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LAURENE, A SESQUITERPENE HYDROCARBON FROM *LAURENCIA* SPECIES[1]

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Abstract—Laurene, a new sesquiterpene hydrocarbon from *Laurencia glandulifera* Kützing and *L. nipponica* Yamada, is shown to possess structure I. Isolaurene (IV) and epilaurene (XX) have been synthesized.

IN A previous paper[2] we described the isolation and structure elucidation of laurencin, a bromo-compound from *L. glandulifera* Kützing (Japanese name, Oosozo; Rhodomelaceae). Our further examination led to the isolation of a new hydrocarbon,[3] which was also obtained from *L. nipponica* Yamada (Urasozo) and was designated as laurene. The present paper deals with the details of the structure determination of laurene and the syntheses of its isomers, isolaurene and epilaurene.[4]

Ether extracts of the dried seaweed* were washed successively with dil KOH soln, dil HCl and water, and the neutral oil thus obtained was chromatographed on standard alumina. The hydrocarbon eluted with n-hexane was separated roughly into two parts (TLC and GLC); one consists mainly of a mixture of aliphatic hydrocarbons and the other that of sesquiterpenes. Careful chromatographic separation of the latter over standard alumina gave a pure sesquiterpene hydrocarbon, laurene (I), $C_{15}H_{20}$, b.p. 131–133°/21 mmHg, $[\alpha]_D$ +48·7°, in 0·11% yield.†

The UV, IR (Fig. 1-A) and NMR (Fig. 2-A) spectra all indicate the presence of a tolyl (probably *p*-tolyl) [λ_{max} 253 mμ (ε 280), 259 (280), 265 (280) and 274 (240); ν_{max} 1512 and 812 cm^{-1}; τ 3·01 (4H, s)‡ and 7·69 (3H, s)], a terminal methylene [1653 and 875 cm^{-1}; τ 5·19 (2H, q, J = 1 c/s)], a secondary Me [τ 9·32 (3H, d, J = 7 c/s)], and a tertiary Me group [τ 8·71 (3H, s)]. In view of the number of unsaturation of I, another carbocyclic ring must be present in the molecule.

Oxidation of I with osmium tetroxide in ether-pyridine afforded a glycol (II), $C_{15}H_{22}O_2$, $[\alpha]_D$ +40°, ν_{max} 3520 and 3380 cm^{-1}, which showed a secondary Me doublet at τ 9·38 and a signal at τ 5·95 due to oxymethylene protons in the NMR spectrum. When treated with periodic acid, II was converted to a 5-membered ring ketone III, $C_{14}H_{18}O$, $[\alpha]_D$ +70°, having an absorption maximum at 1737 cm^{-1} and showing a positive Cotton effect in the ORD curve. The NMR spectrum of III showed peaks attributable to four aromatic protons at τ 2·7 to 3·0 (m), an aromatic Me at τ 7·66, a tertiary Me at τ 8·84 and a secondary Me group at τ 9·04 (d, J = 7 c/s). Thus, laurene has an exocyclic methylene group on a 5-membered ring system, and this is

* *L. glandulifera* was collected in August at Oshiro Bay and *L. nipponica* in June at Hakodate Bay, Hokkaido.

† From *L. nipponica* the yield was poor.

‡ s: singlet, d: doublet, q: quartet, and m: multiplet.

supported by the fact that the IR absorption due to the terminal methylene group is observed at relatively lower frequency (ν 875 cm^{-1}).

Laurene is very unstable in acidic medium; e.g., when a soln of I in n-hexane was passed through a column of silica gel, there was obtained an isomeric hydrocarbon, isolaurene (IV), $C_{15}H_{20}$, b.p. 140–142°/21 mmHg, $[\alpha]_D$ +108·7°, which lacked a peak attributable to a terminal methylene group in the IR spectrum (Fig. 1-C). Furthermore, its NMR spectrum (Fig. 2-C) showed signals due to two Me groups attached to olefinic carbons at τ 8·30 and 8·63* instead of those due to the terminal

