Tetrahedron, 1963, Vol. 19, pp. 1079 to 1090. Pergamon Press Ltd. Printed in Northern Ireland

# TERPENOIDS—XLI

## STRUCTURE AND ABSOLUTE CONFIGURATION OF α-AGAROFURAN, β-AGAROFURAN AND DIHYDROAGAROFURAN*

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(*Received* 8 *January* 1963)

**Abstract**—Three new sesquiterpenic furanoids of the selinane group have been isolated from agarwood oil, obtained from the fungus infected plant *Aquillaria agallocha* Roxb. and their structures and absolute configurations determined (XXII, XX, XXXI) by degradative studies and physical measurements.

THREE new furanoid sesquiterpenes of the selinanic group have been obtained in the pure (VPC) form in small quantities by elaborate column chromatography of the lower boiling fractions of agarwood oil isolated by low temperature solvent extraction procedure from the fungus infected agarwood[1,2] (*Aquillaria agallocha* Roxb.). These are:

(i) Fully saturated dihydroagarofuran, $C_{15}H_{26}O$,
(ii) β-agarofuran, $C_{15}C_{24}O$, containing one double bond,
(iii) α-agarofuran, $C_{15}H_{24}O$, also containing one double bond.

The results of our investigation on the structure and the stereochemistry of these compounds are represented in this paper.

β-Agarofuran which was obtained in comparatively larger quantities correctly analysed for $C_{15}H_{24}O$. On dehydrogenation with selenium it afforded eudalene (I), which accounts for its fourteen carbon atoms. Assuming that β-agarofuran is a true isoprenoid, the 15th carbon atom will be in the form of an angular methyl group at $C_{10}$ and consequently its basic carbon skeleton should be represented by II. β-Agarofuran gives yellow coloration with tetranitromethane. It contains one double bond as shown by peracid titration and confirmed by its catalytic hydrogenation to give dihydro-β-agarofuran.

The double bond in β-agarofuran was proved methylenic ($>C{=}CH_2$) from its I.R. spectrum (Fig. 1, absorptions at 1639 and 898 cm$^{-1}$) and further confirmed by formation of formaldehyde on ozonization. Haloform test was negative with both the trap solution as well as the neutral non-volatile product of ozonolysis, the latter of which is a keto-oxide, $C_{14}H_{22}O_2$, in which the keto group is on a six-membered ring and with a methylenic group next to it (I.R. spectrum, bands at 1712 and 1418 cm$^{-1}$). β-Agarofuran, dihydro-β-agarofuran and the $C_{14}$-keto-oxide, obtained from it by ozonization show a doublet around 1379 and 1361 cm$^{-1}$ in their I.R. spectra, due to

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‡ University of Illinois, Department of Chemistry and Chemical Engineering, Urbana, U.S.A., carried out N.M.R. measurements and interpretation.

[1] A fuller account of the isolation of various constituents will be published separately.

[2] T. C. Jain, M. L. Maheshwari and S. C. Bhattacharyya, *Perf. & Ess. Oil Rec.* 53, 294 (1962).

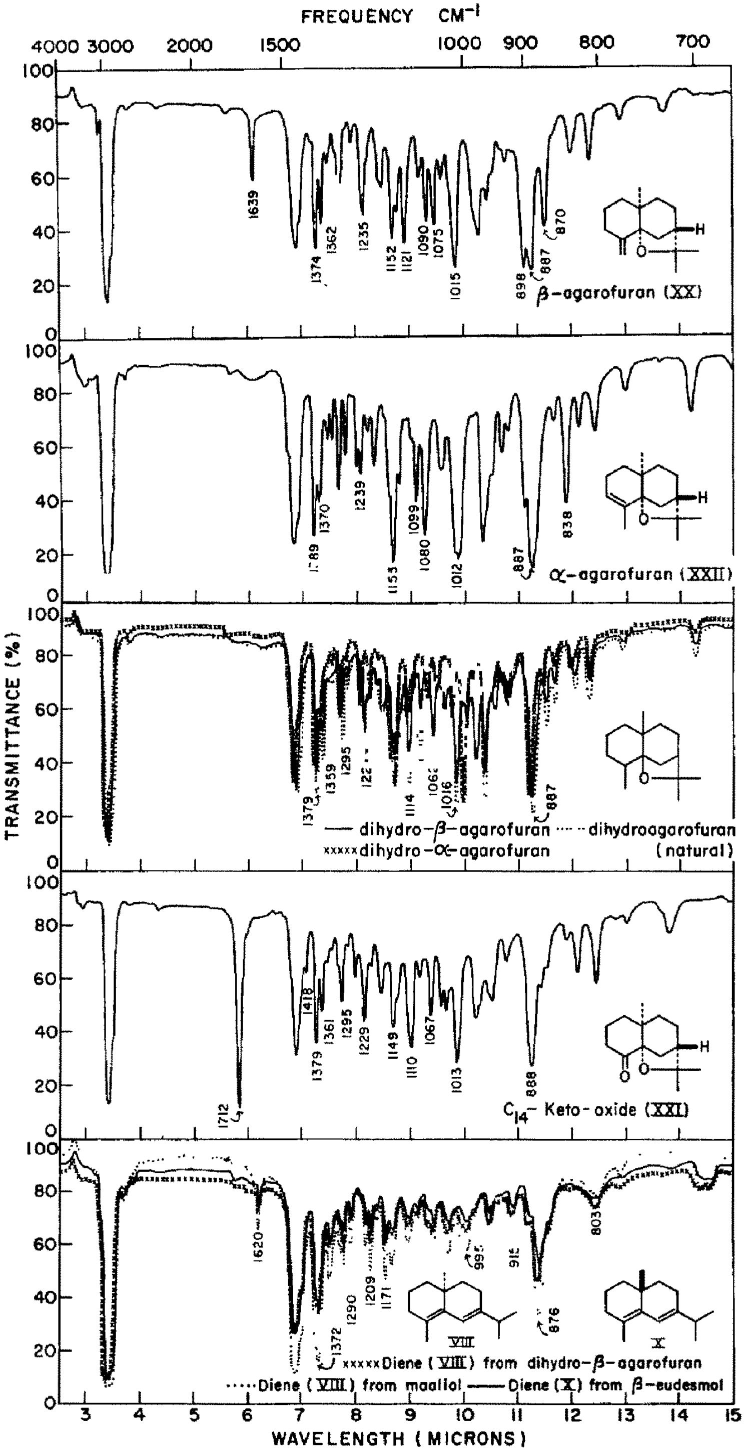
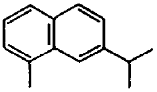

