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LAUREATIN AND ISOLAUREATIN, CONSTITUENTS OF *LAURENCIA NIPPONICA* YAMADA[1]

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Abstract—Laureatin and isolaureatin, new bromo compounds isolated from *Laurencia nipponica* Yamada, are shown to possess structures I and II, respectively.

Two new bromo compounds, designated laureatin and isolaureatin, have been isolated from *L. nipponica* Yamada (Japanese name "Urasozo"; Rhodomelaceae) along with laurene,[2] which has been isolated from *L. glandulifera* Kützing. In the preliminary communications,[3,4] laureatin and isolaureatin have been shown to possess structures I and II, respectively. The present paper deals with the details of the isolation and structural elucidation of these compounds.

A neutral fraction of the methanol extracts of the seaweed[5] was chromatographed on standard alumina. Fractions eluted with n-hexane-benzene (1 :2) were extensively rechromatographed on silica gel to give crystals, which were recrystallized from methanol to yield laureatin (0·07%) and isolaureatin (0·025%) as colourless needles and monoclinics, respectively.

Structure of laureatin

Laureatin (I), $C_{15}H_{20}O_2Br_2$ (M^+ 394, 392, 390), m.p. 82–83°, $[\alpha]_D$ + 96°, shows in its UV [λ_{max} 223 mμ (ε 12,800), λ_{infl} 229 mμ (ε 10,400)] and IR spectra [ν_{max}^{Chf} 3300, 2100, 1140, 1086, 1045, 975 and 965 cm^{-1}; ν_{max}^{KBr} 758 cm^{-1}] that I is an ether having a conjugated enyne or diene group and contains neither OH nor C=O function. The NMR spectrum and the spin decoupling study (Fig. 1) support these findings and provide additional information on the structure. A one-proton sextet (J = 11, 7, 7 Hz) centered at τ 3·97 (A)* and a one-proton finely splitted doublet (J = 11 Hz) at τ 4·47 (B) are ascribed to *cis* olefinic protons.† A signal due to an acetylenic proton appears as a doublet (J = 2 Hz) at τ 6·94 (I). Irradiation at τ 6·94 collapses the finely splitted doublet at τ 4·47 (B) to a broad doublet (J = 11 Hz); conversely, by irradiation at τ 4·47, the doublet at τ 6·94 (I) is simplified to a sharp singlet. Thus, the *cis* double bond is conjugated to the terminal triple bond.

In the higher magnetic field in the spectrum of I there are a couple of 3-proton multiplets centered at τ ca. 7·2 (J) and ca. 7·5 (K), two overlapped one-proton multiplets at τ ca. 8·1 (L_1) and ca. 8·3 (L_2) as well as a sharp triplet (J = 7, 7 Hz) at τ 8·93

* "A" refers to the signal A in the NMR spectrum (Fig. 1).

† From the coupling of 11 Hz, geometry of the double bond could not definitely be determined. However, geometrical isomer of laureatin with coupling of 16 Hz has recently been isolated from the same source[6] and, therefore the double bond of I proved to be *cis*.

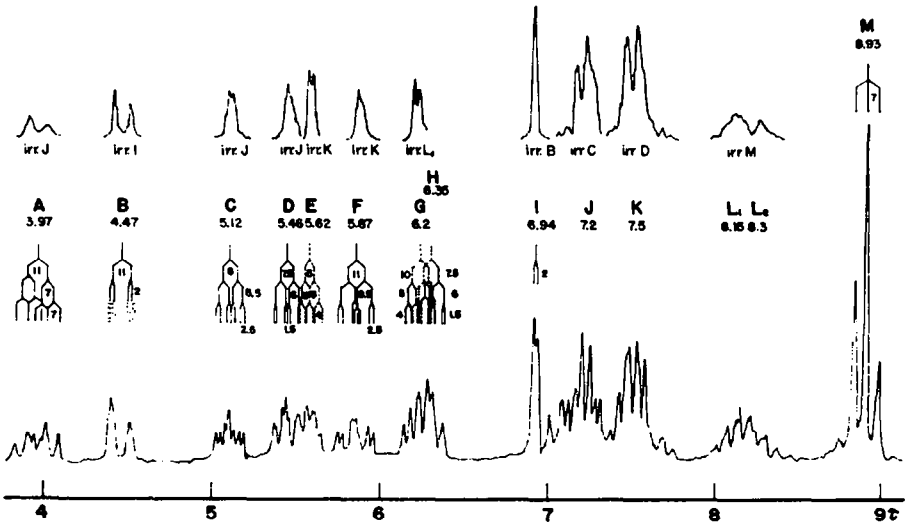


FIG. 1 NMR spectrum of laureatin (I) and its spin decoupling spectra (100 MHz).

(M). Irradiation at τ 8·93 decouples the signals (L_1) and (L_2) to broad singlets, respectively, indicating that these signals (L_1, L_2 and M) are assignable to the methylene and Me protons of an Et group and, moreover, the methylene protons are magnetically nonequivalent to each other. The sextet (A) is changed to a broad doublet (J = 11 Hz) by irradiation at τ 7·2 (J); the olefinic proton H-A* is, therefore, coupled to that H-B with splitting of 11 Hz and to H-J with coupling of 7 Hz. Thus, at least one proton of H-J could be allylic, and this will be discussed later.

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 (C; J = 8, 5·5, 2·5 Hz), 5·46 (D; J = 7·5, 6, 1·5 Hz) and 5·87 (F; J = 11, 8·5, 2·5 Hz), a one-proton broad quartet (J = 5, 5, 4 Hz) at τ 5·62 (E) and two one-proton multiplets centered at τ ca. 6·2 (G) and 6·35 (H). These absorptions might be ascribed to protons on carbons bearing an ether O or Br atom. The signals (C) and (D) are decoupled to a broad doublet (J = 2·5 Hz) and a broad singlet, respectively, by irradiation at τ 7·2. On the other hand, the signals (E) and (F) are simplified to a broad doublet (J = 5 Hz) and a broad singlet, respectively, by irradiation at τ 7·5. On the basis of the results, laureatin should consist of the following units.

$$C_{15}H_{20}O_2Br_2 = \begin{cases} -CH_2-\overset{H}{\underset{}{C}}=\overset{H}{\underset{}{C}}-C\equiv CH \\ -CH_2-CH_3 \\ 2\ >CH-O-CH< \\ 2\ <CH-Br \\ (C_2H_4) \end{cases}$$

* "H-A" refers to the proton of signal A in the NMR spectrum.

In addition, as described later, laureatin has a straight-chained carbon skeleton and groupings $-CH_2-O-\underset{\underset{C}{|}}{\overset{\overset{C}{|}}{C}}-C$ and $-CH_2Br$ are therefore ruled out.

Laureatin (I) consumed 3 moles of H_2 over PtO_2-catalyst in ethanol to yield hexahydrolaureatin (III), $C_{15}H_{26}O_2Br_2$ (M^+ 400, 398, 396), oil; the UV spectrum shows only end absorption and the IR spectrum the presence of an oxido group (ν 1144, 1078, 1050, 975 and 965 cm^{-1}, but no absorption due to unsaturated bond is observed. In the NMR spectrum of III the signals corresponding to those of (A), (B) and (I) in that of I disappear and signals of Me (broad triplet, J = 6, 6 Hz) and methylene protons (6H) are newly centered at τ 9·05 (N) and 8·57 (P), respectively. In the region of τ 7·0 to 7·5 a set of 2-proton multiplets appear at τ ca. 7·1 (J') and 7·3 (K'), indicating that two of six protons in this region of the spectrum of I should be assigned allylic protons. Six one-proton signals comparable to (C) to (H) in the spectrum of I are observed at almost the same field: namely, four septets at τ 4·97 (C; J = 8, 5·5, 2·5 Hz), 5·23 (D; J = 7·5, 6, 1·5 Hz), 5·74 (F; J = 11, 8·5, 2·5 Hz) and 6·39 (H; J = 7·5, 6, 1·5 Hz), a broad quartet (J = 5, 5, 4 Hz) at τ 5·41 (E) and a quintet (J = 10, 5, 4 Hz) at τ 6·15 (G). Furthermore, the signals due to the Et group appear as a triplet (J = 7, 7 Hz) at τ 8·87 (M) and a complicated multiplet at τ ca. 8·1 (L).

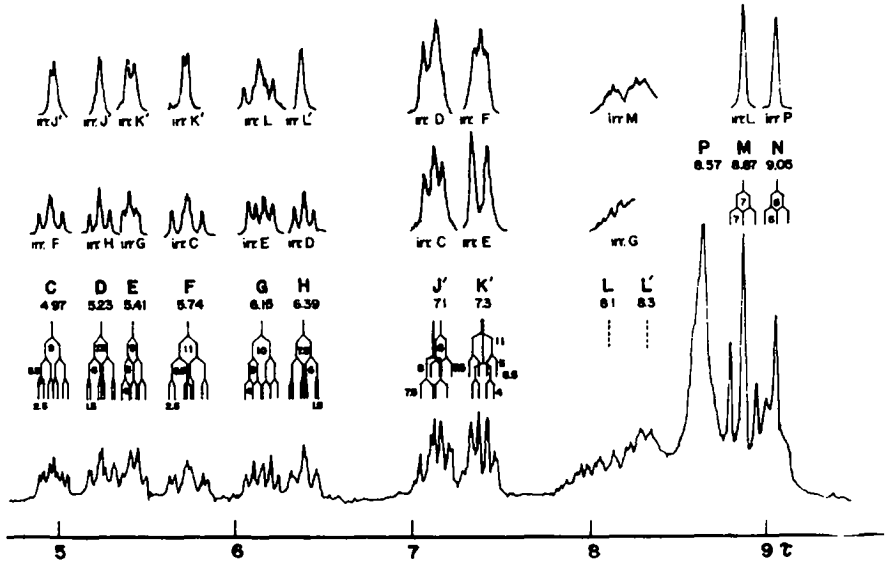


FIG. 2 NMR spectrum of hexahydrolaureatin (III) and its spin decoupling spectra (100 MHz).

