INVESTIGATION ON ESSENTIAL OILS

A
THESIS
SUBMITTED TO
THE UNIVERSITY OF POONA
for
THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN CHEMISTRY

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by

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POONA 8

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INTRODUCTION

Indian subcontinent is rich in diversified flora, many of which yield essential oils. Amongst the various essential oils produced in India[1] vetiver oil obtained by steam distillation of roots of vetiver grass (*Vetiveria zizanioides* Linn.) is of commercial importance. It is used as a fixative in the blending of perfumes for the manufacture of soaps and many other cosmetics[2].

In India, vetiver oil is popularly known as 'khus' and as a perfume 'khus' has been too well known to the Indians since long time[3].

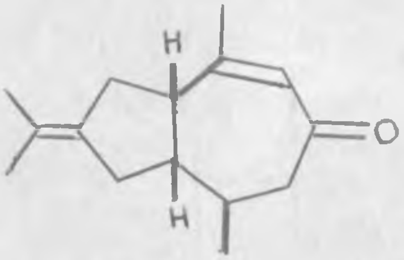
Vetiver grass occurs in wild, semi-wild and cultivated form[2]. In its wild state it is found to grow on slopes of the Himalaya mountains, in parts of India, Ceylon and Malaya. It is cultivated extensively in Java, Reunion Islands, Brazil, Seychelles Islands, Mexico, Central America (Honduras and Guatemala), Belgian Congo and many other sub-tropical countries. In Haiti (West Indies) it grows semi-wild.

In India the grass grows wild in the forests of Uttar Pradesh, Punjab, Bharatpur and parts of Assam and in a semiwild state in Assam, Bihar, Orissa, Hyderabad and Mysore states[3]. In North India there are several important regions which produce vetiver oil namely Bharatpur, Musanagar, Nawabganj and Utarpura. The tillering habit of the grass and scattering of the seeds due to winds have resulted in large scale natural propagation of the plant. Vetiver has also been cultivated as a crop in Kerala state, in east Godavari and Kurnool districts of Andhra Pradesh and in Yellankur district of Madras state.

The oil obtained from the roots of wild origin of North Indian regions is laevorotatory whereas the oil from the roots of cultivated origin from South India is dextrorotatory[4]. The physicochemical properties of South Indian oil are somewhat comparable with those of Java and Reunion Islands. A systematic chemical examination such as isolation and characterisation of the different constituents of vetiver oil from the important regions of India was, therefore, thought to be very desirable. This work was assigned to the Essential Oils Division of the National Chemical Laboratory by the Essential Oils Research Committee of C.S.I.R. New Delhi.

Present knowledge of constituents of Vetiver Oil :

Most important and pioneering work on the chemistry of the constituents of vetiver oil was done by Pfau and Plattner[5]. They isolated the two isomeric ketones, α- and β-vetivones $C_{15}H_{22}O$, from Java and Reunion vetiver oils through their semicarbazones. From a consideration of the optical inactivity of tetrahydro-β-vetivone, tetrahydro-β-vetivol and the ozonolytic cleavage product, hydroxyketone $C_{12}H_{20}O_2$ and different derivatives of these products, Pfau and Plattner[6] concluded that there is a plane of symmetry in the molecule running through the isopropylidene group and that the ring fusion is cis. Naves and Perrottet[7] confirmed the molecular formula and the structure suggested by Pfau and Plattner. By comparison of physical properties and examination of Raman spectra of the two ketones, α-vetivone, m.p. 51.5° and β-vetivone, m.p. 44.5°, Naves and Perrottet concluded that the two ketones differed in configuration at C_4 and that the probable structures for α and β-vetivones would be (1) and (2) respectively.



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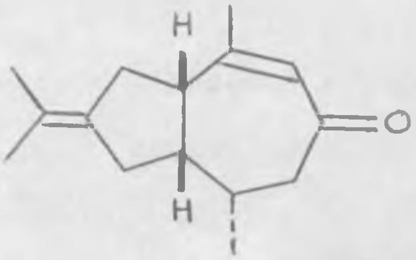

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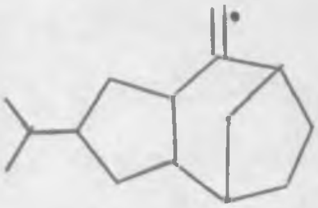
Other workers namely, Ruzicka, Capato and Huyser[8], Pfau and Plattner[5] and Sabetay and Trabaud[9], have reported the presence of bicyclic, tricyclic, primary, secondary and tertiary sesquiterpene alcohols but structures of these compounds have not been established.

Chiurdoglu and Tullen[10] isolated a hydrocarbon, $C_{15}H_{24}$, tricyclovetivene from Belgian Congo vetiver oil and structure (3) was assigned to it, mainly on the basis of degradative experiments.



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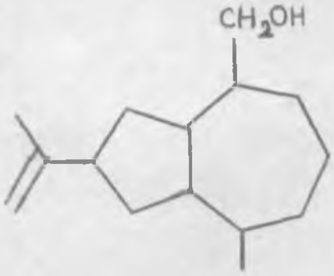

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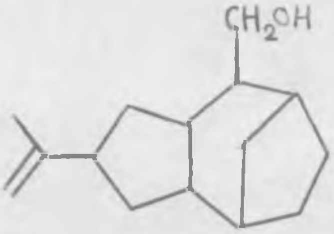

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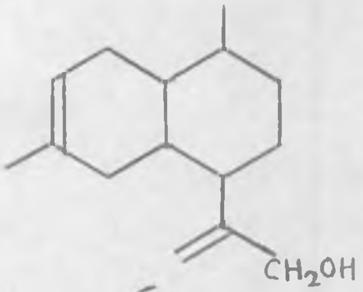
Chiurdoglu and Decot[11] have assigned structures to bicyclovetiverol (4) and tricyclovetiverol (5) though only tricyclovetiverol, $C_{15}H_{24}O$, appears to have been isolated.

Herout and Romanuk[12] isolated α- and β-vetivones and prepared fully reduced hydrocarbons vetivane and isovetivane from the ketones. They also isolated a series of hydrocarbons namely, tricyclovetivene, $C_{15}H_{24}$, bicyclic α- and β-isovetivenenes, and α- and β-vetivenenes with molecular formulae $C_{15}H_{22}$, dehydrovetivenene, $C_{15}H_{20}$, and zizanene, $C_{15}H_{24}$, from Java vetiver oil. The infrared spectra of saturated hydrocarbons of α- and β-vetivenenes were found to be identical with vetivane, the saturated hydrocarbon obtained by reduction of α-vetivone. The infrared spectra of hexahydroderivatives of α-isovetivenene and β-isovetivenene were identical with isovetivane, the product of total reduction of β-vetivone.

<u>Indian Vetiver Oil</u> :

From the North Indian Bharatpur vetiver oil, a new primary sesquiterpene alcohol khusol, $C_{15}H_{24}O$, m.p. 101-102°, was isolated and characterised by Bhattacharyya and coworkers as represented by structure (6).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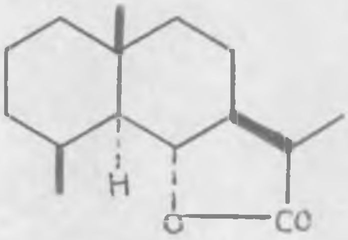
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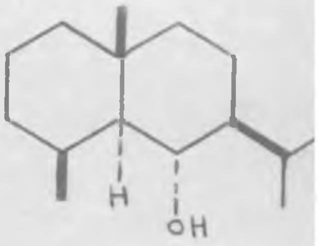
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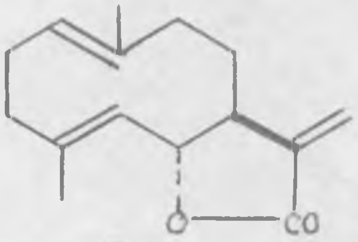
Recently from North Indian Moosanagar vetiver oil a new secondary sesquiterpene alcohol, $C_{15}H_{26}O$, m.p.65° ($[\alpha]_D^{25}$-57°) was isolated in this laboratory by Bhattacharyya and coworkers[14]. On systematic chemical examination, it was found to be an optical antipode of junenol, $C_{15}H_{26}O$, m.p. 63°, ($[\alpha]_D^{20}$+ 59°) isolated by Šorm and coworkers from juniper oil and was therefore named as laevojunenol (12). Dihydrojunenol (8) m.p.115° ([α] ± 0), was synthesised from santanolide 'C' (7). It gave a melting point depression on admixture with dihydrolevojunenol. The absolute configurations of junenol (11) and laevojunenol (12), were determined by Bhattacharyya and coworkers[15] by the synthesis of junenol from the lactone (10) which was obtained from costunolide[16] (9) by partial hydrogenation and cyclisation in acidic medium.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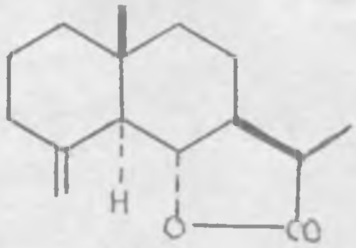
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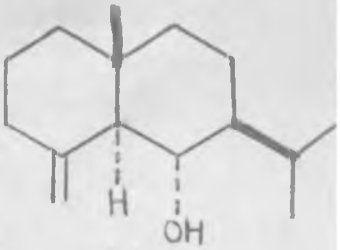
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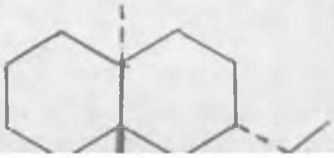

Present Investigation :

In the present investigation, South Indian vetiver oil of cultivated origin (Kerala, South India) and North Indian vetiver oils of Bharatpur and Biswan area were systematically examined for isolation and characterisation of the constituents.

The dextrorotatory South Indian oil is composed of sesquiterpene hydrocarbons, ketones, alcohols and esters. Four new hydrocarbons have been isolated from this oil. Isolation and elucidation of structures of two of these hydrocarbons (A) and (B) have been described in Chapters 1 and 2 of the present thesis.

In Chapter 3 following work has been incorporated :
(i) isolation and partial characterisation of a new tricyclic azulenic hydrocarbon $C_{15}H_{24}$ (C), possessing guaiane type of carbon skeleton,
(ii) isolation and characterisation of a new hydrocarbon $C_{15}H_{22}$ (D), probably with eudesmane carbon skeleton and with three double bonds, two of which are in conjugation and
(iii) isolation and partial characterisation of a new tricyclic secondary sesquiterpene alcohol, $C_{15}H_{24}O$ (E). The alcohol (E) does not possess normal type of carbon frame work encountered in sesquiterpenes such as the substituted napthalenic or azulenic type, but indicated the presence of a carbon skeleton containing fused five and six membered rings.

In Chapter 4, elucidation of structure and absolute configuration of Khusinol, a crystalline secondary alcohol isolated from Bharatpur and Biswan varieties of vetiver oil has been described.

Cadinenes and Cadinols :

Since many of the products isolated from vetiver oil by us possess cadinane skeleton (13), chemistry of compounds belonging to this group is briefly reviewed below.

The term cadinene is generic and is applied to those group of sesquiterpene hydrocarbons and tertiary alcohols which yield crystalline (-)-cadinene dihydrochloride m.p. 118°. (23). There is also a group of compounds, which yield (±) cadinene dihydrochloride m.p. 105-106° and yet another group which yield (+)-cadinene dihydrochloride m.p. 118°. All these compounds give cadalene on dehydrogenation.

β-Cadinene was isolated from the oil of Cubebs (*Piper cubeba* L.) by Soubeiran and Capitaine[17] in 1840, through the crystalline dihydrochloride. Its constitution was not fully established until 1942, when Campbell and Soffer[18] unambiguously labelled the positions of double bonds in the Cadinane skeleton* (13) and expressed its formula as in (14).

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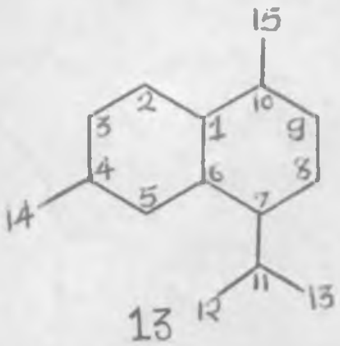
* The numbering of carbon atoms is according to Barton and coworkers[19], which was followed by Herout and Romanuk[20] for the cadinanic compounds.



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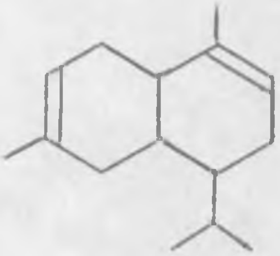
Later on other hydrocarbons with the same carbon framework (13) but differing only in positions of two double bonds were isolated from different essential oils. There are nine theoretically possible isomers (14-22) having double bonds attached to C_4 and C_{10}, capable of yielding the same cadinene dihydrochloride (23).



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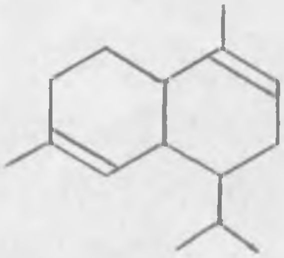

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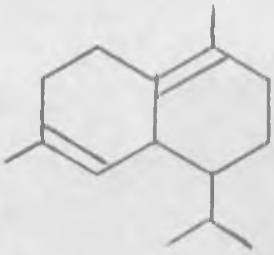

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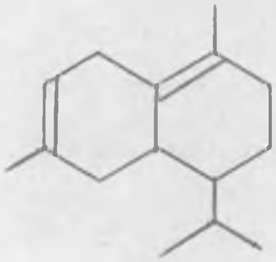

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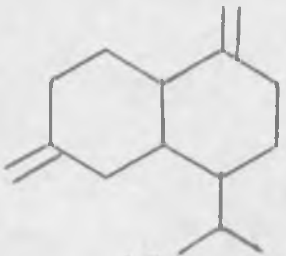

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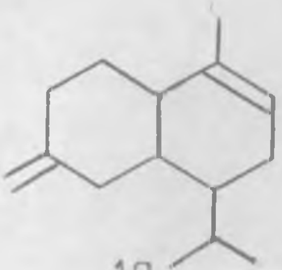

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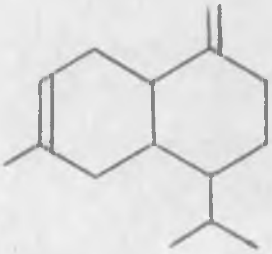

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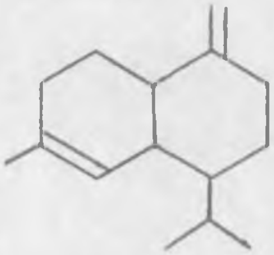

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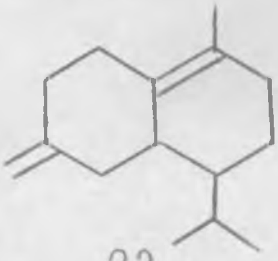

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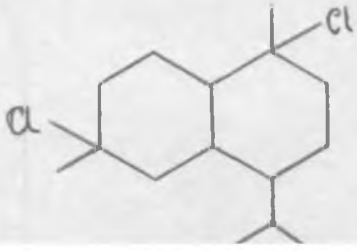
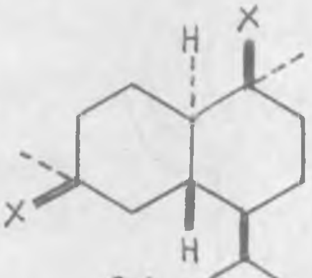


α-Cadinene (15) is not known so far. β-Cadinene (14) is widely distributed in nature. γ-Cadinene (21) is known to be present in citronella oil[21,22]. δ-cadinene (16) occurs in the oil of ylang-ylang[23], citronella[22,24], sweet flag[25] and oil of false cubebs[26]. It gave a crystalline diepoxide, m.p. 84°.5. Herout and his coworkers[27] gave evidence for structure (16) on the basis of failure of Grignard reagent and methyl-lithium to add to the diepoxide; the two double bonds were therefore assigned sterically hindered positions as in (16) consistent with the infrared spectrum and formation of cadinene dihydrochloride (23). ε-Cadinene (18) was isolated from the oil of ylang-ylang[23], which on ozonization gave two moles of formaldehyde and a crystalline diketone, m.p. 113°. γ_1-Cadinene (19) has been isolated by Bhattacharyya and coworkers[28,29] from Malabar lemon-grass oil. Sukh Dev and Guha[30] demonstrated the presence of γ_1-cadinene (19) and ε-cadinene (18) in the oil from oleoresin of Hardwickia pinata. Recently γ_2-cadinene (20) has also been isolated in this laboratory by Bhattacharyya and coworkers[31] from Biswan and Bharatpur vetiver oils.

The isolation of β, γ, δ, ε, γ_1 and γ_2 cadinenes has proved the existence of six isomers of cadinenes.

Stereochemistry of Cadinenes and Cadinols :

Stereochemistry of cadinenes and cadinols is now known through X-ray diffraction analysis of the crystalline cadinene dihydrochloride (m.p. 118°, $[\alpha]_D^{25}$-36°) and cadinene dihydrobromide (m.p. 124°, $[\alpha]_D^{20}$-36°). All isomers which yield the same (-)-cadinene dihydrochloride or dihydrobromide must possess the same configuration at asymmetric carbon atoms 1, 6 and 7 of cadinane (13) skeleton, since these centres are not involved during the course of preparation of this derivative. X-Ray diffraction analysis was carried out by Hanic[32], who represented the steric structure of cadinene dihydrobromide by (24b) or its mirror image, where the two rings are trans fused, the three alkyl groups are equatorial and the two halogens are axial and lie on the same side of the molecule.



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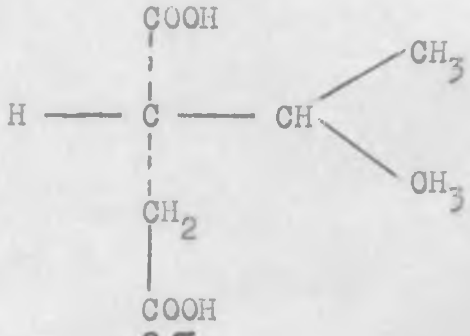
(a) X = Cl

(b) X = Br



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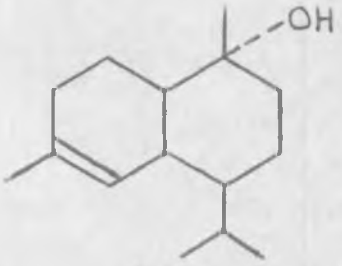
In order to establish the absolute configuration of all centres, it was necessary to establish the absolute configuration of only one of the asymmetric centres C_1, C_6 or C_7. A chemical proof in favour of configuration (24) was put forward by Šorm and coworkers[33], by isolating D-(+)-isopropyl succinic acid (25) of known configuration[34], amongst the degradation products of pure β-cadinene by concentrated nitric acid. The results of dipole moment measurements[35] are also in accordance with structure (24).

Further support in favour of configuration (24) was obtained by the application of optical rotatory dispersion. Sǒrm and coworkers[36] had isolated two crystalline ketones during the course of investigation of the structure of α-cadinol. α-Cadinol m.p. 74°.5 (26) isolated form juniper oil, on treatment with perphthalic acid gave a mixture of oxidoalcohols (27), the predominent isomer of which on reduction with lithium aluminium hydride gave a crystalline diol m.p. 214-216° (28). The diol on chromic acid oxidation gave the ketoalcohol m.p. 109°.5 (29). The dehydration of dihydro-α-cadinol (30) by thionylchloride and pyridine afforded a mixture of hydrocarbons, containing 50% of the hydrocarbon (31), which on ozonolysis gave the ketone, m.p. 73°.5 (32).



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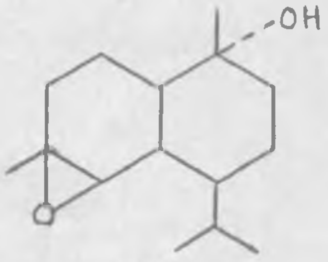

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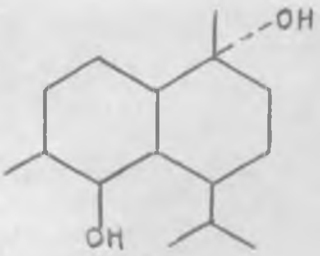

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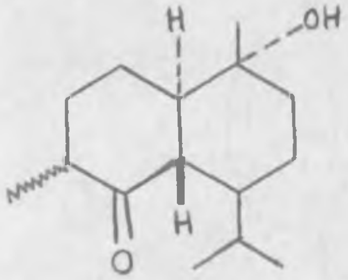

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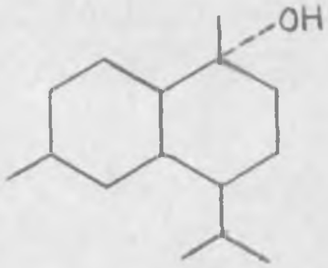

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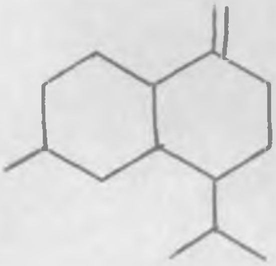

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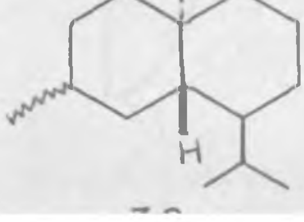
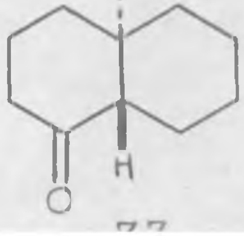
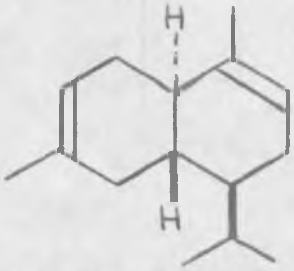


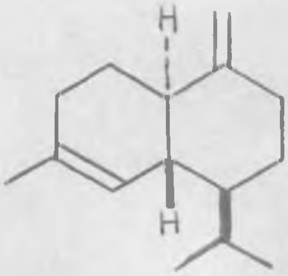


The rotatory dispersion curves of the two ketones (29 & 32) are of antipodal type. The curve of the hydroxy-ketone (29) is of the same type as that of synthetic 9-methyl-trans-decal-4-one[37] with known absolute configuration as represented in (33). The absolute configuration of the ketones can therefore be represented as in the formulae (29 & 32).

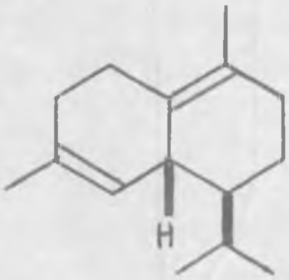
Thus x-ray diffraction analysis, chemical methods of degradation and conclusions from optical rotatory dispersion studies of the ketones (29 & 32) are all in agreement with the configuration (24a) assigned to cadinene dihydrochloride. These findings permit the assignment of configurations to β (34), γ (35), δ (36) and ϵ (37) - cadinenes.



(–)-β-Cadinene (34)



(+)-γ-Cadinene (35)



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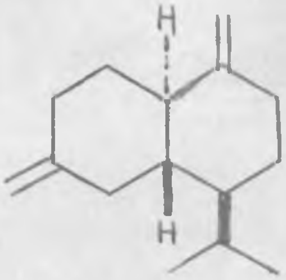
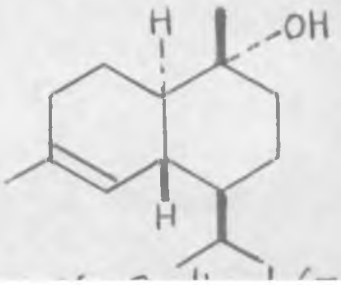


(+)-ϵ-Cadinene (37)

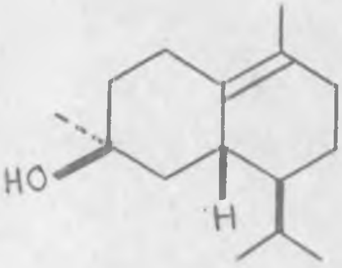


Cadinols :

Of the twelve theoretically possible cadinols which can give rise to (-)-cadinene dihydrochloride, only three isomers so far have been found in nature. α-Cadinol m.p.74°.5 was isolated by Plattner and Markus[38] from Java citronella oil. It was later on found to be present in the oil of Juniperus communis L. and its structure was determined by Šorm and coworkers[36] and Soffer and his collaborators[39] simultaneously and independently, as expressed in (38). Its absolute configuration is also known since it gives (-)-cadinene dihydrochloride; the hydroxy group is assigned α-equational orientation from its ease of esterification and mode of dehydration.