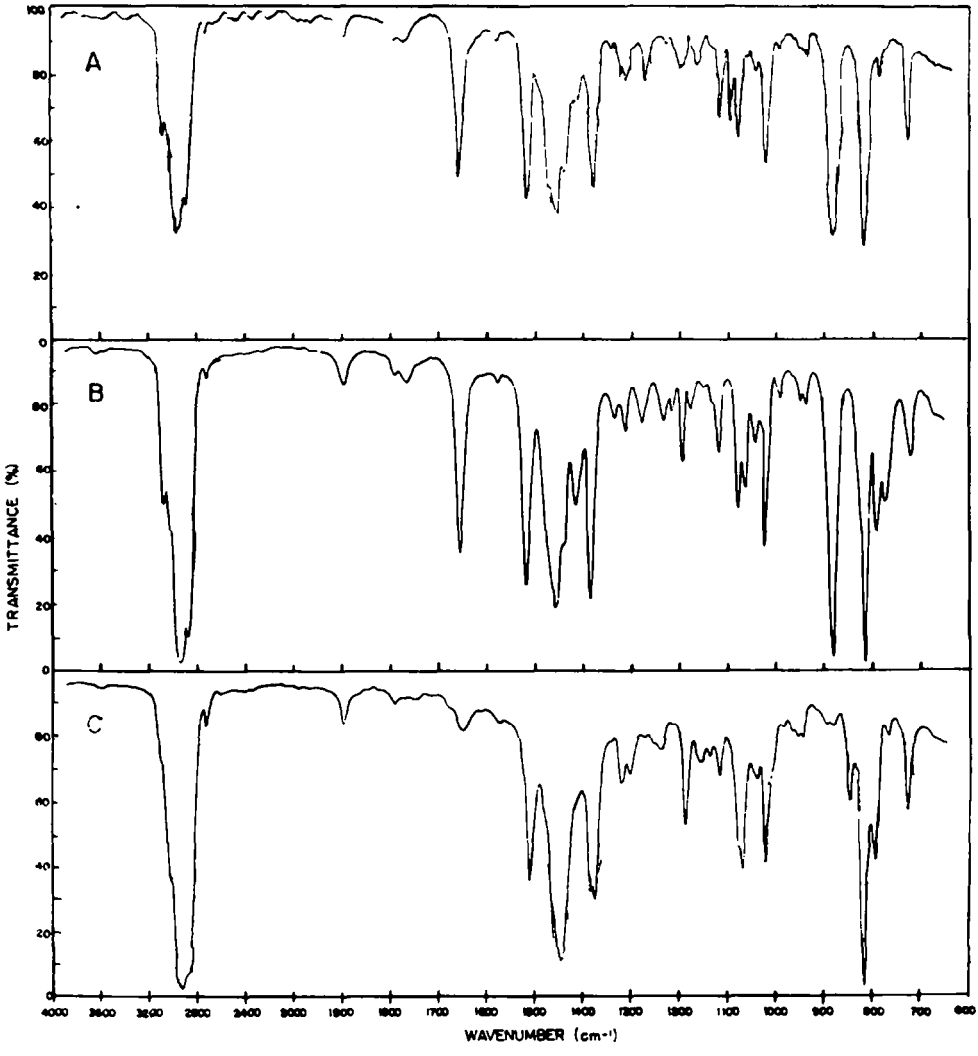


FIG. 1 IR spectra of (A) laurene, (B) epilaurene, and (C) isolaurene.

* The absorption at τ 8·63 appears in the extraordinarily high field as that due to methyl group attached to olefinic carbon, and this abnormality would be caused by a magnetic anisotropy of benzene ring; cf. reference 6.

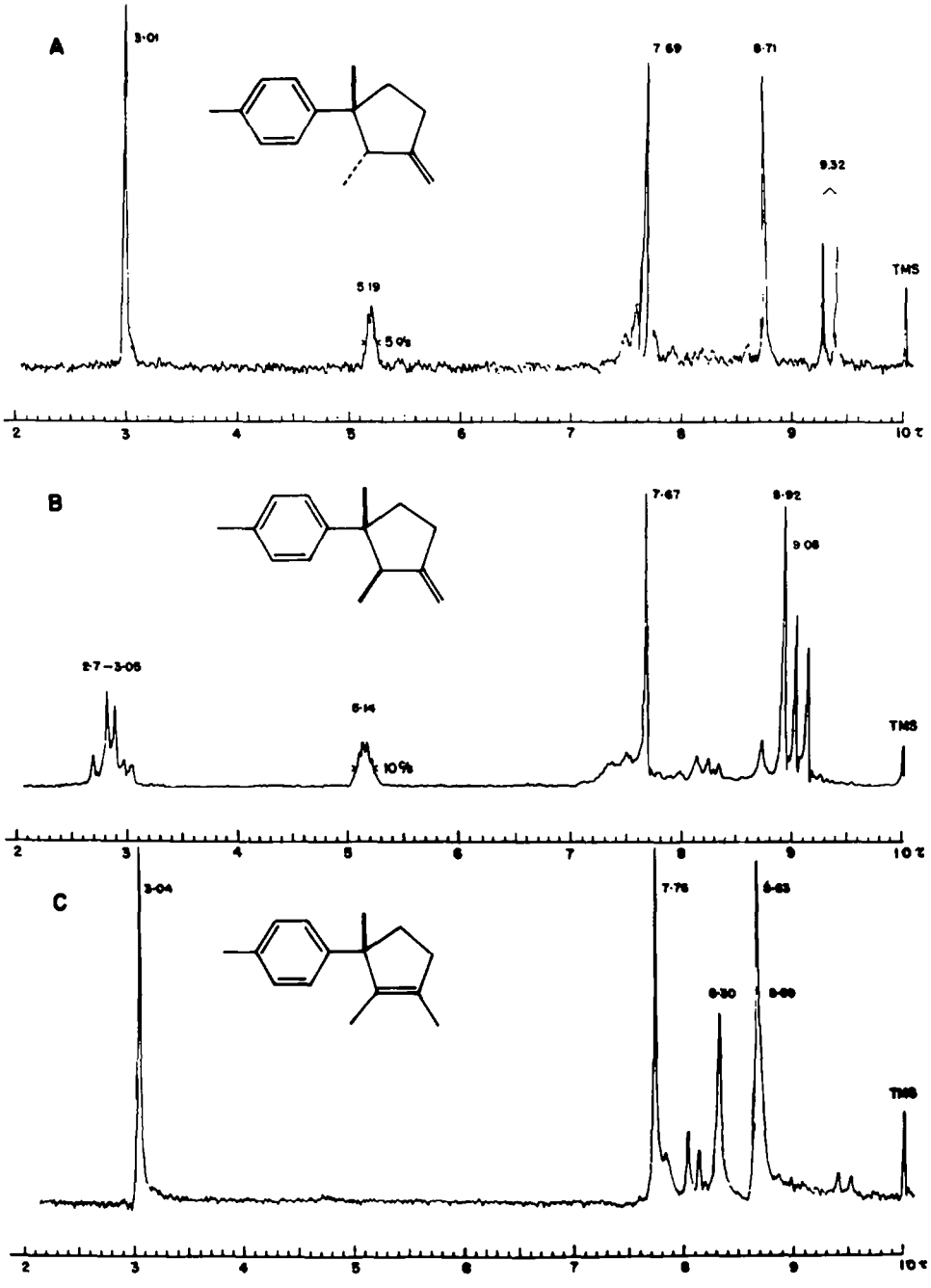
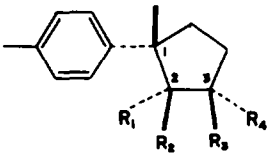
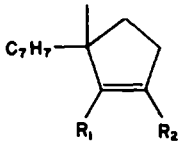


