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LAUREATIN, A CONSTITUENT FROM *LAURENCIA NIPPONICA* YAMADA (1)

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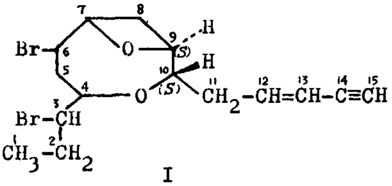
We describe herein the isolation and structural elucidation of a new bromo compound, designated as laureatin, in *Laurencia nipponica* Yamada (Japanese name Urasozo; Rhodomelaceae).

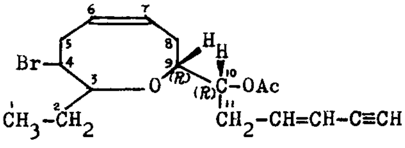
Laureatin (I), $C_{15}H_{20}O_2Br_2$ (M^+ 394, 392 and 390), m.p. 82-83°, $[\alpha]_D$ +96° (CCl_4), was isolated in 0.05% yield by chromatographic purification of the neutral fraction from methanol extracts of the dried seaweed. The UV, λ_{max}^{EtOH} 223 mμ (ε 12,800) and λ_{infl} 229 (10,400), and IR spectra, ν_{max}^{chf} 3300, 2100, 1140, 1086, 1045, 975 and 965 cm^{-1}, indicate that I is an ether having a conjugate enyne group and contains neither hydroxyl nor carbonyl function. The NMR spectrum (2) and the spin decoupling study (Fig. 1A) confirm the presence of groups $-CH_2-C(H\text{-}A)=C(H\text{-}B)-C\equiv C(H\text{-}I)$ (3) and $-C(H\text{-}L_1)(H\text{-}L_2)-C(H\text{-}M)_3$: τ 3.97 (H-A; 1H, sex, J = 11, 7 and 7 c/s), 4.47 (H-B; 1H, finely splitted d, J = 11) and 6.94 (H-I; 1H, d, J = 2), and Irrs B, I and J; τ 8.93 (H-M; 3H, t, J = 7 and 7), ca. 8.15 ($H\text{-}L_1$; 1H, m) and 8.3 ($H\text{-}L_2$; 1H, m), and Irr. M. The spectrum also displays absorptions of six protons in the region of τ 5.0 to 6.5; three one-proton septets at τ 5.12 (H-C; J = 8, 5.5 and 2 c/s), 5.46 (H-D; J = 8, 6 and 1.5) and 5.87 (H-F; J = 10, 8 and 2), a broad quartet(?) at 5.62 (H-E; 1H) and two multiplets centered at τ ca. 6.2 and 6.35 (H-G and H-H; each 1H). These absorptions should be ascribed to protons on carbons bearing an ether oxygen or a bromine atom. Thus, laureatin consists of the following structural units (4).

$-CH_2-CH=CH-C\equiv CH$, $-CH_2-CH_3$, 2 $-C(C)H-O-C(C)H-$, 2 $-C(C)H-Br$ and C_2H_4

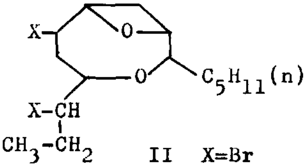
I consumed three moles of hydrogen over platinum catalyst in ethanol to yield hexahydrolaureatin (II), $C_{15}H_{26}O_2Br_2$ (M^+ 400, 398 and 396); ν_{max}^{film} 1144, 1078, 1050 and 975 cm^{-1}. On treatment with zinc in refluxing acetic acid and then with dilute alkali, II gave an unsaturated glycol (III), $C_{15}H_{28}O_2$ (M^+ 240), ν_{max}^{film} 3400 cm^{-1}, τ 6.61 (2H, m, >C$\underline{H}$-OH) and 4.54 (4H, m, olefinic protons), which was converted into the diacetate (IV), τ 7.97 (6H, s, $-OCOC\underline{H}_3$), 7.5-7.9 (4H, m, allylic protons), 7.28 (2H, m, $C=C-C\underline{H}_2-C=C$ (5)), ca. 5.1 (2H, m, >C$\underline{H}$-OAc) and ca. 4.6 (4H, m, olefinic protons). Hydrogenation of III over platinum in ethanol afforded a saturated glycol (V), $C_{15}H_{32}O_2$, m.p. 54-55°, $[\alpha]_D$ -25.4° (CCl_4), ν_{max}^{chf} 3600 and 3450 cm^{-1}, τ 6.72 (2H, m, >C$\underline{H}$-OH). The structure of V was deduced from the mass spectrum of its acetonide (VI), $[\alpha]_D$ -35° (CCl_4), $\underline{m/e}$ 269 (M^+-15), 227 (269 - $CH_2=C=O$), 213 and 171 (6), and confirmed by comparison with a sample derived from laurencin (VII) (7); octahydrolaurencin (VIII) (7) was treated in the same manner as II (Zn-AcOH, OH^- and H_2-Pt), yielding a saturated glycol (V'), m.p. 54-55°, $[\alpha]_D$ +25.5°, which was further transformed to its acetonide (VI'), $[\alpha]_D$ +34.5°. The IR, NMR and mass spectra of V' and VI' were superimposable with those of V and VI, respectively, while their optical rotations were opposite each other. Thus, V is an optical antipode of V' and contains only a straight-chained