FREQUENCY CM$^{-1}$
4000 3000 2000 1500 1000 900 800 700
TRANSMITTANCE (%)
0 20 40 60 80 100
1639
1374
1362
1235
1152
1121
1090
1075
1015
898
887
870
β-agarofuran (XX)
1389
1370
1239
1153
1099
1080
1012
887
838
α-agarofuran (XXII)
1379
1359
1295
122
1114
1062
1016
887
—— dihydro-β-agarofuran ····· dihydroagarofuran (natural)
xxxxx dihydro-α-agarofuran
1712
1418
1379
1361
1295
1229
1149
1110
1067
1013
888
$C_{14}$- Keto-oxide (XXI)
1620
1372
1290
1209
1171
995
915
876
803
VIII
X
xxxxx Diene (VIII) from dihydro-β-agarofuran
····· Diene (VIII) from maaliol —— Diene (X) from β-eudesmol
3 4 5 6 7 8 9 10 11 12 13 14 15
WAVELENGTH (MICRONS)

FIG. 1.

the presence of two symmetrically attached methyl groups. The basic carbon skeleton, taking the nature of double bond into consideration may be therefore extended to III.

β-Agarofuran contains one oxygen function. Its I.R. spectrum does not show any characteristic band of hydroxyl or carbonyl function and it can also be distilled over sodium without any loss. The oxygen atom in β-agarofuran can, therefore, be considered to be either an epoxide or an oxide function. The complete stability of β-agarofuran and dihydro-β-agarofuran towards lithium aluminium hyride, acetic acid etc. rules out the possibility of an epoxide ring. Consequently, the presence of a tetrahydrofuran moiety was suspected in β-agarofuran, which was supported by its I.R. absorption bands at 870, 887, 1015, 1075, 1090, 1121, 1140, 1152, and 1235 cm$^{-1}$ (9·1 to 9·3 μ bands are characteristic of tetrahydrofuran derivatives).[3] Similar bands are also observed in other compounds having tetrahydrofuran rings such as santanolide ether (IV), maalioxide (V), campanulin,[4] grindelic acid[5] etc.



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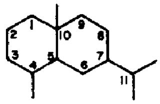

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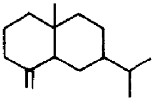

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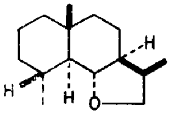

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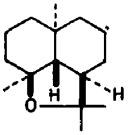

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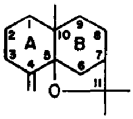

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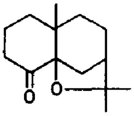

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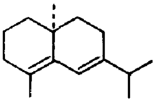

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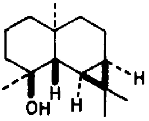

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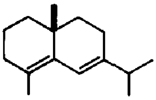
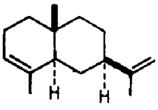


X



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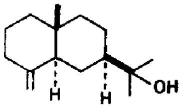

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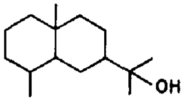

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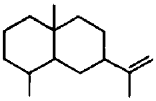

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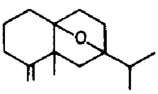

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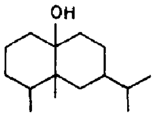
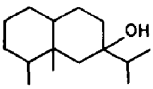


XVI



XVII

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[3] G. M. Borrow, and S. Searles, *J. Amer. Chem. Soc.* **75**, 1175 (1953).

[4] S. Rangaswami and K. Sambamurthy, *Proc. Indian Acad. Sci.* **54A**, 132–9 (1961).

[5] L. Panizzi, L. Mangoni and M. Belardini, *Tetrahedron Letters* No. 11, 376–81 (1961).

The position of fusion of tetrahydrofuran ring was solved by comparing the NMR[6] spectra (Fig. 2) of β-agarofuran and dihydro-β-agarofuran with that of the known compound santonolide ether "a" (IV). The compound (IV) shows three peaks in the 5·9–7·1 τ region, which are due to three protons present on carbon atoms bearing oxygen. The absence of absorption in the NMR spectra of dihydro-β-agarofuran below 7·5τ suggests that it is a ditertiary ether, i.e. there is no proton on the carbons bearing oxygen. Similar absence of absorption in the NMR spectra of β-agarofuran and maalioxide (V) is also observed in the same region. Therefore it can be concluded that in β-agarofuran the oxygen atom is linked to two tertiary carbon atoms leading to the structure (VI) for β-agarofuran and (VII) for the $C_{14}$-keto-oxide obtained from it by ozonization.

In addition, the NMR spectrum of β-agarofuran shows absorption at 5·32 and 5·44τ which is in accordance with the structure (VI) containing two vinyl protons.

The tetrahydrofuran linkage of β-agarofuran was further proved by the treatment of dihydro-β-agarofuran with borontrifluoride ethereate in acteone to furnish a heteroannular diene identical with the diene (VIII) of known stereochemistry obtained by treating maaliol (IX) with formic acid.[7] Their I.R. spectra were also completely superimposable. The diene (VIII) was considered by Büchi *et al.* to be the enantiomer of δ-selinene (X) prepared by isomerization of α-selinene (XI) with sulphuric acid.[8] But Büchi *et al.* did not compare the diene (VIII) and δ-selinene (X) due to non-availability of the latter. Therefore, for the purpose of comparison we prepared δ-selinene (X) by dehydration of β-eudesmol (XII) with acetic acid and perchloric acid.[9] The I.R. spectrum of δ-selinene (X) was completely superimposable over the I.R. spectra of diene VIII and the diene obtained from dihydro-β-agarofuran. U.V. spectra of all the three conjugated dienes showed the same triple absorption (256, 247 and 241 mμ). The optical rotation of δ-selinene (X) is of a very high order ($[\alpha]_D^{30}$ +265·5°, *c*, 6·5) no doubt on account of its purity. All other physical constants of the three dienes are in agreement. By observing the constants and specially the signs and order of rotations it can be said that the dienes from dihydro-β-agarofuran and maaliol are the same and enantiomeric with δ-selinene obtained from β-eudesmol. In the dienes there is only one asymmetric centre, i.e. $C_{10}$. In the case of maaloil and the diene obtained from it, it has been proved that angular methyl group at $C_{10}$ is α-oriented. Hence, it can be concluded that the angular methyl group at $C_{10}$ in the case of thediene and consequently in that of β-agarofuran and dihydro-β-agarofuran is also α-oriented.

