# Terpenoids

# Chemical Investigation
# on Terpenic Constituents of
# Cyperus Scariosus Oil

A Thesis Submitted to the
University of Poona

For the Degree of
Doctor of Philosophy
( In Chemistry )

by

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# Introduction

# INTRODUCTION

India is rich in medicinal plants[1]. The history of medicine in India can be traced to the remote past between 4500 and 1600 B.C. mentioned in the "Rigveda", perhaps the oldest repository of human knowledge. In 'Ayurveda', the properties of various drugs have been described in details.

The indigenous system of medicine has been described extensively in Materia Medica[2]. Out of 2000 items recorded in Indian medicinal literature, less than two hundred are of mineral and animal origin, the rest are derived from vegetable sources.

Most of the drugs used in indigenous medicine are supposed to be specific for particular disease[3]. One of the difficulties confronting research work is the paucity of authentic information on the identity, habitat, conditions of collection and use of these medicinal plants.

The flowers, leaves, barks and roots of many plants contain volatile, odoriferous substances known as essential oils. Essential oils are, thus, the odoriferous principles of an oily nature obtained exclusively from vegetable sources. They are liquids at ordinary temperature and volatile without decomposition[4]. One of the most common essential oils, oil of tuerpentine, was known to the Ancient Greeks. The function of these oils in the plant is not definitely known, but it was thought that the essential oils aided the natural selection by attracting or repelling certain insects in flowers and helped to keep the parasites away from roots, stems and leaves. The oleoresins exuded from the tree trunks acted as a seal against the loss of sap and as a protection against disease.

The isolation of odoriferous principles from plants has developed in modern times into a large industry. Certain perfumery principles are also found in animal sources. The names of musk, castorium and ambergris may be cited as examples.

Essential oils are composed mainly of terpenoids with a few exceptions such as oils of mustard, onion and garlic which contain sulphur compounds and some oils from flowers which have benzenoid compounds. Our knowledge of terpene chemistry is due to the pioneering research by Wallach, Semmler and Simonsen. Wallach in 1887, proposed the 'isoprene' rule for terpenoids.

## CYPERACEAE FAMILY

The plants of cyperaceae family contain essential oils. They are grass or rush-like (marshy plants) and perennial, mostly with rhizomes in the form of partially thickened knobs.

The cyperaceae family[5] has been divided into three sub-families and six tribes by Lemee[6].

One of the important genera of the cyperaceae family is cyperus (the ancient Greek name), which is composed of 700 species widely distributed throughout the world. About 60 species[2,3,7-10] occur in India.

Cyperaceae plants are said to have an antipathy for fertilizers. Certain plants are found to respond well to mineral fertilizer, especially to nitrogen, which increases the yields of the crop[11]. These plants are common pests[12] on irrigated islands and the problem of eradicating the weeds has been subject of detailed study in many countries. Previously farmers used to eradicate it by repeated tillage of the soil, but now many herbicides have come up which selectively affect the pest.

The most commercially important species are, rotundus, scariosus, articulatus and esculentus, which are generally used in indigenous medicine[3] and perfumery. Cyperus rotundus has been studied for its antibacterial[13] and estrogenic[14] activity. Cyperus esculentus contains starch[15] and sucrose and is used in preparation of cold drink[16]. It also yields a flavoured edible oil[17]. Other species like Corymbosus, Malacansis, Papyrus, Longus, Alopeculoides, Organum, Hexangulare, Spalucatus and Textilis are used in mat and paper manufacture; some of them are used as fodder[18], and some yield tuberous rhizomes used as famine food e.g., Cyperus bulbosus[19,20].

The chemical analysis and uses of Cyperaceae family have been described in the Lynn-Index[21] and chemotexonomical discussion by Hagnauer[22].

## CLASSIFICATION OF CYPERUS SCARIOSUS[23-27]

According to Bentham and Hooker, the plant *Cyperus scariosus* R.Br. is classified as follows:

| | | |
|---|---|---|
| Division | .. | Spermatophyta or Siphonogama (Phanerogamia) |
| Subdivision | .. | Monocotyledoneae |
| Order | .. | Glumiflorae |
| Family | .. | Cyperaceae |
| Genus | .. | Cyperus |
| Species | .. | Scariosus R.Br. |

*Cyperus scariosus R.Br.* /̲ Sanskrit - Nagarmusta; Hindi and Bengali - Nagarmotha; Kannada - Konuarigadde; Marathi - Lawala; Tamil - Muttah Kaoh (Koraikkilangu); Burmies - Vomonniu; Arab - Soadekafi; Pers - Mushkizamen_7 is a delicate, slender sedge with small compound umbel, short slender leaves[1], scanty involucre and can be easily distinguished from other members of the genus. The plant produces deep brown or black tubers. The sedge is found in damp places in Bengal, Uttar Pradesh, Eastern and Southern parts of India, common in Sunderband and Ceylon. It is often confused with Cyperus esculentus, bulbosus, scirpus, grossuvar and kyson.

The tubers are said to be diaphoretic and astringent. In indigenous medicine they are given for disorders of the stomach and irritation of the bowels. In the form of decoction it is used in gonorrhoea and in syphillitic affections (Dr. Percock in Watt's Dic.). The root is given along with valerian in case of epilepsy[3]. It is also used in dysentery and other diseases.

Tubers are rich in aromatic odour. The essential oil[20] (0.08%) obtained from these tubers is dark amber coloured viscous liquid resembling the odour of camphor. Rhizomes are used for certain dye preparations to impart perfume to the fabric. Perfumers use it as a fixative for heavy odour blends. It is a substitute for patchouli oil in soaps and is used in the preparation of agarbattis. It is also used as a good tonic for hair[20].

## TERPENIC CONSTITUENTS OF CYPERUS

The physico-chemical properties[20,28-30] of the essential oil from the rhizomes of *Cyperus scariosus* (R.Br.) have been determined (Table I). In 1954, Naves[30] isolated $\alpha$-Cyperone and an $\alpha$-$\beta$ unsaturated Ketone (2,4 dnp, m.p. 228-9$^{\circ}$; dihydro product 2,4 dnp. m.p. 196$^{\circ}$) and noted the presence of tricyclic (40%) and bicylic (33%) sesquiterpenes in the essential oil of *Cyperus scariosus*.

The essential oils of *Cyperus rotundus*[31-41], (Indian, Chinese and Japanese origin) and *Cyperus articulatus*[42] (West Africa) have been examined for their chemical

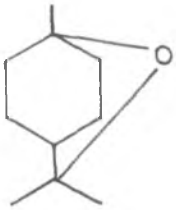
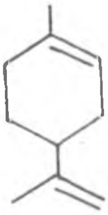
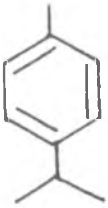
TABLE I

| Authors | Basu et al[20] | Ganeshchandra[28] | S.N.Dingra and D.R.Dingra[29] | | | Naves[30] |
|---|---|---|---|---|---|---|
| Source or Variety | - | - | Red | Black | Dhaulpur | - |
| Yield | 0.75-0.085% | 0.31% | 0.5% | - | - | - |
| Specific gravity | 0.9874-0.9876/30° | 0.9898/20° | 0.9931/31° | -0.9740/30° | 1.013/31° | 0.9671/20° |
| Refractive index | 1.4890-1.4950 | 1.1530/20° | 1.508/24.5° | 1.508/30° | 1.511/28° | 1.5100/20° |
| Optical rotation | - | -9.14 | -6.5 | -2.5 | -10 | -7.8 |
| Acid number | 12.5-14.7 | 5.36 | 7.56 | 6.99 | 31.45 | - |
| Ester number | 38.28-39.48 | 9.0 | 13.75 | 14.36 | 20.59 | - |
| Ester number after Acetylation | 156-161 | 108 | 92.4 | 82.2 | 127.9 | - |
| Carbonyl content Bisulphite Method | - | 25% (by volume) | 3% | 7.8% | 5% | - |
| Hydroxylamine hydrochloride method. | - | - | 48.5% | 36.4% | 68.5% | - |

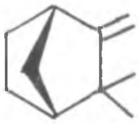
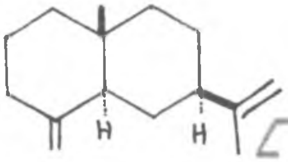
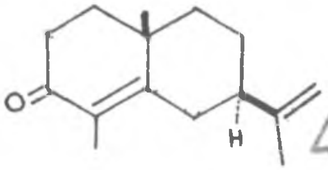
constituents and only $\alpha$-caryophyplene and cadanene have been reported[43] from *Cyperus microsa* of Japanese origin.

Chart I and Chart II show the terpenic constituents isolated from *Cyperus rotundus* and *Cyperus articulatus* respectively.

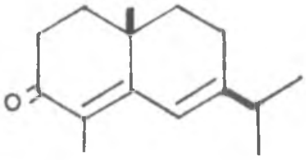
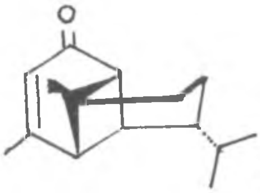
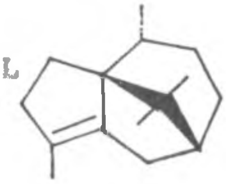
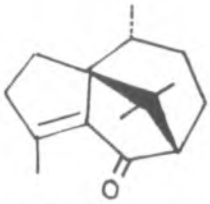
## CHART I

| Sr. No. | SOURCE | STRUCTURE AND NAME | PROPERTIES | REF |
|---|---|---|---|---|
| | Cyperus rotundus.L (Chinese & Indian origin) | | | |
| 1. | " |  1,8-Cineol | $C_{10}H_{18}O$ | 31,32 |
| 2. | " |  Limonene | $C_{10}H_{16}$ | 31 |
| 3. | " |  p-Cymene | $C_{10}H_{14}$ | 31 |

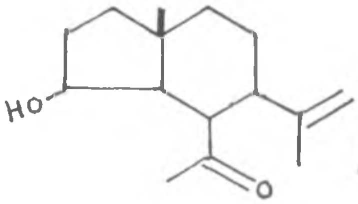
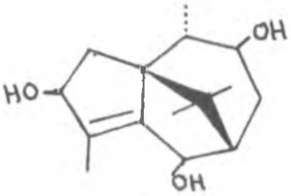
## CHART I (Contd.)

| Sr. No. | SOURCE | STRUCTURE AND NAME | PROPERTIES | REF |
|---|---|---|---|---|
| | Cyperus rotundus.L<br>(Chinese & Indian origin) | | | |
| 4. | " | <br>α-Pinene | $C_{10}H_{16}$<br>$[\alpha]_D$ - 46.55° | 32 |
| 5. | " | <br>β- pinene | $C_{10}H_{16}$<br>$[\alpha]_D$- 22.44° | 31 |
| 6. | " | <br>Camphene | $C_{10}H_{16}$<br>m.p. 51-2°<br>$[\alpha]_D$+103.9-107.7° | 31 |
| 7. | " | <br>β-Selinene | $C_{15}H_{24}$<br>$[\alpha]_D$+40.7° | 31 |
| 8. | " | <br>α-Cyperone | $C_{15}H_{22}O$<br>$[\alpha]_D$+97.5-118° | 35 |

## CHART I (Contd.)

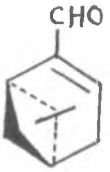
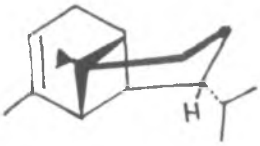
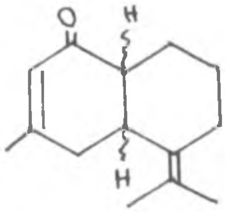
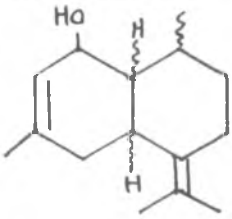
| Sr. No. | SOURCE | STRUCTURE AND NAME | PROPERTIES | REF |
|---|---|---|---|---|
| | Cyperus rotundus.L (Chinese & Indian origin) | | | |
| 9. | " | <br>β-Cyperone | $C_{15}H_{22}O$<br>$[\alpha]_D +239^\circ$ | 36 |
| 10. | " | <br>Mustakone | $C_{15}H_{22}O$<br>$[\alpha]_D +0.34^\circ$ | 37 |
| 11. | " | Iso-Cyperol (bicyclic belongs to eudalene group) | $C_{15}H_{24}O$ | 32 |
| 12. | Cyperus rotundus.L (Chinese origin) | <br>Cyperene | $C_{15}H_{24}$<br>$[\alpha]_D -20^\circ$ | 39 |
| 13. | " | <br>Patchoulenone | $C_{15}H_{22}O$<br>m.p.52.5-53°<br>$[\alpha]_D -97^\circ$ | 40 |

## CHART I (Contd.)

| Sr. No. | SOURCE | STRUCTURE AND NAME | PROPERTIES | REF |
|---|---|---|---|---|
| 14. | Cyperus rotundus.L (Chinese origin) | Selinatriene | $C_{15}H_{22}$<br>$[\alpha]_D +70.5^\circ$ | 31,34 |
| 15. | " |  <br>Cyperelone | $C_{15}H_{24}O$<br>m.p.41-42°<br>$[\alpha]_D +31.4^\circ$ | 38 |
| 16. | " |  <br>Sugetriol | $C_{15}H_{24}O_3$<br>m.p.221-222°<br>$[\alpha]_D +62.4^\circ$ | 41 |
| 17. | " | Cyperol | $C_{15}H_{24}O$<br>$[\alpha]_D + 29.3^\circ$ | 33 |

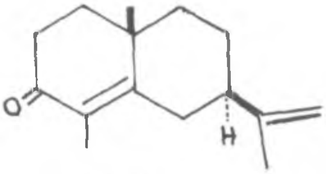
## CHART II

## TERPENIC CONSTITUENTS OF CYPERUS ARTICULATUS

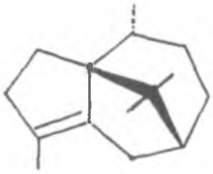
| Sr. No. | SOURCE | STRUCTURE AND NAME | PROPERTIES | REF |
|---|---|---|---|---|
| | Cyperus articulatus (West Africa) | | | |
| 18. | " | <br>(-) Myrtenal | $C_{10}H_{14}O$<br>$[\alpha]_D -14.5^\circ$ | 42 |
| 19. | " | <br>(-) Myrtenol | $C_{10}H_{16}O$<br>$[\alpha]_D -45.8^\circ$ | 42 |
| 20. | " | <br>Copaene | $C_{15}H_{24}$<br>$[\alpha]_D -10.9^\circ$ | 42 |
| 21. | " | <br>Articulone | $C_{15}H_{22}O$<br>$[\alpha]_D -26.6^\circ$ | 42 |
| 22. | " | <br>Articulol | $C_{15}H_{24}O$ | 42 |

## PRESENT WORK

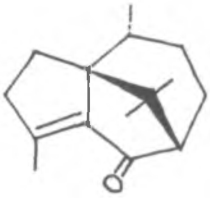
The essential oil from *Cyperus scariosus* (R.Br.), (Indian Origin) has not been examined for its chemical constituents. A systematic chemical examination of the oil of Cyperus scariosus (R,Br.) has been undertaken in this laboratory. Besides known compounds such as α-Cyperone (I), Cyperene (II) and patchoulenone (III), the following six new compounds have been isolated and characterised; Rotundene (IV), Isopatchoulenone[46] (V), Scariodione (VI), Cyperenol[47] (VII), Patchoulenol[47] (VIII) and Rotundenol (IX).



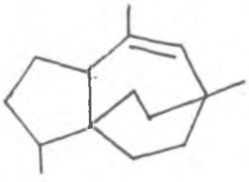
(I)



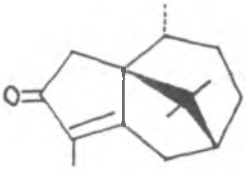
(II)



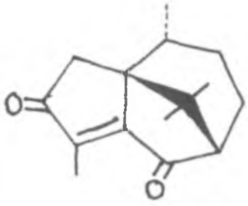
(III)



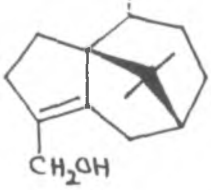
(IV)



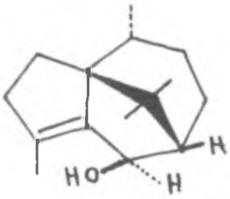
(V)



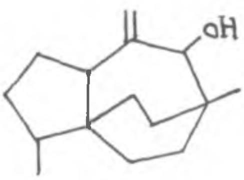
(VI)



(VII)



(VIII)



(IX)

The thesis embodies the results of the systematic chemical examination of the oil of <u>Cyperus scariosus</u> (R.Br.) obtained from the tubers.

In the first Chapter of the thesis, the physico-chemical properties and isolation of various sesquiterpenic constituents from <u>Cyperus scariosus</u> (R.Br.) oil is described. With the help of column chromatography followed by GLC and TLC analysis, the oil has been shown to contain at least twenty one compounds; of these, nine compounds have been characterised as two hydrocarbons, four ketones and three alcohols. An extensive use of spectroscopy and chromatography have been made during isolation and characterisation of the compounds.

The Chapter II deals with the characterisation of the sesquiterpene hydrocarbons namely Cyperene $C_{15}H_{24}$ (II) and a new hydrocarbon Rotundene $C_{15}H_{24}$ (IV).

In the Chapter III of the thesis, the results of structural investigation of the new sesquiterpene ketones Isopatchoulenone $C_{15}H_{22}O$ (V) and Scariodione $C_{15}H_{20}O_2$ (IV) are described. This Chapter also describes the identification of Patchoulenone $C_{15}H_{22}O$, (III) and α-Cyperone $C_{15}H_{22}O$,(I).

The Chapter IV describes the structure elucidation of new crystalline sesquiterpene alcohols, Cyperenol $C_{15}H_{24}O$ (VII), a primary alcohol, Patchoulenol $C_{15}H_{24}O$, (VIII) a secondary alcohol and a liquid secondary alcohol, Rotundenol $C_{15}H_{24}O$, (IX).

One striking feature of <u>Cyperus scariosus</u> (R.Br.) oil is the occurrence of a large number of tricyclic sesquiterpenoids as in Patchouli oil. This is also of obvious biogenetic significance.

Any general introduction to the Chemistry of terpenic compounds has been avoided for the sake of brevity and especially, since a large number of recent monographs and reviews are already available.

## *Chapter I*

# Isolation of Sesquiterpenes from the Oil of Cyperus Scariosus (R. Br.)

## SUMMARY

Isolation of different constituents of the essential oil, obtained from the rhizomes of Cyperus scariosus R.Br. employing elaborate column chromatography on alumina, silicagel, silicagel impregnated with 15% silver nitrate and preparative thin layer chromatography, has been described in this chapter. By GLC and TLC analysis, the oil has been shown to be a complex mixture of at least twentyone compounds. Out of these, two sesquiterpene hydrocarbons, four sesquiterpene ketones and three sesquiterpene alcohols have been isolated in the pure form and their physical properties have been described.

Genuine oil (Cyperus scariosus, R.Br.) was procured from Shree Manaun Lal Ramnarain, Kanuj (U.P.). The crude oil was brown in colour and had pleasant aroma. The physico-chemical properties of the oil are described below :-

Cyperus scariosus (R.Br.) Oil

| | | |
|---|---|---|
| b.p. | ... | 90-155$^{0}$(bath)/1.2 mm. |
| $[\alpha]_{D}^{29}$ | ... | -9.7$^{0}$ (C,5.1) |
| $n_{D}^{26}$ | ... | 1.5110 |
| $d_{4}^{26}$ | ... | 0.9766 |
| Acid number | ... | 6.2 |
| Ester number | ... | 13.07 |
| Ester number after acetylation | ... | 34.37 |
| Carbonyl contents | ... | 40% |
| U.V. absorption $\lambda_{max}$ | ... | 238 & 210 m $\mu$ |

The Infrared Spectrum (Fig.1) of the oil indicates the presence of compounds containing hydroxyl and carbonyl groups.

## ISOLATION OF DIFFERENT CONSTITUENTS OF THE OIL

The free acids present in the oil were removed by treatment with aqueous sodiumbi-carbonate. The neutral oil was separated into three major fractions by column chromatography (Table 1), eluting with petroleum ether (Fraction A), benzene (Fraction B) and ether (Fraction C) respectively.

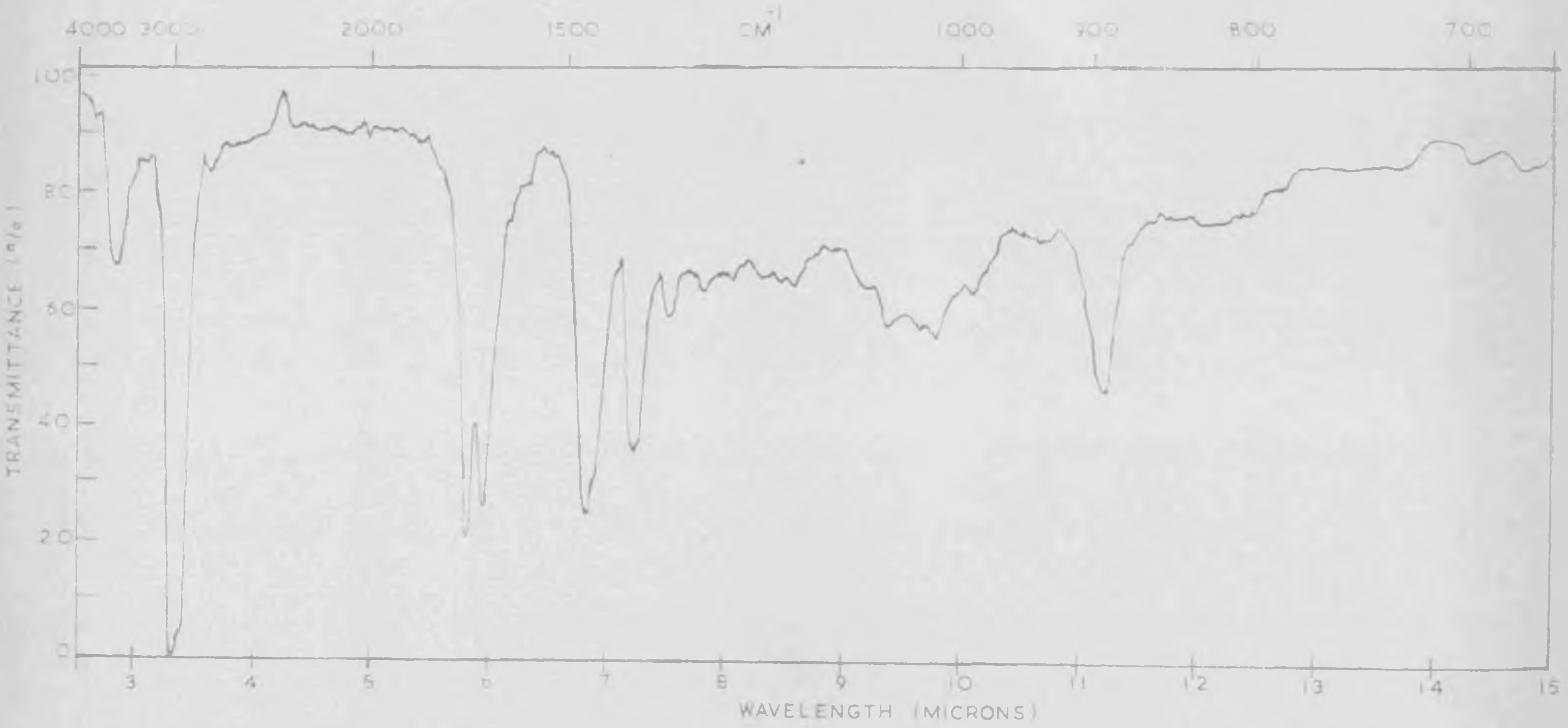


FIG. 1 IR SPECTRUM OF CYPERUS SCARIOSUS (R. Br.) OIL. (LIQUID FILM)

**FRACTION A** : Hydrocarbons, b.p. 88-90°(bath)/1 mm.; $[\alpha]_D^{26}$- 13.98°; (IR Fig.2; GLC Fig.5A).

**FRACTION B** : Ketones, b.p. 120-135°(bath)/0.8 mm.; $[\alpha]_D^{26}$- 9.92°; (IR Fig.3; GLC Fig.5B).

**FRACTION C** : Rich in Alcohols; Carbonyl compounds are also present b.p. 145-155° (bath)/0.8 mm.; $[\alpha]_D^{26}$+9.41°; (IR Fig.4; GLC Fig.5C).

The procedure adopted for the isolation of the different constituents from these fractions is indicated in Chart I. The course of separation was monitored by GLC and TLC on silicagel and $AgNO_3$ impregnated silicagel plates. Based on these data and IR spectra, suitable fractions were taken for the isolation of the compounds.

With the help of column chromatography followed by GLC (Fig.5A,B,C) and TLC analysis the oil has been found to consist of a complex mixture of about twenty one compounds. During the course of this work, two sesquiterpene hydrocarbons, four sesquiterpene ketones and three sesquiterpene alcohols have been isolated in the pure forms from fractions A,B and C.

## ISOLATION OF HYDROCARBONS

Petroleum ether eluted fraction (Fraction A, Table I; Chart I) amounts to 40% of the oil and IR spectrum (Fig.2) showed the absence of Ketones and alcohols. The GLC (Fig.5A) analysis revealed the presence of three

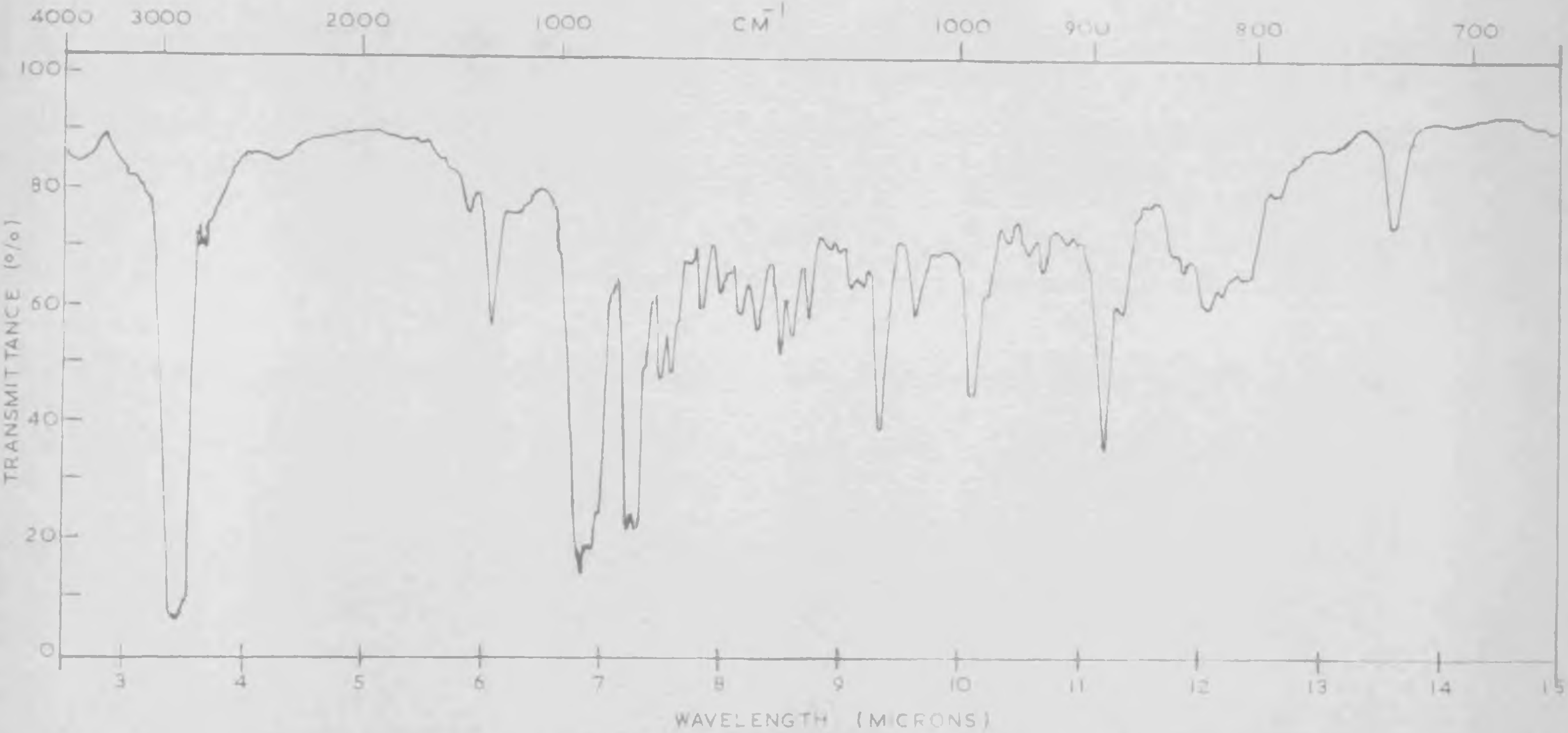


FIG 2 IR SPECTRUM OF PET-ETHER FRACTION (TABLE-I) (LIQUID FILM)

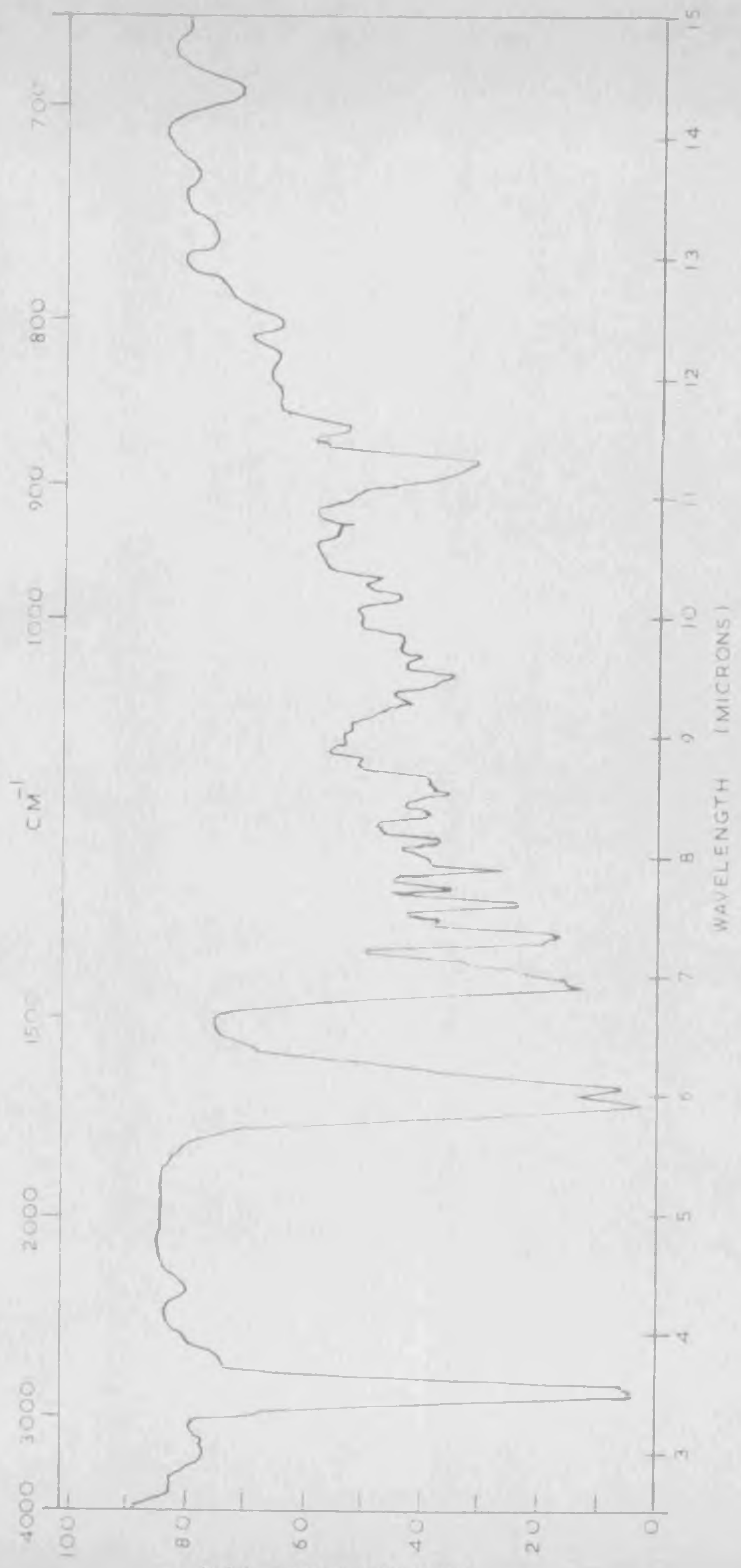


FIG 3 IR SPECTRUM OF BENZENE FRACTION (TABLE-I) (LIQUID FILM)

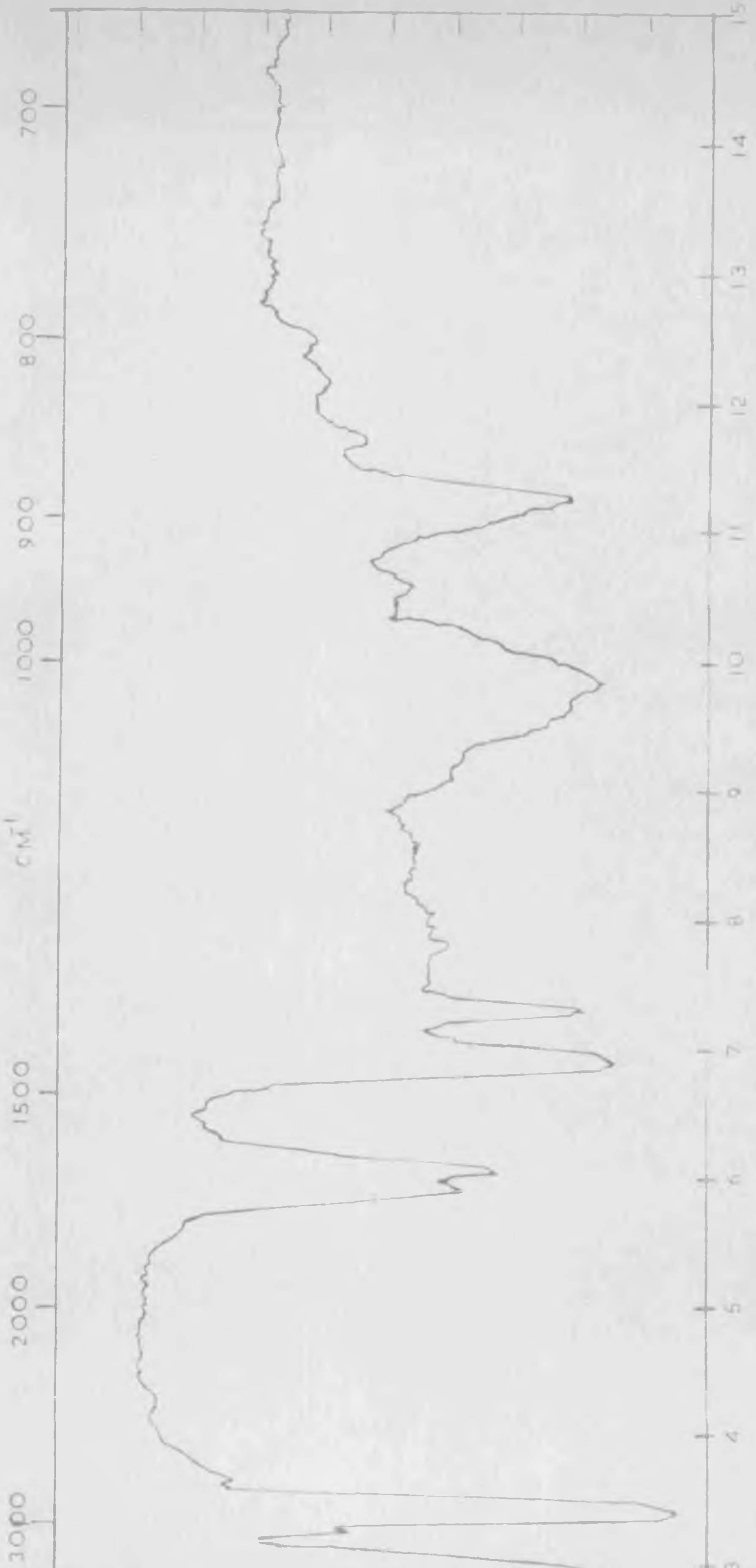


FIG 4 IR SPECTRUM OF ETHER FRACTION (TABLE-I) (LIQUID FILM)

FIG. 5 GLC ANALYSIS OF A B C FRACTIONS

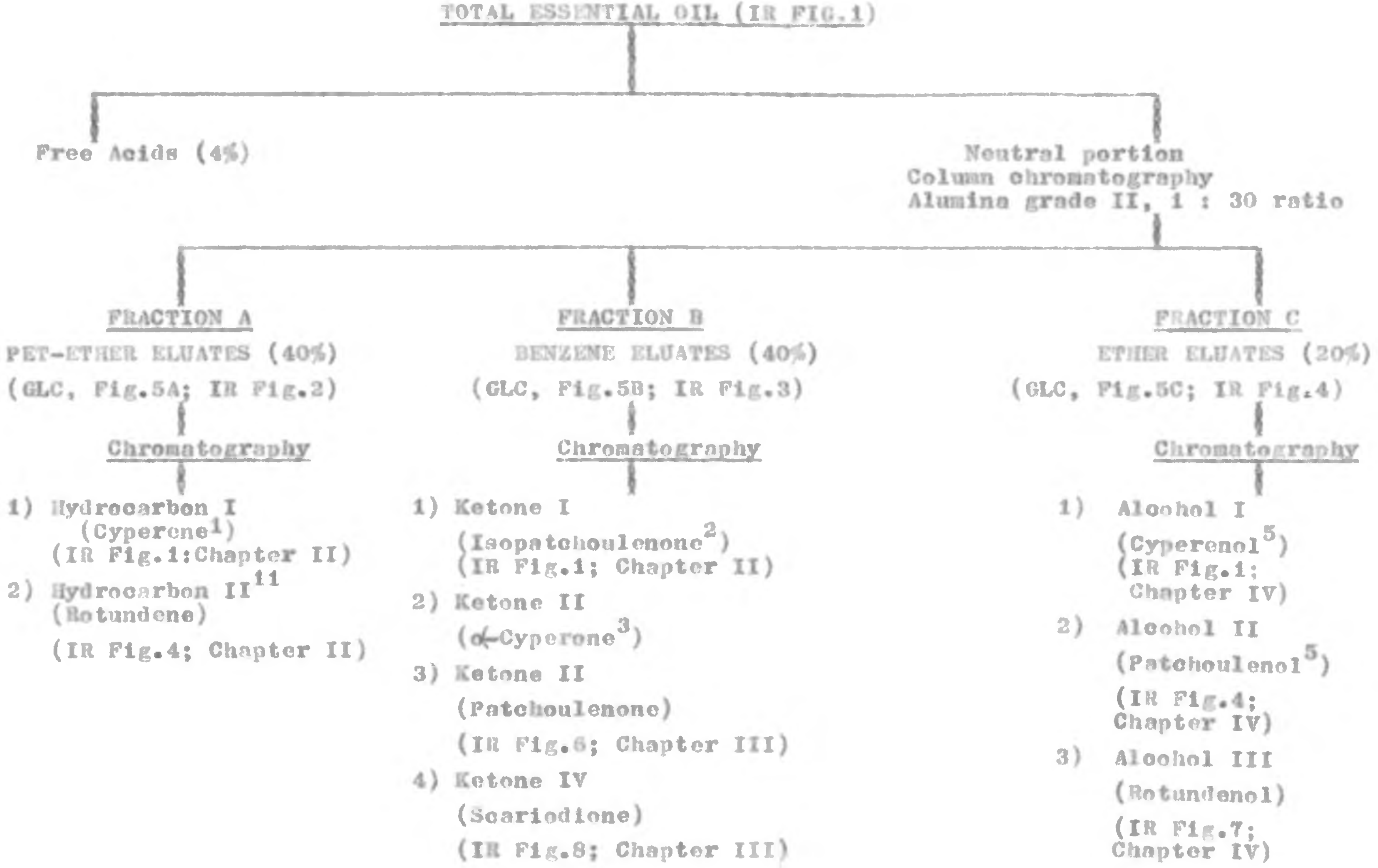
(A) PET. ETHER FRACTION (B) BENZENE FRACTION (C) ETHER FRACTION

**(1) Hydrocarbon I**
**(2) Hydrocarbon II**

**(6) Ketone II**
**(7) Ketone III**
**(8) Ketone I**
**(10) Ketone IV**

**(11) Alcohol II**
**(12) Alcohol III**
**(17) Alcohol I**

CHART I


TOTAL ESSENTIAL OIL (IR FIG.1)
Free Acids (4%)
Neutral portion
Column chromatography
Alumina grade II, 1 : 30 ratio
FRACTION A
PET-ETHER ELUATES (40%)
(GLC, Fig.5A; IR Fig.2)
Chromatography
1) Hydrocarbon I
(Cyperene$^1$)
(IR Fig.1:Chapter II)
2) Hydrocarbon II$^{11}$
(Rotundene)
(IR Fig.4; Chapter II)
FRACTION B
BENZENE ELUATES (40%)
(GLC, Fig.5B; IR Fig.3)
Chromatography
1) Ketone I
(Isopatchoulenone$^2$)
(IR Fig.1; Chapter II)
2) Ketone II
($\alpha$-Cyperone$^3$)
3) Ketone II
(Patchoulenone)
(IR Fig.6; Chapter III)
4) Ketone IV
(Scariodione)
(IR Fig.8; Chapter III)
FRACTION C
ETHER ELUATES (20%)
(GLC, Fig.5C; IR Fig.4)
Chromatography
1) Alcohol I
(Cyperenol$^5$)
(IR Fig.1;
Chapter IV)
2) Alcohol II
(Patchoulenol$^5$)
(IR Fig.4;
Chapter IV)
3) Alcohol III
(Rotundenol)
(IR Fig.7;
Chapter IV)

hydrocarbons in 85:10:5 ratio with close retention times. Two sesquiterpene hydrocarbons were obtained in the pure form by repeated chromatography on alumina of different grades and on $AgNO_3$ impregnated silicagel column.

**HYDROCARBON I, $C_{15}H_{24}$**

The leavorotatory Fraction A, was chromatographed (Table Nos.II and III) on neutral alumina (Gr.I). The combined fraction (2 and 3 Table III) was further chromatographed over silicagel impregnated with $AgNO_3$ and from the middle fraction (Fraction 3, Table IV), a sesquiterpene hydrocarbon (GLC and TLC pure) was isolated. The hydrocarbon I, $C_{15}H_{24}$, had the following properties, b.p.93-94$^{0}$ (bath)/1 mm.; $[\alpha]_D^{27}$- 21.07$^{0}$(C,4).

IR bands at :1701, 1389, 1366, 1070 and 988 $cm^{-1}$. Hydrocarbon I corresponds to GLC peak 1 (Fig.5A).

**HYDROCARBON II: $C_{15}H_{24}$**

Petroleum ether fraction (Fraction No.4, Table IV) was rechromatographed (Table V) on silicagel impregnated with 15% $AgNO_3$, when a hydrocarbon (Fraction No.2, Table V) was obtained. The hydrocarbon was further purified by careful distillation over metallic sodium under reduced pressure. It has the following properties:

Hydrocarbon II, $C_{15}H_{24}$; b.p.118$^{0}$(bath)/1.5 mm.; $[\alpha]_D^{28}$- 15.63$^{0}$; (C,5.28); $n_D^{28}$ 1.5004.

IR bands at: 2778, 1698, 1385, 1362, 1020, 825 and 770 $cm^{-1}$.

Hydrocarbon II corresponds to GLC peak 2 (Fig.5A). Hydrocarbon I has been identified as cyperene[1] and hydrocarbon II is a new hydrocarbon, Rotundene. The structures of these two hydrocarbons are described in Chapter II.

