15)	-0.0030	0.1543	-0.2854
C(6)	0.0738	0.4413	0.1101				

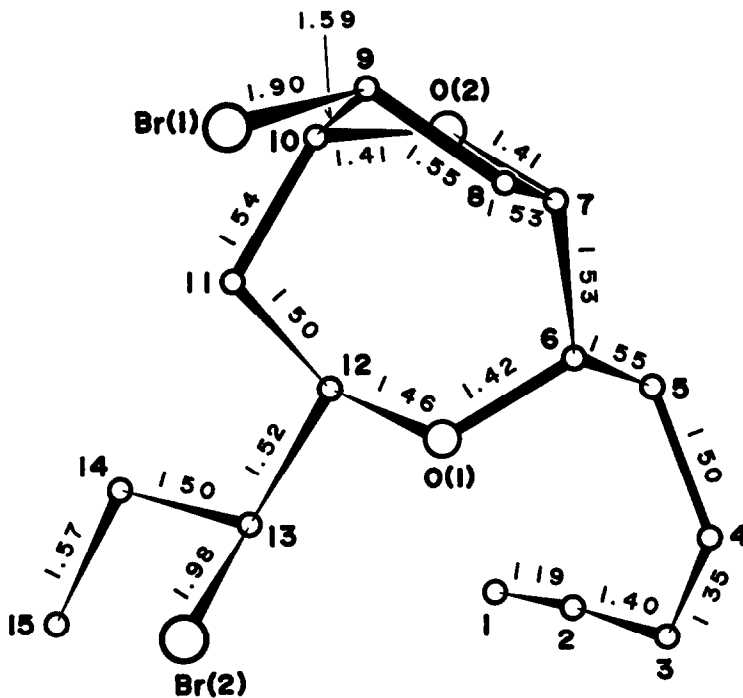


Fig. 1. The molecular configuration.

The molecular framework of isolaureatin thus obtained is shown in Fig. 1. The average standard deviations of the atomic coordinates are about 0.002, 0.010, and 0.017 Å for bromine, oxygen, and carbon atoms respectively. Considering these standard deviations, the bond distances and angles calculated with the final coordinates are all reasonable.

The full structures of laureatin (I) and isolaureatin (II) including the absolute configuration were established and thus, it will be possible to consider their biogenetical pathway from hexadeca-4,7,10,13-tetraenoic acid and laurediol (9) with laurencin (V) and the other bromo cyclic ether compounds (10), expressly regarding the stereochemistry.

#### References

Part XXI of "constituents from Marine Plants". Part XX ref. 9.

The structure and stereochemistry of laurencin were fully established by chemical and crystallographic method (4,5,6).

- (1) T. Irie, M. Izawa and E. Kurosawa, Tetrahedron Letters, 2091 (1968).
- (2) T. Irie, M. Izawa and E. Kurosawa, Tetrahedron Letters, 2735 (1968).
- (3) T. Irie, M. Izawa and E. Kurosawa, Tetrahedron, 26, 851 (1970).
- (4) T. Irie, M. Suzuki and T. Masamune, Tetrahedron Letters, 1091 (1965).
- (5) A. F. Cameron, K. K. Cheung, G. Ferguson and J. Monteath Robertson, Chem. Commun., 638 (1965), J. Chem. Soc. (B), 559 (1969).
- (6) T. Irie, M. Suzuki and T. Masamune, Tetrahedron, 24, 4193 (1968).
- (7) A. Fukuzawa, E. Kurosawa and T. Irie, J. Org. Chem., 37, 680 (1972).
- (8) All calculation necessary for the present study were carried out on a FACOM 230-60 computer at The Computer Center of Hokkaido University, using our own programs.
- (9) E. Kurosawa, A. Fukuzawa and T. Irie, Tetrahedron Letters, 2121 (1972).
- (10) Two new bromo cyclic ether compounds, prelaurefucin and isoprelaurefucin have been isolated from Laurencia nipponica Yamada and will be published in near future.