In view of the fact that both the enantiomeric dienes have now been prepared, it is desirable to assign names to them according to their signs of specific rotations, i.e. the δ-selinene (X) obtained from β-eudesmol as (+)-δ-selinene and the diene (VIII) from maaliol and dihydro-β-agarofuran is (−)-δ-selinene.

The attachment of the tetrahydrofuran ring at $C_{11}$ was confirmed by reductive cleavage of β-agarofuran with lithium in anhydrous ethylene diamine[10] to give the

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[6] N.M.R. spectra were measured by Dr. R. B. Bates on HR-60 and on A-60 (both Varian instruments set at 60 mc). Tetramethyl silane was used as an internal standard, carbon tetrachloride solutions (20%) were used.

[7] G. Büchi, M. Schach. V. Wittenau and Dwain M. White, *J. Amer. Chem. Soc.* **81**, 1968 (1959).

[8] L. Ruzicka and M. Stoll, *Helv. Chim. Acta* **6**, 846 (1923).

[9] S. K. Paknikar and S. C. Bhattacharyya, *Tetrahedron* in press.

[10] L. Reggel, R. A. Friedel, and I. Wender, *J. Org. Chem.* **22**, 891 (1957).

alcohol (XIII), the benzoate of which on pyrolysis under standard conditions as employed in the case of dihydro-β-eudesmol benzoate, furnished a hydrocarbon (XIV) which was sufficient only for examination of I.R. spectrum[11] (1634 and 887 $cm^{-1}$). The formation of hydrocarbon (XIV) proved the location of the hydroxyl group in alcohol (XIII) and consequently that of the attachment of the oxide ring in β-agarofuran at $C_{11}$. It also excluded the possibility of the oxide ring occurring as in the eremophilone type compound (XV), which would form on reductive cleavage with lithium either XVI or XVII, both of which are incapable of giving on pyrolysis a hydrocarbon having methylenic double bond.

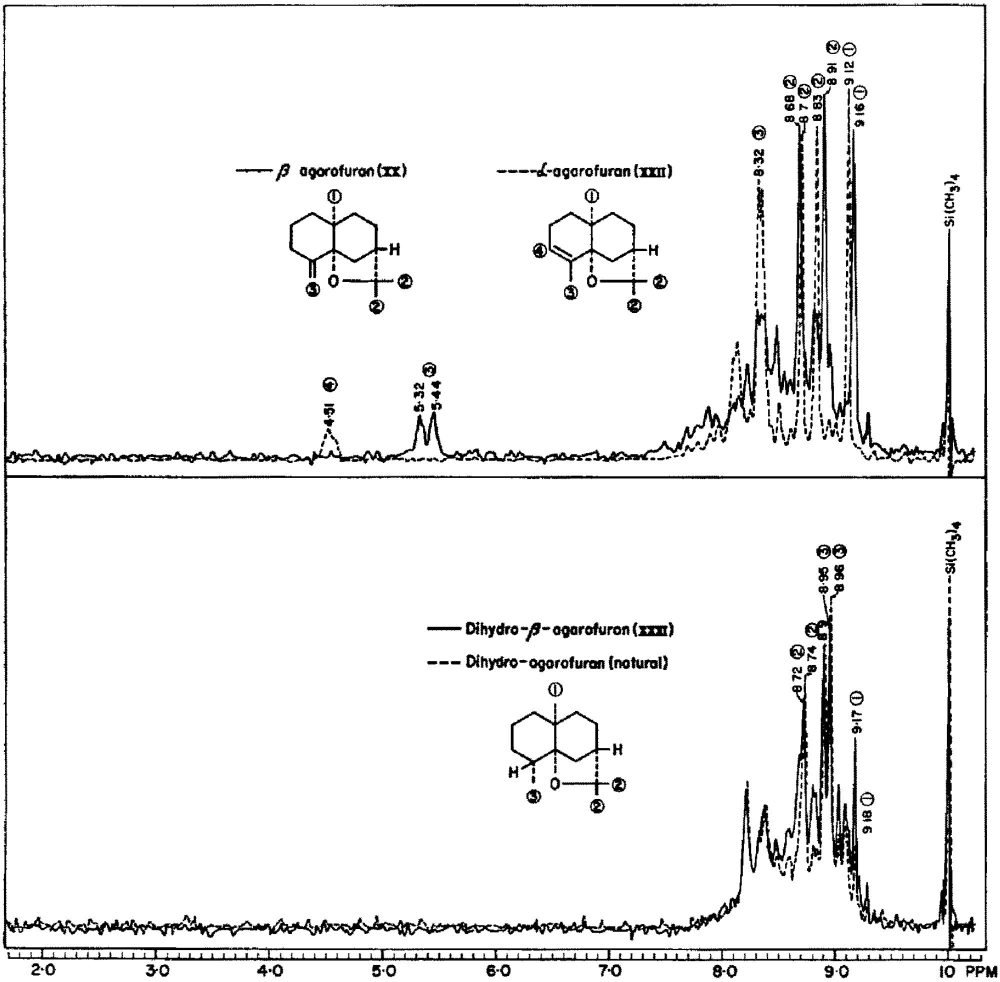

FIG. 2

For determining the stereochemistry of other centres the ORD curve* of the ketone (VII) was measured. It showed negative Cotton effect (Fig. 3). The magnitude of the

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* We thank Prof. W. Klyne, Westerfield College, University of London, for the measurement of the R.D. curve of the compound (VII).