The extensive spin decoupling results are shown in Fig. 2 and Table 1. Thus, the protons H-M, which proved to be Me (C-1) protons of the Et group, are coupled (J = 7 Hz) to H-L, showing H-L are methylene protons of the Et group. These protons H-L are also coupled to a single proton H-G. The protons H-G and H-E are coupled with 5 Hz, and the latter is also split by H-K'. The signal (K') consists of a set

TABLE 1. SPIN DECOUPLING RESULTS OF HEXAHYDROLAUREATIN (III) (IN CCl_4, 100 MHz)

Irradiated			Observed	Multiplicity change[a]	Splitting decoupled[b] (Hz)
8·87 (M)	C—1	$-CH_2-CH_3$	8·1 (L)	(ch)	7
8·1 (L)	C—2	$-CH_2-CH_3$	8·87 (M)	t → S	7, 7
			6·15 (G)	qi → t	10, 4
6·15 (G)	C—3	H^*[c]	8·1 (L)	(ch)	10, 4
			5·41 (E)	q(br) → t(br)	5
5·41 (E)	C—4	H^*	6·15 (G)	qi → q	5
			7·3 (K′)	m → d(br)	5, 4
7·3 (K′)	C—5	$-CH_2-$	5·41 (E)	q(br) → d	5, 4
			5·74 (F)	sp → d	11, 8·5
5·74 (F)	C—6	H^*	7·3 (K′)	m → ds	11, 8·5
			4·97 (C)	sp → t(br)	2·5
4·97 (C)	C—7	H^*	5·74 (F)	sp → t(br)	2·5
			7·1 (J′)	(ch)	8, 5·5
7·1 (J′)	C—8	$-CH_2-$	4·97 (C)	sp → d	8, 5·5
			5·23 (D)	sp → s(br)	7·5, 6
5·23 (D)	C—9	H^*	7·1 (J′)	m → ds	7·5, 6
			6·39 (H)	sp → t (br)	1·5
6·39 (H)	C—10	H^*	5·23 (D)	sp → t(br)	1·5
			8·3 (L′)	(ch)	7·5, 6
8·3 (L′)	C—11	$-CH_2-$	6·39 (H)	sp → s(br)	7·5, 6
8·57 (P)		$-CH_2-$	9·05 (N)	t(br) → s	6, 6

[a] Abbr.: "ch" means change; "t" triplet; "s" singlet; "qi" quintet; "q" quartet; "br" broad; "m" multiplet; "sp" septet; "ds" doublets.

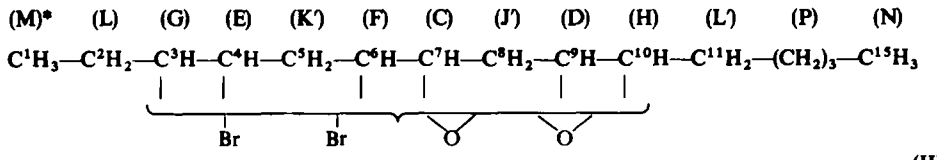
[b] The error limits of J is ± 0·5 Hz.

[c] H^* refers to the proton on carbon bearing Br or ether O atom.

of quartets (J = 11, 5 Hz and J = 8·5, 4 Hz) and is changed by irradiation at τ 5·41 (E) to an overlapped pair of doublets (J = 11 and 8·5 Hz); thus each of two protons H-K′ is coupled to H-E with 5 and 4 Hz. On irradiation at τ 7·3 (K′), both the signals (E) and (F) are collapsed to doublets (J = 5 and 2·5 Hz, respectively). The proton H-F, on the other hand, is split (J = 2·5 Hz) by H-C, which is also coupled to H-J′. Like (K′), the signal (J′) consists of a set of quartets (J = 8, 7·5 and J = 6, 5·5 Hz) and is simplified to an overlapped pair of doublets (J = 7·5 and 6 Hz) by irradiation at τ 4·97 (C). Each of two protons H-J′ is also split (J = 7·5 and 6 Hz) by one proton H-D, and the latter is coupled (J = 1·5 Hz) to a single additional proton H-H, besides being split by H-J′. Furthermore, irradiation at τ 8·57 (P) collapses the broad triplet (N) to a singlet, showing the signal (N) is attributed to the Me of the alkyl group.

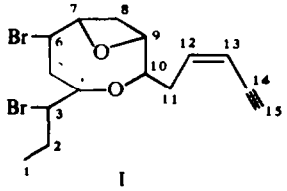
On the basis of the above results, III should consist of a straight C chain and two Br atoms and two ether O atoms should be attached to only the following six carbons in the molecule: C-3, C-4, C-6, C-7, C-9 and C-10 (III_A).

In order to determine the positions of the Br and the ether O atoms in the whole structure, the following experiments were carried out. (i) On treatment with Zn and

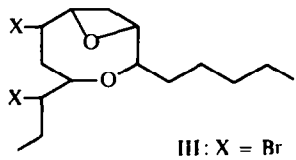


(III$_A$)

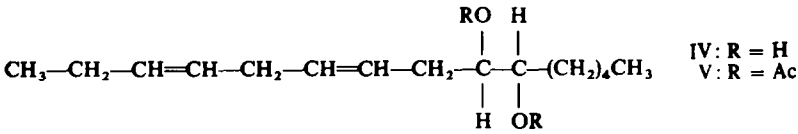
acetic acid and then with dil alkali, III gave an unsaturated glycol (IV), $C_{15}H_{28}O_2$ (M^+ 240), oil, ν 3400, 1130, 1062, 969 cm^{-1}. In the NMR spectrum of IV, two multiplets centered at τ 6·61 (2H) and at τ 4·54 (4H) are ascribed to the protons on carbon atom bearing OH group and olefinic protons, respectively. Acetylation of IV afforded the corresponding diacetate (V), $C_{19}H_{32}O_4$ (M^+ 324), and the NMR spectrum of this acetate exhibits a broad peak centered at τ 7·28 (2H), which is ascribed to doubly allylic methylene protons,[7] and signals at τ 7·6 to 8·2 (4H; allylic protons), ca. 5·1 (2H; >C*H*-OAc) and 7·97 (6H; —OCOC*H*$_3$). Hydrogenation of IV over PtO_2-catalyst in ethanol gave the saturated glycol (VI), $C_{15}H_{32}O_2$ (M^+ 244), m.p. 54–55°, $[\alpha]_D$ − 25·4°. The structure of VI was deduced from the mass spectrum of its acetonide



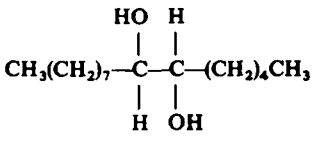
I



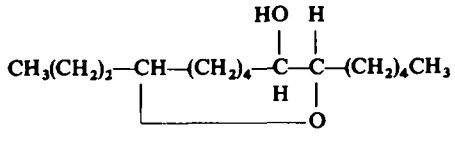
III: X = Br
X: X = I



IV: R = H
V: R = Ac



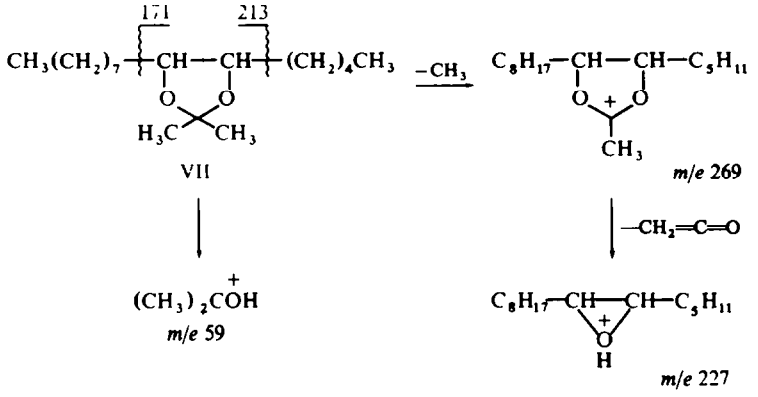
VI



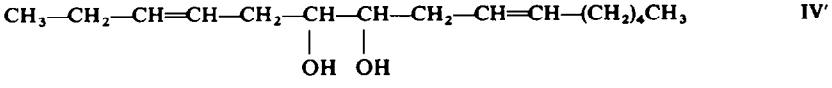
XI

(VII), $[\alpha]_D$ − 35°, and confirmed by comparison with a sample (VII') derived from laurencin (VIII)[8] as described later. The mass spectrum of VII shows characteristic peaks at *m/e* 269, 227, 213, 171 and 59, which are attributed to the fragment ions shown in the following:

* Signals of the corresponding proton in the NMR spectrum.

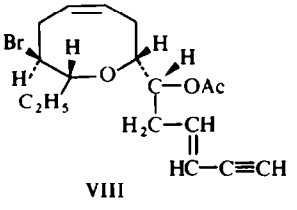


These data are only consistent with the structure IV for the unsaturated glycol. The alternative formula (IV') is excluded by the NMR data of its acetate; i.e., if the relevant compound is represented by IV', which must contain eight allylic protons, the NMR spectrum of its acetate is not in accord with the observed.

