STRUCTURE OF BAZZANENE

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Abstract—A new sequiterpene hydrocarbon, bazzanene, was isolated as a major component from the essential oil of the liverwort, *Bazzania pompeana*. Structural determination of this compound is described.

THE LIVERWORTS (*Hepaticae*) which are taxonomically placed between vascula plants and thallophytes contain, in the cells of gametophytes, several oil bodies which are characteristic for species in the shape and distribution density and are used as a useful factor in the taxonomical diagnosis. The chemical investigation on the essential oil from liverworts was first made by Müller in 1905,[1] but it was interrupted until recent years because of the difficulty in collecting a sufficient amount of the plants and of the dissatisfaction in its botanical homogeneity.

Later, the investigation was resumed by Huneck, Beneŝová and our groups, and several new compounds have been isolated; 1,4-dimethylazulene, 4-methyl-1-methoxycarbonylazulene and 3,7-dimethyl-5-methoxycarbonylindene from *Calypogeia trichomanis* (L.) Corda,[2-4] a furano ketone, pinguisone, from *Aneura pinguis* (L.) Dum.,[5] and an α,β-unsaturated ketone, chiloscyphone, from *Chiloscyphus polyanthus* (L.) Corda.[6, 7]

Bazzania pompeana (Lac.) Mitt. examined in the present work is a leafy liverwort belonging to Jungermaniales and contains 4–10 pieces of colorless globular oil bodies (12–13 × 7–8 μ) in each cell. It is known that the essential oil of this liverwort mainly consists of sesquiterpene hydrocarbons.[8]

In a previous paper,[9] the present authors reported the isolation of a novel sesquiterpene hydrocarbon named bazzanene from this essential oil, and preliminarily determined its structure as formula I. The present paper deals with the detailed chemical evidences for the proposed structure.

The new sesquiterpene hydrocarbon, bazzanene, was isolated from steam-distillate of the McOH extract of the liverwort in homogeneous state, as examined by GLC and TLC, by the combination of fractional distillation and elution chromatography over silica gel impregnated with AgNO₃. Mass and IR spectra of this hydrocarbon are reproduced respectively in Figs 1 and 2.

The appearance of a molecular ion at m/e 204 in the mass spectrum and the result of elementary analysis indicated that the hydrocarbon had a molecular formula of $C_{15}H_{24}$. The IR and NMR spectra of bazzanene revealed the presence of an exo-methylene group (ν_{max}^{liq} 1647 and 886 cm⁻¹; $\delta_{ppm}^{CDCl_3}$ 4·83 and 4·96, each 1H, s) and a trisubstituted double bond bearing a Me group (806 cm⁻¹; δ 1·64, 3H, d, $J = 1\cdot2$ Hz and 5·32, 1H, m) together with one geminal dimethyl group (1379 and 1369 cm⁻¹; δ 0·83 and 1·02, each 3H, s). These two double bonds should be isolated because the

UV spectrum of bazzanene showed no absorption band in the region ascribable to a conjugated diene system. The hydrocarbon was thus characterized as a bicyclic sesquiterpene containing two non-conjugated double bonds, and this structure showed a good agreement with the molecular refraction (obsd. M_D 65·35; calcd. M_D 66·13). In accordance with the above spectral evidence, the hydrocarbon absorbed

