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LAURENCIN, A CONSTITUENT OF *LAURENCIA GLANDULIFERA* KÜTZING[1]

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Abstract—Laurencin, a new bromo compound isolated from *Laurencia glandulifera* Kützing, is represented by formula I on the basis of spectral and chemical evidence.

DURING the search for constituents of marine algae, a crystalline bromo compound was isolated from *Laurencia glandulifera* Kützing (Japanese name, Oosozo; Rhodomelaceae) and designated laurencin. In a preliminary communication,[2] the bromo compound has been shown to possess structure I, which involves an 8-membered cyclic ether ring as well as a triple bond. The present paper describes the full details of the isolation and structural elucidation of the compound.

The dried seaweed was extracted with methanol, and the solution concentrated *in vacuo* to leave resinous substance, which was then percolated with ether. The ethereal solution was washed successively with dilute potassium hydroxide solution, dilute hydrochloric acid and water, and the resulting neutral fraction was extensively chromatographed on alumina. Laurencin (I), m.p. 73–74° and $[\alpha]_D$ +70·2°, was obtained as colorless crystals from n-hexane–benzene eluates together with a sesquiterpene hydrocarbon, laurene,[3] cholesterol* and methyl palmitate. The molecular formula $C_{17}H_{23}O_3Br$ for I was confirmed by the mass spectrum, *m/e* 356 and 354. The IR and UV spectra of I suggest the presence of a terminal methine (ν_{max} 3285 and 2100 cm^{-1}), *trans* and *cis* double bonds (3040, 950 and 750 cm^{-1}), and a conjugated diene or enyne (λ_{max} 224 mμ, ε 16,400 and λ_{infl} 232 mμ, ε 11,000). The NMR spectrum (Fig. 1) supports the presence of these functional groups and also provides additional information on the structure. A sextet centered at τ 3·85 (A),† a multiplet at τ ca. 4·1 (B) and a finely splitted doublet at τ 4·48 (C) are associated with four olefinic protons. An acetylenic proton and protons for an acetoxyl methyl appear as a doublet centered at τ 7·17 (G) and as a singlet at τ 7·97 (K), respectively. Two characteristic one-proton sextets centered at τ 5·02 (D) and at τ 5·93 (E) are ascribed to protons on C atoms bearing an acetoxyl group and a Br atom or *vice versa*, and indicate that each of the relevant C atoms has only one H atom. A triplet centered at τ 9·02 (N) equivalent to three protons indicates the presence of an Et group, which has been confirmed by isolation of propionaldehyde on ozonolysis of I.‡ However,

* The identification of cholesterol was carried out by Dr. N. Katsui, to whom the authors wish to express their thanks.

† "(A)" refers to the signal A in the NMR spectra.

‡ The ozonolysis of laurencin was carried out by Dr. M. Takasugi, to whom the authors wish to express their thanks.

two methylene-protons in the Et group in question appear as multiplets at different fields, one being centered at τ 8·44 (M) and the other at τ ca. 8·0 (L').[4] This assignment will be proved by the spin decoupling study.

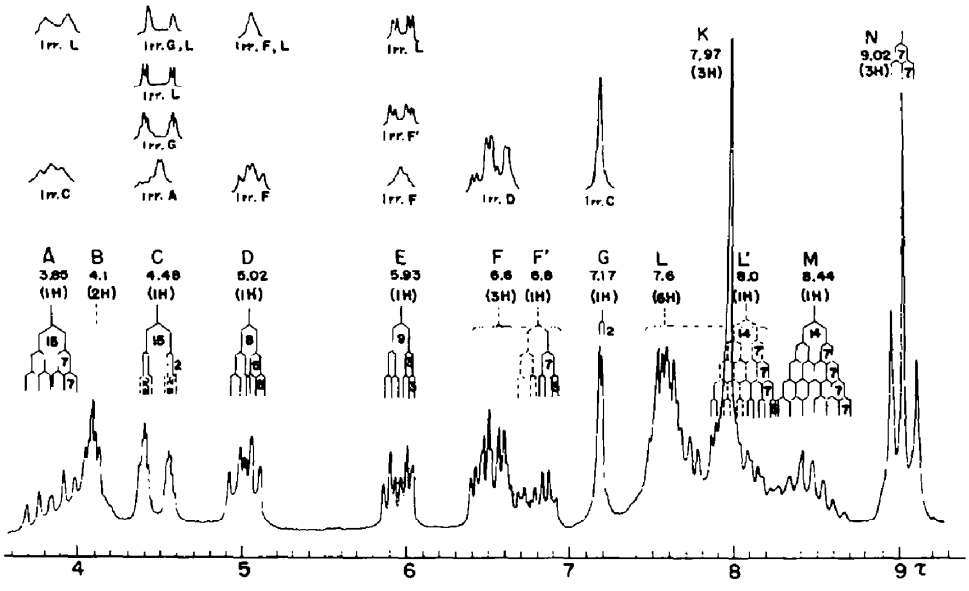


FIG. 1 NMR spectrum of laurencin (I) and its spin decoupling spectra in $CDCl_3$, 100 Mc.

Laurencin (I) gave, on mild hydrolysis with methanolic potassium hydroxide, deacetyllaurencin (II), $C_{15}H_{21}O_2Br$, oil, ν_{max} 3530 and 3420 cm^{-1}, which was reconverted into the original acetate I in good yield by treatment with acetic anhydride and pyridine. The NMR spectrum of II is almost the same as that of I, but the absorptions at τ 7·97 (K) and at τ 5·02 (D) are replaced by a singlet at τ 7·77 due to an OH proton and by a multiplet at τ ca. 6·5, respectively. This confirms that the absorption at τ 5·02 in the spectrum of I is attributable to the proton on the carbon bearing the acetoxyl group and, accordingly, that at τ 5·93 (E) should be ascribed to the proton on the carbon to which the Br atom is attached.