## ISOLATION OF KETONES

Benzene eluted leavorotatory fraction (Fraction B, Table I) amounts to 40% of the oil and IR spectrum (Fig.3) indicated the presence of carbonyl compounds. This fraction consisted of seven compounds (GLC Fig.5B). Out of these four have been isolated by column chromatography (Table VI-VIII) followed by preparative thin layer chromatography. The ketones are present in the ratio of 60:4:20:5 (GLC Fig.5B, Peak Nos.8,6,7 and 10 respectively).

## KETONE I: $C_{15}H_{22}O$

Fraction B, was chromatographed (Table VI) over alumina (Gr.II) and eluted with petether, 1:1 petether: benzene mixture; benzene; 1:1 benzene:ether mixture and ether respectively. The solid obtained from the ether eluents, on crystallisation from pet ether gave colourless crystals, m.p. 48°; $[\alpha]_D^{27}$ + 39.9° (C,3.1): U.V.absorption $\lambda_{max}$ 243 m$\mu$.

IR bands at: 1706, 1667, 1418, 1389, 1377,1330 1282, 1056, 1044, 993 and 892 $cm^{-1}$.

Ketone I corresponds to GLC peak 8 (Fig. 5B)

**KETONE II**: $C_{15}H_{22}O$

Fraction 1 (2.5 g. Table VI) was treated with semicarbazide hydrochloride and sodium acetate, and was allowed to stand overnight. As no crystalline derivative separated, the product was diluted with water, extracted with ether and ether extract dried. The residue after removal of ether was chromatographed (Table VII) over alumina (Gr II) and eluted with petether, benzene, ether and ethanol.

The ethanol fraction on concentration gave crystalline semicarbazone, which on recrystallisation afforded pure semicarbazone m.p. 216°.

The ketone regenerated from the semicarbazone (m.p.216°) distilled at b.p.108°(bath)/1 mm.; $[\alpha]_D^{28}$ +120° (C,3.9). It corresponds to GLC peak 6 (Fig.5B). IR bands at 1665, 1610, 890 $cm^{-1}$.

**KETONE III** $C_{15}H_{22}O$

The benzene fraction (Table VII) was further chromatographed on alumina (Gr II) and was eluted with petether, petether: benzene mixture and ether; the middle fraction eluted with petether: benzene (Fraction 4, Table VIII) gave a solid which on crystallisation from petether gave colourless crystalline ketone III, m.p.53°; b.p.125° (bath)/ 1 mm. $[\alpha]_D^{27}$ -96.3° (C,2.86); U.V. absorption $\lambda_{max}$ 264 m$\mu$.

IR bands at: 1712, 1664, 1389, 1368, 1238, 1207, 1064 and 1020 cm$^{-1}$.

Ketone III corresponds to GLC peak 7 (Fig.5B).

## KETONE IV $C_{15}H_{22}O$

Ketone IV was obtained by preparative thin layer chromatography of fractions (5 and 6 Table VIII); colourless crystals, m.p. 45$^{o}$; $[\alpha]_{D}^{27}$- 107.5$^{o}$(C, 4.2); U.V. absorption $\lambda_{max}$ 267 m$\mu$.

IR bands at : 1709, 1607, 1412, 1389, 1376, 1202, 1174, 940 and 823 cm$^{-1}$.

Ketone IV corresponds to GLC peak 10 (Fig. 5B), Ketone I and IV are new crystalline sesquiterpene ketones isopatchoulenone[2] and scariodione; ketone II and III have been identified as $\alpha$-cyperone [3] and patchoulenone[4].

The structure elucidations of these Ketones are described in Chapter III.

## ISOLATION OF ALCOHOLS

Ether eluted fraction ( Fraction C, Table I) is dextrorotatory and amounts to 20% of the oil. Its IR spectrum (Fig.4) indicated the presence of alcohols and carbonyl compounds, GLC (Fig. 5.C) analysis showed that the fraction C is a complex mixture of eleven compounds.

Three major components corresponding to GLC peaks 11, 12 and 17 (Fig.5,C) were isolated and characterised as new sesquiterpene alcohols.

Fraction C was chromatographed over silicagel (Table IX), when a broad separation of primary and secondary alcohols was effected. Benzene fractions (Fraction Nos. 4-23, Table IX) contained secondary alcohols and later fractions (24 onwards) contained only primary alcohols.

## ALCOHOL I $C_{15}H_{24}O$

Benzene eluted fraction (Fraction 24, Table IX) was concentrated and the concentrate dissolved in petroleum ether and was kept in refrigerator. The separated solid was filtered and crystallised from ethanol, when Alcohol-I was obtained, m.p. 94°; b.p.125°(bath) / 0.05 mm.; $[\alpha]^{30}_{D}$ -12.1° (C, 4.3); U.V.absorption $\lambda_{max}$ 210 m $\mu$.

IR bands at: 3333, 1678, 1408, 1379, 1361, 1018 and 980 $cm^{-1}$.

Alcohol I corresponds to GLC peak 17 (Fig.5,C).

## ALCOHOL II $C_{15}H_{24}O$

Fractions (Fractions 4-12, Table IX) were combined and rechromatographed on silicagel impregnated with 15% $AgNO_3$ and eluted with petether, petether:benzene and ether. Fractions 2 and 3 (Table X) were combined. This fraction was dissolved in alcohol, allowed to crystallise, when alcohol II was obtained as colourless crystals, m.p. 74°; $[\alpha]^{30}_{D}$-54.23° (C,3.8) U.V. absorption $\lambda_{max}$ 210 m $\mu$;

IR bands at: 3333, 1692, 1379, 1361, 1190, 1099, 1064, 1053 and 1020 $cm^{-1}$.

Alcohol II corresponds to GLC peak 11 (Fig.5,C).

ALCOHOL III $C_{15}H_{24}O$

On treatment with 3:5 dinitrobenzoylchloride in Pyridine, the benzene fractions 13-23 (Table IX) gave 3:5 dinitrobenzoate derivative.

On repeated crystallisations from ethanol, the 3:5 dinitrobenzoate derivative was obtained as colourless fine crystals, m.p. 139-140$^0$; $[\alpha]_D^{29}$ - 32.10$^0$ (C, 4.1). The 3:5 dinitrobenzoate derivative analysed for $C_{22}H_{26}O_6N_2$. On alkaline hydrolysis, it yielded a liquid alcohol, b.p. 139-140$^0$ (bath)/0.2 mm; $[\alpha]_D^{28}$ + 55.35$^0$ (C, 3.4), $n_D^{29}$ 1.5205; U.V. absorption $\lambda_{max}$ 210 m $\mu$.

IR bands at: 3509, 3106, 1661, 1418, 1385, 1042, 1020, 990 and 910 cm$^{-1}$.

Alcohol III corresponds to GLC peak 12 (Fig.5,C). Alcohols I, II and III are new sesquiterpene alcohols, Cyperenol[5], Patchoulenol[5] and Rotundenol and the structures of these three alcohols are described in Chapter IV.

## EXPERIMENTAL

The oil (Cyperus scariosus R.Br.) was dried over anhydrous sodium sulphate. The last traces of moisture was removed by heating under reduced pressure. A small fraction (10 g.) was distilled under vacuum and the physico-chemical properties of the distilled oil were determined as follows:

b.p. 90-155$^\circ$(bath)/1.2 mm. $[\alpha]_D^{29}$- 9.7$^\circ$ (C,5.1); $n_D^{26}$ 1.5110; $d^{26}$ 0.9766; Ester number 13.07; Ester number after acetylation 34.37; carbonyl content 40%; Acid number 6.2; U.V. absorption $\lambda_{max}$ 238 and 210 m$\mu$.

IR bands (Fig.1, liquid film) at: 3509, 1715, 1669, 1374, 1058, 1020 and 892 cm$^{-1}$.

GLC (Fig.5, A,B,C) analysis showed the presence of twenty one compounds.

The essential oil (200 g.), dissolved in petroleum-ether (400 ml.), was washed with $NaHCO_3$ solution (10%).The petroleum ether layer was washed with brine (3 x 40 ml.), and dried over anhydrous sodium sulphate. The solvent was removed by distillation, when neutral oil (196 g.) was obtained.

## SEPARATION OF HYDROCARBONS, KETONES AND ALCOHOLS BY COLUMN CHROMATOGRAPHY

The acid free oil was chromatographed over neutral alumina (Gr.II) and the details of the chromatography are described below.

## TABLE I

Weight of oil ... 1 Kg. (in 5 batches)

Weight of neutral alumina Gr.II ... 30 Kg.(in 5 batches)

| Sr. No. | Eluent | Volume of Eluent | Wt. of fraction. | $[\alpha]_D^{26}$ | $d^{26}$ | $n_D^{26}$ |
|---|---|---|---|---|---|---|
| 1. | Pet-ether | 70 lit. | 400 g. | $-13.98^0$ | 0.8636 | 1.5026 |
| 2. | Benzene | 70 lit. | 400 g. | $-9.92^0$ | 1.009 | 1.5093 |
| 3. | Ether | 60 lit. | 185 g. | $+9.41^0$ | 0.9972 | 1.5100 |

Recovery 98.5%

## ISOLATION OF HYDROCARBONS

### FRACTION A

b.p. $88-90^0$ (bath)/1 mm. $[\alpha]_D^{26}$ $-13.98^0$, GLC Fig. 5A; U.V. absorption $\lambda_{max}$ 210 m$\mu$. IR bands (Fig.2, liquid film) at : 1639, 1381, 1366, 1070, 985 and 890 cm$^{-1}$.

The petroleum ether fraction from the column chromatography (vide chart I and Table I) of the oil contains only three hydrocarbons (GLC Fig.5A) and was rechromatographed over neutral alumina. Several fractions were collected by eluting with petroleum ether. The details of chromatography are shown below.

## TABLE II

Weight of fraction A ... 40 g.

Weight of alumina Gr. I ... 2 Kg.

| Sr. No. | Eluent | Volume of eluent (ml.) | Weight of fraction (g) | GLC of Hydrocarbons | | |
|---|---|---|---|---|---|---|
| | | | | I | : | II |
| 1. | Pet-ether | 200 ml. | 2.5250 ) | 55 | : | 45 |
| 2. | " | " | 5.9070 ) | | | |
| 3. | " | " | 5.4690 ) | 80 | : | 20 |
| 4. | " | " | 7.0994 ) | | | |
| 5. | " | " | 5.2670 ) | 9 | : | 10 |
| 6. | " | " | 5.3692 ) | | | |
| 7. | " | " | 3.7834 ) | – | : | – |
| 8. | " | " | 1.9778 ) | | | |
| 9. | " | 1000 ml. | 0.5406 ) | | | |

Recovery 98.66%

Fractions 3 and 4 (12.5684 g. Table II) were mixed and chromatographed over alumina.

## TABLE III

Weight of the fraction ... 10 g.

Weight of alumina Gr. I ... 720 g.

| Sr. No. | Eluent | Volume of Eluent (ml.) | Wt. of fraction (g) | $[\alpha]_D^{27}$ | GLC Hydrocarbons | | |
|---|---|---|---|---|---|---|---|
| | | | | | I | : | II |
| 1. | Pet-ether | 100 ml. | 0.8708 | $- 13.2^\circ$ | 70 | : | 30 |
| 2. | " | " | 4.8016 | $- 16.23^\circ$ | 90 | : | 10 |
| 3. | " | " | 1.3666 | $- 17.5^\circ$ | | | |
| 4. | " | " | 0.5038 | $- 10.3^\circ$ | 20 | : | 80 |
| 5. | " | " | 0.5478 | | | | |
| 6. | " | " | 0.2070 | | | | |
| 7. | " | 1000 ml. | 0.8603 | | | | |
| 8. | " | 2000 ml. | 0.4334 | - | - | : | - |

Recovery 95.88%

### HYDROCARBON I

The fractions (2 and 3 Table III ) were rechromatographed over silicagel impregnated with silver nitrate (15%) as follows:

## TABLE IV

Weight of the fraction ... ... 6 g.

Weight of the silicagel impregnated with 15% $AgNO_3$...150 g.

| Sr. No. | Eluent | Volume of Eluent (ml.) | Weight of fractions (g) | $[\alpha]_D^{27}$ | GLC Hydrocarbons I | : | II |
|---|---|---|---|---|---|---|---|
| 1. | Pet-ether | 70 ml. | 1.4214 | $-16.93^\circ$ | Mixture | | |
| 2. | " | 50 ml. | 0.3411 | $-19.31^\circ$ | 95 | : | 5 |
| 3. | " | 100 ml. | 2.1051 | $-21.07^\circ$ | 100% | | |
| 4. | " | 400 ml. | 2.0850 | $-13.86^\circ$ | 10 | : | 90 |

Recovery 99%

The hydrocarbon I $C_{15}H_{24}$ (2.1 g.) corresponding to GLC peak 1 (Fig. 5A); was distilled over sodium under reduced pressure and the distilled product showed the following properties:-

b.p. 93-94°(bath)/1 mm.; $n_D^{28}$ 1.5030; $[\alpha]_D^{27}$ $-21.07^\circ$ (C,4.0)

ANALYSIS

Found : C, 88.31; H, 11.91

Calculated for $C_{15}H_{24}$ : C, 88.16; H, 11.84%

IR bands (0.05 mm. cell) at: 1701, 1389, 1366, 1333, 1316, 1269, 1250, 1222, 1205, 1181, 1163, 1141, 1070, 1037, 988, 934, 892, 877, 845 and 832 $cm^{-1}$.

### HYDROCARBON II

Fraction 4 (Table IV) was further chromatographed on silicagel impregnated with 15% $AgNO_3$.

TABLE V

Weight of the fraction .. .. 2 g.

Weight of silicagel impregnated with 15% $AgNO_3$ .. 50 g.

| Sr. No. | Eluent | Volume of eluent (ml.) | Weight of fractions (g) | $[\alpha]_D^{26}$ | GLC Hydrocarbons | |
|---|---|---|---|---|---|---|
| | | | | | I | II |
| 1. | Pet-ether | 50 ml. | 1.3403 | $-13.04^\circ$ | 5 | 85 |
| 2. | " | " | 0.3121 | $-15.63^\circ$ | | 100% |
| 3. | " | 25 " | 0.5250 | $-14.87^\circ$ | 7 | 93 |
| 4. | " | " | 0.0248 | | | |
| 5. | " | " | 0.0146 | | | |
| 6. | " | 100" | 0.1470 | | | |
| 7. | " | 200" | 0.0087 | | | |

Recovery 95 %

Fraction 2 (Table V) was distilled over sodium under reduced pressure when hydrocarbon II (0.3121 g) was obtained. It showed the following properties. TLC single spot, GLC single peak corresponding to peak 2 (Fig.5A). b.p. 118° (bath) / 1.5 mm. $[\alpha]_D^{28}$ $- 15.63^\circ$ (c, 5.28); $n_D^{28}$ 1.5004.

ANALYSIS

Found : C, 88.20; H, 11.9

Calculated for $C_{15}H_{24}$ : C, 88.16; H, 11.84%

IR bands at: 2778, 1698, 1385, 1362, 1320, 1205, 1190, 1155, 1100, 1020, 1000, 980, 970, 935, 910, 895, 885, 825, 795 and 770 $cm^{-1}$.

## ISOLATION OF KETONES

### FRACTION B

The benzene fraction from the column chromatography (Chart I and Table I) of the oil was a mixture of seven compounds (GLC Fig. 5B; IR Fig.3). It had the following properties:

b.p. 120-135°(bath) / 0.8 mm.; $[\alpha]_D^{26}$ - 9.92° (C, 3.3); $n_D^{26}$ 1.5093; $d^{26}$ 1.0090.

IR bands (Fig. 3, liquid film) at: 1727 , 1706, 1370, 1321, 1274, 1176, 1053 and 892 $cm^{-1}$.

Fraction B was chromatographed over alumina to isolate the carbonyl constituents in the pure form.

## KETONE I

### TABLE VI

Weight of the fraction B ... 40 g.

Weight of alumina Gr. II ... 2 Kg.

| Sr. No. | Eluent | Ratio by volume | Volume of eluent (ml.) | Wt. of fractions (g) | $[\alpha]^{28}_{D}$ | GLC Ketones |
|---|---|---|---|---|---|---|
| 1. | Pet-ether benzene | 1:1 | 2000 | 2.5 | $-30^{\circ}$ | 50%Ketone III |
| 2. | " | " | 600 | 3.0 | $-44.44^{\circ}$ | 70% " |
| 3. | " | " | " | 5.0 | | |
| 4. | " | " | " | 3.0 | | |
| 5. | Benzene | - | 1000 | 3.6 | $+13.95^{\circ}$ | Ketone<br>I : III<br>50 : 50 |
| 6. | " | - | " | 3.0 | | |
| 7. | " | - | " | 5.01 | $+24.40^{\circ}$ | 65 : 35 |
| 8. | " | - | 3000 | 5.12 | $+36.6^{\circ}$ | |
| 9. | Benzene-ether | 1:1 | 1000 | 3.20 | | |
| 10. | Ether | - | " | 3.80 | $+39.9^{\circ}$ | Ketone I<br>100% |
| 11. | " | - | 2000 | 2.60 | | |

Recovery 99.5%

Fraction 10 and 11(Table VI) were found to be fairly pure (GLC). The combined fraction crystallised from petroleum ether (40-60$^{\circ}$), when ketone I was obtained as a colourless crystalline compound.

Ketone I, $C_{15}H_{22}O$, (TLC single spot, GLC single peak corresponding to peak 8, Fig. 5B) had the following properties:

m.p.48°; b.p.105° (bath)/0.2 mm.; $[\alpha]_D^{27} + 39.9^{\circ}$(C,3.1).

## ANALYSIS

Found : C, 82.64; H, 10.20

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

IR bands at : 1706, 1667, 1418, 1389, 1377, 1330, 1282, 1183, 1056, 1044, 993, 978, 944, 905, 892, 837 and 698 $cm^{-1}$.

## KETONE II

Fraction 1 (2.5 g. Table VI) was dissolved in ethanol (10 ml.) and treated with semicarbazide hydrochloride (1.5 g.) and sodium acetate (0.5 g.) in water (2 ml.). The mixture was heated on a water bath till the solution was clear and kept for 48 hours at room temperature with occasionel shaking. Ethanol was removed by distillation. The residue was diluted with water and extracted with petroleum ether. Petroleum ether extract was washed with water, dried over anhydrous sodium sulphate and concentrated. The product (3.1 g.) was chromatographed on neutral alumina (Gr. II).

## TABLE VII

Weight of the product ... 3 g.

Weight of alumina (Gr. II) ... 100 g.

| Sr. No. | Eluent | Volume of eluent (ml.) | Wt. of fractions (g) | $[\alpha]_D^{26}$ | GLC Ketones |
|---|---|---|---|---|---|
| 1. | Pet-ether | 500 | - | - | - |
| 2. | Benzene | " | 2.0310 | -38.7 | 75% Ketone III |
| 3. | Ether | " | - | - | - |
| 4. | Ethanol | " | 0.6144 | - | (Semicarbazone m.p. 216°) |

Recovery 89.2%

The ethanol eluted fraction (0.614 g.) was repeatedly crystallised from ethanol when a pure semicarbazone was obtained m.p. 216°.

On regeneration from the semicarbazone by treating with oxalic acid, an $\alpha$-$\beta$ unsaturated ketone II corresponding to GLC peak 6 (Fig. 5,B): b.p. 108°(bath)/1 mm., $[\alpha]_D^{28}$ + 120° (C, 3.9) was obtained.

ANALYSIS

Found : C, 82.68; H, 10.31

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

IR bands at: 1665, 1610 and 890 $cm^{-1}$.

KETONE III

Benzene fraction (fraction 2, Table VII; 2 g.) was chromatographed as follows:

## TABLE VIII

Weight of the fraction ... 2 g.

Weight of alumina (Gr.II) ... 100 g.

| Sr. No. | Eluent | Ratio by volume | Volume of eluent (ml.) | Weight of fraction (g) | $[\alpha]_D^{27}$ | Remarks |
|---|---|---|---|---|---|---|
| 1. | Pet-ether | - | 500 | - | - | - |
| 2. | Pet-ether benzene | 9 : 1 | 200 | 0.1464 | $-30.1^0$ | Liquids |
| 3. | " | " | 100 | 0.2704 | | |
| 4. | " | " | " | 0.3970 | $-96.3^0$ | Solid m.p.$53^0$ Ketone III |
| 5. | " | " | " | 0.2146 | $-87.7^0$ | Thick liquid |
| 6. | " | " | " | 0.2246 | | |
| 7. | " | " | 300 | 0.4674 | $-11.8^0$ | Mixtures |
| 8. | Ether | " | 400 | 0.3938 | $+20^0$ | |

Recovery 96.5%

The 4th fraction (Table VIII) was crystallised from petroleum ether to yield a crystalline ketone III, m.p.$53^0$; b.p. $135^0$(bath)/ 1 mm.; $[\alpha]_D^{27}$- $96.3^0$(C,2.86). It corresponds to GLC peak 7 (Fig. 5 B).

ANALYSIS

Found : C, 82.45; H, 10.11

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

IR bands at : 1712, 1664, 1389, 1368, 1287, 1258, 1238, 1207, 1183, 1143, 1098, 1064, 1020, 995, 983, 975, 940, 894, 885, 873, 833, 806 and 785 $cm^{-1}$.

## KETONE IV

Fractions 5 and 6 (Table VIII) were found to contain two components in almost equal quantity. It was not possible to separate the components by column chromatography. The components, however, could be separated on preparative thin layer chromatography.

## PREPARATION OF PREPARATIVE THIN LAYER PLATES

Preparative thin layer plates of homogeneous thickness were prepared by spreading silicagel (20 g. of 200 mesh) on 20 x 20 cm. size glass plates. The plate was dried in air for 2 hours, and was activated at 120° for 4 hours. It was kept in the dessicator for half an hour before use.

## SEPARATION OF INDIVIDUAL COMPONENTS

The material (100 mg.)combined fraction 5 and 6 Table VIII) was injected 2 cm. apart from the side of the glass plate with the help of a smooth capillary. The plate was saturated by solvent vapour in the chromatography chamber for 5 minutes, and was dipped into the solvent (Benzene : ethylacetate 85 : 15). The solvent layer was kept well below the point of injection. Solvent front was run for a distance of 15 cm. from the point of injection. The plate was developed by spraying the sides with 50% ethanolic sulphuric acid and heating only the edges of the plate with burner. The bands were separately cut, the material was recovered by eluting with dry ether. The ketone IV (2 x 65 mg.) was crystallised from 40-60$^{\circ}$ pet-ether, colourless crystals, m.p.45$^{\circ}$; $[\alpha]_D^{27}$- 107.5$^{\circ}$ (C, 4.2). The singlo spot, GLC single peak corresponding to peak 10 (Fig.5B).

ANALYSIS

Found : C, 77.63; H, 8.81

Calculated for $C_{15}H_{20}O_2$ : C, 77.55; H, 8.68%

IR bands at: 1709, 1667, 1412, 1389, 1376, 1307, 1266, 1235, 1202, 1194, 1174, 1099, 1058, 1040, 1018, 998, 975, 940, 895, 863, 823, 797, and 768 cm$^{-1}$.

The other ketone obtained by preparative thin layer chromatography was found to be identical with Ketone I described before.

## ISOLATION OF ALCOHOLS

### FRACTION C

The ether fraction obtained on column chromatography (Chart I, Table I) of the oil was shown to be a mixture of eleven components (GLC Fig.5C). IR spectrum (Fig. 4) showed the presence of alcohols along with carbonyl compounds. The fraction had the following properties: b.p.145-155$^{\circ}$ (bath)/1.5 mm.; $[\alpha]_D^{27}$+ 9.41 (C, 4.5); $n_D^{27}$1.5100; $d^{27}$ 0.9972; U.V. absorption $\lambda_{max}$ 210 m $\mu$.

IR bands ( Fig.4 ) at: 3448, 1695, 1661, 1374, 1370, 1017 and 892 $cm^{-1}$.

Fraction C was chromatographed over silicagel in order to separate the individual components.

## ALCOHOL I

### TABLE IX

Weight of the fraction C ... 20 g.

Weight of silicagel ... 1200g.

| Sr. No. | Eluent | Volume of eluent (ml.) | Wt.of fraction (g) | $[\alpha]^{30}_{D}$ | G L C Alcohols |
|---|---|---|---|---|---|
| (1) | (2) | (3) | (4) | (5) | (6) |
| 1. | Pet-ether | 5000 | - | - | - |
| 2. | Pet-ether: Benzene 3 : 1 | 5000 | - | - | - |
| 3. | " 1:1 | 5000 | - | - | - |
| 4. | Benzene | 1000 | 4.6920 | $-52.8^{\circ}$ | Alcohol II & III are major. |
| 5. | " | " | | | |
| 6. | " | " | | | |
| 7. | " | " | | | |
| 8. | " | " | | | |
| 9. | " | " | | | |
| 10. | " | " | | | |
| 11. | " | " | | | |
| 12 to 23. | " | " | 1.880 | $+50.13^{\circ}$ | Alcohol III is major |

TABLE IX (Contd.)

| (1) | (2) | (3) | (4) | (5) | (6) |
|---|---|---|---|---|---|
| 24. | Benzene | 6000 | 0.6056 | -12.1° | Pure alcohol I m.p.94° |
| 25. | " | 3000 | 0.5556 | - | Mixture |
| 26. | " | 3000 | | | |
| 27. | Ether | 2000 | 9.2784 | +30.82 | Mixture of other alcohols |
| 28. | Ether | 4000 | 1.9120 | | |

Recovery 94.6 %

Fraction 24 on keeping gave a solid which, when crystallised from ethanol yielded colourless crystalline product m.p. 94°; b.p. 125°(bath) / 0.05 mm. $[\alpha]^{30}_{D}$ - 12.1° (C, 4.3); U.V. absorption $\lambda_{max}$ 210 m$\mu$. It corresponds to GLC peak 17 (Fig. 5C).

ANALYSIS

Found : C, 81.49; H, 11.1

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

IR bands at: 3333, 1678, 1379, 1361, 1328, 1302, 1266, 1238, 1220, 1183, 1152, 1139, 1067, 1042, 1018, 980, 935, 913, 897, 875 and 847 cm$^{-1}$.

ALCOHOL II

The fractions from 4 to 12 (Table IX, two spots on TLC, and two peaks on GLC) were mixed and rechromatographed over silicagel impregnated with 15% $AgNO_3$.

## TABLE X

Weight of fraction ... ... 4 g.

Weight of silicagel impregnated with 15% $AgNO_3$ ... 120 g.

| Sr. No. | Eluent | Volume of eluent (ml.) | Wt. of fractions (g) | $[\alpha]_D^{30}$ | G L C Alcohols |
|---|---|---|---|---|---|
| 1. | Pet-ether | 4000 | - | - | - |
| 2. | Pet-ether: Benzene 3:1 | 50 | 1.3400 | $-54.23^{\circ}$ | Pure alcohol II m.p. 74° |
| 3. | " | " | | | |
| 4. | " | " | 0.8624 | $-40.3^{\circ}$ | 80% of alcohol II |
| 5. | " | " | | | |
| 6. | " | " | | | |
| 7. | " | 300 | | | |
| 8. | Ether | 600 | 1.3884 | - | Mixture |

Recovery 89.77 %

The fractions 2 and 3 were crystallised from ethanol when a colourless crystalline product was obtained. m.p. 74°; $[\alpha]_D^{30} - 54.23^{\circ}$ (C,3.8). It corresponds to GLC peak 11 (Fig. 5C). U.V.absorption $\lambda_{max}$ 210 m$\mu$.

ANALYSIS

Found : C, 81.69; H, 11.06

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

IR bands at: 3333, 1692, 1379, 1361, 1304, 1280, 1227, 1190, 1156, 1111, 1099, 1064, 1053, 1020, 1007, 980, 900, 875, 810 and 770 $cm^{-1}$.

ALCOHOL III

Fractions from 13-22 (1.8 g. Table IX) containing one major alcohol, were treated with 3:5 dinitrobenzoyl-chloride (1 g.) in pyridine (15 ml.) and heated on a boiling water bath till the solution was clear ( 4-5 hours). Excess of pyridine was removed by distillation. The residue was diluted with water and extracted with ether, ether layer washed with water, dried over anhydrous sodium sulphate and concentrated to yield a solid product. The product was crystallised repeatedly from ethanol, when pure crystalline 3:5 dinitrobenzoate derivative was obtained. m.p.139-140°. $[\alpha]_D^{29}$- 32.1° (C, 4.17). U.V. absorption $\lambda_{max}$ 210 m$\mu$.

ANALYSIS

Found : C, 63.92; H, 6.42

Calculated for $C_{22}H_{26}O_6N_2$ : C, 63.75; H, 6.32%

IR bands at: 1709, 1626, 1546, 1374, 1342, 1282, 1170, 1073, 962, 943, 917, 730 and 720 $cm^{-1}$.

3:5-dinitrobenzoate derivative (2 g.) was dissolved in 5% ethanolic NaOH (25 ml.) and was refluxed for 2 hours. The excess of ethanol was distilled under reduced pressure and the residue diluted with water. The hydrolysed product extracted with ether, washed with water, dried over anhydrous $Na_2SO_4$ and solvent distilled when Alcohol III, corresponding to GLC peak 12 (Fig. 5C), was

obtained. Its physical properties are as follows:-
b.p. 139-140° (bath) / 0.2 mm.; $[\alpha]_D^{28}$ + 55.35°(C, 3.4);
$n_D^{29}$ 1.5205; U.V. absorption $\lambda_{max}$ 210 m$\mu$.

ANALYSIS

Found : C, 81.86; H, 11.18

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

IR bands at: 3509, 3106, 1818, 1661, 1418, 1385, 1316, 1250, 1190, 1168, 1065, 1042, 1020, 990, 965, 910 and 805 cm$^{-1}$.

-.-

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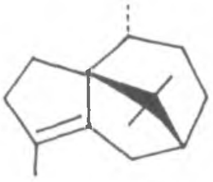
## Chapter II

# Structures of Hydrocarbons

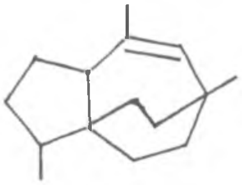
## SUMMARY

By elaborate column chromatography of the hydrocarbon fraction of the oil of *Cyperus scariosus*, (R.Br.). Hydrocarbons I and II have been isolated. On the basis of spectral studies and chemical degradation Hydrocarbon I has been shown to be identical with Cyperene (I).

Hydrocarbon II appears to be identical with Rotundene isolated earlier from the oil of *Cyperus rotundus* (Chinese origin). A provisional structure II has been assigned to the hydrocarbon II.



(I)

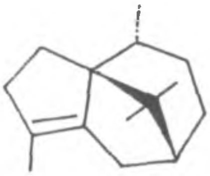


(II)

# CYPERENE

This Chapter deals with structure elucidation of Hydrocarbons I and II.

Hydrocarbon I, $C_{15}H_{24}$ (1), isolated from pet-ether eluted fraction of Cyperus scariosus (R.Br.) oil, [b.p. 78° (bath)/0.2 mm.; $n_D^{28}$ 1.5028; $[\alpha]_D^{27}$ -21.07° (C,4.0) TLC single spot, GLC single peak; mol.wt.204 (Mass spec.)] has been identified as Cyperene[1] (VII). The infrared spectrum (Fig.1) of this hydrocarbon was devoid of any characteristic absorption for unsaturation. However, it showed a weak absorption at 1701 $cm^{-1}$, due to $>C=C<$ stretching frequency. It gives positive tetranitromethane test. It did not show any characteristic absorption in the ultraviolet region indicating the absence of conjugation. The NMR spectrum (Fig.2) did not show any signal below 7 τ, indicating the absence of olefinic hydrogen, but a signal at 8.38 τ clearly indicated the presence of a methyl group on a double bond. The presence of three methyl groups was also shown by singlets at 9.25 and 9.05 τ (3H, each), doublet at 9.16 τ (3H, J = 6cps) in the NMR spectrum.


(VII)

Catalytic hydrogenation of the hydrocarbon I with platinum oxide in acetic acid furnished a dihydroproduct, $C_{15}H_{26}$; b.p. 85-88° (bath)/1 mm. $[\alpha]_D^{26}$ -59.7° (C,3.7);

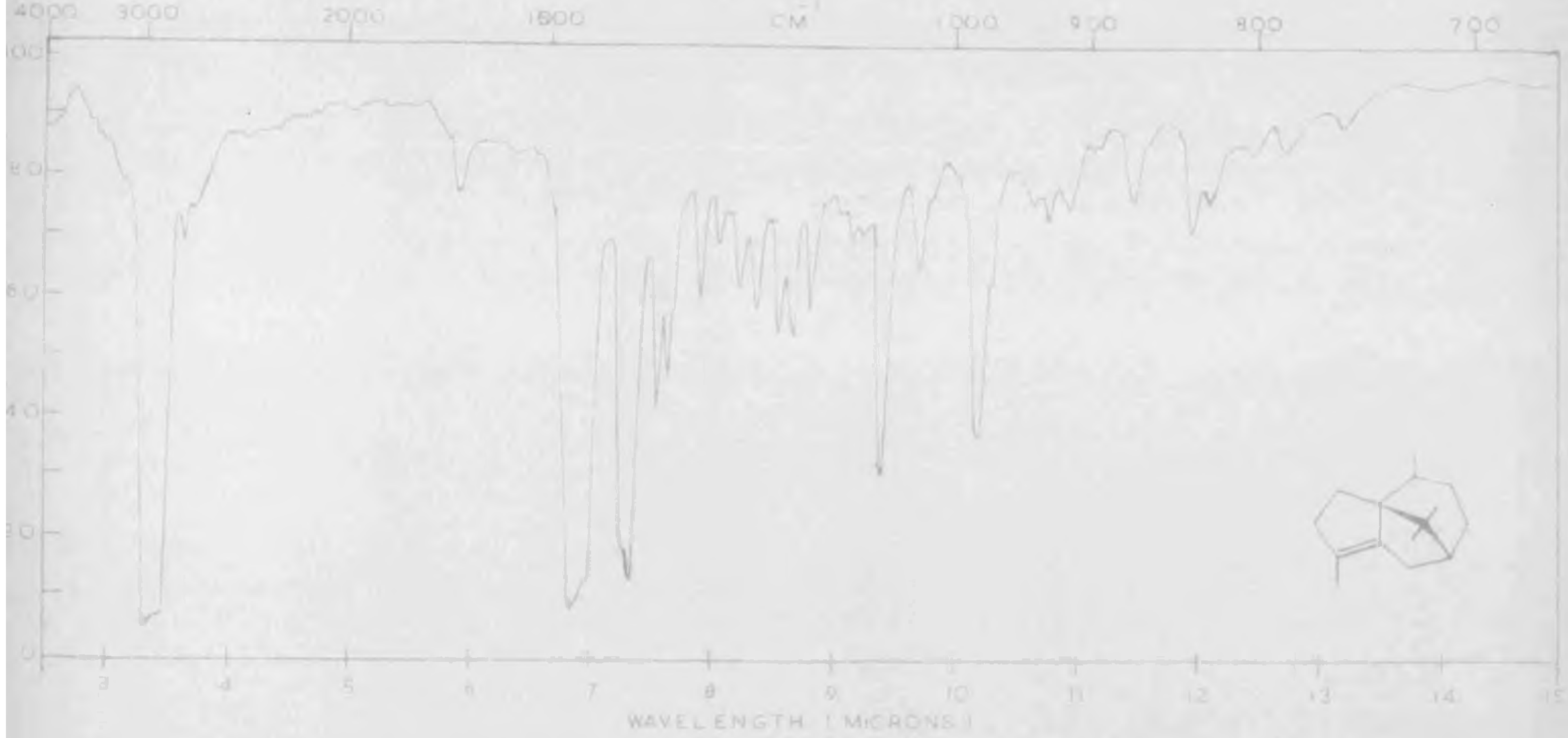


FIG. 1. IR SPECTRUM OF HYDROCARBON-I (CYPERENE) (0.05MM LIQUID CELL)

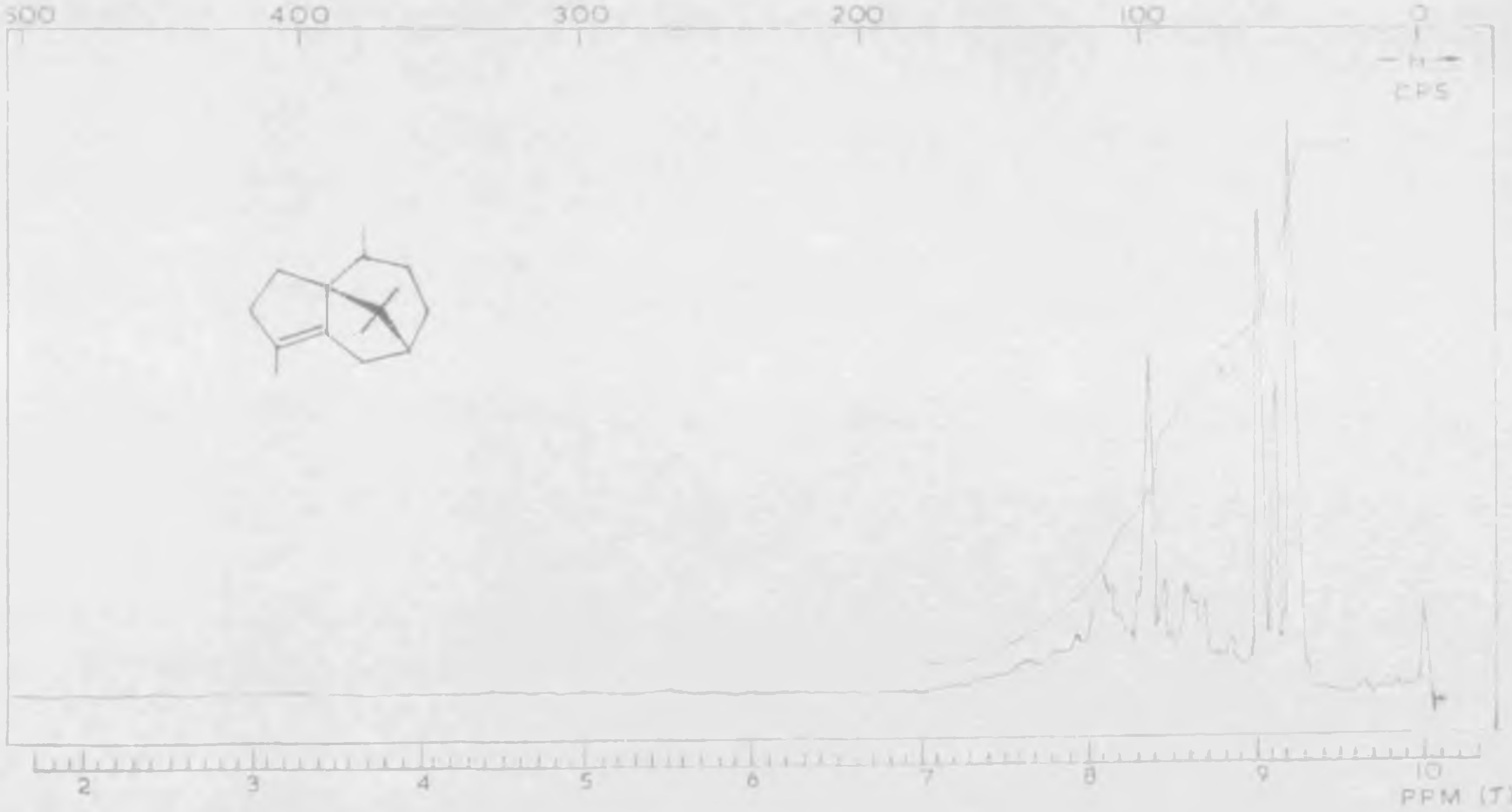


FIG 2 NMR SPECTRUM OF HYDROCARBON – I (CYPERENE)

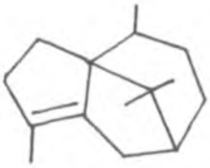
$n_D^{26}$ 1.4955. The dihydroproduct shows two peaks in the GLC in 7:3 ratio, corresponding two stereo isomers formed during hydrogenation. Its IR spectrum (Fig.3) showed the absence of band at 1701 $cm^{-1}$. Thus hydrocarbon I is a tricyclic sesquiterpene containing one tetrasubstituted double bond.

The physical properties of Hydrocarbon I are similar to Cyperene I isolated by Senich[2] from *Cyperus rotundus* (Indian origin) and Cyperene isolated by Sorm et al[1] from *Cyperus rotundus* (Chinese origin). The comparative physical properties are shown in the following Table I.