A crystalline alcohol, m.p. 135°, was isolated by Haagen-Smit and coworkers[40] from the heavy oil fraction of Pinus albicaulis and was named as albicaulol. Albicaulol was also found to be present in the oleoresin of Pinus armandi[41] and in the heartwood of Chamaecyparis lawsoniana[42]. Erdtman and coworkers[43] isolated a crystalline cadinol m.p. 139-140° from the conifer Pilgerodendron uviferum. (D.Don) Florin, which they named as pilgerol. The same cadinol was also found to be present in the oil of Juniperus communis, and Šorm and coworkers[36] named it as δ-cadinol, as it showed the presence of a tetrasubstituted double bond (873 cm^{-1}) and structure (39) was suggested to it.

Anderson and coworkers[44] proved the identity of albicaulol and δ-cadinol, and revised the structure of δ-cadinol, as in (40) on the basis of N.M.R. spectrum of δ-cadinol and of O.R.D. curve of the saturated ketone (41). He further suggested that the name δ-cadinol should be abandoned since it no longer contained a tetrasubstituted double bond. The hydroxy group is assigned β-axial orientation since it is difficult to esterify.



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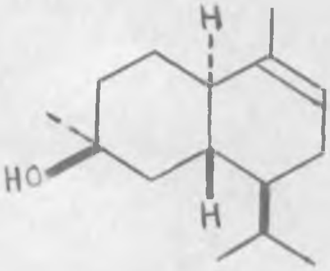

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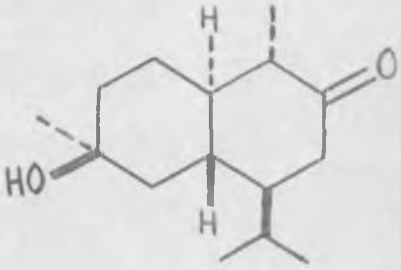

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Another cadinol, m.p. 79°, was isolated by Šorm and coworkers[36] from the oil of Juniperus communis and its structure is being investigated.

The second class of compounds which yield optically inactive cadinene dihydrochloride has long been known. The wood oil of Dysoxylon frazeranum Benth was examined by Penfold[45]. He reported that the sesquiterpene fraction of the oil yielded an optically inactive dihydrochloride. Hellyer and McKern[46] from the same oil prepared the (±) dihydrochloride m.p.105-106° and proved that it was the racemic form of cadinene dihydrochloride, m.p. 119°. The optically inactive sesquiterpene regenerated from (±) cadinene dihydrochloride m.p. 105-106° was named by them as dsysoxylonene.

(±)-Cadinene dihydrochloride m.p. 105-106°, was also obtained from a sesquiterpene fraction of oil of Lantana camara L. named as micranene, by Kafuku and coworkers[47] and Sebe[48]. Sutherland and Hildebrand[49] conclusively proved that dysoxylonene is optically inactive δ-cadinene from degradation experiments and from complete identity of I.R. spectrum of (±) dysoxylonene diepoxide (m.p. 86-87°) and of δ-cadinene diepoxide (m.p. 84°.5, $[\alpha]_D^{20}$ + 13°).

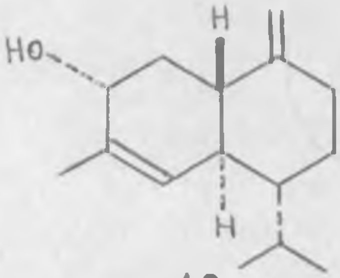
The third class of compounds which yield (+)-Cadinene dihydrochloride (m.p. 118°, $[\alpha]_D^{25}$ + 36°) at present comprises of only a few compounds. These compounds are antipodal to cadinenes and cadinols yielding (-)-cadinene dihydrochloride (m.p. 118°, $[\alpha]_D$ - 36°) described earlier.

The oldest known examples were reported by Grimal[50] in 1902, who prepared (+)-cadinene dihydrochloride (m.p. 118°) from a fraction of Atlas Cedar oil and by Penfold[51] from leaf oil of Eriostemon coxii, Muell. From a sesquiterpene fraction (which was about 95%) of essential oil of Metrosideros scandens, Gardner[52] had obtained (+)-cadinene dihydrochloride (m.p. 119°, $[\alpha]_D$ + 30°). It depressed the melting point of (-)-cadinene dihydrochloride; and from the melting point curve Gardner concluded that the (+)-cadinene dihydrochloride obtained by him was an optical antipode of (-)-cadinene dihydrochloride normally obtained from cadinenes. Later on Birch[53] examined the same oil and separated aromadendrene and a sesquiterpene

([α], -80°), which yielded cadalene on dehydrogenation and (+)-cadinene dihydrochloride (m.p. 117°) with dry hydrogen chloride.

Khusinol :

A new, crystalline sesquiterpene alcohol, khusinol m.p. 87° (42), which was recently isolated and characterised by us (Chapter 4) can now be included in this class of compounds. Khusinol appears to be the first secondary alcohol in this group. Khusinol (42) was converted into a hydrocarbon, identified as (-)-γ-cadinene, an enantiomer of (+)-γ-cadinene[22]. (-)-γ-Cadinene obtained from khusinol, yielded (+)-cadinene dihydrochloride (m.p. 117°.5, $[\alpha]_D^{25}$ + 36°.2) and depressed the melting point of (-)-cadinene dihydrochloride. The O.R.D. curves of the two dihydrochlorides also show enantiomeric relationship. Absolute configuration (42) has therefore been assigned to khusinol.



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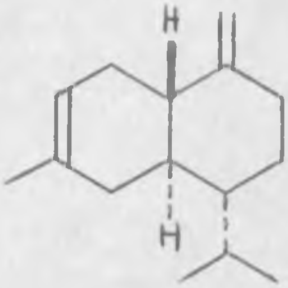

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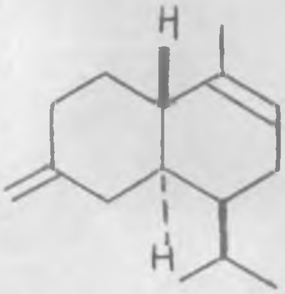

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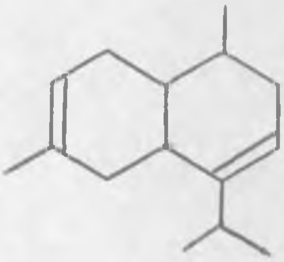
The hydrocarbon γ_2-cadinene[31] (20) recently isolated in this laboratory has also been found to give (+)-cadinene dihydrochloride, and absolute configuration (43) has, therefore, been assigned to it.

It is very interesting to observe that Bharatpur and Biswan varieties of vetiver oil have yielded an alcohol, khusinol (42) and a hydrocarbon γ_2-cadinene (43) which yield (+)-cadinene dihydrochloride. This is very important from biogenetic point of view. Moosanagar variety of vetiver oil has also yielded laevojunenol, an enantiomer of junenol.

γ_1-Cadinene ($[\alpha]_D^{25}$ - 18.°9 (clean)) isolated from Malabar lemongrass oil and characterised by Bhattacharyya and coworkers[28,29] gave cadinene dihydrochloride, m.p. 118°. Its specific rotation, which was not determined at that time has now been found to be + 36.°81. The mixed melting point of (+)-cadinene dihydrochloride derived from khusinol and that obtained from γ_1-cadinene did not show any depression. The O.R.D. curve of (+)-cadinene dihydrochloride from γ_1-cadinene also show enantiomeric relationship with respect to (-)-cadinene dihydrochloride. Absolute configuration (44) can, therefore, be assigned to γ_1-cadinene. Thus it also belongs to the antipodal group.

Isocadinenes and isocadinols :

Besides cadinenes and cadinols, there are several compounds known which possess cadinane skeleton but do not afford crystalline dihydrochloride. These are termed as isocadinenes and isocadinols. Structure (45) has been assigned to isozingiberene by Soffer et al.[54]. During our present investigation we have also isolated from South Indian vetiver oil two new isocadinenes, which have been assigned gross structures (46 and 47). The details are discussed in Chapters 1 and 2 of this thesis.



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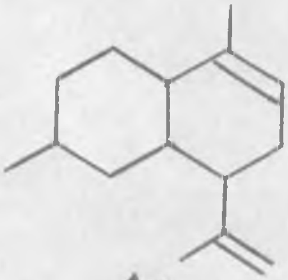

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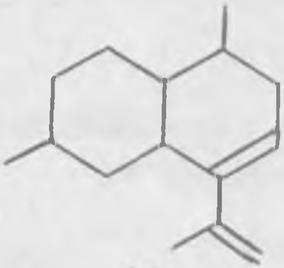

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The primary alcohol khusol[13] (6) may also belong to the group isocadinols. The problem of stereochemistry of isocadinenes and isocadinols still awaits solution.

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CHAPTER - I

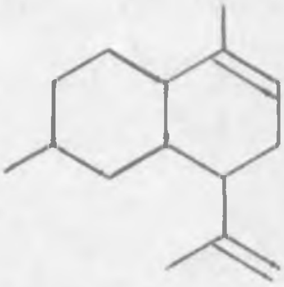
ISOLATION AND CHARACTERISATION OF A NEW SESQUITERPENE HYDROCARBON

HYDROCARBON A

CHAPTER I

SUMMARY

By careful fractionation and elaborate column chromatography over neutral alumina, a new sesquiterpene hydrocarbon, $C_{15}H_{24}$, Hydrocarbon A, with two double bonds has been isolated from the lower boiling hydrocarbon fraction of South Indian vetiver oil. Structure (1) is assigned to it mainly on the basis of its infra-red spectrum, results of dehydrogenation and ozonolysis. The position of the trisubstituted double bond was determined by the labelling method of Campbell and Soffer.



1

Isolation of Hydrocarbon (A)

A genuine sample of vetiver oil (Vetiveria zizaniodides Linn.) supplied by Mr. D.V.Deo of Cochin, obtained by steam distillation of the roots of cultivated variety, was taken up for chemical examination. The crude oil was deep brown in colour. It was dried over anhydrous sodiumsulphate and the last traces of moisture were removed by heating in an oil bath (110°) under water pump suction. The physicochemical properties of the oil were determined after total distillation of the oil under reduced pressure. The oil distilled over a range of 90°-140°/0.3 mm in a yield of 83%. The distilled dextrorotatory oil with a greenish yellow colour was clear and viscous and its properties are described in the experimental.

As a prelude to the isolation of the individual constituents, the distilled oil was separated into two major fractions :

(A) Lower boiling fraction : b.p. 72-98°/0.3 mm, which was mainly rich in sesquiterpene hydrocarbons and

(B) the residue, which mainly comprised of oxygenated constituents and henceforward will be referred to as higher boiling 'Fraction B'.

By fractionation and elaborate column chromatography on neutral alumina of some of the dextrorotatory fractions obtained from the lower boiling fraction, a new sesquiterpene hydrocarbon, Hydrocarbon (A), $C_{15}H_{24}$, containing two double bonds, was isolated in a pure form. It possessed the following physico-chemical constants :

b.p. $94^{\circ}/2$ mm; $[\alpha]_{D}^{25}$ + $68^{\circ}.24$; n_{D}^{30} 1.5033; d_{4}^{30} 0.9030;
$[R_{L}]_{D}$ 65.37; $C_{15}H_{24}\ \sqrt{2}$ requires 66.1
Analysis : Found : C, 88.07; H, 11.90;
$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

Structural features

The infrared spectrum of the hydrocarbon [Fig.1] exhibited strong absorption bands at 891 and 1644 cm^{-1}, characteristic of a methylenic double bond, $\begin{matrix} R_1 \\ R_2 \end{matrix}\!\!>C = CH_2$ and bands at 816 and 1680 cm^{-1} suggestive of a trisubstituted double bond. It did not show any characteristic dienic absorption maximum in the ultraviolet region indicating the absence of conjugation of the methylenic double bond with the trisubstituted double bond.

On dehydrogenation with selenium, the hydrocarbon yielded copious amount of cadalene and a trace of vetivazulene. Cadalene was identified through its picrate and also through its ultraviolet spectrum. Quantitative estimations with perbenzoic acid after different intervals of time indicated the presence of two double bonds in the molecule. On hydrogenation with Adams catalyst in glactal acetic acid, the

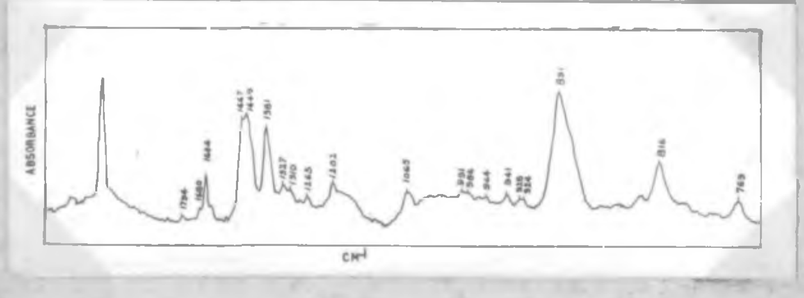


Fig. 1 - Infra-red spectrum (liquid film) of 'Hydrocarbon A'.

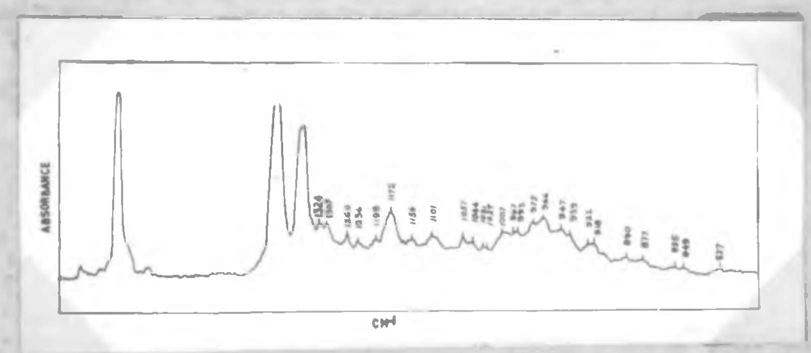
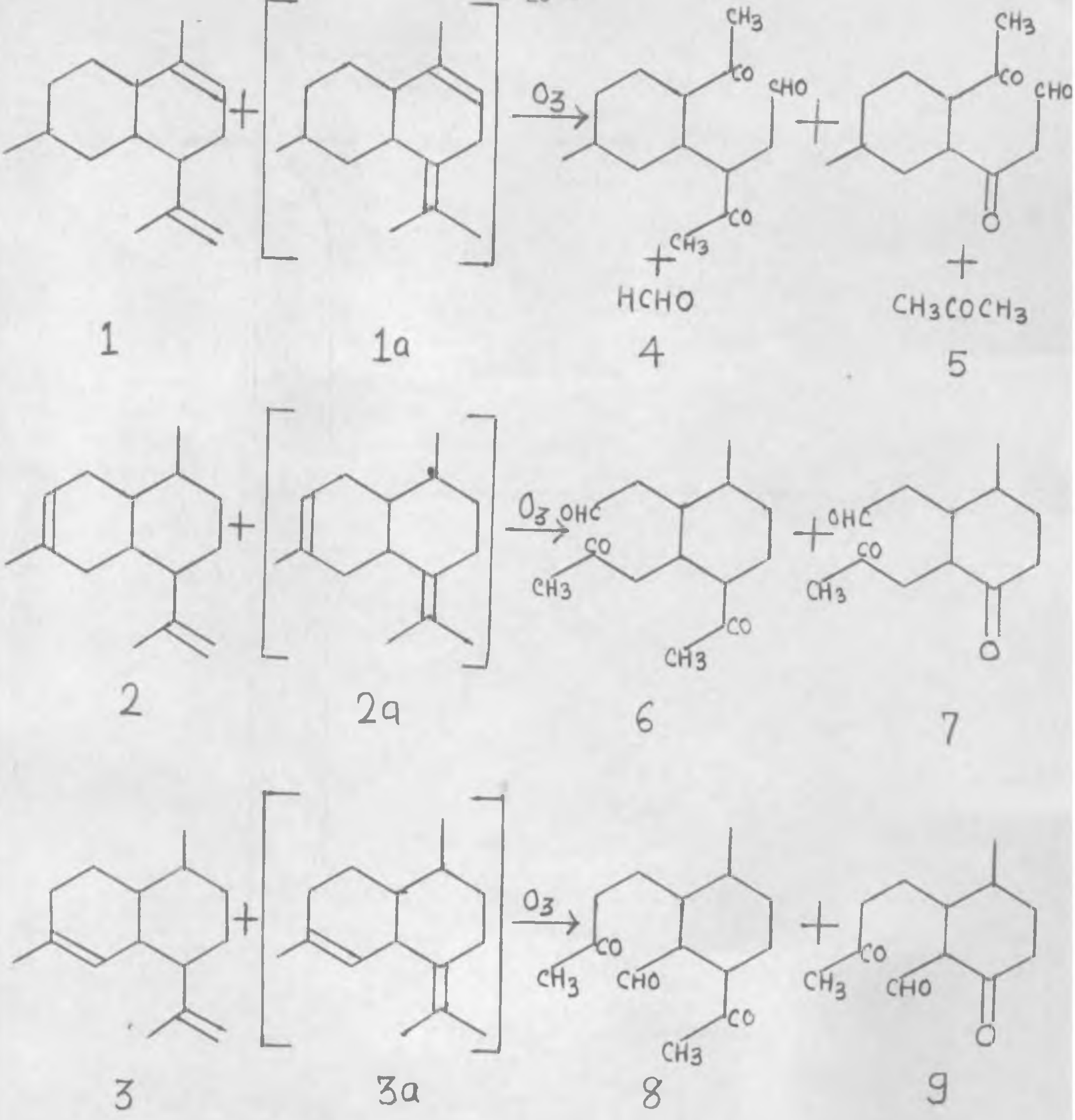


Fig. 2 - Infra-red spectrum (liquid film) of Tetrahydroderivative of 'Hydrocarbon A'.

hydrocarbon absorbed two moles of hydrogen and furnished a tetrahydro derivative whose physicochemical constants do not agree with any of the cadinanes reported so far in the literature[1,2]. Its infrared spectrum is reproduced (Fig.2). On passing dry hydrogen chloride in ethereal solution, the hydrocarbon failed to give any crystalline dihydrochloride and hence it belonged to isocadinane series. Stereochemistry and absolute configuration of isocadinenes is not known so far.

On ozonization in carbontetrachloride, both formaldehyde and acetone were obtained as the volatile fragments. Formaldehyde was identified through its dimedone derivative (m.p. 189°) and acetone through iodoform (m.p.138°). The formation of both formaldehyde and acetone during ozonolysis, indicated that one of double bands was in the form of isopropenyl side chain; acetone evidently was formed as a result of isopropenyl-isopropylidene interconversion during ozonolysis[3-6]. This statement was supported by the infrared curve of the natural product, which showed intensive absorption bands due to a methylenic double bond. The nonvolatile product of ozonolysis showed the presence of aldehyde function (Fehling's solution) and methyl ketone group (iodoform test). It also gave a faint but distinct violet brown colouration with neutral alcoholic ferricchloride solution, indicating the presence of an enolizable hydrogen. All these observations lead to following three possible structures (1), (2) and (3) for the hydrocarbon.



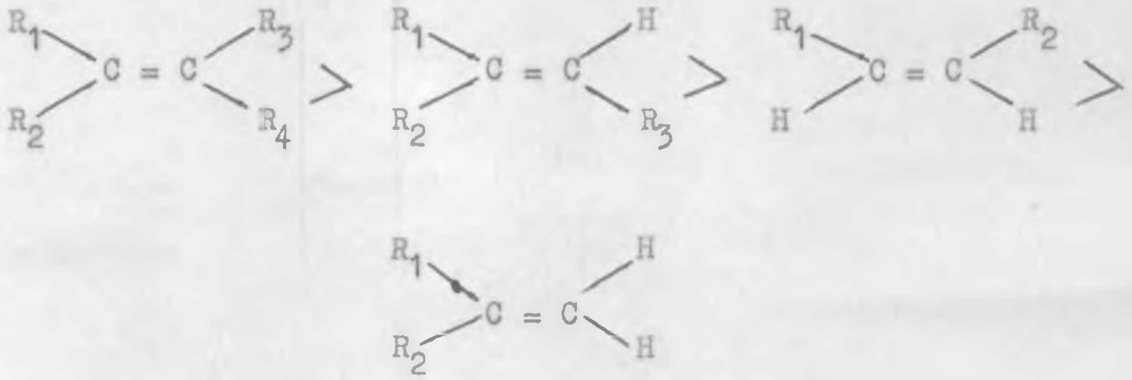
1 1a 4 5

2 2a 6 7

3 3a 8 9

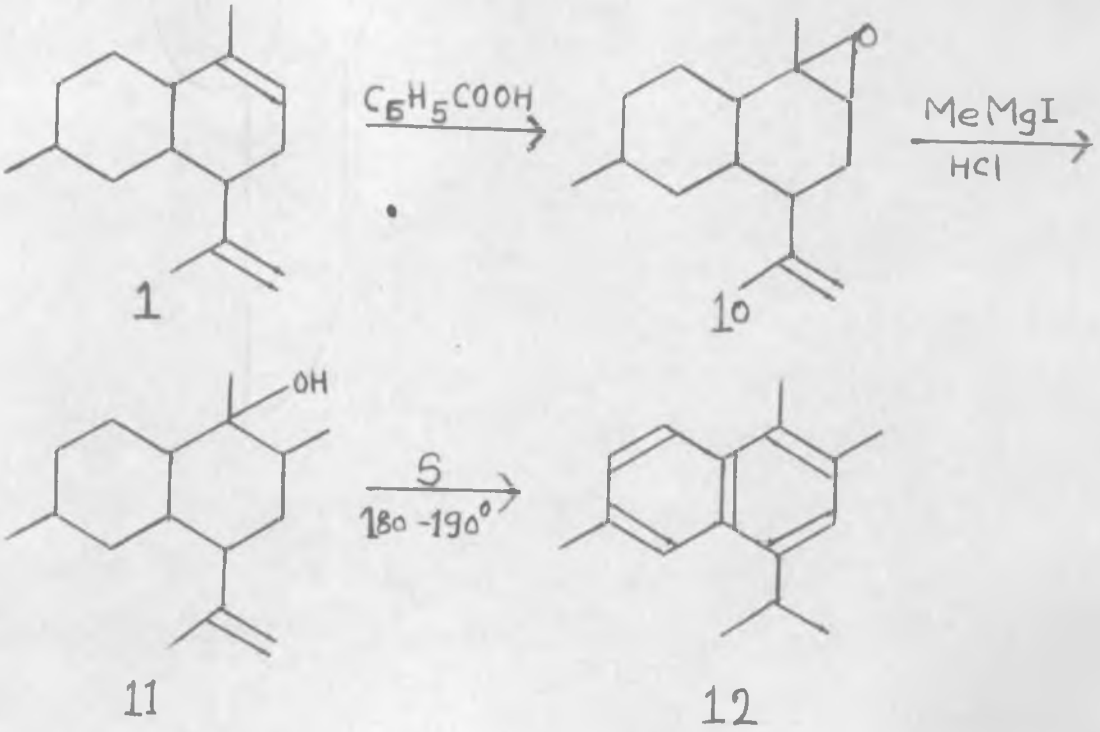
The β-diketoaldehydes (5) and (9) derivable from (1a) and (3a) will respond to ferricchloride colouration, while that from (2a) will not give colouration with ferricchloride. To decide between the two probable structures 1 and 3, the position of the trisubstituted double bond was fixed by the labelling procedure of Campbell and Soffer[7].