FIG. 2 NMR spectra of (A) laurene, (B) epilaurene, and (C) isolaurene.

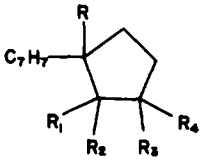
methylene and the secondary Me group of I. Hence, the isomerization involves migration of the exo-cyclic double bond to an endo-cyclic one to which two Me groups are attached and, therefore, the terminal methylene and the secondary Me groups must be located on vicinal carbons in I, as far as no skeletal change occurs during the isomerization. Such a facil migration of an exo-cyclic double bond into



I: $R_1 = CH_3, R_2 = H, R_3R_4 = CH_2$
II: $R_1 = CH_3, R_2 = H, R_3 = OH, R_4 = CH_2OH$
III: $R_1 = CH_3, R_2 = H, R_3R_4 = O$
V: R_1 or $R_2 = CH_3$, R_2 or $R_1 = OH$
R_3 or $R_4 = CH_3$, R_4 or $R_3 = OH$
VI: $R_1 = R_2 = CH_3, R_3R_4 = O$
VII: $R_1R_2 = O, R_3 = R_4 = CH_3$
XV: $R_1 = R_2 = CH_3, R_3 = R_4 = H$



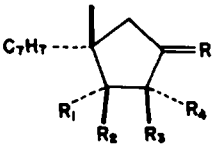
IV: $R_1 = R_2 = CH_3$ (α-C_7H_7)
XII: $R_1 = CH_3, R_2 = H$



(R, R_2, R_3: same side)

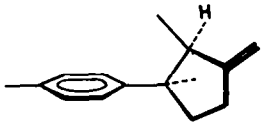
XIX: $R_1 = R_2 = CH_3, R_3R_4 =$ 

XX: $R_1 = H, R_2 = CH_3, R_3R_4 = CH_2$



IX: $R = R_3 = R_4 = H, R_1R_2 = O$
X: $R = CH_3, R_1R_2 = O, R_3 = R_4 = H$
XI: *cis*: $R = R_2 = CH_3, R_1 = OH, R_3 = R_4 = H$
trans: $R = R_1 = CH_3, R_2 = OH, R_3 = R_4 = H$
XIII: $R = R_1 = CH_3, R_2 = R_4 = H, R_3 = OH$
XIV: $R = R_1 = CH_3, R_2 = H, R_3R_4 = O$

VIII: $R_1 = R_2 = R_3 = H, R_4 = CH_3, R = CH_2$
XVI: $R_1 = CH_3, R_2 = H, R_3R_4 = O, R = CHOH$
XVII: $R_1 = CH_3, R_2 = H, R_3R_4 = O, R = CHSC_4H_9$
XVIII: $R_1 = R_2 = CH_3, R_3R_4 = O, R = CHSC_4H_9$



XXI

an endo-cyclic position by the acidic reagents is well known.[4a] In accord with the assigned partial structure, IV afforded a ditertiary glycol (V), m.p. 114–116°, ν_{max} 3320 cm^{-1}, on treatment with osmium tetroxide; that is, the NMR spectrum of V exhibited two sharp signals at τ 8·82 and 8·90 due to the Me groups on vicinal carbons bearing an OH group instead of those at τ 8·30 and 8·63 in IV. With the expectation of formation of α-cuparenone (VI),[5] glycol V was submitted to acid treatment, but the NMR spectrum of the product was not identical with the reported one of VI.[5] It would probably be formulated as VII.

All these results indicate that I is the most preferable structure for laurene, since the possibility of formula VIII is ruled out by the presence of optical activity in isolaurene. It is evident, on the basis of the high τ-value of the secondary Me signals in the NMR spectra of I and II, that the Me group is *cis*-oriented to the tolyl group.[6]

The mass spectrum of I (Fig. 3) is characterized by strong molecular ion at *m/e* 200 and abundant fragments, a few of which can be assigned plausible structures. The parent peak at *m/e* 143 corresponding to molecular formula $C_{11}H_{11}^+$ arises from the expulsion of C_3H_6 from the $M^+ - CH_3$ species (*m/e* 185). The *m/e* 171 ion is suggested