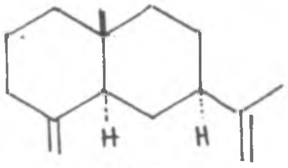
TABLE I

| Hydrocarbon I | Dihydroproduct | Cyperene | Dihydro-Cyperene | Cyperene I |
|---|---|---|---|---|
| $C_{15}H_{24}$ | $C_{15}H_{26}$ | $C_{15}H_{24}$ | $C_{15}H_{26}$ | $C_{15}H_{24}$ |
| $n_D^{28}$ 1.5028 | $n_D^{26}$ 1.4955 | $n_D^{20}$ 1.5058 | $n_D^{20}$ 1.4975 | $n_d^{20}$ 1.5006 |
| $[\alpha]_D^{27}$ -21.07° | $[\alpha]_D^{26}$ -59.7° | $[\alpha]_D^{20}$ -20° | $[\alpha]_D^{20}$ -60.2° | $[\alpha]_D^{20}$ -16° |

Senich[2] in 1959 reported the isolation of Cyperene I (tricyclic) and Cyperene II (bicyclic). These compounds were also isolated by Sorm[1] et al, who assigned the structure I and named it as Cyperene to avoid confusion between Cyperene I and II. Cyperene II was identified as $\beta$-Selinene(II)



(I)



(II)

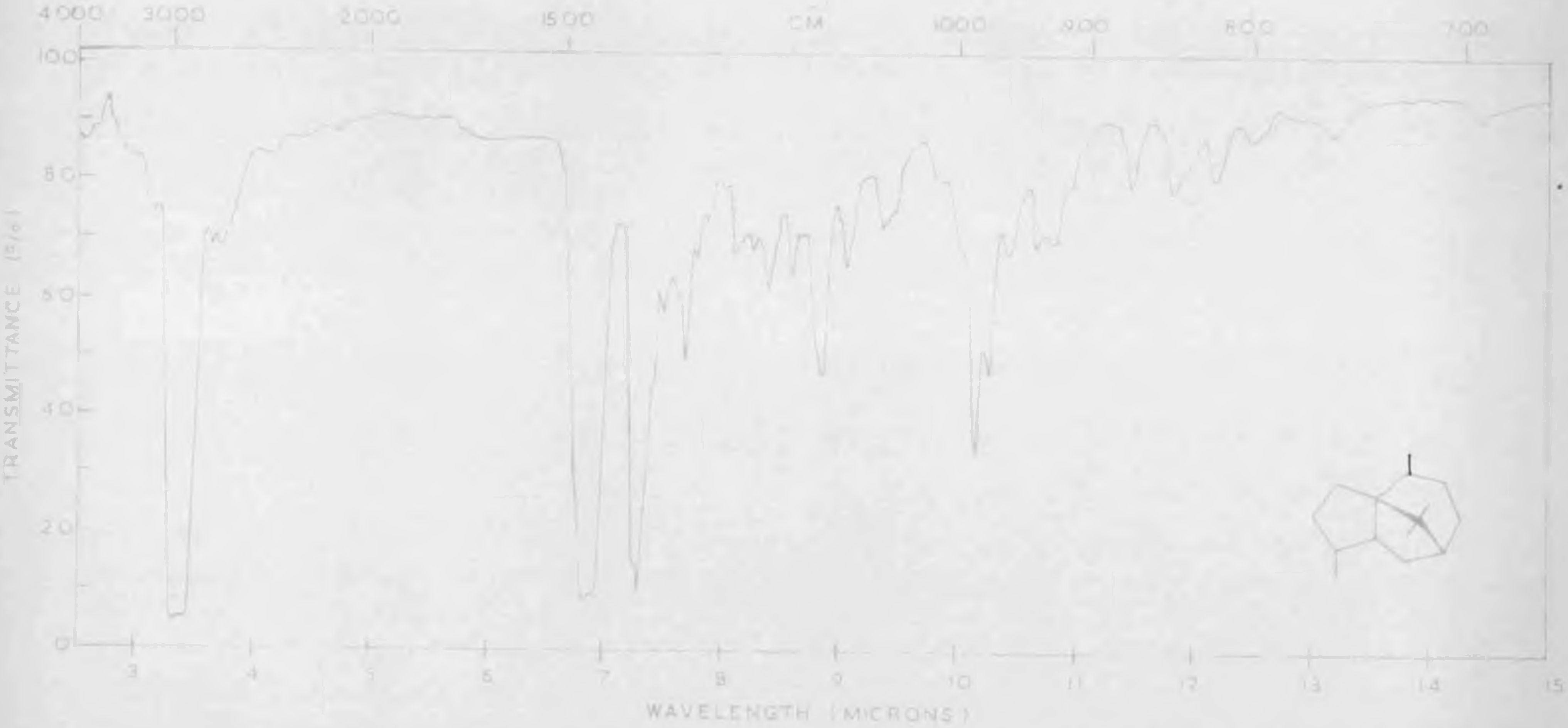
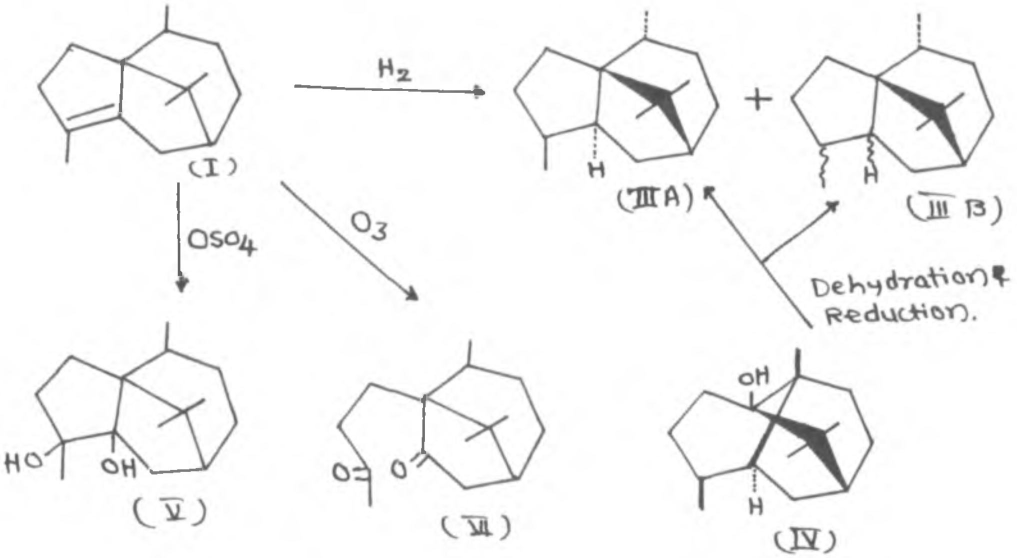


FIG 3. IR SPECTRUM OF DIHYDRO CYPERENE (0.05MM LIQUID CELL)

Sorm et al[1] established the structure of Cyperene (I) as follows:

Raman spectrum of Cyperene (I) showed a band at 1695 $cm^{-1}$, characteristic for the tetrasubstituted olefin. Its dihydro derivative $C_{15}H_{26}$ was completely saturated and showed that the compound was tricyclic. As this compound was identical with the saturated hydrocarbon (III) derived from Patchouli alcohol[3] (IV), the collected data was sufficient to define structure I for Cyperene. On Osmium tetroxide oxidation, it yielded diol (V) m.p. 147.5°.



The NMR spectrum of Cyperene confirmed the absence of any olefinic protons, but exhibited a singlet at 9.25 $\tau$ (6H, gemdimethyls), a doublet at 9.15 $\tau$ (3H,J=6cps, secondary methyl) and an allylic methyl at 8.38 $\tau$ .

Further confirmation of structure of Hydrocarbon I as Cyperene was obtained by ozonolysis of hydrocarbon I to a crystalline diketone (VI), m.p. 78°; $[\alpha]_D^{28}$ + 35.3° (C,3.1). IR spectrum (Fig.10, Chapter III ) indicated presence of $CH_3-CO-$; $-CO-CH_2-$ and five membered ring ketone (1368, 1412 and 1724 $cm^{-1}$ respectively). NMR spectrum (Fig.11, Chapter III) showed signals at 9.28 $\tau$ ($CH_3-CH\!<$ ), 9.00 $\tau$ ($CH_3-C\!\begin{smallmatrix}/\\-\\\backslash\end{smallmatrix}$ ), 8.84 $\tau$ ($CH_3-C\!\begin{smallmatrix}/\\-\\\backslash\end{smallmatrix}$ ), and 7.93 $\tau$ ($CH_3-CO-$ ), 8.08 $\tau$ ($-CH_2-CO-$). This diketone was identical with the diketone (VI) obtained from Cyperene (I) by Sorm et al[1]. Cyperene on catalytic hydrogenation also shows two peaks in the GLC in the ratio of 3:2 as observed for hydrocarbon I, corresponding to two stereo isomers.

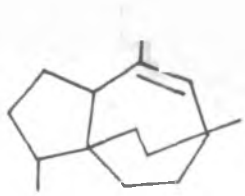
Thus hydrocarbon I (Isopatchoul-4-ene) was established to be Cyperene (I).

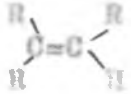
The absolute stereochemistry of Cyperene has been established by the Japanese workers[4], as shown in the structure (VII). The details of this work is described in Chapter III.

(VII)

## ROTUNDENE

Hydrocarbon II, $C_{15}H_{24}$ (VIII) had the following properties: mol. wt. 204 (Mass spec.) GLC single peak, TLC single spot; b.p. 118°(bath)/1.5 mm.; $n_D^{28}$ 1.5004; $[\alpha]_D^{28}$ -15.63° (C, 5.28). It is a new sesquiterpene hydrocarbon; a provisional structure VIII has been assigned to the hydrocarbon.


(VIII)

The infrared spectrum (Fig.4) showed bands at 1675 and 825 $cm^{-1}$ (a trisubstituted double bond  $\genfrac{}{}{0pt}{}{R}{R}\!>C=C<\!\genfrac{}{}{0pt}{}{R}{H}$ ). The ultraviolet absorption showed only end absorption.

The NMR spectrum (Fig.5) showed signals at 9.15 τ (3H, doublet, J = 7 cps) due to a secondary methyl group, 9.01 τ ( 3H, singlet) arising from a quarternary methyl group and 8.3 τ (3H, broad signal) attributable to a methyl group on an ethylenic linkage. The presence of a vinyl proton was revealed by a signal at 4.55 τ ( 1H, unresolved quartet).

On hydrogenation in acetic acid using Adams catalyst, hydrocarbon II afforded a saturated dihydroderivative (IX), $C_{15}H_{26}$; $[\alpha]_D^{26}$- 71.37° (C,4.2); $n_D^{26}$1.4950; b.p. 130 - 135° (bath) / 3.5 mm. Disappearance of infrared absorption (Fig.6) bands at: 825 and 1675 $cm^{-1}$ indicated complete saturation.

NMR spectrum (Fig.7) of dihydrohydrocarbon

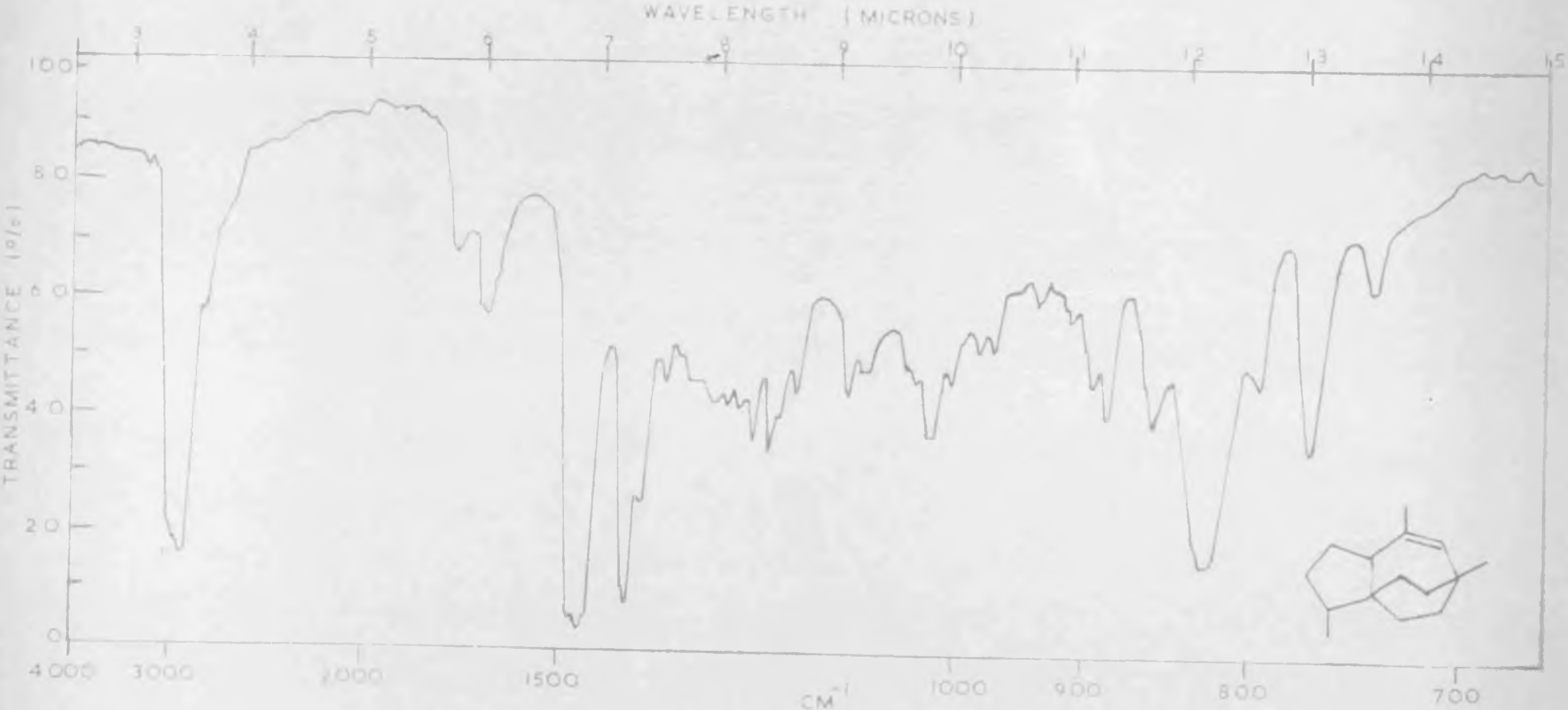


FIG 4 IR SPECTRUM OF HYDROCARBON II (ROTUNDENE)

(0·05MM LIQUID CELL)

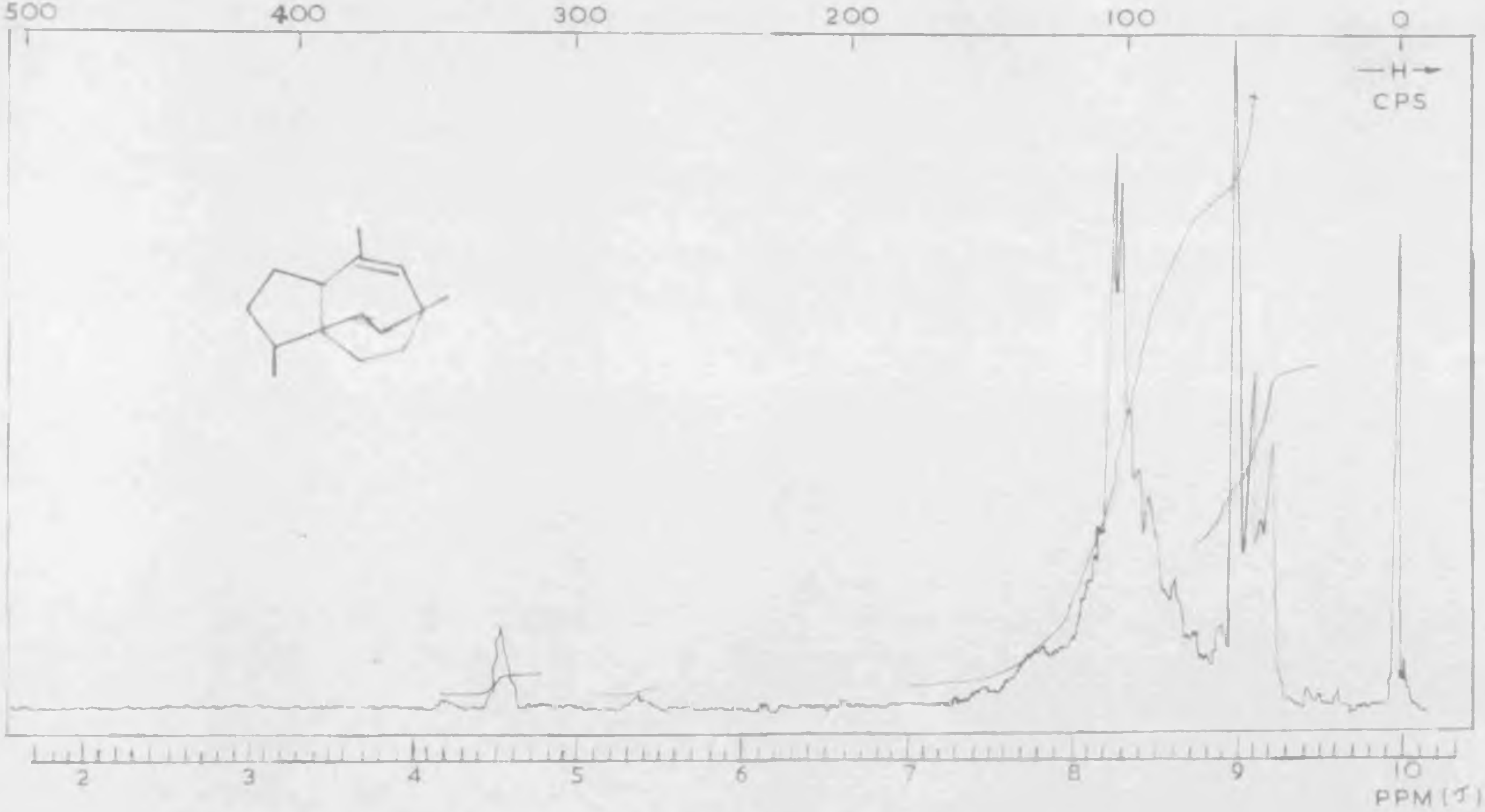


FIG. 5 NMR SPECTRUM OF HYDROCARBON - II ( ROTUNDENE )

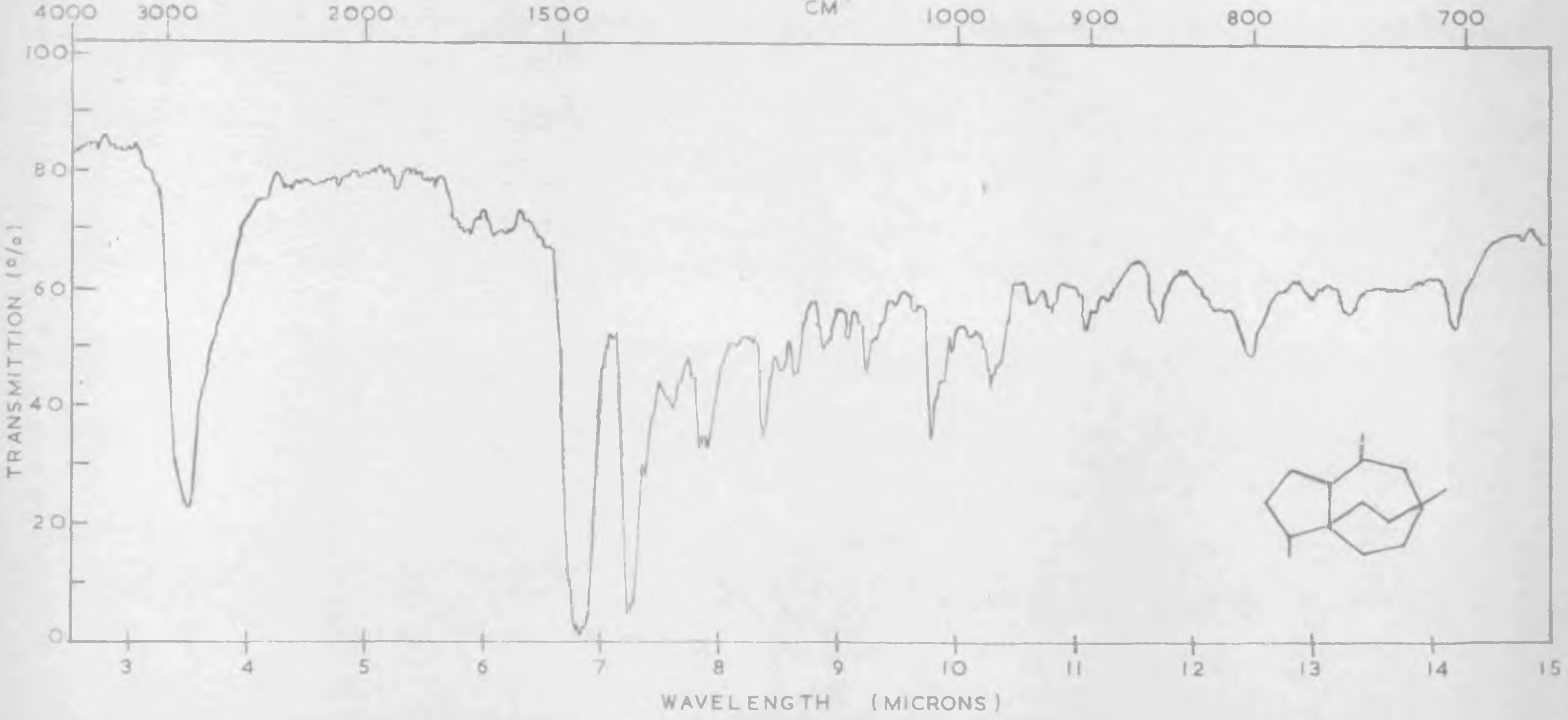
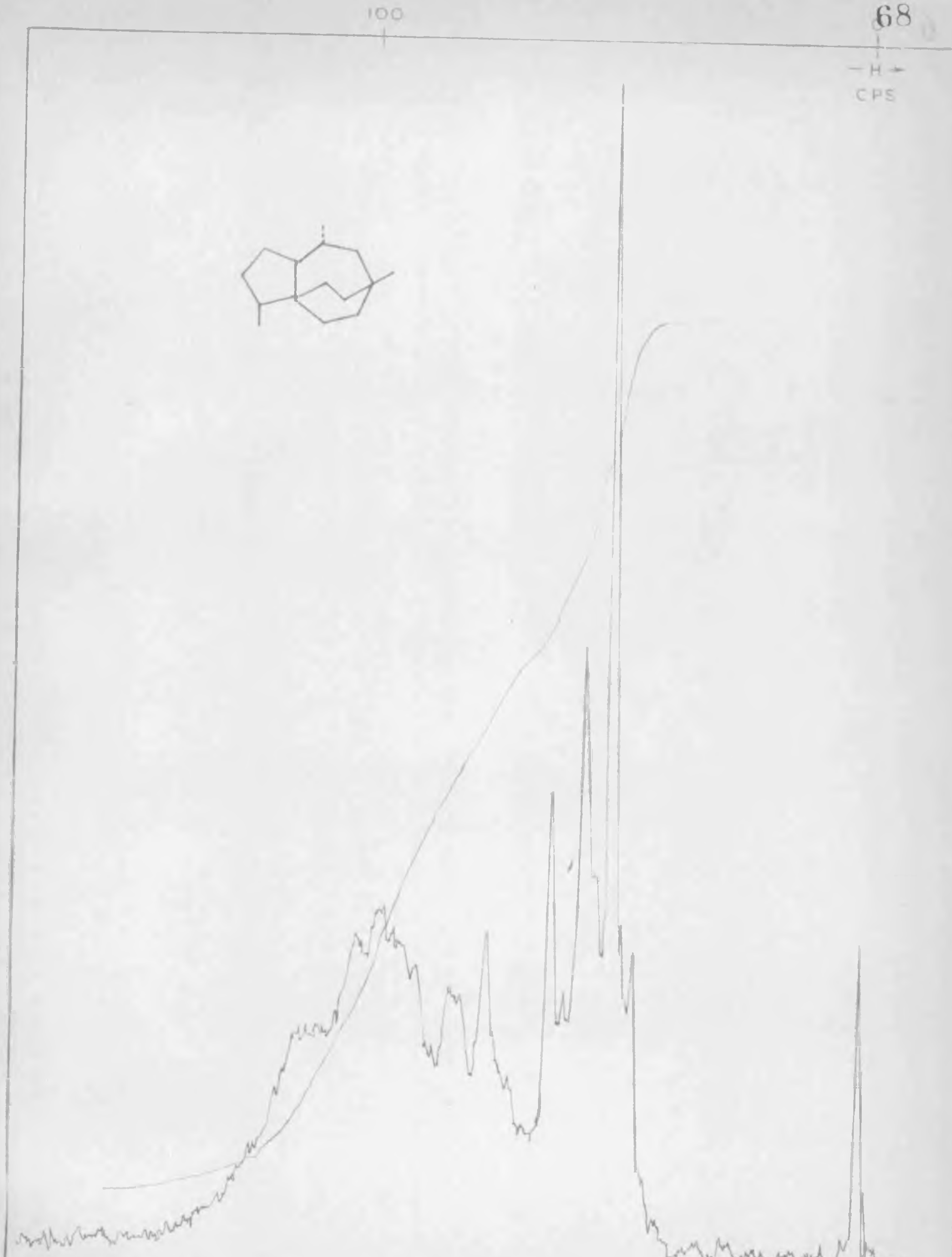


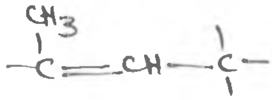
FIG. 6 IR SPECTRUM OF DIHYDRO-ROTUNDENE

(0·05MM LIQUID CELL)


100
H
CPS
7·5
8

clearly accounts for three methyl groups ( signals at 9.17, 9.12 and 9.02 $\tau$. 9 H).

Thus, hydrocarbon II is a tricyclic sesquiterpene hydrocarbon with a trisubstituted double bond and part structure (A).



$-\overset{CH_3}{\overset{|}{C}}=CH-\underset{|}{\overset{|}{C}}-$

(A)

The physical properties of Hydrocarbon II compare well with the tricyclic hydrocarbon (Rotundene)* isolated from <u>Cyperus rotundus</u> (Chinese origin) by Sorm et al[5]. The comparative physical properties are shown in the following Table.

TABLE II

| Hydrocarbon II | Dihydro-product | Rotundene | Dihydrorotundene |
|---|---|---|---|
| $n_D^{28}$ 1.5004 | $n_D^{26}$ 1.4950 | $n_D^{20}$ 1.5035 | $n_D^{20}$ 1.4980 |
| $[\alpha]_D^{28}$ -15.63° | -71.37° | -16.3° | -65.8° |

On epoxidation followed by isomerisation with $BF_3$ etherate[6], Hydrocarbon II (VIII) afforded a ketone (XI), $C_{15}H_{24}O$; $[\alpha]_D^{28}$ - 47.24° (C,2.8); b.p. 138° (bath)/1 mm. The IR (Fig.8) bands at 1709 $cm^{-1}$ suggested that the carbonyl oxygen must be on a saturated six or seven membered ring.

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*The tricyclic hydrocarbon $[\alpha]_D$ -16.3° described in reference No.5, has been named as Rotundene by Prof.F.Sorm (personal communication).

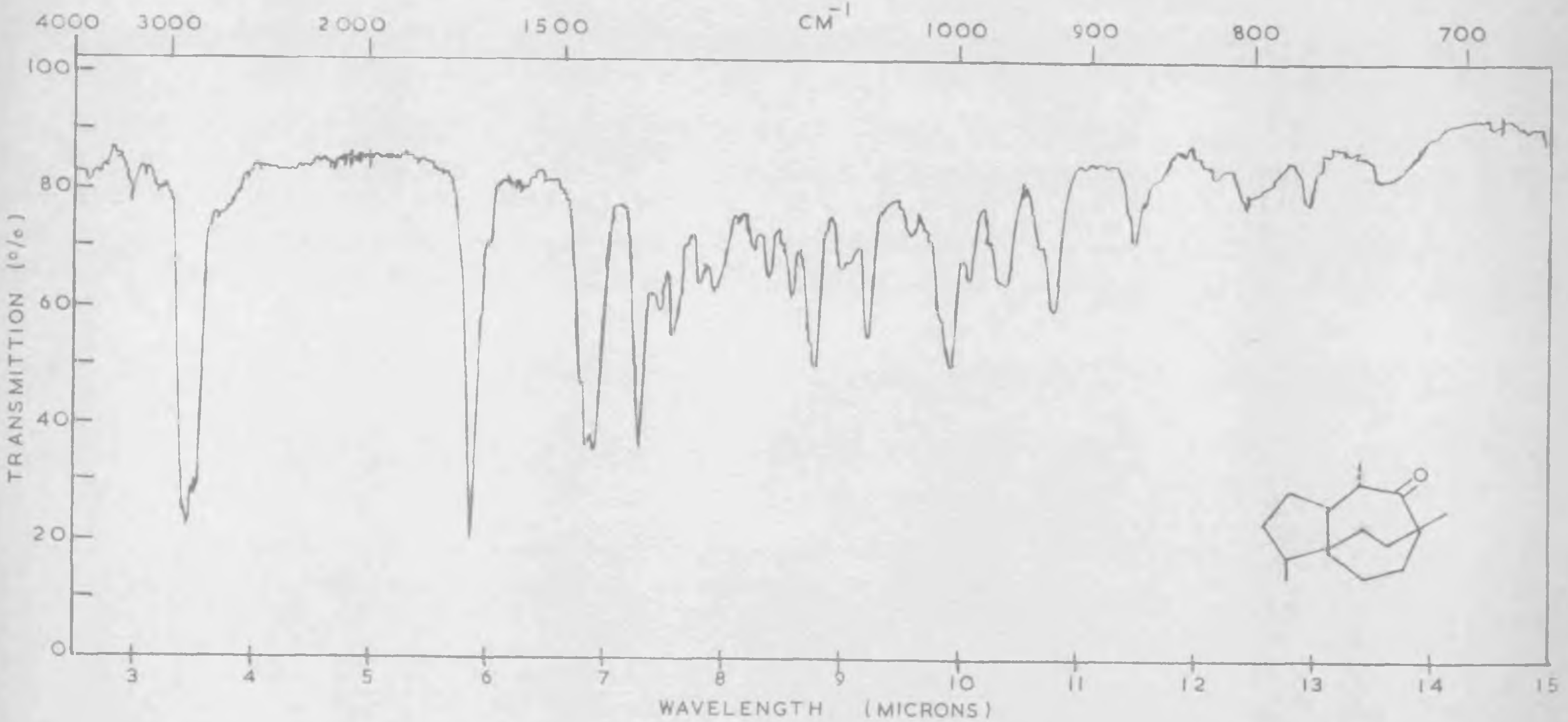
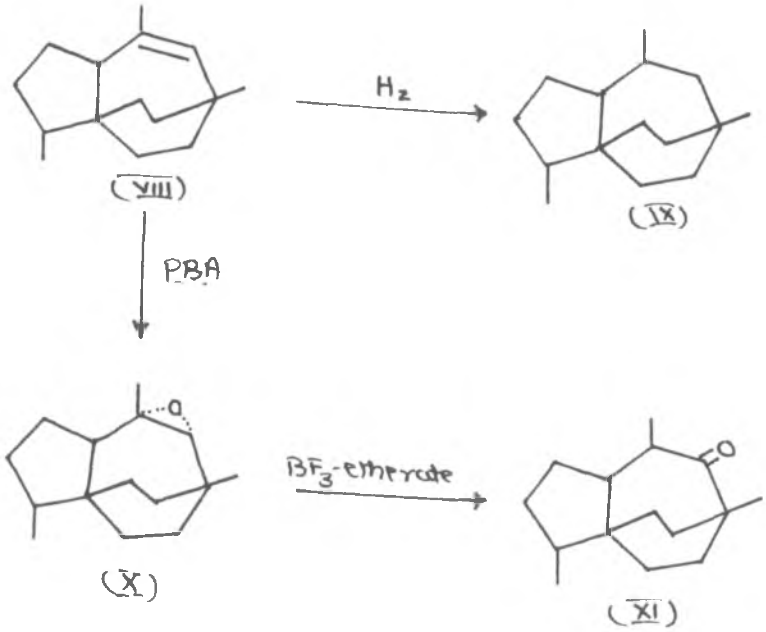


FIG 8 IR SPECTRUM OF KETONE

( LIQUID FILM )

The IR spectrum also indicated the absence of methylene groups adjacent to the ketone as it did not show any band at 1420 $cm^{-1}$. The ketone did not form any carbonyl derivative and was recovered unchanged on an attempted Wolff-Kishner reduction.



The identity of hydrocarbon II was established by a direct comparison (GLC,IR) with Rotundene** $[\alpha]_D -16.3^\circ$; the ketone (XI), $[\alpha]_D -46^\circ$ prepared from Rotundene via hydroboration, oxidation was also identical (IR) with the ketone (XI) $[\alpha]_D - 47.24^\circ$ prepared from hydrocarbon II via epoxidation followed by $BF_3$ etherate treatment.

The hydrocarbon II occurs along with Cyperene. The NMR (Fig.2) of Cyperene shows the presence of four

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** Our thanks are due to Prof.F.Sorm and Dr.O.Motl for kindly supplying a sample of Rotundene and IR spectrum of ketone (XI) prepared by hydroboration and oxidation of Rotundene.

methyl groups (one gemdimethyl, one secondary methyl and one methyl on double bond), whereas Rotundene shows the presence of only three methyl groups (one secondary, one methyl on a double bond and one quarternary methyl group) in NMR spectrum (Fig.5). It is possible that a methyl group of Cyperene might be involved in the ring formation in Rotundene. It is, therefore, proposed to assign a provisional structure (VIII) for Rotundene on biogenetic considerations. The biogenetic path way leading to Rotundene is described in Chapter IV, while discussing the structure of Rotundenol which appears to have the same carbocyclic system.

## EXPERIMENTAL

**CYPERENE** (I) (Hydrocarbon I, isolation Chapter I) $C_{15}H_{24}$ had the following properties:

b.p. 93-94° (bath)/1 mm. $[\alpha]_D^{28}$ - 21.07°(c,4.0); $n_D^{28}$ 1.5030; Mol. wt. 204 (Mass spec.).

**ANALYSIS**

Found : C, 88.31; H, 11.91.

Calculated for $C_{15}H_{24}$ : C, 88.16; H, 11.84%

U.V. absorption $\lambda_{max}$ 210 m$\mu$.

IR bands (Fig.1, 0.05 mm. cell) at: 1701, 1389, 1366, 1333, 1316, 1269, 1250, 1222, 1205, 1181, 1163, 1141, 1070, 1037, 988, 934, 892, 877, 845 and 832 cm$^{-1}$.

NMR spectrum (Fig.2), 9.25 $\tau$ (6H; $CH_3-\overset{|}{\underset{|}{C}}-CH_3$), 9.05 and 9.16 $\tau$ (3H, $CH_3-\overset{|}{C}H-$) and 8.38 $\tau$ (J = 1 cps, $CH_3-\overset{|}{C}=\overset{|}{C}-$).

**DIHYDROCYPERENE** (III)$C_{15}H_{26}$.

**Hydrogenation of Cyperene** (I)

Cyperene (350 mg.) dissolved in glacial acetic acid (20 ml.) was stirred in an atmosphere of hydrogen with pre-reduced Adams $PtO_2$ catalyst (50 mg.). The equivalent of 0.98 mole of hydrogen was absorbed in 25-30 minutes. The catalyst was filtered and solvent was removed in vacuum to furnish dihydroproduct (314 mg.), which on chromatography over 100 fold alumina (Gr.I, 4 g.) followed by vacuum distillation gave dihydrocyperene having the following properties.

b.p. 85-98$^{o}$ (bath) / 1 mm. $[\alpha]_D^{26}$ - 59.7$^{o}$ (C, 3.7); $n_D^{26}$ 1.4955. GLC two peaks in 7:3 ratio (stereoisomers of dihydrocyperene).

ANALYSIS

Found : C, 87.5; H, 12.78

Calculated for $C_{15}H_{26}$ : C, 87.3; H, 12.7%

IR bands (Fig.3, 0.05 mm. cell) at: 1387, 1366, 1342, 1312, 1294, 1251, 1205, 1178, 1139, 1114, 1076, 995, 982, 965, 948, 930, 921, 893, 880 and 852 cm$^{-1}$.

DIKETONE (VI), $C_{15}H_{24}O_2$

Ozonolysis of Cyperene (I)

Ozone was passed in to an ethylacetate (50 ml.) solution of Cyperene (980 mg.) at 0.5$^{o}$. At the end of reaction (after 1/2 hour), the solution turned yellow. Ethylacetate was removed under reduced pressure. After adding water (25 ml.) it was refluxed for 4 hours and extracted with ether (4 x 50 ml.). The combined ether extract was washed with 5% sodium hydroxide solution to remove any acid formed during ozonolysis. Neutral portion was dried ($Na_2SO_4$ anhydrous). Evaporation of solvent yielded a colourless crystalline compound (675 mg.). It was crystallised from petroleum ether m.p. 78$^{o}$ $[\alpha]_D^{26}$ +35.3$^{o}$ (C, 3.1).

ANALYSIS

Found : C, 76.54; H, 10.3

Calculated for $C_{15}H_{24}O_2$ : C, 76.22; H, 10.24%.

IR bands (Fig.10, nujol, Chapter III) at: 1724, 1412, 1379, 1300, 1245, 1224, 1190, 1171, 1157, 1105, 1075, 1058, 1031, 980, 972, 943, 920, 890, 840 and 790 cm$^{-1}$.

NMR spectrum (Fig.11, Chapter III); doublet at: 9.28 $\tau$ (3H J = 6 cps, $CH_3-CH\begin{smallmatrix}\diagup\\ \diagdown\end{smallmatrix}$ ), singlet at 9.06 $\tau$ (3H, $CH_3-C\begin{smallmatrix}\diagup\\ -\\ \diagdown\end{smallmatrix}$), singlet at: 8.84 $\tau$ (3H, $CH_3-C\begin{smallmatrix}\diagup\\ -\\ \diagdown\end{smallmatrix}$), singlet at 7.93 $\tau$ (3H, $CH_3-CO-$), 8.06 $\tau$ (2H, $-CH_2-CO-$).

ROTUNDENE (VIII) (Hydrocarbon II, isolation Chapter I) $C_{15}H_{24}$ b.p. 118° (bath) / 1.5 mm. $[\alpha]_D^{28}$ - 15.63° (C, 5.28); $n_D^{28}$ 1.5004; mol. wt. 204 (Mass spec.) U.V. absorption $\lambda_{max}$ 210 m$\mu$.

ANALYSIS

Found : C, 88.20; H, 11.9

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

IR bands (Fig.4, 0.05 mm. cell) at: 2778, 1698, 1385, 1362, 1320, 1205, 1190, 1155, 1100, 1020, 1000, 980, 970, 935, 895, 885, 825, 795 and 770 cm$^{-1}$.

NMR spectrum (Fig. 5): 9.15 $\tau$ (3H, $CH_3-C\begin{smallmatrix}\diagup\\ -\\ \diagdown\end{smallmatrix}$ ); 9.01 $\tau$ (3H, $CH_3-CH\begin{smallmatrix}\diagup\\ \diagdown\end{smallmatrix}$ ), 8.3 $\tau$ ( 3H, $CH_3-\overset{|}{C}=\overset{|}{C}-$ ), 4.55 $\tau$ ($\rangle C=CH-$).

DIHYDROROTUNDENE (IX) $C_{15}H_{26}$

Hydrogenation of Rotundene (VIII)

Rotundene (130 mg.) was hydrogenated in ethylalcohol (6 ml.) with $PtO_2$ (40 mg.) at room temperature. After the uptake of 1 mole $H_2$, the solution was filtered and filtrate was evaporated to give the product (120 mg.) which on distillation over metallic sodium afforded dihydrorotundene as colourless mobile liquid. b.p. 130–136° (bath) / 3.5 mm; $[\alpha]_D^{26}$ - 71.37° (C, 4.2); $n_D^{26}$ 1.4950.

ANALYSIS

Found : C, 87.54; H, 12.88

Calculated for $C_{15}H_{26}$ : C, 87.3; H, 12.7%

IR bands (Fig. 6, 0.05 mm. cell) at: 1380, 1320, 1270, 1195, 1160, 1130, 1110, 1023, 970, 940, 925, 900, 855, 800, 770 and 750 $cm^{-1}$.

NMR spectrum (Fig.7): singlet at 9.17 τ (3H, $H_3C-\overset{/}{\underset{\backslash}{C}}-$), doublet centered at 9.12 τ (3H, J= 6 cps, $H_3C-\overset{/}{\underset{\backslash}{C}}H$) and doublet centered at 9.02 τ (3H, J = 6 cps, $H_3C-\overset{/}{\underset{\backslash}{C}}H$).

KETONE (XI) $C_{15}H_{26}O$

Epoxidation of Rotundene (VIII)

(1) Rotundene (150 mg.) in dry chloroform (5 ml.) was mixed with a solution of perbenzoic acid in chloroform (20 ml. 1.0 N) and the mixture was kept at 0°C. for 24 hrs. The epoxide was isolated in the usual manner. The crude epoxide (143 mg.), showed weak $\nu_{max}$ 3560 and 1713 $cm^{-1}$, indicating the presence of hydroxyl and ketonic impurities. Chromatography over alumina (Gr.II, 13.0 g.) and elution

with pet-ether gave the epoxide (110 mg.) in the middle fractions (98% pure by GLC). IR 901 cm$^{-1}$ (epoxide), (b.p. 120$^0$ (bath) / 1 mm.).

ANALYSIS

Found : C, 80.71; H, 11.77.
Calculated for $C_{15}H_{24}O$ : C, 81.08; H, 11.71%

### $BF_3$ Etherate rearrangement

(2) To the epoxide (100 mg.) in dry benzene (20 ml.), $BF_3$ etherate (0.2 ml.) was added with cooling and the product left at room temperature for 1 hour. The light brown coloured solutions was washed with $Na_2CO_3$ solution and water and dried over $Na_2SO_4$ (anhydrous). After removal of benzene, the product was chromatographed over alumina (Gr. II, 0.5 g.) and on distillation it gave ketone (XI), as a light green coloured liquid (TLC, GLC pure) b.p.138$^0$ (bath) / 1 mm. $[\alpha]_D^{28}$ - 47.24$^0$ (C, 2.8).

ANALYSIS

Found : C, 81.16; H, 11.73
Calculated for $C_{15}H_{26}O$ : C, 81.08; H, 11.71%

IR bands (Fig.8; liquid film) at: 1709, 1379, 1342, 1328, 1287, 1266, 1195, 1170, 1143, 1114, 1087, 1047, 1010, 995, 961, 926, 870, 805 and 773 cm$^{-1}$.

NMR spectrum (Fig.15, Chapter IV); singlet (3H) at 9.04 $\tau$ ( $CH_3-C\leqslant$ ), two doublets (3H, each) centred at 9.13 and 8.9 $\tau$ (J = 5.5 and 6.5 cps respectively $>CH-CH_3$ ).

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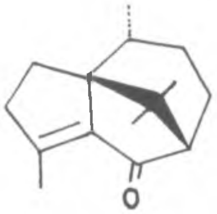
## Chapter III

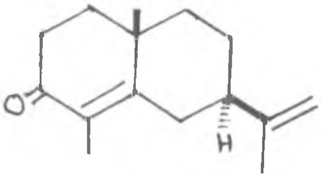
# Structures of Ketones

## SUMMARY

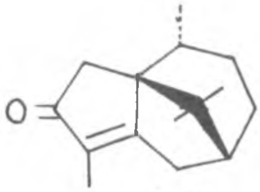
From the carbonyl fraction of the oil of Cyperus-scariosus, Patchoulenone (I), α-Cyperone (II) and two new crystalline ketones, Isopatchoulenone (III) and Scariodione (IV), have been isolated. Isopatchoulenone and Scariodione have been shown to possess stereostructures III and IV respectively.



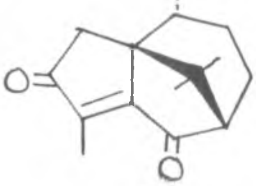
(I)



(II)



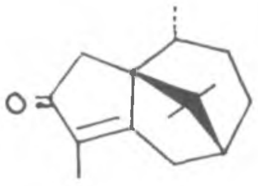
(III)



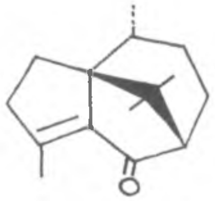
(IV)

## ISOPATCHOULENONE[1]

Ketone I is a new crystalline sesquiterpene Ketone $C_{15}H_{22}O$, (TLC and GLC pure), m.p. 48, molecular weight 218 (mass spec.); $[\alpha]_D^{27}$ + 39.9° (C, 3.1), (positive tetranitromethane test). On the basis of spectral



(IB)



(II)

data and chemical evidences ketone I has been assigned the structure and absolute configuration represented by IB. It has been named Isopatchoulenone, because of its structural similarity to patchoulenone (II) isolated from Cyperus-rotundus (Chinese origin).

IR spectrum (Fig.1) of Isopatchoulenone showed two bands of almost equal intensity at 1663 and 1706 cm$^{-1}$. The ultraviolet absorption ($\lambda_{max}^{EtOH}$ 243 m$\mu$, $\varepsilon$,14,235) showed the presence of conjugation.