Reactivity of perbenzoic acid and peracids, in general, has been known to be in the following increasing order^{8}.



Electrophilic substituents such as alkyl groups increase the rate of reactions. The preferential reactivity of a trisubstituted double bond towards perbenzoic acid over a methylenic double bond is too well known. The hydrocarbon under examination was allowed to react with one mole of perbenzoic acid at 0° for twelve hours. The product was a monoepoxide (10). Its I.R.spectrum indicated that the methylenic double bond had remained in tact (888 and 1638 cm^{-1}) and that the trisubstituted double bond had disappeared with the formation of epoxide. (bands at 1271, 1197, 758, 711 and 1724 cm^{-1}). The band at 1724 cm^{-1} appears to be due to partial isomerization of the epoxide to a cyclic ketone. The Grignard complex of the monoepoxide, prepared by the action of methylmagnesiumiodide, was decomposed by dilute hydrochloric acid and the tertiary alcohol (11) so obtained was dehydrogenated with sulphur at 180-190°. The resultant product was 2-methylcadalene (12) identified through picrate m.p. 142° and T.N.B.

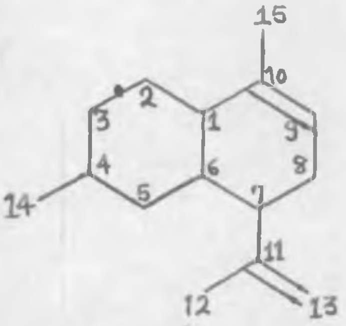
adduct m.p. 167° and mixed melting point. The new sesquiterpene hydrocarbon can, therefore, be represented by the structure (1) and the sequence of reactions involved in the labelling procedure are shown below.



Stereochemistry and nomenclature of the Hydrocarbon

Stereochemistry of cadinenes and cadinols has been determined through X-ray diffraction measurement of the crystalline cadinenedihydrochloride[9]. Since the new hydrocarbon from vetiver oil did not yield crystalline cadinene dihydrochloride, no direct conclusion can be drawn as regards its stereochemistry. The physicochemical constants and the infrared spectrum of the saturated hydrocarbon also do not agree with those reported for the tetrahydroderivatives of β, γ, δ and ε cadinenes[2].

According to the nomenclature suggested by Herout and coworkers[10] and Sorm and his collaborators[11], which is applicable not only to cadinenes which yield cadinene dihydrochloride but also to others possessing cadinane skeleton, the new hydrocarbon can be named as cadina, - 9, 11 (12 or 13) - diene (1).



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An alternative way which can decide the stereochemistry of the hydrocarbon (1) seems to be the study of rotatory dispersion curve of the saturated ketone with the keto group at C_9 position. But due to paucity of material this could not be done at this stage.

EXPERIMENTAL

In this thesis, all melting points and boiling points are uncorrected. Alumina used for chromatography was acid washed neutralised and standardised according to Brockmann's method. Commercial solvents were purified, dried and distilled. Petroleum ether refers to fraction b.p. 65-68°. Specific rotations were taken in chloroform solution. Infra-red spectra were recorded on Grubb-Parson Double Beam Spectrophotometer or on Perkin-Elmer Infracord 137b with sodium chloride optics. Ultra-violet spectra were determined on Unicam SP.500 U.V. spectrophotometer or on Beckman DK2 Recording Spectrophotometer in 95% ethanolic solutions.

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EXPERIMENTAL

Physicochemical Properties of South Indian Vetiver Oil of cultivated origin

The oil (10 lbs) was procured from Mr. D.V.Deo, Cochin, through the Chairman, Essential Oils Research Committee, Council of Scientific & Industrial Research, New Delhi. It was dried over anhydrous sodium sulphate and finally by heating in an oil bath at 110° under water pump suction. The oil was then totally distilled under reduced pressure (boiling range 90-140°/0.3 mm) in an approximate yield of 83%. The physicochemical properties of the distilled oil were determined : d_4^{30} 0.9872; α_D^{25} + 18° (clean); $n_D^{23.5}$ 1.5226; ester no.16.9; ester no. after acetylation 133; carbonyl content by hydroxylamine hydrochloride method (as $C_{15}H_{24}O$) 15.6%; acid no. 7.28; solubility 1 part dissolves in 1.8 vol. of 75% ethanol.

The totally distilled oil was then separated into two major fractions :

(A) Lower boiling fraction, b.p. 72-98°/0.3 mm; and

(B) the residue, which was left over after removing the fraction (A). It was mainly comprised of oxygenated constituents and will be referred to as higher boiling '<u>Fraction</u> (<u>B</u>)' of the oil.

Fractionation of A : This fraction was rich in sesquiterpene hydrocarbons but some ketones were also present as shown by the I.R. spectrum. Its carbonyl content as determined by hydroxylamine hydrochloride method was 10.58%. It was fractionated in a Tower's column using total condensation partial take off type still head and fractions were collected on an equal volume basis. Determination of refractive indices and optical rotations of the various fractions alongwith I.R. observation revealed that separation was not satisfactory. After refractionating some of these fractions, the rotational data showed the presence of both dextro and laevo rotatory hydrocarbons. In one experiment, a charge of 475 g was fractionated in an Emil Greiners' column using a reflux ratio of 1:5 and 32 fractions were collected on an equal volume basis (10 ml). The tail fractions were very viscous and did not appear to be composed of hydrocarbons and were retained in the distillation flask. The column was washed with acetone and the washings after removing the solvent were combined with the residue in the distillation flask. This residue was distilled separately and preserved. The boiling points, refractive indices and optical rotations of various fractions are tabulated in Table 1.

Table - 1

Fr. No.	Still head temp.	Bath temp.	Vac. mm.	no. of ml. collected	n_D^{23}	α_D(clean)	Remarks
1	79°	155°	0.25	5	1.5050	- 8.7	Fractions 1 to 3 combined (A_1)
2	79	155	"	10	1.5043	- 7.6	
3	80	"	"	"	1.5048	- 4.4	
4	81	"	"	"	1.5062	+ 0.5	
5	81-82	"	"	"	1.5078	+ 5.06	
6	83	"	"	"	1.5091	+10.6	
7	84-86	158	"	"	1.5114	+20.16	Fractions 7 to 14 combined (A_2)
8	86-87	"	"	"	1.5103	+16.0	
9	88	"	"	"	1.5130	+23.4	
10	88-88.5	160	"	"	1.5142	+23.4	
11	88.5	"	"	"	1.5149	+21.5	
12	87	158	"	"	1.5151	+20.2	
13	87	"	"	"	1.5155	+19.0	
14	87-88	160	"	"	1.5160	+15.8	
15	88-88.5	"	"	"	1.5178	+ 8.4	
16	89	162	"	"	1.5183	+ 2.54	
17	89	"	"	"	1.5196	- 2.5	
18	89	"	"	"	1.5206	- 6.5	
19	90	"	"	"	1.5220	-16.2	
20	92	"	"	"	1.5242	-29.1	
21	92-92.5	158	"	"	1.5247	-36.26	Fractions 21 to 28 combined (A_3)
22	92	"	"	5	1.5260	-38.9	
23	90-92	165	0.3	5	1.5196	- 2.6	
24	92-93	"	"	10	1.5228	-27.2	
25	94	168	"	"	1.5288	-64.3	
26	96	172	"	"	1.5316	-74.5	
27	97	173	"	"	1.5324	-60.8	
28	98.5	"	"	"	1.5322	-37.4	
29	101-103	180	0.35	"	1.5272	- 6.76	
30	106	183	"	"	1.5272	- 6.76	
31	110	186	"	"	1.5129	+ 3.3	
32	112	186	"	"	1.5149	+ 5.34	

The data in Table 1 revealed that partial separation of three hydrocarbons was achieved. The various fractions were combined into three fractions as follows :

A_1 : laevorotatory fraction nos 1 to 3; b.p.79-80°/0.25 mm; n_D^{23} 1.5043;

A_2 : dextrorotatory fraction nos 7 to 14; b.p.84-88°/0.25 mm; n_D^{23} 1.5145;

A_3 : laevorotatory fraction nos 20 to 28; b.p.92-98°/0.3 mm; n_D^{23} 1.5270.

Isolation of hydrocarbon (A)

The combined fraction A_2 and various other corresponding dextrorotatory fractions obtained during earlier fractionations were chromatographed on neutral alumina (grade I, ratio 1:40) several times. The tail fractions eluted from the column were laevorotatory. Since this dextrorotatory hydrocarbon (A_2) was preceded by a laevorotatory hydrocarbon (A_1) during fractionation and was followed by another hydrocarbon (A_3) which was also laevorotatory, its dextrorotation could be advantageously used during the course of its isolation by chromatography and the same could be regarded as a criterion of its purity (i.e. the higher the dextrorotation, the lesser are the chances of admixture with laevorotatory impurities). The course of chromatography was therefore followed mainly by determining the rotations with occasional check through I.R. spectrum. Chromatography data of one such experiment is presented in Table 2. Part of fraction A_2 (40 g) was chromatographed an alumina (grade I, 1.6 kg, ratio 1:40) and the column eluted with petroleum ether.

Table - 2

Fra. No.	Eluent	no.of ml.	wt. in g	α^{0} (clean)
1	Petroleum ether	75	2.651	+ 36.6
2	"	"	2.373	+ 40.0
3	"	100	3.139	+ 33.2
4	"	"	3.684	+ 30.9
5	"	"	3.367	+ 30.1
6	"	"	3.159	+ 29.5
7	"	"	3.126	+ 28.5
8	"	"	2.854	+ 28.0
9	"	"	2.474	+ 25.6
10	"	"	2.167	+ 13.4
11	"	200	3.810	+ 20.2
12	"	"	2.567	+ 12.4
13	"	300	2.641	- 8.0

Fractions having the same order of rotations from different chromatography batches were combined and rechromatographed several times until finally no further change in the rotations was observed. Such a fraction was distilled (twice) over sodium and was found to possess the following physico-chemical constants.

b.p. 94°/2 mm; $[\alpha]_D^{25}$ + 68°.24; d_4^{30} 0.9230; n_D^{30} 1.5033;
$[R_L]_D$ 65.37; $C_{15}H_{24}\sqrt{\overline{2}}$ requires 66.1.
Analysis : Found : C, 88.07; H, 11,90;
$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

Ultraviolet spectrum was determined on a Unicam spectrophotometer model SP-500 in spectroscopically pure ethyl alcohol. There was no absorption maximum characteristic of a dienic system.

Dehydrogenation of Hydrocarbon (A)

The hydrocarbon (1 g) was heated with selenium powder (1.186 g) at 280-290° for 24 hrs. in nitrogen atmosphere. The dehydrogenated product was taken up in petroleum ether. The extract was concentrated and chromatographed over alumina (grade I, 180 g) and the column eluted with petroleum ether. Two distinct coloured bands were observed on the column. The colourless nonazulenic product was eluted first from the column. The product was separated into five main fractions (1) colourless nonazulenic - 0.216 g. (2) slightly blue coloured - 0.056 g. (3) blue coloured - 0.040 g., (4) blue and violet coloured - 0.025 g. and (5) violet coloured - 0.035 g.

Non-azulenic fraction :

Ethereal solution of'fraction 2' was shaken with cold phosphoric acid to remove traces of azulene. The nonazulenic ether layer was washed free of acid, dried and evaporated and the residue (0.035) was added to nonazulenic fraction 1 above. It gave an orange coloured complex with picric acid which after crystallisation from ethanol had m.p. 115°. Mixed melting point with an authentic sample of cadalene picrate (m.p. 115°) was undepressed.

Blue azulene :

Petroleum ether solution of fraction 3 after shaking with phosphoric acid and decomposing the complex with cold water and extracting with ether, finally yielded 7 mg. of azulene :

Visible spectrum : $\lambda_{max.}$ at 615, 375, 372, 355, 339 mμ ;
Ultraviolet spectrum : $\lambda_{max.}$ 284, 321, 227 mμ

The azulene could not be identified further.

Violet azulene :

Fraction no. 5 after purification through the phosphoric acid complex gave a violet coloured azulene (0.019 g). It gave 1, 3, 5 T.N.B. adduct m.p. 153° after two crystallizations from ethanol. Pure azulene was regenerated from the T.N.B. adduct (m.p. 153°) by passing through alumina column, and eluting with petroleum ether and petroleum ether : benzene mixture (1:1). The combined eluates were concentrated and the visible and ultraviolet spectrum determined in ethanol solution.

Visible spectrum : λ_{max} at 544, 350, 332, 300 mμ ;
Ultraviolet spectrum: λ_{max} at 230, 290 mμ .

The melting point of the T.N.B. adduct and the visible spectrum agree with those of vetivazulene recorded in the literature[12].

Estimation of Unsaturation in the Hydrocarbon (A):

(a) by hydrogenation : The hydrocarbon (2.281 g) in glacial acetic acid (20 ml.) was hydrogenated in the presence of platinumoxide catalyst (16 mg.) at room temperature and atmospheric pressure. It absorbed hydrogen equivalent to 2.1 moles in 5 hrs. The catalyst was then filtered off and the filtrate diluted with water. The hydrogenated product was taken up in petroleum ether. The combined extracts were washed with concentrated sulphuric acid to remove any unsaturated hydrocarbon present, washed with bicarbonate solution and finally with water and dried. Solvent was evaporated and the product was distilled over sodium.

b.p. 83-84°/0.3 mm; n_D^{23} 1.4850; $[\alpha]_D^{23}$ + 7°.39 (C, 4);
Analysis : Found : C, 86.7 ; H, 13.20;
$C_{15}H_{28}$ requires : C, 86.46; H, 13.54%

(b) by perbenzoic acid : Hydrocarbon (50 mg.) was treated with excess of perbenzoic acid solution in chloroform and was kept in the refrigerator. Blank experiments were run simultaneously. The excess of perbenzoic acid was titrated against standardised sodiumthiosulphate solution at different intervals of time. It absorbed (i) 1.799 moles after 8 hrs.; (ii) 1.993 moles after 19 hrs. and (iii) 2.03 moles after 48 hrs.

Hydrochlorination of Hydrocarbon (A)

Dry hydrochloric acid gas was bubbled through dry ethereal solution of the hydrocarbon (1 g. in 50 ml. ether) for sometime and the mixture set aside overnight at 0°. Solvent was removed under suction at 40°. The residue did not deposit any crystals on protracted cooling at -10°.

Ozonolysis of Hydrocarbon (A)

A stream of dry ozonized oxygen was bubbled through a solution of the hydrocarbon (1 g.) in carbontetrachloride (20 ml.) till the absorption was complete. The trap water collected during ozonolysis reduced Fehling's solution, and Tollen's reagent, and gave dimedone derivative (m.p. and mixed melting point with formaldimethone 189°) and iodoform test. (m.p. 138°) indicating the presence of formaldehyde and acetone. The ozonide, after removing solvent at 40°, was decomposed by heating with water (15 ml.) on a water bath for 3 hrs. and the ensuing gases were trapped in water. This water also gave positive tests for formaldehyde and acetone. The decomposed ozonide was taken up in ether and shaken with sodium bicarbonate solution (5%). The neutral ether layer was washed with water and dried. The solvent was evaporated and the residue distilled; b.p. 135° (bath)/0.002 mm. It gave very strong test for an aldehyde group (Fehling's solution), a methyl ketone group (iodoform test in dioxan), and a distinct violet brown colouration with alcoholic ferricchloride.

Analysis : Found : C, 70.6 ; H, 9.5 ;

$C_{14}H_{22}O_3$ requires : C, 70.55; H, 9.31.

The aqueous layer containing sodium salt of the acid was acidified and the product extracted with ether. Ether extract was washed, dried and solvent removed. The residue gave positive iodoform test. Attempts to distill this material gave only polymeric products.

Monoepoxide (10)

Perbenzoic acid solution (1 mole; 55 ml. of 6.27% in chloroform and benzene, 9:1), was added gradually in three instalments at an interval of 15 minutes to the hydrocarbon (5 g.) in cold chloroform (20 ml.) and was kept in the refrigerator overnight. The liberated benzoic acid was removed by washing with sodiumcarbonate solution (5%) and the chloroform layer was washed free of acid, dried over anhydrous sodiumsulphate and the solvent removed by distillation. A small portion of the epoxide was distilled; b.p.115° (bath)/0.0025 mm;

Analysis : Found : C, 80.1 ; H, 10.10;

$C_{15}H_{24}O$ requires : C, 81.76; H, 10.98%.

I.R. Bands at : 1724, 1638, 1271, 1197, 888, 758, 711 cm^{-1}.

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Grignard reaction on monoepoxide (10)

The crude monoepoxide (1.431 g.) in dry ether (20 ml.) was added dropwise under cooling and stirring during 30 minutes to methylmagnesiumiodide prepared from magnesium (0.46 g.) and methyliodide (0.5 ml.) in dry ether (50 ml.). The contents were refluxed for 48 hrs. with stirring. The Grignard complex was then decomposed by the addition of dilute hydrochloric acid. Contents were transferred to a separating funnel, ether layer separated and the aqueous layer was extracted with ether (twice). Combined ether extract was washed free of acid, dried and the solvent removed to give the resulting alcohol (1.379 g.).

Dehydrogenation of (11)

The crude alcohol (1.379 g.) was heated with sulphur (0.8 g.) at 180-190° for 5 hrs. in nitrogen atmosphere. The dehydrogenated product was taken up in petroleum ether, filtered, concentrated and chromatographed over alumina (grade II; 50 g.). The column was eluted with petroleum ether. The residue after evaporation of solvent gave picrate m.p. 135° on treatment with alcoholic solution of picric acid. After two crystallisations from ethanol the melting point became constant at 143°. Picrate (0.027 g.) was passed through alumina column (grade II, 4 g.) and eluted with petroleum ether. The petroleum ether eluate after removal of solvent and on treatment with alcoholic solution of 1,3,5 trinitrobenzene gave 1,3,5-T.N.B. adduct m.p. 167°, after two crystallisations from ethanol. Mixed melting point with an authentic specimen of T.N.B. derivative of 2-methylcadalene was undepressed.

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CHAPTER - II

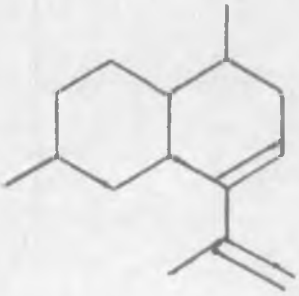
ISOLATION AND CHARACTERISATION OF A NEW SESQUITERPENE HYDROCARBON

HYDROCARBON B

CHAPTER II

SUMMARY

A new sesquiterpene hydrocarbon, $C_{15}H_{24}$, Hydrocarbon (B) with two double bonds, has been isolated from the higher boiling fraction of South Indian vetiver oil. From a systematic study of its degradation products and on the basis of ultra-violet and infrared spectra, it has been assigned the structure (13).



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Isolation of Hydrocarbon (B)

With a view to studying the oxygenated constituents of South Indian vetiver oil, the higher boiling 'Fraction B' (p.23), which mainly consisted of oxygenated constituents, was fractionated in a Tower's column with a batch strip still head and fractions were collected on an equal volume basis. The fractionation data (Table I, p. 51) showed that it was still containing some lower boiling fraction distilling between 97° to 120°/1 mm. The boiling range of these fractions (Nos. 1 and 2, Table I, p. 51) indicated that it might still contain some sesquiterpene hydrocarbons and its infra-red spectrum showed the presence of both ketones and alcohols. The combined fraction (214 g.) was therefore chromatographed on neutral alumina when the hydrocarbons were eluted with hexane, ketones with hexane:benzene mixture (1:1) and alcohols with benzene and ether. The hexane eluted fraction (fraction Nos.1 to 10, Table II,p.52) appeared to consist of at least two sesquiterpene hydrocarbons, one a conjugated diene, (I.R.Bands at 1604 and 1628 cm^{-1}) and the other moving slowly on the column with a higher refractive index, possibly a triene (I.R.Bands at 1603, 1633, 1662 cm^{-1}), both being dextrorotatory. Chromatographic fractions 1 to 6 (Table II, p. 52) were repeatedly chromatographed on grade II and grade I neutral alumina until a homogeneous hydrocarbon fraction was obtained. Henceforward it will be referred to as Hydrocarbon (B) (Table VI, p.55). It was purified by distillation under reduced pressure.

The infra-red spectrum of Hydrocarbon (B) showed strong bands at 1628, 1604, 888 and 814 cm^{-1}, suggesting conjugation of a methylenic double bond with a trisubstituted double bond. It also exhibited a minor absorption peak at 1706 cm^{-1}, indicating the presence of a trace of carbonylic impurity, which accompanied it in spite of repeated column chromatography over grade I alumina. Correct elemental analysis also could not be obtained for it. It was therefore felt necessary to purify it through Girard's reagent to obtain a pure sample free from ketonic impurities. The infra-red spectrum of the purified hydrocarbon (B) is reproduced in Fig. 3. There was no considerable difference in the I.R. spectrum after this treatment except that the absorption peak due to carbonylic impurity was absent. The hydrocarbon exhibited a single absorption maximum in the ultra-violet region at 235 mµ in ethanolic solution (log ϵ, 3.9496). This confirmed the presence of a conjugated dienic system.

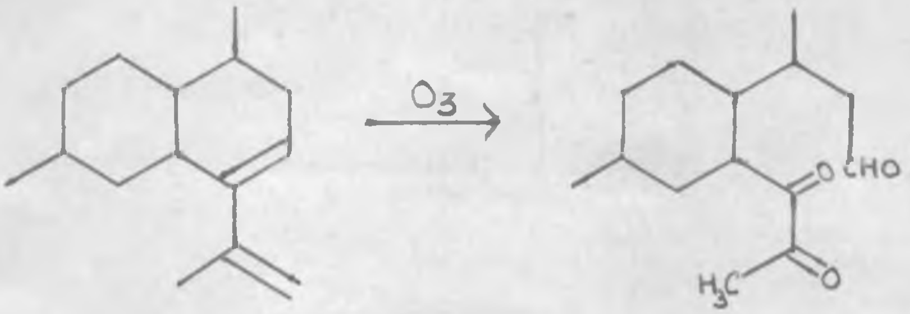
Structural aspects :

The new sesquiterpene hydrocarbon (B), $C_{15}H_{24}$, on hydrogenation in glacial acetic acid using Adams catalyst absorbed two moles of hydrogen and furnished a tetrahydro derivative. Infra-red spectrum of this tetrahydroderivative was identical with that of the tetrahydroderivative of cadina-9, 11 (12 or 13) diene, hydrocarbon (A) (Chapter I) isolated from the same oil (Fig. 4 and 5), though there was slight difference in the physicochemical constants. The molecular formula $C_{15}H_{24}$ and the hydrogenation data suggested that it is a bicyclic sesquiterpene hydrocarbon.

Varying yields of cadalene upto 40% were obtained when the hydrocarbon was dehydrogenated with selenium and sulphur respectively. The hydrocarbon on ozonolysis gave copious amount of formaldehyde (identified through dimedone derivative m.p. and mixed m.p. 189^{0}) as the only volatile fragment and no acetone was detected. The non-volatile portion obtained after decomposition of the ozonide gave the following tests :

(i) a positive iodoform test suggesting the presence of a methyl ketone group;
(ii) Fehling's solution test indicating the presence of an aldehyde function and
(iii) negative test with neutral alcoholic ferric chloride solution indicating absence of an enolisable hydrogen.