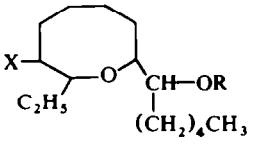


IV'

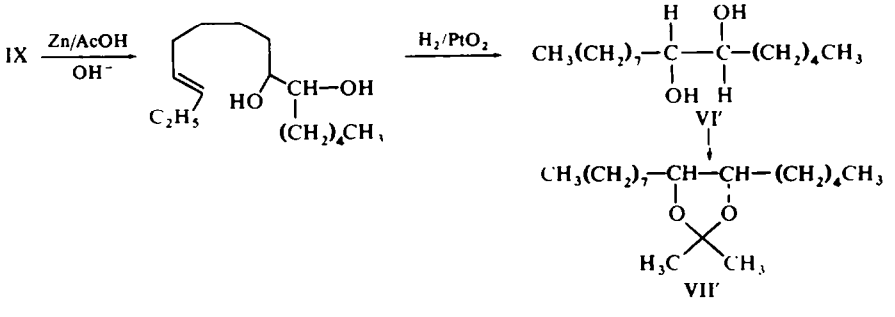
On the other hand, octahydrolaurencin (IX)[8] was treated in the same manner as III (Zn-AcOH, OH^- and H_2/PtO_2), yielding a saturated glycol (VI'), m.p. 54–55°, $[\alpha]_D$ + 25·5°, which was further transformed to its acetonide (VII'), $[\alpha]_D$ + 34·5°. The IR (in Chf), NMR and mass spectra of VI' and VII' are superimposable over those of VI and VII, respectively, while their optical rotations are opposite each other. Thus, VI is an optical antipode of VI', whose structure has been established unambiguously. Since the absolute configuration of both C-9 and C-10 in laurencin (VIII)



VIII

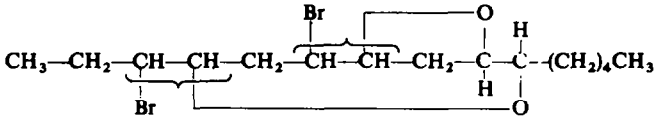


IX: X = Br, R = Ac
XII: X = Br, R = H
XIII: X = R = H

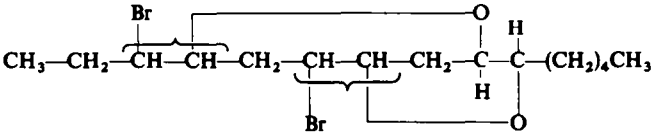


VII'

has been established to be *R*, those of the corresponding carbons in I must be *S* configuration. Considering the structure of the unsaturated glycol (IV), two Br atoms in III can not be located to the vicinal carbons and the compound III must, therefore, be formulated as III_B or III_C.

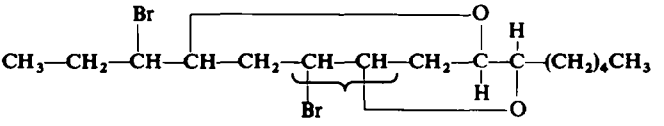


III_B

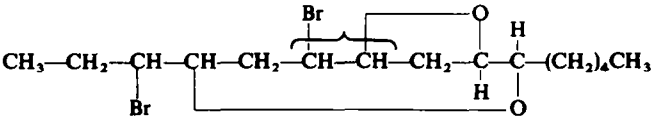


III_C

(ii) Reduction of III with Ra-Ni in alkaline ethanol afforded two major products. One was hexahydrobisdebromolaureatin (X), $C_{15}H_{28}O_2$ (M^+ 240), oil, the IR spectrum of which shows the presence of oxido group(s) (ν 1152, 1061, 1040 and 955 cm^{-1}). The other was a hydroxy ether (XI), $C_{15}H_{30}O_2$ (M^+ 242), oil, whose IR spectrum exhibits the absorptions due to an OH and oxido groups (ν 3460, 1132, 1082 and 1060 cm^{-1}). The mass spectra of III and X (Fig. 3) reveal the presence of groups $CH_3—CH_2—CHBr—$ (*m/e* 277, 275 due to $M^+ - C_3H_6Br$) and $CH_3—CH_2—CH_2—$ (*m/e* 197 due to $M^+ - C_3H_7$), respectively, while in the spectra of octahydrodeacetylaurencin (XII) and its debromo derivative (XIII) the peaSs due to $M^+ - C_2H_5$ appear but no peak due to $M^+ - C_3H_6Br$ nor $M^+ - C_3H_7$ is observed. From these results, the structure of III is limited to III_D or III_E.



III_D



III_E

(iii) The NMR spectrum of hexahydrobisdebromolaureatin (X) (Fig. 4) exhibits a characteristic two-proton multiplet at τ ca. 7·4 (J') and four one-proton signals at τ 5·29 (C; multiplet), 5·58 (D; septet, J = 7·5, 6, 1·5 Hz), 5·83 (E; multiplet) and 6·72 (H; septet, J = 7·5, 6, 1·5 Hz). In view of their splittings as well as chemical shifts, it would be reasonable to assign the latter four signals to those corresponding to (C), (D), (E) and (H), respectively, in the spectrum of III. The spin decoupling study (Table 2) confirm this assignment; of these four protons only H—D and H—H are coupled each other, and H—D is further coupled to protons H—J', which in turn are also split by a single additional proton H—C.

TABLE 2. SPIN DECOUPLING RESULTS OF HEXAHYDROBISDEBROMOLAUREATIN (X) (IN CCl_4, 100 MHz)

Irradiated			Observed	Multiplicity change[a]	Splitting decoupled[b] (Hz)
6·72 (H)	C—10	>CH—O—*CH*<	5·58 (D)	sp → t(br)	1·5
5·58 (D)	C—9	>CH—O—*CH*<	6·72 (H)	sp → t(br)	1·5
			7·4 (J')	(ch)	7·5, 6
7·4 (J')	C—8	—HC—*CH*$_2$CH— (O) (O)	5·58 (D)	sp → s(br)	7·5, 6
			5·29 (C)	sp → d(br)	8, 5·5
5·29 (C)	C—7	>*CH*—O—CH<	7·4 (J')	(ch)	8, 5·5

[a,b] See footnotes of Table 1.

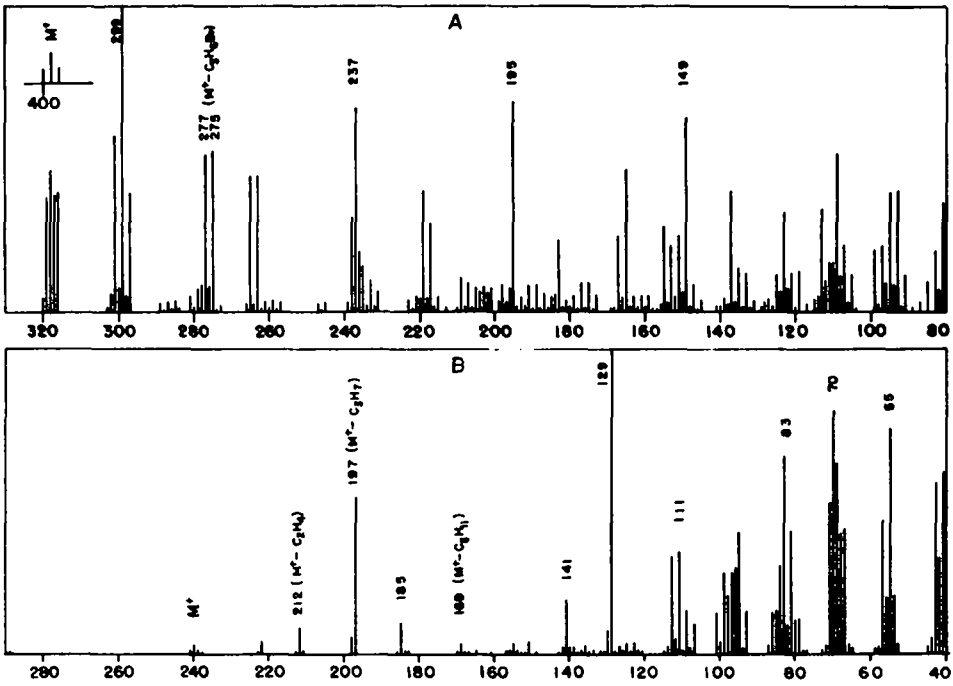
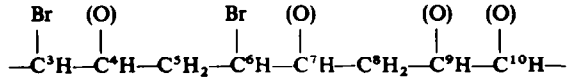


FIG. 3 Mass spectra of (A) hexahydrolaureatin (III) and (B) hexahydrobisdebromolaureatin (X).

These data clearly elucidate the afore-mentioned assignment, which is summarized as follows:



	(G)	(E)	(K)	(F)	(C)	(J)	(D)	(H)
I	6·20	5·62	7·5	5·87	5·12	7·2	5·46	6·34
III	6·15	5·41	7·3	5·74	4·97	7·1	5·23	6·39
X (Br→H)	(8·0–)	5·83*	(8·0–)	(8·0–)	5·29*	7·4	5·58	6·72

(* broad signal)

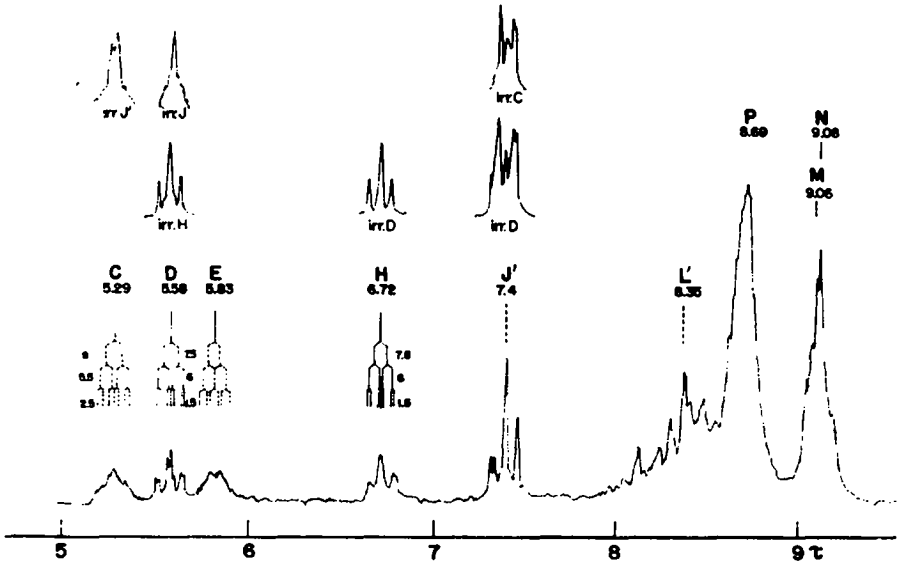
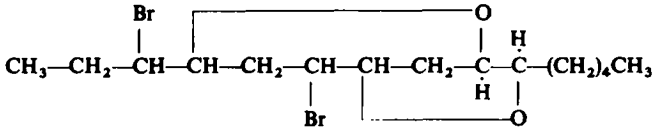
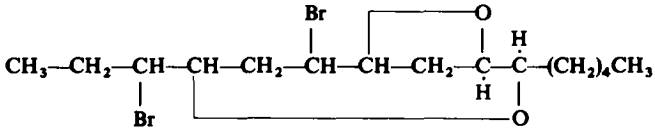


FIG. 4 NMR spectrum of hexahydrobisdebromolaureatin (X) and its spin decoupling spectra (100 MHz).