IR data along with the U.V. absorption maxima suggested the presence of a five membered $\alpha$- $\beta$ unsaturated ketone[2,3,4], the double bond being fully substituted[5]. IR bands at 1418 cm$^{-1}$ accounted for a methylene group adjacent to carbonyl group. Ketone I forms a crystalline 2,4-dinitrophenyl hydrozone derivative (m.p.228°) which

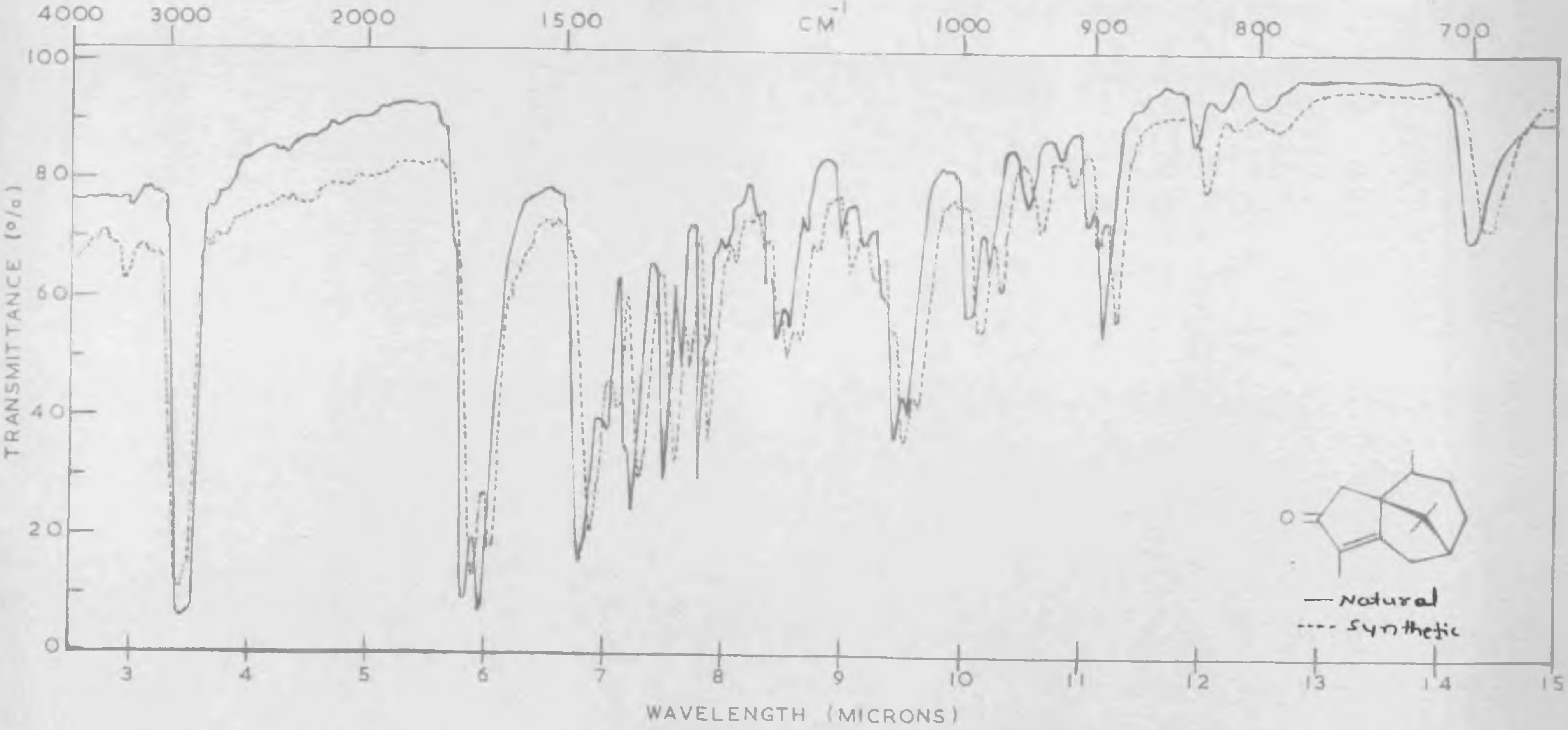
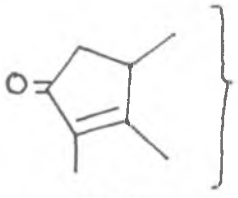


FIG. 1 IR SPECTRUM OF KETONE - I (ISOPATCHOULENONE) (NUJOL)

exhibited U.V. absorption at 392 m/u ($\log_e$ 4.39) indicating the presence of a tetrasubstituted double bond.

On catalytic hydrogenation (Pt / acetic acid) Isopatchoulenone absorbed one mole of hydrogen, giving crystalline, dihydroderivative (III) $C_{15}H_{24}O$; m.p. 74°; $[\alpha]_D^{26}$ - 28.3° (C, 3.3), ( 2,4 d.n.p. 195°). The dihydro compound had no characteristic U.V. absorption and did not give any colouration with tetranitromethane. It displayed IR absorption (Fig.3) bands at: 1742, 1422 $cm^{-1}$, indicating the carbonyl group on a five membered ring. It is therefore, mono-olefinic, tricyclic sesquiterpene having an $\alpha$ - $\beta$ unsaturated carbonyl group on a five membered ring.

The NMR spectrum of Isopatchoulenone (IA) (Fig.2) showed the presence of a secondary methyl (3H, d, 9.36 $\tau$; J = 7 cps), two tertiary methyls (6H, s, 9.2 and 8.87 $\tau$), and methyl on an ethylenic linkage (3H, m, 8.32 $\tau$, $\alpha$ - to carbonyl group) and multiplet at 8.03 $\tau$ represents the two $\alpha$ -protons to the carbonyl group. It also indicated the absence of any vinyl proton. Thus, the spectral data (IR. U.V. and NMR) suggested a part structure (A) for Isopatchoulenone.



(A)

Wolff-Kishner reduction of dihydroisopatchoulenone (III) gave a saturated hydrocarbon (IV), $C_{15}H_{26}$; $[\alpha]_D^{27}$ - 76° (C, 4.1), which

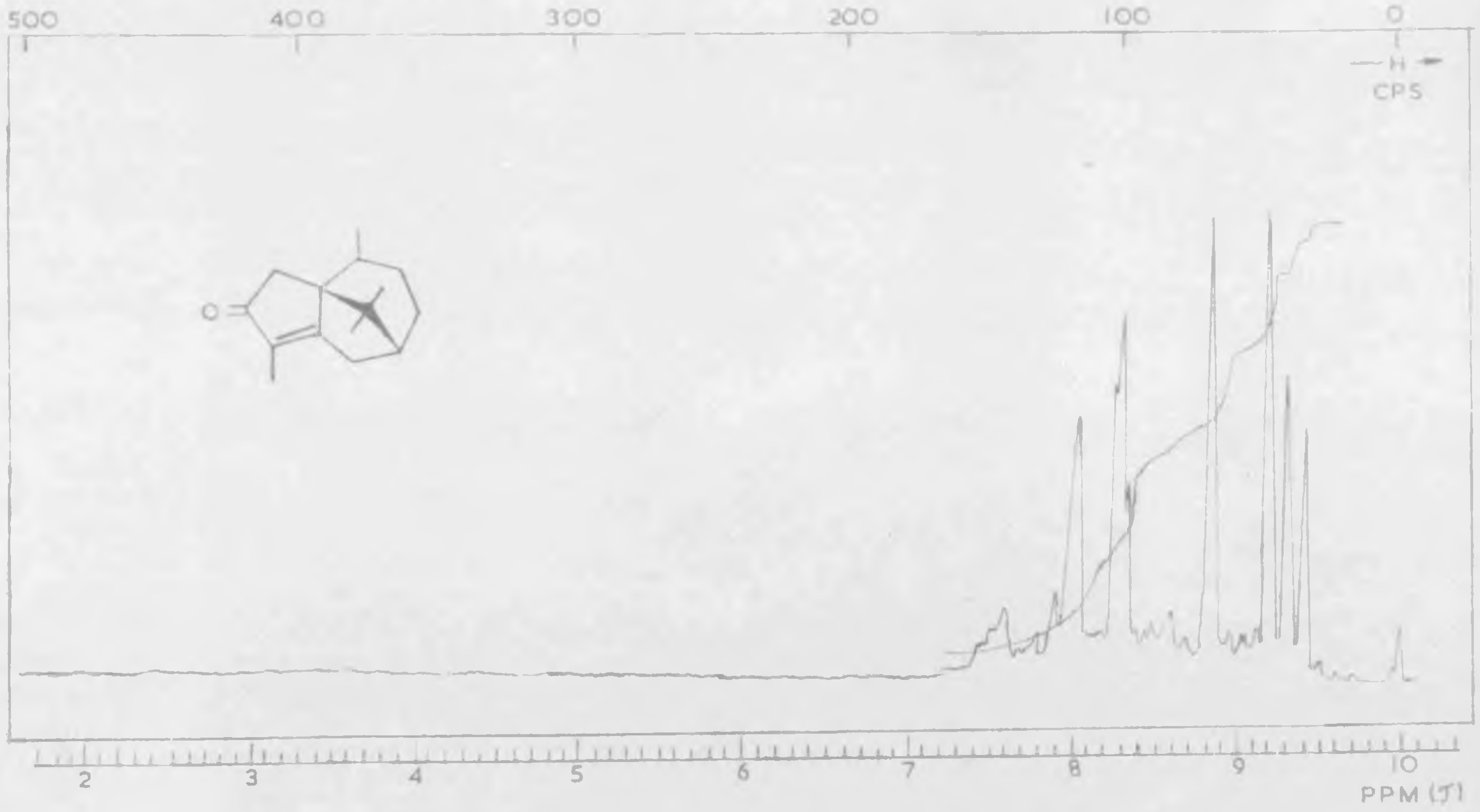


FIG. 2. NMR SPECTRUM OF KETONE - I ( ISOPATCHOULENONE )

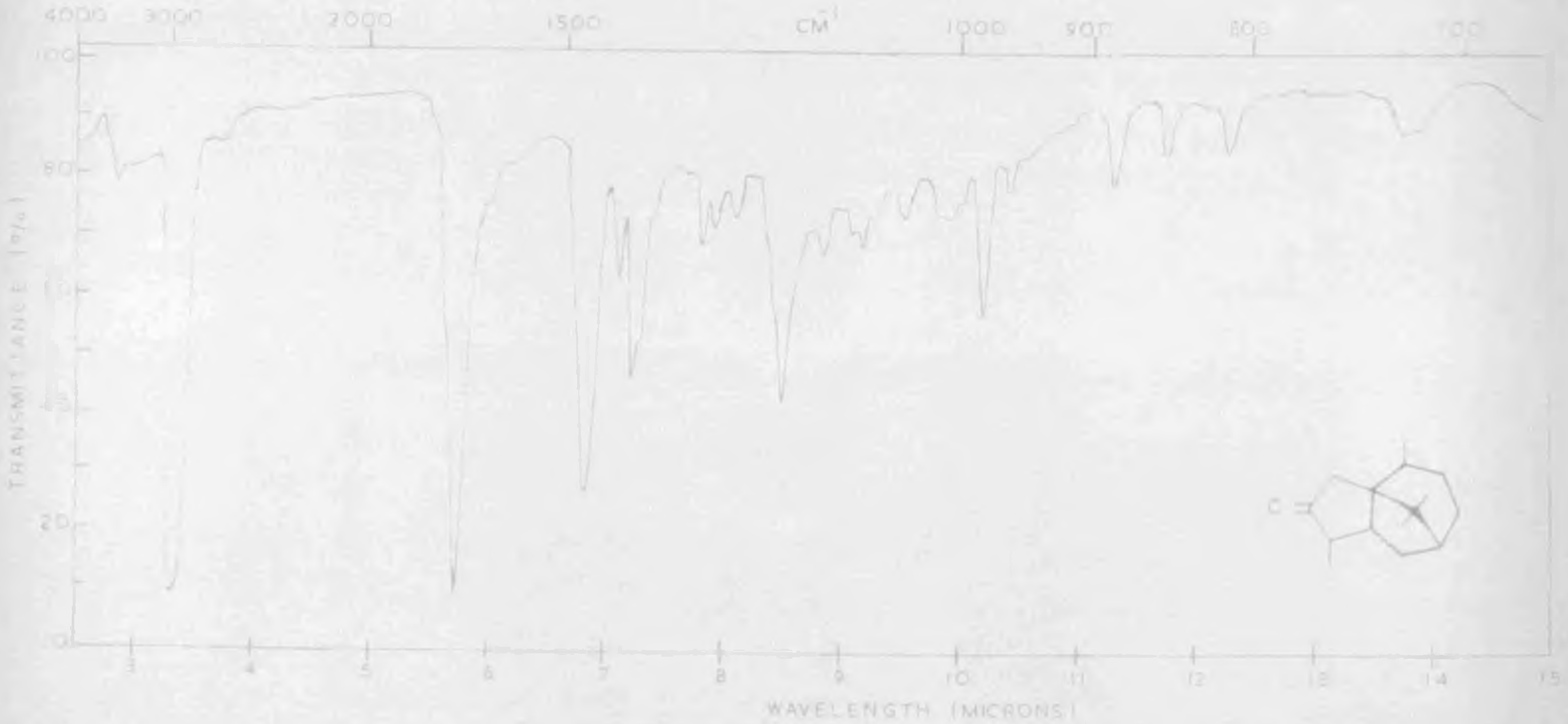


FIG 3 IR SPECTRUM OF DIHYDROISOPATCHOULENONE (NUJOL)

according to its infrared spectrum (Fig.4, intense bands at: 1124, 975, 930 and 848 $cm.^{-1}$) was found to be identical with a stereoisomer of isopatchoulane (IVA) prepared by the reduction of α-patchoulane obtained via dehydration and reduction of patchoulialcohol (V). It has also been observed that cyperene on hydrogenation yields two stereoisomers in 7:3 ratio and the stereoisomers are represented by structures IVB and IVA. IVB represents isopatchoulane.

Reduction of isopatchoulenone (IA) with LAH gave the corresponding alcohol (VI) $C_{15}H_{24}O$; m.p.140°, $[\alpha]_D^{27}$-53° (C, 2.0) (TLC and GLC pure). IR band 3250 $cm^{-1}$ (-OH). The alcohol (VI) on catalytic hydrogenation in ethanol (Adams catalyst), consumed nearly two moles of hydrogen giving a saturated hydrocarbons (IV, stereoisomers in 7:3 ratio GLC) $C_{15}H_{26}$; $[\alpha]_D^{27}$- 62.37° (C, 3.4) indicating the allylic nature of the hydroxyl group. The saturated hydrocarbon (IV) was identical (GLC retention time) with dihydrocyperenes (IV) $C_{15}H_{26}$; $[\alpha]_D^{26}$- 59.7° (C, 3.7); prepared by the hydrogenation of cyperone (VII).

On reduction with LAH-$AlCl_3$, isopatchoulenone (IA) gave an unsaturated hydrocarbon (VII) identical in all respects (NMR, GLC and IR Fig.5) with an authentic sample of cyperene[10]. On ozonolysis it gave a diketone (VIII) m.p. 78°, which was identified as the dione[10]; $[\alpha]_D^{27}$ + 37.2° (C, 2.8) obtained from cyperene. The above results provided unambigous evidence that

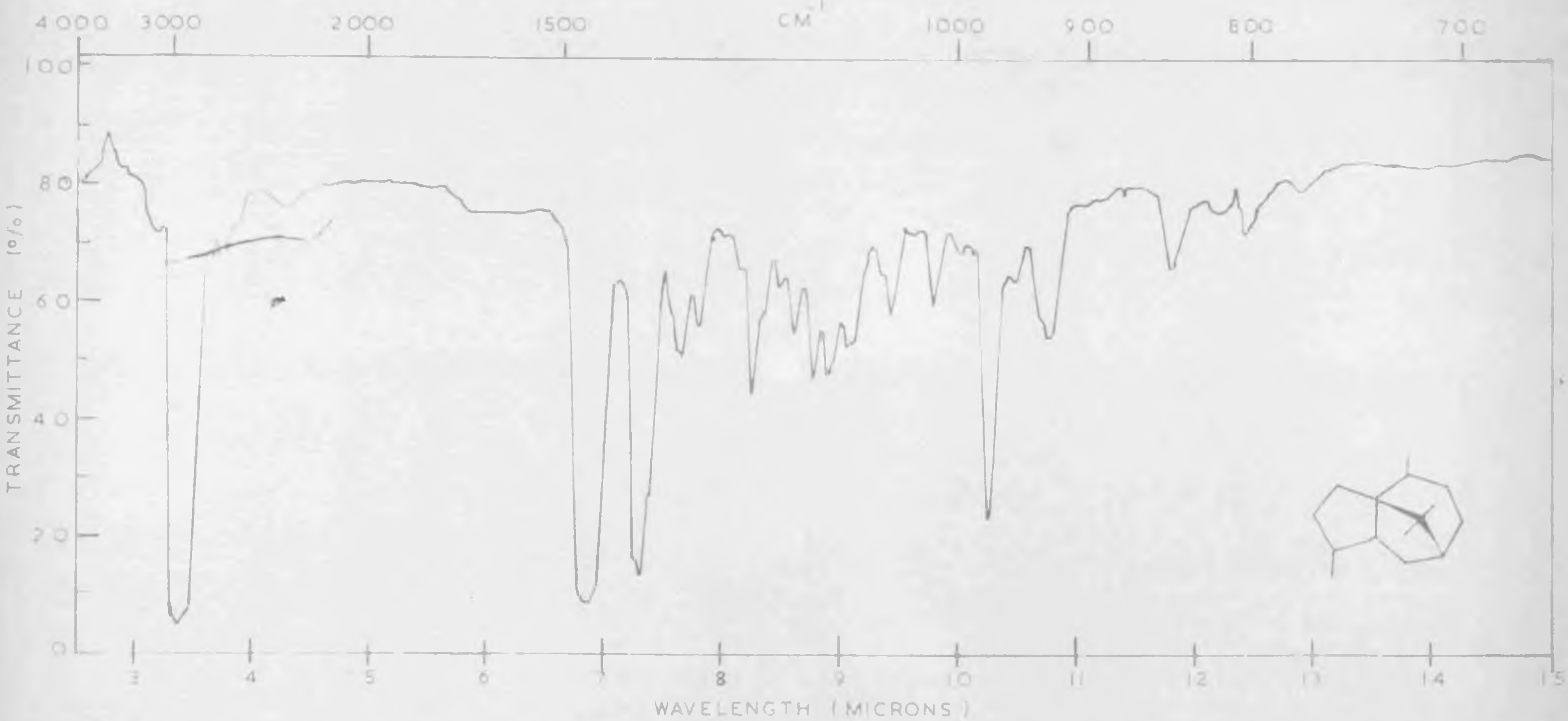


FIG 4 IR SPECTRUM OF ISOPATCHOULANE (0·05MM CELL)

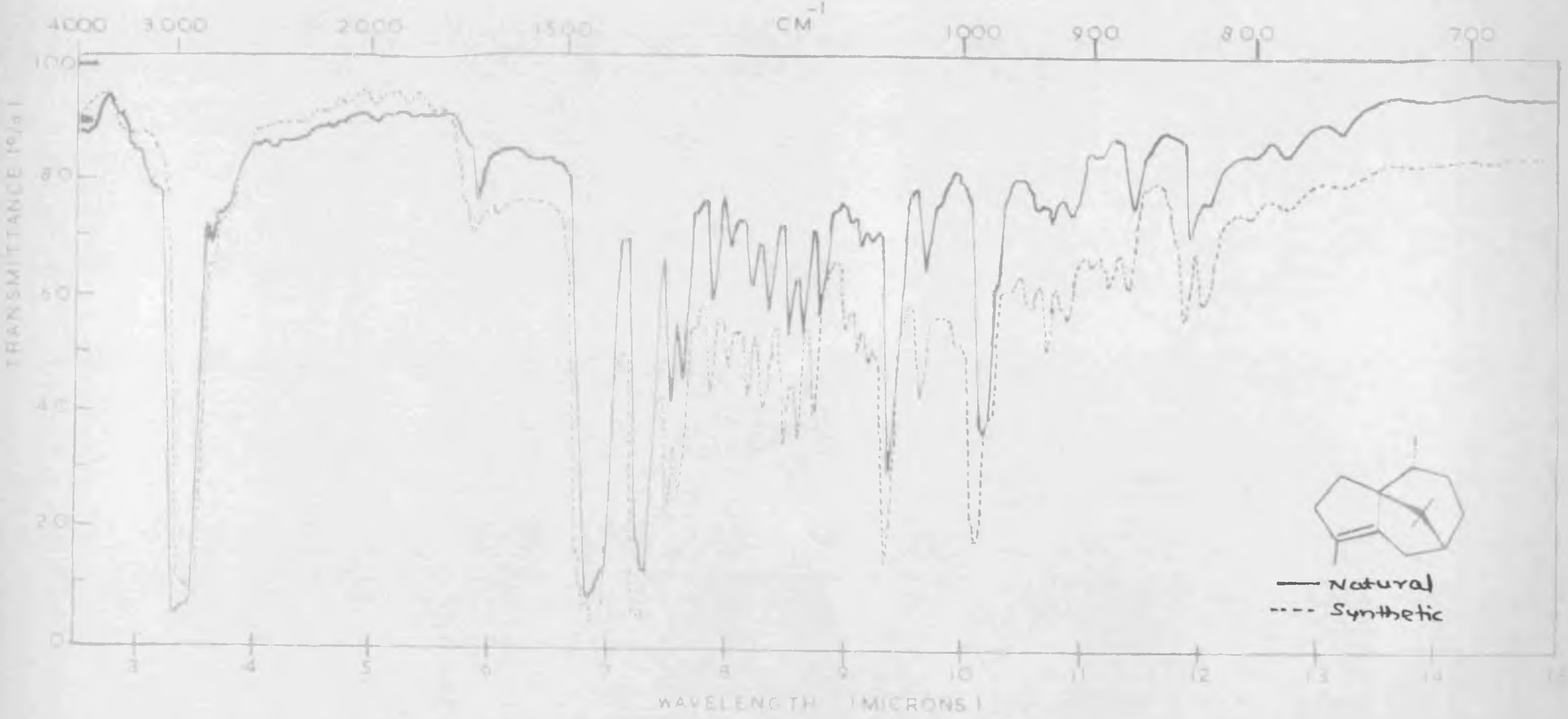
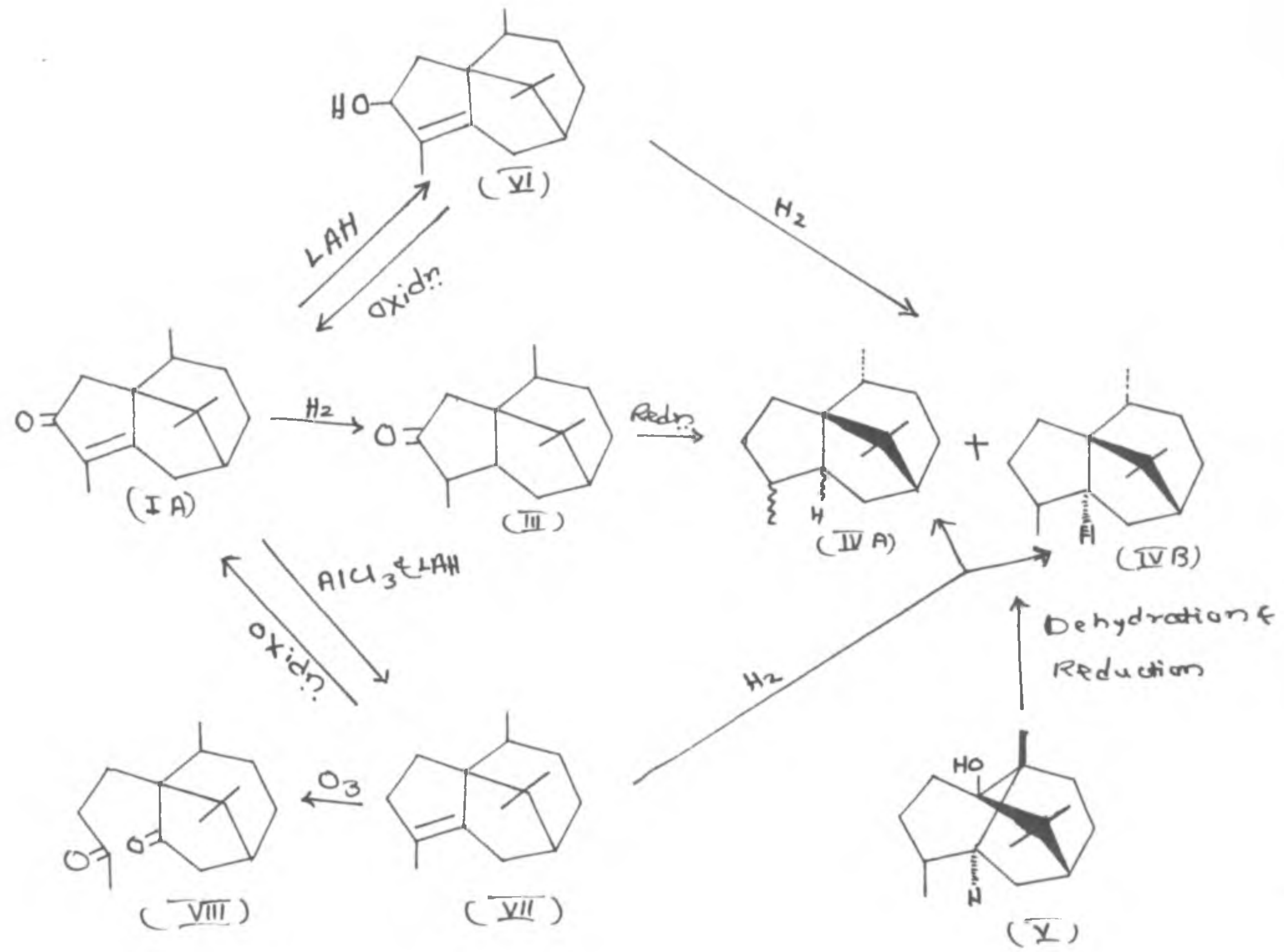


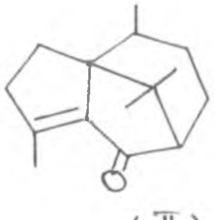
FIG 5 IR SPECTRUM OF CYPERENE (0.05 MM LIQUID CELL)

isopatchoulenone has the same carbon skeleton as cyperene (VII).



On the basis of this data, isopatchoulenone can be represented by the two possible structures (IA) and (II). However, Sörm et al[6] have assigned structure (II) for a ketone, $C_{15}H_{22}O$, m.p. 52.5°; $[\alpha]_D^{20}$ - 97.1° isolated from *Cyperus rotundus* (Chinese origin) and named it as Patchoulenone (II). Isopatchoulenone is therefore, a new isomeric ketone represented by (IA).

(IA)



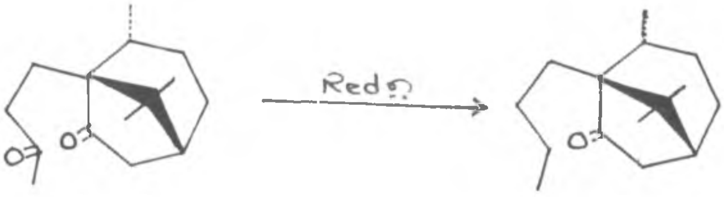
(II)

Further chemical evidence for the confirmation of the structure of isopatchoulenone (IA) was obtained by the oxidation of Cyperene (VII), $[\alpha]_D$ - 21°, (C,4.0). (TLC and GLC pure) isolated from the present oil, with t-butyl chromate[43] to isopatchoulenone (IA). Among the products of oxidation (TLC4-spots), isopatchoulenone (IA) was found to be present by a comparative TLC study with the natural isopatchoulenone. The oxidation product was reduced with LAH to afford the crystalline alcohol, identical with isopatchoulenol (VI, m.p. and mixed m.p. 140°). Oxidation of this crystalline alcohol with Jones reagent gave a ketone m.p. and mixed m.p. 48°; $[\alpha]_D$ + 38°, identical in all respects with the natural isopatchoulenone[1] (IA). In a later experiment, oxidation of cyperene with chromic acid in acetic acid gave isopatchoulenone in a better yield.

As our work was in progress, the Japanese group of workers[12] published in 1965 the isolation and characterisation of a ketone, cyperotundone (IB) from <u>Cyperus rotundus</u> (Japanese origin). Direct comparison[13] of isopatchoulenone and its 2:4 dinitrophenyl hydrozone with cyperotundone and its derivative established the identity of both the ketones. At the same time, Nigam[13] also reported the isolation and characterisation of a new ketone cyperenone (IA) from <u>Cyperus</u> <u>scariosus</u> (Indian origin). This ketone and its derivatives are also identical with isopatchoulenone. Thus isopatchoulenone, cyperotundone and cyperenone are the different names of the same compound (Isopatchoul-4en-3-one).

Table I gives a comparative data of physical and spectral properties of isopatchoulenone, cyperenone and cyperotundone.

The streochemistry of cyperotundone (isopatchoulenone) has been established by the Japanese workers[12]. The absolute configuration of patchouli alcohol was conclusively established as shown in structure[14,15] (V). Hikino et al assigned the β-configuration to the C-11 carbon bridge of isopatchoulenone (IA) as is present in patchouli alcohol (V). This was further confirmed by the fact that the monoketone (IX) obtained from the diketone (VIII) showed in ORD curves a positive cotton effect α = +66 in agreement with that expected for the postulated absolute configuration.



(VIII) (IX)

The $C_{10}$ methyl was shown to have the α-stereochemistry on the following considerations. In the molecule, due to anisotropy of the unsaturated system, α and β methyls on $C_{10}$ or $C_{11}$ cannot be equivalent and a β methyl is expected to be fairly deshielded while an α-methyl should be shielded. Experimentally the $C_{12}$ (i.e. β) and

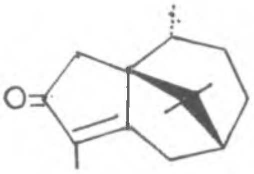
## TABLE I

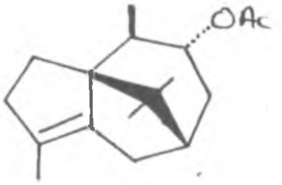
| Properties | Present observation[1] | Nigam[13] | Hikino et al[12] |
|---|---|---|---|
| Source | *Cyperus scariosus*<br>(Indian origin) | *Cyperus scariosus*<br>(Indian origin) | *Cyperus Rotundus*<br>(Japanese origin) |
| Name of compound | Isopatchoulenone | Cyperenone | Cyperotundone |
| M.P. or b.p. | 48° | b.p.136-8°/0.5 mm. | 46-47.5° |
| Optical rotation | + 39.9° | - | + 40.4° |
| Refractive index | - | 1.5130 | - |
| U.V. absorption | | | |
| $\lambda_{max}^{EtOH}$ | 243 mμ<br>$\log_e$ 3.9 | 245.5 mμ.<br>$\log_e$ 3.988 | 245 mμ.<br>$\log_e$ 3.96 |
| IR values | 1706 & 1663 $cm^{-1}$. | 1705 & 1665 $cm^{-1}$. | 1706 & 1667 $cm^{-1}$. |
| 2,4 dnp M.P. | 228° | 227.5° | 224-5° |
| U.V. absorption | | | |
| $\lambda_{max}^{EtOH}$ | 392 mμ.<br>$\log_e$ 4.39 | 390 mμ.<br>$\log_e$ 4.335 | 396 mμ.<br>$\log_e$ 4.76 |

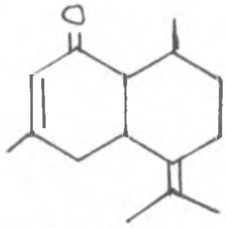
TABLE (Contd)

| Properties | | Present observation | Nigam[13] | Hikino et al[12] |
|---|---|---|---|---|
| NMR values in $\tau$ | | | | |
| $CH_3-CH<$ | d | 9.36 | 9.43 & 9.33 | 9.39 |
| $CH_3-C\overset{/}{\underset{\backslash}{-}}$ | s | 9.2 | 9.24 | 9.25 |
| $CH_3-C\overset{/}{\underset{\backslash}{-}}$ | s | 8.87 | 8.89 | 8.83 |
| $CH_3-\overset{\vert}{C}=C<$ | tri | 8.32 | 8.35, 8.33 & 8.31 | 8.33 |

$C_{13}$ (i.e. $\alpha$ ) methyl protons have their resonance positions at 8.83 and 9.25$\tau$ respectively whereas the $C_{15}$ methyl appears at 9.39$\tau$, the high field of the resonance indicates that it is in $\alpha$-configuration. Hence, the stereostructure for cyperotundone (Isopatchoulenone) is presented as (IB).


(IB)


(X)

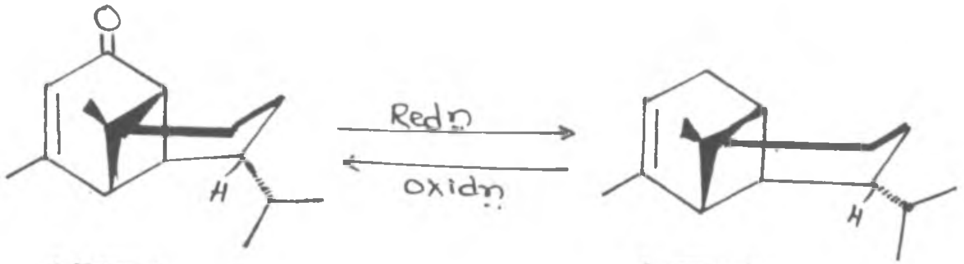

(XI)

In confirmation, the $C_{15}$ methyl protons in a $\beta$-configuration were found to be strongly deshielded occurring at 8.85 , in intermediate (X), prepared during synthesis of patchouli alcohol.

Isolation of an $\alpha$-$\beta$ unsaturated ketone $C_{15}H_{22}O$; 2,4 dnp m.p. 228-9° from the essential oil of *Cyperus scariosus* was reported earlier by Naves and Ardizio[16]. Pinder et al[17] reported the isolation of a ketone-articulone, whose 2,4 dnp (m.p. 231-232°) was identical with 2,4 dnp of the $\alpha$-$\beta$ unsaturated ketone reported by Naves and Ardizio. Pinder et al had assigned the structure XI to articulone, but recently the Japanese workers[19] and Nigam et al[13] have demonstrated that the $\alpha$-$\beta$ unsaturated ketone of Naves et al and Articulone of Pinder et al have the same structure as isopatchoulenone (I).

Hikino et al have also observed that catalytic hydrogenation of deoxocyperotundone gives two products. The major compound was identical with isopatchoulane (IVB) obtained from patchouli alcohol (V) (IR.NMR and retention time) and the minor product was identical with a stereoisomer of isopatchoulane (IVA) which has been obtained by Hikino et al by Wolff-Kishner reduction of dihydrocyprotundone (III).

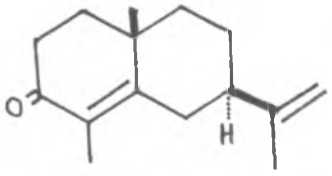
Unlike *Cyperus rotundus*. L species of Japanese and Chinese origin, Sukh Dev et al[2] described the isolation of a tricyclic $\alpha$-$\beta$ unsaturated ketone Mustakone (XII) from *Cyperus rotundus*. L of Indian origin and formulated its structure, based on spectral and photochemical studies and correlation with (-) copaene (XIII) as shown below.



(XII) (XIII)

## α-CYPERONE

The ketone II, (isolation Chapter I.) regenerated from semicarbazone (m.p. 216°) had the following properties: $C_{15}H_{22}O$, b.p.108° (bath)/1 mm. $[\alpha]_D^{28}$ + 120° (C,3.9); U.V.absorption at 244 mμ ($\log_e$ 4.2) has been identified as α-Cyperone (XIV).



( XIV )

The infrared spectrum showed bands at 1665 and 890 $cm^{-1}$ and indicated the presence of a six membered ring ketone and unsymmetrically disubstituted double bond.

The physico-chemical constants of ketone II were found to be identical with that of bicyclic α-β unsaturated ketone, α-Cyperone[44] (XIV) isolated by Hegde and Rao[20] which is the main constituent of Cyperus rotundus oil (Indian origin). The structural formula of Cyperone (XIV), a sesquiterpene ketone was first suggested by Bradfield[21] and Simonsen[22]. Synthesis of α-β Cyperones[23-26] have been achieved and many inter conversions[27-31] in this series have also been described. The identity of ketone II with α-Cyperone was confirmed by the direct comparison of IR spectrum, Gas liquid chromatogram and m.p. and mixed m.p.216° of the semicarbazone with an authentic sample of α-Cyperone* obtained from Cyperus rotundus (Indian origin).

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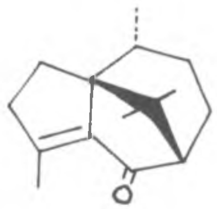
*A sample of α-Cyperone was kindly supplied by Dr.Sukh Dev.

## PATCHOULENONE

Ketone III, $C_{15}H_{22}O$; m.p. 53°; $[\alpha]_D^{28}$ - 96.3° (C. 2.86), molecular weight 218 (mass spec.); was isolated from the benzene eluate by the procedure described in Chapter I, and identified as Patchoulenone (II B).



(IIB)

IR spectrum (Fig.6) showed two absorption bands of equal intensity at 1664 and 1712 $cm^{-1}$, but was devoid of any characteristic frequency for the double bond in the region 700-900 $cm^{-1}$. It displayed U.V.maxima at 264 mμ ( 9,000) characteristic of a highly strained[45,46,39] α-β unsaturated carbonyl system.

IR data 1664 and 1712 $cm^{-1}$ along with the U.V. absorption maxima suggested the location of a carbonyl group on a five membered ring in conjugation with a tetrasubstituted double bond. The ketone III failed to give any carbonyl derivative (2,4 dnp or semicarbazone).

NMR spectrum (Fig.7) showed absence of vinyl protons, but exhibited two singlets at 9.0 and 9.1 τ (tertiary methyls), a doublet at 9.15 τ (J = 6 cps) and a broad signal at 7.90 τ assignable to a β-methyl group of an α-β unsaturated ketone.

A comparison of the spectral data and physical constants showed that ketone III was identical with

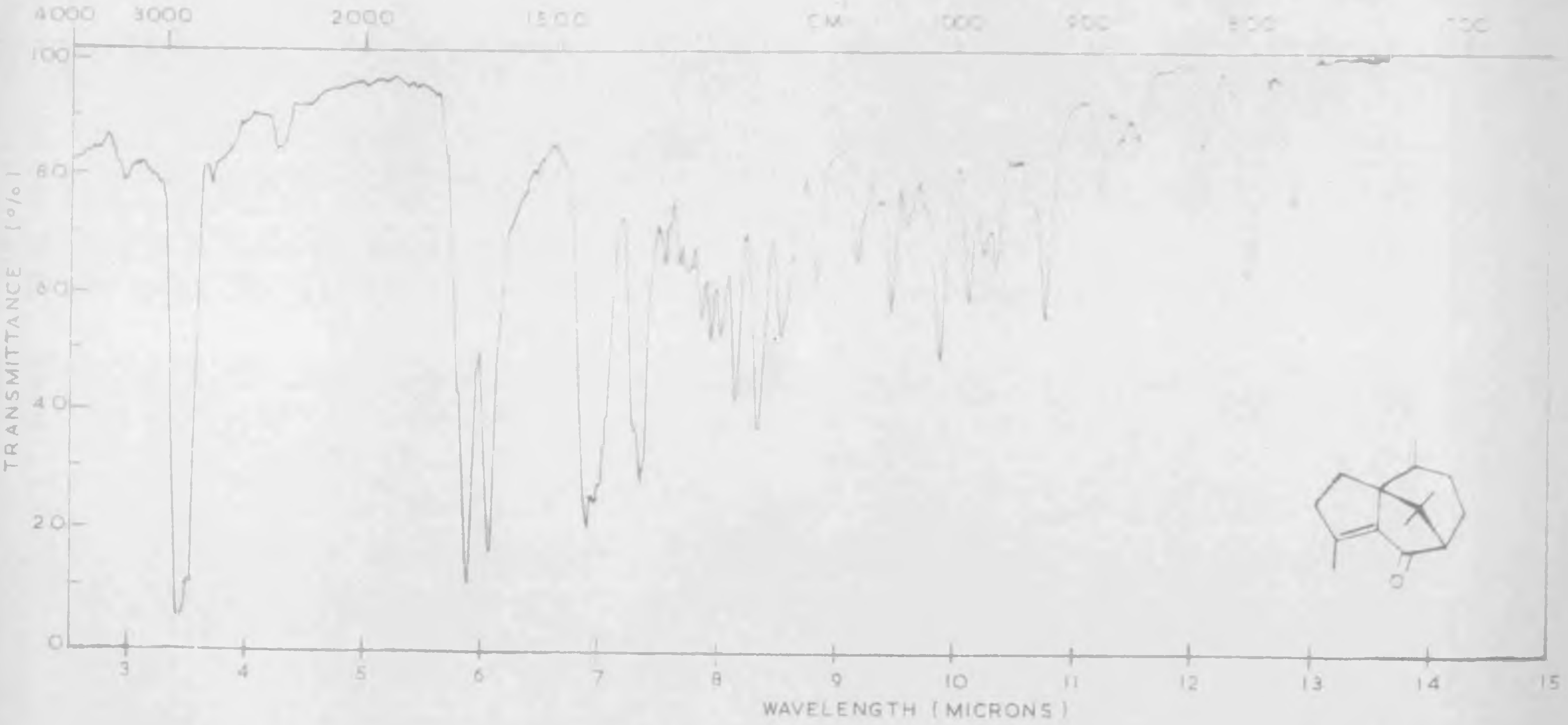


FIG 6 IR SPECTRUM OF KETONE - III ( PATCHOUL-ENONE ) (NUJOL)

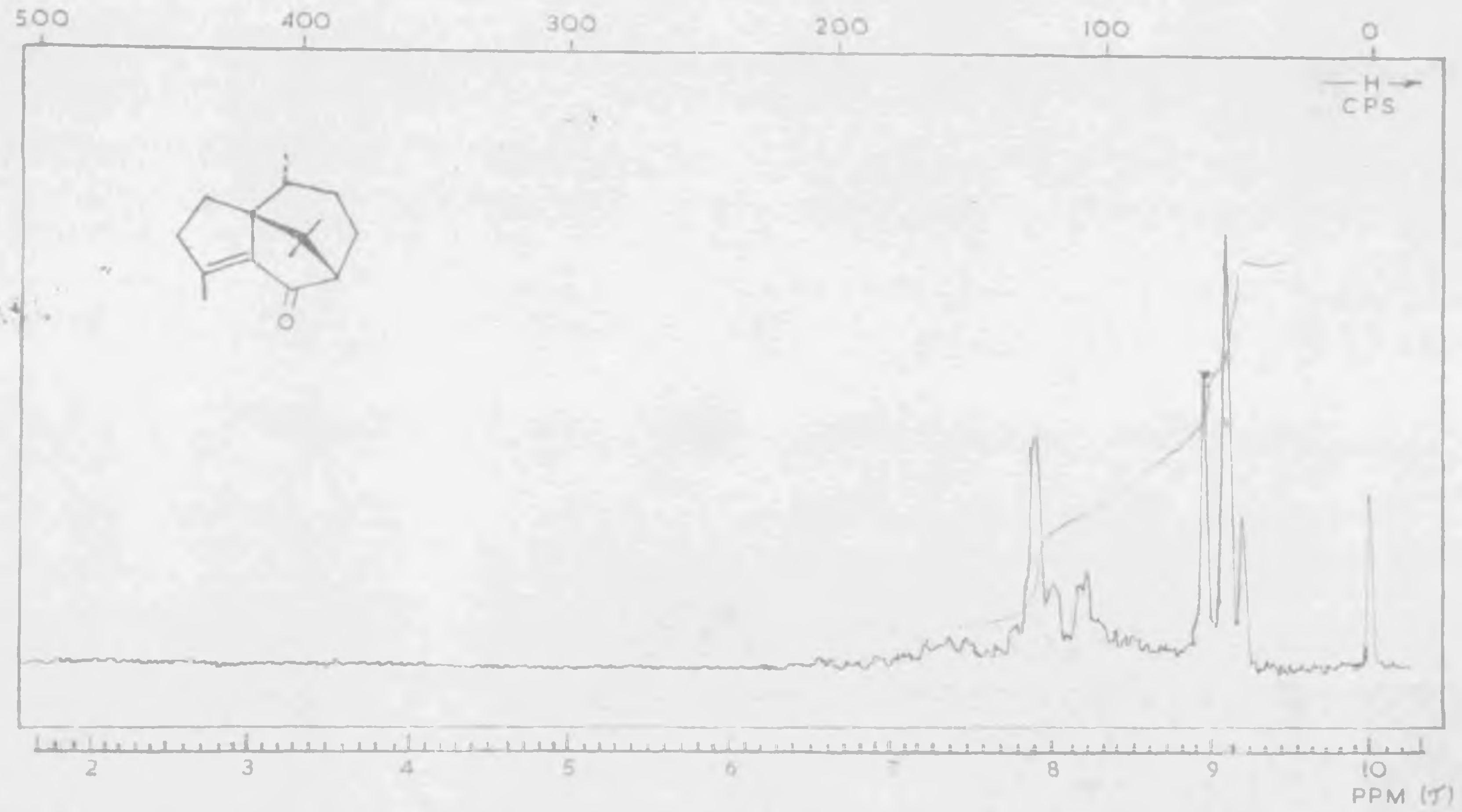
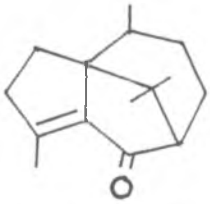


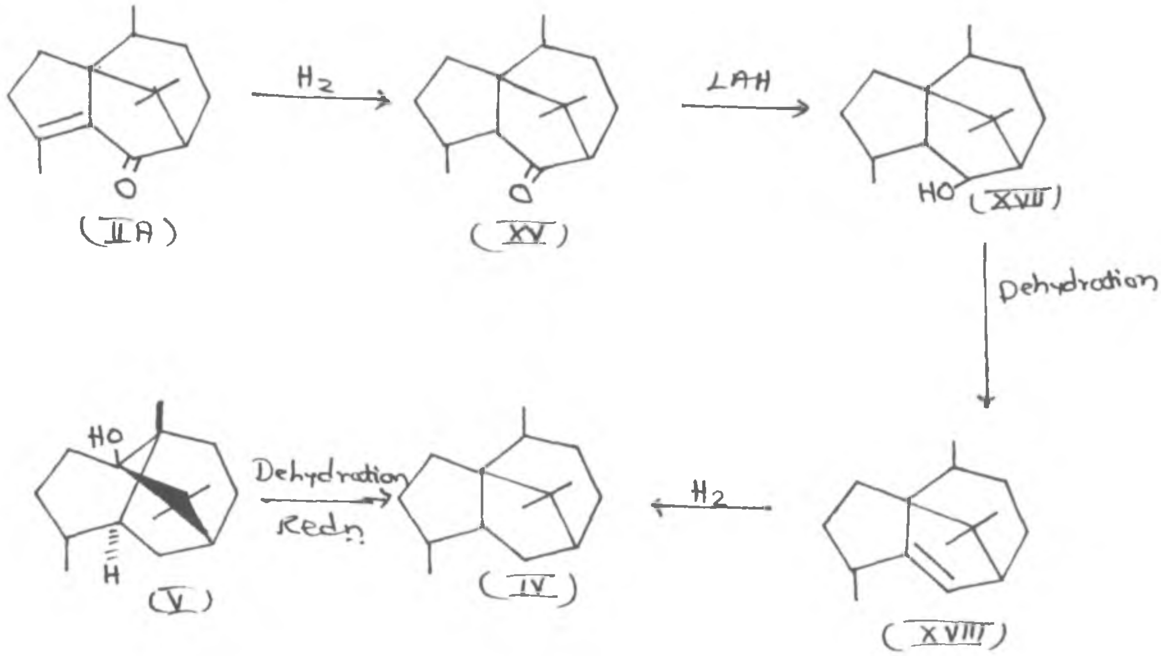
FIG. 7. NMR SPECTRUM OF KETONE - III (PATCHOULENONE)

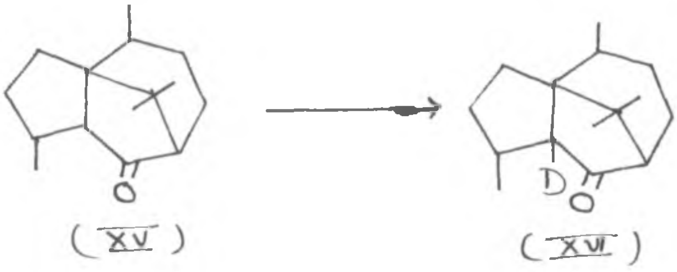
Patchoulenone[6] (IIA), a tricyclic $\alpha$-$\beta$ unsaturated ketone isolated by Sorm et al from Cyperus rotundus of Chinese origin. The structure of Patchoulenone (IIA) has been established by Sorm et al and it is based mostly on comparison of the skeletons of isomerised patchouli alcohol (V).