On the basis of qualitative tests given by the ozonolysis products of the hydrocarbon, its infra-red bands at 1628, 1604, 888 and 816 cm^{-1} and a single absorption maximum at 235 mμ suggestive of a heteroannular dienic system[1] where a trisubstituted double bond is in the ring and the other is an exocyclic methylenic one, a tentative structure (13) could be assigned to the hydrocarbon B. Such a structure would give rise to an α-diketoaldehyde (14) on ozonolysis.



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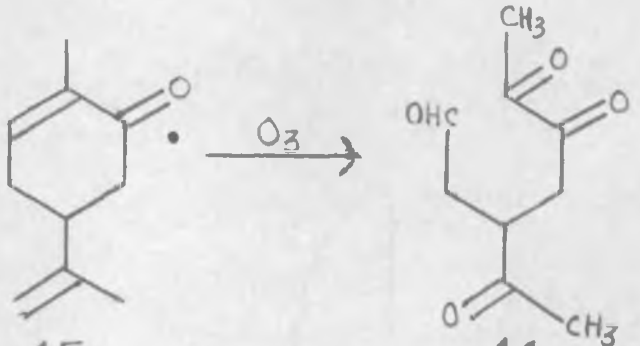
The α-diketoaldehyde (14) will consume one mole of periodate giving a mole of acetic acid as one of the fragments of oxidation. This was confirmed in the following way. Though α-glycols react with metaperiodate very easily, α-diketones are known to be sluggish towards this reagent[2] and much longer time is required for completion of the reaction.

Considering the above factor, carvone (15) was used by us as a model compound. It was ozonized (excessive ozonisation was avoided[3]) and the ozonide decomposed carefully by heating with water at 60° to yield the α-diketoproduct (16) along with certain amount of unchanged starting material. In confirmity with its structure, the compound (16) gave strong iodoform test and reduced Fehling's solution. On treatment with sodiummetaperiodate solution, it consumed 0.43 mole of the reagent after keeping for three days at 28°. After fifteen days the consumption did not substantially increase and was only 0.45 mole. Under parallel conditions the α-diketoaldehyde (14) from our hydrocarbon consumed 0.608 mole of sodiummetaperiodate. After steam distillation of the reaction product and subsequent operations, the volatile component was identified by paper chromatography as acetic acid, using the procedure of Kennedy and Barker[4]. These results confirmed the new sesquiterpene hydrocarbon as represented by the structure (13).



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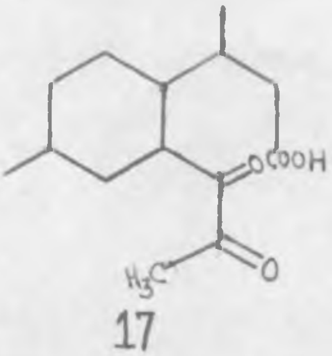
An attempt to prepare the quinoxaline derivative from the α-diketo acid gave only oily products. The α-diketo aldehyde (14) on oxidation with potassium permanganate in acetone gave an acid, $C_{14}H_{22}O_4$, presumably (17).

The hydrocarbon (B) on reduction with sodium and ethanol gave a product which did not show any ultraviolet absorption maximum and its infra-red spectrum showed the presence of both methylenic and trisubstituted double bonds which suggested that the reduced product may be a mixture of isomers (18).



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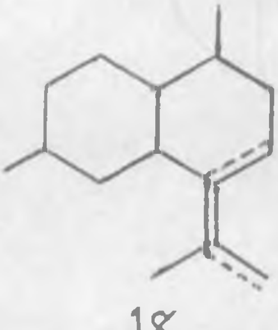

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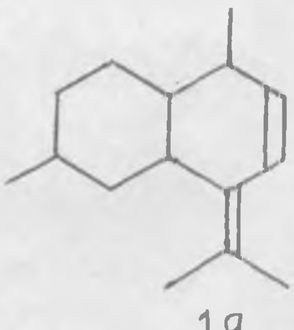

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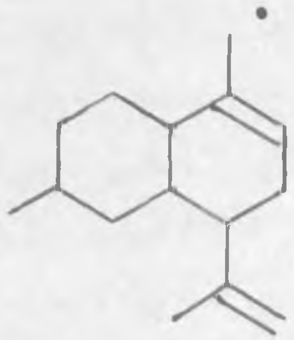
The ultraviolet absorption maximum at 235 mμ is in agreement with Woodward's rule. The low ϵ-value of this class of compounds of semicyclic dienes has been ascribed by Gilam[1] and Savard[5] to the presence of an unconjugated isomer. We did not observe any formation of acetone during ozonolysis of the hydrocarbon. This fact also supports structure (13) and rules out the possibility of the presence of an isomer like (19).



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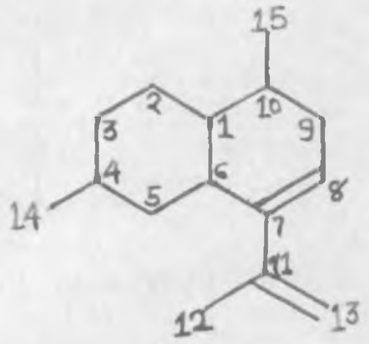

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According to the nomenclature suggested by Herout[6], the new hydrocarbon (B) can be named as cadina-7, 11 (12 or 13)-diene. As stated earlier the infra-red spectra of tetrahydro-derivatives of (13) and (20) are closely similar, it may be quite likely that both the hydrocarbons are stereochemically same as far as ring juncture is concerned.

EXPERIMENTAL

Isolation of hydrocarbon (B)

The higher boiling fraction B was fractionated in a Tower's column with a batch strip still head in four batches. The fractionation data of one such batch are given in Table I.

Table - I

Wt. of fraction B - 420 g.

Fra. No.	Bath Temp.	Still head Temp.	Vac. mm.	No. of ml. collected	n_D^{26}	$[\alpha]_D^{26}$ °
1	133°	97-115°	1	26	1.5170	+ 3.29
2	145	120	"	"	1.5200	+ 8.38
3	160	130	"	"	1.5218	+12.61
4	160	135	"	"	1.5218	+17.62
5	160	135	"	30	1.5218	+12.52
6	160	135-138	"	"	1.5223	+20.46
7	160	138	"	"	1.5226	+19.72
8	160	138	"	"	1.5230	+17.44
9	158	128-132	0.7	"	1.5238	+18.97
10	170	132-138	0.7	"	1.5250	+23.26
11	170-190	138-150	0.9	"	1.5260	+27.35
12	196-205	148-154	0.9	20	1.5280	+40.60

Fractions corresponding to 1 and 2 from four such batches were combined (214 g.) and chromatographed on neutral alumina (grade III, 6.7 Kg.) and the column was eluted successively with hexane (65-68°), benzene : hexane mixture (1 : 1), benzene and finally with ether. The results of chromatography are recorded in table II.

Table - II

Chromatography of combined fractions 1 and 2 (Table I, P.51)

Wt. of fraction - 214 g.

Wt. of Alumina - 6.7 Kg., grade III, ratio 1 : 30.

Frac. No.	Eluent	No. of ml. collected	Wt.in g.	n_D^{24}
1	Hexane	250	5.689	1.5088
2	"	"	12.074	1.5162
3	"	"	11.606	1.5167
4	"	"	9.947	1.5184
5	"	"	9.579	1.5182
6	"	"	10.065	1.5195
7	"	"	6.966	1.5218
8	"	500	9.478	1.5208
9	"	"	5.567	1.5208
10	"	"	2.968	1.5192
11	"	1000	1.943	1.5173
12	"	2000	4.000	1.5173
13	Hexane:Benzene	1000	5.669	1.5092
14	"	500	3.275	1.5110
15	"	1000	6.136	1.5130
16	"	"	5.470	1.5162
17	Benzene	500	4.662	1.5190
18	"	"	4.077	1.5178
19	"	1000	5.402	1.5188
20	"	750	3.419	1.5158
21	"	2000	6.376	1.5123
22	"	2000	5.589	1.5110
23	"	2500	7.217	1.5100
24	"	1000	2.638	1.5103
25	"	2000	7.413	1.5098
26	"	2000	7.119	1.5120
27	Ether	"	20.239	1.5160
28	"	"	12.329	1.5185

Fractions 1 to 6 (Table II) were combined (58.969) and rechromatographed over neutral alumina (grade II, 1.68 Kg. ratio 1 : 30). The column was eluted with hexane and the chromatographic results are given in table III.

Table - III

Fra. No.	Eluent	No. of ml. collected	Wt. in g.	α° clean
1	Hexane	150	3.251	+ 25.3
2	"	"	9.144	+ 22.4
3	"	"	10.255	+ 10.3
4	"	"	11.026	+ 9.8
5	"	"	8.694	+ 8.8
6	"	"	7.737	+ 6.4
7	"	300	3.608	- 4.3
8	"	1000	traces	-

Fractions 3 to 6 (37.71 g. Table III) were combined and chromatographed on neutral alumina. (grade I, 1.11 Kg. ratio 1 : 30) and the column was eluted with hexane. The results are recorded in table IV.

Table - IV

Fr. No.	Eluent	No. of ml. collected	Wt.in g.	n_D^{23}	α^{230} clean
1	Hexane	50	1.305	1.5025	+ 21
2	"	100	7.323	1.5080	+ 26.8
3	"	"	6.765	1.5120	+ 31.8
4	"	"	6.170	1.5140	+ 33.1
5	"	"	5.968	1.5200	+ 10.7
6	"	"	3.916	1.5210	- 9.7
7	"	"	2.305	1.5298	- 40.4
8	"	200	2.195	1.5370	- 43.2
9	"	300	0.729	1.5402	-
10	Hexane : Benzene (1 : 1)	1000	traces brown red in colour		

Fractions 1 and 2 (Tables III and Table IV) were combined (21.023 g.) and chromatographed over neutral alumina (grade I, 1 kg., ratio 1 : 50). The chromatographic results are presented in Table V.

Table - V

Frac. No.	Eluent	No. of ml. collected	Wt.in g.	$\alpha_D^{23^0}$ clean
1	Hexane	100	7.939	+ 24.8
2.	"	"	5.685	+ 28.6
3	"	"	4.050	+ 28.0
4	"	"	1.714	+ 35.4
5	"	"	0.510	-
6	"	200	0.693	-

Fractions 1 to 3 (17.673 g., Table V) were chromatographed on neutral alumina (grade I, 1 kg., ratio 1 : 55). The results of chromatography are presented in Table VI.

Table - VI

Frac. No.	Eluent	No. of ml. collected	Wt. in g.	n_D^{23}	$\alpha_D^{23^\circ}$ clean
1	Hexane	30	0.423	1.4935	-
2	"	"	1.700	1.5020	+ 21.8
3	"	"	1.996	1.5050	+ 27.9
4	"	"	2.151	1.5070	+ 25.2
5	"	"	1.939	1.5068	-
6	"	"	2.050	1.5045	-
7	"	"	1.620	1.5062	+ 27.0
8	"	"	1.562	1.5066	-
9	"	60	2.389	1.5030	+ 27.4
10	"	"	1.272	1.5086	+ 28.7
11	"	100	0.349	1.5140	-

Fractions 2 and 10 (Table VI) were chromatographed separately on alumina (grade I, 30 g.) and 5 ml. fractions were collected. Hydrocarbon with the same refractive index (1.5048) was added to the main fraction (Nos. 3 to 9, Table VI) and the combined fraction was distilled under reduced pressure :

b.p. 72°/0.35 mm; α_D^{23} + 31.47° (clean); n_D^{23} 1.5090;
d_4^{23} 0.9248; $[R_L]_D$ 65.83; $C_{15}H_{24}$ $\sqrt{2}$ requires 66.1

Analysis : Found : C, 86.3 ; H, 10.9 ;

$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

Ultra-violet spectrum : λ_{max} 235 mμ (ϵ 7, 676) ;
I.R.spectrum bands at : 1706, 1628, 1604, 1461, 1446, 1374, 1200, 1160, 1097, 1065, 888, 879, 815 cm^{-1}.

In view of the presence of carbonylic impurity as revealed from microanalysis and infrared spectrum a small portion of the hydrocarbon was further purified by treatment with Girard's reagent. Hydrocarbon (1.763 g.) dissolved in ethanol (10 ml.) and Girard's reagent (0.1945 g. dissolved in ethanol containing 10% acetic acid) were refluxed on a water bath for one hour. Contents after cooling were diluted and taken up in ether. The aqueous layer was rejected and the organic layer was washed free of acid, dried over anhydrous sodiumsulphate and ether evaporated. The residue (1.288 g.) was distilled under reduced pressure and physicochemical constants of Hydrocarbon (B) were determined.
b.p.145-155°(bath)/4.25 mm; $[\alpha]_D^{26}$ +36°.9 (clean); n_D^{28} 1.5078; d_4^{30} 0.9199; $[R_L]_D$ 65.999, $C_{15}H_{24}$ $\sqrt{2}$ requires 66.1.

Analysis : Found : C, 87.8 ; H, 11.23;

$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

Ultraviolet spectrum : λ_{max} 235 mμ (ϵ, 8, 904);
Infrared spectrum is reproduced, in Fig. 3.

Hydrogenation of Hydrocarbon (B)

Hydrocarbon (1.0389) in glacial acetic acid (20 ml.) was stirred with platinumoxide catalyst (50 mg.) in hydrogen atmosphere at room temperature and atmospheric pressure. The uptake of hydrogen (286 ml. in 5 hrs) corresponds to 2.11 moles. Catalyst was then filtered off and the filtrate diluted with water and extracted with hexane (thrice). Hexane solution was washed free of acid, dried over anhydrous sodiumsulphate, and solvent evaporated to give the tetrahydro product which was chromatographed over alumina (grade I, 25 g.). The petroleum ether eluate (50 ml.) after evaporating the solvent was distilled over sodium under reduced pressure.

b.p. 150° (bath)/7.2 mm; $[\alpha]_D^{23}$ + 2.15 (C, 8.8);
$n_D^{23.5}$ 1.4820; d_4^{26} 0.8888; $[R_L]_D$ 66.65, $C_{15}H_{24}\sqrt{\overline{\text{nil}}}$
requires : 67.06.

Analysis : Found : C, 86.78; H, 13.20;
$C_{15}H_{28}$ requires : C, 86.46; H, 13.54%.

Dehydrogenation of Hydrocarbon (B)

On the basis of large number of experiments using both selenium and sulphur, it was found that heating for a long period was harmful and gave rise to bye-products. Best results were obtained using short period of heating. Two typical experiments are described.

(a) With Selenium : Hydrocarbon (0.947 g.) was heated with selenium powder (0.945 g.) at 280-290° for $4\frac{1}{2}$ hrs.

in nitrogen atmosphere. The dehydrogenated product was taken up in dry ether and shaken with 85% phosphoric acid. Azulenes were regenerated by decomposing the complex with cold water and extracting with ether. The ether extract was washed free of acid, dried and ether evaporated to give 0.048 g. azulene. The ether layer containing nonazulenes was washed free of acid, dried and solvent evaporated to give 0.64 g. crude nonazulene, which was chromatographed over alumina (grade I, 25g) when 0.625g colourless nonazulene was obtained. U.V. spectrum : λ_{max} 228 mμ (ϵ 19,420), 285 mμ. It gave picrate m.p. 115° and mixed melting point with an authentic sample of cadalene picrate was undepressed. The violet coloured azulene obtained above gave picrate 123° (brought to a constant melting point by crystallisations). Azulene (0.003 g.) was regenerated from its picrate and its visible spectrum determined in hexane (λ_{max} 555, 650, 350 mμ

(b) With Sulphur : Hydrocarbon (0.474 g) was heated with sulphur (0.247 g) at 185-190° for 3 hrs. in nitrogen atmosphere. No azulenes were formed. The dehydrogenated product was chromatographed over alumina (grade I, 50g) and the petroleum ether eluate after evaporation of solvent gave the dehydrogenated product (0.223g, n_D^{30} 1.5426). It readily furnished cadalene picrate m.p. 115° and mixed melting point with an authentic sample of cadalene picrate was undepressed.

Ozonolysis :

Hydrocarbon B (2.043 g) in pure ethyl acetate (20 ml.

was ozonized at 0-5° during 5 hrs. The trap-water collected during ozonolysis gave copious amount of formaldehyde (identified through dimedone derivative m.p. and mixed melting point 189°) and no acetone was detected (negative iodoform test). After removing the solvent at 40° under suction, the ozonide was decomposed in the usual way by heating with water (15 ml) on a water bath. Contents were then taken up in ether and ether extract dried. On evaporation of solvent ozonolysis product (2.09g) was obtained. It gave following qualitative tests :

(1) strong iodoform test in dioxane;

(2) reduced Felling's solution and ammonical silver nitrate solution;

(3) negative colour reaction with neutral alcoholic ferric chloride solution.

Quantitative reaction with sodiummetaperiodate

(A) α-diketo product obtained by ozonolysis of carvone (0.094 g) was dissolved in ethanol (15 ml) and sodiummetaperiodate solution (100 ml, 0.2804%) and 2N sulphuric acid (10 ml) were added and the contents were kept in a stoppered conical flask for 3 days at room temperature.

(B) A blank experiment was similarly carried out. The contents of flasks A and B were titrated against standard sodium thiosulphate solution.

Experiments were repeated with α-diketoproduct obtained from carvone and sesquiterpene hydrocarbon by keeping the oxidation mixture for a longer time.

(C) α-diketo product from carvone (0.199 g) dissolved in ethanol (50 ml) was treated with 100 ml...N/10 sodiummetaperiodate solution and 10 ml 2N sulphuric acid in a stoppered conical flask and allowed to react at room temperature for 15 days.

(D) A blank experiment was similarly carried out.

(E) α-diketo product from sesquiterpene hydrocarbon B (0.178 g) dissolved in ethanol (50 ml) was treated with 100 ml N/10 solution of sodiummetaperiodate and 10 ml of 2N sulphuric acid in a stoppered conical flask and were allowed to react at room temperature for 12 days.

(F) A blank as in D for 12 days.

Contents of all the flasks were titrated against N/10 standard sodiumthiosulphate solution using starch indicator at the end. The results are tabulated in Table VII.

Table - VII

No.	Name of compound	Wt.in g.	No. of days	ml.of N/10 $Na_2S_2O_3$ solution	ml.of N/10 $Na_2S_2O_3$ soln.reqd. theoretically	%
1.	α-diketo product of carvone	0.094	3	4.44	10.22	43.49
2.	"	0.199	15	9.60	21.14	45.41
3.	α-diketo product of hydrocarbon B	0.178	12	9.15	15.04	60.84

Oxidation with sodiummetaperiodate and isolation of acetic acid

α-diketoaldehyde (14), (1.887 g) dissolved in ethanol (25 ml.) was treated with sodiummetaperiodate solution (160 ml. of N/10 solution) in a stoppered conical flask and the reactants were allowed to stand at room temperature for 20 days. Contents of the flask were steam distilled and the steam distillate (250 ml) containing ethanol was collected. The steam distillate was made alkaline to pH 8 by the addition of sodiumhydroxide solution and concentrated to a small bulk (25 ml). Preliminary experiments for identification of acetic acid (in a standard 1% solution of acetic acid made alkaline by sodium hydroxide to pH 8) by descending paper chromatography using butanol - 1N ammonium hydroxide did not succeed and no movement of the spot was observed. Subsequently, following the procedure of Kennedy and Barker[4] the solutions containing sodium salt of the acid, in both known and unknown were treated with equimolar amounts of ammoniumsulphate and were converted into the ammonium salts and the pH was adjusted to 7.1 by the addition of dilute ammonia solution. These solutions were spotted on a paper pre-treated with oxalic acid and the chromatogram developed with 95% ethanol and ammonia (1 ml.) by ascending paper chromatography. The paper was dried in an oven at 100° for 5 minutes and was then sprayed with bromophenol blue indicator, when blue spots were visible on a yellow background, both with known and unknown solutions at the same distance (R_f 0.33).

Potassiumpermanganate oxidation of α-diketoaldehyde (14)

α-diketoaldehyde (14), (0.845 g) in acetone (10 ml.) was oxidised with saturated solution of potassiumpermanganate (10 ml.) and the contents were stirred for 3 hrs. The sludge of manganesedioxide formed was removed by passing sulphurdioxide. The contents were taken up in ether, washed with water (twice) and was shaken with saturated sodiumbicarbonate solution. The bicarbonate extract after acidifying and extracting with ether gave the acid (0.25 g.) b.p. 210° (bath)/ 0.8 mm.

Analysis : Found : C, 65.09; H, 8.77;

$C_{14}H_{22}O_4$ requires : C, 66.11; H, 8.77%.

Reduction of hydrocarbon (13) with sodium and alcohol

Freshly cut pieces of sodium (14 g.) were carefully added to the solution of hydrocarbon (0.8387 g.) in absolute ethyl alcohol (75 ml.). Another 50 ml. of absolute ethyl alcohol were added at an intermediate stage. The contents were diluted with water (20 times) and taken up in ether. Ether extract was washed free of alkali, dried and ether evaporated to give the crude reduced product (0.519 g.). It was distilled over sodium; b.p. 150-152°(bath)/7 mm; n_D^{26} 1.5020. U.V.Spectrum : It did not show any absorption maximum at 235 mμ. Infrared spectrum showed presence of bands at 1633, 889 and 815 cm^{-1} and absence of band at 1604 cm^{-1}.

Presence of atriene :

Extensive chromatography of fractions 7 to 10 (Table II, P. 52) revealed that it was a mixture of a conjugated diene and triene with a high refractive index, and no homogeneous fraction could be isolated from the same.

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CHAPTER - III

ISOLATION AND PARTIAL CHARACTERISATION OF TWO NEW SESQUITERPENIC HYDROCARBONS C & D AND AN ALCOHOL E

CHAPTER III

SUMMARY

Isolation and partial characterisation of two new hydrocarbons (C & D) and an alcohol (E) isolated from South Indian vetiver oil are described in this chapter.

Hydrocarbon (C), $C_{15}H_{24}$, containing one double bond, appears to be a new tricyclic hydrocarbon possessing guaiane type of carbon skeleton.

Hydrocarbon (D), $C_{15}H_{22}$, is a new sesquiterpene hydrocarbon with an eudalenic carbon skeleton containing three double bonds, two of which are in conjugation.

Alcohol (E), $C_{15}H_{24}O$, is a new tricyclic secondary sesquiterpene alcohol, containing one double bond. The presence of a carbon skeleton containing fused five and six membered ring is postulated.

Isolation and Partial Characterisation of Two New Sesquiterpenic Hydrocarbons and an Alcohol :

In this part we present our results of investigation of three other constituents obtained from South Indian Vetiver Oil, two of these are hydrocarbons (referred to as C and D) and the other one is an alcohol (E). Our results on these constituents are inconclusive and we are not in a position to ascribe definite structures to these. However sufficient amount of valuable data have been collected which would throw light on their structural features.

Isolation of a new Azulenic Tricyclic Hydrocarbon (C)

The combined laevorotatory lower boiling fraction A_1 (p.33), obtained during fractionation of A, after extensive chromatography on neutral alumina gave a homogeneous laevorotatory hydrocarbon (C). It was distilled over sodium and was found to possess the following physicochemical constants : b.p.112-113°/6.5 mm; α_D^{23} $-19^{\circ}.46$ (clean); n_D^{23} 1.5000; d_4^{30} 0.9258; $[R_L]_D$ (i) 64.46; (ii) 64.45;

$C_{15}H_{24}\ \sqrt{\overline{\overline{1}}}$ requires 64.4.

Analysis : Found : C, 87.3 ; H, 11.6 ;

$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

Structural features :

Infra-red spectrum of this hydrocarbon (C) exhibited bands at 890 and 1636 cm^{-1} (Fig.6) characteristic of a methylenic double band. It did not show any absorption in the ultraviolet region.

Its molecular refractivity agrees well with that of a tricyclic monoethylenic sesquiterpene hydrocarbon. Presence of a cyclopropane ring was not indicated as bands in the region 1005-1020 and 3040 cm^{-1} were absent. This was also supported by the absence of any molecular exaltation. Compounds containing cyclopropane ring are known to show exalted molecular refractivity as in the cases of aromadendrene[1], α-gurjunene[2] and copaene[3] etc.