Laurencin consumed four moles of hydrogen over platinum catalyst in ethyl acetate to yield octahydrolaurencin (III), $C_{17}H_{31}O_3Br$, oil; the UV spectrum shows only end absorption and the IR spectrum the presence of an acetoxyl (ν_{max} 1735 and 1237 cm^{-1}) and an oxido group (1189 and 1075 cm^{-1}). In the NMR spectrum of III, absorptions corresponding to those in (D), (E) and (K) in the spectrum of I were observed, although they are shifted to slightly higher fields, τ 5·21, 6·13 and 8·02, respectively, but the signals due to the olefinic protons and that in (G) in the spectrum of I have disappeared, proving the latter signal (G) to be due to the acetylenic proton. It is to be noted that a complex multiplet centered at τ ca. 6·5, comparable with a signal centered at τ ca. 6·6 (3H, (F) including (F')) in the spectrum of I, involves only two protons. On mild hydrolysis with methanolic potassium hydroxide, III gave

octrahydrodeacetyllaurencin (IV), $C_{15}H_{29}O_2Br$, oil, ν_{max} 3590, 3500 and 1090 cm^{-1}, τ 7·76 (1H, singlet, O<u>H</u>) and ca. 6·3 (1H, multiplet, $\rangle$C<u>H</u>-OH), from which III was regenerated in good yield by acetylation.

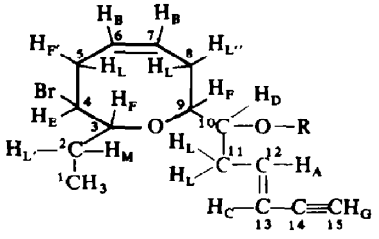
Reduction of III with LAH afforded a debromo alcohol (V), $C_{15}H_{30}O_2$, oil, which was then converted into the corresponding acetate (VI), $C_{17}H_{32}O_3$, oil, ν_{max} 1740 cm^{-1}, which must be a monocyclic compound. Oxidation of V with chromium trioxide in acetic acid gave rise to propionic, caproic and adipic acids after purification by preparative TLC, indicating that a n-pentyl group is involved in a side chain and a tetramethylene unit is part of a ring. The NMR spectrum of VI is almost similar as that of III except for the absence of the signal corresponding to that centered at τ 6·13 in III, which has been assigned to the proton on the carbon bearing the Br atom. It is again emphasized that a broad multiplet centered at τ ca. 6·6 accounts for only two protons. These facts indicate that two of the three protons appearing near this region in the spectrum of I are located on the carbon(s) adjacent to the ether oxygen, and the remaining one proton on the C atom vicinal to a double bond. The signal (F′) of the latter proton is overlapped by that of the former and only its higher field pattern is clearly observable. On the other hand, the absorption (L) in the spectrum of I involves 6 protons and one of them, corresponding to the signal (L′), is the proton of the methylene in the Et group as mentioned. The other 5 protons, the signals of which appear in the region of τ ca. 7·4 to 7·8, must be allylic protons judging from the chemical shifts. On the basis of the facts mentioned above, laurencin (I) should consist of the following units:

$C_{17}H_{23}O_3Br =$ { 3 —C<u>H</u>$_2$—(C=C); —C≡C—<u>H</u>; 2 —C<u>H</u>=C<u>H</u>— (*cis* and *trans*); $\rangle$C<u>H</u>—O—COCH$_3$; $\rangle$C<u>H</u>—Br; $\rangle$C<u>H</u>—O—C<u>H</u>$\langle$ or —C<u>H</u>$_2$—O—C(C)(C)—(C); —C<u>H</u>$_2$—C<u>H</u>$_3$ }

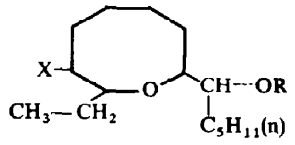
We next attempted to interpret the NMR spectrum of laurencin with the aid of double resonance experiments. Irradiation of τ 7·17 (G) collapses the finely splitted doublet (dodecade or decade) centered at τ 4·48 (C) to a broad doublet (J = 15 c/s) (run 1). Conversely, by irradiation at τ 4·48 (C), the doublet (J = 2 c/s) at τ 7·17 (G) and the sextet (J = 15, 7 and 7 c/s) at τ 3·85 (A) are simplified to a sharp singlet (run 2a) and to a broad triplet (J = 7 and 7 c/s) (run 2b), respectively. Therefore, the olefinic proton H-C* is coupled to that H-A with a large coupling constant of 15 c/s, which indicates the protons to be *trans*-oriented and that the *trans* double bond is located adjacent to the terminal triple bond. In the same double resonance experiment, the signal at τ ca. 7·6 (L) is slightly but definitely changed (run 2c). Not only a similar change

* "H-C" refers to the proton of the signal C in the NMR spectra.

