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# STUDIES IN SESQUITERPENES—XLVI*

## SESQUITERPENES FROM THE OLEORESIN OF *DIPTEROCARPUS PILOSUS*: HUMULENE EPOXIDE-III, CARYOPHYLLENOL-I AND CARYOPHYLLENOL-II†‡

A. S. GUPTA and SUKH DEV

National Chemical Laboratory, Poona 8, India

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**Abstract**—Oleoresin from *Dipterocarpus pilosus* has been shown to be a complex blend of sesquiterpenes (~18%) and triterpenoids—both tetracyclic and pentacyclic. A complete analysis of the sesquiterpene portion is reported. Besides the known caryophyllene, humulene, caryophyllene oxide, humulene epoxide-II and clovane-diol, seven new sesquiterpenes have been isolated and the structure of three of these—humulene epoxide-III, caryophyllenol-I and caryophyllenol-II—elucidated.

*Dipterocarpus pilosus* (Synonym: *D. gracilis* Bl.; Assamese, *Hollong*), a tall tree occurring gregariously in Assam, India, exudes an oleoresin which has a tendency to accumulate in big cracks under dead knots and such other defects in trees. The resin does not appear to have been the subject of a chemical study. In this and the following paper, we, now, report on a fairly complete analysis of this oleoresin, which has been found to be a complex mixture of several sesquiterpenoids and triterpenoids—both tetracyclic and pentacyclic. The sesquiterpenoids form the subject matter of the present communication, while triterpenoids are discussed in the following paper.

The oleoresin was segregated, by trituration, into light petroleum soluble (~67%), benzene soluble (~10%) and ethyl acetate soluble (~8%) parts (by using these solvents in this sequence). Sesquiterpenes are present only in the light petroleum fraction, which was steam-distilled to furnish a volatile part (essential oil, ~25%) and a non-volatile portion (~75%).

Programmed GLC of the essential oil showed it to consist of at least eleven constituents. The oil was fractionated and the various cuts monitored by GLC and TLC on $AgNO_3$–silica gel.[1] Based on this, suitable fractions were selected for the isolation of individual constituents. In this way nine sesquiterpenoids accounting for over 95% of the essential oil could be isolated. Once the pure compounds had been obtained, their positions on the GL Chromatogram were finally ascertained by peak accentuation technique using these products in mixed chromatograms. The identity of known sesquiterpenes *viz* caryophyllene, humulene, caryophyllene oxide, humulene epoxide-II[2] and humulenol-II[3] was established by spectral (IR, PMR) and chromatographic (GLC, TLC) methods using authentic samples. Four new sesquiterpenoids (GLC component ⑧, ⑩, ⑪, ⑪) have been isolated and structures of three of these

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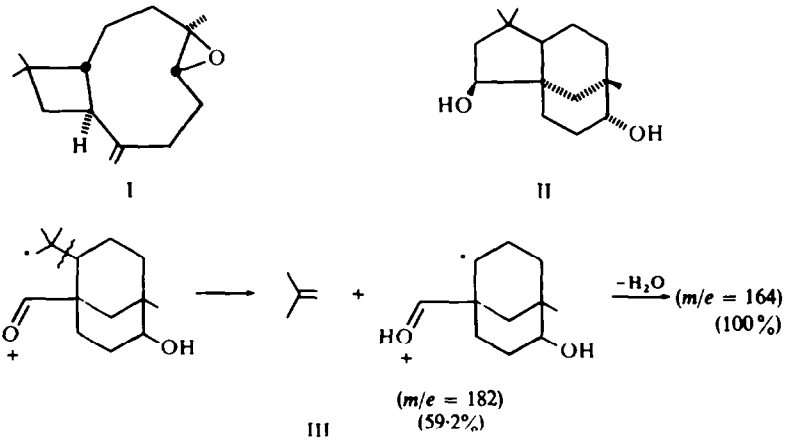
(GLC component ⑧, ⑪, ⑪) are discussed in the sequel. Structure of the fourth new sesquiterpene (GLC component ⑩; m.p. 116–117°) will be reported in another publication. Table 1 gives some pertinent data regarding the components of the essential oil.

The steam non-volatile part was separated ($Na_2CO_3$ aq) into neutral (~95%) and acidic fractions. The acidic part consisted essentially of triterpenoids and these are reported in the following communication. The neutral fraction has been found to be a complex mixture of at least ten components (TLC)—both sesquiterpenoids (~4%) and neutral tetracyclic triterpenoids. By systematic chromatography it has been possible to essentially resolve this mixture. The sesquiterpenoids, thus, obtained, are shown in Table 2, along with their certain characteristics. Surprisingly, one of these compounds (No. 3) has turned out (m.p., IR, PMR of the parent compound and of the derived diacetate; Experimental) to be clovane-diol (II),[4] a product of acid-catalysed cyclization of caryophyllene epoxide (I).* Its mass spectrum (Experimental) is readily rationalised in terms of structure II; the base peak ($m/e$ = 164) appears to arise by loss of $H_2O$ from an ion such as III ($m/e$ = 182) and this is supported by the presence of a metastable peak at $m/e$ = 147·9 (calcd. 147·7). The other three sesquiterpenoids (Table 2) appear to be new and their structures have not yet been clarified.