I II

III

IV V VI

VII VIII IX

X: R = H   XII
XI: R = Ac
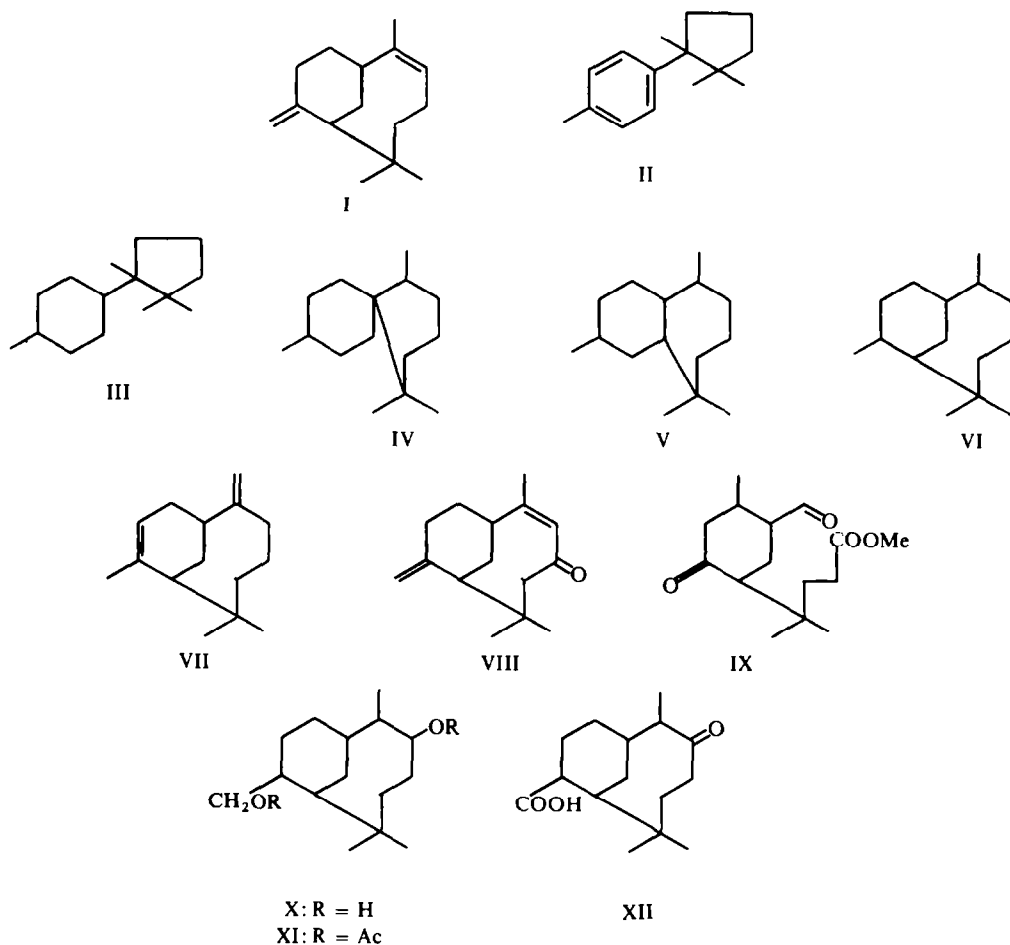
two molar equivalents of hydrogen in catalytic hydrogenation over the Adams catalyst in AcOH to produce two kinds of tetrahydro derivative (M⁺ *m/e* 208) in a ratio of about 2:3. These compounds were considered to be steric isomers with respect to the Me group, since both compounds, after being isolated by preparative GLC, exhibited the same mass spectra (Fig 3) having a M⁺ ion at *m/e* 208.