(run 3b) in the signal at τ ca. 7·6 (L) is observed on irradiation at τ 3·85 (A) but also the signal of the proton H-C is simplified to a broad singlet (run 3a) by removal of the relevant 15 c/s coupling. These facts suggest that an allylic methylene group is adjacent to the *trans* double bond. This inference is confirmed by irradiation at τ ca. 7·6 (L),

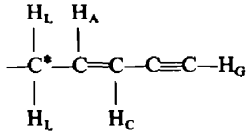


I: R = Ac
II: R = H



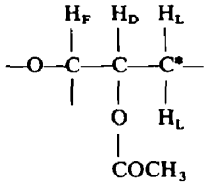
III: X = Br, R = Ac
IV: X = Br, R = H
V: X = R = H
VI: X = H, R = Ac
VII: X = Br, R = $COCOC_6H_5$
VIII: X = Br, R = $CO-\dot{C}(CH_3)(OH)-C_6H_5$

in which experiment the sextet (A) has collapsed to a doublet ($J = 15$ c/s) (run 8a) and the multiple doublet (C) to a double doublet ($J = 15$ and 2 c/s) (run 8b), respectively, *two* 7 c/s couplings and *two* 1·5 c/s splittings being removed in each resonance of the olefinic protons H-A and H-C. Furthermore, when the signal (C) is recorded with simultaneous irradiation at τ 7·17 (G) and τ ca. 7·6 (L), the complex doublet (C) is changed to a simple doublet ($J = 15$ c/s), three splittings, 2, 1·5 and 1·5 c/s, being removed (run 11). The following structural unit (i) is therefore present in laurencin:



(i)

The signals near τ 6·6 (F other than F') and centered at τ ca. 7·6 (L) exhibit significant change on irradiation at τ 5·02 (D) (runs 4a and 4b; Fig. 2B). On the other hand, the sextet ($J = 8$, 5 and 5 c/s) at τ 5·02 (D) is decoupled to a quartet ($J = 8$ and 5 c/s) by irradiation at τ ca. 6·6 (F) (run 6a) and to a broad doublet ($J = 5$ c/s) by that at τ ca. 7·6 (L) (run 8d), respectively, and is simplified to a broad singlet by simultaneous irradiation at τ ca. 6·6 and 7·6 (run 12). Since the signal (D) has been associated with the proton on the carbon bearing the acetoxyl group and the resonance near τ 6·6 with that adjacent to the ether oxygen, the experiments mentioned above indicate that the following structural unit (ii) must be involved in I:



(ii)

TABLE 1. SPIN DECOUPLING RESULTS IN $CDCl_3$ (100 Mc)

Run	Proton[a] (τ) Irradiated				Observed			Multiplicity change[b]	Splitting decoupled[c] (c/s)
1	7·17	(G)	C-15	—C≡CH	4·48	(C)	C-13	de–se	2
2a	4·48	(C)	C-13	—CH=CH—	7·17	(G)	C-15	do–si	2
b				(*trans*)	3·85	(A)	C-12	se–tr	15
c					7·6	(L)		(ch)	v.s.
3a	3·85	(A)	C-12	—CH=CH—	4·48	(C)	C-13	de–si(br)	15
b				(*trans*)	7·6	(L)		(ch)	
4a	5·02	(D)	C-10	—CH(OAc)—	6·6	(F)		(ch?)	
b					7·6	(L)		(ch)	
5a	5·93	(E)	C-4	—CH(Br)—	6·6	(F)		(ch)	
b					6·8	(F′)	C-5	(ch)	
c					7·6	(L)		(ch)	
6a	6·6	(F)	C-3	>CH—O—CH<	5·02	(D)	C-10	se–qu	5
b			and		5·93	(E)	C-4	se–tr(br)	9
c			C-9		8·03	(L′)	C-2	de(?)–se(?)	3
d					8·44	(M)	C-2	sp–se	7
e					7·6	(L)		(ch)	
f					7·8	(L″)	C-8	(ch)	
7a	6·8	(F′)	C-5	allylic proton	5·93	(E)	C-4	se–qu(?)	3
b					4·1	(B)		(ch)	
c					7·6	(L)		(ch)	
8a	7·6	(L)	C-5,	allylic proton	3·85	(A)	C-12	se–do	7, 7
b			C-8		4·48	(C)	C-13	de–qu	1·5, 1·5
c			and		5·93	(E)	C-4	se–qu	3
d			C-11		5·02	(D)	C-10	se–do(?)	5, 8
e					4·1	(B)		(ch)	
f					6·6	(F)		(ch)	
g					6·8	(F′)	C-5	(ch)	
9a	4·1	(B)	C-6	—CH=CH—	6·8	(F′)	C-5	oc(?)–qu	7
b			and	(*cis*)	7·6	(L)		(ch)	
c			C-7		7·8	(L″)		(ch)	
10a	9·02	(N)	C-1	—CH_2—CH_3	8·44	(M)	C-2	sp–qu	7, 7, 7
b					8·03	(L′)	C-2	de(?)–qu	7, 7, 7
11	7·17	(G) and 7·6 (L)			4·48	(C)	C-13	de–do	2, 1·5, 1·5
12	6·6	(F) and 7·6 (L)			5·02	(D)	C-10	se–si(br)	5, 5, 8
13	8·44	(M) and 8·03 (L′)			9·02	(N)	C-1	tr–si(br)	7, 7

[a] "C-15" refers to number of the carbon to which the proton is attached.

[b] Abbr.: "de" means decade; "se" sextet; "do" doublet; "si" singlet; "tr" triplet; "ch" change; "br" broad; "qu" quartet; "sp" septet; "oc" octet; "?" means that the multiplicity is not clear.

[c] Abbr.: "v.s." means "very small coupling constants". The error limits of J is 0·5 c/s.