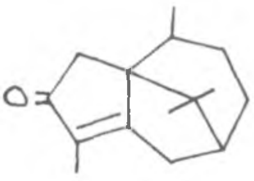

(IIA)

Patchoulenone (IIA) has got $\alpha$-$\beta$ unsaturated chromophore $\lambda_{max}$ 264 m$\mu$, log$_e$ 3.955). The IR spectrum showed two bands of equal intensity at 1663 and 1713 cm$^{-1}$, attributable to a cisoid chromophore. The absence of any olefinic protons in the NMR spectrum established that a double bond was tetrasubstituted. Further, NMR spectrum showed two quarternary methyls (9.0 and 9.1$\tau$, singlets), one secondary methyl (9.15$\tau$, J = 6 cps) and one allylic methyl (7.9$\tau$). As the dihydrocompound showed band at: 1735 cm$^{-1}$ in the infrared spectrum, the carbonyl group must be in a five membered ring.

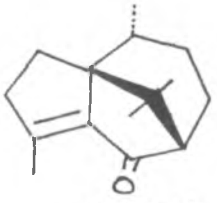
This ketone (IIA) could be converted (Scheme I) to a tricyclic saturated hydrocarbon (IV), identical with the isopatchoulane (IV) obtained by reduction of the dehydration product of patchouli alcohol (V). This leads to structure (IIA) for patchoulenone. The alternate structure (I), which does not contain the cisoid arrangement could be ruled out by deuterium exchange on the dihydro compound (XV) in which only one hydrogen (and not three) was substituted (XVI). Recently Hikino et al[12] assigned stereo formula for







(I)

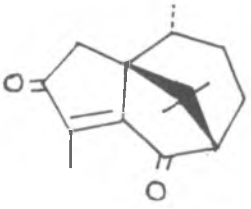


(II B)

Patchoulenone (IIB) along with Cyperene and Cyperotundone (isopatchoulenone) (I).

## SCARIODIONE

From the carbonyl fraction, a leavorotatory crystalline ketone IV, scariodione, $C_{15}H_{20}O_2$; molecular weight 232 (mass spec.); m.p. 45°; $[\alpha]_D^{26}$ - 107.5°; U.V. absorption $\lambda_{max}$ 267 m$\mu$, ($\epsilon$,7,900), has been isolated in pure state (GLC and TLC) and characterised as a new sesquiterpene dione, Scariodione (XIX). The infrared spectrum (Fig.8) showed absorption bands at: 1709 ($>C{=}O$), 1667 ($>C{=}C<$), 1412 ( $-\overset{O}{\overset{\|}{C}}-CH_2-$ ), 1389 and 1376 ( $\begin{matrix}CH_3\\ \diagup\\ C\\ \diagdown\\ CH_3\end{matrix}$ ) $cm^{-1}$. The intensity of carbonyl absorption suggested the presence of two such groupings in the scariodione.



( XIX )

The NMR spectrum (Fig.9) of scariodione displayed a doublet at 9.32 $\tau$ (J = 6 cps) assignable to secondary methyl group and singlet at 9.12 and 8.83 $\tau$ ascribable to two quarternary methyls and singlet at 8.00 $\tau$ for vinyl methyl being $\beta$- to an $\alpha$-$\beta$ unsaturated carbonyl function, thus presence of tetrasubstituted double bond was also confirmed. A signal at 7.77 $\tau$ could be assigned to methylene group adjacent to the carbonyl function, as this signal appeared as a sharp singlet, it indicated that adjacent carbon is fully substituted.

Thus scariodione $C_{15}H_{20}O_2$, is tricyclic with tetrasubstituted double bond.

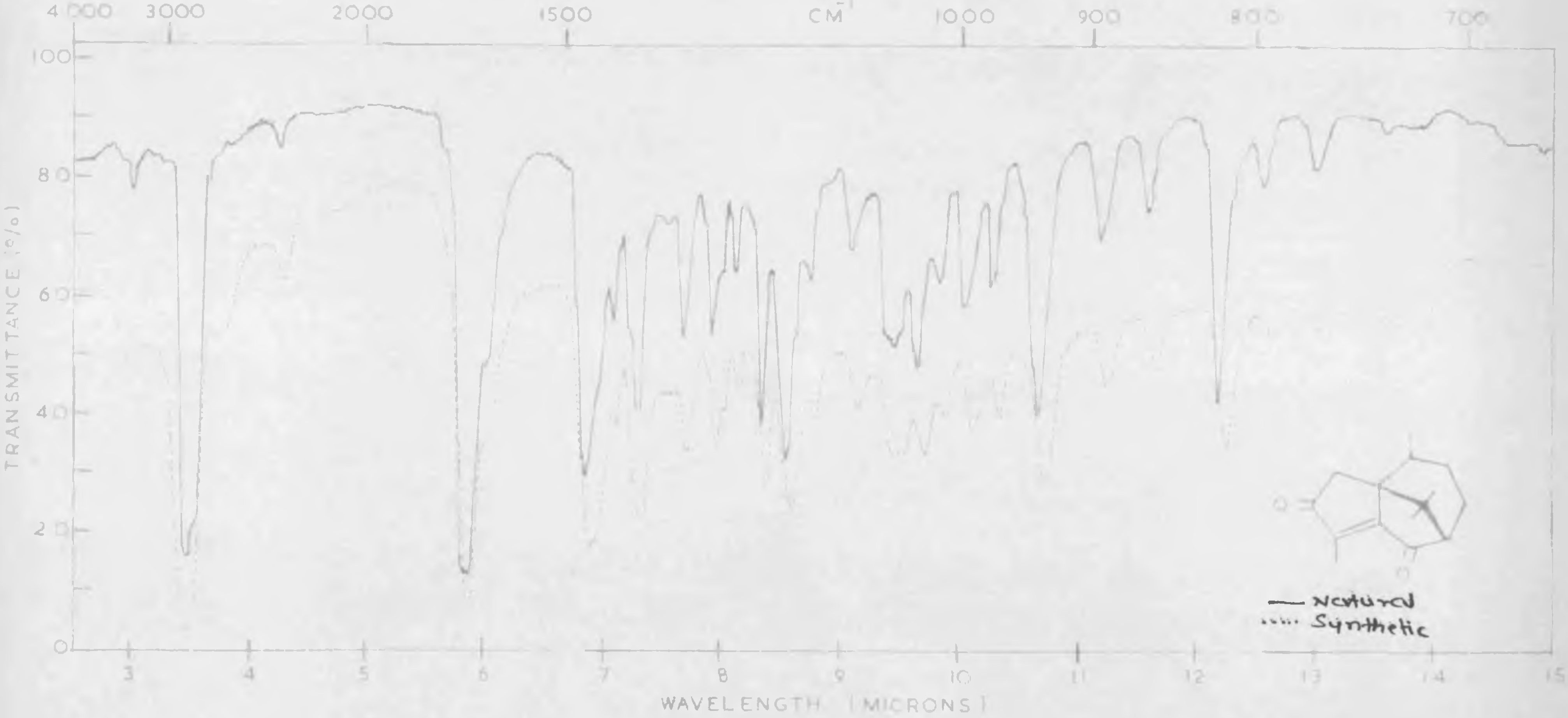


FIG 8 IR SPECTRUM OF KETONE-IV (SCARIODIONE) (NUJOL)

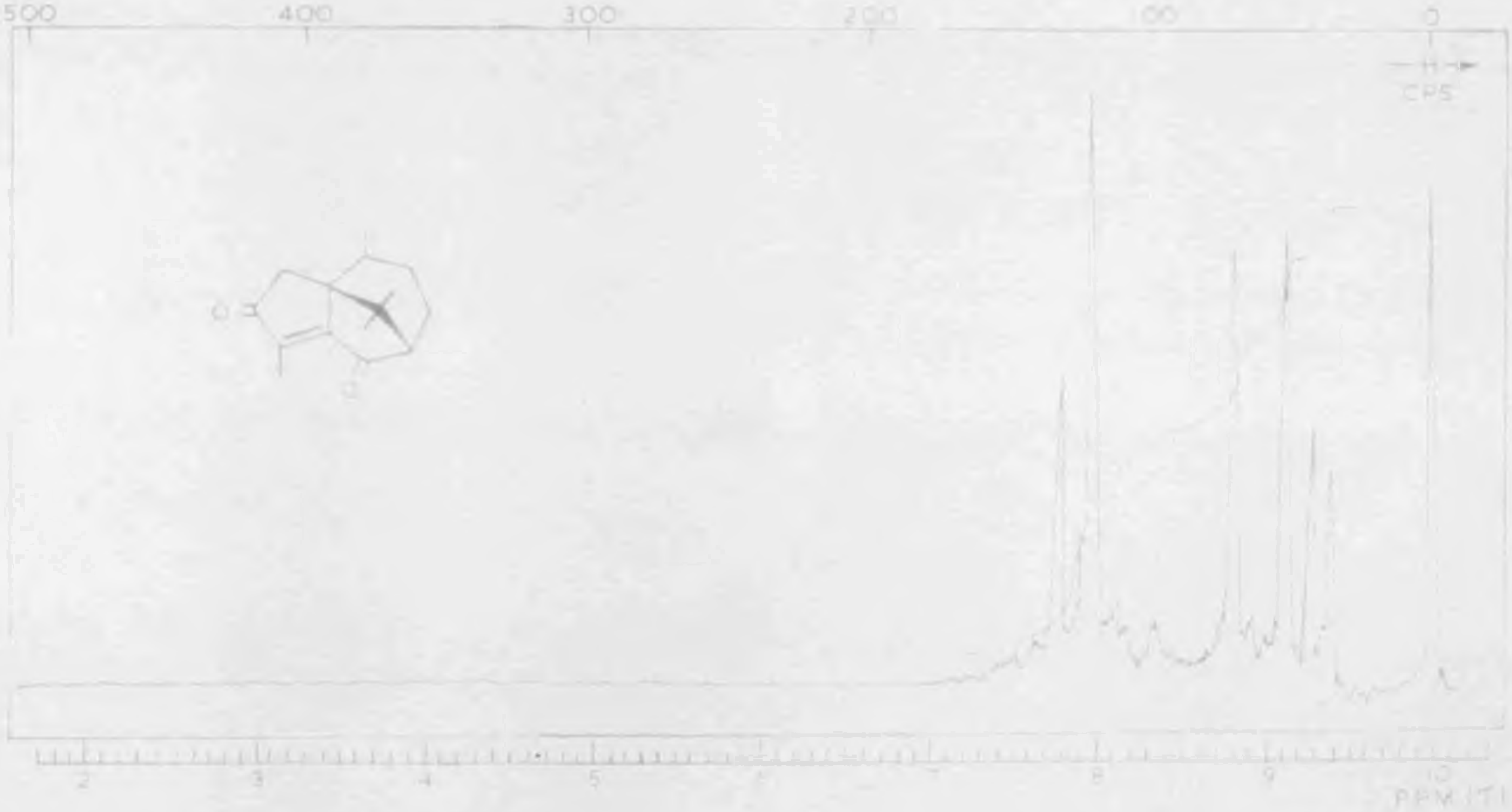
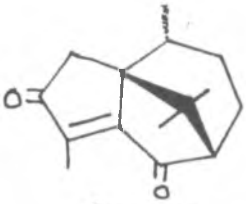
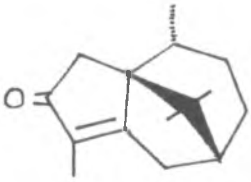
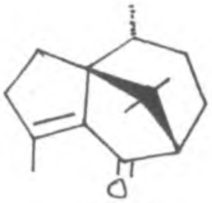


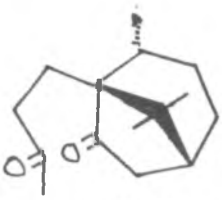
FIG 9 NMR SPECTRUM OF KETONE - IV (SCARIODIONE)

Tricyclic ketones Isopatchoulenone (I) (Cyperotundone, Cyperenone), Patchoulenone (II) and diketone (VIII) obtained from ozonolysis of tricyclic hydrocarbon cyperene.


(XIX)


(I)


(II)


(VIII)

showed the similar range of spectral properties with Scariodione (XIX) as follows:

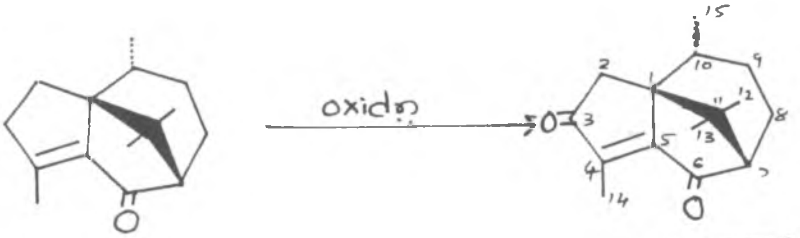
TABLE

| Properties | Present observation | Isopatchoulenone | Patchoulenone | Diketone (VIII) |
|---|---|---|---|---|
| Mol formula | $C_{15}H_{20}O_2$ | $C_{15}H_{22}O$ | $C_{15}H_{22}O$ | $C_{15}H_{24}O_2$ |
| U.V. $\lambda_{max}^{EtoH}$ | 267 mμ | 243~5mμ | 264 mμ | - |
| IR in $cm^{-1}$ | 1709 | 1705~6 | 1712~3 | 1724~35 |
| | 1667 | 1663~7 | 1663~4 | - |
| | 1412 | 1412~8 | - | 1412~5 |
| NMR in $\tau$ | | | | |
| $CH_3-CH<$ | 9.34 | 9.36~9.39 | 9.1 | 9.28 |
| $CH_3-C<$ | 9.12 | 9.2 ~9.25 | 9.0 | 9.06 |
| $CH_3-C<$ | 8.83 | 8.83~8.87 | 9.15 | 8.83 ~8.84 |
| $CH_3-C=C<$ | 8.00 | 8.31~8.33 | 7.9 | - |
| $CH_2-C=O$ | 7.77 | 8.03 | - | 8.08 |

These findings in conjugation with biogenetic considerations clearly suggested structure (XIX) for this enedione. All the spectral and physical properties are consistent with the proposed structure XIX for Isopatchoul-4en-3,6 dione.

## CONVERSION OF PATCHOULENONE TO SCARIODIONE

On oxidation with chromium trioxide in acetic acid patchoulenone (II) of known stereoformula afforded in good yield an enedione, m.p.45°; $[\alpha]_D^{28}$- 105.83°; direct comparison with the natural product established their identity.

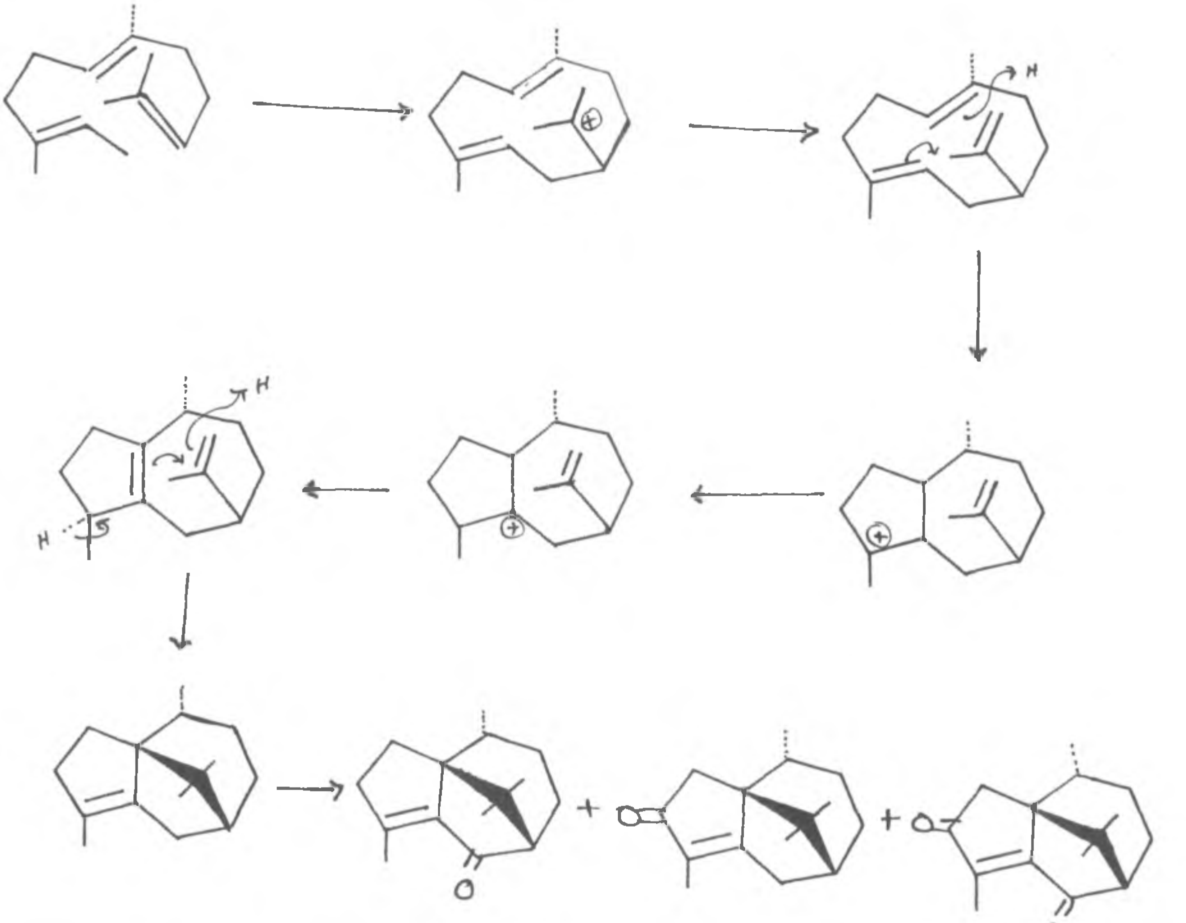


(II) (XIX)

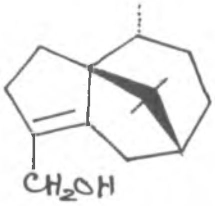
Scariodione should therefore be represented by the stereostructure (XIX).

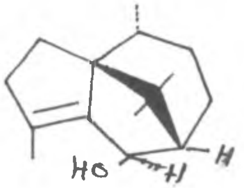
## BIOGENESIS OF ISOPATCHOULANE COMPOUNDS

Recently Parker[32] et al gave a biogenetical relation to this new group of compounds Isopatchoulane, which can be formed by nucleophilic attack of the double bond on the cation derived from epiguaiol. The revised structure of Patchouli alcohol (V) is explained in terms of Wagner-Meerwein migration with concomitant solvent attack in a cation readily derivable from bulnesol.

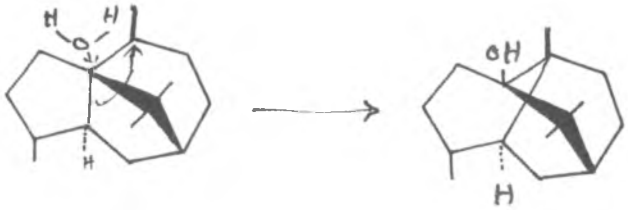


Cyperene Patchoulenone Isopatchoulenone Scariodione





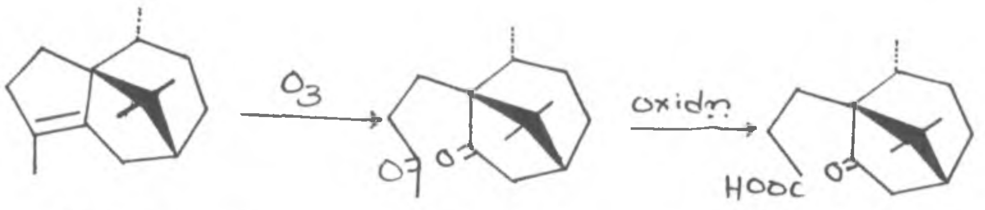
Cyperenol Patchoulenol



Patchouli alcohol

## SOME DEGRADATION PRODUCTS OF CYPERENE (VII) AND ISOPATCHOULENONE (I)

Ozonolysis of Cyperene $C_{15}H_{24}$ (VII) gave a crystalline diketone (VIII) $C_{15}H_{24}O_2$, m.p. 78°; its infra-red spectrum (Fig. 10) indicated the presence of a five membered ring ketone (1724 $cm^{-1}$) and methyl ketone group (1412 and 1360 $cm^{-1}$). The NMR spectrum (Fig.11) clearly revealed a three proton singlet at 7.95 $\tau$ assignable to a methyl of the $-CO-CH_3$ group. It also showed two singlets at 8.83 and 9.06 $\tau$ and a doublet centred at 9.28 $\tau$ (J = 6 cps) attributable to the two quarternary methyls and one secondary methyl. It is significant to note that the removal of the double bond resulted in shielding of the secondary methyl by 0.08 $\tau$, whereas one of the methyl groups has been considerably deshielded by 0.42 $\tau$. It also shows the presence of methylene group $\alpha$-to the ketone as a triplet centred at 7.85 $\tau$ (J = 6 cps). This triplet can be assigned to the methylene group $\alpha$-to the methyl ketone function. A prominent signal at 8.06 $\tau$ can be assigned to a methylene group $\alpha$-to the ring ketone.



(VII) (VIII) (XX)

The diketone (VIII) was subjected to oxidation

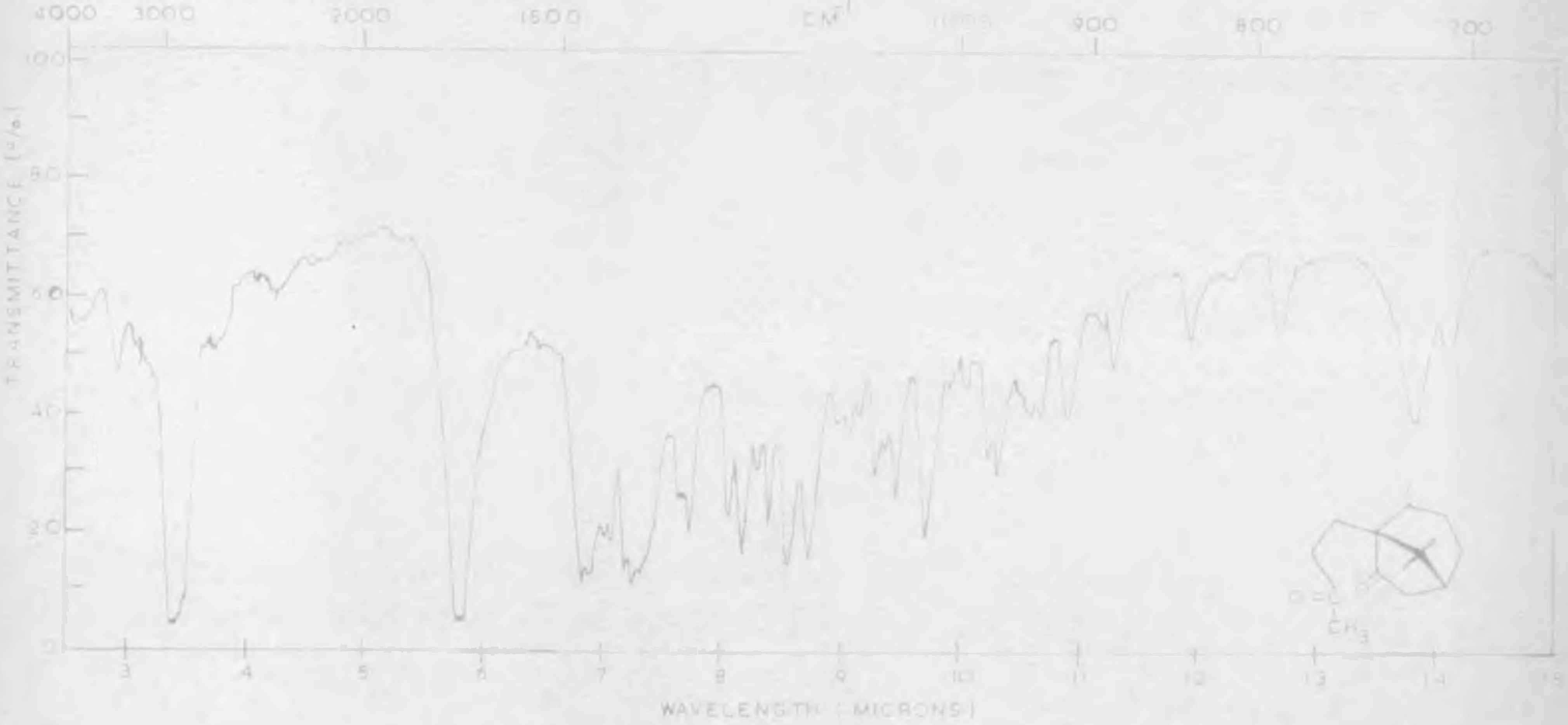


FIG **10** IR SPECTRUM OF DIKETONE (NUJOL)

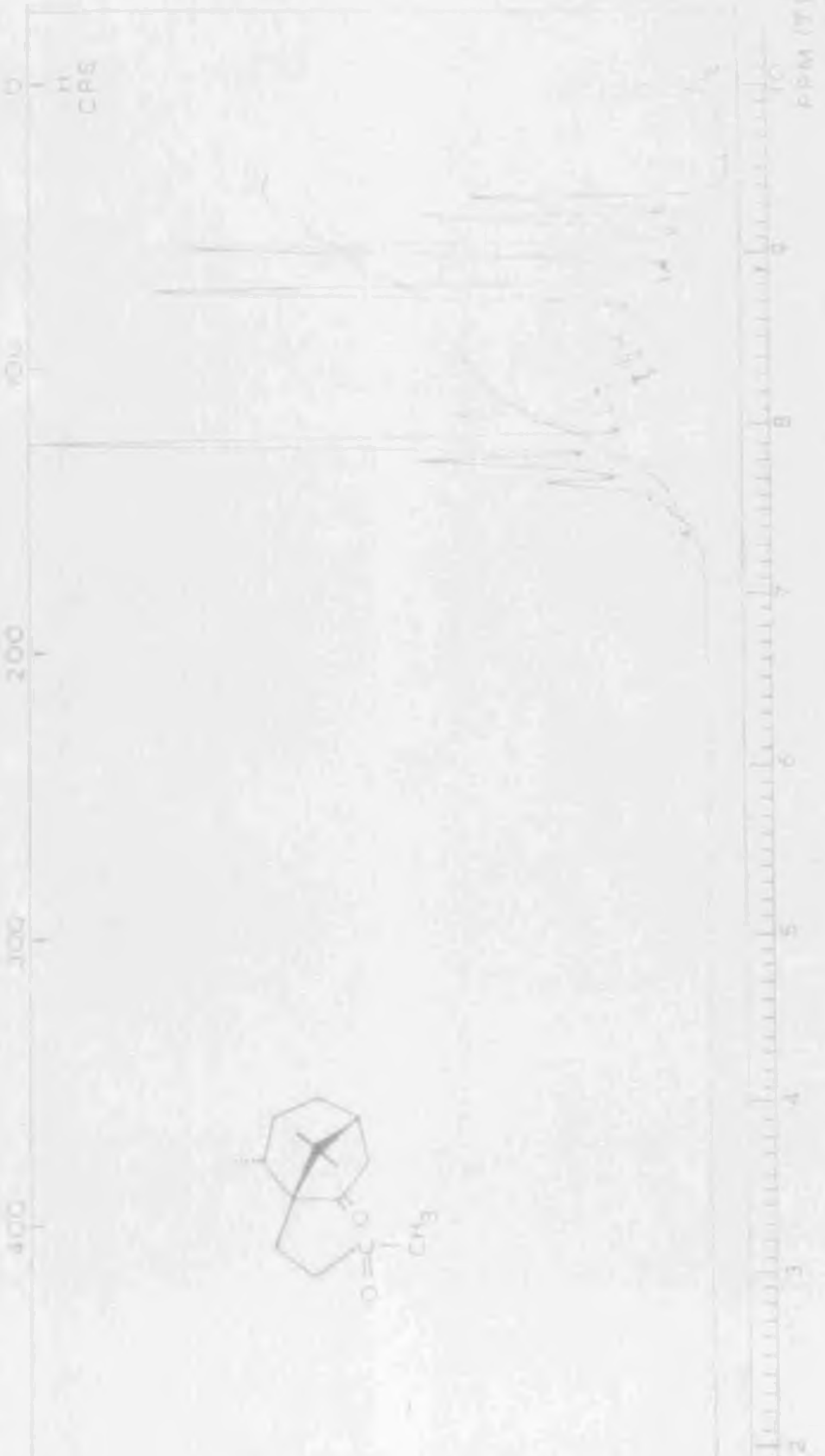
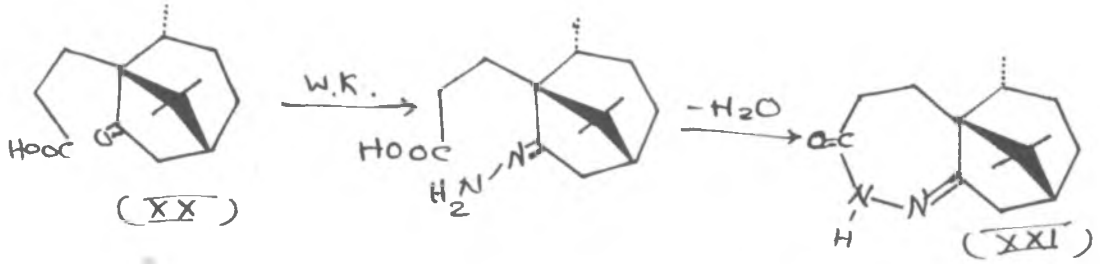


FIG 11 NMR SPECTRUM OF DIKETONE

with chromium trioxide[40,41] in acetic acid. The product $C_{14}H_{22}O_3$(XX), m.p. 177°, was shown by IR (Fig.12) spectrum to contain a five membered ring ketone (1730 $cm^{-1}$.) and an acid function (1709, 2630 and 925 $cm^{-1}$.). The NMR spectrum (Fig.13) of methylester indicated the presence of methyl doublet at 9.19 $\tau$ (J = 7 cps) and two methyl singlets at 9.04 and 8.9 $\tau$. The carbomethoxy methyl was seen as a singlet at 6.4 $\tau$.

Wolff-Kishner reduction of the keto acid, $C_{14}H_{22}O_3$ (XX), gave a product, $C_{14}H_{22}ON_2$ (XXI) m.p. 203-204°, whose IR spectrum (Fig. 14) indicated the absence of any acid function as well as five membered ketone, the only carbonyl absorption appeared at 1675 $cm^{-1}$ ($\rangle$C=O of -CO-NH-& $\rangle$C=N-),



and the characteristic band at: 3175 $cm^{-1}$ (-NH)[33,34] suggested that the cyclisation of the hydrazone occurred to yield a seven membered nitrogen derivative (XXI), such cyclisations have been reported[35,36] to occur during Wolff-Kishner reduction of $\delta$ and $\gamma$ keto acids.

The NMR spectrum (Fig. 15) of the compound showed two methyl singlets at 9.07 and 8.97 $\tau$. The methyl doublet centred at 9.1 $\tau$ (J = 6 cps) could be assigned to secondary

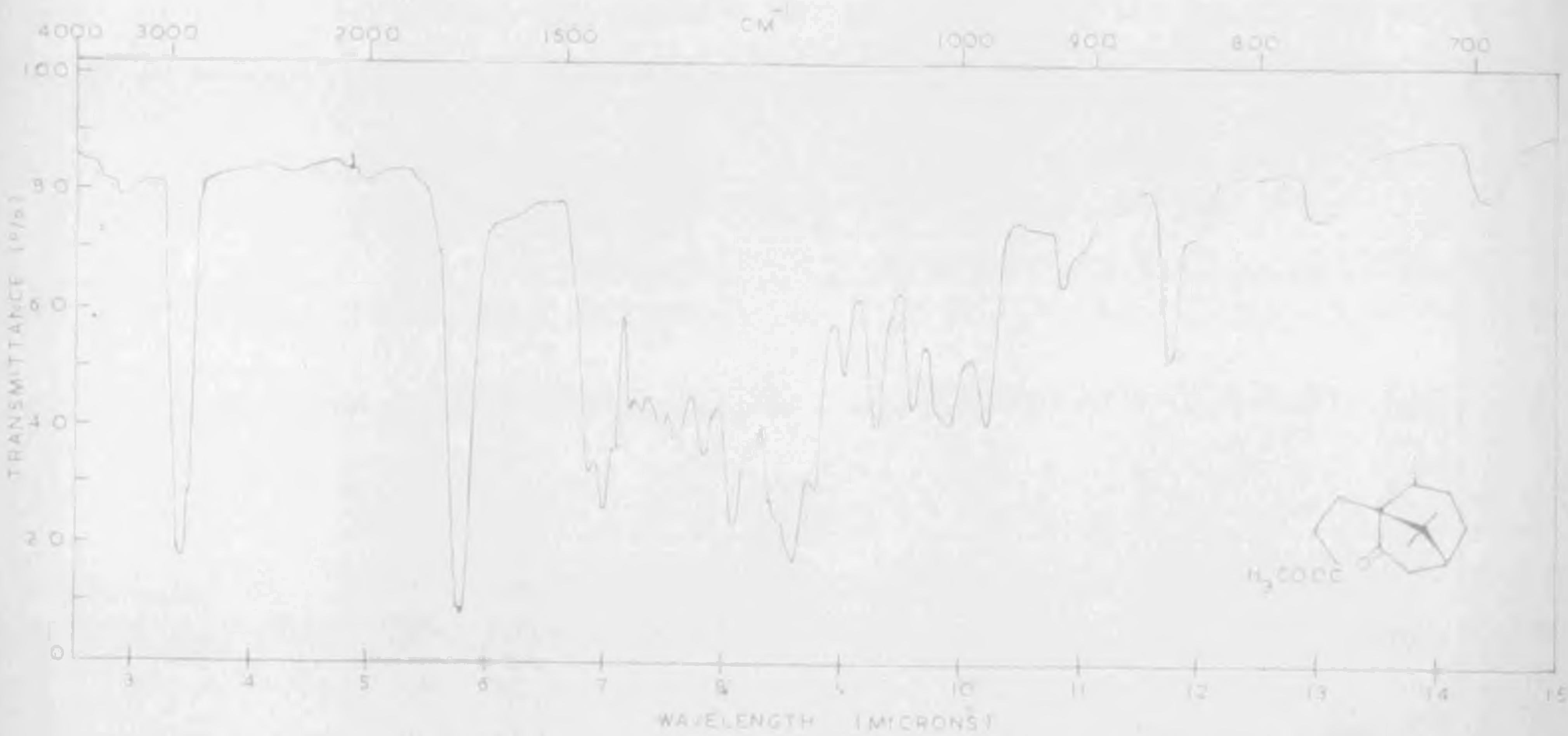


FIG **12** IR SPECTRUM OF METHYL ESTER OF C14 KETO ACID (NUJOL)

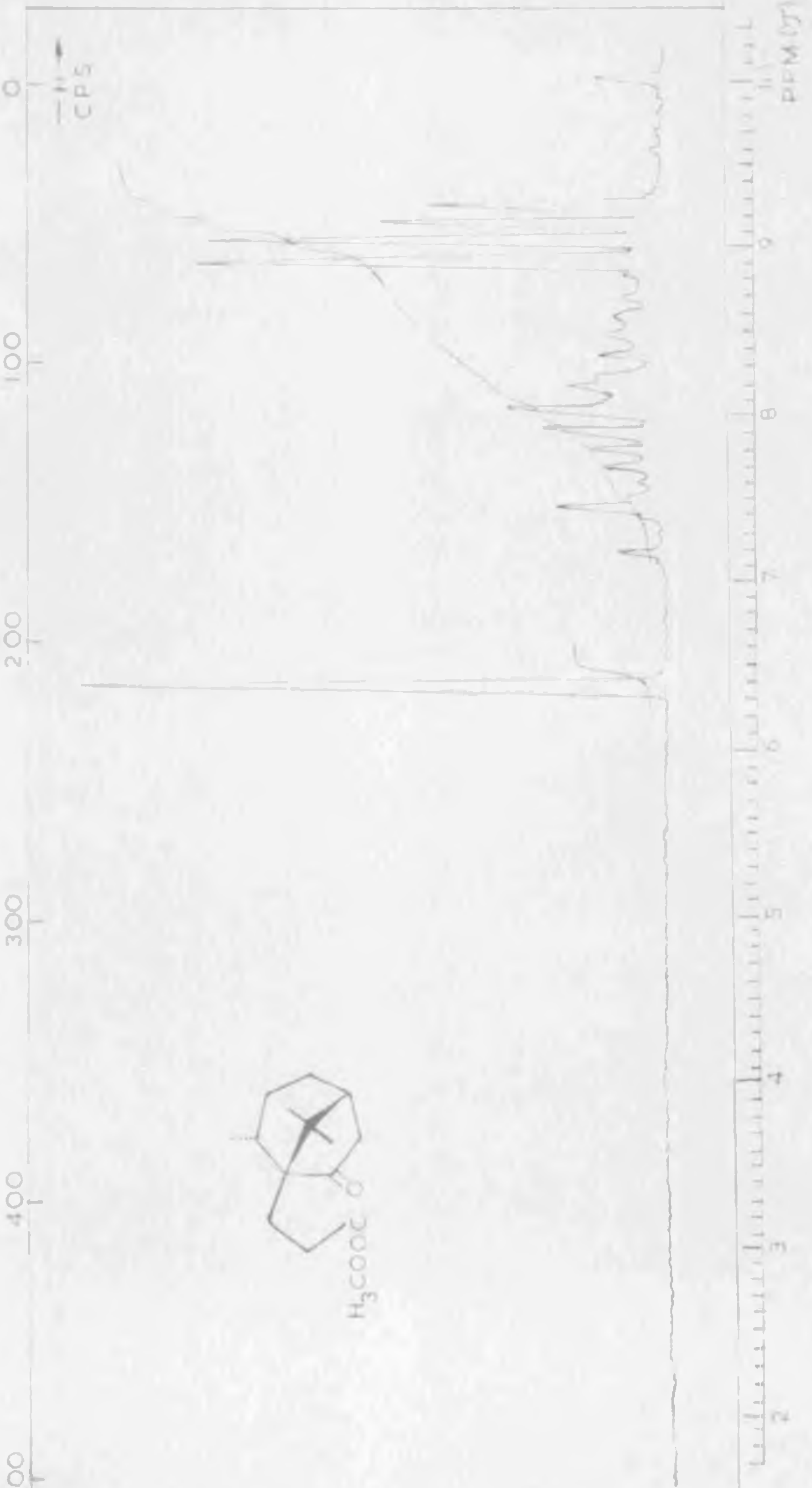


FIG. 13 NMR SPECTRUM OF METHYL ESTER OF $C_{14}$KETOACID

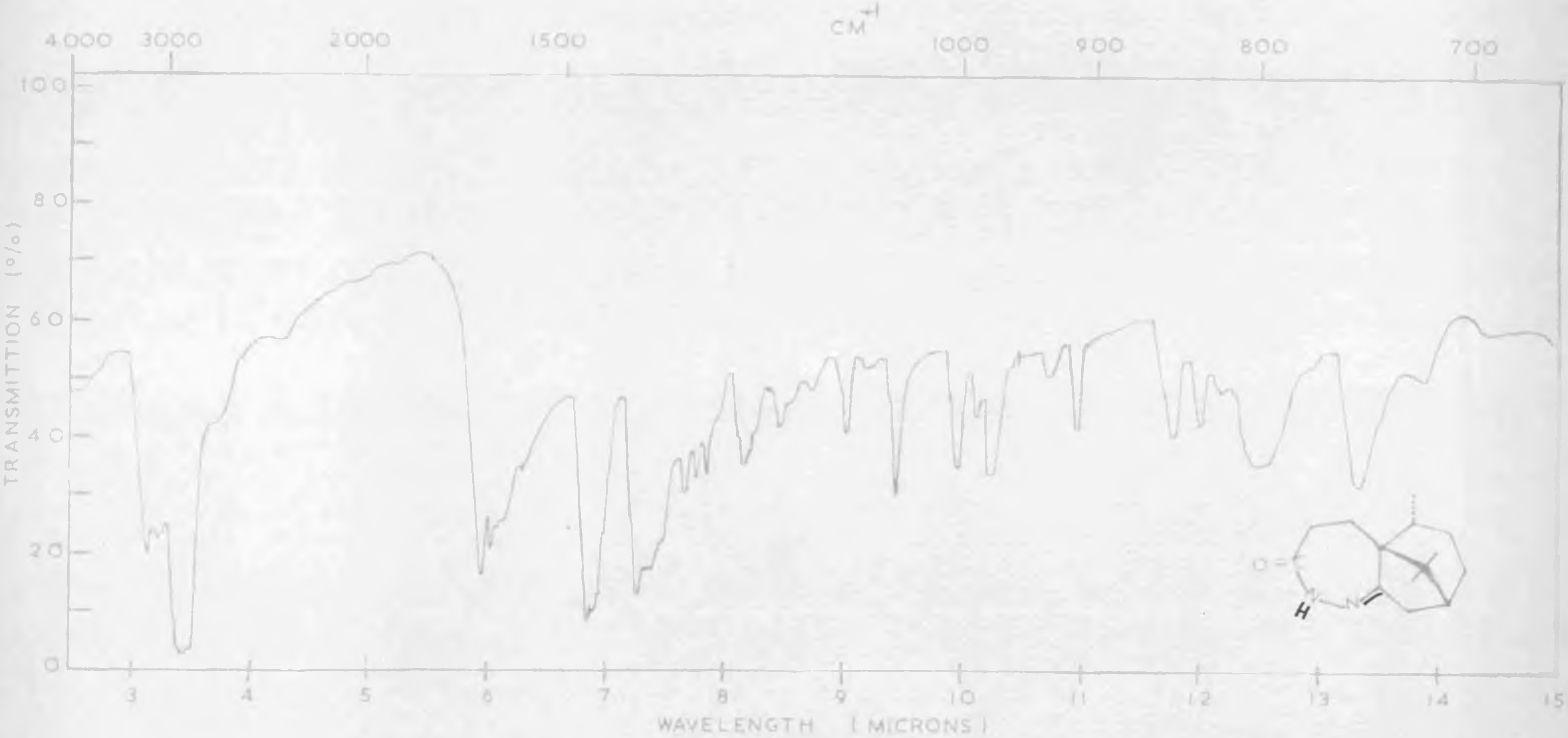


FIG 14 IR SPECTRUM OF CYCLISED PRODUCT (NUJOL)

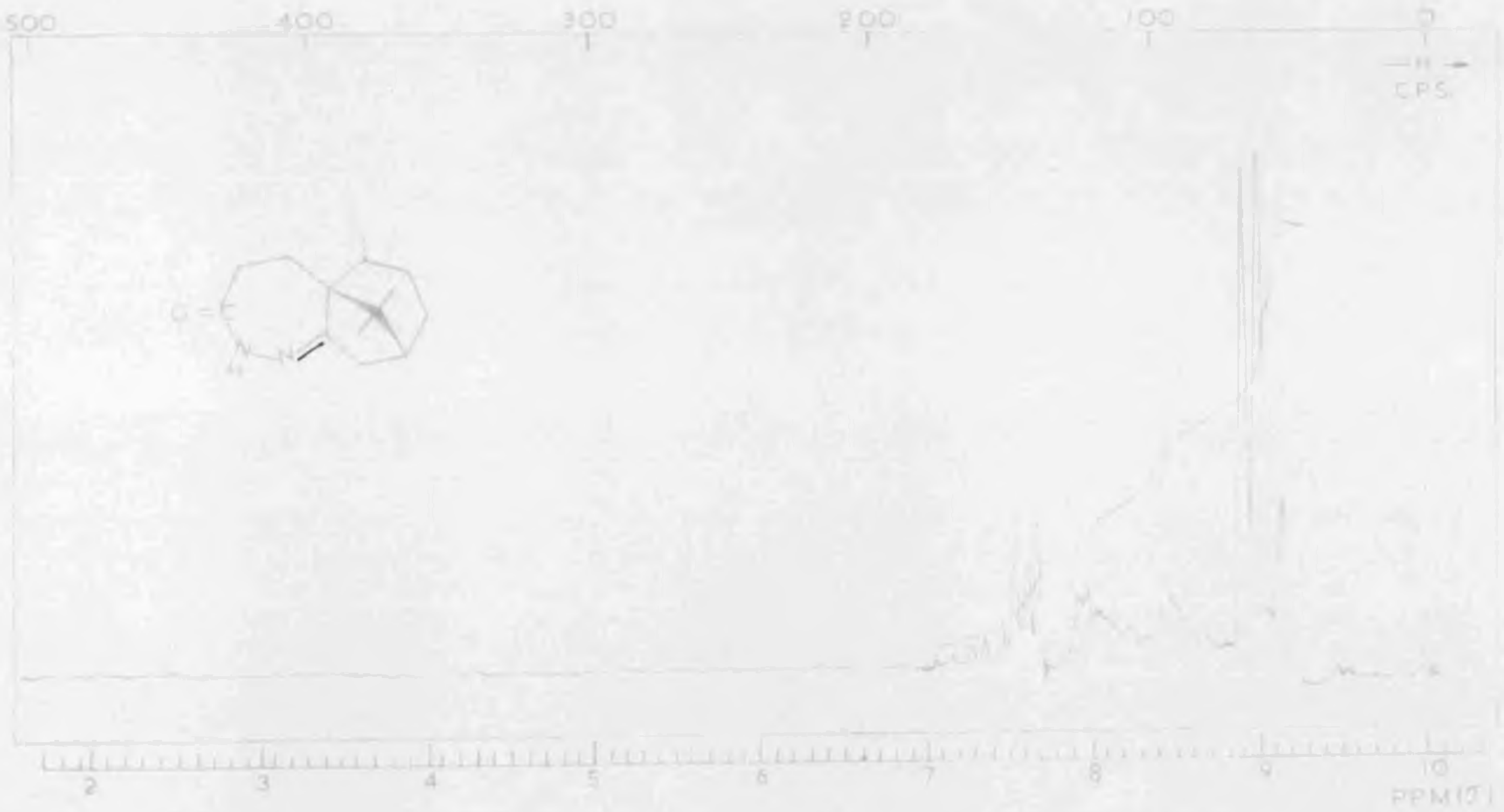
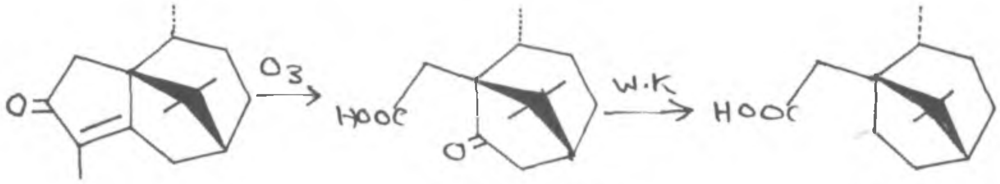


FIG 15 NMR SPECTRUM OF CYCLISED PRODUCT

methyl group. The spectrum showed no absorption below 7.2$\tau$.