I II III

*Humulene epoxide*-III

GLC component ⑧ analyses for $C_{15}H_{24}O$. From its IR spectrum it is clear that the oxygen function must be an ether and from the presence of bands at 810, 910 and 1255 $cm^{-1}$, positions considered characteristic for oxirane system, the ether linkage, in all likelihood, must be an 1,2-epoxide. Its PMR spectrum shows signals for two quaternary Me's (3H, s's at 42, 62 c/s), two vinylic Me's (two 3H, d's centred at 90 and 97 c/s each with $J$ = 1·5 c/s) and two olefin protons (~2H, m centred at 268 c/s);

* It is conceivable that clovane-diol is an artefact arising during steam-distillation of the pet. ether-soluble fraction of the oleoresin, of which caryophyllene epoxide is a component. However, in view of the ready steam-volatility of caryophyllene epoxide, it is more likely that clovane-diol is a product of non-enzymatic cyclization of caryophyllene epoxide during transport and accumulation of the resin (which contains ~15% free acids) in the tree.

Clovane-diol has also been reported[5] to occur in the essential oil of *Mentha piperita*.

TABLE 1. CONSTITUENTS OF THE ESSENTIAL OIL FROM THE OLEORESIN OF *DIPTEROCARPUS PILOSUS*

| GLC peak No. | RRT* | $R_{dye}$[a] | % weight (by GLC) | Remarks |
|---|---|---|---|---|
| ① | 1·00 | 0·34 | 28·0 | (−)-Caryophyllene (VII) |
| ② | 1·42 | 0·15 | 19·7 | Humulene (IV) |
| ③ | 3·41 | — | 2·0 | Unidentified |
| ④ | 3·87 | 0·90 | 30·5 | (−)-Caryophyllene oxide (I) |
| ⑤ | 4·28 | — | 1·0 | Humulene epoxide-I[b] |
| ⑥ | 4·43 | 0·36 | 13·0 | Humulene epoxide-II (V) |
| ⑦ | 4·72 | — | 0·3 | Unidentified |
| ⑧ | 4·92 | 0·70 | 0·4 | A new sesquiterpene epoxide (Humulene epoxide-III) (VI) |
| ⑨ | 5·74 | 0·08 | 3·2 | Humulenol-II (XII) |
| ⑩ | 6·01 | 0·32 | 0·8 | A new sesquiterpene alcohol (sesquiterpene A)[c] |
| ⑪ | 6·27 | 0·27 | 0·2 | A new sesquiterpene alcohol (Caryophyllenol-I) (XV) |
| ⑪ | 6·27 | 0·24 | 0·9 | A new sesquiterpene alcohol (caryophyllenol-II) (XVII) |

* Retention time relative to caryophyllene under conditions of programming (80–190°; 6°/min); column: 2 meter × 6 mm, packed with 20% diethyleneglycol polysuccinate on Chromosorb W; gas flow: 70 ml $H_2$/min.

[a] $R_{dye} = \frac{\text{Movement of substance from start in mm}}{\text{Movement of dye from start in mm}}$

Solvent: $AgNO_3$–silica gel (0·3 mm);
5% acetone in $C_6H_6$ (solvent front 10 mm)

[b] Identified only by retention time.

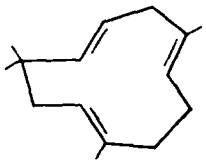
[c] Provisional designation

TABLE 2. SESQUITERPENOIDS FROM STEAM NON-VOLATILE PORTION OF PET. ETHER FRACTION OF *DIPTEROCARPUS PILOSUS* OLEORESIN

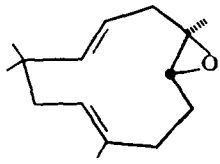
| No. | Mol. formula | $M^+$ (*m/e*) | m.p. | $[\alpha]_D$ | Provisional designation | Remarks |
|---|---|---|---|---|---|---|
| 1 | $C_{17}H_{28}O_3$* | 280 | 131–135° | — | Sesquiterpene B | Sesquiterpene diol ($C_{15}H_{26}O_2$) |
| 2 | $C_{15}H_{26}O_2$ | 238 | 80–82° | −6·5° | Sesquiterpene C | Sesquiterpene diol |
| 3 | $C_{15}H_{26}O_2$ | 238 | 152–153° | +2·2° | — | Clovane-diol (II) |
| 4 | $C_{17}H_{28}O_4$* | 296 | gum | −15·2 | Sesquiterpene D | Parent compound: $C_{15}H_{26}O_3$ |