Irradiation at τ 5·93, a center of the sextet associated with the proton H-E on the carbon to which the Br atom is attached, produces deformation of the resonance patterns near τ 6·6 (F other than F′), 6·8 (F′) and 7·6 (L) (runs 5a, 5b and 5c, respectively). Conversely, the sextet (J = 9, 3 and 3 c/s) in question centered at τ 5·93 (E) is simplified to a broad triplet (J = 3 and 3 c/s) by removal of the large coupling of 9 c/s by irradiation at τ 6·6 (F) (run 6b) and is decoupled to a broad quartet (J = 9 and 3 c/s) by

TABLE 2. SPIN DECOUPLING RESULTS IN BENZENE (100 Mc)

Run	Proton[a] (τ) Irradiated				Observed			Multiplicity change[b]	Splitting decoupled[c] (c/s)
14	6·95	(F)	C-9	—O—C<u>H</u>—CH(OAc)—	5·05	(D)	C-10	se–qu(?)	5
15	7·8	(L)	C-11	allylic proton	5·05	(D)	C-10	se–do	5, 8
16	6·62	(F)	C-3	—O—C<u>H</u>—CH(Br)—	6·15	(E)	C-4	se–tr(br)	9
17	7·6	(L)		allylic proton	6·15	(E)	C-4	se–qu(?)	3
18	7·1	(F')	C-5	allylic proton	6·15	(E)	C-4	se–qu	3
19	6·15	(E)	C-4	—C<u>H</u>(Br)—	7·1	(F')	C-5	(ch)	
20	8·12	(L')	C-2	—C<u>H</u>(H)—CH_3	6·62	(F)	C-3	sp–qu	3
21	8·43	(M)	C-2	—C(H)<u>H</u>—CH_3	6·62	(F)	C-3	sp–qu	7

[a], [b] and [c] See footnotes of Table 1.

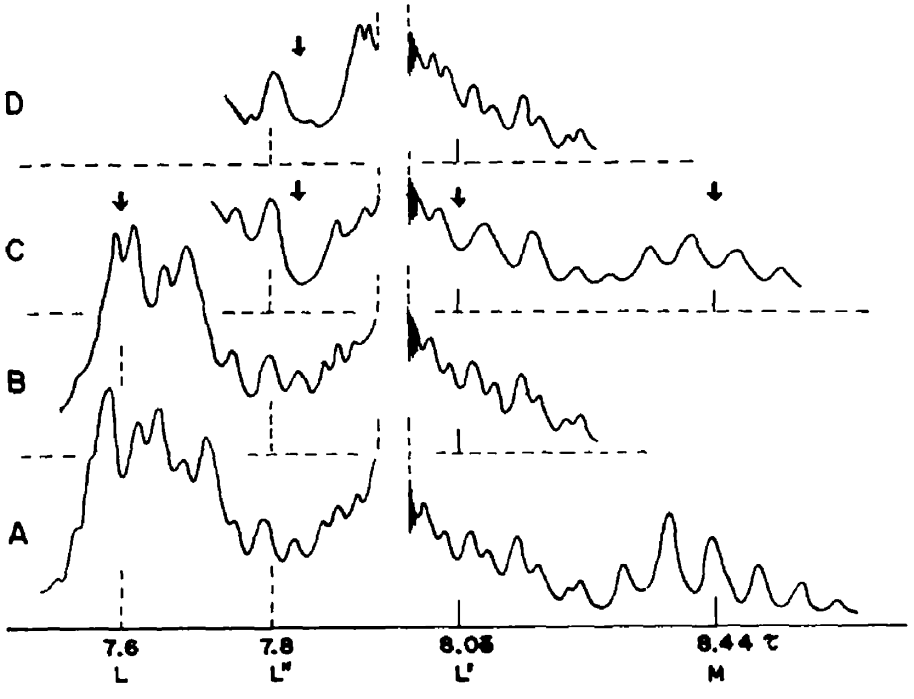
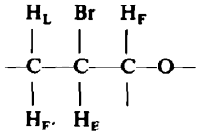


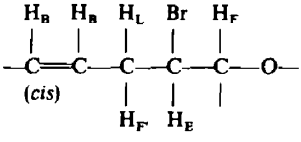
FIG. 2 Spin decoupling spectra of laurencin (I) in $CDCl_3$, 100 Mc.
(A) Standard (B) Run 4b (C) Runs 6c, 6d, 6f (D) Run 9c.

irradiation at τ 6·8 (F′) or at τ 7·6 (L) (runs 7a and 8c), 3 c/s splitting being removed in each run. Thus, the structural unit (iii) described below is deduced.



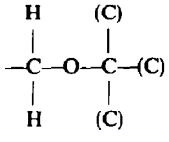
(iii)

As expected from this unit (iii), irradiation at τ 7·6 (L) causes change in the shape of the signal centred at τ 6·8 (F′) (run 8g) and, conversely, that at τ 6·8 deforms the signal of the proton H-L (run 7c). In both the decoupling experiments, the resonance pattern centered at τ ca. 4·1 (B), which is associated with protons on *cis* olefinic carbons, exhibits significant deformation (runs 8e and 7b). This is further clarified by irradiation at τ ca. 4·1 (B), on which the signal (F′) (octet or septet if not disturbed by other signals) is decoupled to a broad quartet ($J = 12$(?) and 3 c/s) by removal of 7 c/s coupling (run 9a), and also that (L) is deformed (run 9b). On the basis of these results, the unit (iii) is extended to the following (iv), and this disposition of the relevant allylic proton H-F′ will be supported in the decoupling studies in benzene (cf. runs 18 and 19), described later.



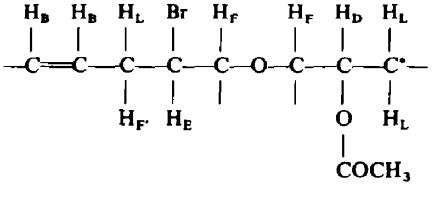
(iv)

As mentioned, both the signals centered at τ 5·02 (D) and at τ 5·93 (E) are clearly simplified by irradiation at τ ca. 6·6 (F), and the resonance pattern at the field, τ 6·6, accounts for only two protons on the carbon(s) adjacent to the ether oxygen. Thus, the possibility of a partial structure (v) is excluded (cf. the decoupling experiments in



(v)

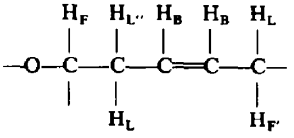
benzene, runs 14 and 16), and the structural units (ii) and (iv) are connected through the ether oxygen to give the sequential order (vi).