When bazzanene was heated with Pd–C at 250° or with Se powder at 300° in a sealed tube, neither naphthalenic nor azulenic hydrocarbons were produced, but only one benzenoid compound, cuparene (II), was obtained in a good yield, which was identified by the measurement of IR, NMR and mass spectra.[10]
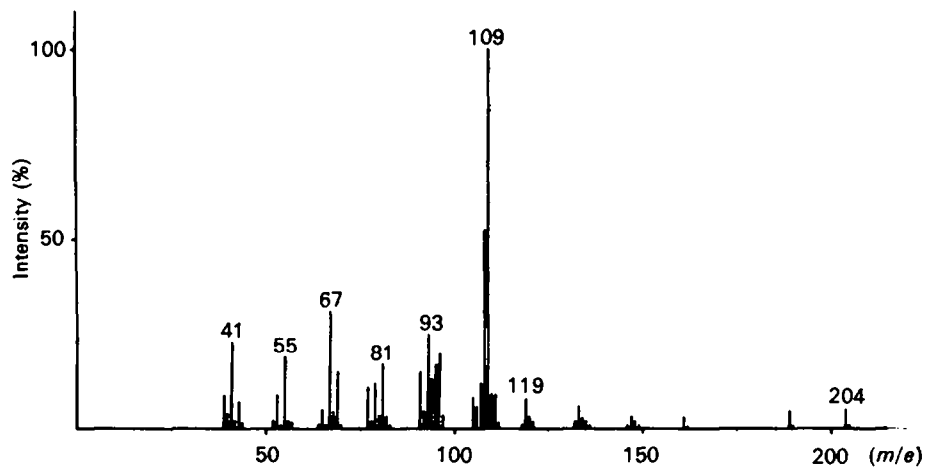
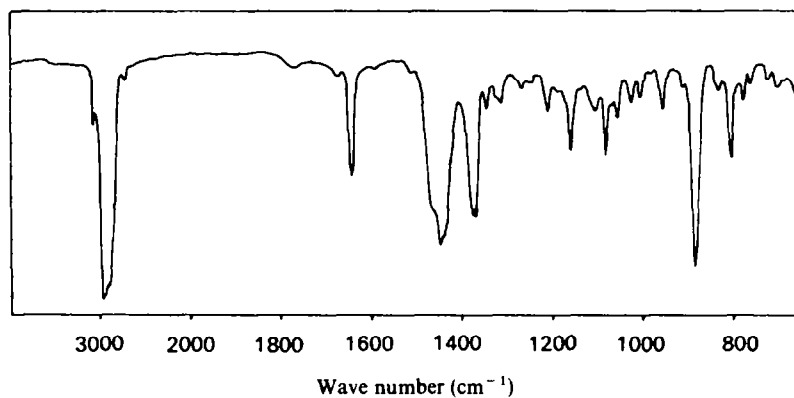FIG. 1 Mass spectrum of bazzanene