[11] K. G. O'Brien, A. R. Penfold, M. D. Sutherland and R. L. Werner, *Austr. J. Chem.* 7, 298 (1954).

curve is not sufficiently high, possibly due to the presence of the oxide ring in the vicinity of the carbonyl group, but negative Cotton effect gives information about the stereochemistry at C$_5$. Comparison of the ORD curves of C$_{14}$-keto-oxide (VII), *trans*-10-methyl-1-decalone (XVIII) and *cis*-10-methyl-1-decalone[12] (XIX) shows the oxide linkage at C$_5$ in C$_{14}$ keto-oxide (VII) should be α-oriented.

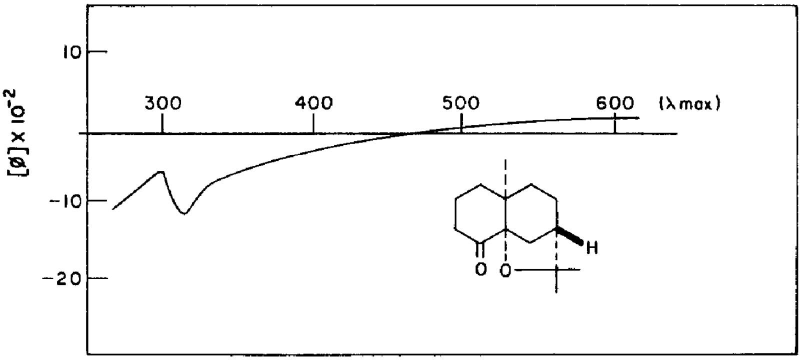
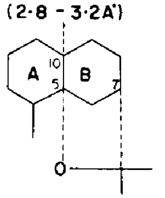
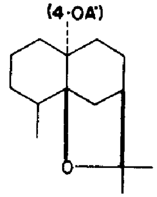


FIG. 3. RD curve of C$_{14}$-keto-oxide (XXI).

Therefore, it may be concluded that the fusion of A and B rings in β-agarofuran is *cis*, which is also supported by its N.M.R. spectrum, showing absorption at 50·0 cps (9·16τ) due to the angular methyl group. Absorption in similar compounds due to angular methyl group in *cis*-fused rings A and B is at 55·6,[13] 54·0,[13] 58·0[14] cps and in *trans*-fused A and B rings is at 47,[13] 45·5,[13] 43[14] cps.

The oxygen atom deshields the angular methyl group more with a *cis*-ring juncture than with a *trans*. The average distance between protons of the methyl group and the oxygen nucleus, as measured from Dreiding models, are in parentheses.*





By model studies it has been observed that the tetrahydro-furan ring can be fused at C$_5$ and C$_7$ only when both the linkage (C$_5$—O and C$_7$—C$_{11}$) are oriented axially. Consequently, since the A and B rings have *cis*-fusion and the angular methyl group and the oxide linkage (C$_5$—O) are α-oriented, the C$_7$—C$_{11}$ bond also automatically becomes α-oriented. Hence the stereochemical structures (XX, XXI) can be assigned to β-agarofuran and C$_{14}$-keto-oxide respectively.

α-Agarofuran also analysed for the molecular formula, C$_{15}$H$_{24}$O and from the experimental evidences recorded herein can be represented by structure XXII. Its I.R. spectrum showed the absence of hydroxyl and carbonyl functions but indicated the presence of tetrahydrofuran ring (887, 1012, 1080, 1099, 1136, 1155, 1164, 1202 and

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* Measurements were carried out by Dr. R. B. Bates.

[12] C. Djerassi, *J. Amer. Chem. Soc.* **80**, 3986 (1958).

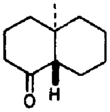
[13] J. I. Musher, *J. Amer. Chem. Soc.* **83**, 1146 (1961).

[14] K. R. Varma, T. C. Jain, and S. C. Bhattacharyya, *Tetrahedron* **18**, 979 (1962).

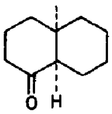
1250 cm$^{-1}$), *gem*-dimethyl group (1389 and 1370 cm$^{-1}$) and a trisubstituted double bond (1653, w, 838, s/cm$^{-1}$). The NMR spectrum also supported the presence of trisubstituted double bond (4·51$\tau$) and further indicated that as in the case of $\beta$-agarofuran the oxygen of oxide ring is also attached to two tertiary carbon atoms.

Oxidation with prebenzoic acid and catalytic hydrogenation showed the presence of only one double bond. It gives eudalene on dehydrogenation with selenium. Infrared spectrum of dihydro-$\alpha$-agarofuran is almost superimposable with that of dihydro-$\beta$-agarofuran, but only the intensities of some of the peaks were slightly different. The specific rotation (—60·8°) was also some what lower than that of dihydro-$\beta$-agarofuran (—76·07°). This is understandable for two closely related isomers.

On treatment with borontrifluoride ethereate, dihydro-$\alpha$-agarofuran also formed (—)-$\delta$-selinene (VIII), which shows that like $\beta$-agarofuran the angular methyl group in $\alpha$-agarofuran and dihydro-$\alpha$-agarofuran is also $\alpha$-oriented.



XVIII



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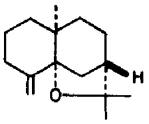

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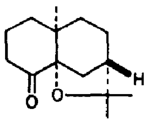
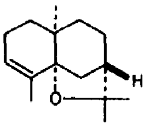


XXI



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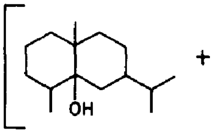

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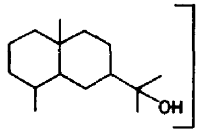

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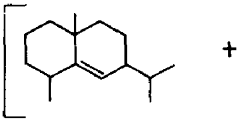
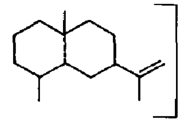
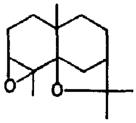


XXV



XXVI



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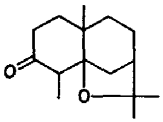
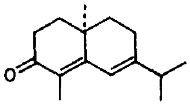
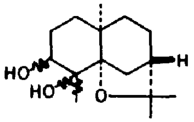


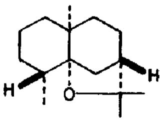
XXVIII



XXIX



XXX



XXXI

The linkage of the oxygen function in α-agarofuran was further confirmed by the formation of the alcohols (XXIII, XXIV) by prolonged hydrogenation for 72 hours in the presence of glacial acetic acid and platinum oxide as a catalyst and subsequently pyrolysis of the mixed benzoate to afford a mixture of hydrocarbons (XXV, XXVI) which showed characteristic I.R. absorptions for trialkylated double bond (1653 and 811 $cm^{-1}$) as well as for methylenic double bond (1637 and 891 $cm^{-1}$).