* Isolated after acetylation ($Ac_2O$, pyridine)

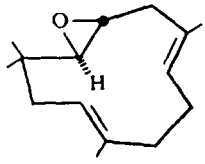
a 2H, m centred at 163 c/s is assigned to two oxirane ring protons. From these data it was concluded that the compound has two olefinic linkages and an oxirane ring and hence must be monocarbocyclic. In view of its co-occurrence with humulene (IV) and humulene epoxide-II (V) in the essential oil it was suspected that this compound may be the hitherto unknown third possible mono epoxide, VI, based on humulene; structure VI being in complete accord with the PMR spectral data (~8H, m located between 116 and 135 c/s can now be assigned to the 8 allylic protons). This has been confirmed by further epoxidation of this compound with percamphoric acid, when a mixture of isomeric humulene trioxides was obtained, from which humulene trioxide[6] of m.p. 121–122° could be isolated and identified (mixed m.p., IR) by comparison



IV



V



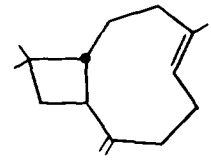
VI

with an authentic sample.[2] In view of its structure, the compound has been named humulene epoxide-III. Since, in an epoxidation reaction the geometry of the olefinic linkage does not change,[7] this correlation with humulene triepoxide also ensures the stereochemistry depicted in VI.

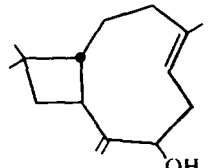
*Caryophyllenol*-I

Two compounds showed the same RRT and corresponded to GLC peak (11) (Table 1). The less abundant component ($R_{dye}$ = 0·27, m.p. 73·5–75°; $[\alpha]_D$ −101·39, $c$ = 0·5% in $CHCl_3$) analyses for $C_{15}H_{24}O$ and shows in its IR spectrum bands for OH (3300, 1020 $cm^{-1}$), —C=$CH_2$ (3070, 1650, 887, 895 $cm^{-1}$). Its PMR spectrum displays signals assignable to: two quaternary Me's (s's at 59, 61 c/s), one vinylic Me (s with a sh, 98 c/s), —C<u>H</u>OH (1H, m centred at 265 c/s), —C=C<u>H</u>$_2$ (2H, s at 286 c/s) and —C=C<u>H</u>— (1H, m centred at 317 c/s). It follows from the functionality revealed above that the compound should be bicyclic. Working on the premise that the oxygenated terpenoids (except triterpenes) generally arise by a separate biological oxidation step from the corresponding hydrocarbons and, that at least some amount of one class invariably co-occurs with the other in a plant tissue,[8] it was suspected that the new alcohol might have been derived from the bicyclic hydrocarbon, caryophyllene (VII), which is an important component of the oleoresin and has all the structural requirements of the new alcohol. Keeping in view all this and the multiplicity of the signal observed for —C=C<u>H</u>— and the chemical shift for —C<u>H</u>OH (the value 265 c/s is rather on the lower side for secondary alcohol protons[9] and suggested its possible allylic character) structures VIII to XI appeared attractive possibilities.

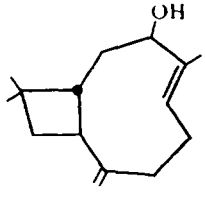
We have already reported[10,3] that humulene epoxide-II (V) on contact with active $Al_2O_3$ is transformed into the allylic alcohol XII (humulenol-II). A similar transformation of caryophyllene oxide (I) can assist in narrowing down the structural



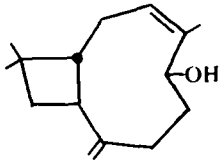
VII



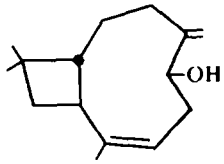
VIII



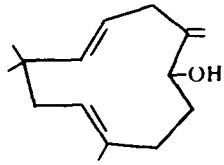
IX




X



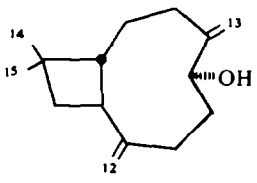

XI



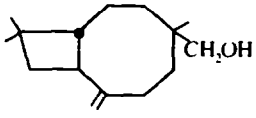

XII

possibilities (VIII → XI) by providing a suitable reference compound. With this aim isomerisation of caryophyllene oxide over $Al_2O_3$ has been investigated and this fortuitously yielded as one of the products, a compound completely identical with the naturally occurring alcohol.