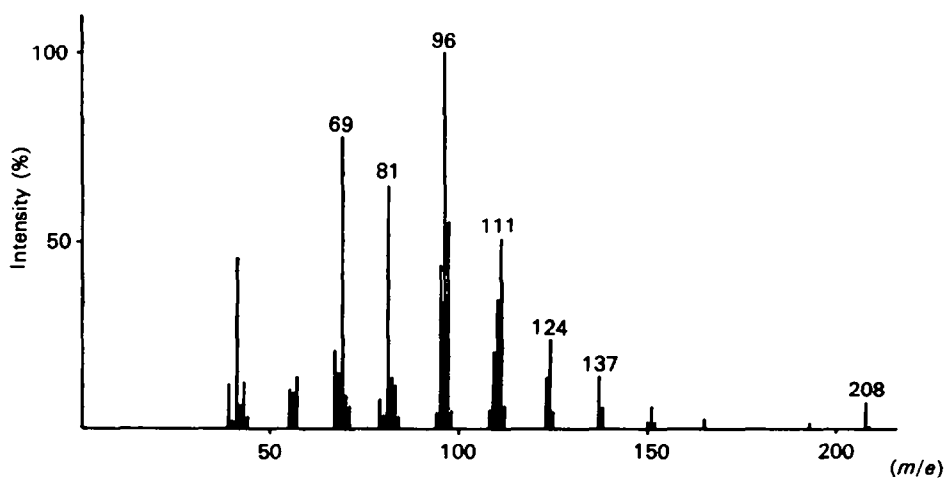Wave number (cm⁻¹)
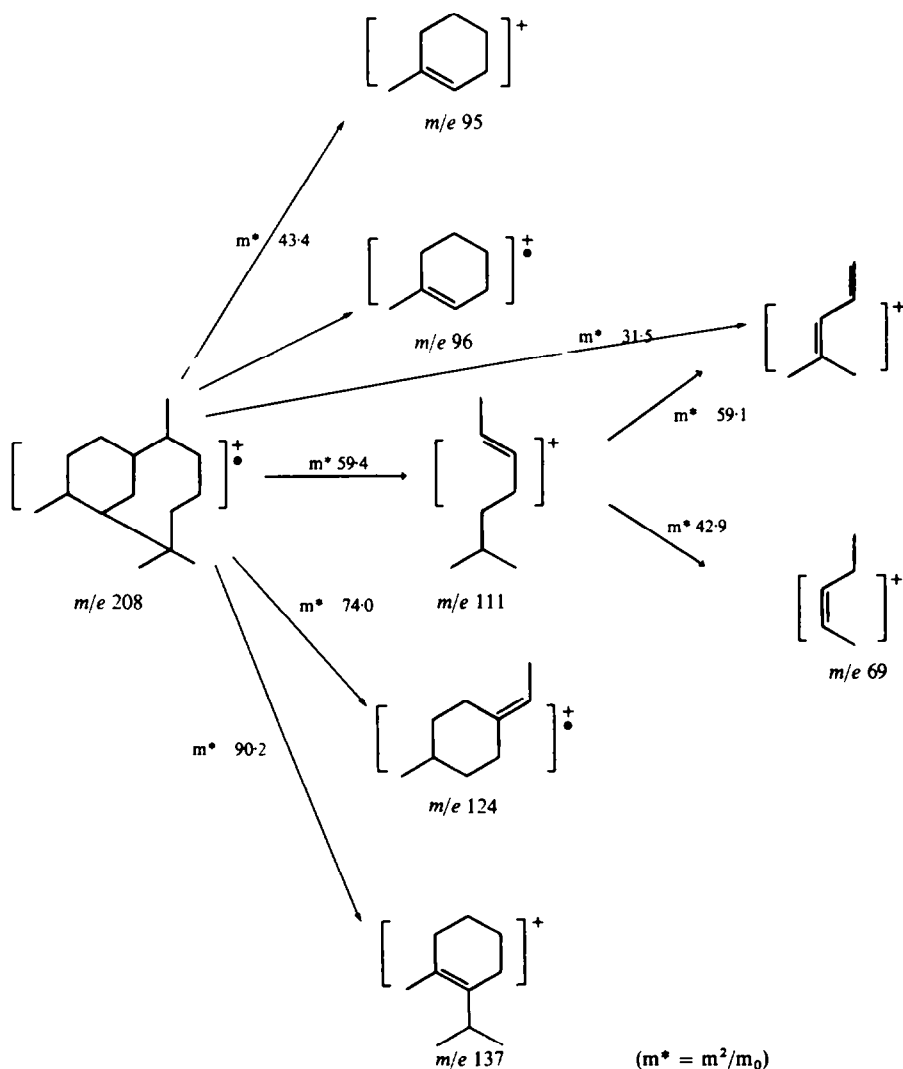
FIG. 2 IR spectrum of bazzanene

FIG. 3 Mass spectrum of tetrahydrobazzanene

Taking the result of this cuparene formation into consideration, the carbon skeleton of bazzanene must be represented by any one of the formulae III, IV, V and VI. Among these formula IV is already known as chamigrane,[11] and V is that of hima-chalane.[12] The IR and mass spectra of tetrahydrobazzanene did not coincide with those of these compounds.[13] Cuparane skeleton (III) was also ruled out because this skeleton could not have, at the same time, such an exomethylene double bond and a trisubstituted double bond bearing a Me group as indicated by the above spectral evidences and the result of catalytic hydrogenation. Accordingly, the carbon skeleton of bazzanene should be the formula VI. The mass spectrum of tetrahydrobaazzanene (Fig 3), having characteristic peaks at m/e 69, 81, 95, 96 (base), 111, 124 and 137, could

CHART 1. Fragmentation course of tetrahydrobazzanene

m/e 95

m* 43·4

m/e 96

m* 31·5

m* 59·1

m/e 208

m* 59·4

m/e 111

m* 74·0

m* 42·9

m/e 69

m* 90·2

m/e 124

m/e 137

$(m^* = m^2/m_0)$

be reasonably explained by this structure, and the fragmentation course, the majority of which was supported by the appearance of metastable ions, is showed in Chart 1.