Consequently, the Br atom must be attached to C-6 and, therefore, the compound III should be represented by III_F or III_G. The latter is preferable to the former on the



III_F



III_G

basis of the following reasons. (a) In the NMR spectra of I, III and X, H—C and H—D resonate at extraordinarily low fields as compared with those on carbon bearing an ether O atom and this downfield shift is explicable well by the assignment of those to α-protons of a 4-membered cyclic ether.[9] (b) The chemical shift (τ 7·4) and the absorption pattern due to H—J' in the spectrum of X are interpretable successfully, if they are located on β-position of the same cyclic ether ring.[10] This pattern was examined by the spin decoupling experiments shown in Fig. 4. Irradiation at τ 7·4 (J') collapses the broad multiplet at τ 5·29 (C) to a broad doublet (J = 2·5 Hz) and the septet (J = 7·5, 6, 1·5 Hz) at τ 5·58 (D) to a broad singlet. Conversely, by irradiation at τ 5·29 (C) and at τ 5·58 (D), the pattern of (J') is changed as shown in Fig. 5. These experiments show that each of the protons H—J' is coupled to H—C with 8 and 5·5 Hz and also to H—D with 7·5 and 6 Hz, respectively. (c) The strong absorptions near ν 975 cm^{-1} in the IR spectra of I, III and X (Fig. 6) are characteristic of C—O

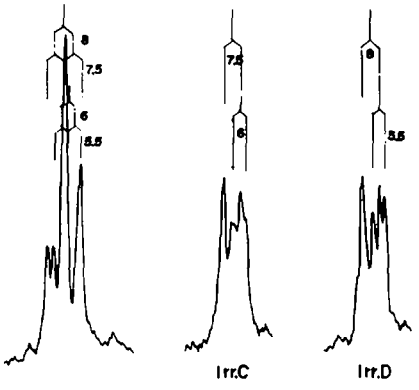


FIG. 5.

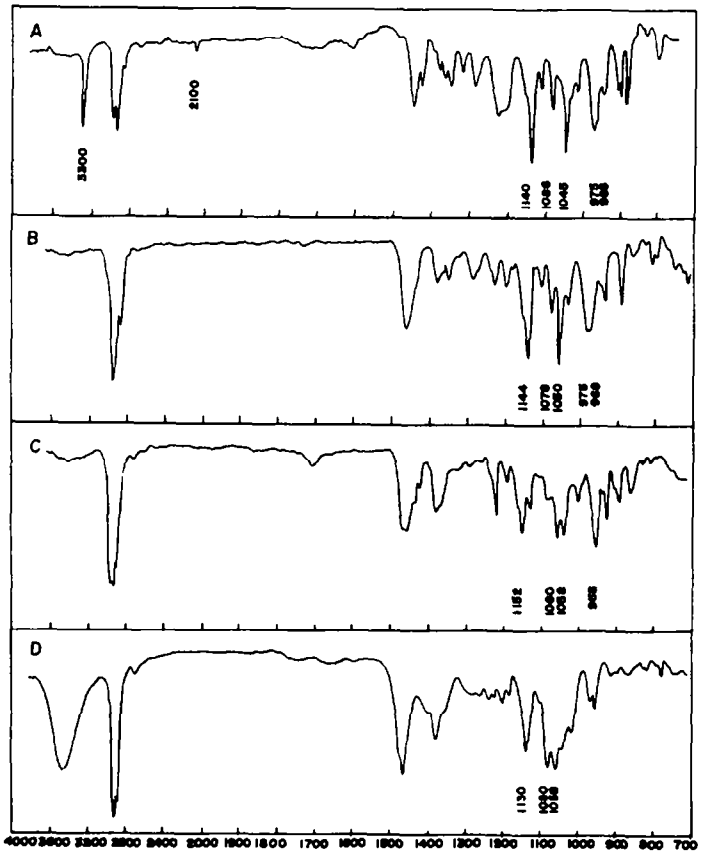
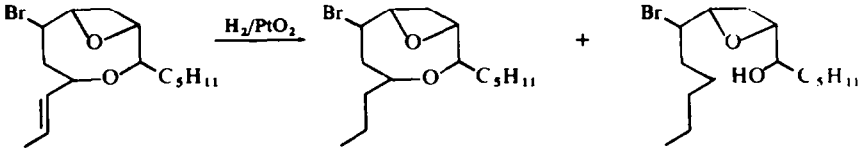


FIG. 6 IR spectra of (A) laureatin (I) in $CHCl_3$, (B) hexahydrolaureatin (III), (C) hexahydrobisdebromo-laureatin (X) and (D) hydroxy ether (XI) in film.

unsymmetrical stretching in a 4-membered cyclic ether.[11] All these results have confirmed that III_G is the most preferable structure for hexahydrolaureatin. Moreover, this conclusion is in good accord with the mass spectra of some derivatives described below.

On treatment with refluxing ethanolic KOH, III gave dehydrobromohexahydrolaureatin (XIV), $C_{15}H_{25}O_2Br$ (M^+ 318, 316), oil, whose IR spectrum displays absorption due to a *trans*-oriented double bond (ν 977 cm^{-1}). When treated with H_2 over 5% Pd—C in acetic acid, XIV afforded more than 6 products (TLC). On the other hand, hydrogenolysis of XIV over Pt in acetic acid yielded two products. One of them was hexahydromonodebromolaureatin (XV), $C_{15}H_{27}O_2Br$ (M^+ 320, 318), oil, whose IR spectrum shows the presence of oxido group(s) (ν 1145, 1082, 1062, 1037 and 974 cm^{-1}), and the other was a hydroxybromo ether (XVI), $C_{15}H_{29}O_2Br$, *m/e* 304, 302 (M^+—H_2O), oil, the IR spectrum of which shows the presence of an OH and oxido groups (ν 3450, 1057 and 972 cm^{-1}). Apparently the unsaturated bromo ether (XIV) was formed by the selective dehydrobromination of the side chain Br atom of III,[12] and the compounds XV and XVI are hydrogenation and hydrogenolysis products of XIV, respectively. In the mass spectrum of XV, the fragment peaks



XIV XV XVI

m/e 277, 275 due to M^+—C_3H_7 and those *m/e* 249, 247 due to M^+—C_5H_{11} appear. The NMR spectrum of XVI exhibits the characteristic signals due to the protons on a 4-membered cyclic ether at τ 5·53, and those of the protons on carbons carrying Br and OH at τ 6·02 and 6·54, respectively. Moreover, the mass spectrum of XVI reveals the presence of groups $CH_3(CH_2)_4$—CHBr— (*m/e* 157 due to M^+—$C_6H_{12}Br$; *m/e* 139 due to M^+—H_2O—$C_6H_{12}Br$) and $CH_3(CH_2)_4$—CHOH— (*m/e* 221, 219 due to M^+—$C_6H_{13}O$), which are attached to α- and α'-positions of the 4-membered cyclic ether.

It is concluded on the basis of these results that the planar structure of hexahydrolaureatin is represented by III_G and, therefore, laureatin by I.

Structure of isolaureatin

Isolaureatin (II), $C_{15}H_{20}O_2Br_2$ (M^+ 394, 392, 390), m.p. 83–84°, $[\alpha]_D$ +40°, shows the UV [λ_{max} 223 mμ (ε 12,400), λ_{infl} 229 mμ (ε 10,300)] and IR spectra [ν_{max}^{Chf} 3300, 2150, 1130, 1108 and 1096 cm^{-1}; ν_{max}^{KBr} 754 cm^{-1}] similar to those of laureatin (I). Hence, II is assignable to be a cyclic ether having a conjugated enyne like I. The mass spectrum of II also shows fragment ions similar to those of I (Fig. 7). The NMR spectrum (Fig. 8) exhibits the signals due to an acetylenic proton at τ 6·94 (1H, doublet, J = 2 Hz), two vinylic protons at τ 3·96 (1H, sextet, J = 12, 7, 7 Hz) and 4·45 (1H, finely splitted doublet, J = 12 Hz) and Me protons at τ 8·94 (3H, triplet, J = 7,

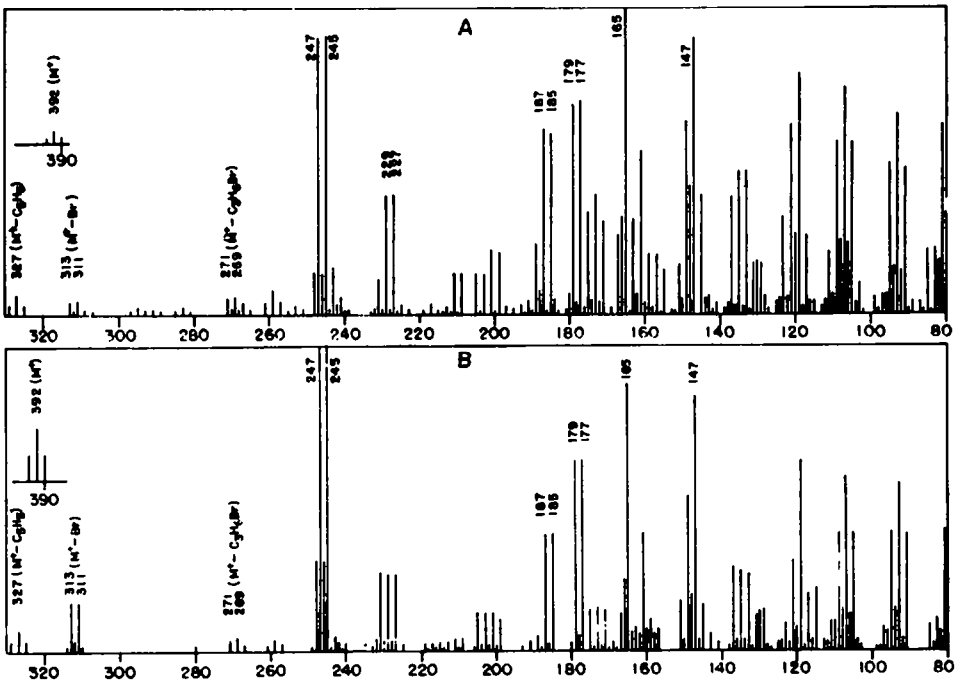


FIG. 7 Mass spectra of (A) laureatin (I) and (B) isolaureatin (II).