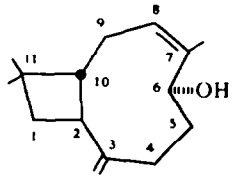
(−)-Caryophyllene epoxide on contact with $Al_2O_3$ under standard conditions[11] yielded a product showing three spots on TLC ($AgNO_3$–silica gel). Column chromatography over $AgNO_3$–silica gel furnished these three compounds. The major component (liquid) from its spectral characteristics (IR: OH 3390, 1025 $cm^{-1}$; —C(=$CH_2$)— 3100, 1650, 910, 890 $cm^{-1}$. PMR: two quaternary Me's, 6H singlet at 59 c/s; —C<u>H</u>OH, 1H, qu centred at 238 c/s; two —C(=$CH_2$)—, 2H, s at 282 c/s, two 1H partly split s's at 292 and 298 c/s) and sufficient analogy[10,11] has been identified as XIII. The next less abundant compound readily crystallised (m.p. 73–75°) and was found to be identical (mixed m.p., IR) with the naturally occurring compound, which can now be formulated[11] as X. The third component (liquid) which is a minor component of this transformation, has been assigned structure XIV in view of its spectral properties (IR: OH 3390, 1058 $cm^{-1}$; —C(=$CH_2$)— 3100, 1650. PMR: three quaternary Me's 51, 60, 60 c/s; C(—C—<u>$CH_2$</u>OH)(—C—)(—C—), 2H s at 193 c/s; —C(=$CH_2$)— two 1H partly split s's at 263 and 275 c/s) and known analogies.[11,*]




XIII




XIV




XV

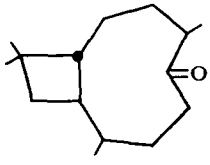
This correlation of the new alcohol with (−)-caryophyllene epoxide also dictates[11] the absolute stereochemistry XV for this compound, which has been named *caryophyllenol*-I. The only point still remaining open, is the configuration of the $\Delta^7$-olefinic linkage.

* Since our preliminary reporting,[10] rearrangement of caryophyllene epoxide on $Al_2O_3$ has been reported from two other laboratories.[12,13] These authors, however, have failed to recognize X and XIV.

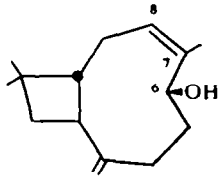
Structure XV has recently[14] been assigned to one of the minor products of Schenck oxidation of (−)-caryophyllene. Physical constants reported (liquid; $[\alpha]_D$ −54°, *c*, 10% in $CHCl_3$) are completely at variance with those of caryophyllenol-I, though the reported PMR spectrum values are in excellent agreement.

*Caryophyllenol*-II

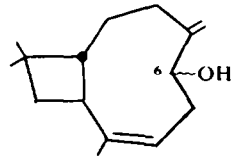
The second compound corresponding to GLC peak (11) ($R_{dye}$ = 0·24; m.p. 89–90°; $[\alpha]_D$ +176·9, *c*, 0·3% in $CHCl_3$) also analyses for $C_{15}H_{24}O$ and is an unsaturated alcohol (IR: OH 3250, 1020 $cm^{-1}$; $-C(=CH_2)-$ 1650, 890 $cm^{-1}$) closely related to caryophyllenol-I, as revealed by its PMR spectrum: two quaternary Me's (3H, s's at 59 and 62·5 c/s), one vinylic Me (s at 95 c/s), $-C(=CH_2)-$ (two 1H, m at 265 and 280 c/s), $-CH(OH)-$ (1H, m centred at 280 c/s; shifts to 331 c/s on acetylation) and $-C=CH-$ (1H, quartet centred at 327 c/s). The alcohol on catalytic hydrogenation consumed two moles of $H_2$ to give a saturated alcohol, which on Jones oxidation, gave a ketone mixture (GLC). This mixture on equilibration over $Al_2O_3$ yielded essentially a single ketone, the IR spectrum of which was found to be identical with that of the ketone XVI reported by Sorm *et al.*[15] This correlation, along with the structural features discussed earlier, limits the structural possibilities (ignoring the geometrical isomerism at the endocyclic olefinic bond) for the new alcohol, which we term caryophyllenol-II, to XVII and XVIII (two $C_6$ epimers), structure XV ($C_6$ epimer of XVII) having already been assigned to caryophyllenol-I.




XVI




XVII




XVIII

A decision between XVII and XVIII could be made on the basis of PMR shifts resulting from esterification of the alcohol with 3,5-dinitrobenzoic acid, an anisotropic moiety. Vinylic Me and the trisubstituted olefin proton undergo significant downfield shift in the 3,5-dinitrobenzoate, where they occur at 111 c/s (*d*, *J* = 1 c/s) and 360 c/s (*m*) respectively; on the other hand, the two vinylidene protons remain practically unaffected (1H, *t*, 269 c/s; 1H, *t*, 282·5 c/s). This clearly supports structure XVII.