In view of the nature of the double bonds mentioned above, the structure of bazzanene should be represented by formula I or VII. In order to clarify this point, bazzanene was oxidized with sodium dichromate in AcOH and a ketonic compound thereby obtained was characterized as β,β'-disubstituted α,β-unsaturated ketone, $C_{15}H_{22}O$, on the basis of its UV (λ_{max}^{EtOH} 239 mμ, ε 8300) and IR spectra (ν_{max}^{liq} 1672 cm^{-1}). Its IR and NMR spectra indicated this ketone to have an active methylene group (ν 1413 cm^{-1}; $\delta_{ppm}^{CDCl_3}$ 2·33, 2H, s) and one olefinic proton adjacent to a carbonyl group (δ 6·50, 1H, q, $J = 1·5$ Hz) together with geminal dimethyl (1383 and 1373 cm^{-1}; δ 0·89 and 1·09, each 3H, s), vinylmethyl (842 cm^{-1}; δ 1·74, 3H, d, $J = 1·5$ Hz) and exomethylene group (892 cm^{-1}; δ 4·83 and 5·05, each 1H, s) which were observed in the original hydrocarbon. The presence of an olefinic proton adjacent to a carbonyl group offered an additional support to the fact that the ketonic derivative from bazzanene was a β,β'-disubstituted α,β-unsaturated ketone, and the singlet signal of the active methylene indicated a carbon atom adjacent to the methylene group to be tertiary. Thus, it is

certain that the ketone has a partial structure of

$$-\overset{\displaystyle |}{\underset{\displaystyle |}{C}}-CH_2-CO-CH=\overset{\displaystyle \overset{CH_3}{|}}{C}- \;.$$

Such a partial structure is only possible in an allylic oxidation product of formula I, although a simple β,β'-disubstituted α,β-unsaturated ketone would be expected for oxidation products from both I and VII. Therefore, the structure of the ketone obtained from the dichromate oxidation of bazzanene should be formula VIII. The mass
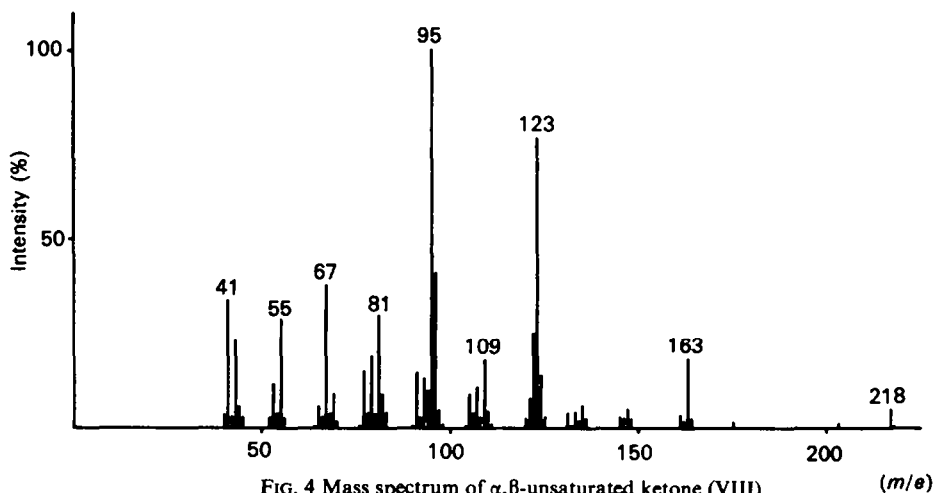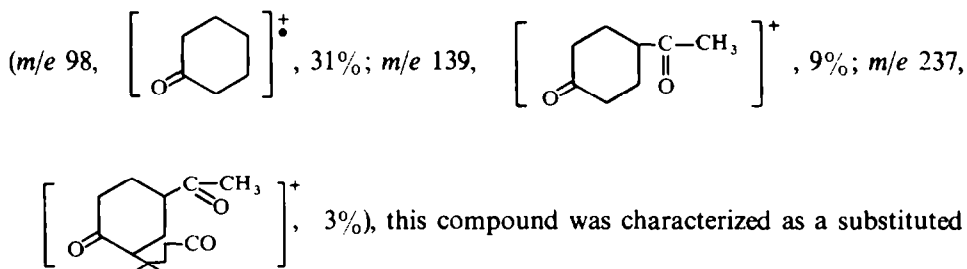