The monoethylenic nature of the hydrocarbon was confirmed by hydrogenation. The hydrocarbon (C) on hydrogenation in glacial acetic acid with Adams catalyst absorbed only one mole of hydrogen and furnished a dihydro derivative. The dihydro derivative did not give any colouration with tetranitromethane and did not consume perbenzoic acid. On dehydrogenation with selenium at 280°, the hydrocarbon afforded azulenes in a yield of 3% when heated for 48 hours and in a yield of 10% when heated for $4\frac{1}{2}$ hours. The non-azulenic portion did not show any absorption in the ultraviolet region. The dehydrogenated product was a mixture of azulenes which was separated by chromatography and fractional crystallisations of the 1,3,5-T.N.B. adducts. One of them was identified as guaiazulene (T.N.B., m.p. 147°); the other one (T.N.B., m.p. 131°) could not be characterised. Its visible and ultraviolet spectrum exhibited maxima at 733,

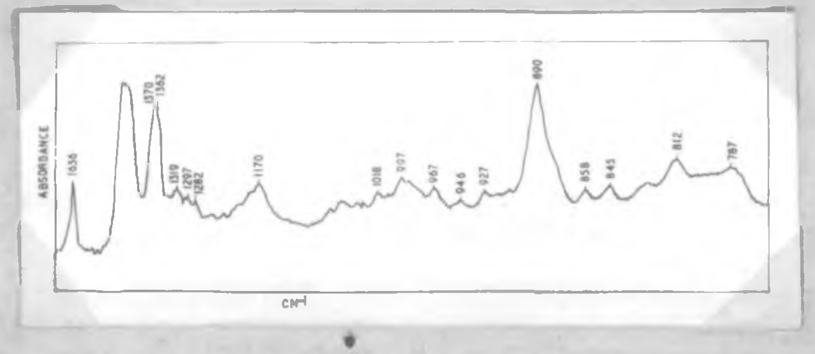


Fig. 6 - Infra-red spectrum (liquid film) of azulenic 'Hydrocarbon C'.

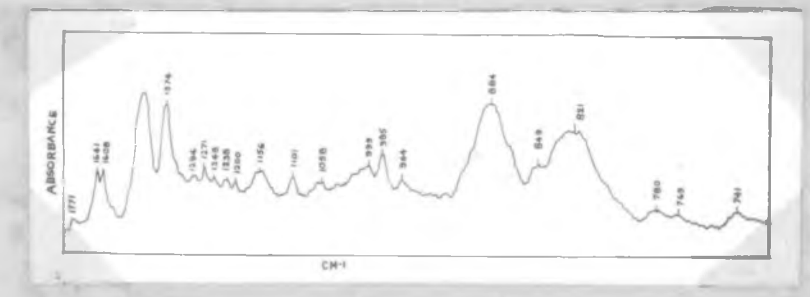
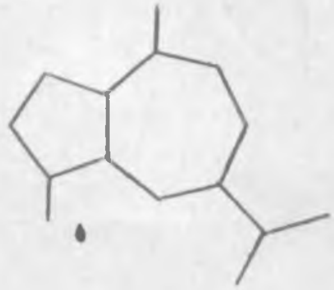


Fig. 7 - Infra-red spectrum (liquid film) of eudalenic conjugated 'Hydrocarbon D'.

710, 699, 661, 607 (principal), 586, 565, 372, 353 mμ. The formation of azulenes clearly indicated the presence of fused five and seven membered ring system in the molecule and a guaiane (21) type of carbon skeleton.



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The hydrocarbon on ozonolysis gave formaldehyde as the only volatile fragment identified through its dimedone derivative (m.p. 189°); no acetone was detected. The non-volatile product of ozonolysis was separated into acidic and neutral parts. The neutral part after chromatography gave a ketone in an yield of 2.5% which gave semicarbazone m.p. 208°. Regeneration of the ketone through semicarbazone and examination of its infrared spectrum was not possible, as the amount of semicarbazone was very little. The acidic product was methylated with diazomethane and the esterified product distilled. Elemental analysis indicated that it contains more than two oxygen atoms and the results are inconclusive.

<u>Isolation of Eudalenic Triene</u> (<u>Hydrocarbon D</u>)

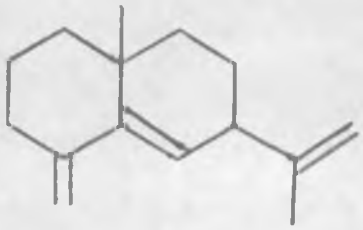
The laevorotatory fractions obtained during fractionation of lower boiling hydrocarbon 'Fraction A' (nos. 17 to 22, Table I, p.33) on extensive column chromatography over neutral alumina gave a hydrocarbon (D), with a high refractive index and was some what unstable.

b.p. 94-96°/0.7 mm; $[\alpha]_D^{26}$ -49°.15 (C, 3.54); n_D^{26} 1.5335.

Analysis : Found : C, 89.0 ; H, 10.63;
$C_{15}H_{22}$ requires : C, 89.04; H, 10.96%.

Infrared spectrum of this hydrocarbon (D) (Fig. 7) exhibited bands at 177[illegible], 1641, 1604, 884, 821 cm^{-1} characteristic of an exocyclic methylenic double bond in conjugation with a trisubstituted double bond. Bands in the region 960-970 and 700-725 cm^{-1} characteristic of a trans or cis disubstituted double bond were absent. Ultraviolet spectrum of the hydrocarbon, λ_{max} 227.5 mμ (log ε 4.24), 235 (4.16), 267 (3.42), indicated that it is a heteroannular diene[4]. Elemental analysis suggested the molecular formula $C_{15}H_{22}$ for the hydrocarbon. On hydrogenation with Adams catalyst in glacial acetic acid it absorbed three moles of hydrogen. The hydrocarbon on ozonolysis, gave copious amount of formaldehyde as the volatile fragment and no acetone was detected. On dehydrogenation with selenium it afforded eudalene (characterised through the T.N.B. adduct m.p. 110°) in an approximate yield of 46%.

In view of all the experimental facts tentative structure (22) has been assigned to it. An alternative structure (23) is also equally tenable as bands due to trisubstituted double bond were intense.



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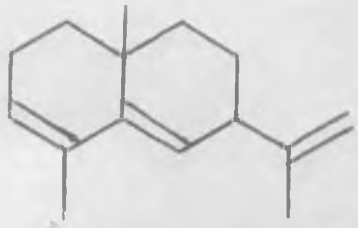

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Oxygenated constituents of Vetiver oil

The tail fractions (Nos. 11 and 12, Table I, p.51) obtained during fractionation of higher boiling fraction B, were combined and chromatographed over neutral deactivated alumina.

Chromatographic fraction 1 (Table VII, p. 87) eluted with petroleum ether was a minor fraction (9 g.) and its infrared spectrum and colour indicated that it was a mixture of conjugated hydrocarbons and azulenes. Considering the amount and complexity of this fraction, its examination was reserved for a future occasion.

Chromatographic fraction 2 (Table VII, p. 87) with benzene was rich in conjugated ketonic constituents (intense I.R. bands at 1675 and 1616 cm^{-1}, λ_{max} 233 (log ε, 4.152), λ_{max} 299 mμ) with traces of alcohols. Examination of this fraction also was kept aside for the time being.

Chromatographic fractions 3 and 4 (Table VII, p.87) eluted with benzene and ether mainly consisted of alcoholic constituents. Both the fractions were chromatographed separately and the relevant fractions were converted into acetates. Acetates of various fractions were chromatographed and separated into acetates and non-reactive alcohols. The alcohol eluted earlier from the column (fractions 2 to 7, Table VIII) gave acetate, which after chromatography was found to give several acetate fractions which possessed different physicochemical constants. The alcohol eluted slowly from the column with benzene (fractions 8 to 12, Table VIII) gave acetate, which after chromatography gave several acetate fractions identical in respect of specific rotations, refractive indices and infrared spectra. All such acetate fractions were combined and the alcohol (E) regenerated by saponification.

Infrared spectrum (Fig. 8) of this sesquiterpene alcohol (E), $C_{15}H_{24}O$, exhibited bands at 3248, 1031, 1087 (hydroxy group); 1780, 1642, 885 (exocyclic methylenic double bond) and 1383, 1366 and 1167 (probably isopropyl group) cm^{-1}. The acetate on hydrogenation with Adams catalyst in glacial acetic acid absorbed one mole of hydrogen, which indicated that the parent compound is a tricyclic sesquiterpene alcohol. When the dihydroalcohol, regenerated from dihydroacetate, was chromatographed, a sample of dihydroalcohol (I), $C_{15}H_{26}O$ along with a saturated hydrocarbon (II), possibly formed by hydrogenolysis of an allylic alcohol present as an impurity were separated. Dihydroalcohol (I) on oxidation with chromiumtrioxide-pyridine complex gave a liquid saturated ketone (III), $C_{15}H_{24}O$. Infrared spectrum of the ketone (Fig.9) indicated that it is a five membered ring ketone (band at 1733 cm^{-1}) and the band at 1404 cm^{-1} also indicated that the keto group is flanked on either or both sides by a methylene group. It readily formed a 2,4 D.N.P. derivative m.p. 133° (ethanol).

The parent alcohol (E) on treatment with p-toluene sulphonyl chloride in pyridine solution, gave the tosylate in a quantitative yield. The product on reduction with lithiumaluminiumhydride afforded a hydrocarbon (IV), $C_{15}H_{24}$. Infrared spectrum (Fig. 10) of this hydrocarbon (IV) exhibited bands at 1788, 1633, 891 cm^{-1} characteristic of an exocyclic-methylenic double band. The hydrocarbon (IV) on ozonolysis gave formaldehyde and a ketone (V), wherein intense I.R.band (Fig.11) at 1706 cm^{-1}, suggested a six or a seven membered ring ketone; doublet at 1364-1380 cm^{-1} and a band at 1154 cm^{-1} indicative probably of an isopropyl group and absence of band in the vicinity of 1420 cm^{-1} suggested that both the carbon atoms adjacent to the carbonyl are substituted. The ketone (V) did not give iodoform test, suggesting thereby that it was not a methyl ketone. The methylenic double bond in the hydrocarbon (IV), therefore, is not present in the isopropenyl side chain but more probably is exocyclic to a six or a seven membered ring.

The alcohol (E) on dehydrogenation with selenium at 280-290° gave a product, which showed ultraviolet absorption maxima at 227.5 and 267 mμ, but it was not a fully aromatised

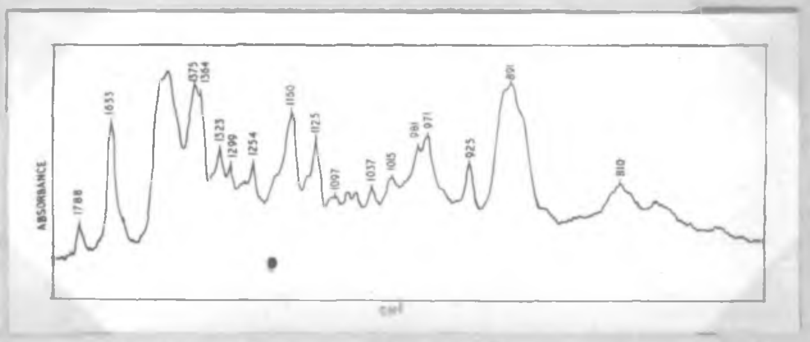


Fig.10 - Infra-red spectrum (liquid cell 0·1mm) of Hydrocarbon (IV) obtained by reduction of tosylate.

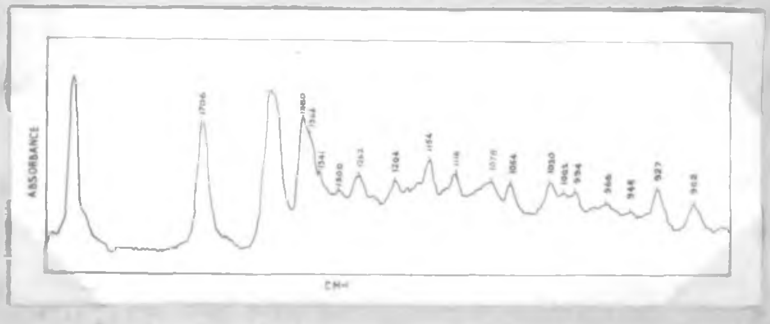


Fig.11 - Infra-red spectrum (liquid film) of Ketone (V) from Hydrocarbon IV by ozonolysis.

product of napthalenic type as it did not form any crystalline adduct with 1,3,5 T.N.B. or picric acid. No azulenes were formed during dehydrogenation. The hydrocarbon (IV), obtained from the tosylate by reduction, on dehydrogenation with selenium at 285-295°, also did not give any fully aromatised product which could be characterised through a crystalline derivative. However, its infra-red spectrum showed weak benzenoid absorption bands (1595, 1493, 828 cm^{-1}) indicating the presence of a small amount of partially aromatised product. The presence of a five and a six or seven membered ring in the molecule was evidenced from earlier experiments. 1-Isopropyl indane and 1-isopropyl hydrindane are known to undergo dehydrogenation with selenium only at 380° and above to yield the expanded product 2,2-dimethyl tetralin[5].

The hydrocarbon (IV) on hydrogenation absorbed one mole of hydrogen. The infrared spectrum (Fig.12) of the saturated hydrocarbon (VI) did not agree with any of the saturated tricyclic hydrocarbons known so far. The infra-red spectrum and specific rotation of this hydrocarbon (VI) and that of II (Fig.13) obtained by hydrogenolysis were however different. The alcohol isolated by us, therefore, appears to be a mixture of two tricyclic sesquiterpene alcohols, one of which is allylic and is responsible for the formation of a hydrocarbon through hydrogenolysis and that the nonallylic alcohol forms the major constituent.

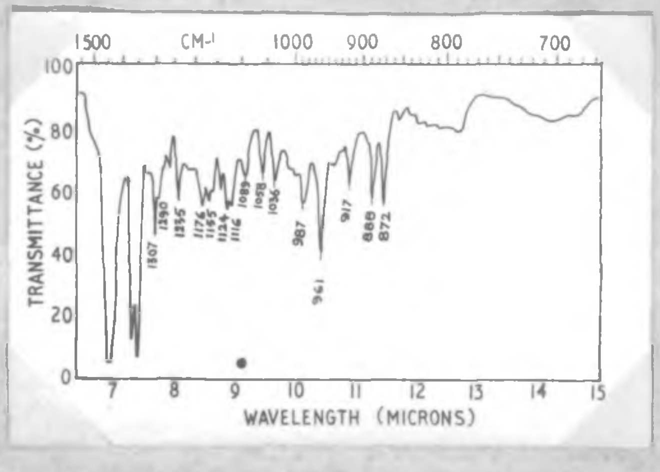


Fig. 12 - Infra-red spectrum (liquid cell, 0.05 mm.) of saturated Hydrocarbon VI from hydrocarbon IV.

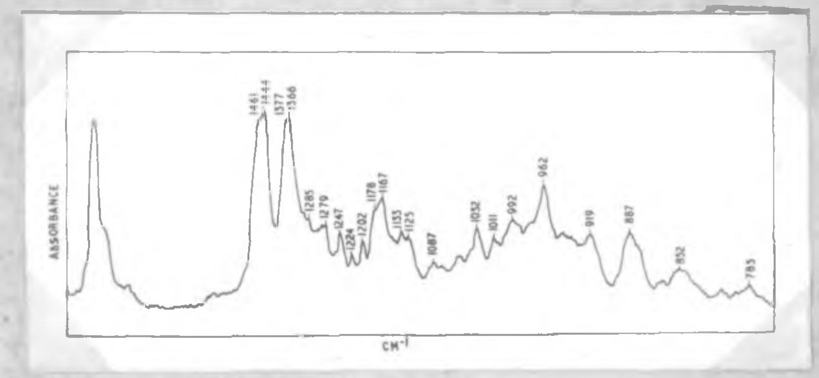
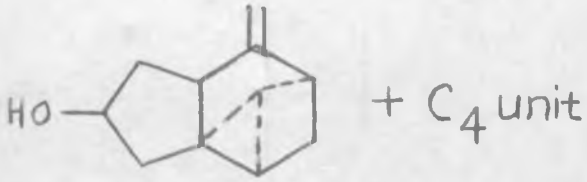


Fig. 13 - Infra-red spectrum (liquid cell, 0.1 mm.) of saturated Hydrocarbon II obtained by hydrogenolysis.

Chromic acid oxidation of the alcohol (E) also gave products which showed intense bands due to a five membered ring ketone (1729, 1408 cm^{-1}) and a six membered α-β-unsaturated ketone (bands at 1672 and 1644 of lesser intensity) arising from an allylic secondary alcohol. The mixture of these two ketones was difficult to separate by chromatography. It, however, gave a 2,4 D.N.P. derivative m.p. 163° (brought to a constant m.p. by crystallisations). Probably the five membered ring ketone, which is the major constituent with a methylene group adjacent to the carbonyl function furnished the derivative with ease. The yields of chromium trioxide-pyridine oxidation products were low and when chromium trioxide in acetic acid was used acetates were also formed in substantial quantities, the former reagent was therefore preferred.

The above experimental facts indicated that the sesquiterpene alcohol examined by us appears to be a mixture of two tricyclic sesquiterpene alcohols, the major constituent of which is nonallylic where the secondary hydroxy group is situated in a five membered ring and the methylenic double bond most probably in a six membered ring as represented by the partial structure (24).



24

It will be premature at this stage to make further structural suggestions.

+ + + + +

EXPERIMENTAL

Isolation of the tricyclic hydrocarbon (C)

The lower boiling laevorotatory hydrocarbon fraction A_1 (29 g., p. 33) was chromatographed on neutral alumina (grade I, 1.5 kg., ratio, 1:50) and the hydrocarbon eluted with petroleum ether. The results are tabulated in Table I.

Table - I

Frac. No.	Eluent	No. of ml. collected	Wt. in g.	n_D^{23}	$\alpha_D^{23^\circ}$ (clean)
1	Petroleum ether	50	3.006	1.4970	- 16.4
2	"	"	4.386	1.5000	- 19.6
3	"	"	4.126	1.5010	- 18.0
4	"	"	3.651	1.5020	- 16.8
5	"	"	3.013	1.5040	- 14.6
6	"	"	2.417	-	- 12.6
7	"	"	3.115	-	- 9.0
8	"	"	1.961	1.5100	+ 3.0
9	"	"	0.700	1.5110	-

Chromatographic fractions 6 and 7 (5.532 g. Table I) were combined and chromatographed on neutral alumina (grade I, 250 g.) and the column eluted with petroleum ether. The results are tabulated in Table II.

Table - II

Frac. No.	Eluent	No. of ml. collected	Wt.in g.	n_D^{23}	$\alpha_D^{23^\circ}$ (clean)
10	Petroleum ether	50	2.885	1.5020	- 16.5
11	"	"	1.226	1.5062	- 10.5
12	"	"	1.022	1.5100	- 0.5

Chromatographic fractions 1 to 5 and 10 were combined (21.068 g.) and rechromatographed on neutral alumina (grade I, 1.04 kg., ratio 1:50). The results are tabulated in Table III.

Table - III

Frac. No.	Eluent	No. of ml. collected	Wt.in g.	$\alpha_D^{23^\circ}$ (clean)
13	Petroleum ether	50	4.646	- 20.0
14	"	"	4.783	- 21.1
15	"	"	3.738	- 20.6
16	"	"	2.194	- 19.0
17	"	100	1.625	- 17.5
18	"	150	1.745	- 11.25
19	"	"	0.261	--

Chromatographic fractions 13 to 16 (above) were combined. The combined fraction did not show any absorption maximum characteristic of conjugated double bonds. It was therefore distilled over sodium (twice) and its physicochemical constants were determined.

b.p. 112-113°/6.5 mm; α_D^{23} $-19^{\circ}.46$ (clean); n_D^{23} 1.5000; d_4^{30} 0.9258;

$[R_L]_D$ (i) 64.46, (ii) 64.45, $C_{15}H_{24}\sqrt{1}$ requires 64.4.

Analysis : Found : C, 87.3 ; H, 11.6 ;

$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

Hydrogenation of hydrocarbon (C)

Hydrocarbon (0.568 g.) was hydrogenated in glacial acetic acid (15 ml.) using platinum oxide catalyst (12 mg.) at room temperature and atmospheric pressure. The absorption of hydrogen (67 ml.) corresponding to 0.92 mole of hydrogen was complete in $4\frac{1}{2}$ hours after which there was no further absorption. Catalyst was filtered off and the filtrate diluted with water and the hydrogenated product was taken up in petroleum ether. The petroleum ether extract was washed free of acid, dried and the solvent evaporated. The residue was distilled.

b.p. 150-152°(bath)/6.2 mm; $[\alpha]_D^{26}$ $-9^{\circ}.938$ (C, 2.515);

Analysis : Found : C, 87.6 ; H, 12.2 ;

$C_{15}H_{26}$ requires : C,87.3 ; H, 12.7 %.

The dihydroproduct did not consume any perbenzoic acid and did not give colouration with tetranitromethane.

Dehydrogenation of hydrocarbon (C)

(1) Hydrocarbon (0.456 g.) was heated with selenium powder (0.58 g.) at 280-290° in nitrogen atmosphere for 48 hours. The dehydrogenated product was taken up in ether, concentrated and chromatographed over alumina (grade I, 40 g.). The colourless nonazulenic product (0.27 g.) did not show any absorption in the ultraviolet region. The coloured azulenic fraction (0.044 g.) was purified through phosphoric acid complex when azulene (0.012 g.) was obtained. It afforded 1,3,5 T.N.B. adduct m.p. 107° (ethanol). Azulene was regenerated from the T.N.B. adduct by passing through alumina column (grade II, 4 g.) and its visible spectrum determined. (λ_{max} 610, 640, 372, 353, 320, 284, 228 mμ).

(2) Hydrocarbon (1.14 g.) was heated with selenium powder (2.2 g.) at 280-290° in nitrogen atmosphere for $4\frac{1}{2}$ hrs. The dehydrogenated product was taken up in ether, concentrated and chromatographed over alumina (grade II, 50 g.). The colourless nonazulenic fraction (0.87 g.) did not show any ultraviolet absorption and did not furnish any crystalline derivative with T.N.B. or picric acid. The petroleum ether solution of the coloured fraction (0.141 g.) was shaken with phosphoric acid repeatedly. The complex was decomposed by shaking with cold water and azulenes were extracted with ether. Ether extract was washed free of acid, dried and ether evaporated when azulenes (0.097 g.) were obtained. From the low melting point of the T.N.B. adduct obtained in the earlier

experiment, it was suspected to be a mixture and was therefore chromatographed on hundred fold alumina (grade I) and the azulenes eluted with petroleum ether in about 13 fractions of 15 ml. each. Fractions 2, 6 and 10 were examined directly with the spectrophotometer in the visible region, when it was clearly indicated that two blue azulenes were formed during dehydrogenation but there was no effective separation. Fraction nos. 1 to 8 were combined. After removal of solvent the residue was converted into 1,3,5 T.N.B. derivative (ethanol). After repeated crystallisations it was brought to a constant m.p. 131° (ethanol).

Visible and U.V. spectrum of azulene (T.N.B. m.p. 131°)

Azulene T.N.B. m.p. 131° (3.1 mg.) was passed through alumina column (grade II, 4 g.) and the azulene eluted with petroleum ether and petroleum ether : benzene (1:1). After evaporation of solvent it was dissolved in spectroscopically pure n-heptane (5 ml, solution I). 1 ml. of solution I was diluted to 5 ml. (solution II) and 1 ml. of solution II was diluted to 10 ml. (solution III). Solution I exhibited maxima at 607 (strong), 555, 586, 661, 699, 710, 733 mμ in the visible region and solution III exhibited maxima at 245, 306, 353, 372 mμ in the ultraviolet region.