α-Agarofuran on treatment with perbenzoic acid affords a crystalline epoxide (XXVII), $C_{15}H_{24}O_2$, m.p. 88°. Its I.R. spectrum shows characteristic bands for epoxide ring (882, 1024 and 1089 $cm^{-1}$), the tetrahydrofuran moiety (898, 1024, 1058, 1089, 1121, 1144, 1160, 1241, 1287 and 1309 $cm^{-1}$) and *gem* dimethyl group (1389 and 1370 $cm^{-1}$). Bands due to the trisubstituted double bond were absent. Treatment of the epoxide (XXVII) with borontrifluoride-ethereate in acetone (possibly containing traces of moisture) furnished three products on chromatography: (i) A liquid keto-oxide (XXVIII) showing I.R. absorption bands at 1712 and 1420 $cm^{-1}$ (characteristic of six-membered ring ketone having —$CH_2$-group in α-position to carbonyl group); 889, 1015, 1047, 1076, 1111, 1235, 1279 and 1304 $cm^{-1}$ (tetrahydrofuran ring), and which furnished a solid semicarbazone, m.p. 210°; (ii) an impure (25%) sample of (—)-β-cyperone[15] (XXIX), which showed characteristic U.V. absorption spectra $\lambda_{max}$ 300 mμ, (ε 6774), and strong laevo-rotation (−164·2°). Due to paucity of material further purification of (—)-β-cyperone was not possible. Formation of (—)-β-cyperone proves the position of olefinic linkage between $C_3$ and $C_4$ and also further confirms that the angular methyl group at $C_{10}$ is α-oriented; (iii) a needle-shaped crystalline diol oxide (XXX), m.p. 176°, $C_{15}H_{26}O_3$. It showed intense I.R. absorption at 3520, 1140 $cm^{-1}$ (—OH groups) and at 881, 1015, 1075, 1089, 1106, 1235, 1295 and 1316 $cm^{-1}$ (tetrahydrofuran ring).

The non-volatile product of ozonization of α-agarofuran showed the presence of an aldehyde function and a methyl ketone group (iodoform test).

All the evidence supports the structure XXII for α-agarofuran.

Along with α- and β-agarofurans we also obtained pure dihydro-agarofuran from agarwood oil, all the properties of which are identical with those of dihydro-β-agarofuran. Their I.R. spectra were also completely superimposable. Their N.M.R. spectra were also identical.

Assuming that during the formation of dihydro-β-agarofuran the hydrogen attack takes place from the less hindered β-face, dihydro-β-agarofuran (which is identical with natural dihydro-agarofuran) can be represented by the structure XXXI.

## EXPERIMENTAL

All m.p.s are uncorrected. The b.p., unless otherwise stated, correspond to bath temps. Rotations were taken in chloroform solution. Neutral alumina, graded according to the Brockmann scale[16,17] of activity was used in chromatography. The pet. ether refers to the fraction boiling between 60–80°. U.V. spectra were measured in ethanol solution on a Beckman ratio recording spectrophotometer, Model DK-2 by Miss Prabhu. The I.R. spectra were recorded as liquid film or in nujol suspension on a Perkin-Elmer Model No. 137B infracord spectrophotometer by Mr. Gopinath. Microanalyses were carried out by Mr. Pansare and colleagues.

*Isolation.* The lower boiling fractions, b.p. 104° at 0·5 mm (actual b.p. Tower's packed column)

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of diffusion pump-distilled agarwood oil (1·2 kg, solvent extracted from 600 kg of the fungus infected wood) were rigorously chromatographed on grade I alumina (50 to 100 times) to furnish dihydroagarofuran (XXXI, 600 mg), β-agarofuran (XX, 5·0 g) and α-agarofuran (XXII, 3·3 g) in the sequence indicated. All the three compounds were eluted with pet. ether. When subjected to VPC analysis they showed single peaks. Their properties are recorded.

*Dihydroagarofuran* (XXXI), b.p. 135°/8 mm, $n_D^{29}$ 1·4912, $[\alpha]_D^{30}$ −77·01° (*c*, 4·4), no coloration with tetranitromethane, I.R. bands at: 1379, 1359, 1295, 1229, 1155, 1144, 1114, 1089, 1062, 1015 998, 980, 952, 887 and 869 cm$^{-1}$. (Found: C, 81·40; H, 12·00. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%).

*β-Agarofuran* (XX), b.p. 130° at 8 mm, $n_D^{28}$ 1·4973, $d_D^{30}$ 0·9646, $[\alpha]_D^{30}$ −127·1°(*c* 8·)3; yellow coloration with tetranitromethane, peracid value 1·01, I.R. bands at: 1639, 1374, 1362, 1299, 1235, 1152, 1140, 1121, 1090, 1075, 1015, 898, 887, and 870 cm$^{-1}$. (Found: C, 81·3; H, 11·1. $C_{15}H_{24}O$ requires; C, 81·7; H, 10·98%).

*α-Agarofuran* (XXII), b.p. 134° at 6 mm, $n_D^{30}$ 1·5061, $[\alpha]_D^{30}$ +37·09° (*c*, 6·12); yellow coloration with tetranitromethane, peracid value 0·9, I.R. bands at: 1653 (w), 1389, 1370, 1326, 1307, 1285, 1250, 1239, 1202, 1164, 1155, 1136, 1099, 1080, 1046, 1012, 965, 950, 935, 887, 856, 838(s), 825, 805, 770, and 703 cm$^{-1}$ (Found: C, 81·64; H, 10·79. $C_{15}H_{24}O$ requires: C, 81·7; H, 10·98%).