(vi)

Irradiation of resonance peak centered at τ 4·1 (B) leads to change of the pattern around τ 7·8 (run 9c and Fig. 2D), and the same is observed on irradiation at τ ca. 6·6 (F) (run 6f, Fig. 2C). The proton in question, whose signal appears around τ 7·8

and is named H-L'', is coupled neither to the protons H-D, H-E nor H-C, since irradiation at τ 5·02, 5·93 or 4·48 causes no significant change in the pattern near τ 7·8 (cf. Fig. 2B). Therefore, a moiety (vii) should be present in the molecule and, accordingly, the methylene group adjacent to the *trans* double bond must be the same as that vicinal to the carbon bearing the acetoxyl group (asterisked C^*H_2 in (i) and (ii) or (vi)).



(vii)

Irradiation at τ 9·02 (N) produces spin decoupling of two sets of signals in the spectrum. First, the seven-line pattern (J = 14, 7, 7, 7 and 7 c/s) centered at τ 8·44 (M) is simplified to a broad quartet (J = 14 and 7 c/s), three 7 c/s couplings being removed (run 10a). Secondly, the signal centered at τ ca. 8·0, whose low-field peaks are hidden under the signal due to the acetoxyl Me protons and whose whole pattern appears clearly as a dodecade (J = 14, 7, 7, 7 and 3 c/s) in the spectrum of II, is collapsed to a broad pattern (doublet or quartet if the whole pattern is visible), by removal of the three 7 c/s splittings (run 10b). Conversely, the triplet (J = 7 and 7 c/s) centered at τ 9·02 is simplified to a singlet on simultaneous irradiation at τ 8·44 and ca. 8·0 (run 13). Furthermore, irradiation at τ ca. 6·6 (F) removes the 7 c/s and 3 c/s splittings in the two one-proton multiplets centered at τ 8·44 (M) and at τ ca. 8·0 (L'), respectively (runs 6d and 6c, Fig. 2C). These experiments and the results mentioned in the preceding section indicate that both the Et group and the methylene group, which is vicinal to the *cis* double bond and includes the proton H-L'', are linked with the two carbons adjacent to the ether oxygen.

The spin decoupling studies of the spectrum of I in benzene (Fig. 3) has revealed that the Et group is combined with the C atom flanked by the ether oxygen and the

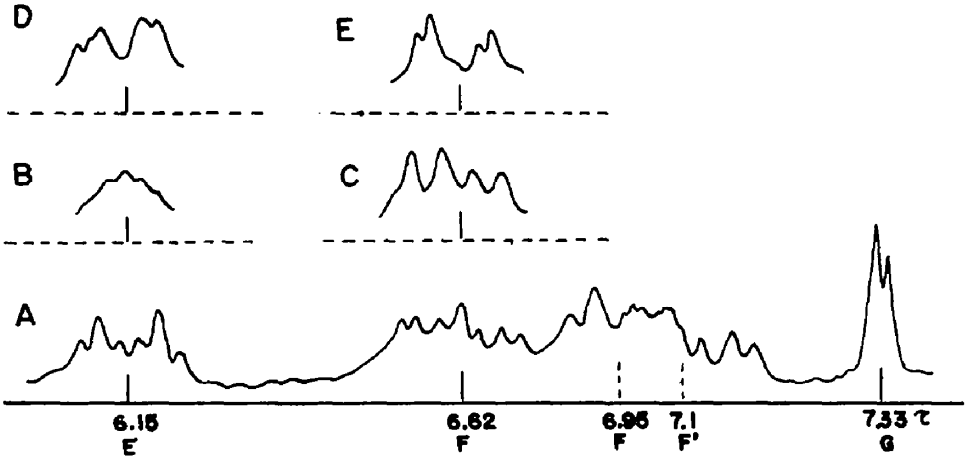
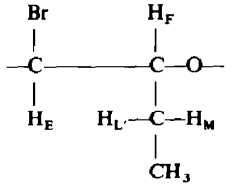


FIG. 3 Spin decoupling spectra of laurencin (I) in benzene, 100 Mc.
(A) Standard (B) Run 16 (C) Run 20 (D) Run 18 (E) Run 21.

carbon bearing the Br atom. The absorption due to the two protons H-F appearing as a confused multiplet around τ 6·6 in chloroform is divided into two parts in the spectrum in benzene, one of them being a clearly resolved septet ($J=9$, 7 and 3 c/s) centred at τ 6·62 and the other a multiplet at τ 6·95. Irradiation at τ 6·62 (F) collapses the sextet (J = 9, 3 and 3 c/s) centered at τ 6·15, which is associated with the proton on the carbon bearing the Br atom, to a broad triplet (run 16, Fig. 3B), removing the 9 c/s coupling. In addition, this septet at τ 6·62 is simplified to a quartet ($J=9$ and 7 c/s) on irradiation at τ 8·12 (run 20, Fig. 3C) and also to that ($J=9$ and 3 c/s) on irradiation at τ 8·43 (run 21, Fig. 3E). Apparently, the protons appearing at these fields, τ 8·12 and 8·43, are not allylic protons but those (H-L′ and H-M) of the methylene adjacent to the Me group, judging from the chemical shifts. Hence, the following structural unit (viii) must be present.



(viii)

Combination of the partial structures (i), (vi), (vii) and (viii) has now established the whole (planer) structure I of laurencin.