The melting point of the T.N.B. adduct (131°) agrees well with that of chamazulene T.N.B., but its visible spectrum is considerably different from that reported by Plattner[6].

Chromatographic fractions 9 to 15 were combined and the T.N.B. adduct prepared (m.p. 125°). After repeated crystallisations from ethanol the m.p. was 147°. Mixed melting point with an authentic sample of guaiazulene, T.N.B. m.p. 151° was undepressed. The amount of T.N.B. adduct left at this stage was insufficient to determine its visible spectrum and the above finding could not be pursued further.

Ozonolysis of hydrocarbon (C)

A stream of dry ozonised oxygen was bubbled through a solution of hydrocarbon (3.3 g.) in ethyl acetate (20 ml.) at 0°, till completion. The solvent was removed under suction at 40°, and the ozonide was heated with water (20 ml.) on a water bath for 3 hours, trapping the ensuing gases in cold water. The trap water collected during ozonolysis and during decomposition of the ozonide gave strong tests for formaldehyde (dimedone derivative m.p. and mixed m.p. 189°) and negative iodoform test indicating absence of acetone. The nonvolatile part was extracted with ether and ether extract was separated into acidic and neutral parts by shaking with sodiumbicarbonate solution. The neutral ether extract (1.35 g.) was chromatographed over alumina (grade III, 30 g.). The product eluted with benzene gave semicarbazone m.p. 208°, but was insufficient for elemental analysis and regeneration of the pure ketone.

The bicarbonate extract after acidification and extraction with ether gave acidic product (2.5 g.). This was esterified with diazomethane and the neutral product was distilled under reduced pressure. The product was collected in three fractions according to boiling ranges :

(i) b.p. 145-150°/3 mm; 0.338 g. [Found : C, 70.34;
H, 8.76];
(ii) b.p. 178-185°/0.2 mm; 0.567 g. [Found : C, 67.9; H, 9.0);
(iii) b.p. 190-195°/0.2 mm; 0.33 g. was very viscous.

Isolation of hydrocarbon (D)

The laevorotatory fractions obtained during fractionation of A, (fractions 17 to 22, p.33 , α_D-2 to -38°) were combined (100 g.) and were chromatographed in two batches, each of 50 g. on neutral alumina (grade III, 1.5 kg.). The column was eluted successively with petroleum ether, petroleum ether : benzene (1:1), benzene and ether. The results of chromatography are presented in Table IV.

Table - IV

Frac. No.	Eluent	No. of ml. collected	Wt.in g.	n_D^{26}	$\alpha_D^{26°}$ (clean)
1	Petroleum ether	200	3.451	1.5155	- 0.3
2	"	"	11.801	1.5238	-26.3
3	"	"	7.437	1.5248	-38.3
4	"	"	1.929	1.5280	-40.3
5	"	500	0.634	1.5202	--
6	"	3000	1.412	1.4910	-28.5
7	Petroleum ether : benzene (1:1)	500	2.257	1.5022	-10.1
8	"	"	2.302	1.5082	+20.3
9	"	"	1.603	1.5118	+13.2
10	"	1000	2.341	1.5118	+15.9
11	Benzene	1000	2.373	1.5080	+ 8.5
12	"	"	1.809	1.5092	+20.1
13	Ether	"	7.108	1.5099	+15.0
14	"	"	2.996	1.5100	+23.3

Chromatographic fractions 2, 3 and 4 (Table IV, 40 g. from two batches) were combined and rechromatographed over alumina (grade III, 2 kg., ratio 1:50) and the column was eluted with petroleum ether. The results are recorded in Table V.

Table - V

Frac. No.	Eluent	No. of ml. eluted	Wt.in g.	n_D^{26}	$\alpha_D^{26°}$ (clean)
1	Petroleum ether	100	6.018	1.5113	+ 0.3
2	"	"	8.533	1.5220	-28.6
3	"	"	9.055	1.5240	-34.5
4	"	"	7.064	1.5263	-39.9
5	"	"	4.371	1.5285	-47.0
6	"	300	2.631	1.5300	-34.0

The laevorotatory fractions 2 to 5 (Table V) were combined and chromatographed repeatedly over grade III and grade II alumina. The earlier fractions eluted from the column, which were dextrorotatory and with a lower refractive index, were thus resolved by repeated column chromatography. The purest hydrocarbon thus obtained had a higher refractive index. During each chromatographic separation some loss of material to the column was also observed, which limited the use of higher ratio of alumina. The hydrocarbon D (2 g.) thus isolated was distilled under reduced pressure (twice) and its physicochemical constants were determined.

b.p. 94-96°/0.7 mm; n_D^{26} 1.5335; $[\alpha]_D^{26}$ -49°.15 (C, 3.54);

Analysis : Found : C, 89.0 ; H, 10.63;

$C_{15}H_{22}$ requires : C, 89.04; H, 10.96%.

Ultraviolet Spectrum :

The ultraviolet spectrum of the hydrocarbon (D) exhibited peaks at 227.5 mμ (ϵ , 17,400), 235 (14,520), 267 (6,524), with ϵ values at 215 (15,340), 211 (14,290), 210 (14,770) mμ respectively.

Hydrogenation of hydrocarbon (D)

Hydrocarbon (0.62 g.) dissolved in glacial acetic acid (15 ml.) was hydrogenated at room temperature and atmospheric pressure in the presence of Adams catalyst (30 mg.). The uptake of hydrogen corresponding to one mole was very quick ($1\frac{1}{2}$ hours) and second mole of hydrogen was absorbed during 13 hours, after which rate of absorption became very slow. The product was not examined further.

Selenium dehydrogenation of hydrocarbon (D)

Hydrocarbon (0.618 g.) was heated with selenium (0.612 g.) at 285° for 19 hours in nitrogen atmosphere. The dehydrogenated product was extracted with petroleum ether, concentrated and chromatographed over alumina (grade II, 20 g.). No azulenes were formed during dehydrogenation. The colourless hydrocarbon (0.452 g.; n_D^{26} 1.5530) was eluted with petroleum ether. Ultra-violet spectrum : λ_{max} 228 (ϵ, 45,220), 261, 280, 320 mμ (approximate yield was 46%). It readily furnished 1,3,5 T.N.B. adduct of eudalene m.p. 110° (ethanol), mixed melting point with an authentic sample was 111°.

Ozonolysis of hydrocarbon (D)

A stream of dry ozonized oxygen was bubbled through a solution of hydrocarbon (0.705 g.) in ethyl acetate (15 ml.) till the absorption was complete. The trap water collected during ozonolysis and during decomposition of the ozonide gave strong positive test for formaldehyde (dimedone derivative m.p. and mixed melting point 189°) and negative iodoform test for acetone. The nonvolatile product of ozonolysis was not examined further.

Oxygenated constituents of Vetiver Oil

Fraction Nos. 11 and 12 (Table I, p. 51) from four fractionation batches were combined (193 g.) and chromatographed over alumina (grade III, 6 kg., ratio 1:30). The column was eluted successively with petroleum ether (10 l.), benzene (25 l.) and ether (22 l.). The results of chromatography are tabulated in Table VI.

Table - VI

Frac. No.	Eluent	No. of litres	Wt.in g.	n_D^{24}	$[\alpha]_D^{24°}$
1	Petroleum ether	10	9.222	1.5250	+ 31.75
2	Benzene	10	55.983	1.5318	+ 47.12
3	"	15	55.469	1.5258	+ 33.13
4	Ether	10	33.559	1.5258	+ 34.36
5	"	12	2.910	dark brown & viscous	

Chromatographic fraction 1 (Table VI) was bluish in colour and from its infrared spectrum appeared to be a complex mixture of conjugated hydrocarbons and azulenes. Its examination was reserved for a future occasion.

Infra-red spectrum of fraction 2 (Table VI) exhibited intense bands at 1725, 1655, 1600 cm^{-1} characteristic of a five membered ring ketone and an α-β-unsaturated ketone and a weak hydroxy band at 3300 cm^{-1}. Its ultraviolet spectrum showed absorption maximum at 233 (ϵ,14,200) and 295 mμ

Chromatographic fraction 3 (55.9 g.) (Table VI) was rich in alcoholic constituents (I.R. band at 3300) and was rechromatographed over alumina (grade III, 1.68 kg., ratio 1:30) and the column was eluted with petroleum ether : benzene (1:1), benzene and ether. The results are recorded in Table VII.

Table - VII

Frac. No.	Eluent	No. of ml. collected	Wt. in g.	n_D^{23}	$[\alpha]_D^{23^\circ}$	Wt. of crude acetate g.
1	Petroleum ether : benzene (1:1)	500	3.464	1.5230		
2	"	"	2.632	1.5240	+ 19.16	7.122
3	"	"	2.683	1.5230		
4	"	"	2.892	1.5238	+ 20.47	11.471
5	"	"	2.092	1.5240		
6	"	500x2	4.59	1.5240	+ 20.15	
7	"	500x3	5.640	1.5248	→	7.396
8	Benzene	500	4.294	1.5266	+ 30.95	8.851
9	"	"	3.553	1.5262	-	
10	"	500x2	5.355	1.5268	+ 36.56	13.768
11	"	500x4	6.306	1.5262	+ 38.74	
12	"	500x7	6.743	1.5270	→	8.231
13	Ether	500x3	2.846	1.5250	→	3.87

Various fractions having similar refractive indices and rotations were combined, and treated with pyridine and acetic anhydride and kept at room temperature for 48 hrs. Crushed ice was added and contents were extracted with ether. Ether extract was washed successively with dilute hydrochloric acid, water, bicarbonate solution and dried. On evaporation of ether crude acetates were obtained. Weights of crude acetates are recorded in the last column of Table VII. Crude acetates of fractions 2 and 3 and 4 to 7 (Table VII) were chromatographed on alumina (grade II, ratio 1:30). Various acetate fractions

(n_D^{23} 1.4995, $[\alpha]_D^{28}$ + 12°) were obtained together with some unchanged alcohol (eluted with ether).

Crude acetate of fractions 8 and 9 (8.89 g., Table VII) was chromatographed over alumina (grade III, 250 g., ratio 1:30) and eluted with petroleum ether. Results are recorded in Table VIII.

Table - VIII

Frac. No.	Eluent	No. of ml. collected	Wt. in g.	n_D^{23}	$[\alpha]_D^{23}$ °
1	Petroleum ether	100	1.3327	1.5020	
2	"	"	1.7851	1.5038	combined & distilled. b.p. 135-140/ 0.2 mm. n_D^{23} 1.5058 $[\alpha]_D^{23}$ +32°.16
3	"	"	1.0850	1.5040	
4	"	200	1.1031	1.5048	
5	"	250	0.6038	1.5050	
6	"	"	0.5060	1.5052	
7	"	"	0.2917	1.5058	
8	Ether	1 l.	1.3270	1.5250	

Chromatography of crude acetates of fractions 10 and 11 (Table VII) in a similar way yielded acetate fractions with identical infrared spectra. These fractions were combined and distilled under reduced pressure. [b.p. 140-145° (bath)/ 0.4 mm, n_D^{21} 1.5060; $[\alpha]_D$ + 32°.4].

Chromatography of crude acetate of fraction 12 (Table VII) similarly yielded acetate fraction. (n_D^{28} 1.5028, $[\alpha]$ + 38°.3).

Chromatographic fraction 4 (Table VI, 33.5 g.) eluted with ether, which was mainly rich in alcoholic constituents with trace impurities of ketones as revealed from its infrared spectrum was chromatographed over alumina (grade III, 1 kg., ratio 1:30) and the column eluted with petroleum ether : benzene (1:1), benzene and ether. The results are recorded in Table IX.

Table - IX

Frac. No.	Eluent	No. of ml. collected	Wt. in g.	$n_D^{28.5}$	Wt. of crude acetate g.
1	Petroleum ether : benzene (1:1)	500x2	0.3472	1.4956	
2	"	500	1.9211	1.5190	
3	"	500	3.8519	1.5236	11.657
4	"	500x2	3.8588	1.5236	
5	"	500x2	4.7160	1.5238	9.921
6	"	500x2	2.7010	1.5242	
7	Benzene	500	1.4784	1.5248	10.326
8	"	500	2.2330	1.5251	
9	"	500x2	2.5600	1.5251	
10	"	500x2	1.6768	1.5262	
11	"	500x2	0.8382	1.5268	
12	"	500x5	0.9660	1.5262	
13	Ether	500x5	4.5986	--	

Chromatographic fractions 1 and 2 (Table IX) were mixture of ketones (I.R. band at 1732 cm^{-1}) and alcohols.

Relevant fractions as shown in Table IX were combined and were converted into their acetates in the usual manner. The weights of crude acetates are recorded in the last column of Table IX. Crude acetate of fractions 3 and 4 (Table IX, 11.6579) was chromatographed over alumina (grade III, 350 g.) and eluted with petroleum ether. The results are recorded in Table X.

Table - X

Frac. No.	Eluent	No. of ml. collected	Wt.in g.	n_D^{28}	$[\alpha]_D^{28}$
1	Petroleum ether	100	1.109	1.5010	
2	"	"	0.914	1.5028	Combined + 37.11°
3	"	"	0.822	1.5028	
4	"	200	1.325	1.5028	
5	"	"	0.635	1.5032	
6	"	"	0.512	1.5028	
7	"	500	0.794	1.5040	
8	Ether	500x2	2.204	1.5182	

Crude acetates of fraction 5 and 6 and 7 to 11 (Table IX) were similarly chromatographed and the relevant fractions were combined.

Acetate of Alcohol (E)

Part of the acetate (fractions 2 to 6; Table X) was distilled under reduced pressure.

b.p.150-155°(bath)/1.5 mm; n_D^{28} 1.5048; $[\alpha]_D^{24}$ +37°.11 (C,1.563)

Analysis : Found : C, 78.02; H, 10.01;

$C_{17}H_{26}O_2$ requires : C, 77.82; H, 9.99%.

Alcohol (E)

The mixture of acetate (6.0768 g.) dissolved in ethyl alcohol (25 ml.) and alcoholic potassium hydroxide solution (51 ml.; 5%) was refluxed on a water bath for 4 hrs. Contents after cooling were extracted with ether. Ether extract was washed free of alkali, dried and ether evaporated to give the regenerated alcohol (5.126 g.). A small part of the alcohol was distilled under reduced pressure.

b.p. 140-148° (bath)/0.4 mm; n_D^{22} 1.5260; $[\alpha]_D^{24}$ + 34°.31

Analysis : Found : C, 81.6 ; H, 10.9 ;

$C_{15}H_{24}O$ requires : C, 81.76; H, 10.98%.

I.R.spectrum (Fig.8) : Bands at 3448, 1642, 1383, 1366, 1167, 1121, 1087, 1064, 1031, 948, 895 cm^{-1}.

Hydrogenation of Acetate

Acetate (5.164 g.) dissolved in glacial acetic acid (25 ml.) was hydrogenated in presence of palladised carbon (11%, 0.51 g.) at room temperature and atmospheric pressure. The uptake of hydrogen was 620 ml. (1.1 moles) in 5 hr., after which there was no further absorption. The catalyst was filtered off, and the filtrate after dilution with water was extracted with hexane. Hexane extract was washed free of acid, dried and hexane evaporated to yield dihydroacetate

(4.842 g.). Part of it was chromatographed and then distilled under reduced pressure.

b.p.138-140°(bath)/0.4 mm; n_D^{22} 1.4920; $[\alpha]_D^{22°}$ + 25.54 (C, 0.7).

Analysis : Found : C, 77.49; H, 10.91;

$C_{17}H_{26}O_2$ requires : C, 77.22; H, 10.62%.

Dihydro alcohol (II)

Dihydroacetate (4.842 g.), dissolved in ethanol (25 ml.), was refluxed with alcoholic potassium hydroxide solution (50 ml, 5%) for 4 hours. The contents were diluted with water and extracted with ether. Combined ether extracts were washed free of alkali, dried and the solvent evaporated to give the residue (4.138 g.). Dihydroalcohol (3.3279) was chromatographed over alumina (grade III, 100 g.) and the column eluted successively with petroleum ether, benzene and ether. Results of chromatography are recorded in Table XI.

Table XI

Frac. No.	Eluent	No. of ml. collected	Wt.in g.	$[\alpha]_D^{26°}$
1	Petroleum ether	200	0.821	+ 3.85
2	Benzene	250	1.796	+ 28.44
3	Ether	250	0.747	+ 29.20

Infrared spectrum (Fig.13) of fraction 1 (Table XI) revealed that it was a saturated hydrocarbon. It did not give colouration with tetranitromethane. It was distilled over sodium.

b.p.138-142°(bath)/6 mm; n_D^{26} 1.4813; $[\alpha]_D^{26}$ $+3^{\circ}.85$

Analysis : Found : C, 86.8 ; H, 13.7 ;

$C_{15}H_{28}$ requires : C, 86.46; H, 13.54%.

Dihydroalcohol (fraction 2, Table XI) was distilled under reduced pressure :

b.p. 152-155° (bath)/0.1 mm; n_D^{28} 1.5058; $[\alpha]$ $+ 28^{\circ}.44$ (C,11.25

Analysis : Found : C, 81.5 ; H, 11.5 ;

$C_{15}H_{28}O$ requires : C, 81.02; H, 11.79%.

$C-CH_3$: (i) 6.83%; (ii) 7.2%.

<u>Chromiumtrioxide-pyridine oxidation of dihydroalcohol</u> (II)

Dihydroalcohol (0.5710 g., not chromatographed) dissolved in pyridine (5 ml.) was added dropwise to the chromiumtrioxide pyridine complex prepared by adding chromiumtrioxide (0.5539) to pyridine (5 ml.) at 0° and was allowed to stand at room temperature overnight. Contents were diluted with water and taken up in ether. Ether extract was washed with dilute hydrochloric acid, water and was given washing with sodiumbicarbonate solution. Aqueous bicarbonate layer was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed with water (twice), dried and the solvent evaporated to give 0.05 g. acidic product. It was not examined further. The neutral ethereal extract was washed free of bicarbonate, dried and the solvent evaporated. The residue (0.464 g.) was chromatographed over alumina (grade III, 25 g.). The petroleum ether eluate (0.1178 g.) gave a saturated hydrocarbon (II). Its infra-red spectrum was identical with the saturated hydrocarbon separated from dihydroalcohol by chromatography. Product (0.152 g.) eluted with petroleum ether : benzene (6:1) was the ketone (III). It readily formed 2,4 D.N.P. derivative m.p. 133° (ethanol). The ketone (III) was distilled, b.p. 145-148°(bath)/0.5 mm.

Analysis : Found : C, 81.45; H, 11.27;

$C_{15}H_{24}O$ requires : C, 81.76; H, 10.98%

I.R.spectrum (Fig.9) : Bands at - 1733, 1404, 1389, 1362, 1245, 1183, 1166, 1134, 1105, 1079, 1039, 1010, 995, 961, 952, 813, 760, 676 cm^{-1}.

Tosylate of alcohol (E)

Alcohol (1.368 g.) dissolved in pyridine (10 ml.) was added to freshly crystallised p-toluenesulphonyl chloride (1.548) dissolved in pyridine (10 ml.) and the reactants were allowed to stand overnight in a stoppered conical flask at room temperature. Contents were diluted with water and taken up in ether. Ether extract was washed successively with water, dilute hydrochloric acid, water, sodiumbicarbonate solution and finally with water. It was dried and evaporated to give 2.098 g. crude tosylate. I.R.spectrum - bands at : 1624, 1589, 1172, 1093 cm^{-1} and hydroxy peak (3448 cm^{-1}) was absent.

Lithiumaluminiumhydride reduction of tosylate

Tosylate (1.6503 g.) dissolved in dry ether (15 ml.) was added to a slurry of lithium aluminium hydride (0.89 g.) in dry ether (25 ml.) during 30 min. with cooling and the contents were refluxed with stirring for 3 hrs. Excess of lithiumaluminiumhydride was decomposed by adding moist ether and water. The hydroxide sludge was decomposed by the addition of dilute hydrochloric acid with stirring. Ether layer was separated and the aqueous layer was extracted with ether. Combined ether extracts were washed free of acid, dried and ether evaporated. The residue (1.05 g.) was chromatographed over alumina (grade I, 25 g.) and eluted with petroleum ether. The hydrocarbon (0.674 g.) after evaporation of solvent was distilled over sodium under reduced pressure, b.p. 145°(bath)/6.5 mm; n_D^{27} 1.5037; $[\alpha]_D^{26}$ + 33.88° (C, 1.8).

Analysis : Found : C, 88.4 ; H, 11.6 ;

$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

I.R.spectrum (Fig.10) - Bands at 1788, 1633, 1375, 1364, 1323, 1299, 1254, 1160, 1125, 1097, 1037, 1015, 981, 971, 925, 891, 810, 709 cm^{-1}.

Ozonolysis of hydrocarbon (IV)

A dry stream of ozonized oxygen was passed into the solution of hydrocarbon (0.673 g.) in dry ethyl acetate (15 ml.) until it was saturated. The trap water collected during ozonolysis gave test for formaldehyde (dimedone derivative m.p. 189°) and a negative iodoform test indicating absence of acetone. After removal of solvent under suction at 40°, the ozonide was heated with water (15 ml.)on a water bath for 3 hrs. Contents were then taken up in ether and the acidic product separated by washing with sodiumbicarbonat solution. The neutral product (0.5045 g.) was chromatographed over alumina (grade III, 25 g.). The petroleum ethe eluate after evaporation gave the ketone (V, 0.199 g.). It did not give iodoform test indicating absence of $CO-CH_3$ group I.R.spectrum is reproduced in (Fig.11).

Dehydrogenation of alcohol (E)

Alcohol (0.918 g.) was heated with selenium powder (0.948 g.) at 285-290°, in nitrogen atmosphere for 24 hours. The dehydrogenated product was taken up in petroleum ether, concentrated and chromatographed over alumina (grade II, 30 g.). The petroleum ether eluate (0.3 g., n_D^{26} 1.5312) showed ultraviolet absorption maxima at 227.5 and 267 mμ . The product was partially soluble in ethanol and the ϵ value could not be calculated.

Dehydrogenation of hydrocarbon (IV)

Hydrocarbon (0.316 g.) was heated with selenium powder (0.301 g.) at 285-295° for six hours in nitrogen-atmosphere. The dehydrogenated product was taken up in ether, concentrated and chromatographed over alumina (grade I, 25 g.). On evaporation of petroleum ether eluate (25 ml.) hydrocarbon (0.263 g., $n_D^{26.5}$ 1.5098) was obtained. No azulenes were formed during dehydrogenation. I.R. spectrum bands at : 1595, 1493, 1379, 1370, 1351, 1300, 878, 828, 750 cm^{-1}.

Hydrogenation of hydrocarbon (IV)

Hydrocarbon (0.346 g.) in glacial acetic acid (15 ml., partially soluble) was hydrogenated in presence of platinumoxide catalyst (10 mg.) for three hours. The uptake of hydrogen (48 ml.) corresponded to 1.1 moles. Catalyst was filtered off and the filtrate after dilution with water was extracted with petroleum ether. Petroleum ether extract was washed free of acid, dried and the solvent evaporated. The residue (0.33 g.) was distilled over sodium. b.p. 145-150°(bath)/6.5 mm; n_D^{27} 1.4925; $[\alpha]_D^{27}$ + 47.78° (C, 1.235). I.R. spectrum (Fig. 12) : Bands at 1307, 1290, 1263, 1235, 1176, 1155, 1142, 1124, 1116 , 1089, 1058, 1036, 987, 961, 917, 888, 872 cm^{-1}.