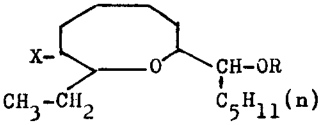
I



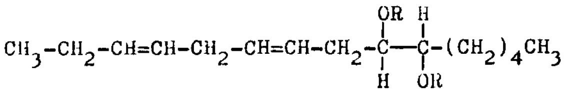
VII



II X=Br
IX X=H

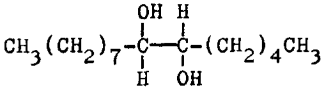


VIII X=Br, R=Ac
XI X=Br, R=H
XII X=R=H



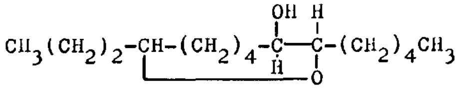
$$CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-\underset{H}{\overset{OR}{C}}-\underset{OR}{\overset{H}{C}}-(CH_2)_4CH_3$$

III R=H
IV R=Ac

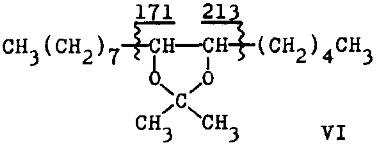


$$CH_3(CH_2)_7-\underset{H}{\overset{OH}{C}}-\underset{OH}{\overset{H}{C}}-(CH_2)_4CH_3$$