Ozonolysis of isopatchoulenone $C_{15}H_{22}O$ (I) furnished a keto acid $C_{13}H_{20}O_3$ (XXII). The methylester of this acid exhibited IR bands (Fig.16) at 1739, and 1724 $cm^{-1}$ (five membered ring ketone and ester).



(I) (XXII) (XXIII)

NMR spectrum (Fig. 17) of the methylester (XXII) showed the presence of only three methyls. The methyl doublet appeared at 9.06$\tau$. The gem dimethyls appeared as widely seperated singlets at 9.05 and 8.73$\tau$. The only lowfield signal was 3 proton singlet at 6.37$\tau$ assignable to carbomethoxy function. These spectral data together with the mode of formation was consistent with structure (XXII).

Wolff-Kishner reduction of this keto acid (XXII), afforded a product XXIII whose methylester $C_{14}H_{24}O_2$, in its IR spectrum (Fig. 18) revealed the presence of only a single carbonyl frequency at 1733 $cm^{-1}$.

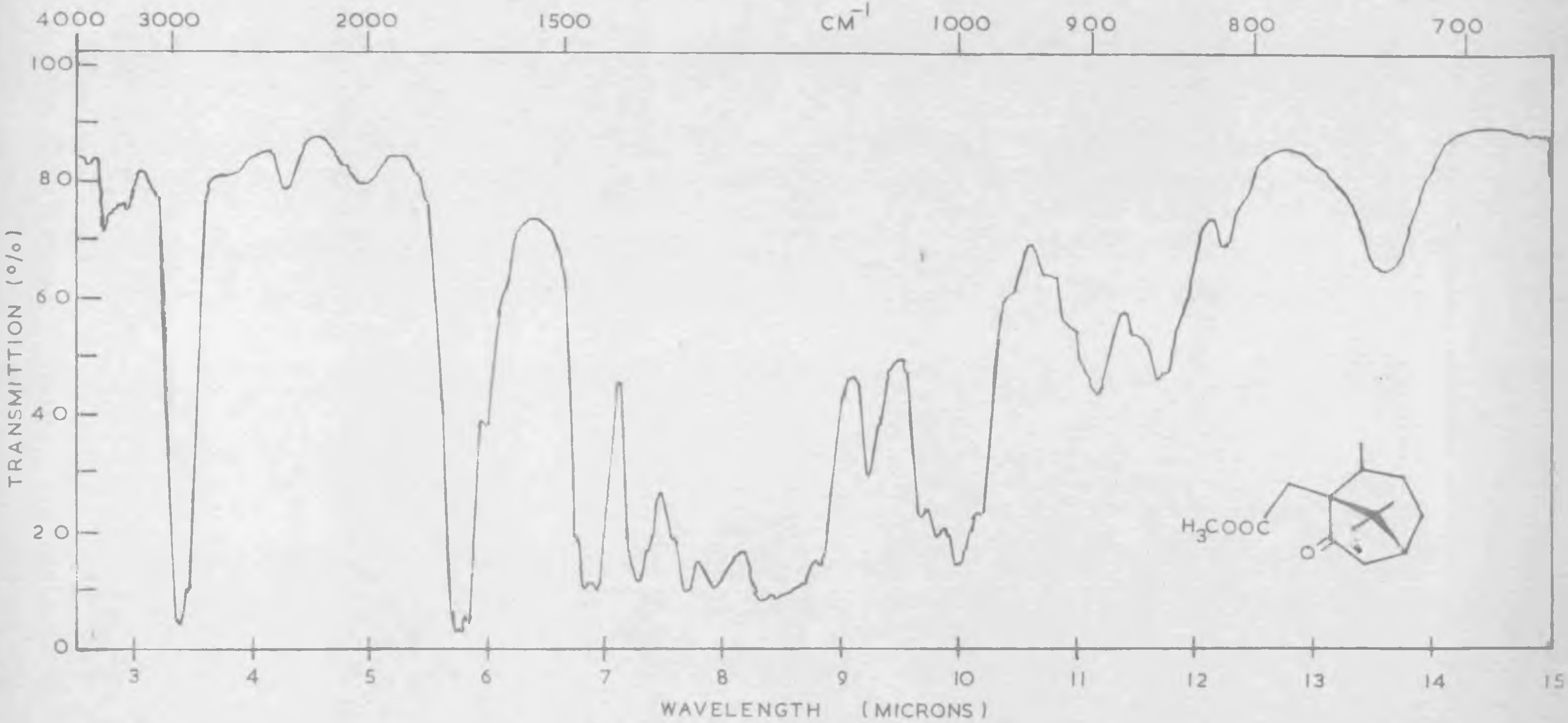


FIG. 16. IR SPECTRUM OF METHYL ESTER OF $C_{13}$ KETOACID
(LIQUID FILM)

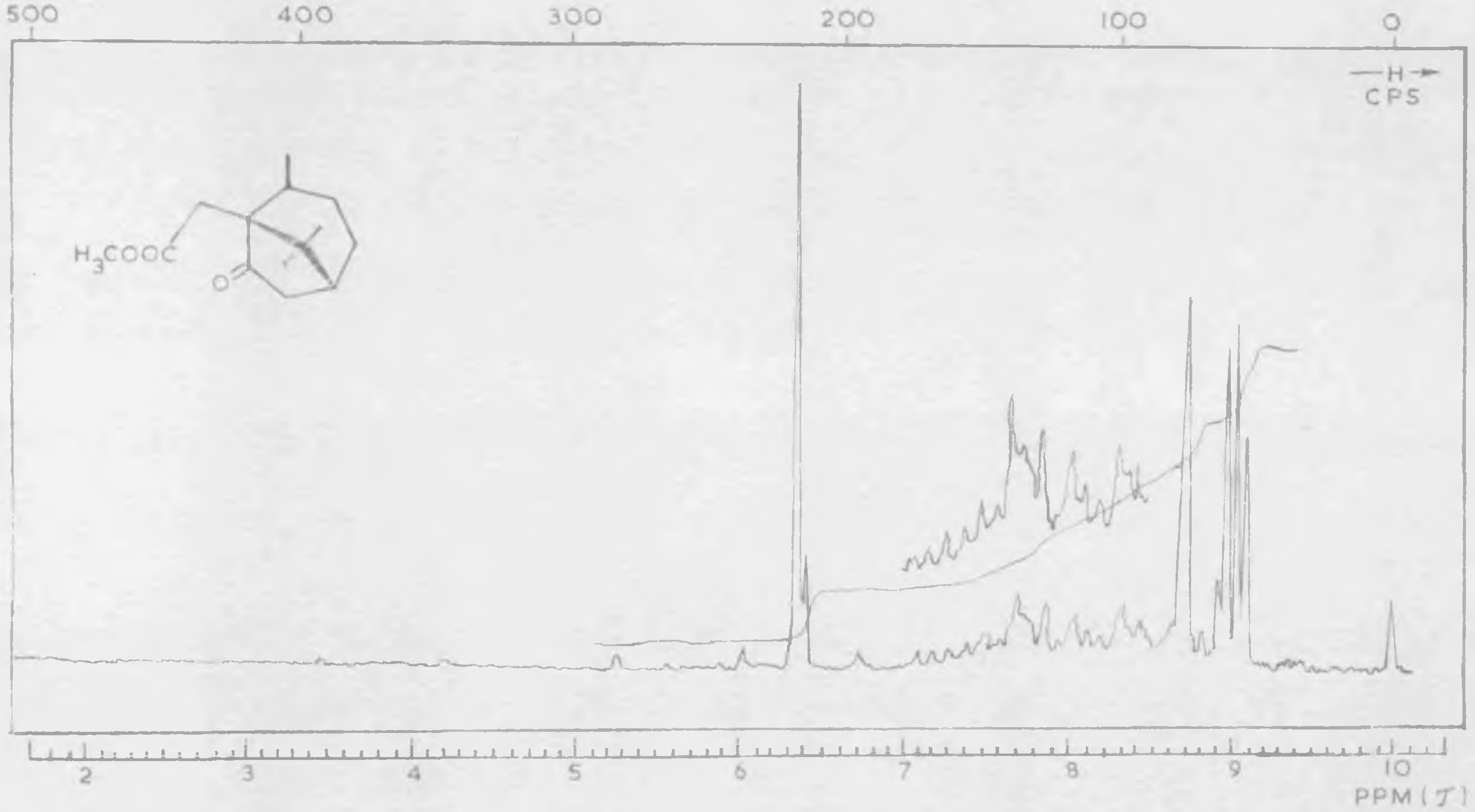


FIG 17 NMR SPECTRUM OF METHYL ESTER OF $C_{13}$ KETO-ACID

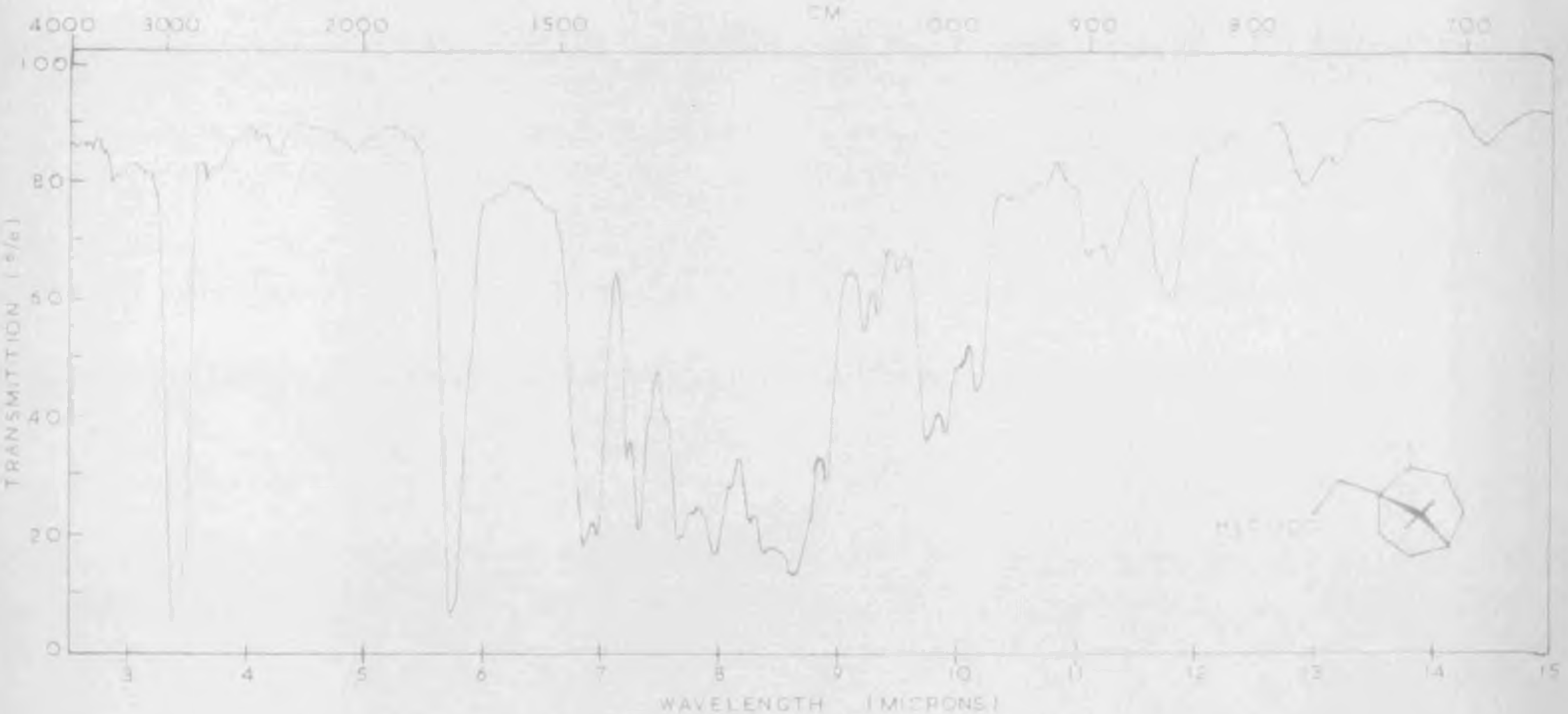


FIG. 18 IR SPECTRUM OF METHYL ESTER OF $C_{13}$ ACID
(LIQUID FILM)

## EXPERIMENTAL

Isopatchoulenone (I) $C_{15}H_{22}O$ (Ketone I, isolation Chapter I) had the following properties, m.p. 48°, b.p. 105° (bath) / 0.2 mm. $[\alpha]^{27}_{D}$ + 39.9° (C, 3.1); molecular weight 218 (mass spec.) U.V. absorption $\lambda_{max}$ 243 m$\mu$(log$_e$ 3.9).

ANALYSIS

Found :C, 82.64; H, 10.2.

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

IR bands (Fig.1, nujol) at: 1706, 1663, 1416, 1389, 1377, 1330, 1304, 1282, 1183, 1168, 1056, 1044, 993, 976, 944, 905, 892, 837 and 698 cm$^{-1}$.

NMR spectrum (Fig.2); doublet (3H) at 9.36 $\tau$ (J = 7 cps; $CH_3-CH\!<$ ), singlet (3H) at 9.2 $\tau$($CH_3-C\!\!\leftarrow$ ), singlet (3H) at 8.87 $\tau$($CH_3-C\!\!\leftarrow$ ), triplet (3H) at 8.32 $\tau$ ($CH_3-C{=}C\!<$), broad signal (2H) at 8.01 $\tau$($-\overset{O}{\overset{\|}{C}}-CH_2$).

2,4-DINITROPHENYLHYDRAZONE OF ISOPATCHOULENONE (I)

To a solution of isopatchoulenone (I, 100 mg.) in ethanol (1 ml.) was added a solution of 2,4-dinitrophenyl hydrazine in sulphuric acid solution. The mixture was heated at 50° for 25-30 min., allowed to stand overnight at room temperature. The separated solid was crystallised to red needles from ethanol, m.p. 228°.

ANALYSIS

Found : C, 63.58; H, 6.41; N, 14.5

Calculated for $C_{21}H_{26}N_4O_4$ : C, 63.3; H, 6.58; N.14.06%

## DIHYDRO-ISOPATCHOULENONE (III) $C_{15}H_{24}O$

### Hydrogenation of Isopatchoulenone (I)

A solution of isopatchoulenone (I, 480 mg.) in acetic acid (10 ml.) was hydrogenated in presence of pre-reduced Adams catalyst (43 mg.). Hydrogen absorbed (60 ml. at 30° and 709 mm. 5 hours) corresponded to 1 mole. The catalyst was filtered off and the acetic acid removed in vacuo on a steam bath. The residue was chromatographed over alumina (Gr.III, 10 g.) and eluted with petether-benzene (1:1, 150 ml.) to yield pure (TLC and GLC) dihydro-isopatchoulenone (III) (450 mg.), m.p. 74° $[\alpha]_D^{28}$ - 28.4° (C, 3.3).

### ANALYSIS

Found : C, 81.56; H, 10.82

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

IR bands (Fig.3, nujol) at: 1742, 1464, 1422, 1389, 1366, 1280, 1179, 985, 885, 853 and 815 $cm^{-1}$.

## DIHYDRO CYPERENE (IV) $C_{15}H_{26}$

### Wolff-Kishner reduction of dihydro-isopatchoulenone (III)

A mixture of dihydroisopatchoulenone (III) (254 mg.) diethylene glycol (10 ml.), potassium hydroxide pellets (approximately 500 mg.) and hydrazin hydrate (1 ml. 85%) was heated to 100° for 4 hours in an atmosphere of nitrogen. Water from the reaction mixture was removed by raising the temperature gradually to 195-200° and then heating continued for 4 hours at 200°. It was diluted with water and made neutral then extracted with ether. Ether layer dried and evaporated. The product (173 mg.) was purified by filtering through alumina (Gr.I, 12 g.) and on elution with pet-ether afforded, colourless mobile product stereo-isomeric isopatchoulane (IVA), b.p. 103° (bath) / 1.3 mm. $[\alpha]_D^{29}$ -76.86° (C, 4.13).

ANALYSIS

Found : C, 87.6; H, 12.61

Calculated for $C_{15}H_{26}$ : C, 87.3; H, 12.7%

I.R. bands (Fig.4, 0.05 mm. cell) at: 1449, 1383, 1368, 1302, 1282, 1211, 1163, 1139, 1124, 1099, 1062, 1020, 975, 928 and 847 $cm^{-1}$.

## ISOPATCHOULANE (IV) $C_{15}H_{26}$

### Hydrogenation of Cyperene (VII)

A solution of cyperene (VII, 300 mg.) in acetic acid (15 ml.) was hydrogenated in the presence of pre-reduced Adams catalyst (30 mg.). It absorbed only one mole of hydrogen and on usual working up afforded dihydro-cyperenes (IVAB, Isopatchoulane), b.p. 105°(batch) / 1.5 mm. $[\alpha]_D^{27}$ - 50.7° (C, 2.4).

ANALYSIS

Found: C, 87.43; H, 12.82

Calculated for $C_{15}H_{26}$: C, 87.3; H, 12.7%

IR bands (0.05 mm. cell) at: 1453, 1388, 1366, 1342, 1312, 1294, 1251, 1205, 1178, 1139, 1114, 1076, 995, 982, 965, 948, 930, 921, 893, 880 and 852 $cm^{-1}$.

## ISOPATCHOULANE (IV) FROM PATCHOULI-ALCOHOL (V)

To a solution of patchouli alcohol (250 mg.) in pyridine (5 ml.), freshly distilled phosphorus oxychloride (5 ml.) was added slowly and the total mixture was refluxed for 6 hours. The purple coloured solution was poured on crushed ice and extracted with ether, ether extract was washed with hydrochloric acid 5%, then with $NaHCO_3$, water, and finally dried over anhydrous $Na_2SO_4$. After removal of the solvent, the residue was distilled under reduced pressure over sodium to afford a mixture of $\alpha$-$\gamma$-patchoulanes as colourless oil. It was then hydrogenated in ethyl acetate (15 ml.) over Pd.C (250 mg.). After working up in the usual procedure it furnished colourless oil, isopatchoulane (IV), b.p. 98° ( bath ) / 0.8 mm. $[\alpha]_D^{26}$ - 50.08° (C, 3.28).

### ANALYSIS

Found : C, 87.60; H, 12.61

Calculated for $C_{15}H_{26}$ : C, 87.3; H, 12.7%

IR bands (liquid film) at: 1385, 1368, 1344, 1312, 1294, 1208, 1180, 1139, 1114, 1075, 997, 984, 965, 946, 930, 918, 890, 879 and 849 $cm^{-1}$.

## ISOPATCHOULENOL (VI) $C_{15}H_{24}O$

### LAH Reduction of Isopatchoulenone (I)

A solution of isopatchoulenone (250 mg.) in dry ether (10 ml.) was added dropwise to a stirred suspension of LAH (50 mg.) in dry ether (25 ml.). The mixture was stirred under reflux for 4 hours and then the excess of reagent was decomposed by addition of moist ether followed by cold dilute HCl. Ether layer was washed free of acid and concentrated. The solid thus obtained was crystallised from pet-ether (235 mg.), m.p.140°; $[\alpha]_D^{30}$ - 53° (c,2 ).

### ANALYSIS

Found : C, 81.70; H, 11.01.

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

IR bands (nujol) at: 3226, 1695, 1380, 1368, 1272, 1218, 1180, 1109, 1092, 1051, 1012, 998, 978, 900 and 875 cm$^{-1}$.

### ISOPATCHOULANE (IV) $C_{15}H_{26}$

### Hydrogenation of Isopatchoulenol (VI)

Isopatchoulenol (VI) (200 mg.) was hydrogenated over pre-reduced $PtO_2$ catalyst (25 mg.) in ethanol (8 ml.) at 28° and 709 mm. Hydrogenation was completed (2 hr.) after the absorption of 1.8 mole $H_2$. The product after the usual work up was chromatographed over alumina (Gr.II, 8 g.) and eluted with per-ether to yield isopatchoulanes (IV) b.p. 110° (bath) / 1.5 mm. $[\alpha]_D^{28}$ - 76° (C, 4.1).

### ANALYSIS

Found : C, 87.50; H, 12.78

Calculated for $C_{15}H_{26}$ : C, 87.3; H, 12.7%

IR bands (0.05 mm. cell) at: 1453, 1388, 1366, 1342,1294, 1250, 1178, 1139, 1124, 975, 930 and 848 cm$^{-1}$. Superimposable on dihydrocyperenes.

## CYPERENE (VII) $C_{15}H_{24}$

## Reduction of Isopatchoulenone with LAH and $AlCl_3$

Isopatchoulenone (I, 300 mg.) in dry ether (15 ml.), was added dropwise into a slurry of LAH (270 mg.) in ether (20 ml.). The mixture was refluxed for 1/2 hour and then cooled in ice and a solution of aluminium-chloride (360 mg.) in ether (20 ml.) was added. After refluxing for 45 minutes, olefin was isolated in the usual way. On distillation over sodium under reduced pressure, colourless mobile liquid, cyperene was obtained. b.p. 110° (bath)/2.5 mm. GLC single peak $[\alpha]_D^{29}$ - 20.17° (C, 2).

### ANALYSIS

Found : C, 88.31; H, 11.91

Calculated for $C_{15}H_{24}$ : C, 88.16; H, 11.84%

IR bands (Fig.5, 0.05 mm. cell) at: 1701, 1389, 1366, 1333, 1316, 1269, 1250, 1222, 1205, 1181, 1163, 1141, 1070, 1037, 988, 934, 892, 877, 845 and 832 $cm^{-1}$.

This olefin on ozonolysis gave a diketone (VIII) m.p. and mixed m.p. with an authentic sample obtained from Cyperene. m.p. 78°; $[\alpha]_D^{28}$ + 35.6° (C, 2.9).

### ANALYSIS

Found : C, 75.94; H, 10.03

Calculated for $C_{15}H_{24}O_2$ : C, 76.22; H, 10.24%

IR bands (nujol) at: 1724, 1412, 1379, 1300, 1245, 1224, 1190, 1170, 1147, 1105, 1075, 1058, 1031, 980, 972, 943, 920, 890, 840 and 790 $cm^{-1}$.

## ISOPATCHOULENONE (I) $C_{15}H_{22}O$

### (i) Oxidation of Cyperene (VII) with t-butyl chromate

A solution of cyperene (2 g.) in carbontetrachloride (10 ml.) was heated to 80° with stirring and tertiary butyl-chromate (30 ml.), glacial acetic acid (5 ml.) and aceticanhydride (2 ml.) were added dropwise over a period of 1 hour. The mixture was stirred at 80° for 10 hours. After cooling to room temperature, oxalic acid (3 g.) in water (30 ml.) was added slowly in 45 minutes. A further quantity of oxalic acid (2 g.) was added and stirring continued for 2 hours. The organic layer was separated, made neutral and dried. The concentrate was purified by passing through alumina (Gr. II, 50 g.) and eluting with pet-ether benzene (50:50). The product (1.8 g.) showed 4 spots on a TLC plate and presence of Isopatchoulenone was ascertained by a comparative TLC study with the natural product.

The oxidation product (1 g.) in dry ether (5 ml.) added dropwise to a stirred suspension of lithium aluminiumhydride (400 mg.) in dry ether (25 ml.). The mixture was refluxed for 5 hours. After working in the usual way, alcohol corresponding to isopatchoulenol (400 mg.) was crystallized from the mixture with pet-ether, m.p. 140°; $[\alpha]_D^{27}$ - 33.85° (C, 3.5).

ANALYSIS

Found : C, 81.60; H, 10.81

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

IR bands (nujol) at: 3209, 1690, 1380, 1366, 1275, 1220, 1183, 1110, 1095, 1053, 1015, 1005, 980, 900 and 875 $cm^{-1}$.

The solution of alcohol (VI, 300 mg.) in acetone (30 ml.) was treated with chromic acid solution in acetone (1.5 ml.). It was allowed to stand at room temperature for 1/2 hour. After the usual working up, the product obtained was chromatographed over alumina (Gr.II, 20 g.). The benzene eluate gave a solid which was crystallised with pet ether m.p. and mixed m.p. 48$^0$; $[\alpha]_D^{29}$ + 38$^0$ (C, 2.1).

IR bands (Fig.1, nujol) at: 1706, 1663, 1416, 1388, 1375, 1323, 1299, 1274, 1235, 1202, 1176, 1139, 1109, 1081, 1053, 980, 970, 938, 885, 833 and 694 $cm^{-1}$.

(ii) Oxidation of cyperene (VII) with chromium trioxide

Cyperene (700 mg.) in glacial acetic acid (12 ml.) was mixed with a solution of chromic acid (1 g.) in water, (2 ml.) and glacial acetic acid (10 ml.). After keeping at room temperature for 30 hours, the mixture was heated on a boiling water-bath for 1 hour. The cold reaction mixture was diluted with water, saturated with NaCl and extracted with ether. The ethereal extract was washed with saturated brine, followed by water and dried over $Na_2SO_4$ (anhydrous). Concentration of solvent gave a crude product, which on distillation under reduced pressure afforded light green coloured liquid (550 mg.), which solidified on cooling and crystallized from pet-ether to colourless crystals, b.p. 125° (bath) / 1 mm. m.p. 48°; $[\alpha]_D^{27}$ +38.48°; (C, 2.4). (GLC and TLC pure).

### ANALYSIS

Found : C, 82.34; H, 10.09

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

IR bands (Fig.1, nujol) at: 1706, 1663, 1416, 1388, 1375, 1299, 1202, 1109, 1081, 980, 938, 833, and 694 $cm^{-1}$, superimposable with natural isopatchoulenone.

### α -CYPERONE (XIV)

Ketone II (Isolation Chapter I) gave a semicarbazone derivative which was purified by repeated crystallisations from ethanol (m.p.216°). α -Cyperone was regenerated from the above semicarbazone by the usual method. It has the following properties, b.p. 108° (bath) / 1 mm. $[\alpha]_D^{28}$ + 120° (C, 3.9). U.V.absorption 244 mμ($\log_e$ 4.2).

### ANALYSIS

Found : C, 82.68; H, 10.31

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

IR bands (liquid film) at: 1665, 1610, 890 $cm^{-1}$.

### PATCHOULENONE (II) $C_{15}H_{22}O$

Benzene fraction, on further chromatography (Isolation Chapter I), gave Patchoulenone (II) which on crystallisation from pet-ether yielded colourless solid m.p. 53°; b.p. 125° (bath) / 1 mm. $[\alpha]_D^{28}$ - 96.3 (C,2.86). Molecular weight 218 (mass spec.) GLC and TLC pure

U.V. absorption $\lambda_{max}$ 264 mμ ($\varepsilon$, 9,000).

### ANALYSIS

Found : C, 82.45; H, 10.11

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

IR bands (Fig.6, nujol) at: 1712, 1664, 1389, 1368, 1287, 1271, 1258, 1238, 1207, 1183, 1143, 1098, 1064, 1020, 995, 983, 975, 940, 894, 885, 873, 833, 806 and 785 cm$^{-1}$.

NMR spectrum (Fig.7) singlet (3H) at 9.1 $\tau$ ($CH_3-\overset{|}{\underset{|}{C}}-$). doublet (3H, J = 6 cps) at 9.15 $\tau$ ($CH_3-CH<$), singlet (3H) at 9.0 $\tau$ ($CH_3-C<$), broad signal (3H) at 7.9 $\tau$ ($CH_3-\overset{|}{C}=C<$).

### SCARIODIONE (XIX) $C_{15}H_{20}O_2$

Scariodione (XIX) isolated from latter fractions of benzene fraction by preparative thin layer chromatography (Isolation Chapter - I), was crystallised from pet-ether to a colourless product, m.p. 45°; $[\alpha]_D^{28}$ - 107.5° (C, 4.2); molecular weight 232 (mass spec.), GLC and TLC pure; U.V. $\lambda_{max}$ 267 mμ ($\log_e$ 3.9).

### ANALYSIS

Found : C, 77.63; H, 8.81

Calculated for $C_{15}H_{20}O_2$ : C, 77.55; H, 8.68%

IR bands (Fig. 8, nujol) at: 1709, 1667, 1412, 1389, 1376, 1307, 1266, 1235, 1202, 1174, 1194, 1099, 1058, 1040, 1018, 998, 975, 940, 895, 863, 823, 797 and 768 cm$^{-1}$.

NMR spectrum (Fig. 9) singlet (3H) at 9.12 $\tau$ ($CH_3-C<$), doublet (3H, J = 6 cps) at 9.32 $\tau$ ($CH_3-CH<$), singlet (3H) at 8.83 $\tau$ ( $CH_3-\underset{\diagdown}{\overset{\diagup}{C}}-$ ), singlet (3H) at 8.0 $\tau$ ( $CH_3-\overset{\backslash}{C}=C<$ ), a signal at 7.77 $\tau$ (2H, $-\overset{\overset{O}{\|}}{C}-CH_2-$ ).

## SCARIODIONE (XIX) $C_{15}H_{20}O_2$

### Oxidation of Patchoulenone (II) with Chromic acid

Patchoulenone (250 mg.) in acetic acid (25 ml.) was mixed with chromic acid (230 mg.) at 15° and kept at room temperature for 36 hours. It was diluted with water and extracted with ether. The ether layer was washed with water, aqueous $Na_2CO_3$ and finally with water and dried, solvent was removed and the product (203 mg.) was filtered through alumina column (Gr.II. 6 g.), the benzene eluate gave a dione which was crystallized from pet-ether (GLC and TLC pure) m.p. 45° undepressed with the natural product $[\alpha]_D^{28}$ - 105.83° (C, 2.1).

### ANALYSIS

Found : C, 77.87; H, 8.73

Calculated for $C_{15}H_{20}O_2$ : C, 77.55; H, 8.68%

IR bands (Fig.8, nujol) at: 1709, 1667, 1412, 1389, 1376, 1307, 1266, 1235, 1202, 1174, 1194, 1099, 1058, 1040, 1018, 998, 975, 940, 895, 863, 823, 797 and 768 $cm^{-1}$.

## DIKETONE (VIII) $C_{15}H_{24}O_2$

### Ozonolysis of Cyperene (VII)

A solution of Cyperene (1.2 g.) in ethylacetate (25 ml.) was ozonised at 0° for 2 hours. Ethyl acetate was removed under vacuum and the residual ozonide was heated with water (20 ml.) for 2 hours and extracted with ether. The ether extract was separated into acidic and neutral portions by treatment with $Na_2CO_3$. The neutral part was purified by chromatography on grade II alumina eluting with petether : benzene (1:1). The pure (TLC and GLC) diketone (VIII) was crystallised twice with pet-ether to a colourless solid m.p. 78°; $[\alpha]_D^{28}$ + 35.3°(C, 3.1).

ANALYSIS

Found : C, 75.81; H, 10.08

Calculated for $C_{15}H_{24}O_2$ : C, 76.22; H, 10.24%

IR bands (Fig.10, nujol) at: 1724, 1412, 1389, 1368, 1300, 1249, 1224, 1190, 1171, 1147, 1105, 1075, 1058, 1031, 980, 972, 943, 920, 890, 840 and 790 $cm^{-1}$.

NMR spectrum (Fig.11) doublet (3H) at 9.28 τ (J = 6 cps; $CH_3-\overset{/}{\underset{\backslash}{CH}}$ ), singlet (3H) at 9.06τ( $CH_3-\overset{/}{\underset{\backslash}{C}}-$), singlet (3H) at 8.84 τ($CH_3-\overset{/}{\underset{\backslash}{C}}-$), singlet (3H) at 7.93 τ ($CH_3-CO-$).

KETOACID (XX) $C_{15}H_{22}O_3$

Oxidation of Diketone (VIII) with Chromium Trioxide

A solution of chromium trioxide (3 g.) in glacial acetic acid (25 ml.) was slowly added with stirring to a solution of diketone (VIII) (3 g.) in glacial acetic acid (8 ml.). The reaction mixture was left for 75 hours at room temperature, diluted with water, and extracted with ether, extract treated with $NaHCO_3$ to facilitate separation of unreacted diketone and keto acid. Aqueous layer acidified, extracted with ether, dried over sodium sulphate (anhydrous). On removal of solvent, solid obtained was crystallised twice with ethanol, m.p. 177°.

ANALYSIS

Found : C, 70.23; H, 9.25

Calculated for $C_{14}H_{22}O_3$ : C, 70.55; H, 9.31%

IR bands (nujol) at: 3125, 1724, 1376, 1366, 1078, 1053, 925 and 862 $cm^{-1}$.

Keto acid (XX) thus obtained was methylated with diazomethane by the usual method. b.p. 140°(bath)/0.7 mm. m.p.63° $[\alpha]_D^{29}$ + 40.78 (C, 4.4).

ANALYSIS

Found : C, 71.68; H, 9.52

Calculated for $C_{15}H_{24}O_3$ : C, 71.39; H, 9.59

IR bands (Fig.12, liquid film) at: 1724, 1456, 1431, 1412, 1389, 1370, 1342, 1316, 1280, 1242, 1163, 1142, 1111, 1079, 1046, 1010, 980 and 851 $cm^{-1}$.

NMR spectrum (Fig.13): two singlets (3H each) at 9.04 and 8.9$\tau$($CH_3-C\leq$ ); doublet (3H) at 9.19$\tau$ (J = 7 cps, $CH_3-CH<$ ); singlet (3H) at 6.4$\tau$($-COOCH_3$).

CYCLISED PRODUCT (XXI) $C_{14}H_{22}ON_2$

Wolff-Kishner Reduction of Ketoacid

The keto acid (XX 700 mg.) in diethylene glycol (10 ml.) was treated with hydrazine hydrate (1 ml.) and potassium hydroxide (1 g.). The solution was heated first at 120° for 3 hours and then the temperature was raised to 200° and heating was continued for further 2 hours. The reaction was, however, carried out in the nitrogen atmosphere. The reaction product was cooled and diluted with water (10 ml.) acidified and extracted with ether, washed with water, dried ($Na_2SO_4$), and ether distilled leaving a colourless solid product (XXI) which was crystallised with pet-ether m.p. 203-204°.

ANALYSIS

Found : C, 71.55; H, 9.52; N, 12.2

Calculated for $C_{14}H_{22}ON_2$ : C, 71.75; H, 9.46; N, 11.96%

IR bands (Fig. 14, nujol) at: 3175, 3058, 1675; 1658, 1460, 1324, 1351, 1304, 1287, 1272, 1229, 1183, 1111, 1060, 1005, 990, 931, 913, 852, 833, 800 and 752 $cm^{-1}$.

NMR spectrum (Fig.15): Two singlets (3H each) at 9.07 and 8.97 $\tau$ ( $CH_3-C\begin{smallmatrix}/\\-\\ \backslash\end{smallmatrix}$ ); one doublet (3H) centred at 9.1 $\tau$ (J = 6 cps $CH_3-\overset{/}{\underset{\backslash}{C}}H$).

KETO ACID (XXII) $C_{14}H_{22}O_3$

Ozonolysis of the Isopatchoulenone

Isopatchoulenone (1.3 g.) was ozonised at 0° in chloroform (20 ml.) for 1 hour. The ozonide, after removing the solvent, was decomposed by boiling with water for 2 hours. The resulting product was treated with sodium bicarbonate and extracted with ether (2 x 35 ml.). The aqueous layer was acidified then extracted with ether, and acid was converted into methylester, b.p. 115-120°(bath)/0.2mm. $[\alpha]_D^{26}$ - 22.98; $n_D^{25}$ 1.4630.

ANALYSIS

Found : C, 70.38; H, 9.62

Calculated for $C_{14}H_{22}O_3$ : C, 70.55; H, 9.31%

IR bands (Fig.16, liquid film) at: 1739, 1724, 1370, 1361, 1299, 1758, 1198, 1130, 1081, 1031, 1019, 1000, 980, 893, 855, and 813 $cm^{-1}$.

NMR spectrum (Fig.17); doublet (3H) at 9.06 $\tau$ ($\rangle CH-CH_3$); two singlets (3H, each) at 9.05 and 8.73 $\tau$ ($\overset{\backslash /}{\underset{/}{C}}-CH_3$), singlet (3H) at 6.37 $\tau$ ( $-COOCH_3$).

ACID (XXIII) $C_{13}H_{22}O_2$

Wolff-Kishner Reduction of Keto Acid

The keto acid (1 g.) dissolved in freshly distilled diethylene glycol (10 ml.) hydrazinehydrate (2 ml.) and KOH pellets (1 g.) were heated at 140-150° for 3 hours under nitrogen atmosphere and then at 185-190° for another 3 hours. It was cooled, diluted with water, extracted with ether. The aqueous layer was acidified and extracted with ether, washed and dried. On removal of the solvent, the acid obtained was converted into its methyl ester by diazomethane method. b.p. 88-90°(bath) / 0.2 mm.; $[\alpha]_D^{27}$+ 83.33° (C, 2.9), $n_D^{25}$ 1.4550.

ANALYSIS

Found : C, 74.78; H, 11.03

Calculated for $C_{14}H_{24}O_2$ : C, 74.95; H, 10.78%

IR bands (Fig.18, liquid film) at : 2941, 1733, 1456, 1429, 1385, 1361, 1304, 1250, 1209, 1190, 1159, 1124, 1085, 1070, 1053, 1020, 1010, 985, 900, 885, 845, 803 and 775 $cm^{-1}$.

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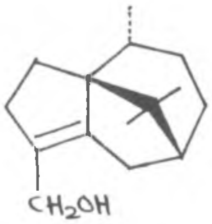
## Chapter IV

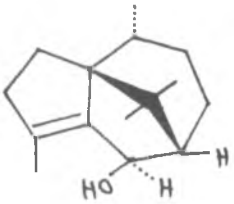
# Structures of Alcohols

## SUMMARY

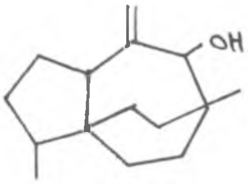
From the ether eluted fraction of the oil of Cyperus scariosus, three new sesquiterpene alcohols have been isolated in pure state. On the basis of chemical and spectral studies, the two crystalline alcohols Cyperenol and Patchoulenol have been assigned structures I and II respectively. The third sesquiterpene alcohol, Rotundenol, has been assigned a provisional structure III.