One of the minor products of Schenck oxidation of (−)-caryophyllene has been assigned[14] structure XVII. Though, the reported PMR spectrum is identical with the PMR spectrum of caryophyllenol-II and the reported m.p. (86–88°) is also close, the reported specific rotation ($[\alpha]_D$ +125°, $CHCl_3$) is considerably lower.

## EXPERIMENTAL

All m.ps and b.ps are uncorrected, the former being determined on a Kofler hot stage. Light petroleum refers to the fraction b.p. 40–60°. Optical rotations were measured at room temp (27 ± 2°) in $CHCl_3$ (except when otherwise stated) on a Perkin–Elmer Polarimeter model 141.

UV spectra were taken on a Perkin–Elmer spectrophotometer, model 350, in 95% EtOH. IR spectra were recorded as smears (liquids) or Nujol mulls (solids), unless otherwise stated, on a Perkin–Elmer Infracord model 137E. PMR spectra were taken in 10–20% soln in $CCl_4$ (exceptions stated) with TMS as internal standard, on a Varian A-60 spectrometer; signals are recorded in c/s relative to TMS as zero. Mass spectra were recorded on a CEC mass spectrometer, model 21-110B, using an ionizing voltage of 70 eV and a direct inlet system. GLC was run on "Aerograph", model A-350-B, using a 150 cm × 0·6 mm column packed with 20% diethylene glycol polysuccinate on Chromosorb W (60–80 mesh) with $H_2$ as carrier gas.

Alumina used for chromatography was made neutral by the $HNO_3$ method[16] and graded according to Brockmann.[17] The silica gel for column chromatography (−100, +200 mesh) was washed with hot distilled water till sulphate-free, dried and activated at 125–130° for 6–8 hr; the product was standardised according to Hernandez *et al.*[18] $AgNO_3$-impregnated silica gel was made by the method of Gupta and Dev[1] and activated and standardised as above. TLC was carried out on silica gel or silica gel-$AgNO_3$ layers, containing 15% gypsum, using the apparatus and technique cited earlier.[1]

Dipterocarpus pilosus *oleoresin*. The oleoresin, which was collected* from the forests around Margherita, Assam, when received was a dark grey, semisolid with a balsamic odour and was contaminated with wood chips.

The oleoresin (100 g) on extraction with EtOAc yielded ~84 g of a clear dark thick gum with the following physicochemical characteristics: acid value, 27·9; saponification value, 47·5; saponification value after acetylation, 113·0; active hydrogen, 0·13%; steam volatile, 21·5%.

*Broad separation*. The crude oleoresin (575 g) was well-stirred with light petroleum (3 l.) and centrifuged to give a light petroleum extract and a residue. The residue was next extracted in a Soxhlet apparatus, successively with light petroleum, benzene and EtOAc. Light petroleum extracts were combined and freed of solvent to give 360–390 g of light *petroleum extract* (viscous brown liquid). Solvent removal from other two extracts yielded 40·2–51·7 g of benzene extract (brown powder) and 39·5–46·0 g of *EtOAc extract* (buff-colored powder).

The light petroleum extract (370 g), along with water (1·5 l.) and NaCl (100 g) was charged in a flask (3 l.) fitted with a Dean–Stark type head[19] and heated in an oil-bath (130–140°) till no more volatile oil was collected (~30 hr). The *essential oil* thus obtained was dried and totally distilled, b.p. 105–130°/2 mm, yield 85 g.

The non-volatile material from the above steam-distillation was collected (~269 g) by filtration. A part of it (195 g) was dissolved in ether (2·5 l.) and separated in the usual fashion into *acidic* (8–9 g) and *neutral portions* (~180 g) by extraction with $Na_2CO_3$ aq (5%, 50 ml × 6).

*Fractionation of essential oil*. The essential oil (40·8 g) as obtained above, was carefully fractionated on a spinning-band column,† at a reflux ratio of 10:1 and the various fractions monitored by GLC and TLC ($AgNO_3$–silica gel) under the conditions specified in Table 1:

TABLE 3. FRACTIONATION OF ESSENTIAL OIL FROM *Dipterocarpus pilosus*

| Fraction No. | B.p./2 mm | Weight (g) | Remarks |
|---|---|---|---|
| 1 | 85–95° | 1·86 | Essentially ①* |
| 2 | 95–98° | 14·11 | ①, ② |
| 3 | 98–103° | 4·51 | Essentially ② |
| 4 | 103–106° | 7·55 | ③, ④(major), ⑥ |
| 5 | 106–108° | 7·32 | ④, ⑥ |
| 6 | 110–125° | 3·71 | ⑥, ⑧, ⑨, ⑩, ⑪ |

*These numbers refer to GLC components (Table 1)

* The supply was made through the courtesy of Dr. N. K. A. Iyer, who kindly identified the trees. Authors wish to record their thanks for this help.