V



X



VI

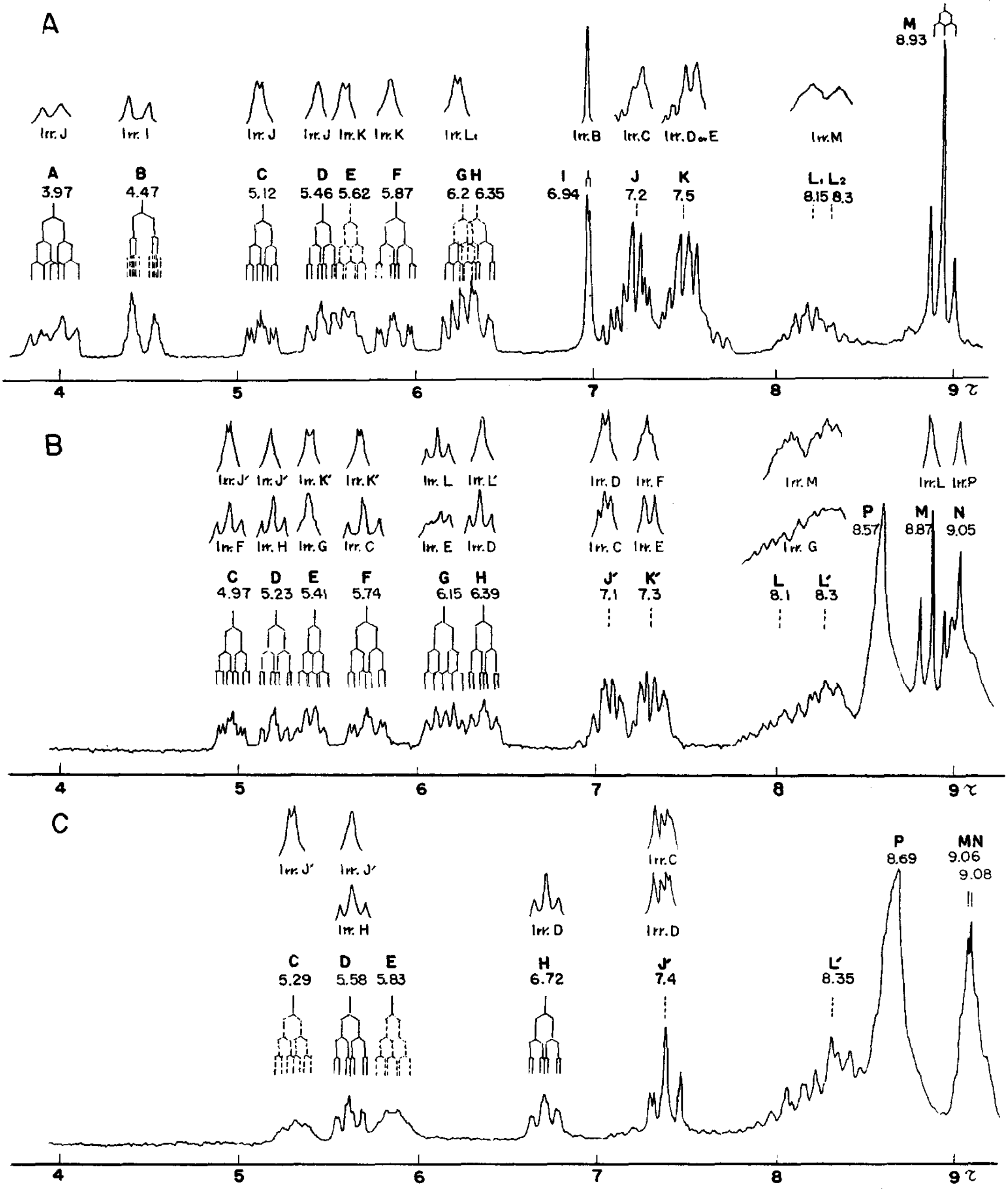
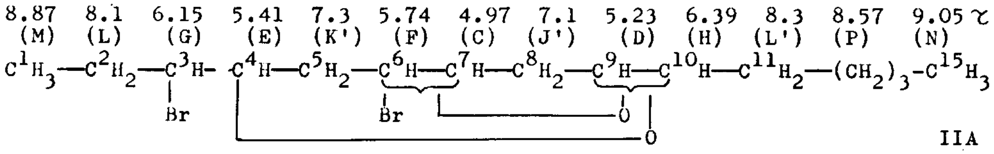


FIG. 1. NMR spectra of (A) Laureatin (I), (B) Hexahydrolaureatin (II) and (C) Hexahydrodebromolaureatin (IX) and their spin decoupled spectra

carbon skeleton. Since the absolute configuration of both C-9 and C-10 in laurencin (VII) has been shown to be <u>R</u> (7b, 8), those of the corresponding carbons in I must be <u>S</u>-configuration.

Reduction of II with Raney nickel in alkaline ethanol afforded two major products; one was hexahydrodebromolaureatin (IX), $C_{15}H_{28}O_2$ (M^+ 240), ν_{max}^{film} 1153, 1060, 1040 and 955 cm^{-1}, and the other a hydroxy ether (X), $C_{15}H_{30}O_2$ (M^+ 242), ν_{max}^{film} 3460, 1130, 1080 and 1057 cm^{-1}. The mass spectra of II and IX revealed the presence of groups CH_3-CH_2-CHBr- (<u>m/e</u> 277 and 275 due to (M^+- C_3H_6Br)) and CH_3-CH_2-CH_2- (<u>m/e</u> 197 due to (M^+- C_3H_7)), respectively; while in the spectra of octahydrodeacetyllaurencin (XI) and its debromo derivative XII (7), the peaks due to (M^+- C_2H_5) appeared.