(I)



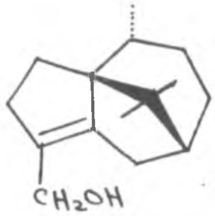
(II)



(III)

## CYPERENOL

Alcohol I $C_{15}H_{24}O$; molecular weight 220 ( mass spec.) colourless crystals, m.p. 94°, $[\alpha]_D^{30}$- 12.1° (C,4.3) (isolation described in Chapter I) is a new alcohol and has been named cyperonol (VI). It exhibited only end-absorption (210 m u, ε,10,500) in the U.V. region indicating the absence of any conjugated chromophore. The infra-red spectrum (Fig.1) displayed absorption bands at: 3333, 1018 cm$^{-1}$ (primary hydroxyl) and 1379, 1361 cm$^{-1}$ (gemdi-methyl group). Cyperenol gave colouration with tetranitromethane.


(VI)

The magnitude of the 'ε' value, together with the absence of any absorption due to the $>C = C<$ stretching vibrations suggested the fully substituted nature of the ethylenic linkage.

NMR spectrum (Fig.2) of cyperenol (1) does not show any signals due to the presence of vinyl protons, thus the only double bond present inthe alcohol is tetrasubstituted. It further exhibited unsplit methyl signals at 9.22 and 9.05τ (6H, $CH_3 - C< - CH_3$ ), and methyl doublet centered at 9.17τ (3H, J = 6 cps, $CH_3-CH<$ ). The broad signal at 5.91 τ(2H) can be assigned to the methylene group of the primary alcohol; its down field position and singlet nature

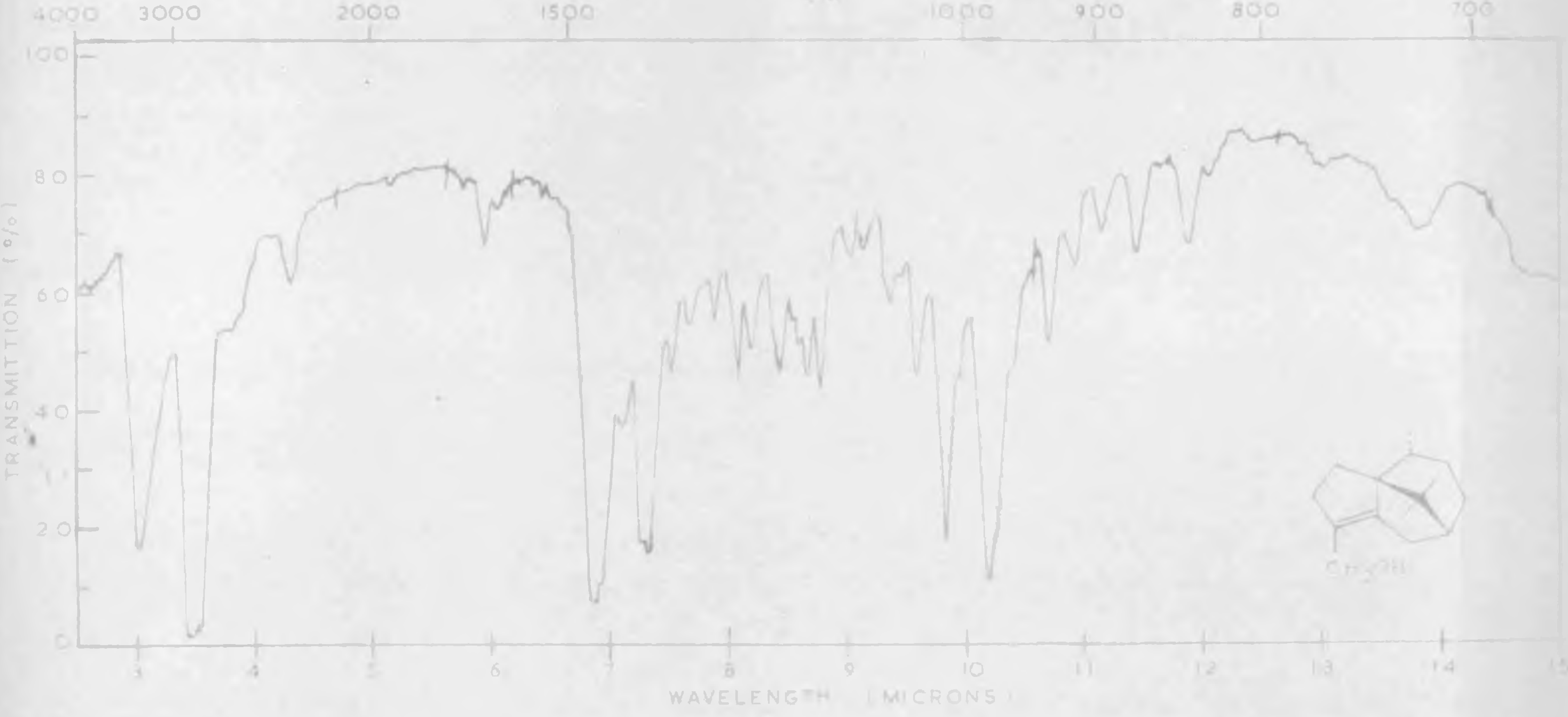


FIG. [illegible] IR SPECTRUM OF ALCOHOL - I (CYPERENOL)

(NUJOL)

FIG 2 NMR SPECTRUM OF ALCOHOL-I ( CYPERENOL )

indicated that the $-CH_2OH$ group is attached to a double bond which carries no hydrogen. The singlet at 7.69 $\tau$ could be assigned to the proton of the hydroxyl group as it disappeared on deuterium exchange. There is no signal attributable to a methyl on a double bond.

The spectral properties along with its molecular formula $C_{15}H_{24}O$, suggested that Cyperenol is a monoethenoid tricyclic sesquiterpene primary alcohol.

On oxidation with Jones reagent[1] Cyperenol (I) gave and $\alpha-\beta$ unsaturated acid (II), $C_{15}H_{22}O_2$, U.V.($\lambda_{max}$ 230 m$\mu$, $\epsilon$,2340) and IR (1704 $cm^{-1}$) confirming the presence of an allylic primary alcohol.

On hydrogenation Cyperenol afforded only a saturated hydrocarbon due to hydrogenolysis. This saturated hydrocarbon (III) $C_{15}H_{26}$, was identical in every respect (IR, GLC, rotation) with dihydro-cyperenes[2] (Isopatchoulanes) (III). These experiments, therefore, suggested the structure (I) for Cyperenol.

The tosyl derivative of Cyperenol on reduction with LAH afforded an unsaturated hydrocarbon (IV) (IR Fig.3), $C_{15}H_{24}$, b.p. 78° (bath) / 0.2 mm.; $n_D^{30}$ 1.5017; $[\alpha]_D^{30}$ - 19.73° in low yield. This hydrocarbon has been identified as cyperene[2] (IV) (GLC, rotation and IR spectrum).

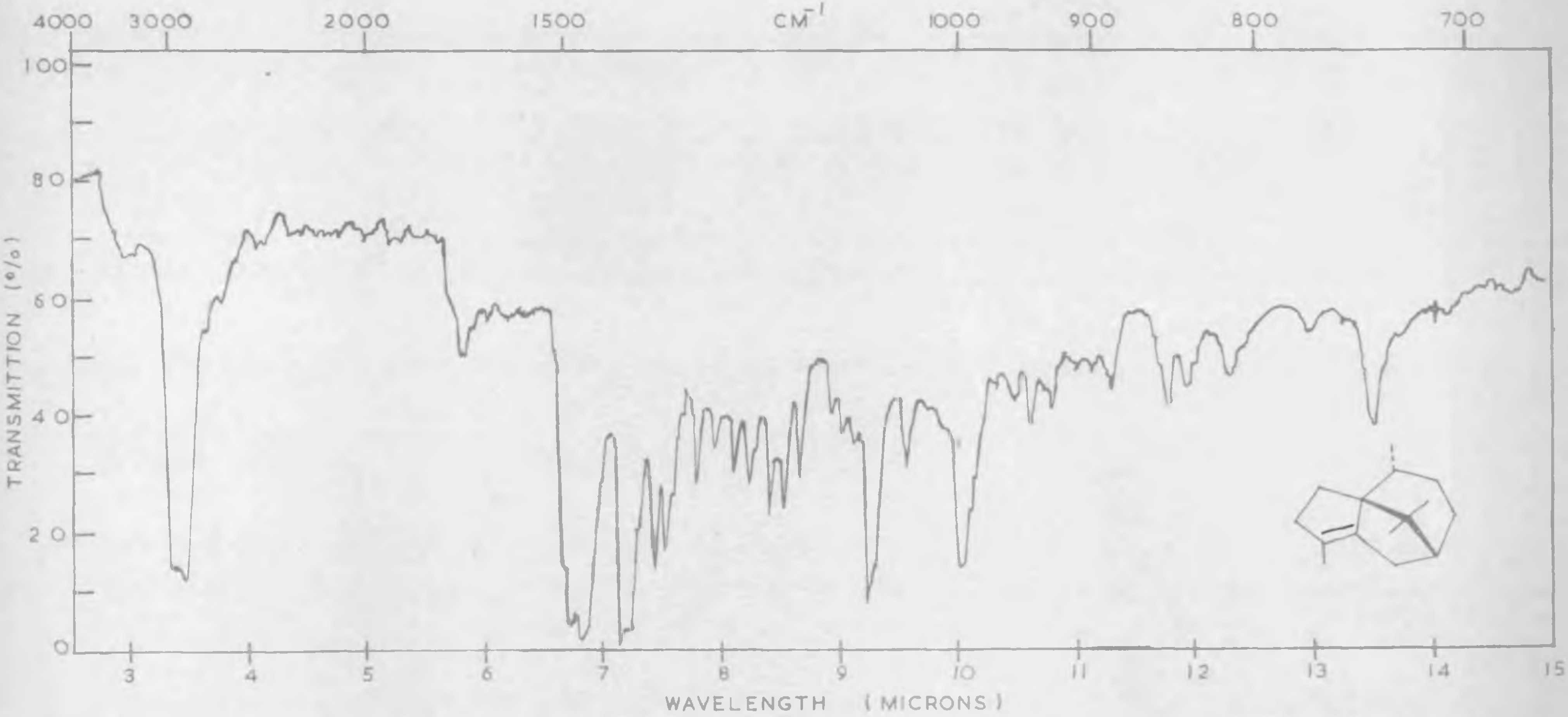
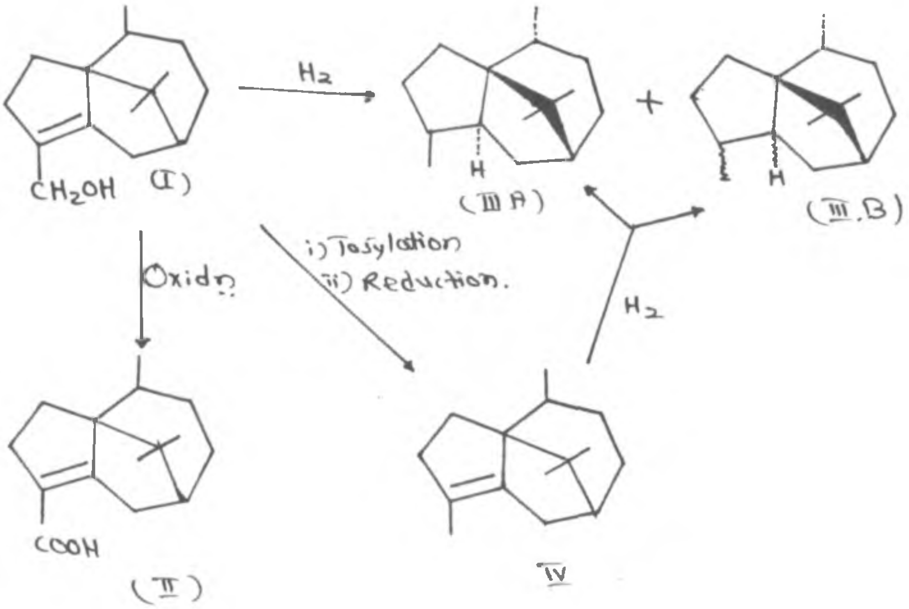
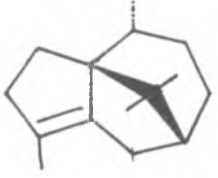


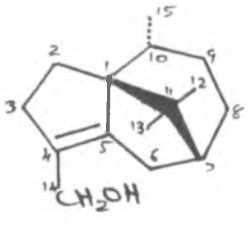
FIG. 3 IR SPECTRUM OF HYDROCARBON (CYPERENE)

(0.05 MM LIQUID CELL)



The stereochemistry of cyperene represented by structure (V) has been established by the Japanese workers[4]. On the basis of these evidences the stereoformula VI represents the structure and stereochemistry of cyperenol[3] (Isopatchoul-4en-14-ol).

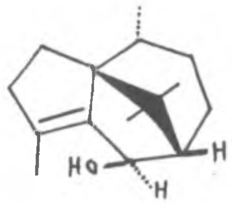

(V)



(VI)

## PATCHOULENOL

Alcohol II, $C_{15}H_{24}O$; m.p. 74°; $[\alpha]_D^{30}$ - 54.23° (C, 3.8) (isolation described in Chapter I), is also a new alcohol and has been named as Patchoulenol (IX). It showed absorption bands at: 3333, 1053, (secondary hydroxyl) 1379, 1361 (gemdimethyl group) and 1064, 1020 cm$^{-1}$ in the infrared spectrum (Fig.4). Its U.V. spectrum displayed absorption at 210 mμ ($\epsilon$,10,500) indicative of end absorption.



( IX )

NMR spectrum (Fig. 5) of Patchoulenol (VII) indicated the absence of any signal due to the presence of olefinic protons. It further showed a quartet between 9.02 and 9.32 $\tau$ corresponding to 9 protons (one gemdimethyl group and one secondary methyl group). A singlet at 8.22 $\tau$ accounted for a methyl group on a double bond. So, the only double bond in the alcohol is tetrasubstituted. Another singlet at 8.45 $\tau$ represents the proton of the hydroxyl group as it disappears on $D_2O$ exchange. A singlet at 5.68 $\tau$ accounts for one proton on an asymmetric carbon atom carrying hydroxyl group and it also indicated the secondary nature of the alcohol.

On hydrogenation with $PtO_2$ and ethanol, Patchoulenol (VII) afforded stereoisomers of dihydrocyperene (III A & B) GLC, IR) through hydrogenolysis, confirming

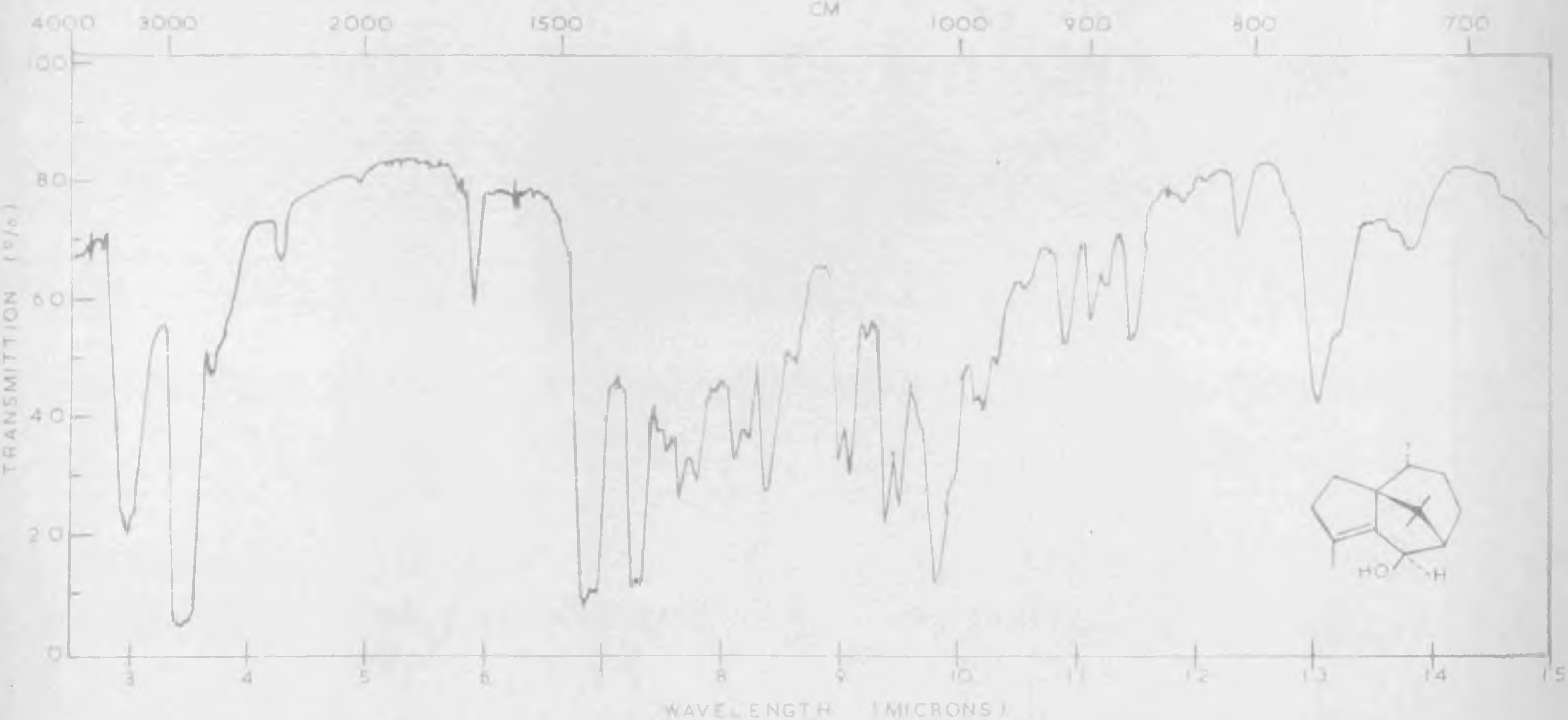


FIG 4 IR SPECTRUM OF ALCOHOL-II (PATCHOULENOL)
(NUJOL)

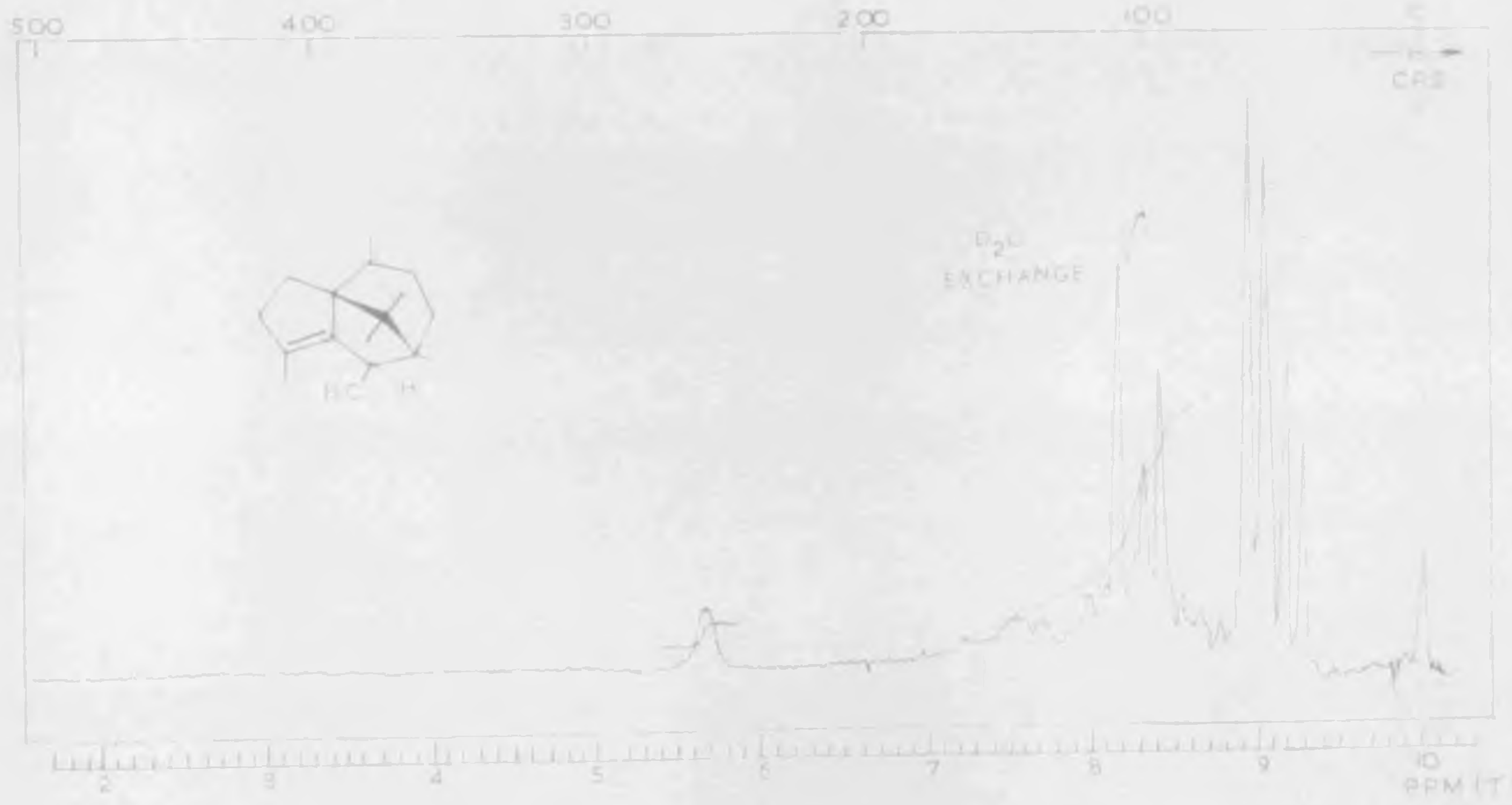
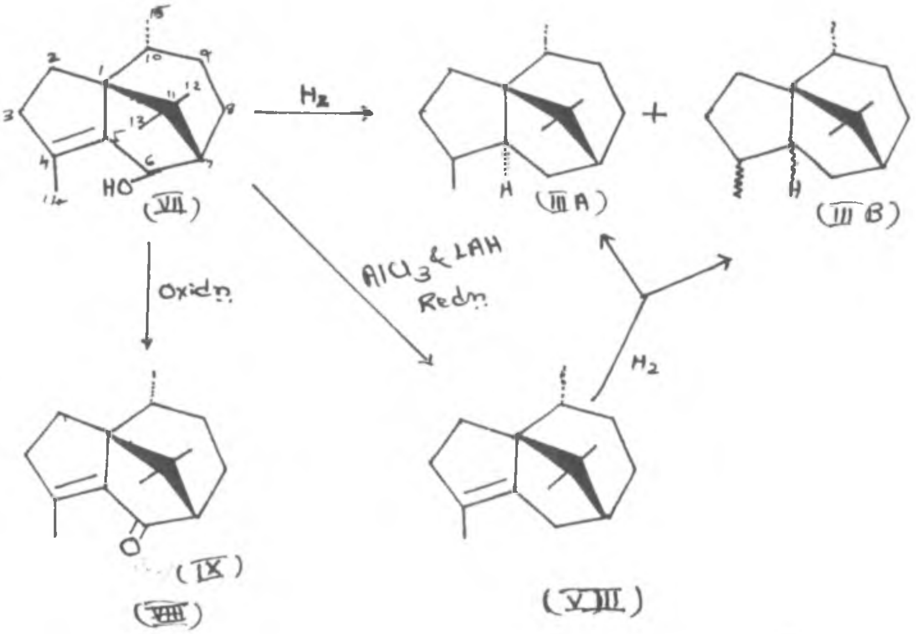


FIG **5.** NMR SPECTRUM OF ALCOHOL – II (PATCHOULENOL) the allylic nature of the alcohol.

Reduction of Patchoulenol (VII) with LAH and $AlCl_3$ gave an unsaturated hydrocarbon (VIII), $C_{15}H_{24}$; $[\alpha]_D^{30}$ - 21°, $n_D^{30}$ 1.5020. This hydrocarbon was found to be identical with cyperene (VIII) (GLC, rotation, IR spectrum).

On oxidation with Jones reagent, Patchoulenol (VII) gave an $\alpha$-$\beta$ unsaturated ketone(IX), $C_{15}H_{22}O$; m.p. 53°; $[\alpha]_D^{30}$ - 93.73° (C, 3.51) $\lambda_{max}$ 263 m$\mu$, $\epsilon$, 9,198 and IR spectrum (Fig.6) bands at 1712 $cm^{-1}$ indicating the allylic nature of the secondary alcohol. The comparison of the properties of the ketone (IX) with Patchoulenone[6] established their identity (GLC, IR, m.p. and mixed m.p. rotation).

Patchoulenol (Isopatchoul-4en-6-ol) was, therefore, assigned structure VII.



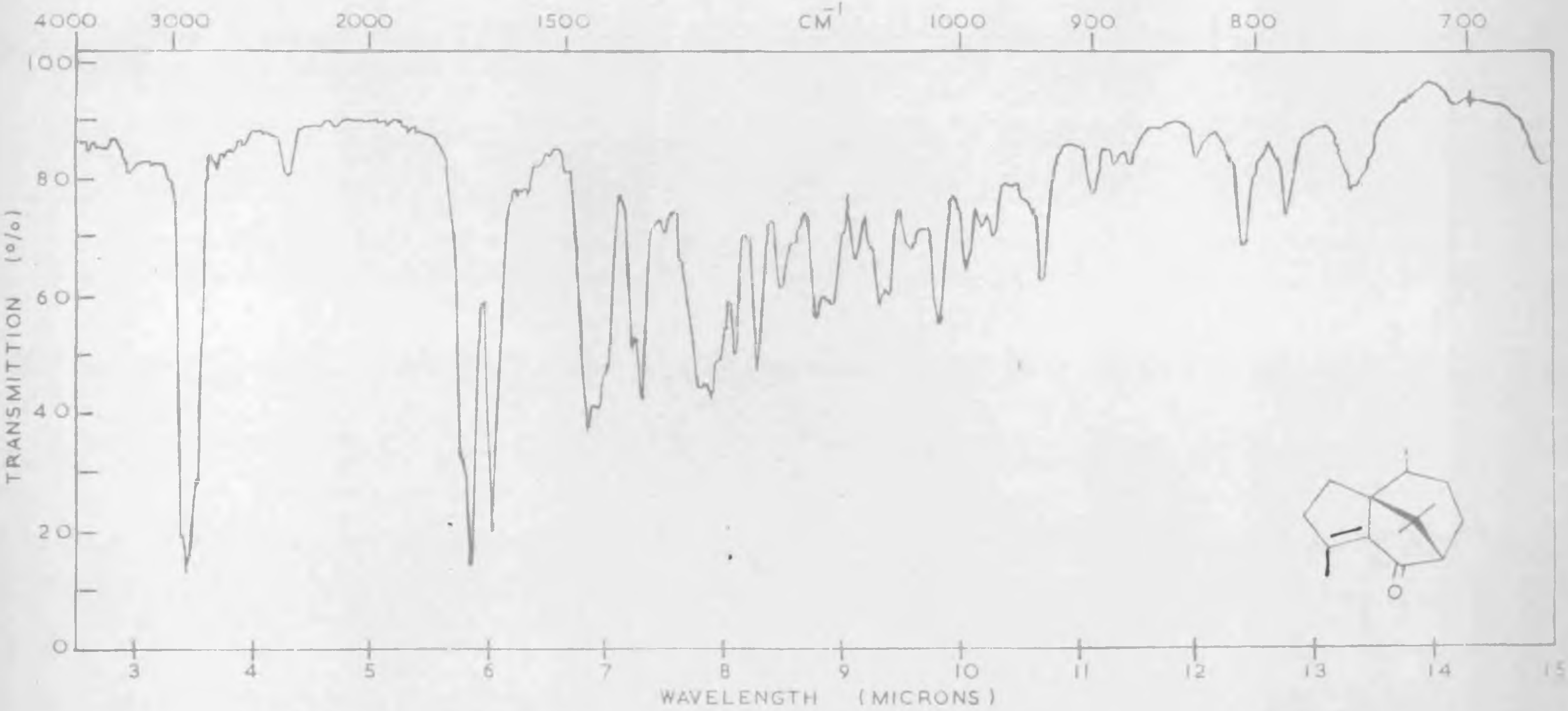
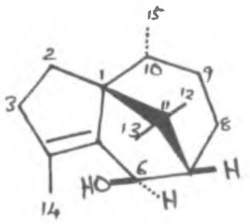


FIG 6 IR SPECTRUM OF KETONE (PATCHOULENONE)
(LIQUID FILM)

The correlation with (-) Cyperone (VIII) and (-) Patchoulenone (IX) of known absolute stereochemistry determined the stereochemistry of patchoulenol (VII) at all the centres of asymmetry except carbon ($C_6$) carrying hydroxyl group.

Stereochemistry of the hydroxyl group was determined from the NMR spectrum, in which the proton on the asymmetric carbon atom ($C_6$) carrying hydroxyl group appears to be axial as it shows a singlet at 5.68 $\tau$.

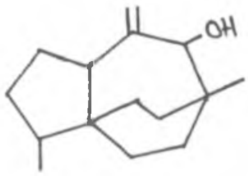
The dihedral angles between $C_6$ and $C_7$ from models is approximately 100 degrees which would result in small coupling. In the opposite orientation ($\alpha$-hydroxyl) the dihedral angle between $C_6$ and $C_7$ would be approximately 20° and this would have resulted in coupling of the order of 6-7 cps. The NMR spectrum therefore indicates the hydroxyl group to be $\beta$-oriented[7]. Patchoulenol is therefore represented by the stereoformula (IX).



( IX )

## ROTUNDENOL

Alcohol III, $C_{15}H_{24}O$, molecular weight 220 (mass spec.) $[\alpha]_D^{27}$ +55.35°, [3:5 dinitrobenzoate, m.p. 139-140° (IR Fig.9, $[\alpha]_D^{28}$ -32.1°) isolation Chapter I ] has been named Rotundenol (X) because of its structural similarity with Rotundene (Hydrocarbon II, Chapter II). It showed absorption bands at 3509 (characteristic of a hydroxyl group) 3106, 1818, 1661, 910 (terminal methylene group) cm$^{-1}$ in the IR spectrum (Fig.7). It gave intense colouration with tetranitromethane and showed end absorption in U.V. $\lambda_{max}$ 210 m$\mu$, $\varepsilon$,3,100.



(X)

NMR spectrum (Fig.8) of rotundenol (X) showed the presence of two methyl groups, one tertiary (3H, singlet 9.17 $\tau$) and the other secondary (3H, doublet 9.1 $\tau$, J = 7 cps), an exocyclic methylene group (2H, doublet 5.01 $\tau$). The signal at 6.16 $\tau$ (1H) is obviously due to the CHOH methine proton, and 8.7 $\tau$ signal could be assigned to the hydroxyl proton as it disappeared on deuterium exchange.

Hydrogenation of rotundenol with platinum oxide in ethylalcohol gave a crystalline dihydroproduct (XI) $C_{15}H_{26}O$ ($M^+$ 222 & 223 after $D_2O$ exchange, mass spec.) m.p. 95-96°, $[\alpha]_D^{28}$ - 31.5° IR spectrum (Fig.12) showed absence of bands at 3106, 1661, 910 cm$^{-1}$ due to the

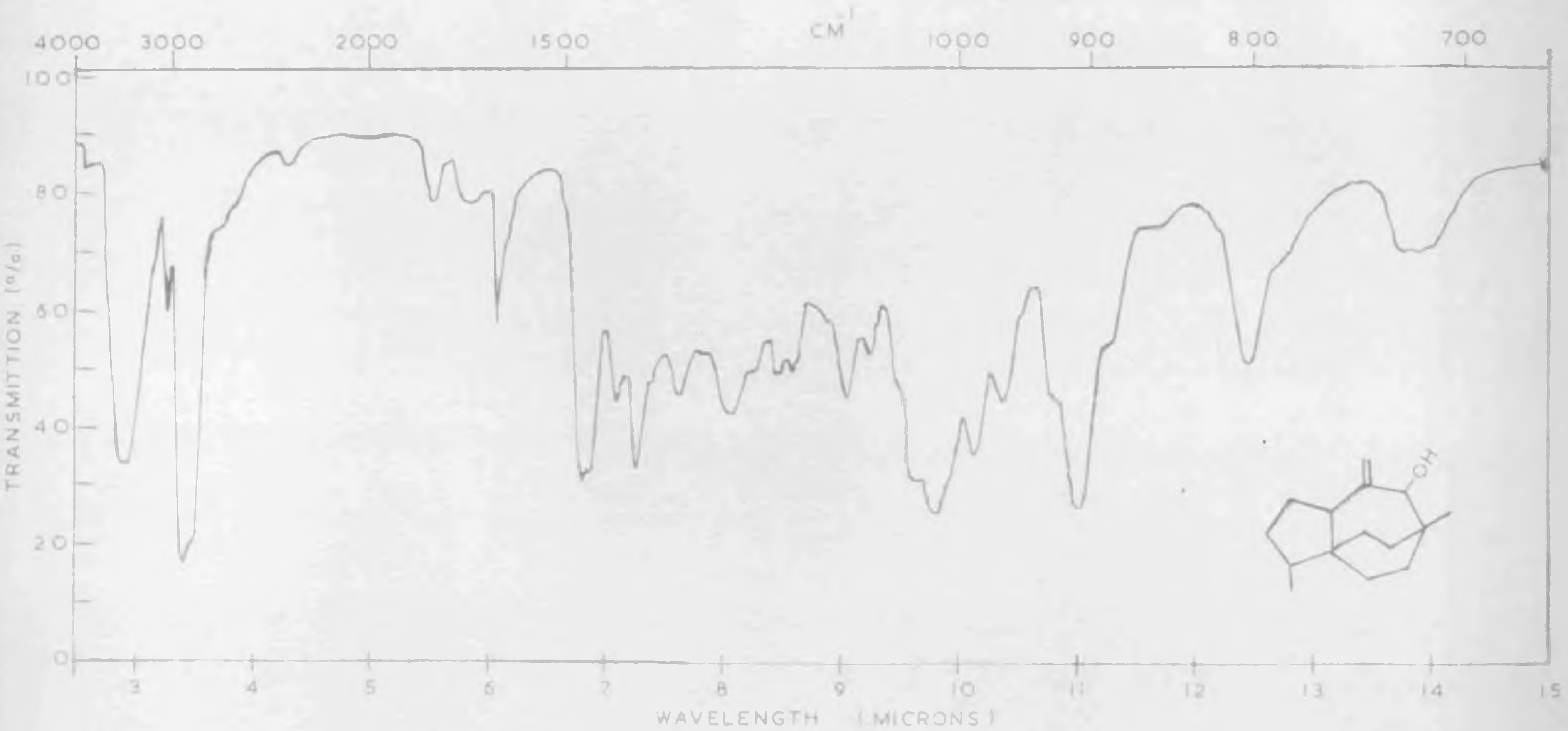


FIG **7** IR SPECTRUM OF ALCOHOL - III (ROTUNDENOL)

(LIQUID FILM)

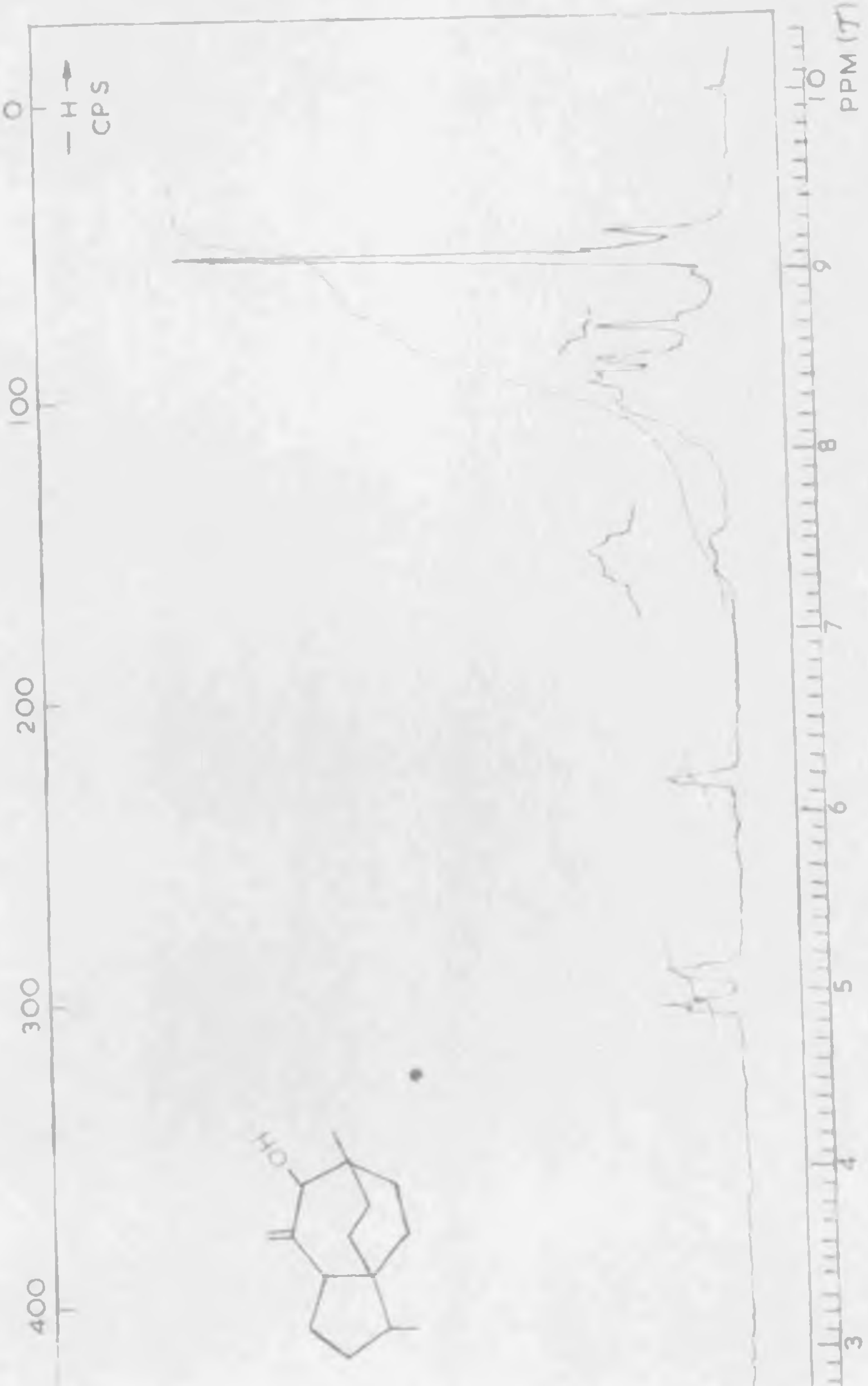


FIG 8 NMR SPECTRUM OF ALCOHOL - III (ROTUNDENOL)

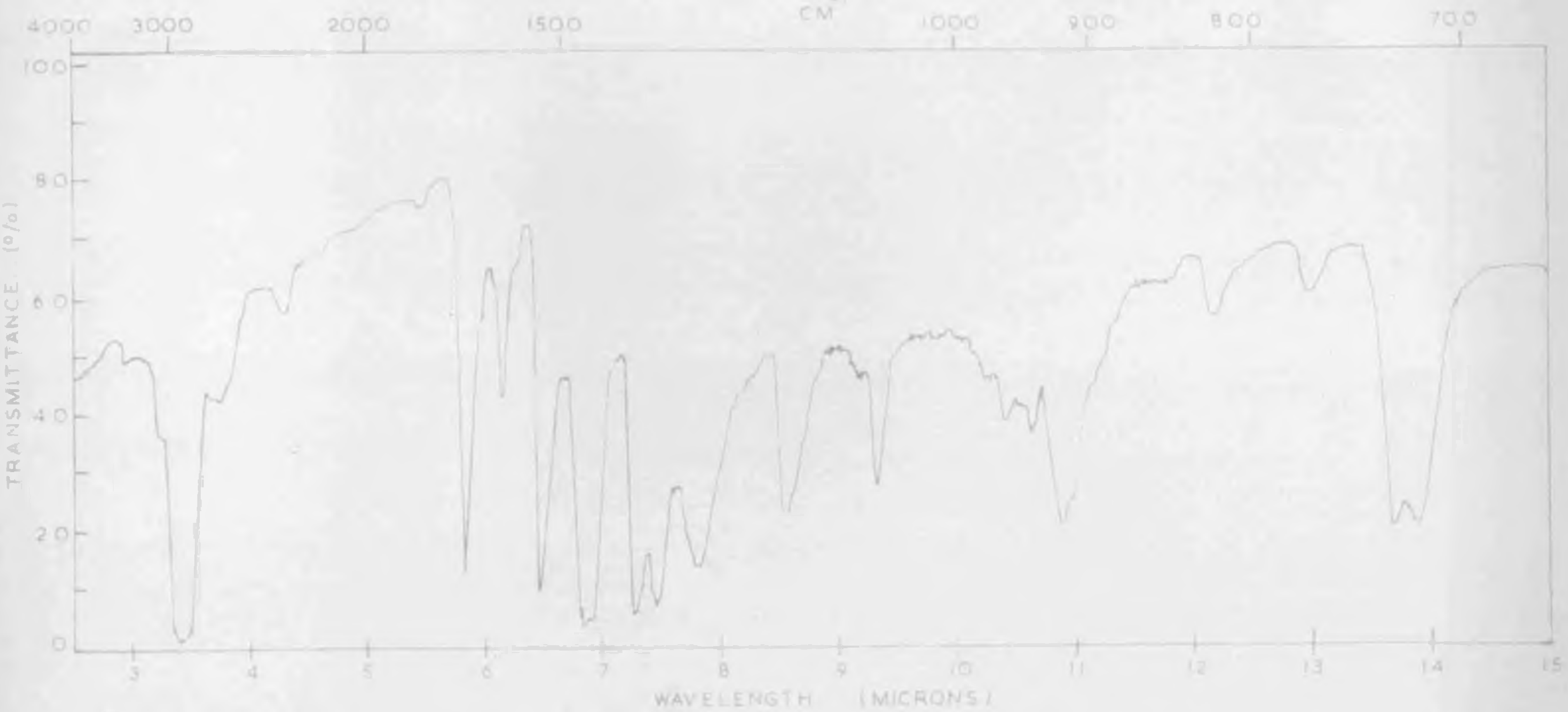


FIG 9 IR SPECTRUM OF 3'5 DINIRO-BENZOATE DERIVATIVE OF ALCOHOL - III (NUJOL)

FIG 10 IR SPECTRUM OF ACETATE DERIVATIVE OF ALCOHOL – III
(LIQUID FILM)