† Model NF 115, manufactured by Nestler and Faust, Newark, USA; theoretical plates: 23.

(−)-*Caryophyllene* (VII). Fraction 1 (Table 4) (1·64 g) in light petroleum (12 ml) was stirred with $AgNO_3$ (3·3 g) in $H_2O$ (3 ml) at 0° for 1 hr. The light petroleum phase was separated, solvent removed to give a product (1·17 g), which was chromatographed over $AgNO_3$–silica gel, as described earlier,[20] to finally give pure (GLC, TLC) (−)-caryophyllene (0·85 g), b.p. 98·5–100°/3 mm, $n_D^{30}$ 1·2922, $[\alpha]_D$ −14·11 ($c$ = 1·63%). (For lit. value, see Ref[20]).

*Humulene* (IV). Fraction 3 (Table 4) (2·0 g) on treatment with $AgNO_3$ aq in the usual manner,[20] furnished humulene–$AgNO_3$ adduct[21] (2·21 g, m.p. 167–170°), which after recrystallisation from 95% EtOH had, m.p. 174–175°; mixed m.p. with an authentic sample remained undepressed (Lit,[21] m.p. 175°).

Humulene was regenerated from the adduct in the usual manner[21] to give a product, b.p. 101–103°/2 mm, $n_D^{30}$ 1·5008, $[\alpha]_D \pm 0$.

(−)-*Caryophyllene oxide* (I). Fraction 4 (Table 4) slowly solidified and, on crystallisation from acetonitrile furnished caryophyllene oxide (3·63 g, m.p. 60–62°) which after recrystallisations from MeOH had m.p. 62–63°, mixed m.p. with an authentic sample[20] remained undepressed, $[\alpha]_D$ −75·0 ($c$ = 0·9%) (Lit.[22], m.p. 64°, $[\alpha]_D$ = −68°).

*Isolation of GLC components* ⑥, ⑧, ⑨, ⑩ *and* ⑪. Fraction 6 (Table 4) (1·52 g) was chromatographed over $AgNO_3$–silica gel (grade IIA; 95 g, 50 cm × 2·2 cm) with TLC ($AgNO_3$–silica gel; solvent: 5% acetone in $C_6H_6$), GLC monitoring:

| | | | |
|---|---|---|---|
| Fraction I | $C_6H_6$ | 600 ml | 290 mg, rejected |
| Fraction II | 1% acetone in $C_6H_6$ | 25 ml × 4 | 97 mg, rich in ⑧* |
| Fraction III | 2% acetone in $C_6H_6$ | 25 ml × 7 | 442 mg, essentially ⑥ |
| Fraction IV | 2% acetone in $C_6H_6$ | 25 ml × 4 | 57 mg, essentially ⑩ |
| Fraction V | 2% acetone in $C_6H_6$ | 25 ml × 3 | 365 mg, rich in ⑪ |
| | 5% acetone in $C_6H_6$ | 25 ml × 3 | |
| | 10% acetone in $C_6H_6$ | 25 ml × 4 | |
| Fraction VI | 50% ether in $C_6H_6$ | 200 ml | 179 mg, essentially ⑨ |

* These numbers refer to GLC components (Table 1)

*Humulene epoxide*-III (VI). Fraction II (64 mg) was rechromatographed over silica gel (grade II, 25 cm × 0·5 cm) using light petroleum as eluent and GLC monitoring to finally give pure ⑧ (23 mg), b.p. 120–130° (bath)/1·5 cm, $n_D^{30}$ 1·4989 $[\alpha]_D$ +2·15 ($c$, 1·25%). (Found: C, 81·83; H, 10·87. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98%).

Humulene epoxide-III (16 mg) in $C_6H_6$ (3·5 ml) was mixed with a $C_6H_6$ soln of percamphoric acid[23] (45 mg of peracid) and left aside at 15° for 4 days. Usual work-up gave a gum which was chromatographed over $Al_2O_3$ (grade II, 1 g). Benzene–light petroleum (1 : 1) eluted fraction (2 ml) after recrystallisation from light petroleum–benzene (1 : 1), yielded humulene trioxide (2·4 mg), m.p. 121–122·5°, mixed m.p. with an authentic sample[2] remained undepressed; IR spectrum: bands at 1450, 1395, 1262, 1250, 1055, 952, 918, 875, 850 and 783 $cm^{-1}$. Benzene eluted fraction, yielded on crystallisation a product (4 mg), m.p. 120–130°, mixed m.p. with humulene trioxide (m.p. 121–122°) remained unchanged.