Chromic acid oxidation of alcohol (E)

To the chromium trioxide pyridine complex prepared by adding chromium trioxide (1.1 g.) to pyridine (10 ml.) at 0°, was added pyridine solution of alcohol (1.03 g. in 10 ml.) and was allowed to stand overnight. Contents were diluted with water and taken up in ether. Ether extract was washed successively with dilute hydrochloric acid, water and sodiumbicarbonate solution to remove acidic constituents. The aqueous layer after acidification and extraction with ether gave 0.2 g. acidic fraction. The neutral ether extract after evaporation of solvent gave 0.9134 g. crude oxidised product. 2:4 D.N.P. in phosphoric acid (0.25 g.) (4 ml.) was added to the neutral product (0.21 g.) in ethanol (20 ml.) and allowed to cool. The derivative immediately separated which was filtered and washed with hydrochloric acid. It was repeatedly crystallised from ethanol and brought to a constant melting point (163°).

Analysis : Found : N, 13.97% ;

$C_{21}H_{26}N_4O_4$ requires : N, 14.06%.

Neutral product (0.7 g.) was chromatographed over alumina (grade III, 30 g.). The ketonic fraction was eluted with benzene : petroleum ether mixture (1:2); ultraviolet spectrum : λ_{max} 245 mμ, (ϵ , 1,557); I.R.spectrum - bands at : 1739, 1672, 1635, 892 cm^{-1}. Subsequent fractions were mixture of ketones and unchanged alcohol.

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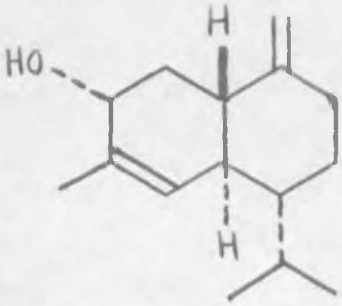
CHAPTER - IV

STRUCTURE AND ABSOLUTE CONFIGURATION OF KHUSINOL

CHAPTER - IV

SUMMARY

Khusinol, a crystalline secondary, sesquiterpene alcohol, $C_{15}H_{24}O$, isolated from North Indian vetiver oil is shown to have the absolute configuration represented by the structure (26), on the basis of degradative experiments and its conversion to (-)-γ-cadinene under mild conditions. It belongs to the unusual antipodal group of cadinenes, γ_1-Cadinene isolated from Malabar lemongrass oil has also been shown to belong to the same antipodal group.



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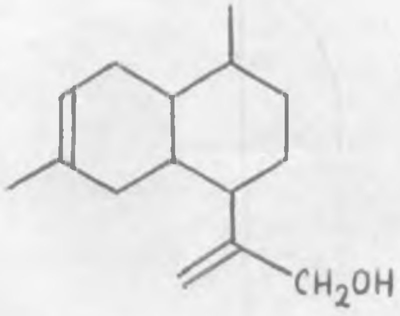
Isolation of Khusinol :

The laevorotatory vetiver oil (*Vetiveria zizanioides* Linn.) from Bharatpur and Biswan area (North India) on careful chromatography over neutral alumina gave a crystalline secondary sesquiterpene alcohol, $C_{15}H_{24}O$, m.p. 87°, as a major constituent in an yield of about 20-30%. In addition to this secondary alcohol, the oil also contained another primary sesquiterpene alcohol, Khusol, m.p. 101-102°, to the extent of about 5%. Khusol wasisolated from Bharatpur vetiver oil by Zutshi and Sadgopal[1] and it was characterised by Bhattacharyya et al[2], as shown in structure (25). We propose to name the secondary alcohol m.p. 87° as 'khusinol' so as to distinguish it from the primary alcohol khusol.

Structure of Khusinol

On the basis of experimental evidences which will be described in the sequel, gross structure (26) and the absolute configuration (27) has been assigned to khusinol.



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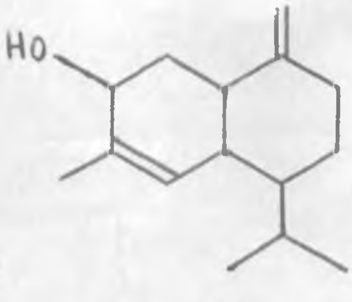

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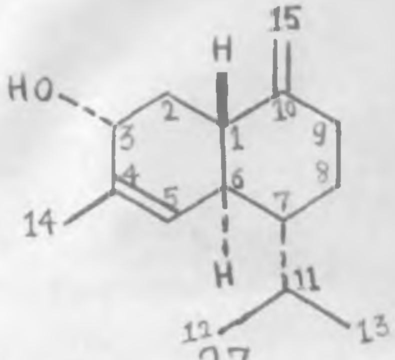

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Khusinol belongs to the unusual antipodal group of cadinenes and is of considerable interest from biogenetic

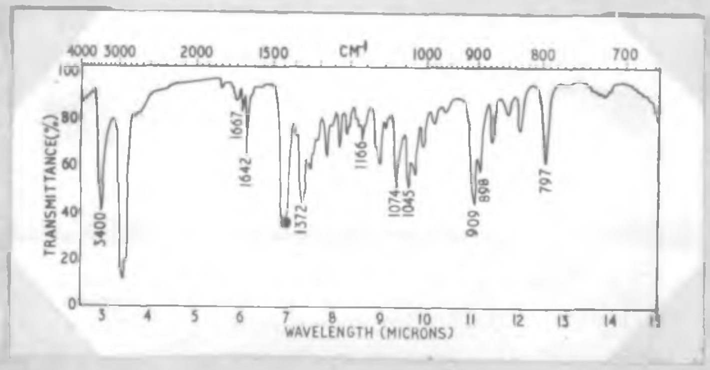


Fig. 14 - Infrared spectrum (in Nujol) of 'Khusinol'.

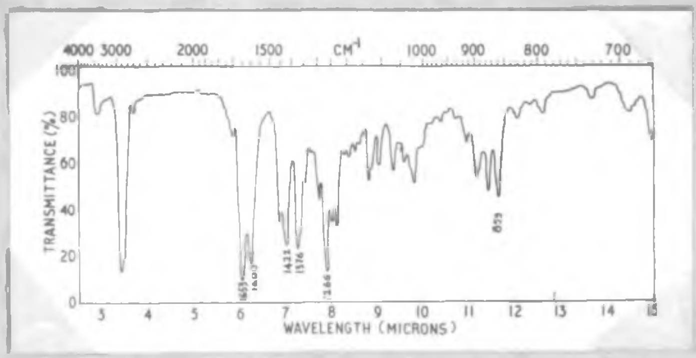


Fig. 15 - Infra-red spectrum (liquid film)
of Ketone (30) from Khusinol.

point of view. Khusinol also appears to be the first secondary alcohol of the cadinane group reported so far.

Infra-red spectrum of khusinol (Fig.14) exhibited bands at 3400, 1074 (hydroxy group), 909, 898 and 1642 (and methylenic double bond), 797 and 1667 (trisubstituted double bond), 1340, 1370 and 1166 (isopropyl group) cm^{-1}.

On hydrogenation with Adams catalyst in glacial acetic acid it absorbed two moles of hydrogen to furnish tetrahydrokhusinol (29), $C_{15}H_{28}O$, m.p. 93-94°. Perbenzoic acid titrations also showed the presence of two double bonds in khusinol. Hence khusinol is a bicyclic sesquiterpene alcohol. It did not show any absorption maximum in the ultra-violet region indicating the absence of conjugation.

Khusinol easily formed a liquid acetate, $C_{17}H_{26}O_2$, on treatment with acetic anhydride and pyridine at room temperature in good yield. On dehydrogenation with selenium at 280-286°, khusinol afforded cadalene (characterised through picrate, m.p. and mixed melting point 115°) in an excellent yield. It is therefore a cadalenic sesquiterpene alcohol. On ozonolysis, it yielded formaldehyde as the only volatile fragment (dimedone derivative, m.p. and mixed m.p. 189°) and no acetone was detected. This further confirmed the presence of an exocyclic methylenic double bond. The nonvolatile portion gave positive tests for a methyl ketone (iodoform test) and an aldehyde function, product arising from ozonolysis of a trisubstituted double bond.

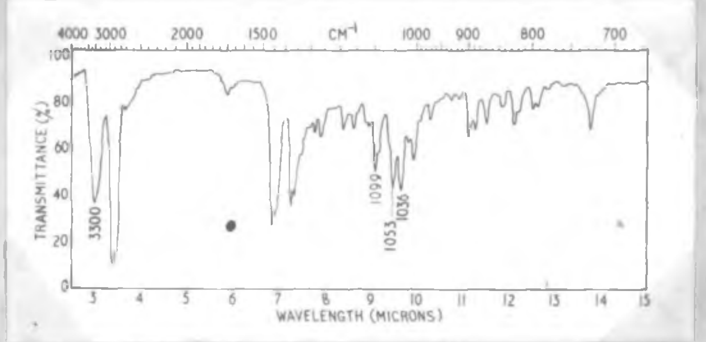


Fig. 16 - Infra-red spectrum (in Nujol) of 'Dihydrokhusinol'

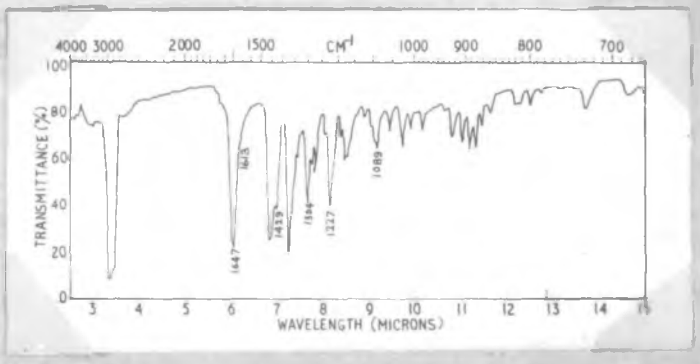


Fig. 17 - Infra-red spectrum (in Nujol) of Ketone (31) from dihydrokhusinol.

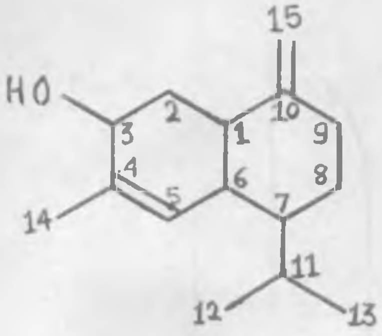
Khusinol on chromic acid oxidation in acetic acid gave an α-β-unsaturated ketone (30), $C_{15}H_{22}O$, (λ_{max} 243 mμ; log ϵ, 4.01). Its infrared spectrum (Fig.15) showed intense bands at 1653 and 1600 cm^{-1}, due to α-β-unsaturated carbonyl group, and further a band at 1422 cm^{-1} suggested the presence of at least one methylene group (CH_2) adjacent to the carbonyl. On partial hydrogenation in presence of palladised carbon in ethanolic solution, khusinol absorbed only one mole of hydrogen and furnished dihydrokhusinol (28), $C_{15}H_{26}O$, m.p. 111°. Its infrared spectrum (Fig. 16) clearly showed absence of methylenic double bond. Dihydrokhusinol (28) on chromic acid oxidation in acetic acid furnished a crystalline α-β-unsaturated ketone (31), $C_{15}H_{24}O$, m.p. 96-97°. Its ultraviolet spectrum (λ_{max} 233 mμ, log ϵ, 4.14) and infrared spectrum (Fig.17, intense bands at 1647 and 1613 cm^{-1}) clearly indicated that the secondary hydroxy group in dihydrokhusinol was allylic to the trisubstituted double bond. On complete hydrogenation with Adams catalyst in glacial acetic acid dihydrokhusinol absorbed another mole of hydrogen and furnished tetrahydrokhusinol (29) $C_{15}H_{28}O$. On chromic acid oxidation, it gave a liquid saturated ketone (32), $C_{15}H_{26}O$, in which I.R. band at 1704 cm^{-1} (Fig.18) indicated the keto group on a six membered ring. Oxidation of khusinol with activated manganese dioxide yielded the ketone in an unsatisfactory yield.

Kuhn-Roth estimations of khusinol and dihydrokhusinol (1.75 and 2.22 respectively) showed a definite rise in the C-CH_3 groups indicating that the methylenic double bond was not present in the C_7 isopropyl side chain, and most probably may be at C_4 or C_{10} .

The location of the secondary hydroxy group was proved in the following way. The saturated ketone (32) obtained by chromic acid oxidation of tetrahydrokhusinol, was treated with methyl magnesium iodide, to yield the carbinol (33), which on dehydrogenation with selenium afforded 7-methyl-cadalene (34). Formation of 7-methyl-cadalene from tetrahydrokhusinol proved the location of the secondary hydroxy group at carbon atom 3 of the cadinane skeleton.

Additional proof for the position of the trisubstituted double bond in khusinol was obtained by the labelling method of Campbell and Soffer[3]. Epoxy alcohol (35) prepared by the action of perbenzoic acid on dihydrokhusinol was treated with methyl magnesium iodide. The diol (36) thus obtained on subsequent dehydrogenation with selenium afforded, 1,2,5-trimethylnapthalene (37) identified through the 1,3,5-T.N.B. and picric acid complexes. Introduction of methyl group at C_5 position, eliminated the bulky isopropyl group at C_7 during dehydrogenation resulting in the formation of 1,2,5-trimethylnapthalene[4].

All these reactions shown schematically in chart I conclusively prove the gross structure (26) assigned to khusinol.



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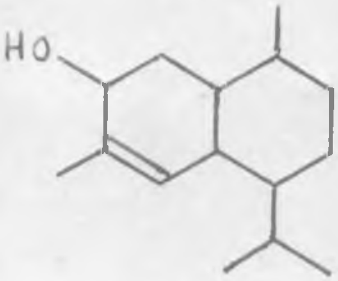

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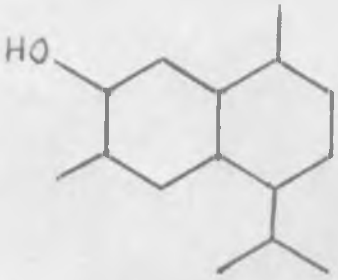

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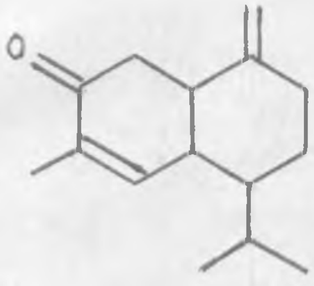

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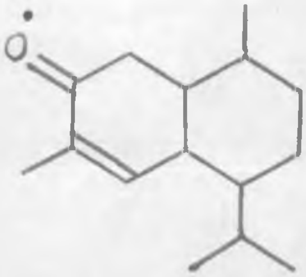

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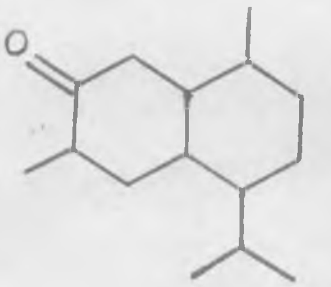

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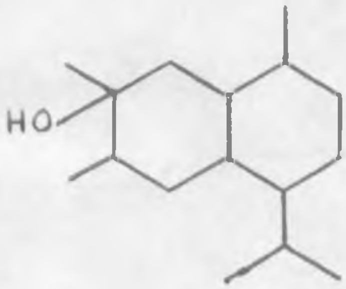

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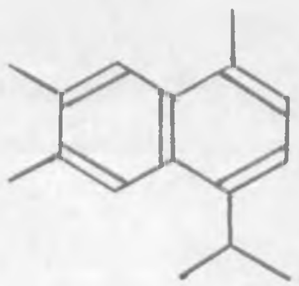

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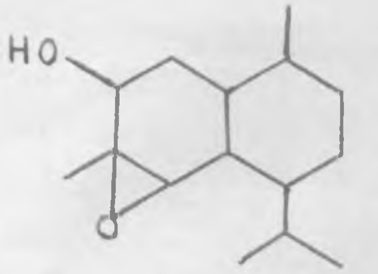

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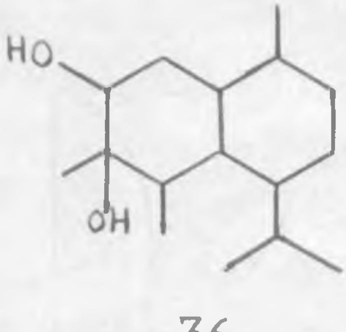

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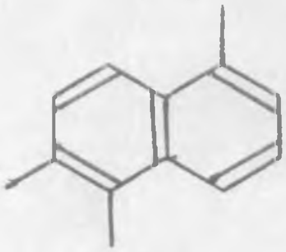

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CHART 1

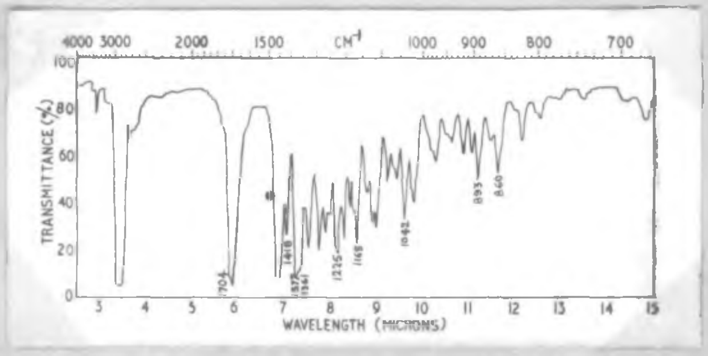

Fig.18 - Infra-red spectrum (liquid cell) of Ketone (32) 0·05 mm. from Tetrahydrokhusinol.

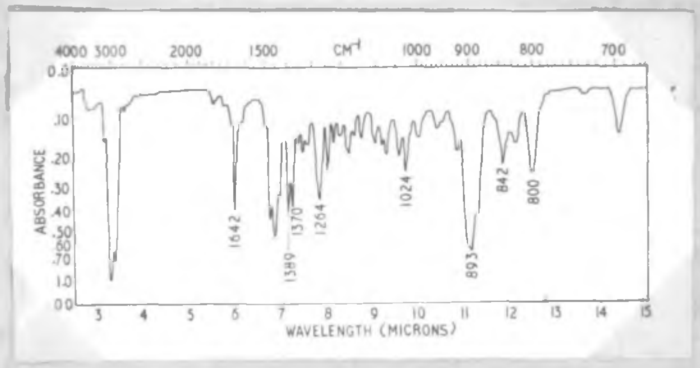

Fig.19 - Infra-red spectrum (liquid film) of Oxide (?) from Khusinol.

Absolute Configuration of Khusinol

With a view to elucidating the absolute configuration of asymmetric centres of khusinol, it was converted to its tosyl derivative by treating with tosyl chloride in pyridine solution at room temperature for 80 hours in an yield of about 80%, a condition which was found to be optimum. Attempts to increase the yield of the tosylate by heating at 50° for 48 hours resulted in the formation of a product, in which nitrogen and sulphur were absent. Absence of ketonic and hydroxy functions was clear from its infra-red spectrum (Fig. 19) and an intense band at 1264 cm^{-1} indicated that probably it may be an oxide, an argument which was supported by its elemental analysis. Infrared spectrum showed the presence of methylenic (1642 and 893 cm^{-1}) and trisubstituted double bonds (1669 and 800 cm^{-1}). It exhibited ultra-violet absorption maximum at 250 mμ (log ϵ, 4.09). It is being further examined.

Attempts to isolate the tosylate in a pure form, which appeared to be a crystalline derivative by rechromatography resulted in decomposition of the tosylate and subsequent formation of conjugated dienes. These products were not studied in details. At one stage we were fortunate to isolate the tosylate in a pure form by careful chromatography. Its infrared spectrum is reproduced in Fig. 20.

The crude tosylate (containing small amount of unchanged alcohol which was not purified for reasons stated

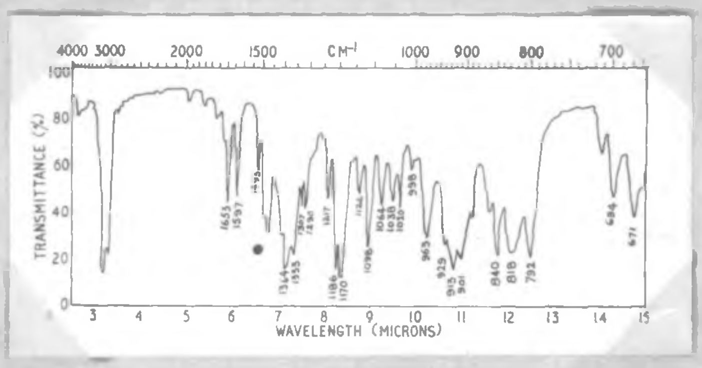

Fig.20 - Infra-red spectrum (liquid film) of Tosylate of Khusinol.

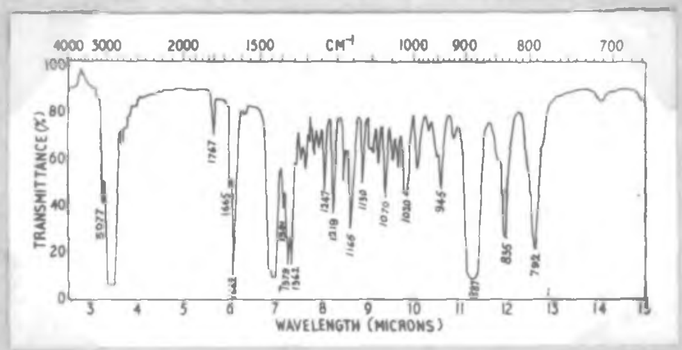

Fig.21 - Infra-red spectrum (liquid cell, 0.1 mm.) of (–)-γ-cadinene from Khusinol.

above) on reduction with lithium aluminium hydride and subsequent chromatography gave a hydrocarbon (39), $C_{15}H_{24}$, in good yield. Its infra-red spectrum (Fig. 21) and other physicochemical constants were identical with those of (+)-γ-cadinene (41, $[\alpha]_D^{26}$ + 148°) isolated by Pliva and coworkers[5] from citronella oil. However, its specific rotation (-153°) clearly indicated that the hydrocarbon (39) obtained from khusinol was the optical antipode of (+)-γ-cadinene (41).

To further confirm the antipodal nature of the hydrocarbon (39), it was converted to its crystalline dihydrochloride (40) by passing dry hydrogen chloride in ethereal solution. Its melting point, 117°.5, was identical with that of normal cadinene dihydrochloride (m.p. 118°), but its specific rotation (+ 36°.2) was equal but opposite in sign to that of normal cadinene dihydrochloride (- 36°).

Mixed melting point of (+)-cadinene dihydrochloride (40) from khusinol with an authentic sample of (-)-cadinene dihydrochloride (42)* showed depression (102°), which is in accordance with expectation, since (±)-cadinene dihydrochloride m.p. 105-6° has been obtained from optically inactive δ-cadinene[6,7] and has also been synthesised[8].

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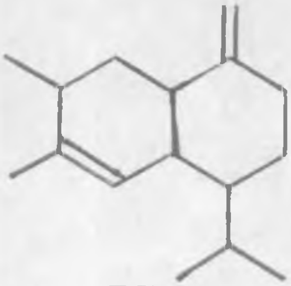
* We are thankful to Dr. Sukh Dev for the sample of (-)-cadinene dihydrochloride m.p. 118°, ($[\alpha]_D^{25}$ - 36) and symmetrical T.N.B. adduct of 1,2,5-trimethyl napthalene.