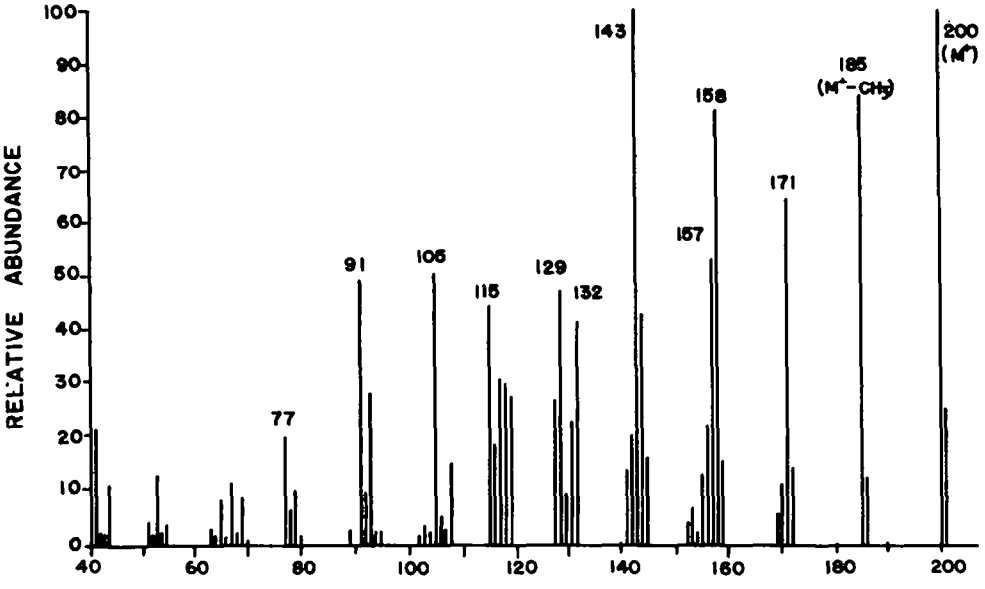


FIG. 3 Mass spectrum of laurene

to be formed by the loss of C_2H_5 from the molecular ion and the *m/e* 157 and 129 ions are by the loss of C_2H_4 and C_4H_8 from the $M^+ - CH_3$ ion, respectively. Moreover, peaks at *m/e* 158 and 132 may be attributed to radical ions $C_{12}H_{14}^+$ and $C_{10}H_{12}^+$ which are formed by the loss of C_3H_6 and C_5H_8 from the molecular ion, respectively, and the *m/e* 91 and 77 peaks are shown to arise from the aromatic group.

The structure I for laurene has been confirmed by the synthesis of ketone III. 2-(*p*-Tolyl)cyclopentanone (IX)[7] was methylated with MeI and $NaNH_2$ to yield 2-methyl-2-(*p*-tolyl)cyclopentanone (X), b.p. 124–126°/5·5 mmHg. The IR spectrum of X showed absorptions at 1737 and 1408 cm^{-1} due to a carbonyl and a methylene group adjacent to the carbonyl, respectively, and the NMR spectrum a tertiary Me signal at τ 8·72. The treatment of X with MeLi in ether afforded stereoisomers of *cis*- and *trans*-1,2-dimethyl-1-(*p*-tolyl)cyclopentan-2-ol (XI). Each compound could be isolated by preparative TLC; one isomer showed in its NMR spectrum a peak due to a methyl group on C-2 at τ 8·85 and the other at τ 9·13. The latter could be assigned as *trans*, and the former *cis*. The relevant upfield shift of the Me signal in the *trans*-isomer is explained due to the magnetic anisotropy of the tolyl group. For the preparative purpose the mixture of two isomers XI could be used without further separation because both the *cis*- and *trans*-isomers afforded the same compound, 1,2-dimethyl-1-(*p*-tolyl)cyclopent-2-ene (XII), on acid dehydration. On hydroboration followed

by oxidation, the cyclopentene XII gave 1,2-dimethyl-1-(*p*-tolyl)cyclopentan-3-ol (XIII) in good yield. The secondary methyl signal at τ 9·38 in the NMR spectrum of XIII indicated that the Me group was oriented *cis* to the tolyl group, as expected from the principle that the hydroboration involves *cis* addition from the less hindered side of the double bond.[8] This alcohol XIII was oxidized with chromic acid-pyridine to yield the corresponding ketone XIV, having the carbonyl frequency at 1737 cm^{-1}. The IR (in $CHCl_3$) and NMR spectra and the R_f-value on TLC of this synthetic *dl*-ketone XIV (semicarbazone, m.p. 214–215°) have been found to be identical with those of the ketone III (*d*-) obtained from I.

The absolute configuration of laurene was established by correlation with (+)-cuparene (XV) as follows. The ketone III was treated with ethyl formate and NaOMe in benzene[9] to yield a hydroxymethylene compound XVI, which on refluxing with n-butyl mercaptan and *p*-toluenesulfonic acid in benzene[10] was converted into the thioether XVII. Methylation of XVII with MeI and KO*t*Bu followed by treatment with KOH in refluxing aqueous diethylene glycol produced a *gem*-dimethyl ketone, $C_{15}H_{20}O$, m.p. 52–53°, $[\alpha]_D$ +170°, the semicarbazone, m.p. 233–234°. This ketone was shown to be identical with α-cuparenone (VI)[5] by a comparison of their optical rotations, IR and NMR spectra and by the mixed melting point method of their semicarbazones.* On the other hand, treatment of the thioketal XIX, prepared from VI and ethanedithiol, with Raney-nickel in refluxing ethanol afforded a hydrocarbon, $C_{15}H_{22}$, $[\alpha]_D$ +60°, which was identical with natural (+)-cuparene† in all respects. Since the absolute configuration of (+)-cuparene[11] and the relative orientation of a tolyl and a secondary Me group in I have been established, the present transformation completes the stereochemistry of laurene and α-cuparenone.