The mass spectra of laurencin and octahydrodebromolaurencin support the structures I and VI, respectively (Fig. 4A and 4B). The spectrum of laurencin (M^+ 356

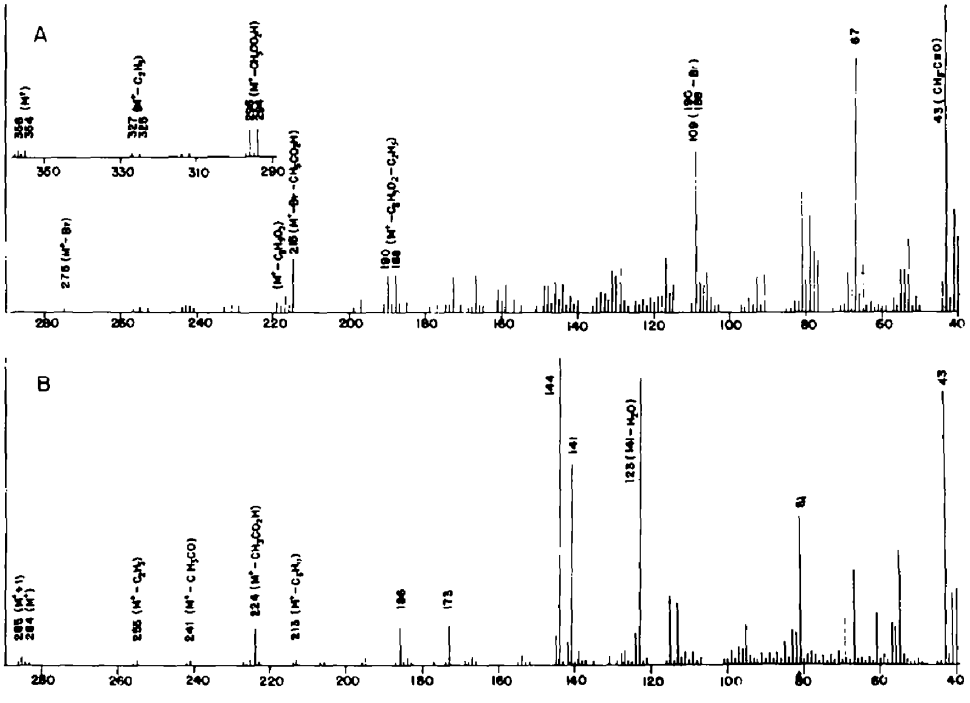
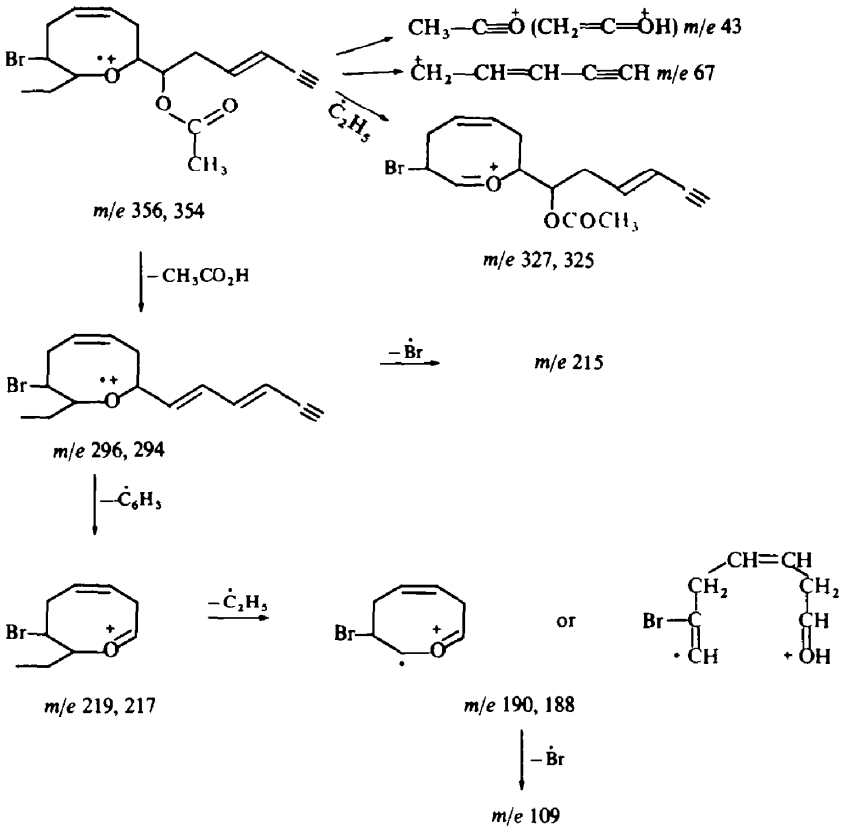
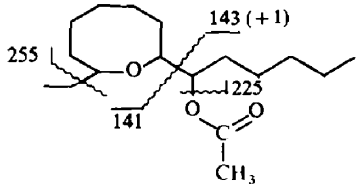


FIG. 4. Mass spectra of (A) lauencin (I) and (B) octahydrodebromolaurencin (VI).

and 354) shows a base peak at *m/e* 43 (CH_3—$C{\equiv}\overset{+}{O}$) and significant peaks at *m/e* 327, 325 ($M^+ - C_2H_5$), 296, 294 ($M^+ - CH_3CO_2H$), 275 ($M^+ - Br$), 219, 217, 215, 190, 188, 109 and 67. The one-step process from *m/e* 296 and 294 to *m/e* 215 is supported by the appearance of a metastable ion at *m/e* 156·5. The other metastable ions around *m/e* 245 and *m/e* 63 arise from the following two one-step processes: from molecular ions to *m/e* 296 and 294, and from *m/e* 190 and 188 to *m/e* 109. The main fragmentations are explicable by the following scheme:

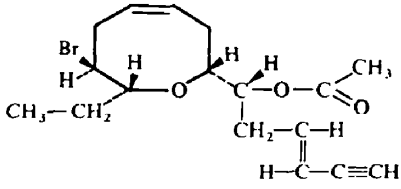


On the other hand, octahydrodebromolaurencin (VI) ($M^+ + 1$ 285, M^+ 284) has a base peak at *m/e* 144 and significant peaks at *m/e* 255, 225, 141, 123 and 43 (CH_3—$C{\equiv}O^+$). The major fragmentations may be shown as follows:



The strong peak at *m/e* 123 may be attributable to an ion produced by the loss of water from the ion of mass 141, as demonstrated by the appearance of a metastable ion at *m/e* 107·5.