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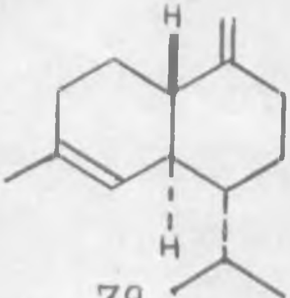

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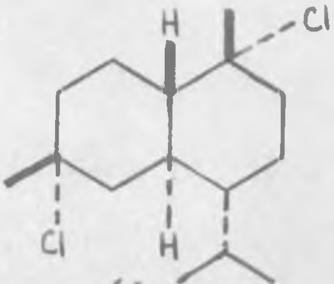

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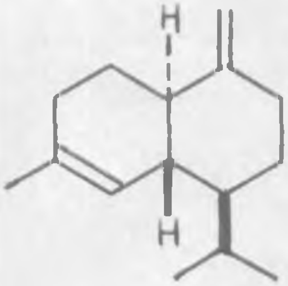

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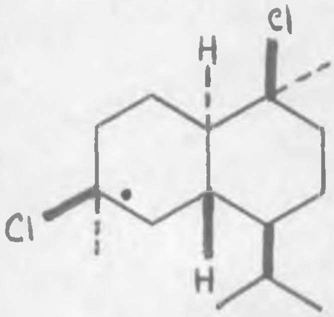

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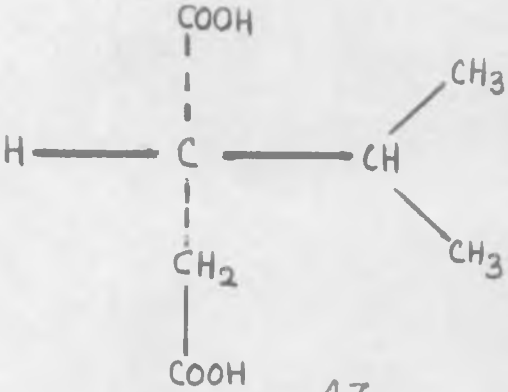

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Absolute configuration of cadinenes and cadinols yielding (-)-cadinene dihydrochloride have been determined on the basis of X-ray diffraction measurement of (-)-cadinene dihydrochloride[9] (42) and also by determining the absolute configuration at C_7 by isolating D-(+) isopropyl succinic acid (43)[10], an ultimate product of oxidative degradation of β-cadinene. Same conclusion has been arrived at by comparative study of the rotatory dispersion curves of the ketones (44) and (45) obtained from α-cadinol[11] with that of ketone (46)[12] whose absolute configuration is known. Consequently, (-)-γ-cadinene from khusinol and (+)-cadinene dihydrochloride obtained from it are represented by the antipodal configurations (39 and 40). The optical rotatory dispersion curves*

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* We are grateful to Prof. W. Klyne for determining the O.R.D. Curves of three samples of cadinene dihydrochloride.

(Fig. 22) of (+) cadinene dihydrochloride from (-)-γ-cadinene obtained through khusinol and the normal (-)-cadinene dihydrochloride also show enantiomeric relationship, showing plain positive and plain negative cotton effect. Khusinol, therefore, can be represented by the absolute configuration (47) where the hydroxy group is assigned α-equatorial orientation from its ease of esterification.

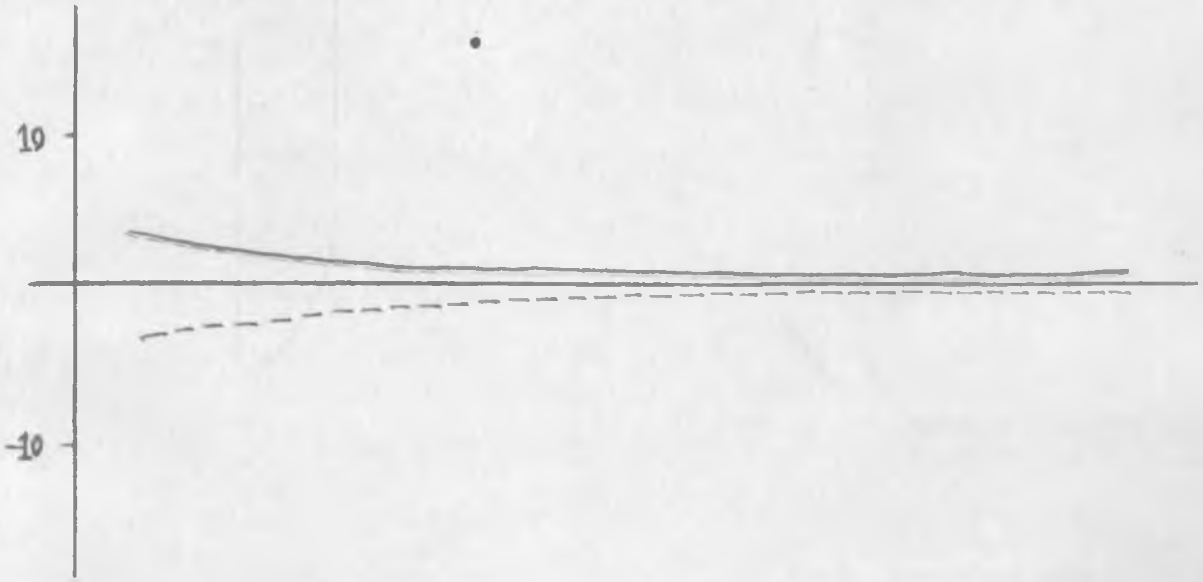
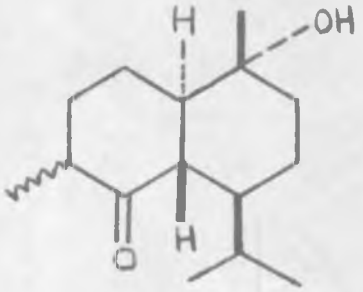


Fig.22 : O.R.D.Curve of
—— (+) Cadinene dihydrochloride (from khusinol)
- - - (+) Cadinene dihydrochloride (from γ_1-cadinene)
— — (-) Cadinene dihydrochloride (in MeOH).



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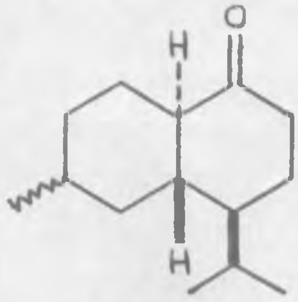

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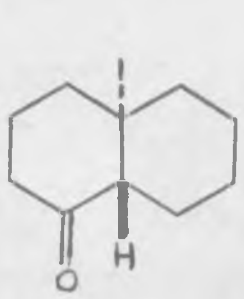

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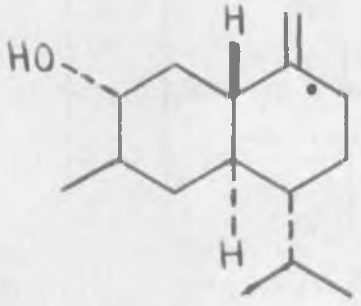

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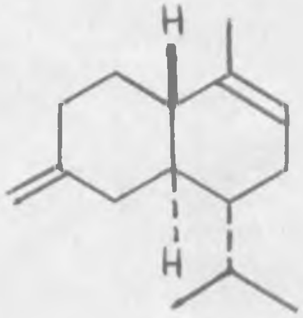

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A survey of literature indicates that (+)-cadinene dihydrochloride has been previously obtained by R.Gardner[13] from a laevorotatory sesquiterpene fraction of the oil of Metrosideros scandens. The dihydrochloride prepared from it had a m.p. 118°, $[\alpha]_D^{26}$ $+30^{\circ}$ (C, 4% in chloroform). From a study of the mixed melting point curve of (+) dihydrochloride and the usual (-) dihydrochloride he concluded that they were optical antipodes. The same oil was later on studied by Birch[14], who separated aromadendrene ($[\alpha] - 22^{\circ}$) and l-cadinene ($[\alpha] - 80^{\circ}$) from it. This l-cadinene again furnished (+) cadinene dihydrochloride.

Previously, γ_1-cadinene has been isolated in this laboratory from Malabar lemongrass oil and its structure elucidated. It also gives cadinene dihydrochloride, m.p. 118°. Its specific rotation which was not determined at that time has now been found to be + 36.8°. It does not depress the melting point of (+)-cadinene dihydrochloride obtained from (-)-γ-cadinene via khusinol but depresses the melting point of (-)-cadinene dihydrochloride. γ_1-Cadinene, therefore, also belongs to antipodal group and is assigned the absolute configuration (48).

Khusinol may be identical with cussol, isolated and preliminarily examined by Zutshi and Sadgopal[17].

EXPERIMENTAL

Vetiver oil was obtained from reliable suppliers at Kannauj, contacted through Government Agencies.

Physicochemical properties of the oil were determined. Sp. gra^{30} 0.9914, n_D^{26} 1.5182, $[\alpha]_D^{25}$ -82.26, ester no., 16.15, acid No.9.7, ester no. after acetylation, 123.3. Carbonyl content 13.7% (Hydroxylamine hydrochloric method).

Isolation of Khusinol (26) :

Vetiver oil (400 g.) was chromatographed on neutral alumina (grade II, 6 kg.) and eluted successively with petroleum ether (15 l.), ether (14 l.) and alcohol (10 l.). The product (250 g.) obtained by elution with ether was rechromatographed on neutral alumina (grade II, 3.3 kg.). The viscous petroleum ether eluate deposited crystals of khusinol on keeping at 0°. The crystals (20% from Bharatpur oil and 30% from Biswan oil) were filtered off and recrystallised from petroleum ether, m.p. 87°; $[\alpha]_D^{25}$ - 174.4° (C, 5.03)

Analysis : Found : C, 81.03; H, 11.1 ;

$C_{15}H_{24}O$ requires : C, 81.76; H, 10.98%.

I.R. spectrum (Fig.14) : Bands at 3400, 1709, 1667, 1642, 1372, 1340, 1282, 1241, 1215, 1166, 1116, 1074, 1045, 1029, 1010, 909, 898, 877, 851, 833 and 797 cm^{-1}.

Khusinol acetate :

Khusinol (0.5 g.) was treated with pyridine (50 ml.) and acetic anhydride (7 ml.) at room temperature for 24 hours. Contents were poured into crushed ice and processed in the usual way. The crude acetate (0.641 g.) was chromatographed on alumina (grade II, 20 g.) and the petroleum ether eluate after evaporation of solvent was distilled (0.503 g.), b.p. 150°(bath)/0.5 mm; n_D^{28} 1.4999; $[\alpha]_D^{28}$ -168°.4 (C, 6.855).

Analysis : Found : C, 78.0 ; H, 10.1 .

$C_{17}H_{26}O_2$ requires : C, 77.82; H, 9.99%.

I.R. spectrum - Bands at : 1715, 1625, 1220, 1050, 890, 795 cm^{-1}.

Dehydrogenation of Khusinol (26)

Khusinol (0.5 g.) was heated with selenium powder (1 g.) at 280-286° for 17 hours in nitrogen atmosphere. The dehydrogenated product was extracted with ether and filtered to give 0.31 g. of dehydrogenation product. Cadalene content was about 90% on the basis of ultraviolet spectrum. It readily formed cadalene picrate, m.p. and mixed m.p. with an authentic specimen was 115°.

Ozonolysis of Khusinol (26)

A stream of dry ozonised oxygen was passed through a solution of Khusinol (0.146 g.) in dry chloroform (20 ml.)

for 3 hrs. at 0°. The ozonised solution was steam distilled and the distillate containing chloroform was treated with dimedone solution (0.52 g. in 200 ml. water). Chloroform was removed by distillation and on cooling formaldimethone separated, which was filtered and dried to constant weight (m.p. and mixed m.p. 189°, 0.052 g.; 26.83% of theory). The steam distillate gave negative iodoform test. The decomposed ozonide was extracted with ether and solvent evaporated. The non-volatile residue gave positive iodoform test in dioxan and reduced Fehling's solution.

Ketone (30) from Khuzinol

A solution of chromium trioxide (2.8 g.) in minimum amount of water was added to a solution of khusinol (5.2 g.) dissolved in glacial acetic acid (15 ml.) under cooling and shaking during 10 minutes, followed by heating on a water bath for one hour and was then left overnight at room temperature. Reaction mixture was diluted with at water and extracted with ether. Ether extract was separated into acidic (0.15 g.) and neutral parts (4.2 g.). The neutr product after chromatography on alumina (grade II, 80 g.) gav the pure ketone (30, 0.45 g.) on elution with petroleum ether, b.p. 155-160°(bath)/2.5 mm; n_D^{27} 1.5315; $[\alpha]_D^{25}$ + 49.86° (C, 5.234).

Analysis : Found : C, 81.79; H, 10.25.

$C_{15}H_{22}O$ requires : C, 82.51; H, 10.16%.

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$C_{15}H_{22}O$ requires : C, 82.51; H, 10.16%.

Ketone (31) from dihydrokhusinol

Chromium trioxide (0.3 g.) dissolved in minimum amount of water was added to a solution of dihydrokhusinol (0.48 g., m.p. 108-110°) in glacial acetic acid (8 ml.) under cooling and shaking during 5 minutes. The reaction mixture was heated on a water bath for 1 hour and was left overnight at room temperature. Contents were diluted with water and extracted repeatedly with ether. Ether layer was washed successively with water, sodium bicarbonate solution (8%) and finally with water and dried. After removal of solvent, residue (0.496 g.) was chromatographed over alumina (grade II, 15 g.). The pure ketone (31) was eluted with a mixture of petroleum ether-benzene (1:1), m.p. 92°, which after careful sublimations was 96-97°; $[\alpha]_D^{26}$ + 48.37° (C, 1.375).

Analysis : Found : C, 81.8 ; H, 10.91.

$C_{15}H_{24}O$ requires : C, 81.76; H, 10.98%.

U.V. spectrum : λ_{max} 233 mμ, $\log \epsilon$, 4.14.

I.R. spectrum (in Nujol, Fig. 17) bands at : 1647, 1613, 1429, 1377, 1366, 1304, 1274, 1227, 1175, 1089, 1056, 1026, 1009, 983, 923, 905, 893, 884, 873, 858, 821, 799 cm^{-1}.

Tetrahydrikhusinol (29)

A solution of dihydrokhusinol (m.p. 107-111°, 3.36 g.) in glacial acetic acid (25 ml.) was hydrogenated at room temperature and atmospheric pressure in the presence of Adams catalyst (0.014 g.). The hydrogenation was complete after the absorption of 350 ml. hydrogen corresponding to 0.85 mole of hydrogen during 5 hours. Catalyst was filtered off and the filtrate neutralised with potassium hydroxide solution (10%) and the hydrogenated product taken up in ether Ether layer was washed till neutral and dried. Tetrahydroproduct (3.22 g.) was chromatographed over alumina (grade III 100 g.) and eluted with petroleum ether and petroleum ether : benzene mixture (1:1) and sublimed to give tetrahydrokhusinol (29), m.p. 93-94°; $[\alpha]_D^{24}$, 20.84°.

Analysis : Found : C, 79.63; H, 12.46;
$C_{15}H_{28}O$ requires : C, 80.29; H, 12.58%.

I.R. spectrum : bands at : 3260, 1376, 1361, 1342, 1269, 1192 1156, 1134, 1099, 1050, 1040, 960, 887, 860, 840, 825, 795 cm

Some slightly lower melting fractions having nearl identical IR spectra were also obtained. This evidently was due to presence of isomers. A trace of hydrocarbon was also formed due to hydrogenolysis of the allylic hydroxyl group.

Ketone (32) from tetrahydrokhusinol

A solution of tetrahydrokhusinol (4 g.) in glacial acetic acid (50 ml.) was oxidised with chromium trioxide (4 g. following the procedure described earlier. Ketone (32) forme was purified by chromatography and distillation;

b.p. 140-50°(bath)/3.5 mm.; $[\alpha]_D^{24}$ +18.8° (C, 5.155); n_D^{24} 1.4849.

Analysis : Found : C, 81.5 ; H, 11.9 ;
$C_{15}H_{26}O$ requires : C, 81.02; H, 11.79%.

I.R. spectrum (Fig. 18) bands at : 1704, 1453, 1418, 1377, 1361, 1326, 1290, 1266, 1225, 1200, 1186, 1168, 1136, 1120, 1111, 1083, 1063, 1042, 1018, 973, 940, 920, 905, 893, 873, 860, 825, 797 cm^{-1}.

Grignard reaction on tetrahydroketone and dehydrogenation of the carbinol (33)

The ethereal solution of tetrahydroketone (32) (0.75 g.) was added dropwise to methyl magnesium/iodide prepared from magnesium (0.49 g.) and methyl iodide (1.5 ml.) in dry ether (10 ml.) with cooling and stirring. The mixture was refluxed for 3 hours. Grignard complex was then decomposed by the addition of saturated ammonium chloride solution at 0°, extracted with ether, washed with water, dried and solvent evaporated when crude carbinol (0.87 g.) was obtained. IR spectrum showed the presence of small amount of ketonic impurities which was removed by chromatography over alumina (grade II, 80 g.) and elution with petroleum ether. A portion of the carbinol (0.19 g.) eluted with petroleum ether : benzene mixture (1:1) was heated with palladised carbon (30%, 0.1 g.) at 300-330° for 20 hours in nitrogen atmosphere. The dehydrogenated product was taken up in ether, washed with caustic soda solution (5%), water and dried, and ether evaporated. The residue (0.145 g.) was chromatographed over alumina (grade II, 20 g.) and eluted with petroleum ether to yield the hydrocarbon (0.11 g.). It furnished 1:3:5 T.N.B. derivative of 7-methylcadalene (34), m.p. 126°.

Analysis : Found : C, 62.5 ; H, 5.2 ; N, 10.0;
$C_{22}H_{23}O_6N_3$ requires : C, 62.36; H, 5.45; N, 9.88%.

Epoxy alcohol (35) from dihydrikhusinol

Dihydrokhusinol (1.7 g.) dissolved in chloroform (5 ml.) was treated with a chloroform solution of perbenzoic acid (120 ml., 0.25N) and kept at 0° for 16 hours. Chloroform solution was washed with bicarbonate, water and dried. Evaporation of solvent gave crude epoxy alcohol (35) (1.86 g.). I.R.spectrum bands at : 3280, 1700, 1263, 1214, 1111, 1089, 1010, 909, 872, 840, 826, 713, cm^{-1}.

Dehydrogenation of diol (36)

A solution of the epoxy alcohol (1.86 g.) in dry ether (10 ml.) was added to methyl magnesium iodide prepared from magnesium (4.1 g.) and methyl iodide (20 ml.) in dry ether (30 ml.) under cooling and stirring during one hour and then refluxed for 47 hours. Ethanol (20 ml.) was added dropwise followed by cold dilute sulphuric acid. Contents were taken up in ether, washed with water till neutral and dried. On evaporation of solvent diol (X, 2.28 g.) was obtained. It was mixed with selenium powder (4.2 g.) and heated at 275-80° for 24 hours in nitrogen atmosphere. The product was taken up in ether, concentrated and passed through alumina column (grade I, 30 g.) to yield 1:2:5-trimethylnaphthalene (1.24 g.) UV spectrum : λ_{max} 227, mμ , log ϵ 4.77; $\lambda_{max.}$ 284 mμ , log ϵ , 3.61. It gave a picrate which after two crystallisations from ethanol melted at 136-39°. Hydrocarbon (0.4386 g.) was regenerated by passing the picrate through alumina column (grade I, 12 g.) and T.N.B. adduct was prepared, m.p. and mixed m.p. with an authentic sample was 160°.

Analysis : Found : C, 59.75; H, 4.2 ; N, 11.5;
$C_{19}H_{17}O_6N_3$ requires: C, 59.53; H, 4.47; N, 10.96%.

Tosylation of Khusinol at 50°

Khusinol (3.1 g.) was dissolved in pyridine (50 ml.) mixed with p-toluene solphonyl chloride (4 g.) in pyridine (10 ml.). The contents in a stoppered conical flask, were kept in a thermostat at 50° for 48 hours. It was processed in the usual way. The crude tosylate (4 g.) was chromatographed on alumina. (grade III, 120 g.). The petroleum ether eluate after evaporation gave the residue (1.056 g.). It was distilled under reduced pressure. b.p.142-145°/2 mm; n_D^{23} 1.5270.

Analysis : Found : C, 78.84; H, 10.3 ;
C, 78.7 ; H, 9.4%.

U.V. spectrum : $\lambda_{max.}$ 250 mμ , ϵ ,12270.

I.R. spectrum (Fig.19) bands at : 3096, 1669, 1642, 1608, 1389, 1370, 1264, 1242, 1220, 1176, 1136, 1099, 1070, 1041, 1024, 998, 893, 842, 800, 694 cm^{-1}.

Tosylation of Khusinol at 40°

Khusinol (4.8 g.) dissolved in dry pyridine (50 ml.) was added to p-toluene sulphonyl chloride (5 g.) dissolved in pyridine (50 ml.) in a stoppered conical flask. The contents were placed in a thermostat at 40° for 48 hours and at room temperature (25°) for 5 days. The crude tosylate (5.29 g.) was isolated in the usual way and was chromatographed over alumina (grade III, 150 g.). The results of chromatography are recorded in Table I.

Table - I

Frac. No.	Eluent	No. of ml. collected	Wt. in g.	Remarks from IR
1	Hexane	200	0.1	Oxide
2	"	300	0.4595	pure tosylate.
3	"	"	0.647	mixture of tosylate and alcohol.
4	"	200	0.457	Unchanged alcohol.
5	"	300	0.267	
6	Benzene	500	2.947	

Fraction 2 (Table I) solidified on cooling. From its infrared spectrum it appeared to be the pure tosylate. I.R. spectrum (Fig.20, melted liquid film) bands at : 1653, 1597, 1493, 1364, 1333, 1307, 1290, 1217, 1186, 1170, 1122, 1095, 1064, 1038, 1028, 998, 963, 929, 913, 901, 881, 853, 840, 818, 792, 707, 694, 671 cm^{-1}.

(-)-γ-cadinene (39)

A mixture of khusinol (2 g.) in dry pyridine (35 ml.) and freshly crystallised p-toluene sulphonyl chloride (2 g.) in dry pyridine (10 ml.) was kept at room temperature for 80 hours. Three such independent batches were then combined and poured into crushed ice and taken up in ether. Ether layer was washed successively with dilute hydrochloric acid, water, sodium bicarbonate solution, finally with water and dried. After evaporating the solvent crude tosylate (6.26 g.) was obtained. The infrared spectrum showed a weak hydroxy band (3300 cm^{-1}) and intense bands due to tosyl group (1603, 1500, 1186, 1170, 1095 cm^{-1}). The tosylate (6.26 g.) in dry ether (25 ml.) was added dropwise to a slurry of lithium aluminium hydride (2.12 g.) in dry ether (50 ml.) at 0^{o} with stirring, which was continued for 30 minutes. The contents were then refluxed for 15 hours. The excess of lithium aluminium hydride was decomposed cautiously by the addition of moist ether and water. Ether layer was separated and the aqueous layer was extracted several times with ether. Combined ether extracts were washed with water till neutral, dried, and ether evaporated. The residue (4.19 g.) was chromatographed over alumina (grade I, 120 g.) and the column eluted with petroleum ether to give (-)-γ-cadinene (2.5 g.) which was distilled over sodium, b.p. 130-33°(bath)/4.3 mm; n_D^{23} 1.5083; d_4^{24} 0.9189; $[\alpha]_D^{24}$ - 153° (C, 2.476);

Analysis : Found : C, 88.22; H, 11.76;
$C_{15}H_{24}$ requires : C, 88.16; H, 11.84%.

I.R.spectrum (Fig.21) bands at : 3077, 1767, 1665, 1642, 1391, 1379, 1362, 1332, 1317, 1285, 1268, 1247, 1218(s), 1187, 1165(s), 1130, 1102, 1089, 1070, 1050, 1040, 1020, 996, 969, 954, 945, 920, 887, 835, 792, cm^{-1}.

Dihydrochloride (40) of (-)-γ-cadinene

Dry gaseous hydrogen chloride was bubbled through ethereal solution of hydrocarbon (1.2 g. in 75 ml.) for 2 hours at -10° and was set aside overnight at 0°. Solvent was removed at 40° under suction. On cooling crystals deposited which after one crystallisation from dry petroleum ether and ether (1:1) gave the dihydrochloride, m.p. 117°.5, $[\alpha]_D^{24}$ +36.27°.

Analysis : Found : Cl, 23.9;
$C_{15}H_{24}Cl_2$ requires : Cl, 25.82%.

Mixed m.p. with an authentic sample of cadinene dihydrochloride (m.p. 118°, $[\alpha]_D^{24}$ - 36°) was depressed to 102°.

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