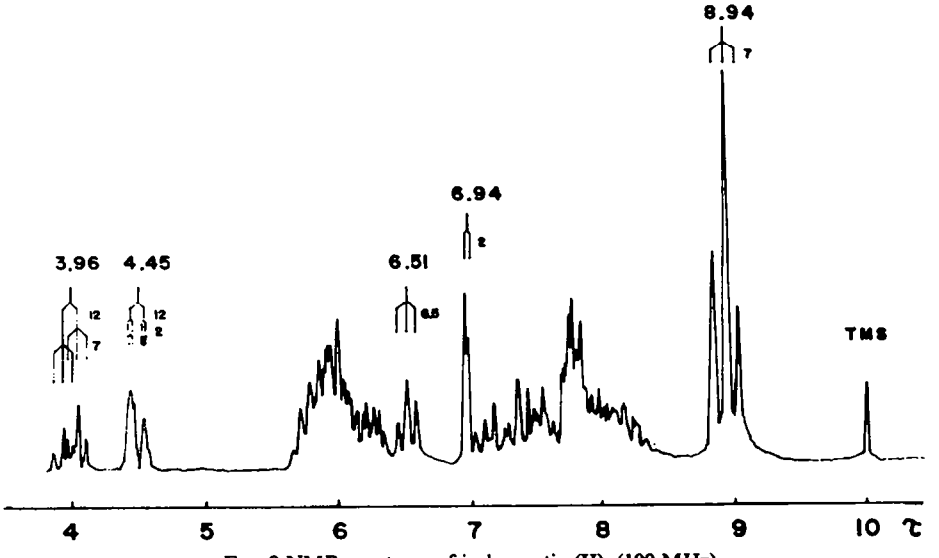
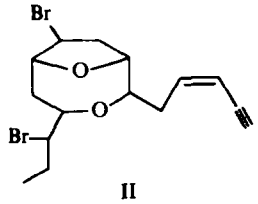


FIG. 8 NMR spectrum of isolaureatin (II). (100 MHz).

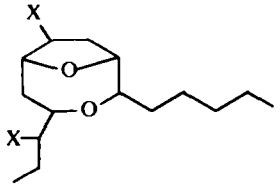
7 Hz). In addition, the signals corresponding to 6 protons appear in the region of τ 5·7 to 6·6, which are ascribed to the protons attached to the carbons carrying the Br or ether O; a one-proton broad triplet (J = 6·5, 6·5 Hz) at τ 6·51, a one-proton double triplet at τ 6·23 and complex, unresolvable four-proton signals at τ 5·7 to 6·1. Thus, II is inferred to be a bicyclic ether having $HC{\equiv}C{-}CH{=}CH{-}CH_2{-}$ (*cis*) and $CH_3{-}CH_2{-}CHBr{-}$ groupings and to possess a structure closely related to I.

Isolaureatin (II) consumed 3 moles of H_2 over PtO_2-catalyst in ethanol to give hexahydroisolaureatin (XVII), $C_{15}H_{26}O_2Br_2$ (M^+ 400, 398, 396), oil, whose IR spectrum shows the presence of oxido group(s) (ν 1140, 1120, 1092 and 1075 cm^{-1}). The NMR spectrum of XVII exhibits two Me signals at τ 9·08 (3H, broad triplet) and 8·93 (3H, triplet, J = 7, 7 Hz), a six-proton broad signal at τ 8·65, eight-proton signals in the region of τ 7·4 to 8·5, a one-proton triplet at τ 6·69 (J = 6·5, 6·5 Hz), a one-proton multiplet centered at τ ca. 6·2 and four-proton multiplets at τ 5·7 to 6·1.

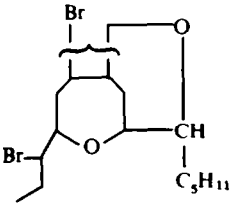
Treatment of XVII with Zn in acetic acid afforded the unsaturated glycol (IV), $C_{15}H_{28}O_2$, which was then hydrogenated to the corresponding saturated glycol (VI), $C_{15}H_{32}O_2$. These glycols, IV and VI, and acetonide of VI were identical with those obtained from hexahydrolaureatin (III) in all respects. These facts indicate the structure of hexahydroisolaureatin must be formulated as III_F or III_G.



II



XVII: X = Br
XVIII: X = H

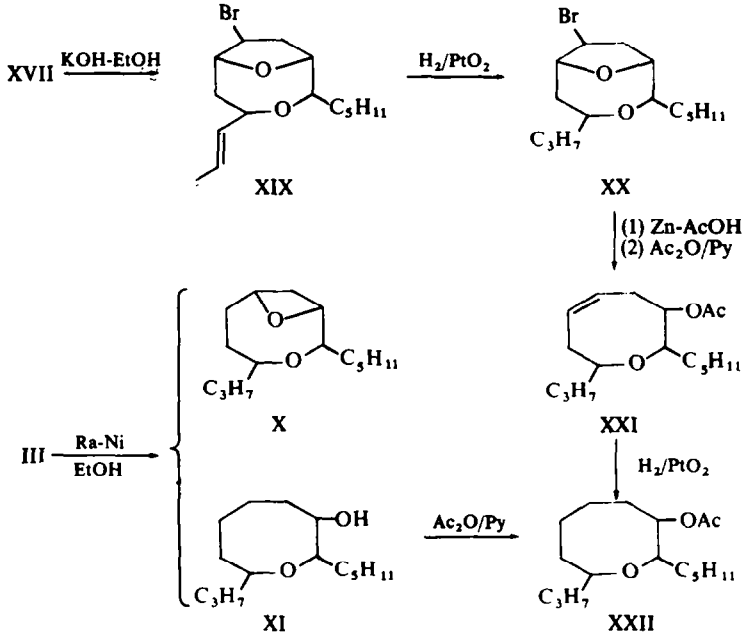


XVII′

On the other hand, treatment of XVII with Ra-Ni and alkali yielded hexahydrobisdebromoisolaureatin (XVIII), $C_{15}H_{28}O_2$ (M^+ 240) as a sole product and no hydroxy ether was obtained. This result is definitely different from that of hexahydrolaureatin (III). The NMR spectrum of XVIII shows only four one-proton signals in the field lower than τ 7·8; a broad triplet at τ 6·73, a broad multiplet at τ 6·21, a broad triplet at τ 5·98 and a broad multiplet at τ 5·77. This spectrum differ from that of hexahydrobisdebromolaureatin (X), especially in the absence of absorption in the region near τ 7·4. These facts indicate that XVII is not a stereoisomer of III. Moreover, the possibility of the alternative structure XVII′ is excluded by the following evidence. Treatment with ethanolic KOH effected dehydrobromination of XVII to yield dehydrobromohexahydroisolaureatin (XIX), $C_{15}H_{25}O_2Br$ (M^+ 318, 316), oil, whose IR spectrum shows absorption due to oxido group(s) and a *trans*-double bond (ν 1677, 1145, 1127, 1097, 1064 and 966 cm^{-1}). In the NMR spectrum of XIX, the signal due to vinylic Me appears at τ 8·28 (broad doublet, J = 5 Hz) and that of olefinic protons at τ ca. 4·5 (2H, multiplet). On hydrogenation over PtO_2-catalyst in ethanol or acetic acid, XIX afforded hexahydromonodebromoisolaureatin (XX), $C_{15}H_{27}O_2Br$

(M^+ 320, 318), oil, whose mass spectrum shows the presence of CH_3—CH_2—CH_2— group (*m/e* 277, 275 due to M^+—C_3H_7).

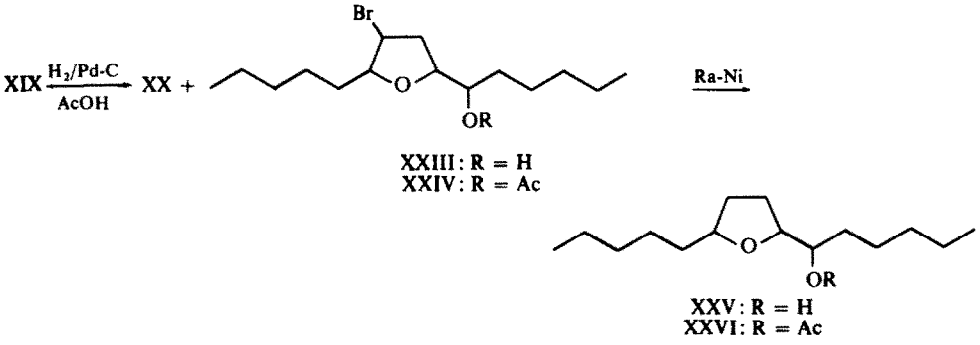
Treatments of XX with Zn in acetic acid and then with acetic anhydride-pyridine gave *cis*-unsaturated acetoxy cyclic ether (XXI),[13] $C_{17}H_{30}O_3$ (M^+ 282), oil; the IR spectrum shows the presence of AcO, *cis*-double bond and oxido group (ν 1745, 1240, 1130, 1082, 1064, 1045, 1024 and 768 cm^{-1}). The NMR spectrum of XXI exhibits the signals due to olefinic protons at τ 4·18 (2H, multiplet), allylic protons at τ 7·1 to 8·2 (4H, multiplet), protons on carbons bearing ether O atom at τ 6·22 (1H, sextet, J = 6, 6, 2 Hz) and 6·06 (1H, multiplet) and on carbon carrying an AcO group at τ 4·97 (1H, octet, J = 8, 4, 2 Hz). *cis*-Double bond was further confirmed by a spin decoupling experiment, the multiplet due to the olefinic protons at τ 4·18 is changed to



a narrower multiplet (half width 12 Hz)[14] on irradiation at τ 7·8 (allylic protons). These spectral data support the structure XXI for the unsaturated acetoxy ether. Hydrogenation of XXI afforded the corresponding saturated acetoxy ether (XXII), $C_{17}H_{32}O_3$ (M^+ 284), oil, which has been found to be identical with the specimen prepared by acetylation of the hydroxy ether XI obtained from hexahydrolaureatin (III), by comparison of their IR, NMR and mass spectra. Hence, it is concluded that hexahydroisolaureatin is represented by XVII.