After publication of our preliminary communication,[2] Professor J. M. Robertson *et al.*[5] have kindly determined the relative configuration of I on the basis of the X-ray crystallographic analysis. The absolute configuration at C-10 has been determined by the application of Prelog's atrolactic acid method[6] to octahydrodeacetyllaurencin (IV). Reaction of IV with phenylglyoxyloyl chloride gave phenylglyoxylic ester VII, which on treatment with methyl magnesium iodide followed by hydrolysis afforded levorotatory atrolactic acid. This proves the asymmetric C atom at the position 10 to have a *R*-configuration.* Therefore, laurencin has been established to possess the structure Ia.



(Ia)

EXPERIMENTAL

All the m.ps are uncorrected. The UV and IR spectra were measured using a Hitachi spectrophotometer and a Nippon Bunko 402-G or IR-S spectrophotometer, respectively. The NMR measurements were performed in CCl_4 or $CDCl_3$ with a Nippon Denshi 60-Mc or Varian 100-Mc spectrometer, TMS being used as an internal reference.

Isolation of laurencin (I). Air dried seaweed (8·5 kg) was extracted with MeOH and the MeOH soln was concentrated *in vacuo*. The residue was percolated with ether and the ethereal soln was shaken with 5% KOH aq and then with 1N HCl to remove acidic and basic components. After evaporation of the solvent, a neutral, pale yellow oil (90 g) was obtained and chromatographed on standard alumina. Fractions eluted with n-hexane–benzene (5:1) on removal of the solvents, left a crystalline substance. Recrystallization from MeOH gave laurencin (I, 4·5 g) as rhombic crystals, m.p. 73–74°; $[\alpha]_D^{27}$ +70·2° (*c*, 1·0; Chf); IR, ν_{max}^{Nujol} 3285, 3040, 2100, 1735, 1627, 1230, 1168, 1080, 1035, 950, 913 and 750 cm^{-1}. (Found: C, 57·42; H, 6·54; Br, 22·15. $C_{17}H_{23}O_3Br$ requires: C, 57·46; H, 6·54; Br, 22·42%).

Ozonolysis of I. A soln of I (100 mg) in AcOH (10 ml) was treated with ozonized O_2 at about 10° for 10 min and then reduced with Zn dust in the usual manner. After being distilled with steam, the distillate was treated with 2,4-DNP; brown ppt thus obtained was purified by preparative silica-gel TLC followed by recrystallization from EtOH to yield brown crystals (5 mg), m.p. 147–149°. This was identified as propionaldehyde 2,4-DNP by the mixed m.p. and by the comparison of its IR spectrum with that of an authentic sample.

Deacetyllaurencin (II). To a soln of 5% methanolic KOH (5 ml) I (50 mg) was added and the mixture refluxed for 5 min in a stream of N_2. The soln was then evaporated *in vacuo*, diluted with water and extracted with ether. The ethereal soln gave after evaporation an oily product, which was purified by chromatography on silica-gel to give II, oil (45 mg); $[\alpha]_D^{17}$ +46·1° (*c*, 1·15; Chf); UV, λ_{max}^{EtOH} 224 mμ (ε 14,000) and λ_{infl}^{EtOH} 232 mμ (ε 11,000); IR, ν_{max}^{film} 3530, 3420, 3035, 2150, 1627, 1167, 955, 910 and 750 cm^{-1}; NMR, τ 9·04 (3H, tr, *J* = 7 and 7 c/s), ca. 8·5–7·8 (2H, m), 7·77 (1H, s), ca. 7·8–7·4 (5H, m), 7·38 (1H, d, *J* = 2 c/s), ca. 7·0–6·5 (3H, m), ca. 6·5 (1H, m), 6·06 (1H, double-tr, *J* = 9, 3 and 3 c/s), 4·63 (1H, double-m, *J* = 15 c/s), ca. 4·1 (2H, m), and 3·85 (1H, double-tr, *J* = 15, 7 and 7 c/s). (Found: C, 57·38; H, 6·75. $C_{15}H_{21}O_2Br$ requires: C, 57·51; H, 6·77%).

* The absolute configuration of laurencin has recently been examined by the X-ray method and it has been shown that the asymmetric C at C-10 has a *R*-configuration. Private communication from Dr. G. Ferguson, The University, Glasgow, Scotland.

Acetylation of II with Ac_2O–Py was carried out in the usual manner. The product (15 mg from 14 mg of II) was identified as I, m.p. and mixed m.p. 73–74°.

Octahydrolaurencin (III). The hydrogenation of I (307 mg) was performed in AcOEt over Adams' catalyst, and ca. 4 moles of H_2 were absorbed after 2 hr. After removal of the catalyst and the solvent, the residual oil was chromatographed on silica-gel to give pure III (305 mg) as a colorless oil; $[\alpha]_D^{20}$ +43·9° (*c*, 3·45; CHf); UV, $\varepsilon_{220\,m\mu}$ 710; IR, ν_{max}^{film} 1735, 1237, 1189 and 1075 cm^{-1}; NMR, τ 8·02 (3H, s), ca. 6·5 (2H, m), 6·13 (1H, m) and 5·21 (1H, m); mass spectrum, M^+ 364 and 362. (Found: C, 56·38; H, 8·67. $C_{17}H_{31}O_3Br$ requires: C, 56·19; H, 8·60%).