FIG. 4 Mass spectrum of α,β-unsaturated ketone (VIII)   (m/e)

spectrum of the ketone (Fig 4) exhibited a base peak at m/e 95 (C_7H_{11}: obsd. m/e 95·086) and a characteristic ion at m/e 123 ($C_8H_{11}O$: obsd. m/e 123·082) which corresponded to those of m/e 109 in bazzanene and of m/e 111 in tetrahydrobazzanene, and also supported by the observation of a metastable ion (m* = 69·3).

From the above evidence it was concluded that the structure of bazzanene was represented by the formula I.

Ozonolysis and hydroboration of bazzanene presented further evidences for this structure. When the hydrocarbon was subjected to ozonolysis in $CHCl_3$ at $-30°$, formaldehyde expected from the exomethylene group in the formula I and an acidic mixture were obtained. Formaldehyde was identified as its dimedone derivative. and the acidic mixture, after its treatment with diazomethane, was chromatographed over a silica gel column with hexane–ethyl acetate (4:1) and an oily methyl ester (v_{max}^{liq} 1735 cm^{-1}; $\delta_{ppm}^{CDCl_3}$ 3·65, 3H, s) was isolated as a main product. This methyl ester contained a methyl-ketone group 1715 cm^{-1}; δ 2·16, 3H, s) and a geminal dimethyl group (1380 and 1372 cm^{-1}; δ 0·97 and 1·02, each 3H, s). On the basis of formaldehyde formation, IR spectrum (1715 cm^{-1}) and abundant peaks in its mass spectrum

(m/e 98, [structure] , 31%; m/e 139, [structure] , 9%; m/e 237,

[structure] , 3%), this compound was characterized as a substituted

cyclohexanone. This spectral evidence well fitted the structure IX expected as the ozonolysis product of I,

By hydroboration, bazzanene was converted into a diol (X), $C_{15}H_{28}O_2$ ([M-H$_2$O]$^+$ 222). Its diacetyl derivative (XI) (v_{max}^{liq} 1737 cm^{-1}; $\delta_{ppm}^{CDCl_3}$ 2·05, 6H, s), prepared by treatment in pyridine–Ac$_2$O, showed the presence of a secondary Me (δ0·93, 3H, d, $J = 5·0$ Hz), a geminal dimethyl (δ 0·99 and 1·05, each 3H, s), a methylene and a methine bearing the Ac group (δ 3·70–4·85, 3H, complex).

The diol was further oxidized with the Jones reagent and a compound showing a broad absorption band at 1702 cm^{-1} was obtained by elution chromatography of the reaction product over silica gel. The broad absorption band should be interpreted as the overlap of a $v_{c=o}$ band due to the eightmembered cyclic ketone and a $v_{C=O}$ band due to a carboxylic group in the expected structure of XII from bazzanene.

From the above experimental evidence, the structure of bazzanene is elucidated as 2,6,6-trimethyl-8-methylenebicyclo[5.3.1]undec-2-ene (I). It is assumed that the hydrocarbon arose from cis-farnesyl pyrophosphate via the cyclization pathway of α-bisabolene.

steam distillation. The volatile oil (17·0 g) was obtained in 1·20% yield: $[\alpha]_D^{25} + 34·7°, n_D^{25}$ 1·5053, d_4^{25} 0·9397.