Moreover, this conclusion is in accord with the mass spectra of the derivatives described below. On treatment with H_2 over 5% Pd-C in acetic acid, dehydrobromohexahydroisolaureatin (XIX) gave two products, hexahydromonodebromoisolaureatin (XX) and a hydroxybromo ether (XXIII), $C_{15}H_{29}O_2Br$ (M^+ 322, 320), oil. The IR spectrum of the latter shows absorption of tetrahydrofuran ring (ν 1075). This hydroxybromo ether (XXIII) was further acetylated to the corresponding acetate

(XXIV), $C_{17}H_{31}O_3Br$ (M^+ 364, 362). The NMR spectrum of XXIV exhibits four one-proton signals in the region of τ 6·53 to 5·14; two signals centered at τ 6·53 and 6·14 are attributed to the protons on carbons bearing ether O, and the signals at τ 5·67 and 5·14 are ascribed to the protons on carbons carrying Br atom and AcO group, respectively.



Reduction of XXIII with Ra—Ni and alkali yielded a hydroxy ether (XXV), $C_{15}H_{30}O_2$ (M^+ 242), which was converted into the corresponding acetate (XXVI), $C_{17}H_{32}O_3$ (M^+ 284). The mass spectra of both XXIII and XXV exhibit the fragment peaks due to $M^+—C_5H_{11}$ and to $M^+—C_6H_{13}O$, and those of XXIV and XXVI reveal the peaks due to $M^+—C_5H_{11}$ and to $M^+—C_8H_{15}O_2$, which are fully consistent with the proposed structures. Treatment of XXIV with zinc-acetic acid followed by acetylation gave an unsaturated glycol diacetate XXVII, $C_{19}H_{34}O_4$ (M^+ 326), $[\alpha]_D$ −14°. All the results mentioned above establish that hexahydroisolaureatin is formulated as XVII and, therefore, isolaureatin as II.

Stereochemistry

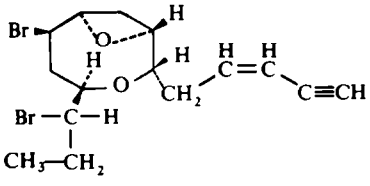
It has already been discussed that the two asymmetric centers C-9 and C-10 of laureatin (I) and isolaureatin (II) have *S* configuration. Now, the stereochemistry of the remaining four asymmetric centers, C-3, C-4, C-6 and C-7, will be discussed.

On treatment with Zn in refluxing acetic acid for 1 hr and then with acetic anhydride-pyridine, hexahydromonodebromolaureatin (XV) gave smoothly a *cis*-unsaturated acetoxy ether XXI as a sole product, while hexahydromonodebromoisolaureatin (XX) afforded the same acetoxy ether (XXI) together with two other products after 37 hr. This type of debromination reaction in the 1,2-haloether is considered to proceed through *E*2 mechanism, in which *trans* elimination occurs. According to the Dreiding model of XV, many convertible conformations are possible and, therefore, XV would readily take a conformation with Br and ether O atoms oriented 1,2-diaxial leading to the formation of *cis*-unsaturated hydroxy cyclic ether. Furthermore, in the NMR spectrum of III, the coupling constant (2·5 Hz) between protons H—F and H—C on the carbons in question gives the dihedral angle of about 60°, which supports the afore-mentioned conformation. Accordingly, each center C-6 and C-7 would reasonably be assigned as *R* configuration, because the hydrogens at C-7 and C-9 would be oriented *cis* each other.

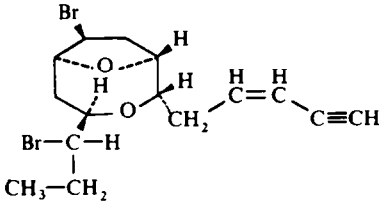
In the NMR spectra of I, III and XV, the signal of H—E (on C-4) appears in considerably low field as that of proton on carbon carrying ether O atom. This downfield shift is easily explicable, since H—E is situated close to the O atom of the oxetane ring. The α-configuration is thus assigned to H—E and, therefore, C-4 has *R* configuration.

Relative relationship concerning C-3 and C-4 will be proposed from a biogenetical point of view; it is presumed that laureatin (I), isolaureatin (II) and laurencin (VIII) would be formed from the same precursor, hexadeca-4,7,10,13-tetraenoic acid,[4,15] *via* a similar biogenetical pathway, at least concerning C-3 and C-4 and, therefore, sterical relationship of the two adjacent asymmetric centers in I might probably be the same as that of laurencin, whose absolute configuration has been established by the chemical[8] and crystallographic methods.[15] Consequently, *S* configuration would be assigned to C-3 in I. These considerations have now realized the absolute configuration Ia for laureatin.

Similarly, in isolaureatin (II) the two relative relationships concerning C-3 and C-4 as well as C-6 and C-7 are presumed to be *erythro* and *threo*, respectively. The asymmetric carbons C-3 and C-4 would, therefore, be assigned as *S* and *R*, respectively, as shown in the case of I. The asymmetric center C-6 would be assigned as *S* because the center C-9 has been established as *S* configuration as mentioned above. Thus, the center C-7 would also be inferred to be *S*, in view of the relative configuration (*threo*) of C-6 and C-7. Consequently, the stereostructure IIa is proposed for isolaureatin.



Ia



IIa

EXPERIMENTAL

All the m.ps are uncorrected. The UV and IR spectra were measured using a Hitachi spectrophotometer and a Nippon-Bunko IR-S spectrophotometer, respectively. The NMR measurements were performed in CCl_4 on a Japan Electron Optics 60 MHz or Varian 100 MHz spectrometer using TMS as internal reference. The NMR spectra were analyzed at first order approximation.

Isolation of laureatin (I) *and isolaureatin* (II). Air-dried seaweed (12 kg), collected at Hakodate Bay in June, was extracted with MeOH and the soln concentrated *in vacuo*. The residue was percolated with ether and the ether soln was shaken with 5% KOH and then with 1N HCl to remove acidic and basic components. After evaporation of the solvent, a neutral, dark brown oil (70 g) was obtained and chromatographed on standard alumina to give laurene,[8] an unidentified bromo ketone, laureatin, isolaureatin, laurenisol,[16] and sterols. From the fractions eluted with n-hexane, a mixture of hydrocarbons was obtained and purified by preparative GLC to yield laurene (0·01%). Fractions eluted with n-hexane-benzene (1 : 2) were extensively rechromatographed on silica gel to give crude laureatin and isolaureatin as colorless crystals. Recrystalization from MeOH afforded laureatin as colorless needles (8 g) and isolaureatin as monoclinics (3 g).

Laureatin (I); m.p. 82–83°, $[\alpha]_D$ +96° (*c*, 2·00; CCl_4); UV, λ_{max}^{EtOH} 223 mμ (ε 12,800), λ_{infl} 229 mμ (ε 10,400); IR, $\nu_{max}^{CCl_4}$ 3300, 2100, 1140, 1086, 1045, 975 and 965 cm^{-1}, ν_{max}^{KBr} 758 cm^{-1}; NMR, τ 8·93 (3H, t, J = 7, J Hz), ca. 8·3 (1H, m), ca. 8·15 (1H, m), ca. 7·5 (3H, m), ca. 7·2 (3H, m), 6·95 (1H, d, J = 2 Hz), 6·35 (1H, m), ca.

6·2 (1H, m), 5·87 (1H, sp, J = 11, 8·5, 2·5 Hz), 5·62 (1H, br. q, J = 5, 5, 4 Hz), 5·46 (1H, sp, J = 7·5, 6, 1·5 Hz), 5·12 (1H, sp, J = 8, 5·5, 2·5 Hz), 4·47 (1H, fine splitted d, J = 11 Hz), 3·97 (1H, sx, J = 11, 7, 7 Hz); mass spectrum, *m/e* 394, 392, 390 (M^+), 329, 327, 325 (7), 313, 311 (3), 271, 269 (6), 247, 245 (90), 229, 227 (40), 187, 185 (60), 179, 177 (70), 165 (100), 147 (90), 119 (80), 107 (75), 93 (65). (Found: C, 45·93; H, 5·16. $C_{15}H_{20}O_2Br_2$ requires: C, 45·92; H, 5·14%).