We now return to the NMR spectrum of II (Fig. 1B). In this spectrum the signals corresponding to those of H-A, H-B and H-I in that of I disappeared and absorptions of methyl (H -N; 3H, br.) and methylene protons (H-P; 6H) were newly centered at τ 9.05 and 8.57, respectively. In the region of τ 7.0 to 7.5 two two-proton multiplets appeared at τ ca. 7.1 (H-J') and 7.3 (H-K'), indicating that two of six protons in this region of the spectrum 1A should be assigned as allylic protons. The signal due to the ethyl group appeared as a triplet (H-M; 3H) at τ 8.87 and a multiplet (H-L) at ca. 8.1. Furthermore, six one-proton signals comparable with those due to H-C to H-H in the spectrum 1A were clearly observable at almost the same fields: four septets at τ 4.97 (H-C), 5.23 (H-D), 5.74 (H-F) and 6.39 (H-H; J = 8, 7 and 1.5 c/s), a broad quartet at 5.41 (H-E; J = 5, 5 and 4) and a quintet at 6.15 (H-G; J = 10, 5 and 5). On the basis of the extensive spin decoupling experiments shown in Fig. 1B, in combination with the mass spectral data described above and the assigned structures for IV and V, the compound II must be formulated as IIA (9).

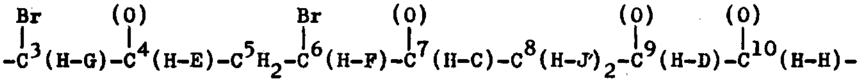


$$\overset{\substack{8.87\\(M)}}{C^1H_3}{-}\overset{\substack{8.1\\(L)}}{C^2H_2}{-}\underset{Br}{\overset{\substack{6.15\\(G)}}{C^3H}}{-}\overset{\substack{5.41\\(E)}}{C^4H}{-}\overset{\substack{7.3\\(K')}}{C^5H_2}{-}\underset{Br}{\overset{\substack{5.74\\(F)}}{C^6H}}{-}\overset{\substack{4.97\\(C)}}{C^7H}{-}\overset{\substack{7.1\\(J')}}{C^8H_2}{-}\overset{\substack{5.23\\(D)}}{C^9H}{-}\overset{\substack{6.39\\(H)}}{C^{10}H}{-}\overset{\substack{8.3\\(L')}}{C^{11}H_2}{-}\overset{\substack{8.57\\(P)}}{(CH_2)_3}{-}\overset{\substack{9.05\,\tau\\(N)}}{C^{15}H_3}$$

IIA

The NMR spectrum of IX (Fig. 1C) exhibited a characteristic two-proton multiplet (10) at τ ca. 7.4 (H-J') and four one-proton signals at τ 5.29 (H-C;

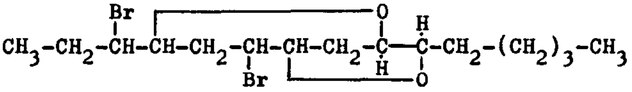
br.), 5.58 (H-D; sep, J = 8, 6 and 1.5 c/s), 5.83 (H-E; br.) and 6.72 (H-H; sep, J = 8, 7 and 1.5). In view of their splittings as well as chemical shifts (11), it would be reasonable to assign the latter four protons as those corresponding to H-C, H-D, H-E and H-H in II, respectively. The spin decoupling study confirms this assignment; of these four protons only the protons H-D and H-H are coupled each other, and the proton H-D is further coupled to those H-J', which in turn are coupled to only the proton H-C besides that in question. This behavior of coupling finely elucidates the afore-mentioned assignment which is summarized as follows (* broad signal):



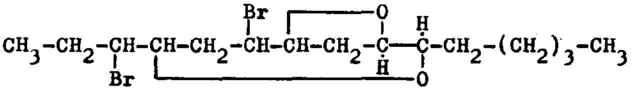
$-\overset{\text{Br}}{\text{C}^3}(\text{H-G})-\overset{(\text{O})}{\text{C}^4}(\text{H-E})-\text{C}^5\text{H}_2-\overset{\text{Br}}{\text{C}^6}(\text{H-F})-\overset{(\text{O})}{\text{C}^7}(\text{H-C})-\text{C}^8(\text{H-J}')_2-\overset{(\text{O})}{\text{C}^9}(\text{H-D})-\overset{(\text{O})}{\text{C}^{10}}(\text{H-H})-$