*Humulene epoxide*-II (V). Fraction III was distilled to give humulene epoxide-II (320 mg), b.p. 119–121°/25 mm, $n_D^{30}$ 1·4973. (Lit.[2] b.p. 105–106°/1·5 cm, $n_D^{30}$ 1·4962).

*Sesquiterpene-A* (*GLC component* ⑩). Fraction IV slowly solidified and was recrystallised from acetonitrile to furnish colourless needles (20 mg), m.p. 116–117°, $[\alpha]_D$ + 66·13° ($c$, 0·44%). PMR: quaternary Me's (3H, s's at 40, 55 and 62 c/s), —CHOH (1H, m centred at 218 c/s), —C=CH$_2$ (1H, broad s's at 270 and 284 c/s). Mass spectrum: $M^+$, $m/e$ = 222. (Found: C, 80·78; H, 11·83. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%).

*Caryophyllenol*-I (XV). Fraction V (365 mg) was rechromatographed over $AgNO_3$–silica gel (grade IIA; 30 g; 42 cm × 1·2 cm) with TLC monitoring ($AgNO_3$–silica gel; solvent: 5% acetone in $C_6H_6$).

| | | | |
|---|---|---|---|
| Fraction VA | 2% acetone in $C_6H_6$ | 5 ml × 3 | 25 mg, rejected |
| Fraction VB | 5% acetone in $C_6H_6$ | 5 ml × 3 | 39 mg |
| Fraction VC | 5% acetone in $C_6H_6$ | 5 ml × 6 | 86 mg |

Fraction VB was recrystallised from acetonitrile to give XV as colourless prisms (20 mg), m.p. 73·5–75°: (Found: C, 81·87; H, 11·14. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98).

*Caryophyllenol*-II (XVII). Fraction VC, above was distilled and the distillate crystallised from acetonitrile to furnish caryophyllenol-II (XVII) as colourless needles (60 mg), m.p. 89–90°. (Found: C, 81·68; H, 10·42. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98%).

*Acetate* ($Ac_2O$ pyridine method), purified by passing through a column of silica gel (grade II; eluent $C_6H_6$) and total distillation, was obtained as a colourless viscous liquid, $[\alpha]_D$ +188·69° (*c*, 0·71%). (Found: C, 78·05; H, 9·92. $C_{17}H_{26}O_2$ requires: C, 77·82; H, 9·99%).

3,5-*Dinitrobenzoate* (3,5-dinitrobenzoyl chloride pyridine method) was purified by passing through a column of silica gel (grade II; eluent 10% $C_6H_6$ in light petroleum) but was still obtained only as a gum.

*Ketone* (XVI). Caryophyllenol-II (XVII; 100 mg) was hydrogenated ($PtO_2$, AcOH) $H_2$ uptake 24·2 cc/25°, 710 mm; required for 2 double bonds 23·8 cc) and the product passed through a column of alumina (grade-II; 3 g). Light petroleum eluted material was discarded and the column was washed with EtOH to collect the tetrahydro derivative (95 mg). This was oxidized by Jones reagent (0·32 ml at 15° for 12 hr). The ketone obtained after work-up and distillation was kept adsorbed overnight on basic alumina (grade I; 6 g, height 33 cm). Elution with ether gave the equilibrated ketone (XVI)[15] GLC pure, $[\alpha]_D$ +32·8° (*c*, 2·1%).

*Humulenol*-II (XII). Fraction VI (179 mg) on total distillation furnished GLC pure humulenol-II[3] (XII) as a colourless viscous liquid, b.p. 125–135° (bath)/2 mm; $n_D^{30}$ 1·5102; $[\alpha]_D$ +13·92° (*c*, 0·67%) (Lit.[3] b.p. 115–116/1 mm, $n_D^{30}$ 1·5127; $[\alpha]_D$ +30·0° (*c*, 3·6%).

*Action of* $Al_2O_3$ *on caryophyllene epoxide.* (−)-Caryophyllene oxide (1·0 g) in light petroleum (2 ml) was added to a slurry of $Al_2O_3$ (grade I, 70 g) in light petroleum (70 ml) and the mixture shaken ($N_2$) for 12 hr at room temp (25–27°), after which the reaction mixture was worked up in the usual manner[11] to give a product (855 mg), a part of which (500 mg) was chromatographed over $AgNO_3$–silica gel (grade IIA; 35 g, 50 cm × 1·2 cm) with TLC monitoring ($AgNO_3$–silica gel; solvent: 5% acetone in $C_6H_6$):

| | | | |
|---|---|---|---|
| Fraction I | 2% acetone in $C_6H_6$ | 5 ml × 15 | 27 mg, discarded |
| Fraction II | 5% acetone in $C_6H_6$ | 5 ml × 5 | 88·7 mg |
| Fraction III | 10% acetone in $C_6H_6$ | 5 ml × 7 | 36·8 mg |
| Fraction IV | ether | 50 ml | 292 mg |

*Caryophyllenol*-I. Fraction II was distilled and the distillate recrystallised from acetonitrile to give caryophyllenol-I (24·3 mg), m.p. 73·5–75°, $[\alpha]_D$ −105·9° (*c*, 0·62%).