Isolaureatin (II), m.p. 83–84°, $[\alpha]_D$ +40° (*c*, 2·00; CCl_4), UV, λ_{max}^{EtOH} 223 mμ (ε 12,400), λ_{infl} 229 mμ (ε 10,300); IR, ν_{max}^{Chf} 3300, 2150, 1130, 1108 and 1096 cm^{-1}, ν_{max}^{KBr} 754 cm^{-1}; NMR, τ 8·94 (3H, t, J = 7, 7 Hz), ca. 8·3–7·0 (8H, m), 6·94 (1H, d, J = 2 Hz), 6·51 (1H, br. t, J = 6·5, 6·5 Hz), 6·23 (1H, dt), 6·1–5·7 (4H, ms), 4·45 (1H, fine splitted d, J = 12 Hz), 3·96 (1H, sx, J = 12, 7, 7 Hz); mass spectrum, *m/e* 394, 392, 390 (M^+), 329, 327, 325 (7), 313, 311 (17), 271, 269 (4), 247, 245 (100), 229, 227 (27), 187, 185 (40), 179, 177 (64), 165 (90), 147 (85), 119 (63), 107 (58), 93 (56). (Found: C, 45·66; H, 5·01. $C_{15}H_{20}O_2Br_2$ requires: C, 45·92; H, 5·14%).

Hexahydrolaureatin (III). The hydrogenation of I (1 g) was performed in EtOH (60 ml) over Adams' catalyst, and ca. 3 moles of H_2 were absorbed after 2 hr. After removal of the catalyst and the solvent, residual oil was purified by column chromatography on silica gel to give III (1·015 g) as colorless oil; $[\alpha]_D$ +32·5° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1144, 1078, 1050, 975 and 965 cm^{-1}; NMR, τ 9·05 (3H, br. t, J = 6, 6 Hz), 8·87 (3H, t, J = 7, 7 Hz), 8·57 (6H, br.), ca. 8·3 (2H, br. m), ca. 8·1 (2H, br. m), ca. 7·3 (2H, m), ca. 7·1 (2H, m), 6·39 (1H, sp, J = 7·5, 6, 1·5 Hz), 6·15 (1H, qi, J = 10, 5, 4 Hz), 5·74 (1H, sp, J = 11, 8·5, 2·5 Hz), 5·41 (1H, q, J = 5, 5, 4 Hz), 5·23 (1H, sp, J = 7·5, 6, 1·5 Hz), 4·97 (1H, sp, J = 8, 5·5, 2·5 Hz); mass, *m/e* 400, 398, 396 (M^+), 319, 317 (35), 318, 316 (37), 301, 299, 297 (100), 277, 275 (50), 265, 263 (42), 237 (63), 195 (64), 149 (59). (Found: C, 45·08; H, 6·66. $C_{15}H_{26}O_2Br_2$ requires: C, 45·20; H, 6·58%).

Unsaturated glycol (IV). To a soln of III (300 mg) in glacial acetic acid (10 ml) was added Zn-dust (400 mg) and the mixture was refluxed for 3 hr. After being cooled, the soln was filtered and the filtrate was evaporated *in vacuo*. To the residual oil was added 5% KOH-MeOH (10 ml) and then the mixture was allowed to stand at room temp overnight. After addition of water and removal of most of MeOH *in vacuo*, the residue was extracted with ether. The ether extracts were washed with water, dried over Na_2SO_4 and evaporated. The oily substance thus obtained was purified by column chromatography on silica gel to give IV (202 mg) as colorless oil; $[\alpha]_D$ −6° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 3400, 1130, 1062, 969 cm^{-1}; NMR, τ 9·07 (3H, br. t), 9·01 (3H, t, J = 7, 7 Hz), 8·2–7·5 (4H, m), ca. 7·2 (2H, m), ca. 6·61 (2H, m), ca. 4·54 (4H, m); mass, *m/e* 240 ($C_{15}H_{28}O_2$).

Diacetate (V). Acetylation of IV (50 mg) was carried out with Ac_2O-Py in the usual manner. The oily product thus obtained was purified by column chromatography over silica gel to give V (50 mg) as colorless oil; IR, ν_{max}^{film} 1748, 1225, 1024, 969 cm^{-1}; NMR, τ 9·07 (3H, br. t), 9·03 (3H, t, J = 7, 7 Hz), 8·2–7·6 (4H, m), 7·97 (6H, s), 7·28 (2H, m), ca. 5·1 (2H, m), ca. 4·6 (4H, m); mass *m/e* 324.

Saturated glycol (VI). The hydrogenation of IV (92 mg) was carried out over Adams' catalyst, and ca. 2 moles of H_2 were absorbed after 2 hr. After removal of the catalyst and the solvent, a crystalline substance was obtained. Recrystallization from n-hexane-benzene (5:1) gave VI (83 mg) as rhombic crystals; m.p. 54–55°, $[\alpha]_D$ −25·4° (*c*, 1·85; CCl_4); IR, ν_{max}^{Chf} 3600, 3400, 1126, 1070, 1020 cm^{-1}; NMR, τ 9·10 (6H, br. t), ca. 6·75 (2H, m); mass, *m/e* 244 ($C_{15}H_{32}O_2$).

Acetonide (VII). To VI (68 mg) was added 5% phosphomolybdic acid in acetone (5 ml), and the soln was stirred at room temp for 2·5 hr. After addition of 15N NH_4OH (2 ml) and water (20 ml), the mixture was extracted with ether and the ether layer was washed with 5% Na_2CO_3 and water, dried and evaporated. The residual oil was purified by column chromatography on silica gel to yield VII (57 mg) as colorless oil; $[\alpha]_D$ −35° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1383, 1371, 1239, 1217, 1170, 1106, 884 cm^{-1}; NMR, τ 9·07 (12H, br. t), 6·55 (2H, m); mass, *m/e* 269 ($C_{17}H_{33}O_2 = M^+ - CH_3$), 227 (25), 213 (11), 171 (10), 169 (14), 142 (11), 127 (13), 125 (12), 111 (25), 97 (45), 59 (100).

Saturated glycol (VI') *from octahydrolaurencin* (IX). Treatment of octahydrolaurencin (IX)[8] (100 mg) with Zn-AcOH and then with alkali was carried out in the similar manner as in the case of III to yield an unsaturated glycol (71 mg); IR, ν_{max}^{film} 3400, 1130, 1072, 969 cm^{-1}. *Diacetate*: oil; NMR, τ 9·08 (3H, br. t), 9·04 (3H, t, J = 7, 7 Hz), 7·94 (6H, s), 5·07 (2H, m), 4·65 (2H, m). Hydrogenation of the unsaturated glycol (80 mg) was performed in EtOH over Adams' catalyst and ca. 1 mole of H_2 was absorbed. The NMR and IR (in Chf) spectra of the crystalline saturated glycol (VI', 68 mg) thus obtained were superimposable over those of VI, respectively, but the optical rotation was opposite: $[\alpha]_D$ +25·5° (*c*, 1·92; CCl_4); mass, *m/e* 244 ($C_{15}H_{32}O_2$).

Acetonide (VII') prepared from VI' as described above; colorless oil, $[\alpha]_D$ +34·5° (*c*, 2·00; CCl_4); the IR (in Chf), NMR and mass spectra were superimposable over those of VII, respectively.

Hexahydrobisdebromolaureatin (X) *and hydroxy ether* (XI). To a soln of III (160 mg) in EtOH (20 ml) was

added freshly prepared W-7 Ra-Ni (from 1 g of Al-Ni alloy) and then 3 drops of 2N KOH. The mixture was refluxed for 1·5 hr. After removal of the catalyst by filtration, water was added and most of the solvent was removed under diminished press. The residue was extracted with ether and the ether extracts were washed with water, dried and evaporated to yield an oily product, which was chromatographed on silica gel. Fractions eluted with benzene afforded X (59 mg) as colorless oil; IR, ν_{max}^{film} 1223, 1152, 1061, 1040, 955, 926 cm^{-1}; NMR, τ 9·08 (3H, br. t), 9·06 (3H, br. t), ca. 7·4 (two 1H, ts, J = 6, 5·5 and J = 8, 7·5 Hz), 6·72 (1H, sp?, J = 7·5, 6, 1·5 Hz), 5·83 (1H, br. m), 5·58 (1H, sp, J = 7·5, 6, 1·5 Hz), 5·29 (1H, m); mass, *m/e* 240 ($C_{15}H_{28}O_2$).

Fractions eluted with benzene–ethyl acetate (10:1) gave XI (44 mg) as colorless oil; IR, ν_{max}^{film} 3460, 1132, 1082, 1060 cm^{-1}; NMR, τ 9·07 (6H, br. t), ca. 6·49 (3H, m); mass, *m/e* 242 ($C_{15}H_{30}O_2$).

Dehydrobromohexahydrolaureatin (XIV). A mixture of III (800 mg) and 2N KOH-EtOH (80 ml) was refluxed for 2 hr. After cooling, water was added and most of EtOH was evaporated *in vacuo*. The residue was extracted with ether and the ether soln was washed with water, dried and evaporated to give an oily product which was chromatographed on silica gel. Fractions eluted with benzene afforded XIV (607 mg) as colorless oil; IR, ν_{max}^{film} 1229, 1165, 1147, 1080, 1020, 977, 935 cm^{-1}; NMR, τ 9·12 (3H, br. t), 8·34 (3H, d, J = 5 Hz), 7·8–7·45 (2H, m), 7·27 (2H, br. t), 6·53 (1H), 5·85 (1H), 5·53 (1H), 5·30 (1H), 5·17 (1H), 4·57 (2H); mass, *m/e* 318, 316 ($C_{15}H_{25}O_2Br$).

Hexahydromonodebromolaureatin (XV) *and hydroxybromo ether* (XVI). The hydrogenation of XIV (110 mg) was carried out in EtOH over Adams' catalyst for 2 hr. After removal of the catalyst and the solvent, the residual oil was chromatographed on silica gel. Fractions eluted with benzene afforded XV (57 mg) as colourless oil; IR, ν_{max}^{film} 1225, 1145, 1082, 1062, 1037, 974, 960, 933 cm^{-1}; NMR, τ 9·09 (3H, br. t), 9·07 (3H, br. t), 7·8–7·5 (2H, m), ca. 7·4 (2H, br. t), 6·62 (1H, br. t), 5·87 (1H), 5·76 (1H), 5·47 (1H), 5·17 (1H); mass, *m/e* 320, 318 ($C_{15}H_{27}O_2Br$).