	C^3(H-G)	C^4(H-E)	C^5H_2	C^6(H-F)	C^7(H-C)	C^8(H-J')$_2$	C^9(H-D)	C^{10}(H-H)
I	6.2	5.62	7.5	5.87	5.12	7.2	5.46	6.35
II	6.15	5.41	7.3	5.74	4.97	7.1	5.23	6.39
IX (Br→H)	(8.0-)	5.83*	(8.0-)	(8.0-)	5.29*	7.4	5.58	6.72

These results indicate that the bromine atom must be attached to C^6 and, therefore, the compound II should be represented by IIB or IIC, and the latter



IIB



IIC

is more preferable to the former on the basis of the following reasons: (i) the protons H-C and H-D in the NMR spectra of I, II and IX resonate at extraordinarily low fields as those on carbons bearing an ether oxygen atom and this downfield shift is explicable well by the assignment of those as α-protons of a four-membered cyclic ether (12). (ii) The chemical shift and the absorption pattern (10) due to the protons H-J' in the spectrum of IX are interpretable successfully, if they are located on the β-position of the same cyclic ether ring (12). (iii) The strong absorptions near 975 cm^{-1} in the IR spectra of I, II and IX are characteristic to C-O stretching vibrations in a four-membered cyclic ether (13). It is now concluded that IIC is the most favorable structure for hexahydrolaureatin and, therefore, the formula I for laureatin.

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REFERENCES

1. Part IX of "Constituents from Marine Plants." Part VIII, T. Irie, M. Suzuki and T. Masamune, Tetrahedron in press.

2. NMR spectra were taken in CCl_4 with TMS as an internal standard on a Varian 100 Mc spectrometer; abbr. "sex" sextet, "d" doublet, "t" triplet, "br." broad, "m" multiplet, "s" singlet and "sep" septet. The spectra were analyzed at first order approximation, and the more precise analysis would be required to discuss the stereochemistry, as the J-values would be accurate to ±1 c/s.

3. "H-A" refers to the proton of the signal A in the NMR spectra.

4. The presence of structural units $-CH_2-Br$ and $-CH_2-O-$ in I is excluded because this compound includes no branched carbon chain.

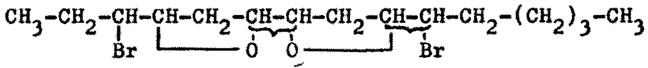
5. Cf. N.S. Bhacca, L.F. Johnson and J.N. Shoolery, NMR Spectra Catalog, Varian Associates, Palo Alto, California, 1962, Spectrum No 337.

6. Cf. R.E. Wolff, G. Wolff and J.A. McCloskey, Tetrahedron 22, 3093 (1966).

7. a) T. Irie, M. Suzuki and T. Masamune, Tetrahedron Letters 1091 (1965).
   b) Part VIII of this series.

8. On the basis of X-ray analysis of laurencin; Private communication from Dr. G. Ferguson, The University, Glasgow, Scotland.

9. An alternative structure IIA' is ruled out because the corresponding structure of IV is inconsistent with the observed NMR spectrum.



$$CH_3-CH_2-\underset{Br}{CH}-CH-CH_2-\underbrace{\underset{O}{CH}-\underset{O}{CH}}-CH_2-\underbrace{CH-\underset{Br}{CH}}-CH_2-(CH_2)_3-CH_3$$

IIA'

10. The pattern of the signal J' in the spectrum 1C is interpretable well as a result of sum of two ABXY-type signals centered at τ 7.35 (J = 8, 8 and 6(?) c/s) and at 7.40 (J = 6, 5.5 and 6(?)).

11. Each signal is shifted to the higher field by 0.3 to 0.4 ppm owing to the replacement of bromine atom by hydrogen.

12. Cf. N.S. Bhacca, L.F. Johnson and J.N. Shoolery, NMR Spectra Catalog Spectrum No 33; F. Piozzi, A. Quilico, T. Ajello, V. Sprio and A. Melera, Tetrahedron Letters 1829 (1965); R. C. Cookson, T.A. Crabb, J.J. Frankel and J. Hudec, Tetrahedron Supplement No 7, p.355 (1966).

13. Cf. G.M. Barrow and S. Searles, J. Am. Chem. Soc. 75, 1175 (1953).