Next, an attempt was made to convert the ketone III into laurene. Contrary to the expectation, the attempt led to the formation of isolaurene (IV) and epilaurene (XX); treatment of III with an excess of methylenetriphenylphosphorane in DMSO at 60°[12] followed by purification of the product by column chromatography over alumina yielded a new hydrocarbon, designated as epilaurene (XX), $C_{15}H_{20}$, $[\alpha]_D$ −3·1°, in about 80% yield, and no laurene could be detected by GLC. On the other hand, by chromatographic separation of the afore-mentioned reaction product over silica gel, epilaurene (XX) and isolaurene (IV) were isolated in the ratio of about 4:1. While epilaurene showed almost the same IR spectrum (Fig. 1-B) as I, the NMR spectrum (Fig. 2-B) was different from that of I; the signal due to the secondary Me group of I appeared at τ 9·32, whereas corresponding peak of XX at τ 9·08. Since both the hydrocarbons I and XX were isomerized to isolaurene (IV) under acidic conditions, epilaurene (XX) should be a C-2 epimer of laurene. The above-mentioned formation of XX from the ketone III indicates that the C atom at position 2 has been epimerized under the reaction conditions used, although III was recovered unchanged on treatment with NaOMe in refluxing MeOH. It is noteworthy that the isomerization of I to IV takes place more readily as compared with that of XX.

Finally, we discuss the chemical shifts of C-2 and C-1 Me groups in the NMR spectra of laurene and its derivatives. In view of the extraordinary upfield shifts of

* The authors wish to express their thanks to Professor Sukh Dev, National Chemical Institute, Poona, for providing an authentic sample of α-cuparenone semicarbazone.

† The authors wish to express their thanks to Professor Sho Ito, Tohoku University, for providing a sample of natural cuparene.

the signals due to the C-2 methyl group in laurene and its derivatives II, XIII and *trans*-XI, as well as one of two C-2 Me groups in cuparene (XV) and α-cuparenone (VI) (Table 1), it is presumed that the 2-Me group oriented *cis* to the tolyl group

TABLE 1. CHEMICAL SHIFTS (τ) OF PROTON RESONANCES IN LAURENE AND ITS RELATED COMPOUNDS

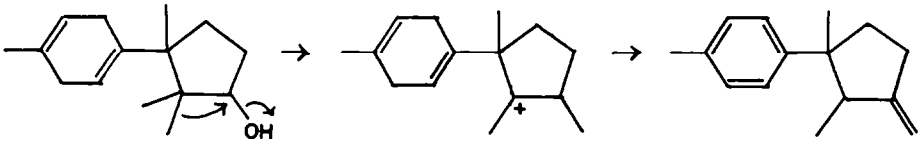
Compound	Arom. H.	Ar-Me	C_1-Me	C_2-Me	C_3-Me
I	3·01 (s)	7·69	8·71	9·32	—
II	3·05 (s)	7·73	8·54	9·38	—
III	2·7–3·0	7·66	8·84	9·04	—
IV	3·04 (s)	7·76	8·67	8·63*	8·30*
V	2·65–3·0	7·69	8·68	8·90†	8·82†
VI	2·7–3·05	7·68	8·77	9·43; 8·88	—
VII	2·7–3·05	7·72	8·72	—	9·07; 8·93
X	2·7–3·05	7·72	8·73	—	—
cis-XI	2·55–3·0	7·67	8·73	8·85†	—
trans-XI	2·65–3·1	7·70	8·70	9·13†	—
XII	3·02 (s)	7·73	8·62	8·55*	—
XIII	3·00 (s)	7·72	8·60	9·38	—
XIV(*dl*-III)	2·7–3·0	7·66	8·84	9·04	—
XV	2·9–3·1	7·72	8·78	9·45; 8·95	—
XX	2·7–3·05	7·67	8·92	9·08	—

* Vinyl methyl.

† Me group attached on a carbon bearing OH.

falls within the diamagnetic screening zone of the aromatic nucleus. This implies that the tolyl group adopts a near-perpendicular orientation with respect to the plane of cyclopentane ring as shown in XXI. On the other hand, the down-field shift of the C-1 Me signals in glycol II (τ 8·54) and alcohol XIII (τ 8·60) should be ascribed to the presence of an OH group at C-3, which is oriented *cis* to the Me group in question and exerts 1,3-interaction to the group.[13] This orientation of the OH group is explicable on the basis of that the reagents (OsO_4 or B_2H_6) approach from the sterically less hindered side.

To our knowledge, laurene is a new type of sesquiterpene, which is presumed to be formed by 1,2-Me shift from cuparene type sesquiterpene.[14]



EXPERIMENTAL

M.ps and b.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 laurene (I). Air dired seaweed (2·3 kg) was extracted with ether and the ether soln concen-

trated to about 2 l. The soln was shaken with 1N KOH and then with 1N HCl to remove acidic and basic components. After removal of the solvent, neutral oily residue (31·7 g) was chromatographed on standard alumina. The hydrocarbon fraction thus obtained was carefully rechromatographed over silica gel to yield I, colorless oil, b.p. 131–133°/21 mmHg, $[\alpha]_D^{23}$ +48·7° (*c*, 1·2; EtOH); UV, λ_{max}^{EtOH} 253, 259, 265 and 274 mμ (ε 280, 280, 280 and 240); IR, ν_{max}^{film} 1653, 1515, 1017, 875, 810 and 725 cm^{-1}; NMR τ 9·32 (3H, d, J = 7 c/s), 8·71 (3H, s), 7·69 (3H, s), 5·19 (2H, m) and 3·01 (4H, m); mass spectrum, *m/e* 200 (M^+), 185 (86), 171 (64), 158 (82), 143 (100), 132 (42), 129 (47), 115 (45), 105 (50), 91 (49) and 77 (19). (Found: C, 89·73; H, 9·40. $C_{15}H_{20}$ requires: C, 89·95; H, 10·05%).