### *Dehydrogenation of β-agarofuran* (XX) *with* Se

β-Agarofuran (202 mg) mixed with Se (202 mg) was heated in an atm. of nitrogen at 300° for 10 hr. The product after extracting with pet. ether was filtered through a column of alumina (grade I, 20 g). The eluate (165 mg), after phosphoric acid washing and working up in the customary manner, afforded eudalene (I, 150 mg), $\lambda_{max}$ 227·5, 279 mμ (log ε 4·5658, 3·3730); picrate m.p. 94° undepressed on admixture with an authentic specimen. (Found: C, 57·81; H, 4·98; N, 10·1. $C_{20}H_{19}O_7N_3$ requires: C, 58·11; H, 4·63; N, 10·17%).

### *Preparation of dihydro-β-agarofuran*

β-Agarofuran (304 mg) dissolved in glacial acetic acid (20 ml) was stirred in an atm. of hydrogen with pre-reduced Adams $PtO_2$ catalyst (50 mg). The equivalent of 0·98 mole hydrogen was absorbed in 30 min. The catalyst was filtered and solvent was removed *in vacuo* to furnish dihydro-β-agarofuran (270 mg) which on chromatography over 100 fold amount of alumina (grade I, 2·7 g) followed by distillation gave the analytical specimen, b.p. 135° at 8 mm, $n_D^{29}$ 1·4910, $[\alpha]_D^{30}$ −76·07° (*c*, 8·29); no coloration with tetranitromethane; I.R. bands at: 1379, 1359, 1155, 1144, 1114, 1089, 1062, 1015, 998, 980, 952, 887, and 869 cm$^{-1}$; no band at 1639 and 898 cm$^{-1}$. (Found: C, 81·32; H, 12·05. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%).

### *Ozonolysis of β-agarofuran*

β-Agarofuran (266 mg) in chloroform (50 ml) was ozonized for 2 hr at 0°. The solvent was distilled off and the residue steam distilled for a short time into dimedone solution. The steam distillate on standing in the freeze overnight gave formaldimedone (176 mg, equivalent to 0·5 mole of $>C{=}CH_2$ grouping), m.p. 187°, undepressed on admixture with an authentic specimen. No acetone was detected.

The non-volatile portion was taken up in ether and worked up in the customary manner to yield the neutral product (180 mg). This was purified by chromatography over alumina (grade II, 10 g), eluted with benzene (50 ml) followed by distillation to give keto-oxide (VII, 122 mg), b.p. 145° at 4 mm, $n_D^{28}$ 1·4946, $[\alpha]_D^{30}$ −69·2° (*c*, 6·9), I.R. bands at: 1712, 1418, 1379, 1361, 1295, 1229, 1149, 1140, 1110, 1092, 1067, 1013, 888 and 875 cm$^{-1}$; negative haloform reaction (Found: C, 75·98; H, 10·40. $C_{14}H_{22}O_2$ requires: C, 75·63; H, 9·97%). Semicarbazone m.p. 195°.

### *Treatment of dihydro-β-agarofuran* (XXXI) *with borontrifluoride ethereate in acetone*

Freshly distilled borontrifluoride ethereate (1 ml) was added to a solution of dihydro-β-agarofuran (500 mg) in dry acetone (20 ml) and kept at room temp for 48 hr. Addition of ice cold water (10 ml) and working up in the customary manner furnished a hydrocarbon (430 mg) which was further purified by chromatography over alumina (grade I, 43 g, elution by 50 ml of pet. ether) followed by distillation to afford diene (VIII, 360 mg), b.p. 120° at 8 mm., $n_D^{31}$ 1·5170, $[\alpha]_D^{30}$ $-188°$ ($c$, 2·18), $\lambda_{max}$ 241, 247, 256 m$\mu$ ($\varepsilon$, 28140, 28540, 16700); I.R. bands at: 2900, 1645 (w), 1620, 1389, 1379, 1355, 1299, 1270, 1215, 1174, 1066, 1034, 995, 953, 877, and 804 cm$^{-1}$. (Found: C, 87·86; H, 11·9. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

### *Dehydration of maaliol* (IX) *to the diene* (VIII)

Maaliol (1 g) was dissolved in anhydrous formic acid (10 ml) and the mixture heated on the steam bath for 5 hr. The material was then poured on ice-water and the hydrocarbon extracted with pet ether. The organic layer was washed repeatedly with aqueous sodium bicarbonate solution and water and after drying it was filtered through a column of alumina (grade I, 20 g) and eluted with pet. ether.

After the solvent had been removed by evaporation the residue was distilled to furnish diene (VIII, 508 mg), b.p. 118–120° at 8 mm, $n_D^{31}$ 1·5169, $[\alpha]_D^{30}$ $-191°$ ($c$, 2·85), $\lambda_{max}$ 241, 247, 256 m$\mu$ ($\varepsilon$, 18870, 19900, 13000), I.R. bands at: 2900, 1645 (w), 1620, 1385, 1375, 1295, 1270, 1215, 1175, 1065, 1030, 995, 955, 876 and 805 cm$^{-1}$. (Found: C, 87·80; H, 12·0. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

### *Dehydration of β-eudesmol* (XII) *to the diene* (X)

To a solution of β-eudesmol (2·5 g) in glacial acetic acid (25 ml) perchloric acid (1 ml, 60%) was added. The reaction mixture was allowed to stand at room temp (25–27°) for 72 hr with continuous stirring. The reaction product was diluted with a large excess of water and extracted with ether. The ethereal extract was washed with aqueous sodium bicarbonate, then with water and dried ($Na_2SO_4$). The solvent was removed and the residue (2·29 g) was taken up for further purification by chromatography over alumina (grade I, 100 g), followed by distillation to furnish analytically pure diene (X, 1·9 g), b.p. 105–110° at 1 mm, $n_D^{31}$ 1·5172, $[\alpha]_D^{30}$ $+265·5°$ ($c$, 6·5), U.V. spectrum: $\lambda_{max}$ 240, 247, 256 m$\mu$ ($\varepsilon$, 31110, 32045, 18615), I.R. bands at: 2900, 1645 (w), 1618, 1385, 1372, 1332, 1290, 1266, 1222, 1209, 1171, 1156, 1112, 1060, 1029, 995, 953, 915, 876, and 803 cm$^{-1}$. (Found: C, 87·85; H, 12·05. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