Isolation of bazzanene. The volatile oil (15·0 g) was precisely fractionated through a spinning band distillation column into 15 fractions. Fractions 9–12, rich in hydrocarbon, was chromatographed over $AgNO_3$ (3·0%)-impregnated silica gel with hexane, and the eluate exhibiting only one peak and one spot respectively on gas (PEG 6000 and DEGS) and thin-layer (silica gel and hexane) chromatography was collected in a yield of 52·1% for the total oil; b.p. 102–103°/2 mm Hg, $[\alpha]_D^{25} + 48·0°, n_D^{25}$ 1·5073, d_4^{25} 0·9295, M_D 65·35, M^+ m/e 204 ($C_{15}H_{24}$). (Found: C, 88·27; H, 11·63. Calcd for $C_{15}H_{24}$: C, 88·16; H, 11·84%).

Catalytic hydrogenation of bazzanene. The hydrocarbon (200 mg) was hydrogenated over the Adams catalyst (10 mg) in glacial AcOH (6 ml) at room temp. The reaction ceased when about 2 molar equivs of hydrogen was taken up. The filtrate, after being diluted with water, was repeatedly extracted with ether. The ether soln was washed with 5% $NaHCO_3$ aq and then with H_2O, dried over anhyd. Na_2SO_4 and distilled to remove solvent. The hydrogenated product ($[\alpha]_D$ − 14 5°) did not show any spot due to unsaturated components on TLC by the fluorescene-bromine test, but its GLC (PEG 6000) showed two peaks in a relative intensity of about 2:3. The two components were isolated by prep. GLC (PEG 6000, 10%), and mass and IR spectra of the major components were taken; M^+ m/e 208 ($C_{15}H_{28}$); $\nu_{max}^{liq.}$ 1455, 1377, 1215, 1152, 1110, 1021 cm^{-1}.

Dehydrogenation of bazzanene—Palladium-charcoal dehydrogenation. Bazzanene (200 mg) was heated with 10% Pd-C (400 mg) in a sealed tube at 250° for 30 min. The dehydrogenated product was taken up into hexane, chromatographed over $AgNO_3$ (1·5%)-impregnated silica gel with hexane, and then subjected to preparative GLC with PEG 6000 (10%). Cuparene was isolated as a major product in 30% yield; $\nu_{max}^{liq.}$ 1640,

1597, 1518, 1192, 1106, 1068, 1020, 958, 812, 722 cm^{-1}; $\delta_{ppm}^{CDCl_3}$ 0·56, 1·07, 1·26 (each 3H, s; —C·—CH₃),

with the —C having a vertical bond above and below (CH₃ substituent shown)

2·32 (3H, s; aro-CH₃), 7·17 (4H, dd, J = 8·5 Hz; aro-H); m/e 41 (31%), 55 (15), 91 (23), 105 (26), 119 (31), 132 (100), 145 (31), 159 (10), 187 (3), 202 (M^+, 17).

Selenium dehydrogenation. A mixture of bazzanene (100 mg) and Se powder (200 mg) was heated at 300° for 1 hr in a sealed tube. From the reaction mixture cuparene was isolated in comparable yield as above, and other aromatic hydrocarbons were not detected.

Allylic oxidation of bazzanene. Bazzanene (1·0 g) was stirred with $Na_2Cr_2O_7$ (3·0 g) in glacial AcOH (45 ml) at 65–70° for 8 hr. The reaction mixture was diluted with EtOH (2·0 ml) and water (30 ml), and extracted 5 times with C_6H_6. The C_6H_6 soln was washed with 5% $NaHCO_3$ aq, dried over Na_2SO_4, and the solvent was evaporated. The oxidized product thus obtained was repeatedly chromatographed over silica gel by using a mixed solvent of hexane-EtOAc (4:1) to isolate an α,β-unsaturated ketone; Rf = 0·64 on