Oxidation of laurene with OsO_4 *and* $NaIO_4$. To a soln of I (826 mg) in a mixture of ether (20 ml) and pyridine (5 ml) was added OsO_4 (551 mg), and the mixture was stirred at room temp for 20 hr. The reaction mixture was poured into water and extracted with ether. The ether soln was washed with 1N HCl and water, dried and evaporated. The residual mass was dissolved in EtOH and the soln was treated with Na_2SO_3 aq, filtered and evaporated. A pale yellow oily residue was purified by chromatography on silica gel to yield pure glycol II (380 mg) as a colorless oil; $[\alpha]_D^{23}$ +40° (*c*, 2·1; Chf); IR, ν_{max}^{Chf} 3520, 3380, 1508, 1012, 975 and 812 cm^{-1}; NMR, τ 9·38 (3H, d, J = 7 c/s), 8·54 (3H, s), 7·73 (3H, s), 5·95 (2H, m) and 3·05 (4H, s).

A mixture of II (267 mg), $NaIO_4$ (270 mg), MeOH (10 ml) and H_2O (5 ml) was stirred at room temp for 10 hr. To the reaction mixture was added water, and after removal of most of MeOH under diminished press the mixture was extracted with ether. The ether soln was washed with water, dried and evaporated. A pale yellow residue (174 mg) was purified by preparative TLC to yield pure ketone III (65 mg), colorless oil, $[\alpha]_D^{23}$ +70° (*c*, 2·0; Chf); IR, ν_{max}^{Chf} 1737, 1512, 1408, 1302, 1066, 1030 and 1014 cm^{-1}; NMR, τ 9·04 (3H, d, J = 6 c/s), 8·84 (3H, s), 7·66 (3H, s) and 2·7–3·0 (4H, m); ORD, pos. Cotton effect, a = 12. Semicarbazone, colorless needles (MeOH), m.p. 227–229°.

Ozonolysis of laurene. A soln of crude hydrocarbon I (2·3 g) in n-hexane (50 ml) was treated with ozonized oxygen at −70° for 1 hr and then reduced with Na_2SO_3 aq in the usual manner. An oily product was purified by chromatography on silica gel to give the ketone III (0·4 g).

Isomerization of laurene to isolaurene (IV). A mixture of I (100 mg) and silica gel (10 g) in n-hexane (100 ml) was allowed to stand at room temp for 2 days. After removal of the silica gel and the solvent, oily residue was chromatographed on silica gel to give pure IV (80 mg), b.p. 140–142°/21 mmHg, $[\alpha]_D^{23}$ +108·7° (*c*, 1·4; Chf); IR, ν_{max}^{film} 1510, 1015, 819 and 720 cm^{-1}; NMR, τ 8·67 (3H, s), 8·63 (3H, s), 8·30 (3H, s), 7·76 (3H, s), 3·04 (4H, s). Isolaurene was also obtained by careful elution of silica gel column chromatography of I.

Oxidation of isolaurene with OsO_4. A soln of IV (100 mg) in ether (10 ml) and pyridine (5 ml) was treated with OsO_4 (103 mg) as in the case of oxidation of I. Di-tertiary glycol V was obtained in colorless crystals, m.p. 114–116° (87·4 mg); IR, ν_{max}^{Chf} 3320, 1512, 1069, 1017 and 810 cm^{-1}; NMR, τ 8·90 (3H, s), 8·82 (3H, s), 8·68 (3H, s), 7·69 (3H, s) and 2·65–3·0 (4H, m).

Pinacolic rearrangement of glycol V. A suspension of V (90 mg) in 20% H_2SO_4 (6 ml) was boiled gently under reflux for 2 hr. After cooling, water was added and the whole mixture was extracted with ether. The ether soln was evapolated and the residue was chromatographed over silica gel to yield ketone VII (26 mg), IR, ν_{max}^{Chf} 1735 cm^{-1}; NMR, τ 9·07 (3H, s), 8·93 (3H, s), 8·72 (3H, s), 7·72 (3H, s) and 2·7–3·05 (4H, m).

2-(p-*Tolyl*)*cyclopentanone* (IX)[7]. A soln of 2-chlorocyclopentanone[15] (41·4 g) in dry ether (400 ml) was added to a stirred, ice-cold soln of *p*-tolylmagnesium bromide, prepared from Mg (8·65 g) and *p*-bromotoluene (56 g) in dry ether (300 ml). After most of the ether was removed by distillation, xylene (100 ml) was added and the soln was heated under reflux for 1 hr. After being cooled, the reaction mixture was poured into a mixture of cracked ice and dil HCl. The mixture was extracted with ether and the organic layer was washed with dil NaOH, water and dried. After removal of the solvent, the residue was distilled under reduced press, and the resulting ketone IX, b.p. 160–170°/20 mmHg, was purified *via* semicarbazone (m.p. 218–219°). IR, ν_{max}^{Chf} 1738, 1510, 1410, 1130, 830 and 805 cm^{-1}; NMR, τ 7·72 (3H, s) and 3·04 (4H, s). (Found: C, 82·51; H, 8·09. Calc. for $C_{12}H_{14}O$: C, 82·72; H, 8·10%).