FIG **11** NMR SPECTRUM OF ACETATE DERIVATIVE OF ALCOHOL-III

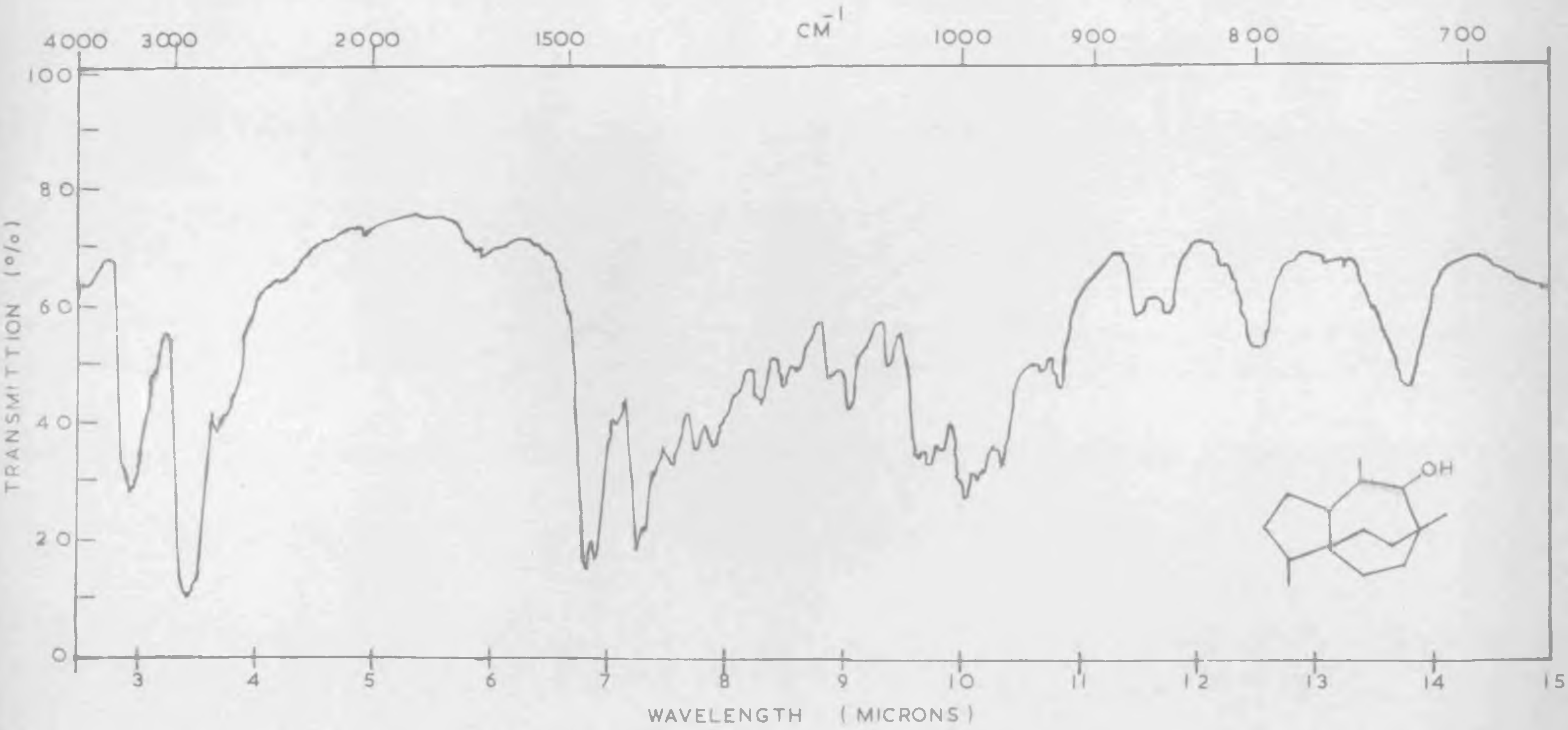


FIG. 18. IR SPECTRUM OF DIHYDRO-ROTUNDENOL
(NUJOL)

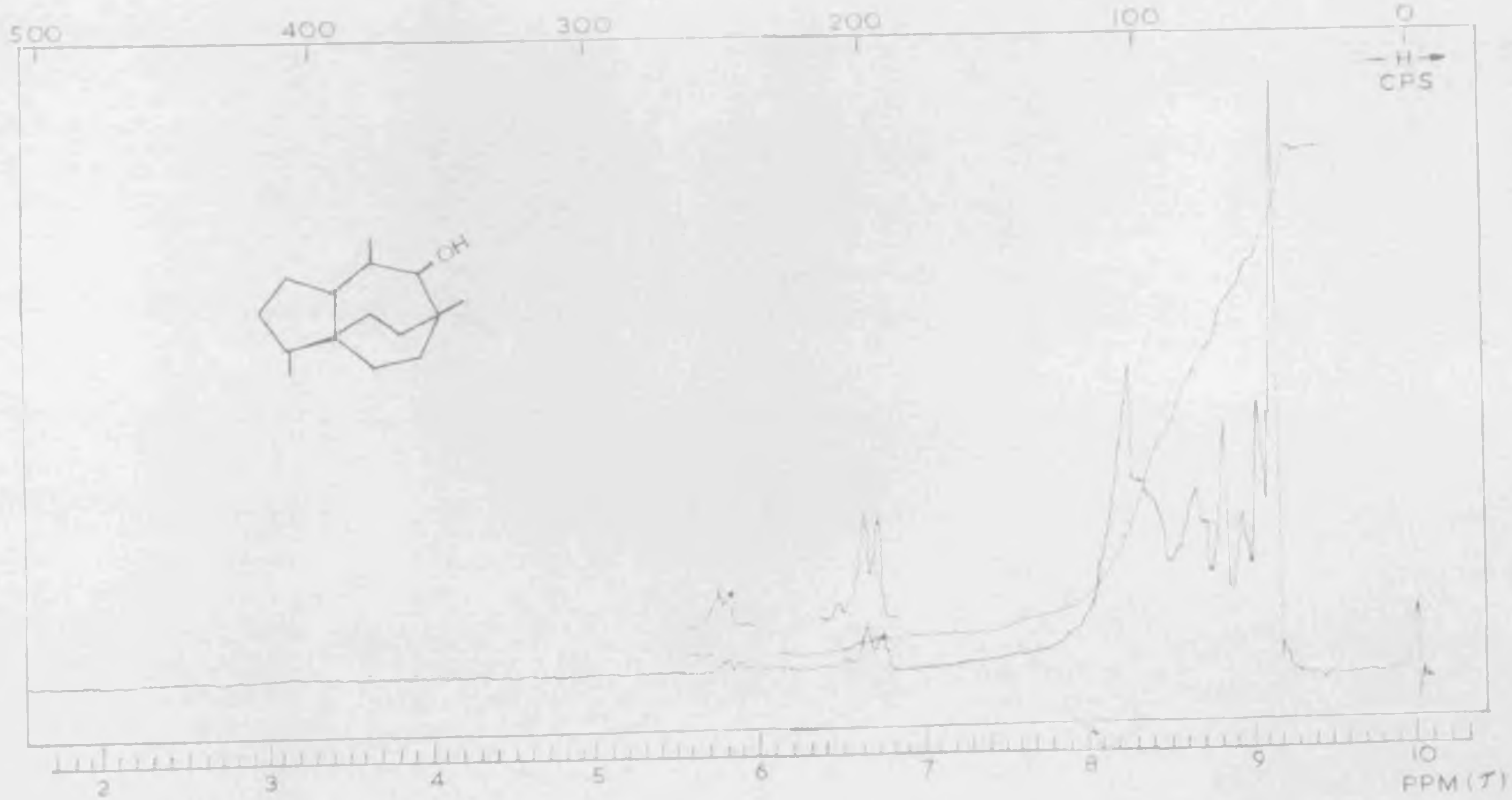


FIG 13 NMR SPECTRUM OF DIHYDRO-ROTUNDENOL

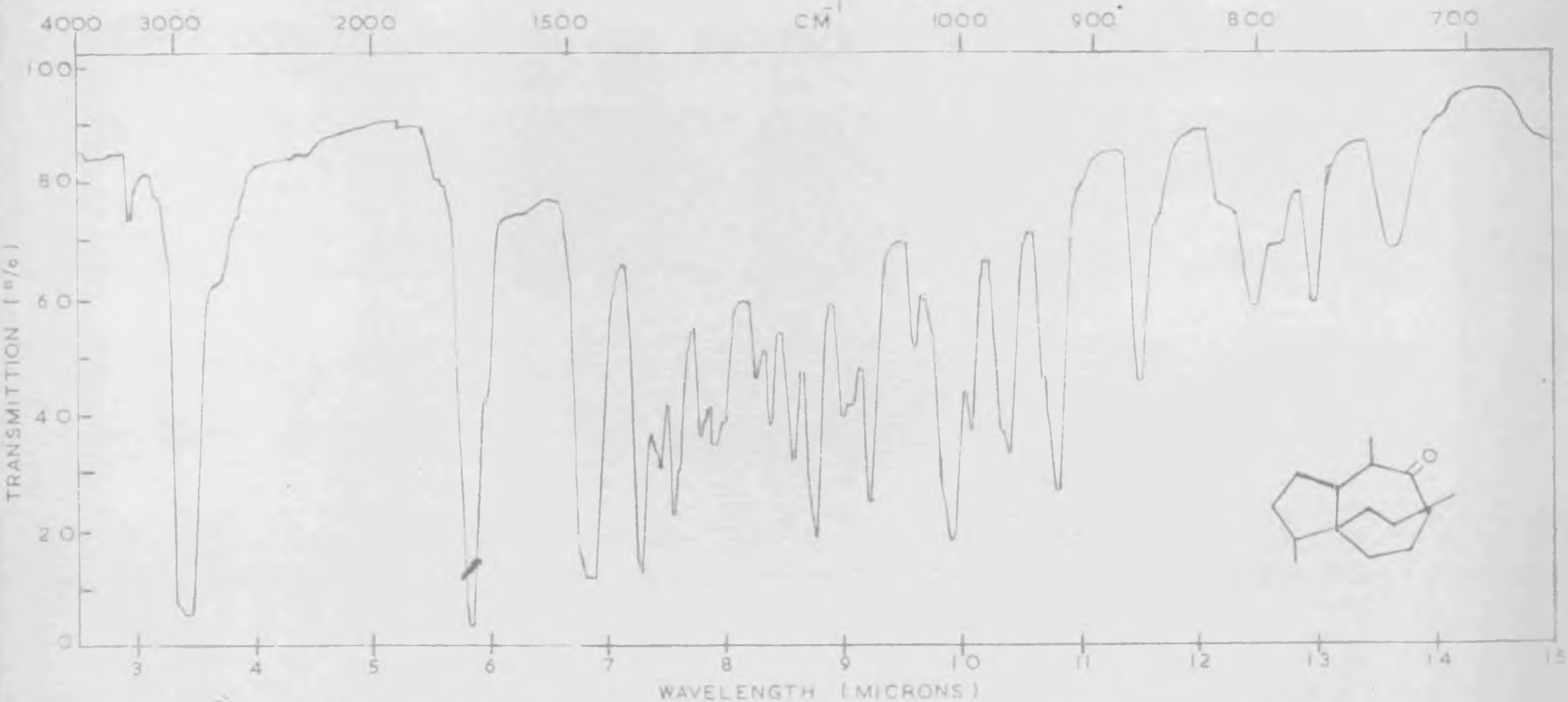


FIG. **14** IR SPECTRUM OF DIHYDROKETONE (LIQUID FILM)

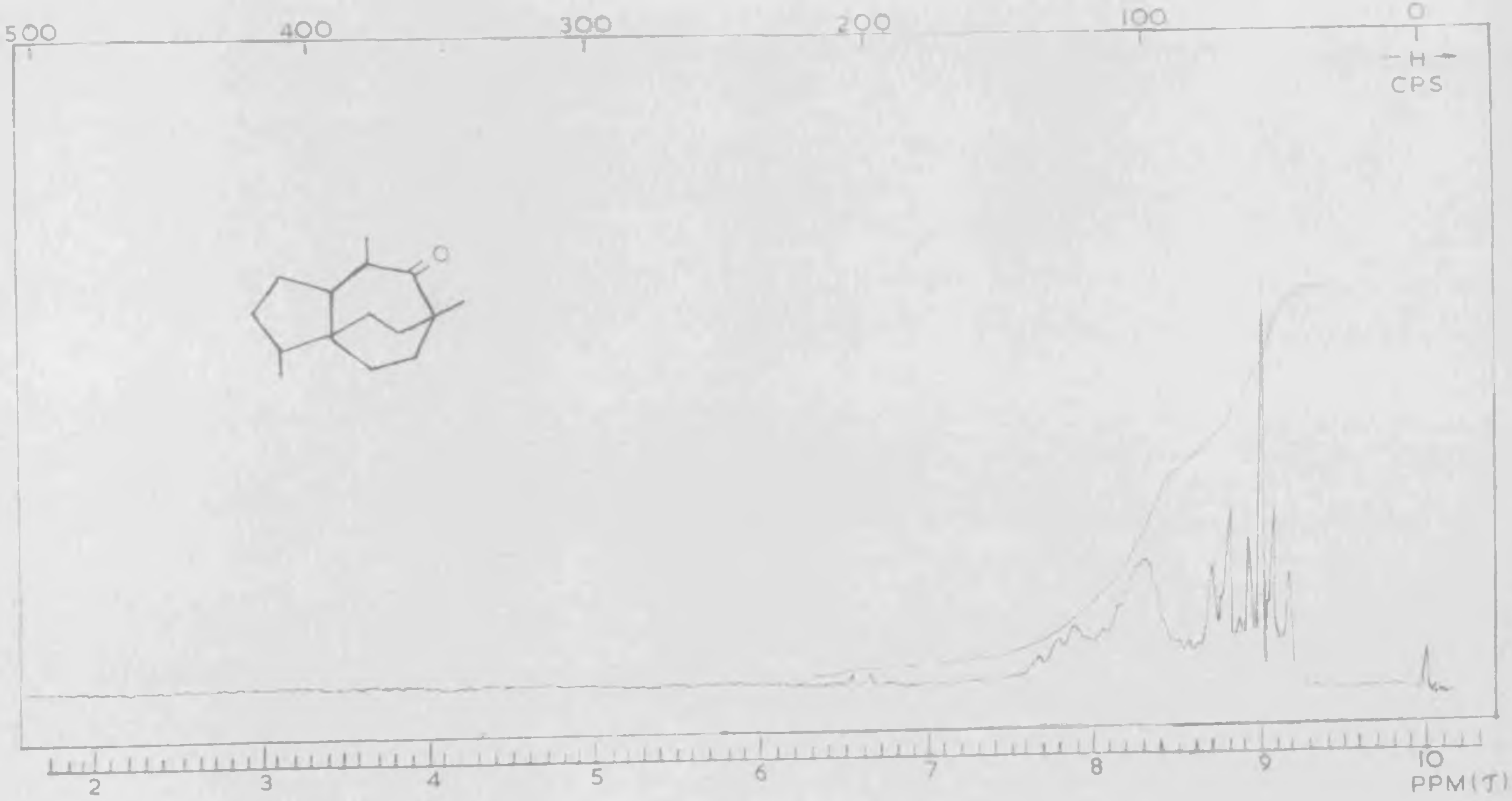


FIG. 15. NMR SPECTRUM OF DIHYDROKETONE.

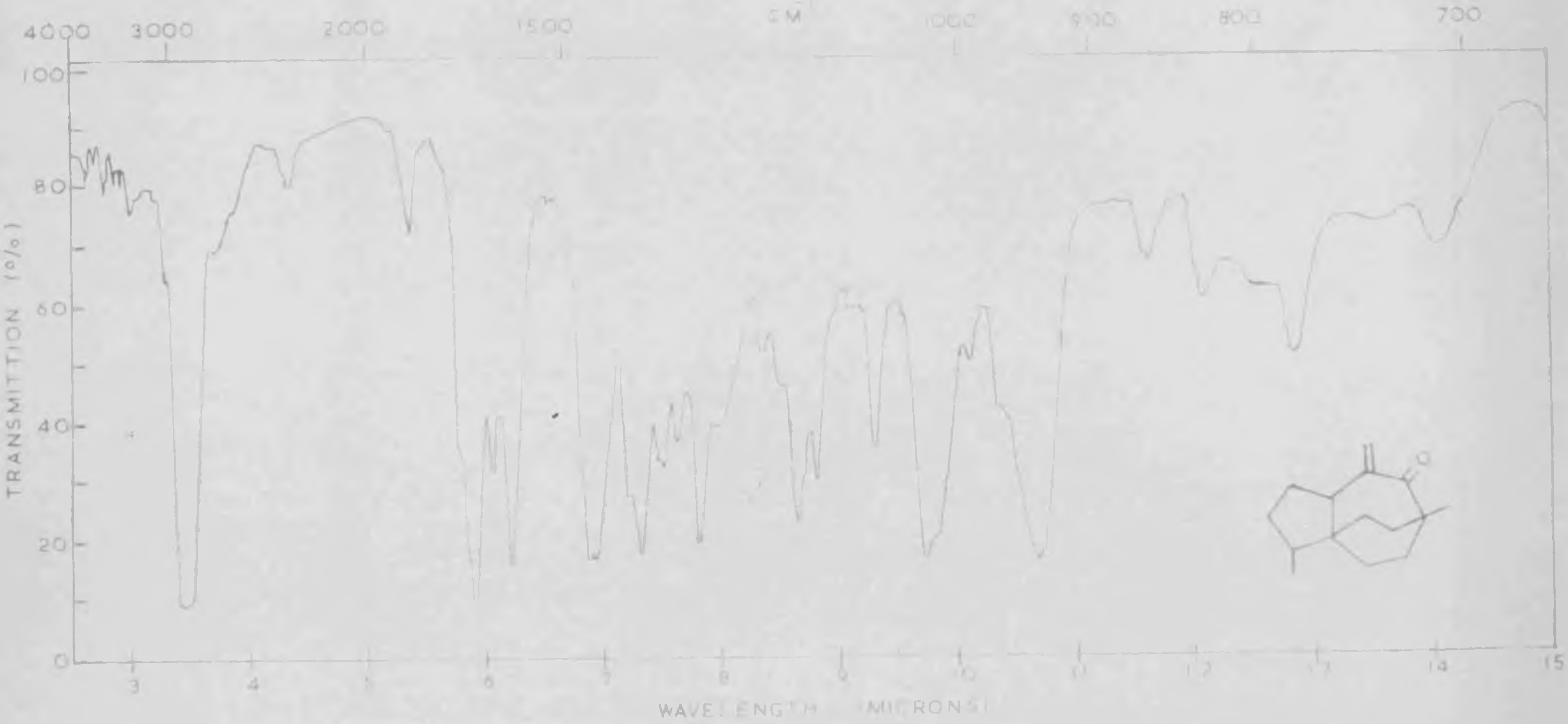


FIG 16 IR SPECTRUM OF KETONE (LIQUID FILM)

terminal methylene group.

NMR spectrum (Fig.13) of the dihydroalcohol (XI) showed the presence of two secondary methyls centered at 9.12 and 8.95 $\tau$ ($J$ = 6 cps, each) and one quarternary methyl at 9.17 $\tau$. The signal at 8.27 $\tau$ could be assigned to the hydroxyl proton as it disappeared after $D_2O$ exchange. Signal of the secondary hydrogen of the alcohol was shifted up field by 0.5 $\tau$ and appeared as a doublet at 6.69 $\tau$ ( $J$ = 5.5 cps).

Thus, Rotundenol (X) is a tricyclic sesquiterpene secondary alcohol having an exocyclic methylene, a tertiary and secondary methyl groups.

Rotundenol readily furnished the monoacetate $C_{17}H_{26}O_2$, b.p. 115° (bath) / 0.1 mm.; $[\alpha]_D^{28}$ - 41.44° (C, 4.3); $n_D^{29}$ 1.4965. U.V. absorption $\lambda_{max}$ 210 mμ $\log_e$ 3.5 and displayed IR bands (Fig. 10) at 1730, 1235 ( acetoxyl ), 1639, 909 ( $>C = CH_2$) cm$^{-1}$.

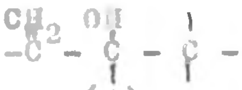
The NMR spectrum (Fig. 11) of the acetate was essentially similar to that of Rotundenol, the major difference being a downfield shift of the hydrogen attached to the carbon carrying the hydroxyl group by 1.53 $\tau$ and appeared as a narrow signal at 4.63 $\tau$.

Jones oxidation of rotundenol gave an $\alpha$-$\beta$ unsaturated ketone (XII), IR spectrum (Fig.16) displayed absorption bands at 1695 (conjugated ketone) and 1695, 1613 and 944 (olefinic linkage) $cm^{-1}$. The absorption band at 944 $cm^{-1}$ was assigned to the unsymmetrically disubstituted double bond, frequency of which is known to be shifted to 930-945 $cm^{-1}$, when it is conjugated with carbonyl function[8]. It also gave an $\alpha$-$\beta$ unsaturated acid, probably formed by allylic rearrangement and oxidation as in the case of oxidation of linalool[9].

Jones oxidation of the dihydro alcohol (XI) resulted in the formation of a saturated ketone (XIII) $C_{15}H_{24}O$, $[\alpha]_D^{29}$ - 47.24°; IR spectrum (Fig.14) did not show any absorption due to the methylene group adjacent to the carbonyl group and band at 1709 $cm^{-1}$ suggested that the keto group must be on a saturated six membered (or larger) ring ketone. The ketone (XIII) did not form any carbonyl derivative and resisted reduction by Wolff-Kishner method.

The NMR spectrum (Fig.15) of the ketone (XIII) indicated the presence of one quarternary methyl (singlet at 9.04 $\tau$) and two secondary methyls (Two doublets at 9.13 $\tau$, J = 5.5 cps; and 8.9 $\tau$, J = 7 cps.).

Rotundenol has, therefore, the following part structure A.

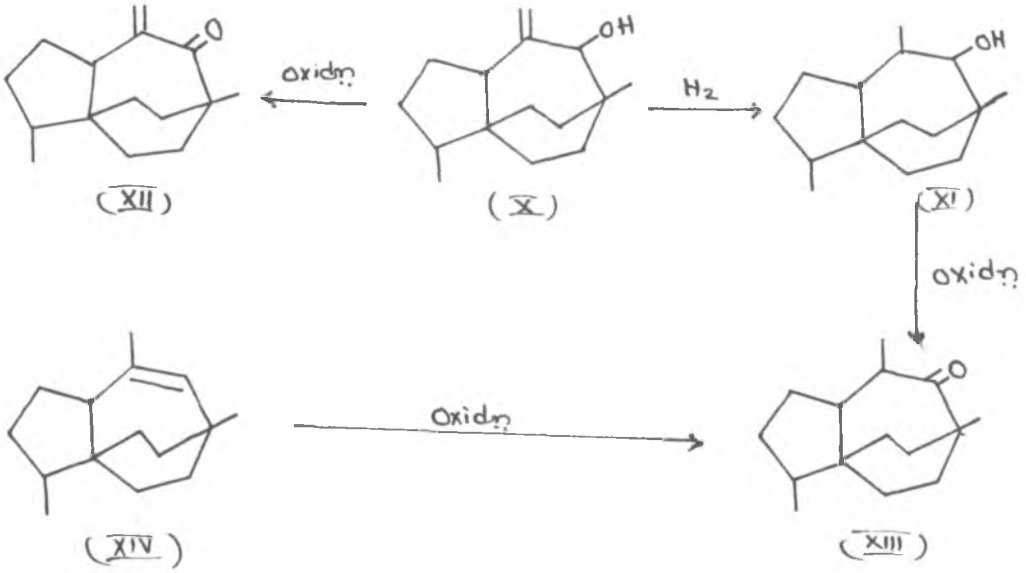


$$-\overset{CH_2}{\overset{\|}{C}}-\underset{|}{\overset{OH}{C}}-\underset{|}{\overset{|}{C}}-$$

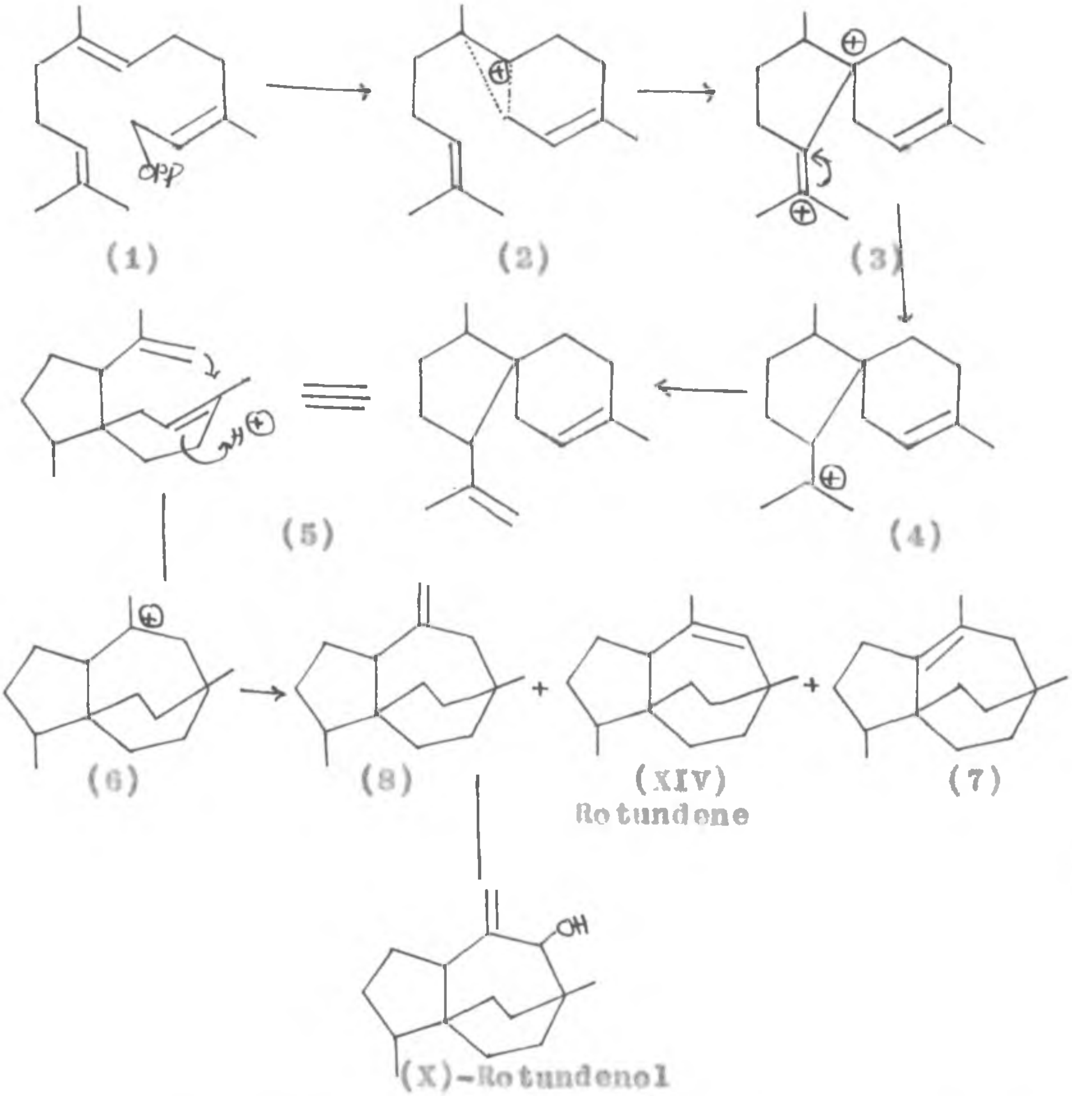
(A)

The dihydro ketone (XIII) obtained from rotundene[10] (XIV) (Hydrocarbon II, Chapter II), via epoxidation and isomerisation on treatment with $BF_3$ etherate was identical (IR, rotation GLC, NMR) with the ketone (XIII) obtained by Jones oxidation of dehydroalcohol (XI).

Hydrocarbon II (Rotundene) has been assigned a provisional structure (XIV). As the basic structures of rotundene and rotundenol are same, Rotundenol has been assigned a provisional structure (X).



The presence of Rotundene (Hydrocarbon II) and Rotundenol along with cyperene and other tricyclic compounds (Isopatchoulanes) in the oil of *cyperus scariosus* is expected from biogenetic considerations. A biogenetic path way leading to rotundene and rotundenol can be derived as follows:



The farnesyl cation could collapse via the non-classical ion 2 to afford the ion 3, an intermediate in the biogenesis of cedrene; this ion undergoes cyclisation to give the ion 4, which by loss of a proton can yield the hydrocarbon 5. Acid catalysed cyclisation of this ion would yield 6 which could afford three possible hydrocarbons one of which is rotundene (XIV). Allylic oxidation of 8 could provide Rotundenol (X).

## EXPERIMENTAL

Cyperenol (VI), $C_{15}H_{24}O$ (Alcohol I, isolation Chapter I) had the following properties: m.p. 94°, b.p. 125° (bath) / 0.05 mm. $[\alpha]^{30}_{D}$ - 12.1° (C, 4.3); molecular weight 220 (mass spec.). U.V. absorption $\lambda_{max}$ 210, $\varepsilon$, 2,340.

## ANALYSIS

Found : C, 81.49; H, 11.1

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

IR bands (Fig.1, nujol) at: 3333, 1678, 1408, 1379, 1361, 1328, 1302, 1266, 1238, 1220, 1183, 1153, 1139, 1067, 1042, 1018, 980, 913, 897, 875 and 842 $cm^{-1}$.

NMR spectrum (Fig.2): unsplit methyl signals (6H) at 9.22 and 9.05 $\tau$ $(CH_3-\overset{/}{\underset{\backslash}{C}}-CH_3)$, doublet (3H, J = 6 cps) at 9.17 $\tau$ $(CH_3-\overset{/}{\underset{\backslash}{C}}-H)$, broad signal (2H) at 5.91 $\tau$ $(-C\underline{H}_2OH)$, singlet (1H) at 7.69 $\tau$ $(-CH_2O\underline{H})$.

## JONES OXIDATION OF CYPERENOL (I)

Jones reagent (0.25 ml.) [chromiumtroxide (2.67 g.) and concentrated sulphuric acid (2.3 ml.) in water (10 ml.)] was added with stirring to a solution of alcohol I (103 mg.) in acetone (5 ml.) at 0-5°. The reaction mixture was further stirred for 15 min. at room temperature, the mixture was poured into ice-water and extracted with ether. Removal of ether yielded acidic product (II) (74 mg.).

**ANALYSIS**

Found : C, 76.65; H, 9.49

Calculated for $C_{15}H_{22}O_2$ : C, 76.88; H, 9.46%

IR bands ( nujol ) at: 3125, 2632, 1818, 1710, 1669, 1460, 1443, 1408, 1389, 1374, 1282, 1115, 1081, 1042, 980, 942, 910, 855, 823 and 760 cm$^{-1}$.

**DIHYDROCYPERENE** (III) $C_{15}H_{26}$

**Hydrogenation of Cyperenol** (I)

Cyperenol (100 mg.) was hydrogenated in ethanol (15 ml.) with Adams platinum oxide (20 mg.); hydrogenation was complete in 4 hours. The catalyst was removed by filtration and the filtrate was evaporated to give a colourless mobile product dihydrocyperene (III), b.p.93-96°(bath)/1.2mm. $[\alpha]_D^{28}$- 58.32° (C, 2.3).

**ANALYSIS**

Found : C, 87.43; H, 12.9.

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

IR bands (0.05 mm. cell) at: 1453; 1388, 1367, 1343, 1312, 1294, 1252, 1209, 1178, 1138, 1116, 1078, 998, 982, 965, 948, 930, 922, 893, 880 and 853 cm.$^{-1}$ (Superimposable with dihydrocyperene).

**CYPERENE** (IV) $C_{15}H_{24}$

(1) **Tosylation of Cyperenol** (I)

Cyperenol (200 mg.) was dissolved in anhydrous pyridine (2.5 ml.) and added to a solution of freshly recrystallised p-toluene sulphonyl chloride (350 mg.) in pyridine (4 ml.). The red solution was kept at room temperature for 24 hours, then poured in ice water (250 ml.). The mixture was extracted with chloroform (25 x 3 ml.).The organic extracts were washed with water (2 x 25 ml.), 10% sulphuric acid (5 ml.) water (25 ml.) and saturated sodium chloride solution (30 ml.). The chloroform extract dried over anhydrous magnesium sulphate, the crude tosylate was obtained after removal of chloroform.

### (ii) LAH reduction of the crude tosylate

The tosylate (130 mg.) was treated overnight at room temperature with LAH (250 mg.) in ether (40 ml.), The mixture was then decomposed with saturated aqueous ammonium chloride and extracted with ether, and the extracts were dried over magnesium sulphate and distilled when cyperene (IV) (43 mg.) was obtained. b.p. 78$^{\circ}$(bath) / 0.2 mm. $[\alpha]_D^{30}$ $-$ 19.73$^{\circ}$; $n_D^{30}$ 1.5017.

### ANALYSIS

Found : C, 88.23; H, 11.96
Calculated for $C_{15}H_{24}$ : C, 88.16; H, 11.84%

IR bands (Fig.3, liquid film) at: 1701, 1389, 1366, 1333, 1316, 1269, 1250, 1222, 1205, 1181, 1163, 1141, 1070, 1037, 988, 934, 892, 877, 845 and 832 cm$^{-1}$.

## PATCHOULENOL (VII) $C_{15}H_{24}O$

Ether eluted fraction on further chromatography (Table ; in Chapter I), gave Patchoulenol (VII) m.p. 74°; $[\alpha]_D^{30}$ - 54.23° (C, 3.8). U.V.absorption $\lambda_{max}$ 210 m$\mu$, ($\epsilon$,10,500).

## ANALYSIS

Found : C, 81.69; H, 11.06

Calculated for $C_{15}H_{24}O$ : C, 81.76, H, 10.98%

IR bands (Fig.4, nujol) at: 3333, 1692, 1379, 1361, 1304, 1280, 1227, 1190, 1156, 1111, 1099, 1064, 1053, 1020, 1007, 918, 900, 875, 810 and 770 cm$^{-1}$.

NMR spectrum (Fig.5) doublet (3H, J = 6 cps) at 9.25$\tau$ ($CH_3-C\langle H$), singlet (3H) at 9.09$\tau$ ($CH-C\langle$ ), singlet (3H) at 9.02$\tau$ ($CH_3-C\langle$); singlet (3H) at 8.22$\tau$ ($CH_3-\overset{\backslash}{C}=\overset{\backslash}{C}-$), broad signal (1H) at 5.68$\tau$ ($\underline{H}-C-OH$), singlet (1H) at 8.45$\tau$ ( $-\overset{|}{\underset{|}{C}}-O\underline{H}$).

## DIHYDROCYPERENE (III) $C_{15}H_{26}$

### Hydrogenation of Patchoulenol (VII)

Patchoulenol (140 mg.), dissolved in ethanol (25 ml.), was stirred in an atmosphere of hydrogen with Adams catalyst (30 mg.). It absorbed two moles of hydrogen during 6 hours. The catalyst was filtered, ethanol removed under vacuum to furnish an oily material which was extracted with ether, dried over anhydrous sodium sulphate and evaporated to give a saturated olefin, dihydrocyperene (III) b.p. 123° (bath) / 3 mm. $[\alpha]_D$ - 55.8° (C, 4.0).

### ANALYSIS

Found : C, 87.23; H, 12.60

Calculated for $C_{15}H_{26}$ : C, 87.3; H, 12.7%

IR bands (0.05 mm. cell) at: 1387, 1366, 1342, 1312, 1294, 1205, 1178, 1139, 1114, 1076, 995, 982, 965, 948, 930, 921, 893, 880 and 852 $cm^{-1}$.

### CYPERENE (V) $C_{15}H_{24}$

### Reduction of Patchoulenol (VII) with LAH and $AlCl_3$

The reagent (LAH-$AlCl_3$) was prepared by the addition of LAH (250 mg., 1.75 mole) to a solution of aluminium chloride (470 mg., 3.5 mole), in ether (20 ml.).After the vigorous reaction had subsided Patchoulenol (22 mg.1 mole) was added in ether during 5-10 min. The total reaction mixture was refluxed for 1 hr. and was further worked out in the usual way with 20% $H_2SO_4$. Removal of ether yielded the crude product, which was purified by column chromatography when cyperene (VII) was obtained. b.p.98°(bath) / 1.2 mm; $[\alpha]_D^{30}$- 21°, (C, 4.3); $n_D^{30}$ 1.5020.

### ANALYSIS

Found : C, 87.98; H, 11.64.

Calculated for $C_{15}H_{24}$ : C, 88.16; H, 11.84%

IR bands (liquid film) at: 1701, 1389, 1366, 1333, 1316, 1269, 1250, 1222, 1205, 1181, 1163, 1141, 1070, 1037, 988, 934, 892, 877, 845 and 832 $cm^{-1}$.

## PATCHOULENONE (VIII) $C_{15}H_{22}O$

### Jones oxidation of Patchoulenol (VII)

To a solution of patchoulenol (VII) (500 mg.) in acetone (20 ml.) at 0-5°, was added 8N, chromic acid solution (10 ml. Jones reagent). After standing at 0° for 1/2 hour, the mixture was poured into water (50 ml.). The aqueous solution was extracted with ether (100 ml.). The ether extract was washed with water and dried. After removal of ether the thick liquid was distilled and the distillate was crystallised from pet ether when colourless solid was separated m.p.53°; $[\alpha]_D^{30}$ - 93.73° (C, 3.5).

### ANALYSIS

Found : C, 82.33; H, 10.13.

Calculated for $C_{15}H_{22}O$ : C, 82.57; H, 10.09%

IR bands (Fig.6, nujol) at: 1712, 1663, 1464, 1388, 1370, 1285, 1271, 1250, 1238, 1210, 1180, 1080, 1069, 1017, 990, 980, 932, 895, 866, 830, 805, 782 and 746 cm$^{-1}$.

## ROTUNDENOL (X) $C_{15}H_{24}O$

Rotundenol (alcohol I, isolation Chapter I) had the following properties: b.p. 139-140° (bath)/0.2 mm., $[\alpha]_D^{28}$ + 55.35°, (C, 3.4); $n_D^{29}$ 1.5205; molecular weight 220 (mass spec.) U.V. absorption $\lambda_{max}$ 210 ($\log_e$ 3.5).

ANALYSIS

Found : C, 81.86; H, 11.18

Calculated for $C_{15}H_{24}O$ : C, 81, 76; H, 10.98%

IR bands (Fig. 7, liquid film) at: 3509, 3106, 1818, 1661, 1418, 1385, 1316, 1250, 1190,1168, 1085, 1042, 1020, 990, 965, 963, 910 and 805 cm$^{-1}$.

NMR spectrum (Fig.8): 9.17τ ($CH_3$-C-), 9.1τ $(-CH\langle^{CH_3}$ , 8.7 (-OH), 6.16τ (CHOH), 5.1 and 4.92τ $(-\overset{CH_2}{\overset{\|}{C}}-)$.

ROTUNDENOL 3:5 DINITROBENZOATE $C_{22}H_{26}O_6N_2$

Rotundenol (450 mg.) was warmed on water bath with 3:5 dinitrobenzoylchloride (120 mg.) in pyridine (1 ml.) and benzene (5 ml.) for 2 hours. After two hours, the solution was poured in ice, and extracted with ether. The ether extract washed with dilute acid, water and dried over anhydrous sodium sulphate. After removal of ether, the crude product was crystallised from methanol, when colourless crystals of 3:5 dinitrobenzoate of rotundenol was obtained m.p. 140°; $[\alpha]_D^{29}$ - 32.10° (C, 4.17).

ANALYSIS

Found : C, 63,92; H, 6.42

Calculated for $C_{22}H_{26}O_6N_2$ : C, 63.75; H, 6.32%

IR bands (Fig.9, nujol) at: 1709, 1626, 1540, 1374, 1342, 1282, 1170, 1073, 962, 943, 917, 730 and 720 cm$^{-1}$.

## DIHYDRO-ROTUNDENOL (XI) $C_{15}H_{24}O$

### Hydrogenation of Rotundenol (X)

A solution of rotundenol (X) (200 mg.) in ethanol (25 ml.) was shaken with Adams catalyst (70 mg.) in a hydrogen atmosphere for 3.5 hours. The catalyst was filtered off and the filtrate was concentrated. The residue obtained was crystallised from petroleum ether to afford colourless crystalline product (XI) (183 mg.) dihydrorotundenol, m.p. 96°; $[\alpha]_D^{28}$ - 31.44 (C, 4.2); molecular weight 222 (mass spec.) and 223 after $D_2O$ exchange (mass spec.).

### ANALYSIS

Found : C, 81.00; H, 11.33

Calculated for $C_{15}H_{26}O$ : C, 81.02; H, 11.79%

IR bands (Fig.12, nujol) at: 3401, 1464, 1440, 1374, 1316, 1105, 1026, 995, 960, 920, 870, 848 and 795 $cm^{-1}$.

NMR spectrum (Fig.13): singlet (3H) at 9.17 $\tau$ ($\rangle$C-$CH_3$); two doublets (3H each) centered at 9.01 and 8.9 $\tau$ (J = 7 and 6 cps. respectively) ($\rangle$CH-$CH_3$), doublet (1H, J = 6 cps) at 6.69 $\tau$ (-CH-OH), singlet at 8.27 $\tau$ (1H, $D_2O$ exchangable, -OH).

## ROTUNDENOLACETATE $C_{17}H_{26}O_2$

Rotundenol (X), (100 mg.) was dissolved in dry pyridine (4 ml.), $AC_2O$ (1.5 ml.) was added and the solution was allowed to stand at room temperature for 48 hours. MeOH was added and after standing at room temperature for 2 min. the mixture was concentrated under reduced pressure, diluted with water (10 ml.), made alkaline by the addition of solid $K_2CO_3$ and extracted with ether. The ether extract was washed several times with water, dried over anhydrous $Na_2SO_4$ and concentrated, distilled to give colourless mobile liquid rotundenol acetate (110 mg.) b.p.115° (bath)/0.1 mm. $[\alpha]_D^{28}$ - 41.44° (C, 4.03); $n_D^{29}$ 1.4965. U.V.absorption $\lambda_{max}$ 210 ($\log_e$ 3.5).

## ANALYSIS

Found : C, 78.05; H, 10.13

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

IR bands (Fig. 10, liquid film) at: 3012, 1730, 1639, 1460, 1366, 1235, 1030, 961, 909, 853 and 805 cm$^{-1}$.

NMR spectrum (Fig.11): singlet (3H) at 9.2 τ ($>$C-CH$_3$), doublet (3H, J = 6 cps) at 9.15 τ ($>$CH-CH$_3$), singlet (3H) at 8.0 τ (-OCOCH$_3$), triplets (2H, J = 1.5 cps) at 5.07 and 4.9 τ ($>$C=CH$_2$, narrow multiplet (1H) at 4.63 τ (CHOAC).

## KETONE (XII) $C_{15}H_{22}O$

### Jones oxidation of Rotundenol (X)

To a solution of rotundenol (210 mg.) in acetone (10 ml.) was added dropwise a solution of Jones reagent (2 ml.) during 10 min. at 5°. The mixture was kept for further 20 min. at the same temperature and was diluted with water and extracted with ether. The ether layer was separated into acidic and neutral parts by washing with sodium bicarbonate.

The neutral ethereal layer was dried. After removal of ether, the product was distilled, when ketone (XII) (48 mg.) was obtained, b.p.138-140° (bath)/0.8 mm.

ANALYSIS

Found : C, 82.7; H, 10.1

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

IR bands (Fig. 16, liquid film) at: 1869, 1695, 1658, 1613, 1460, 1370, 1333, 1285, 1163, 1139, 1081, 1031, 1020 and 944 $cm^{-1}$.

KETONE (XIII) $C_{15}H_{24}O$

Oxidation of dihydrorotundenol (XI)

Dihydrorotundenol (220 mg.), dissolved in acetone (5 ml.) was treated with Jones reagent till a permanent brown colour persisted. It was kept at the room temperature for 1/2 hour and working it in the usual manner gave a ketone(170 mg.) in the neutral portion, b.p.129° (bath) / 1.2 mm. $[\alpha]^{29}_{D}$ - 47.24° (C, 3.5).

ANALYSIS

Found : C, 81.89; H, 10.64.

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

IR bands (Fig. 14, liquid film) at: 1709, 1460, 1379, 1342, 1328, 1287, 1266, 1195, 1170, 1143, 1114, 1087, 1047, 1010, 995, 961, 926, 870, 805 and 773 $cm^{-1}$.

NMR spectrum (Fig. 15) : singlet (3H) at 9.04$\tau$ ($\rightarrow C-CH_3$); two doublets (3H, each) centred at 9.13 and 8.9 $\tau$ (J = 5.5 and 6.5 cps respectively, $\rightarrow CH-CH_3$).

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