Octahydrodeacetyllaurencin (IV). A mixture of III (310 mg) and 5% methanolic KOH was refluxed for 5 min in a stream of N_2. After being worked up in the usual manner, the product was chromatographed on silica-gel to give pure IV (285 mg) as a colorless oil; $[\alpha]_D^{20}$ + 29·4° (*c*, 2·36; Chf); IR, ν_{max}^{film} 3590, 3500, 1185 and 1090 cm^{-1}; NMR, τ 7·76 (1H, s), ca. 6·6 (2H, m), ca. 6·3 (1H, m) and ca. 6·0 (1H, m). (Found: C, 56·18; H, 9·01. $C_{15}H_{29}O_2Br$ requires: C, 56·07; H, 9·10%).

Compound IV (30 mg) was acetylated with Ac_2O–Py at room temp overnight. The product, after being treated by the usual method, was purified by chromatography on silica-gel to yield III (32 mg), which was identified by comparison of R_f values of TLC and IR spectra.

Octahydrodeacetyldebromolaurencin (V). To a soln of III (500 mg) in THF (25 ml) was added LAH (350 mg), and the mixture was refluxed for 7 hr with continuous stirring. After cooling, water was added and the soln filtered. After the solvent of the filtrate were evaporated *in vacuo*, the residue was repeatedly extracted with ether, and the ethereal soln dried over Na_2SO_4 and evaporated. The oily substance obtained was purified by column chromatography on silica-gel to give V (200 mg) as a colorless oil; $[\alpha]_D^{18}$ +21·5° (*c*, 1·86; Chf); IR, ν_{max}^{film} 3570, 3480, 1190 and 1090 cm^{-1}; NMR, τ 7·64 (1H, s), ca. 6·7 (2H, m), and ca. 6·55 (1H, m). (Found: C, 74·18; H, 12·70. $C_{15}H_{30}O_2$ requires: C, 74·32; H, 12·48%).

Compound V (84 mg) was acetylated with Ac_2O–Py. After purification of the product by column chromatography on silica-gel, pure VI (85 mg) was obtained as a colorless oil; $[\alpha]_D^{18}$ +45·7° (*c*, 1·73; Chf); IR, ν_{max}^{film} 1740, 1238, 1200 and 1020 cm^{-1}; NMR, τ 7·95 (3H, s), ca. 6·6 (2H, m), and 5·15 (1H, m); mass spectrum, M^+ 284. (Found: C, 71·58; H, 11·42. $C_{17}H_{32}O_3$ requires: C, 71·78; H, 11·34%).

Oxidation of V. To a soln of V (245 mg) in glacial AcOH (7 ml) a suspension of CrO_3 (500 mg) in AcOH (10 ml) was added dropwise with vigorous stirring. The mixture was continuously stirring for 1 hr at room temp, ice water (ca. 15 ml) was then added and the whole was extracted with ether. The ethereal soln was washed with water, dried over Na_2SO_4 and evaporated. The residue was again extracted with ether and was shaken with 5% $NaHCO_3$ aq. The alkaline layer was acidified with dil HCl and extracted with ether. After being dried over Na_2SO_4, the ethereal soln was evaporated to yield a mixture of carboxylic acids, which was examined by GLC and TLC: propionic acid was identified by the retention time of GLC (P.E.G. 4000, temp 155–156°, carrier gas: He) comparing with that of an authentic sample. Caproic acid was characterized as the crystalline *p*-bromophenacyl ester, m.p. 67–68°. (Found: C, 53·86; H, 5·58. Calc. for $C_{14}H_{17}O_3Br$: C, 53·68; H, 5·47%). Adipic acid was identified by the comparison of *Rf* value on TLC with that of an authentic sample.

Phenylglyoxylic ester of IV (VII). A soln of phenylglyoxyloyl chloride (150 mg) in dry benzene (5 ml) was added to a soln of IV (216 mg) in a mixture of dry benzene (3 ml) and pyridine (2 ml). The mixture was allowed to stand at room temp for 20 hr, and then poured into ice water and extracted with ether. The ethereal soln was washed successively with 1N HCl, 10% Na_2CO_3 aq and water and dried over Na_2SO_4. A crude ester obtained after removal of the solvent was purified by column chromatography on silica-gel to give VII (280 mg), oil; $[\alpha]_D^{18}$ +43·5° (*c*, 1·15; Chf); IR, ν_{max}^{film} 1735, 1689, 1600, 1200, 1175 and 990 cm^{-1}. (Found: C, 60·88; H, 7·28. $C_{23}H_{33}O_4Br$ requires: C, 60·93; H, 7·34%).

Atrolactic acid from VII. A soln of VII (230 mg) in dry ether (20 ml) was added dropwise into an ice-cooled soln of MeMgI prepared from Mg (50 mg) and MeI (200 mg) in dry ether (10 ml). The mixture was stirred for 1 hr at room temp and then refluxed gently for 1·5 hr. The reaction mixture was poured onto cracked ice, diluted with 1N AcOH (10 ml) and then extracted with ether. The ethereal soln was washed with water, dried over Na_2SO_4, and evaporated to give crude VIII (240 mg); IR, ν_{max}^{film} 3520 and 1725 cm^{-1}. The crude sample of VIII was hydrolysed by refluxing with KOH (30 mg) in a 1:5 mixture of water and MeOH (6 ml) for 2 hr. After being cooled the reaction mixture was extracted with ether and the aqueous layer was acidified with 2N HCl and then extracted with ether. The ethereal soln was washed with water, dried over Na_2SO_4 and evaporated to yield atrolactic acid, m.p. 77–86° (70 mg); $[\alpha]_D^{24}$ −4·8° (*c*, 2·69; EtOH).

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