Elution with benzene–ethyl acetate (10:1) yielded XVI (54 mg) as colorless oil; IR, ν_{max}^{film} 3450, 1223, 1057, 972, 854 cm^{-1}; NMR, τ 9·08 (6H, br. t), 7·9–7·5 (2H, m), 7·32 (2H, br. t), 6·54 (1H, m), 6·02 (1H, m), 5·53 (2H, m); mass, *m/e* 304, 302 ($C_{15}H_{27}OBr = M^+ - H_2O$).

Hexahydroisolaureatin (XVII). The hydrogenation of isolaureatin (II; 1·0 g) was performed in EtOH over Adams' catalyst, and ca. 3 moles of H_2 were absorbed after 2 hr. After removal of the catalyst and the solvent, the residual oil was purified by chromatography on silica gel to afford XVII (1005 mg) as colourless oil; $[\alpha]_D \pm 0°$ (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1289, 1201, 1140, 1120, 1092, 1088, 1075, 845, 743 cm^{-1}; NMR, τ 9·08 (3H, br. t), 8·93 (3H, t, J = 7, 7 Hz), 8·65 (6H, br.), 8·5–7·4 (8H), 6·69 (1H, t, J = 6·5, 6·5 Hz), ca. 6·2 (1H, m), ca. 5·9 (4H, m); mass, *m/e* 400, 398, 396 ($C_{15}H_{26}O_2Br_2$).

Saturated glycol (VI) *and its acetonide* (VII) *from hexahydroisolaureatin* (XVII). Treatment of XVII (300 mg) with Zn-AcOH and then with alkali was carried out in the similar manner as in the case of III to afford unsaturated glycol (204 mg) which showed the IR and NMR spectra superimposable upon those of IV, respectively. Diacetate of this unsaturated glycol was also identical with V in all respects.

The hydrogenation of the above-mentioned unsaturated glycol (90 mg) afforded the corresponding saturated glycol (81 mg) which was identical with a sample (VI) obtained from hexahydrolaureatin (III) described above. $[\alpha]_D$ − 24·3° (*c*, 1·85; CCl_4). The saturated glycol (70 mg) was converted to its acetonide VII (61 mg); $(\alpha)_D$ − 35° (*c*, 1·80; CCl_4). The IR, NMR and mass spectra of this compound were identical with those of the acetonide obtained from hexahydrolaureatin (III).

Hexahydrobisdebromoisolaureatin (XVIII). To a soln of XVII (300 mg) in EtOH (20 ml) was added freshly prepared W-7 Ra-Ni (from 1 g of Al-Ni alloy) and then 2N KOH (1 ml) and the mixture was refluxed for 1 hr. The reaction product, after being treated as in the case of III, was purified by chromatography on silica gel to give only XVIII (168 mg) as colourless oil; IR, ν_{max}^{film} 1146, 1081, 1038 cm^{-1}; NMR, τ 9·06 (6H, br. t), 6·70 (1H, br. t), 6·21 (1H, br. m), 5·98 (1H, br. t), 5·77 (1H, br. m); mass, *m/e* 240 ($C_{15}H_{28}O_2$).

Dehydrobromohexahydroisolaureatin (XIX). A mixture of XVII (800 mg) and 2N KOH-EtOH (45 ml) was refluxed for 4 hr. After cooling, water was added and most of EtOH was evaporated *in vacuo*. The mixture was then extracted with ether and the ether soln was washed with water, dried and evaporated to give an oily product which was chromatographed on silica gel. Fractions eluted with n-hexane-benzene (2:1) afforded XIX (564 mg) as colourless oil; IR, ν_{max}^{film} 1677, 1290, 1145, 1127, 1097, 1064, 966, 844, 741 cm^{-1}; NMR, τ 9·08 (3H, br. t), 8·28 (3H, d, J = 5 Hz), ca. 6·7 (1H, m), ca. 6·1–5·6 (4H, m), ca. 4·75–4·2 (2H, m); mass, *m/e* 318, 316 ($C_{15}H_{25}O_2Br$).

Hexahydromonodebromoisolaureatin (XX). The hydrogenation of XIX (291 mg) was carried out in EtOH (60 ml) over Adams' catalyst, and ca. 1 mole of H_2 was absorbed after 2 hr. After removal of the catalyst and the solvent, the residual oil was purified by chromatography on silica gel to give XX (286 mg) as

colourless oil; $[\alpha]_D$ + 14·5° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1290, 1146, 1120, 1090, 825, 742 cm^{-1}; NMR, τ 9·10 (6H, br. t), ca. 6·8 (1H, m), ca. 6·2 (1H, m), ca. 6·1–5·7 (3H, m); mass, *m/e* 320, 318 ($C_{15}H_{27}O_2Br$).

Acetoxy unsaturated cyclic ether (XXI). To a soln of XX (403 mg) in glacial acetic acid (40 ml) was added Zn-dust (400 mg), and the mixture was refluxed for 37 hr. After being cooled, the soln was filtered and evaporated *in vacuo*. The residue was acetylated with Ac_2O-Py in the usual manner. An oily product (293 mg) thus obtained consisted mainly of 3 products (TLC). This was carefully chromatographed over silica gel and the fraction eluted with benzene afforded XXI (143 mg) as colourless oil; $[\alpha]_D$ + 71° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1745, 1240, 1130, 1082, 1064, 1045, 1024, 768 cm^{-1}; NMR, τ 9·11 (3H, br. t), 9·03 (3H, br. t), 7·97 (3H, s), 8·2–7·1 (4H, m), 6·22 (1H, sex, J = 6, 6, 2 Hz), 6·06 (1H, m), 4·97 (1H, oct, J = 8, 4, 2 Hz), 4·18 (2H, m); mass, *m/e* 282 ($C_{17}H_{30}O_3$).

Acetoxy ether (XXII). a) Acetylation of XI (93 mg) with Ac_2O-Py was carried out in the usual manner. An oily product was purified by chromatography on silica gel giving XXII (95 mg) as colourless oil; $[\alpha]_D$ ± 0° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1742, 1240, 1134, 1083, 1022 cm^{-1}; NMR, τ 9·10 (3H, br. t), 9·08 (3H, br. t), 8·02 (3H, s), ca. 6·5 (2H, m), 5·28 (1H, m); mass, *m/e* 284 ($C_{17}H_{32}O_3$). (b) Hydrogenation of XXI (52 mg) was performed in EtOH (10 ml) over Adams' catalyst, and ca. 1 mole of H_2 was absorbed. After removal of the catalyst and the solvent, oily product was purified by chromatography on silica gel to give XXII (43 mg) which was found to be identical with XXII obtained from XI as mentioned above by comparison of their IR, NMR and mass spectra.

Hydroxybromo ether (XXIII). Hydrogenolysis of XIX (480 mg) was carried out in glacial acetic acid (60 ml) over 5% Pd-C for 2 hr. After removal of the catalyst and the solvent under diminished press, the oily product was chromatographed on silica gel. Elution with n-hexane–benzene (1 : 1) afforded oily substance (125 mg) which was identical with XX obtained from XIX by the hydrogenation over Adams' catalyst. Elution with benzene gave XXIII (303 mg) as colourless crystalline solid; $[\alpha]_D$ ± 0° (*c*, 2·00; CCl_4); IR, ν_{max}^{Nujol} 3600, 3480, 1124, 1075, 1024, 947 cm^{-1}; NMR, τ 9·09 (6H, br, t), 6·47 (3H, m), 5·66 (1H, m); mass, *m/e* 322, 320 ($C_{15}H_{29}O_2Br$).

Acetoxybromo ether (XXIV). Acetylation of XXIII (145 mg) was carried out in the usual manner to give XXIV (154 mg) as colourless oil; $[\alpha]_D$ − 23° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1744, 1240, 1027 cm^{-1}; NMR, τ 9·14 (6H, br. t), 8·03 (3H, s), 6·53 (1H, sex, J = 6, 6, 4·5 Hz), 6·14 (1H, sex, J = 6, 6, 4 Hz); mass, *m/e* 364, 362 ($C_{17}H_{31}O_3Br$).

Acetoxy ether (XXVI). To a suspension of W-7 Ra-Ni in EtOH (6 ml) and XXIII (52 mg) was added 3 drops of 2N KOH, and then the mixture was refluxed for 3 hr. After filtration of the catalyst, addition of water and removal of the solvent *in vacuo*, the residue was acetylated with Ac_2O-Py in the usual manner. An oily product thus obtained was purified by chromatography on silica gel to give XXVI (44 mg) as colourless oil; $[\alpha]_D$ − 24° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1744, 1240, 1024, 950 cm^{-1}; NMR, τ 9·09 (6H, br. t), 8·02 (3H, s), 6·26 (2H, m), 5·26 (1H, m); mass, *m/e* 284 ($C_{17}H_{32}O_3$).

Unsaturated diacetate (XXVII). Treatments of XXIV (105 mg) with Zn-AcOH and then with dil alkali were carried out in the similar manner as in the case of III. The acetylation of the oily product thus obtained afforded an oily substance which was purified by chromatography on silica gel to yield XXVII (79 mg) as colourless oil; $[\alpha]_D$ − 14° (*c*, 2·00; CCl_4); IR, ν_{max}^{film} 1748, 1225, 1024, 972 cm^{-1}; NMR, τ 9·11 (6H, br. t), 8·00 (6H, s), 5·15 (2H, m), 4·68 (2H, m); *m/e* 326 ($C_{19}H_{34}O_4$).

Acetoxy unsaturated cyclic ether (XXI) *from hexahydromonodebromolaureatin* (XV). To a soln of XV (42 mg) in glacial acetic acid (3 ml) was added Zn-dust (50 mg) and the mixture was refluxed for 1 hr. After being cooled, the soln was filtered and evaporated *in vacuo* and the residue was acetylated in the usual manner. An oily product (30 mg) was identical with XXI obtained from XX in all respects.

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