2-*Methyl*-2-(p-*tolyl*)*cyclopentanone* (X). A suspension of $NaNH_2$ (400 mg) in dry ether (10 ml) was heated under reflux. To this was added dropwise IX (1·7 g) dissolved in a mixture of dry ether (6 ml) and dry benzene (3·5 ml) over a period of 30 min, and the whole mixture was refluxed for about 1 hr until the evolution of NH_3 had ceased. The reaction mixture was then taken up in ether–water, and the ether layer was separated and washed with water, dried and evaporated. The residue thus obtained was distilled under diminished press to give X (1·29 g), b.p. 124–126°/5·5 mmHg, IR, ν_{max}^{Chf} 1737, 1505, 1408, 1380, 1150, 1120, 1060 and 815 cm^{-1}; NMR, τ 8·72 (3H, s), 7·73 (3H, s) and 2·7–3·05 (4H, m). (Found: C, 83·11; H, 8·78. $C_{13}H_{16}O$ requires: C, 82·93; H, 8·57%).

1,2-*Dimethyl*-1-(p-*tolyl*)*cyclopentan*-2-*ol* (XI). To a soln of MeLi in dry ether, prepared from MeI (1 ml) and Li (300 mg) in dry ether (10 ml), was added a soln of X (67 mg) in the same solvent (10 ml) and the mixture was refluxed under stirring for 48 hr. After cooling, excess of the reagent was decomposed with Na_2SO_4 aq containing a small amount of Na_2SO_3. The ether layer was separated, washed with water and dried. On removal of the solvent, an oily mass was obtained, and then purified by chromatography on silica gel to yield *cis*- (15 mg) and *trans*-alcohol XI (16 mg). IR, *cis*-XI, $\nu_{max}^{CHCl_3}$ 3600, 1505, 1385, 1125 and 830 cm^{-1}, *trans*-XI, 3640, 1510, 1390, 1130 and 830 cm^{-1}; NMR, *cis*-XI, τ 8·85 (3H, s), 8·73 (3H, s), 7·67 (3H, s) and 2·55–3·0 (4H, m), *trans*-XI, τ 9·13 (3H, s), 8·70 (3H, s), 7·70 (3H, s) and 2·65–3·1 (4H, m).

1,2-*Dimethyl*-1-(p-*tolyl*)*cyclopent*-2-*ene* (XII). A soln of XI (mixture, 82 mg, of *cis* and *trans* isomers) in 1N-HCl/MeOH was refluxed for 40 min. After being cooled, the soln was poured into water and most of MeOH removed under reduced press. The resulting mixture was extracted with ether and the ether soln was washed with Na_2CO_3 aq and then with water. The ether soln, after evaporation, gave an oily product, which was purified by chromatography on silica gel to yield XII (72 mg). IR, $\nu_{max}^{CHCl_3}$ 1655, 1505, 1380, 1072, 1020 and 820 cm^{-1}; NMR, τ 8·62 (3H, s), 8·55 (3H, d, J = 2 c/s), 7·73 (3H, s), 4·58 (1H, m) and 3·02 (4H, s). (Found: C, 90·08; H, 9·83. $C_{14}H_{18}$ requires: C, 90·26; H, 9·74%).

1,2-*Dimethyl*-1-(p-*tolyl*)*cyclopentan*-3-*ol* (XIII). To a soln of $NaBH_4$ (380 mg) and XII (72 mg) in diglyme (10 ml) was added BF_3-etherate (2 ml) under stirring in a N_2 atm. After the mixture was set aside at room temp for 2 hr, water (2 ml) was added slowly. The organoborinic acid thus formed was oxidized at 30–50° by addition of 2N NaOH aq (3 ml), followed by the dropwise addition of 30% H_2O_2 (2 ml). The reaction mixture was allowed to stand for an additional hour at room temp and was then taken up with ether. The ether extract was washed four times with ice-water to remove diglyme and evaporated. The oily residue was purified by chromatography on silica gel to give XIII (69 mg). IR, $\nu_{max}^{CHCl_3}$ 3620, 3450, 1510, 1380, 1030 and 820 cm^{-1}; NMR, τ 9·38 (3H, d, J = 7 c/s), 8·60 (3H, s), 7·72 (3H, s), ca. 6·3 (1H, m) and 3·00 (4H, s). (Found: C, 82·02; H, 9·65. $C_{14}H_{20}O$ requires: C, 82·30; H, 9·87%).

1,2-*Dimethyl*-1-(p-*tolyl*)*cyclopentan*-3-*one* (XIV). A mixture of XIII (32 mg) and CrO_3 (60 mg) in pyridine (5 ml) was left at room temp overnight. Water (5 ml) was then added to the mixture and the whole was extracted with ether. The ether extract was washed with 2N HCl, 10% Na_2CO_3 aq and water. After being dried, the ether soln was evaporated to yield ketone XIV, which was shown to be *dl*-III by the comparison of IR and NMR spectra and TLC *Rf*-values. IR, $\nu_{max}^{CHCl_3}$ 1737, 1512, 1408, 1302, 1066, 1030 and 1014 cm^{-1}; NMR, τ 9·04 (3H, d, J = 6 c/s), 8·84 (3H, s), 7·66 (3H, s) and 2·7–3·0 (4H, m). (Found: C, 83·40; H, 8·93. $C_{14}H_{18}O$ requires: C, 83·12; H, 8·97%).

IR spectrum of semicarbazone (m.p. 214–215°) in $CHCl_3$ was also superimposable with that of III-semicarbazone.