TLC with silica gel and hexane-EtOAc (1:1); λ_{max}^{EtOH} 239 mμ (ε 8300, calcd for —C=CH—CO—; 293 mμ); $\nu_{max}^{liq.}$ 1672, 1413, 1383, 1213, 1164, 1077 cm^{-1}.

with CH₃ substituent shown above the —C=CH—CO— group

Ozonolysis of bazzanene. After ozone was absorbed into a solution of bazzanene (1·0 g) in CHCl₃ (20 ml) at − 30°, the mixture was pumped out at reduced pressure to remove the solvent. The ozonide thus obtained was heated with a small amount of water and the distillate was collected. A portion of this distillate was was extracted with ether, which was dried over anhyd. Na_2SO_4 and mixed with an ether soln of CH_2N_2.

ester as an oily substance; R_f = 0·52 on TLC with hexane-EtOAc(1:1); $[\alpha]_D \pm 0°$: $C_{15}H_{24}O_4$ ([M-OCH₃]⁺, m/e 237); $\nu_{max}^{liq.}$ 1735, 1715, 1242, 1167, 1020, 973 cm^{-1}; m/e 43 (100%), 55 (26), 69 (19), 81 (20), 98 (31), 109 (11), 121 (8), 139 (9), 147 (3), 237 ([M-OCH₃]⁺, 3).

The remaining portion of the above distillate was mixed with a saturated solution of dimedone, and a ppt which showed m.p. 118–119° after recrystallization from EtOH was obtained. — — — —

Hydroboration of bazzanene. According to the method of Zweifel and Brown,[14] BF_3 etherate (3·0 ml) was added dropwise into a mixed soln of bazzanene (1·0 g) and $NaBH_4$ (0·2 g) in diglyme (30 ml), at 20–25° in N_2, and the mixture was maintained at this temp for 1 hr. Excess hydride was decomposed with water (5 ml) and an organoborinic acid obtained was then oxidized, at 30–50°, with 3N NaOH (5 ml) and 30% H_2O_2 (5 ml). The resulting mixture was extracted with ether and the extract was chromatographed over a silica gel column. A crystalline diol, m.p. 144–145°, was obtained; R_f = 0·16 on TLC (hexane-EtOAc, 1:1); $C_{15}H_{28}O_2$ ([M-H₂O]⁺ m/e 222. (Found: C, 74·72; H, 11·65. Calcd for $C_{15}H_{28}O_2$: C, 74·95; H, 11·74%); ν_{max}^{KBr} 3300, 1373, 1351, 1314, 1250, 1108, 1036, 1011, 902 cm^{-1}; m/e 41 (48%), 55 (43), 67 (40), 69 (41), 81 (81), 95 (10b), 109 (95), 126 (6), 135 (6), 189 (7), 204 (4), 207 (9), 222 ([M-H₂O]⁺, 7).

Acetylation of the diol. The diol (60 mg) was mixed with Ac_2O (0·9 ml) in pyridine (10 ml) and allowed to stand overnight at room temp. After water (10 ml) was added the mixture was extracted 3 times with ether to obtain an oil acetate; R_f = 0·52 on TLC (hexane-EtOAc, 1:1); $[\alpha]_D$ −69·5°; $C_{17}H_{32}O_4$ ([M-2(AcOH)]$^+$, m/e 204); $v_{max}^{liq.}$ 1737, 1245, 1028 cm^{-1}; m/e 43 (92%), 55 (31), 67 (39), 81 (40), 95 (82), 109 (100), 119 (6), 161 (3), 189 (3), 204 (2).

Jones oxidation of the diol. Jones reagent (0·1 ml) was added to an acetone soln (5 ml) of the diol (20 mg) under cooling in an ice bath. The mixture was stirred for 3 min at room temp and poured into ice water. By the extraction of the aqueous soln with $CHCl_3$, a ketonic derivative was obtained as an oily substance; R_f = 0·48 on TLC (hexane-EtOAc, 1:1); $v_{max}^{liq.}$ 3000–2500, 1702, 1458, 1425, 1393, 1382, 1225, 1170 cm^{-1}.

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