### *Reduction of β-agarofuran* (XX) *with lithium in ethylenediamine*

To a stirred solution of β-agarofuran (400 mg) in anhydrous ethylenediamine (25 ml), lithium (150 mg) was added during 1·5 hr, at a temp of 90–100° in an atm. of anhydrous oxygen free nitrogen. After all of the lithium had been added the mixture was refluxed for 12 hr. The product was then cooled in ice and carefully decomposed by addition of an adequate quantity of water and repeatedly extracted with ether. The combined organic layer was washed with dil. hydrochloric acid, sodium bicarbonate solution, then with distilled water, dried ($Na_2SO_4$), filtered and solvent removed to furnish a viscous residue (360 mg). This was chromatographed over 50 fold alumina (grade II, 18 g, elution with 50 ml benzene) to furnish alcohol (XIII, 300 mg). The alcohol on distillation afforded analytical specimen (241 mg), b.p. 115–120° at 0·3 mm, $n_D^{25}$ 1·5045, $[\alpha]_D^{28}$ $+10·33°$ ($c$, 4·55); no coloration with tetranitromethane, I.R. bands at: 3480, 1136, and 933 cm$^{-1}$ (Found: C, 80·50; H, 12·26 $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%).

### *Preparation of hydrocarbon* (XIV)

(i) Benzoyl chloride (0·1 ml) was added to the solution of alcohol (XIII, 80 mg) in pyridine (0·5 ml) and the mixture kept at room temp for 24 hr and then heated for 2 hr on water bath. After working up the product in the customary way, furnished the benzoate (65 mg), which was chromatographed over alumina (grade II, 5 g) to furnish benzoate (54·6 mg); I.R. bands at: 1721, 1600, 1580, 1383, 1366, 1314, 1282, 1171, 1111, 1067, 1027, 807 and 710 cm$^{-1}$ (characteristic bands for benzoate 1721, 1600, 1580, 1282 and 710 cm$^{-1}$).

(ii) The pyrolysis of benzoate (50 mg) was carried out under a press. of 100 mm and at a temp 200–210° for 15 min. The pyrolysed product was dissolved in pet. ether (2 ml) and transferred to a column of alumina (grade I, 1 g) and eluted with pet. ether (10 ml). After removing the solvent, it afforded hydrocarbon (XIV, 6·8 mg) which was sufficient for I.R. spectrum and showed bands at 2874, 1634, 1439, 1362 and 887 cm$^{-1}$.

### *Dehydrogenation of α-agarofuran* (XXII) *with Se*

α-Agarofuran (211 mg) mixed with Se (220 mg) was dehydrogenated and processed following the procedure as employed in the case of β-agarofuran to furnish eudalene (I, 150·8 mg), characterized through its picrate m.p. and mixed m.p. with an authentic sample, 94° (Found: C, 57·90; H, 4·90; N, 10·38. $C_{20}H_{19}O_7N_3$ requires: C, 58·11; H, 4·63; N, 10·17%).

### *Dihydro-α-agarofuran*

α-Agarofuran (780 mg) dissolved in glacial acetic acid (25 ml) was stirred in an atm. of hydrogen with pre-reduced Adams $PtO_2$ catalyst (50 mg). The hydrogen (100 ml, 1·05 mole) was absorbed in 3 hr. The catalyst was filtered and solvent was removed *in vacuo* to furnish dihydro-α-agarofuran (710 mg), which on chromatography over alumina (grade I, 72·0 g), followed by distillation gave the analytical specimen (680 mg); b.p. 135° at 8 mm, $n_D^{27}$ 1·4923, $[\alpha]_D^{28}$ −60·8° (*c*, 6·045); no coloration with tetranitromethane; I.R. bands at: 1389, 1370, 1307, 1236, 1217, 1155, 1149, 1119, 1075, 1049, 1025, 1002, 963, 925, 888 and 872 cm$^{-1}$, no band at 1653 and 838 cm$^{-1}$. (Found: C, 81·13; H, 11·75. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%).

### *Treatment of dihydro-α-agarofuran with borontrifluoride ethereate in acetone*

Freshly distilled borontrifluoride ethereate (1·0 ml) was added to a solution of dihydro-α-agarofuran (320 mg) in acetone (15 ml) and kept at room temp for 48 hr. Addition of ice cold water (10·0 ml) and working up the product in the customary manner furnished the viscous material (280 mg), which was purified by chromatography over alumina (grade I, 30 g, elution with 30 ml pet. ether) followed by distillation to afford diene (VIII, 190 mg), b.p. 115–120° at 8 mm, $n_D^{30}$ 1·5173, $[\alpha]_D^{30}$ −182° (*c*, 3·72), U.V. spectrum: $\lambda_{max}$ 241, 247, 256 mμ (ε, 18826, 19605, 14312), I.R. bands at: 2900, 1645 (w), 1623, 1389, 1379, 1353, 1295, 1270, 1217, 1175, 1066, 1033, 994, 952, 877 and 806 cm$^{-1}$. (Found: C, 87·82; H, 12·05. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

### *Prolonged hydrogenation of α-agarofuran* (XXII)

α-Agarofuran (800 mg) dissolved in glaical acetic acid (25 ml) was stirred in an atm. of hydrogen with pre-reduced Adams $PtO_2$ catalyst (40 mg), with absorption of hydrogen (170 ml, 1·78 mole) in 72 hr. The catalyst was filtered off and the solvent was removed *in vacuo*, on a steam bath. The residue (720 mg) was chromatographed over alumina (grade II, 72 g). Pet. ether (50 ml) and benzene (125 ml) eluted two fractions: Fraction A (100 mg); Fraction B (511 mg).

*Fraction* A. On distillation furnished dihydro-α-agarofuran, b.p. 135° at 8 mm, $n_D^{27}$ 1·4921, $[\alpha]_D^{28}$ −60·02° (*c*, 2·5), with characteristic I.R. spectrum as previously described. (Found: C, 81·35; H, 11·82. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%).