Formylation of ketone III. To an ice-cold suspension of powdered NaOMe (from 170 mg of Na) in dry benzene (5 ml) was added, under stirring, a mixture of III (126 mg) and ethyl formate (1 ml). The mixture was allowed to stand at room temp overnight in a N_2 atm. Ice water was added, the aq. layer was separated, and the benzene layer was washed with cold dil NaOH aq. All the aq. solns were combined, washed with ether and acidified with dil HCl. The resulting oily suspension was extracted with ether and the ether extracts were washed with sat. salt soln, dried over Na_2SO_4, and evaporated. The crude product was purified by chromatography on silica gel to yield pure hydroxymethylene ketone XVI (98 mg), IR, ν_{max}^{film} ca. 3200 (br.), 1710 and 1620 cm^{-1}.

Thioenolether XVII. A soln of XVI (691 mg) in benzene (25 ml) containing n-butyl mercaptan (320 mg) and *p*-TsOH (15 mg) was refluxed for 2·5 hr under a Dean–Stark water separator in a N_2 atm. When 0·5 ml of water had collected, the reaction mixture was chilled, washed with $NaHCO_3$ aq, water, and dried. After removal of the solvent under diminished press, reddish oily thioenolether XVII (812 mg) was obtained. IR, $\nu_{max}^{CHCl_3}$ 1692 and 1590 cm^{-1}.

Methylation of thioenolether XVII. To a soln of KO^{t}Bu (400 mg K in 15 ml of ^{t}BuOH) was added XVII (780 mg) and the mixture was stirred at room temp for 5 min under a N_2 atm. After the mixture was cooled in an ice-bath, MeI (1 ml) was added and the whole then refluxed for 2·5 hr. After removal of most of the solvent under reduced press, water was added to the residue and the mixture was extracted with ether. The ether soln was washed with sat. salt soln, dried and evaporated. An oily residue (crude XVIII, 689 mg; $\nu_{max}^{CHCl_3}$ 1692 and 1590 cm^{-1}) was used for the following reactions without further purification.

α-*Cuparenone* (VI). A mixture of the foregoing crude XVIII (655 mg), 25% KOH aq (10 ml) and diethylene glycol (10 ml) was refluxed for 15·5 hr in a N_2 atm. After being cooled, the reaction mixture was extracted thoroughly with ether, the ether soln was washed with water, dried and evaporated. An oily residue was chromatographed on silica gel to yield pale yellow crystals. Recrystallization from MeOH—H_2O gave

pure ketone (240 mg), m.p. 52–53°, $[\alpha]_D$ +170° (*c*, 1·05; Chf), which is identical with α-cuparenone (VI). IR, ν_{max}^{Chf} 1738, 1513, 1460, 1417, 1374, 1098, 1058, 1020 and 820 cm^{-1}; NMR, τ 9·43 (3H, s), 8·88 (3H, s), 8·77 (3H, s), 7·68 (3H, s) and 2·7–3·05 (4H, m). (Found: C, 83·15; H, 9·31. Calc. for $C_{15}H_{20}O$: C, 83·28; H, 9·32%).

Semicarbazone, colorless crystals, m.p. 233–234°, showed no melting point depression on admixture with an authentic sample.

(+)-Cuparene from α-cuparenone. A mixture of the above-mentioned α-cuparenone VI (168 mg), ethanedithiol (3 ml) and BF_3-etherate (1 ml) was set aside at room temp for 3 days. To the reaction mixture was added $NaHCO_3$ aq and the whole was extracted with ether. The ether soln was washed with 2N NaOH, water and dried. After removal of the solvent, crude thioketal was obtained. This was dissolved in EtOH and refluxed with Ra-Ni overnight. After cooling and removal of the catalyst and solvent, the oily residue was taken up with ether and the ether soln was washed with water, dried and evaporated. An oily product was purified by chromatography on silica gel to give a hydrocarbon (38 mg), which was identified as (+)-cuparene (XV). $[\alpha]_D$ +40° (*c*, 2·0; Chf); IR, ν_{max}^{film} 1512, 1460, 1380, 1190, 1020, 812 and 723 cm^{-1}; NMR, τ 9·45 (3H, s), 8·95 (3H, s), 8·78 (3H, s), 7·72 (3H, s) and 2·9–3·1 (4H, m).

Epilaurene (XX). Sodium hydride (570 mg) in a flask was washed with several portions of dry n-hexane to remove mineral oil. The flask was evacuated and filled with N_2; DMSO (10 ml) was then introduced and the mixture was heated at 75–80° for 15 min under stirring. To the cooled soln was added Ph_3PMeBr (3·00 g) in DMSO (30 ml). The ketone III (170 mg) was then added to the mixture and stirred at room temp for 6 hr. The reaction mixture was poured into water (ca. 30 ml) and extracted with n-hexane. After removal of the solvent, oily residue was carefully purified by standard alumina chromatography to give epilaurene (XX; 413 mg), $[\alpha]_D$ −3·1° (*c*, 2·1; Chf); IR, ν_{max}^{film} 1650, 1510, 1380, 878 and 810 cm^{-1}; NMR, τ 9·08 (3H, d, J = 7 c/s), 8·92 (3H, s), 7·67 (3H, s), 5·14 (2H, m) and 2·7–3·05 (4H, m).

Isomerization of epilaurene to isolaurene. A mixture of XX (27 mg) and silica gel (1 g) in n-hexane (10 ml) was allowed to stand at room temp for 2 days. After removal of the silica gel and the solvent, oily residue was chromatographed on silica gel to give IV and unchanged XX (IR and R_f-values on TLC).

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