4,10,10-*Trimethyl-4-hydroxymethyl-7-methylene-bicyclo* [6.2.1] *decane* (XIV). Fraction III was distilled and the distillate passed through a column of silica gel (grade II, 2 g). Material eluted with $C_6H_6$ was discarded and the fraction eluted with 1% acetone in $C_6H_6$ (2 ml × 3; 21 mg) was distilled to furnish XIV, $[\alpha]_D$ +18·0° (*c*, 0·92%). (Found: C, 80·37; H, 11·53. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%).

*Caryophylla*-3(12), 7(13)-*dien*-6-*ol* (XIII). Fraction IV was distilled and the distillate passed through a column of silica gel (grade II, 8 g). After rejecting the $C_6H_6$ eluate (negligible), 1% acetone in $C_6H_6$ eluates (5 ml × 3) were collected, freed of solvent and distilled to give XIII (250 mg), viscous liquid, $[\alpha]_D$ +21·08° (*c*, 2·94%). (Lit.: $[\alpha]_D$ +20·8[12], +24[14]). (Found: C, 81·75; H, 11·32. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98%).

*Sesquiterpenoids from the steam non-volatile (neutral) fraction.* Isolation of these compounds (Table 2) is best described along with the isolation of neutral triterpenoids and this is reported in the following communication. Only, some properties of these compounds are described here.

*Sesquiterpene*-B was isolated as its acetate, m.p. 131–135° (Light petroleum-ether); IR (KBr): OH 3390, 1029 $cm^{-1}$; OAc 1700, 1250 $cm^{-1}$. Mass spectrum: major signals at *m/e* 280 (base), 262, 224, 220, 205, 202, 199, 177, 162, 125, 109, 95, 82.

*Sesquiterpene*-C, m.p. 80–82° (light petroleum-ether); IR (KBr): OH 3390, 970 $cm^{-1}$. Mass spectrum: major signals at *m/e* 238, 221, 220 (base), 205, 202, 179, 164, 162, 127, 123, 121, 109, 95, 81. (Found: C, 74·85; H, 11·20. $C_{15}H_{26}O_2$ requires: C, 75·58; H, 11·00%).

*Sesquiterpene*-D was purified as an acetate, which was also obtained as a gum; IR: OH 3400, 1030 $cm^{-1}$; OAc 1720, 1250 $cm^{-1}$; $-\underset{|}{C}=CH_2$ 1645, 890 $cm^{-1}$; PMR: quaternary Me's at 59, 63 and 65·5 c/s; OCOMe (3H, s at 122 c/s): $-\underset{|}{C}=C\underline{H}_2$ and $-C\underline{H}-OAc$ (both signals overlap to give a 3H. m centred at 294 c/s). Mass: major signals at *m/e* 296 (base), 280, 265, 251, 238, 236, 222, 218, 205, 202, 109, 95, 93, 43.

*Clovane-diol* (II) m.p. 152–153° (acetonitrile); IR (KBr): OH 3300, 1078 $cm^{-1}$; PMR (pyridine): quaternary Me's (3H signals at 55, 67·5 and 71 c/s): two $-\underset{|}{C}\underline{H}OH$ (1H, broad s at 212 c/s; 1H, tr centred at 245 c/s, $J$ = 8 c/s). Mass: major signals (relative intensity) at *m/e* 238 (54%), 220 (48%), 182 (59%), 179

(51%), 164 (100%), 163 (53%), 137 (48%), 135 (57%), 107 (44%), 105 (41%), 95 (40%), 93 (42%), 41 (57%). (Lit.[4] m.p. 152–153°, $[\alpha]_D$ +5·0°).

*Acetate* ($Ac_2O$ pyridine method), m.p. 98–99° (ether); IR (KBr): OAc 1715, 1245 $cm^{-1}$; other bands at 1020, 950, 900 $cm^{-1}$; PMR: quaternary Me signals (3H, s's) at 51, 57 and 63·5 c/s; two $OCOCH_3$ (6H, s at 120 c/s); two —CH—OAc (1H, broad s at 271 c/s; 1H, qu centred at 288 c/s with $J_1$ = 6 c/s and $J_2$ = 7·5 c/s). (Lit.[4] m.p. 96–97°).

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