*Fraction* B. On distillation gave a mixture of alcohols (XXIII) and XXIV, 408 mg); b.p. 115–117° at 0·3 mm, $n_D^{26}$ 1·5020, $[\alpha]_D^{30}$ −1·38° (*c*, 2·88); no coloration with tetranitromethane, I.R. bands at 3500(s), 2933, 1451, 1381, 1284, 1250, 1151(s), 1032, 985, 945 and 935 cm$^{-1}$ (Found: C, 80·05; H 12·27. $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%).

### *Preparation of hydrocarbon* (XXV, XXVI) *from alcohol* (XXIII, XXIV)

(i) Benzoyl chloride (0·2 ml) was added to a solution of alcohol (200 mg) in pyridine (1·0 ml) and the mixture kept at room temp for 24 hr and then heated for 2 hr on a water bath. The product was worked up in the customary manner to furnish a viscous benzoate (180 mg), which showed the following I.R. spectrum: 1721, 1600, 1581, 1384, 1364, 1313, 1282, 1172, 1111, 1066, 1025, 807 and 709 cm$^{-1}$ (characteristic bands for benzoate 1721, 1600, 1581, 1282 and 709 cm$^{-1}$).

(ii) The pyrolysis of the benzoate (150 mg) was carried out under a press. of 100 mm and at 200–210° for 15 min. The pyrolysed product was dissolved in pet. ether (5 ml) and transferred to a column of alumina (grade I, 7 g) and eluted with 50 ml pet. ether. After removal of solvent followed by distillation over sodium afforded the mixture of hydrocarbons (XXV and XXVI, 70 mg); b.p. 140–145° at 2 mm, $n_D^{25}$ 1·4998; yellow coloration with tetranitromethane; I.R. bands at: 2950, 1653, 1637, 1462, 1389, 1271, 1174, 1111, 1038, 891, and 811 cm$^{-1}$. (Found: C, 87·22; H, 12·82. $C_{15}H_{26}$ requires: C, 87·30; H, 12·70%).

### *Preparation of epoxide* (XXVII) *of α-agarofuran*

To α-agarofuran (530·7 mg) dissolved in chloroform (5 ml) 10 ml of perbenzoic acid (0·6 N approx.) was added and the mixture kept at 0° for 24 hr; perbenzoic acid equivalent to 0·9 double bonds was absorbed. The product was neutralized with sodium bicarbonate solution, washed with water, dried ($Na_2SO_4$) and the solvent removed. The residue (519 mg) was viscous, which on chromatography over alumina (grade II, 20 g, elution with 50 ml benzene) afforded a white crystalline epoxide (XXVII, 508 mg), m.p. 88°. It was further purified by sublimation (90° at 0·4 mm) but the m.p. could not be raised further; $[\alpha]_D^{30}$ $-39{\cdot}6°$ (*c*, 4·09); I.R. bands at: 1389, 1370, 1309, 1287, 1241, 1160, 1144, 1121, 1089, 1067, 1058, 1049, 1024, 970, 961, 930, 898, 882, 844, 828, 808, 780 and 759 $cm^{-1}$ (Found: C, 75·90; H, 10·00. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%).

### *Treatment of epoxide* (XXVII) *with borontrifluoride ethereate in acetone*

Freshly distilled borontrifluoride ethereate (1·0 ml) was added to a solution of epoxide (415 mg) in acetone (25 ml) and kept for 60 hr at 0°. Addition of ice cold water (10 ml) and working up the product in the customary manner furnished a viscous material (390 mg) showing U.V. spectrum: $\lambda_{max}$ 297 m$\mu$ ($\varepsilon$, 1427). The viscous material was carefully chromatographed over alumina (grade II, 17·0 g). Pet. ether (50 ml), benzene (50 ml) and ether (25 ml) eluted three fractions A (60 mg), B (100 mg) and C (180 mg) respectively.

*Fraction* A was further purified by chromatography over alumina (grade II, 2 g) and distillation to give the keto-oxide (XXVIII, 49 mg); b.p. 150° at 4 mm, $n_D^{26}$ 1·4995; $[\alpha]_D^{29}$ $-53{\cdot}6°$ (*c*, 0·84); I.R. spectrum bands at: 2933, 1712, 1456, 1420, 1383, 1377, 1304, 1279, 1235, 1111, 1076, 1047, 1015, 961 and 889 $cm^{-1}$; no absorption in the U.V. spectrum. (Found: C, 75·99; H, 10·45. $C_{15}H_{24}O_2$ requires C, 76·22; H, 10·24%). Semicarbazone m.p. 210°.

*Fraction* B was a yellowish viscous material, which showed U.V. absorption at $\lambda_{max}$ 300 m$\mu$ ($\varepsilon$, 4934). It was further purified by chromatography over alumina (grade II, 5·0 g, elution with 30 ml of benzene) to give impure (−)-β-cyperone (XXIX, 25%); $n_D^{28}$ 1·5524, $[\alpha]_D^{29}$ $-164{\cdot}2°$ (*c*, 0·335), $\lambda_{max}$ 300 m$\mu$ ($\varepsilon$, 6774); I.R. bands at: 2950, 1667, 1618, 1458, 1425, 1389, and 1362 $cm^{-1}$. Due to paucity of material further purification was not attempted.

*Fraction* C was a white solid, which on crystallization from hot pet. ether gave crystals m.p. 172°. The crystalline material was further purified by vacuum sublimation and two crystallizations from ethyl acetate to furnish needle shape crystals of diol-oxide (XXX, 80 mg) having a constant m.p. 176°, which could not be raised by further crystallizations; $[\alpha]_D^{30}$ $-40{\cdot}6°$ (*c*, 0·32), no absorption in U.V. spectrum, I.R. bands at: 2976, 1473, 1431, 1397, 1389, 1316, 1295, 1235, 1140, 1106, 1089, 1075, 1038, 1015, 983, 962, 945, 933, 909 and 881 $cm^{-1}$. (Found: C, 70·84; H, 10·51. $C_{15}H_{26}O_3$ requires: C, 70·83; H, 10·30%).